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LETTERS TO THE EDITOR

Biginelli Reaction under Microwave Irradiation Conditions without a Solvent

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Scientific interest in 3,4-dihydropyrimidinethiones, structural analogs of 1,4-dihydropyridines, steadily grows in view of their potential biological activity [1].

The Biginelli reaction is a well-studied process, but its principal disadvantage is a long reaction time. In DMF with chlorotrimethylsilane as a catalyst, this reaction completes in 2–3 days [2]. In ethanol with iron(III) or nickel(II) chloride as a catalyst, this reaction proceeds for 6–8 h [3]. Using ruthenium(III) chloride allows the reaction times to be decreased to 30 min [4].

We used the example of condensation of benzaldehyde, thiourea, and ethyl acetoacetate to find out whether the Biginelli reaction can be performed under conditions of microwave irradiation without a solvent. As catalysts we applied *N*-bromosuccinimide and sulfuric acid adsorbed on silica gel.

To carry out this reaction, we mixed in a flat-bottom heat-resistant flask 1.3 g of ethyl acetoacetate, 1.06 g of thiourea, and 1.06 g of benzaldehyde, after which 0.35 g of commercial *N*-bromosuccinimide was added. The reaction mixture was subjected to microwave irradiation. It was found that the best yield can be achieved under irradiation with a power of 150 W for 3–5 min with a 30-min break after every one minute of heating. The product was purified by recrystallization from ethanol, yield 2.07 g (75%).

This synthesis was also carried out on a silica gel support. To 5 g of silica gel we added 0.5 g of conc. H_2SO_4 and 20 ml of ethanol. The mixture was thoroughly stirred, and ethanol was then removed by rotary evaporation. Thus prepared silica gel was placed to a flat-bottom heat-resistant flask, and then 1.06 g (0.014 mol) of thiourea, 1.06 g (1.02 ml, 0.01 mol) of benzaldehyde, and 1.3 g (1.26 ml, 0.01 mol) of acetoacetic ester were added. The mixture was thoroughly stirred and then heated for 30 s in a microwave device at the irradiation power 800 W. The yield of the reaction product was 1.8 g (65%).

The samples of ethyl 4-methyl-6-phenyl-2-thioxo-1,2,3,6-tetrahydropyrimidine-5-carboxylate, obtained by two methods, has similar physicochemical and spectral characteristics (mp 201–203°C). ^{1}H NMR spectrum, δ, ppm: 1.09 t (3H), 2.27 s (3H), 3.99 q (2H), 5.15 d (1H), 7.20–7.35 m (5H), 9.63 s (1H), 10.29 s (1H). IR spectrum, ν, cm^{-1}: 1573.66, 1671.54, 3174.29, 3327.48. Mass spectrum: *m/z* 276.31 (M^+). Found, %: C, 60.78; H, 5.90. $C_{14}H_{16}O_2N_2S$. Calculated, %: C, 60.85; H, 5.84.

The IR spectra were obtained on a NICOLET AVATAR-320 FTIR spectrometer in KBr. The ^{1}H NMR spectra were measured on a Bruker DRX-500 spectrophotometer at 500 MHz in DMSO-d_6 against internal TMS. The mass spectra were taken on an MX-1321 instrument with direct inlet at an ionizing energy of 70 eV. The melting points were measured on a Boetius hot stage. The experiments were performed using an LG MS2022H microwave oven.

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