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RESEARCH PROJECT INITIATION

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Project Director: Dr. E. Grovenstein, Jr.

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National Science Foundation
Washington, D. C. 20550

Reports Required

Annual - Short informal report,
approximately 30 September
1966.

Final - Upon completion of project,
approximately 30 September
1967.

Assigned to: School of Chemistry

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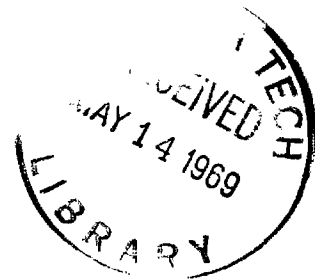
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December 18, 1968

CHEMISTRY

Dr. Donald A. Speer
Program Director for Chemical Dynamics
National Science Foundation
Washington, D. C. 20550



Dear Dr. Speer:

Subject: Final Technical Report for NSF Grant No. GP-297
(Sept. 1, 1962-Sept. 30, 1965) and Renewal
Grant No. GP-5186 (Oct. 1, 1965-Sept. 30, 1968).
"Mechanism of Electrophilic Aromatic Halogenation."

Thank you for your card of December 5th reminding me that you were due a Final Technical Report. While your card indicated that this was for GP-297, my files showed that you had agreed to accept the renewal proposal for the extension of this work under NSF Grant No. GP-5186 in place of this final report. However, since you are now due a Final Technical Report on GP-5186 and since this material so closely overlaps that of GP-297, I have decided to write a Final Technical Report covering both GP-297 and GP-5186.

Since a final write-up of much of this work is now in progress and should be completed within a few months, this report will summarize only the important developments in our work.

Sincerely yours.

Erling Grovenstein, Jr.
Brown Professor of Chemistry

EG: eb
Enclosures

Mechanism of Electrophilic Aromatic Halogenation

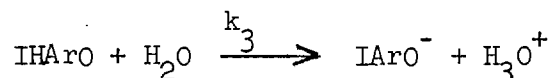
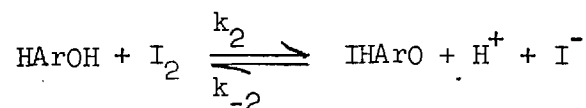
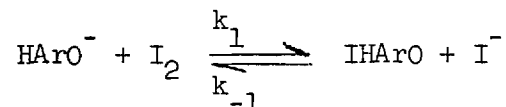
Final Technical Report on National Science Foundation Grants No. GP-297 (Sept. 1, 1962-Sept. 30, 1965) and Renewal Grant No. GP-5186 (Oct. 1, 1965-Sept. 30, 1968).

Our work has been restricted to study of the kinetics and mechanism of iodination in aqueous solution of phenol, 4-nitrophenol, 2,4-dinitrophenol, anisole, benzene, toluene, m-xylene, durene, mesitylene, and azulene. For many of these substances both the protium- and the deuterium-substituted compound have been investigated such that the kinetic isotope effect, k_H/k_D , has been determined. Iodination is an unusual type of electrophilic aromatic halogenation which normally is accompanied by a considerable kinetic isotope effect. Also iodination occurs at a rate which can be greatly accelerated by lowering the iodide ion concentration (and sometimes by regulation of the pH) such that compounds of widely varying reactivity can be studied under similar conditions.

Phenol. - The kinetics of iodination of phenol in water at 25° has now been studied in our laboratory from 0.046 M down to 3.2×10^{-7} M iodide ion concentration.¹ Over this range the isotope effect k_H^*/k_D^* dropped from 6.6

(1) The higher range of iodide ion concentrations was studied prior to work under the present grants by Mr. D. C. Kilby and Dr. N. S. Aprahamian.

