[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF NEBRASKA, LINCOLN, NEBRASKA]

The Iodination of Phenols. II. The Design and Construction of a Reliable Stirred Flow Reactor and its Use in Kinetic Studies on 2,4-Dichlorophenol[1,2]

BY WALDEEN C. BUSS[3] AND JAY E. TAYLOR[4]

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A new, accurate and reliable stirred flow reactor has been developed for the making of kinetic measurements under the conditions of the steady state. The basic features of the apparatus are a synchronous motor which drives a gearbox having a number of outlets of different speeds, a screw drive for a set of specially designed leakproof pistons and a small (3.35 ml.) reaction vessel equipped for the immediate stopping of the reaction in the outflowing solution and for the measurement of *p*H and temperature inside the reactor. Particularly outstanding is the close control (±0.1%) of flow rates. With the apparatus three aspects of the reaction, the iodination of 2,4-dichlorophenol, have been evaluated. (1) Using unbuffered solutions the observed second order rate constants vary with hydrogen ion according to the relationship, $k_{\text{obsd}} = k/(K_i + [H^+])$, where K_i is the ionization constant of phenol. (2) In very low iodide concentrations the variation of the observed rate constant with iodide ion is inversely proportional to $([I^-] + K_2)([I^-])$, where $[I^-]$ is the effective iodide ion concentration and K_2 is the dissociation constant for the I_3^- complex. (3) In the presence of phosphate buffers the increase in rate is proportional to the concentration of $HPO_4^=$. These observations support previous work on the iodination of phenol. Three mechanisms completely satisfy the experimental observations; these are the postulation of the intermediacy of (1) a quinoid complex, (2) the iodinium ion and (3) hypoiodous acid. No one of these can be exclusively supported or eliminated, although it appears that the contribution of the iodinium ion is of least significance.

An accurate experimental investigation of the iodination of phenols is difficult because of three characteristics of the reaction: (1) The possibility of multinuclear substitution by iodine, (2) inhibition by hydrogen ion which is a product of the reaction and (3) inhibition by iodide ion, also a product of the reaction. In previous work these difficulties have been partially overcome by the use of 2,4-dichlorophenol which yields primarily the monosubstitution product, buffers which introduce a further complication in the buffer effect and high iodide concentrations to mask the iodide ion effect.

The work presently described was undertaken to determine the feasibility of applying a rather new kinetic tool to the study of this reaction. This tool is the stirred flow reactor, which permits study under the conditions of a true steady state.

In a stirred flow reactor, solutions containing the reactants are pumped at a constant flow rate into a reactor which is stirred vigorously. The reactor contents flow out at a rate equal to the combined inflow. When the system reaches a steady state, there is no further change in concentration of the reactive species inside the reactor with time. The product of the extent of reaction times the reciprocal of the average time of contact of the reactants is a measure of the rate of reaction. Thus, for a typical second order reaction under conditions of the steady state the rate equation may be expressed as

$$x/t = k(a - x)(b - x) \text{ and } 1/t = u/v \qquad (1)$$

where a and b are the concentrations of reactants flowing into the reactor, x is the amount of a and b which have reacted at the steady state, k is the reaction rate constant, t is the average time spent by a and b in the reactor, u is the combined rate of inflow of a and b and v is the volume of the reactor.

The advantages of this technique are evident. After the steady state is attained the reaction takes place under conditions of constant concentrations of reactants, product, salt, etc., and at a constant *p*H. Thus, it becomes possible to study the iodination reaction without the use of buffers and at low iodide concentrations. It is only necessary that the *p*H and iodide ion concentrations be determined under conditions of the steady state.

A more complete discussion of the theory associated with this technique was first presented by Denbigh[5] and co-workers. Johnson and Edwards[6] and Eldridge and Piret[7] discussed the theory and performance of equipment related to the stirred flow reactor.

Laboratory application of this technique to kinetic studies has been made by Stead, Page and Denbigh,[8] Hammett and co-workers[9] and Page.[10] In all of the previous designs flow rates have been controlled by a flow of solution from a constant height. However, a motor driven glass syringe for introduction of a single component has been used by Hammett[9d,e] and co-workers.

The excellent earlier works of Denbigh, Page and Hammett have clearly demonstrated the potential of this technique. Unfortunately, gravity control of flow is unwieldy to use, and the rate of flow cannot be precisely controlled (±1%). Their apparatuses have not been applicable to extended studies of a routine nature, to very slow reactions or to reactions for which a high degree of precision is required.

In the apparatus to be described the precision in the control of flow rates has been increased by a factor of at least ten. The equipment is permanent,

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(1) The first paper of this series, J. E. Taylor and M. I. Evans, *J. Ohio Acad. Sci.*, **53**, 37 (1953).

(2) Abstracted from the master's and doctor's theses of W. C. Buss, University of Nebraska, 1958 and 1959.

(3) (a) Minnesota Mining and Manufacturing Fellow, 1957–1958; (b) Eastman Kodak Fellow, 1958–1959; (c) California Research Corp., San Francisco 20, Calif.

