[CONTRIBUTION FROM DEFENCE RESEARCH CHEMICAL LABORATORIES, CANADA]

The Reaction of Amines with 3-Nitroso-2-oxazolidone[1]

BY A. F. McKAY AND E. J. TARLTON

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In order to obtain more information on the mechanism of the reaction of amines with nitrosamides their reaction with 3-nitroso-2-oxazolidone was studied. The major products from this reaction were 2-*p*-arylaminoethyl N-*p*-arylcarbamates, N,N'-di-*p*-arylethylenediamines, carbon dioxide and nitrogen. A scheme is presented to explain in part the formation of these products.

Recently[2] a scheme was outlined for the reaction of amines with 1-nitroso-2-nitramino-2-imidazoline.[2-4] The products from these reactions contained large amounts of oils which could not be converted to identifiable products by picrate formation or use of the Hinsberg amine separation technique. An attempt to fractionally distil these oils resulted in some decomposition. The temperature was not taken too high because of the possible presence of nitramines. As a consequence of these unidentified oils, another cyclic nitrosamide, 3-nitroso-2-oxazolidone,[5] was investigated because it was anticipated that the products from the reaction of the latter compound with amines could be examined more fully.

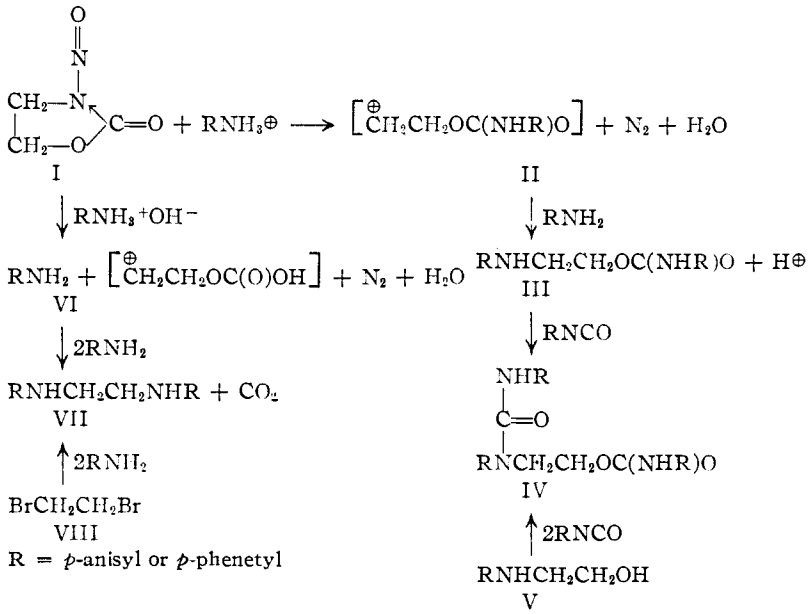
In 1905, Gabriel[5] decomposed 3-nitroso-2-oxazolidone with dilute alkali into carbon dioxide, nitrogen, acetylene and water. The acetylene accounted for only 25–33% of the ethylene group in the oxazolidone. It is quite probable that the remainder of the ethylene group formed acetaldehyde or glycol, since Gabriel showed that other similar nitrosamides gave oxygenated derivatives on decomposition with dilute alkali. More recently Newman[6] has shown that substituted-3-nitroso-2-oxazolidones can be decomposed to give the corresponding aldehydes.

In the present work *p*-anisidine (or *p*-phenetidine) was added to an aqueous ethanol solution of 3-nitroso-2-oxazolidone. The reaction products were divided into solids and filtrate. After evaporation of the filtrate an oil was obtained. The solid fraction consisted almost entirely of 2-*p*-anisylaminoethyl N-*p*-anisylcarbamate (III, R = *p*-anisyl) and N,N'-di-*p*-anisylethylenediamine (VII, R = *p*-anisyl). The structure of 2-*p*-anisylaminoethyl N-*p*-anisylcarbamate was verified by converting it into compound IV (R = *p*-anisyl) which was obtained also from N-β-hydroxyethyl-*p*-anisidine (V, R = *p*-anisyl) and *p*-anisylisocyanate. N,N'-Di-*p*-anisylethylenediamine was prepared by treating 1,2-dibromoethane with *p*-anisidine by a modification of the method of Schouten.[7] In the latter preparation N,N'-di-*p*-anisylpiperazine was obtained as a by-product.

