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> LETTERS TO THE EDITOR

Microwave-Assisted Three-Component Cyclocondensation of Thiourea, Ethyl Acetoacetate, and Substituted Benzaldehydes

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A typical Biginelli reaction involving ethyl acetoacetate, aldehyde, and thiourea under the standard conditions is carried out in the presence of hydrochloric or sulfuric acid, more preferred is the use of inorganic salts, the Lewis acids [1]. The main drawback is the long reaction time. We investigated the three-component condensation of thiourea, ethyl acetoacetate, and *p*-substituted benzaldehyde derivatives in the Biginelli reaction either at the simple heating or microwave irradiation. If the reaction is carred out in the boiling ethyl alcohol using $MnCl_2 \cdot H_2O$ as a catalyst, it is completed within 6–8 h. The use of microwave irradiation makes it possible to reduce the reaction time to 150 min at 750 W.



The optimization of the reaction conditions was carried out by varying the reaction time (from 1 to 180 min) and the irradiation power (from 75 to 750 W) with a frequency of 2450 MHz (LG MS2022G) in the medium of solvents like ethanol and dimethylform-amide.

The structure of the obtained 5-(ethoxycarbonyl)-4-(4-*R*-phenyl)-6-methyl-3,4-di-hydropyrimidine-2(1H)thiones **I–III**) was confirmed by the analytical and spectral data, which were consistent with those of the other 3,4-dihydropyrimidinethiones [1–3]. Thus, the behavior of the reaction components under the microwave irradiation conditions does not differ from that under the conventional heating conditions. Some synthetic features can be attributed to the behavior in the microwave field [4].

The ¹H NMR spectra of compounds **I–III** were recorded on a Bruker AM-400 spectrometer in DMSO d_6 using TMS as a reference. The purity of the compounds obtained was monitored by TLC (Silufol UV-254, eluent CHC1₃–EtOH). The melting points were determined on a Boetius melting point apparatus.

5-Ethoxycarbonyl-4-phenyl-6-methyl-3,4-dihydropyrimidine-2(1*H***)-thione (I). A mixture of 0.55 g of benzaldehyde, 0.48 g of ethyl acetoacetate, 0.3 g of thiourea, 0.25 g of MnCl₂·4H₂O, and 50 ml of DMF was subjected to microwave irradiation for 150 min with intermissions. After cooling, the resulting pre-** cipitate was filtered off, washed with water, dried, and recrystallized from ethanol. Yield 0.63 g (62%), mp 208–210°C. ¹H NMR spectrum (DMSO-*d*₆), δ , ppm: 1.08–1.12 t (3H, <u>CH</u>₃CH₂O), 2.29 s (3H, CH₃C), 4.03 q (2H, CH₃<u>CH</u>₂O, *J* 7.2 Hz), 5.09 s (1H, N<u>CH</u>Ar), 5.16–5.21 d (2H, CH_{Ar}, *J* 8.0 Hz), 7.33–7.37 d (2H, CH_{Ar}, *J* 8.0 Hz), 9.63 s (1H, NH), 10.31 s (1H, NH). Found, %: C 60.91; N 10.20. C₁₄H₁₆N₂O₂S. Calculated, %: C 60.85; N 10.14.

5-Ethoxycarbonyl-4-(4-methoxyphenyl)-6-methyl-3,4-dihydropyrimidine-2(1*H***)-thione (II) was synthesized similarly. Yield 0.58 g (50%), mp 152–153°C. ¹H NMR spectrum (DMSO-d_6), \delta, ppm: 1.10 t (3H, <u>CH</u>₃CH₂O), 2.24 s (3H, CH₃C), 3.71 t (2H, NCH₂<u>CH</u>₂O), 3.98 q (2H, CH₃<u>CH</u>₂O,** *J* **7.0 Hz), 5.09 s (1H, N<u>CH</u>Ar), 6.88 d (2H, CH_{Ar},** *J* **8.0 Hz), 7.15 d (2H, CH_{Ar},** *J* **8.4 Hz), 9.17 br. s (1H, NH), 10.25 s (1H, NH). Found, %: C 58.95; N 9.03. C₁₅H₁₈N₂O₃S. Calculated, %: C 58.80; N 9.14.**

5-Ethoxycarbonyl-4-(4-morpholinophenyl)-6methyl-3,4-dihydropyrimidine-2(1*H***)-thione (III)** was synthesized similarly. Yield 1.05 g (81%), mp 263–264°C. ¹H NMR spectrum (DMSO- d_6), δ , ppm: 1.10–1.13 t (3H, <u>CH</u>₃CH₂O), 2.27 s (3H, CH₃C), 3.05– 3.09 t (2H, N<u>CH</u>₂CH₂O), 3.70–3.73 t (2H, NCH₂<u>CH</u>₂O), 3.98–4.03 q (2H, CH₃<u>CH</u>₂O), 5.07 d (1H, N<u>CH</u>Ar), 6,89 d (2H, CH_{Ar}, J 8.0 Hz), 7.06 d (2H, CH_{Ar}, J 8.6 Hz), 9.56 br. s (1H, NH), 10.20 s (1H, NH). Found, %: C 59.96; N 11.75. C₁₈H₂₃N₃O₃S. Calculated, %: C 59.81; N 11.63.

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