A Facile Baker-Venkataraman Synthesis of Flavones using Phase Transfer Catalysis

P. K. JAIN, J. K. MAKRANDI[1], S. K. GROVER*

Department of Chemistry, University of Delhi, Delhi-110007, India

Flavones are an important class of compounds belonging to the flavonoid group, which have been largely synthesised either by the Allan-Robinson method[2] of dry heating a mixture of an appropriately substituted *o*-hydroxyacetophenone with an acid anhydride in the presence of the sodium salt of the acid or the Baker[3]-Venkataraman[4] method starting from *o*-hydroxyacetophenones, converting them into the corresponding *o*-aroyloxyacetophenones, transformation of these into *o*-hydroxydibenzoylmethanes with pyridine/alkali, followed by cyclisation. The stepwise Baker-Venkataraman synthesis was modified by Seshadri et al.[5] by refluxing *o*-hydroxyacetophenones with aroyl chloride in acetone containing anhydrous potassium carbonate, which gave directly the *o*-hydroxydibenzoylmethanes required for cyclisation to flavones. However, this simplified procedure was reported[5] to have its limitations. Thus, 2-hydroxy-4,6-dimethoxy- and 2-hydroxy-3-methyl-4,6-dimethoxyacetophenones failed to undergo conversion into

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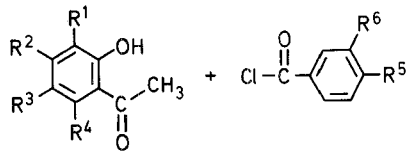
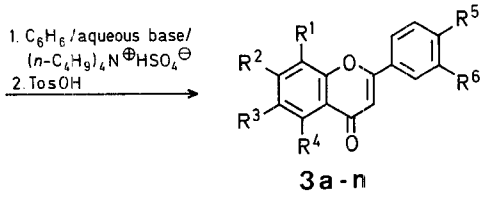
the corresponding dibenzoylmethanes. The inactivity of these acetophenones was attributed to the resonance effect of the methoxy groups[5].

We present below an extremely facile procedure for the synthesis of flavones **3**. An *o*-hydroxyacetophenone **1**, containing methoxy or methyl groups at various positions (Table), was treated with an aroyl chloride **2** in benzene solution under phase transfer-catalysed conditions, using *n*-tetrabutylammonium hydrogen sulphate, resulting in the formation of the corresponding *o*-hydroxydibenzoylmethanes. The benzene solution, on treatment with *p*-toluenesulphonic acid afforded the flavones **3** in excellent yields. However, in the absence of the phase transfer catalyst, *o*-aroyloxyacetophenones were the only products of the reaction in the first step.



1 **2**



3a-n

This method is of general applicability. Even 2-hydroxy-4,6-dimethoxy- and 2-hydroxy-3-methyl-4,6-dimethoxyacetophenones have now been found to undergo smooth conversion under the present conditions.

Flavones 3; General Procedure:

The *o*-hydroxyacetophenone **1** (3.0 mmol) and the aroyl chloride **2** (3.6 mmol) in benzene (20 ml) are magnetically stirred at 80°C with 10% aqueous potassium carbonate or potassium hydroxide solution (20 ml) in the presence of *n*-tetrabutylammonium hydrogen sulphate (1.5 mmol) for 2–3 h until the starting acetophenone and the first formed *o*-aroyloxyacetophenone disappear (T.L.C.). During this period the benzene solution acquires a deep yellow to orange colour. The benzene solution is separated, washed thoroughly with water (3 × 20 ml), and the water removed from it by azeotropic distillation. *p*-Toluenesulphonic acid (9.0 mmol) is added together with dry benzene (25–50 ml) and azeotropic removal of water continued (30–45 min). Excess *p*-toluenesulphonic acid is extracted from the benzene solution with 8% aqueous sodium hydrogen carbonate solution (50 ml). The benzene phase is evaporated and the residue dried in vacuum over phosphorus pentoxide. The residue is recrystallised from ethyl acetate/light petroleum ether or benzene/light petroleum ether to give the desired flavone **3** (Table).

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* Address for correspondence.
[1] Present address: Department of Chemistry, M. D. University, Rohtak-124001, India.

Table. Flavones **3a–n** prepared

Product No.	R^1	R^2	R^3	R^4	R^5	R^6	Base used	Yield [%]	m.p. [°C] found	m.p. [°C] reported
3a	H	H	H	H	H	H	K_2CO_3	92	99–100°	96–97°[6]
3b	H	H	H	H	OCH_3	H	K_2CO_3	92	158–159°	157–158°[7]
3c	H	OCH_3	H	H	H	H	K_2CO_3	95	110°	110°[8]
3d	H	OCH_3	H	H	OCH_3	H	K_2CO_3	92	140–141°	144–146°[9]
3e	H	H	CH_3	H	H	H	K_2CO_3	92	121–122°	122°[6]
3f	H	H	CH_3	H	OCH_3	H	K_2CO_3	95	170–171°	170°[9]
3g	CH_3	OCH_3	H	H	H	H	K_2CO_3	95	174–175°	175–176°[10]
3h	H	OCH_3	CH_3	H	H	H	K_2CO_3	92	158–159°	—[a]
3i	H	OCH_3	H	OCH_3	H	H	K_2CO_3	92	149°	142–143°[11]
3j	H	OCH_3	H	OCH_3	OCH_3	H	K_2CO_3	92	154–155°	156°[8]
3k	CH_3	OCH_3	H	OCH_3	H	H	KOH	95	230–232°	231°[12]
3l	CH_3	OCH_3	H	OCH_3	OCH_3	H	KOH	95	228–229°	230–231°[13]
3m	H	OCH_3	H	H	OCH_3	OCH_3	K_2CO_3	94	173–174°	176°[14]
3n	H	OCH_3	H	OCH_3	OCH_3	OCH_3	K_2CO_3	92	188–189°	190–192°[8]

[a] $C_{17}H_{14}O_3$ (266.3) calc. C 76.68 H 5.30; found 76.50 5.60
^{1}H-N.M.R. ($CDCl_3$/TMS): $\delta = 2.25$ (s, 3H); 3.90 (s, 3H); 6.65 (s, 1H); 6.80 (s, 1H); 7.3–7.9 ppm (m, 6H).

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