

KINETICS OF REACTIONS OF 1,2,4-TRIAZOLE-3-DIAZONIUM IONS WITH PHENOL AND WITH HYDROXYL ION

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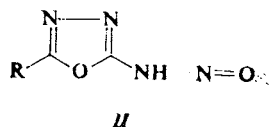
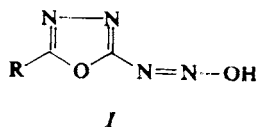
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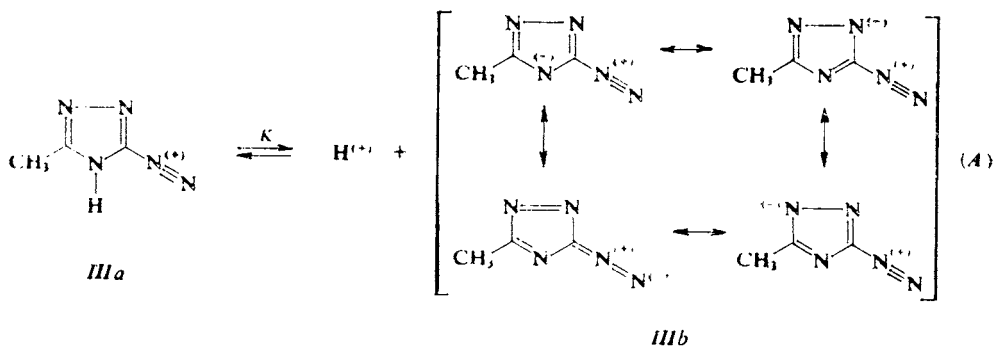
5-Methyl- and 5-phenyl-1,2,4-triazole-3-diazonium ions (*IIIa*, *IIIb*) react with undissociated phenol in diluted hydrochloric acid. At $\text{pH} > 1$ the reactions with phenolate ions become kinetically significant, their bimolecular rate constants approaching those of the diffusion-controlled reactions. At the same time, the diazonium ions are dissociated into the dipolar ions *IIIb* and *IVb*. At $\text{pH} > 4$ (for the phenyl derivative) and $\text{pH} > 5$ (for the methyl derivative), the reaction of the dipolar ions with phenolate ion becomes the main reaction path. The rate constant of the reaction of the dipolar ion *IIIb* with hydroxyl ion ($3 \cdot 10^3 \text{ l mol}^{-1} \text{ s}^{-1}$) is comparable with that of the analogous reaction of benzenediazonium ion, but the reverse reaction of the dipolar ion *IIIb* is slower by about 5 orders of magnitude, and the $\text{p}K_A$ value of the diazo hydroxide formed is higher by about 4 units than that of benzenediazo hydroxide. The high stability of the heterocyclic diazo hydroxide and its low acidity are explained by formation of a strong intramolecular hydrogen bond. In sodium hydroxide solutions, the (*Z*)-diazotate *IIIId* initially formed is transformed into the (*E*)-isomer (the corresponding half-life being about 10 h) which, in contrast to the (*Z*)-isomer, does not practically react with aromatic hydroxy compounds in basic medium. The transformation of the (*E*)-isomer to the diazonium ion is general acid-catalyzed reaction. Transformation of nitrosamine into diazo hydroxide is suggested to be the rate-limiting step of this reaction in solutions of $\text{pH} < 5$.

Five-membered heterocyclic amines with two or more heteroatoms in the nucleus are diazotized to give very reactive diazonium ions. Many of them react with water even in diluted mineral acids to give the corresponding diazo hydroxides (*I*) or isomeric nitrosamines (*II*) which could be isolated in several cases¹. In this respect the heterocyclic diazonium ions differ from the carbo-



cyclic aromatic diazonium ions which react with water or with hydroxyl ions only in basic medium, giving the diazo hydroxides which split off the proton immediately to give the diazotates. The diazotates are more stable in basic medium, hence the reaction mixture contains an only slight amount of diazo hydroxide besides the diazotate and diazonium ion². If the heterocyclic

amine contains an acidic proton bound to the ring nitrogen atom, this proton can be split off from the respective diazonium ion to give a much less reactive dipolar ion (*IIIb*)



The extraordinary stability of the diazo hydroxides derived from five-membered heterocycles is due to strong electron-attracting effect of the ring heteroatoms as well as to intramolecular hydrogen bond.

The equilibrium constant of the reaction of heterocyclic diazonium ion with water was measured³ in the case of one of the most reactive diazonium ions, 5-phenyl-1,3,4-thiadiazole-2-diazonium ion. This ion is converted (5%) to the diazo hydroxide in aqueous sulphuric acid (1.7 mol . l⁻¹), the half-life of the formation of diazo hydroxide being 1 s in H₂SO₄ of 0.1 mol l⁻¹ concentration.

Reactivity of heterocyclic diazonium ions to aromatic hydroxy compounds is so high that in many cases their reaction with phenoxides is diffusion controlled, and — at lower pH values — the diazonium ion reacts with undissociated hydroxy compound⁴. The rate constant of the reaction of 5-methyl-1,3,4-thiadiazole-2-diazonium ion with phenol⁵ in diluted sulphuric acid has the value of 30 l mol⁻¹ s⁻¹. This means that the said diazonium ion reacts by several orders of magnitude faster than the most reactive substituted benzenediazonium ions. In the cases of coupling reactions of the heterocyclic diazonium ions containing an acidic proton in the ring we can consider also the third possibility — reaction of the dipolar ion with phenoxide ion.

This communication deals with coupling kinetics of the diazotized 5-methyl- (*IIIa*) and 5-phenyl-3-amino-1,2,4-triazole (*IVa*) with phenol and with kinetics of the reversible reaction of the 5-methyl derivative *IIIa* with hydroxyl ion.

EXPERIMENTAL

The ¹H and ¹³C NMR spectra were measured with a JNM FX-100 apparatus (JEOL) at 99.602 and 25.047 MHz, respectively. For the measurements, saturated solutions of the compounds in hexadeuteriodimethyl sulphoxide were prepared. The δ(¹H) values are related to hexamethyl-disiloxane, δ(¹³C) are related to the solvent signal (δ 39.60).

The pH values of the reaction solutions were measured by means of a Digital MV 870-pH-Messgerät using a glass and a silver chloride electrodes at 25°C. Standard buffers of pH 1.68 (Forschungsinstitut Meinsberg) and pH 6.96 (Lachema, Brno) were used for calibration.

3-Amino-5-methyl-1,2,4-triazole was prepared by cyclization of acetylamino-guanidine nitrate in sodium carbonate solution⁶, yield 86%, m.p. 144–146°C (ref.⁶ gives m.p. 147–148°C).

