The Abnormal Wallach Rearrangements of 4,4′-Dialkylazoxybenzenes

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The reactions of 4,4′-dialkylazoxybenzenes (**1**) with sulfuric acid afforded 2-alkyl-5-(*p*-alkylphenylazo)phenols (**2**) and 2-alkyl-4-(*p*-alkylphenylazo)phenols (**3**) as novel rearrangement products; in certain cases 4-(*p*-alkylphenylazo)phenols (**4**) were also obtained. The ratios of these azophenols were greatly affected by the alkyl group type. In addition, the reactions gave a very small amount of 5-alkyl-2-(*p*-alkylphenylazo)phenols (**5**), which were considered as normal Wallach rearrangement products.

In 1880, Wallach and Belli[1] found that heating azoxybenzene with sulfuric acid converted it to azobenzene and 4-hydroxyazobenzene. Later, in 1900, Bamberger[2] found that a small amount of 2-hydroxyazobenzene was also formed as a by-product in the reaction. Thereafter, many mechanistic investigations about the Wallach rearrangement have been carried out.[3] But only a few studies have been reported on the Wallach rearrangement of disubstituted azoxybenzenes.[4,5]

The rearrangement reaction of *p*,*p*′-azoxytoluene (**1a**) with sulfuric acid has been anomalous. Bamberger[6] found that **1a** gave a substance having a melting point of 204 °C in this reaction. In 1936, Parsons and Bailar[7] reported that this reaction afforded some alkali soluble (mp 210—212 °C) and alkali insoluble materials (mp 208—210 °C) which both contained a hydroxyl group; they suggested without any sure evidence that the alkali soluble material was 3-hydroxy-4,4′-dimethylazobenzene and the alkali insoluble material was 4-methyl-4′-hydroxymethylazobenzene. Subsequently, Gore and Hughes[4] reported the isolation of a substance having the same melting point in this reaction, and they showed that the two products obtained by Parsons and Bailar[7] were identical. They also proposed, carelessly, that this substance was 2-hydroxy-4,4′-dimethylazobenzene. The result of Gore and Hughes has been widely accepted and cited.[8]

On the other hand, Cumming and Ferrier[9] reported that the irradiation of **1a** gave 5-methyl-2-(*p*-tolylazo)phenol (**5a**) (mp 150 —151 °C). It is generally recognized that 2-hydroxyazobenzenes are exclusively obtained by the photorearrangement of azoxybenzenes. Consequently, on the basis of the substantial difference of their melting points, it appears to be extremely doubtful that the reaction of **1a** with sulfuric acid gave **5a** as the main product.

In the present investigation, we confirm the structure of the rearrangement product of **1a**, and deal with the reactions of some 4,4′-dialkylazoxybenzenes (**1**) and some other disubstituted azoxybenzenes with sulfuric acid.

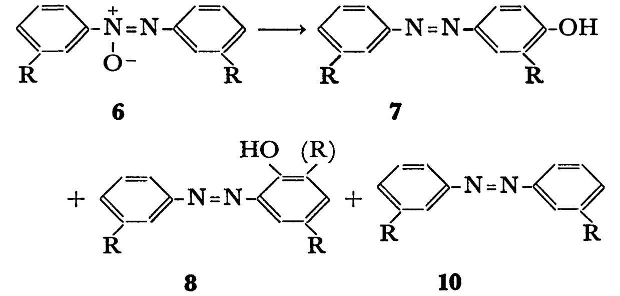
Results and Discussion

The investigation of the Wallach rearrangement of disubstituted azoxybenzenes have been insufficient. Thus, in order to compare with the reaction of **1**, some examples of the normal Wallach rearrangement were carried out; the results are shown in Table 1. The unsubstituted and 3,3′-disubstituted azoxybenzenes (**6**) gave 4-hydroxyazobenzenes (**7**) as the major products and 2-hydroxyazobenzenes (**8**) as by-products, and 4,4′-dihaloazoxybenzenes (**9**) gave **8**. The azoxybenzenes were reduced to a considerable extent to yield the corresponding azobenzenes (**10**), and some resinous meterial was also found.

