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Base-Catalyzed Halogenation of Acetone[1]

Eliana Tapuhi and William P. Jencks*

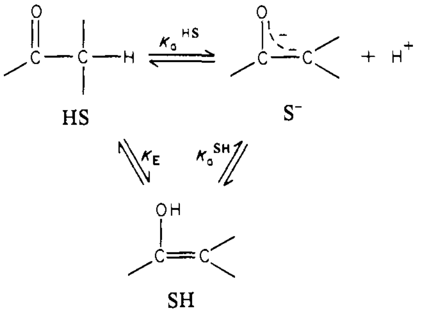
Contribution No. 1420 from the Graduate Department of Biochemistry, Brandeis University, Waltham, Massachusetts 02254. Received February 26, 1982

Abstract: The kinetics of the iodination and bromination of acetone were measured in basic aqueous solutions, buffered with trifluoroethanol, under conditions in which halogenation of the enolate ion is the rate-determining step. With the assumption of diffusion-controlled halogenation of the enolate ion by I_2 and HOBr with $k = 5 \times 10^9$ M^{-1} s^{-1}, rate constants for other halogenating agents (M^{-1} s^{-1}) are BrO^-, 8×10^7; IO^-, 10^8; IOH, 2.5×10^8; and I_3^-, 3.6×10^8; the pK_a of acetone is 18.9 ± 0.3 at 25 °C, ionic strength 1.0 M (KCl) or 1.0 M (KNO_3). Iodoform was identified spectrophotometrically as the product of iodination. Values of pK_a^{SH} = 10.8 and 10.6 for the enol give pK_E = 8.1 and 8.3, respectively, for formation of the enol from acetone. It is suggested that the reactions of IO^- and BrO^- may proceed through the formation of a complex with the enolate, followed by protonation and halogenation, and that I_3^- may serve as an iodine donor through a preassociation mechanism. The observed dependence of the absorbance of I_3^- on buffer concentration and pH indicates the formation of a significant amount of a species with the composition $ROIOH^-$ at high concentrations of trifluoroethoxide and hydroxide ions.

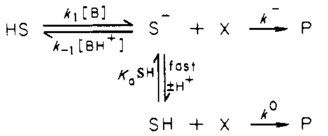
We describe here the initial results of a search for reagents that will trap basic carbanions in alkaline solution at a diffusion-controlled rate. Measurement of the ratio of products from such trapping and from protonation or elimination reactions of the carbanion will give absolute values of the rate constants for the latter processes, i.e., a measure of the lifetime of the intermediate. The lifetime of intermediates determines whether elimination and other reactions of carbanions can proceed through a stepwise mechanism; if the intermediate is too unstable to exist, the reaction must be concerted.[2,3]

We have examined the halogenation of acetone by species derived from iodine and bromine in buffered alkaline solution. Studies of base-catalyzed iodination have generally been avoided because of the instability and complexity of the halogenating species in alkaline solution.[4] However, Bartlett[5] has determined rate constants for the chlorination of ketones at pH >11, and the reactions of hypobromite with ketones have been examined in alkaline solution.[6,7] Guthrie and co-workers have independently determined the rate constants for the reactions of hypobromite and hypochlorite with acetone in alkali and estimated the pK_a of acetone, with results similar to those reported here.[8]

The equilibria for the enolization of acetone are defined in eq 1. The kinetic scheme for the halogenation of acetone in basic solution is described by eq 2.[9]



(1)



(2)

The reaction of acetone, HS, with a halogenating agent, X, can proceed through the enolate, S^-, and the enol, SH. The steady-state treatment gives eq 3, assuming

$$\frac{d[P]}{dt} = \frac{k_1[HS][B]\left(k^-[X] + k^0\frac{[H^+]}{K_a^{SH}}[X]\right)}{k_{-1}[BH^+] + \left(k^-[X] + k^0\frac{[H^+]}{K_a^{SH}}[X]\right)} \qquad (3)$$

fast proton transfer to and from the oxygen atom of the enolate. The usual zero-order kinetics in halogen are obtained when reprotonation is relatively slow, i.e., $k_{-1}[BH^+] << k^-[X] + k^0[H^+][X]/K_a^{SH}$. However, when the halogenating species is at low concentration or has a low reactivity, and especially in the presence of buffers, the opposite inequality holds and the reaction becomes first order in halogenating agent; i.e., $k_{-1}[BH^+] >> k^-[X] + k^0[H^+][X]/K_a^{SH}$. Under these conditions the reaction follows eq 4, in which $K_1 = k_1/k_{-1}$ (eq 2).

$$\frac{d[P]}{dt} = \frac{K_1K_{BH^+}}{[H^+]}[HS]\left(k^- + k^0\frac{[H^+]}{K_a^{SH}}\right)[X] = \left(\frac{K_a^{HS}}{K_w}k^-[OH^-] + k^0K_E\right)[HS][X] \qquad (4)$$

Halogenation of acetone that is first order in halogenating agent was observed by Bartlett for the reaction with hypochlorite in alkaline solution[5] and was utilized by Dubois and Toullec with other halogenating reagents to estimate the keto–enol equilibrium constant K_E in acid solution.[10,11] If the value of k^0 is known, the value of K_E can be calculated from observed rate constants for halogenation (eq 4). The value of K_a^{HS} can be calculated similarly if k^- is known. A value of $K_E = 3.5 \times 10^{-9}$ has been estimated[11] on the basis of the assumption that the similar observed rate constants for halogenation by Cl_2, Br_2, and I_2 represent rate-determining diffusion-controlled reaction of the halogen and enol with $k^0 = 5 \times 10^9$ M^{-1} s^{-1}; earlier estimates[10,12] of $K_E = 1.5 \times 10^{-8}$ and 1.5×10^{-9} were based on estimated values of $k^0 = 10^9$

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[1] Supported by grants from the National Science Foundation (PCM-7708369) and the National Institutes of Health (GM20888). Dr. Tapuhi was supported by a Chaim Weizmann Postdoctoral Fellowship Award (9366).

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Table I. Rate Constants for the Bromination of Acetone in Basic Solution Buffered with Trifluoroethanol[a]

10^3[OH$^-$], M	k_{obsd}/[acetone], M^{-1} s^{-1}	10^3[OH$^-$], M	k_{obsd}/[acetone], M^{-1} s^{-1}
21.5	66	2.40	8.7
15.0	46	2.05	8.1
8.30	27	1.30	4.2
5.00	16.3	1.03	3.5
4.40	16.0	0.65	2.6

[a] Ionic strength 1.0 M (KCl), (2.5-5.0) × 10^{-3} M [acetone], 0.4 M trifluoroethanol buffer, (2-4) × 10^{-4} M [BrO$^-$], 25 °C.

M^{-1} s^{-1} and 10^{10} M^{-1} s^{-1}, respectively. This assumption is reasonable, but not proved. The rate constants for the halogenation of the enol of diethyl malonate by Cl_2, Br_2, and I_2 have all been reported to be within an order of magnitude of 10^6 M^{-1} s^{-1}, well below the diffusion-controlled limit.[13] Similar ratios of rate constants for these halogens, with a relatively slow reaction of Cl_2, were reported at this time for the enol of acetone and for the enolate ion of diethyl malonate, which are expected to be much more reactive.[13,14] The more recent work has indicated that the rate constants for the reactions of acetone enol with these three reagents are essentially the same;[10] however, the reactions of less reactive enols have not been reexamined in order to establish that different rate constants for the three halogens are to be expected if halogenation is slower than diffusion controlled. It has been reported that Cl_2 reacts more slowly than Br_2 with the enols of 2-butanone in aqueous sulfuric acid.[15] The smaller rate constant of 1.5 × 10^8 M^{-1} s^{-1} for halogenation of the enol ether of acetone[16] requires the further condition that enols are substantially more reactive than enol ethers.[11] Somewhat larger values of K_E have been estimated by using kinetic ($K_E = 10^{-7}$, 2.8×10^{-8})[17,18] and thermochemical ($K_E = 6 \times 10^{-8}$)[12] approaches.

