Dealkylation in Connection with Diazo Coupling of Phenol Ethers[1]

BY J. F. BUNNETT AND G. BROOKE HOEY

The literature contains conflicting statements about the coupling of diazonium salts with phenol ethers such as methyl 1-naphthyl ether. Some responsible authors report the predominant formation of dealkylated products (e.g., II) while others describe only normal coupling products with the alkyl group retained (e.g., I). Some believe that dealkylation occurs during coupling while others think it occurs after coupling. We have conducted a systematic study of these phenomena using a photometric method of product analysis. Coupling is found to be a relatively slow reaction at room temperature. Dealkylation is shown to occur *after* coupling. It is shown that dealkylation is an acid-catalyzed hydrolysis which can be avoided by conducting coupling either in the presence of excess sodium acetate or in a strictly anhydrous medium.

In 1913, Meyer and Lenhardt[2] reported that sufficiently reactive diazonium salts will couple with phenol ethers. Subsequent publications from Meyer's[3] and v. Auwers'[4] laboratories extended knowledge of this subject, and further examples have been reported by other authors. These coupling reactions generally gave azoethers as products, but they sometimes yielded the corresponding azophenols with loss of the alkyl group. For example, the reaction of p-nitrobenzenediazonium ion with methyl 1-naphthyl ether (equation 1) was reported by v. Auwers and Michaelis[4a] and by Meyer and Lenhardt[2] to yield methyl 4-(p-nitrophenylazo)-1-naphthyl ether (I) without demethylation, but by Hurd and Bonner[5] to furnish a large proportion of the demethylation product 4-(p-nitrophenylazo)-1-naphthol (II).
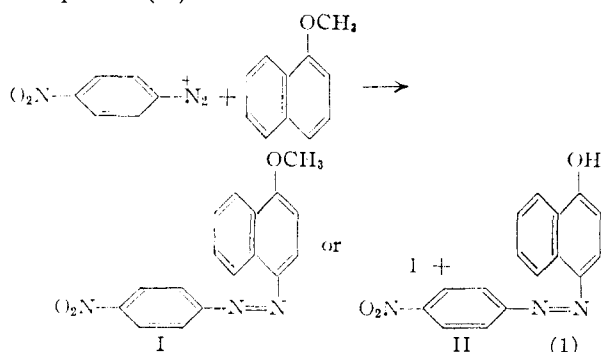
Other examples of coupling with dealkylation were reported both in the earlier papers[3,4] and by later authors.[6-9] De*phenyl*ation also has been observed; from the action of 2,4-dinitrobenzenediazonium ion on phenyl 1-naphthyl ether both the normal coupling product, phenyl 4-(2,4-dinitrophenylazo)-1-naphthyl ether, and the dephenylation product, 4-(2,4-dinitrophenylazo)-1-naphthol, have been obtained.[3,9b] Dealkylation has been observed only rarely in connection with coupling of

monocyclic aryl ethers (e.g., benzene derivatives), frequently with coupling of naphthyl ethers and exclusively with coupling of 9-methoxyanthracene.[3]

It is pertinent to ask whether dealkylation occurs before, during or after coupling. The stability of phenol ethers in the glacial or aqueous acetic acid media customarily used for coupling is obvious and the first alternative therefore has been rejected. Most chemists who have dealt with this question have concluded that dealkylation occurs *during* coupling; some have stated this opinion forthrightly[3,4a,7] and others by inference.[5,6] Ettel, et al.,[8] on the other hand, averred that dealkylation occurred subsequent to coupling. They supported their position by showing that the azoethers, the products of coupling without dealkylation, are rapidly dealkylated by boiling dilute mineral acid in acetic acid. This observation also was made by Meyer, et al.,[3] who did not, however, consider it relevant to the matter of dealkylation with coupling. In actual fact, the Czech workers[8] did not demonstrate that the azoethers were cleaved under the true conditions of coupling, since boiling the reaction mixture was not part of their coupling procedure.

