ALKYLATION OF 5-NITRO-1, 2, 4-TRIAZOL-3-ONE

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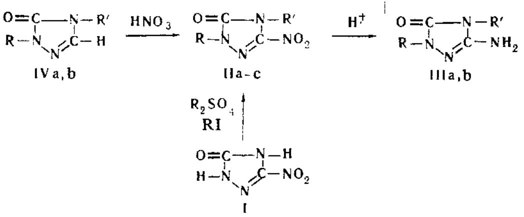
Khimiya Geterotsiklicheskikh Soedinenii, Vol. 5, No. 1, pp. 159–161, 1969

UDC 547.792.5: 542.951

The alkylation of 5-nitro-1, 2, 4-triazol-3-one with dialkyl sulfates and alkyl iodides has given N-alkyl-5-nitro-1, 2, 4-triazolones. The structure of the compounds obtained has been shown by independent synthesis via the corresponding N-alkyl derivatives of 1, 2, 4-triazol-3-one.

Alkyl derivatives of 5-nitro-1, 2, 4-triazol-3-one have not been described in the literature. The N-alkyl derivatives of unsubstituted 1, 2, 4-triazol-3-one have been obtained by cyclizing N-methylsemicarbazides with ethyl orthoformate [1] and by the deamination of 4-amino-2-ethyl-1, 2, 4-triazol-3-one [2].

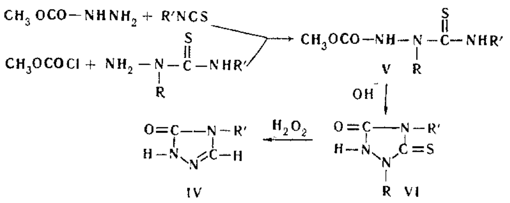
Alkylation of 5-nitro-1, 2, 4-triazol-3-one (I) with dimethyl sulfate or methyl iodide in an alkaline medium (with one equivalent of alkali) forms 4-methyl-5-nitro-1, 2, 4-triazol-3-one (**IIa**). However, increasing the concentration of alkali (3–5 mole of alkali per mole of nitro compound) in alkylation with dimethyl sulfate leads to the formation of 2-methyl-5-nitro-1, 2, 4-triazol-3-one (IIb). The higher alkyl iodides (ethyl, propyl, isopropyl, etc. iodides) do not react with nitrotriazolone under the conditions of this experiment. Alkylation of the silver salt of the nitrotriazolone with methyl iodide in methanol leads to the formation of an unstable intermediate compound which decomposes with the formation of the nitrotriazolone. Introduction of a second alkyl group into the molecule of a monosubstituted nitrotriazolone is difficult: in an alkaline medium, the dialkyl sulfates and alkyl halides hydrolyze more readily than they alkylate the corresponding compounds.



a R=H, R′=CH$_3$; b R=CH$_3$, R′=H; c R=H, R′=C$_2$H$_5$

The N-alkylnitrotriazolones II are colorless crystalline substances readily soluble in water and ethanol. The potassium and sodium salts of these compounds are readily soluble in water. Compounds **IIa, b** hydrolyze on being boiled with concentrated hydrochloric acid but are stable to the action of alkalies. After alkaline solutions of **IIa** and **b** have been boiled, acidification liberates a yellow compound with the same empirical composition and melting point. The reduction of both the yellow and the colorless forms of each of the alkylnitrotriazolones **IIa, b** forms one and the same amino compound **IIIa, b**, respectively, in each case but, for example, the colorless form of **IIa** forms a yellow silver salt and the yellow form of the same compound forms a brown salt. The structure of the yellow forms of the alkylnitrotriazolones has not been established.

The position of the alkyl group in the molecule of an alkylnitrotriazolone was determined by nitrating the corresponding N-alkyl derivatives of 1, 2, 4-triazol-3-one, which we obtained by the alkylation and cyclization of 2-methylsemicarbazide hydrochloride in formic acid by a published method [3], and from the corresponding monothiourazoles [4, 5] in the following way:



a R=R′=H; b R=H, R′=CH$_3$; c R=CH$_3$, R′=H

By the catalytic reduction of the N-alkylnitrotriazolones **IVa, b** over Adams catalyst we have obtained for the first time N-alkyl derivatives of 5-amino-1, 2, 4-triazol-3-one (**IIIa, b**).

