[CONTRIBUTION FROM DEFENCE RESEARCH CHEMICAL LABORATORIES]

N-β-Nitraminoethyl-N'-methyl-N''-nitroguanidine[1]

BY A. F. MCKAY AND W. G. HATTON

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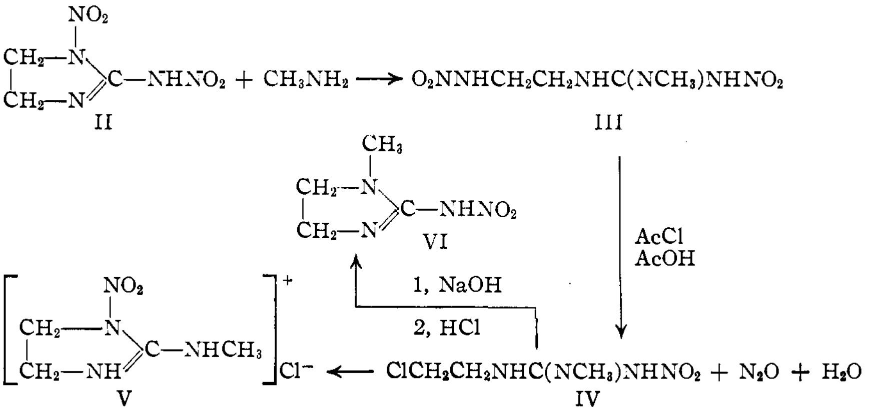
The chemistry involved in the reaction of N-β-nitraminoethyl-N'-methyl-N''-nitroguanidine with acetyl chloride in glacial acetic acid and absolute nitric acid in acetic anhydride is discussed in detail. Their reactions are similar in that the aliphatic nitramino group is replaced by a chloro and a nitroxy group respectively as preliminary reactions to cyclization.

Wright and his co-workers[2,3] have assigned cyclic or acylic configurations to the amine addition products of 1-nitro-2-nitramino-2-imidazoline depending on their behavior on potentiometric titration. On the other hand, ultraviolet studies[4,5] have shown that all the ammonia and amine addition products of 1-nitro-2-nitramino-2-imidazoline possess the same type of configuration and that this structure is acyclic I. Thus the reaction of acetyl chloride with these addition products is not as complex as indicated by Hall and Wright.[2] Moreover this reaction is the same as the previously described decomposition of primary nitramines by acid chlorides.[6] The reactions of acetyl chloride–glacial acetic acid and nitric acid–acetic anhydride media with the methylamine addition product (III) of 1-nitro-2-nitramino-2-imidazoline (II) described below are in agreement with the assigned[4,5] linear structure (III).[7]

$$NO_2NHCH_2CH_2NH—C(NR)NHNO_2$$

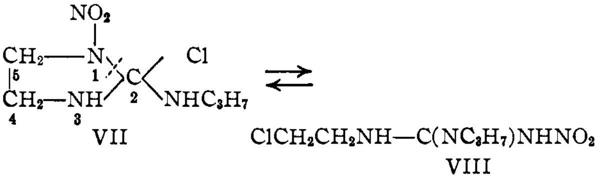
I



$$O_2NNHCH_2CH_2NHC(NCH_3)NHNO_2$$

$$ClCH_2CH_2NHC(NCH_3)NHNO_2 + N_2O + H_2O$$

N-β-Nitraminoethyl-N'-methyl-N''-nitroguanidine (III) was heated carefully in an acetyl chloride–acetic acid–acetic anhydride medium until the evolution of nitrous oxide ceased. The products of the reaction were isolated without the use of basic solutions. In this manner two crystalline products, N-β-chloroethyl-N'-methyl-N''-nitroguanidine (IV) and 1-nitro-2-methylamino-2-imidazolinium chloride (V) along with a trace of oil were obtained. Since the conditions of the experiment are unavoidably those conducive to the cyclization[8] of N-β-halogenoethyl-N'-nitroguanidines, it is not unexpected to find a large portion of the N-β-chloroethyl-N'-methyl-N''-nitroguanidine (IV) converted into 1-nitro-2-methylamino-2-imidazolinium chloride (V). Hall and Wright[2] considered that treatment of the *n*-propylamine addition product of 1-nitro-2-nitramino-2-imidazoline with acetyl chloride in acetic anhydride must give rise to structure VII to account



$$ClCH_2CH_2NH—C(NC_3H_7)NHNO_2$$

for the formation of 1-nitro-2-*n*-propylamino-2-imidazoline although it had been demonstrated previously[8] that warming N-β-chloroethyl-N'-nitroguanidines alone or in solvent gave the hydrochlorides of 1-nitro-2-amino-2-imidazolines. Also since the N_1–C_2 bond is more susceptible to cleavage than the N_1–C_5 bond, it is very unlikely that an equilibrium between VII and VIII could possibly exist.

