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LETTERS TO THE EDITOR

Unusual Chemical Behavior of 1-(2-Chloroethyl)-4-hydroxymethylpyrazoles at Heating

O. S. Attaryan, A. A. Sahakyan, and G. V. Asratyan

Institute of Organic Chemistry, Scientific and Technological Center of Organic and Pharmaceutical Chemistry, National Academy of Sciences of Armenia, pr. Azatutyan 16, Yerevan, 0014 Armenia
e-mail: sahakyan.arsen@gmail.com

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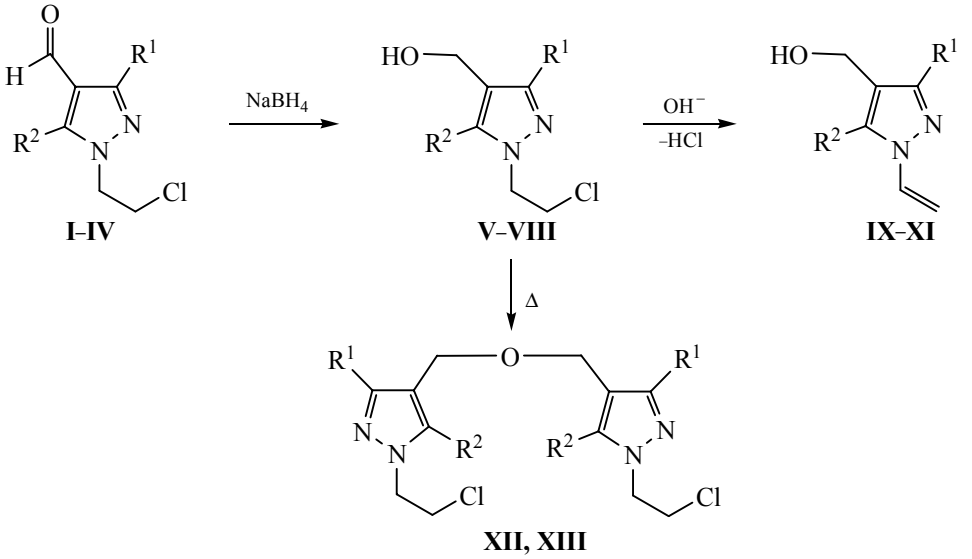
Previously we have shown that 1-(2-chloroethyl)-3,5-dimethyl-4-hydroxymethylpyrazole is thermally unstable and undergoes some transformation when distilling [1]. To investigate the nature of the observed phenomenon, we synthesized a series of 4-hydroxymethylpyrazoles **V**–**VII**: 1-(2-chloroethyl)- (**V**), 1-(2-chloroethyl)-3-methyl- (**VI**) and 1-(2-chloroethyl)-5-methyl-4-hydroxymethylpyrazole (**VII**).



$R^1 = R^2 = H$ (**I, V, IX, XII**); $R^1 = CH_3$, $R^2 = H$ (**II, VI, X**); $R^1 = H$, $R^2 = CH_3$ (**III, VII, XI, XIII**); $R^1 = R^2 = CH_3$ (**IV, VIII**).

It has been found that the obtained 4-hydroxymethylpyrazoles **V**, **VII** were isolated by distillation only in 20–30% yield except for compound **VI**, whose yield reached ~75%. The main portion of 4-hydroxymethylpyrazoles **V**, **VII** is converted via cross-coupling into compounds **XII**, **XIII**. Synthesis of hydroxymethyl derivatives **V**–**VII** via reduction of the initial aldehydes

I–**III** with satisfactory yields and their subsequent conversion into the corresponding vinylpyrazoles **IX**–**XI** with yields up to 59–60% is possible only by avoiding the isolation and purification of the compounds by distillation.

The same abnormal behavior of the compounds under distillation has been observed earlier in a series of *N*-alkyl-4-hydroxymethylpyrazoles [2].

One of the factors that allows the understanding of this phenomenon may be the presence of hydrogen bonding in these compounds. To determine the nature

of the association in the compounds **V**–**VIII**, we carried out a series of infrared spectral studies using solutions of varying concentrations of the test compounds (0.5–0.05 M) in chloroform.

The IR spectra of the diluted solutions of the samples contain narrow bands at 3615 (**V**, **VII**, **VIII**) and 3612 cm^{-1} (**VI**) belonging to the free OH-group. In the spectra of concentrated solutions there is a difference in the intensity of the stretching vibrations: about 3 times in the case of compound **VIII** and 2 times in the case of compounds **V**–**VII** as compared with compound **VI**. This indicates the prevalence of the association in solutions of compounds **V**, **VII**, **VIII** in contrast to compound **VI**, which hinders their distillation from the reaction mixture and leads to the formation of bispyrazoles **XII**–**XIII**.

