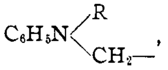
yields first a compound which contains the unit  $C_6H_5N\genfrac{}{}{0pt}{}{\diagup R}{\diagdown CH_2—}$, reducible to methylalkylaniline. The formation of the anhydro-*p*-alkylaminobenzyl alcohol salts, which eventually occurs under the same conditions but in absence of reducing agent, is therefore not the result of a special primary condensation, but of a secondary intra- or intermolecular action, probably a coupling of the units shown in (1).

4. By the procedures described either nuclear or N-methylation of alkylanilines can be effected by means of formaldehyde.

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Alkyl-Nitroguanidines. Dearrangement and Preparation by Nitration[1]

BY TENNEY L. DAVIS AND ROBERT C. ELDERFIELD

Nitroguanidine dearranges in two modes and may be used for synthesis in two ways by taking advantage of the products which result from its dearrangement in one manner or the other. Thus, with ammonium carbonate it yields guanidine carbonate, and with primary aliphatic amines it gives N-alkyl-N′-nitroguanidines.[2] These alkyl-nitroguanidines, having a hydrogen atom attached to each of the guanidine nitrogens, are capable of dearrangement in two modes, as follows.

$$RNH—C(NH)—NH—NO_2 \rightleftharpoons \begin{cases} RNH_2 + HNCN—NO_2 & \text{(I)} \\ RNCNH \text{ (or } RNHCN) + NH_2—NO_2 & \text{(II)} \end{cases}$$

The first of these modes corresponds to the method by which the substances have been synthesized from nitroguanidine; the second opens new possibilities of synthesis. We have therefore wished to determine whether the alkyl-nitroguanidines dearrange in the predicted manner and to investigate their usefulness for the easy preparation of monoalkyl- and N,N′-dialkyl-guanidines by reaction with ammonia and with primary amines, respectively.[3]

As no alkyl-nitroguanidines have heretofore been prepared by the nitration of alkyl-guanidines, we have studied that reaction in an effort to gain a further insight into the mechanism of the nitration of amines, and have found that the only alkyl-nitroguanidines which we have been able to

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(1) A summary of part of the Doctor's Dissertation of Robert C. Elderfield, Massachusetts Institute of Technology, June, 1930.

(2) Davis and Abrams, *Proc. Am. Acad. Arts Sci.*, **61**, 437 (1926); Davis and Luce, THIS JOURNAL, **49**, 2303 (1927).

(3) Other papers on the urea dearrangement: Davis and Underwood, *ibid.*, **44**, 2595 (1922); Davis and Blanchard, *ibid.*, **45**, 1816 (1923); Davis, *Proc. Nat. Acad. Sci.*, **11**, 68 (1925); Davis and Blanchard, THIS JOURNAL, **51**, 1790, 1801, 1806 (1929).

produce by this method are identical with those resulting from the other method of synthesis. The relation of this finding to the question of the basicity of the substituted guanidines is discussed.

Dearrangement of the N-Alkyl-N'-nitroguanidines and its Application in Synthesis.—When methyl-nitroguanidine was refluxed with water, it decomposed slowly into gaseous products, methylamine carbonate collected in the condenser, and the solution, after one hundred hours of boiling, yielded no residue on evaporation to dryness. No cyanic acid could be detected in the solution, and no trimethylisomelamine, from the polymerization of methylcyanamide, could be isolated. The facts agree with the belief that dearrangement under these conditions occurred according to the second of the above-indicated modes. If the dearrangement had produced methylamine and nitrocyanamide, then the nitrocyanamide, decomposing in the manner usual with nitroamines, would have formed nitrous oxide and cyanic acid, the cyanic acid would have combined with the methylamine and methylurea would have been found when the solution was evaporated to dryness. If the dearrangement produced methylcyanamide and nitroamide, the nitroamide would have decomposed into nitrous oxide and water, and the methylcyanamide, being extremely stable to polymerization in neutral solution, would have hydrolyzed slowly to methylamine, ammonia and carbon dioxide. In other experiments we have found positive proof of the presence of the alkylcyanamide, both by the production from it of mono- and dialkyl-guanidines and by the isolation of the trialkylmelamine.

