137. *Nitrous Acid as a Nitrating and Oxidising Agent. Part V. Reactions with the Four 3-Halogenodimethylanilines.*

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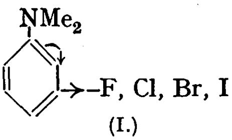
The four 3-halogenodimethylanilines all react similarly with nitrous acid in excess to form mixtures of the 3-halogeno-2-nitro-, -4-nitro-, and -4-nitroso-dimethylanilines.

When an aqueous solution of sodium nitrite reacts with 3-chloro-, 3-bromo-, and 3-iodo-dimethylaniline in dilute hydrochloric acid according to the directions of Hodgson and Wignall (J., 1927, 1144), the hydrochlorides of the 3-halogeno-4-nitrosodimethylanilines are precipitated, and this result is also partly obtained with 3-fluorodimethylaniline. When, however, the sodium nitrite is added in excess and in one batch as a finely divided solid, considerable nitration takes place with all four analogues in the 2- and the 4-position, but in each case nitrosation in the 4-position also occurs. 6-Nitration appears to be excluded.

The 3-*fluoro-* and 3-*chloro-2-nitro-* and -4-*nitro-dimethylanilines* have been compared with synthetically prepared 3-fluoro- and 3-chloro-4-nitro- and -6-nitro-dimethylanilines (cf. Hodgson and Kershaw, J., 1930, 497), and the constitutions of the 2-nitro-compounds derived by exclusion. Similarly the steam-volatile 3-bromo- and 3-iodo-2-nitrodimethylanilines are different from the corresponding 6-nitro-isomerides. Owing to their similarity in m. p. (38° and 50°) to 3-fluoro-2-nitrodimethylaniline (liquid) and 3-chloro-2-nitrodimethylaniline (m. p. 36°), and also their ready solubility in cold light petroleum, these two compounds may reasonably be assigned a 2-nitro-structure. On the other hand, the m. p.'s of the non-steam-volatile 3-bromo- and 3-iodo-4-nitrodimethylanilines (128° and 140°) correspond to those of the authentic non-steam-volatile 3-fluoro- and 3-chloro-analogues (120° and 126° respectively), as does also their insolubility in cold light petroleum. Hence the 4-nitro-structure appears to be justified by analogy.

The general occurrence of 2-nitration instead of the expected 6-nitration would appear to indicate that the structures of the 3-halogenodimethylanilines when reaction takes place have their conjugate systems as in (I), a result brought about by the powerful (— *I*) inductive effect of the halogen. The 2-position may be further activated by the direct field (*D* or *F*) effect of the halogen, and also by its mesomeric effect (Bennett, Brooks, and Glasstone, J., 1935, 1821).



(I.)

The general mechanism of nitration in the 2-position has already been discussed by Hodgson and Kershaw (J., 1930, 277) for the nitration of dimethyl-*p*-toluidine, and nitrosation and nitration in the 4-position by Hodgson and Nicholson (this vol., p. 470) for some *N*-dialkylanilines.

3-Fluoro-6-nitroaniline resisted acetylation by acetic anhydride or acetyl chloride separately, but was acetylated by their combination, indicating a chelation of considerable strength between the nitro- and the amino-group. The m. p.'s of 3-fluoro-4-nitro- and -6-nitro-acetanilides are lower than those of the free amines.

Contrary to the experience of Hodgson and Wignall (*loc. cit.*), 3-iodo-4-nitrosodimethylaniline is now found to give 3-iodobenzoquinone-4-oxime when it is heated for a short time with aqueous sodium hydroxide, the solution being filtered before all the dimethylamino-compound has been decomposed. It thus comes into line with the 3-chloro- and the 3-bromo-derivative.

Of the four 3-halogeno-4-nitrodimethylanilines, only the 3-fluoro-derivative is attacked easily by boiling aqueous alkaline hydroxide with replacement of its fluorine by the hydroxyl group, the other three analogues remaining unchanged under the same conditions. Similarly, 3-fluoro-4-nitrosodimethylaniline is converted into 4-nitrosoresorcinol instead of the expected 3-fluoro-4-nitrosophenol.

Although only under special conditions which exclude water does dimethylaniline itself form a hydrochloride, which is very hygroscopic, the four 3-halogenodimethylanilines form hydrochlorides which separate from dilute hydrochloric acid and are stable towards atmospheric moisture. This enhanced capacity for salt formation would appear to be connected with the mesomeric effects of the halogens (cf. Bennett, Brooks, and Glasstone, *loc. cit.*). The picrates of the halogeno-compounds have much higher m. p.'s than that of dimethylaniline picrate.

