167. p-*Aminodimethylaniline. Part II. The* o-*Chloro- and -Nitro-derivatives.*

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Methods are described for the preparation of 2-chloro-, 2 : 6-dichloro-, and 2-chloro-6-nitro-4-aminodimethylaniline. A novel reaction is recorded in which bromine removes an *N*-methyl group, leading to the formation of 2-chloro-6-nitro- and 2 : 6-dinitro-4-acetamidomethylaniline.

In Part I (J., **1941**, 613) the authors showed that the sluggishness of the reaction between diazotised *p*-aminodimethylaniline and amines or phenols, and the poor yields of azo-compound, can be attributed to the strong tautomeric influence of the dimethylamino-group, which hinders the formation of a positive charge at the diazo-group. In order to study the possible modification of this effect by nuclear substituents, such as chlorine and the nitro-group, in the *o*-position to the dimethylamino-group, it was necessary to examine the mode of formation and the properties of such compounds, only 2 : 6-dinitro-4-aminodimethylaniline (Hodgson and Crook, J., **1934**, 873) having previously been described.

Although 2-nitro-4-aminodimethylaniline is known as its acetyl and formyl derivatives (*idem*, J., **1932**, 2976; Pinnow and Pistor, *Ber.*, **1894**, **27**, 605), the free base has not been isolated, since it suffers decomposition during its liberation by hydrolysis. An attempt to obtain the base by partial reduction of 2 : 4-dinitrodimethylaniline yielded only 4-nitro-2-aminodimethylaniline (compare Heim, *Ber.*, **1888**, **21**, 2308), and the nitration of *p*-aminodimethylaniline gave the 2 : 6-dinitro-base.

2-*Chloro*-4-*aminodimethylaniline* was obtained by hydrolysis of its *acetyl* derivative, formed in the chlorination of *p*-acetamidodimethylaniline in chloroform. It was also readily obtained not only from 2-nitro-4-acetamidodimethylaniline, by reduction of the nitro-group and replacement of the resulting amino-group by chlorine by means of the diazo-reaction and subsequent hydrolysis, but also by reduction of 2-chloro-4-nitrodimethylaniline (compare van Duin, *Rec. Trav. chim.*, 1932, **51**, 878). The latter compound results from direct chlorination of 4-nitrodimethylaniline or from the diazo-reaction on 4-nitro-2-aminodimethylaniline, which, when diazotised, resembles diazotised *p*-aminodimethylaniline (Ayling, Gorvin, and Hinkel, *loc. cit.*) in its anomalous reaction with copper bronze but reacts normally with cuprous chloride.

When nitrated in acetic acid solution, the 2-nitro- or 2-chloro-4-acetamidodimethylaniline acquires a nitro-group in the 6-position and a nitroso-group replaces an *N*-methyl group (compare Meldola and Hollely, J., 1915, **107**, 610). In hydrochloric acid (*d*, 1·2), however, the reaction can be arrested at the first stage to give 2 : 6-dinitro- and 2-*chloro*-6-*nitro*-4-*acetamidodimethylaniline*, respectively. The latter compound also resulted from direct chlorination of 2-nitro-4-acetamidodimethylaniline. The acetyl group could not be removed by hydrolysis without decomposition of the base (compare 2-nitro-4-acetamidodimethylaniline). Replacement of the nitro-group in 2-nitro-6-chloro-4-acetamidodimethylaniline by chlorine, through the amine by means of the diazo-reaction in the usual manner, yielded 2 : 6-*dichloro*-4-*acetamidodimethylaniline*. This compound also results from the direct chlorination of 2-chloro-4-acetamidodimethylaniline.

A new example of the weakening of the bond between the *N*-methyl groups and the nitrogen atom by *o*-substituents (compare Hodgson, *J. Soc. Dyers Col.*, 1930, **46**, 183; Emerson, *J. Amer. Chem. Soc.*, 1941, **63**, 2023) is provided by the action of bromine on 2-chloro-6-nitro-4-acetamidodimethylaniline and on 2 : 6-dinitro-4-acetamidodimethylaniline. In each case there is an elimination of an *N*-methyl group to give the corresponding monomethylaniline derivative (compare Leymann, *Ber.*, 1882, **15**, 1234).

