EXPERIMENTAL

The ^{13}C NMR spectra were obtained with a Brucker WH-90 spectrometer at 22.63 MHz and 27 ± 1°C, the solvents (d_6-DMSO, d_5-pyridine, d_7-DMF, and d_9-trimethyl phosphate) were dried over 4-Å molecular sieves, and cyclohexane and dioxane (for the aqueous solutions) were used as the internal standards. The accuracy in the measurement of the chemical shifts was ±0.03 ppm. The concentrations of the solutions were no higher than 10%.

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HETEROCYCLIC NITRO COMPOUNDS.

27.* METHODS FOR THE SYNTHESIS OF 3-NITRO-5-R-1,2,4-TRIAZOLES

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and M. S. Pevzner

UDC 547.792.07

A method for the preparation of 3-nitro-5-R-1,2,4-triazoles by reaction of 1-(3'-oxobutyl)-3,5-dinitro-1,2,4-triazole with nucleophilic reagents with various structures with replacement of the nitro group in the 5 position of the triazole ring during subsequent elimination of the oxobutyl fragment in an alkaline medium is examined. A number of previously undescribed NH acids, viz., 1,2,4-triazole derivatives, including 3-nitro-5-azolyl-1,2,4-triazoles, were obtained, and the ionization constants were determined for some of them.

One of the widely used methods for the synthesis of 3-nitro-5-R-1,2,4-triazoles is diazotization of 3-amino derivatives of 1,2,4-triazole and subsequent reaction of the diazo compounds with nitrite ion [2]. However, its application is not always possible in view of the limitations involved in varying the substituents in the 5 position of the starting amine. At the same time, it has been shown in the case of reactions of 1-methyl-3,5-dinitro-1,2,4-triazole with nucleophilic reagents [1, 3-5] that 3,5-dinitro-1,2,4-triazole derivatives can be used as starting substances for expanding the series of compounds of the triazole series,

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*See [1] for Communication 26.

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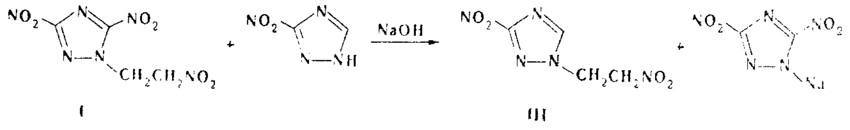
Because of the low lability of the nitro groups in the 3,5-dinitro-1,2,4-triazole anion, the latter is virtually inapplicable to the synthesis of nitrogen-unsubstituted 3-nitro-5-R-1,2,4-triazoles by this method. For their preparation in the reaction with nucleophilic reagents with various structures we propose the use of 3,5-dinitro-1,2,4-triazole derivatives that have a substituent of this type attached to the N_1 atom, which can be easily eliminated after replacement of the nitro group in the 5 position of the ring. As possible subjects for this reaction we examined the products of addition of 3,5-dinitro-1,2,4-triazole to compounds with an activated double bond, viz., 1-(2'-nitroethyl)-3,5-dinitro-1,2,4-triazole (I) [6] and 1-(3'-oxobutyl)-3,5-dinitro-1,2,4-triazole (II) [7].

In the reaction of I with 3-nitro-1,2,4-triazole in the presence of a base by the method in [1], instead of the expected replacement of the nitro group by a triazole fragment, we observed the formation of 1-(2'-nitroethyl)-3-nitro-1,2,4-triazole (III). This pathway is evidently due to the facile cleavage of I as a result of a reverse Michael reaction and subsequent reaction of the resulting nitroethylene with the more nucleophilic nitrotriazole anion. Ketone II proved to be more stable under these conditions, and replacement of the nitro group in the 5 position in this triazole proceeded with retention of the oxobutyl fragment both in reactions with heteryl- [1] and alkoxy-, phenoxy-, and alkylnitramino anions.