The assumption that the reaction of the enolate anion of acetone with reactive halogenating agents is diffusion controlled rests on firmer ground. Rate constants for the halogenation of several acyclic enolate anions have been reported to be ~10^5 larger than those for the corresponding enols,[13,19] and the enolate anion of acetone is protonated by acetic acid and other acids ~10^5 times faster than the enol.[20] The increased reactivity of the enolate relative to the enol should, therefore, give diffusion-controlled halogenation even if the rate constant for halogenation of the enol is no larger than that of the enol ether. Determination of the second-order rate constants for halogenation will then give a value for pK_a^{HS} of acetone that is as accurate as the estimated value of the diffusion-controlled rate constant k^- (eq 4), and the equilibrium constant for enolization can be calculated from pK_a^{HS} if the acidity of the enol can be estimated (eq 1, pK_E = pK_a^{HS} - pK_a^{SH}).

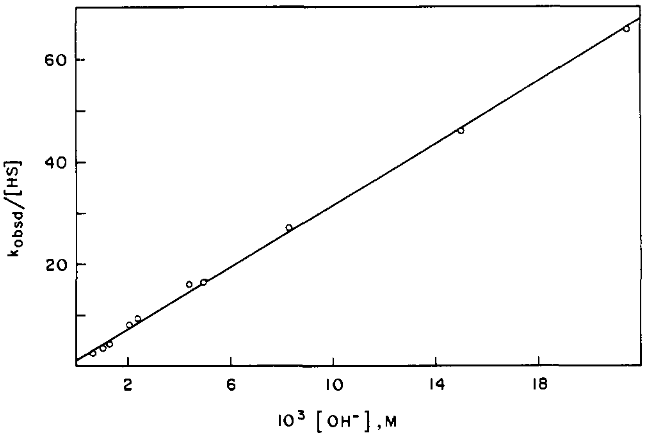

Figure 1. Bimolecular rate constants for the bromination of acetone in basic media as a function of [OH$^-$] at 25 °C and I = 1 M (KCl).

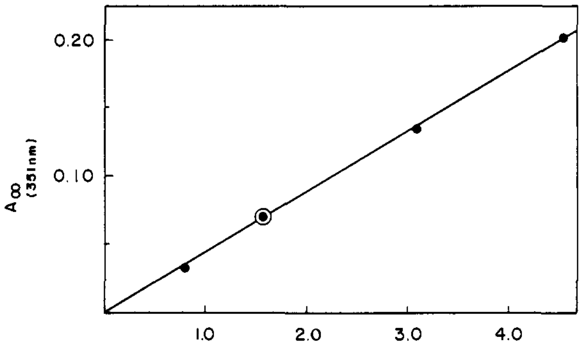

Figure 2. Absorbance of the product from the iodination of excess acetone as a function of the total iodine concentration: (●) pH 11.5 and 11.7; (⊙) pH 10.6-11.8.

Results

Bromination of Acetone. The disappearance of 3 × 10^{-4} M hypobromite ion in the presence of 2.5 × 10^{-3} M acetone was found to follow zero-order kinetics for >50% reaction at pH 11.7, ionic strength 1.0 M, in agreement with the results of previous studies.[5,6] However, in the presence of 0.4 M trifluoroethanol buffer under the same conditions, the disappearance of BrO$^-$ follows first-order kinetics because the rate of reprotonation of the enolate ion is increased by the acidic component of the buffer (k_{-1}[BH$^+$], eq 3). The first-order rate constant was found to be independent of buffer concentration in the range 0.4-0.9 M. The observed rate constants at different concentrations of hydroxide ion are given in Table I.

The observed first-order rate constants are related to the elementary rate and equilibrium constants for bromination of the enolate and enol by HOBr and BrO$^-$ according to eq 5, in which

$$\frac{k_{obsd}}{3[\mathrm{HS}]}\frac{C_t}{[\mathrm{BrO^-}]} = \frac{K_a^{HS}}{K_w}k^-_{\mathrm{BrO^-}}[\mathrm{OH^-}] + \frac{K_a^{HS}}{K_a^{HOBr}}k^-_{\mathrm{HOBr}} + k_E k^0_{\mathrm{BrO^-}} + \frac{K_w K_E k^0_{\mathrm{HOBr}}}{K_a^{HOBr}[\mathrm{OH^-}]} \qquad (5)$$

C_t is the total halogen concentration and K_a^{HOBr} is the dissociation constant of HOBr. Equation 5 is obtained from eq 4, taking into account that three molecules of halogen are consumed in the reaction.[5,6]

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(19) Bell, R. P.; Davis, G. G. *J. Chem. Soc.* **1965**, 353-361. Several cyclic enols and enolate anions are brominated with similar rate constants for reasons that are not well understood.

(20) The ratio of the rate constants for protonation of the enol and enolate ion of acetone by different acid species can be calculated from the following equation:

$$\begin{tikzcd}
\mathrm{HS} + \mathrm{B} \arrow[r, shift left, "k^-_1"] \arrow[d, shift left] & \mathrm{S^-} + \mathrm{BH^+} \arrow[l, shift left, "k^-_{-1}"] \arrow[d, shift left] \\
\mathrm{HS} + \mathrm{BH^+} \arrow[u, shift left, "K_{HA}/H^+"] \arrow[r, shift left, "k^0_1"] & \mathrm{SH} + \mathrm{BH^+} \arrow[l, shift left, "k^0_{-1}"] \arrow[u, shift left, "K_a^{SH}/H^+"]
\end{tikzcd}$$

$$\frac{k^-_{-1}}{k^0_{-1}} = \frac{K_{HA}}{K_a^{SH}}\frac{k^-_1}{k^0_1}$$

For B = acetate the value of K_{HA} is $10^{-4.7}$ M and the forward rate constants (ref 9, p 150) are $k^-_1 = 15 \times 10^{-6}$ M^{-1} min^{-1} and $k^0_1 = 5 \times 10^{-6}$ M^{-1} min^{-1}. A value of pK_a^{SH} = 10.8 (see Discussion) gives the ratio $k^-_{-1}/k^0_{-1} = 4 \times 10^6$. Analogous calculations for B = OH$^-$ and B = H_2O give ratios of k^-_{-1}/k^0_{-1} between 3.4 × 10^5 and 1 × 10^6.

The second-order rate constants for bromination show a linear increase with increasing hydroxide ion concentration (Figure 1). The absence of upward curvature at low concentrations of hydroxide ion shows that the reaction of enol with HOBr is negligible under the conditions of these experiments (eq 5). The best fit of the line was calculated by the least mean squares method and gives a slope of (3.01 ± 0.05) × 10^3 M^{-2} s^{-1} and an intercept of 1.2 ± 0.3 M^{-1} s^{-1}. From the slope a value of $K_a^{HS}k^-_{BrO^-} = 1.0 \times 10^{-11}$ s^{-1} is obtained for the reaction between enolate and BrO^-. The intercept represents the kinetically ambiguous reactions of enolate with HOBr or enol with BrO^- and corresponds to approximate values of $K_a^{HS}k^-_{HOBr} = (8 \pm 2) \times 10^{-10}$ s^{-1} (with $K_{HOBr} = 2 \times 10^{-9}$ M^{-1})[21] or $K_Ek^0_{BrO^-} = 0.4 \pm 0.1$ M^{-1} s^{-1}.

Iodination of Acetone. Formation of Iodoform. The product from the iodination of 2 × 10^{-3} to 1 × 10^{-2} M acetone was found to have an absorbance at 351 nm that is independent of pH in the range 10.6–12.0 and is proportional to the initial concentration of total iodine (Figure 2). An absorption maximum was found at 336 nm and is identical with that of iodoform. The slope of (4.4 ± 0.1) × 10^2 M^{-1} cm^{-1} in Figure 2 is one-third the extinction coefficient of iodoform, (1.35 ± 0.05) × 10^3 M^{-1} cm^{-1} (determined at 351 nm in 3/1 water/ethanol (v/v); the extinction coefficient of the product does not change in the presence of 25% ethanol). A similar slope of (4.7 ± 0.3) × 10^2 M^{-1} cm^{-1} at 351 nm was observed at ionic strength 1.0 M maintained with potassium nitrate.

