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Mechanism of azo coupling reactions. Part 34.¹ Reactivity of five-membered ring heteroaromatic diazonium ions

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This paper is dedicated to Professor Arthur N. Bourns

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The azo coupling reactions of six five-membered ring heteroaromatic diazonium ions with 2-naphthol-3,6-disulfonic acid are investigated kinetically at various pH values. The dependence of the measured rate constants on the acidity of the aqueous reaction system is evaluated. It can be shown that the 2-naphtholate-3,6-disulfonate trianion reacts $4 \times 10^8 - 8 \times 10^8$ times faster than the 2-naphthol-3,6-disulfonate dianion. The rate constants of the six diazonium ions vary by more than four orders of magnitude. The logarithms of the rate constants of all comparable diazonium ions correlate linearly with ¹H nmr chemical shifts of the respective unsubstituted heteroaromatic parent compounds. An analogous correlation was found for azo couplings with substituted benzenediazonium ions. Diazotization of heteroaromatic amines does not go to completion, rather to an equilibrium. It is shown therefore that in acidic coupling systems the azo compound is only the kinetically controlled product. The thermodynamic products are 1-nitroso-2-naphthol-3,6-disulfonic acid and the heteroaromatic amine.

HEINZ DIENER et HEINRICH ZOLLINGER. Can. J. Chem. 64, 1102 (1986).

Opérant à divers pH, on a étudié la cinétique de réactions de couplage azo entre six ions diazonium d'hétérocycles aromatiques à cinq chaînons et l'acide naphtol-2 disulfonique-3,6. On a évalué la dépendance des constantes de vitesses mesurées sur l'acidité du système aqueux de la réaction. On peut démontrer que le trianion naphtolate-2 disulfonate-3,6 réagit de 4×10^8 à 8×10^8 plus rapidement que le dianion naphtol-2 disulfonate-3,6. Les constantes de vitesse pour les six ions diazonium varient par plus de quatre ordres de grandeurs. Il existe une corrélation linéaire entre les constantes de vitesse de tous les ions diazonium comparables et les déplacements chimiques en rmn du ¹H des composés hétéroaromatiques de base qui ne sont pas substitués. On a pu établir une corrélation analogue pour les couplages azo avec des ions benzènediazonium substitués. La réaction de diazotation des amines hétéroaromatiques n'est pas complète; il s'agit plutôt d'un équilibre. On démontre alors que, dans les systèmes de couplages acides, les composés azo ne sont que les produits de contrôle cinétique. Les produits de contrôle thermodynamique sont l'acide nitroso-1 naphtol-2 disulfonique-3,6 et l'amine hétéroaromatique.

[Traduit par la revue]

Introduction

In contrast to the large number of investigations of the reactivity of carboaromatic diazonium ions in general and of the mechanism of their azo coupling reactions, very few comparable investigations have been made with heteroaromatic diazonium ions. Goerdeler and Haubrich (2) have made a semiquantitative comparison of the reactivity of 3-phenyl-1,2,4-thiadiazole-5diazonium ion with 2-naphthol and the respective reaction with 2,4-dinitrobenzenediazonium ion. Sawaguchi et al. (3) have measured the rate of azo coupling of various heteroaromatic diazonium ions with 2-naphthol-3,6-disulfonic acid. There exists an extensive patent literature on azo dyes synthesized with heteroaromatic diazonium ions since Dickey and Towne realized in the early 1950s that industrially interesting disperse dyes can be obtained on this basis. Weaver and Shuttleworth (4) have reviewed that subject, but give no information on reactivities and yields.

Relations between the structure of heteroaromatic parent compounds and the reactivity of the respective diazonium ions have not been investigated in the past. The goal of this investigation is the measurement of the rates of azo coupling reactions of a series of five-membered ring heteroaromatic diazonium ions with the tri- and, if possible, the di-basic anion of 2-naphthol-3,6-disulfonic acid, and the correlation of the kinetic results with the chemical shift in ¹H nmr of the heteroaromatic compound that contains a hydrogen atom instead of the diazonio group. In addition, 1-nitroso-2-naphthol-3,6-disulfonic acid was identified as a by-product, as it is known that the yields of azo coupling reactions with heteroaromatic diazonium ions are in most cases significantly lower than those with carboaromatic diazonium ions.

