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KINETIC STUDY OF THE MECHANISM
OF THE IODINATION OF PHENOL

A THESIS

Presented to

the Faculty of the Graduate Division

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Donald Charles Kilby

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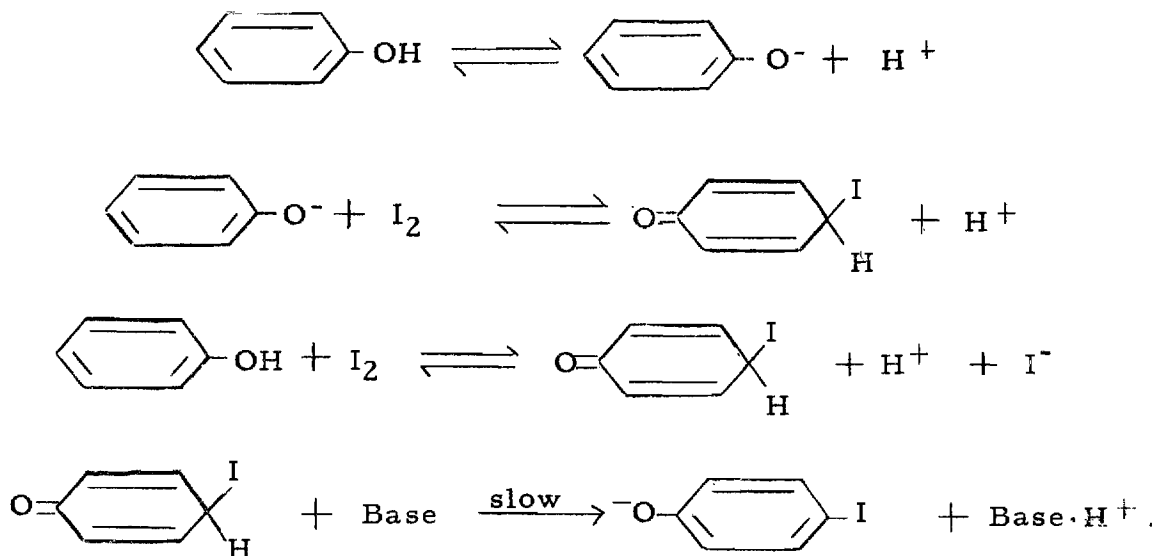
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SUMMARY

The mechanism of the mono-iodination of phenol to give chiefly *p*-iodophenol has been studied previously, especially by E. Berliner. Berliner has proposed that the mechanism involves the rate-determining attack upon phenoxide ion of hypiodous acidium ion (or iodine cation) and of hypiodous acid catalyzed by a general acid. The mechanism as proposed by Berliner agrees with the known kinetic data according to which the rate follows the expression

$$\text{rate} = \frac{k_1 [\text{PhOH}] [\text{I}_2]}{[\text{H}^+] [\text{I}^-]} + \frac{k_2 [\text{PhOH}] [\text{I}_2] [\text{HOAc}]}{[\text{H}^+]^2 [\text{I}^-]}$$

Grovenstein and Henderson have studied the bromination of 2, 4-dibromophenol and 2, 6-dibromophenol and their work suggested to them that another mechanism could exist for the iodination of phenol. The rate expression for their mechanism has the same kinetic form as Berliner's for ranges of iodide ion concentrations as previously studied. They proposed that the mechanism involved an equilibrium of iodine and phenol or phenoxide ion with a intermediate which lost a proton in a subsequent slow step. Specifically, their mechanism is



With water and acetate ion as the general bases and at sufficiently high iodide ion concentration the rate expression is

$$\text{rate} = \frac{k_3 [\text{PhOH}] [\text{I}_2] [\text{H}_2\text{O}]}{[\text{H}^+] [\text{I}^-]} + \frac{k_4 [\text{PhOH}] [\text{I}_2] [\text{Ac}^-]}{[\text{H}^+] [\text{I}^-]}$$

In order to distinguish between these and other mechanisms a study was made of the rate of iodination as a function of iodide ion concentration. In particular the reaction was studied at low iodide ion concentrations in order to determine whether or not the rate-determining step would become the attack of iodine molecule upon phenol or phenoxide ion at sufficiently low iodide ion concentration. Such a result would be indicated by the rate of iodination becoming independent of iodide ion concentration save for any concomitant formation of tri-iodide ion.

The iodination of phenol was studied in a buffered solution of sodium acetate-acetic acid. The hydrogen ion concentration of the

reaction mixture was 3.17×10^{-4} moles per liter and the concentrations were such that this hydrogen ion concentration did not change appreciably during iodination. From the data collected in a particular run, apparent integrated bimolecular rate constants were calculated from the equation

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

in which \underline{b} is the initial stoichiometric phenol concentration, \underline{a} is the initial stoichiometric iodine concentration, \underline{t} is the time elapsed between the mixing of the reactants and the stopping of the reaction, and \underline{x} is the concentration of either reactant consumed or the concentration of product formed at time \underline{t} . Since the apparent rate constants decreased with per cent reaction due to iodide ions produced in the reaction, an apparent rate constant at the initial stoichiometric iodide ion concentration of the reaction was obtained by extrapolating to zero time or, when the rate constants did not drop more than nine per cent during a run by averaging the rate constants; and on the basis of Berliner's mechanism, a constant k' was calculated from the apparent rate constant k_{app} by the relationship

$$k' = \frac{k_{\text{app}} \times 768 (I_2) [I^-]^2}{[I_3^-]}$$

In this discussion and elsewhere, a term enclosed in square brackets, $[\]$, indicates an actual concentration of a particular molecular species, while a term enclosed in parentheses, $(\)$, indicates a stoichiometric concentration.

The rate of the iodination of phenol in buffered sodium acetate-acetic acid was studied in the iodide ion concentration range of 0.08 M to 0.0005 M. The value of k' at 0.08 M sodium iodide was $3.28 \times 10^{-4} \text{ sec.}^{-1}$ and the value at 0.0005 M sodium iodide was $3.01 \times 10^{-4} \text{ sec.}^{-1}$. Since the value of k' did not decrease a significant amount in the above study it was deemed of interest to lower the iodide ion concentration further; however, the pH of the reaction had to be lowered in order to be able to make accurate rate measurements at smaller iodide ion concentrations by the techniques employed. To do this the buffered sodium acetate-acetic acid solution was no longer used; instead a solution of 0.0174 M perchloric acid was employed. The rate of the iodination of phenol in 0.0174 M perchloric acid was studied in the iodide ion concentration range of 0.0005 M to 1.99×10^{-5} M. The value of k' at 0.0005 M sodium iodide was $4.53 \times 10^{-6} \text{ sec.}^{-1}$ and the value at 1.99×10^{-5} M sodium iodide was $4.06 \times 10^{-6} \text{ sec.}^{-1}$. A first-order differential equation was used to obtain k' values as a check upon the values of k' obtained by graphical methods.

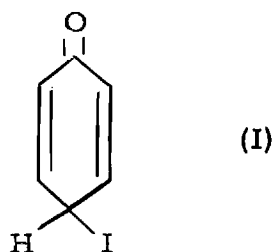
As the k' values did not decrease a significant amount in

going from iodide ion concentrations of 0.08 M to $1.99 \times 10^{-5} \text{ M}$ the present kinetic work cannot in itself disprove Berliner's mechanism. The mechanism of Grovenstein and Henderson, however, unlike the mechanism preferred by Berliner, leads to the prediction of an isotope effect as their rate-determining step involves the release of the proton by a base. To test this hypothesis a study was made of the rate of iodination of phenol-2, 4, 6-d₃ as compared with the rate of iodination of ordinary phenol to see if there is an appreciable isotope effect.

Phenol-2, 4, 6-d₃ was prepared by the general procedure of Ingold and co-workers. After two equilibrations of phenol with heavy water, a product which is estimated to be at least 99 per cent phenol-2, 4, 6-d₃ was obtained. This phenol undergoes iodination at one fourth the rate of ordinary phenol. Thus in a typical experiment at 25° at initial concentrations of 0.0080 M in phenol and 0.00196 M in iodine, in aqueous solvent that was 0.500 M in acetic acid, 0.050 M in sodium acetate, 0.230 M in sodium perchlorate, and 0.020 M in sodium iodide, the initial apparent second order rate constants were 1.21×10^{-3} (l./mole sec.) for ordinary phenol and 3.05×10^{-4} (l./mole sec.) for phenol-2, 4, 6-d₃. These data give a value of k_H/k_D of 3.97. In related runs with perchloric acid in place of the acetate buffer, isotope effects of similar magnitude were obtained.

This example shows that a phenol need not necessarily be

hindered to give an isotope effect. Phenols are just the type of compound that would be expected to give stable reactive intermediates. A structure like (I) could be the stable reactive intermediate in the iodination of phenol



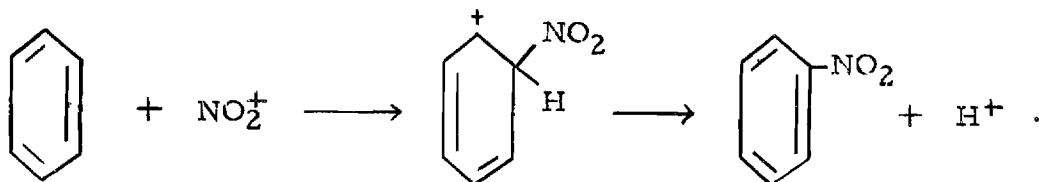
Substances analogous to (I) have been isolated from reactions of 2,4,6-trisubstituted phenols. General evidence, therefore, favors (I) as an intermediate in the iodination of phenol.

On this basis, in order to account for both the kinetic evidence and isotope effect, intermediate (I) must, under the experimental conditions which have been studied, be transformed back to reactants considerably faster than into the final products, i. e., (I) must be essentially at equilibrium with the reactants. From such kinetic data, therefore, the nature of the iodinating agent for phenol cannot be specified.

CHAPTER I

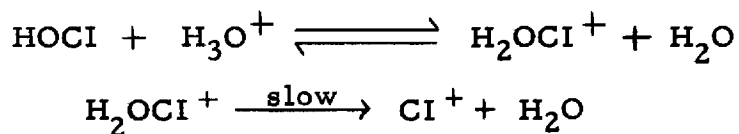
INTRODUCTION

Electrophilic aromatic substitution is a reaction in which Lewis acids, or substances capable of giving up the elements of Lewis acids, attack aromatic molecules, usually to replace hydrogen atoms, e. g.

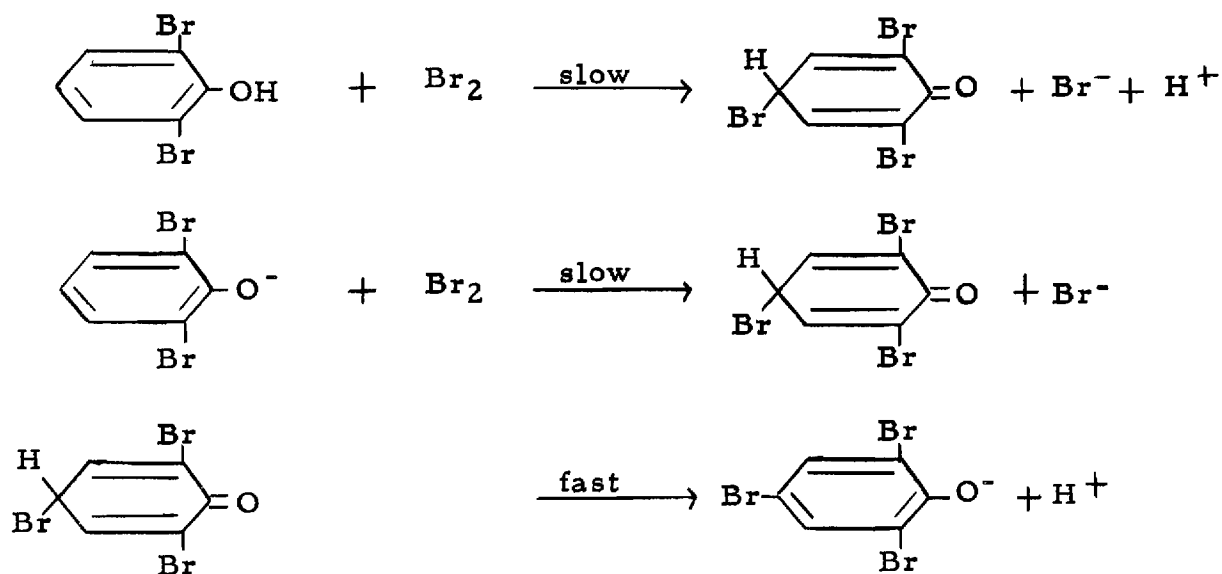


One factor of interest concerning an electrophilic aromatic substitution reaction is the detailed mechanism whereby the reaction proceeds. To know the mechanism of the reaction involves knowing what the reacting species are; what intermediates, if any, are formed; and what is the rate-determining step. The rate-determining step may be the formation of the Lewis acid, and thus the reaction rate may be independent of the aromatic molecule. An example is the chlorination of phenol in a solution of hypochlorous acid and perchloric acid (1).

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



On the other hand, the rate-determining step in an electrophilic aromatic substitution may be the bimolecular reaction of the Lewis acid with the aromatic molecule. An example is the bromination of 2,6-dibromophenol and 2,4-dibromophenol (2).

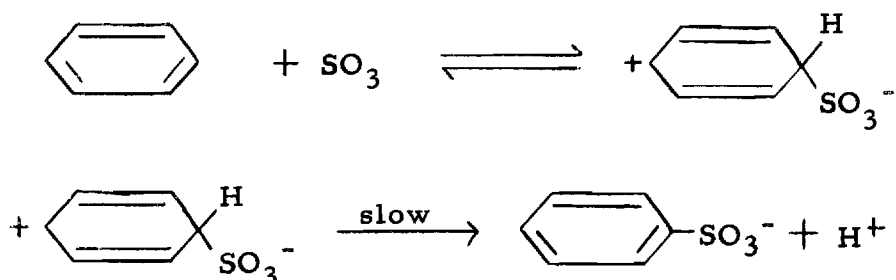


Finally, the rate-determining step of an electrophilic aromatic substitution may be the release of the proton from the carbon atom undergoing electrophilic attack. An example of this type of rate-determining step is the sulphonation of benzene or bromobenzene with weak oleum (3, 4).

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

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

4. L. Melander, Arkiv Kemi, 2, 211 (1950).



The principle that is used to distinguish the release of the proton as the rate-determining step in an electrophilic aromatic substitution reaction is as follows: The zero-point energy of a bond holding a deuterium atom differs considerably from the zero-point energy of a bond holding a proton. Only part of such differences of energy appears in the transition stages of reactions if the bond is partially broken. This difference of energy leads to a difference of activation energy and rate. A complete discussion of the theory of such isotope effects is given by Melander (3, 4, 5).

One of the more interesting questions concerning the halogenation of aromatic compounds is that of whether substitution ever takes place through the pre-formed free halogenium ion, or whether it is always conveyed to the aromatic nucleus by a carrier such as, for iodination, H_2OI^+ , I_2 , HOI , or even perhaps I_3^- .

Painter and Soper (6), in studying the iodination of phenol in aqueous solution, concluded that the iodinating species is the hypoiodous

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

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

acidium ion. Since water is in constant active mass, the iodine cation will bear a constant ratio to the hypiodous acidium ion and thus could be the iodinating species (6). Berliner (7) concluded that the hypiodous acidium ion or alternatively the iodine cation is the attacking reagent in the iodination of aniline. Berliner (7) likewise concluded that the powerful agent in aqueous iodination of phenol is a cation, either the iodine cation, or the hypiodous acidium ion, and that it is very much more powerful than either molecular iodine, or any anionic species, such as triiodide ion. Ingold (8a) has stated that there is no evidence as yet that any iodine carrier other than the cationic species, is effective for aromatic iodination in hydroxylic solutions. Ingold (8b) has further stated that the mode of attack of electrophilic halogenating agents on the benzene ring is very probably similar to that of nitrating agents, and the results encourage one to believe that in halogenation the loss of the aromatic proton is not kinetically significant.

Molecular iodine has been found to be the effective iodinating species for the iodinolysis of p-methoxybenzeneboronic acid in aqueous

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

8a. C. K. Ingold, Structure and Mechanism in Organic Chemistry. Ithaca: Cornell University Press, 1953, p. 291.

8b. Ibid., p. 295.

solution at iodide ion concentrations of 0.1 to 0.5 M (9), and is apparently responsible for the exchange reaction between radioactive iodine and diiodotyrosine (10).

To distinguish between the stoichiometric concentration of a species and the actual concentration, the stoichiometric concentration will be designated in this thesis by enclosure in parentheses, (), and the actual concentration by enclosure in square brackets [].

Berliner (11) has proposed a mechanism for the iodination of phenol in phosphate or acetate buffers containing an iodide ion concentration of 0.12 M. His experimental data agreed with the following rate expression:

$$\text{rate} = \frac{k_1 [\text{PhOH}] [\text{I}_2]}{[\text{H}^+] [\text{I}^-]} + \frac{k_2 [\text{PhOH}] [\text{I}_2] [\text{HA}]}{[\text{H}^+]^2 [\text{I}^-]}$$

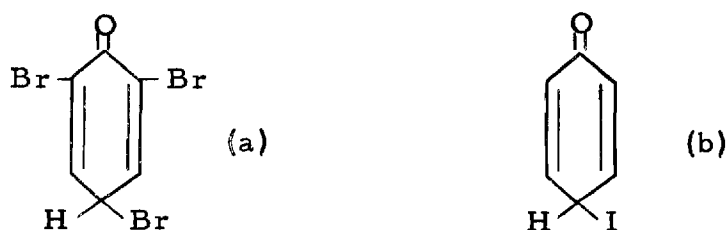
where HA is a buffer acid such as acetic acid. The first term was interpreted as involving attack of H_2OI^+ or alternatively I^+ upon phenoxide ion while the second term involved attack of HOAc and HOI upon phenoxide ion. The author has stated that the proton loss in iodination of phenol is kinetically insignificant and takes place after the rate-determining step (11).

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

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

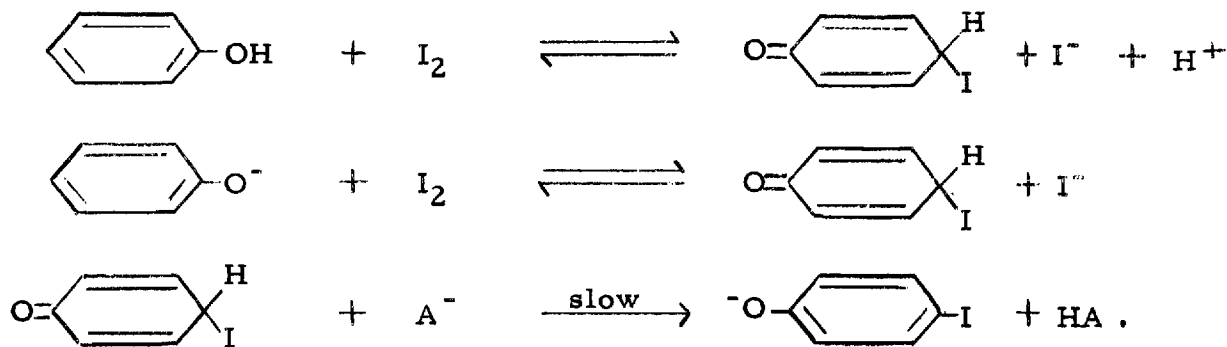
11. E. Berliner, J. Am. Chem. Soc., 73, 4307 (1951).

Grovenstein and Henderson (2) have proposed a mechanism for the iodination of phenol. In the bromination of 2,6-dibromophenol they found that under the experimental conditions the intermediate (a) showed little if any tendency to react with bromide ion, but it occurred to them that in the iodination of phenol an intermediate such as (b) should have a greater tendency to react with iodide ion.



This idea is supported by the greater nucleophilic character of iodide ion than bromide ion (12) and by the probable greater ease of nucleophilic displacement upon iodine than bromine (13).

They proposed the following mechanism:



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

13. J. Hine and W. H. Brader, Jr., J. Am. Chem. Soc., 77, 361 (1955).

The kinetic form of this mechanism is the same as that demanded by Berliner, Soper and co-workers' experimental results on the iodination of phenol. If this mechanism is the correct one, then molecular iodine is the effective iodinating agent, and the rate-determining step is the release of the proton from the aromatic nucleus.

The purpose of this thesis is to elucidate the true mechanism of the iodination of phenol. In particular in this investigation an answer was sought as to whether in solutions of high or moderately high iodide ion concentration, the concentration of the hypiodous acidium ion is sufficiently great to compete successfully as the iodinating agent with the much larger concentration of molecular iodine. This work will cover a study of the kinetics of iodination at much lower iodide ion concentrations than used previously and a study of a possible hydrogen isotope effect as a function of the iodide ion concentration. Knowledge of the exact mechanism of the iodination of phenol should contribute to an understanding of the mechanism of the iodination of similar substances such as tyrosine (14, 15, 16), aniline (7), and pyrole (17).

14. C. H. Li, J. Am. Chem. Soc., 64, 1147 (1942).

15. J. Roche, S. Lissitzky, O. Michel and R. Michel, Compt. rend., 232, 357 (1951).

16. J. Roche, S. Lissitzky, O. Michel and R. Michel, Annales pharmaceutiques francaises, 9, 163 (1951).

17. K. W. Doak and A. H. Corwin, J. Am. Chem. Soc., 71, 159 (1949).

CHAPTER II

SURVEY OF RELATED WORK

The Iodination of Phenol. --The mechanism of the iodination of phenol was investigated by Cofman (18), who showed that in acid solution molecular iodine does not iodinate, while in alkaline solution the iodine consumed in the reaction was equal to the concentration of hypiodous acid as calculated from the known kinetics of iodate formation. Cofman proposed that iodine is incapable of iodination and that hypiodous acid or the iodine cation is the halogenating agent.

The reaction was further studied by Soper and Smith (19) who used phosphate-buffered solutions in the near-neutral range and iodide ion concentrations such that the iodine existed practically entirely in the form of the tri-iodide ion. With such solutions containing phenol in excess with respect to the iodine, it was observed that the reaction was pseudo-unimolecular. The speed was found to be directly proportional to the phenol concentration and to the stoichiometric iodine concentration and inversely proportional to the square

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

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

of the actual iodide ion concentration.

Experiments carried out at different hydrogen-ion concentration showed that the velocity coefficient varied more rapidly than the inverse of the actual hydrogen ion concentration of the mixture, but less rapidly than its inverse square. Soper and Smith concluded that the iodination of phenol appears not to be caused by the iodine cation, but that the main reactions are those between the hypoiodous acid and the unionised and ionised phenol.

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

A kinetic study of the N-chlorination of amides indicated that, in addition to chlorination by the hypochlorite ion, certain amides are also N-chlorinated at a rate dependent on the product of the concentration of hypochlorous acid and the acid present as a component of the buffer (20). Painter and Soper (21) therefore re-examined the iodination of phenol in order to determine whether the kinetic effects observed in N-chlorination are paralleled by similar effects in C-iodination. The re-examination of the reaction showed that at constant pH the rate of iodination is greatly affected by the concentration of the buffer, being

20. R. P. Mauger and F. G. Soper, J. Chem. Soc., 71 (1946).

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

approximately a linear function of the concentration of the buffer acid,

$$\text{velocity} = k_o [\text{PhOH}] [\text{I}_3^-] + k_{\text{HA}} [\text{PhOH}] [\text{I}_3^-] [\text{HA}]$$

The term involving catalysis by acetic acid was interpreted by the authors as showing reaction between acetyl hypoiodite and the phenoxide ion. The authors concluded that the kinetics of the iodination conform with either (a) or (b):

$$\text{velocity} = k_o [\text{HOI}] [\text{PhOH}] + k_{\text{HA}} [\text{AcOI}] [\text{PhO}^-] \quad (\text{a})$$

$$\text{velocity} = k_o [\text{I}^+] [\text{PhO}^-] + k_{\text{HA}} [\text{AcOI}] [\text{PhO}^-]. \quad (\text{b})$$

By analogy with the chlorination of phenol by hypochlorous acid which also involves the phenoxide ion only (22), Painter and Soper preferred mechanism (b).

Berliner (11) studied the mechanism of the iodination of phenol in order to add further evidence in favor of a reaction involving the phenoxide ion. A possible distinction between the two mechanisms was approached from the electronic theory which demands that the order of activation by different substituents on the benzene ring toward an electrophilic reagent should be $-\text{O}^- > -\text{NH}_2 > -\text{OH}$ (23). Since the

22. F. G. Soper and G. F. Smith, J. Chem. Soc., 1582 (1926).

23. C. K. Ingold, Chem. Revs., 15, 225 (1934).

kinetics of the iodination of aniline had been reported by Berliner (7) it should be possible to establish the relative order of reactivity.