EXPERIMENTAL

4-Methyl-5-nitro-1, 2, 4-triazol-3-one (IIa, colorless form). a) A mixture of 10.4 g (0.08 mole) of the nitrotriazolone, 5 ml (0.08 mole) of methyl iodide, and 4.5 g (0.08 mole) of caustic potash in 20 ml of water was kept at 100° C in a sealed tube for 6 hr. After cooling **IIa** crystallized out. Yield 5.7 g (50%), mp 179° C (decomp., from water). Found, %: C 25.10; H 2.73; N 38.73. Calculated for $C_3H_4N_4O_3$, %: C 25.01; H 2.79; N 38.87.

b) With stirring, 2 ml (0.02 mole) of dimethyl sulfate was added to a solution of 3.36 g (0.02 mole) of the potassium salt of the nitrotriazolone [3] in 30 ml of water, and the mixture was left a room temperature for 14 hr. Compound **IIa** crystallized out. Yield 0.77 g (26.6%), mp 179° C (decomp.).

The silver salt (yellow) precipitated when equimolar solutions of the methylnitrotriazolone and silver nitrate were mixed. Found, %: C 14.15; H 1.27. Calculated for $C_3H_3N_4O_3Ag$, %: C 14.36; H 1.21 .

2-Methyl-5-nitro-1, 2, 4-triazol-3-one (IIb). With stirring, 1.88 ml (0.02 mole) of dimethyl sulfate was added to a solution of 2.6 g (0.02 mole) of the nitrotriazolone and 3.36 g (0.06 mole) of caustic potash in 10 ml of water. After cooling, the mixture was acidified with hydrochloric acid to pH ~2. Compound **IIb** crystallized out. Yield 2.6 g (92.8%). After recrystallization from ethanol, mp 227–228° C (decomp.). Found, %: C 24.15; H 3.01; N 39.00. Calculated for $C_3H_4N_4O_3$, %: C 25.01; H 2.79; N 38.86.

4-Ethyl-5-nitro-1, 2, 4-triazol-3-one (IIc). This was obtained by alkylating the nitrotriazolone with diethyl sulfate in a similar manner to the synthesis of **IIa**. Mp 165° C (decomp.). Found, %: N 35.97. Calculated for $C_4H_6N_4O_3$, %: N 35.43.

Yellow forms of the N-alkylnitrotriazolones. These were obtained by boiling the corresponding N-alkylnitrotriazolones in 20% caustic potash solution for 1 hr. After cooling, the solution was acidified with concentrated hydrochloric acid to pH ~2. The yellow forms of the N-alkylnitrotriazolones precipitated.

The silver salts of these compounds were obtained as described above for **IIa**.

Yellow form of compound **IIa**. Mp 179° C (decomp., from water). Found, %: C 25.29; H 3.06. Calculated for $C_3H_4N_4O_3$, %: C 25.01; H 2.79. Silver salt—brown. Found, %: C 14.00; H 1.74. Calculated for $C_3H_3N_4O_3Ag$, %: C 14.36; H 1.21.

Yellow form of compound **IIb**. Mp 228–229° C (decomp.). Found, %: C 25.12; H 2.68; N 39.08. Calculated for $C_3H_4N_4O_3$, %: C 25.01; H 2.79; N 38.86.

Yellow form of compound **IIc**. Mp 186° C (decomp.). Found, %: N 35.34. Calculated for $C_4H_6N_4O_3$, %: N 35.43.

Reduction of the N-alkylnitrotriazolones. A solution of 0.005 mole of **IIa** (colorless or yellow form) or **IIb** (colorless or yellow form) in 80 ml of water was treated with 0.1 g of Adams catalyst and reduced with hydrogen. The theoretical amount of hydrogen was absorbed in 4 hr. After the catalyst had been filtered off, the solution was evaporated to dryness and the residue was recrystallized from a suitable solvent.

5-Amino-4-methyl-1,2,4-triazol-3-one. Yield 49%, mp 228–229° C (from water). Found, %: C 31.73; H 5.58; N 48.91. Calculated for $C_2H_4N_4O$, %: C 31.58; H 5.30; N 49.08.

5-Amino-2-methyl-1,2,4-triazol-3-one. Yield 63%, mp 211° C (from ethanol). Found, %: C 31.88; H 5.60; N 48.72. Calculated for $C_2H_4N_4O$, %: C 31.58; H 5.30; N 49.08.

