

## 2-Nitroguanidine Derivatives: X.\* Synthesis and Nitration of 4-Nitriminotetrahydro-1,3,5-oxadiazine and 2-Nitriminohexahydro-1,3,5-triazine and Their Substituted Derivatives

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**Abstract**—A new synthetic procedure was developed to obtain 1-hydroxymethyl-2-nitroguanidine from 2-nitroguanidine and formaldehyde without catalyst. Reactions of 2-nitroguanidine and its 1-methyl- and 1-phenyl-substituted derivatives with formaldehyde and urotropin under acid catalysis resulted in 4-nitriminotetrahydro-1,3,5-oxadiazine and 2-nitriminohexahydro-1,3,5-triazine and their methyl- and phenyl-substituted derivatives, whose nitration with concn. HNO<sub>3</sub> in the presence of acetic anhydride and concn. H<sub>2</sub>SO<sub>4</sub> depending on the temperature conditions led to the formation of 4-nitrimino-3,5-dinitrotetrahydro-1,3,5-oxadiazine, 3-methyl-4-nitrimino-5-nitrotetrahydro-1,3,5-oxadiazine, 2-nitrimino-5-nitrohexahydro-1,3,5-triazine, and 1,3,5-trinitro-hexahydro-1,3,5-triazine-2-one.

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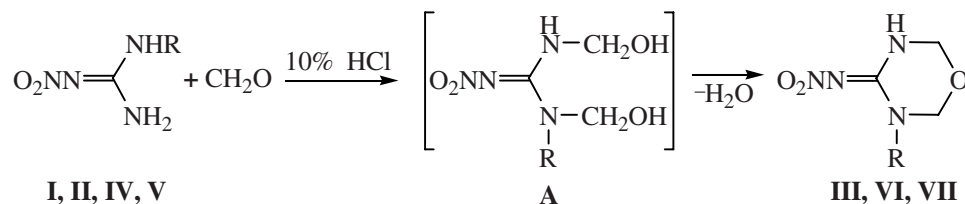
The reaction of 2-nitroguanidine with formaldehyde under catalysis with alkali is known to result in 1-hydroxymethyl-2-nitro-guanidine [2]. However the consideration of acid-base characteristics of the 2-nitroguanidine in the series of nitroamides and nitroamines permitted a suggestion that the nucleophilicity of the nitrogen in the molecule of 2-nitroguanidine is sufficient for this reaction to occur also without catalyst. We actually established that boiling of the 2-nitroguanidine with a triple excess of formaldehyde water solution for 3–5 min provided a hydroxymethyl derivative of 2-nitroguanidine **II** in 85% yield.

Inasmuch as in the molecules of 2-nitroguanidine (**I**) and 1-hydroxymethyl-2-nitroguanidine (**II**) a second, less reactive nucleophilic site was present we attempted to

add the formaldehyde to this site under conditions of acid catalysis.

The experiments showed that the heating of compounds **I** and **II** in 10% hydrochloric acid and excess formaldehyde solution at 80–85°C led to the formation of a heterocyclic compound, 4-nitriminotetrahydro-1,3,5-oxadiazine (**III**). Under similar conditions the reaction of 1-methyl- and 1-phenyl-2-nitroguanidine (**IV** and **V**) with formaldehyde water solution gave rise to new representatives of this series compounds, 3-methyl- and 3-phenyl-4-nitriminotetrahydro-1,3,5-oxadiazines (**VI** and **VII**).

The intermediate products of these reactions are evidently dihydroxymethyl derivatives **A** whose dehydration results in the cyclization.