to 3.1. The detailed kinetics can be accounted for in terms of the mechanism (Mechanism I):



where HArO^- represents phenoxide ion, HArOH unionized phenol, and IHArO a sigma complex of likely quinoid structure. If we define the rate of the iodination as

$$-d(\text{I}_2)/dt = k^*[\text{HArOH}][\text{I}_2]$$

where concentration terms in parenthesis represent stoichiometric concentrations (which for iodine would be the concentration as determined suitably by a thiosulfate titration) and those in brackets are actual concentrations of the species shown (for iodine the stoichiometric concentration must be corrected for iodine in the form of I_3^- and/or HOI). For the above mechanism, detailed considerations based on the steady-state assumption on the intermediate sigma complex leads to the relationship:

$$\frac{1}{k^*[\text{H}^+]} = \left(\frac{k_{-1}}{k_1 k_3 K_2} \right) [\text{I}^-] + \frac{1}{k_1 K_2 + k_2 [\text{H}^+]} \quad (1)$$

where K_2 is the acidic ionization constant of phenol which at the present ionic strength (0.30) has an effective value in terms of concentrations of 2.6×10^{-10} M. The kinetic constants at 25° are k_1 , 3.6×10^8 l/mole sec; k_2 , ca 5 l/mole sec; k_{-1}/k_3 , 1.4×10^6 l/mole. For phenol-2,4,6-d₃ these constants are all considered to be about the same ($\pm 10\%$) as those for ordinary

phenol save for k_{-1}/k_3 which has the value of 9.3×10^6 l/mole.

The very high value of k_1 for the rate of combination of phenoxide ion with iodine is notable; this value is near the diffusion-controlled limit. We cannot, of course, be certain that the actual mechanism does not involve a prior reversible combination of iodine with the much more plentiful phenol to give a weak π -complex which rearranges with loss of the elements of HI to the σ -complex.² No evidence was found for combination of phenol (or

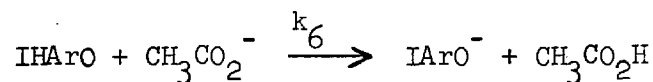
(2) Cf similar considerations for the nitration of aromatic amines in sulfuric acid [S. R. Hartshorn and J. H. Ridd, J. Chem. Soc. (B), 1068 (1968)].

phenoxide ion) with hypoiodous acid (HOI) or hypoiodous acidium ion (H_2OI^+) even at 3.2×10^{-7} M iodide ion concentration. The reaction of iodine with phenoxide ion is so much more faster than that of iodine with phenol that only an approximate estimate of the rate constant of the latter reaction is possible.

Berliner³ has studied acetate ion catalysis of the iodination of phenol

(3) E. Berliner, J. Am. Chem. Soc., 73, 4037 (1951).

at 0.12 M iodide ion concentration. At such high iodide ion concentrations, the proton removal step of mechanism I must be completely rate-determining; in addition to proton removal by water, proton removal must also be effected by acetate ion:



Experiments⁴ show that the isotope effect for proton removal by acetate ion

(4) Unpublished work at Georgia Tech of Mr. D. C. Kilby.

is about the same as for proton removal by water at such high iodide ion concentrations. The modified kinetic equation for such conditions becomes:

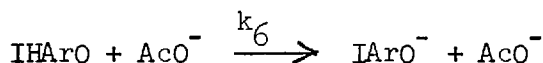
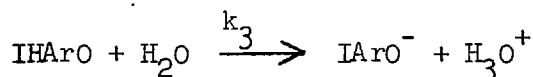
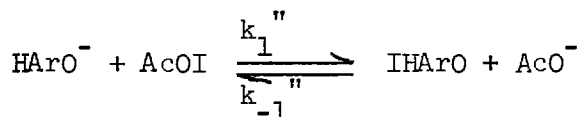
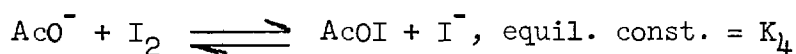
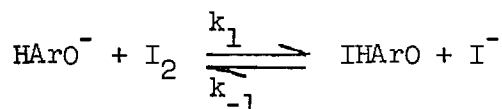
$$\frac{1}{k^*[\text{H}^+]} = \left\{ \frac{k_{-1}}{k_1 K_2 (k_3 + k_6 [\text{CH}_3\text{CO}_2^-])} \right\} [\text{I}^-] + \frac{1}{k_1 K_2} \quad (2)$$

where it is assumed that the only effect of acetate is catalysis of proton removal from the intermediate. If these considerations hold accurately at low iodide ion concentrations, then addition of acetate should reduce the isotope effect by making the first term on the right side of eq. 2 smaller relative to the second term. Also the limiting value of $k^*[\text{H}^+]$ at infinite acetate ion concentration should be $k_1 K_2$, which for phenol at 25.0° and 0.30 ionic strength is 0.0926 sec.⁻¹ (or 0.022 sec. at 10° and 0.60 μ). In fact as seen from Table I, while acetate ion catalyzes the iodination of phenol at

