

Semisynthetic studies of melleins using cashew nut shell liquid

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Mellein and the related 3,4-dihydroisocoumarins are a family of natural products which are mainly isolated from fungi such as *Aspergillus*, *Ceratocystis*, *Cladosporium*, *Fusarium* and *Penicilium*. Other sources of mellein-type 3,4- dihydroisocoumarins are bacteria, lichens, higher plants, insects and marine sponges. These natural products are known to exhibit interesting biological properties such as phytotoxic, neurotoxic, antibacterial and antifungal properties. This dissertation reports on the synthesis of the mellein-type 3,4-dihydroisocoumarin 39 {i.e., 8-methoxy-3-tridecyl-3,4-dihydroisocoumarin or 8-methoxy-3-tridecylisochroman-1 - one), and its precursors, namely, methyl 2-methoxy-6-pentadecylbenzoate (37), methyl 2-methoxy-6-pentadecanoylbenzoate (38) and (£)-methyl 2-methoxy-6- (pentadec-1-enyl)benzoate (19). Anacardic acid (12), which is the starting material in the synthesis of compounds 19, 37, 38 and 39, was obtained from Cashew Nut Shell Liquid (CNSL) in an overall yield of 78%. The transformation of 12 to 39 involved protection of the reactive phenolic and carboxylic acid groups of compound 12 through methylation followed by hydrogenation so as to saturate the mono-, di- and tri-unsaturated C15 chains of anacardic acid (12). Subsequent benzylic oxidation and reduction of the keto functional group with concomitant dehydration of the alcohol led to the formation of 19. Deprotection of the carboxyl group using AlCl_3 followed by lactonization under the same reaction conditions led to the mellein-type 3,4- dihydroisocoumarin 39. On the other hand, 3-hydroxybenzaldehyde (43) and tetradecanal (44) were inadvertently obtained following a similar route as the one described for the synthesis of compound 19 but using acetic anhydride as a reagent for protecting the phenolic group in anacardic acid. However, ozonolysis of the product obtained after reduction and dehydration of what was thought to be a 6-pentadecanoylbenzoic acid derivative similar to 38 gave compounds 43 and 44 in 38% and 45% yields, respectively.