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PREPARATION AND REACTIONS OF DIAZONIUM SALTS.
II. REACTIONS OF ArN_2^+

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4 Reactions of Arenediazonium Salts with Nucleophiles

Arenediazonium salts can react with nucleophiles in three ways (also see Introduction): (1) The substitution of diazonium group by a nucleophile (Part (6), (2) the substitution of a substituent at *ortho* or *para* position by a nucleophile (Part 5), (3) the addition of a nucleophile to the diazonium group producing the corresponding diazo compound Ar-N=N-Nu or a five- or six-membered ring if the nucleophile is represented by an *ortho*-standing substituent with regard to the diazonium group.

This section will deal with the third type of reactions. A stable diazo compound is formed if (a) the nucleophile is relatively strong and shows a low tendency for homolytic splitting to radicals or (b) if the product is converted to its conjugated base, e.g. $ArN_2OH \rightarrow ArN_2O^- + H^+$ or $Ar{-}N{=}N{-}N^+H_2Ar' \rightarrow Ar{-}N{=}N{-}NH{-}Ar' + H^+$, or (c) isomerized to a much more stable isomer. The role of nucleophilic atoms is played mainly by N, C, O, and six valent sulfur. As most reactions of diazonium salts with nucleophiles take place in aqueous solutions, this section will give the greatest space to the reactions of diazonium ions with OH^-.

4.1 Reactions of Arenediazonium Ions with OH^- Ion

4.1.1 Equilibria Arenediazonium Ion ⇌ Diazo Hydroxide ⇌ Diazotate

In aqueous alkaline medium, the following consecutive reversible reactions of diazonium ions take place

$$ArN_2^+ + OH^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} syn\text{-}ArN_2OH \qquad K_1 \tag{4.1}$$

$$syn\text{-}ArN_2OH + OH^- \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} syn\text{-}ArN_2O^- + H_2O \qquad K_2 \tag{4.2}$$

$$syn\text{-}ArN_2OH \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} anti\text{-}ArN_2OH \qquad K_3 \tag{4.3}$$

$$syn\text{-}ArN_2O^- \underset{k_{-4}}{\overset{k_4}{\rightleftharpoons}} anti\text{-}ArN_2O^- \qquad K_4 \tag{4.4}$$

$$anti\text{-}ArN_2OH + OH^- \underset{k_{-5}}{\overset{k_5}{\rightleftharpoons}} anti\text{-}ArN_2O^- + H_2O \qquad K_5 \tag{4.5}$$

The formation of the potassium salt of benzenediazonium ion with potassium hydroxide was described as early as 1866 by P. Griess[43] who recognized the reaction as being reversible. The transformation of diazonium ion into diazotate consumes two equivalents of OH^- ion. Hantzsch[44] monitored this reaction conductometrically but he presumed it to proceed in two separated steps similar to those of other dibasic acids, and he even described the isolation of a compound which he believed to be the diazo hydroxide. Only after 90 years from the first published paper in this field, Zollinger[45] measured the equilibrium diazonium $\rightleftharpoons$ diazotate with three substituted benzenediazonium ions for which the subsequent *syn-anti* isomerization is slow and does not interfere with the estimation of equilibrium of the acid-base reaction. He found that the neutralization curve only shows a single step although each diazonium ion consumed two OH^- ions. A similar case was described before by Schwarzenbach[46]. The diazonium ion reacts with OH^- ion as a Lewis acid to give the respective diazo hydroxide. The equilibrium constant K_1 of this reaction is lower (!) than the equilibrium constant K_2 of the reaction of diazo hydroxide with OH^-. The diazo hydroxide formed is rapidly transformed into the diazotate, hence its concentration is low throughout the measurement. This result was confirmed later also by spectral determination of the diazonium $\rightleftharpoons$ diazotate equilibrium[47]. The spectrum only contained the absorption bands corresponding to the starting diazonium ion and diazotate. The slope of the pH dependence of $[ArN_2^+]/[ArN_2O^-]$ had the value of -2 in accordance with the fact that the diazonium ion reacts with two equivalents of OH^- ion practically in a single step.

The transformation of diazonium ion into *syn*-diazotate can also be expressed by the following equations:

$$ArN_2^+ + H_2O \rightleftharpoons syn\text{-}ArN_2OH + H^+ \qquad K_{a1} \tag{4.6}$$

$$syn\text{-}ArN_2OH \rightleftharpoons syn\text{-}ArN_2O^- + H^+ \qquad K_{a2} \tag{4.7}$$

The equilibrium constants of the reactions (4.1), (4.2) and (4.6), (4.7) are defined by the following relations:

$$K = K_1 K_2 = \frac{[\mathrm{ArN_2O^-}]}{[\mathrm{ArN_2^+}][\mathrm{OH^-}]^2} \tag{4.8}$$

$$K_a = K_{a1} K_{a2} = \frac{[\mathrm{ArN_2O^-}][\mathrm{H^+}]^2}{[\mathrm{ArN_2^+}]} = K K_{\mathrm{H_2O}}^2 \tag{4.9}$$

where $K_{H_2O} = [\mathrm{H^+}][\mathrm{OH^-}]$

In aqueous alkaline solution both the diazonium ion and the diazo hydroxide react faster with OH^- ion than with water, but the estimation of equilibrium does not depend on the pathway by which the equilibrium had been attained, hence both equations (4.8) and (4.9) are correct. The application of the equations (4.6) and (4.7) and Eq. (4.9) is more common and more advantageous in determining the acid-base equilibria. Taking logarithms in Eq. (4.9) we obtain the relation:

$$\frac{\mathrm{p}K_{a1} + \mathrm{p}K_{a2}}{2} + \log \frac{[\mathrm{ArN_2O^-}]}{[\mathrm{ArN_2^+}]} = \mathrm{pH} \tag{4.10}$$

This means that $(\mathrm{p}K_{a1} + \mathrm{p}K_{a2})/2$ equals to the pH of the medium in which it is $[\mathrm{ArN_2^+}] = [\mathrm{ArN_2O^-}]$. This pH value has been called pH_m(Ref.[47]). The value of equilibrium constant K (and hence also pH_m) depends on the ionic strength of the medium. If I is increased from 0.1 to 1 mol l^{-1}, the K value decreases by about one order of magnitude. Table 4.1 presents the K and pH_m values measured at room temperature at the ionic strength I = 1 mol l^{-1}.

The ratio $[\mathrm{ArN_2^+}]/[\mathrm{ArN_2O^-}]$ is changed by a factor of 100 when pH is changed by 1; at $\mathrm{pH} = \mathrm{pH}_m + 1$ the reaction mixture only contains 1% diazonium ion and 99% diazotate. The concentration of diazo hydroxide always is negligible except for extremely reactive diazonium ions at $\mathrm{pH} = \mathrm{pH}_m$.

The dependence of log K upon the Hammett σ constants is linear with the slope $\rho = 6.6$. This very large value arises from the fact that K is a product of two equilibrium constants, hence ρ is a sum of ρ_1 and ρ_2 corresponding to the equilibrium constants K_1 and K_2, respectively. The slope of the dependence of pH_m vs. σ is one half of that for log K, which follows from Eq. (4.10). The substituents *o*- and *p*-NR_2 and -O^- exhibit such high negative σ values that the pH_m values of the respective diazonium ion cannot be measured.

4.1.2 Kinetics and Mechanism of Reaction Diazonium Ion $\rightleftharpoons$ *syn*-DiazoHydroxide $\rightleftharpoons$ *syn*-Diazotate

As it is $K_2 > K_1$, the partial constants K_1 and K_2 cannot be found by measuring the pH dependence of the concentrations of reacting components. For estimation of the constants of both steps it is necessary to determine the rate constant of the reaction of diazonium ion with OH^- ion and that of the reverse reaction of *syn*-diazo hydroxide giving the diazonium ion. The rate of formation of *syn*-diazo hydroxide is given by Eq. (4.11) and that of the reverse reaction by the relation (4.12).

Table 4.1 Equilibrium constants K ($l^2\ mol^{-2}$) of reaction $XC_6H_4N_2^+ = 2OH^- \rightleftharpoons XC_6H_4N_2O^- + H_2O$ and the corresponding pH_m values

X	pH_m	$K \times 10^{-4}$
4-NO_2	9.44	130 000
4-CN	9.77	29 000
3-CF_3	10.34	2 100
4-CF_3	10.55	790
4-SO_3^-	10.48	1 100
3-Cl	10.70	400
3-$COCH_3$	10.71	380
4-I	11.21	38
4-Br	11.09	66
4-Cl	11.21	38
4-CO_2^-	11.24	33
3-CO_2^-	11.54	8.3
4-F	11.53	8.7
H	11.90	1.6
3-CH_3	12.22	0.36
4-CH_3	12.59	0.066

$$\vec{v} = k_1[ArN_2^+][OH^-] \tag{4.11}$$

$$\overleftarrow{v} = k_{-1}[ArN_2OH] = k_{-1}\frac{[ArN_2O^-]}{K_2[OH^-]} = k_1\frac{[ArN_2O^-]}{K_1K_2[OH^-]} \tag{4.12}$$

The resulting velocity was determined by measuring the absorbance changes at a suitable wavelength and at various $[OH^-]$ concentrations or pH (Refs[48,49]). The dependence of the observed rate constants K_{obs} vs. $[OH^-]$ is defined by Eq. (4.13);

$$k_{obs} = k_1 [OH^-] + \frac{k_1}{K_1 K_2 [OH^-]} = k_1 \left([OH^-] + \frac{1}{K[OH^-]} \right) \qquad (4.13)$$

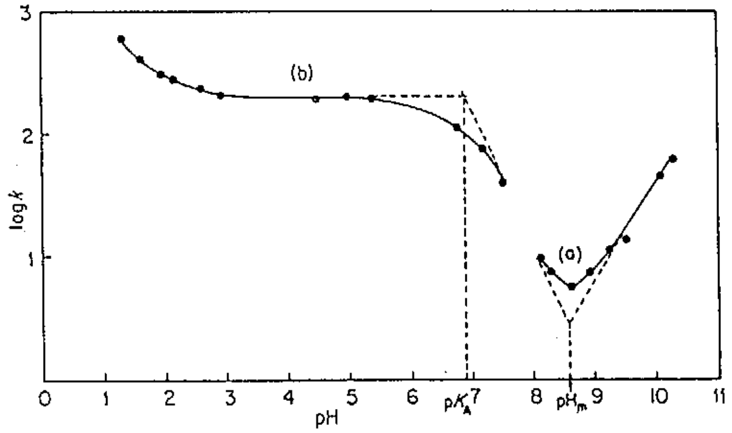
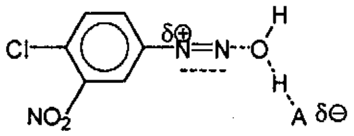


Fig. 1 The pH dependence of $\log k_{obs}$ of the reaction 3-nitro-4-chlorobenzenediazonium ion ⇌ *syn*-diazohydroxide ⇌ *syn*-diazotate at 20 °C. (a) Transformation of diazonium ion into the diazotate; (b) transformation of diazohydroxide (in equilibrium with diazotate) into diazonium ion

the pH dependence of log k_{obs} is given in Fig. 1 for the reaction of 3-nitro-4-chlorobenzene-diazonium ion. At pH > 8, the starting component was the diazonium ion, whereas at pH < 8 it was the *syn*-diazotate. In dilute hydrochloric acid, the k_{obs} value increases with increasing proton concentration, although in the reaction mixture practically all the diazotate is immediately transformed into diazo hydroxide. The transformation of diazo hydroxide is acid-catalyzed in this region (pH < 3), and the reaction course is really expressed by Eq. (4.6) at these proton concentrations, whereas at higher pH values it is defined by Eq. (4.1). Beside the proton also the acid component HA of the buffer used catalyzes the splitting off of OH group, hence the reaction exhibits the general acid catalysis[26]; the activated complex can be expressed by structure I.



I

The logarithms of the constants found (Table 4.2) correlate with σ constants.

$$\log k_1 = 2.1\sigma + 3.97 \tag{4.14}$$

$$\log k_{-1} = -3.4\sigma + 5.4 \tag{4.15}$$

$$\log K_{a2} = 1.3\sigma - 8.1 \tag{4.16}$$

The value of ρ constant of $K = k_1/k_{-1}$ calculated from the ρ values for k_1 and k_{-1} is 5.4. Although OH^- ion is a much stronger base than are the anions of aromatic hydroxy compounds, the rate constants of its reaction with diazonium ions are usually by several orders of magnitude lower than those of the azo coupling reactions with anions of aromatic hydroxy compounds. The OH^- ion is strongly solvated in water; before forming the N-O bond it must be partially desolvated, and this process needs a considerable amount of energy. As a result the reaction rate is substantially lowered.

Table 4.2 Rate and equilibrium constants of the reaction

$$ArN_2^+ + OH^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} syn\text{-diazohydroxide} \overset{K_{a2}}{\rightleftharpoons} syn\text{-diazotate} + H^+$$

Substituent(s)	$k_1 \times 10^{-5}$ $1\,mol^{-1}s^{-1}$	$k_{-1} \times 10^{-2}$ s^{-1}	$K_1 \times 10^{-3}$	pK_{a2}	ArN_2OH^a %
4-Cl-3-NO_2	7.4	1.95	3.8	6.90	2.05
3,5-Br_2	3.6	4.96	7.3	7.00	0.79
3,5-Cl_2	3.8	6.03	6.3	7.05	0.90
3-NO_2	4.5	5.34	8.4	7.15	1.11
3,4-Cl_2	1.3	3.00	4.5	7.30	0.28

[a] At pH = pH_m.

The K_1 and K_2 values can be used to calculate the maximum concentration of *syn*-diazo hydroxide (at pH = pH_m). The concentrations are very low (Table 4.2) but increase with increasing σ value (i.e. with increasing reactivity of the diazonium salt) because the K_1 values increase much more steeply than the K_2 constants do.

4.1.3 Kinetics and Mechanism of *syn* $\rightleftharpoons$ *anti* Isomerization

The *syn*-diazo hydroxides and diazotates rearrange to give the *anti*-isomers. The isomerization is usually slow, e.g. *syn*-benzenediazotate rearranges to the *anti*-isomer with the half life of about 100 h at room temperature. The isomerization of diazotates is considerably accelerated if there is a -M substituent at *ortho* or *para* position; 4-nitrobenzenediazotate is rearranged by more than 4 orders faster than the parent diazotate. From the measurements of the isomerization kinetics it was possible to derive the following relation of log k_4 vs. σ (Ref.[50]):

$$\log k_4 = 2.2[\sigma + 2.4(\sigma^- - \sigma)] - 5.6 \tag{4.17}$$

The general form of the equation is $\log k = \rho[\sigma + r(\sigma^- - \sigma)] + \log k_0$; the r value (which is usually less than 1) expresses the extent to which the conjugation of substituent with reaction centre makes itself felt in the given reaction as compared with that in the reaction serving as the standard for determination of σ^-. The value of 2.4 in Eq. (4.17) probably is the highest one out of the values given in literature so far.

