150. Stereochemistry of the σ-Complex Intermediate in Sterically Hindered Electrophilic Aromatic Substitutions

(20th communication on diazo coupling reactions)[1])

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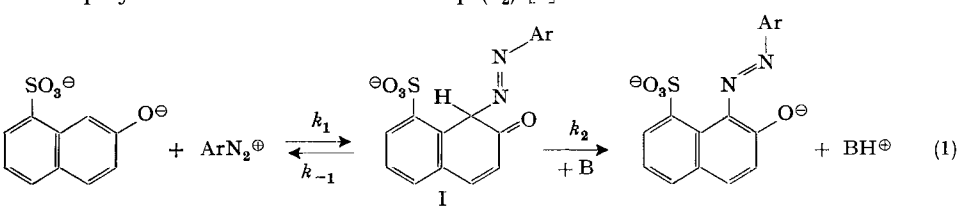
(8. VI. 70)

Summary. The kinetics of the diazo coupling reactions of diazotized sulfanilic acid with 9 derivatives of 2-naphthol, each containing a substituent in the 8-position, have been measured. The reactions proceed by general base catalysis. The rate constants (k_1) for the formation of the steady-state intermediate in the presence of varying concentrations of a base (pyridine) have been evaluated from rate measurements. Similarly the ratios k_2/k_1 (where k_2 is the rate constant for proton transfer from the steady-state intermediate to the base, and k_{-1} is the rate constant for the dissociation of the intermediate) have been determined. The dependence of $\log k_1$ on σ_m^+ and of the ratio k_2/k_{-1} on a steric parameter R^f (defined in this paper) is interpreted as evidence for the steady-state intermediate existing as a benzodienone σ-complex with the sp^3-bound hydrogen in a pseudo-equatorial position and the electrophile pseudo-axial. A sterically caused destabilisation of the intermediate can be excluded. The steric influence on the ratio k_2/k_{-1} is therefore due to the steric influence on k_2 only. Diazo coupling of 8-(2′-pyridyl)-2-naphthol is subject to intramolecular base catalysis, as demonstrated by kinetic hydrogen isotope effects.

1. *Introduction.* Sterically induced base catalysis in diazo coupling reactions was found for 2-naphthol-6.8-disulfonic acid [2] and 2-naphthol-8-sulfonic acid [3]. The explanation was sought in the steric crowding of the σ-intermediate I in equation (1). This was assumed to lead to a destabilisation of the σ-complex and a relative increase of k_{-1} in the kinetic equation (2). The influence of steric conditions in the base B (e.g. decreased catalytic effect of α-picoline relative to its isomers) demonstrated that steric effects play a role also in the second step (k_2) [4].



(1)

$$\frac{d(Az)}{dt} = [R\text{–}H]\,[ArN_2^{\oplus}]\,\frac{k_1 k_2[B]/k_{-1}}{1 + k_2[B]/k_{-1}} \qquad (2)$$

In the steady-state equation (2) only the ratio k_2/k_{-1} can be determined. It is therefore impossible to decide if both effects or only one of them is the cause of the measured small value of that ratio.

In order to investigate this problem, the diazo coupling rate of a series of 8-substituted 2-naphthols were measured. In this manner the influence of a variation of the size of the sterically hindering group can be determined.

[1]) 19th communication: *Jermini, Koller & Zollinger* [1].

2. *Results and Discussion.* The rates of nine 8-substituted 2-naphthols with diazotized sulfanilic acid were measured in aqueous buffer solutions (pH range 6.4–7.2, ionic strength $I = 0.20$) at 20.0° ± 0.5°C in the presence of pyridine (0–0.1 mol/l). Recognising that the diazonium sulfonate zwitter ion and the naphtholate anion are the two species which enter the substitution proper [5] (overall rate constants $k = (k_1\, k_2[B])/(k_{-1} + k_2[B])$, the constants k_1 and k_2/k_{-1} were calculated in the usual way [2] [6a]. In Table 1 the results for all coupling components are given. In the cases where the k_2/k_{-1} ratio is omitted, no base catalysis was observed.

Table 1. *Diazo coupling reaction rates of diazotized* p-*sulfanilic acid with 8-substituted 2-naphthols*

	$10^{-6} \times k_1$ $l \cdot mole^{-1} \cdot min^{-1}$	$10^{-2} \times k_2/k_{-1}$ $l \cdot mole^{-1}$
8-Methyl-2-naphthol	4.99	1.06
8-Ethyl-2-naphthol	8.83	1.22
8-Isopropyl-2-naphthol	10.65	1.07
8-Phenyl-2-naphthol	5.15	–
8-Chloro-2-naphthol	0.373	3.93
8-Bromo-2-naphthol	0.627	1.93
8-Iodo-2-naphthol	0.988	1.57
7-Hydroxy-1-naphthoic acid (as carboxylate)	7.0	–
3-Phenanthrol	0.614	0.91

The rate constants, k_1, in the series of alkyl groups of increasing size in the 8-position of the substituted 2-naphthol (methyl, ethyl, isopropyl)[2]) as well as the sequence of 8-chloro-, 8-bromo- and 8-iodo-2-naphthol already demonstrate qualitatively that the size of the *peri* group does not significantly influence the rate of formation of the steady-state intermediate.

Figure 1 is a plot of the $\log k_1$ values versus the *Hammett-Brown* [7] σ_m^+ substituent constants. σ_m^+ is selected since the *peri* position can be considered to be a *pseudo meta* position.

