

289. Chemical Selectivities Disguised by Mass Diffusion. V. Mixing-Disguised Azo Coupling Reactions¹⁾²⁾

6th Communication on the Selectivity of Chemical Processes¹⁾

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Summary

The results of this study show that, for given initial and boundary conditions, four parameters are sufficient to describe the final product distribution of azo coupling reactions influenced by mixing. This is in agreement with the prediction of the mixing-reaction model developed previously [4] [5]. In order to explain the pH-dependence of the measured mixing-disguised product distribution, it is necessary to assume that a selectivity-determining, local pH-gradient exists even though the solution is macroscopically buffered.

1. Introduction. - A knowledge of the influence of mixing on the behaviour of a chemical process is of decisive importance in the control and optimization of the distribution of the products formed. In previous parts [4] [5] of this series criteria have been derived which allow an appraisal of a possible interplay between the diffusive flow occurring during the mixing process and the product distribution in chemical reactions. These criteria have been employed to interpret successfully the observed substrate selectivity in fast reactions such as nitration of aromatic compounds with nitronium salts in nitromethane [1] [6].

In the present study further evidence for the general validity of these criteria is presented from an analysis of a mixing-disguised azo coupling. Some coupling components, for example 1-naphthol, 1-naphthylamine, resorcinol or 1,8-dihydroxy-4-sulfonaphthalene, have more than one reactive position available for azo coupling. As a consequence, polyazo compounds can be formed in a competitive, consecutive reaction. Whether or not the yield of these compounds is influenced by the mixing process depends on the ratio of the relaxation times of the mixing to the bond-making and bond-breaking events.

As early as 1891, *Noelting & Grandmougin* [7] reported that in the azo coupling reaction of equimolar amounts of 1-naphthol and diazotized 4-chloroaniline an

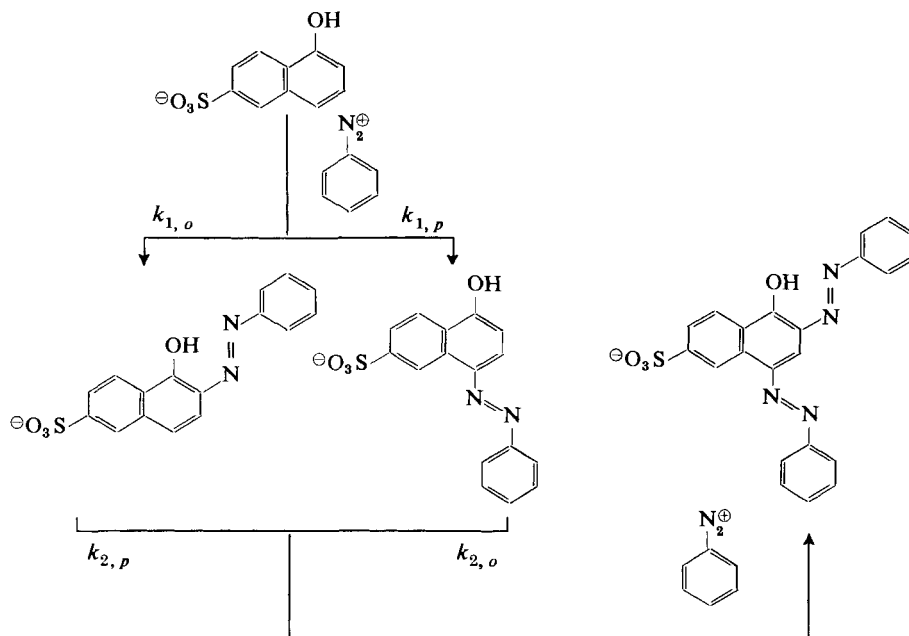
¹⁾ 4th (Part IV) and 5th Communication *cf.* [1] and [2], respectively.

²⁾ Results taken from the PhD. thesis of *E. Crivelli* [3].

appreciable amount of disazo compound is obtained. Particularly under alkaline coupling conditions [8], this amount is much higher than would be expected from the ratio of the intrinsic rate constants for the primary and the secondary substitution steps. For highly reactive diazonium ions, such as the 4-nitrophenyldiazonium ion, the values of these rate constants approach those of encounter controlled reactions [9]. Despite the great industrial importance of azo coupling reactions, only a few studies have appeared [10] in which the possibility of a mixing-dependent product distribution is mentioned.

2. The Model Reaction and its Characteristics. - 2.1. *The System of Competitive Azo Coupling Reactions.* To demonstrate the disguise of chemical selectivities by mixing we chose as a model reaction the azo coupling of 1-naphthol-6-sulfonic acid with phenyldiazonium ion (*Scheme 1*):

Scheme 1



Following the nomenclature in Part I [4] and Part III [5]:

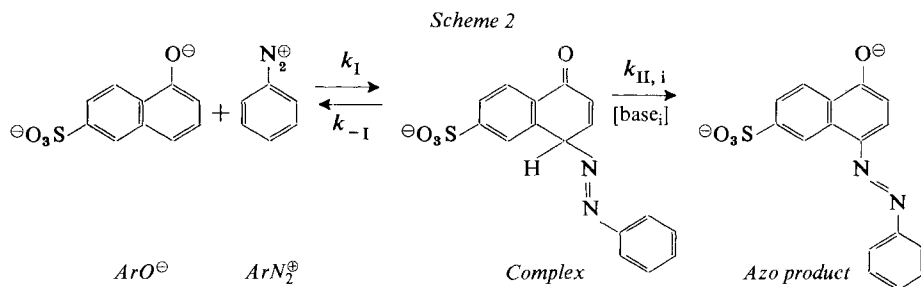
- Reactant *A* 1-Naphthol-6-sulfonic acid;
- Reactant *B* Phenyldiazonium ion;
- Product *R_o* *o*-Monoazo product: 2-Phenylazo-1-naphthol-6-sulfonic acid;
- Product *R_p* *p*-Monoazo product: 4-Phenylazo-1-naphthol-6-sulfonic acid;
- Product *S* Disazo product: 2,4-Bis(phenylazo)-1-naphthol-6-sulfonic acid.

