



Research Article

Efficient Synthesis of Flavones Derivatives from Aromatic Acids

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ABSTRACT

A series of flavones derivatives were synthesized from reaction of o-hydroxyacetophenone and various acids via ester and β -diketone using traditional Baker-Venkatraman rearrangement. Even if the method used is traditional, the noteworthy aspect of the protocol is yields obtained were excellent. The synthesized compounds are having various well known applications like antibacterial application.

Keywords: Flavones; 2-Hydroxyacetophenones; Antibacterial compounds

1. INTRODUCTION

Flavonoids, a vital class of organic compounds displays wide range of pharmacological activities such as anti-cancer¹, anti-inflammatory², anti-osteoporotic³, anti-diabetic⁴ and metal chelating⁵ activities. Flavones are the naturally occurring compounds in fruits, vegetables, flowers and nuts etc.⁶⁻⁸ Moreover, flavones and its derivatives are important intermediates in vital anti-bacterial and anti-AIDS drugs.⁹ Due to their above mentioned astonishing applications flavones are thoroughly investigated for last few decades.

Synthesis of flavones can be achieved by cyclization of 2'-hydroxy chalcones using various catalysts.¹⁰⁻¹² This method suffer from drawbacks such as high reaction temperature along with 2'-hydroxychalcones synthesized from 2-hydroxyacetophenones and benzaldehyde utilize long reaction time and affords low yield. Moreover, these flavones can be synthesized traditionally by Baker-Venkatraman rearrangement which involves the conversion of 2-hydroxyacetophenones into benzoyl esters, followed by rearrangement in base to 1,3-diphenylpropane 1,3-diones, which upon cyclization under acidic conditions furnishes flavones.¹³

Thus, to render efficient method with high yields in this report we accepted the later traditional method and synthesized various flavones from 2-hydroxyacetophenones and substituted acids.

2. EXPERIMENTAL

a) Synthesis of Benzoyloxy Ester of o-Hydroxyacetophenones

o-Hydroxyacetophenone (0.04 mol) and aromatic acid (0.05 mol) were dissolved in pyridine (20ml). To this solution, distilled phosphorus oxychloride (5ml) was added slowly with constant stirring and maintaining the temperature below 40°C. The reaction mixture was poured on a mixture of crushed ice (100 g) containing concentrated HCl (5ml). Usually a colorless solid separated which was filtered, washed successively with water, 2% sodium hydroxide and water. The ester obtained was recrystallized using proper solvent.

b) Synthesis of β -diketone

All the β -diketones were synthesized using Baker-Venkatraman transformation.

A mixture benzoyloxy ester of respective hydroxyacetophenone (0.01 mol), dry pyridine (20 ml) and solid KOH (0.04 mol) was stirred for 20 min. and kept for half an hour. Then the reaction

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mixture was acidified by pouring it on ice and concentrated HCL (5 ml). Usually a yellow product was obtained. It was filtered, washed with water and recrystallized.

c) Synthesis of Substituted Flavones

A mixture of the β -diketone (1 gm), glacial acetic acid (10 ml) and concentrated HCL (1ml) was refluxed for 1 hr. The reaction mixture was then poured over crushed ice and the solid obtained was washed with water and then recrystallized.

Spectral data:

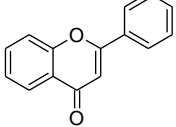
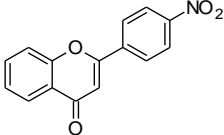
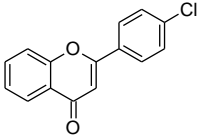
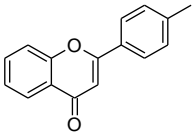
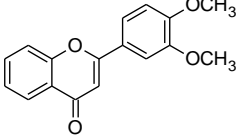
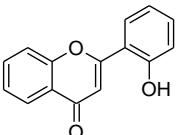
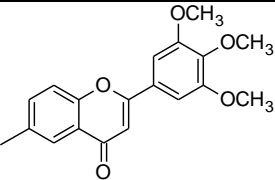
Entry 5g:

IR (KBr) max (cm^{-1}): 2950, 1650, 1470.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz) δ (ppm): 2.54 (s, 3H, CH_3), 4.1 (s, 9H, OCH_3), 6.85 (s, 1H, Ar-H), 7.25 (s, 2H, Ar-H), 7.6 (s, 1H, Ar-H), 8.1 (s, 1H, Ar-H).

