THE KINETICS OF THE DIAZO COUPLING REACTION

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I. INTRODUCTION

Nearly one hundred years ago (1858) Peter Griess discovered the then unknown class of the diazo compounds, the high reactivity of which has made them so valuable. The most important technical use of these compounds is as reactants for the coupling reaction in order to synthesize the azo dyestuffs, which probably still form the most-produced and most remarkable class of dyestuffs. The coupling reaction is practically the only synthetic method which is used industrially.[2]

The preparative methods for the manufacture of the azo compounds are based upon a series of well-known rules which were discovered empirically. Although these rules are of great practical importance, their basic principles, i.e., their explanation by means of physical-organic chemistry, have been surprisingly little investigated.

The monograph of Holzach (27) and the new edition of the textbook by Saunders (36) cover the whole field of the chemistry of diazo compounds primarily on a technological and preparative basis; therefore their reviews of the principles of the coupling reaction are in a rather condensed form. Furthermore, some important publications which have appeared in the last two years could not be considered in those books, because they were published in 1947 and 1949, respectively. The present review deals therefore primarily with recent work in the *fundamental* research in this field. The older views with respect to the mechanism of the coupling reaction which were held, until the 1920's, by Hantsch,

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[1] Visiting Guest at the Massachusetts Institute of Technology, Cambridge, Massachusetts, 1951–52. A condensed review of this subject was presented in the Physical Organic Seminar at Harvard University (under Professor P. D. Bartlett) on December 21, 1951.

[2] An exception is Ziegler's synthesis of tartrazine.

Dimroth, Karrer, Meyer, and others, will be passed over. (Saunders (36) has presented this subject comprehensively.) This review will consider kinetic investigations first, since they afford, in the opinion of the author, the best basis for the determination of the probable reaction mechanism and the explanation of the preparative rules mentioned at the beginning.

II. METHODS OF KINETIC MEASUREMENTS

In principle there are three possibilities of determining the rate of the coupling reaction: (*1*) measurement of the disappearance of the diazo component, (*2*) measurement of the coupling reactant, or (*3*) measurement of the formation of the azo compound. Up to the present time only the first and the third methods have been used.

At the turn of the century Goldschmidt and Merz carried out the first kinetic investigation by means of the first method (14). The amount of diazo compound present after a certain time of reaction was determined by addition of sulfuric acid, which stopped the reaction. By heating the solution the unreacted part of the diazo compound was decomposed; the evolved nitrogen was then measured.

Recently the change in concentration of the diazo component was followed polarographically (6). With an applied potential of 0.3 v. *versus* a saturated calomel electrode the dropping mercury electrode can be used for the measurement of the concentration of diazotized amines. This potential is well below that which leads to the reduction of the azo group of the formed dyestuff. Some examples show that this method is quite generally applicable and has advantages over the other ways of determination, because fast reactions are comparatively easy to follow.

The third method consists in the measurement of the formation of the dyestuff by a colorimeter. Veley (37) was the first investigator proceeding in this way as early as 1909. With one exception (6) all later research work was done by this method (3, 28, 29, 31, 32, 33, 35, 39, 43). As is known, all azo compounds are intensively colored, whereas the commonly used coupling components and a great number of the diazo components show practically no absorption in the visible range. This method cannot be used if colored reaction partners are involved, if colored by-products are formed (e.g., by decomposition of the diazo components), or if the reaction product is completely or partially insoluble in the medium. As pointed out by Elofson, Edsberg, and Meckerly (6), the polarographic method is more suitable for these cases.

III. RESULTS OF THE EARLY KINETIC INVESTIGATIONS

In a series of papers Goldschmidt (10, 11, 12, 13, 14) reported investigations of the kinetics of the coupling of phenol, dimethylaniline, and some of their derivatives. Since, at that time, the use of buffer solutions was unknown, his work has but limited value today. As is known, the acidity of the medium plays an important part in the kinetics of the coupling reaction. Nevertheless, Goldschmidt recognized that a second-order reaction was involved. The formulation of the kinetic equation therefore appeared to be:

$$\frac{d(\mathrm{Az})}{dt} = k_s(\mathrm{D})(\mathrm{C}) \qquad (1)$$

(Az), (D), and (C) are the concentrations of the azo compound, the diazo compound, and the coupling component, respectively. k_s is the reaction rate constant. The subscript s is here intended to show that the constant is determined with the aid of stoichiometric concentrations.