When the alkyl-nitroguanidines were warmed with water and a large excess of ammonium carbonate, nitrous oxide was liberated and unsubstituted guanidine carbonate was the principal product. Dearrangement occurred in the first mode corresponding to the process by which the alkylnitroguanidine was produced in the first place from nitroguanidine, nitroguanidine was formed and dearranged in its turn to give nitroamide, which decomposed, and cyanamide which combined with the ammonia to form guanidine as has been demonstrated earlier. Methyl-, *n*-butyl- and benzyl-nitroguanidine thus yielded guanidine carbonate in 72–74% of the theoretical amount. In the experiment with *n*-butyl-nitroguanidine, a small amount of *n*-butylguanidine (4.2%) was isolated, indicating that dearrangement in the second mode took place to a small extent.

When the alkyl-nitroguanidines were refluxed in water solution with the corresponding primary amine, nitrous oxide came off, and, instead of the expected dialkylguanidine, about 70% of the theoretical amount of the monoalkylurea was obtained. In some experiments, however, a certain quantity of the dialkylguanidine was isolated. At first sight the production of the mono-substituted urea seems explainable in two ways. Either dearrangement took place in the first mode, and the nitrocyanamide lost nitrous oxide to form cyanic acid which combined with the amine to produce the substituted urea; or, the dearrangement being in the second mode, the alkylcyanamide was hydrolyzed to the alkylurea by the action of the bases which were present. An experiment with N,N-dimethyl-N′-nitroguanidine cast doubt upon the first explanation. This substance can dearrange in only one manner, namely, into dimethylamine and nitrocyanamide. After refluxing for twelve hours with a water–alcohol solution of an excess of trimethylamine (chosen because it supplied alkalinity and would form a cyanate but not a urea derivative), 92% of it was recovered unchanged, no allophanic ester was found, and the solution gave no test for cyanate. The second explanation is supported by the fact that a decrease in the alkalinity of the reaction mixture leads to a decrease in the amount of alkylurea which is formed and to an increase in the amount of dialkylguanidine.

Cyanamide itself combines with water readily, especially in alkaline solution, to produce urea. Hetherington and Braham[4] have studied the polymerization and hydrolysis of cyanamide in 0.01, 0.1 and 1.0 molal solutions of sodium hydroxide, and have found that urea is formed as well as dicyandiamide, increased alkalinity resulting in increased urea formation. Buchanan and Barsky[5] in an exhaustive and careful study have confirmed these results; cyanamide polymerizes to dicyandiamide in moderately alkaline solutions, but in strongly alkaline solutions it is entirely hydrolyzed to urea. Since the alkylcyanamides are not known to form dimers corresponding to dicyandiamide, they would be expected—as we have found to be the case—to polymerize to trialkylisomelamines in solutions which are not strongly alkaline enough to hydrolyze them to urea derivatives. Two sources of alkalinity existed in our experiments; the reaction mixtures were about three molal in amine at the start, and the dialkylguanidines which are produced are strong bases, as we have reported,[6] and increased the alkalinity as the reaction progressed, thus militating against their further formation.

Experiments were tried in which the alkalinity of the reaction mixtures was reduced by the addition of varying amounts of acetic acid. The increased hydrogen-ion concentration had the effect of inhibiting the dearrangement, and it was necessary to heat the materials in sealed tubes at 175°. The primary amine, reacting with the alkyl-nitroguanidine, gave the best yields of N,N′-dialkylguanidine (about 40 to about 50% according to the alkyl group) when the *P*H at the beginning of the experiment was about 6.13. This *P*H also corresponded to the lowest yields of the urea derivative. In more alkaline solutions the yields of the urea derivative were greater because of increased hydrolysis of the alkylcyanamide. In

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[4] Hetherington and Braham, THIS JOURNAL, **45**, 828 (1923).

[5] Buchanan and Barsky, *ibid.*, **52**, 195 (1930).

[6] Davis and Elderfield, *ibid.*, **54**, 1499 (1932).

more acid solutions they were greater because, as we believe, the increased acidity inhibited the addition of the amine to the alkylcyanamide and so left the latter material available only for polymerization or for hydrolysis by the hot solution. We expect in the future to investigate more fully the conditions which influence the combination of a cyanamide with an ammonia derivative. In these sealed tube experiments, the products of the hydrolysis of the alkylcyanamides were isolated in the form of N,N′-dialkylureas, as would be expected, for the mono-substituted ureas, by dearrangement, would change over to these substances at the high temperature which was used.