EXPERIMENTAL.

Preparation of 3-*Fluorodimethylaniline.*—A mixture of 3-fluoroaniline (5·5 g.), methyl alcohol (12 c.c.), and methyl sulphate (15 c.c.) was heated in a sealed tube at 160—170° for 6 hours. The reaction mixture when cold was poured into water and rendered just alkaline to litmus, and the separated oil heated with acetic anhydride and then steam-distilled. 3-*Fluorodimethylaniline* passed over and was purified by distillation, b. p. 198—199°/752 mm. (Found : N, 10·2. $C_8H_{10}NF$ requires N, 10·1%). The filtered flask liquor, on cooling, deposited 3-*fluoro*-N-*methylacetanilide* in colourless square plates, m. p. 113° (Found : N, 8·6. $C_9H_{10}ONF$ requires N, 8·4%).

3-Chloro-, 3-bromo-, and 3-iodo-dimethylaniline were made according to the directions of Hodgson and Wignall (*loc. cit.*), purified by steam-distillation after prior treatment with acetic anhydride, and subsequently distilled. Their picrates crystallised readily from methyl alcohol.

3-*Fluorodimethylaniline hydrochloride*, colourless micro-prisms, m. p. 153° (Found : N, 8·1. $C_8H_{10}NF,HCl$ requires N, 8·0%). 3-*Chlorodimethylaniline hydrochloride*, colourless plates, m. p. 170° (Found : N, 7·5. $C_8H_{10}NCl,HCl$ requires N, 7·3%). 3-*Bromodimethylaniline hydrochloride*, colourless plates, m. p. 194° (Found : N, 6·1. $C_8H_{10}NBr,HCl$ requires N, 5·9%). 3-*Iododimethylaniline hydrochloride*, colourless plates, m. p. 165° (Found : N, 4·8. $C_8H_{10}NI,HCl$ requires N, 4·9%). 3-*Fluorodimethylaniline picrate*, greenish-yellow plates, m. p. 181° (Found : N, 15·3. $C_8H_{10}NF,C_6H_3O_7N_3$ requires N, 15·2%). 3-*Chlorodimethylaniline picrate*, greenish-yellow spears, m. p. 179° (Found : N, 14·3. $C_8H_{10}NCl,C_6H_3O_7N_3$ requires N, 14·5%). 3-Bromodimethylaniline picrate, greenish-yellow spears, m. p. 182° (Vorländer and Siebert, *Ber.*, 1919, **52**, 288, give m. p. 134—138°) (Found : N, 13·2. Calc. : N, 13·0%). 3-*Iododimethylaniline picrate*, greenish-yellow spears, m. p. 182° (Found : N, 11·8. $C_8H_{10}NI,C_6H_3O_7N_3$ requires N, 11·8%).

General Procedure for the Action of Excess of Nitrous Acid on the Four 3-*Halogenodimethylanilines.*—A solution of the 3-halogenodimethylaniline (2 g.) in hydrochloric acid (20 c.c., *d* 1·16) and water (100 c.c.) at 0° (floating ice) was shaken vigorously with finely powdered sodium nitrite (2 g.), added in one batch. In all four cases a greenish-yellow solid was precipitated, which was collected after 10 minutes' shaking. The filtrate was then made just alkaline at 0°, and the precipitate removed. The subsequent operations for the individual amines were as follows :

(1) 3-*Fluorodimethylaniline.* The initial greenish-yellow precipitate, which was 3-*fluoro*-4-*nitrodimethylaniline*, remained unchanged when treated with warm aqueous sodium carbonate or with boiling water, the absence of a hydrochloride thus being proved. It crystallised from 50% aqueous alcohol in golden-yellow needles, m. p. 120° (Found : N, 15·4. $C_8H_9O_2N_2F$ requires N, 15·2%), which were not volatile in steam. On boiling with 2N-sodium hydroxide, it dissolved to give a golden-yellow fluorescent solution ; this on acidification with hydrochloric acid precipitated 4-*nitro*-3-*hydroxydimethylaniline*, which crystallised from 50% aqueous alcohol in slender golden-yellow parallelepipeds, m. p. 141—142° (Found : N, 15·5. $C_8H_{10}O_3N_2$ requires N, 15·4%). The filtrate from the initial precipitate above, when made just alkaline, afforded a green precipitate of 3-*fluoro*-4-*nitrosodimethylaniline*, which crystallised from methyl alcohol in deep green, rectangular prisms, m. p. 119° (Found : N, 16·6. $C_8H_9ON_2F$ requires

