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# STEREO- AND REGIOSELECTIVE CYCLOADDITION OF NORBORNENE TO 2,4,9-TRIAZIDOPYRIDINE

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*4-(3-Azatricyclo[3.2.1.0]oct-3-yl)-2,6-diazido-3,5-dicyanopyridine has been obtained by the reaction of 2,4,6-triazido-3,5-dicyanopyridine with an equimolar quantity of norbornene. The product reacted readily at room temperature with an excess of norbornene giving the corresponding trisazatricyclooctane cycloadduct. An analogous trisadduct was obtained in the reaction of 4-(3-azatricyclo[3.2.1.0]oct-3-yl)-1,6-diazido-3-chloro-5-cyanopyridine with norbornene on boiling in $CCl_4$, and also in ether at room temperature in the presence of the complexes $Rh_2(OAc)_4$ and $Cu(AcAc)_2$. The cycloaddition proceeds stereoselectively in all cases with the exclusive formation of exo-conformers. Calculations have been carried out using the PM3 and RHF/3-21G* methods on 2,4,6-triazido-3-chloro-5-cyanopyridine and on 2,4,6-triazido-3,5-dicyanopyridine and also on the cycloadducts of these compounds with one or two molecules of norbornene. It was established that the addition of norbornene at the azide groups of pyridine is a dipole–LUMO controlled type of reaction and leads to the formation of cycloadducts having higher LUMO energy than the initial azides. The energy of the LUMO is increased to a lesser extent as a result of the addition of norbornene to a triazide containing identical substituents in the β positions of the pyridine ring, and is due to the special features of the symmetry of the LUMO of the cycloadducts formed.*

The present work is a continuation of the systematic investigations carried out by us on clarifying the rules for the selective addition of dipolarophiles at the azide groups of 2,4,6-triazidopyridines (see [1-3]).

We showed previously that the 1,3-dipolar cycloaddition reaction of pyridine (Ia) with norbornene occurs stereo- and regioselectively giving the exo-cycloadduct (IIIa) as the sole product [1, 2]. A quantum chemical study of the nature of the exceptionally high reactivity of the γ azide group of the (Ia, b) molecules showed that these groups are distinguished by an increased electrophilicity of the terminal nitrogen atoms, a higher contribution of the AO (atomic orbital) to the LUMO (lowest unoccupied molecular orbital), and a significant degree of curvature of the N—N—N atom chain. The ease of addition of the molecules (Ia, b) to the dipolarophile is determined by the difference in energies of the LUMO of the dipole and the HOMO (highest occupied molecular orbital) of the dipolarophile. The ability of the reaction to stop at the stage of forming monoadducts is determined by the ratio of the energies of the LUMO of the adduct formed and of the initial compounds (Ia, b). It is evident from these data that the low reactivity of cycloadduct (IIIa) towards norbornene is caused by the electron-donating character of the aziridine ring formed and by the insufficiently strong electron-accepting properties of the other substituents in the pyridine ring. Consequently there is considerable interest in the study of the cycloaddition of norbornene to compound (Ib) which contains stronger electron-accepting groups than (Ia). Furthermore, the problem of what conditions enable the azide groups of pyridine (IIIa) to interact with norbornene remains unclarified.

The aim of the present work was to study the special features of the cycloaddition of norbornene to the azide groups of compound (Ib) and also to develop a method for the synthesis of the tris adduct by the reaction of norbornene with the diazidopyridine (IIIa).

The reaction of compound (Ib) with an excess of norbornene was carried out in ether at room temperature, analogous to the synthesis of compound (IIIa) described previously in [2]. Monitoring the reaction by TLC showed that compound (Ib)

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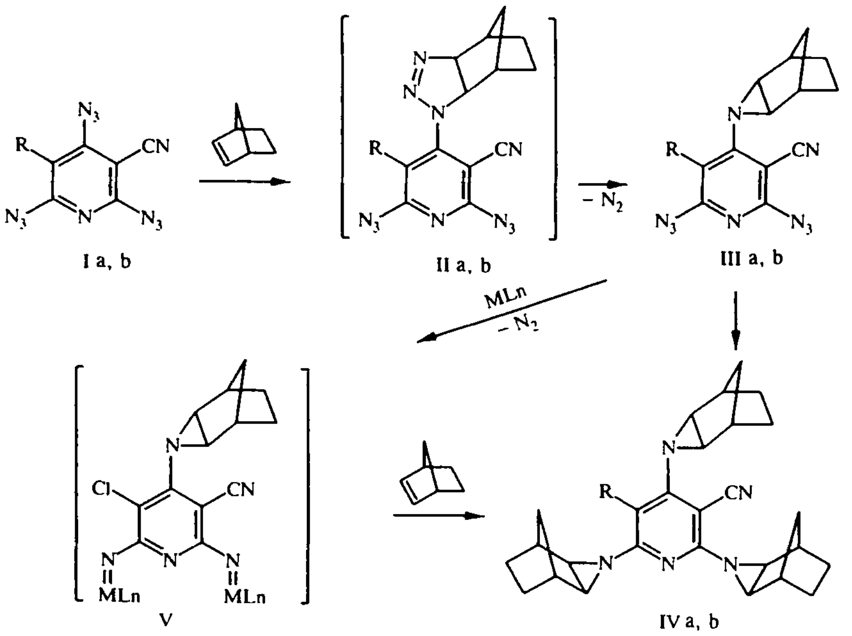
had undergone complete conversion after only 10 min from the start of the reaction, forming the tris adduct (IVb) as sole product in 92% yield.



