The Thermal Reaction of Azoxybenzenes

Ichiro Shimao and Hirokazu Hashidzume

Department of Industrial Chemistry, Faculty of Engineering, Toyama University, Takaoka-shi, Toyama 933

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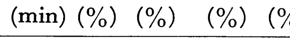
Azoxybenzenes (**1**) were heated at 245—250 °C to give azobenzenes (**2**), 2-hydroxyazobenzenes (**3**), 2-hydroxyazoxybenzenes (**4**), 4-hydroxyazobenzenes (**5**), and 4-hydroxyazoxybenzenes (**6**). Compounds **4** and **6** were mostly composed of α-isomers. In the reaction of azoxytoluenes, their methyl groups were oxidized to formyl groups. It was proposed that **4** and **6** were the intermediates of the thermal rearrangement of **1** to **3** and **5**.

The Wallach rearrangement[1)] and photorearrangement[2)] of azoxybenzenes (**1**) have been extensively investigated, and it is well known that azobenzenes (**2**) can be prepared by a dry distillation of **1**. Recently, Feinstein and Fields[3)] have investigated the reaction of azoxybenzene with benzene at elevated temperatures. However, only one work on the thermal rearrangement has been done. About seventy years ago, Knipscheer[4)] reported that **1** decomposed thermally to give **2**, 2-hydroxyazobenzenes (**3**), and 4-hydroxyazobenzenes (**5**) at 240—250 °C in a carbon dioxide atmosphere. Azoxybenzenes gave mostly **5** in a Wallach rearrangement, and exclusively **3** in a photorearrangement, but they gave **3** and **5** in a thermal reaction. Consequently, it seemed that the thermal rearrangement may proceed by a mechanism different from those presented for the other rearrangements of **1**. In this paper, we will deal in detail with the thermal reaction of unsubstituted, 4-bromo-, 3,3′-, and 4,4′-disubstituted azoxybenzenes.

Results and Discussion

It was found by the differential thermal analysis that the exothermic reaction occurred when **1** was heated at 245—250 °C. The thermal decomposition of **1** at 245—250 °C gave **2**, **3**, 2-hydroxyazoxybenzenes (**4**), **5**, and 4-hydroxyazoxybenzenes (**6**), while the formation of **2**, **3**, and **5** has previously been reported by Knipscheer.[4)] The results are shown in Table 1.

Table 1. Thermal reaction of azoxybenzenes

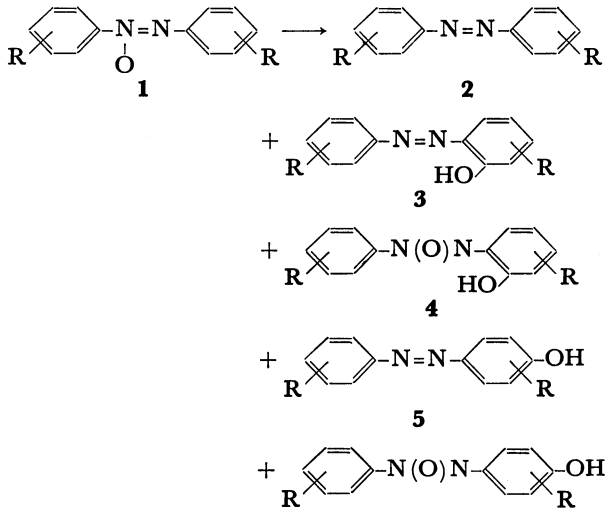


$RC_6H_4\underset{O^-}{\underset{|}{N^+}}=NC_6H_4R'$

R	R′	Time (min)	**1** (%)	**2** (%)	**3** (%)	**4** (%)	**5** (%)	**6** (%)
H	H	60	27	25.9	4.1	1.2	1.2[b)]	
4-Cl	4-Cl	30	70	7.5	1.3	1.1		
3-Cl	3-Cl	30	50	14.5	3.6[c)]	0.8[c)]	0.9	1.8
4-CH_3	4-CH_3	60	15	36.9	1.2	0.5		d)
3-CH_3	3-CH_3	30	38	20.4			0.4	d)
4-OCH_3	4-OCH_3	60	12	23.9	1.0			
3-OCH_3	3-OCH_3	30	45	14.8	3.1[c)]	0.5[c)]	0.5	1.5
H	4-Br	30	52	16.0	2.3[e)]	1.1		
4-Br	H	30	8	38.4	2.7[e)]	trace		

