

### 353. Studies on Nitroamines. Part III. The Reactions of Nitroamines with Formaldehyde.

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The *N*-hydroxymethyl compounds (I; R = CH<sub>2</sub>·OH; *n* = 1, 3, or 4) and (II; R = CH<sub>2</sub>·OH) have been prepared by utilising the reversible reaction between the corresponding nitroamine and formaldehyde. Characteristic derivatives (I; R = morpholinomethyl; *n* = 3 or 4) and (II; R = morpholinomethyl) are formed with morpholine.

FRANCHIMONT (*Rec. Trav. chim.*, 1910, **29**, 306) showed that nitroamines reacted with formaldehyde in the presence of piperidine or piperazine, but stated that no reaction took place in the absence of bases (*ibid.*, 1895, **14**, 48; 1910, **29**, 306). It has now been found that ethylenedinitroamine (I; *n* = 2; R = H) condenses with 40% formaldehyde to form *N*-hydroxymethylethylenedinitroamine (II; R = CH<sub>2</sub>·OH), m. p. 127—129° (decomp.), but attempts to obtain the *NN'*-bishydroxymethyl derivative (I; *n* = 2; R = CH<sub>2</sub>·OH) were unsuccessful even in the presence of a large excess of formaldehyde.



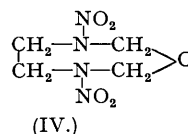
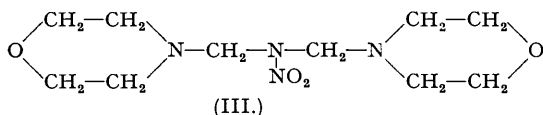
The product (II; R = CH<sub>2</sub>·OH) reacts with morpholine to give a crystalline *derivative* (II; R = morpholinomethyl), but with an excess of the base in the presence of an excess of formaldehyde gives the *compound* (I; *n* = 2; R = morpholinomethyl). These morpholine derivatives are highly characteristic and can be accurately titrated with 0.1*N*-sodium hydroxide using thymolphthalein as indicator, and the formaldehyde liberated (see Part V) can be conveniently determined.

Treatment of ethylenedinitroamine with excess of piperidine in the presence of excess of 40% formaldehyde gave the compound (I; *n* = 2; R = piperidinomethyl), m. p. 112—114° (decomp.) (cf. Franchimont, *Rec. Trav. chim.*, 1910, **29**, 207), but diethylamine or monomethyl-aniline failed to give crystalline products.

Methylenedinitroamine (I; *n* = 1; R = H), when treated in ethyl acetate solution with dry gaseous formaldehyde, formed the *compound* (I; *n* = 1; R = CH<sub>2</sub>·OH), but the yield was poor and erratic under a variety of conditions. Confirmation of the structure of this product was obtained by its conversion by acetyl chloride into *NN'*-bisacetoxymethylmethylenedinitroamine (I; *n* = 1; R = CH<sub>2</sub>·OAc) (first prepared by Roberts, private communication).

Treatment of the diol (I; *n* = 1; R = CH<sub>2</sub>·OH) with excess of morpholine failed to give the dimorpholino-compound; the water-soluble product evolved formaldehyde readily on warming the solution, and gave elementary analysis results in good agreement with those required for *substance* (III). Its formation is apparently made possible by a breakdown of the

nitroamine into nitroamine in the presence of morpholine and formaldehyde, and the structure was confirmed by synthesis from these components.



Trimethylenedinitroamine (I;  $n = 3$ ; R = H) and tetramethylenedinitroamine (I;  $n = 4$ ; R = H) condensed with warm 40% aqueous formaldehyde to give the *diols* (I; R = CH<sub>2</sub>·OH;  $n = 3$  or 4, respectively), which with excess of morpholine yielded characteristic derivatives (I; R = morpholinomethyl,  $n = 3$  or 4, respectively); both these and the diols were accurately titratable using 0.1N-sodium hydroxide and thymolphthalein.