The reactions were performed at high iodide ion concentration (0.12 M) using a 4 to 1 ratio of phenol to iodine. The total ionic strength was 0.3 (Na Cl). Reactions were performed with phosphate buffers where both secondary and primary phosphate are catalytically active. The observed rate constants can be expressed by:

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

Using five different buffer ratios (pH 5.71-6.61) and plotting $k_{\text{obsd.}} (\text{H}^+)$ versus the primary phosphate ion concentration, Berliner obtained observed rate constants which are possibly true rate constants for phenol. Using these observed rate constants and calculating the phenoxide ion concentration at each pH, Berliner obtained the rate constants for the phenoxide ion reaction. A comparison with the aniline reaction showed that the uncatalyzed reaction of the phenoxide ion is 25,000 times faster than the uncatalyzed reaction of aniline.

Another comparison was made through the energies of activation. From the plot of $k_{\text{obsd.}} (\text{H}^+)$ versus primary phosphate at five different buffer ratios (pH 6.01-5.61) at 35° and 25° the energy of activation for the observed uncatalyzed reaction of phenol is 25.2 kcal; the activation energy of the uncatalyzed phenoxide ion reaction was

calculated to be 19.4 ± 0.4 kcal; the activation energy of the uncatalyzed aniline reaction was calculated to be 23.9 ± 0.5 kcal.

Berliner used another analogy of the aniline reaction where the reaction is expressed by the rate equation

$$\text{velocity} = k_o [\text{PhNH}_2] [\text{HOI}] [\text{H}^+] + k_{\text{cat}} [\text{PhNH}_2] [\text{HOI}] [\text{acid}]$$

and when this analogy is applied to the iodination of phenol it demands that the reaction involves the phenoxide ion.

$$\text{velocity} = k_o [\text{PhO}^-] [\text{HOI}] [\text{H}^+] + k_{\text{cat}} [\text{PhO}^-] [\text{HOI}] [\text{acid}]$$

There have been a number of halogenation reactions in water which show the same kinetic form as the two above mechanisms.

Wilson and Soper (24) have observed acid catalysis in the bromination of *o*-nitroanisole and of benzene with hypobromous acid. Derbyshire and Waters (25) have noted the same in the bromination of *w*-toluene-sulfonic acid.

Berliner concluded that the iodination of phenol involves, first, a preliminary equilibrium between HOI and H^+ to give H_2OI^+ or I^+ and, second, the rate-determining attack by the latter and by hypoiodous acid-buffer acid complex upon phenol. He also noted that

24. W. J. Wilson and F. G. Soper, J. Chem. Soc., 3376 (1949).

25. D. H. Derbyshire and W. A. Waters, J. Chem. Soc., 564 (1950).

this mechanism depends upon the assumption that the breaking of C-H bond of phenol occurs in a later fast step (11).

Tronov and Kolesnikova (26) studied the iodination of phenol in the presence of pyridine, nitrobenzene, hydrochloric acid, potassium fluoride, and sodium iodide. In alcohol the iodination proceeded rapidly and normally. The rate of iodination was increased by addition of pyridine which the authors assumed formed the molecular compound $[C_6H_5NI]^+ I^-$ which was presumed to be of high reactivity like the iodine cation. In the presence of sodium iodide the rate of iodination was lowered. Nitrobenzene and HCl also lowered the rate of iodination. The effect of potassium fluoride was not made clear. The authors did not propose a mechanism.

Taylor and Evans (27) conducted a study on the effects of variation of pH, potassium iodide concentration, and temperature on the iodination of 2, 4-dichlorophenol. The rate of iodination of 2, 4-dichlorophenol varies markedly with the pH. It was concluded by the authors that the reaction takes place between the phenolate ion and the iodine molecule; however, their rate constants assuming the iodine molecule is the halogenating agent is not constant with a variation of

26. B. Tronov and S. Kolesnikova, Soobshcheniya Mauch. Rabot. Vsesoyuz. Khim. Obshchestva im. Mendeleeva, 1, 46 (1953).

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

iodide ion concentration.

Berliner, Berliner and Nelidow (28) studied the relative rates of iodination of para-alkyl phenols in order to evaluate the effect of the alkyl groups on the meta position. All comparative rates were determined at a constant buffer concentration. In all runs, the stoichiometric iodine concentration was 0.002 M and that of the phenol was 0.008 M; the concentration of the potassium iodide was 0.12 M. The rate constants (in units of liter mole⁻¹ min.⁻¹) and the relative rates (enclosed in parentheses) are for the para-alkyl group equal Me, Et, iso-Pr, and tert-Bu respectively: 1.18(100), 1.44(122), 1.69(143), 2.16(183) in 10 per cent acetic acid as solvent. Other rate constants were determined in 25 per cent methyl alcohol and also 30 per cent dioxane. In each of these solvent mixtures the relative rates indicate the predominant operation of the inductive effect in the order Me₃C > Me₂CH > Et > Me. The rate constants for the reaction of the four p-alkyl phenols in 30 per cent methyl alcohol were determined at three different buffer concentrations at constant pH, and the rate constants for the uncatalyzed reaction were obtained. The relative rate constants for the uncatalyzed reactions show the same order of reactivity as the constants obtained at constant buffer concentration. No mechanisms were given by the authors, but

28. E. Berliner, F. Berliner and I. Nelidow, J. Am. Chem. Soc., 76 507 (1954).

it was assumed that the iodinating species is a positive entity - either I^+ or H_2OI^+ .

Li (14) has studied the iodination of tyrosine at 25° in acetate buffers. He has stated that the reaction involves four paths: namely, iodine and hypiodous acid reacting with phenol and phenoxide ion. He further noted that the most reactive pair is hypiodous acid and phenoxide ion, whereas the reaction between iodine and phenol is the least active. He claimed that the tyrosine molecule reacts with two molecules of iodinating agent simultaneously or that tyrosine reacts with the first molecule of iodine in a slow step and with the second in a subsequent fast step. This interpretation has been confuted by Roche and co-workers (15, 16) who found that disubstitution occurs in a second slower step. Li (29) has further studied the rate of the reactions between iodine and p-chlorophenol, tyramine and glycylytyrosine at 25° in acetate buffers. He interpreted the mechanisms for these reactions as similar to the mechanism for tyrosine; presumably the same confutation as indicated above exists for this interpretation.

Bromination of 2, 4-and 2, 6-dibromophenol. --Grovenstein and Henderson (2) in their work on the kinetics and mechanism of bromodecarboxylation of 3, 5-dibromo-2-hydroxy-and 3, 5-dibromo-4-hydroxybenzoic acids

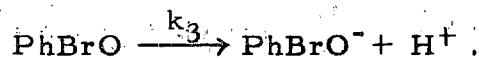
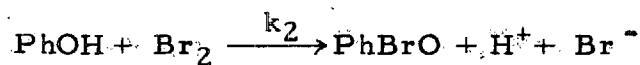
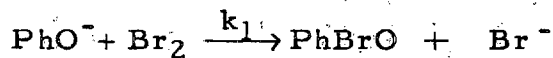
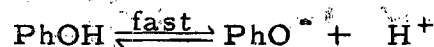
studied the bromination of 2,4- and 2,6-dibromophenol. At constant hydrogen ion concentration, the values of k^* were found to be constant within 11 per cent over a threefold variation of bromide ion concentration.

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

This bromide ion dependence indicated to the authors that molecular bromine (Br_2) is the effective brominating agent. A plot of k^* at constant bromide ion concentration versus the reciprocal of the hydrogen ion concentration revealed a linear relationship with k^* increasing as the hydrogen ion concentration decreases. The data fairly closely fit the relationship:

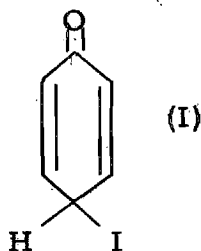
$$\frac{k_{app} K_1 (Br_2) [Br^-]}{[Br_3^-]} = k + \frac{k_3}{[H^+]} = k^*$$

or

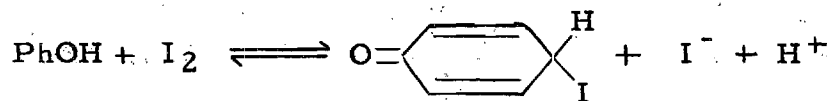
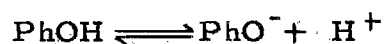


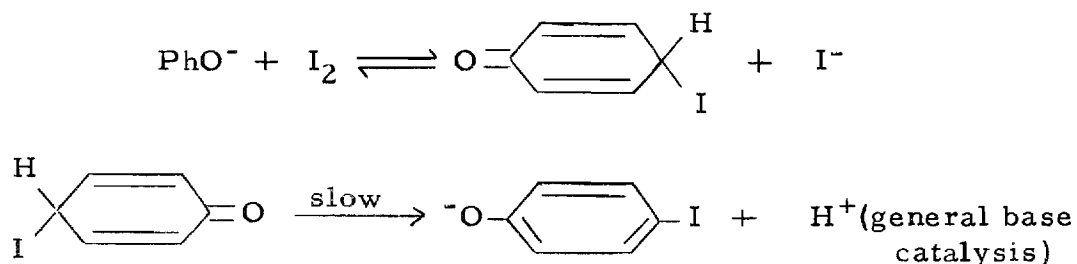
The rate-determining step is the attack of molecular bromine on phenol or the phenoxide ion. There appeared little, if indeed any, tendency for the PhBrO intermediate to revert to the starting phenol.

Grovenstein and Henderson (2), using analogies from their work on bromination of dibromophenols and bromodecarboxylation, have proposed a new mechanism for the iodination of phenol. In the bromination of 2,6-dibromophenol, they found that the intermediate formed from the initial reactants showed little, if any, tendency under the experimental conditions to revert to the starting phenol by reaction with halide ion; however, it occurred to the authors that an intermediate such as (I) from the iodination of phenol should show a greater tendency to do so.



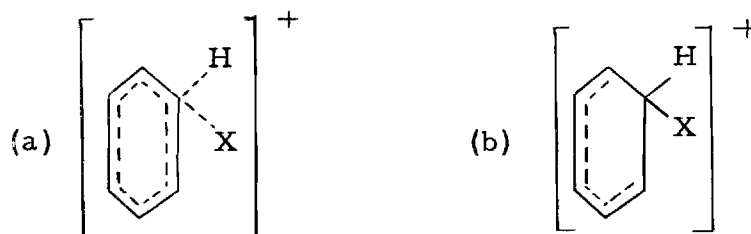
The authors presented the following mechanism which is in agreement with the kinetic data of Berliner and of Soper and co-workers.





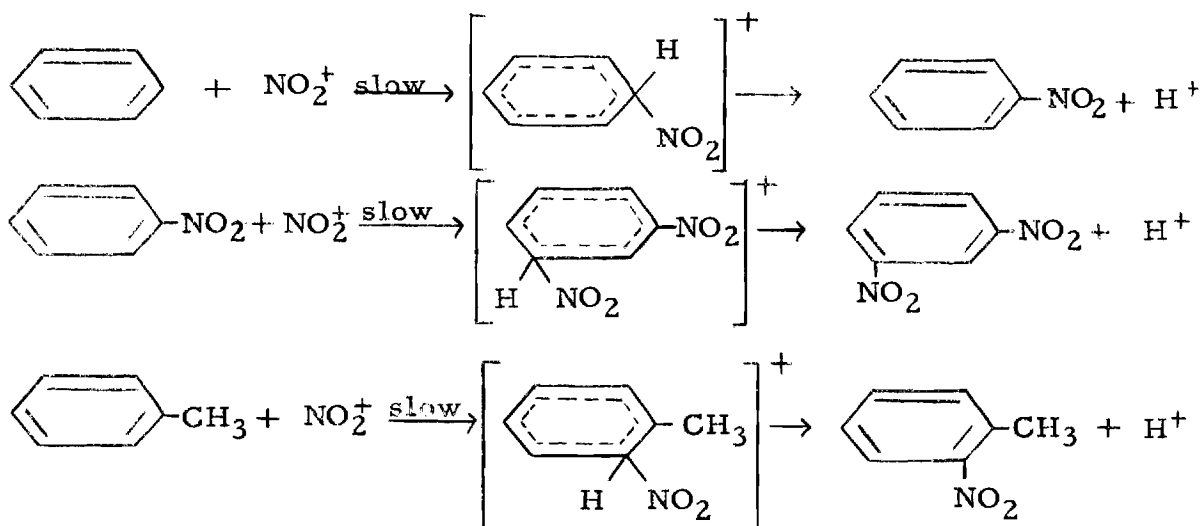
If this mechanism is correct, then molecular iodine is the effective iodinating agent, and the rate-determining step is the release of the proton. This iodinating agent has been shown to be responsible for the iodinolysis of *p*-methoxybenzeneboronic acid in aqueous solution at iodide ion concentrations of 0.1 to 0.5 M (9) and is apparently responsible for the exchange reaction between radioactive iodine and diiodotyrosine (10).

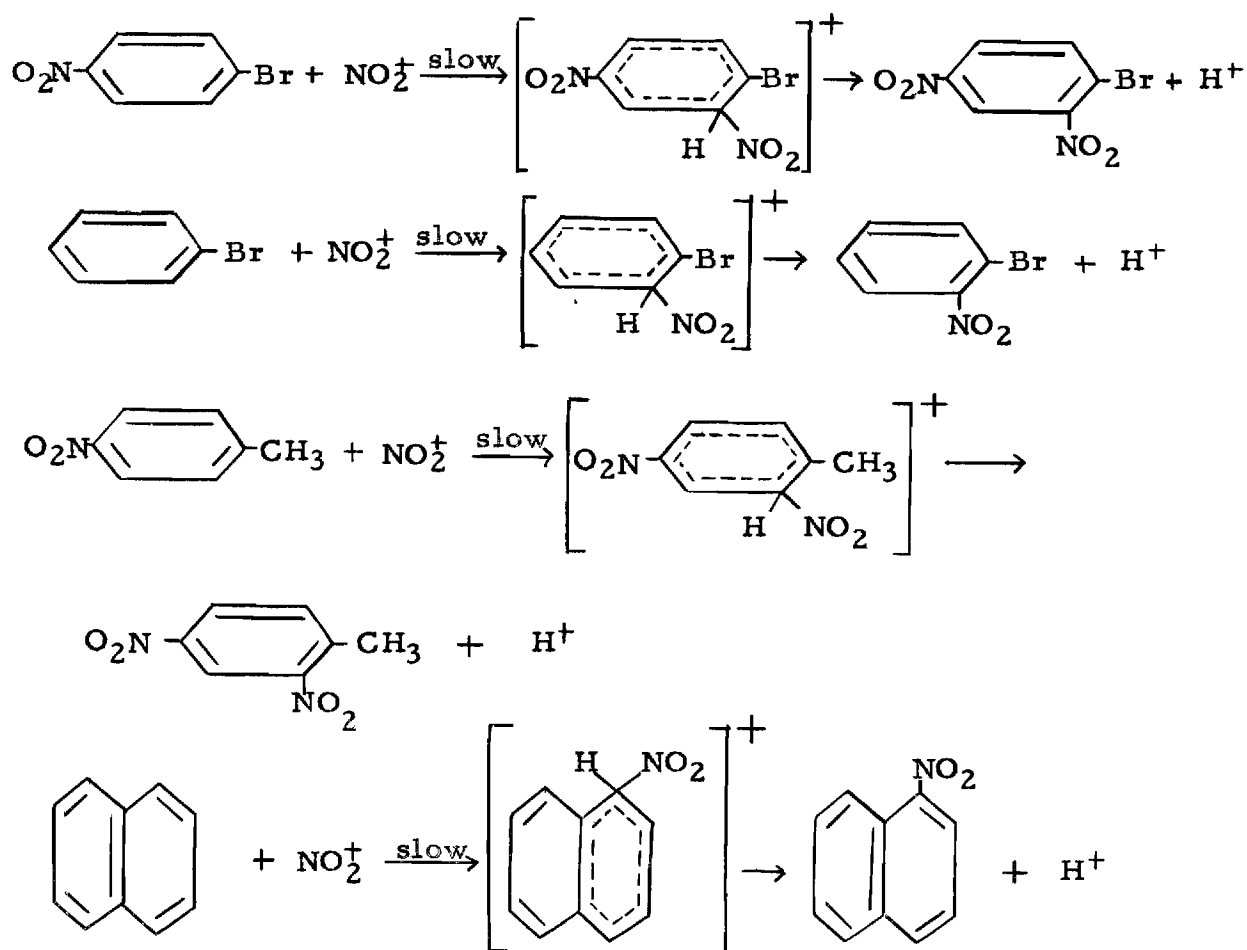
Survey of Kinetic Isotope Effects During Aromatic Electrophilic Substitution. -- Melander (4), in a detailed discussion of the mechanism of aromatic electrophilic substitution, considered the hydrogen isotope effect in the two alternative $\text{S}_{\text{E}}2$ processes - the single step replacement with the activated complex (a), and the two stage process with an intermediate addition compound (b).



In the limiting case (a) the π -electrons of the benzene ring do not take part in the formation of π -bonds; while in (b), two π -electrons are used for the addition of the cation with resulting appearance of four bonds of sp^3 type at the nuclear carbon atom. If, experimentally, identical rates of substitution for hydrogen isotopes are found, the stepwise reaction occurs with a rate-determining first step; if a substantially slower rate is observed for the heavy isotope the substitution may occur either by the stepwise reaction with the second step rate-determining, or by the single-step replacement.

Melander (3, 4) conducted a number of nitrations of aromatic compounds and their tritium analogues using relatively high proportions of nitric acid and aromatic compound to sulfuric acid (there was lack of homogeneity in some cases). Within the accuracy of the method the rates were found to be equal. He found that the following nitrations take place according to the two-step mechanism with the first-step rate-determining:





Bonner, Bowyer and Williams (30) studied the rates of nitration of nitrobenzene and pentadeuteronitrobenzene in 97.4 per cent and 86.72 per cent sulfuric acid and found that the rates are very nearly the same. Lauer and Noland (31) found that nitration of benzene

30. T. G. Bonner, F. Bowyer and G. Williams, J. Chem. Soc., 2650 (1953).

31. W. M. Lauer and W. E. Noland, J. Am. Chem. Soc., 75, 3691 (1953).

containing 91.5 per cent monodeuterobenzene gave nitrobenzene containing 74.9 mole per cent monodeuteronitrobenzene and m-dinitrobenzene containing 60.9 mole per cent monodeutero-m-dinitrobenzene. The authors state that these are the concentrations expected if there is no hydrogen isotope effect.

In halogenations little has been done to establish the steps of the reaction after the attack of the electrophilic reagent. Molecular halogens as the electrophilic reagent often involve complicated pre-equilibria reactions, and it has been argued by Robertson (32) that the proton-loss is probably rapid and not rate-determining. Melander (4) found that in the iodine-catalysed bromination of toluene and of tritiated toluene the rates proceeded with no preferential displacement of either isotope. P. B. D. de la Mare, Dunn and Harvey (33) studied the rates of bromination of benzene and of hexadeuterobenzene by aqueous hypobromous acid containing perchloric acid and found that the rates were the same within experimental error. Zollinger (34) reported, but without experimental details, that an isotope effect ($k_H/k_D = 2.0 \pm 0.6$) exists in the reaction of molecular bromine and 2-naphthol-6,8-disulphonic acid.

32. P. W. Robertson, J. Chem. Soc., 1269 (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).

Berglund-Larsson and Melander (35) studied the sulphonation of bromobenzene containing tracer amounts of bromobenzene-4-t. The reactions were carried out with oleum, partly without solvent, and partly in nitrobenzene solution. The rates of reactions in nitrobenzene solution gave an isotope ratio (k_T/k_H) of 0.55 ± 0.09 at 0° . In pure oleum lack of homogeneity caused some discrepancies but the value seems to be in reasonable agreement with the same figure.

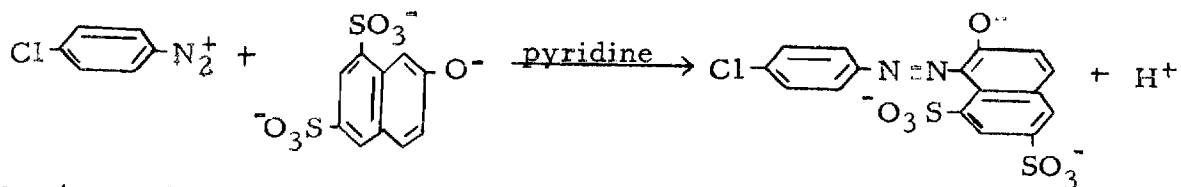
Bonner and Wilkins (36) have observed a small, but definite, isotope effect in the cyclodehydration of 2-(2, 4, 6-trideuteroanilino) pent-2-en-4-one and its protium analogue. The authors considered this reaction to be an intramolecular electrophilic substitution.

Zollinger (37a) has studied the azo coupling reaction of 2-naphthol-6, 8-disulphonic acid and the 1-deutero-2-naphthol-6, 8-disulphonic acid with 4-chlorobenzenediazonium ion. He found the reaction to be strongly base catalyzed and the relative reaction rates gave a isotope effect of 6.55. The following reactions were studied:

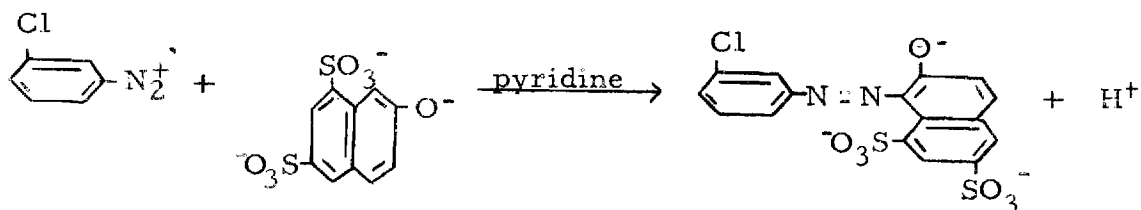
35. U. Berglund-Larsson and L. Melander Arkiv Kemi, 6, 219 (1954).

36. T. G. Bonner and J. M. Wilkins, J. Chem. Soc., 2358 (1955).

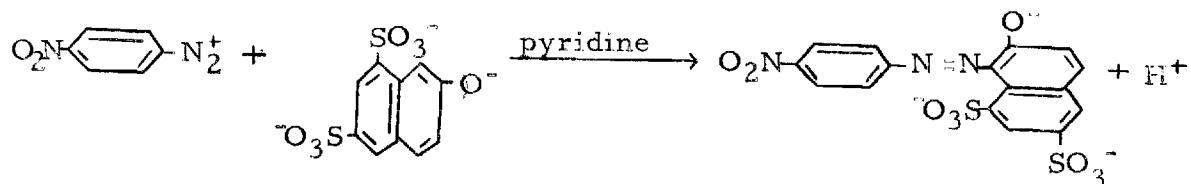
37a. H. Zollinger, Helvetica Chimica Acta, 38 1603 (1955).



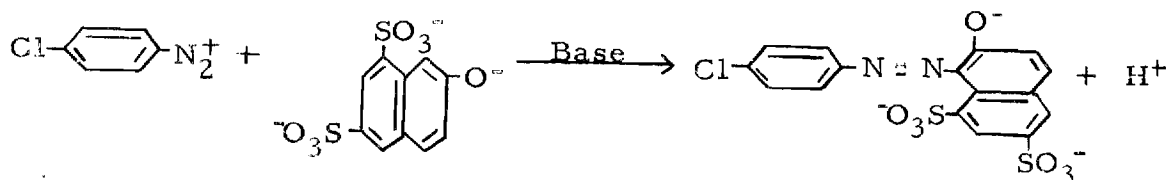
$$k_{\text{H}}/k_{\text{D}} = 6.55$$



$$k_{\text{H}}/k_{\text{D}} = 5.48 \text{ (37b)}$$



$$k_{\text{H}}/k_{\text{D}} = 4.78 \text{ (37b)}$$



Base

 $k_{\text{H}}/k_{\text{D}}$ (37c)

55.6 M Water

6.55

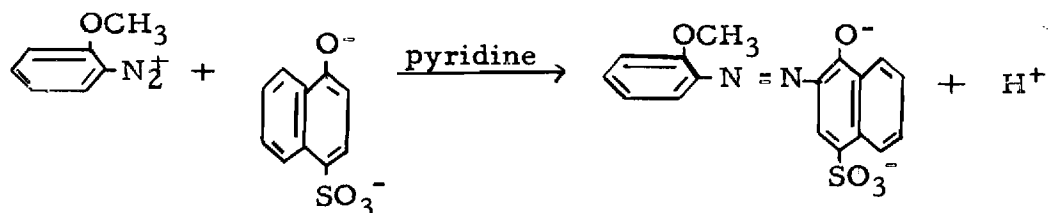
0.0232 M Pyridine

6.01

0.905 M Pyridine

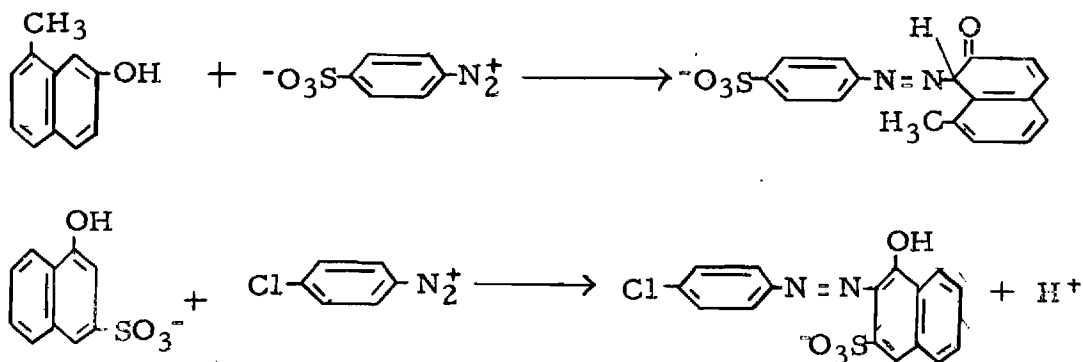
3.62

37b. Ibid., p. 1620.37c. Ibid., p. 1619.



$$k_H / k_D \approx 1 \text{ (37a).}$$

Recently Zollinger (34) reported two azo coupling reactions, but he did not give complete experimental data concerning the reactions.



$$k_H / k_D = 3.0$$

The first reaction was reported by Zollinger (unpublished work of O. Stamm) to be catalyzed by bases and thus presumably would show an isotope effect. The results of the second reaction were taken from the unpublished work of R. Ernst.

