

KINETICS AND MECHANISM OF DIAZO COUPLING. XX.*

COUPLING KINETICS
OF SUBSTITUTED BENZENEDIAZONIUM IONS
WITH SUBSTITUTED ω -METHYLGLYOXAL PHENYLHYDRAZONES

V. MACHÁČEK, O. MACHÁČKOVÁ and V. ŠTĚRBA

*Department of Organic Chemistry,
Institute of Chemical Technology, Pardubice*

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The substituted ω -methylglyoxal phenylhydrazones in the form of conjugate bases react with diazonium salts at $\text{pH} > 5$. The respective overall coupling rate is higher than that of the same diazonium salt with acetone at the same pH and substrate concentrations by 7 orders of magnitude. The logarithms of the coupling rate constants of anions of the hydrazones with *p*-sulfobenzenediazonium ion correlate satisfactorily with the Hammett σ constants (or σ^- in the case of *p*-nitro derivative). On the contrary, the correlation of $\text{p}K_a$ of the substances mentioned with σ as well as σ^- constants is very poor, especially so in the case of *p*-methyl and *p*-methoxy derivatives. This fact is explained by the existence of *syn* and *anti* forms differing considerably in their acidities. Very good linear relations having the slopes $\rho = 2.62$ and 2.73 have been found when correlating $\log k$ of coupling of substituted benzenediazonium ions with anions of ω -methylglyoxal *p*-tolyl- and *p*-nitrophenylhydrazones respectively with σ constants.

When studying the coupling kinetics of substituted benzenediazonium ions with acetone¹, we found that the reaction was of the first order with respect to acetone and diazonium ion in the whole course. However, 1,5-diaryl-3-acetylformazane and not the expected ω -methylglyoxal arylhydrazone was the product of the reaction. As the formation of the formazane necessitates two molecules of diazonium ions, we explained the kinetic dependence found in that way that a reaction of the diazonium ion with acetone giving the hydrazone is the rate determining step, whereas the subsequent reaction producing the formazane is far quicker.

One of the aims of this work was to confirm the correctness of the abovementioned explanation by direct measurements of rates of reactions of substituted benzenediazonium ions with substituted ω -methylglyoxal phenylhydrazones. At the same time we wanted to ascertain the pH dependence of the reaction rate (and hence to tell whether the neutral hydrazone molecule or its conjugate base reacts) and the influence of substituents of the benzenediazonium ion and ω -methylglyoxal phenylhydrazone on the reaction rate.

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EXPERIMENTAL

Reagents

The preparation of the substituted ω -methylglyoxal phenylhydrazones was described in our previous paper¹. In addition to it ω -methylglyoxal *m*-chlorophenylhydrazone (m.p. 130–132°C; for $C_9H_9N_2ClO$ (196.6) calculated: 54.97% C, 4.61% H, 14.25% N; found: 55.27% C, 4.73% H, 13.95% N) and ω -methylglyoxal *m*-tolylhydrazone (m.p. 112–114°C; for $C_{10}H_{12}N_2O$ (176.2) calculated: 68.16% C, 6.86% H, 15.90% N; found: 68.43% C, 7.05% H, 15.78% N) were prepared in the same way.

Stock solutions of the hydrazones (concentrations $5 \cdot 10^{-5}$ – $5 \cdot 10^{-4}$ mol/l) were prepared as follows: The weighed amount of the substance was dissolved in a minimum amount of chloroform directly in the calibrated flask. After an addition of about a half volume of water the mixture was heated at 50°C and shaken until the chloroform evaporated. The volume was then adjusted at 20°C. The buffer stock solutions were prepared by dissolving the p.a. chemicals in deionized water which was redistilled with potassium permanganate and alkali in a glass apparatus. The diazonium salt solutions (concentration $5 \cdot 10^{-3}$ mol/l) were prepared in the way described previously^{2,3}.