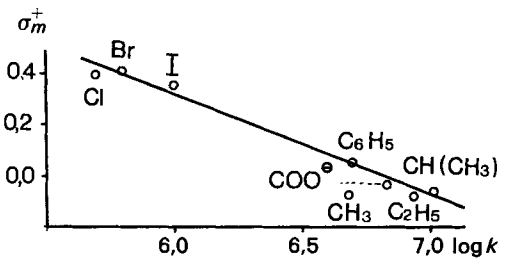


Fig. 1. *Correlation of the rate of the first step in diazo coupling reactions of 8-substituted 2-naphthols with* Hammett-Brown's σ_m^+ *constant*

A reasonable agreement exists. Thus the 8-substituents influence the rate of formation of the intermediate only by their electronic properties and not by their size. The same can be said for the energy of the first transition state, since it is directly related to k_1. As σ_m^+ refers to complexes with σ-bonds (not to charge-transfer complexes), the

[2]) Attempts to synthesize 8-*t*-butyl-2-naphthol were not successful.

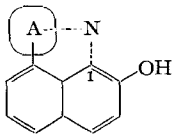
correlation of Figure 1 indicates that the steady state intermediate is a σ and not a π-complex [8].

It is accepted that in diazo coupling reactions the intermediate is closely approximated by the transition state of the first step [9]. Any factor which substantially destabilizes the intermediate would therefore also influence the energy of the transition state. On the basis of the above mentioned results a sterically caused destabilisation of the intermediate can be excluded. Thus k_{-1} is also essentially uninfluenced by steric factors.

However, the ratio of k_2/k_{-1} changes if the size of the 8-substituent changes. To illustrate this steric effect of the *peri* group, a free radius R^f is defined as follows:

$$R^f = AN - R^W \tag{3}$$

AN is the distance between the centre A of the hindering atom in 8-position and a point N to which the nitrogen of the azo group attached to the sp^3-carbon atom in the σ-complex will «swing» during the conversion to products in the second step of the reaction (1). R^W is the *van der Waals* radius of the *peri* group.



The distance between N and C-1 is taken to be the same as the carbon-nitrogen single bond length in azobenzene (1.43 Å) [10]. A is taken to be the centre of the hindering atom in the cases of the halogen derivatives, and the centre of one of the hydrogen atoms in the case of the methyl derivative. The usual values for the bond lengths [11] and the structural data for naphthalene [12] and phenanthrene [13] were used.

The values R^W for the ethyl and isopropyl groups were obtained by adding a small, arbitrary increment (0.03 Å) to the *van der Waals* radius of the methyl group. The experimental k_2/k_{-1} ratios exclude free rotation of the ethyl and isopropyl groups during the conversion to products. Thus the steric volume of these groups is not considerably larger than that of the methyl group. However, the hindering of rotation is expected to result in an increase of the energy of the second transition state, comparable to the effect of a small increase in the size of the group.

In Table 2 these radii R^f are tabulated against the ratios of k_2/k_{-1} found experimentally. Figure 2 is a graphical representation of the logarithms of these values.

Table 2. *Free radius R^f and k_2/k_{-1} ratios for diazo coupling reactions of 8-substituted 2-naphthols and of 3-phenanthrol with diazotized sulfanilic acid*

8-Substituent of 2-naphthol	Free radius R^f Å	$10^{-2} \times k_2/k_{-1}$ $l \cdot mole^{-1}$
–Cl	0.65	3.93
–Br	0.47	1.93
–I	0.31	1.57
$-CH_3$	0.29	1.06
$-C_2H_5$	0.26	1.22
$-CH(CH_3)_2$	0.23	1.07
3-Phenanthrol	0.64	1.96

It may thus be assumed that the steric effect of the *peri* group operates mainly in the second step of the reaction, i.e. the transformation of the intermediate to the products; k_2 (and not k_{-1}) is influenced[3]).

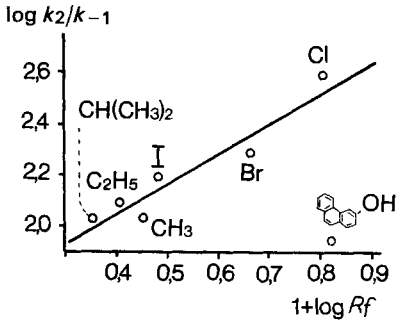


Fig. 2. *Correlations of the free radii and the ratios* (k_2/k_{-1})

It has been suggested [14] that the σ-intermediate does not possess the symmetrical *Wheland* structure [15]. Our results indicate that the introduction of a sp^3-hybridized carbon atom does indeed lead to an asymmetric intermediate. The preferred conformation of a σ-complex of this type is illustrated in Figure 3. This formulation is confirmed by an inspection of models.

The pseudo-axial position of the electrophile would decrease the steric interaction between this group and the *peri* substituent. The virtual absence of steric effects during the formation of the σ-complex strongly supports this representation.

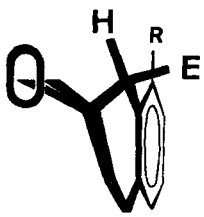


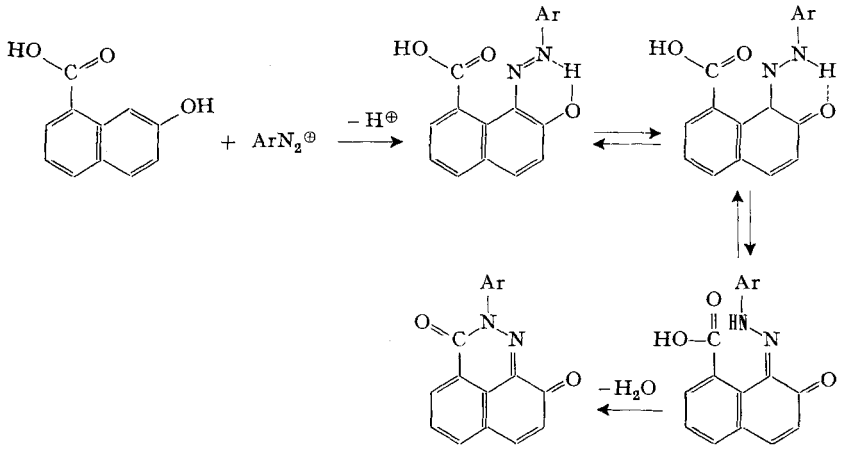
Fig. 3. *Diagrammatic representation of the preferred conformation of a σ-complex in substitution of 8-substituted 2-naphtholate anions by the electrophile* $E^{\oplus}$

