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PREPARATION AND REACTIONS OF AZO COMPOUNDS

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Contents

1 Introduction

The term azo compounds involves the compounds of general formula R-N=N-R' where the nitrogen atoms of the azo group N=N are bound with carbonatoms of the groups R and R'. From among the large variety of such combinations

practically important are those in which both groups (R, R') or at least one of them have aromatic character. Extraordinarily important are compounds having hydroxy and/or amino groups in positions conjugated with the azo group since they are intensively coloured, can be widely modified to obtain various physico-chemical properties, and are relatively easily available: that is why they form the greatest class of commercial dyestuffs - azo dyestuffs.

The most important reaction producing azo dyestuffs is azo coupling. It consists in the reaction of aromatic diazonium compounds with aromatic hydroxy or amino compounds or with some aliphatic compounds. The reaction can be schematically represented as follows

$$R\text{-}N_2^{\oplus} + H\text{-}R'\text{-}X \rightarrow R\text{-}N{=}N\text{-}R'\text{-}X + H^{\oplus} \qquad (X = OH,\ NH_2) \qquad (1)$$

The diazonium compound is referred to as "diazo component" and the other reaction partner as "coupling component".

The reaction is carried out in aqueous medium. The diazonium compound prepared by the reaction of aromatic primary amine with sodium nitrite in acid medium is not usually isolated but its solution or suspension is mixed with the solution or suspension of coupling component. The coupling reaction proper proceeds, after adjusting the optimum pH range, very rapidly in most cases. The usual reaction temperature is within 0 - 20 °C. Very often it is possible to adopt equivalent amounts of the two components or an only slight excess of the coupling component, which is enabled by the fact that the coupling reaction is much faster than possible side reactions. The present paper deals mainly with the problem of coupling reaction (the problems of diazo compounds are dealt with by V. Štěrba elsewhere in this Journal).

There also exist other ways of producing azo dyestuffs. Sometimes they are even adopted commercially if the compound required cannot be obtained by azo coupling. These methods will be mentioned here too.

2 Azo Coupling Reactions of Aromatic Compounds

2.1 Theoretical

Considerable attention was paid to azo coupling mechanism in the past. As early as at the beginning of this century it was found by Goldschmidt et al.[1-5] that azo coupling reaction obeys the kinetic equation (2).

$$\frac{d[\text{Azo}]}{dt} = k'[\text{D}][\text{K}] \qquad (2)$$

where $d[\text{Azo}]/dt$ is the rate of formation of azo compound, and [D] and [K] are the analytical concentrations of the diazonium and coupling components, respectively. However, the rate equation (2) had a drawback in that the k'

constant changed with a change in acidity of medium. The subsequent development was characterized by a series of errors and inaccurate interpretations. Their main reason was in the fact that the azo coupling reaction is accompanied by acid-base equilibria whose nature then was unknown since the theory of acids and bases was still in its infancy. Hence as late as the 40's and 50's the rate equation (2) was replaced by another one whose rate constant was independent of the acidity of medium. It was found[6,7] that the azo coupling proper is preceded by the equilibria (3-6), its reaction partners comprising the diazonium ion and phenoxide (naphtholate) ion or free aromatic amine[8,9]. The way to deriving the kinetic equations (7-8), which are generally accepted at present, was then relatively short.

$$R\text{-}N_2^{\oplus} + OH^{\ominus} \overset{K_1}{\rightleftharpoons} R\text{-}N{=}N\text{-}OH \tag{3}$$

$$R\text{-}N{=}N\text{-}OH + OH^{-} \overset{K_2}{\rightleftharpoons} R\text{-}N{=}N\text{-}O^{\ominus} + H_2O \tag{4}$$

$$R'\text{-}OH \overset{K_{A(ROH)}}{\rightleftharpoons} R'\text{-}O^{\ominus} + H^{\oplus} \tag{5}$$

$$R'\text{-}NH_3^{\oplus} \overset{K_{A(RNH_2)}}{\rightleftharpoons} R'\text{-}NH_2 + H^{\oplus} \tag{6}$$

$$\frac{d[\mathrm{Azo}]}{dt} = k_{\mathrm{R\text{-}OH}}\left[R\text{-}N_2^{\oplus}\right]\left[R'\text{-}O^{\oplus}\right] \tag{7}$$

$$\frac{d[\mathrm{Azo}]}{dt} = k_{\mathrm{R\text{-}NH_2}}\left[R\text{-}N_2^{\oplus}\right]\left[R'\text{-}NH_2\right] \tag{8}$$

The relation between the constants K and k' is clearly shown in Fig. 1. If pH is increased up to the value of pK_A of the coupling component used, the k' value is increased proportionally to the concentration increase of phenoxide (naphtholate) anion or free amine, respectively. At $pH > pK_A$ the k' value should not change any further since the concentration of coupling partners proper has reached its maximum ($k' = k$). In reality, however, when crossing a certain pH value we can observe a rate decrease which is steeper than the above-mentioned increase. This is due to operation of the equilibria (3-4) transforming the reactive diazonium cation into the nonreactive diazohydroxide and diazotate, respectively. The concentration of diazonium ion[7] is given by Eq. (9). This relation and the fact that $K_2 \gg K_1$ (i.e. the concentration of diazo hydroxide is negligibly low) have the consequence that for $pH \gg (pK_1 + pK_2)/2$ the value of log k' is indirectly proportional to $2\times$pH, i.e. an increase in pH by

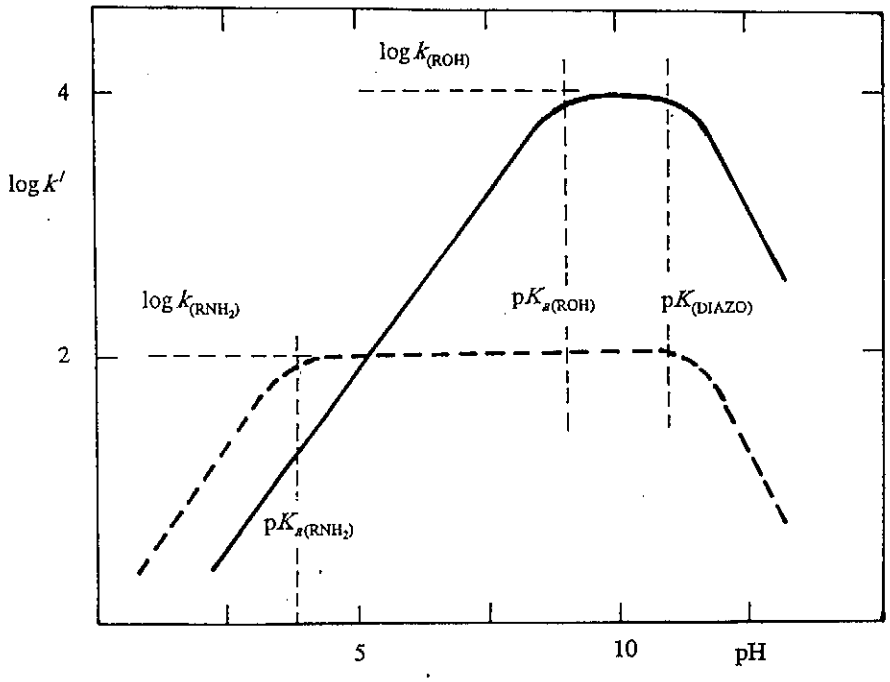


Fig. 1 Schematic representation of dependences of $\log k$ and $\log k'$ vs. pH (Refs[7,9,10]): ———— coupling of hydroxy compounds (here $pK_A = 9$, $\log k = 4$); - - - - - - - coupling of amino compounds (here $pK_A = 4$, $\log k = 2$); $pK_{(DIAZO)} = (pK_1 + pK_2)/2$ (here $pK_{(DIAZO)} = 11$)

one unit will decrease the reaction rate constant k' by a factor of 100.

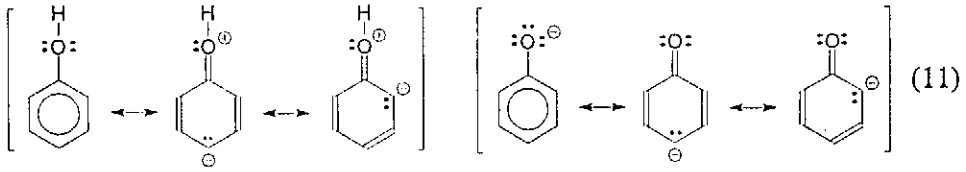
$$\mathrm{pH} = \frac{pK_1 + pK_2}{2} + \frac{1}{2}\log\frac{[\mathrm{R{-}N{=}N{-}O^{\ominus}}]}{[\mathrm{R{-}N_2^{\oplus}}]} \tag{9}$$

$$\log k' \approx \log[\mathrm{RN_2^{\oplus}}] \approx 2(\mathrm{const} - \mathrm{pH}) \tag{10}$$

The main difference between hydroxy and amino compounds is in that pK_A values of the latter are generally lower than those of the former, hence the maximum reaction rate of RNH_2 is reached at lower pH values and is lower than the maximum reaction rate for ROH. Hence, in the azo coupling reactions with amino coupling components there is usually a relatively broad pH region of pH-independence of coupling rate.

The reason why the reactive partners of azo coupling reaction are diazonium cation at one side and phenoxide (naphtholate) anion or nonprotonated amine at the other follows from the general principles of electron theory. The diazonium ion, having a positive charge at nitrogen atom, is decidedly a stronger electrophilic agent than diazohydroxide or even diazotate.

In phenoxide anion (in contrast to the nondissociated ArOH) the shift of negative charge into the aromatic nucleus is much facilitated as compared with the nondissociated phenol.



(11)

The difference between the reactivities of protonated and free amine is still more distinct. Amino group belongs among electron donors, whereas ammonium group is strongly electron-attracting.

To have a full picture, it should be noted that also the nondissociated hydroxy compounds can undergo azo coupling reactions, however, very slowly. E.g. phenol itself reacts more slowly than phenoxide anion by the factor of 10^{10}, the respective ratios being 10^7 - 10^9 for 1-naphthol derivatives.

Formation of azo dyestuffs was also observed with other aromatic coupling components, e.g. aryl ethers[13-16] or some aromatic hydrocarbons[17-19]. Even the simplest aromatic hydrocarbon - benzene - was "persuaded" to undergo azo coupling reaction, of course, by using extremely reactive diazonium compounds[20]. Such reactions, however, have no practical significance.

A number of authors have studied the effect of reactivity of diazonium ion upon the azo coupling reaction rate. In general, the more negative substituent is present in the diazonium ion the faster is the coupling reaction. Out of many papers dealing with the relation of log k vs. Hammett σ constants let us mention here one concerning the azo coupling reaction of phenol and 1-naphthol[21] - (Fig. 2).

Table I Azo coupling reaction rates (log k) of benzenediazonium ion with various coupling components[a]

No.	Coupling component	log k	Substitution position	Ref.
1	phenol	2.65	4	21
2	4-methylphenol	1.44	2	22
3	4-methoxyphenol	2.72	2	22
4	1-naphthol	5.72	4	23
5	2-naphthol	4.48	1	21
6	6-hydroxynaphthalene-2-sulfonic acid	2.98	5	24
7	6-aminonaphthalene-2-sulfonic acid	0.35	5	9

[a] In all the cases the conjugated base was the reagent proper; k (l mol^{-1} s^{-1}).

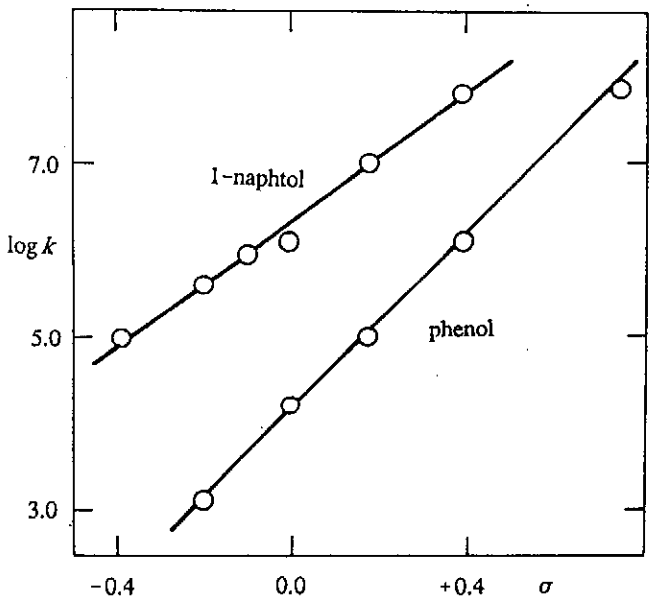
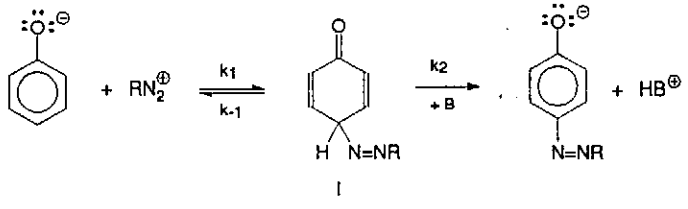


Fig. 2 Dependence of $\log k$ on Hammett σ constants for the azo coupling reactions of substituted benzenediazonium ions with phenol and 1-naphthol[21]: 1. 4-OCH_3, 2. 4-CH_3, 3. 3-Cl, 4. H, 5. 4-Cl, 6. 3-Cl, 7. 3-NO_2

It is self-evident that the character of coupling constant affects there action rate too. Table I presents values of rate constants of azo coupling reactions of benzenediazonium ion with some simple coupling components. It can be seen that the dependence is considerable. Generally: (a) aromatic hydroxy compounds are more reactive than the corresponding amines (Nos 6 and 7), (b) negative and positive substituents slow down and accelerate the reaction, respectively (Nos 2,3 and 5,6), (c) benzene derivatives usually react more slowly than similar naphthalene derivatives (Nos 1 and 4,5). Further details and/or exceptions will be discussed below in context with individual coupling components.

