106. p-*Aminodimethylaniline. Part III. The Orientation of Groups in the Disubstituted Molecule.*

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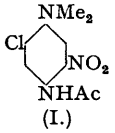
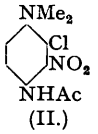
The study of the influence of nuclear substituents on the coupling power of diazotised *p*-aminodimethylaniline (compare Parts I and II, *J.*, 1941, 613; 1942, 755) required the preparation of derivatives of the base having chloro- or nitro-groups in the *o*- and *m*-positions to the dimethylamino-group. 2-Chloro-4-acetamidodimethylaniline yields the 5-nitro-derivative by nitration in sulphuric acid. In the chlorination of 3-nitro-4-acetamidodimethylaniline and in the nitration of 3-chloro-4-acetamidodimethylaniline substitution occurs in the 2- instead of the 6-position.

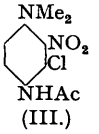
As a result of the exceptionally strong *op*-directing activity of the dimethylamino-group, substituents normally enter *p*-acetamidodimethylaniline in one or both of the *o*-positions (compare Part II). A single nitro-group can, however, be introduced into the *m*-position by nitration in concentrated sulphuric acid (Hodgson and Crook, *J.*, 1932, 2976), the point of attack being here determined by the acetamido-group. In a similar manner,



(I.)



(II.)



(III.)

2-*chloro*-5-*nitro*-4-*acetamidodimethylaniline* (I) was obtained by the nitration of 2-chloro-4-acetamidodimethylaniline (compare Part II) in concentrated sulphuric acid; its structure was verified by deacetylation and deamination of the resulting *base* to 2-chloro-5-nitrodimethylaniline (compare van Duin, *Rec. Trav. chim.*, 1932, **51**, 878).

Since in the nitration of 3-nitro-4-acetamidodimethylaniline the second nitro-group had been reported to enter the 6-position to give the compound usually termed 2 : 5-dinitro-4-acetamidodimethylaniline (Hodgson and Crook, *J.*, 1934, 873), it was expected that chlorination would yield the red 2-chloro-5-nitro-compound (I).

Instead, however, the product consisted entirely of a pale yellow substance considered to be 2-*chloro*-3-*nitro*-4-*acetamidodimethylaniline* (II), since the compound obtained on deacetylation and deamination of the resulting *base* was identical with 2-*chloro*-3-*nitrodimethylaniline* prepared by methylation of 2-chloro-3-nitroaniline (compare Wallagh and Wibaut, *Rec. Trav. chim.*, **1936**, **55**, 1074). Similarly, the nitration of 3-chloro-4-acetamidodimethylaniline with nitrous acid, with a mixture of nitric acid and hydrochloric acid (compare Part II), or with nitric acid in concentrated sulphuric acid, gave only 3-*chloro*-2-*nitro*-4-*acetamidodimethylaniline* (III); this compound, by hydrolysis to the free *base* and subsequent deamination, was converted into 3-chloro-2-nitrodimethylaniline (compare Hodgson and Nicholson, *J.*, 1941, 766).

Substitution in the 2- rather than in the 6-position of the 3-chloro-compound is readily accounted for by the mechanism suggested by Hodgson and Nicholson (*loc. cit.*) for the comparable case of nitration of the 3-halogenodimethylanilines which gives the 2- as well as the 4-nitro-derivatives. Since, however, the 4-position is now occupied, the most strongly activated point in 3-chloro-4-acetamidodimethylaniline will be the 2-position, and the resulting yield of 2-nitro-derivative is high. Similar considerations apply to the chlorination of 3-nitro-4-acetamidodimethylaniline, especially as it has now been found possible to isolate some 2-chloro-3-nitrodimethylaniline from the product of chlorination of 3-nitrodimethylaniline.

