[CONTRIBUTION FROM THE CHEMICAL LABORATORY, UNIVERSITY OF TORONTO]

Nitroguanidines as Pseudo-acids

BY S. S. BARTON, ROSS H. HALL AND GEORGE F WRIGHT

Nitroguanidine has been found not to form a sodium salt in 0.1 alkali within the time required for a potentiometric titration, but ten to twenty hours later it behaves as if it were an acid. A similar behavior for 2-nitriminoimidazolidone-2 (but not 1-nitro-2-nitramino-Δ^2-imidazoline) is more amenable for study since subsequent decomposition is minimized and capable of evaluation. The aci-forms, which are considered to be the tautomeric nitramines, revert to the pseudo-acid forms in 50–85% recovery when the neutralized solutions are evaporated. The reclassification of these nitroguanidines as nitrimines rather than primary nitramines removes previous anomalies respecting stability and reactivity.

During Thiele's[1] study of nitroguanidine he assigned the structure as 1-nitroguanidine, I, rather than 2-nitroguanidine, II, after some deliberation. We believe this assignment was incorrect since nitroguanidine, unlike aliphatic or aromatic primary nitramines, does not ordinarily function as an acid. For example, one equivalent of normal alkali is insufficient for its rapid dissolution. When

$$\underset{II}{H_2NC(=NNO_2)NH_2} \rightleftharpoons \underset{I}{H_2NC(=NH)NHNO_2}$$

its freshly-prepared solution in two equivalents of 2.5 *N* alkali is chilled, the precipitate is ordinary nitroguanidine and not the sodium salt. Furthermore, potentiometric titration indicates that the compound is not an acid. Curve 1, Fig. 1, represents titration with 0.1140 *N* hydrochloric acid of a freshly-prepared solution containing 0.0006 mole of nitroguanidine in 15 ml. of 0.0875 *N* aqueous sodium hydroxide. Although these equivalent amounts should involve neutralization of the alkali by the nitroguanidine in the region indicated by the dimension on the upper abcissa, it may be seen by comparison with curve 2 (representing acetic acid titrated under the same conditions) that the nitro compound is not functioning either as an acid, base or amino-acid.

When the titration of the 0.1 *N* alkaline solution described above is delayed for twelve hours the titer follows curve 3, Fig. 1. The inflection which has developed is accentuated (curve 4, Fig. 1) if the titration is delayed for thirty-six hours. These inflections are easily recognized by comparison with a titer curve for hydrochloric acid and ammonia as typical of the latter substance. Indeed the odor of ammonia is discernible in these aged solutions. If this ammonia is removed by evacuation for three hours of a solution containing 0.0006 mole of nitroguanidine in 15 ml. of 0.0875 *N* alkali (prepared eighteen hours previously) then subsequent potentiometric titration follows curve 5, Fig. 1. It may be seen from the displacement of the vertical part of the curve, that about 0.65 equivalent of acidic substance has been formed.

Several causes of this phenomenon may be considered. Firstly the acidic function might be thought to be due to carbonic acid. The latter might be formed by total hydrolytic decomposition of nitroguanidine. However, the behavior of sodium carbonate on titration with hydrochloric acid ought to be observed as an inflection in the curve at approximately *p*H 8. This inflection is not present in curves 3, 4 and 5, although it may be seen in the titer curve when nitroguanidine is deliberately allowed to decompose completely in 2 *N* alkali. The inflection also is apparent on titration of a freshly prepared solution of nitroguanidine, sodium carbonate and ammonia in quantities such as to simulate 40% decomposition according to the equation outlined above. A final proof that presence of carbonic acid is not appreciable in the systems described by curves 3, 4 and 5 is obtained when the acidified solutions are swept with nitrogen which would remove carbon dioxide. Subsequent titration with alkali reproduces curves 3, 4 and 5 exactly for their respective solutions.

