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

THE STRUCTURE OF NITROGUANIDINE AND OF ITS DERIVATIVES

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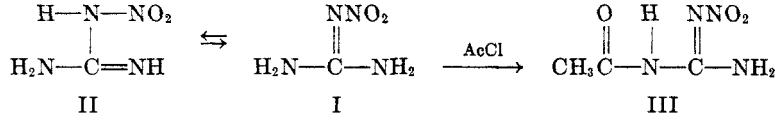
Received July 22, 1952

Recently evidence has been presented on the basis of titrimetric data to show that nitroguanidine and many of its derivatives exist in the nitrimino rather than the nitramino form, although conversion to the latter tautomer may occur in alkaline solution (1). The prevalence of the nitrimino form in such compounds has been confirmed by others who have evaluated the titrimetric data and the dipole moments of nitroguanidine and its derivatives (2, 3). On the other hand McKay, Picard, and Brunet (3a) have seemingly contradicted these opinions on the basis of some ultraviolet absorption spectroscopy. It seemed to us worthwhile to reexamine the chemistry of nitroguanidines in order to resolve this discrepancy.

The opinion (1) that nitroguanidine exists normally as the neutral nitrimine (I) rather than the acidic nitramine (II) was based originally upon the observation that the substance could be precipitated unchanged from the alkaline solution in which it had previously been dissolved with difficulty. This nonacidic character was confirmed by potentiometric titration of a dilute alkaline solution. If now, this alkaline solution was allowed to stand for some hours under conditions such that ammonia could not induce autocatalytic decomposition, the subsequent titration showed the appearance of an acidic function. This function was attributed to a primary nitramino group in the tautomeric 1-nitroguanidine (II) because at least 70% of the original nitroguanidine could be recovered from the alkaline solution. Furthermore the decomposition products to which the acidic behavior might have been attributed are not neutralized in the manner observed for the properly manipulated aged alkaline solutions of nitroguanidine.



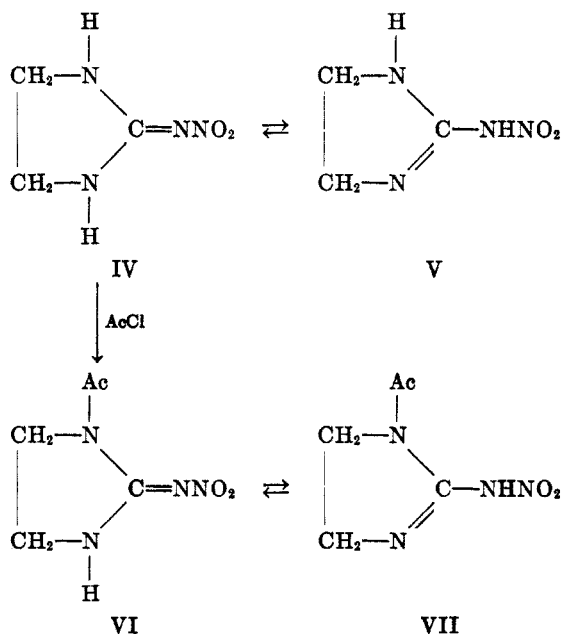
The spectrophotometric studies by McKay, Picard, and Brunet (3a) on aged alkaline solutions of nitroguanidine have been interpreted in contradiction of our results. Unfortunately, the reported experimental work by these authors comprises three lines descriptive only of the spectrophotometer, so we cannot properly evaluate their method of manipulating alkaline solutions of nitroguanidine. The original report (1), which we have confirmed, specifies that these solutions must be handled with great care in respect of time, temperature, and concentration of ammonia.

The absence of a primary nitramino group in ordinary nitroguanidine is also attested by its inertness toward diazomethane (4), which reacts readily with

authentic nitramines such as N-methyl-1,2-dinitraminoethane. Another test for the presence of primary nitramino groups has been found in the reaction with acetyl chloride which converts them to alcohols or chlorides with the elimination of nitrous oxide (5–7). When this reaction is applied to nitroguanidine, no nitrous oxide is evolved after ten hours of reflux with excess acetyl chloride. Instead acetylation occurs and a good yield of 1-aceto-2-nitroguanidine (III) may be obtained. The product has been assigned this structure because it is evidently stable in acetyl chloride and it does not react with diazomethane. Unfortunately this assignment cannot be confirmed by potentiometric titration; the curve which is obtained indicates that decomposition is occurring in alkaline solution. The decomposition product, 2-nitroguanidine, is not unexpected in consideration of the behavior of a homologous analog, 1-methyl-1,3-dinitroguanidine (8).

Evidence provided by methods other than absorption spectroscopy (or its interpretation) thus seem to favor assignment of the nitro group to the 2-position in nitroguanidine. A similar situation exists for 2-nitriminoimidazolidine (IV) which was found (1) to behave like nitroguanidine in basic aqueous solution, but which McKay, Picard, and Brunet believe to exist as 2-nitraminoimidazoline (V). However V ought to react with diazomethane because of its primary nitramino group. Actually the compound is recovered unchanged after treatment with this reagent.

Furthermore, the nitrimino structure IV is indicated by treatment with acetyl chloride in acetic acid at temperatures up to 100°. No gas is evolved during reaction periods of four to six hours. Instead, like nitroguanidine, 2-nitriminoimidazolidine (IV) is acetylated under these conditions.



