II.1: INTRODUCTION

II.1.1: Task Specific Ionic Liquids (TSILs)

Recently, the synthesis of ionic liquids with special functions according to the requirement of a specific reaction has become an attractive field due to their tunable features for various targeted chemical tasks and their advantages as reusable homogeneous supports, reagents, and catalysts with green credentials. All these studies offer the possibility of designing suitable catalysts for the appointed reactions. Task specific ionic liquids (TSILs) have been defined as ionic liquids bearing a functional group covalently tethered to the cation or anion or both. The first report of their application was that of thiazolium ionic liquid (IL) that could interact specifically with a solute and function both as a solvent and a catalyst for the benzoin condensation. The idea was that the incorporation of one or several functional groups into the ions of an ionic liquid should confer special properties or reactivities upon them such as the capacity to behave as reagents, catalysts or new reaction media. TSILs often serve the dual role of catalyst and reaction medium and are finding an increasing number of applications in synthesis, separations, catalysis and electrochemistry.

Recently, ILs based on different cations and anions bearing functional groups have been the object of several recent reviews. The acidity/basicity of the reaction media has a substantial influence on the efficiency of many reactive processes. Therefore, a new class of acidic or basic ionic liquids is gaining special attention due to the possibility of increasing the efficiency of many processes by a wise manipulation of their properties. The acid or basic function can be attached either on the anion or the cation (Figure II.1).
Acidic Ionic Liquids

The acidic ionic liquids, having one or more acidic activity sites in the framework of the ionic liquids, are one of the most important and extensively used TSILs. Based on the acidic property of the activity site, they are divided into three categories. First category is Lewis acidic ionic liquids whose activity sites have Lewis acid characteristics which can accept the isolated pair of electron from the Lewis base. The second category is Bronsted acidic ionic liquids or protic ionic liquids which have acidic activity sites with protic acidic characteristics and its key properties that distinguish from other ionic liquids are the proton transfer from the acid to the base, leading to the presence of proton-donor and acceptor site. The third category is Bronsted-Lewis combined acidic ionic liquids in which Bronsted and Lewis acidic characteristics exist simultaneously. Nowadays, acidic ionic liquids, which posses the advantageous characteristics of solid acids and mineral acids, have been successfully applied as dual solvents-catalysts for lots of organic unit reactions.

**Lewis Acidic Ionic Liquids**

Lewis acidic ionic liquids are usually distributed into organoaluminate ionic liquids which are the most intensively investigated ones. The non-organoaluminate ionic
liquids have one or more non-aluminum metal elements, such as zinc, gallium, indium or tin. They are easily prepared by mixing quaternary ammonium salts, especially $N$-alkylpyridinium chlorides and 1,3-dialkylimidazolium chlorides with metal chlorides (Scheme II.1). Their acidity could be regulated by varying the ratio of quaternary ammonium salt and metal chloride.

![Scheme II.1](image)

The ionic liquids are often loaded onto solid carrier to reduce recycling loss and separation complexity and are used for a number of organic reactions. The solid carriers are usually inorganic or organic compounds, such as activated carbon, silica gel, molecular sieves, carbon nanotubes, modified montmorillonite and organic polymers with high surface area on which ionic liquids are more evenly distributed.

**Bronsted Acidic Ionic Liquids**

Bronsted acidic ionic liquids can either have -SO$_3$H or -COOH or -H functional group as cation and a HSO$_4^-$ or other monoacid radicals as anions. The acidity of these ionic liquids is usually weak. Bronsted acidic ionic liquids having two acid sites at different locations where both positive and negative ions contribute to the acidity of the ionic liquids are also known.

**Bronsted-Lewis Combined Acidic Ionic Liquids**

The Bronsted-Lewis combined acidic ionic liquids are the ones where Bronsted and Lewis acidic character exists simultaneously. Shen *et al.*$^{11}$ have synthesised a novel ionic liquid by three steps. In the first step, zwitterion was obtained through the
condensation of pyridine and 1,4-butane sulfonate. The zwitterion and sulfuric acid were then mixed together to form the homogeneous liquid phase. Some $\text{H}^+$ ions were substituted by $\text{Fe}^{3+}$ in the third step (Scheme II.2).

![Scheme II.2](image)

**Basic Ionic Liquids**

The basic ionic liquids also fall into two categories: Lewis basic ionic liquids and Brönsted basic ionic liquids. The former refer to the basic ionic liquids with the ability to donate one or more electron pairs; the latter are the basic ionic liquids having the ability to accept one or more protons.

**Lewis Basic Ionic Liquids**

These kind of basic ionic liquids are mainly divided into two classes. The first class is the basic ionic liquids with the cation containing one $\text{-NH}_2$ or $\text{-NH}$ group which can provide isolated pair of electron and the second class is the basic ionic liquids with the anions, such as $\text{CH}_3\text{COO}^-$, $\text{CH}_3\text{CH(OH)COO}^-$, $\text{CN}^-$ and other anions which can also supply an isolated pair of electrons. Increasing the number of base sites is the best way to enhance the basicity of the basic ionic liquids. A novel normal Lewis basic ionic liquid with two base sites individually located in the cation and anion, 1-(2-piperidyl-ethyl)-3-methylimidazolium-2-morpholinyl-4-ethane sulfonate (Figure II.2) was prepared by Liu and co-workers.

![Figure II.2](image)
**Bronsted Basic Ionic Liquids**

The Bronsted basic ionic liquids with the OH\(^-\) anion are the most important ones in Brönsted basic ionic liquids, especially [bmim]OH (1-butyl-3-methylimidazolium hydroxide). Ranu et al. have prepared [bmim]OH via ion exchange reaction between potassium hydroxide and the intermediate ionic liquid, [bmim]Br, formed by the alkylations of N-methylimidazole and 1-bromobutane (Scheme II.3)\(^{13}\).

\[
\text{N} = \text{N} \quad \text{BuBr} + \text{KOH} \quad \rightarrow \quad \text{N} = \text{N} \quad \text{BuOH} + \text{Br}^-
\]

Scheme II.3

[bmim]OH has been employed in numerous organic reactions in place of traditional bases, wherein [bmim]OH plays the dual role of catalyst and solvent. [bmim]OH not only provides a green reaction medium but also could be recycled and reused for several times without loss of activity unlike conventional sodium hydroxide and ammonia. A brief review of [bmim]OH mediated reactions is given below.

**II.1.2: Reactions catalyzed by [bmim]OH**

Knoevenagel condensation of aliphatic and aromatic carbonyl compounds with a variety of active methylene compounds has been carried out using [bmim]OH (eq. 1)\(^{14}\). A series of 5-arylidene thiazolidine-2,4-diones have been synthesized by the Knoevenagel condensation of thiazolidine-2,4-dione with aromatic aldehydes by using [bmim]OH, acting both as solvent and catalyst (eq. 2)\(^{15}\).

\[
R^1O \quad + \quad E^1 \quad \text{[bmim]OH} \quad \rightarrow \quad R^1O \quad E^1 \quad \text{...(1)}
\]

\[
\text{ArCHO} + \quad \text{S}_{\text{NH}} \quad \text{O} \quad \text{[bmim]OH} \quad \rightarrow \quad \text{Ar} \quad \text{S}_{\text{NH}} \quad \text{O} \quad \text{...(2)}
\]
[bmim]OH has been used as a catalyst and reaction medium for the Markovnikoff addition of \(N\)-heterocycles to vinyl esters under mild conditions (eq. 3).\(^{16}\)

\[
\begin{align*}
\text{R}^2 \text{N} - \text{R}^1 & + \text{O} - \text{O} - \text{R}^3 \quad \text{[bmim]OH} \\
\text{R}^2 \text{N} - \text{R}^1 & \quad \text{(3)}
\end{align*}
\]

Michael addition of \(N\)-heterocycles to \(\alpha,\beta\)-unsaturated compounds at room temperature was developed using [bmim]OH, as reagent as well as reaction medium (eq. 4).\(^{17}\) It also catalyzes the addition of thiols to \(\alpha,\beta\)-acetylenic ketones (eq. 5) and alkylation of 1,3-dicarbonyl/1,3-dicyano compounds (eq. 6).\(^{18}\)

\[
\begin{align*}
\text{Nu}-\text{H} & + \quad \text{R}^1 \quad \text{EWG} \quad \text{[bmim]OH} \\
\text{Nu} & \quad \text{EWG} \\
\text{EWG} & = \text{CN, COMe, COOMe} \\
\text{[bmim]OH} & \quad \text{(4)}
\end{align*}
\]

\[
\begin{align*}
\text{Ar} & + \quad \text{SR} \quad \text{[bmim]OH} \\
\text{Ar} & \quad \text{(5)}
\end{align*}
\]

\[
\begin{align*}
\text{R}^3\text{Br} & + \quad \text{R}^1 \quad \text{[bmim]OH} \\
\text{R}^1 & \quad \text{or} \quad \text{R}^2 \quad \text{R}^3 \quad \text{(6)}
\end{align*}
\]

\(R^1 = R^2 = \text{COOMe, COOEt, CN, NO}_2; R^3 = \text{Alkyl, benzyl, allyl}\)

Three component Mannich-type reaction of ketone, aromatic aldehydes, and aromatic amines was catalyzed by [bmim]OH,\(^{19}\) at room temperature to give various \(\beta\)-amino carbonyl compounds in high yields (eq. 7).

\[
\begin{align*}
\text{O} & + \quad \text{NH}_2 \quad \text{CHO} \\
\text{O} & \quad \text{HN} \quad \text{[bmim]OH} \\
\text{[bmim]OH} & \quad \text{(7)}
\end{align*}
\]

Furans could be prepared in two steps using [bmim]OH and [pmim]Br under solvent-free conditions at 70-75\(^\circ\)C (Scheme II.4).\(^{20}\)
An efficient protocol for Henry reaction using [bmim]OH as catalyst and reaction medium has been reported (eq. 8). Three component coupling reaction of nitromethane, aromatic aldehydes and trimethylsilyl cyanide (TMSCN) or ammonium thiocyanate had been reported for the synthesis of β-nitrocarbonitriles or β-nitrothiocyanates respectively, via C-C and C-S bond forming reactions by Yadav and co-workers. The reaction involved a one pot sequential Henry reaction and a Michael addition efficiently promoted by the same ionic liquid [bmim]OH (eqs. 9-10).