(4) Department of Chemistry, Kent State University, Kent, Ohio.

(5) K. G. Denbigh, *Trans. Faraday Soc.*, **40**, 352 (1944); K. G. Denbigh, M. Hicks and F. M. Page, *ibid.*, **44**, 479 (1946); K. G. Denbigh and F. M. Page, *Discussions Faraday Soc.*, **17**, 145 (1954).

(6) J. D. Johnson and L. J. Edwards, *Trans. Faraday Soc.*, **45**, 286 (1949).

(7) J. W. Eldridge and E. L. Piret, *Chem. Eng. Progr.*, **46**, 290 (1950).

(8) B. Stead, F. M. Page and K. G. Denbigh, *Discussions Faraday Soc.*, **2**, 263 (1947).

(9) (a) H. H. Young, Jr., and L. P. Hammett, THIS JOURNAL, **72**, 280 (1950); (b) J. Saldick and L. P. Hammett, *ibid.*, **72**, 283 (1950); (c) M. J. Rand and L. P. Hammett, *ibid.*, **72**, 287 (1950); (d) H. M. Humphreys and L. P. Hammett, *ibid.*, **78**, 521 (1956); (e) R. L. Burnett and L. P. Hammett, *ibid.*, **80**, 2415 (1958).

(10) F. M. Page, *Trans. Faraday Soc.*, **49**, 635, 1033 (1953).

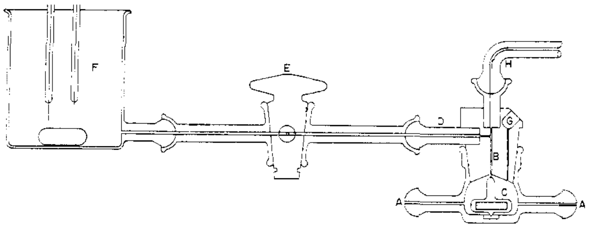

Fig. 1.—Reactor vessel and titration assembly: A, inlet to reactor vessel; B, Teflon plug; C, magnetic stirrer; D, outlet for reactants and stopping solution; E, three-way stopcock; F, titration assembly; G, well for pH electrodes; H, inlet for stopping solution.

and it is adapted to the study of almost any type of reaction. In short, it is a new and highly practical piece of equipment designed for great versatility.

Experimental

Description of the Stirred Flow Reactor.—The essential parts of the apparatus are a synchronous motor, a gear box with variable speed outlets, a screw drive with three interchangeable screws for a set of leak proof pistons and a small (3.35 ml.) reaction vessel with a very efficient stirrer. The mechanism provides 21 different rates of flow varying between 77.6 and 0.0249 ml. per min. with an average deviation of ± 0.1% for single units or 0.14% for two units working together. The reaction vessel is equipped so that a stopping solution may be added immediately to the outflowing solution and a sample collected and titrated. Equipment for the measurement of pH and temperature are also provided.

The glass cylinders containing the pistons were each made of 1 ± 0.0002 inch precision bore tubing, 11 inches in length, with a capacity of 100 ml. All tubes in one set were cut from a single length of tubing. The pistons were designed so that only glass or Teflon is in contact with the solution. The distinctive feature is two expandable Teflon rings separated by a glass tube which, by means of a threaded nut, may be forced against the silicone oil coated glass surface of the cylinders. This system was found to be completely leak proof at all flow rates.

The flow rates were determined by measuring the amount of water flowing from each of the cylinders using each of the gear ratios and each of the screws over the different sections of each of the tubes. Connections to the reactor vessel were made with capillary tubing and 12/2 ball joints.

The reactor vessel and stirrer were the subjects of extensive experimentation. Of the types tried the most generally efficient stirrer was a simple propellor blade rotating at about 1800 r.p.m. In order to support the stirrer inside the reactor, it was first attempted to devise a leak proof, corrosion proof seal which would withstand continuous high rotation speeds. This attempt was not successful.

A design, employing a magnetic stirrer, is shown at Fig. 1. Note that the stirring motor is immersed in the bath and is protected from it by a can open only at the bottom. The stirrer C is supported by two Teflon bearings, one in the Teflon plug B and the other recessed into the bottom of the reactor vessel. The reactants flow into the reactor vessel from A and out through B. The stopping solution flows through H and the mixture out through D. The stopcock at E may direct the solution from D either into the titration vessel at F or to waste. The vessel at F is a 100 ml. beaker equipped with a 12/2 ball joint so that the solution is directed into the bottom, and the possibility of loss of iodine by evaporation is thereby largely eliminated. A well in the Teflon plug at G is designed to accomodate a Leeds and Northrup Miniature pH Electrode assembly. To measure pH the flow of stopping solution is halted, and the reactants are directed into G. The time required for the solution to flow from the reactor to the electrodes is very small in comparison with the value of t in equation 1. The measurement of temperature was achieved by means of two thermistors, one in the constant temperature bath for comparison and the other in the reactor inserted through plug B. The temperature differential was usually about 0.1°.