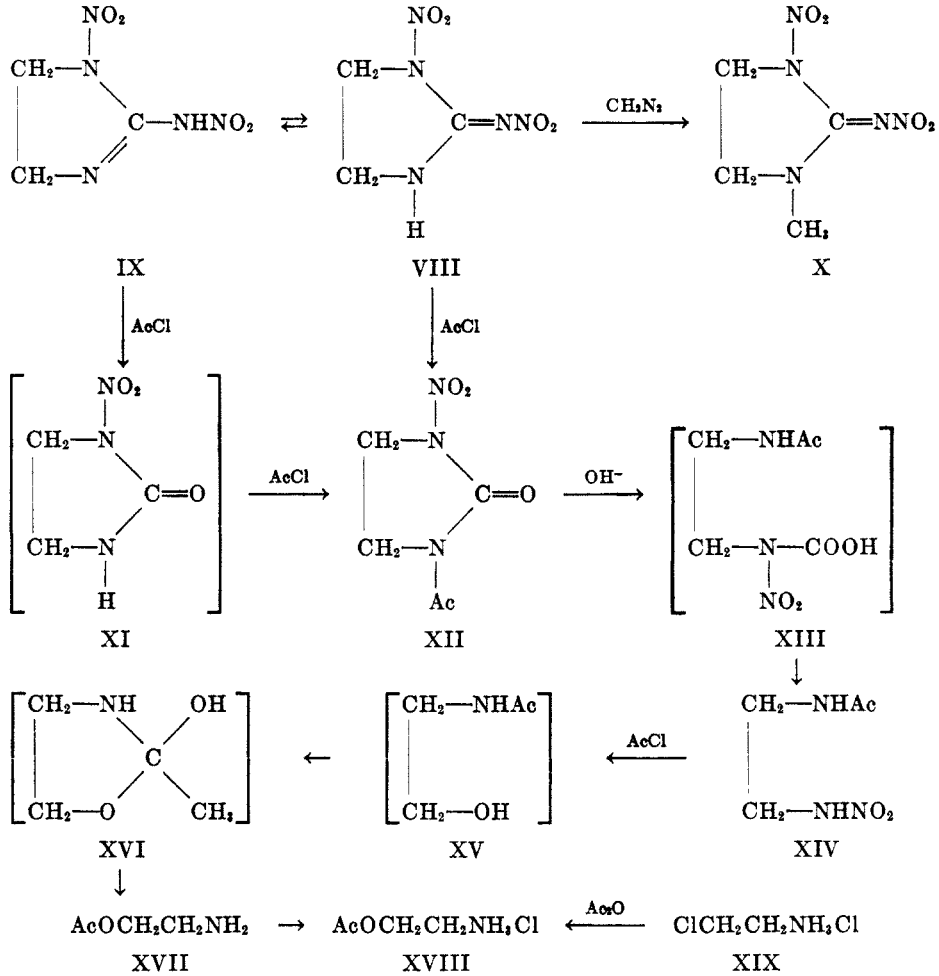
The acetylated product has been designated 1-aceto-2-nitriminoimidazolidine (VI) although some of its properties might be ascribed to 1-aceto-2-nitraminoimidazoline (VII). It will not react with diazomethane or acetyl chloride, but its titration in freshly prepared alkaline solution shows that it behaves as a very weak acid ($K_A = 1 \times 10^{-9}$) with negligible amino acid characteristic. In this respect it behaves like 2-nitriminoöxazolidine, which was thought (7) to exist in labile equilibrium with its tautomer. When the acetylated 2-nitriminoimidazolidine is first prepared it melts at 141°, but this form gradually changes to one melting at 126°. There is at present no evidence to show that these are not simple polymorphs. Both forms are assigned structure VI, largely by analogy with the analogous 1-nitro-2-nitriminoimidazolidine (VIII).

This nitration product (VIII) of 2-nitriminoimidazolidine (IV) was originally designated as 1-nitro-2-nitraminoimidazoline (IX) because of its behavior as a relatively strong acid ($K_A = 3 \times 10^{-7}$) in freshly prepared alkaline solution (1). In this single instance McKay, Picard, and Brunet seem to agree with Barton, Hall, and Wright. However the dipole moment determination ($\mu = 7.65$ D) by Kumler (3) indicates that both groups of authors are incorrect. Indeed we have now found that the reaction of VIII with diazomethane and with methyl sulfate in aqueous sodium bicarbonate supports the opinion of Kumler.

A dioxane solution of this dinitro compound reacts vigorously with an ether solution of diazomethane which has been standardized colorimetrically with respect to benzoic acid. Titration of the dioxane solution to the first permanent yellow color requires 1.03 equivalents of diazomethane for each molar equivalent of the dinitro compound. In order to isolate the methylation products, a suspension of the dinitro compound has been treated with an excess of diazomethane. Evaporation yields a solid and an oil which can be separated. The oil detonates upon attempted distillation; it is probably an isonitramine. The solid is found to be 1-nitro-2-nitrimino-3-methylimidazolidine (X), which had previously been prepared by an unequivocal method (9). The position of this methyl group designates the structure of the dinitro compound as the nitrimine, VIII.

However the reaction of the dinitro compound with acetyl chloride in acetic acid seems to indicate the presence of 1-nitro-2-nitramino-Δ^2-imidazoline (IX), although the conditions of the reaction are severe. Ordinarily a primary nitramine decomposes in the presence of acetyl chloride at temperatures of 30–60°, but nitrous oxide is not released from the dinitro compound except over long periods of time at 90–100°. Under these conditions some carbon dioxide is also formed; nevertheless a 50% yield of 1-aceto-3-nitroimidazolidone-2 (XII) can be obtained. Presumably this substance is formed by ketonization of the original enol remaining after loss of nitrous oxide from IX. Acetylation of this 1-nitroimidazolidone-2 (XI) would thus yield XII. While the alternative route involving acetylation of VIII with subsequent loss of nitrous oxide from the nitrimine cannot entirely be excluded, this alternative is improbable to the extent that 2-nitroguanidine and 2-nitriminoimidazolidine can be acetylated under the same severe conditions without loss of nitrous oxide. It seems more reasonable

to presume that the drastic reaction conditions are required in order that the tautomeric equilibrium VIII ⇆ IX, in which VIII is largely predominant, may be shifted in favor of IX.



