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

The Scission of New 1-Alkyl-1,3-dinitroguanidines and an Analog

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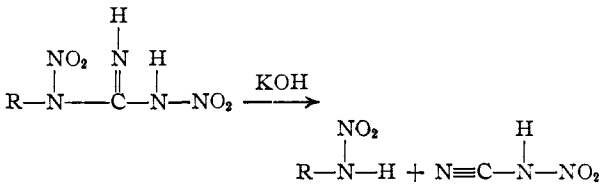
The number of known linear dinitroguanidines has been increased to include 1-methyl- and 1-*n*-butyl-1,3-dinitroguanidine. These compounds are rapidly cleaved by dilute potassium hydroxide to the potassium salts of nitrocyanamide and the corresponding primary nitramines. In a similar manner 1-nitro-2-amino-2-imidazoline isomerizes in aqueous alkali to the linear compound N-nitro-N′-cyano-1,2-diaminoethane.

Since both of the known linear 1-substituted 1,3-dinitroguanidines[2,3] have substituents in the β-position it seemed worthwhile to determine whether β-substitution was a requirement for the introduction of a second nitro group into a nitroguanidine structure. Although 1-methyl-2-nitroguanidine has been reported[4,5] to be completely resistant to further nitration, we have found that both methyl- and butylnitroguanidine were converted to the corresponding 1,3-dinitroguanidines by treatment with nitric acid and acetic anhydride.

The report that much gas was evolved during similar nitrations[2,3] was confirmed in the present instances. This gas was identified as nitrous oxide in amounts approximately complementary to the fair yields of dinitroguanidines. The gas evolution was most vigorous during the initial part of the reaction. This might indicate that the gas was evolved at the expense of the starting material. However when 1-methyl-1,3-dinitroguanidine was separately subjected to the nitration conditions nitrous oxide was also evolved.

While we confirmed the previous report[4] that 1-methyl-2-nitroguanidine could be largely recovered unchanged from absolute nitric acid at 0°, we also obtained small yields (*ca.* 1%) of 1-methyl-1,3-dinitroguanidine from both 97 and 99.9% nitric acid. When the dinitroguanidine was treated with 97% nitric acid under the same conditions 1-methyl-2-nitroguanidine was obtained in 59% yield. Evidently in nitric acid solution the nitration is reversible.

Both methyl and 1-butyl-1,3-dinitroguanidine[6] were readily soluble in two equivalents of 0.1 *N* potassium hydroxide, but when such a solution was titrated at once potentiometrically with standard hydrochloric acid, two equivalents of acid function were indicated. One acid function was relatively weak (K_A about 4×10^{-7}) while the other resembled the strong mineral acids. These acids were identified as the corresponding primary nitramines and nitrocyanamide. The isolation was facilitated by the different acidity of the compounds. This reaction appears to be identical with that reported[7] for 1-methyl-1-nitroso-3-nitroguanidine.



A similar fission also occurs with 1-nitro-2-amino-2-imidazoline (I). Since recent papers[8,9] have indicated rather labile ring openings and closures with certain nitroguanidines, it seemed possible despite the demonstrated cyclic structure of its salts[2] that compound I might have a linear structure such as the acid corresponding to II, or be easily isomerized to this acid. In agreement with structure I an aqueous solution of I was found by potentiometric titration (curve 1, Fig. 1) to be a monoacidic base. When the titration was completed, evaporation of the solution regenerated the hydrochloride salt[2] of I in 84% yield. However when I was first dissolved in 2.19 equivalents (20.0 cc.) of 0.1040 *N* sodium hydroxide and then very rapidly titrated with hydrochloric acid (curve 2) the basic function had almost disappeared and in its place were two equivalents of acid function. The presence of the weaker acid function is observable by comparison with curve 3, obtained from 20.0 cc. of sodium hydroxide. When at the end of the titration the excess of hydrochloric acid was neutralized at once with an equivalent amount of sodium hydroxide, the *p*H rose over 60 minutes from about 4.4 to a steady value of 7.6. Evaporation of the solution yielded 62% of unchanged 1-nitro-2-amino-2-imidazoline (I). The drift in the direction of higher *p*H was also observed whenever the time taken for the titration of sodium hydroxide solutions of I was greater than a few minutes. For example when the time was increased from 5 minutes (curve 2) to 35 minutes 0.8 equivalent of

(1) Senior author.

(2) A. F. McKay and J. E. Milks, THIS JOURNAL, **73**, 1616 (1950).

