

ISATIN-BASED BIGINELLI-LIKE REACTIONS

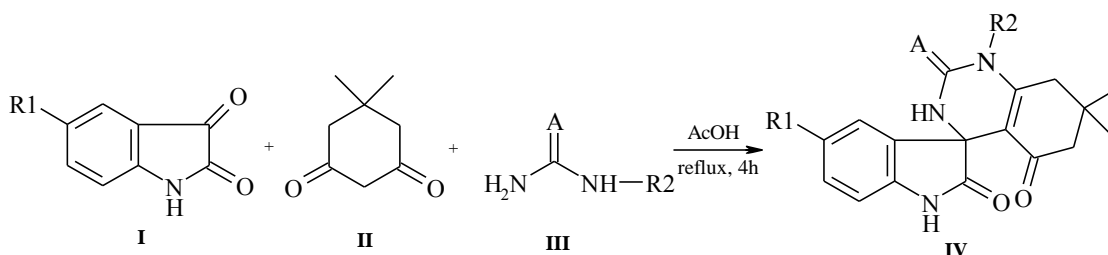
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Introduction. More than 100 years ago Italian chemist Pietro Biginelli discovered the acid-catalyzed three-component interaction of ethyl acetoacetate with benzaldehyde and urea that led to 3,4-dihydropyrimidin-2(1*H*)-ones. At first it didn't draw a lot of attention, but later the products were considered to reveal such valuable biological activities as anticancer, anti-inflammatory, antibacterial, antiviral, calcium channel blocking etc. Therefore the scope of this reaction has been extended broadly. Nowadays literature data include different structural variations of initial compounds, catalysts applied and reaction modes of classical Biginelli reaction. Nevertheless the selection of the most suitable conditions for each type of possible interactions remains a challenging task.

Aim. Our research was dedicated to the study of Biginelli-like interaction of isatins with dimedone and (thio)ureas (or their N-substituted derivatives) in acetic acid medium. We also aimed to determine the structure of the obtained compounds.

Materials and methods. Isatins, dimedone, (thio)ureas and their N-substituted derivatives were used as starting materials. In order to achieve the research goals, the methods of organic synthesis and ¹H NMR spectroscopy were also used.

Results and discussion. Previously the reaction between isatin, dimedone and urea was reported to pass smoothly in ethanol using HCl as a catalyst. We applied a new reaction conditions for such type of interaction, namely glacial acetic acid was used as solvent and acidic catalyst simultaneously. In general the studied interaction of isatins (I) with dimedone (II) and (thio)ureas (III) (the molar ratio 1:1:1.25) was carried out in refluxing AcOH for 4 hours. As a result compounds IV were isolated in high yields. The products are yellow precipitates, which can be recrystallized from ethanol. The structures of obtained compounds were confirmed using ¹H NMR spectroscopy.



R₁ = H, CH₃; R₂ = H, Ph, Ac; A = O, S

Conclusions. Thus, we have demonstrated convenient and beneficial novel reaction mode for the Biginelli-like interaction of isatins with dimedone and (thio)ureas, which led to the formation of compounds IV in high yield.