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Halide Catalysis in the Bromination of Deoxybenzoin

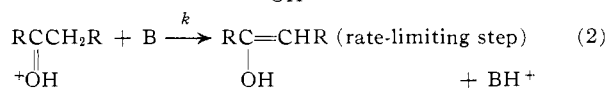
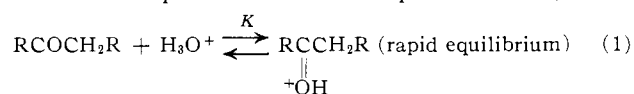
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RECEIVED MARCH 9, 1963

The rate of bromination of deoxybenzoin in aqueous acetic acid solution, in the presence of perchloric acid and at constant formal ionic strength, is zero order in bromine, first order in h_0 and in the concentrations of deoxybenzoin and water. The bromination in 97.9% acetic acid proceeds 43 times more rapidly with 0.1 *M* HBr, and 26 times more rapidly with 0.1 *M* HCl, than with 0.1 *M* perchloric acid. The superiority of the halogen acids decreases markedly in more aqueous solvents. For the portion of the reaction in 97.9%, 91.0%, and 79.9% acetic acid which is specifically catalyzed by the halogen acids, the addition of LiClO₄ sharply decreases k/h_0 , but the addition of LiCl increases this ratio. At constant formal ionic strength, the reaction is zero order in bromine, first order in h_0 , in the concentration of deoxybenzoin, and in the stoichiometric concentration of halide ions. These data have been discussed in terms of the tentative hypothesis that halide ions function as bases in 79.9, 91.0, and 97.9% acetic acid, where they are only partially hydrated. In this formulation, the ketone is first protonated and a hydrogen ion is then removed from the α -carbon atom by a halide ion (or possibly by a closely related ion-pair).

Introduction

The halogenation of ketones provides a convenient measure of the rate of enolization.² In acid solution, the reaction proceeds³ in two steps. The enol, formed



in the rate-limiting⁴ step, is then rapidly halogenated. In dilute aqueous solutions of mineral acids, the base which removes the proton is a water molecule. When weak acids are present, the effective bases include corresponding anions; the kinetic equation for reactions 1 and 2 is $v = (\text{ketone})[k(\text{H}^+) + k_{\text{HA}}(\text{HA})]$. Studies of the halogenation of ketones in solutions of strong acids have generally been concerned with the appropriate acidity function which should be applied to the reaction.⁵

In the present study, deoxybenzoin was brominated in 79.9%, 91.0%, and 97.9% acetic acid, in the presence of perchloric, hydrochloric, and hydrobromic acids. The rates with 0.1 *M* HBr and HCl, in 97.9% acetic acid solution, were 43 and 26 times as fast as with 0.1 *M* perchloric acid, despite the greater acid strength of the latter, and therefore the greater h_0 values of its solutions. Similar and less spectacular findings were obtained in 91.0% acetic acid; the specific catalytic effect of the halogen acids in 79.9% acetic acid is small. The interpretation of these results is complicated by the incomplete dissociation of the acids into ions; in 97.9% acetic acid, ion-pairs predominate. However, the results are best understood on the basis of general acid catalysis by the halogen acids. An understanding of the special circumstances which permit such catalysis is offered in the Discussion.

Experimental

Materials.—One batch (600 ml.) of du Pont C.P. Reagent grade acetic acid was purified by adding 6 g. of chromium trioxide to the hot acid and allowing it to stand overnight. It was flash-distilled under vacuum and then carefully fractionated with a 26-cm. column packed with glass helices. The main fraction,

boiling at $118.0 \pm 0.2^\circ$, had a melting point of $16.59 \pm 0.01^\circ$ (N.B.S. thermometer). This corresponds to 99.975% acetic acid, assuming that water is the dominant impurity.⁶ Four other batches of du Pont C.P. Reagent acetic acid were used without purification; the data were accepted if they corresponded to those from the purified acid. One batch of acetic acid was found to contain a trace of an aldehydic impurity (2,4-dinitrophenylhydrazine test) tentatively identified as glyoxal at perhaps 3×10^{-4} *M*. The H_0 measurements made with this batch of solvent differed by as much as 0.15 unit from those in purified acetic acid, presumably because the glyoxal reacts selectively with the basic form of the indicator. The suspected H_0 values were discarded. Rates of bromination determined in this solvent were consistent with those found with other batches.

