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LETTERS TO THE EDITOR

Synthesis of 1-Vinyl-3,5-dimethyl-4-hydroxymethylpyrazole

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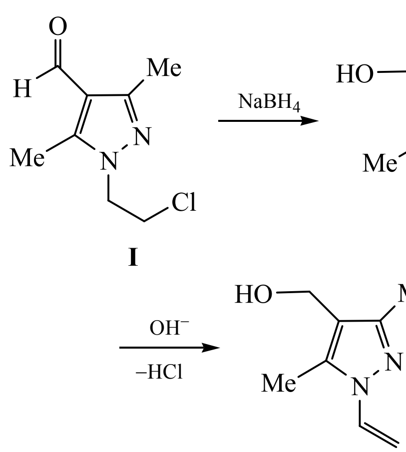
By the introduction of the reactive functional groups into the pyrazole ring a new series of the 1-vinylpyrazole derivatives can be obtained, which might be of interest in the various fields of science, technology, and medicine [1–3].

The available 1-(2-chloroethyl)-3,5-dimethyl-4-formyl-pyrazole **I** [4] is a promising synthon for the synthesis of new 4-substituted 1-vinylpyrazoles [5, 6].

Aiming to obtain 1-vinyl-3,5-dimethyl-4-hydroxy-methylpyrazole **III** we studied the reduction of 1-(2-chloroethyl)-3,5-dimethyl-4-formylpyrazole **I** with sodium borohydride in methanol. The dehydro-chlorination of the resulting 1-(2-chloroethyl)-3,5-dimethyl-4-hydroxymethylpyrazole **II** yields the target compound **III**.



I **II** **III**

1-(2-Chloroethyl)-3,5-dimethyl-4-hydroxymethyl-pyrazole **II** is thermally unstable. Therefore at distilling the reaction mixture it was isolated in 22% yield. The rest of compound **II** transformed into a series of compounds **III**–**VI**.

By the route *a*, compound **II** is dehydrochlorinated to give 1-vinyl-3,5-dimethyl-4-hydroxymethylpyrazole **III**, which undergoes mainly the thermal polymeriza-tion to form poly-1-vinyl-3,5-dimethyl-4-hydroxymethyl-pyrazole **IV**.

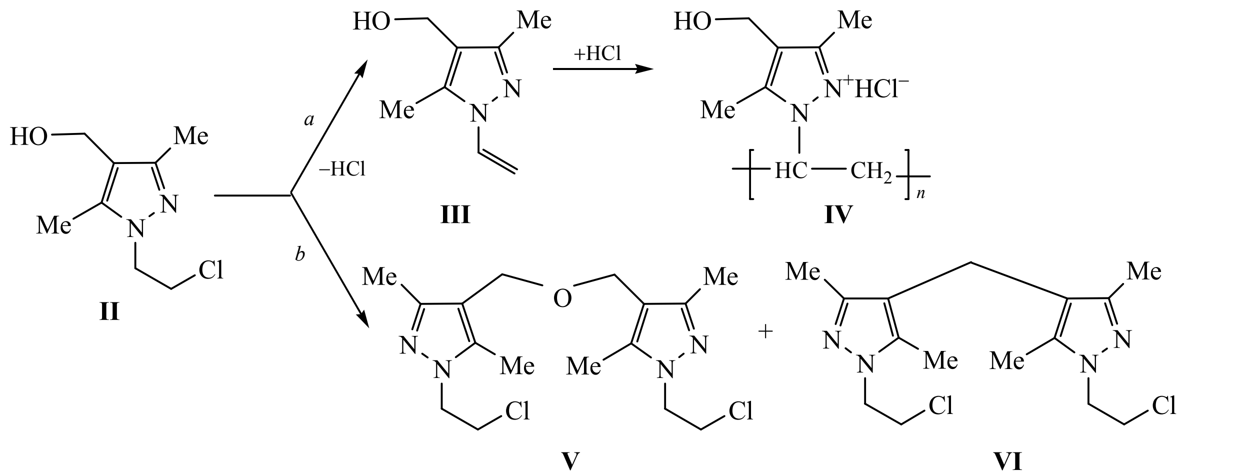
Another part of 1-(2-chloroethyl)-3,5-dimethyl-4-hydroxymethylpyrazole **II** is subjected to a cross-coupl-ing (*b*) to give a symmetrical di-(1,1'-chloroethyl)-3,5-dimethylpyrazol-4-yl)dimethyl ether **V** in 7.2% yield. Such reaction among the pyrazoles series was first noted in [7].