I-IV a R = Cl, b R = CN

The composition and structure of compound (IVb) were in complete agreement with the data of elemental analysis, and of IR, PMR, and $^{13}C$ NMR spectroscopy. Since the cycloaddition of a molecule of norbornene at an azide group of (Ib) is theoretically capable of forming exo and endo conformers [the stereoselectivity of these reactions may be different for the various azide groups of (Ib)], consideration of the PMR spectrum of compound (IVb) deserves particular attention. Analysis of this spectrum showed that the addition of a molecule of norbornene at all three azide groups of compound (Ib) leads to the formation of aliphatic fragments each of which has the most favored exo conformation. Only four singlets of twelve protons were present in the PMR spectrum of compound (IVb) at 2.56-2.78 ppm. Two of these had double intensity and belong to the protons in the bridgehead of the aliphatic fragments (2.56 ppm) and the aziridine rings (2.68 ppm) assigned to the substituents in the $\alpha$ positions of the pyridine ring. The protons in the bridgehead of the aliphatic fragment and the aziridine ring for a $\gamma$ substituent are displayed as two other singlets at 2.64 and 2.78 ppm respectively. These data indicate conclusively the absence of coupling between the protons in the bridgehead of the aliphatic fragments and the aziridine rings of all three 3-azatricyclo[3.2.1.0]octane substituents in cycloadduct (IVb). The PMR spectrum of compound (IVb) also exposes significant differences in the signals of the 8-$H_{exo}$ bridge protons for its $\alpha$ and $\gamma$ azatricyclooctane substituents. Thus the signals for protons of this type for two substituents in the $\alpha$-positions of the pyridine ring are displayed as a doublet at 1.37 ppm with coupling constant $J = 10$ Hz. A similar picture was observed previously in the PMR spectra of other cycloadducts obtained in reactions of $\alpha$-monoazidopyridines with norbornene [4]. On the other hand the signal of the 8-$H_{exo}$ proton of the $\gamma$-substituent of compound (IVb) was displaced markedly towards high field and overlapped the signals of the 6- and 7-$H_{ax}$ protons of the $\alpha$ and $\gamma$ substituents, which gave a multiplet at 1.18 ppm. The same regularity was observed for the 8-$H_{exo}$ proton signal in the PMR spectrum of cycloadduct (IIIa) [1, 2]. This comparison shows that the position of the azatricyclooctane substituents in pyridines may be reliably identified by PMR from the position of the signals characteristic of the 8-$H_{exo}$ protons. It is evident from the $^{13}C$ NMR spectrum of compound (IVb) that the carbon atoms of $CH_2$ groups remote from the pyridine ring of all three aliphatic substituents are equivalent and are displayed as two signals at 25.44 ($CH_2-CH_2$) and 28.56 ppm ($CH-CH_2$). The effect of the pyridine ring proved to be only on the position of the signals of the bridgehead and aziridine ring carbon atoms of the aliphatic substituents of compound (IVb). The signals of the $\gamma$ substituent are displaced towards low field and were recorded at 36.63 and 42.39 ppm respectively. This is linked to the strong conjugation of this substituent with the pyridine ring of compound (IVb) [5]. The signals of the analogous carbon atoms of the $\alpha$ substituents have significantly higher intensity and are observed at 35.92 and 42.19 ppm respectively. The $C_{(2)}$, $C_{(3)}$, and $C_{(4)}$ carbon atoms of the pyridine ring of cycloadduct (IVb) give signals at 167.17, 83.40, and 164.35 ppm and the carbon atoms of the cyano groups give one signal at 114.09 ppm.

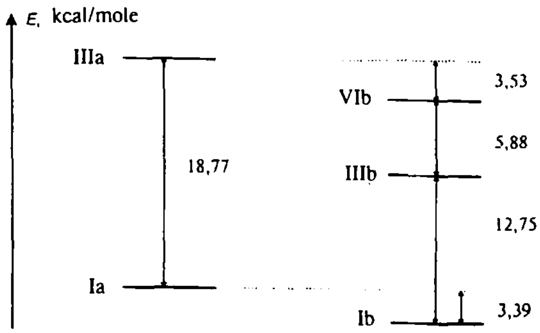


Fig. 1. Diagram of the energy levels of the LUMO of azidopyridines (Ia, b), (IIIa, b), and (VIa, b).

The formation of the tris adduct (IVb) in the reaction of compound (Ib) with an excess of norbornene indicates that, unlike (IIIa), the cycloadduct (IIIb) formed as an intermediate possesses significantly higher reactivity towards norbornene and readily adds it at room temperature at the azide groups in the $\alpha$ positions of the pyridine ring. However the problem of whether the initial pyridine (Ib) can interact regioselectively with norbornene at room temperature remains open. We therefore studied the reaction of compound (Ib) with an equimolar quantity of norbornene at room temperature.

The reaction of (Ib) with an equimolar quantity of norbornene was carried out by slowly adding an ether solution of the dipolarophile to a solution of the azide in ether. Even at 10 min after the addition of norbornene the initial substance (Ib) had disappeared completely from the reaction mixture forming compound (IIIb) in 86% yield.

As for compound (IIIa) [2], the IR spectrum of compound (IIIb) recorded the presence of two intense absorption bands at 2178 and 2128 $cm^{-1}$, belonging to the two azide groups, in addition to the absorption band at 2229 $cm^{-1}$ of the $C \equiv N$ group. As might have been expected, the cycloadduct (IIIa) has the most favored exo conformation. This follows from the absence of coupling of the bridgehead CH protons of the aliphatic fragment and the aziridine ring, which give two singlets in the PMR spectrum at 2.78 and 3.02 ppm respectively. The significant displacement of these signals towards low field indicates the very strong character of the conjugation of the azatricyclooctane substituent with the pyridine ring of cycloadduct (IIIb). As in the case of derivative (IIIa), the signal of the 8-$H_{exo}$ proton of compound (IIIb) overlaps with the signals of the 6- and 7-$H_{ax}$ protons, which give a multiplet at 1.22 ppm. The 8-$H_{exo}$ proton is displayed as a well resolved doublet at 0.97 ppm with coupling constant $J = 10.6$ Hz. In the $^{13}C$ NMR spectrum of compound (IIIb) there were signals for the pyridine ring carbon atoms at 159.97 ($C_{(2)}$), 85.40 ($C_{(3)}$), and 165.26 ppm ($C_{(4)}$), for the $C \equiv N$ group at 112.27 ppm, and four signals for the aliphatic fragment at 44.07 (NCH), 37.63 (CH), 29.33 ($CH-CH_2$), and 25.92 ppm ($CH_2-CH_2$). The presence of only three signals for the carbon atoms of the pyridine ring indicates conclusively that the addition of a molecule of norbornene to a molecule of (Ib) occurs regioselectively at the azide group at position 4 of the pyridine ring.

The regioselective synthesis of compound (IIIb) indicates that, in spite of the fairly high reactivity at room temperature of the $\alpha$-azide groups of pyridines (Ib) and (IIIb), the $\gamma$-azide group of the initial pyridine (Ib) is the strongest dipole when interacting with norbornene. As might have been expected, the reaction of cycloadduct (IIIb) with an excess of norbornene gave the trisadduct (IVb), the yield of which was 94%.

