KINETICS AND MECHANISM OF *syn–anti* ISOMERIZATION
OF SUBSTITUTED BENZENEDIAZOHYDROXIDES AND DIAZOTATES;
SUGGESTION OF *cis*-CONFIGURATION FOR *anti*-DIAZOTATES

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Isomerization rate constants of 2-nitro-4 resp. 5-substituted benzenediazohydroxides and diazotates have been determined and their logarithms correlated with σ and σ^- constants. The influence of inductive and especially mesomeric effects of substituents on the isomerization rate is far greater in the case of diazotates than it is with diazohydroxides. On the basis of the polar effects found the rotation about N–N bond of tautomeric N-nitrosamines has been suggested to be the most probable mechanism of the isomerization of diazohydroxides. The influence of pH and substituents on reaction mechanism of transformation of *anti*-diazotate into diazonium ion has been discussed. The dependence of rate and equilibrium constants of the isomerization reaction of substituted benzenediazotates on steric effects of *ortho*-substituents suggests that, in contrast to the existing opinion, *anti*-diazotates have *cis*-configuration.

In alkaline solutions substituted benzenediazonium ions react quickly with hydroxyl ions to give *syn*-diazotates which, in turn, rearrange to more stable *anti*-isomers. The isomerization is facilitated by the presence of electron-withdrawing substituents, especially *ortho*- and *para*-substituents having —M effect[1]. The isomerization rate constants were measured[1–3] for several substituted benzenediazonium ions, but the reaction conditions were inasmuch different (temperature 20—100°C, OH⁻ concentration 10^{-4}—10M) that not even a rough quantitative estimate of substituent effects was possible. Kinetics and mechanism of the reverse transformation of *anti*-diazotates into diazonium ions were studied in six cases of substituted benzenediazonium ions[3,4] in pH range 9—2. Rearrangement of *anti*-diazohydroxide to *syn*-diazohydroxide was found to be the rate-limiting step for the two derivatives having the substituents with highest σ constants (p-NO$_2$, p-N$_2^+$). The value 1·1 was obtained[4] for ϱ constant of the isomerization reaction from the isomerization rate constants of these two derivatives and the corresponding σ_p constants.

The aim of this work was to evaluate quantitatively the effects of substituents on the isomerization rate of diazohydroxides and diazotates and find reaction mechanism of the transformation of *anti*-diazotates into diazonium ions in the broadest possible pH range. The results obtained also should have verified and completed those of previous works[5,6]. Isomerizations of the diazotates having a substituent with a low σ constant value are so slow, that it is necessary to work at high temperatures and hydroxide concentrations. Therefore, 4- resp. 5-substituted 2-nitrobenzene-

diazonium ions were chosen for these kinetic studies so that even the slowest measured reactions proceeded with half-lives of maximum several hours at 20°C.

EXPERIMENTAL

The substituted anilines prepared by known methods were diazotized in diluted hydrochloric acid (1 : 1) with solid $NaNO_2$ and transformed into crystalline fluoroborates[7]. As 2-nitro-4-acetylbenzenediazonium fluoroborate was not stable (it decomposed completely within two days), the diazotization of 2-nitro-4-acetylaniline was carried out in a mixture of acetic and diluted sulphuric acid[8], and the diazonium salt solution formed was added to a sufficient amount of 0·5M-NaOH to give an about 5 . 10^{-4} diazotate solution in 0·2M-NaOH. The diazotate solution was quite stable and was used for further experiments.

Kinetic measurements were carried out in usual buffer solutions (chloroacetate, acetate, phosphate, borax, carbonate) and 0·1M-NaOH. Ionic strength was adjusted at 0·2 by addition of KCl and the temperature was maintained at 20°C.

