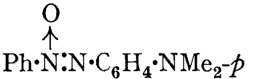
319. *Condensation of* N-*Phenylhydroxylamine with* NN-*Dimethyl*-p-*nitrosoaniline. The Azoxy-compounds derived from* p-*Dimethylaminoazobenzene.*

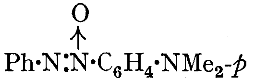
By W. Anderson.

α- and β-*p*-Dimethylaminoazoxybenzene (I and II) are both obtained on condensation of *N*-phenylhydroxylamine with *NN*-dimethyl-*p*-nitrosoaniline. Absorption-spectrum measurements were used to assign the structures to the compounds. The course of the reaction, which was studied in some detail, was contrary to that generally found for reactions between *N*-arylhydroxylamines and arylnitroso-compounds possessing different aryl residues.

The main object of the present investigation was the preparation of the isomeric azoxy-compounds (I) and (II) derived from *p*-dimethylaminoazobenzene. Direct oxidation of


$\mathrm{Ph{\cdot}\overset{\overset{O}{\uparrow}}{N}{:}N{\cdot}C_6H_4{\cdot}NMe_2}$-*p*

α-Isomer (I)

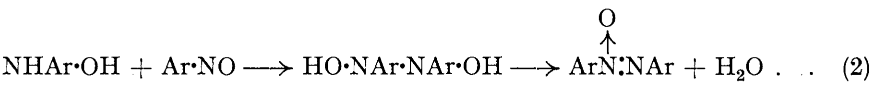

$\mathrm{Ph{\cdot}N{:}\overset{\overset{O}{\uparrow}}{N}{\cdot}C_6H_4{\cdot}NMe_2}$-*p*

β-Isomer (II)

the azo-compound with peracetic acid is unsuitable, since according to Angeli (*Atti R. Accad. Lincei*, 1915, **24**, 1190) it leads to the amine oxide of (II). Furthermore, interaction of *N*-arylhydroxylamines and arylnitroso-compounds possessing different aryl residues generally produces symmetrical azoxy-compounds (Bamberger and Renauld, *Ber.*, 1897, **30**, 2278; Renauld, Thesis, Rennes, 1896; Bamberger, *Viert. Naturforsch. Gess. Zürich*, 1896, **41**, 174; Müller, *Annalen*, 1932, **495**, 132; Taylor and Baker in Sidgwick's "Organic Chemistry of Nitrogen," Oxford Univ. Press, 1942, p. 427). This has been represented as a process of mutual oxidation and reduction :

$$\mathrm{2NHAr{\cdot}OH + 2Ar'{\cdot}NO \longrightarrow Ar{\cdot}N_2O{\cdot}Ar + Ar'{\cdot}N_2O{\cdot}Ar'} \quad . \quad . \quad . \quad . \quad (1)$$

There were indications however that the compounds desired might be formed in a hydroxylamine–nitroso-compound reaction. Thus, Bamberger and Bernays (*Ber.*, 1902, **35**, 1624) obtained one of the isomeric *p*-hydroxyazoxybenzenes from *N*-phenylhydroxylamine and *p*-nitrosophenol. Bamberger and Renauld (*loc. cit.*) suggested that unsymmetrical compounds, although not isolated, may have been present as products of other reactions of this type. Of interest also was that the rate of formation of azoxy-compounds is greatly increased by alkali (see Brand and Mahr, *J. pr. Chem.*, 1931, **131**, 97; 1935, **142**, 153). The following scheme analogous to that for the aldol-type condensation has been proposed :


$$\mathrm{NHAr{\cdot}OH + Ar{\cdot}NO \longrightarrow HO{\cdot}NAr{\cdot}NAr{\cdot}OH \longrightarrow Ar\overset{\overset{O}{\uparrow}}{N}{:}NAr + H_2O} \quad . \quad . \quad (2)$$

This alkali effect seems to have been studied only in reactions with hydroxylamines and nitroso-compounds possessing the same aryl residue; other reactions have generally been conducted in neutral solution. In the present work the reaction of *N*-phenylhydroxylamine with *NN*-dimethyl-*p*-nitrosoaniline was studied under various reaction conditions.*

When *N*-phenylhydroxylamine condensed with dimethyl-*p*-nitrosoaniline in alcohol in the presence of alkali, chromatography of the crude reaction product yielded two pale orange crystalline substances, m. p. 126·2—126·6° and 122·5—123·2° respectively, further characterised as their picrates. The separation on the column was quite definite and the melting points were strongly depressed on admixture. The substances were shown to be the azoxy-compounds (I) and (II).