N, 16·6%). It dissolved in boiling 2N-sodium hydroxide with evolution of dimethylamine to give a deep red solution, from which 4-nitrosoresorcinol was precipitated on acidification. This compound had no m. p., gave no Liebermann nitroso-reaction [showing it to be different from the expected 3-fluoro-4-nitrosophenol (Hodgson and Nicholson, *loc. cit.*)], and appeared to be identical with the substance produced by the action of boiling 2N-sodium hydroxide on 4-nitroso-3-hydroxydimethylaniline.

However gradually the excess of sodium hydroxide, either as solid or in solution, was added to the acid solution of *m*-fluorodimethylaniline, the initial crystallisation always contained 3-fluoro-4-nitrodimethylaniline, but later fractions were mainly 3-*fluoro*-4-*nitrosodimethylaniline hydrochloride*, which separated from hydrochloric acid in yellow crystals (Found : HCl, 18·0. $C_8H_9ON_2F,HCl$ requires HCl, 17·8%). Steam-distillation of the original reaction mixture yielded the very volatile 3-*fluoro*-2-*nitrodimethylaniline*, b. p. 184°/752 mm. (Found : N, 15·3. $C_8H_9O_2N_2F$ requires N, 15·2%).

The Action of Sodium Nitrite on 3-*Fluorodimethylaniline in Acetic Acid Solution.*—3-Fluorodimethylaniline (2 c.c.), dissolved in glacial acetic acid (10 c.c.), was treated gradually with sodium nitrite (4 g.) dissolved in the minimum amount of water; the mixture at once became dark green. The precipitate of 3-fluoro-4-nitrosodimethylaniline which gradually separated was collected after 2 hours and crystallised from methyl alcohol, forming green rectangular prisms, m. p. and mixed m. p. with the above product 119° (Found : N, 16·7%).

Synthesis of 3-*Fluoro*-4- *and* -6-*nitrodimethylanilines.*—*Preparation of* 3-*fluoro*-4- *and* -6-*nitroanilines.* 3-*Fluoroacetanilide*, prepared from 3-fluoroaniline and acetic anhydride, crystallised from water in colourless rectangular plates, m. p. 85° (Found : N, 9·0. C_8H_8ONF requires N, 9·1%). A solution of 3-fluoroacetanilide (15·4 g.) in acetic anhydride (20 c.c.) and oleum (10 c.c., 27% SO_3) was gradually treated at 0° with nitric acid (7 c.c., *d* 1·5) in oleum (10 c.c., 27% SO_3). After 2 hours, the mixture was poured on ice, and the precipitate of 3-fluoro-4- and -6-nitroacetanilides collected, washed with cold water, and refluxed for 6 hours with 50% sulphuric acid (90 c.c.) and alcohol (90 c.c.). Steam-distillation removed 3-*fluoro*-6-*nitroaniline*, which crystallised from water in bright yellow, feathery needles, m. p. 97° (Found : N, 18·2. $C_6H_5O_2N_2F$ requires N, 17·9%). Yield, 3·4—3·8 g. Acetylation with a mixture of acetic anhydride and acetyl chloride gave 3-*fluoro*-6-*nitroacetanilide*, which crystallised from water in very pale yellow, almost colourless needles, m. p. 85° (Found : N, 14·2. $C_8H_7O_3N_2F$ requires N, 14·1%).

When the steam flask liquor was rendered faintly alkaline at 0° with aqueous sodium hydroxide, 3-*fluoro*-4-*nitroaniline* separated; it crystallised from aqueous alcohol in yellow needles, m. p. 153° (Found : N, 18·1%). 3-*Fluoro*-4-*nitroacetanilide* crystallised from water in colourless needles, m. p. 138° (Found : N, 14·3%).

Alternative preparation of 3-*fluoro*-4-*nitroaniline.* 3-Fluoroaniline (5 g.) and benzaldehyde (5 g.) were refluxed on the water-bath for 30 minutes, and the mixture dissolved in sulphuric acid (20 c.c., *d* 1·84), nitrated below 5° by the addition during 90 minutes of nitric acid (3 c.c., *d* 1·5) and sulphuric acid (10 c.c., *d* 1·84), and then poured into water. On steam-distillation, a little benzaldehyde and 3-fluoro-6-nitroaniline (0·1 g.) passed over. The non-volatile 3-fluoro-4-nitroaniline was purified as above.