Table I
 Acetate-Catalyzed Iodination of Phenol at Iodide Ion
 Concentration of 0.33×10^{-6} M

[AcO ⁻] mole/l	°C	[H ⁺] x 10 ⁶ mole/l	μ	k _H [*] [H ⁺] sec. ⁻¹	k _H [*] /k _D [*]
0.000	25.0	100	0.30	0.074	3.2
0.060	25.0	294	0.53	0.118	3.6
0.180	25.0	116	0.67	0.221	3.3
0.018	10.0	93	0.56	0.018	4.5
0.180	10.0	93	0.60	0.037	4.5
0.019	10.0	107	1.20	0.025	4.8
0.360	10.0	107	1.20	0.080	3.5

0.33×10^{-6} M iodide ion concentration, the observed values of $k^*[\text{H}^+]$ are considerably in excess of this limiting value and moreover no appreciable drop in isotope effect with increasing acetate ion concentration is observed. While some of the variation of rate in Table I is due to variations in ionic strength, other data indicate that this should not be the major effect and moreover protium- and deuterium compounds should be affected in about the same way by ionic strength. All of the data can be reconciled if acetyl hypoiodite, AcOI, is considered to be an effective iodinating agent in addition to molecular iodine. A possible detailed mechanism (Mechanism II) is:



The corresponding rate expression is then:

$$\frac{1}{k^*[\text{H}^+]} = \left\{ \frac{k_{-1}}{k_1 K_2 (k_3 + k_6 [\text{AcO}^-])} \right\} [\text{I}^-] + \frac{1}{\frac{k_1 K_2 + k_1'' K_2 K_4 [\text{AcO}^-]}{[\text{I}^-]}} \quad (3)$$

A possible alternative explanation of the role of acetate ion in the iodination of phenol is that a concerted attack of acetyl hypoiodite upon

phenoxide ion occurs. The steps corresponding to k_1'' and k_6 are then fused into one process. It is impossible to distinguish this process from mechanism II at the present time.

Recently Ogata and Aoki⁵ found that the rate of reaction of m-xylene with

(5) Y. Ogata and K. Aoki, J. Am. Chem. Soc., 90, 6187 (1968).

a mixture of iodine and peracetic acid in acetic acid solution follows the rate equation:

$$\text{rate} = k[\text{I}_2][\text{CH}_3\text{CO}_2\text{H}]$$

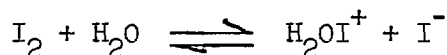
and explained the kinetic result on the basis of a rate-determining reaction of iodine with peracetic acid to give an active iodinating agent, which was thought to be acetyl hypoiodite. Our present work, therefore, confirms Ogata and Aoki's speculation.

p-Nitrophenol. - This compound has been previously studied by Grovenstein and Aprahamian⁶ down to iodide ion concentrations of 2.3×10^{-5} M; these

(6) E. Grovenstein, Jr., and N. S. Aprahamian, J. Am. Chem. Soc., 84, 212 (1962).

workers concluded that the iodination of p-nitrophenol follows Mechanism I (see section on phenol) with iodine as the effective iodinating agent. Since a new spectroscopic technique of following the kinetics of iodination was at hand and since this technique permitted studying the iodination down to lower iodide ion concentrations than previously, p-nitrophenol was studied at 50° by the new technique with iodide ion concentrations in the range of 2.7×10^{-5} M to 1.95×10^{-7} M wherein the isotope effect k_H^*/k_D^* fell from 4.1 to 1.28.