Even with a fore-knowledge of the properties of 3-*p*-anisyl-2-oxazolidone,[8] and a very careful screening of the reaction products from *p*-anisidine with 3-nitroso-2-oxazolidone, none could be detected. The products to be expected by the replacement of the nitrosamine group by an OH group are N-β-hydroxyethyl-*p*-anisidine and β-hydroxyethyl N-*p*-anisylcarbamate. Both these compounds and some of their derivatives were prepared for comparison with the reaction products from *p*-anisidine with 3-nitroso-2-oxazolidone. These compounds were either absent or present only in traces.

The residual oil from the original filtrate on distillation gave *p*-anisidine, a trace of *sym*-di-*p*-anisylurea and a small viscous oily residue. The residue became more viscous with continued heating. Since *sym*-di-*p*-anisylurea is not present before distillation it most probably arises from the heating of *p*-anisidine carbonate and *p*-anisidine. When the oil is strongly acidified to liberate the base from the carbonate and the solution made basic to recover the oil, then no urea derivative forms during distillation.

On addition of amine to 3-nitroso-2-oxazolidone a gaseous mixture of CO_2 and N_2 was evolved. When



(1) Issued as DRCL Report No. 70.

(2) A. F. McKay, *J. Org. Chem.*, **16**, 1395 (1951).

(3) A. F. McKay, W. R. R. Park and S. J. Viron, THIS JOURNAL, **72**, 3659 (1950).

(4) A. F. McKay, *J. Org. Chem.*, **16**, 1846 (1951).

(5) S. Gabriel, *Ber.*, **38**, 2405 (1905).

(6) M. S. Newman, THIS JOURNAL, **71**, 378 (1949).

(7) A. E. Schouten, *Rec. trav. chim.*, **56**, 541 (1937).

(8) A. F. McKay and R. O. Braun, *J. Org. Chem.*, **16**, 1829 (1951).

gassing had ceased, the reaction mixture was acidified, whereupon a trace (0.46%) of acetylene was obtained. As no acetylene formed during the main reaction it was considered that decomposition of one of the products was responsible for its formation. At the end of one run the reaction mixture was acidified and heated until all the acetaldehyde (0.98%) had distilled. As this acetaldehyde does not appear to be present as a Schiff base, it is considered also to arise from hydrolysis of one of the reaction products, *e.g.*, a vinyl ester. The only probable product possessing this group would be vinyl N-*p*-anisylcarbamate. This compound was not isolated and an attempt to prepare it by the dehydrohalogenation of β-chloroethyl N-*p*-anisylcarbamate was unsuccessful.

p-Phenetidine with 3-nitroso-2-oxazolidone gave products analogous to those obtained with *p*-anisidine, *viz.*, 2-*p*-phenetylaminoethyl N-*p*-phenetylcarbamate (III, R = *p*-phenetyl), N,N'-di-*p*-phenetylethylenediamine (VII, R = *p*-phenetyl), carbon dioxide and nitrogen.

The mechanism outlined for the reaction of amines with 3-nitroso-2-oxazolidone is similar to that described for the reaction of primary aromatic amines with 1-nitroso-2-nitramino-2-imidazoline.[2] It also has points in common with the mechanism recently described by Newman and Kutner[9] for the reaction of alkali with 3-nitroso-2-oxazolidones. Although the reactions are outlined as occurring in discrete steps and the intermediates are indicated as discrete entities, it is realized that the sequence of reactions may be entirely different. However, the carbonium ion intermediates II and VI offer a reasonable explanation for the products obtained. In this reaction as in the reaction of amines with 1-nitroso-2-nitramino-2-imidazoline,[2,4] the types of products obtained depend upon the basicity of the amines. This will be described in a forthcoming paper.