Diazo hydroxides are rearranged faster than diazotates, e.g. 4-chlorobenzenediazo hydroxide is rearranged almost by 4 orders faster than the corresponding diazotate. The values of k_3 and k_{-3} increase but slowly with increasing σ values (assessed $\rho = 1$ and $r < 1$ for equations of the type (4.17)), hence in the case of the 4-nitro derivative the diazo hydroxide reacts faster by only about 1 order of magnitude. Therefore, in the case of substituents having low positive σ values the main reaction pathway is the isomerization of diazo hydroxide (in mildly basic media), whereas in the case of reactive diazonium ions (high σ constant values) it is predominantly or exclusively the *syn*-diazotate which is rearranged.

Some experimental values of the isomerization rate constant and pK_{a5} values are given in Table 4.3 for illustration. In contrast to *syn*-diazo hydroxides, which split off the OH^- ion with half lives of several ms or even faster, the *anti*-diazo hydroxides are much more stable. Thus e.g. the rate of splitting of benzene-*syn*-diazo hydroxide is higher than that of the *anti*-isomer by about 7 orders of magnitude. As a consequence, the dissociation constants of *anti*-diazo hydroxides can be determined by usual methods. The *syn*/*anti* ratio of *m*- and *p*-derivatives is practically independent of polar effects of the substituents; the K_4 values are about 10^3 (see Ref.[51]). With increasing sterical demands of *o*-substituents, the K_4 value rapidly decreases, which contradicts the current ideas. A similar case was described in the study of *syn*/*anti* configuration of N-alkyl-N-nitrosoanilines where *o*-substituents shift the equilibrium in favour of *syn* isomer, too[52].

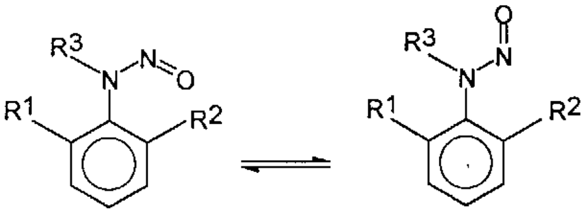
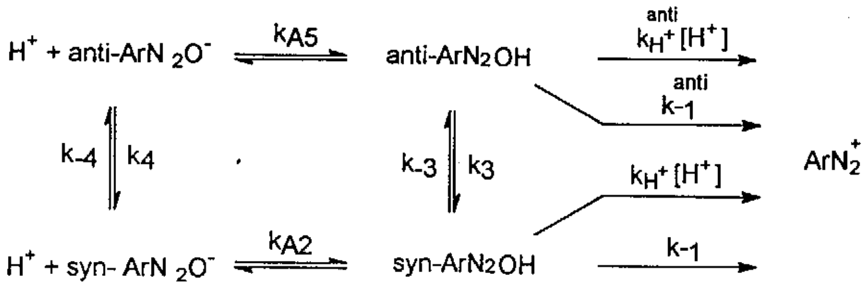


Table 4.3 Rate constants (s^{-1}) and equilibrium constants of isomerization of substituted benzenediazotates and diazo hydroxides (k_{-3}) and dissociation constants of *anti*-diazo hydroxides at 20 °C (Ref.[50])

Substituent(s)	k_4	k_{-4}	k_{-3}	K_4	pK_{as}
H	2.0×10^{-6}	$\approx 2 \times10^{-9}$	$\approx 5 \times10^{-4}$	1 000	7.29
4-NO_2	5.4×10^{-2}	9×10^{-5}	4.8×10^{-3}	600	6.13
2-Cl-4-NO_2	3.2×10^{-2}	9.2×10^{-5}		350	
2-NO_2	1.5×10^{-3}	8.3×10^{-5}	1.9×10^{-2}	18	6.15
4-Cl-2-NO_2	4.3×10^{-3}	3.7×10^{-4}	2.7×10^{-2}	11.5	5.80
5-Cl-2-NO_2	1.0×10^{-2}	8.3×10^{-4}	4×10^{-2}	12	5.60
2,4-$(NO_2)_2$	20.9		$2{,}4\times10^{-1}$		5.00
2,6-Cl_2-4-NO_2	5.5×10^{-3}	1.8×10^{-5}	6.4×10^{-2}	3.0	4.65

Interesting results were obtained from investigations of the reverse transformation of *anti*-diazotate to diazonium ion. *anti*-Diazotates derived from reactive diazonium ions can be prepared be merely pouring the solution of diazonium salt into a dilute sodium hydroxide solution. With little reactive diazonium ions, the rearrangement is carried out in more concentrated solutions (the higher the pH_m the more concentrated solution in order to reduce the decomposition of diazonium salt) and at higher temperatures. The transformation of *anti*-diazotate into the diazonium ion is monitored in the following way: the diazotate solution is injected into the buffer (or acid) solution containing a sufficient amount of a reactive coupling component which is able to react immediately with the diazonium ion formed to give the corresponding coloured azo compound, which prevents the reverse reaction. The reaction course is given in Scheme 4.1 (Ref.[53]).



Scheme 4.1

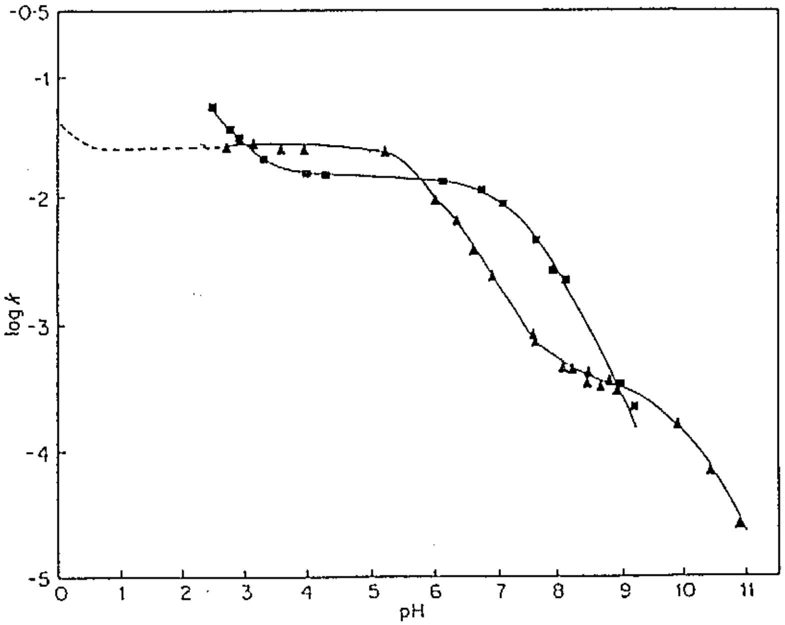


Fig. 2 pH-Dependence of $\log k_{obs}$ of conversion of nonsubstituted (■) and *anti*-2-nitro-4-chlorobenzenediazotates (▲) into the respective diazonium ions

Figure 2 shows the course of transformation of non-substituted benzene-*anti*-diazotate and *anti*-2-nitro-4-chlorobenzenediazotate to the corresponding diazonium ions depending on the pH value of medium. The *anti-syn* isomerization is very slow with the benzenediazotate, hence the main pathway consists in splitting off of OH^- ion from *anti*-diazo hydroxide (Scheme 4.2),

$$H^+ + \mathit{anti}\text{-}C_6H_5N_2O^- \rightleftharpoons \mathit{anti}\text{-}C_6H_5N_2OH \xrightarrow{k_{1\,anti}} C_6H_5N_2^+$$

Scheme 4.2

which is ca 7 orders faster than that from the *syn*-diazotate (see above). At the high pH values, k_{obs} increases with increasing proton concentration, because the diazo hydroxide concentration increases. At pH < pK_{a5} (7.29; see Table 4.3) k_{obs} becomes independent of $[H^+]$ because practically all the starting compound is present as the *anti*-diazo hydroxide. At pH < 3, the proton-catalyzed splitting of *anti*-diazo hydroxide begins to make itself felt, and the slope of log k_{obs} vs. pH dependence approaches -1.

With increasing σ constant values the rate of splitting of *anti*-diazo hydroxide decreases; the dependence of log k_{-1anti} upon σ constants

$$\log k_{-1anti} = -2.6\sigma - 1.89 \tag{4.18}$$

is similar to that for *syn*-diazo hydroxides (see Eq. (4.15)), but the rate constants are lower by many orders of magnitude[53]. At the same time, the isomerization rate increases too. With 2-nitro-4-chloro derivative (in the whole pH range), the splitting of *anti*-diazotate is slower than the isomerization of diazotate and (at lower pH values) diazo hydroxide with subsequent splitting of OH^- bond in *syn*-diazo hydroxide,* hence the transformation to diazonium ion takes the pathways given in Schemes 4.3 and 4.4.

$$anti\text{-}ArN_2O^- \rightleftharpoons syn\text{-}ArN_2O^- \overset{H^+}{\rightleftharpoons} syn\text{-}ArN_2OH \xrightarrow{k_1} ArN_2^+$$

Scheme 4.3

$$H^+ + anti\text{-}ArN_2O^- \rightleftharpoons anti\text{-}ArN_2OH \xrightarrow{k_3} syn\text{-}ArN_2OH \xrightarrow{k_1} ArN_2^+$$

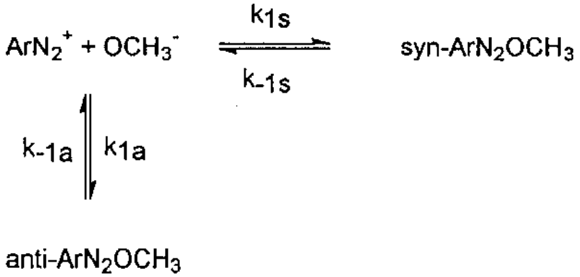
Scheme 4.4

At the highest pH values, *anti*-ArN_2O^- stands in equilibrium with a slight amount of *syn*-ArN_2OH, and the rate is limited by the splitting of *syn*-ArN_2OH; the log k_{obs} vs. pH dependence is linear with the slope of -1. Increasing proton concentration makes the transformation of *syn*-ArN_2OH to ArN_2^+ faster than its dissociation to diazotate, and the rate-limiting step is the isomerization of *anti*-diazotate to *syn*-diazotate; the dependence of log k_{obs} on pH has a slope near to zero (pH > 9); further increasing of $[H^+]$ makes the *anti*-diazo hydroxide concentration so high (p$K_{a5} \approx 5.8$) that the rate of its isomerization is higher than that of isomerization of diazotate (pH < 8); dependence of log k_{obs} on pH at first increases because of increasing concentration of diazo hydroxide but in the end it becomes pH independent since almost all diazotate has been transformed to diazo hydroxide. Although both the diazonium ions differ very much in their reactivities (the ratio of rate constants of the reactions with current nucleophiles is often above 4 orders of magnitude), the differences between the rates of transformation of the *anti*-diazotates to diazonium ions are small and the reactivity ratio may even be reversed in some pH regions. This is the consequence of the transformations going via different reaction pathways which are the most suitable ones for the given medium and substances.

4.2 Reactions of Diazonium Ions with Other Nucleophiles

4.2.1 Arenediazo Ethers

The reactions of diazonium ions with alkoxide anions differ fundamentally in several respects from those of diazonium ions with hydroxyl ion. The primary reaction product - diazo ether - cannot react with a further alkoxide ion to form a stable anion. The alkoxide ions are much less solvated in alcohols than is OH^- ion in water, and the relative permittivity of alcohols is substantially lower than that of water. As a consequence, the reaction of ArN_2^+ with RO^- is much faster and the reverse reaction much slower. The mechanism of *syn-anti* transformation is different from that operating with diazo hydroxides (Scheme 4.5)[54].



Scheme 4.5

The reaction takes two kinetically rather different steps. In the first one, the diazonium ion reacts very rapidly with alkoxide ion to give the corresponding *syn*-isomer. The rate constant of reaction of 4-nitrobenzenediazonium ion with methoxide at 23 °C is $k_{1s} = 3.10^8$ l mol^{-1} s^{-1} (Ref.[55]) and that for the reverse reaction is $k_{-1s} = 5.4$ s^{-1}. The equilibrium constant $K_{1s} = 5.6.10^7$ l mol^{-1}, i.e. more than 4 orders higher than K_1 for the reaction of 4-nitrobenzene-diazonium ion with hydroxyl ion; the difference between these values is due to the faster formation of diazo ether (by about 2.5 orders of magnitude) and to its slower dissociation into the starting substances (by almost 2 orders). In the second, far slower step (which is finished within ca 1 min) a small amount of the diazonium ion which is in equilibrium with *syn*-diazo ether reacts with methoxide ion to give the *anti*-diazo ether. The rate constant of this reaction is $k_{1a} = 2.5.10^6$ l mol^{-1} s^{-1} (it is 120 times smaller than that for the formation of *syn*-derivative); the rate constant of dissociation of *anti*-isomer (measured at 30 °C) is $k_{-1a} = 2.9.10^{-4}$ s^{-1} (which means that the equilibrium constant of isomerization is about

500, i.e. approximately the same as K_4 for 4-nitrobenzenediazotate in water) (Ref.[54]). The values of ρ constant of the dependence of log k_{-1a} on σ constants are -2.8 and -3.2 for the *meta* and *para* derivatives, respectively (see Fig. 3), i.e. somewhat higher than that for *anti*-diazo hydroxides, which is typical of reactions in media which less solvate ions. In the case of the reaction of diazonium ions with ethoxide anion in ethanol, the ρ constant has an even greater negative value (-4.2), and k_{-1a} for 4-nitro derivative ($1.9.10^{-5}$ s^{-1}) is more than one order of magnitude smaller than that in methanol[56]. Also measured in ethanol were the K_{-1s} values for substituted 2-nitro derivatives[57]; the found value ρ = - 5.4 is higher than that for the *anti*-isomer in analogy with the reverse reaction of diazo hydroxides in water.

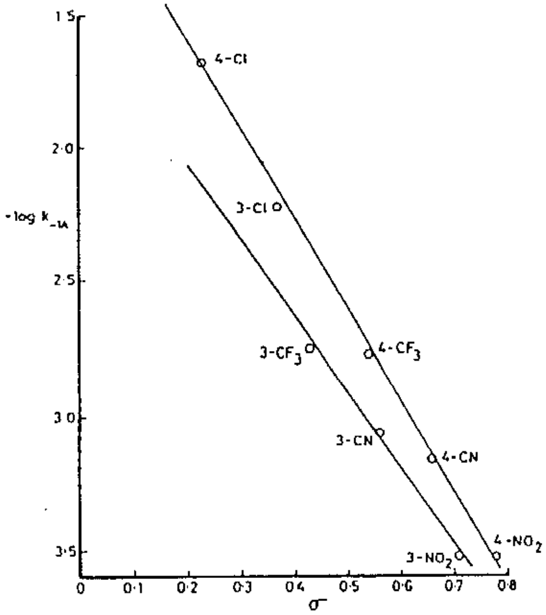


Fig. 3 Hammett plot for the ionization of *anti*-arylazo methyl ethers (k_{-1A}) in methanol at 30 °C

Phenoxide ions in water are very weak nucleophiles, hence the equilibrium constants of formation of ArN=NOAr′ are very small. So far no reliable value has been found for the equilibrium constant of this reaction.