The new data fully confirm the old data and interpretation down to 1×10^{-6} M iodide ion concentration; however, at lower iodide ion concentration the rate of iodination is faster than predicted by extrapolations based on Mechanism I and the isotope effect does not drop as much as expected. We believe that at ca. 2×10^{-7} M iodide ion concentration iodination by hypiodous acidium ion (H_2OI^+) becomes important. Hypiodous acidium ion can arise by hydrolysis of iodine:



While an accurate value of this equilibrium constant is not known, the value cannot be greater than 1×10^{-10} mole/l. at 25° according to Allen and Keefer,⁷

(7) T. L. Allen and R. M. Keefer, J. Am. Chem. Soc., 77, 2957 (1955).

while a value as low as 10^{-20} has been considered possible.⁸ In any event it

(8) J. Hine, "Physical Organic Chemistry," 2nd ed., McGraw-Hill Co., Inc., New York, N. Y., 1962, pp. 362-363.

is reasonable that hypiodous acidium ion should be an important iodinating agent only at very low iodide ion concentrations. A more detailed study of iodination by this species has been made upon 2,4-dinitrophenol.

2,4-Dinitrophenol. - The kinetics of iodination of 2,4-dinitrophenol and 2,4-dinitrophenol-6-d has been investigated in aqueous solution at 50° at iodide ion concentrations of 8.5×10^{-3} to 2.6×10^{-7} M and at hydrogen ion concentrations of 1.9×10^{-4} to 1.7×10^{-6} M. Some of the pertinent data are summarized in Table II. The rate constant k_{H}^* is defined on the basis

$$-d(\text{I}_2)/dt = k_{\text{H}}^* [\text{HArO}^-][\text{I}_2]$$

where $[HArO^-]$ refers to the concentration of 2,4-dinitrophenoxide anion and the subscript on k^* refers to the protium compound. It is seen from Table II

Table II

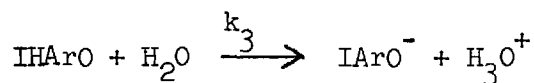
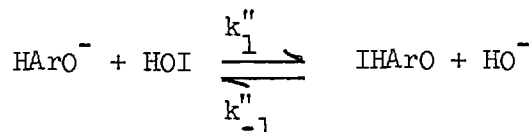
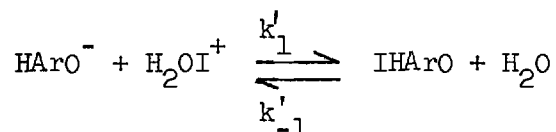
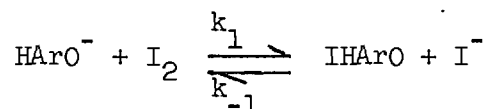
Iodination of 2,4-Dinitrophenol and 2,4-Dinitrophenol-6-d
 at 50.0°; μ , 0.30; $[H^+]$, 7.0×10^{-5} M

$[I^-] \times 10^6$ (mole/l)	k_H^* (1/mole sec)	$k_H^*[I^-] \times 10^6$ (sec ⁻¹)	k_H^*/k_D^*
3890	0.0059	22.8	4.3
1940	0.0113	21.9	4.1
995	0.0196	19.5	3.9
486	0.0330	16.0	3.4
97	0.114	11.1	2.9
49	0.188	9.2	2.4
10.0	0.78	7.8	2.5
5.1	1.54	7.8	2.4
2.6	2.61	6.8	2.4

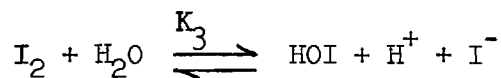
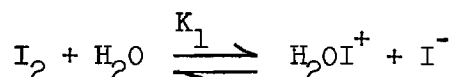
that the isotope effect k_H^*/k_D^* starts at 4.3 and falls to a final constant value of 2.4 as the iodide ion concentration is lowered; during the same interval $k_H^*[I^-]$ falls to a final constant value of 7.5 ± 0.4 . The data indicate that, at this or higher acidity, iodine was the effective iodinating agent at the higher iodide ion concentrations and that hypiodous acidium ion becomes the predominant iodinating agent at the lower iodide concentrations. At low iodide (10^{-4} to 10^{-6} M), k^* was found, at constant iodide ion concentration, to increase as hydrogen ion concentration was decreased and moreover the isotope effect rose to 3.0 at 1.7×10^{-6} M hydrogen ion concentration.

This information is interpreted as indicating that hypiodous acid is a significant iodinating agent at such low acidities and low iodide ion concentrations.

