ORGANIC AND BIOLOGICAL CHEMISTRY

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, GEORGIA INSTITUTE OF TECHNOLOGY]

Decarboxylation. III. The Kinetics and Mechanism of Bromodecarboxylation of 3,5-Dibromo-2-hydroxy- and 3,5-Dibromo-4-hydroxybenzoic Acids[1,2]

BY ERLING GROVENSTEIN, JR., AND U. V. HENDERSON, JR.

RECEIVED AUGUST 1, 1955

The kinetics of the bromination of 3,5-dibromo-2-hydroxy- and 3,5-dibromo-4-hydroxybenzoic acids and of the corresponding phenols, 2,4-dibromo- and 2,6-dibromophenol, have been studied in 70 to 80% acetic acid at 20°. At constant hydrogen ion and bromide ion concentrations, these compounds undergo bromination to give tribromophenol at a rate proportional to the stoichiometric concentration of the reactants. The apparent second-order rate constants ($k_{app.}$) so obtained, however, vary widely with hydrogen ion and bromide ion concentration. After correction for conversion by the bromide ion of much of the bromine to unreactive tribromide ion, the second-order rate constants, k^*, still diminish at constant ionic strength with increasing bromide ion concentration. This decrease is almost negligible for 2,6-dibromophenol. For 3,5-dibromo-4-hydroxybenzoic acid, on the other hand, k^* is almost inversely proportional to the bromide ion concentration at bromide ion concentrations of 0.04 M or greater. The bromide ion dependency of 3,5-dibromo-2-hydroxybenzoic acid falls in between these two extremes. These bromide ion, as well as the observed hydrogen ion, dependencies are explained on the basis of a mechanism involving attack of molecular bromine to give a reactive cyclohexadienone intermediate which is reverted in part to starting compound by bromide ion or loses carbon dioxide (or hydrogen ion in the case of the dibromophenols) to give tribromophenol. The reversion of the intermediate cyclohexadienone to starting compound is most evident for 3,5-dibromo-4-hydroxybenzoic acid and is slight or even negligible for 2,6-dibromophenol. It is pointed out that similar mechanisms can explain the kinetics of the iodination of phenol and aniline at iodide ion concentrations of 0.1 M or larger and thus that the effective iodinating agent here may be molecular iodine instead of those previously postulated (I^+, H_2OI^+, IOAc, etc.).

The stereochemistry and mechanism of the conversion of *cis*- and *trans*-cinnamic acid dibromides to β-bromostyrene has been reported earlier from this Laboratory.[2] These studies were concerned with the general process

$$RCH{=}CHCO_2H + Br_2 \longrightarrow RCHBrCHBrCO_2H \xrightarrow{\text{base}} RCH{=}CHBr + CO_2 + (HBr) \quad (1)$$

whose over-all result is the replacement of a carboxyl group by halogen. It seemed of interest to study the mechanism of the more nearly direct replacement of carboxyl by halogen

$$RCO_2H + Br_2 \longrightarrow RBr + CO_2 + HBr \quad (2)$$

We shall call this process "bromodecarboxylation."[3] In order to avoid the possible complication of formation of intermediate dibromides (see eq. 1), aromatic rather than olefinic carboxylic acids have been studied. In particular, 3,5-dibromo-2-hydroxy- and 3,5-dibromo-4-hydroxybenzoic acids were studied.

Salicylic acid has been reported[4-8] to react with bromine to form dibromosalicylic acid, which then may undergo replacement of carboxyl group by bromine to give tribromophenol, which finally may take up a fourth bromine atom to yield "tribromophenol bromide." Carbon dioxide is liberated quantitatively[6] during the bromodecarboxylation in water. *p*-Hydroxybenzoic acid behaves similarly on bromination[5,9] or iodination.[10] Rather analogous halodecarboxylations have been reported for *p*-aminobenzoic acid,[11-13] anthranilic acid,[14] pyrrole-α-carboxylic acids[15] and α-furoic acids.[16]

It may be concluded from these references that halodecarboxylation occurs readily with aromatic carboxylic acids if the carboxyl group is located on a position of an aromatic ring which is readily susceptible to attack by electrophilic reagents. In other words the halodecarboxylations under consideration appear to involve electrophilic aromatic substitutions of a carboxyl group by halogen. Furthermore, halodecarboxylations probably involve reaction of the ionized form of the acid since such decarboxylations are retarded by strong acid and proceed readily with alkali metal salts of the acid.[17] The present paper is concerned with the detailed mechanism of bromodecarboxylation as deduced from a kinetic study of 3,5-dibromo-2-hydroxy- and 3,5-dibromo-4-hydroxybenzoic acids in aqueous acetic acid.

(1) Abstracted in part from the Ph.D. thesis of U. V. Henderson, Jr, Georgia Institute of Technology, April, 1954.

(2) Papers I and II, E. Grovenstein, Jr., and D. E. Lee, THIS JOURNAL, **75**, 2639 (1953); E. Grovenstein, Jr., and S. P. Theophilou, *ibid.*, **77**, 3795 (1955).

(3) This name is in accord with the suggestions for systematic nomenclature of substitution reactions as proposed by J. F. Bunnett and reported by A. M. Patterson, *Chem. Eng. News*, **32**, 4019 (1954). An alternative name, which has sometimes been used to denote this reaction and also the Hunsdiecker silver salt reaction, is "brominative decarboxylation."

(4) M. A. Cahours, *Ann. chim. phys.*, [3] **13**, 87 (1845).

(5) R. Benedikt, *Ann.*, **199**, 127 (1879).

(6) I. M. Kolthoff, *Pharm. Weekblad*, **69**, 1159 (1932).

(7) L. H. Farinholt, A. P. Stuart and D. Twiss, THIS JOURNAL, **62**, 1237 (1940).

(8) (a) E. J. Smith, *Ber.*, **11**, 1225 (1878); (b) E. Lellmann and R. Grothman, *ibid.*, **17**, 2724 (1884); (c) W. Robertson, *J. Chem. Soc.*, **81**, 1475 (1902); (d) R. B. Earle and H. L. Jackson, THIS JOURNAL, **28**, 104 (1906).

(9) F. G. Pope and A. S. Wood, *J. Chem. Soc.*, **101**, 1823 (1912).

(10) P. Weselsky, *Ann.*, **174**, 99 (1874).

(11) F. Beilstein and P. Geitner, *ibid.*, **139**, 1 (1866).

(12) E. H. Wells, *J. Assoc. Offic. Agr. Chemists*, **25**, 537 (1942).

(13) H. L. Wheeler and L. M. Liddle, *Am. Chem. J.*, **42**, 441 (1909).

(14) H. L. Wheeler and C. O. Johns, *ibid.*, **43**, 398 (1910); F. Ullman and E. Kopetschni, *Ber.*, **44**, 425 (1911).

(15) Thus see A. H. Corwin, W. A. Bailey and P. Viohl, THIS JOURNAL, **64**, 1267 (1942); H. Fischer, P. Halbig and B. Walach, *Ann.*, **452**, 283 (1927).

(16) Thus see H. B. Hill and G. T. Hartshorn, *Ber.*, **18**, 448 (1885); H. Gilman, H. E. Mallory and G. F. Wright, THIS JOURNAL, **54**, 733 (1932); A. P. Dunlop and F. N. Peters, "The Furans," Reinhold Publishing Corp., New York, N. Y., 1953, pp. 84, 116-121.

(17) The reaction of bromine with a wide variety of sodium salts of carboxylic acids has been investigated recently from the standpoint of structural requirements by C. C. Price and J. D. Berman, *Am. Chem. Soc. Abst.*, Cincinnati, March, 1955, p. 12 N.

Experimental Details[18]

Reagents.—Acetic acid (du Pont C.P. glacial grade) was purified by refluxing over chromium trioxide according to the method of Bradfield and Orton[19] and then was distilled through a three foot, $1^3/_8$ in. bore column packed with $^3/_{16}$ in. glass helices. The fraction boiling at 116–117° was collected and was analyzed for water content by titration with Karl Fischer reagent.[20] Acetic acid prepared by this method contained less than 1% water and the amount of water was known to within 0.01%. The composition of acetic acid–water mixtures is always expressed in terms of percentage by weight.

