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## SHORT COMMUNICATIONS

# Synthesis of 3-(2-Azidoethyl)-1,5-dinitro-1,3,5-triazacycloheptane

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Cyclic nitroamines are known as important energy-rich compounds [1] and biologically active nucleosides [2, 3]. Owing to the easily departing nitro group heterocyclic *N*-nitroamines are used as mild N- [4] and C-nitrating agents [2, 5].

Introduction of functional groups into the side chain of the cyclic nitroamines extends the synthetic potential of these compounds. In particular, the presence of an azido group not only increases the energy-content of nitroamines but also opens new opportunities to apply them as energy-rich precursors in preparation of a wide range of new derivatives [6, 7]. One of the widely spread and swiftly developing methods of synthetic application of azides is the 1,3-dipolar cycloaddition of these compounds to acetylene systems for preparation of versatile 1,2,3-triazoles interesting for medicine [8], nanoparticles generation [9, 10], producing functionalized oligosaccharides [11] and dendrimers [9].

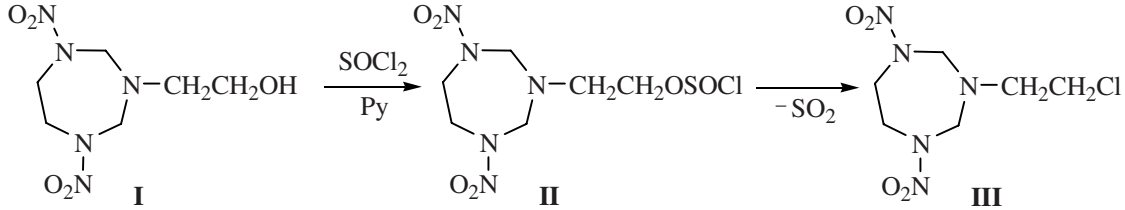
The reactivity of functionalized nitroamines may be governed both by the character of the functional groups and/or by the relatively weak chemical bond N–$NO_2$ sensitive to the action of bases [12] and acids [2]. The lability of the bond requires special mild conditions for chemical transformations in the side chain of cyclic nitroamines.

The information on cyclic azidonitroamines [13] is very limited for they are inaccessible and instable. Organic azides are sensitive to mechanical actions [6] that limits their application. The presence of a seven-membered heterocycle should favor increased stability of azidonitroamines. Aiming at preparation of azidonitroamines stable under common conditions we carried out a synthesis of previously unknown 3-(2-azidoethyl)-1,5-dinitro-1,3,5-triazacycloheptane.

In the published description of the synthesis of 3-(2-hydroxyethyl)-1,5-dinitro-1,3,5-triazacycloheptane (**I**) obtained by Mannich reaction through condensation of *N,N'*-ethylenedinitroamine with formaldehyde and monoethanolamine [14] no spectral characteristics of the compound were given. For subsequent introduction of an azido group into the side chain of heterocyclic nitroamine **I** we investigated the electrophilic substitution of the hydroxy group by chlorine and tosyl group.

The chlorination of heterocyclic alcohol **I** with thionyl chloride in a mixture of dichloromethane and pyridine at 42–70°C within 6 h occurred with the formation of intermediate themally unstable chlorosulfite **II**. After recrystallization compound **II** from chloroform we isolated previously unknown 1,5-dinitro-3-(2-chloroethyl)-1,3,5-triazacycloheptane (**III**) in 30% yield, mp

**Scheme 1.**



198–199°C (Scheme 1). The structure and composition of compound **II** are confirmed by $^1$H NMR spectrum and elemental analysis. The $^1$H NMR spectrum alongside the singlets of methylene protons belonging to the seven-membered heterocycle (4.17 and 5.12 ppm) and a triplet at 2.90 ppm ($NCH_2$, side chain) contains a triplet of $CH_2O$ at 4.02 ppm.

The IR spectrum of compound **III** contains absorption bands of the stretching vibrations of the nitro group in the region 1340, 1500 cm$^{-1}$. $^1$H NMR spectrum is characterized by the signals of the methylene protons of the ring and the side chain. In the $^{13}$C NMR spectrum signals are observed from the fragments $NCH_2N$, $NCH_2CH_2N$, $CH_2Cl$, and $NCH_2$ (side chain).

