

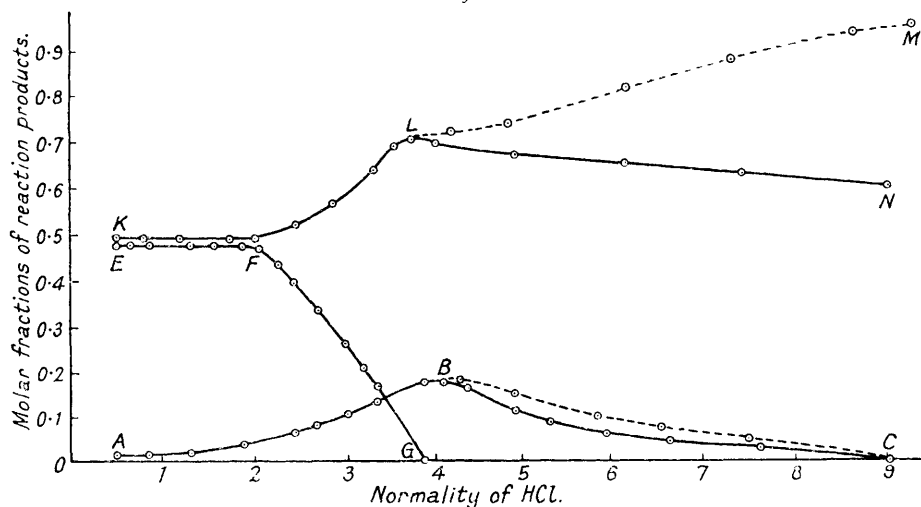
11. The Action of Nitrous Acid on Tertiary Amines: the Influence of Acidity.

By CHARLES DONALD and T. HAROLD READE.

THIS communication records the behaviour of Michler's ketone (4:4'-bisdimethylaminobenzophenone), Michler's hydride (4:4'-bisdimethylaminodiphenylmethane), and the corresponding bisdiethyl base towards aqueous sodium nitrite and hydrochloric acid at various dilutions at 0°.

FIG. 1.

Nitrous acid and 4:4'-bisdimethylaminodiphenylmethane in hydrochloric acid of various concentrations at 0°. Products of the reaction.



EFG—*p*-Nitrodimethylaniline.

ABC—4:4'-Bismethylnitrosoaminodiphenylmethane:
single line, 4 mols. nitrite: 1 mol. base.
dotted line, 8 mols. nitrite: 1 mol. base.

KLN—3:3'-Dinitro-4:4'-bisdimethylaminodiphenylmethane,
4 mols. nitrite: 1 mol. base.

KLM—8 mols. nitrite: 1 mol. base.

With Michler's hydride, the products isolated by Pinnow (*Ber.*, 1894, **27**, 3867), namely, 3:3'-dinitro-4:4'-bisdimethylaminodiphenylmethane, 4:4'-bismethylnitrosoaminodiphenylmethane, and *p*-nitrodimethylaniline, were again obtained: they represent three types of action, (1) nuclear nitration, (2) nitrosoamine formation by loss of alkyl groups from the nitrogen atoms, and (3) fission (accompanied by nitration), respectively. We find that the type of action which predominates is influenced by the normality of the mineral acid solution, fission being characteristic of low concentrations, nuclear nitration of high, and nitrosoamine formation reaching a true maximum at intermediate concentrations (normality, 3.8), as is shown in Fig. 1, where allowance has been made for 2 mols.

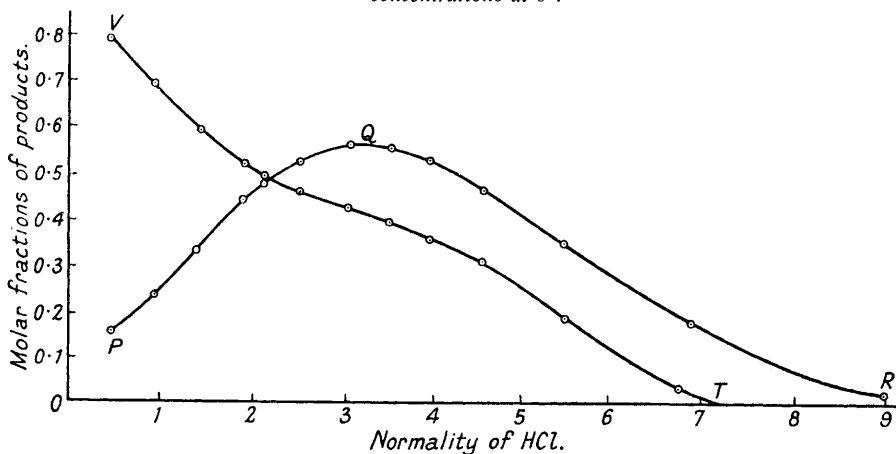
of hydrogen chloride used in dissolving the base, and 4 mols. used in attacking 4 mols. of sodium nitrite. The corresponding bisdiethyl-hydride behaved analogously. Michler's ketone, however, gave only mono- and di-nitrosoamines, the latter reaching a true maximum in 3*N*-hydrochloric acid (Fig. 2).