To place solutions in the reactor it is necessary to remove the syringes and cylinders. Since the water-bath surrounds all parts of the apparatus which contains solutions, a Montgomery Ward, two ton, scissors auto jack with a rise of 16 inches was installed to raise and lower the bath.

The Titration.—The method of Scully,[11] a modified dead-stop titration technique, was used. Two platinum electrodes are immersed in the iodine solution. In the presence of iodine the polarization voltage, measured by a line operated direct reading pH meter, is nearly zero. As the last traces of iodine disappear the voltage rapidly rises to 0.4 volt.

In carrying out the titration approximately 20 ml. of distilled water is placed in the beaker F, Fig. 1, along with about 5 ml. of 2 M acetic acid and about 5 mg. of potassium iodide. Stopcock E is then turned to direct the flow of reactants into beaker F. A "split timer" stopwatch (two hands move around the dial and one may be stopped at any time and then recoördinated with the moving hand) is activated as soon as the presence of iodine is indicated in the beaker by a drop in the polarization voltage. The iodine is kept nearly but not completely neutralized by adding 0.03 N thiosulfate continuously from a silicone coated 5 ml. buret. After about 2.0 ml. of thiosulfate have been added, a very slight excess is introduced and the end-point of the titration is determined as the time at which a voltage surge to 0.4 volt is observed. With the split timing device it is possible to repeat observations of the end-point several times in succession and thereby obtain recheck values.

Description of a Typical Rate Determination.—The routine begins with the placing of the iodine-iodide solution, the phenol solution and the stopping solution (2 M acetic acid) in three syringes and positioning these underneath the drive block. The constant temperature bath is raised into position, and after coming to temperature the flow of reactants is started. The time required to fill the reactor is carefully measured and the value of t, equation 1, is thus directly obtained. To prevent entry of the stopping solution into the reactor vessel, the tube at H is not connected until after the reactor is filled.

A short period of time is allowed for the attainment of steady state conditions since the solutions are very nearly at this condition by the time the reactor is filled. The solution is then directed through stop-cock E into beaker F and a series of titrations is made until the values are found to be clearly reproducible.

After completion of the titrations the pH of the contents of the reactor are measured by directing the outflow of solution through G and inserting the pH electrodes. Also the temperature inside the reactor must be checked sometime during the course of the run. A standardization of the thiosulfate is made by directing the flowing iodine directly into the titration vessel and following the above titration procedure. If a different time of reaction measurement on this same sample is desired, it is necessary only to change the speed of flow and repeat the same measurements. The values of $a - x$ and $b - x$ and from these the rate constants are then calculated.

For the study of the iodination of phenols the major source of error is pH, which unfortunately leads to an over-all uncertainty of about 4% based on an uncertainty of 0.03 pH. The titration gives values of $a - x$ having a reproducibility of 0.3% or better from which the rate constant can be calculated to ± 1% or better.

The first test of the validity of the technique and the new apparatus was made in a brief study of the rearrangement of N-chloroacetanilide. This compound was prepared according to the procedure of Percival and La Mer[12] and was stored in the dark over P_4O_{10}. Fresh solutions were prepared for each run. The extent of rearrangement was determined by a thiosulfate-iodide titration. Using 0.980 M HCl and 0.025 M N-chloroacetanilide at 24.91° rate constants of 0.1022, 0.1037 and 0.1019 min.$^{-1}$ giving an average of 0.1026 ± 0.0007 min.$^{-1}$ were obtained in successive runs. For comparison values of 0.1035 and 0.1055 min.$^{-1}$ under comparable conditions were extrapolated from data listed by Rivett[13] and Harned and Seltz,[14] respectively.

Purification of Reagents.—2,4-Dichlorophenol was purified by the zone refining technique. The material was placed

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[11] B. D. Scully, *Chem. and Ind.* (*London*), 1146 (1955).

[12] J. O. Percival and V. K. La Mer, THIS JOURNAL, **58**, 2413 (1936).

[13] A. C. D. Rivett, *Z. physik. Chem.*, **82**, 201 (1913).

[14] H. S. Harned and H. Seltz, THIS JOURNAL, **44**, 1475 (1922).

in a 1.2 × 50 cm. tube closed at one end and a P_4O_{10} drying tube was attached to the open end. Fourteen passes of a liquid zone moving at a rate of two inches per hour yielded a product which, from its physical appearance, was excellent. The product was stark white and upon breaking the tube in which it was contained the phenol was found to be in the form of long asbestos-like crystals which ran lengthwise in the tube. Since this material has a pronounced tendency to absorb small amounts of moisture and since a means of handling the dry sample was not available it was not possible to determine precisely the purity of the sample.

The iodine solution was prepared by mixing the desired quantities of solutions of potassium iodide, potassium iodate and excess perchloric acid immediately preceding each run. To adjust the solution to the desired *p*H it was back titrated with sodium hydroxide. Stock solutions of 0.01500 *M* 2,4-dichlorophenol and 0.0300 *N* potassium iodate were prepared and used for all the work to be described in this paper. In all runs the concentration of phenol was twice the concentration of iodine.