IV. INFLUENCE OF THE ACIDITY ON THE COUPLING RATE

The acidity of the medium is a dominating factor in the kinetics of any particular combination of reactants. Many qualitative observations have been reported in the early and the more recent literature on this subject. The preparative methods for the production of the azo compounds in the laboratory and in the plant are based on the fact that the pH must be kept above a certain value in order for the reaction to proceed rapidly. On the other hand, there is an optimal range; with very high concentrations of hydroxide ions a decrease in rate is generally observed.

The first attempts to investigate the fundamentals of the relation between the pH and the reaction rate were those of Conant and Peterson (3). It appeared that in the coupling of some naphtholsulfonic acids between pH 4.50 and 9.15, the hydroxyl-ion concentration and the rate were proportional. This showed that the measured rate was governed by an acid–base equilibrium in *one* of the reactants. The conclusion was drawn that the coupling takes place with the free (undissociated) phenol and the diazohydroxide, and that this reaction is preceded by an equilibrium between the diazonium ion and the diazohydroxide:

$$\mathrm{ArN_2^{\oplus}} + {}^{\ominus}\mathrm{OH} \rightleftarrows \mathrm{ArN{=}NOH} \qquad (2)$$

This conclusion coincided with the then accepted views as to the mechanism of this reaction (9, 38a, and others).

Eleven years after the publication of this paper, Wistar and Bartlett (39) demonstrated that not only the mechanism mentioned above, but also a second mechanism, coincides with these kinetic measurements. Both the diazo reactant and the coupling component are in an acid–base equilibrium. In the case of a phenol as reactant we have:

$$\mathrm{ROH} \rightleftarrows \mathrm{RO^{\ominus}} + \mathrm{H^{\oplus}} \qquad (3)$$

or, with an aromatic amine:

$$\mathrm{RNH_3^{\oplus}} \rightleftarrows \mathrm{RNH_2} + \mathrm{H^{\oplus}} \qquad (4)$$

The general shape of the curves of the relationship between acidity and reaction rate was discussed for all the different pairs of molecular species resulting from the equilibria 2 and 3 (for a phenol coupling) or 2 and 4 (for an amine coupling), respectively. In both cases there are four possibilities (table 1).

From model curves of the logarithms of velocity constants as a function of the acidity, assuming the reactive pairs of table 1, it is seen that the curves for cases A and B are identical in shape with each other but completely different from those of the last two possibilities, C and D.

In some experiments with naphthylaminesulfonic acids as coupling reactants, Wistar and Bartlett were able to show that their curves coincided with those of mechanism A or B. Since it was known at that time that anilinium ions have no nucleophilic character at all or practically none, case A could be excluded, thus establishing that the reaction takes place between diazonium ion and free amine.

Analogously, the same behavior was to be expected for phenol couplings. Here the choice is between the pair diazohydroxide + phenol or diazonium ion + phenoxide ion. At that time, little experimental evidence was present for the decision as to whether the undissociated phenol or the phenoxide ion is more reactive in electrophilic substitutions. By analogy with the amine coupling and on theoretical grounds the second mechanism was considered to be probable. Later these theoretical considerations will be referred to briefly.

TABLE 1

Combinations of the reactants in the rate-determining step

CASE	DIAZO COMPONENT	COUPLING COMPONENT
A	Diazohydroxide	Ammonium ion or free phenol
B	Diazonium ion	Free amine or phenoxide ion
C	Diazonium ion	Ammonium ion or free phenol
D	Diazohydroxide	Free amine or phenoxide ion

The experimental answer to this problem on a kinetic basis recently came from two sources: Pütter (35) studied the kinetics of the coupling of 1-naphthol-4-sulfonic acid, 1-naphthol-2-sulfonic acid, and 1-naphthol-8-sulfonic acid with the diazo derivative of 4-(acetylamino)aniline-2-sulfonic acid. The reaction rate was found to be proportional to the OH-dissociation of the particular coupling component. The acidity constants of these three naphtholsulfonic acids differ within a large range (the pK values are 8.2, 9.4, and 12.6, respectively). The measurements made between pH 7.4 and pH 9.8 show that the expected proportionality between hydroxyl-ion concentration and reaction rate is present only at acidities higher than that corresponding to the pK value of the naphtholsulfonic acid used. In a more alkaline range, the curve of the logarithm of the rate as a function of pH becomes horizontal.