When the alkyl-nitroguanidines were made to react in water solution with the corresponding amines by refluxing under a pressure (above atmospheric pressure) of 508 cm. of mercury while carbon dioxide was bubbled through the liquid, about 40% of the material was obtained in the form of N,N′-dialkylguanidine and about 40% in the form of trialkylisomelamine. The carbon dioxide reduced the alkalinity enough to prevent any considerable hydrolysis of the alkylcyanamide resulting from the dearrangement and, in the less strongly heated solution, created a condition favorable for the polymerization of that portion of the substance which did not combine with the amine.

The dearrangement of the alkyl-nitroguanidines to form alkylcyanamide and nitroamide appears to be fully demonstrated by the isolation of the polymer of the alkylcyanamide and of the several substances which correspond to the interaction of the alkylcyanamide with water, with ammonia and with amines, respectively, by the evolution of nitrous oxide from the reaction mixtures, and by the fact, previously reported, that the alkyl-nitroguanidines give up their nitro group nitrogen quantitatively in the nitrometer. The conditions which promote the dearrangement are clearly not the conditions which most promote the addition of ammonia or of amines to the alkylcyanamide and at the same time most reduce the tendency of the alkylcyanamide to enter into the side reactions of hydrolysis and polymerization. We conclude that the dearrangement of the alkyl-nitroguanidines does not supply the best method for the synthesis of substituted guanidines.

The results however have another interest. They show that the mechanism of the hydrolysis of the alkyl-nitroguanidines is first dearrangement and then hydrolysis of the dearrangement products. The hydrolysis cannot be the replacement of the NH group by an oxygen atom with the formation of an alkyl-nitrourea, as would be expected if one accepts the conclusions of Bell,[7] who supposes that the production of urea from guanidine, under the conditions where this "hydrolysis" occurs, is due to the hydrolysis of the guanidine molecule as a whole. We believe, on the

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(7) Bell, *J. Chem. Soc., London*, **118**, 1213 (1926); **120**, 2074 (1928).

contrary, that the urea results from the hydrolysis of the cyanamide produced by the dearrangement of the guanidine—just as in our experiments, where the alkyl group serves as a label or marker for the nitrogen atom to which it is attached, the alkylurea is certainly produced by the hydrolysis of the alkylcyanamide.

Nitration of Alkylguanidines.—In guanidine salts the acid is possibly combined with one of the amino nitrogen atoms (or amino groups) in the same way, whatever that way may be, that hydrochloric acid, say, is combined with the ammonia nitrogen atom (or the ammonia molecule) in ammonium chloride. There is also the possibility that the acid may be combined in some manner with the guanidine molecule as a whole. The introduction of an alkyl group into ammonia increases its basicity, and the introduction of an alkyl group into guanidine would be expected to increase the basicity of the nitrogen atom to which it is attached and hence to impart greater basicity to the molecule as a whole. In a salt of such an alkylguanidine, it would be expected that the acid would be in combination with the alkylated nitrogen atom or amino group. If, now, the salt being a nitrate, an alkyl-nitroguanidine is formed from it by a process of dehydration, the nitro group in the resulting compound would be attached to the nitrogen atom to which the nitric acid of the nitrate was previously attached, that is, to the nitrogen which carries the alkyl group.

We have found that the nitrates of methyl-, *n*-butyl-, *n*-heptyl- and N,N-dimethylguanidine, when treated with concentrated sulfuric acid, yielded alkyl-nitroguanidines identical with those already known in which the nitro group is attached to a different nitrogen atom from that which carries the alkyl group or groups. If the nitro compound is produced by a process of dehydration, then the nitric acid in the nitrate was not attached to the alkylated amino group. If the nitrate reacts with the sulfuric acid to produce nitric acid which then nitrates the substance, then the nitric acid in the original nitrate may have been attached to the base in any manner whatever, whether to the alkylated or the non-alkylated amino group or to the molecule as a whole.

Benzylguanidine nitrate carbonized on treatment with concentrated sulfuric acid producing sulfur dioxide; piperidylguanidine nitrate gave a yellow solution and some sulfur dioxide, and neither substance yielded a nitro compound. The nitrates of N,N′-dimethyl- and N,N′,N″-trimethylguanidine dissolved in sulfuric acid to yield solutions from which no nitro compound could be isolated and from which the bases (87%) were recovered in the form of picrates.

