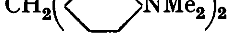
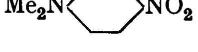
243. *The Action of Nitrous Acid on Tertiary Amines: The Influence of Acidity.*

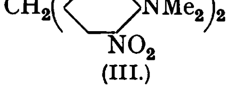
By Gerald P. Crowley, George J. G. Milton, T. Harold Reade, and William M. Todd.

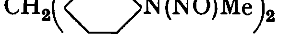
The concentration of mineral acid has a marked influence on the yields of nitration, nitrosation, and fission products obtained by the action of nitrite on bis-(*p*-dimethylaminophenyl)methane in various acids, but it has little effect on the yields of products from dimethyl-*p*-toluidine in hydrochloric acid. In *p*-nitromethylethylaniline the ethyl group is eliminated more easily than the methyl group during formation of its nitrosoamines.

Bis-(*p*-dimethylaminophenyl)methane (I) reacts with nitrite in aqueous acids, forming three compounds, *viz.*, *p*-nitrodimethylaniline (II) by fission and nitration, bis-(3-nitro-4-dimethylaminophenyl)methane (III) by nitration of the benzene nuclei, and bis-(*p*-*N*-nitroso-*N*-methylaminophenyl)methane (IV) by nitrosation of the amino-nitrogen atom and loss of a methyl group. The yields are dependent on the concentration of mineral acid in excess of that required to dissolve the amine and convert the sodium nitrite into nitrous acid (Donald and Reade, J., 1935, 53). These authors found (*a*) that substances (II), (III), and (IV) were produced at a hydrogen chloride concentration below 3·9N, but that (II) was not produced in more concentrated acid; (*b*) that the nitration/nitrosation ratio, *i.e.*, (III)/(IV), tended to increase as the hydrogen chloride concentration increased, provided that excess of nitrite was employed. To account for this they suggested a mechanism analogous to the shift caused by acids in the position of equilibrium between diazonium salts and diazo-compounds, nitration being assumed to occur *via* the diazonium form, [R·N(NO)Me$_2$]Cl, and nitrosation *via* the diazo-form, R·NMe·NCl·OMe.


(I.)


(II.)


(III.)


(IV.)

This communication records experiments made in three other mineral acid systems to test the validity of these authors' results and theoretical assumptions.

To avoid the interference caused by combination of the evolved nitric oxide with air and water to form more nitrous acid, the experiments were carried out in nitrogen, and are recorded in tabular form on p. 1287.

Molar Fractions per 1 *Mol. of* (I) *and* 4 *Mols. of* $NaNO_2$.

[The concentration of acid refers to its normality in excess of that required to dissolve the amine and react with sodium nitrite (see p. 1288).]

Acid, N.	H_2SO_4.	H_2SO_4 + HBr.	HCl + HBr.	Acid, N.	H_2SO_4.	H_2SO_4 + HBr.	HCl + HBr.
Fission product (II).							
1	0·30	0·34	0·37	3	0·20	0·18	0·18
1·5	0·31	0·36	0·36	3·5	0·04	0·03	0·07
2	0·31	0·37	0·34	3·9	nil	nil	nil
2·5	0·305	0·34	0·26	and over			
This affords confirmation of (*a*).							
Nitration product (III).							
1	0·66	0·62	0·59	4·5	0·77	0·78	0·71
1·5	0·65	0·59	0·56	5	0·73	0·74	0·67
2	0·64	0·60	0·57	5·5	0·71	0·71	0·62
2·5	0·65	0·61	0·61	Maxima occur at			
3	0·70	0·74	0·65	3·6	0·80	—	—
3·5	0·80	0·80	0·70	3·5	—	0·80	—
4	0·79	0·80	0·74	3·9	—	—	0·742
Nitrosation product (IV).							
1	0·016	0·023	0·013	4·5	0·137	0·105	0·152
1·5	0·024	0·030	0·030	5	0·120	0·104	0·138
2	0·033	0·038	0·050	5·5	0·070	0·096	0·130
2·5	0·039	0·047	0·070	Maxima occur at			
3	0·055	0·062	0·093	4·6	0·14	—	—
3·5	0·069	0·086	0·130	4·5	—	0·105 *	—
4	0·093	0·105	0·155	4·1	—	—	0·156

* Possibly slightly too low.