It appears that another factor enters into the nitration of the 3-nitro-derivatives. Forster and Coulson (*J.*, 1922, **121**, 1988) commented on the absence of 2 : 3-dinitrodimethylaniline from the nitration products of 3-nitrodimethylaniline (compare also Macmillan and Reade, *J.*, 1929, 2865; Hodgson and Smith, *J.*, 1931, 1508). Similarly, Hodgson and Crook (*loc. cit.*) recorded 2 : 5-dinitro-4-acetamidodimethylaniline (*i.e.*, 3 : 6-dinitro-) as the only nitration product of 3-nitro-4-acetamidodimethylaniline. These observations rested on the conclusion of Forster and Coulson (*loc. cit.*) that the red dinitrodimethylaniline, m. p. 112°, of van Romburgh (*Rec. Trav. chim.*, 1887, **6**, 253; compare also Vorländer and Siebert, *Ber.*, 1919, **52**, 297, and Swann, *J.*, 1920, **117**, 3) was in fact the 2 : 5-compound; this has now been confirmed by its preparation from 2 : 5-dinitroaniline by methylation.

The preferential formation of the 2 : 5-dinitro-derivative would seem to be a steric effect; the amount of space available in the 2-position, when the 3-position is occupied by a nitro-group, is not great, particularly as the mesomerism of the dimethylamino-group requires that the *N*-methyl groups should tend to lie in the plane of the benzene ring (Birtles and Hampson, *J.*, 1937, 10). Thus, although the space in the 2-position may be quite adequate to receive a chloro-group, the larger nitro-group is diverted into the 6-position, even though this may be less strongly activated. Nevertheless, there does appear to be some tendency towards 2-substitution, for the nitration of *p*-acetamidodimethylaniline in sulphuric acid and the nitration of 3-nitro-4-acetamidodimethylaniline with nitrous acid or with a mixture of nitric acid and hydrochloric acid give, in addition to the deep red 2 : 5-dinitro-compound of Hodgson and Crook (*loc. cit.*), a smaller amount of an orange-yellow *dinitro*-derivative which, by exclusion, must be the 2 : 3-compound. Like certain other 2-nitro-compounds of this type (compare Part II), it cannot be deacetylated without decomposition, and it has therefore not been possible to verify its structure by degradation.

Experimental.

2-*Chloro*-5-*nitro*-4-*acetamidodimethylaniline* (I).—To a solution of 2-chloro-4-acetamidodimethylaniline (2·12 g.) (cf. Part II) in concentrated sulphuric acid (8 c.c.) was added a mixture of nitric acid (1·4 c.c., *d* 1·5) and sulphuric acid (6 c.c.) at 0°. After an hour the mixture had become deep yellow; it was poured on to ice, filtered to remove traces of nitrosoamine, and neutralised with ammonia. 2-*Chloro*-5-*nitro*-4-*acetamidodimethylaniline* (1·34 g., 52%) was precipitated, and crystallised from alcohol as a coppery-red felted mass of fine needles, m. p. 124° (Found : Cl, 13·9. $C_{10}H_{12}O_3N_3Cl$ requires Cl, 13·8%). The compound was soluble in 10% sodium hydroxide solution and could be recovered unchanged by acidification and neutralisation with ammonia.

2-*Chloro*-5-*nitro*-4-*aminodimethylaniline*.—The acetyl derivative was hydrolysed by boiling for 3 minutes with 40% sulphuric acid. On cooling and basifying, 2-*chloro*-5-*nitro*-4-*aminodimethylaniline* separated; it crystallised from ligroin (b. p. 80—100°) in dark red square plates, m. p. 92—93° (Found : Cl, 16·5. $C_8H_{10}O_2N_3Cl$ requires Cl, 16·5%).

A solution of the base (1 g.) in 40% sulphuric acid (5 c.c.) was diazotised with sodium nitrite and refluxed with alcohol (50 c.c.) for 30 minutes. On concentration of the solution and addition of ammonia, 2-chloro-5-nitrodimethylaniline was obtained; it crystallised from alcohol, after treatment with charcoal, in bright yellow prismatic rods, m. p. 64—65°, and was identical with an authentic specimen prepared in 90% yield from *o*-chlorodimethylaniline by the method of van Duin (*loc. cit.*).

