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REGIOSELECTIVE AND REGIOSPECIFIC CYCLOADDITION OF ACETYLENES TO 2,4,6-TRIAZIDOPYRIDINE

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The cycloaddition of tert-butylacetylene to 2,4,6-triazido-3,5-dicyanopyridine and 2,4,6-triazido-3-chloro-5-cyanopyridine occurs regioselectively and regiospecifically at the azide group in position 4 of the pyridine ring leading to the formation of the corresponding 4-(4'-tert-butyl-1H-1,2,3-triazolyl)pyridines as the sole products. Analogous reactions with the less sterically hindered n-butylacetylene are characterized by less regiospecificity and give a mixture of the isomeric 4'- and 5'-n-butyl-substituted triazoles at ratios of 96 : 4 and 91 : 9 respectively for the two different triazides. The interaction energies of the pyridine α- and γ-azide groups with the acetylene molecules, and the energies of the transition states for these reactions have been calculated by the PM3 method. It was established that the high reactivity of the γ-azide group of the triazidopyridines in relation to the acetylenes is caused by the anomalously low distribution of bonding orbital density on these groups, leading to substantially lower activation energies in 1,3-dipolar cycloaddition reactions.

Keywords: azides, pyridines, triazoles, regioselectivity, regiospecificity, cycloaddition.

The present work is a continuation of the systematic investigations carried out by us on clarifying the rules for the selective addition of dipolarophiles to the azide groups of 2,4,6-triazidopyridines [1-5].

We showed previously that the 1,3-dipolar cycloaddition of compounds **1a,b** to *tert*-butylphosphaacetylene occurs regioselectively and regiospecifically at the azide group in position 4 of the pyridine ring with the formation of the corresponding 4-(5'-*tert*-butyl-3H-1,2,3,4-triazaphospholo)pyridines as intermediate products [3]. From an analysis of the energies of the frontier orbitals for the initial and intermediately resulting azides it followed that addition of the given dipolarophile to the γ-azide group of pyridines **1a,b** is approximately 10 kcal/mole more favorable than reaction at the α-azide group of the same compounds [4]. At the same time the nature of the detected effect remained unclear. The given reactions might be controlled by both kinetic and by thermodynamic parameters with equal probability. In the first case it was necessary to look for the reason for the selective addition of phosphaacetylene at the γ-azide group of pyridines **1a,b** in the different stabilization energies of the transition states for reaction at the azide groups at positions 2 and 4 of the pyridine ring. In the case of equal activation energy for both processes the choice of reaction pathways should be determined by the interaction energies of the reaction centers described by the equation:

$$\Delta E = -\sum_{ab}\sum (q_a + q_b)\,\gamma_{ab} S_{ab} - \sum_{ab} Q_a Q_b\,\Omega/\varepsilon + 2\sum_{R}\sum_{S} - \sum_{R}\sum_{S} \Big(\sum_{rs} c_a c_b \gamma_{ab}\Big)^2 / E_R - E_S, \qquad (1)$$

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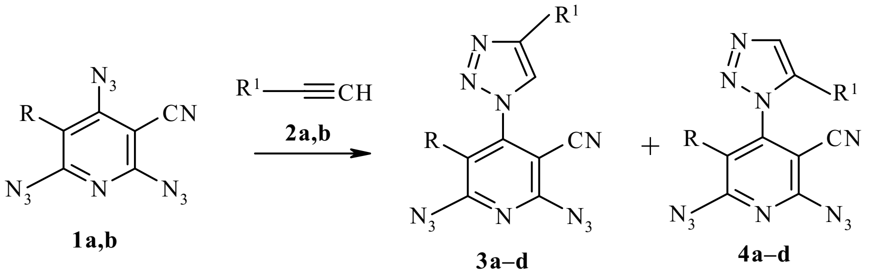
Where q_a, q_b and Q_a, Q_b are the orbital and total electron density at AO *r* and MO *R* of molecule *a* and at AO *s* and MO *S* of molecule *b*, γ_{ab} is the interaction integral, S_{ab} is the overlap integral between the two AO, Ω is a term for the Coulombic repulsion between the atoms, ε is the local dielectric constant of the solvent, c_a and c_b are the AO coefficients, E_R and E_S are the energies of the frontier MO of compounds **a** and **b** [6,7]. The data obtained by us enabled assessment of only the contribution of the third term of equation (1) to the overall energy of interaction of the azide groups of pyridines **1a,b** with the phosphaacetylene molecule and might not explain completely the reasons for the observed effect. In addition there is considerable interest in the study of the reactions of compounds **1a,b** with other dipolarophiles to clarify the dependence of the selectivity of such reactions on the properties of the dipolarophiles.



1 a R = CN, **b** R = Cl; **2 a** R^1 = *t*-Bu, **b** R^1 = *n*-Bu; **3, 4 a** R = CN, R^1 = *t*-Bu, **b** R = Cl, R^1 = *t*-Bu, **c** R = CN, R^1 = *n*-Bu, **d** R = Cl, R^1 = *n*-Bu

In the present work the reactions of triazidopyridines **1a,b** with acetylenes **2a,b** have been studied. The interaction energies of the azide groups with the acetylene molecules and the stabilization energies of the different transition states have been calculated by semiempirical method.

