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# 207. Electrophilic Aromatic Substitution of Groups other than Hydrogen. Part II: $S_N1$-Type Desulfonation of 2-Naphthol-1-sulfonic Acid by Diazonium Ions in Aprotic Apolar Solvents

27th communication on diazo coupling reactions[1])

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(10. V. 72)

*Summary.* The rates of formation of 1-(4'-chlorophenylazo-)-2-naphthol by $SO_3$ of release from the $\pi$-complex [2-naphthol-1-sulfonate anion $\cdots$ *p*-chlorobenzenediazonium cation] have been measured in chloroform and in methylene chloride; they are first-order with respect to the complex. They are catalysed by pyridine and co-catalysed by acetic acid. Acids alone, in stoichiometric or higher concentrations, inhibit the reaction. A mechanism is postulated involving proton transfer to the sulfonate group, followed by rearrangement to the $\sigma$-complex which, in the catalysed reaction, first loses a proton to the base and then releases $SO_3$, but in the uncatalysed reaction loses $SO_3H^{\oplus}$. The function of the co-catalyst (pyridinium ion) is explained (see text). This reaction is – in contrast to electrophilic aromatic substitutions in which the leaving group is a proton – an $S_N1$-type re-aromatization of the $\sigma$-complex to the product.

**1. The Sulfonic Group as an Electrofugal Leaving Group in Aromatic Substitutions.** – In the field of electrophilic aromatic substitution many reactions exist for which an electrofugal leaving group is other than a proton. The leaving capacities of a number of substituents have been reviewed systematically by *Perrin* in 1971 [2]: The sulfonic group is a relatively good electrofugal leaving group. Qualitatively this is understandable because the bond between carbon and tetrahedral sulfur appears to be relatively weak and, furthermore, the released $SO_3$ molecule is stable.

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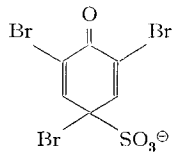
[1]) 26th communication: *Fischer & Zollinger* [1].

On the other hand, the large sulfonic acid group hinders the attack of an electrophile at the adjacent carbon atom, the so-called *ipso* position[2]). This steric hindrance is, however, not too difficult to overcome since bromo-desulfonations are known [4]. A particularly favourable reaction is proto-desulfonation; thus sulfonations (sulfodeprotonation) are – besides *Friedel-Crafts* reactions – the only reactions of the more common electrophilic aromatic substitutions that are significantly reversible.

The relatively high stability of the $\sigma$-complex **1** in the bromo-desulfonation of 2,6-dibromophenol-4-sulfonic acid, investigated by *Cannell* [4], appears to be in contradiction to the above statement. However, the related observations of *Ershov & Volod'kin* and *de la Mare et al.* [5] concerning the electrophilic substitution of 2,6-di-*t*-butylphenol show that the stability of cyclohexadienones is greatly increased when large substituents are present in both the 2- and 6-positions.




**1**

Both from the technological and the mechanistic point of view, substitutions of sulfonic groups by diazonium ions are particularly interesting: The observation [6] that 1-arylazo-2-naphthylamine dyes can be obtained by diazo coupling reactions with 2-naphthylamine-1-sulfonic acid as easily as with 2-naphthylamine is technologically important because the use of the highly carcinogenic 2-naphthylamine can be avoided.

This reaction is also interesting because one might expect that 2-naphthol-1-sulfonic acid could be desulfonated in exactly the same way. Astonishingly enough, however, this is the case only under particular reaction conditions. Normally a completely different reaction takes place. The reaction has been investigated by *Bucherer et al.*, *Rowe et al.*, *Vaughan* [7] and recently by *Jaecklin, Skrabal & Zollinger* [8].