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

(4) A. F. McKay and G. F Wright, THIS JOURNAL, **69**, 3028 (1947).

(5) A. F. McKay, *Chemistry in Canada*, **3**, 37 (1951).

(6) The instability of these dinitroguanidines toward base prevented the application of the potentiometric methods of Wright, *et al.* (THIS JOURNAL, **73**, 2201 (1951)) for distinguishing between the 3-nitro- and the 2-nitroguanidine structures. However, the 3-nitroguanidine structure has been assigned, since aqueous solutions of the dinitroguanidines were distinctly acidic. The *p*H of 0.05 and 0.001 *N* solutions of both compounds was 4.2 and 5.2, respectively (15% of acetone was included to increase the solubility of butyldinitroguanidine). In contrast 2-nitroguanidine did not affect the *p*H of pure water or aqueous acetone.

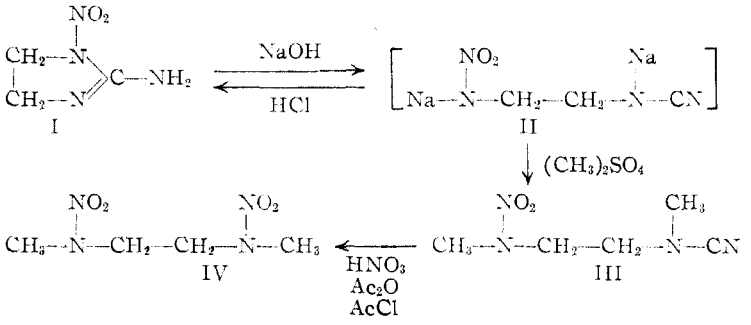
If the acidity displayed by these dinitroguanidines were due only to traces of impurity such as nitric acid, the addition of diazoethane ought to consume this impurity and then coexist with the remaining non-acidic compound. Such is the case with 2-nitroguanidine and 2-nitriminoimidazolidine. In contrast, 1-methyl-1,3-dinitroguanidine reacts with diazoethane rapidly and completely.

In favor of the 3-nitro structure it was also noted that only two or three seconds were required for the dissolution of either of the dinitroguanidines in 3 equivalents of 2.5 *N* potassium hydroxide. On this basis we also suggest the same structure for 1-methyl-1-nitroso-3-nitroguanidine.

(7) A. F. McKay, *et al.*, *Can. J. Research*, **28B**, 683 (1950).

(8) R. H. Hall, A. F. McKay and G. F Wright, THIS JOURNAL, **73**, 2205 (1951).

(9) R. H. Hall and G. F Wright, *ibid.*, **73**, 2208 (1951).



basic function appeared. These effects are interpreted as indicating that in basic solution the ring of I is opened to give the dibasic acid, II, and on neutralization of such a solution I is reformed.

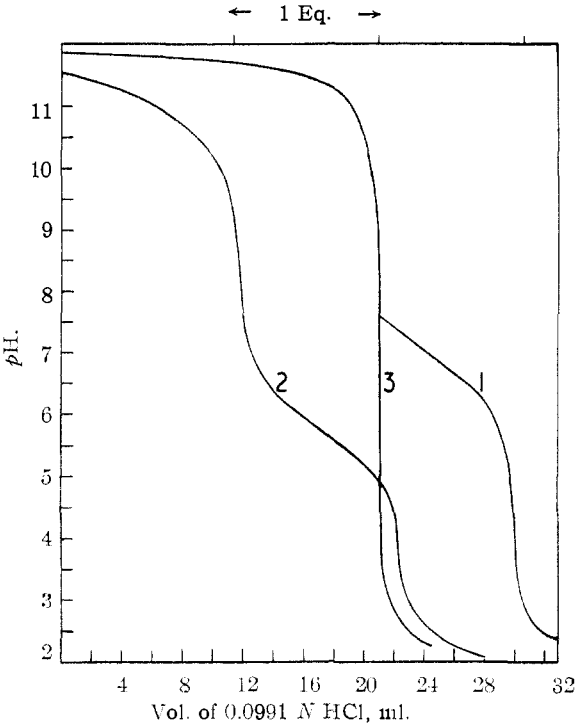


Fig. 1.