During experiments with *N*-hydroxymethylethylenedinitroamine (II; R = CH<sub>2</sub>·OH) it was found that heating at 130–140° gave an alkali-insoluble substance, m. p. 154–155°, in 15% yield. Analytical figures suggested that this was 3:6-dinitro-1-oxa-3:6-diazacycloheptane (IV), and 98% nitric acid at –20° gave the ether-insoluble *NN'*-bisnitroxymethylethylenedinitroamine (I;  $n = 2$ ; R = CH<sub>2</sub>·O·NO<sub>2</sub>) which was converted into the *dimethoxy*- (I;  $n = 2$ ; R = CH<sub>2</sub>·OMe) and *diacetoxy*-compound (I;  $n = 2$ ; R = CH<sub>2</sub>·OAc) (Myers and Wright, "Nitrolysis of Hexamine, Part IV," *Canadian J. Res.*, in the press) by methyl alcohol and acetic acid, respectively.

Attempts to synthesise (IV) by treating ethylenedinitroamine and excess of 40% aqueous formaldehyde with acetic anhydride at 65° were unsuccessful; (II; R = CH<sub>2</sub>·OH) was usually obtained, but in one experiment a small amount of *NN'*-bisacetylethylenedinitroamine (I;  $n = 2$ ; R = COMe) was isolated by evaporation of the solution in a vacuum below 70°. In view of statements in the literature (Franchimont and Klobbie, *Rec. Trav. chim.*, 1889, 8, 297; 1910, 29, 303; Thomas, *ibid.*, 1890, 9, 85) that smooth acylation of primary nitroamines has seldom been realised, it is of interest to record that *NN'*-bisacetylethylenedinitroamine can be prepared by stirring ethylenedinitroamine with acetic anhydride at 65°; at higher temperatures no solid product could be isolated.

#### EXPERIMENTAL.

*N*-Hydroxymethylethylenedinitroamine (II; R = CH<sub>2</sub>·OH).—40% Aqueous formaldehyde (20 c.c.; 2 mols.) was added to ethylenedinitroamine (20 g.) in boiling water (110 c.c.). The *product* (22.1 g.) which crystallised from the cooled mixture in stout prisms, m. p. 127–130° (decomp.), was collected and dried (Found: C, 20.3, 20.4; H, 4.5, 4.0; N, 31.1, 31.4; CH<sub>2</sub>O, 16.4; equiv., 89.8, 90.8. C<sub>3</sub>H<sub>8</sub>O<sub>5</sub>N<sub>4</sub> requires C, 20.0; H, 4.4; N, 31.1; CH<sub>2</sub>O, 16.6%; equiv., 90). Prolonged heating on a water-bath caused decomposition with loss of formaldehyde, and attempted recrystallisation from hot methyl, ethyl, or butyl alcohol yielded only ethylenedinitroamine. The product was insoluble in cold ether, chloroform, and methyl or ethyl alcohol, moderately soluble in acetone, and readily soluble in warm acetic anhydride.

*N*-Morpholinomethylethylenedinitroamine (II; R = morpholinomethyl).—*N*-Hydroxymethylethylenedinitroamine (0.45 g.) was dissolved in a warm mixture of morpholine (0.22 c.c.; 1 mol.) and ethyl acetate (3 c.c.); the *product* obtained after cooling crystallised in rosettes of monoclinic prisms (0.52 g.), m. p. 128–130° (decomp.) (Found: C, 34.0; H, 6.0; CH<sub>2</sub>O, 12.2; equiv., 124.0. C<sub>17</sub>H<sub>15</sub>O<sub>5</sub>N<sub>5</sub> requires C, 33.7; H, 6.0; CH<sub>2</sub>O, 12.0%; equiv., 124.5).

*NN'*-Bismorpholinomethylethylenedinitroamine (I;  $n = 2$ ; R = morpholinomethyl).—Ethylenedinitroamine, *N*-hydroxymethylethylenedinitroamine, or the monomorpholinomethyl compound described above, was warmed with excess of 40% formaldehyde and morpholine in ethyl acetate for 5 minutes; on cooling the mixture, the *product* separated in a mass of felted needles, m. p. 170–171° (reddening and decomp.) (Found: C, 41.0; H, 6.8; CH<sub>2</sub>O, 19.7; equiv., 174.0. C<sub>12</sub>H<sub>24</sub>O<sub>6</sub>N<sub>6</sub> requires C, 41.3; H, 6.9; CH<sub>2</sub>O, 17.2%; equiv., 174.0).