A number of authors[2,3,4,10-13] have discussed the mechanism of the dealkylation, mostly on the assumption that dealkylation occurs *during* coupling, and a variety of interesting suggestions have been put forth. At the same time some recognized that the chronological relationship of dealkylation to coupling was not well established. The need for further research has been pointed out.[10]

We have conducted a systematic investigation of this phenomenon with particular attention to the reaction represented in equation 1. Our conclusions are that dealkylation occurs *after* coupling and that the cleavage reaction is an acid-catalyzed hydrolysis. Dealkylation can, we find, be avoided by conducting the coupling reaction either in the presence of excess base or in strictly anhydrous acetic acid.

In all previous investigations of this phenomenon, the products formed have been determined by actual isolation and weighing. The advantage of directness in this procedure is offset by the time it

(1) Research supported by the National Science Foundation, via grant No. NSF-G2359.

(2) K. H. Meyer and S. Lenhardt, Ann., 398, 74 (1913).

(3) K. H. Meyer, A. Irschick and H. Schlösser, Ber., 47, 1741 (1914).

(4) (a) K. v. Auwers and F. Michaelis, ibid., 47, 1281 (1914); (b) K. v. Auwers and E. Borsche, ibid., 48, 1716 (1915).

(5) C. D. Hurd and W. A. Bonner, THIS JOURNAL, 71, 3241 (1949).

(6) G. B. Jambuserwala and F. A. Mason, J. Soc. Dyers Col., 46, 339 (1930).

(7) J. van Alphen and G. Drost, Rec. trav. chim., 68, 54 (1949).

(8) V. Ettel, J. Weichet and J. Spacil, Coll. Czech. Chem. Comm., 15, 204 (1950).

(9) (a) J. Haginiwa and I. Murakoshi, J. Pharm. Soc. Japan, 71, 1460 (1951); (b) 73, 287 (1953).

(10) K. H. Saunders, "The Aromatic Diazo-Compounds and Their Technical Applications," 2nd ed., Edward Arnold and Co., London, England, 1949, p. 218.

(11) S. N. Boyd, in H. A. Lubs, "The Chemistry of Synthetic Dyes and Pigments," Reinhold Publishing Corp., New York, N. Y., 1955, p. 106.

(12) K. Venkataraman, "The Chemistry of Synthetic Dyes," Vol. I, Academic Press, Inc., New York, N. Y., 1952, p. 429.

(13) H. Gilman and D. R. Swayampati, THIS JOURNAL, 78, 2163 (1956).

requires, by the difficulty of isolating products quantitatively and by the possibility that the products might undergo chemical change during isolation. Also, in order to get amounts of products convenient for isolation, it is necessary to conduct reactions in relatively concentrated solution from which some products, such as II, precipitate with resulting disturbance of concentration relationships. We have used a photometric method of product analysis which is much more satisfactory. This method depends on the fact that, although the spectra of I and II are similar in neutral solution, solutions of II in alcoholic alkali are blue (λ_{max} 600 mμ) while I in the same solvent is yellow-orange (λ_{max} 430 mμ). With this method of analysis, it has been possible to conduct coupling in dilute solution in which homogeneity is preserved throughout. In addition to the further advantages of speed and accuracy, the photometric method of analysis also allows the rate of the coupling reaction to be estimated since the reactants (the diazonium salt and the naphthyl ethers) are colorless in dilute solution in alcoholic alkali.

Results from a set of significant experiments are displayed in Table I. In these experiments the coupling of p-nitrobenzenediazonium sulfate with methyl 1-naphthyl ether was allowed to occur in 85.7% aqueous acetic acid solution under various conditions of acidity. Samples of the reaction mixture were analyzed at various times and so some insight into chronological relationships is provided.

Attention should first be paid to part A of Table I which concerns coupling carried out with no added base or acid other than a small amount of sulfuric acid (about 2.7×10^{-3} M) carried through from the preparation of the diazonium salt. It will be noted that under the conditions employed (room temperature, [methyl 1-naphthyl ether]$_0$ ca. 0.064 M, [ArN$_2$$^+$]$_0$ 2.25 $\times$ 10^{-4} M) coupling was rather slow, the maximum yield being obtained only after several hours of reaction. The product formed during the first three hours was almost exclusively I, the result of normal coupling without dealkylation. However, with the passage of time the dealkylated product II was formed at the expense of I and at the end of three days dealkylation was complete. It is thus shown that dealkylation follows coupling. The data of part A of Table I are displayed graphically in Fig. 1. The plot is a typical example of concentration–time relationships for a sequence of two first-order reactions.[14]

Part B of Table I shows what happens when coupling is carried out in the presence of a substantial amount (0.057 M) of sulfuric acid. The over-all rate of coupling is similar to that in part A, but the product after the first hour is mostly if not entirely that of dealkylation (II). This indicated that in this definitely acidic medium the normal product (I) is dealkylated soon after it is formed.