Direct evidence for the existence of II was obtained by treating a basic solution of I with dimethyl sulfate. The methylated product (III) was isolated in 37% yield. This compound was converted by a chloride-catalyzed nitration[10] to N,N′-dimethyl-N,N′-dinitro-1,2-diaminoethane (IV).[11]

Experimental[12]

1-Methyl-1,3-dinitroguanidine. A. From Acetic Anhydride Nitric Acid at 40°.—To a stirred solution of 0.067 mole (2.82 cc.) of 99.9% nitric acid and 0.15 mole (14.2 cc.) acetic anhydride, prepared at 0° was added at once 0.030 mole (3.54 g.) of 1-methyl-2-nitroguanidine. The mixture was allowed to warm spontaneously for 10 minutes, when at about 20° an exothermic reaction started with rapid solution of the solid and vigorous evolution of a gas. After the temperature had been maintained at 38–40° for 20 minutes, 0.014 mole of nitrous oxide (47%) was collected and the evolution of gas almost stopped. The solution was vacuum concentrated at 8 mm. to a viscous oil. Crystallization occurred on stirring with 10 cc. of ice-water. The crystals were separated by filtration, and after washing with 10 cc. of ice-water weighed 2.52 g. (52%), m.p. 80–82°. Vacuum concentration of the combined filtrate and washings gave a second crop of 0.26 g. (5%), m.p. 79–81°. After recrystallization from hot benzene or from ethyl ether (26 cc. per g.) by dilution with petroleum ether (20 cc. per g., b.p. 60–70°) the melting point was 81.5–82.5°. A strong green Franchimont test[13] was obtained using N-diethylaniline. The compound is soluble to the extent of 4 g./100 ml. of water at 25° and is quite soluble in most organic solvents.

We suspect that a case of dermititis was caused by repeated exposure of the skin to this compound.

Anal. Calcd. for $C_2H_5N_5O_4$: C, 14.7; H, 3.09; N, 42.9. Found: C, 14.7; H, 3.04; N, 43.0.

X-Ray diffraction with CuKα gave powder spacings (Å.) with the following intensities [I/I_0]: [10] 3.53; [9] 4.13; [8] 5.34, 3.72; [6] 2.75; [5] 4.52, 2.66; [3] 3.10, 2.27, 2.22, 2.14; [2] 9.06, 4.75; [1] 3.28, 3.18, 2.98, 2.82, 2.55, 2.46, 2.37, 2.06, 1.99, 1.90, 1.85, 1.58.

The ultraviolet absorption spectrum as determined in absolute ethanol on a Beckman D.U. spectrometer (slit 1 mm. at 2700 Å. and 2 mm. at 2300 Å.) consisted of $E_{max.}$ 9740 at $\lambda_{max.}$ 2690 Å. with decrease in absorption to $E_{min.}$ 7100 at $\lambda_{min.}$ 2400 Å. and then slight increase to the limit at 2250 Å.

The reactivity of 1-methyl-1,3-dinitroguanidine toward diazoethane was determined by addition of 2 ml. of a half-saturated solution of the latter at 25° to 3 mg. of the former in 0.25 ml. of dioxane. Gas evolution was vigorous, and the solution was bleached in 5 seconds. In contrast, comparable treatment of nitroguanidine and 2-nitroiminoimidazolidine gave no more gas evolution than a control, and the test mixtures, like the control, did not bleach until three hours had elapsed.

When 0.0040 mole (0.652 g.) of methyldinitroguanidine was treated according to the preceding conditions of preparation, 0.0018 mole of nitrous oxide (45%) was collected. Only 0.33 g. (51%) of the starting material could be recovered.

B. From Acetic Anhydride Nitric Acid at 15°.—A solution of 0.004 mole (0.47 g.) of 1-methyl-2-nitroguanidine in 0.009 mole (0.38 cc.) of 99.9% nitric acid, 0.04 mole (3.8 cc.) of acetic anhydride and 40 cc. of acetic acid was maintained at 13–15° for 30 hours, and then concentrated by a high vacuum at a temperature below 18°. Treatment of the residue with 1.5 cc. of ice-water gave 0.35 g. (52%) of crystals, m.p. 80–82°.

C. From Absolute Nitric Acid.—A solution of 0.004 mole (0.472 g.) of methylnitroguanidine in 0.080 mole (3.5 cc.) of 97% nitric acid was prepared at −30° and allowed to stand at 0° for 3 hours. The solution was recooled to −30° and 18 g. of ice was added. Vacuum evaporation at 0.06 mm. left a solid residue which was extracted with 40 cc. of ether. The residue after washing with 4 cc. of ice-water consisted of 0.40 g. (85%) of unchanged methylnitroguanidine, m.p. 160–161°. The ether extracts were vacuum concentrated to an oily residue which was re-extracted with 0.5 cc. of ether. When the ether was diluted with 3 cc. of petroleum ether (b.p. 60–70°) crystallization occurred after several days at −70°. The product, 0.004 g. (0.6%), m.p. 72–77°, was impure but gave an X-ray diffraction pattern identical with methyldinitroguanidine from method A.