CHAPTER III

SOURCE, PREPARATION, AND PURIFICATION OF MATERIALS

Acetic Acid. -- The acetic acid used for all preparations and for kinetic runs was purified by a senior at Georgia Tech on November 11, 1954. The label indicated that the acetic acid was purified by the method of Bradfield and Orton (38). The acetic acid was used without further purification.

Calcium Chloride. -- Mallinckrodt, Analytical Reagent, anhydrous calcium chloride was used without further purification.

Calcium Sulfate. -- Hammond Drierite, anhydrous calcium sulfate, 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. This method of preparation of deuterium chloride was used by Langseth and Klit (39). Ten milliliters of heavy water was slowly dropped from an equal

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

39. A. Langseth and A. Klit, Kgl. Danske Videnskab. Seiskab, Math. -fys. Medd., 15, No. 13 (1937).

pressure funnel into a 100 ml. three neck round bottom flask containing 25 ml. of purified thionyl chloride. Dried nitrogen was continuously swept through the apparatus to help drive the deuterium chloride gas through the system. From the round bottom flask the gases, sulfur dioxide and deuterium chloride, were passed through two glass traps which were cooled by acetone and solid carbon dioxide. The boiling point of sulfur dioxide is -10° and the freezing point is -75.5° (40a), and deuterium chloride has a boiling point of approximately -85° and a freezing point of approximately -115° .¹ A trap cooled with a slurry of acetone and solid carbon dioxide has a temperature of around -80° thus the sulfur dioxide was crystallized out and the deuterium chloride gas passed through the traps. The deuterium chloride was then bubbled through a glass bulb containing several small pin-point holes into 50 ml. of heavy water. The end of the system was open to the atmosphere, but a calcium chloride drier was used to prevent water from entering the system. The deuterium chloride solution was titrated with standard sodium hydroxide solution and found to be 8.57 M. To check the solution for oxidizing agents, a sample of deuterium

40a. N. A. Lange, Handbook of Chemistry. Sixth Edition, Sandusky: Handbook Publishers, Inc., 1946, p. 262.

¹ The indicated temperatures are for hydrogen chloride but as an approximation deuterium chloride should have a boiling point and freezing point within two or three degrees of these temperatures.

chloride solution was added to a potassium iodide-sulfuric acid solution. Starch was then added and no visible blue color was present.

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

Heavy Water. --Heavy water was purchased from the Stuart Oxygen Co., 211 Bay Street, San Francisco, California. The chemical was labeled as batch IV and 99.5 per cent pure deuterium oxide.

Hydrochloric Acid. --DuPont, C. P. Reagent, hydrochloric acid was used without further purification.

Iodine. --Merck Resublimed - U. S. P. iodine was used without further purification. Two types of iodine solutions were used in this work. Where a high iodine concentration was desired an iodine-iodide ion solution was prepared by weighing the solutes and diluting to the desired volume. When a low iodine concentration was desired, the solution was prepared as follows. Solid iodine was ground in an agate mortar and excess iodine was added to a one liter volumetric flask. Approximately 800 ml. of distilled water was then added and the flask shaken for approximately ten hours. The flask was then filled to exactly one liter and the solution filtered through a sintered-glass funnel. The concentration of the solution was always about 0.0013 M. This solution was then diluted to any desired

concentration for use as a stock solution for kinetic runs. It was found that iodine solutions are unstable with the iodine being reduced to iodide ions. It was found that the stock iodine solutions should be used within 24 hours especially when working at extremely low iodide ion concentrations.

Linseed Oil. --Raw, refined, unboiled linseed oil was used without further purification.

Magnesium Sulfate. --Mallinckrodt, Analytical Reagent, anhydrous magnesium sulfate (powder) was dried in vacuum for three hours at 130° . The anhydrous salt was then used without further purification.

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

Nitrogen. --Marks, compressed, cylinder, nitrogen gas was always dried over calcium chloride, but was otherwise used without further purification.

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

Phenol. --Baker U. S. P. phenol was purified by distilling through a ten inch column packed with 3/16 inch glass helices at atmospheric pressure. The whole distillation system was wrapped with asbestos string in order

to prevent loss of heat during distillation. The phenol distilling in the range of 175° - 185° was collected. This distillation was then repeated. The twice distilled phenol was then heated for four hours at 50° over anhydrous calcium sulfate. The phenol was decanted and then dried over anhydrous calcium chloride for 30 minutes at 50° . The phenol was filtered while warm and distilled in vacuum through a ten inch column packed with 3/16 inch glass helices. Ten milliliter samples of phenol were poured into glass vials and sealed under nitrogen for future use. A sample of purified phenol melted sharply at 40° - 41° . The recorded melting point of phenol is 41° (41). Stock phenol solutions of 0.08 to 0.02 M were found to be stable at room temperature for at least two months.

Phenol-2, 4, 6-d₃. -- Phenol-2, 4, 6-d₃ was prepared by the general procedure of Ingold and co-workers (42, 43). According to Ingold one-half of the phenol should be present as the phenoxide ion in order to have maximum deuteration at the end of a specified time.

Sodium deuterioxide was prepared by adding very slowly 100 grams of heavy water to 1.8370 grams of sodium metal. This reaction

41. C. D. Hodgmann, Handbook of Chemistry and Physics. Thirty-third Edition, Cleveland: Chemical Rubber Publishing Co., 1951, p. 1050.

42. C. K. Ingold, C. G. Raisin and C. L. Wilson, J. Chem. Soc., 1637 (1936).

43. A. P. Best and C. L. Wilson, J. Chem. Soc., 28 (1938).

was performed in a 200 ml. three neck round bottom flask in which nitrogen gas was continuously let into the system from the top-neck; a water condenser was used to condense any heavy water that might be evaporated and a 100 ml. dropping funnel was used to control the rate of reaction.

The sodium deuteroxide was divided into two equal volumes and then placed into 50 ml. reaction tubes. To one tube was added 7.5127 grams of phenol and to the other was added 7.5204 grams of phenol. The tubes were sealed at atmospheric pressure; however, it was found that the reaction tubes should have been sealed under a nitrogen atmosphere as a little of the phenol was destroyed by oxidation as judged by development of an orange color during the heating period. The tubes were placed in a liter round bottom flask containing water and heated at the boiling point of water for ninety-six hours. The tubes were then broken open and the homogenous solution placed in a 250 ml. round bottom flask. The flask was then connected to a distillation system. Sodium metal (1.8614 grams) was then added to the solution through the connecting, parallel sidearm distillation tube. Nitrogen gas was continuously let into the system as the sodium metal was added. This sodium metal converted all the phenol to the sodium salt. The heavy water was then distilled using an oil-bath. The heavy water distilled at 101° - 101.5° at atmospheric pressure. The salt was then dried for three hours while still in the distillation system using a vacuum pump and an oil bath temperature of 105° .

While the deuterated sodium phenoxide was still in the round bottom flask, 9.32 ml. of 8.57 M deuterium chloride was added to neutralize one-half of the sodium phenoxide. The flask was neither cooled nor nitrogen present during this operation; however, these precautions should have been taken because the heat of the reaction may have initiated oxidation of some of the phenol. One hundred grams of fresh 99.5 per cent heavy water was then added to the phenol solution. The solution was then divided into two equal volumes and transferred to the reaction tubes. The reaction tubes were sealed under nitrogen and then placed into a liter round bottom flask containing water and heated at the boiling point of water for ninety-six hours. The reaction tubes were then broken open and the solution placed in a 250 ml. round bottom flask and 1.8370 grams of sodium metal was added by the same method indicated above. The heavy water was then distilled by the same method indicated above, but the deuterated sodium phenoxide was not dried for three hours as was previously done. Thirty milliliters of 8.57 M deuterium chloride was added to the round bottom flask. The flask was cooled with ice water and nitrogen gas was swept into the flask during this operation. The solution was checked with pH paper and found to be acidic.

The deuterated phenol was extracted from the solution by shaking with 50 ml. of anhydrous diethyl ether. This process was repeated two times. The ether solutions were decanted into a separatory funnel

and anhydrous magnesium sulfate was added to the solution to extract any heavy water that might be present.

The ether solution was transferred to a 200 ml. round bottom flask and the ether was distilled at atmospheric pressure using an oil-bath. The distilling apparatus was then modified for vacuum distillation and the deuterated phenol distilled at 100 mm. pressure under a nitrogen atmosphere. The distillation had to be done at a temperature below the normal boiling point of phenol because of the possibility that the deuterium on the -OD group might exchange with meta hydrogens. (44).

The phenol-2,4,6-d₃ was placed in a round bottom flask under nitrogen for future use. The percentage yield based on the starting weight of phenol was 50.4 per cent. The purity of the phenol-2,4,6-d₃ was calculated to be 99 per cent pure using the partition ratio given by Ingold (42). See Appendix B for the calculation.

Potassium Dichromate. --Merck Reagent Potassium dichromate was purified as indicated by Kolthoff and Sandell (45a). Potassium dichromate was twice recrystallized from water, followed by drying of the pulverized

44. A. I. Brodskii, G. P. Mukluktiin, I. I. Kukhtenko and I. P. Gragerov, Doklady Akad. Nauk S. S. S. R., 57, 463 (1947).

45a. I. M. Kolthoff and E. B. Sandell, Textbook of Quantitative Inorganic Analysis. Third Edition, New York: The MacMillan Co., 1952, p. 579.

crystals at 150° to 200° in an electric oven.

Potassium Iodate. -- Baker Analyzed Reagent potassium iodate was purified as indicated by Kolthoff and Sandell (45b). Potassium iodate was recrystallized from water, followed by drying of the crystals at 180° in an electric oven.

Potassium Iodide. -- Merck Reagent potassium iodide was used without further purification. The potassium iodide was checked for iodate by a procedure indicated by Kolthoff and Sandell (45c). There was no iodate present.

Potassium Acid Phthalate. -- Baker Analyzed potassium acid phthalate was used without further purification.

Quinoline. -- The Matheson Co., Inc. quinoline was used without further purification.

Sodium Metal. -- Baker Reagent Grade freshly cut sodium metal was used without further purification. The sodium metal was always stored in toluene until needed.

Sodium Acetate. -- Baker Analyzed Reagent Grade sodium acetate tri-

45b. Ibid., p. 594.

45c. Ibid., p. 592.

hydrate was decomposed to the anhydrous salt. The tri-hydrate was heated for forty-eight hours at 125° - 130° . Sodium acetate tri-hydrate decomposes to give anhydrous sodium acetate at 120° (40b). The sodium acetate was then used without further purification. This salt was found to be impure (note Table 8) and sodium acetate was then prepared by the reaction of purified acetic acid with sodium hydroxide using a Beckman pH meter. The sodium acetate was then dried as described above. The salt was found to be pure (note Table 11).

Sodium Carbonate. --Mallinckrodt Analytical Reagent anhydrous sodium carbonate was used without further purification.

Sodium Chloride. --Baker Analyzed Reagent sodium chloride was used without further purification.

Sodium Hydroxide. --Fisher Certified Reagent Grade sodium hydroxide was used without further purification in the preparation of sodium acetate and sodium perchlorate. In making standard solutions of sodium hydroxide, the sodium hydroxide was purified by dissolving 50 grams in 50 ml. of water in a Pyrex flask (45d). The sodium carbonate remains in sus-

40b. N. A. Lange, Handbook of Chemistry. Sixth Edition, Sandusky: Handbook Publishers, Inc., 1946, p. 250.

45d. I. M. Kolthoff and E. B. Sandell, Textbook of Quantitative Inorganic Analysis. Third Edition, New York: The MacMillan Co., 1952, p. 526.

pension and the solution is filtered through a sintered-glass crucible. The concentrated sodium hydroxide was diluted to the desired molarity with distilled water that had been freed of carbon dioxide by the use of nitrogen gas. The molarity of stock solutions of sodium hydroxide was determined by titration against a known molarity of potassium acid phthalate solution. Phenolphthalein was used as the indicator.

Sodium Iodide. -- Baker Analyzed Reagent sodium iodide was used without further purification. This sodium iodide was used in all kinetic reactions; however, Merck, U. S. P. sodium iodide was used without further purification to stop all kinetic reactions.

Sodium Perchlorate. -- Sodium perchlorate was prepared by reacting perchloric acid with solid sodium hydroxide. Near the end point a solution of sodium hydroxide was titrated using a Beckman pH meter until the perchloric acid solution was neutral. The salt was then evaporated to dryness in an electric oven in vacuum (29 in.) at 130° - 140° for nine hours. Sodium perchlorate monohydrate decomposes to give anhydrous sodium perchlorate at 130° (40c).

Sodium Thiosulfate. -- Merck Reagent sodium thiosulfate pentahydrate was used without further purification to prepare solutions of approximately

40c. N. A. Lange, Handbook of Chemistry. Sixth Edition, Sandusky: Handbook Publishers, Inc., 1946, p. 256.

0.1 M as indicated by Kolthoff and Sandell (45c). Stock solutions of sodium thiosulfate pentahydrate were prepared by dissolving 25 grams of sodium thiosulfate in one liter of freshly boiled, cooled water. To this solution was added 0.1 grams of sodium carbonate. The solution was allowed to stand one day before standardizing. To standardize the solution potassium iodate or potassium dichromate in a sulfuric acid solution were used. These methods are described by Kolthoff and Sandell (45b). It was found that potassium iodate using starch solution as an indicator gave a much clearer end-point as compared to potassium dichromate.

Starch. --Baker, C. P. potato starch was used without further purification. Starch solutions were prepared as indicated by Kolthoff and Sandell (45e). Two grams of starch and 10 milligrams of mercuric iodide were triturated with a little water, and the suspension added slowly to one liter of boiling water. The solution was boiled until it was clear. The solution was then cooled and stored for use.

Sulfuric Acid. --DuPont C. P. sulfuric acid was used without further purification.

Thionyl Chloride. --Thionyl chloride was purified by the method recom-

mended by Fieser (46). Eastman Organic thionyl chloride (200 ml.) was thoroughly mixed in a round bottom flask with 40 ml. of quinoline and distilled. The open system was protected from moisture in the air by calcium chloride. After distillation the thionyl chloride was mixed with 52 ml. of linseed oil and distilled. The observed boiling point was 73.0° - 73.5° . The recorded boiling point of thionyl chloride is 78.8° (40d).

Toluene. --Eastman Kodak (Practical) toluene was used without further purification.

46. L. F. Fieser, Experiments in Organic Chemistry. Third Edition, Boston: D. C. Heath and Company, 1955, p. 345.

40d. N. A. Lange, Handbook of Chemistry, Sixth Edition, Sandusky: Handbook Publishers, Inc., 1946, p. 264.

CHAPTER IV

EXPERIMENTAL TECHNIQUES FOR KINETIC MEASUREMENTS

General. -- The iodination of phenol in buffered aqueous solutions has been found to be first order in stoichiometric iodine and first order in phenol (19, 21). In this work integrated second order rate constants were calculated on this basis. The rate equation used was the conventional second order equation

$$\frac{dx}{dt} = k_{app} (a - x) (b - x)$$

in which a is the initial stoichiometric molar concentration of iodine, b is the initial molar concentration of phenol, and x is the molar concentration of stoichiometric iodine reacted (or product formed) at time t (47). The integrated form of this equation that was used to calculate the integrated rate constants is

$$k_{app} = \frac{2.303}{(b - a)t} \log \frac{a(b - x)}{b(a - x)} \quad (47).$$

The units of k_{app} are (liter) (mole⁻¹) (sec.⁻¹) or (l./mol. sec.). All

of the rate constants cited in the tables were calculated on this basis except in Table 3 where t is in terms of minutes.

Throughout the course of the experimental work, two general techniques for measuring the kinetics of the reactions were used. In Runs 1-9, 11-14 and 17-22, the reactions were carried out in a single flask and aliquots were withdrawn at noted times and the unconsumed iodine titrated after stopping the reaction. In the remainder of the runs, the reaction was run concurrently in a number of flasks. The reaction was then stopped in individual flasks at noted times and the contents analysed for unconsumed iodine.

In all cases, analysis for iodine was by titration with standard sodium thiosulfate solution. The standard sodium thiosulfate solution was prepared fresh each day by diluting a stock solution of approximately 0.1 M sodium thiosulfate. The stock solution of sodium thiosulfate was standardized against potassium iodate every two months and was found not to change concentration more than 0.07 per cent during this interval. A definite volume of potato starch solution, depending on the volume of iodine solution to be titrated, was used as an indicator. Kolthoff and Sandell (45f) recommend the use of five ml. of 0.2 per cent starch solution for each 100 ml. of solution to be titrated. In all cases a 10 ml. buret was used which could be read to an accuracy of ± 0.01 ml.

45f. I. M. Kolthoff and E. B. Sandell, Textbook of Quantitative Inorganic Analysis. Third Edition, New York; The MacMillan Company, 1952, p. 590.

All runs were thermostated in a Sargent Constant Temperature Water Bath, model S-84805, equipped with a H-B Instrument Company hermetically sealed, hydrogen filled mercurial thermoregulator having a sensitivity of 0.01° . The bath temperature was set at $25.0 \pm 0.1^{\circ}$ as checked against a Bureau of Standards thermometer. The bath temperature was found to be $25.0 \pm 0.1^{\circ}$ and was observed to stay constant within 0.02° .

Sample Withdrawal Method. --Runs 1-9, 11-14 and 17-22 were all performed by this technique. In a typical run of this type, stock solutions of iodine, sodium iodide, acetic acid, sodium acetate and sodium perchlorate and water were buretted into a 100 ml. red, low actinic, volumetric flask fitted with a ground glass stopper. The molarity of the stock solutions were such that when the flask was filled to exactly 100 ml. the molarity of the chemicals was that desired. The flask was then thermostated to $25.0 \pm 0.1^{\circ}$ by placing in the water bath. A volume of phenol from a stock solution previously thermostated at $25.0 \pm 0.1^{\circ}$ was then pipetted into the volumetric flask and the flask shaken vigorously. The volumes of stock solutions were found to be additive and thus the volume of phenol added made the total volume of the solution exactly 100 ml. A 10 ml. sample of the solution was quickly withdrawn and drained into an Erlenmeyer flask containing 20 ml. of 1 N sulfuric acid. As the solution passed the half-way mark on the pipette, the stopwatch was started; and this was designated as zero time for the reaction. The iodine solu-

tion was quickly titrated with freshly prepared sodium thiosulfate solution, and starch solution was added as an indicator. The stoichiometric iodine concentration in the first aliquot was considered the blank, and this concentration represented zero per cent reaction. Seven 10 ml. aliquots of solution were then withdrawn at definite intervals of time, and as the solution passed the half-way mark of the pipette, the time was recorded. A run was usually followed to 60 per cent reaction.

Since the rate of the iodination of phenol is expressed by two terms, one involving an inverse first power of hydrogen ion concentration and the other involving an inverse second power of hydrogen ion concentration, and both terms are inversely proportional to the square of the iodide ion concentration, 20 ml. of 1 N sulfuric acid was able to slow the reaction to a very slow rate at iodide ion concentrations of 0.008 to 0.08 M (21). At iodide ion concentrations below this, the rate of reaction was not slowed to a point where accurate titrations of iodine could be made. The test of this hypothesis, Run 22, was made by allowing a stopped reaction mixture to stand for varying periods of time before titration. As shown in Table 1, this had a significant effect on the titer of thiosulfate and indicated that the reaction of iodine and phenol was not stopped by 20 ml. of 1 N sulfuric acid at iodide ion concentrations below 0.008 M.

In this procedure the glass stoppers on the low actinic, volumetric flasks were not greased. In performing kinetic runs at low iodide

Table 1

Effect of Standing upon Accuracy of Titration

Run 22, Phenol in 0.00420 M Sodium Iodide Solution at 25° $(\text{Phenol})_0 = 0.007990 \text{ M}$ $(\text{HC}_2\text{H}_3\text{O}_2) = 0.500 \text{ M}$ $(\text{I}_2)_0 = 0.001950 \text{ M}$ $(\text{NaC}_2\text{H}_3\text{O}_2) = 0.0500 \text{ M}$ $(\text{NaI})_0 = 0.00420 \text{ M}$ $(\text{NaClO}_4) = 0.2458 \text{ M}$ $(\text{Na}_2\text{S}_2\text{O}_3) = 0.005054 \text{ M}$

10.0 ml. aliquots withdrawn

Time elapsed (sec.)	Titer (ml.)	Per cent reaction
0	7.23	0.00
290	6.94	4.01
0	5.83	0.00
900	5.46	6.35

ion concentration there exists the problem of volatilization of iodine.

To learn how much iodine at low iodide ion concentration was being lost by volatilization each time the stopper was removed to withdraw a sample, a blank run was conducted at 0.00420 M sodium iodide. It was found that there was a significant loss of iodine during a reaction using this sample withdrawal method. See Table 2, Run 21, for the results of this experiment.

Multiple Flask Method. -- This method of conducting kinetic runs was used on all reactions not indicated in the tables as 10 ml. aliquot withdrawals. This method was adopted in order to alleviate the problems encountered with the sample withdrawal method.

In a typical run of this type, stock solutions of iodine, sodium iodide, acetic acid, sodium acetate, sodium perchlorate and water were usually buretted into a 50 ml. red, low actinic, volumetric flask fitted with a ground glass stopper; however, a 100 ml. or even 200 ml. volumetric flask was sometimes used depending on the iodine concentration of the reaction. The 200 ml. volumetric flasks were not colored; instead black ink was added to the water in the water bath in order to filter out most of the light. The molarity of the stock solutions was such that when the flask was filled to exactly the required volume the molarity of the chemicals was that desired. The flask was then thermostated to 25.0^o by placing in the water bath. A volume of stock phenol solution pre-

Table 2

Check for Volatilization of I_2 Run 21, Blank in 0.00420 M Sodium Iodide Solution at 25.0°

(Phenol) ₀ - Zero	($HC_2H_3O_2$) - <u>0.500 M</u>
(I_2) ₀ - <u>0.001950 M</u>	($NaC_2H_3O_2$) - <u>0.0500 M</u>
(NaI) ₀ - <u>0.00420 M</u>	($NaClO_4$) - <u>0.2458 M</u>
	($Na_2S_2O_3$) - <u>0.005054 M</u>

10.0 ml. aliquots withdrawn

Time elapsed (sec.)	Titer (ml.)	Per cent loss of (I_2)
(blank)	7.72	0.00
420	7.73	0.00
840	7.73	0.00
1560	7.73	0.00
4020	7.72	0.00
4860	7.71	0.13
6060	7.73	0.00
7620	7.67	0.78
10,320	7.62	1.42

viously thermostated at 25.0° was then pipetted into the volumetric flask. The zero time for the reaction was taken when one-half of the phenol had drained into the flask from the pipette. It took about 10 seconds to drain a five ml. pipette. The flask was then shaken vigorously. At a definite interval of time a flask was removed; and when the second hand of the watch reached the time desired to stop the reaction, 1 ml. per 50 ml. of solution of 8 M sodium iodide solution was injected into the reaction flask with a syringe, and the flask quickly shaken. This operation required about 10 seconds. The contents of the reaction flask were then drained into a Erlenmeyer flask, and the syringe and flask were thoroughly washed with distilled water. The flask was washed three times using approximately 15 ml. of water each time. The iodine solution was quickly titrated with freshly prepared sodium thiosulfate solution using starch solution as an indicator.

