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Total Synthesis of 3,3′-Biflavone

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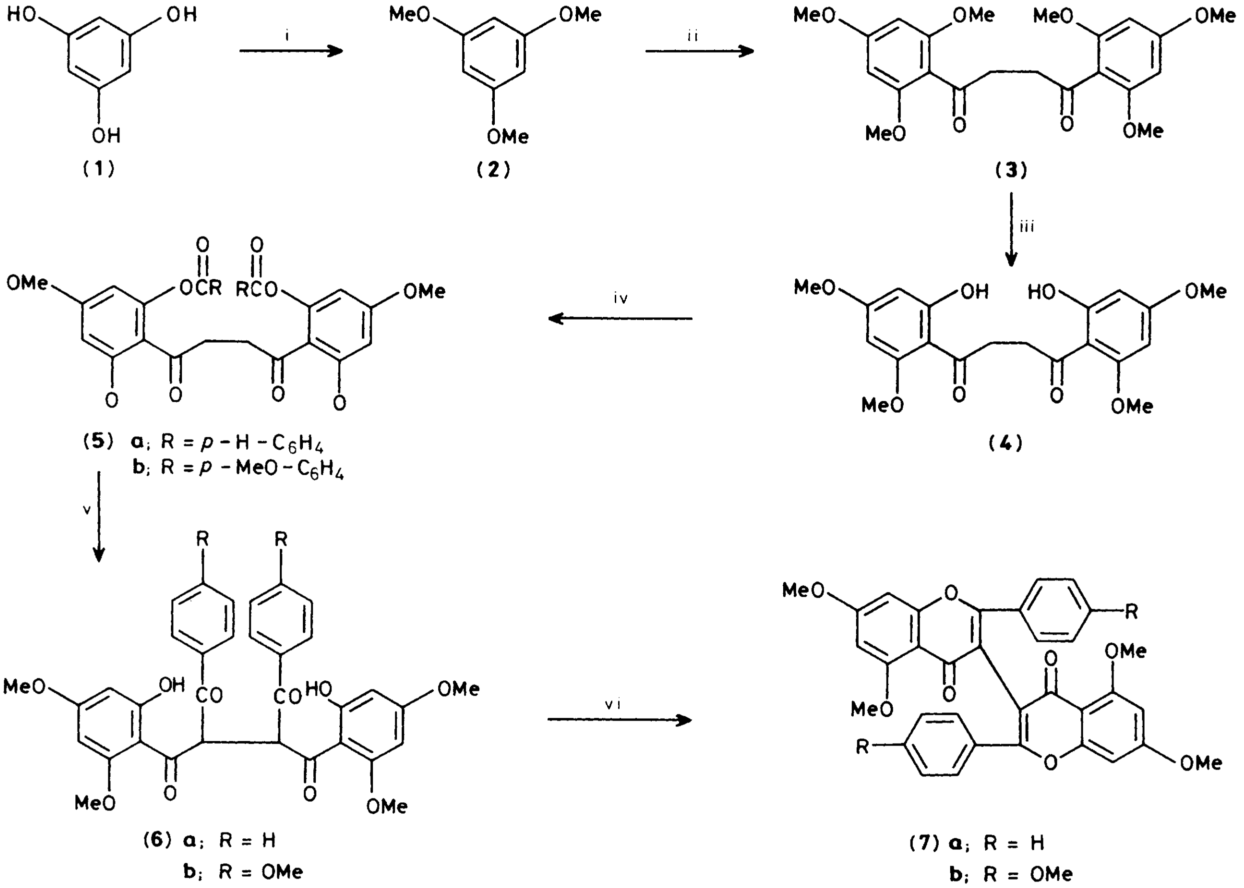
3,3′-Biflavones (**7a**) and (**7b**) have been successfully synthesized.

Large numbers of biflavonoids have been isolated from a variety of natural sources, but biflavonoids possessing a 3,3′-linkage are not common. Chamaejasmine, isolated from *Stellera chamaejasmae L.* by Professor Huang in 1979,[1] was the first example of this class. It is constructed with two units of naringenin linked by a carbon–carbon bond between the two C-3 atoms. 7-Methoxychamaejasmine,[2] chamaejasmine A,B,C,[3] neochamaejasmine A,B,[4] and isochamaejasmine[5] have been isolated from the same plant.

3,3′-Biapigenin has been prepared by phenolic oxidative



Scheme 1. *Reagents and conditions:* i, K_2CO_3, Me_2CO, Me_2SO_4; ii, $AlCl_3$, $(CH_2COCl)_2$, $(CHCl_2)_2$; iii, BCl_3, CH_2Cl_2; iv, pyridine, C_6H_5COCl or anisoyl chloride; v, NaH, toluene; vi, H_2SO_4, HOAc.

coupling of apigenin using alkaline potassium ferricyanide as the oxidizing reagent,[6] but the yield was very poor (only 5%).

In searching for a synthesis of chamaejasmine and other 3,3′-biflavonoids, we have designed a synthetic route and successfully synthesized 3,3′-biflavones (**7a**) and (**7b**), (Scheme 1). Phloroglucinol reacted with dimethyl sulphate in the presence of potassium carbonate and dry acetone to give the trimethyl ether (**2**) in 92% yield. Friedel–Crafts reaction of (**2**) with succinyl chloride provided butane-1,4-dione (**3**) in 65% yield. Selective demethylation of (**3**) with boron trichloride gave (**4**) in 98% yield. Esterification of (**4**) with benzoyl chloride or anisoyl chloride in pyridine afforded the ester (**5a**) or (**5b**), yield 85% and 81% respectively, which was converted to the phenol (**6a**), yield 90%, or (**6b**), yield 89% by the Baker–Venkataraman rearrangement.[7] Finally, ring closure of (**6a**) or (**6b**) yielded 3,3′-biflavone (**7a**) or (**7b**) in yields of 95% and 88% respectively.†

The catalytic hydrogenation of compounds (**7a**) and (**7b**) is in progress.

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† The structure of compounds (**2**)—(**7**) was determined by i.r., ^{1}H n.m.r., and mass spectral data. The high resolution m.s. of compound (**7**) was: (**7a**), M = 562.1595 (calc. 562.1627); (**7b**), M = 622.1827 (calc. 622.1838).

‡ Revised version of Com. 1425, original version received 30th September 1987.