The phenomenon of general base catalysis in these electrophilic aromatic substitutions is closely associated with the presence of a hindering group in the *peri* position of the 2-naphthol derivative. This fact led to attempts to combine both effects, *i.e.* steric hindrance and base catalysis, in one molecule. In other words, the introduction of a hindering group with a basic centre of suitable geometry (to allow direct approach to the proton in the splitting-off phase) should lead to intramolecular base catalysis.

We attempted to detect a change in the pH-independent second order rate constant of the diazo coupling reaction of 7-hydroxy-1-naphthoic acid as the pH value of the reaction solution approaches the buffer region of the carboxylic acid $\rightleftarrows$ carboxylate equilibrium. It was, however,

[3]) It is of interest to note that the phenanthrene derivative does not fall into the series of Figure 2. Thus the assumption that 3-phenanthrol may be treated as a naphthol derivative seems to be incorrect.

not possible to obtain reproduceable results at these low pH-values (ca. pH 3.7) because the reaction times were extremely long. This caused extensive decomposition of the diazonium ion and, in addition, formation of a pyridazone derivative (4). Similar observations have been made by *Dziewonski & Stolyhwo* [16] and by *Willstätter et al.* [17].



(4)

The mechanism probably involves an attack of the lone-pair electrons of the saturated nitrogen atom of the hydrazone form on the carbon atom of the carboxyl group. That this reaction will be of the first order with respect to the naphthoquinonehydrazone derivative is to be expected and was demonstrated in preliminary kinetic experiments. The acceleration of this reaction by an increase in hydrogen ion concentration can be explained by considering the electrophilicity of the carboxyl carbon atom. This will increase when going from $-COO^{\ominus}$ to –COOH and $-COOH_2^{\oplus}$. Thus, as the acidity of the reaction medium increases, the electrophilicity of this carbon atom will increase and facilitate the attack of the nitrogen.

The instrumental analysis (NMR., IR. und UV.) of the pyridazone formed in (4), sodium 2,3-diaza-2,4-dihydro-2-(4′-benzenesulfonate)-phenalene-1,4-dione, is described elsewhere [6b].

As 7-hydroxy-1-naphthoic acid was not suitable for the detection of intramolecular base catalysis, we chose 8-(2′-pyridyl)-2-naphthol. By a comparison of the kinetic hydrogen isotope effect of the 1-position ($k_H/k_D = 0.9$) in the diazo coupling of this derivative with that observed for 8-phenyl-2-naphthol ($k_H/k_D = 2.7$), it was possible to demonstrate that intramolecular base catalysis takes place [18]. Furthermore it was possible to show that the attack of the base on the leaving proton takes place *before* the electrophile swings into the plane of the naphthalene nucleus and, also, that a linear transition state for the proton transfer is not a necessary requirement for base catalysis.

Experimental Part

1. Syntheses of the coupling components. – 1.1. *8-Methyl-2-naphthol.* – *7-Methoxy-1-tetralone* was synthesized using the method described by *Haworth & Sheldrick* [19], with the modification of *Howell & Taylor* [20]. Yield 48%, m.p. 66° as in [19]. This ketone (5g, 0.028 mole) was dissolved in dry ether (20 ml) and treated with a methyl-magnesium solution [prepared from magnesium turnings (1.1 g, 0.046 mole), methyl iodide (6.4 g, 0.045 mole) and ether (20 ml)]. The mixture was refluxed for 2 h and then decomposed with dilute sulfuric acid. The ether layer was separated, dried (Na_2SO_4) and evaporated. The residue was distilled (40–65°/0.1 Torr) and yielded *3,4-dihydro-7-methoxy-1-methyl-naphthalene* (3.6 g). This distillate was heated with selenium (6 g), first at 220° for 1 hour and then at 295° for 40 h. The dehydrogenated product was isolated by chloroform extraction of the reaction mixture, followed by vacuum distillation. The distillate

crystallized on standing (1.5 g *7-methoxy-1-methyl-naphthalene*, 29%), m.p. 45° (lit. [19]: m.p. 47 to 48°). NMR. ($CDCl_3$ solution): Peaks at 2.64 ppm (3H, *s*, $-CH_3$), 3.93 ppm (3H, *s*, $-OCH_3$), and 7.1 to 7.9 ppm (6H, aromatic multiplet).

7-Methoxy-1-methyl-naphthalene (1.5 g, 0.0087 mole) was heated with acetic acid (20 ml) and hydrobromic acid (48%, 12 ml) for 1 hour. After evaporating the excess acetic and hydrobromic acid, the residue was treated with water. The product was then isolated *via* chloroform extraction and subsequent chromatography [SiO_2 (50 g), column packed in petroleum ether (b.p. 60–90°) and eluted with petroleum ether/benzene mixtures with increasing benzene content (0–100%)]. The chromatographed product was then vacuum distilled and yielded the pure solid *8-methyl-2-naphthol* (0.72 g, 53%), m.p. 61° (lit. [19]: m.p. 70–71°). NMR. ($CDCl_3$ solution): Peaks at 2.50 ppm (3H, *s*, $-CH_3$), 5.42 ppm (1H, *s*, –OH), and 6.9 to 7.8 ppm (6H, aromatic multiplet). IR.: ν_{max} (nujol) 3300 cm^{-1} (OH).

