Chemistry of Heterocyclic Compounds, Vol. 39, No. 1, 2003

SELECTIVE THERMOLYSIS OF AZIDE GROUPS IN 2,4,6-TRIAZIDOPYRIDINES

S. V. Chapyshev

When refluxed in 1,4-dichlorobenzene, the compound 2,4,6-triazido-3,5-dichloropyridine and its 3,5-dicyano derivative undergo selective thermolysis of the γ-azide groups, forming the corresponding 4-amino-2,6-diazidopyridines in high yields. According to quantum-chemical calculations, the selectivity of thermolysis of the γ-azide groups in triazides is due to the weaker bonding interactions between the $N_{(\alpha)}$ and $N_{(\beta)}$ atoms in these azide groups.

Keywords: azidopyridines, aminopyridines, orbital control, selective thermolysis.

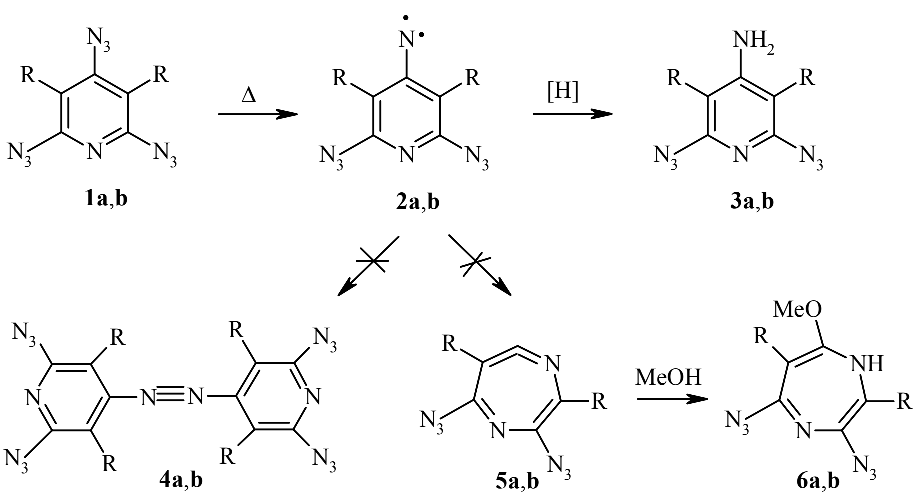
This paper is a continuation of systematic investigations to identify rules for selective chemical reactions at nonequivalent azide groups of heterocyclic polyazides [1-8].

It was shown previously that α- and γ-azide groups of pyridines **1a,b** are characterized by non-identified electron density distributions in the HOMO [highest occupied molecular orbital] and LUMO [lowest unoccupied molecular orbital] and consequently react selectively in 1,3-dipolar cycloaddition with electron-rich [1-3] and electron-deficient [2, 4] dipolarophiles, in nucleophilic addition at the terminal atoms of azide groups [5], and also in photolytic decomposition on exposure to light [6, 7]. The study of selective thermolysis of azide groups of pyridines **1a,b** was of no less interest for developing new methods for obtaining various pyridine derivatives. The low bonding orbital density on the $N_{(\alpha)}$ and $N_{(\beta)}$ atoms in the γ-azide groups of these compounds (Fig. 1) provided a basis for assuming that these groups specifically should be the most unstable toward heat treatment. These conclusions were also confirmed by the results of studies of thermolysis of triazides **1a,b** by chromato-mass spectrometry [8]. However, the prospects for using such selective reactions for preparative synthesis of new compounds remained undetermined.

With the aim of developing new preparative methods for obtaining polyfunctional pyridines, in this work we studied thermolysis of triazides **1a,b** in 1,4-dichlorobenzene.

Thermolysis of triazides **1a,b** was carried out at a temperature of 155-160°C, observing the course of the reaction by TLC. Although thermal decomposition of compounds **1a,b** at the given temperature occurred rather slowly (80% conversion of the starting compounds was achieved after 12 h of thermolysis), such conditions were favorable for preferential formation of one new compound in each of the reactions, specifically the aminoazidopyridines **3a,b**.