1-Methoxycarbonylthiosemicarbazide (Va). a) At 50–60° C over 30 min, 23 ml (0.3 mole) of methyl chloroformate was added to a solution of 27.3 g (0.3 mole) of thiosemicarbazide in 330 ml of 50% ethanol. On cooling, **Va** crystallized out. Yield 35.5 g (79.4%). Mp 190° C (decomp.). After crystallization from ethanol or acetic acid, mp 198° C (decomp.). Found, %: N 28.15. Calculated for $C_3H_7N_3O_2$, %: N 28.17.

b) A solution of 2.53 g (0.02 mole) of methyl hydrazinecarboxylate hydrochloride and 1.94 g (0.02 mole) of potassium thiocyanate in 40 ml of water was evaporated to dryness on the water bath. Another 40 ml of water was added and evaporation was repeated twice. The residue was extracted with 30 ml of hot anhydrous ethanol. On cooling, 0.25 g of **Va** crystallized out. Mp 198° C (decomp., from ethanol). A mixture with the substance obtained by method (a) gave no depression of the melting point.

1-Methoxycarbonyl-4-methylthiosemicarbazide (Vb). a) A suspension of 6.3 g (0.06 mole) of 4-methylthiosemicarbazide in 30 ml of ethanol was treated with 4.8 ml (0.06 mole) of methyl chloroformate, and the solution was heated to the boil. On cooling, **Vb** crystallized out. Yield 7.3 g (74.6%), mp 185° C (decomp., from water). Found, %: C 29.81; H 5.54, N 25.61. Calculated for $C_4H_9N_3O_2$, %: C 29.44; H 5.55; N 25.73.

b) A mixture of 2.52 g (0.02 mole) of methyl hydrazinecarboxylate hydrochloride, 1.12 g (0.02 mole) of caustic potash, and 1.46 g (0.02 mole) of methyl isothiocyanate in 15 ml of water was boiled for 4 hr. On cooling, **Vb** crystallized out. Yield 1.1 g (33.6%), mp 185° C (decomp.). It gave no depression of the melting point with the substance obtained by method (a).

4-Methylmonothiourazole (VIb). A mixture of 1.63 g (0.012 mole) of **Vb**, 1.05 g (0.01 mole) of sodium carbonate, and 5 ml of water was boiled for 1 hr. After neutralization with hydrochloric acid, **VIb** separated out. Yield 0.6 g (45.8%), mp 212° C (decomp., from water) [6]. Found, %: C 27.51; H 3.35; N 31.78. Calculated for $C_3H_5N_3OS$, %: C 27.49; H 3.84; N 32.04.

1-Methylmonothiourazole (VIc). A mixture of 2.1 g (0.02 mole) of 2 methylthiosemicarbazide and 1.5 ml (0.02 mole) of methyl chloroformate in 25 ml of 50% ethanol was boiled for 15 min. The solvent was distilled off in vacuum and the residue was treated with 3 ml of 95% ethanol. The precipitate of **Vc** that deposited was boiled with 1 g (0.01 mole) of sodium carbonate in 5 ml of water for 1 hr. On neutralization with hydrochloric acid, **VIc** separated out. Yield 1.0 g (40%), mp 258° C (decomp., from water). Found, %: C 27.38; H 3.93; N 32.04. Calculated for $C_3H_5N_3OS$, %: C 27.49; H 3.84; N 31.34.

4-Methyl-1,2,4-triazol-3-one (IVa). A solution of 13.1 g (0.1 mole) of **VIb** in 40 ml of water was slowly treated with 50 ml of 30% hydrogen peroxide. The solution was heated to the boil and then evaporated to dryness, the residue was dissolved in 30 ml of water, and the solution was neutralized with sodium bicarbonate and again evaporated. The residue was extracted with hot ethyl acetate (6 × × 50 ml). Evaporation of the solvent yielded 3.1 g (45%) of **IVa**, mp 158° C (decomp., from ethyl acetate) [1]. Found, %: C 36.10; H 5.06; N 43.04. Calculated for $C_3H_5N_5O$, %: C 36.37; H 5.08; N 42.39.

2-Methyl-1,2,4-triazol-3-one (IVb). A mixture of 2.3 g of 2-methylsemicarbazide hydrochloride and 3 ml of 95% formic acid was boiled for 3 hr and cooled. **IVb** crystallized out, yield 0.6 g (33.3%), mp 178° C (decomp., from ethyl acetate) [1,2]. Found, %: C 36.55; H 5.29; N 42.68. Calculated for $C_3H_5N_3O$, %: C 36.37; H 5.08; N 42.39.

Nitration of the N-alkyltriazolones. A N-alkyltriazolone (0.66 g; 0.0066 mole) was treated with 0.4 ml of water and 0.8 ml of fuming nitric acid (d 1.495). The mixture was heated until the reaction began. On cooling, the corresponding N-alkyltriazolone **IIa** or **b** crystallized out.

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21 June 1966

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