CCCXXI.—*Studies in the Nitration of Substituted Tertiary Aromatic Amines.*

By GEORGE ROGER CLEMO and JAMES MUIR SMITH.

ALTHOUGH the literature contains a great number of papers on the subject of nitration, this major reaction is still imperfectly understood. The preliminary experiments which led to this investigation were carried out several years ago by one of us (G. R. C.) and C. M. McLeod, but at the time it was not possible to pursue the subject. It has been pointed out by, amongst others, Noelting and Collin (*Ber.*, 1884, **17**, 261) and Pinnow (*Ber.*, 1894, **27**, 3161), that the products of the nitration of certain aniline derivatives vary with the amount of concentrated sulphuric acid used to dissolve the base.

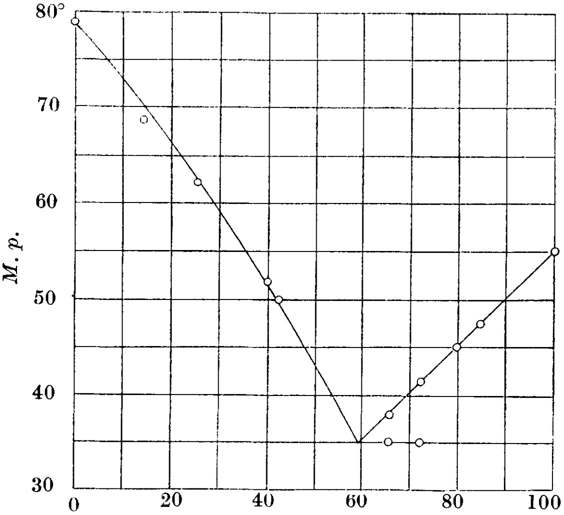
It has now been found that variation of the strength of the sulphuric acid used as the medium for the nitration has in many cases a striking effect on the particular nitro-compound formed.

The experiments of Flürscheim and Holmes on the nitration of benzyldiethylamine (J., 1926, 1562), and of Pollard and Robinson on benzylpiperidine (J., 1927, 2770), which showed that the addition of certain salts to the reaction medium had a marked effect in reducing the proportion of the *m*-nitro-compound formed, are of interest in this connexion.

The bases selected for our experiments were, in the first instance, *p*-chloro-, *p*-bromo-, and *p*-methyl-dimethylaniline, and subsequently more complicated dialkylanilines, including tetramethylbenzidine and 4 : 4′-tetramethyldiaminodiphenylmethane, were employed.

FIG. 1.

Composition–melting point curve for mixtures of 4-chloro-2-nitro- and 4-chloro-3-nitro-dimethylaniline.



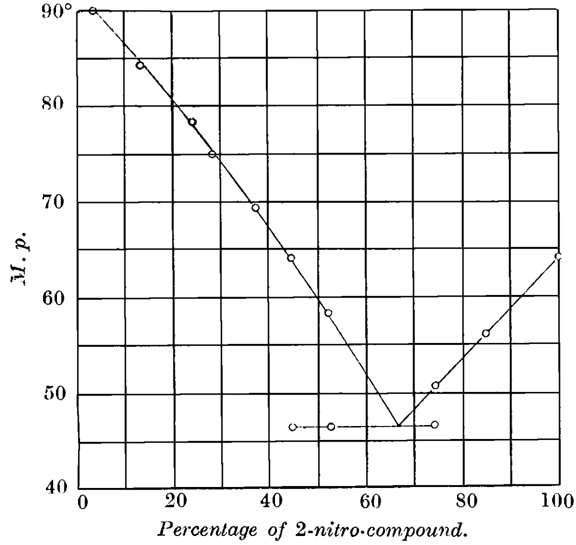
Percentage of 2-nitro-compound.

Thus, *p*-chlorodimethylaniline on nitration in concentrated sulphuric acid gives a good yield of the almost pure *m*-nitro-derivative (*Ber.*, 1898, **31**, 2984), whilst in dilute sulphuric acid (75% H_2SO_4 by weight) a good yield of the pure *o*-nitro-compound results—this compound was prepared by Heidlberg (*Ber.*, 1887, **20**, 151) by the action of nitrous acid on the base. With *p*-bromodimethylaniline, approximately parallel results have been obtained, and in both cases the presence of urea inhibits ortho-nitration in dilute sulphuric acid, whilst improving the purity of the *m*-nitro-derivative when concentrated sulphuric acid is used. That the ortho- and meta-nitrations involve essentially different mechanisms for the two reactions is seen also from the fact that, in the latter case, when the nitration mixture is removed from the cooling bath, the temperature quickly rises some degrees above that of the room, during which time the reaction is completed, whilst, in the former, nitration only occurs with rapid rise of temperature and slight effervescence some 1—4 hours after room temperature has been attained.