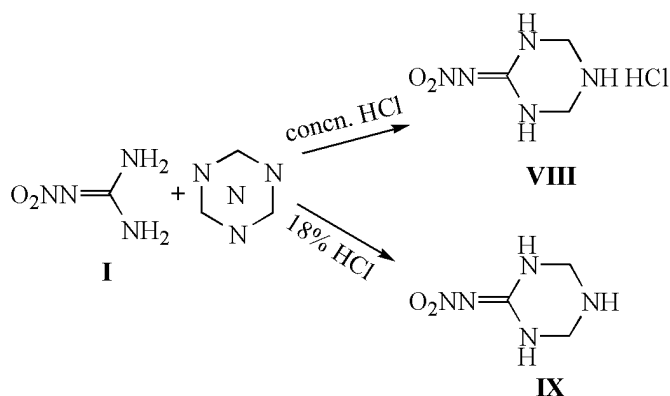
R = H (**I,III**), CH<sub>2</sub>OH (**II**), Me (**IV,VI**), Ph (**V,VII**).

\*For Communication IX, see [1].

Synthesized compounds **III**, **VI**, and **VII** are stable colorless crystalline substances, whose composition and structure was confirmed by elemental analyses and  $^1\text{H}$  NMR spectra. The character of  $^1\text{H}$  NMR spectra of compounds **III**, **VI**, and **VII** is similar for the spectra contain the methylene group signals in the region 5.10–5.32 ppm and downfield signals of the protons from the NH groups in the oxadiazine ring at 9.35–10.13 ppm

It was presumable that analogously to the reaction with formaldehyde the 2-nitroguanidine would take up urotropin in hydrochloric acid medium.

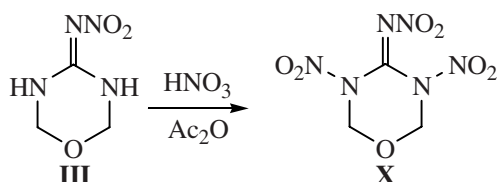
Actually, it was experimentally established that the reaction of 2-nitroguanidine (**I**) with urotropin in concn. HCl at room temperature led to the formation of 2-nitriminohexahydro-1,3,5-triazine monohydrochloride (**VIII**), and after heating the reagents in 18% hydrochloric acid at 50–55°C for 3 h we isolated a compound which was assigned the structure of nitrimine (**IX**) based on the elemental analysis and  $^1\text{H}$  NMR spectrum.



In the  $^1\text{H}$  NMR spectrum of 2-nitriminohexahydro-1,3,5-triazine (**IX**) in the downfield region appear three singlets of amine protons at  $\delta$  8.49, 9.11, and 9.49 ppm at the integral intensity ratio 1:1:1. In the upfield region the methylene groups signals are observed at  $\delta$  5.13 and 4.60 ppm (2:2).

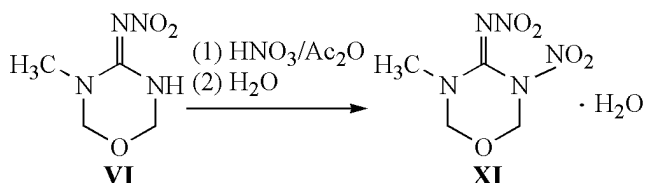
To prepare more nitrated analogs of compounds **III**, **VI**–**IX** nitration procedures were developed by concn.  $\text{HNO}_3$  in the presence of acetic anhydride and concn.  $\text{H}_2\text{SO}_4$ .

As a result of investigations it was established that the nitration of 4-nitriminotetrahydro-1,3,5-oxadiazine



(**III**) with concn.  $\text{HNO}_3$  in acetic anhydride at  $-2\pm 0^\circ\text{C}$  4-nitrimino-3,5-dinitrotetrahydro-1,3,5-oxadiazine (**X**) formed in a good yield.