The diazonium ions of the following amines were included in this investigation: thiazole-2-, -4-, and -5-diazonium ions (1, 2 and 3), 1,2,4-thiadiazole-5-diazonium ion (4), 1,3,4-thiadiazole-2-diazonium ion (5), and 1,3,4-triazole-2-diazonium ion (6).



Experimental and kinetic results

The diazonium ions 1-6 were obtained by diazotization of the respective amines. For 2-aminothiazole the synthesis of Traumann (5) was used.

4-Aminothiazole was synthesized from chloroacetonitrile and sodium thiocyanate, which form cyanomethylthiocyanate (NC—CH₂—S—CN). This compound was cyclized to 2-bromo-4-aminothiazole hydrobromide with HBr following a procedure described by Johnson and Nasutavicus (6). For the debromination of 2-bromo-4-aminothiazole the amino group has to be protected by acylation. Johnson and Nasutavicus used acetic anhydride for this purpose. We obtained

¹Part 33: Kaminski et al. (1).

insufficient yields by using their procedure. Therefore we acylated with trifluoroacetanhydride: 28.6 g (0.11 mol) 2-bromo-4-aminothiazole hydrobromide was added in four batches to 75 g (0.36 mol) trifluoroacetanhydride. After 1 h at room temperature the solution was evaporated in vacuo. Yield: 34,75 g (81%) of the 1:1 addition product of 2-bromo-4-trifluoroacetamidothiazole with trifluoroacetic acid. Of this, 31.0 g were dissolved in 125 mL EtOH and purified on 80 g Amberlite IRC-50 (pretreated with 2 M NaOH and washed with 2 L water and afterwards with 200 mL ethanol). Afterwards, the EtOH solution was extracted with 150 mL hexane and treated at the boiling temperature with 0.5 g charcoal. After filtration and cooling, colorless needles precipitated, 16.78 g (76.6%) 2-bromo-4-trifluoroacetamidothiazole, mp 58°C; 16.78 g (61 mmol) of this product was debrominated with H_2 at normal pressure in a solution of 7.30 g (89 mmol) NaOAc in 500 mL absolute EtOH in the presence of 3 g Pd on coal (10%). After 6 h the filtrate was evaporated. The residue was extracted with warm CH₂Cl₂ and recrystallized from EtOH, 8.11 g (67.8%) 4-trifluoroacetamidothiazole, mp 139°C. Anal. calcd. for C5H3N2OSF3 (196.15): C 30.62, H 1.54, N 14.28%; found: C 30.57, H 1.65, N 14.31%. Then 392 mg (2 mmol) 4-trifluoroacetamidothiazole was dissolved in 3 mL water and 0.25 mL 50% NaOH. After 6 h at 35°C under Ar the solution was cooled in an ice bath and glacial acetic acid was added to pH 8. Water was evaporated under rotation at 40°C in an Ar atmosphere. The residue was distilled at 0.01 Torr/85°C (1 Torr = 133.3 Pa). We obtained a colorless oil that crystallized out at deep-freezer temperatures, 42 mg (21%). The melting point was not determined because the product rapidly became black. Anal. calcd. for C3H4N2S (100.14): C 35.98, H 4.03, N 27.97%; found: c 35.69, H 4.01, N 27.74%.

5-Aminothiazole was synthesized from aminoacetonitrile. Reaction with formic acid ethyl ester gave N-cyanomethylacetamide, as described by Sekiya and Osaki (7). As we were not successful in following the procedure of these authors for the next step, namely the addition of H₂S at the cyano group in order to form 2-formamido-thioacetamide, we used the method described by Sen *et al.* (8), in which gaseous H_2S was introduced into a pyridine solution of the substrate. As we did not obtain the desired product, rather again the substrate after evaporation at normal pressure, we evaporated the solvent in vacuo and did not purify the residue, but made the cyclocondensation to 5-aminothiazole directly with the help of POCl₃ as described by Masui and Tamura (9): 18.79 g raw 2-formamidothioacetamide gave 1.32 g 5-aminothiazole, which was chromatographed (CHCl₃/CH₃OH 9:1, Kieselgel) and recrystallized from isopropanol under Ar, 0.537 g (3.5%) colorless crystals, mp 81°C (dec.). Anal. calcd. for C₃H₄N₂S (100.14): C 35.98, H 4.03, N 27.97%; found: C 35.80, H 4.13, N 27.74%.

