[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

Kinetics and Mechanism of the Coupling of Diazonium Salts with Aromatic Amines in Buffer Solutions

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A kinetic study of the coupling of a series of diazonium salts with phenols in different buffer solutions[2] revealed that the rate of coupling, measured colorimetrically, was proportional to the hydroxyl ion concentration and independent of other bases. This indicated that the measured rate was governed by an acid–base equilibrium in one or the other of the reactants. Both reactants are capable of such equilibria:

$$ArN_2^+ + OH^- \rightleftharpoons ArN_2OH \qquad (1)$$

$$ArOH \rightleftharpoons ArO^- + H^+ \qquad (2)$$

In conformity with the usual views[3] about the coupling reaction, Conant and Peterson concluded that the reaction was between the undissociated phenol and the undissociated diazo-hydroxide, and that alkali promoted the reaction by increasing the amount of the diazo-hydroxide present in equilibrium with the diazonium ion.

The present work[4] consists of a kinetic study of the coupling of diazonium salts with aromatic amines under conditions similar to those of Conant and Peterson. In this case instead of Equilibrium (2) we have

$$ArNH_2 + H^+ \rightleftharpoons ArNH_3^+ \qquad (3)$$

In contrast to the ionization of phenol, this acid–base equilibrium reaches 50% in the region of acidity in which the coupling proceeds with measurable speed. Therefore a graph of the logarithm of the observed rate constant plotted against the *p*H cannot be a straight line as in the phenol case.

The interpretation of the results with the amines is helped by considering the general shapes of the curves which would be expected if different pairs of the molecular species in Equations 1 and 3 are active in the coupling. There are four possibilities.

(1) The diazo-hydroxide couples with the ammonium ion
(2) The diazonium ion couples with the free amine
(3) The diazonium ion couples with the ammonium ion
(4) The diazo-hydroxide couples with the free amine

For a model case in which the dissociation constant of the ammonium ion is 1×10^{-4} and that of the diazo-hydroxide is 1×10^{-8}, we can calculate the fractions of the total amine existing as free base and as ammonium ion in buffer solutions of different *p*H's, and we can likewise calculate the fractions of the total diazonium compound existing as the diazonium ion and as the undissociated diazo-hydroxide in these same buffers. If Case 1 represents the facts, then the velocity constant for the rate of coupling will change with *p*H in proportion to the change in the product

$$\frac{(ArN_2OH)}{(ArN_2OH) + (ArN_2^+)} \times \frac{(ArNH_3^+)}{(ArNH_2) + (ArNH_3^+)}$$

and correspondingly for the other three cases. Plots of these products therefore indicate the general shape of the rate–*p*H curve which should result for each of the eligible mechanisms.

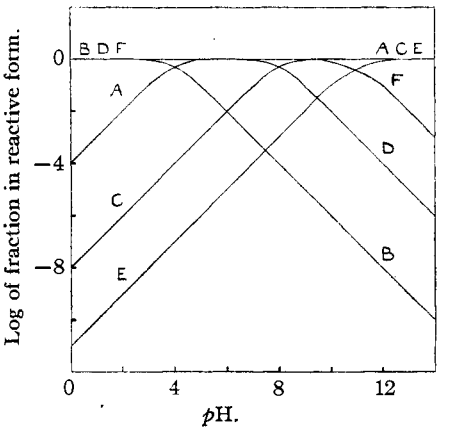

Fig. 1.—Effect of *p*H on fraction of each component in acid and basic form.

A, $\frac{ArNH_2}{ArNH_2 + ArNH_3^+}$; B, $\frac{ArNH_3^+}{ArNH_2 + ArNH_3^+}$;

C, $\frac{ArO^-}{ArOH + ArO^-}$; D, $\frac{ArOH}{ArOH + ArO^-}$;

E, $\frac{ArN_2OH}{ArN_2OH + ArN_2^+}$; F, $\frac{ArN_2^+}{ArN_2OH + ArN_2^+}$.