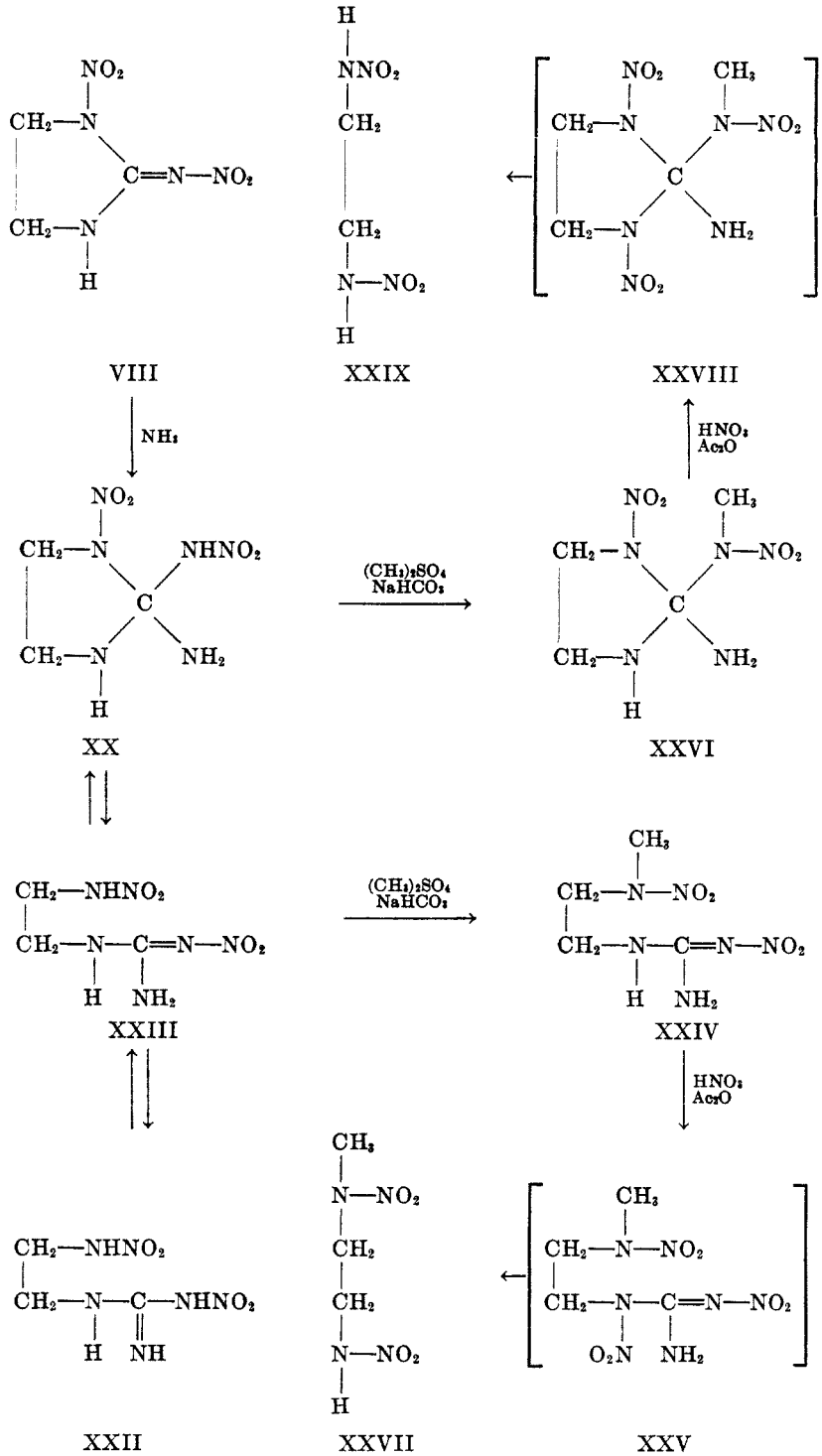
The structure of 1-aceto-3-nitroimidazolidone-2 (XII) has been demonstrated by means of its instability toward alkali. When the alkaline solution of XII is acidified carbon dioxide is evolved from the intermediate nitrocarbamic acid (XIII), and 2-acetaminoethylnitramine (XIV) is formed. This aliphatic primary nitramine is shown by potentiometric titration to be a relatively strong acid ($K_A = 2 \times 10^{-6}$). It decomposes typically under mild conditions with acetyl chloride to liberate nitrous oxide, but the remainder is not 2-acetaminoethanol (XV) but rather the hydrochloride of 2-aminoethyl acetate (XVII), evidently *via* the cyclic intermediate XVI. Identity of XVII should be established by comparison with the compound prepared from ethanolamine and

hydrogen chloride in acetic acid (10). However we were unable to prepare the compound in this manner. Instead we have treated 2-chloroethylammonium chloride (XIX) with acetic anhydride. The 2-acetoxyethylammonium chloride (XVIII) thus obtained is identical with the reaction product from XIV and acetyl chloride.

It would seem that McKay, Picard, and Brunet are unable to find evidence for any nitrimine linkage when a nitramine linkage is alternatively possible. Thus they consider that the addition product of ammonia with 1-nitro-2-nitriminoimidazolidine (VIII) not only comprises the linear isomer rather than the cyclic isomer (XX), but must also exist in the dinitramine form (XXII) rather than the nitramine-nitrimine form (XXIII). They disregard entirely an earlier opinion regarding ring-chain isomerism that "the facile cyclization and fission encountered among certain of these substituted nitroguanidines makes a choice of structure difficult and perhaps not too significant" (5). In order to maintain their opinion they advance the evidence afforded by absorption spectrum measurements and also a Franchimont test to which they have ascribed a new meaning. On the other hand, they disregard the titrimetric criterion (5), although there is no evidence that they have tested its authenticity. In view of this diversity of opinion it seemed worthwhile to us to evaluate the acidity of the addition product of ammonia with 1-nitro-2-nitriminoimidazolidine by methods other than potentiometric titration.

The first of these methods involves the fixation of the species existent in alkaline solution by methylation with methyl sulfate at the *p*H of saturated aqueous sodium bicarbonate. The principal product of this reaction (85% yield) is 1-[β-N-methylnitramino]ethyl-2-nitroguanidine (XXIV). The structure has been established firstly by the observation that this monomethyl derivative (of XX or XXIII but not of XXII) is non-acidic. The methyl group must therefore have replaced the acidic hydrogen. Secondly, this monomethyl derivative reacts in a nitration medium comprising acetic anhydride and nitric acid. The system, after treatment with alkali and then acid, yields N-methyl-1,2-dinitraminoethane (XXVII). This product would be expected if the imido hydrogen in XXIV were replaced by a nitro group and the trinitro derivative (XXV or the analogous urea) thus formed were to decompose hydrolytically to XXVII. The principal monomethylation product is thus shown to be XXIV which must have been formed by methylation of XXIII.

