Synthesis of 2'-Hydroxydihydrochalcone from Flavone

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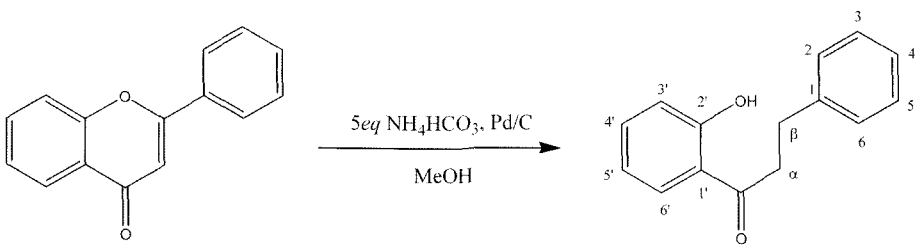
To establish the synthetic method for dihydrochalcones as an important bioactive compounds, 2'-hydroxydihydrochalcone has been synthesized from the reduction of flavone in 20% yield. Flavone with five equivalents of ammonium formate in the presence of Pd/C in methanol under N_2 atmosphere produced the C-ring opened product. It was characterized by UV-VIS, ESI-MS and ^{1}H-NMR spectroscopy, and identified as 2'-hydroxydihydrochalcone.

Key words: *flavone, flavonoids, 2'-hydroxydihydrochalcone, Pd/C, reduction*

Dihydrochalcones are minor flavonoids found from some plants [Fuchs *et al.*, 1984; Zheng *et al.*, 2004] and show various biological activities. Derivatives of phlozirin are known to be potent inhibitors of *Plasmodium falciparum*-induced erythrocyte permeation [Silfen *et al.*, 1988] and C-benzylated dihydrochalcones show cytotoxicity toward human promyelocytic leukemia HL-60 cells [Ichimaru *et al.*, 2004]. Hence, simple preparation of dihydrochalcones can provide many useful bioactive compounds. Flavones are structurally robust and more than hundreds derivatives are available. If flavones can be used for the synthesis of dihydrochalcones through C-ring cleavage, numerous dihydrochalcones can be obtained for the relevant study. Here we report simple and convenient synthetic method of 2'-hydroxydihydrochalcone from flavone, as a possible expansion to the general synthesis of dihydrochalcones.

The preparation and identification of 2'-hydroxydihydrochalcone were done as follows: The reduction of flavone was carried out in the presence of ammonium formate and Pd/C (Aldrich) in an inert atmosphere glove box (Fig. 1). Flavone (600 mg, 2.70 mmol), Pd/C (550 mg), NH_4HCO_3 (1050 mg, 13.3 mmol) were dissolved in anhydrous MeOH (50 ml). The reaction mixture was stirred for a day and Pd/C was filtered off through cotton-plugged Pasteur pipette. More than 8 compounds were identified on silica gel TLC plate after developing in chloroform and the product with R_f= 0.6 (2'-dihydroxydihydrochalcone) was isolated in 20% yield (120 mg, 0.53 mmol), by using prepTLC with concentrating zone (Merck # 13793/7). UV-Vis spectrum of the 2'-hydroxydihydrochalcone showed λ_{max} at 323 nm, 251 nm and 218 nm in MeCN. ESI-MS measurement identified the molecular ion peak at 226.7 *m/z* and the peak at 267.7 *m/z*



flavone 2'-hydroxydihydrochalcone

Fig. 1. Synthesis of 2'-hydroxydihydrochalcone.

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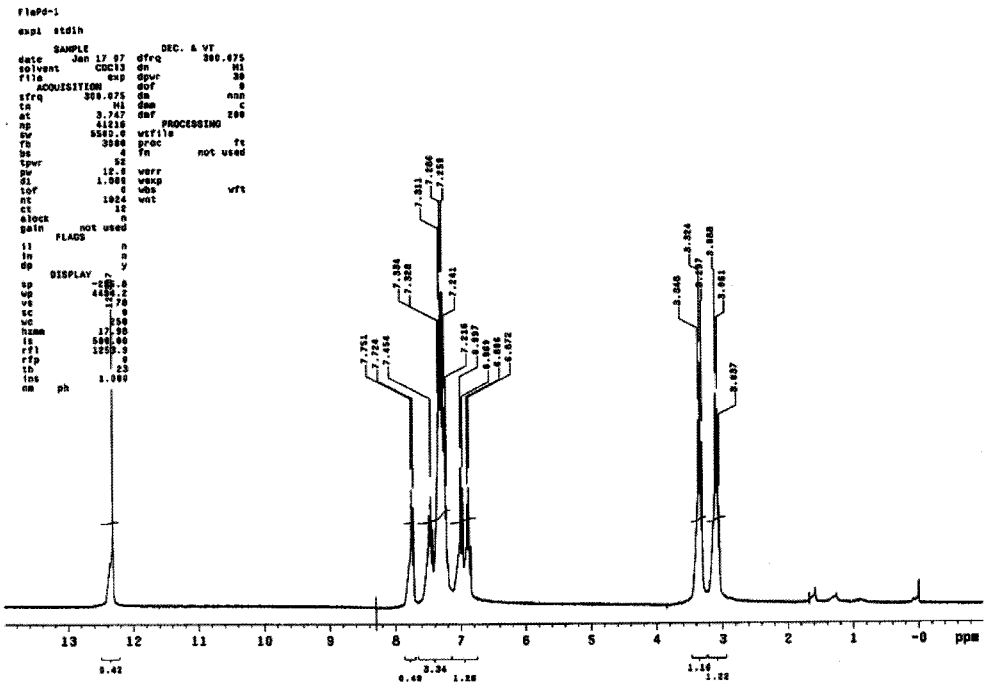
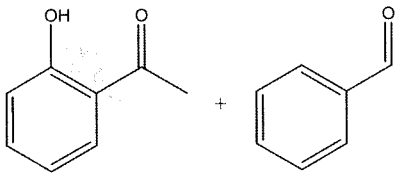
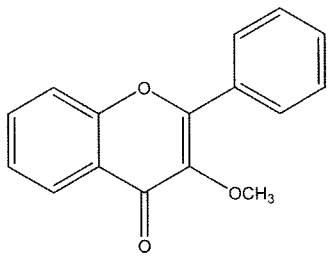
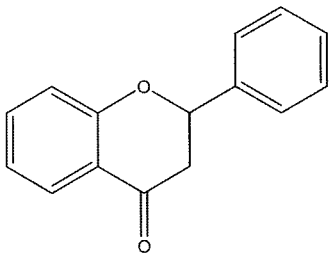


Fig. 2. ^{1}H-NMR spectrum of 2'-hydroxydihydrochalcone.

Table 1. Synthetic methods for 2'-hydroxydihidrochalcone

Reaction conditions	Reference
	Cho and Shim, 2006
	Sweeny *et al.*, 1979
	Ibrahim and Abul-Hajj, 1990

was assigned as a MeCN adduct. The proton of 2'-OH on A-ring appeared at 12.3 ppm and α- and β-methylenyl protons were found at 3.32 ppm and 3.06 ppm, respectively, on 300 MHz ^{1}H-NMR spectrometer (Fig. 2).

2'-Hydroxydihydrochalcone has been prepared by several methods as shown at Table 1. Recently, dihydrodaidzein was synthesized from daidzein by α, β-reduction under the similar reaction conditions [Wang *et al.*, 2005]. But, synthesis of 2'-hydroxydihydrochalcone from flavone has never been reported to the best of our

knowledge. The reduction of flavones with excess amount of ammonium formate in the presence of Pd/C could provide general procedure for the synthesis of dihydrochalcones from flavones.

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