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.

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

OTTAWA, ONTARIO

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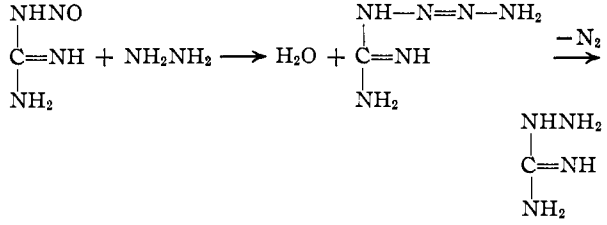
Representative examples of the previously unreported 1-(alkylamino)-guanidines have been prepared by the catalytic hydrogenation of the corresponding guanyl hydrazones. Methylhydrazine and nitrosoguanidine react to give principally 1-methyl-1-aminoguanidine; however, a small amount (*ca.* 4%) of 1-(methylamino)-guanidine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

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

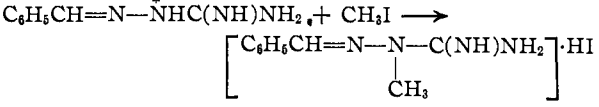
This method is similar to that employed for the reduction of semicarbazones to semicarbazides.[3] The general procedure is described in the experimental section; the results are outlined in Table I. These compounds do not form hydrazones with benzaldehyde in contrast to the behavior of the isomeric alkylaminoguanidines.

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



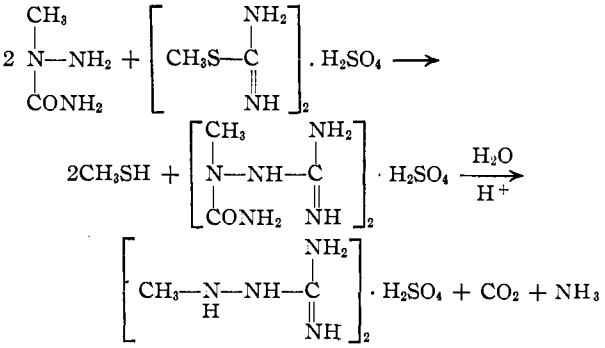
On this basis, one might expect the reaction of methylhydrazine and nitrosoguanidine to give 1-(methylamino)-guanidine; however, only about 4% of the latter is formed. The principal product is the isomeric compound, 1-methyl-1-aminoguanidine.[2] Guanidine, which results from the denitrosation of the 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]

(1) G. W. Kirsten and G. B. L. Smith, THIS JOURNAL, **58**, 800 (1936).

(2) A. H. Greer and G. B. L. Smith, *ibid.*, **72**, 874 (1950).

(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).

(4) J. Thiele, *Ann.*, **273**, 133 (1893).

(5) T. L. Davis and E. N. Rosenquist, THIS JOURNAL, **59**, 2112 (1937).

(6) C. Vogelesang, *Rec. trav. chim.*, **62**, 5 (1943).

TABLE I

COMPARISON OF GUANYL HYDRAZONES WITH THE CORRESPONDING 1-(ALKYLAMINO)-GUANIDINES, $RNHC(NH)NH_2$

	Hydrochlorides			Picrates		
		Nitrogen, %			Nitrogen, %	
R	M.p., °C.[a]	Calcd.	Found	M.p., °C. (dec.)[a]	Calcd.	Found
$CH_2{=}N-$	....	...	...	199.5	31.15	31.00
CH_3NH-	154.5–156	44.98	44.06[b]	193–194[c]	30.92	30.88[d]
$CH_3(CH_2)_2CH{=}N-$	....	...	...	198.5–199.5	27.45	27.38
$CH_3(CH_2)_3NH-$	....	...	...	174–175	27.29	27.14, 27.29[e]
$CH_3(CH_2)_5CH{=}N-$	....	...	...	186–187	24.56	24.53
$CH_3(CH_2)_6NH-$	....	...	...	163–164	24.43	24.44
$(CH_3)_2C{=}N-$	....	...	...	205.5–206.5	8.16[f]	8.16[f]
$(CH_3)_2CHNH-$	....	...	...	195–196[g]	28.40	28.58
$C_6H_{10}{=}N-$	208–210	29.38	29.50	187–187.5	25.59	25.51, 25.67
$C_6H_{11}NH-$	159–161	29.08	29.09	196–196.5[h]	25.45	25.49[i]
$4\text{-}CH_3C_6H_9{=}N-$	190–191	13.67[f]	13.77[f]	188–189	7.05[f]	7.02[f]
$4\text{-}CH_3C_6H_{10}NH-$	156–157	26.97	26.95	196–198	24.49	24.54
$C_6H_5CH{=}N-$	139–140	14.10[f]	14.01[f]	255–256	7.16[f]	7.08[f]
$C_6H_5CH_2NH-$	147–148[j]	27.92	27.60[k]	233	24.94	25.20

