

206. Electrophilic Aromatic Substitution of Groups other than Hydrogen. Part I: *Ipso* Factors and Rate-Limiting Steps in Dehalogenations by Diazonium Ions

26th communication on diazo coupling reactions¹⁾

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(10. V. 72)

Summary. The rates of substitution of the group X in 1-X-2-naphthol-6-sulfonic acids (X = H, Cl, Br, and I) by *p*-chlorobenzenediazonium ions in aqueous solution have been measured. The rates of the halogenated naphthols relative to that of the parent compound (X = H) are 0.0070:0.0089:0.149 for X = Cl, Br, and I respectively. The reaction of 1-bromo-2-naphthol-6-sulfonic acid is catalysed by thiosulfate ions; the relative rate observed for this compound does not, therefore, represent the *ipso* factor. It is postulated that in its substitution the release of the electrofugal leaving group (Br[⊖]) is rate-limiting.

1. Influence of Electrofugal Leaving Groups on the Rate of Electrophilic Aromatic Substitution. – Studies of electrophilic aromatic substitution reactions have been outstanding in the establishment of our present understanding of the electronic influence of substituents on organic compounds in solution. Until recently, the enormous amount of data concerning these reactions referred solely to replacements of hydrogen and its isotopes bonded to aromatic carbon. If we compare these reactions, classified today as electrophilic aromatic deprotonations [2], with other types of substitutions, e.g. nucleophilic aromatic or aliphatic substitutions, it is fair to say that the earlier progress made in the field of electrophilic aromatic substitution was, to a large extent, due to the fact that the leaving group attached at the carbon atom was always the same and therefore a constant factor in the reactions. In nucleophilic substitutions, however, experimental data for reactions involving a large variety of leaving groups had to be compared, so that a further factor to the reaction behaviour had to be considered.

Electrophilic aromatic substitution is, however, not restricted to deprotonation. Substitution of groups other than hydrogen²⁾ is by no means uncommon, but it was not until recently that these reactions were investigated on the same systematic basis as nucleophilic reactions, particularly nucleophilic aliphatic substitution reactions.

It is, for example, significant that the term 'leaving group' was used for decades for nucleophilic substitutions only. The distinction in nomenclature suggested by *Mathieu et al.* [3] and used extensively by *Grob et al.* [4] for leaving groups in electrophilic and nucleophilic substitutions ('elektrofuge Abgangsgruppe' and 'nukleofuge Abgangsgruppe') is therefore unfortunately little used²⁾. It may be noted also, that in spite of the detailed discussions of electrophilic aromatic

¹⁾ 25th communication: *Jaecklin, Shrabal & Zollinger* [1].

²⁾ This becomes evident by the fact that there seems to be no generally accepted English translation for these classifications: The words *nucleofugic/electrofugic* are used occasionally, but *nucleofugal/electrofugal* are the correct words to use from the linguistic point of view.

substitution found in all textbooks of organic chemistry, the attention of the reader is seldom drawn to substitutions of electrofugal leaving groups other than protons. To our knowledge, treatises of aromatic chemistry and related subjects have devoted specific chapters to other electrofugal leaving groups, e.g. [2] and [5], only in the last few years.

Recently, *Perrin* [6] discussed electrofugal leaving groups in terms of a sequence of relative leaving capacities. So far as we know, this is the first attempt to systematize electrofugal leaving groups in aromatic substitutions. Using his own experimental data and related data from the literature, *Perrin* suggested the following sequence of increasing leaving capacity:

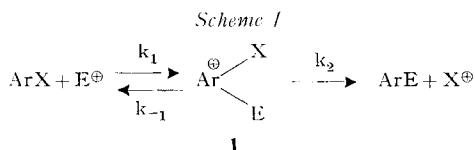


In a subsequent paper *Perrin & Skinner* [7] proposed that in addition to the well known partial rate factors, o_f^X , m_f^X , and p_f^X , representing the rates of attack at a single position ortho, meta, or para to the substituent X relative to the rate of attack at a single position of benzene an *ipso partial rate factor*, i_f^X should be introduced. In the case of a compound ArX, this factor represents the rate of attack at the position bearing the substituent X, relative to the rate of attack at the same position in the parent compound (X = H).