This result agrees with mechanism B (diazonium ion + phenoxide ion) but not with the views of Conant and Peterson, as there should always be the same dependence upon pH regardless of the character of the coupling component, inasmuch as the same diazo reactant is used.

Furthermore, the results of Pütter show that the equation of the relationship between pH and rate constant, formulated by Conant and Peterson as

$$\log k_s = \log k_0 + \mathrm{pH} \tag{5}$$

holds only for a limited pH range, that is, for a medium where an increase of 1 pH unit effects a tenfold increase in the concentration of the reactive species of the coupling reactant.

On the other hand, the coupling of a number of dihydroxynaphthalenesulfonic acids was investigated by Zollinger and Büchler (42). For the question under discussion, the 1,8-dihydroxynaphthalene-4-sulfonic acid is especially important, because it carries both hydroxyl groups in α-positions and the sulfo group does not sterically influence the reaction in the 2- and 7-positions. It is a principal characteristic of this compound that the coupling takes place exclusively in the ring which contains the sulfo group (2, 40), i.e., in the 2-position. By a comparison of the dissociation constants of the hydroxyl groups of 1-naphthol-4-sulfonic acid and 1-naphthol-5-sulfonic acid it can be determined which of the two hydroxyl groups in 1,8-dihydroxynaphthalene-4-sulfonic acid is the more acid, i.e., the more dissociated. The 1-naphthol-4- and -5-sulfonic acids have pK values of 8.2 and 9.0, respectively (41); in 1,8-dihydroxynaphthalene-4-sulfonic acid, therefore, the hydroxyl group in the 1-position is the more acidic. This result is understandable if the electrostatic effect exerted by the dipole of the sulfo group is kept in mind. The coupling reaction, therefore, takes place with the more acid hydroxyl group, thus establishing that the dissociated hydroxy compound is better qualified to enter the rate-determining step.

It should also be mentioned that the difference in acid strength in the case of this dihydroxy compound is very great. The more acid hydroxyl group has a pK value of 5.33; the second hydroxyl group dissociates above pH 13. The exact pK value is probably of the same magnitude as that of 1,8-dihydroxynaphthalene-3,6-disulfonic acid, which Heller and Schwarzenbach (22) determined recently (pK = 15.6). These results signify an extraordinarily strong hydrogen bond between the two hydroxyl groups.

Now that the coupling components involved in the substitution steps have been determined for amine couplings as well as, more recently, for phenol couplings, the proposal has been made (43) correspondingly to change the kinetic equation (equation 1) by replacing the stoichiometric concentrations by the concentrations of the effective reactants, i.e., of the free amine or the phenoxide ion and of the diazo component:[3]

$$\frac{\mathrm{d(Az)}}{\mathrm{d}t} = k(\mathrm{D})[\mathrm{RO}^{\ominus}] \tag{6}$$

$$\frac{\mathrm{d(Az)}}{\mathrm{d}t} = k(\mathrm{D})[\mathrm{RNH_2}] \tag{7}$$

The constant k in these equations is, in contrast to k_s of equation 1, independent of the acidity. This is clearly apparent from the kinetic data, published by several authors. Their evaluation (table 2) shows the rather good constancy of the values of k. Exact constants are, of course, to be expected only when the kinetic

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[3] Stoichiometric concentrations are designated by parentheses, concentrations of effective reactants by square brackets.

measurements, as well as the determination of the dissociation constants of the coupling component, take place at the same ionic strength. This is true in only one of the reactions mentioned in table 2 (*p*-diazotoluene + 2-naphthol-6-sulfonic acid).

Examples of how these kinetic equations can be used will be reviewed in the last sections of this paper.

Although most of the recent investigators assume the diazonium ion as the reacting species, the general term "D" (= diazo component), and not "$ArN_2^{\oplus}$" (= diazonium ion), is still used in equations 6 and 7. This is done—in order to be very exact—because the diazo–diazonium equilibrium has not been measured in connection with these kinetic studies nor has the kinetics of couplings in the buffer range of this equilibrium (probably pH > 10) been investigated. There is only one modern study in the field of diazo equilibria in aqueous medium which is easily available (1). Only abstracts of some recent and interesting papers of Russian chemists are known to the present author (15, 16, 17, 18, 34). The question of the reacting form of the diazo partner will be referred to in a later section.

