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Aqueous Hydrolysis of 3-[2-(3-Methyl-1*H*-pyrazol-1-yl)-ethylamino]- and 3-[2-(5-methyl-1*H*-pyrazol-1-yl)ethylamino]-propanoates

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Abstract—Noncatalytic hydrolysis of methyl 3-[2-(3-methyl-1*H*-pyrazol-1-y)ethylamino]- and methyl 3-[2-(5-methyl-1*H*-pyrazol-1-yl)ethylamino]propanoates at 200°C was performed. According to X-ray diffraction data, the resulting acids exist exclusively as salts.

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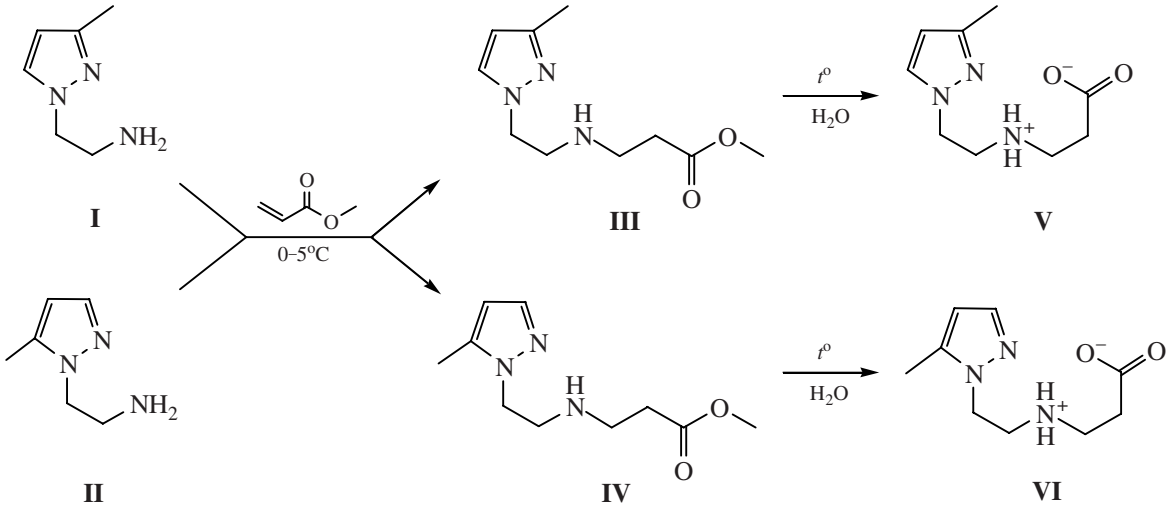
As is known, esters, including pyrazole derivatives [1–4], are hydrolyzed in the presence of acids or bases. We are the first to find that heating of compounds **III** and **IV** with water results in substitution of the methoxy group by the hydroxy group of water.

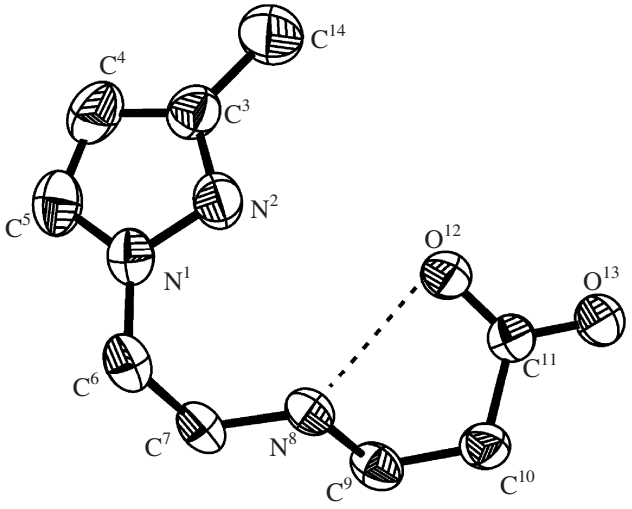
By X-ray structural analysis on an example of compound **V** we established that compounds **V** and **VI** exist exclusively in the salt form. A general view of a molecule of compound **V** is shown in the figure.

EXPERIMENTAL

The IR spectra were registered on a Specord UR-75 instrument from thin layers and KBr pellets. The ^{1}H NMR spectra were measured on a Varian Mercury-300 instrument.

Methyl 3-[2-(3-methyl-1*H*-pyrazol-1-yl)ethylamino]propanoate (III). Methyl acrylate, 25.8 g, was added dropwise with stirring to 12.5 g of 1-(β-aminoethyl)-3-methyl-1*H*-pyrazole (**I**) at 5–10°C, and the mixture was left to stand for one day at room temperature. Excess methyl acrylate was then distilled off, and the residue was distilled in a vacuum. Yield 85%, bp 130–135°C (1 mm Hg), n_D^{20} 1.4890. IR spectrum, ν, cm^{-1}: 1510 (ring), 1670 (C=O). ^{1}H NMR spectrum (DMSO-d_6, 300 MHz), δ, ppm: 1.65 br (1H, NH), 2.19 s (3H, 3-CH_3), 2.36 t (2H, CH_2CO, *J* 6.6 Hz), 2.80 t





General view of a molecule of compound **V**. Hydrogen atoms are omitted, the intramolecular H bond is shown by a broken line.

(2H, NC*H*$_2$CH$_2$CO, *J* 6.2 Hz), 2.91 t (2H, NCH$_2$, *J* 6.2 Hz), 3.60 s (3H, OCH$_3$), 4.00 t (2H, CH$_2$Ar, *J* 6.2 Hz), 5.82 d (1H, 4-H$_{pyr}$, *J* 2.2 Hz), 7.38 d (1H, 5-H$_{pyr}$, *J* 2.2 Hz). Found, %: C 56.39; H 8.32; N 19.68. $C_{10}H_{17}N_3O_2$. Calculated, %: C 56.87; H 8.06; N 19.91.