*NN'*-Bishydroxymethylmethylethylenedinitroamine (I;  $n = 1$ ; R = CH<sub>2</sub>·OH).—Gaseous formaldehyde was passed to saturation through a solution of methylenedinitroamine (0.5 g.) in ethyl acetate (1 c.c.); the mixture was cooled to 0°, and the *product*, rosettes of prisms (0.53 g.), m. p. 70–75° (decomp.), collected (Found: C, 19.3; H, 4.1; N, 27.8; equiv., 98.1. C<sub>3</sub>H<sub>8</sub>O<sub>5</sub>N<sub>4</sub> requires C, 18.4; H, 4.1; N, 28.6%; equiv., 98.0). The yields from three similar experiments were 0.39, 0.34, 0.30 g., respectively; however, on many occasions the product failed to crystallise, and the solution was then evaporated in vacuo and acetylated, as described below, to give the diacetate.

*NN'*-Bisacetoxyethylmethylethylenedinitroamine (I;  $n = 1$ ; R = CH<sub>2</sub>·OAc).—This was first prepared by Roberts (private communication). The above-mentioned diol (0.2 g.) was heated under reflux with acetyl chloride (1 c.c.) for 5 minutes; after removal of excess of solvent in a vacuum, the residue was triturated with water (5 c.c.), and the solid (0.26 g.) was collected and dried in a vacuum; recrystallisation from methyl alcohol gave prisms (0.18 g.), m. p. 103–104° (Found: C, 30.4; H, 4.6; N, 19.9; CH<sub>2</sub>O, 31.6. Calc. for C<sub>7</sub>H<sub>12</sub>O<sub>8</sub>N<sub>4</sub>: C, 30.0; H, 4.3; N, 20.0; CH<sub>2</sub>O, 32.1%). Attempted acetylation of the diol with acetic anhydride at 70° yielded methylenedinitroamine, and at 140° an amorphous product; no reaction occurred at room temperature.

*Bismorpholinomethylnitroamine* (III).—(a) A solution of methylenedinitroamine (0.54 g.) in 40%

aqueous formaldehyde (0.60 c.c.) was cooled below 0°, and morpholine (0.70 c.c., 2 mols.) added with stirring. After half an hour, the white solid (1.05 g.), m. p. 95—97° (decomp.), was collected and dried (Found: C, 45.7; H, 7.7; N, 20.6; CH<sub>2</sub>O, 24.6, 24.2, 23.7; *M* (cryoscopic in benzene), 210. C<sub>10</sub>H<sub>20</sub>O<sub>4</sub>N<sub>4</sub> requires C, 46.1; H, 7.7; N, 21.5; CH<sub>2</sub>O, 23.0%; *M*, 260). (b) A solution of methylenedinitroamine (0.5 g.) in ethyl acetate (0.8 c.c.) was saturated with gaseous formaldehyde at 0°, and morpholine (0.7 c.c., 2 mols.) added with shaking. After standing overnight at 0°, the solid (0.82 g.), m. p. 96—100° (decomp.), undepressed by admixture with the product from (a), was collected, washed with ether, and dried in a vacuum. (c) A solution of nitroamide (0.15 g.) in 40% aqueous formaldehyde (0.6 c.c., 3 mols.) was cooled to -10°, and morpholine (0.44 c.c., 2 mols.) added with stirring. After being kept at 0° for 3 hours, during which some effervescence was observed, the white solid (0.15 g.), m. p. 98—100° (decomp.), undepressed by admixture with products from (a) or (b), was collected, washed with ether, and dried.