The nitration/nitrosation ratios when the fission product (II) is not formed are recorded below :

Ratio (III)/(IV).

Acid, N.	H_2SO_4.	H_2SO_4 + HBr.	HCl + HBr.
4	8·5	7·6	4·8
4·5	5·8	7·4	4·7
5	6·1	7·1	4·8
5·5	10·1	7·4	4·8
Average	7·6	7·4	4·8

The fact that, although the ratios show considerable fluctuations, they afford no real evidence of rising as the acid concentration increases, deprives conclusion (*b*)—and the assumptions made to account for it—of a satisfactory experimental foundation; and the following additional points may be cited against it.

1. The supposed intermediate compounds have never been isolated, although special experiments were made in alcoholic solution, amyl nitrite and sulphuric acid being used, followed by ether, in the hope of obtaining them.

2. The average values of the ratio (III)/(IV) tend to be higher in solutions containing sulphuric acid than in those containing hydrochloric acid of the same normality. The higher hydrogen-ion concentration of the hydrochloric acid might have been expected to favour the diazonium form assumed to be the precursor of (III), thus giving a higher ratio of (III)/(IV) than in the sulphuric acid; but the reverse is the case.

3. If the assumption was valid that compounds (III) and (IV) were obtained by a reaction similar to diazotisation, whereas fission to form compound (II) was of a different sort, the ratio [(III) + (IV)]/(II) would be expected to rise in media which favoured rapid diazotisation, *e.g.*, in hydrobromic acid (cf. Ueno and Suzuki, *J. Soc. Chem. Ind. Japan*, 1933, **36**, 615); but experimentally the average value (1·8) in H_2SO_4 + HBr is lower than that in H_2SO_4 alone (2·2) :

Ratios [(III) + (IV)]/(II).

Acid, N.	H_2SO_4.	H_2SO_4 + HBr.	HCl + HBr.
1	2·2	1·9	1·6
1·5	2·2	1·7	1·6
2	2·2	1·7	1·8
2·5	2·3	1·9	1·9
Average	2·2	1·8	1·7

4. In nitrosoamine formation at low concentration of nitrite the methyl group eliminated was converted into formaldehyde, not into methyl nitrate as previously assumed. One of us (W. M. T.) isolated both the compounds which formaldehyde forms with *p*-nitrophenylhydrazine by filtering the basified solution, adding ammonia, evaporating to dryness, and regenerating formaldehyde from the hexamethylenetetramine so formed. As formaldehyde was also obtained during nitrosoamine formation from the action of nitrous acid on *p*-nitrodimethylaniline, which does not contain a methylene group, it evidently originates from the alkyl group (cf. Halliday and Reade, this vol., p. 138), and the same is probable for its formation from the methane base (I).

For these reasons many points in Donald and Reade's proposals are now regarded as erroneous. The existence of an intermediate compound analogous in valency to a diazonium salt is not, however, improbable; for Meisenheimer's assumption (*Ber.*, 1913, **46**, 1150) that an intermediate compound $NMe_3Cl{\cdot}Cl$ was formed in the reaction of a neutral hypochlorite on trimethylamine hydrochloride, whereby formaldehyde, dimethylamine, and ultimately the chloroamine, NMe_2Cl, were produced, is essentially similar to the assumption of a diazonium analogue $[NR_3{\cdot}NO]Cl$ which by elimination of an alkyl group R as formaldehyde, ultimately gave the nitrosoamine, $NR_2{\cdot}NO$; for nitrous and hypochlorous acids have a number of points of similarity. It is not clear, however, exactly how this is brought about, or by what steps the nitration product (III) and the fission product (II) come to be formed. The following points are noteworthy.