Small amounts of N-β-chloroethyl-N'-*n*-propylurea (IX) were obtained in the reaction of acetyl chloride with N-β-nitraminoethyl-N'-*n*-propyl-N''-nitroguanidine. It was suggested[2] that the former compound might arise by the hydrolysis of N-β-chloroethyl-N'-*n*-propyl-N''-nitroguanidine. However, this would not occur under the conditions of the reaction described because other substituted nitroguanidines, *e.g.*, N-β-nitraminoethyl-N'-aryl-N''-nitroguanidines[9] and N,N'-disubstituted-N''-nitroguanidine[10] require prolonged refluxing with 10% sodium hydroxide solution to effect their hydrolyses to the corresponding ureas. It is more probable that the following reaction is involved. This is in agreement with the fact that N-β-nitraminoethyl-N'-aryl-N''-nitroguanidines treated with acetyl

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[1] Issued as D.R.C.L. Report No. 88.

[2] R. H. Hall and G. F. Wright, THIS JOURNAL, **73**, 2208 (1951).

[3] R. H. Hall, A. F. McKay and G. F. Wright, *ibid.*, **73**, 2205 (1951).

[4] A. F. McKay, J. P. Picard and P. E. Brunet, *Can. J. Chem.*, **29**, 746 (1951).

[5] A. F. McKay and C. Sandorfy, *ibid.*, in press.

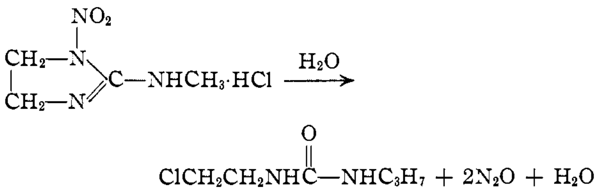
[6] F. B. Ahrens, *Sammlung Chemischer und Chemisch, Technischer Vortrage*, **18**, 414 (1912).

[7] For convenience the nitramino form is used although nitroguanidine derivatives could exist as hybrids of several electronic structures.[4]

[8] A. F. McKay and J. E. Milks, THIS JOURNAL, **72**, 1616 (1950).

[9] A. F. McKay, W. R. R. Park and S. J. Viron, *ibid.*, **72**, 3659 (1950).

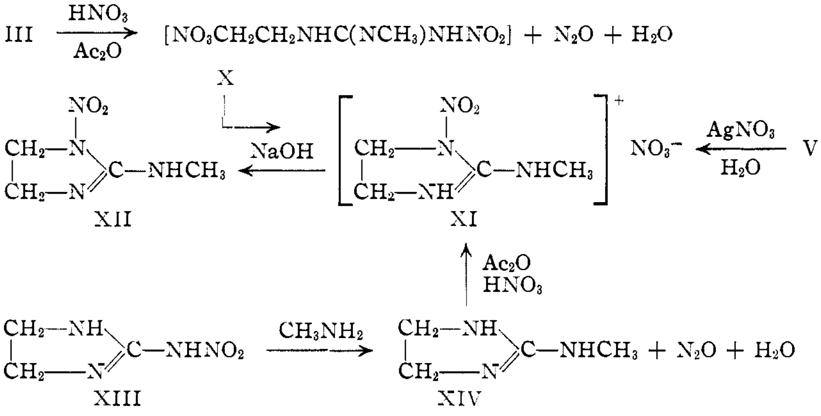
[10] A. F. McKay, *J. Org. Chem.*, **16**, 1395 (1951).



