2-(4-Ethyl-3,5-di-n-propyl-1-pyrazolyl)-8-n-propylhypoxanthine (VIII). A mixture of 6.1 g of IV, 3.2 g of 5-ethylnonane-4,6-dione, and 50 ml of DMF was refluxed for 2 h, after which it was poured into 300 ml of water. The precipitate was removed by filtration, washed on the filter with water, and dried to give 3.0 g of VIII.

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α-OXIDES IN REACTION WITH N – H ACIDS OF THE HETEROCYCLIC SERIES

IV.* ALKYLATION OF 1-METHYL-3-NITRO-1,2,4-TRIAZOL-5-ONE WITH OLEFIN OXIDES

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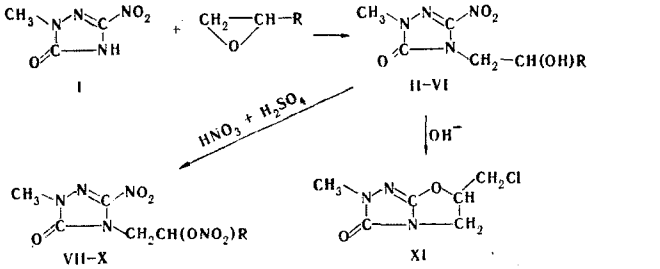
Anumber of 1-methyl-4-(2-hydroxyalkyl)-3-nitro-1,2,4-triazol-5-ones and their derivatives were obtained by reaction of 1-methyl-3-nitrol,2,4-triazol-5-one with α-epoxides. The fact of intramolecular nucleophilic substitution of the nitro group in hydroxy derivatives of 3-nitro-1,2,4-triazol-5-one with cyclization to 2-methyl-3-oxo-5,6-dihydrooxazolo[3,2-b]-1,2,4-triazoline was established.

The available data on the alkylation of 3-nitro-1,2,4-triazol-5-one are extremely contradictory. According to the data in [2], methylation with dimethyl sulfate in alkaline media leads to 1,4-dimethyl-3-nitro-1,2,4-triazol-5-one, whereas it has been reported [3] that exclusively monosubstitution products are formed, which Chipen and Bokaldere [3] explain by rapid hydrolysis of the alkylating agent and the relatively low reactivity of the secondary reaction center.

We have established that 1-methyl-3-nitro-1,2,4-triazol-5-one (I) is alkylated successfully at the second center (N_4) in aqueous media in the presence of bases when α-epoxides, which are relatively stable with respect to hydrolysis, are used. The alkylation conditions are similar to the conditions previously described for 3-nitro-5-bromo-1,2,4-triazole [4], the acidity of which is close to that of triazolone I (pK_a 3.05 and 3.67, respectively, determined potentiometrically).



II, VII R=H; III, VIII R=CH_3; IV, IX R=CH_2Cl; V, X R=CH_2ONO_2; VI R=CH_2OH

*See [1] for communication III.

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TABLE 1. 1-Methyl-3-nitro-4-R-1,2,4-triazol-5-ones

Compound	R_1	mp, °C (crystallization solvent)	Found, % C	Found, % H	Found, % N	Empirical formula	Calc., % C	Calc., % H	Calc., % N	M found	M calc.	PMR spectra, chemical shifts, δ, ppm (J, Hz) CH_3	$-CH_2-N$	CH_2-C	CH	IR spectra, cm⁻¹ ν_{CO}	ν_{NO_2}	ν_{OH}	ν_{ONO_2}	Yield, %
II	CH_2CH_2OH	100—101 ($CHCl_3$—CCl_4, 1 : 1)	32,0	4,2	30,1	$C_5H_8N_4O_4$	31,9	4,3	29,8	207	198	3,60 s	4,33 t (6)	3,80 t (6)	—	1735	1350, 1560	1040, 3200, 3600	—	41
IV	$CH_2CH(OH)CH_2Cl$	96—97 (water)	29,9	3,4	23,7	$C_6H_9ClN_4O_4$[a]	30,4	3,8	23,7	222	236	3,60 s	4,30 d (6)	4,30 d (6)	4,0 m	1730	1360, 1560	1080, 3200, 3600	—	45
V	$CH_2CHCH_2CNO_2$ | OH	106—107 ($CHCl_3$—CCl_4, 1 : 1)	27,5	3,2	26,9	$C_6H_9N_5O_7$	27,4	3,4	26,6	267	263	3,61 s	4,37 d (5)	4,74 d (5)	4,2 m	1725	1360, 1555	1080, 3350	1290, 1640	56
VII	$CH_2CH_2ONO_2$	121—122 (ethanol)	29,9	3,4	25,7	$C_5H_7N_5O_6$	30,1	3,0	25,8	237	233	3,51 s	4,49 t (6)	4,90 t (6)	—	1740	1340, 1550	—	1280, 1670	80
VIII	CH_2CHCH_3 | ONO_2	117—118 (ethanol)	29,3	3,5	28,2	$C_6H_9N_5O_6$	29,1	3,6	28,3	238	247	3,55 s 1,45 d (6)	4,39 d (6)	—	5,69 m	1750	1350, 1550	—	1290, 1645	30
IX	CH_2-CHCH_2Cl | ONO_2	174—175 (dichloroethane)	25,4	3,1	24,8	$C_6H_8ClN_5O_6$[b]	25,6	2,8	24,9	276	281	3,54 s	4,51 d (6)	4,09 d (6)	5,77m	1750	1350, 1545	—	1290, 1650	45
X	$CH_2CHCH_2ONO_2$ | ONO_2	106—107 (ethanol)	23,1	2,7	27,3	$C_6H_8N_6O_9$	23,4	2,6	27,3	304	308	3,53 b	4,60 d (6)	5,09 d (6)	5,90 m	1735	1350, 1560	—	1290, 1660	57