For the purpose of rationalizing the possible influence of mixing on the product distribution, it is convenient to subdivide this model reaction (*Scheme 1*) into various

competitive events: First, two isomeric monoazo products R,o and R,p are formed. The relative rate of formation is given by the positional selectivity and therefore, in general, will not be influenced³⁾ by the diffusion rate of the reactants A and B [4] [11]. Second, formation of the disazo product occurs and the product ratios $[S]/[R,o]$ and $[S]/[R,p]$ will be given by the substrate selectivity and can therefore be diffusion-dependent. The fact that this reaction system consists of a superposition of two mixing-disguised, competitive, consecutive reactions renders its representation by a mathematical model rather complicated.

Before discussing the simplifications which have to be made (*Section 2.3*), we will consider the intrinsic behaviour of the model reaction not disguised by the mixing process.

2.2. The Intrinsic Kinetics of the Azo Coupling. Investigations of *Bartlett* [12], *Pütter* [13] and *Zollinger* [14] have shown that in azo coupling reactions with naphthols the reacting species are the naphtholate ion and the diazonium ion. The bond-making and bond-breaking events are commonly formulated as depicted in *Scheme 2* for the primary *para*-coupling in the reaction system under investigation. Similar mechanistic considerations apply also for the secondary coupling. In this case ArO^\ominus is understood to be the naphtholate anion of R .



If the steady-state approximation

$$\left| \frac{d[\text{Complex}]}{dt} \right| \ll k_1 [ArO^\ominus] [ArN_2^\oplus] \quad (1)$$

applies, the coupling rate can be expressed as:

$$r = \frac{k_1 \sum_i k_{II,i} [\text{base}_i]}{k_{-1} + \sum_i k_{II,i} [\text{base}_i]} [ArO^\ominus] [ArN_2^\oplus] \quad (2)$$

r molar rate of production of the azo product [$M s^{-1}$];
 $[ArO^\ominus]$ concentration of the naphtholate anion [M];
 $[ArN_2^\oplus]$ concentration of the phenyldiazonium ion [M];
 $[\text{base}_i]$ concentration of the base i [M];
 $k_1, k_{-1}, k_{II,i}$ intrinsic n -order rate constants [$M^{1-n} s^{-1}$].

³⁾ This holds only if both monoazo products are formed from the same reacting species, that is from the naphtholate anion and the phenyldiazonium ion, and if the reactions have the same kinetic order and molecularity.

Assuming that the acid-base equilibria of the reacting species are established at a much faster rate than the substitution reaction occurs, we can rewrite equation (2) in terms of the total concentrations of the reactants present. For this purpose the following expressions have to be considered:

$$[ArOH]_{\text{tot}} = [ArOH] + [ArO^{\ominus}] \quad (3)$$

$$K_{OH} = [ArO^{\ominus}][H^{\oplus}]/[ArOH] \quad (4)$$

$$[ArN_2^{\oplus}]_{\text{tot}} = [ArN_2^{\oplus}] + [ArN_2OH] + [ArN_2O^{\ominus}] \quad (5)$$

$$K_1 = [ArN_2OH][H^{\oplus}]/[ArN_2^{\oplus}] \quad (6)$$

$$K_2 = [ArN_2O^{\ominus}][H^{\oplus}]/[ArN_2OH] \quad (7)$$

As $K_1 < K_2$, the concentration of the phenyldiazohydroxide can be neglected ($[ArN_2OH] \approx 0$). One obtains then

$$r = k [ArOH]_{\text{tot}} [ArN_2^{\oplus}]_{\text{tot}} \quad (8a)$$

$$k = \frac{k_1 \sum_i k_{II,i} [\text{base}_i]}{k_{-I} + \sum_i k_{II,i} [\text{base}_i]} \left(\frac{K_{OH}}{K_{OH} + [H^{\oplus}]} \right) \left(\frac{[H^{\oplus}]^2}{K_1 K_2 + [H^{\oplus}]^2} \right) \quad (8b)$$

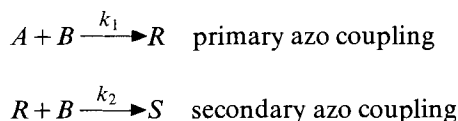
k experimentally measured second-order rate constant for a given constant pH and given, constant concentrations of the bases i [$M^{-1}s^{-1}$].

According to equation (8b) the rate constants $k_{1,o}$, $k_{1,p}$, $k_{2,o}$ and $k_{2,p}$ can be formulated for the primary (index I) and the secondary (index 2) coupling in the *ortho* (index o) and the *para* (index p) positions (*Scheme 1*) using the appropriate acidity constants of the respective coupling components.

Several studies on azo coupling reactions of 1-naphthols [15] have indicated that reaction in the *ortho* as well as in the *para* position can exhibit general base catalysis. From the experimental results presented in *Table 3*, however, we conclude that in the reaction under study a slight general base catalysis occurs for the primary coupling reaction in the *para* position only. Thus, for the buffer system used the condition $k_{-I} < \sum_i k_{II,i} [\text{base}_i]$ applies for the primary coupling in the *ortho* position and for both secondary reactions.