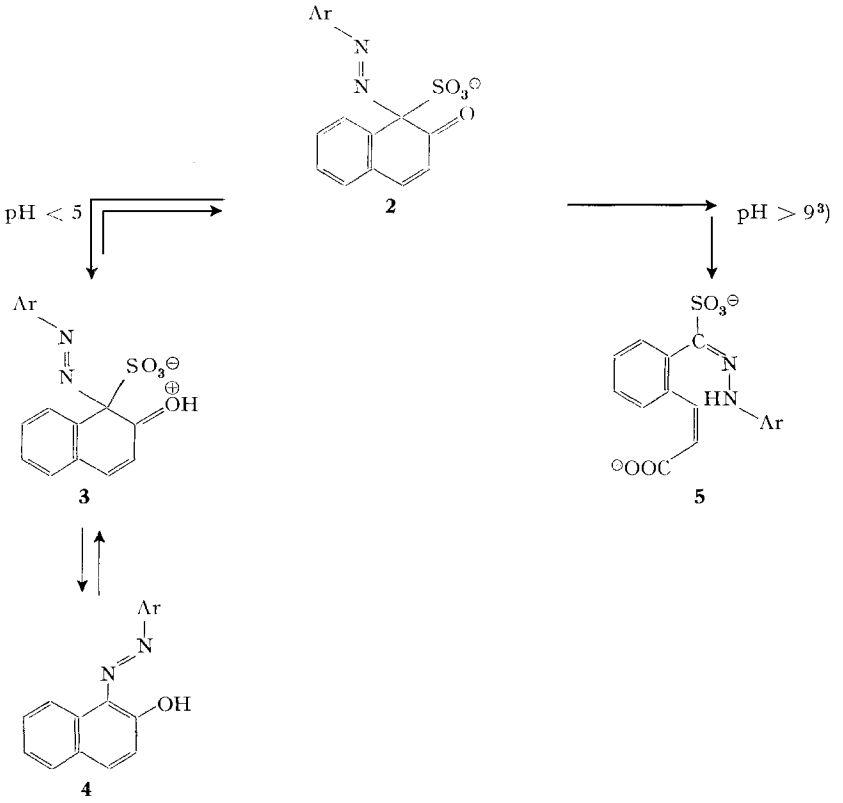
The $\sigma$-complex **2** is formed from 2-naphthol-1-sulfonic acid and an aryldiazonium salt in a slightly alkaline medium; its constitution was verified by NMR. spectroscopy [9] [10] [11]. It yields the azo substitution product [4] by release of the sulfonic group only after acidification (Scheme 1). Under alkaline conditions nucleophilic addition of hydroxyl ions to the carbonyl group takes place. This leads to a fragmentation in which the *cis*-cinnamic acid derivative (**5**) is formed. Recently its structure and mechanism of formation have been described in detail [8].

That such a fragmentation was never observed with $\sigma$-complexes having a proton as an electrofugal leaving group, but only with sulfonic leaving groups, can be explained by the fact that protons are successful competitors for the carbonyl group in reactions with bases such as hydroxyl ions, whereas an (anionic) sulfonic groups does not need – at least formally – an acceptor to be released as a $SO_3$ molecule.

However, it is still open to question if water molecules are involved in the release of the $SO_3$ molecule and if the spontaneous release of $SO_3$ is slower than the release with water as an acceptor for $SO_3$.

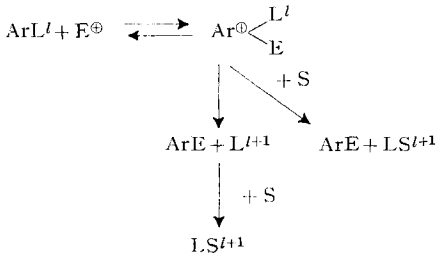
[2]) *Perrin & Skinner* [3] propose to call that position of benzene which bears the substituent, the *ipso* position.