EXPERIMENTAL.

2-Nitro-4-acetamidodimethylaniline, prepared in 90% yield from *p*-acetamidodimethylaniline (Auwers and Wehr, *Annalen*, 1904, **344**, 311) by Pinnow and Pistor's method (*loc. cit.*) for the formyl analogue, crystallised from hot water, or appropriately seeded benzene solutions, in maroon parallelepipeds, m. p. 132° (cf. Hodgson and Crook, *loc. cit.*), or from benzene in orange-yellow needles, m. p. 122—123° (Found : N, 18·3. Calc. : N, 18·8%). The orange form also separated as a crystalline powder on neutralising cold, dilute aqueous acid solutions; van Alphen (*Rec. Trav. chim.*, 1932, **51**, 458) quotes many examples of dimorphism in nitro-compounds of similar type. The compound reacted readily with hot mineral acids but formed red tarry products.

When the filtrate from the above preparation was made alkaline with ammonia and evaporated to small bulk under reduced pressure, N-*nitroso*-4-*acetamidomethylaniline* (0·88 g., 6%) separated; after decolorisation, it crystallised from water in colourless plates, m. p. 146° (Found : C, 55·9; H, 5·7; N, 21·5. $C_9H_{11}O_2N_3$ requires C, 55·9; H, 5·7; N, 21·8%). The compound gives a positive reaction in the Liebermann nitrosoamine test (Hodgson and Crook, *loc. cit.*, obtained an *N*-nitroso-compound, m. p. 146°, when the above nitration was carried out in dilute hydrochloric acid).

Nitration of p-*Aminodimethylaniline*.—Nitric acid (*d* 1·5; 1·9 c.c., 2 mols.) in acetic acid (5 c.c.) was added to an ice-cooled solution of *p*-aminodimethylaniline (2·7 g., 1 mol.) in acetic acid (20 c.c.) containing sulphuric acid (1·2 c.c., 1 mol.). Reaction was rapid, and when the product was poured into water (250 c.c.) 2 : 6-dinitro-4-aminodimethylaniline (0·24 g.) separated; after decolorisation, this crystallised from aqueous alcohol in orange-red needles, m. p. 157°, unchanged by admixture with an authentic specimen prepared by the method of Hodgson and Crook (*loc. cit.*).

2 : 4-*Dinitrodimethylaniline*.—Following a method mentioned, but not detailed, by Orton (*Ber.*, 1907, **40**, 374), nitric acid was added to a solution of dimethylaniline (60 g.) in acetic acid (225 c.c.). On addition of a little sodium nitrite a rapid reaction set in, during which the mixture was kept below 15° by cooling in ice. When crystals appeared in the solution, the temperature was no longer controlled and, at the end of the reaction, 2 : 4-dinitrodimethylaniline (78 g., 77%) was obtained by filtration below 0°. On dilution with water, more of the compound was obtained. Crystallisation from alcohol gave golden prisms, m. p. 87°.

4-*Nitro*-2-*aminodimethylaniline*.—A solution of crystalline stannous chloride (67·8 g.) in alcoholic hydrogen chloride (100 c.c.) was added to a warm solution of 2 : 4-dinitrodimethylaniline (21·1 g.) in alcohol (100 c.c.). The mixture was cooled, diluted to 800 c.c., and 50% sodium hydroxide solution added until all the precipitated stannic hydroxide had redissolved. The red crystals which separated overnight were dissolved in warm hydrochloric acid (20 c.c.) and the solution was diluted. A small amount of unchanged 2 : 4-dinitrodimethylaniline separated and was removed. Addition of alkali to the filtrate liberated 4-nitro-2-aminodimethylaniline (13 g., 72%), which crystallised from water in orange-yellow needles, m. p. 63° (cf. Heim, *loc. cit.*). The base (2 g.) and acetic anhydride (2 g.) were boiled for 3 mins.; cooling and basification then yielded 4-*nitro*-2-*acetamidodimethylaniline*, which crystallised from alcohol in long, straw-coloured needles, m. p. 163° (Found : N, 19·0. $C_{10}H_{13}O_3N_3$ requires N, 18·8%).