Parts C and D of Table I show the effect of buffering the coupling reaction with sodium acetate; the two parts differ in the concentration of sodium acetate employed. In these runs the normal product predominates even after three days time. It is evident that the dealkylation is an acid-catalyzed

(14) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1953, p. 154.

TABLE I

REACTION OF p-NITROBENZENEDIAZONIUM ION WITH METHYL 1-NAPHTHYL ETHER IN AQUEOUS ACETIC ACID[a]

Time, hr.	Absorbance of quenched samples At 430 mμ	At 600 mμ	Yields, % I	II	Total yield, %
A. With no added acid or base[b]					
0.35	0.037	0.016	19.1	3.5	22.6
0.97	.066	.015	34.2	3.2	37.4
1.65	.082	.014	40.9	3.0	43.9
2.10	.096	.014	49.6	3.0	52.6
2.58	.098	.010	50.6	2.1	52.7
3.15	.118	.025	61.9	5.5	67.4
23.60	.077	.211	39.8	46.2	86.0
45.40	.035	.332	17.8	71.4	89.2
74.20	− .005	.385	0.0	82.8	82.8
B. With added sulfuric acid (0.057 M)					
0.35	0.014	0.010	7.3	2.1	9.4
0.97	.025	.035	13.0	7.6	20.6
1.65	.024	.072	12.4	15.5	27.9
2.10	.022	.100	11.3	21.7	33.0
2.58	.026	.135	13.4	29.0	42.4
3.15	.027	.173	14.1	37.2	51.3
23.60	− .011	.446	0.0	96.0	96.0
45.40	− .023	.431	0.0	93.0	93.0
74.20	− .035	.430	0.0	93.0	93.0
C. With added sodium acetate (1.46 $\times$ 10^{-2} M)					
0.35	0.029	0.019	16.3	4.1	20.4
0.97	.063	.024	32.5	5.5	38.0
1.65	.078	.015	40.2	3.2	43.4
2.10	.080	.012	41.3	2.6	43.9
2.58	.098	.015	50.7	3.2	53.9
3.15	.110	.010	53.2	6.1	59.3
23.60	.132	.038	68.3	8.2	76.5
45.40	.120	.072	62.0	15.5	77.5
74.20	.106	.094	54.8	20.2	75.0
D. With added sodium acetate (7.32 $\times$ 10^{-2} M)					
0.35	0.023	0.014	11.9	3.0	14.9
0.97	.047	.010	24.3	2.1	26.4
1.65	.064	.010	33.1	2.1	35.2
2.10	.084	.015	44.0	3.2	47.2
2.58	.093	.006	48.0	1.2	49.2
3.15	.096	.005	49.6	1.1	50.7
23.60	.114	.020	59.1	4.3	63.4
45.40	.108	.036	55.3	8.7	64.0
74.20	.116	.054	60.0	11.7	71.7

[a] See Experimental for details of procedure; reaction (room) temperature was 27–30°. [b] Run A contained sulfuric acid, ca. $2.7 \times 10^{-3}M$, carried through from preparation of the diazonium solution.

process which is held to a minimum by addition of acetate ion, the strongest base possible in acetic acid solution. A small amount of dealkylation is, however, evident at the later times and it is interesting to note that the additional concentration of sodium acetate in part D was somewhat more effective in repressing this complication. Acetic acid itself apparently catalyzed dealkylation to a small extent in these runs.

