CCCLXXXVIII.—*The Formation of* N-*Nitrosoamines from Tertiary Amines. Part I. The Conversion of Derivatives of Dimethylaniline by Nitrous Acid into the Corresponding Nitrosoamines and Monomethylanilines.*

By WILLIAM GEORGE MACMILLAN and THOMAS HAROLD READE.

ABNORMAL reactions between nitrous acid and tertiary aromatic amines, leading to the formation of (a) nuclear nitro-compounds by loss of hydrogen or halogen and (b) *N*-nitrosoamines by loss of an alkyl group, have been recorded by several workers (Wurster and Scheibe, *Ber.*, 1879, **12**, 1816; Heidlberg, *Ber.*, 1887, **20**, 149; Koch, *ibid.*, p. 2460; Pinnow, *Ber.*, 1898, **31**, 2982; Van Romburgh and Jansen, *Proc. K. Akad. Wetensch. Amsterdam*, 1911, **13**, 820; Aitken and Reade, J., 1926, 1896).

With nitrodimethylanilines, both types of reaction occur, (b)

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* Attention is directed to a misprint (this vol., p. 1775), of which a correction has already been issued, whereby nicotine was cited as an example of this rule, whereas the small high-frequency term is actually of the same sign as the large low-frequency term.

predominating at room temperature, but often being accompanied by (a) if the temperature is allowed to rise.

TABLE I.

The Action of Nitrous Acid in Excess on Tertiary Amines without External Cooling.

Under " Products," col. A gives the weight and yield % of the *N*-nitrosoamine of the corresponding monomethylaniline, col. B the weight and positions of the substituents of the polynitrodimethylaniline, and col. C the weight of unchanged tertiary amine.)

Initial materials.					Products.		
Deriv. of $NPhMe_2$ used.	Wt. (g.).	HCl (c.c.).	Water (c.c.).	$NaNO_2$ (c.c. of 50%).	A.	B.	C.
3-Nitro*	10	30	70	25	4; 37	4; 3 : 4-Dinitro 0·5; 3 : 6-Dinitro	Nil
4-Nitro†	10	100	50	25	5; 46	Nil	3
3 : 6-Dinitro‡	10	120	40	20	7·8; 73	,,	Pract. nil
4-Bromo-2-nitro§	10	200	100	25	8·5; 80	,,	Nil
4-Bromo-3-nitro‖	10	100	100	25	6; 57	0·6; 4-Bromo-3 : 6-dinitro	1·5

* Groll (*Ber.*, 1886, **19**, 198). † Weber (*Ber.*, 1877, **10**, 761).

‡ Romburgh (*Rec. trav. chim.*, 1887, **6**, 253).

§ Koch (*Ber.*, 1887, **20**, 2460). ‖ Forster and Coulson (J., 1922, **121**, 1995).

Since nitrosoamine formation takes place to a considerable extent in each of the experiments recorded, and is the principal reaction in several, its occurrence can no longer be regarded as a distinctive property of secondary amines only. In the nuclear nitro-compounds produced, the nitro-group enters preferentially position 4 or 6.

A second series of experiments was carried out at constant temperature, the initial molecular concentrations of amine and of nitrous acid being the same in all cases.

TABLE II.

Amount of Nitrosoamine produced in 12 Hours, at 17° from 20 c.c. of 50% Aqueous Sodium Nitrite and 0·0475 G.-mol. of Amine in 200 c.c. of Hydrochloric Acid and 100 c.c. of Water.