Reaction of aldehydes, malononitrile and α-naphthol or β-naphthol catalyzed by [bmim]OH in aqueous media afforded corresponding 2-amino-2-chromenes (eqs. 11-12).
Synthesis of 4\(H\)-benzo[\(b\)]pyrans (eq. 13),\(^{24}\) polyfunctionalized pyridines (eq. 14),\(^{25}\) pyrroles (eq. 15)\(^{26}\) and highly stereoselective synthesis of (\(Z\))-vinyl bromides (eq. 16)\(^{27}\) by the debrominative decarboxylation of \(\alpha,\beta\)-dibromocarboxylic acids have been reported by using \([\text{bmim}]\text{OH}\).

\([\text{bmim}]\text{OH}\) has been used for an efficient synthesis of \(1\)-\(H\)-pyrazolo[1,2-\(b\)]phthalazine-5,10-diones by one pot cyclocondensation reaction of phthalhydrazide, aromatic aldehydes and malononitrile or ethyl cyanoacetate under microwave irradiation by Singh et al. (eq. 17).\(^{28}\)
A one pot synthetic protocol for 3-benzamidocoumarins using \([\text{bmim}]\text{OH}\) as a catalyst has been reported in acetonitrile (eq. 18).\textsuperscript{29} Synthesis of disubstituted ureas has also been reported from amines and \(\text{CO}_2\) using \([\text{bmim}]\text{OH}\) (eq. 19).\textsuperscript{30}

\[
\begin{align*}
\text{CHO} & \quad \text{N} \quad \text{O} \\
\text{CH}_3\text{CN}, \text{r.t.} & \quad \text{H} \\
\end{align*}
\]

...(18)

\[
\begin{align*}
2 \text{RNH}_2 & \quad \text{CO}_2 \quad \text{[bmim]}\text{OH} \\
\text{H} & \quad \text{N} \quad \text{N} \quad \text{H} \\
\text{H}_2\text{O} & \quad \text{[bmim]}\text{OH} \\
\end{align*}
\]

...(19)

Ultrasound promoted synthesis of oximes using basic ionic liquid \([\text{bmim}]\text{OH}\) (eq. 20)\textsuperscript{31} and oxidative homocoupling of terminal alkynes to symmetrical 1,4-disubstituted 1,3-diynes using copper(I) iodide in \([\text{bmim}]\text{OH}\) in the absence of any palladium compound has been reported (eq. 21).\textsuperscript{32}

\[
\begin{align*}
\text{R}_1\text{R}_2^\text{O} & \quad \text{H}_2\text{NOH.HCl} \quad \text{[bmim]}\text{OH} \\
\text{H} & \quad \text{N} \quad \text{OH} \\
\text{[bmim]}\text{OH} & \quad \text{[bmim]}\text{OH} \\
\end{align*}
\]

...(20)

\[
\begin{align*}
\text{R} & \quad \equiv \quad \equiv \quad \equiv \quad \text{R} \\
\text{[bmim]}\text{OH}, \text{r.t.} & \quad \text{CuI} (5 \text{ mol}\%) \\
\end{align*}
\]

...(21)

Synthesis of 3-styrylchromones from 3-formylchromones and 4-nitrophenylacetic acid/4-nitrotoulene in the presence of \([\text{bmim}]\text{OH}\) under microwave irradiation (eq. 22)\textsuperscript{33} and synthesis of quinazoline-2,4(1\(H,3\text{H}\))-diones from carbon dioxide and 2-aminobenzonitriles (eq. 23)\textsuperscript{34} using \([\text{bmim}]\text{OH}\) have been reported.
[bmim]OH is used as a green recyclable reaction medium and reagent for the alkylation of phenols in excellent yields by Mohanazadeh and Aghvami (eq. 24).\(^{35}\)

\[
\begin{align*}
\text{OH} & \quad \text{RX} \quad \text{[bmim]OH, 70}^\circ \text{C} \quad \text{OR} \quad \text{OH} \\
\text{Y} & \quad \text{Y} 
\end{align*}
\]

...(24)

[bmim]OH mediated synthesis of \(N\)-heterocyclic carbamates from \(N\)-heterocycles and dimethyl carbonate (DMC) (eq. 25)\(^ {36}\) and \(N\)-alkylation of benzotriazole with alkyl halides at room temperature has been reported (eq. 26).\(^ {37}\)

\[
\begin{align*}
\text{N} & \quad \text{H} \quad \text{[bmim]OH} \quad \text{DMC} \quad \text{N} \quad \text{O} \\
\text{N} & \quad \text{N} 
\end{align*}
\]

...(25)

\[
\begin{align*}
\text{N} & \quad \text{N} \quad \text{RX} \quad \text{[bmim]OH} \quad \text{r.t.} \quad \text{N} \quad \text{N} \\
\text{N} & \quad \text{N} \quad \text{R} \quad \text{R} 
\end{align*}
\]

...(26)

An environment friendly approach to the diastereoselective synthesis of trans-4-oxo-3-aryl-3,4-dihydro-2\(H\)-furo[3,2-\(c\)]coumarin-2-carbonitriles, trans-2-benzoyl-3-aryl-2\(H\)-furo[3,2-\(c\)]chromen-4(3\(H\))-ones and trans-ethyl-4-oxo-3-aryl-3,4-dihydro-2\(H\)-furo[3,2-\(c\)]chromene-2-carboxylates has been reported via sequential multicomponent reactions of 4-hydroxycoumarin, aromatic aldehydes and \textit{in situ} generated cyanomethyl pyridinium, phenacylpyridinium/ (2-ethoxy-2-oxoethyl) pyridinium ylides, in presence of [bmim]OH (eq. 27).\(^ {38}\)

\[
\begin{align*}
\text{Z = CN, COPh, COOEt}
\end{align*}
\]
II.1.3: Synthesis of 4H-pyrans, 4H-pyrano[2,3-c]pyrazoles and 4H-benzo[g]chromenes

Polyfunctionalized 4H-pyran derivatives are versatile synthons because of the inherent reactivity of the pyran ring and are biologically interesting compounds as they possess various pharmacological activities, e.g. antiallergic and antitumor activities. The synthesis of 4H-pyran derivatives by one pot condensation of aromatic aldehydes, malononitrile and β-dicarboxyl compounds can be achieved by using tetramethylguanidine in [bmim]BF$_4$, magnesium oxide, 1-methyl-3-(2-aminoethyl)imidazolium hexafluophosphate, Cu(II) oxymetasilicate, silica nanoparticles, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and also by a recyclable temperature-dependent phase-separation catalytic system comprising of PEG$_{1000}$-based functional dicationic acidic ionic liquid and ethylene glycol monomethyl ether (eq. 28).

\[
\text{ArCHO} + \text{R} = \text{CH}_3, \text{OEt} + \text{CN} \rightarrow \begin{array}{c}
\text{O} \\
\text{Ar}
\end{array} \begin{array}{c}
\text{CN} \\
\text{O}
\end{array} \begin{array}{c}
\text{O} \\
\text{NH}_2
\end{array} 
\]  

Pyrano[2,3-c]pyrazoles also hold a position of prominence due to their potential antibacterial, antifungal, anti-inflammatory and molluscidal activity besides being identified as a screening kit for Chk1 kinase inhibitor. Synthesis of 4H-pyrano[2,3-c]pyrazoles has been reported by using four component cyclocondensation of hydrazine monohydrate/ phenyl hydrazine, ethyl acetoacetate, aldehydes and malononitrile in presence of L-proline in [bmim]BF$_4$, γ-alumina in aqueous medium, imidazole, piperidine, triethylamine as catalysts and also under solvent free conditions using per-6-amino-β-cyclodextrin or silicotungstic acid (eq. 29).

\[
\text{ArCHO} + \text{CN} + \text{NH}_2\text{NH}_2 + \begin{array}{c}
\text{O} \\
\text{HN}
\end{array} \begin{array}{c}
\text{O} \\
\text{NH}_2
\end{array} \rightarrow \begin{array}{c}
\text{O} \\
\text{Ar}
\end{array} \begin{array}{c}
\text{CN} \\
\text{O}
\end{array} \begin{array}{c}
\text{O} \\
\text{NH}_2
\end{array} 
\]  

Moreover, benzo[g]chromenes are known as antimalarial, anti-inflammatory, and anti-cancer agents besides demonstrating pesticide activities. Synthesis of functionalized 4H-benzo[g]chromenes has been reported by reaction between aldehydes, malononitrile and 2-hydroxynaphthalene-1,4-dione using catalytic Et$_3$N in...
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CH$_3$CN,$^{68}$ triethylbenzylammonium chloride under solvent-free conditions$^{69}$ and DBU in water under reflux $^{70}$ (eq. 30).

