Abnormal Wallach Rearrangement of 4-Alkylazoxybenzenes

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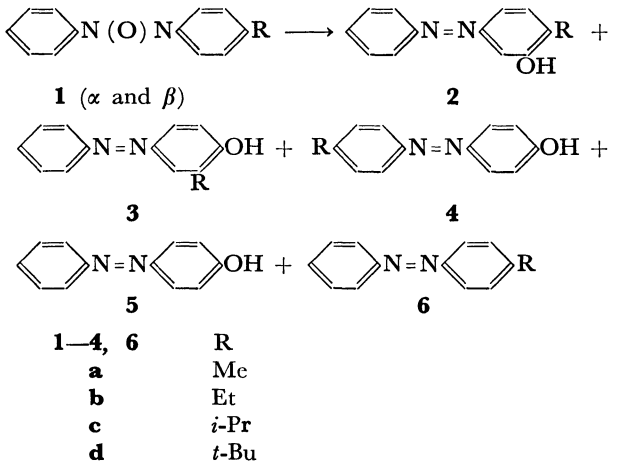
The major product in the reaction of 4-alkylazoxybenzenes with sulfuric acid is not 4-(*p*-alkylphenylazo)phenol, which is regarded as the usual product of Wallach rearrangement. The following azophenols were obtained as major products; 2-alkyl-5-(phenylazo)phenol (R : Me), 2-alkyl-4-(phenylazo)phenol (R : Et), and 4-(phenylazo)phenol (R : *i*-Pr and *t*-Bu).

In a previous paper,[1] the present authors reported abnormal Wallach rearrangement for 4,4'-dialkylazoxybenzenes. For example, it was found that, in the reaction of 4,4'-dimethylazoxybenzene, the hydroxyl group was mainly introduced into the meta position of the azo group, and that reactions of 4,4'-dialkylazoxybenzenes take place more rapidly than does that of azoxybenzene.

On the other hand, it was reported that, when α-4-methylazoxybenzene was treated with concentrated sulfuric acid, the main product is 4-(*p*-tolylazo)phenol.[2,3] In order to evaluate the effect of the alkyl group, it appears important to investigate the rearrangement of 4-alkylazoxybenzenes (**1**). It was found that the main rearrangement product of 4-methylazoxybenzene (**1a**) differs from that described in the literature.[2,3] Furthermore, in the present paper, the reactions of some 4-alkylazoxybenzenes are discussed.

Results and Discussion

4-Alkylazoxybenzenes were treated with 85% sulfuric acid at 50 °C. The reaction products were separated by column chromatography in most cases.



1—4, 6 R
a Me
b Et
c *i*-Pr
d *t*-Bu

Table 1 shows the results for the reactions of *p*-tolyl-NNO-azoxybenzene (**1aα**) and *p*-tolyl-ONN-azoxybenzene (**1aβ**). Both **1aα** and **1aβ** gave 2-methyl-5-(phenylazo)phenol (**2a**) as the major rearrangement product. The structure of **2a** was confirmed in the following way. This compound (**2a**) was acetylated using a conventional method. The acetate was identified by comparison with a sample obtained by condensation of 3-acetoxy-4-methylaniline and nitrosobenzene. Contrary to earlier reports,[2,3] 4-(*p*-tolylazo)-phenol (**4a**) was obtained only as a minor product.

The α isomer of **1a** reacted somewhat faster than the β isomer. This agrees with the results of kinetic studies reported by Hahn, *et al.*[4] The mp and IR spectra of the recovered azoxy compounds were identical with those the respective starting materials. Consequently, **1aα** and **1aβ** do not rapidly isomerize with each other under the reaction conditions. Furthermore, **1aα** and **1aβ** gave similar proportions of reaction products.

Since the α and β isomers of **1** were not separately available, excepting **1a**, mixtures of α and β isomers of **1** were used. These were prepared by hydrogen peroxide oxidation of the corresponding 4-alkylazobenzene (**6**). It has been reported that the oxidation of asymmetrical azobenzenes give a mixture of azoxybenzene isomers (the isomer ratio is about 1 : 1), excepting azobenzenes having special substituents in the ortho position.[5] The results for the reaction of **1** (in a mixture of the α and β isomers) are also shown in Table 1.