$$H_2NCNHNHNO_2 + H_2O \longrightarrow 2NH_3 + H_2CO_3 + N_2O$$

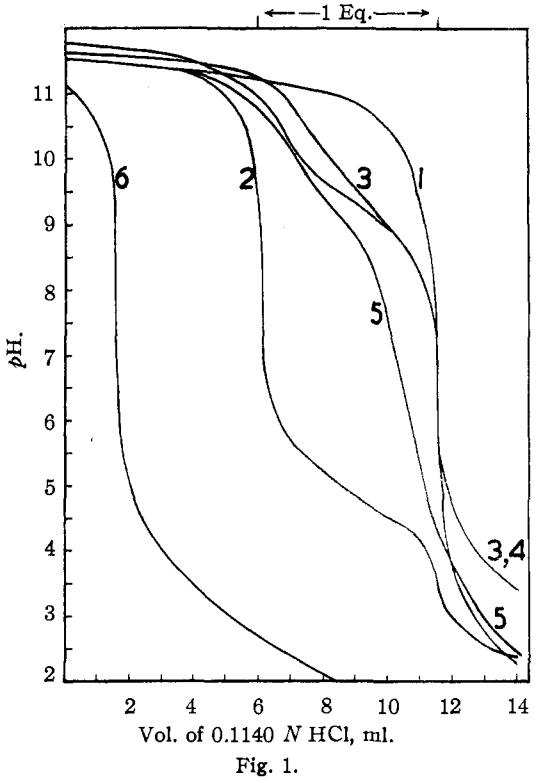


Fig. 1.

A less-complete hydrolytic decomposition of nitroguanidine would yield ammonia and nitrourea. This would indeed account for the volatile base as well as the generation of the acidic function indicated by curves 3, 4 and 5, Fig. 1. The nitrourea might be derived from either the nitramino (I) or nitrimine (II) form of nitroguanidine. Actually a few per cent. of nitrourea may be detected

(1) J. Thiele, *Ann.*, **270**, 16 (1892).

in the aged solutions, as well as its decomposition products, urea[2] and nitric acid. However, the marked acidity (displaced curve 6, Fig. 1) of nitrourea is absent in curve 5.

Indeed the presence of nitrourea and nitric acid cannot account for the appearance of 0.65 equivalent of acidic function because the recovery of nitroguanidine from such solutions exceeds 70% of the amount originally introduced. Since no reaction is known to account for its resynthesis *in situ* from the products of decomposition, it must therefore have been present in the aged solution as an aci-form, in contrast to the pseudo-acid form in which it originally existed.

One might attempt to explain the non-acidic nature of ordinary nitroguanidine by the amino-acid structure, I. However, the titration of a freshly prepared alkaline solution (curve 1, Fig. 1) is not characteristic of amino-acids, although a resemblance to such intramolecular salts[3] is found in curves 3, 4 and 5 which depict the titration of aged solutions. Furthermore, the slow appearance of the acidic function is not characteristic of the reversible ionic behavior of a zwitterion type of bifunctional compound. Such a delay is more satisfactorily explained by a tautomeric displacement of hydrogen

Several such displacements are possible. Hantzsch and Dollfus,[4] originally postulated the existence of a pseudo- and aci-form of phenylnitramine by analogy with the nitroalkanes. Their

$$C_6H_5\underset{\underset{H}{|}}{N}NO_2 \rightleftharpoons C_6H_5N{=}NOOH$$

postulation was based on delayed precipitation of the ammonium salt from benzene and on abnormal conductivity. However, Euler[5] showed that the delayed precipitation was merely a supersaturation phenomenon (later admitted by Hantzsch) and that the conductivity of the supposed pseudo-form approximated that of acetic acid. A possible example of neutral and aci-forms of primary nitramines was briefly suggested[6] between the proposal by Hantzsch and the repudiation by Euler but no case has been authenticated. The titration of 1,2-dinitraminoethane, for example, is entirely like that of a normal dicarboxylic acid. While the existence of two isomeric alkyl derivatives of primary nitramines indicates that two tautomeric forms of the acid probably exist, it would seem that the interconversion is immeasurably fast. A delay of many hours in the appearance of the aci-form of nitroguanidine cannot therefore find a reasonable explanation in the nitramine-isonitramine equilibrium.