II.2: RESULTS AND DISCUSSION

It can be inferred from the above review (II.1.3) that penta-substituted 4$H$-pyrans, 4$H$-pyrano[2,3-c]pyrazoles and 4$H$-benzo[g]chromenes have broad utility range. It has also been reviewed above that [bmim]OH (II.1.2) is a useful reaction medium and also catalyzes a variety of reactions. In view of the importance of 4$H$-pyrans, 4$H$-pyrano[2,3-c]pyrazoles, 4$H$-benzo[g]chromenes and the fact that reported methods have their own merits and demerits, we decided to investigate the possibility of synthesizing these compounds by utilizing [bmim]OH which can act both as reaction medium and catalyst.

II.2.1: Synthesis of 4$H$-Pyrans

With the objective of the project for the one pot synthesis of 4$H$-pyrans in mind, a reaction of 4-chlorobenzaldehyde (Ia) (1.0 mmol), ethyl acetoacetate (1.0 mmol) and malononitrile (1.0 mmol) was carried out in presence of 10 mol% of [bmim]OH at 50-60°C. Reaction progress was monitored by TLC using petroleum ether: ethyl acetate (60:40, v/v) as eluent. TLC showed complete disappearance of 4-chlorobenzaldehyde and malononitrile after 30 min but showed the presence of ethyl acetoacetate besides formation of a new product. We believed that simple Knoevenagel condensation could have taken place between the aldehyde and malononitrile and ethyl acetoacetate could have remained unreacted. This was confirmed by co-TLC analysis that the new spot corresponded with 2-(4-chlorobenzylidene)-malononitrile generated by the Knoevenagel condensation of 4-chlorobenzaldehyde and malononitrile. The heating was continued and another new spot appeared after 1 h as observed by TLC. However, the reaction did not proceed to completion even after 6 h of heating and was worked up. The new product was separated by preparative TLC (run 1). The isolated product was
characterized to be ethyl 6-amino-4-(4-chlorophenyl)-5-cyano-2-methyl-4H-pyran-3-carboxylate (IIa), by m.p., IR and NMR analysis albeit in only 65% yield.

The effect of amount of [bmim]OH on the reaction time and yield of the product was then investigated. The above reaction of Ia, malononitrile and ethyl acetoacetate was performed using 15 mol%, 20 mol% and 25 mol% of [bmim]OH. It was observed that the reaction using 15 mol% of [bmim]OH was complete in 4 h yielding 75% of IIa (run 2), while the reaction was complete in 30 min using 20 mol% of [bmim]OH, yielding 91% of IIa (run 3). When the same reaction was attempted using 25 mol% of [bmim]OH, the reaction was complete in 30 min and yielded 92% of IIa (run 4). The reaction conducted using 20 mol% of [bmim]OH at room temperature remained incomplete and resulted in the formation of only 30% of IIa after 6 h (run 5), whereas no appreciable effect on the reaction time or yield was observed when the reaction was attempted at 80°C under otherwise similar conditions (run 6).

The effect of other ionic liquids on the reaction was also examined. [bmim]Br and [bmim]BF$_4$ were found to be ineffective for this condensation, yielding only 15-20% of the desired product (IIa) even after 6 h (runs 7-8). This confirms the vital role of the hydroxyl counter anion of [bmim]OH functionalized ionic liquid in this transformation. All these results are listed in Table II.1.

Table II.1: Optimization of reaction conditions for the condensation of equimolar amounts of 4-chlorobenzaldehyde, malononitrile and ethyl acetoacetate

<table>
<thead>
<tr>
<th>Run</th>
<th>Ionic liquid</th>
<th>Mol %</th>
<th>Temp (°C)</th>
<th>Time (h)</th>
<th>% Yield (IIa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>[bmim]OH</td>
<td>10</td>
<td>50-60</td>
<td>6</td>
<td>65&lt;sup&gt;ab&lt;/sup&gt;</td>
</tr>
<tr>
<td>2.</td>
<td>[bmim]OH</td>
<td>15</td>
<td>50-60</td>
<td>4</td>
<td>75</td>
</tr>
<tr>
<td>3.</td>
<td>[bmim]OH</td>
<td>20</td>
<td>50-60</td>
<td>0.5</td>
<td>91</td>
</tr>
<tr>
<td>4.</td>
<td>[bmim]OH</td>
<td>25</td>
<td>50-60</td>
<td>0.5</td>
<td>92</td>
</tr>
<tr>
<td>5.</td>
<td>[bmim]OH</td>
<td>20</td>
<td>r.t.</td>
<td>6</td>
<td>30&lt;sup&gt;ab&lt;/sup&gt;</td>
</tr>
<tr>
<td>6.</td>
<td>[bmim]OH</td>
<td>20</td>
<td>80</td>
<td>0.5</td>
<td>93</td>
</tr>
<tr>
<td>7.</td>
<td>[bmim]Br</td>
<td>20</td>
<td>50-60</td>
<td>6</td>
<td>15&lt;sup&gt;ab&lt;/sup&gt;</td>
</tr>
<tr>
<td>8.</td>
<td>[bmim]BF$_4$</td>
<td>20</td>
<td>50-60</td>
<td>6</td>
<td>20&lt;sup&gt;ab&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Incomplete reaction  
<sup>b</sup>Mixture of products
It can be concluded from the results summarized in Table II.1 that 20 mol% of [bmim]OH at 50-60°C is the optimum system for the condensation reaction of 4-chlorobenzaldehyde, ethyl acetoacetate and malononitrile to afford 91% of ethyl 6-amino-4-(4-chlorophenyl)-5-cyano-2-methyl-4H-pyran-3-carboxylate (IIa) (eq. 31).

The recyclability of the ionic liquid was also investigated. The recovered ionic liquid gave comparable yields of the product (IIa) in second and third cycles. However, the yields decreased gradually in fourth and fifth cycles as depicted in Figure II.3.

![Figure II.3: Recycling yields; Reaction of equimolar amounts of 4-chlorobenzaldehyde, malononitrile and ethyl acetoacetate in [bmim]OH at 50-60°C](image)

The scope of the optimized protocol was then extended to a variety of aromatic aldehydes. Aromatic aldehydes such as 3-chlorobenzaldehyde (Ib), benzaldehyde (Ic), 4-methylnbenzaldehyde (Id), 2,4-dichlorobenzaldehyde (Ie), 4-nitrobenzaldehyde (If), 4-methoxybenzaldehyde (Ig), 3-nitrobenzaldehyde (Ih), 4-hydroxybenzaldehyde (II), 3-hydroxybenzaldehyde (Ij), piperonal (Ik) and 2-chlorobenzaldehyde (Il) underwent successful condensation with ethyl acetoacetate and malononitrile using 20 mol% of [bmim]OH at 50-60°C, to afford corresponding 4H-pyran derivatives viz. ethyl 6-amino-
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4-(3-chlorophenyl)-5-cyano-2-methyl-4H-pyran-3-carboxylate (IIb), ethyl 6-amino-5-cyano-2-methyl-4-phenyl-4H-pyran-3-carboxylate (IIc), ethyl 6-amino-5-cyano-2-methyl-4-(4-methylphenyl)-4H-pyran-3-carboxylate (IId), ethyl 6-amino-5-cyano-4-(2,4-dichlorophenyl)-2-methyl-4H-pyran-3-carboxylate (IIe), ethyl 6-amino-5-cyano-2-methyl-4-(4-nitrophenyl)-4H-pyran-3-carboxylate (IIf), ethyl 6-amino-5-cyano-4-(4-methoxyphenyl)-2-methyl-4H-pyran-3-carboxylate (IIg), ethyl 6-amino-5-cyano-2-methyl-4-(3-nitrophenyl)-4H-pyran-3-carboxylate (IIh), ethyl 6-amino-5-cyano-4-(4-hydroxyphenyl)-2-methyl-4H-pyran-3-carboxylate (IIi), ethyl 6-amino-5-cyano-4-(3-hydroxyphenyl)-2-methyl-4H-pyran-3-carboxylate (IIj), ethyl 6-amino-4-(benzo[1,3]dioxol-5-yl)-5-cyano-2-methyl-4H-pyran-3-carboxylate (IIk) and ethyl 6-amino-4-(2-chlorophenyl)-5-cyano-2-methyl-4H-pyran-3-carboxylate (III) respectively in high yields (Table II.2, runs 9-19) (eq. 32).

