

2-Nitroguanidine Derivatives: IX.* Reaction of 1-Amino-2-nitroguanidine with Oxalic Acid as a Method of Synthesis of 3(5)-Nitroamino-1,2,4-triazole-5(3)-carboxylic Acid and 5,5'-Bi(3-nitroamino-1,2,4-triazole) Salts

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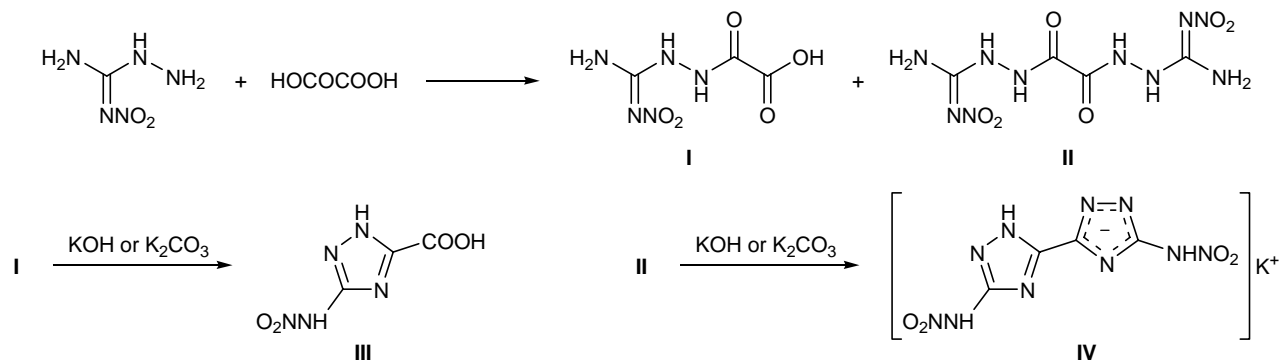
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Abstract—A new procedure for the synthesis of 5(3)-nitroamino-1,2,4-triazole-3(5)-carboxylic acid and 5,5'-bi(3-nitroamino-1,2,4-triazole) potassium salt has been developed. It includes cyclization of [2-(N^2 -nitrocarbamidoyl)hydrazino]oxoacetic acid and 2,2'-bis(N^2 -nitrocarbamidoyl)oxalohydrazide, respectively, which are prepared by reaction of 1-amino-2-nitroguanidine with oxalic acid. The reaction of 5(3)-nitroamino-1,2,4-triazole-3(5)-carbohydrazide with 1-methyl-2-nitro-1-nitrosoguanidine leads to N' -(N^2 -nitrocarbamidoyl)-5(3)-nitroamino-1,2,4-triazole-3(5)-carbohydrazide whose intramolecular cyclization in the presence of bases may be regarded as a new method of synthesis of 5,5'-bi(3-nitroamino-1,2,4-triazole) salts.

Methods of synthesis of 5(3)-amino-1,2,4-triazole-3(5)-carboxylate [2, 3] and 5,5'-bi(3-amino-1,2,4-triazole) [4, 5] have been reported. These compounds were prepared by cyclization of N -guanidinoxamate and N^1, N^2 -bis(carbamimidoyl)oxalohydrazide, respectively, which were obtained in turn by condensation of aminoguanidinium carbonate with oxalic acid. Taking into account anomalously high nucleophilicity of 1-amino-2-nitroguanidine, we anticipated that its reaction with oxalic acid should also lead to formation of both [2-(N^2 -nitrocarbamidoyl)hydrazino]oxoacetic acid (**I**) and N^1, N^2 -bis(N^2 -nitrocarbamidoyl)oxalohydrazide (**II**) whose cyclization should give the corresponding nitroaminotriazole derivatives.