In addition to the principal monomethylation product (XXIV), a second one is obtained in small yield by the treatment with methyl sulfate. This minor monomethylation product is also alkali-insoluble, and therefore could not have been derived from 3-β-nitraminoethyl-1-nitroguanidine (XXII). When it is treated with an acetic anhydride-nitric acid mixture, a gas is evolved slowly which contains nitrogen oxides. Subsequent treatment of the system with alkali, and then acid, yields 1,2-dinitraminoethane (XXIX). Isolation of this product designates the minor monomethylation product as 1-nitro-2-amino-2-methylnitraminoimidazolidine (XXVI). The intermediate nitration product (XXVIII


VIII
XXIX
XXVIII
NH₃
HNO₃ Ac₂O
(CH₃)₂SO₄ NaHCO₃
XX
XXVI
XXIII
XXIV
XXII
XXVII
XXV

or the analogous linear urea) which is indicated in the chart is probably isolable, but in the present work it was converted directly into the characterizing nitramine because the nitration was carried out on a small scale. Such a procedure is reliable because it is known that neither 1,2-diaminoethane (11) nor 2-aminoethylnitramine (7) can be nitrated under these conditions.

Since XXVI must have been derived by methylation of 1-nitro-2-amino-2-nitraminoimidazolidine (XX), it is probable that XX and 3-β-nitramino-2-nitroguanidine (XXIII) are both present in aqueous solution. XXII is evidently absent since neither an alkali-soluble monomethylation product nor a dimethylation product is found among the methylation products. The comparative yields of XXIV and XXVI show that in aqueous solution, XXIII must be the predominant form. However the work which we now shall describe shows that this dominance of XXIII does not seem to maintain in a solvent mixture such as ethyl ether-dimethylformamide.

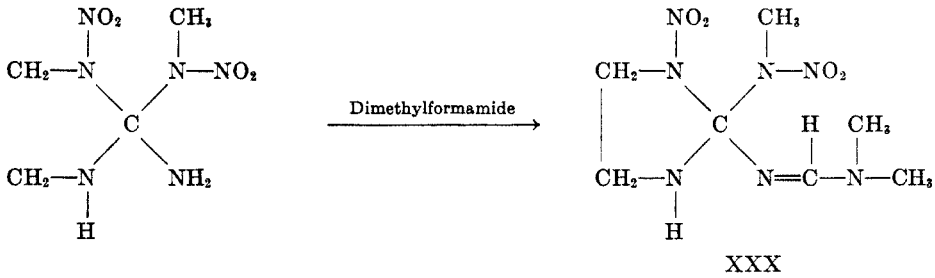
The second method used to establish a choice between structures XX, XXII, and XXIII for the addition product from ammonia and nitronitriminoimidazolidine (VIII) is reaction with diazomethane. This reaction has been evaluated both qualitatively and quantitatively. The colorimetric quantitative determination described earlier in this report gives anomalous results with the addition product, but a gasometric method confirms the presence of only one acidic group per formula weight of the compound.

Titration of the addition product with ethereal diazomethane indicates the consumption of about 1.4 moles of the titrant per mole of addition product. This value does not vary according to the duration of time over which the reaction takes place. Therefore it cannot be caused either by slow reaction of a second functional group or by a tautomeric change, since eventual consumption of 2 moles of titrant would be expected under these circumstances.

Alternatively, one may assume that the consumption of diazomethane in excess of one equivalent involves an addition reaction in which the entire diazomethane molecule is retained in the product. This type of reaction does not occur at an acidic linkage. If this assumption were valid, then the amount of nitrogen evolved during the reaction ought to be more correctly a criterion for amount of active hydrogen than is the disappearance of diazomethane color. In actual fact the amount of nitrogen which is released corresponds closely with that obtained from an equivalent weight of benzoic acid in the same reaction medium, ether-dimethylformamide. Thus the presence of only one acidic group is indicated. This excludes structure XXII but does not permit a choice between structures XX and XXIII.

The qualitative evaluation with diazomethane in ether-dimethylformamide solution depends on the isolation of the products obtained from the fixation by the methyl group of the acidic linkages in the compound which may be XX or XXIII. Three products have been obtained. The one obtained in lowest yield (2%) is most easily isolated because of its relative insolubility in water. The structure of this compound is yet uncertain, but its empirical formula indicates

that it is a condensation product (XXX) of 1-nitro-2-amino-2-methyl-nitramino-imidazolidine (XXIV) and dimethylformamide.



XXX

The low yield of this product has prevented extensive investigation; a single nitration yielded no identifiable product, and all attempts to synthesize it from the other reaction products have been unsuccessful.

The second isolable product is obtained in 7% yield and is found to be 1-[β-N-methylnitramino]ethyl-2-nitroguanidine (XXIV). The third, and most prevalent product (29% yield), is 1-nitro-2-amino-2-methylnitraminoimidazolidine (XXVI). It may be seen that XXVI, which was obtained in negligible yield by methylation in aqueous solution, becomes the main isolable product from methylation in non-aqueous solution. Conversely, XXIV becomes a minor product from the diazomethane methylation of the addition product of ammonia and 1-nitro-2-nitriminoimidazolidine in ether-dimethylformamide solution.

The methylation studies firstly disprove the contention of McKay, Picard, and Brunet that the structure, 3-β-nitraminoethyl-1-nitroguanidine, is properly descriptive of the addition product of ammonia and 1-nitro-2-nitriminoimidazolidine. Secondly, these methylation studies tend to support the opinion (5) that ring-chain isomerism is prevalent among these negatively-substituted imidazolidines. However, the idea (5) that this isomerization is not very significant is contradicted by the present study, which shows that the reaction environment contributes largely to the significance of ring-chain isomerism. In retrospect one might have anticipated this significance by analogy with carbohydrate chemistry.

The opinions expressed by McKay, Picard, and Brunet are in a certain sense vague and self-contradictory. Thus, when they define nitroguanidine and some of its derivatives in terms of resonance hybridization, the degenerate structure which they imply is actually an approximation of the nitrimine of which they deny the existence. On the other hand they attribute salt-like properties to the compounds, which essentially denies the existence of the resonance hybrid. However they do state without equivocation, on the basis of ultraviolet absorption spectroscopy, (a) that the structures defined by Barton, Hall, and Wright as 2-nitroguanidine and 2-nitriminoimidazolidine are actually internal salts of primary nitramines, (b) that the structure defined by Kumler as 1-nitro-2-nitriminoimidazolidine is a primary nitramine, and (c) that the addition product of ammonia and 1-nitro-2-nitriminoimidazolidine is a dinitramine. It may be

seen in the present report that these statements are all contradicted by the chemical evidence. It would seem that in the present state of development, ultraviolet absorption spectra are not reliable criteria for structure assignment to nitroguanidine and its derivatives.

