KINETICS OF COUPLING OF 4-METHOXYBENZENEDIAZONIUM ION WITH 2,6-DIHYDROXYPYRIDINE

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The kinetics of reaction of 4-methoxybenzenediazonium ion (**3**) with 2,6-dihydroxypyridine (**1**) has been studied in methoxyacetate, acetate, and phosphate buffers. The rate-limiting step is the formation of the reaction intermediate and not the splitting off of the proton (which was detected in the cases of citrazinic acid and its methyl ester). Therefrom it follows that for 2,6-dihydroxypyridine derivatives the steric hindrance to the formation of the Wheland intermediate exerted by CO_2^- and CO_2CH_3 groups represents a necessary condition for the rate-limiting splitting off of the proton and, hence, for the existence of general base catalysis.

Key words: Chemical kinetics; Azo coupling reaction; Electrophilic aromatic substitution; Dissociation constant.

Recently we have published[1] a study of coupling kinetics of substituted benzenediazonium ions with the dianion of citrazinic acid. The coupling rate constants increased linearly with the concentration of basic buffer component (the dependence of log k rate constant of the base-catalyzed reaction versus pK_a of the acid buffer components exhibited the value of $\beta = 0.38 \pm 0.02$), i.e. the rate-limiting step of the reaction is the splitting off of the proton from the intermediate formed by addition of a substituted benzenediazonium ion to the dianion of citrazinic acid (Scheme 1) and not the formation of this intermediate which is usual with azo coupling reactions[2]. The rate-limiting splitting off of the proton from the reaction intermediate was found[2–4] in the coupling reactions using – as the azo component – naphthols with sulfonic acid groups adjacent or in peri position to the site of attack, and it was interpreted as a result of steric effect of sulfonic acid group interfering with the transformation of the intermediate into the product[5].

In the reactions with citrazinic acid, the change of rate-limiting step could be explained by the steric effect of adjacent CO_2^- group which, however, is substantially smaller than that of SO_3^- group. This interpretation became rather doubtful when it was found that in the coupling reactions of substituted benzenediazonium ions with the primary coupling products, 2,6-dioxo-3-(*p*-substituted phenylhydrazono)-1,2,3,6-tetrahydropyridine-4-carboxylic acid[6], where the steric effect should have been increased by the buttressing effect[7] of the adjacent hydrazono group, the general base catalysis made itself felt to a far lower extent and was not observed at all with the most reactive 4-nitrobenzenediazonium ion. There arises a question whether the rate-limiting transformation of the intermediate into the product is really a consequence of the steric effect of CO_2^- or is characteristic of 2,6-dihydroxypyridine and its derivatives. Therefore, the kinetics of the reaction of 2,6-dihydroxypyridine with 4-methoxybenzenediazonium ion has been studied in a series of buffers.

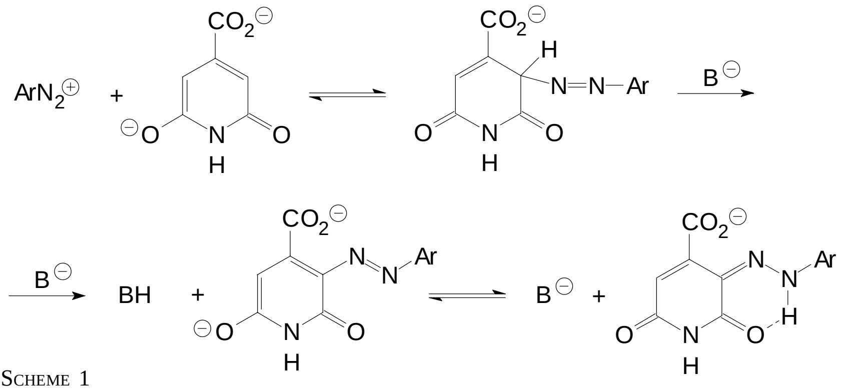
EXPERIMENTAL

Measurements. The electronic spectra were measured with a Hewlett–Packard 8452A Diode Array instrument. The kinetic and dissociation constant measurements were carried out spectrophotometrically using the same apparatus. The pH values of buffers were determined with the help of an MV 870 apparatus (VEB Pröcitronic) using a combined glass and silver chloride electrode at 25 °C.