Reaction of compounds **1a,b** with an excess of acetylene **2a** was carried out in ether solution at room temperature during three weeks. The course of the reactions was checked by TLC. After the indicated time the initial triazides had undergone almost complete conversion with the formation of the sole product, *viz*. compounds **3a,b**.

The composition and structure of pyridines **3a,b** were in complete agreement with data of elemental analysis, IR, ^{1}H and ^{13}C NMR spectroscopy, and mass spectrometry (Tables 1-3). Thus the presence in the ^{13}C NMR spectrum of compound **3a** of only three signals for the carbon atoms of the pyridine ring at 160.4, 150.4, and 89.8 ppm shows that addition of a molecule of *tert*-butylacetylene to triazide **1a** occurs regioselectively at the azide group in position 4 of the pyridine ring. The ^{13}C NMR spectra also enabled to determine the position of the *tert*-butyl fragment in the triazole ring of adducts **3a,b**. It was established previously that the signals of the $C_{(4')}$ carbon atoms for 4-alkyl substituted 1H-1,2,3-triazoles are usually displayed at 120 ppm and are displaced by approximately 10 ppm towards low field compared with the signals of the $C_{(5')}$ atoms [8-10]. Consequently the signal at 119 ppm in the ^{13}C NMR spectra of compounds **3a,b** (Table 3) may confidently be assigned to the $C_{(4')}$ atom of the triazole ring and the signal at 110 ppm to the $C_{(5')}$ atom.

The significantly lower intensity of the $C_{(4')}$ atom signal shows unequivocally that the *tert*-butyl substituent is located precisely at this carbon atom. It should be noted that analysis of the ^{1}H NMR spectra for the reaction mixture did not reveal the presence of the possible isomers **4a,b** as minor reaction products. The results show that cycloaddition of a molecule of *tert*-butylacetylene to triazides **1a,b** occurs regioselectively with the formation of 4'-*tert*-butyl substituted 1H-1,2,3-triazoles exclusively.

The reaction of triazidopyridines **1a,b** with *n*-butylacetylene **2b** was carried out under conditions analogous to those described above for the synthesis of compounds **3a,b**. Analysis of the reaction mixture by ^{1}H NMR spectroscopy showed that together with the cycloadducts **3c,d** a small amount of the 5' substituted triazoles **4c,d** is formed in the reactions. As might have been expected [8-10], the signals of the $H_{(4')}$ protons in compounds **4c,d** were displaced towards high field compared with the signals of the $H_{(5')}$ protons in the isomeric triazoles **3c,d** (Table 2). It follows from a comparison of the integrated intensities of these signals that the ratio of isomers **3c**/**4c** and **3d**/**4d** in the reaction mixture are equal to 96/4 and 91/9 respectively. Only compounds **3c,d** were isolated from the reaction mixture in yields of 80-85%. The main spectral characteristics of the compounds obtained are given in Tables 1-3.

TABLE 1. Characteristics of Compounds **3a-d**

Compound	Empirical formula	Found, % Calculated, % C			mp, °C	Mass spectrum, *m/z* (I_{rel}, %)	Yield, %
		C	H	N			
3a	$C_{13}H_{10}N_{12}$	46.86 46.70	3.22 3.02	49.92 50.28	190-192	306 (44) $[M-N_2]^+$, 291 (100) $[M-N_2-CH_3]$, 278 (4) $[M-2N_2]$	86
3b	$C_{12}H_{10}ClN_{11}$	42.15 41.93	3.26 2.93	44.56 44.83	61-62	343 (52) $[M-N_2]^+$, 328 (100) $[M-N_2-CH_3]$, 315 (12) $[M-2N_2]$	82
3c	$C_{13}H_{10}N_{12}$	46.90 46.70	3.16 3.02	49.94 50.58	183-185	306 (40) $[M-N_2]^+$, 291 (100) $[M-N_2-CH_3]$, 278 (7) $[M-2N_2]$	85
3d	$C_{12}H_{10}ClN_{11}$	42.22 41.93	3.23 2.93	44.67 44.83	55-56	343 (46) $[M-N_2]^+$, 328 (100) $[M-N_2-CH_3]$, 315 (10) $[M-2N_2]$	80

TABLE 2. IR and ^{1}H NMR Spectra of Compounds **3a-d** and **4c,d***

Compound	IR spectrum, ν, cm^{-1}			^{1}H NMR spectrum, CDCl$_3$, δ, ppm, *J* (Hz)	
	N_3	C≡N	C=N, C=C	$CH_{(5')}$	R^1
3a	2160	2230	1580, 1555, 1542	7.88	1.34 (9H, s, $C(CH_3)_3$)
3b	2148, 2125	2230	1583, 1556, 1536	7.60	1.35 (9H, s, $C(CH_3)_3$)
3c	2160	2230	1580, 1557, 1544	7.91	0.88 (3H, t, *J* = 7.3, CH_3); 1.36 (2H, m, γ-CH_2); 1.65 (2H, m, β-CH_2); 2.75 (2H, t, *J* = 7.5, α-CH_2)
3d	2145, 2120	2225	1580, 1556, 1540	7.63	0.88 (3H, t, *J* = 7.3, CH_3); 1,35 (2H, m, γ-CH_2); 1.66 (2H, m, β-CH_2); 2.76 (2H, t, *J* = 7.5, α-CH_2)

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* ^{1}H NMR spectra of compounds **4c** 7.59 (1H, s, $CH_{(4')}$); 2.61 (2H, t, *J* = 7.5, α-CH_2); 1.54 (2H, m, β-CH_2); 1.27 (2H, m, γ-CH_2); 0.84 (3H, t, *J* = 7.3, CH_3); **4d** 7.57 (1H, s, $CH_{(4')}$); 2.46 (2H, t, *J* = 7.5, α-CH_2); 1.52 (2H, m, β-CH_2); 1.25 (2H, m, γ-CH_2); 0.84 (3H, t, *J* = 7.3, CH_3).