1.2. *8-Ethyl-2-naphthol.* 1-Ethyl-7-methoxy-naphthalene was synthesized in the same way as the methyl derivative. The *Grignard* reagent (prepared from ethyl bromide 7 g, 0.064 mole) was reacted with the tetralone (5 g, 0.028 mole). Dehydration, dehydrogenation with selenium (6.5 g) and chromatography yielded *1-ethyl-7-methoxy-naphthalene* (3.2 g, 60%). This product was vacuum distilled to give the pure substance (2.95 g, 56%) as a light oil. NMR. ($CDCl_3$ solution): Peaks at 1.38 ppm (3H, *t*, J = 7 cps, $-CH_3$), 3.08 ppm (2H, *q*, J = 7 cps, $-CH_2-$), 3.94 ppm (3H, *s*, $-OCH_3$), and 7.1 to 7.9 ppm (6H, aromatic multiplet).

The naphthol ether (2.95 g, 0.016 mole) was split as described and yielded, after the usual column chromatography and distillation, the pure *ethylnaphthol* (2.0 g, 73%), which crystallized on standing, m.p. 85°. NMR. ($CDCl_3$ solution): Peaks at 1.26 ppm (3H, *t*, J = 7 cps, $-CH_3$), 2.90 ppm (2H, *q*, J = 7 cps, $-CH_2-$), 5.40 ppm (1H, *s*, –OH), and 6.9 to 7.8 ppm (6H, aromatic multiplet). IR.: ν_{max} (nujol) 3210 cm^{-1} (OH).

$C_{12}H_{12}O$ Calc. C 83.69 H 7.02% Found C 83.81 H 7.07%

1.3. *8-Isopropyl-2-naphthol.* Preparation as above, using a larger excess of *Grignard* reagent [prepared from isopropyl bromide (11 ml, 0.117 mole)] over ketone (5 g, 0.028 mole). In this case the reaction product was separated from residual ketone by column chromatography [SiO_2 (45 g), column packed in petroleum ether (60–90°) and eluted with petroleum ether/benzene mixtures with increasing benzene content (0–100%)], to yield the *3,4-dihydro-1-isopropyl-7-methoxy-naphthalene* (0.9 g) as an oil. NMR. ($CDCl_3$ solution): Peaks at 1.14 ppm (6H, *d*, J = 7 cps, 2× $-CH_3$), 2.0 to 2.9 ppm (5H, *m*, 2×$-CH_2-$, $-CH<$), 3.80 ppm (3H, *s*, $-OCH_3$), 5.92 (1H, *t*, broad, J = 5 cps, vinylic H), and 6.6 to 7.2 ppm (3H, *m*, aromatic protons). Dehydrogenation with selenium (1.5 g) and chromatography gave *1-isopropyl-7-methoxy-naphthalene* (0.3 g, 5.3%) as an oil. NMR. ($CDCl_3$ solution): Peaks at 1.38 ppm (6H, *d*, J = 7 cps, 2×$-CH_3$), 3.58 ppm (1H, *m*, J = 7 cps, $-CH<$), 3.90 ppm (3H, *s*, $-OCH_3$), and 7.0 to 7.8 ppm (6H, aromatic multiplet).

The ether (2.0 g, 0.01 mole) was split as usual. Chromatography and vacuum distillation yielded the pure *8-isopropyl-2-naphthol* (0.7 g, 35%) as an oil. NMR. ($CDCl_3$ solution): Peaks at 1.32 ppm (6H, *d*, J = 7 cps, 2×$-CH_3$), 3.51 ppm (1H, *m*, J = 7 cps, $-CH<$), 5.48 ppm (1H, *s*, –OH), and 7.0 to 7.9 ppm (6H, aromatic multiplet). IR.: ν_{max} (liq. film) 3320 cm^{-1} (OH).

$C_{13}H_{14}O$ Calc. C 83.83 H 7.58% Found C 83.78 H 7.83%

1.4. *8-Phenyl-2-naphthol.* The method is the same as above, using bromobenzene (18 g, 0.115 mole) and the tetralone (5 g, 0.028 mole). Distillation and chromatography gave the *3,4-dihydro derivative* (4.5 g). NMR. ($CDCl_3$ solution): Peaks at 2.35 ppm (2H, *m*, $-CH_2-CH=$), 2.77 ppm (2H, *t*, J = 7 cps, ar-CH_2-), 3.63 ppm (3H, *s*, $-OCH_3$), 6.07 ppm (1H, *t*, J = 5 cps, $-CH=$), and 6.5 to 7.4 ppm (8H, aromatic multiplet). Selenium dehydrogenation followed by chromatography yielded *7-methoxy-1-phenyl-naphthalene* (3.2 g, 48%) as an oil. NMR. ($CDCl_3$ solution): Peaks at 3.72 ppm (3H, *s*, $-OCH_3$), and 7.0 to 7.9 ppm (11H, aromatic multiplet).

Demethylation of the methyl ether was accomplished as usual. The oily product (1.35 g *8-phenyl-2-naphthol*, 45%) was purified by chromatorgraphy and vacuum distillation. NMR ($CDCl_3$ solution): Peaks at 5.06 ppm (1H, *s*, –OH), 7.38 ppm (5H, *s*, $-C_6H_5$), and 6.9 to 7.9 ppm (6H, aromatic multiplet). IR.: ν_{max} (liq. film) 3330 cm^{-1} (OH).

