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Ionic Liquid Promoted Expeditious Synthesis of Flavones

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A smooth conversion of substituted 1-(2-hydroxy phenyl)-3-phenyl-1,3-propane diones to flavones has been done using *n*-butyl-3-methyl-imidazolium tetrafluoroborate ionic liquid.

Keywords: 1,3-Dicarbonyl compounds, Dehydrative cyclization, Ionic liquid, Flavones

INTRODUCTION

Flavones are naturally occurring compounds widely distributed in the plant kingdom. Members of the class of flavones show a wide spectrum of biological activities [1-2]. Recently they have been reported to be reteroviral transcriptases, protein tyrosine kinase [3] and serine/threonine kinase inhibitors [4].

Currently a number of methods have been reported for the synthesis of flavones [5] including Allan-Robinson synthesis [6], synthesis from chalcones [7], and *via* an intramolecular wetting strategy [8]. The most common method is Baker-Venkatramn reaction representing the convenient route from 2-hydroxy acetophenone. In this method, acid induced dehydrative cyclization of 1,3-(diaryl) diketones obtained by intramolecular claisen condensation of *o*-benzoyl acetophenone to 75% flavones [9] is introduced. Recently the flavones synthesis was reported using different catalysts such as Amberlyst15 [10], Co^{III}(sulpr)OH [11], FeCl₃ [12], Br₂/CHCl₃ [13], EtOH/HCl [14], clay [15], NaOAc/AcOH [16], and H₂SO₄ under microwave irradiation [17]. All these reported methods suffer from strong acidic conditions, prolonged reaction times, low yields and high cost of the

reagents.

This obviously warranted further investigation into finding an alternative method to afford mild reaction conditions, short reaction times, and better yields. Our experiments using ionic liquids (ILs) as green solvents provided the answer.

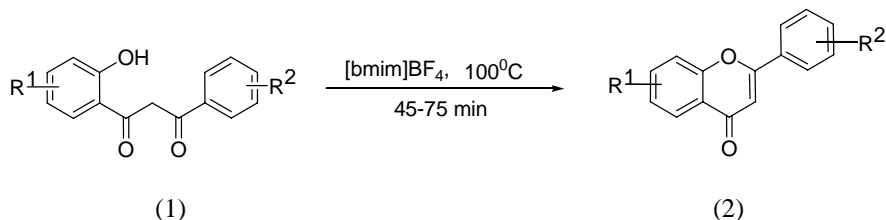
In recent times, the use of ionic liquids (ILs) as green solvents in organic synthesis process has gained considerable significance because of their negligible vapor pressure, solvating ability and easy recyclability [18]. Additionally, some ILs possesses inherent Lewis/Bronsted acidity which promotes and catalyzes organic transformations in excellent yields [19].

On the basis of the findings of our research into flavones synthesis [20], herein we report a mild and efficient protocol promoted by ionic liquid, 1-*n*-butyl-3-methyl-imidazolium tetrafluoroborate ([bmim]BF₄) in excellent yield and short reaction times (Scheme 1). The non-volatile ionic liquids were effectively recovered and reused. The process does not require any additional catalyst or hazardous organic solvent.

GENERAL EXPERIMENTAL PROCEDURE

1,3-(Diaryl) diketone **1** (1 mmol) in ionic liquids [bmim]BF₄ (3 mmol) was stirred at 100 °C temperature. After the completion of reaction (monitored by TLC), the reaction

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Scheme 1

mixture was poured onto crushed ice and further stirred for 10-15 min. The separated solid was filtered, washed with ice cold water and recrystallized from petroleum ether to offer pure flavones **2**. The combined aqueous filtrate was concentrated under reduced pressure to recover the ionic liquid for reuse. The product **2a-h** was identified by comparison with authentic samples ¹H NMR and their melting points.

