2.7 ml. of 12% hydrochloric acid the solvent was removed *in vacuo*. The residue was extracted with 150 ml. of boiling acetone. This solvent was vacuum evaporated to leave 0.89 g. (70% recovery) of III, m.p. 220–222°.

The experiment was repeated with an ageing period of 8 or 10 hours. Evaporation of the acetone yielded 0.30 g., m.p. 220–221° (23% recovery) of III. The acetone insoluble residue was dissolved in 6.5 ml. of hot water, adjusted to *p*H 5, and evaporated to half volume. The residual solution, when chilled, precipitated 0.75 g. of 2-hydroxy-2-nitraminoimidazolidine, V, m.p. 136° dec. This was quickly crystallized from 1 ml. of hot water to avoid decomposition. The purified material melted at 137° with decomposition. It gave a weakly positive Franchimont test with dimethylaniline.

Anal. Calcd. for $C_3H_8N_4O_3$: C, 24.3; H, 5.42; N, 37.8. Found: C, 24.0; H, 5.32; N, 37.9.

A further repetition of this experiment was effected with an ageing period of thirteen hours. The recovery of III, m.p. 220–222°, was 20%.

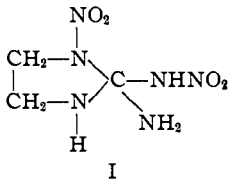
TORONTO 5, CANADA RECEIVED SEPTEMBER 13, 1950

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF TORONTO]

The Chemistry of Linear Substituted Nitroguanidines

BY R. H. HALL, A. F. MCKAY[1] AND GEORGE F WRIGHT

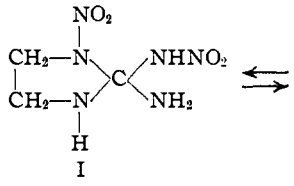
It was formerly[2] stated that the treatment of 1-nitro-2-nitriminoimidazolidone-2 with concentrated ammonia solution gave 1-nitro-2-amino-2-nitraminoimidazolidine (I), after subsequent acidification. Although this compound gave a negative secondary nitramine test,[3] a cyclic structure was assigned to it. This assignment was based on the fact that a small yield (26.5%) of 1,3-dinitroimidazolidone-2 was obtained[2] by nitrating this substance in a nitric acid–acetic anhydride medium.



I

Later work[4] has shown that 1-β-substituted ethyl-3-nitroguanidines are readily cyclized. Since this implies that ring fission is also likely, it seemed worthwhile to reinvestigate the structure of the compound from ammonia and 1-nitro-2-nitriminoimidazolidone-2 in order to confirm either a linear or a cyclic structure.

Two alternative structures, both linear, can be written instead of the cyclic structure, I. Thus



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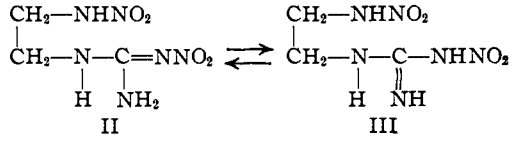
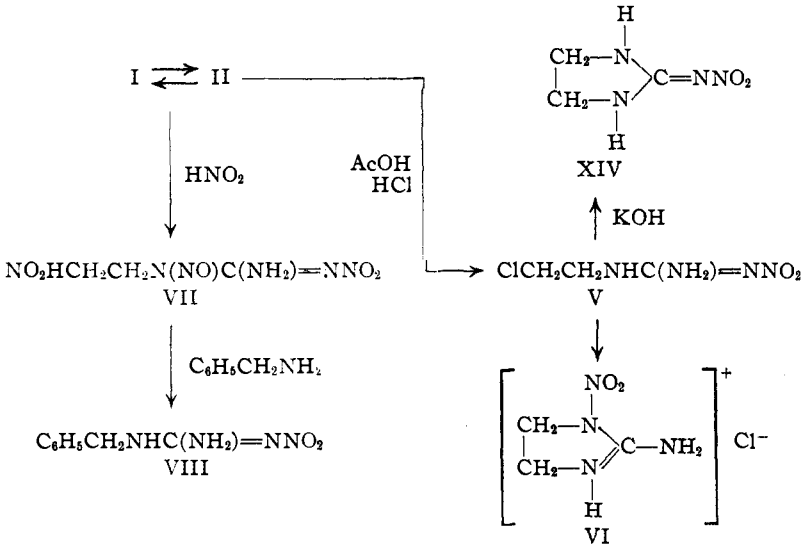


II III

β-nitraminoethyl-2-nitroguanidine (II) or 3-nitroguanidine (III) would be formed by ring fission between atoms 1 and 2 by removal of hydrogen from either the nitramino group or the amino group, respectively. Alternatively, either II or III might be formed initially and then transformed to the other by a 1,3-hydrogen rearrangement.



