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2-Nitroguanidine Derivatives: XI.* Reactions of *N*′-Nitrohydrazinecarboximidamide and 2-Methylidene-*N*′-nitrohydrazinecarboximidamide with Glyoxal

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Abstract—The reaction of glyoxal with *N*′-nitrohydrazinecarboximidamide (1-amino-2-nitroguanidine) in the presence of sodium hydroxide at a molar ratio of 1 : 1 : 1 gave *N*′-nitro-2-(2-oxoethylidene)hydrazinecarboximidamide as a mixture of *syn* and *anti* isomers, whereas at a reactant ratio of 1 : 2 : 2 *N*′-nitro-2-[(5-nitroamino-2*H*-1,2,4-triazol-3-yl)methyl]hydrazinecarboximidamide and 3-nitroamino-4,5-dihydro-1,2,4-triazin-5-ol were formed. *N*′-Nitro-2-(2-oxoethylidene)hydrazinecarboximidamide reacted with *N*′-nitrohydrazinecarboximidamide in boiling ethanol to give *N*′-nitro-2-[(5-nitroamino-2*H*-1,2,4-triazol-3-yl)methyl]hydrazinecarboximidamide, while in glacial acetic acid 2,2′-(ethane-1,2-diylidene)bis(*N*′-nitrohydrazinecarboximidamide) was obtained. The latter was also formed in the reaction of glyoxal with *N*′-nitrohydrazinecarboximidamide in acetic acid at room temperature. The reaction of 2-methylidene-*N*′-nitrohydrazinecarboximidamide with glyoxal led to the formation of 3-nitroimino-2,3,4,5-tetrahydro-1,2,4-triazine-5-carbaldehyde or 1-(methylideneamino)-2-(nitroimino)imidazolidine-4,5-diol, depending on the conditions.

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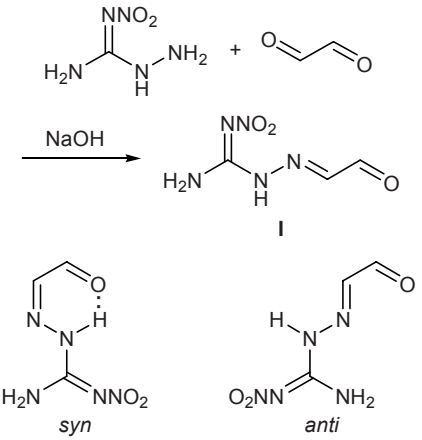
It is known that aminoguanidine nitrate and hydrochloride react with glyoxal in aqueous medium at room temperature to give the corresponding monohydrazone which reacts with the second aminoguanidine molecule on heating, yielding glyoxal bis-hydrazone [2]. Erickson later reported [3] that aminoguanidine bicarbonate reacts with glyoxal and biacetyl in aqueous medium at room temperature to produce 3-amino-1,2,4-triazine and 3-amino-5,6-dimethyl-1,2,4-triazine, respectively. The author believed that the monohydrazones formed by reactions of glyoxal and biacetyl with aminoguanidine bicarbonate, which is relatively insoluble in water, "are given a greater chance to cyclize before reacting further with aminoguanidine to form the osazones," for the concentration of the bicarbonate in the reaction medium is much lower than of the corresponding nitrate or hydrochloride.

Taking into account that dicarbonyl compounds (dialdehydes and diketones) react with hydrazine in a stepwise mode (initially one carbonyl group is involved, and then the other [4]), the reaction of 1-amino-2-nitroguanidine with glyoxal in the presence of sodium hydroxide was studied. The reaction was carried out at room temperature (2–3 h), and the subsequent acidification gave glyoxal monohydrazone **I** in 79% yield (Scheme 1). Compound **I** is a colorless crystalline substance, and its structure was confirmed by elemental analysis and ^{1}H NMR spectroscopy. According to the ^{1}H NMR data, hydrazone **I** is a mixture of *syn* and *anti* isomers at a ratio of 1 : 1.

Scheme 1.