TABLE 1. REACTIONS OF AZOXYBENZENES $RC_6H_4N(O)NC_6H_4R$, WITH SULFURIC ACID(85%) (Reaction conditions: 50 °C, 30 min)

R	Yield (%)			
	6	**10**	**7**	**8**
H	45	7	42	1.6
3,3′-Me_2	29	14	43	0.8[a)]
3,3′-Cl_2[b)]	75		16	1.0[c)]
4,4′-Cl_2[b)]		58		13
4,4′-Br_2[b)]		59		15

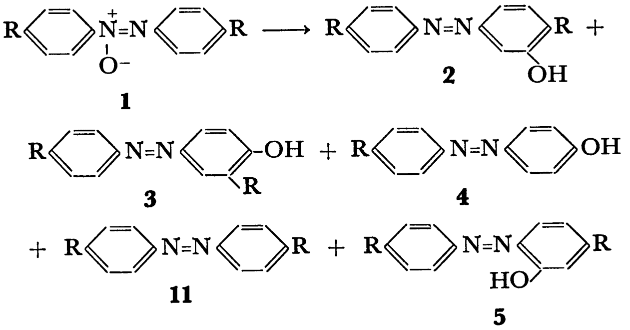
a) Mixture of **8a** and **8b**. b) 92% H_2SO_4. c) 4-Chloro-2-(*m*-chlorophenylazo)phenol.



The 2-hydroxyazo compound **8** obtained from *m*,*m*′-azoxytoluene (**6a**) was a mixture of 4-methyl-2-(*m*-tolylazo)phenol (**8a**) and 6-methyl-2-(*m*-tolylazo)pnenol (**8b**). The ratio of **8a** to **8b** was determined by gas chromatography to be 2.5 : 1. On the other hand, the compound **8** obtained from 3,3′-dichloroazoxybenzene (**6b**) was 4-chloro-2-(*m*-chlorophenylazo)phenol.

TABLE 2. REACTION OF 4,4′-DIALKYLAZOXYBENZENES **1** WITH 85% SULFURIC ACID (50 °C, 30 min)

	R	Yield (%)				
		1	**11**	**2**	**3**	**4**
1a	Me	3	18	21		
1b	Et	3	22	8	22	2
1c	*n*-Pr	4	25	19	4	6
1d	*i*-Pr	4	30		2	33
1e	*t*-Bu	7	33			51



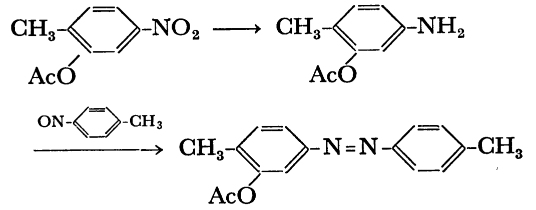
1—5, 11	R
a	Me
b	Et
c	*n*-Pr
d	*i*-Pr
e	*t*-Bu

Unlike the photorearrangement,[10] in the reaction with sulfuric acid the isomer ratios of **8** were affected by the substituents of **6**.

The compounds **1** were treated with 85% sulfuric acid at 50 °C and the reaction products were separated by column chromatography. The results are shown in Table 2.

As in the reactions of 3,3'- and 4,4'-dichloroazoxybenzenes, **1a** reacted faster than the *meta* isomer **6a**. Such results can probably be attributed to the stabilization effect of these *p*-substituents on the cationic intermediate.

The main rearrangement product of **1a** was 2-methyl-5-(*p*-tolylazo)phenol (**2a**). This compound **2a** was acetylated with acetic anhydride; then the structure of **2a** acetate was confirmed by a comparison with the sample obtained by the following synthesis:

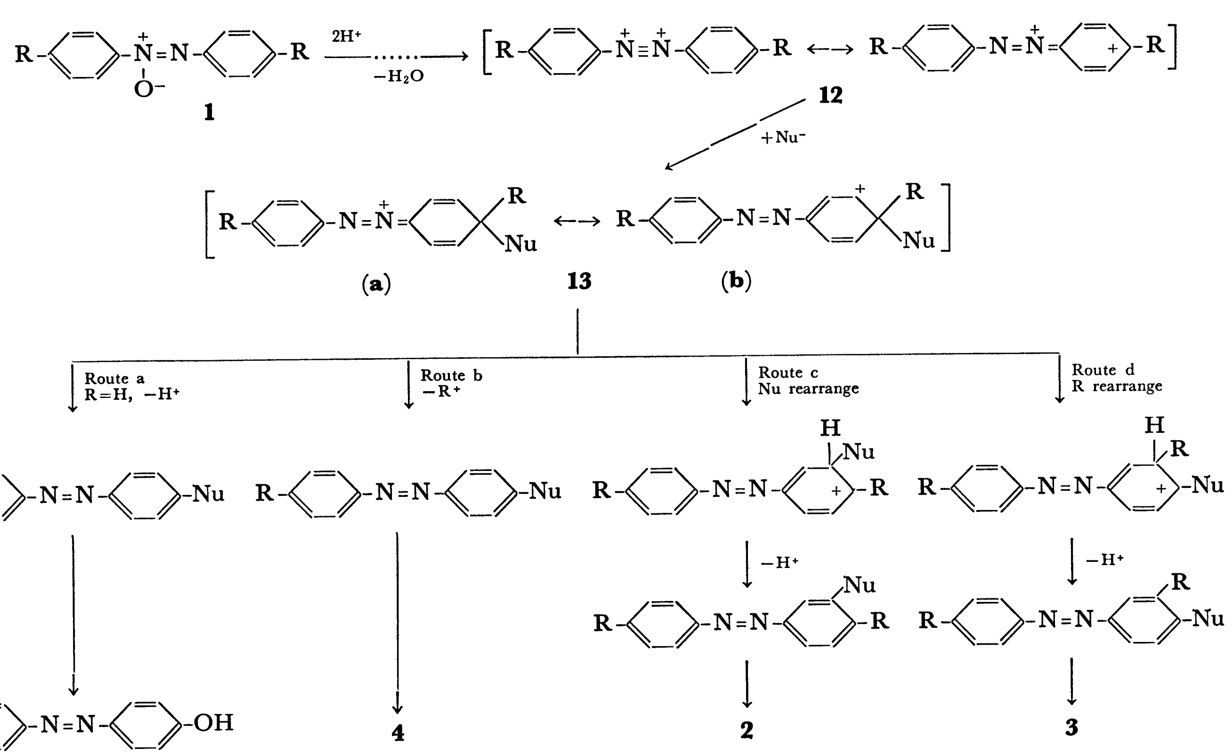


2a acetate

The melting point(211—212 °C) of **2a** was close to those[4,7] reported previously for the main product of the Wallach rearrangement of **1a**. Therefore it is evident that the conclusion of Gore and Hughes[4] is incorrect.[11] Although 5-alkyl-2-(*p*-alkylphenylazo)-phenols (**5**) appear to be the normal Wallach rearrangement products of **1**, **5a** was formed in only 0.2% yield. It is well-known that an irradiation of **1a** gives **5a**.[9,10] In order to conform the structure of **5a**, it was independently prepared by the condensation of 4-methyl-2-benzyloxyaniline and *p*-nitrosotoluene and then the debenzylation with hydrobromic acid. The gas chromatographic analysis showed that a trace amount of **5** was formed in the reaction of **1b**—**e**.

The 4,4'-diethylazoxybenzene (**1b**) and 4,4'-dipropylazoxybenzene (**1c**) afforded the corresponding 3-hydroxyazo compounds, **2b** and **2c**, respectively. Furthermore, **1b** and **1c** rearranged peculiarly to the 2-alkyl-4-(*p*-alkylphenylazo)phenols, **3b** and **3c**, respectively. The propyl group did not rearrange to an isopropyl group in this rearrangement.

The reactions of **1d** and **1e** yielded 4-(*p*-alkylphenylazo)phenols, **4d** and **4e**, respectively as the main products. Recently, Cox and Buncel[3] briefly communicated the formation of the same products. The rearrangement accompanied by the dealkylation was also ob-



Scheme 1.

served in the reaction of **1b** and **1c**. In the reaction of **1d**, **3d** was formed as a by-product.

The mechanism shown in Scheme 1 accounts nicely for the formation of the various azophenols, except **5**: First, **1** undergoes diprotonation and then dehydration to yield the dicationic intermediate (**12**). Subsequently the nucleophile, probably HSO_4^-, attacks the dication to form the complex (**13**). When R=H, the deprotonation occurs to afford the 4-hydroxyazobenzenes (Route a). This mechanism has been proposed as a pathway of the Wallach rearrangement.[3)]

On the other hand, the compounds **4** were formed by the separation of a alkyl carbonium ion from the complex **13** (Route b). When the carbonium ion is more stable, such as an isopropyl or *tert*-butyl group, the reaction proceeds preferentially by this route. In route c, the nucleophile group migrates to its *ortho* position in the complex **13** and then the deprotonation occurs to yield **2**. The compound **1a** rearranges mostly by this route. In Route d, the alkyl group migrates to its *ortho* position in **13** and then the deprotonation occurs. The compounds, **1b**, **1c**, and **1d**, which have the primary or secondary alkyl groups, rearrange by this route to form **3**.