It was then decided to submit *p*-chloro- and *p*-bromo-dimethylanilines to a series of nitration experiments in sulphuric acid of various strengths. The analyses of the resulting nitration products were carried out according to the well-known method of Holleman (see Figs. 1 and 2), and, contrary to expectations, it has been found that the change over from the *o*- to the *m*-nitro-compound is not a gradual process. Thus the chloro-base in sulphuric acid (86% H_2SO_4) gives a product containing 92% of the *o*-compound, whilst in 92% acid a theoretical yield of the *m*-nitro-compound results. With 88 and 90% acid, however, the product is an oil containing both of the nitro-compounds and unchanged base (eutectic temperature of the two nitro-compounds, 35·1°).

FIG. 2.

Composition-melting point curve for mixtures of 4-*bromo*-2-*nitro*- *and* 4-*bromo*-3-*nitro*-*dimethylaniline*.



The pure materials necessary for the construction of Figs. 1 and 2 were made by the above methods and crystallised from alcohol. The results of the nitrations are summarised in the following tables.

Nitration of 4-Chlorodimethylaniline in Sulphuric Acid of Various Concentrations.

Conc. of H_2SO_4 (% by weight).	Total yield of nitro-compound from 6·2 g. of base.	Proportion of 2- to 3-nitro-compound in product.
50	7·4 g.	95 : 5 *
70	6·5	85 : 15
70 (Urea present)	Nil	—
74·5	6·5	100 : 0
79·4	6·5	100 : 0
83·9	6·3	100 : 0
86·0	5·0	92 : 8
88·3	Oil	Indefinite
90·0	,,	,,
92·0	8·0	9 : 91
93·8	7·5	6 : 94
98·0	7·4	6 : 94
98·0 (Urea present)	7·2	3·5 : 96·5

* All nitrations were effected by the general method described on p. 2420. with the exception of that in 50% sulphuric acid which took two weeks for completion at room temperature.

Nitration of 4-Bromodimethylaniline in Sulphuric Acid of Various Concentrations.

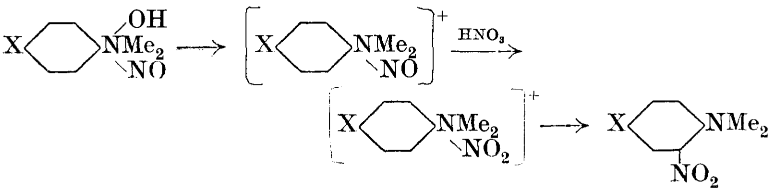
Conc. of H_2SO_4 (% by weight).	Total yield of nitro-compound from 6 g. of base.	Proportion of 2- to 3-nitro-compound in product.
70	7·0 g.	88 : 12
70 (Urea present)	Nil	—
75	5·4	92 : 8
79·4	5·4	97 : 3
83·9	5·5	92 : 8
90·0	3·2	Indefinite
98·0 (Urea present)	7·0	4 : 96

Although no special accuracy is claimed for the figures in column 3 of the above tables, a test in which known amounts of one of the pure isomerides were added to the product of nitration gave composition values from the graph which were within 0·5% of the calculated ones. In marked contrast to the two previous cases, however, *p*-methyldimethylaniline gives a good yield of *o*-nitro-product (*Ber.*, 1895, **28**, 3041; 1897, **30**, 3119) in dilute sulphuric acid in the presence of urea, whilst nitration in concentrated acid gives the normal *m*-nitro-derivative (D.R.-P. 69188; *J. pr. Chem.*, 1902, **65**, 247). It is therefore clear that the nature of the para-substituent plays an important part in ortho-nitration.

Attention was then turned to bases having a para-substituent more powerfully *op*-directing than either Cl, Br, or CH_3, and *p*-dimethylaminobenzyl alcohol was the first selected for study. A difficulty was encountered here, however, as the literature records no suitable method for its preparation (see, however, following paper), and hence a detailed study of its nitration has not yet been carried out. Nevertheless, it has been found in preliminary experiments that this alcohol undergoes nitration in 70% sulphuric acid in presence of urea so readily that the reaction is difficult to control at − 5°. The benzoyl derivative of *p*-dimethylaminobenzyl alcohol, on the other hand, is recovered largely unchanged under these conditions. Tetramethylbenzidine readily undergoes ortho-nitration in 70% sulphuric acid in the presence of urea (*Ber.*, 1881, **14**, 2164; J., 1926, 2712), whilst in concentrated sulphuric acid meta-nitration proceeds equally easily (*Ber.*, 1904, **37**, 29), and parallel results are obtained with 4:4′-tetramethyldiaminodiphenylmethane (*Ber.*, 1894, **27**, 3161).