As expected, during the distillation ether **V** partially transforms into bispyrazolylmethane **VI** in a 9.1% yield. The formation of bispyrazolylmethanes we have studied in detail in [8, 9].

The dehydrochlorination of 1-(2-chloroethyl)-3,5-dimethyl-4-hydroxymethylpyrazole (without the preliminary distillation) under the phase-transfer catalysis at 70°C in an aqueous alkali–catalyst–sub-strate–benzene system proceeds over 1 h with a 62% yield. Triethylbenzylammonium chloride was used as a phase transfer catalyst.

The structure and composition of the obtained compounds **II**–**VI** were confirmed by the IR, ^{1}H NMR spectroscopy and elemental analysis.

In the IR spectrum of compound **II** do not appear the strong absorption band of the carbonyl group at 1680 cm^{-1} and the broad absorption band at 3200–3400 cm^{-1} of the OH group is observed. The IR spectrum of compound **III** contains an intensive absorption band at 1640 cm^{-1} corresponding to the vibrations of the vinyl group and an absorption band of the pyrazole ring at 1570 cm^{-1}.



In the [1]H NMR spectra of 1-vinyl-4-hydroxymethylpyrazole **III** the methyl protons signals are recorded in a strong field at 2.19 (3-CH_3) and 2.27 ppm (5-CH_3). The signals of the vinyl protons are registered as an ABX-system at δ 4.65 (H_A), 5.49 (H_B) and 6.92 ppm (H_X) with the coupling constants J_{AX} 15.2, J_{BX} 8.9 and J_{AB} 0 Hz.

The [1]H NMR spectra of compounds **V** and **VI** along with the signals of methyl and ethyl groups contain the characteristic singlet signals of the protons of the ester moiety (**V**) at 4.18 ppm and the methylene protons of Ar-CH_2-Ar fragment in a strong field at 3.34 ppm (**VI**).

1-(2-Chloroethyl)-3,5-dimethyl-4-hydroxymethylpyrazole (II). To the ice-cold solution of 8.16 g of 1-(2-chloroethyl)-3,5-dimethyl-4-formylpyrazole **I** in 100 ml of methanol was added by portions 1.8 g of sodium borohydride over 0.5 h maintaining the temperature of the reaction mixture no higher than 10°C. The mixture was stirred under cooling with ice water for 2 h, and then at room temperature for ~3 h. After removal of methanol in a vacuum, the formed complex was treated with the concentrated sodium hydroxide solution, extracted with chloroform, and dried over magnesium sulfate. After removal of chloroform the residue was distilled in a vacuum. Yield 4.1 g (22%), bp 139–142°C (1 mm Hg), crystallizes on standing, mp 98–102°C (ethanol–water, 1:9). IR spectrum, ν, cm^{-1}: 1570 (pyrazole ring), 3200–3400 (OH). [1]H NMR spectrum, δ, ppm (*J*, Hz): 2.13 s (3H, 3-CH_3), 2.24 s (3H, 5-CH_3), 3. 85 s (2H, CH_2Cl, *J* 6.2), 4.08 t (1H, $CH_2\underline{OH}$, *J* 5.3), 4.21 t (2H, NCH_2, *J* 6.8), 4.22 d (2H, CH_2OH, *J* 5.3). Found, %: C 50.61; H 7.11; Cl 18.41; N 14.34. $C_8H_{13}ClN_2O$. Calculated, %: C 50.92; H 6.89; Cl 18.83; N 14.85.

