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SHORT COMMUNICATIONS

Hydroxymethylation with Formaldehyde of Substituted 3-(4-Methoxyphenyl)-5-nitromethyl-1,2,4-oxadiazoles

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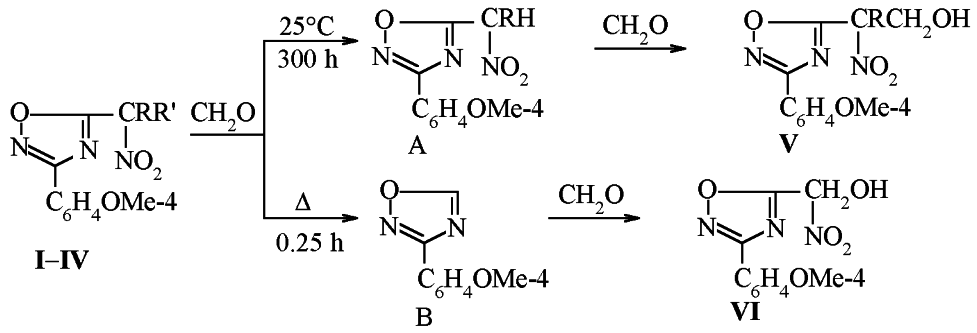
Halopolynitromethanes and tetranitromethane in reaction with formaldehyde undergo substitution of one or two functional groups by a hydroxymethyl function [1, 2]. However no published data exist describing reaction between formaldehyde and analogous derivatives of 1,2,4-oxadiazoles. We carried out reaction of formaldehyde with a series of substituted 3-(4-methoxyphenyl)-5-nitromethyl-1,2,4-oxadiazoles and obtained as a result various hydroxymethylation products of oxadizoles **V** and **VI**. The



R = NO_2, R' = CO_2Et (**I, V**); R = R' = NO_2 (**II**); R = NO_2, R' = Cl (**III**); R = CO_2Et, R' = Cl (**IV**).

reactions occur more readily than with halonitromethanes presumably because of higher acceptor quality of the 1,2,4-oxadiazole ring.

Hydroxymethylation of ester **I** or trinitroalkane **II** proceeds under mild conditions and is completed by elimination of the ethoxycarbonyl or nitro groups yielding compound **V**. Dinitrochloroalkane **III** and ester **IV** do not react with formaldehyde under mild conditions. The reaction occurs at heating, with a loss of substituents in *5* position of the heterocycle, and provides as a result hydroxymethyloxadiazole **VI**. The nature of products **V, VI** suggests that these processes follow the mechanism assumed for formaldehyde reaction with polynitromethanes [3]. In the course of electrophilic attack of nitroalkanes on the carbonyl oxygen of formaldehyde compounds I–IV are reduced to the corresponding intermediates A and B. The latter undergo condensation with excess formaldehyde along Henri reaction [4] to furnish alcohols **V, VI**. The direction of hydroxymethylation is governed presumably by the electrophilicity of the substituent in the *5* position of the oxadiazole.

1-Hydroxy-2-[3-(4-methoxyphenyl)-1,2,4-oxadiazol-5-yl]-2,2-dinitroethane (V). To 6 mmol of compound **I** or **II** [5] was added 40 ml of formalin, and the mixture was stirred 300 h at 25°C. Then the products were extracted into ether (2 × 10 ml), the extract was evaporated, the residue was subjected to chromatography on a column (250 × 10 mm) packed with activated Silicagel 100/400 μ, eluent benzene. Yield 53%, mp 107–108°C. IR spectrum, ν, cm^{-1}: 3560 (OH); 1570, 1330 (NO_2). ^1H NMR spectrum, δ, ppm: 7.80–6.82 m (C_6H_4); 5.54 t (OH); 4.86 d (CH_2); 3.81 c (CH_3O). Found, %: C 42.47; H 3.14; N 17.95. $C_{11}H_{10}N_4O_7$. Calculated, %: C 42.58; H 3.23; N 18.07.

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5-Hydroxymethyl-3-(4-methoxyphenyl)-1,2,4-oxadiazole (VI). To 6 mmol of compound **III** or **IV** [5] was added 40 ml of formalin, and the mixture was boiled for 15 min, cooled, and extracted with ether (2 × 10 ml), the solvent was evaporated, and the residue was subjected to chromatography under similar conditions (eluent ethyl ether). Yield 67%, mp 131°C. IR spectrum, ν, cm^{-1}: 3580 (OH). ^1H NMR spectrum, δ, ppm: 7.74–6.80 m (C_6H_4); 5.51 t (OH); 4.68 d (CH_2); 3.80 s (CH_3O). Found, %: C 58.14; H 4.78; N 13.47. $C_{10}H_{10}N_2O_3$. Calculated, %: C 58.25; H 4.85; N 13.59.

IR spectra were recorded on spectrophotometer IKS-29 from solutions in chloroform. ^1H NMR spectra were registered on spectrometer Tesla BS-487C (80 MHz) in acetone-d_6, internal reference HMDS.

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