The potassium iodate was purified by dual recrystallization. Purified sodium perchlorate was prepared from several times recrystallized sodium carbonate and reagent perchloric acid. All other chemicals were of reagent grade and were used without further purification.

Discussion and Results

Although the literature on the iodination of phenols is quite extensive, only one earlier article[1] deals with the mechanism of the reaction of iodine with 2,4-dichlorophenol. This reaction is second order[15] and to account for the *p*H and iodide ion effects it must be first order with respect to each iodine and phenol. Berliner[16] in a study of the reaction of iodine chloride with 2,4-dichlorophenol has also demonstrated that this reaction is first order with respect to each component and has characteristics similar to the iodination reaction.

The Effect of *p*H.—Since the use of the stirred flow reactor has made it possible to measure the rate of iodination of 2,4-dichlorophenol without the use of buffers, it is now possible to determine directly the influence of *p*H upon the rate of reaction. The major uncertainty, as previously indicated, is in the measurement of *p*H. The results of these observations are shown in Table I. There are several possible explanations of the effect of hydrogen ion on this reaction. One which must be taken into account is the ionization of phenol, since this is a known equilibrium. If the phenoxide ion is assumed to be the reactive species, then

$$k_{\text{obsd}} = kK_{\text{i}}/(K_{\text{i}} + [\text{H}^+]) \qquad (2)$$

where k_{obsd} is the apparent second order rate constant, k is the corrected rate constant and K_{i} is the ionization constant. To determine if the above relationship is followed, the value[17] of 1.41 × 10^{-8} for the ionization constant at 25° is used, and it may be seen in Table I, column E, that reasonably constant values of k_{obsd}. times (K_{i} + [H^+]) are obtained. For simplicity and because of the uncertainties in the evaluation of activities, concentrations are used in this paper with the exception of hydrogen ion whose activity was measured with respect to the glass electrode. For this set of runs moderately high iodide concentrations were used and the per cent. completion was kept between the limits of 36–49%; thus, the total iodide (I^- + I_3^-) at the steady state varied between the limits of 0.02073 and 0.02053 *M*. The uncertainty introduced is well within experimental error due to *p*H measurement.

In Table I a slight upward trend of the values of column E (based on K_{i} = 1.41 × 10^{-8}) is observable, and there are several possible explanations for this. It may be that the estimated error is too small or there may be another equilibrium which has not been evaluated. If a value of 1.0 × 10^{-8} is used for the ionization constant, a better correlation is obtained; see column F, Table I. Again, this may only be a salt effect caused by changing ionic species or due to the basic nature of the phenoxide ion, there may be some relationship to the buffer effect as discussed below.

TABLE I

EFFECT OF *p*H ON THE RATE OF REACTION IN THE ABSENCE OF BUFFERS AND AT CONSTANT IODIDE CONCENTRATIONS

Initial concentrations: I_2 = 0.001505 *M;* 2,4-dichlorophenol = 0.003010 *M;* I^- = 0.02000 *M;* ionic strength = 0.060; steady state concentrations: (I^- + I_3^-) = 206.5 ± 0.4 × 10^{-4}; temperature = 25.13°.

A *p*H	B Contact time, *t*, sec.	C % completion at steady state	D $k_{\text{obsd.}}$ l. mole^{-1} sec.$^{-1}$	$E^{a,c}$ ([H^+] + K_{i}) × $k_{\text{obsd.}}$ × 10^8	F^{b,c} ([H^+] + K_{i}) × $k_{\text{obsd.}}$ × 10^8
7.02	939.7	44.97	0.373	4.09	3.94
7.33	582.0	49.23	.735	4.48	4.17
7.45	381.7	44.85	.912	4.51	4.15
7.73	233.3	44.78	1.49	4.87	4.26
7.94	151.2	40.30	1.85	4.74	3.98
7.99	147.7	42.71	2.13	5.17	4.31
8.18	89.2	35.54	2.47	5.11	4.10
				Av.	4.13 ± 0.11

[a] K_{i} = 1.41 × 10^{-8} from ref. 17. [b] K_{i} is arbitrarily taken to be 1.0 × 10^{-8}. [c] The high experimental error is due mainly to the uncertainty in the measurement of *p*H.

The Effect of Iodide Ion.—The stirred flow technique has also made it feasible to measure the rate of reaction at low iodide ion concentrations. In order to eliminate the necessity of measuring *p*H and applying corrections due to varying *p*H in different runs a single phosphate buffer was used for all solutions. The data are recorded in Table II.

TABLE II

THE IODIDE ION EFFECT AT CONSTANT *p*H

Initial concentrations: 2,4-dichlorophenol = 0.001505 *M;* KH_2PO_4 = 0.080 *M;* Na_2HPO_4 = 0.020 *M*. Steady state conditions: *p*H 6.17; ionic strength = 0.14; temperature 25.02°.