In Fig. 1, curves A and B represent the logarithms of the fractions of total amine existing as free amine and as ammonium ion, respectively; and curves E and F the logarithms of the fractions of total diazonium compound existing as diazo-hydroxide and as diazonium ion. Figure 2

(1) Present address: Mills College, Oakland, California.
(2) Conant and Peterson, THIS JOURNAL, **52**, 1220 (1930).
(3) See Fieser in Gilman's "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1938, pp. 128–140.
(4) This problem was assigned to the junior author in 1930 by Professor J. B. Conant. Work on it was interrupted for a number of years and resumed in 1938.

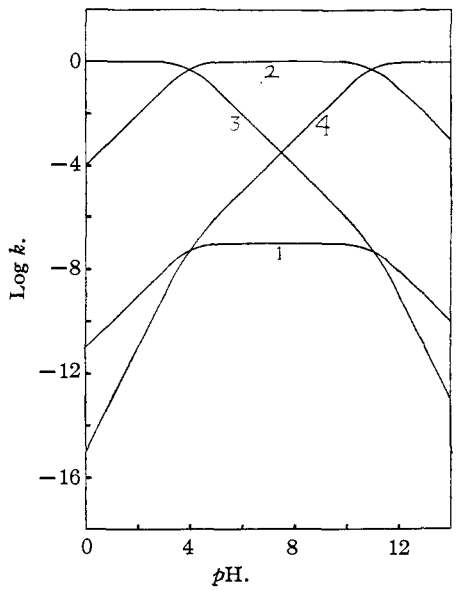

Fig. 2.—Model curves of logarithm of velocity constant of diazo coupling reaction as a function of pH assuming the following reactive pairs: 1, $ArN_2OH + ArNH_3^+$; 2, $ArN_2^+ + ArNH_2$; 3, $ArN_2^+ + ArNH_3^+$; 4, $ArN_2OH + ArNH_2$.

shows the logarithms of the products of reactive forms corresponding to mechanisms 1, 2, 3 and 4. The shapes of these curves would be the same for different ionization constants from those assumed, only the positions of the inflections being shifted. In our work the amines used were 1-naphthylamine-4- and 8-sulfonic acids, of which the former has $K_a = 1.02 \times 10^{-5}$ at 25°.[5] The diazonium salts used were diazotized aniline and sulfanilic acid. According to Hantzsch and Davidson,[6] the ionization constant of benzenediazohydroxide at 0° is 1.25×10^{-3}. Thus the values assumed in constructing the model curves are near the ones pertaining to our experiments.

From Fig. 2 it is seen that the curves for mechanisms 1 and 2 are identical with each other but entirely different from those for mechanisms 3 and 4. The experimental curves, shown in Figs. 3 and 4, are of the type called for by mechanisms 1 and 2. In each figure the exact coincidence in the shape of the curves is shown by making the slight necessary shift of assumed K_a to superpose the theoretical curve upon the experimental. Mechanism 4, often considered the most probable, is definitely eliminated.

The part of the model curves occurring in the alkaline region, where the inflection due to formation of molecular diazo-hydroxide is encountered has been simplified by neglecting the acidic character of the diazo-hydroxide. If this were taken into account, all the curves would descend more steeply toward the right than has been represented as a result of conversion of diazonium compound into diazoate anion. This is of no importance experimentally, since our observations are limited to the pH range 2.04 to 6.25, where this effect is negligible. Despite the fact that we have only a portion of the experimental curve, this portion is ample to show the type to which it belongs.

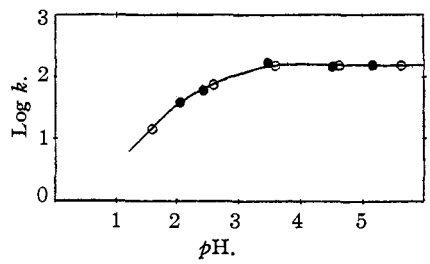

Fig. 3.—Velocity constants for coupling of 1-naphthylamine-4-sulfonic acid with diazotized sulfanilic acid at 25° in buffer solutions of ionic strength 0.24. Solid circles, experimental points; open circles, model curve superposed.