Calculation of the geometry and the electronic properties of compounds **2a,b**, **3a-d**, and **4c,d** was carried out by the PM3 semiempirical method [11] with the Spartan set of programs [12]. The molecular structures of the compounds were calculated with full optimization of the geometric parameters.

The energies of the frontier orbitals in acetylenes **2a,b** and azidopyridines **1a,b**, **3a-d**, and **4c,d** are given in Table 4. Comparison of the energy values shows that addition of acetylenes **2a,b** to triazidopyridines **1a,b** belongs to a type of dipole–LUMO controlled reaction occurring as a result of the interaction of the LUMO of the dipole with the HOMO of the dipolarophile, the difference in energy between which is 1.5-2.5 eV less than the difference in energies of the LUMO of the dipolarophile and the HOMO of the triazide. Analogously to the reaction with *tert*-butylphosphaacetylene [4], the addition of one molecule of acetylenes **2a,b** to triazidopyridines **1a,b** leads to the formation of cycloadducts having a lower energy of the LUMO than for the initial compounds. The least reduction in energy of the LUMO in the azidopyridines is recorded when forming a triazole substituent having a *tert*-butyl group (by 5.60-5.70 kcal/mole), and the greatest on forming cycloadducts **3c,d** (by 5.74-5.93 kcal/mole, Table 4). Analysis of the effective charges, bond lengths, and torsion angles revealed that the difference in energies of the LUMO in the series of isomers **3a**, **3c**, and **4c** and also **3b**, **3d**, and **4d** is caused by the different

TABLE 3. Parameters of the ^{13}C NMR Spectra for Compounds **3a-d** (δ, ppm, $CDCl_3$)

Compound	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	C≡N	$C_{(4')}$	$C_{(5')}$	R^1
3a	160.4	89.8	150.4	89.8	160.4	109.7	110.3	119.2	31.0; 29.8
3b	154.8	110.3	149.3	88.2	154.3	108.3	110.6	119.9	30.9; 29.9
3c	160.4	89.9	150.4	89.9	160.4	109.7	110.3	121.2	13.6; 22.0; 24.9; 30.7
3d	154.8	110.3	149.3	88.2	154.3	108.3	110.6	121.9	13.6; 22.0; 24.9; 30.9

spatial orientation of the triazole ring in relation to the plane of the pyridine ring (Table 5), affecting the character of the electron density distribution in the molecules of these compounds (effective Mulliken charges and partial electron density in the frontier orbitals).

The distribution of orbital density in the LUMO of azidopyridines **1a,b** and **3a,b** (all the cycloadducts **3a-d** and **4c,d** have the same LUMO symmetry) is shown in Fig. 1. It is very obvious that the triazide molecule **1a** has practically the same orbital density at the azide groups in positions 2 and 4 of the pyridine ring. Approximately the same distribution of orbital density at the same groups is also observed in the molecule of triazide **1b**. This is a basis for proposing that the essentially differing reactivity of these groups in reactions with acetylenes is not linked with the properties of the LUMO in the initial triazides. The fairly high orbital density at one of the azide groups in the LUMO of cycloadducts **3a,b** (Fig. 1) indicates that the reaction of these compounds with acetylenes is allowed

TABLE 4. Energies of the Frontier Orbitals of Compounds **1a,b**, **2a,b**, **3a-d**, and **4c,d** and the Differences of the LUMO Energies for Cycloadducts **3a-d** and **4c,d** and the Initial Pyridines **1a,b**

Compound	E_{HOMO}, eV	E_{LUMO}, eV	ΔE_{LUMO}, kcal/mole
1a*	-9.661	-1.707	
1b*	-9.077	-1.488	
2a	-11.031	1.944	
2b	-10.762	1.882	
3a	-9.832	-1.950	5.60
3b	-9.317	-1.735	5.70
3c	-9.822	-1.956	5.74
3d	-9.312	-1.745	5.93
4c	-9.848	-1.953	5.67
4d	-9.386	-1.739	5.79

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* Data of [4].

TABLE 5. Torsion angles (φ, deg) in the Cycloadduct Molecules **3a-d** and **4c,d**

Compound	Parameter	φ, deg
3a	$C_{(3)}$–$C_{(4)}$–$N_{(1)}$–$N_{(2)}$	58.4
3b	$C_{(3)}$–$C_{(4)}$–$N_{(1)}$–$N_{(2)}$	48.3
3c	$C_{(3)}$–$C_{(4)}$–$N_{(1)}$–$N_{(2)}$	52.7
3d	$C_{(3)}$–$C_{(4)}$–$N_{(1)}$–$N_{(2)}$	46.3
4c	$C_{(3)}$–$C_{(4)}$–$N_{(1)}$–$N_{(2)}$	68.5
4d	$C_{(3)}$–$C_{(4)}$–$N_{(1)}$–$N_{(2)}$	65.7