As far as the mechanism of azo coupling reaction is concerned, it is generally accepted to correspond to S_E2 with a reaction intermediate. In the first step the diazonium ion attacks the substrate to form the intermediate I which is transformed into the reaction product on splitting off of a proton[25-27]



(12)

I

Supposing the reaction intermediate to be present at a low and constant

concentration throughout the reaction, the coupling course can be described by the following equation

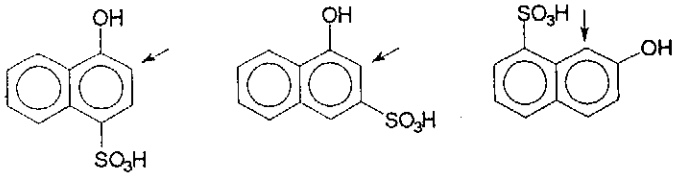
$$\frac{d[\text{Azo}]}{dt} = \frac{k_1 k_2 [\text{B}]/k_{-1}}{1 + k_2 [\text{B}]/k_{-1}} \left[\text{R}-\text{N}_2^{\oplus}\right]\left[\text{R}'-\text{O}^{\ominus}\right] \qquad (13)$$

where [B] means concentration of the base which assists in the splitting off of the proton from the reaction intermediate. The role of this base can be played by anions of some acids, hydroxyl ion, or water. Extraordinarily efficient are nitrogen heterocyclic aromatic amines such as pyridine and its derivatives or some heterocyclic nonaromatic amines such as N,N'-dimethylpiperazine, N-methylmorpholine, or 1,4-diazabicyclo[2,2,2]octane. Similar relations are also valid for azo coupling reactions with aromatic amines.

Let us consider equation (13) in more detail. First suppose the extreme case of $k_2[\text{B}] \gg k_{-1}$: then k from Eqs (7) and (8) reduces to k_{-1} of Eq. (13), i.e. $k = k_{-1}$. This situation is encountered when the second reaction step is faster than the first one, hence the formation of intermediate I is rate limiting.

If, on the contrary, it is $k_2[\text{B}] \ll k_{-1}$, then the constant k is given by the relation $k = k_1 k_2 [\text{B}]/k_{-1}$. In such case the rate limiting step is the decomposition of intermediate I, i.e. the second step, and the reaction will exhibit the primary H isotope effect and base catalysis. With increasing base concentration, the rate ceases to be linearly dependent on its concentration, $k_2[\text{B}] \approx k_{-1}$. The dependence on base is decreased until finally the rate is independent of the base concentration, since $k_2[\text{B}] \gg k_{-1}$. All the three possibilities discussed are represented in Fig. 3. Detailed measurements of this kind have the drawback in that only the k_1 values and k_2/k_{-1} ratios are directly measurable, while the values of the individual constants k_2 and k_{-1} are not.

The isotope effect is observed if the coupling component contains a bulky substituent near the reaction centre, as it can be seen from the following data



1.04 3.1 6.2

k_H/k_D in azo coupling reactions with 4-chlorobenzenediazonium ion

An increase in steric effect (either by a suitable mutual arrangement of substtuents or by increase in their size) has no substantial influence upon the k_1 value, whereas the k_2 value is decreased[28]. The small influence of substituent upon k_1 can be interpreted as follows: the intermediate I formed in the first step

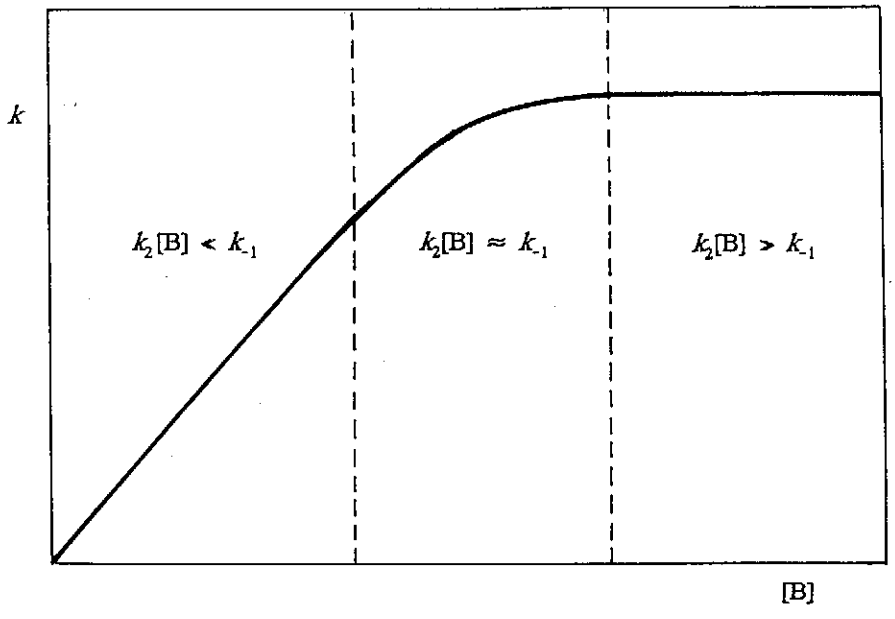
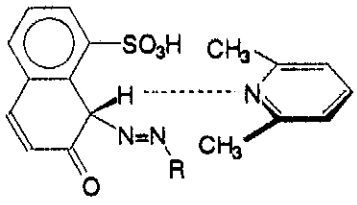


Fig. 3 Schematic representation of effect of base B concentration upon azo coupling rate constant k value

suffers from relatively little steric hindrance, since the carbon atom of the reaction centre has the sp^3 hybridization, i.e. the hydrogen atom and the azo group are in pseudoequatorial and pseudoaxial positions, respectively, whereas the splitting off of the proton is realized in the plane of the aromatic nucleus.

An increase in electrophilicity of diazonium component facilitates the splitting off of the proton from the reaction centre, i.e. k_2 is increased and, consequently, the isotope effect is decreased. This statement can be illustrated by the k_H/k_D values of 6.55, 5.48, and 4.78 found in the azo coupling reactions of 7-hydroxynaphthalene-1,3-disulfonic acid with 4-chloro-, 3-chloro-, and 4-nitrobenzenediazonium ions, respectively[26].

The studies of base catalysis have paid the greatest attention to the influence of heterocyclic or alicyclic nitrogen bases upon the azo coupling reaction of 7-hydroxynaphthalene-1-sulfonic acid and its derivatives. The effects of the individual bases depend on their respective pK_A values: the greater the pK_A the higher accelerating effect of the base. This is manifested by the linear course of the dependence of $\log(k_2/k_{-1})$ vs. pK_A of the bases[29]. A distinct deviation from the said dependence was found with 2-methylpyridine and especially 2,6-dimethylpyridine. These compounds show a lower catalytic effect than that expected on the basis of their basicity.The reason is in the steric hindrance of *o*-methyl groups which prevent any close approach of the basic centre to the proton to be split off by the base. The transition state of this protolysis is represented in the formula II.



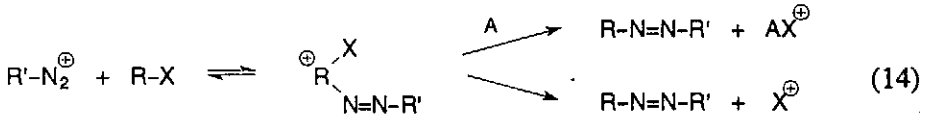
II

Hence, if bases increase the azo coupling reaction rates with the second step rate-limiting, then their effects must also be manifested in the isotope effect. This is what was really proved experimentally: the isotope effect is lowered with increasing base concentration[26]. On the whole, this is self-evident, since the k_2 value affects the k value through the $k_2[B]/k_{-1}$ ratio. The greater is the value of this expression the lower is the effect of k_2 upon k. Then the ratio k_{2H}/k_{2D} is independent of the base concentration, but it is changed when a base of some other kind is adopted. It was found[30] that the dependence of $\log(k_{2H}/k_{2D}$ vs. pK_A of the bases used crosses the maximum at pK_A 1. That means that at pH 1 it is possible to expect the pK_A values of the azo coupling intermediates[30].

In the equation (13) the transformation of intermediate I into the final product is considered to be an unidirectional process. This presumption, however, is contradicted by the finding that e.g. 1-arylazo-4-hydroxy-naphthalene-2-sulfonic acids can be isomerized to the 3-arylazo derivatives at enhanced temperatures[31]. However, the comparison of the rate of formation of the azo compounds with the rate of their decomposition by acids at the same reaction conditions indicates a much lower rate of the reverse reaction[31]. Hence, the azo coupling reaction can be considered irreversible with a sufficient accuracy.

So far the azo coupling reaction has been considered to be a replacement of the proton by azo group. Generally, however, other substituents can play the role of the leaving group too, e.g. halogen[32,33], sulfonic group[34], carboxyl group[35], or even another arylazo group[36].

The azo coupling reactions with such different leaving groups were studied far less extensively than those with the proton as the leaving group. Nevertheless, it is obvious that the basic reaction scheme is the same for all these cases. The interaction of diazonium ion $R'N_2^{\oplus}$ with the corresponding $RO^{\ominus}$ or RNH_2 derivatives produces the reaction intermediate III which - in the second step - looses the leaving group X with the assistance of some auxiliary reagent (denoted A in scheme (14)) or spontaneously to give the expected product.



III

The replacement of 5-H atom in 6-hydroxynaphthalene-2-sulfonic acid by halogen reduces considerably the corresponding azo coupling reaction rate with 4-chlorobenzenediazonium chloride[33]; for the substitutions of 5-H, 5-Cl, 5-Br, and 5-I by 4-Cl-$C_6H_4N_2^{\oplus}$ the found ratio of rates is 1 : 0.007 : 0.0089 : 0.149. In the cases of chloro and iodo derivatives the rate-limiting step is the formation of the reaction intermediate, whereas in the case of the bromoderivative the decomposition of intermediate is rate limiting, which is indicated by a distinct catalytic effect of thiosulfate anion (A = $S_2O_3^{2-}$)[1].

The azo coupling reaction of 2-hydroxynaphthalene-1-sulfonic acid also produces the reaction intermediate III[33,39,40] which, however, is so stable that it was possible to determine its structure. Hence, its transformation into 1-arylazo-2-naphthol must be the slowest step of the azo coupling reaction. This reaction will be discussed in more detail in Section 2.2.

The replacement of an arylazo group by another one is very significant from the point of view of dyestuff production, since such a reaction can be a source of undesirable side products in the production of disazo, trisazo, or higher polyazo dyestuffs. So far the reaction was observed with some naphthalenic and heterocyclic coupling components. Generally, the replacement is the easier the more electrophilic is the attacking diazonium ion[36].

2.2 Azo Coupling Reactions of Aromatic Hydroxy Compounds

The simplest aromatic hydroxy compound - phenol - reacts with diazonium ions in alkaline medium to give two isomers: e.g. with benzenediazonium chloride it forms 2-(phenylazo)phenol (IV) and 4-(phenylazo)phenol (V), the latter product being predominant[41].

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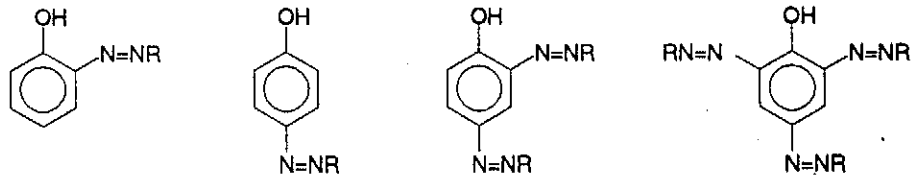
[1] In earlier papers[37,38], the positive effect of sodium thiosulfate upon the rate of azo coupling reaction of 1-bromo-2-naphthol and its derivatives was interpreted by the reduction of the $Br^{\oplus}$ ion (released in azo coupling reaction) with the $S_2O_3^{2-}$ ion thus preventing oxidation reactions of the components with $Br^{\oplus}$. If this interpretation were correct, a similar effect of $S_2O_3^{2-}$ ion would have to be found also with 1-chloro-2-naphthol. But this is not the case[33].

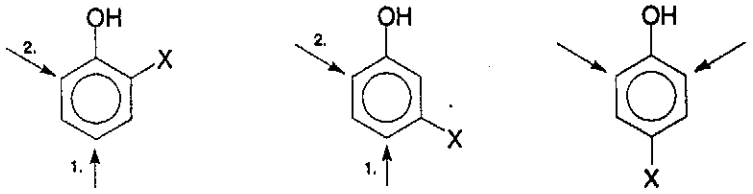


IV V VI VII

R = phenyl

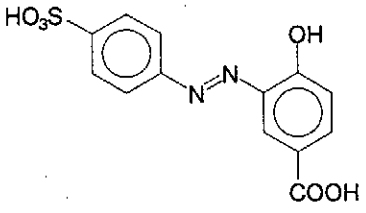
With excess diazo component the reaction continues and gives 2,4-bis(phenylazo)phenol (VI) and finally.2,4,6-tris(phenylazo)phenol (VII)[42,43]. Disazo and trisazo dyestuffs such as VI and VII, respectively, are formed less easily than the monoazo dyestuffs IV and V because the azocoupling reaction is retarded by the presence of one or two phenylazo groups in the molecule of coupling component due to lowering of electron density in the position of attack by the next benzenediazonium cation. As a consequence, the coupling rate is lowered and undesirable side reactions such as decomposition of diazonium cation become more significant. When carrying out the reaction in aqueous medium one encounters another problem. The relatively lower solubility of the monoazo and disazo dyestuffs resulting in their precipitation, which further reduces the coupling rate.

The character of substituents of aromatic nucleus of phenol affects both the coupling rate and position of attack by the diazonium cation.

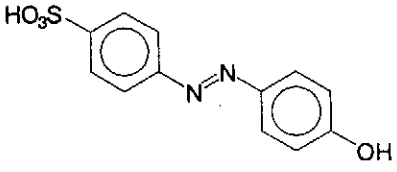


the arrows and numbers show the positions and order of the attacks

If phenol is substituted at the *o*- or *m*-position with respect to hydroxy group, then the arylazo group preferably enters the *p*-position. If the p-position is occupied, then azo coupling takes place at the *o*-position with the exception of the cases where X is a good leaving group and the arenediazonium ion is sufficiently reactive: then the X substituent is replaced by ArN_2 group. As an example we can give the azo coupling reaction of diazotized 4-aminobenzene-sulfonic acid with 4-hydroxybenzoic acid: the reaction products involve, besides the expected *o*-derivative VIII, also 4-hydroxyazobenzene-4'-sulfonic acid (IX)[44].

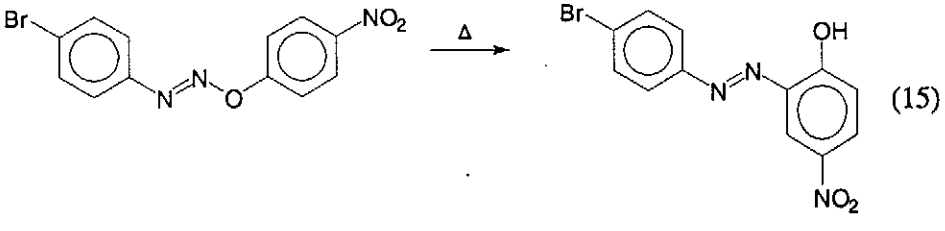


VIII



IX

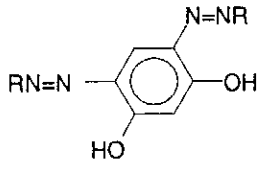
The reactivity of phenol derivatives as coupling components decreases in the sequence of X = OCH_3 > CH_3 > Cl > NO_2. The reactivity of 4-nitrophenol is so low that at usual reaction conditions only its phenoxide O atom is attacked to give the so-called diazo ether. These are unstable compounds readily decomposing into the starting components. However, heating of the dry diazoether prepared from 4-bromobenzenediazonium ion and 4-nitrophenol above 100 °C results in its rearrangement to 2-(4-bromophenylazo)-4-nitrophenol[45].