When this procedure was repeated with 99.9% nitric acid for 1 hour at 0°, 97% of the methylnitroguanidine was recovered unchanged and the yield of crude methyldinitroguanidine was 0.9%.

When methyldinitroguanidine was treated by the same procedure with 97% nitric acid for 3 hours at 0° 8% was recovered unchanged and 59% was recovered as methylnitroguanidine, m.p. 158–160°.

In control experiments methyldinitroguanidine was recovered unchanged from 20% nitric acid.

1-*n*-Butyl-1,3-dinitroguanidine.—1-*n*-Butyl-2-nitroguanidine was treated as described for the preparation of methyl-

(10) W. J. Chute, *et al.*, *Can. J. Research*, **26B**, 114 (1948).

(11) H. J. Backer, *Rec. trav. chim.*, **31**, 142 (1912).

(12) All melting points have been corrected against reliable standards.

(13) A. P. N. Franchimont, *Rec. trav. chim.*, **16**, 226 (1897).

dinitroguanidine, part A, except that the reaction was carried out for 1 hour at 20–22°. The crude product, 2.24 g., m.p. 64–68° (soft 57°) was dissolved in 15 cc. of chloroform and treated with 0.5 g. of decolorizing charcoal. The chloroform solution was vacuum concentrated to 4 cc. Dilution with 20 cc. of carbon tetrachloride gave 1.45 g. (24%) of crystals, m.p. 69–70°. Repeated recrystallizations raised the melting point to 71–72°.

Anal. Calcd. for $C_6H_{11}N_5O_4$: C, 29.3; H, 5.41; N, 34.1. Found: C, 29.7; H, 5.52; N, 34.1.

The compound is 0.4% soluble in water at 25°, but is very soluble in most organic solvents. A strong Franchimont test was obtained. In a smaller preparation 0.0040 mole of butylnitroguanidine evolved 0.0033 mole (82%) of nitrous oxide.

Scission of Dinitroguanidines by Dilute Potassium Hydroxide.—A solution of 0.00346 mole (0.564 g.) of 1-methyl-1,3-dinitroguanidine in 0.00692 mole of 0.1 *N* potassium hydroxide was prepared at 15° and then neutralized with 0.00346 mole of 0.3 *N* hydrochloric acid. By continuous ether extraction an oil was obtained which after crystallization from ethyl ether, petroleum ether weighed 0.128 g. (49%), m.p. 34–36°. X-Ray diffraction with CuKα gave powder spacings (Å) with intensities $[I/I_0]$ identical with authentic methylnitramine,[14] m.p. 38°: [10] 3.31; [9] 5.68, 3.52; [8] 2.64; [7] 2.47; [6] 4.82, 3.95, 2.82; [5] 4.45, 3.74, 2.21; [4] 2.13, 1.92; [3] 1.65; [2] 1.70; [1] 3.10, 2.95, 2.56, 1.85, 1.81, 1.75.

The aqueous phase from the ether extraction was vacuum evaporated to dryness and the residue was extracted with 50 cc. of acetone. Evaporation of the acetone and recrystallization of the residue, 0.38 g., m.p. 131–135°, from absolute ethanol gave 0.33 g. (76%) of crystals that melted at 135–137° alone and on admixture with an authentic sample[7] of potassium nitrocyanamide.

When the above procedure was repeated with 1-*n*-butyl-1,3-dinitroguanidine, potassium nitrocyanamide was obtained in 60% yield and *n*-butylnitramine was isolated quantitatively as the monohydrate of the barium salt. X-Ray diffraction by this salt with CuKα gave powder spacings (Å.) with intensities $[I/I_0]$ identical with an authentic sample[15]: [10] 4.06; [9] 3.69; [8] 2.91, 2.32; [7] 3.25, 2.75, 2.59; [6] 3.42; [5] 3.10, 2.22; [4] 5.86, 2.02; [3] 2.16, 2.11; [2] 1.73, 1.56; [1] 2.44, 1.88, 1.82.