Experimental[10,11]

2-Oxazolidone.—This compound (m.p. 89–90°) was prepared in 62% yield by the method of Homeyer.[12]

3-Nitroso-2-oxazolidone.—Oxazolidone-2 (47 g., 0.54 mole) was dissolved in a solution of 75 cc. of 70% nitric acid in 100 cc. of water at 10°. The temperature was maintained at 70 while a saturated aqueous solution of sodium nitrite (69 g., 1.0 mole) was added beneath the surface of the solution. After the addition of the sodium nitrite, which required 17 minutes, the reaction mixture was cooled to 0° over a period of five minutes. The yellow crystals were removed by filtration and washed with water, yield 43.1 g. (68.8%). This crude product melted at 52–53°. It was used without further purification. Gabriel reports a melting point of 53°. *Note: 3-Nitroso-2-oxazolidone decomposes spontaneously after standing 4–36 hours. This decomposition produces large volumes of gases and flames. It must be dried and stored with adequate precautions.*

Reaction of *p*-Anisidine with 3-Nitroso-2-oxazolidone.—3-Nitroso-2-oxazolidone (20 g., 0.172 mole) was added portionwise over a period of 20 minutes to 59.2 g. (0.481 mole) of *p*-anisidine dissolved in 50% aqueous ethanol (170 cc.). The temperature of the reaction mixture was kept below 25° by periodic cooling. After the evolution of gas had ceased, the reaction remained at room temperature overnight. A copious light brown crystalline precipitate (m.p. 93–99°) formed which was removed by filtration and washed with 50% aqueous ethanol (2 × 50 cc.), yield 32 g. This crude material after washing with ether (2 × 200 cc.) melted at 96–110° with a few crystals melting at 74–76°, yield 27.1 g. One crystallization from 80 cc. of ethyl acetate gave 11.58 g. (34.3%) of impure N,N'-di-*p*-anisylethylenediamine (m.p. 101–104°). Petroleum ether (200 cc.) was added to the ethyl acetate filtrate after which crystals separated with a melting point of 115–119°, yield 14.0 g. (35.7%). The latter crop, after several recrystallizations from absolute alcohol, gave pure N-*p*-anisyl 2-*p*-anisylaminoethylcarbamate (m.p. 123–124°), yield 4.13 g.

Anal. Calcd. for $C_{17}H_{20}N_2O_4$: C, 64.65; H, 6.48; N, 8.85. Found: C, 64.42; H, 6.30; N, 9.13.

N-*p*-Anisyl 2-*p*-anisylaminoethyl carbamate on treatment with one mole equivalent of *p*-anisyl isocyanate gave an 83.1% yield of compound IV (R = *p*-anisyl) (m.p. 158–159°). One crystallization from 95% ethanol raised the melting point to 159.5–161°.

Anal. Calcd. for $C_{25}H_{27}N_3O_6$: C, 64.50; H, 5.85; N, 9.03. Found: C, 64.39; H, 5.79; N, 9.10.

An authentic sample of compound IV (R = *p*-anisyl) prepared by the reaction of N-β-hydroxyethyl *p*-anisidine with 2 mole equivalents of *p*-anisyl isocyanate did not depress the melting point of the above sample.

The melting point of the crude N,N'-di-*p*-anisyl ethylenediamine[13] was raised to 104–105° by crystallization from ethyl acetate or absolute ethanol, yield 8.45 g.

Anal. Calcd. for $C_{16}H_{20}N_2O_2$: C, 70.50; H, 7.42; N, 10.28. Found: C, 70.25; H, 7.38; N, 10.55.