EXPERIMENTAL

General. All melting points have been corrected against reliable standards. When a Franchimont test is designated as negative or positive, the meaning of Franchimont himself is conveyed. X-Ray diffraction powder patterns are reported at relative intensities $[I/I_1]$ for d spacings in Angstroms using Cu K_α Ni-filtered radiation.

1-Aceto-2-nitroguanidine (III). A mixture of 1.04 g. (0.01 mole) of nitroguanidine, 2.14 ml. (0.03 mole) of acetyl chloride, and 15 ml. of glacial acetic acid was heated under reflux for 8 hours. No gas evolution could be detected. The clear solution was eventually evaporated under reduced pressure to leave a white solid which was washed with 3 ml. of ethanol. When dry it weighed 0.99 g. (68%), m.p. 200–205° (decomp.). Two crystallizations from hot acetonitrile (20 ml. per g.) raised this melting point with decomposition to 214.5–215.3°. The substance gave a negative Franchimont test with dimethylaniline.

Anal. Calc'd for $C_3H_6N_4O_3$: C, 24.7; H, 4.14; N, 38.3.

Found: C, 24.8; H, 4.30; N, 39.1.

This compound gave the following x-ray diffraction pattern: [10] 10.11, 9.71, 3.23, 3.19; [7] 4.86, 3.92; [6] 4.33, 4.07; [5] 6.94, 6.53; [4] 3.78, 2.84, 2.66; [1] 3.44, 2.22; [0.5] 3.29, 2.44, 2.35.

When 1 ml. of acetic anhydride was added to the original reaction mixture the yield was raised to 77%. When 1.46 g. (0.01 mole) of acetonitroguanidine was added to 100 ml. (0.01 mole) of ice-cold 0.1 *N* aqueous potassium hydroxide, it dissolved after about 4 minutes of shaking. After 80 minutes at 28° the solution was extracted with chloroform to remove 20 mg. of unchanged acetonitroguanidine and then was chilled to 0°. A precipitate of 0.25 g. was filtered off. This yield of pure nitroguanidine, m.p. 228–230°, was augmented by evaporation of the neutralized solution to a volume of 18 ml. (precipitating 0.58 g., m.p. 215–216°), and then to 4 ml. (precipitating 0.09 g., m.p. 177–183°). The whole represents about 90% of the possible nitroguanidine, evidently contaminated with nitrourea since all fractions gave positive Franchimont tests with diethylaniline.

1-Aceto-2-nitriminoimidazolidine (VI). A mixture of 1.30 g. (0.01 mole) of 2-nitriminoimidazolidine, 2.14 ml. (0.03 mole) of acetyl chloride, and 13 ml. of glacial acetic acid was stirred and heated under reflux at 60–65° for 6 hours. Gas evolution could not be detected, even when the temperature was increased to 90–95°. The resulting clear solution was vacuum-evaporated. The residue, 1.58 g. (92%), m.p. 135–140°, was thrice crystallized from hot water (12 ml. per g.), m.p. 141.1–141.9°.

Anal. Calc'd for $C_5H_8N_4O_3$: C, 34.9; H, 4.68.

Found: C, 34.7; H, 4.51.

The x-ray diffraction pattern was determined as follows: [10] 4.04; [7] 6.13; [6] 3.77, 3.08; [5] 9.77, 6.44, 3.90; [4] 6.84, 3.15, 2.73; [3] 3.25; [2] 4.19; [1] 4.97, 4.41; [0.5] 5.50, 4.59, 3.02, 2.62, 2.46, 2.36, 2.15.

When this compound was heated at 3° rather than at 10° per minute, or at either rate when it was kept in absence of light for a few weeks, it melted at 125.3–126.0°. This low-melting form, which turned yellow on exposure to light, could not be reconverted to the high-melting form by crystallization from hot water. However this conversion could be effected by heating the low-melting form at 118° for 12 hours. The low-melting form gave a negative Franchimont test with dimethylaniline.

Anal. Calc'd for $C_5H_8N_4O_3$: C, 34.9; H, 4.68; N, 32.6.

Found: C, 34.6; H, 4.96; N, 32.5.

Neither the high- nor the low-melting form reacted with acetyl chloride (70–80°) or with diazomethane (0°).

1-Nitro-2-nitriminoimidazolidine. In order to insure uniformity in this reagent it was

periodically examined by x-ray diffraction. No change was found in the powder pattern: [10] 11.55; [9] 9.08, 8.14, 7.46; [7] 12.53; [6] 14.24; [5] 9.94, 5.97; [4] 7.10, 6.61, 4.11; [3] 4.21; [2] 3.77; [1] 5.52, 5.26, 4.72, 3.55; [0.5] 8.40, 7.72, 5.76, 5.04.

1-Methyl-3-nitro-2-nitriminoimidazolidine (*X*). (*A*) *by diazomethane methylation.* To an ethereal solution containing an excess of diazomethane was added 3 g. (0.017 mole) of 1-nitro-2-nitriminoimidazolidine over a period of 5 minutes. Within 30 minutes gas evolution had ceased. After 2 hours the crude product (0.61 g., 19%) was filtered off, m.p. 165–166°. Following 3 crystallizations from hot acetonitrile (9.5 ml. per g.) this melted at 166.8–167.2°. It gave a faint yellow-green coloration in the Franchimont test. It was insoluble in water but dissolved in 5% aqueous sodium hydroxide; however it was not reprecipitated by the addition of dilute hydrochloric acid. Its identity was shown by precise elemental analysis and by mixture melting point with an authentic sample, for which we are indebted to Dr. A. F. McKay. The x-ray diffraction pattern of this has also been used for comparison: [10] 3.52; [9] 6.17, 5.20; [8] 3.91; [7] 4.84, 4.52; [6] 3.81; [5] 2.73, 2.57, 2.49, 2.41; [3] 2.62, 2.26, 2.08; [2] 2.19; [1] 2.86, 1.89, 1.77; [0.5] 2.01, 1.74.

Evaporation of the ethereal filtrate from which this compound had been removed left 2.60 g. of reddish oil which detonated when an attempt was made to distil it under a vacuum (15 mm.).