Methyl-, *n*-butyl- and N,N-dimethylguanidine sulfate, on treatment with concentrated sulfuric acid and potassium nitrate, nitrated in the unsubstituted amino group as before, but now under conditions in which it is difficult to believe that the formation of the nitro compound was due to a process of dehydration. In a similar experiment with the sulfate of N,N′-diethylguanidine, and in an attempt to nitrate N,N′,N″-trimethylguanidine with mixed acid, no nitro compound could be isolated and the bases were recovered in large part in the form of their picrates. We conclude that only those alkylguanidines which contain an unsubstituted amino group form nitro compounds by direct nitration, the nitro group entering the non-alkylated amino group.

Since it seems less likely that the acid in the guanidine salt is attached to the unalkylated amino group than to the more basic alkylated one, and in view of the nitrations which have been accomplished without the preliminary preparation of the nitrate, we conclude that the mechanism of the nitration is probably not dehydration. To test the matter further we have treated guanidine nitrate with a mixture of phosphoric acid and phosphorus pentoxide, a mixture which ought to be as strong and as prompt a dehydrating agent as concentrated sulfuric acid, and have recovered over 95% of the guanidine after thirty minutes heating at 65° and after thirty hours standing at room temperature. After forty-eight hours at room temperature, during which time nitric acid or nitrophosphoric acid was doubtless produced, an 82% yield of nitroguanidine was secured.

If the basicity of guanidine is a property of one of the nitrogen atoms (or amino groups) rather than of the molecule as a whole, then the introduction of alkyl groups would be expected to increase the basicity of the substance, or certainly not to reduce it.[6] We have found that the monoalkylguanidines (which form nitro compounds) are as strong bases as guanidine itself, but that the N,N′-dialkylguanidines (which do not nitrate) are markedly weaker. The facts so far can be explained on the unlikely supposition, suggested above, that the strong basicity of guanidine and its monoalkyl derivatives is resident in the unsubstituted NH_2 group (where nitration occurs). But that supposition is contradicted by the fact that N,N′,N″-trimethylguanidine (which does not nitrate) is again as strong a base as guanidine. The facts altogether suggest that the acid in guanidine salts is not attached to any particular part of the molecule but is attached to the molecule as a whole.

Experiments

Experiments which are indicated with sufficient fullness in the foregoing are not again described in this section. Experiments are reported in the order in which their results are discussed in the first section of the paper.

Methyl-nitroguanidine and Ammonium Carbonate.—Ten grams of methyl-nitroguanidine, 350 g. of ammonium carbonate, and 200 cc. of water were warmed together under reflux in the water-bath at 65–70° for five hours until everything had gone into solution. The liquid was evaporated to dryness, and the residue, after twice dissolving in water and precipitating with alcohol. yielded pure guanidine carbonate, 72% of the theoretical amount, identified by its melting point and by the melting points of the picrate, nitrate and nitro compound prepared from it.

n-Butyl-nitroguanidine and Ammonium Carbonate.—A mixture of 20 g. of n-butyl-nitroguanidine, 500 g. of ammonium carbonate and 500 cc. of water required about seven hours of heating at 65–70° before all of the n-butyl-nitroguanidine went into solution. Precipitation by alcohol yielded 8.31 g. of guanidine carbonate, 74%. The liquor from the precipitation yielded a gummy mass on evaporation, and this, on treatment with ammonium picrate, gave 2.1 g. of a crystalline picrate. Four recrystallizations from 20% alcohol gave the pure substance, bright yellow needles, melting sharply at 154.5° and identified as butylguanidine picrate by analysis.[8]

Methyl-nitroguanidine and Methylamine.—Ten grams of methyl-nitroguanidine, 9 g. of a 33% methylamine solution, and 50 cc. of water were refluxed together on the boiling water-bath for three hours. A constant slow evolution of nitrous oxide took place. Evaporation gave a thick sirup which yielded 8.00 g. of crystals upon treatment with dilute nitric acid. These, recrystallized from water, melted at 127–128° with slight decomposition, in agreement with the melting point of methylurea nitrate reported by Franchimont.[9] The nitrate, evaporated with a solution of an equivalent amount of potassium carbonate and worked up from acetone, yielded methylurea, m. p. 101°, identified by mixed melting point with a known sample. The yield of methylurea amounted to 69%.