Six hundred milliliters of Baker analyzed C.P. bromine was refluxed for three hours over 60 g. of potassium bromide. The mixture was fractionally distilled and the middle cut boiling at 57–58° was used in the kinetic runs.[21]

2,4-Dibromophenol (Eastman Kodak Co., white label, m.p. 32.5–36°) was recrystallized twice from chloroform at −40° to give a product of m.p. 36.2–37° (recorded[22] m.p. 40°). 2,6-Dibromophenol (Eastman Kodak Co., white label) was distilled at 18 mm. pressure and recrystallized from cold chloroform to give a product of m.p. 56–57° which agrees with that recorded.[22] *p*-Hydroxybenzoic acid and salicylic acid were from Matheson and Eastman Kodak Co. and were recrystallized from water before use.

Hydrobromic acid solutions were prepared from Matheson C.P. anhydrous hydrogen bromide; the concentration was determined by titration with standard barium hydroxide solution and this titration was checked in several instances by titration for bromide ion with standard silver nitrate solution with eosin as indicator. Lithium bromide solutions were prepared from Coleman and Bell C.P. lithium bromide and assayed by titration with standard silver nitrate solution. Baker and Adamson Reagent potassium dichromate, which was used as primary standard for assaying the sodium thiosulfate solutions, was recrystallized from hot water and dried *in vacuo* at 156°. Other reagents were C.P. or Reagent Grade and were used without further purification.

3,5-Dibromo-2-hydroxybenzoic Acid.—This compound was prepared by bromination of salicylic acid in glacial acetic acid according to the procedure of Earle and Jackson[8d] and was twice recrystallized from glacial acetic acid. Thirty grams of the product was refluxed for four hours in 1500 ml. of 1 *N* potassium hydroxide to saponify any esters which might have been formed in the bromination step. The mixture was neutralized with 200 ml. of 85% phosphoric acid and filtered while hot. The precipitate was washed several times with water, sucked dry, and then shaken successively with 100-ml. and 50-ml. portions of *n*-pentane to extract any phenols present. The dried product was suspended in 300 ml. of water and titrated to a phenolphthalein end-point with a *ca.* 0.1 *N* solution of barium hydroxide. The new solid formed in this process was indicated by the titer of base to be the barium salt formed by neutralization of one acidic hydrogen per molecule of dibromosalicylic acid. The barium salt was filtered, washed with water, then decomposed by triturating with 120 ml. of 2 *N* hydrochloric acid. The dibromosalicylic acid so obtained was filtered, washed three times with water, dried in air, recrystallized from acetonitrile and finally dried *in vacuo* at 56° to give a product of m.p. 228–230° (m.p. recorded[23] 228°).

3,5-Dibromo-4-hydroxybenzoic Acid.—This compound was prepared by bromination of *p*-hydroxybenzoic acid according to the procedure used above for 3,5-dibromo-2-hydroxybenzoic acid. The product after one recrystallization from glacial acetic acid was obtained in 55% yield and had m.p. 275–276° (m.p. recorded[24] 267–268°). The product was subjected to about the same purification procedure as used above for 3,5-dibromo-2-hydroxybenzoic acid except that the barium salt formed from neutralization of both acidic hydrogen atoms of the *p*-hydroxy acid was water soluble and was precipitated by addition of ethanol. A final addition crystallization from chloroform gave a product which still had m.p. 275–276°.

Anal.[25] Calcd. for $C_7H_4O_3Br_2$: Br, 54.0. Found: Br, 54.3.

Kinetic Measurements.—A stock solution of solvent of the desired water–acetic acid composition (reported on the basis of the percentage by weight of acetic acid present) was prepared so as to contain the required concentration of electrolytes. With this solvent 250 ml. of solution of the compound being brominated was prepared in the desired concentration (0.0025–0.0125 *M*) and either 20.0 or 40.0 ml. of the solution was placed in each of a number of 50-ml. or 100-ml. red, low actinic, volumetric flasks fitted with ground glass stoppers. A like volume of the solvent was also placed in each of several volumetric flasks to serve as blanks. A bromine solution was prepared by adding a few tenths of a milliliter of bromine to 100 ml. of the solvent. All solutions were kept at the temperature of the water-bath which was 20.0 ± 0.1°. The reaction was started by pipetting at a noted time 5.0 or 10.0 ml. of the bromine solution into each of the prepared flasks so as to make, respectively, 25.0 or 50.0 ml. of reaction mixture. The reaction was stopped at the desired time by injecting with a syringe 4 ml. of 1 *N* potassium iodide solution followed by 10 ml. of 4 *N* potassium hydroxide (to decrease the acidity of the solution and help prevent air oxidation of iodide ion). The solution was rinsed into 10 ml. of water and the iodine equivalent of the unreacted bromine was determined by titration with standard sodium thiosulfate solution to visual disappearance of the iodine color. It seemed possible that the iodine (or triiodide ion) formed in stopping the reaction might itself continue to react with the remaining dibromohydroxybenzoic acid in the solution. This was proved to be unimportant since titers upon runs with dibromo-*p*-hydroxybenzoic acid, in which the reaction mixture after addition of potassium iodide and sodium hydroxide was allowed to stand for 20 to 30 min. before titration, were not appreciably different from those which were run similarly but were titrated immediately (within 1 to 2 min.) after stopping the reaction.

Apparent second-order rate constants (k_{app}) were calculated from each point by use of the integrated rate equation

$$k_{app} = \frac{2.303}{(b - a)t} \log \frac{a(b - x)}{b(a - x)}$$

where k_{app} is expressed in units of liter mole^{-1} second^{-1}, a is the initial molar concentration of substrate being brominated, b is the initial molar concentration of bromine (stoichiometric concentration as determined by thiosulfate titration), and x is the molar concentration of substance reacted (or product formed) at time t.

Bromination Products.—In preliminary experiments upon bromination of dibromosalicylic acid in 40% by volume dioxane in a chloroacetic acid buffer at *p*H 3.4, "tribromophenol bromide"[6,26] was obtained as a light yellow precipitate. Tribromophenol upon bromination under similar conditions gave the same product. In the same solvent but 0.1 *N* in perchloric acid, tribromophenol bromide formation was greatly retarded and 50% yield of tribromophenol was obtained (by isolation) upon bromination of dibromosalicylic acid with excess of bromine. No evidence for tribromophenol bromide formation was obtained during the present brominations conducted in aqueous acetic acid as solvent with hydrobromic or perchloric acid concentrations as low as 0.05 *M*. Infinity titers upon bromine consumption indicate that dibromosalicylic acid and dibromo-*p*-hydroxybenzoic acid react with exactly one molar equivalent of bromine under the conditions of the present kinetics. Thus dibromosalicylic acid (in 70.0% HOAc, 0.300 *M* in HBr) gave 99.6% of this theoretical amount of

(18) All melting points and boiling points are uncorrected unless otherwise specified.

(19) K. J. P. Orton and A. E. Bradfield, *J. Chem. Soc.*, 960 (1924).

(20) J. Mitchell, Jr., and D. M. Smith, "Aquametry," Interscience Publishers, Inc., New York, N. Y., 1948.

(21) *Cf.* H. G. Kuivila and E. K. Esterbrook, THIS JOURNAL, **73**, 4629 (1951).

(22) I. M. Heilbron and H. M. Bunbury, "Dictionary of Organic Compounds," Oxford University Press, New York, N. Y., 1943, Vol. I, p. 713.

(23) Reference 22, p. 720.

(24) Reference 22, p. 700.

(25) Analysis by Clark Microanalytical Laboratory, Urbana, Ill.

(26) For some recent discussions of the structure of such compounds see (a) L. C. Raiford and A. L. LeRosen, THIS JOURNAL, **68**, 397 (1946); (b) G. Wittig and F. Vidal, *Ber.*, **81**, 368 (1948); (c) C. H. R. Elston, A. T. Peters and F. M. Rowe, *J. Chem. Soc.*, 367 (1948); (d) L. E. Forman and W. C. Sears, THIS JOURNAL, **76**, 4977 (1954); (e) J. A. Price, *ibid.*, **77**, 5136 (1955).

bromine consumption in 256 hours and nine runs upon dibromo-*p*-hydroxybenzoic acid (in 80% acetic acid, 0.1 or 0.3 *M* in HBr) gave infinity titers which averaged 99.8 ± 0.5% of this theoretical consumption of bromine.

The amount of carbon dioxide evolved during the bromination of dibromo-*p*-hydroxybenzoic acid in 80.2% acetic acid, which was 0.10 *M* in both perchloric acid and lithium bromide, was determined by measuring the volume of carbon dioxide evolved from the well shaken solution which had been saturated with carbon dioxide before breaking a capsule of bromine in the solution. Two such experiments indicated that about 97% of the theoretical amount of carbon dioxide was evolved.