Reagent grade bromine (Merck) was fractionated from 0.5% of potassium bromide (to remove traces of chlorine). Matheson 99.0% (min.) hydrogen bromide was passed through a drying tube packed with Drierite; Matheson 99.0% (min.) hydrogen chloride was dried with calcium chloride. Merck 70% perchloric acid was standardized before use. Analytical reagent lithium chloride (Mallinckrodt) was dried for 5 hr. at 210° ; lithium perchlorate (prepared from reagent grade lithium carbonate and reagent grade 70% perchloric acid) was dried to the anhydrous salt by heating to 230° for 20 hr. Mallinckrodt N.F. grade lithium bromide was recrystallized from water, then dried first over phosphorus pentoxide, and finally at 100° and 0.2 μ pressure for 3 hr. Mallinckrodt Reagent grade acetic anhydride was fractionated through a 46-cm. Vigreux column. Stuart Oxygen Co. deuterium oxide, 99.5%, was used without purification. Acetic acid-1-*d* was prepared by refluxing a slight excess of deuterium oxide with acetic anhydride for about 8 hr. Excess deuterium oxide was removed by azeotropic distillation with benzene through a 35-cm. column packed with glass helices. Fractionation produced acetic acid-1-*d*, b.p. $117\text{--}118.5^\circ$. The melting point of this acid, determined 34 months after its preparation, was $15.25 \pm 0.02^\circ$ (N.B.S. thermometer), lit.⁷ $15.66 \pm 0.05^\circ$. Deoxybenzoin, after recrystallization from 95% ethanol, melted at $55.7\text{--}56.3^\circ$, lit.⁸ $54.5\text{--}55.7^\circ$; desyl bromide, recrystallized from 95% ethanol, melted at $57.1\text{--}57.5^\circ$, lit.⁹ $54\text{--}55^\circ$. Dibromodeoxybenzoin, recrystallized from acetic acid, melted at $111.8\text{--}112.7^\circ$, lit.¹⁰ 112° . *o*-Nitroaniline, from ethanol, melted at $71.7\text{--}72.5^\circ$; *p*-nitroaniline, from 50% ethanol, melted at $148.4\text{--}149.1^\circ$. Other chemicals were reagent grade.

Solutions.—The "97.9%," "91.0%," and "79.9%" acetic acid were made up accurately by weight¹¹ from distilled water and from "glacial" acetic acid of known melting point (and hence of known water content). The standard sample of 97.9% acetic acid melted at $13.29 \pm 0.02^\circ$. One batch of 97.9% acid which melted at $13.13 \pm 0.02^\circ$ presumably contained 0.07–0.08% excess water.

"97.9%" acetic acid-1-*d* was prepared so as to be 1.1620 *M* in deuterium oxide in acetic acid-1-*d*, and so correspond to the solvent with ordinary water. The solution of DCl in this solvent was made by adding acetyl chloride and D₂O to acetic acid-1-*d* in quantities calculated to yield the appropriate acid solution.

Stock solutions of hydrogen halides in aqueous acetic acid were prepared by bubbling the dry gas into the appropriate solvent

(1) National Science Predoctoral Fellow, 1955–1959.

(2) A. Iapworth, *J. Chem. Soc.*, **85**, 30 (1904).

(3) For a discussion of the mechanism of enolization see R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959.

(4) For the definition of "rate-limiting," see J. Rocek, F. H. Westheimer, A. Eschenmoser, L. Moldovanyi, and J. Schreiber, *Helv. Chim. Acta*, **45**, 2554 (1962), footnote 7.

(5) L. Zucker and L. P. Hammett, *J. Am. Chem. Soc.*, **61**, 2785 (1939); D. P. N. Satchell, *J. Chem. Soc.*, 2878 (1957); G. Archer and R. P. Bell, *ibid.*, 3228 (1959); H. J. Campbell and J. T. Edward, *Can. J. Chem.*, **38**, 2109 (1960); C. G. Swain and A. S. Rosenberg, *J. Am. Chem. Soc.*, **83**, 2154 (1961).

(6) J. S. Fritz and G. S. Hammond, "Quantitative Organic Analysis," John Wiley and Sons, Inc., New York, N. Y., 1957, p. 229.

(7) H. Linschitz, M. E. Hobbs, and P. M. Gross, *J. Am. Chem. Soc.*, **63**, 3234 (1941).

(8) A. C. Cope, P. A. Trumbull, and E. R. Trumbull, *ibid.*, **80**, 2844 (1958).

(9) E. Knoevenagel, *Chem. Ber.*, **21**, 1355 (1888).