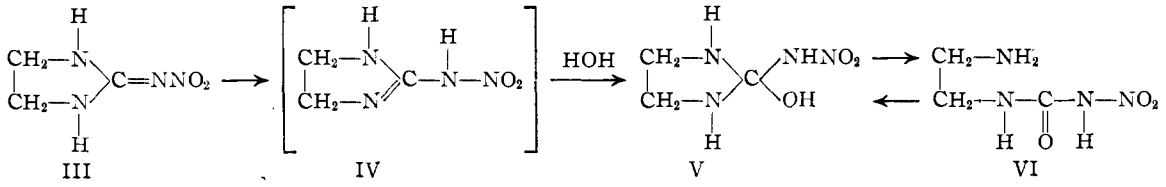
On the other hand slow formation of the sodium salt is characteristic of the conversion of some nitrimines to nitramines.[7] Thus 2-nitrimino-4-methylpentene - 3 - one - 2 and 2 - nitrimino - 3,3-dimethylbutanone-2 are insoluble in cold alkali, but can be dissolved when the alkali is warm. Nitriminocamphor dissolves easily in alkali, but acidification yields a labile isomer, m.p. 39°, which gradually reverts to the stable form melting at 70°.[8] Hantzsch and Barth considered this to be a nitrimine-nitramine conversion. Analogously the ordinary form of nitroguanidine may be thought to be the non-acidic nitrimine, II, which tautomerizes to the nitramine, I, in alkaline solution. Curves 3, 4 and 5, Fig. 1, suggest that this amino-acid tautomer, I, is stabilized as its hydrochloride by acidification. The nitrimino form, II, is regenerated when crystallization occurs from the neutral solution.

The nitrimino structure, 2-nitroguanidine, is not new. Both Pellizzari[9] and Franchimont[10] approved it. Even Thiele[1] when he abandoned this structure for that of 1-nitroguanidine expressed his doubt. He prepared a silver salt (which, he noted, was alkaline in reaction) but considered it to be relatively meaningless as a criterion of acidity since guanidine itself forms a silver salt. Actually the properties of nitroguanidine are more satisfactorily explained by the nitrimine rather than the nitramine structure. Thus its high melting point and thermal stability are characteristic of a high order of symmetry. Its preparation by direct nitration of guanidine in sulfuric-nitric acids would be unique if it were 1-nitroguanidine since authentic primary nitramines are unstable in this medium. Finally its non-corrosive behavior toward metals, which is advantageous for its use in explosive munitions, is practical evidence that it is not acidic in nature.

Some of the cyclic nitroguanidines also are non-acidic. When 2-nitriminoimidazolidone-2 (III, formerly designated as 2-nitramino-Δ^2-imidazoline or 2-nitramino-Δ^2-1,3-diazacyclopentene) is dissolved in 1.4 equivalents of cold 2.5 *N* alkali and the solution is chilled from 0 to −20° after thirty minutes 40% of the original compound is precipitated unchanged, and not as the sodium salt. Confirmation that the compound does not originally behave as an acid is shown by curve 1, Fig. 2, when a solution in 0.1 *N* alkali is immediately titrated with 0.1104 *N* hydrochloric acid. It may be seen that the titration is essentially that of the strong acid and base. The equivalent of nitro-compound shown on the upper abscissa is not indicated at all.

When the alkaline solution is allowed to stand for twelve hours before it is titrated, curve 2, Fig. 2 shows an inflection which begins to deviate rapidly at the equivalence point where the nitramine, if present, ought to be effective; it continues in the manner expected for an amino acid. This effect, which is independent of vacuum evacuation of the solution is accentuated (curve 3, Fig. 2) when the alkaline solution is allowed to stand thirty-six hours before titration. The system now behaves as if it were relatively stable. If it is titrated with 0.1 *N* alkali after thirteen hours, then let stand for nine hours and re-titrated with