That the normal coupling product I is dealkylated under conditions typically used for coupling was further established by exposing I to 85.7% aqueous acetic acid and to solutions of sodium acetate (0.0732 M), sulfuric acid (0.054 M) and hydrobromic acid (0.10 M) in this solvent. The results are
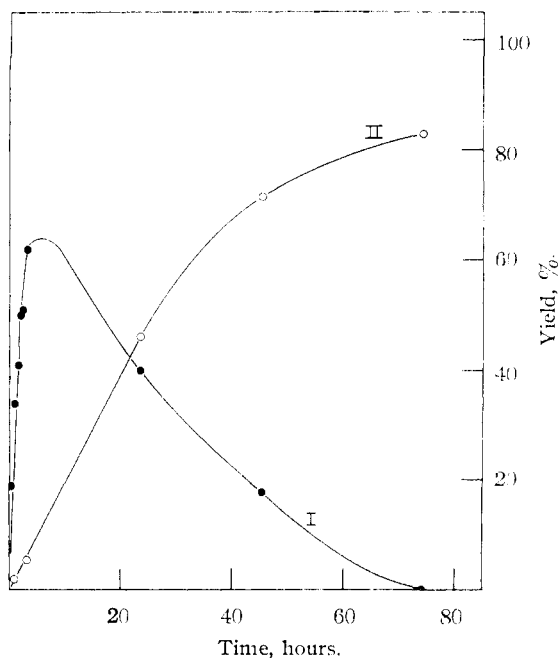
Fig. 1.—Yields at various times of normal (I) and dealkyl-
ated (II) products of coupling of p-nitrobenzenediazonium
ion with methyl 1-naphthyl ether in 85.7% acetic acid solu-
tion.

shown graphically in Fig. 2. The first three hours
of the experiment were devoted to preparing a solu-
tion of I in 85.7% acetic acid by shaking powdered
I with this solvent; it is clear that some dealkyla-
tion occurred during this period. The other chem-
icals then were added. The graph shows that the
two acids cause very rapid dealkylation. Plain
aqueous acetic acid causes some dealkylation, and
added sodium acetate is a protective agent.

In the experiment set forth in part B of Table I
no strong nucleophilic reagent was present. The
cleavage therefore appeared to be a hydrolysis, and
this led to the expectation that cleavage could be
avoided, regardless of the acidity, if coupling were
run in strictly anhydrous acetic acid. This ex-
pectation has been realized. Strictly anhydrous
acetic acid was prepared by refluxing stock "glacial"
acetic acid with excess acetic anhydride. In this
solvent, as shown in Table II, dealkylation did not
accompany coupling even when a substantial con-
centration of hydrochloric acid was present. Nor

TABLE II

COUPLING OF p-NITROBENZENEDIAZONIUM ION WITH
METHYL 1-NAPHTHYL ETHER IN ANHYDROUS ACETIC ACID
CONTAINING HYDROGEN CHLORIDE[a]

Time, hr.	Absorbance of quenched samples		Yields, %	
	At 430 mμ	At 600 mμ	I	II
0.78	0.039	0.011[b]	15.8	2.0[b]
3.00	.071	.008[b]	29.2	1.5[b]
6.00	.107	.010[b]	46.4	1.7[b]
25.50	.196	.021	81.7	3.7
44.61	.202	.027	83.5	4.7

[a] See Experimental for details of procedure: room tem-
perature ca. 30°; [HCl] in reaction solution ca. 0.12 M.
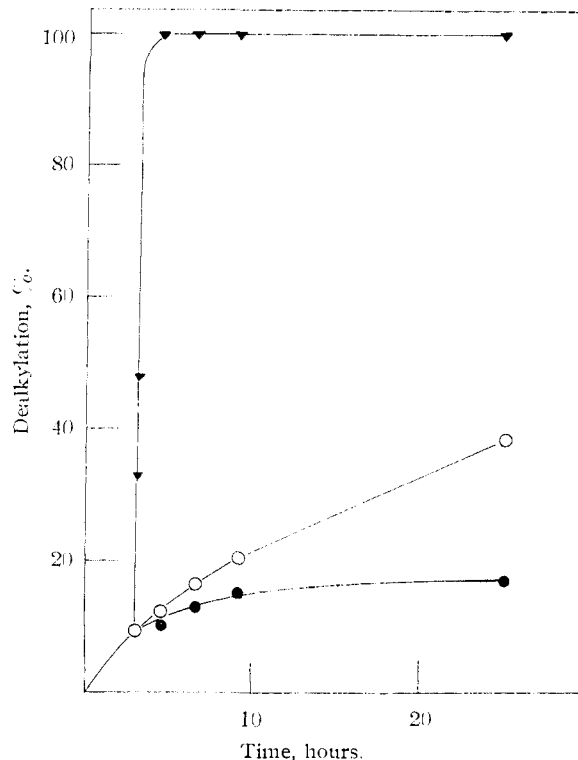[b] These figures are not considered to be significantly different
from zero.