Initial I_2, mole/l. × 10^4	Initial I^-, mole/l. × 10^3	Contact time, *t*, sec.	% completion at steady state	[I^-] at steady state, mole/l. × 10^3	$k_{\text{obsd.}}$ l. mole^{-1} sec.$^{-1}$	[I^-] (K_2 + [I^-]) × $k_{\text{obsd.}}$ × 10^3
6.58	2.528	382.8	47.25	2.610	1.96	2.02[a]
5.57	1.834	230.2	48.28	1.933	3.28	2.07
7.51	1.256	147.7	46.35	1.399	5.05	1.93
6.44	1.133	86.9	41.13	1.217	6.48	2.01

[a] K_2 = 1.33 × 10^{-3}, see ref. 18.

Iodide ion in moderately high concentration is known to affect the rate of reaction according to the inverse square, and this relationship is the one assumed in the early papers. If the I_2 molecule is assumed to be the reactant, the triiodide equilibrium ($I_3^- \rightleftarrows \text{I}_2 + \text{I}^-$) must be considered. At best, however, this can account for only an inverse dependence on the first power of iodide ion as implied by the following

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[15] M. I. Evans, M. S. Thesis, Miami University, 1951.

[16] E. Berliner, THIS JOURNAL, **80**, 856 (1958).

[17] C. M. Judson and M. Kilpatrick, *ibid.*, **71**, 3110 (1949).

$$k_{\text{obsd}} = kK_2/(K_2 + [\text{I}^-]) \qquad (3)$$

where K_2 represents the dissociation constant for the triiodide equilibrium[18] which is given as 1.33 × 10^{-3}.

To explain the square relationship a second equilibrium may be invoked. The iodine is assumed to form in part iodide ion plus an undefined reaction intermediate whose concentration is so small that there is no detectable change in the actual concentration of iodine, iodide ion or phenol. Disregarding the triiodide equilibrium the concentration of the intermediate is obviously proportional to iodine concentration and inversely proportional to iodide ion. A general expression which incorporates both the triiodide and the above equilibria is

$$\mathrm{d}x/\mathrm{d}t = k_{\text{obsd}}\,(a - x)(b - x) = kF_{\text{HI}} \qquad (4)$$

where $F_{\text{HI}} = K_iK_2(a - x)(b - x)/(K_i + [\text{H}^+])(K_2 + [\text{I}^-])([\text{I}^-])$. The constant k is invariant with varying pH or iodide concentrations.

That equation 4 quite satisfactorily correlates the observed data is seen in the last column of Table II in which the values of k_{obsd}, taken at a constant pH and multiplied by $[\text{I}^-]\ (K_2 + [\text{I}^-])$, are constant within experimental error.

One of the distinct advantages of the stirred flow technique is that the actual effective iodide concentrations may be readily determined, and the rate equations may be derived in terms of these quantities rather than the total iodide concentrations. The iodide concentration is calculated from $K_2 = [\text{I}^-][\text{I}_2]/[\text{I}_3^-]$ by setting $[\text{I}^-] = i + x - [\text{I}_3^-]$ and $[\text{I}_2] = b - x - [\text{I}_3^-]$ where i and b are starting concentrations of iodide and iodine, respectively, and x is the amount of iodide formed as a reaction product. The equation is

$$[\text{I}^-] = {}^1/_2(K_2 + b - i - 2x)\left(\sqrt{1 + \frac{4K_2(i + x)}{(K_2 + b - i - 2x)^2}} - 1\right) \qquad (5)$$

If standard techniques are used in place of stirred flow techniques at low iodide concentrations, it would be necessary to substitute (5) into (4) and integrate to evaluate k, the rate constant.

The Effect of Phosphate Buffers.—That there is a pronounced buffer effect on the iodination of phenol has been observed by several investigators.[19,20,21] To determine if this effect applies to other phenols, the rate of iodination of 2,4-dichlorophenol was investigated in the presence of varying concentrations of phosphates. Two series of runs were made: one with a 1:1 ratio of $\text{HPO}_4^=$ to H_2PO_4^- and the other with a 3:1 ratio. The ionic strength was maintained at 0.50 using sodium perchlorate for all experiments. The results of these experiments are given in Table III and the data incorporating the necessary corrections are shown in the last column. Since it is evident from the data that the rate of reaction does increase with increasing concentrations of buffer, previous observations on buffer effects are at least qualitatively supported using in this case a different phenol.

Following the suggestion of Berliner[21] the buffer effect may be incorporated empirically into equation 4 by

$$\mathrm{d}x/\mathrm{d}t = (k + k_{\text{cat}}\,[\text{base}])F_{\text{HI}} \qquad (6)$$

where k_{cat} is the catalytic constant for the particular base species. In setting down this equation there are presumed to be two reactions taking place concurrently. One, the "normal" reaction in the presence of water the other the "base catalyzed" reaction. Whether or not the concept of "base catalysis" is appropriate remains to be determined by further research. It may be that the variation in rate is due to some other kind of activity effect.[22]

TABLE III

EFFECT OF PHOSPHATE BUFFERS

Initial concentrations: I_2 = 0.001505 M; 2,4-dichlorophenol = 3.010 × 10^{-3} M; I^- = 0.02000 M; ionic strength = 0.50; temperature = 25.02°.