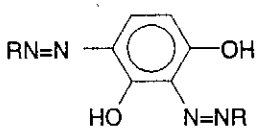
(15)

Out of three isomeric benzenediols - pyrocatechol, hydroquinone, and resorcinol - the first two compounds do not undergo azo coupling reactions in alkaline media[46]. Instead of this they undergo oxidation-reduction processes liberating elementary nitrogen from the diazo component. In the case of pyrocatechol, however, these undesirable processes can be minimized by carrying out the azo coupling reaction in acid medium with aluminium complex of pyrocatechol[47]. The third substance mentioned - resorcinol - is considerably important in dyestuff production.

Due to the presence of two hydroxy groups, resorcinol undergoes azocoupling reactions very easily; with benzenediazonium ion resorcinol dianion reacts faster than phenoxide anion by the factor of 10^4 (Ref.[48]). First the reaction produces 4-arylazo-1,3-benzenediol, and with excess diazo component two isomeric disazo dyestuffs are formed, viz. 4,6- (X) and 2,4-bis(arylazo)-1,3-benzenediol (XI).



X



XI

The ratio of products X:XI depends on the acidity of reaction medium: in alkaline and acid media the isomers X and XI, respectively, are the major products. The reason is that the azo coupling at 4-position is more positively influenced by bases than that at 2-position[49].

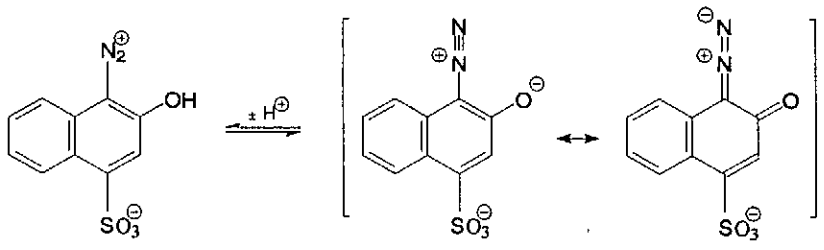
Monohydroxynaphthalenes (1- and 2-naphthols) and the sulfonic acids derived therefrom are very important in dyestuff production.

1-Naphthol couples in both weak acid and weak alkaline media. Its reactivity is high (see Table I), which allows reactions also with little reactive diazo components. Like with phenol the reaction product involves the o- and *p*-azo compounds, however, in contrast to phenol, the product ratio is shifted in favour of *o*-isomer. The two isomers differ in their properties and only one of them is usually suitable for a given purpose. Hence the undesirable isomer must be removed from the product or the reaction must be conducted in such a way as to entirely suppress its formation.

The azo coupling reaction of parent 1-naphthol was investigated by Stepanov et al.[55-59]. The authors found that in the reaction of benzenediazonium chloride with 1-naphthol the proportion of *o*-product increases with increasing basicity of medium but only if this basicity increase is due to hydroxyl ion and not to buffers. The ratios of 2-phenylazo-, 4-phenylazo-, and 2,4-bis(phenylazo)-1-hydroxynaphthalenes found at pH 7 and 12 were 5.4 : 86 : 8.6 and 27.4 : 42.6 : 29, respectively.

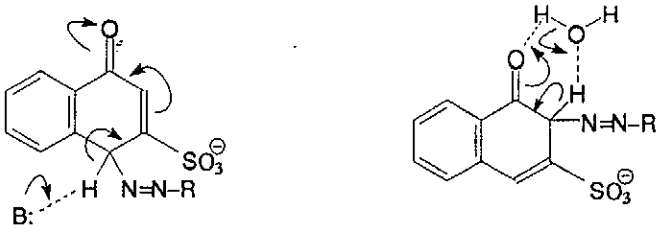
Substituents in diazo component significantly affect the *o/p* ratio of the azo coupling reaction: electron-donor substituents decrease the proportion of *o* - isomer whereas electron-acceptor substituents have the opposite effect[59].

The above-mentioned results, however, disagree with the well-known fact concerning 1-diazonium-2-hydroxynaphthalene-4-sulfonate (XII): this diazo component reacts with 1-naphthol selectively at its 2-position only in very strong alkali medium. If the basicity of medium decreases, also the reaction at 4-position becomes significant. At present, this fact is interpreted by a distinct lowering of electrophilic reactivity of this diazo component after deprotonation of its OH group[60] (XIIa,b), which results in the increase of selectivity of reaction in favour of the 2-position of 1-naphthol.



XII XIIa XIIb

The most integral theoretical study is that by Zollinger et al. who investigated in detail the azo coupling reaction of 4-hydroxynaphthalene-2-sulfonic acid and found that the essential difference between *o*- and *p*-coupling reactions lies in different mechanisms of splitting off of the proton from the corresponding reaction intermediates. This process is strongly catalyzed by bases in the case of *p*-coupling reaction (XIII) whereas the assistance of base is substantially lower in the splitting off of proton during the *o*-coupling reaction[31,50]. This is due to the intramolecular base catalysis by the neighbouring oxygen atom assisted by a water molecule which completes the six-membered cyclic transition state (XIV).



XIII XIV

The results given follow (a) from the found dependence of *o/p* product ratio upon the buffer concentration in the azo coupling reactions of 2-nitrobenzenediazonium ion with 4-hydroxynaphthalene-2-sulfonic acid[31] and (b) from the different isotope effects of the *o*- and *p*-substitution in the coupling of the same diazo component with 1,3-dideuterio-4-hydroxynaphthalene-2-sulfonic acid[27].

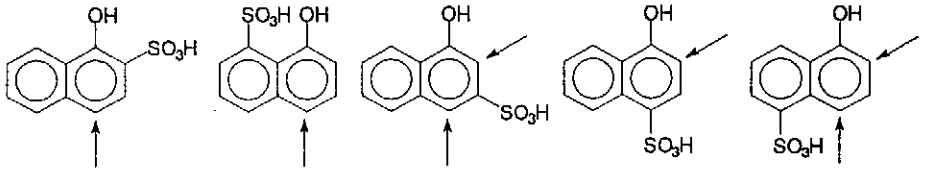
The *o/p* product ratio also depends on the temperature[31]: a temperature increase favours the *o*-coupling reaction. Thus in the azo coupling reaction of 2-nitrobenzenediazonium ion with 4-hydroxynaphthalene-2-sulfonic acid in acetate buffer the *o/p* ratios found at the temperatures of 10, 20, and 30 °C were 3.20, 4.35, and 7.55, respectively.

The catalytic effect of bases at *p*-position decreases with increasing electronegativity of the diazo component[53]. Therefrom follows the well-known fact: the more electronegative diazo component is used in a coupling reaction

the higher proportion of *p*-isomer in the product[54].

From what has been said one can draw several conclusions for practical applications. The aim of the highest proportion of *o*-isomer in the coupling products of 4-hydroxynaphthalene-2-sulfonic acid and other sulfonic acids of 1-naphthol which structurally allow the azo coupling at both *o*- and *p*-positions is best attained if the following rules are observed: (a) the lowest possible pH value of reaction mixture, (b) the absence or at least reduced presence of buffers (the role of a base can be played by anions of current weak acids such as acetic, oxalic, phosphoric, carbonic, or by nitrogen bases such as pyridine, di- and trialkylamines etc.), (c) the highest possible temperature.

From practical point of view, the most important sulfo derivatives of 1-naphthol are its mono-, di-, and trisulfonic acids. Obviously, the effect of sulfonic group on azo coupling is the greater the nearer the group is to the position of attack by arenediazonium ion.



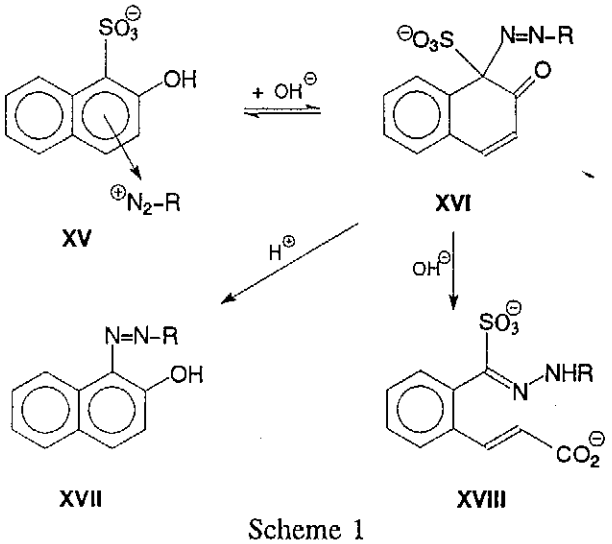
A sulfonic acid group at 2-position allows the azo coupling reaction to proceed at the 4-position only. The sulfonic groups at 2- and 8-positions accelerate the reaction considerably[62] (by 3-4 orders of magnitude as compared with the other derivatives), and the sulfonic groups at 3- and 5-positions increase the trend of azo coupling reaction at 2-position, the group at 3-position being more efficient in this respect[52]. The dependence of *o*/*p* ratio on the medium and on electrophilicity of diazo component are the same as those for 1-naphthol. They only differ in absolute values.

The azo coupling reactions of disulfo and trisulfo derivatives of 1-naphthol obey the same rules as those valid for monosulfonic acids.

2-Naphthol reacts more slowly than 1-naphthol in alkaline medium, the difference being in the order of magnitude (Table I), and the azo coupling reaction only produces a single isomer: the arylazo group exclusively enters the 1-position. The reaction at other positions (where it could be expected from analogy with benzene derivatives, i.e. at 3- and 6-positions) was never observed.

If the 1-position is occupied by a substituent, then either the reaction fails to proceed or the substituent is replaced. The problem of coupling reactions of 1-substituted-2-naphthols was mentioned in Section 2.1. Here we will deal with rather unusual reactions of arenediazonium ions with 2-hydroxynaphthalene-1-sulfonic acid[40]. In the medium of a weak acid, a relatively stable π complex XV is formed which is transformed into σ complex XVI in weak alkali. 1-Arylazo-2-hydroxynaphthalene (XVII) is obtained from the intermediate XVI by acidification to pH 5. If the reaction mixture remains alkaline, then the

aromatic ring is opened to form a cinnamic acid derivative XVIII.



Scheme 1

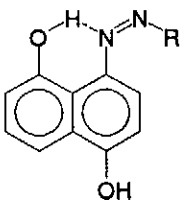
The reaction is interesting from theoretical point of view since understanding it will undoubtedly extend our knowledge about the effect of leaving group on the course of azo coupling reaction. First steps to solving this problem have been already realized[33].

The azo coupling reaction of 2-naphthol is considerably influenced by 8-substituent (see Section 2.1) whereas substituents at other positions have smaller effects.

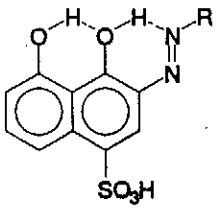
Dihydroxynaphthalenes obey similar rules as those valid for the monohydroxy derivatives. In addition some extra regularities are observed which follow from possible existence of hydrogen bonds in the starting dihydroxy compound or in its first coupling product.

1,5-Dihydroxynaphthalene, 4,5-dihydroxynaphthalene-1-sulfonic acid (Dioxy-S-Acid), 4,5-dihydroxynaphthalene-2,7-disulfonic acid (chromotropic acid), and 4,6-dihydroxynaphthalene-2-sulfonic acid (Dioxy-G-Acid) react in the presence of weak alkali with exceptional ease to give the respective monoazo dyestuffs XIX-XXII.

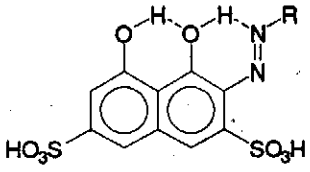
Introduction of a further azo group into *o*- or *p*-position with respect to the second hydroxy group is considerably difficult. The second azo coupling of the azo dyestuffs XIX-XXII takes place only after the deprotonation of hydroxy groups which is possible in strong alkali only (due to the relatively strong hydrogen bonds present)[63-65]. For instance, the dissociation of hydroxy groups in chromotropic acid exhibits[66] the values $pK_1 = 5.53$ and $pK_2 \approx 12$. At the respective reaction conditions, most arenediazonium salts are rapidly



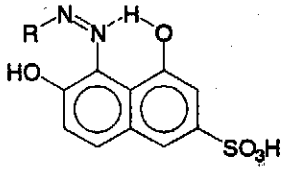
XIX



XX



XXI

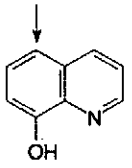


XXII

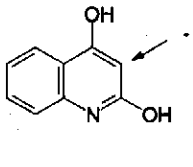
decomposed or transformed into the nonreactive diazotate. Hence, a complete reaction of the coupling component requires a considerable excess of diazo component, which causes problems of isolation of the desirable product. The limitations due to the hydrogen bond can be crossed in the case of double coupling of chromotropic acid if the reaction is carried out with the calcium complex of the monoazo dyestuff[67,68].

Dioxy-S-Acid and Dioxy-G-Acid are unsymmetrical, which allows isomers to be formed in the first azo coupling reaction. The former reacts preferably at the *o*-position to the more acidic hydroxy group[66], i.e. at 3-position (XX), whereas the latter prefers 5-position (XXII) to 3-position. An interesting way of influencing the isomer ratio was found in the azo coupling reaction of Dioxy-G-Acid with diazotized 2-aminobenzoic acid. An addition of sodium thiosulfate to the reaction mixture resulted in the 3-isomer being the main product[65].

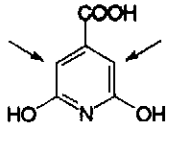
Out of other aromatic hydroxy compounds, some hydroxy or dihydroxy derivatives of nitrogen-containing heterocyclic compounds are important in dyestuff production, e.g. 8-hydroxyquinoline (XXIII)[69,70], 2,4-dihydroxyquinoline (XXIV)[71], and 2,6-dihydroxypyridine-4-carboxylic acid (XXV)[72,73].