$C_{16}H_{12}O$ Calc. C 87.24 H 5.49% Found C 87.06 H 5.56%

Attempts to synthesize the *8-(2'-pyridyl)-* and *8-(t-butyl)-2-naphthols* by this route were not successful.

1.5. *8-Chloro-2-naphthol.* 8-Amino-2-naphthol (16 g, 0.1 mole) was treated, first with water (100 ml), then with a solution of sodium nitrite (7.05 g, 0.102 mole) and copper sulfate (0.5 g) in water (25 ml), and lastly, at 0°, with concentrated hydrochloric acid (60 ml) [17]. The resulting diazonium salt solution was reacted with a solution of copper(I) chloride (15 g) in concentrated hydrochloric acid (100 ml) at 60°. The product was isolated by ether extraction and chromatographed [SiO_2 (150 g), column packed in petroleum ether (60–90°) and eluted with mixtures of petroleum ether and benzene with increasing benzene content (0–100%)]. The chromatographed naphthol was recrystallised from petroleum ether to yield the pure product (2.3 g, 12.8%), m.p. 100–101° (lit. [21]: m.p. 101°). NMR. ($CDCl_3$ solution): Peaks at 5.41 ppm (1H, *s*, –OH) and 6.9 to 7.8 ppm (6H, aromatic multiplet).

1.6. *8-Bromo-2-naphthol.* This compound was prepared as described above, using copper(I) bromide and concentrated hydrobromic acid (48%). The pure product (2.4 g, 10.7%) crystallised from petroleum ether, m.p. 112–113° (lit. [22]: m.p. 113–114°). NMR. ($CDCl_3$ solution): Peaks at 5.62 ppm (1H, *s*, –OH) and 7.0 to 7.9 ppm (6H, aromatic multiplet). IR.: ν_{max} (nujol) 3330 cm^{-1} (OH). Mass spectrum: M^+ at *m/e* 222/4.

1.7. *8-Iodo-2-naphthol.* This derivative was also prepared as above, utilising potassium iodide and dilute sulfuric acid (4N). The pure compound (3.3 g, 12.1%) was recrystallised from petroleum ether: m.p. 109°. NMR. ($CDCl_3$ solution): Peaks at 5.50 ppm (1H, *s*, –OH) and 6.9 to 8.2 ppm (6H, aromatic multiplet). IR.: ν_{max} (nujol) 3330 cm^{-1} (OH). Mass spectrum: M^+ at *m/e* 270.

$C_{10}H_7IO$ Calc. C 44.47 H 2.61% Found C 44.36 H 2.60%

1.8. *3-Phenanthrol.* This compound was synthesized via phenanthrene-3-sulfonic acid. The latter was prepared from phenanthrene (50 g, 0.28 mole) in the usual way [23]. The pure potassium salt of the sulfonic acid (6.5 g, 7.8%, 0.022 mole) was treated with molten potassium hydroxide [24], from which mixture, after distillation and recrystallisation from petroleum ether (60–90°), the pure phenanthrol (2.9 g, 68%) was obtained, m.p. 121° (lit. [24]: m.p. 122–123°). NMR. ($CDCl_3$ solution): Peaks at 5.0 ppm (1H, *s*, –OH), 7.1 (1H, *q*, $J_{1,2} = 9$, $J_{2,4} = 2.5$ cps, H–C2), 7.4 to 8.0 ppm (7H, aromatic multiplet), and 8.45 ppm (1H, *m*, H–C5). IR.: ν_{max} (nujol) 3280 cm^{-1} (OH).

1.9. *7-Hydroxy-1-naphthoic acid.* This compound was synthesized starting from 8-aminonaphthalene-2-sulfonic acid (15 g, 0.064 mole). The method described by *Royle & Schedler* [25] was used, except that the intermediate products were not isolated. Instead, the crude solutions of the intermediates were evaporated to dryness and these residues were used for the following steps. This resulted in an increase in yield. The pure hydroxynaphthoic acid was crystallised from water (1.87 g, 15%), m.p. 253° (lit. [25]: m.p. 253–254°). NMR. [$(CD_3)_2SO$ solution]: Peaks at 7.19 ppm (1H, *q*, $J_{3,4} = 9$, $J_{1,3} = 2.5$ cps, H–C3), 7.36 ppm (1H, *q*; $J_{5,6}$, $J_{6,7} = 8$, 7.5 cps; H–C6), 8.37 ppm (1H, *d*, $J_{1,3} = 2.5$ cps, H–C1), and 7.7 to 8.3 ppm (3H, aromatic multiplet). IR.: ν_{max} (KBr) 3320 (OH), 1680 cm^{-1} (C=O). Mass spectrum: M^+ at *m/e* 188.