(*B*) *By methyl sulfate methylation.* A suspension of 3.50 g. (0.02 mole) of 1-nitro-2-nitriminoimidazolidine and 6.72 g. (0.08 mole) of sodium bicarbonate in 40 ml. of water was stirred at 25° with 3.80 ml. (0.04 mole) of methyl sulfate for 7 hours. Concentrated hydrochloric acid was then added to *p*H 2. The product was filtered and washed with water, 0.87 g. (23%), m.p. 169.5–170°. A mixture melting point with an authentic sample was not depressed. Evaporation of the aqueous filtrate yielded an oil which probably contains some isonitramine, although it was not identified. The oil probably also contains methylated β-nitraminoethylnitrourea since the latter substance is found by alkaline hydrolysis of nitronitriminoimidazolidine as is shown by the next experiment.

3-β-Nitraminoethyl-1-nitrourea. A mixture of 3.50 g. (0.02 mole) of 1-nitro-2-nitriminoimidazolidine and 2.52 g. (0.03 mole) of sodium bicarbonate was stirred in 40 ml. of water for 12 hours at 28°. The clear solution was acidified to *p*H 5 with concentrated hydrochloric acid. The precipitate, 1.12 g., melted at 151–152°. A second crop, 0.44 g., melted at 145–146°. The total recovery of nitronitriminoimidazolidine was thus 45%. The filtrate was evaporated in an air stream to a volume of 6 ml. and then was acidified to *p*H 1. The precipitate weighed 0.63 g., m.p. 97–98°. Further evaporation yielded 0.49 g., m.p. 90–91°. The total yield of β-nitraminoethylnitrourea was thus 29% of theoretical. This product was twice crystallized from hot water (2 ml. per g.), m.p. 104–104.5°. A strong Franchimont test was observed with dimethylaniline.

Anal. Calc'd for $C_3H_7N_5O_5$: C, 18.7; H, 3.65; N, 36.3.
Found: C, 18.7; H, 3.58; N, 36.5.

The yield is doubled by the use of aqueous sodium hydroxide (10%) instead of sodium bicarbonate.

1-Aceto-3-nitroimidazolidone-2 (XII). A mixture of 8.75 g. (0.05 mole) of 1-nitro-2-nitriminoimidazolidine, 10.7 ml. (0.15 mole) of acetyl chloride, and 80 ml. of glacial acetic acid was heated under reflux at 90–95° for 12 hours. Absorption of the effluent gas in alkali showed that it contained 90 cc. of carbon dioxide, while combustion of the remainder with hydrogen showed that 424 cc. (38% based on 1 nitramino group) of nitrous oxide was present. Vacuum evaporation of the homogeneous reaction system left a yellow solid which was washed with 10 ml. of cold ethanol. The ethanol-insoluble product weighed 4.59 g. (52%), m.p. 121–124°. Crystallization from hot ethanol (10 ml. per g.) raised this m.p. to 124.9–125.3°. The purified product gave a positive lanthanum nitrate test for an acetyl group. The x-ray diffraction pattern was determined as follows: [10] 5.89, 3.88; [9] 3.05; [8] 2.91; [7] 2.98; [6] 5.23, 4.47, 3.53, 2.74; [5] 4.12, 2.66, 2.39; [3] 2.32; [2] 3.72, 2.24; [1] 5.05, 4.63, 2.01, 1.90, 1.72; [0.5] 6.46, 4.84, 3.63, 2.20, 2.17, 2.13, 2.08, 2.05, 1.96.

Anal. Calc'd for $C_5H_7N_3O_4$: C, 34.7; H, 4.08; N, 24.3.
Found: C, 34.9; H, 4.02; N, 24.3.

Because of high temperature of this reaction, acetyl chloride was sometimes lost or consumed to the extent that reaction was incomplete. When a test portion showed this had occurred, the reaction was reheated 2 or 3 hours with an additional amount of acetyl chloride.

2-Acetaminoethylnitramine (XIV). Addition of 3 g. (0.017 mole) of 1-aceto-3-nitroimidazolidone-2 in 20 ml. (0.04 mole) of 2 *N* aqueous sodium hydroxide was carried out during 10 minutes. The solid was dissolved by shaking for 30 minutes; heat was evolved. After the system had cooled spontaneously to 25° the acidity was increased to *p*H 3 with 22.7 ml. of 2 *N* hydrochloric acid. Much carbon dioxide was evolved. The solution was vacuum-evaporated to dryness and extracted with 20 ml., and then 10 ml., of hot ethanol. The hot extracts were filtered, combined and evaporated in an air-stream. The residue, 2.40 g. (94%), m.p. 120–128°, was crystallized 4 times from hot water (3.9 ml. per g.), m.p. 134.5–135.5°.

Anal. Calc'd for $C_4H_9N_3O_3$: C, 32.7; H, 6.17; N, 28.6.

Found: C, 32.6; H, 6.00; N, 29.1.

The compound reacted vigorously with ethereal diazomethane, and showed positive lanthanum nitrate and Franchimont tests for acetyl and nitramino groups.

2-Acetoxyethylammonium chloride (XVIII) (*A*) *from 2-acetaminoethylnitramine* (XIV). A mixture of 0.74 g. (0.005 mole) of XIV, 1.07 ml. (0.015 mole) of acetyl chloride, and 7.4 ml. of glacial acetic acid was heated at 50–55° for 90 minutes. During this time 70 cc. (63% on the basis of 1 nitramino group) of nitrous oxide was collected and identified by combustion analysis with hydrogen. The homogeneous reaction system was vacuum-evaporated, treated with 4 ml. of ethanol, and re-evaporated under reduced pressure to leave 0.59 g. of an oil which was dissolved in 5 ml. of chloroform. Evaporation of this solution left 0.10 g. (16%) of white needles, m.p. 125–128°. This product was crystallized from hot ethanol (3 ml. per g.), m.p. 130–130.9°. Silver chloride was precipitated at once when the compound was treated with cold aqueous silver nitrate.

Anal. Calc'd for $C_4H_{10}ClNO_2$: C, 34.4; H, 7.22, N, 10.04.

Found: C, 34.5; H, 7.42; N, 9.71.

The following x-ray diffraction pattern was obtained: [10] 6.60, 4.55, 3.62, 3.29, 2.58; [9] 3.37; [7] 3.00, 2.79; [6] 3.18, 2.74; [2] 4.32, 2.07; [1] 5.05, 3.99, 2.68, 2.01; [0.5] 9.88, 6.89, 6.00, 4.69, 4.15, 3.86, 3.72, 2.63, 2.46, 2.36, 1.98, 1.92, 1.88, 1.85, 1.81, 1.74, 1.68, 1.64, 1.60, 1.58.