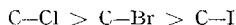
In particular, *Perrin & Skinner* investigated the formation of *p*-nitroanisole, a compound which is formed, besides other products, in the nitrations of anisole, 4-chloro-, 4-bromo- and 4-iodoanisole in acetic anhydride. The evaluation of the product ratios yielded the following *ipso* factors for the halogens:

$$i_f^{\text{Cl}} = 0.061, i_f^{\text{Br}} = 0.079, i_f^{\text{I}} = 0.18$$

Therefore, the halogens deactivate the *ipso* position, a result which is to be expected for an electron-withdrawing substituent. The qualitative sequence is also that expected if one considers the electronic effects of these three halogen substituents on the benzene nucleus and therefore on its capacity for adding an electrophilic reagent in the *ipso* position, i.e. if only the formation of the benzenium-type σ -complex (**1**) is rate-determining (Scheme 1).



The same sequence is, however, obtained also if the second step (k_2), i.e. the release of the electrofugal leaving group, is rate-limiting. It is feasible to assume that the energy needed for carbon-halogen bond dissociation into carbanion + halogenium ion decreases in the order



It should be emphasized, however, that this sequence is not as easy to predict as one might assume; for example the acidity or basicity sequences observed in solutions for amines change to a remarkable extent in the gas phase [8]. Thus solvation effects will definitely influence the reactivity of halogenium ions very strongly and therefore the solvent reorganization which occurs in going from the σ -complex to the transition state of the halogenium ion may influence the values

of k_2 for $X = \text{Cl}, \text{Br},$ and I to differing extents. However *Perrin & Skinner* [7] have presented arguments to show that in the reactions they studied k_1 is the product-determining step.

Their kinetic data exclude the possibility that they were dealing with reactions which exhibited 'disguised kinetics' [9], namely reactions which are not controlled by the rate of reaction of two species, but by the process of mixing. Such cases have been reported and discussed recently by *Schofield et al.* [10], *Ridd* [11] and by one of us [12].

2. Diazo Coupling Reactions with Halogens as Electrofugal Leaving Groups.

In the present paper we communicate data on dehalogenations of 1-halogeno-2-naphthol-6-sulfonic acids by diazonium ions.

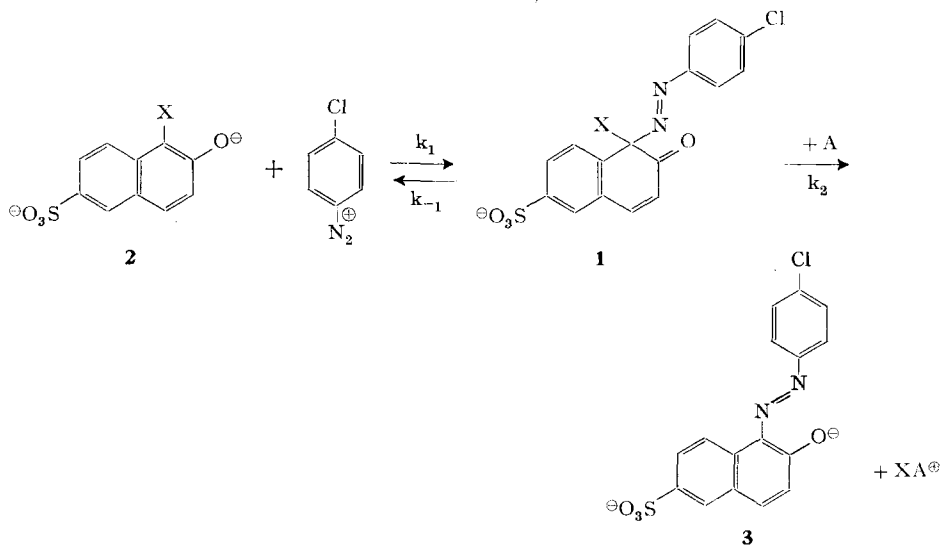
Although we are not able at the present time to rationalize our results fully, in our opinion an interesting comparison can be made with the data of *Perrin & Skinner* since

a) we obtained our *ipso* factors directly from independent rate measurements and not from product ratios,

b) we found at least one case in which the release of the electrofugal leaving group is rate-limiting.