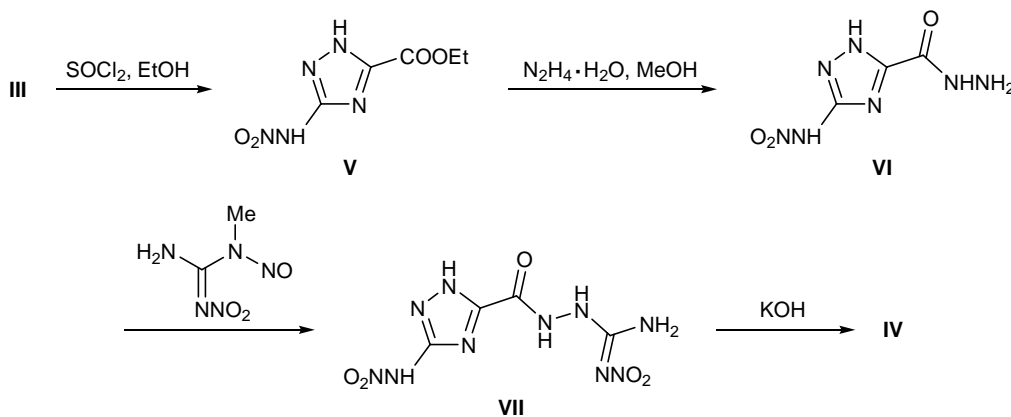
Our experiments showed that the reaction of 1-amino-2-nitroguanidine with oxalic acid in water at 92–94°C (reaction time 8 h) leads to the corresponding mono- and dihydrazides **I** and **II**. The subsequent heating of compounds **I** and **II** with potassium hydroxide or carbonate led to their cyclization to 5(3)-nitroamino-1,2,4-triazole-3(5)-carboxylic acid (**III**) and 5,5'-bi(3-nitroamino-1,2,4-triazole) potassium salt (**IV**), respectively (Scheme 1). The yields of condensation products **I** and **II** were 51 and 18%, respectively, when the ratio of 1-amino-2-nitroguanidine and oxalic acid was 1:1 or 2:1. Compounds **I** and **II** can readily be separated due to their different solubilities in water. The greater yield of monohydrazide **I** as compared to

Scheme 1.



* For communication VIII, see [1].

Scheme 2.



dihydrazide **II** may result from the fact that acid **I** exists as the corresponding dipolar ion in which the carboxylic group is deprotonated; therefore, its further reaction with 1-amino-2-nitroguanidine is slower.

Cyclization of hydrazides **I** and **II** to the corresponding nitroaminotriazoles **III** and **IV** was smoothly effected by the action of basic reagents, and the product yields were nearly quantitative (98 and 94%, respectively). Compound **III** can be obtained without isolation of intermediate condensation product **I**; for this purpose, the precipitate of dihydrazide **II** formed in the reaction of 1-amino-2-nitroguanidine with oxalic acid should be filtered off, potassium carbonate should be added to the filtrate, and the mixture should be heated for 8 h more. After acidification of the reaction mixture and cooling, compound **III** was isolated in 50% yield calculated on the initial 1-amino-2-nitroguanidine.

The structure of compounds **I–IV** was confirmed by the UV and ^1H NMR spectra. 5(3)-Nitroamino-1,2,4-triazole-3(5)-carboxylate (**III**) is characterized by a red shift of the main absorption maximum in the electron spectrum ($\Delta\lambda = 18$ nm) relative to the corresponding maximum in the spectrum of **I** ($\lambda_{\text{max}} 267$ nm, $\log \varepsilon = 4.5$), typical of the $\text{C}=\text{N}=\text{N}(\text{O})=\text{O}$ nitroguanidine fragment. This maximum is located at $\lambda 285$ nm, and it originates from $\pi-\pi^*$ transitions in the triazole ring conjugated with the nitroamino and carbonyl groups.

Study of the chemical transformations of 5(3)-nitroamino-1,2,4-triazole-3(5)-carboxylate (**III**) led us to develop a new procedure for the preparation of 5,5'-bi(3-nitroamino-1,2,4-triazole) potassium salt (**IV**). Treatment of compound **III** with thionyl chloride in ethanol gave ethyl 5(3)-nitroamino-1,2,4-triazole-3(5)-carboxylate (**V**). Ester **V** was brought into reac-

tion with hydrazine hydrate in methanol to obtain 5(3)-nitroamino-1,2,4-triazole-3(5)-carbohydrazide (**VI**), and the latter reacted with 1-methyl-2-nitro-1-nitrosoguanidine to afford N' -(N^2 -nitrocarbamiimidoyl)-5(3)-nitroamino-1,2,4-triazole-3(5)-carbohydrazide (**VII**). By heating compound **VII** in water in the presence of potassium hydroxide or carbonate we obtained 5,5'-bi(3-nitroamino-1,2,4-triazole) potassium salt (**IV**) (Scheme 2). When the cyclization of **VII** was carried out in the presence of sodium hydroxide or carbonate or guanidinium and aminoguanidinium carbonates, the products were the corresponding 5,5'-bi(3-nitroamino-1,2,4-triazole) salts **VIII–X** which were synthesized previously by cyclization of N^1, N^2 -bis(N^2 -nitrocarbamiimidoyl)oxalohydrazide [1].

EXPERIMENTAL

The ^1H NMR spectra were recorded on a Tesla BS-487C spectrometer (80 MHz) from solutions in $\text{DMSO}-d_6$ using HMDS as external reference. The UV spectra were measured on an SF-9 spectrophotometer equipped with an automatic recorder.