a) Reaction temperature, 245—250 °C. b) Crude product, mixture of **5** and **6**. c) Mixture of 2-hydroxy compound and 6-hydroxy compound. d) Tolylazobenzaldehyde was obtained. e) Mixture of 5-bromo-2-(phenylazo)phenol and 2-(4-bromophenylazo)phenol.

Significant amounts of black resinous substances were also formed as by-products.



After long heating **4** and **6** were not isolated, because of their lability under these conditions. Figure 1 shows the influence of the heating time on the yields of **2**, **3**, and **4** for the thermal reaction of azoxybenzene. The 2-hydroxyazoxybenzenes obtained by the thermal reaction were exclusively 2-(phenyl-ONN-azoxy)phenols (α-isomers). The α- and β-isomers of **4** were easily distinguished by their NMR spectra. The OH proton signal of the β-isomer appeared in a lower magnetic field than that of the α-isomer (2-hydroxyazoxybenzene: β-isomer, δ 11.73 ppm; α-isomer, δ 7.66 ppm). This may be attributed to the formation of an intramolecular hydrogen bond between the hydroxyl group and the

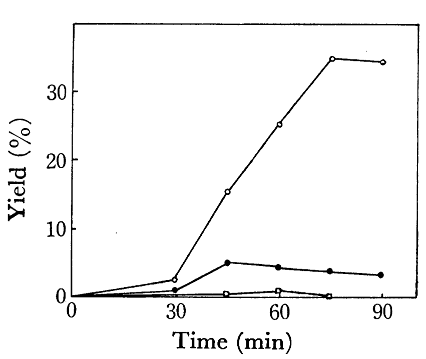
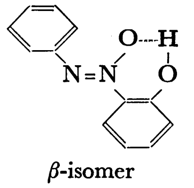
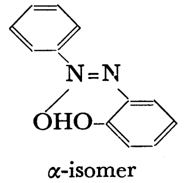


Fig. 1. The effect of the heating time on the yield of products, **2**, **3**, and **4**, for thermal reaction of azoxybenzene. At 245—250 °C.
○: **2**, ●: **3**, □: **4**.

oxygen atom of the azoxy group in the β-isomer. On the other hand, in the α-isomer the formation of the analogous intramolecular hydrogen bond is impossible, because of a steric strain present in its coplanar seven-membered ring. Those results agreed with those postulated by Digiavi[5] from the fact that the α-isomer is more liable to undergo oxidation with a potassium permanganate solution than is the β-isomer. In addition, the presence of the intramolecular hydrogen bond in the β-isomer was also shown by an absorption near 3400 cm^{-1} in its IR spectrum and by a higher R_f value in TLC on silica gel.



β-isomer



α-isomer

The ratio of 2-(3-chlorophenylazo)-4-chlorophenol to 2-(3-chlorophenylazo)-6-chlorophenol was determined by gas chromatography to be 1: 1. 2-(3-Methoxyphenylazo)-4-methoxyphenol and 2-(3-methoxyphenylazo)-6-methoxyphenol were separated by column chromatography on silica gel, and the ratio of the 4-methoxy isomer to the 6-methoxy isomer was 1: 2.1. Those ratios were analogous to that in the photorearrangement of the corresponding **1**. Tanikaga[6] reported that the substituents on 3,3′-positions do not have a steric effect on the isomer ratios upon the photorearrangement. Interestingly, it was found that, on the irradiation of an ethanolic solution of 3,3′-dimethoxyazoxybenzene, the oxygen atom rearranged preferentially to the *o*-position of methoxy group (4-methoxy isomer: 6-methoxy isomer=1: 2.5).