Reagents. Methoxyacetic and acetic acids were commercial products of p.a. purity grade. 2,6-Dihydroxypyridine (Aldrich) of 97% purity was used without purification. The preparation of the solution of 4-methoxybenzenediazonium ion is described elsewhere[1]. The buffers were prepared from redistilled water, the acids given, and sodium hydroxide. The 1 : 1 phosphate buffer was prepared from NaH_2PO_4 and Na_2HPO_4.

Dissociation constant of 2,6-dihydroxypyridine. The dissociation constant of 2,6-dihydroxypyridine was determined spectrophotometrically in acetate buffers by measuring the absorbance at the wavelength of 340 nm at 25 °C at the ionic strength of 0.5 mol l^{-1} adjusted by addition of potassium chloride. The absorbances of the neutral form and the anion were measured in $5 \cdot 10^{-3}$ mol l^{-1} hydrochloric acid and in $2 \cdot 10^{-2}$ mol l^{-1} Na_2HPO_4 solutions, respectively. All the spectra formed a sharp isosbestic point at 305 nm. The dissociation constant was calculated from the dependence (*1*) where $R = [\mathbf{1}]/[\mathbf{2}] = (A - A_\mathbf{2})/(A_\mathbf{1} - A)$, the symbols A, $A_\mathbf{1}$, and $A_\mathbf{2}$ representing the absorbances in the buffers, the Na_2HPO_4 solution, and hydrochloric acid, respectively. The pK_a value of 2,6-dihydroxypyridine is 4.4 ± 0.08.

$$pK_a = pH + \log R \qquad (1)$$



SCHEME 1

Kinetic measurements. The first kinetic measurements adopted the same procedure as that used for the reactions of citrazinic acid with substituted benzenediazonium ions[1]. A solution of 2,6-dihydroxypyridine in buffer and KCl (ionic strength 0.5 mol l^{-1}) was treated with a solution of 4-methoxybenzenediazonium ion injected at 25 °C (the resulting concentration of 4-methoxybenzenediazonium ion was $1 . 10^{-5}$ mol l^{-1}) and the absorbance was measured in the region from 390 to 500 nm. In all the cases the excess of 2,6-dihydroxypyridine was tenfold at least, hence the reaction kinetics was of the pseudofirst order. The observed rate constants were calculated from the absorbances at 446 nm according to a program present in the spectrophotometer Hewlett–Packard 8452A. As 2,6-dihydroxypyridine undergoes decomposition – especially in basic acetate buffers and phosphate buffer – already before injecting the diazonium salts, the reverse procedure was adopted in the respective experiments. A solution of $(4–16) . 10^{-4}$ mol l^{-1} 2,6-dihydroxypyridine in $1 . 10^{-3}$ mol l^{-1} hydrochloric acid (25 μl) was injected into a solution of diazonium salt ($5 . 10^{-5}$ to $2 . 10^{-4}$ mol l^{-1}) and KCl.

RESULTS AND DISCUSSION

The kinetics of azo coupling of 4-methoxybenzenediazonium ion with 2,6-dihydroxypyridine was studied in methoxyacetate, acetate, and phosphate buffers. In all the cases a tenfold excess of diazonium salt was adopted, so the reactions were the pseudofirst order kinetically. The reaction mechanism is given in Scheme 2 and its course is defined by the rate equation (*2*):

$$v = \mathrm{d[product]}/\mathrm{d}t = k_{\mathrm{obs}}c_{(\mathbf{1}+\mathbf{2})} = k_{\mathrm{s}}c_{(\mathbf{1}+\mathbf{2})}[\mathbf{3}] = k_2[\mathbf{3}][\mathbf{2}] = k_2[\mathbf{3}]c_{(\mathbf{1}+\mathbf{2})}(K_{\mathrm{a}}/(K_{\mathrm{a}} + a_{\mathrm{H^+}})) \ , \qquad (2)$$

where $k_s = k_{obs}/[\mathbf{3}]$ and k_2 is defined by Eq. (*3*):

$$k_2 = k_1(k_2^0/(k_{-1} + k_2^0) + k_2^{\mathrm{B}}[\mathrm{B}]/(k_{-1} + k_2^{\mathrm{B}}[\mathrm{B}]) \ . \qquad (3)$$

Table I presents the k_s values in the individual buffers and Fig. 1 depicts the dependence of k_2 on the concentration of the basic buffer components.