The above ethereal washings (400 cc.) on evaporation gave an oily residue (4.9 g.). This residue was separated by fractional distillation and crystallization into pure *p*-anisidine (0.50 g.), N,N'-di-*p*-anisylethylenediamine (0.17 g.), 2-*p*-anisylaminoethyl N-*p*-anisylcarbamate (0.61 g.), *sym*-di-*p*-anisylurea (0.06 g.) and material melting at 268.5–270° (0.21 g.). The *sym*-di-*p*-anisylurea melted at 242–243° alone and on admixture with a sample prepared from *p*-anisidine and 1,3-dinitro-2-imidazolidone.[3] The crystals, which melted at 268.5–270°, gave analytical values in agreement with the required for 1,3-di-*p*-anisyl-2-imidazolidone.

Anal. Calcd. for $C_{17}H_{18}N_2O_3$: C, 68.50; H, 6.08; N, 9.40. Found: C, 68.48; H, 6.07; N, 9.67.

The main aqueous ethanol filtrate and washings from above were acidified to decompose the carbonates and then made strongly alkaline. After the oil was removed by extraction with ether, the ethereal solution was dried over anhydrous sodium sulfate and evaporated to dryness. The residual oil, on distillation *in vacuo* under nitrogen, gave 28.1 g. of *p*-anisidine and a residue of 3.03 g. Since the amount of *p*-anisidine consumed in this reaction is 30.58 g. (0.248 mole) the above yields are based on this figure.

Another run of *p*-anisidine (15.17 g., 0.123 mole) with 5.13 g. (0.044 mole) of 3-nitroso-2-oxazolidone was allowed to proceed to completion. The reaction mixture was acidified by addition of 87 cc. of 25% sulfuric acid solution after which part of the aqueous solution was distilled at atmospheric pressure into a cooled receiver. The first 25 cc. of distillate contained all the obtainable acetaldehyde, which was isolated as the 2,4-dinitrophenylhydrazone (m.p. 150–160°), yield 0.115 g. (0.98%). One crystallization from 95% ethanol raised the melting point to 167–168°. A mixed melting point with an authentic sample of acetaldehyde 2,4-dinitrophenylhydrazone was not depressed.

The gaseous products from the reaction of amines with 3-nitroso-2-oxazolidone consist mainly of nitrogen and carbon dioxide. Carbon dioxide and acetylene were determined quantitatively. *p*-Anisidine (7.44 g., 0.06 mole) dissolved in 50 cc. of 50% aqueous ethanol was placed in a three-neck flask fitted with a nitrogen lead-in, an addition funnel and a lead-off to three gas washing towers. 3-Nitroso-2-oxazoli-

(9) M. S. Newman and A. Kutner, THIS JOURNAL, **73**, 4199 (1951).

(10) All melting points were determined on a Kofler block and are corrected unless specified otherwise.

(11) Microanalyses by C. W. Beazley, Skokie, Illinois.

(12) A. H. Homeyer, U. S. Patent 2,399,118; *C. A.*, **40**, 4084 (1946).

(13) Frequently N,N'-di-*p*-anisylethylenediamine was obtained melting over a range of 102–110° with gassing. This material could not be purified by crystallization from the usual solvents. This melting point range was observed also with material prepared from *p*-anisidine and 1,2-dibromoethane. It could be purified readily by melting the solid and keeping it in the liquid state until all bubbling had ceased. When the liquid was poured onto a watch glass, it solidified immediately. It then melted at 103–104° without gassing.

done (2.515 g., 0.0217 mole) was added *en masse* and the evolved gases swept through the gas washing bottles with dry, oxygen-free nitrogen. The first two wash bottles contained barium hydroxide solution while the third contained a solution of cuprous chloride in pyridine. Freshly precipitated cuprous chloride[14] was used in the preparation of the pyridine solution for acetylene determination as described by Siggia.[15] After gas evolution had ceased 10% sulfuric acid solution was added through the addition funnel under a positive pressure of nitrogen to free the carbon dioxide held in the reaction mixture as amine carbonates. The carbon dioxide was determined by filtering off the barium carbonate from the barium hydroxide solutions, drying and weighing. The yield of barium carbonate was 1.9801 g. (46.3% based on release of one mole equivalent of carbon dioxide from 3-nitroso-2-oxazolidone). A duplicate determination gave 45.9%.