4.2.2 Arenediazo Thioethers

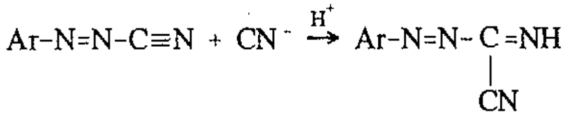
Diazo thioethers are formed very easily and rapidly by the reaction of diazonium salts with thiolate anions, however, they are extraordinarily unstable and decompose often explosively, hence it is quite dangerous to handle with them. The reason of the low stability lies in much higher tendency of N-S bond to split homolytically to radicals $ArN_2\cdot$ and $RS\cdot$ as compared with much less easy homolysis of N-O bond. With regard to their low stability, diazo thioethers should not actually be treated within this chapter, but nevertheless the reactions of diazonium ions with substituted thiophenolate ions are given here to illustrate the tremendous difference in nucleophilicity as compared with the much more basic phenoxide anions. The rate constant of reaction:

$$4\text{-}NO_2C_6H_4N_2^+ + C_6H_4S^- \underset{k_1}{\overset{k_1}{\rightleftharpoons}} syn\text{-}4\text{-}NO_2C_6H_4N_2SC_6H_5 \tag{4.19}$$

measured[55] in methanolic buffers at 23 °C is $8.7.10^9$ l mol^{-1} s^{-1}, i.e. almost 1.5 orders higher than that of the reaction with methoxide ion, and the equilibrium constant is $K_1 = 1.9.10^{10}$, i.e. even by 2 orders higher. The rate constant k_1 already approaches the values of diffusion-controlled reactions, and the effect of substituents upon k_1 is much smaller than that in the reactions with other nucleophiles.

4.2.3 Arenediazo Cyanides

Substituted benzenediazonium ions react rapidly and reversibly with cyanide ions in aqueous media to give the corresponding *syn*-diazo cyanides which are slowly isomerized to the much more stable *anti*-isomers[59]. For their preparation one must add the solution of cyanide to the solution of diazonium salt. Otherwise the excess CN^- ions react with the primary diazo cyanide since the -C≡N group is easily attacked by nucleophiles:



$$Ar{-}N{=}N{-}C{\equiv}N + CN^- \xrightarrow{H^+} Ar{-}N{=}N{-}\underset{\displaystyle CN}{\underset{|}{C}}{=}NH \tag{4.20}$$

The *syn*-isomers are relatively unstable and can explode on heating. The substituent effects on the rate of formation of the *syn*-isomer (k_1) and on the equilibrium constant of the formation (K_1) are expressed quantitatively in the following Hammett relations[59]:

$$\log k_1 = 2.31\sigma + 2.32 \tag{4.21}$$

$$\log K_1 = 3.53\sigma + 1.82 \tag{4.22}$$

The relatively low value of $\rho = 3.53$ (as compared e.g. with the value of 5.4 for the reaction of diazonium ions with OH^- ion) is due to the strong -M effect of CN group. This effect also has the consequence that, in contrast to diazotates and diazo hydroxides, the isomerization is retarded by electron-attracting substituents[60]; e.g. in benzene solution at 25 °C the half life of isomerization of non-substituted *syn*-isomer is 0.12 h, those of 4-bromo and 4-nitro derivatives being 12 and 27 h, respectively.

Although the CN^- ion is more basic than $C_6H_5S^-$, and carbanions usually are strong nucleophiles, its reaction with diazonium ions in water is slower than the reaction of $C_6H_5S^-$ in methanol. For the 4-nitro derivative the differences in k_1 and K_1 are almost 6 orders. The main reason of this relatively low reactivity lies (cf. OH^- ion) in strong solvation of CN^- ion with water. Thus e.g. in dimethyl sulfoxide, in which CN^- ion is much less solvated, the k_1 value of 4-chloro derivative is more than 5 orders higher than in water, the corresponding difference in K_1 being almost 7 orders of magnitude[59].

4.2.4 Arenediazo Sulfonates

A preparation of diazo sulfonate was described[61] as early as 1869, and the reaction has been intensively studied since the products were of considerable technical importance in the past. The reaction is carried out at pH 7 - 8; at higher pH values nonreactive diazotates are formed, and in the presence of excess sulfite a second equivalent of SO_3H is added to give arylhydrazinedisulfonic acid, which is hydrolyzed to arylhydrazine in acid media at higher temperatures.

The rate of formation of diazo sulfonate is directly proportional to the concentrations of diazonium ion and SO_3^{2-}; no reaction takes place between HSO_3^- and diazonium ion[62]. The first, very fast step ($k_1 = 4.5.10^8$ l mol^{-1} s^{-1} for 4-nitro derivative) produces the *syn*-isomer; the K_1 value of formation of the 4-nitro derivative is 3.10^8 l mol^{-1}, and the ρ constant is 5.5, i.e. similar to that of diazo hydroxides; the reaction is reversible, the rate of the reverse reaction is increased with decreasing σ value of substituent as it is the case with diazo hydroxides, too; for the 4-chloro derivative the half life of the reverse reaction is 15 ms (Ref.[63]). The isolated *syn*-isomers are usually contaminated with the *anti*-isomer because they are very soluble in water and relatively rapidly are transformed to *anti*-isomers; the half life of isomerization is 6 - 10 min at 0 °C. The *anti*-isomers are extremely stable. As solids they can be kept for years. The equilibrium constant of isomerization reaction of 4-methoxy derivative is 10^7, and the rate constant of reverse transformation is 10^{-10} s^{-1} (i.e. a half life of more than 100 years)[64]. The *anti* → *syn* transformation rate is very much accelerated by irradiation; the *anti*-isomer is regenarated again in darkness.

The yields of diazo sulfonates from the reaction of 1- and 2-naphthalenediazonium ions with sulfite are very low - there takes place a consecutive reaction:

$$2\,C_{10}H_7N_2^+ + NaHSO_3 \rightarrow C_{10}H_7\text{-}N{=}N\text{-}C_{10}H_7 + N_2 \tag{4.23}$$

The highest yields of the azo compound are obtained with the application of 1/2 equivalent of sodium hydrogensulfite[65].

4.2.5 Arenediazoamino Compounds (1,3-Diaryltriazenes)

On reacting with nucleophiles, diazonium ions produce a number of compounds containing the reactive centre -NH-. The most important and thoroughly studied among them are triazenes which are formed by reacting diazonium ions with primary and secondary aliphatic and aromatic (or heteroaromatic) amines.

$$ArN_2^+ + HNR^1R^2 \underset{k_1}{\overset{k_1}{\rightleftharpoons}} ArN{=}N{-}\overset{\oplus}{N}HR^1R^2 \rightleftharpoons ArN{=}N{-}NR^1R^2 + H^+ \qquad (4.24)$$

So far it has not been proved that these products undergo a *cis-trans* isomerization. The dipole moments measured indicate that the isolated products are *trans*-isomers[66].

The reaction of diazonium ion with an aromatic amine can result either in a reversible attack of amine nitrogen atom to give triazene or in an attack of aromatic carbon atom to give a very stable azo compound. The azo coupling reaction is negligible when reacting aniline in mildly acid medium, it takes place to a small extent with alkylanilines, but it becomes the chief reaction in the cases of more reactive aromatic amines such as naphthylamines. Increasing acidity of medium speeds up the reverse reaction of triazene, and the content of azo compound in the reaction mixture increases.

The reaction with primary amines is connected with another complication: two tautomers of triazene are formed, and the acid catalyzed splitting of triazene can lead to an amine and a diazonium ion different from those present as the starting substances. If in R-N=N-NH-R' both R and R'are aryl groups, the splitting preferably produces the less reactive diazonium ion and the less basic amine. If R is an alkyl, the triazene is split into the aromatic amine and alcohol or, as the case may be, other products obtainable from the primary cation R^+.

The reactions of diazonium ions with aromatic amines are dealt with in more detail in the section about azo coupling reactions.

The rate constants of reaction of diazonium ions with aliphatic amines and of the reverse reaction of the triazenes formed were measured in a series of *m*- and *p*-substituted benzenediazonium ions reacting with dimethylamine in water at 25 and 20 °C (Ref.[67]). The ρ constants observed for the formation of triazene and its reverse reaction are 3.47 and - 3.8, respectively. The resulting ρ constant is 7.28 for the equilibrium constant:

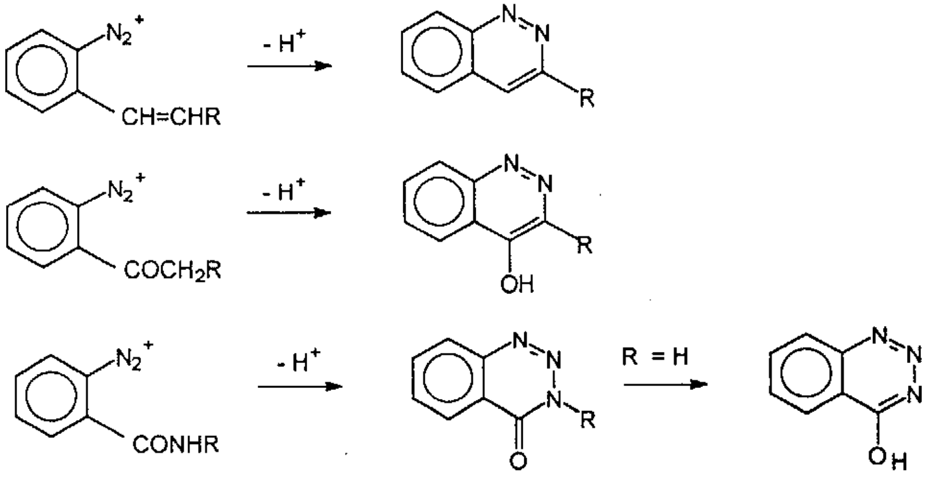
$$K = \frac{[ArN{=}N{-}N(CH_3)_2]\,[H^+]}{[ArN_2^+]\,[HN(CH_3)_2]} \qquad (4.25)$$

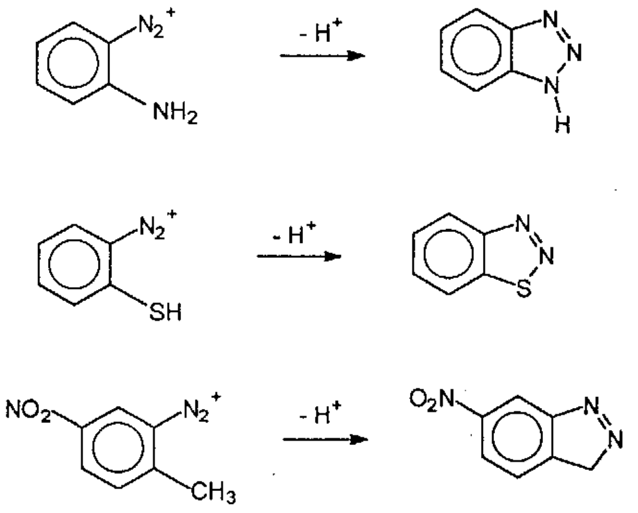
i.e. it is only slightly higher than the value found for the reaction of diazonium ion with OH^- ion. The calculated rate constant k_1 of the reaction of benzenediazonium ion is 450 l mol^{-1} s^{-1}, i.e. 3 orders lower than that of azo coupling reaction with 1-naphtholate ion and about 1 order lower than that of the reaction with OH^- ion.

4.3 Reactions of Diazonium Group with Nucleophilic *o*-Substituents

If there is a substituent present in *ortho* position to diazonium group, and this substituent is able to react as a nucleophile, an intramolecular reaction will take place - a cyclization giving five- or six-membered rings. The reaction can take place rapidly already during the diazotization, or the cyclization can proceed slowly after finished diazotization, or - as the case may by - after changing the reaction conditions. In some cases the reaction is reversible, hence after an addition of sufficiently reactive coupling component (e.g. an aromatic hydroxy compound) azo coupling will take place. The cyclization occurs even if the *ortho* standing substituent is a very weak nucleophile such as a carbon atom with activated double bond, because the rate of intramolecular reaction usually is by several orders of magnitude higher than the rates of intermolecular reactions.

Literature gives many examples of reactions of diazonium group with an *ortho*-standing nucleophilic substituent[3]; some typical examples will be presented here for illustration:

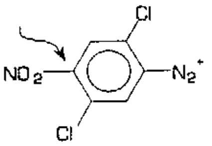




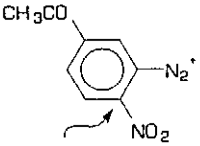
5 Nucleophilic Aromatic Substitutions

As already stated in Introduction the $-N_2^+$ group strongly attracts electrons from the aromatic nucleus, much more than any other group, e.g. more strongly than two nitro groups. This has two opposite effects on the reactivity of the aromatic nucleus. Due to a severe electron deficit in the aromatic nucleus no current electrophilic substitutions (such as nitration, sulfonation, halogenation etc.) can take place in the arenediazonium ions. Only with quinonediazides it is possible to perform some electrophilic substitutions since the negatively charged oxygen atom to a certain extent neutralizes the unfavourable polar effect of diazonium group. Electrophilic aromatic substitution reactions in adjacent ring of naphthoquinonediazides are easier than those in benzene series: 1-diazo-2-hydroxynaphthalene-4-sulfonic acid can be nitrated at 6 position.

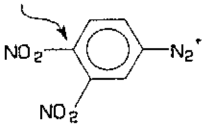
On the other hand the $-N_2^+$ group is the best activator for nucleophilic aromatic substitutions especially (or better: exclusively) so for the substitution reactions at *ortho* and *para* positions to the diazonium group. From the difference 1, 3 between σ_m and σ_p^- of N_2^+ group (Ref.[2]) and from the value of ρ constant for aromatic nucleophilic substitution with current nucleophiles ($\rho \approx$ 3 - 5) it can be assessed that the difference between the rates of substitution of a substituent at *meta* and *para* positions to N_2^+ group will be 3 - 5 orders of magnitude. If there is only one substituent in the benzene ring at *ortho* or *para* positions, the rate of its replacement is low even with strong nucleophiles. In the naphthalene series the reactions are much faster, hence even a single substituent with a sufficiently strong tendency to splitting (e.g. nitro group) will be easily replaced by a nucleophile if there is an *ortho*- or *para*-standing N_2^+ group. For the reaction to be fast in the benzene nucleus it is necessary that an additional substituent with a great value of σ constant (e.g. one or two halogens at *meta* and *ortho* position) or better still a substituent with strong -M effect (i.e. great value of σ_p^-) were present at *ortho* or *para* position to the substituent replaced. In the structures I - IV given below, the arrows denote the groups which will be replaced by a nucleophile.