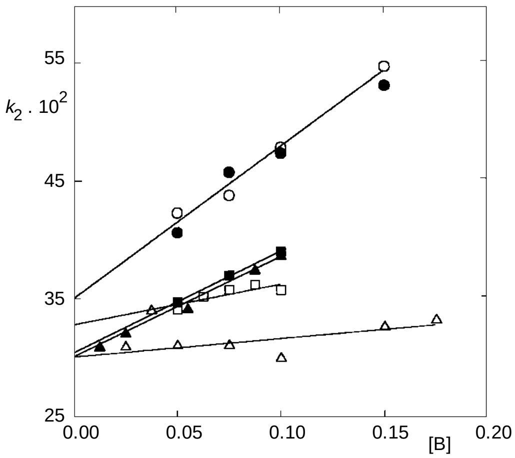


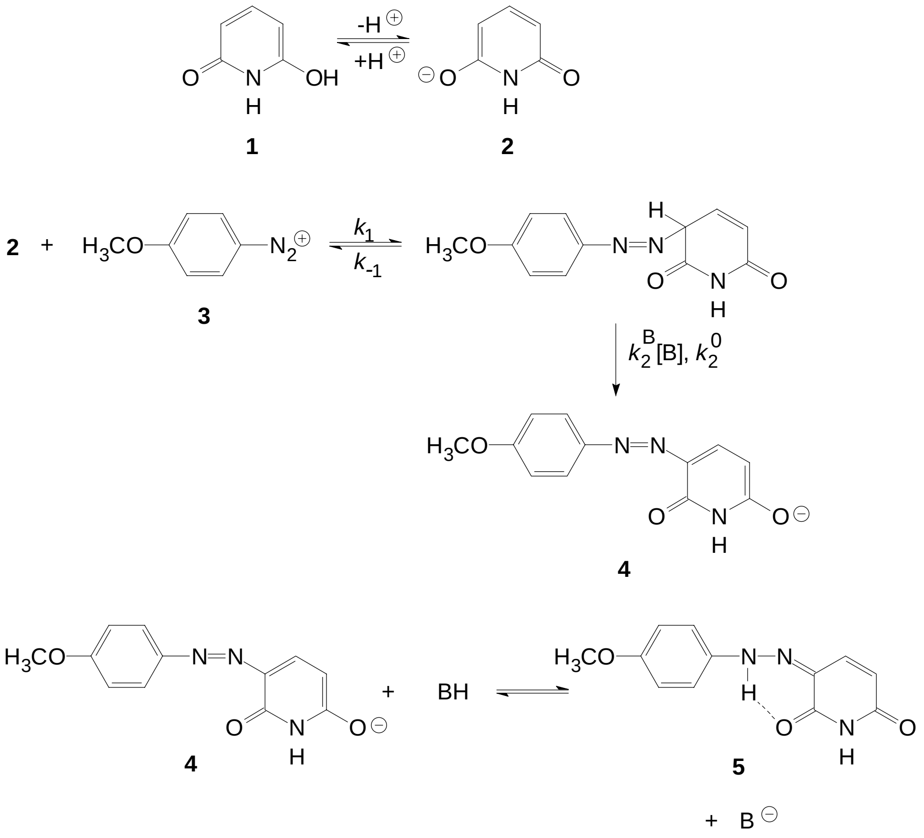
FIG. 1
Dependence of k_2 (l mol^{-1} s^{-1}) on molar concentration of basic buffer component ([B], mol l^{-1}) for reactions of 2,6-dihydroxypyridine (**1**) with 4-methoxybenzenediazonium ion (**3**) in various buffers: ❍ 1 : 1, ● 1 : 2 methoxyacetate; ❐ 5 : 1, ■ 1 : 1, Δ 1 : 2 acetate; ▲ 1 : 1 phosphate

TABLE I
Rate constants k_s (l mol^{-1} s^{-1}) of reaction of 2,6-dihydroxypyridine (**1**) with 4-methoxybenzenediazonium ion (**3**) in methoxyacetate (1), acetate (2), and phosphate (3) buffers at 25 °C