5-Amino-1,2,4- and 2-amino-1,3,4-thiadiazole were synthesized by the methods of Goerdeler (10) and Stolle and Fehrenbach (11), respectively.

2-Amino-1,3,4-triazole: Fluka product, puriss; mp 154–155°C. Anal. calcd. for $C_2H_4N_4$ (84.08): C 28.57, H 4.80, N 66.63%; found: C 28.62, H 4.82, N 66.48%.

Methods of diazotization and azo coupling

After comparative studies of various methods, we used the following two procedures, which gave the best results with our amines 1-6.

Method A: 1.0 mmol amine was dissolved in 5 mL 72% H₂SO₄ and diazotized by addition of 1.0 mmol powdered NaNO₂ at -10° C. After 1 h the solution was diluted to 50 mL with 72% H₂SO₄. For preparative azo coupling reactions 1 mmol of 2-naphthol-3,6-disulfonic acid (disodium salt, purified, containing 9% crystal water) was added. After 1 h the solution was carefully neutralized with Na₂CO₃. The precipitate consisted of a mixture of the azo compound, Na2SO4, and the products of decomposition, which were separated by preparative paper chromatography (n-butanol/ethanol/water 4:3:3). The colored zone on the paper was cut out and the azo compond extracted with water. Yields were low (1 to 5% pure azo compound). For kinetic measurements a 5-µL droplet of the diazo solution was put on the Teflon stopper of an uv cell that contained 3.0 mL buffer solution and 50 µL 0.211 M solution of 2-naphthol-3,6-disulfonic acid. The reaction was started by the shaking of the cell. Initial concentrations: 2-naphthol-3,6-disulfonic acid, $3.52 \times 10^{-3} M$; diazonium salt, $3.33 \times 10^{-5} M$ (or lower).

TABLE 1. Azo couplings of thiazole-2-diazonium ion^a

pH	$\frac{10^3 k_{\rm ps}}{({\rm s}^{-1})}$	$\frac{10^{-8}k_1}{(L \text{ mol}^{-1} \text{ s}^{-1})}$	k_2 (L mol ⁻¹ s ⁻¹)
-1.72 ^b	0.63 ± 0.03		1.79×10^{-1}
0.51	1.15 ± 0.03	1.15	
1.10	2.75 ± 0.07	1.56	
1.55	7.18 ± 0.11	1.44	
2.00	18.50 ± 0.38	1.32	
Mean			
value (µ)		1.37 ± 0.18^{c}	

^aDiazotization method A in 72% H₂SO₄; λ_{max} of azo compound: 486 nm. ^b30% H₂SO₄ ($H_0 = -1.72$).

⁶95% confidence limits: $1.19 \times 10^8 < \mu < 1.55 \times 10^8$.

Method B: 1.0 mmol amine was dissolved in 1.0 mL 50% or 90% H₂SO₄ and diazotized at -10° C with 1.0 mL 1 M nitrosyl sulfuric acid (50% or 90% H₂SO₄). This solution was used directly for reactions on a preparative scale as described for method A. For kinetic measurements a 50-mL volumetric flask was filled with buffer and 100 µL of a 0.25 M solution of 2-naphthol-3,6-disulfonic acid and thermostatted. The diazo solution (5-20 µL) was dropped on the stopper. The volumetric flask was scaled with the stopper and the reaction was started by shaking. Afterwards a sample of the reacting solution was transferred into a quartz cell for spectrophotometric analysis. Initial concentrations: 2-naphthol-3,6-disulfonic acid, $5.00 \times 10^{-4} M$; diazo solution, $1.25-5.00 \times 10^{-5} M$.

Method C: Due to the very low stability of 4-aminothiazole, the following procedure was used for diazotization: 0.196 g (1 mmol) 4-trifluoroacetamidothiazole was dissolved in 1.5 mL water by adding 0.125 mL 50% NaOH. The solution was stirred under Ar at room temperature for 24 h. After cooling to -10° C we added dropwise 2.5 mL (4.59) 96% H₂SO₄. This yielded a solution of 4-aminothiazole in 72% H₂SO₄. It was diazotized by adding 1.0 mL of 1 *M* nitrosylsulfuric acid (72% H₂SO₄) at -10° C.