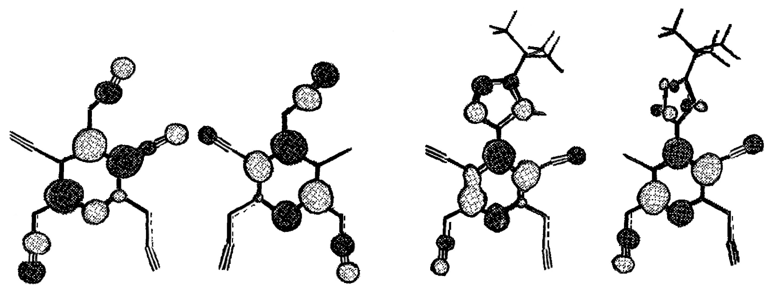
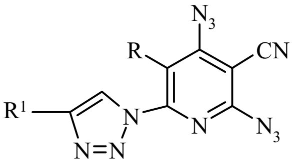


Fig. 1. Distribution of orbital density in the LUMO of pyridines **1a,b** and **3a,b**.

according to the orbital selection rule [7]. On comparing the LUMO of compounds **3a** and **3b** it is not difficult to notice that at a more coplanar disposition of the two heterocyclic fragments in the cycloadduct molecules the azide groups have a lower orbital density and consequently must be less reactive in relation to a polarophile rich in electrons. Considering that the reactivity of the azide groups is linked not only with the values of the AO coefficients for the atoms of these groups but also with a whole series of other parameters [see equation (1)], further analysis of the thermodynamic preference for the interaction of acetylenes **2a,b** with the α- and γ-azide groups of pyridines **1a,b**, **3a-d**, and **4c,d** was carried out on the basis of determining the total energy of interaction of the reactants. According to chemical reaction theory, such energy is equal to the difference between the total energy of the isolated initial molecules and the total energy of the cycloadducts [7].



5a–d

5 a R = CN, R^1 = *t*-Bu, **b** R = Cl, R^1 = *t*-Bu,
c R = CN, R^1 = *n*-Bu, **d** R = Cl, R^1 = *n*-Bu

In order to determine the interaction energies of the α- and γ-azide groups of pyridines **1a,b** with acetylenes **2a,b** the heats of formation for these compounds and also for the cycloadducts **3a-d** and **4c,d** and the hypothetical compounds **5a-d** were calculated (Table 6). The energies of interaction were found as the difference between the total heat of formation for the initial compounds and the heat of formation for the corresponding cycloadduct. It was revealed that for triazide **1a** the energy of interaction with a molecule of acetylene **2a** at the γ-azide group was 0.7 kcal/mole less than at the azide group at position 2 of the pyridine ring (Table 7). This means that thermodynamically the reaction at the α-azide group of pyridine **1a** must be the somewhat more preferred direction for the interaction of these compounds. Since experimentally the cycloaddition of acetylene **2a** to triazide **1a** proceeds exclusively at the γ-azide group then it is obvious that the direction of the reaction in this case is not determined by thermodynamic parameters.

Unlike the case of the dicyano derivative **1a** the LUMO of triazide **1b** is characterized by a higher orbital density at the γ-azide group compared with the azide group in position 2 of the pyridine ring (Fig. 1, the AO coefficients at the $N_{(\gamma)}$ atoms of these groups were respectively 0.45 and -0.37 according to the data of calculations by the STO-3G method [4]). Consequently it is fully conforming to principle that the energy of interaction of acetylene **2a** with pyridine **1b** at the γ-azide group is 4.9 kcal/mole greater than at the α-azide group (Table 7). Although these data are in good agreement with experiment it is not at all certain that the reaction is subject to thermodynamic control.

TABLE 6. Heats of Formation for Pyridines **1a,b**, **2a,b**, **3a-d**, and **4c,d**, the Hypothetical Compounds **5a-d** and **6** and the Transition States **7a,b**, **8a,b**, and **9**

Compound	H_f, kcal/mole	Compound	H_f, kcal/mole	Compound	H_f, kcal/mole
1a	329.6	**3d**	262.3	**6**	290.6
1b	286.8	**4c**	307.3	**7a**	387.0
2a	25.1	**4d**	263.2	**7b**	344.6
2b	24.6	**5a**	311.1	**8a**	392.5
3a	311.8	**5b**	268.7	**8b**	350.1
3b	263.8	**5c**	310.1	**9**	373.0
3c	306.8	**5d**	267.7		

TABLE 7. Interaction Energies (ΔE, kcal/mole) of the Azide Groups in Pyridines **1a,b** and **3a** with Molecules of Acetylenes **2a,b**

Group	Acetylene **2a**	Acetylene **2b**	
		orientation $N_{(\gamma)}$–$C_{(2)}$	orientation $N_{(\gamma)}$–$C_{(1)}$
γ-N_3 **1a**	42.9	47.4	46.9
α-N_3 **1a**	43.6	44.1	—
γ-N_3 **1b**	48.1	49.1	48.2
α-N_3 **1b**	43.2	43.7	—
α-N_3 **3a**	46.3	—	—