(2) T. L. Davis and Blanchard, THIS JOURNAL, **51**, 1790 (1929).
(3) G. E. K. Branch and S. M. Mamoto, *ibid.*, **52**, 863 (1930).
(4) A. Hantzsch and F. E. Dollfus, *Ber.*, **35**, 258 (1902).
(5) H. Euler, *ibid.*, **39**, 1612 (1906).
(6) J. P. Orton, *J. Chem. Soc.*, **81**, 965 (1902).
(7) J. W. Suggitt, G. S. Myers and George F. Wright, *J. Org. Chem.*, **12**, 373 (1947).
(8) A. Hantzsch and Barth, *Ber.*, **35**, 260 (1902).
(9) G. Pellizzari, *Gazz. chim. ital.*, **21**, 2, 405 (1891).
(10) A. P. N. Franchimont, *Rec. trav. chim.*, **10**, 231 (1891).



0.1 *N* acid, curve 3 is reproduced in both titrations within experimental error.

Two compounds are obtained when the acidified solution is evaporated. If the solution is adjusted to *p*H 7 the first to appear is the original 2-nitriminoimidazolidone-2. Subsequent adjustment of acidity to *p*H 4.5 usually yields, on further evaporation, a compound melting at 137° with decomposition which, like the parent nitrimine (III), gives a negative Franchimont test. Although the empirical formula is identical with that of 3-β-hydroxyethylnitroguanidine,[11] its properties differ, and indicate that it is either 3-β-aminoethyl-1-nitrourea (VI) or 2-hydroxy-2-nitraminoimidazolidine (V). Since a choice between these closely-related structures is not significant to the present report, the compound will be discussed by the latter designation.

The relative yields of III and V obtained from the neutralized solution depend on time and concentration of alkali. Table I shows that the yield of 1-hydroxy-1-nitraminoimidazolidine (V) increases while the amount of regenerated 2-nitraminoimidazolidone-2 (III) becomes less as the reaction proceeds.

TABLE I

RECOVERY BY ACIDIFICATION OF ALKALINE NITRIMINOIMIDAZOLIDONE SOLUTION

Time, hr.	Normality alkali	III %	V %
4	0.20	70	15
8	.20	23	58
13	.20	20	
9	.16	32	31
12	.10	40	23

Since the titration curves for V resemble closely that of an aged solution of the nitrimine, III, it might be thought that V was formed directly from III without intermediate conversion to the nitramine (IV). However, this seems not to be the case. If aliquots from an ageing solution of the nitrimine (III) in 0.2 *N* alkali are titrated at intervals of zero, 0.5, 1.5, 3, 4, 6, 8.5, 10.5 and 12.5 hours, a family of curves shown in Fig. 3 is obtained. If rate curves at two convenient *p*H ranges (11.0 and 9.25) are compared with the data in Table I, it may be seen that the recovery of nitrimine is always greater than would be expected if it were to be considered entirely as material which had not yet undergone reaction. Indeed 20% of the original amount of III may be recovered after the alkaline reaction has proceeded to completion after twelve hours. This 20% does not represent an equilibrium because an alkaline solution of 1-hydroxy-1-nitraminoimidazolidine (V) does not precipitate any of the nitrimine when it is acidified.

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

It seems necessary therefore to consider that the nitrimine (III) is converted by alkali to the sodium salt of an intermediate form. We consider this intermediate to be 2-nitramino-Δ^2-imidazoline (IV) which, upon acidification, may revert to the nitrimine (III) unless it suffers hydration to give V.