(10) T. Curtius and H. Lang, *J. prakt. Chem.*, [2] **44**, 547 (1891).

(11) "International Critical Tables," Vol. 11, McGraw-Hill Book Co., Inc., New York, N. Y., 1928, p. 324.

and standardizing the resulting solution by potentiometric titration for halide.¹² Solutions of hydrogen bromide and lithium bromide had to be freshly prepared every few days; they became yellow on prolonged standing. Solutions of bromine were prepared each day.

Methods.—The acidity function, H_0 , was determined spectrophotometrically¹³ with a Beckman quartz DU spectrophotometer equipped with a specially constructed thermostated cell compartment, maintained at $30.15 \pm 0.01^\circ$.

Two indicators (*o*- and *p*-nitroaniline) were used. The absorbance of the acid form, IH^+ , of *o*-nitroaniline was neglected, but that of *p*-nitroaniline at $375 \text{ m}\mu$ was taken into account as a small correction.¹⁴ The absorbancies of the fully basic forms of the indicators were measured when sodium acetate was added to the solvent. The value 0.99 was assigned¹³ to the $\text{p}K$ of *p*-nitroaniline, and a value of -0.48 was then found for *o*-nitroaniline, from measurements with both indicators in 79.9% acetic acid. Although the $\text{p}K$ of *o*-nitroaniline in water¹⁵ is $+0.29$, our result is consistent with those of others who worked in glacial or aqueous acetic acid as solvent.^{14,16}

Experiments with carefully prepared solutions of 97.71 and 98.00% acetic acid showed that the values of H_0 generally run about 0.05 unit more negative in the less aqueous solvent. Since some of the measurements were made in solvent containing about 0.1% extra water, all the measurements were corrected to a common basis. The corrections were small, and the error in the correction is probably negligible. The detailed data are available elsewhere.¹⁴

The rate of bromination of deoxybenzoin was followed by observing the disappearance of the specific absorbance of bromine and tribromide ion at their isosbestic point; in the presence of chloride ion, the isosbestic point for bromine and bromochloride ion was used. The needed data are presented in Table I.

TABLE I

ISOSBESTIC POINTS FOR BROMINE AND COMPLEX IONS

Solvent, wt. % AcOH	—Br ₂ —Br ₂ —		—Br ₂ —Br ₂ Cl—	
	λ , m μ	ϵ	λ , m μ	ϵ
97.9	450	119	429	152
91.0	448	122	429	150.5
79.9	448	117	429	147

The rate measurements usually were conducted with 0.0200 *M* deoxybenzoin and 0.002 *M* bromine. Thus all the bromine was consumed when only 10% of the deoxybenzoin had reacted, and the reaction therefore followed nearly perfect zero-order kinetics. The recorded first-order rate constants are the quotient of the observed zero-order rate divided by the concentration of deoxybenzoin. (Only in 97.9% acetic acid, with perchloric acid as catalyst, was a special situation encountered; there the strong catalytic influence of HBr made itself felt in autocatalysis.)

Most experiments were carried out in duplicate or triplicate; one set (used to standardize the solvents) was repeated six times. The spread between duplicates was seldom as great as 5%; the average deviation of the sextet was 1%.

Product.—The product of bromination was determined in 97.9% acetic acid after ten half-lives in the presence of HCl. The solvent was removed by evaporation under vacuum and a weighed sample of the residue dissolved in carbon disulfide. The infrared spectrum was virtually identical with that obtained with pure desyl bromide; none of the bands characteristic of either deoxybenzoin or α,α -dibromodeoxybenzoin appeared in the product, which was at least 98% pure. In other experiments, the rate of bromination of desyl bromide was determined; it is only about $1/200$ that of deoxybenzoin. Although the bromination of deoxybenzoin is promoted by strong illumination, no appreciable photochemical reaction occurred because of brief illumination in the spectrophotometer during measurements, or in the diffuse light of the laboratory while the solutions were prepared. The rate with a degassed sample under vacuum was the same as that obtained in ordinary runs.

Results

H_0 -Values.—The H_0 -values for the acids and acid-salt mixtures used are presented in Table II. These data are consistent with those found by others for aqueous acetic acid solutions.^{14,17,18}

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(13) M. A. Paul and F. A. Long, *Chem. Rev.*, **57**, 1 (1957).

(14) J. Roček, *Collection Czech. Chem. Commun.*, **22**, 1 (1957).

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(17) K. B. Wiberg and R. J. Evans, *J. Am. Chem. Soc.*, **80**, 3019 (1958).