Table II.2: Synthesis of 4H-pyrans by condensation of aldehydes, malononitrile and ethylacetoacetate/ acetyl acetone (molar ratio 1: 1: 1) catalyzed by [bmim]OH

<table>
<thead>
<tr>
<th>Run</th>
<th>Ar (ArCHO)</th>
<th>R</th>
<th>Product</th>
<th>Time (min)</th>
<th>% Yield (II)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.</td>
<td>3-ClC₆H₄</td>
<td>OEt</td>
<td>IIb</td>
<td>50</td>
<td>91</td>
</tr>
<tr>
<td>10.</td>
<td>C₆H₅</td>
<td>OEt</td>
<td>IIc</td>
<td>45</td>
<td>90</td>
</tr>
<tr>
<td>11.</td>
<td>4-CH₂C₆H₄</td>
<td>OEt</td>
<td>IId</td>
<td>60</td>
<td>87</td>
</tr>
<tr>
<td>12.</td>
<td>2,4-Cl₂C₆H₄</td>
<td>OEt</td>
<td>IIe</td>
<td>45</td>
<td>91</td>
</tr>
<tr>
<td>13.</td>
<td>4-O₂NC₂H₄</td>
<td>OEt</td>
<td>IIf</td>
<td>30</td>
<td>90</td>
</tr>
<tr>
<td>14.</td>
<td>4-CH₂OC₂H₄</td>
<td>OEt</td>
<td>IIg</td>
<td>55</td>
<td>88</td>
</tr>
<tr>
<td>15.</td>
<td>3-O₂NC₂H₄</td>
<td>OEt</td>
<td>IIh</td>
<td>35</td>
<td>90</td>
</tr>
<tr>
<td>16.</td>
<td>4-HOC₂H₄</td>
<td>OEt</td>
<td>IIi</td>
<td>40</td>
<td>87</td>
</tr>
<tr>
<td>17.</td>
<td>3-HOC₂H₄</td>
<td>OEt</td>
<td>IIj</td>
<td>35</td>
<td>88</td>
</tr>
<tr>
<td>18.</td>
<td>Piperonyl</td>
<td>OEt</td>
<td>IIk</td>
<td>45</td>
<td>87</td>
</tr>
<tr>
<td>19.</td>
<td>2-ClC₆H₄</td>
<td>OEt</td>
<td>III</td>
<td>35</td>
<td>92</td>
</tr>
<tr>
<td>20.</td>
<td>C₆H₅</td>
<td>CH₃</td>
<td>IIm</td>
<td>35</td>
<td>90</td>
</tr>
<tr>
<td>21.</td>
<td>4-CH₂C₆H₄</td>
<td>CH₃</td>
<td>IIl</td>
<td>35</td>
<td>88</td>
</tr>
<tr>
<td>22.</td>
<td>4-CH₂OC₂H₄</td>
<td>CH₃</td>
<td>IIo</td>
<td>40</td>
<td>89</td>
</tr>
</tbody>
</table>

*Reactions were carried out using 20 mol% of [bmim]OH at 50-60°C
The condensation of benzaldehyde (Ic), 4-methylbenzaldehyde (Id) and 4-methoxybenzaldehyde (Ig) could also be carried out with malononitrile and acetyl acetone, under otherwise identical reaction conditions. The reactions were complete in 35-40 min and the isolated products were identified to be 5-acetyl-2-amino-6-methyl-4-phenyl-4H-pyran-3-carbonitrile (IIm), 5-acetyl-2-amino-4-(4-methylphenyl)-6-methyl-4H-pyran-3-carbonitrile (IIn) and 5-acetyl-2-amino-3-cyano-6-methyl-4-(4-methoxy phenyl)-4H-pyran (IIo) respectively (Table II.2, runs 20-22) (eq. 32).

\[
\text{ArCHO} + \begin{array}{c}
\text{CN} \\
\text{R}
\end{array} \begin{array}{c}
\text{CN} \\
\text{CN}
\end{array} \rightarrow \begin{array}{c}
\text{CN} \\
\text{Ar}
\end{array} + \begin{array}{c}
\text{CN} \\
\text{NH}_2
\end{array}
\] 

\(50-60^\circ\text{C}\) ...(32)

The structures of all the synthesized pyrans IIa-o were in accordance with their spectroscopic data. The IR spectra of all the products showed the characteristic absorption bands for amine, carbonyl and nitrile functionalities. For example, the IR spectrum of compound IIh (Figure II.4, page 71) displayed absorption bands at 3403 cm\(^{-1}\) and 3328 cm\(^{-1}\) for NH stretch of NH\(_2\) group of pyran ring. Bands at 2191 cm\(^{-1}\) and 1691 cm\(^{-1}\) correspond to C≡N stretch of nitrile and C=O stretch of carbonyl group, respectively. In the \(^1\text{H}\) NMR spectrum of compound IIh (Figure II.5, page 72), a singlet of methine-proton (CHAr) appeared at \(\delta 4.56\), while another singlet of three protons of methyl group appeared at \(\delta 2.39\). Four aromatic protons appeared as multiplets in the range of \(\delta 8.10-8.04\) and 7.58-7.45, while the two protons corresponding to NH\(_2\) appeared as a broad singlet at \(\delta 4.62\). The methyl protons of ethoxy group appeared as triplet at \(\delta 1.12\), whereas the two methylene protons were observed as multiplet in the range of \(\delta 4.06-4.00\). \(^{13}\text{C}\) NMR spectrum of compound IIh (Figure II.6, page 73) showed fifteen signals corresponding to fifteen non-equivalent carbons present in the compound as mentioned in the experimental spectral data.

A plausible mechanism for the formation of 4H-pyran from aldehydes, malononitrile and ethyl acetoacetate/acetylacetonate is proposed in Scheme II.5.
Chapter II

The initial condensation of aromatic aldehyde with malononitrile in the presence of [bmim]OH led to the formation of arylidenemalononitrile with the loss of a water molecule. The nucleophilic addition of the enolizable ethyl acetoacetate to arylidene malononitrile followed by intramolecular cyclization of the resulting species produce the 2-amino-4H-pyran. The reaction pathway was confirmed by an independent reaction of 2-(4-chlorobenzylidene)-malononitrile with ethyl acetoacetate in the presence of [bmim]OH which gave the desired 4H-pyran (IIa).

II.2.2: Synthesis of 4H-pyrano[2,3-c]pyrazoles

The protocol employed for the synthesis of 4H-pyrans as described in section II.2.1 was investigated for the condensation of aldehyde, 5-methyl-2,4-dihydropyrazol-3-one and malononitrile. A reaction of 4-bromobenzaldehyde (Im) (1.0 mmol), malononitrile (1.0 mmol), 5-methyl-2,4-dihydro-pyrazol-3-one (1.0 mmol) and 20 mol% of [bmim]OH was carried out at 50-60°C. The reaction was complete in 5 min as monitored by TLC using petroleum ether: ethyl acetate (70:30, v/v) as eluent unlike the synthesis of 4H-pyrans which required 30-60 min for completion. After work up, 6-amino-4-(4-bromophenyl)-3-methyl-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (IIIa) was obtained as identified by spectral data in 91% yield (Table II.3, method A, run 23) (eq. 33).
The IR spectrum of compound IIIa displayed absorption bands at 3397, 3223 and 3182 cm\(^{-1}\) for NH stretch of NH\(_2\) group of pyran ring and NH group of pyrazole ring, respectively (Figure II.7, page 74). Band at 2190 cm\(^{-1}\) correspond to C≡N stretch of nitrile. The \(^1\)H NMR spectrum of compound IIIa (Figure II.8, page 75) showed six signals indicating that the molecule possesses six sets of non-equivalent protons. A singlet of one proton at δ 12.11 was assigned to NH of pyrazole ring, another singlet for NH\(_2\) group attached to pyran ring appeared at δ 6.91. Two doublets of two protons each appeared at δ 7.48 and δ 7.10 due to protons of 4-bromophenyl ring showing para-substitution. A singlet of methine-proton (CHAr) appeared at δ 4.58, while another singlet appeared at δ 1.75 for three protons of methyl group. \(^{13}\)C NMR spectrum of compound IIIa (Figure II.9, page 76) showed twelve signals corresponding to twelve non-equivalent carbons present in the compound as mentioned in the experimental spectral data.

Further, we decided to investigate whether the synthesis of 4H-pyrano[2,3-c]pyrazoles, could also be achieved via four component cyclocondensation of hydrazine monohydrate, ethyl acetoacetate, aldehydes and malononitrile using 20 mol% of [bmim]OH at 50-60°C. Therefore, a mixture of 4-bromobenzaldehyde (1.0 mmol), malononitrile (1.0 mmol), hydrazine hydrate (1.0 mmol), ethyl acetoacetate (1.0 mmol) and [bmim]OH (0.2 mmol) was heated in an oil-bath maintained at 50-60°C. TLC showed complete disappearance of the starting materials after 10 min of heating and a simple work up yielded 90% of 6-amino-4-(4-bromophenyl)-3-methyl-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (IIIa) (eq. 34) (Table II.3, run 23, method B).
Thus having established the reaction conditions for the synthesis of 4H-pyran[2,3-c]pyrazole (IIa), we aimed at checking the applicability of the protocols for different aromatic aldehydes under both the conditions i.e. via three component condensation of aldehydes, malononitrile and pyrazolone (Method A) or via four component condensation of aldehydes, malononitrile, ethyl acetoacetate and hydrazine monohydrate (Method B) using [bmim]OH as task specific ionic liquid (Scheme II.6).