Formation of iodoform is consistent with the expected haloform reaction in basic media, and it is known that rate constants for enolization of iodoacetones are larger than for acetone.[22] However, under the conditions of these experiments it is the concentration of the enolic species of mono- and diiodoacetone and the rate constants for the iodination of these species, not the rate constants for enolization, that are responsible for the uptake of the second and third equivalents of iodine. The fact that the reaction follows first-order kinetics accurately throughout the observed reaction shows that these equilibrium and rate constants are relatively large, so that the second and third iodination steps are fast and not kinetically significant even in the presence of a large excess of acetone.

Iodinating Species in Alkaline Solution. The iodine-containing species described in eq 6–10 must be considered as possible iodinating reagents in the range pH 10–12.[23,24] In addition, the absorbance of triiodide ion under equilibrium conditions was found to decrease with increasing concentration of trifluoroethanol buffer at constant pH, which shows that a component of the buffer forms a complex with iodine. The decrease is 40% at pH 11.75 and 13% at pH 11.10 in the presence of 0.4 M buffer and 1 M potassium chloride. The apparent equilibrium constant for the formation of the complex increases sharply with increasing pH and requires a composition containing trifluoroethoxide ion, iodine, and hydroxide ion: $[ROIOH]^-$ (eq 11). The dependence of the amount of complex on the concentrations of hydroxide and iodide ions at different concentrations of total iodine is shown in Figure 3 and corresponds to an equilibrium constant of $K_{RO^-} = 2.7 \times 10^4$ M^{-1} at 25 °C, ionic strength 1.0 M (KCl); a smaller value of 1.3 × 10^4 M^{-1} was obtained from measurements with a series of buffer concentrations at pH 11.75 in which the ionic strength was maintained with KNO_3. The absence of an intercept in Figure 3 shows that there is no significant formation of a complex with the composition I_2OR^-, analogous to I_2OH^-.

$$I_2 + OH^- \underset{}{\overset{K_{IOH}}{\rightleftharpoons}} IOH + I^- \tag{6}$$

$$IOH \overset{K_a^{IOH}}{\rightleftharpoons} IO^- + H^+ \tag{7}$$

$$I_2 + OH^- \overset{K_{I_2OH^-}}{\rightleftharpoons} I_2OH^- \tag{8}$$

$$I_2 + I^- \overset{K_{I_3^-}}{\rightleftharpoons} I_3^- \tag{9}$$

$$I_2 + Cl^- \overset{K_{I_2Cl^-}}{\rightleftharpoons} I_2Cl^- \tag{10}$$

$$I_2 + RO^- + OH^- \overset{K_{RO^-}}{\rightleftharpoons} ROIOH^- + I^- \tag{11}$$

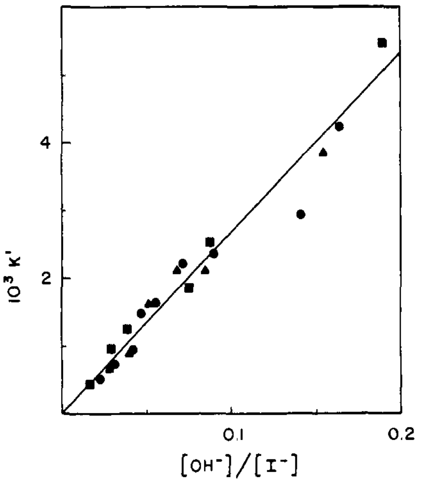

Figure 3. The ratio $K' = [ROIOH^-]/[I_2][RO^-]$ as a function of $[OH^-]/[I^-]$ at 25 °C and I = 1 M (KCl); $[RO^-]$ = 0.05–0.19 M. Legend: (●) $[I^-] = 5.3 \times 10^{-2}$ M, $[I_2]_T = 1.04 \times 10^{-4}$ M; (■) $[I^-]$ = 0.1 M, $[I_2]_T = 1.02 \times 10^{-4}$ M; (▲) $[I^-] = 5.6 \times 10^{-2}$ M, $[I_2]_T = 1.73 \times 10^{-4}$ M.

The concentrations of iodine-containing species were calculated from the equilibrium constants of eq 6–11 according to eq 12 by

$$C_t = [I_2]\left(1 + K_{I_3^-}[I^-] + \frac{K_{IOH}[OH^-]}{[I^-]} + K_{I_2OH^-}[OH^-] + \frac{K_{IOH}K_a^{IOH}[OH^-]^2}{K_w[I^-]} + K_{I_2Cl^-}[Cl^-] + K_{RO^-}\frac{[RO^-][OH^-]}{[I^-]}\right) \tag{12}$$

using the values $K_{I_3^-}{}^{24} = 750$ M^{-1}, $K_{IOH}{}^{23} = 54$, $K_a^{IOH\,23} = 3.0 \times 10^{-11}$ M, $K_{I_2OH^-}{}^{23} = 4.5 \times 10^3$ M^{-1}, $K_{I_2Cl^-}{}^{24} = 1.66$ M^{-1}, and $K_{RO^-} = 2.7 \times 10^4$ M^{-1}. These values were found to give good agreement with the observed absorbance of triiodide ion at 351 nm[25] and the total iodine concentration, usually to much better than ±10%.

Kinetics of Iodination. Iodination by ~10^{-4} M total iodine in the presence of 2 × 10^{-3} M to 1 × 10^{-2} M acetone was followed by measuring the disappearance of the absorbance of triiodide ion at 351 nm and was found to follow first-order kinetics in the presence of 0.4 M trifluoroethanol buffers at pH >11. At pH <11 the disappearance of triiodide ion was initially close to zero order (because of the higher concentration of the reactive I_2 species), but satisfactory first-order kinetics were observed under all conditions examined for at least two and usually more than three half-lives. The reactions were >90% complete in <1 min; the rate of iodine decomposition in the absence of acetone is not significant under these conditions.

The observed pseudo-first-order rate constants are dependent on the concentrations of acetone, hydroxide ion, and iodide ion and may be described by eq 13, in which the parameters a, b, and

$$\frac{k_{obsd}C_t}{[HS][OH^-][I_2]} = a[I^-] + \frac{b}{[I^-]} + c \tag{13}$$

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(25) The other species that may absorb at this wavelength have a negligible contribution: ϵ_{IO^-} ~ 30 M^{-1} cm^{-1} (Haimovich, O.; Treinin, A. *Nature (London)* **1965**, *207*, 185–186); for $\epsilon_{I_2OH^-}$ a value of 4.6 × 10^2 M^{-1} cm^{-1} was estimated from different spectra and equilibrium constants (Connick, R. E.; Chia, Y. Ph.D. Thesis, University of California Radiation Laboratory—8311, 1958).

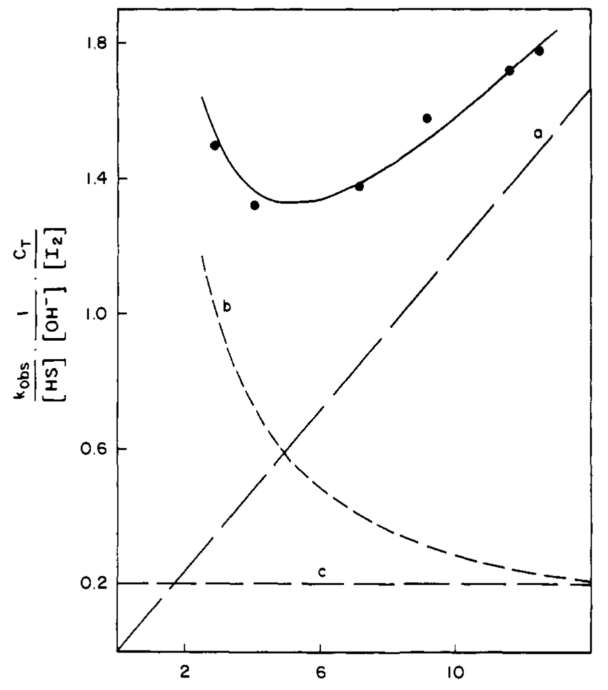

Figure 4. Value of $k_{obsd}C_T/([HS][OH^-][I_2])$ as a function of $[I^-]$ at constant $[OH^-] = 6.1 \times 10^{-3}$ M and I = 1 M (KCl), 25 °C. The solid line was calculated from the final a, b, and c parameters at different hydroxide ion concentrations. The contributions of a, b, and c to this graph are shown as dashed lines.