TABLE 2

Reaction rates and acidities of some couplings with phenols and amines

REACTANTS		pK OF COUPLING COMPOUND	pH OF MEDIUM	RATE CONSTANTS		REFERENCE
Diazo compound	Coupling compound			log k_s	log k	
Aniline	1-Naphthylamine-8-sulfonic acid	5.03	4.32	2.82	3.5	(39)
			4.95	3.30	3.6	
			6.25	3.48	3.5	
Sulfanilic acid	1-Naphthol-4-sulfonic acid	8.2	4.50	2.04	5.7	(3)
			4.94	2.48	5.7	
			5.27	2.82	5.7	
p-Toluidine	2-Naphthol	9.91	6.4	1.97	5.5	(6)
			6.6	2.11	5.4	
			7.0	2.57	5.5	
			7.4	2.99	5.5	
p-Toluidine	2-Naphthol-6-sulfonic acid	8.94	5.09	−0.15	3.71	(43)
			5.71	0.42	3.65	
			6.24	1.02	3.72	
			6.71	1.45	3.68	
			7.18	1.91	3.67	

V. ELECTRONIC CONSIDERATIONS OF THE REACTION MECHANISM

Although this review deals first of all with the kinetics of the coupling reaction, it appears to be appropriate to mention briefly the more recent papers which treat this reaction from the standpoint of the electronic theory, for there are some connections with the kinetic investigations of Wistar and Bartlett (39).

It has already been mentioned that up to the 1930's the generally accepted view was that the diazohydroxides enter the coupling reaction. Hammett (20) was the first, so far as is known, to point out on the background of the new theories that the diazonium ion, too, is an electrophilic reactant. Hauser and Breslow (21) explained these considerations in an article which accompanied the paper of Wistar and Bartlett. The diazonium ion may be represented as a resonance hybrid:

$$\underset{\text{I}}{\mathrm{Ar{-}\overset{\oplus}{N}{\equiv}\bar{N}}} \quad \leftrightarrow \quad \underset{\text{II}}{\mathrm{Ar{-}\bar{N}{=}\overset{\oplus}{\bar{N}}}} \tag{8}$$

It is obvious that II is strongly electron-attracting. On the other hand, the free amine and the phenoxide ion are more active electron donors than the ammonium ion and the undissociated phenol, respectively. The authors refer to the fact that addition of bases to the medium would convert *reversibly* a portion of the diazonium ion into the diazohydroxide. As already mentioned, only few data are known in the field of these equilibria.

The conclusions of Hauser and Breslow, as well as those resulting from the kinetic measurements made by Wistar and Bartlett, were criticized by Hodgson (23, 24, 25, 26). First of all, he gives a different interpretation of the conclusions drawn by the other authors. Hodgson thinks that Wistar and Bartlett's mechanism must follow first-order kinetics, although it was clearly pointed out that the rate-determining step is the reaction between a diazonium ion and a molecule of the coupling component. Furthermore, he says that a coupling reaction at pH > 7 could not be due to a diazonium ion, because the real existence of this species would be impossible in an alkaline medium. This assertion is at least not permissible so long as the values of the equilibrium diazonium ion $\rightleftarrows$ diazohydroxide $\rightleftarrows$ diazotate are unknown. It may be added that in case the equilibrium favors the diazohydroxide strongly in weakly alkaline solutions, the diazonium ion is still present in low concentrations, provided the reaction is reversible.

Hodgson proposes his "polarization theory of the coupling reaction" and concludes that the reaction is a condensation between the polarized, undissociated electrophilic diazo compound

$$\mathrm{R{-}N{=}\overset{\delta\oplus}{N}{-}\overset{\delta\ominus}{X}}$$

(where X is OH or the anion of an acid) and the nucleophilic phenol, phenoxide ion, or amine.

At all events it is, with this theory, difficult to interpret the known kinetic data of the amine and the phenol couplings. Hodgson's investigations show that the concentration of the effective diazo reactant has to be constant at all the measured pH's. This pH range covers generally 1–2 pH units between pH 3 and 9. It is not probable that the concentration of the diazohydroxide fits this condition. The author is therefore of the opinion that Hodgson's theory can hardly be accepted for the reactions mentioned.

This does not mean that a diazohydroxide is not capable of reacting at all. In other solvents or with certain components this species may couple very well (see Section X).

In a series of more recent publications (4, 5, 38b) the diazonium-ion mechanism proposed (20, 21, 39) has been accepted, but because these papers do not contribute to the basic principles of the coupling reaction, they will not be reviewed here in detail.

