Chemistry of Heterocyclic Compounds, Vol. 42, No. 9, 2006

REACTIONS OF 3-NITRO-1,2,4-TRIAZOLES WITH ALKYLATING AGENTS. 3*. ALKYLATION OF A NEUTRAL HETEROCYCLE BY DIETHYL SULFATE

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The reaction of 3-nitro-5-R-1,2,4-triazoles with diethyl sulfate gives 1-ethyl-3-R-5-nitro-, 4-ethyl-3-nitro-5-R-1,2,4-triazoles, 1,4-diethyl-, 1,4-diethyl-3-methyl-1,2,4-triazol-5-ones, and 1,4-diethyl-3-nitro-5-R-1,2,4-triazolium salts. When compared with the use of dimethyl sulfate as alkylating agent the ethylation products have a markedly increased fraction of triazolones (up to 30-37%) and a somewhat lowered yield of nitrotriazolium salts (up to 6-10%). The reaction time is increased by an order.

Keywords: N-alkyl-3-nitro-1,2,4-triazoles, N,N-dialkyl-3-nitro-1,2,4-triazolium salts, N,N-dialkyl-1,2,4-triazol-5-ones.

We have previously reported the alkylation of 3-nitro- and 3-methyl-3-nitro-1,2,4-triazoles (**1** and **2**) using dimethyl sulfate (DMS). Later and under similar conditions the alkylation of the nitrotriazoles **1,2** by diethyl sulfate (DES) gave the ethyl sulfate salts of 1,4-diethyl- and 1,4-diethyl-5-methyl-3-nitro-1,2,4-triazoles (**3** and **4**) and also their perchlorate salts (**5** and **6**). The overall reaction schemes for the nitrotriazoles **1** and **2** with DMS and DES are similar. However, the change in alkylating agent leads to a marked change in the reaction conditions and the ratio of N-mono- and complete alkylation products.

The main reaction products of the alkylation of the nitrotriazoles **1** and **2** using DMS are the N-monomethyl nitrotriazoles (yield 53-73%). Ratio of $N_{(1)}$, $N_{(2)}$, and $N_{(4)}$-methyl-3-nitro-5-R-1,2,4-triazoles 0.035:1:7.75; fraction of 1,4-di- and 1,3,4-trimethyl-1,2,4-triazol-5-ones in the reaction product 3-6%; 1,4-di- and 1,4,5-trimethyl-3-nitro-1,2,4-triazolium salt content 8-12% [1]. The use of DES as alkylating agent gives an order increase in the reaction time. The products of interaction of nitrotriazoles **1** and **2** with DES from the N-mono-substituted 3-nitro-5-R-1,2,4-triazoles gave only the $N_{(2)}$ isomers – 1-ethyl-5-nitro- and 1-ethyl-3-methyl-5-nitro-1,2,4-triazoles (**7** and **8**) and $N_{(4)}$ isomers – 4-ethyl-3-nitro- and 4-ethyl-5-methyl-3-nitro-1,2,4-triazoles (**9** and **10**). The overall yield of N-mono-substituted 3-nitro-5-R-1,2,4-triazoles and the fraction of $N_{(4)}$-isomers was lowered (yield of **7** + **8** 26.3%, **9** + **10** 45.3%, ratio of **7**:**9** = 1:2.7 and **8**:**10** 1:2.3).

The selectivity of the N-mono alkylation of the triazoles **1** and **2** using DES when compared with their alkylation by DMS is shifted to an increase in the yield of the $N_{(2)}$-substituted nitrotriazoles **7,8** relative to the $N_{(4)}$-substituted nitrotriazoles **9,10**. This leads to an increase in the fraction of 2,4-diethyl secondary diethylation alkylation salts 1,4-diethyl- and 1,4-diethyl-3-methyl-5-nitrotriazole (**11** and **12**) (being triazolone precursors) when compared to the fraction of the 1,4-alkylation salts 1,4-diethyl- and 1,4-diethyl-5-methyl-3-nitro-1,2,4-

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* For Communication 2 see [1].

