SYNTHESIS AND TRANSFORMATIONS OF 3-AZIDO-5-AMINO-1,2,4-TRIAZINES

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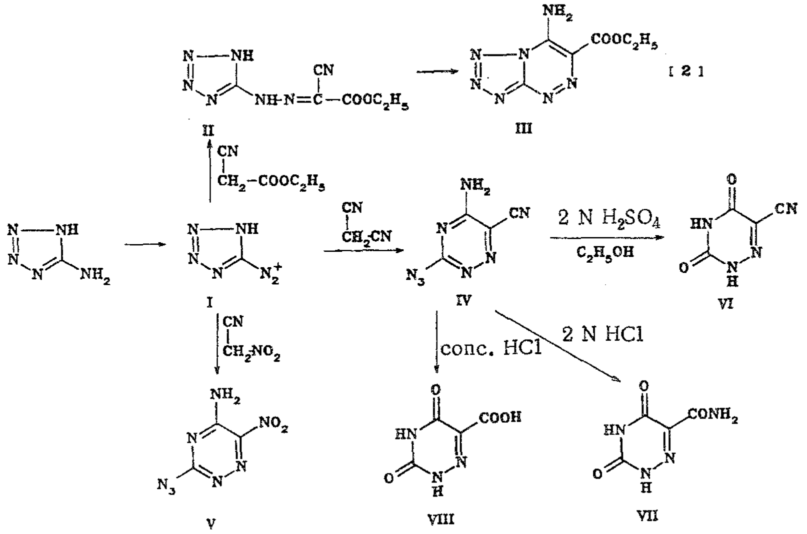
The reaction of the tetrazolediazonium ion with malonic acid dinitrile and nitroacetonitrile leads to the formation of 3-azido-5-amino-1,2,4-triazine derivatives. According to the mass-spectrometric data and the results of X-ray diffraction analysis, the crystalline compounds exist in the amino form. The facile hydrolysis of the amino and azido groups to azauracils is an argument in favor of the existence of the imino form in solution.

The reaction of diazoazoles with carbonyl compounds that have an active methylene group is a convenient method for the synthesis of azoloannelated 1,2,4-triazine derivatives. Diazonium salts obtained from aminopyrazole, imidazole, or triazole are used for this purpose (see, for example [1]). The behavior of 5-aminotetrazole in this reaction remains virtually uninvestigated. Only one case [2] of coupling of a 5-tetrazolediazonium salt (I) with cyanoacetic ester is known; hydrazone II, heating of which in acetic acid gives 6-ethoxycarbonyl-7-aminotetrazolo[5,1-c][1,2,4]triazine (III), was obtained in the presence of sodium acetate.

In the present communication we present data on the condensation of the 5-tetrazolediazonium ion with other CH-active derivatives of acetonitrile, viz., malonic acid dinitrile and nitroacetonitrile. We observed that the introduction into the acetonitrile molecule of stronger (than the ethoxycarbonyl group) acceptor substituents, viz., a cyano or nitro group, substantially changes the course of the reaction (see the scheme presented below). In contrast to the reaction with cyanoacetic ester [2], a 1,2,4-triazine ring is formed immediately as a result of reaction of the tetrazolediazonium ion with malonodinitrile, and the tetrazole ring is opened to form an azido group (IV). The use of nitroacetonitrile gives 3-azido-5-amino-6-nitro-1,2,4-triazine (V), which is inaccessible by other methods. In this case ring closing takes place at the nitrile fragment, and alternative condensation with splitting out of a nitro group [3] is not realized.



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Triazines IV and V are formed when the reaction is carried out in the presence of sodium acetate (the conditions for the formation of tetrazolylhydrazone II [2]) and when sodium carbonate or alkali is used.

A comparison of the synthesized IV and V with triazine III, and also with tetrazolo-[5,1-b][1,2,4]triazine [4] shows that the increase in the acceptor properties of the substituent in the 6 position of the triazine ring when a cyano or nitro group is introduced leads to a pronounced shift in the equilibrium to favor azides, which exist in the azido form even in the crystalline state.

Bands of vibrations of azido, amino, cyano (for IV), or nitro (for V) groups are observed in the IR spectra of the compounds obtained.