Eleven reaction flasks were usually prepared with two of the flasks serving as blanks in order to determine the initial stoichiometric iodine concentration. The initial stoichiometric iodine concentration using the multiple flask method was determined by two different procedures. The blanks for Runs 23-25 were prepared by diluting a definite volume of stock iodine solution to the marked level on the volumetric reaction flask with water. It was found that this method was inaccurate because as the water was added, iodine volatilized. See Table 26 for the results of this experiment. The ground glass stoppers for the volumet-

ric flasks were not greased for the runs just indicated. Even though it seemed unlikely that iodine could volatilize from a ground glass stoppered flask, it was found that a blank containing all reaction chemicals except phenol lost a significant amount of iodine. See Table 26 for the results of this experiment.

All other runs not mentioned above and using the multiple flask method were performed in volumetric flasks with silicone greased ground glass stoppers. The blanks for the determination of the initial stoichiometric iodine concentration were prepared just as a typical run except water was added to fill the flask to the required volume instead of phenol. Before this method was used, it was checked by preparing blank solutions containing all the required reagents except phenol and using greased ground glass stoppers. After an interval of time that would represent 70 per cent reaction, there was no loss of iodine concentration. See Table 26 for the results of this experiment.

CHAPTER V

KINETIC MEASUREMENTS IN AQUEOUS BUFFER
OF SODIUM ACETATE-ACETIC ACID

To distinguish between the stoichiometric concentration of a reagent and the actual concentration of a particular molecular species, the stoichiometric concentration will be designated in this thesis by enclosure in parentheses, (), and the actual concentration of a species by enclosure in square brackets [].

The mechanism of the iodination of phenol in water containing acetate-acetic acid buffer as given by Berliner has the following rate expression:

$$\text{rate} = \frac{k_1 [\text{PhOH}] [\text{I}_2]}{[\text{H}^+][\text{I}^-]} + \frac{k_2 [\text{PhOH}] [\text{I}_2] [\text{HOAc}]}{[\text{H}^+]^2 [\text{I}^-]}$$

At iodide ion concentrations where approximately all the stoichiometric iodine is present as tri-iodide ion Berliner's rate expression has the form:

$$\text{rate} = \frac{k'_1 [\text{PhOH}] (\text{I}_2)}{[\text{H}^+][\text{I}^-]^2} + \frac{k'_2 [\text{PhOH}] (\text{I}_2) [\text{HOAc}]}{[\text{H}^+]^2 [\text{I}^-]^2}$$

since

$$K_{\text{eq.}} = \frac{[\text{I}_3^-]}{[\text{I}_2] [\text{I}^-]} .$$

The mechanism proposed by Grovenstein and Henderson leads to the following rate expression at high iodide ion concentration:

$$\text{rate} = \frac{k'_3 [\text{PhOH}] [\text{I}_3^-] [\text{H}_2\text{O}]}{[\text{H}^+] [\text{I}^-]^2} + \frac{k'_4 [\text{PhOH}] [\text{I}_3^-] [\text{HOAc}]}{[\text{H}^+]^2 [\text{I}^-]^2}$$

At iodide ion concentrations where approximately all the stoichiometric iodine is present as tri-iodide ion, this rate expression is the same as Berliner's. See Appendix D for the justification of this statement.

At iodide ion concentrations where the stoichiometric iodine is mainly present as the tri-iodide ion the two mechanisms are indistinguishable, but the two mechanisms are distinguishable at low iodide ion concentrations where Berliner's rate expression approaches infinity while Grovenstein and Henderson's rate expression assumes the form:

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

In this thesis study the first approach to distinguish between the two mechanisms was to lower the iodide ion concentration at a constant pH and ionic strength. According to the mechanism of Grovenstein

and Henderson as the iodide ion concentration is lowered Berliner's rate constants should eventually decrease.

As the iodination of phenol proceeds the iodide ion concentration increases since hydrogen iodide is a product of the iodination. Since the rate of the iodination is diminished by an increasing iodide ion concentration, the apparent second order rate constant falls. In order to obtain an apparent rate constant at a definite stoichiometric iodide ion concentration a plot was made of per cent reaction versus the integrated rate constant calculated as described in Chapter IV. By extrapolating the curve to zero per cent reaction this gave an apparent rate constant at the initial stoichiometric iodide ion concentration of the reaction. When the initial iodide ion concentration was of sufficient molarity such that the increase in iodide ion concentration produced by the reaction did not diminish the apparent rate constant by more than nine per cent, an average of the apparent rate constants was taken.

Since the zero time apparent rate constant depends on the initial actual iodide ion concentration present, a rate constant, k' , was calculated for each kinetic run. The rate constant, k' , was based on Berliner's mechanism and takes into account the actual iodide ion dependence in the reaction. The rate constant, k' , was derived as follows:

$$\text{rate} = k_{\text{app}} (\text{PhOH}) (I_2)$$

$$\text{rate} = k_o [\text{PhOH}] [\text{I}^+] \quad (\text{Berliner's mechanism})$$

$$k_{\text{app}} (\text{PhOH}) (\text{I}_2) = k_o [\text{PhOH}] [\text{I}^+]$$

$$K_2 = \frac{[\text{I}^+] [\text{I}^-]}{[\text{I}_2]}$$

$$k_{\text{app}} (\text{PhOH}) (\text{I}_2) = \frac{k_o K_2 [\text{PhOH}] [\text{I}_2]}{[\text{I}^-]}$$

$$K_1 = \frac{[\text{I}_3^-]}{[\text{I}_2] [\text{I}^-]} = 768 \quad (48)$$

$$k_{\text{app}} (\text{PhOH}) (\text{I}_2) = \frac{k_o K_2 [\text{PhOH}] [\text{I}_3^-]}{768 [\text{I}^-]^2}$$

$$(\text{PhOH}) = [\text{PhOH}]^*$$

$$k_o K_2 = k' = \frac{k_{\text{app}} \times 768 \times (\text{I}_2) \times [\text{I}^-]^2}{[\text{I}_3^-]}$$

Kinetic Reactions of Phenol. -- The first kinetic run was a duplication of Berliner's (11) iodination of phenol at 0.08 M sodium iodide. This run was performed in order to obtain experience in doing kinetic measurements and to check the apparent rate constant value obtained by Berliner. Berliner obtained an apparent rate constant of 0.665 (l./mole min.), and the duplication run gave a value of 0.675 ± 0.012 (l./mole min.).

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

* At a pH of 3.50 the phenoxide ion concentration in 0.008 M phenol is approximately 2.5×10^{-9} M.

See Table 3, Run 1, for the details of this experiment. The withdrawal method using an ungreased glass stopper was used in this run. No further duplication work was done since it was felt that Berliner's work could be duplicated with good accuracy.

In the iodination of phenol at lower iodide ion concentrations several reaction conditions were changed from those used by Berliner. To obtain an ionic strength of 0.3, Berliner used sodium chloride; however, sodium perchlorate was used in this study since it was possible that the chloride ion might react with iodine to form I_2Cl^- or ICl (49). Since the present work was performed at lower iodide ion concentrations than Berliner's the pH had to be lowered in order to be able to follow the rate conveniently. Berliner used a pH of 5.60 while all kinetic runs described in this chapter had a pH of 3.50 by using 0.0500 M sodium acetate and 0.500 M acetic acid. This pH represents a hydrogen ion concentration of 3.17×10^{-4} moles per liter.¹

The first run using these new conditions was the iodination

49. W. M. Latimer, The Oxidation States of the Elements and Their Potentials in Aqueous Solutions. New York: Prentice Hall, 1952, p. 65.

50. H. S. Harned and B. B. Owen, The Physical Chemistry of Electrolytic Solutions. Second Edition, New York: Reinhold Publishing Corp., 1950, p. 523.

¹ This hydrogen ion concentration was calculated using the equilibrium constant (3.20×10^{-5} liter mole⁻¹) at 25° and ionic strength of 0.3 given by Harned and Owen (50).

Table 3

Run 1, Phenol in 0.0800 M Sodium Iodide Solution at 25.0°

(Phenol) ₀ - <u>0.007990 M</u>	(HC ₂ H ₃ O ₂) - <u>0.0100 M</u>
(I ₂) ₀ - <u>0.002070 M</u>	(NaC ₂ H ₃ O ₂) - <u>0.100 M</u>
(NaI) ₀ - <u>0.0800 M</u>	(NaCl) - <u>0.120 M</u>
	(Na ₂ S ₂ O ₃) - <u>0.2050 M</u>

10.0 ml. aliquots withdrawn

Time elapsed (min.)	Titer (ml.)	Rate constant (l. /mole min.)	Per cent reaction
(blank)	2.02		0.00
20.0	1.82	0.701	4.95
43.0	1.61	0.678	20.30
70.0	1.42	0.677	29.70
101.0	1.22	0.663	39.60
141.0	1.00	0.679	50.49
190.0	0.82	0.653	59.41

Average value of rate constant (k_{app}) = 0.675 ± 0.012

of phenol at 0.08 M sodium iodide. In all kinetic runs indicated in this thesis the phenol concentration was always at least four times the concentration of iodine. The use of excess phenol prevents the complication of disubstitution and other complications which Berliner (11) indicated in his work but was unable to explain. The withdrawal method using an ungreased glass stopper was used in this run. Since the apparent rate constants did not decrease by more than nine per cent, an average of the apparent rate constants was taken to give a value of $0.785 \pm 0.025 \times 10^{-4}$ (l./mole sec.). See Table 4, Run 2, for the details of this experiment. A duplicate run was made as a check, and an averaged apparent rate constant value of $0.777 \pm 0.010 \times 10^{-4}$ (l./mole sec.) was obtained (see Table 5, Run 3).

Two sets of blank reactions were used to check the iodination of phenol at 0.08 M sodium iodide for side-reactions and possible volatilization of iodine. At the end of a period of time that would represent 63 per cent reaction for the normal run, 4.10 and 4.09 per cent reaction had occurred in the blanks (see Tables 6 and 7, Runs 4 and 5). The withdrawal method using ungreased glass stoppers was used in these blanks. This loss of iodine seemed too large to represent volatilization of iodine, so three sets of blanks containing only iodine and sodium iodide with a respective chemical, either acetic acid, sodium acetate or sodium perchlorate, were run in order to check for side-reactions. At the end

Table 4

Run 2, Phenol in 0.0800 M Sodium Iodide Solution at 25.0°

(Phenol) ₀ - 0.00799 <u>M</u>	(HC ₂ H ₃ O ₂) - 0.500 <u>M</u>
(I ₂) ₀ - 0.002097 <u>M</u>	(NaC ₂ H ₃ O ₂) - 0.0500 <u>M</u>
(NaI) ₀ - 0.0800 <u>M</u>	(NaClO ₄) - 0.170 <u>M</u>
	(Na ₂ S ₂ O ₃) - 0.005054 <u>M</u>

10.0 ml. aliquots withdrawn

Time elapsed (sec.)	Titer (ml.)	Rate constant x10 ⁴ (l./mole sec.)	Per cent reaction
(blank)	8.30		0.00
159,660	7.46	0.847	10.12
249,780	7.10	0.798	14.46
349,380	6.75	0.761	18.67
1,127,760	4.37	0.766	47.35
1,452,900	3.66	0.772	55.90
1,803,180	3.07	0.767	63.01

Average value of rate constant (k_{app}) = $0.785 \pm 0.025 \times 10^{-4}$

Table 5

Run 3, Phenol in 0.0800 M Sodium Iodide Solution at 25.0°

(Phenol) ₀ - 0.007990 <u>M</u>	(HC ₂ H ₃ O ₂) - 0.500 <u>M</u>
(I ₂) ₀ - 0.002097 <u>M</u>	(NaC ₂ H ₃ O ₂) - 0.0500 <u>M</u>
(NaI) ₀ - 0.0800 <u>M</u>	(NaClO ₄) - 0.170 <u>M</u>
	(Na ₂ S ₂ O ₃) - 0.005054 <u>M</u>

10.0 ml. aliquots withdrawn

Time elapsed (sec.)	Titer (ml.)	Rate constant x 10 ⁴ (l./mole sec.)	Per cent reaction
(blank)	8.30		0.00
160,800	7.50	0.799	9.64
251,220	7.12	0.779	14.22
350,700	6.75	0.758	18.67
585,180	5.87	0.773	29.28
783,480	5.24	0.776	36.87

Average value of rate constant (k_{app}) = $0.777 \pm 0.010 \times 10^{-4}$

Table 6

Run 4, Blank in 0.0800 M Sodium Iodide Solution at 25.0°

(Phenol) ₀ - Zero	(HC ₂ H ₃ O ₂) - 0.500 <u>M</u>
(I ₂) ₀ - 0.002097 <u>M</u>	(NaC ₂ H ₃ O ₂) - 0.0500 <u>M</u>
(NaI) ₀ - 0.0800 <u>M</u>	(NaClO ₄) - 0.170 <u>M</u>
	(Na ₂ S ₂ O ₃) - 0.005054 <u>M</u>

10.0 ml. aliquots withdrawn

Time elapsed (sec.)	Titer (ml.)	Per cent reaction
(blank)	8.30	0.00
63,060	8.28	0.24
191,940	8.24	0.72
317,220	8.24	0.72
1,132,080	8.03	3.25
1,457,700	7.98	3.85
1,803,180	7.96	4.10

Table 7

Run 5, Blank in 0.0800 M Sodium Iodide Solution at 25.0°

(Phenol) ₀ - Zero	(HC ₂ H ₃ O ₂) - 0.500 <u>M</u>
(I ₂) ₀ - 0.002102 <u>M</u>	(NaC ₂ H ₃ O ₂) - 0.0500 <u>M</u>
(NaI) ₀ - 0.0800 <u>M</u>	(NaClO ₄) - 0.170 <u>M</u>
	(Na ₂ S ₂ O ₃) - 0.005054 <u>M</u>

10.0 ml. aliquots withdrawn

Time elapsed (sec.)	Titer (ml.)	Per cent reaction
(blank)	8.32	0.00
63,840	8.22	1.20
192,840	8.26	0.72
318,480	8.25	0.84
587,340	8.20	1.44
772,740	8.08	2.88
1,133,100	8.05	3.24
1,459,080	7.98	4.09

of a period of time that would normally represent 50 per cent reaction for the normal run, the sodium acetate blank had a 4.01 per cent reaction while the acetic acid and sodium perchlorate blanks indicated zero per cent reaction (see Tables 8, 9 and 10, Runs 6, 7 and 8). These experiments definitely showed that the sodium acetate was the cause for the side-reaction, and it must have contained a reactive impurity. In order to solve this problem, sodium acetate was prepared by neutralizing purified acetic acid with sodium hydroxide as indicated under sodium acetate in Chapter III. To learn whether this sodium acetate would cause a side-reaction, a blank containing iodine, sodium iodide and the prepared sodium acetate was run. At the end of a period of time that would normally represent 50 per cent reaction for a normal run there appeared only a 0.40 per cent side-reaction in the blank (see Table 11, Run 9). This per cent reaction could certainly be due to an error in reading the buret. The prepared sodium acetate was used in all the future kinetic runs. Values of k' were not calculated for the 0.08 M sodium iodide runs because of the apparent side-reaction. The reaction of the iodination of phenol was repeated later using the multiple flask method and greased glass stoppers. An average of the apparent rate constants gave a value of $0.691 \pm 0.006 \times 10^{-4}$ (l./mole sec.), and the value of k' was 3.28×10^{-4} sec.⁻¹ (see Table 12, Run 10).

Table 8

Check for Side-reaction of Iodine with Sodium Acetate

Run 6, Blank in 0.0800 M Sodium Iodine Solution at 25.0°

(Phenol) ₀ - Zero	(HC ₂ H ₃ O ₂) - Zero
(I ₂) ₀ - <u>0.001993 M</u>	(NaC ₂ H ₃ O ₂) - <u>0.0500 M</u>
(NaI) ₀ - <u>0.0800 M</u>	(NaClO ₄) - Zero
	(Na ₂ S ₂ O ₃)* - <u>0.005070 M</u>

10.0 ml. aliquots withdrawn

Time elapsed (sec.)	Titer (ml.)	(Iodine) concentration	Per cent reaction
(blank)	7.89	0.001993	0.00
1,294,020	7.55	0.001913	4.01

*Blank titrated with 0.005054 M Na₂S₂O₃ solution

Table 9

Check for Side-reaction of Iodine with Acetic Acid

Run 7, Blank in 0.0800 M Sodium Iodide Solution at 25.0°

(Phenol) ₀ - Zero	(HC ₂ H ₃ O ₂) - 0.500 <u>M</u>
(I ₂) ₀ - 0.002006 <u>M</u>	(NaC ₂ H ₃ O ₂) - Zero
(NaI) ₀ - 0.0800 <u>M</u>	(NaClO ₄) - Zero
	(Na ₂ S ₂ O ₃)* - 0.005070 <u>M</u>

10.0 ml. aliquots withdrawn

Time elapsed (sec.)	Titer (ml.)	(Iodine) concentration	Per cent reaction
(blank)	7.94	0.002006	0.00
1,293,660	7.92	0.002007	0.00

*Blank titrated with 0.005054 M Na₂S₂O₃ solution

Table 10

Check for Side-reaction of Iodine with Sodium Perchlorate

Run 8, Blank in 0.0800 M Sodium Iodide Solution at 25.0°(Phenol)₀ - Zero(HC₂H₃O₂) - Zero(I₂)₀ - 0.002003 M(NaC₂H₃O₂) - Zero(NaI)₀ - 0.0800 M(NaClO₄) - 0.170 M(Na₂S₂O₃)* - 0.005070 M

10.0 ml. aliquots withdrawn

Time elapsed (sec.)	Titer (ml.)	(Iodine) concentration	Per cent reaction
(blank)	7.93	0.002003	0.00
1,292,640	7.90	0.002002	0.05

* Blank titrated with 0.005054 M Na₂S₂O₃ solution

Table 11

Check for Side-reaction of Iodine with Sodium Acetate

Run 9, Blank in 0.0800 M Sodium Iodide Solution at 25.0°

(Phenol) ₀ - Zero	(HC ₂ H ₃ O ₂) - 0.500 <u>M</u>
(I ₂) ₀ - 0.001977 <u>M</u>	(NaC ₂ H ₃ O ₂) - 0.0500 <u>M</u>
(NaI) ₀ - 0.0800 <u>M</u>	(NaClO ₄) - 0.170 <u>M</u>
	(Na ₂ S ₂ O ₃) - 0.005070 <u>M</u>

10.0 ml. aliquots withdrawn

Time elapsed (sec.)	Titer (ml.)	(Iodine) concentration	Per cent reaction
(blank)	7.80	0.001977	0.00
(blank)	7.80	0.001977	0.00
1, 157, 520	7.76	0.001967	0.50
1, 158, 120	7.77	0.001969	0.40

Table 12

Run 10, Phenol in 0.0800 M Sodium Iodide Solution at 25.0°

(Phenol) ₀ - 0.008000 <u>M</u>	(HC ₂ H ₃ O ₂) - 0.500 <u>M</u>
(I ₂) ₀ - 0.002006 <u>M</u>	(NaC ₂ H ₃ O ₂) - 0.0500 <u>M</u>
(NaI) ₀ - 0.0800 <u>M</u>	(NaClO ₄) - 0.170 <u>M</u>
	(Na ₂ S ₂ O ₃) - 0.02030 <u>M</u>

50.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mole sec.)x10 ⁴	Per cent reaction
(blank)	9.88		0.00
162,060	9.05	0.685	8.40
270,000	8.51	0.701	13.87
392,460	8.00	0.688	19.03
656,400	6.97	0.690	29.45
961,740	6.00	0.684	39.27
1,355,160	4.95	0.684	49.90

Average value of rate constant (k_{app}) = $0.691 \pm 0.006 \times 10^{-4}$

$k' = 3.28 \times 10^{-4}$ sec.⁻¹

A kinetic run at 0.06 M sodium iodide was made using the withdrawal method and an ungreased glass stopper. The apparent rate constants drifted upward in this run; this drift could be due to an error in determining the blank. Since the upward drift was not very large the apparent rate constants were averaged to give the value $1.272 \pm 0.030 \times 10^{-4}$ (1./mole sec.). This run was repeated and the same upward drift was observed. An average of the apparent rate constants gave a value of $1.279 \pm 0.037 \times 10^{-4}$ (1./mole sec.) (see Tables 13 and 14, Runs 11 and 12). Even though these two runs were in error, k' was calculated using an average of the two apparent rate constants. The value of k' was $3.37 \times 10^{-4} \text{ sec.}^{-1}$.

A kinetic run at 0.02 M sodium iodide was made using the withdrawal method and an ungreased glass stopper. The plot of apparent rate constants versus per cent reaction when extrapolated to zero time gave an apparent rate constant value of 0.001244 (1./mole sec.) for the kinetic run. The calculation of k' gave a value of $3.35 \times 10^{-4} \text{ sec.}^{-1}$. The run was repeated as a check, and an apparent rate constant value of 0.001244 (1./mole sec.) was obtained by extrapolation. The calculation of k' gave a value of $3.36 \times 10^{-4} \text{ sec.}^{-1}$ (see Tables 15 and 16, Runs 13 and 14). In later work the run at 0.02 M sodium iodide was repeated using the multiple flask method with greased glass stoppers. The plot of apparent rate constants versus per cent reaction when extrapolated

Table 13

Run 11, Phenol in 0.0600 M Sodium Iodide Solution at 25.0°

(Phenol) ₀ - 0.007990 M	(HC ₂ H ₃ O ₂) - 0.500 M
(I ₂) ₀ - 0.002021 M	(NaC ₂ H ₃ O ₂) - 0.0500 M
(NaI) ₀ - 0.0600 M	(NaClO ₄) - 0.190 M
	(Na ₂ S ₂ O ₃) - 0.005054 M

10.0 ml. aliquots withdrawn

Time elapsed (sec.)	Titer	Rate constant x 10 ⁴ (l./mole sec.)	Per cent reaction
(blank)	8.00		0.00
70,740	7.48	1.196	6.50
114,600	7.15	1.245	10.62
163,620	6.80	1.267	15.00
204,840	6.52	1.281	18.50
345,000	5.73	1.260	28.37
496,080	4.91	1.302	38.62
686,580	4.11	1.306	48.62
1,104,600	2.80	1.321	65.00

Average value of rate constant (k_{app}) = $1.272 \pm 0.030 \times 10^{-4}$ $k' = 3.37 \times 10^{-4} \text{ sec.}^{-1}$

Table 14

Run 12, Phenol in 0.0600 M Sodium Iodide Solution at 25.0°

(Phenol)₀ - 0.007990 M

(HC₂H₃O₂) - 0.500 M

(I₂)₀ - 0.002021 M

(NaC₂H₃O₂) - 0.0500 M

(NaI)₀ - 0.0600 M

(NaClO₄) - 0.190 M

(Na₂S₂O₃) - 0.005054 M

10.0 ml. aliquots withdrawn

Time elapsed (sec.)	Titer (ml.)	Rate constant x 10 ⁴ (l. / mole sec.)	Per cent reaction
(blank)	8.00		0.00
70,740	7.49	1.176	6.37
114,600	7.15	1.245	10.62
163,620	6.80	1.267	15.00
204,840	6.50	1.301	18.75
345,000	5.67	1.301	29.12
496,080	4.91	1.302	38.62
686,580	4.11	1.306	48.62
884,580	3.38	1.333	57.75

Average value of rate constant (k_{app}) = $1.279 \pm 0.037 \times 10^{-4}$

$k' = 3.37 \times 10^{-4} \text{ sec.}^{-1}$

Table 15

Run 13, Phenol in 0.020003 M Sodium Iodide Solution at 25.0°

(Phenol) ₀ - 0.007987 <u>M</u>	(HC ₂ H ₃ O ₂) - 0.500 <u>M</u>
(I ₂) ₀ - 0.002041 <u>M</u>	(NaC ₂ H ₃ O ₂) - 0.0500 <u>M</u>
(NaI) ₀ - 0.020003 <u>M</u>	(NaClO ₄) - 0.230 <u>M</u>
	(Na ₂ S ₂ O ₃) - 0.005054 <u>M</u>

10.0 ml. aliquots withdrawn

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mole sec.)	Per cent reaction
(blank)	8.08		0.00
10,800	7.27	0.001239	10.02
22,680	6.54	0.001198	19.06
34,380	5.88	0.001202	27.23
51,540	5.12	0.001170	36.63
74,340	4.26	0.001158	47.28
102,480	3.40	0.001160	57.92
142,680	2.57	0.001128	68.19
186,060	1.83	0.001146	77.35

Rate constant extrapolated to zero time (k_{app}) = 0.001244

$$k' = 3.35 \times 10^{-4} \text{ sec.}^{-1}$$

Table 16

Run 14, Phenol in 0.020005 M Sodium Iodide Solution at 25.0° $(\text{Phenol})_0 - 0.007985 \underline{\text{M}}$ $(\text{HC}_2\text{H}_3\text{O}_2) - 0.500 \underline{\text{M}}$ $(\text{I}_2)_0 - 0.002039 \underline{\text{M}}$ $(\text{NaC}_2\text{H}_3\text{O}_2) - 0.0500 \underline{\text{M}}$ $(\text{NaI})_0 - 0.020005 \underline{\text{M}}$ $(\text{NaClO}_4) - 0.230 \underline{\text{M}}$ $(\text{Na}_2\text{S}_2\text{O}_3) - 0.005054 \underline{\text{M}}$

10.0 ml. aliquots withdrawn

Time elapsed (sec.)	Titer (ml.)	Rate constant (l. mole sec.)	Per cent reaction
(blank)	8.07		0.00
10,800	7.26	0.001273	10.04
22,680	6.54	0.001190	18.96
34,380	5.87	0.001205	27.26
51,540	5.11	0.001170	36.68
74,340	4.26	0.001156	47.21
102,480	3.40	0.001158	57.87
142,680	2.56	0.001131	68.28
186,060	1.84	0.001141	77.20

Rate constant extrapolated to zero time (k_{app}) = 0.001244 $k' = 3.28 \times 10^{-4} \text{ sec.}^{-1}$

to zero time gave an apparent rate constant of 0.001208 (l./mole sec.). The calculation of k' gave a value of $3.28 \times 10^{-4} \text{ sec.}^{-1}$ which is in agreement with the value obtained at 0.08 M sodium iodide (see Table 17, Run 15).

