[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, ILLINOIS INSTITUTE OF TECHNOLOGY AND CHEMISTRY DIVISION, RESEARCH DEPARTMENT, U. S. NAVAL ORDNANCE TEST STATION]

ACETYLATION AND RING CLOSURE IN REDUCTION OF NITRO- AND NITROAMINO-GUANIDINE[1]

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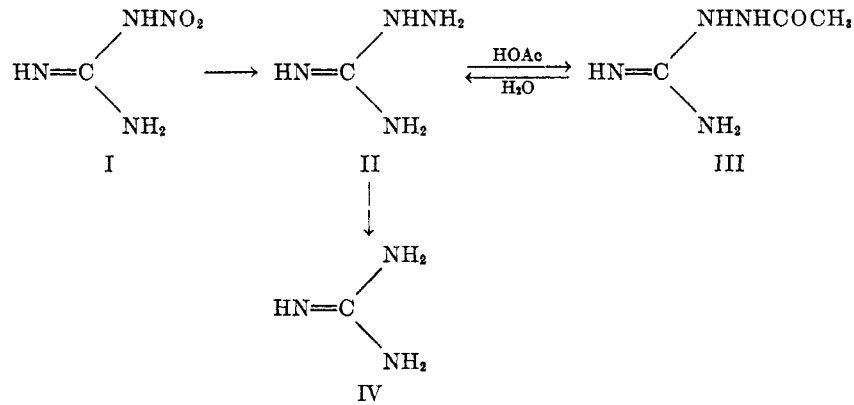
This investigation was prompted by repeated failure to obtain diaminoguanidine by the zinc-acetic acid reduction of nitroaminoguanidine as described by Phillips and Williams (1). This procedure involves the evaporation of the aqueous acetic acid solution of the reduction product, after removal of the zinc, to a residue which is recrystallized in the form of a hydrochloride. We have shown that the product obtained under these conditions is not diaminoguanidine hydrochloride and have identified it as 3-methyl-4,5-diamino-1,2,4-triazole (IX). Similar difficulties with the Phillips and Williams procedure were experienced by O'Connor, Horgan, and Reilly (2) who indicated that the contaminants were triazole derivatives. Evidence for triazole formation, however, was not presented.[4] The same difficulties are experienced in attempts to prepare diaminoguanidine by hydrogenation of nitroaminoguanidine in acetic acid using a platinum catalyst. Besides unidentified products, it is significant to note that small amounts of aminoguanidine have been isolated (3, 4) indicating hydrogenolysis of a hydrazino-group. In view of this it was deemed important to re-examine the hydrogenation of nitroguanidine in acetic acid for products resulting from hydrogenolysis, acetylation, and ring closure not previously reported (5). The present investigation will also show the course of the reactions taken by nitroaminoguanidine in its reduction in acetic acid media.

The hydrogenation of nitroguanidine (I) in acetic acid resulted in the isolation of two additional products not previously reported by Lieber and Smith (5).



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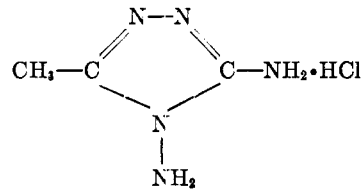
[4] *Note Added in Proof.* Sometime after this manuscript had been accepted for publica-

Aminoguanidine (II), 1-acetamidoguanidine (III), and guanidine (IV), are formed in approximately equal quantities. The method of recovery of II, as described by Lieber and Smith (5), in the form of the sulfate or hydrochloride salt results in higher yields of II due to the ready hydrolysis of III to II.

In contrast to nitroguanidine, the hydrogenation of nitroaminoguanidine (V), in acetic acid, using low ratios of catalyst to substrate, proceeds very sluggishly and with incomplete absorption of hydrogen. However, as the ratio of catalyst to V increases, the rate of reduction and percent hydrogen absorption markedly increases. The use of 1.5 g. of PtO_2 for 0.05 mole of V was found to result in the theoretical absorption of hydrogen within several hours. Using the Phillips and Williams (1) isolation procedure the product obtained was not diaminoguanidine hydrochloride but was subsequently identified as 3-methyl-4,5-diamino-1,2,4-triazole hydrochloride (IX).