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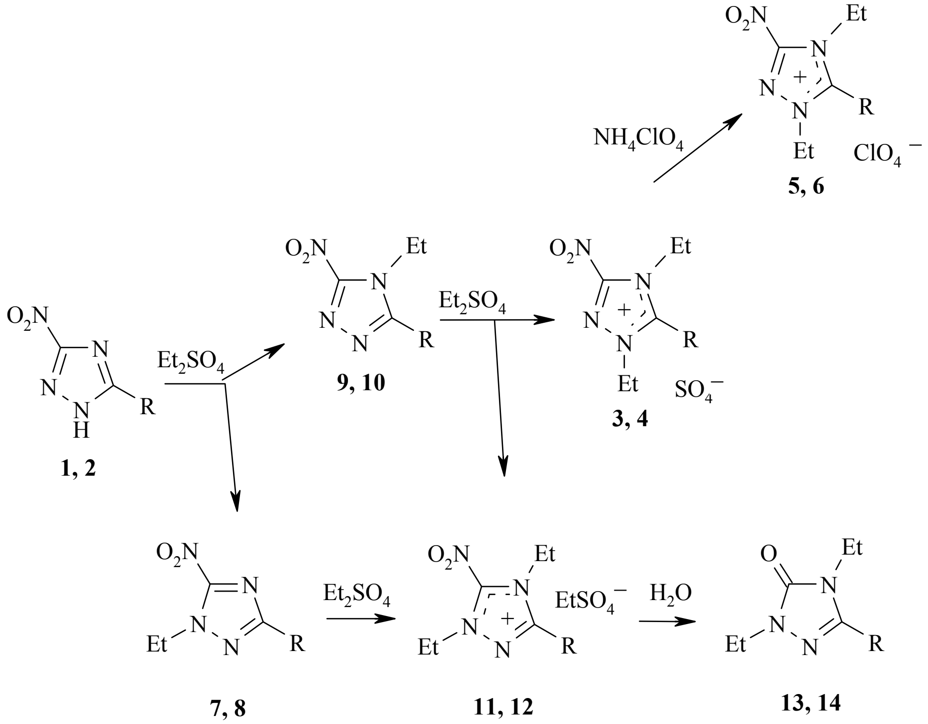

1, **3**, **5**, **7**, **9**, **11**, **13** R = H; **2**, **4**, **6**, **8**, **10**, **12**, **14** R = Me

triazoles (**5** and **6**). As a result, when comparing with the products of N,N-dimethylation [1] there is a significant increase in the yield of 1,4-diethyl- and 1,4-diethyl-3-methyl-1,2,4-triazol-5-ones (**13** and **14**) to 36.7 and 29.4% respectively. The yield of salts **5** and **6** (the products of 1,4-ethylation of triazoles **1** and **2**) are somewhat lowered (9.7 and 5.5% respectively).

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-400 spectrometer (400 and 100 MHz respectively) using DMSO-d$_6$ and with TMS as internal standard. IR spectra were taken on a Perkin-Elmer instrument as KBr tablets. UV spectra were recorded on a Specord instrument. Gas chromatographic analysis of the reaction products was carried out by the internal standard method on a Chrom-5 chromatograph with flame ionization detection, a glass column (l = 200 mm, d = 3 mm) packed with SE-30 siloxane elastomer, nitrogen gas carrier (40 ml/min), oven temperature 180°C, evaporator 220°C, and detector 220°C.

The N-alkyl-3-nitro-5-R-1,2,4-triazoles and triazolones **7-10, 13, 14** as starting materials and comparison materials for ^{1}H NMR spectroscopy and GLC were synthesized by methods [1-3].

