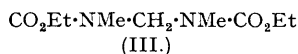
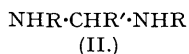
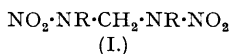


### 352. Studies on Nitroamines. Part II. The Nitration of Some Methylenebisamides and Related Compounds.

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Methylenebisacetamide (II; R = Ac, R' = H) is convertible, by nitration and subsequent hydrolysis, into methylenedinitroamine (I; R = H). Attempts to prepare methylenedinitroamine and its analogues from related bisamides were unsuccessful.

IN the course of work undertaken primarily to provide a synthetical proof of the structure of methylenedinitroamine (I; R = H), first isolated, as a degradation product during nitrolysis of hexamine, by workers at Bristol University (private communication), the nitration of a number of bisamides (II; R = Ac, R' = H, Me, or Ph; R = CO<sub>2</sub>Et, R' = H or Me; or R = CO·NMe<sub>2</sub>, R' = H) and (III) has been studied. Cleavage of the N-C-N linkages



appeared to be the commonest reaction, but methylenebis-*N*-acetamide (II; R = Ac, R' = H) was unaffected by cold 98% nitric acid. Whilst addition of ether precipitated the *mono-nitrate*, introduction of acetic anhydride led to the formation of *methylenebis-N-(N-nitro)-acetamide* (I; R = Ac), from which methylenedinitroamine could best be obtained by hydrolysis with aqueous ammonia.

Ethylidenebis-*N*-acetamide (II; R = Ac, R' = Me) was less stable to 98% nitric acid than was the methylene homologue, and no isolable nitration product could be obtained from nitric acid-acetic anhydride mixtures. Benzylidenebis-*N*-acetamide (II; R = Ac, R' = Ph) yielded nitrobenzylidenebisacetamides with 98% nitric acid, the *p*-isomer being predominant. Introduction of acetic anhydride caused cleavage to *p*-nitrobenzaldehyde.

Nitric acid treatment of methylenebis-*N*-urethane (II; R = CO<sub>2</sub>Et, R' = H) yielded nitrourethane and an (unidentified) neutral oil. Similar treatment of ethylidenebis-*N*-urethane (II; R = CO<sub>2</sub>Et, R' = Me) gave a greater yield of nitrourethane, but no neutral product. The stability of nitrourethane in nitric acid was greater than anticipated (Thiele and Lachmann, *Ber.*, 1894, **27**, 1519; *Annalen*, 1895, **288**, 269), and a direct preparation from urethane and nitric acid compares favourably with the traditional method. *Methylenebis-(N-methylurethane)* (III) yielded methylnitroamine on treatment with 98% nitric acid and subsequent ammonolysis, whilst from methylenebis-(*as*-dimethylurea) (II; R = CO·NMe<sub>2</sub>, R' = H) there was obtained a small yield of dimethylnitroamine.

#### EXPERIMENTAL.

*Methylenebis-N-acetamide* (II; R = Ac, R' = H).—Acetamide (118 g.) and paraformaldehyde (33 g.) were heated in an oil-bath at 155° for 17 hours with, and for a further 90 minutes without, a

reflux condenser. The melt yielded methylenebis-*N*-acetamide (60 g.), m. p. 196°, on crystallisation from alcohol (350 ml.); a further 20 g. were obtainable by evaporation and reheating of the residue. This method, based on G.P. 164611 (*Centr.*, 1905, II, 1751), appeared more convenient than that of Noyes and Forman (*J. Amer. Chem. Soc.*, 1933, **55**, 3493).

*Methylenebis-N-acetamide Mononitrate*.—Methylenebisacetamide (5 g.) was added at  $-5^\circ$  to 98% nitric acid (30 ml.); the product appeared to be stable since, after 25 minutes at  $<+5^\circ$  and precipitation at about  $-30^\circ$  by the dropwise addition of precooled ether (105 ml.), the *nitrate* (6.4 g., after washing with ether) could be collected. This crystallised from chloroform in needles, m. p.  $102^\circ$  (Found: equiv., 195.  $C_5H_{10}O_2N_2, HNO_3$  requires equiv., 193), which gave potassium nitrate and methylenebis-*N*-acetamide on neutralisation with alcoholic potassium hydroxide.