Rate constants of syn–anti *isomerization of diazotates* were obtained as follows: 0·5 ml 5 . 10^{-4}M substituted benzenediazonium fluoroborate solution in 10^{-3}M-HCl was injected into 4·5 ml 0·05M-NaOH in a 3 cm cell placed in the thermostated cell compartment of a Zeiss VSU-2P spectrophotometer. The time dependence of extinction was followed in the range 270—300 nm (according to the compound being measured), and the rate constants were obtained from the equation $kt = \log (E_\infty - E_t) + const.$ as usual. This method of rate constant determination failed in the case of rapid isomerization of 2-nitro-5-acetyl derivative. Therefore, the stock solution of the respective diazotate was diluted with a fivefold amount of 0·01M-HCl and mixed with equal amount of 0·1M-NaOH in a Durrum Stopped Flow Spectrophotometer. The reaction half-life ($t_{1/2}$) was read directly from the oscillograph record of extinction *vs* time dependence at 300 nm, and the rate constant was calculated from the equation $k = 0.693/t_{1/2}$.

Rate constants of transformation of diazotate into diazonium ion were obtained as follows: 0·5 ml 2 . 10^{-4}M *anti*-diazotate solution in 0·05M-NaOH was injected into 4·5 ml buffer in a 3 cm cell placed in a Zeiss VSU-2P spectrophotometer. The buffer contained resorcinol (for pH > 10), 2-hydroxynaphthalene-3,6-disulfonic acid (pH 10—5), or 1,8-dihydroxynaphthalene-3,6-disulfonic acid (pH < 5), their amount being at least 100 times greater than that of diazotate. The time dependence of extinction of the respective azo dyestuff was followed, and the rate constants were calculated as usual. Dissociation constant of *syn*-2-nitrobenzenediazohydroxide and rate constant of its splitting into diazonium ion and OH^- ion were measured with the use of Durrum Stopped Flow Spectrophotometer in the same way as those of 3- resp. 4-substituted benzenediazohydroxides[9].

Equilibrium ratio of anti- *and* syn-2-nitro-4,6-dichlorobenzenediazotates was determined as follows: 0·5 ml 2 . 10^{-4}M diazotate solution in 0·05M-NaOH was injected into 4·5 ml mixture of acetate resp. chloroacetate buffer and 1,8-dihydroxynaphthalene-3,6-disulfonic acid (10^{-3}M) in a 3 cm cell placed in the thermostated (20°C) cell compartment of the Zeiss VSU-2P apparatus. The time dependence of extinction increase of the azo dyestuff was measured. The equilibrium concentrations of the both forms were calculated from the value obtained by extrapolation to $t = 0$ of the linear part of the dependence $\log (E_\infty - E_t)$ *vs* time and from the found value of $\log (E_\infty - E_0)$.

pH's of the reaction mixtures were measured with the use of a Radiometer Copenhagen pHM 4c apparatus after each kinetic experiment.

RESULTS AND DISCUSSION

Table I gives the rate constants k_1 of *syn–anti* diazotate isomerization. Logarithms of the rate constants were correlated with the substituent constants according to Eq. (1) (ref.[10]).

$$\log k_1 = (2.1 \pm 0.2)(\sigma + 2.4(\sigma^- - \sigma)) - (2.83 \pm 0.05). \qquad (1)$$

The value $r = 2.4$, which expresses the relative significance of mesomeric effect, is one of the greatest given in literature so far.

The remaining rate and equilibrium constants were obtained from pH dependence of experimental rate constant of the transformation of *anti*-diazotates into diazonium ions. The overall reaction scheme is following:
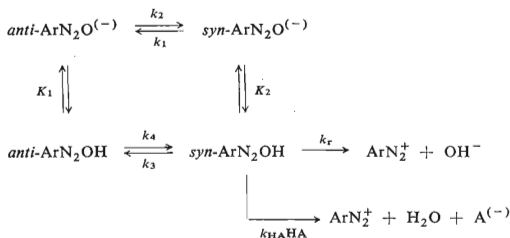
$$Ar = aryl$$