Formal examination of these structures shows that I and II should act as mono-acids while III should be functionally diacidic because of its two primary nitramino groups. Potentiometric titration of a freshly prepared alkaline solution (curve 1, Fig. 1) discloses only one acidic function, thus excluding structure III as the normal state of the compound. By analogy with nitroguanidine or 2-nitriminoimidazolidone-2 and its 1-nitro derivative one might expect[5] that structure II, if present, would be transformed to III if the alkaline solution were aged for sixteen hours prior to titration. Curve 2, Fig. 1, which is almost identical

(1) Defence Research Chemical Laboratories, Ottawa, Canada.

(2) A. F. McKay and George F Wright, THIS JOURNAL, **70**, 3990 (1948).

(3) A. P. N. Franchimont, *Rev. trav. chim.*, **16**, 226 (1897).

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

(5) S. S. Barton, R. H. Hall and George F Wright, *ibid.*, **73**, 2201 (1951).

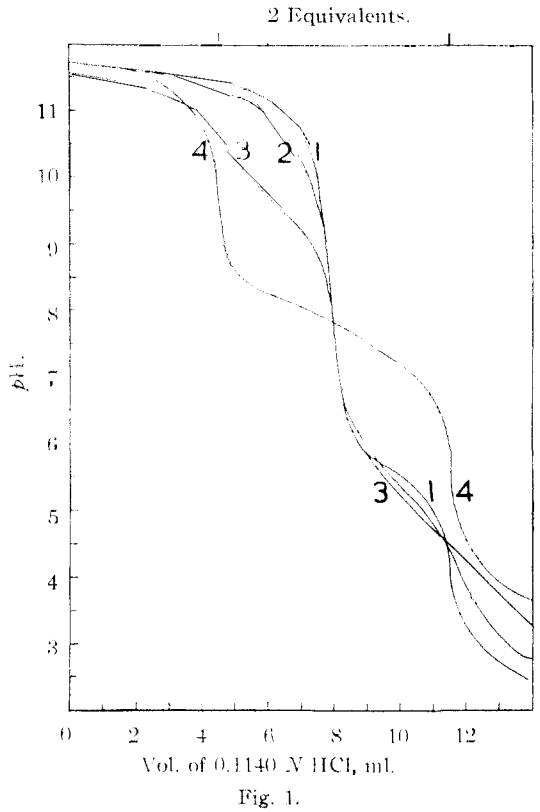


Fig. 1.

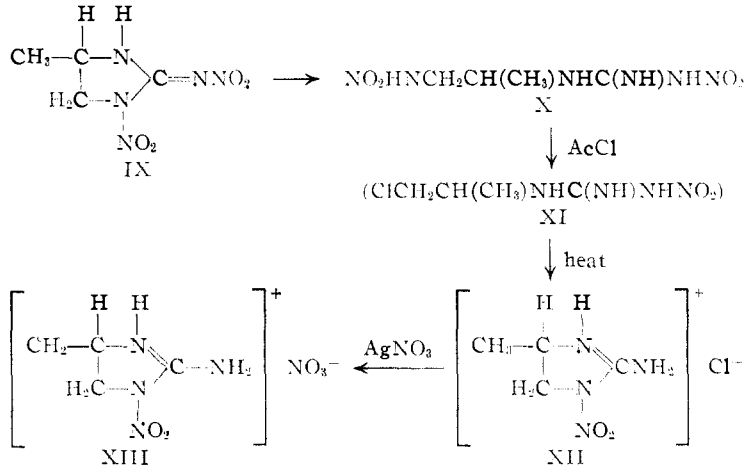
with that of curve 1 shows this not to be the case. However, when the alkaline solution is aged for ninety hours it may be seen (curve 3, Fig. 1) that a new inflection indicative of a second acidic function does appear. The final state of the ammonia–nitronitriminoimidazolidine addition product in alkaline solution must thus be the disodium salt of 1-β-nitraminoethyl-3-nitroguanidine, III. At present we consider the equilibria formulated above must be preponderantly in the direction of 1-nitro-2-amino-2-nitraminoimidazolidine (I) principally because the transformation to the disodium salt of III is much slower than might be expected for β-nitraminoethyl-2-nitroguanidine (II) by analogy with the behavior of 2-nitroguanidine and 2-nitriminoimidazolidone-2.