3-Amino-5-phenyl-1,2,4-triazole was prepared by reaction of aminoguanidine nitrate with benzimidazole ether hydrochloride in the presence of triethylamine and was isolated as the nitrate⁷. Yield 90%, m.p. 204–208°C (ref.⁸ gives m.p. 208–209°C). The corresponding base was crystallized from water, m.p. 185–187°C (ref.⁸ gives m.p. 186–187°C).

Diazotization of 3-amino-5-methyl-1,2,4-triazole: Solution of 2 g (about 20 mmol) amine in a mixture of 2.5 ml concentrated sulphuric acid and 15 ml water and ice was treated with solution of 1.6 g (23 mmol) sodium nitrite in 5 ml water (added at once). 2.7 ml of this solution of diazonium salt was diluted with 5 ml ice water, whereupon 5 ml sodium hydroxide solution (concentration of 1 mol l^{-1}) was added. The volume was adjusted at 50 ml by addition of ice water, the final concentration of the diazonium salt being about 0.04 mol l^{-1} and pH 3.4. The diazonium salt stock solution prepared in this way (*IIIb*) was kept in the refrigerator, and a part of this solution was diluted with water to required concentration before each measurement.

Preparation of the (E)-diazotate IIIc: 5 ml of fresh solution of the diazonium salt *IIIb* (concentration of about 0.8 mol l^{-1}) was added to 35 ml sodium hydroxide (1 mol l^{-1}) with stirring and cooling at 0°C. Within 2 days, practically all the (*Z*)-diazotate *IIIc* initially formed was transformed into the (*E*)-isomer. The (*E*)-diazotate *IIIc* prepared in this way was kept in darkness at 0°C and was diluted with water to required concentrations before each measurement.

5-Methyl-3-(4-hydroxyphenylazo)-1,2,4-triazole: 3-Amino-5-methyl-1,2,4-triazole (1 g, about 0.01 mol) was dissolved in 10 ml fluoroboric acid. After cooling to 0°C, solid sodium nitrite (0.7 g, 0.01 mol) was added gradually. The diazonium salt solution was added to a cold emulsion of 3 g (0.03 mol) phenol in 10 ml water. After several minutes, the suspension of the azo compound formed was neutralized with saturated sodium carbonate solution, and the excess of phenol was removed by extraction with CCl_4 . The product was collected by suction and recrystallized twice from 50% aqueous acetic acid. Yield 0.9 g (45%), m.p. 255°C with decomposition. For $\text{C}_9\text{H}_9\text{N}_5\text{O}$ (203.2) calculated: 53.19% C, 4.46% H, 34.47% N; found: 52.89% C, 4.30% H, 34.63% N. ^1H NMR spectrum: $\delta(\text{C}_6\text{H}_4)$ 7.84 and 6.99 (AA'XX' quartet, 4 H), $\delta(\text{CH}_3)$ 2.45 (singlet, 3 H). ^{13}C NMR spectrum: δ_3 168.20; δ_5 154.44; δ_1 145.53; δ_0 125.09; δ_m 116.05; δ_p 161.61; $\delta(\text{CH}_3)$ 12.13.

Diazotization of 3-amino-5-phenyl-1,2,4-triazole: 0.5 g (about 3 mmol) 3-amino-5-phenyl-1,2,4-triazole was dissolved in 3 ml solution of sodium hydroxide (1 mol l^{-1}), 0.24 g (3.5 mmol) sodium nitrite was added, and the solution was cooled to 0°C. This solution was added drop by drop to an ice-cold solution of 2.5 ml concentrated sulphuric acid and 2 ml water. After about 10 min, the precipitated dipolar ion of 3-diazo-5-phenyl-1,2,4-triazole (*IVb*) was collected by suction, again dissolved in sodium hydroxide solution (1 mol l^{-1}), and the solution was diluted to final volume of 50 ml with solution of sodium hydroxide (1 mol l^{-1}). For kinetic experiments, the diazotate solution was diluted in the ratio 1 : 3 with hydrochloric acid (0.4 mol l^{-1}). The obtained solution contained $2\text{--}5 \cdot 10^{-3} \text{ mol l}^{-1}$ diazonium salt, the $[\text{H}^+]$ concentration being 0.1 mol l^{-1} .

3-(4-Hydroxyphenylazo)-5-phenyl-1,2,4-triazole: 1 g (4.5 mmol) 3-amino-5-phenyl-1,2,4-triazole nitrate was dissolved in saturated solution of 0.5 g (4.7 mmol) Na_2CO_3 , 0.34 g (4.9 mmol) sodium nitrite was added thereto, and the solution was cooled to 0°C. The solution obtained was added drop by drop to 10 ml sulphuric acid (10 mol l^{-1}) with stirring and cooling at 0°C. The suspension formed was added portionwise to the emulsion of 1.3 g (14 mmol) phenol in 10 ml water. After several minutes, the excess phenol was removed by extraction with CCl_4 , the azo compound was collected by suction and recrystallized twice from acetic acid. Yield 0.4 g (34%), m.p. 301–302°C. From the ^1H NMR spectrum it is obvious that the compound forms a solvate with acetic acid (molar ratio 1 : 1) (nitrogen content calculated 21.53%, found 21.65%). After

5 h drying at 110°C at 300 Pa, the ^1H NMR spectrum of the compound showed the absence of acetic acid. M.p. of the compound 304–305°C. For $\text{C}_{14}\text{H}_{11}\text{N}_5\text{O}$ (265.3) calculated: 63.38% C, 4.18% H, 26.40% N; found: 63.79% C, 4.32% H, 26.67% N, ^1H NMR spectrum: $\delta(\text{C}_6\text{H}_4)$ 7.99 and 7.06 (AA'XX' quartet, 4 H). $\delta(\text{C}_6\text{H}_5)$ 8.25–7.35 (multiplet, 5 H). ^{13}C NMR spectrum: δ_3 168.70; δ_5 158.91; for the phenyl group: δ_i 129.47; δ_o 126.25; δ_m 125.69; δ_p 130.50; for the 4-hydroxyphenyl group: δ_i 145.40; δ_o 129.09; δ_m 116.90; δ_p 164.02.