Reactions of different substituted aromatic aldehydes such as 4-chlorobenzaldehyde (Ia), benzaldehyde (Ic), 4-methylbenzaldehyde (Id), 4-nitrobenzaldehyde (If), 4-methoxybenzaldehyde (Ig), 3-nitrobenzaldehyde (Ih), 4-hydroxybenzaldehyde (ii), 2-chlorobenzaldehyde (II), 3,4,5-trimethoxybenzaldehyde (In), 4-fluorobenzaldehyde (Io), 4-dimethylaminobenzaldehyde (Ip), 2-methoxybenzaldehyde (Iq), 3-bromobenzaldehyde (Ir), 2-nitrobenzaldehyde (Is), furfuraldehyde (It) and 1-naphthaldehyde (Iu) were carried out in the presence of [bmim]OH (20 mol%) by both Methods A and B at 50-60°C.

All the reactions afforded corresponding pyranopyrazole derivatives viz. 6-amino-4-(4-chlorophenyl)-3-methyl-2,4-dihydropyran[2,3-c]pyrazole-5-carbonitrile (IIIb), 6-amino-3-methyl-4-phenyl-2,4-dihydropyran[2,3-c]pyrazole-5-carbonitrile (IIIc), 6-amino-3-methyl-4-(4-methylphenyl)-2,4-dihydropyran[2,3-c]pyrazole-5-carbonitrile (IIId), 6-amino-3-methyl-4-(4-nitrophenyl)-2,4-dihydropyran[2,3-c]pyrazole-5-carbonitrile (IIle), 6-amino-4-(4-methoxyphenyl)-3-methyl-2,4-dihydropyran[2,3-c]pyrazole-5-carbonitrile (IIIf), 6-amino-3-methyl-4-(3-nitrophenyl)-2,4-dihydropyran[2,3-c]pyrazole-5-carbonitrile (IIIg), 6-amino-4-(4-hydroxyphenyl)-3-methyl-2,4-dihydropyran[2,3-c]pyrazole-5-carbonitrile (IIH), 6-amino-4-(2-chlorophenyl)-3-methyl-2,4-dihydro-pyran[2,3-c]pyrazole-5-carbonitrile (IIi), 6-amino-3-methyl-4-(3,4,5-trimethoxyphenyl)-2,4-dihydropyran[2,3-c]pyrazole-5-carbonitrile (IIj), 6-amino-4-(4-fluorophenyl)-3-methyl-2,4-dihydropyran[2,3-c]pyrazole-5-carbonitrile (IIk), 6-amino-4-(4-dimethylaminophenyl)-3-methyl-2,4-dihydropyran[2,3-c]pyrazole-5-carbonitrile (IIl), 6-amino-4-(2-methoxyphenyl)-3-methyl-2,4-dihydropyran[2,3-c]pyrazole-5-carbonitrile (IIm), 6-amino-4-(4-bromophenyl)-3-methyl-2,4-dihydropyran[2,3-c]pyrazole-5-carbonitrile (IIm), 6-amino-3-methyl-4-(2-nitrophenyl)-2,4-dihydropyran[2,3-c]pyrazole-5-carbonitrile (IIIo), 6-amino-4-(4-fluoro-2-yl)-3-methyl-2,4-dihydropyran[2,3-c]pyrazole-5-carbonitrile (IIIp) and 6-amino-3-methyl-4-(1-naphthyl)-2,4-dihydropyran[2,3-c]pyrazole-5-carbonitrile (IIIq) in high yields by both methods (Scheme II.6). These results are compiled in Table II.3 (runs 24-39).
**Table II.3: Syntheses of 4H-pyran-2,3-c|pyrazoles catalyzed by [bmim]OH**

<table>
<thead>
<tr>
<th>Run</th>
<th>Ar (ArCHO)</th>
<th>Product</th>
<th>Method A&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Method B&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Time (min)</td>
<td>(%) Yield</td>
</tr>
<tr>
<td>23.</td>
<td>4-BrC₆H₄(Im)</td>
<td>IIIa</td>
<td>5</td>
<td>91</td>
</tr>
<tr>
<td>24.</td>
<td>4-ClC₆H₄(Ia)</td>
<td>IIIb</td>
<td>5</td>
<td>94</td>
</tr>
<tr>
<td>25.</td>
<td>C₆H₅ (Ic)</td>
<td>IIIc</td>
<td>5</td>
<td>90</td>
</tr>
<tr>
<td>26.</td>
<td>4-CH₃C₆H₄(Id)</td>
<td>IIId</td>
<td>5</td>
<td>96</td>
</tr>
<tr>
<td>27.</td>
<td>4-O₂NC₆H₄(If)</td>
<td>IIIe</td>
<td>5</td>
<td>94</td>
</tr>
<tr>
<td>28.</td>
<td>4-CH₂OC₆H₄(Ig)</td>
<td>IIIf</td>
<td>5</td>
<td>94</td>
</tr>
<tr>
<td>29.</td>
<td>3-O₂NC₆H₄(Ih)</td>
<td>IIIg</td>
<td>5</td>
<td>85</td>
</tr>
<tr>
<td>30.</td>
<td>4-HOC₆H₄(Ii)</td>
<td>IIIh</td>
<td>5</td>
<td>87</td>
</tr>
<tr>
<td>31.</td>
<td>2-ClC₆H₄(II)</td>
<td>IIIi</td>
<td>5</td>
<td>89</td>
</tr>
<tr>
<td>32.</td>
<td>3,4,5-(CH₃O)₃C₆H₂(In)</td>
<td>IIIj</td>
<td>5</td>
<td>84</td>
</tr>
<tr>
<td>33.</td>
<td>4-FC₆H₄(Io)</td>
<td>IIIk</td>
<td>5</td>
<td>86</td>
</tr>
<tr>
<td>34.</td>
<td>4-(CH₃)₂NC₆H₄(Ip)</td>
<td>IIIl</td>
<td>10</td>
<td>95</td>
</tr>
<tr>
<td>35.</td>
<td>2-CH₂OC₆H₄(Iq)</td>
<td>IIIm</td>
<td>5</td>
<td>92</td>
</tr>
<tr>
<td>36.</td>
<td>3-BrC₆H₄(Ir)</td>
<td>IIIn</td>
<td>5</td>
<td>90</td>
</tr>
<tr>
<td>37.</td>
<td>2-O₂NC₆H₄(Is)</td>
<td>IIIo</td>
<td>5</td>
<td>87</td>
</tr>
<tr>
<td>38.</td>
<td>2-Furanyl (It)</td>
<td>IIIp</td>
<td>5</td>
<td>93</td>
</tr>
<tr>
<td>39.</td>
<td>1-Naphthyl (Iu)</td>
<td>IIIq</td>
<td>5</td>
<td>86</td>
</tr>
</tbody>
</table>

<sup>a</sup>Reactions of equimolar amounts of aldehydes, malononitrile and pyrazolone were carried out using 20 mol% of [bmim]OH at 50-60°C

<sup>b</sup>Reactions of equimolar amounts of aldehydes, malononitrile, ethyl acetoacetate and hydrazine monohydrate were carried out using 20 mol% of [bmim]OH at 50-60°C
The possible reaction pathway for the synthesis of dihydropyrano[2,3-c]pyrazole derivatives (IIIa-IIIq) in the presence of [bmim]OH is given in Scheme II.7.

The first step involves the condensation of aromatic aldehydes with malononitrile to afford the corresponding \( \alpha \)-cyanocinnammonitrile derivative (1). Ethyl acetoacetate condenses with hydrazine to give 3-methyl-1,4-dihydropyrazol-5-one (2). The active methylene of pyrazolone (2) underwent Michael addition with the electrophilic C=C double bond of \( \alpha \)-cyanocinnammonitrile to give the intermediate 3 which tautomerizes to the intermediate 4. The intermediate 4 undergoes intramolecular nucleophilic attack on the cyano group to give the intermediate 5, which undergoes tautomerization to give the desired product. The proposed mechanism was confirmed by an independent reaction between 2-(4-bromobenzylidene)malononitrile (prepared from Knoevenagal condensation of 4-bromobenzaldehyde and malononitrile) and 3-methyl-1,4-dihydropyrazol-5-one (prepared from condensation of ethyl acetoacetate and hydrazine hydrate) in equimolar ratio which gave quantitative yield of IIIa.

II.2.3: Synthesis of 4H-benzof[g]chromenes

The protocol employed for the synthesis of 4H-pyrans and 4H-pyran[2,3-c]pyrazoles as described in Sections II.2.1 and II.2.2 was further explored for the condensation of
aldehydes, 2-hydroxy-1,4-naphthoquinone and malononitrile to give 4H-benzo[g]chromene derivatives. A reaction of 4-bromobenzaldehyde (Im) (1.0 mmol), malononitrile (1.0 mmol), 2-hydroxynaphthalene-1,4-dione (1.0 mmol) and [bmim]OH (20 mol%) was carried out at 50-60°C. The reaction was complete in 1.5 h as monitored by TLC using petroleum ether: ethyl acetate (70:30, v/v) as eluent. After work-up, 90% of 2-amino-4-(4-bromophenyl)-5,10-dioxo-5,10-dihydro-4H-benzo[g]chromene-3-carbonitrile (IVa) (run 40) was obtained as characterized by m.p. and spectral analysis (eq. 35).

