THE KINETICS OF IODINATION AND BROMINATION OF 2,6-DIBROMOPHENOL AND 2,6-DIBROMOPHENOL-4-D

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SUMMARY

In order to add to the general fund of information regarding the nature of the electrophile and other reacting species and the presence of intermediates, if any, the kinetics of the iodination of 2,6-dibromophenol and 2,6-dibromophenol-4-d were studied at constant hydrogen ion concentration and varying iodide ion concentration, but at constant ionic strength and temperature.

It was demonstrated that the reaction is first-order in stoichiometric iodine and first-order in the phenol. The ionic strength was kept constant at 0.300 and the temperature at 50.0°. The reaction was run in 50 ml., 100 ml., or 250 ml. red, low-actinic volumetric flasks and the rate measured by stopping the reaction with a saturated solution of sodium iodide at measured time intervals. The concentration of unreacted iodine was determined by titration with standard sodium thiosulfate solution to the starch-iodine end point.

Second order rate constants were calculated at each per cent reaction by the integrated rate equation

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

in which $\underline{a}$ and $\underline{b}$ designate the initial stoichiometric iodine and phenol concentrations, respectively, $\underline{t}$ is the elapsed time in seconds, and $\underline{x}$ is the concentration of iodine consumed in time $\underline{t}$.

The apparent rate constants generally showed a downward drift as the reaction proceeded. Such a drift was more pronounced at low iodide

ion concentration and, therefore, apparent rate constants were plotted versus the per cent reaction and extrapolated to zero per cent reaction to give the initial apparent rate constant. However, at high iodide ion concentrations, the apparent rate constants remained essentially constant throughout a reaction and an average was taken.

One reason for the variation of apparent rate constants with the concentration of iodide ion is the conversion of iodine into unreactive triiodide ion by the reaction

$$I_2 + I^- \overset{K_1}{\rightleftarrows} I_3^- \quad ; \quad K_1 = \frac{[I_3]}{[I_2][I^-]}$$

The apparent rate constants were corrected for triiodide formation through the equation

$$k^x = k_{app} \frac{(I_2)}{[I_2]}$$

where $[I_2]$ refers to the actual concentration and (I_2) refers to the stoichiometric concentration. The values of k^x were calculated for each run at zero per cent reaction. Similarly, the rate constant k'

$$k' = k_{app} \frac{(I_2)[I^-]}{[I_2]} = k^x\,[I^-]$$

which should be constant according to Berliner's mechanism of iodination, was calculated for each run at different iodide ion concentrations.

The data are consistent with a mechanism in which molecular iodine reacts with both the phenol and phenoxide ion in a reversible step to yield an intermediate having a cyclohexadienone structure. The intermediate then in a rate-determining-step loses a proton to a Bronsted base such as the solvent.

$$\mathrm{ArHOH} \rightleftarrows \mathrm{ArHO}^- + \mathrm{H}^+$$

$$\mathrm{ArHO}^- + \mathrm{I}_2 \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \mathrm{ArHOI} + \mathrm{I}^-$$

$$\mathrm{ArHOH} + \mathrm{I}_2 \underset{k_{-2}}{\overset{k_2}{\rightleftarrows}} \mathrm{ArHOI} + \mathrm{I}^- + \mathrm{H}^+$$

$$\mathrm{ArHOI} + \mathrm{H_2O} \xrightarrow[k_3]{\text{slow}} \text{products}$$

Such a mechanism demands that a plot of $1/(k^x[H^+])$ versus $[I^-]$ give a straight line. The experimental results were in agreement with the postulated mechanism since a straight line was obtained with an intercept of 70 sec.$^{-1}$ and a slope of 152 x 10^4 l./mole sec. This mechanism also demands a maximum isotope effect at high iodide ion concentrations which diminishes with decreasing iodide ion concentration. The maximum isotope effect (k^H_{app}/k^D_{app}) observed was 5.8 ± 0.6 at high iodide ion concentration and it dropped to 4.0 ± 0.4 at very low iodide ion concentration.

Other mechanisms, such as Berliner's and its modifications were considered. According to this mechanism, the reaction proceeds via a rate-determining attack of hypoiodous acidium ion (H_2OI^+) or (I^+) upon the phenoxide ion followed by a fast proton removal.

$$\mathrm{I}_2 + \mathrm{H_2O} \rightleftarrows \mathrm{H_2OI}^+ + \mathrm{I}^-$$

$$\mathrm{H_2OI}^+ + \mathrm{ArHO}^- \xrightarrow{\text{slow}} \mathrm{ArHOI} + \mathrm{H_2O}$$

$$\mathrm{ArHOI} + \mathrm{H_2O} \xrightarrow{\text{fast}} \text{products}$$

Such a mechanism demands that the values of k' remain constant with varying iodide ion concentration. This mechanism was discarded since the values of k' were observed to diminish with decreasing iodide ion concentration.

The possibility of iodination by both I^+ and H_2OI^+ was also considered. However, a plot of k^x versus $1/[I^-]$ did not give a straight line as required and this mixed mechanism was also discarded.

Iodination at extremely low but constant iodide ion concentration was studied by the use of thallium perchlorate, which acts as iodide ion regulator by precipitating iodide ion formed during the reaction. Such an experiment was useful in that it allowed the measurement of deuterium isotope effect at very low iodide ion concentration.

Bromination of 2,6-dibromophenol was studied under conditions similar to those employed by Grovenstein and Henderson in order to determine if a deuterium isotope effect could be detected in such a bromination reaction. A deuterium isotope effect of 1.30 ± 0.10 (k^H_{app}/k^D_{app}) was observed in 80.0 per cent acetic acid by weight at 20.0° and 1.33 ± 0.02 in water at 0°.

CHAPTER I

INTRODUCTION

Electrophilic aromatic substitution is a reaction wherein a Lewis acid, or a substance capable of giving up a Lewis acid, attacks an aromatic molecule displacing, most commonly, a hydrogen atom. However, other suitably activated groups may be displaced in preference to a hydrogen atom as in the bromination of dibromobenzoic acid in aqueous acetic acid[1] (where Ar is $C_6H_2Br_2$).

$$Ar(OH)(COOH) + Br_2 \longrightarrow ArBr(OH) + CO_2 + HBr$$

Hydrogen substitution reactions could proceed conceivably by a one step termolecular mechanism which might involve an activated complex such as (X---ArH---B), where X is the attacking electrophile, ArH is the substrate, and B is a base. This mechanism has been discarded,[2] but not yet disproved.[3] The more generally accepted mechanism is that in which the aromatic nucleus is first attacked by the electrophile and the proton removed in the following step. In this latter mechanism, the rate-determining step may be either the attack of the electrophile or the removal of the proton. A few cases have also been noted in

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(1) E. Grovenstein, Jr. and U. V. Henderson, Jr., *J. Am. Chem. Soc.*, *78*, 569 (1956).

(2) C. K. Ingold, *Structures and Mechanisms in Organic Chemistry*, Ithaca, N. Y.: Cornell University Press, 1953, pp. 207-212.

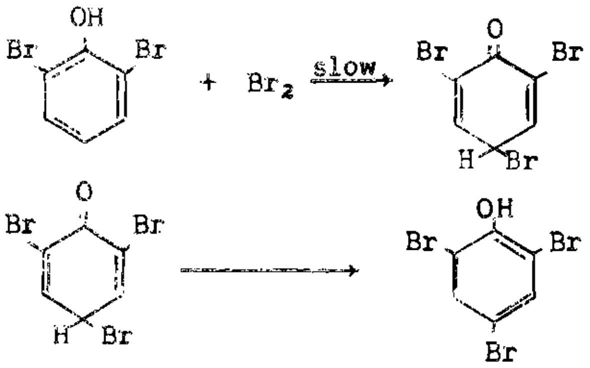
(3) G. S. Hammond, *J. Am. Chem. Soc.*, *77*, 334 (1955).

which the rate-determining step is the formation of the electrophile and the rate of the reaction independent of the aromatic species. This is illustrated in the chlorination of phenol in a solution of hypochlorous acid and perchloric acid.[4]

$$HOCl + H_3O^+ \rightleftarrows H_2OCl^+ + H_2O$$

$$H_2OCl^+ \xrightarrow{slow} Cl^+ + H_2O$$

An example of a reaction in which the attack of the electrophile on the aromatic nucleus is the slow step in the bromination of 2,6-dibromophenol.[1]



The rate-determining step may also be the release of a proton from the carbon atom undergoing attack by the electrophile. This is exemplified by the sulfonation of benzene.[5,6]

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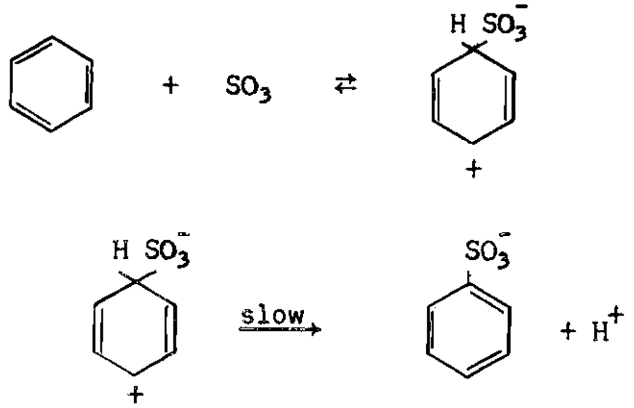
(4) P. B. de la Mare, E. D. Hughes and C. A. Vernon, Research (London), 3, 192 (1950).

(5) L. Melander, Acta Chem. Scand., 3, 95 (1949).

(6) L. Melander, Arkiv Kemi, 7, 287 (1954).



In reactions in which C-H bond breaking is the slow step, it is expected that a C-D or C-T bond will be broken more slowly than the C-H bond. This is largely due to the decreased reactivity of bonds to deuterium or tritium as a result of the difference in zero-point energy between a bond to deuterium or to tritium and a bond to protium.[7,8] A complete discussion of the theory of such isotope effects is given by Melander.[9] It has also been argued that the absence of an isotope effect does not necessarily eliminate the possibility of the slow proton removal as the rate-determining step[3] as the isotope effect may be too small to detect.

Painter and Soper[10] concluded that the iodinating species in the aqueous iodination of phenol is the hypoiodous acidium ion, while Berliner[11] concluded that the hypoiodous acidium or iodine cation is

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(7) L. Melander, Nature, 163, 599 (1949).

(8) L. Melander, Arkiv Kemi, 7, 287 (1954).

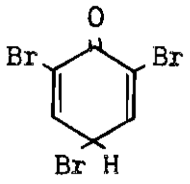
(9) L. C. Melander, Isotope Effects on Reaction Rates, New York: Ronald Press Co., 1960.

(10) B. S. Painter and F. G. Soper, J. Chem. Soc., 342, (1947).

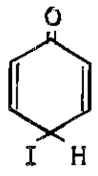
(11) E. Berliner, J. Am. Chem. Soc., 72, 4003 (1950).

the iodinating species in the iodination of aniline. Ingold[12] has stated that there is no evidence as yet that any iodine carrier other than the cationic species is effective in aromatic iodination in aqueous solution. Ingold is of the opinion that the mode of attack of the electrophilic halogenating agents on the benzene ring is similar to that of nitrating agents in which the loss of a proton from the aromatic nucleus is kinetically insignificant.[13]

Molecular iodine has been found to be the effective iodinating agent for the iodination of p-methoxybenzeneboronic acid in aqueous solution,[14] and is apparently responsible for the exchange reaction between radioactive iodine and diiodotyrosine.[15] Grovenstein and coworkers[1,16] have proposed a mechanism for the iodination of phenol. In the bromination of 2,6-dibromophenol they found that the intermediate (a) showed little tendency to react with bromide ion,[1] while they argued that intermediate (b) should show a greater tendency to react with iodide ion.



(a)



(b)

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(12) Ingold, op. cit., p. 291.

(13) Ibid., p. 295.

(14) H. G. Kuvika and R. M. Williams, J. Am. Chem. Soc., 76, 2679 (1954).

(15) A. H. Zeltman and M. Kahn, J. Am. Chem. Soc., 76, 1554 (1954).

(16) E. Grovenstein, Jr. and D. C. Kilby, J. Am. Chem. Soc., 79 2972 (1957).

This argument is supported by the greater nucleophilic character of iodide ion than bromide ion[17] and the increased ease of nucleophilic displacement upon iodine than bromine.[18] The mechanism proposed by Grovenstein and co-workers involves the rapid, reversible attack of molecular iodine on the aromatic nucleus to give an intermediate (b), which suffers the loss of a proton to a base in the slow step of the reaction.

The purpose of this research is to attempt to elucidate the mechanism of iodination and bromination of aromatic molecules with special regard to the nature of the attacking species, the presence of intermediates, if any, and the determination of the rate-determining step. A study has been made of the iodination and bromination of 2,6-dibromophenol and its deuterated derivative at various iodide ion and bromide ion concentrations. Knowledge of the mechanism for the iodination and bromination of 2,6-dibromophenol should contribute toward an understanding of the mechanism for the iodination and bromination of related compounds.

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(17) C. G. Swain and C. B. Scott, J. Am. Chem. Soc., 75, 141 (1953).

(18) J. Hine and W. H. Brader, Jr., J. Am. Chem. Soc., 75, 3964 (1953).

CHAPTER II

SURVEY OF RELATED WORK

The Iodination of Phenols.--A literature survey reveals a considerable amount of mechanistic investigation of the halogenation of phenols. Cofman[19] concluded that molecular iodine is incapable of iodinating aromatic compounds on the basis that molecular iodine did not iodinate phenol in acid solution, while in basic solution, where iodine is converted to hypoiodous acid, the iodination proceeded smoothly.

Soper and Smith studied the iodination of phenol in nearly neutral, phosphate-buffered solutions at high iodide ion concentrations such that essentially all the iodine was complexed to triiodide ion.[20] These authors found the rate of the reaction to be directly proportional to the concentrations of phenol and stoichiometric iodine, but inversely proportional to the square of the iodide ion concentration. The reaction also varied inversely to more than the first power and less than the second power of the actual hydrogen ion concentration. The authors concluded that both the phenol and phenoxide ion are iodinated by hypoiodous acid.

$$\text{rate} = k_1[\text{PhOH}][\text{HOI}] + k_2[\text{PhO}^-][\text{HOI}]$$

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(19) V. Cofman, J. Chem. Soc., 115, 1040 (1919).

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

Painter and Soper[10] found that the rate of iodination in acetate buffer varied inversely with the hydrogen ion concentration and with the square of the iodide ion concentration. They concluded that the reaction may involve interaction of hypoiodous acid with phenol or iodine cations with phenoxide ions. The rate of iodination was also found to increase linearly with the concentration of the buffer acid at constant pH. They interpreted this catalytic effect in terms of an interaction of acetyl hypoiodite with phenoxide ions.

$$\frac{dx}{dt} = k_0[\mathrm{PhOH}][\mathrm{HOI}] + k_{cat}[\mathrm{PhO^-}][\mathrm{AcOI}]$$

or

$$\frac{dx}{dt} = k_0[\mathrm{PhO^-}][\mathrm{I^+}] + k_{cat}[\mathrm{PhO^-}][\mathrm{AcOI}]$$

Breliner[21] studied the kinetics of the iodination of phenol at high iodide ion concentration (0.12 M) in phosphate buffers in which both secondary and primary phosphate are catalytically active. The phenol to iodine ratio was 4 to 1 and the ionic strength was kept constant at 0.300 by the addition of NaCl. His experimental data agreed with the following rate expression:

$$\text{rate} = \frac{k_1[\mathrm{PhOH}][\mathrm{I_2}]}{[\mathrm{H^+}][\mathrm{I^-}]} + \frac{k_2[\mathrm{PhOH}][\mathrm{I_2}][\mathrm{HA}]}{[\mathrm{H^+}]^2[\mathrm{I^-}]} \quad ,$$

where HA is a buffer acid. It seems probable from his results that the phenoxide ion is the reactive species and the kinetics are compatible with a general acid catalyzed iodination by HOI. Berliner then stated,

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(21) E. Berliner, J. Am. Chem. Soc., 73, 4307 (1951).

without direct experimental evidence, that the proton loss in the iodination of phenol is probably kinetically insignificant and takes place after the rate-determining step. His observed rate constants are expressed as

$$k_{obs} = \frac{k_0}{[H^+]} + \frac{k'_{cat}(\text{base}')}{[H^+]} + \frac{k''_{cat}(\text{base}'')}{[H^+]}$$

where k_{obs} is the observed rate constant and k_0 refers to the uncatalyzed rate constant. The rate constants k'_{cat} and k''_{cat} are the catalytic rate constants of the primary and secondary phosphate, respectively. The true rate constants were then obtained by plotting $k_{obs}[H^+]$ versus the primary phosphate ion concentration using five different buffer ratios (pH 5.71-6.61). Berliner then concluded that the halogenation of phenol involves the phenoxide ion as an active substrate.

$$\text{rate} = k_0[\text{PhO}^-][\text{HOI}][H^+] + k_{cat}[\text{PhO}^-][\text{HOI}][\text{Acid}]$$

Li,[22] studying the iodination of p-chlorophenol at varying iodide ion concentrations, concluded that the active halogenating species is hypoiodous acid, the rate being given by

$$\text{rate} = k_1[\text{PhOH}][\text{HOI}] + k_2[\text{PhO}^-][\text{HOI}] \;.$$

Taylor and Evans[23] found an inverse hydrogen ion dependence in the iodination of 2,4-dichlorophenol and concluded that the phenolate

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(21) E. Berliner, J. Am. Chem. Soc., 73, 4307 (1951).