Fig. 2.—Dealkylation of methyl 4-(p-nitrophenylazo)-1-
naphthyl ether (I) by various reagents in 85.7% acetic acid
solution: open circles, no added reagent; solid circles,
sodium acetate added (at time 3 hours); solid triangles,
hydrobromic or sulfuric acid added (at time 3 hours).
Experiment conducted at room temperature with photo-
metric determination of the extent of cleavage.

did the presence of added lithium chloride (0.1 M),
sodium bromide (0.05 M) or sodium acetate (0.05
M) cause dealkylation in strictly anhydrous acetic
acid (see Table III). The anions of these salts all
have marked nucleophilic reactivity, and it is sig-
nificant that they are ineffective in cleaving I.

The coupling of p-nitrobenzenediazonium ion
with ethyl and isopropyl 1-naphthyl ethers also has
been investigated, in both aqueous and anhydrous
acetic acid, and similar results have been obtained.
Results are set forth briefly in Table III which is a
resumé of all our experiments of this type except
those already presented in Tables I and II. It will
be noted that the ethyl and isopropyl ethers couple,
in unbuffered aqueous acetic acid, to give initially
an azo-ether which is slowly converted to the azo-
phenol II. In strictly anhydrous acetic acid an azo-
ether is formed and is stable in this medium.

It is of interest that coupling with methyl 1-
naphthyl ether in the presence of sodium bromide
in anhydrous acetic acid gave only 36% of I and no
II (see Table III). The yield did not increase be-
tween the 25.5-hour and the 44.6-hour samples, in-
dicating that a competing reaction forming a color-
less product was interfering. The competing reac-
tion is probably attack of bromide ion on p-nitro-
benzenediazonium ion to form p-bromonitroben-
zene.[15] That this reaction did not interfere in
85.7% acetic acid (Table III) is probably due to de-

(15) E. S. Lewis and W. H. Hinds, THIS JOURNAL, 74, 304 (1952).

TABLE III

RESUMÉ OF EXPERIMENTS ON COUPLING OF p-NITROBEN-
ZENEDIAZONIUM SULFATE WITH ALKYL 1-NAPHTHYL ETHERS
IN VARIOUS MEDIA[a]

Alkyl group in ether	Acetic acid in solvent, %	Added substance	Product formed	Max. time, hr.	Max. total yield, %
Methyl	85.7	None[b]	I, then II	20.5	94
		LiCl, 0.1 M^b	I, then II	20.5	94
		NaBr, 0.05 M^b	I, then II	20.5	96
		HCl, 0.11 M	II	20.5	80
Ethyl	85.7	None[b]	Azo-ether, then II	24.9	c
Isopropyl	85.7	None[b]	Azo-ether, then II	24.9	c
Methyl	100	None[b]	I	44.6	80
		LiCl, 0.1 M^b	I	44.6	94
		NaBr, 0.05 M^b	I[d]	44.6	36[d]
Ethyl	100	None[b]	Azo-ether	50.0	82
Isopropyl	100	None[b]	Azo-ether	50.0	89
Methyl	100	NaC₂H₃O₂, 0.05 M	I	118.4	60
Ethyl	100	NaC₂H₃O₂, 0.05 M	Azo-ether	118.4	68
Isopropyl	100	NaC₂H₃O₂, 0.05 M	Azo-ether	118.4	75
		None[b]	Azo-ether	118.4	92

[a] Each entry represents a separate run. These experiments are all of the general type of those in Tables I and II. All were conducted at room temperature (22–32°). [b] However, some H_2SO_4 (ca. 0.0027 M) carried through from the diazotization. [c] The yield was not accurately determined. [d] p-Bromonitrobenzene probably was formed also (see text).

celeration of this anion–cation reaction by change to a solvent of higher dielectric constant.