The iodination of phenol at 0.00801 M sodium iodide was run using the withdrawal method with an ungreased glass stopper. The plot of apparent rate constants versus per cent reaction when extrapolated to zero time gave an apparent rate constant of 0.00874 (l./mole sec.). The calculation of k' gave a value of $3.27 \times 10^{-4} \text{ sec.}^{-1}$ (see Table 18, Run 17). The run was repeated as a check, and an apparent rate constant value of 0.00839 (l./mole sec.) was obtained by extrapolation. The calculation of k' gave a value of $3.14 \times 10^{-4} \text{ sec.}^{-1}$ (see Table 19, Run 18).

The iodination of phenol at 0.004251 M sodium iodide was run using the withdrawal method with an ungreased glass stopper. The plot of apparent rate constants versus per cent reaction when extrapolated to zero time gave an apparent rate constant of 0.03370 (l./mole sec.). The calculation of k' gave a value of $3.17 \times 10^{-4} \text{ sec.}^{-1}$ (see Table 20, Run 19). The run was repeated as a check, and an apparent rate constant value of 0.03240 (l./mole sec.) was obtained by extrapolation. The calculation of k' gave a value of $3.08 \times 10^{-4} \text{ sec.}^{-1}$ (see Table 21, Run 20).

Table 17

Run 15, Phenol in 0.0200 M Sodium Iodide Solution at 25.0°

(Phenol) ₀ - 0.008020 <u>M</u>	(HC ₂ H ₃ O ₂) - 0.500 <u>M</u>
(I ₂) ₀ - 0.001975 <u>M</u>	(NaC ₂ H ₃ O ₂) - 0.0500 <u>M</u>
(NaI) ₀ - 0.0200 <u>M</u>	(NaClO ₄) - 0.230 <u>M</u>
	(Na ₂ S ₂ O ₃) - 0.02030 <u>M</u>

50.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mole sec.)	Per cent reaction
(blank)	9.73		0.00
10,800	8.79	0.001189	9.66
17,400	8.28	0.001177	14.90
25,200	7.72	0.001176	20.66
39,000	6.90	0.001142	29.08
60,420	5.84	0.001113	39.98
86,460	4.80	0.001098	50.67
118,500	3.81	0.001083	60.84

Rate constant extrapolated to zero time (k_{app}) = 0.001208

$k' = 3.28 \times 10^{-4} \text{ sec.}^{-1}$

Table 18

Run 17, Phenol in 0.00801 M Sodium Iodide Solution at 25.0°

(Phenol) ₀ - 0.007980 <u>M</u>	(HC ₂ H ₃ O ₂) - 0.500 <u>M</u>
(I ₂) ₀ - 0.001996 <u>M</u>	(NaC ₂ H ₃ O ₂) - 0.0500 <u>M</u>
(NaI) ₀ - 0.00801 <u>M</u>	(NaClO ₄) - 0.242 <u>M</u>
	(Na ₂ S ₂ O ₃) - 0.005054 <u>M</u>

10.0 ml. aliquots withdrawn

Time elapsed (sec.)	Titer (ml.)	Rate constant (l /mol. sec.)	Per cent reaction
(blank)	7.90		0.00
1800	7.01	0.00845	11.26
2700	6.63	0.00831	16.07
3780	6.20	0.00828	21.52
6180	5.54	0.00751	29.87
9240	4.75	0.00730	39.87
13,020	4.03	0.00696	49.99
21,120	2.89	0.00659	63.42
25,320	2.48	0.00641	68.61

Rate constant extrapolated to zero time (k_{app}) = 0.00874

$$k' = 3.27 \times 10^{-4} \text{ sec.}^{-1}$$

Table 19

Run 18, Phenol in 0.008015 M Sodium Iodide Solution at 25.0°

(Phenol) ₀ - 0.007975 <u>M</u>	(HC ₂ H ₃ O ₂) - 0.500 <u>M</u>
(I ₂) ₀ - 0.001991 <u>M</u>	(NaC ₂ H ₃ O ₂) - 0.0500 <u>M</u>
(NaI) ₀ - 0.008015 <u>M</u>	(NaClO ₄) - 0.242 <u>M</u>
	(Na ₂ S ₂ O ₃) - 0.005054 <u>M</u>

10.0 ml. aliquots withdrawn

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mol.sec.)	Per cent reaction
(blank)	7.88		0.00
1800	7.03	0.00806	10.28
2580	6.74	0.00774	14.47
3780	6.28	0.00775	20.30
6180	5.53	0.00749	29.82
9240	4.75	0.00727	39.72
13,020	4.64	0.00692	48.73
16,020	3.55	0.00678	54.95
29,820	2.12	0.00623	73.10

Rate constant extrapolated to zero time (k_{app}) = 0.00839

$$k' = 3.14 \times 10^{-4} \text{ sec.}^{-1}$$

Table 20

Run 19, Phenol in 0.004251 M Sodium Iodide Solution at 25.0° $(\text{Phenol})_0 = 0.007939 \text{ M}$ $(\text{HC}_2\text{H}_3\text{O}_2) = 0.500 \text{ M}$ $(\text{I}_2)_0 = 0.001945 \text{ M}$ $(\text{NaC}_2\text{H}_3\text{O}_2) = 0.0500 \text{ M}$ $(\text{NaI})_0 = 0.004251 \text{ M}$ $(\text{NaClO}_4) = 0.2458 \text{ M}$ $(\text{Na}_2\text{S}_2\text{O}_3) = 0.005054 \text{ M}$

10.0 ml. aliquots withdrawn

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mol.sec.)	Per cent reaction
(blank)	7.70		0.00
420	6.90	0.03333	10.39
840	6.33	0.03006	17.79
1560	5.56	0.02725	27.79
4020	3.95	0.02242	48.70
4860	3.60	0.02132	53.25
6060	3.13	0.02048	59.35
7620	2.60	0.01989	66.23
10,320	2.06	0.01813	73.25

Rate constant extrapolated to zero time (k_{app}) = 0.03370 $k' = 3.17 \times 10^{-4} \text{ sec.}^{-1}$

Table 21

Run 20, Phenol in 0.004263 M Sodium Iodide Solution at 25.0° $(\text{Phenol})_0 = 0.007927 \text{ M}$ $(\text{HC}_2\text{H}_3\text{O}_2) = 0.500 \text{ M}$ $(\text{I}_2)_0 = 0.001933 \text{ M}$ $(\text{NaC}_2\text{H}_3\text{O}_2) = 0.0500 \text{ M}$ $(\text{NaI})_0 = 0.004263 \text{ M}$ $(\text{NaClO}_4) = 0.2458 \text{ M}$ $(\text{Na}_2\text{S}_2\text{O}_3) = 0.005054 \text{ M}$

10.0 ml. aliquots withdrawn

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mol. sec.)	Per cent reaction
(blank)	7.65		0.00
420	6.96	0.02884	9.02
1080	6.05	0.02822	20.91
1740	5.37	0.02669	29.80
3300	4.33	0.02313	43.39
4560	3.70	0.02169	51.63
6480	2.98	0.02012	61.04
9900	2.18	0.01795	71.50
11,700	1.82	0.01757	76.20

Rate constant extrapolated to zero time (k_{app}) = 0.03240 $k' = 3.13 \times 10^{-4} \text{ sec.}^{-1}$

In all of the kinetic runs that have been described so far, the iodine concentration was approximately 0.002 M. At iodide ion concentrations where the iodine is mainly in the form of the tri-iodide ion, the problem of volatilization is not too great; however, at iodide ion concentrations in the range of 0.004 M sodium iodide the problem of volatilization might be serious, especially when using the withdrawal technique where there is an increasing head space above the solution, and also when using ungreased glass stoppers. To check for the presence of these problems a blank at 0.0042 M was run. Ten ml. aliquots were withdrawn at intervals of time where the total time represented approximately 70 per cent reaction for a normal run. There was no loss of iodine until the aliquots for the 60 and 70 per cent reaction time were withdrawn. These aliquots indicated that there was a loss of iodine concentration of 0.78 and 1.42 per cent respectively (see Table 2, Run 21). This loss of iodine was attributed to an increase in head space above the reaction mixture as samples were withdrawn. A check was made at 0.0042 M sodium iodide as to whether 20 ml. of 1 N sulfuric acid could stop the reaction for titration. A kinetic run was prepared and two aliquots were withdrawn. The first aliquot was titrated immediately and the other aliquot was titrated 290 seconds later. The second aliquot required less thiosulfate titer as compared to the first aliquot, and represented a 4.01 per cent reaction. Two further

aliquots were withdrawn from the reaction solution. The first aliquot was titrated immediately and the other aliquot was titrated 900 seconds later. The second aliquot required less thiosulfate as compared to the first aliquot, and represented a 6.35 per cent reaction (see Table 1, Run 22). Thus at low iodide ion concentration 20 ml. of 1 N sulfuric acid could not stop the reaction for accurate titrations as the average time for a titration was approximately three to four minutes.

To eliminate these problems all future kinetic runs were performed by the multiple flask method. To stop the reaction 1 ml. of approximately 8 M sodium iodide per 50 ml. of reaction solution was injected into the reaction solution. Sulfuric acid was no longer used in addition to the sodium iodide solution as 1 ml. of 8 M sodium iodide would make the reaction solution have an iodide ion concentration of 0.08 M, and as seen in Table 12, Run 10, the iodination of phenol is very slow at 0.08 M sodium iodide. For a complete discussion of the multiple flask method and the method of stopping the reactions with sodium iodide solution see Chapter IV.

Because of the errors that were present in the withdrawal method the reaction of iodine and phenol at 0.0042 M sodium iodide was repeated. The multiple flask method was used with greased glass stoppers. The plot of the apparent rate constants versus per cent reaction when extrapolated to zero time gave an apparent rate constant

of 0.02030 (l./mole sec.). The calculation of k' gave a value of $3.13 \times 10^{-4} \text{ sec.}^{-1}$ (see Table 22, Run 23).

In order to go to lower iodide ion concentration in the kinetic runs and yet be able to follow the reaction it was felt that the phenol concentration should be lowered. The reaction of iodine and phenol at 0.0042 M sodium iodide was repeated but the phenol concentration was reduced by a factor of four. Even though the phenol was reduced by a factor of four, the ratio of phenol to iodine (5 to 1) was still large enough to prevent the problem of disubstitution. The multiple flask method was used with ungreased glass stoppers. This was done unintentionally, and should not have been done. The apparent rate constants for the reaction were found to drift upward which certainly represents an error. The error could be due to the volatilization of iodine around the ungreased glass stopper. An average of the apparent rate constants was taken and the value of 0.02042 ± 0.00051 (l./mole sec.) was obtained. The calculation of k' gave a value of $3.16 \times 10^{-4} \text{ sec.}^{-1}$ (see Table 23, Run 24).

To obtain further data at low iodide ion concentrations a kinetic run at 0.002 M sodium iodide was run using the multiple flask method with greased glass stoppers. The plot of apparent rate constants versus per cent reaction when extrapolated to zero time gave an apparent rate constant of 0.07955 (l./mole sec.). The calculation of

Table 22

Run 23, Phenol in 0.00420 M Sodium Iodide Solution at 25.0°

(Phenol) ₀ - 0.008016 <u>M</u>	(HC ₂ H ₃ O ₂) - 0.500 <u>M</u>
(I ₂) ₀ - 0.000432 <u>M</u>	(NaC ₂ H ₃ O ₂) - 0.0500 <u>M</u>
(NaI) ₀ - 0.00420 <u>M</u>	(NaClO ₄) - 0.2458 <u>M</u>
	(Na ₂ S ₂ O ₃) - 0.005070 <u>M</u>

50.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mol. sec.)	Per cent reaction
(blank)	8.52		0.00
1560	6.62	0.02022	22.30
2160	6.04	0.02009	29.11
3900	4.60	0.02003	46.01
5400	3.65	0.01995	57.16
7320	2.77	0.01963	67.49
9900	1.92	0.01933	77.46

Rate constant extrapolated to zero time (k_{app}) = 0.02030

$$k' = 3.13 \times 10^{-4} \text{ sec.}^{-1}$$

Table 23

Run 24, Phenol in 0.00420 M Sodium Iodide Solution at 25.0°

(Phenol) ₀ - 0.002004 <u>M</u>	(HC ₂ H ₃ O ₂) - 0.500 <u>M</u>
(I ₂) ₀ - 0.000424 <u>M</u>	(NaC ₂ H ₃ O ₂) - 0.0500 <u>M</u>
(NaI) ₀ - 0.00420 <u>M</u>	(NaClO ₄) - 0.2458 <u>M</u>
	(Na ₂ S ₂ O ₃) - 0.005070 <u>M</u>

50.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mol. sec.)	Per cent reaction
(blank)	8.37		0.00
7200	6.36	0.01960	24.01
9600	5.80	0.01972	30.70
13,200	4.96	0.02081	40.74
17,400	4.29	0.02040	48.74
24,000	3.30	0.02095	60.57
30,600	2.58	0.02103	69.17

Average value of rate constant (k_{app}) = 0.02042 ± 0.00051

$$k' = 3.16 \times 10^{-4} \text{ sec.}^{-1}$$

k' gave a value of $3.15 \times 10^{-4} \text{ sec.}^{-1}$ (see Table 24, Run 25).

The reaction of iodine and phenol at 0.001 M sodium iodide was run using the multiple flask method with ungreased glass stoppers. The apparent rate constants were found to drift upward, then to fall. This error was probably due to the method of determining the iodine concentration of the blank. This error will be discussed later in this chapter. An average of the apparent rate constants gave a value of 0.17722 ± 0.0022 (l./mole sec.). The calculation of k' gave a value of $2.45 \times 10^{-4} \text{ sec.}^{-1}$ (see Table 25, Run 27). Because of the error in this experiment, blanks were run to check for side-reactions at this low iodide ion concentration, for volatilization of iodine, and for a method of determining iodine concentration of the blanks. The previous method of determining the iodine concentration of the blank was to dilute the required volume of stock iodine solution that was added to all flasks with water to the total volume of the reaction. The kinetic runs that were performed using this method of determining the iodine concentration were Runs 23-25.

A set of blanks at 0.001 M sodium iodide were prepared using all the reagents except phenol. The glass stoppers were not greased. The initial iodine concentration was determined and then the concentration of iodine in the individual flasks was determined at definite intervals of time that would represent 70 per cent reaction for a

Table 24

Run 25, Phenol in 0.00200 M Sodium Iodide Solution at 25.0°

(Phenol) ₀ - 0.002004 <u>M</u>	(HC ₂ H ₃ O ₂) - 0.500 <u>M</u>
(I ₂) ₀ - 0.000497 <u>M</u>	(NaC ₂ H ₃ O ₂) - 0.0500 <u>M</u>
(NaI) ₀ - 0.00200 <u>M</u>	(NaClO ₄) - 0.248 <u>M</u>
	(Na ₂ S ₂ O ₃) - 0.005070 <u>M</u>

50.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mol. sec.)	Per cent reaction
(blank)	9.80		0.00
720	8.77	0.07766	10.51
1500	7.85	0.07585	19.90
2580	6.75	0.07544	31.12
3600	5.92	0.07399	39.59
5100	4.91	0.07320	50.00
7200	3.87	0.07077	60.51
9660	2.94	0.06966	70.00

Rate constant extrapolated to zero time (k_{app}) = 0.07955

$$k' = 3.15 \times 10^{-4} \text{ sec.}^{-1}$$

Table 25

Run 27, Phenol in 0.00100 M Sodium Iodide Solution at 25.0°

(Phenol)₀ - 0.002004 M

(HC₂H₃O₂) - 0.500 M

(I₂)₀ - 0.000408 M

(NaC₂H₃O₂) - 0.0500 M

(NaI)₀ - 0.00100 M

(NaClO₄) - 0.249 M

(Na₂S₂O₃) - 0.005070 M

50.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate Constant (l. /mol. sec.)	Per cent reaction
(blank)	8.05		0.00
480	6.80	0.1772	15.53
840	6.05	0.1736	24.84
1020	5.67	0.1779	29.56
1440	4.89	0.1804	39.25
1980	4.08	0.1813	49.32
2580	3.43	0.1768	57.39
3780	2.42	0.1734	69.94

Average value of rate constant (k_{app}) = 0.1772 ± 0.0022

$k' = 2.45 \times 10^{-4} \text{ sec.}^{-1}$

normal run at this iodide ion concentration; there was a 1.33 per cent loss of iodine concentration. This indicated that iodine was being lost by volatilization around the glass stoppers. Two blanks were prepared by the previous method of diluting stock iodine solution with water. The comparison of the concentration of iodine in the blank by this method and the method of adding all the reagents except phenol indicated an error of 3.33-3.55 per cent loss of iodine concentration. This error was probably due to pushing iodine vapors out of the flask when the water was added as compared to the iodine being held in solution when the blank contained sodium iodide. Three more blanks were prepared by adding all the reagents except phenol, and the glass stoppers were greased. The titers of these blanks indicated that there was no loss of iodine by volatilization, and no side-reactions. See Table 26, Run 28, for the results of these experiments. All kinetic runs in the future were performed using greased glass stoppers, and all blanks were prepared by using all the reagents except phenol. A discussion of these techniques is given in Chapter IV.

In view of the errors in technique in the reaction at 0.001 M sodium iodide the reaction was repeated. The plot of apparent rate constants versus per cent reaction when extrapolated to zero time gave an apparent rate constant of 0.2132 (l./mole sec.). The calculation of k' gave a value of $2.94 \times 10^{-4} \text{ sec.}^{-1}$ (see Table 27, Run 29).

Table 26

Check for Side-reaction, Volatization of Iodine and Methods of Determining Iodine Concentration for Blanks

Run 28, Blank in 0.00100 M Sodium Iodide Solution at 25°

(Phenol) ₀ - Zero	(HC ₂ H ₃ O ₂) - 0.500 <u>M</u>
(I ₂) ₀ - given in table	(NaC ₂ H ₃ O ₂) - 0.0500 <u>M</u>
(NaI) ₀ - 0.00100 <u>M</u>	(NaClO ₄) - 0.249 <u>M</u>
	(Na ₂ S ₂ O ₃) - 0.005070 M

50.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	(I ₂) moles/l.	Per cent reaction
(blank)	8.88	0.000450	0.00
(blank)	8.88	0.000450	0.00
(blank)*	8.58	0.000435	3.33
(blank)*	8.57	0.000434	3.55
480	8.89	0.000450	0.00
840	8.88	0.000450	0.00
1020	8.89	0.000450	0.00
1440	8.86	0.000449	0.22
1980	8.85	0.000449	0.22
2580	8.83	0.000448	0.44
3780	8.76	0.000444	1.33
(blank)**	8.57	0.000434	0.00
3780**	8.56	0.000434	0.00
3780**	8.57	0.000434	0.00

* Determining iodine concentration by diluting 25.0 ml. of stock iodine solution to 50.0 ml. with water.

** Greased ground glass stoppers.

Unless otherwise indicated the blanks were diluted to 50 ml. with sodium iodide-buffer solution.

Table 27

Run 29, Phenol in 0.00100 M Sodium Iodide Solution at 25°

(Phenol) ₀ - 0.002004 <u>M</u>	(HC ₂ H ₃ O ₂) - 0.500 <u>M</u>
(I ₂) ₀ - 0.000414 <u>M</u>	(NaC ₂ H ₃ O ₂) - 0.0500 <u>M</u>
(NaI) ₀ - 0.00100 <u>M</u>	(NaClO ₄) - 0.249 <u>M</u>
	(Na ₂ S ₂ O ₃) - 0.005070 <u>M</u>

50.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mol. sec.)	Per cent reaction
(blank)	8.17		0.00
360	7.06	0.2044	13.59
660	6.30	0.2005	22.89
1440	4.85	0.1891	40.64
1980	4.11	0.1842	49.69
3780	2.49	0.1721	69.52

Rate constant extrapolated to zero time (k_{app}) = 0.2132

$$k' = 2.94 \times 10^{-4} \text{ sec.}^{-1}$$

As the value k' had not dropped a significant amount a kinetic run was made at 0.0005 M sodium iodide. This run was very fast (12 per cent reaction in 120 seconds). The plot of apparent rate constants versus per cent reaction when extrapolated to zero time gave an apparent rate constant of 0.5970 (1./mole sec.). The calculation of k' gave a value of $3.01 \times 10^{-4} \text{ sec.}^{-1}$ (see Table 28, Run 30).

The iodination of phenol has now been studied in iodide ion concentrations of 0.08 M to 0.0005 M. The values of k' at 0.08 M to 0.0005 M sodium iodide have remained fairly constant (3.28×10^{-4} to 3.01×10^{-4}). In order to follow the reaction at even lower iodide ion concentrations, the hydrogen ion concentration will have to be increased. Chapter VI describes the iodination of phenol in perchloric acid solution where it was possible to study the reaction at extremely low iodide ion concentration.

Kinetic Reactions of Phenol-2, 4, 6-d₃. -- The preparation of phenol

2, 4, 6-d₃ was described in Chapter III. Grovenstein and Henderson (2) indicated that their mechanism would involve as the rate-determining step the release of the proton at high or moderately high concentrations of iodide ion. In order to test this hypothesis, the iodination of phenol-2, 4, 6-d₃ was run at 0.02 M sodium iodide. So that the apparent rate constants at a definite iodide ion concentration could be compared all reactions of phenol-2, 4, 6-d₃ were run under the same conditions as

Table 28

Run 30, Phenol in 0.000500 M Sodium Iodide Solution at 25.0°(Phenol)₀ - 0.002004 M(HC₂H₃O₂) - 0.500 M(I₂)₀ - 0.000503 M(NaC₂H₃O₂) - 0.0500 M(NaI)₀ - 0.000500 M(NaClO₄) - 0.2495 M(Na₂S₂O₃) - 0.005070 M

50.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mol. sec.)	Per cent reaction
(blank)	9.92		0.00
120	8.71	0.5559	12.20
180	8.18	0.5456	17.54
210	8.00	0.5222	19.35
360	7.02	0.4988	29.23
570	6.03	0.4600	39.21
870	4.97	0.4268	49.90
1260	4.00	0.3941	59.68
1800	3.05	0.3652	69.25

Rate constant extrapolated to zero time (k_{app}) = 0.5970 $k' = 3.01 \times 10^{-4} \text{ sec.}^{-1}$

the protium analogue.

The iodination of phenol-2, 4, 6-d₃ at 0.02 M sodium iodide was run using the multiple flask method with greased glass stoppers. The plot of apparent rate constants versus per cent reaction when extrapolated to zero time gave an apparent rate constant value of 3.05×10^{-4} (1./mole sec.) (see Table 29, Run 16). The apparent rate constant of the iodination of phenol at 0.02 M sodium iodide was 12.08×10^{-4} (1./mole sec.); the ratio of k_{app}^H / k_{app}^D at 0.02 M sodium iodide gave an isotope ratio of 3.96.

To check this isotope ratio a kinetic run was made at 0.002 M sodium iodide using the multiple flask method with greased glass stoppers. The plot of apparent rate constants versus per cent reaction when extrapolated to zero time gave an apparent rate constant value of 0.0205 (1./mole sec.) (see Table 30, Run 26). The apparent rate constant at 0.002 M sodium iodide for phenol was 0.07955 (1./mole sec.), and the ratio of k_{app}^H / k_{app}^D gave an isotope ratio of 3.88.