The large yields of mononitrosoamine obtained at low concentrations of hydrogen chloride are probably due mainly to its being removed from the sphere of action owing to its low solubility in the dilute acid.

Important theoretical issues arise from these observations. In the first place, the constitution of the amine has an over-riding influence, and Hodgson's generalisation (*J. Soc. Dyers and Colourists*, 1931, April), that positive substituents (which increase the basicity of the amine) favour nuclear nitration whereas negative substituents favour the formation of nitrosoamines, is confirmed; for Michler's ketone is a much weaker base than either of the hydrides investigated. Secondly, the fact that the concentration of external acid has a lesser but nevertheless a decided effect upon the nature of the end products obtained from these hydrides recalls the fact that these two influences—internal substituents and external acidity—are those known to govern the diazonium \rightleftharpoons diazo

FIG. 2.

Nitrous acid (4 mols.) and 4 : 4'-bisdimethylaminobenzophenone (1 mol.) in hydrochloric acid of various concentrations at 0°.

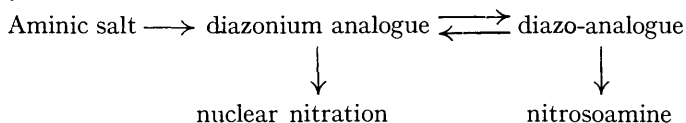


PQR—4 : 4'-Bismethylnitrosoaminobenzophenone.

VT—4-Dimethylamino-4'-methylnitrosoaminobenzophenone.

change, and strongly suggests that an interchange between unstable intermediate compounds analogous to diazonium and diazo-forms plays a part in the reactions of these tertiary amines with nitrous acid also.

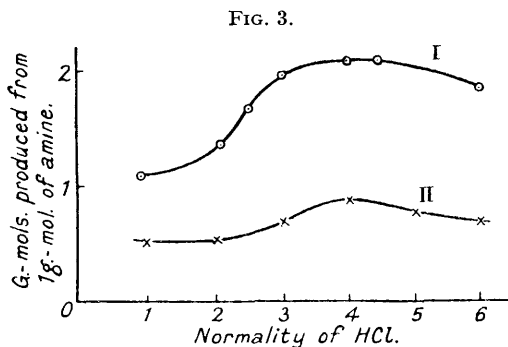
The rate of diazotisation of the salts of primary amines is greatly accelerated by increase of the concentration of mineral acid up to 4*N* (Ueno and Suzuki, *J. Soc. Chem. Ind. Japan*, 1933, **36**, 615*B*), and if this applies also to the transposition of the salts of tertiary amines into their diazonium analogues, the shapes of the nitrosoamine graphs which show true maxima are qualitatively accounted for, and also that for the nuclear nitration product, provided that a diazonium form is the precursor of nuclear nitration, a diazo-form of nitrosoamine formation; for the production of the latter is hindered by acidity greater than 4*N*, and yet the diazo-form must be produced from its diazonium analogue whose formation from the aminic salt is favoured by increasing acidity up to 4*N ex hypo*th. The process may be written :



If the nitrite in our experiments at 0° was wholly replaced by sodium nitrate, no action was discernible; hence the usual equations, $3\text{HNO}_2 \longrightarrow \text{HNO}_3 + 2\text{NO} + \text{H}_2\text{O}$ and $\text{RH} + \text{HNO}_3 \longrightarrow \text{R}\cdot\text{NO}_2 + \text{H}_2\text{O}$, employed to represent nitration by (initially) nitrous acid are inadequate. At higher temperatures, however, the nitro-compound was obtained, but neither nitrosoamine nor fission product, when nitrate was used.