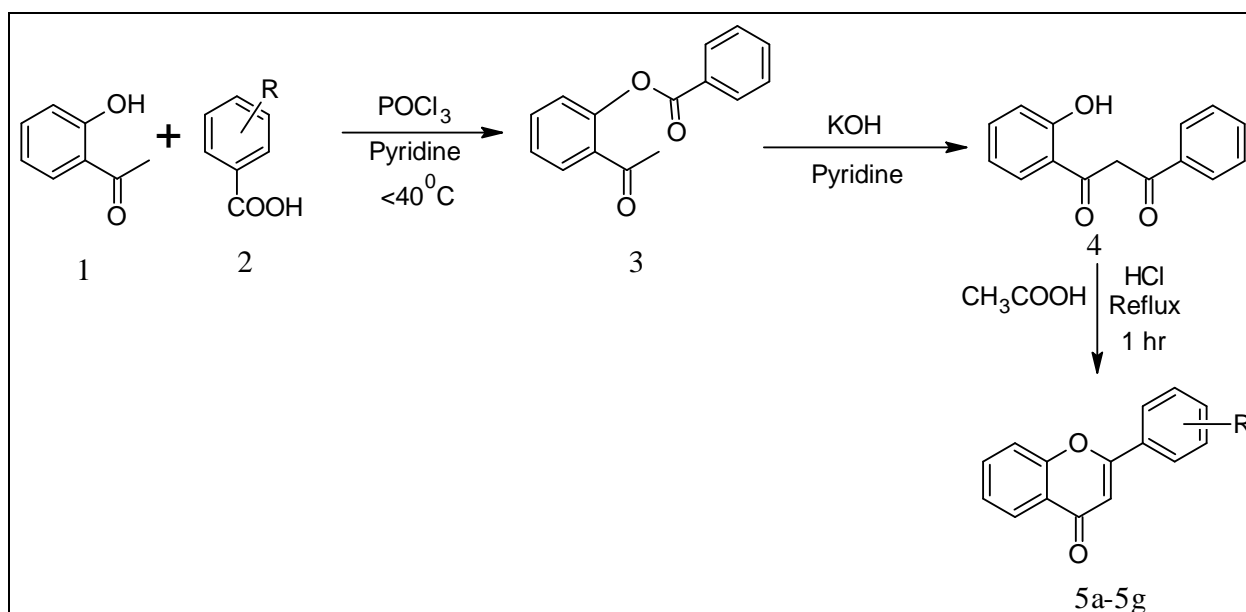
Anal Calcd for $\text{C}_{19}\text{H}_{18}\text{O}_5$: C, 69.93; H, 5.52. Found: C, 70.00; H, 5.92.

Table 1: Synthesis of various flavones from substitutes aromatic acids

Sr. No.	Product	Entry	Yield (%) ^a	Melting point m.p. ($^{\circ}\text{C}$)/lit. m.p ($^{\circ}\text{C}$) [Ref]
1		5a	82	94-95 [14]
2		5b	80	155 [14]
3		5c	84	185 [14]
4		5d	85	112 [14]
5		5e	83	178 [14]
6		5f	79	209-211 [14]
7		5g	85	Novel 190

a – isolated yields

Fig. 1 Synthesis of various flavones from substitutes aromatic acids



3. RESULTS AND DISCUSSION

Initially, we carried out the reaction using benzoic acid. In first step 2-hydroxyacetophenone was converted to its benzoyl ester by reaction with benzoic acid in presence of POCl_3 . In second step using KOH the ester was converted to β -diketone. Finally, cyclization of β -diketone was achieved using HCl as catalyst in acetic acid to give respective flavones. In each step yield obtained was excellent, which boost us to try various substituted benzoic acids. Thus, to explore the scope of protocol we synthesized various substituted flavones using substituted benzoic acid. (Table 1, Fig. 1).

Some negative results were obtained while using acid like aryloxyacetic acid. The reaction proceeds smoothly only up to ester and didn't proceeds further might be the rearrangement is restricted.

We tried the same protocol by grinding method using all the catalyst as it is. But negligible yields were obtained.

In order to achieve higher yields we used the traditional method instead of modern one pot via chalcone method.

4. CONCLUSION

We have developed efficient synthesis of flavones by reaction of 2-hydroxy acetophenones and substituted carboxylic acids. Higher yields, clean procedure are the noteworthy aspects of

the protocol. Flavones can be synthesized efficiently using substitutes acids via ester and β -diketone is depicted by our protocol.

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