2.3. *A Simplified Reaction Scheme.* In order to relate the experimental results to a mixing-dependent product distribution, the investigated azo coupling (*Scheme 1*) will be approximated by the simplified *Scheme 3*. The justification for such a simplification follows from the data presented in *Table 3*: The secondary

Scheme 3



coupling in the *para* position of *R,o* is only about 4 times faster than the corresponding *ortho* coupling. As in the primary coupling approximately 10 times more *R,p* than *R,o* is formed⁴⁾, the disazo product arises mainly by the route $A \rightarrow R, p \rightarrow S$. Therefore, the following approximations can be made:

$$k_1 = k_{1,o} + k_{1,p} \quad \text{and} \quad k_2 = k_{2,o}$$

A comparison of the calculated *intrinsic* (not mixing-disguised) selectivity behaviour of the unmodified (*Scheme 1*) with that of the simplified reaction system (*Scheme 3*) shows a difference in the relative yields X_S of less than 0.1%. The difference is greater, but still very small, (1%), if the rate constant of the primary coupling is assumed to be 100 times smaller, thereby allowing for a possible inhibition by diffusion.

3. The Mixing-Disguised Selectivity Behaviour. - 3.1. *The Selectivity-Determining Criteria.* In the previous Parts I [4] and III [5] of this series it was demonstrated that the final product distribution observed in second-order, consecutive reactions influenced by the mixing rate is fully described by the four parameters α , E , $\varphi_{B,1}^2$, $\varphi_{B,2}^2$ and the initial and boundary conditions. For consecutive azo coupling reactions these parameters can be derived from equation (8) and application of the procedure described elsewhere [4] [5].

$$\alpha = \frac{V_A}{V_B}; \quad E = \frac{[A]_0}{[B]_0} \quad (9a, b)$$

$$\varphi_{B,1}^2 = \frac{\bar{R}^2 [B]_0}{D} \frac{k_{1,1} \sum_i k_{1,II,i} [\text{base}_i]}{k_{1,-1} + \sum_i k_{1,II,i} [\text{base}_i]} \left(\frac{K_{OH,A}}{K_{OH,A} + [H^\oplus]} \right) \left(\frac{[H^\oplus]^2}{K_1 K_2 + [H^\oplus]^2} \right) \quad (9c)$$

$$\varphi_{B,2}^2 = \frac{\bar{R}^2 [B]_0}{D} \frac{k_{2,1} \sum_i k_{2,II,i} [\text{base}_i]}{k_{2,-1} + \sum_i k_{2,II,i} [\text{base}_i]} \left(\frac{K_{OH,R}}{K_{OH,R} + [H^\oplus]} \right) \left(\frac{[H^\oplus]^2}{K_1 K_2 + [H^\oplus]^2} \right) \quad (9d)$$

V_A, V_B	volume of solution of the coupling component (<i>A</i>) and the diazonium salt (<i>B</i>), respectively [l];
$[A]_0 = [ArOH]_{\text{tot},0}$	initial total concentration of the coupling component (<i>cf.</i> equation (3)) [M];
$[B]_0 = [ArN_2^\oplus]_{\text{tot},0}$	initial total concentration of the diazonium salt (<i>cf.</i> equation (5)) [M];
$k_{j,1}, k_{j,-1}, k_{j,II,i}$	intrinsic <i>n</i> -order rate constants of the bond-making and bond-breaking events in the primary (<i>j</i> =1) and the secondary (<i>j</i> =2) azo coupling reactions (<i>cf.</i> <i>Scheme 2</i>) [$M^{1-n} s^{-1}$];
$K_{OH,A}, K_{OH,R}$	acidity constants of the reactants <i>A</i> and <i>R</i> , respectively (defined in equation (4)) [M];
K_1, K_2	acidity constants of the diazonium ion (defined in equations (6) and (7)) [M];
\bar{R}	mean radius of the eddies (<i>cf.</i> [4] [5]) [cm];
D	mean diffusion coefficient of the reactants [$cm^2 s^{-1}$]. (For solvents of low viscosity: 10^{-5} - $10^{-6} cm^2 s^{-1}$).

It follows that the pH of the reaction medium will also determine whether or not the mixing process influences the selectivity in azo coupling.

3.2. *The Problem of Local pH-Gradients.* The fact that in each azo coupling step a proton is released makes it extremely difficult to set up a comprehensive

⁴⁾ The ratio $R,p/R,o$ depends on the buffer system used as the primary azo coupling in the *para* position exhibits a general base catalysis (*Table 3*).

mathematical model for mixing-disguised azo coupling reactions. In order to predict quantitatively the influence of the space- and time-dependent pH-value on the mixing moduli $\varphi_{B,1}^2$ and $\varphi_{B,2}^2$, and thus on the product distribution, it would be necessary to consider an additional diffusion-reaction equation for the hydronium ion (for spherical eddies):

$$\frac{\partial [H^{\oplus}]}{\partial t} = D_H \left(\frac{\partial^2 [H^{\oplus}]}{\partial r^2} + \frac{2}{r} \frac{\partial [H^{\oplus}]}{\partial r} \right) + r_H \quad (10)$$

D_H diffusion coefficient of the hydronium ion [cm^2s^{-1}];
 r_H molar rate of production of the hydronium ion [Ms^{-1}],
 r polar coordinate [cm].