The mass-spectrometric fragmentation and the character of the mass spectra constitute evidence for the cyclic structure of the products. If it is assumed that tetrazolyl-NHN=$C(CN)_2$ is formed as a result of the reaction of the tetrazolediazonium ion with malononitrile, typical (for hydrazones) cleavage of the N—N bond with the formation of fragment ions at 84 and 78,* or at 97 and 65 for the isomeric azo product tetrazolyl-N=N—$CH(CN)_2$ [5, 6] in the case of cleavage of the γ-N—C bond should be observed upon electron impact. The absence of peaks of the indicated ions in the mass spectrum of IV excludes a noncyclic structure. At the same time, a molecular-ion peak (M^+, 162), for which an accurate mass of 162.0432, which corresponds to the empirical composition $C_4H_2N_8$ (calculated value 162.0402), is recorded in the spectrum. The fragmentation of the M^+ ion is associated with the successive elimination of N_2 (134), CN (108), and NH_2 (79) particles. Splitting out of a molecule of N_2 is realized from the azido group, since the energy of activation in this case is lower by a factor of approximately two to four than in the case of ejection of N_2 from the triazine ring [7]. An investigation of the spectra of the metastable ions showed that the formation of the ion at 79 is realized via two pathways:

$$\begin{tikzcd}
M^+ \arrow[r, "-N_2"] & {[M-N_2]^+} \arrow[r, "-CN^\cdot"] \arrow[rr, bend right, "-HCN_3^\cdot"'] & {[M-N_2, -CN]^+} \arrow[r, "-N_2H^\cdot"] & 79
\end{tikzcd}$$

This fragmentation pathway, as well as the appearance of an ion peak at 68, which corresponds to a tetrazolium cation, proves the presence of an azido group and characterizes the orientation of the heteroatoms relative to the $N_{(3)}$ group. The detachment of a CN radical from the $[M - N_2]^+$ ion is associated with contraction of the triazine ring rather than the elimination of a nitrile substituent; this is confirmed by the subsequent fragmentation of the $[M - N_{(2)} - CN]^+$ ion [8, 9]. This molecular-ion peak in the mass spectrum of nitrotriazole V is found at m/z 182 (the value determined was 182.0312, as compared with a value of 182.0300 calculated for the composition $C_3H_2N_8O_2$). The pathway of the fragmentation of the M^+ ion is similar to the fragmentation of the molecular ion of IV, which indicates that their structures are similar. In addition to ions at 154, 128, 99, and 68, which determine the presence of an azido group and its position in the ring, the peak of an $[M - NO_2]^+$ ion (136) is also observed.

In order to make a detailed study of the structure we investigated the molecular-crystal structure of IV by X-ray diffraction analysis. The bond lengths and bond angles averaged with respect to two crystallographically independent A and B molecules are shown in Fig. 1. These data are in good agreement with the published values [10]. Both molecules are virtually planar with maximal deviation of the $N_{(8)}$ atom of the azido group (0.076 Å in the A molecule and 0.145 Å in the B molecule) from the average plane passing through the $N_{(1)}$, $N_{(2)}$, $C_{(3)}$, $N_{(3)}$, $C_{(1)}$, and $C_{(2)}$ atoms. In fact, the dihedral angles formed by this plane with the $C_{(1)}-N_{(4)}-H_{(1)}-H_{(2)}$ and $C_{(3)}-N_{(6)}-N_{(7)}-N_{(8)}$ planes are small and are euqal to 4.4 and 2.1° in the A molecule and 8.4 and 3.2° in the B molecule.

Both the A and B molecules furnish two hydrogen atoms of the amino group for the formation of intermolecular hydrogen bonds joining these molecules in the crystal.

The pronounced shortening of the C—NH_2 bond (up to 1.326 Å) as compared, for example, with the bond of 2-aminopyridine (1.351 Å [11]) or 2-aminopyrazine (1.341 Å [12]) constitutes evidence for significant conjugation of the amino group with the ring and for the possibility of manifestation of amine—imine tautomerism [13].

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*Here and subsequently, the numbers that characterize the ions are the mass-to-charge ratios (m/z).