(22) C. H. Li, J. Am. Chem. Soc., 70, 1716 (1948).

(23) J. Taylor and M. Evans, Ohio Journal of Science, 53, 507 (1954).

ion and molecular iodine are the active species.

The iodination of phenol in the presence of pyridine was studied by Tronov and Kolesnikova.[24] The rate of iodination was increased by the addition of pyridine and the authors assumed the formation of a highly reactive species $[C_6H_5NI^+][I^-]$ which was believed to be the iodinating agent.

Berliner, Berliner and Nelidow[25] studied the relative rates of iodination of <u>para</u>-alkyl phenols in different aqueous solutions of acetic acid, methyl alcohol, and dioxane. In each case the relative rates indicated the predominate operation of inductive effect in the order $Me_3C > Me_2C > Et > Me$. The authors gave no mechanism, but assumed the iodinating agent to be either I^+ of H_2OI^+.

Berliner[26] has studied the kinetics of iodination of <u>p</u>-chlorophenol with ICI in aqueous perchloric acid at constant ionic strength and high chloride ion concentrations. The reaction was found to be first order in <u>p</u>-chlorophenol and ICl concentrations and inversely dependent upon the hydrogen ion and chloride ion concentrations. Berliner[27] also studied the iodination of 2,4-dichlorophenol and anisole with ICl in aqueous perchloric acid solution at high chloride ion and hydrogen ion concentrations. Both reactions were found to be first order in 2,4-dichlorophenol and ICl concentrations. The 2,4-dichloro-

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(24) B. Tronov and S. Kolesnikova, <u>Soobscheniya</u> <u>Mauch</u> <u>Rabot</u>. <u>Vsesoynz</u> <u>Khim</u>. <u>Obshchestva</u> <u>im</u>. <u>Mendeleeva</u>, <u>1</u>, 46 (1953); <u>C.A</u>, <u>49</u>, 8173 (1955).

(25) E. Berliner, F. Berliner and I. Nelidow, <u>J</u>. <u>Am</u>. <u>Chem</u>. <u>Soc</u>., <u>76</u>, 507 (1954).

(26) E. Berliner, <u>J</u>. <u>Am</u>. <u>Chem</u>. <u>Soc</u>., <u>78</u>, 3632 (1956).

(27) E. Berliner, <u>J</u>. <u>Am</u>. <u>Chem</u>. <u>Soc</u>., <u>80</u>, 856 (1958).

phenol was found to be inversely dependent upon the chloride ion and hydrogen ion concentrations. Anisole was found to be independent of the hydrogen ion concentration except at very high concentrations.

Buss and Taylor[28] investigated the iodination of 2,4-dichlorophenol in aqueous phosphate buffers with molecular iodine. The reaction was found to be first order in 2,4-dichlorophenol and iodine concentrations overall and inversely dependent upon the iodide ion and hydrogen ion concentrations.

Bromination of 2,4- and 2,6-dibromophenol.--Grovenstein and Henderson[1] in their work on the kinetics and mechanism of bromodecarboxylation of 3,5-dibromo-2-hydroxy- and 3,5-dibromo-4-hydroxybenzoic acids studied the bromination of 2,4- and 2,6-dibromophenol. At constant hydrogen ion concentration, their values of k^x were found to be constant within 11 per cent over a three fold variation in bromide ion concentration. This bromide ion dependence indicated that molecular bromine is the effective brominating agent. A plot of k^x at constant bromide ion concentration versus the reciprocal of the hydrogen ion concentration revealed a linear relationship with k^x increasing as the hydrogen ion concentration decreases. The data closely fitted

$$k^x = \frac{k_{app} K_1 (Br_2)[Br^-]}{[Br_3^-]} ,$$

where k_{app} is the observed rate constant, K_1 is the equilibrium constant for tribromide ion formation, and k^x is the actual rate constant.

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(28) W. C. Buss and J. E. Taylor, J. Am. Chem. Soc., 82, 5991 (1960).

Here the parentheses ( ) indicate stoichiometric concentration, and the square bracket [ ] indicates actual concentration. This convention will be used throughout this thesis.

The mechanism fitting this k^x relationship is:

$$ArHOH \overset{fast}{\rightleftarrows} ArHO + H^+$$

$$ArHO^- + Br_2 \xrightarrow{k_1} Br^- + ArHBrO$$

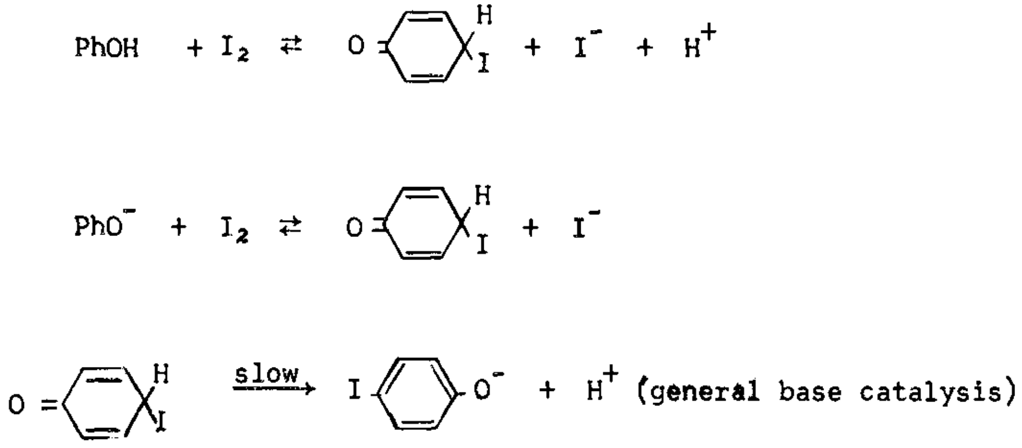
$$ArHOH + Br_2 \xrightarrow{k_2} Br^- + H^+ + ArHBrO$$

$$ArHBrO \xrightarrow{k_3} ArBrO^- + H^+$$

The rate-determining step is the attack of molecular bromine on the phenol or phenoxide ion. There appeared to be little tendency for the ArHBrO intermediate to revert to the starting phenol.

These authors then proposed a new mechanism for the iodination of phenols based on analogies from the bromination of the dibromophenols and bromodecarboxylations. This mechanism which, is in agreement with the data of Berliner and Soper and co-workers for phenol, is as follows:

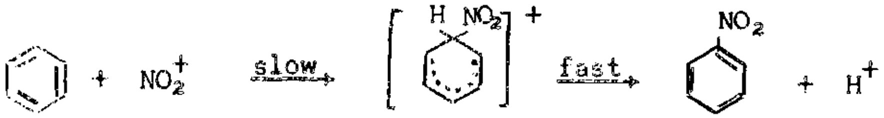
$$PhOH \rightleftarrows PhO^- + H^+$$



(general base catalysis)

If this mechanism is correct, then molecular iodine is the effective iodinating agent, and the rate-determining step is the release of the proton. This iodination agent has been shown to be responsible for the iodination of p-methoxybenzeneboronic acid the aqueous solution at iodide ion concentrations of 0.1 to 0.5 M[14] and is apparently responsible for the exchange reaction between radioactive iodine and diiodotyrosine[15].

Deuterium Isotope Effects in Electrophilic Aromatic Substitution.--Melander[5,6] conducted a number of nitrations of aromatic compounds and their tritium analogues using relative high proportions of nitric acid and aromatic compound to sulfuric acid in early attempts to determine isotope effects in electrophilic aromatic substitution. No detectable tritium isotope effect was observed and he concluded that the substraction of the proton was not the rate-controlling step. Melander decided that if the attack of NO_2^+ is rate-determining, then there should be no observable isotope effect.



Melander's mechanism of aromatic substitution was confirmed by Bonner, Bowyer and Williams[29] in the nitration of nitrobenzene and pentadeuterionitrobenzene. Lauer and Noland[30] also concurred after studying the nitration of benzene and monodeuteriobenzene. Bonner and

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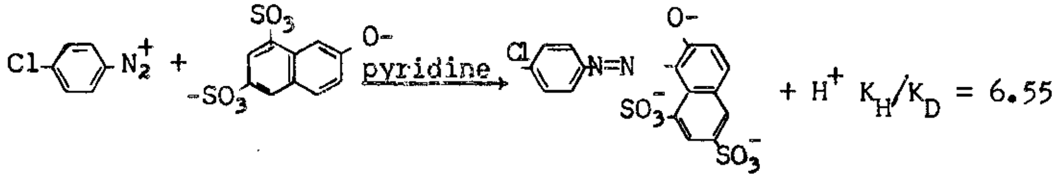
(29) T. G. Bonner, F. Bowyer and G. Williams, J. Chem. Soc., 3274 (1952).

(30) W. M. Lauer and W. E. Noland, J. Am. Chem. Soc., 75, 3689 (1953).

Wilkens[31] observed a small isotope effect in the cyclodehydration of 2-(2,4,6-trideuterioaniline)-pent-2-en-4-one and its protium analogue. They considered this to be an intramolecular electrophilic substitution.

Robertson[32] pointed out that the proton loss is probably rapid in aromatic halogenation and not rate-determining. Melander[6] reported that the rates of iodine-catalyzed bromination of toluene and tritiated toluene were identical. de la Mare, Dunn and Harvey[33] studied the bromination of benzene and hexadeuteriobenzene by aqueous hypobromous acid and obtained no deuterium isotope effect. However, bromination of 2-naphthol-6,8-disulphonic acid gave a deuterium isotope effect of 2.0.[34] Zollinger[35] studied the base catalyzed azo coupling reaction of 2-naphthol-6,8-disulphonic acid and the 1-deuterio-2-naphthol-6,8-disulphonic acid with the 4-chlorobenzenediazonium ion and found an isotope effect of 6.55. A similar deuterium isotope effect was obtained in the diazo coupling reaction of related compounds.



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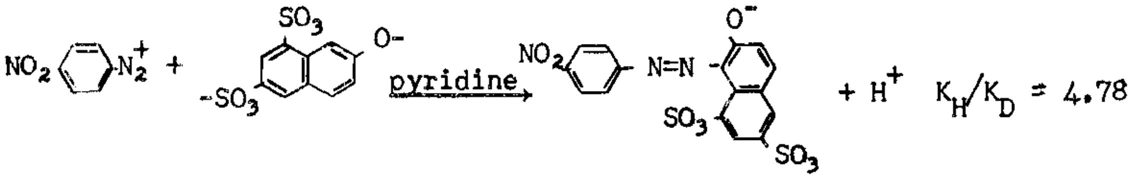
(31) T. G. Bonner and J. M. Wilkens, J. Chem. Soc., 2358 (1955).

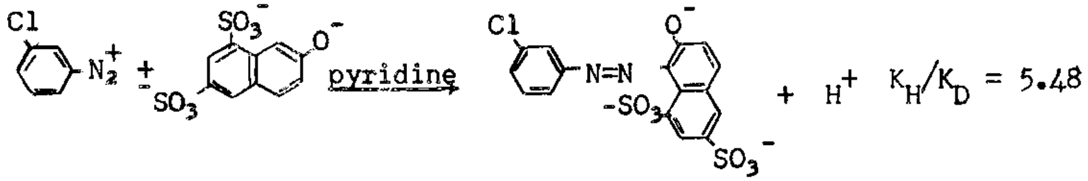
(32) P. W. Robertson, J. Chem. Soc., 1267 (1954).

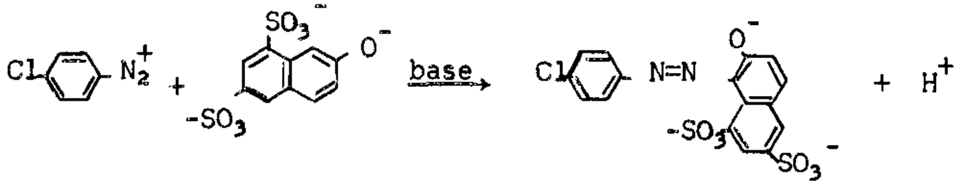
(33) P. B. D. de la Mare, T. M. Dunn and J. T. Harvey, J. Chem. Soc., 923 (1957).

(34) H. Zollinger, Experientia, 12, 165 (1956).

(35) H. Zollinger, Helv. Chim. Acta., 38, 1603 (1955).







Base	K_H/K_D
55.6 <u>M</u> Water	6.55
0.0232 <u>M</u> Pyridine	6.01
0.905 <u>M</u> Pyridine	3.62

The iodination of 2,4,6-trideuterioaniline and related compounds was studied by Shilov and Weinstein.[36] They found that the introduction of a sulphonic group in the <u>meta</u>-position diminished the isotope effect

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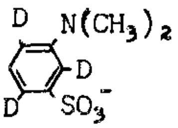
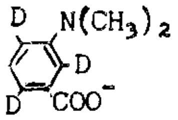
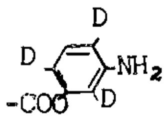
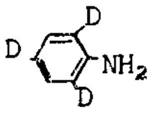
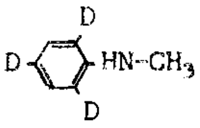
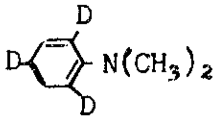
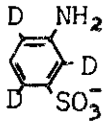
(36) E. Shilov and F. Weinstein, <u>Nature</u>, <u>132</u>, 1300 (1958).

appreciably and attributed this decrease to "energetic pecularities" of the reacting aromatic molecule. The following compounds were iodinated:

Compound	K_H/K_D
	1
	1.4
	4.8
	3.5
	3.2
	3.0
	2.0

An isotope effect of 1.8 for the bromination of dimethylaniline and its 2,4,6-trideuterio derivative was reported by Farrell and Mason.[37]

Berliner[38,39] has recently reinvestigated the mechanism of iodination of anisole and anisole-2,4,6-d_3 by ICl in acetic acid containing chloride ion (0.3 to 0.9 M) and perchloric acid (0.1 to 0.0001 M). He reports a maximum isotope effect of 3.8 and states that the reaction is independent of both the hydrogen ion and chloride ion concentration.

Berliner and Schuller[40] report an isotope effect of 1.15 in the bromination of biphenyl in 50 per cent acetic acid. Kinetic runs were made at two different temperatures, 25° and 35°, in the presence of sodium bromide (0.1 M) and Sodium perchlorate (0.4 M). Another kinetic run was made at 35° with 0.2 M sodium bromide and a deuterium isotope effect of 1.15 obtained. On the basis of this last experiment, the authors concluded that this was a secondary isotope effect.

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(37) P. G. Farrell and S. F. Mason, Nature, 133, 183 (1959).

(38) E. Berliner, Chemistry and Industry, 177 (1960).

(39) E. Berliner, private communication, (1960).

(40) E. Berliner and K. E. Schuller, Chemistry and Industry, 1444 (1960).

CHAPTER III

SOURCE, PREPARATION AND PURIFICATION OF MATERIALS

Acetic Acid.--The acetic acid for all preparations and kinetic runs 66-70 was Ross and Company glacial acetic acid. The fraction boiling at 115-116° was treated by the method of Bradfield and Orton.[41] Three and one-half liters of the freshly distilled acetic acid were refluxed for two hours over 80 grams of chromium trioxide. The solution was distilled through a four foot, 1-3/8 inch bore, jacketed column packed with 3/16 inch glass helices and the fraction boiling at 116-117° collected (ca. 2-3/4 liters). This process was repeated on a second three liter portion of acetic acid and the distillates were combined. The purity of the acetic acid was then determined by measuring the freezing point depression. The acetic acid was found to be 0.44 molal in water. The acetic acid was then diluted with sufficient redistilled water to give an 80.0 per cent acetic acid solution by weight.

Bromine.--Merck, Reagent Grade, bromine was used for all preparations and for runs 66-79. The bromine used was that purified by Henderson[1] in 1954, and was used without further purification.

Calcium Chloride.--Fisher Laboratory Chemicals, anhydrous calcium chloride, was used without further purification.

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

Calcium Sulfate.--Hammond Drierite, anhydrous clacium sulfate was used without further purification.