1. The yield of *p*-nitrodimethylaniline due to fission is less in sulphuric acid, or in the mixed acids, than in hydrochloric acid.
2. In sulphuric acid the curve for the dinitration compound has a true maximum even when 8 mols. of nitrite are used; whereas in hydrochloric acid, the yield increased continuously as the normality increased without giving a true maximum, in Donald and Reade's experiments.
3. For 4 mols. of nitrite, the normalities at which the dinitration and the dinitrosation curves reach their maxima are more widely spaced in sulphuric acid, or in the mixed acids, than in hydrochloric acid.
4. From sulphuric acid of high normality a small quantity of a by-product was isolated; this was bis-(3-nitro-4-*N*-nitroso-*N*-methylaminophenyl)methane, which appears to be produced by the nitrosation of the bis-(3-nitro-4-dimethylaminophenyl)methane present in solution in the reaction mixture. In an attempt to determine whether the nitration/nitrosation ratio obtained from dialkylanilines in general was influenced by the concentration of mineral acid when no fission occurred, one of us (G. P. C.) investigated the behaviour of acid solutions of dimethyl-*p*-toluidine when treated with nitrite (3 and 6 mols.). At all concentrations of excess hydrochloric acid between 2·9N and 7N the variations in yields were small; and because by-products were obtained in small amounts and were difficult to separate quantitatively, the variations were regarded as being less than the possible experimental error. The nitration product, 3-nitro-4-dimethylaminotoluene, amounted to 83%, and the nitrosation product, *N*-nitrosomethyl-*p*-toluidine, to 16% (± 5%).

As mentioned by Hodgson (*J. Soc. Dyers Col.*, 1931, April), the main factor governing the nitration/nitrosation ratio obtained from tertiary amines and nitrous acid appears to be the polarity of the substituent present in the *p*-position to the dialkylamino-group.

Although the formation of nitrosoamines from *p*-nitrodialkylanilines is a general reaction of nitrite and acid, it was not known which alkyl group in unsymmetrical amines, *e.g.*, *p*-nitromethylethylaniline, was the more easily eliminated. The point was therefore investigated, and the amine was found to yield 17·4% of the ethyl and 82·6% of the methyl *p*-nitrophenylnitrosoamine from 4N-hydrochloric acid.

EXPERIMENTAL.

Action of Nitrous Acid on Bis-(p-*dimethylaminophenyl*)*methane.*—Experiments were carried out in conical flasks from which the air had been removed by a stream of nitrogen. The nitric oxide evolved was allowed to escape *via* a bubbler which prevented ingress of air. Mixed acids were made up from 4 mols. of hydrobromic acid per 1 mol. of methane base, the remainder being aqueous sulphuric or hydrochloric acid. The normality of acid shown in the tables is that calculated after allowing 2 equivs. for combination with each mol. of methane base, and 1 equiv. for each mol. of sodium nitrite, of which 4 or 8 mols. were used, the yields being practically identical in the two sets of experiments.

The method of separation and analysis of products was similar to that used by Donald and Reade, and allowance was made for the solubilities of the fission product and the nitrosoamine in acid.

Solubility (S) *of* p-*nitrodimethylaniline in* 100 *c.c. of aqueous sulphuric acid at* 0°.

Acid, N	3·65	3·51	3·45	3·35	3·25	3·11	3·02	2·83	2·77
S, g.	0·48	0·44	0·41	0·36	0·32	0·27	0·24	0·182	0·157
Acid, N	2·57	2·45	2·30	2·10	1·90	1·77	1·53	0·92	0·85
S, g.	0·110	0·091	0·075	0·069	0·057	0·042	0·031	0·018	0·010

Solubility (S) *of bis-*(p-N-*nitroso*-N-*methylaminophenyl*)*methane in* 100 *c.c. of aqueous sulphuric acid at* 0°.

Acid, N	5·87	5·62	5·23	5·08	4·92	4·81	4·66
S, g.	0·036	0·034	0·030	0·027	0·024	0·021	0·018
Acid, N	4·32	4·19	3·82	3·54	3·22	2·89	2·22
S, g.	0·013	0·011	0·010	0·009	0·008	0·007	0·006