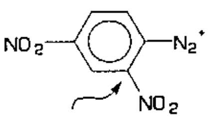
I



II



III



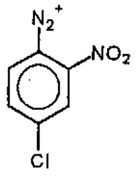
IV

The chlorine atoms at 2 and 5 positions with respect to nitro group (I) will accelerate the substitution by several orders. In the molecule II the nitro group react readily since the $COCH_3$ group exerts a strong -M effects (a high value of σ_p^- constant), and a substituent at *ortho* position to N_2^+ group is activated more strongly than that at *para* position. Particularly clearly this can be seen in 2,4-dinitrobenzenediazonium ion (IV) where the *ortho*-standing nitro group is replaced preferably. The replacement of this nitro group, of course, is much slower (at comparable conditions) than that of 4-nitro group in 3,4-dinitrobenzenediazonium ion (III) since a nitro group at *ortho* position to the substituent replaced activates more strongly than the same group at *meta* position ($\sigma_{m\text{-}NO_2}$ = 0.71; $\sigma^-_{p\text{-}NO_2}$ = 1.25; $\rho \approx 4$; hence the difference between the rate constants is $(1.25 - 0.71) \times 4$ = ca 2 orders of magnitude). The role of nucleophile can be played by e.g. Cl^-, Br^-, $RCOO^-$, SCN^-, CN^-, RO^-, H_2O, and particularly HO^-. In the last case it must not be forgotten that OH^- can realize both the substitution and the reaction with N_2^+ giving the diazo hydroxide and diazotate, which has two consequences: (1) At the $[OH^-]$ concentration corresponding to pH > pH_m the ArN_2^+ concentration decreases with the square of hydroxyl ion concentration, so the substitution rate becomes inversely proportional to $[OH^-]$. (2) At pH close to pH_m, various side reactions become more or less significant, which is usually connected with splitting off of nitrogen (see Section 6). If a substituent is replaced by OH^- ion, the corresponding quinonediazide is formed in which the reactivity of nucleus to nucleophilic substitution is lowered so strongly that further substitution does not proceed even at severe conditions.

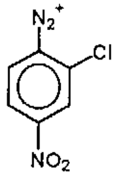
The tendency of substituents to be split off decreases in the series: $N_2^+ > NO_2 > Cl > Br > RCOO > RO$. According to this sequence, e.g. the compound I should most rapidly split off the nitrogen molecule. However, one must also take into account the mutual influences of both groups (NO_2, N_2^+) on their reactivities which in this case are quantitatively expressed by the values of the corresponding σ_p^- constants. The σ_p^- value of N_2^+ group is by almost 2 units higher than that of nitro group; even if we took $\rho = 3$ for nucleophilic substitution (usually it is grater), the acceleration of the replacement of nitro group caused by p-N_2^+ would be almost a million times greater than that of the replacement of N_2^+ caused by p-NO_2. Hence in arenediazonium ions an *ortho* or *para*-standing substituent (to N_2^+) is replaced almost always and not the diazonium group itself. A different situation is encountered with heterocyclic diazonium ions (see Section 7) where the heteroatoms in the nucleus strongly affect the substitution of N_2^+ but cannot react themselves.

The most important nucleophiles are H_2O and OH^- which are always present in aqueous solutions of diazonium salts. Which group and how rapidly will be replaced by OH group is governed by the abilities of individual groups to be split off together with bonding electron pair, their effects on the substitution rates of the other groups, the mutual positions of groups, the concentration of OH^- and the presence of further bases which can be catalytically active. Below we will mention several cases studied with regard to both the reaction products and the kinetics and mechanism of the substitution reaction.

The reactions of 2-nitro-4-chloro- and 4-nitro-2-chlorobenzenediazonium ions were studied in buffers of pH 2.9 - 7.9 (Ref.[68]):



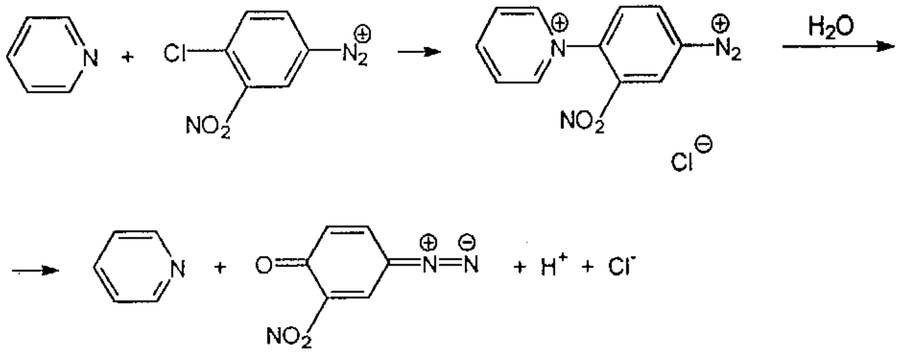
V



VI

In compound V, 2-NO_2 group is exclusively replaced by OH in the whole pH range studied. Although nitro group more strongly facilitates the splitting off of Cl^- than *vice versa*, nevertheless, (1) nitro group is a better nucleofuge and (2) *ortho* position is more activated than *para* position by the N_2^+ group. In compound VI both Cl and NO_2 groups are replaced by OH (the ratio is 3:7). The reactivity of chlorine has been strongly increased (it is *ortho* to N_2^+ and, on the other hand, that of nitro group has been decreased. The overall rate was 3 - 5 times lower. At first the reaction rate increased linearly with OH^- concentration. At $pH = pH_m$ (7.2 and 6.4 for V and VI, respectively) it reached its maximum whereafter it decreased again. At constant concentration of OH^- ions the rate increased with increasing buffer concentration (by as much as ca 2 orders of magnitude), which means that beside the reaction with OH^- also significant is the reaction with water catalyzed by the basic buffer component which facilitates the reaction by assisting dehydration and deprotonation in the activated complex.

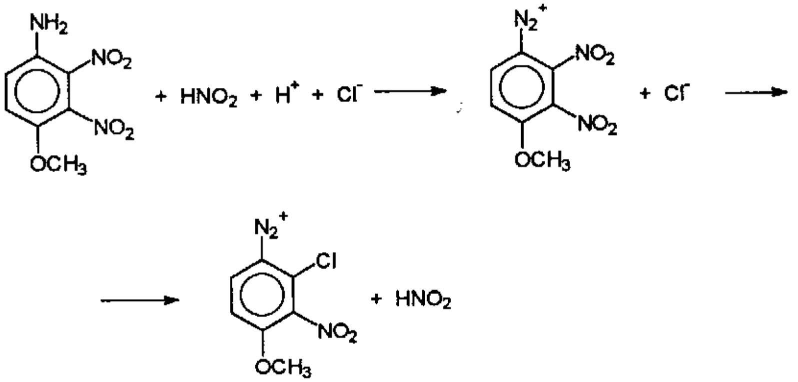
In the reactions of 3-nitro-4-halogenobenzenediazonium ions[69] halogen is exclusively replaced; the nitro group is at *meta* position to N_2^+ group and *ortho* to halogen, i.e. it strongly accelerates the replacement. At pH < 5, the substitution rate was independent of OH^- concentration, i.e. a water molecule played the role of nucleophile. The reaction half life at 20 °C was ca 100 h for the 4-chloro and 4-bromo derivatives but only 1 min for the 4-fluoro derivative! Whereas the chloro and bromo derivatives could be prepared by diazotizations in dilute hydrochloric acid, the diazotization of 4-fluoro-3-nitroaniline required sulfuric acid. After addition of water to the diazotization mixture the hydrolysis was the faster the higher was the water content. In 5M H_2SO_4 the reaction half life was below 0.5 h already. At pH > 5 the rate of reaction of 4-chloro and 4-bromo derivatives increased with increasing concentration of hydroxyl ion and reached the maximum at pH ≈ 8.5 (≈ pH_m) when the half life was 25 s for the reaction of 4-chloro derivative. At the same time it was possible to observe an increasing extent of substitution of N_2^+ by OH^- group. At a constant pH value the rate increased (similarly to the above-mentioned chloronitro derivatives V and VI) with increasing buffer concentration; again 3-nitroquinonediazide was the product of the reaction catalyzed by the basic buffer component. In this case, however, when the reaction was performed in the pyridine buffer solution, it was possible to observe spectroscopically the intermediate of reaction of diazonium ion with pyridine which reacted rapidly with water with a catalysis by another pyridine molecule to give the final quinonediaziode (Scheme 5.1).



Scheme 5.1

From the examples given it can be seen that both the reaction rate and mechanism and composition of products depend considerably upon the mutual positions of substituents, pH of medium, and - as the case may be - the type and concentration of buffer.

An easy replacement of some substituents in reactive diazonium ions by Cl^- has the consequence that it is impossible to carry out the corresponding diazotization reactions in hydrochloric acid; the Cl^- ions are much stronger nucleophiles than H_2O, so a substituent practically inert to water can react with Cl^-. If a substituent readily reacts even with water molecules, the respective diazotization must be carried out in anhydrous medium although the diazotization reaction proper may proceed at a sufficient rate in dilute acids (see the cases of 4-chloro-3-nitroaniline and 4-fluoro-3-nitroaniline) In conclusion let us consider a case of synthetical utilization of a fast replacement of nitro group by a nucleophile. During the diazotization of 4-methoxy-2,3-dinitroaniline with sodium nitrite in hydrochloric acid, chloride anions very rapidly replaced the nitro group at *ortho* position to N_2^+ (Eq. (5.1)); the nitrous acid thus liberated reacts with another amine molecule and the whole process is repeated. The diazotization only needs a small amount of nitrite for starting the reaction[70]:



(5.1)

If the nitro group stands at 5 position instead of 2 position, then the OCH_3 group is replaced since now the two nitro groups are mutually at *meta* position, being also *meta* to N_2^+, and, on the other hand, the methoxy groups is *ortho* to both nitro groups and *para* to N_2^+ group.

6 Splitting off of Nitrogen Molecule and Subsequent Reactions

6.1 Introduction

There are a large number of reactions of diazonium ions in which at first a nitrogen molecule is split off and then the aromatic residue forms a new bond with another substance (neutral molecule, ion, or radical). As a result, the N_2^+ group is replaced by some other group.

The splitting off of a nitrogen molecule produces either an aryl cation or an aryl radical. In a few cases also the formation of aryl anion is presumed. As already stated in part 1 the diazonium group tends to heterolytic splitting of C-N bond to give the extraordinarily stable N_2 molecule and aryl cation (6.1). On the other hand, a homolysis (radical splitting) of the C-N bond would produce the very unstable radical-cation $N_2^{+\cdot}$ (6.2), which process is so unfavourable energetically that it does not occur at all.

$$ArN_2^+ \rightarrow Ar^+ + N_2 \qquad (6.1)$$

$$ArN_2^+ \rightarrow Ar\cdot + N_2^{+}\cdot \qquad (6.2)$$

If the radical splitting should take place, the N_2^+ group must be given an electron at first whereby it is enabled to split off as a neutral N_2 molecule. In principle this can be done in two ways: (1) The arenediazonium ion forms a bond with such a nucleophile Nu that the N-Nu bond formed is easily homolyzed (6.3); the radical $ArN_2\cdot$ formed is very unstable and rapidly decomposes to a nitrogen molecule and aryl radical $Ar\cdot$.

$$ArN_2^+ + Nu^- \rightleftharpoons Ar{-}N{=}N{-}Nu \rightarrow ArN_2\cdot + \cdot Nu \qquad (6.3)$$

(2) The diazonium ion forms a "nonbonding" complex with a compound having a low reduction-oxidation potential (Cu^I, I^-, hydroquinone) and the complex formed undergoes an electron transfer. Especially suitable are such compounds which in some later stage easily accept an electron, i.e. act as true catalysts (their concentration does not substantially change during the reaction, hence only a small amount is necessary); there results a catalyzed decomposition to aryl radicals. The action of cuprous salts can serve as an example:

$$\begin{aligned} &ArN_2^+ + Cu^ICl_2^- \rightleftharpoons ArN_2^+.Cu^ICl_2^- \rightarrow ArN_2Cu^{II}Cl_2 \rightarrow \\ &Ar\cdot + N_2 + Cu^{II}Cl_2 \rightarrow ArCl + Cu^ICl + N_2 \end{aligned} \qquad (6.4)$$

Also nitrite anion belongs among the substances with low reduction-oxidation potential, and especially at higher temperatures catalyzes the radical decomposition of diazonium ions and lowers the yields of ionic reactions (e.g. in the preparation of phenols via thermal decomposition of diazonium salt solutions).

6.2 Non-Catalyzed Decomposition of Diazonium Ions in Media of Low Nucleophilicity

If a solution of diazonium salt contains neither strong nucleophiles (and the solvent has no distinct nucleophilic character either) nor compounds with low reduction-oxidation potential, then the only reaction is heterolysis of arenediazonium ion giving aryl cation. This also is practically the only passable pathway for preparation of aryl cation. What is the effect of medium upon the reaction rate and composition of products, what is the reaction mechanism, and what are the substituent effects on the reaction rate. The effect of medium upon the reaction rate and (partially) composition of products is shown in Tables 6.1 and 6.2.

The rate constant of splitting of benzenediazonium tetrafluoroborate (BF_4^-

exhibits a negligible nucleophilicity) falls to one half on going from 0.001% H_2SO_4 to 96% H_2SO_4 and it is four times smaller in pure dioxane, i.e. the effects of both acidity and polarity of medium are very small, hence there is a small solvation difference between the starting ion (or ion pair) and the activated complex. A big difference in the concentration of benzenediazonium chloride in water also has a small effect on the rate constant (the maximum increase is 1.34 times) but the yield of phenol strongly decreases in favour of formation of other substances, especially chlorobenzene.

Table 6.1 Effect of medium upon decomposition rate constant k (s^{-1}) of benzenediazonium tetrafluoroborate at 25 °C (Ref.[74])

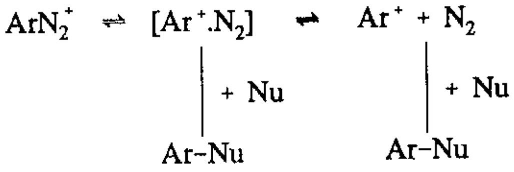
Solvent	$k \times 10^5$	Solvent	$k_1 \times 10^5$
0.001 % H_2SO_4	4.59	CH_3COOH	2.26
9.5 % H_2SO_4	4.12	CH_2Cl_2	2.20
50 % H_2SO_4	2.68	dioxane	1.15
96 % H_2SO_4	2.11		

Table 6.2 Effect of concentration of benzenediazonium chloride on decomposition rate constant k (s^{-1}) and content of phenol at 35 °C (Ref.[58])

$H_2O : ArN_2^+$ Mol ratio	Phenol, %	$k \times 10^5$
600	95	19.5
48	60	23.4
12	40	25.3
3.1	30	26.8
2.4	24	26.2

An investigation[71] of influence of anions with different nucleophilicities on the rate constant and composition of products in dilute aqueous solutions of diazonium salts showed that the presence of anions has an only small effect on the value of rate constant but a considerable effect on the composition of products. Increasing concentration of X^- resulted in an increase of yield of substituted benzene C_6H_5X to the detriment of phenol. The ratio of rate constants calculated from the composition of products and concentration of anions (referred to unimolar concentrations of the participating nucleophiles inclusive of water) k_X/k_{H_2O} was 1.4 (SO_4^{2-}), 3.0 (Cl^-), 6.0 (Br^-), 6.0 (SCN^-, sulfur as the nucleophile), and 3.0 (SCN^-, nitrogen as the nucleophile), i.e. the aryl cations are very little selective, much less than most carbenium ions.

