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# 4-Functionally-substituted 3-Heterylpyrazoles: XVI.* 3-(3-Arylpyrazol-4-yl)propyonic Acids

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**Abstract**—Bromination of 3-(3-arylpyrazol-4-yl)acrylic acids led to the formation of 2-bromo-3-(3-arylpyrazol-4-yl)acrylic acids that were converted into 3-(3-arylpyrazol-4-yl)propynoic acids by treatment of potassium hydroxide with an alcoholic solution.

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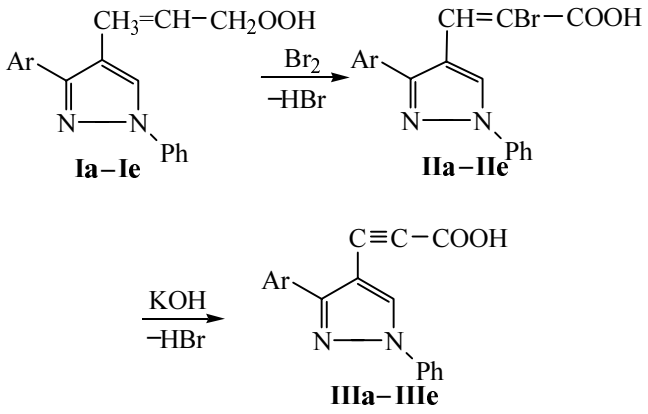
We reported formerly on convenient approach to a number of synthetically important pyrazole derivatives containing carboxy groups: 4-pyrazolecarboxylic [2], 4-pyrazoleacetic [3], 4-pyrazoleacrylic and propanoic [4] acids. Considering the chemical and biological importance of pyrazole acetylene derivatives [5–7] the development of convenient preparative synthesis of 3-pyrazolylpropynoic acids is urgent for the published data on these substances [8] are limited to two compounds, 3-(1-phenylpyrazol-4-yl)- and 3-(3,5-dimethyl-1-phenylpyrazol-4-yl)propynoic acids which were prepared by reaction of ethyl 2-bromo-3-(pyrazol-4-yl)-acrylates with the water solution of sodium hydroxide. At the use in this reaction of the 2-bromo-3-(pyrazol-4-yl)acrylic acids proper only the products were isolated of further transformations of pyrazolepropynoic acids, 4-acetylpyrazoles.

We found that certain structural changes in the position *3* of the pyrazole ring of the initial underlying compounds, 3-(pyrazol-4-yl)-acrylic acids, and also the use of a milder dehydrobrominating agent made it possible to obtain the target 3-(pyrazol-4-yl)propynoic acids directly from 2-bromo-3-(pyrazol-4-yl)-acrylic acids. To this end by bromination of (3-aryl-1-phenylpyrazol-4-yl)acrylic acids **Ia–If** with bromine in chloroform at room temperature we obtained in virtually quantitative yields (according to the data of $^1$H NMR spectra) 2-bromo-3-(pyrazol-4-yl)acrylic acids **IIa–IIf**. It is rational to use the latter in further transformations without additional purification since it has been demonstrated by an example of compound **IIc** that its recrystallization from the aqueous acetic acid has resulted in significant reduction of the yield. We carried out the dehydrobromination of acids **IIa–IIf** by heating them in 10% alcoholic solution of potassium hydroxide and obtained 3-(3-arylpyrazol-4-yl)propynoic acids **IIIa–IIIf** in 46-66% yields with respect to initial compounds **Ia–If**.




**I–III**, Ar = Ph (**a**), 4-$FC_6H_4$ (**b**), 4-$MeC_6H_4$ (**c**), 4-$PhC_6H_4$ (**d**), 3,4-$(MeO)_2C_6H_3$ (**e**), 3,4-$(OCH_2)_2C_6H_3$ (**f**).