By comparing the interaction energies of acetylenes **2a** and **2b** with the α- and γ-azide groups of triazides **1a,b** (Table 7) it is possible to assess the dependence of these characteristics on the properties of the dipolarophiles. Thus in comparison with acetylene **2a** the isomer **2b** is characterized by a higher energy of the HOMO (by 1.5 kcal/mole, Table 4), a somewhat enhanced orbital density in the HOMO at the $C_{(1)}$ atom (Fig. 2), and a less bulky substituent at the triple bond. Starting from the general theory of 1,3-dipolar cycloaddition it follows that higher regioselectivity must be observed in reactions with the participation of more reactive compounds [13]. As the calculations showed (Table 7), in reality the interaction energy of a molecule of acetylene **2b** with triazide **1a** at the γ-azido group is 3.3 kcal/mole greater than at the azide group at position 2 of the pyridine ring. For the reaction of acetylene **2b** with triazide **1b** the corresponding difference in energies was 5.4 kcal/mole. In addition, the overall interaction energy of a molecule of acetylene **2b** with the γ-azide groups of triazides **1a,b** was 1.0-4.5 kcal/mole greater than for acetylene **2a**. Considering that in the reactions of triazides **1a,b** with acetylene **2b** the formation of two types of isomers, *viz*. compounds **3c,d** and **4c,d**, was observed, it is expedient to compare the interaction energy of acetylene **2b** with the γ-azide groups of triazides **1a,b** for two different orientations of the interacting centers. As is seen from the data of Table 7, the more preferred orientation (by 0.5-0.9 kcal/mole) is that at which triazoles **3c,d**, the main reaction products, are formed. Paying attention to the

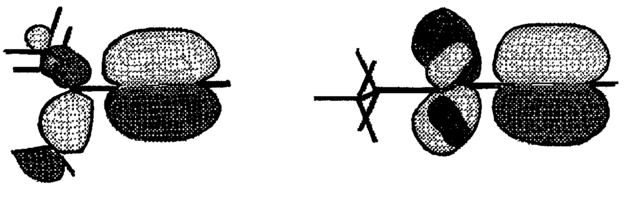
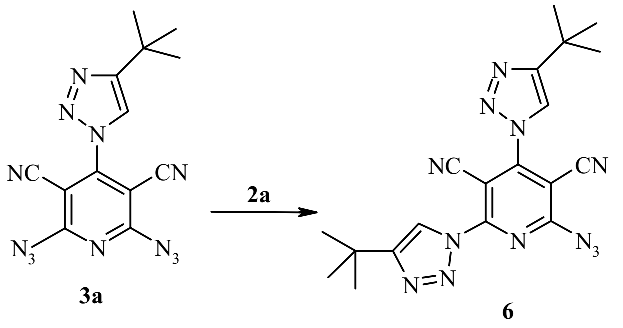

HOMO **2a** HOMO **2b**

Fig. 2. Distribution of orbital density in the HOMO of acetylenes **2a,b**.

fact that the higher orbital density in the HOMO of acetylene **2b** is concentrated on the $C_{(1)}$ atom (Fig. 2), it may be asserted that the difference in energies for the two types of interaction only partially characterize the contribution of steric factors to the regiospecificity of the acetylene **2b** addition to the γ-azide group of pyridines **1a,b**. The same orbital density at the $C_{(1)}$ and $C_{(2)}$ atoms in the HOMO of acetylene **2a** (Fig. 2) indicates that the absolute regiospecificity for the addition of this dipolarophile at the γ-azide group of pyridines **1a,b** is caused exclusively by steric factors. The same regiospecificity of cycloaddition of azides to the triple bond was observed previously in reactions involving *tert*-butylphosphaacetylene and adamantylacetylene [3,8].

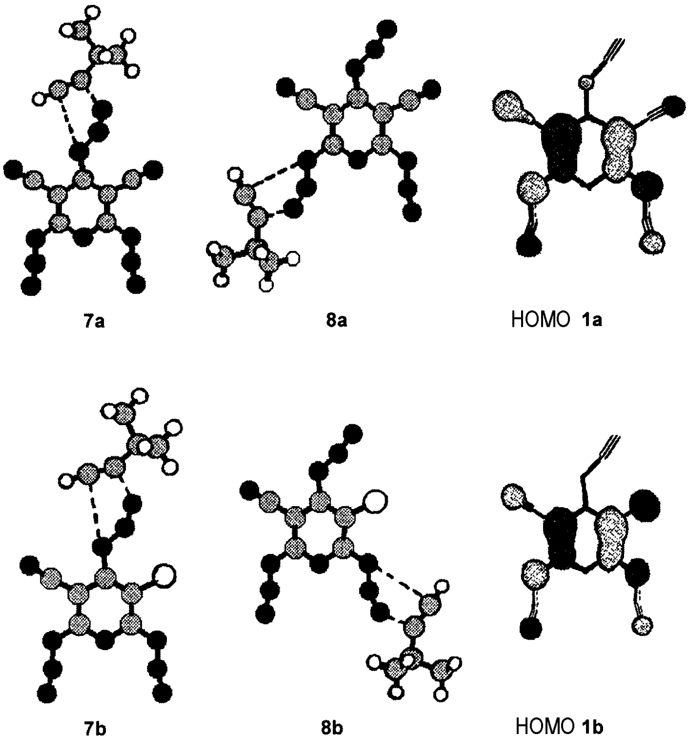
In order to answer the problem as to why the reaction of compounds **1a,b** with acetylenes stops at the stage of adding only one molecule of dipolarophile, the interaction energy of acetylene **2a** with an azide group of the monoadduct **3a** was calculated. This energy was found as the difference between the total heat of formation for the isolated compounds **2a** and **3a** and the heat of formation for the hypothetical bis-adduct **6** (Table 6).