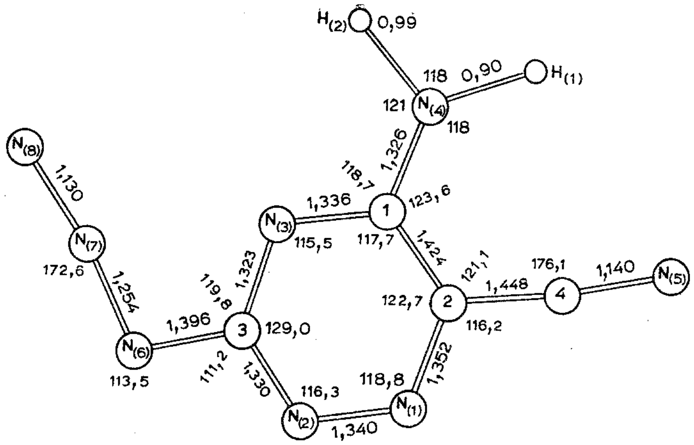

Fig. 1. Bond lengths (Å) and bond angles (degrees) in crystals of IV.

To study the structure of the triazine in solutions we carried out its hydrolysis. 3,5-Dioxo-2,3,4,5-tetrahydro-6-cyanotriazine (VI) was obtained when triazine IV was heated in a mixture of 2 M H_2SO_4 and alcohol, whereas the corresponding amide VII was obtained in a mixture of 2 N HCl and alcohol. Carboxylic acid VIII was obtained in concentrated hydrochloric acid. A signal of a nitrile group is present in the IR spectrum of VI. The UV spectra of VI-VIII are identical in character and coincide with the spectrum of azauracil.

Such facile hydrolysis of the amino and azido groups in triazine IV is an argument in favor of the existence of the compound in the imino form in solution. In addition, this transformation can be regarded as a convenient one-step method for the preparation of carbonyl derivatives of azauracil such as the previously undescribed VI and the previously obtained [14] (in several steps) VII and VIII.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-20 spectrometer. The UV spectra of alcohol solutions were obtained with a Specord UV-vis spectrophotometer. The electron-impact mass spectra were obtained with a Varian MAT-311 spectrometer under standard operating conditions (at an ionization energy of 70 eV, an emission current of 300 μA, and an accelerating voltage of 3 kV). The high-resolution mass spectra were obtained with the same apparatus at $M/\Delta M = 15{,}000$ with polyphosphoric acid (PPA) as the standard. The X-ray diffraction study was carried out with a Syntex P11400 diffractometer with $F \geqslant 2\sigma$. The IV crystals were monoclinic and had the following parameters: $a = 7.851(3)$, $b = 11.804(3)$, $c = 15.246(6)$ Å, $V = 1382.9(9)$ Å^3, $\beta = 101.82(3)°$, $\rho_{calc} = 1.56$ g/cm^3, $z = 8$ (two independent molecules), and space group $P2_1/c$. The structure was determined by the direct method and was refined by the method of least squares with an anisotropic (isotropic for the H atoms) temperature factor. The final deviations of the factors were $R = 0.065$ and $R_W = 0.070$. The coordinates of the atoms and their temperature factors are presented in Tables 1 and 2.

3-Azido-5-amino-6-cyano-1,2,4-triazine (IV). A 2-g (0.02 mole) sample of aminotetrazole was dissolved in 100 ml of water and 5 ml of hydrochloric acid, the solution was cooled to −2°C, a solution of 1.4 g (0.02 mole) of $NaNO_2$ in 20 ml of water was added dropwise with vigorous stirring, and the mixture was maintained at −2°C for 30 min. A mixture of 1.32 g (0.02 mole) of malonic acid dinitrile and 4.9 g of sodium acetate in 5 ml of water and 15 ml of ethanol was added to the resulting diazonium salt, and the mixture was stirred at 0°C for 30 min and at 20°C for 1 h. It was then filtered to give 2 g (62%) of triazine IV with mp 208-210°C [from aqueous ethanol (1:1)]. IR spectrum: 2140 (N_3), 2238 (CN), and 3380 cm^{-1} (NH_2). Mass spectrum, m/z (%): 52 (6.9), 53 (94.1), 54 (100.0), 55 (5.1), 66 (29.9), 67 (6.7), 68 (41.9), 69 (6.0), 79 (23.1), 108 (7.9), 143 (7.0), 152 (29.2). Found: C 29.6; H 1.2; N 69.4%. $C_4H_2N_8$. Calculated: C 29.6; H 1.2: N 69.1%.