The iodination of phenol-2, 4, 6-d₃ at 0.0005 M sodium iodide was run using the multiple flask method with greased glass stoppers. The plot of apparent rate constants versus per cent reaction when extrapolated to zero time gave a value of 0.1502 (1./mole sec.) (see Table 31, Run 31). The value of the apparent rate constant at 0.0005 M sodium iodide for phenol is 0.5970 (1./mole sec.), and the ratio of k_{app}^H / k_{app}^D gave an isotope ratio of 3.98.

Table 29

Run 16, Phenol-2,4,6-d₃ in 0.0200 M Sodium Iodide Solution at 25°

(Phenol) ₀ - 0.007983 <u>M</u>	(HC ₂ H ₃ O ₂) - 0.500 <u>M</u>
(I ₂) ₀ - 0.001953 <u>M</u>	(NaC ₂ H ₃ O ₂) - 0.0500 <u>M</u>
(NaI) ₀ - 0.0200 <u>M</u>	(NaClO ₄) - 0.230 <u>M</u>
	(Na ₂ S ₂ O ₃) - 0.02026 <u>M</u>

50.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mol.sec.) x 10 ⁴	Per cent reaction
(blank)	9.63		0.00
43,080	8.70	2.999	9.70
66,900	8.25	2.964	14.37
94,920	7.72	3.001	19.87
150,600	6.80	3.013	29.42
220,860	5.94	2.895	38.35
392,580	4.22	2.863	56.20
564,900	3.11	2.788	67.70

Rate constant extrapolated to zero time (k_{app}) = 3.050×10^{-4}

$k' = 0.830 \times 10^{-4}$ sec.⁻¹

Table 30

Run 26, Phenol -2,4,6-d₃ in 0.00200M Sodium Iodide Solution
at 25.0°

(Phenol) ₀ - 0.002179 M	(HC ₂ H ₃ O ₂) - 0.500 M
(I ₂) ₀ - 0.000439 M	(NaC ₂ H ₃ O ₂) - 0.0500 M
(NaI) ₀ - 0.00200 M	(NaClO ₄) - 0.248 M
	(Na ₂ S ₂ O ₃) - 0.005065 M

50.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mol. sec.)	Per cent reaction
(blank)	8.67		0.00
2400	7.80	0.0204	10.03
3600	7.45	0.0197	14.07
5700	6.86	0.0194	20.88
9000	6.00	0.0194	30.79
13,020	5.20	0.0189	40.02
18,600	4.20	0.0190	51.26
24,660	3.50	0.0182	59.63

Rate constant extrapolated to zero time (k_{app}) = 0.0205

$$k' = 0.843 \times 10^{-4} \text{ sec.}^{-1}$$

Table 31

Run 31, Phenol -2,4,6-d₃ in 0.000500 M Sodium Iodide Solution
at 25°

(Phenol) ₀ - 0.002174 <u>M</u>	(HC ₂ H ₃ O ₂) - 0.500 <u>M</u>
(I ₂) ₀ - 0.000432 <u>M</u>	(NaC ₂ H ₃ O ₂) - 0.0500 <u>M</u>
(NaI) ₀ - 0.000500 <u>M</u>	(NaClO ₄) - 0.2495 <u>M</u>
	(Na ₂ S ₂ O ₃) - 0.005065 M

50.0 ml of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mol. sec.)	Per cent reaction
(blank)	8.54		0.00
360	7.66	0.1387	10.30
360	7.65	0.1421	10.42
540	7.25	0.1411	15.10
750	6.87	0.1353	19.55
1500	5.78	0.1233	32.32
2040	5.15	0.1188	39.69
2280	4.93	0.1157	42.27
3300	3.95	0.1143	53.75
4440	3.40	0.1035	60.19

Rate constant extrapolated to zero time (k_{app}) = 0.1502

$$k' = 0.785 \times 10^{-4} \text{ sec.}^{-1}$$

CHAPTER VI

KINETIC MEASUREMENTS IN PERCHLORIC ACID SOLUTION

The rate of the iodination of phenol at 0.0005 M sodium iodide in sodium acetate-acetic acid solution was considered the limit for accurate kinetic measurements by the technique employed. As indicated in Table 28, Run 30, there was 12.2 per cent reaction of stoichiometric iodine with phenol in 120 seconds. As the value, k' , had not dropped a significant amount in the iodide ion concentration range of 0.08 M to 0.0005 M in sodium acetate-acetic acid buffer solution, it was desirable to lower the iodide ion concentration even more in order to try to distinguish between Berliner's mechanism and Grovenstein and Henderson's mechanism. In order to lower the iodide ion concentration and yet be able to follow the reaction, the hydrogen ion concentration in the reaction was increased. The hydrogen ion concentration in the sodium acetate-acetic acid solution was 3.17×10^{-4} moles per liter. The concentration of perchloric acid employed was 1.74×10^{-2} moles per liter. At this hydrogen ion concentration the rate at 0.0005 M sodium iodide should be more than fifty-five times slower, and thus the rate of the iodination of phenol in perchloric acid could be followed at very low iodide ion concentrations.

Kinetic Reactions of Phenol. --The first kinetic run in perchloric acid solution was the iodination of phenol in 0.0005 M sodium iodide. The run was performed using the multiple flask method with greased glass stoppers. The plot of apparent rate constants versus per cent reaction when extrapolated to zero time gave an apparent rate constant of 0.008870 (l./mole sec.). The calculation of k' gave a value of $4.65 \times 10^{-6} \text{ sec.}^{-1}$ (see Table 32, Run 32). This value for perchloric acid solution was sixty-five times smaller than the corresponding value in sodium acetate-acetic acid solution where k' was approximately $3.01 \times 10^{-4} \text{ sec.}^{-1}$. The kinetic run was repeated as a check using a fresh iodine solution. The plot of apparent rate constants versus per cent reaction when extrapolated to zero time gave an apparent rate constant of 0.008580 (l./mole sec.). The calculation of k' gave a value of $4.53 \times 10^{-6} \text{ sec.}^{-1}$ (see Table 33, Run 33).

To obtain further values of k' in perchloric acid solution, a kinetic run at 0.0001 M sodium iodide was performed using the multiple flask method with greased glass stoppers. The plot of apparent rate constants versus per cent reaction when extrapolated to zero time gave an apparent rate constant of 0.04800 (l./mole sec.). The calculation of k' gave a value of $4.08 \times 10^{-6} \text{ sec.}^{-1}$ (see Table 34, Run 35).

It was felt that the iodination of phenol should be studied with no added sodium iodide. Thus, a run at zero molar sodium iodide was

Table 32

Run 32, Phenol in 0.000500 M Sodium Iodide Solution at 25.0°

(Phenol)₀ - 0.002030 M

(HClO₄) - 0.0174 M

(I₂)₀ - 0.000433 M

(NaClO₄) - 0.2821 M

(NaI)₀ - 0.000500 M

(Na₂S₂O₃) - 0.005072 M

50.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant (l. /mol. sec.)	Per cent reaction
(blank)	8.54		0.00
10,800	7.17	0.008059	16.04
13,800	6.86	0.007975	19.67
21,600	6.19	0.007564	27.52
37,980	5.20	0.006726	39.11
54,120	4.40	0.006415	48.48
78,120	3.35	0.005970	58.43
98,520	2.93	0.005823	65.49
120,180	2.48	0.005579	70.96

Rate constant extrapolated to zero time (k_{app}) = 0.008870

$k' = 4.65 \times 10^{-6} \text{ sec.}^{-1}$

Table 33

Run 33, Phenol in 0.000500 M Sodium Iodide Solution at 25.0°

(Phenol)₀ - 0.002030 M

(HClO₄) - 0.0174 M

(I₂)₀ - 0.000409 M

(NaClO₄) - 0.2821 M

(NaI)₀ - 0.000500 M

(Na₂S₂O₃) - 0.005072 M

50.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mol. sec.)	Per cent reaction
(blank)	8.06		0.00
5400	7.40	0.007986	8.19
9600	6.93	0.007964	14.02
14,400	6.50	0.007497	19.35
20,400	6.03	0.007200	25.19
26,400	5.64	0.006899	30.02
51,000	4.40	0.006175	45.41

Rate constant extrapolated to zero time (k'_{app}) = 0.008580

$k' = 4.53 \times 10^{-6} \text{ sec.}^{-1}$

Table 34

Run 35, Phenol in 0.000100 M Sodium Iodide Solution at 25.0°

(Phenol)₀ - 0.002030 M

(HClO₄) - 0.0174 M

(I₂)₀ - 0.000429 M

(NaClO₄) - 0.2825 M

(NaI)₀ - 0.000100 M

(Na₂S₂O₃) - 0.005072 M

50.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mol. sec.)	Per cent reaction
(blank)	8.46		0.00
1200	7.65	0.04165	9.57
2400	7.10	0.03665	16.07
3480	6.70	0.03368	20.80
6120	5.95	0.02923	29.67
10,560	5.11	0.02468	39.60
15,180	4.45	0.02204	47.40
25,620	3.43	0.01873	59.46

Rate constant extrapolated to zero time (k_{app}) = 0.04800

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

performed using the multiple flask method with greased glass stoppers. The plot of apparent rate constants versus per cent reaction could not be extrapolated to zero time because of the very fast drop in rate with increasing iodide ion concentration produced by the reaction. In order to calculate a k' value and to eliminate the error caused by not knowing the infinitesimal iodide ion concentration produced by the reaction of iodine and water, the rate of the reaction at 10 per cent reaction was taken from the plot. The initial stoichiometric iodine concentration was 0.000422 M so that at 10 per cent reaction the iodide ion concentration was $42.2 \times 10^{-6} \text{ M}$ and the stoichiometric iodine concentration was 0.000380 M . The apparent rate constant at 10 per cent reaction was $0.1240 \text{ (l./mole sec.)}$ and the calculation of an average k' from zero to 10 per cent is $4.15 \times 10^{-6} \text{ sec.}^{-1}$ (see Table 35, Run 44).

To eliminate in this particular run the problem of not knowing the true apparent rate constant at a known iodide ion concentration, the tangent method was applied. The tangent method consisted of plotting stoichiometric iodine concentration versus time and taking a tangent to the normal at a definite stoichiometric iodine concentration. The tangent of the point was determined by taking a polished metal bar and rotating the bar on the point until the curve of the plot made a continuous smooth line with its reflection. When the curve appeared smooth, a line was drawn through the point using the bar as a straight-edge. This

Table 35

Run 44, Phenol in Zero M Sodium Iodide Solution at 25.0°

(Phenol)₀ - 0.002030 M

(HClO₄) - 0.0174 M

(I₂)₀ - 0.000422 M

(NaClO₄) - 0.2826 M

(NaI)₀ - Zero

(Na₂S₂O₃) - 0.005072 M

50.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mol.sec.)	Per cent reaction
(blank)	8.32		0.00
390	7.54	0.1270	9.37
540	7.35	0.1140	11.66
840	7.07	0.09807	15.02
1080	6.81	0.09376	18.15
1320	6.65	0.08583	20.07
1920	6.26	0.07549	24.76
2940	5.82	0.06208	30.05
4440	5.30	0.05210	36.30
6120	4.85	0.04563	41.71

Rate constant extrapolated to 10 per cent reaction (k_{app}) = 0.1240

Average k' from zero to ten per cent reaction = 4.15×10^{-6} sec.⁻¹

line represented the normal to the point and by drawing a line perpendicular to the normal through the point a tangent was obtained.

The slope of this tangent gave the rate of loss of stoichiometric iodine with respect to time or dx/dt where x is the stoichiometric concentration of iodine. By knowing the initial iodine and phenol concentrations, the concentration of phenol was known at the appropriate iodine concentration. Using the simple second order rate equation

$$\frac{dx}{dt} = k_{app} (\text{PhOH}) (I_2)$$

values of apparent rate constants were calculated at definite stoichiometric iodine concentrations during the reaction.

Using the curve of stoichiometric iodine concentration versus time obtained from the zero molar sodium iodide reaction, values of apparent rate constants at 40×10^{-6} and 64×10^{-6} M sodium iodide were calculated. The apparent rate constant at 40×10^{-6} M sodium iodide was 0.08219 (l./mole sec.), and the instantaneous k' at 9.5 per cent reaction is 2.61×10^{-6} sec.⁻¹. This k' value represents a decrease of 43.8 per cent from the k' value obtained at 0.0005 M sodium iodide. The apparent rate constant at 64×10^{-6} M sodium iodide was 0.06516 (l./mole sec.), and the instantaneous k' at 15 per cent reaction is 3.42×10^{-6} sec.⁻¹.

In order to check whether the k' value obtained at 10 per cent

reaction as discussed above was valid, a reaction at 40×10^{-6} M sodium iodide was performed. The multiple flask method was used with greased glass stoppers. The plot of apparent rate constants versus per cent reaction when extrapolated to zero time gave an apparent rate constant of 0.1312 (l./mole sec.). The calculation of k' gave a value of 4.11×10^{-6} sec.⁻¹ (see Table 36, Run 36). This value of k' while comparable to the initial estimate of k' obtained at 10 per cent reaction was inconsistent with the more reliable value obtained by the tangent method. In the kinetic run of initial stoichiometric iodine concentration of 0.000412 M there was some doubt in the extrapolation of the curve as the slope increased rather rapidly as the plot approached zero. To help eliminate this problem the kinetic run was repeated using an initial stoichiometric iodine concentration of 0.000217 M. The plot of apparent rate constants versus per cent reaction when extrapolated to zero time gave an apparent rate constant of 0.1124 (l./mole sec.). The calculation of k' gave a value of 3.90×10^{-6} sec.⁻¹. (see Table 37, Run 37). The value of 3.90×10^{-6} sec.⁻¹ for k' was 4.5 per cent smaller than the k' value obtained at the higher iodine concentration but was within experimental error.

Since the values of k' had not dropped a significant amount in going from iodide ion concentrations of 5×10^{-4} M to 4×10^{-5} M, it was decided to perform a kinetic run at 1.99×10^{-6} M sodium iodide.

Table 36

Run 36, Phenol in 40×10^{-6} M Sodium Iodide Solution at 25.0°

(Phenol)₀ - 0.002030 M

(HClO₄) - 0.0174 M

(I₂)₀ - 0.000412 M

(NaClO₄) - 0.28256 M

(NaI)₀ - 0.000040 M

(Na₂S₂O₃) - 0.005072 M

50.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant (l. /mol. sec.)	Per cent reaction
(blank)	8.12		0.00
270	7.68	0.1054	5.42
480	7.43	0.09192	8.50
840	7.09	0.08016	12.68
1380	6.77	0.06660	16.62
2220	6.26	0.05965	22.91
2760	6.06	0.05399	25.37
3660	5.71	0.04884	29.68

Rate constant extrapolated to zero time (k'_{app}) = 0.1312

$k' = 4.11 \times 10^{-6} \text{ sec.}^{-1}$

Table 37

Run 37, Phenol in 40×10^{-6} M Sodium Iodide Solution at 25.0°

(Phenol)₀ - 0.002030 M

(HClO₄) - 0.0174 M

(I₂)₀ - 0.000217 M

(NaClO₄) - 0.28256 M

(NaI)₀ - 0.000040 M

(Na₂S₂O₃) - 0.005072 M

100.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate Constant (l./mol. sec.)	Per cent reaction
(blank)	8.55		0.00
540	7.68	0.1028	10.17
960	7.25	0.0882	15.20
1500	6.76	0.0792	20.93
2400	6.00	0.0743	29.82
5520	4.85	0.0528	43.27
7908	4.15	0.0467	51.46
10,260	3.68	0.0422	56.96

Rate constant extrapolated to zero time (k_{app}) = 0.1124

$k' = 3.90 \times 10^{-6}$ sec.⁻¹

The multiple flask method was used with greased glass stoppers. The plot of apparent rate constants versus per cent reaction could not be extrapolated to zero time (see Table 41, Run 40). A further discussion of this kinetic run is presented in this chapter under the kinetic runs of phenol-2, 4, 6-d₃.

The reaction at 1.99×10^{-6} M sodium iodide was repeated at a lower initial stoichiometric iodine concentration so that there would not be a rapid decrease in rate with increasing per cent reaction. The initial stoichiometric iodine concentration in this reaction was 0.0000966 M and to obtain accuracy in titration 100 ml. volumetric flasks were used in order to increase the quantity of iodine. In titrating this concentration of iodine with sodium thiosulfate, the end-point was observed to fade very slowly, and thus a highly precise end-point was not obtained. The plot of apparent rate constants versus per cent reaction when extrapolated to zero time gave an apparent rate constant of 0.3140 (l./mole sec.). The calculation of k' gave a value of 0.582×10^{-6} sec.⁻¹ (see Table 38, Run 42). This represents an 87.5 per cent decrease in k' value as compared to the k' value of 4.65×10^{-6} sec.⁻¹ obtained at 0.0005 M sodium iodide. This value of k' is considered to be of only limited interest because of the weak end-points in titration and because of doubt of the true stoichiometric iodide ion concentration. The initial added stoichiometric sodium iodide concentration was

Table 38

Run 42, Phenol in 1.99×10^{-6} M Sodium Iodide Solution at 25.0°

(Phenol)₀ - 0.0010025 M

(HClO₄) - 0.0174 M

(I₂)₀ - 0.0000966 M

(NaClO₄) - 0.2826 M

(NaI)₀ - 0.00000199 M

(Na₂S₂O₃) - 0.002026 M

100.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mol. sec.)	Per cent reaction
(blank)	9.545		0.00
360	8.63	0.2786	9.54
720	8.00	0.2460	16.14
1020	7.59	0.2254	20.44
1320	7.37	0.1965	22.75
2220	6.36	0.1854	33.33
2302	6.38	0.1774	33.12
2604	6.15	0.1689	35.53

Rate constant extrapolated to zero time (k_{app}) = 0.3140

$k' = 0.582 \times 10^{-6} \text{ sec.}^{-1}$

1.99×10^{-6} M (this value corresponds to an actual iodide concentration of 1.85×10^{-6} M); however, it was calculated that if the initial actual iodide ion concentration was approximately 4.89×10^{-6} M a k' value of $4.06 \times 10^{-6} \text{ sec.}^{-1}$ would have been obtained. Thus an error of only 3.04×10^{-6} M in sodium iodide would cause an error of approximately 80 per cent in the value of k' . Such iodide ion concentrations might arise from reduction of iodine to iodide during preparation of the iodine solution.

In order to obtain k' values at iodide ion concentrations of less than 40×10^{-6} M and yet not use such dilute sodium iodide solutions that large errors would be introduced in k' by small spurious concentrations of iodide ion, a reaction at 19.9×10^{-6} M sodium iodide was performed. The reaction was performed in 200 ml. volumetric flasks in order to obtain sharper end-points in titration. The multiple flask method was used with greased glass stoppers. The plot of apparent rate constants versus per cent reaction when extrapolated to zero time gave an apparent rate constant of 0.2145 (l./mole sec.). The calculation of k' gave a value of $4.06 \times 10^{-6} \text{ sec.}^{-1}$ (see Table 39, Run 38).

Kinetic Reactions of Phenol-2, 4, 6-d₃. --The kinetic isotope effect

k'_H / k'_D of the iodination of phenol and phenol-2, 4, 6-d₃ in sodium acetate-acetic acid solution was in the range of 3.73 to 3.95. It was desirable to conduct a kinetic isotope effect study in perchloric acid

Table 39

Run 38, Phenol in 19.9×10^{-6} M Sodium Iodide Solution at 25°

(Phenol)₀ - 0.0010312 M

(HClO₄) - 0.0174 M

(I₂)₀ - 0.0000892 M

(NaClO₄) - 0.28258 M

(NaI)₀ - 0.0000199 M

(Na₂S₂O₃) - 0.004052 M

200.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mol. sec.)	Per cent reaction
(blank)	8.81		0.00
540	7.97	0.1806	9.53
720	7.75	0.1730	12.03
1080	7.42	0.1544	15.78
1380	7.15	0.1480	18.84
2400	6.41	0.1301	27.24

Rate constant extrapolated to zero time (k_{app}) = 0.2145

$k' = 4.06 \times 10^{-6}$ sec.⁻¹

solution in order to determine whether the same isotope ratio of k'_H / k'_D existed in perchloric acid. Also it was important to determine whether the isotope ratio remained constant in going from 0.0005 M to extremely low iodide ion concentrations.

The iodination of phenol-2, 4, 6-d₃ in 0.0005 M sodium iodide was performed using the multiple flask method with greased glass stoppers. The plot of apparent rate constants versus per cent reaction when extrapolated to zero time gave an apparent rate constant of 0.002240 (l./mole sec.). The calculation of k' gave a value of 1.14×10^{-6} sec.⁻¹ (see Table 40, Run 34). The k' value at 0.0005 M sodium iodide in perchloric acid solution for the protium compound as indicated in this chapter was 4.53×10^{-6} sec.⁻¹. The kinetic isotope ratio of k'_H / k'_D gave a value of 3.97. This isotope ratio is thus of the same magnitude as that obtained in sodium acetate-acetic acid solutions.

The iodination of phenol in 1.99×10^{-6} M sodium iodide was discussed earlier in this chapter, and it was stated that the plot of apparent rate constants versus per cent reaction could not be extrapolated to zero time because of the low initial iodide ion concentration with extremely high increasing concentrations of iodide ion produced by the reaction. The iodination of phenol-2, 4, 6-d₃ was performed using the multiple flask method with greased glass stoppers. The same stock iodine solution was used for this run as the protium run; however,

Table 40

Run 34, Phenol -2,4,6-d₃ in 0.000500 M Sodium Iodide Solution
at 25.5°

(Phenol)₀ - 0.002141 M

(HClO₄) - 0.0174 M

(I₂)₀ - 0.000466 M

(NaClO₄) - 0.2821 M

(NaI)₀ - 0.000500 M

(Na₂S₂O₃) - 0.005065 M

50.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant (l. /mol. sec.)	Per cent reaction
(blank)	9.20		0.00
14,040	8.62	0.002152	6.30
24,600	8.26	0.002087	10.22
43,200	7.65	0.002047	16.85
59,700	7.23	0.001937	21.41
102,600	6.30	0.001792	31.52
164,640	5.33	0.001631	42.06
243,600	4.36	0.001531	52.61
340,740	3.53	0.001424	61.63

Rate constant extrapolated to zero time (k_{app}) = 0.002240

$k' = 1.14 \times 10^{-6}$ sec. ⁻¹

25 hours elapsed between the deuterium and protium run. Since neither of these reactions could be extrapolated to zero time it was decided to compare the ratio of apparent rate constants at a definite iodide ion concentration. A plot of apparent rate constants versus per cent reaction was made for each reaction. In knowing the initial stoichiometric concentration of the iodine in the phenol-2, 4, 6-d₃ reaction and the stoichiometric concentration of iodine at x per cent reaction the stoichiometric concentration of iodide ion produced at x per cent was known. Also at x per cent reaction the apparent rate constant was known. By knowing the initial stoichiometric iodine concentration in the phenol reaction a calculation was made to determine what per cent reaction in the phenol run gave the same stoichiometric iodide ion concentration as that produced in the phenol-2, 4, 6-d₃ run at x per cent reaction. From the plot in the phenol run the apparent rate constant was obtained by knowing the calculated per cent reaction coordinate. A comparison was made of the two apparent rate constants k_{app}^H / k_{app}^D and an isotope ratio was obtained. These comparisons were made over the iodide ion concentration range of 41×10^{-6} to 212×10^{-6} M (see Tables 41, 42 and 43, Runs 40 and 41).

