ISSN 1070-3632, Russian Journal of General Chemistry, 2008, Vol. 78, No. 3, pp. 508–509. © Pleiades Publishing, Ltd., 2008.
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LETTERS TO THE EDITOR

Synthesis of 1-(2-Hydroxyethyl)-3,5-dimethyl-1*H*-pyrazole-4-carbaldehyde

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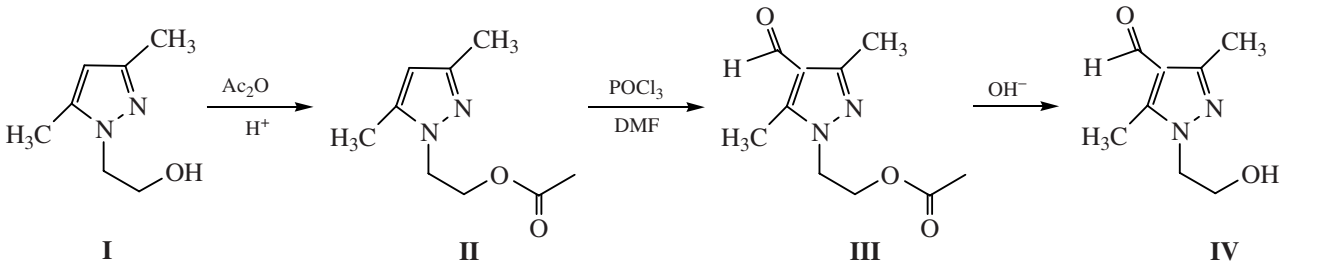
Received August 24, 2007

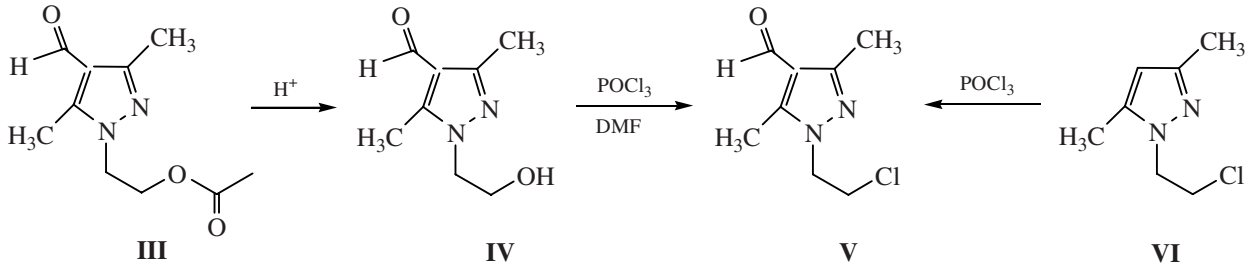
DOI: 10.1134/S1070363208030298

We previously reported [1] that 1-(2-hydroxyethyl)-3,5-dimethyl-1*H*-pyrazole (**I**) does not undergo formylation according to Vilsmeier–Haack and that the reaction occurs as substitution of the hydroxy group in the 2-hydroxyethyl moiety by chlorine atom. We now propose a procedure for the synthesis of 1-(2-hydroxyethyl)-3,5-dimethyl-1*H*-pyrazole-4-carbaldehyde (**IV**) from accessible 1-(2-hydroxyethyl)-3,5-dimethylpyrazole (**I**) according to the following scheme.



I **II** **III** **IV**

Acylation of **I** with acetic anhydride gives 1-(2-acetoxyethyl)-3,5-dimethyl-1*H*-pyrazole (**II**) which readily undergoes Vilsmeier–Haack formylation with formation of 1-(2-acetoxyethyl)-3,5-dimethyl-1*H*-pyrazole-4-carbaldehyde (**III**). Hydrolysis of **III** leads to 1-(2-hydroxyethyl)-3,5-dimethyl-1*H*-pyrazole-4-carbaldehyde (**IV**). We also isolated from the reaction mixture 1-(2-chloroethyl)-3,5-dimethyl-1*H*-pyrazole-4-carbaldehyde (**V**, yield 7%); presumably, the latter was formed as shown in the following scheme.