A	B	C	D	E	F	G[a]
$\text{HPO}_4^=$, mole/l.	H_2PO_4^-, mole/l.	pH	% completion	Contact time, t, sec.	$k_{\text{obsd.}}$ l. mole^{-1} sec.$^{-1}$	$([\text{H}^+] + K_i) \times k_{\text{obsd.}} \times 10^7$
0.100	0.100	6.54	45.52	940	0.382	1.14
.050	.050	6.60	37.87	940	.266	0.70
.010	.010	6.38	20.55	940	.102	0.45
.100	.033	7.01	46.16	381.1	.972	1.05
.060	.020	6.89	37.66	381.1	.649	0.90
.020	.0066	6.78	35.44	592.9	.375	0.66
...	....					0.413[b]

$k_{\text{cat.}}$ (for $\text{HPO}_4^=$ only) = 15 ± 2^c; k_0 = 0.935 ± 0.25^c

[a] The high experimental error is due to the uncertainty in pH measurement. [b] Averaged from column F, Table I; ionic strength = 0.060. [c] See equation 6.

By comparison of columns A and B with G (Table III) it may be seen that the variation in rate with varying buffer concentration correlates reasonably well with the variation in $\text{HPO}_4^=$ but not H_2PO_4^-. Because of the uncertainty in the measurement of pH, the experimental error makes it difficult to evaluate the data with any degree of quantitative precision; howbeit, there is support, though not proof, of the concept of base catalysis. The basis of this proposal is that the catalytic action is due to the basicity of the negative ion, and because of this property it assists in the removal of the proton in the final step of the reaction. The greater effectiveness of $\text{HPO}_4^=$, as compared with H_2PO_4^-, therefore correlates with this idea and with the previous observations on other phenols. It was attempted to find other buffers in this pH range to give a further check on the validity of this concept, but none was found which would withstand an attack by iodine.

It was earlier observed in this paper that the predicted values of the rate constant do not correlate precisely with the observed values as they vary with pH. It is suggested that this is simply another demonstration of a buffer or base catalysis effect due to the variation with pH of the hydroxide and phenoxide ion concentrations; these act in a manner similar to phosphate and other buffer ions.

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(18) L. I. Katzin and E. Gebert, THIS JOURNAL, **77**, 5814 (1955).

(19) C. H. Li, *ibid.*, **66**, 228 (1944).

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

(21) E. Berliner, THIS JOURNAL, **73**, 4307 (1951).

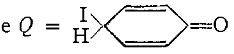
(22) It has been very appropriately emphasized by the referees that the base catalysis interpretation should be taken as highly speculative.

The Mechanism of the Reaction.—Iodine is known to be in equilibrium with several possible forms including $I^+ \cdot H_2O$, HOI, IO_3^-, I· and I_3^-. Upon postulating that any one of these forms could react with either phenol or the phenolate ion or upon postulating an iodine–phenol quinoid intermediate,[23] three mechanisms which acceptably correlate the experimental data as summed in equation 6 may be derived. The base catalysis concept is incorporated into the proposals in each case.

I. The quinoid intermediate:

$$I_2 + C_6H_5O^- \rightleftharpoons I^- + Q \xrightarrow{H_2O \text{ or base}} IC_6H_4O^- + H_3O^+ \ (H^+ \cdot \text{base})$$

where Q =



$$dx/dt = k_3[Q] = (k_3K_3 + k_{cat}\,[\text{base}])F_{HI} \qquad (7)$$

II. The iodinium ion intermediate:

$$I_2 + H_2O \ (\text{or base}) \rightleftharpoons I^- + I^+ \cdot (H_2O \text{ or base}) \xrightarrow{C_6H_5O^-} IC_6H_4O^- + H_3O^+ \ (H^+ \cdot \text{base})$$

$$dx/dt = k_4[I^+ \cdot H_2O][C_6H_5O^-] = (k_4K_4 + k_{cat}[\text{base}])F_{HI} \qquad (8)$$

III. The hypoiodous acid intermediate:

$$I_2 + H_2O + (H_2O \text{ or base}) \rightleftharpoons HOI + H_3O^+ \ (H^+ \cdot \text{base}) + I^-$$

$$HOI + C_6H_5O \longrightarrow IC_6H_4O^- + H_2O$$

$$dx/dt = k_5[HOI][C_6H_5OH] = (k_5K_5/K_i + k_{cat}[\text{base}])F_{HI} \qquad (9)$$

where $K_3 = [Q][I^-]/[I_2][C_6H_5O^-]$; $K_4 = [I^+ \cdot H_2O^-][I^-]/[I_2]$; and $K_5 = [H^+][I^-][HOI]/[I_2]$.