No acetylene was evolved during the course of the reaction until the sulfuric acid solution was added. Then only a trace (0.46%) was obtained.

Reaction of *p*-Phenetidine with 3-Nitroso-2-oxazolidone.—To a solution of 32.9 g. (0.240 mole) of *p*-phenetidine in 50% aqueous ethanol was added 10 g. (0.086 mole) of 3-nitroso-2-oxazolidone. The reaction was carried out in the manner described above for *p*-anisidine and 3-nitroso-2-oxazolidone. The unreacted *p*-phenetidine was not recovered so the yields are based on nitrosoöxazolidone used. In several runs the crude solid products weighed 14.7–17.7 g. They were separated into N-*p*-phenetyl 2-*p*-phenetylaminoethylcarbamate and N,N'-*p*-phenetylethylenediamine by crystallizing from ethyl acetate to obtain the former and treating the ethyl acetate filtrates with petroleum ether to obtain the latter. In this manner pure N-*p*-phenetyl 2-*p*-phenetylaminoethylcarbamate (m.p. 143–144°) was obtained, yield 2.13–3.87 g. (7.2–13.06%).

Anal. Calcd. for $C_{19}H_{24}N_2O_4$: C, 66.20; H, 7.01; N, 8.13. Found: C, 66.47; H, 7.10; N, 7.94.

From the ethyl acetate filtrates N,N'-*p*-phenetylethylenediamine (m.p. 99–100°) was obtained, yield 6.56–7.97 g. (25.4–30.9%).

Anal. Calcd. for $C_{18}H_{24}N_2O_2$: C, 71.95; H, 8.06; N, 9.33. Found: C, 72.10; H, 7.86; N, 9.15.

This sample did not depress the melting point of a sample of N,N'-*p*-phenetylethylenediamine prepared from *p*-phenetidine and 1,2-dibromoethane.

Preparation of 2-Hydroxyethyl N-*p*-Anisylcarbamate and Ethylene Glycol Bis-[N-(*p*-anisyl)-carbamate].—To ethylene glycol (2 g., 0.032 mole) in dry benzene (35 cc.) was added 4.79 g. (0.032 mole) of *p*-anisyl isocyanate. This mixture was refluxed for 15 minutes and left to cool in the refrigerator. A white solid separated which was removed by filtration and washed with benzene, yield 1.91 g. (16.5%). Two crystallizations from ethanol raised the melting point of the ethylene glycol bis-[N-(*p*-anisyl)-carbamate] from 173–175° to 174.8–175.2°.

Anal. Calcd. for $C_{18}H_{20}N_2O_6$: C, 59.99; H, 5.61; N, 7.77. Found: C, 60.15; H, 5.73; N, 7.80.

The benzene filtrate was diluted with petroleum ether until an oily layer separated. After it had stood for three days in refrigerator at 4° crystals were obtained, yield 3.78 g. (56%). These crystals melted at 57–99°. This low melting solid was dissolved in 4 cc. of ethyl acetate. When the solution cooled 240 mg. of high melting product (m.p. 171–173°) was obtained. The filtrate was diluted with petroleum ether until turbid. On standing in the refrigerator several days 1.36 g. of β-hydroxyethyl N-*p*-anisylcarbamate (m.p. 90–91° (uncor.)) was obtained.

Anal. Calcd. for $C_{10}H_{13}NO_4$: C, 56.90; H, 6.16; N, 6.63. Found: C, 56.78; H, 6.15; N, 6.53.