This confirmation of the cyclic structure (I) must, however, be considered tentative. Evidence is at hand to show that, if 1-β-nitraminoethyl-2-nitroguanidine (II) is not present initially, it is easily derived from I during chemical reaction. Thus so mild a reaction as nitrosation converts the ammonia–nitronitriminoimidazolidine addition product to 1-β-nitraminoethyl-1-nitroso-2-nitroguanidine (VII)[6] in low yield. The position of the nitroso group has been demonstrated by conversion with benzylamine to 1-benzyl-2-nitroguanidine (VIII) in 82% yield.

(6) These alkali-unstable compounds are now described as nitrimines by analogy with nitroguanidine and 2-nitriminoimidazolidine since no strict structure proof for them has yet been devised.

Thus the nitroso derivative (VII) probably is derived from the linear fission product 1-β-nitraminoethyl-2-nitroguanidine (II). The product of reaction from treatment of the ammonia–nitronitriminoimidazolidone addition product with acetyl chloride, 1-β-chloroethyl-2-nitroguanidine (V) is also shown as a derivative of II. The ostensible by-product of this reaction, 1-nitro-2-amino-Δ^4-imidazoline hydrochloride (VI, identified as its picrate) is shown as a cyclization product of V because the latter is converted to the former when V is heated alone above its melting point or in hydrolytic solvent.[7] However it might also be considered as the initial product arising by elimination of nitrous oxide from the cyclic 1-nitro-2-amino-2-nitraminoimidazolidine (I), in which case the 1-β-chloroethyl-2-nitroguanidine could arise as its fission product. Indeed the facile cyclization and fission encountered among certain of these substituted nitroguanidines makes a choice of structure difficult and perhaps not too significant.

However, it should not be inferred that the addition products of amines and alcohols to nitriminoimidazolidones are always unstable cyclic compounds. Thus the addition product of ammonia and 1-nitro-2-nitrimino-4-methylimidazolidone-2 (IX, previously reported[8] as the tautomer) is evidently the linear primary dinitramine, 1-(α-methyl-β-nitraminoethyl)-3-nitroguanidine (X) since its freshly-prepared alkaline solution consumes two equivalents of the base, as shown by the curve for potentiometric titration (curve 4, Fig. 1).



The structure of X is of additional interest since the position of the methyl group provides an absolute proof for the position occupied by the nitro group when 4-methyl-2-nitriminoimidazolidone-2 (IX, previously reported as its tautomer) is converted to X. This proof firstly involves the failure to nitrosate X since any derivative of nitroguanidine (such as 1-isopropylnitroguanidine

(7) An alternative ring closure of 1-β-chloroethyl-2-nitroguanidine (V) to 2-nitriminoimidazolidone-2 (XIV) can be accomplished by treatment of 1-β-chloroethyl-2-nitroguanidine (V) for four minutes with boiling 18% ethanolic potassium hydroxide. After acidification and evaporation a 20% yield was obtained.

(8) A. F. McKay and D. F. Manchester, THIS JOURNAL, 71, 1970 (1949).

and 1-cyclohexyl-2-nitroguanidine) having a secondary alkyl group attached to the amido group fails to nitrosate. Secondly treatment of 1-(α-methyl-β-nitraminoethyl)-3-nitroguanidine with acetyl chloride preferentially replaces the nitramino rather than the nitramido group by chlorine to give an intermediate oil to which is attributed the structure 1-(α-methyl-β-chloroethyl)-3(or 2)-nitroguanidine, (XI).

When this oil is boiled in isobutyl alcohol it is converted to 2-amino-4-methyl-1-nitroimidazolinium chloride, (XII). The ionizable chlorine in this substance may be exchanged for nitrate ion by treatment with silver nitrate. The 2-amino-4-methyl-1-nitroimidazolinium nitrate (XIII) thus formed, according to melting point, is not identical with the 2-amino-5-methyl-1-nitroimidazolinium nitrate reliably prepared previously by synthesis.[4]

Acknowledgment.—The authors wish to thank the Defence Research Board of Canada for support of this work.

Experimental[9]

1-Nitro-2-amino-2-nitraminoimidazolidine (I).—The compound 1-nitro-2-nitriminoimidazolidone-2 was converted to 1-nitro-2-amino-2-nitraminoimidazolidine (I) in 93.9% yield (m. p. 180–181° with decomposition) using the conditions previously described.[2] One crystallization from water (19.5 cc./g.) raised the melting point to 184.8–185.3° with decomposition.