Kinetics Measurements

The kinetics measurements were carried out at $20 \pm 0.2^\circ\text{C}$ and ionic strength 0.1. Two methods were adopted for the reaction rate determination:

1. The reaction course of the coupling of substituted ω -methylglyoxal phenylhydrazones with *p*-sulphobenzendiazonium chloride giving well water-soluble products was followed with the use of Unicam SP 800 apparatus. To a thermostated phenylhydrazone solution in a buffer of ionic strength 0.1 such an amount of the diazonium salt was added to make its concentration equal $2 \cdot 10^{-5}$ mol/l. A part of the solution was placed into a 3 cm quartz cell located in the thermostated cell holder of the spectrophotometer. The same solution without the diazonium salt was placed in the reference cell. At definite time intervals a 100 nm wide section of spectrum was recorded in the region of the λ_{max} of the formazane formed (about 450 nm). In most cases the hydrazone concentration was more than $10\times$ greater than that of the diazonium ion. The rate constants were calculated from the Eq. (1) In the case of *p*-nitrophenylhydrazone a concentration ratio of hydrazone and diazonium ion 2 : 1 was used. Eq. (2) was used for graphical calculation of rate constants: B_0 and A_0 are the initial concentrations of hydrazone and diazonium ion respectively, E_t and E_∞ are the extinctions of the formazane at a time t and $t = \infty$ respectively.

$$k't = -2.303 \log (E_\infty - E_t) + \text{const.} \quad (1)$$

$$k't = (1/(B_0 - A_0)) 2.303 \log ((2E_\infty - E_t)/(E_\infty - E_t)) + \text{const.} \quad (2)$$

2. The products formed during the coupling reactions of the substituted ω -methylglyoxal phenylhydrazones with the other diazonium ions are practically insoluble and separate from the solution in the course of kinetic experiments already. In these cases the reaction was followed by ascertaining the decrease of the diazonium salt. At definite time intervals 20 ml samples were withdrawn and added to 5 ml $5 \cdot 10^{-3}\text{M}$ 1,8-dihydroxynaphthalene-3,6-disulfonic acid solution or 20 ml $1 \cdot 10^{-3}\text{M}$ 2-amino-5-hydroxynaphthalene-7-sulfonic acid solution (in the case of *p*-methyl- and unsubstituted benzenediazonium chlorides) placed in 50 ml calibrated flasks. After addition of 5 ml 2.5M-HCl, 5 ml acetone and eventually water (adjusting of the volume) the

solutions were filtered into dry flasks. The extinction of the solutions was measured in 3 cm quartz cells at 505 nm (495 nm in the case of dyestuffs from 2-amino-5-hydroxynaphthalene-7-sulfonic acid⁴) using a VSU-2P apparatus (Zeiss, Jena). The reactions half-lives of couplings of *m*-nitrobenzenediazonium chloride with ω -methylglyoxal *p*-tolylhydrazone were shorter than 1 minute. In this case 1 ml $4 \cdot 10^{-4}$ M diazonium salt solution was injected in 20 ml hydrazone solution in buffer under stirring and after a definite time interval the reaction was stopped by injecting 5 ml $5 \cdot 10^{-3}$ M 1,8-dihydroxynaphthalene-3,6-disulfonic acid solution. About 8 experiments having different time intervals were carried out to determine one rate constant in this way. The further working up of the samples was identical to the previous case. As an at least tenfold excess of the hydrazone (as compared to the diazonium ion) was used in all the cases, the rate constant k' was found graphically from Eq. (3):

$$k't = -2.303 \log (E_t - E_\infty) + \text{const.}, \quad (3)$$

where E_t and E_∞ are the extinctions of the dyestuff formed by coupling of the remaining diazonium salt with 1,8-dihydroxynaphthalene-3,6-disulfonic acid or 2-amino-5-hydroxynaphthalene-7-sulfonic acid at a time t and $t = \infty$ respectively.

pK_a Determination

Spectra of $5 \cdot 10^{-5}$ M solutions of all the prepared substituted ω -methylglyoxal phenylhydrazones were measured in acetate buffer, phosphate buffer (pH 11.4) and 0.1M-NaOH. Isosbestic points were found in all the cases. The extinctions of the conjugate base of the given hydrazone were measured at the respective λ_{\max} found in acetate buffer, in a series of phosphate buffers, and potassium hydroxide (ionic strength was adjusted at 0.1 by addition of 1M-KCl). The extinction of the pure base was determined by measuring in 1M and 2M-KOH. The extinctions were measured immediately after mixing the thermostated solutions of the buffer and hydrazone in 1 cm quartz cell at 20°C using a VSU-2P apparatus (Zeiss, Jena). The measurements were carried out with fresh hydrazone solutions, after 3–4 days, and after about 3 weeks. The differences found were within experimental errors. The pK_a calculation was carried out according to Eq. (4). E_K and