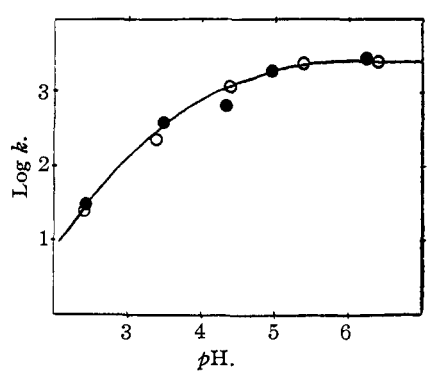

Fig. 4.—Velocity constants for coupling of 1-naphthylamine-8-sulfonic acid with diazotized aniline at 25° in buffer solutions of ionic strength 0.24. Solid circles, experimental points; open circles, model curve superposed.

We are left to decide between a mechanism (1) in which the undissociated diazo-hydroxide attacks the substituted anilinium ion, and another (2) in which the diazonium ion attacks the free substituted aniline. There is a wealth of evidence that of these two only the latter can be correct. In those cases in which aromatic substitution reactions have been carried out on anilinium ions, these ions have proved both very unreactive and powerfully meta-directing. Neither property qualifies the anilinium ion as the active intermediate in a reaction which fails to occur except with highly activated benzene derivatives, and which always

(5) Ebersbach, *Z. physik. Chem.*, **11**, 624, 627 (1893).
(6) Hantzsch and Davidson, *Ber.*, **31**, 1616 (1898).

results in para or ortho substitution. This makes mechanism 1 highly improbable. Mechanism 2, on the other hand, fits excellently into modern theories of aromatic substitution which require the substituting reagent to be an electron-acceptor attacking a region of high electron availability on the nucleus. The diazonium ion obviously has the required electrophilic character, which the diazo-hydroxide has not.[7] The fact that electron-attracting substituents activate the diazonium component and deactivate the amine or phenolic component,[2] is also consistent with mechanism 2.

It is readily seen that the phenol coupling of Conant and Peterson is subject to the same kind of analysis. Curves C and D of Fig. 1 show the change in fraction of phenoxide ion and phenol ($K_a = 1 \times 10^{-8}$) with *p*H, while Fig. 5 shows the model log *k*-*p*H curves for the phenol coupling. Only curves 6 and 7 have any portion that is linear with a slope of 1, as observed. The choice here is between the reactive pair, diazohydroxide and phenol, or the pair, diazonium ion and phenoxide ion. On theoretical grounds the second mechanism here, too, is to be preferred, although we are hampered by scant experimental knowledge of substitution reactions which surely proceed through the phenoxide ion. For this reason the study of the amines has proved more conclusive for the selection of a mechanism.

It is of interest that excess of alkali has been reported to retard the coupling reaction,[8] as it should according to curves 6 and 7.

Experimental

Kinetic Measurements.—The progress of the coupling reaction was followed colorimetrically using a Campbell-Hurley colorimeter as modified by Conant and Peterson.[9] The tube in which the reaction took place was thermostated by means of a water-bath which was maintained at 25.00 ± 0.01°. Using pipets, 50.0 ml. of the stock solution of naphthylamine sulfonic acid was placed in the reaction tube and 1.00 ml. was removed. This was given at least twenty-five minutes to come to temperature. Five seconds before the time counted as the start of the run 1.00 ml. of the diazonium solution was added from a specially calibrated, rapid delivery pipet. The reaction mixture was drawn up twice into the pipet and a gentle stream of air was blown through to complete the mixing.

In the measuring tube was placed 75 ml. of a "completely reacted"[10] solution of the run being studied. This was diluted with an equal volume of the corresponding buffer. With 50 ml. of completely reacted solution in the reaction tube, it takes 100 ml. of the solution in the measuring tube to match it in depth of color. Thus, the reading in the measuring tube corresponds directly to per cent. reaction.

Measurements were started as soon as the color was deep enough to read. This was usually about 6% reaction. They were continued until about 75% reaction, with ten or more readings being made in the interval.

