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Synthesis of 1,7-Bis(4-hydroxyphenyl)-3-hydroxy-1,3-heptadien-5-one

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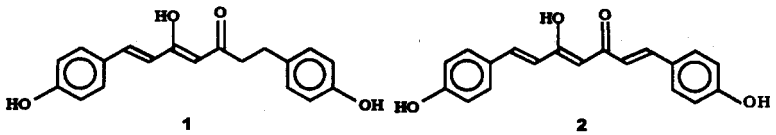
Abstract: A facile synthesis of the analog of curcumin, 1,7-bis (4-hydroxyphenyl)-3-hydroxy-1,3-heptadien-5-one **1** was achieved. The key step was completed through the regioselective condensation of ketone **5** and acyl chloride **7**.

Keywords: 1,7-Bis (4-hydroxyphenyl)-3-hydroxy-1, 3-heptadien-5-one, regioselectivity, synthesis.

1,7-Bis (4-hydroxyphenyl)-3-hydroxy-1, 3-heptadien-5-one **1**[1] was firstly isolated from the seeds of *Alpinia blepharocalyx* K.Schum. (Zingiberaceae) as a novel diarylheptanoid. Meanwhile, 1,7-bis (4-hydroxyphenyl)-3-hydroxy-1, 3,6-heptatrien-5-one **2**, a known diarylheptanoid, was isolated as well. The recent publication[1] reported that **1** strongly inhibited the aggregation of platelet induced by collagen, arachidonic acid and adenosine diphosphate. Additional research[2] proved that **2** could act as an inhibitor of the HIV-1 integrase. By our findings, the synthesis of **1** has not been reported yet. Herein, this paper describes a convenient synthetic route for **1.** Based on this method, a new feasible route for **2** which was much simpler than the previous one[3], could be achieved.

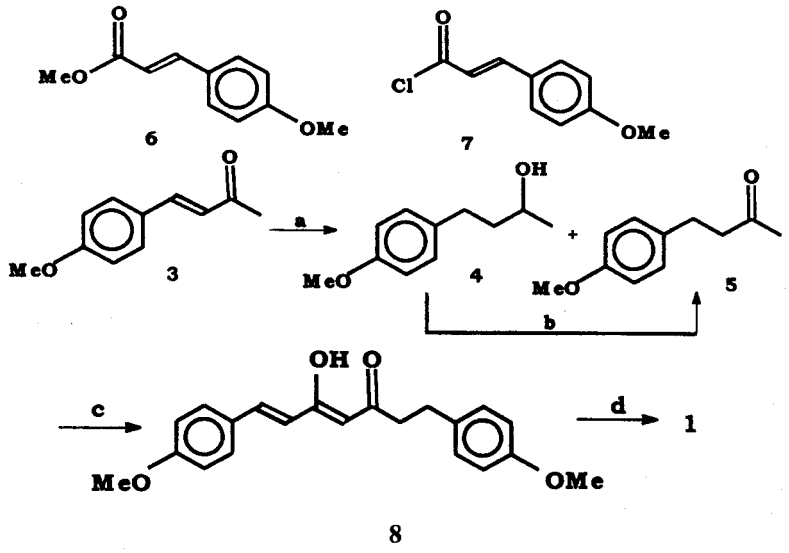
Scheme 1



The synthetic method for **1** is depicted in **Scheme 2**. The experiment started with (4-methoxyphenyl)-3-buten-2-one **3**, which was reduced in hydrogen atmosphere to give **5** and the over-reduced product **4** in a ratio of 2:1. The mixture was oxidized by PCC under mild conditions, and **4** was converted to **5** completely. In the attempt to condense **5** and methyl 4-methoxycinnamate **6**, the reaction, however, failed to form **8**. By using **7** instead of **6**, the condensation for **8** successfully proceeded, and **1**[4] was finally obtained by the demethylation of **8** with BBr_3. In the condensation, LDA was employed which reacted with **5** at first, and both C-1 and C-3 could be attacked to produce kinetically and

thermodynamically controlled products respectively. In order to make kinetically controlled product as the major species, very low temperature was required. By the condensation of **3** and **7**, compound **2** could be synthesized following a similar way as described above.

Scheme 2



Reagents and conditions:

a) 5% Pd-C, H_2, MeOH, r.t. 40min; b) PCC, CH_2Cl_2, r.t., 6h, 85%; c) LDA, -78℃, THF, then **7**. 30min, 75%; d) BBr_3, -78℃ to r.t., 1h, 90%.

References and Notes

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4. Compound **1**: yellow needles, mp: 130-132℃ (Lit[1]: 143-145℃).
   ^{1}HNMR (ppm) δ : 2.66 (2H, dd, *J*=4.2, 5.5 Hz), 2.79 (2H, dd, *J*=4.1, 5.3 Hz), 5.78(1H, s), 6.51(1H, d, *J*=16.0 Hz), 6.75 (2H, d, J=8.7 Hz), 6.89 (2H, d, *J*=8.5 Hz), 7.08 (2H, d, *J*=8.4 Hz), 7.53 (2H, d, *J*=8.8 Hz), 7.55 (1H, d, *J*=15.7 Hz), 15.52 (1H, s); EIMS: 310 (M^+, 15), 292 (7), 203 (15), 189 (32), 161 (42), 147 (100), 107 (79).

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