(*B*) *From 2-chloroethylammonium chloride* (XIX). To a warm solution (50°) of 5.0 g. (0.043 mole) of 2-chloroethylammonium chloride in 50 ml. of water was added 4.7 ml. (0.05 mole) of acetic anhydride. The mixture was stirred vigorously until the anhydride dissolved; then a solution of 3.9 g. (0.048 mole) of sodium acetate trihydrate in 12.2 ml. of water was added. After 7 hours at +3° the system was vacuum-evaporated to leave a semisolid residue which was extracted with three 10-ml. portions of cold ethanol. The filtered extracts were combined and evaporated in an air stream. The amber-colored oil (4.94 g.) was dissolved in 10 ml. of cold ethanol, to which 50 ml. of ether was then added. After 12 hours, 2.50 g. (42%) of white solid, m.p. 60–100°, was filtered off. Four crystallizations from hot ethanol (3 ml. per g.) raised the melting point to 130.1–131.0°. This melting point was not depressed by admixture of the product obtained by procedure *A*.

2-Acetoxyethylamine (XVII). To a solution of 0.98 g. (0.007 mole) of 2-acetoxyethylammonium chloride in 10 ml. of ethanol was added a solution prepared from 0.18 g. (0.0078 mole) of sodium in 6 ml. of ethanol. The sodium chloride (0.4 g., 97%) was filtered off and the filtrate was vacuum-evaporated. The residual oil was distilled, b.p. 134–138° (0.3 mm.). The distillate (0.14 g., 19%) gave a positive carbylamine test.

1-[β-N-Methylnitramino]ethyl-2-nitroguanidine (XXIV). A mixture of 25.2 g. (0.3 mole) of sodium bicarbonate, 9.6 g. (0.054 mole) of 1-nitro-2-amino-2-nitraminoimidazolidine, and 65 ml. of water reacted vigorously with evolution of carbon dioxide. The suspension was stirred at 25° while 9.5 ml. (0.1 mole) of methyl sulfate was added over a 2-hour period. After stirring 5 more hours, the system was treated with 20 ml. (0.1 mole) of 18% hydrochloric acid. It was then filtered to remove 7.8 g., m.p. 130.7–131.2°. The filtrate was evaporated under reduced pressure. The dry residue was extracted with three 25-ml. portions of acetonitrile. Vacuum evaporation of the latter solution left an oil which was boiled 5

minutes with 10 ml. of water. When this solution was cooled, it yielded 1.44 g., m.p. 122–124°. Further concentration of the filtrate yielded 0.3 g., m.p. 94–96°. Total yield of the principal product, based on the first 2 crops, is 86% of theoretical. This 9.54 g. was crystallized from hot dioxane (20 ml. per g., 60% recovery), m.p. 131.5–133.4°. Recrystallization from dioxane raised this melting point to 133.4–134°. After precipitation of a formic acid solution with water it melted at 134.7–135.5°.

Anal. Calc'd for $C_4H_{10}N_6O_4$: C, 23.3; H, 4.88; N, 40.7.
Found: C, 23.4; H, 5.10; N, 40.4.

The following x-ray powder diffraction pattern was obtained: [10] 5.20, 3.76; [9] 10.39, 4.74, 3.05; [8] 4.56; [7] 2.77; [6] 4.43–4.13; [5] 3.42; [4] 4.02–3.87; [3] 5.50; [1] 9.07, 7.49, 6.28, 3.35, 3.22, 3.14; [0.5] 3.57, 2.92, 2.59, 2.48.

1-Nitro-2-amino-2-methylnitraminoimidazolidine (XXVI). If the 0.5 g. fraction described in the previous experiment were XXVI, it would be present in 2.5% of theoretical yield. This crude product was crystallized from hot ethanol (1 g. per 5 cc.) and from hot acetone (1 g. per 3.5 cc.), m.p. 103–103.7°. The compound gave a positive Franchimont test with diethylaniline.

Anal. Calc'd for $C_4H_{10}N_6O_4$: C, 23.3; H, 4.88; N, 40.7.
Found: C, 23.8; H, 4.89; N, 40.3.

The x-ray powder diffraction pattern was found to be: [10] 3.42; [9] 5.57, 4.27, 4.12, 3.36, 3.04; [8] 2.01; [7] 2.17; [6] 4.91, 2.24; [5] 6.89, 6.46, 2.78–2.55; [4] 2.43, 2.40; [3] 3.60, 2.35; [2] 3.76, 3.16, 1.79, 1.74; [1] 5.38, 3.91, 2.95, 2.47, 2.07; [0.5] 5.86, 4.71, 1.70.

1,2-Dinitraminoethane (XXIX). To a solution of 0.22 ml. (0.0051 mole) of 100% nitric acid in 1 ml. (0.011 mole) of acetic anhydride (prepared at −30° and warmed to 0°) was added 0.24 g. (0.00116 mole) of 1-nitro-2-amino-2-methylnitraminoimidazolidine (XXVI). After 6 hours of reaction with slow evolution of nitrogen oxide, the excess nitric acid and acetic anhydride was distilled off under 15 mm. pressure. The residual semisolid was boiled with 4 ml. of water until 2.5 ml. had distilled off. The resulting solution was cooled, made alkaline, and extracted with ether. The aqueous layer was evaporated to 1 ml., acidified with 12% hydrochloric acid, and chilled until 40 mg. (24%) of crude 1,2-dinitraminoethane crystallized, m.p. 164–165°. After crystallization from absolute ethanol (25 cc. per g.), it melted at 175–176°; a mixture melting point with authentic material was not lowered.

N-Methyl-1,2-dinitraminoethane (XXVII). When 1.03 g. (0.005 mole) of 1-[β-methylnitramino]ethyl-2-nitroguanidine was added at 0° to a solution (prepared at −50°) of 0.43 ml. (0.01 mole) of 100% nitric acid in 1.94 ml. (0.02 mole) of acetic anhydride and allowed to warm to room temperature, it dissolved slowly over 4 hours, but evolution of a colorless gas accompanied this solution. When reaction was complete the system was diluted with ice, made alkaline with aqueous sodium hydroxide, and warmed 5 minutes at 50°. It was then chilled, acidified with nitric acid, and vacuum-evaporated to dryness. The residue was extracted with six 5-ml. portions of acetonitrile. Vacuum evaporation of this solution left 0.76 g. which was crystallized from 2 ml. of hot water, weight 0.28 g. (34%), m.p. 118–119°. Recrystallization from hot water raised this to 120.5–121.8°. A mixture melting point with an authentic sample was not lowered.