N-β-Hydroxyethyl-*p*-anisidine.—*p*-Anisidine (50 g., 0.406 mole) was treated with 16.0 g. (0.198 mole) of ethylene chlorohydrin and the products distilled *in vacuo* as described by Jacobs and Heidelberger.[16] After the excess *p*-anisidine (31.5 g.) had distilled over, a fraction (b.p. 140–150° (0.3 mm.); m.p. 41–43°) was obtained which consisted mainly of N-β-hydroxyethyl-*p*-anisidine, yield 22.7 g. (73.9%). A third fraction (b.p. 150–164° (0.3 mm.) was obtained which partly crystallized in the receiver, yield 3.1 g. This third fraction, after three crystallizations from acetone–petroleum ether, melted at 71.5–73°, yield 0.56 g. Anker, Cook and Heilbron[17] report the melting point of N-bis-(β-hydroxyethyl)-*p*-anisidine as 73°.

N-β-Hydroxyethyl-*p*-anisidine, after a second distillation under nitrogen and *in vacuo*, melted at 43.4–44°.

N-β-Hydroxyethyl-*p*-anisidine (300 mg., 0.0019) on treatment with excess phenyl isocyanate (1 cc.) gave 710 mg. (97.5%) of N-(N-phenylcarbamyl-β-hydroxyethyl)-N-*p*-anisyl-N'-phenylurea melting at 141–143°. One crystallization from 95% ethanol raised the melting point to 145–146.5°.

Anal. Calcd. for $C_{23}H_{23}N_3O_4$: C, 68.13; H, 5.72; N, 10.36. Found: C, 68.34; H, 5.87; N, 10.60.

Another sample (1.67 g., 0.098 mole) of N-β-hydroxyethyl *p*-anisidine in dry benzene (20 ml.) was treated with 1.47 g. (0.098 mole) of *p*-anisyl isocyanate. On addition of petroleum ether an oil (1.175 g., 51.5%) separated which crystallized on long standing. This crude N-(N-*p*-anisylcarbamyl-β-hydroxyethyl)-N,N'-di-*p*-anisylurea (IV, R = *p*-anisyl) melted at 156–158°. One crystallization from 95% ethanol raised the melting point to 160–161°.

β-Chloroethyl-N-*p*-anisylcarbamate.—This compound (m.p. 86–87°) was prepared in quantitative yield as previously described.[8]

Attempted Preparation of Vinyl N-*p*-Anisylcarbamate.—β-Chloroethyl N-*p*-anisylcarbamate (5.0 g., 0.0218 mole) was added to a solution of sodium ethoxide (0.0218 mole). The sodium ethoxide solution was prepared by addition of 5.0 g. (0.0218 mole) of sodium to 40 cc. of absolute ethanol. After the addition of the carbamate only a slight heat of reaction was observed. When the reaction had stirred for one hour the crystals were removed by filtration and washed with water. The crude product (3.1 g., 73.8%) melted at 105–106°. After one crystallization from ethanol the melting point was 109–111° alone and on admixture with an authentic sample of 3-*p*-anisyl-2-oxazolidone.[8]

Addition of water to the original filtrate gave 1.0 g. of impure β-chloroethyl N-*p*-anisylcarbamate (m.p. 67–84°). One crystallization from 95% ethanol raised the melting point to 85.5–86.5°. A mixed melting point determination with the starting material was not depressed.

N,N'-Di-*p*-anisylethylenediamine.—A mixture of 53 g. (0.430 mole) of *p*-anisidine and 20.1 g. (0.107 mole) of 1,2-dibromoethane was heated on the steam-bath for one-half hour. Then 150 cc. of water was added and the reaction mixture was heated for an additional 18 minutes. The product was filtered and washed with warm water (50 cc.) to yield 30.5 g. of crystals melting at 96–109°. The product was crystallized from 35% ethanol (800 cc.). Some crystals (2.75 g.) which remained undissolved in the hot solution, were filtered. The filtrate on standing deposited 18.0 g. (97.9%) of impure N,N'-di-*p*-anisylethylenediamine. A portion (14.95 g.) of these crystals was melted in an open beaker until bubbling ceased. The melt was then poured onto a watch glass where it crystallized (m.p. 104–105°). One crystallization from ethyl acetate did not raise the melting point. This sample did not depress the melting point of a sample of N,N'-di-*p*-anisylethylenediamine obtained from the reaction of *p*-anisidine with 3-nitroso-2-oxazolidone.