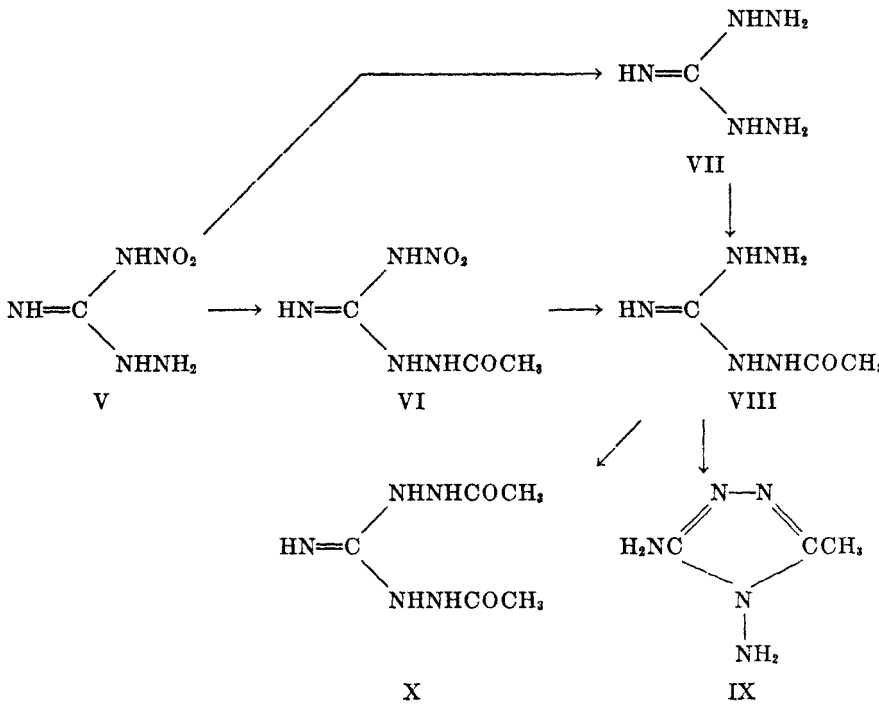


IX

This product was isolated, in yields ranging from 20 to 65%, on many repetitions of the zinc-acetic acid reduction procedure of Phillips and Williams (1). If the evaporative step be eliminated in both the hydrogenation and zinc-acetic acid reductions then diaminoguanidine (VII) and 1-acetamido-2-aminoguanidine (VIII) can be isolated from the solution containing the reduction products. If the reduction be carried out under conditions in which acetylation is not possible, *i.e.*, by zinc-hydrochloric acid, then diaminoguanidine can be isolated as the picrate in yields up to 80%.

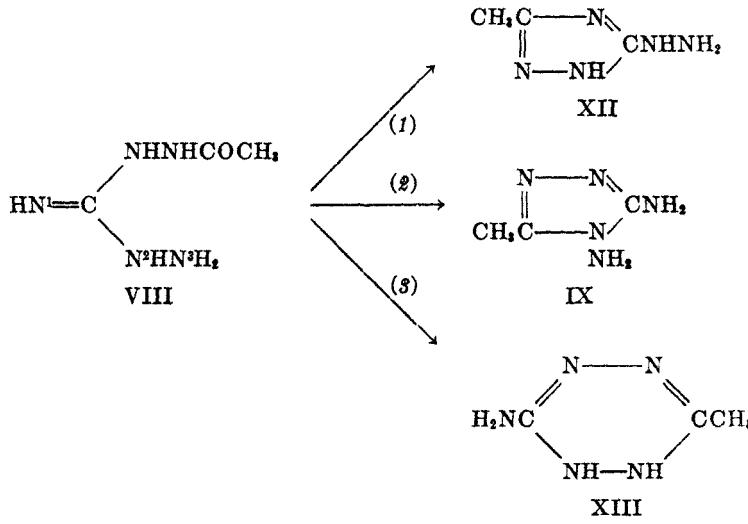
The formation of the triazole (IX) arises from the *a priori* acetylation of V and its reduction product, diaminoguanidine (VII), as evidenced by the isolation of both of these species from the reduction solution and the demonstration that IX can be prepared independently by acetylation of VII. The ease of acetylation of hydrazino-groups was further evidenced by the isolation of 1,2-diacetamidoguanidine (X). Henry (6) has shown that 1-acetamido-2-nitroguanidine (VI) can be independently prepared by heating nitroaminoguanidine with acetic anhydride-acetic acid at 85–90°. The present work has demonstrated that nitroaminoguanidine can be acetylated by merely shaking with acetic acid at room temperature. The further observation arose that VI hydrogenates with much greater ease than the parent substance under the same conditions of catalyst to substrate ratio. Derivatives of 1-acetamido-2-aminoguanidine (VIII) were then isolated by an independent study of the zinc-acetic acid reduction of VI.

tion, our attention was directed to an article by Scott, O'Sullivan, and Reilly [*J. Applied Chem.*, **2**, 184 (1952)] in which limited evidence was presented that this compound was 3-methyl-4,5-diamino-1,2,4-triazole. This is the same conclusion reached in this paper on the basis of more evidence.



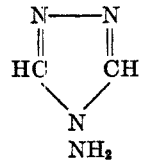
Further recovery of the reduction products from solution, *i.e.*, under mild conditions, fails to yield any cyclized products; however, evidence for extensive acetylation, under relatively mild conditions, was readily demonstrated.

