A FACILE AND EFFICIENT SYNTHESIS OF FLAVANONES BY USING NOVEL IONIC LIQUID


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ABSTRACT
An efficient method for the conversion of substituted 1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one to the corresponding substituted flavanones under eco-friendly condition using novel ionic liquid is reported in this article. The method describes the synthesis of flavanones in single step with excellent yield and it was revealed that position and number of substituent’s on aromatic aldehydes played a very crucial and key role in the construction of flavanones derivatives.

KEYWORD: Flavanones, 2'-Hydroxychalcones, Ionic liquid, Green synthesis.

INTRODUCTION
Chalcones and flavanones, originally isolated from natural sources are an outstanding class of naturally occurring bioactive compounds. The Flavanone structure is abundant in natural products that possess a broad array of biological activity.[1] Due to their favorable anti-cancer, anti-estrogen and anti-inflammatory properties, flavanones have been investigated as selective estrogen receptor modulators and tumor necrosis factor (TNF) -α inhibitors.[2] These compounds have been synthesized by the cyclization of 2'-hydroxychalcones, that is, by an intramolecular oxa-Michael addition using various reagents, such as iodine[3], thiourea catalyst[4], alkali metal carbonates[5] and trifluoroacetic acid[6] and Microwave assisted solvent-free synthesis[7]. Flavanones shows activities like Anticancer[8], antimitotic[9], anti-inflammatory[10], antimalarial[11], antiangiogenic[12], Antimicrobial[13], antioxidant.[14] Several methods have been reported for the synthesis of 2'-hydroxychalcones[15a] and Flavanones.[15a],[15b],[15c]
The chemical and pharmaceutical industries are always under pressure to develop more environmentally friendly organic reaction methodologies. Therefore, ionic liquid is used for a variety of organic reactions due to its use in more rapid and cleaner synthesis of organic compounds. Ionic liquids are the salts of organic cations and inorganic anions. They exist in liquid state at ambient temperature; hence the reactions in presence of ionic liquids need no additional solvent. Ionic liquids have attracted much attention due to their mild reaction conditions, short reaction times and better yield, solvating ability, and easy recyclability.  

Various reactions have been reported recently using ionic liquids as a catalyst, reaction media, as rate enhancers and in peptide synthesis. New Ionic liquid had been used in synthesis pyranopyrazole, the same ionic liquid had been used as catalyst.

**Figure1: Structure of Ionic liquid.**

**MATERIALS AND METHODS**

All Chemicals & Reagents were purchased from Merck & S.D.fine chemicals. TLC pre-coated Silica gel Plates (60F254, 0.2 mm Layer E. Merck). Melting points were determined in open glass capillaries and are uncorrected. Infrared spectra were recorded on Perkin-Elmer 1310 infrared Spectrometer. 1HNMR and 13CNMR spectra were recorded at room temperature on a 300 MHz Varian Inova Spectrometer in CDCl3 using TMS as internal reference standard.

**GENERAL PROCEDURE FOR SUBSTITUTED FLAVANONES**

1mole of 2-hydroxy chalcone was added in previously prepared ionic liquid (10 mole %) in 250ml RBF. The reaction mixture was stirred on magnetic stirrer at 60-65°C. The reaction was monitored by TLC (30:70 Ethyl acetate and n-Hexane). After completion of reaction the mixture was poured in ice. The solid obtained was filtered, washed with cold water and recrystallized using ethanol.
Figure 2: The scheme for synthesis of target compounds

### SPECTRAL DATA

**Synthesis of 2-phenylchroman-4-one:**
- **IR (KBr cm⁻¹):** 1637, 1570, 1470, 1730, 1201, 1151, 975.
- **¹H NMR (300 MHz, CDCl₃):** δ 7.18 (dd, 1H CH), 7.25 (dd, 1H CH), 7.7 (dd, 1H CH), 5.51 (t, 1H CH), 3.38 (d, 2H CH₂), 7.4 (dd, 1H CH), 6.85 (m, 1H CH), 6.96 (dd, 1H CH).
- **¹³C (CDCl₃):** 127.1, 129.0, 127.7, 140, 79, 42, 198, 120, 129, 158.