$$pK_a = \text{pH} + \log ((E_B - E)/(E - E_K)) \quad (4)$$

E_B are the extinctions of the hydrazone and its conjugate base respectively and E is the extinction measured in phosphate buffers or diluted potassium hydroxide solution. pH Values were determined with the use of a PHM 4c apparatus (Radiometer, Copenhagen) and a glass (Radiometer type G 202 B) and a saturated calomel electrodes. 0.01M- $\text{Na}_2\text{B}_4\text{O}_7$ was used as a standard.

Spectral Measurements

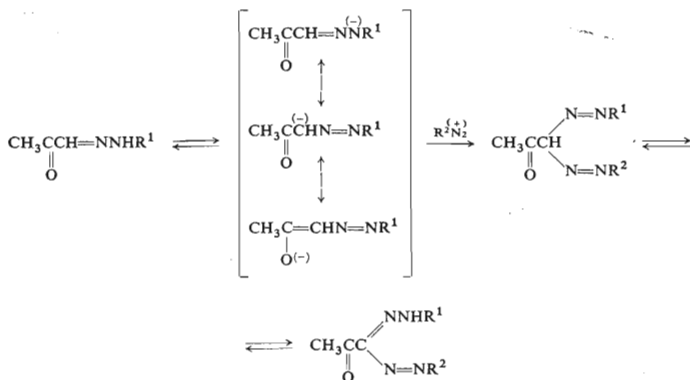
NMR spectra of the substituted ω -methylglyoxal phenylhydrazones were measured in CDCl_3 solution (concentration about 10%) at $25 \pm 2^\circ\text{C}$ using a Tesla BS 487B apparatus at 80 Mcps. Tetramethylsilane was used as the internal standard.

RESULTS AND DISCUSSION

Very good linear relationships were found between $\log (E_\infty - E_t)$ resp. $\log (E_t - E_\infty)$ and the time t up to at least three half-lives in all the cases of measurements of the reaction course of substituted diazonium ions with substituted ω -methylglyoxal

phenylhydrazones except for the reaction of *p*-methyl- and *p*-methoxyphenylhydrazones with *p*-sulfobenzenediazonium ion at pH < 5.5. Also the experiments having the concentration ratio of hydrazone and diazonium ion 2 : 1 show a linear dependence between $\log ((2E_\infty - E_t)/(E_\infty - E_t))$ and time *t* in the whole range studied. The reaction rate found was always of the first order in hydrazone. In the range of pH 6.0 to 7.5 a linear dependence between $\log k_s$ ($k_s = k'/[\text{hydrazone}]$) and pH was found for all the hydrazones, the slope being unity. From these results it follows that, in the pH range given, an equilibrium between the hydrazone and its conjugate base is established rapidly in the first reaction step, and, in a subsequent rate determining step, the conjugate base reacts with diazonium ion giving bisazo compound². As a formazane is the final reaction product, and as neither any intermediate formation nor any deviation from linearity in evaluating the kinetic experiments were observed during the spectral tracing of the reaction, the formation of bisazo compound must be far slower than its rearrangement into formazane.

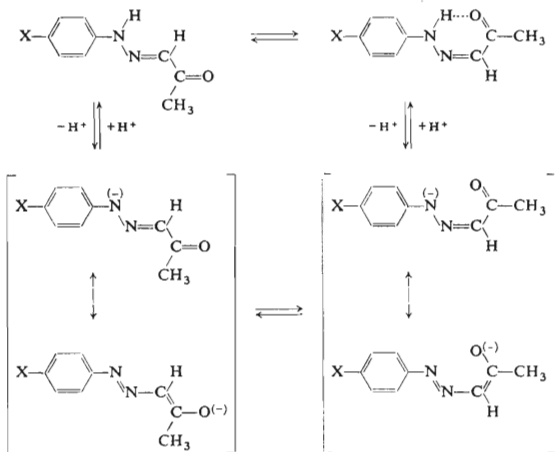
In coupling reactions of benzenediazonium chloride with substituted benzaldehyde phenylhydrazones² the reaction rate was independent of pH in the range of pH 4.0–6.5, a formation of yellow bisazo compounds being observed; these compounds underwent an isomerization into formazanes in the course of reaction. The difference in the behaviour of the both types of hydrazones is obviously due to the presence of an acetyl group which stabilizes strongly the conjugate base of hydrazone, and facilitates the splitting off of the C—H proton of the bisarylazo compound (Scheme 4).