The cyclization of 1-acetamido-2-aminoguanidine (VIII) can theoretically give rise to three products:



depending on whether the ring closure takes place at N^1, N^2, or N^3. However, the evidence indicates that this ring closure takes place predominately through N^2

rather than N^1 or N^3 and that the product has structure IX. 3-Methyl-5-hydrazino-1,2,4-triazole (XII) can be excluded immediately since it was synthesized independently by the reduction of 3-methyl-5-nitroamino-1,2,4-triazole (6) and was found to have distinctly different physical and chemical properties than those observed for compound IX. For example, the latter compound does not react with benzaldehyde in acid medium, whereas XII forms a mono-benzal hydrazone under these conditions; on the other hand, compound IX does react with two moles of benzaldehyde in basic medium. Furthermore, the methylhydrazinotriazole (XII) rapidly reduces ammoniacal silver nitrate, while compound IX only reduces this reagent very slowly. This latter behavior is similar to that observed with 4-amino-1,2,4-triazole;



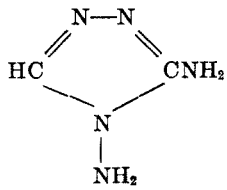
XIV

a homolog of IX, which was synthesized by the method of Allen and Bell (7).

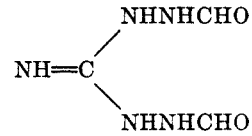
The possibility that the cyclization of acetamidoaminoguanidine (VIII) led to 3-amino-6-methyl-1,2-dihydro-1,2,4,5-tetrazine (XIII) can also be eliminated directly on the basis of the evidence presented in the following paragraph and more indirectly by the fact that the compound under question (IX) could not be oxidized to anything which corresponded to an intensely, red-colored tetrazine.

The presence of a triazole ring in compound IX was shown in two ways: (a) When 3-methyl-4,5-diamino-1,2,4-triazole (IX) is diazotized at $-5°$ to $0°$ with two moles of nitrous acid, there is an immediate, vigorous evolution of gas and the resulting diazonium solution couples with 2-naphthol to give 1-(3-methyl-1,2,4-triazole-5-azo)-2-naphthol. The latter compound was prepared for comparison by diazotizing an authentic sample of 3-methyl-5-amino-1,2,4-triazole with one mole of nitrous acid and coupling with 2-naphthol. (b) When IX is diazotized with two moles of nitrous acid in the presence of hypophosphorous acid, 3-methyl-1,2,4-triazole can be isolated.

The reaction of diaminoguanidine with formic acid was also investigated and two products were isolated: 3,4-diamino-1,2,4-triazole (XV) and 1,2-diformamidoguanidine (XVI),



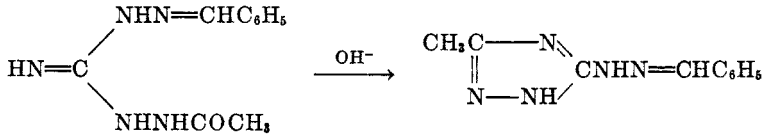
XV



XVI

in the form of their respective nitrate salts. The structure of XV has not been rigorously proved and is assigned only by analogy to IX.

Although 1-acylamino-2-aminoguanidines cyclize in acidic medium to give predominantly 4,5-diamino-1,2,4-triazoles (ring closure on N^2), in basic medium ring closure involves N^1 and derivatives of 5-hydrazino-1,2,4-triazole are formed predominantly. This was demonstrated by a study of the alkali-catalyzed cyclization of benzal 1-acetamido-2-aminoguanidine (XVII):



XVII XVIII

The product was benzal 3-methyl-5-hydrazino-1,2,4-triazole (XVIII), and was identical with the benzal hydrazone derived from compound XII. The ring closure in basic medium is strictly an extension of the method of Thiele and Heidenreich (8) for the synthesis of 5-amino-1,2,4-triazoles from 1-(acylamino)guanidines.

EXPERIMENTAL

Melting points are uncorrected unless otherwise stated. Micro analyses by Micro Tech Laboratory, Skokie, Illinois and Dr. Adalbert Elek, Los Angeles, California.

Catalytic hydrogenation of nitroguanidine. Nitroguanidine (10.49 g., 0.1 mole) and 0.3 g. of platinum oxide catalyst were suspended in 150 ml. of glacial acetic acid. The hydrogenation was started at 50 pounds pressure and room temperature. Slightly more than 0.3 mole of hydrogen was absorbed in three hours. The catalyst was removed by filtration and the filtrate diluted with water to 250 ml. Potentiometric titration of 1-ml. aliquots with standard potassium iodate solution (9) indicated that about 31.5% free *aminoguanidine*, 34.9% *1-acetamidoguanidine* and, by difference, 33.6% *guanidine* were formed.

Nitric acid (9 g. of 70% acid) and 10.6 g. (0.1 mole) of benzaldehyde were added to the balance of the diluted filtrate and the solution was allowed to stand overnight at 0°. Since no precipitate formed, a solution of 23.9 g. (0.1 mole) of picric acid in 100 ml. of hot methyl alcohol was added, and the precipitated picrates were removed by filtration. The mixture of picrates, after drying, amounted to 20.0 g. A portion was titrated potentiometrically with iodate solution (9) and found to contain 53.7% *benzalaminoguanidine picrate*. Based on nitroguanidine the conversion to aminoguanidine was 27.5%. The balance of this fraction is essentially *guanidine picrate;* by difference, therefore, the yield of guanidine is calculated to be about 32% based on the nitroguanidine. By slurrying the mixture repeatedly with hot water to extract benzalaminoguanidine picrate, some of the *guanidine picrate* could be recovered in a reasonably pure state (m.p.>300°); the x-ray powder pattern was identical with that of an authentic sample.