The nucleophile attacks mostly the carbon atom attached the alkyl group. Thus the 2-hydroxyazo compounds **5** were only slightly formed. This can probably be attributed to the fact that the electron-releasing effect of the alkyl group accelerates the formation of the dicationic intermediate **12** and therefore the formation of **5** is hindered. Shemyakin and coworkers showed that the formation of 2-hydroxyazobenzenes appears to proceed by an intramolecular pathway different from that in the formation of 4-hydroxyazobenzenes.[12)]

The migration of the alkyl group or the nucleophile group may be caused by the positive charge on the *ortho* carbon atom of complex **13b**. Although the methyl group does not migrate, the ethyl and propyl groups do. This is probably due to the increasing electron density on the α-carbon atom by the electron-releasing effect of the alkyl group. The secondary and tertiary alkyl groups, in which the effect of the alkyl group is larger than that of the primary alkyl group, leave as the carbonium ion (Route b). It is of interest that the reaction route is greatly affected by the type of the alkyl group. These reactions appear to be explained by the monocationic mechanism[3)] proposed for the Wallach rearrangement; however, the formation of **2** and **3** may be more reasonably interpreted by the dicationic mechanism.

In analogy with the usual Wallach rearrangement, considerable amounts of azobenzenes were formed in these reactions. The formation of azobenzenes has been known for a long time; however, the mechanism is still not elucidated.[13)] In addition, the reaction afforded a small amount of some unidentified products. Further work is under way to isolate and identify these products and to determine the mechanism of the formation of azobenzenes.

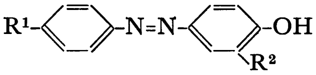
Experimental

The IR spectra were recorded with a JASCO IRA-1 spectrophotometer. The NMR spectra were obtained with a JEOL MH-100 spectrometer using TMS as the internal standard. The gas chromatographic analysis was carried out using a Shimadzu GC-2C apparatus on a 0.75 m×3 mm column packed with 2% Silicone OV-225. The melting points are uncorrected.

Materials. 4,4′-Dipropyl- and diisopropylazoxybenzenes (**1c** and **1d**) were prepared by the oxidation of the corresponding azo compounds. **1c** mp 63—64 °C. Found: C, 76.56; H, 7.90; N, 9.97%. Calcd for $C_{18}H_{22}N_2O$: C, 76.56; H, 7.85; N, 9.92%. **1d** mp 62—63 °C (lit,[14)] 62—63 °C). The other azoxybenzenes were prepared according to the method given in the previous work.[14)]

Reaction of 4,4′-Dialkylazoxybenzenes (1) with Sulfuric Acid. A solution of **1** (0.02 mol) in 85% sulfuric acid (12 ml) was heated for 30 min at 50 °C. The reaction mixture was poured into cold water, and then extracted with chloroform

Table 3. Syntheses of azophenols, **3** and **4**,



	R¹	R²	Yield %	Mp °C	Molecular formula	Found (Calcd) % C	H	N
3b	Et	Et	34	119—120		75.82	7.20	11.29
					$C_{16}H_{18}N_2O$	(75.56)	(7.13)	(11.02)
3c	*n*-Pr	*n*-Pr	20	56—58		76.39	8.08	9.75
					$C_{18}H_{22}N_2O$	(76.56)	(7.85)	(9.92)
3d	*i*-Pr	*i*-Pr	21	86—87		76.60	7.90	9.98
					$C_{18}H_{22}N_2O$	(76.56)	(7.85)	(9.92)
4b	Et	H	29	121—122		74.30	6.12	12.50
					$C_{14}H_{14}N_2O$	(74.31)	(6.24)	(12.38)
4c	*n*-Pr	H	18	76—77		75.04	6.67	11.43
					$C_{15}H_{16}N_2O$	(74.97)	(6.71)	(11.66)
4d	*i*-Pr	H	30	114—115		74.87	6.67	11.83
					$C_{15}H_{16}N_2O$	(74.97)	(6.71)	(11.66)
4e	*t*-Bu	H	56	127—128[a)]				

a) Lit,[15)] 125 °C.

or benzene. The extract was washed with water. After removal of the solvent, the residue was chromatographed on a silica gel column using benzene as a solvent. Unless otherwise noted, all the products were identified by a comparison of these mp and IR spectra with those of authentic samples.

The first fraction gave the crude **11**, contaminated by **1** and **5**, as analyzed by gas chromatography. In the reaction of **1a**, this fraction was again chromatographed on alumina using benzene as a solvent, and the residue on the column was extracted with methanol. The extract gave **5a** mp 150—151 °C (yield 0.2%).