The accuracy of the method for delivering the naphthylamine sulfonic acid was checked gravimetrically and found to be good within 0.2%. Fifty ml. of water in the reaction tube at 19° was placed in the thermostat and it came to 25° in less than fifteen minutes. The pipet used for delivery of the diazonium solution was standardized under the same operating conditions using sodium hydroxide solution and titrating the amount delivered with standard hydrochloric acid. The results checked within 0.5%.

The greatest single source of error was in making the colorimetric measurements. Using various amounts of completely reacted solution in the reaction tube the method was checked for accuracy with the following results:

Reacted, per cent.	20	40	60	80
Average deviation, per cent.	4	3	2	2

Purification of Materials.—Aniline was distilled once from zinc dust and then at reduced pressure. The final material was practically water white and boiled between 82.4 and 83° at 19 mm. Sulfanilic acid was purified by the method recommended by Fierz-David.[11]

1-Naphthylamine-4-sulfonic acid (naphthionic acid) was obtained from the du Pont Company as the sodium

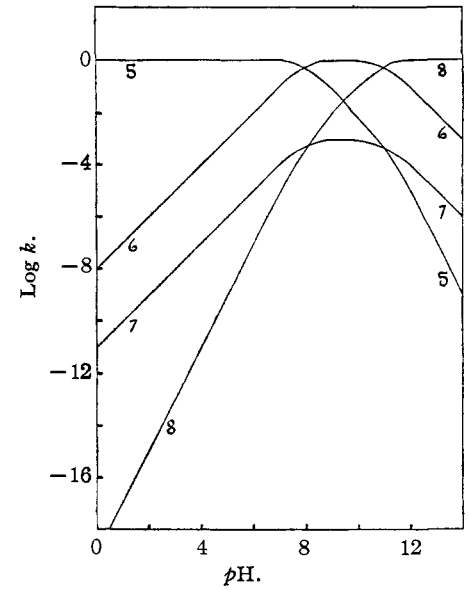

Fig. 5.—Model curves of logarithm of velocity constant of diazo coupling reaction as a function of *p*H assuming the following reactive pairs: 5, $ArN_2^+ + ArOH$; 6, $ArN_2^+ + ArO^-$; 7, $ArN_2OH + ArOH$; 8, $ArN_2OH + ArO^-$.

(7) Hauser and Breslow, THIS JOURNAL, **63**, 418 (1941), have independently come to the same conclusion.

(8) Goldschmidt and Merz, *Ber.*, **30**, 670 (1897).

(9) Reference 2, page 1222.

(10) In the "completely reacted" solution reaction was at least 98% complete as calculated from the rate constant determined by preliminary experiments.

(11) Fierz-David, "Fundamental Processes of Dye Chemistry," translated by Mason, London, 1921, p. 225.

salt about 97% pure. It was precipitated as the acid, dissolved as the sodium salt and reprecipitated as the acid. The acid was recrystallized twice from water and stored in a desiccator over sulfuric acid. Neutral equivalent: calcd., 223; found, 224.

1-Naphthylamine-8-sulfonic acid (peri acid) was obtained as crude material from the du Pont Company. After two extractions with methyl alcohol, it was dissolved in ammonia, boiled with Norit and precipitated with hydrochloric acid. Another treatment with ammonia and hydrochloric acid and one recrystallization from water gave a product pink in color and only slightly soluble in water. This was placed in a steam-heated funnel and boiling water was dripped through it. Most of the colored impurities were soon removed, and the filtrate was then colorless. The acid precipitated from the filtrate in fine white needles. These kept best when in a desiccator over sulfuric acid and stored in a dark closet. Neutral equivalent: calcd., 223; found, 232.

Any important impurities in the reagents should be revealed in deviations of the kinetic graphs from linearity. Such deviations would also surely be observed if the formation of the final colored coupling product were not, as assumed, the rate-determining step in the reaction and the only step producing appreciable color. No such deviations were observed.

Preparation of Solutions.—Using the effective molecular weights of the naphthylamine sulfonic acids as determined above, the stock solutions were made up by dissolving the calculated amounts of acid and diluting to the required volume using the proper buffer solution. The concentrations of the stock solutions were so chosen that when 49 ml. was diluted to 50 ml. in the reaction tube, the desired concentration of naphthylamine sulfonic acid would result.