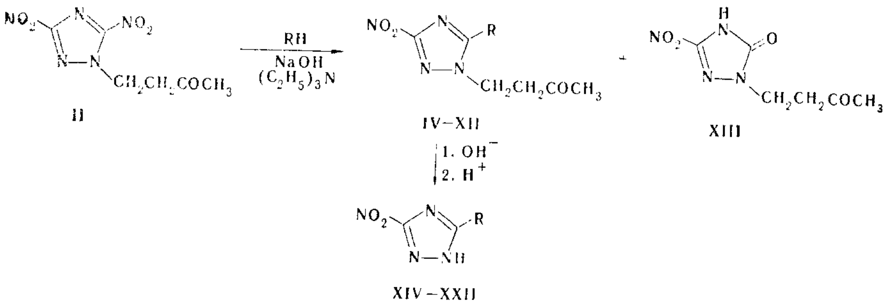


In addition to the desired products (IV-XII), we observed the formation of 1-(3'-oxobutyl)-3-nitro-1,2,4-triazol-5-one (XIII), which is due to the reaction of ketone II with hydroxide ion. Ketones IV-XII were obtained in 20-70% yields, while triazolone XIII was obtained in 30-50% yields.

Another side process was found to be splitting out of methyl vinyl ketone from starting II and resulting ketones IV-XII. 3,5-Dinitro-1,2,4-triazole and NH acids XIV-XXII, which correspond to ketones IV-XII, were detected in the reaction products [by thin-layer chromatography (TLC)]. We were able to isolate only 3-nitro-5-(1,2,4-triazol-1-yl)-1,2,4-triazole (XVII) in appreciable amounts from the reaction medium. It is significant that the yield of the preceding ketone VII decreases up to its complete conversion to NH acid XVII as the time is increased. Products of the addition of methyl vinyl ketone to the attacking nucleophilic reagents were not detected.

The contribution of side reactions becomes extremely substantial when the anions of weak acids (pK_a > 10) are introduced; this is most likely explained by an increase in the pH of the medium.

All of the 1-(3'-oxobutyl)-3-nitro-5-R-1,2,4-triazoles, both those obtained for the first time and those described in [1] (VIII-XII),



IV, XIV R=OCH_3; V, XV R=OC_6H_5; VI, XVI R=$N(NO_2)CH_3$; VII, XVII R=1,2,4-triazol-1-yl; VIII, XVIII R= 3-nitro-1,2,4-triazol-1-yl; IX, XIX R = 3-nitro-5-methyl-1,2,4-triazol-1-yl, X, XX R = 3-chloro-1,2,4-triazol-1-yl XI, XXI R = 3-bromo-1,2,4-triazol-1-yl; XII, XXII R=4-nitro-1-pyrazolyl

Compound XVIII was identical to the product obtained in [8].

