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LETTERS TO THE EDITOR

Synthesis, Structure and Hydrazinolysis of 4-(4-Bromo-3,5-dimethyl-1*H*-pyrazol-1-yl)benzaldehyde

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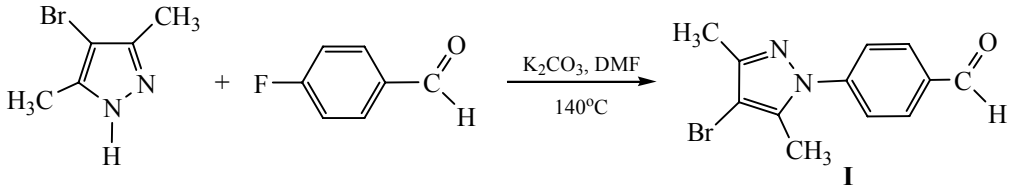
Pyrazole derivatives are used as anti-inflammatory and analgesic drugs, so the synthesis of new representatives of this class of compounds is one of the most promising directions in the search for new biologically active compounds [1, 2]. Since aldehydes are important reagents in organic synthesis of various compounds including heterocyclic, it was interesting to obtain an aromatic aldehyde based on 4-bromo-3,5-dimethylpyrazole and 4-fluoro-benzaldehyde.

However, the nucleophilic substitution reaction involving fluorobenzaldehyde requires prolonged heating [3], due to the nature of the C–F bond. We found that the synthesis of 4-(4-bromo-3,5-dimethyl-1*H*-pyrazol-1-yl)benzaldehyde **I** can be successfully carried out in DMF under the microwave activation and the catalysis with a specially prepared catalyst supported on silica gel Silpearl activated with potassium carbonate (Scheme 1).

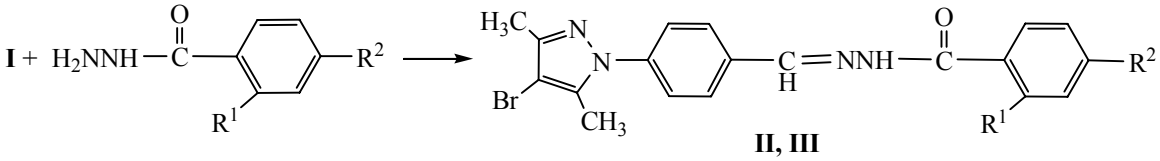
In addition, we performed this reaction under classical conditions (K_2CO_3, DMF, reflux, 18–20 h). The synthesized 4-(4-bromo-3,5-dimethyl-1*H*-pyrazol-1-yl)benzaldehyde **I** is a reactive synthon which is of

Scheme 1.



I

Scheme 2.



II, III

R^1 = OH, R^2 = H (**II**); R^1 = H, R^2 = OH (**III**).

interest for a variety of chemical transformations. Thus, the reaction of aldehyde **I** with hydrazides of *ortho*- and *para*-hydroxybenzoic acids in alcoholic medium resulted in the formation of hydrazones **II** and **III** in 85 and 44% yields respectively (Scheme 2).

Composition and structure of the synthesized compounds **I**–**III** were confirmed by elemental analysis, ^{1}H NMR and IR spectra.

4-(4-Bromo-3,5-dimethyl-1*H*-pyrazol-1-yl)benzaldehyde (I). *a. Under microwave irradiation.* To a solution of 0.62 g (0.005 mol) of 4-fluorobenzaldehyde in 10 mL of DMF was added 1 g (0.0056 mol) of 4-bromo-3,5-dimethylpyrazole and 1.54 g of catalyst. The reaction mixture was subjected to microwave irradiation in a Monowave 300 Anton Paar (Austria) apparatus at 140°C for 5 h. After the reaction completion the mixture was filtered and evaporated. The resulting precipitate was recrystallized from 2-propanol. Yield 0.92 g (66%), mp 109–110°C. IR spectrum, ν, cm^{-1}: 1685 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.12 s (3H, CH_3), 2.39 s (3H, CH_3), 7.79 d (1H, CH_{arom}, J_{HH} 7.8 Hz), 8.05 d (1H, CH_{arom}, J_{HH} 7.9 Hz), 10.07 s [1H, C(O)H]. Found, %: C 52.83; H 4.17; N 10.19. $C_{12}H_{11}N_2OBr$. Calculated, %: C 51.63; H 3.97; N 10.04.