On the basis of studies of the dependence of reaction rate upon the concentration of N_2 in trifluoroethanol and with the ^{15}N nitrogen (Refs[72,73]) it was possible to suggest the following mechanism:



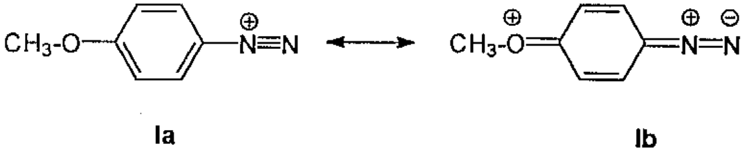
Scheme 6.1

The first step produces the "intimate" ion-molecule pair which can be reverted to the starting diazonium ion, or dissociate to solvated aryl cation and N_2 molecule, or react with a nucleophile. In solutions with relatively high nucleophilicity (H_2O) the solvent molecule reacts with aryl cation in the phase of intimate pair before recombination to diazonium ion can take place; little nucleophilic solvents mainly react with the solvated aryl cation; as only a part of the intimate pair dissociates to the solvated aryl cation, the rate constants are lower in little nucleophilic solvents. Negatively charged nucleophiles react in aqueous medium with the intimate pair, too, and since they are more nucleophilic than water, the proportion of C_6H_5X is higher than it should be according to their population; the effect on the rate constant is small because even in water alone most of the aryl cation has reacted with water and only a small part has recombined to diazonium ion.

Table 6.3 Effect of substituents on decomposition rate constant k (s^{-1}) of benzenediazonium chloride at pH 1.6 - 1.8 at 28.8 °C (Ref.[89])

Substituent	$k \times 10^7$ for the position of substituent		
	ortho	*meta*	*para*
OH	6.8	9 100	0.93
OCH_3		3 400	0.11
C_6H_5	1 100	1 700	37
CH_3	3 700	3 400	91
H	-	740	-
COOH	140	410	
SO_3^-	91	150	42
Cl	0.14	31	1.4
NO_2	0.37	0.69	3.1

The effect of substituents upon the decomposition rate constant of $XC_6H_4N_2^+$ is presented in Table 6.3. All strongly electron-attracting substituents retard the decomposition of diazonium ion. The substituents which attract electrons only a little more strongly than hydrogen does (little positive σ values) or even less strongly exert strongly position-depending effects, which is the more pronounced the higher is the +M effect of substituent, i.e. its ability to delocalize free electron pair as far as the reaction centre - diazonium group. Thus e.g. 4-methoxy-benzenediazonium ion is the most stable among the ions given, but 3-methoxy derivative belongs to the least stable ones. The difference in the rate constants is more than 4 orders of magnitude! Every strong electron-acceptor substituent destabilizes the aryl cation and retards its formation. On the other hand, an electron-donor substituent with +I effect stabilizes the aryl cation and accelerates its formation. The same effect is exerted by a *meta*-substituent with +M effect since it partially delocalizes electrons into the nucleus of aryl cation. If the +M substituent is present at *para* position the free electron pair is considerably delocalized into the diazonium group in the starting state already:



Thereby the whole system is stabilized and the C-N bond possesses a partially double bond character, hence its splitting is made very difficult. The logarithms of rate constants of *meta* and *para* substituted derivatives were correlated with the F (field) and R (resonance) constants according to the relation:

$$\log \frac{k_m}{k_0} = f_m F + r_m R \tag{6.5}$$

valid for the *meta* derivatives and the analogous one ($\log (k_p/k_0)$) for *para* derivatives[74]. The F values correspond to inductive effects of substituents and the R values correspond to resonance or mesomeric effects of substituents[75]. The values f and r found (which correspond to ρ constants of the Hammett equation) are $f_m = -2.7$, $r_m = -3.2$, $f_p = -2.6$, $r_p = +5.1$. The f_m and f_p values are practically the same, and also the r_m value is similar, but the r_p value is much greater and of opposite sign! The inductive and mesomeric effects of *para* substituents are opposite, the mesomeric effect being predominant to such an extent that 4-methoxy derivative decomposes more slowly than 4-nitro derivative by a factor of 10.

6.3 Noncatalyzed Reactions of Diazonium Ions in Aqueous Alkaline Media and Organic Solvents

6.3.1 Reactions in Aqueous Alkaline Medium

Increasing pH value of aqueous solutions of diazonium ion makes the reaction (6.6) and other reactions (such as (6.7) particularly at higher concentrations of diazonium ion) gradually more important.

$$ArN_2^+ + OH^- \rightleftharpoons ArN_2OH \rightleftharpoons ArN_2O^- \qquad (6.6)$$

$$ArN_2^+ + ArN_2O^- \rightleftharpoons ArN_2\text{-}O\text{-}N_2Ar \qquad (6.7)$$

The concentrations of ArN_2OH and $(ArN_2)_2O$ reach the maxima at pH = pH_m (see Section 4; in the case of diazonium ions with strong -M type *ortho* and *para* substituents, the *syn*-diazotate rearranges relatively rapidly to the more stable *anti*-isomer, and the concentration of *syn*-diazohydroxide considerably decreases). Whereas diazonium ions are relatively stable and diazotates are very stable, diazo hydroxides and diazo ethers are very unstable and decompose to radicals which undergo a number of further reactions (such as (6.10) - (6.12)) which often are difficult to identify. Ar'H denotes any aromatic compound formed during the reactions.

$$ArN_2OH \rightarrow ArN_2\cdot + \cdot OH \rightarrow Ar\cdot + N_2 + \cdot OH \qquad (6.8)$$

$$(ArN_2)_2O \rightarrow ArN_2\cdot + \cdot ON_2Ar \rightarrow Ar\cdot + N_2 + \cdot ON_2Ar \qquad (6.9)$$

$$Ar\cdot + \cdot OH \rightarrow ArOH \rightleftharpoons ArO^- + H^+ \qquad (6.10)$$

$$ArN_2^+ + ArO^- \rightarrow ArN{=}N\text{-}ArO^- + H^+ \qquad (6.11)$$

$$Ar\cdot + Ar'H + ArN_2O\cdot \rightarrow Ar\text{-}Ar' + ArN_2OH \qquad (6.12)$$

Beside these reactions there also occur heterolyses of diazonium ion to the aryl cation which reacts with water to give the hydroxy compound ArOH, nucleophilic aromatic substitutions of reactive diazonium ions with -M type substituents (Section 5), and to a lesser extent the reverse reaction of diazonium ion to the arylamine (6.13) which rapidly gives triazene on the reaction with the diazonium ion left[76].

$$ArN_2^+ + H_2O \rightarrow ArNH_2 + HNO_2 \xrightarrow{OH^-} ArNH_2 + NO_2^- \qquad (6.13)$$

At low pH values the concentrations of diazo hydroxide and diazo ether are slight, and the heterolysis only takes place giving ArOH; the reaction rate depends on [OH$^-$]. With increasing pH value the radical splitting becomes gradually more and more significant; the rate increases and usually reaches its maximum at pH = pH$_m$. The more reactive is the diazonium ion the smaller is the pH$_m$ value and, usually, the lower is the pH value at which the rate increase becomes to make itself felt.

The reactions proceeding in aqueous alkaline medium continue to be very little investigated due mainly to their complexity and dependence of their course upon many factors such as the kind and position of substituent, concentration of OH$^-$, light, whether the reaction is carried out in an open vessel or under nitrogen, and even the material of wall of the reaction vessel.

The decomposition of 4-chlorobenzenediazonium tetrafluoroborate was studied at pH 9 - 10.3 at 20 °C, and eleven low-molecular products were identified beside high-molecular resins with considerable nitrogen content which even predominated under certain conditions[77].

In contrast to the heterolysis of diazonium ions, there exists no relation between the nature and position of substituent and reaction rate. Thus e.g. the m-nitro derivative, which is very stable in acid solution, will decompose within less than 1 min at pH = pH$_m$ (Ref.[53]).

6.3.2 Reactions in Organic Solvents

From among organic solvents, alcohols are the media in which the reactions have been most thoroughly studied. In comparison with the reactions in water, we can observe several important differences here which affect both the rate and - even more - the composition of products. (a) The equilibrium constant of the reaction $ArN_2^+ + RO^- \rightleftharpoons ArN_2OR$ is much higher than the corresponding constant of reaction with OH$^-$. (b) The diazo ether formed cannot react with the second alkoxide anion to give an anion, hence its concentration increases with increasing [RO$^-$] concentration until all ArN_2^+ is transformed into ArN_2OR. (c) The radical Ar· formed by decomposition of diazo ether reacts with a solvent molecule, and a chain reaction is started which produces ArH (sometimes in quantitative yields):

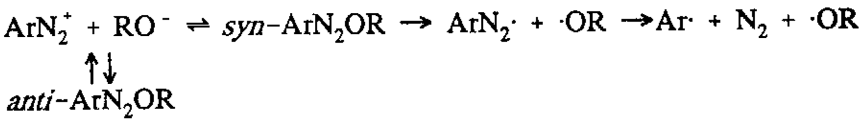
$$Ar\cdot + RCH_2OH \rightarrow ArH + RCHOH\cdot \tag{6.14}$$

$$\begin{aligned} ArN_2^+ + RCHOH\cdot &\rightarrow ArN_2\cdot + RCH{=}OH^+ \rightarrow \\ &Ar\cdot + N_2 + RCH{=}O + H^+ \end{aligned} \tag{6.15}$$

Analogous reactions are impossible in water because the reaction $Ar\cdot + HOH \rightleftharpoons ArH + \cdot OH$ requires very high energy (O-H bond energy is much higher than C-H bond energy).

The mechanism of formation of aryl radicals is represented in Scheme 6.2 (Ref.[54]) and the dependence of energy on reaction coordinate is shown in Fig. 4

for the reaction of 4-nitrobenzenediazonium cation with methoxide anion.



$$\begin{array}{l} \mathrm{ArN_2^+} + \mathrm{RO^-} \rightleftharpoons \textit{syn}\text{-}\mathrm{ArN_2OR} \rightarrow \mathrm{ArN_2}\cdot + \cdot\mathrm{OR} \rightarrow \mathrm{Ar}\cdot + \mathrm{N_2} + \cdot\mathrm{OR} \\ \quad\uparrow\downarrow \\ \textit{anti}\text{-}\mathrm{ArN_2OR} \end{array}$$

Scheme 6.2

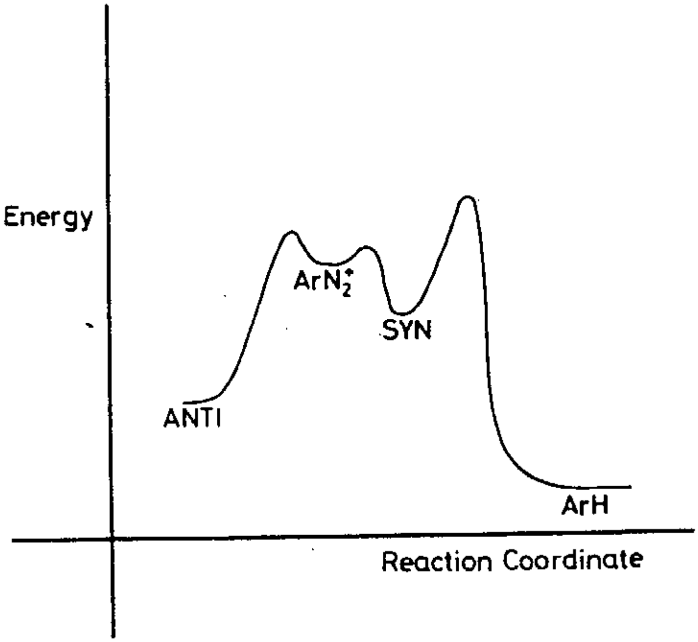


Fig. 4 Free energy diagram for the reactions of the *p*-nitrobenzenediazonium salt, the *syn*- and the *anti*-arylazo methyl ethers in basic methanol

Immediately after the reactants have been mixed, the equilibrium: diazonium ion ⇌ *syn*-diazo ether is established; in the next phase, which is finished in ca 1 min at 30 °C, the *syn*-isomer is reversibly transformed into *anti*-isomer and irreversibly split into aryl radical which reacts with methanol to give nitrobenzene. In the last phase (with the half life of about 2 h) the *anti*-isomer is slowly transformed via *syn*-isomer into aryl radical and further to nitrobenzene. If the separately prepared *anti*-isomer is added to methoxide solution, then only the third slow phase takes place.

The effects of substituents and reaction conditions are given in Tables 6.4 and 6.5. In acid medium (Table 6.4) benzenediazonium ion gives methoxybenzene almost quantitatively both under oxygen and under nitrogen. In neutral medium, radical splitting is significant to a little extent and a small amount of benzene is formed. Benzene and polymeric products are only formed in 1.1M CH_3ONa under nitrogen.

Table 6.4 Decomposition products of benzenediazonium tetrafluoroborate and 4-bromobenzenediazonium tetrafluoroborate in methanol[90]

Substituent	Temperature °C	ArH %	$ArOCH_3$ %	Medium[a]
H	65	0	92	0.1 M $TsOH/O_2$
H	65	0	88	0.1 M $TsOH/N_2$
H	30	3	66	neutral
H	30	64	0	1.1 M CH_3O^-/N_2
4-Br	65	4	72	0.1 M $TsOH/O_2$
4-Br	65	73	19	0.1 M $TsOH/N_2$
4-Br	30	82	5	neutral
4-Br	30	66	0	0.01 M CH_3O^-/N_2

[a] TsOH = 4-methylbenzenesulfonic acid

Table 6.5 Decomposition products of substituted benzenediazonium salts in boiling methanol[91]

Substituent	$ArOCH_3$, %	ArH, %
4-CH_3	84 - 91	6 - 14
4-OCH_3	1 - 18	76 - 99
3-OCH_3	94	2
4-Br	17 - 31	66 - 84
3-Br	53 - 76	18 - 40
3-Br[a]	12	85
4-NO_2	9 - 14	79 - 83
3-NO_2	4	85
3-CH_3	95	5

[a] Under nitrogen.

The 4-bromo derivative gives bromobenzene as the main product even in acid medium under nitrogen, but in the presence of oxygen the product ratio is reversed. In basic medium the yields of bromobenzene decrease because side products begin to increase in amount.

Table 6.5 gives the effect of substituents on the composition of product in neutral boiling methanolic solution. The content of hydrocarbon increases with increasing electron-acceptor ability of the m-substituent, but with *p*-substituents the situation is more complex again (as was the case with the heterolysis). The more resistant is the substituent to heterolysis the lower is the amount of ether and the higher is the amount of substituted benzene formed.

The data of both tables can be interpreted as follows: The easier is the C-N bond heterolysis the lower amount of substituted benzenes are formed in acid to neutral medium. Increasing CH_3O^- concentration increases the significance of the radical splitting and reduction of diazonium ion to substituted benzene. The less reactive is the diazonium ion the higher CH_3O^- concentration is usually needed. At high methoxide ion concentrations, side reactions become considerably significant and the yield of substituted benzenes is lowered. Oxygen acts as a scavenger of radicals, it interrupts the radical chain reaction and thus lowers the yields of substituted benzenes[78].

In ethanolic solutions at otherwise the same conditions, even greater amounts of substituted benzenes are formed than in methanol; the reduction of ArN_2^+ to ArH by heating the diazonium salt in alcohol represents one of the oldest methods of two-step elimination of amino group. Thus e.g. when an ethanolic solution of 2,4,6-tribromoaniline is treated with two equivalents of sulfuric acid and solid sodium nitrite, nitrogen is liberated on heating and a high yield of sym-tribromobenzene is formed.