Methyl 3-[2-(5-methyl-1*H*-pyrazol-1-yl)ethylamino]propanoate (IV) was prepared similarly from 12.5 g of 1-(β-aminoethyl)-5-methyl-1*H*-pyrazole (**II**). Yield 80%, bp 140–145°C (1 mm Hg), n_D^{20} 1.4912. IR spectrum, ν, cm^{-1}: 1520 (ring), 1670 (C=O). ^{1}H NMR spectrum (DMSO-d_6, 300 MHz), δ, ppm: 1.60 br (1H, NH), 2.29 s (3H, 5-CH$_3$), 2.38 t (2H, CH$_2$CO, *J* 6.6 Hz), 2.78 t (2H, NCH$_2$CH$_2$O, *J* 6.6 Hz), 2.91 t (2H, NCH$_2$, *J* 6.6 Hz), 3.61 s (3H, OCH$_3$), 4.03 t (2H, CH$_2$Ar, *J* 6.2 Hz), 5.88 d (1H, 4-H$_{pyr}$, *J* 1.9 Hz), 7.17 d (1H, 3-H$_{pyr}$, *J* 1.9 Hz). Found, %: C 56.45; H 8.51; N 20.2. $C_{10}H_{17}N_3O_2$. Calculated, %: C 56.87; H 8.06; N 19.91.

3-[2-(3-Methyl-1*H*-pyrazol-1-yl)ethylamino]propanoic acid (V). Compound **I,** 5 g**,** and 15 ml of water were placed in a glass ampule. The ampule was sealed and heated in an oil bath at 200°C for 6 h. After cooling, the content was extracted with chloroform, and the aqueous layer was evaporated to dryness. The residual crystals were recrystallized. Yield 3.2 g (70%), mp 173°C (from isopropanol). IR spectrum, ν, cm^{-1}: 1540 (ring), 1670 (C=O). ^{1}H NMR spectrum (DMSO-d_6, 300 MHz), δ, ppm, *J* , Hz: 2.14 s (3H, CH$_3$), 2.29 t (2H, CH$_2$CO, *J* 6.6 Hz), 2.74 t (2H, NHC*H*$_2$CH$_2$CO, *J* 6.6 Hz), 2.91 t (2H, NHC*H*$_2$CH$_2$Ar, *J* 6.3 Hz), 4.08 t (2H, CH$_2$Ar, *J* 6.3 Hz), 4.36 br (2H, NH and COOH), 5.97 d (1H, 4-H$_{pyr}$, *J* 2.2 Hz), 7.55 d (1H, 5-H$_{pyr}$, *J* 2.2 Hz). Found, %: C 54.56; H 7.83; N 21.89. $C_9H_{15}N_3O_2$. Calculated, %: C 54.82; H 7.61; N 21.32.

3-[2-(5-Methyl-1*H*-pyrazol-1-yl)ethylamino]propanoic acid (VI) was prepared similarly from 5 g (0.024 mol) of compound **II**. Yield 3.4 g (72%), mp 178°C (from isopropanol). IR spectrum, ν, cm^{-1}: 1550 (ring), 1670 (C=O). ^{1}H NMR spectrum (DMSO-d_6, 300 MHz), δ, ppm, *J* , Hz: 2.25 s (3H, CH$_3$), 2.30 t (2H, CH$_2$CO, *J* 6.6 Hz), 2.76 t (2H, NHC*H*$_2$CH$_2$CO, *J* 6.6 Hz), 2.93 t (2H, NHC*H*$_2$CH$_2$Ar, *J* 6.4 Hz), 4.08 t (2H, CH$_2$Ar, *J* 6.4 Hz), 4.64 br (2H, NH and COOH), 5.99 d (1H, 4-H$_{pyr}$, *J* 1.9 Hz), 7.29 d (1H, 3-H$_{pyr}$, *J* 1.9 Hz). Found, %: C 54.31; H 7.72; N 22.16. $C_9H_{15}N_3O_2$. Calculated, %: C 54.82; H 7.61; N 21.32.

X-ray diffraction analysis. A crystal with the dimensions 0.3×0.25×0.2 mm was used. An Enraf Nonius CAD-4 automatic diffractometer was used to measure 4836 unique reflections. Compound **V** crystallizes in a monoclinic syngony [space group *C*2/*c*, *a* 24.246(6) Å, *b* 9.919(2) Å, *c* 10.619 (3) Å, β 115.46(3)°]. The structure was decoded by a direct method using the SHELXTL program. Hydrogen atoms were located from a difference Fourier syntheses. In the final step, the coordinates of all atoms, including hydrogens, and anisotropic thermal parameters of non-hydrogen atoms were refined together by full-matrix least squares. The atomic coordinates and other crystallographic data are available from the authors.

REFERENCES

1. Attaryan, O.S, Baltayan, A.O., and Matsoyan, S.G., *Chem. J. Arm.*, 2005, vol. 58, no. 4, p. 68.
2. Attaryan, O.S, Baltayan, A.O., and Matsoyan, S.G., *Zh. Obshch. Khim.*, 2007, vol. 77, no. 2, p. 325.
3. Attaryan, O.S, Antanosyan, S.K., Panosyan, G.a., Asratyan, G.V., and Matsoyan, S.G., *Zh. Obshch. Khim.*, 2006, vol. 76, no. 11, p. 1901.
4. Reutov, O.A., *Teoreticheskie problemy organicheskoi khimii* (Trheoretical Problems of Organic Chemistry), Moscow: Mosk. State Univ., 1956.