*NN'-Biscarbomethoxytrimethylenediamine*.—The instructions of Ing and Manske (*J.*, 1926, 2349) led to a low yield of poor quality  $\alpha\gamma$ -diphthalimidopropane. The following modification was therefore adopted. Finely powdered potassium phthalimide (Hale and Britton, *J. Amer. Chem. Soc.*, 1919, **41**, 844) (96.5 g.) and trimethylene dibromide (30 c.c., 0.6 mol.) were heated in an oil-bath at 180—200° for 2.5 hours, and any unchanged bromide was removed in steam. The residual sticky mass, crystallised from glacial acetic acid, yielded  $\alpha\gamma$ -diphthalimidopropane (64.2 g.), m. p. 194—196°.

This product (25 g.) was heated in boiling 95% ethyl alcohol (70 c.c.) with hydrazine hydrate (100% ; 7.5 c.c.); a clear solution was obtained after 5 minutes, but in a further 10 minutes a gelatinous precipitate had formed. After cooling, excess of 2*N*-hydrochloric acid was added, and the phthalhydrazide collected; the filtrate was concentrated and cooled, and a further amount of hydrazide collected. The aqueous solution of trimethylenediamine dihydrochloride was cooled to <0° and stirred during the addition of sodium hydroxide (6.25 g., 2 mols.) in water (10 c.c.), and again during the simultaneous dropwise addition of methyl chloroformate (11.5 c.c., 2 mols.) and sodium hydroxide (6.25 g., 2 mols.) in water (10 c.c.). After the mixture had been stirred for a further 0.5 hour, the product was extracted with chloroform, dried, and freed from solvent, and the residue distilled. The distillate (7.3 g.), b. p. 154—156°/0.4 mm., solidified on cooling and crystallised from ether—light petroleum (b. p. 40—60°) in plates, m. p. 63—68°. Franchimont and Klobbie (*Rec. Trav. chim.*, 1888, **7**, 747) give m. p. 74—75°.

*Trimethylenedinitroamine* (I; *n* = 3; R = H).—The foregoing compound was converted into the *NN'*-dinitro-derivative (I; *n* = 3; R = CO<sub>2</sub>Me), m. p. 89—90°, by the method of Franchimont and Klobbie (*loc. cit.*), but their method of hydrolysis was modified as follows. The dinitro-compound (4 g.) was warmed with aqueous ammonia (8 c.c., *d* 0.88) for 5 minutes, water (5 c.c.) added, and excess of ammonia removed by evaporation at 100°. The oily residue was cooled, acidified with 2*N*-hydrochloric acid (Congo-red), extracted with ethyl acetate, dried, and freed from solvent. The solid residue (m. p. 58—64°) crystallised from water or ether—light petroleum (b. p. 40—60°) in stout prisms (1.46 g.), m. p. 68—69°. The mother-liquors gave a further amount (0.56 g.), m. p. 63—68°. Franchimont and Klobbie give m. p. 67°.

*NN'-Bishydroxymethyltrimethylenedinitroamine* (I; *n* = 3; R = CH<sub>2</sub>·OH).—Trimethylenedinitroamine (0.5 g.) was dissolved in warm 40% aqueous formaldehyde (1 c.c., 2 mols.), the solution cooled to 0°, and the product, which formed plates (0.58 g.), m. p. 88—92°, collected [Found: C, 26.1; H, 5.3; N, 25.3; CH<sub>2</sub>O, 26.2; equiv., 111.5, 112.3. C<sub>5</sub>H<sub>12</sub>O<sub>6</sub>N<sub>4</sub> requires C, 26.8; H, 5.4; N, 25.0; CH<sub>2</sub>O (2 mols.), 26.8%; equiv., 112.0].

*NN'-Bismorpholinomethyltrimethylenedinitroamine* (I; *n* = 3; R = morpholinomethyl).—The preceding compound (0.5 g.) was dissolved in ethyl acetate (1 c.c.), and morpholine (0.5 c.c., 2 mols.) was added. After 1 hour at 0°, the solid product was collected and dried. Recrystallisation from ethyl acetate gave rosettes of prisms (0.68 g.), m. p. 130—132° [Found: C, 42.9; H, 7.0; CH<sub>2</sub>O, 16.7, 17.2; equiv., 177.5. C<sub>13</sub>H<sub>26</sub>O<sub>8</sub>N<sub>6</sub> requires C, 43.1; H, 7.2; CH<sub>2</sub>O (2 mols.), 16.6%; equiv., 181].