(18) T. L. Smith and J. H. Elliott, *ibid.*, **75**, 3566 (1953).

TABLE II
 H_0 -VALUES FOR AQUEOUS ACETIC ACID SOLUTIONS

Acid	Mole/l.	Salt	Mole/l.	— H_0 in aqueous acetic acid		
				97.9% ^a	91.0%	79.9%
HClO ₄	0.100	1.44	0.02	-0.65
	.100	LiClO ₄	0.200	1.62	.20	-.48
	.300	2.22	.75	+.01
HBr	.020	0.61		
	.020	LiClO ₄	.080	.63		
	.02573		
	.025	LiClO ₄	.075	.75		
	.100	1.44		
HCl	.100	LiClO ₄	.100	1.47		
	.025	0.44		
	.025	LiCl	.075	.48		
	.025	LiClO ₄	.075	.58		
	.025	LiClO ₄	.275	.60		
	.100	1.12	0.03	-.65
	.100	LiClO ₄	.200	1.35	.18	-.51
.100	LiCl	.200		.16		
.30071	+.01	

^a Some measurements in 97.9% acetic acid corrected by 0.05 unit to allow for 0.1% error in water content; see Experimental.

Kinetics. (a) **Perchloric Acid.**—The results of a kinetic run with 0.100 *M* HClO₄, 0.0202 *M* deoxybenzoin, and 0.0020 *M* bromine in 97.9% acetic acid are shown in Fig. 1. Autocatalysis is clearly visible. Experiments showing that HBr is a much more powerful catalyst than perchloric acid suggest that the former is responsible for the observed autocatalysis. When the effect of HBr was taken into account, the corrected zero-order plot of Fig. 1 was obtained. The method of correction is given in the Appendix. Experiments in the presence of HBr or HCl gave excellent zero-order curves without correction; further, in 91.0% and 79.9% acetic acid, the autocatalysis was negligible, even with perchloric acid as catalyst.

The rates are first order in the concentration of deoxybenzoin over the range from 0.02 to 0.06 *M*, and each run was zero order in bromine. The data for 97.9% acetic acid are collected in Table III, those for 91.0% acetic acid in Table IV, and those for 79.9% acetic acid in Table V. The observed zero-order rates divided by the concentrations of deoxybenzoin are given as k_1 .

(b) **HBr and HCl.**—Inspection of the data in Table III shows that the order of the reaction in HCl and HBr is considerably greater than unity. Thus, at a constant formal ionic strength of 0.100 *M*, an increase in the concentration of HBr from 0.020 to 0.050 *M* increases the first-order rate constant from 7.12 to 33.3; an increase of the concentration of HBr to 0.100 *M* increases the rate constant to 126. In 79.9% and 91.0% acetic acid, the rates for hydrogen chloride and hydrogen bromide are larger than but comparable to that for perchloric acid; the specific effect of the halogen acids must be separated from their catalytic effect as acids.

The data here reported for the rate of bromination can be expressed by the equation

$$v = - (d(\text{Br}_2)/dt) = k_{\text{obs}} h_0(\text{deoxy}) = h_0(\text{deoxy}) [k_A + k_X(\text{MX})] \quad (3)$$

where k_A is the rate constant for perchloric acid and k_X is the specific catalytic constant for the halides present (*i.e.*, both HX and LiX). Figure 3 shows the data for 97.9% and 98.0% acetic acid; the numerical results for 91.0% and 79.9% acetic acid are presented in Tables VI and VII.

Solvent Isotope Effect.—The reaction catalyzed by 0.0367 *M* DCl in "97.9%" DOAc-D₂O proceeds about