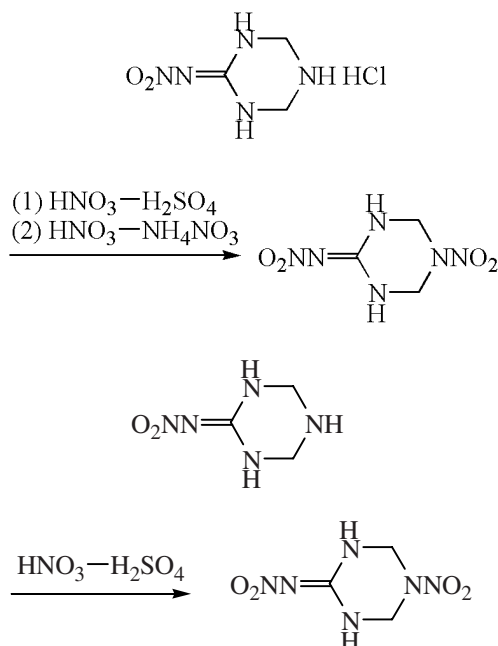
The nitration of 3-methyl-4-nitriminotetrahydro-1,3,5-oxadiazine (**VI**) with concn.  $\text{HNO}_3$  in acetic anhydride at  $-5^\circ\text{C}$  gave 3-methyl-4-nitrimino-5-nitrotetrahydro-1,3,5-oxadiazine (**XI**) that was isolated as hydrate.



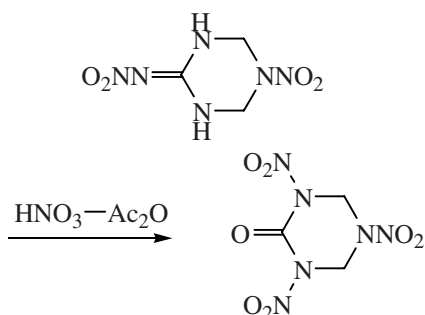
The composition and structure of nitro compounds **X** and **XI** were confirmed by elemental analyses and  $^1\text{H}$  NMR spectra.

In the  $^1\text{H}$  NMR spectrum of compound **X** the signals of methylene protons are present as singlets at  $\delta$  5.02 and 5.47 ppm, and in the spectrum of compound **XI** the singlets of methyl and methylene protons appear at  $\delta$  3.02, 5.11, and 5.74 ppm with the integral intensity ratio 3:2:2 respectively. Besides at  $\delta$  3.55 ppm a signal of protons from the water molecule appears as a singlet of integral intensity equal 2.

The treating of 2-nitriminohexahydro-1,3,5-triazine (**IX**) and its monohydrochloride **VIII** with nitrating mixtures  $\text{HNO}_3$ – $\text{H}_2\text{SO}_4$  and  $\text{HNO}_3$ – $\text{NH}_4\text{NO}_3$  provided 2-nitrimino-5-nitrohexahydro-1,3,5-triazine (**XII**).



The nitration of compound **XII** with concn.  $\text{HNO}_3$  in acetic anhydride at 15–45°C yielded its analog of a higher nitration degree, 1,3,5-trinitrohexahydro-1,3,5-triazin-2-one (**XIII**).



The composition and structure of nitro compounds **X–XIII** were confirmed by elemental analyses and  $^1\text{H}$  NMR spectra. Compounds **X** and **XII** were formerly described [3], but the nitration conditions of compounds **III** and **VIII** were not revealed.

## EXPERIMENTAL

$^1\text{H}$  NMR spectra were registered on spectrometers Tesla BS-487C (80 MHz) and Bruker AC-200 (200 MHz) in  $\text{DMSO}-d_6$ , external reference HMDS.

**1-Hydroxymethyl-2-nitroguanidine (II).** To a dispersion of 2.08 g (0.02 mol) of 2-nitroguanidine in 8 ml of water was poured 6 ml of 32% formaldehyde water solution, then the mixture was brought to boiling. After 2–3 min the formed solution was cooled, the separated amorphous precipitate was filtered off and recrystallized from water. Yield 2.55 g (85%), mp 220°C. Found, %: C 17.93; H 4.47; N 42.04.  $\text{C}_2\text{H}_6\text{N}_4\text{O}_3$ . Calculated, %: C 17.91; H 4.48; N 41.79.