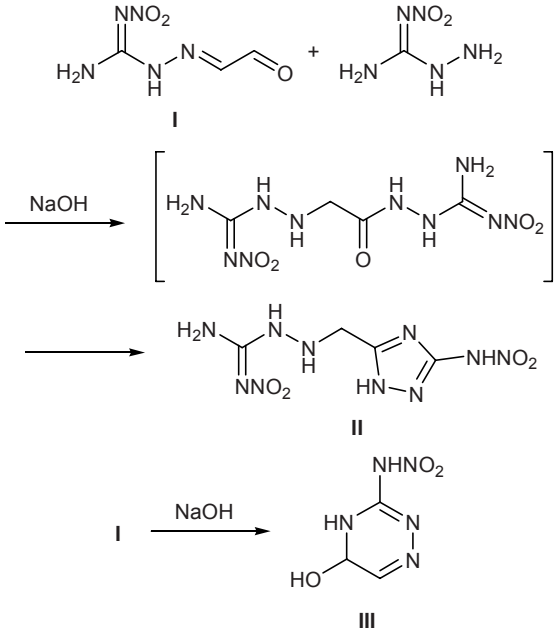


In order to obtain the corresponding glyoxal dihydrazone, 1-amino-2-nitroguanidine was brought into reactions with both hydrazone **I** and glyoxal. The reac-

* For communication X, see [1].

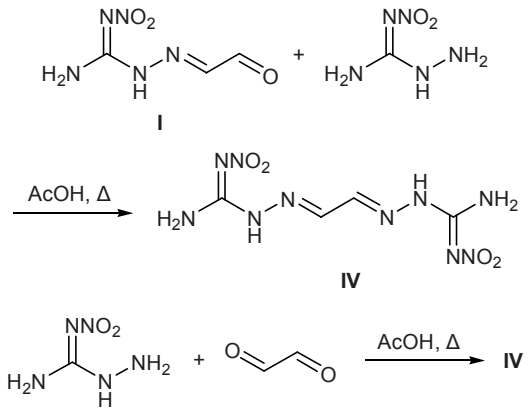
tion of **I** with 1-amino-2-nitroguanidine in the presence of sodium hydroxide, as well as the reaction of glyoxal with 2 equiv of 1-amino-2-nitroguanidine in alkaline medium, at room temperature gave compounds **II** and **III** decomposing at 187 and 123°C, respectively. Compound **II** is also readily formed by heating hydrazone **I** with 1-amino-2-nitroguanidine in boiling ethanol (reaction tome 12 h); here, the yield of **II** is quantitative. According to the ^{1}H NMR data, compound **II** is not an osazone. We presumed that hydrazone **I** in the presence of bases undergoes intramolecular redox transformation, which favors formation of *N*′-nitro-2-[(5-nitroamino-2*H*-1,2,4-triazol-3-yl)methyl]hydrazinecarboximidamide (**II**) (Scheme 2). The structure of **II** was confirmed by elemental analysis and ^{1}H and ^{13}C NMR spectra. The cyclization of hydrazone **I** in the reaction with 1-amino-2-nitroguanidine in aqueous medium in the presence of sodium hydroxide afforded 3-nitroamino-4,5-dihydro-1,2,4-triazin-5-ol (**III**).

Scheme 2.



Glyoxal dihydrazone **IV** was synthesized only when hydrazone **I** was heated with 1-amino-2-nitroguanidine for a long time in boiling glacial acetic acid. Compound **IV** was also formed directly from 1-amino-2-nitroguanidine and glyoxal on heating in glacial acetic acid (Scheme 3). Compound **IV** was isolated as a dark brown solid which is insoluble in water and most common organic solvents (except for DMSO). Purification by recrystallization from DMSO gave colorless glyoxal dihydrazone **IV**. In the ^{1}H NMR spectrum of **IV**, protons in the =CH groups resonated

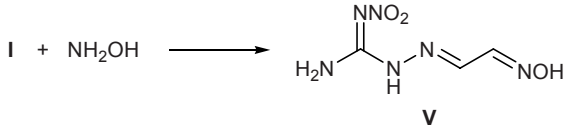
Scheme 3.



at δ 7.85 ppm, while protons in the amino groups gave rise to two separate signals. Presumably, magnetic nonequivalence of the NH_2 protons results from the presence in the molecule of a bulky electron-withdrawing substituent which is capable of stabilizing rotational isomers.