The substances were soluble in warm dilute acids, giving colourless or slightly pink solutions. White crystalline hydrochlorides were formed under anhydrous conditions but sulphates were not obtained, presumably owing to their ready hydrolysis. Subjected to the Wallach reaction (Taylor and Baker, *op. cit.*, p. 428), both isomers yielded *p*-dimethylamino-*p*'-hydroxyazobenzene almost quantitatively. Most reactions of this type have been applied to only one compound of an isomeric pair although rearrangements of both to the same phenol are not unknown (Angeli, *Gazzetta*, 1916, **46**, ii, 82). On reduction, both substances gave *p*-dimethylaminoazobenzene.

Absorption spectra (see below) provide good evidence that the substance with m. p. 126·2—126·6° is the α-isomer (I) and that with m. p. 122·5—123·2° is the β-isomer (II). The spectra also show that both compounds possess the *trans*-azo-configuration. This is confirmed by the stability of the compounds at temperatures well above their melting points.

The isolation of the α- and the β-azoxy-compound discussed above appears to be the first example of a reaction of this type from which both isomers have been obtained. It is in keeping with the theoretical scheme (2). The reaction was studied more fully both in presence and in absence of alkali, in order to provide a comparison with similar reactions where the scheme (1) appears to apply.

In the reaction in presence of alkali the following substances were isolated: α- and β-*p*-dimethylaminoazoxybenzene, large quantities of azoxybenzene, a small quantity of *pp*'-bisdimethylaminoazoxybenzene, a trace of azobenzene, and a small impure fraction which may have been *pp*'-bisdimethylaminoazobenzene. The reaction without alkali, under the conditions used by Bamberger and Bernays (*loc. cit.*) for hydroxylamine–nitroso-compound reactions, gave the same products with a small amount of *p*-dimethylaminoazobenzene in addition; the yields of the azoxy-isomers were considerably smaller.

The occurrence of large amounts of azoxybenzene was due to the direct decomposition of the *N*-phenylhydroxylamine, and the other symmetrical azoxy-compound was only a trace product of the reaction. It would thus appear that the oxidation–reduction mechanism plays a very minor role in the interaction of *N*-phenylhydroxylamine with dimethyl-*p*-nitrosoaniline. Condensation proceeds, giving the unsymmetrical compounds, and this is aided by the presence of alkali.

The course of the reaction is in sharp contrast to that generally accepted for similar hydroxylamine–nitroso-compound reactions. This may be in part only apparent since the reaction products are always complex and information obtained from separations dependent on fractional crystallisation, as used in previous studies, is less complete than that gained by employing chromatography. However, there is no doubt that the production of symmetrical compounds is in general an important feature of these reactions. It is significant that in most cases nuclear-substituted *N*-phenylhydroxylamines were caused to react with nitrosobenzene. A study of the decomposition of nitrosobenzene under the conditions employed by Bamberger *et al.* for the production of azoxy-compounds, but without the addition of the hydroxylamine, showed that 15% of the nitrosobenzene was converted into azoxybenzene. This fact and the probability of similar decomposition of hydroxylamines indicate that the production of symmetrical azoxy-compounds is at least