IX

chloride give higher yields of the corresponding N-β-chloroethyl-N′-arylureas.[11]

When N-β-nitraminoethyl-N′-methyl-N″-nitroguanidine is added to an absolute nitric acid–acetic anhydride medium nitrous oxide is evolved and the reaction proceeds in a manner similar to the reaction with acetyl chloride. The final product isolated in 56% yield was 1-nitro-2-methylamino-2-imidazolinium nitrate (XI). This would be expected if the primary nitramino group of compound III was replaced by a nitroxy group to give N-β-nitroxyethyl-N′-methyl-N″-nitroguanidine (X). The cyclization of the latter compound would then give the final product, 1-nitro-2-methylamino-2-imidazolinium nitrate, analogous to the previously described[8] cyclizations of N-β-nitroxyethyl-N′-nitroguanidines. If the methylamino group of 1-nitro-2-methylamino-2-imidazoline is replaced by an amino group then further nitration occurs to give 1,3-dinitro-2-imidazolidone.[8] This nitration mechanism explains the small yield (26%) of 1,3-dinitroimidazolidone obtained[12] on nitration of the ammonia addition product of 1-nitro-2-nitramino-2-imidazoline.



The structure of 1-nitro-2-methylamino-2-imidazolinium nitrate (XI) was confirmed by synthesis from 2-nitramino-2-imidazoline.[13]

The nitration of the cyclic compound 2-methylamino-2-imidazoline under the same conditions used for the nitration of N-β-nitraminoethyl-N′-methyl-N″-nitroguanidine gave a higher yield (90%) of 1-nitro-2-methylamino-2-imidazolinium nitrate (XI) which is in agreement with the mechanism suggested for the nitration of the linear compound III.

N-β-Chloroethyl-N′-methyl-N″-nitroguanidine warmed in sodium hydroxide solution gave the known 1-methyl-2-nitramino-2-imidazoline.[14]

When N-β-nitraminoethyl-N′-ethyl-N″-nitroguanidine was nitrated in acetic anhydride–nitric acid medium, a 49% yield of 1-nitro-2-ethylamino-2-imidazolinium nitrate was obtained.

Experimental[15,16]

1-Nitro-2-nitroamino-2-imidazoline.—1-Nitro-2-nitramino-2-imidazoline (m.p. 150–151.5° with dec.) was prepared in 83.5% yield by the nitration of 2-nitramino-2-imidazoline[13] in nitric acid–acetic anhydride medium as previously[12] described. One crystallization from acetone raised the melting point to 152.5° with decomposition.

N-β-Nitraminoethyl-N′-methyl-N″-nitroguanidine.—Fifteen grams (0.085 mole) of 1-nitro-2-nitramino-2-imidazoline was dissolved in 41 cc. of a 25% aqueous methylamine solution. This solution was acidified immediately to *p*H 1 while the temperature was held below 20° with an ice–salt-bath. The acidified mixture was cooled to 0° and the white solid removed by filtration and washed with water. The crude yields of several runs varied from 90.2–98%. Crystallization of the crude products from acetone did not affect the melting points. The crystallized material decomposed at 184.7 to 187.5° depending on the rate of heating.

Anal. Calcd. for $C_4H_{10}N_6O_4$: C, 23.30; H, 4.85; N, 40.77. Found: C, 23.44; H, 4.82; N, 41.01.

Acetyl Chloride Reaction of N-β-Nitraminoethyl-N′-methyl-N″-nitroguanidine.—Five grams (0.024 mole) of N-β-nitraminoethyl-N′-methyl-N″-nitroguanidine, 7.63 g. (0.097 mole) of acetyl chloride and 3.48 g. (0.034 mole) of acetic anhydride was added *en masse* to a flask containing 50 cc. of glacial acetic acid. The stirred reaction mixture was continuously swept with dry nitrogen over a period of 1 hour and 35 minutes while the temperature was maintained at 39–41°. During this period, the solid dissolved and gas (N_2O)[2] was evolved. The clear solution was cooled to room temperature and the volatile materials were removed at reduced pressure (11 mm.). The temperature was not allowed to rise above 40° during the distillation. The solid residue was triturated twice with methanol (20 cc.) and each time the methanol was removed *in vacuo*. Finally the solid was suspended in benzene (75 cc.) and filtered from solvent and oil; yield 2.96 g. (67.6%). This product decomposed at 198°. One crystallization from 95% ethanol (45 cc.) raised the decomposition point to 207°. The Franchimont[17] nitramine test using dimethylaniline gave a deep green color in agreement with the presence of a secondary nitramino group.

Anal. Calcd. for $C_4H_9ClN_4O_2$: C, 26.59; H, 4.99; Cl, 19.67; N, 31.02. Found: C, 26.87; H, 5.05; Cl, 19.45; N, 31.44.