Finally tribromophenol was isolated in 23% yield from dibromosalicylic acid under similar conditions of concentration as in the kinetic runs (75% acetic acid, 0.100 *M* HBr, 0.200 *M* LiBr) but at *ca.* 40° and similarly in 55% yield from dibromo-*p*-hydroxybenzoic acid (80% acetic acid, 0.300 *M* HBr).

Equilibrium Constant for Tribromide Ion Formation.—The equilibrium constant K_1 for the reaction $Br_2 + Br^- = Br_3^-$, as defined by

$$K_1 = [Br_3^-]/[Br_2][Br^-] \quad (3)$$

where K_1 is expressed in liters/mole, was determined by the general method of Popov, *et al.*,[27] with use of a model DU Beckman quartz spectrophotometer thermostated at 20°. The solutions were contained in ground-glass stoppered Corex cells of 1.000 ± 0.001 cm. optical path length. All solutions were made up to an ionic strength of 0.300 by addition of appropriate amounts of perchloric and hydrobromic acids. The bromine concentration of the solutions was determined by titration as described in the kinetic measurements. The molar absorbancy indices[28] in the solvents 70.0, 75.0 and 80.0% acetic acid were within experimental error not measurably different over this range of solvent composition and the average values of these indices are recorded in Table I.

TABLE I

MOLAR ABSORBANCY INDICES FOR BROMINE AND TRIBROMIDE ION IN 70–80% ACETIC ACID AT 20°

λ, mμ	Bromine a_M	Tribromide ion a_M
360	106	966
380	165	755
400	179	556
420	159	309

The absorbancy index of bromine in these 0.300 *M* perchloric acid solutions is essentially the same as that reported[29] at 400 mμ in glacial acetic acid. Furthermore the absorptivity of bromine in 80% acetic acid, 0.300 *M* in lithium bromide, is indistinguishable from that in the same solvent 0.300 *M* in hydrobromic acid. These results show that the bromine spectrum, while dependent upon bromide ion concentration, is relatively independent of the concentration of strong acids. This fact argues against the presence of appreciable amounts of any bromine species whose concentration is acid dependent.

From the data at each of the four wave lengths shown in Table I and from the absorbance of solutions 0.003–0.005 *M* in bromine, 0.0010 to 0.0015 *M* in hydrogen bromide, and containing enough perchloric acid to make the solutions 0.300 *M* in strong acid, the equilibrium constant (expressed in terms of concentration) for tribromide ion formation was calculated to be 84 in 70.0%, 88 in 75.0%, and 92 l./mole in 80.0% acetic acid, with an average deviation of the individual values from these mean values of ±6%. The value obtained in 75% acetic acid may be compared with the value of 91 ± 3 reported[30] in the same solvent at about 0.01–0.02 ionic strength by an aspiration technique.

(27) A. I. Popov, K. C. Brinker, L. Campanaro and R. W. Rinehart, THIS JOURNAL, **73**, 514 (1951).

(28) For spectrometric nomenclature and definition of terms see National Bureau of Standards, Letter-Circular LC-857 (1947).

(29) R. E. Buckles and J. F. Mills, THIS JOURNAL, **75**, 552 (1953).

(30) A. E. Bradfield, G. I. Davies and E. Long, *J. Chem. Soc.*, 1389 (1949).

Results

Preliminary experiments of Table II—runs 1 and 2 for dibromosalicylic acid; runs 8, 9, 13 and 14 for dibromo-*p*-hydroxybenzoic acid—indicated that for comparisons at equal hydrogen and bromide concentrations the bromodecarboxylations were first order in both the stoichiometric concentration of bromine and that of the dibromocarboxylic acid.

TABLE II

KINETIC DATA FOR BROMODECARBOXYLATION AT 20.0°

Run	Solvent, wt. % HO-Ac	10^3 (Ar-H_2)$_0$, moles/l.	10^3 (Br_2)$_0$, moles/l.	(HCl-O_4)$_0$, mole/l.	(HBr)$_0$, mole/l.	(LiBr)$_0$, mole/l.	$10^2 k_{app}$, l./mole sec.
			ArH_2 = 3,5-Dibromo-2-hydroxybenzoic acid				
1	75.0	5.01	3.76	0.100			5.8[a]
2	75.0	5.01	7.50	.100			5.8
3	75.0	5.01	7.44	.100		0.0042[c]	4.7
4	75.0	5.08	4.86	.100		.0040[d]	5.6
5	75.2	5.03	3.93	.100		.102	0.49
			ArH_2 = 3,5-Dibromo-4-hydroxybenzoic acid				
6	75.0	5.00	5.79	0.100			200
7	80.0	5.01	5.82	.100			63
8	80.2	4.97	4.17	.100		0.103	1.29
9	80.2	5.05	8.12	.100		.102	1.31
10	80.2	6.69	5.57	.100		.095	1.52
11	80.2	4.61	7.87	.050		.104	3.4
12	80.0	4.91	8.02		0.107		0.72 ± 0.05[b]
13	80.0	5.18	8.05		.222		.064 ± .001[b]
14	80.0	8.93	5.10		.2225		.061 ± .001[b]
15	80.0	4.46	8.14		.200	.100[c]	.060 ± .001[b]

[a] The values of k_{app} are initial rate constants (obtained by extrapolation) unless otherwise specified. [b] Average value of k_{app} and mean deviation. [c] KBr rather than LiBr. [d] $KClO_4$ rather than LiBr.

Hence apparent second-order rate constants (k_{app}) were calculated on this basis. These constants are highly dependent upon the hydrogen and bromide ion concentrations as is shown by the exploratory runs of Table II and by the more detailed experiments of Table III, which latter were all performed at ionic strength of 0.300. In view of this depend-

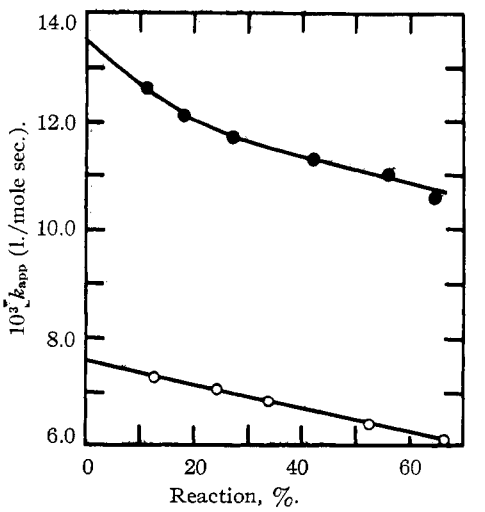


Fig. 1.—Integrated second-order rate constants *vs.* percentage reaction for 3,5-dibromo-2-hydroxybenzoic acid (●) in 75.0% acetic acid, $(HBr)_0 = 0.0100$ *M*, $(HClO_4) = 0.290$ *M*; 3,5-dibromo-4-hydroxybenzoic acid (○) in 80.0% acetic acid, $(HBr)_0 = 0.050$ *M*, $(HClO_4) = 0.250$ *M*.

TABLE III

KINETIC DATA FOR BROMODECARBOXYLATION AT 20.0°, $(ArH_2)_0 \cong 0.005$ M, $\mu = 0.300$

$10^4(Br_2)_0$, moles/l.	$(HClO_4)_0$, mole/l.	$(HBr)_0$, mole/l.	$(LiBr)_0$, mole/l.	$10^3[Br_3^-]_0$, moles/l.	10^3k_{app}, l./mole sec.	$10^4k'$, (moles/l.)^2 sec.$^{-1}$	10^2k^*, l./mole sec.
3,5-Dibromo-2-hydroxybenzoic acid in 75.0% acetic acid							
7.94	0.300				25.5[a]		2.55
7.93	.290	0.0100		3.02	13.5[a]	0.137	2.18
8.00	.250	.0500		6.34	3.47[a]	0.66	1.68
7.97	.200	.100		7.10	1.37[a]	1.05	1.25
7.95	.100	.200		7.50	0.440 ± 0.002[b]	1.37	0.79
8.37		.300		8.05	.233 ± .008	1.64	0.62
7.96		.200	0.100	7.67	.428 ± .003	1.34	1.14
7.90		.100	.200	7.60	1.15 ± .02	0.90	3.07
8.12		.300			1.18 ± .02[c]		
7.87		.300			0.0293 ± .0003[d]		
3,5-Dibromo-4-hydroxybenzoic acid in 80.0% acetic acid							
8.19	0.300			(0.42)[e]	300[a]	(0.16)[e]	30
8.13	.250	0.050		6.50	7.6[a]	1.49	3.80
8.17	.200	.100		7.31	1.82 ± 0.03[b]	1.45	1.73
8.24	.100	.200		7.80	0.50 ± .01	1.60	0.92
8.06		.300		7.78	.222 ± .003	1.62	0.62
8.25		.200	0.100	7.96	.52 ± .01	1.70	1.45
8.12		.100	.200	7.82	2.00 ± .04	1.63	5.58
8.16		.050	.250	7.86	6.9 ± .2	1.40	19.2
8.04		.300			1.97 ± .04[f]		
7.51		.300			11.6 ± .1[c]		