3-Azido-5-amino-6-nitro-1,2,4-triazine (V). The reaction of 2 g (0.02 mole) of aminotetrazole and 1.6 g (0.02 mole) of nitroacetonitrile via the method described above gave 2 g (60%) of V with mp 158°C (dec.). IR spectrum: 2169 (N_3); 1510 and 1315 (NO_2); 3340

TABLE 1. Coordinates of the Atoms in IV Crystals ($\cdot 10^4$; $\cdot 10^{-3}$ for H)

Atom	Molecule A			Molecule B		
	x	*y*	*z*	*x*	*y*	*z*
$N_{(1)}$	5909 (7)	932 (4)	7005 (3)	10720 (7)	1559 (4)	1896 (4)
$N_{(2)}$	5245 (7)	876 (5)	7752 (3)	9963 (8)	1600 (5)	2602 (4)
$N_{(3)}$	4905 (7)	−1130 (4)	7588 (3)	10130 (7)	3629 (4)	2621 (3)
$N_{(4)}$	5705 (7)	−2042 (4)	6408 (3)	11243 (7)	4580 (4)	1558 (4)
$N_{(5)}$	7368 (7)	131 (5)	5150 (4)	12698 (9)	2407 (5)	199 (4)
$N_{(6)}$	4137 (8)	−101 (5)	8774 (4)	8958 (8)	2566 (5)	3660 (4)
$N_{(7)}$	3663 (8)	−1050 (6)	9010 (4)	8768 (8)	3508 (6)	4005 (4)
$N_{(8)}$	3142 (10)	−1833 (6)	9301 (4)	8549 (9)	4303 (6)	4371 (4)
$C_{(1)}$	5563 (8)	−1088 (5)	6843 (3)	10856 (7)	3606 (5)	1906 (4)
$C_{(2)}$	6065 (7)	−11 (5)	6568 (4)	11183 (8)	2524 (5)	1556 (4)
$C_{(3)}$	4812 (8)	−146 (5)	7987 (4)	9726 (8)	2630 (5)	2922 (4)
$C_{(4)}$	6827 (9)	100 (5)	5776 (4)	12012 (9)	2422 (5)	802 (4)
$H_{(1)}$	626 (8)	−206 (5)	597 (4)	1175 (7)	459 (5)	105 (4)
$H_{(2)}$	569 (8)	−274 (6)	665 (4)	1063 (7)	529 (5)	182 (4)

TABLE 2. Parameters of the Anisotropic Temperature Factors in the Form $T = \exp[-1/4(B_{11}h^2a^{*2} + \ldots + 2B_{23}klb^*c^*)]$

Atom	Molecule A					
	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
$N_{(1)}$	6,0 (3)	2,3 (2)	4,2 (2)	−0,0 (2)	1,1 (2)	−0,3 (2)
$N_{(2)}$	5,3 (3)	3,1 (3)	4,1 (2)	0,1 (2)	1,8 (2)	−0,4 (2)
$N_{(3)}$	4,8 (3)	2,7 (3)	3,3 (2)	0,1 (2)	1,7 (2)	0,1 (2)
$N_{(4)}$	6,4 (3)	2,2 (2)	3,9 (2)	−0,2 (2)	2,4 (2)	−0,0 (2)
$N_{(5)}$	6,4 (3)	4,6 (3)	4,6 (3)	−0,6 (2)	2,9 (3)	0,0 (2)
$N_{(6)}$	7,0 (4)	4,0 (3)	4,6 (3)	0,3 (2)	3,6 (3)	−0,4 (2)
$N_{(7)}$	5,9 (3)	4,8 (3)	4,0 (2)	0,7 (3)	2,5 (2)	−0,3 (2)
$N_{(8)}$	8,5 (4)	5,7 (4)	5,8 (3)	0,1 (3)	3,4 (3)	0,6 (3)
$C_{(1)}$	4,7 (3)	2,2 (2)	3,0 (2)	−0,0 (2)	0,6 (2)	0,2 (2)
$C_{(2)}$	3,8 (3)	2,8 (3)	3,2 (3)	−0,2 (2)	1,1 (2)	−0,1 (2)
$C_{(3)}$	5,3 (3)	2,4 (3)	3,7 (3)	0,4 (2)	1,1 (2)	−0,2 (2)
$C_{(4)}$	5,1 (3)	2,6 (3)	4,0 (3)	−0,1 (2)	0,7 (3)	0,0 (2)