[a] All melting points are corrected. [b] Calcd. for $C_2H_9N_4Cl$: C, 19.28; H, 7.28. Found: C, 19.42; H, 7.05. [c] A polymorphic form melting at 182–183° was also obtained. A mixed melting point of this high melting form with the corresponding hydrazone was 187–187.5°; X-ray powder patterns were distinctly different. [d] Calcd. for $C_8H_{11}N_7O_7$: C, 30.29; H, 3.50. Found: C, 30.29; H, 3.57. [e] Calcd. for $C_{11}H_{17}N_7O_7$: C, 36.77; H, 4.77. Found: C, 36.53; H, 4.92. [f] Hydrazine nitrogen. [g] Mixed melting point with hydrazone was 185–187°. [h] Mixed melting point with hydrazone was 177–178°. [i] Calcd. for $C_{13}H_{19}N_7O_7$: C, 40.50; H, 4.97. Found: C, 40.43; H, 5.08. [j] Mixed melting point with hydrazone was 112–120°. [k] Calcd. for $C_8H_{13}N_4Cl$: C, 47.87; H, 6.53. Found: C, 48.09; H, 6.56.

Experimental[7]

1-(Alkylamino)-guanidines.—Recrystallized aminoguanidine hydrochloride (11.1 g., 0.1 mole) was suspended in 100 ml. of glacial acetic acid and 0.11 mole of aldehyde or ketone added with stirring. The mixture was heated at 60° until solution was complete and then transferred to a 375-ml. Parr hydrogenation bottle. Alternatively, the suspension could be shaken at room temperature in a closed flask until solution occurred.

The hydrogenation was performed over Adams platinum oxide (0.1 g.) and at an initial pressure of 50 p.s.i. In general, the hydrogen uptake was rapid and reached the theoretical limit of 0.1 mole in less than two hours; some hydrogenations were completed in about 30 minutes. The catalyst was removed by filtration and the filtrate concentrated to a sirup *in vacuo* on a steam-bath.

The methods used to purify the products varied. In a few cases it was possible to recrystallize the hydrochlorides from absolute ethanol or from mixtures of ethanol and diethyl ether. More often it was necessary to convert the very soluble, poorly crystallizable, hygroscopic 1-(alkylamino)-guanidine hydrochloride to the corresponding picrate and to recrystallize the latter from water, 95% ethanol, or mixtures thereof. Since the yields were not easy to ascertain, due to difficulties encountered in the purification and isolation of the hydrochlorides and picrates, they have not been listed.

The guanyl hydrazones listed in Table I for purposes of comparison were prepared by reacting 0.1 molar quantities of aminoguanidine hydrochloride and the carbonyl compound in 50 ml. of water at room temperature. If the hydrochloride of the hydrazone separated as a solid after cooling the solution to 0°, it was removed by filtration and recrystallized from water. If the hydrazone separated as an oil, it was recovered by extraction with diethyl ether which contained about 20% ethanol; the ethereal solution was carefully dried before evaporation. In general these hydrazones were then obtained as solids which could be recrystallized from absolute ethanol plus diethyl ether.

If the hydrochloride of the hydrazone did not separate from the aqueous solution, it was precipitated by conversion to the picrate using ammonium picrate. The picrates of these guanyl hydrazones were conveniently recrystallized from 95% ethanol.

Reaction of Methylhydrazine and Nitrosoguanidine.—A slurry of 13.2 g. of nitrosoguanidine (0.15 mole), 21.6 of methylhydrazine sulfate (0.15 mole), 12.0 g. of sodium hydroxide (0.30 mole) and 250 ml. of water was heated at 40–45° for five hours. The nitrosoguanidine dissolved completely during this period and there was a slow steady evolution of gas. The resulting solution was adjusted to *p*H 7 with concentrated sulfuric acid and evaporated to dryness on the steam-bath. By extracting the residue with eight 120-ml. portions of 79% ethanol and cooling the combined alcoholic extracts at 0°, there was recovered 9.1 g. (47.7%) of solid, m.p. 255–275°. (The mother liquors were retained for D.)

A.—When a small portion of this solid product was converted to the picrate and the latter recrystallized from water, yellow, dendritic needles were obtained which melted at 229° (dec.) and which were identical with an authentic sample of **1-methyl-1-aminoguanidine picrate** (m.p. 229.5–230.5°; mixed melting point 229°).

Anal. Calcd. for $C_8H_{11}N_7O_7$: N, 30.90. Found: N, 31.19.