TABLE I

Rate Constants (in s^{-1}) of Isomerization *syn-anti* of Substituted Benzenediazotates and Diazohydroxides and Dissociation Constants of *anti*-Diazohydroxides at 20°C

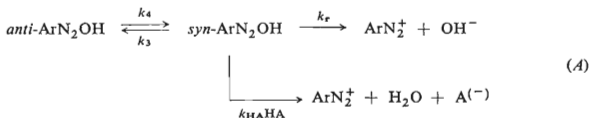| Substituents		k_1	$k_2 \cdot 10^5$	$k_4 \cdot 10^2$	pK_1
2-NO$_2$, 4-CH$_3$	(*I*)	$(7.8 \pm 0.6) \cdot 10^{-4}$	4.2 ± 1	1.2 ± 0.1	6.35 ± 0.1
2-NO$_2$	(*II*)	$(1.5 \pm 0.1) \cdot 10^{-3}$	8.3 ± 1.5	1.9 ± 0.2	6.15 ± 0.1
2-NO$_2$, 4-Cl	(*III*)	$(4.3 \pm 0.2) \cdot 10^{-3}$	37 ± 5	2.7 ± 0.2	5.80 ± 0.1
2-NO$_2$, 5-Cl	(*IV*)	$(1.0 \pm 0.3) \cdot 10^{-2}$	83 ± 20	4.0 ± 0.5	5.60 ± 0.1
2-NO$_2$, 4-COCH$_3$	(*V*)	1.0 ± 0.1		8.25 ± 0.6	
2,4-(NO$_2$)$_2$[a]	(*VI*)	20.9 ± 0.5		24 ± 3	5.0 ± 0.1

[a] Ref.[6].

Experimental rate constant k' is defined by Eq. (2) which

$$k' = \frac{(k_{HA}[HA] + k_r)\left(k_4 \dfrac{[H^+]}{K_1 + [H^+]} + k_2 \dfrac{K_1}{K_1 + [H^+]}\right)}{k_{HA}HA + k_r + k_3 + k_1K_2/[H^+]} \qquad (2)$$

was derived by steady state treatment from the above scheme. This treatment is quite justified, because the concentration of *syn*-diazohydroxide is at least $20 \times$ lower than the sum of *anti*-diazotate and *anti*-diazohydroxide concentrations in all the cases investigated.

Fig. 1 gives the dependence log k' *vs* pH for 2-nitro-4-chlorobenzenediazonium ion. At pH < 5 the slope of the dependence equals zero. The *anti*-isomer is present almost exlusively in the form of diazohydroxide, so that (A) represents the only significant reaction. For this case k' is defined by Eq. (3). As it is $k_r \geqslant k_3$ for all the deriva-

$$anti\text{-}ArN_2OH \underset{k_3}{\overset{k_4}{\rightleftarrows}} syn\text{-}ArN_2OH \overset{k_r}{\longrightarrow} ArN_2^+ + OH^-$$

$$\Big\downarrow_{k_{HA}HA} \longrightarrow ArN_2^+ + H_2O + A^{(-)} \qquad (A)$$

$$k' = k_4(k_r + k_{HA}[HA])/(k_3 + k_r + k_{HA}[HA]) \qquad (3)$$

tives studied except for 4-acetyl and 4-nitro derivatives, k' is practically equal to k_4. In the case of 4-acetyl and 4-nitro derivatives the determination of k_4 was enabled by the fact that the splitting of *syn*-diazohydroxide is a generally acid-catalyzed
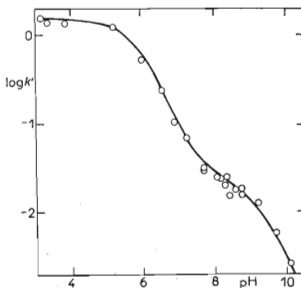

FIG. 1
pH-Dependence of Logarithm of Experimental Rate Constant k' of Conversion of *anti*-2--Nitro-4-chlorobenzenediazotate into Diazonium Ion