The detailed mechanism of iodination of 2,4-dinitrophenoxide under the conditions of the present study is:



and some pertinent equilibria are:



The corresponding rate expression is

$$\frac{1}{k^*} = \left(\frac{k_{-1}}{k_1 k_3} \right) [\text{I}^-] + \frac{1}{\frac{k_1}{[\text{I}^-]} + \frac{k'_1 K_1}{[\text{I}^-]} + \frac{k''_1 K_3 [\text{OH}^-]}{[\text{I}^-]}} \quad (4)$$

For the protium compound at 50.0° and 0.30 ionic strength, k_1 is $0.10 \text{ M}^{-1} \text{ sec}^{-1}$,

$k_1'K_1$ is $1.0 \times 10^{-5} \text{ sec}^{-1}$, k_1'' is $4.7 \text{ M}^{-1} \text{ sec}^{-1}$, K_3 is $9.5 \times 10^{-12} \text{ M}^2$, k_{-1}/k_3 is $4.2 \times 10^3 \text{ M}^{-1}$, k_{-1}'/k_3 is 0.42. For 2,4-dinitrophenol-6-d the values of these constants are believed to be about the same save that k_{-1}/k_3 is $1.9 \times 10^4 \text{ M}^{-1}$ and k_{-1}'/k_3 is 1.3.

Phosphate catalysis of the iodination of 2,4-dinitrophenoxide at 10^{-4} to 10^{-6} M iodide ion concentrations increased the reaction rate but did not lower the isotope effect as expected on the basis of catalysis of the proton-removal step. This result suggests monohydrogen phosphoryl hypiodite (HPO_4I^-) as an iodinating agent in either a two-step or a concerted mechanism.

Anisole. - The kinetics of iodination of anisole has been studied in aqueous solution at 50° at iodide ion concentrations of 9.2×10^{-4} to $3 \times 10^{-7} \text{ M}$. Over this range the rate constant k^* varied inversely with iodide ion

$$-d(\text{I}_2)/dt = k^*[\text{ArH}][\text{I}_2] = k \frac{[\text{ArH}][\text{I}_2]}{[\text{I}^-]} \quad (5)$$

concentration such that the product of $k^*[\text{I}^-]$ was a constant k of $1.35 (\pm 0.07) \times 10^{-7} \text{ sec}^{-1}$ at 0.0030μ . The isotope effect, $k_{\text{H}}^*/k_{\text{D}}^*$, for anisole and anisole-2,4,6-d₃ was also constant at 3.1 ± 0.1 over this range of iodide ion concentrations. Essentially the same isotope effect, 3.0, was obtained at $3.4 \times 10^{-11} \text{ M}$ iodide ion concentration at 25° with use of silver ion to maintain the iodide ion concentration. While the possibility that molecular iodine was the iodinating agent over the entire iodide range could not be rigorously excluded, quantitative considerations of the data show that this is unlikely and that hypiodous acidium ion was probably the effective agent. For a more detailed discussion on this point see the section on mesitylene.

Mesitylene. - The iodination of mesitylene in aqueous solution at 50.0° was found to follow the rate equation:

$$-d(I_2)/dt = k \frac{[ArH][I_2]}{[I^-]} \quad (6)$$

This equation was tested over concentrations of mesitylene from 6.6×10^{-6} to 381×10^{-6} M, iodine of 2.0×10^{-6} to 88×10^{-6} M, iodide ion of 0.20×10^{-6} to 483×10^{-6} M, hydrogen ion of 30×10^{-6} to 3000×10^{-6} M, and ionic strength of 0.30×10^{-4} to 30×10^{-4} . The average value of k was $3.56 (\pm 0.18) \times 10^{-7} \text{ sec}^{-1}$ and for mesitylene-2,4,6- d_3 $1.56 (\pm 0.13) \times 10^{-7} \text{ sec}^{-1}$. Hence the isotope effect k_H/k_D had a value of 2.3 ± 0.3 ; if only experiments run at the same time under the same conditions are compared, the isotope effect had a value of 2.31 ± 0.16 .