2-*Chloro*-3-*nitro*-4-*acetamidodimethylaniline* (II).—3-Nitro-4-acetamidodimethylaniline was prepared in 65% yield by the method of Hodgson and Crook (*J.*, 1932, 2976). After treatment of its alcoholic solution with charcoal it crystallised in deep red prisms, m. p. 124° (Found : N, 18·5. Calc. : N, 18·8%). (Hodgson and Crook record m. p. 116°.) Chlorine was passed into a solution of this compound (2·23 g.) in dry chloroform at room temperature. The colourless hydrochloride which separated was washed with chloroform and its aqueous solution basified; 2-*chloro*-3-*nitro*-4-*acetamidodimethylaniline* (2·05 g., 80%) separated and crystallised from aqueous methanol in pale yellow leaflets, m. p. 159—160° (Found : Cl, 13·8. $C_{10}H_{12}O_3N_3Cl$ requires Cl, 13·8%). This compound was not affected by further treatment with chlorine in chloroform solution. It did not react with nitrous acid, but gave a nitrosoamine derivative on dissolving in nitric acid (*d* 1·4).

2-*Chloro*-3-*nitro*-4-*aminodimethylaniline*.—A solution of the foregoing acetyl derivative in 40% sulphuric acid was raised to the boiling point. On cooling and basifying 2-*chloro*-3-*nitro*-4-*aminodimethylaniline* separated. The base was very soluble in most organic solvents, but crystallised from ligroin (b. p. 80—100°) in yellowish-red needles, m. p. 57·5° (Found : Cl, 16·4. $C_8H_{10}O_2N_3Cl$ requires Cl, 16·5%).

2-*Chloro*-3-*nitrodimethylaniline*.—(*a*) A solution of 2-chloro-3-nitro-4-aminodimethylaniline (1 g.) in hydrochloric acid (5 c.c., *d* 1·2) and water (5 c.c.) was diazotised with sodium nitrite (0·32 g.) in water (5 c.c.). The solution was refluxed with alcohol (50 c.c.) for 30 minutes, made alkaline and steam-distilled. 2-*Chloro*-3-*nitrodimethylaniline* passed over very readily and was recovered by extraction with ether. Crystallisation from aqueous alcohol gave golden-yellow leaflets or long flattened needles (0·75 g., 80%), m. p. 41°, having a faint but characteristic odour (Found : Cl, 17·7. $C_8H_9O_2N_2Cl$

requires Cl, 17·7%). The substance was very soluble in light petroleum. It was unaffected by boiling with aqueous sodium hydroxide.

(*b*) *o*-Chloronitrobenzene (100 g.) was nitrated by the procedure of Ostromisslensky (*J. pr. Chem.*, 1908, **78**, 261), and a large amount of crystalline 1-chloro-2 : 4-dinitrobenzene was removed from the ethereal solution of the product. The residual oil (14·5 g.), consisting mainly of the two isomeric dinitro-compounds, was treated with ethyl acetoacetate and sodium methoxide (Borsche and Rantscheff, *Annalen*, 1911, **379**, 152) in order to remove the remainder of the 1-chloro-2 : 4-dinitrobenzene. The unreacted part of the oil was dissolved in benzene and passed through a column of alumina; on removal of the benzene, 2-chloro-1 : 3-dinitrobenzene (3·1 g., 2%) was obtained, which crystallised from alcohol in yellow needles m. p. 88°. This was reduced to 2-chloro-3-nitroaniline by the method of Wallagh and Wibaut (*loc. cit.*), using the calculated amount of 0·1N-titanous chloride solution. The resulting base, which crystallised from aqueous alcohol in fine yellow needles, m. p. 95—96°, was methylated by heating with methyl sulphate for 3 hours at 150—160°. Subsequent steam-distillation of the alkaline solution gave 2-chloro-3-nitrodimethylaniline identical with the compound obtained by the method (*a*) above.