1-Nitro-2-amino-2-nitraminoimidazolidine (XX) *with diazomethane.* To a solution of 9.60 g. (0.054 mole) of 1-nitro-2-amino-2-nitraminoimidazolidine in 190 ml. of dimethylformamide was added at 3° an ethereal solution of diazomethane sufficient to impart a permanent yellow color to the solution. The volume of gas (1550 cc., N.T.P.) which evolved during 30 minutes was 1.06 times that produced from benzoic acid when it was treated under identical conditions.

After 1 hour at 25° the system was vacuum-evaporated to leave an oil which was dissolved in 20 ml. of ethanol. After 1 week at 3° a white solid was filtered off; 4.40 g., m.p. 120–175°. This solid was eluted with 105 ml. of water at 40°. The insoluble portion weighed 0.27 g. (2%), m.p. 174–179°. When crystallized from hot water (50 ml. per g.), it melted at 182.5–183° (decomp.).

Anal. Calc'd for $C_7H_{15}N_7O_4$: C, 32.2; H, 5.79; N, 37.6.
Found: C, 32.4; H, 5.67; N, 37.5.

The following diffraction pattern was obtained: [10] 3.57; [8] 6.46; [7] 6.80; [6] 5.21; [1] 3.85; [0.5] 12.55, 4.02, 3.75, 3.22.

We have yet been unable to prepare this compound from either monomethyl derivative XXIV or XXVI by solution in dimethylformamide followed by precipitation, after a time, with ether, chloroform, or water. In each case the monomethyl derivative was recovered unchanged.

The aqueous eluate from which $C_7H_{15}N_7O_4$ was isolated was vacuum-evaporated. The residue was dissolved in 10 ml. of warm ethanol. This solution yielded 0.53 g., m.p. 124–128°. Partial evaporation of the filtrate, followed by addition of ether, precipitated 0.28 g., m.p. 90–110°. Crystallization from ethanol raised this melting point to 118–127°. The combined weight represents a 7% yield of 1-[β-N-methylnitramino]ethyl-2-nitroguanidine. This product melted at 131–132° after crystallization from dioxane, and a mixture melting point with the product previously described (XXIV) was not lowered.

TABLE I

TITRATIONS IN (a) DIOXANE OR (b) DIMETHYLFORMAMIDE WITH ETHEREAL SOLUTIONS OF DIAZOMETHANE

MOLE^{-3}	OF REAGENT	MOLE^{-3} OF DIAZOMETHANE	CONSUMPTION PER ACIDIC FUNCTION, %
0.251	1-Nitro-2-nitriminoimidazolidine a	0.249	99
0.267	1-Nitro-2-nitriminoimidazolidine a	0.279	105
0.256	1-Nitro-2-nitriminoimidazolidine a	0.272	106
0.261	Benzoic acid b	0.269	103
0.261	Benzoic acid b	0.270	104
0.324	Benzoic acid b	0.350	108
0.294	1-Nitro-2-amino-2-nitraminoimidazolidine, b	0.416	142
0.249	1-Nitro-2-amino-2-nitraminoimidazolidine, b	0.354	142
0.236	1-Nitro-2-amino-2-nitraminoimidazolidine, b	0.329	139
0.285	β-N-Methylnitraminoethylnitramine a	0.270	95
0.316	β-N-Methylnitraminoethylnitramine a	0.342	108

The combined ether-ethanolic filtrates were evaporated under reduced pressure. The residue was dissolved in 5 ml. of acetone to which ether was added until turbid. A further crop (80 mg.) of impure XXIV was filtered off. Further dilution with ether precipitated 2.21 g. (29%), m.p. 93–94°. Crystallization from acetone raised this melting point to 101.5–102.3°. A mixture melting point with the low-melting monomethyl derivative, XXVI, was not lowered.

Titration with diazomethane. An ethereal solution, approximately 0.15 N, in diazomethane is prepared from an ethereal suspension of N-nitroso-N-methylurea and 50% aqueous potassium hydroxide. This solution is standardized by titrating it (most conveniently in a refrigerated room at +3°) against benzoic acid dissolved in ether or, sometimes, the solvent used in nitramine solution. The endpoint is defined as the first permanent yellow color that may be observed under a blue light. This standardization is reproducible, and the values are comparable with those obtained by the method of Acree and Marshall (12).

The nitramine to be analyzed (0.2–0.3 millimole) is weighed and dissolved in purified dioxane or dimethylformamide (never in alcohols, which cause anomalous results). To this solution at +3° is added standard ethereal diazomethane solution until a pale yellow color persists. After a standard time period of 15 minutes, titration with a standard solution of benzoic acid in ether is carried out until the yellow hue defined by diazomethane standardization against benzoic acid is reached.

The equivalence of active hydrogen is determined by subtracting from the measured excess of normal diazomethane solution the ml. of normal diazomethane solution con-

sumed over the same time period by the solvent alone, and the ml. of normal benzoic acid solution required for back-titration of the diazomethane not consumed by the nitramine. Typical results are shown in Table I.

SUMMARY

1. The absence of a primary nitramino group in nitroguanidine and 2-nitriminoimidazolidine is confirmed, since they do not react with diazomethane, nor lose nitrous oxide with acetyl chloride.

2. The behavior of nitrated 2-nitriminoimidazolidine toward diazomethane indicates a nitrimino structure, while its behavior toward acetyl chloride shows it to be a nitramine. The dual nature is probably due to labile tautomerism with the nitrimino form most prevalent in the equilibrium mixture.

3. Reaction of the three compounds with acetyl chloride also induces acetylation. The acetamino derivatives resemble their nitramino analogs in chemical behavior.

4. The reactions of the addition compound comprising ammonia and 1-nitro-2-nitriminoimidazolidine which occur with diazomethane and with bicarbonate and methyl sulfate show that it exists in solution as the ring-chain isomers, 1-nitro-2-amino-2-nitraminoimidazolidine and 1-β-nitraminoethyl-2-nitroguanidine; the former is more prevalent in non-aqueous media and the latter in aqueous media.

5. All of these chemical evaluations are contrary to the predictions based on ultraviolet spectrophotometry. It is suggested that the latter criteria are at present unreliable.

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