TABLE 1. 1-R-3-Nitro-5-R_1-1,2,4-triazoles

Compound	R^{a}	mp,^{b} °C	PMR spectra, chemical shifts, δ, ppm (J, Hz)	IR spectra, cm^{-1}	pK_a	Found				Emprical formula	Calculated				Yield, %
						C, %	H, %	N, %	M^{c}		C, %	H, %	N, %	M	
III	H	111—112	CH_2 5,20 ; $C_{(5)}H$ 8,80 s	845, 880, 890, 960, 980, 1040, 1210, 1260, 1320, 1340, 1360, 1390, 1420, 1450, 1575, 1560	—	25,6	2,8	37,7	191	$C_4H_5N_5O_4$	25,7	2,7	37,4	185	80
IV	OCH_3	134—135	CH_2 3,15 t (12), 4,25 t (12); CH_3, 2,15 s , 4,18 s	840, 870, 995, 1020, 1030, 1060, 1140, 1180, 1190, 1220, 1240, 1270, 1310, 1350, 1380, 1420, 1460, 1505, 1515, 1540, 1570, 1580, 1715	—	39,3	4,8	26,6	221	$C_7H_{10}N_4O_4$	39,2	4,7	26,2	214	60
V	OC_6H_5	91—92	CH_2 3,25 t (10), 4,50 t (10); CH_3 2,18 s : CH_{ar} 7,52 s	820, 852, 910, 960, 1000, 1035, 1085, 1145, 1180, 1230, 1260, 1295, 1360, 1375, 1390, 1405, 1460, 1470, 1520, 1560, 1600, 1723	—	52,4	4,5	20,5	270	$C_{12}H_{12}N_4O_4$	52,1	4,3	20,3	276	35
VI	$N(NO_2)CH_3$	108—109	CH_2 3,29 t (7), 4,52 t (7); CH_3 3,79 s , 2,15 s	840, 860, 930, 1030, 1060, 1110, 1150, 1350, 1380, 1420, 1430, 1450, 1485, 1540, 1560, 1720	—	32,4	4,0	32,7	254	$C_7H_{10}N_6O_5$	32,6	3,9	32,6	258	45
VII	1,2,4-Triazol-1-yl	—	CH_2 3,30 t (6), 4,90 t (6); CH_3 2,20 s; CH_{tr} 8,45 s , 9,30 s	850, 960, 990, 1010, 1090, 1110, 1140, 1180, 1220, 1290, 1320, 1390, 1440, 1520, 1590, 1735	—	—	—	40,1	—	$C_8H_9N_7O_3$	38,2	3,6	39,0	251	21
XIV	OCH_3	144—145	CH_3 4,20 s ; NH ~ 8,0	800, 840, 880, 920, 980, 1020, 1075, 1150, 1190, 1300, 1380, 1415, 1440, 1520, 1560, 1620	5,35	25,0	2,7	39,0	152	$C_3H_4N_4O_3$	25,0	2,8	38,9	144	65
XV	OC_6H_5	159—160	CH_{ar} 7.50 s ; NH ~ 9,0	800, 840, 920, 1020, 1040, 1070, 1150, 1160, 1180, 1320, 1400, 1450, 1495, 1540, 1560, 1580, 1620	4,20	46,6	2,9	27,4	191	$C_8H_6N_4O_3$	46,6	2,9	27,7	206	60
XVI	$N(NO_2)CH_3$	157,5—158,5	CH_3 4,00 s ; NH ~ 8,6	840, 870, 900, 950, 1040, 1060, 1090, 1120, 1140, 1165, 1210, 1280, 1305, 1340, 1420, 1440, 1540, 1560, 1600	3,12	19,5	2,2	44,8	187	$C_3H_4N_6O_4$	19,5	2,1	44,7	188	60
XVII	1,2,4-Triazol-1-yl	208—209	CH_{ar} 8,35 s 9,30 s; NH ~ 10	860, 890, 950, 980, 1020, 1125, 1180, 1225, 1270, 1300, 1320, 1390, 1400, 1480, 1525, 1570, 1610, 1680	2,00	25,8	2,1	53,8	190	$C_4H_3N_7O_2$	26,2	1,7	54,0	181	80
XVIII	3-Nitro-1,2,4-triazol-1-yl	227—228	CH_{tr} 9,60 s, NH ~ 11,6	850, 880, 900, 970, 1020, 1095, 1060, 1090, 1125, 1175, 1265, 1370, 1385, 1430, 1465, 1575, 1610	0,92	21,6	1,1	49,8	221	$C_4H_2N_8O_4$	21,2	0,9	49,7	226	70
XIX	3-Nitro-5-methyl-1,2,4-triazol-1-yl	230—231	CH_3 2,95 s ; NH ~ 7,5	850, 880, 980, 1010, 1020, 1040, 1090, 1130, 1175, 1215, 1285, 1315, 1380, 1400, 1435, 1480, 1500, 1565, 1590	—	25,0	1,7	46,7	235	$C_5H_4N_8O_4$	25,0	1,7	46,7	240	80
XX	3-Chloro-1,2,4-triazol-1-yl	214—215	CH_{tr} 9,35 s; NH ~ 11,5	840, 880, 890, 965, 1010, 1040, 1140, 1240, 1275, 1290, 1310, 1385, 1410, 1460, 1500, 1510, 1555, 1610	1,59	22,8	1,5	45,5	220	$C_4H_2ClN_7O_2$^{e}	22,2	0,9	45,5	215	86
XXI	3-Bromo-1,2,4-triazol-1-yl	246—247	CH_{tr} 9,50 s ; NH ~ 11,0	855, 890, 970, 1010, 1030, 1140, 1160, 1240, 1250, 1260, 1295, 1310, 1390, 1420, 1560, 1620	1,63	18,9	0,9	38,2	265	$C_4H_2BrN_7O_2$^{f}	18,4	0,8	37,7	260	70
XXII	4-Nitro-1-pyrazolyl	202—203 (ethyl acetate—petroleum ether)	CH_{pyr} 8,65 s, 9,45 s; NH ~ 10,0	830, 850, 875, 920, 935, 990, 1010, 1075, 1110, 1170, 1225, 1285, 1320, 1355, 1390, 1460, 1520, 1560, 1610	—	26,6	0,9	43,4	232	$C_5H_3N_7O_4$	26,6	1,3	43,5	225	70