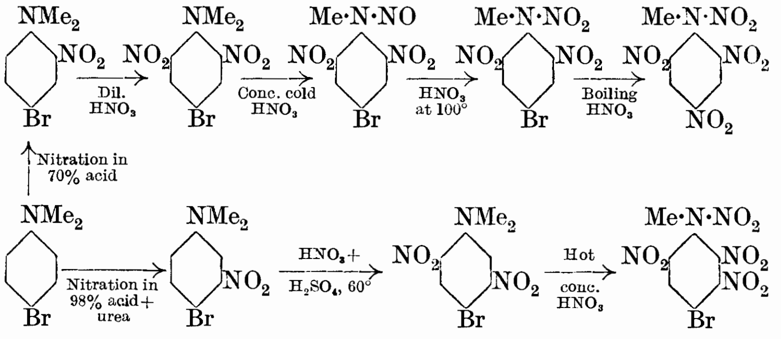
The explanation at present accepted for the meta-nitration of bases dissolved in concentrated sulphuric acid is that it is the kation of the ionised ammonium salt, $[R{\cdot}NMe_2H]^+$, which undergoes nitration. It is somewhat difficult to understand, however, why such a reaction should proceed smoothly in 92% sulphuric acid, but not in 90 or 88% acid, whilst with 86% acid ortho-nitration occurs, involving a different mechanism. The above explanation, if correct, leads to the curious inference that no ammonium ions are present in the 86% acid (H_2SO_4,H_2O corresponds to 84·5% H_2SO_4), since it has been shown for *p*-chloro- and *p*-bromo-dimethylaniline that the meta-nitration is more rapid than the ortho.

The inhibition by urea in the cases of the two bases just mentioned suggests strongly that nitrous acid plays a fundamental part in the nitration process. This contention is supported by the fact that many such nitro-compounds have been prepared by the action of nitrous acid on a dilute acid solution of the para-substituted dialkylaniline (*Ber.*, 1887, **20**, 151, 2460; 1898, **31**, 2982; 1918, **51**, 1036; J., 1926, 1896). In these cases, however, it is usual to obtain considerable quantities of nitrosoamines on account of the partial dealkylation of the tertiary amino-group, and the fact that these products are not formed in the cases under consideration seems to preclude the explanation that ortho-nitration is due solely to the action of nitrous acid. The best explanation which can be offered is that shown by the following scheme, which involves the prior addition of nitrous acid, followed by ionisation to give the ammonium ion, and oxidation of the nitroso- to the nitro-group, which then migrates into an unoccupied ortho-position.



The fact that urea prevents the reaction when X is Cl or Br, but not when it is $\cdot CH_3$, $\cdot CH_2\cdot OH$, $\cdot CH_2\cdot C_6H_4\cdot NMe_2(p)$, or $\cdot C_6H_4\cdot NMe_2(p)$, may be ascribed to the more acid character of the first two bases, as it is probable that urea will not react with concentrations of nitrous acid sufficient to start the process of ortho-nitration for the other (stronger) bases.

Attention was turned finally to the problem of the further nitration of some of the aforementioned mono-ortho- and -meta-nitro-compounds, and it has been found that, generally, a second nitro-group can be introduced into the *m*-nitro-derivative by nitration in sulphuric acid at 60°, and that the same dinitro-compound is formed directly when the base is treated in concentrated sulphuric acid at 60° with 2 mols. of nitric acid. In the case of *p*-bromodimethylaniline, the resulting dinitro-compound has the same melting point as the compound obtained by the bromination of 3 : 6-dinitrodimethylaniline (Forster and Coulson, J., 1922, **121**, 1995), and hence the second nitro-group in all probability occupies the 6-position. The final stage of the reaction is the production of a trinitro-nitroamine as shown below. The further nitration of the *o*-nitro-derivatives also results in the introduction of a second nitro-group in the 6-position, and the end stage in the nitration of 4-bromo-2-nitrodimethylaniline is tetryl, whilst with the corresponding chloro-base the last stage of the above reaction cannot be carried out, for the chlorine atom is not removed by boiling with fuming nitric acid.



EXPERIMENTAL.

The following general method of nitration was used in the experiments recorded in the tables on p. 2417, with the exception that all the nitration mixtures were allowed to stand together over-night at room temperature, before being poured on ice and worked up.