Kinetic measurements. The following procedure was used for measurement of the coupling rate with phenol in HCl and buffer solutions: In a 10 ml calibrated flask a solution was prepared containing $2 \cdot 10^{-2}$ – $2 \cdot 10^{-3}$ mol l^{-1} phenol and HCl or buffer of required concentration. In the case of buffers, the ionic strength of the solution was adjusted at 0.5 by addition of KCl. 2 ml of this solution was pipetted into a quartz cell located in the tempered cell compartment of a Specord UV VIS spectrophotometer. After reaching the temperature of 25°C, one drop of the diazonium salt solution of $5 \cdot 10^{-3}$ mol l^{-1} concentration was added, and the absorbance was measured at 345 nm (the methyl derivative) or 375 nm (the phenyl derivative). The rate constants k_{obs} were determined from the relation $\log(A_\infty - A_t)$ vs time according to Eq. (1).

$$k_{\text{obs}} \cdot t = -2.303 \log(A_\infty - A_t) + \text{const} \quad (1)$$

In the case of coupling reactions of the methyl derivative with phenoxide ion in NaOH solutions the following procedure was adopted: one drop of the diazonium salt solution (concentration about 10^{-2} mol l^{-1}) was added to 1.8 ml tempered NaOH solution (0.1 – $2.5 \cdot 10^{-2}$ mol $\cdot \text{l}^{-1}$) followed by 0.2 ml phenol solution (0.2 mol l^{-1}). Then the time dependence of the absorbance of the solution was followed at 415 nm, and the rate constants were calculated according to Eq. (1).

Transformation of the (*E*)-diazotate *III*d into the diazonium ion *III*a or the dipolar ion *III*b was followed in the following way: A solution was prepared in a calibrated flask containing diluted hydrochloric acid or chloroacetate or acetate or phosphate buffers ($I = 0.5$) and phenol ($2 \cdot 10^{-2}$ to $2 \cdot 10^{-3}$ mol l^{-1}) or 1,8-dihydroxynaphthalene-3,6-disulphonic acid (10^{-3} mol l^{-1}), respectively. This solution (2 ml) was tempered at 25°C, and a drop of $5 \cdot 10^{-3}$ mol l^{-1} solution of (*E*)-diazotate *III*d was added thereto, whereupon the time dependence of absorbance was measured at 345 nm (for phenol) or 500 nm (for 1,8-dihydroxynaphthalene-3,6-disulphonic acid). The rate constants were obtained from Eq. (1).

The rate of the reaction of the dipolar ion *III*b with hydroxyl ion was measured with a Durrum Gibson Stopped Flow spectrophotometer at 300 nm at 25°C. The reaction was realized by mixing of the dipolar ion solution ($c \sim 5 \cdot 10^{-4}$ mol l^{-1} , pH 3.2) placed in one reservoir of the spectrophotometer with the buffer solution (phosphate, borax, carbonate) or NaOH placed in the other reservoir. The reaction half-lives were read from the oscilloscope of the spectrophotometer, and the rate constants were obtained from the relation $k_{\text{obs}} = 0.693/t_{1/2}$.

The acid–base equilibrium constant of the diazonium ion *III*a was determined by measuring the absorbances of the diazonium ion solutions ($c \sim 8 \cdot 10^{-5}$ mol l^{-1}) in diluted hydrochloric acid at 280 nm at 25°C using a Zeiss VSU 2P spectrophotometer. The equilibrium constant was calculated from the relation (2), where A^0 and A^+ mean the absorbances of the dipolar ion *III*b and diazonium ion *III*a, respectively, and A stands for the absorbance of the solution measured.

$$K = ((A^0 - A)/(A - A^+)) \cdot [\text{H}^+] \quad (2)$$

The $\text{p}K_{\text{A}2}$ value of the (*Z*)-diazo hydroxide *III*c was determined by measuring the absorbance of the mixture of *III*c and *III*d at 278 nm at 25°C in phosphate buffers and NaOH solutions (pH 11.3–13) using the Zeiss VSU 2P spectrophotometer: 0.2 ml solution of the dipolar ion

IIIb ($c \sim 10^{-3} \text{ mol l}^{-1}$) was injected into 1.8 ml buffer solution in a quartz cell, and absorbances of the solution were measured in short time intervals. The $\text{p}K_{A2}$ value was calculated from the absorbances obtained by extrapolation to the time of mixing of the solutions. The equilibrium constant K_2 was calculated from Eq. (3)

$$K_2 = ((A_{\text{OH}} - A)/(A - A_0)) \cdot 10^{-\text{pH}}, \quad (3)$$

where A_0 means the absorbance of the (*Z*)-diazotate *IIId* found by measurement in NaOH solution of concentration of 0.5 mol l^{-1} , A_{OH} means the absorbance of (*Z*)-diazo hydroxide *IIIc* which could not be obtained by direct measurement, because at $\text{pH} < 11.5$ the transformation of diazo hydroxide *IIIc* into the dipolar ion *IIIb* becomes increasingly significant: hence, this value had to be obtained by the trial-and-error method. The error introduced by this method of determination of A_{OH} is not large, because the absorbance A_{OH} of the diazo hydroxide *IIIc* does not much differ from that of the dipolar ion *IIIb* at the wavelength of 278 nm. A means the absorbance of the mixture of the (*Z*)-diazo hydroxide *IIIc* and (*Z*)-diazotate *IIId* in the buffer.

RESULTS AND DISCUSSION

Preparation of the Diazonium Salts

Both 5-amino-3-methyl-1,2,4-triazole and the diazonium ion *IIIa* are very well soluble in diluted mineral acids, hence the diazonium salt solution can be prepared in usual way. The diazonium salts derived from substituted amino-1,2,4-triazoles react with chloride ion to give the substituted chlorotriazoles⁹, and, therefore, the diazotization was carried out in sulphuric acid for the kinetic experiments. The diazonium salt prepared in this way was decomposed within several days. At higher pH values the diazonium ion *IIIa* is transformed into the dipolar ion *IIIb* ($\text{p}K_A$ 1.50). The dipolar ion prepared by partial neutralization of the diazonium ion to pH 3.4 is much more stable than the diazonium ion itself, its concentration being decreased by decomposition by as little as several per cent only after a week at 0°C. Therefore, we used the solution of the dipolar ion *IIIb* for the investigation of its coupling with phenol and phenoxide ion.

The preparation of 3-diazo-5-phenyl-1,2,4-triazole is more complicated, because both the starting amine and its salts (nitrate, sulphate, fluoroborate) are very little soluble in water, and the diazonium salt *IVa* formed by the diazotization is separated from the solution in the form of little soluble dipolar ion *IVb*. Therefore, the inversed method was used for the diazotization of 3-amino-5-phenyl-1,2,4-triazole, the solution of sodium salt of the triazole and NaNO_2 being added to diluted H_2SO_4 .