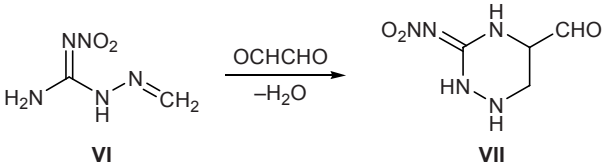
Unlike 1-amino-2-nitroguanidine, hydrazone **I** reacted with hydroxylamine in aqueous alkali at room temperature to produce 2-[2-(hydroxyimino)ethylidene]-*N*′-nitrohydrazinecarboximidamide (**V**) (Scheme 4).

Scheme 4.

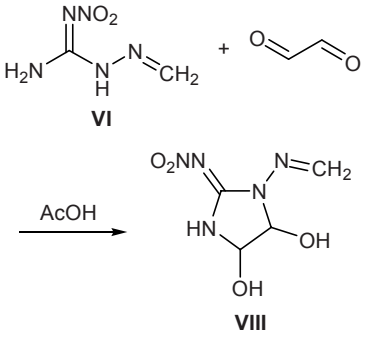


2-Methylidene-*N*′-nitrohydrazinecarboximidamide (**VI**) is characterized by π–*p*–π conjugation which should favor reaction of the amino group in the nitroguanidine fragment with glyoxal. Compound **VI** reacted with glyoxal in water at pH 8 (45–48°C, 10 h) to produce 3-nitroimino-2,3,4,5-tetrahydro-1,2,4-triazine-5-carbaldehyde (**VII**) (Scheme 5) as a colorless crystalline substance whose structure was confirmed by elemental analysis and ^{1}H NMR spectrum. The reaction of compound **VI** with glyoxal in glacial acetic acid at 50°C (10 h) lead to the formation of 1-(methylideneamino)-2-(nitroimino)imidazolidine-4,5-diol (**VIII**) (Scheme 6).

Scheme 5.



Scheme 6.



EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Bruker AC-200 spectrometer (200 MHz) from solutions in DMSO-d_6 using HMDS as external reference.

***N′*-Nitro-2-(2-oxoethylidene)hydrazinecarboximidamide (I).** A solution of 1.19 g (0.01 mol) of 1-amino-2-nitroguanidine and 0.04 g (0.01 mol) of sodium hydroxide in 20 ml of water was added over a period of 2.5 h to 1.93 g (0.01 mol) of 30% glyoxal in 40 ml of water under stirring at room temperature. The mixture was acidified with 20% sulfuric acid to pH 2 and kept for 20 h in a refrigerator, and the colorless precipitate was filtered off, washed with cold water, and dried at 50°C. Yield 1.27 g (79%), decomposition point 147°C (from alcohol). ^{1}H NMR spectrum, δ, ppm: 7.18 s (=CH), 7.26 s (=CH), 8.68 d (NH_2), 10.34 s (CHO), 10.61 s (CHO), 11.85 s (NH), 12.00 s (NH). Found, %: C 22.69; H 3.01; N 43.96. $C_3H_5N_5O_3$. Calculated, %: C 22.64; H 3.14; N 44.02.

***N′*-Nitro-2-[(5-nitroamino-2*H*-1,2,4-triazol-3-yl)methyl]hydrazinecarboximidamide (II) and 3-nitroamino-4,5-dihydro-1,2,4-triazin-5-ol (III).** *a*. A solution of 0.04 g (0.01 mol) of sodium hydroxide in 3 ml of water was added to 1.59 g (0.01 mol) of hydrazone **I** in 15 ml of water, and a solution of 1.19 g (0.01 mol) of 1-amino-2-nitroguanidine and 0.04 g (0.01 mol) of sodium hydroxide in 30 ml of water was then added under stirring. The mixture was stirred for 3 h, and the resulting dark red solution was acidified with 20% sulfuric acid to pH 2. The solution was kept for 16 h in a refrigerator, and the precipitate of **II** was filtered off, washed with cold water, and dried at 50°C. Yield 1.75 g (67%), decomposition point 192°C (from water). ^{1}H NMR spectrum, δ, ppm: 4.99 s (CH_2), 5.95 s (NH), 7.05 s (=CH), 7.96 s and 8.62 s (NH_2), 9.67 s (NH), 10.03 s (NH), 11.54 s (NHN=). ^{13}C NMR spectrum, δ_C, ppm: 162.9 s ($C{=}NNO_2$), 153.0 s ($CNHNO_2$), 138.7 s (HN–C=N), 61.4 s (CH_2). Found, %: C 18.61; H 3.28; N 53.74. $C_4H_8N_{10}O_4$. Calculated, %: C 18.46; H 3.08; N 53.85.