Carbon Disulfide.--Baker Analyzed Reagent carbon disulfide was distilled on a steam bath and stored for use over silica gel.

Carbon Tetrachloride.--Dow, Technical Grade, carbon tetrachloride was used for all preparations. The carbon tetrachloride was purified by the method of Fieser.[42] The carbon tetrachloride was first washed with 1/10 of its volume of a mixture of concentrated potassium hydroxide and ethanol three times. The carbon tetrachloride was then washed with water, stirred with small portions of concentrated sulfuric acid until there was no further discoloration of the acid, washed again with water and dried over calcium chloride. The carbon tetrachloride was then distilled and the fraction boiling at 76° collected and stored for use.

Chloroform.--Commercial chloroform was used without further purification.

Chromium Trioxide.--Baker, Technical Grade, chromium trioxide was used without further purification.

Deuterium Chloride.--A solution of deuterium chloride in heavy water was prepared by the reaction of thionyl chloride and heavy water, after Langseth and Klit.[43] Seventeen milliliters of heavy water was slowly dropped from an equal pressure funnel into a 100-milliter three-neck

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(42) Louis F. Fieser, Experiments in Organic Chemistry, Part II, Second Edition, Boston, Mass.: D. C. Heath and Co., 1941, p. 283.

(43) A. Langseth and A. Klit, Kgl. Danske Videnskab. Seiskab., Math.-fys. Medd., 15, No. 13 (1937); C. A., **32**, 2515 (1938).

round-bottom flask containing 25 milliters of thionyl chloride. Dried nitrogen was continuously swept through the apparatus to help drive the deuterium chloride through the system. The gas stream was then passed through two cold traps, cooled by acetone-dry-ice, to separate out the sulfur dioxide generated with the deuterium chloride. Sulfur dioxide has a boiling point of -10° and a freezing point of -75.5°,[44] while deuterium chloride has a boiling point of approximately -85° and a freezing point of approximately -115°.* Since dry ice-acetone bath has a temperature of approximately -78°, the sulfur dioxide crystallized out in the cold trap and the deuterium chloride passed through the series of traps. The deuterium chloride was then bubbled through 74 ml. of heavy water (99.5 per cent minimum) and the excess vented to the atmosphere through a calcium chloride drying tube. The deuterium chloride solution was titrated with standard sodium hydroxide solution and found to be 2.44 M.

Deuterium Oxide.--Stuart Oxygen Company, 99.5 per cent minimum, deuterium oxide was used without further purification.

2,6-Dibromophenol (DBP).--Eastman Kodak, White Label, m.p. 54-56°, was purified and used in all preparations and kinetic runs. Thrity-five grams of DBP was distilled at 5 mm. and the fraction boiling between 107-115° collected. The distillate was dissolved in 150 ml. of

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(44) N. A. Lange, Handbook of Chemistry, Sixth Edition, Sandusky: Handbook Publishers, Inc., 1946, p. 262.

*The temperatures reported are for hydrogen chloride, but the corresponding boiling point and freezing point of deuterium chloride should be approximately the same.

chloroform and cooled in a dry ice-acetone bath until DBP crystallized. The DBP was then dried under vacuum at room temperature for one hour. The DBP yield was 24.8 grams, m.p. 56-57° which agrees with the reported value.[45]

<u>2,6-Dibromophenol-4-d_1 (DBP-d)</u>.--2,6-Dibromophenol-4-d_1 was prepared by the general method of Ingold and co-workers.[46,47] Ingold states that one-half of the phenol should be present as the phenoxide ion in order to obtain the maximum rate of exchange. Sodium deuterioxide was prepared by adding 100 grams of heavy water (99.5 per cent minimum) to 1.7953 grams (0.0781 mole) of sodium metal very slowly while passing a stream of nitrogen gas through the system. The reaction was performed in a 200 ml. three-neck round-bottom flask fitted with a condenser and a 100 ml. dropping funnel. The sodium deuterioxide was divided into two equal volumes and placed in two 50 ml. reaction tubes.

To one tube was added 7.0758 grams (0.028 mole) of DBP and to the other was added 7.3059 grams (0.029 mole) of DBP. The tubes were flushed with nitrogen and sealed under a nitrogen atmosphere. The tubes were then placed in a five-liter round-bottom flask containing water and heated at the boiling point of water for 672 hours. The tubes were broken open and the contents placed in a 250 ml. round-bottom flask. The heavy water was distilled off under reduced pressure and the sodium

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(45) I. M. Heilbron and H. M. Bunbury, <u>Dictionary of Organic Compounds</u>, New York: Oxford University Press, 1943.

(46) C. K. Ingold, C. G. Raisin and C. L. Wilson, <u>J. Chem. Soc.</u>, 1637 (1936).

(47) A. P. Best and C. L. Wilson, <u>J. Chem. Soc.</u>, 28 (1938).

salt of the DBP and the DBP collected. The sodium salt and DBP were then sealed in a reaction tube and equilibrated under a nitrogen atmosphere with fresh heavy water (99.5 per cent minimum) at 100° for 336 hours. The tube was broken open and sodium metal, 2.170 grams, was added to the DBP-heavy water mixture and the heavy water distilled off.

Deuterium chloride, 74 ml. of 2.44 M, was added to give the solution a pH of less than one. The solution was heated to 60° for one-half hour, cooled, extracted four times with 50 ml. volumes of anhydrous diethyl ether, and the ether solution dried over anhydrous magnesium sulfate. The mixture was filtered and the ether distilled. The residue was sublimed at 20-25 microns pressure in the temperature range 25-75°. The DBP-d was sublimed two more times to give a constant melting point of 56.0° and a yield of 8.1 grams, or 56.3 per cent. Since the deuterium isotope effect was within the expected range, deuteriation was considered complete.

Diethyl Ether.--Merck, Reagent anhydrous diethyl ether, was stored in a brown bottle over sodium wire and was used without further purification.

Hydrochloric Acid.--du Pont, Reagent hydrochloric acid, was used without further purification.

Hydrogen Bromide.--Baker Analyzed Reagent, aqueous 48-50 per cent, hydrogen bromide was used without further purification.

Iodine.--Baker Analyzed Reagent iodine was used without further purification. The aqueous iodine solutions used were made by extracting a saturated solution of iodine in carbon tetrachloride (200 ml.) with redistilled water three times. The fourth and subsequent extracts were used for the kinetic experiments. This method was adopted to eliminate, as nearly as possible, any extraneous triiodide ion present in the original iodine-carbon tetrachloride solution.

Lithium Perchlorate.--Baker Analyzed Reagent lithium perchlorate was dried in a vacuum oven, 29 inches vacuum and 155°,[48] for four hours and used without further purification.

Magnesium Sulfate.--Mallinckrodt, Reagent Grade, anhydrous magnesium sulfate was used without further purification.

Mercuric Iodide.--Baker Analyzed Reagent mercuric iodide was used without further purification.

Nitrogen.--Marks compressed cylinder dry nitrogen was used without further purification.

Perchloric Acid.--Baker Analyzed Reagent, 70-72 per cent, perchloric acid was used without further purification.

Potassium Dichromate.--Baker Analyzed Reagent potassium dichromate was used without further purification.

Potassium Hydroxide.--Baker Analyzed Reagent potassium hydroxide was used without further purification.

Potassium Iodide.--Fisher Laboratory Chemicals, Reagent Grade, potassium iodide was used without further purification.

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(48) Lange, *op. cit.*, p. 165.

Potassium Permanganate.--Baker Analyzed Reagent potassium permanganate was used without further purification.

Sodium.--Baker Analyzed Reagent freshly cut sodium metal was used without further purification.

Sodium Carbonate.--Baker Analyzed Reagent sodium carbonate was used without further purification.

Sodium Hydroxide.--Baker Analyzed Reagent sodium hydroxide was used without further purification.

Sodium Iodide.--Baker Analyzed Reagent sodium iodide was used after drying in a vacuum oven at 28 inches vacuum and 120°C for two hours. Sodium iodide stock solutions were made by dissolving the dried sodium iodide in redistilled water.

Sodium Perchlorate.--Amend Drug and Chemical, hydrated chemically pure, sodium perchlorate was used after drying under vacuum at 150° for ten hours. The sodium perchlorate was then removed, ground with mortar and pestle, and dried again under the same conditions for an additional ten hours.[49]

Sodium Thiosulfate.--Baker Analyzed Reagent sodium thiosulfate was used without purification. The sodium thiosulfate solutions were standardized against potassium dichromate. Potassium dichromate, 5 ml. aliquots, was treated with 0.2 gram of potassium iodide, 1 ml. of concentrated

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(49) *Ibid.*, p. 256.

hydrochloric acid, and titrated with the sodium thiosulfate solution to a yellow-green color. Starch indicator, 1 ml. of a 0.2 per cent solution, was added and the titration continued to the end-point, a sharp change from dark blue to light green. The sodium thiosulfate solutions were stabilized by adding enough sodium carbonate to give a 0.01 per cent solution of sodium carbonate.[50] Sodium thiosulfate solutions prepared in this manner were found to be relatively stable, changing in molarity to the extent of only one to two per cent per month.

<u>Starch</u>.--Baker Analyzed Reagent, Chemically Pure, potato starch was used without further purification. Starch solutions, 0.2 per cent, used for indicators were prepared by triturating two grams of starch and 10 mgms. of mercuric iodide with a little water to give a paste which was added to one liter of boiling water. The solution was boiled until clear, cooled and stored for use in a brown bottle.[51]

<u>Sulfuric Acid</u>.--du Pont, Chemically Pure Reagent, sulfuric acid was used without further purification.

<u>Thallium Perchlorate</u>.--City Chemical Corporation, Reagent Grade, thallium perchlorate was dried in an oven at 125° for three hours and then in a drying pistol which was heated for two hours by the vapor of boiling chlorobenzene. The pistol was connected to a water aspirator

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(50) I. M. Kolthoff and E. B. Sandell, <u>Textbook of Quantitative Analysis</u>, Third Edition, New York: The MacMillan Co., 1952, p. 594.

(51) <u>Ibid</u>., p. 589

through a calcium chloride drying tube and evacuated during the heating. The thallium perchlorate solution was then made by dissolving the thallium perchlorate in redistilled water.

Thionyl Chloride.--Eastman Kodak, White Label, thionyl chloride was used without further purification.

Water.--Distilled water was redistilled from potassium permanganate, 10 grams, and potassium hydroxide, 40 grams, in four liter volumes as needed.

CHAPTER IV

EXPERIMENTAL TECHNIQUES FOR KINETIC MEASUREMENTS

Iodination.--The multiple flask technique was employed throughout the course of the experimental work. The solvent used for all kinetic runs and stock solutions was redistilled water (see Chapter III). Kinetic runs were carried out in 50 ml., 100 ml., or 250 ml. red, low actinic volumetric flasks fitted with ground-glass stoppers which were lightly coated with silicone grease. All the stock solutions were thermostated in a Sargent constant temperature bath Model S-W 3c-82055 equipped with an automatic thermoregulator. For kinetic runs on 2,6-dibromophenol, the bath temperature was set at 50.0 ± 0.1^{0} as determined by a thermometer calibrated by the National Bureau of Standards.

Generally, a stock solution of sodium iodide, perchloric acid, and sodium perchlorate (enough to give the final solution an ionic strength of 0.300 $\underline{M}$) was first introduced into the reaction flasks at 50.0^{0}. The iodine solution was then added and finally 5.0 ml., 10.0 ml., or 25.0 ml. of a 4.4×10^{-4} $\underline{M}$ to 6.6×10^{-4} $\underline{M}$ solution of 2,6-dibromophenol. The flask was then shaken vigorously and the zero time of reaction was taken when one half of the solution of 2,6-dibromophenol had been introduced into the flask. To stop the reaction, a freshly prepared saturated solution of sodium iodide (one ml. per 50 ml. of reaction mixture) was injected into the reaction flasks with a syringe, the time recorded, and the flask shaken vigorously. The contents of the reaction flasks were rinsed into Erlenmeyer flasks and titrated to a starch end-point with a standard sodium thiosulfate solution (6.3×10^{-3} M to 1.3×10^{-2} M). Nine reaction flasks were used in each kinetic run, three of which contained all the reactants except 2,6-dibromophenol and were used as blanks in order to determine the initial stoichiometric iodine concentration. These blanks were determined near the beginning, middle, and end of the kinetic runs and were found to remain essentially constant at the iodide ion concentrations investigated.

Kinetic Runs in the Presence of Thallium Perchlorate.--Thallium perchlorate was used in kinetic runs in order to maintain a fairly low and constant iodide ion concentration. However, a major source of difficulty is encountered in the use of thallium perchlorate. It has been established that crystalline thallium iodide reacts with iodine and forms molecular complexes in the solid phase:[52,53]

$$6TlI + I_2 \longrightarrow Tl_6I8.$$

This reaction occurs at 25° at iodine concentrations greater than 0.76×10^{-5} M at iodine concentrations greater than 3.3×10^{-4} M a second complex is formed

$$Tl_6I_8 + 5I_2 \longrightarrow 6TlI_3$$

in which the per cent iodine tied up in the complex is still greater. Thus, it was found necessary to perform kinetic runs at iodine concentrations below 3.3×10^{-4} M in order to keep the major portion of iodine

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(52) W. Maitland and R. Abegg, Z. anorg. Chem., 49, 341 (1906).

(53) A. G. Sharpe, J. Chem. Soc., 2165 (1952).

from being precipitated as TlI_3. It was necessary to keep the iodine concentration above 2.0 x 10^{-4} M in order to have sufficient iodine for accurate titration.

Generally, a stock solution of perchloric acid, sodium perchlorate, and thallium perchlorate was pipetted into 50 ml. volumetric flasks thermostated at 50.0°. To reaction flasks containing this stock solution, sufficient sodium iodide was added to give a final iodide ion concentration of 1.5 x 10^{-4} M. Iodine solution of such a concentration that the final stoichiometric concentration would be below 3.3 x 10^{-4} M was then added. The sodium iodide was added in order to form seed crystals to induce the precipitation of the additional iodide ions formed in the course of the reaction. The reactants were usually allowed to equilibrate about an hour before the addition of 5.0 ml. of 2,6-dibromophenol solution. The reaction was stopped by pouring the contents of the flask into an Erlenmeyer flask containing an excess of standardized sodium thiosulfate solution. The contents of the reaction flask were rinsed with water and then 2.0 ml. of a saturated solution of sodium iodide was added to precipitate the thallium remaining in solution. The solution was then filtered through two medium porosity filter papers under mild suction. Five ml. of starch solution was added and the pale yellow solution was back-titrated with standardized iodine-sodium iodide solution until a pale blue-green color was attained and then back-titrated to a pale yellow solution with sodium thiosulfate solution.

Bromination.--The multiple flask technique was employed throughout the experimental work. The solvent used for kinetic runs 67-70 and stock solutions was 80.0 per cent, by weight, acetic acid. The solvent used for kinetic runs 74-79 was redistilled water. These kinetic runs were carried out in 50 ml. red, low actinic, volumetric flasks fitted with ground-glass stoppers which were lightly lubricated with silicone grease. All the stock solutions for kinetic runs at 20.1^{0} were thermostated in a Sargent constant temperature bath Model S-W 3c-82055 equipped with an automatic thermoregulator and cooled with a coil through which ethylene glycol was circulated by an "Aminco" refrigeration unit. For kinetic experiments at 0^{0}, an ice-water slurry in a Dewar flask was used as a constant temperature bath.

Generally, a stock solution of lithium perchlorate (sufficient to give a final ionic strength of 0.300 M) and hydrogen bromide was first introduced into the reaction flasks. Five ml. of a solution of 2,6-dibromophenol were then added. The reaction was started by the addition of 5 ml. of *ca*. 0.04 M bromine solution and the zero time of reaction was taken when one half of the bromine solution had drained into the reaction flask. The reaction was stopped by the addition of 2 ml. of saturated aqueous sodium iodide and the solution shaken and poured into 10 ml. of 4 M potassium hydroxide to prevent the oxidation of iodide to iodine. The solution was then titrated to a starch end-point with a standard sodium thiosulfate solution delivered from a 10.0 ml. burette. Nine reaction flasks were used in each kinetic run, three of which contained all the reactants except 2,6-dibromophenol and were used to determine the initial stoichiometric bromine concentration. These blanks were determined near the beginning, middle, and end of the kinetic run and were found to remain essentially constant.

Calculation of Apparent Rate Constants.--It was initially assumed that the reaction of 2,6-dibromophenol was first order in stoichiometric iodine or bromine and first order in the phenol. This assumption was later confirmed by experiment. A similar order has been established for phenol, anisole, and 4-nitrophenol. The apparent rate constants were calculated by the integrated rate equation

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

in which a and b designate the initial stoichiometric molar concentrations of iodine or bromine and substrate respectively and x is the molar concentration of stoichiometric iodine or bromine consumed in time t.[54] The units of k_{app} are (liter)$(\text{mole}^{-1})(\text{sec.}^{-1})$. In a typical run, this equation was used to calculate the apparent rate constants for various times and the calculated rate constants were extrapolated to zero time.

