HETEROCYCLIC NITRO COMPOUNDS

II. Alkylation Of Nitro-1, 2, 4-Triazoles*

L. I. Bagal, M. S. Pevzner, N. I. Sheludyakova, and V. M. Kerusov

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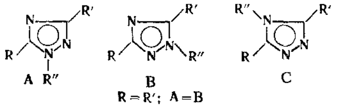
The methylation of 3-nitro-1, 2, 4-triazole (I), 3-nitro-5-methyl-1, 2, 4-triazole (II), 3-nitro-5-methoxycarbonyl-1, 2, 4-triazole (III), and 3, 5-dinitrotriazole (IV) with dimethyl sulfate in alkaline media takes place in the 1-position of the triazole ring. Alkylation of I and II with diazomethane gives a mixture of the N_1 and N_2 products. 3, 5-Dinitrotriazole gives a single, N_1-alkylation product under various conditions.

Alkylation of 1, 2, 4-triazoles which are unsymmetrically substituted in the 3(5) positions, can, theoretically, give three isomers (A, B, and C):


A B C

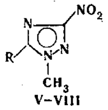
R=R'; A=B

Alkylation of unsymmetrically substituted 1, 2, 4-triazoles, depending on the conditions (solvent, reagent), gives a mixture of isomers containing predominantly the N_1 or N_2 substituted products, but the formation of the N_4 substituted products has not been observed [2–5]. Only in the case of the alkylation of 5-furyl-substituted 3-amino-1, 2, 4-triazoles [6] with methyl iodide in neutral media does N_4-alkylation occur. Literature references to the alkylation of nitro-1, 2, 4-triazoles is confined to a paper [7] in which the preparation of a methyl derivative of 3, 5-dinitro triazole is mentioned, the position of the methyl group not being established.

In continuation of investigations into the reactions and properties of nitro-1, 2, 4-triazoles [1], we have examined the N-alkylation of 3-nitro-1, 2, 4-triazole (I), 3-nitro-5-methyl-1, 2, 4-triazole (II), 3-nitro-5-methoxycarbonyl-1, 2, 4-triazole (III), and 3, 5-dinitro-1, 2, 4-triazole (IV).

Reaction of compounds I–IV with dimethyl sulfate in acetone, alcohol, or in their mixtures with water, in presence of sodium carbonate or hydroxide, introduces a single methyl group.

Thin-layer chromatographic examination of the products of alkylation shows that only one isomer is formed in all cases, and establishes that methylation takes place in the 1-position (V–VIII). The location of the methyl group in V (R_f 0.39) was determined by comparing it with the isomeric 1-methyl-5-nitro-1, 2, 4-triazole XII [1] (R_f 0.61), and 3-nitro-4-methyl-1, 2, 4-triazole [1] (R_f 0.20).


V–VIII

V R=H;
VI R=CH_3;
VII R=$COOCH_3$;
VIII R=NO_2

We have also synthesized by this method [1] the isomers of **VI**: 1, 3-dimethyl-5-nitro-1, 2, 4-triazole (IX), and 3-nitro-4, 5-dimethyl-1, 2, 4-triazole (X). Comparison of the methylation products of 3-nitro-5-methyl-1, 2, 4-triazole showed that a single isomer was obtained, namely, 1, 5-dimethyl-3-nitro-1, 2, 4-triazole (VI).

The location of the methyl group in the methoxycarbonyl derivative VII was established by comparison with the isomeric 1-methyl-3-methoxycarbonyl-5-nitro-1, 2, 4-triazole (XI), and also by hydrolysis of the ester group,

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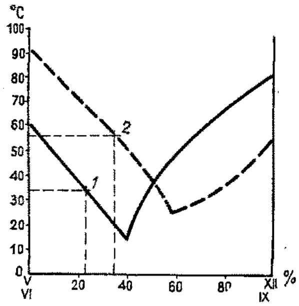
*For part I, see [1].

followed by decarboxylation to give 1-methyl-3-nitro-1, 2, 4-triazole (V). The structure of VIII was established by indirect synthesis from 1-methyl-3, 5-diamino-1, 2, 4-triazole, by the Sandmeyer reaction.

Composition diagrams: 1) System V–XIII;
2) System VI–IX.