Dealkylation in the Literature.—We now know that dealkylation can be avoided if coupling is conducted: (a) in the presence of excess sodium acetate or (b) in truly anhydrous acetic acid, and that it can be held to a low level if (c) an aqueous acetic acid medium of low mineral acid content is used provided the product is removed from the coupling medium soon after being formed. In earlier work, conditions (a) appear to have been employed only in Meyer's initial research[2] in which no cases of dealkylation with coupling were observed.[16] In most previous work on this type of reaction, the aromatic amine (usually nitro-substituted) was diazotized in acetic acid containing sulfuric acid with an alkyl nitrite being the source of nitrous acid. The diazonium salt was precipitated by addition of ether, separated, redissolved in acetic acid and reprecipitated, and this cycle was repeated about two more times. The salt finally was dissolved in acetic acid in which medium the coupling was allowed to occur. Elaborate though it is, this procedure does not eliminate sulfuric acid from the eventual reaction mixture. The ether-precipitated diazonium salt is probably a bisulfate and may contain additional sulfuric acid of solvation; it has frequently been described as oily in nature. Furthermore, an equivalent of acid is liberated in the cou-

(16) Hurd and Bonner[5] obtained much dealkylation when reaction 1 was performed in a medium stated to be buffered with sodium acetate. However, the amount of sodium acetate they used was approximately equivalent to the amount of sulfuric acid carried through from the diazotization. Bearing in mind that in preparative work measurements of quantity are not ordinarily made with analytical balances and precision volumetric glassware, we deem it not improbable that sufficient sulfuric acid remained unneutralized to cause rapid dealkylation of I after coupling. Jambuserwala and Mason[8] observed dealkylation in some but not all of a number of couplings of various diazonium ions with 3-methoxy-2-naphthoic acid in aqueous solution "in presence of sodium carbonate." They gave no experimental details and it is not possible to judge the adequacy of their buffering.

pling reaction itself. In the relatively concentrated solutions used in preparative work the mineral acid introduced from these two sources may accumulate in concentration sufficient to cause relatively fast dealkylation. Many times the coupling mixture was allowed to stand overnight before the product was collected, thus providing time in which additional dealkylation might occur. That coupling without dealkylation often was observed, even in the formation of sensitive ethers, probably stems from the fortunate choice of conditions approaching (b) or (c).

The Mechanism of Dealkylation.—The mechanism of the facile acid-catalyzed hydrolytic cleavage of azo-ethers such as I is of interest. Several features of this process—the great sensitivity to dilute acid, the fact that phenyl ethers cleave readily, and the lack of requirement of strong nucleophilic reagents such as bromide or iodide ion—suggest it is to be differentiated from ordinary ether cleavage. The following mechanism is not improbable
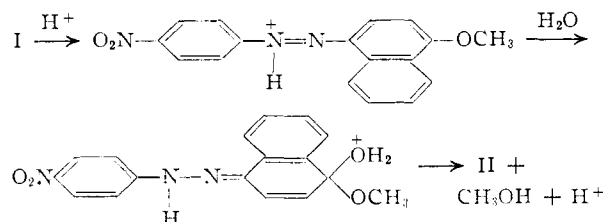
This question is now receiving our experimental attention.

Experimental

Materials. Acetic Acid.—Aqueous acetic acid (85.7%) was prepared by mixing six volumes of reagent grade glacial acetic acid with one volume of distilled water. Strictly anhydrous acetic acid was prepared by refluxing reagent grade glacial acetic acid with acetic anhydride (60 cc. per liter of acetic acid) for several hours in an apparatus protected by a calcium chloride drying tube. The cooled solvent was stored in a bottle with a buret attached in such a way that there was no exposure to the laboratory atmosphere during transfer from bottle to buret; openings to the room were protected by activated alumina drying tubes.

Methyl 1-naphthyl ether was purified by steam distilling the commercial product from alkali, extracting the distillate with ethyl ether, drying and evaporating the ether extract and finally distilling at reduced pressure. Material of b.p. 90–91° (2 mm.), n^{25}D 1.6210, was so obtained.