Dilution of the filtrate with about 200 ml. of water precipitated 6.9 g. of a picrate, m.p. 218–220°. Recrystallization from hot water raised the melting point to 222.5–223.5°. A mixture melting point with an authentic sample (10) of *1-acetamidoguanidine picrate* was not depressed and an x-ray powder pattern of the product was identical with that of 1-acetamidoguanidine picrate.

Anal. Calc'd for $C_9H_{11}N_7O_8$: Hydrazine nitrogen, 8.12. Found: Hydrazine nitrogen, 8.03, 8.08.

Further dilution of the mother liquors with water did not precipitate additional picrate, so the filtrate was concentrated under reduced pressure on a steam-bath to about 100 ml. and cooled. The precipitated picrate (5.3 g.) was removed by filtration, dried, and identified as *benzalaminoguanidine picrate*, m.p. 254–255° (10, 11). Further concentration yielded precipitates consisting mostly of picric acid. It is presumed that heating the filtrate during

concentration hydrolyzed the remaining 1-acetamidoguanidine to aminoguanidine which separated as the picrate of the benzal derivative.

Titration of a similar hydrogenation made in 50% aqueous acetic acid indicated that about 60% free aminoguanidine, 15.5% 1-acetamidoguanidine and, by difference, 24.5% guanidine were formed.

Reduction of nitroaminoguanidine with zinc and hydrochloric acid. Activated zinc dust (12) (35 g.) and 5.95 g. of nitroaminoguanidine (13) were placed in a 2-liter beaker together with 100 ml. of an ice-water mixture. An acid solution, consisting of 40 ml. of conc'd hydrochloric acid and 110 ml. of ice-water was slowly added to the zinc-nitroaminoguanidine mixture. The mixture was stirred for an hour while ice was being added to keep the temperature below 10°. The zinc metal was filtered off and the filtrate was evaporated until a viscous liquid formed. On cooling, a gum was obtained. This was dissolved in 200 ml. of warm water and filtered. The filtrate was treated with a saturated solution of picric acid and cooled in the refrigerator overnight and 12.21 g. (76.7%) of crude *diaminoguanidine picrate* was filtered off. A portion was purified for analysis by recrystallization from alcohol; m.p. 192–194° (14); the melting point was not depressed on admixture with an authentic sample of diaminoguanidine picrate.

Anal. Calc'd for $C_7H_{10}N_8O_7$: N, 35.22. Found: N, 35.46.

Reduction of nitroaminoguanidine with zinc and acetic acid. Preparation of dibenzaldiaminoguanidine picrate. A solution of 25 ml. of glacial acetic acid in 225 ml. of ice-cold water was added with vigorous agitation during 80 minutes to a slurry of 5.95 g. (0.05 mole) of nitroaminoguanidine, 35 g. of zinc dust, and 50 ml. of ice-water; the temperature was maintained at 7–10° by cooling. When the addition of acid was completed, the solution was allowed to warm to 15° during 40 minutes, then heated to and maintained at 35–40° for 30 minutes. The unreacted zinc was removed and the filtrate saturated with hydrogen sulfide for one hour. The precipitated zinc sulfide was removed and washed several times with cold water. The combined filtrates were acidified with 10 ml. of 70% nitric acid, heated to 50°, and shaken with 12 ml. of benzaldehyde. The granular white precipitate, which separated almost immediately, was removed after the solution had been chilled to 0°. The hydrazone was first washed with two 50-ml. portions of cold water, and then with two 50-ml. portions of petroleum ether to remove excess benzaldehyde. The impure, air-dried *dibenzaldiaminoguanidine nitrate* (12.9 g., m.p. 175–185° dec.) was dissolved in 200 ml. of boiling 95% ethanol and treated with 10 g. of picric acid in 100 ml. of hot 95% ethanol. After the solution had been recooled to room temperature, the picrate was removed and washed several times with cold ethanol. The yield of dried product was 18.7 g. (75.7%) of practically pure *dibenzaldiaminoguanidine picrate*; m.p. 240–241° (dec.). A mixture melting point with an authentic sample of dibenzaldiaminoguanidine picrate (11) (m.p. 241–242°) was 242–243° (dec.).

Reaction of nitroaminoguanidine and acetic acid. Preparation of 1-acetamido-2-nitroguanidine. Nitroaminoguanidine (5.95 g., 0.05 mole) was shaken with 150 ml. of glacial acetic acid at room temperature for 18 hours. The reaction mixture was diluted to 350 ml. with water and vacuum-evaporated to dryness on a steam-bath. The residue was washed with 75 ml. of water and filtered. The filtrate (A) was retained. The residue was washed with 125 ml. of ethanol yielding a residue (B) and filtrate (C). The melting point of (B) was found to be 205–208° (dec.). Two recrystallizations of (B) yielded 2.86 g. of a product, m.p. 203–206°. A mixture melting point with an authentic sample of 1-acetamido-2-nitroguanidine (6) (m.p. 199–201°) was 203–206° dec. Evaporation of filtrate (C) gave an additional 0.39 g. of 1-acetamido-2-nitroguanidine. Total yield 3.25 g. (40.4%).