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[a] R = $CH_2CH_2NO_2$ for III, R = $(CH_2)_2COCH_3$ for IV-VII, and R = H for XIV-XXII. [b] Crystallization solvents: ethanol for III-VI and XVII, chloroform for XIV and XIX, water for XV, carbon tetrachloride for XVI, and ethyl acetate—petroleum ether for XVIII and XX-XXII. [c] By inverse ebullioscopy in acetone. [d] The chemical shifts of the methylene groups coincide (the signal is recorded in the form of a pronounced triplet with a CH_2:CH_{tr} intensity ratio of 4:1. [e] Found: Cl 16.5%. Calculated: Cl 16.4%. [f] Found: Br 30.4%. Calculated: Br. 30.8%.

upon treatment with an aqueous solution of alkali split out methyl vinyl ketone with conversion to the salt of the corresponding acid and upon treatment with acid are converted to an NH acid in high yield.

The structures of III-VII and XIV-XXII were confirmed by their analytical and spectral data, while the affilitation of triazoles XVI-XVIII, XX, XXX, and XXI with NH acids was confirmed by the determination of their ionization constants (Table 1). The pK_a values of XIV and XV are close to the values calculated from the correlation equation for 3-nitro-5-R-1,2,4-triazoles [9] by means of the σ_M constants of the corresponding substituents. The ionization constants of triazoles XVI-XVIII, XX, and XXI constitute evidence for the substantial acceptor contribution of the substituent attached to the ring C_5 atom closest to the reaction center.

EXPERIMENTAL

The PMR spectra of solutions of the compounds in d_6-acetone 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. The spectrophotometric determination of the pK_a values was carried out with an SF-16 spectrophotometer at 20°C, while potentiometric titration was carried out with an LPM-60M pH meter; the pK_a values were calculated in conformity with the method in [10]. Thin-layer chromatography (TLC) was carried out on Silufol UV-254, the chromatograms were developed by means UV irradiation. Starting ketones VII-XII were obtained by the method in [1].

1-(2'-Nitroethyl)-3-nitro-1,2,4-triazole (III). A solution of 1.37 g (12 mmole) of 3-nitro-1,2,4-triazole and 0.44 g (11 mmole) of sodium hydroxide in 5 ml of water was added to a solution of 2.8 g (12 mmole) of I [6] in 25 ml of acetone, and the mixture was stirred at 20°C for 30 min [the reaction was monitored by TLC with respect to the disappearance of I with R_f 0.78 in an ethyl acetate—dioxane—petroleum ether system (4:1:2)]. The solvent was evaporated, and the residue was washed with water and crystallized.