[a]Found: Cl 14.1%. Calculated: Cl 14.6%. [b]Found: Cl 12.6%. Calculated: Cl 12.6%.

TABLE 2. Alkylation of 1-Methyl-3-nitro-1,2,4-triazol-5-one with Epichlorohydrin (ECH) (0.526 mole/liter of I and 1.052 mole/liter of ECH in 80% Ethanol)

NaOH, M	0,1052	0,1573	0,0526	0
Temp., °C	20	20	80	80
Time,* h	190	168	5,5	8

*This is the time required for an increase in the pH of the medium of 2.5-2.7 pH units.

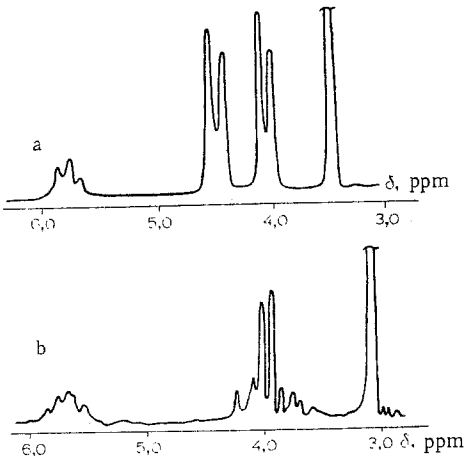

Fig. 1. PMR spectra: a) 1-methyl-3-nitro-4-(2-nitrato-3-chloropropyl)-1,2,4-triazol-5-one; b) 2-methyl-3-oxo-6-chloromethyl-5,6-dihydroox-azolo[3,2-b]-1,2,4-triazoline.

Compounds II, IV, and V were isolated in pure form and nitrated thoroughly to give the corresponding nitrate derivatives; alcohols III and VI were identified only in the form of the nitrates (Table 1). As in the case of 1,2,4-triazole derivatives [1, 4, 5], secondary alcohols are formed in the reaction of triazolone I with unsymmetrically substituted α-epoxides (evidence for this is provided by the PMR spectra of the alcohols and their nitrates). The stability of the signal of the methylene group bonded to the triazolone ring for the primary (II) and secondary (IV, V) alcohols and their nitrates (VII-X), the nonequivalence of the methylene groups in the spectrum of dinitrate X, and the shift to weak field of the signal of the methylidyne proton on passing from alcohols IV and V to their nitrates IX and X make it possible to regard the 1-methyl-3-nitro-4-(2-hydroxyalkyl)-1,2,4-triazol-5-one structure as valid for hydroxyalkyl-substituted triazolones I.

Because of the acidity of triazolone I, its alkylation with α-epoxides can be carried out in the absence of external catalysts [4]. The use of aprotic solvents, in which solvation of the anion of the nucleophile and the oxygen atom of the oxide ring, at which primary attack by the N–H acid takes place, is preferable for the realization of this process. However, triazolone I is practically insoluble in aprotic solvents (acetone, ether, and dioxane), and its solubility in alcohols at room temperature is limited. In view of the low concentration of the nucleophile and its solvation, alkylation in ethanol at room temperature cannot be carried out. At high temperatures alkylation by epichlorohydrin is observed when bases are absent (Table 2); this is undoubtedly due to the rather high acidity of triazolone I. The process is accelerated when a base is introduced and its concentration is increased, during which the general principles of the alkylation of N–H acids of the triazole ring by α-epoxides are retained [1, 4]. Alkylation is accompanied by an increase in the pH of the medium; this was used to monitor and comparatively evaluate the reaction rate.