[a] Initial rate constant (extrapolated). [b] Average value of k_{app} and mean deviation. [c] In 70.0% acetic acid. [d] In 80.0% acetic acid. [e] Calculated on the basis of an assumed stoichiometric concentration of Br^- of 0.0010 M. [f] In 75.0% acetic acid.

ence, the individual apparent second-order rate constants calculated for each run generally decreased with time since hydrogen bromide is formed as a product of the bromodecarboxylations as shown by equation 2. This decrease was, to be sure, largest for those reactions with small initial hydrogen or bromide ion concentrations and was almost negligible when both of these concentrations were 0.3 M. When the fall in k_{app} was 8% or less (from 0 to 70% reaction) during a run, the individual values of k_{app} were averaged (thus see Table IV); in other cases the values of k_{app} were obtained by extrapolation of the individual values of k to zero percentage reaction (thus see Fig. 1).

TABLE IV

KINETICS OF BROMODECARBOXYLATION OF 3,5-DIBROMO-4-HYDROXYBENZOIC ACID IN 80% ACETIC ACID AT 20.0°

$(ArH_2)_0 = 0.005128$ M, $(Br_2)_0 = 0.008240$ M, $(HBr)_0 = 0.200$ M, $(HClO_4)_0 = 0.100$ M; 50.0 ml. of reaction mixture titrated with 0.02185 M $Na_2S_2O_3$

Time × 10^{-3}, sec.	Titer, ml.	$k_{app} \times 10^3$, l./mole sec.	Reaction, %
0	37.71		0
25.32	35.41	0.511	9.8
76.14	31.92	.492	24.7
175.3	27.28	.484	44.4
263.9	24.36	.492	56.9
360.8	21.82	.520	67.6
446.6	21.00	.474	71.2
		Av. .496 ± 0.014	

For the sake of comparison, the kinetics of the bromination of 2,6-dibromophenol was studied as recorded in Table V, in which also are recorded a few runs upon 2,4-dibromophenol.

TABLE V

KINETIC DATA FOR BROMODEPROTONATION AT 20.0°

$10^3(Br_2)_0$, moles/l.	$(HClO_4)_0$, mole/l.	$(HBr)_0$, mole/l.	$(LiBr)_0$, mole/l.	$10^3[Br_3^-]_0$, moles/l.	k_{app}, l./mole sec.	k^*, l./mole sec.
2,6-Dibromophenol, $(ArOH)_0 \cong 0.0025$ M, in 80.0% Acetic Acid $\mu = 0.300$						
3.71	0.200	0.100		3.34	0.513 ± 0.004[a]	5.08
3.75	.100	.200		3.56	.244 ± .001	4.66
4.06		.300		3.92	.160 ± .003	4.52
3.73		.200	0.100	3.60	.199 ± .003	5.61
7.98		.150	.150	7.70	.232 ± .003	6.48
3.69		.100	.200	3.56	.302 ± .008	8.53
2,4-Dibromophenol, $(ArOH)_0 \cong 0.005$ M						
3.77	0.100		0.100		0.53[b,c]	
7.47	.100		.137		.24[b,d]	

[a] Average value of k_{app} and mean deviation. [b] Initial rate constant (extrapolated). [c] In 72.2% acetic acid. [d] In 80.2% acetic acid.

Discussion

3,5-Dibromo-4-hydroxybenzoic Acid.—This acid underwent bromodecarboxylation at a rate such that k_{app} was approximately inversely proportional to both the square of the bromide ion and the square of the hydrogen ion concentrations[31] over the range of about 0.05 to 0.3 M in each ion. This is illustrated by the near constancy of k' of Table III, where

$$k' = k_{app} K_1[Br^-]^2(Br_2)[H^+]^2/[Br_3^-] \quad (4)$$

In this equation as elsewhere in this paper the entities enclosed in brackets refer to the actual concentration of the species shown, while those in pa-

(31) It is assumed throughout the present work that the hydrogen ion concentration is equal to the sum of the molar concentrations of HBr and $HClO_4$ and thus that any contribution of the acetic acid to the hydrogen ion concentration is negligible for these solutions which were always at least 0.05 M in mineral acid.

rentheses refer to the stoichiometric concentration of a material, in this case the concentration of bromine as determined by thiosulfate titration. In view of the magnitude of the bromine–tribromide ion equilibrium constant, K_1, as defined by equation 3, 80% or more of the bromine is present as tribromide ion under the present conditions. The term $K_1[Br^-](Br_2)/[Br_3^-]$ is accordingly used in equation 4 to correct k_{app} for bromine which has been converted to unreactive[32] tribromide ion, in other words

$$\text{rate} = k'[Br_2](ArH_2)/[Br^-][H^+]^2 \quad (5)$$

where (ArH_2) is the stoichiometric concentration of dibromo-*p*-hydroxybenzoic acid. The inverse squared hydrogen ion dependence and the inverse bromide ion dependence imply that the transition state complex of the rate-determining step has two less protons and one less bromide ion under the reaction conditions specified than do the assumed reactants. One possible mechanism fulfilling these requirements is (mechanism I)

$$Br_2 + H_2O \underset{}{\overset{K_2}{\rightleftharpoons}} H_2OBr^+ + Br^- \quad (6)$$

$$[H_2OBr^+] = K_2[Br_2]/[Br^-] \quad (6')$$

$$ArH_2 \overset{K_3}{\rightleftharpoons} Ar^{--} + 2H^+ \quad (7)$$

$$[Ar^{--}] = K_3[ArH_2]/[H^+]^2 \quad (7')$$

$$\text{rate} = k''[H_2OBr^+][Ar^{--}] \quad (8)$$

Then from substitution of (6′) and (7′) into (8)

$$\text{rate} = k''K_2K_3[Br_2][ArH_2]/[Br^-][H^+]^2 = k'[Br_2][ArH_2]/[Br^-][H^+]^2 \quad (9)$$

Since in a medium as acidic as the present the concentration of un-ionized dibromo-*p*-hydroxybenzoic acid must be equal essentially to the stoichiometric concentration of this acid, then mechanism I leads to a kinetic result (equation 9) identical with that found (equation 5). It should be noted that somewhat different brominating agents, Br^+ and $CH_3CO_2HBr^+$ (from acetolysis rather than hydrolysis of bromine) or any combination of these and hypobromous acidium ion (H_2OBr^+), lead also to the observed kinetic result. Finally the present kinetics cannot distinguish between protons having been lost from the brominating agent or from the dibromo-*p*-hydroxybenzoic acid. Thus the observed kinetics are also in agreement with a rate-determining interaction between hypobromous acid and mono-ionized dibromo-*p*-hydroxybenzoic acid or between hypobromite ion and un-ionized dibromo-*p*-hydroxybenzoic acid. The former of these possibilities seems improbable under our conditions of acidity on the basis of studies upon the bromination of substances which cannot undergo complicating ionizations.[32,33] These studies indicate that hypobromous acidium ion (or brominium ion, Br^+) is a much more reactive brominating agent than hypobromous acid and on general evidence hypobromite ion should be even less reactive than hypobromous acid.[34]

While the kinetics of the bromodecarboxylation of dibromo-*p*-hydroxybenzoic acid fit equation 4 or 5 moderately well in the range of bromide and hydrogen ion concentrations of 0.04 to 0.3 *M*, the computed values of k' show some tendency to diminish (by as much as some 15%) toward the lower limits of these concentrations. Moreover when no bromide ion was initially added to the reaction mixture the estimated value of k' was no more than about a tenth of the values previously calculated. This estimation involves an assumption as to what the effective concentration of bromide ion was corresponding to the value of k_{app}, here obtained by extrapolation back to zero per cent. reaction. To the extent that this extrapolation is accurate, the correct value to use for the bromide ion concentration is to be computed from the solvolysis constant of bromine. From the hydrolysis constant of bromine,[35] the bromide ion concentration may be computed to be 10^{-5} *M* for water as solvent; a lower value doubtless is attained in 80% acetic acid. As a much more conservative estimate a value of 10^{-3} *M* was used here for the stoichiometric bromide ion concentration in the calculation of k' (Table III); this bromide ion concentration corresponds to the bromide formed by 25% reaction and thus should lead to an estimate of a maximum value for k'.