The 2-hydroxyazoxybenzenes obtained from 3,3′-dichloro- and 3,3′-dimethoxyazoxybenzenes were a mixture of the α-isomers; however, because of difficulties in the separation, the ratios of the 2-hydroxy isomer to the 6-hydroxy isomer could not be determined. The mixture of 3,3′-dichloro-**4** was reduced with lithium aluminum hydride in ethyl ether to give the corresponding **2** and a mixture of the corresponding substances **3**. It was presumed, by a comparison of the retention time in high-speed liquid chromatography with that of the authentic samples,[7] that 4-hydroxyazoxybenzene was composed mostly of α-isomers.

The thermal reactions of 3,3′- and 4,4′-azoxytoluenes gave 3-(*m*-tolylazo)benzaldehyde (yield, 2.1%) and 4-(*p*-tolylazo)benzaldehyde (yield, 2.5%) respectively. The methyl group was oxidized to only the formyl group, and the hydroxymethyl and carboxyl groups have not been found in the reaction products, which did not show a characteristic absorption of the carboxyl group in the IR spectra or a signal of the benzyl methylene proton in the NMR spectra.

The ratios of 2-phenylazo-5-bromophenol to 2-(4-bromophenylazo)phenol obtained from 4-bromo-ONN- and 4-bromo-NNO-azoxybenzenes were 2.5: 1 and 1: 3 respectively. These ratios were determined by means of the strength of the OH proton signal of the mixture on the NMR spectra (2-phenylazo-3-bromophenol, δ 13.30 ppm; 2-(4-bromophenylazo)phenol, δ 12.88 ppm). The hydroxyl group was preferentially introduced in the benzene ring remote from the oxygen atom of the azoxy group; however, the selectivity was significantly lower than that in the photorearrangement. 4-Bromo-ONN-azoxybenzene reacted faster than the NNO-isomer, and the **1** was recovered from the reaction mixture without isomerization to the other azoxy isomer.

In order to examine the pathway of the formation of **4** and **6**, mixtures of **1** and **3**, or **5** (1: 1), were heated at 245—250 °C for 30 min. If **3** or **5** were oxidized to **4** or **6**, a large quantity of **4** or **6** should be formed in this condition. Azobenzene was formed in a larger quantity than when azoxybenzene was heated alone (yield of azobenzene: azoxybenzene+2-hydroxyazobenzene, 44%; azoxybenzene+4-hydroxyazobenzene, 53%; azoxybenzene alone, 2.6%); however, **4** or **6** were not isolated. These results show that **4** or **6** is not formed by the oxidation of **3** or **5** with **1**. The absence of **4** or **6** may be attributed to the fact that **1** was readily reduced with **3** or **5** to give **2**. This is reflected by the increasing yield of **2**. On the other hand, azoxybenzene was easily reduced to azobenzene on heating with phenols, such as naphthols; the resinous material and water were then formed.

Since **1** served as oxidizing agent at high temperatures and was converted to **2**, the *o*- or *p*-position of **1** was oxidized to the hydroxyl group. The formation of **4** or **6** is a novel reaction in which the aromatic nucleus is directly oxidized to phenols. The formation of the α-isomer of **4** or **6** is due to the ready oxidation of the benzene ring apart from the oxygen atom of the azoxy group. This may be explained in terms of the resonance of **1** and the nucleophilic attack.

In addition, 2-hydroxyazoxybenzene and 3,3′-dichloro-4-hydroxyazoxybenzene gave 2-hydroxyazobenzene (yield, 17%) and 3,3′-dichloro-4-hydroxyazobenzene (yield, 18%) respectively on heating at 245—250 °C for 5 min. Thus, we may conclude that the thermal rearrangement of **1** to **3** or **5** involves the disproportionation of **1** to **2** and **4** or **6** (oxidation and reduction), and then the reduction of **4** or **6** to **3** or **5**:

$$2C_6H_5N(O)NC_6H_5 \longrightarrow$$

$$C_6H_5N_2C_6H_5 + C_6H_5N(O)NC_6H_4(OH)\ (o\text{- or } p\text{-})$$

$$C_6H_5N(O)NC_6H_4(OH) \xrightarrow{\text{Reduction}}$$

$$C_6H_5N_2C_6H_4(OH)\ (o\text{- or } p\text{-})$$

However, it is possible that the thermal rearrangement proceeds partly by the pathway[8] proposed for the Wallach rearrangement, which includes protonation and a symmetrical intermediate ion, or by the intramolecular pathway[9] proposed for the photorearrangement.

