New Approach for the Construction of the Coumarin Frame and Application in the Total Synthesis of Natural Products

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A new synthetic approach is described for building the coumarin scaffold through the *Lewis* acid-promoted cyclization of novel aryl 3-(dimethylamino)prop-2-enoates **2a**–**2f**. The latter precursors were prepared *via* aminomethylenation of the corresponding aryl acetates **4a**–**4f** with the *Bredereck* reagent. This approach was used for the synthesis of biologically active natural compounds **1a**–**1f**, through a three-step procedure starting from the corresponding phenols.

1. Introduction. – Coumarins (=2*H*-1-benzopyran-2-ones) are some of the most abundant metabolites found in extracts of many plant families, such as *Orchidaceae*, *Rutaceae*, *Euphorbiaceae*, and *Asteraceae*, among others, and occur in several parts of the plant [1]. The biogenetic route of coumarins follows the shikimate biosynthesis [2]. They have attracted widespread interest in view of their biological activity and potential as pharmacological agents [3], since they have exhibited inhibitory properties in platelet aggregation [4], as well as antibacterial action [5], and antifungal [6], antitumor [7], and antiviral activities [8]. Accordingly, diverse synthetic strategies have been reported to build their benzo-heterocyclic scaffold [9]. Among them, *Pechmann* reaction is a common and useful method, starting from phenols and β-dicarbonyl compounds, or the latter can be replaced by a propiolate or a 5-alkylidene *Meldrum*'s acid [10]. Both methods involve a C(4)–C(4a) bond-formation through the cyclization step. Moreover, the coupling reactions, catalyzed by transition-metal complexes, the *Wittig* reaction, and the ring-closing metathesis, among others, have resulted in very efficient strategies to prepare functionalized coumarins [11].

Recently, we designed a new method for the preparation of benzofurans [12], which was successfully extended to the synthesis of indoles [13]. This method was based on the formation of the heterocycle by a *Lewis* acid-promoted cyclization of the properly functionalized enaminones. With the aim of evaluating the versatility of this strategy in the construction of the benzo-six-membered heterocyclic framework, we investigated the preparation of coumarins, and their application in the total synthesis of naturally occuring metabolites. Among these targets, we chose the biologically active coumarin