

295. *The Reactivity of the Aromatic Nucleus. Part I.*  
*Karrer's Theory of Coupling.*

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It has been found impossible to repeat Karrer's observations on the coupling of dibutylaniline and of *diisoamyl*aniline. These amines react normally with diazotised sulphanilic acid, and no indication was obtained of the elimination of an alkyl group during the reaction. It is also found that tertiary amines with even larger alkyl groups couple normally. It is concluded that there is no experimental foundation for Karrer's theory of coupling.

A method is described for the purification of dialkylarylamines through their picrates.

KARRER (*Ber.*, 1915, **48**, 1398) reported that dibutyl- or *diisoamyl*-aniline reacts in aqueous acetic acid solution with diazotised sulphanilic acid to form alkylaminoazobenzenes,  $\text{NHR}\cdot\text{C}_6\text{H}_4\cdot\text{N}_2\cdot\text{C}_6\text{H}_4\cdot\text{SO}_3\text{H}$  ( $\text{R} = \text{C}_4\text{H}_9$  or  $\text{C}_5\text{H}_{11}$ ), with the elimination of an alkyl group. As a preliminary to an investigation of the factors influencing the nuclear reactivity of the dialkylarylamines towards diazo-compounds, it was necessary to re-examine these reported abnormalities.

A repetition of the coupling of *diisoamyl*aniline with diazotised sulphanilic acid yielded an aminoazo-sulphonic acid, and analysis of its *potassium* salt indicated that it was *diisoamyl*aminoazobenzenesulphonic acid. This was confirmed by its reduction to *p*-amino-*diisoamyl*aniline, the *dihydrochloride* of which is readily distinguished from that of the monoalkyl compound, which should result if an alkyl group were eliminated. The coupling product was shown to be homogeneous by reducing the unpurified potassium salt obtained from the coupling and then benzoylating the resulting diamine. The crude product, washed and dried, had m. p. 97—100°, raised by further purification to 101°.

It is concluded that *diisoamyl*aniline couples normally with diazosulphanilic acid, and that there is no appreciable elimination of the alkyl group during the process. *Diisobutyl*aniline was also found to couple normally with this diazo-acid without any appreciable loss of an alkyl group, and a repetition of the coupling of di-*n*-butylaniline confirmed the earlier results of Reilly and Hickinbottom (*J.*, 1918, **113**, 99) that this amine also couples without the loss of an alkyl group. The coupling of these three dialkylanilines with diazotised *p*-nitroaniline was also found to proceed normally. These results lead to the conclusion that Karrer's observations were faulty, and that there is no experimental basis for the theory of coupling which he based upon them. An extension of the work to other dialkylanilines, which on Karrer's view might be expected to couple abnormally,

failed to provide any evidence of the elimination of an alkyl group. For instance, dicetyl- and di-*n*-octyl-aniline both couple normally with diazotised *p*-nitroaniline, and even methyl-*tert*-butylaniline reacts with it without the expulsion of an alkyl group, although it has been shown (Hickinbottom, J., 1933, 949, 1072) that the *tert*-butyl group may be eliminated relatively easily by warming with aqueous mineral acids or even by treatment with methyl iodide.

A method has been worked out for the preparation and purification of *N*-dialkylarylamines. It depends on the observation (Reilly and Hickinbottom, J., 1920, 117, 103) that their picrates are, in general, less soluble than those of the corresponding secondary amines. The preparation by this method of pure specimens of diisoomyl-, diisobutyl-, and di-*n*-butyl-anilines, dimethyl-*p*-xylydine, 2-dimethylamino-*m*-xylene, and *o*-chlorodimethylaniline is now described. This method seems to be of fairly wide application for the preparation of dialkylarylamines with not too large alkyl groups, for it has also been used for the preparation of methyl- and ethyl-*n*-butylanilines (Reilly and Hickinbottom, *loc. cit.*) and of *tert*-butyl- and *tert*-hexyl-methylanilines (Hickinbottom, J., 1933, 946). The method fails if the alkyl groups are too large: di-*n*-octyl- and dicetyl-aniline cannot be purified thereby, but the latter is readily purified by crystallisation of its hydriodide from methyl alcohol.

#### EXPERIMENTAL.

*Coupling of Diisoomylaniline.*—(a) *With diazosulphanilic acid: formation of 4-diisoomylaminoazobenzene-4'-sulphonic acid.* A solution of diisoomylaniline (1.5 g.) in glacial acetic acid (5 g.) was cooled and stirred mechanically while diazotised sulphanilic acid (from 1.11 g. of the acid) was added gradually. Potassium acetate (2 g.) was added after  $\frac{1}{2}$  hour and a further 2 g. after 2 hours. The stirring was continued for a further 2 hours, and the brownish product was then cooled in ice and diluted with 10 c.c. of water. Addition of an ice-cold solution of 10 g. of potassium hydroxide in 25 c.c. of water caused the separation of the *potassium* salt as a red sticky solid. For analysis it was purified by three crystallisations from aqueous alcohol (90%) and dried at 100° (Found: C, 57.6; H, 6.5.  $C_{22}H_{30}O_3N_3SK$  requires C; 58.0; H, 6.6%). It formed small, yellow-orange, glistening plates, readily soluble in water, sparingly soluble in alcohol.