**4-Nitriminotetrahydro-1,3,5-oxadiazine (III).** *a.* To a dispersion of 1.04 g (0.01 mol) of 2-nitroguanidine in 6 ml of 10% hydrochloric acid was added at stirring 4 ml of 35% formaldehyde water solution, and the mixture was heated for 3 h at 80–85°C. On cooling the separated precipitate was filtered off, washed with water, and dried at 50–55°C. Yield 0.84 g (56%), mp >300°C. Found, %: C 24.28; H 4.02; N 38.49.  $\text{C}_3\text{H}_6\text{N}_4\text{O}_3$ . Calculated, %: C 24.32; H 4.05; N 38.35.

*b.* To a dispersion of 1 g (8 mmol) of reagent **II** in 6 ml of 10% hydrochloric acid was added at stirring 4 ml of 35% formaldehyde water solution, and the mixture was heated for 3 h at 80–85°C. On cooling the separated

precipitate was filtered off, washed with water, and dried at 50–55°C. Yield: 0.56 g (51%), mp >300°C.  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 5.10 s (4H, 2 $\text{CH}_2$ ), 9.35 s (2H, 2NH). Found, %: C 24.28; H 4.02; N 38.49.  $\text{C}_3\text{H}_6\text{N}_4\text{O}_3$ . Calculated, %: C 24.32; H 4.05; N 38.35.

Compounds **VI** and **VII** were similarly obtained.

**3-Methyl-4-nitriminotetrahydro-1,3,5-oxadiazine (VI).** From 2.36 g (0.02 mol) of 1-methyl-2-nitroguanidine (**IV**) and 8 ml of 35% formaldehyde water solution we obtained 2.02 g (63%) of compound **VI**, mp 134–135°C (from water).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 3.10 s (3H, Me), 5.10 s (4H, 2 $\text{CH}_2$ ), 9.85 s (1H, NH). Found, %: C 29.92; H 5.11; N 35.34.  $\text{C}_4\text{H}_8\text{N}_4\text{O}_3$ . Calculated, %: C 30.00; H 5.00; N 35.00.

**3-Phenyl-4-nitriminotetrahydro-1,3,5-oxadiazine (VII).** From 1.8 g (0.01 mol) of 1-phenyl-2-nitroguanidine (**V**) in 6 ml of 10% hydrochloric acid and 4 ml of 35% formaldehyde water solution we obtained 0.89 g (40%) of compound **VII**, mp 155–156°C (from water).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 5.22 s (2H,  $\text{CH}_2$ ), 5.32 s (2H,  $\text{CH}_2$ ), 7.53 s (5H, Ph), 10.13 s (1H, NH). Found, %: C 48.46; H 4.58; N 25.41.  $\text{C}_9\text{H}_{10}\text{N}_4\text{O}_3$ . Calculated, %: C 48.65; H 4.54; N 25.23.

**2-Nitriminohexahydro-1,3,5-triazine monohydrochloride (VIII).** To a dispersion of 2.5 g (0.024 mol) of 2-nitroguanidine in 11 ml of concn. HCl was added at room temperature while stirring 2.6 g of urotropin. After the halogenization of the mixture (2 h) the flask was stoppered and put into a desiccator. After 3 days the formed solid was dissolved in 50 ml of water. The crystals precipitated on the next day were filtered off, washed with ethanol, and dried at 30°C. Yield 4.2 g (96%), mp 176°C. Found, %: C 19.78; H 4.51; N 38.57.  $\text{C}_3\text{H}_7\text{N}_5\text{O}_2 \cdot \text{HCl}$ . Calculated, %: C 19.84; H 4.408; N 38.45.