	Percentage of pure products isolated.			
Amine used.	Nitroso-amine.	Polynitro-derivatives.	Un-changed.	Total.
3-Nitrodimethylaniline	33	Nil	48	81
4-Nitrodimethylaniline	30	,,	51	81
3 : 6-Dinitrodimethylaniline ...	47	,,	40	87
4-Bromo-2-nitrodimethylaniline	37	,,	37	74
4-Bromo-3-nitrodimethylaniline	32	*ca.* 5% of 4-bromo-3 : 6-dinitrodimethylaniline	37	74

It is seen that nuclear substitution hardly occurs at all at 17°, whereas nitrosoamine production is only slightly less than that shown in Table I. The tendency to nitrosoamine formation seems to be greatest when both ortho-positions to the dimethylamino-group are occupied by nitro-groups; further constitutional inferences, however, are meanwhile deferred.

The constitutions of the nitrosoamines were established by (a) hydrolysis to the corresponding secondary amine, and (b) formation from the secondary amine by means of dilute nitrous acid.

EXPERIMENTAL.

Action of Nitrous Acid on Tertiary Amines.—The general procedure was to dissolve the nitrodimethylaniline in hydrochloric acid, dilute the solution with water (avoiding precipitation), add slowly 50% aqueous sodium nitrite at laboratory temperature, and leave the mixture over-night. The solution first became deep yellow and then the nitrosoamine and feebly basic compounds began to separate, the precipitation often being accompanied by evolution of oxides of nitrogen. After the nitrosoamine had been collected, the bases in the acid mother-liquor were precipitated by dilution with water and addition of alkali. Mixtures of bases were separated by dissolution in acid and fractional precipitation with water or dilute alkali solution.

On 3-nitrodimethylaniline (m. p. 61°). The quantities of reactants were those given in Table I. A flocculent yellow precipitate separated over-night which gave, by crystallisation from alcohol, yellow needles, m. p. 176°, of α-3 : 4-dinitrodimethylaniline, identical with a specimen prepared according to Swann (J., 1920, **117**, 3) (Found: C, 45·4; H, 4·5; N, 20·1. Calc. for $C_8H_9O_4N_3$: C, 45·5; H, 4·3; N, 19·9%). From the alcoholic mother-liquor, by concentration, followed by dilution with water, crystals were obtained which separated from ligroin in yellow needles, m. p. 77°, of 3-nitrophenylmethylnitrosoamine. These gave the Liebermann reaction, and were identical with a specimen prepared according to Ullmann (*Annalen*, 1903, **327**, 112) (Found: C, 46·2; H, 4·2; N, 23·2. Calc. for $C_7H_7O_3N_3$: C, 46·4; H, 3·9; N, 23·2%). Concentration of the ligroin mother-liquor yielded a mixture of nitrosoamine and scarlet needles. This was dissolved quickly in cold hydrochloric acid, water added to precipitate the nitrosoamine, and the filtered solution made alkaline. The red precipitate thus obtained crystallised from alcohol in scarlet needles, m. p. 112°, identical with a specimen of 3 : 6-dinitrodimethylaniline prepared according to Swann (*loc. cit.*) (Found: C, 45·5; H, 4·3; N, 19·9. Calc. for $C_8H_9O_4N_3$: C, 45·3; H, 4·4; N, 20·4%).

On 4-nitrodimethylaniline (m. p. 163°). The precipitate obtained over-night gave pale yellow needles, m. p. 104°, from alcohol. These gave the Liebermann nitrosoamine reaction and were identical with a specimen of 4-nitrophenylmethylnitrosoamine made according to Ullmann (*loc. cit.*) (Found : C, 46·3; H, 4·3; N, 23·1. Calc. for $C_7H_7O_3N_3$: C, 46·4; H, 3·9; N, 23·2%). The yield of the nitrosoamine was raised to 75% of the theoretical by a fourfold increase in the amount of nitrite.

On 3 : 6-dinitrodimethylaniline (m. p. 112°; prepared according to Swann, *loc. cit.*). The precipitate produced over-night crystallised from alcohol in orange needles or plates, m. p. 128°, of 3 : 6-*dinitrophenylmethylnitrosoamine* (Found : C, 37·4; H, 2·7; N, 24·8. $C_7H_6O_5N_4$ requires C, 37·2; H, 2·8; N, 24·8%). This gave the Liebermann nitrosoamine reaction and was insoluble in dilute acids, sparingly soluble in carbon tetrachloride, ligroin, and ether, and soluble in chloroform, acetone, benzene, methyl and ethyl alcohol, and glacial acetic acid.