The initial 1-(2-chloroethyl)-4-formylpyrazole **I** [bp 125–127°C (1 mm Hg), n_D^{20} 1.5410], 1-(2-chloroethyl)-3-methyl-4-formylpyrazole **II** [bp 130–135°C (1 mm Hg), n_D^{20} 1.5400] and 1- (2-chloroethyl)-5-methyl-4-formylpyrazole **III** (mp 42°C) were synthesized by the known methods [3].

1-(2-Chloroethyl)-4-hydroxymethylpyrazole (V). To a solution of 15.8 g of 1-(2-chloroethyl)-4-formylpyrazole **I** in 100 ml of methanol was added by portions 1.8 g of sodium borohydride within 0.5 h under cooling. The reaction temperature did not exceed 10°C. The mixture was stirred under cooling for 2 h and then at room temperature for ~3 h. Methanol was removed and the formed complex was treated with concentrated NaOH, extracted with chloroform, and dried over magnesium sulfate. After removing chloroform, the residue was distilled in a vacuum to give 4.8 g (30%) of 1-(2-chloroethyl)-4-hydroxymethylpyrazole **V** and 5.1 g (33%) of 4,4'-oxybismethylenebis(1,1'-chloroethylpyrazole) **XII**.

1-(2-Chloroethyl)-4-hydroxymethylpyrazole (V). Bp 118–120°C (1 mm Hg), n_D^{20} 1.5273. IR spectrum, ν, cm^{-1}: 1650 (ring), 3200–3400 (OH). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J,* Hz): 2.43 br.s (1H, OH), 3.84 t (2H, CH_2Cl, *J* 6.0), 4.36 t (2H, NCH_2, *J* 6.0), 4.54 s (2H, OCH_2), 7.43 s (1H, 3-H), 7.45 d (1H, 5-H). Found, %: C 44.37; H 5.21; Cl 22.51; N 17.84. $C_6H_9ClN_2O$. Calculated, %: C 44.85; H 5.60; Cl 22.11; N 17.44.

4,4'-Oxybismethylenebis(1,1'-chloroethylpyrazole) (XII). Bp 180–200°C (1 mm Hg), n_D^{20} 1.5585. IR spectrum, ν, cm^{-1}: 1560 (ring), 1100 (CH_2OCH_2). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J,* Hz): 3.86 t (4H, CH_2Cl, *J* 6.0), 4.42 t (4H, CH_2N, *J* 6.0), 4.61 s [4H, $O(CH_2)_2$], 7.41 s (1H, 3-H) 7.82 s (1H, 5-H). Found, %: C 47.91; H 5.78; Cl 23.20; N 18.13. $C_{12}H_{16}Cl_2N_4O$. Calculated, %: C 47.52; H 5.28; Cl 23.43; N 18.48.

1-(2-Chloroethyl)-3-methyl-4-hydroxymethylpyrazole (VI) was prepared similarly from 17.3 g of 1-(2-chloroethyl)-3-methyl-4-formylpyrazole **II**. Yield 12.8 g (75%), bp 128–130°C (1 mm Hg), mp 40–41°C, n_D^{20} 1.5310. IR spectrum, ν, cm^{-1}: 1560 (ring), 3100–3500 (OH). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J,* Hz): 2.15 br.s (3H, CH_3), 3.85 t (2H, CH_2Cl, *J* 6.1), 4.27 t (2H, NCH_2, *J* 6.1), 4.29 s (2H, OCH_2), 4.29 br.s (1H, OH), 7.39 s (1H, 5-H). ^{13}C NMR spectrum, δ_C, ppm: 11.2 (3-CH_3), 42.5 (CH_2Cl), 52.3 (NCH_2), 53.7 (OCH_2), 119.4 (C^4), 129.4 (C^3), 146.1 (C^2). Found, %: C 48.51; H 7.21; Cl 20.85; N 16.38. $C_7H_{11}ClN_2O$. Calculated, %: C 48.13; H 7.45; Cl 20.34; N 16.04.

1-(2-Chloroethyl)-5-methyl-4-hydroxymethylpyrazole (VII) and 4,4'-oxybismethylenebis(1,1'-chloroethyl-5-methylpyrazole (XIII) were prepared similarly from 17.3 g 1-(2-chloroethyl)-5-methyl-4-formylpyrazole **III**.

1-(2-Chloroethyl)-5-methyl-4-hydroxymethylpyrazole (VII). Yield 4.2 g (24.5%), bp 135°C (1 mm Hg), n_D^{20} 1.5316, viscous substance. IR spectrum, ν, cm^{-1}: 1560 (ring), 3100–3500 (OH). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J,* Hz): 2.25 br.s (3H, CH_3), 3.85 t (2H, CH_2Cl, *J* 6.2), 4.26 t (2H, NCH_2, *J* 6.2), 4.30 s (2H, CH_2OH), 7.23 s (1H, 3-H). ^{13}C NMR spectrum, δ_C, ppm: 8.75 (5-CH_3), 42.5 (CH_2Cl), 49.3 (NCH_2), 53.8 (OCH_2), 118.8 (C^4), 135.9 (C^3), 138.3 (C^2). Found, %: C 48.48; H 7.67; Cl 20.59; N 16.44. $C_7H_{11}ClN_2O$. Calculated, %: C 48.13; H 7.45; Cl 20.34; N 16.04.