*Methylenebis-N-(N-nitro)acetamide* (I; R = Ac).—98% Nitric acid (190 ml.) was added at  $15^\circ$  during 30 minutes to a vigorously stirred suspension of methylenebis-*N*-acetamide (65 g.) in acetic anhydride (190 ml.). After 3 hours at  $15^\circ$ , the solution was run in a stream during 30 minutes into vigorously stirred ice (800 g.) and ice-water (1 l.). The crude nitration product was collected and washed with water; it could be hydrolysed to methylenedinitroamine without further treatment but, if it was dried in a vacuum, the yield was 60 g. *Methylenebis-N-(N-nitro)acetamide* separated from aqueous methyl alcohol in rhombic plates, m. p.  $63^\circ$ , insoluble in water or ligroin, sparingly soluble in ether, moderately soluble in alcohol, and easily soluble in ethyl acetate, acetone, benzene, chloroform, nitromethane, or dioxan (Found: C, 27.3; H, 3.9; N, 25.7.  $C_6H_8O_6N_4$  requires C, 27.2; H, 3.6; N, 25.4%). The solid was reasonably stable after crystallisation, and has been kept on porcelain in a desiccator for 3 years, though extensive decomposition occurred in 3 months on storage in glass screw-capped bottles.

The yield was unaffected by the order of addition of the components, and the quantities of both acid and anhydride could be doubled without decrease of yield, but a decrease in the quantity of acid was markedly deleterious. None of the product was obtained in 98% nitric acid alone, or in a 98% nitric acid-fuming sulphuric acid mixture. At  $0^\circ$  the yield rose smoothly to about 40% after  $3\frac{1}{2}$  hours and thereafter fell very slowly; at higher temperatures greater maxima were obtained more rapidly (e.g., 55% after  $2\frac{1}{2}$  hours at  $16^\circ$ ), but the subsequent fall in yield was also accelerated, and only an oil (presumably tetranitromethane) was produced at  $30^\circ$ .

*Methylenedinitroamine* (I; R = H).—The precipitate of crude methylenebis-*N-(N-nitro)acetamide* (from 65 g. of methylenebisacetamide) was collected, washed with water, drained, and added portionwise to well-stirred aqueous ammonia [100 ml. ( $d$  0.88) in 140 ml. of water] kept at  $<20^\circ$ . After a further 5 minutes, barium chloride solution (85 g. of the dihydrate in 250 ml. of water) was run in, and the suspension cooled in about 20 minutes to  $4^\circ$ . The barium salt of methylenedinitroamine was collected, washed with cold 50% aqueous acetone, and added to hydrochloric acid (60 ml. of conc. acid in 140 ml. of water); after the solution had been filtered, extracted with ether (7  $\times$  100 ml.), dried ( $Na_2SO_4$ ), and concentrated to about 60 ml., methylenedinitroamine (28 g.), m. p.  $98-101^\circ$  (decomp.), was precipitated by the addition of two volumes of warm ligroin (b. p.  $40-60^\circ$ ). This method, based on a knowledge of the stability of methylenedinitroamine in aqueous solutions at certain pH values (Part VII of this series) produced methylenedinitroamine (in 25% w/w yield, calc. on acetamide) of quality satisfactory for preparative work; pure material was obtained by one crystallisation from ether. Owing to decomposition, the m. p. is less satisfactory as a criterion of purity than is titration with alkali hydroxide to thymolphthalein.

*Attempted Nitration of Ethylidenebis-N-acetamide* (II; R = Ac, R' = Me).—(a) Ethylidenebis-*N*-acetamide (1.5 g.) (Noyes and Forman, *loc. cit.*) was added to 98% nitric acid (9 ml.) in 6 minutes at  $-5^\circ$ . After a further 9 minutes at  $-5^\circ$ , the mixture was run dropwise into cooled ether; on decantation and stirring in fresh ether the resultant oil solidified (0.47 g.) and yielded ethylidenebis-*N*-acetamide (0.22 g.), m. p.  $177^\circ$ , on crystallisation from alcohol. No insoluble material was obtained by running a similar nitration mixture into water.

(b) Ethylidenebis-*N*-acetamide in acetic anhydride was treated with nitric acid as detailed for the methylene homologue; no water-insoluble solid was obtained at any time during ageing at  $15^\circ$ ,  $0^\circ$ , or  $-10^\circ$ .

*Nitration of Benzylidenebis-N-acetamide* (II; R = Ac, R' = Ph).—(a) Benzylidenebis-*N*-acetamide (2 g.) (Noyes and Forman, *loc. cit.*) was added to 98% nitric acid (10 ml.) in 10 minutes at  $0^\circ$ . After 20 minutes at  $1^\circ$ , the mixture was run dropwise into cooled ether (60 ml.). The mixture of nitrobenzylidenebis-*N*-acetamides (1.83 g.), m. p.  $230-240^\circ$ , was collected and twice crystallised from alcohol-water (9 : 1); needles, m. p.  $260-262^\circ$  (Found: C, 52.7; H, 5.3. Calc. for  $C_{11}H_{13}O_4N_3$ : C, 52.6; H, 5.2%), were obtained (Ittyerah and Pandya, *Proc. Indian Acad. Sci.*, 1942, **15**, A, 258, give  $272^\circ$  as the m. p. of the pure *p*-isomer). 0.25 G. of the crude nitrobenzylidenebis-*N*-acetamides, m. p.  $230-240^\circ$ , was heated at  $90^\circ$  for 4 hours with 2*N*-hydrochloric acid (20 ml.). Insoluble material was collected; *p*-nitrobenzaldehyde (0.06 g.), m. p.  $99-102^\circ$ , separated on cooling.