Dissolution of the diazonium salt *IIIa* in sodium hydroxide solution (1 mol l^{-1}) results in formation of the (*Z*)-diazotate *IIId* which is transformed into the (*E*)-diazotate *IIId* with the half-life of 10 h. The (*E*)-diazotate *IIId* exhibits almost unlimited stability at 0°C, its concentration being decreased by only several per cent after several weeks. The difference in stability of the diazotates *IIId* consists in that the

(*Z*)-diazotate and the dipolar ion *IIIb* stand in a rapid equilibrium even in borax buffer, the latter species being able to couple rapidly with phenoxide ion. The (*E*)-diazotate is transformed into the diazonium ion able of coupling in acid medium only. In the case of the phenyl derivative the stable (*E*)-diazotate was not formed even after three days, the (*Z*)-diazotate being decomposed (more than a half) during the same period.

Coupling Kinetics with Phenol and Phenoxide Ion

The reactions of the diazonium ions *IIIa* and *IVa* with phenol give 3-(4-hydroxyphenylazo)-5-methyl-1,2,4-triazole and 3-(4-hydroxyphenylazo)-5-phenyl-1,2,4-triazole, respectively. The $\delta(^{13}\text{C})$ chemical shifts of the carbon atoms of 5-hydroxyphenylazo group are very close to those of the same carbon atoms of 4-hydroxyazobenzene¹⁰. Therefrom it follows that the two compounds exist exclusively in azo form, as it is the case with 4-hydroxyazobenzene.

The kinetic experiments with reaction of the ions *IIIa* and *IVa* (or *IIIb* and *IVb*) were carried out with at least tenfold excess of phenol. The reactions proceeded as pseudomonomolecular reactions, and the found time dependences of $\log(A_\infty - A_t)$ were linear at least up to 2–3 reaction half-lives. The found k_{obs} values (s^{-1}) were directly proportional to phenol concentration at any given pH value. Dividing of k_{obs} by the phenol concentration gave the stoichiometric rate constants k_s ($1 \text{ mol}^{-1} \text{ s}^{-1}$).

The coupling kinetics have been followed in the media of diluted HCl (0.01 to 4.5 mol l^{-1}), sulphate, chloro acetate, acetate, and phosphate buffers at 25°C. The reactions of the diazonium ions with phenol produce the corresponding azo compounds as the only products, which was confirmed by identity of electronic spectra of the reaction products obtained after the couplings were finished with those of specially prepared solutions of the identified azo compounds of the same concentrations in the same media. The k_s rate constants were independent of the buffer concentrations. The found dependences of $\log k_s$ on pH and H_0 are given in Fig. 1. These dependences can be divided in several sections:

a) At the HCl concentrations above 1 mol l^{-1} predominant part of the diazonium ion is present in the form of *IIIa* and *IVa*, respectively. The main reaction path consists in the coupling of this ion with undissociated phenol. The k_s values should be independent of acid concentration in this region. The probable reason of the increase in k_s with increasing acid concentration will be explained below.

b) With decreasing acid concentration (pH > 0 for the diazonium ion *IVa*, pH > 1 for *IIIa*) the dissociation of the diazonium ions into much less reactive dipolar ions *IIIb* and *IVb*, respectively, becomes increasingly significant, and the k_s value is decreased in the case of the phenyl derivative.

c) At $\text{pH} > 1$ the other reaction path gradually becomes significant, *viz.* the reaction of the diazonium ions *IIIa* and *IVa* with phenoxide ion, which causes a slight increase in k_s in the case of the methyl derivative. This path becomes predominant at $\text{pH} > 2$. The k_s value becomes pH-independent, because the concentration decrease of the diazonium ions *IIIa* and *IVa* is compensated by increasing concentration of phenoxide ions.

d) At $\text{pH} > 4$ the dipolar ions *IIIb* and *IVb* begin to be kinetically significant (in this medium their concentrations are several orders of magnitude higher than those of the diazonium ions *IIIa* and *IVa*) in the reaction with phenoxide ions, and the coupling rate increases. Dependence of $\log k_s$ on pH approaches the unit slope.

The whole dependence of k_s on $[\text{H}^+]$ can be described by Eq. (4). The three terms in this equation correspond to the cases a), c), d). The equilibrium constants K_A and K are defined by Eqs (5) and (6), respectively. The k_0 and k_2^+ constants mean the coupling rate constants of the diazonium ion *IIIa* (*IVa*) with phenol and phenoxide ion, respectively, and k_2 stands for the rate constant of the dipolar ion *IIIb* (*IVb*) with phenoxide ion. The values of the rate constants k_0 , k_2^+ ,

$$k_s = (k_0[\text{H}^+] + k_2^+K_A + k_2KK_A/[\text{H}^+])/([\text{H}^+] + K) \quad (4)$$

$$K_A = [\text{C}_6\text{H}_5\text{O}^-][\text{H}^+]/[\text{C}_6\text{H}_5\text{OH}] \quad (5)$$

$$K = [\text{IIIb}][\text{H}^+]/[\text{IIIa}] \quad (6)$$

and k_2 (Table I) were calculated on the basis of comparison of the experimental k_s values with those calculated from Eq. (4). For phenol the value $K_A = 10^{-10}$ was

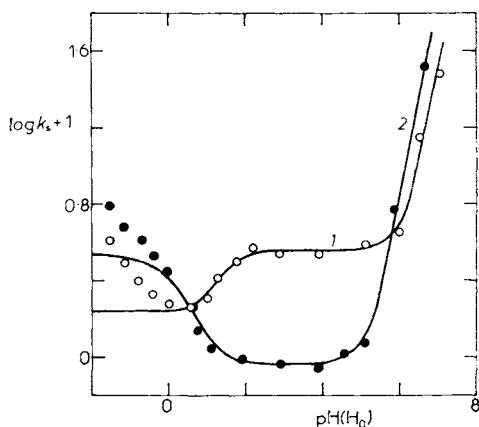


FIG. 1

Dependence of logarithm of stoichiometric rate constant k_s ($\text{l mol}^{-1} \text{s}^{-1}$) of coupling reaction of diazonium ions with phenol and with phenoxide ion on pH and H_0 . The solid lines were calculated according to Eq. (4) from the values given in Table I. 1 5-Methyl-1,2,4-triazole-3-diazonium ion; 2 5-phenyl-1,2,4-triazole-3-diazonium ion

used¹¹. The K value of the diazonium ion *IVa* could not be found experimentally, because this ion is decomposed in diluted hydrochloric acid. Besides that, the difference between the spectra of compounds *IVa* and *IVb* is not distinct. Therefore the K value and, hence, the k_2^+ are determined less accurately for the phenyl derivative than for the methyl derivative.