One of the main problems of the present work was the development of a method of synthesizing the trisadduct (IVa) by the reaction of diazidopyridine (IIIa) with norbornene. We therefore studied the reaction of compound (IIIa) with norbornene at various temperatures.

The reaction of compound (IIIa) with an excess of norbornene was carried out by boiling in $CCl_4$ solution. It turned out that under these conditions the diazide (IIIa) underwent complete conversion only after 48 h reaction giving the trisadduct (IVa) in 56% yield. A large number of polymeric products was also formed in the reaction in addition to the desired compound.

As in the case of trisadduct (IVb) all three aliphatic fragments of compound (IVa) had the more favored exo conformation indicated by the absence from the PMR spectrum of coupling between the bridgehead and aziridine CH protons of these fragments. Due to the absence of symmetry in the (IVa) molecule all the CH protons were nonequivalent and were displayed as six singlets at 2.43, 2.49, 2.52, 2.55, 2.56, and 2.63 ppm. By analogy with the PMR spectrum of compound (IVb) it may be suggested that the signal displaced most towards low field in this set corresponds to the protons of the aziridine ring at the $\gamma$ position of the pyridine ring of cycloadduct (IVa). The character of the disposition of the signals of the 8-$H_{exo}$ protons

TABLE 1. Energies of the HOMO and LUMO of Compounds (Ia, b), (IIIa, b), and (VIa, b) Calculated by the PM3 and RHF/3-21G* Methods

| Compound | HOMO, eV | | LUMO, eV | |
|---|---|---|---|---|
| | PM3 | 3-21G* | PM3 | 3-21G* |
| Ia | -9,077 [4] | -8,895 | -1,488 [4] | 1,287 |
| Ib | -9,661 [4] | -9,255 | -1,707 [4] | 1,140 |
| IIIa | -9,098 | -8,621 | -1,235 | 2,101 |
| IIIb | -9,546 | -8,955 | -1,494 | 1,693 |
| VIa | -9,022 | — | -0,977 | — |
| VIb | -9,349 | -8,833 | -1,306 | 1,948 |

TABLE 2. Charges on the Azide Group Atoms of Compounds (Ia, b), (IIIa, b), and (VIa, b) Calculated by the PM3 Method

| Compound | Group | Atom | | |
|---|---|---|---|---|
| | | $N_{(\alpha)}$ | $N_{(\beta)}$ | $N_{(\gamma)}$ |
| Ia | 2-$N_3$ | -0,42 | 0,75 | -0,28 |
| | 4-$N_3$ | -0,42 | 0,72 | -0,26 |
| | 6-$N_3$ | -0,43 | 0,75 | -0,28 |
| Ib | 2-$N_3$ | -0,41 | 0,75 | -0,27 |
| | 4-$N_3$ | -0,41 | 0,71 | -0,24 |
| | 6-$N_3$ | -0,42 | 0,75 | -0,26 |
| IIIa | 2-$N_3$ | -0,42 | 0,75 | -0,29 |
| | 6-$N_3$ | -0,42 | 0,75 | -0,29 |
| IIIb | 2-$N_3$ | -0,42 | 0,75 | -0,27 |
| | 6-$N_3$ | -0,42 | 0,75 | -0,27 |
| VIa | 6-$N_3$ | -0,43 | 0,76 | -0,29 |
| VIb | 6-$N_3$ | -0,42 | 0,76 | -0,28 |

TABLE 3. Coefficients of the AO for the Azide Group Atoms in LUMO of Compounds (IIIa, b) and (VIa, b) Calculated by the PM3 and STO-3G Methods

| Compound | Group | Atom | | | | | |
|---|---|---|---|---|---|---|---|
| | | $N_{(\alpha)}$ | | $N_{(\beta)}$ | | $N_{(\gamma)}$ | |
| | | PM3 | STO-3G | PM3 | STO-3G | PM3 | STO-3G |
| IIIa | 2-$N_3$ | 0,02 | -0,11 | 0,26 | 0,49 | -0,26 | -0,49 |
| | 6-$N_3$ | 0,00 | -0,01 | 0,10 | 0,27 | 0,10 | -0,26 |
| IIIb | 2-$N_3$ | -0,03 | -0,06 | -0,22 | -0,40 | 0,22 | 0,40 |
| | 6-$N_3$ | 0,03 | 0,06 | 0,22 | 0,40 | -0,22 | -0,40 |
| VIa | 6-$N_3$ | -0,01 | — | -0,22 | — | 0,22 | — |
| VIb | 6-$N_3$ | 0,03 | — | 0,26 | — | -0,26 | — |

in the PMR spectra of compounds (IVa, b) is also extremely complex, the only difference being that the protons of this type for substituents of the pyridine ring of (IVa) were not equivalent to one another and were displayed as a multiplet with center at 1.31 ppm. The main difference between the $^{13}C$ NMR of compounds (IVa) and (IVb), apart from the signals of the pyridine ring carbon atoms, was the nonequivalence of the carbon atoms of the bridgehead and aziridine rings for the α azatricyclooctane fragments of trisadduct (IVa), which were displayed together with the analogous atoms of the γ substituent as two groups of three signals at 36.68-37.25 and 42.73-43.87 ppm.

The low yield of compound (IVa) from the reaction of diazidopyridine (IIIa) with norbornene by boiling in $CCl_4$ solution indicates that an increase in temperature affects the course of the reaction significantly by initiating side reactions. However the analogous reaction at lower temperatures (45-60°C) and in other solvents led to a significant reduction in yield (< 20%) of cycloadduct (IVa) while at 40°C there was no reaction.