Several other organic solvents are used beside alcohols as reducing agents, e.g. dioxane, tetrahydrofurane, dimethylformamide; the yields are usually better than in alcohols. For the application to be possible the solvent must react readily with the aryl radical formed by splitting of the diazonium ion. A small amount of suitable reduction-oxidation catalyst (such as Cu^I salts) are added to reduce the induction period of formation of the aryl radical:

$$ArN_2^+ + Cu^I \rightarrow ArN_2\cdot + Cu^{II} \rightarrow Ar\cdot + N_2 + Cu^{II} \tag{6.16}$$

$$Ar\cdot + RCH_2OR \rightarrow ArH + RCHOR\cdot \tag{6.17}$$

$$ArN_2^+ + RCHOR\cdot \rightarrow ArN_2\cdot + RCH{=}OR^+ \tag{6.18}$$

The reduction of diazonium ions with hypophosphorous acid takes a similar mechanism as that with alcohols. The hypophosphorous acid is taken in excess (up to 10:1 equiv.) and the reaction is performed at room temperature. The reduction is usually very slow (even several days) but the yields are generally much higher. The elimination of amino group from trinitroaniline can serve as an example: Excess hypophosphorous acid (50%) is added to a cold solution of nitrosylsulfuric acid, and a solution of 2,4,6-trinitroaniline in acetic acid is added there to at 0 °C. After 24 h, the reaction mixture is poured onto ice. Yield 65 % of 1,3,5-trinitrobenzene. The reaction mechanism is represented in Eqs (6.19) - (6.22).

$$\mathrm{ArN_2^+} + \mathrm{H_2PO_2^-} \rightleftharpoons \mathrm{ArN{=}N{-}OPOH_2} \rightarrow \mathrm{ArN_2\cdot} + \mathrm{H_2PO_2\cdot} \tag{6.19}$$

$$\mathrm{ArN_2\cdot} \rightarrow \mathrm{Ar\cdot} + \mathrm{N_2} \tag{6.20}$$

$$\mathrm{Ar\cdot} + \mathrm{H_3PO_2} \rightarrow \mathrm{ArH} + \mathrm{H_2PO_2\cdot} \tag{6.21}$$

$$\mathrm{ArN_2^+} + \mathrm{H_2PO_2\cdot} \rightarrow \mathrm{ArN_2\cdot} + \mathrm{H_2PO_2^+} \tag{6.22a}$$

$$\mathrm{H_2PO_2^+} + \mathrm{H_2O} \rightarrow \mathrm{H_3PO_3} + \mathrm{H^+} \tag{6.22b}$$

6.4 Catalytic Decomposition of Diazonium Salts. Sandmeyer Reaction

Only in few cases it has been possible to prepare good yields of ArX (where X is a nucleophile) from $\mathrm{ArN_2^+}$ by thermal decomposition of $\mathrm{ArN_2^+}$ solutions with excess $\mathrm{X^-}$. Very good yields are obtained with some nucleophiles if the corresponding salt with univalent copper, $\mathrm{Cu^{I}X}$, is used as the catalyst. In the presence of CuX the electron transfer from univalent copper to the diazonium ion is very easy and gives the $\mathrm{ArN_2\cdot}$ radical which is rapidly decomposed to $\mathrm{Ar\cdot}$ and $\mathrm{N_2}$; in the subsequent phase, the aryl radical is combined with the $\mathrm{X\cdot}$ group from the salt of divalent copper, $\mathrm{Cu^{II}X_2}$, with regeneration of $\mathrm{Cu^{I}X}$ and formation of ArX. Scheme 6.2 represents the course of reaction for the particular case of replacement of diazonium group by chlorine (x = Cl):

$$\mathrm{ArN_2^+} + \mathrm{Cu^{I}Cl_2^-} \rightleftharpoons [\mathrm{ArN_2^+.Cu^{I}Cl_2^-}] \rightarrow [\mathrm{ArN_2\cdot.Cu^{II}Cl_2}] \rightarrow$$

$$\mathrm{Ar\cdot} + \mathrm{N_2} + \mathrm{Cu^{II}Cl_2} \rightarrow \mathrm{ArCl} + \mathrm{N_2} + \mathrm{Cu^{I}Cl}$$

Scheme 6.2

Electron-acceptor substituents facilitate the formation of complex of diazonium ion with $\mathrm{Cu^{I}X_2^-}$ anion and hence also the overall reaction. The reaction can be realized with catalytic amount of $\mathrm{Cu^{I}}$ (0.05 equivalents for nitro derivatives, ca 0.2 equivalents for 4-methyl and 4-methoxy derivatives). Cuprous oxide or even activated powder copper can be used instead of cuprous salts but the yields are usually much lower. Most often this method is used for replacing the diazonium group by Cl, Br, or CN. The best results are obtained if the diazonium salt solution is added to the solution of the corresponding, specially prepared salt $\mathrm{Cu^{I}X_2^-Na^+}$; if X = CN then the diazonium salt solution must be neutralized first. In this reaction the yields usually are lower because the *syn*-diazo cyanide, which is very rapidly and reversibly formed, is partially isomerized to the stable *anti*-isomer from wherefrom ArCN is not formed.

The diazonium group can be replaced also for other nucleophilic groups with the catalysis by copper, but the procedure must be modified accordingly. In the substitution by nitro group it is impossible to prepare the corresponding salt of univalent copper, and application of even catalytic amount of Cu^{I} salt with another anion would reduce the yield considerably. A possible procedure consists in diazotization of the corresponding amine in sulfuric acid (HSO_4^- anions are very weak nucleophiles, hence their presence does not interfere) or in hydrochloric acid, in which case the diazonium salt is isolated as $ArN_2^+BF_4^-$. The diazonium salt is added to a mixture of sodium nitrite solution and powder copper or cuprous oxide.

The replacement of N_2^+ by iodine does not need any catalyst. Iodide anion can transfer an electron to ArN_2^+ and after decomposition of $ArN_2\cdot$ to $Ar\cdot$ and N_2 a bond is formed between aryl radical and iodine atom. Fluoro derivatives are not prepared by the Sandmeyer reaction either, but can be prepared in good yields by thermolysis of arenediazonium tetrafluoroborates (see Section 6.4). As in the replacement of N_2^+ by iodine the replacement by SR group does not use the Sandmeyer reaction either. In the reaction of ArN_2^+ cations with SR^- anions (R = H, alkyl, aryl) the diazo ether is formed first very rapidly (see Section 4) and, being very unstable, decomposes to the sulfide ArSR sometimes even explosively. The synthesis of ArSR usually consists in slow addition of diazonium salt solution to hot thiolate solution; the diazo thioether formed is rapidly decomposed, hence its concentration is small throughout the reaction. A relatively safe procedure for preparation of sulfides involves a reaction of diazonium salts with potassium xanthate and subsequent thermolysis of the product formed (6.23); alkali splitting produces the thiol ArSH.

$$ArN_2^+ + {}^-S\text{-}CS\text{-}OR \rightarrow ArS\text{-}CS\text{-}OR + N_2 \rightarrow ArSR + COS + N_2 \qquad (6.23)$$

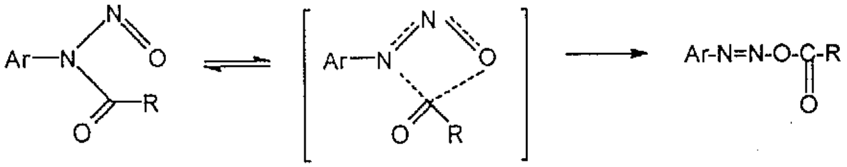
6.5 Arylation

Arenediazonium ions represent one of the main sources of not only aryl cations but also aryl radicals. This section deals with formation of C-C bond between the aryl cation or aryl radical and an aromatic, heteroaromatic, or even unsaturated alipahtic compound. The reactions can proceed both in the presence of a catalyst and without any catalyst (in this case the catalyst is a substance easily providing an electron to the diazonium group). In the former case the reaction species is a radical, in the latter case it is either a radical or a cation depending on the medium, reaction conditions (particularly pH), and structure of the diazonium salt. The reaction can proceed either in an organic solvent (which usually is the second reactant, too), water, or a mixture (usually heterogeneous) of water and organic compound.

The arylation in organic solvent starts from a solid diazonium salt, usually $ArN_2^+BF_4^-$ or some other more soluble form, such as quinonediazide, triazene

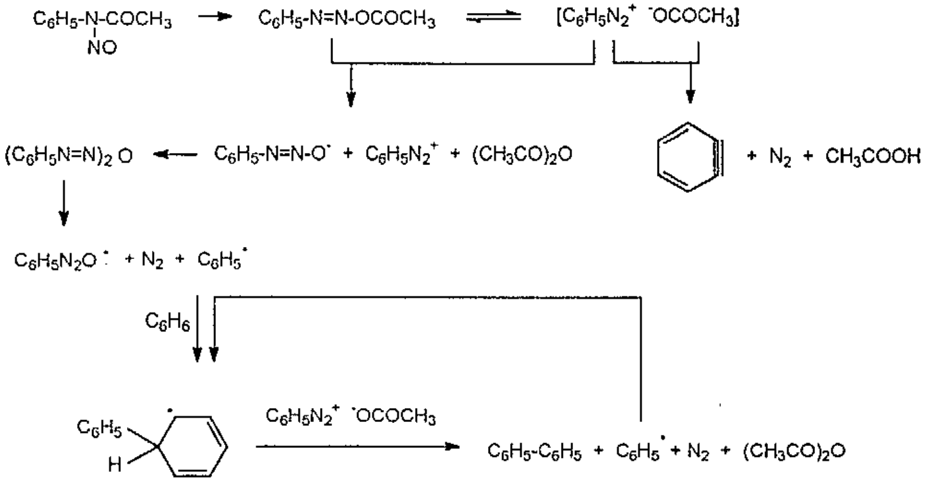
ArN=N-NR$_2$, or N-nitroso-N-arylamide of carboxylic acid, RCON(NO)Ar. The thermolysis of fluoroborates is accompanied by little arylation, the main reaction being the replacement of diazonium group for fluorine. The products of thermolysis of benzenediazonium tetrafluoroborate in nitrobenzene[79] contained 95% fluorobenzene;the ratio of *o*-, *m*-, and *p*-biphenyls was 1:4:0, i.e. typical of a reaction with aryl cations. For comparison, the isomer ratio found in the arylation of nitrobenzene with dibenzoyl peroxide (where the reaction of aryl radicals is presumed) was *o*:*m*:*p* = 6:1:3. The decomposition products of diazonium salt depend on the medium and substituent(s). In dimethyl sulfoxide (a more basic solvent than nitrobenzene), bezenediazonium cation was heterolyzed to phenyl cation but 4-nitrobenzenediazonium cation was homolyzed to the respective aryl radical.

Most intensively studied was the decomposition of N-aryl-N-nitrosoamides of carboxylic acids, which are well soluble in organic solvents and are excellent sources of aryl radicals. They are very unstable compounds which rapidly rearrange to diazo esters RCOON$_2$Ar *via* a cyclic mechanism at room temperature[80]:



Scheme 6.3

Several mechanisms were suggested for the consecutive reactions leading to the arylation products. Scheme 6.4 represents a reaction mechanism which is in the best accordance with experimental facts[81].



Scheme 6.4

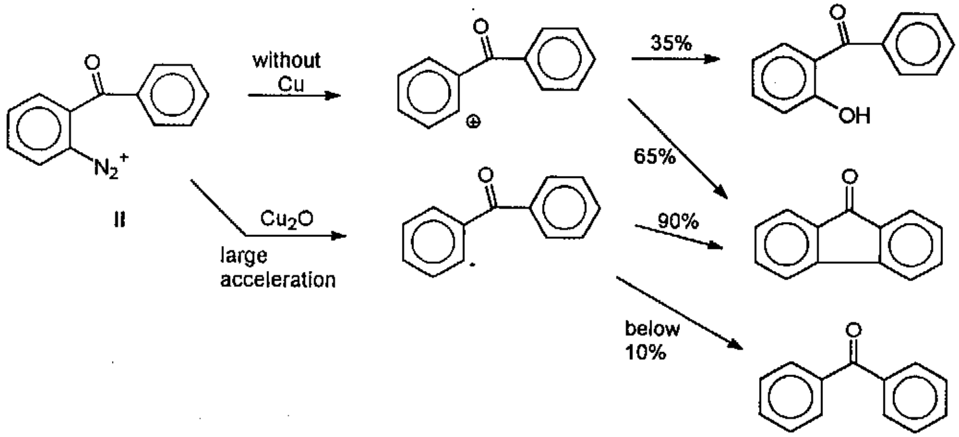
If a scavenger of radicals (e.g. an unsaturated compound) had been added into the reaction mixture, the radical chain reaction was interrupted and the formation of dehydrobenzene (C_6H_4) became the main reaction pathway.

The arylation in a two-phase system: aqueous solution of diazonium salt and an organic layer (usually the compound to be arylated) is known under the name of Gomberg-Bachmann reaction[82]. The reaction is started by addition of base to the aqueous solution. The more reactive is diazonium ion the weaker base usually is sufficient. The reactive species usually is the aryl radical. Arylation studies of mono-substituted benzenes with the splitting product of bezenediazonium ion showed, that nitrobenzene reacts three times as fast as toluene, the ratio of *o*-, *m*-, *p*-derivatives being 6:1:5 (Ref.[83]). The reactionof ArN_2^+ with Ar'H exclusively produces the unsymmetrical biaryl Ar-Ar'; the concentration of Ar· is so low (due to its high reactivity) that the recombination of radicals is improbable. Another situation is encountered if the reaction mixture contains a compound R-H which easily provides a hydrogen atom (e.g. alcohol or ether). Then the radical Ar· produced by splitting of ArN_2^+ reacts with R-H to give ArH, and the reaction of ArH with Ar· leads to the symmetrical biaryl Ar-Ar.

The Gomberg-Bachmann reaction usually gives rather low yields, especially so in such cases when the aromatic compound is solid at the reaction temperature and another organic compound (solvent) must be added which need not be quite inert to radicals. Usually the yields are considerably improved by addition of a catalyst, most often univalent copper. In contrast to the Sandmeyer reaction, the procedure is reversed: the cuprous salt solution is added to the diazonium salt solution. If the cuprous salt solution is added to a solution of diazonium salt alone, symmetrical biaryls are formed in good yields provided there are electronegative substituents present in the diazonium salts. For instance, the decomposition of 3-nitroaniline (diazotized in sulfuric acid) by addition of CuCl in hydrochloric acid gave 87% yield of 3,3'-dinitrobiphenyl and only ca 10% *m*-nitrochlorobenzene[84].