The term r_H contains not only the production rate of the proton, but also the rates of the acid-base equilibria of the reactants and of the buffer species. Furthermore, the concentration gradients of these species are described by their own diffusion-reaction equations, leading to a family of coupled partial differential equations. This formalism is complicated to use in practice and will not be applied in the present study. The problem of the local pH-gradient will only be discussed qualitatively⁵⁾. Figure 1 and Table 4 show experimental data which demonstrate the pH-dependent disguise of the product distribution by mixing: At a constant mol-ratio of *A* and *B* ($\alpha E = 2$) and a given macroscopic pH, the relative final yield X_S of the disazo product increases with increasing initial concentration of the diazonium salt. X_S is defined as the fraction of the diazonium salt which has reacted after 100% conversion to the disazo product. The experimental behaviour is in accord with calculated predictions [4] [5]. However, what is surprising is the change in product distribution with changing pH: With the help of equation (9), the pK -values of the reactants (Table 1) and the pH-values of the applied buffer solutions, the ratio of the mixing moduli $\varphi_{B,1}^2$ and $\varphi_{B,2}^2$ can be calculated (Table 5). The experimental results which, for a constant value of k_2 and thus for a constant value of $\varphi_{B,2}^2$, show a decrease of X_S with a decreasing ratio $\varphi_{B,1}^2/\varphi_{B,2}^2$ contradict the calculated predictions [4] [5]. This contradiction can be rationalized if it is assumed that the effective, local values for $\varphi_{B,2}^2$ are also changing due to the pH-gradients in the reaction zone. A further argument for a selectivity-determining local pH-gradient is the increasing ratio of the relative yields of the monoazo products $X_{R,o}/X_{R,p}$ with decreasing pH of the applied buffer solutions (Table 4). As the pK -value of 2-phenylazo-1-naphthol-6-sulfonic acid (*R,o*) is higher than that of the *para* isomer the secondary azo coupling reaction in the *para* position is retarded more by a local pH-drop. We plan to investigate this problem further.

3.3. *The Influence of the Stirring Rate on the Selectivity.* The concept of the mixing-reaction model presented previously [4] [5] is based on the assumption that, during the addition of one reactant solution to another, spherical eddies having a limited lifetime are formed. The mean radius \bar{R} of these eddies depends on the turbulence created during the mixing process and can be controlled, for example, by mechanical stirring. It is possible to estimate this parameter [1] [16] from the theory

⁵⁾ A quantitative, comprehensive treatment is in preparation.

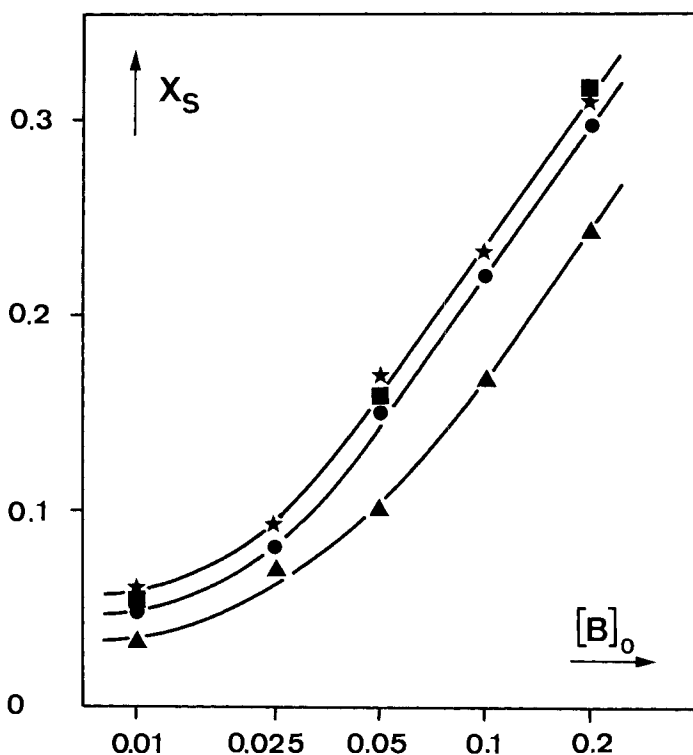


Fig. 1. pH-Dependence of the Product Distribution in the Mixing-Disguised Azo Coupling of 1-Naphthol-6-sulfonic Acid with Phenyl diazonium Salt

-■- pH = 11.06; -★- pH = 10.51; -●- pH = 9.88; -▲- pH = 9.26
 $[B]_0$ in M. For the experimental conditions see Table 4

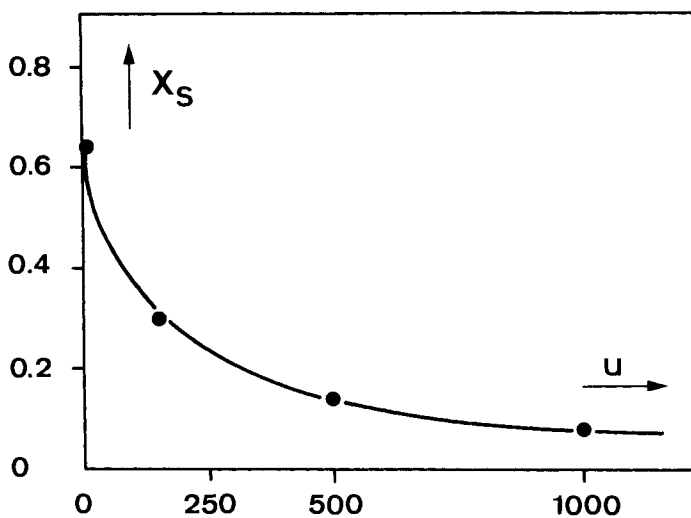


Fig. 2. The Influence of the Stirring Rate on the Product Distribution
 X_S relative yield of the disazo product S at 100% conversion; u rate of stirring [rev. min⁻¹]

of turbulence [17]. As \bar{R} appears also in the mixing moduli $\varphi_{B,1}^2$ and $\varphi_{B,2}^2$ (equation (9)) X_S is expected to depend on the mixing rate. The results in *Figure 2* and *Table 6* confirm this expectation.