When a portion only of the nitrite was replaced by nitrate at 0°, full yields of the nitration product were obtained with diminished yields of nitrosoamine proportional to the molar fraction of nitrite used. A formulation is given later which takes these observations into account, the final change being akin to a nitroamine transformation into the nuclear nitro-compound.

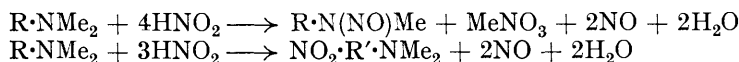
Fig. 3 shows that in the nitrite experiments the quantity of nitric oxide evolved at 19.3° under liquid paraffin B.P. is nearly proportional to the sum of the yields at 0° of



I. Nitric oxide.

II. Sum of nitroamine and dinitro-compound.

nuclear nitro-compound and nitrosoamine, the fission product being formed without evolution of gas. The equations



represent the stoichiometric proportions, but are of too high an order to be probable as a guide to the mechanism, which probably involves consecutive reactions of a lower order. Since 70% of the gas was evolved in about 7 minutes (mechanical stirring), the reactions involved must be rapid. The blank experiment without amine gave a negligible quantity of gas in an hour.

In 6.0, 4.5, 4.0, and 3.0*N*-hydrochloric acid, the times (*t*, mins.) taken for evolution of 70% of the total gases were nearly the same, but the speed was diminished in more dilute solutions, as shown below :

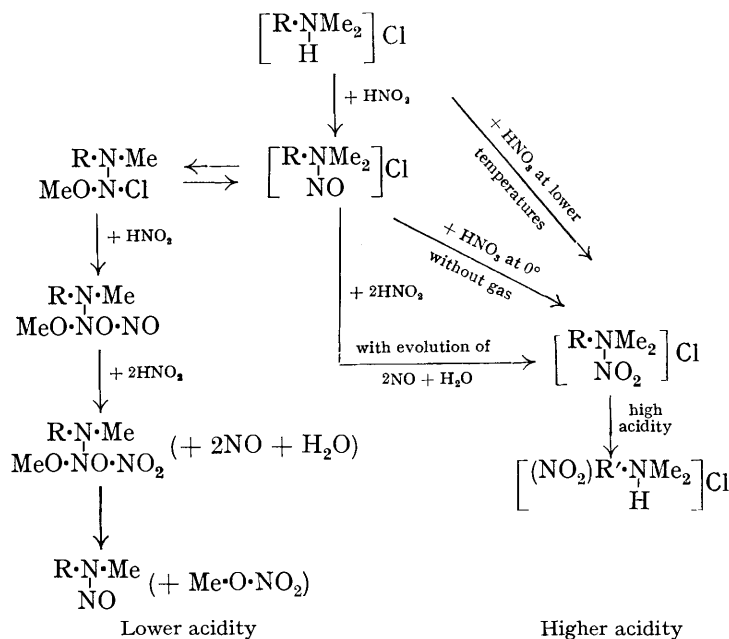
G.-mol. NO	1.90 (1.86)	2.09	2.01 (2.07)	1.95	1.65	1.36	1.06
G.-mol. N.....	0.20 (0.24)	0.11	0.10 (0.11)	0.10	0.10	0.10	0.11
<i>t</i>	5.6	6.6	6.7	6.5	8.9	19.4	37.3
Normality of HCl	6.0	4.5	4.0	3.0	2.4	2.1	0.94

The nitrogen (7 to 17 c.c.) is of uncertain origin, but it would be formed if a small amount of the amine became dealkylated.

These observations can be fairly expressed by the following scheme, in which there is no reaction of a higher order than termolecular; substances favoured by high acidity are on the right (diazonium analogues) and those favoured by lower acidity (diazo-analogues) are on the left. The fission reactions are omitted because all that is known about them is that (1) nitrous acid is the only substance which produces fission and (2) no gas is given off in the process. The formulæ used for the diazo-analogues are conjectural but likely.

The main features are capable of wide extension to cover other classes of amines,

e.g., the velocity measurements for aliphatic amines recorded by T. W. J. Taylor and his collaborators in this Journal in 1925 and the following years.



EXPERIMENTAL.

4 : 4'-Bisdimethylaminodiphenylmethane was prepared according to Mohlau and Heinze (*Ber.*, 1902, **35**, 359) and before use was recrystallised from ethyl and from methyl alcohol; m. p. 91° (Found : C, 79.9; H, 8.6. Calc. : C, 80.2; H, 8.6%).