XXIII



XXIV



XXV

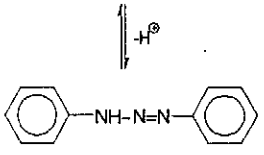
2.3 Azo Coupling Reactions of Aromatic Amino Compounds

Generally, aromatic amino compounds undergo azo coupling reactions less easily than the corresponding hydroxy compounds. This is manifested in lower reaction rates of coupling of amino compounds as compared with those of structurally similar hydroxy compounds with the same diazo component (Table I, Nos 6 and 7). This lowered reactivity has the consequence in that less reactive diazo components do not at all react with amino coupling components; e.g. 1-diazonium-2-hydroxynaphthalene-4-sulfonate reacts relatively slowly with 1-naphthol, whereas no azo coupling reaction takes place with 1-naphthylamine.

Azo coupling reactions of primary aromatic amines (especially benzene derivatives) is often complicated by a side reaction - formation of the respective diaryltriazene (diazoamino compound). Arylazo group not only replaces an aromatic hydrogen atom but can also replace hydrogen atom of amino group, i.e. C-coupling is accompanied by N-coupling reaction. The mutual relations of the two reactions will be explained on the most typical example - preparation of 4-aminoazobenzene (XXVI).

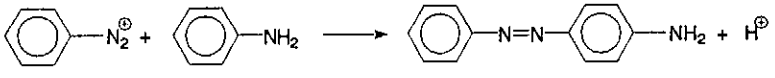
4-Aminoazobenzene should be formed by azo coupling reaction of benzenediazonium ion with aniline but upon mixing equivalent amounts of the two components in mild acid, neutral, or mild alkali media (i.e. media most suitable for azo coupling reaction according to the principles outlined in Section 2.1) we obtain predominantly diphenyltriazene (XXVII). The rate of its formation is - with respect to low acidity of medium - much higher than that of C-coupling reaction giving 4-aminoazobenzene. At a high acidity of medium, the equilibrium (16) is shifted towards the starting reactants but, at the same time, the acid-base equilibrium (17) is shifted to the left too. This lowers the content of aniline free base, and the coupling reaction (18) is slow.

(16)



XXVII

(17)

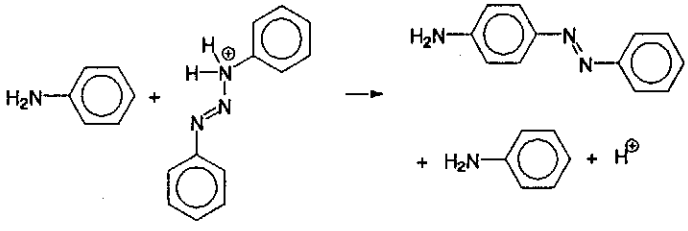


XXVI

(18)

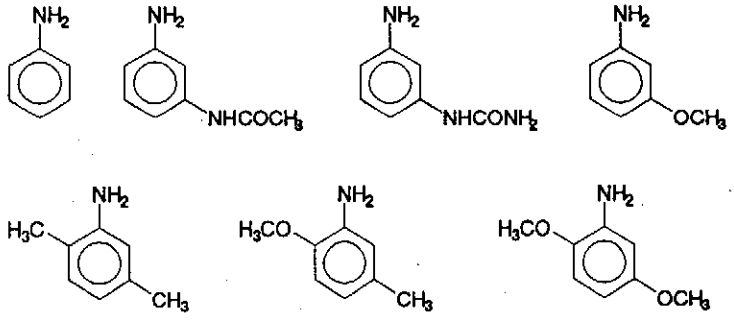
The desirable reaction (18) can, however, be accelerated, and the side decomposition reactions of diazonium ion can be suppressed, by increasing the temperature and the excess of aniline and anilinium chloride and decreasing the water content in the reaction mixture. These are conditions at which 4-aminoazobenzene is really produced industrially in good yields and purity[74,75]; the triazene prepared separately is "rearranged" to the required product at the conditions mentioned.

The formation of triazene does not represent a necessary condition for the realization of the synthesis, only the step (18) is decisive[76]. The mechanism of this reaction was elucidated mainly in the papers by Frieswell, Green, Suizu, and Yokozima[77-79]. In addition, Goldschmidt et al. proved that in anhydrous media the diphenyltriazene cation can react directly with aniline without preceding splitting to the starting diazonium ion and aniline[80-85], see Eq. (19).



(19)

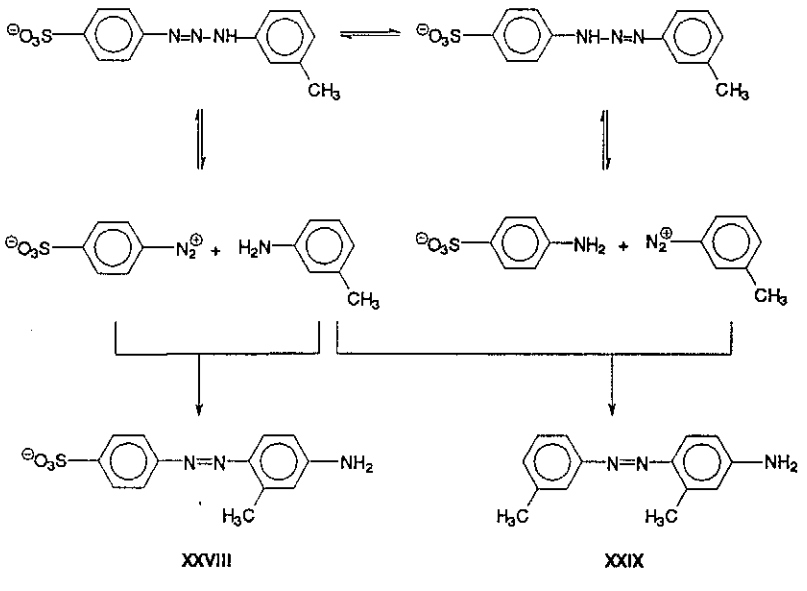
Negative substituents in aniline nucleus at any position (e.g. nitro or sulfonic group) prevent the *C*-coupling so that only the diazoamino compounds can be produced. On the other hand, the presence of electron-donor groups at *m*-, or *m*- and *o*-positions makes it possible for the expected 4-aminoazobenzene derivatives to be produced (sometimes in quite high yields) from equivalent amounts of the diazo and coupling components in water at about 0 °C. The aniline derivatives used industrially as coupling components in production of azo dyestuffs of various types are listed below.



In the azo coupling reactions of amino compounds, a variable extent of the so-called "trans-diazotization" is observed[86]. This is a side reaction which can cause serious troubles in industrial production of dyestuffs. Its nature will be explained on the example of azo coupling reaction of diazotized sulfanilic acid with 3-aminotoluene: the reaction product involves, beside the expected

3-methyl-4-aminoazobenzene-4'-sulfonic acid (XXVIII), also 2,3'-dimethyl-4-aminoazobenzene (XXIX).

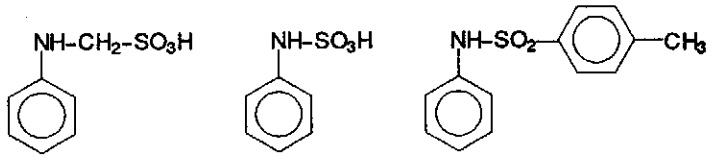
The reason of trans-diazotization is the existence of tautomeric equilibrium (20)[87-90]. The extent to which trans-diazotization will take place depends on the choice of diazo and coupling components. Generally, the trend to the transformation of an amino group into diazonium group increases with increasing basicity of the amino group and vice versa[88,89]. This means that the stronger electrophile is the diazonium ion and the stronger base is the amino compound, the higher tendency to trans-diazotization is observed. Fortunately, the same factors also increase the tendency for C-coupling, hence the final ratio of the products required and those formed by trans-diazotization need not be



(20)

critical for industrial practice even when choosing a strongly electrophilic diazo component or, on the other hand, a strongly basic coupling component. No kinetic measurements of the above-mentioned competitive reactions have been published yet.

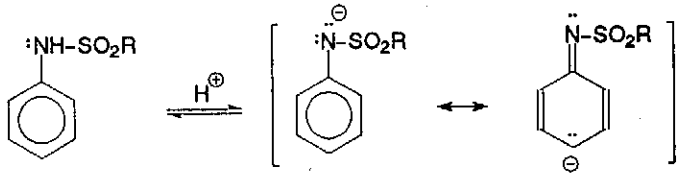
The troubles due to the transformations of diazoamino compounds can in some cases be avoided by replacing the amino hydrogen atom by such a substituent which can positively affect *C*-coupling and can be easily removed after the coupling. The following compounds, e.g., were suggested for this purpose: phenylaminomethanesulfonic acid (XXX), N-phenylsulfamidic acid (XXXI), and N-phenyl-4-methylbenzenesulfonamide (XXXII).



XXX XXXI XXXII

Phenylaminomethanesulfonic acid undergoes azo coupling reaction at *p*-position in mildly acidic, neutral, or alkaline media[91]. The monoazo dyestuff formed is then hydrolyzed in acidic or alkaline medium to remove the CH_2SO_3H group. In some cases the alkaline hydrolysis was accompanied by formation of undesirable side products[92]. The advantage of this procedure is in easy preparation of the coupling component. The synthesis takes place inaqueous medium after mixing equivalent amounts of aromatic amine, formaldehyde, and sodium hydrogensulfite. The procedure mentioned can, of course, be used not only for azo coupling reactions of the parent aniline but also for its methyl, methoxy, or chloro derivatives with free p-position[91].

The compounds XXXI and XXXII have similar properties[93,94]. In alkaline media, both undergo coupling reactions selectively at *p*-position. The reason why electron-acceptor substituents such as sulfonic or arylsulfonyl groups at amino group make the *C*-coupling reaction easier must be looked for in the increased acidity of NH group: it is readily deprotonated in alkaline medium, and the conjugated base formed behaves like phenoxide ion in electrophilic substitutions.



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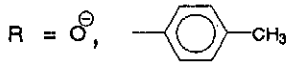
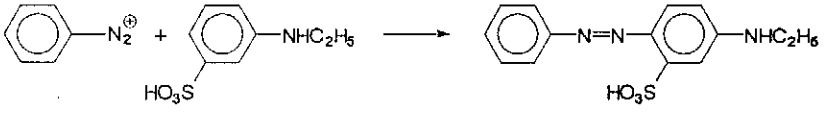


In further treatment, i.e. splitting off of the auxiliary substituent from nitrogen atom, the coupling products from XXXI and XXXII behave differently. Whereas sulfonic group is split off from the nitrogen atom extremely easily in acidic medium (it is even possible to split it off during subsequent diazotization - if the aminoazo compound is designed for this purpose - so that no special hydrolysis operation need be included in the synthesis[94]), arylsulfonyl groups are not. They must be removed by action of sulfuric acid of high concentration[93], which would be rather inconvenient on industrial scale. On the other hand, application of N-sulfo derivatives of aromatic amines has a drawback in their complicated preparation.

Table II Rate constants of azo coupling reactions of diazotized sulfanilic acid with 3-aminotoluene and its N-alkyl derivatives[95]

Amine	pK_A	k, $l\,mol^{-1}s^{-1}$
3-aminotoluene	4.80	27.8
N-methyl-3-aminotoluene	4.94	206.7
N,N-dimethyl-3-aminotoluene	5.47	256.7

Replacement of amino hydrogen atom(s) by one or two alkyl groups increases the azo coupling rate (Table II). In some cases, only one alkyl group is sufficient for the coupling to take place, whereas the corresponding primary amine exclusively forms the diazoamino compound. Thus N-ethyl-3-aminobenzenesulfonic acid reacts with diazonium ion to give the 4-azo derivative[96], whereas 3-aminobenzenesulfonic acid only gives triazene at the same conditions:



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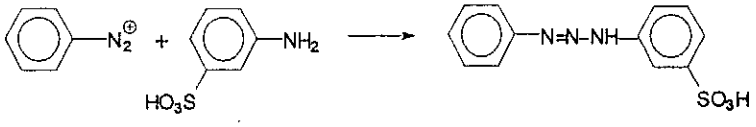


(23)

Industrially important are the azo coupling reactions of N,N-dialkylaniline derivatives which can have further substituent(s) in the alkyl groups. These compounds react usually very easily in acidic medium, the coupling reaction taking place at *p*-position to amino group. Their high reactivity often allows azo coupling reactions to be carried out even in media of 10-20% sulfuric acid if the diazo component is strongly electrophilic. Generally, the azo coupling is the faster the more basic is the amino component used (Fig. 4).

The difference greater than one order of magnitude between the reaction rates of aniline derivatives and 2-aminotoluene derivatives indicates a considerable steric effect of *o*-standing substituent(s) on dialkylamino group. An *o*-methyl group causes the dialkylamino group to rotate out of coplanarity with the benzene nucleus, which - on one hand - increases the basicity of amino group but - on the other hand - decreases the electron transfer from amino group to nucleus, i.e. lowers the reactivity. Two *o*-standing substituents represent a still greater steric hindrance to N,N-dialkylamino group. Thus N,N-2,6-tetramethylaniline (XXXIII) reacts extremely slowly even with 4-nitrobenzenediazonium ion which is a relatively reactive diazo component[97]. On the other hand, julolidine (XXXIV) reacts very easily[98].