(*c*) To 3-nitrodimethylaniline (1·7 g., 1 mol.) dissolved in carbon tetrachloride (5 c.c.) was added a solution of chlorine (0·82 g., 1 mol.) in the same solvent (10 c.c.); the mixture became warm and an orange-yellow oil separated. The solvent was removed under reduced pressure and the residue made alkaline and steam-distilled, the initial distillate being collected in four small fractions. The first two of these fractions, when extracted with ether, gave oils which, after crystallisation from aqueous alcohol, yielded 2-chloro-3-nitrodimethylaniline identical with that prepared by methods (*a*) and (*b*). The oils obtained from the third and fourth fractions could not be crystallised.

3-Chloro-4-acetamidodimethylaniline.—This compound, which crystallised from aqueous alcohol in needles, m. p. 117—118°, was prepared substantially as described by Fieser and Thompson (*J. Amer. Chem. Soc.*, 1939, **61**, 383). The intermediate 3-chloro-4-aminodimethylaniline (cf. also Bayer and Co., G.P. 197,035; *Chem. Zentr.*, 1908, I, 1507) crystallised from ligroin (b. p. 40—60°) in prisms, m. p. 40—42°. Unlike 2-chloro-4-aminodimethylaniline (Part II) and 3-nitro-4-aminodimethylaniline, the base gave a positive reaction (a violet colour) in Lauth's test for *p*-diamines.

Nitration of 3-Chloro-4-acetamidodimethylaniline.—(*a*) The acetyl derivative (1 g.) dissolved in hydrochloric acid (2 c.c., *d* 1·2) and water (4 c.c.) was treated with sodium nitrite (0·5 g.) in water (3 c.c.) at 0°. After being left overnight the mixture was made alkaline; the precipitated *3-chloro-2-nitro-4-acetamidodimethylaniline* (III) (0·88 g., 75%) crystallised from alcohol in yellowish-red prisms, m. p. 166° (Found : Cl, 13·6. $C_{10}H_{12}O_3N_3Cl$ requires Cl, 13·8%).

(*b*) 3-Chloro-4-acetamidodimethylaniline (1 g.) dissolved in hydrochloric acid (6 c.c., *d* 1·2) was treated with nitric acid (3 c.c., *d* 1·42) at room temperature. An immediate reaction ensued and, after pouring the mixture into water and making alkaline with ammonia, 3-chloro-2-nitro-4-acetamidodimethylaniline was the only compound which could be isolated.

(*c*) The acetyl derivative (1·95 g.) dissolved in concentrated sulphuric acid (8 c.c.) was treated with nitric acid (1·4 c.c., *d* 1·5) in sulphuric acid (6 c.c.) at 0° and kept overnight in the cold. On pouring into ice-water a solid nitrosoamine derivative (0·37 g.) separated. When the filtered solution was basified a precipitate of 3-chloro-2-nitro-4-acetamidodimethylaniline (1·4 g., 62%) was obtained, identical with that prepared by methods (*a*) and (*b*).

3-Chloro-2-nitro-4-aminodimethylaniline.—The foregoing acetyl derivative (1 g.) was boiled for 2 minutes with 40% sulphuric acid (10 c.c.). On addition of ammonia an oil was obtained, which soon solidified. By fractional extraction and crystallisation from ligroin (b. p. 80—100°) the crude reaction product, which contained some tarry matter, gave *3-chloro-2-nitro-4-aminodimethylaniline* in the form of black plates or needles, m. p. 53—54°, appearing deep red by transmitted light (Found : Cl, 16·5. $C_8H_{10}O_2N_2Cl$ requires Cl, 16·5%).

3-Chloro-2-nitrodimethylaniline.—When 3-chloro-2-nitro-4-aminodimethylaniline was deaminated by a procedure similar to that previously described for related bases, the product of steam-distillation crystallised from aqueous alcohol or ligroin to give 3-chloro-2-nitrodimethylaniline in long, bright yellow needles, m. p. 39° (Found : Cl, 17·7. Calc. : Cl, 17·7%). There was no m. p. depression on admixture with an authentic specimen, m. p. 39°, prepared by the method of Hodgson and Nicholson (*loc. cit.*) who, however, record m. p. 36°.