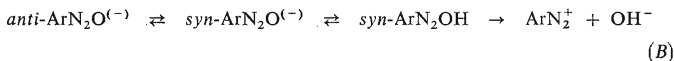Full line was computed from Eq. (2) and measured resp. calculated rate and equilibrium constants.

reaction[5,6] (see the above scheme), so that k' again approaches k_4 at a sufficient concentration of acids. The values k_4 found are given in Table I. Again, log k_4 were correlated with substituent constants to give Eq. (4).

$$\log k_4 = 1.0 \left(\sigma + 0.65(\sigma^- - \sigma)\right) - (1.80 \pm 0.05). \qquad (4)$$

The constant k' decreases with increasing pH, as the dissociation of *anti*-diazohydroxide becomes more and more significant. The dissociation constants K_1 of the derivatives $I-IV$ were calculated from the k' values of that pH region where k' begins to decrease markedly up to pH where k' is smaller than k_4 by about one order of magnitude according to Eq. (5) which was also obtained by simplification of general Eq. (2).

$$k' = k_4 [\text{H}^+]/(K_1 + [\text{H}^+]). \qquad (5)$$

At higher pH the simplified Eq. (5) ceases to hold, because the pH-independent transformation of *anti*-diazotate to *syn*-diazotate becomes gradually more significant. At pH > 9 almost all diazonium ion is formed by reaction (B), and k'

$$anti\text{-}ArN_2O^{(-)} \; \rightleftarrows \; syn\text{-}ArN_2O^{(-)} \; \rightleftarrows \; syn\text{-}ArN_2OH \; \rightarrow \; ArN_2^+ + OH^- \qquad (B)$$

should be independent of pH. With increasing pH, however, the reverse transformation of *syn*-diazohydroxide to *anti*-diazotate becomes faster than splitting of *syn*-diazohydroxide to diazonium ion. Instead of the *anti* to *syn* diazotate transformation, the splitting of *syn*-diazohydroxide to diazonium ion becomes rate-limiting. Hence, the dependence log k' vs pH again becomes linear, the slope being unity (Eq. (6)).

$$k' = k_r k_2 [\text{H}^+]/k_1 K_2. \qquad (6)$$

In the pH range where the k' value depends mainly on the *anti* to *syn* diazotate rearrangement rate (*e.g.* pH 7·5−9·5 for the derivative *III*) it is possible to calculate the rate constants k_2 of the derivatives $I-III$ from Eq. (7) obtained by modification of Eq. (2). For this calculation of k_2

$$k_2 = k' + k' k_1 K_2/k_r [\text{H}^+] - k_4 [\text{H}^+]/K_1 \qquad (7)$$

(Table I) from Eq. (7) it is necessary to know the value of the dissociation constant K_2 of *syn*-diazohydroxide and the rate constant k_r of its splitting into diazonium ion. These values could be directly measured for the derivative *II* ($k_r = 9 \cdot 10^2 \text{ mol}^{-1} \text{ s}^{-1}$;

pK_2 5·86), whereas they were experimentally inaccessible for the derivatives *I*, *III* and *IV*, because either the isomerization (derivative *I*) or the splitting of *syn*-diazo-hydroxide (derivatives *III* and *IV*) were too fast. Therefore, these constants were calculated from the Hammett equation using the ϱ constant of 3- and 4-substituted *syn*-benzenediazohydroxides[9] and presuming that this constant will hold for *o*-nitro derivatives, too.

From the rate constants k_2 and k_1 it is possible to calculate the equilibrium constants K_{iso} of the *syn–anti* isomerization of diazotates; K_{iso} values are within 12 to 18·5 for the derivatives *I*–*IV*. Polar effects have great but comparable influence on k_1 and k_2, so that the effect of substituents on K_{iso} is relatively small.