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(54) A. A. Frost and R. G. Pearson, Kinetics and Mechanism, New York: John Wiley and Son, Inc., 1953, p. 17.

CHAPTER V

KINETIC MEASUREMENTS UPON 2,6-DIBROMOPHENOL

Iodination.--Grovenstein and Henderson[1] found that their proposed mechanism for the iodination of phenol in water containing acetate-acetic acid buffer has the following rate expression at high iodide ion concentration:

$$\text{rate} = \frac{k_1[\text{ArHOH}][\text{I}_3^-][\text{H}_2\text{O}]}{[\text{H}^+][\text{I}^-]^2} + \frac{k_2[\text{ArHOH}][\text{I}_3^-][\text{HoAc}]}{[\text{H}^+]^2[\text{I}^-]^2} .$$

At low iodide ion concentration their rate expression assumes the form:

$$\text{rate} = k'_1[\text{ArHOH}][\text{I}_2] + \frac{k'_2[\text{ArHOH}][\text{I}_2]}{[\text{H}^+]}$$

in which k'_1 and k'_2 designate the rate constant for iodination by molecular iodine of phenol and phenoxide ion respectively.

Berliner's mechanism[21] for the iodination of phenol in acetate-acetic acid buffer leads to the rate expression of Grovenstein and Henderson at high iodide ion concentration. According to Berliner's mechanism, this expression should hold for the entire iodide ion range. However, the expression was only tested at rather high iodide ion concentration.

$$\text{I}_2 + \text{I}^- \overset{K_1}{\rightleftarrows} \text{I}_3^- \quad ; \quad K_1 = \frac{[\text{I}_3^-]}{[\text{I}_2][\text{I}^-]}\ ^{\star}$$

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*The equilibrium constants defined throughout this thesis are expressed in terms of concentrations rather than activities.

the two mechanism are kinetically indistinguishable at high iodide ion concentrations. However, if the reaction proceeds according to Grovenstein and Henderson's mechanism, it is expected that Berliner's rate constants should decrease with decreasing iodide ion concentration at low iodide ion concentrations.

At low iodide ion concentrations, the second order apparent rate constant (k_{app}) falls sharply as the reaction proceeds. This decrease is expected because the iodide ion concentration increases significantly as the reaction progresses. To obtain an apparent rate constant at the known initial iodide ion concentration, k_{app} was plotted versus the per cent reaction and the apparent rate constant at zero per cent reaction was obtained. At initially high iodide ion concentration where the per cent increase in iodide ion concentration is small relative to the initial iodide ion concentration, the values of k_{app} were relatively constant, and an average was taken.

Berliner's rate constant, defined as

$$k' = \frac{k_{app}K_1(I_2)[I^-]^2}{[I_3^-]} ,$$

was also calculated for each run from the extrapolated apparent rate constant. The rate constant k^x, defined as

$$k^x = k_{app}\frac{(I_2)}{[I_2]} ,$$

was calculated to account for the iodide tied up as triiodide ion.

Kinetic Reactions of 2,6-Dibromophenol.--In order to determine the effect of iodide ion concentration on the rate of reaction of 2,6-

dibromophenol, a wide range of iodide ion concentrations was studied at constant hydrogen ion concentration. The first kinetic run was performed at 25.055 x 10^{-4} M sodium iodide in the presence of perchloric acid and sodium perchlorate at 50.0° and ionic strength of 0.300. The results (Table 1, Run 16) indicate that there was no appreciable drop in the apparent rate constant throughout the reaction. This is expected at relatively high iodide ion concentration, since the amount of iodide ion formed during the reaction is relatively small. The plot of apparent rate constant versus per cent reaction, when extrapolated to zero per cent reaction, gave an apparent rate constant of 5.91 ± 0.35 x 10^{-3} l./mole sec. and a calculated value of k' of 3.19 x 10^{-5} sec.$^{-1}$ (see Table 1). Duplication of the same run gave an apparent rate constant of 5.97 ± 0.21 x 10^{-3} l./mole sec. and a calculated value of k' of 3.10 x 10^{-5} sec.$^{-1}$ (Table 2, Run 17).

Iodination of 2,6-dibromophenol at 5.612 x 10^{-4} M sodium iodide showed no appreciable drop in the apparent rate constant. The apparent rate constants were averaged to give an apparent rate constant of 3.90 ± 0.15 x 10^{-2} l./mole sec. and a calculated k' of 2.60 x 10^{-5} sec.$^{-1}$ (Table 3, Run 5). Duplication of the same kinetic run gave an apparent rate constant of 3.65 ± 0.14 x 10^{-2} l./mole sec. and a calculated value of k' of 2.46 x 10^{-5} sec.$^{-1}$ (Table 4, Run 6).

Iodination of 2,6-dibromophenol at 1.604 x 10^{-1} M sodium iodide gave an extrapolated value of the apparent rate constant of 1.19 ± 0.04 x 10^{-1} l./mole sec. and a calculated value of k' of 2.07 x 10^{-5} sec.$^{-1}$ (Table 5, Run 10). A duplicate kinetic run gave an extrapolated apparent rate constant of 1.20 ± 0.04 x 10^{-1} l./mole sec. and a calculated value of k' of 1.86 x 10^{-5} sec.$^{-1}$ (Table 6, Run 13).

The iodination of 2,6-dibromophenol at 0.5011 x 10^{-4} M sodium iodide gave an extrapolated apparent rate constant of 3.97 x 10^{-1} l./mole sec. and a calculated value of k' of 1.82 x 10^{-5} sec.$^{-1}$ (Table 7, Run 14). Duplication of the kinetic run gave an extrapolated apparent rate constant of 4.02 x 10^{-1} l./mole sec. and a calculated value of k' of 1.97 x 10^{-5} sec.$^{-1}$ (Table 8, Run 15).

The iodination of 2,6-dibromophenol at lower iodide ion concentration was desirable. However, due to difficulties in extrapolating at low iodide ion concentrations, no firm conclusion could be reached regarding the effect of iodide ion concentration on reaction rate at low iodide ion concentration. Therefore, the use of thallium ion to regulate the iodide ion concentration was next studied. In the presence of a high thallous ion concentration, the iodide ion concentration should remain constant during a kinetic run if the solution is initially saturated in thallium iodide since any additional iodide formed during the reaction should precipitate as thallium iodide.

A preliminary experiment on iodination of 2,6-dibromophenol in the presence of thallium ion indicated that the reaction was too fast to be studied in 0.021379 M $HClO_4$. The iodination was successfully carried out in the presence of thallium perchlorate (0.0500 M) at higher acidity (0.064137 M). The apparent rate constants were constant throughout the kinetic run and were averaged to give a value of 2.40 ± 0.03 x 10^{-1} l./mole sec. (Table 9, Run 60). A duplicate kinetic run was performed and gave an average apparent rate constant of 2.56 ± 0.14 x 10^{-1} l./mole sec. (Table 10, Run 62).

Kinetic Reactions of 2,6-Dibromophenol-4-d .--The preparation of 2,6-dibromophenol-4-d is described in Chapter III. The iodination of once equilibrated 2,6-dibromophenol (this compound is designated as partially deuterated 2,6-dibromophenol) was studied under the conditions of 5.612×10^{-4} M (Tables 11 and 12, Runs 33 and 38) and 0.5011×10^{-4} M (Tables 13 and 14, Runs 28 and 29) sodium iodide, 0.021379 M perchloric acid and 0.300 ionic strength at 50.0°. The extrapolated value of the apparent rate constant at 5.612×10^{-4} M sodium iodide was 8.40×10^{-3} l./mole sec. and 8.65×10^{-3} l./mole sec. in a duplicate run. The average value of the two rate constants of the protio compound (Tables 3 and 4, Runs 5 and 6) and a deuterium isotope effect of $(k^{H}_{app}/k^{D}_{app})$ of 4.43 was obtained. The iodination of partially deuterated 2,6-dibromophenol at 0.5011×10^{-4} M sodium iodide gave extrapolated values of the apparent rate constant of 9.04×10^{-2} l./mole sec. and 9.02×10^{-2} l./mole sec. (Tables 13 and 14, Runs 28 and 29). Comparison with the average values for the protio compound (Tables 7 and 8, Runs 14 and 15) gave a deuterium isotope effect of 4.42.

The iodination of 2,6-dibromophenol-4-d (prepared by two equilibrations with heavy water) was studied at 5.612×10^{-4} M sodium iodide in order to see if any change in the magnitude of the deuterium isotope effect resulted. The average value of the apparent rate constant gave a value of $6.66 \pm 0.37 \times 10^{-3}$ l./mole sec. and a calculated value of k' of 4.07×10^{-6} sec.$^{-1}$ (Table 15, Run 46). Duplication of the kinetic run gave an apparent average rate constant of $6.43 \pm 0.41 \times 10^{-3}$ l./mole sec. and a calculated value of k' of 4.09×10^{-6} sec.$^{-1}$ (Table 16, Run 48). Comparison with the values of the protio compound

(Tables 3 and 4, Runs 5 and 6) gives a value of 5.8 ± 0.6 for the deuterium isotope effect (k^{H}_{app}/k^{D}_{app}).

The iodination of 2,6-dibromophenol-4-d in 1.604 x 10^{-4} M sodium iodide was performed and the average value of the apparent rate constant was 2.53 ± 0.03 x 10^{-2} l./mole sec. with a calculated k' of 4.06 x 10^{-6} sec.$^{-1}$ (Table 17, Run 49). Duplication of the kinetic run gave an average apparent rate constant of 2.53 ± 0.09 x 10^{-2} l./mole sec. and a calculated k' of 4.08 x 10^{-6} sec.$^{-1}$ (Table 18, Run 50). Comparison with the protio compound (Tables 5 and 6, Runs 10 and 13) gives a deuterium isotope effect of 4.7 ± 0.2 (k^{H}_{app}/k^{D}_{app}).

The iodination of 2,6-dibromophenol-4-d in 0.5011 x 10^{-4} M sodium iodide gave an extrapolated value for the apparent rate constant of 7.88 x 10^{-2} l./mole sec. and a calculated k' of 3.90 x 10^{-6} sec.$^{-1}$ (Table 19, Run 41). Duplication of the kinetic run gave an apparent rate constant of 7.90 x 10^{-2} l./mole sec. and a calculated k' of 3.91 x 10^{-6} sec.$^{-1}$ (Table 20, Run 42). Comparison with the values for the corresponding protio runs gives an isotope effect of 5.1 ± 0.1 (k^{H}_{app}/k^{D}_{app}).

The iodination of 2,6-dibromophenol-4-d in the presence of thallium perchlorate (0.0500 M) was performed in perchloric acid solution (0.064137 M). The average value of the apparent rate constant was 6.22 ± 0.33 x 10^{-2} l./mole sec. (Table 21, Run 63). Duplication of the kinetic run gave a value of 6.27 ± 0.58 x 10^{-2} l./mole sec. for the apparent rate constant (Table 22, Run 64). Comparison with apparent rate constants of the protio compound gives a deuterium isotope effect of 4.0 ± 0.4 (k^{H}_{app}/k^{D}_{app}).

Table 1

Run 16, 2,6-Dibromophenol in 25.055×10^{-4} M Sodium Iodide Solution at 50.0°

$(DBP)_0$ - 0.0006576 M

$(I_2)_0$ - 0.0002024 M

$(NaI)_0$ - 25.055×10^{-4} M

$(HClO_4)$ - 0.021379 M

$(NaClO_4)$ - 0.2761 M

$(Na_2S_2O_3)$ - 0.006300 M

100.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate Constant x 10^3 (l./mole sec.)	Per cent reaction
(blank)	6.42		0.00
84,030	4.56	6.52	29.03
167,507	3.74	6.11	59.23
250,293	2.62	5.78	66.38
421,078	2.16	6.13	76.34
524,285	1.27	5.61	80.23

Average value of rate constant $(k_{app}) = 5.91 \pm 0.35 \times 10^{-3}$ l./mole sec.

$k' = 3.19 \times 10^{-5}$ sec.$^{-1}$

$k^x = 1.32 \times 10^{-2}$ l./mole sec.

$1/k^x \times [H^+] = 3.54 \times 10^3$ sec.

$[I^-]_0 = 23.962 \times 10^{-4}$ M

Table 2

Run 17, 2,6-Dibromophenol in 25.055 x 10^{-4} M Sodium Iodide Solution at 50.0°

$(DBP)_0$ - 0.0006576 M

$(I_2)_0$ - 0.0002032 M

$(NaI)_0$ - 25.055 x 10^{-4} M

$(HClO_4)$ - 0.021379 M

$(NaClO_4)$ - 0.2761 M

$(Na_2S_2O_3)$ - 0.006300 M

100.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant x 10^4 (l./mole sec.)	Per cent reaction
(blank)	6.45		0.00
79,796	4.38	6.35	32.10
153,217	3.77	5.74	41.56
246,374	2.65	6.15	58.92
336,951	2.20	5.54	65.87
411,851	1.63	6.00	74.73
412,107	1.60	6.03	75.20

Average value of rate constant (k_{app}) = 5.97 ± 0.21 x 10^{-3} l./mole sec.

k' = 3.10 x 10^{-5} $sec.^{-1}$

k^x = 1.29 x 10^{-2} l./mole sec.

$1/k^x$ x $[H^+]$ = 3.62 x 10^3 sec.

$[I^-]_0$ = 23.958 x 10^{-4} M

Table 3

Run 5, 2,6-Dibromophenol in 5.612 x 10^{-4} M Sodium Iodide Solution at 50.0°

$(DBP)_0$	- 0.0006458 M	$(HClO_4)$	- 0.021379 M
$(I_2)_0$	- 0.0001544 M	$(NaClO_4)$	- 0.2776 M
$(NaI)_0$	- 5.612 x 10^{-4} M	$(Na_2S_2p_3)$	- 0.004519 M

100.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant x 10^2 (l./mole sec.)	Per cent reaction
(blank)	6.83		0.00
3389	6.27	3.95	8.22
3578	6.25	3.91	8.55
5426	6.03	3.63	11.79
6835	5.80	3.79	16.05
10,319	5.21	4.20	25.22

Average value of rate constant $(k_{app}) = 3.90 \pm 0.15 \times 10^{-2}$ l./mole sec.

$k' = 2.60 \times 10^{-5}$ sec.$^{-1}$

$k^x = 4.90 \times 10^{-2}$ l./mole sec.

$1/k^x \times [H^+] = 9.55 \times 10^2$ sec.

$[I^-]_0 = 5.294 \times 10^{-4}$ M

Table 4

Run 6, 2,6-Dibromophenol in 5.612 x 10^{-4} M Sodium Iodide Solution at 50.0°

$(DBP)_0$ - 0.0006458 M

$(I_2)_0$ - 0.0001320 M

$(NaI)_0$ - 5.6120 x 10^{-4} M

$(HClO_4)$ - 0.021379 M

$(NaClO_4)$ - 0.2776 M

$(Na_2S_2O_3)$ - 0.004519

100.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant x 10^2 (l./mole sec.)	Per cent reaction
(blank)	5.83		0.00
2792	5.44	3.97	6.86
5526	5.15	3.56	11.78
5665	5.10	3.76	12.69
7808	4.91	3.51	15.96
10,081	4.62	3.68	20.88
12,836	4.44	3.40	23.99
15,137	4.12	3.69	29.45

Average value of rate constant $(k_{app}) = 3.65 \pm 0.14 \times 10^{-2}$ l./mole sec.

$k' = 2.46 \times 10^{-5}$ sec.$^{-1}$

$k^x = 4.60 \times 10^{-2}$ l./mole sec.

$1/k^x \times [H^+] = 1.02 \times 10^3$ sec.

$[I^-]_0 = 5.338 \times 10^{-4}$ M

Table 5

Run 10, 2,6-Dibromophenol in 1.604×10^{-4} M Sodium Iodide Solution at 50.0°

$(DBP)_0$ - 0.0005928 M	$(HClO_4)$ - 0.021379 M
$(I_2)_0$ - 0.0001240 M	$(NaClO_4)$ - 0.2782 M
$(NaI)_0$ - 1.604×10^{-4} M	$(Na_2S_2O_3)$ - 0.003013 M

100.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant x 10^4 (l./mole sec.)	Per cent reaction
(blank)	8.23		0.00
1367	7.42	1.28	9.84
2034	7.15	1.18	13.12
2585	6.90	1.17	16.16
3120	6.64	1.19	19.32
3694	6.48	1.12	21.26

Average value of rate constant $(k_{app}) = 1.19 \pm 0.04 \times 10^{-1}$ l./mole sec.