B.—Nine grams of the solid product from A was dissolved in 50 ml. of water at 60° and shaken with 6.5 ml. of benzaldehyde for several hours until the latter was completely reacted. The solution was evaporated to dryness in a vacuum desiccator and the residue extracted with one 200-ml. portion and two 50-ml. portions of 95% ethanol. There was left 1.6 g. of insoluble material melting above 255°. When this residue was recrystallized several times from 70% ethanol, white needles, melting at 280–281°, were obtained. This compound proved to be a 1:1 **double salt of benzal-1-methyl-1-aminoguanidine sulfate and guanidine sulfate** and was conveniently prepared as follows: 0.05 mole of benzal-1-methyl-1-aminoguanidine sulfate was dissolved in 250 ml. of 95% ethanol and treated with 0.05 mole of guanidine sulfate in 100 ml. of hot water. Upon cooling the solution, rosettes of feathery needles separated; m.p. 280–282° (dec.).

Anal. Calcd. for $C_{10}H_{20}N_7SO_4$: C, 36.03; H, 5.74; N, 29.41. Found: C, 36.31, 36.13; H, 5.91, 5.78; N, 29.54.

C.—When the alcoholic extract from B was chilled at 0°, 11.0 g. of **benzal-1-methyl-1-aminoguanidine sulfate** was recovered as large hydrated prisms (12.9% H_2O; 3.5 H_2O requires 12.3%). Recrystallization of 3.36 g. from 100 ml. of 95% ethanol did not raise the melting point of 229–230° (dec.).

Anal. Calcd. for $C_{18}H_{26}N_8SO_4$: C, 47.99; H, 5.82; N, 24.87. Found: C, 48.13; H, 5.98; N, 24.54, 24.43.

The picrate, derived from this sulfate, decomposed at 220–221° after recrystallization from 95% ethanol and was identical with an authentic sample of **benzal-1-methyl-1-aminoguanidine picrate** (orange needles), prepared from benzal-1-methyl-1-aminoguanidine.[2]

Anal. Calcd. for $C_{15}H_{15}N_7O_7$: C, 44.45; H, 3.73. Found: C, 44.50; H, 3.60.

(7) All melting points have been corrected against known standards.

TABLE II

X-RAY POWDER PATTERN DATA FOR VARIOUS SAMPLES OF 1-(METHYLAMINO)-GUANIDINE PICRATE

Low melting form from hydrogenation[a]			High melting form from hydrogenation[a]			From methylhydrazine and nitrosoguanidine[b]		
2θ	d, Å.	I/I_0	2θ	d, Å.	I/I_0	2θ	d, Å.	I/I_0
7.8°	11.3	0.73	8.1°	10.9°	0.17	8.1°	10.9	0.4
9.9	8.93	.27	10.8	8.18	.08	10.7	8.25	.2
...	...	..	...	...	..	13.5	6.55	.05
15.0	5.90	.40	15.3	5.78	.22	15.6	5.67	.3
...	...	..	17.7	5.00	.39	[c]	...	..
18.2[c]	5.63	.60	18.3	5.61	.30	18.2	5.64	.8
21.3	4.16	.63	20.7[c]	4.27	1.00	21.1	4.20	1.0
23.2[c]	3.82	.17	...	...	..	23.4	3.80	0.1
...	...	..	24.2	3.67	0.13	23.9	3.72	.1
25.3	3.52	.57	25.5	3.49	.65	25.8	3.45	.7
...	...	..	26.3	3.38	.09	...	...	..
27.5	3.24	1.00	28.0	3.18	.74	28.1	3.17	.7
30.0	2.97	0.33	...	...	..	29.7	3.00	.05
...	...	..	30.8	2.90	.13	31.0	2.89	.2
32.9	2.72	.13	32.5	2.75	.09	32.8	2.73	.1
35.1	2.48	.11	34.8	2.57	.09	....	...	..

[a] Determined directly with CuKα, Ni filter, on Norelco Recording Spectrogoniometer. [b] Determined with CuKα, Ni filter, on Norelco X-Ray Diffraction Unit; lines measured on photograph; visual estimation of intensities. [c] Line at 18.2° may be double, 2 mm. wide.

D.—When the original ethanolic mother liquors were evaporated to dryness there was left 11.6 g. of gummy material. This residue was triturated with five 30-ml. portions of hot 95% ethanol to leave 7.2 g. of solid material. The extracts were retained for E. The solid was dissolved in 35 ml. of warm water and the solution shaken with 5 ml. of benzaldehyde until the latter dissolved. Upon cooling the solution at 0° for several hours a small amount of solid crystallized; it was removed, washed with small volumes of water, petroleum ether and ethanol. The yield was 0.95 g. and the material, after recrystallization, was identical with the double salt reported under B. The washings and the aqueous filtrate were combined, extracted with petroleum ether to remove excess benzaldehyde, and treated with 9 g. of picric acid in 150 ml. of hot water. The orange precipitate, which formed immediately, was removed by filtration after the solution had been chilled to 0°. The yield was 9.2 g.; m.p. 181–182° after softening. By fractional recrystallization from 95% ethanol the bulk of this picrate was found to be benzal-1-methyl-1-aminoguanidine picrate, m.p. 219–220°. A very sparingly soluble material (1.5–2 g.; 3.1–4.2%) was also recovered which melted at 189° (dec.) after recrystallization from water. A mixed melting point with a sample of 1-(methylamino)-guanidine picrate was 188–189°; the X-ray powder pattern for this compound was also identical with that for 1-(methylamino)-guanidine picrate (Table II).