TABLE III
KINETICS FOR THE BROMINATION OF DEOXYBENZON IN 97.9% ACETIC ACID

Acid	Mole/l.	Salt	Mole/l.	Remarks	$10^5 k_1$, sec. ⁻¹	h_0	$10^5 k_1/h_0$
HClO ₄	0.100				2.64	27.5	0.096
	.100	LiClO ₄	0.200		3.25	41.7	0.078
	.100	NaClO ₄	.200		3.14		
	.200	NaClO ₄	.100		7.56		
	.300				14.3	166	0.086
HBr	0.020			98.0% HOAc	23.2	4.58	5.06
	.020	LiClO ₄	0.080	98.0% HOAc	7.12	4.8	1.48
	.025			98.0% HOAc	26.7	6.03	4.4
	.025	LiClO ₄	0.075	98.0% HOAc	9.63	6.3	1.52
	.025			0.075 M HClO ₄ , 98.0% HOAc	37.3	31.0	1.20
	0.025	LiBr	0.075	98.0% HOAc	29.3	6.3	4.6
	.050	LiClO ₄	0.050	98.0% HOAc	34.5	14	2.43
	.100			98.0% HOAc	126	31.1	4.06
	.100				114	27.5	4.16
	.100	LiClO ₄	0.100	98.0% HOAc	80.9	32.7	2.47
	.100	LiClO ₄	0.200	98.0% HOAc	65.8	41.7	1.6
	.010			0.090 M HClO ₄ , 98.0% HOAc ^a	15.6	31.0	0.53
	HCl	0.0166	NaClO ₄	0.0834		2.53	
.0330		NaClO ₄	0.0668		8.72		
.0323					16.6		
.0330		LiClO ₄	0.0670		8.77		
.0330		LiCl	0.0670		19.5		
.0999					59.3		
.0250		LiClO ₄	0.0750		6.1	3.8	1.6
.0250		LiCl	.0250	0.050 LiClO ₄	10.5	3.5	3.0
.0250		LiCl	.0750		16.5	3.0	5.6
.050		LiCl	.050		34.2	6.3	5.4
.100				98.0% HOAc	70.5	13.7	5.13
.100					67.9	13.1	5.18
.100		LiClO ₄	0.200		35.3	22.4	1.62
.0367			DCl in DOAc - D ₂ O	57.8			

^a Set of three experiments, with initial concentrations of bromine of 0.00065, 0.0020, and 0.0086; average deviation 5%.

TABLE IV
KINETICS FOR THE BROMINATION OF DEOXYBENZON IN 91.0% ACETIC ACID

Acid	Mole/l.	Salt	Mole/l.	Remarks	$10^5 k_1$, sec. ⁻¹	h_0	$10^5 k_1/h_0$
HClO ₄	0.100				0.504	1.05	0.48
	.100	LiClO ₄	0.200		0.610	1.57	.39
	.300				1.87	5.60	.33
HCl	.0300	LiClO ₄	0.070		0.387		
	.0300	LiCl	0.070		9.767		
	.100				2.78	1.08	2.59
	.100	LiClO ₄	0.200		2.00	1.51	1.33
	.100	LiCl	0.200		4.44	1.46	3.04
	.100			0.200 M HClO ₄	6.70	5.5	1.2
	.300				15.1	5.13	2.95

TABLE V
KINETICS FOR THE BROMINATION OF DEOXYBENZON IN 79.9% ACETIC ACID

Acid	Mole/l.	Salt	Mole/l.	$10^5 k_1$, sec. ⁻¹	h_0	$10^5 k_1/h_0$
HClO ₄	0.100			0.240	0.225	1.07
	.100	LiClO ₄	0.160	.265		
	.100	LiClO ₄	0.200	.281	0.333	0.845
.300			.783	1.02	0.765	
HBr	.100			.278	0.226	1.23
HCl	.100			.333	.226	1.45
	.100	LiClO ₄	0.200	.368	.312	1.15
	.300			1.64	1.00	1.64

2.9 times as fast as the corresponding reaction (interpolated from the data of Table III) in HOAc-H₂O.

Salt Effects.—The data in Tables III, IV, and V show that the rate of the reaction catalyzed by perchloric acid increases with increasing salt concentration, but so