*Scheme 1*




As seen from the generalized scheme 2 for electrophilic substitutions of the aromatic compound $ArL^l$ (where L refers to the leaving group with charge $l$, e.g. L = H, $l = 0$ or $L = -SO_3^{\ominus}$, $l = -1$) by the electrophilic reagent $E^{\oplus}$, there are two possibilities for the re-aromatization of the $\sigma$-complex $E\text{–}Ar^{\oplus}\text{–}L^l$, i.e. for the second part of the substitution proper. The first involves a rate-limiting monomolecular release of the leaving group in the form of the particle $L^{l+1}$, followed by fast reaction of that particle with the solvent (S) or other chemical species which may be present in the system and

*Scheme 2*



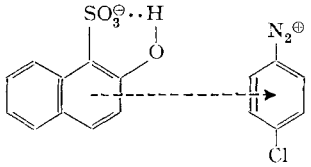

[3]) Mechanistic details see *Jaecklin, Skrabal & Zollinger* [8].

which react with $L^{l+1}$. This is a mechanism which is analogous to the $S_N1$ mechanism in nucleophilic aliphatic substitution.

The $S_N2$ counterpart is the alternative mechanism in scheme 2, namely a bimolecular reaction of the $\sigma$-complex with a solvent molecule S or other reactive particles in the system. This mechanism is well documented by general base-catalyzed deprotonations (L = H, S = general base).

In order to investigate the question of whether $SO_3$ is released by the $S_N1$- or by the $S_N2$-type mechanism, we studied the desulfonation of 2-naphthol-1-sulfonic acid by diazonium ions in aprotic apolar media.

**2. Results.** – An aqueous acidic solution of *p*-chlorobenzene diazonium chloride forms a precipitate with 2-naphthol-1-sulfonic acid. The precipitate can be isolated; it is sufficiently stable to be analysed. The analysis and NMR. spectrum indicate that the structure is similar to that of a $\pi$-complex (**6**) [8] [9] [10][4]). Formation constants for complexes of naphthalene, 2-naphthol-1-sulfonic acid and other naphthalene derivatives with *o*-nitrobenzene diazonium ions in acetic acid/water 4:1 are in agreement with this conclusion [11].




**6**

The complex **6** is soluble in a variety of polar and apolar solvents: In water, ethanol or dimethylsulfoxide no diazo coupling takes place[5]); in acetone or glacial

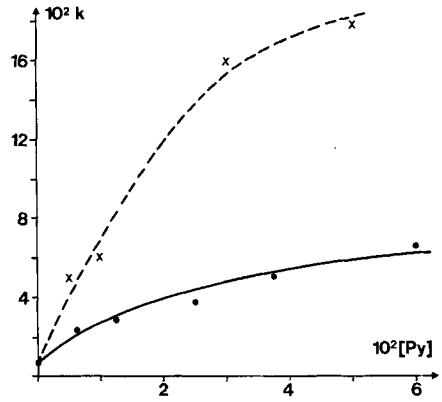



Fig. 1. *Rate constants for diazo coupling reactions of complex* **6**, catalysed by pyridine (•) and by pyridine and acetic acid (×)[6])

[4]) With respect to stability and nomenclature of these complexes see footnote 5 in [11] as well as *Banthorpe*'s review [12].