The α-epoxides investigated in the reaction with triazolone I can be arranged in the following order of decreasing reactivities: propylene oxide, ethylene oxide, nitroglycidol, epichlorohydrin, glycidol.

The alkylation of triazolone I by α-oxides with different structures shows that, as in the case of 3-nitro-5-bromo-1,2,4-triazole, propylene oxide is more reactive than epoxides with electron-acceptor substituents. The latter fact and the fact of alkylation in the absence of bases constitute evidence in favor of primary acid catalysis of the process.

Treatment of halohydrin IV with alklai leads to the synthesis of halo derivative XI, which does not contain a nitro group, instead of the expected α-epoxide. The 2-methyl-3-oxo-6-chloromethyl-5,6-dihydro-oxazolo[2,3-b]-1,2,4-triazoline (XI) structure was assigned to the compound on the basis of the analytical and spectral data. In contrast to the simple first-order spectrum obtained for alcohol IV and its nitrate IX, nonequivalence of the methylene group protons is observed in the PMR spectrum of derivative XI of halohydrin IV (a spectrum of the ABX type); this constitutes evidence for the development of a rigid system of rings as a result of cyclization (Fig. 1).

As in the case of hydroxy derivatives of 3,5-dinitro-1,2,4-triazole [5], elimination of the nitro group to give a two-ring structure was found to be preferable to dehydrochlorination in the alkyl substituent.

EXPERIMENTAL

The PMR spectra of deuteroacetone solutions of the compounds were recorded with a Perkin–Elmer R-12 spectrometer (60 MHz) with hexamethyldisiloxane as the internal standard. The IR spectra of films of the compounds were recorded with a UR-20 spectrometer.

1-Methyl-4-(2-hydroxyalkyl)-3-nitro-1,2,4-triazol-5-ones (II-VI). A mixture of 3.8 g (26 mmole) of triazolone I, 0.21 g (5.2 mmole) of sodium hydroxide, and 52 mmole of the epoxide was dissolved in 50 ml of 80% ethanol, and the solution was allowed to stand in a closed volume with monitoring of the pH of the medium. When the pH reached 6.5-6,8 (pH_0 4.0-4.1), the mixture was diluted with water to twice its original volume, the ethanol was evaporated, and the residual mixture was extracted with ethyl acetate. The extract was washed with water and dried over calcined magnesium sulfate. The solvent was removed, and the alcohols were purified by crystallization (Table 1) or nitrated without purification.

1-Methyl-4-(2-nitratoalkyl)-3-nitro-1,2,4-triazol-5-ones (VII-X). A 20-mmole sample of alcohol II-VI was added with cooling and stirring to 20 ml of an acidic mixture consisting of equal volumes of H_2SO_4 (sp. gr. 1.83) and NHO_3 (sp. gr. 1.51), and the mixture was allowed to stand at 10-15°C for 4 h. It was then poured over ice, and the resulting solution was neutralized with sodium carbonate and extracted with ethyl acetate. The solvent was removed from the extract, and the residue was crystallized (Table 1).

2-Methyl-3-oxo-6-chloromethyl-5,6-dihydrooxazolo[3,2-b]-1,2,4-triazoline (XI). A solution of 1.28 g (31.8 mmole) of sodium hydroxide in 10 ml of water was added in portions to 5 g (21.2 mmole) of halohydrin IV in 50 ml of dioxane, and the mixture was stirred at 20°C for 3 h. It was then diluted to twice its original volume with water and extracted with methylene chloride. The extract was dried over anhydrous magnesium sulfate, the solvent was evaporated, and the residue was crystallized from carbon tetrachloride to give XI, with mp 73-74°C, in 52% yield. IR spectrum: 820 s, 1000 m, 1230 w, 1290 s, 1340 w, 1385 m, 1420 w, 1510 vs, 1660 vs, and 1730 vs cm^{-1}. Found: C 37.5; H 4.1; Cl 18.2; N 22.1%; M 185. $C_6H_8ClN_4O_4$. Calculated: C 37.9; H 4.2; Cl 18.7; N 22.1%; M 189.5.

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