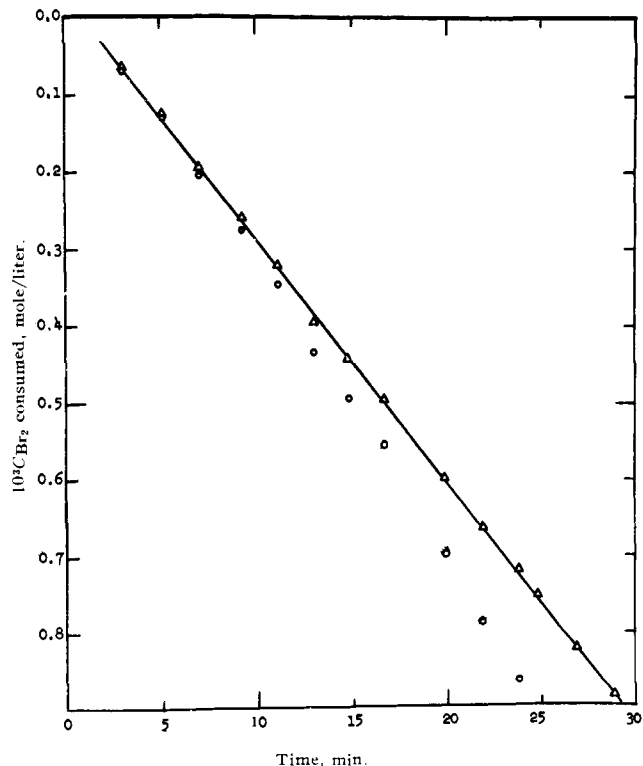


Fig. 1.—Bromination of deoxybenzoin in 97.9% acetic acid, catalyzed by perchloric acid. The observed points are shown by the open circles; the data corrected for autocatalysis (see Appendix) are represented by triangles and by the solid line.

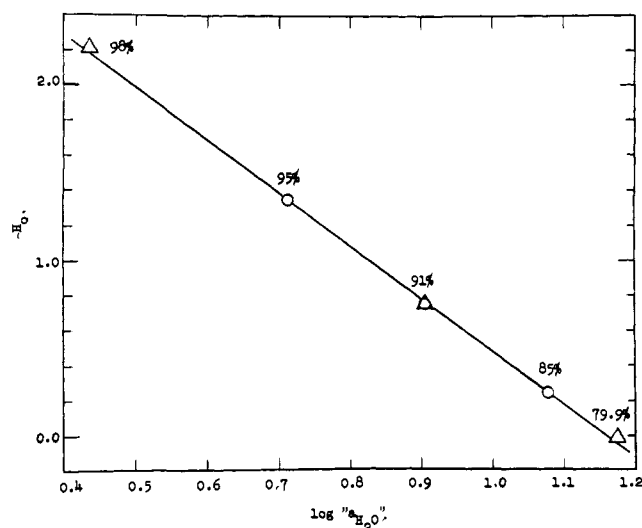


Fig. 2.—The dependence of $-H_0$ on the activity of water for 0.300 M $HClO_4$ in acetic acid-water mixtures. The circles are from the data of Wiberg and Evans, the triangles from our data,

TABLE VI

PARTIAL RATES IN 91% ACETIC ACID FOR BROMINATION
CATALYZED SPECIFICALLY BY HYDROGEN CHLORIDE

System	$10^3 h_0 k_X (MX)$	$10^3 k_X (MX)$	$10^3 k_X$
0.100 M HCl	2.30	2.13	21.3 ^a
.100 M HCl	1.41	0.93	9.3
.200 M $LiClO_4$			
.100 M HCl	3.96	2.72	9.1
.200 M $LiCl$			
.100 M HCl	4.88	0.89	8.9
.200 M $HClO_4$			
.300 M HCl	13.4	2.62	8.7

^a Formal ionic strength, 0.100 M .

TABLE VII

PARTIAL RATES IN 79.9% ACETIC ACID FOR BROMINATION
CATALYZED SPECIFICALLY BY HYDROGEN CHLORIDE

System	$10^3 h_0 k_X (MX)$	$10^3 k_X (MX)$	$10^3 k_X$
0.100 M HCl	0.093	0.41	4.1 ^a
.100 M HCl	.104	.33	3.3
.200 M $LiClO_4$			
.300 M HCl	.875	.88	2.9

^a Formal ionic strength, 0.100 M .

does h_0 , so that the quotient k/h_0 decreases slightly as salt is added. In sharp contrast, the rates in the presence of hydrochloric and hydrobromic acids are subject to a large negative salt effect; since salt increases the value of h_0 , the salt effect upon the quotient, k/h_0 , is even more pronounced. Thus the addition of 0.2 M lithium perchlorate to 0.100 M hydrogen chloride in 97.9% acetic acid decreases the quotient, $10^3 k/h_0$, from 5.13 to 1.62; the same change in 91.0% acid decreases the quotient from 2.59 to 1.33.

Discussion

H_0 Function.—As Wiberg and Evans have pointed out,¹⁷ the values of H_0 increase linearly with the concentration of perchloric acid, provided that a constant formal ionic strength is maintained. This applies to our data in 79.9% and 91.0% acetic acid, and approximately to our data in 97.9% acetic acid, as well as to their data in 85%, 91%, and 95% acetic acid.