TABLE 2 (Continued)

Atom	Molecule B					
	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
$N_{(1)}$	5,4 (3)	2,7 (2)	5,4 (3)	0,1 (2)	2,6 (2)	−0,0 (2)
$N_{(2)}$	6,2 (3)	2,6 (3)	5,2 (3)	−0,2 (2)	2,5 (2)	0,2 (2)
$N_{(3)}$	5,3 (3)	2,6 (3)	4,0 (2)	−0,0 (2)	1,8 (2)	0,2 (2)
$N_{(4)}$	5,7 (3)	2,2 (2)	4,3 (2)	−0,1 (2)	2,3 (2)	0,4 (2)
$N_{(5)}$	8,3 (4)	4,6 (3)	5,3 (3)	0,8 (3)	3,3 (3)	−0,3 (2)
$N_{(6)}$	6,7 (3)	3,6 (3)	4,8 (3)	−0,3 (2)	2,4 (3)	0,3 (2)
$N_{(7)}$	5,4 (3)	5,4 (4)	4,0 (3)	−0,2 (3)	2,0 (2)	0,3 (2)
$N_{(8)}$	7,5 (4)	6,6 (4)	5,6 (3)	−0,6 (3)	3,5 (3)	−0,7 (3)
$C_{(1)}$	3,5 (3)	2,9 (2)	3,5 (3)	0,0 (2)	1,6 (2)	0,0 (2)
$C_{(3)}$	4,9 (3)	2,4 (3)	4,0 (3)	0,3 (2)	1,3 (2)	−0,2 (2)
$C_{(2)}$	4,1 (3)	3,2 (3)	4,3 (3)	−0,2 (2)	1,9 (2)	0,2 (2)
$C_{(4)}$	5,5 (4)	2,6 (3)	4,6 (3)	0,3 (2)	1,8 (3)	−0,3 (2)

cm^{-1} (NH_2). Mass spectrum, m/z (%): 52 (7.4), 53 (27.5), 54 (7.4), 66 (4.9), 67 (4.2), 68 (100.0), 69 (8.0), 86 (3.3), 99 (3.0), 128 (4.2), 136 (4.0), 154 (17.9), 182 (76.9).

3,5-Dioxo-2,3,4,5-tetrahydro-6-cyano-1,2,4-triazine (VI). A 1.62-g (0.01 mole) sample of triazine IV was refluxed in a mixture of 15 ml of 2 M H_2SO_4 and 20 ml of ethanol for 1 h, after which the alcohol was removed by distillation, and the residue was filtered to give 1.2 g (90%) of VI with mp 210-211°C (from ethanol). UV spectrum, λ_{max} (log ε): 207 (3.82) and 283 nm (3.90). Found: C 34.6; H 1.5; N 40.4%. $C_4H_2N_4O_2$. Calculated: C 34.8; H 1.4; N 40.6%.

3,5-Dioxo-2,3,4,5-tetrahydro-6-amido-1,2,4-triazine (VII). A 1.62-g (0.01 mole) sample of triazine IV was refluxed for 1 h in a mixture of 15 ml of 2 N HCl and 20 ml of ethanol, after which the excess solvent was removed by distillation *in vacuo* to give 0.9 g (55%) of VII with mp ⩾ 300°C (mp > 300°C [14]). UV spectrum, λ_{max} (log ε): 210 (3.77) and 277 nm (3.84). Found: C 30.6; H 2.5%. $C_4H_4N_4O_3$. Calculated: C 30.8; H 2.6%.

3,5-Dioxo-2,3,4,5-tetrahydro-6-carboxy-1,2,4-triazine (VIII). A 1.62-g (0.01 mole) sample of triazine IV was refluxed in 20 ml of concentrated HCl for 1 h, after which the mixture was cooled, and the precipitate was removed by filtration to give 1.0 g (60%) of VIII with mp 235-236°C (mp 235°C [14]). UV spectrum, λ_{max} (log ε): 203 (3.79) and 268 nm (3.42). Found: C 30.9; H 2.1%. $C_4H_3N_3O_4$. Calculated: C 30.6; H 1.9%.

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