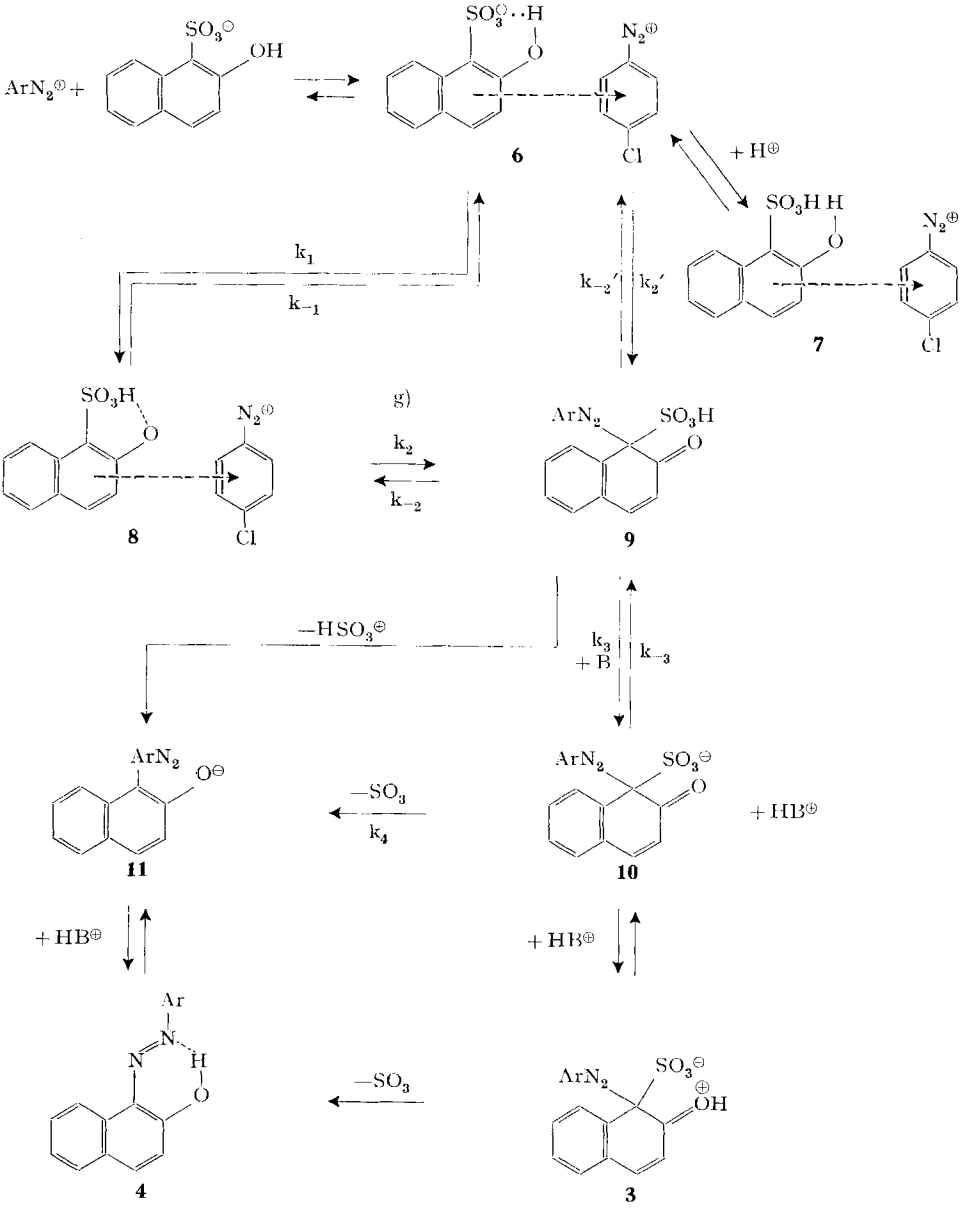
[5]) For the reaction in water after increasing the pH-value (formation of $\sigma$-complex **2**) followed by reacidification, see however [7] [8] [10].

[6]) The abscissae of the points referring to rate measurements in the presence of pyridine and hydrochloric acid represent the concentration of the remaining pyridine assuming that all the hydrochloric acid reacts to form pyridinium chloride.

acetic acid a small amount of the azo compound is slowly formed. In methylene chloride, chloroform, benzene or pyridine, however, a slow but quantitative formation of the azo compound **4** is observed.

We measured the rates of formation of the azo compound in methylene chloride and in chloroform. The rates were measured spectrophotometrically [13] and evaluated

*Schème 3*



by *Guggenheim's* method [14]. It was demonstrated that the rates are first order by varying the initial concentration[7]) of the complex.

The rate constants in the two solvents are very similar: k (methylene chloride) = $1.0 \times 10^{-2}$ min$^{-1}$, k (chloroform) = $0.75 \times 10^{-2}$ min$^{-1}$.