Wiberg and Evans correlated their data with the molarity of water in the acetic acid solvent. Bascombe and Bell¹⁹ have suggested that H_0 should be correlated

(19) K. N. Bascombe and R. P. Bell, *Discussions Faraday Soc.*, **24**, 158 (1957); cf. P. A. H. Wyatt, *ibid.*, **24**, 162 (1957).

with the activity (rather than the molarity of water) and have offered the approximate equation

$$-H_0 = \log(H^+) - n \log a_{H_2O} + \log(f_1 f_{H^+} / f_{IH^+}) \quad (4)$$

where n is the average hydration number of the proton and f_1 and f_{IH^+} represent the activity coefficients of the Hammett indicator and its conjugate acid. Our data and those of Wiberg and Evans are plotted in Fig. 2 against the logarithm of the activity of water²⁰ in solutions of aqueous acetic acid. A good straight line of slope three is obtained, suggesting that the proton holds three more water molecules than the conjugate acids, IH^+ , of the indicator bases used in this study.

Mechanism of the Bromination Catalyzed by Perchloric Acid.—The rate of the bromination of deoxybenzoin, catalyzed by perchloric acid, is well correlated by the expression

$$v = k_{H_2O} h_0 (\text{deoxy})(H_2O) \quad (5)$$

TABLE VIII

KINETIC DATA FOR BROMINATION CATALYZED BY 0.100 M
PERCHLORIC ACID

Wt. % HOAc	$10^3 k_1$, sec. ⁻¹	$10^3 k_1 / h_0$	C_{H_2O} , moles/l. (in solvent)	$10^3 k_1 /$ (h_0)(C_{H_2O})
97.9	2.64	0.096	1.22	0.079
91.0	0.504	0.48	5.30	.091
79.9	0.240	1.07	11.88	.090

The data agree then with eq. 1 and 2, where B is a water molecule. The prior equilibrium should be fast, reversible, and unfavorable to protonation; the most acid solutions employed in this study had an H_0 value of -2 , whereas the pK of deoxybenzoin is unlikely to be very different from -6.15 , the value for acetophenone.²¹ The transition state and the starting materials each have one positive charge but the somewhat greater delocalization of the charge of the transition state should lead to a small negative salt effect, as observed for k_1/h_0 .

Nature of the Ionic Species in 79.9%–97.9% Acetic Acid.—Kolthoff and Willman²² concluded from conductivity measurements that perchloric acid is completely ionized to ion-pairs in glacial acetic acid and that these ion-pairs are slightly dissociated; hydrochloric acid is only slightly ionized in the anhydrous acid, but ionized and (like perchloric acid) partially dissociated in the presence of 1–2% water.

More recently, Wiberg and Evans¹⁷ measured the conductivity of sodium perchlorate in 91% and 95% acetic acid; treating their data by Shedlovsky's equation,²³ they found dissociation constants for the ion-pairs of 5.25×10^{-4} and 4.5×10^{-3} , respectively; the dissociation constant for the salt in 85% acetic acid is large. These are thermodynamic dissociation constants; in order to calculate concentrations, appropriate activity coefficients must be taken into account. Wiberg and Evans estimated, for example, that 0.0017 M sodium perchlorate is 73% dissociated in 95% acetic acid as solvent and almost completely dissociated in 91% acid, but of course the extent of dissociation will be much less at the concentrations here used. Their data, as well as those of others,^{18,24} suggest that even in solutions which are 0.01–0.3 M dissociation is extensive in 79.9% acetic acid as solvent

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and important in 91% acid, but the ion-pairs present in 98% acetic acid are not extensively dissociated.

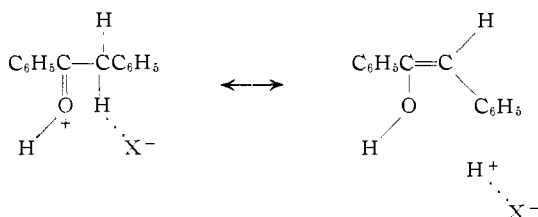
Mechanism of Bromination in the Presence of HCl and HBr.—The data for the bromination of deoxybenzoin show a catalytic role for HCl and HBr in 97.9%, 91.0%, and 79.9% acetic acid solutions, but the specific effect of the halogen acids decreases with increasing water content of the solvent. The rates are independent of the concentration of bromine and vary linearly with the concentration of deoxybenzoin, with h_0 , and with the stoichiometric concentration of halide present in the solution. The data correlated by eq. 3 and 5 lead to the catalytic constants presented in Table IX; see Fig. 3.