By reaction of alcohol **I** with *p*-toluenesulfonyl chloride in pyridine we obtained a previously unknown 1,5-dinitro-3-(2-tosylethyl)-1,3,5-triazacycloheptane (**IV**) in 73% yield (Scheme 2). In the IR spectrum of tosylate **IV** the stretching vibrations bands are present from the nitro group and the phenyl ring. $^1$H NMR spectrum contains the signals from the methylene protons of the aza ring $NCH_2CH_2N$ and $NCH_2N$, and also of the side chain $NCH_2$, $CH_2O$, the resonances of phenyl and methyl groups.

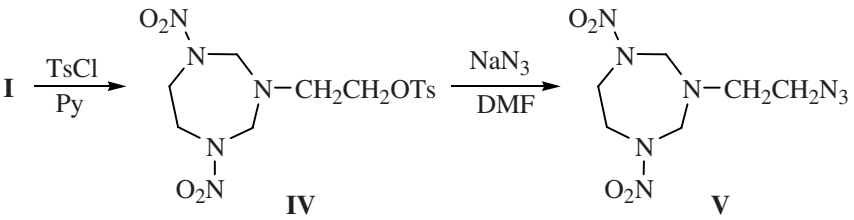
The synthesis of the target azidonitroamine was performed by replacing with azide ion the tosyl group of compound **IV** obtained in a preparative yield. It is known that 1-(bromomethyl)-3,5,7-trinitro-1,3,5,7-tetraazacyclooctane is inert to the treatment with sodium azide, and the bromine is readily substituted at the use of generated in situ acyl azide [13].

By reaction of tosylate **IV** with sodium azide in DMF within 15 h at 95–100°C we obtained previously unknown 3-(2-azidoethyl)-1,5-dinitro-1,3,5-triazacycloheptane (**V**) in 54% yield. The IR spectrum of azidonitroamine **V** contains the absorption bands of the stretching vibrations of the nitro group and a strong band corresponding to the stretching vibrations of the azido group. $^1$H NMR spectrum of compound **V** is characterized by the signals of the methylene protons of the ring and the side chain.

**3-(2-Hydroxyethyl)-1,5-dinitro-1,3,5-triazacycloheptane (I)**. Yield 71%, mp 105–106°C (104–105°C [14]). IR spectrum, ν, cm$^{-1}$: 720, 750, 798, 880, 930, 950, 1005, 1015, 1050, 1070, 1130, 1160, 1195, 1240, 1260, 1295, 1300, 1340, 1400, 1500, 1505, 2850, 2890, 2940, 3060, 3400 br. $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm: 2.56 t (2H, $NCH_2$, side chain, $^3J$ 6.1 Hz), 3.52 t (2H, $CH_2O$, $^3J$ 6.1 Hz), 4.19 C (4H, $NCH_2CH_2N$), 4.62 C (1H, OH), 5.14 C (4H, $NCH_2N$).

**1,5-Dinitro-3-(2-chloroethyl)-1,3,5-triazacycloheptane (III).** To a mixture of 2.0 g (8.5 mmol) of alcohol **I**, 0.7 ml (8.5 mmol) of pyridine, and 7 ml of dichloromethane at cooling with ice a solution was added of 0.7 ml (9.5 mmol) of thionyl chloride in 6 ml of dichloromethane. The reaction mixture was stirred for 4 h at 40°C, the solvent was distilled off, 6 ml of pyridine was added, and the stirring was continued for 2 h at 70°C. On cooling the mixture was poured on ice, the oily layer was separated, diluted with 5 ml of dichloromethane, the separated precipitate was filtered off and dried in a vacuum. We isolated 0.97 g of powdery chlorosulfite **II**. $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm: 2.90 t (2H, $NCH_2$, side chain, $^3J$ 5.1 Hz), 4.02 t (2H, $CH_2O$, $^3J$ 5.1 Hz), 4.17 s (4H, $NCH_2CH_2N$), 5.12 s (4H, $NCH_2N$). Found, %: C 23.51; H 4.23; Cl 10.30; N 21.20; S 11.16. $C_6H_{12}ClN_5O_6S$. Calculated, %: C 22.67; H 3.78; Cl 11.18; N 22.04; S 10.07. On recrystallization of compound **II** from chloroform we isolated 0.64 (30%) of colorless crystals of compound **III**, mp 198–199°C. IR spectrum, ν, cm$^{-1}$: 700, 750, 785, 800, 880, 905, 935, 945, 960, 1000, 1020, 1070, 1100, 1130, 1150, 1180, 1220, 1240, 1260, 1290, 1305, 1340 [$\nu_s(NO_2)$], 1370, 1395, 1430, 1450, 1490, 1500 [$\nu_{as}(NO_2)$], 1605 sh. $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm: 2.97 t (2H, $NCH_2$, side chain, $^3J$ 6.8 Hz), 3.73 t (2H, $CH_2Cl$, $^3J$ 6.8 Hz), 4.21 s (4H, $NCH_2CH_2N$), 5.16 s (4H, $NCH_2N$). $^{13}$C NMR spectrum (DMSO-$d_6$), δ, ppm: 67.45 ($NCH_2N$), 50.77 ($NCH_2CH_2N$), 46.35 ($CH_2Cl$), 41.73 ($NCH_2$, side chain).