1-(α-Methyl-β-nitraminoethyl)-3-nitroguanidine (X).—The compound (m. p. 163–164.5° with decomposition) was prepared from 1-nitro-2-nitrimino-4-methylimidazolidone-2 (IX) under the above described conditions in 89.4% yield. One crystallization from 95% ethanol raised the melting point to 172.7° with decomposition.

Anal. Calcd. for $C_4H_{10}N_6O_4$: C, 23.3; H, 4.85; N, 40.7. Found: C, 23.3; H, 4.75; N, 40.5.

1-β-Nitraminoethyl-1-nitroso-2-nitroguanidine (VII).—The compound 1-nitro-2-amino-2-nitraminoimidazolidine (I) (3.07 g., 0.016 mole) was dissolved in 30 cc. of 70% nitric acid. This solution was cooled to 10° and diluted with 75 cc. of water. The 2.3 g. (0.033 mole) of sodium nitrite in 25 cc. of water was added portionwise while the temperature was held at 8–12°. It was necessary to add a second portion to 2.3 g. (0.033 mole) of sodium nitrite (not in solution) before any product could be obtained. The yellow crystals which separated were filtered off and washed with water. These crystals weighed 1.0 g. (28.4%) and melted at 106° with decomposition. One crystallization from absolute methanol (8 cc./g.) raised the melting point to 113° with decomposition.

Anal. Calcd. for $C_3H_7N_7O_3$: C, 16.2; H, 3.16; N, 44.4. Found: C, 16.4; H, 3.09; N, 44.6.

When the nitrosamine was treated with benzylamine as previously described[5] an 81.7% yield of 1-benzyl-2-nitroguanidine (m. p. 180–181°) was obtained. After one crystallization from 95% ethanol the product melted at 183.5° alone and on admixture with an authentic sample of 1-benzyl-2-nitroguanidine.

Electrometric Titrations.—The potentiometric titrations were performed with a Coleman Electrometer. Each sample (0.0004 mole) was dissolved in excess 0.0875 *N* sodium hydroxide solution (15 ml.) and then titrated with 0.1140 *N* hydrochloric acid solution. The titration curves are shown in Fig. 1.

Effect of Acetyl Chloride on 1-Nitro-2-amino-2-nitraminoimidazolidine, (I).—Eight and nine-tenths grams (0.05 mole) of 1-β-nitraminoethyl-3-nitroguanidine was mixed with 80 cc. of glacial acetic acid to which a 0.10 mole of acetyl chloride was added. The temperature was maintained at 52–60° for five and one-half hours during which nitrous oxide was evolved (1.08 g. of 1-β-nitraminoethyl-3-nitroguanidine gave 40 cc. of nitrous oxide collected over water at 22°). The final solution was diluted with 40 cc. of absolute ethanol and evaporated *in vacuo*. After addition of 12 cc. of water to the residue 3.58 g. of solid remained. This solid melted at 107.8–109.5°, resolidified and melted at 147°; yield 49.8%. One crystallization from 16 cc. of water gave 1.21 g. of crystals melting at 115.2°, resolidifying and melting with decomposition at 189°. A mixed melting point determination with an authentic sample of 1-β-chloroethyl-2-nitroguanidine (V) was not depressed.

Anal. Calcd. for $C_3H_7ClN_4O_2$: C, 21.6; H, 4.20; N, 33.6. Found: C, 21.8; H, 4.23; N, 33.5.

A second crop of crystals (1.38 g.) was obtained by evaporation of the aqueous filtrate to one-half its original volume and diluting with 5 cc. of absolute alcohol and 10 cc. of ether. This material melted at 183.2° with decomposition and without preliminary melting. This solid was identified as 1-nitro-2-amino-Δ^2-imidazoline hydrochloride (VI) by a mixed melting point determination with an authentic sample.[4]

The filtrate from the second crop of crystals was evaporated to dryness *in vacuo* and the residue treated with 22 cc. of absolute ethanol. One and one-tenth grams of 1-nitro-2-amino-Δ^2-imidazoline hydrochloride (m. p. 192° with decomposition) was obtained. The total yield of hydrochloride was 2.48 g. (34.4%). After one crystallization from absolute ethanol, the hydrochloride melted at 193.6–193.8° with decomposition.