In the authors' experience, the " initial yellow precipitate " (Hodgson and Nicholson, *loc. cit.*) consisted only of 3-chloro-4-nitrodimethylaniline hydrochloride, whereas the 3-chloro-2-nitrodimethylaniline was present in the filtrate, from which it was readily recovered by steam-distillation. Though considerably less volatile in steam than 3-chloro-2-nitrodimethylaniline, the isomeric 3-chloro-4-nitrodimethylaniline cannot accurately be described as " non-volatile."

2 : 5-*Dinitrodimethylaniline.*—The mixture of dinitroacetanilides resulting from the nitration of *m*-nitroacetanilide was separated by the usual procedure (cf. Welsh, *J. Amer. Chem. Soc.*, 1941, **63**, 3276) and the 2 : 5-compound was deacetylated to give 2 : 5-dinitroaniline, m. p. 137°. The base (0·62 g.) was heated with methyl sulphate (2 c.c.) at 150—160° for 4 hours and the mixture then made almost alkaline. The dark red precipitate was filtered off and boiled with alcohol, decanting from insoluble tarry matter. The alcoholic solution was evaporated to dryness and the residue warmed with acetic anhydride (1 c.c.), excess of this reagent being removed under reduced pressure. The solid residue was dissolved in hydrochloric acid and the solution extracted several times with ether before final neutralisation. The product (0·4 g., m. p. 105°) was crystallised from aqueous alcohol, filtering through charcoal, to give 2 : 5-dinitrodimethylaniline in red needles (0·33 g.), m. p. 114° (earlier authors record m. p. 112°; Hodgson and Crook give m. p. 114°). The m. p. was not depressed by the compound prepared by nitration of dimethylaniline (van Romburgh, *loc. cit.*) and by deamination of 2 : 5-dinitro-4-aminodimethylaniline (Hodgson and Crook, *J.*, 1934, 873).

2 : 3-*Dinitro-4-acetamidodimethylaniline.*—(*a*) *p*-Acetamidodimethylaniline (16 g.) was nitrated by the method of Hodgson and Crook (*loc. cit.*). The crude reaction product was dissolved in warm alcohol, filtered through charcoal, and allowed to crystallise. A quantity of 2 : 5-dinitro-4-acetamidodimethylaniline separated from the alcoholic solution, and the concentrated filtrate was finally evaporated to dryness and extracted with benzene. The crystals obtained on evaporating the benzene solution were further purified by addition of carbon tetrachloride to their solution in chloroform; crystallisation from alcohol gave a felted mass of orange-yellow needles, m. p. 171·5—172·5° (Found : C, 44·9; H, 4·5; N, 20·2. $C_{10}H_{12}O_5N_4$ requires C, 44·8; H, 4·5; N, 20·9%). Since this compound did not correspond with any of the dinitro-4-acetamidodimethylanilines isolated by Hodgson and Crook, it was considered to be 2 : 3-*dinitro-4-acetamidodimethylaniline*. Treatment with hot mineral acid resulted only in the formation of tarry products. (*b*) 3-Nitro-4-acetamidodimethylaniline (0·5 g.) dissolved in hydrochloric acid (3 c.c., *d* 1·2) was treated with nitric acid (1·5 c.c., *d* 1·42) at room temperature. After 30 seconds the solution was made alkaline. The crude product (0;44 g.) contained some unchanged 3-nitro-compound (at least 0·13 g.) which was recovered in the later stages of crystallisation. By a separation similar to that described above there were obtained 2 : 5-dinitro-4-acetamidodimethylaniline (0·14 g., approx. 31%), 2 : 3-dinitro-4-acetamidodimethylaniline (0·04 g., 9%), and a mixture of the two (0·08 g., 18%). (*c*) 2 : 3-Dinitro-4-acetamidodimethylaniline was similarly obtained from the product of nitration of 3-nitro-4-acetamidodimethylaniline with nitrous acid according to the method of Hodgson and Crook (*loc. cit.*).

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