A kinetic run at 1.99×10^{-6} M sodium iodide was performed using the multiple flask method with greased glass stoppers. The initial stoichiometric iodine concentration was 0.0000956 M as compared

Table 41

Run 40, Phenol in 1.99×10^{-6} M Sodium Iodide Solution at 25°

(Phenol)₀ - 0.002005 M

(HClO₄) - 0.0174 M

(I₂)₀ - 0.000341 M

(NaClO₄) - 0.2826 M

(NaI)₀ - 0.00000199 M

(Na₂S₂O₃) - 0.005065 M

50.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mol. sec.)	Per cent reaction
(blank)	6.74		0.00
360	6.09	0.1422	9.64
840	5.55	0.1167	17.65
1380	5.22	0.0944	22.55
1800	5.04	0.0824	25.22
3840	4.27	0.0614	36.65
7200	3.48	0.0480	48.37
12,600	2.72	0.0381	59.64

Table 42

Run 41, Phenol -2,4,6-d₃ in 1.99×10^{-6} M Sodium Iodide Solution
at 25°

(Phenol)₀ - 0.001979 M

(HClO₄) - 0.0174 M

(I₂)₀ - 0.000347 M

(NaClO₄) - 0.2826 M

(NaI)₀ - 0.00000199 M

(Na₂S₂O₃) - 0.005065 M

50.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mol. sec.)	Per cent reaction
(blank)	6.85		0.00
1500	6.09	0.0406	11.09
2100	5.96	0.0338	12.99
3600	5.65	0.0276	17.52
7740	4.99	0.0212	27.15
15,360	4.27	0.0162	37.66
28,860	3.49	0.0124	49.05
50,400	2.70	0.0101	60.58

Table 43

Ratio of k_{app} for Phenol to k_{app} for Phenol-2,4,6- d_3 from Runs 41 and 42

$(I^-) \times 10^6$	k_{app}	k_{app} for	$k_{app}(H)$	Per cent
<u>M</u>	Phenol	2,4,6- d_3 Phenol	$\frac{k_{app}(H)}{k_{app}(D)}$	difference (3.34)
41	0.1355	0.0406	3.34	0
46	0.1300	0.0352	3.69	10.4
55	0.1200	0.0305	3.93	17.7
83	0.0895	0.0232	3.85	15.3
120	0.0655	0.0175	3.74	12.0
148	0.0546	0.0145	3.77	12.9
212	0.0372	0.0101	3.70	10.8

to 0.000347 M for the previous reaction. This change was made in order to prevent a rapid decrease in rate with increasing per cent reaction. The same stock iodine solution was used for this run as the protium run; however, 104 hours elapsed between the deuterium and protium run. The plot of apparent rate constants versus per cent reaction when extrapolated to zero time gave an apparent rate constant of 0.0842 (l./mole sec.). The calculation of k' gave a value of $0.159 \times 10^{-6} \text{ sec.}^{-1}$ (see Table 44, Run 43). As compared to the value of k' of $1.14 \times 10^{-6} \text{ sec.}^{-1}$ at 0.0005 M sodium iodide the value of $0.159 \times 10^{-6} \text{ sec.}^{-1}$ indicated a decrease of 86 per cent. This value of k' is of only limited interest because of the same errors that were mentioned earlier in this chapter in the iodination of phenol in $1.99 \times 10^{-6} \text{ M}$ sodium iodide. The calculated isotope ratio $k'_{\text{H}} / k'_{\text{D}}$ is 3.66

A kinetic run at $19.9 \times 10^{-6} \text{ M}$ sodium iodide was performed using the multiple flask method with greased glass stoppers. This kinetic run was performed in order to obtain an isotope ratio at this extremely low iodide ion concentration. The same stock iodine solution was used for the protium run; however, 22 hours elapsed between the deuterium and protium run. The plot of apparent rate constants versus per cent reaction when extrapolated to zero time gave an apparent rate constant of 0.0621 (l./mole sec.). The calculation of k' gave a value of $1.18 \times 10^{-6} \text{ sec.}^{-1}$ (see Table 45, Run 39). The calculation of the isotope ratio $k'_{\text{H}} / k'_{\text{D}}$ gave a value of 3.43.

Table 44

Run 43, Phenol -2,4,6-d₃ in 1.99×10^{-6} M Sodium Iodide Solution at 25°

(Phenol)₀ - 0.0009872 M

(HClO₄) - 0.0174 M

(I₂)₀ - 0.0000956 M

(NaClO₄) - 0.2826 M

(NaI)₀ - 0.00000199 M

(Na₂S₂O₃) 0.002026 M

100.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mol. sec.)	Per cent reaction
(blank)	9.44		0.00
1380	8.54	0.0738	9.53
2280	8.13	0.0665	13.88
3120	7.88	0.0591	16.52
4320	7.50	0.0544	20.55
5940	7.02	0.0512	25.63
9900	6.25	0.0429	33.79

Rate constant extrapolated to zero time (k_{app}) = 0.0842

$k' = 0.159 \times 10^{-6} \text{sec.}^{-1}$

Table 45

Run 39, Phenol -2,4,6-d₃ in 19.9×10^{-6} M Sodium Iodide Solution
at 25°

(Phenol)₀ - 0.0010325 M

(HC10₄) - 0.0174 M

(I₂)₀ - 0.0000915 M

(NaC10₄) - 0.28258 M

(NaI)₀ - 0.0000199 M

(Na₂S₂O₃) - 0.004052 M

200.0 ml. of reaction mixture per flask

Time elapsed (sec.)	Titer (ml.)	Rate constant (l./mol. sec.)	Per cent reaction
(blank)	9.03		0.00
2400	7.97	0.0510	11.74
2460	7.95	0.0507	11.96
4680	7.32	0.0440	18.94
5520	7.14	0.0417	20.93
6780	6.88	0.0393	23.81
8100	6.66	0.0368	26.25
10,260	6.26	0.0351	30.67
13,320	5.88	0.0317	34.88

Rate constant extrapolated to zero time (k_{app}) = 0.0621

$k' = 1.18 \times 10^{-6}$ sec.⁻¹

Kinetic Equation for the Iodination of Phenol. --In the kinetic run of the iodination of phenol at zero molar sodium iodide the plot of apparent rate constants versus per cent reaction could not be extrapolated to zero time. Values of k' were obtained at certain per cent reactions by a method indicated earlier in this chapter. In order to obtain more exact values of k' and also to obtain a series of k' values covering the range of increasing iodide ion concentration in the reaction, the kinetic equation for the second-order reaction for Berliner's rate-determining step was derived. The complete derivation and solution to the first-order differential equation is given in Appendix C. By knowing two sets of limits - time and iodide ion concentration produced by the reaction - a series of integrated k' values were obtained for the appropriate iodide ion concentration ranges. Using the data in Run 44 the solution of the integral gave the results indicated in Table 46. The results of the k' values certainly indicated that there was a definite decrease in k' with decreasing iodide ion concentration. However, there was definitely one error in that the initial solution did not contain zero molar sodium iodide as was assumed in solution of the equation but contained at least some iodide ions produced by the reaction of iodine with water.

In order to help eliminate this error, the determination of k' values was repeated for this run, but the initial iodide ion concentration

Table 46

The Mathematical Evaluation of Table 35, Run 44

Time Limits (sec.)	Stoichiometric Iodide Ion Concentration Range x 10 ⁶	k' x 10 ⁶ sec.
0 - 390	0 - 40	1.94
0 - 540	0 - 49	2.25
0 - 840	0 - 64	2.55
0 - 1080	0 - 77	2.99
0 - 1320	0 - 85	3.07
0 - 1920	0 - 105	3.43
0 - 2940	0 - 127	3.56
0 - 4440	0 - 153	3.76
0 - 6120	0 - 176	3.94

was set at 40×10^{-6} M and the appropriate changes in initial stoichiometric concentrations of iodine and phenol were made. The results of this evaluation are given in Table 47. The k' values indicated in Table 47 are more consistent than the k' values indicated in Table 46; thus, by using the lower iodide ion limit as 40×10^{-6} M the error in k' by not knowing the initial iodide ion concentration is reduced.

To check the results obtained from the second evaluation of Run 44 the k' values for Run 36 were determined by the solution of the differential equation and are recorded in Table 48. The resulting k' values in the same iodide ion concentration range indicated there was no decrease of k' with decreasing iodide ion concentration.

An evaluation of Run 15 which had an initial iodide ion concentration of 0.02 M in buffered sodium acetate-acetic acid solution was made in order to obtain k' values at higher ranges of iodide ion concentration. The results of this evaluation are given in Table 49. The values of k' are fairly consistent although the iodide ion concentration only increases six per during the reaction; however, k_{app} decreases 8.9 per cent during the run. The calculation of these k' values indicated that the mathematics of the solution of the differential equation was correct and that the fall in k_{app} during the run can be explained by Berliner's mechanism at least at high iodide ion concentrations. At low iodide ion concentrations, however, computations

Table 47

The Mathematical Evaluation of Table 35, Run 44*

Time Limits (sec.)	Stoichiometric Iodide Ion Concentration Range $\times 10^6$	$k' \times 10^6$ sec.
390 - 540	40 - 49	3.01
390 - 840	40 - 64	3.03
390 - 1080	40 - 77	3.54
390 - 1320	40 - 85	3.51
390 - 1920	40 - 105	3.78
390 - 2940	40 - 127	3.75
390 - 4440	40 - 153	3.90
390 - 6120	40 - 176	4.05

*Initial iodide ion concentration was 40×10^{-6} in this case.

Table 48

The Mathematical Evaluation of Table 36, Run 36

Time Limits (sec.)	Stoichiometric Iodide Ion Concentration Range x 10 ⁶	k'x10 ⁶ sec.
0 - 270	40 - 63	4.37
270 - 480	63 - 75	4.20
480 - 840	75 - 92	4.38

Table 49

The Mathematical Evaluation of Table 17, Run 15

Time Limits (sec.)	Stoichiometric Iodide Ion Concentration Range	k_{app} (l./mole sec.)*	$k' \times 10^6$ sec.
0 - 10,800	0.02 - 0.02019	0.001189	3.29
10,800 - 17,400	0.02019 - 0.02029	0.001177	3.30
17,400 - 25,200	0.02029 - 0.02041	0.001176	3.42
25,200 - 39,000	0.02041 - 0.02057	0.001142	3.23
39,000 - 60,420	0.02057 - 0.02079	0.001113	3.30
60,420 - 86,460	0.02079 - 0.02100	0.001098	3.44
86,460 - 118,500	0.02100 - 0.02120	0.001083	3.51

*The value of k_{app} was integrated from zero time to the time indicated in the second column.

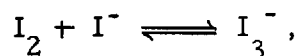
of k' were inconsistent in comparisons between runs. A likely cause of this inconsistency is that the true initial stoichiometric iodide concentrations were in error and consequently all iodide ion concentrations were in error during the runs at low iodide ion concentration.

CHAPTER VII

THE MECHANISM OF THE IODINATION OF PHENOL

The rate constants that have been tabulated in Chapters V and VI have all been calculated on the basis of a second order reaction, first order in iodine and first order in phenol. This is justified on the grounds that at constant hydrogen ion and iodide ion concentrations the rate is constant throughout the reaction, e. g., see Table 12. That there is a variation between runs is quite true, but it is this variation with iodide ion concentration which is indicative of the true mechanism.

The variation in any one run is due to two factors: the first is that if there is an error in the initial concentration of either reagent, the integrated rate constants will deviate from constancy; the second is that due to various equilibria, including the following example



the iodide ion liberated in the reaction is continually altering the concentration of the iodinating species and possibly also altering the concentration of a reactive iodinated intermediate from phenol.

Since the error in the initial concentration is subject to only limited control (the technique and accuracy of the experimenter) and is

not easily measurable, it must for the most part be ignored. It was shown that the rate is greatly slowed by added iodide ion, and thus any rate constant calculated by using a stoichiometric iodine concentration and ignoring the iodide ion concentration is really only an apparent rate constant.

It has been demonstrated by Soper and Smith (19) that the rate of the iodination of phenol is dependent on the inverse square of the actual iodide ion concentration. The dependence upon hydrogen ion and buffer concentration has also been studied in some detail by Painter and Soper (6), and the following relation for hydrogen ion dependence was found

$$k_{app} = \frac{k_o}{[H^+]} + \frac{k_{cat} \text{ (acid)}}{[H^+]^2} .$$

In order to take into consideration the dependence of rate on iodide ion concentration, a k' value was obtained for each kinetic run. The derivation of k' was based on Berliner's mechanism in which the rate expression is

$$\text{rate} = k_o [PhO^-] [I^+] + k_{cat} [PhO^-] [HOI] [HAc] .$$

The derivation of k' is given in Chapter V.

In this thesis one of the methods of distinguishing between Grovenstein and Henderson's mechanism and Berliner's mechanism

was the lowering of the iodide ion concentration in order to observe whether k' would remain constant. According to Grovenstein and Henderson's mechanism a decrease of k' would be observed if the reaction of iodine with phenol or phenoxide ion became the rate-determining step; whereas, if Berliner's mechanism holds, k' should remain constant. It was found from the kinetic runs indicated in Chapters V and VI that the value of k' did not decrease a significant amount in the iodide ion concentration range of 0.08 M to $1.99 \times 10^{-5} \text{ M}$. A summary of the kinetic runs that were felt to be accurate and their appropriate k' value is given in Tables 50 and 51. The slight decrease in the k' values in Tables 50 and 51 with decreasing iodide ion concentration may be due to an error in knowing the true stoichiometric iodide ion concentration or to a salt effect. The fact that k' did not decrease significantly in going to low iodide ion concentrations does not disprove Grovenstein and Henderson's mechanism. The intermediate proposed by these workers could still be in equilibrium with the reactants at the extremely low iodide ion concentrations used in the present work.

Another method of distinguishing between Grovenstein and Henderson's mechanism and Berliner's mechanism was the study of an isotope effect in the iodination of phenol. In Grovenstein and Henderson's mechanism, at a sufficiently high iodide ion concentration, the rate-determining step is the removal of a proton from an intermediate

Table 50

Evaluation of k' From k_{app} for Phenol and Phenol-2, 4, 6-d₃

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

$$K_1 = 768 \text{ liter mole}^{-1}$$

All runs were made in buffered sodium acetate-acetic acid, at an ionic strength of 0.300 at 25.0°.

Phenol						
Table No.	$(I_2)_0 \times 10^3$ (M)	$(I^-)_0 \times 10^2$ (M)	$[I^-]_0 \times 10^2$ (M)	$[I_3^-]_0 \times 10^3$ (M)	k_{app} (L./mole sec.)	$k' \times 10^4$ (sec. ⁻¹)
12	2.006	8.00	7.80	1.97	0.0000691	3.28
17	1.975	2.00	1.82	1.84	0.001208	3.28
18	1.996	0.801	0.635	1.66	0.00874	3.27
22	0.432	0.420	0.388	0.323	0.02030	3.13
23	0.424	0.420	0.388	0.317	0.02042	3.16
24	0.497	0.200	0.172	0.282	0.07955	3.15
27	0.414	0.100	0.0838	0.162	0.2132	2.94
28	0.503	0.0500	0.0386	0.114	0.5970	3.01
Phenol-2, 4, 6-d ₃						
29	1.952	2.00	1.82	1.82	0.000305	0.830
30	0.439	0.200	0.175	0.251	0.0205	0.843
31	0.432	0.0500	0.0399	0.101	0.1520	0.785

Table 51

Evaluation of k' From k_{app} for Phenol and Phenol-2, 4, 6-d₃

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

$$K_1 = 768 \text{ liter mole}^{-1}$$

All runs were made in 0.0174 M perchloric acid, at an ionic strength of 0.300 at 25.0°.

Phenol						
Table No.	$(I_2)_o \times 10^6$ (M)	$(I^-)_o \times 10^6$ (M)	$[I^-]_o \times 10^6$ (M)	$[I_3^-]_o \times 10^6$ (M)	k_{app} (l./mole sec.)	$k' \times 10^6$ (sec. ⁻¹)
31	433	500	399	101	0.00887	4.65
32	409	500	403	96.7	0.00858	4.53
33	429	100	77	23	0.0480	4.08
35	412	40	30.6	9.44	0.1312	4.11
36	217	40	34.3	5.66	0.1124	3.90
38	89.2	19.9	18.7	1.27	0.2145	4.06 ²
37	96.6	1.99	1.85	0.137	0.3140	0.582 ¹
Phenol-2, 4, 6-d ₃						
39	466	500	392	108	0.00224	1.14 ²
44	91.5	19.9	18.7	1.29	0.0621	1.18 ²
43	95.6	1.99	1.86	0.134	0.0842	0.159 ¹

¹ Possible error in initial stoichiometric iodide ion concentration. Same stock iodine solution was used in runs upon protium and deuterium compound; however, 104 hours elapsed between performing run 37 and then run 43.

² Same stock iodine solution was used in both runs. The stock iodine was two hours from time of preparation when used in the deuterium run and 24 hours from time of preparation when used in the protium run.

by a base; while in Berliner's preferred mechanism this is a subsequent fast step. The comparison of the rate of iodination of phenol and phenol-2, 4, 6-d₃ under the same conditions indicated an isotope effect of approximately four. This isotope effect indicated that the rate-determining step in the iodination of phenol under the experimental conditions is the release of the proton from an intermediate and not the attack of the iodine cation on the phenoxide molecule as suggested by Berliner and Soper and co-workers.

It was not possible to determine the halogenating agent from the data obtained in this study. In view of the following experimental results there exist a number of plausible mechanisms for the iodination of phenol:

- a. In this investigation it was not possible to distinguish between the following potential halogenating agents: I_2 , I^+ , H_2OI^+ , CH_3COOI and I_3^- (although this depends upon what mechanism is assumed).
- b. The rate-determining step is the release of the proton from an intermediate by a general base and may possibly involve attack by a halogenating agent as well.
- c. The rate is inversely proportional to the square of the actual iodide ion concentration.
- d. The rate is inversely proportional to more than the first and less than the second power of the actual hydrogen ion concentration.

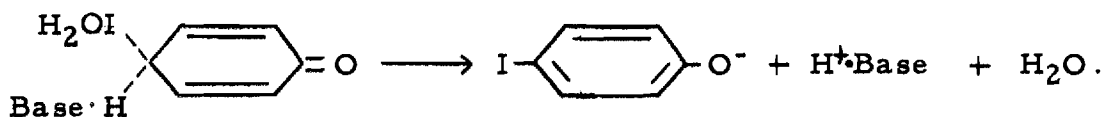
In considering plausible mechanisms for the iodination of phenol the one proposed by Grovenstein and Henderson agrees with the experimental results indicated above if the general bases are considered water and acetate ion. The derivation of the kinetic equation is given in Appendix D. The rate expression of the mechanism is

$$\text{rate} = \frac{k'_3 [\text{PhOH}] [\text{I}_3^-] [\text{H}_2\text{O}]}{[\text{H}^+] [\text{I}^-]^2} + \frac{k'_4 [\text{PhOH}] [\text{I}_3^-] [\text{HOAc}]}{[\text{H}^+]^2 [\text{I}^-]^2} .$$

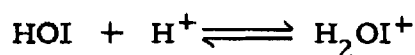
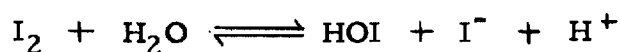
Assuming an equilibrium condition exists in Grovenstein and Henderson's mechanism any of the halogenating agents (I^+ , H_2OI^+ , CH_3COOI and I_3^-) fit the kinetic requirements. Although I^+ , H_2OI^+ and CH_3COOI are reasonable species for halogenation, I_3^- does not appear to be a reasonable halogenating species because in halogenation of other aromatic molecules it has been shown that I_3^- is a poor halogenating species. In the mechanism shown in Appendix D if I_2 is replaced by either I^+ , H_2OI^+ , or CH_3COOI and if the appropriate iodine equilibrium are considered with the general bases water and acetate ion, the rate expression of the mechanism is the same as given above.

A concerted termolecular mechanism has not been ruled out

(7). One possible termolecular mechanism is



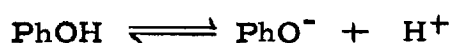
$$\text{rate} = k_0 [\text{PhO}^-] [\text{H}_2\text{OI}^+] [\text{Base}] \quad (1)$$



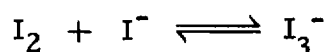
$$K_3 = \frac{[\text{H}_2\text{OI}^+]}{[\text{HOI}][\text{H}^+]}$$

$$K_4 = \frac{[\text{HOI}][\text{I}^-][\text{H}^+]}{[\text{H}_2\text{O}][\text{I}_2]}$$

$$\text{H}_2\text{OI}^+ = \frac{K_3 K_4 [\text{H}_2\text{O}][\text{I}_2]}{[\text{I}^-]} \quad (2)$$



$$\text{PhO}^- = \frac{K_5 [\text{PhOH}]}{[\text{H}^+]} \quad (3)$$



$$\text{I}_2 = \frac{[\text{I}_3^-]}{K_1 [\text{I}^-]} \quad (4)$$

Substitution of equations 2, 3, and 4 into equation 1 gives the rate expression

$$\text{rate} = \frac{k [\text{PhOH}][\text{I}_3^-][\text{Base}]}{[\text{H}^+][\text{I}^-]^2}$$

Considering water and acetate ion as the general bases a rate expression is obtained which conforms to the requirements indicated previously.

The halogenating species I^+ or CH_3COOI would give the same results in the above concerted termolecular mechanism. A summary of mechanisms of the iodination of phenol is given in Table 52. This table indicates as well some mechanisms that do not fit the requirements indicated earlier in this chapter.

Table 52

Possible Mechanisms of the Iodination of Phenol

Aromatic Species		Iodinating Species				
		I_2	I^+	H_2OI^+	CH_3COOI	I_3^-
I.	Rate determining attack upon					
	a. PhOH	No (1)	No (1)	No (1)	No (1)	No (1)
	b. PhO^-	No (1)	No (1)	No (1)	No (1)	No (1)
II.	Attack to give possible equilibrium with					
	a. PhOH	Yes	Yes	Yes	Yes	Yes
	b. PhO^-	Yes	Yes	Yes	Yes	Yes
III.	Concerted termolecular reaction upon					
	a. PhOH	No (2)	Yes	Yes	Yes	No (2)
	b. PhO^-	No (2)	Yes	Yes	Yes	No (2)

¹ Rate-determining step has been found to be the release of the proton.

² Does not give the correct iodide ion dependency.

CHAPTER VIII

SUGGESTIONS FOR FUTURE EXPERIMENTAL WORK

There are several aspects of the iodination of phenol that are in need of further clarification by experimental means. One is a determination of whether or not molecular iodine is the effective halogenating agent. In order to elucidate this point the iodide ion concentration will have to be lowered to an extremely low value. In this work the problems that existed at low iodide ion concentration were knowing the actual iodide ion concentration and maintaining a low iodide ion concentration throughout the reaction. Some method of ascertaining and maintaining an extremely low iodide ion concentration will have to be found. Maybe with the use of some metal iodide which has a small dissociation constant the iodide ion concentration might be controlled. If by controlling the iodide ion concentration negative results are obtained it might be due to the fact that the proposed intermediate is too sensitive even to an extremely small concentration of iodide ions. In this case it might be possible to use another aromatic compound such as *p*-nitrophenol that should give an intermediate which should lose a proton more readily and might react with iodide ion less readily than the intermediate from phenol. If a condition can be found that will prove iodine is the halogenating species then the kinetics at the iodide ion concentration studied in the present

work will demand a mechanism involving an equilibrium with an intermediate complex.

A second aspect for future investigation is of special importance if iodine cannot be shown to be the halogenating species. If this is the case, then there are two possible mechanisms for the iodination of phenol. One involves an intermediate in equilibrium with reactants and the other a concerted termolecular mechanism. If an equilibrium exists with an intermediate complex then it might be possible to prove this point by performing the reaction in an ultraviolet spectrophotometer. If the spectrophotometer indicates a compound that is absorbing ultraviolet light in a different region and/or intensity from phenol, iodine, triiodide ion or iodophenol and then slowly disappearing, an intermediate could be indicated.

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.,

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

in which k is the rate constant (l./mole sec.), t is the time in seconds elapsed for any point, a is the initial stoichiometric molar concentration of iodine, b is the initial molar concentration of phenol, and x is the molar concentration of stoichiometric iodine reacted (or product formed) at time t. The sample calculation will be on Run 33, Table 33.

$$\begin{array}{lll} a = 0.000409 \underline{M} & a/b = 0.2015 & [\text{Na}_2\text{S}_2\text{O}_3] = 0.005072 \underline{M} \\ b = 0.002030 \underline{M} & b - a = 0.001621 & (50 \text{ ml. samples}) \end{array}$$

<u>t</u> (sec.)	Titer (ml.)	(<u>b - x</u>)	(<u>a - x</u>)	(<u>x</u>)	$\frac{(b - x)}{(a - x)}$
5,400	7.40	0.001996	0.000375	0.000034	5.323
9,600	6.93	0.001972	0.000351	0.000058	5.618
14,400	6.50	0.001951	0.000330	0.000079	5.912
20,400	6.03	0.001927	0.000306	0.000103	6.297
26,400	5.64	0.001907	0.000286	0.000123	6.668
51,000	4.40	0.001844	0.000223	0.000186	8.269

$$k = \frac{2.303}{(0.00162)t} \log(0.2015) \frac{(b-x)}{(a-x)}$$

t (sec.)	$\frac{2.303}{(b-a)t}$	$\frac{a(b-x)}{b(a-x)}$	$\log \frac{a(b-x)}{b(a-x)}$	$\frac{2.303}{(b-a)t} \log \frac{a(b-x)}{b(a-x)}$
5400	0.2631	1.072	0.03035	0.007986
9600	0.1480	1.132	0.05381	0.007964
14,400	0.09866	1.191	0.07598	0.007497
20,400	0.06964	1.269	0.1034	0.007200
26,400	0.05381	1.343	0.1282	0.006899
51,000	0.02786	1.666	0.2217	0.006175

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

APPENDIX B

THE CALCULATION OF THE PURITY OF PHENOL-2, 4, 6-d₃

For a quantitative estimate of the purity of the prepared product, phenol-2, 4, 6-d₃, a calculation was made based on Ingold's partition ratio. A further calculation was made based on a partition ratio of unity.