3a

6

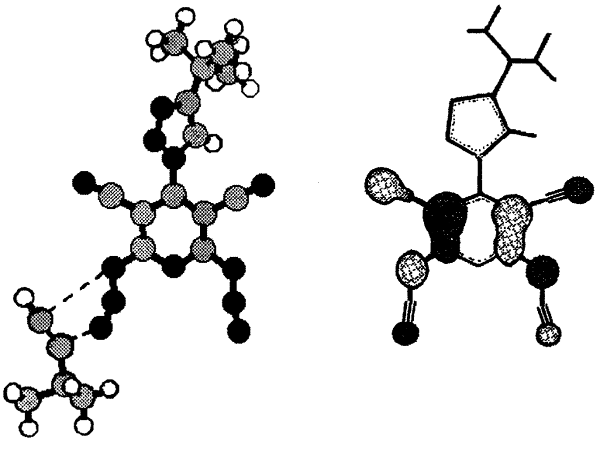
It turned out that the interaction energy of compounds **2a** and **3a** was 3.4 kcal/mole greater than the interaction energy of acetylene **2a** with the γ-azide group of pyridine **1a** (Table 7). This means that with the accumulation of the cycloadduct **3a** in the reaction mixture the addition of a molecule of acetylene **2a** at the azide



7a **8a** HOMO **1a**

7b **8b** HOMO **1b**

Fig. 3. Geometry of the transition states **7a,b** and **8a,b** and distribution of orbital density in the HOMO of pyridines **1a,b**.



9 HOMO **3a**

Fig. 4. Geometry of the transition state **9** and distribution of orbital density in the HOMO of pyridine **3a**.

group of this compound must be the preferred direction for the subsequent reaction. Meanwhile the experimental data indicate the reverse, confirming indirectly that the reaction of acetylenes **2a,b** with azidopyridines **1a,b**, **3a-d**, and **4c,d** is probably subject to kinetic and not thermodynamic control.

The heats of formation for the transition states **7a,b**, **8a,b**, and **9** were calculated with the aim of determining the activation energies for the reaction of acetylenes **2a,b** with the γ- and α-azide groups of pyridines **1a,b** and **3a** (Table 6, Figs. 3 and 4). Calculation of the total energy and geometry of the transition states was carried out analogously to the method described in [14].

The results of the calculations, represented in Figs. 5 and 6, show that of the two possible directions for the addition of a molecule of acetylene **2a** to pyridines **1a,b** the lower energy of activation (by 5.5 kcal/mole) is possessed by the reactions occurring at the azide group in position 4 of the pyridine ring. In addition the activation energy for the reaction of acetylene **2a** with the γ-azide group of pyridine **1a** is 3.8 kcal/mole less than for the reaction of compounds **2a** and **3a** (Figs. 5 and 7). The differences in the activation energies revealed for the competing processes explain completely the observed effect of regioselective addition of acetylenes to the γ-azide group of pyridines **1a,b**. Thus, in accordance with literature data, a gain in energy of 1.5 kcal/mole or more for one of the reaction routes turns out to be adequate for the reaction to proceed exclusively by this route [13].

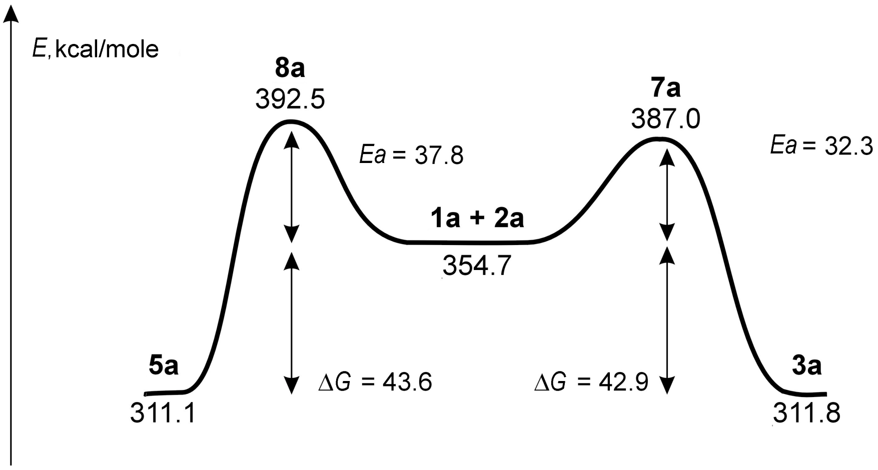


Fig. 5. Energy profile for the reaction of acetylene **2a** with the α- and γ-azide group of pyridine **1a**.

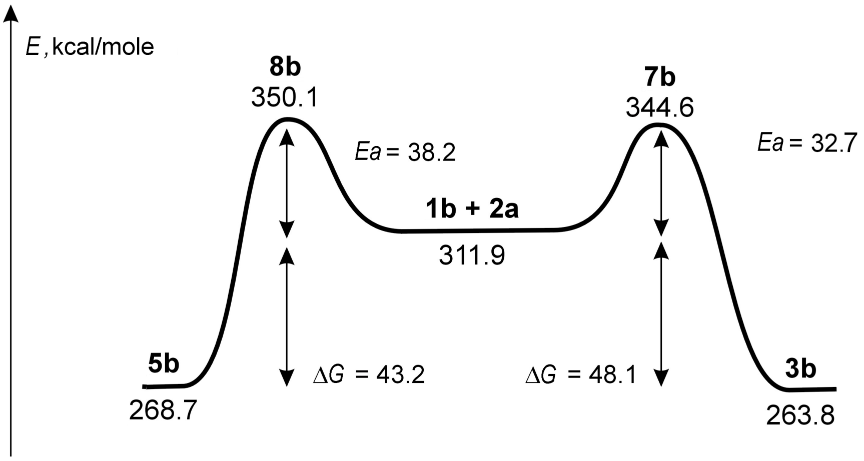


Fig. 6. Energy profile for the reaction of acetylene **2a** with the α- and γ-azide group of pyridine **1b**.