Anal. Calcd. for $C_3H_7N_4O_2$: C, 21.6; H, 4.20; N, 33.6. Found: C, 21.5; H, 4.28; N, 33.2.

A 0.01-g. sample of 1-nitro-2-amino-Δ^2-imidazoline hydrochloride was dissolved in 1 cc. of water and treated with aqueous picric acid solution. A yellow crystalline picrate separated immediately which melted at 186–187°; yield 0.15 g. (65.6%). After one crystallization from 95% ethanol the picrate melted at 188.6–189.8°.

Anal. Calcd. for $C_9H_9N_7O_9$: C, 30.2; H, 2.51; N, 27.3. Found: C, 30.2; H, 2.81; N, 27.5.

1-Nitro-2-amino-4-methyl-2-imidazoline Hydrochloride.—The compound 1-(α-methyl-β-nitraminoethyl)-3-nitroguanidine (9.03 g., 0.043 mole) was added to a solution of 40 g. (0.509 mole) of acetyl chloride in 60 cc. of glacial acetic acid. This mixture was heated at 60° for one hour during which time nitrous oxide was evolved and the solid dissolved. Acetic acid and excess acetyl chloride were removed *in vacuo* (20 mm.) leaving a colorless viscous oil (9.1 g.).

The oil was dissolved in 16 cc. of 3-methyl-1-butanol and transferred to an erlenmeyer flask. This solution was refluxed for about three minutes after which a considerable quantity of white solid separated. The solid was removed by filtration and washed with benzene; yield 4.9 g. (62%). The crude product melted at 186° with decomposition. One crystallization from absolute ethanol (14.8 cc./g.) raised the melting point to 187.5° (uncor.) with decomposition. These crystals of 1-nitro-2-amino-4-methyl-Δ^2-imidazoline hydrochloride gave a strong secondary nitramine test.[2]

Anal. Calcd. for $C_4H_9ClN_4O_2$: C, 26.6; H, 5.02; Cl, 19.6; N, 30.9. Found: C, 26.9; H, 5.15; Cl, 19.5; N, 31.0.

1-Nitro-2-amino-4-methyl-2-imidazoline Nitrate.—The compound 1-nitro-2-amino-4-methyl-Δ^2-imidazoline hydrochloride was wastefully converted into the nitrate (m. p. 150° (uncor.) with decomposition) in 43% yield on treatment with aqueous ethanolic silver nitrate solution.[4]

Anal. Calcd. for $C_4H_9N_5O_5$: C, 23.2; H, 4.38; N, 33.7. Found: C, 23.4; H, 4.48; N, 33.69.

Summary

1. A cyclic and a linear structure may be written for the addition product comprising ammonia and 1-nitro-2-nitriminoimidazolidone-2 on the basis of its titration as a monobasic acid, but the cyclic structure previously assigned to this compound is tentatively favored because its conversion

(9) All melting points have been corrected against reliable standards except those signified otherwise.

to the sodium salt of a dibasic acid requires a longer time than that found for the nitrimine linkage inherent in the linear structure.

2. The addition product comprising ammonia and 1-nitro-2-nitrimino-4-methylimidazolidone-2 is not cyclic, since its titration is that of a dibasic acid.

3. The ring fission by ammonolysis to give this 1-(α-methyl-β-nitraminoethyl)-3-nitroguanidine serves to specify the position of methyl as (4) rather than (5) in the nitrimine formerly designated in its tautomeric form as 1-nitro-2-nitramino-4(or 5)-methyl-Δ^2-imidazoline.

TORONTO, ONTARIO RECEIVED JANUARY 28, 1950

[CONTRIBUTION FROM THE UNIVERSITY OF TORONTO]

Reactions of 1-Nitro-2-nitramino-2-propylaminoimidazolidine with Acetyl Chloride

BY ROSS H. HALL AND GEORGE F WRIGHT[1]

The action of acetyl chloride on 1-nitro-2-nitramino-2-propylaminoimidazolidine causes replacement of the nitramino group by chlorine. The primary reaction product may be represented as a system comprising 1-β-chloroethyl-3-propyl-2-nitroguanidine and its cyclic isomer 1-nitro-2-chloro-2-propylaminoimidazolidine. The linear component can be made to undergo an alternative ring closure to 2-nitrimino-3-propylimidazolidone-2. The unsubstituted ring nitrogen in this compound can be nitrated, the ring cleaved by hydrolysis, and the resulting two nitramino groups eliminated by treatment with acetyl chloride to yield β-chloroethylaminopropane.