Increasing σ value results in decreasing k_r and increasing k_2 values, the latter being, moreover, strongly affected by —M effect. The consequence is that, in the series of the derivatives *I*–*IV*, the splitting of *syn*-diazohydroxide acts as the rate-limiting step at gradually lower and lower pH values and to a gradually smaller and smaller extent. In the case of the derivative *V* the dependence log k' *vs* pH shows only a slight inflex (in the pH region 6—9) wherefrom k_2 cannot be computed, and in the case of the derivative *VI* at pH < 6 this dependence is completely linear, the slope being equal to −1.

From the isomerization rate constants of diazohydroxides and diazotates (Table I) and Eqs (3) and (6) it can be seen that the isomerization of diazohydroxides is substantially faster, but polar and especially mesomeric effects are far less significant. These findings enable the determination of probable isomerization mechanism of diazohydroxides. Two mechanisms are considered for isomerization of diazotates[1] — rotation about the N—N bond (*A*) or overturning around the positively charged nitrogen atom (*B*). In addition to it a further mechanism of isomerization can be

A ,   *B*
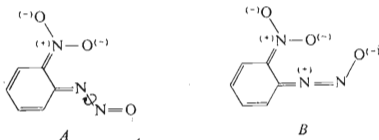
considered for diazohydroxides *viz.* rotation about N—N bond in the nitrosamine tautomer[4]. This mechanism is supposed by us to be the most probable. According to the first mechanism the isomerization of diazotates should be faster than that of diazohydroxides, because the formation of the activated complex *A* is less energy-demanding as compared to that of the corresponding diazohydroxide. Mesomeric effect should be considerably significant with the both mechanisms. In fact, the iso-

merization of diazotates is slower, and the influence of mesomeric effect on the iso-merization of diazohydroxides is relatively small.

Substituents of $-I$ and $-M$ type facilitate the isomerization of N-nitrosamines, because the contribution of the structure C to the resonance hybrid is relatively

$$C \longleftrightarrow D$$
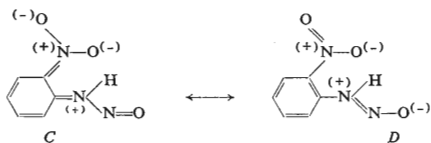
larger than that of structure D. At the same time, however, the concentration of diazo-hydroxide is increased to the detriment of the N-nitrosamine tautomer. Hence, the polar effects of substituents affect the both steps (antecedent equilibrium diazohydro-xide ⇌ N-nitrosamine and subsequent isomerization) antagonistically, and the result-ing effect is small.

Although the real structure of *syn-* and *anti-*diazotates has not yet been determined, it is presumed, on the basis of analogy with the structure and stability of *cis-* and *trans-*azobenzenes and diazocyanides, that the *syn* and *anti* isomers have the *cis* (E) and *trans* (F) configurations, respectively[11]. Littler[12] calculated the value $6 . 10^2$ for the equilibrium constant of this isomerization reaction of 4-nitro and 4-diazo derivatives. During study of the isomerization reactions of 2,6-dichloro-4-nitro-

$$E \qquad\qquad F$$

benzenediazotate it was found[5] that the equilibrium constant of the isomerization had the value 3. This value is inconsistent with the presumed steric effect of the both *ortho-*chloro substituents on the relative stability of the two isomers. In this case the *syn-*isomer, having *cis-*structure, should be far less stable than *anti-*isomer, as compared to 4-nitrobenzenediazotates, and hence on the contrary the K value should have increased. The observed change in equilibrium constant can be explained only by that the configuration of the both diazotates is opposite to what was supposed. In order to verify that the anomaly was not accidental, we determined the isomeriza-tion equilibrium constants of several further substituted benzenediazotates the sub-stituents of which should show different measure of steric hindrance to *cis-*isomer formation. In the case of 2-chloro-4-nitro- and 2-nitrobenzenediazotates the equi-librium constants were computed from the found isomerization rate constants k_1