That this value of k' is considerably smaller than the values calculated at higher bromide concentrations leads to the conclusion that mechanism I, in any of its modifications mentioned above, is basically incorrect. This view is substantiated by the fact that in previous brominations in water or in aqueous acetic acid in which molecular bromine was used as the brominating agent, the kinetic evidence has been that the effective brominating agent was Br_2,[33,36] sometimes accompanied by $(Br_2)_2$.[37] These previous brominations, it is true, involved electrophilic substitution of bromine for hydrogen rather than carboxyl, but it is difficult to see why the relative order of activity of brominating agents should vary greatly with the nature of the displaced group (barring steric effects) provided that aromatic halogenation follows the general pattern of nitration,[38] namely, that the entering group has become more or less fully bonded before the bonding of the old group is substantially broken. Further discussion of the mechanism of bromodecarboxylation of dibromo-*p*-hydroxybenzoic acid is deferred until after a discussion of 2,6-dibromophenol and dibromosalicylic acid.

2,6-Dibromophenol.—In order to compare more fully the mechanism of bromodecarboxylation with that of bromodeprotonation, the kinetics of the bromination of 2,6-dibromophenol has been studied

(32) Thus see D. H. Derbyshire and W. A. Waters, *J. Chem. Soc.*, 564 (1950).

(33) W. J. Wilson and F. G. Soper, *ibid.*, 3376 (1949); E. Shilov and N. Kanyaev, *Compt. rend. acad. sci. U.R.S.S.*, **24**, 890 (1939); *Chem. Abst.*, **34**, 4062(1940); S. J. Branch and B. Jones, *J. Chem. Soc.*, 2317 (1954).

(34) For a general survey of aromatic electrophilic halogenation see C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, Ithaca, N. Y., 1953, pp. 288–295.

(35) H. A. Liebhafsky, THIS JOURNAL, **56**, 1500 (1934).

(36) A. E. Bradfield, B. Jones and K. J. P. Orton, *J. Chem. Soc.*, 2810 (1929).

(37) A. E. Bradfield, G. I. Davies and E. Long, *ibid.*, 1389 (1949); P. W. Robertson, P. B. D. de la Mare and W. T. G. Johnston, *ibid.*, 276 (1943).

(38) See ref. 34, pp. 279–281.

under the same general conditions as those used for 3,5-dibromo-4-hydroxybenzoic acid. The available data are given in Table V. The apparent second-order rate constant (k_{app}) can be corrected for bromine which has been converted to tribromide ion by the relation

$$k_{app}K_1(Br_2)[Br^-]/[Br_3^-] \equiv k^* \qquad (10)$$

At constant hydrogen ion concentration, the values of k^* are constant within 11% over a threefold variation of bromide ion concentration as can be seen from the table. This bromide ion dependence indicates that molecular bromine (Br_2) is the effective brominating agent. Such variation as exists in k^* here may be the result of specific salt effects; an alternative interpretation will be given later.

A plot (Fig. 2) of k^* at constant bromide ion concentration *versus* the reciprocal of the hydrogen ion concentration reveals a linear relationship with k^* increasing as the hydrogen ion concentration decreases. The data therefore fairly closely fit the relationship

$$k_{app}K_1(Br_2)[Br^-]/[Br_3^-] = k_0 + k_-/[H^+] = k^* \qquad (11a)$$

or

$$\text{rate} = k_{app}(ArOH)(Br_2) = \{k_0(ArOH) + k_-(ArOH)/[H^+]\}[Br_3^-]/K_1[Br^-] \qquad (11b)$$

where (ArOH) is the concentration of the 2,6-dibromophenol, k_0 equals 2.5 l./mole sec., and k_- equals 0.60 sec.$^{-1}$. Since the term $[Br_3^-]/K_1[Br^-]$ equals the concentration of bromine, equation (11b) corresponds to the expected kinetic equation for the attack of molecular bromine upon ionized and unionized 2,6-dibromophenol (mechanism II).

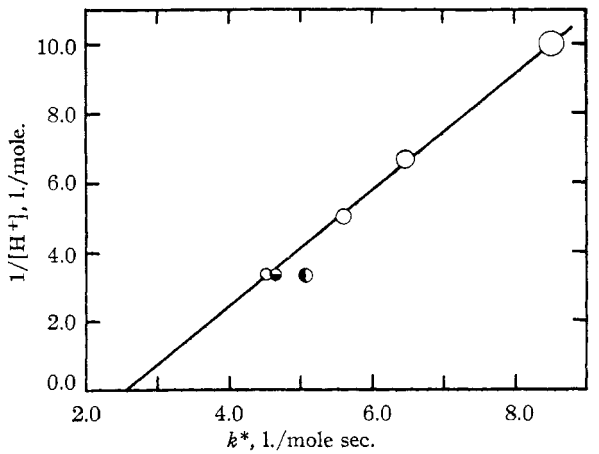


Fig. 2.—Variation of k^* with $1/[H^+]$ for 2,6-dibromophenol at $[Br^-]$ equal 0.292–0.296 M (○), 0.196 M (◒), and 0.097 M (◐). Points drawn with radius equal 2% of k^*.

2,6-Dibromophenol undergoes bromination in 80% acetic acid to give an apparent second-order rate constant which is some 150 to over 700 times greater than that of dibromo-*p*-hydroxybenzoic acid under identical conditions of hydrogen and bromide ion concentrations as can be seen by comparison of the values of k_{app} in Tables III and V. The rate of bromination of the phenol relative to the acid increases as the concentration of hydrogen and bromide ions increases. These data clearly eliminate the possibility that the bromodecarboxylation of dibromo-*p*-hydroxybenzoic acid proceeds by way of a fast, presumably acid-catalyzed, protodecarboxylation to give 2,6-dibromophenol followed by a rate-determining bromination of the latter. Such a mechanism would demand that the rate of the apparent bromodecarboxylation be the same as the rate of bromination of 2,6-dibromophenol. The possibility of a slow rate-determining protodecarboxylation of dibromo-*p*-hydroxybenzoic acid followed by a fast bromination of the resulting phenol is, of course, eliminated by the kinetic dependence upon bromine concentration shown by the acid. Similar considerations hold for the bromodecarboxylation of 3,5-dibromo-2-hydroxybenzoic acid which is brominated at an apparent second-order rate of less than one-hundredth that of 2,4-dibromophenol as is shown by the data of Tables II and V.

3,5-Dibromo-2-hydroxybenzoic Acid.—This acid underwent bromodecarboxylation at a rate such that neither k' nor k^* (as previously defined) were constant at constant hydrogen ion concentration (see Table III). Moreover the trend of these values indicates that k_{app} follows a non-integral bromide ion dependence, somewhere between an inverse first- and second-power dependence. In other words bromination of dibromosalicylic acid (3,5-dibromo-2-hydroxybenzoic acid) follows a bromide dependence which lies in between that previously generally noted for 3,5-dibromo-4-hydroxybenzoic acid and for 2,6-dibromophenol. This result suggests that perhaps dibromosalicylic acid reacts by a mixture of mechanisms I and II. Such a possibility leads to the rate expression

$$\text{rate} = k''[H_2OBr^+][Ar^{--}] + k_0[Br_2][ArH_2] + k_-[Br_2][ArH^-]$$

where $[ArH_2]$, $[ArH^-]$ and $[Ar^{--}]$ represent the concentration of dibromosalicylic acid in its unionized, mono-ionized and di-ionized forms, respectively. Terms for the attack of H_2OBr^+ (as well as any species of similar bromide ion dependency as discussed under mechanism I) and Br_2 upon all three of these forms of dibromosalicylic acid might be included in the above rate expression, but at constant hydrogen ion concentration, in any event, all such expressions reduce to

$$\text{rate} = k_0'[ArH_2][Br_2] + k'''[ArH_2][Br_2]/[Br^-] \qquad (12)$$

where k''' and k_0' include any hydrogen ion dependency. An analogous mixture of mechanisms has been proposed to account for the iodination of tyrosine,[39] histidine,[40] as well as certain pyrroles.[41] As a test of this mechanism for dibromosalicylic acid, since by definition of k_{app}

$$\text{rate} = k_{app}(ArH_2)(Br_2) \qquad (13)$$

and since under our conditions of acidity, to a good approximation $(ArH_2) = [ArH_2]$, then

$$k_{app}(Br_2)/[Br_2] \equiv k^* = k_0' + k'''/[Br^-] \qquad (14)$$

Hence for this mixed mechanism to hold, a plot of k^* *vs.* $1/[Br^-]$ should give a straight line. Such a plot at constant hydrogen ion concentration is

(39) C. H. Li, THIS JOURNAL, **64**, 1147 (1942); **66**, 228 (1944).
(40) C. H. Li, *ibid.*, **66**, 225 (1944).
(41) K. W. Doak and A. H. Corwin, *ibid.*, **71**, 159 (1949).

given in Fig. 3 and the marked deviation from linearity argues strongly against this mechanism for the bromodecarboxylation.