**2-Nitriminohexahydro-1,3,5-triazine (IX).** To a dispersion of 2.08 g (0.02 mol) of 2-nitroguanidine in 80 ml of 18% hydrochloric acid was added at stirring 3 g of urotropin in 7 ml of water, and the mixture was heated for 3 h at 55°C. The solution obtained was evaporated on a rotary evaporator. The colorless precipitate was filtered off and recrystallized from water. Yield 2.2 g (78%), t.decomp. 200–205°C. Found, %: C 24.78; H 4.84; N 48.51.  $\text{C}_3\text{H}_7\text{N}_5\text{O}_2$ . Calculated, %: C 24.82; H 4.82; N 48.27.

**4-Nitrimino-3,5-dinitrotetrahydro-1,3,5-oxadiazine (X).** At 0°C to 2.2 g (0.02 mol) of acetic anhydride was added dropwise at stirring 1.5 ml (0.035 mol) of concn.  $\text{HNO}_3$  ( $d$  1.51 g/cm<sup>3</sup>). Then at –2°C within 5 min

was added 0.5 g (3.5 mol) of reagent **III** which dissolved, and 20 min later a precipitate separated that was in 1 h filtered off, washed with cold water, and dried at 30–40°C. Yield 0.48 g (56%), t.decomp. 85°C. <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 5.20 s (CH<sub>2</sub>), 5.47 s (CH<sub>2</sub>). Found, %: C 15.35; H 1.98; N 35.47. C<sub>3</sub>H<sub>4</sub>N<sub>6</sub>O<sub>8</sub>. Calculated, %: C 15.25; H 1.69; N 35.59.

**3-Methyl-4-nitrimino-5-nitrotetrahydro-1,3,5-oxadiazine (XI).** To 1.5 g (14 mmol) of acetic anhydride was added at –5°C while stirring 0.6 ml (14 mmol) of concn. HNO<sub>3</sub> (*d* 1.50 g/cm<sup>3</sup>). To the solution obtained was added at –5°C within 20 min 1.1 g (7 mmol) of reagent **VI**. The mixture was stirred for 1.5 h at –5°C, then it was poured into ice mixed with water, at 0–5°C the formed precipitate was filtered off, washed with cold water, and dried in air. Yield 0.98 g (70%), t.decomp. 108°C. Found, %: C 21.96; H 4.16; N 31.12. C<sub>4</sub>H<sub>7</sub>N<sub>5</sub>O<sub>5</sub>·H<sub>2</sub>O. Calculated, %: C 21.53; H 4.04; N 31.38.

**2-Nitrimino-5-nitrohexahydro-1,3,5-triazine (XII).**  
*a.* At 0°C to 1.8 ml of concn. HNO<sub>3</sub> (*d* 1.51 g/cm<sup>3</sup>) was added at stirring 5.4 ml of 95% H<sub>2</sub>SO<sub>4</sub>. To the nitrating mixture at 0°C was added by small portions within 40 min 4.2 g (0.023 mmol) of 2-nitriminohexahydro-1,3,5-triazine monohydrochloride (**VIII**), then the mixture was warmed to 24°C and stirred at this temperature for 1 h. The reaction mixture was afterwards poured into ice water, the separated precipitate was filtered off, washed with cold water, and dried. Yield 3.9 g (94%), mp 187°C. Found, %: C 19.20; H 3.21; N 44.76. C<sub>3</sub>H<sub>6</sub>N<sub>6</sub>O<sub>4</sub>. Calculated, %: C 19.11; H 3.33; N 44.68.

*b.* At 0°C to 1.25 ml of concn. HNO<sub>3</sub> (*d* 1.51 g/cm<sup>3</sup>) was added at stirring 3.75 ml of 95% H<sub>2</sub>SO<sub>4</sub>. To the nitrating mixture at 0°C was added by small portions within 10 min 1.44 g (8 mmol) of 2-nitriminohexahydro-1,3,5-triazine (**IX**), then the mixture was warmed to 20–25°C, and the reaction mixture was kept at this temperature for 30–35 min. The reaction mixture was afterwards poured into ice water, the separated precipitate was filtered off, washed with cold water, and dried. Yield 1.2 g (82%), mp 187°C (from water). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 4.87 s (CH<sub>2</sub>), 5.31 s (CH<sub>2</sub>), 9.14 s (NH), 9.22 s (NH). Found, %: C 19.22; H 3.34; N 44.74. C<sub>3</sub>H<sub>6</sub>N<sub>6</sub>O<sub>4</sub>. Calculated, %: C 19.11; H 3.33; N 44.68.