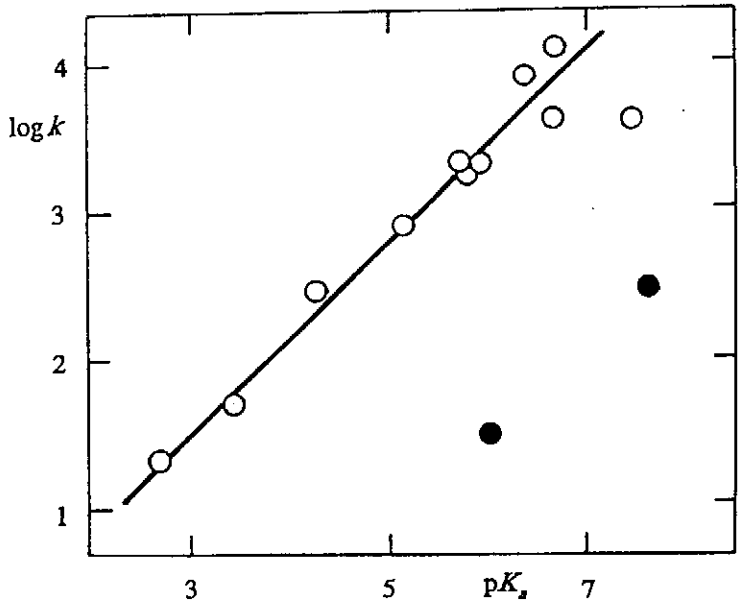
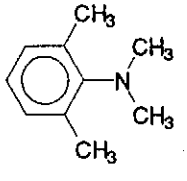
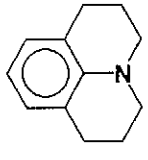


Fig. 4 Dependence of $\log k$ vs. pK_A of amines in azo coupling reactions of diazotized 4-aminobenzenesulfonic acid with N,N-disubstituted aniline (○) and 2-aminotoluene derivatives (●), t = 20 °C (Ref.[95]): 1. NMe_2, 2. NMeEt, 3. NEt_2, 4. $N(n\text{-}Pr)_2$, 5. $N(i\text{-}Pr)_2$, 6. $N(n\text{-}Bu)_2$, 7. $NEt(CH_2Ph)$, 8. $NEt(CH_2CH_2OH)$, 9. $N(CH_2CH_2OH)_2$, 10. $NEt(CH_2CH_2CN)$, 11. $N(CH_2CH_2OH)(CH_2CH_2CN)$, 12. NMe_2, 13. NEt_2

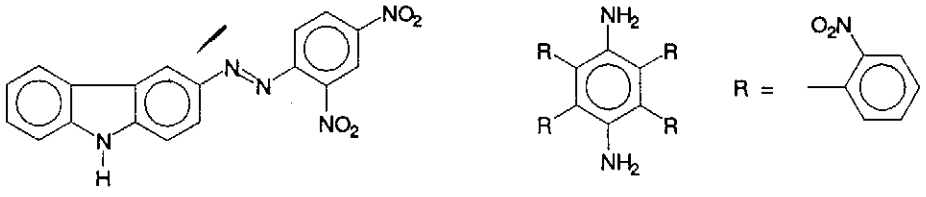


XXXIII



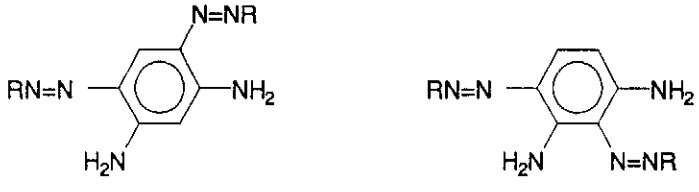
XXXIV

N-Arylanilines also undergo azo coupling reactions. The simplest of them -diphenylamine - even is an important dyestuff intermediate. Its coupling[99] is not slow but the compound is sparingly soluble in water, which may prevent its azo coupling reactions to go to completion. Formally similar to diphenylamine is carbazole which reacts only with very reactive diazo components, the arylazo group entering its 3-position[100]:



XXXV

Out of three isomeric benzenediamines only the *m*-isomer is important in dyestuff production. The *o*- and *p*-isomers treated with diazonium ion undergo oxidation-reduction reactions only. For example, the reaction of 2-nitrobenzenediazonium chloride with 1,4-bezenediamine produces 2,3,5,6-tetrakis(2-nitrophenyl)-1 ,4-benzenediamine (XXXV). On the other hand, 1,3-benzenediamine reacts very quickly also with little reactive diazo components in neutral as well as slightly acidic or alkaline media. Its azo coupling reaction resembles that of resorcinol in many respects. The first coupling product is the 4-arylazo derivative; the ratio of possible disazo compounds depends on the acidity of medium. With decreasing acidity the yield of 4,6-bisarylazo-1,3-benzenediamine (XXXVI) increases to the detriment of 2,4-isomer XXXVII[102].



XXXVI XXXVII

Two amino groups in one aromatic nucleus make it very reactive toward diazonium ions, and the reactivity is still sufficient in the presence of one electron-acceptor group, hence azo coupling reactions with 4-nitro-1,3-benzenediamine as well as with 2,4-diaminobenzenesulfonic acid proceed readily[103].

Naphthaleneamines react with diazo components faster than benzeneamines: e.g. diazotized sulfanilic acid reacts with 1- and 2-naphthaleneamines faster than with 3-aminotoluene the respective factors being 40 and 25 (Ref.[95]).

1-Naphthaleneamine reacts in slightly acidic media to give *o*- and *p*-azo derivatives[104], the second equivalent of diazo component leads to 2,4-bisarylazo-1-naphthaleneamine[105]. The formation of disazo dyestuffs indicates a high reactivity of naphthaleneamines as compared with benzeneamines which normally do not form disazo dyestuffs.

The most significant substitution derivatives of 1-naphthaleneamine are the corresponding sulfonic acids. The sulfonic groups at 2-, 3-, 4-, and

5-positions determine the position of attack considerably. 1-Aminonaphthalene-2-sulfonic acid can only form 4-arylazo compounds. Sulfonicacid groups at 3- and 5-positions increase the proportion of 2-arylazo dyestuff[52,106]. In this respect more efficient is the 3-sulfonic acid group than the 5-sulfonic acid group (cf. analogous situation with 1-naphthol).

2-Naphthaleneamine reacts exclusively at 1-position, and if this is occupied by a sulfonic acid group, it is replaced[107]. At present, the azo coupling reaction of 2-aminonaphthalene-1-sulfonic acid represents the main route to syntheses of 1-arylazo-2-naphthaleneamines because this method makes it possible to avoid handling 2-naphthaleneamine whose production was stopped by all main producers of dyestuff intermediates for hygienic reasons. An 8-sulfonic acid group makes the azo coupling reactions of 1-naphthaleneamine considerably difficult or even impossible[108,109]

2.4 Azo Coupling Reactions of Aromatic Amino Hydroxy Compounds

The presence of both amino and hydroxy groups in a molecule means that the rules controlling the two classes of compounds operate side by side. In alkaline medium the azo coupling reaction takes place at *o*- or *p*-position with respect to hydroxyl group, whereas in acidic medium amino group determines the attack. Of course, there exists a pH region where a mixture of both types of isomers is formed. Hence the expression (24) for the total reaction rate of amino hydroxy compounds was derived[9] as a sum of expressions for the coupling rates of hydroxy compounds (7) and amino compounds (8).

$$v = \left[\mathrm{R\text{-}N_2^{\oplus}}\right]\left(k_{\mathrm{R\text{-}NH_2}}\left[\mathrm{HO\text{-}R\text{-}NH_2}\right] + k_{\mathrm{R\text{-}OH}}\left[{}^{\ominus}\mathrm{O\text{-}R\text{-}NH_2}\right]\right) \tag{24}$$

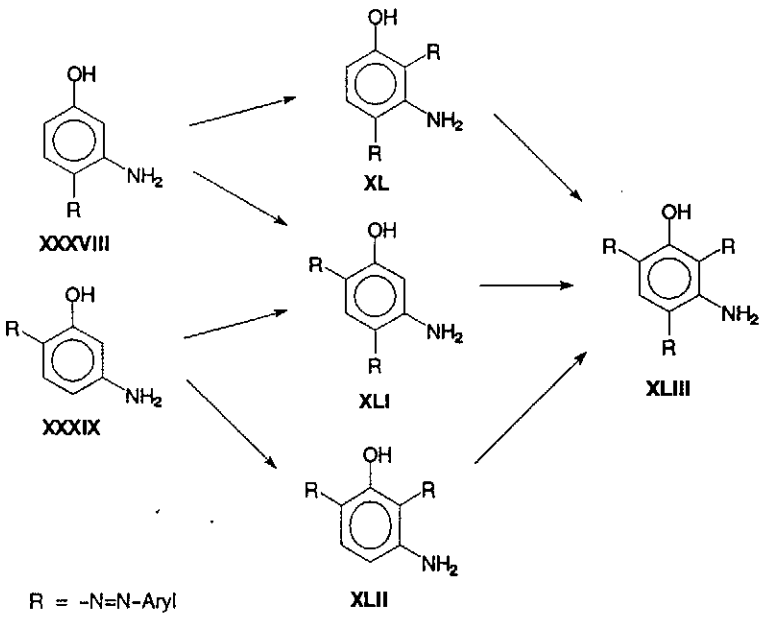
The ratio of amounts of the azo dyestuffs produced by coupling to hydroxyl group and by coupling to amino group is expressed by Eq. (25), and its magnitude depends on the magnitudes of $k_{\mathrm{RNH_2}}$ and k_{ROH} constants as well as on the actual concentrations of aminophenol and aminophenoxide (or aminonaphthol and aminonaphtholate).

$$\frac{X_{\mathrm{R\text{-}NH_2}}}{Y_{\mathrm{R\text{-}OH}}} = \frac{k_{\mathrm{R\text{-}NH_2}}\left[\mathrm{HO\text{-}R\text{-}NH_2}\right]}{k_{\mathrm{R\text{-}OH}}\left[{}^{\ominus}\mathrm{O\text{-}R\text{-}NH_2}\right]} \tag{25}$$

The $k_{\mathrm{RNH_2}}$ and k_{ROH} constants depend on the kinds of the diazo and coupling components used. As for the effect of arenediazonium ion, the higher its electrophilicity, the greater tendency for azo coupling at *o*- and *p*-positions to amino group[110]. This finding was interpreted by differences in the Hammett ρ constants of azo coupling reactions of amino and hydroxy compounds[111]. The concentrations of $\mathrm{HO\text{-}R\text{-}NH_2}$ and ${}^{\ominus}\mathrm{O\text{-}R\text{-}NH_2}$ depend on the kind of the

coupling component adopted, more precisely on the pK_A values of the amino and hydroxy groups present, and, hence, on the acidity of medium.

From among aminohydroxybenzene derivatives industrially important is 3-amino-phenol, which reacts at *p*-position to OH group in alkaline medium (XXXVIII) and at *p*-position to NH_2 group in acidic medium (XXXIX)[112]. In the second step, three isomeric disazo dyestuffs are formed (XL-XLII), and in the third step a single trisazo dyestuff is produced (XLIII).



Scheme 3

In alkaline medium, the formation of disazo dyestuff XLI is preferred from both monoazo dyestuffs XXXVIII and XXXIX. The preferred formation of symmetrical disazo dyestuff XLI in alkaline medium indicates the similarity between 3-aminophenol, resorcinol, and 1,3-benzenediamine. Interesting is the occurrence of the disazo dyestuff XLII found as the single product of azo coupling reaction of monoazo dyestuff XXXIX in strongly alkaline medium. Formation of analogous compounds in the coupling reactions of 1,3-bezenediol and -diamine was not observed.

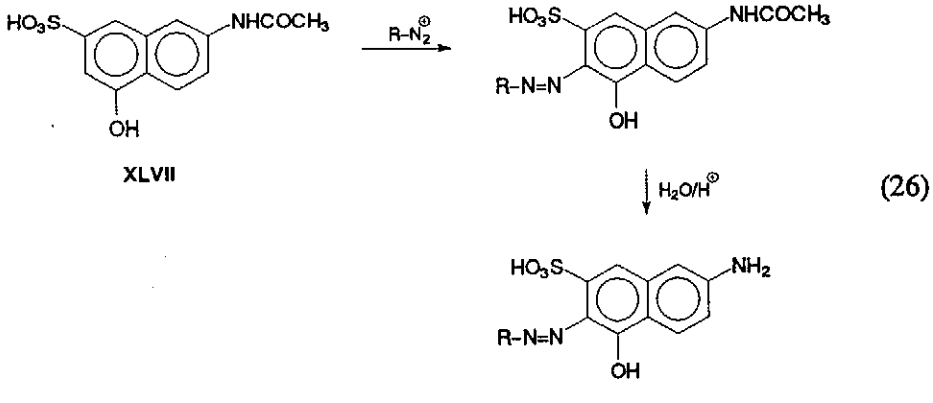
In dyestuff production highly important are amino hydroxy derivatives of naphthalenesulfonic acids, in particular 7-amino-4-hydroxynaphthalene-2-sulfonic acid (I-Acid, XLIV), 6-amino-4-hydroxynaphthalene-2-sulfonic acid (Gamma-Acid, XLV), and 4-amino-5-hydroxynaphthalene-2,7-disulfonic acid (H-Acid, XLVI).

The ratio of products formed by azo coupling reactions at *o*- and *p*-positions to the hydroxy and/or amino groups is determined by the properties of individual diazo and coupling components and by acidity of medium. Azo

coupling reactions of compounds XLIV-XLVI were kinetically investigated by a number of authors[51,52,200-202]. In all the papers the classic scheme by Zollinger was confirmed but also further relationships were discovered. It was found, e.g., that strongly alkaline medium favours coupling reaction at *o*-position to NH_2 group. This can be interpreted by a nucleophilicity increase of amino group due to positive effect of $O^{\ominus}$ group in the adjacent aromatic nucleus. A noteworthy paper by Kaminski, Lauk, Skrabal, and Zollinger[52] describes significant differences in proportions of isomers formed by coupling reactions of Gamma-Acid with strongly electronegative diazonium ions at high concentrations of the reactants (i.e. at the conditions close to industrial realization of the process) as compared with the proportions obtained in experiments at the conditions currently used in kinetic studies. The increased concentrations in the azo coupling reactions in alkaline media increase the amounts of the coupling product to NH_2 group and of disazo dyestuffs. These findings are interpreted by the so-called micro-stirring effect[61].

I-Acid reacts with 4-nitrobenzenediazonium ion[114] at the o-position to amino group or at *o*- and *p*-positions to hydroxyl group in strongly acidic or strongly alkaline media, respectively. In slightly acidic (CH_3COOH - CH_3COONa) or slightly alkaline media ($NaHCO_3$) mixtures of coupling products to amino and hydroxyl groups are formed besides the corresponding disazo dyestuff. In strongly alkaline medium (Na_2CO_3), a considerable amount of product is formed by azo coupling at *p*-position to OH group.

Hence the azo coupling reaction of 4-nitrobenzenediazonium ion (or a diazo component of similar activity) cannot lead to a pure 3-arylazo isomer of I-Acid, but, on the other hand, such dyestuffs are practically demanded. A feasible procedure for their production involves preparation of 7-acetyl-amino-4-hydroxynaphthalene-2-sulfonic acid (XLVII) and its azocoupling reaction with the chosen diazo component in neutral or slightly acidic medium (containing the lowest possible amount of buffers)[115]. The auxiliary acetyl group is split off by hydrolysis after the coupling.

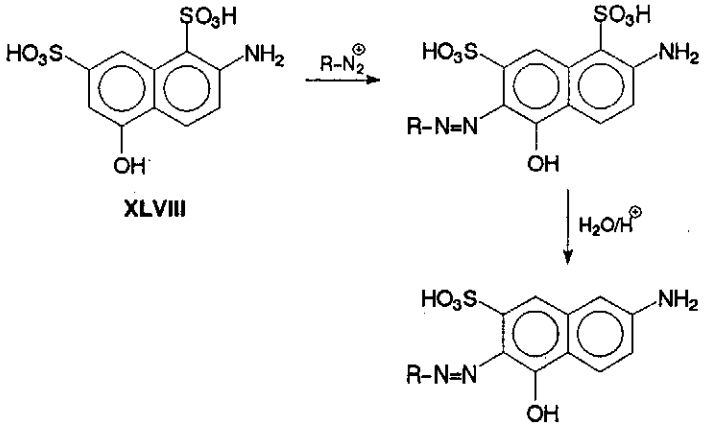


XLVII (26)

The acetylation of amino group prevents formation of the 8-arylazo

derivative. In neutral or slightly acidic medium, the coupling rate to hydroxyl group is sufficiently high, and the absence of general bases will reduce the formation of coupling product at *p*-position to hydroxyl group.