1.10. *8-(2'-Pyridyl)-2-naphthol.* 8-Amino-2-naphthol (63.6 g, 0.4 mole) was acetylated with acetic anhydride (120 g, 1.16 mole) and sodium acetate (33 g, 0.4 mole) in acetic acid (200 ml) at 100°. After evaporation of the excess acetic acid and anhydride, the residue was treated with ice and water. The oily crude product was crystallized from ethyl acetate to yield the pure *acetylamino-acetoxynaphthalene* (19.6 g, 20%), m.p. 182°. This material (19.0 g, 0.078 mole) was now nitrosated with acetic acid (200 ml), acetic anhydride (100 ml), sodium acetate (15 g), phosphorus pentoxide (1 g) and nitrosyl chloride (6.5 g, 0.1 mole) at 8°. The mixture was then poured into ice and water and the precipitated, slightly wet N-nitroso derivative (26 g, ca. 100%) was used without further purification. It was slowly added to pyridine (200 ml) at room temperature. Gradual heating after completion of the addition caused a lively reaction with evolution of nitrogen. After standing overnight at 80°, excess pyridine was evaporated and the residue extracted with a boiling mixture of hydrochloric acid (20 ml), methanol (50 ml) and water (100 ml). This was followed by further extraction with dilute hydrochloric acid (10%, 1500 ml). The combined extracts were washed with chloroform and then neutralized with sodium carbonate. The resulting suspension was thoroughly extracted with chloroform, the extract evaporated and chromatographed [SiO_2 (100 g), column packed and eluted with chloroform]. This yielded, after recrystallisation from ethyl acetate, the required product (0.45 g, 2.6%), m.p. 207–208°. NMR. [$(CD_3)_2SO$ solution]: Peaks at

7.1 to 8.1 ppm (9H, aromatic multiplet) and 8.86 ppm (1H, *m*, α-H of pyridine nucleus). IR.: ν_{max} (nujol) 3020 cm^{-1} (OH). Mass spectrum: M^+ at *m/e* 221.

2. Syntheses of azo compounds. – Sulfanilic acid (0.25 g, 0.0015 mole) was diazotized with conc. HCl (0.5 ml) and $NaNO_2$ (0.11 g, 0.0016 mole) in water (20 ml) at 0°. This mixture was mixed with a solution of 8-methyl-2-naphthol (0.22 g, 0.0014 mole) and sodium hydroxide (0.5 g) in water (20 ml). After completion of the reaction and acidification (to about pH 5), the precipitated dye was filtered off and recrystallized from methanol (0.3 g, 59%). NMR [$(CD_3)_2SO$]: Peaks at 2.88 ppm (3H, *s*, $-CH_3$), 6.86 ppm (1H, *d*, J = 10 cps, H–C3 of naphthalene nucleus), and 7.4 to 8.2 ppm (8H, aromatic multiplet). UV.: λ_{max} (water) 480, 415 (*s*) and 305 nm.

All the other azo compounds were synthesized and characterized similarly, see [6].

3. Deuterations. – 3.1. *1-[²H]-8-(2'-Pyridyl)-2-naphthol.* 8-Pyridyl-2-naphthol (0.11 g, 0.0005 mole) was treated with sodium hydroxide (0.015 g, 0.00037 mole) in deuterium oxide (10 g) under nitrogen at 110° for 5 days. Isolation by acidification and chloroform extraction, and recrystallisation from ethyl acetate gave the deuterated napthol (0.06 g, 54%), NMR. [$(CD_3)_2SO$]: Peaks at 7.20 ppm (1H, *d*, J = 8.5 cps, H–C3 of naphthalene nucleus), 7.3 to 8.2 ppm (7H, aromatic multiplet), and 8.83 ppm (1H, *m*, α-H of pyridine nucleus).

3.2. *1-[²H]-8-Phenyl-2-naphthol.* 8-Phenyl-2-naphthol (0.44 g, 0.002 mole) was dissolved in a solution of sodium hydroxide (0.04 g, 0.001 mole) in deuterium oxide (20 g) and dioxane (20 ml). The mixture was sealed under nitrogen and heated at 110° for 5 days. Isolation by acidification, chloroform extraction and subsequent vacuum distillation yielded the deuterated phenylnaphthol (0.3 g, 68%, about 50% deuteration). NMR. ($CDCl_3$ solution): Peaks at 5.17 ppm (1H, *s*, –OH), 7.22 ppm (1H, *m*, superposition of the quartet of the undeuterated compound and the doublet of the deuterated derivative, H–C3 of naphthalene nucleus), and 7.25 to 8.1 ppm (ca. 10H, aromatic multiplet).

4. Acidity constants of the naphthol derivatives (see Table 3). – The constants were determined spectrophotometrically [26], to within ± 0.02 units. The molar extinction coefficients of the naphthols and the naphtholates were measured in 0.2N hydrochloric acid and 0.2N sodium hydroxide solutions, respectively. The concentration of the naphthol derivative was 1×10^{-4}M, the same as was used in the kinetic determinations. The ionic strength of the solutions was 0.2 and the temperature 20°.

Table 3. *Acidity constants of the naphthol derivatives*

Naphthol derivatives	pK	Wavelength (nm)
8-Methyl-2-naphthol	9.42	353
8-Ethyl-2-naphthol	9.54	355
8-Isopropyl-2-naphthol	9.52	357
8-Phenyl-2-naphthol	9.38	360
8-Chloro-2-naphthol	8.96	355
8-Bromo-2-naphthol	8.94	362
8-Iodo-2-naphthol	8.98	362
8-(2'-Pyridyl)-2-naphthol	4.95, 9.36	354, 360
7-Hydroxy-1-naphthoic acid	3.69, 9.60	280, 363
3-Phenanthrol	9.28	373

5. Kinetics. – 5.1. *Method of measurement.* The variation of the concentration of the reaction product was determined photometrically. The actual measurement was carried out on a *Beckman* DBG spectrophotometer, with the reaction mixture in the cuvette. The constant reaction temperature was 20.0° ± 0.5°C. The ionic strength of the solution was maintained at 0.2. The buffer capacity was chosen to avoid a pH variation larger than 0.02 units during the reaction. The coupling component (*i.e.* the naphthol derivative) was used in 10 times excess over the diazotized sulfanilic acid, the concentration of which was either 1×10^{-5}M or 5×10^{-6}M (the latter indicated in tables 4

and 5). That this excess suffices to bring about a pseudo first-order reaction was confirmed by the excellent straight lines obtained in *Guggenheim* evaluations [27]. The pH value of the reaction solutions was determined after completion of the reaction and was taken to represent the pH during the reaction within 0.02 units. In the tabulations below k_{pfo} represents the measured pseudo first-order rate constant, and k the pH-independent second-order rate constant (derived from k_{pfo}, see [5]).