Preparation of Solutions.—40.000 G. of the above base were dissolved and made up to 1 l. in 11.63*N*-hydrochloric acid. 25.0 C.c. portions of this solution were diluted with water to give a range of hydrogen chloride concentrations from 9.035*N* to 0.663*N*, allowance being made for the acid used up by the sodium nitrite (4 mols.), for that used by the base in forming its dihydrochloride (2 mols.), and for the water in which the nitrite was dissolved. Each solution was cooled in ice-water, 5 c.c. of a sodium nitrite solution added containing 4.01 mols. of nitrite to 1.0 mol. of the base, and the reaction continued for 24 hours. The reaction mixture consisted of a precipitate and a solution, each of which was analysed.

Analysis of the precipitate. The precipitate, consisting of the bisnitrosoamine and *p*-nitrodimethylaniline, was collected on a Jena glass filter crucible, washed with 200 c.c. of ice-cold water, dried at 40°, and weighed. The *p*-nitro-compound was then dissolved in 5.5*N*-hydrochloric acid and the bisnitrosoamine (washed and dried as before) was weighed, a correction being applied for its solubility in 5.5*N*-hydrochloric acid : it crystallised from methyl or ethyl alcohol in straw-yellow needles, m. p. 102° (compare Pinnow, *Ber.*, 1894, **27**, 3867) (Found : C, 63.1; H, 5.6. Calc. : C, 63.3; H, 5.6%). The *p*-nitrodimethylaniline was estimated by difference, its solubility in the reaction mixture being allowed for : after crystallisation from ethyl alcohol it had m. p. and mixed m. p. 163°.

Solubility of p-nitrodimethylaniline and of 4 : 4'-bismethylnitrosoaminodiphenylmethane in 100 c.c. of hydrochloric acid of various concentrations at 0°.

(1) *p*-Nitrodimethylaniline.

Normality of HCl	3.620	2.439	1.796	1.198	0.898	0.787
Solubility in grams.....	0.460	0.086	0.043	0.019	0.011	0.008

(2) 4 : 4'-Bismethylnitrosoaminodiphenylmethane.

Normality of HCl	5.939	5.344	4.443	3.819	2.853	1.326
Solubility in grams.....	0.036	0.031	0.014	0.010	0.008	0.006

Analysis of the filtrate after removal of the insoluble reaction products. The nitration product of the reaction, 3:3'-dinitro-4:4'-bisdimethylaminodiphenylmethane (Pinnow, *Ber.*, 1894, 27, 3165), was precipitated by sodium hydroxide as a viscous oil, which crystallised from alcohol or glacial acetic acid in slender red needles, m. p. 124° (Found: C, 59.1; H, 5.8. Calc.: C, 59.3; H, 5.8%).

Since accurate weighing of the oily product was impracticable, the acid filtrate was treated with urea at 25–30° to destroy any nitrous acid and made up to standard bulk by addition of dilute hydrochloric acid, and the nitrate estimated in a portion by titanous chloride. The organic dinitro-compound was similarly determined by titanous chloride at 100° (see Knecht and Hibbert, "New Reduction Methods in Volumetric Analysis").

Laboratory Preparation of p-Nitrodimethylaniline.—100 G. of 4:4'-bisdimethylaminodiphenylmethane are dissolved in 300 c.c. of concentrated hydrochloric acid and cooled to 0°, 800 c.c. of water added, and 100 g. of sodium nitrite in 200 c.c. of water slowly poured into the solution. After 1 hour's stirring, 28 g. of *p*-nitrodimethylaniline are obtained, m. p. 159°. After one crystallisation from glacial acetic acid the product may be taken as pure.

Action of Nitrous Acid on 4:4'-Bisdimethylaminobenzophenone.—The ketone, kindly supplied for research purposes by Imperial Chemical Industries Ltd., melted at 179° after repeated crystallisation from ethyl alcohol (Found: C, 76.0; H, 7.3; N, 10.4. Calc.: C, 76.1; H, 7.5; N, 10.4%)

Preparation of Solutions.—12.50 G. of the ketone were dissolved and made up to 500 c.c. with 11.55*N*-hydrochloric acid. 20 C.c. portions of this solution were diluted with water to give a range of acid concentration from 9.18*N* to 0.46*N*, allowances being made for acid used by nitrite, etc., as in the experiments with 4:4'-bisdimethylaminodiphenylmethane. Each solution was treated in an exactly similar manner to that previously described under the "methane base" experiments.