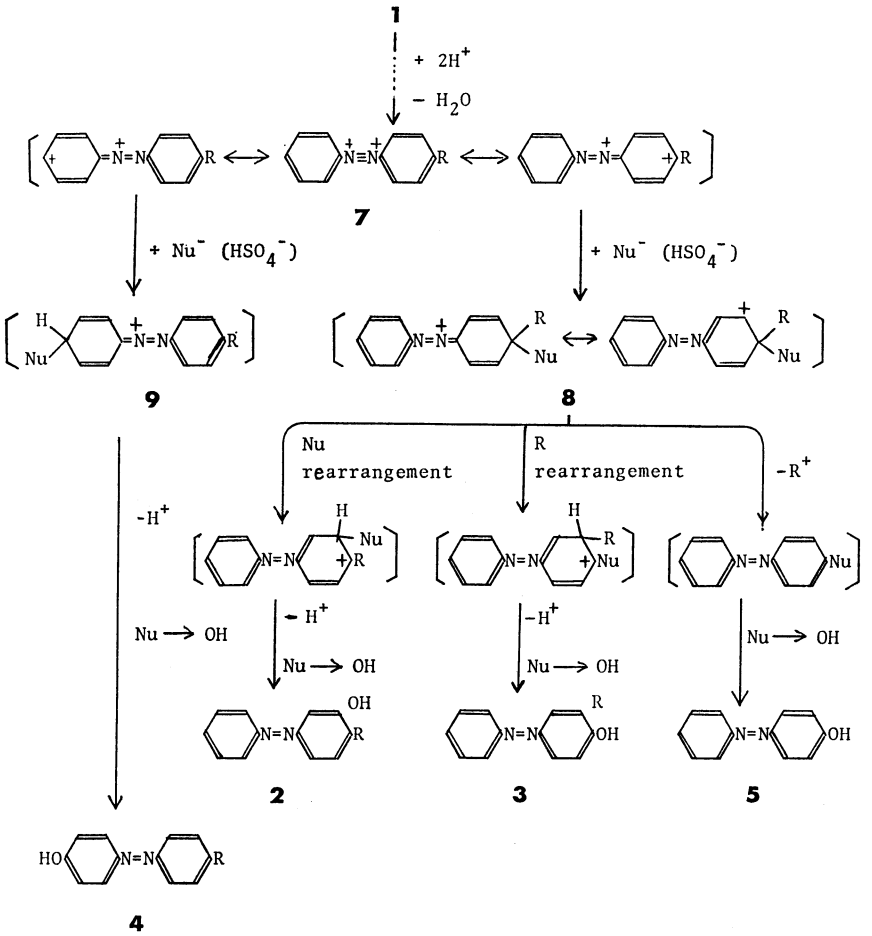
In the reaction of **1b**, the main rearrangement product was 2-ethyl-4-(phenylazo)phenol (**3b**), and azophenols, **2b**, **4b**, and **5**, were also formed. 4-Isopropyl- and 4-*t*-butyl-azoxybenzenes, **1c** and **1d**, gave mainly **5**. The reaction products varies with the type of alkyl group. Except for the formation of **4**, the effect of the alkyl group on the distribution of reaction products is similar to that in reactions of 4,4'-dialkylazoxybenzenes.[6] Gaschromatographic analysis of the reaction products showed that a small amount of a 2-hydroxyazo compound was formed in each case. However, it could not be determined whether the azophenol was 5-alkyl-2-(phenylazo)phenol or 2-(*p*-alkylphenylazo)phenol.

The formation of various azophenols may be interpreted by the mechanism shown in Scheme 1. Normal Wallach rearrangement is generally explained by a dicationic intermediate mechanism,[7] which consists of

Table 1. Reaction of 4-alkylazoxybenzenes with sulfuric acid

	Yield (%)					
	1	**2**	**3**	**4**	**5**	**6**
1aα	26	37	6	7		7
1aβ	60	24	3	4		2
1a[a]	22	41	7	8		8
1b[a]	24	10	28	3	7	9
1c[a]	25		1		42	8
1d[a]	26				57	10

a) A mixture of α and β isomers.



Scheme 1.

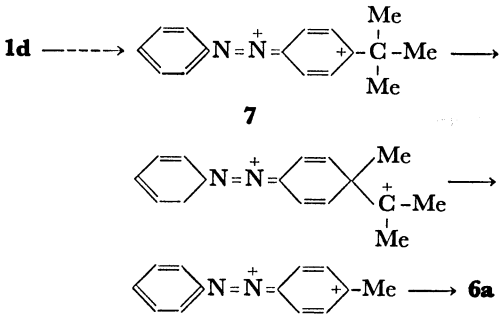
the formation and the nucleophilic attack of dicationic intermediate (**7**), followed by the deprotonation of **9**, and the conversion of the nucleophilic group into a hydroxyl group to give **4**. The following explanations involve some modification of the dicationic mechanism.