Proof of the constitutions of the 3-*fluoro*-4-*nitro*- *and* -6-*nitro*-*anilines.* The fluoronitroaniline (3·2 g.), dissolved in sulphuric acid (3 c.c., *d* 1·84) and water (8 c.c.), was stirred into a solution of sodium nitrite (1·5 g.) in water kept below 5°. After 10 minutes, the excess of nitrous acid was destroyed with urea, and the filtered solution added to boiling 50% sulphuric acid through which a current of steam was passing (cf. Hodgson, E.P. 200,714). The assumed 3-fluoro-6-nitroaniline was converted into the steam-volatile 3-fluoro-6-nitrophenol (Hodgson and Nixon, J., 1928, 1880), which passed over as a brown oil that solidified on cooling and crystallised from light petroleum in yellow needles, m. p. and mixed m. p. with an authentic specimen 32° (Found : N, 9·1. Calc. : N, 8·9%). The assumed 3-fluoro-4-nitroaniline was converted into the non-steam-volatile 3-fluoro-4-nitrophenol, which separated from the flask liquor on cooling and crystallised from light petroleum in long colourless needles, m. p. and mixed m. p. with an authentic specimen 42° (Found : N, 9·1%).

Dimethylation of the 3-*fluoro*-4-*nitro*- *and* -6-*nitro*-*anilines.* The amine (3·5 g.) was heated in a sealed tube with methyl alcohol (6 c.c.) and methyl sulphate (7·5 c.c.) for 6 hours at 170°. After cooling, the mixture was poured into water and made alkaline; the dimethylated amine then separated. 3-Fluoro-4-nitrodimethylaniline crystallised from 50% aqueous alcohol in fine golden-yellow needles, m. p. 120° (Found : N, 15·3. Calc. : N, 15·2%), identical with the compound prepared by the action of nitrous acid on 3-fluorodimethylaniline. 3-*Fluoro*-6-

nitrodimethylaniline crystallised from 50% aqueous alcohol in yellow rectangular plates, m. p. 39° (Found: N, 15·3. $C_8H_9O_2N_2F$ requires N, 15·3%).

(2) 3-*Chlorodimethylaniline*.—The initial yellow precipitate was a mixture of the unstable hydrochlorides of 3-*chloro*-2-*nitro*- and 3-*chloro*-4-*nitro-dimethylanilines*, which were readily hydrolysed by water or when left exposed to the atmosphere. On steam distillation, the very volatile 3-chloro-2-nitrodimethylaniline passed over; it crystallised from light petroleum, in which it was very soluble, in long, bright yellow, rectangular prisms, m. p. 36° (Found: N, 14·3. $C_8H_9O_2N_2Cl$ requires N, 14·0%). The mixture of this compound with authentic 3-chloro-6-nitrodimethylaniline (Hodgson and Kershaw, *loc. cit.*) is liquid at room temperature. It is very stable to boiling aqueous potassium hydroxide. The non-volatile residue was 3-chloro-4-nitrodimethylaniline, which crystallised from alcohol in yellow needles, m. p. and mixed m. p. with a synthetic specimen (see below) 125—126° (Found: N, 14·2%). The initial filtrate above, when immediately neutralised, gave a precipitate of 3-chloro-4-nitrosodimethylaniline, which crystallised from methyl alcohol in green needles, m. p. 130° (Hodgson and Wignall, *loc. cit.*, give m. p. 130°) (Found: Cl, 19·1. Calc.: Cl, 19·2%).

When the filtrate was kept for 3 hours before neutralisation, the product subsequently obtained was a mixture, from which boiling water extracted 3-chloro-4-nitrosodimethylaniline, which separated on cooling. Boiling light petroleum extracted 3-chloro-4-nitrodimethylaniline, which was identified by comparison with the authentic specimen described below.

Synthesis of 3-*chloro*-4-*nitro- and* -6-*nitro-dimethylanilines*. 3-Chloroacetanilide (16 g.) was added gradually to a mixture of concentrated nitric acid (10 c.c., *d* 1·42) and sulphuric acid (20 c.c., *d* 1·84) kept at 0°. The whole was kept for 12 hours at 30° and then poured on ice. The yellow precipitate which separated was removed and refluxed for 2 hours with 50% sulphuric acid (80 c.c.), and the product steam-distilled. The steam-volatile 3-chloro-6-nitroaniline passed over and solidified in golden-yellow plates, m. p. 126° (Lobry de Bruyn, *Rec. Trav. chim.*, 1917, **36**, 148, gives m. p. 126°) (Found: N, 16·4. Calc.: N, 16·2%).