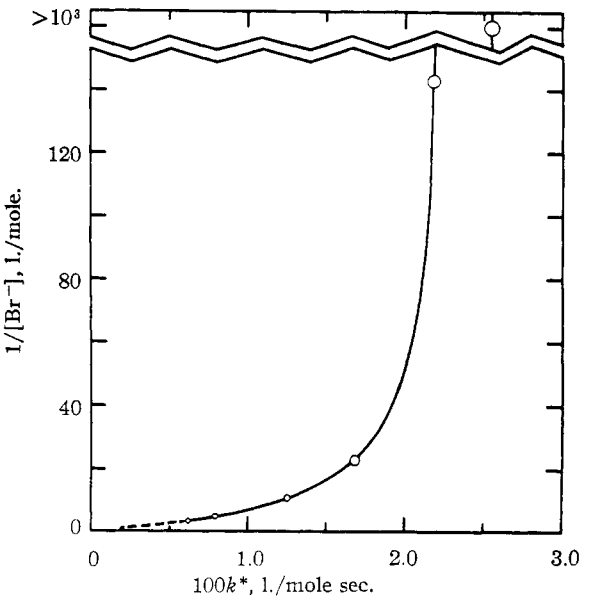


Fig. 3.—Variation of k^* with $1/[Br^-]$ for 3,5-dibromo-2-hydroxybenzoic acid at $[H^+] = 0.300\ M$; points drawn with radius equal 2% of k^*.

The following mechanism (III) is therefore postulated to account for the observed bromide ion and hydrogen ion dependency of k_{app}

$$ArH_2 \overset{\text{fast}}{\rightleftharpoons} ArH^- + H^+;\ K_4 = [H^+][ArH^-]/[ArH_2] \quad (15)$$

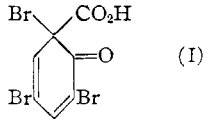
$$ArH^- + Br_2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ArHBr + Br^- \quad (16)$$

$$ArH_2 + Br_2 \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} ArHBr + H^+ + Br^- \quad (17)[42]$$

$$ArHBr \overset{\text{fast}}{\rightleftharpoons} ArBr^- + H^+;\ K_5 = [ArBr^-][H^+]/[ArHBr] \quad (18)$$

$$ArBr^- \overset{k_3}{\longrightarrow} Ar'Br^- + CO_2 \quad (19)$$

where $Ar'Br^-$ is the anion of tribromophenol. Here the reactive intermediate ArHBr is presumed for dibromosalicylic acid to have the structure I.



(I)

This intermediate ArHBr is assumed under the conditions of the kinetics to be formed in low concentration relative to ArH_2. Then on the basis of the steady-state approximation

$$k_1[ArH^-][Br_2] + k_2[ArH_2][Br_2] = k_{-1}[ArHBr][Br^-] + k_{-2}[ArHBr][H^+][Br^-] + k_3[ArBr^-] \quad (20)$$

Substitution for $[ArH^-]$ from (15) and for [ArHBr] from (18) and solving for $[ArBr^-]$ gives

$$[ArBr^-] = \frac{[ArH_2][Br_2]\{k_2 + k_1K_4/[H^+]\}}{(k_{-1}/K_5)[H^+][Br^-] + (k_{-2}/K_5)[H^+]^2[Br^-] + k_3} \quad (21)$$

Since

$$\text{rate} = k_3[ArBr^-] = k_{app}(Br_2)(ArH_2) \quad (22)$$

substitution of (21) into (22) gives

$$\frac{k_{app}(Br_2)[H^+]}{[Br_2]} = k^*[H^+] = \frac{k_2[H^+] + k_1K_4}{(k_{-2}/k_3K_5)[H^+]^2[Br^-] + (k_{-1}/k_3K_5)[H^+][Br^-] + 1} \quad (23)$$

Application of equilibrium statistics and the principle of microscopic reversibility[43] to reactions 15, 16, and 17 leads to the relationship

$$k_1K_4/k_{-1} = k_2/k_{-2} \quad (24)$$

which must hold even away from equilibrium. From (23) and (24) there may be obtained

$$1/k^*[H^+]^2 = k_{-1}[Br^-]/k_1K_4k_3K_5 + 1/\{k_2[H^+]^2 + k_1K_4[H^+]\} \quad (25)$$

According to (25) a plot of $1/k^*[H^+]^2$ *vs.* $[Br^-]$ should give a series of parallel straight lines for each hydrogen ion concentration. Such a plot for dibromosalicylic acid is given in Fig. 4 in which the radii of the points are drawn equal to 3% of $1/k^*[H^+]^2$ save for the point at zero bromide ion concentration where the radius is 5%. Extensive data are available only at 0.300 M hydrogen ion concentration; the data here do indeed fall rather well upon a straight line all the way down to an initial bromide ion concentration of essentially zero.

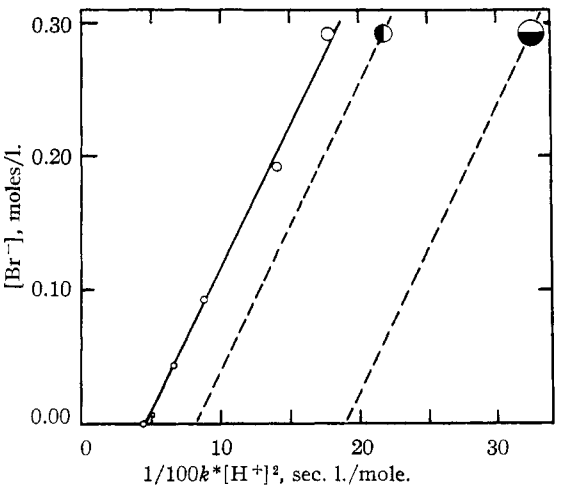


Fig. 4.—$[Br^-]$ *vs.* $1/100k^*[H^+]^2$ for 3,5-dibromo-2-hydroxybenzoic acid at $[H^+]$ equal 0.300 M (○), 0.200 M (◐), and 0.100 M (◒).

At negligible bromide ion concentrations equation 25 reduces to

$$k^* = k_2 + k_1K_4/[H^+] \quad (26)$$

which equation is entirely analogous to that (11a) obtained with 2,6-dibromophenol. By extrapolation of the data at 0.200 and 0.100 M hydrogen ion concentrations to zero bromide ion concentration as suggested by equation 25 and as shown in Fig. 4, values of k^* at zero bromide ion concentration

(42) To be sure the proton formed here is affixed to some base; this step is presumed to be subject to general base catalysis.

(43) Thus see A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1953, p. 202.

may be obtained and these upon substitution into (26) permit approximate evaluation of k_1K_4 and k_2, which are found to be, respectively, 0.0042 ± 0.002 sec.$^{-1}$ and 0.0103 ± 0.0005 l./mole sec. From this value of k_1K_4 and the slope of the lines of Fig. 4, k_{-1}/k_3K_5 is calculated to be 20 (l./mole)^2 and k_{-2}/k_3K_5 49 (l./mole)^3.

Rediscussion of 3,5-Dibromo-4-hydroxybenzoic Acid.—The above discussion upon dibromosalicylic acid suggests that perhaps mechanism III also applies to dibromo-*p*-hydroxybenzoic acid. A plot of $1/k^*[H^+]^2$ *vs.* $[Br^-]$ at a hydrogen ion concentration of 0.300 *M* gives a good straight line for this acid. It is notable that the point at zero initially added bromide ion falls on this line. This latter point is much nearer the origin than the corresponding point for dibromosalicylic acid; this means that the second term on the right of equation 25 is quite small compared to the first term. To the extent that the second term is negligibly small, then equation 25 reduces to equation 4 which was previously shown to hold approximately for dibromo-*p*-hydroxybenzoic acid. Mechanism III, therefore, offers an alternative and superior explanation for this kinetic form to that considered under mechanism I.[44]

The points for smaller hydrogen ion concentration for dibromo-*p*-hydroxybenzoic acid fall much closer to the line for 0.300 *M* hydrogen ion concentration than did the corresponding points for dibromosalicylic acid. This makes evaluation of k_1K_4 and k_2 difficult for the *p*-hydroxy acid. If the point at 0.05 *M* hydrogen ion concentration is considered to be accurate, then k_1K_4 and k_2 are found by the method previously discussed to be approximately 0.05 sec.$^{-1}$ and 0.12 l./mole sec., respectively; from these values and the slope of the line, k_{-1}/k_3K_5 and k_{-2}/k_3K_5 are, respectively, ~300 (l./mole)^2 and ~700 (l./mole)^3. On the basis of these constants, errors as small as 6% on the evaluation of k_{app} can account for the rather inconsistent location of the points at 0.2 and 0.1 *M* hydrogen ion concentration.