The dicationic intermediate (**7**) is formed by the diprotonation and subsequent dehydration of **1**. Subsequently, when the nucleophile, probably HSO_4^-, attacks the carbon atom having an alkyl group in **7**, the intermediate ion (**8**) is formed. The routes for the formation of azophenols, **2**, **3**, and **5**, from **8** are similar to those proposed previously for the Wallach rearrangement of 4,4'-dialkylazoxybenzenes.[1]

It is generally stated that 4-substituted 4'-hydroxyazobenzenes are the main products of Wallach rearrangement of 4-monosubstituted azoxybenzenes.[2,3,8] However, **1a** and **1b** gave only small amounts of **4**, that is, the reactions proceed weakly along this route in the case of **1**. The benzene ring having an alkyl group of **7** is preferentially attacked by a nucleophile yielding **8**, because of the electron-releasing effect of the alkyl group.

Similarly, in the reaction of an azoxybenzene with an electron-releasing group at its meta position, a hydroxyl group was found to be introduced mainly into the benzene ring having the substituent. For example, 3-methylazoxybenzene (a mixture of the α and β isomers) gave 2-methyl-4-(phenylazo)phenol (yield 30%) and only a 2% yield of 4-(*m*-tolylazo)-phenol,[9] while 3-methoxyazoxybenzene (a mixture of the α and β isomers) gave 2-methoxy-4-(phenylazo)-phenol (yield 26%).

In all case, substituted azobenzenes were also formed. Furthermore, **1d** gave **6a** in a 5% yield, namely, the *t*-butyl group was replaced by a methyl group. The mechanism of azobenzene formation is still unknown. Although the pathway from **7** to **6** is obscure, it appears likely that a methyl group in the *t*-butyl group migrates to the carbon atom of the benzene ring in **7** and then the isopropyl moiety is eliminated.



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 high-speed liquid-chromatographic analysis was carried out using a JASCO-FLC 150 apparatus on a 0.5 m × 2.1 mm column packed with JASCODAC SV-02 (the solvent was methanol–water), JASCOSIL WC-01 (the solvent was hexane–chloroform), or WC-03 (the solvent was hexane). All melting points are uncorrected.

Azoxybenzenes. 4-Methylazoxybenzenes, **1a**α and **1a**β, were prepared using methods described in the literature. **1a**α, mp 50.5—51.5 °C (lit,[10] 50—51 °C). **1a**β, mp 62—64 °C (lit,[5] 63.5—64 °C). Compounds **1a—1d** were obtained by oxidation of the corresponding azobenzenes with hydrogen peroxide.[11] The products were recrystallized from hexane, or subjected to chromatography on an alumina column (the solvent was benzene), yield: 85%. It was shown by a comparison of their NMR spectra with those of **1a**α and **1a**β that the products were mixtures of the α and β isomers. However, the isomer ratios, α/β, could not be determined. **1a**, mp 30—36 °C (lit,[12] 30—35 °C). **1b**, oil, Found: C, 74.48; H, 6.40; N, 12.34%. Calcd for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.24; N, 12.38%. **1c**, mp 36—45 °C. Found: C, 75.05; H, 6.83; N, 11.59%. Calcd for $C_{15}H_{16}N_2O$: C, 74.97; H, 6.71; N, 11.66%. **1d**, mp 25—36 °C. Found: C, 75.40; H, 7.00; N, 11.15%. Calcd for $C_{16}H_{18}N_2O$: C, 75.56; H, 7.13; N, 11.02%.

4-Alkylazobenzenes. Compounds **6a—6d** were prepared by the condensation of nitrosobenzene and the corresponding 4-alkylaniline in acetic acid.[13] The products were purified by chromatography on alumina column (the solvent was benzene) and by recrystallization from ethanol. **6a**, mp 66—67 °C (lit,[14] 66—67 °C). **6b** (yield, 71%), mp 26—27 °C. Found: C, 79.69; H, 6.84; N, 13.33%. Calcd for $C_{14}H_{14}N_2$: C, 79.96; H, 6.71; N, 13.32%. **6c** (yield, 76%), mp 46.5—47.5 °C. Found: C, 80.15; H, 7.44; N, 12.54%. Calcd for $C_{15}H_{16}N_2$: C, 80.32; H, 7.19; N, 12.49%. **6d** (yield, 70%) mp 48—49 °C. Found: C, 80.82; H, 7.60; N, 11.70%. Calcd for $C_{16}H_{18}N_2$: C, 80.63; H, 7.61; N, 11.76%.

The Reactions of 4-Alkylazoxybenzenes with Sulfuric Acid. A solution of **1** (0.005 mol) in 85% sulfuric acid (25 ml) was heated at 50 °C for 30 min. The reaction mixture was poured into cold water and then extracted with chloroform. The organic phase was washed with water, and dried over anhydrous sodium sulfate. After removal of the solvent, the residue was subjected to chromatography on a silica gel (Wakogel C-200) column using benzene as the solvent.