The picrate of this compound, 1-nitro-2-methylamino-2-imidazolinium chloride, was formed in the usual manner. This picrate melted at 163.5° with decomposition after one crystallization from water.

Anal. Calcd. for $C_{10}H_{11}N_7O_9$: C, 32.17; H, 2.95; N, 26.27. Found: C, 32.32; H, 2.95; N, 25.98.

The benzene filtrate from above was taken to dryness *in vacuo* at a temperature below 35° and the residual oil was dissolved in 95% ethanol. On cooling in a chloroform–Dry Ice-bath crystals separated; yield 1.22 g. (30.0%). These crystals melted at 101–103°, resolidified at 105–106° and decomposed at 200°. Since heating this compound causes it to cyclize to 1-nitro-2-methylamino-2-imidazolinium chloride, it was crystallized by dissolving in a minimum of ethanol at room temperature and then cooling the

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[11] A. F. McKay, W. G. Hatton and G. W. Taylor, to be published.

[12] A. F. McKay and G. F. Wright, This Journal, **70**, 3990 (1948).

[13] A. F. McKay and G. F. Wright, *ibid.*, **70**, 430 (1948).

[14] A. F. McKay, J. R. G. Bryce and D. E. Rivington, *Can. J. Chem.*, **29**, 382 (1951).

[15] All melting points are uncorrected.

[16] Microanalyses by C. W. Beazley, Skokie, Illinois.

[17] A. P. N. Franchimont, *Rec. trav. chim.*, **16**, 213 (1897).

solution in chloroform–Dry Ice. This treatment removed the small amount of oil present with crystals, but it did not affect the melting point.

Anal. Calcd. for $C_4H_9ClN_4O_2$: C, 26.59; H, 4.99; Cl, 19.67; N, 31.02. Found: C, 26.95; H, 5.30; Cl, 19.40; N, 31.15.

Although care was exercised in the purification of the latter compound, N-β-chloroethyl-N′-methyl-N″-nitroguanidine, it may have been contaminated with a trace of the cyclic rearrangement product, 1-nitro-2-methylamino-2-imidazolinium chloride. This contamination would not affect the analysis.

1-Methyl-2-nitramino-2-imidazoline.—N-β-Chloroethyl-N′-methyl-N″-nitroguanidine (0.5 g., 0.003 mole) was heated for 2 minutes at reflux temperature with 120 mg. (0.003 mole) of sodium hydroxide in 3 cc. of water. Two volumes of absolute alcohol was added and the sodium chloride filtered from the solution. The clear solution was taken to dryness and 1 cc. of water added. On standing several days in the refrigerator, after which some of the water had evaporated, beautiful crystals separated; yield 110 mg. (27.3%). These crystals melted at 115–116° alone and on admixture with an authentic sample of 1-methyl-2-nitramino-2-imidazoline (m.p. 115–116°).[14]

2-Methylamino-2-imidazoline.—Twenty-five grams (0.19 mole) of 2-nitramino-2-imidazoline and 125 cc. of 25% aqueous methylamine solution were placed in an erlenmeyer flask. This mixture was left at room temperature until gas evolution ceased and a clear solution resulted. The excess aqueous methylamine solution was removed *in vacuo* (40 mm.) and the residual yellow-orange oil distilled. A white hygroscopic solid (b.p. 120–122° (1.0 mm.)) was obtained; yield 16.5 g. (87.6%). A sample of this product was distilled (b.p. 103° (0.5 mm.)) into a tube, and its setting point (66.9–67.5°) determined under an atmosphere of dry nitrogen.

A sample of the 2-methylamino-2-imidazoline was converted into its picrate (m.p. 196–197°) in the usual manner. Aspinall and Bianco[18] report a melting point of 193–194°.

Anal. Calcd. for $C_{10}H_{12}N_6O_7$: C, 36.60; H, 3.66; N, 25.60. Found: C, 36.86; H, 3.87; N, 25.80.

1-Nitro-2-methylamino-2-imidazolinium Nitrate. A. From 2-Methylamino-2-imidazoline.—A solution of 7.1 g. (0.072 mole) of 2-methylamino-2-imidazoline in 40 cc. of glacial acetic acid was added over a period of 28 minutes to a nitrating solution of 45.2 g. (0.72 mole) of absolute nitric acid in 73.1 g. (0.72 mole) of acetic anhydride. During the addition of 2-methylamino-2-imidazoline solution, the temperature of the stirred solution was held at 0–10°. After the addition was complete, the reaction was allowed to stand for a half-hour at 18°. It was poured onto 150 g. of crushed ice and the aqueous solution extracted with ether (2 × 150 cc.). The ethereal solution was washed with water and the water washings were combined with the original aqueous phase. After the aqueous solution was evaporated to dryness, the residual white crystals were suspended in cold absolute alcohol and filtered; yield 13.47 g. (90.0%). The melting point of 172° with decomposition was not altered by crystallization from absolute alcohol.