c represent the terms that are dependent on, inversely dependent on, and independent of the concentration of iodide ion, respectively. These parameters each depend on hydroxide ion concentration because of the stoichiometry of the different possible iodinating species, as described in eq 6–11, and because of the possibility of reaction with both the enolate ion (k^-) and the enol (k^0) of acetone. The composition of the a, b, and c terms is given in eq 14–16, taking into account the stoichiometry of 3 for the iodination

$$\frac{a}{3} = \frac{K_E K_{I_3^-} k^0{}_{I_3^-}}{[OH^-]} + \frac{K_a{}^{HS}}{K_w} K_{I_3^-} k^-{}_{I_3^-} \tag{14}$$

$$\frac{b}{3} = K_E K_{IOH} k^0{}_{IOH} + K_E \frac{K_a{}^{IOH} K_{IOH}}{K_w} k^0{}_{IO^-}[OH^-] + \frac{K_a{}^{HS}}{K_w} K_{IOH} k^-{}_{IOH}[OH^-] + \frac{K_a{}^{HS}}{K_w} \frac{K_a{}^{IOH} K_{IOH}}{K_w} k^-{}_{IO^-}[OH^-]^2 + K_E K_{RO^-} k^0{}_{RO^-}[RO^-] + \frac{K_a{}^{HS}}{K_w} K_{RO^-} k^-{}_{RO^-}[RO^-][OH^-] \tag{15}$$

$$\frac{c}{3} = K_E \frac{(k^0{}_{I_2} + K_{I_2Cl^-}[Cl^-] k^0{}_{I_2Cl^-})}{[OH^-]} + K_E K_{I_2OH^-} k^0{}_{I_2OH^-} + \frac{K_a{}^{HS}}{K_w} k^-{}_{I_2} + K_{I_2Cl^-}[Cl^-] k^-{}_{I_2Cl^-} + \frac{K_a{}^{HS}}{K_w} k_{I_2OH^-} k^-{}_{I_2OH^-}[OH^-] \tag{16}$$

and assuming that the reactions of eq 6–11 are at equilibrium.

The parameters a, b, and c were evaluated from a series of experiments in which the concentration of iodide ion was varied and the hydroxide ion concentration was constant, in the range 6×10^{-4} to 1×10^{-2} M. Typical experimental results are shown in Figures 4 and 5. Both figures show two branches that are dependent on $[I^-]$ and $1/[I^-]$, as well as a term that is independent of $[I^-]$. The term proportional to $1/[I^-]$ is larger at the higher pH value of Figure 4. The best parameters a, b, and c were calculated for each set of measurements at constant $[OH^-]$ as a linear regression in two variables and are given in Table II. The relative contributions of the three terms at two pH values are shown as the dashed lines in Figures 4 and 5.

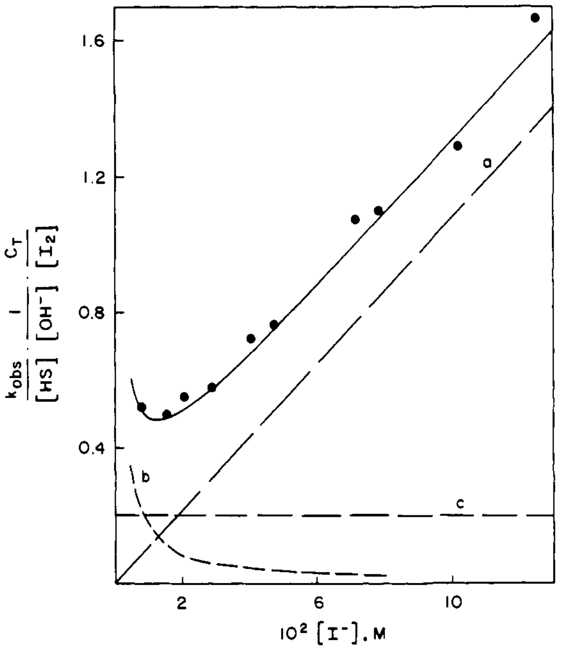

Figure 5. Same as Figure 4, at $[OH^-] = 1.25 \times 10^{-3}$ M.

Table II. Calculated Parameters for the Dependence of k_{obsd} for the Iodination of Acetone on Iodide Concentration, Eq 13[a]

$10^3[OH^-]$	$10^{-6}a$, $M^{-3}\,s^{-1}$	$10^{-3}b$, $M^{-1}\,s^{-1}$	$10^{-5}c$, $M^{-1}\,s^{-1}$
	I = 1 M (KCl)		
8.40	9.6 ± 0.9	56 ± 5	3.3 ± 1.5
6.10	11.1 ± 0.5	29 ± 2	1.7 ± 0.7
5.00	10.6 ± 0.9	19 ± 4	1.8 ± 1.3
3.55	11.5 ± 0.4	11 ± 1	1.4 ± 0.5
2.25	11.4 ± 0.3	3.8 ± 0.4	1.5 ± 0.3
1.25	11.7 ± 0.2	2.0 ± 0.3	1.9 ± 0.2
0.83[b]	10.6 ± 0.4	1.1 ± 0.5	2.3 ± 0.4
	I = 1 M (KNO_3)		
10.00[c]	8.7 ± 0.7	41 ± 6	1.6 ± 1.4
8.70	9.0 ± 0.7	32 ± 6	1.7 ± 1.5
4.90	8.0 ± 0.1	8.2 ± 0.6	1.9 ± 0.2
3.00	9.7 ± 0.5	2.6 ± 1.3	1.7 ± 0.7
2.20	9.4 ± 0.4	2.3 ± 1.1	1.1 ± 0.6
1.30	10.2 ± 0.2	0.5 ± 0.06	1.4 ± 0.3
0.61	12.0 ± 0.3	0.6 ± 0.5	1.0 ± 0.4

[a] At 25 °C, ionic strength 1.0 M, in the presence of 0.4 M trifluoroethanol buffer. [b] Buffer concentration also 0.8 M. [c] Buffer concentration = 0.8 M.

Table II shows that the a and c parameters do not vary significantly with $[OH^-]$, in contrast to the b parameter that increases with increasing $[OH^-]$. The a parameter of $(10.9 \pm 0.6) \times 10^6$ $M^{-3}\,s^{-1}$ corresponds to the kinetically unambiguous reaction of the enolate ion and I_3^- with the rate constant $k_{I_3^-}K_a{}^{HS} = (4.8 \pm 0.3) \times 10^{-11}\,s^{-1}$ at 25 °C, ionic strength 1.0 M (KCl); with KNO_3 instead of KCl the corresponding values are $a = (9.6 \pm 1.3) \times 10^6$ $M^{-3}\,s^{-1}$ and $k_{I_3^-}K_a{}^{HS} = (4.3 \pm 0.6) \times 10^{-11}\,s^{-1}$.

The value of $c = (2.0 \pm 0.6) \times 10^5$ $M^{-2}\,s^{-1}$ at ionic strength 1.0 M (KCl) can be attributed to three different reactions: the reaction of the enolate ion with I_2, or with I_2Cl^-, and the reaction of the enol with I_2OH^-. A similar value of $c = (1.5 \pm 0.3) \times 10^5$ $M^{-2}\,s^{-1}$ from experiments in which the ionic strength was maintained with KNO_3 (Table II) shows that I_2Cl^- is not the main contributor to the reaction. The absence of a dependence of the c parameter on $[OH^-]$ shows that there is no significant reaction of I_2OH^- with the enolate ion. It is therefore reasonable to assume that there is no significant reaction of I_2OH^- with the less reactive enol, which is expected to be present in comparable or smaller concentrations compared with the enolate ion under the conditions of the experiments, so that the c parameter can be assigned to the reaction of the enolate and I_2 with $k^-{}_{I_2}K_a{}^{HS}$ $(6.7 \pm 2.0) \times 10^{-10}$ s^{-1} (KCl) and $k^-{}_{I_2}K_a{}^{HS} = (5.0 \pm 1.0) \times 10^{-10}$ s^{-1} (KNO_3).

