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Synthesis Of (±)-2-Methyl-(2'-Hydroxy-4'- Methylphenyl)-2-Hepten-4-One (Turmeronol B)

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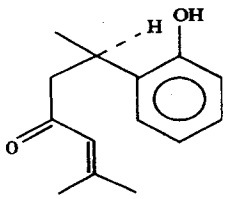
Abstract: The first total synthesis of the racemic compound is described. 2-hydroxy-4-methylacetophenone was used as starting material and transformed into the target molecule in 6 steps. The synthetic Turmeronol B displays spectral properties identical to those reported for the natural compound leading to the confirmation of the proposed structure.

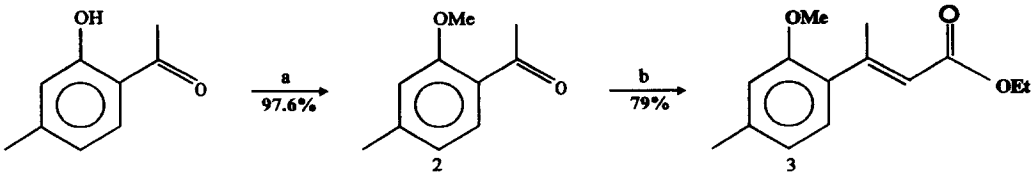
The various functional properties of Soybean protein such as emulsifying, foaming, and hydration, render it as a good food processing material. The large quantities of lipoxygenase present in soybean seeds catalyses the oxidation of useful unsaturated fatty acids possessing cis, cis-1,4-pentadiene moieties such as linoleic acid, arachidonic acid etc., into volatile carbonyl compounds (mainly aldehydes), causes an undesirable greasy-beany flavor of soybean material during food processing.

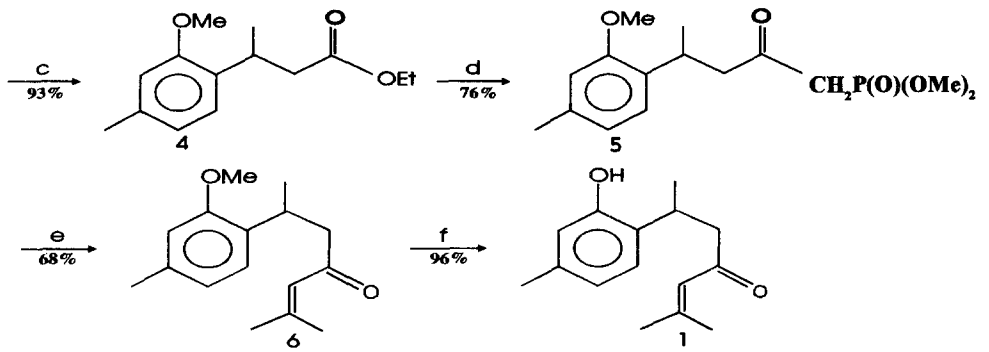
To overcome this problem for food processing, associated with soybean protein, Imai et al[1]. isolated a new phenolic sesquiterpene ketone, Turmeronol B, as an inhibitor of soybean lipoxygenase from the spice turmeric (dried rhizome of *Curcuma longa L.*). The compound was assigned the structure 1 on the basis of its physical and spectral properties.



Turmeronol
1

Literature does not seem to record any attempt toward the synthesis of the above compound. We hereby report the first synthesis of racemic 1 using 2 – hydroxy – 4 – methylacetophenone from Fries rearrangement of commercially available m-cresyl acetate[2].





a: $(CH_3)_2SO_4$, NaOH, H_2O, Microwave irradiations, 1min ; b: $(MeO)_2P(O)CH_2COOEt$, K_2CO_3, H_2O, reflux, 6 hr. ; c: Mg, absolute MeOH, N_2 atm ; d: $(MeO)_2P(O)Me$, n - BuLi, N_2 atm, — 78° ; e: NaH, THF, acetone, 0° ; f : BBr_3, CH_2Cl_2 , 78° to r.t.

2-Hydroxy-4-methylacetophenone was converted into methylated product **2**, by microwave irradiation in the presence of dimethyl sulphate in 10% aq. NaOH.[3] The resulting substituted acetophenone **2** was then subjected to a modified Wittig reaction with ethyl dimethyl phosphonoacetate using K_2CO_3 as base in refluxing aqueous media[4] to get the conjugate ester **3**. Reduction[5] of α, β -unsaturated ester **3** with Mg-MeOH afforded the saturated ester **4**. Acylation[6] of lithium dimethyl methyl phosphonate using the ester **4** at low temperature in anhyd. THF in an inert atmosphere yielded the β-ketophosphonate **5**. Modified-Wittig reaction of acetone with **5** using NaH in THF afforded the methylated Turmeronol B. Demethylation[7] of **6** with boron tribromide in CH_2Cl_2 at low temperature afforded pure racemic turmeronol B in quantitative yield identical in its spectral properties to the product reported in literature[1,8].

The synthesis of **1** in optically active form is presently underway.

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8. All products gave satisfactory spectral data. Spectral data of synthetic **1** : IR υ (neat) : 3350, 2960, 1690, 1610, 1480, 1030, 920, 740 cm^{-1}. EIMS, m/z : 232[M^+], 176, 149, 107, 83, 41. ^{1}HNMR (δ ppm, $CDCl_3$, 300MHz) : 8.06 (brs,1H,OH,D_2O exchangeable), 7.2 (d,1H,aromatic, J=4 Hz), 6.9 (s,1H, olefinic), 6.7 (s,2H,aromatic), 3.4 (m,1H, benzylic methine), 2.63 (s,3H, $ArCH_3$), 2.3 (d,2H,-CH_3CO, J=8Hz), 1.8 (s,3H), 1.7 (s,3H), 1.2 (d,3H, J=4Hz). ^{13}CNMR (ppm, $CDCl_3$,75.5MHz) :218,158.2,153.7 ,137.2, 131.4, 126.1, 123.3, 121.8, 118.4, 54.2, 27.8, 25.4, 21.7, 21.2, 20.8.

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