In the above equation activities are disregarded and the proposed intermediate in each case is assumed to be very low in concentration. If the reaction is carried out at extremely low iodine and iodide ion concentrations (lower than those which are now practically feasible), corrections for activities are no longer of concern but the transformation of iodine into the various equilibrium species does become significant. Under these conditions $a - x$ and $b - x$ should be replaced by $a - x - [I^+ \cdot H_2O] - [HOI] - [Q]$ and $b - x - [Q]$. Although the equations become far more complex, the three proposed mechanisms still yield the same basic rate equations. In all of the above discussion the rate of intermediate formation is assumed to be rapid with respect to the decomposition; that is, reversibility of the intermediate is assumed. If irreversibility is the case, then the kinetics must be much more complex and out of keeping with the experimental data.

Each of the above proposals has been supported by previous investigators, and all of the arguments have in effect been this: since the specific proposals under consideration explains the data, it is therefore the mechanism. The fault of such logic is obvious.

The iodinium ion mechanism has been widely supported.[24,25] In contrast, on the basis of the low observed activation energy[1] and the low iodinium ion concentration,[26] this mechanism has been deemed unlikely. In Table IV it is shown that absolute rate constants for the phenol and 2,4-dichlorophenol reactions by the iodinium ion mechanism are much larger than those by the hypoiodous acid mechanism. Upon comparing these values to those from another very simple reaction,[27] hydrogen ion with hydroxyl ion whose rate constant is 1.5×10^{11}, they are seen to be high indicating that the iodinium ion mechanism is of a low order of acceptability. By a similar logic the brominium ion mechanism is even less probable. With aniline the case is reversed, but the iodinium ion rate constant is still very large. This mechanism cannot be completely discredited, however, since the various species are in equilibrium and the iodinium ion must be present even if in very small amounts.

TABLE IV

	Ref.	k_4[a]	k_5[b]
Phenol	(21)	7×10^{12}	3×10^5
2,4-Dichlorophenol	Table III	1×10^{11}	4×10^4
Aniline[c]	(24a)	2×10^9	2×10^{20}

[a] See equation 8, $K_4 = 1.2 \times 10^{-11}$; [b] see equation 9, $K_5 = 3 \times 10^{13}$; [c] assumes $I^+ \cdot H_2O$ + aniline and HOI + anilinium ion.

It has been suggested[26] that the buffer effect is well explained by the quinoid intermediate proposal since there is a proton release during the rate controlling step. However, a similar condition is to be observed for each of the other two mechanisms so all three are equally supported; see equations 7 to 9.

Further argument for the quinoid intermediate has been made on the basis of isotope studies.[28] But, since the explanation of the isotope effect is again based upon the elimination of a proton during a rate controlling step, all three proposals satisfy this condition and no selection can be made.

In studies on the bromination of 3,5-dibromo(2 or 4)-hydroxybenzoic acid[26] and sodium 3,5-dibromo-4-hydroxybenzenesulfonate[29] the identification of quinoid intermediates has been claimed. From this it was argued[26] that the iodination mechanism must proceed by a similar mechanism. This reasoning is faulty on two counts. First, using presently available techniques it is quite impossible to establish that the quinoid complex is a specific intermediate for the bromination reaction. A very similar situation is discussed for the periodate–glycol reaction[30] where it is shown that the mere identification of an appropriate complex does not indicate its part in the mechanism of product formation. There is then *no experimental proof of the intermediacy of the quinoid complex.* Secondly, even if it could be shown that the quinoid complex were an intermediate for the bromination reaction, then it cannot by analogy be assumed that the iodination reaction proceeds in a similar manner. Identification of an iodination quinoid complex would lend credence

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[23] See ref. 1 and a succeeding discussion in ref. 26.

[24] (a) E. Berliner, THIS JOURNAL, **72**, 4003 (1950); (b) **78**, 3632 (1956); (c) *Chem. and Ind.* (*London*), 177 (1960).

[25] See also C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 290, for favoring arguments and earlier references. The hypoiodous acidium ion and hydrated iodinium ion refer to the same species.

[26] E. Grovenstein, Jr., and U. V. Henderson, Jr., THIS JOURNAL, **78**, 569 (1956).

[27] M. Eigen, *Z. physik. Chem.* (*Frankfurt*) *N. F.*, **1**, 176 (1954).

[28] E. Grovenstein, Jr., and D. C. Kilby, THIS JOURNAL, **79**, 2972 (1957); for similar studies see ref. 24c.

[29] L. G. Cannell, *ibid.*, **79**, 2927, 2932 (1957).

[30] J. E. Taylor, *ibid.*, **75**, 3912 (1953).

though not proof to the intermediacy proposal; further work is planned by one of the authors (WCB).

Branch and Jones[31] have attempted to show that the brominium ion and not hypobromous acid is the intermediate in the bromination of aromatic ethers, but they have neglected to take all possible explanations into consideration and their logic is therefore inconclusive.

In discussion of reactions where there are multiple mechanistic proposals which equally and completely explain the observed data, it cannot be emphatically stated that one mechanism is exclusive; rather the reactants may be thought of as following the simplest path under the immediate conditions. It is only appropriate to think of the most probable reaction pathway rather than an exclusive mechanism.