Benzaldehyde (1·5 g.) was added to a boiling solution of 4-nitro-2-aminodimethylaniline (2 g.) in alcohol (20 c.c.). On cooling, the *benzylidene* derivative separated; it crystallised from alcohol in golden needles, m. p. 128° (Found : N, 15·2. $C_{15}H_{15}O_2N_3$ requires N, 15·6%).

2-*Chloro*-4-*acetamidodimethylaniline*.—(a) *From* p-*acetamidodimethylaniline*. Chlorine was passed into a solution of the base (20 g.) in dry chloroform (300 c.c.) at room temperature. The mixture developed an intensely crimson colour, due probably to the formation of a Wurster salt (cf. Sidgwick, " The Organic Chemistry of Nitrogen," 1937, 99); this colour gradually disappeared with the separation of a colourless, crystalline hydrochloride. This was washed with chloroform, dissolved in warm water, and the solution made alkaline, whereupon 2-*chloro*-4-*acetamidodimethylaniline* (13·8 g., 58%) separated; several crystallisations from alcohol yielded colourless prisms, m. p. 119—120° (Found : N, 13·0. $C_{10}H_{13}ON_2Cl$ requires N, 13·2%).

(b) *From* 2-*nitro*-4-*acetamidodimethylaniline*. The nitro-compound (3 g.) in alcohol (15 c.c.) was reduced with a warm saturated aqueous solution of sodium hyposulphite (dithionite). After cooling to 0°, hydrochloric acid was added, and the solution diazotised with sodium nitrite. Cuprous chloride in hydrochloric acid (10% solution) was added, and the solution warmed; cooling and addition of excess of ammonia then gave a small amount of 2-chloro-4-acetamidodimethylaniline (mixed m. p.).

2-*Chloro*-4-*aminodimethylaniline*.—The foregoing compound was hydrolysed by 3 mins.' boiling with concentrated hydrochloric acid. On cooling and basifying, 2-*chloro*-4-*aminodimethylaniline* separated as a colourless solid, which crystallised from light petroleum (b. p. 60—80°) in prisms or leaflets, m. p. 61·5—63° (Found : Cl, 20·9. $C_8H_{11}N_2Cl$

requires Cl, 20·8%). The base, which is somewhat soluble in water, does not give Lauth's test for *p*-diamines; it does not darken in air.

Action of Copper-bronze on Diazotised 4-*Nitro*-2-*aminodimethylaniline*.—The base (1 g.) in hydrochloric acid (5 c.c.) was diazotised with sodium nitrite (0·38 g.) in water. Copper-bronze (0·5 g.) was added, and the solution filtered and made alkaline with ammonia; *p*-nitrodimethylaniline separated, and crystallised from alcohol in needles, m. p. 163°, unchanged by an authentic specimen. The same compound was obtained when the above diazo-solution was refluxed with methyl alcohol and when solutions of the diazotised base in nitric acid were treated with copper-bronze or with freshly prepared cuprous oxide.

2-*Chloro*-4-*nitrodimethylaniline*.—(a) *From* p-*nitrodimethylaniline*. Chlorine was led into a solution of the nitro-compound (8·3 g., 1 mol.) (Weber, *Ber.*, 1877, **10**, 761) in chloroform (200 c.c.) at room temperature until the increase in weight was 3·6 g. (1 mol. of chlorine). The solution was then extracted with concentrated hydrochloric acid and the acid extract, after being boiled to remove chloroform, was cooled and basified. 2-Chloro-4-nitrodimethylaniline (7·5 g., 75%) separated; it crystallised from alcohol in golden plates, m. p. 78° (cf. van Duin, *loc. cit.*) (Found: Cl, 17·5. Calc., Cl, 17·7%).

(b) *From* 4-*nitro*-2-*aminodimethylaniline*. The base (30 g.), dissolved in hydrochloric acid (50 c.c.) and water (50 c.c.), was diazotised at 10° with sodium nitrite (11·5 g.), and the solution slowly poured into 100 c.c. of a 10% solution of cuprous chloride in boiling hydrochloric acid. After the mixture had cooled, excess of ammonia was added, and the resulting precipitate removed, dried, and extracted (Soxhlet) with alcohol. The extract yielded 2-chloro-4-nitrodimethylaniline (24 g., 70%).