Anal. Calc'd for $C_3H_7N_5O_3$: N, 43.47. Found: N, 43.20.

Evaporation of filtrate (A) and recrystallization of the residue from water-alcohol mixture gave 1.68 g. (28.2%) of recovered nitroaminoguanidine.

Benzal 1-acetamido-2-aminoguanidine nitrate. Glacial acetic acid (26 ml.) was added with stirring during 30 minutes to a slurry of 10.0 g. of 1-acetamido-2-nitroguanidine, 16 g. of zinc dust, and 90 ml. of water. The temperature was held at 23–28° by cooling in an ice-

water bath. After the acid had been added, the stirring was continued for another 30 minutes. Unreacted zinc dust was then removed and washed with 10 ml. of water. The filtrate was acidified with 5 ml. of 70% nitric acid and shaken for 10 minutes with 6.5 ml. of benzaldehyde. When the resulting homogeneous solution was chilled to 0° and seeded, the hydrazone crystallized slowly. After overnight cooling, the product was removed and dried; the yield was 12.1 g. (69.2%). The m.p. after one recrystallization from water, was 170–171°.

Anal. Calc'd for $C_{10}H_{14}N_6O_4$: C, 42.55; H, 5.00.
Found: C, 42.71; H, 5.62.

The *picrate* after recrystallization from 50% aqueous ethanol melted at 223–224° (dec.).

Anal. Calc'd for $C_{16}H_{16}N_8O_8$: N, 24.99. Found: N, 24.57.

The *free base* recrystallized from 50% aqueous ethanol as fluffy rosettes of fine, white needles, m.p., 250–252° (dec.).

Anal. Calc'd for $C_{10}H_{12}N_6O$: C, 54.78; H, 5.98; N, 31.95.
Found: C, 54.63; H, 6.13; N, 32.06.

Hydrogenation of nitroaminoguanidine. Formation of diaminoguanidine and 1-acetamido-2-aminoguanidine. Nitroaminoguanidine (5.95 g., 0.05 mole) and 1.5 g. of platinum oxide catalyst were suspended in 150 ml. of glacial acetic acid. The hydrogenation was started at 50 pounds hydrogen pressure and room temperature and approximately complete absorption of hydrogen was obtained in 24 hours. The catalyst was then removed by filtration.

Nitric acid (9 g. of 70% acid) and 10.6 g. (0.1 mole) of benzaldehyde were then added. The solution was allowed to stand for one hour and then cooled to 10°. The white crystalline solid which was removed by filtration weighed 0.9 g. after drying. It was identified as *benzalnitroaminoguanidine* by m.p. (187°) and mixture melting point with an authentic sample. The recovery corresponds to 8.4% nitroaminoguanidine.

Ammonium picrate (12.3 g., 0.05 mole) in a minimum volume of hot water was added to the filtrate and the solution diluted with water to about 800 ml. The precipitated picrate, after filtration and drying weighed 7.8 g., m.p. 217–219°. Recrystallization from 50% aqueous ethanol raised the melting point to 222–223°. A mixture melting point with the *benzal-1-acetamido-2-aminoguanidine*, prepared above, was not depressed.

Anal. Calc'd for $C_{16}H_{16}N_8O_8$: C, 42.86; H, 3.60; N, 24.99.
Found: C, 43.04; H, 3.91; N, 24.63.

The conversion to 1-acetamido-2-aminoguanidine, based on nitroaminoguanidine, was 47%.

The insoluble residue from the recrystallization of the benzal 1-acetamido-2-aminoguanidine amounted to 0.62 g., m.p. 240–244°. A mixture melting point with an authentic sample of *dibenzaldiaminoguanidine picrate* was not depressed. This yield represents a 2.5% conversion.

Concentration of the mother liquors under reduced pressure on the steam-bath yielded mainly ammonium picrate.

The material balance of products isolated amounted to 57.9% based on nitroaminoguanidine.

1,2-Diacetamidoguanidine hydrochloride. Nitroaminoguanidine (5.95 g., 0.05 mole), 1.5 g. platinum oxide catalyst, and 150 ml. of glacial acetic acid were shaken with hydrogen at an initial pressure of 42 pounds and room temperature. The theoretical absorption of hydrogen required two hours. The catalyst was then removed. The filtrate was diluted to 300 ml. with water, 5 ml. of concentrated hydrochloric aicd was added, and the mixture was vacuum-evaporated to dryness on the steam-bath. The residue was recrystallized from ethanol; m.p. 209–210°. Successive recrystallizations from ethanol yielded white needles, the melting point on each successive crystallization being 197–203°.

Anal. Calc'd for $C_5H_{12}ClN_5O_2$: N, 33.40, Cl, 16.91.
Found: N, 33.65; Cl, 17.12.

By working up the mother liquors successive increments of a white solid melting above 260° and identified as ammonium chloride was obtained.