b. Under classical conditions. To a solution of 1.24 g (0.01 mol) of 4-fluorobenzaldehyde in 20 mL of DMF was added 2 g (0.0113 mol) of 4-bromo-3,5-dimethylpyrazole and 2.07 g (0.015 mol) of potassium carbonate. The reaction mixture was heated on a glycerol bath at 140–150°C for 20 h. The reaction progress was monitored by TLC. After cooling potassium carbonate was filtered off, and the solvent was evaporated. The residue was recrystallized from 2-propanol. Yield 1.68 g (60%).

2-Hydroxy-*N*-[4-(4-bromo-3,5-dimethyl-1*H*-pyrazol-1-yl)benzylidene]benzoylhydrazide (II). To a solution of 0.23 g (0.00083 mol) of benzaldehyde **I** in 5 mL of ethanol was added 0.13 g (0.00083 mol) of *o*-hydroxybenzoic acid hydrazide. The reaction mixture was heated at 50°C for 15 min. The resulting precipitate was filtered off, washed with ethanol, and recrystallized from 2-propanol. Yield 0.15 g (44%), yellow powder, mp 169–170°C. IR spectrum, ν, cm^{-1}: 1665 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.21 s (3H, CH_3), 2.34 s (3H, CH_3), 7.59 d (1H, CH_{arom}, J_{HH} 7.4 Hz), 7.87 d (1H, CH_{arom}, J_{HH} 7.8 Hz), 6.71 d (1H, CH^1_{arom}, J 8.7 Hz), 7.21 t (1H, CH^2_{arom}, J 7.8 Hz), 6.59 t (1H, CH^3_{arom}, J 7.4 Hz), 7.82 d (1H, CH^4_{arom}, J 8.7 Hz), 8.39 s (1H, CH=N), 14.02 br.s (1H, OH), 14.08 br.m (1H, NH). Found, %: C 55.72; H 4.65; N 14.06. $C_{19}H_{17}BrN_4O_2$. Calculated, %: C 55.22; H 4.15; N 13.56.

4-Hydroxy-*N*-[4-(4-bromo-3,5-dimethyl-1*H*-pyrazol-1-yl)benzylidene]benzoylhydrazide (III) was prepared similarly from benzaldehyde **I** and *p*-hydroxybenzoic acid hydrazide. Yield 85%, mp 248–249°C (2-propanol). IR spectrum, ν, cm^{-1}: 1668 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.19 s (3H, CH_3), 2.32 s (3H, CH_3), 7.59 d (1H, CH_{arom}, J_{HH} 7.4 Hz), 7.87 d (1H, CH_{arom}, J_{HH} 7.8 Hz), 6.68 d (1H, CH_{arom}, J_{HH} 8.7 Hz), 7.75 d (1H, CH_{arom}, J_{HH} 8.7 Hz), 8.4 s (1H, CH=N), 13.95 br.s (1H, OH), 14.05 br.m (1H, NH). Found, %: C 55.57; H 4.49; N 13.81. $C_{19}H_{17}BrN_4O_2$. Calculated, %: C 55.22; H 4.15; N 13.56.

IR spectra of the compounds **I**–**III** were recorded on a Nicolet Avatar-320 spectrometer from KBr pellets. ^{1}H NMR spectra were registered on a Bruker DRX500 spectrometer (500 MHz) in DMSO-d_6 solution, internal reference TMS. Melting points were determined on a Boetius instrument. TLC analysis was performed using Sorbfil plates, eluting with 2-propanol–benzene–ammonia mixture (10 : 5 : 2) and detecting with iodine vapor.

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