On 4-bromo-3-nitrodimethylaniline (m. p. 95°; prepared by the methods of Forster and Coulson, *loc. cit.*, and Clemo and Muir, J., 1928, 2421). The precipitate obtained yielded, by crystallisation from methyl alcohol, 4-*bromo*-3-*nitrophenylmethylnitrosoamine* in yellow needles, m. p. 78°, soluble in cold chloroform, acetone, benzene, and glacial acetic acid and in warm alcohol, carbon tetrachloride, and ligroin (Found : C, 32·4; H, 2·5; N, 16·2. $C_7H_6O_3N_3Br$ requires C, 32·3; H, 2·5; N, 16·2%). The acid filtrate, when made alkaline, yielded a mixture from which were isolated 4-bromo-3 : 6-dinitrodimethylaniline, scarlet plates from alcohol, m. p. 109° (Found : C, 32·9; H, 3·4; N, 14·2. Calc. for $C_8H_8O_4N_3Br$: C, 33·0; H, 3·1; N, 14·4%), and unchanged bromonitrodimethylaniline.

On 4-bromo-2-nitrodimethylaniline (m. p. 66°; obtained by the method of Clemo and Muir, J., 1928, 2420). This gave 4-*bromo*-2-*nitrophenylmethylnitrosoamine*, which crystallised from methyl alcohol in large rhombs, m. p. 73°, soluble in cold acetone, chloroform, benzene, glacial acetic acid and in hot alcohol, carbon tetrachloride, and ligroin (Found: C, 32·3; H, 2·4; N, 16·3. $C_7H_6O_3N_3Br$ requires C, 32·3; H, 2·3; N, 16·2%).

Conversion of Nitrosoamines into the Corresponding Monomethylanilines.—The elimination of the nitroso-group was effected by hydrolysis, in the presence of urea and sulphuric acid, as previously described for 3- and 4-nitrophenylmethylnitrosoamines (this vol., p. 585). The following four monomethylanilines are soluble in cold chloroform, acetone, and glacial acetic acid and in warm dilute mineral acids, alcohol, carbon tetrachloride, and ligroin.

3 : 6-*Dinitromonomethylaniline* (3·8 g.), obtained from 5 g. of 3 : 6-dinitrophenylmethylnitrosoamine, crystallised from alcohol in red needles, m. p. 163° (Found: C, 43·0; H, 3·7; N, 21·3. $C_7H_7O_4N_3$ requires C, 42·6; H, 3·5; N, 21·3%).

4-*Bromo*-3-*nitromonomethylaniline* (7·5 g.) was obtained, together with a small amount of a less basic yellow by-product of m. p. 196° (decomp.), from 10 g. of 4-bromo-3-nitrophenylmethylnitrosoamine: it crystallised from ligroin in long, claret-coloured needles, m. p. 81° (Found : C, 36·6; H, 3·3; N, 12·2. $C_7H_7O_2N_2Br$ requires C, 36·4; H, 3·0; N, 12·1%).

4-*Bromo*-2-*nitromonomethylaniline* (8·4 g.) was obtained from 10 g. of 4-bromo-2-nitrophenylmethylnitrosoamine; it crystallised from alcohol in orange needles or plates, m. p. 103° (Found : C, 36·6; H, 3·2; N, 12·0%).

4-Bromo-2 : 6-dinitromonomethylaniline (8·5 g.) was obtained from 10 g. of 4-bromo-2 : 6-dinitrophenylmethylnitrosoamine; it separated from alcohol or ligroin in small yellow crystals, m. p. 106°.

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MARISCHAL COLLEGE,
UNIVERSITY OF ABERDEEN.

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