Reduction with sodium hyposulphite in aqueous alkaline solution gave *p*-aminodiisoomylaniline, which was isolated as its *hydrochloride* by adding ethereal hydrogen chloride to a dried ethereal solution of the crude amine from the reduction. The salt separates from alcohol-ether as a white crystalline magma (Found: C, 59.6; H, 9.4.  $C_{16}H_{23}N_2 \cdot 2HCl$  requires C, 59.8; H, 9.4%); an aqueous solution gives a brilliant red coloration with ferric chloride solution, quickly fading to yellow.

4-Benzamidodiisoomylaniline, prepared from a suspension of the diamine in aqueous alkali, separates from aqueous alcohol as small glistening needles, m. p. 101° (Found: C, 78.3; H, 9.3.  $C_{23}H_{32}ON_2$  requires C, 78.4; H, 9.2%). Benzoylation of the crude diamine from reduction of the unpurified coupling product, gave a product which, washed with water and dried, had m. p. 97–100° (identity confirmed by mixed m. p.).

(b) *With p-nitrobenzenediazonium chloride: formation of 4'-nitro-4-diisoomylaminoazobenzene.* Diazotised *p*-nitroaniline (from 1 g. of base in 13.8 c.c. of 24% hydrochloric acid, 2 g. of ice, and 5.1 c.c. of 10% sodium nitrite solution) was filtered into a solution of 1.7 g. of diisoomylaniline in 20 c.c. of acetone, and 3 g. of sodium acetate added; the solution was stirred mechanically for 2 hours, and water added. The precipitated *azo*-compound separated from aqueous alcohol as small crimson crystals, m. p. 120° (Found: C, 68.7; H, 7.6; N, 14.7.  $C_{22}H_{30}O_2N_4$  requires C, 69.1; H, 7.9; N, 14.6%).

*Coupling of isoAmylaniline.*—(a) *With diazosulphanilic acid: formation of 4'-amylaminoazobenzene-4'-sulphonic acid.* Sulphanilic acid (5.3 g.) was diazotised and added to a mechanically stirred solution of isoamylaniline (5 g.) in 15 c.c. of glacial acetic acid. Coupling occurred immediately, and after 1 hr. potassium acetate (5 g.) was added, and after a further hour's stirring, the reddish-orange reaction mixture was neutralised by addition of an ice-cold solution of 25 g. of potassium hydroxide in 75 c.c. of water. The *potassium* salt of the *azo*-compound separated as a yellowish-orange solid admixed with some red oily matter. After crystallisation from 90% alcohol, it was obtained as golden-orange plates (Found: C, 52.6; H, 5.3.  $C_{17}H_{20}O_3N_3SK$  requires C, 52.9; H, 5.2%).

Reduction of the aminoazo-compound with an alkaline solution of sodium hyposulphite

yielded *p*-aminoisoamylaniline, which was isolated as its *dihydrochloride*, glistening plates from alcohol (Found : C, 52.4; H, 7.8.  $C_{11}H_{18}N_2 \cdot 2HCl$  requires C, 52.6; H, 8.0%). Its aqueous solution gives a green coloration with ferric chloride.

(b) *With p-nitrobenzenediazonium chloride: formation of 4'-nitro-N-isoamyl diazoaminobenzene.* Reaction of diazotised *p*-nitroaniline with isoamyl aniline under the conditions described for diisoamylaniline (p. 1384) gave a red oil which gradually solidified to a mass of dark red crystals having a green reflex. Extraction with boiling light petroleum (b. p. 40–60°) removed 4'-nitro-N-isoamyl diazoaminobenzene, which separated from alcohol as yellow aggregates of needles, m. p. 72–73° (Found : C, 65.4; H, 6.4.  $C_{17}H_{20}O_2N_4$  requires C, 65.3; H, 6.5%). Treatment with cold concentrated sulphuric acid and subsequent cautious dilution gave a solution containing a diazo-compound, as shown by its reaction with alkaline  $\beta$ -naphthol.

The dark red oil, remaining after extraction of the crude product with light petroleum, presumably contained the corresponding aminoazo-compound, but it could not be isolated in a pure state.