3.4. *Comparison of the Measured and Predicted Product Distributions.* The initial concentrations $[A]_0$ and $[B]_0$ of 1-naphthol-6-sulfonic acid and phenyldiazonium salt, respectively, as well as the volume ratio α of their solutions, are the most easily measurable and experimentally variable quantities in the selectivity-determining parameters $\alpha, E, \varphi_{B,1}^2, \varphi_{B,2}^2$. According to both versions of the diffusion-reaction model discussed elsewhere [5], these quantities determine fully the final product distribution of mixing-disguised reactions, provided the mixing conditions

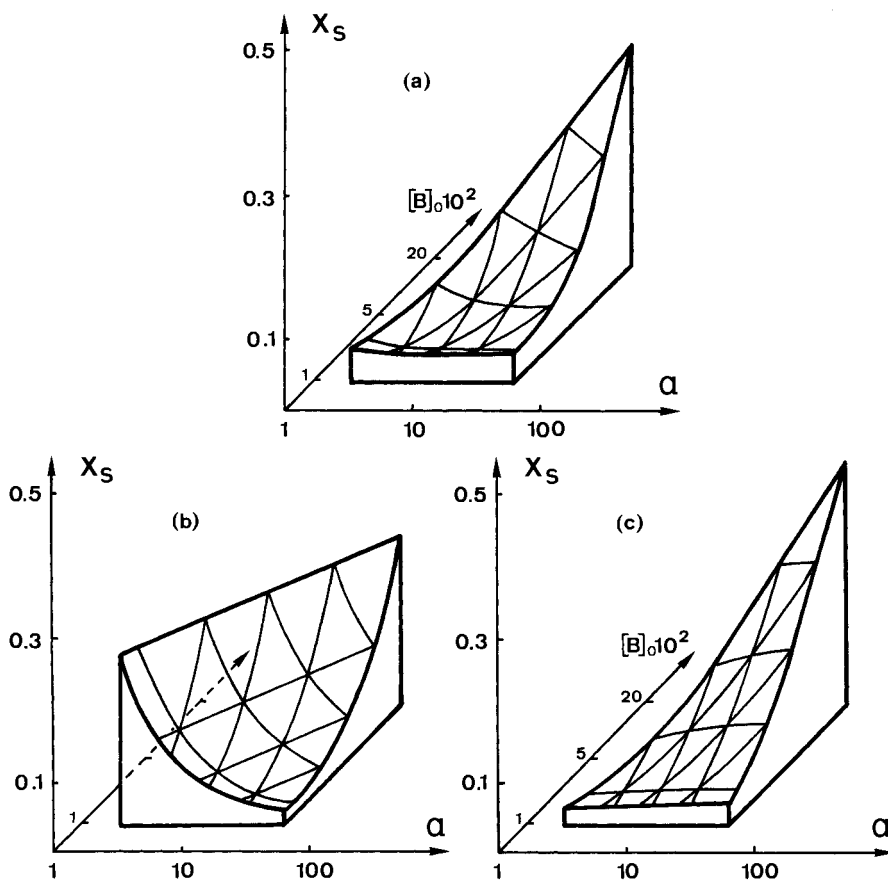


Fig. 3. Comparison of the Experimentally Measured and the Calculated Product Distribution in the Mixing-Disguised Azo Coupling of 1-Naphthol-6-sulfonic Acid with Phenyldiazonium Salt

$[B]_0$ in M

- (a) Experimental results, see *Table 7*;
- (b) Calculated behaviour assuming mobile *B* and immobile *A, R* and *S* (Version I) [4]: $R^2/D = 50$ s, see *Table 8*;
- (c) Calculated behaviour assuming immobile *B* and mobile *A, R* and *S* (Version II) [5]: $R^2/D = 1$ s, see *Table 8*

and the temperature are kept constant. Therefore, a comparison of the experimental results with the predicted behaviour calculated with the help of the two different versions is easily possible.

Figure 3a and Table 7 summarise the experimental results for a buffer system of pH = 10.8. At this pH, effects of local pH-gradients as well as the decomposition of the diazonium ion can be neglected. The calculated reaction behaviour is presented in Figure 3b and 3c and in Table 8.

The best agreement of the predicted and the experimental product distribution is obtained by choosing the values 1s and 50s for the ratio \bar{R}^2/D when applying the model versions II [5] and I [4], respectively. A comparison of the data shown in Figure 3 demonstrates an excellent agreement between the experimental results and the predictions made from the model version II.

4. Conclusion. - The product distribution of azo coupling reactions can be influenced by the mixing rate of the reactant solutions. An analysis of the experimental results demonstrates that this influence can be adequately described by our diffusion-reaction model. General criteria can be derived from this model which allow an understanding and control of mixing effects encountered in daily laboratory syntheses. These criteria are also useful for appraising the efficiency of mixing devices and thus the degree of segregation in the reaction vessel. Furthermore, the discussion of the experimental results has also raised the question of the extent to which concentration gradients of the product formed can influence the rate and the selectivity of mixing-disguised chemical transformations. It has been shown that in fast azo coupling reactions appreciable local pH-gradients have to be assumed in order to understand the measured selectivity behaviour. Such pH-gradients can occur despite the fact that the macroscopically measured pH remains constant. Their values will depend on the ratio of the relaxation times of diffusion and proton release as well as on the local buffer capacities.

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5. Experimental Part. - *General Remarks.* The preparative and the thin layer chromatography were performed on precoated silica gel (Merck PF₂₅₄ and HF₂₅₄) and on cellulose (Schleicher & Schuell) plates. For paper chromatography, pre-washed Whatman No. 3 and Ederol-E 202 paper was used. The UV/VIS. spectra were determined on a Beckman-Acta III spectrophotometer and are reported in $\lambda_{\max}(e)$. The pH-values were measured using a digital pH-meter (Metrohm, E 532). For the determination of the intrinsic kinetics, a stopped-flow mixing chamber equipped with a spectrophotometer (Durrum Instr. Corp.) was used. In the mixing experiments a stirrer IKA-motor RM 18 (Janke and Kunkel, AG.) with variable stirring rate was employed.