5.2. *Results from coupling reactions* (s. Tables 4 and 5):

Table 4. *Diazo coupling reactions of the phenolic derivatives*

Phenolic derivative, Conditions	pH	Pyridine conc. (mole/l)	k_{pfo} (min^{-1})	$k \times F$ ($l \cdot mole^{-1} \cdot min^{-1}$)	
8-Methyl-	6.56	0.00	0.52	3.74	$F = 10^{-6}$
2-naphthol,	6.56	0.00	0.52	3.74	
measured at	6.57	0.00	0.52	3.68	
480 nm	6.59	1.92×10^{-3}	0.65	4.43	
	6.58	1.92×10^{-3}	0.68	4.74	
	6.58	1.92×10^{-3}	0.66	4.58	
	6.61	4.82×10^{-3}	0.84	5.46	
	6.61	4.82×10^{-3}	0.83	5.39	
	6.61	4.82×10^{-3}	0.85	5.49	
	6.65	9.67×10^{-3}	1.08	6.38	
	6.64	9.66×10^{-3}	1.06	6.38	
	6.71	1.94×10^{-2}	1.40	7.17	
	6.71	1.94×10^{-2}	1.35	6.94	
	6.84	4.89×10^{-2}	2.02	7.68	
	6.83	4.89×10^{-2}	2.13	8.29	
	6.84	4.89×10^{-2}	2.02	7.70	
8-Ethyl-	6.42	0.00	0.25	3.29	$F = 10^{-6}$
2-naphthol,	6.42	0.00	0.25	3.32	
measured at	6.42	0.00	0.25	3.32	
482 nm	6.45	1.90×10^{-3}	0.39	4.82	
	6.45	1.90×10^{-3}	0.40	4.98	
	6.45	1.90×10^{-3}	0.39	4.83	
	6.49	4.76×10^{-3}	0.58	6.50	
	6.49	4.76×10^{-3}	0.57	6.40	
	6.49	4.76×10^{-3}	0.58	6.47	
	6.54	9.57×10^{-3}	0.78	7.77	
	6.54	9.57×10^{-3}	0.81	8.09	
	6.54	9.57×10^{-3}	0.80	8.02	
	6.62	1.93×10^{-2}	1.17	9.74	
	6.62	1.93×10^{-2}	1.14	9.47	
	6.77	4.87×10^{-2}	1.91	11.23	
	6.77	4.87×10^{-2}	1.75	10.34	
	6.77	4.87×10^{-2}	1.76	10.38	
8-Isopropyl-	6.43	0.00	0.11	2.68	$F = 10^{-6}$
2-naphthol,	6.43	0.00	0.12	2.85	
measured at	6.45	1.90×10^{-3}	0.21	4.82	
484 nm,	6.45	1.90×10^{-3}	0.20	4.73	
[naphthol] $= 5 \cdot 10^{-5}$ M	6.45	1.90×10^{-3}	0.20	4.77	
[diaz.salt] $= 5 \cdot 10^{-6}$ M	6.50	4.77×10^{-3}	0.31	6.52	
	6.50	4.77×10^{-3}	0.31	6.53	

Table 4 (continued)

Phenolic derivative, Conditions	pH	Pyridine conc. (mole/l)	k_{pfo} (min^{-1})	$k \times F$ ($l \cdot mole^{-1} \cdot min^{-1}$)	
	6.50	4.77×10^{-3}	0.32	6.60	
	6.54	9.57×10^{-3}	0.44	8.37	
	6.54	9.57×10^{-3}	0.45	8.59	
	6.54	9.57×10^{-3}	0.43	8.24	
	6.61	1.93×10^{-2}	0.64	10.43	
	6.61	1.93×10^{-2}	0.63	10.29	
	6.61	1.93×10^{-2}	0.65	10.49	
	6.77	4.87×10^{-2}	1.05	11.85	
	6.77	4.87×10^{-2}	1.05	11.80	
	6.77	4.87×10^{-2}	1.06	11.93	
8-Phenyl-	6.44	0.00	0.56	4.86	$F = 10^{-6}$
2-naphthol,	6.44	0.00	0.52	4.50	
measured at	6.44	0.00	0.56	4.85	
490 nm	6.45	4.74×10^{-4}	0.56	4.76	
	6.45	4.74×10^{-4}	0.57	4.89	
	6.45	4.74×10^{-4}	0.57	4.85	
	6.46	9.49×10^{-4}	0.58	4.80	
	6.46	9.49×10^{-4}	0.61	5.04	
	6.46	9.49×10^{-4}	0.61	5.06	
	6.48	1.90×10^{-3}	0.64	5.12	
	6.47	1.90×10^{-3}	0.63	5.16	
	6.50	4.77×10^{-3}	0.70	5.34	
	6.51	4.77×10^{-3}	0.74	5.47	
	6.51	4.77×10^{-3}	0.72	5.32	
	6.56	9.59×10^{-3}	0.78	5.16	
	6.56	9.59×10^{-3}	0.78	5.13	
8-Chloro-	6.52	0.00	0.29	7.92	$F = 10^{-5}$
2-naphthol,	6.52	0.00	0.29	8.02	
measured at	6.52	0.00	0.29	7.96	
474 nm	6.54	9.57×10^{-4}	0.34	9.00	
	6.54	9.57×10^{-4}	0.34	8.99	
	6.54	9.57×10^{-4}	0.34	8.98	
	6.56	1.92×10^{-3}	0.38	9.68	
	6.56	1.92×10^{-3}	0.38	9.53	
	6.56	1.92×10^{-3}	0.38	9.61	
	6.59	4.81×10^{-3}	0.42	9.97	
	6.58	4.80×10^{-3}	0.43	10.26	
	6.63	9.65×10^{-3}	0.53	11.27	
	6.62	9.64×10^{-3}	0.51	11.14	
	6.64	9.66×10^{-3}	0.51	10.69	
	6.71	1.94×10^{-2}	0.67	11.91	
	6.70	1.94×10^{-2}	0.64	11.71	
8-Bromo-	6.46	0.00	0.081	4.89	$F = 10^{-5}$
2-naphthol,	6.46	0.00	0.084	5.09	
measured at	6.49	1.92×10^{-3}	0.122	6.90	
484 nm	6.49	1.92×10^{-3}	0.116	6.53	
[naphthol] = $5 \cdot 10^{-5}$ M	6.52	4.85×10^{-3}	0.150	7.91	
[diaz. salt] = $5 \cdot 10^{-6}$ M	6.52	4.85×10^{-3}	0.150	7.92	