The results obtained permit a qualitative description of the electron density distribution and the relative nucleophilicities of the nitrogen atoms in the nitrotriazole anion. Starting from information on the structure of triazole anions [8], and also by analogy with the anion of 4-nitroimidazole [9], and taking into account the inductive effect of the nitro group, it is possible to postulate with a fair degree of certainty that the greatest electron density in the nitrotriazole anion will be found at the N_2 nitrogen atom, and consequently the greatest polarizability will occur at N_1.

Steric factors apparently play a lesser role in the alkylation with dimethyl sulfate, and do not influence the isomer composition, since replacement of the hydrogen atom in the 5-position by methyl or methoxycarbonyl groups does not change the position of alkylation. Methylation of I and II with diazomethane affords a mixture of isomers. In the first case, the mixture consists of 1-methyl-3-nitro-1, 2, 4-triazole (V, 76%) and 1-methyl-5-nitro-1, 2, 4-triazole (XII, 24%); and in the second case, 1, 3-dimethyl-5-nitro-1, 2, 4-triazole (IX, 36%) and 1, 5-dimethyl-3-nitro-1, 2, 4-triazole (VI, 64%). In no case was N_4-substitution observed.

In order to establish the quantitative composition of the isomer mixtures, the melting point diagrams of the systems 1-methyl-3-nitro-1, 2, 4-triazole (V), 1-methyl-5-nitro-1, 2, 4-triazole (XII), and 1, 3-dimethyl-5-nitro-1, 2, 4-triazole (IX), 1, 5-dimethyl-3-nitro-1, 2, 4-triazole (VI) were examined (see Figure).

All these facts are in agreement with the low selectivity of the alkylating agent involving the carbonium ion reaction mechanism, as in the case of diazomethane [10].

Alkylation of the dinitrotriazole IV with diazomethane, and of its silver salt with methyl iodide, gave a single reaction product, 1-methyl-3, 5-dinitro-1, 2, 4-triazole (VIII), no N_4-substitution being observed.

EXPERIMENTAL

1-Methyl-3-nitro-1, 2, 4-triazole (V). Two grams (0.0176 mole) of I [1] was dissolved in 40 ml of acetone, and 6 ml of 10% sodium hydroxide added, followed by 2.2 g (0.0176 mole) of dimethyl sulfate. After 8 hr, the acetone was evaporated, and the residue dissolved in water and extracted with ethyl acetate. Yield 1.5 g (66%), mp 63–64° C (from ethanol). R_f 0.39. Found, %: C 27.80; H 3.49; N 43.95; mol wt 131. Calculated for $C_3H_4N_4O_2$, %: C 28.10; H 31.3; N 43.70; mol wt 128.

1, 5-Dimethyl-3-nitro-1, 2, 4-triazole (VI). This was obtained by the methylation of II with dimethyl sulfate [1], as for V. Yield 1.2 g (55%), mp 89–90° C (from benzene). R_f 0.50. Found, %: C 33.78; H 4.43; N 39.48; mol wt 141.5. Calculated for $C_4H_6N_4O_2$, %: C 33.80; H 4.23; N 39.50; mol wt 142.

1-Methyl-3-nitro-5-methoxycarbonyl-1, 2, 4-triazole (VII). Obtained similarly to V and VI, from III. Yield 51%, mp 120–121° C (from alcohol). Found, %: C 32.17; H 3.56; N 29.73; mol wt 180. Calculated for $C_5H_6N_4O_4$, %: C 32.25; H 3.22; N 30.10; mol wt 186.

Methylation of nitrotriazoles with diazomethane. Ethereal diazomethane was added in 50% excess to a dioxane solution of I and II. The mixture was evaporated, and the residual product examined by thin-layer chromatography.

1, 3-Dimethyl-4-nitro-1, 2, 4-triazole (IX). A 6.5 g amount (0.031 mole) of 1, 3-dimethyl-5-amino-1, 2, 4-triazole sulfate [11] in 50 ml of 5% H_2SO_4 was added at 0° C to a solution of 30 g of sodium nitrite in 60 ml of water. The mixture was heated for 30 min at 60° C and then extracted with ethyl acetate. The extract was evaporated and the residue recrystallized from 50% aqueous ethanol with the addition of activated charcoal. Yield 3.0 g (52%), mp 55–56° C. R_f 0.69. Found, %: C 33.93; H 4.60; N 39.35; mol wt 137. Calculated for $C_4H_6N_4O_2$, %: C 33.80; H 4.23; N 39.50; mol wt 142.