3-METHYL-4,5-DIAMINO-1,2,4-TRIAZOLE HYDROCHLORIDE

(*A*) *By hydrogenation of nitroaminoguanidine.* Nitroaminoguanidine (5.95 g.), 1.5 g. of platinum oxide catalyst, and 150 ml. of glacial acetic acid were shaken with hydrogen at an initial pressure of 45 pounds and room temperature. Absorption of the theoretical quantity of hydrogen required 21 hours at which time the reaction mixture had solidified to a grey mass. The grey mass was dissolved in 200 ml. of water and filtered. The filtrate was treated with 5 ml. of concentrated hydrochloric acid and vacuum-evaporated on a steam-bath until incipient crystallization occurred. After cooling, the crystals were removed and identified as ammonium chloride.

The filtrate was evaporated on the steam-bath to 10 ml. and a white powder was obtained on cooling. Re-concentration of the mother liquors yielded further quantities of the white powder, which were combined and recrystallized from ethanol. The total yield was 0.89 g. (11.9%).

Anal. Calc'd for $C_3H_8ClN_5$: C, 24.08, H, 5.39; Cl, 23.70; N, 46.82.
Found: C, 24.23; H, 5.40; Cl, 23.20; N, 47.00.

3-Methyl-4,5-diamino-1,2,4-triazole hydrochloride is a white powder whose uncorrected melting point was found to be 244–248° when taken on the Fisher-Jones block. The compound sublimes at about 205° and covers the upper slide on the block, thus making it difficult to observe the melting point. When the melting point is taken in a sealed capillary, in a Thiele tube, the compound decomposes into an orange-pink liquid at 243–246°, uncorrected; 250–253°, corrected. It is completely soluble in water, slightly soluble in alcohol, and insoluble in ethyl ether, dioxane, chloroform, benzene, and carbon tetrachloride. With ammoniacal silver nitrate a white precipitate is first formed; this gradually turns grey and finally black, indicating a slow reduction. Fehling's solution is not reduced by the compound even on prolonged heating.

The *picrate*, by reaction of the hydrochloride with a saturated aqueous picric acid solution, consists of small yellow needles which, after recrystallization from water, melt at 188°.

Anal. Calc'd for $C_9H_{10}N_8O_7$: C, 31.60; H, 2.95; N, 32.75.
Found: C, 31.76; H, 3.16; N, 32.50.

The *nitrate* was prepared by double decomposition with silver nitrate. After removal of the silver chloride, the residue obtained on evaporation of the filtrate was recrystallized to constant melting point from ethanol. Two recrystallizations produced a melting point of 187–188°.

Anal. Calc'd for $C_3H_8N_6O_3$: N, 47.73. Found: N, 48.01.

(*B*) *By zinc-acetic acid reduction of nitroaminoguanidine.* Zinc dust (35 g.), 5.95 g. of nitroaminoguanidine, and 50 g. of an ice-water mixture were placed in a 3-necked 2-liter flask which was equipped with a stirrer and immersed in an ice-bath. An acetic acid solution (25 ml. of glacial acetic acid and 225 ml. of ice-water) was slowly added to the mixture in the flask with stirring. After the addition of the acid, mixing was maintained for one hour at 10° and then allowed to warm to 25°. The unreacted zinc dust was filtered off and the solution was saturated with H_2S. The zinc sulfide was removed by filtration.

The clear filtrate was treated with 5 ml. of concentrated hydrochloric acid and evaporated to dryness on the steam-bath. Then 60 ml. of 1.2 *N* hydrochloric acid was added to the residue and the solution was re-evaporated to dryness. The yellow residue was taken up in hot ethanol, charcoaled, and filtered into 50 ml. of ether. The warm solution was cooled in the refrigerator. A white powder was filtered off and air-dried. The melting point was found to be 244–248° and the yield of *3-methyl-4,5-diamino-1,2,4-triazole hydrochloride* was 4.87 g. (64.9%). The melting point was not depressed on admixture with the compound obtained by hydrogenation (*A*).

(*C*) *By hydrogenation of 1-acetamido-2-nitroguanidine.* 1-Acetamido-2-nitroguanidine (6.04 g., 0.037 mole), 1.5 g. of PtO_2 catalyst, and 150 ml. of glacial acetic acid were shaken with hydrogen at an initial pressure of 35 pounds and room temperature. Absorption of the theoretical quantity of hydrogen required 15 min. The reaction mixture was diluted to 225 ml. with water and filtered. The filtrate was treated with 4 ml. of concentrated hydro-

chloric acid and evaporated to dryness in a vacuum on a steam-bath. The residue was dissolved in ethanol and ether was added to the cooled solution until precipitation occurred. The precipitate was removed and identified as ammonium chloride. The ethanol-ether mother liquor was evaporated to a gummy liquid, and the gum dissolved in hot ethanol. On cooling a white powder melting at 240–244° was obtained. The yield of *3-methyl-4,5-diamino-1,2,4-triazole hydrochloride* was 0.45 g. (8.1%). A mixture melting point with an authentic sample of the salt showed no depression.