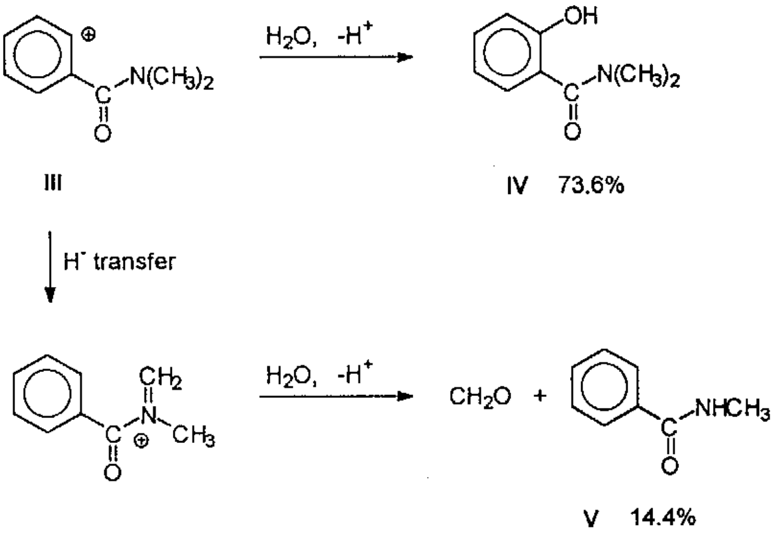
Water soluble heteroaromatic bases represent a special case since both reaction components are present in a single phase - water. If the heterocyclic base is strong enough (e.g. pyridine) or if the diazonium ion is reactive, no alkalies need be added; the amount of base must be large enough to neutralize all mineral acid present.

When both reactants are parts of the same molecule and in favourable mutual positions, intramolecular processes can take place with formation of five- or six-membered (exceptionally seven-membered) cycles. These reaction are referred to as the Pschorr reaction[85]. In the presence of Cu catalysts the reaction takes a radical mechanism, in the absence of catalyst the mechanism is ionic in acid media and usually predominantly radical in alkaline media. A clear example of the catalyst effect is given in Scheme 6.5 which presents the product composition from decomposition of *o*-benzoylbenzenediazonium salt (II) in acid medium.

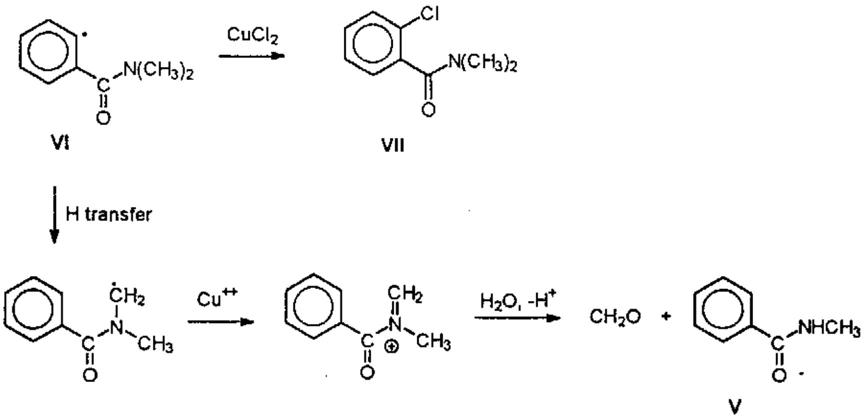


Scheme 6.5

If the catalyzed reaction is carried out in the presence of a hydrogen donor (alcohol, dioxane), the reduction product predominates. A very detailed study was undertaken in the case of decomposition of *o*-(dimethylamino-carbonyl)-benzenediazonium tetrafluoroborate without added CuCl (Scheme 6.6) and with 1.1 equivalents of CuCl (Scheme 6.7), Ref.[86]. The reaction of aryl cation III with water is about five times as fast as the intramolecular hydride transfer. In the "intimate" pair of aryl cation and nitrogen molecule, the nitrogen molecule obviously hinders the attack of hydrogen of methyl group by the positively charged carbon atom more than the reaction of the latter with water.



Scheme 6.6



Scheme 6.7

When the radical decomposition of diazonium ion was performed in the presence of only 1.1 equivalents of CuCl, the yield of N-methylbenzamide (V) was almost quantitative. After adding 75 equivalents of NaCl, 92% amide V and 7% chloroderivative VII were obtained; after additional addition of 4 equivalents of $Cu(NO_3)_2$ the yield of chloro derivative VII increased to 44.6%.

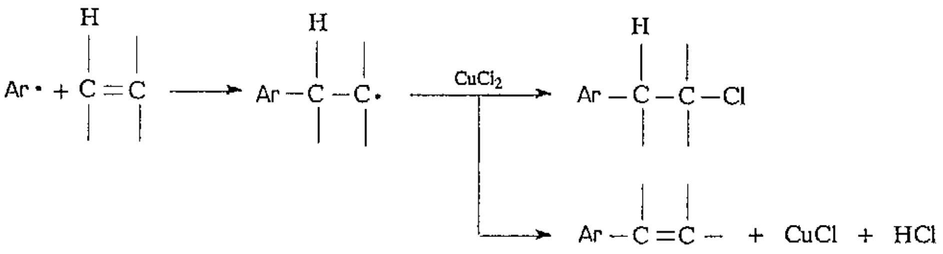
The radical reaction in the first case gave no product of the Sandmeyer reaction - *o*-chloro derivative VII; the intramolecular hydrogen transfer was many times faster than the transfer of chlorine. Even in the presence of 75 fold excess of Cl^- ions only 7% chloro derivative was produced. Only after addition of a 4 fold exces of cupric salt the both products were present in comparable amounts. This also shows that $CuCl_2$ is an especially efficient carrier of chlorine atom to aryl radical.

The most complex arylation undoubtedly is the Meerwein arylation of α,ß-unsaturated organic compounds[87]. Usually, a concentrated solution of diazonium salt is added to a 2 - 3 fold volume of acetone containing the unsaturated compound, ca 0.2 equivalents of $CuCl_2$, and 1 - 2 equivalents of base (acetate, pyridine); the temperature is usually maintained in the interval of 0 - 30 °C. A likely mechanism is represented in Scheme 6.8.

$$2CuCl_2 + CH_3COCH_3 \rightarrow 2CuCl + HCl + ClCH_2COCH_3$$

$$ArN_2^+ + CuCl + Cl^- \rightarrow Ar\cdot + N_2 + CuCl_2$$

The most serious side reactions are the formation of resinous substances and the reaction $Ar\cdot + CuCl_2 \rightarrow CuCl + Ar{-}Cl$ which is especially significant at higher concentrations of $CuCl_2$ and thus lowers the yields of the main products. If there are electron-acceptor substituents next to the double bond, the yields are much worse than those with the parent olefins, but even in these cases the results are better than those of the other methods.



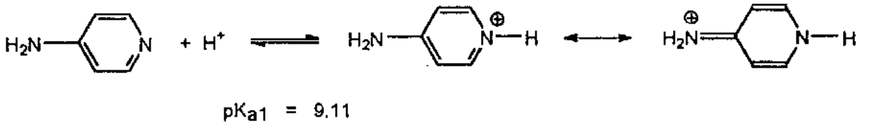
Scheme 6.8

7 Heterocyclic Diazonium ions

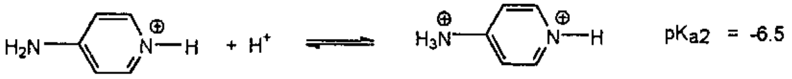
Heterocyclic diazonium ions differ considerably from carbocyclic arenediazonium ions in several aspects, particularly in their stabilities in solutions and in reactions with water and hydroxyl ion. This is particularly true of the five-membered heterocyclic diazonium ions. Although literature provides much more papers about these cycles than about six-membered heterocyclic diazonium ions (for a survey see Ref.[92]), the papers contain but few data about rate and/or equilibrium constants of their reactions and practically no data on kinetics of the diazotization reactions; many data are contradictory or rather questionable. One of the reasons lies in their high reactivity, particularly prominent with the diazonium salts containing O and S atoms in the heterocycle. This results in instability in solutions and rather complex reactions even if compared with those of six-membered heterocyclic diazonium ions. With the latter ones the situation is much more favourable in this respect; especially detailed studies concern the diazotization kinetics of aminopyridines and their derivatives[93-96].

7.1 Six-Membered Heterocyclic Diazonium Ions

Amino derivatives of six-membered heteroaromatics substantially differ from carbocyclic aromatic amines in two properties: (1) The nitrogen atom in heterocyclic ring has a similar polar effect as nitro group in benzene nucleus, which considerably reduces the basicity of the amino group present. (2) Due to the lowered basicity of amino group and, on the other hand, its high +M effect, this amino group is not protonated in acid media, the heterocyclic nitrogen atom being protonated instead, as shown in the given example of 4-aminopyridine:



(7.1)



(7.2)

The protonated nitrogen atom of pyridine possesses a polar effect as large as that of N_2^+ group, hence the basicity of amino group in monoprotonated 4-aminopyridine is many orders lower than that in the neutral molecule (cf. Eqs (7.1) and (7.2); the pK_{a2} value is even lower than pK_{a2} of 2,4-dinitroaniline (-4.5) by as much as 2 units). The high basicity of neutral 4-aminopyridine and the very low basicity of 4-aminopyridinium ion have several consequences: (a) the diazotization mixture contains only negligible amounts of neutral amine; (b) because of the very low basicity of monoprotonated 4-aminopyridine, its diazotization in dilute mineral acids is very slow as it is the case of very little basic carbocyclic aromatic amines; (c) the diazonium ions formed are very reactive, especially so if the diazonium group is at 2 or 4 position. These diazonium ions react rapidly with nucleophiles in solution (inclusive of the water molecules). In contrast to carbocyclic diazonium ions, the main reaction is the nucleophilic substitution of N_2^+ group. 4-Pyridinediazonium ion reacts with water to give 4-pyridone, the reaction half life being as low as 17 s at 25 °C! The diazonium group at 2 position is replaced even much faster[97]. The diazotization in hydrochloric acid produces a mixture of pyridone and chloropyridine instead of the diazonium ion. In contrast to 2- and 4-aminopyridines, the diazotization of 3-aminopyridine proceeds at normal conditions and the diazonium ion formed is relatively stable even in solution. The hetero nitrogen atom at 3 position exerts a much smaller effect on the basicity of amino group (pK_{a2} = -1.4) as well as on the reactivity of diazonium group; 3-aminopyridine resembles 2- or 4-nitroaniline, and 3-pyridinediazonium ion resembles 2- or 4-nitrobenzenediazonium ion. The diazotization of 2- and 4-aminopyridines is carried out either by the action of nitrosylsulfuric acid or with alkyl nitrite in an organic solvent in the presence of a strong base such as $NaNH_2$. The diazotates formed (probably *anti*-isomers) are relatively stable in aqueous alkaline solutions. Upon lowering pH, they are gradually converted into the respective diazonium ions, similarly to substituted benzenediazotates (Section 4), which undergo rapid azo coupling in the presence of reactive phenols or naphthols. The rate of these azo coupling reactions is limited by the formation of the diazonium ion; the subsequent azo coupling is faster than the reverse transformation of diazonium ion into diazotate[97].

Investigations[93-96] of diazotization of aminopyridines and their derivatives in solutions of perchloric acid at the ionic strength $I = 3$ mol l^{-1} at 2 °C revealed that either the base or its monoprotonated form can react depending on the pK_{a1} and pK_{a2} values and the acidity of medium. The pathway through the monoprotonated form becomes increasingly significant with increasing concentration of perchloric acid. Table 7.1 presents the pK_{a1} values and some pK_{a2} values and the rate constants of the reaction of the protonated form. The diazotization rate constants of free base should have similar values as those of nitroanilines, i.e. $\leq 10^3$ l^2 mol^{-2} s^{-1}. For comparison, the table also presents the rate constants of diazotization of 4-nitroaniline and 2,4-dinitroaniline. From the k_3 values in Table 7.1 it can be seen that (a) the protonated form is the less reactive and the k_3 value is the lower the greater negative value is observed for pK_{a2}; (b) the k_3 value of the 2,4-dinitro derivative corresponds to the interrelation between pK_{a2} and k_3 in spite of dinitroaniline reacting as the base (two nitro groups at *ortho* and *para* positions exhibit about the same polar effect upon the reactivity of amino group as that of positively charged nitrogen atom in the heterocycle). The main difference is observed as late as after diazotization in the behaviour of the diazonium ions in solution; in 2,4-dinitrobenzenediazonium ion, OH replaces the 2-nitro group and not the diazonium group.

The greater is pK_{a1} the lower is the concentration of free base in acid solution and the more likely is the diazotization *via* the protonated form. On the other hand, the greater is the negative pK_{a2} value the slower is the diazotization of the monoprotonated form and the more likely is the reaction path *via* the base (see Table 7.1).

Table 7.1 Rate constants k_3 (l^2 mol^{-2} s^{-1}) of diazotization of protonated aminopyridines and their derivatives

Substrate	pK_{a1}	pK_{a2}	$k_3 \times 10^2$
4-aminopyridine[a]	9.11	- 6.55	3.03
2-aminopyridine[a]	6.82	- 7.6	2.54
2-amino-4-chloropyridine[b]	4.83	≈ - 8.5	0.78
4-aminopyridine-1-oxide[b]	3.69	- 6.27	0.78
2-aminopyridine-1-oxide[b]	2.67		0.16
2-amino-5-chloropyridine-1-oxide[c]	1.73		≈ 0
3-aminopyridine[a]	6.0	- 1.4	$\approx 2 \times 10^4$
4-nitroaniline[c]	1		$\approx 9 \times 10^4$
2,4-dinitroaniline[c]	- 4.5		≈ 25

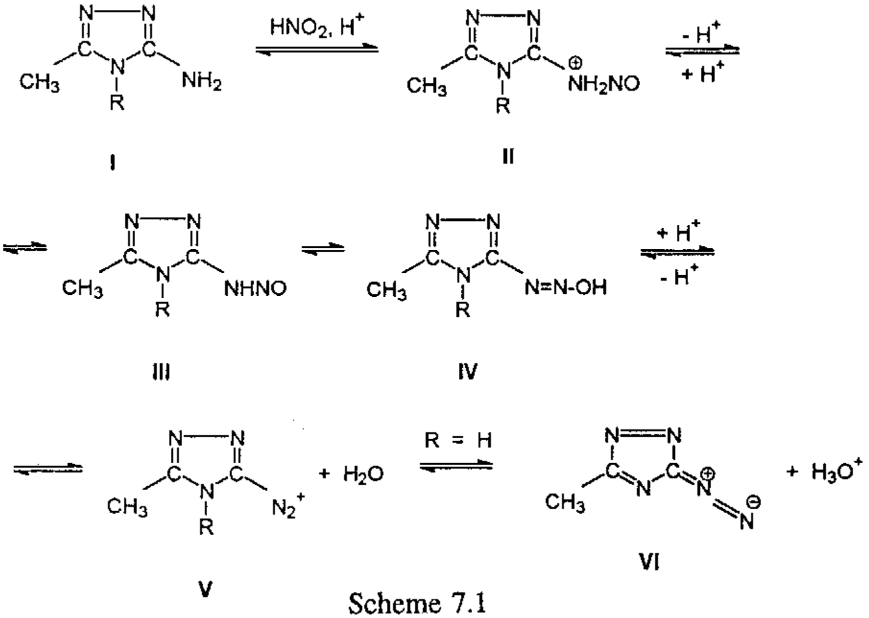
[a] The protonated form reacts.