Kinetic measurements were made in thermostatted 1.0-cm cells at 20.0 \pm 0.1°C. Based on eq. [1], pseudo-first-order rate constants (k_{ps}) were obtained by linear regression from plots of $-\ln (A_{\infty} - A_t)$ against time (A_{∞} , A_t = optical density at the visible absorption maximum λ_{max} of the azo compound formed at times $t = \infty$, i.e. at least 10 half-life times, and t). All rate constants are mean values of the rate constants determined in three independent runs. Buffer solutions were made on the basis of the CRC Handbook (12).

[1]
$$-\ln (A_{\infty} - A_t) = k_{\text{ns}}t + C$$

Equation [1] has the advantage that k_{ps} can be determined without knowing the molar extinction coefficient of the azo compound at λ_{max} . The second-order rate constant is calculated as usual (13). Due to the high reactivity of the diazonium ions used and the relatively low pH values of the reacting solution (pH 1.72–5.97, see Results), the reaction rate consists of the sum of two independent reactions, namely that of the 2-naphtholate-3,6-disulfonate trianion RO⁻ (k_1) and that of the 2-naphthol-3,6-disulfonate dianion ROH (k_2). Equation [2] shows that by plotting log k_{ps} against pH, a straight line with a slope of 1.0 ± 0.1 is obtained if the reaction with RO⁻ is dominant. If k_2 [ROH] $\gg k_1$ [RO⁻] the overall rate is independent of pH.

[2]
$$\frac{d[Azo]}{dt} = k_{ps}[D] = k_1[RO^-][D] + k_2[ROH][D]$$

where D = diazonium ion. [RO⁻] and [ROH] were calculated as usual with the help of the acidity constant of the OH group of the coupling component: $pK_3 = 9.76$. This constant was calculated from data of Hashida *et al.* (14) for the ionic strength (I = 0.08-0.10) used in our experiments except for azo couplings of thiazole-2-diazonium (Table 1), which were run at I = 0.20-0.25. We determined $pK_3 = 9.40$ at this ionic strength. Results are given in Tables 1–6.

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TABLE 2. Azo couplings of thiazole-4-diazonium ion^a

pH	k _{ps} (s ⁻¹)	$\frac{10^{-6}k_1}{(L \text{ mol}^{-1} \text{ s}^{-1})}$	$\frac{k_2}{(L \operatorname{mol}^{-1} \operatorname{s}^{-1})}$
-0.31 ^b	$(7.94\pm0.37)\times10^{-6}$		1.59×10 ⁻²
1.01	$(1.62\pm0.04)\times10^{-5}$	9.29	
2.02	$(7.46\pm0.18)\times10^{-5}$	7.33	
3.03	$(5.75\pm0.13) \times 10^{-4}$	6.18	
4.01	$(6.52\pm0.19)\times10^{-3}$	7.33	
4.53	$(1.89\pm0.12)\times10^{-2}$	6.42	
5.03	$(6.97\pm0.31)\times10^{-2}$	7.49	
μ		7.34 ± 0.82^{c}	

"Diazotization method C in 72% H_2SO_4 ; λ_{max} of azo compound: 485 nm. ^b10% H_2SO_4 .

°95% confidence limits: $6.62\times10^6 < \mu < 8.06\times10^6.$

TABLE 3. Azo couplings of thiazole-5-diazonium ion^a

pH	k_{ps} (s ⁻¹)	$\frac{10^{-5}k_1}{(L \text{ mol}^{-1} \text{ s}^{-1})}$
4.01	$(4.49\pm0.13)\times10^{-4}$	5.05
5.03	$(3.72\pm0.13)\times10^{-3}$	4.00
5.97	$(2.95\pm0.08)\times10^{-2}$	3.64
μ	_	4.23±0.73 ^b

^aDiazotization method B in 90% H_2SO_4 ; λ_{max} of azo compound: 473 nm.

 $^{b}95\%$ confidence limits: $3.40 \times 10^{5} < \mu < 5.06 \times 10^{5}$.

