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A Short Synthesis of Cordiachromene

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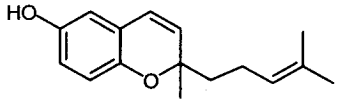
Abstract: Cordiachromene was synthesized from 5-methyl hept-5-en-2-one by using a Claisen rearrangement

Keywords: benzopyrans, chromenes, rearrangements, alkynes.

There are many examples of biologically active compounds containing the benzopyran or 3,4-dihydrobenzopyran nucleus. These nuclei are present in cannabinoids such as cannabichromene[1], ubichromenol[2] or cordiachromene. At first, cordiachromene was isolated from *Cordia alliodora* Ruiz. and Pav.[3] which is a native tropical American tree whose wood is recognized for its durability in marine use.[4] More recently, cordiachromene was isolated from *Aplidium antillense*[5] and *Aplidium constellatum*.[6] This chromene shows antibacterial activity against *Staphylococcus aureus*.[5] It also demontrates anti-inflammatory activity[7] and seems to act by a specific inhibition of cyclooxygenase.[7]



Cordiachromene

Syntheses of substituted 3,4-dihydrobenzopyran nuclei can be achieved by using a cyclization of phenols substituted by an *ortho* isoprenic side chain followed by a dehydrogenation with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ),[8] by using a cyclization of substituted quinones in refluxing pyridine,[9] or by using a Claisen rearrangement of propargyl ethers.[10] Of the methods available, we found that a Claisen rearrangement applied to propargyl ether **4** was the most suitable method to synthesize cordiachromene. After treatment of 5-methyl hept-5-en-2-one with ethynylmagnesium bromide (ether/THF: 1/1; yield: 90%), propargyl alcohol **2** was obtained and condensed with hydroquinone monoacetate **3** [$(CF_3CO)_2O$; DBU; CH_3CN, 0 °C][11] to produce propargyl ether **4** (yield: 75%). The transformation of propargyl ether **4** to the corresponding 2*H*-1-benzopyran **5** was achieved by heating **4** at 150 °C in DMF containing *N*,*N*-diethylaniline[12] (85% yield). After alkaline

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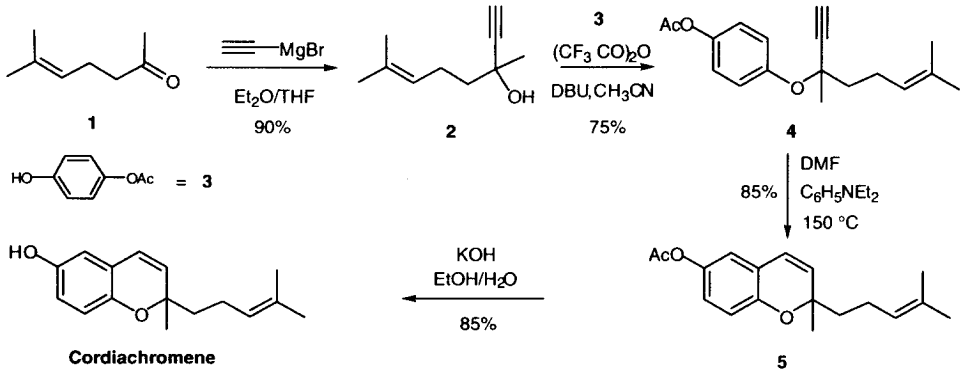
hydrolysis (KOH, EtOH/H_2O), cordiachromene was isolated with a yield of 85%. Cordiachromene was synthesized from 5-methyl hept-5-en-2-one, in 4 steps with an overall yield of 50%

Scheme: Synthesis of cordiachromene from 5-methyl hept-5-en-2-one.



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