VI. EFFECT OF THE TEMPERATURE ON THE REACTION RATE

In the early papers (11, 12) on the kinetics of the coupling reaction some experiments were described which were intended to investigate the applicability of the equation of Arrhenius:

$$\ln k = -\frac{E}{RT} + \ln A \tag{9}$$

Conant and Peterson (3) measured some coupling reactions at 15°C. and 25°C. In this way a temperature coefficient of the rate constant was obtained. They assumed that the reaction constant A is the same at both temperatures, and calculated the activation energy E. For couplings with two simple diazo components and two naphtholsulfonic acids they found values between 14,200 and 17,200 cal. The correctness of their assumption may be doubted, because there are cases where A is definitely not independent of the temperature (40), but the error caused thereby is probably very small.

VII. EFFECT OF ADDITIONS TO THE REACTION MEDIUM

Some azo coupling processes of great technical significance can be executed in a satisfactory way only in a mixture of water and pyridine. The addition of pyridine effects a substantially higher reaction rate as compared with the analogous reaction carried out at the same acidity in water. Some other organic bases have a similar effect.

Although a large number of examples of this effect have been published in the patent literature, only one paper concerning the fundamental kinetic research in this field is available today. Pütter (35) studied the influence of a small addition of pyridine (1 per cent calculated on the amount of water) on the kinetics of the reaction of eight different naphtholsulfonic acids with three diazo components. It can be seen that pyridine causes a higher rate with certain combinations only. Whereas the velocity of the reaction of 4-diazophenol-2,6-disulfonic acid with 1-naphthol-8-sulfonic acid is increased in the presence of pyridine, the rate of the analogous reaction with 1-naphthol-5-sulfonic acid is not altered by this addition. On the other hand, with 4-(acetylamino)diazobenzene-2-sulfonic acid the rate of the reaction of 1-naphthol-5-sulfonic acid, but not that of 1-naphthol-8-sulfonic acid, will be accelerated by pyridine. The change in rate is illustrated by a 2- to 28-fold increase of the rate constant. The examples mentioned here show that pyridine does not raise the reactivity of *one* of the reactants, either the diazo component alone or the naphthol alone. Such an effect should be detectable in each combination of that particular compound. The ideas suggested in the literature for the mechanism of coupling reactions in the presence of pyridine (26) are inconsistent with these experimental results, because they are based on an intermediate of a pyridine molecule with the diazo partner only. Pütter assumes in his explanation of the facts that the coupling reactant and the diazo component at first form an intermediate in a reversible reaction; the second step consists in the release of a proton from the reacting carbon atom at the aromatic ring of the coupling partner. This second step is influenced by strong proton acceptors like pyridine, but this effect is recognizable only if the rate of the reverse reaction of the first step is not negligibly slow compared with the proton release.

A similar explanation may be applied to the reaction of 1-naphthol-3-sulfonic acid, 1-naphthol-5-sulfonic acid, and related coupling reactants. With these compounds a certain ratio of dyestuff coupled in the 2-position to that coupled in the 4-position is obtained. This ratio is not the same with or without the addition of pyridine. Pyridine favors the reaction in the 4-position more than it does in the 2-position.

Pütter's experiments were done in buffered solutions; therefore the pyridine neither has an effect on the pH of the medium nor does it seem to have a mere buffering action. On the other hand, it may be concluded from Pütter's explanation that other proton acceptors would have an analogous effect. In fact, this is known for the influence of hydroxyl ions on the *o/p* coupling ratio of 1-naphthol-3-sulfonic acid and 1-naphthol-5-sulfonic acid. The published observations (8) are of purely qualitative nature only; a recent, more detailed investigation will not be referred to here, because it has not been published in the generally available literature (40). Considerable knowledge from practical experience exists in the industry, but this has not been published and perhaps has not been evaluated as to kinetic principles, except for Pütter's work.

Basic and profound studies in this field, including the question of a general acid–base catalysis, are desirable. Conant and Peterson (3) carried out a few experiments to obtain an idea concerning the nature of the salt effect. They used a series of phosphate and acetate buffers of constant acidity but varying ionic strength. Three combinations showed a positive but small salt effect; another was unaffected by the ionic strength within the limits of experimental error. An interpretation of the data by means of Brønsted's theory was impossible, because of the necessity of using sufficiently buffered solutions which, on the other hand, were not dilute enough for this purpose.