First fraction. This fraction was a mixture of **1**, **6** and small amounts of 2-hydroxy-4-(or 4′-)alkylazobenzenes which were analyzed using gas chromatography. Furthermore, the mixture was again subjected to chromatography on an alumina column using hexane–benzene (2:1) as the solvent. Fraction 1 gave **6** and fraction 2 gave **1**. In the case of **1d**, fraction 2 upon rechromatography gave **6a**, mp 66.5—67 °C, and fraction 3 gave **1d**. The mp and IR spectra of azobenzenes **6a—6d** and of the recovered **1a**α and **1a**β were in good agreement with those of respective authentic samples. Other recovered **1a—1d** were identified by comparing their IR spectra and GC retention times with those of the corresponding starting materials.

Second fraction. Recrystallization from benzene gave 2-alkyl-5-(phenylazo)phenol (**2**). **2a**, mp 153.5—154.5 °C. Found: C, 73.49; H, 5.61; N, 13.40%. Calcd for $C_{13}H_{12}N_2O$: C, 73.56; H, 5.70; N, 13.20%. **2b**, mp 136—137 °C. Found: C, 74.35; H, 6.19; N, 12.29%. Calcd for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.24; N, 12.38%.

Azophenol **2a** and **2b** were acetylated with acetic anhydride and pyridine. The products were recrystallized from hexane. The acetate of **2a**, mp 73—73.5 °C (yield 70%). The acetate of **2b**, mp 29—30 °C (yield 75%). The mp and IR spectra of both acetates were identical with those of respective authentic samples.

Third fraction. Recrystallization from hexane or ethanol-water gave 2-alkyl-4-(phenylazo)phenol (**3**). **3a**, mp 130—131.5 °C. **3c**, mp 126.5—128 °C. Since the **3b** was impure, crude **3b** was acetylated with acetic anhydride in pyridine. The product was recrystallized form hexane to yield acetate of **3b**, mp 47—48 °C. These compounds were identified by comparing their mp and IR spectra with those of authentic samples.

Fourth fraction. In the case of **1a**, recrystallization from ethanol-water gave **4a**, mp 154—155 °C. In the case of **1b**, this fraction was found by high-speed liquid-chromatographic analysis to be a mixture of **4b** and **5**. The mixture was acetylated with acetic anhydride and pyridine, and the resulting acetate was also analyzed by high-speed liquid-chromatography. In the cases of **1c** and **1d**, recrystallization from benzene gave **5**, mp 155—156 °C (lit,[15] 152 °C).

The Reactions of 3-Methyl- and 3-Methoxy-azoxybenzenes with Sulfuric Acid. The azoxy compounds were treated with sulfuric acid using the procedure described above. 3-Methylazoxybenzene gave 3-methylazobenzene (yield 6.5%) and a mixture of 2-methyl-4-(phenylazo)phenol (yield 30%) and 4-(*m*-tolylazo)phenol (yield 2%) which was analyzed by high-speed liquid-chromatography. 3-Methoxyazoxybenzene gave 3-methoxyazobenzene (yield 12%) and 2-methoxy-4-(phenylazo)phenol, mp 69—70 °C (lit,[16] 70.5—71.5 °C).

Preparation of Authentic Samples. Azophenols, **3** and **4**, were prepared by diazo-coupling of the corresponding phenols and diazonium salts.[17] The products were subjected to chromatography on a silica gel column (the eluent was benzene), and then recrystallized from hexane–benzene. **3a**, mp 132—133 °C (lit,[18] 129—130 °C) (yield 55%). **3b**, mp 89—89.5 °C (yield 40%). Found: C, 74.37; H, 6.44; N, 12.55%. Calcd for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.24; N, 12.38%. **3c**, mp 127.5—128 °C (yield 30%). Found: C, 74.97; H, 6.72; N, 11.63%. Calcd for $C_{15}H_{16}N_2O$: C, 74.97; H, 6.71; N, 11.66%. **4a**, mp 154—154.5 °C (lit,[19] 152 °C). Compounds **4b**, **4c**, and **4d** have been repotred previously.[1]

3-Ethyl-4-acetoxyazobenzene, the acetate of **3b**, was prepared by the acetylation of **3b** with acetic anhydride and pyridine, and then recrystallized from hexane (yield 86%), mp 48—49 °C. Found: C, 71.43; H, 5.94; N, 10.66%. Calcd for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44%.

3-Acetoxy-4-alkylazobenzenes, the acetate of **2a** and **2b**, were prepared by condensation of 3-acetoxy-4-alkylaniline and nitrosobenzene according to the method given in a previous report.[1] The acetate of **2a**, mp 72.5—73.5 °C from hexane (yield 21%). Found: C, 71.10; H, 5.51; N, 11.28%. Calcd for $C_{15}H_{14}N_2O_2$: C, 70.85; H, 5.55; N, 11.02%. The acetate of **2b**, mp 29—30 °C from hexane (yield 28%). Found: C, 71.90; H, 6.09; N, 10.63%. Calcd for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44%.

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