Another way to 3-arylazo isomers of I-Acid consists in azo coupling reactions of 2-amino-5-hydroxynaphthalene-1,7-disulfonic acid (XLVIII) and subsequent splitting off of 1-sulfonic acid group by refluxing the product in mineral acid[116]. The 1-sulfonic acid group prevents the arylazo group from entering not only the 1-position but also the 8-position. Hence - in contrast to the previous method - the coupling reaction can be performed in alkaline medium.

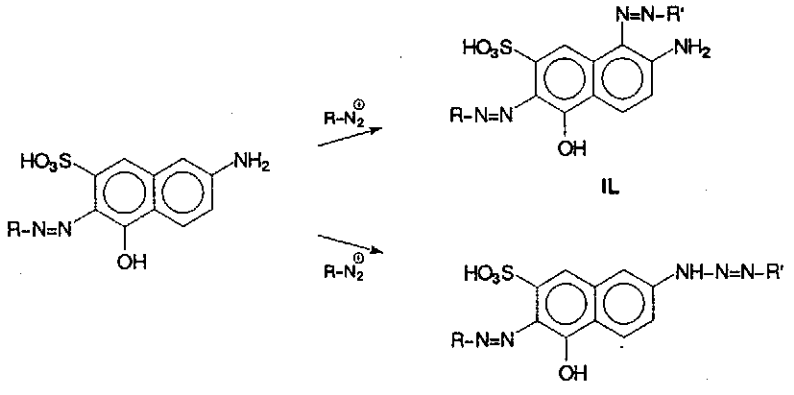


(27)

On the other hand, the azo coupling reactions of Gamma-Acid at *o*-positions to both amino and hydroxy groups proceed without any serious problems with most arenediazonium salts: sufficiently pure *o*-hydroxy- and *o*-aminoazo dyestuffs are formed in alkaline and acidic media, respectively.

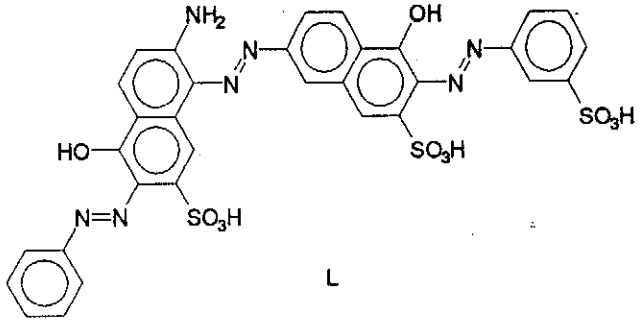
The azo coupling reactions of H-Acid at *o*-position to amino group, however, can be realized at usual reaction conditions only with considerably reactive diazo components, e.g. 4-nitrobenzenediazonium ion. With benzenediazonium ion and diazo components of similar reactivity it proceeds very slowly. In such cases it is recommended to carry out the coupling reaction in the presence of urea, dimethylformamide, or mixture of both compounds[117,118].

The monoazo dyestuffs prepared by azo coupling reactions at *o*-position to hydroxyl group of all the three coupling components mentioned (XLIV-XLVI) undergo further coupling step only very unwillingly. In slightly acidic medium, a mixture of the required disazo dyestuff and triazene is usually formed. Their ratio depends on the kind of coupling component adopted as well as on the ratio of electrophilicities of both diazo components. The more positive substituents there are in the diazonium ion of the first coupling reaction, and the more negative substituents there are in the diazonium ion used in the second coupling step, the greater amount of disazo dyestuff IL can be found in the product.



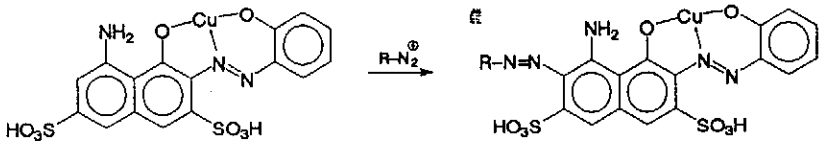
If strongly electrophilic diazonium ions are let to react with *o*-hydroxyazo dyestuffs in alkaline medium, the original arylazo group is replaced[114].

Formation of triazene enables a trans-diazotization, and the diazo component newly formed can participate in further coupling reaction. Only in this way we can explain the occurrence of trisazo dyestuff L among the reaction products formed from 7-amino-4-hydroxy-3-phenylazonaphthalene-2,3'-disulfonic acid and some reactive diazo components in acid medium[119].



L

The *o*-hydroxyazo dyestuffs prepared by alkaline coupling reactions from Gamma-Acid and H-Acid behave during the second coupling reaction like the analogous derivatives of I-Acid. An exception was observed with H-Acid in the case of Cu complexes of *o,o'*-dihydroxyazo dyestuffs which undergo azo coupling reaction to amino group relatively easily[119]

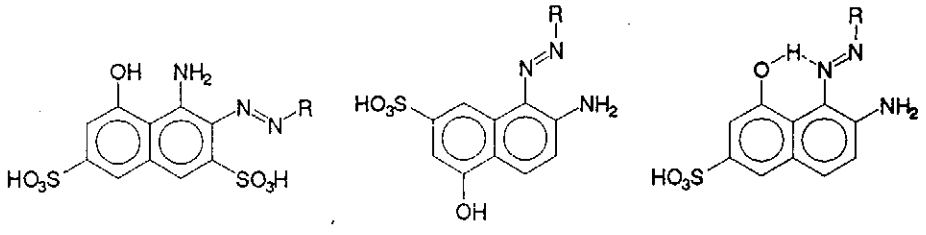


(28)

For R = 3-sulfophenyl and 30% excess of diazo component, the required disazo dyestuff was formed in the yield of 67%, and for R = 4-nitrophenyl and

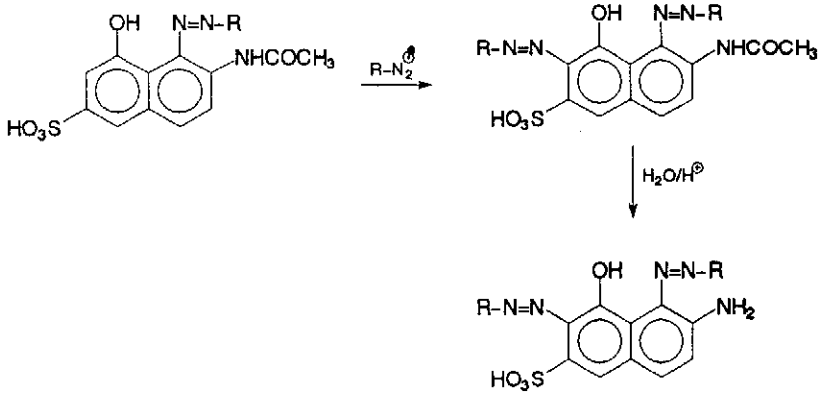
equivalent ratio of both reaction partners the yield was as high as 91%.

The monoazo dyestuffs formed by azo coupling reactions of the above-discussed amino hydroxy compounds at *o*-position to amino group (LI-LIII) show different willingness in further transformation to disazo dyestuffs by treatment of a diazo component.



LI LII LIII

The monoazo dyestuffs LI and LII react as coupling components in alkaline medium, whereas the azo coupling reaction of monoazo dyestuff LIII does not take place at all at usual reaction conditions. The reason of these differences in behaviour lies in the presence of a hydrogen bond between hydroxyl group and azo group which prevents deprotonation of hydroxyl group and, hence, the coupling reaction. The same phenomenon was observed also in the coupling reactions of dihydroxynaphthalenesulfonic acids (see Section 2.1). However, the azo coupling reactions of monoazo dyestuff LIII or other 1-arylazo-2-amino-8-hydroxy-naphthalenesulfonic acids are possible, viz. in strongly alkaline medium (e.g. in NaOH medium), after deprotonation of the hydroxyl group[120-123]. An interesting way of enabling the second coupling step of monoazo dyestuff LIII was published by authors from Sandoz Company[124,125] who found that the coupling at 3-position is possible if the amino group *ortho* to azo group is acetylated. The acetyl group is removed by hydrolysis after the coupling reaction is finished.

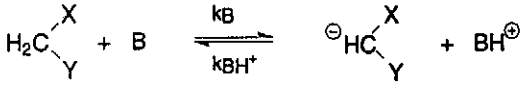


(29)

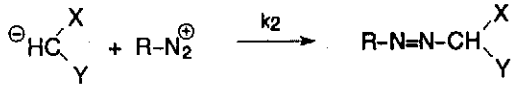
3 Azo Coupling of Compounds with Activated Methyl or Methylene Groups

Azo coupling reaction of diazonium salts with a methyl or methylene group is only possible if there is one or several substituents attached to it which are electrophilic enough to ensure formation of the corresponding carbanion under the conditions of sufficient stability of the diazo component.

The mechanism of the coupling proper is similar to that of coupling reactions of aromatic hydroxy compounds[126]. The first step consists in the dissociation of C-H bond (the equilibrium (30)) and the second in the electrophilic substitution itself of the carbanion formed (Eq. (31)). The reaction scheme involves one more equilibrium, viz. the tautomerism (32) which is shifted to the right. That is why the products of coupling reactions of this sort are represented as the hydrazones LV and not azo compounds LIV.



(30)



(31)

(32)

LIV LV

B and $BH^{\oplus}$ denote a base and its conjugated acid, respectively;
X and Y are substituents out of which at least one is distinctly electrophilic

The dissociation of C-H bond to give the carbanion is a slower process than that of phenols or naphthols. This fact is reflected in the azo coupling reactions at aliphatic carbon atoms in that the rate-limiting step need not be the electrophilic attack of carbanion by diazo component (31) but the formation of carbanion (30). Thus e.g. the kinetic equations (33) and (34) were found for the coupling reaction of 4-nitrobenzenediazonium chloride with nitroethane and its anion, respectively[128,129].

$$\textit{reaction rate} = k[\mathrm{B}][\mathrm{CH_3CH_2NO_2}] \tag{33}$$

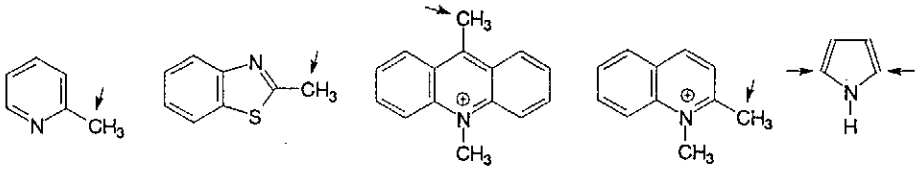
$$\textit{reaction rate} = k[\mathrm{CH_3CHNO_2^{\ominus}}][4\text{-}\mathrm{NO_2}\text{-}\mathrm{C_6H_4}\text{-}\mathrm{N_2^{\oplus}}] \tag{34}$$

The character of substituents near the reaction centre affects the coupling

reaction in opposite sense than that in the coupling reactions of aromatic amino and hydroxy compounds. Whereas the coupling of aromatic substrates is retarded or even prevented by electron-acceptor substituents, quite the opposite is true of the coupling reactions at aliphatic carbon atoms: the stronger the electron-acceptor effect upon the reaction centre the easier the formation of carbanion. Hünig and Boes[127] arranged substituents by their decreasing activating effects

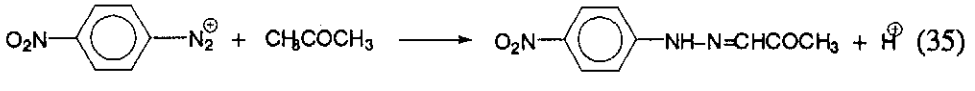
$$NO_2 > CHO > COCH_3 > CN > COOC_2H_5 > CONH_2 > \\ > COOH > SO_2CH_3 > SOCH_3 > C_6H_5$$

Besides the activating groups mentioned some others are also capable to enable azo coupling, especially heterocycles: thus the azo coupling reaction at carbon atom was successful with 2-methylpyridine (LVI)[130], 2-methylbenzo-1,3-thiazole (LVII)[131], 1,6-dimethylacridinium cation (LVIII)[132], 1,2-dimethyl-quinolinium cation (LIX)[133], or pyrrole (LX)[134, 135].



LVI LVII LVIII LIX LX

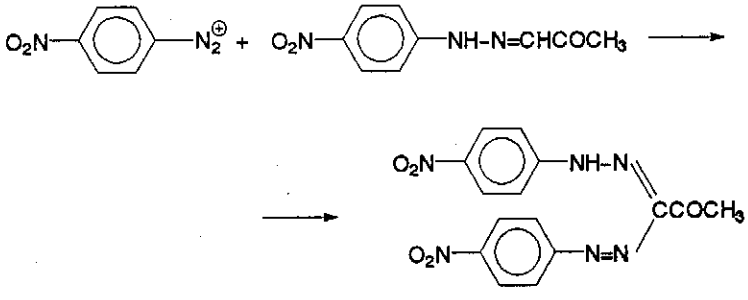
Out of the large number of compounds capable of azo coupling reaction at aliphatic carbon atom the greatest practical importance belongs to those whose methyl or methylene group is activated by at least one carbonyl group. The simplest compound of this type is acetone which reacts in acid medium to give the monoazo dyestuff LXI[136] and in alkaline medium to give the disazo dyestuff LXII[137,138] even in the presence of considerable excess of the coupling component as compared with the diazo component.



(35)

In accordance with what is generally presumed, acetone anion is the reactive species[139]. Its concentration in reaction medium, however, is extremely low in weak alkali or even in weak acid ($pK_A \approx 19-20$). Nevertheless, this drawback is counterbalanced by high reactivity of the carbanion, hence it is possible to find reaction conditions at which the reaction is completed within a reasonable time period. The product of the first coupling, ω-methyl-glyoxal 4-nitrophenylhydrazone (LXI) reacts faster than acetone by seven orders of magnitude, which is due to enhanced activation of C-H bond by the additional electron-acceptor substituent introduced: the hydrazone LXI has $pK_A = 11.54$.