The crystals insoluble in the dilute alcohol melted at 190–218°. This melting point was raised to 234–235° after three crystallizations from pyridine (54 cc./g.), yield 0.65 g. (4.09%). Bischoff[18] reported a melting point of 233° for N,N'-di-*p*-anisylpiperazine.

N,N'-Di-*p*-phenetylethylenediamine.—*p*-Phenetidine (59.0 g., 0.430 mole) and 1,2-dibromoethane (20 g., 0.107 mole) were combined in the same manner as *p*-anisidine and 1,2-dibromoethane described above. The crude product (56.6 g.) melted at 92–180°. It was dissolved in 95% ethanol (300 cc.) which deposited 26.27 g. of crystals (m.p. 176–220°) on cooling to room temperature. The filtrate was diluted with water (300 cc.) to yield 10.51 g. of solid (m.p. 92–95°). The first crop of crystals was then refluxed with 200 cc. of ether and the insoluble material (4.16 g.) re-

(14) L. F. Fieser, "Experiments in Organic Chemistry," 2nd Edition, D. C. Heath and Co., New York, N. Y., 1941, p. 215.

(15) S. Siggia, "Quantitative Organic Analysis via Functional Groups," John Wiley and Sons, Inc., New York, N. Y., 1949, p. 57.

(16) W. A. Jacobs and M. Heidelberger, *J. Biol. Chem.*, **21**, 403 (1915).

(17) R. M. Anker, A. H. Cook and I. M. Heilbron, *J. Chem. Soc.*, 917 (1945).

(18) C. A. Bischoff, *Ber.*, **22**, 1777 (1889).

moved by filtration. The melting point of the insoluble material was raised from 218–220.5° to 223–223.5° by one crystallization from pyridine (56 cc.), yield 2.46 g. Bischoff and Trapesonzjanz[19] report a melting point of 223° for N,N′-di-*p*-phenetylpiperazine.

The ether filtrate on evaporation left 20.4 g. of solid, which melted at 89–92°. This gave a total yield of 30.51 g. (95%) of crude N,N′-di-*p*-phenetylethylenediamine. One crystallization from 95% ethanol (65 cc.) raised the melting point to 98–98.5°. This melting point was not depressed on admixture with a sample of the N,N′-di-*p*-phenetylethylenediamine from the reaction of *p*-phenetidine with 3-nitroso-2-oxazolidone.

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(19) C. A. Bischoff and Ch. Trapesonzjanz, *Ber.*, **23**, 1977 (1890).

[CONTRIBUTION FROM THE INORGANIC CHEMISTRY BRANCH, CHEMISTRY DIVISION, U. S. NAVAL ORDNANCE TEST STATION]

1-(Alkylamino)-guanidines

BY WILLIAM G. FINNEGAN, RONALD A. HENRY AND G. B. L. SMITH

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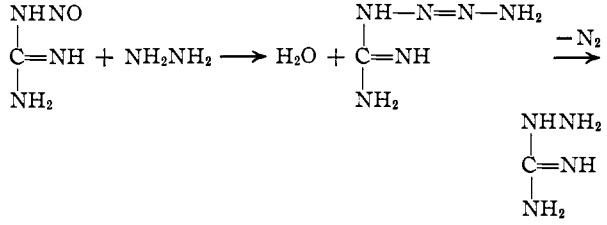
Representative examples of the previously unreported 1-(alkylamino)-guanidines have been prepared by the catalytic hydrogenation of the corresponding guanyl hydrazones. Methylhydrazine and nitrosoguanidine react to give principally 1-methyl-1-aminoguanidine; however, a small amount (*ca.* 4%) of 1-(methylamino)-guanidine is also formed.