TABLE II

Isomerization Rate and Equilibrium Constants of Substituted Benzenediazotates

Substituent	$k_1 . 10^3$	$k_2 . 10^5$	K
4-NO$_2$	30.5 ± 1.0^a		600^b
2-Cl, 4-NO$_2$,	32 ± 1.0	9.2 ± 0.5	350 ± 40
2-NO$_2$	1.50 ± 0.20	8.3 ± 0.5	18 ± 3
2,6-Cl$_2$, 4-NO$_2$^{c}	5.5 ± 0.8	1.8 ± 0.3	3.0 ± 0.5
2-NO$_2$, 4,6-Cl$_2$	—	—	0.70 ± 0.05

^{a} Ref.[3]; ^{b} ref.[1]; ^{c} ref.[5].

and k_2. In the case of 2-nitro-4,6-dichlorobenzenediazotate it was impossible to de-
termine the rate constants, however, the equilibrium content of the both isomers
could be determined by kinetic method[3]. The method made use of the fact that, after
injection of the equilibrium mixture of diazotates into chloroacetate or acetate buffer
containing 1,8-dihydroxynaphthalene-3,6-disulfonic acid, the reaction *syn*-diazo-
hydroxide → diazonium ion → azo dyestuff was much faster than the *anti* to *syn*
isomerization. From the time dependence of extinction of the azo dyestuff solution
being formed it was possible to calculate the content of the both isomers. The found
rate and equilibrium constants are given in Table II.

From the data given it can be seen that increasing steric requirements result in a de-
crease of the equilibrium constant. The decrease is by no means due to a change
of polarity of substituents. Polar effects have a large influence on the rates of iso-
merization reactions, which can be seen from Eq. (*1*), but their influence on equi-
librium constants is small. On the contrary, *e.g.* the difference between the isomeriza-
tion constant of 2-chloro-4-nitrobenzenediazotate and that of 2,6-dichloro-4-nitro
derivative is more than a hundredfold. Steric effects are obviously decisive for the value
of isomerization equilibrium constant, and the most acceptable explanation is that,
in fact, the *syn*-derivative has *trans*-configuration, and the *anti*-derivative has
cis-configuration.

G   *H*
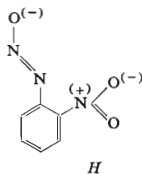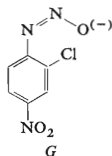
The isomerization equilibrium constant of 2-chloro-4-nitrobenzenediazotate is only $2\times$ smaller than that of 4-nitro derivative, which could be explained by the configuration G of the *cis*-derivative being sterically disadvantageous and practically insignificant. In the case of 2-nitro derivative only *trans*-configuration H and the corresponding *cis*-isomer can be considered.

Its equilibrium constant is about $30\times$ smaller than that of 4-nitro derivative, which suggests that the repulsive forces between the electron pair of the azo-nitrogen atom connected with benzene ring and those of oxygen atoms are greater in the *cis*-isomer. 2,6-Dichloro-4-nitro derivative has both its *ortho*-positions occupied, and the equilibrium constant is about $200\times$ smaller than that of 4'-nitro derivative. In the case of 2-nitro-4,6-dichloro derivative the equilibrium mixture contains predominantly the *syn*-isomer. The isomerization reaction rates of *ortho*-derivatives are affected by both polar and steric effects. If an at least rough estimate of polar effects is carried out on the basis of Eq. (*1*), the conclusion can be drawn that the decrease of the equilibrium constants is caused mainly by the decrease of k_1 values as a consequence of steric effects.

ortho-Substituents displace the azo group of the plane of aromatic ring by their steric effects, and hence during isomerization reactions they should decrease the energy of the activated complex B, and on the contrary they should increase the energy of the activated complex A. From our results it follows that steric effects slow down fundamentally the isomerization, and the rearrangement goes probably *via* the activated complex A.

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