![Reaction Scheme](image)

The IR spectrum of compound IVa showed absorption bands at 3407 and 3330 cm\(^{-1}\) corresponding to NH stretch of NH\(_2\) group and band at 2205 cm\(^{-1}\) corresponding to C≡N stretch of nitrile group (Figure II.10, page 77). The streching due to carbonyl group was observed at 1669 cm\(^{-1}\). In \(^1\)H NMR spectrum of compound IVa, the CH (ArCH) was observed as singlet at δ 4.61 while the two protons corresponding to NH\(_2\) were observed as a singlet at δ 7.38. The eight aromatic protons appeared as their usual patterns of doublets and multiplets in the range of δ 8.0-7.28 (Figure II.11, page 78). \(^{13}\)C NMR spectrum of compound IVa showed eighteen signals corresponding to eighteen non-equivalent carbons present in the compound (Figure II.12, page 79).

Thereafter, reactions of other aromatic aldehydes such as 4-chlorobenzaldehyde (Ia), 3-chlorobenzaldehyde (Ib), benzaldehyde (Ic), 4-methylbenzaldehyde (Id), 2,4-dichlorobenzaldehyde (Ie), 4-nitrobenzaldehyde (If), 4-methoxybenzaldehyde (Ig), 4-hydroxybenzaldehyde (II), 2-chlorobenzaldehyde (II), 4-fluorobenzaldehyde (Io), 3-bromobenzaldehyde (Ir) and 2-naphthaldehyde (Iv) were carried out with malononitrile and 2-hydroxynaphthalene-1,4-dione using [bmim]OH at 50-60°C. The corresponding
benzo[g]chromene derivatives obtained were 2-amino-4-(4-chlorophenyl)-5,10-dioxo-5,10-dihydro-4H-benzo[g]chromene-3-carbonitrile (IVb), 2-amino-4-(3-chlorophenyl)-5,10-dioxo-5,10-dihydro-4H-benzo[g]chromene-3-carbonitrile (IVc), 2-amino-5,10-dioxo-5,10-dihydro-4-phenyl-4H-benzo[g]chromene-3-carbonitrile (IVd), 2-amino-5,10-dioxo-5,10-dihydro-4-(4-methylphenyl)-4H-benzo[g]chromene-3-carbonitrile (IVe), 2-amino-4-(2,4-dichlorophenyl)-5,10-dioxo-5,10-dihydro-4H-benzo[g]chromene-3-carbonitrile (IVf), 2-amino-5,10-dioxo-5,10-dihydro-4-(4-nitrophenyl)-4H-benzo[g]chromene-3-carbonitrile (IVg), 2-amino-5,10-dioxo-5,10-dihydro-4-(4-methoxyphenyl)-4H-benzo[g]chromene-3-carbonitrile (IVh), 2-amino-4-(4-hydroxyphenyl)-5,10-dioxo-5,10-dihydro-4H-benzo[g]chromene-3-carbonitrile (IVi), 2-amino-4-(2-chlorophenyl)-5,10-dioxo-5,10-dihydro-4H-benzo[g]chromene-3-carbonitrile (IVj), 2-amino-5,10-dioxo-5,10-dihydro-4-(4-fluorophenyl)-4H-benzo[g]chromene-3-carbonitrile (IVk), 2-amino-4-(3-bromophenyl)-5,10-dioxo-5,10-dihydro-4H-benzo[g]chromene-3-carbonitrile (IVl) and 2-amino-5,10-dihydro-4-(naphthalene-2-yl)-4H-benzo[g]chromene-3-carbonitrile (IVm). The results have been summarized in Table II.4 (runs 41-52) and generalized in eq. 36.

A plausible mechanism for the formation of 4H-benzo[g]chromene derivatives (IVa to IVm) is proposed in Scheme II.8, wherein the initial step is the fast Knoevenagel condensation of malononitrile and aromatic aldehyde. The subsequent step presumably involves the ortho C-alkylation of 2-hydroxy-1,4-naphthoquinone by reaction with electrophilic C-C double bond. Subsequently, the hydroxyl group undergoes fast nucleophilic addition to the CN group producing the final 4H-benzo[g]chromenes (Scheme II.8).
Table II.4: Synthesis of 4H-benzo[g]chromene derivatives by condensation of equimolar ratio of aldehydes, malononitrile and 2-hydroxy-1,4-naphthoquinone

<table>
<thead>
<tr>
<th>Run</th>
<th>Ar (ArCHO)</th>
<th>Product</th>
<th>Time (h)</th>
<th>% Yield (IV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40.</td>
<td>4-BrC₆H₄ (IIm)</td>
<td>IVa</td>
<td>1.5</td>
<td>90</td>
</tr>
<tr>
<td>41.</td>
<td>4-ClC₆H₄ (Ia)</td>
<td>IVb</td>
<td>1</td>
<td>91</td>
</tr>
<tr>
<td>42.</td>
<td>3-ClC₆H₄ (Ib)</td>
<td>IVc</td>
<td>1.5</td>
<td>91</td>
</tr>
<tr>
<td>43.</td>
<td>C₆H₅ (Ic)</td>
<td>IVd</td>
<td>1.5</td>
<td>86</td>
</tr>
<tr>
<td>44.</td>
<td>4-CH₃C₆H₄ (Id)</td>
<td>IVe</td>
<td>2</td>
<td>86</td>
</tr>
<tr>
<td>45.</td>
<td>2,4-Cl₂C₆H₃ (Ic)</td>
<td>IVf</td>
<td>1.5</td>
<td>89</td>
</tr>
<tr>
<td>46.</td>
<td>4-O₂NC₆H₄ (If)</td>
<td>IVg</td>
<td>1</td>
<td>90</td>
</tr>
<tr>
<td>47.</td>
<td>4-CH₃OC₆H₄ (Ig)</td>
<td>IVh</td>
<td>1.5</td>
<td>88</td>
</tr>
<tr>
<td>48.</td>
<td>4-HOC₆H₄ (Ii)</td>
<td>IVi</td>
<td>1.5</td>
<td>87</td>
</tr>
<tr>
<td>49.</td>
<td>2-ClC₆H₄ (II)</td>
<td>IVj</td>
<td>1</td>
<td>92</td>
</tr>
<tr>
<td>50.</td>
<td>4-FC₆H₄ (Io)</td>
<td>IVk</td>
<td>1</td>
<td>90</td>
</tr>
<tr>
<td>51.</td>
<td>3-BrC₆H₄ (Ir)</td>
<td>IVl</td>
<td>1</td>
<td>88</td>
</tr>
<tr>
<td>52.</td>
<td>2-Naphthyl (Iv)</td>
<td>IVm</td>
<td>2</td>
<td>92</td>
</tr>
</tbody>
</table>

*aReactions were carried out using 20 mol% of [bmim]OH at 50-60°C*

In conclusion, we have investigated [bmim]OH as an effective catalyst which provides a new and useful method for the synthesis of 4H-pyrans, 4H-pyran[2,3-c]pyrazoles.
and 4H-benzo[g]chromenes by the condensation of aldehydes, malononitrile and ethyl acetoacetate/ acetylacetone/ pyrazolone/ 2-hydroxy-1,4-naphthoquinone. The procedure offers advantages such as high yields, operational simplicity and clean reaction conditions.

II.3: EXPERIMENTAL

All the chemicals used were purchased from Sigma-Aldrich or Spectrochem and used without further purification. All melting points were recorded on a Tropical Labequip apparatus and are uncorrected. Thin layer chromatography was used to monitor reaction progress and was performed using silica gel 60 F$_{254}$ (precoated aluminium sheets) from Merck. The products were confirmed by their m.p., IR, NMR and mass spectra. IR spectra were recorded on Perkin-Elmer FT-IR-1710 instrument. NMR spectra were recorded on Bruker Avance Spectrospin (300 MHz) and Jeol JNM ECX-400P (400 MHz) using TMS as internal standard. Mass spectra were recorded on KC-455-TOF mass spectrometer (Micromass, Manchester, U.K.). The chemical shift values are recorded on δ scale and the coupling constants ($J$) are in Hertz (Hz). [bmim]OH was prepared by the reported method.$^{13}$

**Preparation of [bmim]OH$^{13}$**

Solid potassium hydroxide (40 mmol) was added to a solution of [bmim]Br (40 mmol) in dry methylene chloride (20 mL). The mixture was stirred vigorously at room temperature for 10 h. The precipitated KBr was filtered off, and the filtrate was evaporated to leave the crude [bmim]OH as a viscous liquid. The viscous liquid so obtained was washed well with diethyl ether (2×20 mL) and dried at 90°C on a rotary evaporator to yield [bmim]OH.

**General procedure for the synthesis of 4H-pyran derivatives (IIa-IIo)**

A mixture of aldehyde (1.0 mmol), malononitrile (1.0 mmol), ethyl acetoacetate or acetylacetone (1.0 mmol) and [bmim]OH (20 mol%) was placed in a 50 mL round bottomed flask mounted over a magnetic stirrer. The reaction mixture was stirred
magnetically in an oil-bath maintained at 50-60°C for an appropriate time as mentioned in Table II.2. After completion of the reaction as monitored by TLC using petroleum ether: ethyl acetate (60:40, v/v) as eluent, the reaction mixture was allowed to cool to room temperature and quenched with water (~5 mL). The solid product obtained was filtered, washed with water and dried. The crude product was washed well with hot ethanol to yield pure 4H-pyran derivatives.