The iodination of mesitylene was also studied in aqueous solution at 25° in presence of silver ion. This study was undertaken in order to extend the study of iodination to very low iodide ion concentrations. To suppress excessive hydrolysis of iodine, the kinetics were run in solutions which were at least 0.05 M in hydrogen ion. Experiments showed that, if conditions were properly regulated, the iodination followed equation 6 or, since the ionic strength was generally high, the modified equation (7), where γ is the mean ionic activity coefficient and K_{sp} is the solubility product of silver iodide.

$$-d(K_2)/dt = k \frac{[ArH][I_2]}{[I^-] \gamma^2} = k \frac{[ArH][I_2][Ay^+]}{K_{sp}} \quad (7)$$

The main difficulty in fitting equation 7 arose in the case of reactions which were fast with times for 25% consumption of iodine of less than 700 sec. Such fast reactions gave low values of k ; evidently the rate of precipitation of silver iodide was not great enough to establish equilibrium between silver ions and iodide ions.⁹ In thirteen kinetic runs in which initial concentrations

(9) An alternative interpretation is that for the fast reactions the hydrolysis of iodine to hypoiodous acidium ion occurs too slowly to keep the concentration of this ion at its equilibrium value; our kinetic results would then suggest that silver ion catalyzes this hydrolyses.

of mesitylene varied from 1.0×10^{-6} to 5.6×10^{-6} M, iodine from 1.7×10^{-6} to 3.5×10^{-6} M, silver ion from 4.2×10^{-6} to 25.8×10^{-6} M, and hydrogen ion from 0.10 to 0.30 M, the average value of k was $7.5 (\pm 0.6) \times 10^{-9}$ sec^{-1} . For mesitylene-2,4,6- d_3 under similar conditions the average value of k was $3.5 (\pm 0.5) \times 10^{-9}$. Hence the isotope effect under these conditions was 2.1 ± 0.4 . In Table III the values of k for mesitylene at various temperatures are listed.

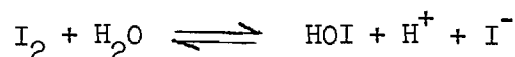
Table III

Iodination of Aromatic Hydrocarbons in Aqueous Solution

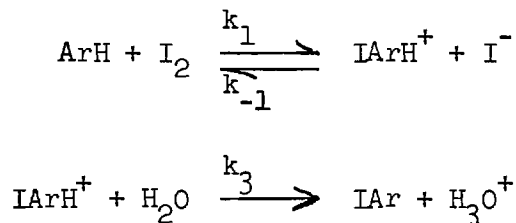
Hydrocarbon	Catalyst	Temp. °C	k sec^{-1}	Rel. Rate at 35°	ΔH^\ddagger kcal/mole	ΔS^\ddagger cal/deg
Benzene	Ag^+	35.0	9.4×10^{-15}	1.00		
Toluene	Ag^+	25.0	2.3×10^{-13}		35.1	+2.0
	Ag^+	35.0	23.0×10^{-13}	2.4×10^2		
Durene	Ag^+	35.0	1.2×10^{-10}	1.3×10^4		
<u>m</u> -Xylene	Ag^+	25.0	1.02×10^{-10}		33.6	+8.4
	Ag^+	35.0	6.7×10^{-10}	7.1×10^4		
Mesitylene	Ag^+	25.0	0.75×10^{-8}		23.0	-18.5
	Ag^+	35.0	2.8×10^{-8}	3.0×10^6		
	None	40.0	9.7×10^{-8}			
	None	50.0	35×10^{-8}			
	None	60.0	108×10^{-8}			

It is notable that the value of k obtained in presence of silver ion is essentially that expected by extrapolation from values of k obtained in absence of silver ion. Hence the only important role of silver ion seems to be that of regulation of the iodide ion concentration.

What is the detailed mechanism of iodination of mesitylene? The large isotope effect makes it relatively certain that cleavage of the aromatic C-H bond is part of the rate-determining step. If we assume the usual two-step mechanism, I_2 , HOI, or H_2OI^+ are reasonable a priori possible iodinating agents. Of these hypoiodous acid may be discarded since its concentration is inversely proportional to the hydrogen ion concentration as demanded by the equilibrium:



Only in the very unlikely event that proton removal from the intermediate sigma complex were acid catalyzed could HOI be an iodinating agent for mesitylene since the rate of iodination of mesitylene was found to be independent of the acidity both in presence and in absence of silver ion. If I_2 were the iodinating agent, the detailed mechanism would be:



By the steady-state approximation:

$$-d(I_2)/dt = \frac{k_1 k_3 [ArH][I_2]}{k_{-1}[I^-] + k_3} \quad (8)$$

This expression reduces to that (eq. 7) found by experiment only if

$k_{-1}[I^-] \gg k_3$. If we assume that $k_{-1}[I^-]$ is 100 times as large as k_3 and that the intermediate is never present in more than 0.01 times the concentration of mesitylene, then for the experiment at $[Ag^+] = 14.5 \times 10^{-6} \text{ M}$ and for $[I_2] = 1.06 \times 10^{-6} \text{ M}$ which at 25° and $\mu = 0.10$ corresponds to $[I^-] = 0.89 \times 10^{-11} \text{ M}$

$$k_1[ArH][I_2] \approx k_{-1}[IArH^+][I^-]$$

or

$$k_1[1.06 \times 10^{-6}] \approx k_{-1}[10^{-2}][0.89 \times 10^{-11}] \quad (9)$$

Since the rate of the overall reaction is given by:

$$\begin{aligned} -d(I_2)/dt &= \frac{k [ArH][I_2]}{[I^-]^2} \\ &= \frac{7.5 \times 10^{-9}[ArH][I_2]}{[0.89 \times 10^{-11}][0.80]^2} \\ &= 1.3 \times 10^3 [ArH][I_2] \end{aligned}$$

But if only one hundredth of the intermediate goes to final product and the remainder returns to reactants then k_1 must be $100 \times 1.3 \times 10^3$ or ca 1.3×10^5 .

Substitution of this result back into eq. 9 gives:

$$1.3 \times 10^5 [1.06 \times 10^{-6}] \approx k_{-1} [10^{-2}][0.89 \times 10^{-11}]$$

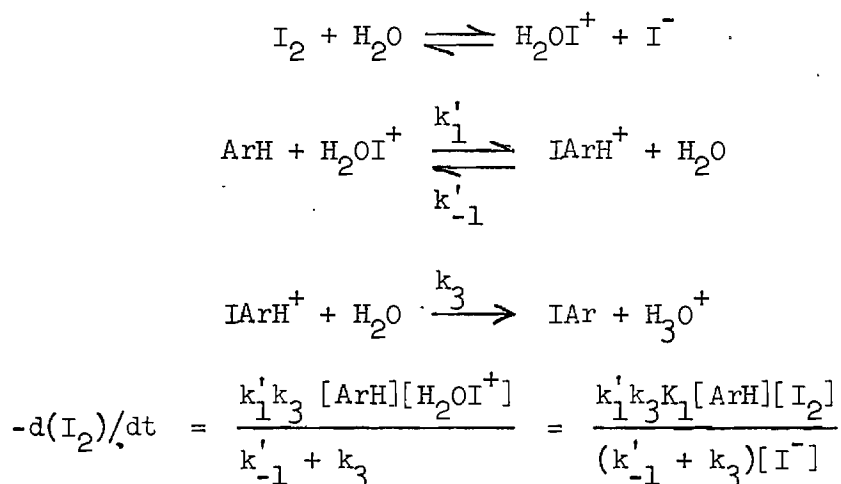
or

$$k_{-1} \approx 1.5 \times 10^{12} \text{ M}^{-1} \text{ sec}^{-1}$$

This value for k_{-1} exceeds the "typical" upper limit¹⁰ of $4 \times 10^9 \text{ M}^{-1} \text{ sec}^{-1}$

(10) I. Amdur and G. G. Hammes, "Chemical Kinetics, Principles and Selected Topics," McGraw-Hill, New York, 1966, p. 62.

for diffusion controlled reactions in aqueous solution. Regardless of the details of the above calculation, we believe that it is unlikely that iodide ion can remove I^+ from the intermediate at near the diffusion-controlled rate and hence that I_2 is not an important iodinating agent for mesitylene. We are left then with hypiodous acidium ion which seems to be able to fulfill nicely its role in the expected mechanism: [Mechanism III)



Mechanism III requires that the equilibrium constant K_1 for the hydrolysis of iodine to hypiodous acidium ion:

$$K_1 = \frac{[H_2OI^+][I^-]}{[I_2]}$$

be greater than 2×10^{-18} M in order that k'_1 not exceed the diffusion controlled limit. A value of K_1 of less than 2×10^{-18} M is reasonable since previous estimates^{7,8} have placed this at greater than 10^{-10} M and up to as high as 10^{-20} M.