The filtrate was evaporated, and the precipitate of compound **III** was filtered off, washed with cold water, and dried at 50°C. Yield 0.52 g (33%), decomposition point 138°C (from aqueous alcohol, 1:1). ^{1}H NMR spectrum, δ, ppm: 5.21 s (OH), 6.79 s (CH), 7.14 s (=CH), 10.33 s (NH), 11.83 s (NH).

b. A solution of 2.38 g (0.02 mol) of 1-amino-2-nitroguanidine and 0.08 g (0.02 mol) of sodium hydroxide in 50 ml water was added over a period of 1.5 h to 1.9 g (0.01 mol) of 30% glyoxal in 30 ml of water under stirring at room temperature. The mixture was stirred for 4 h, left to stand for 16 h, and acidified with 20% sulfuric acid. The precipitate was filtered off, washed with cold water, and dried at 50°C. Yield of **II** 1.42 g (55%), decomposition point 192°C (from water). ^{1}H NMR spectrum, δ, ppm: 4.97 s (CH_2), 5.89 s (NH), 7.04 s (=CH), 7.90 s and 8.62 s (NH_2), 9.67 s (NH), 10.03 s (NH), 11.50 s (NHN=). Found, %: C 18.65; H 3.26; N 53.76. $C_4H_8N_{10}O_4$. Calculated, %: C 18.46; H 3.08; N 53.85.

The filtrate was evaporated in a hood, and the precipitate of compound **III** was filtered off, washed with cold water, and dried at 50°C. Yield 0.70 g (44%), decomposition point 138°C (from water). Found, %: C 22.67; H 2.95; N 43.88. $C_3H_5N_5O_3$. Calculated, %: C 22.69; H 3.14; N 44.02.

c. 1-Amino-2-nitroguanidine, 0.23 g (2 mmol), was added in portions over a period of 10 min to a solution of 0.32 g (2 mmol) of hydrazone **I** in 30 ml of ethanol, heated to 42°C. The mixture was heated for 11 h under reflux and cooled, and the colorless precipitate was filtered off. Yield of **II** 0.53 g (100%), decomposition point 195°C. ^{1}H NMR spectrum, δ, ppm: 4.98 s (CH_2), 5.91 s (NH), 7.04 s (=CH), 7.91 s and 8.62 s (NH_2), 9.67 s (NH), 10.03 s (NH), 11.51 s (NHN=).

2,2′-(Ethane-1,2-diylidene)bis(*N′*-nitrohydrazinecarboximidamide) (IV). *a*. 1-Amino-2-nitroguanidine, 0.23 g (2 mmol), was added to a suspension of 0.32 g (2 mmol) of hydrazone **I** in 10 ml of glacial acetic acid, and the mixture was heated for 5 h under reflux and cooled. The dark brown precipitate was filtered off, washed with water, and dried at 50–55°C. Yield 0.31 g (59%), decomposes above 300°C. Found %: C 18.54; H 2.98; N 53.72. $C_4H_8N_{10}O_4$. Calculated, %: C 18.46; H 3.07; N 53.84

b. 1-Amino-2-nitroguanidine, 0.46 g (4 mmol), was dispersed in 10 ml of glacial acetic acid at room temperature, and 0.5 g of 40% glyoxal in 6 ml of glacial

acetic acid was added. The mixture was heated for 17 h under reflux and evaporated under reduced pressure, and the dark red precipitate was washed with water and dried at 50°C. Yield 0.38 g (78%), decomposes above 300°C. ^{1}H NMR spectrum, δ, ppm: 7.85 s (=CH), 8.41 s and 8.85 s (NH_2), 12.08 s (NH).