(*D*) *By acetylation of diaminoguanidine hydrochloride.* One ml. of acetic anhydride, 4 ml. of glacial acetic acid, and 0.4 g. (0.0032 mole) of diaminoguanidine hydrochloride were heated on the steam-bath under a cold-finger condenser. After 1.5 hours of heating the solution became clear and it was poured into a small flask. The reaction tube was washed out with 25 ml. of ether which was added to the original reaction solution which had become cloudy. No crystallization took place on refrigeration. The solution was then evaporated to dryness and the residue was treated with 25 ml. of concentrated hydrochloric acid and again evaporated to dryness. The residue was dissolved in hot ethanol and cooled. A white powder was filtered off which sublimed at 200° and melted at 240–245°. The yield of *3-methyl-4,5-diamino-1,2,4-triazole hydrochloride* was 0.17 g. (35%). A mixture melting point with an authentic sample of the salt showed no depression.

Dibenzal 3-methyl-4,5-diamino-1,2,4-triazole. A solution of 2.0 g. of the hydrochloride, 1.2 g. of piperidine, and 2.8 g. of benzaldehyde in 25 ml. of 95% ethanol was refluxed for two hours. The yellow-colored solution was cooled to room temperature, diluted with 25 ml. of water, and chilled overnight at 0°. The felted, yellow needles were removed, washed with 30% ethanol, and dried; yield; 1.7 g., m.p. 160–165°. One recrystallization from 50 ml. of 50% ethanol raised the melting point to 167.5–168.5°.

Anal. Calc'd for $C_{17}H_{15}N_5$: C, 70.57; H, 5.23; N, 24.21.

Found: C, 70.33; H, 5.52; N, 24.28.

There was no evidence of reaction when an aqueous solution of the hydrochloride was shaken for three days at room temperature with one equivalent of benzaldehyde.

1-(3-Methyl-1,2,4-triazole-5-azo)-2-naphthol from 3-methyl-4,5-diamino-1,2,4-triazole. A solution of 1.35 g. (0.0196 mole) of sodium nitrite in 10 ml. of cold water was added all at once to a stirred mixture of 1.45 g. (0.0097 mole) of 3-methyl-4,5-diamino-1,2,4-triazole hydrochloride, 2 ml. of concentrated hydrochloric acid, 30 g. of crushed ice, and 20 ml. of ice-water. The stirring was continued for 20 minutes; the temperature was maintained at −5 to 0°. Gas was evolved and the solution assumed a deep yellow color. When the diazotization was completed, a cold solution of 1.44 g. (0.01 mole) of 2-naphthol, 0.45 g. of sodium hydroxide, and 30 ml. of water was added all at once. There was an immediate precipitation of the orange azo compound; stirring was continued for one hour at 5–10°. After the solution had been adjusted to *p*H 7, the compound was removed, washed with cold water, and recrystallized from 100 ml. of 95% ethanol; orange crusts of needles, which melt at 199–202°, change color, resolidify, and remelt at 215–216°. Morgan and Reilly (15) report m.p. 213–215° for 1-(3-methyl-1,2,4-triazole-5-azo)-2-naphthol. The melting point was not depressed when the compound was mixed with a sample of azo compound prepared from authentic 3-methyl-5-amino-1,2,4-triazole.

3-Methyl-1,2,4-triazole from 3-methyl-4,5-diamino-1,2,4-triazole. A solution consisting of 6.65 g. (0.0445 mole) of recrystallized 3-methyl-4,5-diamino-1,2,4-triazole hydrochloride, 13.2 g. (0.099 mole) of 50% hypophosphorous acid, and 45 ml. of water was cooled to 10°. A solution of 6.2 g. (0.09 mole) of sodium nitrite in 15 ml. of water was added during one hour with agitation while the temperature was maintained between 10 and 15° by external cooling. One hour more was allowed to complete the reaction. After the solution had been adjusted to *p*H 8, it was evaporated to dryness at water-aspirator pressure. The residue was extracted with one 50-ml. and four 25-ml. portions of boiling ethyl acetate, the extracts combined, and evaporated to dryness. The weight of impure product melting about 80° was 2.3 g. (63%). Recrystallization from benzene raised the melting point to 94–95°; the reported value (16) for 3-methyl-1,2,4-triazole is 95°.

Reaction of diaminoguanidine nitrate with formic acid. 3,4-Diamino-1,2,4-triazole and 1,2-diformamidoguanidine. Two ml. of 88% formic acid, 4.56 g. (0.03 mole) of diaminoguanidine nitrate, and 6 ml. of dioxane were refluxed on a steam-bath for 2 hours. After 10 minutes of heating, two layers formed and after 30 minutes crystals had formed in the lower layer. The mixture was cooled and a slightly yellow precipitate (A) was filtered off, washed with mother liquor and air-dried. The filtrate (B) still contained two layers and was replaced in the refrigerator. The yield of (A), m.p. 188–194° was 2.91 g. On recrystallization from a water-ethanol mixture, the product melted at 197–199°. A recrystallization from ethanol gave white needles, m.p. 198–199°; the yield was 1.95 g. (40%). The analyses are in agreement with those expected for 3,4-diamino-1,2,4-triazole.

Anal. Calc'd for $C_2H_6N_6O_3$: C, 14.82; H, 3.73; N, 51.85.

Found: C, 14.94; H, 4.00; N, 52.08.