A second product of the original reaction behaves as the hydrochloride of the system comprising 1-β-aminoethyl-1-nitro-3-propylurea and its cyclic isomer 1-nitro-2-hydroxy-2-propylaminoimidazolidine. The free base decomposes to give 1-β-nitraminoethyl-3-propylurea, which on treatment with acetyl chloride yields 1-β-chloroethyl-3-propylurea. This compound also is obtained in trace from the original reaction mixture.

The dual melting points found for these compounds seem not to indicate polymorphism but rather ring opening and closure. The ease of these transformations seems to indicate that addition compounds of guanidines are quasi-stable. It is suggested that the mechanisms of reactions involving nitroguanidines can better be expressed in terms of addition intermediates than by the "dearrangement" mechanism formerly used.

Nitrous oxide is evolved when acetyl chloride reacts with a primary nitramine, and chlorine replaces the nitramino group when the system is anhydrous.[2,3] It has been shown that this reaction is applicable to either cyclic[4] or linear[5] nitroguanidines, although the chlorine may not remain at the original site of replacement (atom No. 2) in the cyclic compounds.

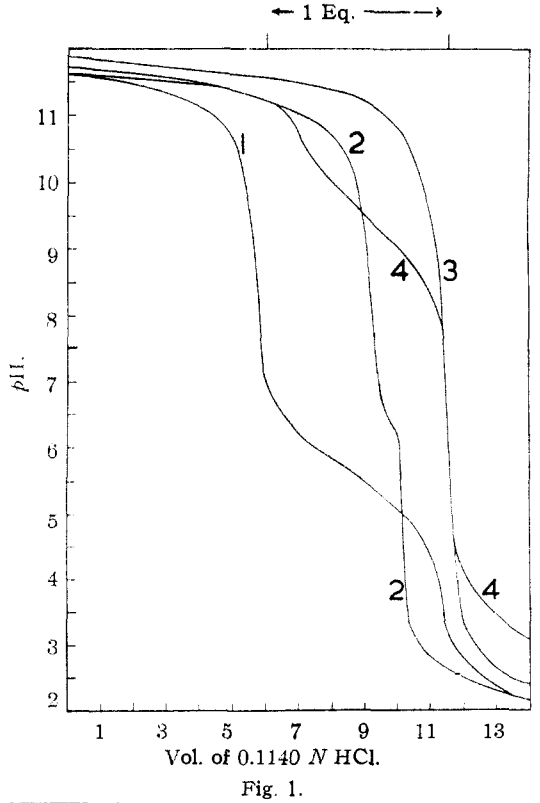


Fig. 1.

In continuation of such studies we have examined the effect of acetyl chloride on 1-nitro-2-nitramino-2-propylaminoimidazolidine (I). This compound, which was prepared by addition of *n*-propylamine to 1-nitro-2-nitriminoimidazolidone-2,[4] has been found by potentiometric titration (curve 1, Fig. 1) of a 0.04 *N* solution in 0.0875 *N* alkali either at once or after one week to possess and retain in alkaline solution the cyclic structure which originally was assigned to it. When this 1-nitro-2-nitramino-2-*n*-propylaminoimidazolidine (I) is treated with acetyl chloride in acetic acid previously saturated with dry hydrogen chloride, nitrous oxide is evolved, and three products have been isolated. These are the compounds listed in the formulation as II, III and VII. The first two are obtained in fair yield but only traces of the third can be found.

When the reaction is carried out in excess acetic acid which initially contains no hydrogen chloride then compound II is not found among the products. Its absence is not surprising since it is found to be relatively unstable. Thus in presence of hydrolytic solvents it is transformed to III. Compound II has a double melting point (91–92°, then resolidifies and remelts at 162–163°). For reasons which will be outlined below we consider that the form stable at the lower temperature is 1-β-chloroethyl-2-nitro-3-*n*-propylguanidine (IIb) while the higher melting form is either 2-chloro-1-nitro-2-propylaminoimidazolidine (IIa) or else the hydrochloride of the corresponding imidazoline.

(1) Senior author.

(2) F. B. Ahrens, *Sammlung Chemischer und Chemisch-Technischer Vortrage*, **18**, 359 (1912).

(3) A. P. N. Franchimont, *Rec. trav. chim.*, **29**, 304 (1910).

(4) A. F. McKay and G. F Wright, THIS JOURNAL, **70**, 3990 (1948).

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