VIII. KINETICS OF THE COUPLING REACTION WITH DIHYDROXY COMPOUNDS

Conant and Peterson (3) observed that, in couplings with resorcinol, the reaction rate per pH unit did not increase tenfold but rather more than tenfold; this observation was confirmed in recent measurements (6). The explanation for the deviating behavior of this dihydroxy compound follows directly from the new kinetic equation (equation 6): resorcinol is a dibasic acid; therefore in its aqueous solution the singly as well as the doubly negatively charged ions, which may be designated as $RH^{\ominus}$ and $R^{\ominus\ominus}$, are present together with the undissociated molecule RH_2. It is to be expected that the reaction rate of these two ions is not

$$RH_2 \rightleftarrows RH^{\ominus} + H^{\oplus} \rightleftarrows R^{\ominus\ominus} + 2H^{\oplus} \tag{10}$$

the same. This means that, kinetically viewed, two parallel reactions proceed: on the one hand coupling with $RH^{\ominus}$, and on the other hand coupling with $R^{\ominus\ominus}$.

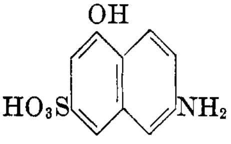
Assuming that the reaction rate of the undissociated molecule is very small, the kinetic equation for the coupling with resorcinol is:

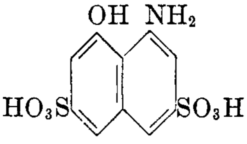
$$\frac{d(Az)}{dt} = (D)(k_1[RH^{\ominus}] + k_2[R^{\ominus\ominus}]) \qquad (11)$$

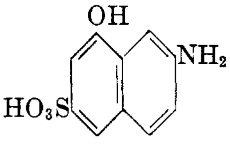
From the measurement of the total reaction rate at two different acidities, the rate constants k_1 and k_2 can be calculated. It has been shown (43) that the doubly charged negative ion has a constant which is more than 10,000 times larger than that of the singly charged ion. This result is readily understandable from the standpoint of electron theory.

IX. THE SELECTIVE COUPLING OF THE AMINONAPHTHOLS

Some aminonaphtholsulfonic acids are of great technical importance as coupling components. Among these, particular mention may be made of I acid (III), H acid (IV), and γ-acid (V). Depending upon reaction conditions, the coupling can be caused to take place at the six-membered ring which carries the hydroxyl group or at the ring which carries the amino group. It is a long-known rule that in acid solution, preferably acetate buffer solution, substitution occurs in the ring containing the amino group, while in weakly to strongly alkaline solution, substitution occurs in the ring containing the hydroxyl group. By observing this rule, it is possible to prepare so-called primary disazo dyestuffs which carry, on the hydroxy as well as on the amino side, an arylazo group, which need not be the same on the two sides. Details of the technology of these compounds may be found in the handbooks of dyestuff chemistry (7 and others).


III
I acid


IV
H acid


V
γ-Acid

Very little work has hitherto been done with respect to the basic principles of this behavior of the aminonaphthols. Some years ago, the effect of the pH of the medium on the reacting position in the naphthalene nucleus was explained on the basis of the resonance theory (25). It was, in this connection, asserted that a different resonance structure prevails in acid solution from that in alkaline solution. However, there is no proof whatever for this assertion. It seems, in the opinion of the present author, that this is a case where the concept of the resonance hybrid was confused with the existence of structurally different forms of a compound.

A recent explanation rests upon kinetic principles and is rather simple (43). The equation for the entire reaction, i.e., hydroxy *and* amino coupling, is the following:[4]

[4] Az_{NH_2}, Az_{OH} = aminoazo compound and hydroxyazo compound, respectively.
k_{NH_2}, k_{OH} = rate constants for the coupling on the ring containing the amino and the hydroxyl group, respectively.
$HORNH_2$ = aminonaphtholsulfonic acid.

$$\frac{d(\mathrm{Az_{NH_2}} + \mathrm{Az_{OH}})}{dt} = (\mathrm{D})(k_{\mathrm{NH_2}}[\mathrm{HORNH_2}] + k_{\mathrm{OH}}[{}^{\ominus}\mathrm{ORNH_2}]) \qquad (12)$$

Since a competitive reaction is involved, it is possible from the ratio of the formed isomeric products to determine the reaction rate ratio:

$$\frac{(\mathrm{Az_{NH_2}})}{(\mathrm{Az_{OH}})} = \frac{k_{\mathrm{NH_2}}[\mathrm{HORNH_2}]}{k_{\mathrm{OH}}[{}^{\ominus}\mathrm{ORNH_2}]} \qquad (13)$$