III **IV** **V** **VI**

The structure of compound **V** was proved by the ^{1}H NMR and IR spectra, elemental analysis, and independent synthesis via formylation of 1-(2-chloroethyl)-3,5-dimethyl-1*H*-pyrazole (**VI**).

Formylation of 1-(2-acetoxyethyl)-3,5-dimethyl-1*H*-pyrazole (II). A mixture of 0.1 mol of compound **II** and 0.6 mol of dimethylformamide was heated under stirring to 90°C, and 0.2 mol of phosphoryl chloride was carefully added dropwise under stirring, maintaining the temperature not exceeding 120°C. The mixture was cooled with ice water, neutralized with aqueous sodium hydroxide, and extracted with chloroform, the extract was dried over magnesium sulfate, the solvent was distilled off, and the residue was subjected to fractional distillation under reduced pressure to isolate 15.3 g of a product with bp 150–170°C (1 mm), n_D^{20} = 1.5270. According to the ^{1}H NMR data, the product was compound **IV** containing 10% of 1-(2-chloroethyl)-3,5dimethyl-1*H*-pyrazole-4-carbaldehyde (**V**), which was separated after hydrolysis.

1-(2-Hydroxyethyl)-3,5-dimethyl-1*H*-pyrazole-4-carbaldehyde (IV). A mixture of 21 g of the crude product (see above), 4 g of sodium hydroxide, and 50 ml of water was stirred for 3–4 h at 30°C. The mixture was extracted first with diethyl ether and then with chloroform, and the extracts were dried over magnesium sulfate. After removal of the solvent, the residue was subjected to fractional distillation under reduced pressure. From the diethyl ether extract we isolated 1.4 g of 1-(2-chloroethyl)-3,5-dimethyl-1*H*-pyrazole-4-carbaldehyde (**V**), bp 135–140°C (1 mm), n_D^{20} = 1.5390. IR spectrum, ν, cm^{-1}: 1530 (ring), 1660 (C=O), 640–650 (C–Cl). ^{1}H NMR spectrum, δ, ppm, (*J*, Hz): 2.36 s (3H, 3-CH_3), 2.54 s (3H, 5-CH_3), 3.93 t (2H, NCH_2, *J* = 5.9), 4.31 t (2H, CH_2Cl, *J* = 5.9), 9.84 s (1H, CHO). Found, %: C 51.84; H 6.01; N 15.04; Cl 19.25. $C_8H_{11}N_2OCl$. Calculated, %: C 51.34; H 5.88; N 14.97; Cl 19.25.

From the chloroform extract we isolated 11.76 g (70%) of compound **IV**, bp 173°C (1 mm), mp 64–66°C (from CCl_4). IR spectrum, ν, cm^{-1}: 1510 (ring), 1680 (C=O), 3200–3400 (OH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.34 s (3H, 3-CH_3), 2.52 s (3H, 5-CH_3), 2.73 q (2H, OCH_2, *J* = 5.4), 4.02 t (2H, NCH_2, *J* = 5.4), 4.68 t (1H, OH, *J* = 5.4), 9.81 s (1H, CHO). Found, %: C 57.84; H 8.06; N 18.32. $C_8H_{12}N_2O_2$. Calculated, %: C 57.14; H 7.14; N 16.67.

The ^{1}H NMR spectra were recorded on a Varian Mercury-300 spectrometer (300 MHz). The IR spectra were obtained on a Specord 75-IR instrument from thin films. GLC analysis was performed on an LKhM-8MD chromatograph equipped with a 1.5-m×3-mm column packed with 10% of Carbowax-20M on Inerton AW-HMDS (0.20–0.25 mm); carrier gas helium, flow rate 50 ml min^{-1}.

Initial compounds **I** and **II** were synthesized according to the procedures described in [2, 3].

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