KINETICS OF SUBSTITUTION OF 4-METHOXYPHENYLAZO GROUPS OF 2,6-DIOXO-5(3)-(4-METHOXYPHENYLAZO)-3(5)-(4-METHOXYPHENYLHYDRAZONO)-1,2,3,6-TETRAHYDROPYRIDINE-4-CARBOXYLIC ACID BY REACTION WITH 4-NITROBENZENEDIAZONIUM CATION

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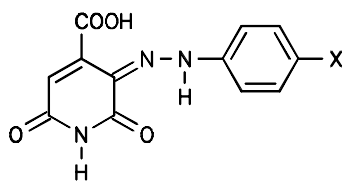
Kinetics have been studied of gradual replacement of 4-methoxyphenylazo groups in 2,6-dioxo-5(3)-(4-methoxyphenylazo)-3(5)-(4-methoxyphenylhydrazono)-1,2,3,6-tetrahydropyridine-4-carboxylic acid (*IIIa*) by 4-nitrophenylazo groups using the reaction with 4-nitrobenzenediazonium cation (*IIc*) in acetate and phosphate buffers. The rate constant of replacement of the second methoxyphenylazo group is lower by a factor of ca 60. From the experimentally found pK_a values of the corresponding azohydrazone compounds with methoxy, chloro, or nitro substituent at 4-position (*IIIa – IIIf*) it has been concluded that the 5(3)-(4-methoxyphenylazo)-3(5)-(4-nitrophenylhydrazono) derivative is formed in the first step.

The azo coupling products formed by the reaction at an activated CH_2 group exist exclusively in the respective hydrazone form[1]. Such hydrazones also involve azo coupling products of 2,6-dihydroxypyridine derivatives and some fivemembered heterocyclic compounds such as 1-substituted pyrazolin-5-ones[2,3,4]. A reaction of these hydrazones with substituted benzenediazonium cations produces an unstable bisarylazo intermediate which again forms the hydrazone upon splitting off of the less electrophilic diazonium cation[5,6]. The reactions of benzenediazonium ions with phenols produce azo compounds almost exclusively[3,7,8], whereas the reactions with 1- or 2-naphthols result in mixtures of azo and hydrazone compounds[3,7,8]. In none of these cases any substitution of phenylazo group by a more electrophilic diazonium cation has been described yet. Only in the cases of 5-X-6-hydroxynaphthalene-2-sulfonic acids[9] (X = F, Cl, I) and 2-hydroxynaphthalene-1-sulfonic acid[10], the substitution of X and SO_3^- groups, respectively, by *p*-chlorobenzenediazonium ion was observed.

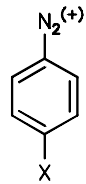
Our previous report[2] dealt with azo coupling kinetics of 2,6-dioxo-3-(*p*-substituted phenylhydrazono)-1,2,3,6-tetrahydropyridine-4-carboxylic acids *Ia – Ic* with *p*-substituted benzenediazonium ions *IIa – IIc*. In the reactions of 4-nitrobenzenediazonium

ion (*IIc*) with 4-chloro- (*Ib*) and 4-methoxyphenylhydrazono (*Ia*) derivatives and in those of 4-chlorobenzenediazonium ion (*IIb*) with 4-methoxyphenylhydrazono derivative (*Ia*), the azo coupling reaction was accompanied by substitution of 4-chloro- and 4-methoxyphenylhydrazono groups, respectively, by the 4-nitro- and 4-chlorophenylhydrazono groups, respectively. Since a similar reaction (though slower) must be encountered with the resulting azohydrazone compounds *IIIa* – *IIIf*, the respective kinetics have now been studied too.

The present communication describes the kinetics of gradual substitution of 4-methoxyphenylazo and -hydrazono groups in the reaction with 4-nitrobenzenediazonium ion (*IIc*). The rate constant of substitution of 4-chloro- for 4-nitrophenylazo group and of 4-methoxy- for 4-chlorophenylazo group could not be determined with sufficient accuracy because of rather extensive decomposition of the benzenediazonium ions and their consecutive reactions with the azohydrazone compounds.