Two of the three possible structural isomers of methylaminoguanidine have been previously reported: namely, 1-methyl-2-aminoguanidine[1] and 1-methyl-1-aminoguanidine.[2] The third isomer, 1-(methylamino)-guanidine, $CH_3NHNHC(NH)NH_2$, and several other 1-(alkylamino)-guanidines have now been synthesized by the hydrogenation of guanyl hydrazones (generally as their hydrochlorides) in acetic acid over Adams platinum catalyst at room temperature and three atmospheres pressure

$$RCH{=}NNHC(NH)NH_2 + H_2 \longrightarrow RCH_2NHNHC(NH)NH_2$$

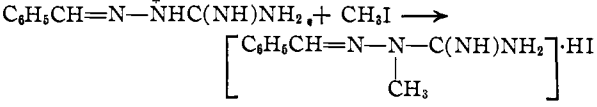
This method is similar to that employed for the reduction of semicarbazones to semicarbazides.[3] The general procedure is described in the experimental section; the results are outlined in Table I. These compounds do not form hydrazones with benzaldehyde in contrast to the behavior of the isomeric alkylaminoguanidines.

An attempt was also made to synthesize 1-(methylamino)-guanidine by a method similar to that developed by Thiele[4] for the preparation of aminoguanidine. He demonstrated that the latter compound was formed when equimolecular quantities of nitrosoguanidine and hydrazine hydrate reacted, and proposed the mechanism



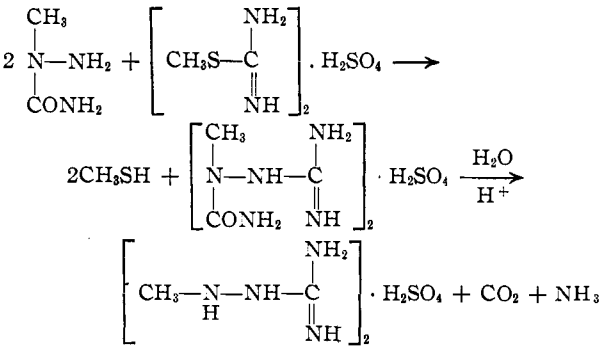
On this basis, one might expect the reaction of methylhydrazine and nitrosoguanidine to give 1-(methylamino)-guanidine; however, only about 4% of the latter is formed. The principal product is the isomeric compound, 1-methyl-1-aminoguanidine.[2] Guanidine, which results from the denitrosation of the nitrosoguanidine, was also identified. Obviously, Thiele's explanation is incorrect or inadequate. A more plausible explanation involves the addition of methylhydrazine at its nucleophilic center either to cyanamide, which arises from the dearrangement[5] of nitrosoguanidine in aqueous systems, or to the electrophilic center of nitrosoguanidine, followed by elimination of nitrosamine.

Methyl iodide and benzalaminoguanidine react in methanol at room temperature to yield benzal-1-methyl-1-aminoguanidine hydroiodide. The methylation is essentially quantitative and appears to take place exclusively on the nitrogen atom indicated in the equation



Benzal semicarbazone and methyl iodide under comparable conditions do not react.

An attempt to prepare 1-(methylamino)-guanidine by the following reactions was also unsuccessful.



Under the conditions employed for the first step, the only product recovered was 3-methylbiurea, $H_2NCON(CH_3)NHCONH_2$, identical with the compound obtained from 2-methylsemicarbazide and cyanic acid.[6]

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(3) D. W. Neighbors, A. L. Foster, S. M. Clark, J. E. Miller and J. R. Bailey, *ibid.*, **44**, 1557 (1922); E. J. Poth and J. R. Bailey, *ibid.*, **45**, 3001 (1923); K. A. Taipale and S. A. Smirnoff, *Ber.*, **56**, 1794 (1923).

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