$k' = 2.07 \times 10^{-5}$ sec.$^{-1}$

$k^x = 1.36 \times 10^{-1}$ l./mole sec.

$1/k^x \times [H^+] = 3.44 \times 10^2$ sec.

$[I^-]_0 = 1.518 \times 10^{-4}$ M

Table 6

Run 13, 2,6-Dibromophenol in 1.604×10^{-4} M Sodium Iodide Solution at 50.0°

$(DBP)_0$ - 0.0006420 M

$(I_2)_0$ - 0.0002478 M

$(NaI)_0$ - 5.612×10^{-4} M

$(HClO_4)$ - 0.021379 M

$(NaClO_4)$ - 0.2782 M

$(Na_2S_2O_3)$- 0.006026 M

100.0 ml. of reaction mixture per flask.

Time elapsed (sec.)	Titer (ml.)	Rate constant x 10^4 (l./mole sec.)	Per cent reaction
(blank)	8.23		0.00
1631	7.23	1.26	12.08
2347	6.86	1.24	16.58
3269	6.43	1.23	21.80
4267	6.17	1.11	24.87
5162	5.68	1.20	30.93
6076	5.36	1.18	34.87

Average value of rate constant $(k_{app}) = 1.20 \pm 0.04 \times 10^{-1}$ l./mole sec.

$k' = 1.86 \times 10^{-5}$ sec.$^{-1}$

$k^x = 1.29 \times 10^{-1}$ l./mole sec.

$1/k^x \times [H^+] = 3.64 \times 10^2$ sec.

$[I^-]_0 = 1.440 \times 10^{-4}$ M

Table 7

Run 14, 2,6-Dibromophenol in 0.5011×10^{-4} M Sodium Iodide Solution at 50.0°

$(DBP)_0$	- 0.0006420 M	$(HClO_4)$	- 0.021379 M
$(I_2)_0$	- 0.0002581 M	$(NaClO_4)$	- 0.2786 M
$(NaI)_0$	- 0.5011×10^{-4} M	$(Na_2S_2O_3)$	- 0.006026 M

100.0 ml. of reaction mixture per flask.

Time elapsed (sec.)	Titer (ml.)	Rate constant x 10 (l./mole sec.)	Per cent reaction
(blank)	8.57		0.00
477	7.71	3.52	10.01
884	7.17	3.27	16.31
1465	6.63	2.86	22.61
2089	6.15	2.63	28.21
2612	5.86	2.43	21.60
3037	5.60	2.36	34.64

Rate constant extrapolated to zero time $(k_{app}) = 2.97 \times 10^{-1}$ l./mole sec.

$k' = 1.82 \times 10^{-5}$ sec.$^{-1}$

$k^x = 4.07 \times 10^{-1}$ l./mole sec.

$1/k^x \times [H^+] = 1.15 \times 10^2$ sec.

$[I^-]_0 = 0.4461 \times 10^{-4}$ M

Table 8

Run 15, 2,6-Dibromophenol in 0.5011 x 10^{-4} M Sodium Iodide Solution at 50.0°

$(DBP)_0$ - 0.0005136 M

$(I_2)_0$ - 0.0001016 M

$(NaI)_0$ - 0.5011 x 10^{-4} M

$(HClO_4)$ - 0.021379 M

$(NaClO_4)$ - 0.2786 M

$(Na_2S_2O_3)$ - 0.005649 M

250.0 ml. of reaction mixture per flask.

Time elapsed (sec.)	Titer (ml.)	Rate constant x 10^4 (l./mole sec.)	Per cent reaction
(blank)	8.99		0.00
686	7.84	3.93	12.77
1278	7.07	3.74	21.35
1315	7.04	3.70	21.69
1900	6.45	3.52	28.25
2399	5.90	3.55	34.37

Rate constant extrapolated to zerp times (k_{app}) = 4.02 x 10^{-1} l./mole sec.

k' = 1.97 x 10^{-5} sec.$^{-1}$

k^x = 4.11 x 10^{-1} l./mole sec.

$1/k^x \times [H^+]$ = 1.14 x 10^2 sec.

$[I^-]_0$ = 0.4779 x 10^{-4} M

Table 9

Run 60, 2,6-Dibromophenol in 0.0500 M Thallium Perchlorate Solution at 50.0°

$(DBP)_0$ - 0.0004351 M

$(I_2)_0$ - 0.0003380 M

$(NaI)_0$ - 0.00015 M

$(TlClO_4)_0$ - 0.0500 M

$(HClO_4)$ - 0.064137 M

$(NaClO_4)$ - 0.1857 M

$(Na_2S_2O_3)$ - 0.008414 M

50.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant x 10 (l./mole sec.)	Per cent reaction
(blank)	4.02		0.00
483	3.83	2.35	4.78
973	3.64	2.41	9.32
1379	3.52	2.38	12.63
1769	3.38	2.40	15.86
2210	3.28	2.48	19.82

Average value of rate constant $(k_{app}) = 2.40 \pm 0.03 \times 10^{-1}$ l./mole sec.

Table 10

Run 62, 2,6-Dibromophenol in 0.0500 M Thallium Perchlorate Solution at 50.0°

$(DBP)_0$ - 0.0004351 M

$(I_2)_0$ - 0.0002707 M

$(NaI)_0$ - 0.00015 M

$(TlClO_4)_0$ - 0.0500 M

$(HClO_4)$ - 0.064137 M

$(NaClO_4)$ - 0.1857 M

$(Na_2S_2O_3)$ - 0.008414

50.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant x 10 (l./mole sec.)	Per cent reaction
(blank)	3.24		0.00
895	2.89	2.80	10.01
1337	2.80	2.46	12.81
1822	2.65	2.62	17.75
2421	2.56	2.30	20.27
3497	2.25	2.60	29.89

Average value of rate constant $(k_{app}) = 2.56 \pm 0.14 \times 10^{-1}$ l./mole sec.

Table 11

Run 33, 2,6-Dibromophenol-4-d in 6.612 x 10^{-4} M Sodium Iodide Solution at 50.0°

$(DBP\text{-}d)_0^*$ - 0.0006337 M
$(HClO_4)$ - 0.021379 M

$(I_2)_0$ - 0.002393 M
$(NaClO_4)$ - 0.2776 M

$(NaI)_0$ - 5.612 x 10^{-4} M
$(Na_2S_2O_3)$ - 0.01260 M

100.0 ml. of reaction mixture per flask.

Time elapsed (sec.)	Titer (ml.)	Rate constant x 10^3 (l./mole sec.)	Per cent reaction
(blank)	3.80		0.00
20,566	3.43	8.00	9.72
33,191	3.23	7.94	14.99
49,036	3.01	7.81	20.77
68,782	2.78	7.58	26.83
86,994	2.60	7.36	31.57
104,479	2.48	6.94	34.73

Rate constant extrapolated to zero time (k_{app}) = 8.40 x 10^{-3} l./mole sec.

k' = 5.41 x 10^{-6} $sec.^{-1}$

k^x = 1.05 x 10^{-2} l./mole sec.

$1/k^x \times [H^+]$ = 4.44 x 10^3 sec.

$[I^-]_0$ = 5.132 x 10^{-4} M

---

*This compound was partially deuterated.

Table 12

Run 38, 2,6-Dibromophenol-4-d in 5.612×10^{-4} M Sodium Iodide Solution at 50.0^{0}

$(\text{DBP-d})_0^*$	- 0.0006144 M	$(HClO_4)$	- 0.021379 M
$(I_2)_0$	- 0.0002584 M	$(NaClO_4)$	- 0.2776 M
$(NaI)_0$	- 5.612×10^{-4} M	$(Na_2S_2O_3)$	- 0.01260 M

100.0 ml. of reaction mixture per flask.

Time elapsed (sec.)	Titer (ml.)	Rate constant x 10^3 (l./mole sec.)	Per cent reaction
(blank)	4.10		0.00
20,780	3.70	8.26	9.81
21,262	3.70	8.07	9.81
33,175	3.55	7.31	13.47
63,857	3.20	6.66	22.00
72,690	3.10	6.64	24.44
88,204	2.98	6.29	27.36

Rate constant extrapolated to zero time $(k_{app}) = 8.65 \times 10^{-3}$ l./mole sec.

$k' = 5.64 \times 10^{-6}$ sec.$^{-1}$

$k^x = 1.11 \times 10^{-2}$ l./mole sec.

$1/k^x \times [H^+] = 4.21 \times 10^3$ sec.

$[I^-]_0 = 5.106 \times 10^4$ M

---

*This compound was partially deuterated.

Table 13

Run 28, 2,6-Dibromophenol-4-d in 0.5011 x 10^{-4} M Sodium Iodide Solution at 50.0°

$(DBP\text{-}d)_0^*$ - 0.0006391 M

$(I_2)_0$ - 0.0002262 M

$(NaI)_0$ - 0.5011 x 10^{-4} M

$(HClO_4)$ - 0.021379 M

$(NaClO_4)$ - 0.2786 M

$(Na_2S_2O_3)$ - 0.006293 M

100.0 ml. of reaction mixture per flask.

Time elapsed (sec.)	Titer (ml.)	Rate constant x 10^2 (l./mole sec.)	Per cent reaction
(blank)	7.19		0.00
1086	6.73	9.62	6.39
1582	6.57	9.05	8.62
2399	6.42	7.76	10.70
3996	6.09	6.68	15.29
7546	5.49	5.90	23.64
11,043	5.10	5.15	29.06

Rate constant extrapolated to zero time (k_{app}) = 9.04 x 10^{-2} l./mole sec.

k' = 3.98 x 10^{-6} $sec.^{-1}$

k^x = 8.84 x 10^{-2} l./mole sec.

$1/k^x \times [H^+]$ = 5.29 x 10^2 sec.

$[I^-]_0$ = 0.4501 x 10^{-4} M

---

*This compound was partially deuterated.

Table 14

Run 29, 2,6-Dibromophenol-4-d in 0.5011×10^{-4} M Sodium Iodide Solution at 50.0°

$(DBP\text{-}d)_0^*$ - 0.0006393 M

$(I_2)_0$ - 0.0001114 M

$(NaI)_0$ - 0.5011×10^{-4} M

$(HClO_4)$ - 0.021379 M

$(NaClO_4)$ - 0.2786 M

$(Na_2S_2O_3)$ - 0.008390 M

100.0 ml. of reaction mixture per flask.

Time elapsed (sec.)	Titer (ml.)	Rate constant x 10^2 (l./mole sec.)	Per cent reaction
(blank)	2.65		0.00
1759	2.43	7.93	8.52
2399	2.35	8.04	11.49
3507	2.24	7.69	15.63
5179	2.11	7.07	20.53
6790	1.98	6.92	25.42
8377	1.89	6.52	28.81

Rate constant extrapolated to zero time (k_{app}) = 9.02×10^{-2} l./mole sec.

$k' = 4.39 \times 10^{-6}$ sec.$^{-1}$

$k^x = 9.23 \times 10^{-2}$ l./mole sec.

$1/k^x \times [H^+] = 5.07 \times 10^2$ sec.

$[I^-]_0 = 0.4758 \times 10^{-5}$ M

---

*This compound was partially deuterated.

Table 15

Run 46, 2,6-Dibromophenol-4-d in 5.612 x 10^{-4} $\underline{M}$ Sodium Iodide Solution at 50.0°

$(DBP)_0$	- 0.0006002 $\underline{M}$	$(HClO_4)$	- 0.021379 $\underline{M}$
$(I_2)_0$	- 0.0001624 $\underline{M}$	$(NaClO_4)$	- 0.21379 $\underline{M}$
$(NaI)_0$	- 5.612 x 10^{-4} $\underline{M}$	$(Na_2S_2O_3)$	- 0.008370 $\underline{M}$

100.0 ml. of reaction mixture per flask.

Time elapsed (sec.)	Titer (ml.)	Rate constant x 10^4 (l./mole sec.)	Per cent reaction
(blank)	3.88		0.00
18,300	3.58	7.41	7.73
29,816	3.44	6.83	11.37
43,216	3.28	6.61	15.46
59,511	3.12	6.28	19.58
78,588	2.87	6.17	26.03

Average value of rate constant (k_{app}) = 6.66 ± 0.37 x 10^{-3} l./mole sec.

$k' = 4.07 \times 10^{-6}$ sec.$^{-1}$

$k^x = 7.75 \times 10^{-3}$ l./mole sec.

$1/k^x \times [H^+]_0 = 5.262 \times 10^{-4}$ $\underline{M}$

Table 16

Run 48, 2,6-Dibromophenol-4-d in 5.612 x 10^{-4} M Sodium Iodide Solution at 50.0°

$(DBP)_0$	- 0.0006100 M	$(HClO_4)$	- 0.021379 M
$(I_2)_0$	- 0.0001745 M	$(NaClO_4)$	- 0.2776 M
$(NaI)_0$	- 5.612 x 10^{-4} M	$(Na_2S_2O_3)$	- 0.008370 M

100.0 ml. of reaction mixture per flask.

Time elapsed (sec.)	Titer (ml.)	Rate constant x 10^4 (l./mole sec.)	Per cent reaction
(blank)	4.17		0.00
21,776	3.80	7.09	8.87
35,393	3.62	6.70	13.19
45,058	5.50	6.53	16.07
56,718	3.40	6.07	18.46
71,349	3.27	5.77	21.58

Average value of rate constant $(k_{app}) = 6.43 \pm 0.41 \times 10^{-3}$ l./mole sec.

$k' = 4.09 \times 10^{-6}$ sec.$^{-1}$

$k^x = 7.80 \times 10^{-3}$ l./mole sec.

$1/k^x \times [H^+] = 6.01 \times 10^3$ sec.

$[I^-]_0 = 5.255 \times 10^{-4}$ M

Table 17

Run 49, 2,6-Dibromophenol-4-d in 1.604 x 10^{-4} M Sodium Iodide Solution at 50.0°

$(DBP\text{-}d)_0$ - 0.0005978 M

$(I_2)_0$ - 0.0001526 M

$(NaI)_0$ - 1.604 x 10^{-4} M

$(HClO_4)$ - 0.021379 M

$(NaClO_4)$ - 0.2782 M

$(Na_2S_2O_3)$ - 0.008370 M

100.0 ml. of reaction mixture per flask.

Time elapsed (sec.)	Titer (ml.)	Rate constant x 10^2 (l./mole sec.)	Per cent reaction
(blank)	3.65		0.00
7143	3.28	2.51	10.05
7335	3.27	2.52	10.32
10,663	3.10	2.60	14.99
14,564	2.94	2.54	19.38
18,443	2.78	2.54	23.77
18,577	2.80	2.46	23.22
22,562	2.62	2.57	27.49

Average value of rate constant (k_{app}) = 2.53 ± 0.03 x 10^{-2} l./mole sec.

k' = 4.06 x 10^{-6} $sec.^{-1}$

k^x = 2.71 x 10^{-2} l./mole sec.

$1/k^x \times [H^+]$ = 1.73 x 10^3 sec.

$[I^-]_0$ = 1.499 x 10^{-4} M

Table 18

Run 50, 2,6-Dibromophenol-4-d in 1.604×10^{-4} M Sodium Iodide Solution at 50.0°

$(DBP\text{-}d)_0$ - 0.0005962 M

$(I_2)_0$ - 0.0001667 M

$(NaI)_0$ - 1.604×10^{-4} M

$(HClO_4)$ - 0.021379 M

$(NaClO_4)$ - 0.2782 M

$(Na_2S_2O_3)$ - 0.008370 M

100.0 ml. of reaction mixture per flask.

Time elapsed (sec.)	Titer (ml.)	Rate constant x 10^2 (l./mole sec.)	Per cent reaction
(blank)	3.98		0.00
6198	3.61	2.70	9.37
6283	3.63	2.51	8.87
6377	3.62	2.55	9.13
10,643	3.43	2.40	13.89
14,172	3.21	2.63	19.41
17,427	3.12	2.43	21.67
20,314	2.98	2.49	25.19

Average value of rate constant $(k_{app}) = 2.53 \pm 0.09 \times 10^{-2}$ l./mole sec.

$k' = 4.08 \times 10^{-6}$ sec.$^{-1}$

$k^x = 2.74 \times 10^{-2}$ l./mole sec.

$1/k^x \times [H^+] = 1.71 \times 10^3$ sec

$[I^-]_0 = 1.491 \times 10^{-4}$ M

Table 19

Run 41, 2,6-Dibromophenol-4-d in 0.5011 x 10^{-4} $\underline{M}$ Sodium Iodide Solution at 50.0°

$(DBP\text{-}d)_0$ - 0.0006176 $\underline{M}$

$(I_2)_0$ - 0.0001356 $\underline{M}$

$(NaI)_0$ - 0.5011 x 10^{-4} $\underline{M}$

$(HClO_4)$ - 0.021379 $\underline{M}$

$(NaClO_4)$ - 0.2786 $\underline{M}$

$(Na_2S_2O_3)$ - 0.006298 $\underline{M}$

100.0 ml. of reaction mixture per flask.