[b] At a lower proton concentration, the neutral form reacts predominantly.

[c] The neutral form reacts.

7.2 Five-Membered Heterocyclic Diazonium Ions

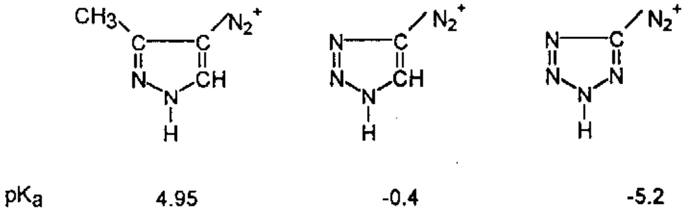
Scheme 7.1 presents the mechanism of diazotization of a five-membered heteroaromatic amine (an aminotriazole derivative in particular).



Scheme 7.1

If R = H, then an equilibrium is established between the diazonium ion V and dipolar diazo compound VI; at a sufficiently low proton concentration the diazo compound usually separates in solid state. In this respect the case is analogous to that of diazophenols but the reactivities of both the diazonium ion V and the dipolar diazo compound VI are many orders higher than those of diazophenols and quinonediazides, respectively.

The acidity of N-H bond increases with increasing number of nitrogen atoms in the cycle; the pK_a values were measured for a series of azoles at 0 °C (Ref.[98]):



If there is no acidic proton in the five-membered ring, the diazotization product is a mixture of nitrosamine and/or diazo hydroxide and diazonium cation. Nitrosamines are often isolated as the product of diazotization of amines; in this respect they differ from carbocyclic and six-membered heteroaromatic diazonium ions with which no stable nitrosamine have been isolated. The tendency to form nitrosamines (and tautomeric diazo hydroxides) again increases with increasing number of heteroatoms in the cycle and (for the same number of heteroatoms) in the series N < O < S. High yields of nitrosamines were obtained from substituted aminotriazoles and aminotetrazoles, thiadiazoles and oxadiazoles[99-101]. The yields depend on many factors such as the solubility of products, consecutive reactions with nucleophiles, rate of decomposition of both the diazonium ion and nitrosamine. 5-Amino-1,3,4- and -1,2,4-thiadiazoles give high yields of nitrosamines[99,101], but 5-substituted amino-1,2,4-thia-diazoles form only relatively unstable diazonium salts[102-103]. The diazotization of 4-N-aryl-5-alkyl-3-aminotriazole with sodium nitrite in 18% hydrochloric acid produces the stable nitrosamine. In dilute hydrochloric acid, the diazoamino compound is formed predominantly, and after 12 h stirring of the reaction solution in 20% hydrochloric acid the substituted 3-chlorotriazole was formed[100].

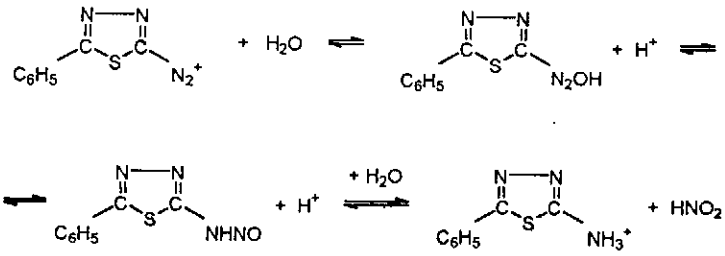
The rate constants k_1 of the reaction with hydroxyl ion and k_{-1} of the reverse reaction, the dissociation constant K_a of diazo hydroxide (or nitrosamine) and the rate constant k_2 of the reaction with phenoxide ion were measured[104] for the dipolar diazo compound VI and compared with the corresponding constants of benzenediazonium ion (Table 7.2).

The rate constants of the dipolar ion VI with hydroxyl and phenoxide ions are comparable with the corresponding rate constants of benzenediazonium ion, but k_{-1} is by five orders of magnitude smaller and K_a by ca four orders smaller than the corresponding values of benzenediazonium ion. The high stability of the heterocyclic diazo hydroxide and its low acidity are mainly due to the strong intramolecular hydrogen bond between N_2OH group and heterocyclic nitrogen atom. At pH < 5 it is the diazonium ion V which reacts with phenoxide, being by five orders of magnitude more reactive than the dipolar diazo compound VI, and at pH < 1 the diazonium ion reacts with the nondissociated phenol.

Table 7.2. Rate constants for the reaction of compound VI and benzenediazonium ion with hydroxyl and phenoxide ion and the pK_A values of their diazohydroxides

Diazonium ion	k_1	k_{-1}	pK_A	k_2
VI	3×10^3	2.0	11.8	3×10^3
Benzenediazonium ion	1×10^4	2.5×10^5	8.1	2.25×10^3

Not only the rate of reaction of diazonium ion with hydroxyl ion and other nucleophiles but also the rate of reverse reaction giving the amine increases with increasing number of heteroatoms in the ring and in the series N < O < S. One of the most reactive heterocyclic diazonium ions, 5-phenyl-1,3,4-thiadiazole-2-diazonium ion, exhibits the half life of 1 s for the reaction with water in 0.1M H_2SO_4, i.e. all the diazonium ion is converted into the diazo hydroxide within less than ten seconds[105]. The sulfuric acid concentration must be as high as 1.7M to obtain the ratio of diazonium ion / diazo hydroxide = 1. The rate of transformation of diazonium ion to the amine (7.3) increases with concentration of sulfuric acid up to 2.3M H_2SO_4; at this concentration the half life of reaction (7.3) is as low as 35 s.



(7.3)

Another piece of evidece of the extreme reactivity of thiadiazolediazonium ions is given by the rate constant of azo coupling reaction of 5-methyl-1,3,4-thiadiazolediazonium ion with nondissociated phenol, k_2 = 3 mol^{-1} $^{-1}$, i.e. 200 times as high as the value for 5-methyl- 1,2,4-triazole-3-diazonium ion.

8 Stabilized Diazo Compounds

Sometimes it happens that a diazonium ion solution is not used immediately but after a certain time or in another plant. In such cases it is often necessary to isolate the diazonium salt in solid state so that it could be better stored or transported. This is connected with several problems: how to obtain the diazonium salt from the solution without any large loss due to high solubility or partial decomposition during the isolation; how to ensure a sufficient stability of the diazonium salt during storage and prevent the hazard of explosive decomposition; how to achieve a good solubility of the diazonium salt (before use) in cold water with formation of a clear solution Depending on the form of the isolated diazonium salt two cases are recognized: the so-called "active stabilized diazo compounds" and "passive stabilized diazo compounds". The former ones are stable in acid and neutral media and upon dissolution they immediately exhibit the reactions characteristic of diazonium ions. In fact, they are real diazonium salts containing a suitable anion. This group includes simple diazonium salts such as chlorides or sulfates, salts with a nonmetallic complex anion, double salts, and arenediazonium arenesulfonates. "Passive stabilized diazo compounds" are stable in neutral and/or alkaline media and need acid treatment, steam, oxidation agents etc. to exhibit the properties of diazonium ions. This group includes metal salts of *anti*-diazotates, triazenes, diazo sulfonates. The majority of simple salts are much too soluble in water, hence the isolation from aqueous solution is difficult and is connected with a high loss. In solid state they are little stable and cannot be stored in large quantities because of the danger of explosion. Due to this reason quite unsuitable are anions with oxidation effects such as chlorates, perchlorates, and nitrates. Sulfates are much more convenient than chlorides or bromides since they are usually less soluble and more stable. Diazonium sulfates can often be salted out by addition of sodium sulfate or precipitated by addition of an organic solvent (ethanol, acetone). If the diazonium salts are too water soluble, it is more convenient to carry out the diazotization in an organic solvent (see Section 2). Sometimes, before further treatment, the aqueous solution of diazonium salt is concentrated by vacuum distillation at low (!) temperatures. This procedure is applied only rarely since it is connected with a hazard of local overheating and explosive decomposition.

Some amines having a negatively charged substituent in the molecule (COO^-, SO_3^-) give little soluble inner salts which often separate from solution during diazotization.

The decomposition of diazonium salts is highly exothermic; if the molecule is bigger, the amount of mass capable of absorption of energy is greater, and the temperature increase and explosion hazard are smaller. Due to that, benzenediazonium ions of relatively low molecular weight are not suitable for preparation of solid salts.

Further treatment consists in adding sodium sulfate to the solid (usually still wet) diazonium salt; this additive binds the water present and "dilutes" the diazonium salt and hence lowers the explosion hazard; a similar effect is achieved by adding partially dehydrated aluminium sulfate; magnesium carbonate is added in the cases where it is necessary to neutralize the residues of occluded mineral acid; in some cases such substances are added which stabilize the diazonium salt, e.g. salts of naphthalenesulfonic acids. These admixtures amounts to 75% of the final product weight. The substances mentioned are also added to other types of stabilized diazo compounds. From among the salts with nonmetallic complex anion the most frequently used are tetrafluoroborates. They are little soluble in water, but they can be recrystallized from water and prepared in a very pure state, and they are considerably stable. Therefore they are used for special purposes necessitating a high purity of diazonium salt such as e.g. theoretical studies of reactions of diazonium ions.

One of the biggest groups of "stabilized diazo compounds" is that of double salts with zinc chloride, i.e. the type $(ArN_2^+)_2(ZnCl_4^{2-})$. They are easily prepared (Sect. 2), inexpensive, well soluble in water, and considerably stable. The Zn^{2+} cation cannot be oxidized to a higher valency and thereby enable formation of aryl radicals, and the $ZnCl_4^{2-}$ anion is less nucleophilic than chloride ion. Diazonium ions with electron-acceptor substituents show diminished tendency to formation of double salts with $ZnCl_2$, thus e.g. 2,4,6-trinitro-benzenediazonium ion does not form the double salts.

Very useful and very stable are salts of arenediazonium ions with anions of naphthalenesulfonic acids. They are used e.g. in the cases where the double salts with zinc chloride are too soluble or little stable (or are not formed).

Naphthalenesulfonic acids stabilize diazonium ions not only in solid state but also in solution. The reason is formation of molecular complexes between diazonium ion and naphthalenesulfonate anion[106]; these complexes have almost no effect on coupling rates. When preparing them we can either add the solution of diazonium salt into a solution of naphthalene sulfonic acid or *vice versa* Usually used are free naphtahlenesulfonic acids since they are more soluble than their salts; the excess acidity is removed by addition of magnesium carbonate. In many cases, particularly with little soluble and little basic amines, the solution of naphthalenesulfonic acid is not added after but before the diazotization - the amine is dissolved in a concentrated solution of naphthalenesulfonic acid and diazotized. A particularly convenient procedure consists in the application of raw mixture obtained by sulfonation of naphthalene (which contains predominantly 1-naphthalenesulfonic acid, free sulfuric acid, and 3-5 parts of water): the amine is dissolved in this mixture and diazotized by adding sodium nitrite. The presence of naphthalenesulfonic acids not only stabilizes the diazonium salt formed but also considerably reduces the decomposition of nitrous acid in the medium used (see Section 2), hence the diazotizations can be carried out on large scale at temperatures as high as 40 - 50 °C with high yields.

Out of the class of "passive stabilized diazo compounds", diazo sulfonates were often applied in the past; the diazonium ion was regenerated by treatment with oxidation reagents or light. Nowadays these products are replaced by other types. The most frequently adopted types are diazoamino compounds (triazenes). They are obtained by reaction of diazonium ions with amines of various basicities depending on the reactivity of the particular diazonium salt (see Section 2 - Azo coupling reactions). The prerequisite is that there must not occur any azo coupling reaction. Particularly useful are aromatic amines with *para*-standing hydrophilic groups such as COO^-, SO_3^-. They are usually prepared as mixtures with the azo coupling component, e.g. with compounds of the type of 3-hydroxynaphthalene-2-carboxanilides (Naphthol AS, Ultrazol).

Metal salts of *anti*-diazotates are obtained by adding a solution of diazonium salt to concentrated sodium or potassium hydroxide solution at or above room temperature (depending on the isomerization rate). The isolation is achieved either by salting out or by precipitation with an water-soluble organic solvent (usually alcohol). They are also mainly used as mixtures with the respective azo coupling component (a powder consistence is usually attained by admixing anhydrous sodium acetate).

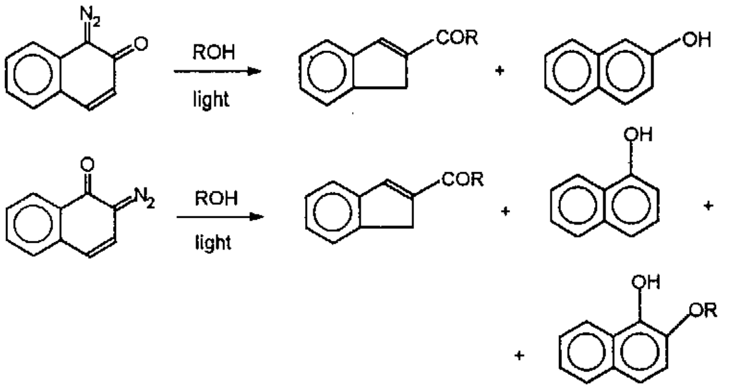
9 Effect of Light on Diazonium Ions

Many diazonium ions are sensitive to light especially in ultraviolet region both in dissolved and solid states. Irradiation accelerates the decomposition of diazonium salts by several orders of magnitude (as much as 10^7). The photolysis of diazonium salts in acid aqueous solutions exclusively has a heterolytic mechanism and produces the respective phenol and N_2 (Ref.[107]) even in cases when thermolysis leads to different products. Thus e.g. the photolysis of solution of 2,4,6-tribromobenzenediazonium ion quantitatively gives tribromophenol, whereas the thermolysis produces tribromobenzene[108].

The quantum yields are both pH and temperature independent. They are always below 1 and decrease with increasing wavelength of light and increasing electron-acceptor effects of substituents[109].

In alcoholic solutions the splitting is both heterolytic and homolytic. The composition of products depends on the wavelength and substituent(s): e.g. the photolysis of 4-nitro-benzenediazonium ion in methanol predominantly leads to nitrobenzene (Table 9.1), 4-methyl-benzenediazonium ion gives comparable amounts of toluene and 4-methoxytoluene, 2,4,6-tribromobenzenediazonium ion gives 2,4,6-tribromoanisol (in methanol), tribromophenyl acetate (in acetic acid), or tribromobenzene (in formic acid). At higher wavelenghts, products of homolytic (radical) splitting are formed in increasing amounts.

In some cases, complex reactions occur upon irradiation (Scheme 9.1)[110]. In the absence of light, the same reactions do not proceed until 180 - 190 °C, the yields being much lower.



Scheme 9.1

Table 9.1 Photolysis products from $4\text{-}NO_2\text{-}C_6H_4\text{-}N_2^+.1/2\ SnCl_4$ in various solvents

Products, %	Solvent				
	C_2H_5OH	CH_3OH	H_2O	9M HCl	4.3M H_2SO_4
$C_6H_5NO_2$	77	72	0	0	0
$4\text{-}NO_2C_6H_4OR$	5.3	3.5	73.5	23	84
$4\text{-}NO_2C_6H_4Cl$	0	0	7.4	62	0

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