TABLE 4. Bond Lengths in the Azide Groups of Pyridines (Ia, b), (IIIa, b), and (VIa, b) Calculated by the PM3 and RHF/3-21G* Methods

| Compound | Group | Bond length (Å) | | | | | |
|---|---|---|---|---|---|---|---|
| | | C–N(α) | | N(α)–N(β) | | N(β)–N(γ) | |
| | | PM3 | 3-21G* | PM3 | 3-21G* | PM3 | 3-21G* |
| Ia | 2-$N_3$ | 1,4167 | 1,3928 | 1,2777 | 1,2896 | 1,1221 | 1,0975 |
| | 4-$N_3$ | 1,4152 | 1,3883 | 1,2773 | 1,2927 | 1,1228 | 1,0974 |
| | 6-$N_3$ | 1,4173 | 1,3941 | 1,2790 | 1,2880 | 1,1216 | 1,0974 |
| Ib | 2-$N_3$ | 1,4126 | 1,3872 | 1,2809 | 1,2928 | 1,1211 | 1,0963 |
| | 4-$N_3$ | 1,4111 | 1,3833 | 1,2807 | 1,2965 | 1,1218 | 1,0962 |
| | 6-$N_3$ | 1,4135 | 1,3882 | 1,2818 | 1,2937 | 1,1207 | 1,0960 |
| IIIa | 2-$N_3$ | 1,4181 | 1,3956 | 1,2772 | 1,2876 | 1,1222 | 1,0979 |
| | 6-$N_3$ | 1,4180 | 1,3962 | 1,2776 | 1,2859 | 1,1221 | 1,0981 |
| IIIb | 2-$N_3$ | 1,4146 | 1,3919 | 1,2802 | 1,2898 | 1,1212 | 1,0971 |
| | 6-$N_3$ | 1,4146 | 1,3919 | 1,2802 | 1,2898 | 1,1212 | 1,0971 |
| VIa | 6-$N_3$ | 1,4193 | — | 1,2774 | — | 1,1221 | — |
| VIb | 6-$N_3$ | 1,4159 | 1,3926 | 1,2799 | 1,2904 | 1,1214 | 1,0968 |

TABLE 5. Valence Angles (ω, deg) in the Azide Groups of Compounds (Ia, b), (IIIa, b), and (VIa, b) Calculated by the PM3 and RHF/3-21G* Methods

| Compound | Group | Parameter | | | |
|---|---|---|---|---|---|
| | | N–N–N | | C–N–N | |
| | | PM3 | 3-21G* | PM3 | 3-21G* |
| Ia | 2-$N_3$ | 169,67 | 171,77 | 122,04 | 113,07 |
| | 4-$N_3$ | 166,35 | 166,50 | 126,28 | 119,37 |
| | 6-$N_3$ | 169,70 | 172,22 | 122,04 | 113,41 |
| Ib | 2-$N_3$ | 169,68 | 171,76 | 122,27 | 113,43 |
| | 4-$N_3$ | 166,29 | 166,70 | 126,59 | 119,43 |
| | 6-$N_3$ | 169,70 | 171,94 | 122,15 | 113,31 |
| IIIa | 2-$N_3$ | 169,62 | 171,91 | 121,95 | 113,08 |
| | 6-$N_3$ | 169,66 | 172,25 | 122,09 | 113,47 |
| IIIb | 2-$N_3$ | 169,65 | 172,01 | 122,18 | 113,37 |
| | 6-$N_3$ | 169,65 | 172,01 | 122,18 | 113,47 |
| VIa | 6-$N_3$ | 169,47 | — | 121,83 | — |
| VIb | 6-$N_3$ | 169,49 | 172,24 | 121,91 | 113,09 |

With the aim of developing a more efficient synthesis of compound (IVa) we studied the reaction of diazidopyridine (IIIa) with norbornene at room temperature in the presence of the complex $Rh_2(OAc)_4$. We showed recently that this complex is able to decompose the highly stable diazadimedone readily at room temperature and the diketocarbenoid formed in this way displays high reactivity towards unsaturated compounds [6]. It might be expected that the rhodium tetraacetate complex would prove to be efficient for decomposing α-azide groups also. Analogous reactions involving palladium, copper, and several other metal complexes have been used more than once in azide chemistry [7].

The reaction of diazidopyridine (IIIa) with norbornene in the presence of $Rh_2(OAc)_4$ was carried out at room temperature in an atmosphere of nitrogen. Addition of the first portions of azide solution to the suspension of catalyst in ether was accompanied by a vigorous evolution of nitrogen gas from the reaction mixture and a change in its color from transparent to the color of the sea. Analysis of the reaction mixture showed that the sole reaction product was the trisadduct (IVa), the yield of which was 89%.

In addition to $Rh_2(OAc)_4$ the copper acetylacetonate complex is another widely used catalyst for decomposing diazoketones [8]. It seemed of interest to compare the catalytic activity of two of these complexes in the decomposition of diazidopyridine (IIIa). Study of the reaction of azide (IIIa) with norbornene at room temperature in the presence of $Cu(AcAc)_2$ showed that the use of this complex is also fairly effective and enabled the trisadduct (IVa) to be obtained in 76% yield. In addition, the lower yield of the desired product indicates that copper acetylacetonate is superseded somewhat by $Rh_2(OAc)_4$ in catalytic activity.

The high yield of compound (IVa) in the reactions of diazidopyridine (IIIa) with norbornene in the presence of the complexes $Rh_2(OAc)_4$ and $Cu(AcAc)_2$ shows that these traditional catalysts for decomposing diazoketones [8] may be of considerable interest for initiating reactions of weakly active azides with unsaturated compounds, particularly for the subsequent modification of the α-azide groups in 2,6-diazidopyridines. However, it is important to note that reactions of 2,6-diazidopyridines with olefins in the presence of metal complexes occurs by a mechanism completely different from the 1,3-dipolar cycloaddition reaction and excludes the stagewise addition of olefin molecules. It was shown in [9, 10] that in the presence of metal complexes the azide group undergoes rapid decomposition with the elimination of a molecule of nitrogen and the formation of a very reactive metal-bound nitrene of general formula (V). Such a nitrene reacts readily with an unsaturated bond by a type of [2+2]-cycloaddition and in the absence of olefin in the reaction mixture undergoes various conversions depending on its structure and the properties of the surrounding medium [7, 9, 10]. On the other hand in the absence of metal the azides react with olefins as 1,3 dipoles [3+2]-cycloaddition) giving as a rule a five-membered cycloadduct [11]. The formation of aziridine cycloadducts (IIIa, b) and (IVa, b) in the reaction of (Ia, b) with norbornene is determined by the exceptionally general instability of triazoline rings linked with the electron-accepting nature of the pyridine ring [intermediates (IIa, b)] [11, 12]. Since thermolysis of aromatic azides occurs at temperatures not less than 100°C [11], it may be affirmed that the reaction of compound (IIIa) with norbornene on boiling in $CCl_4$ solution also has a [3+2]-cycloaddition mechanism.