Institute of Problems of Chemical Physics, Russian Academy of Sciences, Chernogolovka 142432, Moscow Region, Russia; e-mail: chap@icp.ac.ru. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 87-90, January, 2003. Original article submitted December 15, 2000.

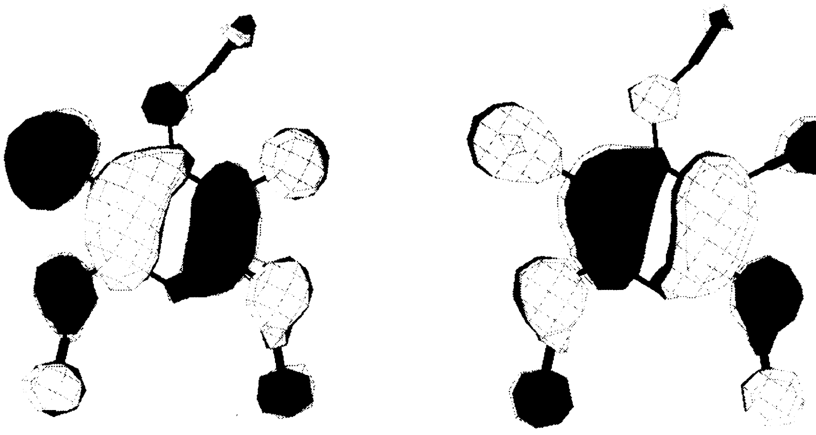


1–3 a R = Cl, **b** R = CN

The composition and structure of compounds **3a,b** completely correspond to elemental analysis as well as IR, ^{1}H NMR, and ^{13}C NMR spectroscopy data. Thus the presence in the IR spectra of compounds **3a,b** of two intense absorption bands at 3500-3350 cm^{-1} and 3400-3230 cm^{-1} (due to asymmetric and symmetric stretching vibrations of the N–H bonds of the primary amino groups) and also intense absorption bands at 1685-1630 cm^{-1} (due to bending vibrations of the N–H bonds) is convincing evidence for the presence of a primary amino group in the molecules of the compounds obtained. Furthermore, the presence in the IR spectra of compounds **3a,b** of two intense absorption bands for azide groups at 2172-2158 and 2143 cm^{-1} that are typical for many 2,6-diazidopyridines [9] indicates the presence of two azide groups in the 2 and 6 positions of the pyridine ring of compounds **3a,b**. The latter also is confirmed by ^{13}C NMR spectra, which has three signals at 100.0 ppm, 147.7 ppm, and 150.8 ppm for the carbon atoms of the pyridine ring in compound **3a** and three signals at 80.4 ppm, 160.6 ppm, and 161.0 ppm for the analogous atoms in compound **3b**.

The mechanism for thermal conversion of triazides **1a,b** to aminodiazides **3a,b** obviously includes intermediate formation of triplet nitrenes **2a,b**. It has been shown that specifically triplet nitrenes are the major primary products of thermolysis for most aromatic azides, which then dimerize to form the corresponding azo compounds, undergo intramolecular insertion of nitrenes into the aromatic ring, and also are converted to amines as a result of abstraction of a proton from the solvent [10-12]. The absence of diazo compounds of the type **4a,b** as thermolysis products of triazides **1a,b** shows that dimerization of triplet arylnitrenes is inefficient in the presence of two substituents *ortho* to the nitrene center in the aromatic ring. Steric hindrances on the side of the *ortho* substituents in molecules of compounds **2a,b** probably also make difficult the reaction of intramolecular insertion of nitrenes into the pyridine ring. Thus our previous study of the properties of polysubstituted triplet pyridyl nitrenes, isolated in cryogenic matrices, also did not observe isomerization of the given compounds to 1,4-diazaheptatetraenes of the type **5a,b** [13]. As a result, the major direction for further conversion of triplet nitrenes **2a,b** becomes abstraction of a proton from the solvent and formation of aminodiazides **3a,b**.