Time elapsed (sec.)	Titer (ml.)	Rate constant x 10^2 (l./mole sec.)	Per cent reaction
(blank)	4.31		0.00
2433	3.85	7.37	10.60
4603	3.52	7.07	18.27
5790	3.35	7.03	22.21
6790	3.25	6.74	24.54
6986	3.23	6.70	25.00

Rate constant extrapolated to zero time (k_{app}) = 7.88 x 10^{-2} l./mole sec.

k' = 3.90 x 10^{-6} $sec.^{-1}$

k^x = 8.28 x 10^{-2} l./mole sec.

$1/k^x \times [H^+]$ = 5.65 x 10^2 sec.

$[I^-]_0$ = 0.4713 x 10^{-4} $\underline{M}$

Table 20

Run 42, 2,6-Dibromophenol-4-d in 0.5011 x 10^{-4} M Sodium Iodide Solution at 50.0°

$(DBP\text{-}d)_0$ - 0.0005907 M	$(HClO_4)$ - 0.021379 M
$(I_2)_0$ - 0.0001324 M	$(NaClO_4)$ - 0.2786 M
$(NaI)_0$ - 0.5011 x 10^{-4} M	$(Na_2S_2O_3)$ - 0.0006298 M

100.0 ml. of reaction mixture per flask.

Time elapsed (sec.)	Titer (ml.)	Rate constant x 10^2 (l./mole sec.)	Per cent reaction
(blank)	4.20		0.00
2409	3.78	7.55	10.07
2400	3.78	7.58	10.07
3680	3.57	7.48	15.06
4935	3.41	7.41	18.87
5815	3.28	7.01	21.96
6933	3.18	6.76	24.34
8214	3.06	6.76	27.20

Rate constant extrapolated to zero time (k_{app}) = 7.90 x 10^{-2} l./mole sec.

$k' = 3.91 \times 10^{-6}$ sec.$^{-1}$

$k^x = 8.29 \times 10^{-2}$ l./mole sec.

$1/k^x \times [H^+] = 5.63 \times 10^2$ sec.

$[I^-]_0 = 0.4715 \times 10^{-4}$ M

Table 21

Run 63, 2,6-Dibromophenol-4-d in 0.0500 M Thallium Perchlorate Solution at 50.0°

(DBP-d)$_0$ - 0.0004308 M

(HClO$_4$) - 0.064137 M

(I$_2$)$_0$ - 0.0002740 M

(NaClO$_4$) - 0.1857 M

(NaI)$_0$ - 0.00015 M

(Na$_2$S$_2$O$_3$) - 0.008414 M

(TlClO$_4$)$_0$ - 0.0500 M

50.0 ml. of reaction mixture per flask.

Time elapsed (sec.)	Titer (ml.)	Rate constant x 10^2 (l./mole sec.)	Per cent reaction
(blank)	3.27		0.00
5270	2.86	5.93	12.12
7964	2.76	6.27	18.25
10,095	2.49	6.93	24.18
11,111	2.49	6.29	24.18
12,116	2.52	5.68	24.10

Average value of rate constant (k_{app}) = $6.22 \pm 0.33 \times 10^{-2}$ l./mole sec.

Table 22

Run 64, 2,6-Dibromophenol-4-d in 0.0500 M Thallium Perchlorate Solution at 50.0°

$(\text{DBP-d})_0$ - 0.0004308 M

$(I_2)_0$ - 0.0002725 M

$(\text{NaI})_0$ - 0.00015 M

$(\text{TlClO}_4)_0$ - 0.0500 M

(HClO_4) - 0.064137 M

(NaClO_4) - 0.1857 M

$(\text{Na}_2\text{S}_2\text{O}_3)$ - 0.008414 M

50.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant x 10^2 (l./mole sec.)	Per cent reaction
(blank)	4.24		0.00
4336	2.95	5.05	8.95
5570	2.82	6.05	12.95
6697	2.69	6.84	16.95
7881	2.68	5.93	17.30
8955	2.49	7.41	23.20

Average value of rate constant $(k_{app}) = 6.27 \pm 0.58 \times 10^{-2}$ l./mole sec.

Bromination.--Grovenstein and Henderson[1] found the rate of bromination of 2,6-dibromophenol to be proportional to the actual bromine concentration and inversely dependent upon the hydrogen ion concentration between zero and first power. Their proposed mechanism, in which molecular bromine reacts with both the phenol and phenoxide ion, may be expressed as

$$\text{rate} = k^x(\text{ArHOH})[\text{Br}_2] = k[\text{Br}_2](\text{ArHOH}) + k_2 \frac{(\text{ArHOH})}{[\text{H}^+]} .$$

The constant k^x should remain constant at constant hydrogen ion concentration and may be calculated from k_{app} by the relationship

$$k^x = \frac{k_{app}K_1(\text{Br}_2)[\text{Br}^-]}{[\text{Br}_3^-]} ,$$

where K_1 is the equilibrium constant for the reaction

$$\text{Br}_2 + \text{Br}^- \overset{K_1}{\rightleftarrows} \text{Br}_3^- \quad ; \quad K_1 = \frac{[\text{Br}_3^-]}{[\text{Br}_2][\text{Br}^-]}$$

Kinetic Reactions of 2,6-Dibromophenol and 2,6-Dibromophenol-4-d.--In order to determine the magnitude of the deuterium isotope effect in the bromination of 2,6-dibromophenol, conditions closely corresponding to Gorvenstein and Henderson's were employed. Hydrogen bromide (0.100 M) and lithium perchlorate (0.200 M) were used to give an ionic strength of 0.300 in 80.0 per cent acetic acid (by weight) at 20.0°. The results show no appreciable drop in the apparent rate constants throughout the course of the reaction and average of the apparent rate constants was used. The first run on the protium compound gave an apparent rate constant of 1.03 ± 0.05 l./mole sec. (Table 23, Run 67).

Table 23

Run 67, 2,6-Dibromophenol in 80.0 per cent acetic acid at 20.1°

$(DBP)_0$ - 0.002453 M

$(Br_2)_0$ - 0.003567 M

(HBr) - 0.100 M

$(LiClO_4)$ - 0.200 M

$(Na_2S_2O_3)$ - 0.02050 M

50.0 ml. of reaction mixture per flask.

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mole sec.)	Per cent reaction
(blank)	17.40		0.00
121	13.31	1.12	23.5
182	12.40	1.00	29.8
300	10.45	1.08	39.9
449	9.20	1.04	47.1
642	8.28	0.97	52.4
929	7.30	0.96	58.0

Average value of rate constant (k_{app}) = 1.03 ± 0.05 l./mole sec.

$[Br^-]_0 = 9.679 \times 10^{-2}$ M

h^x = 1.03 l./mole sec.

Table 24

Run 68, 2,6-Dibromophenol in 80.0 per cent acetic acid at 20.1°

$(DBP)_0$ - 0.002453 M

$(Br_2)_0$ - 0.003433 M

(HBr) - 0.100 M

$(LiClO_4)$ - 0.200 M

$(Na_2S_2O_3)$ - 0.02050 M

50.0 ml. of reaction mixture per flask.

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mole sec.)	Per cent reaction
(blank)	17.29		0.00
180	12.05	1.09	30.3
481	8.80	1.07	49.1
480	8.80	1.07	49.1
596	8.35	0.99	51.7
910	7.15	1.00	58.6

Average value of rate constant (k_{app}) = 1.04 ± 0.04 l./mole sec.

$[Br^-]_0 = 9.672 \times 10^{-2}$ M

k^x = 1.02 l./mole sec.

Table 25

Run 69, 2,6-Dibromophenol-4-d in 80.0 per cent acetic acid at 20.1°

$(\text{DBP-d})_0$ - 0.002238 M

$(\text{Br}_2)_0$ - 0.003481 M

(HBr) - 0.100 M

(LiClO_4) - 0.200 M

$(\text{Na}_2\text{S}_2\text{O}_3)$ - 0.02050 M

50.0 ml. of reaction mixture per flask.

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mole sec.)	Per cent reaction
(blank)	16.98		0.00
196	12.78	0.817	24.7
317	11.60	0.776	31.7
521	9.92	0.777	41.6
631	9.35	0.818	44.9
900	8.00	0.823	52.9

Average value of rate constant (k_{app}) = 0.802 ± 0.019 l./mole sec.

$[\text{Br}^-]_0$ - 9.687×10^{-2} M

k^x = 0.802 l./mole sec.

Table 26

Run 70, 2,6-Dibromophenol-4-d in 80.0 per cent acetic acid at 20.1°

$(DBP\text{-}d)_0$ - 0.002265 M (HBr) - 0.100 M

$(Br_2)_0$ - 0.003428 M $(LiClO_4)$ - 0.200 M

$(Na_2S_2O_3)$ - 0.0205 M

50.0 ml. of reaction mixture per flask.

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mole sec.)	Per cent reaction
(blank)	16.72		0.00
191	12.75	0.784	23.7
312	11.15	0.817	33.3
480	9.88	0.787	40.9
600	9.08	0.811	45.7
600	9.08	0.811	45.7

Average value of rate constant (k_{app}) = 0.802 ± 0.013 l./mole sec.

$[Br^-]_0$ - 9.69×10^{-2} M

k^x = 0.799 l./mole sec.

Table 27

Run 74, 2,6-Dibromophenol in 2.000 M Hydrogen Bromide at 0°

$(DBP)_0$ - 0.0003737 M (HBr) - 2.000 M

$(Br_2)_0$ - 0.001246 M $(Na_2S_2O_3)$ - 0.02050 M

50.0 ml. of reaction mixture per flask.

Time elapsed (sec.)	Titer (ml.)	Rate constant x (l./mole sec.)	Per cent reaction
(blank)	6.08		0.00
90	5.40	4.78	39.0
180	4.98	4.62	60.0
300	4.65	4.83	78.5
720	4.35	4.20	97.0

Average value of rate constant $(k_{app}) = 4.61 \pm 0.21$ l./mole sec.

$[Br^-]_0 = 1.9987$ M

$h^x = 1.80$ l./mole sec.

Table 28

Run 75, 2,6-Dibromophenol in 2.000 M Hydrogen Bromide at 0°

$(DBP)_0$ - 0.0003737 M

(HBr) - 2.000 M

$(Br_2)_0$ - 0.001246 M

$(Na_2S_2O_3)$ - 0.02050 M

50.0 ml. of reaction mixture per flask.

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mole sec.)	Per cent reaction
(blank)	6.08		0.00
180	5.00	4.47	59.0
300	4.68	4.56	79.0
720	4.31	5.08	97.0
900	4.30	4.33	98.0

Average value of rate constant (k_{app}) 4.86 ± 0.36 l./mole sec.

$[Br^-]$ = 1.9987 M

k^x = 189.0 l./mole sec.

Table 29

Run 78, 2,6-Dibromophenol-4-d in 2.000 M Hydrogen Bromide at 0°

$(DBP\text{-}d)_0$ - 0.0003777 M HBr - 2.000 M

$(Br_2)_0$ - 0.001226 M $(Na_2S_2O_3)$ - 0.02050 M

50.0 ml. of reaction mixture per flask.

Time elapsed (sec.)	Titer (ml.)	Rate constant x (l./mole sec.)	Per cent reaction
(blank)	5.98		0.00
180	5.08	3.99	53.0
300	5.74	3.68	67.5
480	4.60	4.00	81.3
720	4.26	3.15	98.0

Average value of rate constant (k_{app}) = 3.56 ± 0.37 l./mole sec.

$[Br^-]_0 = 1.998$ M

k^x = 139.0 l./mole sec.

Table 30

Run 79, 2,6-Dibromophenol-4-d in 2.000 M Hydrogen Bromide at 0°

$(DBP\text{-}d)_0$ - 0.0003777 M

(HBr) - 2.000 M

$(Br_2)_0$ - 0.001226 M

$(Na_2S_2O_3)$ - 0.02050 M

50.0 ml. of reaction mixture per flask.

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mole sec.)	Per cent reaction
(blank)	5.98		0.00
180	5.05	3.87	50.5
300	4.72	3.72	66.6
480	4.56	4.11	82.0
720	4.27	3.12	98.0

Average value of rate constant $(k_{app}) = 3.54 \pm 0.38$ l./mole sec.

$[Br^-]_0 = 1.998$ M

$k^x = 138.0$ l./mole sec.

Duplication of the kinetic run gave an apparent rate constant of 1.04 ± 0.04 l./mole sec. (Table 24, Run 68). The deuterium derivative gave values of 0.802 ± 0.019 l./mole sec. (Table 25, Run 69) and 0.802 ± 0.013 l./mole sec. (Table 26, Run 70). The deuterium isotope effect was 1.30 ± 0.10 (k^H_{app}/k^D_{app}).

It was desirable to study the bromination of 2,6-dibromophenol at a higher hydrogen bromide concentration (2.000 M). Preliminary experiments in 80.0 per cent acetic acid showed that the phenol was salted out. Therefore, redistilled water was used for the kinetic runs at 0°. The first kinetic run with the protium compound gave an average apparent rate constant of 4.61 ± 0.21 l./mole sec. (Table 27, Run 74). Duplication of the kinetic run gave an apparent rate constant of 4.86 ± 0.36 l./mole sec. (Table 28, Run 75). The deuterium compound gave values of 3.56 ± 0.37 l./mole sec. (Table 29, Run 78) and 3.54 ± 0.38 l./mole sec. (Table 30, Run 79) for the apparent rate constants and an isotope effect of 1.33 ± 0.02 (k^H_{app}/k^D_{app}).

Due to the low deuterium isotope effects obtained in these bromination experiments, it was thought that the highly acidic conditions used may have allowed the exchange of hydrogen for deuterium on the 2,6-dibromophenol-4-d. Therefore, a sample of both the protium and deuterium compounds were separately treated under the conditions of the acetic acid kinetic runs without bromine, but with a hydrogen bromide concentration of 2.000 M. The reaction mixtures were extracted with carbon tetrachloride, shaken with 5 ml. portions of aqueous five per cent sodium bicarbonate, the phases separated, and the organic phase dried over magnesium sulfate. The infrared spectrum of each solution was run on a Perkin Elmer Infrared Spectrometer (Model 221) and compared with the spectra of the pure compounds. No apparent change in the deuterium content of the deuterium derivative was observed after exposure to the acetic acid reaction mixture.

Wave lengths at which the protium and deuterium compounds were different were: 5.24 microns, 5.41 microns, 6.01 microns, 7.05 microns, 7.20 microns, 7.95 microns, 8.70 microns, 9.13 microns, 10.39 microns, and 11.10 microns.

CHAPTER VI

THE MECHANISM OF IODINATION OF 2,6-DIBROMOPHENOL

Introduction.--Apparent second-order rate constants were calculated on the basis of the reaction's being first-order in stoichiometric concentration of both the phenol and iodine. Such rate constants remain constant at high iodide ion concentration and an average value of k_{app} was taken. For runs at the lowest iodide ion concentration the values of k_{app} fell throughout a run and k_{app} was extrapolated to zero per cent reaction in order to obtain a value of k_{app} at a definite iodide ion concentration.

The iodide ion dependency is demonstrated in Table 31. It can be seen that during a 50 fold decrease in stoichiometric iodide ion concentration (at constant hydrogen ion concentration) the values of k' decreased nearly two fold whereas k^x increased by approximately 30 fold. The values of k^x and k' (as previously defined) follow a trend indicating that k_{app} follows a non-integral iodide ion dependence. Alternatively, k^x has an iodide ion dependence between inverse zero order and first order.

Part of the iodide ion dependence may be attributable to the formation of triiodide through the equilibrium

$$I_2 + I^- \overset{K_1}{\rightleftarrows} I_3^- \quad ; \quad K_1 = \frac{[I_3^-]}{[I_2][I^-]} \quad , \qquad (1)$$

Table 31

Effect of Iodide Ion Concentration upon the Rate of Iodination of 2,6-Dibromophenol

All runs were made in aqueous solution, 0.021379 M perchloric acid, at an ionic strength of 0.300 at 50.0°.

$[I^-] \times 10^4$ (mole/l.)	k_{app} (l./mole sec.)	$k^x \times 10^3$ (l./mole sec.)	$k' \times 10^6$ (sec.$^{-1}$)	Ref Table
23.962	5.91×10^{-3}	13.2	31.9	1
23.958	5.97×10^{-3}	12.9	31.0	2
5.294	3.90×10^{-2}	49.0	26.0	3
5.338	3.65×10^{-2}	46.0	24.6	4
1.518	1.19×10^{-1}	136.0	20.7	5
1.440	1.20×10^{-1}	129.0	18.6	6
0.4461	3.97×10^{-1}	407.0	18.2	7
0.4779	4.02×10^{-1}	411.0	19.7	8

Table 32

Effect of Iodide Ion Concentration on the Rate of Iodination of 2,6-Dibromophenol-4-d

All runs were made in aqueous solution, 0.021379 M perchloric acid, at an ionic strength of 0.300 at 50.0°.