The solid lines in Fig. 1 were calculated from Eq. (4) with the use of the constants given in Table I. In the case of the both diazonium ions the coupling rate is higher than that according to the calculated dependence at $H_0 < 0$. This acceleration is probably due to formation of hydrogen bonds to nitrogen atoms of the heterocycle and, hence, to increased reactivity of the diazonium ions. A similar acceleration was also found in coupling of 2-diazo-5-methyl-1,3,4-thiadiazole with phenol⁵. Another possible explanation of the acceleration of the reaction in the medium of dilute hydrochloric acid is as follows: Diazotized aminotriazoles react with HCl to give chlorotriazoles⁹. In such case, the k_{obs} rate constant would represent a sum of the coupling rate constant and rate constant of nucleophilic substitution of the diazonium group by chlorine. In order to verify this possibility, we investigated separately the decompositions of the diazonium ion *IIIa* in 1–5 mol l⁻¹ HCl, and we found that the decomposition rate was lower by several orders of magnitude than the coupling rate with phenol at the same conditions.

In strongly acidic medium with $\text{pH} < 1$ the coupling of the phenyl derivative *IVa* is faster than that of the methyl derivative *IIIa*, because phenyl group increases the diazonium ion reactivity by its polar effects to a higher extent than methyl group. At $\text{pH} \sim 0.6$ the two dependences of $\log k_s$ on pH intersect each other (Fig. 1), and at $\text{pH} > 2$ the methyl derivative *III* reacts about $4 \times$ faster than the phenyl derivative *IV*. In this region, the main reaction path consists in coupling of the diazonium ions *IIIa* (*IVa*) which are in equilibrium with the dipolar ions *IIIb* (*IVb*). The value of the k_2^+ rate constant of the phenyl derivative *IVa* is about $5 \times$ higher than that of the methyl derivative *IIIa*, but, on the contrary, the concentration of the

TABLE I

Rate constants k_0 , k_2^+ , k_2 (l mol⁻¹ s⁻¹) of coupling reactions of the diazonium ions *III* and *IV* with phenol and dissociation constants K (mol l⁻¹) of the diazonium ions *IIIa* and *IVa* into the dipolar ions *IIIb* and *IVb*

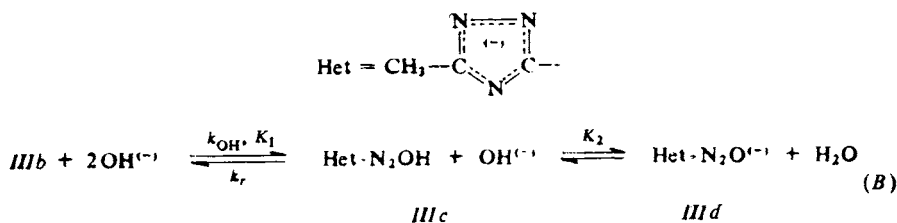
Diazonium ion	k_0	k_2^+	k_2	K
<i>III</i>	0.175	$1.0 \cdot 10^8$	$3.0 \cdot 10^3$	$3.15 \cdot 10^{-2}$
<i>IV</i>	0.35	$5 \cdot 10^8$	$7 \cdot 10^3$	0.6

diazonium ion *IVa* is about $20 \times$ lower. The result is that the reaction of the diazonium ion *IIIa* is about $4 \times$ faster. This situation is due to the fact that the phenyl group strongly increases acidity of the NH proton in the heterocycle,* but the reactivity of the distant diazonium group is increased much less. The reaction of the dipolar ion *IVb* with phenoxide ion begins to make itself felt (as the main reaction path) sooner than in the case of the methyl derivative *IIIb*, because the ratio $[IVb] : [IVa]$ is $20 \times$ higher than the corresponding ratio for the methyl derivative.

The ratio of rate constants k_2^+/k_2 is $3.3 \cdot 10^4$ and $7 \cdot 10^4$ for the methyl and phenyl derivatives, respectively. It means that the diazonium ions are more than four orders of magnitude more reactive than the corresponding dipolar ions. The rate constant k_0 of the diazonium ion *IIIa* is about $200 \times$ smaller than the coupling rate constant of 2-diazo-5-methyl-1,3,4-thiadiazole with phenol⁵. Phenoxide ion reacts with the diazonium ion by about 9 orders of magnitude faster than the undissociated phenol ($k_2^+/k_0 = 5.7 \cdot 10^8$ and $1.4 \cdot 10^9$ for the methyl and phenyl derivatives, respectively). The rate constants k_2^+ of the reactions of the diazonium ions *IIIa* and *IVa* with phenoxide ion approach the rate values of the diffusion-controlled reaction¹³ ($k \sim 10^9$ to $10^{10} \text{ l mol}^{-1} \text{ s}^{-1}$). In this respect the diazonium ions *IIIa* and *IVa* resemble the most reactive diazonium ions¹⁴.

Study of the Reversible Reaction of Dipolar Ion *IIIb* with Hydroxyl Ion**

3-Diazo-5-methyl-1,2,4-triazole undergoes the reactions given by Eq. (B) in basic media.



The formation of (*Z*)-diazo hydroxide *IIIc* by reaction of the dipolar ion *IIIb* with hydroxyl ion was studied in borax, carbonate, and phosphate buffers and the dilute NaOH solutions in the pH range 9.2–12.6. The rate constants k_{obs} obtained by the stopped-flow method were plotted against the hydroxyl ions activities, and the found dependence was linear. The dependence of k_{obs} vs a_{OH} can be linear, if one of the two following simplifying presumptions is fulfilled at different a_{OH} values:

* A similar acidity difference was also found between 3-methyl- and 3-phenyl-1,2,4-triazole¹².

** The analogous reactions of the phenyl derivative *IVb* could not be followed, because the (*Z*)-diazo hydroxide *IVc* is decomposed very rapidly.

a) In the borax and carbonate buffers the final reaction mixture only contains the dipolar ion *IIIb* and the (Z)-diazo hydroxide *IIIc*. The diazotate *IIId* is practically absent. At this conditions the found rate constant k_{obs} is given by Eq. (7).

$$k_{\text{obs}} = k_{\text{OH}} \cdot a_{\text{OH}} + k_r \quad (7)$$

The intercept at the y axis of the plot of k_{obs} vs a_{OH} gives the value of the rate constant k_r of the reverse reaction, and the slope gives the k_{OH} value.

b) In the phosphate buffers and solutions of sodium hydroxide the dissociation of the (Z)-diazo hydroxide *IIIc* into (Z)-diazotate *IIId* becomes increasingly significant (the value of the dissociation constant of the (Z)-diazo hydroxide $\text{p}K_{\text{A}2} = -\log K_2 + 14$ was found spectrophotometrically to be equal to 11.8). However, the k_{obs} value is not practically affected by this dissociation, because k_r is negligible as compared with $k_{\text{OH}} \cdot a_{\text{OH}}$ ($k_{\text{obs}} \approx k_{\text{OH}} \cdot a_{\text{OH}}$). The found values of the rate and equilibrium constants k_{OH} , k_r , K_1 , $\text{p}K_1$, $\text{p}K_{\text{A}2}$ are given in Table II along with the corresponding constants for 3-nitro-4-chlorobenzenediazonium ion² and benzenediazonium ion².