The detailed, numerical procedure has been described elsewhere [4] [5]. The computer program was written in FORTRAN and the calculations were carried out on a CDC 6400/6500 computer.

Materials. - *Phenyldiazonium Tetrafluoroborate.* The synthesis was performed according to the procedure described elsewhere [18].

1-Naphthol-6-sulfonic Acid. The commercial product was separated from its isomers by paper chromatography using the following solvent system: *t*-butanol/butanol/ethanol 4:3:3 (v/v). After extraction with methanol the paper impurities were removed by chromatography on aluminium oxide (act. V, M. Woelm).

2- and 4-Phenylazo-1-naphthol-6-sulfonic Acid. These monoazo compounds were synthesized according to the procedure of Szy [19]. The purification was carried out by chromatography on cellulose

plates using the solvent system: butyl acetate/pyridine/ammonia conc./water 30:47:3:20 (v/v). - VIS. spectra (water, pH = 10, [R] = 10⁻⁶M): *o*-isomer λ_{max} = 495 nm (7280); *p*-isomer λ_{max} = 482 nm (15840).

2,4-Bis(phenylazo)-1-naphthol-6-sulfonic Acid. This disazo compound was synthesized by the method of Krohn [20]. It was purified by the method used for the monoazo compounds. VIS. spectrum (water, pH = 10, [S] = 10⁻⁶M): λ_{max} = 530 nm (9630).

Determination of the pK-values: The pK-values of the reactants were determined by the method of Hammett [21].

Table 1. pK-values of the Reactants at 20.0° and I = 0.2

Compound	pK _{OH}	(pK ₁ + pK ₂)/2	Ref.
A 1-Naphthol-6-sulfonic Acid	9.88		[22]
R, <i>o</i> 2-Phenylazo-1-naphthol-6-sulfonic Acid	8.28		measured
R, <i>p</i> 4-Phenylazo-1-naphthol-6-sulfonic Acid	7.30		measured and [23]
B Phenyldiazonium Ion		11.50	[24]

Determination of the Intrinsic Kinetics: The kinetic measurements were carried out in a stopped-flow mixing chamber connected to a spectrophotometer. The rate of the primary azo coupling reaction was measured at λ = 490 nm. After the reaction was finished the monoazo products were separated using cellulose plates. The relative rate constants were calculated from the ratio of *R,*o** and *R,*p**. The secondary azo coupling rate was measured at λ = 600 nm. Of the two reactant solutions only the naphthol solution was buffered. However, both solutions were brought to the same ionic strength of I = 0.2 with sodium chloride. The buffer systems used are given in Table 2.

Table 2. Composition and pH of the Buffer Systems (22.0°; I = 0.2)

Buffer No.	pH	Composition
1	9.26	[NaHCO ₃] = 1.21 × 10 ⁻¹ M [Na ₂ CO ₃] = 2.64 × 10 ⁻² M
2	9.88	[NaHCO ₃] = 8.01 × 10 ⁻² M [Na ₂ CO ₃] = 4.00 × 10 ⁻² M
3	10.51	[NaHCO ₃] = 1.09 × 10 ⁻¹ M [NaOH] = 9.50 × 10 ⁻² M
4	10.80	[Na ₂ B ₄ O ₇ · 10 H ₂ O] = 3.70 × 10 ⁻² M [NaOH] = 8.10 × 10 ⁻² M
5	11.06	[KH ₂ PO ₄] = 1.25 × 10 ⁻¹ M [NaOH] = 7.50 × 10 ⁻² M

Table 3. Rate Constants for the Azo Coupling of 1-Naphthol-6-sulfonic Acid with Phenyldiazonium Salt (22.0°; I = 0.2)

The concentrations are initial concentrations before mixing
 Index 1: primary reaction; Index 2: secondary reaction; Index *o*: reaction in *ortho* position;
 Index *p*: reaction in *para* position
 Volume ratio of the reactant solutions: α = 1

[CO ₃ ²⁻] × 10 ² [M]	pH	[A] ₀ = 3.60 × 10 ⁻⁴ M		[R, <i>p</i>] ₀ = 2.80 × 10 ⁻³ M		[R, <i>o</i>] ₀ = 2.36 × 10 ⁻⁴ M	
		[B] ₀ = 2.30 × 10 ⁻⁴ M		[B] ₀ = 1.04 × 10 ⁻³ M		[B] ₀ = 1.80 × 10 ⁻³ M	
		k _{1,<i>o</i>} × 10 ⁻⁴ [M ⁻¹ s ⁻¹]	k _{1,<i>p</i>} × 10 ⁻⁴ [M ⁻¹ s ⁻¹]	k _{2,<i>o</i>} × 10 ⁻¹ [M ⁻¹ s ⁻¹]		k _{2,<i>p</i>} × 10 ⁻² [M ⁻¹ s ⁻¹]	
0.50	9.78	0.41 ± 0.01	2.92 ± 0.10	5.06 ± 0.24		1.79 ± 0.12	
1.88	9.82	0.42 ± 0.02	3.44 ± 0.17	5.77 ± 0.41			
2.90	9.85	0.44 ± 0.02	3.79 ± 0.15	5.44 ± 0.34			
3.99	9.88	0.44 ± 0.04	4.63 ± 0.44	5.44 ± 0.47		2.02 ± 0.10	

Mixing experiments. The same thermostated ($22.0 \pm 0.1^\circ$) reaction vessel was used in all experiments. It consisted of a two-necked flask of 50 ml volume and 4.7 cm diameter equipped with a stirrer which had a symmetrical three-wing propeller (height: 1.5 cm, diameter: 1.0 cm). The blades of the stirrer were arranged at an angle of 20° with respect to the rotational axis. The rate of stirring could be varied from 150 to 2000 rev. min^{-1} . The buffered solution of *A* ($I=0.2$) was thermostated at 22.0° in the reaction vessel and the non-buffered solution of *B* ($I=0.2$), thermostated at the same temperature, was added by means of a pipette. The pipette outlet had a diameter of 0.02 cm, and the flow rate at the outlet was always 0.1 m/s. After completion of the reaction the products were separated using cellulose plates. The product distribution was then determined spectrophotometrically.

