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The use of type-MCM-48/TiO₂ mesoporous materials in the Betti Reaction to synthesize hybrids 1,3-oxazines-4-methyl coumarins, potential anticancer hits.

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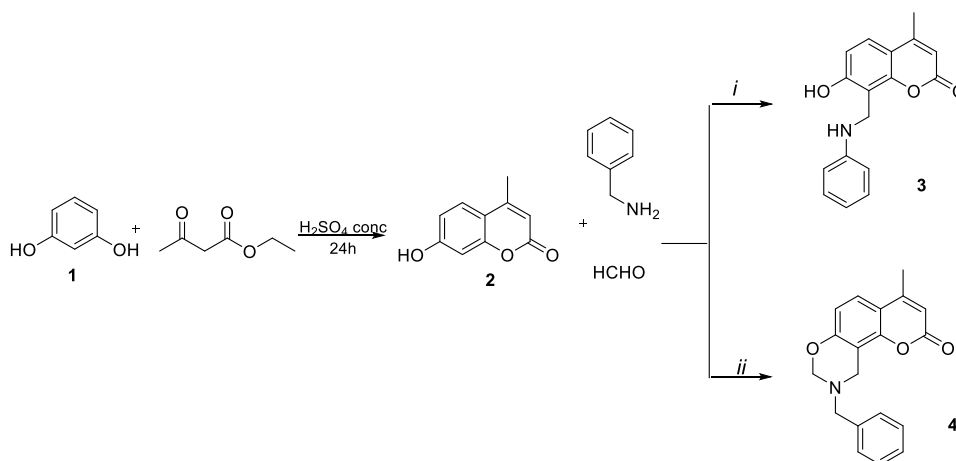
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ABSTRACT

Coumarins are oxygenated heterocycles, widely distributed in nature, that have several pharmacological activities, including anticancer. These facts attract medicinal chemists to the synthesis of compounds containing this fragment.¹ The Betti reaction is a multicomponent reaction that consists of a α -aminomethylation of phenolic compounds. In this work, we used Betty reaction with coumarin **2**, HCHO and benzylamine or propylamine in various situations. The following three components conditions were tested: a) reactions at room temperature (7 days), under reflux (overnight) or in microwaves (7 minutes) b) in water or water:ethanol mixture c) without catalyst d) with catalyst (zeolites). The conditions that provided the 1,3-oxazine-coumarin hybrid **4** and compound **3** was the use of type-MCM-48/TiO₂ mesoporous materials, ethanol in reflux (overnight) as depicted in Fig.1. Initial yields are moderate (<50%) but we are optimizing the reaction conditions as well as performing with other aldehydes and amines.



Conditions: i) MCM-48/TiO₂, 10%, EtOH, reflux, overnight, coumarin1 (1 equiv.), benzylamine (1 equiv.), HCHO (1 equiv.) ii) MCM-48/TiO₂, 10%, EtOH, reflux, overnight, coumarin1 (1 equiv.), benzylamine (1 equiv.), HCHO (2 equiv.)

Figure 1

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