The K_1 values of the dipolar ion *IIIb* and of 3-nitro-4-chlorobenzenediazonium ion are comparable, which, however, is not due to their comparable reactivities but to large stability of the diazo hydroxide *IIIc*, as it follows from comparison of the k_r and $\text{p}K_{\text{A}2}$ values. The (Z)-diazo hydroxide *IIIc* is obviously stabilized by a strong intramolecular hydrogen bond. The reactivity of the dipolar ion *IIIb* to nucleophiles is rather comparable with that of benzenediazonium ion. The two diazonium ions have similar k_{OH} values as well as similar k_2 constants of coupling reaction with phenoxide ion² (the k_2 values of benzenediazonium ion is valid for

TABLE II

Rate and equilibrium constants k_{OH} ($\text{l mol}^{-1} \text{s}^{-1}$), k_r (s^{-1}), K_1 (mol l^{-1}), $\text{p}K_{\text{A}1}$, $\text{p}K_{\text{A}2}$, k_2 ($\text{l mol}^{-1} \text{s}^{-1}$) of the reactions of the dipolar ion *IIIb*, 3-nitro-4-chlorobenzenediazonium ion² (*V*) and benzenediazonium ion² (*VI*) with hydroxyl ion and phenoxide ion

Diazonium ion	k_{OH}	k_r	K_1	$\text{p}K_{\text{A}1}^a$	$\text{p}K_{\text{A}2}^b$	k_2
<i>IIIb</i>	$3 \cdot 10^3$	2.0	$1.5 \cdot 10^3$	10.8	11.8	$3 \cdot 10^3$
<i>V</i>	$7.4 \cdot 10^5$	195	$3.8 \cdot 10^3$	10.4	6.9	$2.3 \cdot 10^3$
<i>VI</i>	$1 \cdot 10^4$	$2.5 \cdot 10^5$	$4 \cdot 10^{-2}$	15.4	8.1	$2.25 \cdot 10^3$

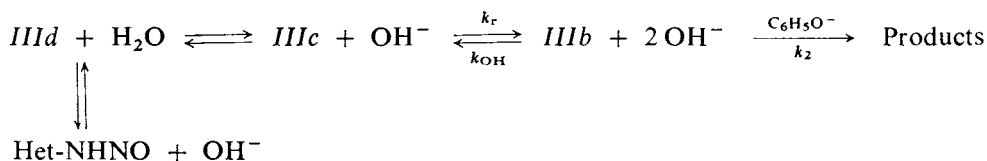
^a $\text{p}K_{\text{A}1} = -\log ([\text{ArN}_2\text{OH}] \cdot [\text{H}^+]/[\text{ArN}_2^+]) = -\log K_1 \cdot K_{\text{H}_2\text{O}}$; ^b $\text{p}K_{\text{A}2} = -\log ([\text{ArN}_2\text{O}^-] \cdot [\text{H}^+]/[\text{ArN}_2\text{OH}])$.

20°C). The strong intramolecular hydrogen bond in (Z)-diazohydroxide *IIIc* has the consequence that its pK_{A2} value is by about 4 units lower than that of benzenediazohydroxide, and the rate of splitting off of OH group, which must be preceded by splitting of the hydrogen bond, is lower by about 5 orders of magnitude.

Coupling of Dipolar Ion IIIb with Phenol in Diluted NaOH Solutions

In contrast to the reactions taking place at low pH values, the first added reagent was the diazonium salt solution followed by phenol, because the rates of the reactions of the diazonium ion with phenoxide and hydroxyl ions are so high that with the reversed order of the operations the reaction rate is largely dependent on the rate of mixing of the components.

The reaction course is given in Scheme 1. The phenoxide



SCHEME 1

ion concentration is (at the hydroxyl ion concentrations used) practically equal to the analytical concentration of phenol, and the concentration of the dipolar ion *IIIb* is negligible as compared with those of the diazotate *III d* and diazohydroxide

TABLE III

The measured (k_{obs}) and calculated rate constants (k , $l \text{ mol}^{-1} \text{ s}^{-1}$) of the coupling reaction of the dipolar ion *IIIb* with phenoxide ion in diluted NaOH solutions

$[C_6H_5OH]$	$[OH^-]$	k_{obs}	k^a
$2 \cdot 10^{-2}$	$6.8 \cdot 10^{-2}$	$2.4 \cdot 10^{-2}$	$3.5 \cdot 10^{-2}$
$2 \cdot 10^{-3}$	$4.6 \cdot 10^{-2}$	$5.8 \cdot 10^{-3}$	$8.9 \cdot 10^{-3}$
		$6.6 \cdot 10^{-3}$	
$2 \cdot 10^{-3}$	$2.1 \cdot 10^{-2}$	$5.3 \cdot 10^{-3}$	$3.8 \cdot 10^{-2}$
		$2.1 \cdot 10^{-2}$	

^a The values of the rate constants k were calculated from Eq. (8).

IIIc. The rate constant of formation of the azo compound can be calculated by means of the Bodenstein steady-state treatment (8).

$$k = (10^{(\text{p}K_{\text{A}2} - \text{pH})} + 1)^{-1} \cdot \frac{k_r \cdot k_2 [\text{C}_6\text{H}_5\text{OH}]_{\text{anal}}}{k_{\text{OH}}[\text{OH}^-] + k_2 [\text{C}_6\text{H}_5\text{OH}]_{\text{anal}}} \quad (8)$$