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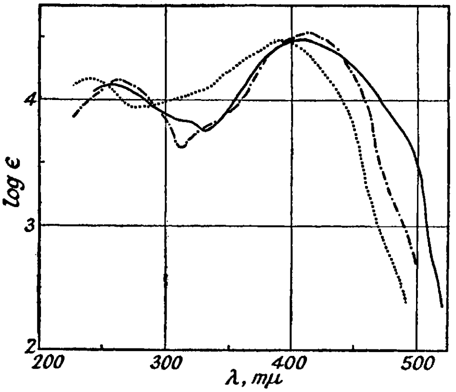
* The following errors in the literature should be noted. (1) Bigelow (*Chem. Reviews*, 1931, **9**, 157) states that Fischer and Wacker (*Ber.*, 1888, **21**, 2609) condensed dimethyl-*p*-nitrosoaniline with phenylhydroxylamine in absolute alcohol, obtaining *p*-azoxydimethylaniline. The reaction actually conducted was a condensation of dimethyl-*p*-nitrosoaniline with phenylhydrazine in absolute ether. (2) In *Chem. Abs.*, 1936, **30**, 9996, 2934^5, a substance listed as "Aniline, *NN*-dimethylphenylazoxy," $C_{14}H_{15}N_3O$ (Bigiavi and Albanese, *Gazzetta*, 1935, **65**, 773), was actually the oxide, $C_{14}H_{15}N_3O_2$, of this substance.

in part independent of any direct interaction of the nitroso-compound and the hydroxylamine. Further assessment of the relative importance of the different processes is prevented by absence, from the literature, of information on the yields of azoxy-compounds obtained. In the present study the nitroso-compound carries a dimethylamino-group, and again in the synthesis of one of the isomeric *p*-hydroxyazoxybenzenes by Bamberger and Bernays (*loc. cit.*) the hydroxyl group was attached to the nitroso-compound. On the other hand, Müller (*loc. cit.*) obtained only symmetrical azoxy-compounds from *o*-bromonitrosobenzene with *N*-*o*-chlorophenylhydroxylamine. The operation of the condensation mechanism in the reactions with the nitrosoaniline and the nitrosophenol may well be related to the profound influence of the amino- and hydroxyl radicals on the structure of these nitroso-compounds (see Taylor and Baker, *op. cit.*, p. 217).

Our intention to study the reaction of nitrosobenzene with *N*-*p*-dimethylaminophenylhydroxylamine has so far not been possible owing to the failure to prepare this hydroxylamine.

Spectrographic Data.—The absorption spectra of the isomers and their parent azo-compound *p*-dimethylaminoazobenzene, measured in 0·01% ethanolic solution, are shown in the Fig. The values for *p*-dimethylaminoazobenzene are in good agreement with those recorded by Pongratz *et al.* (*Ber.*, 1938, **71**, 1287) for 0·05% ethanolic solution; there is a slight difference in the $\varepsilon_{\text{max.}}$ values of the bands of shorter wave-length.



Absorption of : p-*dimethylaminoazobenzene* ————; *the azoxy-compound, m. p.* 122·5°, ...; *and the azoxy-compound, m. p.* 126°, — · — · —.

The features significant to the present work are (1) the similarity for the three compounds of the $\varepsilon_{\text{max.}}$ values in the comparable bands, (2) the larger shift of $\lambda_{\text{max.}}$ for the azoxy-compound, m. p. 122·5—123·2°, relative to the azo-compound and towards shorter wave-length, and (3) the closer relation of the general shape of the curve of the azoxy-compound, m. p. 126·2—126·6°, to that of the azo-compound.

The first point shows that the isomers possess a *trans*-configuration, since Müller's *cis*-azoxy-compounds (*loc. cit.*; *Annalen*, 1932, **493**, 166) have absorption intensities about half of those of the *trans*-stereoisomers, while the *trans*-compounds have values similar to those of the related azo-compounds. The second and third points together provide strong evidence that the azoxy-compound, m. p. 122·5—123·2°, is the β- and the other the α-isomer. This is based on Szegö's results (*Ber.*, 1929, **62**, 736) for numerous pairs of isomeric azoxy-compounds containing strongly directive groups; both points (2) and (3) are characteristic features of Szegö's spectra.

EXPERIMENTAL

Spectra were measured with a Hilger " Spekker " photometer and Medium Quartz Spectrograph, with a condensed spark between tungsten steel electrodes as light source. The recordings were made on Ilford Rapid Panchromatic Process plates, sensitive to 650 mμ. The ethanol employed was purified according to Leighton *et al.* (*J. Amer. Chem. Soc.*, 1931, **53**, 3017). The sample of *p*-dimethylaminoazobenzene, m. p. 117·5—117·8°, had been purified by chromatography.