Experimental

The IR spectra were recorded with a JASCO IRA-1 spectrometer. 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 1.5 m×3 mm column packed with 5% SE-52. 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 JASCO-DAC SV-02 (solvent: methanol–water). The differential thermal analysis was carried out using a Mitamura-Riken 2-100 DTA-S apparatus with a sample packed as a layer in α-alumina. The melting points are uncorrected.

The azoxybenzenes were prepared by the methods described in the literature.[10–12]

Thermal Reaction of 1. *General Procedure*: About a 0.2 g portion of **1** was placed in a small glass tube and heated at 245—250 °C in a silicone oil bath. After cooling, the reaction mixture was extracted with benzene, and then the extract was further extracted with a dilute sodium hydroxide solution. The alkali extract was acidified with hydrochloric acid, and the resulting precipitate was collected and chromatographed on silica gel by the use of chloroform as the solvent. The elution was in the following order: **3**, **4**, **5**, and **6**.

The alkali-insoluble material was chromatographed on alumina by the use of benzene as the solvent; the elution was in the following order: **2** and **1**.

Each eluent was evaporated and recrystallized from hexane or ehanol. These products were identified by a comparison of their mp and their IR and NMR spectra with those of the corresponding authentic samples, or by chromatographic analysis.

Tolylazobenzaldehydes: These compounds were obtained as second fractions in chromatography, on silica gel, of the alkali-insoluble parts in the reaction of azoxytoluenes. 4-(*p*-Tolylazo)benzaldehyde was recrystallized from acetone and sublimed under reduced pressure; mp 177—178 °C (lit,[13] 177.5 °C). 3-(*m*-Tolylazo)benzaldehyde, obtained as an oil (IR: 1700 cm^{-1}, NMR: δ 9.82 ppm (COH)), was oxidized with silver oxide to the carboxylic acid. The acid was esterified with methanol in the presence of sulfuric acid; subsequent recrystallization from petroleum ether gave methyl 3-(*m*-tolylazo)benzoate; mp 66.5—68 °C; Found: C, 70.85; H, 5.40; N, 10.97%. Calcd for $C_{15}H_{14}N_2O_2$: C, 70.85; H, 5.55; N, 11.02%.

Preparation of the Authentic Samples. The compounds **3**, except for 2-(3-chlorophenylazo)-6-chlorophenol, were synthesized by the photorearrangement of **1**, or by the coupling of the corresponding phenols and diazonium salts. 2-(3-Methoxyphenylazo)-4-methoxyphenol; mp 80.5—81.5 °C. Found: C, 64.82; H, 5.25; N, 11.08%. Calcd for $C_{14}H_{14}N_2O_3$: C, 65.10; H, 5.46; N, 10.85%. 2-(3-Methoxyphenylazo)-6-methoxyphenol, mp 128.5—129.5 °C. Found: C, 65.07; H, 5.31; N, 10.68%. Calcd for $C_{14}H_{14}N_2O_3$: C, 65.10; H, 5.46; N, 10.85%.

The compounds **5** were prepared by diazo-coupling in the usual method. 4-(3-Chlorophenylazo)-2-chlorophenol, mp 127—128 °C. Found: C, 54.17; H, 2.81; N, 10.67%. Calcd for $C_{12}H_8Cl_2N_2O$: C, 53.95; H, 3.02; N, 10.49%. 4-(3-Methoxyphenylazo)-2-methoxyphenol, mp 88—89 °C. Found: C, 64.91; H, 5.24; N, 10.88%. Calcd for $C_{14}H_{14}N_2O_3$: C, 65.10; H, 5.46; N, 10.85%.