**Synthesis of 2-(4-Bromophenyl) chroman-4-one:**
- **IR (KBr cm⁻¹):** 1640, 1460, 1537, 1214, 1105, 987.
- **¹H NMR (300 MHz, CDCl₃):** δ 7.08 (dd, 1H CH), 7.36 (dd, 1H CH), 5.55 (t, 1H CH), 3.38 (d, 2H CH₂), 7.40 (d, 1H CH), 6.9 (m, 1H CH), 7.5 (m, 1H CH), 6.8 (d, 1H CH).
- **¹³C (CDCl₃):** 129.3, 131.8, 196, 122, 120, 129, 139, 79, 42, 133, 114.0.

**Synthesis of 2-(4-Chlorophenyl) chroman-4-one:**
- **IR (KBr cm⁻¹):** 1706, 1631, 1217, 1100, 987.
- **¹H NMR (300 MHz, CDCl₃):** δ 7.13 (dd, 1H CH), 7.20 (dd, 1H CH), 5.5 (t, 1H CH), 3.3 (t 2H CH₂), 7.30 (dd 1H CH), 7.50 (dd, 1H CH).
- **¹³C (CDCl₃):** 128, 129, 79, 196, 42, 130, 133, 138, 129.

**Synthesis of 2-(4-Nitrophenyl) chroman-4-one:**
- **IR (KBr cm⁻¹):** 1635, 1560, 1465, 1217, 1118, 996.
- **¹H NMR (300 MHz, CDCl₃):** δ 7.63 (dd, 1H CH), 8.5 (dd 1H CH), 5.2 (t, 1H CH), 3.38 (2h CH₂), 7.40 (dd, 1H CH), 6.85 (dd, 1H CH).
- **¹³C (CDCl₃):** 128, 146, 79, 42, 124, 164, 133, 196.

**Synthesis of 2-(4-Methoxyphenyl) chroman-4-one:**
- **IR (KBr cm⁻¹):** 1670, 1500, 1640, 1205, 1113, 985, 1090.
- **¹H NMR (300 MHz, CDCl₃):** δ 7.0 (dd, 1H CH), 6.7 (dd 1H CH), 3.72 (s, 3H CH₃), 5.5 (t, 1H CH), 3.38 (d 2H CH₂), 7.40 (dd, 1H CH), 6.8 (dd 1H CH), 6.9 (m 1H CH).
- **¹³C (CDCl₃):** 128, 114, 159, 55, 132, 79, 42, 196, 133, 124.
RESULT AND DISCUSSION

We report the synthesis of flavanones promoted by the ionic liquid catalyst, in excellent yield. The ionic liquid was prepared by the literature method.\textsuperscript{[20]} Simple intramolecular cyclization reaction of chalcone in a specific time is observed. The progress of reaction was monitored by TLC. After completion of the reaction, aqueous work-up afforded pure flavanones in 80-90 % yield. The ionic liquid is water-soluble and therefore goes into the aqueous layer. The reaction proceeds cleanly without formation of any side product except water. The protocol of the process offers advantages in terms of simple procedure and work up, mild reaction conditions and excellent yields.

Tab1. Physical data of synthesized flavanones derivative compounds

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Flavanone Derivatives</th>
<th>Melting Point (°C)</th>
<th>Time (Min)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>2-phenylchroman-4-one</td>
<td>75</td>
<td>60</td>
<td>85.94%</td>
</tr>
<tr>
<td>2.</td>
<td>2-(4-Bromophenyl) chroman-4-one</td>
<td>90</td>
<td>55</td>
<td>82.16%</td>
</tr>
<tr>
<td>3.</td>
<td>2-(4-Chlorophenyl) chroman-4-one</td>
<td>98</td>
<td>60</td>
<td>87.95%</td>
</tr>
<tr>
<td>4.</td>
<td>2-(4-nitropheynyl) chroman-4-one</td>
<td>88</td>
<td>40</td>
<td>90.21%</td>
</tr>
<tr>
<td>5.</td>
<td>2-(4-Methoxyphenyl) chroman-4-one</td>
<td>80</td>
<td>60</td>
<td>88.65%</td>
</tr>
</tbody>
</table>

CONCLUSION

In summary, we demonstrated an efficient and mild protocol for the intramolecular cyclization of 2-hydroxy chalcone to flavanones in the presence of the ionic liquid. Simple reaction conditions, higher yield and an eco-friendly approach are reported.

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