$[I^-] \times 10^4$ (mole/l.)	k_{app} (l./mole sec.)	$k^x \times 10^3$ (l./mole sec.)	$k' \times 10^6$ ($sec.^{-1}$)	Ref Table
5.132	8.40×10^{-3}	10.5	5.41	11
5.106	8.65×10^{-3}	11.1	5.64	12
0.4501	9.04×10^{-2}	88.4	3.98	13
0.4758	9.02×10^{-2}	92.3	4.39	14
5.262	6.66×10^{-3}	7.75	4.07	15
5.255	6.43×10^{-3}	7.80	4.09	16
1.499	2.53×10^{-2}	27.1	4.06	17
1.491	2.53×10^{-2}	27.4	4.08	18
0.4713	7.88×10^{-2}	82.8	3.90	19
0.4715	7.90×10^{-2}	82.9	3.91	20

$$K_1 = 490^{55} \text{ at } 50^\circ$$

Thus the concentration of iodine is inversely proportional to the concentration of the iodide ion.

If the possible hydrolysis of iodine in an aqueous medium is considered then,

$$I_2 + 2\,H_2O \overset{K_2}{\rightleftarrows} HOI + H_3O^+ + I^- \;;$$

$$K_2 = \frac{[HOI][H_3O^+][I^-]}{[I_2][H_2O]^2} \tag{2}$$

$$HOI + H_3O^+ \overset{K_3}{\rightleftarrows} H_2OI^+ + H_2O$$

$$K_3 = \frac{[H_2OI^+][H_2O]}{[HOI][H_3O^+]} \tag{3}$$

or

$$I_2 + H_2O \overset{K_5}{\rightleftarrows} H_2OI^+ + I^- \tag{4}$$

then

$$[HOI] = \frac{K_2[H_2O]^2[I_2]}{[I^-][H_3O^+]}\;, \tag{3'}$$

$$[H_2OI^+] = \frac{K_2K_3[H_2O][I_2]}{[I^-]}\;, \tag{4'}$$

and

$$[H_2OI^+] = \frac{K_5[I_3^-][H_2O][I_2]}{[I^-]} \tag{5}$$

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(55) M. Davis and E. Gwynne, J. Am. Chem. Soc., 74, 2748 (1952).

It can be seen that the concentration of H_2OI^+ is directly proportional to the concentration of iodine and inversely proportional to the concentration of iodide ion. Since the concentration of I^+ is directly proportional to the concentration of H_2OI^+, these two iodinating species are indistinguishable under most conditions.

Several feasible mechanisms can be evaluated from the data obtained.

Mechanism I.--

$$\mathrm{ArHOH} \overset{K_4}{\rightleftarrows} \mathrm{ArHO^-} + \mathrm{H^+} \quad ; \quad K_4 = \frac{[\mathrm{ArHO^-}][\mathrm{H^+}]}{[\mathrm{ArHOH}]} \tag{6}$$

$$\mathrm{ArHO^-} + \mathrm{H_2OI^+} \overset{k_1}{\rightleftarrows} \mathrm{ArHOI} \tag{7}$$

$$\mathrm{ArHOI} + \mathrm{H_2O} \xrightarrow{k_2} \mathrm{ArOI^-} + \mathrm{H_3O^+} \tag{8}$$

$$\mathrm{rate} = k_1[\mathrm{ArHO^-}][\mathrm{H_2OI^+}] \tag{7'}$$

Three forms of mechanism I may be considered. For the first k_2 k_{-1} and therefore, step 7, involving k_1, is rate-determining. Substitution of the appropriate equilibrium concentrations, (5) and (6), into the rate expression for step 7 gives

$$\mathrm{rate} = \frac{k_1K_4K_5[\mathrm{ArHOH}][\mathrm{I_2}]}{[\mathrm{H^+}][\mathrm{I^-}]} \tag{8'}$$

By equating the rate as given by (8') to that given by (9)

$$\mathrm{rate} = k_{app}(\mathrm{ArHOH})(\mathrm{I_2}) \tag{9}$$

and on the assumption that under the present conditions of acidity

$$(\mathrm{ArHOH}) = [\mathrm{ArHOH}] \ ,$$

then

$$k' = \frac{k_{app}(I_2)[I^-]}{[I_2]} = k_1 K_4 K_5 \frac{[H_2O]}{[H^+]} \quad . \qquad (10)$$

Equation (10) is similar to Berliner's and demands that k' be constant in a medium of constant hydrogen ion concentration and varying iodide ion concentration. Table 31 shows that k' gradually drops with decreasing iodide ion concentration and, therefore, this mechanism is probably disproven. Stronger evidence against the mechanism is that a large kinetic isotope effect was found while only a small or secondary isotope effect is expected for this mechanism.

Mechanism I', involves the attack of H_2OI^+ on the phenol and phenoxide ion in a fast and reversible step ($k_2 \ll k_{-1}$) followed by slow removal of a proton. This mechanism, however, has iodide ion dependence similar to that of mechanism I and is made unlikely both on the basis of the observed drop in k' and the decrease in isotope effect with decreasing iodide ion concentration.

The termolecular mechanism in which steps 7 and 8 take place simultaneously may be discarded for the same reasons as Mechanism I'.

Mechanism II.--To account for the non-integral iodide ion dependence and the observed trend in the values of k^x and k', it is possible to postulate a second mechanism which involves iodination by molecular iodine instead of hypoiodous acidium ion or iodine cation (indistinguishable as iodinating species by mechanism I or I'). Such a possibility leads to the rate expression

$$\text{rate} = k_0[\text{ArOH}][I_2] + k_1 \frac{[\text{ArOH}][I_2]}{[I^-]} \qquad (11)$$

where k_0 and k_1 include any hydrogen ion dependency. Equation (12) may be rearranged to a form including k_{app}

$$k_{\text{app}}\frac{(I_2)}{[I_2]} = k^x = k_0 + \frac{k_1}{[I^-]} \quad . \qquad (12)$$

Therefore, for this mixed mechanism to hold, a plot of k^x versus $1/[I^-]$ should give a straight line. Such a plot at constant hydrogen ion concentration is shown in figure 1 and the deviation from linearity argues against this mechanism for the iodination of 2,6-dibromophenol.

Mechanism III.--

$$\text{ArHOH} \overset{K_4}{\rightleftarrows} \text{ArHO}^- + H^+ \;\; ; \;\; K_4 = \frac{[\text{ArHO}^-][H^+]}{[\text{ArHOH}]} \qquad (6)$$

$$\text{ArHO}^- + I_2 \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \text{ArHOI} + I^- \qquad (13)$$

$$\text{ArHOH} + I_2 \underset{k_{-2}}{\overset{k_2}{\rightleftarrows}} \text{ArHOI} + I^- + H^+ \qquad (14)$$

$$\text{ArHOI}^{*} \xrightarrow{k_3} \text{ArOI}^- + H^+ \qquad (15)$$

where ArHOI is a reactive intermediate having a <u>para</u>-quinoid structure

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[*] To be sure the proton formed here is affixed to some base; this step is assumed to be subject to general base catalysis.

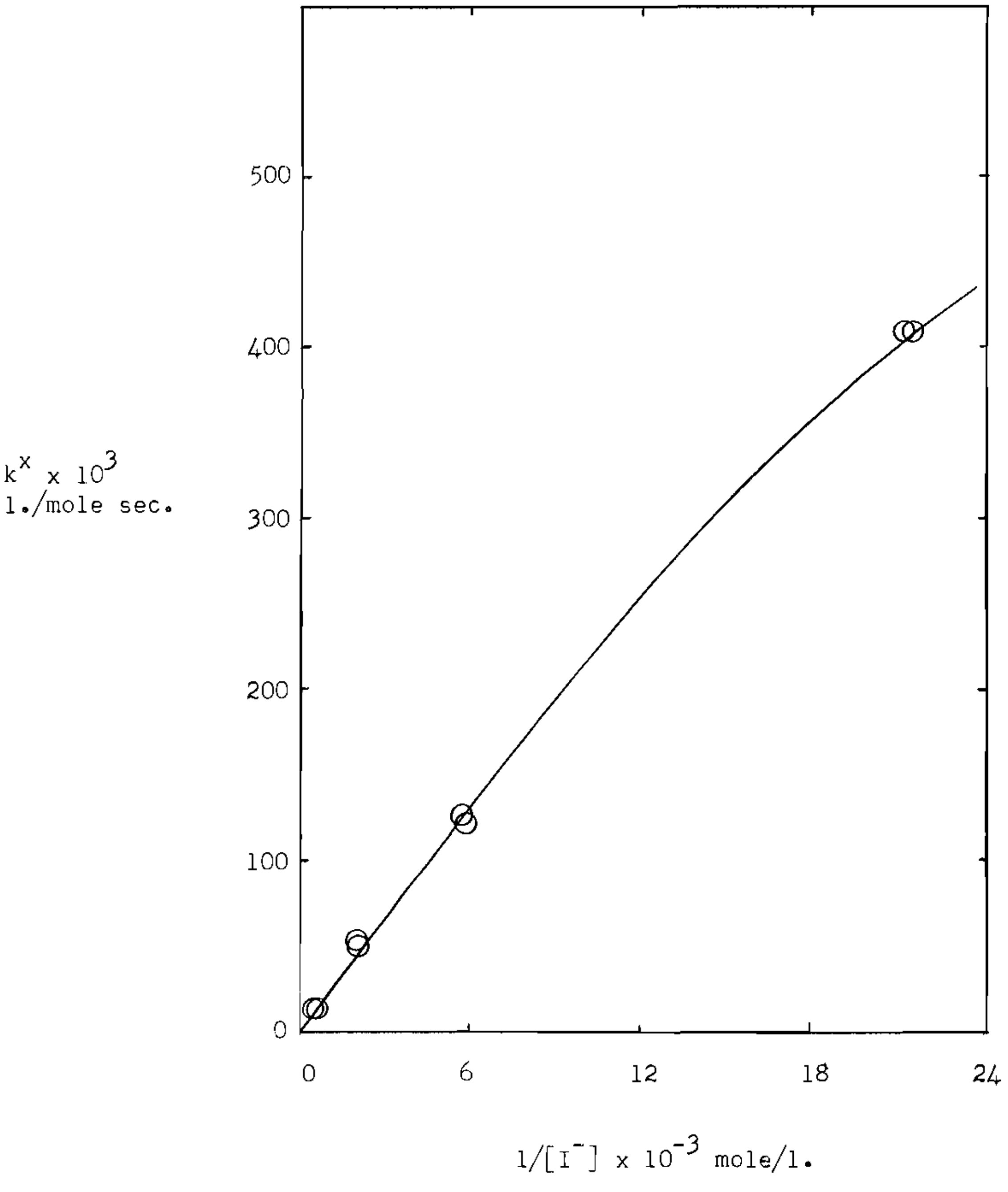
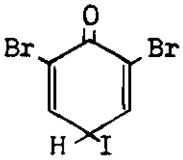


Fig. 1. 2,6-Dibromophenol in 0.021379 M Perchloric Acid



Such an intermediate is assumed to be formed in small concentrations relative to ArHOH. The application of steady state approximation gives

$$k_1[\mathrm{ArHO^-}][I_2] + k_2[\mathrm{ArHOH}][I_2] = k_{-1}[\mathrm{ArHOI}][I^-] + k_{-2}[\mathrm{ArHOI}][H^+][I^-] + k_3[\mathrm{ArHOI}] \;. \qquad (16)$$

Eauation (17) can be rearranged to

$$[\mathrm{ArHOI}] = \frac{k_1[\mathrm{ArHO^-}][I_2] + k_2[\mathrm{ArHOH}][I_2]}{k_{-1}[I^-] + k_{-2}[H^+][I^-] + k_3} \;. \qquad (17)$$

Substitution of equation (6) into (18) gives

$$[\mathrm{ArHOI}] = \frac{k_1K_4[\mathrm{ArHOH}][I_2] + k_2[\mathrm{ArHOH}][I_2][H^+]}{k_{-1}[I^-] + k_{-2}[H^+][I^-] + k_3 \quad [H^+]} \qquad (18)$$

since

$$\mathrm{rate} = k_3[\mathrm{ArHOI}] = k_{\mathrm{app}}(I_2)(\mathrm{ArHOH}) \qquad (19)$$

substitution of (19) into (20) gives

$$k_{\mathrm{app}}\,\frac{(I_2)[H^+]}{[I_2]} = k^x[H^+] = \frac{k_1K_4 + k_2[H^+]}{k_{-1}/k_3\;[I^-] + k_{-2}/k_3\;[H^+][I^-] + 1} \qquad (20)$$

Application of the principle of microscopic reversibility[56] and

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(56) Frost and Pearson, <u>op</u>. <u>cit</u>., p. 202.

equilibrium statistics to reactions (6), (14) and (15) leads to the relationship

$$\frac{k_1 K_4}{k_{-1}} = \frac{k_2}{k_{-2}} \tag{21}$$

From equations (20) and (21) there may be obtained

$$\frac{1}{k^x[H^+]} = \frac{k_{-1}[I^-]}{k_1 k_3 K_4} + \frac{1}{k_1 K_4 + k_2[H^+]} \quad . \tag{22}$$

According to equation (22) a plot of $1/(k^x[H^+])$ versus $[I^-]$ should give a straight line at constant hydrogen ion concentration ion. Figure 2 shows that the available data do indeed fall on a straight line.

By extrapolating the plot of $1/(k^x[H^+])$ versus $[I^-]$ to zero iodide ion concentration, the value of $k_1K_4 + k_2[H^+]$ may be obtained from the intercept. The slope corresponds to $k_{-1}/k_1K_4k_3$. The values of $k_1K_4 + k_2[H^+]$ and $k_{-1}/k_1k_3K_4$ were found to be 70 sec.$^{-1}$ and 152 x 10^4 l/mole sec. respectively (see Appendix B).

It is of interest to note that a similar plot for iodination of the deuterium derivative gives about the same intercept, but a different slope. A similar intercept is not unusual since the magnitude of $k_1K_4 + k_2[H^+]$ is similar for the protium and deuterium compounds.

Since it was assumed that proton removal occurs in the slow step, the deuterium isotope effect presents strong evidence in favor of mechanism III. Furthermore, according to mechanism III the maximum isotope effect expected should be at high iodide ion concentrations and the isotope effect should decrease with decreasing iodide ion concen-

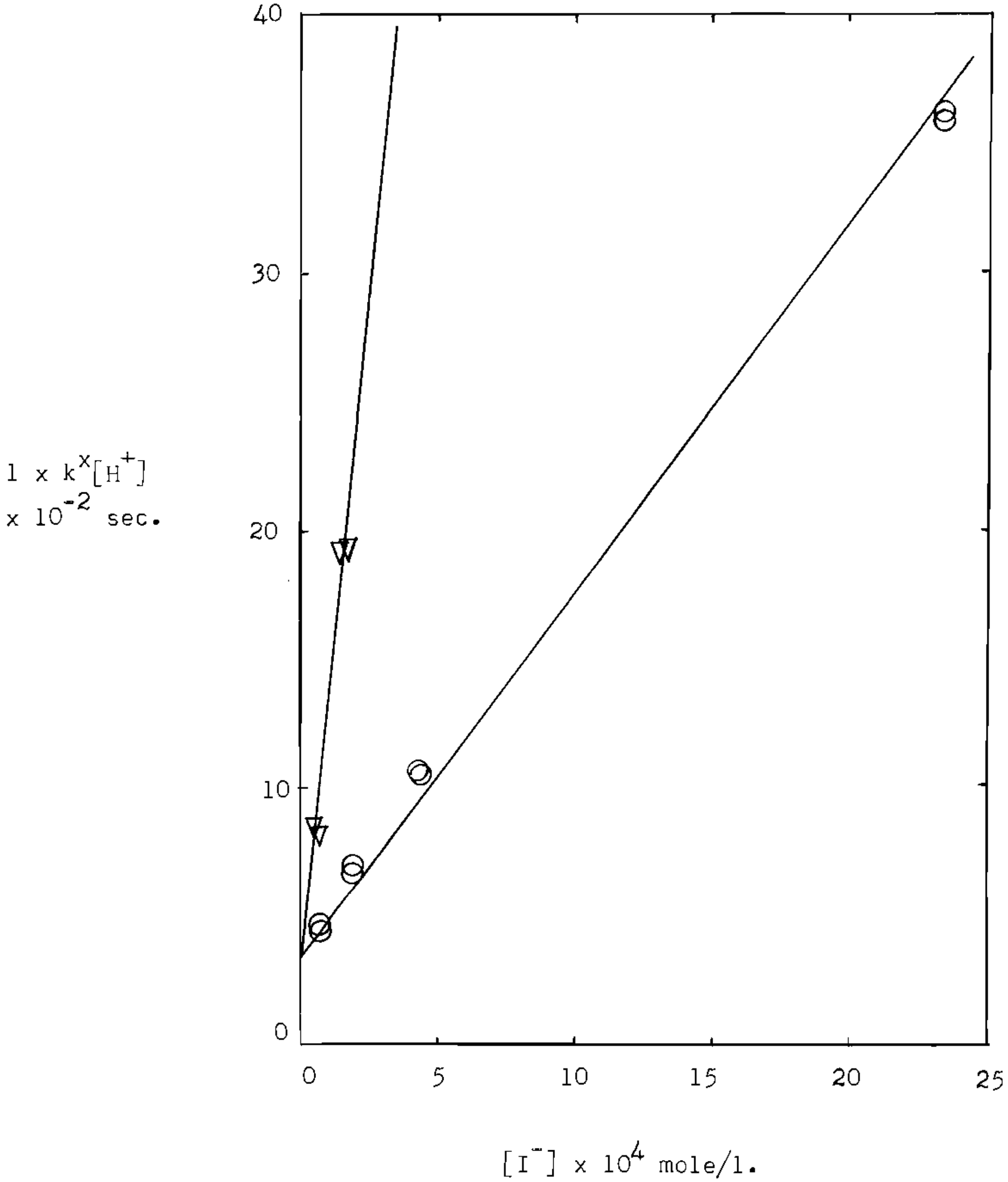

Fig. 2. 2,6-Dibromophenol and 2,6-Dibromophenol-4-d in 0.021379 M Perchloric Acid

Legend: (1) ○ - 2,6-Dibromophenol
(2) Δ - 2,6-Dibromophenol-4-d

tration. Such a prediction is based primarily on the reversibility of the first step. At high iodide ion concentration the intermediate ArHOI is formed at small, near equilibrium concentration and the rate-determining step is the reaction of equation (15). Since this reaction involves loss of a proton bound to carbon, a large primary isotope effect is expected. At low iodide ion concentration reactions (13) and (14) should not be appreciably reversed and these reactions correspond to the rate-determining steps of the reaction and only a small secondary isotope effect is expected.