Light petroleum refers to the fraction of b. p. 60—80°. M. p.s are corrected.

Preparation of the Azoxy-compounds (I *and* II).—*N*-Phenylhydroxylamine was prepared by reduction of nitrobenzene with zinc dust and aqueous ammonium chloride, dried quickly on porous plate, and used immediately. Commercial dimethyl-*p*-nitrosoaniline was recrystallised from light petroleum; this gave material with m. p. 85°.

Solutions of the nitroso-compound (1 g. in 12 c.c.) and the hydroxylamine (2 g. in 12 c.c.) in ethanol were mixed and a few drops of 50% aqueous potassium hydroxide added immediately with shaking. The mixture was heated at 70—80° for 10 minutes, then cooled and poured into water (400 c.c.). After 24 hours in the refrigerator the precipitated material was filtered off and dried, to give a brown powder (1·5 g.). (With some batches the precipitated material was soft and difficult to manipulate. In these cases extraction with benzene proved satisfactory but the chromatogram was more complex. Generally the bulk of the material was precipitated and little was gained by extraction of the diluted mother-liquor.) The brown material was poured on to an alumina column (10 × 1·5″) in benzene; aluminium oxide for chromatographic adsorption analysis supplied by Messrs. British Drug Houses Ltd., Dorset, gave satisfactory separations. The material separated into numerous zones. On development with benzene a broad orange zone appeared, preceded by a trace of yellow-orange material and followed by various orange, scarlet, and other zones. The broad orange zone was finally resolved into two bands which were eluted separately. Each part was subjected to two further chromatographic procedures. The lower band yielded trans-β-p-*dimethylaminoazoxybenzene* (II) (0·17 g.). After sublimation at 135°/0·05 mm. it was obtained from light petroleum as pale yellow-orange needles, m. p. 122·5—123·2° ± 0·3° (Found: C, 69·9; H, 6·2; N, 17·3. $C_{14}H_{15}ON_3$ requires C, 69·7; H, 6·3; N, 17·4%). The *picrate* prepared and crystallised from ethanol formed stout yellow prisms, m. p. 149—151° (decomp.) (Found: C, 51·2; H, 3·9. $C_{14}H_{15}ON_3,C_6H_3O_7N_3$ requires C, 51·1; H, 3·9%). The upper band yielded the trans-α-*isomer* (I), which was obtained from light petroleum as small pale orange prisms, m. p. 126·2—126·6° ± 0·3° (Found: C, 70·0; H, 6·3; N, 16·9%). The *picrate*, prepared and crystallised from ethanol, formed fine yellow needles, m. p. 155—157° (decomp.) (Found: C, 51·15; H, 3·9%).

The yields recorded are the highest of numerous runs. Similar yields were obtained from reactions at room temperature but the precipitates were finer and difficult to handle. Heating for more than 10 minutes also resulted in fine precipitates. The yields were lower when the hydroxylamine was not in excess of the theoretical quantity.

Chemical Properties of the Azoxy-compounds.—Reactions confirming structures assigned to compounds were as follows.

Hydrochlorides. White crystalline hydrochlorides were obtained by passing dry hydrogen chloride through dry benzene solutions of the materials. These hydrochlorides were quickly hydrolysed in the laboratory atmosphere and unsuitable for routine analysis. Handled with as little exposure to moisture as possible, they did not give sharp m. p.s even in sealed tubes. The hydrochloride of the β-isomer (II) decomposed from 140° to 152°; the other hydrochloride decomposed from 150° to 165°.

Wallach transformation. Solutions of the isomers (0·05 g.) in concentrated sulphuric acid (5 c.c.) were heated in the water-bath for 10 minutes. The reaction mixtures were cooled, stirred into water (50 c.c.), neutralised with sodium hydroxide (2N), and extracted with ether. Both extracts yielded bright red solids (0·045 g.), each with m. p. 201—202° (decomp.). In solubilities and colours with dilute acids these solids were identical with *p*′-dimethylamino-*p*-hydroxyazobenzene, m. p. 201—202° (decomp.). The identity of the materials was confirmed by mixed melting point determinations.