Ethyl-nitroguanidine and Ethylamine.—A mixture of 13.2 g. of ethyl-nitroguanidine, 15 g. of a 33% solution of ethylamine, and 50 cc. of water, after refluxing for three hours, was evaporated to a thick sirup which deposited 6.38 g. of crystals after standing for several days, m. p. 92° after recrystallization from acetone, identified as ethylurea by mixed melting point with a known sample; yield, 72.5%.

n-Butyl-nitroguanidine and n-Butylamine.—Ten grams of n-butyl-nitroguanidine, 9 g. of n-butylamine and 30 cc. of water were heated together under reflux for five hours in a water-bath at 80° and for three hours in a boiling water-bath. Evaporation yielded a thick sirup which would not crystallize. Taken up in water and treated with an ammonium picrate solution, it gave 3.2 g. of a picrate, m. p. 122.5° after recrystallization from dilute alcohol.

Anal. Calcd. for di-n-butylguanidine picrate: N, 21.00. Found: N, 21.59, 21.35, 21.29. Yield of di-n-butylguanidine, 12.80%. The oil remaining from the picrate precipitation could not be made to crystallize or to yield any precipitate with a variety of reagents.

Effect of Hydrogen-Ion Concentration on the Reaction of an Amine with an Alkylnitroguanidine.—Approximately 3 N solutions of the amines were made up and their exact strengths were determined by titration with standard acid. To portions of these solutions acetic acid was added in such amounts that the ratios of acetic acid to amine were known, and the hydrogen-ion concentrations of the mixtures were determined electrometrically. Weighed portions of the alkylnitroguanidines were heated in sealed tubes at 175° for eight hours with quantities of the various solutions which contained in every case 1.1 molecular equivalents of the corresponding amine. After the heating the tubes contained considerable gas under pressure.

In the experiments with n-butylamine and n-butyl-nitroguanidine, no attempt was made to obtain dibutylurea because of the difficulties attendant upon the quantitative estimation of that substance. The contents of the sealed tubes were washed out, and the dibutylguanidine was precipitated as picrate, which was collected, washed, dried, weighed, recrystallized from benzene and identified by mixed melting point with a known sample.

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[8] Analyses of nearly all the sulfates, nitrates and picrates which are mentioned in this paper have been reported in an earlier article.[6]

[9] Franchimont, *Rec. trav. chim. Pays-bas.*, **3**, 220 (1884).

In the experiments with *n*-amylamine and *n*-amyl-nitroguanidine, the contents of the sealed tubes were washed onto filters, the solid matter was washed with cold water until the washings gave no precipitate with ammonium picrate, and the diamylurea which remained was dried, weighed, recrystallized from water, and identified by mixed melting point, 92.8°, with a known sample. The filtrates were precipitated with ammonium picrate, and the precipitates collected, etc., and recrystallized from benzene to constancy of melting point at 108°.

In the experiments with the *n*-heptyl derivatives, the reaction mixture was worked up in the same manner. The di-*n*-heptylurea, after recrystallization from dilute alcohol, melted at 91° as reported by Manuelli and Ricca-Rosellini,[10] and its melting point was not lowered by mixture with a sample, m. p. 91°, prepared from nitrourea and *n*-heptylamine. The di-*n*-heptylguanidine picrate, after recrystallization from alcohol, melted at 278° with decomposition.

Anal. Calcd. for di-*n*-heptylguanidine picrate: N, 17.35. Found: N, 17.21, 17.51.

In the experiments with the benzyl derivatives, the dibenzylguanidine could not be determined as picrate for the reason that benzylamine picrate precipitated at the same time and could not be separated from it. The dibenzylurea was collected by filtering the reaction mixture, recrystallized from dilute alcohol, and identified by mixed melting point with a known sample.

The results of the series of experiments are summarized in Table I.