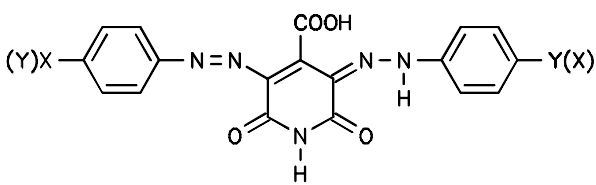


I



II

In formulae *I* and *II* : *a*, X = OCH_3; *b*, X = Cl; *c*, X = NO_2



III

	a	*b*	*c*	*d*	*e*	*f*
X	OCH_3	Cl	NO_2	OCH_3	OCH_3	Cl
Y	OCH_3	Cl	NO_2	Cl	NO_2	NO_2

EXPERIMENTAL

Chemicals

The preparation of 2,6-dioxo-5(3)-(4-methoxyphenylazo)-3(5)-(4-methoxyphenylhydrazono)-1,2,3,6-tetrahydropyridine-4-carboxylic acid (*IIIa*) and 2,6-dioxo-5(3)-(4-nitrophenylazo)-3(5)-(4-nitrophenylhydrazono)-1,2,3,6-tetrahydropyridine-4-carboxylic acid (*IIIc*) were described in our previous report[2].

Preparation of Nonsymmetrical Azohydrazones *IIId* and *IIIe*. General Procedure

The respective hydrazones[2] *Ib*, *Ic* (3.3 mmol) were dissolved in 1 M sodium carbonate (15 ml) and a 0.4 M solution of diazonium salt *IIa* (8.5 ml) was added. The reaction mixture was stirred 20 min, left to stand 1 h, and then the dyestuff was collected by filtration, washed with water, and dried in air. The nonsymmetrical azohydrazono compounds *IIId* and *IIIe* were purified by dissolving a 0.5 g sample in 0.1 M NaOH (40 ml), filtering with charcoal, and pouring the filtrate into 0.1 M HCl (50 ml) at about 60 °C. The suspension was stirred for another 10 min and left to stand overnight in darkness. Then the precipitates were collected by filtration, washed with water and dried in air. Their purity was checked by TLC (Silufol, Lucefol; propanol–ammonia 2 : 1; R_F(*IIId*) = 0.67, R_F(*IIIe*) = 0.60). UV spectra of compounds *IIId* and *IIIe* (acetate buffer 1 : 1, pH 4.5), λ_{max} in nm (log ε): 494 (4.380); 505 (4.418). For the kinetic and pK_a measurements we prepared 10^{-3} M solutions of the symmetrical and nonsymmetrical azohydrazono compounds in 0.01 M borax. All the measurements were carried out at 25 °C at the ionic strength of 0.5 mol l^{-1} adjusted by the addition of potassium chloride.

4-Nitrobenzenediazonium Tetrafluoroborate

4-Nitroaniline (5.52 g, 40 mmol) was dissolved in hot 5 M HCl (30 ml) and the solution was cooled to 0 °C with stirring, whereafter a solution of 2.5 M $NaNO_2$ (16 ml) was quickly added with stirring and cooling. The solution of diazonium salt was filtered with charcoal and diluted to the required concentration of $4 . 10^{-1}$ mol l^{-1}. This solution (50 ml) was treated with 3 g sodium tetrafluoroborate. The precipitate formed was collected by filtration, washed with alcohol and anhydrous ether, predried on the filter in a stream of argon, and dried in air in darkness.

The buffers were prepared from redistilled water and chemicals of p.a. purity grade. The pH values of solutions were determined with an MV 870 apparatus (VEB Procitronic) using a combined glass–silver chloride electrode at 25 °C. The electronic spectra were measured with a Unicam SP 1800 Ultraviolet Spectrophotometer.

Determination of pK_a

The spectra of solutions of nonsymmetrical azohydrazono compounds *IIId* and *IIIe* were measured in glycinamide buffers in the wavelength region of 350 – 600 nm. The spectra of monoanions *IV* were measured in acetate buffer 1 : 1 and those of dianions *V* in carbonate basic buffer 1 : 3; at higher pH values the amide group dissociation became spetrophotometrically observable. In all the cases the spectra showed well-developed isosbestic points. The absorbances in buffer solutions were measured at a selected wavelength, and the pK_a values (Table I) were calculated from Eq. (*1*),

$$\mathrm{p}K_a = \log I + \mathrm{pH} , \qquad (1)$$

where $I = (A_S - A)/(A - A_{SH})$, where A_S, A_{SH}, and A stand for the absorbances of dianion, monoanion, and their mixture in the buffer, respectively.