*Action of Nitrous Acid on Dimethyl-*p-*toluidine.*—From amine, hydrochloric acid, and sodium nitrite in the molar proportions 1 : 19·4 : 3 with water as diluent, the main products after 16 hours at 0° were the same as those previously isolated from dilute solution by Hodgson and Kershaw (J., 1930, 277), *viz.*, (1) *N*-nitrosomethyl-*p*-toluidine and (2) 3-nitro-4-dimethylaminotoluene, from 2—5·5N-acid, after allowance for 4 mols. of acid—1 mol. for the amine and 3 mols. for the nitrite. These were accompanied—especially at higher normalities—by (3) 3-nitro-4-*N*-nitrosomethylaminotoluene, (4) 3-nitro-4-methylaminotoluene, and (5) 3 : 5-dinitro-4-*N*-nitrosomethylaminotoluene. The average yield of (1) was 16% from 2—7N-acid, but it fell rapidly at higher normality. The difficulty of perfect separation of products made quantitative experiments unreliable.

A typical experiment is the following: To the amine (5 g.), dissolved in 11·6N-hydrochloric acid (62 c.c.) and diluted with water (62 c.c.), a solution of sodium nitrite (7·6 g.) in water (25 c.c.) was slowly added at 0°. The mixture was kept for 16 hours and then diluted to 250 c.c. with water, cooled to 0° for 2 hours, and the mixed nitrosoamines (1·1 g.) filtered off. They were fractionally crystallised from ethanol to yield, in order of solubility, (*a*) 3 : 5-dinitro-4-nitrosomethylaminotoluene, which recrystallised from hot ethanol in pale yellow needles, m. p. 124° (Found: C, 40·1; H, 3·2; N, 23·4. Calc. for $C_8H_8O_5N_4$: C, 40·0; H, 3·3; N, 23·3%) (cf. von Romburgh, *Ber.*, 1896, **29**, 1016); (*b*) nitrosomonomethyl-*p*-toluidine, which, recrystallised from ethanol, had m. p. 49·5° (cf. Hodgson and Kershaw, *loc. cit.*); (*c*) 3-nitro-4-nitrosomethylaminotoluene, m. p. 40° (not obtained pure owing to decomp.) (Found, by determination with $TiCl_3$: $NO_2 + NO$, 42·5. Calc. for $C_8H_9O_3N_3$: $NO_2 + NO$, 46·3%); (*d*) a residual yellow oil which on addition of a few drops of concentrated hydrochloric acid gave a red precipitate of 3-nitro-4-methylaminotoluene, which recrystallised from aqueous ethanol in bright red needles, m. p. 84° (Found: C, 57·9; H, 5·9; N, 16·9; NO_2, 27·3. Calc. for $C_8H_{10}O_2N_4$: C, 57·8; H, 6·0; N, 16·9; NO_2, 27·7%) (cf. Gattermann, *Ber.*, 1885, **18**, 1487).

The acid filtrate obtained after separation of the mixed nitrosoamines was treated with urea at 30° to remove excess nitrous acid, and sodium hydroxide was added to reduce the acidity to 0·5N. A small quantity of 3-nitro-4-methylaminotoluene separated as a red precipitate. The solution was then neutralised at 0° and 3-nitro-4-dimethylaminotoluene was precipitated as fine yellow crystals (4 g.), which recrystallised from aqueous alcohol in needles, m. p. 25° (cf. Pinnow, *Ber.*, 1897, **30**, 3119; Hodgson and Kershaw, *loc. cit.*).

Nitrosation of p-*Nitromethylethylaniline.*—A mixture of *p*-nitrophenyl-methyl- and -ethyl-nitrosoamine was obtained from 4N-hydrochloric acid at 15° in 80% yield after 18 hours. After collection on a glass filter the substances were successively washed with acid, water, alkali, and water (until neutral), and then were dried in a vacuum for 14 days. The composition of the mixture was obtained by thermal analysis. It had m. p. 87·97° ± 0·08°. After admixture with the pure ethyl compound to give 28·8% of the latter, it had m. p. 80·27° ± 0·15°, corresponding satisfactorily with 80·2° read from the m. p. graph; the original mixture therefore consisted of 17·4% of the ethyl and 82·6% of the methyl *p*-nitrophenylnitrosoamine. Of these two alkyl groups, therefore, the ethyl was much the more completely removed during nitrosoamine formation.

MARISCHAL COLLEGE, UNIVERSITY OF ABERDEEN.

[*Received, May* 10*th*, 1940.]