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SHORT COMMUNICATIONS

Alkylation of 3-Nitro-1,2,4-triazole with Allyl Bromide and Cyclohexa-1,3-diene in Acid Medium

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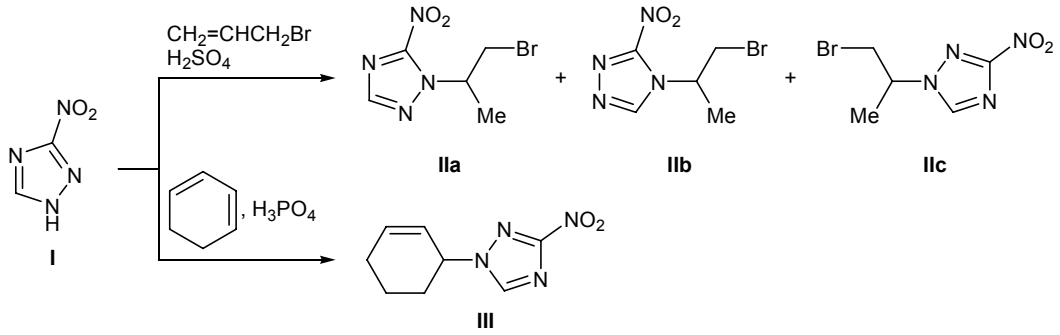
Nitro derivatives of 1,2,4-triazoles possess a combination of unique properties, such as high energy capacity but considerable heat resistance, biological activity, and complexing ability. Therefore, these compounds are promising from the viewpoint of their application in various fields of human activity, specialty devices, industry, agriculture (as fungicides and herbicides), biochemistry, and pharmacology [1]. Elaboration of methods for the synthesis of nitro-substituted 1,2,4-triazoles seems to be important for the development of the reactivity theory of heterocycles and procedures for regioselective functionalization of ambident compounds.

Up to now, alkylation of relatively accessible 5-substituted 3-nitro-1,2,4-triazoles has been studied in sufficient detail. The presence in their molecules of three potential reactions centers for attack by electrophilic reagents, one pyrrole- and two pyridine-type nitrogen atoms, implies that the alkylation may involve either of them. In fact, treatment of these compounds with alkyl halides, dialkyl sulfates [2–7], halocarboxylic acid esters [8, 9], chloroethanol, and oxirane [10] in basic or neutral medium often leads to formation of three isomeric N-substituted 3-nitro-1,2,4-triazoles.

Some advances were achieved in the alkylation of 5-R-3-nitro-1,2,4-triazoles with alcohols in acid medium. In particular, Saraev et al. [11] reported on their selective alkylation at N^1 with adamantan-1-ol and *tert*-butyl alcohol in sulfuric acid, whereas the alkylation with isopropyl alcohol afforded exclusively the corresponding N^2-derivative [12]. The observed regioselectivity may be interpreted in terms of weakly basic properties of triazoles which undergo protonation at the most basic nitrogen atom. Obviously, the nature of alkylating agent is also an important factor responsible for the reaction selectivity. Taking the above stated into account, it seemed reasonable to examine the behavior of nitro-substituted 1,2,4-triazoles in reactions with other alkylating agents, specifically with allyl bromide and cyclohexa-1,3-diene which were successfully used by us previously for N-functionalization of tetrazole ring [13, 14].

We found that the alkylation of 3-nitro-1*H*-1,2,4-triazole (**I**) with allyl bromide under conditions analogous to the alkylation of 5-R-tetrazoles (concentrated sulfuric acid, 7 days) [13] gave 65% of a mixture of isomeric *N*-alkyl derivatives with appreciable prevalence of 1-(1-bromopropan-2-yl)-5-nitro-1*H*-1,2,4-triazole (**IIa**). The ratio of regioisomers **IIa**, **IIb**, and **IIc** was estimated at 1 : 0.3 : 0.2 by the intensities of NMR signals from the CH proton in the triazole ring. Predominant formation of isomer **IIa** is likely to be determined by protonation of initial triazole **I** in sulfuric acid with formation of 3-nitro-1*H*-1,2,4-triazol-4-ium cation where only the N^2 atom is accessible to attack by the cation generated from allyl bromide. This mechanism was recently proposed to rationalize selective alkylation of triazole (**I**) with *tert*-butyl alcohol [12] and was based on the data for selective acid-catalyzed N^2-alkylation of tetrazoles as structural analogs of **I** [15]. Isomeric products **IIb** and **IIc** may be formed as a result of electrophilic attack on unprotonated 3-nitro-1,2,4-triazole species present in the reaction mixture at a small concentration.