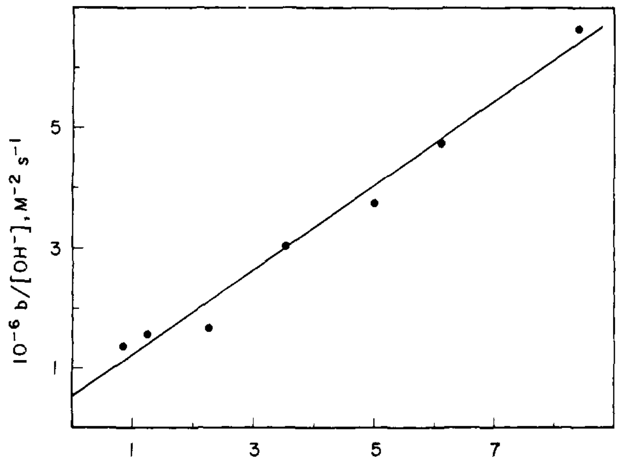

Figure 6. $b/[OH^-]$ term as a function of $[OH^-]$ at $I = 1$ M (KCl) and 25 °C.

The b parameter increases with more than the first power of the hydroxide ion concentration. A plot of $b/[OH^-]$ against $[OH^-]$ (Figure 6) gives the best fit to a line of slope $(7.0 \pm 0.4) \times 10^8$ $M^{-2}\ s^{-1}$ and intercept $(5.0 \pm 2.0) \times 10^5$ $M^{-1}\ s^{-1}$. No effect on k_{obsd} was found upon doubling the buffer concentration at the highest pH value examined. There is, therefore, no significant contribution from iodination by $ROIOH^-$, and the slope of Figure 6 can be attributed entirely to reaction of the enolate ion and IO^- with a rate constant of $k^-_{IO^-}/K_a^{HS} = (1.30 \pm 0.07) \times 10^{-11}\ s^{-1}$. The intercept is kinetically ambiguous, as in the bromination reaction, between reaction of the enol and IO^-, with $k^0_{IO^-} K_E = (1.0 \pm 0.4)\ M^{-1}\ s^{-1}$, or the enolate ion and IOH, with $k^-_{IOH}K_a^{HS} = (3.3 \pm 1.3) \times 10^{-11}\ s^{-1}$.

Discussion

Assignment of Reacting Species. The observed rate constants for reactions of the enolate ion of acetone with different halogenating species, $k^-K_a^{HS}$, are summarized in Table III. The table includes rate constants for HOCl and ClO^- based on measurements by Bartlett at 35 °C[5] and for HOCl, ClO^-, HOBr, and BrO^- obtained recently by Guthrie et al. at 25 °C.[8]

There is a large reactivity of IO^- and BrO^- in spite of the poor leaving group and unfavorable electrostatic interaction of these anions with the enolate anion, as found also by Guthrie et al.[8] for BrO^-. The rate constants for IO^- and BrO^- measured in this work are almost equal and only ~50 times less than that for I_2; however, the rate constant for ClO^- is more than 10^3 smaller. The same relative reactivities have been observed for the enolate of diisopropyl ketone.[7]

The rate constants for the reactions of the enolate anion with HOI, HOBr, and HOCl could also be interpreted as the kinetically ambiguous reactions of the enol with IO^-, BrO^-, and ClO^- (eq 5). There are several reasons for assigning these reactions to the enolate anion and hypohalous acid. (1) The reactivities of HOI and HOBr are expected to be at least as large as those of IO^- and BrO^- because HO^- is a better leaving group than O^{2-}. Since the rate constants for the reactions of the enolate ion with IO^- and BrO^- are large and unambiguous, similar or larger rate constants are expected for the reactions of enolate ion with HOI and HOBr. (2) There is no measurable reaction of HOI with the enol at the lowest pH values examined, so that a significant reaction of IO^- with the enol would not be expected; the ratio $[HOI]/[IO^-]$ is ~0.4 under these conditions. (3) The enolate ion is a much more reactive species than the enol, so that a reaction of HOI, HOBr, and HOCl with the enolate is expected, especially because the concentration of enolate is comparable to that of enol under the conditions of these experiments (see below). (4) The observed reactivities of IO^- and BrO^- with the enolate are $>10^3$ larger than that of ClO^- (Table III), and a similar or larger selectivity would be expected for the less reactive enol. This is inconsistent with the ratios of $k_{IO^-}/k_{ClO^-} = 50$ and $k_{BrO^-}/k_{ClO^-} = 20$ (Table III, footnote c) for the assignment to a reaction of XO^- with the enol. (5) Similarly, the ratio k_{I_2}/k_{IO^-} for the enolate ion is 51 (Table III), which is larger than the ratio $k_{I_2}/k_{IO^-} = 17$ that would be required for the enol according to the alternative assignment, based on a previously reported rate constant for the reaction of the enol with I_2.[9] This would require that the IO^- reaction with enol be only slightly slower than the I_2 reaction, which is close or equal to diffusion controlled,[10] while the observed selectivity of these species with the more reactive enolate is significantly larger. (6) The absolute values of the rate constants for the reactions of the enol with BrO^- ($(0.4–1.1) \times 10^8$ $M^{-1}\ s^{-1}$) and IO^- ($(1–3) \times 10^8$ $M^{-1}\ s^{-1}$), calculated from values of pK_E in the range 8.0–8.5, are larger than those for the enolate anion (Table III, see also footnote c), which is a more reactive species. The assignment to a reaction of HOX with the enolate ion gives rate constants for the reactions of HOBr and HOCl that are similar to that for I_2 and are presumably diffusion controlled, confirming the assumption of Guthrie et al.[8] The rate constant for the reaction of enolate ion with HOI is, if anything, smaller than expected; the reason for this is not understood.

Table III. Apparent Rate Constants for the Reactions of Different Halogen Species with Acetone Enolate in Aqueous Solution at 25 °C and I=1.0 M (KCl)[a]

species	$10^{10}k^-K_a^{HS}$, s^{-1}	k^-, $M^{-1}\ s^{-1}$
BrO^-	0.100 ± 0.002	8×10^7
	0.045^b	$2.8 \times 10^{7\,b}$
HOBr	8 ± 2^c	5×10^9
	3^b	$1.7 \times 10^{9\,b}$
IO^-	0.130 ± 0.007	10^8
IOH	0.33 ± 0.13^c	2.5×10^8
I_2	6.7 ± 2.0	5×10^9
	5.0 ± 1.0^d	
I_3^-	0.48 ± 0.03	3.6×10^8
	0.43 ± 0.06^d	
ClO^-	$3.3 \times 10^{-5\,e}$	2.5×10^4
	$8.7 \times 10^{-6\,b}$	$2 \times 10^{4\,b}$
HOCl	$6.9^{c,e}$	5×10^9
	0.74^b	$1.7 \times 10^{9\,b}$

[a] Unless otherwise stated. [b] Given or calculated from data in ref 8; the data are at I = 0.1 M (KCl) and k^- was taken as 1.7×10^9 $M^{-1}\ s^{-1}$ for diffusion-controlled halogenation. [c] These terms are kinetically ambiguous and can also be interpreted as a reaction of the enol and hypohalite ion, with values of $K_Ek^0_{BrO^-} = 0.4\ M^{-1}\ s^{-1}$, $K_Ek^0_{IO^-} = 1.0\ M^{-1}\ s^{-1}$, and $K_Ek^0_{ClO^-} = 0.02\ M^{-1}\ s^{-1}$. [d] Data obtained in I = 1.0 M (KNO_3). [e] Calculated from data in ref 5 at 35 °C.

Reactivity of Halogenating Species. The reaction of I_2 with the enolate ion of acetone is expected to be diffusion controlled because the reactions of halogens with the much less reactive enol and enol ether are close or equal to diffusion controlled,[10,11] as discussed in the introduction. This conclusion is supported by reported rate constants in the range 10^9–10^{11} $M^{-1}\ s^{-1}$ for the halogenation of acyclic enolate anions of β-diketones,[13,26] which are also less reactive than the enolate of acetone. These rate constants are based on indirect estimates of the pK_a values for the diketones, but they are certainly at or close to the diffusion-controlled limit. The rate constants for halogenation by HOBr and by HOCl (at 35 °C) are equal to that for I_2 (Table III), so that these reactive halogenating agents also react at a diffusion-controlled rate.