TABLE IX
CATALYTIC CONSTANTS FOR ACID-CATALYZED ENOLIZATION OF DEOXYBENZOIN

	$I,^a M$	Solvent, wt. % HOAc		
		79.9%	91.0%	97.9%
$10^5 k_{H_2O}$	0.1	0.090	0.091	0.08
	.3	0.068	0.068	0.067
$10^5 k_{Cl^-}$.1	4.1	21.3	58
	.3	3.1	9.0	15
$10^5 k_{Br^-}$.1	1.7	...	46 ^b

^a Formal ionic strength. ^b 98.0% HOAc.

These data are most simply explained by the scheme shown in eq. 1 and 2, where the base B is halide ion. The large negative salt effect is consistent with this formulation and with the transition state



Further, an increase in water content should diminish the basicity of halide ions and therefore their catalytic efficiency, in conformity with our observations. The finding that chloride and bromide ions participate as bases, but only in dry or nearly dry solvents, is consistent with previous knowledge.^{25, 26} In particular, Cromwell, Kevill, and their collaborators have shown that these ions, in solution in acetonitrile, function as bases in the dehydrohalogenation of 2-benzyl-2-bromo-4,4-dimethyl-1-tetralin, and of other ketones.²⁷ Catalysis by hydrogen bromide for the racemization of optically active ketones²⁸ in glacial acetic acid has also been observed. (Catalysis by the relatively basic fluoride ion²⁹ in enolization is of course well known.) Similar increase in the effective activity of cations with decreasing hydration accounts for the increase in the h_0 function¹⁹ and for the increase in the rate of mercuration of benzene³⁰ which accompanies a decrease in the activity of water.

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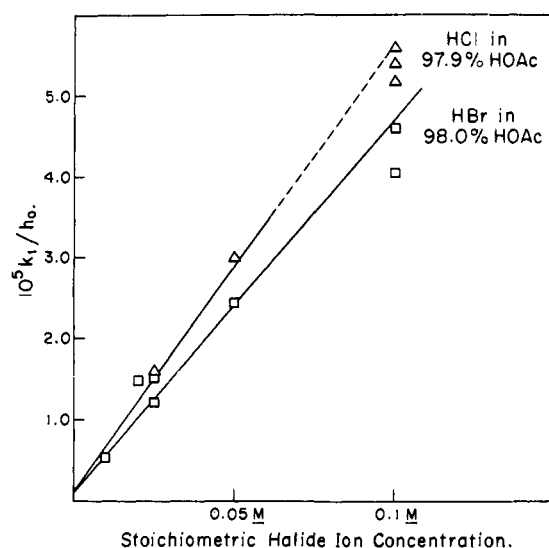


Fig. 3.—Dependence of k_1/h_0 on the stoichiometric concentration of halide ion for the bromination of deoxybenzoin catalyzed by HCl in 97.9% acetic acid or by HBr in 98.0% acetic acid, at a constant formal ionic strength of 0.1 M.

Furthermore, the solvent deuterium isotope effect is that to be anticipated when a proton is transferred to the substrate prior to the rate-limiting step; the ratio is consistent with that observed in aqueous solutions³¹ for the mechanism shown in eq. 1 and 2.

Although this mechanism has some plausibility for solutions in 79.9 and 91.0% acetic acid, it cannot be applied directly to solutions in 97.9% acetic acid, where both the halogen acids and salts are present largely as ion pairs. Furthermore, even the extent of ionic dissociation in solutions in 79.9% and 91.0% acetic acid has been extrapolated from the prior work of other investigators who operated under experimental conditions^{17, 22-24} somewhat different from ours. Therefore the possible roles of ion pairs, ion triplets, or even undissociated molecules of hydrogen halides have not yet been fully explored. Nevertheless, at least at the lower concentrations of acetic acid, where dissociated ions are presumably present in moderate concentrations,¹⁷ the mechanism of eq. 1 and 2 appears plausible, whereas an alternative explanation in terms of ion pairs is difficult to reconcile with the observed effects of salt, water, and deuterium oxide. A further investigation into the ionic composition of solutions of HBr and LiBr, etc., in 79.9, 91.0, and 98.7% acetic acid must precede any firm conclusions on mechanism. The extraordinary catalytic efficiency of the hydrogen halides is real, and at least in the more dilute acetic acid solutions may tentatively be assigned to general base catalysis by halide ions on protonated deoxybenzoin.

Appendix

Correction for Autocatalysis.—Integration of eq. 3 gives the expression

$$\frac{1}{k_A} \ln \left[1 + \frac{k_X}{k_A} (\text{Br}^-) \right] = h_0(\text{deoxy})t$$

The value of k_X/k_A estimated independently is about 500 l./mole. This value was used for the data plotted in Fig. 1.

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