*NN'-Biscarbomethoxytetramethylenediamine*.—Adipyl chloride (from 20 g. of adipic acid; cf. Fuson and Walker, *Org. Synth.*, 1933, **13**, 32) in an equal volume of chloroform was added slowly, with vigorous stirring, to aqueous ammonia (100 c.c., *d* 0.88). The product was collected and boiled in water containing a little charcoal until the chloroform had been removed; the filtered solution was cooled, and the adipamide (17 g.), m. p. 219°, collected. This was dissolved in a solution of bromine (13 c.c.) in 10*N*-sodium hydroxide (100 c.c.) and poured on ice (140 g.). After 1 hour the solution was heated under reflux for 3 hours, set aside overnight, and steam-distilled, the distillate being made acid with 2*N*-hydrochloric acid (120 c.c.) and evaporated to dryness. The residue of hydrochloride (9 g.) was collected and dissolved in 4*N*-sodium hydroxide (60 c.c.); the mixture was extracted with ether, the solvent removed, and the residual putrescine (3.0 g.) distilled, b. p. 140—150°/750 mm. (cf. Braun and Lemke, *Ber.*, 1922, **55**, B, 3549). The base was dissolved in water (10 c.c.), cooled in ice-salt, and stirred during the gradual addition of methyl chloroformate (6 c.c.). When about half of the latter had been added, 10*N*-sodium hydroxide (6.2 c.c.) was added at twice the rate, and, after the mixture had been kept for 2 hours at room temperature, *NN'*-biscarbomethoxytetramethylenediamine (4.0 g.), m. p. 128—130°, was collected, washed with water, and dried at 100°.

*Tetramethylenedinitroamine* (I; *n* = 4; R = H).—The preceding compound was converted into, successively, the *NN'*-dinitro-derivative and dinitroamine (cf. Dekkers, *Rec. Trav. chim.*, 1890, **9**, 96).

*NN'-Bishydroxymethyltetramethylenedinitroamine* (I; *n* = 4; R = CH<sub>2</sub>·OH).—Tetramethylenedinitroamine (I; *n* = 4; R = H) (0.6 g.) was dissolved in warm 40% aqueous formaldehyde (0.5 c.c.), and the solution kept overnight at 0°. The product was collected, washed with a little water, and dried (0.5 g.), m. p. 86—90° (Found: C, 30.4; H, 5.5; N, 23.6. C<sub>6</sub>H<sub>14</sub>O<sub>6</sub>N<sub>4</sub> requires C, 30.3; H, 5.9; N, 23.5%).

*NN'-Bismorpholinomethyltetramethylenedinitroamine* (I; *n* = 4; R = morpholinomethyl).—The diol (I; *n* = 4; R = CH<sub>2</sub>·OH) (0.4 g.) was dissolved in a warm mixture of ethyl acetate (5 c.c.) and morpholine (0.3 c.c.). The solid dinitroamine (0.42 g.), which separated on cooling, crystallised from ethyl acetate in minute prisms, m. p. 156—159° (Found: C, 44.4; H, 7.3; N, 21.6. C<sub>14</sub>H<sub>28</sub>O<sub>6</sub>N<sub>6</sub> requires C, 44.7; H, 7.7; N, 22.3%).

3 : 6-Dinitro-1-oxa-3 : 6-diazacycloheptane (IV).—*N*-Hydroxymethylethylenedinitroamine (5 g.) was heated at 140—145° for 1 hour in an open tube; formaldehyde and water were eliminated. The product was stirred with excess of sodium hydrogen carbonate solution, and the insoluble cyclic compound (0.85 g.), m. p. 150—152°, was collected, washed with water, and dried at 100°. It crystallised from hot water or acetone-benzene in a mass of fine needles, m. p. 154—155° (Found : C, 25.5; H, 4.3; N, 30.0; *M* (Rast), 187, 196.  $C_4H_8O_5N_4$  requires C, 25.0; H, 4.2; N, 29.1%; *M*, 192). Acidification of the sodium hydrogen carbonate liquors and extraction with ethyl acetate, yielded ethylenedinitroamine, m. p. 170—172° (decomp.), undepressed by admixture with an authentic specimen.