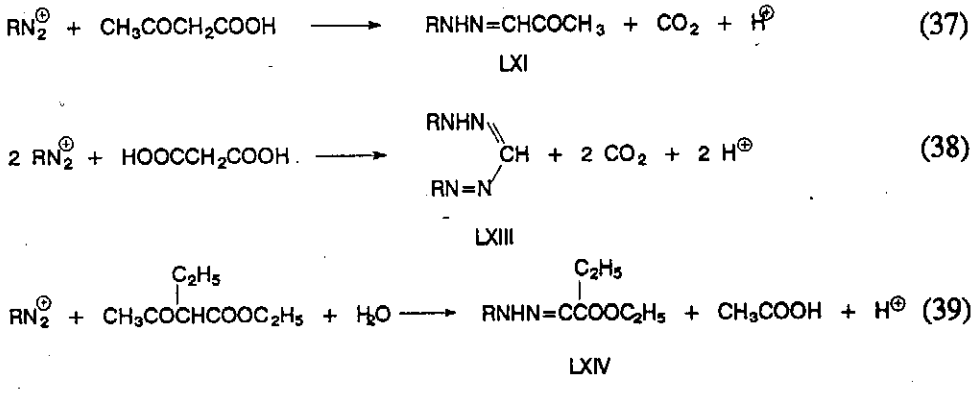
Although the substituent mentioned lowers the coupling rate proper by about one order of magnitude, this effect is negligible as compared with the considerable increase in concentration of reactive coupling component[139,140]. The disazo compounds of the type LXII are generally referred to as formazanes.



(36)

LXII

If the groups X, Y in the compounds $X-CH_2-Y$ or X-CH(Z)-Y are readily split off, the azo coupling is accompanied by their elimination (Japp-Klingemann reaction). Thus the coupling products of acetone and acetoacetic acid are identical[141], malonic acid reacts with elimination of both carboxylic groups to give N,N'-diarylformazane LXIII[142], and ethyl 2-ethylaceto-acetate gives ethyl ester of 2-oxobutyric acid arylhydrazone LXIV[143].



(37)

LXI

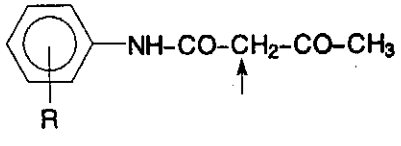
(38)

LXIII

(39)

LXIV

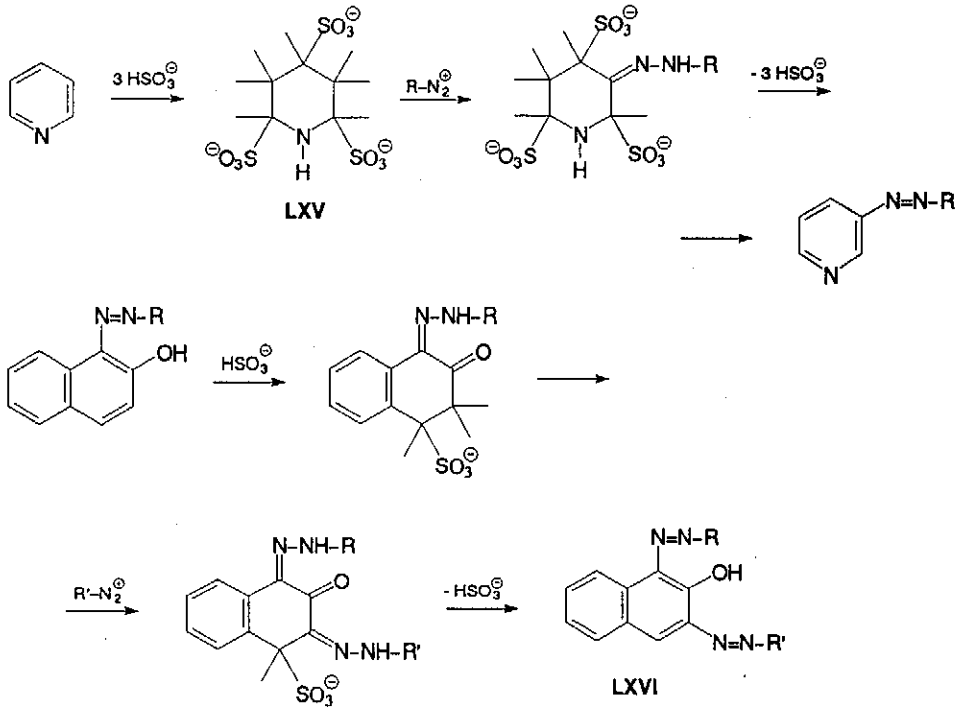
Azo coupling reactions of acetoacetanilide and its ring-substituted derivatives are of high technical importance:



R = H, halogen, alkyl, alkoxyl, sulfonic group etc.

These compounds react very easily in slightly acidic, neutral, as well as alkaline media even with relatively "weak" diazo components. The corresponding kinetic measurements show that the electrophilic attack by diazo component is rate limiting[144].

The class of compounds undergoing azo coupling reactions at aliphatic carbon atom also includes adducts of aromatic compounds with hydrogensulfite: e.g. pyridine is a compound which cannot act as a coupling component at any circumstances. It can, however, be transformed into the hydrogensulfite adduct LXV which undergoes coupling at current conditions, and in the end the auxiliary hydrogensulfite ion can be eliminated from the dyestuff obtained[146,147]. In this way it is possible to obtain 3-arylazopyridines which are inaccessible by direct azo coupling. Similarly it is possible to prepare 1,3-bisaryl-azo-2-naphthol LXVI from 1-arylazo-2-naphthol[145].



Scheme 5

4 Preparation of Azo Compounds by Other Ways than Azo Coupling Reactions

Aromatic azo compounds can be prepared by a number of other procedures beside azo coupling. Out of them the most important for industrial production

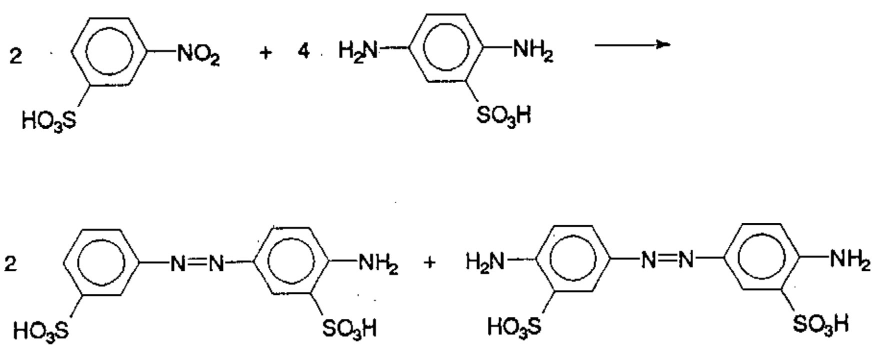
of dyestuffs are the syntheses based on condensations of amino with nitro compounds, reduction of nitro compounds, and oxidation of amino compounds. Let us discuss in some detail these three types of syntheses.

The condensation of aromatic amino and nitro compounds proceeds in strongly alkaline media (1-5% NaOH) at 40-120 °C and involves linking of two nitrogen atoms. Schematically, the reaction can be represented as in Eq. (40) or (41) under the presumption that azoxy compound is formed.

$$R\text{-}NO_2 + R'\text{-}NH_2 \xrightarrow{2\,H} R\text{-}N{=}N\text{-}R' + 2\,H_2O \qquad (40)$$

$$R\text{-}NO_2 + R'\text{-}NH_2 \longrightarrow R\text{-}\overset{\oplus}{\underset{O^{\ominus}}{N}}{=}N\text{-}R' + H_2O \qquad (41)$$

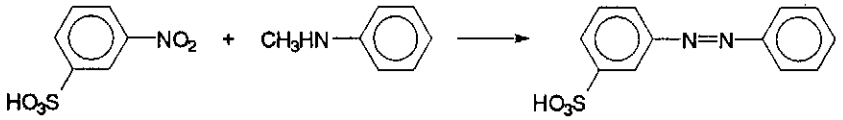
The course of the reactions (40) and (41) is not yet known, and in the case of (40) even the stoichiometry is known only incompletely. The electron source for accomplishing the reduction (in Eq. (40) represented as hydrogen atoms) is only known in the cases of readily oxidized amines. The reaction product of condensation of 3-nitrobenzenesulfonic acid with 3,5-diaminobenzenesulfonic acid includes, beside the expected dyestuff 4-aminoazobenzene-3,3′-disulfonic acid (LXVII), also the oxidation product of starting amino compound, i.e. 4,4′-diaminoazobenzene-3,3′-disulfonic acid (LXVIII)[148], which compensates the electron balance of process.



(42)

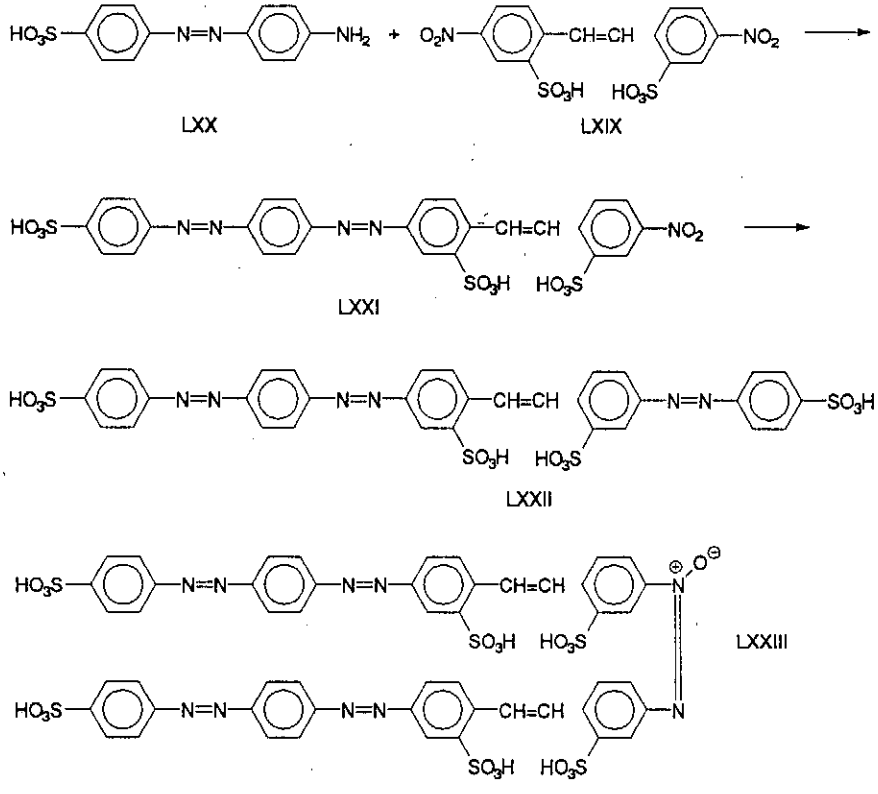
LXVII LXVIII

N-Alkylamino compounds undergo the condensation too, the alkyl group being split off during the reaction[149,150]. The alkyl group does not retard the process, on the contrary, it seems to facilitate it by serving as a source of necessary hydrogen. But N,N-dialkylamino compounds fail to react.



(43)

In industrial dyestuff production the most important condensation is that of 4,4'-dinitrostilbene-2,2'-disulfonic acid (LXIX) with amino compounds, particularly with 4-aminoazobenzene derivatives. The condensation of LXIX with 4-aminoazo-benzene-4'-sulfonic acid (LXX) is presented below as an example[151].



(41)

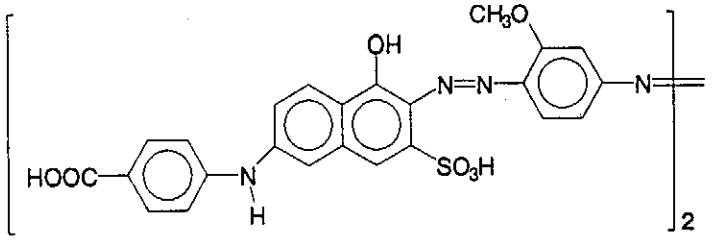
The stilbene derivative LXIX is a bifunctional compound, which enables the condensation to be carried out either at one side or at both (products LXXI or LXXII, respectively). In addition, some side products are formed too such as the pentakisazo dyestuff LXXIII, the product of reduction dimerization of the nitrodisazo dyestuff LXXI[152]. The composition of reaction mixture depends on the ratio of the two starting components LXIX : LXX and on the reaction conditions. In the above scheme the products LXIX and LXXII are written as

azoxy compounds but in fact a mixture of azo and azoxy compounds is obtained. Sometimes, a reducing agent (such as glucose or sodium sulfide) is added after the condensation to remove the azoxy compounds[152].

Another way of preparation of azo compounds consists in reduction of aromatic nitro compounds:

$$2RNO_2 + 8H \rightarrow R\text{-}N{=}N\text{-}R + 4H_2O \qquad (45)$$

A large number of suitable reducing agents have been suggested: alcohols[153], glucose[154], hydrazine[155], zinc[156], silicon[157], ferrosilicon[157], arsenites[158], sulfides[159], or electrochemical pathway[160]. Practicable reagents, however, are only those producing the minimum amounts of products of total reduction (amines) and/or avoiding the splitting of the azo groups already present in the starting compounds. Another condition to be fulfilled is availability of the reducing agent and easy isolation of the required product in pure form. These conditions are well fulfilled by glucose which is therefore adopted in these reductions on industrial scale. The reduction of nitro compounds serves for production of symmetrical tris- and polyazo dyestuffs. Thus e.g. the trisazo dyestuff LXXIV can be obtained by treatment of 7-(4-carboxyphenylamino)-3-(2-methoxy-4-nitrophenylazo)-4-hydroxynaphthalene-2-sulfonic acid with glucose in 1.5% NaOH medium at 75 °C (Ref.[161]).



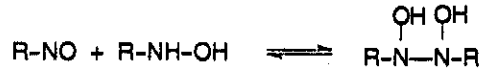
LXXIV

The above-mentioned condensations of nitro and amino compounds giving azo compounds and the reductions of nitro compounds have not been investigated theoretically yet. It can be presumed that their mechanism involves a transformation of nitro group into nitroso and hydroxylamino groups. These products undergo subsequent reactions, mutual condensation (Eq. (46)) or the nitro compound is condensed with amino compound (47).

$$R\text{-}NO + R\text{-}NHOH \longrightarrow R\text{-}\overset{\oplus}{N}(\overset{\ominus}{O})\text{=}N\text{-}R \qquad (46)$$

$$R\text{-}NO + R\text{-}NH_2 \longrightarrow R\text{-}N{=}N\text{-}R \qquad (47)$$

The reactions (46) and (47) take place in acidic, neutral, as well as alkaline media, usually quite rapidly and with good yields. However, they are not technically important due to limited availability of the starting materials. Both reactions were studied by a number of workers[162-169]. At present it is obvious that the first step of reaction produces intermediates LXXV or LXXVI and the second involves their condensation (with elimination of a water molecule) giving azoxy (from LXXV) or azo products (from LXXVI).