The composition and structure of acids **IIIa–IIIf** are consistent with elemental analyses, IR and $^1$H NMR spectra. In the IR spectra appear the absorption band of the stretching vibrations of C=O (1700–1720 cm$^{-1}$), C≡C(2230–2235 cm$^{-1}$), and OH (2650–3000 cm$^{-1}$) bonds, whereas the range of the latter indicates the dimeric structure of the compounds in the solid state. $^1$H NMR spectra alongside the signals from the substituents Ar and

* For Communication XV, see [1].

Ph contain the singlets belonging to $C^5H$ protons of the pyrazole ring in the region 9.06–9.16 ppm.

Note in conclusion that acids **IIIa–IIIf** are hetero-analogs of phenylpropiolic acid which is widely used as a synthon in preparation of flavones and chromones [9–11], and consequently acids **IIIa–IIIf** also may be promising in this kind syntheses.

## EXPERIMENTAL

IR spectra of compounds were recorded on a spectrophotometer UR-20 from KBr pellets. $^1H$ NMR spectra were registered from solutions of compounds in DMSO-$d_6$ on a spectrometer Varian Gemini (300 MHz), internal reference TMS.

**3-(3-Aryl-1-phenylpyrazol-4-yl)propynoic acids IIIa–IIIf.** To a dispersion of 5 mmol of acid **Ia–If** in 20 ml of chloroform was added at stirring a solution of 1 g (6.25 mmol) of bromine in 10 ml of chloroform. After stirring for 2 h the reaction mixture was evaporated to dryness to obtain acids **IIa–IIf**. To the latter 30 ml of 10% solution of potassium hydroxide in ethanol was added, and the mixture was boiled for 3 h. On cooling to the reaction mixture 50 ml of water was added, the solution was filtered, the filtrate was acidified with 12% hydrochloric acid, the separated precipitate was filtered off, washed with water, dried, and crystallized from a mixture acetic acid–water, 2:1.

**Compound IIIa.** Yield 48%, mp 184–186°C. IR spectrum, $cm^{-1}$: 1700 (C=O), 2230 (C≡C), 2650–2980 (OH). $^1H$ NMR spectrum (DMSO-$d_6$)*, δ, ppm: 7.38–7.61 m ($6H_{arom}$), 7.92 d ($2H_{arom}$), 8.06 d (2H), 9.17 s (1H, $C^5H$). Found, %: C 74.61; H 4.09; N 9.48. $C_{18}H_{12}N_2O_2$. Calculated, %: C 75.00; H 4.17; N 9.72.

**Compound IIIb.** Yield 56%, mp 163–165°C. IR spectrum, $cm^{-1}$: 1710 (C=O), 2230 (C≡C), 2650–2900 (OH). $^1H$ NMR spectrum (DMSO-$d_6$), δ, ppm: 7.25–7.51 m ($5H_{arom}$), 7.93 d ($2H_{arom}$), 8.14 t ($2H_{arom}$), 9.08 s (1H, $C^5H$). Found, %: C 70.32; H 3.43; N 8.97. $C_{18}H_{12}FN_2O_2$. Calculated, %: C 70.59; H 3.59; N 9.15.

**Compound IIIc.** Yield 47%, mp 159–161°C. IR spectrum, $cm^{-1}$: 1715 (C=O), 2235 (C≡C), 2700–2950 (OH). $^1H$ NMR spectrum (DMSO-$d_6$), δ, ppm: 2.40 s (3H, $CH_3$), 7.29–7.52 m ($5H_{arom}$), 7.84–7.98 m ($4H_{arom}$), 9.09 s (1H, $C^5H$). Found, %: C 75.37; H 4.50; N 9.32. $C_{19}H_{14}N_2O_2$. Calculated, %: C 75.50; H 4.63; N 9.27.

**Compound IIId.** Yield 66%, mp 225–227°C. IR spectrum, $cm^{-1}$: 1720 (C=O), 2235 (C≡C), 2650–2900 (OH). $^1H$ NMR spectrum (DMSO-$d_6$), δ, ppm: 7.38–7.92 m ($14H_{arom}$), 9.17 s (1H, $C^5H$). Found, %: C 79.53; H 4.28; N 7.56. $C_{24}H_{16}N_2O_2$. Calculated, %: C 79.12; H 4.40; N 7.69.