We studied the reaction of 1-X-2-naphthol-6-sulfonic acids (**2**, $X = \text{H}, \text{Cl}, \text{Br},$ or I) with *p*-chlorobenzenediazonium chloride in various aqueous buffer solutions ($\text{pH} = 4.28$ to 6.22 , ionic strength $I = 0.25$) at 15° . In these reactions X is replaced by the *p*-chlorophenylazo group (Scheme 2). The pH-dependence of the rate constant shows that it is, as usual, the naphtholate dianion (**2**) which undergoes the actual substitution [13].

Scheme 2³⁾



The rates were determined from measurements of the optical density of the azo compound formed (**3**). The results obtained for 2-naphthol-6-sulfonic acid (**1**, $X = \text{H}$) agreed with previous kinetic measurements of the same reaction [13, 14]. In particular,

³⁾ A refers to an appropriate acceptor for the electrofugal leaving group X^\oplus . A may bear a negative charge (see text).

the reaction was not general base catalysed. This shows that the attack of the electrophile is the rate-limiting step (k_1).

The rates of all four naphthol derivatives are given in Table 1 together with the *ipso* factors which, for reasons given below, are called 'apparent *ipso* factors'. They refer to the ratio of the respective rate constant ($X =$ halogen) to that of the parent compound ($X = H$).

Table 1. Rates and apparent *ipso* factors of reactions of 1-*X*-2-naphthol-6-sulfonic acid with *p*-chlorobenzenediazonium ions

X	k ($M^{-1} \cdot \text{min}^{-1}$)	i_f^X (app.)
H	4.18×10^5	—
Cl	2.92×10^3	0.0070
Br	3.73×10^3	0.0089
I	6.21×10^4	0.149

The sequence of rates $Cl < Br < I < H$ is that expected. It is found also for the pK_a values of the naphthol-naphtholate equilibrium of the compounds 1: pK_a (Cl) = 7.27; pK_a (Br) = 7.30; pK_a (I) = 7.40; pK_a (H) = 8.95. The linear relationship between the pK_a values and the logarithms of the rate constants⁴⁾ is poor however. That a good relationship cannot be expected in this series of reactions becomes clear from the following section of this paper.

3. Catalysis by Thiosulfate Ions. – The observation by *Joffe* in 1936 and 1937 [16] that diazo coupling reactions of 1-bromo-2-naphthol can be catalysed by thiosulfate ions prompted us to investigate the effect of this ion in our reactions. We found indeed that added thiosulfate ion catalysed the reaction with $X = Br$ (Fig. 1), but astonishingly had no influence on the rate of the chloro and iodo compounds.

Fig. 1 demonstrates that the accuracy of the rate measurements in the presence of thiosulfate ions is poor.

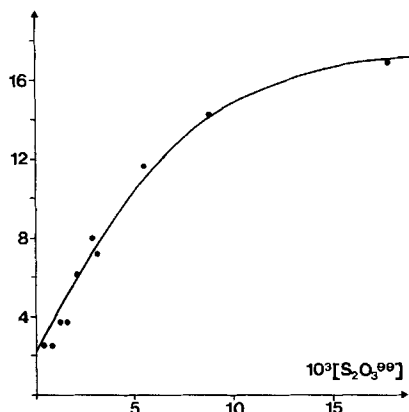


Fig. 1. Thiosulfate catalysis of the debromination of 1-bromo-2-naphthol-6-sulfonic acid with *p*-chlorobenzenediazonium ions

⁴⁾ This problem has been mentioned already briefly in a review paper [15].

This is one reason for not proposing a specific mechanism for this catalytic reaction. Another is the well-known fact that thiosulfate reacts with chlorine, bromine and iodine molecules and their derivatives (e.g. I_3^- , $BrOH$ etc.) in a variety of reactions. One well-known reaction is that with triiodide ions (I_3^-) in water which under neutral or slightly acidic conditions yields the tetrathionate ion ($S_4O_4^{2-}$), but in an alkaline medium sulfate ions are formed. Almost all other familiar oxidising reagents except iodine oxidise thiosulfate to sulfate rather than to tetrathionate. The reactions are, however, not sufficiently quantitative to be understood from a mechanistic point of view [17].