A quantum chemical study of the geometry and electronic properties of azidopyridines (Ia, b), (IIIa, b), and (VIa, b) {(VIa, b) are the bisadducts of structure 2,4-bis(3-azatricyclo[3.2.1.0]oct-3-yl)-6-azido-3-chloro-5-cyano (or 3,5-dicyano) pyridine} has been carried out with the purpose of clarifying the rules for the selective addition of norbornene at the azide group of compounds (Ia, b). Methods used were the semiempirical PM3 calculation [13] included in the Spartan set of programs [14] and nonempirical calculations based on STO-3G and 3-21G* carried out with the aid of the GAMESS program [15] on a DEC Alpha 3000/600 computer. The molecular structures of compounds were calculated with full optimization of the geometric parameters. The use of the PM3 method enabled a comparative analysis to be carried out on the characteristics of compounds (IIIa, b) and (VIa, b) and the analogous characteristics of the cycloadducts formed in the reaction of azidopyridines (Ia, b) with t-butylphosphaacetylene [16]. The STO-3G nonempirical calculations describe precisely the contribution of the atomic orbitals of the azide group to the LUMO of the pyridines [16]. The nonempirical calculation using 3-21G* was chosen since the use of 6-312G, 6-31G*, and 6-31G** leads to significant deviations between the values calculated and those obtained experimentally for the molecular characteristics of organic azides [17]. The calculated data are given in Fig. 1 and in Tables 1-5.

According to the calculations by the PM3 and 3-21G* methods the molecules of cycloadducts (IIIa, b) are characterized by absolutely identical orientations of the azatricycloactane fragments relative to the plane of the pyridine ring with a line of symmetry passing through the pyridine ring nitrogen atom and along the $C_{(4)}-N$ bond. It follows from this that the different reactivity of diazidopyridines (IIIa) and (IIIb) towards norbornene is determined exclusively by the specific electronic effects in the given molecules. Both aziridine substituents in the molecules of bisadducts (VIa) and (VIb) have the same spatial orientation as the aziridine substituents in the molecules of the monoadducts (Ia, b) but are arranged relative to one another at an angle of 180°. It is interesting that owing to the weak electron-accepting character of the pyridine ring the barrier for rotation of the aliphatic substituents in the molecules of the trisadducts (IVa, b) does not exceed 40 kcal/mole. The rotational isomers of compounds (IVa, b) have the least energy. Their α substituents look at a different side of the plane of the pyridine ring.

From an analysis of the HOMO and LUMO energy characteristics of azidopyridines (Ia, b), (IIIa, b), and (VIa, b) (Table 1) it is seen that the sequential addition of norbornene molecules at an azide group of (Ia, b) leads to the formation of cycloadducts having higher values of the HOMO and LUMO energies, and the change in the latter is displayed to a greater extent. Such a rule is often observed in those cases when the electron-donating properties of substituents in azide molecules are strengthened [18]. It is evident that the increase in HOMO and LUMO energies in the series of compounds (Ia, b), (IIIa, b), and (VIa, b) is caused by the increase in the number of aziridine substituents in their pyridine rings. Calculation of the HOMO and LUMO energy values for norbornene using PM3 shows that these characteristics are −9.783 and +1.086 eV respectively, which is not in bad agreement with the experimental data on the measurement of the ionization potential of norbornene (−8.97 eV [19]). The smaller difference in energy values of the LUMO of azides (Ia, b), (IIIa, b), and (VIa, b) and of the HOMO of norbornene compared with the difference in the HOMO energies of the azides and the LUMO energy of norbornene indicates that the addition of norbornene at the azide group of pyridines (Ia, b), (IIIa, b), and (VIa, b) belongs to a type of dipole – LUMO controlled reaction [18]. The ease of carrying out such type of cycloaddition reaction is determined by the properties of the LUMO of the dipole. Consequently further analysis of the reactivity of azides (Ia, b), (IIIa, b), and (VIa, b) was based on a comparison of the LUMO energy values of these compounds. Since the nonempirical calculation using 3-21G$^*$ enables the properties of the azides to be described with a higher precision than with the PM3 semiempirical method of calculation [17], a comparative analysis of the LUMO energies of the azidopyridines (Ia, b), (IIIa, b), and (VIa, b) was carried out using calculations by the 3-21G$^*$ method.

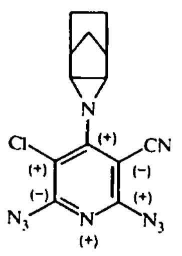
The diagram of the LUMO energy levels of compounds (Ia, b), (IIIa, b), and (VIa, b) given in Fig. 1 enables a quantitative estimate to be made of the change in the LUMO energies of azides arising from the sequential addition of norbornene molecules at the azide groups of (Ia, b). It is evident from the data in Fig. 1 that the addition of one molecule of norbornene at the $\gamma$ azide group of (Ia) leads to the formation of cycloadduct (IIIa), the LUMO energy of which is 18.77 kcal/mole greater than for the initial azide. Somewhat different regularities were observed in the series of compounds (Ib), (IIIb), and (VIb). The addition of one molecule of norbornene at the $\gamma$ azide group of pyridine (Ib) leads to the formation of cycloadduct (IIIb), the LUMO energy of which is 12.75 kcal/mole greater than that of the initial compound and 9.41 kcal/mole less than the LUMO energy of derivative (IIIa). These data suggest that the strongly differing reactivities of (IIIa) and (IIIb) towards norbornene are caused mainly by the significant difference in the energies of their LUMO. It is also evident from Fig. 1 that the addition of norbornene at one of the azide groups of pyridine (IIIb) leads to the formation of the cycloadduct (VIb), the LUMO energy of which is 3.53 kcal/mole less than that of (IIIa). It is interesting that approximately the same difference in LUMO energy values (3.39 kcal/mole) was also observed for the initial molecules (Ia, b), which reacted with norbornene at room temperature significantly differently [1, 2]. Thus the reaction with pyridine (Ia) took place smoothly after a certain time [2] and the reaction of derivative (IIIb) with norbornene occurred within seconds and was accompanied by a considerable evolution of heat. In view of these data it may be assumed that the difference in LUMO energy values of the azidopyridines (IIIa) and (VIb) of the order of 3.5 kcal/mole reflects quite adequately the significant difference in reactivity of these compounds. It is important to note that the LUMO energy of the azide is not by far the only factor determining the reactivity of this class of compound [10]. Factors of no less importance in this series are the electronic properties of the azide groups themselves and also their geometry [16]. Consequently the difference in LUMO energies of compounds (IIIa) and (VIb) may be considered as only one of the reasons for the higher reactivity of the bisadduct (VIb) compared to the monoadduct (IIIa).