The diazonium salt solutions were prepared fresh each day. A stock solution 0.100 molar in sulfanilic acid was prepared by dissolving 8.65 g. (0.05 mole) of the acid in some water containing 5 ml. of concentrated ammonia solution. This was diluted to 500 ml. To 10.00 ml. of this standard solution of sulfanilic acid in a 50-ml. Erlenmeyer flask was added 5.00 ml. of 0.6 molar hydrochloric acid. This mixture was cooled in an ice–water-bath for ten minutes. Then 5.00 ml. of a 0.200 molar sodium nitrite solution was added dropwise from a buret while the flask was gently rotated to facilitate mixing and cooling. The diazotization was permitted to continue at the temperature of the ice-bath for half an hour, and then 20.00 ml. of water was added. This solution is 0.025 molar in diazonium ion, and 1.00 ml. of it diluted to 50 ml. in the reaction mixtures gives a solution which is 0.0005 molar.

A solution 0.200 molar in aniline and 0.600 molar in hydrochloric acid was prepared by dissolving 4.656 g. (0.05 mole) of aniline and 27.43 g. (0.15 mole) of constant boiling hydrochloric acid in water and diluting to 250 ml. After cooling 5.00 ml. of this standard solution in an ice–water-bath for ten minutes, 5.00 ml. of a 0.200 molar sodium nitrite solution was added dropwise from a buret. After adding 10.00 ml. of water the diazotization was permitted to continue at the temperature of the ice-bath for half an hour, and then 20.00 ml. of water was added, making the solution 0.025 molar in diazonium ion.

The buffer solutions were prepared to have an ionic strength of 0.24. The composition of the solutions is given in Table I in grams per liter of solution. Although the best grade of material obtainable was used in all cases, the *p*H of the two acetate buffers was not reproduced in making up a fresh lot of solution. Acetate buffers IA and IIIA were used only in runs with 1-naphthylamine-4-sulfonic acid and diazotized sulfanilic acid, and acetate buffers IB and IIIB were used only in the runs with 1-naphthylamine-8-sulfonic acid and diazotized aniline.

TABLE I

Buffer	*p*H	Composition
Phosphate III	6.25	11.4 g. KH_2PO_4 22.2 g. Na_2HPO_4
Acetate III A	5.18	32.66 g. $NaC_2H_3O_2 \cdot 3H_2O$ 3.6 g. $HC_2H_3O_2$
Acetate IIIB	4.95	Same as Acetate IIIA
Acetate IA	4.51	32.66 g. $NaC_2H_3O_2 \cdot 3H_2O$ 16.22 g. $HC_2H_3O_2$
Acetate IB	4.32	Same as Acetate IA
Phthalate III	3.49	49.0 g. $KHC_8H_4O_4$ 6.497 g. (0.036 mols) Constant boiling HCl
Phosphate II	2.43	32.68 g. KH_2PO_4 16.77 g. 50% H_3PO_4
Phosphate I	2.04	32.68 g. KH_2PO_4 31.38 g. 50% H_3PO_4

The *p*H values of the buffer solution were determined potentiometrically using a quinhydrone electrode and the values for reference solutions accepted by Clark.[12]

Treatment of Data.—For convenience in plotting, the following forms of the integrated second order rate equation were used

$$k = \frac{Z}{tc(1 - Z)} \text{ and } k = \frac{2.303}{tc(m - 1)} \log \frac{m - Z}{m(1 - Z)}$$

in which Z is fraction reacted in t minutes, c is initial concentration of reactants, and m is ratio of concentrations of reactants in the cases in which they are not equal. In the latter case c is lower of two initial reactant concentrations. The values for the velocity constants were always determined graphically. The sample data presented in Fig. 6 indicate that the reaction is well represented by the second order equation. The ratio of reactants is 2:1 in one case and 5:1 in the other, and both of the reactions were followed to more than 75% completion. The points all fall close to a straight line and the constants check each other well.