Isopropyl 1-naphthyl ether was prepared by the method of Dermer and Dermer.[17] Eastman Kodak Co. ethyl 1-naphthyl ether was used.

Reagent grade sodium acetate was fused in an evaporating dish. Reagent grade sodium bromide and lithium chloride were dried overnight in an oven at 110°. These three chemicals were stored in a vacuum desiccator over phosphorus pentoxide.

J. T. Baker Chemical Co. 1-naphthylamine hydrochloride was crystallized several times from water with use of boneblack, and was recrystallized before each use for analysis of diazonium solutions. Eastman Kodak Co. p-nitroaniline was used. All other chemicals were reagent grade and were used without further purification.

Ethyl 4-(p-Nitrophenylazo)-1-naphthyl Ether.—A solution of p-nitrobenzenediazonium sulfate was prepared[18] from 24 cc. of concentrated sulfuric acid, 3.4 g. (0.049 mole) of sodium nitrite, 6.0 g. (0.044 mole) of p-nitroaniline and 72 cc. of stock glacial acetic acid.

The cool diazonium solution so formed was added to a solution of 7.2 g. of ethyl 1-naphthyl ether in 25 cc. of glacial

(17) V. H. Dermer and O. C. Dermer, J. Org. Chem., **3**, 289 (1938).
(18) H. H. Hodgson and J. Walker, J. Chem. Soc., 1620 (1933).

acetic acid in a beaker surrounded by an ice-bath. A purple precipitate formed. After 15 minutes in the ice-bath, the mixture was allowed to stand in the room (temperature 27°) for 80 minutes and it was then poured into 100 g. of ice and 300 cc. of water. A deep orange precipitate was collected by filtration and washed with water. A small amount of this precipitate gave no blue color when dissolved in aqueous alcoholic potassium hydroxide. Crystallization from ethanol afforded beautiful, deep red crystals of m.p. 154–156°.

Anal. Calcd. for $C_{18}H_{15}N_3O_3$: C, 67.29; H, 4.71; N, 13.09. Found[19]: C, 66.99; H, 5.31; N, 12.95.

The above preparation was carried out before the factors responsible for dealkylation were understood; its success (yield about 80%) probably stems from low water content in the acetic acid plus a rather short reaction time.

Isopropyl 4-(p-Nitrophenylazo)-1-naphthyl Ether.—The preparation was conducted essentially as described in the preceding experiment except that strictly anhydrous acetic acid was used to dissolve the isopropyl 1-naphthyl ether. The yield of crude product was 87%. Recrystallization from ethanol afforded fluffy orange plates of m.p. 133.5–135° which gave no blue color when combined with alcoholic potassium hydroxide.

Anal. Calcd. for $C_{19}H_{17}N_3O_3$: C, 68.06; H, 5.07; N, 12.54. Found[19]: C, 68.39; H, 5.25; N, 12.20.

Methyl 4-(p-Nitrophenylazo)-1-naphthyl Ether (I).—This preparation was performed much as described for the corresponding ethyl ether. Compound I was obtained, after crystallization from ethanol, as orange-red crystals of m.p. 168–169.5° (lit.[2] 169°).

4-(p-Nitrophenylazo)-1-naphthol (II), m.p. 287–289° dec. (lit.[5] 284–285° dec.), was prepared by coupling p-nitrobenzenediazonium sulfate with 1-naphthol.

4-(p-Nitrophenylazo)-1-naphthylamine, m.p. 249–251° (lit.[20] 252°), was prepared by coupling of p-nitrobenzenediazonium sulfate with 1-naphthylamine in acetic acid solution and eventual crystallization of the product from toluene. This azo-amine was converted to its hydrochloride by treatment with hydrochloric acid in hot ethanol and subsequent cooling to cause crystallization.