Reduction of 2-*Chloro*-4-*nitrodimethylaniline*.—A solution of the base (36 g.) and crystalline stannous chloride (170 g.) in hydrochloric acid (300 c.c.) was heated to boiling. On cooling, 2-*chloro*-4-*aminodimethylaniline stannichloride* (77 g., 86%) separated in silvery needles, purified by boiling with alcohol (Found: Sn, 23·4. $C_8H_{11}N_2Cl,H_2SnCl_6$ requires Sn, 23·6%). The amine separated when a solution of the stannichloride in water was decomposed with excess of 50% sodium hydroxide solution.

Nitration of 2-*Nitro*-4-*acetamidodimethylaniline*.—(i) *In acetic acid*. Nitric acid (*d* 1·42, 4 c.c.) was added to a solution of the acetyl compound (2 g.) in acetic acid (16 c.c.) at 15°. After an hour the solution was diluted with water (200 c.c.); 2 : 6-dinitro-*N*-nitroso-4-acetamidomethylaniline (2 g.) separated, and crystallised from alcohol in colourless needles, m. p. 152°, unchanged by an authentic specimen prepared according to Meldola and Hollely (*loc. cit.*).

(ii) *In hydrochloric acid*. Hydrochloric acid (10 c.c.) was used as solvent, the other conditions being as in (i). After several minutes the clear golden solution was diluted and made alkaline, whereupon 2 : 6-dinitro-4-acetamidodimethylaniline (1·6 g.) separated; it crystallised from alcohol in orange prisms, m. p. 195°, unchanged by a specimen prepared according to Hodgson and Crook (*loc. cit.*).

Nitration of 2-*Chloro*-4-*acetamidodimethylaniline*.—(i) *In acetic acid*. The procedure was exactly analogous to that in (i) above. 2-*Chloro*-6-*nitro*-N-*nitroso*-4-*acetamidomethylaniline* (1·8 g.) separated; it was crystallised several times from chloroform–carbon tetrachloride and finally from aqueous alcohol, forming colourless needles, m. p. 132—133° (Found: N, 20·0; Cl, 13·2. $C_9H_9O_4N_4Cl$ requires N, 20·6; Cl, 13·0%); it gave a positive reaction in the Leibermann nitrosoamine test.

(ii) *In hydrochloric acid*. Nitric acid (*d* 1·42; 15 c.c.) was added to a solution of the base (5 g.) in hydrochloric acid (30 c.c.) at room temperature. After several minutes the clear golden solution was diluted and basified; 2-*chloro*-6-*nitro*-4-*acetamidodimethylaniline* (5·2 g., 86%) separated, and crystallised from aqueous acetic acid or aqueous alcohol in orange-yellow prisms or needles, m. p. 165—166° (Found: Cl, 13·85. $C_{10}H_{12}O_3N_3Cl$ requires Cl, 13·8%).

Oxidation of 2-*Chloro*-6-*nitro*-N-*nitroso*-4-*acetamidomethylaniline*.—The nitrosoamine (2 g.) was dissolved in nitric acid (15 c.c., *d*, 1·5) at 0°, and the solution kept for an hour at room temperature. Dilution with water yielded 2-*chloro*-6:*N*-*dinitro*-4-*acetamidomethylaniline*, which crystallised from ethyl acetate–light petroleum (b. p. 80—100°) and then from aqueous alcohol in colourless needles, m. p. 152—153° (Found: Cl, 12·1. $C_9H_9O_5N_4Cl$ requires Cl, 12·3%). When this compound is dissolved in acetic acid containing α-naphthylamine and warmed with zinc dust, a red colour develops (Franchimont–Bamberger test for *N*-nitro-compounds).

Chlorination of 2-*Nitro*-4-*acetamidodimethylaniline*.—Chlorine was led into a solution of the base (18 g.) in dry chloroform (300 c.c.) at room temperature. The white solid which separated was washed with chloroform and treated with water at 100°. The 2-chloro-6-nitro-4-acetamidodimethylaniline (2·2 g.) obtained on cooling the solution, crystallised from aqueous alcohol in orange-yellow needles, m. p. 165—166°, unchanged by admixture with the compound obtained by nitration of 2-chloro-4-acetamidodimethylaniline. When the aqueous filtrate from the reaction was basified, much unchanged 2-nitro-4-acetamidodimethylaniline was recovered.

