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REACTIONS OF 4-NITRO-1,2,3-TRIAZOLE WITH ALKYLATING AGENTS

AND COMPOUNDS WITH ACTIVATED MULTIPLE BONDS

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When 4-nitro-1,2,3-triazole is alkylated, a mixture of N_1 - and N_2 -isomers is formed, with the latter usually predominating. The same behavior is also observed in addition reactions of 4-nitrotriazole to activated multiple bonds.

Electrophilic substitution reactions in a number of vicinal triazoles have been studied very insufficiently. Thus, on alkylation of mono-and di-substituted 1,2,3-triazoles, a mixture of all three isomers [1], the 1,4- and 2,4-isomers with one of them predominating [2-5], as well as only the N₁ or N₂ alkylation products [2, 3, 5] were obtained. Not only the nature of the substitutent in the ring but also the reaction conditions have a given orienting effect on the direction of attack of the electrophile. It is shown, for example [5], that reaction of unsubstituted 1,2,3-triazole with picryl fluoride under conditions of basis catalysis leads to the formation of 2-picryltriazole, while without catalyst 1-picryltriazole is formed. As far as 4-nitrotriazole is concerned, it is known [5] that when it is alkylated with picryl fluoride in DMF only 1-picryl-4-nitrotriazole is obtained.

In order to elucidate the orienting role of the nitro group, the alkylation of 4-nitro-1,2,3-triazole (I) with various alkylating agents has been examined. Owing to the fact that triazole I has three potential reaction centers, the formation of all three alkyltriazoles is possible. The interaction of the Na salt of I with alkyl halides (II) and dimethyl sulfate was studied in acetone at 25°C. It transpired that in all cases a mixture of two isomeric products -1-R- and 2-R-4-nitrotriazoles (III and IV) with the N₂-isomer often predominating — was formed. The absence of the 1,5-isomer may be explained by steric factors and also the negative inductive effect of the nitro group, lowering the nucleophilicty of the neighboring nitrogen atom.



 $\begin{array}{rcl} II-IV & a & R=CH_3; & b & R=C_2H_5; & c & R=n\cdot C_3H_7; & d & R=iso\cdot C_3H_7; & e & R=C_2H_5O_2CCH_2, \\ & f & R=C_6H_5CH_2; & g & R=C_6H_5COCH_2; & IIa & X=I; & b-e, & g & X=Br; & e, & f & X=CI \end{array}$

Institute of Petrochemical and Coal Chemicals Synthesis, A. A. Zhdanov Irkutsk State University, Angarsk 665813. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 932-935, July, 1986. Original article submitted March 12, 1985; revision submitted October 9, 1985.

	Time	Found, The				Calculated, %			Yield, %		
Reaction products	of reac- tion	С	н	N	Empirical formula	с	н	N	111+IV	N ₁ - isomer	N ₂ - isome
$\begin{array}{c} IIIa + IVa^{a}\\ IIIa + IVa^{b}\\ IIIb + IVb\\ IIIc + IVc\\ IIIc + IVc\\ IIIc + IVe^{c}\\ IIIc + IVe^{d}\\ IIIc + IVe^{f}\\ III$	1 24 24 156 156 24 120 204 24	28,9 28,3 33,8 39,2 38,9 35,7 36,3 53,9 51,8	3,0 3,3 4,4 4,9 5,3 4,0 3,7 4,1 3,7	44,0 43,6 39,8 36,3 35,4 28,5 28,7 26,3 23,8	C3H4N4O2 C3H4N4O2 C4H6N4O2 C3H8N4O2 C3H8N4O2 C6H8N4O2 C6H8N4O4 C6H8N4O4 C6H8N4O2 C10H8N4O3	28,1 23,8 38,5 38,5 36,0 36,0 52,9 51,7	3,1 3,1 4,2 5,1 5,1 4,0 3,9 3,5	43,7 43,7 39,4 35,9 28,0 28,0 27,5 24,1	90 94 85 70 20 87 50 87 87 80	40 40 45 30 67 70 65 33	60 60 55 70 33 30 35 67

TABLE 1. Alkylation Products of 1,2,3-Triazole (I) in Acetone at 25°C

^a $II = CH_{31}$, ^b $II = (CH_{3})_{2}SO_{4}$, ^c $II = C_{2}H_{5}O_{2}CCH_{2}Br$, ^d $II = C_{2}H_{5}O_{2}CCH_{2}CI$.