Because the acidity constant of the ammonium group of a naphthylaminesulfonic acid is of the magnitude 10^{-4} (pK = 4) and because the pK value of naphtholsulfonic acids is about 9, it may be assumed that these constants are of like magnitude in the case of the aminonaphthols. This assumption was confirmed in the case of the constants of H acid (IV). Therefore, at pH values of 9 and above, the concentrations of the two species $[\mathrm{HORNH_2}]$ and $[{}^{\ominus}\mathrm{ORNH_2}]$ are practically the same, whereas in a more acid medium

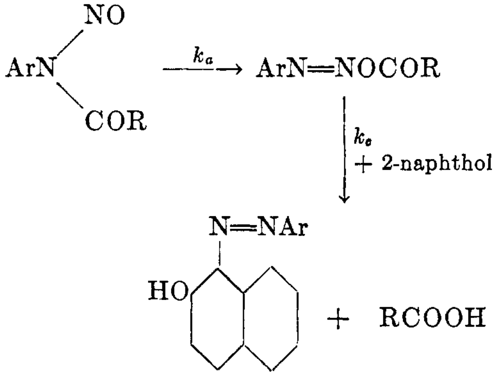
$$[\mathrm{HORNH_2}] \gg [{}^{\ominus}\mathrm{ORNH_2}]$$

It follows that the constant k_{OH} must be considerably greater than $k_{\mathrm{NH_2}}$, because the rate of the hydroxy coupling is at pH > 9 faster than the amino reaction, i.e., the product $k_{\mathrm{OH}}[{}^{\ominus}\mathrm{ORNH_2}]$ must have a larger value than $k_{\mathrm{NH_2}}[\mathrm{HORNH_2}]$ in this pH range. Because the two concentrations are practically the same, the constant k_{OH} therefore must be greater than $k_{\mathrm{NH_2}}$.

The conclusion that $k_{\mathrm{OH}} > k_{\mathrm{NH_2}}$ could be verified by testing the reaction of diazotized *p*-toluidine with 2-naphthol-6-sulfonic acid on the one hand and with 2-naphthylamine-6-sulfonic acid on the other (43). This gives good evidence for the correctness of the kinetic explanation of the aminonaphthol coupling.

X. COUPLING IN NONAQUEOUS MEDIA

There are several experimental indications that the mechanism of the coupling reaction in nonaqueous solutions is not the same as in water. Direct kinetic investigations in this field have not been made. However, the work of Huisgen on the rearrangement of the nitrosoacylanilides is of some importance for the knowledge of the coupling reaction in a nonaqueous medium. He studied the rearrangement of these compounds to the diazoacetates kinetically by colorimetric measurements of the azo compound which is formed from the diazoacetates (28, 29, 31, 32, 33):



(14)

The results show that the coupling is much faster than the rearrangement, i.e., $k_a \ll k_c$. Therefore, the formation of the azo compound can be used for the kinetic investigation of the rearrangement. For the subject of this review the following conclusion is important (29): Huisgen shows that in mixtures of benzene and glacial acetic acid the covalent diazoacetate is in equilibrium with the ionized diazonium acetate, whereas in benzene practically only the diazoacetate is present. Because of the decrease in the rate of formation of the azo compound, which can be observed with increasing content of acetic acid in the solvent, it is inferred that only the diazoacetate is capable of the coupling in this solvent. It seems that this work is a good starting point, not only for investigations concerning the acyl rearrangement of the nitrosoacylanilides but also for the knowledge of the coupling reaction in nonaqueous media and the reactivities of other diazo compounds like the diazonium ions.

The result that diazoacetate has a much higher reactivity than the diazonium acetate is very interesting compared with the conclusions of Wistar, Bartlett, and others concerning the measurements in aqueous medium. There may be some correlation between Huisgen's work and the investigations of Grachev (17).

At the moment it does not seem impossible that there is a different mechanism, depending on the type of solvent. Some unpublished investigations of Huisgen (30) indicate that the rate of coupling reactions with phenol ethers in water is not independent of the acidity, as one would expect by analogy with the data of Bartlett and of Pütter. The reaction rate of phloroglucinol trimethyl ether (1,3,5-trimethoxybenzene) with diazotized 2,4-dinitroaniline increases between pH 1 and 5.