A comparison between the kinetics of bromodecarboxylation of 3,5-dibromo-2-hydroxy- and 3,5-dibromo-4-hydroxybenzoic acids is of interest. An obvious point of distinction is that the apparent second-order rate constant for the *p*-acid is 7.6, 8.5 or 9.8 times that of the *o*-acid depending upon whether the comparison is being made in 80, 75 or 70% acetic acid at a hydrogen bromide concentration of 0.300 *M*. According to equations 25 and 11a the apparent second-order rate constants at a given bromine, bromide and hydrogen ion concentration are a moderately complex function of the constants k_1, k_{-1}, k_2, k_3, k_4 and K_4. While these constants have not yet all been evaluated separately and while those for the *p*-acid refer to 80% and those for the *o*-acid to 75% acetic acid, certain correlations are possible. In these two solvents at hydrogen bromide concentration of 0.3 *M* the *o*- and *p*-hydroxy acids undergo bromodecarboxylation at nearly the same rate. This is due to the fact that while k_1K_4 and k_2 for the *p*-hydroxy acid are some ten times larger than the corresponding constants for the *ortho*-hydroxy acid, this effect is approximately compensated by some 15-fold larger values for the reversibility ratios, k_{-1}/k_3K_5 and k_{-2}/k_3K_5 for the *p*-hydroxy acid. Upon going from 80 to 75% acetic acid k_1K_4 and k_2 would both be expected to increase for the *p*-hydroxy acid (the former largely because of increase in K_4) and k_{-1}/k_3K_5 and k_{-2}/k_3K_5 would be expected to decrease (largely because of increase in K_5 and decrease in k_{-2}) on the basis of current theories[45] of solvent effects. In this way, therefore, the relative reactivities of the *o*- and *p*-hydroxydibromobenzoic acids in 75% acetic acid may be rationalized in terms of mechanism III; similar explanations apply also to the relative reactivities in the other solvent mixtures. A point worth emphasizing is how large these solvent effects are. Thus in presence of 0.3 *M* HBr for dibromo-*p*-hydroxybenzoic acid, k_{app} increases 8.9-fold in going from 80 to 75% acetic acid and 5.9-fold from 75 to 70% acetic acid; the corresponding factors for dibromosalicylic acid are 8.0- and 5.1-fold. Such large solvent effects demanded very accurate preparation of the mixed solvents and doubtless were a major source of error in our present work. Salt effects are expected to be correspondingly large for the present reactions and for this reason quantitative comparisons have all been made at a large and constant ionic strength of 0.300.

That k_1K_4 and k_2 in a given medium should be larger for dibromo-*p*-hydroxybenzoic acid than for dibromo-*o*-hydroxybenzoic acid might *a priori* have been predicted on the basis that the bromination of phenol gives 90.2% *para* and 9.8% *ortho* derivative[46,47] and hence occurs some twenty times faster in the *para* position than in a single *ortho* position. More suitable for comparison with the dibromohydroxybenzoic acids are the relative rates of bromination of 2,6- and 2,4-dibromophenol. Such data as are available upon these phenols in Table V suggests that 2,6-dibromophenol is brominated more readily under fixed conditions than 2,4-dibromophenol but that the differences in reactivity are not as great as the phenol analogy suggests.

Rediscussion of 2,6-Dibromophenol.—It is of interest to consider the possibility that 2,6-dibromophenol, ArOH, may undergo bromination according to a mechanism somewhat analogous to mechanism III, namely, by the process (mechanism III′)

$$ArOH \overset{\text{fast}}{\rightleftharpoons} ArO^- + H^+;\ K_4' = [H^+][ArO^-]/[ArOH] \quad (15')$$

$$ArO^- + Br_2 \underset{k'_{-1}}{\overset{k_1'}{\rightleftharpoons}} ArBrO + Br^- \quad (16')$$

$$ArOH + Br_2 \underset{k'_{-2}}{\overset{k_2'}{\rightleftharpoons}} ArBrO + H^+ + Br^- \quad (17')[42]$$

(44) Additional evidence for mechanism III for 3,5-dibromo-4-hydroxybenzoic acid recently has been provided by study of carbon-13 isotope fractionation as a function of bromide ion concentration for the bromodecarboxylation (Gus A. Ropp and E. Grovenstein, Jr., work done at the Oak Ridge National Laboratory; details to be reported later).

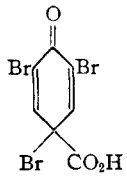
(45) See ref. (34), pp. 345–350.

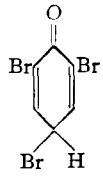
(46) A. F. Holleman, *Chem. Revs.*, **1**, 218 (1924).

(47) For a possible explanation of this *ortho–para* ratio see P. W. Robertson, P. B. D. de la Mare and B. E. Swedlund, *J. Chem. Soc.*, 782 (1953).

$$ArBrO \xrightarrow{k_3'} Ar'Br^- + H^+ \qquad (19')^{42}$$

$Ar'Br^-$ is the anion of tribromophenol and the reactive intermediate ArBrO is presumed to have the structure III analogous to that (II) from the


II

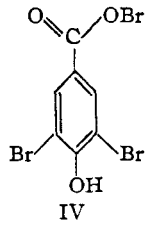

III

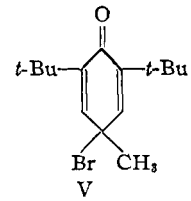
corresponding carboxylic acid. Such a mechanism leads to the kinetic consequence

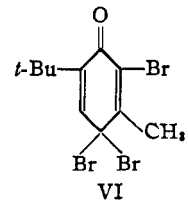
$$1/k^*[H^+] = k'_{-1}[Br^-]/k_1'k_3'K_4' + 1/\{k_2'[H^+] + k_1'K_4'\} \qquad (27)$$

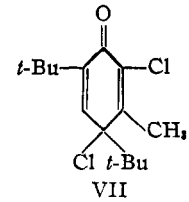
This mechanism offers an alternative explanation to that given earlier for the small decrease in k^* with increase in bromide ion concentration. If the first term on the right-hand side of equation 27 is small compared to the second right-hand term, then equation 27 reduces to equation 11a. Evaluation of the constants of equation 27 by a method similar to that used for dibromosalicylic acid gives k' equal 3.2 l./mole sec., $k_1'K'$ 0.63 sec.$^{-1}$, and k'_{-1}/k_3' 0.26 l./mole. The values of k_2' and $k_1'K_4'$ are close to the values of k_0 and k_- given earlier (see equation 11a) and the reversibility ratio k'_{-1}/k_3' is indeed so small that the first term on the right-hand side of equation 27 makes no more than a 17% contribution to the sum of the right-hand terms at the highest bromide ion concentration studied. Thus in contrast to intermediate II from dibromo-*p*-hydrobenzoic acid, intermediate III from 2,6-dibromophenol shows little, if indeed any, tendency to revert to the starting phenol; this fact must result chiefly because intermediate III loses a proton much faster than II loses carbon dioxide. Finally $k_1'K_4'$ and k_2' for 2,6-dibromophenol are some ten and thirty times larger than the corresponding constants for dibromo-*p*-hydroxybenzoic acid; such is to be expected for an electrophilic substitution since the carboxyl group relative to hydrogen must lower the availability of electrons at the atom to which it is attached.