*c.* To 10 ml of concn. HNO<sub>3</sub> (*d* 1.51 g/cm<sup>3</sup>) was added at stirring 5 g of ammonium nitrate, then at room temperature 0.5 g of 2-nitriminohexahydro-1,3,5-triazine monohydrochloride (**VIII**) was added. The reaction mixture was stirred for 1 h at 55°C, then it was cooled to

5°C, and poured into ice water. In 2.5 h the separated precipitate was filtered off, washed with cold water, and dried. Yield 0.35 g (67%), mp 187–188°C (from water). Found, %: C 19.16; H 3.28; N 44.62. C<sub>3</sub>H<sub>6</sub>N<sub>6</sub>O<sub>4</sub>. Calculated, %: C 19.11; H 3.33; N 44.68.

**1,3,5-Trinitrohexahydro-1,3,5-triazin-2-one (XIII).**  
*a.* At 0°C to 2.7 g (0.025 mol) of acetic anhydride was added 1.5 ml (0.035 mol) of concn. HNO<sub>3</sub> (*d* 1.51 g/cm<sup>3</sup>), then the mixture was heated to 45°C, and within 5 min was added at stirring 0.5 g (3 mmol) of compound **XII** that dissolved in 5–6 min, and within another 5 min a precipitate separated. After 1 h the reaction mixture was cooled to 10°C, the separated precipitate was filtered off, washed thrice with cold dichloromethane, and dried. Yield 0.32 g (53%), t.decomp. 173°C. <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 5.4 s (CH<sub>2</sub>), 6.05 s (CH<sub>2</sub>). Found, %: C 15.12; H 2.23; N 34.98. C<sub>3</sub>H<sub>6</sub>N<sub>7</sub>O<sub>4</sub>. Calculated, %: C 15.25; H 1.69; N 35.59.

*b.* To 2.7 g (0.025 mol) of acetic anhydride was added at 0°C 1.5 ml (0.035 mol) of concn. HNO<sub>3</sub> (*d* 1.51 g/cm<sup>3</sup>), then the mixture was warmed to 24°C, and within 5 min was added at stirring 0.5 g (3 mmol) of compound **XII**. After 25–30 min a precipitate started to form that 2 h later after cooling the reaction mixture to 5°C was filtered off, washed with cold water, and dried. Yield 0.3 g (50%), t.decomp. 173°C. Found, %: C 15.39; H 2.24; N 34.96. C<sub>3</sub>H<sub>6</sub>N<sub>7</sub>O<sub>4</sub>. Calculated, %: C 15.25; H 1.69; N 35.59.

*c.* At 0°C to 2.7 g (0.025 mol) of acetic anhydride was added 1.5 ml (0.035 mol) of concn. HNO<sub>3</sub> (*d* 1.51 g/cm<sup>3</sup>), then the mixture was warmed to 15°C, and within 5 min was added at stirring 0.5 g (3 mmol) of compound **XII**. After 40–45 min a precipitate started to form that 2 h later after cooling the reaction mixture to 5°C was filtered off, washed with cold dichloromethane, and dried at room temperature. Yield 0.3 g (50%), t.decomp. 173°C. Found, %: C 15.22; H 2.16; N 34.95. C<sub>3</sub>H<sub>6</sub>N<sub>7</sub>O<sub>4</sub>. Calculated, %: C 15.25; H 1.69; N 35.59.

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