The second fraction gave **2**, which was recrystallized from benzene. **2a** mp 211—212 °C. Found: C, 74.38; H, 5.95; N, 12.26%. Calcd for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.24; N, 12.38%. **2b** mp 152.5—153 °C. Found: C, 75.35; H, 7.06; N, 11.25%. Calcd for $C_{16}H_{18}N_2O$: C, 75.56; H, 7.13; N, 11.02%. **2c** mp 126.5—127 °C. Found: C, 76.55; H, 8.01; N, 9.92%. Calcd for $C_{18}H_{22}N_2O$: C, 76.56; H, 7.85; N, 9.92%.

The azophenols, **2a**, **2b**, and **2c**, were acetylated with acetic anhydride and pyridine. The products were recrystallized from hexane. Acetate of **2a** mp 105—106 °C. Acetate of **2b** mp 78.5—80 °C. Acetate of **2c** mp 46—47 °C. Found: C, 74.27; H, 7.34; N, 8.46%. Calcd for $C_{20}H_{24}N_2O_2$: C, 74.04; H, 7.46; N, 8.64%. The mp and the IR and NMR spectra of the acetates of **2a** and **2b** were identical with those of an authentic sample prepared independently. The **2c** acetate was identified by a comparison of its IR and NMR spectra (particularly, the characteristic signals due to aryl protons) with those of the **2a** and **2b** acetates. **2c** acetate: IR (KBr): 1750 (C-O), 1220 cm^{-1} (CO-O-Ar); NMR ($CDCl_3$): δ 1.00 (t, $2CH_3$), 1.68 (m, $2CH_2$), 2.35 (s, CH_3-COO), 2.58, 2.68 (t, $2CH_2Ar$), 7.3—8.0 (m, ArH).

The third fraction gave **3**. These products were recrystallized from hexane or ethanol-water. **3b** mp 116—117 °C. **3c** mp 55—56 °C. **3d** mp 86—88 °C.

The fourth fraction gave **4**, which was recrystallized from hexane. **4b** mp 122—123 °C. **4d** mp 115—116 °C. **4e** mp 127—128 °C. Since **4c** was impure, the crude **4c** was acetylated by the usual method. After purification by column chromatography (silica gel, benzene), recrystallization from hexane afforded **4c** acetate mp 80—81 °C.

The other fractions gave a small amount of unidentified substances.

Preparation of the Authentic Samples. *(A) 2-Alkyl-4-(*p-*alkylphenylazo)phenols (3) and 4-(*p-*Alkylphenylazo)phenols (4):* These azophenols were prepared by diazocoupling of the corresponding phenols and diazonium salts. These were purified by the use of column chromatography on silica gel and recrystallization from hexane or hexane-benzene. The results are shown in Table 3.

*(B) 5-Methyl-2-(*p-*tolylazo)phenol (5a):* The azophenol **5a** was obtained by the irradiation of the ethanolic solution of **1a**, and **5a** was also prepared by the method previously reported for 6-chloro-2-(3-chlorophenylazo)phenol.[16] 4,4′-Dimethyl-2-benzyloxyazobenzene, mp 95—96 °C (yield, 20%), Found: C, 79.90; H, 6.60; N, 8.85%. Calcd for $C_{21}H_{20}N_2O$: C, 79.71; H, 6.37; N, 8.85%. The **5a** mp 151—152 °C (yield, 69%).

(C) Acetate of ***2a:*** 3-Acetoxy-4-methylaniline was prepared by catalytic hydrogenation of 2-acetoxy-4-nitrotoluene. Mp 78—79 °C. Found: C, 65.53; H, 6.85; N, 8.63%. Calcd for $C_9H_{11}NO_2$: C, 65.44; H, 6.71; N, 8.48%.

A solution of the acetoxyaniline (0.67 g) and *p*-nitrosotoluene (0.49 g) in acetic acid was allowed to stand overnight at room temperature. The reaction mixture was poured into water, and extracted with benzene. After removal of the solvent, the extract was chromatographed on silica gel (solvent: benzene). The third fraction was recrystallized from hexane to give 3-acetoxy-4,4′-dimethylazobenzene (**2a** acetate) mp 104—105 °C. Found: C, 71.44; H, 5.79; N, 10.82%. Calcd for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44%.

2b acetate was prepared by the same method. Mp 78—79 °C. Found: C, 72.82; H, 6.86; N, 9.38%. Calcd for $C_{18}H_{20}N_2O_2$: C, 72.95; H, 6.80; N, 9.45%.

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