In Table II are summarized the results of the rate measurements. All of the runs were at 25° and at an ionic strength of 0.24. In all cases except one, two different concentration ratios were

(12) W. M. Clark, "Determination of Hydrogen Ions," 3rd ed., Williams and Wilkins Co., Baltimore, Md., 1928, p. 672.

studied at each *p*H interval. The values reported in the table are the averages of from four to six runs.

TABLE II

1-NAPHTHYLAMINE-4-SULFONIC ACID COUPLING WITH DIAZOTIZED SULFANILIC ACID			1-NAPHTHYLAMINE-8-SULFONIC ACID COUPLING WITH DIAZOTIZED ANILINE		
*p*H	log *k*	log *k* av.	*p*H	log *k*	log *k* av.
5.18	2.16		6.25	3.47	
	2.20			3.49	3.48
	2.20	2.19			
			4.95	3.32	
4.51	2.17			3.28	3.30
	2.18	2.18			
			4.32	2.81	
3.49	2.24			2.82	2.82
	2.21	2.23			
			3.49	2.54	
3.43	1.78			2.65	2.59
	1.79	1.79	2.43	1.49	1.49
2.04	1.62				
	1.58	1.60			

The corresponding values of log *k* and *p*H for 1-naphthylamine-4-sulfonic acid and diazotized sulfanilic acid from Table II are plotted in Fig. 3. It can be seen that the rate is very constant above *p*H 3.4. It drops off at lower *p*H values and has apparently just reached a slope of one at the lowest *p*H measured. Accurate rate measurements could not be made below *p*H 2 because the dye formed was very insoluble in this range.

Referring to the theoretical curves presented in Fig. 2 it can be seen that curves 3 and 4 represent mechanisms definitely inconsistent with the kinetic data. Although curve 4 has a somewhat similar shape to the experimental one, the *p*H at which the rate approaches a constant value is associated with the K_b for the diazo-hydroxide which is very far from the K_a for the naphthylamine sulfonic acid.

The data for 1-naphthylamine-8-sulfonic acid and diazotized aniline from Table II have been plotted in Fig. 4. The peri acid couples more rapidly than naphthionic acid does under corresponding circumstances. The value for K_a for the peri acid is lower than for naphthionic acid, so the flat portion of the curve for the former comes

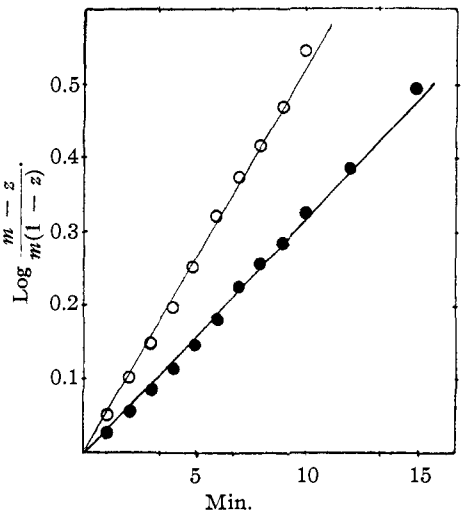

Fig. 6.—Data of a typical run on coupling of 1-naphthylamine-4-sulfonic acid with diazotized sulfanilic acid, plotted as a bimolecular reaction: acetate buffer, *p*H 4.51, ionic strength 0.24, at 25°; solid circles, $m = 2$; open circles, $m = 5$.

at a higher *p*H. Even though diazotized aniline was the other coupling component, the reaction could be studied at a *p*H well below the point where the slope of the curve approached unity. It appears to have levelled off at the highest *p*H studied.

Summary

The influence of *p*H on the rate of the coupling reaction between 1-naphthylamine-4-sulfonic acid and diazotized sulfanilic acid and between 1-naphthylamine-8-sulfonic acid and diazotized aniline has been studied.

An examination has been made of several possible mechanisms for the coupling reaction between diazonium salts and aryl amines or phenols. The kinetic study is consistent with only two of these mechanisms. Only one of these is in harmony with the facts regarding activating and directive influence of aromatic substituents upon the coupling reaction. It is thus shown that the active components in the coupling reaction are the diazonium cation and the free amine or phenoxide ion.

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