The precipitate (C), which separated from the bottom layer of filtrate (B), was removed by filtration, and vacuum-dried. The yield of (C), m.p. 126–129°, was 1.10 g. One recrystallization of (C) from ethanol gave silky white needles, m.p. 154–155°. The melting point after one further recrystallization from ethanol was 155° and the yield of pure *1,2-diformamidoguanidine nitrate* was 0.32 g. (5%).

Anal. Calc'd for $C_3H_8N_6O_5$: C, 17.31; H, 3.88; N, 40.39.

Found: C, 16.84; H, 3.98; N, 40.81.

3-Methyl-5-hydrazino-1,2,4-triazole. To a slurry of 28.6 g. (0.2 mole) of 3-methyl-5-nitroamino-1,2,4-triazole (6) and 52 g. of zinc dust in 300 ml. of water was added 85 ml. of glacial acetic acid with stirring during 1.75 hours; the temperature was maintained at 25–30°. The mixture was next stirred for 45 minutes at 35–40° after which it was warmed to 50° and filtered from unreacted zinc. The filtrate was saturated with H_2S for 5 hours to insure complete precipitation of zinc sulfide. The latter was then removed and washed with several small volumes of cold water. After 20 ml. of concentrated hydrochloric acid had been added to the filtrate, it was evaporated to dryness under reduced pressure. The solid residue was extracted with one 75-ml. and three 50-ml. portions of absolute ethanol, followed by two 55-ml. portions of 85% ethanol; the remaining residue was retained (B).

(*A*). When the combined alcoholic extracts were concentrated to 125 ml. and chilled to 0°, 3.75 g. of material, melting at 235–236° (dec.), crystallized. Upon further evaporation of the mother liquors to 15 ml. and cooling an additional 1.25 g. was obtained. These two crops were combined and recrystallized from 120 ml. of 83% aqueous methanol; the recovery of *3-methyl-5-hydrazino-1,2,4-triazole hydrochloride was* 2.35 g., m.p. 236–239° (dec.). This compound was readily soluble in water and showed strong reducing properties.

Anal. Calc'd for $C_3H_8ClN_5$: C, 24.08; H, 5.39; N, 46.82.

Found: C, 24.36; H, 5.57; N, 47.01.

(*B*). The residue from the alcohol extractions was dissolved in 75 ml. of water, warmed to 50°, and shaken with 5 ml. of benzaldehyde; 7.65 g. of impure *benzal 3-methyl-5-hydrazino-1,2,4-triazole hydrochloride* was recovered. Two wasteful recrystallizations from 95% ethanol gave rosettes of very fine needles, decomposing at 219–220°.

Anal. Calc'd for $C_{10}H_{12}ClN_5$: N, 29.47. Found: N, 29.57.

The *free base*, benzal 3-methyl-5-hydrazino-1,2,4-triazole, melted at 267–268° after recrystallization from 80% ethanol.

Anal. Calc'd for $C_{10}H_{11}N_5$: C, 59.68; H, 5.51; N, 34.81.

Found: C, 59.67; H, 5.50; N, 34.94.

The *picrate* of the *benzal hydrazone* crystallized from 95% ethanol as needles, m.p. 247–248° (dec.).

Anal. Calc'd for $C_{16}H_{14}N_8O_7$: N, 26.04. Found: N, 26.19.

Cyclization of benzal 1-acetamido-2-aminoguanidine nitrate. Benzal 1-acetamido-2-aminoguanidine nitrate (2.8 g.) was dissolved in 50 ml. of hot 50% aqueous ethanol and made just alkaline to phenolphthalein with sodium hydroxide. The solution was refluxed for 2 hours on the steam-bath; some pale yellow flat needles began to crystallize before the heating was completed. After the solution had been cooled slowly to 30°, the

product was removed by filtration and washed with two 10-ml. portions of 50% ethanol. The yield of *benzal 3-methyl-5-hydrazino-1,2,4-triazole* was 0.65 g. (33%); the melting point was 267–268° and was not depressed by admixture with the benzal derivative prepared in the previous experiment.

The only other product recovered (66%) from the mother liquors was uncyclized starting material.

SUMMARY

Guanidine and 1-acetamidoguanidine have been isolated from the hydrogenation of nitroguanidine in acetic acid. Large ratios of catalyst to substrate are necessary for the successful hydrogenation of nitroaminoguanidine in this media. Nitroaminoguanidine undergoes acetylation in acetic acid under mild conditions and the 1-acetamido-2-nitroguanidine hydrogenates with much greater ease than the parent substance.

1-Acetamido-2-aminoguanidine can be recovered as derivatives from the reduction products if mild conditions are employed; generally, however, this compound undergoes cyclization to 3-methyl-4,5-diamino-1,2,4-triazole under the conditions of recovery from acidic medium. Acetylation or formylation of diaminoguanidine salts also yields similarly substituted triazoles. Evidence is presented to support the structure assigned to these cyclized products. In basic medium benzal 1-acetamido-2-aminoguanidine undergoes ring closure to benzal 3-methyl-5-hydrazino-1,2,4-triazole.

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