It is suggested that this uncertainty in the evaluation of the pathway of a chemical reaction may be referred to as the *principle of mechanistic indeterminancy.* A forthcoming publication on the periodate–glycol reaction will discuss this in more detail. Systems of this type appear to be very common; in fact, it is an exceptional reaction to which this idea cannot be applied. The only qualification is that a simple equilibrium must be associated with the reaction under consideration. A complete evaluation of the mechanism of any reaction cannot be made until all plausible mechanisms are assembled and are assumed to be contributors of varying importance to the over-all system.

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[31] S. J. Branch and B. Jones, *J. Chem. Soc.*, 2317 (1954); 2921 (1955).

[CONTRIBUTION FROM THE UNIVERSITY OF WASHINGTON, SEATTLE 5, WASHINGTON]

Kinetics of the Thermal Unimolecular Isomerization Reactions of Cyclopropane-d_2[1]

BY E. W. SCHLAG[2] AND B. S. RABINOVITCH

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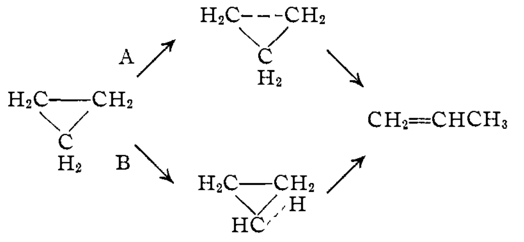
The structural and geometric thermal unimolecular isomerization of cyclopropane-d_2 has been studied at 718°K. over a pressure range. The fall-off behavior was found to be the same as that of light cyclopropane at this temperature, a fact difficult to interpret by the Slater theory. A value of $n = 14$ fits both isomerization processes. Activation energies were measured at several pressures in the fall-off regions. Relevant reaction mechanisms are discussed in light of the findings. Comparison to previous data for light cyclopropane at 773°K. is made. An improved method for graphically determining k_∞ is suggested.

An important example of a unimolecular reaction is the isomerization of cyclopropane to propylene.[3] This reaction has gained particular prominence as the first to which the theory of Slater has been applied in detail.[4,5] Two mechanisms for this reaction proposed by Chambers and Kistiakowsky[3] have been the most important:



On the basis of the pressure fall-off predicted by the Slater analysis for the two mechanisms ($n = 13$ for mechanism B, $n = 3$ for mechanism A), it has been concluded that "hydrogen transfer" as in mechanism B accorded best with the experimental findings.[4–6] If, however, the reaction coördinate for "ring opening" by mechanism A were not a highly symmetrical coördinate as was used[4] but was instead a more complex coördinate,[7] this would increase the theoretically predicted value of n, and then ring enlargement[8] is not necessarily excluded. In fact, "ring opening" by mechanism A could result in the geo-

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[2] Department of Chemistry, Northwestern University, Evanston, Illinois.

[3] T. S. Chambers and G. B. Kistiakowsky, THIS JOURNAL, **56**, 399 (1934).

[4] N. B. Slater, *Proc. Roy. Soc.* (*London*), **A218**, 224 (1953).

[5] H. O. Pritchard, R. G. Sowden, A. F. Trotman-Dickenson, *ibid.*, **A217**, 563 (1953).

[6] This conclusion contained the implicit, though reasonable, assumption that "ring opening" as in mechanism A is not characterized by a bond dissociation energy significantly less than the 65 kcal. observed value for isomerization; an energy below 65 kcal. for ring opening has been proposed by many investigators.

[7] B. S. Rabinovitch and K.-W. Michel, THIS JOURNAL, **81**, 5065, (1959). (It should be noted that the values of k_∞ and of n for cyclobutane, given in this reference, were based on an unfortunate error in transcription of the literature rate data and are incorrect.)

[8] The terminology "trimethylene biradical" and "ring opening" has been employed to describe an intermediate species in mechanism A. This name and description must not be taken too literally since the opening ends of the cyclopropane structure would not be removed from each other's sphere of influence, nor are they in trimethylene. The exact nature of this expanded ring is open to discussion; *cf.* our previous note[9] and Smith.[10]

NOTE ADDED IN PROOF.—M. C. Flowers and H. M. Frey [*J. Chem. Soc.*, 2758 (1960)] have concluded recently, on the basis of certain experimental tests, that the occurrence of a biradical intermediate in the thermal isomerization of cyclopropane is ruled out. We believe that these tests are intrinsically incapable of providing the criterion alleged. In addition, their results actually may be interpreted as being suggestive of the existence of an appreciable reorganization energy upon ring opening and, hence, suggestive of the existence of an appreciable barrier to recyclization of a singlet trimethylene biradical. If this were to be confirmed by further experimental tests which can be performed, then it would indeed be quite meaningful to speak of the existence of a singlet biradical as an entity with operational significance. B. S. R. thanks Dr. Frey for a preprint of this paper.