TABLE I

EFFECT OF HYDROGEN-ION CONCENTRATION ON THE PRODUCTS OF THE REACTION OF A PRIMARY AMINE WITH THE CORRESPONDING ALKYLNITROGUANIDINE

			Yield, %	
Alkyl	Ratio of acetic acid to amine	PH	Dialkylurea	Dialkylguanidine
n-Butyl	1.1	5.34	..	13.5
n-Butyl	1.0	5.59	..	32.6
n-Butyl	0.9	6.13	..	38.2
n-Butyl	0.8	9.51	..	17.6
n-Amyl	1.1	5.67	37.1	16.0
n-Amyl	1.0	6.13	28.1	47.0
n-Amyl	0.9	9.46	33.0	42.1
n-Amyl	0.8	9.90	45.3	32.9
n-Heptyl	1.1	5.63	39.5	41.4
n-Heptyl	1.0	6.12	20.5	52.8
n-Heptyl	0.9	8.61	49.0	37.2
n-Heptyl	0.8	9.07	53.9	21.2
Benzyl	1.1	6.06	8.2	..
Benzyl	1.0	7.96	11.1	..
Benzyl	0.9	8.56	13.1	..
Benzyl	0.8	8.84	15.1	..

Effect of Carbon Dioxide.—Ten grams of methyl-nitroguanidine and 150 cc. of 21% methylamine solution were refluxed together under a pressure (above atmospheric pressure) of 508 cm. of mercury while carbon dioxide was bubbled through the solution. At the end of ten hours all of the methyl-nitroguanidine had disappeared and the solution no longer gave a blue color when a test portion was treated with a solution of diphenylamine in concentrated sulfuric acid. The reaction mixture, evaporated to a small volume and chilled, gave a white solid which, after recrystallization from a little

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(10) Manuelli and Ricca-Rosellini, *Gazz. chim. ital.*, **29**, II, 135 (1899).

water, showed the double melting point which has been reported for trimethylisomelamine,[11] namely, 123–124° and 179°; yield, 41.3%.

Anal. Calcd. for trimethylisomelamine: N, 50.00. Found: N, 49.41. The filtrate from the trimethylisomelamine, on precipitation with ammonium picrate, gave 11.8 g. (40.2%) of N,N'-dimethylguanidine picrate, m. p. 178° after recrystallization from water.

Ten grams of *n*-butyl-nitroguanidine, 20 g. of *n*-butylamine, and 150 cc. of water were similarly refluxed for twelve hours under pressure and in the presence of carbon dioxide. Two liquid phases remained. The aqueous phase, on precipitation with ammonium picrate, yielded 11.05 g. (42.4%) of N,N'-di-*n*-butylguanidine picrate, m. p. 122.5° after recrystallization from benzene. The oily phase, consisting probably of tri-*n*-butylisomelamine, could not be made to crystallize.

Ten grams of benzyl-nitroguanidine, 20 g. of benzylamine, and 150 cc. of water were similarly refluxed for fifteen hours. The solution on cooling deposited a white solid which, collected, dried and recrystallized from *n*-butyl alcohol, yielded 5.95 g. of tribenzylisomelamine (46.3%). Strakosch[12] previously prepared this substance but did not report the melting point. We find that it melts first at 146–147°, then solidifies, and finally melts again with decomposition at 157–158°.

Anal. Calcd. for tribenzylisomelamine: N, 21.21. Found: N, 21.01, 20.92. The dibenzylguanidine in the reaction mixture was not determined because of the difficulty of separating its picrate from the picrate of benzylamine.

Action of Concentrated Sulfuric Acid on Alkylguanidine Nitrates.—Four grams of methylguanidine nitrate was stirred slowly into 5 cc. of concentrated sulfuric acid cooled in a freezing mixture. The resulting thick paste was drowned in 30 cc. of cracked ice and water, and the material which precipitated, recrystallized once from alcohol, yielded 3.2 g. (91%) of N-ethyl-N'-nitroguanidine, m. p. 160–161°, identified by mixed melting point with a known sample, m. p. 160.5–161°.

Four grams of *n*-butylguanidine nitrate, by the same procedure, gave 3.1 g. (93%) of N-*n*-butyl-N'-nitroguanidine, m. p. 84.5°.

Three grams of N,N-dimethylguanidine nitrate, treated similarly with 4 cc. of concentrated sulfuric acid, gave 2.29 g. (87%) of N,N-dimethyl-N'-nitroguanidine, m. p. 194.5°.

N-*n*-Heptyl-N-nitroguanidine has not heretofore been described. A sample prepared by the action of 2 cc. of concentrated sulfuric acid on 0.3 g. of heptylguanidine nitrate was found to be identical with material prepared from heptylamine and nitroguanidine,[2] as follows. Twenty grams of nitroguanidine, 25 g. of *n*-heptylamine and 100 cc. of water were heated together in the water-bath at 65–70° for about an hour until all of the nitroguanidine had gone into solution. The reaction mixture was then chilled and saturated with carbon dioxide, and the heptyl-nitroguanidine which separated was collected and recrystallized from alcohol to constancy of melting point at 115°, 5 g. (13.5%).