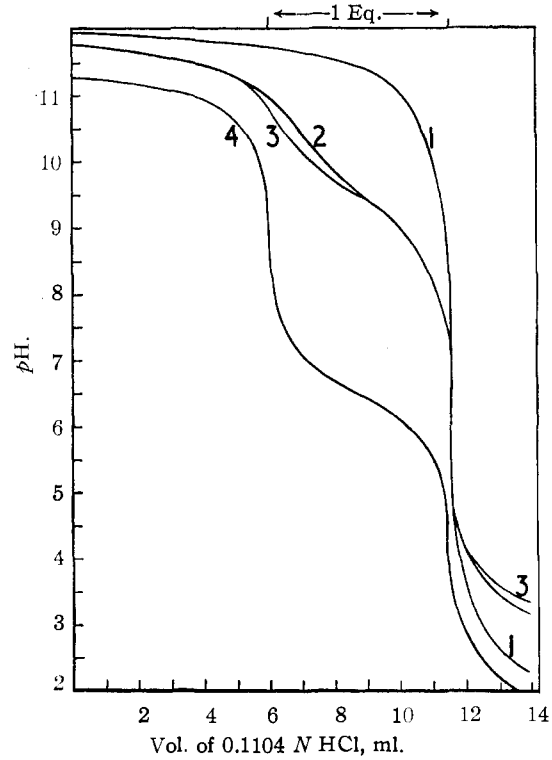


Fig. 2.

Two examples of initially non-acidic nitroguanidines have been presented, but it must not be inferred that the nitrimino structure will be characteristic of all compounds of this type. A typical exception is 1-nitro-2-nitramino-Δ^2-imidazoline, VII, which differs from the compounds described previously in several respects. It gives a positive Franchimont test with dimethylaniline whereas negative tests are obtained with the others. It is relatively unstable, as compared with the compounds described earlier in this report. Thus the nitro group in nitroguanidine and the alkylnitroguanidines is not displaced in media containing an excess of nitric acid. The attempted nitration of nitronitraminoimidazoline, on the other hand, leads to 1,3-dinitroimidazolidone-2, IX. Since authentic primary nitramines lose nitrous oxide with ease, this result is not unexpected if a nitramino group is actually present at the 2-position. Loss of nitrous oxide in the acidic nitration medium would result initially in the enolic form of 1-nitroimidazolidone-2 (VIII), which would yield the expected

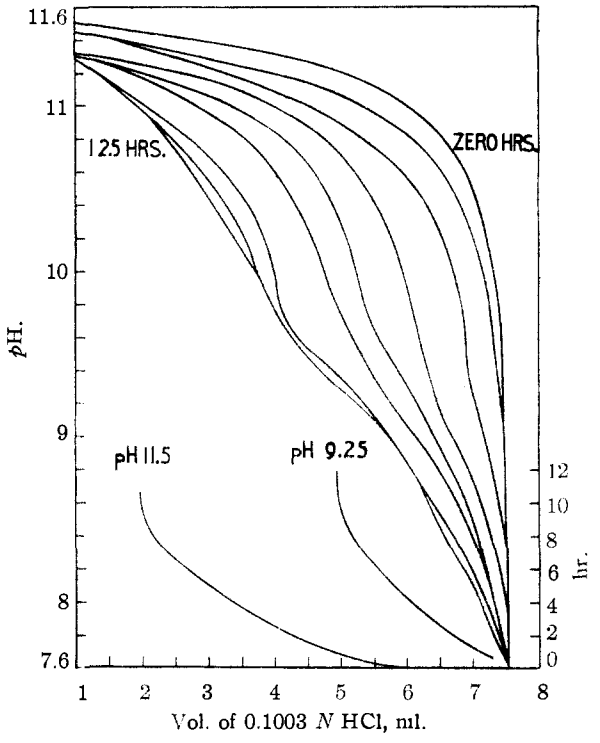
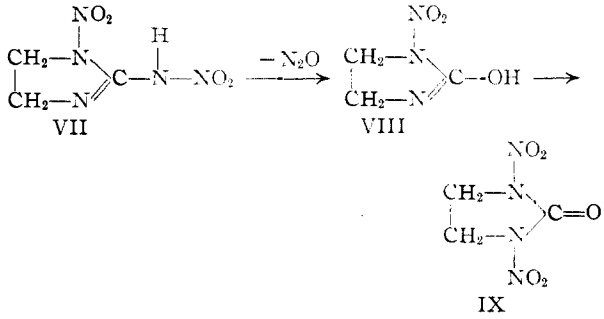


Fig. 3.

product if it became nitrated after ketonization. In consideration of these contrasts to the other nitroguanidines discussed in this report it might then be expected that the nitration product of 2-nitriminoimidazolidone-2 would possess the nitramino structure, VII.