Concentrated phosphoric acid turned out to be the most efficient medium for the alkylation of triazole **I** with cyclohexa-1,3-diene. Such acids as sulfuric and perchloric could not be used because of oligo- and



polymerization of the alkylating agent. The alkylation of **I** with cyclohexa-1,3-diene in phosphoric acid occurred at a fairly high rate (50–60 min) at room temperature, and 1-(cyclohex-2-en-1-yl)-3-nitro-1*H*-1,2,4-triazole was selectively formed in a good yield (60%). The product was assigned the structure of 1-substituted triazole on the basis of its ^{1}H and ^{13}C NMR spectra which were consistent with published data for analogous 1-substituted 3-nitro-1,2,4-triazoles [4–6].

The selective formation of compound **III** was surprising. It may be rationalized assuming isomerization of the initially formed N^2-derivative into the N^1-isomer in a way similar to the isomerization of 2-cyclohexenyltetrazole under analogous conditions [14]. The driving force of such isomerization is higher thermodynamic stability of 1-alkyl-3-nitro-1,2,4-triazoles compared to 2- and 4-alkyl derivatives [16].

Alkylation of 3-nitro-1*H*-1,2,4-triazole with allyl bromide. Allyl bromide, 1.3 g (0.011 mol), was added under stirring to a solution of 1.0 g (0.0088 mol) of 3-nitro-1*H*-1,2,4-triazole in 7 ml of 96% sulfuric acid. The mixture was stirred for 7 days at room temperature, poured onto ice, and extracted with methylene chloride (4×25 ml), the combined extracts were washed with 10 ml of water, 10 ml of 5% aqueous sodium carbonate, and 10 ml of water again, and dried over anhydrous magnesium sulfate, and the solvent was distilled off under reduced pressure. The residue, 1.3 g (65%), was a viscous oily material containing isomeric *N*-(1-bromopropan-2-yl)-3-nitro-1,2,4-triazoles **IIa**–**IIc**.

1-(1-Bromopropan-2-yl)-5-nitro-1*H*-1,2,4-triazole (IIa). ^{1}H NMR spectrum, δ, ppm: 1.62 d (3H, CH_3), 3.93 m (2H, CH_2), 5.53 sext (1H, CH), 8.32 s (1H, HC=N). ^{13}C NMR spectrum, δ_C, ppm: 18.6 (CH_3), 35.6 (CH_2), 58.4 (CH), 149.5 (C^3), 152.7 (C^5).

4-(1-Bromopropan-2-yl)-3-nitro-4*H*-1,2,4-triazole (IIb). ^{1}H NMR spectrum, δ, ppm: 1.49 d (3H, CH_3), 3.83 m (2H, CH_2), 4.83 sext (1H, CH), 8.11 s (1H, HC=N). ^{13}C NMR spectrum, δ_C, ppm: 19.1 (CH_3), 35.6 (CH_2), 56.3 (CH), 149.4 (C^5), 152.3 (C^3).

1-(1-Bromopropan-2-yl)-3-nitro-1*H*-1,2,4-triazole (IIc). ^{1}H NMR spectrum, δ, ppm: 1.73 d (3H, CH_3), 3.76 m (2H, CH_2), 4.67 sext (1H, CH), 8.87 s (1H, HC=N). ^{13}C NMR spectrum, δ_C, ppm: 146.1 (C^5), 162.9 (C^3); the other signals were not assigned unambiguously.

1-(Cyclohex-2-en-1-yl)-3-nitro-1*H*-1,2,4-triazole (III). Cyclohexa-1,3-diene, 0.44 g (0.0055 mol), was added dropwise over a period of 10 min under stirring at room temperature to a solution of 0.57 g (0.005 mol) of 3-nitro-1*H*-1,2,4-triazole in 10 ml of 87% phosphoric acid. The mixture was stirred for 50–60 min at room temperature, poured into water (50 ml), and extracted with methylene chloride (2×25 ml). The combined extracts were dried over anhydrous magnesium sulfate and filtered, and the solvent was distilled off under reduced pressure. Yield 0.57 g (60%), viscous oily substance. ^{1}H NMR spectrum, δ, ppm: 1.04–2.18 m (6H, CH_2), 5.14–5.23 m (1H, CH), 5.76–5.82 m (1H, CH=), 6.08–6.15 m (1H, =CH), 8.86 s (1H, 5-H). ^{13}C NMR spectrum, δ_C, ppm: 18.5 (CH_2), 23.9 (CH_2), 28.8 (CH_2), 56.4 (CH), 123.4 and 133.5 (CH=CH), 145.7 (C^5), 161.9 (C^3). Found, %: C 49.12; H 5.31; N 28.49. $C_8H_{10}N_4O_2$. Calculated, %: C 49.48; H 5.19; N 28.85.

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance-500 spectrometer at 500 and 100 MHz, respectively, using DMSO-d_6 as solvent.

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