Finally we observed a difference between the electronic spectra of kinetic runs carried out in the presence of *low* concentrations of thiosulfate ions (below 1.5×10^{-3} M) and the spectra obtained using higher concentrations of this ion. Whereas while measurements were taken the latter spectra were identical with those of reactions without the additive, the spectra of runs with small concentrations of thiosulfate ion had a shoulder on the long wavelength side of the 487 nm band in the visible spectrum. After 2 to 3 hours the shoulder disappeared and the spectra became identical with that of the azo compound **3**.

As a tentative explanation for these observations the possibility exists that the shoulder is caused by the absorption of a primary or a side product of a reaction of the σ -complex with thiosulfate which then forms the azo compound **3**, either in a fast reaction in the presence of more thiosulfate ion⁵⁾ or in a slower reaction involving other components in the system.

4. Conclusions. – The following conclusions have been drawn on the basis of the observations mentioned above:

1. The debromination of 1-bromo-2-naphthol-6-sulfonic acid with diazonium ions is catalysed by thiosulfate ion. Although the mechanism of this catalysis seems to be complex, in our opinion the thiosulfate ion is involved in the second step of the substitution proper (2), i.e. it acts as an acceptor for the bromonium ion in the σ -complex **1**. The measured rates (Fig. 1) are consistent, in a semiquantitative manner, with the usual steady-state kinetics, i.e. equation (3).

$$\frac{d[\text{azo}]}{dt} = [N][D] \frac{k_1(k_2 + k_2'[T])}{k_{-1} + k_2 + k_2'[T]} \quad (3)^6$$

2. The rearomatization of this debromination is therefore definitely bimolecular, similar to deprotonations which are general base-catalysed. It will be shown in the following paper [18] that this debromination and all deprotonations are S_N2 -type rearomatizations. Unassisted (monomolecular) release of leaving groups (S_N1 -type) is, however, also possible. An example described in the following paper [18] is the desulfonation of 2-naphthol-1-sulfonic acid by diazonium ions in aprotic media.

⁵⁾ If in that reaction with a second thiosulfate ion another reducing reagent is generated, no second order rate dependence on thiosulfate is necessarily to be expected.

⁶⁾ N = 1-bromo-2-naphtholate-6-sulfonic acid dianion, D = *p*-chlorobenzenediazonium ion, T = thiosulfate ion. k_2 refers to that fraction of the second step which is not catalysed by thiosulfate (but perhaps by water). k_2 is a first-order, k_2' a second order rate constant.

3. The *ipso* factor for this debromination contains therefore a complex factor originating in the second step of the substitution. For this reason it does not conform to *Perrin's* definition of *ipso* factors; we call it therefore an *apparent ipso* factor.

4. The respective dechlorinations and deiodinations are, within the accuracy of the measurements, not catalysed by thiosulfate ion. Therefore the measured rate constant may either refer to reactions in which the first step (k_1) is rate-limiting or in which the acceptor for the halogenium ion, A in (2), corresponds to a species which is present in constant concentration. This might be a water molecule, but not the σ -complex itself. We found no evidence for the formation of 1-(4'-chlorophenylazo)-4-halogeno-naphthol-6-sulfonic acid, the presence of which would indicate the occurrence of a *Reverdin* rearrangement [19].

Experimental Part

1-X-2-naphthol-6-sulfonic acids. – 2-Naphthol-6-sulfonic acid was purified as described previously [13].

1-Chloro-2-naphthol-6-sulfonic acid: 30 g 2-naphthol-6-sulfonic acid (sodium salt, 0.122 mole) were dissolved in dilute NaOH, and the solution was added dropwise to a solution of 0.125 mole NaOCl. After stirring overnight, the compound was precipitated by the addition of sodium chloride, recrystallized from water and ethanol, and dried.

1-Bromo-2-naphthol-6-sulfonic acid (sodium salt): prepared by the bromination (Br_2) of 2-naphthol-6-sulfonic acid [20].

1-Iodo-2-naphthol-6-sulfonic acid (sodium salt): 16.8 g 2-naphthol-6-sulfonic acid (sodium salt, 0.069 mole) and 17.4 g I_2 (0.069 mole) were dissolved in water and acetic acid. After addition of a little HgO the solution was refluxed for $1\frac{1}{2}$ hours. After cooling, the precipitate was separated, recrystallized from water and ethanol, and dried.