In the opinion of the present author, this is a very promising way in which to attack the problem of the reacting form of the diazo partner as well as the question whether there are different mechanisms of the coupling reaction depending on the solvent and the type of reactants. Additional help toward solving these problems may come from further studies in the field of the structures and equilibria of diazo compounds.

XI. QUANTITATIVE DATA ON THE REACTIVITY OF DIAZO AND COUPLING COMPOUNDS

The reaction rate constants give quantitative data on the electrophilic reactivity of diazo compounds as well as on the nucleophilic reactivity of aromatic amines and phenols. These values provide possibilities of comparison as to the influence exerted on the reactivity of these compounds by other substituents which may be in different positions in the molecule.

Conant and Peterson (3) have already tried to relate the coupling tendency of various diazo compounds to their structure. Because of the dependence of their rate constants on the pH (k_s in equation 1), they represented the results as the "coupling value," which is, by definition, the pH at which the logarithm of the rate constant has the value 1. The coupling value consists of two numbers assigned to the particular diazo and the coupling reactant (A and B, respectively) according to the relationship:

$$A + B = \text{coupling value} \qquad (15)$$

In table 3 some of the experimentally found coupling values are given, together with the value of A for six diazo compounds. It is clearly apparent from these data that the electrophilic reactivity of the diazo compounds will be increased by positive and decreased by negative substitution.

With the new kinetic equations 6 and 7 it is possible to compare the reactivity by means of the rate constants directly, i.e., without introduction of a new constant like Conant's coupling value. The k values (but not the k_s values!) provide a means of studying, for example, the influence exerted on the nucleophilic reactivity of the naphthol molecule by sulfo groups which are in different positions in the naphthalene nucleus. In table 4 this is done with the experimental data of Pütter (35) for couplings with diazotized 4-(acetylamino)aniline-2-sulfonic acid. The evaluation of these results (especially the reasons for the extremely high reactivity of 1-naphthol-8-sulfonic acid) is still to be made.

TABLE 3

Experimentally found coupling values and calculated A values of Conant and Peterson

SUBSTITUENT IN THE DIAZO COMPOUND	VALUE OF A	COUPLING VALUE WITH NAPHTHOLDISULFONIC ACIDS		
		2-Naphthol-3,6-disulfonic acid	2-Naphthol-6,8-disulfonic acid	1-Naphthol-3,8-disulfonic acid
p-NO_2	−2.0			
p-SO_3H	0.0	4.28	6.48	4.90
p-Br	0.0	4.43	6.10	4.77
H	1.1	5.22	7.60	6.37
p-CH_3	1.5	5.60	8.02	6.83
o-OCH_3	2.1	6.22		7.35

TABLE 4

Relative coupling rate constants of diazotized 4-(acetylamino)aniline-2-sulfonic acid with naphtholsulfonic acids (after Pütter)

COUPLING REACTANT	pK	k
1-Naphthol-2-sulfonic acid	9.4	1200
1-Naphthol-3-sulfonic acid	8.5	2
1-Naphthol-4-sulfonic acid	8.2	1
1-Naphthol-5-sulfonic acid	9.0	11
1-Naphthol-8-sulfonic acid	12.6	120,000
2-Naphthol-6-sulfonic acid	9.15	3.2

If, conversely, the same coupling component is coupled with various benzene diazo compounds, substituted in the m- or p-position, it should be possible in this way to calculate the reaction constant ρ of Hammett's formula (19) for the respective coupling reaction. In table 5 this is done in connection with a number of values published by Conant and Peterson. As one may see from these examples, a constant value[5] for ρ is not obtained. This is additional evidence that the explanation of the reactivity is still rather complex for the diazo reactants.

It seems that whereas the fundamental principles concerning the reactivity of the amines and the phenols in coupling in an aqueous medium are today rather clear with regard to the most important points, the kinetics of the diazo reactant still presents many interesting problems.

TABLE 5

ρ-Values for couplings with 2-naphthol-3,6-disulfonic acid at pH = 5.80

DIAZO REACTANT	LOG k_2	VALUE OF ρ
Diazobenzene	1.553	
p-Diazotoluene	1.104	2.64
p-Bromodiazobenzene	2.346	3.42

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[5] Strictly speaking, the rate constants used in calculating the Hammett rho constant should be corrected so as to refer only to the active reactants; hence the values in table 5 are questionable.

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