% H ₂ SO ₄	k _{ps} (s ⁻¹)	$\frac{k_2^b}{(\text{L mol}^{-1} \text{ s}^{-1})}$
30	$(3.81\pm0.22) \times 10^{-3}$	7.62 ± 0.44
50	$(2.62\pm0.32) \times 10^{-3}$	5.25 ± 0.65

TABLE 4. Azo couplings of 1,2,4-thiazole-5-diazonium ion^a

^aDiazotization method B in 90% H_2SO_4 ; λ_{max} of azo compound: 541 nm.

 ${}^{b}k_{2} = k_{\rm sp}/[{\rm ROH}]; k_{1}[{\rm RO}^{-}] \ll k_{2}[{\rm ROH}].$ Štěrba and co-workers (19) and we (this paper) found ratios of reactivities of 2-naphtholate-3,6-disulfonate dianion $k_{1}/k_{2} = 5.69 \times 10^{8} - 7.94 \times 10^{8}$. Therefore we can calculate approximately k_{1} for the azo coupling reaction of 1,2,4-thiadiazole-5-diazonium ion, based on k_{2} in 30% H₂SO₄: $k_{1} \approx 5.4 \times 10^{9}$ L mol⁻¹ s⁻¹.

TABLE 5. Azo couplings of 1,3,4-thiazole-2-diazonium ion^a

	k _{ps} ^b (s ⁻¹)	$\frac{k_2^c}{(L \text{ mol}^{-1} \text{ s}^{-1})}$	
30	$(1.87\pm0.13) \times 10^{-3}$	3.74±0.26	
50	$(5.33\pm0.85) \times 10^{-4}$	1.07±0.17	

<code>aDiazotization method B in 50% H_2SO4; λ_{max} of azo compound: 544 nm.</code>

^bCalculated on the basis of initial rates.

^cSee footnote b of Table 4, $k_1 \approx 2.7 \times 10^9 \text{ L mol}^{-1} \text{ s}^{-1}$.

In the azo coupling of the 1,3,4-thiadiazole-2-diazonium ion in 50% H_2SO_4 one observes that the absorption at $\lambda_{max} = 544$ nm goes through a maximum at approximately 1 h and decreases asymptotically thereafter (Fig. 1). Simultaneously, the optical density at 380 nm increases. This secondary band corresponds to the absortion maximum of 1-nitroso-2-naphthol-3,6-disulfonic acid. Pure 1-(1',3',4'-thiazolyl-2'-diazo)-2-naphthol-3,6-disulfonic acid in 50% H_2SO_4 solution shows the same

TABLE 6. Azo couplings of 1,3,4-thiazole-2-diazonium ion^a

pH	k_{ps} (s ⁻¹)	$\frac{10^{-5}k_1}{(L \text{mol}^{-1} \text{s}^{-1})}$
4.01	$(1.66\pm0.10) \times 10^{-4}$	1.87
5.03	$(1.89\pm0.15) \times 10^{-3}$	2.03
5.97	$(1.13\pm0.11)\times10^{-2}$	1.39
μ		1.76 ± 0.33^{b}

^aDiazotization method B in 50% H_2SO_4 ; λ_{max} of azo compound: 495 nm.

^b95% confidence limits: $1.39 \times 10^5 < \mu < 2.13 \times 10^5$.



FIG. 1. Absorption of a mixture of the 1,3,4-thiadiazole-5-diazonium ion and 2-naphthol-3,6-disulfonic acid in 50% H₂SO₄ at 544 nm as a function of time.

decrease and increase, respectively, at the 544-nm and 380-nm bands, respectively. From such an experiment the rate of the retro-azo coupling reaction, i.e. the substitution of the heteroaryldiazo group by a proton, can be calculated: $k = (1.03 \pm 0.10) \times 10^{-4} \text{ s}^{-1}$ (mean value of 3 measurements), 95% confidence limits; $0.92 \times 10^{-4} < \mu < 1.14 \times 10^{-4} \text{ s}^{-1}$.

Discussion

The pseudo-first-order rate constants (k_{ps}) of the azo coupling reactions of the diazonium ions of six five-membered ring heteroaromatic amines with 2-naphthol-3,6-disulfonic acid show the typical dependence on the acidity of the aqueous solvent system that is known from respective investigations of carboaromatic diazonium ions with naphthols. The classical case is shown in Fig. 2 for the azo coupling of the thiazole-5-diazonium ion for the pH range 4–6: the measured values for log k_{ps} increase proportionally to pH, i.e. the rate is linearly dependent on the concentration of hydroxyl ions and therefore also linearly dependent on the concentration of the naphtholate ion (RO⁻). It is the naphtholate ion that reacts with the diazonium ion (see ref. 13 and reviews (15, 16)).