Reactive Intermediates in a Halogenation of Phenols.—We have proposed that reactive intermediates of structures I, II and III are formed during the bromination of the present phenols. An alternative structure for the intermediate from the phenolic carboxylic acids is of type IV as represented for dibromo-*p*-hydroxybenzoic acid. We favor structures I and II, however, since they give a simpler mechanism for the bromodecarboxylation. For structure IV to give the final products rearrangement of bromine must occur before or simultaneously with the decarboxylation step of mechanism III. Stronger evidence in favor of structures I–III is provided by the formation and isolation of analogous, though more stable, intermediates, from 2,4,6-trisubstituted phenols. Thus Coppinger and Campbell[48] have described the preparation of the cyclohexadienone V from the bromination of 4-methyl-2,6-di-*t*-butylphenol in 80% acetic acid. Bromination of 2,4-dibromo-3-methyl-6-*t*-butylphenol gives VI according to Forman and Sears[26d]; likewise chlorination of 2,4-di-*t*-butyl-5-methylphenol yields VII. Analogous products of nitration have been described[49] and the reaction[50] of 2,4,6-trialkylphenols with alkylperoxy radicals gives products of related structure. The structure of these products has been established especially on the basis of their ultraviolet and infrared absorption spectra. That such 2,4,6-trisubstituted phenols undergo halogenation and nitration chiefly at the position *para* to the phenolic hydroxyl group is in agreement with the fact that dibromo-*p*-hydroxybenzoic acid gives intermediate II considerably faster than dibromosalicylic acid gives I.

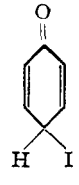

IV


V


VI


VII

Mechanism of Iodination of Phenols.—While we have shown that the intermediate III from 2,6-dibromophenol shows little if any tendency under our experimental conditions to revert back to the starting phenol by reaction with halide ion, as opposed to loss of a proton, it occurs to us that an intermediate such as VII from the iodination of phenol should show a greater tendency to do so.


VII

This idea is supported by the greater nucleophilic character[51] of iodide ion *versus* bromide ion and by the probably greater ease of nucleophilic displacement[52] upon iodine as opposed to bromine. Additional evidence is supplied by the work of Soper and Smith[53] upon the kinetics of the iodination of phenol. These workers found that for iodination with iodine in aqueous solution containing much iodide ion (0.1–0.4 *M*) that the variation of the apparent second-order rate constant with iodide ion concentration was in agreement with a species such

(48) G. M. Coppinger and T. W. Campbell, THIS JOURNAL, **75**, 734 (1953).

(49) H. E. Albert and W. C. Sears, *ibid.*, **76**, 4979 (1954).

(50) T. W. Campbell and G. M. Coppinger, *ibid.*, **74**, 1469 (1952); A. F. Bickel and E. C. Kooyman, *J. Chem. Soc.*, 3211 (1953).

(51) C. G. Swain and C. B. Scott, THIS JOURNAL, **75**, 141 (1953).

(52) For some evidence see J. Hine and W. H. Brader, *ibid.*, **77**, 361 (1955).

(53) F. G. Soper and G. F. Smith, *J. Chem. Soc.*, 2757 (1927).

as hypoiodous acid as the effective iodinating agent. A more complete study[54] gave the empirical result

$$\text{rate} = k_0'[\text{PhOH}][I_2]/[H^+][I^-] + k'_{HA}[\text{PhOH}][I_2][HA]/[H^+]^2[I^-] \quad (28)$$

where HA is a buffer acid such as acetic acid. The first term was interpreted as involving attack of HOI upon un-ionized phenol or alternatively I^+ (or H_2OI^+) upon phenoxide ion while the second term involved attack of acyl hypohalite upon phenoxide ion (or a general acid-catalyzed attack of hypoiodous acid upon phenoxide ion). We wish to point out that equation 28 is just the kinetic form which would be expected for mechanism III′ (involving iodine in place of bromine) with steps 16′ and 17′ essentially at equilibrium and, therefore, with the second right-hand term of equation 27 small relative to the first. The first right-hand term of equation 28 would then result from water being the general base which accepted the proton of step 19′ while the second term would involve the base A^- conjugate to the buffer acid. Moreover if mechanism III′ corresponds to the true mechanism of halogenation of phenol, then molecular iodine is seen to be the effective iodination agent. This iodinating agent has been shown to be responsible for the iodinolysis of *p*-methoxybenzeneboronic[55] acid in aqueous solution at iodide ion concentrations of 0.1 to 0.5 *M* and is apparently responsible for the exchange reaction between radioactive iodine and diiodotyrosine.[56]

At extremely low iodide concentrations such as are maintained by excess silver ion, the hypoiodous acidium ion (or iodinium ion) is probably the effective iodinating agent[57]; our question is whether in solution of high or moderately high iodide ion concentration the concentration of the hypoiodous acidium ion is sufficiently great to compete successfully with the much larger concentration of molecular iodine.[58] A final answer to this question for phenol must await a study of the kinetics of iodination to much lower iodide ion concentration or, perhaps better, a study of a possible hydrogen isotope effect here as a function of the iodide ion concentration. If mechanism III′ can be shown to apply to the kinetics of the iodination of phenol,[59] then probably a similar mechanism holds for the iodination of aniline.[60]

Acknowledgments.—The authors are indebted to the Graduate School for a fellowship to U. V. H. which made part of this work possible and to Dr. Jack Hine for helpful discussions.

(54) B. S. Painter and F. G. Soper, *J. Chem. Soc.*, 342 (1947); see also E. Berliner, THIS JOURNAL, **73**, 4307 (1951).

(55) H. G. Kuivila and R. M. Williams, THIS JOURNAL, **76**, 2679 (1954).

(56) A. H. Zeltmann and M. Kahn, *ibid.*, **76**, 1554 (1954).

(57) D. H. Derbyshire and W. A. Waters, *J. Chem. Soc.*, 3694 (1950); I. R. L. Barker and W. A. Waters, *ibid.*, 150 (1952); R. P. Bell and E. Gelles, *ibid.*, 2734 (1951).

(58) For a similar and more detailed argument concerning the reaction of oxalic acid with bromine *versus* hypobromous acidium ion see Y. Knoller and B. Perlmutter-Hayman, THIS JOURNAL, **77**, 3212 (1955).

(59) A somewhat similar mechanism has been considered for the iodination of 2,4-dichlorophenol but without appreciable experimental confirmation (J. E. Taylor and M. I. Evans, *Ohio J. Sci.*, **53**, 37 (1953)).

(60) E. Berliner, THIS JOURNAL, **72**, 4003 (1950).

ATLANTA, GEORGIA

[CONTRIBUTION FROM THE COLLEGE OF CHEMISTRY AND PHYSICS, PENNSYLVANIA STATE UNIVERSITY]

Carbonium Ions. III. Aromatic Nitration and the C_0 Acidity Function[1]

BY N. C. DENO AND RICHARD STEIN

RECEIVED SEPTEMBER 8, 1955

The rates of aromatic nitrations have been studied as a function of sulfuric acid concentration.

The work reported in this paper is part of the third step in a series of investigations carried out in aqueous sulfuric acids whose ultimate goal is to determine whether or not aliphatic tertiary alkyl cations exist as reaction intermediates. The first step in the program was to evaluate an acidity function (C_0), defined by eq. 1, where pK_{R^+} is the negative logarithm of the equilibrium constant for eq. 2.

$$C_0 = (pK_{R^+}) + \log(c_{ROH}/c_{R^+}) \quad (1)$$

$$H_2O + R^+ = ROH + H^+ \quad (2)$$

The second step was to test the generality of eq. 1 with data from a variety of equilibria in aqueous sulfuric acid. These two steps were accomplished in the initial paper of the series[2] in which a number of triaryl, diaryl and monoaryl groups were used for "R."

(1) Grateful acknowledgment is made of the support of this research by a grant from the Petroleum Research Fund of the American Chemical Society.

(2) N. Deno, J. J. Jaruzelski and A. Schriesheim, THIS JOURNAL, **77**, 3044 (1955).

The third step in the program involved testing the generality of eq. 3 with kinetic data from appropriate acid-catalyzed reactions of the type of eq. 4 in which the group R was varied as widely as possible. Equation 3 follows directly from reaction path 4 if eq. 5 is valid.[2] In eq. 5, R^+ on the right-hand side of the equation represents the cations used to evaluate C_0 and R on the left-hand side refers to the same R as in reaction path 4. The superscript ($\neq$) in eq. 5 signifies the transition state for path 4, and "*f*" is an activity coefficient.

$$\log k = -C_0 + \text{constant} \quad (3)$$

$$ROH + H^+ = H_2O + R^+ \xrightarrow[\text{rate determining}]{+\,A} \text{products} \quad (4)$$

$$d\log(f_A f_{ROH}/f^{\neq})d\,\%\,H_2SO_4 = d\log(f_{ROH}/f_{R^+})/d\,\%\,H_2SO_4 \quad (5)$$

The fourth step can be undertaken if eq. 3 proves satisfactory for a wide variety of R groups. This