The calculation of the purity of phenol-2, 4, 6-d₃ based on Ingold's partition ratio was 99.00 per cent and 99.13 per cent based on a partition ratio of unity. The per cent purity was calculated as follows:

Grams atoms of H present in phenol -

$$\frac{15.0331 \text{ g.}}{94.11 \text{ g./mole}} = 0.1597 \text{ moles of phenol}$$

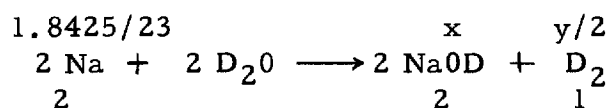
$$0.1597 \text{ moles} \times 4\text{H atoms/mole} = 0.6388 \text{ gram atoms of exchangeable H.}$$

Gram atoms of D present in 100 grams of 99.5% D₂O -

$$\frac{99.5 \text{ g.}}{20.0162 \text{ g./mole}} = 4.971 \text{ moles of D}_2\text{O}$$

$$4.971 \text{ moles} \times 2\text{D atoms/mole} = 9.942 \text{ gram atoms of D.}$$

Loss of gram atoms of D in reaction of sodium -



$$x = 0.0801 \text{ moles of NaOD}$$

$$y = 0.0801 \text{ gram atoms of D}$$

Total gram atoms of D present in solution -

$$\begin{array}{r} 9.9420 \text{ gram atoms} \\ -0.0801 \text{ gram atoms} \\ \hline 9.8619 \text{ gram atoms of D} \end{array}$$

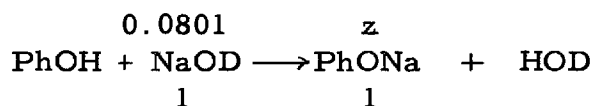
Gram atoms of H present in 99.5 per cent D_2O -

$$\frac{0.50 \text{ g.}}{18.016 \text{ g./mole}} = 0.02775 \text{ moles of } H_2O$$

$$0.02775 \text{ moles} \times 2H \text{ atoms} = 0.0555 \text{ gram atoms of H.}$$

Loss of gram atoms of H from phenol because of reaction with

NaOD:



$$z = 0.0801 \text{ moles of PhONa or gram atoms of H lost.}$$

Total gram atoms of H now in solvent -

$$\begin{array}{r} 0.0801 \text{ gram atoms} \\ + 0.0555 \text{ gram atoms} \\ \hline 0.1356 \text{ gram atoms of H} \end{array}$$

Define Ingold's partition ratio as:

$$\frac{(D)_{\text{PhOH}} \quad (H)_{\text{Solvent}}}{(H)_{\text{PhOH}} \quad (D)_{\text{Solvent}}} = 0.91$$

where at equilibrium

$(D)_{\text{PhOH}}$ equals the gram atoms of exchangeable D in phenol

$(H)_{\text{Solvent}}$ equals the gram atoms of H in solvent

$(H)_{\text{PhOH}}$ equals the gram atoms of exchangeable H in phenol

$(D)_{\text{Solvent}}$ equals the gram atoms of D in solvent.

Let x equal the number of gram atoms of exchangeable H present in phenol after first deuteration, and then solve the value of x -

$$\frac{(0.5587 - x) (0.1356 + 0.5587 - x)}{(x) (9.8619 - 0.5587 + x)} = 0.91$$

$x = 0.0400$ gram atoms of H left in phenol.

Gram atoms of D now in phenol and purity -

$$\begin{array}{r} 0.5587 \text{ gram atoms} \\ -0.0400 \text{ gram atoms} \\ \hline 0.5187 \text{ gram atoms of D now in phenol} \end{array}$$

$$\frac{0.5187 \times 100}{0.5587} = 92.84 \text{ per cent}$$

Using Ingold's partition ratio but replacing the value of 0.91 by unity gives an x value of 0.0367 gram atoms. The purity based on a partition ratio of unity was

$$\begin{array}{r} 0.5587 \text{ gram atoms} \\ -0.0367 \text{ gram atoms} \\ \hline 0.5220 \text{ gram atoms of D} \end{array}$$

$$\frac{0.5220 \times 100}{0.5587} = 93.43 \text{ per cent}$$

For second deuteration phenol was present at first as PhONa

then 9.32 ml. of DCl heavy water solution was added. An assumption is made here that the D and H gram atoms added come from the heavy water only and the DCl or HCl is not considered. This may cause about a one per cent error in the final purity of the phenol-2,4,6-d₃.

Total gram atoms of D and H present from 9.32 ml. of D₂O

$$1.107 \text{ g/ml.} \times 9.32 \text{ ml.} = 10.317 \text{ grams}$$

$$10.317 \text{ g.} \times 0.005 = 0.05158 \text{ grams of H}_2\text{O}$$

$$10.317 \text{ g.} \times 0.995 = 10.2654 \text{ grams of D}_2\text{O}$$

$$\frac{0.05158 \text{ g.} \times 2 \text{ g. atoms/mole}}{18.016 \text{ g/mole}} = 0.0057 \text{ gram atoms of H}$$

$$\frac{10.2654 \text{ g.} \times 2 \text{ g. atoms/mole}}{20.016 \text{ g/mole}} = 1.0257 \text{ gram atoms of D}$$

Upon adding 100 grams of 99.5 per cent pure D₂O the total gram atoms of D and H present is

9.9420 gram atoms	0.0555 gram atoms
1.0257 gram atoms	0.0057 gram atoms
<hr style="width: 100%; border: 0.5px solid black;"/>	<hr style="width: 100%; border: 0.5px solid black;"/>
10.9677 gram atoms of D	0.0612 gram atoms of H

Let y equal net gram atoms of D transferred from solvent to phenol -

$$\frac{(0.5187 + y)(0.0612 + y)}{(0.0400 - y)(10.9677 - y)} = 0.91$$

$$y = 0.0344 \text{ gram atoms of D}$$

Gram atoms of D now in phenol and purity -

0.5187 gram atoms

0.0344 gram atoms

0.5531 gram atoms of D

$$\frac{0.5531 \times 100}{0.5587} = 99.00 \text{ per cent}$$

For partition ratio of unity -

$$y = 0.0351 \text{ gram atoms of D}$$

0.0351 gram atoms

0.5187 gram atoms

0.5538 gram atoms

$$\frac{0.5538 \times 100}{0.5587} = 99.13 \text{ per cent}$$

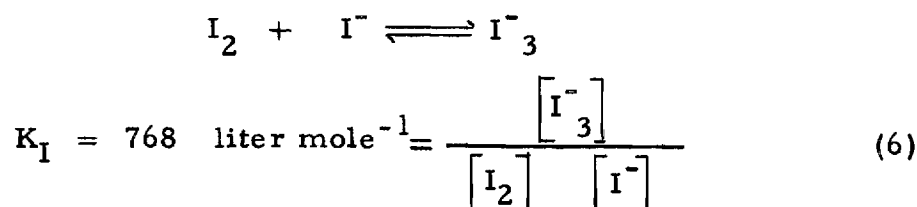
APPENDIX C

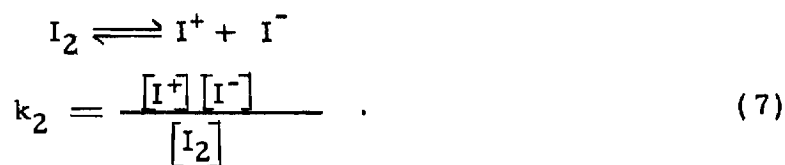
DERIVATION AND SOLUTION OF A FIRST-ORDER DIFFERENTIAL EQUATION FOR THE IODINATION OF PHENOL

In the iodination of phenol Berliner has proposed that the rate-determining step is the attack of the iodine cation or the hypiodous acidium ion upon the phenoxide ion. At constant buffer concentration at acidities in the range of the present work, Berliner's mechanism can be expressed as

$$\frac{-d(I_2)}{dt} = (\text{PhOH}) [I^+]. \quad (5)$$

This first-order differential equation was integrated in order to obtain a mathematical evaluation of kinetic runs. This evaluation gave integrated k' values for iodide ion concentration ranges. The following equilibria had to be considered in order to help solve the differential equation:





Substitution of $[I^+]$ from equation 7 into equation 5 gave the following relation:

$$\frac{-d(I_2)}{dt} = \frac{k_0 K_2 (\text{PhOH}) [I_2]}{[I^-]} \quad . \quad (8)$$

In the iodide ion concentration range of most of the present work the following relation existed between the actual iodine concentration and the stoichiometric concentration (since I^+ , H_2OI^+ and HOI are of negligible concentration):

$$(I_2) = [I_2] + [I_3^-] \quad . \quad (9)$$

Substitution of the $[I_3^-]$ from equation 6 into equation 9 gave the following relation:

$$(I_2) = [I_2] \left\{ 1 + K_1 [I^-] \right\} \quad . \quad (10)$$

Substitution of the actual iodine concentration from equation 10 into equation 8 gave the following relation:

$$\frac{-d(I_2)}{dt} = \frac{k_0 K_2 (\text{PhOH}) (I_2)}{[I^-] + K_1 [I^-]^2} \quad . \quad (11)$$

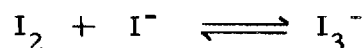
In order to know what relation existed at time \underline{t} between the actual iodide ion concentration and the actual concentration of the tri-iodide ion the following substitutions were made:

Let $x = (I_2)$ which has reacted at time \underline{t} .

$z = I_3^-$ at time \underline{t} .

$(I_2)_0 =$ initial stoichiometric iodine concentration.

$(I^-)_0 =$ initial stoichiometric iodide ion concentration.



$$K_1 \left[(I_2)_0 - x - z \right] \left[(I^-)_0 + x - z \right] = z. \quad (12)$$

The solution of equation 12 for the value of \underline{z} in terms of K_1 , $(I_2)_0$, $(I^-)_0$ and \underline{x} gave the following relation:

$$z = \frac{\left[(I^-)_0 K_1 + (I_2)_0 K_1 + 1 \right] - \sqrt{a}}{2K_1} \quad (13)$$

$$\text{where } a = 4K_1^2 x^2 + 4K_1^2 (I^-)_0 x - 4K_1^2 (I_2)_0 x + (I^-)_0^2 K_1^2 - 2K_1^2 (I_2)_0 (I^-)_0 + 2K_1 (I^-)_0 + K_1^2 (I_2)_0^2 + 2K_1 (I_2)_0 + 1$$

At any time \underline{t} equation 11 has the following form:

$$\frac{-d(I_2)}{dt} = \frac{k_o k_1 \left[(PhOH)_0 - x \right] \left[(I_2)_0 - x \right]}{\left[(I^-)_0 + x - z \right] + K_1 \left[(I^-)_0 + x - z \right]^2} \quad (14)$$

Substitution of the value of \underline{z} from equation 13 into equation 14 and simplification gave the following general form:

$$\frac{-dx}{dt} = \frac{k_o K_1 \left[(\text{PhOH})_o - x \right] \left[(\text{I}_2)_o - x \right]}{b}$$

$$\text{where } b = 2K_1 x^2 + x \left[2K_1 (\text{I}^-)_o - 2K_1 (\text{I}_2)_o \right] + \left[0.5 (\text{I}^-)_o - (\text{I}_2)_o (\text{I}^-)_o K_1 + 0.5 (\text{I}^-)_o^2 K_1 + 0.5 (\text{I}_2)_o^2 K_1 + 0.5 (\text{I}_2)_o \right] + \left[0.5 (\text{I}^-)_o + x - 0.5 (\text{I}_2)_o \right] \sqrt{a} \cdot (15)$$

To illustrate this general form a sample calculation will be made on Run 36, Table 36. Substitution of the following initial stoichiometric concentrations of species into equation 15 with simplification give the following relation:

$$\begin{aligned} (\text{PhOH})_o &= 0.002030 \text{ M} \\ (\text{I}_2)_o &= 0.000412 \text{ M} \\ (\text{I}^-)_o &= 0.000040 \text{ M} \\ K_1 &= 768 \text{ liter mole}^{-1} \end{aligned}$$

$$\int dt = \frac{1}{k_o K_1} \left[\int \frac{1536x^2 dx}{x^2 - 0.002442x + 0.8364 \cdot 10^{-6}} - \int \frac{0.5714x dx}{x^2 - 0.002442x + 0.8364 \cdot 10^{-6}} + \int \frac{2.791 \cdot 10^{-4} dx}{x^2 - 0.002442x + 0.8364 \cdot 10^{-6}} + \int \frac{(x - 0.000186) \sqrt{2,359,296x^2 - 877.66x + 1.775}}{x^2 - 0.002442x + 0.8364 \cdot 10^{-6}} \right] \cdot (16)$$

The first three integrals on the right side of equation 16 were solved by the method of completing the square of a quadratic equation, and the use of definite integral relationships. The following integral will serve as an illustration and was applicable to the solution of the other two integrals:

$$\int \frac{1536x^2 dx}{x^2 - 0.002442x + 0.8364 \cdot 10^{-6}} \quad (17)$$

Upon dividing the numerator by the denominator the following relation was equal to equation 17:

$$1536 \left[x + 0.002442 \int \frac{x dx}{x^2 - 0.002442x + 0.8364 \cdot 10^{-6}} - 0.8364 \int \frac{dx}{x^2 - 0.02442x + 0.8364 \cdot 10^{-6}} \right] .$$

Completion of the square of the denominator and substitution gave:

$$x^2 - 0.002442x + 0.8364 \cdot 10^{-6} = (x - 0.001221)^2 + 0.8364 \cdot 10^{-6} - 1.491 \cdot 10^{-6} \\ (x - 0.001221)^2 - 0.6545 \cdot 10^{-6}$$

With $x' = (x - 0.001221)$, equation 17 is thereby shown to equal equation 18:

$$1536 \left[x + 0.002442 \int \frac{(x' + 0.001221) dx'}{(x')^2 - (0.809 \cdot 10^{-3})^2} - 0.8364 \int \frac{dx'}{(x')^2 - (0.809 \cdot 10^{-3})^2} \right] \quad (18)$$

From the relationships

$$\int \frac{x dx}{x^2 - a^2} = \frac{2.303}{2} \log (x^2 - a^2)$$

$$\int \frac{dx}{x^2 - a^2} = \frac{2.303}{2} \log \frac{(x - a)}{(x + a)} \quad (51a)$$

the solution of the integrals of equation 18 gave the following relation for equation 17:

$$\int \frac{1536 x^2 dx}{x^2 - 0.002442x + 0.8364 \cdot 10^{-6}} = 1536x + 4.319 \log (x^2 - 0.002442x + 0.8364 \cdot 10^{-6}) + 4.691 \log \frac{(x - 0.002030)}{(x - 0.000412)} \quad (19)$$

Upon solving the second and third integrals in equation 16 the differential equation had the following form:

$$dt = \frac{1}{k_0 K_2} \left[1536x + 3.661 \log (x^2 - 0.002442x + 0.8364 \cdot 10^{-6}) + 4.094 \log \frac{(x - 0.002030)}{(x - 0.000412)} + \frac{(x - 0.000186) \sqrt{2,359,296x^2 - 877.66x + 1.775}}{x^2 - 0.002442x + 0.8364 \cdot 10^{-6}} \right] \quad (19)$$

There is no simple direct integration of the last integral of equation 19. In order to solve this integral the I. B. M. 650 Electronic Computer was used. By the use of Simpson's equation (51b) and a General Bell System Program the solution of the above integral was found between any set of limits for x . It is beyond the scope of this thesis to go into the programming for the 650 computer and the ultimate solution of this integral; however, the reader is referred to reference 52. The specific program for this particular integration is given in Table 53, and although it was written for this reaction it can be modified to fit any of the reactions performed in this thesis by use of suitable constants calculated from the appropriate initial stoichiometric concentrations of phenol, iodine and sodium iodide and the limits for the equation. The k' values that were obtained from equation 19 are given in Table 48.

51b. Ibid., p. 276

52. R. W. Hamming and R. A. Weiss, The General Purpose System for the 650. Bell Telephone Laboratories, reproduced by Georgia Tech - Rich Electronic Computer Center, [undated].

Table 53

General Bell System Program for the 650 Computer for Kinetic Run 36

$$\int \frac{(x - 0.000186) \sqrt{2,359,296x^2 - 877.66x + 1.775}}{x^2 - 0.002442x + 0.8364 \cdot 10^{-6}}$$

Drum position		Floating point Representation of numbers
510	0000	0000000050
511	$0.1667 \cdot 10^{-6}$ (h/3)	1666700043
512	2,359,296	2359296056
513	877.66	8776600052
514	1.7749	1774900050
515	0.000186	1860000046
516	0.002442	2442000047
517	$0.8364 \cdot 10^{-6}$	8364000043
518	$0.50 \cdot 10^{-6}$ (h)	5000000043
519	4	4000000050

Card No.	Operation	Drum Positions	
00	0129	col's 77, 78, 79, 80	Problem number
01	+ 9	800 002 000	Program point 2
02	+ 2	510 510 520	x · x in 520
03	+ 2	520 512 521	$2,359,296x^2$ in 521
04	+ 2	510 513 000	877.66x in 000
05	- 1	521 000 000	$2,359,296x^2 - 877.66x$

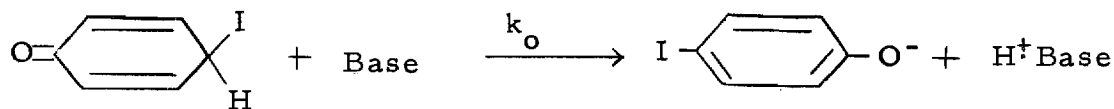
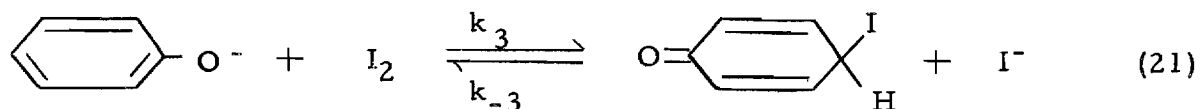
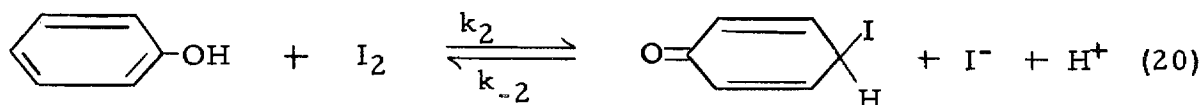
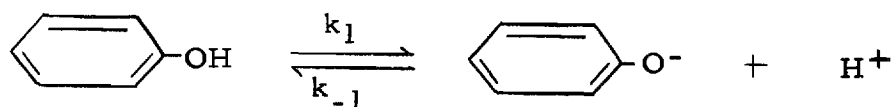
06	+ 1	000	514	000	$2,359,296x^2 - 877.66x + 1.7749$
07	+ 0	300	000	522	$\sqrt{2,359,296x^2 - 877.66x + 1.7749}$
08	- 1	510	515	000	$x - 0.000186$
09	+ 2	000	522	522	$(x - 0.000186) \sqrt{\text{term}}$
10	+ 2	510	516	000	$0.002442x$
11	- 1	520	000	000	$x^2 - 0.002442x$
12	+ 1	000	517	000	$x^2 - 0.002442x + 0.8364 \cdot 10^{-6}$
13	+ 3	522	000	523	$\frac{(x - 0.000186) \sqrt{\text{term}}}{x^2 - 0.002442x + 0.8364 \cdot 10^{-6}}$
14	+ 9	800	001	000	Program point 1
15	+ 1	510	518	510	$x_0 + h = x_1$ in 510
16	+ 2	510	510	520	$x_1 \cdot x_1$ in 520
17	+ 2	520	512	521	$2,359,296x_1^2$
18	+ 2	510	513	000	$877.66x_1$
19	- 1	521	000	000	$2,359,296x_1^2 - 877.66x_1$
20	+ 1	000	514	000	$2,359,296x_1^2 - 877.66x_1 + 1.7749$
21	+ 0	300	000	522	$\sqrt{\text{term}}$
22	- 1	510	515	000	$x_1 - 0.000186$
23	+ 2	000	522	522	$x_1 - 0.000186 \sqrt{\text{term}}$
24	+ 2	510	516	000	$0.002442x_1$
25	- 1	520	000	000	$x_1^2 - 0.002442x_1$
26	+ 1	000	517	000	$x_1^2 - 0.002442x_1 + 0.8364 \cdot 10^{-6}$

27	+ 9	100	001	000	Store in two positions
28	+ 3	522	000	524	f_1 in 524; f_2 in 525
29	+ 8	101	002	001	transfer to program point 1
30	+ 2	524	519	000	$4f_1$
31	+ 4	902	525	526	$2f_2 + 4f_1$ in 526
32	+ 1	526	523	523	$f_0 + 4f_1 + 2f_2$
33	+ 8	200	040	001	$f_0 - - - 2f_{80}$
34	- 1	523	525	000	$f_0 - - - f_{80}$
35	+ 2	000	511	509	$h/3 (f_0 - - - f_{80})$
36	+ 7	300	509	510	Punch $f(dx)$, upper limit
37	+ 7	000	033	033	Read a card
38	+ 8	000	000	002	Transfer to program point 2
39		510 to 515	6 constants	shown above	
40		516 to 519	4 constants	shown above	
41		0000			
42	033 1+8	200	012	014	
43	033 1+8	200	017	014	
44	033 1+8	200	017	014	
45	033 1+8	200	026	014	
46	033 1+8	200	010	014	
47	033 1+8	200	017	014	

APPENDIX D

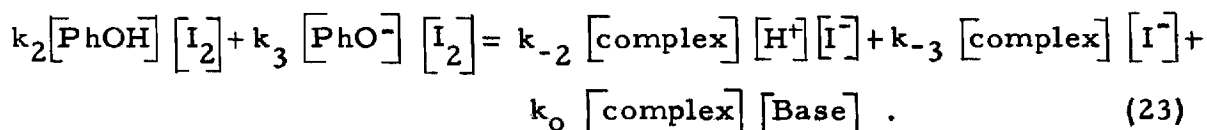
DERIVATION OF KINETIC EQUATION FOR A
MECHANISM FOR THE IODINATION OF PHENOL

A plausible mechanism for the iodination of phenol which conforms to the dependency of iodide ion and hydrogen ion required by results obtained by other workers is



$$\text{rate} = k_0 \left[\text{C}_6\text{H}_4(\text{O})(\text{I})\text{H} \right] [\text{Base}] \quad (22)$$

The derivation of the mathematics of this mechanism was as follows: On the basis of the steady-state approximation



Substitution of the concentration of complex intermediate calculated from equation 23 into equation 22 gave the rate expression

$$\text{rate} = k_0[\text{Base}] \left\{ \frac{k_2[\text{PhOH}][\text{I}_2] + k_3[\text{PhO}^-][\text{I}_2]}{k_{-2}[\text{H}^+][\text{I}^-] + k_{-3}[\text{I}^-] + k_0[\text{Base}]} \right\} \quad (24)$$

To agree with the kinetic results, the third term in the denominator must be negligible compared to the first two terms. Application of equilibrium statistics and the principle of microscopic reversibility to reactions 20 and 21 lead to the relationship

$$\frac{[\text{PhOH}] k_2 k_{-3}}{[\text{PhO}^-] k_3} = k_{-2} [\text{H}^+] \quad (25)$$

Substitution of $k_{-2} [\text{H}^+]$ from equation 25 into the denominator of equation 24 with simplification gave

$$\text{rate} = \frac{k_0[\text{Base}][\text{I}_2]}{k_{-3}[\text{I}^-]} \left\{ \frac{k_2[\text{PhOH}] + k_3[\text{PhO}^-]}{k_2[\text{PhOH}] + 1} \frac{1}{k_3[\text{PhO}^-]} \right\}$$

$$= \frac{k_o k_3 [\text{Base}] [\text{I}_2] [\text{PhO}^-]}{k_{-3} [\text{I}^-]} \left\{ \frac{k_2 [\text{PhOH}] + k_3 [\text{PhO}^-]}{k_2 [\text{PhOH}] + k_3 [\text{PhO}^-]} \right\} \quad (26)$$

Substitution of the following equilibria:

$$K_1 = \frac{[\text{I}_3^-]}{[\text{I}_2] [\text{I}^-]}$$

$$K_5 = \frac{[\text{PhO}^-] [\text{H}^+]}{[\text{PhOH}]}$$

$$K_6 = \frac{[\text{Ac}^-] [\text{H}^+]}{[\text{HAc}]}$$

into equation 26 gives the final result

$$\text{rate} = \frac{k_o (\text{H}_2\text{O})^5 k_3 [\text{PhOH}] [\text{I}_3^-] [\text{H}_2\text{O}]}{K_1 k_{-3} [\text{H}^+] [\text{I}^-]^2} + \frac{k_o (\text{Ac}^-) K_5 K_6 k_3 [\text{PhOH}] [\text{I}_3^-] [\text{HAc}]}{K_1 k_{-3} [\text{H}^+]^2 [\text{I}^-]^2} :$$

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