Much attention is paid in the theory of chemical reactions to the clarification of the distance between the interacting centers of molecules of two reactants in the transition state [15]. In particular the value of the interaction integral γ_{ab} in equation 1 depends on these distances [6]. It was established with the aid of CNDO/2 calculations that the $N_{(\gamma)}$–C distance in the transition states for the reaction of azides with dipolarophiles was on average 1.75 Å [6]. Calculations by the PM3 method for the reaction of methylsulfanilyl azide with 5-alkylidenedihydrotetrazole showed that for a given pair of reactants the distance $N_{(\gamma)}$–C and $N_{(\alpha)}$–C in the transition state were 1.87 and 3.11 Å respectively [14].

Practically the same distances between the interacting centers (1.83-1.85 and 3.19-3.31 Å) were also observed in the transition states **7a,b** (Table 8). At the same time the $N_{(\gamma)}$–$C_{(2)}$ bond in the transition states **8a,b** and **9** were shortened to 1.71-1.77 Å, while the $N_{(\alpha)}$–$C_{(1)}$ bond was lengthened to 3.37-3.49 Å (Figs. 3 and 4, Table 8).

The most significant changes in the geometry of the azide molecules in the transition states **7a,b**, **8a,b**, and **9** are the decrease to 146.7-152.6° in the valence angles of the azide group participating in the reaction and the lengthening of the $N_{(\beta)}$–N(γ) bond by 0.03 Å. For the acetylene molecule in the transition state a bend develops in the $C_{(1)}$–$C_{(2)}$–$C_{(3)}$ chain of atoms (angle CCC 146.9-151.5°) and also the $C_{(1)}$–$C_{(2)}$ bond is lengthened by 0.03 Å (Table 8). Analysis of the charge distribution in the transition states **7a,b**, **8a,b**, and **9** shows that, independent of the reaction center position in the pyridine ring, the charges on the $N_{(\alpha)}$, $N_{(\beta)}$, $N_{(\gamma)}$, $C_{(1')}$, and $C_{(2')}$ atoms remain

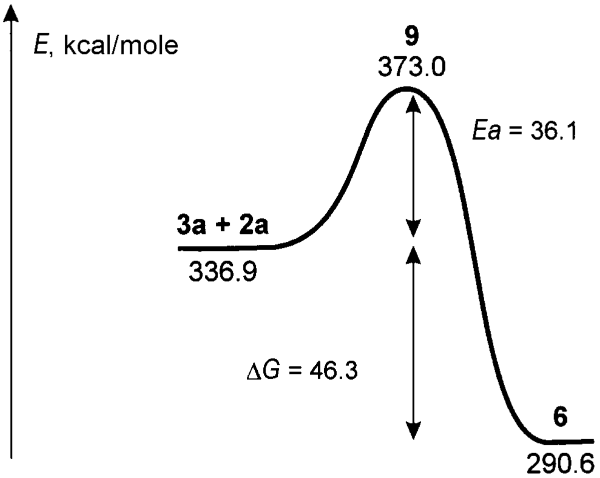


Fig. 7. Energy profile for the reaction of acetylene **2a** with pyridine **3a**.

TABLE 8. Geometric Parameters of the Reaction Centers in the Transition States **7a,b**, **8a,b**, and **9**

Transition state	Bond length (d, Å)		Valence angle (ω, deg)	
	$N_{(\gamma)}–C_{(2)}$	$N_{(\alpha)}–C_{(1)}$	$N_{(\alpha)}–N_{(\beta)}–N_{(\gamma)}$	$C_{(1)}–C_{(2)}–C_{(3)}$
7a	1.85	3.19	146.7	150.7
7b	1.84	3.31	150.0	151.5
8a	1.77	3.37	150.5	147.6
8b	1.76	3.49	154.4	148.7
9	1.71	3.45	152.6	146.9

practically unchanged and are -0.38, 0.54, -0.15, -0.19, and -0.10 eV respectively. This in its turn indicates that the differences in stabilization energies of the transition states **7a,b**, **8a,b**, and **9** are in no way linked with the features of charge distribution on the atoms of their reaction centers.