NN'-Bisnitroxymethylethylenedinitroamine (I;  $n = 2$ ;  $R = CH_2 \cdot O \cdot NO_2$ ).—The cyclic compound (IV) (0.5 g.) was added gradually with stirring to 98% nitric acid (5 c.c.) at -15°. After 10 minutes the mixture was added dropwise to anhydrous ether (50 c.c.) at -40°. The diester (0.64 g.) was collected, washed with dry ether, and dried; m. p. 112—117° (decomp.) (Found : C, 16.6; H, 2.7;  $O \cdot NO_2$ , 40.0;  $CH_2O$ , 19.8.  $C_4H_8O_{10}N_4$  requires C, 16.0; H, 2.7;  $O \cdot NO_2$ , 41.3;  $CH_2O$ , 20.0%). At > -40°, reduced yields were obtained.

NN'-Bismethoxymethylethylenedinitroamine (I;  $n = 2$ ;  $R = CH_2 \cdot OMe$ ).—The foregoing diester (0.1 g.) was heated under reflux with methyl alcohol (2 c.c.) for 0.5 hour, and the solution concentrated and allowed to cool. The product (0.07 g.), which separated on cooling and scratching, crystallised from methyl alcohol in nacreous plates, m. p. 79—80° (Found : C, 30.7; H, 5.9; N, 23.6.  $C_6H_{14}O_8N_4$  requires C, 30.2; H, 5.9; N, 23.5%).

NN'-Bisacetoxymethylethylenedinitroamine (I;  $n = 2$ ;  $R = CH_2 \cdot OAc$ ).—The dinitroxy-compound (I;  $n = 2$ ;  $R = CH_2 \cdot O \cdot NO_2$ ) (0.16 g.) was heated under reflux for 5 minutes with sodium acetate (0.16 g.) and glacial acetic acid (1 c.c.), the solvent was removed in a vacuum, and the residue triturated with water. The resultant sticky gum, which gradually solidified, was collected, washed with water, and crystallised from ethyl alcohol. The product (0.1 g.), m. p. 67—70°, crystallised from glacial acetic acid in large colourless plates, m. p. 67—69°, undepressed by admixture with a specimen, m. p. 67—70°, prepared as described by Myers and Wright ("Nitrolysis of Hexamine, Part IV," *Canadian J. Res.*, in the press.)

The diacetoxo-compound (1.0 g.) was added to 98% nitric acid (10 c.c.) at 5° and, after 15 minutes, the nitration mixture was added dropwise to anhydrous ether (50 c.c.) at <10°. The micro-crystalline precipitate was collected, washed with dry ether, and dried in a vacuum; the product (0.42 g.) had m. p. 115—120° (decomp.), undepressed by admixture with the product, m. p. 112—117° (decomp.), obtained by nitration of compound (IV). The identity of the substance was further confirmed by boiling with methyl alcohol which yielded the dimethoxy-compound (I;  $n = 2$ ;  $R = CH_2 \cdot OMe$ ), m. p. 79—80°.

Acetylation of Ethylenedinitroamine.—Finely powdered ethylenedinitroamine (1.5 g.) was stirred with acetic anhydride (25 c.c.) at 65° for 6 hours, the solution evaporated in a vacuum at <65°, and the residue treated with excess of sodium bicarbonate solution. The product (0.24 g.), m. p. 133—134° (decomp.), which was collected, washed with water, and dried at 100°, crystallised from acetone-ligroin (b. p. 40—60°) in nacreous plates, m. p. 135—136° (decomp.) (Found : C, 31.2; H, 4.2; N, 24.5. Calc. for  $C_6H_{10}O_6N_4$ : C, 30.8; H, 4.3; N, 23.9%). W. E. Bachmann (private communication) reports m. p. 132—133°.

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