Figure 3 demonstrates that the pH dependence of the azo coupling reaction of the thiazole-2-diazonium ion is in part different from that of the 5-isomer: the logarithm of the rate constant k_{ps} shows a linear dependence on pH with a slope of 1 only above pH 1. At lower pH values the curve gradually becomes horizontal. A similar figure results if our results with the 4-isomer are plotted. This is consistent with a dominant reaction of the naphthol relative to that of the naphtholate in the pH range below 0.5 ($k_2[ROH] > k_1[RO^-]$, because [ROH] \gg [RO⁻]): in eq. [2] the first term can be neglected due to the ex-







FIG. 3. Rate of azo coupling of a mixture of the thiazole-5-diazonium ion and 2-naphthol-3,6-disulfonic acid as a function of acidity.

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FIG. 4. Correlation between azo coupling rates of heteroaromatic diazonium ions with 2-naphtholate-3,6-disulfonate trianion and the chemical shifts of protons at the position of the diazonio group in ¹H nmr spectra of the respective heteroaromatic parent compound (nmr data from refs. 20 and 21).



FIG. 5. Correlation between azo coupling rates of substituted benzenediazonium ions with the 2-naphtholate-3,6-disulfonate trianion (from ref. 15, p. 241) and the chemical shifts of protons at the position of the diazonio group in 1 H nmr spectra of the respective monosubstituted benzenes (nmr data from ref. 20).

tremely low numerical value of [RO⁻]. For example, at pH 0, the equilibrium concentration of the naphtholate is $10^{9.76}$ times lower than that of the naphthol. An analogous pH dependence is expected for the thiazole-2-diazonium ion at lower pH values. Rates at pH < -2 are, however, too small to be measured accurately.

Semiquantitative work carried out in the fifties (17) suggests that undissociated naphthols and phenols do react with carboaromatic diazonium ions, but at rates that are several orders of magnitude lower than those of the respective naphtholates and phenolates. Quantitative evaluations of kinetic measurements carried out by Štěrba and co-workers (18, 19) in the seventies demonstrate that the naphtholates are 10^8-10^9 times more reactive than the naphthols.

The evaluation of the rate constants k_{ps} of the azo couplings of thiazole-2- and -4-diazonium ions with eq. [2] gives k_1 and k_2 , i.e. the rate constants for reaction with the naphtholate and the naphthol, respectively (Tables 1 and 2). The ratios k_1/k_2 are 7.65×10^8 and 5.69×10^8 . Very good agreement exists with the ratio k_1/k_2 of the reaction of the 3-nitrobenzenediazonium ion with 2-naphthol-3,6-disulfonic acid reported by Štěrba and co-workers (19): $k_1/k_2 = 7.94 \times 10^8$. This indicates strongly that, in this respect, azo coupling reactions of the heteroaromatic diazonium ion are mechanistically similar to those of carboaromatic analogs.

An interesting problem is the influence of the structure of the heteroaromatic ring on the reactivity of the respective diazonium ions. The results in Tables 1–6 show that the reactivities of the

six diazonium ions with the naphtholate ion (k_1) cover a range of more than 4 orders of magnitude $(1.76 \times 10^5 - 5.4 \times 10^9 \text{ L} \text{mol}^{-1} \text{ s}^{-1})$.

Is there a rationale behind the sequence of reactivities that we found? One may consider checking the results from MO calculations made with heteroaromatic compounds of the types used for this study. Literature data which we found could, however, not be compared because they were either not obtained with the same type of MO treatment or obtained with outdated methods. We preferred, therefore, a comparison with an experimental probe for the reactivity of heteroaromatic compounds, namely the ¹H nmr chemical shifts of the heteroaromatic compounds on which our six diazonium ions are based. In Fig. 4 we plotted the logarithms of our azo coupling rate constants k_1 against the chemical shift of that proton in the respective heteroaromatic parent compound which is substituted by the diazonio group in our diazonium ions. We found a surprisingly good linear relationship for all but one rate. This results should, in fact, not be astonishing: a change of the chemical shifts to lower field indicates lower nucleophilicity (i.e. higher electrophilicity) of a heteroaromatic compound, which is reflected in the higher electrophilicity of the diazonio group. More astonishing, in our opinion, is the fact that, to our knowledge, such a correlation between chemical shifts and a series of comparable electrophilic aromatic substitutions has not yet been reported in the literature.