c. 1-Amino-2-nitroguanidine, 0.24 g (2 mmol), was added under stirring to a mixture of 8 ml of glacial acetic acid and 0.4 g of 30% glyoxal. After 1 h, the mixture was heated to 90°C on a water bath until it became homogeneous. The solution was cooled to 20°C, stirred for 3 h at that temperature, and left overnight. The precipitate was filtered off, washed with water and alcohol, and dried at 75–80°C. Yield 0.19 g (73%), decomposes above 300°C. ^{1}H NMR spectrum, δ, ppm: 7.85 s (=CH), 8.42 s and 8.86 s (NH_2), 12.08 s (NH).

2-[2-(Hydroxyimino)ethylidene]-*N*′-nitrohydrazinecarboximidamide (V). A solution of 0.4 g (0.01 mol) of sodium hydroxide in 6 ml of water was added to a solution of 1.59 g (0.01 mol) of hydrazone **I** in 10 ml of water, and a solution of 0.4 g (0.012 mol) of hydroxylamine [prepared by alkalization of 0.81 g (0.012 mol) of hydroxylamine hydrochloride] and 0.47 g (0.012 mol) of sodium hydroxide in 10 ml of water was slowly added under stirring. The mixture was left to stand overnight at room temperature, acidified with 10% hydrochloric acid to pH 2, and kept for 3 h in a refrigerator, and the precipitate was filtered off, washed with water, and dried at 50–60°C. Yield 0.2 g (70%), decomposes above 250°C. ^{1}H NMR spectrum, δ, ppm: 7.25 d (C**H**=NOH), 7.81 q (CH=N), 8.31 d (C**H**=NOH), 8.35 s and 8.83 s (NH_2), 11.89 d (NHN=), 12.01 s (=NOH). Found, %: C 20.73; H 3.28; N 48.05. $C_3H_6N_6O_3$. Calculated, %: C 20.69; H 3.45; N 48.27.

3-Nitroimino-2,3,4,5-tetrahydro-1,2,4-triazine-5-carbaldehyde (VII). A solution of 0.2 g (1 mmol) of 30% glyoxal in 5 ml of water was adjusted to pH 8 by adding 20% aqueous potassium hydroxide and heated to 42–45°C, a solution of 0.13 g (1 mmol) of compound **VI** in 7 ml of water was added dropwise under stirring, and the mixture was stirred for 10 h at 45–48°C. After cooling, the precipitate was filtered off, washed with water, and dried at 70°C. Yield 0.08 g (45%), decomposes above 250°C. ^{1}H NMR spectrum, δ, ppm: 5.21 s (CH), 6.77 d (CH=N), 7.11 s (NH), 10.30 s (CH=O), 11.80 s (NH). Found, %: C 28.29; H 2.84; N 40.81. $C_4H_5N_5O_3$. Calculated, %: C 28.07; H 2.92; N 40.92.

1-(Methylideneamino)-2-(nitroimino)imidazolidine-4,5-diol (VIII). Compound **VI**, 0.13 g (1 mmol), was added under stirring to a mixture of 0.3 g (1.5 mmol) of 30% glyoxal and 7 ml of glacial acetic acid, and the mixture was stirred for 10 h at 50°C. The mixture was cooled, the solvent was removed under reduced pressure, and the precipitate was filtered off, washed with water, and dried at 70°C. Yield 0.08 g (45%), decomposition point 236°C. ^{1}H NMR spectrum, δ, ppm: 4.97 s (CH), 5.44 s (CH), 6.77 s (OH), 7.25 s (OH), 7.87 d and 7.94 d (N=CH_2), 10.00 s (NH). Found, %: C 25.82; H 2.52; N 36.43. $C_4H_5N_5O_4$. Calculated, %: C 25.66; H 2.67; N 36.41.

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