2-(3-Chlorophenylazo)-6-chlorophenol: This compound was formed during the irradiation of 3,3′-dichloroazoxybenzene; however, its separation from its isomer was difficult. Consequently, the following synthesis was carried out. A mixture of 2-chloro-6-nitrophenol (9.1 g), benzyl chloride (13.3 g), and 3% sodium hydroxide solution (186 ml) was stirred for 4 hr at 50—60 °C. A subsequent recrystallization of the oily substance from methanol gave *benzyl 2-chloro-6-nitrophenyl ether*; mp 49 °C (yield, 17%). Found: C, 59.66; H, 3.85; N, 5.35%. Calcd for $C_{13}H_{10}ClNO_3$: C, 59.50; H, 3.70; N, 5.39%.

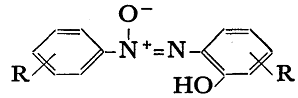
The catalytic hydrogenation of the benzyl ether (2.4 g) in ethanol using the Pt catalyst gave *3-chloro-2-benzyloxyaniline*. The treatment of the aniline with hydrochloric acid gave the amine hydrochloride (yield, 83%). The *acetanilide*; mp 84—85 °C. Found: C, 69.20; H, 5.27; N, 5.13%. Calcd for $C_{15}H_{14}ClNO_2$: C, 69.36; H, 5.43; N, 5.39%.

A mixture of the amine hydrochloride (2.4 g), 3-chloronitrosobenzene (1.1 g), and anhydrous sodium acetate (0.1 g) in acetic acid (11 ml) and benzene (10 ml) was stirred for 15 hr at room temperature. The reaction mixture was then steam-distilled, and the residue was collected. After purification by column chromatography on alumina, recrystallization from ethanol gave *3-chloro-2-benzyloxy-(3-chlorophenylazo)-benzene*; mp 74—75 °C (yield, 21%). Found: C, 63.63; H, 3.79; N, 7.86%. Calcd for $C_{19}H_{14}Cl_2N_2O$: C, 63.88; H, 3.95; N, 7.84%.

A mixture of the benzyloxyazobenzene (0.6 g), acetic acid (3.7 ml), and 47% hydrobromic acid (3.7 ml) was stirred for 8 hr at 45 °C. The mixture was then poured into cold water. The recrystallization of the resulting precipitate from ethanol gave 6-chloro-2(3-chlorophenylazo)phenol; mp 143.5—145 °C (yield, 74%); lit,[6] mp 144 °C.

α-2-Hydroxyazoxybenzenes: The 2-hydroxyazobenzenes were oxidized by 30% hydrogen peroxide in acetic acid according to the usual method.[14] The product was chromatographed on silica gel, using petroleum benzine–benzene as the developing solvent, to separate the α-isomer from the β-isomer and the unchanged azo compound, and then recrystallized from petroleum benzine. The results are shown in Table 2.

TABLE2. PREPARATION OF α-2-HYDROXYAZOXYBENZENES,



R	R′	Yield (%)	Mp (°C)	Found (Calcd)		
				C %	H %	N %
4-Cl	4′-Cl	16	145.5—147	50.69	2.60	9.64
				(50.91	2.85	9.89)
5-Cl	3′-Cl	31	172 —173	50.76	2.65	9.61
				(50.91	2.85	9.89)
3-Cl	3′-Cl	31	128.5—129.5	51.00	3.01	10.00
				(50.91	2.85	9.89)
4-CH$_3$	4′-CH$_3$	9	107.5—108	69.57	5.64	11.39
				(69.40	5.83	11.56)
4-OCH$_3$	4′-OCH$_3$	2.5	114.5—116	61.18	4.93	10.06
				(61.31	5.15	10.21)
5-OCH$_3$	3′-OCH$_3$	3.5	84.5—86	61.10	5.10	10.05
				(61.31	5.15	10.21)
3-OCH$_3$	3′-OCH$_3$	8	69 — 71	61.04	5.13	10.12
				(61.31	5.15	10.21)
4-Br	H	33	101.5—102	49.32	3.08	9.85
				(49.17	3.09	9.56)
H	4′-Br	21	127 —128	49.35	3.12	9.85
				(49.17	3.09	9.56)

We wish to express our thanks to Professor Syuzi Hirooka for his valuable suggestions.

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