TABLE 2. PMR Spectra of Alkylation Products (III + IV)

	δ _n ,	ppm	δ _R (111+1V)., ppm		
Mixture of isomers	N ₁ -isomer III (s)	N ₂ -isomer IV (s)			
$\begin{array}{c} 111a + 1Va \\ 111b + 1Vb \\ 111c + 1Vc \\ 111d + 1Vd \\ 111e + 1Ve \\ 111f + 1Vf \\ 111g + 1Vg \end{array}$	8,40 8,73 8,92 8,42 8,95 8,00 9,09	8,12 8,15 8,10 8,17 8,41 7,87 8,54	4,15 s; 4,10 s 3,47 t; 1,51 m 4,59 t; 2,07—1,97m; 0,96 t; 0,94 t 5,49 s; 4,92 m; 1,69 d; 1,65 d 5,38 s; 5,30 s; 4,13 q 1,25 t 7,35—7,14 m; 4,58 s; 3,66 s 8,18—7,55 m; 6,37 s		

In order to elucidate the influence of the nature of solvent on the rates of reaction and ratio of isomers, the alkylation of the Na salt of I with methyl iodide in the absence of acetone was conducted in DMF, DMSO, MeOH, and EtOH. If this reaction takes 1 h in acetone (Table 1), then it takes 2 h in DMSO, 3 h in DMF, 30 h in MeOH, and 48 h in EtOH. The ratio of isomers in fact changes very little.

In a number of works information is given about the migration of substituents in vicinal triazoles from the 1-position to the 2-position of the heterocycle [6, 7]. Experiments have shown that on standing mixture IIIa + IVa at room temperature without solvent for 2 years the proportion of N₂-isomer increased from 60 to 74%, while on maintaining this same mixture at 120°C in DMSO for 8 h, there was an increase of 4-5%. An experiment, specially set in an ampul used for NMR spectroscopy, on the methylation of I with methyl iodide showed that even in the first moment of reaction the N₁- and N₂-isomers are formed simultaneously in the ratio 2:3, which remains practically unchanged during the reaction.

Separation of the isomeric reaction products III and IV, with the exception of 1(2)methyl- (IIIa + IVa) and 1(2)-ethylnitrotriazoles (IIIb + IVb) (see experimental section), was not achieved. Thus, fractional crystallization does not give positive results owing to their solubility being the same, while fractionation by vacuum distillation is complicated by the closeness of their boiling points and by partial isomerization and thermal decomposition.

Identification and determination of the ratio of isomers in the mixture of alkylation products was conducted with the help of PMR spectroscopy from the position and intensity of the signal from the proton at C_5 in the heterocycle. It is known [8] that this signal in 1-R-nitrotriazole occurs at lower field than the corresponding signal in the N₂-isomer.

Thus, in alkylation reactions of triazole I the 1,4- and 2,4-isomers are formed, more often with the latter predominating. The inductive and shielding effects of the nitro group hinder attack by the electrophile on the 3-position of the heterocycle.

TANTE 2. OPECTAT LIOPELCIES OF MUDICION LIOUNCES AN'D-AIT	lucts Va.b-VIIa	Products	Addition	of	Properties	Special	3.	Table
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	Content in			Cher			
Mixture of isomers	mixtu	re, %	ð			TD and a furness	
	isomer	isomer	isomer (\$)	isomer (\$)	δ_{R}	cm ⁻¹	
Va + (V.b (H ₉ PQ	5	95	9,12	8,48	5,94 q, 3,61-3,32 m, 1,53- 1,37 m, 1,37-1,20 m, 0,82 t	1100—1230, 1535 1565	
Catalyst) Va+Vb (without catalyst)	14	86	9,12	8,46	6,06 q, 5,94 q, 3,67-3,29 m, 1,56-1,39 m, 1,39-1,16 m,	1100—1230, 1535 1565	
VIa+VIb	45	55	9,12	8,52	4,97 t, 4,95 t, 3,34 t, 3,31 t	1530, 1540, 1560	
VIIa+VIIb	39	61	9,06	8,51	8,14-7,33 m, 6,73 d, 6,70 d, 5,63 d, 5,59 d	1600, 1611, 1678	

Analogous behavior is also observed in addition reactions of triazole I to multiple bonds. Thus, addition of I to vinyl butyl either proceeds smoothly both in the presence of a catalytic quantity of orthophosphoric acid and without it, that is to say, nitrotriazole itself catalyzes this reaction. In both cases a mixture of 1(2)-(1-butoxyethyl)-4-nitrotriazoles(Va + Vb) is formed. Without the catalyst the ratio of N₁- to N₂-isomers is 1:6, and with the addition of catalyst the ratio is 1:19.