An understanding of the nature of the different activation energy for the cycloaddition of the acetylenes at the α- and γ-azide groups of pyridines **1a,b** and **3a** is possible from an analysis of the character of the orbital density distribution in the HOMO of these compounds. Thus, according to the general theory of chemical reactions, the formation of a new bond for two molecules includes destabilization of the initial system due to redistribution of the bonding interactions in the reactant molecules. In this way transfer of electrons from the initial MO of the reactants to the bonding orbital of the new bond in the transition states is accompanied by the simultaneous disappearance of the previously existing bonding orbitals in the interacting fragments. It has been shown in many examples that the most preferred reaction direction is that in which the fewest reactant bonding orbitals disappear [7] (for azide groups such bonding orbitals are the AO of the $N_{(\alpha)}$ and $N_{(\beta)}$ atoms in the HOMO [16,17]). It is seen from Fig. 3 that the HOMO of pyridines **1a,b** are characterized by relatively high bonding orbital density at the α-azide groups and less at the azide group in position 4 of the pyridine ring (the coefficients at the $N_{(\alpha)}$ and $N_{(\gamma)}$ atoms for the α-azide group, according to data from STO-3G calculations, were 0.38 and 0.04 respectively, while for the γ-azide group they were 0.09 and 0.01). This enables the conclusion that the higher stability of transition states **7a,b** compared with **8a,b** and **9** is caused by the retention in the first of stronger bonding interactions in the azide groups. In other words the lower activation energy for the reaction of acetylenes **2a,b** with the γ-azide groups of pyridines **1a,b** is caused by the lower energy outlay of the system on overcoming the weaker bonding interactions in the azide groups on changing their geometry in the transition state. Consequently it is remarkable that the γ-azide groups of pyridines **1a,b** undergo the most important changes of geometry in the transition state (Table 8). It is important to note that the weakness of the bonding interactions in the γ-azide groups in compounds **1a,b** are also displayed in essentially a greater degree of curvature of these groups compared with the α-azide groups of the pyridines (angle NNN of γ-azide groups 166.3°, for α-azide groups 169.7° [4,5]). Previously we suggested that precisely the high degree of curvature of the γ-azide group in compounds **1a,b** serves as one of the principal reasons for their high reactivity in relation to a dipolarophile [4]. Allowing for the data obtained in the present work it should be specified that the origin for the high reactivity of the γ-azide groups of pyridines **1a,b** in relation to dipolarophiles is covered in the distribution, untypically low for the majority of azides, of bonding orbital density on the $N_{(\alpha)}$ and $N_{(\beta)}$ atoms of these groups, thanks to which these groups are distinguished by a particular geometry and reduced energy of activation in 1,3-dipolar cycloaddition reactions.

The investigations carried out have shown that the selectivity of the acetylenes **2a,b** addition to the γ-azide group of pyridines **1a,b** is caused exclusively by the lower energy of activation for this reaction pathway, when the least bonding orbitals in the azide groups of the initial compounds disappear. For the same reason, in spite of the lower energy for the LUMO of the resulting monoadducts **3a-d** and **4c,d**, the initial pyridines **1a,b** remain the more reactive azides in the reaction with acetylenes. In addition transition from kinetic to thermodynamic control in the reactions of triazides **1a,b** with dipolarophiles must evidently occur in the case when the azide groups of the monoadducts formed as intermediates also have very low bonding orbital density. A particular example of this is the reaction of triazide **1b** with *tert*-butylphosphaacetylene, in which the monoadduct formed as intermediate, having a very low bonding orbital density at the azide groups, readily adds two other molecules of phosphaacetylene [3,4]. Thermodynamic control in the reactions of triazides **1a,b** with dipolarophiles might also be expected at increased temperatures. In view of the data obtained in the present work (Table 7), it might be assumed that at increased temperature the reaction of acetylene **2a** with triazide **1a** will proceed at the azide groups at positions 2 and 4 of the pyridine ring to an equal extent. For the reactions of triazide **1b** with acetylenes **2a,b** and also of compound **1a** with acetylene **2b** at increased temperature the thermodynamically more preferable direction must remain reaction at the azide group in position 4 of the pyridine ring. On the strength of the lower energy of the LUMO for the monoadducts **3a-d** and **4c,d** formed as intermediates, the corresponding tris-adducts must be the final products of the reaction of triazides **1a,b** with acetylenes **2a,b**.

EXPERIMENTAL

The IR spectra were obtained on a Specord M-80 spectrometer, and the ^{1}H NMR spectra on a Bruker AMX-400 (400 MHz) instrument using TMS as internal standard. The ^{13}C NMR spectra were recorded on a Bruker AM-400 (100.6 MHz) instrument, and the mass spectra on a Finnigan MAT-90 at an ionization energy of 70 eV. A check on reactions was effected by TLC on Silufol UV-254 plates.

The method for obtaining the initial **1a,b** was described in [2,3].

2,6-Diazido-4-(4'-*tert*-butyl-1H-1,2,3-triazolyl)-3,5-dicyanopyridine (3a). A solution of acetylene **2a** (0.164 g, 2 mmol) in dry diethyl ether (20 ml) was added to a stirred solution of compound **1a** (0.126 g, 0.5 mmol) in dry diethyl ether (30 ml). The reaction mixture was then left stirring in the dark at room temperature for three weeks. The solvent was distilled off under vacuum, the residue was washed with boiling pentane (3 × 30 ml), and recrystallized from ethanol.

2,6-Diazido-4-(4'-*tert*-butyl-1H-1,2,3-triazolyl)-3-chloro-5-cyanopyridine (3b), 2,6-Diazido-4-(4'-*n*-butyl-1H-1,2,3-triazolyl)-3,5-dicyanopyridine (3c), and 2,6-Diazido-4-(4'-*n*-butyl-1H-1,2,3-triazolyl)-3-chloro-5-cyanopyridine (3d) were obtained similarly to the method described above.

The properties of compounds **3a-d** are given in Tables 1-3.

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