E.—The first ethanolic extract from D was heated to boiling with 4 g. of picric acid, filtered and cooled to 0°. The mixture of picrates which crystallized melted at 150–155°. Small amounts of three products were isolated by fractional recrystallization from 95% ethanol. They were analyzed but not identified.

E-1.—A sparingly soluble material; yellow, feathery dendrites from water; m.p. 264° (dec.); a mixed melting point with ammonium picrate was 245–255°.

Anal. Found: C, 32.14, 32.08; H, 2.71, 2.64; N, 33.70, 33.66.

E-2.—A more soluble material; orange-yellow prisms; m.p. 157–159° (dec.) after recrystallization from 95% ethanol; a mixed melting point with 2-methylsemicarbazide picrate (m.p. 157°) was 140–145°.

Anal. Found: C, 30.71, 31.02; H, 3.42, 3.70; N, 29.97, 30.10. For methylamino-guanidine picrate ($C_8H_{11}N_7O_7$): C, 30.29; H, 3.50; N, 30.90.

E-3.—A still more soluble material; yellow spherulites; m.p. 163°; mixed melting points with E-2, methylhydrazine picrate (m.p. 170°), and 2-methylsemicarbazide picrate (m.p. 157°) were 142–145°, 145–155° and 150–153°, respectively.

Anal. Found: C, 30.51; H, 2.73.

Benzal-1-methyl-1-aminoguanidine Hydroiodide.—To a solution of 1.62 g. (0.01 mole) of benzalaminoguanidine in 25 ml. of absolute methanol was added 1.42 g. (0.01 mole) of methyl iodide. The solution was allowed to stand at room temperature for two days and then cooled to 0°. The crystalline product after filtration and drying weighed 2.1 g. (82.5% yield); it melted at 278–280° after five recrystallizations from hot methanol.

Anal. Calcd. for $C_9H_{13}N_4I$: C, 35.54; H, 4.31; N, 18.43. Found: C, 35.28; H, 4.43; N, 18.34.

The picrate prepared from the iodide and ammonium picrate in hot methanol solution, melted at 219–220° (dec.). A mixed melting point with an authentic sample of benzal-1-methyl-1-aminoguanidine picrate (above) was not depressed.

1-Methylbiurea. A.—A solution of 8.9 g. of 2-methylsemicarbazide (0.1 mole) and 13.9 g. of S-methylisothiourea sulfate (0.05 mole) in 50 ml. of water was refluxed for 48 hours. Methyl mercaptan was evolved very slowly. After the solution was cooled, the white, crystalline product was removed by filtration and dried; yield 8.0 g. (60.5%); m.p. 211–224°. A further quantity (3.1 g.) of very impure product (m.p. 200–210°) was obtained by refluxing the mother liquors for several days more. One recrystallization of the first crop from 50 ml. of water gave a compound which melted at 226–226.5° (dec.), and which did not give a test for sulfate or form a hydrazone with benzaldehyde.

Anal. Calcd. for $C_3H_8N_4O_2$: C, 27.27; H, 6.10; N, 42.41. Found: C, 27.29; H, 5.92; N, 42.02.

B.—A solution of 4.45 g. of 2-methylsemicarbazide, 4.1 g. of potassium cyanate and 3.0 g. of acetic acid in 50 ml. of water was evaporated to dryness on the steam-bath. When the residue had been recrystallized once from a minimum volume of hot water, the melting point of the product was 221–224° (dec.). Further recrystallization gave a product identical with that obtained in A.

2-Methylsemicarbazide picrate, yellow needles from 95% ethanol: m.p. 157–157.5°.

Anal. Calcd. for $C_8H_{10}N_6O_8$: N, 26.41. Found: N, 26.70.

Benzal-2-methylsemicarbazide picrate, orange needles from 95% ethanol; m.p. 146.5–147.5° (dec.).

Anal. Calcd. for $C_{15}H_{14}N_6O_8$: C, 44.34; H, 3.47. Found: C, 44.39; H, 3.10.

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INYOKERN, CHINA LAKE, CALIF.