Benzene, Toluene, m-Xylene, and Durene. - The kinetics of iodination of these compounds has been investigated in aqueous solution in presence of silver ion. While these studies have been in less detail than those for

mesitylene, the data agree with the same kinetic expression (eq. 7). The isotope effect, k_H/k_D , for iodination of toluene at 25° is 2.3.

The kinetic data for iodination of these compounds is summarized in Table III. A plot of log k of iodination versus log K for the equilibrium constant¹¹ of protonation by HF-BF₃ gives a good linear plot. This correla-

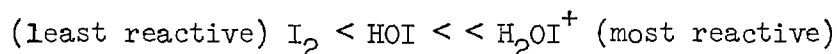
(11) E. L. Mackor et al., Trans Faraday Soc., 53, 186 (1957).

tion suggests that the sigma complex is a good model for the transition state in electrophilic aromatic iodination. Indeed Pariser-Parr-Pople calculations based on this assumption and an induction-hyperconjugation model correlate well with the present data. The success of such correlations suggests that about the same fraction of sigma complex goes on to give the final product for all of the present aromatic hydrocarbons. This conclusion is in accord with the similarity of the isotope effect k_H/k_D for toluene and mesitylene.

Azulene. - Azulene undergoes iodination in aqueous solution by a mechanism which is similar to that of phenol. The kinetic isotope effect k_H/k_D is 3.1 ± 0.2 for proton removal from the sigma complex by water, chloroacetate, acetate, and HPO₄⁻ but is 2.0 ± 0.2 for pyridine and 6.5 ± 1.3 for 2,4,6-trimethylpyridine. The general details of this work and some likely conclusions have already been published.¹²

(12) E. Grovenstein, Jr., and F. C. Schmalstieg, J. Am. Chem. Soc., 89, 5084 (1967).

Conclusions. - Kinetic studies show that under the conditions of the present work phenol, chiefly in the form of phenoxide anion, is iodinated in aqueous solution through attack by I_2 even down to 3×10^{-7} M iodide ion concentration; if acetate ion is present and if the concentration of iodide ion is low (ca. 3×10^{-7} M), CH_3CO_2I becomes an effective electrophilic agent for phenoxide ion. For p-nitrophenoxide ion, I_2 is the effective electrophile save at very low iodide ion concentrations (ca. 2×10^{-7} M) where H_2OI^+ appears to become important. For 2,4-dinitrophenoxide ion I_2 is the chief iodinating agent down to ca. 10^{-4} M iodide ion concentration; at lower iodide ion concentrations H_2OI^+ is the chief electrophile unless the acidity is so low (ca. 2×10^{-6} M) that HOI becomes important; at low iodide ion concentrations in presence of $HPO_4^{=}$, HPO_4I^- becomes an important electrophile. For less reactive compounds—anisole, mesitylene, m-xylene, durene, toluene, benzene—hypoiodous acidium ion (H_2OI^+) is apparently the only effective iodinating agent. The order of reactivity of iodinating agents appears to be:



It will be observed that the most reactive compound (phenoxide ion) seeks the least reactive iodinating and that the least reactive compounds (the aromatic hydrocarbons) seek the most reactive iodinating agent. For compounds of intermediate reactivity (the nitrophenoxide ions) the electrophilic agent chosen depends upon its concentration, I_2 at high iodide ion and HOI or H_2OI^+ at low iodide ion concentrations. The present work also demonstrates that the molecules CH_3CO_2I and HPO_4I^- are considerably more powerful electrophilic reagents than I_2 ; comparisons of these reagents with H_2OI^+ is not possible because the equilibrium concentrations are unknown.

Publication of Work

To date the only portion of this work which is published is:

"Kinetics of Iodination of Azulene. Amplification of Isotope Effects by Steric Hindrance," E. Grovenstein, Jr., and F. C. Schmalstieg, J. Am. Chem. Soc., 89, 5084 (1967).

Other publications of this work are in active preparation and it is to be hoped that most of these will be completed within a few months.

Names of People whose Work Was Aided under the Present

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