It was therefore imperative to check if the same type of correlation also exists for azo coupling reactions of substituted benzenediazonium ions with 2-naphthol-3,6-disulfonic acid. This is indeed the case, as shown in Fig. 5.

The only heteroaromatic diazonium ion whose rate of azo coupling does not follow the linear relationship with the ¹H nmr data in Fig. 4 is the 1,3,4-triazole-2-diazonium ion. This apparent discrepancy is most likely based on the fact that the ion is easily deprotonated at the heterocyclic nitrogen atom in the 1-position. Under our azo coupling conditions (pH 4.01-5.97) the equilibrium is almost completely on the side of the zwitterion 7 in eq. [3]. The mesomeric structure 7b demonstrates



that the reactivity of 7 is expected to be lower than that of 6 and the diazonium ions 1-5 used in this study. In Fig. 4 the chemical shift of 1,3,4-triazole is plotted (8.31 ppm). For the corresponding anion of 1,3,4-triazole a chemical shift of 8.10 ppm is reported (21). This value hardly improves the position of this diazo compound relative to the five others.

A comparison of Figs. 4 and 5 also offers an explanation for the deviation of the 1,3,4-triazole-2-diazonium zwitterion (7) in Fig. 4. The straight lines have different slopes. This is obviously due to the fact that the aromatic ring current is influenced by the type of aromatic systems involved, namely benzene (Fig. 5) and various heteroaromatic five-membered ring compounds (Fig. 4). It seems that the number and type of heteroatoms in these rings is of minor importance except for a (formally) anionic nitrogen as present in 7.² An additional factor for a decreased reactivity may be the addition (equilibrium [4]) of water to the diazo compound 7 to

.. .

$$\begin{bmatrix} 4 \end{bmatrix} \xrightarrow{N-N}_{N} \xrightarrow{+}_{N} = N + H_{2}O \rightleftharpoons \bigvee_{N} \xrightarrow{N-N}_{H} \xrightarrow{N}_{H}$$

form the diazohydroxide $\mathbf{8}$, which is probably not electrophilic at all. This possibility was, however, not investigated in more detail because of the low stability of solutions of this diazo compound.³

We explain the spectral change in kinetic runs of the azo coupling of the 1,3,4-thiadiazole-2-diazonium ion with time (Fig. 1) by the mechanism [5]. The diazonium ion 5 is present in



equilibrium with the nitrosating reagent⁴ and forms the azo compound 9 as a kinetically controlled reaction product, whereas 1-nitroso-2-naphthol-3,6-disulfonic acid (10) is the thermodynamically controlled product. The back reaction of the azo coupling reaction $9 \rightarrow 5$ has been described in various cases involving carboaromatic diazonium ions.⁵ Our results confirm that heteroaromatic diazonium ions also show the same behavior in this respect.

We will report on the mechanism of diazotization of heteroaromatic amines later (see ref. 22). In contrast to the diazotization of carboaromatic amines, which give quantitative yields of diazonium ions under the usual conditions, heteroaromatic amines are in equilibrium with the respective diazonium ions in the presence of nitrosating reagents. The formation of 1-nitroso-2-naphthol-3,6-disulfonic acid in reaction [5] is a consequence of that equilibrium.

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³Note added Dec. 19, 1985: We only now became aware of the recent paper of Macháček *et al.* (23), who investigated the azo coupling mechanism of 5-methyl- and 5-phenyl-1,2,4-triazole-3-diazonium ions with phenols. In the context of diazo acid-base equilibria, they discuss structures analogous to **8** as potential intermediates.

⁴The formulation of the nitrosating reagent does not imply that it is not an ionic species.

⁵See summary, ref. 15, p. 241.

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 $^{^{2}}$ A referee suggested that 1,3,4-triazole is the only compound in which the proton in question resides between two nitrogen atoms. This may be the cause for the deviation.

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