*Coupling of Diisobutylaniline.*—(a) *With diazosulphanilic acid: formation of 4'-diisobutylaminoazobenzene-4-sulphonic acid.* The coupling was effected under conditions similar to those employed for diisoamylaniline. The potassium salt of 4'-diisobutylaminoazobenzene-4-sulphonic acid separates from 90% alcohol as small, orange-brown crystals (Found : C, 56.3; H, 6.0; K, 9.2.  $C_{20}H_{26}O_3N_3SK$  requires C, 56.2; H, 6.1; K, 9.2%). Reduction in aqueous alkaline solution with sodium hyposulphite gave *p*-aminodiisobutylaniline, the hydrochloride of which separates from aqueous alcohol as small colourless crystals, m. p. 223–224° after darkening from about 210° (Found : C, 56.9; H, 8.9.  $C_{14}H_{24}N_2 \cdot 2HCl$  requires C, 57.3; H, 8.9%). Its aqueous solution gives with ferric chloride an intense red coloration which rapidly fades to yellow.

4-Benzamidodiisobutylaniline separates from alcohol as small white crystals, m. p. 111° (Found : C, 77.5; H, 8.8.  $C_{21}H_{28}ON_2$  requires C, 77.7; H, 8.7%). The crude diamine isolated directly from the reduction of the unpurified coupling product gave a benzoyl derivative which had m. p. 105–107° when washed with water and dried.

*p*-Aminodiisobutylaniline was also prepared by reduction of *p*-nitrosodiisobutylaniline hydrochloride in diluted hydrochloric acid with zinc. The benzoyl derivative of the diamine from this source was identical with that derived from the reduction of the coupling product. As Karrer (*loc. cit.*) failed to obtain this nitroso-compound, its preparation is given.

A solution of diisobutylaniline (2.1 g.) in 8 c.c. of diluted hydrochloric acid (1 : 2) was cooled in ice and salt and then treated with 1.6 c.c. of aqueous sodium nitrite (48%) with mechanical stirring. After 2 hours, the resulting precipitate of orange-brown crystals was collected, and purified by two crystallisations from alcohol-ether. *p*-Nitrosodiisobutylaniline hydrochloride was obtained as yellow-brown needles having no definite m. p. (Found : C, 62.5; H, 8.7.  $C_{14}H_{22}ON_2 \cdot HCl$  requires C, 62.1; H, 8.6%). The free base, liberated from the aqueous solution of the salt by the addition of ice-cold sodium carbonate solution, separates from light petroleum (b. p. 40–60°) as green needles, m. p. 62–63° (Found : C, 71.9; H, 9.7.  $C_{14}H_{22}ON_2$  requires C, 71.8; H, 9.5%).

(b) *With p-nitrobenzenediazonium chloride: formation of 4'-nitro-4-diisobutylaminoazobenzene.* The coupling product was obtained as described on p. 1384. It separates from alcohol as minute crimson needles, m. p. 122–123° (Found : C, 67.9; H, 7.3.  $C_{20}H_{26}O_2N_4$  requires C, 67.8; H, 7.4%).

Coupling of methyl-*tert.*-butylaniline in aqueous acetone with diazotised *p*-nitroaniline gave 4'-nitro-4-methyl-*tert.*-butylaminoazobenzene, which formed crimson needles from alcohol, m. p. 133–134° (Found : C, 65.5; H, 6.7.  $C_{17}H_{20}O_2N_4$  requires C, 65.3; H, 6.5%). Similar coupling of *tert.*-butylaniline gives as the main product 4'-nitro-N-*tert.*-butyldiazoaminobenzene, shining yellow plates from alcohol, m. p. 142–143° (Found : C, 64.3; H, 6.0.  $C_{16}H_{18}O_2N_4$  requires C, 64.4; H, 6.1%).

4'-Nitro-4-di-*n*-octylaminoazobenzene, obtained by the coupling of di-*n*-octylaniline with diazotised *p*-nitroaniline in aqueous acetone solution in presence of potassium acetate, separates from alcohol as clusters of crimson needles, m. p. 66–67° (Found : C, 71.5; H, 8.9.  $C_{28}H_{42}O_2N_4$  requires C, 72.1; H, 9.1%); and by a reaction under the same conditions, *n*-octylaniline gave 4'-nitro-N-*n*-octylaminodiazoaminobenzene as principal product; yellow, felted needles, m. p. 61–62° (Found, C, 67.7; H, 7.7.  $C_{20}H_{28}O_2N_4$  requires C, 67.8; H, 7.4%).

4'-Nitro-4-dicetylaminoazobenzene, prepared by coupling dicetylaniline with diazotised *p*-nitroaniline in aqueous acetone solution, separates from acetone as bright red crystals, m. p. 70–71° (Found : C, 76.4, 76.9; H, 10.8, 10.9.  $C_{44}H_{74}O_2N_4$  requires C, 76.4; H, 10.8%).