Absolute values of the rate constants for the reactions of the enolate ion with halogenating agents are given in column 3 of Table III. These rate constants are based on the assumption that diffusion-controlled halogenation occurs with a rate constant of 5×10^9 $M^{-1}\ s^{-1}$, in agreement with some previous estimates.[11,27] Rate constants in the range 10^9–10^{10} have been assumed previously for diffusion-controlled halogenation and the variation in these values accounts for some of the variation in estimated values of K_E.[10-12] The value of $k = 5 \times 10^9$ $M^{-1}\ s^{-1}$ is consistent with a

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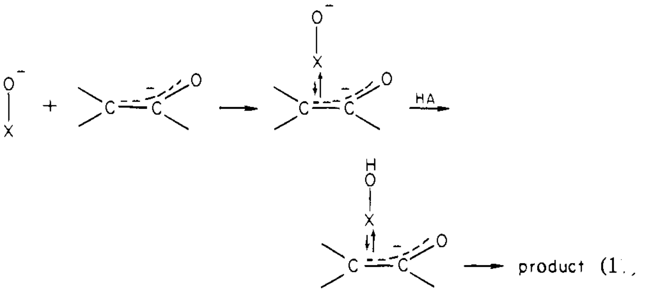
(26) Bell, R. P.; Engel, P. *J. Chem. Soc.* **1957**, 247-253. Bell, R. P.; Vogelsong, D. C. *Ibid.* **1958**, 243-245.

(27) Young, P. R.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 8238-8248.

measured rate constant of 6×10^9 M^{-1} s^{-1} for the reaction of I_2 with I^- to give I_3^- and 8.2×10^9 M^{-1} s^{-1} for the combination of $2I\cdot$ to give I_2.[28,29] Correction for differences in diffusion coefficients and effective radii gives $k = 4 \times 10^9$ M^{-1} s^{-1} for I_2 and the enolate ion, assuming that acetate ion is a model for the enolate of acetone.[30,31] Larger rate constants close to 10^{10} M^{-1} s^{-1} have been reported for the bromination of anions of phenols and uracil derivatives by Br_2,[32-34] but some of the larger numbers are based on limited data[32] or on pK values measured at a lower ionic strength than was used for the experimental measurements;[33] there may also be a larger effective radius for initial combination with these aromatic molecules. Calculated rate constants according to the Smoluchowski equation[28] are approximately 10^{10} M^{-1} s^{-1}, but other calculations give lower values,[29] and experimental rate constants for thermodynamically favorable proton transfer between electronegative atoms of acids and bases in aqueous solution[35,36] are usually close to 10^9 M^{-1} s^{-1}. Rate constants for reactions of Br_2 with four disulfone carbanions of pK_a = 10.7–14.6 are in the range $(0.9–1.6) \times 10^9$ M^{-1} s^{-1}.[37] The differences in these rate constants presumably reflect differences in the rate constant for the final step of diffusion due to desolvation or steric effects.[28,36]

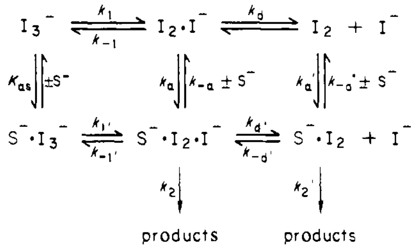
The large rate constants of $(6–8) \times 10^7$ M^{-1} s^{-1} for halogenation by BrO^- and IO^- (Table III) are surprising because a simple one-step halogenation by these species would require the expulsion of O^{2-}, an exceptionally poor leaving group. It is conceivable that halogenation is concerted with protonation of oxygen and expulsion of OH^-, but no rate increase from the general acid catalysis that might be expected for such protonation was observed upon doubling the buffer concentration from 0.4 to 0.8 M.

The simplest explanation for the high reactivity of these species is that the reaction is stepwise, with rate-determining formation of a donor–acceptor complex between the enolate and halogenating agent followed by protonation and expulsion of oxygen in one or more subsequent steps (eq 17). The existence of halogen com-



plexes, including trihalide ions such as I_3^-, π complexes, and bromonium addition compounds, is well-known,[38-40] and there is evidence that bromonium ions can be intermediates in the halogenation of alkenes;[41-44] π complexes (or charge-transfer complexes) have also been suggested as intermediates in the halogenation of olefins and aromatic compounds.[40,42,45,46] The smaller ability of chlorine derivatives[47] to form such complexes is consistent with the 10^3 slower reaction rate of ClO^- compared with BrO^- and IO^- (Table III). The electronic structure of the proposed complex is uncertain, but it presumably involves electron donation from the enolate (HOMO) to the lowest antibonding orbital of the halogen (LUMO).[48] Back-bonding from occupied orbitals of the halogen with proper energy and symmetry, possibly with a contribution of d orbitals, to an antibonding π orbital of the enolate may provide additional stabilization. Analogous bonding is well-known for metal–olefin complexes, including enols,[49,50] and has been postulated for the bromination of olefins.[41,46] The bonding in such a complex of an enolate ion is expected to be strongest at the terminal carbon atom,[48,50,51] so that collapse to the haloacetone can occur with little further rearrangement.

Scheme I



The rate constant of 3.6×10^8 M^{-1} s^{-1} for the reaction of I_3^- with the enolate is 13 times smaller than that for I_2. This result is surprising, because the ratios of $k_{I_2}/k_{I_3^-}$ = 17–100 for iodination of the much less reactive enols of ketones are only slightly larger.[10,52] This suggests that the reactivity ratios of 13–28 are not caused by an ordinary chemical barrier for the reaction of I_3^-. If the rate constant for I_3^- is less than that for I_2 because there is an ordinary chemical barrier for the I_3^- reaction with enols, it would be expected that this barrier would decrease or disappear with the more reactive enolate ion. The rate constant for the reaction of I_3^- would then be expected to be diffusion controlled, close to that of I_2.

These rate constant ratios can be accounted for if the role of I_3^- is simply to act as a carrier to deliver I_2 to the enol or enolate through a preassociation mechanism (Scheme I, pathway through K_{as}, k_1', and k_2).[2,53] If the reactions of I_2 with I^- and with the enolate, S^-, are diffusion controlled, the complexes $S^- \cdot I_2$ and $S^- \cdot I_2 \cdot I^-$

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(28) Turner, D. H.; Flynn, G. W.; Sutin, N.; Beitz, J. V. *J. Am. Chem. Soc.* **1972**, *94*, 1554–1559. Rosman, H.; Noyes, R. M. *Ibid.* **1958**, *80*, 2410–2415. The same rate constants have been calculated for diffusion in carbon tetrachloride and in water. (See ref 29.)

(29) Ridd, J. H. *Adv. Phys. Org. Chem.* **1979**, *16*, 1–49.

(30) The corrections are based on reported diffusion coefficients, D, of 2.25×10^{-5}, 2.05×10^{-5}, 4.2×10^{-5}, and 1.09×10^{-5} cm^2 s^{-1} and radius, r, of 2.52×10^{-8}, 2.16×10^{-8}, 2×10^{-8}, and 1.56×10^{-8} cm for I_2, I^-, $I\cdot$, and acetate ion, respectively, and on the Smoluchowski equation.[28,31]

$$k = \frac{4\pi N(r_1 + r_2)}{1000}(D_1 + D_2)$$

The contact distance for an ion that has a peripheral charge site can be determined by an effective electrostatic radius that is smaller than the overall ionic radius. (Gordon, J. E. "The Organic Chemistry of Electrolyte Solutions"; Wiley: New York, 1975; p 396.)

(31) Albery, W. J.; Greenwood, A. R.; Kibble, R. F. *Trans. Faraday Soc.* **1967**, *63*, 360–368.

(32) Bell, R. P.; Rawlinson, D. J. *J. Chem. Soc.* **1961**, 63–68.

(33) Kulič, J.; Večeřa, M. *Collect. Czech. Chem. Commun.* **1970**, *39*, 171–176.

(34) Tee, O. S.; Berks, C. G. *J. Org. Chem.* **1980**, *45*, 830–835.

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(37) Bell, R. P.; Cox, B. G. *J. Chem. Soc. B* **1971**, 652–656.