Buffer	[BH]/[B^-]	pH	[B^-]	k_s
1	1 : 1	3.38	0.0500	368.50
			0.0750	381.50
			0.1000	415.75
			0.1500	475.75
	1 : 2	3.70	0.0500	676.00
			0.0750	760.50
			0.1000	791.25
			0.1500	881.75
2	5 : 1	3.89	0.0125	869.00
			0.0250	715.00
			0.0375	715.40
			0.0500	805.00
			0.0625	830.20
			0.0750	843.20
			0.0875	842.40
	1 : 1	4.77	0.0250	2 046.00
			0.0500	2 424.00
			0.0750	2 592.00
			0.1000	2 985.00
			0.1500	2 709.00
	1 : 2	4.95	0.0250	2 576.00
			0.0500	2 432.00
			0.0750	2 432.00
			0.1000	2 344.00
			0.1500	2 548.00
			0.1750	2 592.00
3[a]	1 : 1	7.03	0.0125	3 106.00
			0.0250	3 222.00
			0.0375	3 532.00
			0.0500	3 554.00
			0.0625	3 267.00
			0.0750	3 306.00
			0.0875	3 748.00
			0.1000	3 903.00

[a] BH = $H_2PO_4^-$.

The k_2 value extrapolated to zero buffer concentration (see Fig. 1) is 3 144 ± 120 l mol^{-1} s^{-1}. The slope of dependence of k_2 vs buffer concentration (which should give the value of the rate constant $k_B = k_1k_2^B/(k_{-1} + k_2^B)$ of the base-catalyzed reaction if the splitting off of the proton from the intermediate were the rate-limiting step) has the value of $1.3 \, . \, 10^4$ l^2 mol^{-2} s^{-1} in the methoxyacetate buffers. The ratio of the slope to the extrapolated value of k_2 is 3.7 l mol^{-1}, the same ratio for citrazinic acid dianion being 4.9 l mol^{-1}. In acetate and phosphate buffers, where this ratio should exhibit an increasing value (it was 13.2 and 170 l mol^{-1} for citrazinic acid), its value varies from 0.5 to 2.5. This means that in these buffers the base catalysis is not operating and the formation of intermediate is rate limiting. This also must be true of the reaction in methoxyacetate buffers, since it is impossible that the rate constants k_2 for the rate-limiting transformation of the intermediate into the product should have a higher value (see Fig. 1 for the k_2 values in methoxyacetate buffers) than that in the buffers in which the formation of intermediate is rate limiting.



SCHEME 2

Obviously, the increase in k_2 with increasing buffer concentrations is due to a specific effect of the buffers on the reaction rate. This is also indicated by the fact that the above ratio for the coupling reactions of citrazinic acid is 2.7 times greater in acetate buffers and 1.4 times smaller in chloroacetate buffers than in ethoxyacetate buffers, i.e. specific buffer effects contribute to the slope values in these cases too.

Another piece of evidence in favour of the rate-limiting formation of intermediate in the case of 2,6-dihydroxypyridine is the fact that the extrapolated k_2 value is 7.5 times higher than that for citrazinic acid[1] (420 l mol^{-1} s^{-1}) in spite of the polar effect of CO_2^- which should facilitate the formation of intermediate.

The extrapolated k_2 value for the coupling reaction of citrazinic acid methyl ester[1] (85 l mol^{-1} s^{-1}) is only 5 times lower than that for the citrazinic acid dianion. The ρ constant of coupling reactions of *p*-substituted phenols with diazotized sulfanilic acid[8] is –3.77 and the difference between the σ_{para} constants of CO_2^- and CO_2CH_3 is 0.49 (ref.[9]). Presuming that the same ρ value applies to 4-substituted derivatives of 2,6-dihydroxypyridine and using σ_{para} values for the corresponding *ortho* substituents we can calculate the ratio of k_2 values of citrazinic acid and its methyl ester: it is ca 70. With *ortho* substituted derivatives, both the values ρ and σ_{ortho} are usually higher than those for the *para* derivatives[10], hence the difference in the reactivities should be even greater. The small difference can probably be due to the fact that the steric effect of solvated CO_2^- group is much greater than that of the ester group, hence the coupling rate of citrazinic acid is lowered by steric effects more than that of its methyl ester.

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