4-*Chloro*-2-*nitrodimethylaniline*.—4-Chlorodimethylaniline (6·2 g.;

0·04 mol.) was dissolved in sulphuric acid (20 c.c.; 75% H_2SO_4 by weight*), cooled in an ice-bath, and stirred whilst a mixture of nitric acid (2·9 c.c.; 66% HNO_3) and sulphuric acid (10 c.c.; 75% H_2SO_4) was run in during ½ hour, the temperature meanwhile being kept at 3—5°. The reaction mixture was allowed to warm to room temperature (21°), and then about 4½ hours later a rapid rise of temperature to 35° occurred, whereupon nitration took place with slight effervescence. After the temperature had fallen again, the mixture was poured on ice, neutralised with caustic soda, the red precipitate collected, well washed with water, and dried in a vacuum (6·5 g.; m. p. 56°). The product was crystallised from methyl alcohol, giving 5 g. of red prisms, m. p. 56° (corr.). If urea (2 g.) was added to the above experiment, and the nitration mixture left overnight at room temperature, 5·8 g. of chlorodimethylaniline were recovered unchanged. 4-*Chloro*-2-*aminodimethylaniline* was obtained as an oil, b. p. 158°/22 mm., by reducing the nitro-compound with iron and hydrochloric acid (Found : N, 16·6. $C_8H_{11}N_2Cl$ requires N, 16·5%); it forms an *acetyl* derivative, colourless plates from ligroin, m. p. 90° (Found : N, 12·9. $C_{10}H_{13}ON_2Cl$ requires N, 13·1%).

4-*Chloro*-3-*nitrodimethylaniline.*—This compound was prepared by substituting an equal volume of concentrated sulphuric acid for the 75% acid used above, and nitration was completed with slight rise of temperature as soon as the mixture had reached room temperature. The yield from 6·2 g. of 4-chlorodimethylaniline was 7·5 g., which gave yellow needles (7 g.) from methyl alcohol, m. p. 79° (corr.). The same yield of rather purer nitro-compound was formed when urea was present. 4-*Chloro*-3-*aminodimethylaniline*, obtained by the reduction of the nitro-compound with iron and hydrochloric acid, forms colourless plates from ligroin; m. p. 54° (Found : N, 16·3. $C_8H_{11}N_2Cl$ requires N, 16·5%); this compound, which darkens after a time in air, forms an *acetyl* derivative, colourless prisms, m. p. 97° (Found : N, 13·0. $C_{10}H_{13}ON_2Cl$ requires N, 13·1%).

4-*Bromo*-2-*nitrodimethylaniline.*—4-Bromodimethylaniline (8 g.; 0·04 mol.), when nitrated as described above for the corresponding chloro-base, gave 7·2 g. of product containing 92% of the 2-nitro-compound, which crystallised from methyl alcohol in orange-coloured prisms, m. p. 64° (*Ber.*, 1887, **20**, 2460) (Found : N, 11·6. Calc. for $C_8H_9O_2N_2Br$: N, 11·4%). In this case reaction set in one hour after the nitration mixture had reached room temperature (21°), but if urea was present nitration was inhibited. 4-*Bromo*-2-*aminodimethylaniline* was obtained as an oil, b. p. 165°/23 mm., by

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* All subsequent acid percentages are by weight.

reduction of the nitro-compound with iron and hydrochloric acid (Found: N, 13·05. $C_8H_{11}N_2Br$ requires N, 13·0%); its *acetyl* derivative formed colourless, glistening prisms from ligroin, m. p. 111° (Found: N, 10·7. $C_{10}H_{13}ON_2Br$ requires N, 10·9%).

4-*Bromo*-3-*nitrodimethylaniline*.—Nitration was carried out in the presence of urea as for the corresponding chloro-compound, and the product gave orange-coloured needles from methyl alcohol, m. p. 93·5° (Found: N, 11·5. $C_8H_9O_2N_2Br$ requires N, 11·4%).

3 : 3′-*Dinitro*-4 : 4′-*tetramethyldiaminodiphenylmethane*.—4 : 4′-Tetramethyldiaminodiphenylmethane (10·2 g.) and urea (4 g.) were dissolved in sulphuric acid (60 c.c.; 70%), and a mixture of nitric acid (5·8 c.c.; 66%) and sulphuric acid (20 c.c.; 70%) was added at − 5°. After standing for 1 hour at room temperature, the mixture was worked up in the usual way and gave 9·2 g. of red prisms, m. p. 121° after crystallising from acetic acid.

3 : 3′-*Dinitrotetramethylbenzidine*.—Tetramethylbenzidine (9·6 g.) was nitrated as in the preceding case and gave 7·4 g. of red needles, m. p. 188°, from acetic acid.