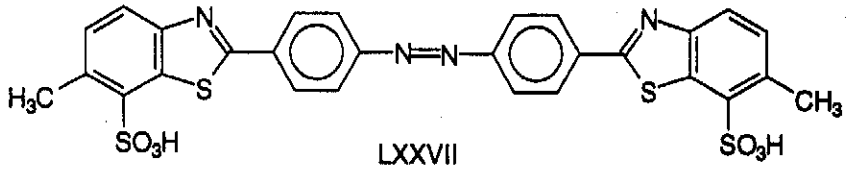
(48)

LXXV

(49)

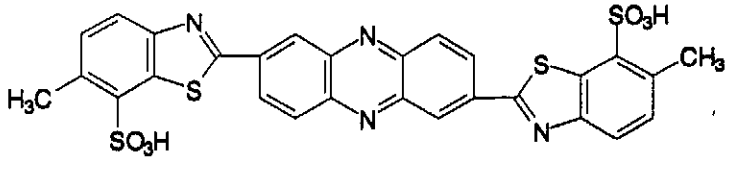
LXXVI

Another way of preparation of azo dyestuffs is based on oxidation of amino compounds: $2ArNH_2 + 2"O" \rightarrow Ar-N=N-Ar + 2H_2O$. The following oxidizing agents were suggested: hydrogen peroxide[170], air[171,172], sulfur[173], chromic acid[174], potassium permanganate[175], and, above all, hypochlorites which have found widest applications. A typical example of application of sodium hypochlorite is the oxidation of 6-methyl-2-(4-aminophenyl)-benzo- 1,3-thiazole-7-sulfonic acid (referred to as dehydrothio-*p*-toluidinesulfonic acid) giving a valuable yellow dyestuff LXXVII[176].



LXXVII

Detailed investigation of the reaction product showed that it contains, beside the required dyestuff LXXVII, also the phenazine derivative LXXVIII[177].



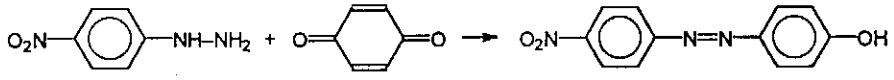
LXXVIII

The phenazine derivative is not formed if both *o*-positions of the starting

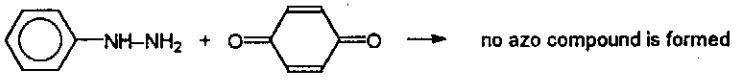
amino component are blocked by substituents[177].

From among other methods of preparation of azo compounds let us mention the condensation reactions of arylhydrazines and reductions of diazonium compounds.

Arylhydrazines react with quinones to give the corresponding hydroxyazo compounds. Success of the reaction depends on the ratio of oxidation and reduction potentials of both components. Quinones with high oxidation potentials react with hydrazines having high reduction potentials only with formation of the respective hydroquinones and liberation of nitrogen molecule. Therefore, the condensation of quinones with high oxidation potentials requires negatively substituted arylhydrazines: e.g. 1,4-benzoquinone can be condensed with 4-nitrophenylhydrazine[178] but not with phenylhydrazine.



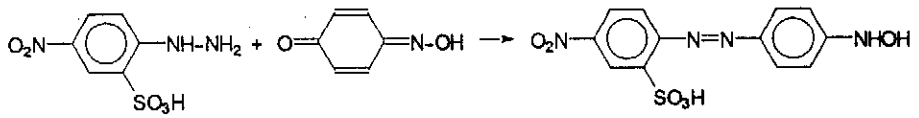
(51)



(52)

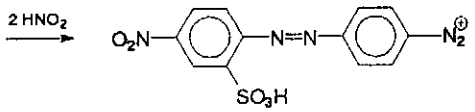
However, 1,2- and 1,4-naphthoquinones can be condensed with phenylhydrazine[179,180]. The former exclusively provides 2-phenylazo-1-naphthol. The reaction is usually carried out in acidic media either in water or aqueous alcohol or in acetic acid at the temperatures up to 100 °C.

The reactions of this type can also be applied to quinone derivatives such as quinone monooximes. Such reactions produce hydroxylaminoazo compounds. The condensation of 2-hydrazino-5-nitrobenzenesulfonic acid (LXXIX) with 1,4-bezoquinone monooxime (LXXX) gives 4-nitro-4'-hydroxylamino-azobenzene-2-sulfonic acid (LXXXI) which can be transformed into the corresponding diazonium compound by treatment with nitrous acid[181]. The diazonium compound thus obtained can serve for production of otherwise inaccessible azo dyestuffs .



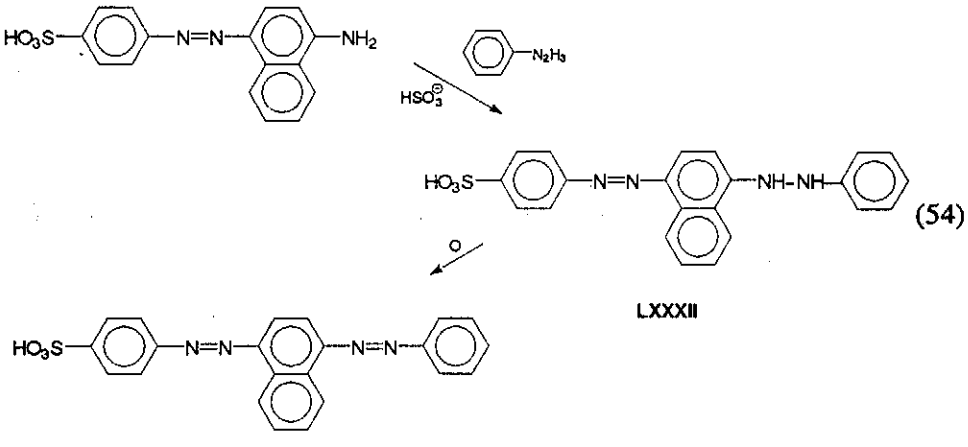
LXXIX LXXX LXXXI

(53)



Another possibility of application of arylhydrazines to preparation of azo

dyestuffs consists in their condensations with *o*- and *p*-hydroxyazo dyestuffs in the presence of sodium hydrogen sulfite. In principle, this is an analogy of the Bucherer reaction. The products are hydrazine derivatives (compound LXXXII in the case given) which must be oxidized to give azo dyestuffs: the oxidation is accomplished with air, sodium hypochlorite in alkaline medium, or with nitrous acid in acidic medium[182].



(54)

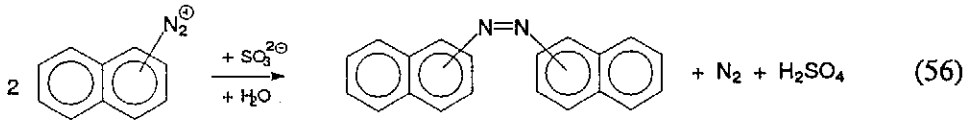
LXXXII

N,N'-Diarylhydrazines can be obtained by other methods, e.g. nucleophilic substitution of halogens or other good leaving groups with arylhydrazines. Thus it is possible to prepare 2,4-dinitrohydrazobenzene by reaction of phenylhydrazine with 2,4-dinitrochlorobenzene, and subsequent oxidation produces 2,4-dinitroazobenzene[183].

Under special conditions it is also possible to reduce diazonium ions to azo compounds:

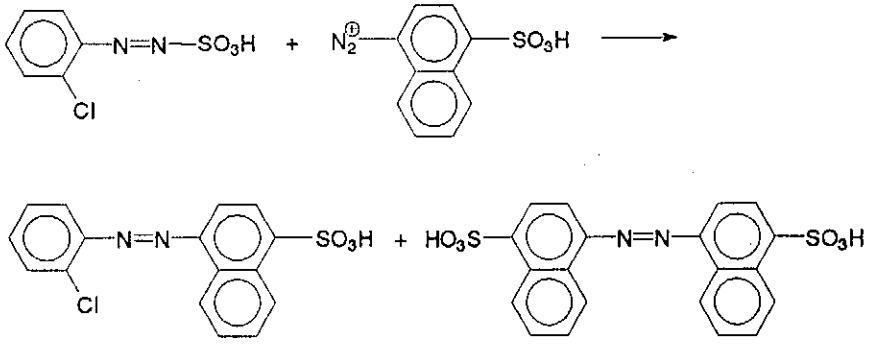
$$2RN_2^{\oplus} + 2e^{\ominus} \rightarrow R\text{-}N{=}N\text{-}R + N_2 \qquad (55)$$

The reaction, however, needs certain structural features in $ArN_2^{\oplus}$ and suitable oxidizing agent and medium. The application of $Cu^{\oplus}$ ion in (55) was published[184-189], but cuprous ions can catalyze a number of other reactions of diazonium ions, so the reaction usually produces mixtures of products. A more suitable agent is sulfite ion but its action is limited to some types of diazonium compounds. Thus it is possible to prepare 1,1'- and 2,2'-azo-naphthalenes upon treating 1- and 2-naphthylamines, respectively, with sodium sulfite in slightly acidic, neutral, or slightly basic media at the temperatures up to 20 °C (Ref.[190]).



(56)

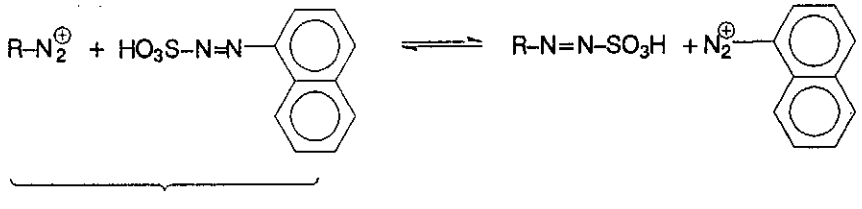
Benzenic diazonium compounds give other products at the same conditions. Suckfüll and Dittmer found that the procedure is applicable to preparation of benzene-azo-naphthalene (i.e. unsymmetrical) dyestuffs. According to the procedure suggested by them one diazonium salt (either benzene or naphthalene derivative) is converted into the corresponding syn-diazo sulfonate which then reacts with the second diazonium compound[191,192].



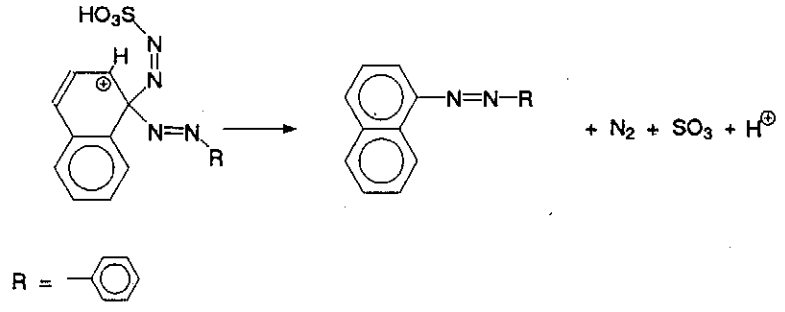
(57)

LXXXIII

The symmetrical dyestuff LXXXIII (containing two naphthalene residues) was found as a side product, whereas the other expected symmetrical side product (2,2'-dichloroazobenzene) was not observed. A more detailed study showed that the nitrogen molecule released always comes from the naphthalenic compound. Zollinger et al.[193] suggest a likely mechanism consisting in a rapid preequilibrium (58) which, however, is strongly shifted to the left. Then follows the attack of the naphthalenic diazo sulfonate by the benzenic diazonium ion and decomposition to final products (59).

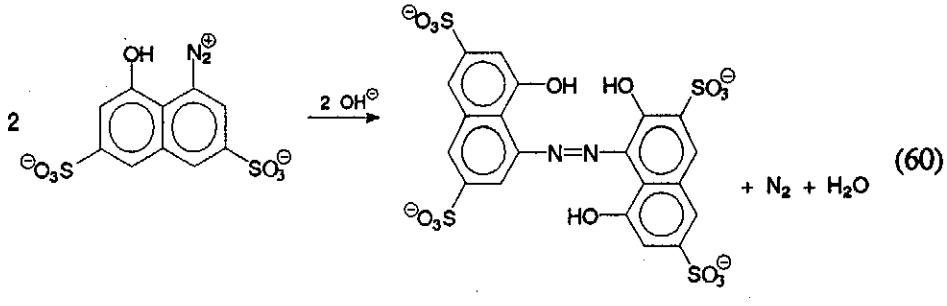


(58)



Scheme 5

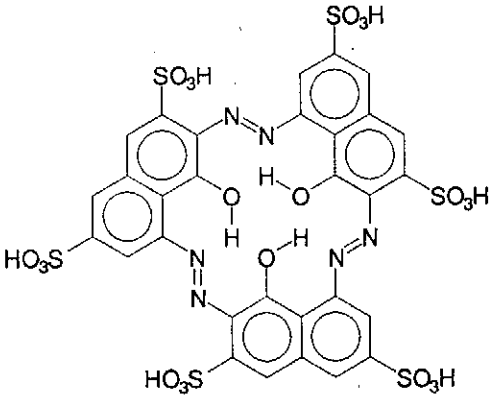
The reactions of *syn*-diazotates with diazonium compounds are similar to those of *syn*-diazo sulfonates[192-194]. In this case, however, the overall electron balance is compensated by introduction of another hydroxyl group into the molecule of the azo dyestuff formed. Thus e.g. alkalinization of the suspension of diazotized 4-amino-5-hydroxynaphthalene-2,7-disulfonic acid results in formation of a high yield of compound LXXXIV.



LXXXIV

The basic principles of reaction mechanism are obviously the same as in the reactions of diazo sulfonates. One particular problem, however, has not yet been explained: the hydroxyl group only enters the *o*-position to the reaction centre and if this is blocked, the reaction does not take place[195].

Note:
Formation of coloured products after alkalinization of diazotized aminohydroxynaphthalenesulfonic acids was observed as early as the end of 19th century[196], however, the products were assigned unlikely structures. In 1960 Close and West[197] found that the compound formed upon alkalinization of the suspension of diazotized 4-amino-5-hydroxynaphthalene-2,7-disulfonic acid can be used as an analytical reagent for calcium, and it was introduced into analytical practice under the name of Calcichrom. Close and West presumed that the compound results from auto coupling reaction of diazotized H-Acid and therefore suggested the cyclic structure LXXXV for it.



LXXXV

However, it was found later by Stead[198] that Calcichrom corresponds to the formula LXXIV. The compound LXXXV was prepared too[199], however, by a procedure quite different from that used for preparation of Calcichrom.

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