Kinetic Measurements

A 10 ml calibrated flask was charged with the chosen amounts of buffer, solution of potassium chloride, solution of symmetrical (*IIIa*) or nonsymmetrical (*IIIe*) azohydrazono compound of precise concentration, and redistilled water. The final volume was 10 ml, and the substrate concentration was $4 \cdot 10^{-5}$ mol l^{-1}. This solution (2 ml) was transferred into a 1 cm quartz cell at 25 °C, and 100 µl of diazonium salt of $4 \cdot 10^{-2}$ or $8 \cdot 10^{-2}$ mol l^{-1} concentration was added from a syringe. The absorbance changes with time were monitored at a selected wavelength (Table II). In acetate buffers the measurements were carried out at the wavelength corresponding to the isosbestic point of methoxynitro derivative *IIIe* and dimethoxy derivative *IIIa*. The remaining solution in the flask was used for pH measurement. The rate constants were calculated from Eq. (*2*).

$$k_{obs} = (1/t) \ln (A_{oo} - A_t) + \text{const.} \qquad (2)$$

TABLE I

pK_a Values of hydrazone compounds *Ia – Ic* (ref.[2]), symmetrical azohydrazone compounds *IIIa – IIIc* (ref.[2]) and nonsymmetrical azohydrazone compounds *IIId*, *IIIe* measured in aqueous solutions at 25 °C

Compound	*Ia*	*Ib*	*Ic*	IIIa	*IIIb*	*IIIc*	*IIId*[a]	*IIIe*[b]
pK_a	9.16	9.10	8.93	8.45	7.60	7.04	8.35	8.20

[a] λ_{anal} = 416.7 nm, λ_{iso} = 452.3 nm; [b] λ_{anal} = 455 nm, λ_{iso} = 520 nm.

TABLE II

Rate constants k_S (l mol^{-1} s^{-1}) and k_2 (l mol^{-1} s^{-1}) of azo coupling reactions of benzenediazonium ion *IIc* with the symmetrical azo compound *IIIa* and nonsymmetrical azohydrazone compound *IIIe* in aqueous acetate (1) and phosphate (2) buffers at 25 °C

Compound	Buffer	[BH]/[B$^-$]	k_S	pH	k_2[a]	λ
IIIa	1	1 : 4	4.37	5.18	$8.12 \cdot 10^3$	562.0
		1 : 2	2.33	4.89	$8.46 \cdot 10^3$	562.0
		1 : 1	1.29	4.61	$8.90 \cdot 10^3$	562.0
IIIe	2	1 : 1	3.68	6.63	144.5	581.0
		1 : 1[b]	3.58	6.62	144.5	581.0
		1 : 3	9.40	7.10	127.0	571.0

[a] Average values $(8.50 \pm 0.4) \cdot 10^3$ and 138 ± 8; [b] starting compound *IIIa*.

RESULTS AND DISCUSSION

pK_a Values

The pK_a values of nonsymmetrical azohydrazono compounds *IIId* and *IIIe* are presented in Table I. The pK_a difference between 4-methoxy- *Ia* and 4-nitrophenylazo derivative *Ic* of citrazinic acid is 0.23, which corresponds to an abnormally low ρ value of ca 0.25. On the other hand, with the symmetrical derivatives in which one group is in its azo form and the other in hydrazone form, the pK_a difference between the symmetrical dimethoxy derivative *IIIa* and dinitro derivative *IIIc* is 1.41. Presuming the substituent effect on pK_a in the hydrazone forms of compounds *IIIa*, *IIIc* to be similar to that in the hydrazone derivatives *Ia* and *Ic*, the estimated pK_a difference due to the replacement of 4-methoxy group by a 4-nitro group is 1.18 in the azo form. Hence the effect of substituent in phenylazo group upon pK_a and ρ values is almost 5 times as much as that in phenylhydrazone group.

The pK_a difference between the symmetrical dimethoxy derivative *IIIa* and unsymmetrical methoxynitro derivative *IIIe* is 0.25, which is again a similar value to the pK_a difference between nitrohydrazone derivative *Ic* and methoxyhydrazone derivative *Ia*.

Similarly, the gradual replacement of chlorine in symmetrical dichloro derivative *IIIb* by methoxy groups is connected with the pK_a changes of 0.75 and 0.10. Therefrom it follows that in the nonsymmetrical methoxynitro derivative *IIIe* the nitro group is in the phenyl nucleus of phenylhydrazone substituent, since the replacement of methoxy group in dimethoxy derivative *IIIa* by a nitro group has an only small effect on pK_a, which is typical of a hydrazone form, and, on the other hand, the replacement of methoxy group of methoxynitro derivative *IIIe* by a nitro group is connected with a large pK_a change in accordance with the methoxy group being located in the benzene nucleus of phenylazo group. Similarly, in the chloromethoxy derivative *IIId* chlorine is predominantly located in the benzene nucleus of phenylhydrazone group. The stability of nonsymmetrical azohydrazone compounds *IIId* and *IIIe* is increased by electron delocalization, as represented in Scheme 1 for the example of resonance structures of compound *IIIe*.