4-*Bromo*-2 : 6-*dinitrodimethylaniline*.—4-Bromo-2-nitrodimethylaniline (3 g.) was added in portions to nitric acid (35 c.c.; 52% HNO_3), the temperature being maintained meanwhile at 10°, and subsequently raised to 35° for ½ hour. The resulting acid solution was then gradually diluted with water until the dinitro-compound began to separate, and when precipitation was complete the solid was collected and recrystallised from alcohol, giving orange-coloured diamond-shaped plates (1 g.), m. p. 118° (Found: N, 14·2. $C_8H_8O_4N_3Br$ requires N, 14·4%). 4-Bromo-2 : 6-dinitrophenylmethylnitrosoamine (see below) was also isolated from this reaction.

4-*Bromo*-2 : 6-*dinitrophenylmethylnitrosoamine*.—4-Bromodimethylaniline (14 g.) was dissolved in sulphuric acid (56 c.c.; 50%) by warming on a water-bath. Water (48 c.c.) was then added, the solution cooled to 12°, and a mixture of nitric acid (80 c.c.; 66% HNO_3) and sulphuric acid (120 c.c.; 96%) added. After a short time a vigorous reaction set in, and the temperature was kept under 40° by cooling; the nitrosoamine then separated as small, pale yellow needles, which were collected and recrystallised from alcohol (18 g.; m. p. 124°) (Found: C, 27·9; H, 1·55; N, 18·7. $C_7H_5O_5N_4Br$ requires C, 27·6; H, 1·6; N, 18·4%).

4-*Bromo*-2 : 6-*dinitromonomethylaniline*.—This was prepared as orange-coloured needles, m. p. 104—105°, by refluxing the above nitrosoamine for 6 hours with methyl-alcoholic hydrogen chloride (Found: N, 15·8. $C_7H_6O_4N_3Br$ requires N, 15·2%).

4-*Bromo*-2 : 6-*dinitrophenylmethylnitroamine*.—4-Bromo-2 : 6-dinitrophenylmethylnitrosoamine (1 g.) was dissolved in fuming nitric acid (15 c.c.) and heated on a water-bath for ten minutes. Water was then added, and the precipitated nitroamine collected and recrystallised from alcohol, giving pale yellow needles, m. p. 113—114°; yield 0·8 g. (Found: C, 26·3; H, 1·9. Calc. for $C_7H_5O_6N_4Br$: C, 26·2; H, 1·6%) (Blanksma, *Rec. trav. chim.*, 1902, **21**, 272).

2 : 4 : 6-*Trinitrophenylmethylnitroamine* (*Tetryl*).—4-Bromo-2 : 6-dinitrophenylmethylnitrosoamine (3 g.) was boiled under reflux with fuming nitric acid (25 c.c.) for 5½ hours, and the resulting solution cooled and poured into water. The yellow solid was collected and crystallised from alcohol, 1 g. of diamond-shaped plates being obtained, m. p. 127°, not depressed when mixed with an authentic specimen of tetryl. The compound gave 2 : 4 : 6-trinitroaniline (m. p. 186°) when treated with ammonia.

4-*Bromo*-3 : 6-*dinitrodimethylaniline*.—4-Bromodimethylaniline (6 g.) was dissolved in sulphuric acid (20 c.c.; 96%) at 40°, the solution stirred, and a mixture of nitric acid (4 c.c.; 66%) and concentrated sulphuric acid (10 c.c.) slowly added. The reaction mixture was allowed to stand over-night, then poured on ice, and neutralised with caustic soda. The precipitate consisted of a mixture of the 3-nitro- and the 3 : 6-dinitro-compound, and was separated by dissolving it in concentrated hydrochloric acid and gradually diluting the solution with water, the less basic dinitro-compound being precipitated; it crystallised from alcohol in deep red plates, m. p. 107° (compare Forster and Coulson, J., 1922, **121**, 1995).

4-*Bromo*-2 : 3 : 6-*trinitrophenylmethylnitroamine*.—Fuming nitric acid (20 c.c.) was added all at once to 4-bromo-3-nitrodimethylaniline (3 g.); a vigorous reaction took place, and when it had subsided the solution was heated for ½ hour on a water-bath and then poured on ice with stirring. The resulting yellow solid was collected, extracted with a small volume of alcohol, and the residue recrystallised from alcohol, pale yellow needles being obtained, m. p. 158° (Found: N, 19·2. Calc. for $C_7H_4O_8N_5Br$: N, 19·1%) (compare Forster and Coulson, *loc. cit.*, who, however, give m. p. 165°).

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