(b) Benzylidenebis-*N*-acetamide (5 g.) was suspended in acetic anhydride (20 ml.) and 98% nitric acid (21 ml.) added at  $15^\circ$  in 15 minutes. After 3 hours at  $15^\circ$  the mixture was poured into ice and water (250 ml.). The resultant oil was extracted with ether, washed with sodium bicarbonate, dried, and evaporated; after 3 weeks, *p*-nitrobenzaldehyde (0.3 g.), m. p.  $95-98^\circ$ , was deposited. A similar experiment showed that nitrobenzylidenebis-*N*-acetamides, isolable at first by running into ether, were destroyed during the ageing process.

*Nitration of Methylene- and Ethylidene-bisurethanes* (II; R =  $CO_2Et$ , R' = H or Me).—(a) Methylenebisurethane (5 g.) (better prepared by condensation in 0.1*N*-hydrochloric acid in place of the 0.02*N*-acid of Conrad and Hock, *Ber.*, 1903, **36**, 2206) was added in 7 minutes to 98% nitric acid (25 ml.) at  $-8^\circ$ . After a further 8 minutes at  $-8^\circ$ , the mixture was poured on ice (300 g.) and extracted with ether, and the extract washed with sodium hydrogen carbonate solution. The residual ether yielded on evaporation a neutral oil (1.7 g.) from which no crystalline material could be isolated. The carbonate washings were acidified and extracted with ether; passage of gaseous ammonia through the extract precipitated ammonium nitrourethane (1.74 g.), m. p.  $162^\circ$  (decomp.), identified by comparison with an authentic sample and by conversion into the free acid.

(b) Ethylidenebisurethane (5 g.) [prepared in 78% yield by treatment of urethane (17.8 g.) in water (55 ml.) with acetaldehyde (4.6 g.) and concentrated hydrochloric acid (1 ml.); cf. Nencki, *Ber.*, 1874, **7**, 160] yielded, on similar treatment, no neutral oil, and an enhanced yield (5.6 g.) of ammonium nitrourethane, m. p. 160° (decomp.).

*Direct Nitration of Urethane.*—Urethane (4.45 g.) was added to 98% nitric acid (21 ml.) in 10 minutes at  $-5^{\circ}$ . After 25 minutes at  $0^{\circ}$  the mixture, worked up as described for the nitration of methylenebisurethane, yielded ammonium nitrourethane (7.26 g.), m. p. 156°; crystallisation from methylated spirits (40 ml.) yielded the pure salt (4.7 g.), m. p. 171°.

*Methylenebis-(N-methylurethane)* (III).—*N*-Methylurethane (30 ml.) was shaken for 36 hours with 0.1*N*-hydrochloric acid (180 ml.) and 38% formaldehyde (14 ml.). The oil which separated was extracted with ether, dried, and distilled. The *product* (III) (16 g.) had b. p. 136–142°/14 mm. (Found: C, 49.8; H, 8.4.  $C_9H_{18}O_4N_2$  requires C, 49.5; H, 8.3%). By nitration and working up as described for methylenebisurethane, a neutral oil was obtained; passage of ammonia through an ethereal solution of this product precipitated the hygroscopic ammonium methylnitroamine as a yellow oil. Excess of anhydrous sodium sulphate was added, the solid collected, decomposed with acid, and extracted with ether. Methylnitroamine (1.1 g.), m. p. 37°, not depressed by an authentic specimen, was obtained on evaporation.

*Nitration of Methylenebis-(as-dimethylurea)* (II; R = CO·NMe<sub>2</sub>, R' = H).—Methylenebis-(as-dimethylurea) (2 g.) (Einhorn, *Annalen*, 1908, **361**, 136; for dimethylurea, see Davis and Blanchard, *J. Amer. Chem. Soc.*, 1929, **51**, 1798) was added to 98% nitric acid (10 ml.) in 15 minutes at  $-8^{\circ}$ . Slight evolution of gas occurred during dissolution, and after a further 4 minutes at  $-8^{\circ}$  the mixture was poured on ice (100 g.). Extraction with ether yielded only dimethylnitroamine (0.2 g.), m. p. 53–56°, identified by comparison with an authentic sample.

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