Table 4. *pH-Dependence of the Product Distribution of the Mixing-Disguised Azo Coupling of 1-Naphthol-6-sulfonic Acid with Phenylidiazonium Salt (22.0° ; $I=0.2$)*

The concentrations are initial concentrations before mixing. The errors are calculated to a confidence level of 95%

$$[A]_0 = 10^{-2} \text{M}; \text{Mol-ratio: } \alpha E = 2; \text{Rate of stirring: } u = 150 \text{ rev. min}^{-1}$$

Buffer No.	pH	$[B]_0 \times 10^2$ [M]	α	$X_{R,o} \times 10^2$	$X_{R,p} \times 10^2$	$\frac{X_{R,o}}{X_{R,p}} \times 10^2$	$X_S \times 10^2$
1	9.26	1	2	7.3 ± 0.3	89.5 ± 1.1	8.1	3.2 ± 0.8
		2.5	5	6.3 ± 1.6	86.5 ± 1.3	7.3	7.2 ± 0.9
		5	10	6.5 ± 0.2	83.3 ± 2.0	7.8	10.2 ± 1.4
		10	20	6.0 ± 0.2	77.0 ± 1.2	7.8	17.0 ± 0.8
		20	40	5.3 ± 0.5	70.0 ± 1.8	7.6	24.5 ± 1.9
2	9.88	1	2	6.2 ± 1.0	88.9 ± 0.3	7.0	4.9 ± 1.0
		2.5	5	5.6 ± 1.0	86.4 ± 1.0	6.5	8.0 ± 0.9
		5	10	5.0 ± 0.3	79.6 ± 1.4	6.3	15.4 ± 1.2
		10	20	4.2 ± 0.6	73.7 ± 2.0	5.8	22.1 ± 2.3
		20	40	4.0 ± 0.3	66.0 ± 1.4	6.0	30.0 ± 1.4
3	10.51	1	2	5.3 ± 0.5	88.3 ± 1.3	6.0	6.0 ± 1.0
		2.5	5	5.0 ± 0.5	85.9 ± 1.0	5.8	9.1 ± 1.3
		5	10	4.1 ± 0.7	78.8 ± 1.7	5.2	17.1 ± 1.4
		10	20	3.7 ± 0.3	72.7 ± 1.7	5.1	23.6 ± 1.5
		20	40	3.1 ± 0.2	66.1 ± 2.0	4.7	31.0 ± 1.8
5	11.06	1	2	5.4 ± 0.6	89.0 ± 1.4	6.1	5.6 ± 1.5
		5	10	4.2 ± 0.8	79.8 ± 1.9	5.3	16.0 ± 0.7
		20	40	3.0 ± 0.2	66.6 ± 1.5	4.5	31.4 ± 1.4

Table 5. *Calculated pH-Dependence of the Rate Constants in various Buffer Systems*
For definitions see equations (8b), (9c) and (9d)

Buffer No.	pH	k_1 [$\text{M}^{-1} \text{s}^{-1}$]	k_2 [$\text{M}^{-1} \text{s}^{-1}$]	$\varphi_{B,1}^2 / \varphi_{B,2}^2$
1	9.26	2.0×10^4	55.8	356
2	9.88	5.1×10^4	55.8	920
3	10.51	8.2×10^4	55.3	1480
5	11.06	8.5×10^4	49.3	1720

Table 6. *The Influence of the Stirring Rate on the Product Distribution (22.0°; I=0.2)*

The concentrations are initial concentrations before mixing. The errors are calculated to a confidence level of 95%

Volume ratio of the reactant solutions: $\alpha = 40$; Mol-ratio: $\alpha E = 2$; Buffer 2 (cf. Table 2): pH = 9.88; $[A]_0 = 10^{-2} \text{M}$; $[B]_0 = 0.2 \text{M}$

Rate of stirring u [rev. min ⁻¹]	$X_{R,o} \times 10^2$	$X_{R,p} \times 10^2$	$X_S \times 10^2$
0	2.3 ± 0.3	33.0 ± 2.2	64.7 ± 3.1
150	4.0 ± 0.3	66.0 ± 1.4	30.0 ± 1.4
500	5.2 ± 0.9	80.7 ± 1.0	14.1 ± 1.1
1000	6.3 ± 0.7	85.9 ± 1.3	7.8 ± 0.8

 Table 7. *Product Distribution in the Mixing-Disguised Azo Coupling of 1-Naphthol-6-sulfonic Acid with Phenyldiazonium Salt (22.0°; I=0.2)*

The concentrations are initial concentrations before mixing

The errors are calculated to a confidence level of 95%

Mol-ratio: $\alpha E = 2$; Buffer 4 (cf. Table 2): pH = 10.80; Rate of stirring: $u = 150 \text{ rev. min}^{-1}$