Chlorination of 2-*Chloro*-4-*acetamidodimethylaniline*.—Chlorine was led into a solution of the base (10 g.) in chloroform (160 c.c.) at room temperature, the white solid (10·5 g.) being treated as in the preceding case. The 2 : 6-*dichloro*-4-*acetamidodimethylaniline* (1·74 g.), obtained when the solution was cooled and filtered, crystallised from aqueous alcohol in colourless plates, m. p. 153—154° (Found: Cl, 29·0. $C_{10}H_{12}ON_2Cl_2$ requires Cl, 28·7%). Again, much unchanged starting material was recovered.

A similar reaction to the above occurred when the requisite amount of "dichloramine" was added to 2-chloro-4-acetamidodimethylaniline in chloroform solution.

2-*Chloro*-6-*amino*-4-*acetamidodimethylaniline*.—2-Chloro-6-nitro-4-acetamidodimethylaniline (5 g.) in alcohol (75 c.c.) was reduced with a saturated aqueous solution of sodium hyposulphite (dithionite). Basification and concentration of the solution yielded the 6-*amino*-compound, which crystallised from aqueous alcohol in colourless plates, m. p. 152° (Found: Cl, 15·5. $C_{10}H_{14}ON_3Cl$ requires Cl, 15·6%).

2 : 6-*Dichloro*-4-*acetamidodimethylaniline*.—2-Chloro-6-amino-4-acetamidodimethylaniline (1·5 g.) in hydrochloric acid (10 c.c.) and water (5 c.c.) was diazotised at 10° with sodium nitrite (0·45 g.) in water (5 c.c.), and copper-bronze (0·5 g.) added. Filtration and addition of ammonia yielded 2 : 6-dichloro-4-acetamidodimethylaniline (1·3 g., 80%) (m. p. and mixed m. p.).

2 : 6-*Dichloro*-4-*aminodimethylaniline*.—The foregoing compound was hydrolysed by 3 mins.' boiling with concentrated hydrochloric acid. Cooling and basification then yielded 2 : 6-*dichloro*-4-*aminodimethylaniline* as a colourless solid, which crystallised from light petroleum (b. p. 80—100°) or from aqueous alcohol in needles, m. p. 90—91° (Found: Cl, 34·8. $C_8H_{10}N_2Cl_2$ requires Cl, 34·6%).

2-*Chloro*-6-*nitro*-4-*acetamidomethylaniline*.—2-Chloro-6-nitro-*N*-nitroso-4-acetamidomethylaniline was boiled with excess of phenol for 15 minutes. Cooling and basification yielded 2-*chloro*-6-*nitro*-4-*acetamidomethylaniline*, which separated from alcohol as a bright red, crystalline powder, m. p. 208—209° (Found: Cl, 14·6. $C_9H_{10}O_3N_3Cl$ requires Cl, 14·55%). The same product was obtained when 2-chloro-6 : *N*-dinitro-4-acetamidomethylaniline was submitted to this procedure.

Action of Bromine on 2-*Chloro*-6-*nitro*-4-*acetamidodimethylaniline*.—Bromine (0·64 g.) in chloroform (20 c.c.) was added to a solution of the base (1·04 g.) in chloroform (10 c.c.). The oil which separated crystallised overnight to a yellow solid, which with boiling water yielded 2-chloro-6-nitro-4-acetamidomethylaniline (0·87 g., 94%) (m. p. and mixed m. p.).

Action of Bromine on 2 : 6-*Dinitro*-4-*acetamidodimethylaniline*.—The base (0·7 g.) was treated as above with bromine (0·42 g., 1 mol.) in chloroform. The resulting 2 : 6-dinitro-4-acetamidomethylaniline separated from alcohol as a red crystalline powder, m. p. 196—197°, unchanged by an authentic specimen prepared according to Meldola and Hollely (*loc. cit.*).

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