Potentiometric Titrations (Fig. 1).—These were performed with a Coleman Electrometer. In the determination represented by curve 1, a solution of 0.000950 mole (0.1235 g.) of 1-nitro-2-amino-2-imidazoline, (I)[2] in 25 cc. of water was titrated with 0.00119 mole (12 cc.) of 0.0991 *N* hydrochloric acid. Vacuum evaporation of this solution left a residue, 0.17 g., which on crystallization from absolute ethanol gave 0.133 g. (84%) of crystals that melted at 195–196° both alone and on admixture with authentic[2] 1-nitro-2-amino-2-imidazoline hydrochloride.

In the determination represented by curve 2, 0.000950 mole of (I) was dissolved in 0.00208 mole (20.0 cc.) of 0.1040 *N* sodium hydroxide during 5 minutes. The resulting solution was titrated during the next 5 minutes with 0.00257 mole (26.0 cc.) of 0.0991 *N* hydrochloric acid. After neutralization of the excess acid with 0.00049 mole (4.7 cc.) of sodium hydroxide, the solution was allowed to stand for 60 minutes and then evaporated *in vacuo*. The residue was extracted with 30 cc. of acetone. Vacuum evaporation of the acetone to 3 cc. gave 0.077 g. (62%) of crystals, m.p. 131–133°. A mixed melting point with the original 1-nitro-2-amino-2-imidazoline was not depressed. X-Ray diffraction by these crystals with CuKα gave powder spacings (Å.) with intensities $[I/I_0]$ identical with an authentic sample: [10] 3.37; [9] 4.21; [8] 7.49, 5.52, 5.20, 4.06, 2.74; [7] 4.54, 3.17, 2.90; [6] 3.72, 3.12, 2.59, 2.16, 1.98; [5] 2.31; [4] 2.23, 1.86; [3] 2.53, 1.91, 1.65; [2] 2.47, 1.71, 1.68; [1] 6.25, 2.65, 2.07, 1.80, 1.51.

N,N'-Dimethyl-N-nitro-N'-cyano-1,2-diaminoethane (III).—A vigorously stirred solution of 0.008 mole (1.04 g.) of 1-nitro-2-amino-2-imidazoline in 0.017 mole of aqueous sodium hydroxide (15.5 cc., 1.08 *N*) was aged for 5 minutes at 0° and then treated with 0.030 mole (2.8 cc.) of dimethyl sulfate. During 2 hours at 25–35° the reaction mixture was kept basic by the portionwise addition of 0.014 mole (5.5 cc., 2.6 *N*) of sodium hydroxide. The homogeneous reaction mixture was extracted with a total of 25 cc. of chloroform. Vacuum evaporation of the solvent left a viscous oil which on dilution with 2 cc. of absolute ethanol gave, at −70°, 0.54 g. of solid, m.p. 50–53°. Recrystallization from absolute ethanol (3 cc. per g., 40 to 0°) gave 0.47 g., 37% of crystals, m.p. 55.5–57°. Repeated recrystallizations from ethanol and from acetone water mixtures gave a constant melting point of 57.0–57.3°.

Anal. Calcd. for $C_5H_{10}N_4O_2$: C, 38.0; H, 6.37; N, 35.4. Found: C, 38.2; H, 6.53; N, 35.2.

N,N'-Dimethyl-N,N'-dinitro-1,2-diaminoethane (IV).—A solution of 0.002 mole (0.084 cc.) of 99.9% nitric acid, 0.003 mole (0.27 cc.) of acetic anhydride, 0.0002 mole (0.014 cc.) of acetyl chloride and 0.4 cc. of acetic acid, prepared at 0° was used to dissolve 0.0004 mole (0.063 g.) of 2-nitro-5-cyano-2,5-diazahexane (III). The temperature was kept at 0° for 30 minutes and then at 25° for 38 hours. During this period a colorless gas was evolved and a crystalline precipitate appeared. It weighed 0.013 g., m.p. 129/134°. The filtrate was poured into 10 g. of ice. The resulting solution was vacuum concentrated to yield an additional 0.012 g. of crystal, m.p. 129–132°. The crude products were combined, and after recrystallization from absolute ethanol weighed 0.013 g. (18%) and melted at 134–135°. The melting point was not depressed on admixture with authentic (IV).[11]

(14) A. P. N. Franchimont, *Rec. trav.chim.*, **13**, 308 (1894).

(15) H. Van Erp, *ibid.*, **14**, 1 (1895).

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