Whereas additions of (gaseous) hydrochloric acid in excess inhibit the reaction, additions of pyridine increase the reaction rate. In Fig. 1 the measured rates in chloroform are plotted as a function of the pyridine concentration. Addition of acetic acid to reactions with added pyridine (Py) increased the rate still further. Addition of acetic acid alone decreased the rate slightly.

The corresponding complex of 2-naphthol-1-sulfonic acid with *p*-nitrobenzenediazonium ion instead of the *p*-chloro derivative reacts in a similar way but, as expected, the reaction is faster (in $CHCl_3$ k = $7.14 \times 10^{-2}$ min$^{-1}$).

**3. Discussion.** – The kinetic results are consistent with the reaction scheme 3: In our opinion the hydroxyl group in the zwitterionic $\pi$-complex **6** forms an intramolecular hydrogen bond with the sulfonate group when the complex is dissolved in an aprotic solvent[8]). Addition of acid yields the cationic complex **7** which does not react further.

Complex **6**, however, is in equilibrium with the tautomeric $\pi$-complex **8** or the cyclohexadienone-type $\sigma$-complex **9**.

The following step in the reaction is the release of the proton attached to the sulfonic acid group. It is general base catalysed, e.g. by pyridine. The curvilinear dependence of the rate upon the pyridine concentration is consistent with **9** being a steady-state intermediate and, therefore, with the general rate equation (4)[10]).

The anionic $\sigma$-complex **10** has a better electrofugal leaving group ($-SO_3^{\ominus}$) than has **9** ($-SO_3H$), therefore it rearomatizes easily into the 1-arylazonaphtholate ion **11**, which is protonated by the conjugate acid $HB^{\oplus}$ to give **4**.

The leaving capacity of the sulfonate group in **10** can be improved by protonation of the carbonyl group (**3**), i.e. by general acid catalysis. The conjugate acid $HB^{\oplus}$ may be so effective as a catalyst that the path **10** → **3** → **4** is preferred to **10** → **11** → **4**. A kinetic differentiation between them is not possible however. The reaction through **3** is consistent with the observed catalysis by acetic acid which either reacts as a co-catalyst *per se* or by forming pyridinium ions, both being general acid catalysts in step **10** → **3**.

The best representation for the reaction without added catalyst is probably sequence **9** → **11** → **4** in which $-SO_3H$ is the leaving group, forming $SO_3H^{\oplus}$ which then acts as a proton donator for step **11** → **4**. It is unlikely that the solvent is the proton

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[7]) Apparently slower rates are obtained only at high concentrations where decomposition reactions become dominant.

[8]) The observation that the diazo coupling reaction does not proceed in dimethylsulfoxide suggests that strong intermolecular hydrogen bonds between the hydroxyl group and a dimethylsulfoxide molecule are formed.

[9]) As discussed elsewhere [15], it is not possible to decide if a $\pi$-complex (like **7**) is an intermediate in the reaction path in the formation of a $\sigma$-complex or if the $\pi$-complex is a product of a side equilibrium and the $\sigma$-complex is formed directly from the reactants.

[10]) Equation (4) is based on the assumption of a sequence **6** → **8** → **9** and $k_1 > k_{-1} \gg k_{-2} > k_2$. If **9** is formed directly from **6**, a slightly different rate equation results; yet, it has still the characteristics of the curvilinear rate dependence on base concentration.

acceptor for the path **9** → **10** → **11** (or **3**) → **4**. Base catalysis by a preceeding intermediate (e.g. **8**) or by the products (**11** or **4**) is not consistent with the experimental data as these two mechanisms should be second-order for **6** and autocatalysed respectively.

In conclusion, we see that $SO_3$ is indeed able to be an electrofugal leaving group without assistance of the solvent, i.e. in a $S_NI$-type reaction. It is not possible to decide on the basis of these data if, in water, there is solvent participation.