[2-(N^2 -Nitrocarbamiimidoyl)hydrazino]oxoacetic acid (I**) and N^1, N^2 -bis(N^2 -nitrocarbamiimidoyl)-oxalohydrazide (**II**).** A solution of 2.44 g (0.02 mol) of oxalic acid in 5 ml of water was added under stirring to a mixture of 2.38 g (0.02 mol) of 1-amino-2-nitroguanidine and 10 ml of water, heated to 60°C . The mixture was heated for 8 h at $90\text{--}95^\circ\text{C}$. The colorless precipitate was filtered off at $60\text{--}65^\circ\text{C}$, washed with methanol and diethyl ether, and dried at $50\text{--}55^\circ\text{C}$. We thus isolated 0.51 g (17.4%) of compound **II**, decomposition point 207°C . UV spectrum: $\lambda_{\text{max}} 269$ nm ($\log \varepsilon 4.43$). ^1H NMR spectrum, δ , ppm: 8.73 s (2H, NH_2), 9.95 s (1H, NH). Found, %: C 16.34; H 2.78;

N 48.06. $C_4H_8N_{10}O_6$. Calculated, %: C 16.46; H 2.74; N 47.97.

The filtrate was cooled, and the precipitate of compound **I** was filtered off and washed with alcohol and diethyl ether. Yield 1.41 g (50%), mp 174–175°C (from water). UV spectrum: λ_{\max} 269 nm ($\log \epsilon$ 4.00). 1H NMR spectrum, δ , ppm: 8.74 s (2H, NH_2), 9.97 s ($NHC=NO_2$), 11.02 s ($NHC=O$). Found, %: C 18.40; H 2.52; N 36.66. $C_3H_5N_5O_5$. Calculated, %: C 18.32; H 2.61; N 36.64.

5(3)-Nitroamino-1,2,4-triazole-3(5)-carboxylate (III). *a.* Potassium carbonate, 1.1 g (7.9 mmol), was added to a solution of 1.40 g (7.4 mmol) of compound **I** in 15 ml of water, heated to 50–55°C. The mixture was heated for 8 h on a water bath, cooled, and acidified with 10% sulfuric acid. After cooling for 40 min in a refrigerator, the precipitate was filtered off, washed with alcohol, and dried at 50–55°C. Yield 1.25 g (98%), mp 197–198°C (from water). IR spectrum, ν , cm^{-1} : 3600 (OH), 3430 (NH), 3200, 1650 (C=O), 1580, 1520, 1440 ($\nu_{as}NO_2$), 1320 (ν_sNO_2), 1300, 1240, 1100. UV spectrum: λ_{\max} 285 nm ($\log \epsilon$ 4.09). Found, %: C 20.96; H 2.22; N 40.44. $C_3H_3N_5O_4$. Calculated, %: C 20.81; H 1.73; N 40.46.

b. A solution of 2.44 g (0.02 mol) of oxalic acid in 6 ml of water was added under stirring to a mixture of 2.38 g (0.02 mol) of 1-amino-2-nitroguanidine and 10 ml of water, heated to 60°C. The mixture was heated for 8 h at 90–95°C, the colorless precipitate of compound **II** was filtered off at 60–65°C, and 1.1 g (7.9 mmol) of potassium carbonate was added to the filtrate. The mixture was heated for 8 h on a boiling water bath, cooled to room temperature, and acidified with 10% sulfuric acid. After cooling in a refrigerator, the precipitate was filtered off, washed with water, and dried at 50–55°C. Yield 1.76 g (50%), mp 198–199°C (from water). Found, %: C 20.72; H 2.10; N 40.65. $C_3H_3N_5O_4$. Calculated, %: C 20.81; H 1.73; N 40.46.

5,5'-Bi(3-nitroamino-1,2,4-triazole) potassium salt (IV). A solution of 0.24 g (4.3 mmol) of potassium hydroxide in 15 ml of water was added to a suspension of 0.5 g (1.7 mmol) of compound **II** in 20 ml of water. The mixture was heated for 1.5 h at the boiling point, cooled to 50°C, and acidified to pH 3 with nitric acid. The mixture was cooled over a period of 6 h, and the precipitate was filtered off, washed with cold water, and dried at 70–80°C. Yield 0.48 g (94%), decomposition point 234°C. UV spectrum: λ_{\max} 298 nm ($\log \epsilon$ 4.31). 1H NMR spectrum, δ , ppm: 7.46 s (1H, NH). Found, %: C 16.48; H 1.42; N 47.73. $C_4H_3KN_{10}O_4$. Calculated, %: C 16.32; H 1.02; N 47.62.