This seems to be the case. When 1-nitro-2-nitramino-Δ^2-imidazoline (VII) is dissolved in 2.5 *N* alkali (with great ease) the compound cannot be removed either by chilling the solution or by extracting it with chloroform. When a freshly-prepared solution of VII in 0.1 *N* alkali is titrated potentiometrically, curve 4, Fig. 2 shows that it is a relatively strong acid with little amino acid character. From the acidified solution 73% of VII can be recovered.

Experimental[12]

Potentiometric Titrations.—A Coleman *p*H electrometer was used at 26 ± 2° with glass and calomel electrodes in a 150 ml. beaker containing a stainless steel gas disperser from which nitrogen saturated and blanketed the liquid. The samples of nitroguanidines (0.0006 mole) were dissolved in a solution of 0.00131 mole of sodium hydroxide made up closely 0.1 normal in conductivity water.

(12) All melting points are uncorrected.

Recovery of Nitroguanidine A. From 1.9 *N* Alkali.—To 130 ml. of stirred 1.9 *N* aqueous sodium hydroxide was added 10.4 g. (0.1 mole) of nitroguanidine. The temperature decreased as solution occurred over forty-five minutes. The solution, which now was ammoniacal in odor, was chilled. The precipitate was filtered off and washed with methanol. It weighed 3.2 g., m.p. 233–236° and was pure nitroguanidine uncontaminated with sodium salt, as shown by ignition. The cold filtrate was chilled and 30 ml. of 10% hydrochloric acid was added. After five seconds 2.4 g. more nitroguanidine began to precipitate.

B. **From 1.5 *N* Alkali.**—A suspension of 52 g. of nitroguanidine (0.5 mole) in 375 ml. (0.56 mole) of 1.5 *N* aqueous sodium hydroxide was placed under 22 mm. pressure with a fine air stream passing through for 13 hours. The clear solution was chilled and acidified to *p*H 7.2 and filtered to remove 0.5 g. of nitroguanidine. The filtrate was evaporated under 20 mm. pressure until sodium chloride and 0.15 g. of nitroguanidine appeared. These were filtered off; the solution had to be acidified to *p*H 2 before 21 extractions with a total of 500 ml. acetonitrile were efficient in removal of 6.0 g., m.p. 60–80°. The crude product was wastefully separated by solution in acetonitrile and precipitation with ethyl and petroleum ethers (b.p. 60–70°) into 1.1 g. of an unidentified component, m.p. 164–165° and 2.17 g. of the more soluble nitrourea, identified as its lilac colored complex with copper sulfate and pyridine[2] and by its X-ray powder diffraction pattern.

In an otherwise identical experiment the vacuum evaporation was continued to complete dryness. The residue was dissolved in hot absolute ethanol. After fractional crystallization with ethanol to remove ammonium chloride, 4.3 g. of urea was the only product obtained.

C. **From 1.25 *N* Alkali.**—A suspension of 10.4 g. (0.1 mole) of nitroguanidine in 90 ml. (0.112 mole) of 1.25 *N* aqueous alkali was stirred with a fine air stream under 25 mm. pressure for 17 hours. It is important to maintain this air-stream in order to prevent accumulation of ammonia, which seems to autocatalyze the decomposition. The clear solution was chilled to precipitate 0.4 g. of pure nitroguanidine. The chilled filtrate was cautiously acidified to *p*H 4 with 25 ml. of 25% hydrochloric acid; slight gas evolution occurred. A precipitate appeared slowly. Filtration yielded 9.0 g. of crude nitroguanidine, m.p. 228–229°, which gave a positive Franchimont test with dimethylaniline. In this instance the test is presumptive for nitrourea.

Large amounts of old samples of nitroguanidine always gives a positive Franchimont test which disappears if the substance is crystallized from boiling water. When the 9 g. of crude product was crystallized from 100 ml. of 4% aqueous acetic acid, 8.2 g. of pure nitroguanidine was obtained which gave a negative Franchimont test. A comparable crystallization of 9.0 g. of pure nitroguanidine yielded 8.6 g. The crude sample must therefore have contained not more than 0.4 g. (5%) of nitrourea and it thus represents a 95% recovery of nitroguanidine from the alkaline solution.