RESULTS AND DISCUSSION

In a model reaction, 1,3-diketones (**1**) in 1-*n*-butyl-3-methyl imidazolium tetrafluoroborate [bmim]BF₄ was stirred at 100 °C temperature. The progress of the reaction was monitored by TLC. After completion of reaction the aqueous work-up afforded pure flavones (**2**) in considerably high yields. To evaluate the synthetic utility of the process, several substituted diketones were prepared by the established procedure [9] and subjected to the same reaction. The results are presented in (Table 1).

The reaction proceeds cleanly to afford flavones bearing NO₂, Cl, methoxy and hydroxy groups in the aromatic rings in high yields. No undesirable side reactions were observed. The protocol offers advantages in terms of simple and easy procedure, fast reaction rate, mild reaction conditions and excellent yields.

Similar reactions have been also carried out in the absence of ionic liquid [bmim]BF₄ at 100 °C using toluene as a solvent. But the reaction does not proceed evenly after 3-4 h under reflux conditions.

The used ionic liquid was recovered and reused for several reactions with identical results. Thus the recyclability of ionic liquid was confirmed (Table 2).

In summary, we have demonstrated an efficient and mild protocol for the dehydrative cyclization of 1,3-(diaryl) diketones to flavones in ionic liquids. This protocol does not

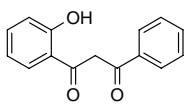
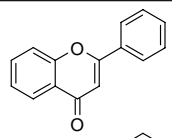
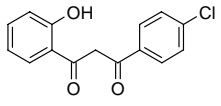
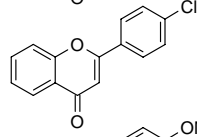
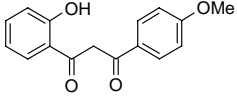
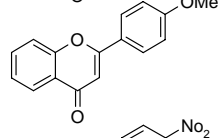
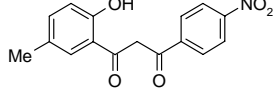
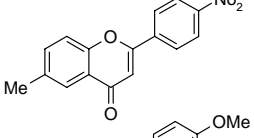
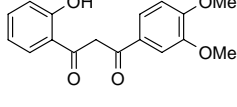
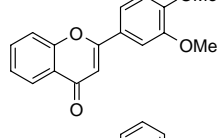
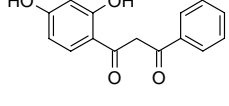
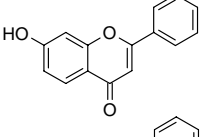
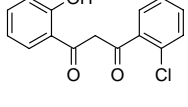
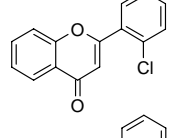
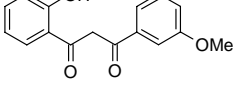
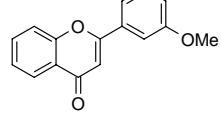
need any additional catalyst and hazardous solvents. This method does not generate any byproducts except water. We hope this simple procedure finds wide utility in organic synthesis.

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Ionic Liquid Promoted Expeditious Synthesis of Flavones

Table 1. Synthesis of Flavones **2(a-h)** in Ionic Liquid [bmim]BF₄

Entry	1,3-diketones 1(a-h)	Product 2(a-h)	Time(min)	Yield(%) ^a	M.P.(°C) ^b
a			60	93	97
b			50	90	185-187
c			45	91	155-156
d			75	88	277
e			65	90	154
f			70	89	240-241
g			60	87	118
h			50	92	128-129

^aIsolated yields. ^bMelted points are uncreated and compare with reported compounds reference [12].

Table 2. Synthesis of Flavones **2(a-b)** with Recovered Ionic Liquid [bmim]BF₄

Entry	1,3-diketone	product	Time(min)	Yield(%)		
				Cycle 1	Recycle 1	Recycle 2
1	1a	2a	60	93	91	91
2	1b	2b	50	90	88	88

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