In assuming that an appreciable isotope effect exists only for step (15), and neglecting secondary isotope effects and the effect of

$$\mathrm{ArHOI} \xrightarrow{k_{3H}} \mathrm{ArOI}^- + \mathrm{H}^+ \tag{15}$$

$$\mathrm{ArDOI} \xrightarrow{k_{3D}} \mathrm{ArOI}^- + \mathrm{H}^+ \tag{15'}$$

isotopic substitution on the ionization constant of 2,6-dibromophenol there will be two equations analogous to (22), one for the deuterium and the other for the protium compound. Division of one by the other gives:

$$\frac{k_D^x[H^+]_D}{k_H^x[H^+]_H} = \frac{[k_{-1}[I_H^-]/k_1k_3K_4] + [I/)k_1K_4 + k_2[H_H^+])]}{[k_{-1}[I_D^-]/k_1k_3K_4] + [I/(k_1K_4 + k_2[H_D^+])]} \ . \tag{23}$$

Thus, at relatively high iodide ion concentration, when

$$\frac{k_{-1}[I^-]}{k_{3H}} \gg 1 \quad \text{and} \quad \frac{k_{-1}[I^-]}{k_{3D}} \gg 1 \quad , \text{then}$$

$$\frac{k_D^x}{k_H^x} = \frac{k_{3D}}{k_{3H}} \tag{24}$$

or

$$\frac{k_H^x}{k_D^x} = \frac{\dfrac{k_{3H}}{k_{-1}}}{\dfrac{k_{3D}}{k_{-1}}} \times 7.25^{*} \tag{25}$$

and substitution equation (25) into equation (23)

$$\frac{k_H^x}{k_D^x} = \frac{7.25 \times \dfrac{k_{-1}[I^-]}{k_1 k_{3H} K_4} + 1/(k_2[H^+] + k_1 K_4)}{\dfrac{k_{-1}[I^-]}{k_1 k_{3H} K_4} + 1/(k_2[H^+] + k_1 K_4)}$$

Since the value of $k_{-1}/k_1 k_{3H} K_4$ can be determined from the slope and intercept of figure 2, then the magnitude of the deuterium isotope effect can be calculated at any iodide ion concentration. The results of such calculations are tabulated in Table 33 along with those experimentally determined. The trend is similar in both cases and the magnitude of the deuterium isotope effect diminishes with decreasing iodide ion concentration.

Therefore, the preceeding discussion strongly supports mechanism III for the iodination of 2,6-dibromophenol.

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*This value was calculated from the ratio of the slopes of protio and deuterio compounds in figure 2.

Table 33

Effect of Iodide Ion Concentration on the Magnitude of the Deuterium Isotope Effect at 50.0°

Reference Table Protium	Deuterium	$(I)_0 \times 10^4$ (mole/l.)	$k_H^x \times 10^3$ $k_D^x \times 10^3$ (l./mole sec.)	$\left[\frac{k_H^x}{k_D^x}\right]$ obs.	$\left[\frac{k_H^x}{k_D^x}\right]$ calc.
3	15	5.612	49.0	6.32	6.85
5	17	1.604	136.0	5.05	5.55
8	20	0.5011	411.0	4.98	4.20
9	21	$TlClO_4$=0.0500	240.0*	3.85*	**
10	22	$TlClO_4$=0.0500	256.0*	4.09*	**

*Apparent second-order rate constants were used for evaluation of deuterium isotope effect since the actual iodide ion concentration is not known at 50.0°.

**An $(I^-)_0$ of 0.4500×10^{-4} M would be required for an isotope effect of 4.00.

CHAPTER VII

THE MECHANISM OF BROMINATION OF 2,6-DIBROMOPHENOL

Grovenstein and Henderson[1] investigated the bromination of 2,6-dibromophenol in 80.0 per cent acetic acid and found an inverse hydrogen ion dependence between zero and first power. These authors also found the rate to be proportional to the actual concentration of bromine. This was interpreted as bromination by molecular bromine upon both the phenol and phenoxide ion. Since the actual concentration of bromine is a function of the bromide ion concentration,

$$Br_2 + Br^- \rightleftarrows Br_3^- \quad ; \quad K_1 = \frac{[Br_3^-]}{[Br_2][Br^-]} \; ; \qquad (1)$$

$$K_1 = 93 \text{(80.0 per cent acetic acid at } 20.0^\circ)^{1}$$

$$K_1 = 19.6 \text{ (water at } 0^\circ)^{57}$$

The data of Grovenstein and Henderson can be expressed by the rate equation

$$\text{rate} = k[Br_2] \quad (ArHOH) + \frac{k_1(ArHOH)}{[H^+]} \quad . \qquad (2)$$

Equating this to

$$\text{rate} = k_{app}(Br_2)(ArHOH). \qquad (3)$$

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(57) G. A. Linhart, *J. Am. Chem. Soc.*, **40**, 158 (1918).

and incorporating equation (1)

$$\text{rate} = k_{\text{app}}(\text{ArHOH})(\text{Br}_2) = k\,\frac{[\text{Br}_3^-]}{K_1[\text{Br}^-]}\,(\text{ArHOH}) + \frac{k'(\text{ArHOH})}{[\text{H}^+]}\;. \qquad (4)$$

Then

$$k^x = \frac{k_{\text{app}}K_1(\text{Br}_2)[\text{Br}^-]}{[\text{Br}_3^-]} = k_0 + \frac{k_-}{[\text{H}^+]}\;, \qquad (5)$$

where k_0 equals 2.5 l./mole sec. and k_- equals 0.60 sec.$^{-1}$. Equation (4) corresponds to the expected kinetic equation for the attack of molecular bromine upon ionized and unionized 2,6-dibromophenol.

If a mechanism analogous to mechanism III for the iodination is considered,

$$\text{ArHOH} \overset{\text{fast}}{\rightleftarrows} \text{ArHO}^- + \text{H}^+ \;;\; K_4 = \frac{[\text{H}^+][\text{ArHO}^-]}{[\text{ArHOH}]} \qquad (6)$$

$$\text{ArHO}^- + \text{Br}_2 \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \text{ArHBrO} + \text{Br}^- \qquad (7)$$

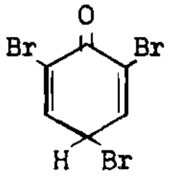
$$\text{ArHOH} + \text{Br}_2 \underset{k_{-2}}{\overset{k_2}{\rightleftarrows}} \text{ArHBrO} + \text{Br}^- + \text{H}^+ \qquad (8)$$

$$\text{ArHBrO} \xrightarrow{k_3} \text{ArBrO}^- + \text{H}^+ \qquad (9)$$

then the rate expression becomes

$$\frac{1}{k^x[\text{H}^+]} = \frac{k_{-1}[\text{Br}^-]}{k_1k_3K_4} + \frac{1}{k_2[\text{H}^+] + k_1K_4} \qquad (10)$$

In this case, ArHBrO is presumed to have the structure



In the present work in 80.0 per cent acetic acid, 0.100 M hydrogen bromide, an isotope effect (k^{H}_{app}/k^{D}_{app}) of 1.30 ± 0.10 was found in the bromination of 2,6-dibromophenol-4-d at 20°. In water, 2.00 M in hydrogen bromide, an isotope effect of 1.33 ± 0.02 was obtained at 0°.

These observed isotope effects are not too disimilar from those obtained by Berliner[40] in the bromination of biphenyl ($\frac{k^H}{k_D}$ = 1.15). Berliner concluded that his isotope effect was largely a secondary isotope effect and that proton removal was not the rate-determining step.

The data of Grovenstein and Henderson[1] indicate that the rate-determining step is the attack of the electrophile. On this basis and on the essentially constant isotope effect at the different bromide ion concentrations, it appears that the present isotope effect is a secondary one and reflects the effect of isotopic substitution on steps k_1 and k_2 in the above mechanism. Therefore, proton-removal (step k_3) appears to occur after the rate-determining steps (k_1 and k_2).

CHAPTER VIII

SUGGESTIONS FOR FUTURE EXPERIMENTAL WORK

It is apparent from the literature cited that there is a need for more work on the bromination of phenols. It is suggested that the kinetics of bromination of phenol, *o*-nitrophenol, *p*-nitrophenol, *o*-bromophenol and *p*-bromophenol be investigated at varying hydrogen ion and bromide ion concentrations and that the deuterium isotope effect be studied as a function of the bromide ion concentration in each case.

It should also be informative to investigate the kinetics of bromination and iodination of 2,6-dichlorophenol and its deuterium derivative. It is hoped that a study of this type, at varying hydrogen ion, bromide ion, and iodide ion concentrations, would clarify factors effecting the reversibility of the first step in the halogenation of phenols.

APPENDICES

APPENDIX A

SAMPLE CALCULATION OF INTEGRATED RATE CONSTANTS

The rate constants were calculated from the integrated form of the second-order rate equation, i.e.,

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

in which k_{app} is the rate constant (l./mole sec.), t is the elapsed time in seconds, a is the initial stoichiometric iodine or bromine concentration, b is the initial stoichiometric concentration of 2,6-dibromophenol, and x is the molar concentration of iodine reacted at time t. The sample calculation will be on Run 14, Table 7.

a = 0.0002581 M

b = 0.0006420 M

$(Na_2S_2O_3)$ = 0.006026 M

(c-a) = 0.0003839 M

(100.0 ml. samples)

t (sec.)	Titer (ml.)	$(a-x) \times 10^4$	$(b-x) \times 10^4$	$10^5(x)$	$\frac{a(b-x)}{b(a-x)}$
477	7.71	2.3229	6.1619	2.5826	1.0665
884	7.17	2.1602	5.9993	4.2095	1.1165
1465	6.63	1.9976	5.8366	5.8365	1.1747
2089	6.15	1.8529	5.6919	7.2827	1.2350
2612	5.86	1.7656	5.6046	8.1564	1.2762
3037	5.60	1.6872	5.5262	8.9400	1.3168

$$k_{app} = \frac{2.303}{(0.0003839)t} \log \frac{a(b-x)}{b(a-x)}$$

t (sec.)	$\frac{2.303}{(b-a)t}$	$\log \frac{a(b-x)}{b(a-x)}$	$\frac{2.303}{(b-a)t} \log \frac{a(b-x)}{b(a-x)}$
477	12.5764	0.02796	0.352
884	6.7862	0.04825	0.327
1465	4.0984	0.06993	0.286
2089	2.8717	0.09167	0.263
2612	2.2967	0.10592	0.243
3037	1.9753	0.11952	0.236

Extrapolated value of rate constant k_{app} = 0.397 l./mole sec.

For the calculation of k', the following equation was employed.

$$k' = \frac{k_{app} K_1 (I_2)_0 [I^-]_0^2}{[I_3^-]_0}$$

in which K_1 is the iodine-triiodide equilibrium constant at the designated temperature which is represented by

$$K_1 = \frac{[I_3^-]}{[I_2][I^-]} ,$$

$(I_2)_0$ is the initial stoichiometric iodine concentration, $[I^-]_0$ is the actual iodide ion concentration and $[I_3^-]_0$ is the actual initial triiodide concentration. The sample calculation will be on the same run represented above.

$$\begin{array}{ccccc} I_2 & + & I^- & \rightleftarrows & I_3^- \\ (2.581 \times 10^{-4}-x) & & (0.5011 \times 10^{-4}-x) & & (x) \end{array}$$

$$K_1 = \frac{x}{(5.011 \times 10^{-5}-x)(2.581 \times 10^{-4}-x)} = 490$$ [56]

$$490x^2 - 1.151033x + 6.337853 \times 10^{-6} = 0$$

Solving for x via the quadratic equation, then

$$x = \frac{1.151033 - 1.324876 - 1.2422 \times 10^{-2}}{980}$$

$$x = \frac{1.151033 - 1.145647}{980} = 0.5495 \times 10^{-5}\ \underline{M}$$

$$[I^-]_0 = 0.5011 \times 10^{-4} - 0.05495 \times 10^{-4} = 0.4461 \times 10^{-4}\ \underline{M}$$

$$k' = \frac{(0.397)(490)(2.581 \times 10^{-4})(0.4461 \times 10^{-4})^2}{(5.495 \times 10^{-6})}$$

$$k' = 1.816 \times 10^{-5}\ \text{sec.}^{-1}$$

Similar calculations were made for the bromination reactions using

$$K_1 = \frac{[Br_3]}{[Br_2][Br^-]} .$$

K_1 in 80.0 per cent acetic acid at 20.0° was taken as 93[1] and in redistilled water at 0° as 19.6[58].

All calculations of this type were made on an electric calculating machine with the number of significant figures shown.

APPENDIX B

FIGURE 2 SLOPE CALCULATION

The slopes for both the protium and deuterium compounds were calculated by the expression

$$\text{slope} = \frac{\dfrac{1}{k^{x}[H^{+}]} - \text{intercept}}{[I^{-}]_{0}} .$$

An intercept was assumed and the slope of each point with respect to this intercept was calculated. The slope with the lowest average deviation for the protium compound was 152×10^{4} l./mole sec. with an intercept of 70 sec.^{-1}. This same intercept was assumed for the deuterium compound and a slope of 1100×10^{4} l./mole sec. was calculated. The calculated slopes with the assumed intercepts are shown in the table below.

Assumed Intercept (sec.^{-1})	Calculated Slope (l./mole sec.)
85	$141 \pm 38 \times 10^{4}$
80	$145 \pm 34 \times 10^{4}$
75	$148 \pm 32 \times 10^{4}$
70	$152 \pm 28 \times 10^{4}$
67	$154 \pm 29 \times 10^{4}$
65	$156 \pm 29 \times 10^{4}$
70 (Deuterium Compound)	$1100 \pm 3 \times 10^{4}$

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BIOGRAPHICAL SKETCH

Coleman Jennings Bryan, son of Hazel S. and William K. Bryan, Sr., was born October 2, 1936, in St. Augustine, Florida. He attended public elementary school in Arlington, Virginia. He attended secondary schools in Paris, France; Athens, Greece; Tripoli, Libya; and graduated from Washington-Lee High School in Arlington, Virginia, in June 1954.

In September, 1954, he entered the Georgia Institute of Technology and completed his work for the degree of B.S. in Chemistry in June, 1958. Immediately thereafter, he entered graduate school at the same institution. His first year of graduate work was supported by the National Science Foundation, his second by serving as a Graduate Assistant, and his third year was spent working as a Research Assistant at the Engineering Experiment Station.

In December, 1960, he married Sarah Catherine Little of Bankston, Alabama.

Upon completing work for his master's degree, he will be employed by the Dow Chemical Company at Plaquemine, Louisiana.