In the addition reactions of I to acrylonitrile and benzoylacetylene in the presence of bases, mixtures of 1(2)-cyanoethyl-4-nitrotriazoles (VIa + VIb) and 1-phenyl-3-[4-nitro-1(2)-triazolyl]propen-1-ones (VIIa + VIIb) are formed. The structures of the addition products V-VII were confirmed by IR and PMR spectroscopy (Table 3). The quantity of isomers in the mixture and their ratio were determined from the presence and intensity in the PMR spectra of two signals in the regions 9.06-9.12 and 8.46-8.52 ppm from the ring protons at C₅ in the heterocycle. The proton signal at lower field, as in the case of alkylation, was assigned to the N₁-isomer.

EXPERIMENTAL

PMR spectra were recorded on Varian XL-100/12 (100.1 MHz) and Bruker WP-200-34 (200.13 MHz) spectrometers. The accuracy of chemical shift measurement was \pm 0.02 ppm. IR spectra were recorded on a UR-20 instrument in petrolatum oil, as a thin layer of pure samples and in carbon tetrachloride. The course of the reactions was monitored by TLC on plates with Al₂O₃ in an ether-hexane (3:1) system and on Silufol plates in an ether-petroleum ether (3:1) system. 4-Nitro-1,2,3-triazole was obtained according to the method in [9].

General Method for Alkylation of Triazole I. To a suspension of 5 mmole (0.68 g) of the Na salt of I in 10 ml of acetone was added 6 mmole of alkylating agent II, and the mixture was stirred at 25°C (monitoring on Silufol plates). The time of reaction for every specific case is given in Table 1. The precipitate inorganic salt was filtered off, the filtrate was evaporated, and the residue was recrystallized from aqueous alcohol and dist tilled under vacuum. The ratio of isomers was determined both in the reaction mass and after isolation and purification of the mixture of isomers. Mixtures of alkylation products IIIa-g + IVa-g were obtained, the properties of which are given in Tables 1 and 2. Isomers IIIa and IVa were separated by chromatography on an Al_2O_3 plate (standard activity II), the eluent was ether-petroleum ether (3:1); IIIa: mp 122-123°C; IVa: mp 92-94°C. Isomers IIIb and IVb were separated by vacuum distillation; IIIb: bp 57-60°C (3 mm); IVb was isolated by recrystallization of the indigo-colored residue from aqueous alcohol, mp 48-61°C. Separation of the remaining isomer mixtures was not achieved.

1(2)-(1-Butoxyethyl)-4-nitrotriazoles (Va + Vb). To a suspension of 6 mmole (0.7 g) of triazole I in 10 ml of chloroform was added 6 mmole (0.6 g) of vinyl butyl ether and 1 drop of orthophosphoric acid at 25°C. The reaction mixture was stirred while boiling for 8 h, then washed with a 5% solution of sodium carbonate and dried over MgSO4. The solvent was distilled off and the residue was distilled under vacuum, bp 71-80°C (3 mm), yield 63%. Found: C 44.6; H 6.6; N 25.8%. C_{9H_14}N_4O_3. Calculated: C 44.8; H 6.5; N 26.2%.

<u>1(2)-Cyanoethyl-4-nitro-1,2,3-triazoles (VIa + VIb).</u> To a solution of 6 mmole (0.7 g) of triazole I in 10 ml of acrylonitrile at room temperature was added 0.6 mmole (0.03 g) of anhydrous KOH, and the mixture was stirred at 30-40 °C for 7 h. The excess acrylonitrile was distilled off and the residue, a mixture of isomers VIa and VIb, was recrystallized from aqueous alcohol. Yield 78%. Found: C 36.5; H 3.2; N 42.2%. C₃H₅N₅O₂. Calculated: C 35.9; H 3.0; N 41.9%.

<u>1-Phenyl-3-[4-nitro-1(2)-triazolyl]propen-1-ones (VIIa + VIIb)</u>. To a suspension of 8 mmole (1 g) of triazole I in 10 ml of dichlorethane was added 8 mmole (1.6 g) of benzoylace-tylene and 2-3 drops of triethylamine. The reaction mass stirred at 80°C until the benzoylace-acetylene had disappeared (monitored on Al₂O₃ plates). The solvent was distilled off and the residue was recrystallized from acetone. The yield of the mixture of isomers VIIa and VIIb was 94%. Found: C 54.5; H 3.3; N 22.1%. $C_{11}H_8N_4O_3$. Calculated: C 54.1; H 3.3; N 22.3%.

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