The dicetylaniline was obtained by heating cetylaniline (7 g.) with cetyl iodide (7.7 g.) at 110° for 4 hours. The amines isolated from the reaction product were distilled up to 280°/0.025 mm. to remove the bulk of the unchanged cetylaniline. The residue was converted into hydriodide, which was recrystallised several times from methyl alcohol; the base isolated from this salt and repeatedly crystallised from methyl alcohol separates from this solvent as small, soft, white crystals, m. p. 30° (Found: C, 84.1; H, 13.4.  $C_{38}H_{71}N$  requires C, 84.2; H, 13.2%).

Cetylaniline couples with diazotised *p*-nitroaniline under conditions similar to those used for dicetylaniline to give 4-nitro-*N*-cetyldiazoaminobenzene, pale yellow crystals from alcohol, m. p. 77° (Found: C, 72.0; H, 9.5.  $C_{28}H_{42}O_2N_4$  requires C, 72.1; H, 9.1%).

*Preparation of N-Dialkylarylamines.—Diisoamylaniline.* *iso*Amyl bromide (50 g.) and aniline (25 g.) were heated under reflux at 120° for 2 hours and then at 140° for 1 hour. The product was treated with an excess of aqueous sodium hydroxide, and the liberated amines, after drying, were distilled. The distillate above 190° (43.9 g.) was heated with 25 g. of *iso*amyl bromide for 3 hours at 100° followed by 5 hours at 140°. The amines liberated from this product were distilled, the fraction, b. p. 190—270° (37.4 g.), being subjected to a further 7 hours' heating at 150° with *iso*amyl bromide (25 g.). The amines from this last heating were distilled, and the fraction, b. p. >260°, was combined with that from the previous alkylation boiling above 270° (yield, 52.3 g.). These combined fractions, consisting largely of diisoamylaniline, were converted into picrate by warming with picric acid (48 g.) in ethereal solution, and the crude *picrate* of diisoamylaniline was recrystallised to constant m. p. 146° from absolute alcohol (yellow crystals. Found: C, 57.5; H, 6.7.  $C_{16}H_{27}N_2C_6H_3O_7N_3$  requires C, 57.1; H, 6.5%). The pure amine was liberated from the purified *picrate* by adding an excess of ammonia and distilling in steam; yield, 21.5 g., b. p. 166—168°/18 mm.

*Diisobutylaniline.* This base was prepared and purified similarly. Its *picrate* separated from alcohol as yellow crystals, m. p. 141° (Found: C, 55.2; H, 6.0.  $C_{14}H_{23}N_2C_6H_3O_7N_3$  requires C, 55.3; H, 6.0%), and the regenerated base had b. p. 142—144°/21 mm.

*Dimethyl-*p*-xylydine.* *p*-Xylydine (40 g.) was heated for 5 hours in a boiling water-bath with methyl iodide (141 g.) and a solution of 40 g. of anhydrous sodium carbonate in 400 c.c. of water. The crude amine, after being separated from the aqueous layer and dried, was heated with alcohol (300 g.) and picric acid (68 g.); after standing overnight, the *picrate* was collected and purified by further recrystallisation from alcohol, forming yellow needles, m. p. 159—160° (von Braun, Arkuszewski, and Köhler, *Ber.*, 1918, 51, 290, record orange-red needles, m. p. 158°). The pure regenerated amine (28 g.) had b. p. 198—199°.

*2-Dimethylamino-*m*-xylene.* The methylation was carried out as in the preceding preparation, and the product converted directly into *picrate*; yellow crystals from alcohol, m. p. 154—155° (Found, C, 50.6; H, 4.8; N, 14.8.  $C_{10}H_{15}N_2C_6H_3O_7N_3$  requires C, 50.8; H, 4.8; N, 14.8%). The yield of pure amine, b. p. 82—82.5°/18 mm., was 8.5 g. from 14.2 g. of 2-amino-*m*-xylene.

*o*-Chlorodimethylaniline. *o*-Chloroaniline (25.3 g.), methyl iodide (84 g.), sodium carbonate (27 g.), and water (400 c.c.) were heated together in a boiling water-bath for 15 hours. The crude product, heated with picric acid (36 g.) in alcohol, furnished a *picrate*, which after crystallisation from alcohol had m. p. 133—134° (Found: C, 44.1; H, 3.5; N, 14.9; Cl, 9.4.  $C_8H_{10}NCl_2C_6H_3O_7N_3$  requires C, 43.7; H, 3.4; N, 14.6; Cl, 9.2%). The regenerated amine (18 g.) had b. p. 101—103°/28 mm.