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Abstract

Synthesis and Chemical Reactivity of Novel Polyhydroxylated *Bis*-Chalcones †

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Abstract: Chalcones, a class of compounds characterized by two aromatic rings linked through a three carbon α,β-unsaturated carbonyl system, aroused widespread interest due to their (bio)synthesis and broad biological activities. However, less attention has been given to a subcategory of chalcones, *bis*-chalcones, despite some studies suggesting that they have improved bioactivities in comparison to their mono derivatives. Their synthesis is relatively less explored and typically requires longer reaction times and harder purifications, especially for derivatives with free hydroxy groups. This issue is relevant because several activities of *bis*-chalcones have been associated with the presence of hydroxy groups in the structure. In this context, the objectives of this work were to establish an efficient methodology for the synthesis of novel polyhydroxylated *bis*-chalcones and *bis*-chalcones containing other substituent groups such as halogen, methoxy, and prenyl groups and explore their chemical reactivity for further transformation into other potentially bioactive flavonoids. Herein, we report our most recent results on the synthesis of *bis*-chalcones and their transformation into *bis*-flavones. *Bis*-chalcones were obtained in good yields (50–80%) by basic catalyzed Claisen–Schmidt condensation of methoxymethyl (MOM)/Me-protected *bis*-acetophenones with aromatic aldehydes, followed by deprotection of MOM groups in an acidic medium. In turn, a prenylated *bis*-chalcone was prepared by O-prenylation of the hydroxylated *bis*-acetophenone followed by Claisen rearrangement and Claisen–Schmidt condensation with 4-methoxymethylbenzaldehyde. Afterwards, some unprotected *bis*-chalcones were successfully cyclized into *bis*-flavones through cyclodehydrogenation with I_2/ dimethyl sulfoxide (DMSO). In the future we intend to evaluate the anti-inflammatory activity of these compounds.

Keywords: *bis*-chalcones; flavonoids; synthesis; Claisen–Schmidt condensation; cyclodehydrogenation

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