Reaction of 3-Nitro-1,2,4-triazole with Diethyl sulfate. A suspension of 3-nitro-1,2,4-triazole (0.2 mol) and DES (0.15 mol) was stirred at 78-80°C for 28 h, cooled to 30°C, and extracted with methylene chloride. The ^{1}H NMR and GLC of the extract pointed to identification of the following compounds: DES, **7, 9, 13**. Yield, %: 1.4:32.9:4.3:61.4 respectively (overall yield of the reaction mixture after distillation of methylene chloride under vacuum = 4.42 g). The residual mass was treated with stirring with water (25 ml) and extracted with methylene chloride. The extract was analyzed by ^{1}H NMR and GLC using the reference compounds and contained DES, **7, 9, 13**, and non-identified material. Yield, %: traces, 2.1, 68.1, 21.7, 8.0% respectively (overall yield of the reaction product after distillation of methylene chloride under vacuum = 5.72 g). Extraction of this mixture with hexane, evaporation of solvent, and fractionation in vacuo gave compound **7** with bp 65°C (0.5 mm Hg). IR spectrum, ν, cm^{-1}: 1558, 1336. UV spectrum, λ_{max}, nm: 267, 218. ^1H NMR spectrum, δ, ppm: 1.49 (3H, t, *J* = 7.2, CH_3); 4.61 (2H, q, *J* = 7.2, CH_2); 8.12 (1H, s, CH). ^{13}C NMR spectrum, δ, ppm: 14.15 (CH_3); 47.73 (CH_2); 149.08 (CH); 151.99 ($C{-}NO_2$). Recrystallization of the indigo residue from 2-propanol and water gave substance **9** with mp 83-84°C. ^1H NMR spectrum, δ, ppm: 1.44 (3H, t, *J* = 7.2, CH_3); 4.38 (2H, q, *J* = 7.2, CH_2); 8.93 (1H, s, CH). ^{13}C NMR spectrum, δ, ppm: 14.82 (CH_3); 42.93 (CH_2); 147.20 (CH); 153.92 ($C{-}NO_2$). Ammonium perchlorate (3.2 g) was added to the reaction mixture (after two extractions with methylene chloride) at 78-80°C and the product was cooled to 20°C and filtered. Yield of substance **5** 2.12 g (9.7%); mp 150-151°C (water). IR spectrum (KBr tablet), ν, cm^{-1}: 1562 (NO_2); 1325 (NO_2), 1080 (ClO_4). ^1H NMR spectrum, δ, ppm: 1.52 (3H, t, *J* = 7.2, CH_3); 1.55 (3H, t, *J* = 7.2, CH_3); 4.53 (2H, q, *J* = 7.2, CH_2); 4.57 (2H, q, *J* = 7.2, CH_2); 10.42 (1H, s, CH). ^{13}C NMR spectrum, δ, ppm: 13.36 (CH_3); 13.62 (CH_3); 46.72 (CH_2); 49.09 (CH_2); 145.78 (CH); 150.92 ($C{-}NO_2$).

Reaction of 5-methyl-3-nitro-1,2,4-triazole with diethyl sulfate. A suspension of 5-methyl-3-nitro-1,2,4-triazole (0.2 mol) and diethyl sulfate (0.15 mol) was stirred at 75-80°C for 30 h, cooled to 30°C, and extracted with methylene chloride. The ^1H NMR spectrum and GLC pointed to the identification of the compounds: DES, **8, 10, 15**, and non identified material. Yield, %: 1.6; 51.8; 13.1; 19.0; 14.5 respectively (overall yield of the reaction mixture after distillation of the methylene chloride = 3.2 g). The residual reaction mass was stirred with water (1:1 by weight) and extracted with methylene chloride. ^1H NMR and GLC with the reference compounds showed the presence of the following compounds: DES, **8, 10, 14**, and non identified material. Yield, %: 0.28, 0.27, 79.2; 9.7; 10.5 respectively (overall yield of the reaction product after distillation of methylene chloride = 4.1 g). Ammonium perchlorate (3.6 g) was added to the reaction mixture (after two extractions with methylene chloride) at 75-80°C and the product was cooled to 20°C and filtered. Yield of substance **6** 0.69 g (5.5%); mp 158-160°C (water). ^1H NMR spectrum, δ, ppm: 1.44 (3H, t, *J* = 7.2, CH_3); 1.47 (3H, t, *J* = 7.2, CH_3); 2.94 (3H, s, $C{-}CH_3$); 4.49 (2H, q, *J* = 7.2, CH_2); 4.53 (2H, q, *J* = 7.2, CH_2). ^{13}C NMR spectrum, δ, ppm: 9.98 ($C{-}C\underline{H}_3$); 13.11 ($CH_2C\underline{H}_3$); 13.17 ($CH_2C\underline{H}_3$); 44.89 (CH_2); 47.14 (CH_2); 150.39 ($C{-}NO_2$); 155.32 ($C{-}CH_3$).

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