All the products of the reaction, being weakly basic, were precipitated from solution. The feebly basic bisnitrosoamine separated even in the strongly acid solutions and the more basic mononitrosoamine was precipitated on dilution with water.

Analysis of the precipitate. The precipitate, consisting of a mixture of mono- and bisnitrosoamines, was collected on a tared Jena glass filter, washed with 200 c.c. of ice-cold water, and dried at 60°. The mononitrosoamine was removed by allowing 50 c.c. of 5*N*-hydrochloric acid to percolate through the crucible, and the bisnitrosoamine (washed and dried as before) was weighed, a correction being applied for its solubility in 5*N*-hydrochloric acid. The mononitroso-compound was estimated by difference, its solubility in the reaction mixture being allowed for: it crystallised from ethyl alcohol in bright yellow plates, m. p. 183° (compare Herzberg and Polonowsky, *Ber.*, 1891, 24, 3198) (Found: C, 70.3; H, 6.2; N, 15.4. Calc.: C, 70.3; H, 6.4; N, 15.3%).

4:4'-Bismethylnitrosoaminobenzophenone crystallised from benzene in pale yellow needles, m. p. 234° (compare v. Braun, *Ber.*, 1904, 37, 2677) (Found: C, 60.4; H, 4.7; N, 18.8. Calc.: C, 60.3; H, 4.7; N, 18.9%).

Solubility of 4:4'-bismethylnitrosoaminobenzophenone and of 4-dimethylamino-4'-methylnitrosoaminobenzophenone in 100 c.c. of hydrochloric acid of various concentrations at 0°.

(1) The bismethylnitrosoamine.

Normality of HCl	7.58	5.05	3.79	2.53	0.76
Solubility in grams.....	0.034	0.025	0.020	0.019	0.018

(2) The monomethylnitrosoamine.

Normality of HCl	5.68	3.79	2.53	1.52	0.76
Solubility in grams.....	large	0.671	0.127	0.045	0.037

Action of Nitrous Acid on 4:4'-Bisdiethylaminodiphenylmethane.—To 5 g. of the base, dissolved in 100 c.c. of 11.5*N*-hydrochloric acid and diluted with 30 c.c. of water, a solution of 4.5 g. of sodium nitrite in 10 c.c. of water was slowly added at 0°. Evolution of nitric oxide proceeded steadily for hours; the solution turned red, and after 90 minutes began to precipitate 4:4'-bisdiethylnitrosoaminodiphenylmethane, of which 0.5 g. had separated as colourless plates after 24 hours; it melted at 83° after crystallisation from alcohol and gave the Liebermann nitroso-reaction strongly (Found: C, 65.3; H, 6.4; N, 17.8. C₁₇H₂₀O₂N₄ requires C, 65.4; H, 6.4; N, 17.9%).

Neutralisation of the remaining solution precipitated 4.5 g. of an oil, which solidified in

red needles soluble in ether and sparingly soluble in alcohol or glacial acetic acid, melted at 39—40° after crystallisation from alcohol, did not give the Liebermann nitroso-reaction, and consisted of *dinitro-4 : 4'-bisdiethylaminodiphenylmethane* (the nitro-groups are probably in positions 3 and 3') (Found : C, 62.8; H, 7.2; N, 14.1; NO₂, 22.7. C₂₁H₂₈O₄N₄ requires C, 63.0; H, 7.0; N, 14.0; NO₂, 23.0%).

In a similar experiment with 50 c.c. of hydrochloric acid and 150 c.c. of water, the gassing was less vigorous and precipitation began in 20 minutes. After 24 hours, 1.3 g. of a mixture, m. p. 70—80°, had been precipitated. This was dissolved in hydrochloric acid; cautious addition of water then precipitated 0.8 g. of yellow *p*-nitronitrosoethylaniline, m. p. and mixed m. p. 116° (Found : C, 49.3; H, 4.8; N, 21.5. Calc. : C, 49.3; H, 4.6; N, 21.5%). Neutralisation then precipitated 0.5 g. of *p*-nitrodiethylaniline, yellow needles, m. p. 77.5°, and 78.0° after admixture with an authentic specimen (Found : C, 61.8; H, 7.2; N, 12.5. Calc. : C, 61.9; H, 7.2; N, 14.4%). From the original mother-liquor, alkali precipitated 3.5 g. of the same dinitrobisdiethylaminodiphenylmethane as was obtained in the previous experiment.

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MARISCHAL COLLEGE, UNIVERSITY OF ABERDEEN.

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