$\text{R}^1, \text{R}^2 = \text{aryl}$

SCHEME 1

The dependence $\log k_s$ vs pH (Fig. 1) diminished gradually when lowering the pH value below about 6. At the same time the formazane amount found in products diminished too. *E.g.* at pH 4.84 the coupling rate found for ω -methylglyoxal *p*-tolylhydrazone with *p*-sulfobenzendiazonium chloride was $3 \times$ greater than it would correspond to the linear dependence on pH, and about 30% only of the expected formazane amount was formed. At a pH ~ 4 the formazane was formed in such a slight amount that the reaction could not be followed by direct spectral methods. When the kinetic experiments were followed by measuring the diazonium salt decrease under the same conditions, the dependence of $\log k_s$ on pH was roughly linear for this range, too (Fig. 1). We cannot yet explain this anomalous dependence and we intend to study the reaction course at pH < 5.5 at a later time.



SCHEME 2

The coupling rate constants (k_s) of substituted diazonium ions with substituted ω -methylglyoxal phenylhydrazones carrying the same substituent as the diazonium ion are greater than the k_s of coupling of these diazonium ions with acetone at the same pH by about 7 orders of magnitude. In the kinetic study of the coupling of acetone with diazonium ions¹ the concentration of acetone was greater than that of diazonium ion by about 4.5 orders of magnitude. Hence it follows that the concentration of the intermediate hydrazone was $100 \times$ smaller than that of diazonium ion in the reaction mixture. At such a small hydrazone concentration the reaction proceeds

as a first order reaction with respect to the diazonium ion (except for the first 1–2%). In this way our previous assumption that the hydrazone formation was the rate determining step¹ was confirmed. To say it more precisely, the rate determining step is the formation of an azo compound of the type $\text{CH}_3\text{C}(\text{O})\text{CH}_2\text{N}=\text{NR}$ (*I*) which splits off the proton rapidly to give the conjugate base of hydrazone which, in turn, reacts with a further molecule of the diazonium ion.

The $\text{p}K_a$ values 11.5–12.5 were found for ω -methylglyoxal phenylhydrazones. As these compounds exist in the hydrazo form predominantly, the respective azo tautomers must be much more acidic ($\text{p}K < 11$). The rate constant k of the reaction of acetoacetanilide ($\text{p}K_a$ 10.68) with water and acetate ion (ref.⁵) is $1.6 \cdot 10^{-1} \text{ min}^{-1}$ and $2.5 \cdot 10^1 \text{ l mol}^{-1} \text{ min}^{-1}$ respectively. As the value of the Brönsted coefficient β is about 0.6 (ref.⁶) for the C-acids of comparable strength, the estimated half-life of the reaction of the azo compound *I* with hydroxyl ion is 0.1–0.01 seconds in borax buffers. Anyway, the proton splitting cannot be the rate determining step.

For the purpose of calculation of bimolecular rate constants of reactions of substituted benzenediazonium ions with conjugate bases of substituted ω -methylglyoxal phenylhydrazones it was necessary to measure the dissociation constants of the hydrazones. The $\text{p}K_a$ values found are given in Table I. From Fig. 2 it is obvious that the correlation between $\text{p}K_a$ values of the substituted ω -methylglyoxal phenylhydrazones and the Hammett σ constants is very poor, the *p*-methoxy derivative

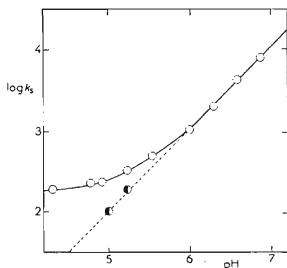


FIG. 1

The pH Dependence of Rate Constant of Reaction of *p*-Sulfobenzene diazonium Chloride with ω -Methylglyoxal *p*-Tolylhydrazone Found from Formazane Increase (O) resp. Diazonium Ion Decrease (●) at 20°C and Ionic Strength 0.1

