Effects of nanosized metal oxides on regio- and stereo-features for the synthesis of dihydroazolopyrimidines

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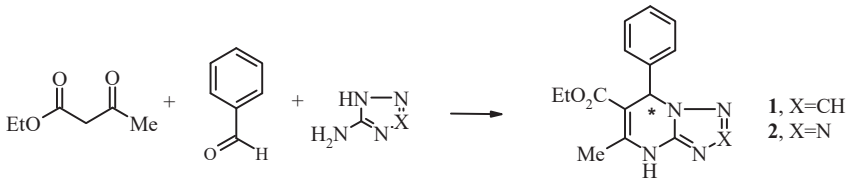
Substituted dihydroazolopyrimidines **1** and **2** have been prepared by the multicomponent Biginelli reaction with urea isosteres, such as 3-amino-1,2,4-triazole and 5-aminotetrazole [1]. It has been established that the formation of dihydroazolopyrimidines requires a more hard reaction conditions (7-8 hours of reflux in DMF) and proved to be a less selective process than the classical Biginelli reaction leading to dihydropyrimidines [2].

For the first time the effects of nanosized metal oxides (CuO, Al_2O_3, ZnO, MgO, TiO_2-SiO_2), including the presence of chiral modifiers, on regio- and stereoselective features of the multicomponent synthesis of dihydroazolopyrimidines **1** and **2** have been studied (scheme 1). Using of nanosized system TiO_2-SiO_2 allowed one to optimize the synthesis of **2,** to reduce the reaction temperature from 80 °C to 22 °C, and to enhance content of the target compound up to 90-92% according to HPLC. It has been shown that the presence of nanosized TiO_2-SiO_2, ZnO and chiral modifiers (quinine sulfate, *L*-proline, *D*-proline, 5-oxy-*L*-proline, *D*-aspartic acid) enables one to improve stereoselectivity of the synthesis of dihydroazolopyrimidines **1** and **2**. Also it is worth to note that use of chiral modifiers without nanosized metal oxides has no effect on stereoselectivity of the reaction.

Dependence of enantiomeric excess of **1** on the ratio of SiO_2 and TiO_2 has shown that the best results can be achieved with the catalyst bearing 18% of TiO_2. By using of this nanosized metal oxide, *L*-proline and DMF as solvent the *ee* has been enhanced up to 30-45%. In case of derivatives **2** the presence of ZnO and *L*-proline provided the value of 20% for the dihydrotetrazolopyrimidines **2**.



Scheme 1. Synthesis of dihydroazolopyrimidines

Reference

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