The filtered flask liquors, when rendered faintly alkaline at 0° with aqueous sodium hydroxide, gave 3-chloro-4-nitroaniline, which crystallised from water in yellow needles, m. p. 158° (Lobry de Bruyn, *loc. cit.*, gives m. p. 158°) (Found: N, 16·2. Calc.: N, 16·2%).

These amines were dimethylated as described for the corresponding fluoro-analogues. 3-Chloro-4-nitrodimethylaniline crystallised from alcohol in yellow needles, m. p. 125—126° (Found: N, 14·4%), and 3-*chloro*-6-*nitrodimethylaniline* from ligroin in pale yellow plates, m. p. 49° (Found: N, 14·2%).

(3) 3-*Bromodimethylaniline*.—The initial yellow precipitate (1·1 g.), when washed with cold water, was unchanged, and afforded no soluble matter, thereby indicating absence of hydrochlorides. On steam-distillation, 3-*bromo*-2-*nitrodimethylaniline* passed over; it crystallised from water in bundles of long, pale yellow needles, m. p. 38° (Found: N, 11·7. $C_8H_9O_2N_2Br$ requires N, 11·4%), which were very soluble in light petroleum. Its mixture with 3-bromo-6-nitrodimethylaniline (Hodgson and Kershaw, *loc. cit.*) was liquid at room temperature. The steam flask liquors on cooling deposited 3-*bromo*-4-*nitrodimethylaniline*, which was much less soluble in light petroleum than the 2-nitro-isomeride and crystallised from 50% aqueous alcohol in bright greenish-yellow, rectangular prisms, m. p. 128° (Found: N, 11·2%), which resisted hydrolysis by boiling 2N-sodium hydroxide. The filtrate from the initial yellow precipitate, when neutralised, afforded only a small amount of 3-bromo-4-nitrosodimethylaniline, which crystallised from aqueous methyl alcohol in green needles, m. p. 129° (Hodgson and Wignall, *loc. cit.*, give m. p. 129°) (Found: N, 12·1. Calc.: N, 12·2%). On boiling with 2N-sodium hydroxide, this was converted into 3-bromobenzoquinone-4-oxime, with evolution of dimethylamine.

(4) 3-*Iododimethylaniline*.—Most of the initial precipitate (*ca.* 1 g.) was very soluble in cold light petroleum, from which on slow evaporation 3-*iodo*-2-*nitrodimethylaniline* crystallised in bright yellow, rectangular prisms, m. p. 50° (Found: N, 9·7. $C_8H_9O_2N_2I$ requires N, 9·6%). When mixed with authentic 3-iodo-6-nitrodimethylaniline (Hodgson and Kershaw, *loc. cit.*), it liquefied, and it was also volatile in steam.

The residue of insoluble 3-*iodo*-4-*nitrodimethylaniline* which was not volatile in steam crystallised from its solution in benzene, on the addition of light petroleum, in yellow-brown needles, m. p. 140° (Found: N, 9·7%), which resisted hydrolysis by boiling 2N-sodium hydroxide.

The initial filtrate, when neutralised, afforded a small amount of 3-iodo-4-nitrosodimethylaniline, m. p. 128° (decomp.) (Hodgson and Wignall, *loc. cit.*, give m. p. 128°) (Found: I, 46·2. Calc.: I, 46·0%), and of 3-iodo-4-nitrodimethylaniline, which were separated by boiling light petroleum, in which the former product was insoluble. When 3-iodo-4-nitrosodimethylaniline was boiled for 5 minutes with 2N-sodium hydroxide, dimethylamine was evolved; the filtered liquid on acidification gave 3-iodobenzoquinone-4-oxime, m. p. 190° (decomp.), identified by comparison with an authentic product (Hodgson and Moore, J., 1925, **127**, 2260).

When 3-iododimethylaniline was dissolved in excess of nitric acid (*d* 1·42), and the solution immediately poured on ice, the *nitrate* was precipitated; it crystallised from water in colourless rectangular plates, which reddened at 120° and decomposed at 202° (Found: HNO_3, 20·5. $C_8H_{10}NI,HNO_3$ requires HNO_3, 20·3%).

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