Anal. Calcd. for heptyl-nitroguanidine: N, 27.92. Found: N, 27.86, 27.87.

The filtrate from the carbon dioxide treatment was divided into two portions. One portion on precipitation with ammonium picrate gave *n*-heptylguanidine picrate, light yellow needles from 20% alcohol, m. p. 140.5°. The other, evaporated to dryness and treated with dilute nitric acid, yielded *n*-heptylguanidine nitrate, stout colorless needles from water, m. p. 86°. The total amount of heptylguanidine obtained from this experiment was 38%.

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[11] Freund and Schwartz, *Ber.*, **29**, 2498 (1896); McKee. *Am. Chem. J.*, **36**, 208 (1906).

[12] Strakosch. *Ber.*, **5**, 694 (1872).

Nitration of Alkylguanidine Sulfates.—Three grams of methylguanidine sulfate was slowly stirred into 5 cc. of concentrated sulfuric acid chilled in a freezing mixture, 2.50 g. of potassium nitrate was added, the mixture was allowed to stand for five minutes and was drowned in 30 cc. of cracked ice and water. The product, after recrystallization from alcohol, amounted to 2.15 g. (75%) of N-methyl-N′-nitroguanidine.

An experiment with 2.15 g. of *n*-butylguanidine sulfate, 5 cc. of concentrated sulfuric acid and 1.85 g. of potassium nitrate yielded 1.95 g. (87%) of N-*n*-butyl-N′-nitroguanidine.

One with 3 g. of N,N-dimethylguanidine sulfate, 5 cc. of concentrated sulfuric acid and 2.43 g. of potassium nitrate gave 2.09 g. (75%) of N,N-dimethyl-N′-nitroguanidine.

Five grams of guanidine sulfate, 10 cc. of concentrated sulfuric acid. and 4.80 g. of potassium nitrate gave 4.18 g. (87%) of nitroguanidine.

Attempts to Nitrate N,N′,N″-Trimethylguanidine Nitrate.—Three grams of N,N′.N″-trimethylguanidine nitrate was stirred slowly into a mixture of 4 cc. of concentrated sulfuric acid and 2 cc. of nitric acid (1.42). Eighty-six per cent. of the material was recovered in the form of picrate. Three grams of the nitrate was added to 10 cc. of absolute white nitric acid; after half an hour at room temperature the mixture was drowned—and 78% of the material was recovered. Two grams of the nitrate, evaporated to dryness on the steam-bath with 20 cc. of absolute nitric acid, left a residue of 1.4 g. of the unchanged nitrate.

Action of Phosphoric Acid on Guanidine Nitrate.—Twenty cc. of 85% phosphoric acid was mixed with a 50 cc. volume of phosphorus pentoxide, 5 g. of guanidine nitrate was added, and the mixture was heated to 65° and held there for thirty minutes without signs of decomposition. When the mixture was drowned, there was no precipitate and 97% of the guanidine was recovered in the form of picrate.

Similar mixtures were allowed to stand at room temperature for periods up to thirty hours, and in each case 95% or more of the guanidine was recovered. A mixture which stood for forty-eight hours at room temperature. and was then drowned. yielded 3.5 g. (82%) of nitroguanidine.

Summary

N-Alkyl-N′-nitroguanidines dearrange in aqueous solution to form alkylcyanamides from which N,N′-dialkylguanidines may be produced by combination with primary amines. The tendency of the alkylcyanamides to hydrolyze or to polymerize impairs the usefulness of the synthesis. If the reaction mixtures are acidified with acetic acid to *P*H about 6.13, yields of 40–50% of the dialkylguanidines may be obtained.

The hydrolysis of the N-alkyl-N′-nitroguanidines is really the hydrolysis of their dearrangement products.

Monoalkylguanidines and N,N-dialkylguanidines nitrate on the non-alkylated nitrogen atom. We have not been able to nitrate other alkylguanidines.

The mechanism of the nitration is evidently not loss of water from the nitrate.

The basicity of guanidine and its derivatives is evidently a property of the molecule as a whole and not a property of any particular nitrogen atom.

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