Reduction. The substances (0·05 g.) were suspended in ethanol (5 c.c.), and 25% aqueous sodium hydroxide (10 c.c.) was added. An excess of zinc dust was added during 10 minutes with vigorous stirring. The reaction mixtures were diluted with water (100 c.c.) and extracted with light petroleum. Chromatography of each extract on alumina with light petroleum gave bright orange crystalline substances (0·02 g.), each with m. p. 115—117°. In chromatographic behaviour, solubilities, and colours with dilute hydrochloric acid these substances were identical with *p*-dimethylaminoazobenzene, m. p. 117·5—117·8°. The identity of the materials was confirmed by mixed melting point determinations.

Effect of heat. After being heated in sealed tubes at 200° for 1 hour both compounds were largely unchanged. Only the α-isomer showed slight decomposition.

Reactions of N-*Phenylhydroxylamine with Dimethyl*-p-*nitrosoaniline.*—The nitroso- and hydroxylamine compounds were of the same grade as those used for the preparation of the azoxy-compounds. The *N*-phenylhydroxylamine contained 6—10% of azoxybenzene. Treatment of *N*-phenylhydroxylamine under the conditions used in the reactions below with the omission of the nitroso-compound gave azoxybenzene and azobenzene in quantities similar to those obtained in the reactions themselves. The various substances described were identified by their chromatographic behaviour, colour reactions with dilute hydrochloric acid, and mixed melting points with authentic compounds. Attention should be drawn to variations in the appearances of the materials on different batches of alumina. For example, the symmetrical azoxy-compound described was scarlet on some batches and a dull orange on others.

Reaction in presence of alkali. Solutions of the hydroxylamine (5 g. in 30 c.c.) and the nitroso-compound (5 g. in 60 c.c.) in ethanol were mixed and a few drops of 1 : 1 aqueous potassium hydroxide added immediately, with shaking. The reaction was then conducted as in the preparation of the azoxy-compounds. In the chromatography all the solvent which passed through before the elution of the main orange zones was collected. Removal of the solvent from this fraction and rechromatography of the material in light petroleum gave rise to a small, rapidly eluted, pale orange zone which yielded a few mg. of azobenzene. Further washing of this column, now colourless, with light petroleum gave an eluate which yielded pure azoxybenzene (1·5 g.) From the main column the two broad orange zones were eluted as before, to give β- (0·6 g.) and α-*p*-dimethylaminoazoxybenzene (0·8 g.). These two orange zones were followed by a third orange zone and then a scarlet zone. The alumina was pushed out and the region containing these two zones was cut off, made into a small column, and washed clear with hot benzene. Rechromatography on a small column with benzene effected a separation. The orange zone gave impure material (0·005 g.), m. p. 250—265°; this may have been *pp'*-bisdimethylaminoazobenzene, m. p. 266°. The scarlet zone yielded *pp'*-bisdimethylaminoazoxybenzene (0·05 g.).

Reaction without alkali. A solution of the nitroso-compound (5 g.) in ethanol (60 c.c.) was cooled in ice. The hydroxylamine (5 g.) was added and the mixture kept at room temperature for 30 minutes, and then refluxed for 1·75 hours. The alcohol was removed by distillation and the residue taken up in 1 : 4 benzene–light petroleum. This was chromatographed on an alumina column (8 × 1·25"). The chromatography conducted as above gave a trace of azobenzene, azoxybenzene (2·2 g.), *p*-dimethylaminoazobenzene (0·037) g.), β- (0·045 g.) and α-*p*-dimethylaminoazoxybenzene (0·15 g.). Zones were present corresponding to the symmetrical azo- and azoxy-compounds but separations of these were not effected.

Decomposition of Nitrosobenzene.—Nitrosobenzene (2 g.), purified by steam distillation, was suspended in dry ethanol (20 c.c.), and the mixture refluxed for 1·75 hours. The ethanol was removed by distillation and the residue extracted with cold light petroleum (3 × 30 c.c.). The extract was poured on to an alumina column. This was washed with light petroleum and the colourless eluate collected in fractions until a fraction devoid of dissolved material was obtained. Pure azoxybenzene (0·3 g.) was recovered from the various fractions. It was identified by direct comparison with a known sample of the substance. No azoxybenzene was detected in an untreated sample of the nitrosobenzene.

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