**Compound IIIe.** Yield 52%, mp 165–166°C. IR spectrum, $cm^{-1}$: 1710 (C=O), 2235 (C≡C), 2670–2990 (OH). $^1H$ NMR spectrum (DMSO-$d_6$), δ, ppm: 3.84 s (3H, $CH_3O$), 3.89 s (3H, $CH_3O$), 7.02 d ($1H_{arom}$), 7.34–7.70 m ($5H_{arom}$), 7.93 d ($2H_{arom}$), 9.08 s (1H, $C^5H$). Found, %: C 68.64; H 4.48; N 8.01. $C_{20}H_{16}N_2O_4$. Calculated, %: C 68.97; H 4.60; N 8.05.

**Compound IIIf.** Yield 46%, mp 203–205°C. IR spectrum, $cm^{-1}$: 1715 (C=O), 2230 (C≡C), 2650–3000 (OH). $^1H$ NMR spectrum (DMSO-$d_6$), δ, ppm: 4.30 s (4H, $OCH_2CH_2O$), 6.90 d ($1H_{arom}$), 7.34 t ($1H_{arom}$), 7.50–7.61 m ($4H_{arom}$), 7.93 d ($2H_{arom}$), 9.07 s (1H, $C^5H$). Found, %: C 69.04; H 4.09; N 8.15. $C_{20}H_{14}N_2O_4$. Calculated, %: C 69.36; H 4.07; N 8.09.

**2-Bromo-3-[3-(4-tolyl)pyrazol-4-yl]acrylic acid (IIc).** Yield 51%, mp 275–278°C (acetic acid–water, 3:1). $^1H$ (DMSO-$d_6$), δ, ppm: 2.45 s (3H,$CH_3$), 7.36–7.49 m ($7H_{arom}$), 7.94 d ($2H_{arom}$), 8.11 s (1H, CH=), 9.22 s (1H, $C^5H$).

## REFERENCES


1. Bratenko, M.K., Panimarchuk, O.I., Mel'nichenko, N.V., and Vovk, M.V., *Zh. Org. Khim.,* 2005, vol. 41, p. 247.
2. Bratenko, M.K., Chornous, V.A., and Vovk, M.V., *Zh. Org. Khim.,* 2001, vol. 37, p. 587.
3. Vovk, M.V., Chornous, V.A., Tsymbal, I.F., and Bratenko, M.K., *Ukr. Khim. Zh*., 2002, vol. 68, p. 59.
4. Bratenko, M.K., Chornous, V.A., and Vovk, M.V., *Zh. Org. Khim.,* 2002, vol. 38, p. 1223.
5. Seela, F. and Zulauf, M., *J. Chem. Soc., Perkin Trans. 1*, 1999, vol. 4, p. 479.
6. Vasilevsky, S.F., Tretyakov, E.V., and Elguero, J., *Adv. Heterocycl. Chem*., 2002, vol. 81, p. 1.
7. Vasilesky, S.F., Klyatskaya, S.V., Tretyakov, E.V., and Elguero, J., *Heterocycles*, 2003, vol. 60, p. 879.
8. Finar, Y.F. and Okoh, E., *J. Chem. Soc., Perkins Trans. 1*, 1973, vol. 18, p. 2008.
9. McGarry, L.W. and Detty, M.R., *J. Org. Chem*., 1990, vol. 55, p. 4349.
10. Singh, I., Kour, I., Nayyor, S., and Kad, G., *J. Chem. Res. Synop*., 1998, vol. 5, p. 280.
11. Jia, Ch., Lu, W., Oyamoda, J., Kitamura, T., Matsuda, V., and Fujiwara, T., *J. Am. Chem. Soc*., 2000, vol. 122, p. 7252.


* Proton signals of the COOH group coincide with the proton signals of $H_2O$ (3.30–3.60 ppm) present in the DMSO-$d_6$.