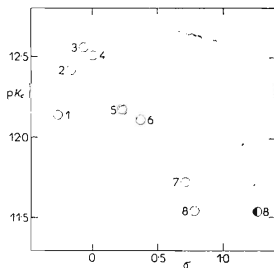


FIG. 2

The Dependence of $\text{p}K_a$ of Substituted ω -Methylglyoxal Phenylhydrazones on σ Constants^{12,13}

For numbers see Table I; ● σ^- .

being quite deviated. In the case of *p*-nitro derivative it would be better to use the respective σ_p^- constant, but, even then, the correlation will not improve substantially. Aldehyde phenylhydrazones are known to exist as *syn* and *anti* isomers². In our case the both isomers can be supposed to differ in their acidities strongly. In the *syn* isomer there is an intramolecular hydrogen bond whereas in the *anti* isomer there is not (Scheme 2). *E.g.* in the case of arylazonaphthols the *o*-derivatives with an intramolecular hydrogen bond are less acidic than the *p*-isomers by about 3 pK_a units⁸. The presence of the both hydrazone isomers was proved by measuring their NMR spectra in $CDCl_3$. The signals of the protons in acetyl groups belonging to the individual isomers were found in the spectra of all the derivatives. The chemical shifts of the methyl groups of the both isomers as well as the difference in chemical shifts $\Delta\tau$ of various derivatives differed only very slightly (the average values: *syn*- CH_3 , 7.78 τ , *anti*- CH_3 , 7.63 τ , $\Delta\tau = 0.1-0.2$ p.p.m.). The ratio of signal intensities of the methyl groups I_{anti}/I_{syn} varied within the limits 1 to 2. The signals of the methyl group were ascribed on the basis of a comparison of their intensities of absorption with those of NH protons.

The NMR spectra of the substances in water could not be measured because of slight solubility. In spite of this we believe that the both isomers are present there, too. A slow interconversion of the isomers after dissolving in water could be one of the possible explanations of the very poor correlation of pK_a vs σ constants. Therefore, we have measured the pK_a values using the hydrazones stock solutions after various storage times (see Experimental). As the differences found were within the experimental errors, we exclude this possibility.

TABLE I

pK_a and Rate Constants of Reaction of Substituted ω -Methylglyoxal Phenylhydrazones with *p*-Sulfobenzendiazonium Chloride at 20°C and Ionic Strength 0.1

Compound No	Substituent	pK_a	$k \cdot 10^{-8}$ $l \text{ mol}^{-1} \text{ min}^{-1}$
1	<i>p</i> -OCH ₃	12.14 ± 0.02	99.80 ± 20.03
2	<i>p</i> -CH ₃	12.42 ± 0.02	27.20 ± 1.44
3	<i>m</i> -CH ₃	12.56 ± 0.02	26.80 ± 2.04
4	H	12.51 ± 0.02	18.53 ± 1.67
5	<i>p</i> -Cl	12.17 ± 0.02	10.02 ± 0.50
6	<i>m</i> -Cl	12.11 ± 0.02	6.030 ± 0.608
7	<i>m</i> -NO ₂	11.72 ± 0.02	1.762 ± 0.113
8	<i>p</i> -NO ₂	11.54 ± 0.02	0.387 ± 0.052

We take it for the most probable explanation that the concentration ratio of the both isomers depends on some other factors (as *e.g.* solvation) which, as a rule, do not depend linearly on the substituent polar effects expressed by the respective σ constants. Therefore, the dependence $\text{p}K_a$ vs σ is not linear either.

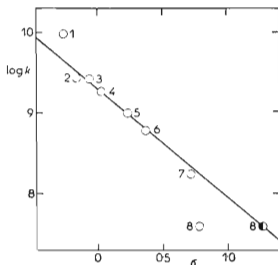


FIG. 3

The Dependence of Logarithms of Rate Constants of Reaction of *p*-Sulfobenzenediazonium Chloride with Substituted ω -Methylglyoxal Phenylhydrazones on σ Constants^{12,13} at 20°C and Ionic Strength 0.1

For numbers see Table I; \bullet σ^- .