1-Vinyl-3,5-3,5-dimethyl-4-hydroxymethylpyrazole (III). Yield 1.5 g (10%), bp 119–125°C (1 mm Hg), n_D^{20} 1.5472, d_4^{20} 1.1099. IR spectrum, ν, cm^{-1}: 1570 (pyrazole ring), 1640 (CH=CH_2), 3000–3500 (OH). [1]H NMR spectrum, δ, ppm (*J*, Hz): 2.19 s (3H, 3-CH_3), 2.27 s (3H, 5-CH_3), 4.18 m (1H, $CH_2\underline{OH}$), 4.24 m (2H, $\underline{CH_2}OH$), 4.65 d (1H, CH=$\underline{CH_2}$, *J* 8.9), 5.49 d (1H, CH=$\underline{CH_2}$, *J* 15.2), 6.92 d. d (1H, $\underline{CH}$=CH_2, *J* 8.9, 15.2). Found, %: C 63.48; H 7.51; N 18.01. $C_8H_{12}N_2O$. Calculated, %: C 63.15; H 7.89; N 18.42.

Compounds **V** and **VI** were separated by the fractional crystallization. Yield 5.2 g, bp 220–260°C (1 mm Hg).

4,4'-Oxymethylenebis(1,1'-chloroethyl-3,5-dimethylpyrazole) (V). Yield 1.3 g (7.2%), mp 97–99°C (water). IR spectrum, ν, cm^{-1}: 1570 (pyrazole ring). [1]H NMR spectrum, δ, ppm (*J*, Hz): 2.09 s (6H, 3-CH_3), 2.20 s (6H, 5-CH_3), 3.86 t (4H, CH_2Cl, *J* 6.1), 4.16 s (4H, Ar-CH_2OCH_2-Ar), 4.22 t (4H, NCH_2, *J* 6.1). Found, %: C 53.82; H 6.21; Cl 19.37; N 15.73. $C_{16}H_{24}Cl_2N_4O$. Calculated, %: C 53.48; H 6.68; Cl 19.77; N 15.59.

Bis[(1,1'-chloroethyl)-3,5-dimethylpyrazol-4-yl]-methane (VI). Yield 1.5 g (9.1%), mp 101–109°C (water–ethanol). IR spectrum, ν, cm^{-1}: 1570 (pyrazole ring). [1]H NMR spectrum, δ, ppm (*J*, Hz): 1.94 s (6H, 3-CH_3), 2.10 s (6H, 5-CH_3), 3.34 s (4H, CH_2Cl, *J* 6.1), 3.34 s (4H, Ar-CH_2-Ar), 3.82 t (4H, CH_2Cl, *J* 6.1), 4.19 t (4H, NCH_2, *J* 6.1). Found, %: C 54.32; H 6.91; Cl 21.22; N 17.31. $C_{15}H_{22}Cl_2N_2$. Calculated, %: C 54.71; H 6.68; Cl 21.58; N 17.02.

Poly-1-vinyl-3,5-dimethyl-4-hydroxymethylpyrazole (IV). Poly-1-vinyl-3,5-dimethyl-4-hydroxymethylpyrazole hydrochloride (2.4 g) was dissolved in 20 ml of water and neutralized with NaOH aqueous solution. Compound **IV** precipitates as a viscous substance. Yield 1.6 g, the intrinsic viscosity is 0.04 dl g^{-1}. The IR spectrum of **IV** lacks the intensive absorption band of the vinyl group (1640 cm^{-1}). The absorption bands of pyrazole ring (1570 cm^{-1}) and hydroxy group (3200–3400 cm^{-1}) are unchanged.

1-Vinyl-3,5-3,5-dimethyl-4-hydroxymethylpyrazole (III). A mixture of 20 g of 1-(2-chloroethyl)-3,5-dimethyl-4-hydroxymethylpyrazole **II** (without the preliminary distillation), 1.2 g of potassium hydroxide, 1.2 g of triethylbenzylammonium chloride, 5 ml of water and 50 ml of benzene was vigorously stirred at 70–75°C for 1 h. After cooling the benzene layer was separated, washed with water, dried over magnesium sulfate, and concentrated in a vacuum. Yield 9.4 g (62%), bp 120–121°C (1 mm Hg), n_D^{20} 1.5473, d_4^{20} 1.1210.

The IR spectra were taken on a Specord 75-UR instrument (thin layer). The ^{1}H NMR spectra were registered on a Varian Mercury spectrometer (300 MHz) using DMSO-d_6 as a solvent.

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