

## Note

### Synthesis of genkwainin

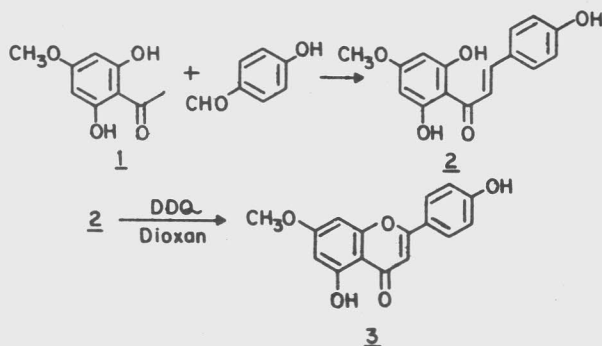
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Genkwainin **3** isolated from a Chinese drug *Yuen Hua* has been synthesized. 2,6-Dihydroxy-4-methoxyacetophenone **1** is condensed with *p*-hydroxybenzaldehyde to give the chalcone **2** which on DDQ oxidation afford the genkwainin **3**. All the compounds have been characterized on the basis of spectral data and microanalysis.

Flavones and their derivatives are naturally occurring and have a variety of biological properties such as fish toxicity<sup>1</sup> coronary vasodilator<sup>2</sup> and antitumour activity<sup>3</sup>. Nakao *et al.*<sup>4</sup> have reported the isolation of 5,4'-dihydroxy-7-methoxyflavone **3** (genkwainin) from a Chinese drug *yuen hua*. The structure was assigned to it on the basis of spectral data but no synthetic proof was provided. In this note we describe the synthesis of genkwainin **3** starting from phloroacetophenone. Phloroacetophenone on methylation with dimethyl sulphate yielded three products<sup>5</sup>, viz. 2-hydroxy-4,6-dimethoxyacetophenone, 2,6-dihydroxy-4-methoxyacetophenone **1** and 2,4-dihydroxy-6-methoxyacetophenone. Alkaline condensation of **1** with *p*-hydroxybenzaldehyde gave the chalcone **2**. DDQ oxidation of **2** afforded the title compound **3**, (Scheme I) which



Scheme I

was identical with the natural sample of genkwainin (superimposable TLC, mixed melting point, superimposable IR and <sup>1</sup>HNMR).

### Experimental

Melting points were determined using an electrothermal melting point apparatus (Gallenkamp) and are uncorrected. IR spectra were recorded (KBr discs) on a Pye-Unicam SP3-300 IR spectrophotometer ( $\gamma_{\max}$  in  $\text{cm}^{-1}$ ); <sup>1</sup>HNMR spectra were recorded on a Perkin-Elmer R-32 (90 MHz) instrument in  $\text{CDCl}_3$  with TMS as an internal standard (chemical shifts in  $\delta$ , ppm). UV spectra were recorded on LKB 4053 spectrophotometer Ultrospek in methanol ( $\lambda_{\max}$  in nm). TLC was performed using silica gel 60G. Satisfactory elemental analysis were obtained for all the compounds and structures are in accord with the UV, IR and <sup>1</sup>HNMR data. Mass spectra were recorded on VG 7070E analytical mass spectrometer. (Scheme I).

**2,6,4-Trihydroxy-4'-methoxychalcone 2.** A mixture of 2,6-dihydroxy-4-methoxyacetophenone<sup>5</sup> (**1**, 1.82 g) and *p*-hydroxyacetophenone (1.32 g) in ethanolic solution of KOH (50%, 50 mL) was kept at room temperature for about 75 hr. The reaction mixture was diluted with ice cold water, acidified with dil. HCl and extracted with ether. The ether layer was washed with water, dried over  $\text{Na}_2\text{SO}_4$  and evaporated to dryness. The solid obtained was crystallized from petrol as pale yellow crystals (2.49 g), m.p. 169°C,  $R_f$  0.65 (benzene-acetone; 15:1), ( $M^+$ , 286), UV: 228, 260, 376; IR: 3470, 1645; <sup>1</sup>HNMR: 3.98 (s, 3H, -OCH<sub>3</sub>), 6.25 (d, 1H,  $J=2.5$  Hz, H-3'), 6.68 (dd, 1H,  $J=2.5$  & 9 Hz, H-5'), 6.98 (d, 2H,  $J=9$  Hz, H-5 & H-3), 7.18 (d, 2H,  $J=9$  Hz, H-2 & H-6), 7.45 (d, 1H,  $J=9$  Hz, H- $\alpha$ ), 8.01 (d, 1H,  $J=9$  Hz, H- $\beta$ ), 8.78 (s, 1H, -OH), 12.73 (s, 2H, -OH $\times$ 2) (Found: 67.4; H, 4.7.  $\text{C}_{16}\text{H}_{14}\text{O}_5$  requires C, 67.1; H, 4.9%).

**5,4'-Dihydroxy-7-methoxyflavone (genkwainin, 3).** A mixture of **2** (1 g) in dry dioxan (50 mL) and DDQ (200 mg) was refluxed for 3 hr. Dioxan was

removed by distillation. Water was added to the residue. It was extracted with ether, dried over anhydrous  $\text{Na}_2\text{SO}_4$  and evaporated to dryness. The reaction mixture was purified by preparative TLC over silica gel 60 G using benzene-acetone (7:1) as developing solvent. It crystallized from methanol as yellow needles (0.72 g), m.p. 281-83°C [lit.<sup>4</sup> m.p. 282°C], it gave the green colour with alcoholic ferric chloride solution and red colour with  $\text{MgHCl}$ ,  $R_f$  0.71 (benzene),  $M^+$ , 284; UV: 235, 365; IR: 3450, 1640;  $^1\text{HNMR}$ : 4.00 (s, 3H,  $-\text{OCH}_3$ ), 6.13 (s, 1H, H-3), 6.45 (d, 1H,  $J=2.5$  Hz, H-8), 6.78 (dd, 1H,  $J=2.5$  and 9 Hz, H-6), 6.92 (d, 2H,  $J=9$  Hz, H-5' & H-3'), 7.14 (d, 2H,  $J=9$  Hz, H-2' & H-6'), 13.01 (s, 2H,  $-\text{OH}\times 2$ ) (Found: 67.8; H, 4.6.  $\text{C}_{16}\text{H}_{12}\text{O}_5$  requires C, 67.6; H, 4.9%).

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