Anal. Calcd. for $C_4H_9N_5O_5$: C, 23.19; H, 4.34; N, 33.81. Found: C, 23.12; H, 4.52; N, 34.01.

B. From 1-Nitro-2-nitramino-2-imidazolinium Chloride.—Five hundred milligrams (0.0028 mole) of 1-nitro-2-nitramino-2-imidazolinium chloride was dissolved in *ca.* 5 cc. of water and treated with 0.475 g. (0.0028 mole) of silver nitrate in 3 cc. of water. The heavy precipitate of silver chloride was removed by filtration and the filtrate taken to dryness *in vacuo*. The residual white solid decomposed at 159°; yield (76.4%). One crystallization from absolute ethanol raised the melting point to 171° with decomposition. A sample of this product did not depress the melting point of a known sample of 1-nitro-2-methylamino-2-imidazolinium nitrate.

C. From N-β-Nitraminoethyl-N′-methyl-N″-nitroguanidine.—To a nitrating medium consisting of 15.3 g. (0.243 mole) of absolute nitric acid in 24.8 g. (0.243 mole) of acetic anhydride (mixed at 0°), 5 g. (0.024 mole) of N-β-nitraminoethyl-N′-methyl-N″-nitroguanidine was added portionwise over a period of 7 minutes. After the addition was complete, the stirred solution was held at 24 to 28° for 55 minutes. The product (m.p. 165° with dec.) was obtained by the procedure outlined above in section A; yield 2.81 g. (56.1%). One crystallization from absolute ethanol (200 cc.) raised the melting point to 170° with decomposition. A sample did not depress the melting point of an authentic sample of 1-nitro-2-methylamino-2-imidazolinium nitrate.

1-Nitro-2-methylamino-2-imidazoline.—One gram (0.0048 mole) of 1-nitro-2-methylamino-2-imidazolinium nitrate was added to a solution of 0.193 g. (0.0048 mole) of sodium hydroxide in 11 cc. of water. After standing at room temperature for one day, the aqueous solution was extracted with ether (5 × 25 cc.) and the ethereal solution taken to dryness. The white crystalline residue weighed 530 mg. (76.2%). One crystallization from ether raised the melting point from 71–73.5° to a constant value of 76.5–77°. The pure crystals gave a deep green color with the Franchimont nitramine test using dimethylaniline.

Anal. Calcd. for $C_4H_8N_4O_2$: C, 33.33; H, 5.56; N, 38.88. Found: C, 33.36; H, 5.74; N, 38.86.

N-β-Nitraminoethyl-N′-ethyl-N″-nitroguanidine.—N-β-Nitraminoethyl-N′-ethyl-N″-nitroguanidine (m.p. 107–108°) was prepared in 72% yield using the same procedure given above for N-β-nitraminoethyl-N′-methyl-N″-nitroguanidine.

Anal. Calcd. for $C_5H_{12}N_6O_4$: C, 27.28; H, 5.45; N, 38.18. Found: C, 27.24; H, 5.64; N, 38.17.

1-Nitro-2-ethylamino-2-imidazolinium Nitrate.—N-β-Nitraminoethyl-N′-ethyl-N″-nitroguanidine (4.88 g., 0.022 mole) was nitrated in a solution of 13.9 g. (0.22 mole) of absolute nitric acid in 22.6 g. (0.22 mole) of acetic anhydride under conditions given above for the nitration of N-β-nitraminoethyl-N′-methyl-N″-nitroguanidine. The product (m.p. 157.5° with dec.) was obtained in 45.1% yield. One crystallization from methanol (2.21 g./7 cc.) did not change the melting point.

Anal. Calcd. for $C_5H_{11}N_5O_5$: C, 27.15; H, 4.98; N, 31.67. Found: C, 27.18; H, 5.00; N, 32.02.

OTTAWA, CANADA

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[18] S. R. Aspinall and E. J. Bianco, THIS JOURNAL, **73**, 602 (1951).