The rather high yield of aminodiazidopyridines **3a,b** upon thermolysis of triazidopyridines **1a,b** confirms that using selective thermal decomposition of nonequivalent azide groups in heterocyclic polyazides is a promising approach for preparative chemistry. Aminodiazidopyridines **3a,b** may be of considerable interest as starting compounds for synthesis of various polyfunctionally-substituted derivatives of pyridine, and also as the objects of photochemical studies. Thus the recently studied photolysis of 3-azatricyclooctane derivatives of compound **1b** that are substituted at the 4 position of the pyridine ring made it possible to obtain in high yield the corresponding quintet dinitrenes, which are a novel type of organic molecular magnets [14].



HOMO **1a** HOMO **1b**

Fig. 1. Orbital density distribution in HOMOs of pyridines **1a,b**.

EXPERIMENTAL

The IR spectra were obtained on a Perkin-Elmer FTIR-2000. The ^{1}H NMR spectra were recorded on a Bruker DPX-250 (250 MHz) using TMS as an internal standard; the ^{13}C NMR spectra were recorded on a Bruker DPX-250 (62 MHz). The reactions were monitored by TLC on Silufol UV-254 plates.

The geometry and electronic properties of compounds **1a,b** were calculated using the PM3 semiempirical method [15] included in the Spartan software package [16]. The molecular structures of the compounds were calculated with full optimization of the geometric parameters.

4-Amino-2,6-diazido-3,5-dichloropyridine (3a). A solution of compound **1a** (0.271 g, 1 mmol) in dry 1,4-dichlorobenzene (30 ml) was stirred at a temperature of 155-160°C for 12 h, after which it was cooled down to room temperature and poured into ice water (300 ml). The reaction product was extracted three times with portions (50 ml) of diethyl ether; ether was distilled off from the combined extract at reduced pressure, and the residue was chromatographed on a column with silica gel, using the system benzene–ethyl acetate 9:1 as the eluent. The product obtained was recrystallized from a benzene–ethyl acetate mixture. After drying, 0.142 g (58%) of compound **3a** was obtained; mp 170-171°C. IR spectrum, (microcrystalline film), ν, cm^{-1}: 3502 (ν_{as} NH), 3399 (ν_s NH), 2172 and 2143 (N_3), 1629 (δ_s NH), 1576 and 1544 (C=N, C=C), 1413, 1390, 1354, 1316, 1230, 1096, 1004, 828, 737, 678, 635, 540. ^{1}H NMR spectrum, (acetone-d_6), δ, ppm: 6.28 (2H, br. s, NH_2). ^{13}C NMR spectrum (acetone-d_6), δ, ppm: 100.0 ($C_{(3,5)}$); 147.7 ($C_{(2,6)}$); 150.8 ($C_{(4)}$). Found, %: C 24.68; H 0.93; N 45.62. $C_5H_2Cl_2N_8$. Calculated, %: C 24.51; H 0.82; N 45.73.

4-Amino-2,6-diazido-3,5-dicyanopyridine (3b). A solution of compound **1b** (0.252 g, 1 mmol) in dry 1,4-dichlorobenzene (50 ml) was stirred at a temperature of 155-160°C for 12 h, after which it was cooled down to room temperature and poured into ice water (300 ml). The reaction product was extracted with three portions (50 ml) of diethyl ether; the ether was distilled off from the combined extract at reduced pressure, and the residue was chromatographed on a column with silica gel, using the system benzene–ethyl acetate, 4:1, as the eluent. The product obtained was recrystallized from ethanol. After drying, 0.140 g (62%) of compound **3b** was obtained; mp 155-156°C. IR spectrum, (microcrystalline film), ν, cm^{-1}: 3352 (ν_{as} NH), 3232 (ν_s NH), 2234 (C≡N), 2158 and 2143 (N_3), 1683 (δ_s NH), 1588 and 15460 (C=N, C=C), 1411, 1321, 1233, 1199, 767, 665, 592, 544, 515, 492. ^{1}H NMR spectrum, (acetone-d_6), δ, ppm: 7.24 (2H, br. s, NH_2). ^{13}C NMR spectrum (acetone-d_6), δ, ppm: 80.4 ($C_{(3,5)}$); 113.0 (CN); 160.6 ($C_{(4)}$); 161.0 ($C_{(2,6)}$). Found, %: C 37.31; H 0.97; N 61.72. $C_7H_2N_{10}$. Calculated, %: C 37.19; H 0.85; N 61.96.

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