Table 4 (continued)

Phenolic derivative, Conditions	pH	Pyridine conc. (mole/l)	k_{pfo} (min^{-1})	$k \times F$ ($l \cdot mole^{-1} \cdot min^{-1}$)	
	6.57	9.65×10^{-3}	0.19	8.98	
	6.57	9.65×10^{-3}	0.20	9.19	
	6.64	1.94×10^{-2}	0.26	10.21	
	6.64	1.94×10^{-2}	0.25	9.80	
	6.79	4.90×10^{-2}	0.39	11.00	
	6.79	4.90×10^{-2}	0.38	10.66	
8-Iodo-	6.56	0.00	0.24	6.32	$F = 10^{-5}$
2-naphthol,	6.56	0.00	0.25	6.51	
measured at	6.56	0.00	0.25	6.70	
495 nm	6.60	4.81×10^{-3}	0.45	10.94	
	6.62	4.82×10^{-3}	0.46	10.47	
	6.61	4.82×10^{-3}	0.46	10.89	
	6.65	9.67×10^{-3}	0.59	12.55	
	6.64	9.66×10^{-3}	0.57	12.62	
	6.64	9.66×10^{-3}	0.57	12.53	
	6.71	1.94×10^{-2}	0.71	13.50	
	6.71	1.94×10^{-2}	0.72	13.64	
	6.84	4.89×10^{-2}	0.99	13.79	
	6.83	4.89×10^{-2}	1.05	15.00	
	6.97	9.83×10^{-2}	1.62	16.78	
	6.98	9.84×10^{-2}	1.45	14.65	
3-Phenanthrol,	6.59	0.00	0.050	2.43	$F = 10^{-5}$
measured at	6.59	0.00	0.052	2.57	
525 nm	6.61	1.93×10^{-3}	0.072	3.39	
[phenanthrol] =	6.61	1.93×10^{-3}	0.073	3.42	
$5 \cdot 10^{-5}$ M	6.61	1.93×10^{-3}	0.073	3.43	
[diaz.salt] = $5 \cdot 10^{-6}$ M	6.63	4.83×10^{-3}	0.099	4.43	
	6.63	4.83×10^{-3}	0.097	4.35	
	6.67	9.68×10^{-3}	0.135	5.49	
	6.66	9.67×10^{-3}	0.132	5.50	
	6.74	1.95×10^{-2}	0.183	6.36	
	6.74	1.95×10^{-2}	0.181	6.29	
	6.74	1.95×10^{-2}	0.183	6.37	
	6.87	4.90×10^{-2}	0.290	7.49	
	6.87	4.90×10^{-2}	0.287	7.41	
7-Hydroxy-	6.74	0.00	0.95	6.89	$F = 10^{-6}$
1-naphthoic acid,	6.76	0.00	0.92	6.38	
measured at	6.87	1.96×10^{-3}	1.34	7.21	
484 nm	6.88	1.96×10^{-3}	1.29	6.78	
	7.00	4.92×10^{-3}	1.64	6.55	
	6.98	4.92×10^{-3}	1.87	7.81	
	7.12	9.88×10^{-3}	2.42	7.33	
	7.12	9.88×10^{-3}	2.46	7.45	
	7.28	1.99×10^{-2}	3.25	6.82	
	7.27	1.98×10^{-2}	3.36	7.07	

Table 5. *Determination of intramolecular base catalysis*

Compound	pH	k_{pfo} (min^{-1})	$k \times 10^{-6}$ ($l \cdot mole^{-1} \cdot min^{-1}$)
1-[^{1}H]-8-(2'-Pyridyl)-2-naphthol	6.40	0.24	2.17
	6.40	0.24	2.21
1-[^{2}H]-8-(2'-Pyridyl)-2-naphthol	7.18	1.41	2.15
	7.18	1.56	2.38
	6.41	0.24	2.17
	6.41	0.30	2.68
1-[^{1}H]-8-Phenyl-2-naphthol	6.45	0.28	4.74
	6.45	0.28	4.78
	6.45	0.28	4.80
1-[^{2}H]-8-Phenyl-2-naphthol	6.45	0.20	3.44
	6.45	0.21	3.56
	6.45	0.20	3.47

These determinations were made at 490 nm (for the phenylnaphthol) and 487 nm (for the pyridylnaphthol). The concentration of the naphthols was 5×10^{-6} M and that of the diazonium salt 5×10^{-6} M.

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