Azo Coupling Kinetics

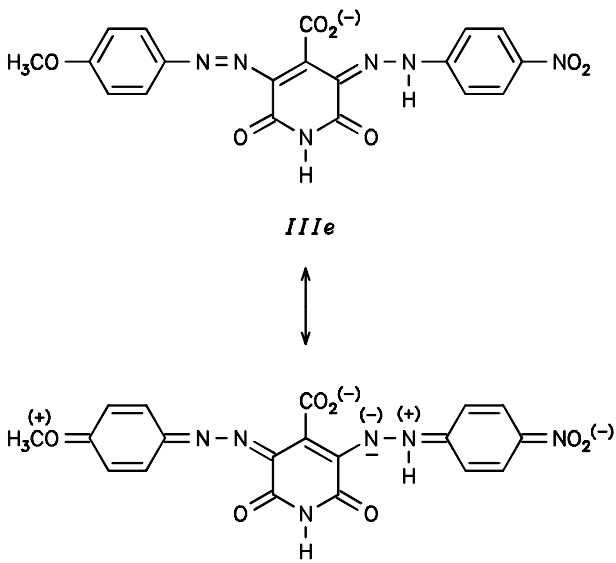
The reaction of symmetrical dimethoxyazohydrazono compound *IIIa* with 4-nitrobenzenediazonium cation (*IIc*) is accompanied by gradual replacement of 4-methoxy- by 4-nitrophenylazo group (Scheme 2). The replacement of the first 4-methoxyphenylazo group resulting in the formation of nonsymmetrical azohydrazone compound is almost two orders of magnitude faster, hence the two steps can be monitored separately. The first step was measured in acetate buffers and the second step in phosphate buffers (Table II). When measuring the kinetics, we adopted a tenfold excess of diazonium salt at

least, hence the reaction was of pseudo-first order in the whole range measured (4 – 5 half-lives). The rate constants were independent of the concentrations of buffers and increased with increasing proton concentration in accordance with Eq. (*3*).

$$v = \mathrm{d[Prod]}/\mathrm{d}t = k_{\mathrm{obs}}\, c_{\mathrm{diaza}} = k_2(K_a/(K_a + [\mathrm{H}^+]))\, c_{\mathrm{diaza}}[\mathrm{ArN}_2^+] \qquad (3)$$

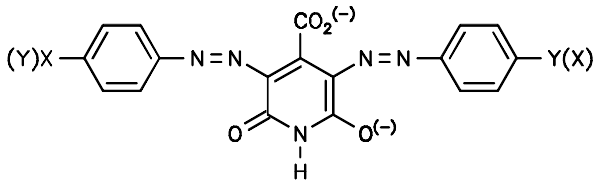
The rate of replacement of methoxyphenylazo group by nitrophenylazo group in the nonsymmetrical azohydrazone compound *IIIe* is lower than that in the first step by a factor of 62, which is similar to the ratio of coupling rates of nitrophenylhydrazono *Ic* and methoxyphenylhydrazono *Ia* derivatives of citrazinic acid ($9.3 \cdot 10^{-2}$ l mol^{-1} s^{-1}/ $9 \cdot 10^{-4}$ l mol^{-1} s^{-1} = 97, ref.[2]), in which azo couplings involve the substitution of proton. The same rate constant was found in phosphate buffers when the dimethoxy derivative *IIIa* was adopted instead of the methoxynitro derivative *IIIe* (Table II); the dimethoxy derivative was transformed almost completely into the methoxynitro derivative as early as the first spectral record.

The replacement of methoxyphenylazo group of nonsymmetrical azohydrazone compound *IIIe* by the nitrophenylazo group is slower by a factor of 6.8 as compared with the substitution of hydrogen in the nitrophenylhydrazono derivative *Ic* of citrazinic acid, being 10.6 times slower with the symmetrical dimethoxy derivative *IIIa* as compared with the substitution of hydrogen in the methoxyphenylhydrazono derivative *Ia* of citrazinic acid, which values again are similar. In the second case it is of course impossible to establish whether in the dimethoxyazohydrazone compound *IIIa* the

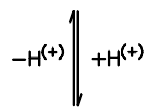


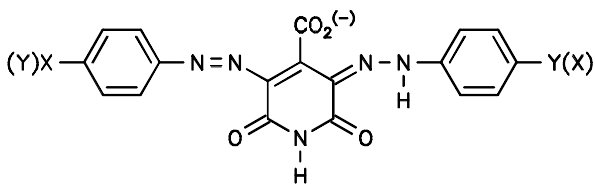
SCHEME 1

methoxyphenylazo group substituted is in its azo or hydrazone form or both forms are substituted simultaneously.



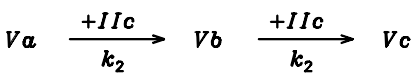
V





IV

	a	*b*	*c*
X	OCH_3	OCH_3	NO_2
Y	OCH_3	NO_2	NO_2



SCHEME 2

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