It is possible but difficult to duplicate this high recovery. After the autocatalytic effect of ammonia has been excluded the critical step is in the acidification of the alkaline solution. It is characteristic of most sodium salts of primary nitramines that they lose nitrous oxide with great ease if acidification is effected carelessly.

D. **From 0.1 *N* Alkali.**—The acidified solution after potentiometric titration of an alkaline solution which had been aged for 12 hours, was evaporated under reduced pressure until a crystal crop appeared. This was filtered off and vacuum evaporation continued until chloride began to appear. The yield of nitroguanidine (m.p. 232°, inserted at 200°) was 68% in comparison with 90% from a freshly-prepared alkaline solution.

Recovery of 2-Nitriminoimidazolidone-2, III. A. From 2.5 *N* Alkali.—A solution of 1.30 g. (0.01 mole) of nitriminoimidazolidone in 5.5 ml. (0.014 mole) of 2.5 *N* aqueous sodium hydroxide was maintained at +2° for thirty minutes and then chilled to −20° and filtered. The precipitate weighed 0.5 g. and its melting point (219–220°) showed that it constituted a 38% recovery of the original material, III. Ignition tests showed that this was not contaminated with a significant amount of any sodium salt.

B. **From 0.2 *N* Alkali.**—A solution of 1.30 g. (0.01 mole) of III in 50 ml. (0.01 mole) of 0.2 *N* aqueous sodium hydroxide was aged at 25° for 4 hours. After acidification with

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%.

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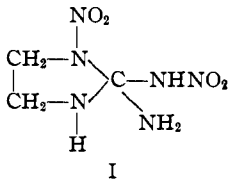
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF TORONTO]

The Chemistry of Linear Substituted Nitroguanidines

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

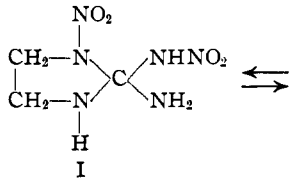
It was formerly[2] stated that the treatment of 1-nitro-2-nitriminoimidazolidone-2 with concentrated ammonia solution gave 1-nitro-2-amino-2-nitraminoimidazolidine (I), after subsequent acidification. Although this compound gave a negative secondary nitramine test,[3] a cyclic structure was assigned 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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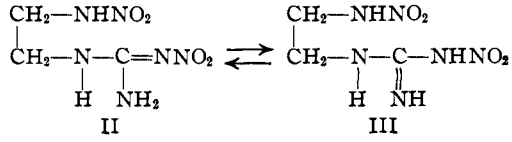
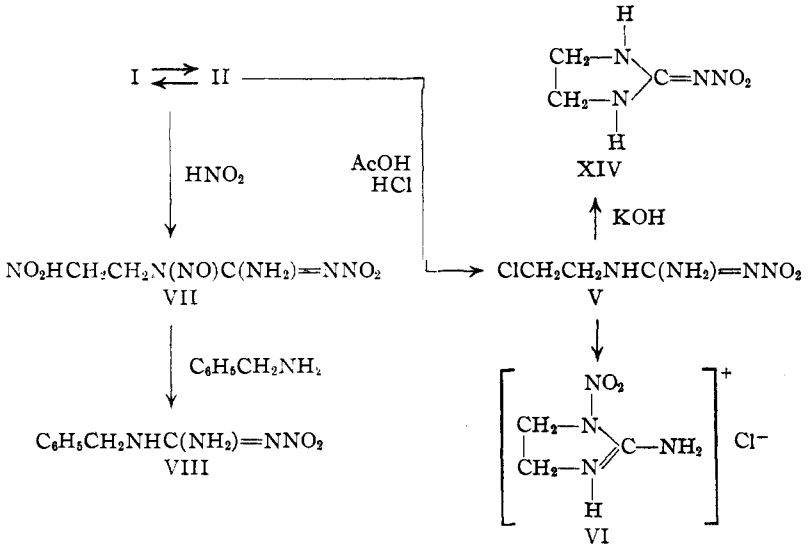


II III

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).