For all halogenated compounds the sulfur: halogen ratio was determined by microanalysis: S:Cl = 1:0.99; S:Br = 1:1.01; S:I = 1:1.02. It was extremely difficult to obtain 1-halogenated 2-naphthol-6-sulfonic acids which did not contain traces of the unhalogenated acid ($X = \text{H}$). As 2-naphthol-6-sulfonic acid reacts faster and kinetic runs were made with excess of the naphthols, these trace amounts influence the measured rate when reactions with halogenated compounds are carried out. For this reason the first-mentioned rate constant of Table 4 (diazo coupling of 1-bromo-2-naphthol-6-sulfonic acid) without addition of thiosulfate is lower, by 40%, than the average of the respective constants in Table 3.

Table 2. Rate measurements of $5 \times 10^{-4} \text{ M}$ 1-chloro-2-naphthol-6-sulfonic acid (sodium salt) with 10^{-6} M p-chlorobenzenediazonium chloride, buffered at 5.86, $l = 0.25$, $T = 15^\circ$

t min.	pH	measured dye concentration	$10^2 k_s$ $\text{M}^{-1} \text{min}^{-1}$	$10^{-3} k$ $\text{M}^{-1} \text{min}^{-1}$
3	5.86	1.00	1.53	1.82
6	5.85	2.15	1.77	2.13
10	5.84	3.55	1.90	2.35
15	5.85	4.60	1.78	2.20
20	5.84	5.65	1.81	2.24
25	5.84	6.45	1.80	2.23
32	5.84	7.40	1.84	2.27
37	5.84	7.90	1.83	2.26
45	5.83	8.35	1.74	2.20
50	5.83	8.90	1.92	2.45

All rate data are summarized in Tables 3 and 4.

Table 3. Summary of rate measurements of diazo couplings of 1-X-2-naphthol-6-sulfonic acids

X	pH	k M ⁻¹ min ⁻¹
H	4.28	3.41 × 10 ⁵
H	4.67	4.92 × 10 ⁵
H	5.83	4.22 × 10 ⁵
Cl	5.81	2.22 × 10 ³
Cl	6.22	3.62 × 10 ³
Br	4.64	4.03 × 10 ³
Br	5.84	3.40 × 10 ³
Br	5.79	3.76 × 10 ³
I	4.72	6.44 × 10 ⁴
I	5.88	5.98 × 10 ⁴

Table 4. Catalysis of the debromination by thiosulfate ion 10⁻³M 1-bromo-2-naphthol-6-sulfonic acid (sodium salt), 2 × 10⁻⁵M p-chlorobenzenediazonium chloride, buffered at pH = 6.02, I = 0.25 (except the 3 last runs), T = 15°

10 ³ S ₂ O ₃ ²⁻ M	pH	10 ⁻³ k M ⁻¹ min ⁻¹
0	6.02	2.18
0.35	6.08	2.41
0.70	6.10	2.36
1.07	6.02	3.92
1.32	6.10	3.83
2.05	6.08	6.31
2.59	6.02	8.04
2.92	6.08	6.94
5.36	6.02	11.72
8.95	6.02	14.11
17.92	6.01	19.22
32.90	6.00	19.22
82.20	5.91	18.92

pK_a values. – They were measured by titration of the 1-X-2-naphthol-6-sulfonic acids with 0,1M NaOH at 15° and I = 0.25 (KCl). pH measurements were made using a *Methrom* E-305 potentiograph with a *Beckman* glass electrode, NBS standard buffers (pH 6.88 and 9.22).

Kinetic measurements. – The experimental technique has been described [13], but a *Cary* 11 and a *Beckman* D4 spectrophotometer were used for the spectrophotometric measurements.

Table 2 gives the results of a representative run: *k_s* is the so-called stoichiometric rate constant, based on the overall concentration of the naphthol, *k* refers to the rate constant based on the equilibrium concentration of the naphtholate ion at the given pH value.

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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 reactions¹⁾

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(10. V. 72)

Summary. The rates of formation of 1-(4'-chlorophenylazo)-2-naphthol by SO₃ of release from the π -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 σ -complex which, in the catalysed reaction, first loses a proton to the base and then releases SO₃, but in the uncatalysed reaction loses SO₃H[⊕]. 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 σ -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 SO₃ molecule is stable.

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