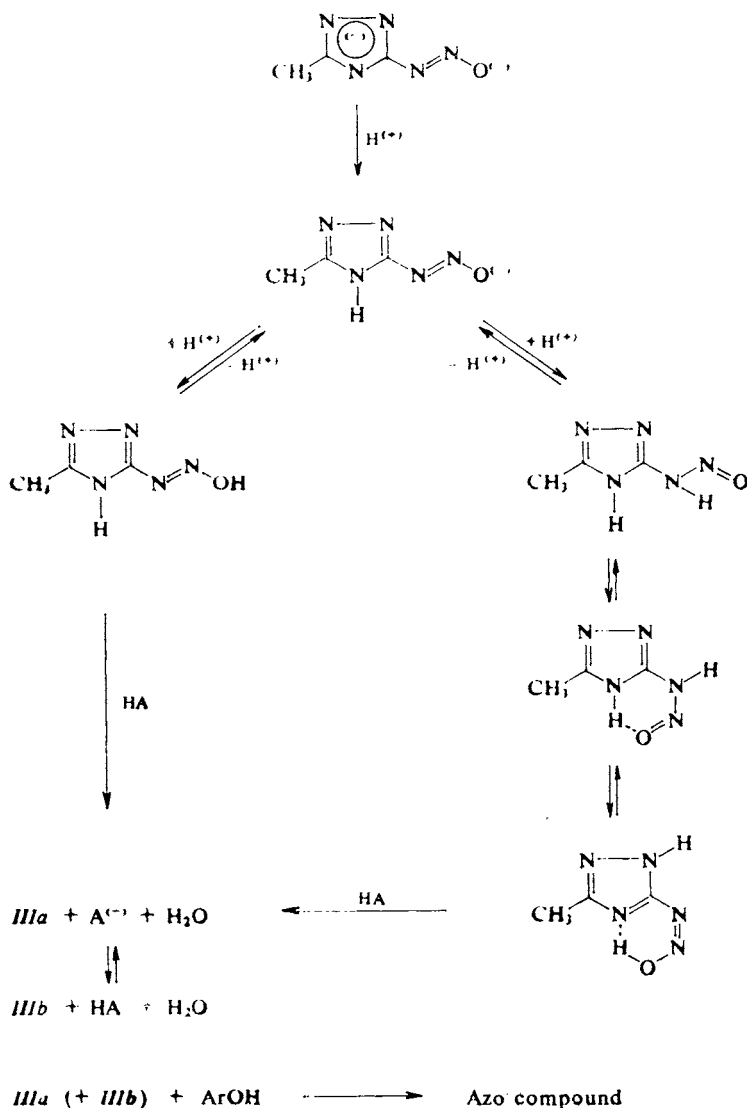
Table III gives the values of the rate constants k found experimentally and those calculated from Eq. (8). The calculated values are higher by about 50%, which can at least partially be due to the fact that the k_r value was determined by the stopped-flow method at $\text{pH} \leq 10$, so that the equilibrium between the diazo hydroxide *IIIc* and nitrosamine Het-NHNO need not to have been established. In such case the k_r values measured would be higher, and the rate constants calculated from Eq. (8) would be increased, too.

Transformations of (E)-Diazotate IIIc into Diazonium Ion IIIa or Dipolar Ion IIIb

The reactions given in Scheme 2 can take place after addition of the solution of (*E*)-diazotate *IIIc* to solution of aromatic hydroxy compound in diluted HCl or buffer solution of $\text{pH} \leq 7$. The protonation of the (*E*)-diazotate *IIIc* at nitrogen atom is practically quantitative, because the $\text{p}K_{\text{A}}$ value of its protonated form is greater than 9*, and $\text{p}K_{\text{A}}$ of the negatively charged (*E*)-diazo hydroxide *IIIc* is about 7–7.5 (in analogy with the (*E*)-benzenediazo hydroxide¹⁵ whose $\text{p}K_{\text{A}} = 7.29$). The rate-limiting step of formation of the diazonium ion *IIIa* (or the dipolar ion *IIIb*) can consist in splitting off of OH group from the (*Z*)- or (*E*)-diazo hydroxides *IIIc*, or in isomerization of the nitrosamine, or in transformation of the nitrosamine into the (*Z*)-diazo hydroxide.

The reactions given in Scheme 2 were followed in diluted HCl, chloro acetate and acetate buffers in an indirect way by trapping the dipolar ion by its reaction with 1,8-dihydroxynaphthalene-3,6-disulphonic acid. In phosphate buffers, phenol was used as the aromatic hydroxy compound, because the coupling reaction with phenoxide ion is very fast in this medium, and, hence, the dipolar ion *IIIb* is not accumulated in the reaction mixture. In acetate buffers the diazonium ion is formed faster, and, on the contrary, the coupling with phenol is slower than in phosphate buffers. Therefore, substantial increase of the diazonium ion concentration took place in the initial phases of the reaction, and the measured time dependence of $\log(A_{\infty} - A_t)$ had the S-shape course characteristic for consecutive reactions. With 1,8-dihydroxy-

* The $\text{p}K_{\text{A}} = 10.73$ for 3-methyltriazole¹²; the $-\text{N}_2\text{O}^{(-)}$ group has a relatively small effect on the acidity.



SCHEME 2

naphthalene-3,6-disulphonic acid the coupling reactions had pseudomonomolecular course even in diluted HCl. In acetate and chloro acetate buffers, the k_{obs} rate constants increased with increasing concentration of the acid component of the buffers (Fig. 2), which indicates that the reaction is subject to general acid catalysis. The

k_{obs} values extrapolated to the zero buffer concentration correspond to the rate constants of the non-catalyzed and the proton-catalyzed reactions (9).

$$k_{\text{extr}} = k^0 + k_{\text{H}^+}[\text{H}]^+ \quad (9)$$

From the dependence of the rate constants k_{obs} on concentration of the acid buffer component it was possible to determine the rate constants of formation of the diazonium ion in the reaction catalyzed by chloroacetic acid ($k = 3.3 \cdot 10^{-2} \text{ l mol}^{-1} \cdot \text{s}^{-1}$) and by acetic acid ($k = 1.1 \cdot 10^{-2} \text{ l mol}^{-1} \text{ s}^{-1}$). From the dependences of k_{extr} and k_{obs} found in HCl solutions on H^+ concentration it was possible to find the values of the proton-catalyzed reaction rate constant ($k_{\text{H}^+} = 1.01 \text{ mol}^{-1} \text{ s}^{-1}$) and that of the non-catalyzed reaction ($k^0 = 4.0 \cdot 10^{-3} \text{ s}^{-1}$). No dependence of the reaction rate on buffer concentration was found in the phosphate buffers.

Figure 3 gives the pH dependences of $\log k_{\text{obs}}$ or $\log k_{\text{extr}}$ (for the reactions in acetate and chloro acetate buffers). The curvature of the dependence at higher pH values

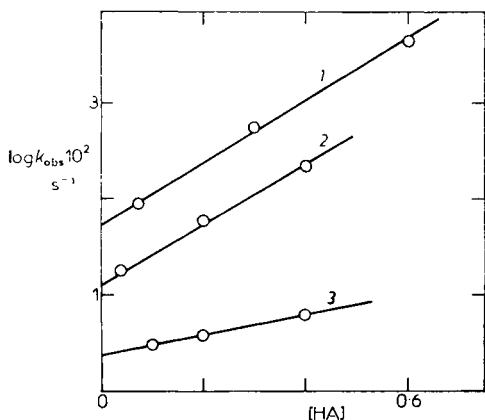


FIG. 2

Dependence of the rate constants k_{obs} (s^{-1}) of formation of the diazonium ion *IIIa* and dipolar ion *IIIb* from the (*E*)-diazotate *IIIc* on concentration of acids in buffers at $I = 0.5$ and at the temperature 25°C . 1 Chloro acetate buffer, $[\text{ClCH}_2\text{CO}_2\text{H}] : [\text{ClCH}_2\text{CO}_2\text{Na}] = 3$; 2 chloro acetate buffer, $[\text{ClCH}_2\text{CO}_2\text{H}] / [\text{ClCH}_2\text{CO}_2\text{Na}] = 1$; 3 acetate buffer, $[\text{CH}_3\text{CO}_2\text{H}] / [\text{CH}_3\text{CO}_2\text{Na}] = 1$