1-(3'-Oxobutyl)-3-nitro-5-methoxy-1,2,4-triazole (IV). A 1-ml sample of triethylamine was added to a solution of 3 g (13.1 mmole) of II [7] in 30 ml of methanol, and the mixture was heated at 50°C [the reaction was monitored by TLC with respect to the disappearance of ketone II with R_f 0.52 in a hexane—acetone system (2:1)]. The solvent was evaporated, and the residue was washed with water. The undissolved material was crystallized (IV), and the wash waters were acidified to pH 1 with 10% H_2SO_4 and extracted with ethyl acetate (two 30-ml portions). The solvent was evaporated, and triazolone XIII [1] was crystallized from ethanol.

1-(3'-Oxobutyl)-3-nitro-5-phenoxy-1,2,4-triazole (V). A solution of 0.8 g (8.5 mmole) of phenol and 1.6 ml of triethylamine in 5 ml of dioxane was added to a solution of 2 g (8.7 mmole) of ketone II in 15 ml of dioxane, and the mixture was heated with stirring to 55-60°C and maintained at this temperature for 4 h (the reaction was monitored by TLC with respect to ketone II). The reaction mixture was worked up as in the preceding experiment.

1-(3'-Oxobutyl)-3-nitro-5-(N-methyl-N-nitramino)-1,2,4-triazole (VI). A solution of 1.28 g (13.1 mmole) of the sodium salt of methylnitramine in 5 ml of water was added to a solution of 3 g (13.1 mmole) of ketone II in 20 ml of ethyl acetate, and the mixture was heated with stirring to 55-60°C and maintained at this temperature for 6 h (the reaction was monitored by TLC with respect to ketone II). The reaction mixture was cooled, and the organic layer was washed with water. The solvent was evaporated, and the residue (ketone VI) was crystallized. The aqueous layer and the wash waters were combined and worked up to isolate XIII as in the preceding experiment.

1-(3'-Oxobutyl)-3-nitro-5-(1,2,4-triazol-1-yl)-1,2,4-triazole (VII). This compound was obtained from ketone II and 1,2,4-triazole in the presence of NaOH as in the preceding experiment.

3-Nitro-5-R-1,2,4-triazoles (XIV-XXII). A 4-mmole sample of ketone IV-XII was added with stirring at room temperature to a solution of 0.48 g (12 mmole) of sodium hydroxide in 25 ml of water, and the mixture was allowed to stand until it became completely homogeneous. The solution was extracted with 20 ml of ether (to remove the methyl vinyl ketone), and the aqueous part was acidified to pH 1 with 10% H_2SO_4 and extracted with ethyl acetate (three 25-ml portions). The combined extracts were washed with water, the solvent was evaporated, and the residue was crystallized.

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SYNTHESIS AND THERMAL DECOMPOSITION OF HALOALKOXY-sym-TRIAZINES.

6.* SYNTHESIS AND THERMOLYSIS OF 2-(2-CHLOROETHOXY)-4-N-METHYL-N-CYANOAMINO-6-DIALKYLAMINO-syn-TRIAZINES

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K. A. Eliazyan, and R. G. Mirzoyan

UDC 547.873'781.3'-785.5.07

2-(2-Chloroethoxy)-4-N-methyl-N-cyanoamino-6-dialkylamino-sym-triazines were synthesized. It was established that thermolysis of the indicated compounds in xylene is accompanied by dechloroalkylation; however, it takes place at the site of both the dialkylamino and alkylcyanoamino groups to give a mixture of two imidazo-sym-triazines. The structures of the latter were confirmed by data from the IR, PMR, and mass spectra.

It has been shown [1] that the thermolysis of 2-(2-chloroethoxy)-4,6-bis(dialkylamino)-sym-triazines proceeds unambiguously to give 2-dialkylamino-4-oxo-8-alkyl-6,7-dihydroimidazo[1,2-a]-sym-triazines.

The aim of the present research was to study the specificity of the analogous reaction in the case of 2-(2-chloroethoxy)-4-N-methyl-N-cyanoamino-6-dialkylamino-sym-triazines, the rearrangement-cyclization of which may proceed with the elimination of both alkyl chlorides and cyanogen chloride.

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*See [4] for Communication 5.

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