Calculated data on the charge distribution, the contribution of the AO to the LUMO, and the geometric parameters of the azide groups of pyridines (Ia, b), (IIIa, b), and (VIa, b) are given in Tables 2-4.

By comparing the sizes of the charges on the azide group atoms of compounds (Ia, b), (IIIa, b), and (VIa, b) it is seen that the electron-donating influence of the aziridine rings on the azide group atoms of the pyridines (IIIa, b) and (VIa, b) is expressed weakly and is displayed only as a small (0.01) increase of the negative charge on the $N_{(\gamma)}$ atoms in the cycloadducts (IIIa, b) compared with the initial molecules (Ia, b). Comparison of the charges on the $N_{(\gamma)}$ atoms in the azide groups of compounds (IIIb), (VIb), and (IIIa) shows that these characteristics for the reactive azides (IIIb) and (VIb) are 0.02 in absolute value lower than for the chloropyridine (IIIa). Precisely the same difference in the charges on the $N_{(\gamma)}$ atoms was observed for the $\alpha$ and $\gamma$ azide groups of pyridines (Ia, b) (Table 2), characterizing the strongly different reactivity towards the dipolarophile [1, 2, 16]. It is evident from these comparisons that one of the reasons for the higher reactivity of azidopyridines (IIIb) and (VIb) compared to (IIIa) is the increased electrophilicity of the terminal nitrogen atoms in the azide groups of compounds (IIIb) and (VIb) at which the initial attack of the dipolarophile occurs [16, 21].

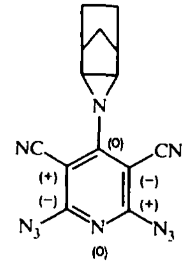
The data of Table 3 enable comparison of the AO coefficients of the azide groups with the LUMO of compounds (IIIa, b) and (VIa, b). Similar characteristics were given in [16] for the azide groups in the initial molecules (Ia, b). As is evident from the data of Table 3 the highest contribution of the AO of the $N_{(\beta)}$ and $N_{(\gamma)}$ atoms to the LUMO is found in the molecule of chloropyridine (IIIa) (0.49 and $-0.49$ respectively for the azide group at position 2 of the pyridine ring). At the same time this azide is less reactive towards norbornene compared with (IIIb) and (VIb) [1-3]. It may be concluded from these data that the contribution of the azide group AO to the LUMO of the pyridines does not show a marked effect on the reactivity of the azides and only controls the stereoselectivity and stereospecificity of their cycloaddition to the dipolarophile [16, 18]. The higher contribution of the AO to the LUMO for the azide group in position 2 of the pyridine ring in (IIIa) suggests that diazidopyridine (IIIa) must add a molecule of norbornene at precisely this group, forming bisadduct (VIa) as an intermediate compound.

The principal difference in the electronic properties of cycloadducts (IIIa, b) is the different symmetry of their LUMO. In the case of cycloadduct (IIIb) the LUMO has a nodal plane passing through the N atoms and $C_{(4)}$ of the pyridine ring, while the LUMO of derivative (IIIa) is characterized by a large number of antibonding interactions between the AO of the pyridine ring.



IIIa

$\Psi_{LUMO} = 0{,}15\ C_1 - 0{,}45\ C_2 + 0{,}27\ C_3 +$
$+ 0{,}22\ C_4 - 0{,}40\ C_5 + 0{,}27\ C_6 + M$

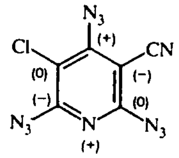


IIIb

$\Psi LUMO = -0{,}41(C_2 - C_6) +$
$+ 0{,}34\ (C_3 - C_5) + M$

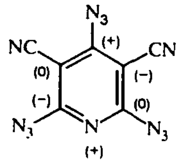
The molecules of the initial pyridines (Ia, b) are characterized by the same symmetry of the LUMO which has a nodal plane passing through the $C_{(3)}$ and $C_{(6)}$ atoms of the pyridine ring. It may be assumed that the different character of the increase in energy of the LUMO of the pyridines as a result of adding a molecule of norbornene at the $\gamma$ azide group of (Ia, b) is caused by the different symmetry of the LUMO of the resulting cycloadducts (IIIa, b). The lower difference in LUMO energies of azidopyridines (Ib) and (IIIb) indicates that the symmetrical molecules of the norbornene adducts with the triazides are characterized by lower values of the LUMO energies.

It is evident from a comparison of the bond lengths of compounds (Ia, b), (IIIa, b), and (VIa, b) (Table 4) that elongation of the $C-N_{(\alpha)}$ and $N_{(\beta)}-N_{(\gamma)}$ bonds and shortening of the $N_{(\alpha)}-N_{(\beta)}$ bond, depending on the electron-donating properties of the substituents in the pyridine ring, is a general tendency for all the azidopyridines. Such a change of character of bond lengths in the azide groups indicates a reduction in reactivity towards dipolarophiles in the compounds (Ia, b), (IIIa, b), and (VIa, b) [12, 13]. The lengthened $C-N_{(\alpha)}$ bond and the shortened $N_{(\alpha)}-N_{(\beta)}$ bond in the azide groups of (IIIa) compared with (IIIb) and (VIb) show that the lower reactivity of compound (IIIa) towards norbornene is partially caused by the weak conjugation of its azide groups with the pyridine ring.