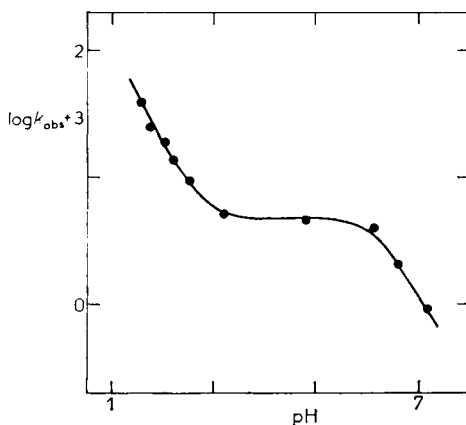


FIG. 3

pH Dependence of logarithm of the rate constants k_{obs} and k_{extr} of formation of the diazonium ion *IIIa* and dipolar ion *IIIb* from the diazotate *IIIc* (for the reactions in chloro acetate and acetate buffers)

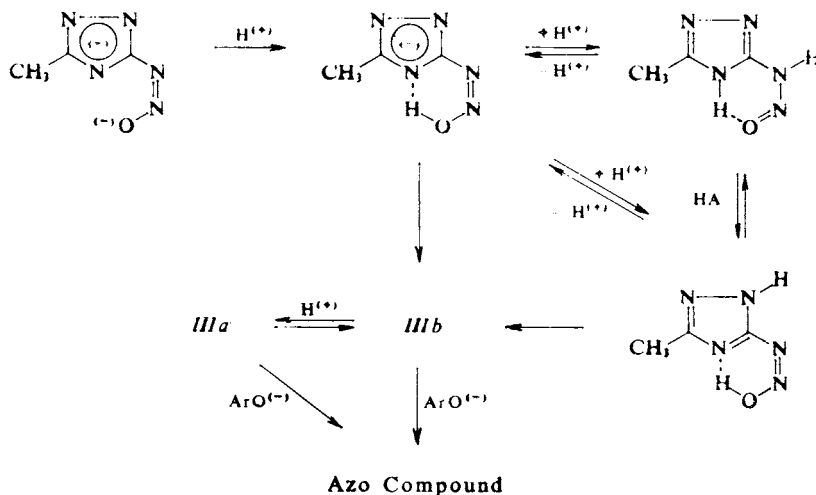
can be due to a change in the rate-limiting step or to an acid-base equilibrium. The latter possibility is more probable, because the value pK_A 6.5 found from the dependence in Fig. 3 corresponds to dissociation of (*E*)-diazohydroxides into (*E*)-diazotates². At lower pH values the reaction is subject to general acid catalysis, which most probably excludes the isomerization of nitrosamines to be the rate-limiting step. Splitting of (*E*)-diazohydroxide cannot be considered the rate-limiting step either, because the k_{obs} value is (in the region of pH independence) only $4 \times$ lower than the splitting rate of (*E*)-benzenediazohydroxide¹⁶ and, generally, the splitting rate decreases rapidly with introduction of electron-withdrawing substituents ($\rho = -2.6$)¹⁶. The triazole ring attracts electrons much more strongly than benzene ring, which is also obvious from comparison of the coupling rate constants with phenoxide ion.

The rate-limiting step consists most probably in splitting off of OH group from the (*Z*)-diazohydroxide which has been in equilibrium with the nitrosamine and (*Z*)-diazotate. The formation of diazonium ions from (*Z*)-diazohydroxides represents a general acid-catalyzed reaction, and the found values² of the Brønsted coefficient $\alpha \sim 0.2$ are similar to those in the case studied.

If our presumptions are correct, the same rate constants have also to be obtained in the case of addition of the freshly prepared (*Z*)-diazotate (instead of (*E*)-diazotate) to solution of buffer and aromatic hydroxy compound. But, after the addition of (*Z*)-diazotate, the reaction proceeded in two steps of considerably different rates: Within 2–3 seconds after mixing with acetate buffer, about 20% of the starting (*Z*)-diazotate reacted to the corresponding azo compound, whereas further azo product was formed with a half life of about 120 s. The rate constants measured for the slower reaction were practically identical with k_{obs} of the transformation of the (*E*)-diazotate into diazonium ion in the same medium. In phosphate buffers (pH ~ 7), the half life of the slower reaction was about 10 s, whereas in borax buffer practically all diazotate reacted immediately to the azo compound. The results found can be explained by Scheme 3.

In borax buffers the reaction mixture predominantly contains the negatively charged (*Z*)-diazohydroxide *IIIc* (in a rapid equilibrium with the neutral form of (*Z*)-diazohydroxide *IIIc* and neutral form of nitrosamine) which reacts within about 2 s to the azo compound *via* the dipolar ion *IIIb*. In acetate buffers a mixture of the neutral nitrosamine and neutral (*Z*)-diazohydroxide *IIIc* is formed immediately, the two species being in equilibrium with a slight amount of the negatively charged (*Z*)-diazohydroxide *IIIc*. The neutral (*Z*)-diazohydroxide rapidly and irreversibly splits off OH group with formation of the diazonium ion which reacts with 1,8-dihydroxynaphthalene-3,6-disulphonic acid to give the corresponding azo compound. This reaction is finished within several seconds. In the subsequent phase there takes place the slower, rate-limiting transformation of the nitrosamine into diazohydroxide, and the latter species, again, splits off OH group to give the diazonium ion. This

transformation of nitrosamine into diazo hydroxide can be catalyzed by the proton (at $\text{pH} < 3$), hydroxyl ion (at $\text{pH} > 6$) as well as by carboxylic acids. In acetate buffers of $\text{pH} \leq 5$ the second slow reaction phase involves establishment of the equilibrium with (*E*)-diazo hydroxide and (*E*)-diazotate, so that the reaction course and the coupling rate are the same as in the cases starting from the (*E*)-diazo hydroxide *III d*.



SCHEME 3

So far the available literature has given no case in which the transformation of nitrosamine into diazo hydroxide would represent the rate-limiting step of formation of diazonium ion from diazotate. Thus, although this reaction mechanism agrees with experimental findings, it must only be considered a working hypothesis in further studies of heterocyclic diazonium compounds.

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