The filtrate was concentrated under reduced pressure and dried at 100°C to recover the ionic liquid for subsequent use. The recovered ionic liquid was reused for the condensation reaction involving 4-chlorobenzaldehyde, malononitrile and ethyl acetoacetate in consecutive runs.

**Ethyl 6-amino-4-(4-chlorophenyl)-5-cyano-2-methyl-4H-pyran-3-carboxylate (IIa, C_{16}H_{15}ClN_{2}O_{3})**

Colorless solid; Yield: 93%; M.p.: 171-173°C (Lit. 172-174°C); $^{44}$IR (KBr) $\nu_{\text{max}}$, cm$^{-1}$: 3411, 3333, 2194, 1696; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 7.27 (d, $J$ = 8.2 Hz, 2H, Ar), 7.15 (d, $J$ = 8.2 Hz, 2H, Ar), 4.53 (brs, 2H, NH$_2$), 4.42 (s, 1H, CH), 4.05 (q, $J^{1,2}$ = 6.9 Hz, $J^{1,3}$ = 3.4 Hz, 2H, OCH$_2$), 2.37 (s, 3H, CH$_3$), 1.13 (t, $J$ = 7.1 Hz, 3H, CH$_3$).

**Ethyl 6-amino-4-(3-chlorophenyl)-5-cyano-2-methyl-4H-pyran-3-carboxylate (IIb, C_{16}H_{15}ClN_{2}O_{3})**

Colorless solid; Yield: 91%; M.p.: 153-155°C (Lit. 153-156°C); $^{44}$IR (KBr) $\nu_{\text{max}}$, cm$^{-1}$: 3400, 3329, 2191, 1693; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.27-7.25 (m, 2H, Ar), 7.16-7.11 (m, 2H, Ar), 4.55 (brs, 2H, NH$_2$), 4.42 (s, 1H, CH), 4.08-4.00 (m, 2H, OCH$_2$), 2.37 (s, 3H, CH$_3$), 1.11 (t, $J$ = 7.2 Hz, CH$_3$).

**Ethyl 6-amino-5-cyano-2-methyl-4-phenyl-4H-pyran-3-carboxylate (IIc, C_{16}H_{16}N_{2}O_{3})**

Colorless solid; Yield: 90%; M.p.: 195-197°C (Lit. 195-196°C); $^{44}$IR (KBr) $\nu_{\text{max}}$, cm$^{-1}$: 3403, 3329, 2190, 1693; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.28-7.25 (m, 2H, Ar), 7.20-7.16 (m, 3H, Ar), 4.48 (brs, 2H, NH), 4.41 (s, 1H, CH), 4.03-3.97 (m, 2H, OCH$_2$), 2.34 (s, 3H, CH$_3$), 1.08 (t, 3H, CH$_3$).
Ethyl 6-amino-5-cyano-2-methyl-4-(4-methylphenyl)-4H-pyran-3-carboxylate (IId, C_{17}H_{18}N_{2}O_{3})

Colorless solid; Yield: 87%; M.p.: 177-179°C (Lit. 177-179°C);\textsuperscript{44} IR (KBr) $\nu_{\text{max}}$, cm\textsuperscript{-1}: 3414, 3336, 2202, 1693; $^1$H NMR (400 MHz, CDCl\textsubscript{3}): $\delta = 7.06$ (s, 3H, Ar), 4.43 (s, 1H, CH), 4.42 (brs, 2H, NH\textsubscript{2}), 4.04-3.98 (q, 2H, $J_{1,2} = 7.3$ Hz, $J_{1,3} = 14.6$ Hz, OCH\textsubscript{2}), 2.33 (s, 3H, CH\textsubscript{3}), 2.28 (s, 3H, CH\textsubscript{3}), 1.11 (t, 3H, $J_{1,2} = 7.7$ Hz, CH\textsubscript{3}).

Ethyl 6-amino-5-cyano-4-(2,4-dichlorophenyl)-2-methyl-4H-pyran-3-carboxylate (IIe, C_{16}H_{14}Cl_{2}N_{2}O_{3})

Colorless solid; Yield: 91%; M.p.: 166-168°C; IR (KBr) $\nu_{\text{max}}$, cm\textsuperscript{-1}: 3410, 3325, 2199, 1713; $^1$H NMR (400 MHz, DMSO-d\textsubscript{6}): $\delta = 7.51-7.50$ (m, 1H, Ar) 7.36-7.33 (m, 1H, Ar), 7.20-7.18 (m, 1H, Ar), 6.96 (brs, 2H, NH\textsubscript{2}), 4.81 (s, 1H, CH), 4.66 (brs, 2H, OCH\textsubscript{2}), 2.30 (s, 3H, CH\textsubscript{3}), 0.95-0.92 (m, 3H, CH\textsubscript{3}).

Ethyl 6-amino-5-cyano-2-methyl-4-(4-nitrophenyl)-4H-pyran-3-carboxylate (IIf, C_{16}H_{15}N_{3}O_{5})

Colorless solid; Yield: 90%; M.p.: 179-181°C (Lit. 180-183°C);\textsuperscript{44} IR (KBr) $\nu_{\text{max}}$, cm\textsuperscript{-1}: 3395, 3318, 2188, 1710; $^1$H NMR (400 MHz, CDCl\textsubscript{3}): $\delta = 8.15$ (d, 2H, $J = 8.8$ Hz, Ar) 7.36 (d, 2H, $J = 8.0$ Hz, Ar), 4.66 (brs, 2H, NH\textsubscript{2}), 4.53 (s, 1H, CH), 4.69-4.62 (m, 2H, OCH\textsubscript{2}), 2.38 (s, 3H, CH\textsubscript{3}), 1.09 (t, 3H, $J_{1,2} = 6.6$ Hz, CH\textsubscript{3}).

Ethyl 6-amino-5-cyano-4-(4-methoxyphenyl)-2-methyl-4H-pyran-3-carboxylate (IIg, C_{17}H_{18}N_{2}O_{4})

Colorless solid; Yield: 88%; M.p.: 140-142°C (Lit. 142-144°C);\textsuperscript{44} IR (KBr) $\nu_{\text{max}}$, cm\textsuperscript{-1}: 3405, 3323, 2210, 1693; $^1$H NMR (400 MHz, CDCl\textsubscript{3}): $\delta = 6.96$ (d, $J = 14.6$ Hz, 2H, Ar), 6.66 (d, $J = 14.6$ Hz, 2H, Ar), 5.53 (s, 2H, NH\textsubscript{2}), 4.21 (s, 1H, CH), 3.92-3.84 (m, 2H, OCH\textsubscript{2}), 3.61 (s, 3H, OCH\textsubscript{3}), 2.19 (s, 3H, CH\textsubscript{3}), 1.12 (t, $J_{1,2} = 7.1$ Hz, 3H, CH\textsubscript{3}).

Ethyl 6-amino-5-cyano-2-methyl-4-(3-nitrophenyl)-4H-pyran-3-carboxylate (IIh, C_{16}H_{15}N_{3}O_{5})

Colorless solid; Yield: 90%; M.p.: 180-183°C (Lit. 182-183°C);\textsuperscript{44} IR (KBr) $\nu_{\text{max}}$, cm\textsuperscript{-1}: 3403, 3328, 2191, 1691; $^1$H NMR (400 MHz, CDCl\textsubscript{3}): $\delta = 8.10-8.04$ (m, 2H, Ar), 7.58-
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7.56 (m, 1H, Ar), 7.49-7.45 (m, 1H, Ar), 4.62 (brs, 2H, NH₂), 4.56 (s, 1H, CH), 4.06-4.00 (m, 2H, OCH₂), 2.39 (s, 3H, CH₃), 1.12 (t, J₁,₂ = 7.3 Hz, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ = 165.25, 157.94, 157.76, 148.47, 146.07, 134.01, 129.50, 122.54, 122.40, 118.35, 106.92, 60.96, 38.72, 18.64, 13.90.

Ethyl 6-amino-5-cyano-4-(4-hydroxyphenyl)-2-methyl-4H-pyran-3-carboxylate (IIi, C₁₆H₁₆N₂O₄)⁴⁶

Colorless solid; Yield: 87%; M.p.: 175-177°C; IR (KBr) νₘₐₓ, cm⁻¹: 3490, 3448, 3275, 2216, 1718, 1679; ¹H NMR (400 MHz, DMSO-d₆): δ = 8.32 (brs, 1H, OH), 7.43 (d, J = 8.01 Hz, 2H, Ar), 7.21 (d, J = 8.0 Hz, 2H, Ar), 6.69 (brs, 2H, NH₂), 5.12 (s, 1H, CH), 4.16 (q, J = 7.23 Hz, 2H, OCH₂), 2.39 (s, 3H, CH₃), 1.16 (t, J = 7.23 Hz, 3H, CH₃).