Preparation and Analysis of Diazonium Solutions for Quantitative Studies.—For runs in 85.7% acetic acid, diazotization was effected by adding a solution of sodium nitrite (about 0.20 g.) in about 1.5 cc. of concentrated sulfuric acid (see above) to a solution of p-nitroaniline (about 0.30 g.) in the aqueous acetic acid solvent. The resulting diazonium solution was transferred to a 100-cc. volumetric flask and diluted to the mark with 85.7% acetic acid. For runs in strictly anhydrous acetic acid, the same general procedure was used except that the p-nitroaniline was first dissolved in stock glacial acetic acid. (Strictly anhydrous acetic acid, which contained free acetic anhydride, might have acetylated the amine.) The diazonium solution was then diluted to the mark in a 100-cc. volumetric flask with strictly anhydrous acetic acid.

(19) Carbon and hydrogen analyses by Micro-Tech Laboratories, Skokie, Ill.; nitrogen analysis by Miss Betty Jean Pegram, Venereal Disease Experimental Laboratory, U. S. Public Health Service, through courtesy of Dr. Leon Freedman.

(20) R. Meldola, *J. Chem. Soc.*, **43**, 425 (1883).

The concentration of diazonium ion in such solutions was determined as follows: A 5.00-cc. aliquot of the diazonium solution was transferred to a 100-cc. volumetric flask, diluted to the mark with the appropriate solvent and mixed thoroughly. Two 1.00-cc. aliquots of this 1:20 strength solution were added to solutions of excess 1-naphthylamine hydrochloride in 95% ethanol in 100-cc. volumetric flasks, and each was then diluted to the mark with 95% ethanol and mixed thoroughly. The absorbance of these solutions at 520 mμ was determined by means of a Beckman model B spectrophotometer. It was separately determined that a solution of 6.35 mg. of 4-(p-nitrophenylazo)-1-naphthylamine hydrochloride per liter (1.93×10^{-5} M) of 95% ethanol containing also 0.25 cc. of concentrated sulfuric acid had an absorbance of 0.802 at 520 mμ, and that solutions of this substance obeyed Beer's law. From these measurements, the concentration of diazonium ion in the initial 100 cc. of diazonium solution was easily calculated.

Quantitative Analysis for Products in Reaction Mixtures.—The spectra of I and II in neutral media are similar, but in ethanol containing excess potassium hydroxide I has an absorption peak at 430 mμ (ϵ 1.72×10^4) while II has an absorption peak at 600 mμ (ϵ 4.13×10^4) and absorbs more weakly at 430 mμ (ϵ 3.49×10^3). Absorption by I at 600 mμ is negligible. (Absorption measurements were made with a Beckman model B spectrophotometer the wave length scale of which is not perfectly accurate.) It was shown that Beer's law was obeyed by solutions of I and II in ethanolic potassium hydroxide.

Coupling reactions for photometric analysis were carried out in 100-cc. volumetric flasks. About 75 cc. of the reaction solvent, 1 cc. of a naphthyl ether (a large excess) and any additional substances were placed in such a flask and 1.00 cc. of a diazonium solution was added. About the same time, aliquots of the diazonium solution were taken for analysis (see above). The solutions were diluted to the mark with the reaction solvent and shaken well. Coupling was allowed to occur at room temperature in a dark place. Aliquots of 5.00 cc. were withdrawn at recorded times and run into 100-cc. volumetric flasks containing about 25 cc. of 95% ethanol each. Immediately thereafter, 50.0 cc. of a 15% solution of potassium hydroxide in ethanol was added to each analysis flask, and after the heat of neutralization had dissipated each flask was filled to the mark with 95% ethanol. Duplicate samples of the reaction solution were usually withdrawn at each time interval. These analysis solutions were kept in the dark until their absorbances were determined at 430 and 600 mμ by means of the Beckman model B spectrophotometer. There was no evidence of change of absorbance in the analysis solutions with time when the above procedure was followed, and thus it is indicated that treatment with ethanolic potassium hydroxide stopped the coupling reaction and that no degradation of the reaction products occurred in these solutions. In some cases, a "blank coupling reaction" was run (that is, everything was done as in a usual coupling reaction except that no naphthyl ether was added), and it was established that aliquots of this solution treated in the usual way with potassium hydroxide gave no color. From the absorbances of the analysis solutions and the concentration of the diazonium solution determined as described above, the yields of both I and II were easily calculated.

CHAPEL HILL. N. C.