3-Nitro-4, 5-dimethyl-1, 2, 4-triazole (X). This was obtained from 3-amino-4, 5-dimethyl-1, 2, 4-triazole [11] as for IX. Yield 4.0 g (69%), mp 66–67° C (from benzene), R_f 0.37. Found, %: C 34.23; H 4.68; N 39.60; mol wt 141. Calculated for $C_4H_6N_4O_2$, %: C 33.80; H 4.23; N 39.50; mol wt 142.

1-Methyl-3-methoxycarbonyl-5-nitro-1, 2, 4-triazole (XI). To 0.8 g (0.0047 mole) of 1-methyl-3-carboxy-5-nitro-1, 2, 4-triazole [1] in 20 ml of dioxane was added an ethereal solution of 0.4 g of diazomethane. The solution was evaporated and the residue crystallized from ethanol to give 0.6 g (69%), mp 84° C. Found, %: C 32.20; H 3.29; N 30.23; mol wt 180. Calculated for $C_5H_6N_4O_4$, %: C 32.25; H 3.22; N 30.10; mol wt 186.

Hydrolysis and decarboxylation of 1-methyl-3-nitro-5-methoxycarbonyl-1, 2, 4-triazole (VII). A 1.3 g (0.007 mole) amount of VII was heated at 100° C in 25 ml of 15% H_2SO_4 for 12 hr. The mixture was extracted with ethyl acetate, and the residue after evaporation of the ethyl acetate (0.6 g, 67%) was identical by mp (62–63° C), IR spectrum and R_f 0.64. Found, %: C 20.60; H 2.06; N 40.49; mol wt 174. Calculated for $C_3H_3N_5O_4$, %: C 20.80; H 1.73; N 40.45; mol wt 173.

B) To a solution of 0.6 g (0.0038 mole) of IV in 20 ml of ether was added an ethereal solution of 0.3 g of diazomethane. The solution was evaporated, giving 0.6 g (90%) of compound, R_f 0.64, mp 95–96° C (from ethanol), which gave no depression of mp on admixture with material obtained by method (A).

C) Six grams (0.023 mole) of the silver salt of dinitrotriazole [7] was dissolved in 60 ml of acetonitrile, 50 ml of methyl iodide added, and the mixture kept in the dark for 48 hr. The precipitate of silver iodide was filtered off, the filtrate evaporated to dryness, and the residue extracted with hot methanol. On cooling, the methanolic solution deposited crystals which were filtered off, and the mother liquors were evaporated to dryness. Both the residue and the crystalline material had the same R_f value (0.64) and mp 95–96° C (from ethanol). Yield 2.3 g (59%). No depression of mp was observed on admixture with material obtained by methods (A) and (B).

D) To a solution of 20 g of copper nitrate and 40 g of sodium nitrite in 100 ml of water at 50–60° C was added dropwise a solution of 3 g (0.0142 mole) of 1-methyl-3, 5-diamino-1, 2, 4-triazole sulfate [12] in 50 ml of water. The mixture was heated for 2 hr at 50–60° C, cooled, and filtered. The filtrate was acidified with dil H_2SO_4 until oxides of nitrogen were no longer evolved, then treated with urea to destroy dissolved oxides of nitrogen. The solution was extracted with ethyl acetate, the extract washed with 3–4% sodium hydroxide followed by water, dried over calcium chloride, and the solvent removed to give 0.7 g (29%), mp 95–96° C (from ethanol). The product was identical in its properties with that obtained by methods (A), (B), and (C).

Thin-layer chromatography of the nitro triazoles. Chromatography was carried out on "chromatography grade" alumina, the layers being without a binder. The plate dimensions were 9 × 15 cm, and the solvent was acetone–heptane (1 : 1). The chromatograms were visualized in UV light (Brumberg ultrachemiscope).

Chromatography of 1-methyl-3, 5-dinitrotriazole was carried out using alumina which had previously been treated with 15% acetic acid, since without this treatment the compound decomposed on the adsorbent. System: dioxane–heptane (2 : 3).

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Lensovet Leningrad Technological Institute