**Scheme 2.**



Found, %: C 28.20; H 5.13; Cl 14.13; N 27.20. $C_6H_{12}ClN_5O_4$. Calculated, %: C 28.41; H 4.76; Cl 13.97; N 27.60.

**1,5-Dinitro-3-(2-tosylethyl)-1,3,5-triazacycloheptane (IV).** To a solution of 1.18 g (5 mmol) of alcohol I in 10 ml of anhydrous pyridine at –2...–4°C was added by portions 1.4 g (7 mmol) of *p*-toluenesulfonyl chloride within 30 min. The reaction mixture was stirred at room temperature for 4 h, the solution was poured into a mixture of 30 g of ice and 4 ml of concn. HCl. The precipitated crystals were filtered off and dried in a vacuum. Yield 1.52 g (73%), mp 113–115°C (chloroform–hexane). IR spectrum, ν, $cm^{-1}$: 700, 720, 745, 790, 810, 880, 885, 945, 1010, 1055, 1070, 1080, 1140, 1170, 1180, 1220, 1260, 1265, 1295, 1345 [$\nu_s(NO_2)$], 1490, 1510 [$\nu_{as}(NO_2)$], 1595 (Ph). $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 2.44 C (3H, $CH_3$), 3.00 t (4H, $NCH_2$, side chain, $^3J$ 5.1 Hz), 4.09 t (2H, $CH_2O$, $^3J$ 5.1 Hz), 4.18 s (4H, $NCH_2CH_2N$), 5.02 s (4H, $NCH_2N$), 7.34 d (2H, Ph), 7.79 d (2H, Ph). Found, %: C 40.01; H 5.02; N 17.90; S 7.95. $C_{13}H_{19}N_5O_7S$. Calculated, %: C 40.09; H 4.91; N 17.98; S 8.23.

**3-(2-Azidoethyl)-1,5-dinitro-1,3,5-triazacycloheptane (V).** A mixture of 1.0 g (2.5 mmol) of tosylate **IV**, 0.2 g (3.0 mmol) of sodium azide, and 15 ml of anhydrous DMF was stirred for 15 h at 95–100°C. The reaction mixture was cooled to 10°C and poured into 20 ml of ice water. The crystalline precipitate was filtered off, washed with water and ether, and dried under a reduced pressure. Yield 0.35 g (54%), mp 115–117°C (chloroform–hexane). IR spectrum, ν, $cm^{-1}$: 700, 750, 795, 800, 850, 895, 945, 980, 1020, 1050, 1070, 1130, 1170, 1230, 1235, 1260, 1290, 1305, 1340 [$\nu_s(NO_2)$], 1505 [$\nu_{as}(NO_2)$], 2100 C ($N_3$). $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 2.96 t (2H, $NCH_2$, side chain, $^3J$ 6.8 Hz), 3.46 t (2H, $CH_2N_3$, $^3J$ 6.8 Hz), 4.22 s (4H, $NCH_2CH_2N$), 5.12 s (4H, $NCH_2N$). Found, %: C 27.68; H 4.85; N 43.50. $C_6H_{12}N_8O_4$. Calculated, %: C 27.69; H 4.65; N 43.06.

IR spectra were recorded on a spectrophotometer Specord 75IR from pellets with KBr or mulls in mineral oil. $^1$H and $^{13}$C NMR spectra were registered on a spectrometer Bruker DPX-400 (operating frequencies 400.13 and 100.62 MHz respectively), internal reference HMDS. *N,N'*-Ethylenedinitroamine was prepared by procedure [15].

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