The influence of the *syn-anti* isomerism on the rate constants should be less than that on $\text{p}K_a$. This presumption was confirmed as it can be seen in Fig. 3 where the $\log k$ of coupling of substituted ω -methylglyoxal phenylhydrazones with *p*-sulfobenzenediazonium chloride are plotted against σ constants. The better correlation with the use of the σ_p^- constant for the *p*-nitro derivative stands in accord with that the free electron pair at the nitrogen atom is conjugated with the nitro group. When excluding the *p*-methoxy derivative whose deviation from the regression line is substantially greater than the standard deviation s , the following regression equation was obtained:

$$\log k = 9.270 - 1.34\sigma; \quad r = 0.997; \quad s = \pm 0.060. \quad (5)$$

The difference between the kinetics and $\text{p}K_a$ in correlating with σ can also be explained as follows*: If two forms A and B are in equilibrium (equilibrium constant

* The authors are indebted to the reviewer for this interpretation.

K) and each of them dissociates (constants K_A and K_B), the observable constant K_{exp} equals to $(K_A + K.K_B)/(1 + K)$. If we express each constant by the Hammett equation, we obtain the relationship $\log K_{\text{exp}} = \log (K_1^0 10^{\rho_1 \sigma} + K^0 K_2^0 10^{\rho_2 \sigma}) / (1 + K^0 10^{\rho_0 \sigma})$ which is not linear function of σ . But in the case of kinetics the matter is quite different. If two substances A and B are in equilibrium and each of them undergoes a reaction (rate constants k_A and k_B), the observed velocity depends on the ratio of the equilibrium velocity and k_A and k_B . The above expression holds, if the equilibrium is slow; if it is rapid, the observed velocity approaches the velocity of the more quickly reacting isomer and the Hammett equation may hold.

In the case of ω -methylglyoxal *p*-tolyl- and *m*-nitrophenylhydrazones the influence of substituents in diazonium ion on the coupling rate was determined too (Table II) and expressed quantitatively by means of the Hammett equation (Eqs (6) and (7) respectively). The difference in ρ values of coupling of ω -methylglyoxal *m*-nitrophenylhydrazone (2.73 ± 0.07) and *p*-tolylhydrazone (2.62 ± 0.18) are within the experimental error.

$$\log k = (8.606 \pm 0.071) + (2.62 \pm 0.18) \sigma; \quad r = 0.993, \quad (6)$$

$$\log k = (7.482 \pm 0.026) + (2.73 \pm 0.07) \sigma; \quad r = 0.999. \quad (7)$$

The ρ constants found are smaller than those found in coupling with acetylacetone⁹ and acetoacetanilide⁵ which is in accord with that the ω -methylglyoxal phenylhydrazones are somewhat weaker acids. Also the magnitude of the rate constants of coupling of substituted ω -methylglyoxal phenylhydrazones with benzenediazonium ion fits roughly the previously found relationship between $\log k$ of coupling and pK_a of the C-acid⁹.

TABLE II

Rate Constants (k) of Reactions of Substituted Benzenediazonium Ions with ω -Methylglyoxal *p*-Tolyl (A) and *m*-Nitrophenylhydrazone (B) at 20°C and Ionic Strength 0.1

Benzenediazonium ion	$k, \text{l mol}^{-1} \text{ min}^{-1}$		σ^a
	A	B	
<i>p</i> -CH ₃	$1.355 \cdot 10^8$	$8.782 \cdot 10^6$	-0.20
Unsubst.	$4.254 \cdot 10^8$	$3.274 \cdot 10^7$	0.00
<i>p</i> -Cl	$1.327 \cdot 10^9$	$1.010 \cdot 10^8$	0.20
<i>m</i> -Cl	$2.793 \cdot 10^9$	$3.050 \cdot 10^8$	0.39
<i>m</i> -NO ₂	$3.479 \cdot 10^{10}$	$2.705 \cdot 10^9$	0.70

^a Most σ constants were taken from literature¹⁰. The value 0.29 ($\sigma^+ - \sigma$) was added to constants of *p*-Cl and *p*-CH₃ according to the literature¹¹.

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