Ia

$\Psi\ LUMO = 0{,}31\ C_1 - 0{,}39\ C_2 +$
$+ 0{,}41\ C_4 - 0{,}36\ C_5 + P$



Ib

$\Psi\ LUMO = 0{,}30\ C_1 - 0{,}39\ C_2 + 0{,}39\ C_4 +$
$+ 0{,}36\ C_5 + Q$

Analysis of the size of the $N-N-N$ and $C-N-N$ valence angles in pyridines (Ia, b), (IIIa, b), and (VIa, b) (Table 5) did not reveal any significant differences for the azide groups of cycloadducts (IIIa), (IIIb), and (VIb) to characterize the different reactivity towards norbornene. It may only be stated that the $N-N-N$ angle is increased and the $C-N-N$ angle is reduced when the electron-donating properties of the substituent in the pyridine ring are strengthened, indicating a reduction in reactivity towards norbornene in the series (Ia, b), (IIIa, b), and (VIa, b) [16, 22, 23].

The data of calculations of the $C-N-N$ and $N-N-N$ valence angles in (Ia, b) using 3-21G* deserve special consideration (Table 5). It has been shown using the PM3 method of calculation that the exceptionally high reactivity of the $\gamma$ azide group in (Ia, b) towards the dipolarophile was caused mainly by the strong curvature of the $N-N-N$ chain of atoms and the high values of the $C-N-N$ valence angles [16]. It is seen from the data of Table 5 that the $N-N-N$ and $C-N-N$ valence angles differ more significantly for the $\alpha$ and $\gamma$ azide groups of (Ia, b) than from the calculation using 3-21G*. The $C-N-N$ and $N-N-N$ angles in compounds (Ia, b), (IIIa, b), and (VIa, b) calculated by this method are in good agreement with x-ray crystallographic data for the p-nitrophenyl azide molecule (115.0 and 173.40° respectively [24]).

By correlating the results of the comparative analysis of the electronic properties and geometric parameters of compounds (Ia, b), (IIIa, b), and (VIa, b) it may be concluded that the different character of the course of the reactions of (Ia, b) with norbornene is caused not only by the different electronic properties of their $\beta$ substituents but also by the different symmetry of the LUMO of the cycloadducts formed. Triazidopyridines which contain identical substituents in the $\beta$ positions of the pyridine ring are less inclined to stop reacting at the stage of adding one molecule of norbornene.

## EXPERIMENTAL

The IR spectra were obtained on a Specord M 80 instrument, and the PMR spectra on a Bruker AC 200 (200 MHz) instrument using TMS as internal standard. The $^{13}$C NMR spectra were recorded on a Bruker AM 400 (100.6 MHz) instrument. The monitoring of reactions was effected by TLC on Silufol UV 254 plates. The complexes $Rh_2(OAc)_4$ and $Cu(AcAc)_2$ used were from Aldrich.

Methods for obtaining (Ia), (Ib), and (IIIa) have been described in [2, 3].

**4-(3-Azatricyclo[3.2.1.0]oct-3-yl)-2,6-diazido-3,5-dicyanopyridine (IIIb).** A solution of norbornene (0.094 g, 1 mmole) in dry diethyl ether (300 ml) was added dropwise to a stirred solution of compound (Ib) (0.252 g, 1 mmole) in dry diethyl ether (100 ml). The reaction mixture was stirred for a further 0.5 h. The solvent was distilled off under vacuum, and the white crystalline residue recrystallized from a hexane–benzene mixture. After drying, compound (IIIb) (0.274 g, 86%) was obtained having mp > 260°C. IR spectrum, 2229 (C≡N); 2172, 2128 cm$^{-1}$ ($N_3$). PMR spectrum ($CDCl_3$): 0.94 (1H, d, J = 11.6 Hz, 8-$H_{endo}$); 1.25 (3H, m, 8-$H_{exo}$, 6- and 7-$H_{ax}$); 1.56 (2H, m, 6- and 7-$H_{eq}$); 2.72 (2H, s, $H_{br}$); 2.99 (2H, s, NCH). $^{13}$C NMR spectrum ($CDCl_3$): 25.92 ($CH_2-CH_2$); 29.33 ($CH-CH_2$); 37.63 (CH); 44.07 (NCH); 85.40 ($C_{(3,5)}$); 112.47 (C≡N); 159.97 ($C_{(2,6)}$); 165.26 ($C_{(4)}$). Found, %: C 52.95; H 3.21; N 43.85. $C_{14}H_{10}N_{10}$. Calculated, %: C 52.82; H 3.17; N 44.00.

**2,4,6-Tris(3-azatricyclo[3.2.1.0]oct-3-yl)-3,3-dicyanopyridine (IVb).** A solution of norbornene (0.376 g, 4 mmole) in dry diethyl ether (100 ml) was added dropwise to a stirred solution of compound (Ib) (0.252 g, 1 mmole) in dry diethyl ether (100 ml) at room temperature. The reaction mixture was stirred for a further 0.5 h. The solvent was distilled off under vacuum, and the white crystalline residue recrystallized from a hexane–benzene mixture. After drying, compound (IVb) (0.414 g, 92%) was obtained having mp 251-253°C. IR spectrum: 2216 (C≡N). PMR spectrum ($CDCl_3$): 0.81 (3H, m, 8-$H_{endo}$); 1.18 (7H, m, 8-$H_{exo}$, 6- and 7-$H_{ax}$); 1.37 (2H, d, J = 10 Hz, 8-$H_{exo}$); 1.43 (6H, m, 6- and 7-$H_{eq}$); 2.56 (4H, s, $\alpha$-$H_{br}$); 2.64 (2H, s, $\gamma$-$H_{br}$); 2.68 (4H, s, $\alpha$-NCH); 2.78 (2H, s, $\gamma$-NCH). $^{13}$C NMR spectrum ($CDCl_3$): 25.44 ($CH_2-CH_2$); 28.56 ($CH-CH_2$); 35.92 ($\alpha$-CH); 36.63 ($\gamma$-CH); 42.19 ($\alpha$-NCH); 42.39 ($\gamma$-NCH); 83.40 ($C_{(3,5)}$); 114.09 (C≡N); 164.35 ($C_{(4)}$); 167.17 ($C_{(2,6)}$). Found, %: C 74.85; H 6.63; N 18.52. $C_{28}H_{30}N_6$. Calculated, %: C 74.63; H 6.71; N 18.65.