(38) Banthorpe, D. V. *Chem. Rev.* **1970**, *70*, 295–322.

(39) Hanna, M. W.; Lippert, J. L. In "Molecular Complexes"; Foster, R., Ed.; Elek Science: London, 1973; Vol. 1, pp 1–48. Tamres, M. *Ibid.* 1973; pp 49–116.

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(42) Freeman, F. *Chem. Rev.* **1975**, *75*, 439–490.

(43) Melloni, G.; Modena, G.; Tonellato, U. *Acc. Chem. Res.* **1981**, *14*, 227–233.

(44) Dubois, J. E.; Mouvier, G. *Tetrahedron Lett.* **1963**, 1325–1331.

(45) Olah, G. A. *Acc. Chem. Res.* **1971**, *4*, 240–248.

(46) Olah, G. A.; Schilling, P.; Westerman, P. W.; Lin, H. C. *J. Am. Chem. Soc.* **1974**, *96*, 3581–3589.

(47) Heublein, G. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 881.

(48) Fleming, I. "Frontier Orbitals and Organic Chemical Reactions"; Wiley: London, 1976; p 43.

(49) Reference 21, p 95.

(50) Albright, T. A.; Hoffmann, R.; Thibeault, J. C.; Thorn, D. L. *J. Am. Chem. Soc.* **1979**, *101*, 3801–3812.

(51) Chang, T. C. T.; Foxman, B. M.; Rosenblum, M.; Stockman, C. *J. Am. Chem. Soc.* **1981**, *103*, 7361–7362. Eisenstein, O.; Hoffmann, R. *Ibid.* **1980**, *102*, 6148–6149.

(52) The rate constant for the reaction of the enol of acetone itself with I_3^- has not been reported; it is known to be less than half of the rate constant for I_2.[10]

(53) Jencks, W. P. *Chem. Soc. Rev.* **1981**, *10*, 345–375.

collapse to products faster than they separate into their components. In Scheme I this corresponds to $k_2, k_{-1}' > k_{-a}$ and $k_2' > k_{-a}'$. This means that the lowest energy pathway for halogenation by I_3^- in this scheme is through the lower, preassociation pathway rather than the upper mechanism through k_1 and the diffusion-controlled step k_a.[2,53] The rate constants for the reactions with I_2 and I_3^- are then given by eq 18 and 19, respectively, in which

$$k^-_{I_2} = k_a' = 5 \times 10^9\ M^{-1}\ s^{-1} \tag{18}$$

$$k^-_{I_3} = k_pK_{as} = 3.6 \times 10^8\ M^{-1}\ s^{-1} \tag{19}$$

$k_p = k_1'k_2/(k_{-1}' + k_2)$. If it is assumed that the dissociation constant for I_3^- is not altered by the presence of S^-, then taking $k_1'/k_{-1}' = K_{as}/K_{I_3^-} = 0.1\ M^{-1}/750\ M^{-1} = 1.3 \times 10^{-4}$ and $k_{-1}' = k_2$ gives a value of $\sim 5 \times 10^{13}\ s^{-1}$ for k_{-1}' and k_2. This estimate for k_{-1}' and k_2 is on the order of a vibration frequency. It is consistent with the hypothesis that there is essentially no chemical barrier for the reaction of I_2 with either I^- or enolate ion after encounter and that the barrier for halogenation of the enolate by I_3^- is simply provided by the unfavorable equilibrium for the formation of I_2 from I_3^- within the encounter complex. This could be considered a "preassociation uncoupled concerted" mechanism.[53]

No reaction was detected with the anions I_2OH^- and $ROIOH^-$. Upper limits for the rate constants corresponding to halogenation of the enolate ion by these species are $2 \times 10^8\ M^{-1}\ s^{-1}$ for I_2OH^- and $6 \times 10^7\ M^{-1}\ s^{-1}$ for $ROIOH^-$.[54] This value for I_2OH^- and the rate constants in Table III for I_3^- and IOH are not consistent with the suggestion that the reactions of these species with the enolate ion are diffusion controlled.[11]

The species $ROIOH^-$ does not appear to have been described previously. The structure is formally analogous to that of I_3^- and I_2OH^- and may represent the same type of bonding.[55] We are not aware of evidence that IO^- does not exist partly as the corresponding hydrate $HOIOH^-$ in aqueous solution. Halogenation by this species (and the corresponding bromine species) provides a conceivable alternative to the intermediate complex mechanism proposed above for halogenation by IO^- (and BrO^-).

pK_a of Acetone. The observed rate constants for halogenation of the enolate ion of acetone by I_2 and by HOBr, $k^-K_a^{HS}$ (Table III), and the value of $k^- = 5 \times 10^9\ M^{-1}\ s^{-1}$ for diffusion-controlled halogenation give a value of $K_a^{HS} = 1.3 \times 10^{-19}$ M or $pK_a^{HS} = 18.9$ for the acid dissociation of acetone at 25 °C, ionic strength 1.0 M (KCl). In 1.0 M KNO_3 the value of pK_a^{HS} is 19.0. We estimate an uncertainty of approximately ±0.3 pK units for these values. The rate constant for chlorination of the enolate ion by HOCl at 35 °C[5] also gives $pK_a^{HS} = 18.9$, assuming the same value for diffusion-controlled encounter at this temperature.

This pK_a is lower than the traditional value of $pK_a^{HS} = 20$ that was based on an extrapolation of a correlation between rate constants for enolization and ΔpK of a series of ketones and base catalysts;[56] however, these data can be fit by different correlation lines for mono-, di-, and tricarbonyl compounds,[57] and the estimated pK_a has a considerable uncertainty. Guthrie[57] has calculated a value of $pK_a^{HS} = 19.1$ from the data of Bartlett and Vincent,[5] assuming a diffusion-controlled reaction of HOCl and the enolate anion with $k = 1 \times 10^{10}\ M^{-1}\ s^{-1}$. More recently, Guthrie et al. have obtained values of $pK_a^{HS} = 18.8$ and 19.4 from the observed rate constants for halogenation by HOBr and HOCl, respectively, assuming a rate constant of $1.7 \times 10^9\ M^{-1}\ s^{-1}$ for diffusion-controlled halogenation.[8]

The rate constants for protonation of the enolate ion by water and by the proton are $k_{-1}' = k_1'K_w/K_a^{HS} = 1 \times 10^4\ s^{-1}$ and $k_{-1} = k_1/K_a^{HS} = 3.5 \times 10^9\ M^{-1}\ s^{-1}$, respectively, from $pK_a^{HS} = 18.9$ and the known rate constants for enolization induced by hydroxide ion and by water in the reverse direction.[58] The latter value corresponds to a rate constant of $k_{-1} = 6 \times 10^{-2}\ s^{-1}$ for the kinetically equivalent protonation of the enol by water, assuming $pK_a^{SH} = 10.8$ (see below). This rate constant corresponds to a half-life of 12 s and suggests that it should be possible to follow reactions of the enol directly at the minimum of the pH-rate profile for ketonization.

The rate constant for catalysis by water of the enolization of acetone falls about 6-fold above the Brønsted line for general base catalysis of enolization by carboxylate ions;[59] it falls close to a linear Brønsted plot for catalysis by substituted pyridines.[60] This is surprising, because proton transfer to or from carbon by the proton or water is usually abnormally slow compared with other acids and bases.[61] Deviations from a Brønsted plot are the same in both directions of a reaction for a given acid-base pair. Thus, the well-known negative deviation of hydroxide ion from the Brønsted plot for enolization[59] corresponds to a negative deviation of 10^3 of the rate constant for protonation of the enolate ion by water. Similarly, the negative deviation for catalysis by the proton of acetone enolization by a factor of ~20[59] corresponds to the same negative deviation for reaction of a proton with the enol in the ketonization direction.