4,4'-Oxybismethylenebis(1,1'-chloroethyl-5-methylpyrazole (XIII). Yield 4.5 g (27.2%), bp 210–230°C (1 mm Hg), n_D^{20} 1.5565. IR spectrum, ν, cm^{-1}: 1560 (ring), 1100 (CH_2OCH_2). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J,* Hz): 2.23 s (6H, CH_3), 3.9 t [4H, $(CH_2)_2Cl$, *J* 6.1], 4.21 s [4H, $O(CH_2)_2$], 4.32 t [4H, $(CH_2)_2N_2$, *J* 6.1] 7.21 s (2H, 3-H). Found, %: C 50.25; H 6.48; Cl 21.15; N 16.39. $C_{12}H_{16}Cl_2N_4O$. Calculated, %: C 50.75; H 6.04; Cl 21.45; N 16.91.

1-Vinyl-4-hydroxymethylpyrazole (IX). A mixture of 16.0 g of the freshly prepared 1-(2-chlororethyl)-4-hydroxymethylpyrazole **V** (without previous distillation), 11.2 g of potassium hydroxide, 1.2 g of triethyl-

benzylammonium chloride, 5 ml of water, and 50 ml of benzene was vigorously stirred at 70–75°C for 1 h. After cooling the organic layer was separated, washed with water, and dried over magnesium sulfate. Then benzene was removed, and the residue was distilled in a vacuum. Yield 7.4 g (59.6%), bp 105–110°C (1 mm Hg), n_D^{20} 1.5430. IR spectrum, ν, cm^{-1}: 1580 (ring), 1650 (C=C), 3100–3500 (OH). ^1H NMR spectrum (DMSO-d_6), δ, ppm (*J,* Hz): 2.63 t (1H, OH, *J* 4.8), 4.54 d (2H, OCH_2, *J* 4.8), 4.79 d. d (1H, $=CH_2$, *J* 8.9, 1.3), 5.43 d. d (1H, $=CH_2$, *J* 15.7, 8.9), 7.50 s (1H, 3-H), 7.56 s (1H, 5-H). Found, %: C 58.39; H 6.85; N 22.31. $C_6H_8N_2O$. Calculated, %: C 58.06; H 6.45; N 22.58.

1-Vinyl-3-methyl-4-hydroxymethylpyrazole (X) was prepared similarly from 17.4 g 1-(2-chloroethyl)-3-methyl-4-hydroxymethylpyrazole **VI**. Yield 11 g (80%), bp 101–102°C (1 mm Hg), n_D^{20} 1.5385, d_4^{20} 1.1064. IR spectrum, ν, cm^{-1}: 1580 (ring), 1640 (C=C), 3100–3500 (OH). ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J,* Hz): 2.20 s (3H, 3-CH_3), 4.31–4.33 m (2H, OCH_2), 4.39–4.42 m (1H, OH), 4.61 d (1H, $=CH_2$, *J* 8.8), 5.35 d (1H, $=CH_2$, *J* 15.7), 6.94 d. d (1H, =CH, *J* 15.7, 8.8), 7.59 s (1H, 5-H). Found, %: C 60.44; H 7.51; N 20.45. $C_7H_{10}N_2O$. Calculated, %: C 60.86; H 7.24; N 20.28.

1-Vinyl-5-methyl-4-hydroxymethylpyrazole (XI) was prepared similarly from 17.4 g of the freshly prepared 1-(2-chloroethyl)-3-methyl-4-hydroxymethylpyrazole **VII** (without previous distillation). Yiled 8.4 g (60%), bp 114–115°C (1 mm Hg), n_D^{20} 1.5412, d_4^{20} 1.1094. IR spectrum, ν, cm^{-1}: 1580 (ring), 1640 (C=C), 3100–3400 (OH). ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J,* Hz): 2.30 s (3-H, 5-CH_3), 4.23–4.26 m (2H, OCH_2), 4.16–4.20 m (1H, OH), 4.75 d (1H, $=CH_2$, *J* 8.8), 5.58 d (1H, $=CH_2$, *J* 15.3), 7.01 d. d (1H, =CH, *J* 15.3, 8.8), 7.36 s (1H, 3-H). Found, %: C 60.48; H 7.58; N 20.51. $C_7H_{10}N_2O$. Calculated, %: C 60.86; H 7.24; N 20.28.

The IR spectra were taken on a Specord 75-UR instrument (thin layer). The ^1H and ^{13}C NMR spectra were recorded on a Varian Mercury instrument (300 MHz).

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