**2,4,6-Tris(3-azatricyclo[3.2.1.0]oct-3-yl)-3-chloro-5-cyanopyridine (IVa). A.** A mixture of compound (IIa) (0.328 g, 1 mmole) and norbornene (0.376 g, 4 mmole) in $CCl_4$ (200 ml) was boiled for 48 h, after which the solvent was distilled off in vacuum. The yellow crystalline residue was recrystallized from a hexane–benzene mixture. After drying, compound (IVa) (0.257 g, 56%) was obtained having mp 131-132°C. IR spectrum: 2212 (C≡N). PMR spectrum ($CDCl_3$): 0.74 (3H, m, 8-$H_{endo}$); 1.10 (7H, m, 8-$H_{exo}$, 6- and 7-$H_{ax}$); 1.31 (2H, m, $H_{exo}$); 1.37 (6H, m, 6- and 7-$H_{eq}$); 2.43 (2H, s, $\alpha$-$H_{br}$); 2.49 (2H, s, $\alpha$-$H_{br}$); 2.52 (2H, s, $\gamma$-$H_{br}$); 2.55 (2H, s, $\alpha$-NCH); 2.56 (2H, s, $\alpha$-NCH); 2.63 (2H, s, $\gamma$-NCH). $^{13}$C NMR spectrum ($CDCl_3$): 26.56 ($CH_2-CH_2$); 29.33 ($CH-CH_2$); 36.68 ($\alpha$-CH); 36.75 ($\alpha$-CH); 37.25 ($\gamma$-CH); 42.73 ($\alpha$-NCH); 43.14 ($\alpha$-NCH); 43.37 ($\gamma$-CH); 87.09 ($C_{(3)}$); 106.71 ($C_{(5)}$); 115.71 (C≡N); 158.82 ($C_{(4)}$); 162.04 ($C_{(6)}$); 164.62 ($C_{(2)}$). Found, %: C 70.65; H 6.63; N 15.12. $C_{27}H_{30}N_5Cl$. Calculated, %: C 70.49; H 6.57; N 15.23.

**B.** A solution of compound (IIIa) (0.328 g, 1 mmole) in dry diethyl ether (100 ml) was added dropwise at room temperature in an atmosphere of nitrogen to a stirred solution of norbornene (0.376 g, 4 mmole) and rhodium(II) acetate (0.013 g, 0.03 mmole) in dry diethyl ether (100 ml). The reaction mixture was then stirred for a further 30 min. The solvent was distilled off under vacuum, and the residue chromatographed on a column of silica gel using a hexane–benzene, 2:1 mixture as eluent. Compound (IVa) (0.409 g, 89%) was obtained after recrystallization and drying.

**C.** A solution of compound (IIIa) (0.328 g, 1 mmole) in dry diethyl ether (100 ml) was added dropwise at room temperature in an atmosphere of nitrogen to a stirred solution of norbornene (0.376 g, 4 mmole) and copper(II) acetylacetonate (0.016 g, 0.06 mmole) in dry diethyl ether (100 ml). The reaction mixture was then stirred for a further 1 h. The solvent was distilled off under vacuum, and the residue chromatographed on a column of silica gel using a hexane–benzene, 2:1 mixture as eluent. Compound (IVa) (0.35 g, 76%) was obtained after recrystallization and drying.

## REFERENCES

1. S. V. Chapyshev and T. Ibata, Heterocycles, **36**, 2185 (1993).
2. S. V. Chapyshev, Khim. Geterotsikl. Soedin., No. 12, 1650 (1993).
3. S. V. Chapyshev, U. Bergstrasser, and M. Regitz, Khim. Geterotsikl. Soedin., No. 1, 67 (1996).
4. S. V. Chapyshev and N. V. Chapysheva, Khim. Geterotsikl. Soedin., No. 5, 666 (1994).
5. S. V. Chapyshev and T. Ibata, Izv. Akad. Nauk, Ser. Khim., No. 11, 2702 (1996).
6. S. V. Chapyshev and T. Ibata, Izv. Akad. Nauk, Ser. Khim., No. 2, 491 (1996).
7. E. F. V. Scriven and K. Turnbull, Chem. Rev., **88**, 297 (1988).
8. A. Padwa and S. F. Hornbuckle, Chem. Rev., **91**, 263 (1991).
9. H. Takeuchi, Y. Shiobara, M. Mitani, and K. Koyama, J. Chem. Soc., Chem. Commun., No. 11, 1251 (1985).
10. H. Takeuchi, K. Koyama, M. Mitani, R. Ihara, T. Uno, Y. Okazaki, Y. Kai, and N. Kasai, J. Chem. Soc., Perkin Trans. I, No. 3, 677 (1985).
11. G. L'Abbe, Chem. Rev., **69**, 345 (1969).
12. I. R. A. Bernard, G. E. Chivers, R. J. W. Cremlyn, and K. G. Mootoosamy, Aust. J. Chem., **27**, 171 (1974).
13. J. J. P. Stewart, J. Comput. Chem., **10**, 209 (1989).
14. Spartan version 4.0, Wavefunction Inc., 18401 Van Karman Ave., #370 Irvine, CA 92715, USA (1995).
15. M. W. Schmidt, K. K. Baldridge, J. A. Boatz, S. T. Elbert, M. S. Gordon, J. H. Jensen, S. Koseki, N. Matsunaga, K. A. Nguyen, S. J. Su, T. L. Windus, M. Dupius, and J. A. Montgomery, J. Comput. Chem., **14**, 1347 (1993).
16. S. V. Chapyshev and V. M. Anisimov, Khim. Geterotsikl. Soedin., No. 5, 676 (1997).
17. M. L. Costa, B. J. Costa Cabral, M. A. Almoster Ferreira, J. Mol. Struct., **249**, 181 (1991).
18. A. Padwa (ed.), 1,3-Dipolar Cycloaddition Chemistry, Wiley, New York (1984), p. 559.
19. P. Bischof, Helv. Chim. Acta, **53**, 1677 (1970).
20. K. N. Houk, J. Sims, C. Watts, and L. Luskus, J. Am. Chem. Soc., **95**, 7301 (1973).
21. R. Sustmann, W. Sicking, and H. Quast, J. Comput. Chem., **13**, 314 (1992).
22. M. Tsuda, S. Oikawa, and K. Nagayama, Photogr. Sci. and Eng., **27**, 118 (1983).
23. S. Gronowitz and P. Zanirato, J. Chem. Soc., Perkin Trans. II, No. 8, 1815 (1994).
24. A. Mugnoli, C. Mariani, and M. Simonetta, Acta Crystallogr., **19**, 367 (1965).