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_2Et, R′ = H or Me; or R = CO·NMe_2, 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 *mononitrate,* 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.

$NO_2{\cdot}NR{\cdot}CH_2{\cdot}NR{\cdot}NO_2$ (I.)   NHR·CHR′·NHR (II.) $CO_2Et{\cdot}NMe{\cdot}CH_2{\cdot}NMe{\cdot}CO_2Et$ (III.)

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_2Et, R′ = H) yielded nitrourethane and an (unidentified) neutral oil. Similar treatment of ethylidenebis-*N*-urethane (II; R = CO_2Et, 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_2, 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° to 98% nitric acid (30 ml.); the product appeared to be stable since, after 25 minutes at $<+5°$ and precipitation at about −30° 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° (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° during 30 minutes to a vigorously stirred suspension of methylenebis-*N*-acetamide (65 g.) in acetic anhydride (190 ml.). After 3 hours at 15°, 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°, 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° the yield rose smoothly to about 40% after 3½ hours and thereafter fell very slowly; at higher temperatures greater maxima were obtained more rapidly (*e.g.*, 55% after 2½ hours at 16°), but the subsequent fall in yield was also accelerated, and only an oil (presumably tetranitromethane) was produced at 30°.

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°. 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°. 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 × 100 ml.), dried (Na_2SO_4), and concentrated to about 60 ml., methylenedinitroamine (28 g.), m. p. 98—101° (decomp.), was precipitated by the addition of two volumes of warm ligroin (b. p. 40—60°). 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°. After a further 9 minutes at −5°, 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°, 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°, 0°, or −10°.

*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°. After 20 minutes at 1°, the mixture was run dropwise into cooled ether (60 ml.). The mixture of nitrobenzylidenebis-*N*-acetamides (1·83 g.), m. p. 230—240°, was collected and twice crystallised from alcohol–water (9 : 1); needles, m. p. 260—262° (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° as the m. p. of the pure *p*-isomer). 0·25 G. of the crude nitrobenzylidenebis-*N*-acetamides, m. p. 230—240°, was heated at 90° for 4 hours with 2N-hydrochloric acid (20 ml.). Insoluble material was collected; *p*-nitrobenzaldehyde (0·06 g.), m. p. 99—102°, 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° in 15 minutes. After 3 hours at 15° 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 (0·8 g.), m. p. 95—98°, 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 0·1N-hydrochloric acid in place of the 0·02N-acid of Conrad and Hock, *Ber.*, 1903, **36**, 2206) was added in 7 minutes to 98% nitric acid (25 ml.) at −8°. After a further 8 minutes at −8°, 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° (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 $-5°$. After 25 minutes at 0° 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 0·1N-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 = $CO{\cdot}NMe_2$, 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 $-8°$. Slight evolution of gas occurred during dissolution, and after a further 4 minutes at $-8°$ 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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