The water-catalyzed enolization reaction corresponds to protonation of the enolate ion by the solvated proton in the reverse direction. The traditional value of $pK_a^{HS} = 20$ gives a rate constant of $k_{-1} \sim 5 \times 10^{10}\ M^{-1}\ s^{-1}$ for this protonation, which corresponds to a diffusion-controlled reaction.[35] However, the rate constant of $k_{-1} = 4 \times 10^9\ M^{-1}\ s^{-1}$ from $pK_a^{HS} = 18.9$ is significantly smaller than expected for a diffusion-controlled reaction of the proton[35] and means that there is a significant barrier for this protonation. Nevertheless, the unexpectedly large rate constant for water-catalyzed enolization and, therefore, for this protonation of the enolate ion indicates that this barrier is smaller than expected. We suggest that this represents catalysis through a modest stabilization of the transition state by hydrogen bonding of the solvated proton to the oxygen anion of the enolate for the reaction in both directions. We prefer this mechanism to a fully concerted cyclic proton transfer from the hydroxyl group to carbon in the enol because it is likely that the immediate protonating reagent is H_3O^+. The existence of a significant barrier for protonation of carbon means that this protonation is slower than both diffusion away of H_3O^+ and protonation of the oxygen anion of the enolate; i.e., both of these steps are at equilibrium. A similar, but larger, facilitation by a neighboring nitrogen atom of the protonation of a nitronate anion has been reported by Bernasconi and Carrê and was ascribed to an intramolecular proton switch mechanism.[62]

The enol of acetone dissociates to the enolate ion with an estimated value of $pK_a^{SH} = 10.8$, based on a value of $pK_a^{SH} = 10.34$ for the enol of acetophenone that was measured by a flash-spectroscopic method.[63] The difference between the values for the enols of acetone and acetophenone is based on the difference of 0.45 unit between $pK_a = 10.45$ for $CH_3C(OH)_2CF_3$ and $pK_a = 10.0$ for $PhC(OH)_2CF_3$.[64] This value of pK_a^{SH} is significantly smaller than a previous estimate of $pK_a^{SH} = 11.8$ that was based on an indirect value for the pK_a^{SH} of acetophenone enol[17,65] and values for the enols of cyclopentanone and cyclohexanone that were estimated from halogen titration.[66]

The dependence on pH of the observed rate constants for iodination provides a method to confirm this pK_a value of 10.8 for

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[54] The rate constant of $2 \times 10^8\ M^{-1}\ s^{-1}$ for I_2OH^- corresponds to an increase in the *c* term by $2 \times 10^5\ M^{-2}\ s^{-1}$ at $[OH^-] = 8.4 \times 10^{-3}$ M; the rate constant is smaller than this because no increase was observed up to $[OH^-] = 10^{-2}$ M (Table II). The rate constant for $ROIOH^-$ was calculated with the assumption that all of the *b* term represents reaction by this species; however, this assumption was ruled out because doubling the buffer concentration does not increase the rate.

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the enol and/or the assumption that iodination of the enol is diffusion controlled. As the pH decreases the enol and enolate will exist in comparable concentrations so that there will be an increase in the observed rate constant for halogenation over that expected for the enolate alone (eq 16); if the enol and enolate both react with I_2 at a diffusion-controlled rate there will be a 2-fold increase of the observed rate constant at pH = pK_a^{SH}.

In fact, there is no significant increase in the *c* term, which would represent a reaction of I_2 with the enol, at pH 10.8, the lowest pH examined (Table II). If it is assumed that a 30% increase occurs but was not detected at pH 10.8, the value of pK_a^{SH} is 10.6; alternatively, if pK_a^{SH} is 10.8, the rate constant for reaction of the enol with I_2 is $\lesssim 0.5$ that for the enolate anion.

The relationship between the enolization and dissociation constants of acetone (eq 1) gives a value of $pK_E = pK_a^{HS} - pK_a^{SH} = 18.9 - 10.8 = 8.1$ for enolization of the ketone. This is somewhat smaller than a value of $pK_E = 8.5$ that was reported recently,[11] based on the assumption that halogenation of the enol in acid solution is diffusion controlled with $k^0 = 5 \times 10^9$ M^{-1} s^{-1}.

We conclude from these comparisons that pK_E is in the range 8.1–8.5 and that the rate constant for halogenation of the enol by I_2 is close to that of a diffusion-controlled reaction, confirming the earlier assumption.[10] A value of $pK_a^{SH} = 10.6$ is within the uncertainty of the estimate in view of the ionic strength of 1.0 M for the experiments described here and 0.1 M for the determination of pK_a^{SH} for acetophenone enol;[63] this p*K* value gives $pK_E = 8.3$. This value is significantly larger than estimates in the range $pK_E = 7.0$–7.5 based on thermochemical and kinetic approaches and the assumption that the enol and enol ether have identical properties;[12,17,67] it therefore supports the conclusion[11] that this assumption is incorrect. The values of $pK_E = 8.1$–8.5 and the observed rate constants for halogenation in acid solution[10] give rate constants in the range $k^0 = 2 \times 10^9$ to 5×10^9 M^{-1} s^{-1} for reaction of the enol with I_2, Br_2, and Cl_2.

There is also no detectable reaction of the enol with HOBr or HOI under the conditions of these experiments. Such a reaction would give upward curvature with decreasing $[OH^-]$ in the plots of Figures 1 and 6, respectively. It can be concluded, as in the case of the I_2 reaction, that the rate constants for reaction of the enol with these species are smaller than those for reaction with the enolate ($k^- = 5 \times 10^9$ and 2.5×10^8 M^{-1} s^{-1} for HOBr and HOI, respectively, Table III) or that pK_a^{SH} is slightly smaller than 10.8.

Trapping of Carbanions. This work has demonstrated that it is possible to sort out the complex equilibria among the different species of iodine that exist in buffered alkaline solutions, in spite of their instability, and to obtain rate constants for halogenation that permit a determination of the p*K* of acetone by assuming a diffusion-controlled halogenation of acetone enolate by I_2. Bromination by HOBr provides a similar system, and the agreement of the rate constants for halogenation by HOBr and I_2 suggests that the HOBr reaction is also diffusion controlled. However, the concentration of these reactive species in strongly alkaline solutions is too small to permit diffusion-controlled trapping of much more basic carbanions. A less accurate estimate of the pK_a of weaker carbon acids may be possible by determining the rate constant for reaction of the carbanion with BrO^- and assuming that the rate constant for this reaction is 10^1–10^2 times smaller than diffusion-controlled, as it is for the anion of acetone.

Experimental Section

Reagents. Fresh solutions of acetone were made by volume daily from Fisher HPLC grade acetone that was used without further purification. Potassium hypobromite was prepared by adding bromine (99.7%, Baker analyzed reagent) to cold aqueous solutions of potassium hydroxide. The solutions were kept at ~0 °C and were used for kinetic studies as long as no change was observed[68] in the absorption of BrO^- at 330 nm (ϵ 300).[69] Stock solutions of iodine were prepared from Fisher resublimed reagent iodine in the presence of potassium iodide and were stored under argon. Solutions of potassium iodide (Fisher) were prepared at the same time and were also stored under argon. When a pale yellow color was observed in the iodide solutions indicating the formation of I_3^-, both solutions of iodine and iodide were replaced. The iodine concentration was determined by thiosulfate titration and by I_3^- absorption at 351 nm (ϵ_{I_3}- 26 000 + 2200$[I^-]$).[24] Buffer solutions were made by mixing Aldrich 2,2,2-trifluoroethanol (>99%) and potassium hydroxide solutions in glass-distilled water.

Measurements. The kinetics and equilibria of the reactions were monitored spectrophotometrically with a Cary 118 spectrophotometer with a thermostated cell compartment. All reactions were started by adding the halogen, ~10^{-4} M, to the cuvette containing acetone in the buffered solution. The pseudo-first-order rate constants obtained graphically were divided by acetone concentration to obtain the second-order rate constants. These rate constants were not affected by doubling the acetone concentration. Between pH 10.55 and 11.74 for concentrations of total iodine in the range 5×10^{-5} to 1.5×10^{-4} M, a decomposition of 2–6% was observed in 1 min. The percentage of decomposition decreases with decreasing total iodine concentration and increasing $[I^-]$.

The pH was measured with an Orion Research Model 701A pH meter standardized at pH 12.45 with $Ca(OH)_2$[70] at 25 °C. The concentration of hydroxide ion was obtained from calibration graphs that were made for different concentrations of potassium hydroxide at ionic strength 1.0 M, maintained with potassium chloride or potassium nitrate. All measurements were made at 25 °C and 1.0 M ionic strength.

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