## Experimental Part

*Isolation and characterisation of complex* **6**. – A solution of 3.19 g *p*-chlorobenzenediazonium chloride (0.025 mole) in 25 ml cold water and 50 ml 1 N HCl was added to a solution of 6.31 g 2-naphthol-1-sulfonic acid (sodium salt, 0.025 mole) in 50 ml water at 50°. The yellowish precipitate was separated, washed with water and dried in the dark at 5° in vacuo (ca. 0.1 Torr). The complex has to be stored at low temperature (< – 5°).

| | | | | |
|---|---|---|---|---|
| $C_{16}H_{11}ClN_2O_4S$ | Calc. | C 52.92 | H 2.99 | N 7.72 S 8.84% |
| | Found | ,, 53.10 | ,, 2.94 | ,, 7.56 ,, 8.84% |

Table 1. *Kinetic run of the diazo coupling reaction of complex* **6** ($6 \times 10^{-5}$ M), T = 25° in chloroform, $\Delta t = 60$ min.

| t min. | y | y′ | $10^2 k$ (min$^{-1}$) |
|---|---|---|---|
| 15 | 0.067 | 0.305 | 0.621 |
| 35 | 0.157 | 0.368 | 0.655 |
| 55 | 0.238 | 0.422 | 0.702 |
| 75 | 0.305 | 0.465 | 0.794 |
| 95 | 0.368 | 0.505 | 0.644 |
| 115 | 0.422 | 0.542 | – |

Table 2. *Summary of kinetic measurements* (25.0°)

| Substituent[a] | Solvent | Complex concentration $10^5$ M | Acetic acid $10^2$ M | Pyridine $10^2$ M | $10^2 k$ (min$^{-1}$) |
|---|---|---|---|---|---|
| *p*-Cl | $CHCl_3$ | 2 | – | – | 0.834 |
| | | 4 | – | – | 0.698 |
| | | 5 | – | – | 0.760 |
| | | 6 | – | – | 0.726 |
| | | 5 | 2.00 | – | 0.570 |
| | | 10 | – | 0.65 | 2.16 |
| | | 10 | – | 1.26 | 2.97 |
| | | 10 | – | 2.59 | 3.83 |
| | | 10 | – | 3.75 | 5.44 |
| | | 10 | – | 6.00 | 6.42 |
| | | 10 | 1.00 | 1.00 | 6.14 |
| | | 10 | 1.00 | 3.00 | 16.1 |
| | | 10 | 1.00 | 5.00 | 17.9 |
| | | 10 | 2.00 | 0.50 | 5.11 |
| *p*-Cl | $CH_2Cl_2$ | 5 | – | – | 1.00 |
| *p*-$NO_2$ | $CHCl_3$ | 2 | – | – | 7.47 |
| | | 4 | – | – | 6.82 |

[a] Substituent on diazonium component of the complex

Determination of the percentage of substance able to undergo a coupling reaction: A measured amount of complex **6** (ca. 100–200 mg) was dissolved in a buffer solution (pH = 5) containing the three-fold amount (w/w) of 2-naphthol-6-sulfonic acid. The azo compound formed, 1-(4'-chlorophenylazo)-2-naphthol-6-sulfonic acid [1] [16], was determined spectrophotometrically in the usual way [16].

*Kinetic measurements.* – *Guggenheim*'s method [14] was used because the start of the reaction cannot be determined accurately. 18.8 mg of complex **6** was dissolved in 100 ml chloroform or methylene chloride at 25°. For a kinetic run with $5 \times 10^{-5}$ M, 5 ml of this solution were diluted to 50 ml. The solution was kept in a thermostat at 25.0 ± 0.10°. The optical densities of samples taken from this solution at 20 min. intervals were measured at 490 nm in a *Cary* 11 or a *Beckman* DU spectrophotometer. Measurements at time intervals of 60 or 100 min. ($t + \Delta t$; optical densities y and y') were used to evaluate the rate constant using *Guggenheim*'s equation (5).

$$kt + \log(y - y') = \log(y_0 - y_\infty)\,(1 - e^{-k\Delta t}) = \text{const.} \qquad (5)$$

The results of a typical kinetic run are shown in Table 1. In Table 2 the results of all kinetic runs are summarized.

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