$[A]_0 \times 10^2$ [M]	$[B]_0 \times 10^2$ [M]	α	$X_S \times 10^2$
0.25	2.5	20	6.4 ± 0.65
0.25	5.0	40	9.4 ± 0.75
0.50	2.5	10	6.0 ± 0.30
0.50	5.0	20	12.5 ± 1.00
0.50	10.0	40	18.2 ± 2.20
1.00	1.0	2	5.0 ± 1.20
1.00	2.5	5	9.4 ± 0.85
1.00	5.0	10	15.6 ± 0.60
1.00	10.0	20	23.3 ± 1.50
1.00	20.0	40	30.9 ± 2.10

 Table 8. *Calculated Product Distribution in a Mixing-Disguised Competitive, Consecutive Second-Order Reaction⁶⁾*

The concentrations are initial concentrations before mixing

Mol-ratio: $\alpha E = 2$; $k_1 = 10.2 \times 10^4 \text{M}^{-1} \text{s}^{-1}$; $k_2 = 55.8 \text{M}^{-1} \text{s}^{-1}$

$[A]_0 \times 10^2$ [M]	$[B]_0 \times 10^2$ [M]	α	Version I [4]			Version II [5]		
			$R^2/D = 50 \text{ s}$, see Fig. 3b			$R^2/D = 1 \text{ s}$, see Fig. 3c		
			$\varphi_{B,1}^2 \times 10^{-4}$	$\varphi_{B,2}^2$	X_S	$\varphi_{B,1}^2 \times 10^{-2}$	$\varphi_{B,2}^2$	X_S
0.25	2.5	20	12.8	69.8	0.06	25.5	1.4	0.09
0.25	5.0	40	25.5	139.5	0.06	51.0	2.8	0.15
0.50	2.5	10	12.8	69.8	0.12	25.5	1.4	0.08
0.50	5.0	20	25.5	139.5	0.12	51.0	2.8	0.15
0.50	10.0	40	51.0	279.0	0.12	102.0	5.6	0.24
1.00	1.0	2	5.1	27.9	0.23	10.2	0.6	0.02
1.00	2.5	5	12.8	69.8	0.23	25.5	1.4	0.07
1.00	5.0	10	25.5	139.5	0.23	51.0	2.8	0.14
1.00	10.0	20	51.0	279.0	0.23	102.0	5.6	0.24
1.00	20.0	40	102.0	558.0	0.23	204.0	11.2	0.34
2.00	10.0	10	51.0	279.0	0.35	102.0	5.6	0.21
2.00	20.0	20	102.0	558.0	0.35	204.0	11.2	0.31
2.00	40.0	40	204.0	1116.0	0.35	408.0	22.3	0.44
4.00	10.0	5	51.0	279.0	0.46	102.0	5.6	0.19

⁶⁾ The calculated product distribution for other k_1 - and k_2 -values is practically the same as long as $k_1/k_2 > 1000$.

Appendix

List of Symbols

A	Coupling component: 1-Naphthol-6-sulfonic acid;
ArN_2^{\oplus}	Phenyldiazonium ion;
ArN_2O^{\ominus}	Phenyldiazotate;
ArN_2OH	Phenyldiazohydroxide;
ArO^{\ominus}	Naphtholate anion;
$ArOH$	Naphthol;
B	Diazo component: Phenyldiazonium salt;
D	Mean diffusion coefficient of the reactants [cm^2s^{-1}];
D_H	Diffusion coefficient of hydronium ion [cm^2s^{-1}];
I	Ionic strength [M];
K_1, K_2	Acidity constants of ArN_2^{\oplus} and ArN_2OH , respectively (cf. equations (6) and (7)) [M];
K_{OH}	Acidity constant of $ArOH$ (cf. equation (4)) [M];
$K_{OH,A}, K_{OH,R}$	Acidity constants of A and R , respectively [M];
k_j	Experimentally measured overall second-order rate constants for the primary ($j=1$) and the secondary ($j=2$) azo coupling reaction [$M^{-1}s^{-1}$];
$k_{j,o}, k_{j,p}$	Experimentally measured second-order rate constants for the primary ($j=1$) and the secondary ($j=2$) azo coupling reactions in <i>ortho</i> (index <i>o</i>) and <i>para</i> (index <i>p</i>) position for a given, constant pH and given constant concentrations of bases [$M^{-1}s^{-1}$];
$k_{j,I}, k_{j-1}, k_{j,II,i}$	Intrinsic n -order rate constants of the bond-making and bond-breaking events in the primary ($j=1$) and the secondary ($j=2$) azo coupling reactions for the base i [$M^{1-n}s^{-1}$];
r	Molar rate of production of the azo product [Ms^{-1}];
r_H	Molar rate of production of the proton [Ms^{-1}];
r	Polar coordinate [cm];
\bar{R}	Mean radius of the eddies [cm];
R,o	<i>o</i> -Monoazo product: 2-Phenylazo-1-naphthol-6-sulfonic acid;
R,p	<i>p</i> -Monoazo product: 4-Phenylazo-1-naphthol-6-sulfonic acid;
S	Disazo product: 2,4-Bis(phenylazo)-1-naphthol-6-sulfonic acid;
u	Stirring rate [rev. min^{-1}];
V_A, V_B	Volume of solution of the coupling component A and the diazonium salt B , respectively [l];
$X_{R,o}, X_{R,p}, X_S$	Fraction of the diazonium salt which has reacted after 100% conversion to R,o , R,p or S , respectively;
$\alpha = V_A/V_B$	Ratio of solution volumes of A and B [-];
$E = [A]_0/[B]_0$	Ratio of the initial total concentrations of A and B [-];
$\phi_{B,j}^{\ddagger}$	Normalized rate constant of the reaction step j (cf. equations (9c) and (9d)) [-];
$[i]_0$	Initial concentration of the component i before mixing [M].

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