Ethyl 5(3)-nitroamino-1,2,4-triazole-3(5)-carboxylate (V). Freshly distilled thionyl chloride, 0.43 ml (6 mmol), was added dropwise to a suspension of 0.86 g (5 mmol) of compound **III** in 5 ml of anhydrous ethanol, cooled to 0–5°C. The cooling bath was removed, and the mixture became homogeneous in 30 min. It was kept for 48 h at room temperature, and the precipitate was filtered off, washed with water, and dried at 50°C. Yield 0.9 g (96%), mp 159–160°C. UV spectrum: λ_{\max} 285 nm ($\log \epsilon$ 4.09). Found, %: C 29.92; H 3.64; N 34.97. $C_5H_7N_5O_4$. Calculated, %: C 29.85; H 3.48; N 34.83.

5(3)-Nitroamino-1,2,4-triazole-3(5)-carbohydrazide (VI). Hydrazine hydrate, 0.4 ml, was added under stirring to a suspension of 0.47 g (2.5 mmol) of compound **V** in 10 ml of methanol. The mixture was heated for 30 min at 35–40°C and was left to stand for 4 h at room temperature. The slightly colored precipitate was filtered off and dispersed in water, and the mixture was acidified to pH 3.5–5 with dilute hydrochloric acid. The colorless precipitate was filtered off and washed with water and alcohol. Yield 0.32 g (84%), decomposition point 234°C. UV spectrum: λ_{\max} 288 nm ($\log \epsilon$ 4.10). Found, %: C 19.48; H 2.76; N 52.48. $C_3H_5N_7O_3$. Calculated, %: C 19.25; H 2.67; N 52.41.

N'-(N²-Nitrocarbamimidoyl)-5(3)-nitroamino-1,2,4-triazole-3(5)-carbohydrazide (VII). A solution of 0.147 g (1 mmol) of 1-methyl-1-nitroso-2-nitroguanidine in 7 ml of methanol was added under stirring to a suspension of 0.187 g (1 mmol) of compound **VI** in 7 ml of water. The mixture was heated for 40 min at the boiling point and cooled, and the precipitate was filtered off, washed with water, and dried at 50°C. Yield 0.24 g (88%), mp 155–157°C. UV spectrum: λ_{\max} 285 nm ($\log \epsilon$ 4.18). Found, %: C 16.72; H 1.94; N 48.42. $C_4H_6N_{10}O_6$. Calculated, %: C 16.55; H 2.06; N 48.27.

5,5'-Bi(3-nitroamino-1,2,4-triazole) potassium salt (IV). A solution of 0.12 g (2.1 mmol) of potassium hydroxide in 5 ml of water was added to a suspension of 0.24 g (0.83 mmol) of compound **VII** in 8 ml of water. The mixture was heated for 3 h at the boiling point, cooled to 50°C, and acidified to pH 3 with nitric acid. After cooling for 4 h, the precipitate was filtered off, washed with cold water, and recrystallized from water. Yield 0.23 g (93%), decomposition point 232°C. Found, %: C 16.58; H 1.14; N 47.92. $C_4H_3KN_{10}O_4$. Calculated, %: C 16.32; H 1.02; N 47.62. Compounds **VIII–X** were synthesized in a similar way.

5,5'-Bi(3-nitroamino-1,2,4-triazole) sodium salt (VIII) was obtained from 0.29 g (1 mmol) of compound **VII** and 0.1 g (2.5 mmol) of sodium hydroxide or 0.132 g (1.3 mmol) of sodium carbonate in 12 ml of water. Yield 0.25 g (86%), decomposition point 224°C. Found, %: C 17.54; H 1.82; N 50.21. $C_4H_3NaN_{10}O_4$. Calculated, %: C 17.27; H 1.08; N 50.36.

5,5'-Bi(3-nitroamino-1,2,4-triazole) guanidinium salt (IX) was obtained from 0.29 g (1 mmol) of compound **VII** and 0.22 g (1.3 mmol) of guanidinium carbonate in 12 ml of water. Yield 0.3 g (81%), decomposition point 235°C. Found, %: C 19.17; H 2.59; N 57.52. $C_5H_6N_{13}O_4$. Calculated, %: C 19.04; H 2.85; N 57.77.

5,5'-Bi(3-nitroamino-1,2,4-triazole) aminoguanidinium salt (X) was obtained from 0.29 g (1 mmol) of compound **VII** and 0.3 g (1.1 mmol) of aminoguanidinium hydrogen carbonate in 15 ml of water. Yield 0.29 g (83%), decomposition point 234°C. Found, %:

C 18.39; H 2.76; N 59.50. $C_5H_{10}N_{14}O_4$. Calculated, %: C 18.18; H 3.03; N 59.39.

The properties of compounds **IV** and **VIII–X** were identical to those reported in [1].

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