Ethyl 6-amino-5-cyano-4-(3-hydroxyphenyl)-2-methyl-4H-pyran-3-carboxylate (IIj, C₁₆H₁₆N₂O₄)

Colorless solid; Yield: 88%; M.p.: 165-167°C (Lit. 164–165°C); IR (KBr) νₘₐₓ, cm⁻¹: 3414, 3336, 2202, 1693; ¹H NMR (400 MHz, DMSO-d₆): δ = 8.85 (s, 1H, OH), 7.07 (t, J = 8.0 Hz, 1H, Ar), 6.67–6.64 (m, 3H, Ar), 5.74 (s, 2H, NH₂), 4.31 (s, 1H, CH), 4.05–4.02 (m, 2H, OCH₂), 2.35 (s, 3H, CH₃), 1.13 (t, J = 7.1 Hz, 3H, CH₃).

Ethyl 6-amino-4-benzo[1,3]dioxol-5-yl-5-cyano-2-methyl-4H-pyran-3-carboxylate (IIk, C₁₇H₁₆N₂O₅)

Colorless solid; Yield: 87%; M.p.: 136-138°C; IR (KBr) νₘₐₓ, cm⁻¹: 3429, 3332, 2195, 1686; ¹H NMR (400 MHz, CDCl₃) δ = 6.74-6.71 (m, 3H, Ar), 5.90 (s, 2H, CH₂), 4.43 (s, 2H, NH₂), 4.34 (s, 1H, CH), 4.08-4.00 (m, 2H, OCH₂), 2.33 (s, 3H, CH₃), 1.13 (t, 3H, J₁,₂ = 7.3 Hz, CH₃).

Ethyl 6-amino-4-(2-chlorophenyl)-5-cyano-2-methyl-4H-pyran-3-carboxylate (IIl, C₁₆H₁₅ClN₂O₃)

Colorless solid; Yield: 92%; M.p.: 167-169°C; IR (KBr) νₘₐₓ, cm⁻¹: 3405, 3329, 2194, 1691; ¹H NMR (400 MHz, CDCl₃): δ = 7.33-7.29 (m, 1H, Ar), 7.22-7.11 (m, 3H, Ar), 5.04 (s, 1H, CH), 4.47 (brs, 2H, NH₂), 4.02-3.94 (m, 2H, OCH₂), 2.39 (s, 3H, CH₃),
1.05 (t, 3H, $J^{1,2} = 7.1$ Hz, CH$_3$); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta = 165.00$, 157.94, 157.76, 148.37, 146.07, 134.31, 126.50, 124.54, 124.40, 117.31, 106.92, 59.92, 38.62, 17.54, 13.70; MS (ESI) calcd. for: C$_{16}$H$_{15}$ClN$_2$O$_3$ 318.07, found: $m/z = 319.06$ [M$^+$/H], 321.06 [(M$^+$/H)+2].

5-Acetyl-2-amino-6-methyl-4-phenyl-4$H$-pyran-3-carbonitrile (IIm, C$_{15}$H$_{14}$N$_2$O$_2$)

Colorless solid; Yield: 90%; M.p.: 158-160°C (Lit. 158-160°C); IR (KBr) $\nu_{\text{max}}$, cm$^{-1}$: 3409, 3330, 2929, 2189, 1680, 1650, 1510, 1383, 1198; $^1$H NMR (400 MHz, DMSO-d$_6$): $\delta = 7.18-7.15$ (m, 5H, Ar), 6.80 (brs, 2H, NH$_2$), 4.78 (s, 1H, CH), 2.30 (s, 3H, CH$_3$), 2.05 (s, 3H, CH$_3$).

5-Acetyl-2-amino-4-(4-methylphenyl)-6-methyl-4$H$-pyran-3-carbonitrile (IIn, C$_{16}$H$_{16}$N$_2$O$_2$)

Colorless solid; Yield: 88%; M.p.: 138-140°C (Lit. 135-137°C); IR (KBr) $\nu_{\text{max}}$, cm$^{-1}$: 3410, 3333, 2932, 2191, 1682, 1651, 1512, 1381, 1196, 1134; $^1$H NMR (400 MHz, DMSO-d$_6$): $\delta = 7.23-7.15$ (m, 3H, Ar), 7.06-7.05 (m, 1H, Ar), 6.87 (brs, 2H, NH$_2$), 4.81 (s, 1H, CH), 2.30 (s, 3H, CH$_3$), 2.13 (s, 3H, CH$_3$), 2.05 (s, 3H, CH$_3$).

5-Acetyl-2-amino-3-cyano-6-methyl-4-(4-methoxyphenyl)-4$H$-pyran (IIo, C$_{16}$H$_{16}$N$_2$O$_3$)

Colorless solid; Yield: 89%; M.p.: 158-160°C (Lit. 157-159°C); IR (KBr) $\nu_{\text{max}}$, cm$^{-1}$: 3460, 3300, 3170, 2180, 1695, 1660, 1600, 1510; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.12$ (d, $J = 8.8$ Hz, 2H, Ar), 6.86 (d, $J = 8.8$ Hz, 2H, Ar), 4.48 (brs, 2H, NH$_2$), 4.39 (s, 1H, CH), 3.78 (s, 3H, OCH$_3$), 2.28 (s, 3H, CH$_3$), 2.05 (s, 3H, CH$_3$).

General procedure for the synthesis of 4$H$-pyrano[2,3-c]pyrazoles (IIIa-IIIq)

**Method A**

In a 50 mL round bottomed flask mounted over a magnetic stirrer, a mixture of 5-methyl-2,4-dihydro-pyrazol-3-one (1.0 mmol), aldehyde (1.0 mmol), malononitrile (1.0 mmol) and [bmim]OH (20 mol%) was placed. The mixture was stirred and heated in an oil-bath maintained at 50-60°C for 5-10 min. Progress of the reaction was monitored by TLC using ethyl acetate: petroleum ether (30:70, v/v) as eluent. Upon completion of the
reaction, the mixture was cooled to room temperature and water (~5 mL) was added. The contents were stirred magnetically. The solid product obtained was filtered at pump, washed with water and dried to afford the crude product, which was recrystallised from ethanol to yield pure 4\(H\)-pyrano[2,3-c]pyrazoles.

**Method B**

A mixture of hydrazine hydrate (96%) (1.0 mmol), ethyl acetoacetate (1.0 mmol), aldehyde (1.0 mmol), malononitrile (1.0 mmol) and [bmim]OH (20 mol%) was taken in a 50 mL round bottomed flask mounted over a magnetic stirrer. The mixture was stirred at 50-60°C in an oil-bath for 10-15 min until completion of the reaction as monitored by TLC. The reaction was worked up as in Method A to yield pure products (IIIa-IIIq).

6-Amino-4-(4-bromophenyl)-3-methyl-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (IIIa, C_{14}H_{11}BrN_{4}O)

Colorless solid; Yield : 91%; M.p. 248°C (Lit. 249-250°C); \(^{73}\) IR (KBr) \(\nu_{\text{max}}\), cm\(^{-1}\): 3397, 3223, 3182, 2190, 1643, 1598, 1490, 1402, 1045; \(^1\)H NMR (300 MHz, DMSO-d\(_6\)): \(\delta = 12.11\) (s, 1H, NH), 7.48 (d, \(J = 7.8\) Hz, 2H, Ar), 7.10 (d, \(J = 7.8\) Hz, 2H, Ar), 6.91 (s, 2H, NH\(_2\)), 4.58 (s, 1H, CH), 1.75 (s, 3H, CH\(_3\)); \(^{13}\)C NMR (100 MHz, DMSO-d\(_6\)): \(\delta 160.94, 154.72, 143.95, 135.73, 131.42, 129.79, 120.73, 119.80, 97.15, 56.63, 35.90, 9.79.

6-Amino-4-(4-chlorophenyl)-3-methyl-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (IIIb, C_{14}H_{11}ClN_{4}O)

Colorless solid; Yield: 94%; M.p.: 233°C (Lit. 234-235°C); \(^{72}\) IR (KBr) \(\nu_{\text{max}}\), cm\(^{-1}\): 3410, 3308, 3177, 2188, 1645, 1600, 1490, 1401, 1047; \(^1\)H NMR (300 MHz, DMSO-d\(_6\)): \(\delta = 12.17\) (s, 1H, NH), 7.39 (d, \(J = 8.4\) Hz, 2H, Ar), 7.21 (d, \(J = 8.4\) Hz, 2H, Ar), 6.95 (s, 2H, NH\(_2\)), 4.63 (s, 1H, CH), 1.79 (s, 3H, CH\(_3\)).

6-Amino-3-methyl-4-phenyl-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (IIIc, C_{14}H_{12}N_{4}O)

Colorless solid; Yield: 90%; M.p.: 244°C (Lit. 245-246°C); \(^{72}\) IR (KBr) \(\nu_{\text{max}}\), cm\(^{-1}\): 3374, 3311, 3172, 2193, 1649, 1611, 1489, 1402, 1045; \(^1\)H NMR (300 MHz, DMSO-d\(_6\)): \(\delta = \delta\)
11.99 (brs, 1H, NH), 7.32-7.14 (m, 5H, Ar), 6.72 (br s, 2H, NH₂), 4.57 (s, 1H, CH), 1.77 (s, 3H, CH₃).

6-Amino-3-methyl-4-(4-methylphenyl)-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (IIId, C₁₅H₁₄N₄O)
Pale Yellow; Yield: 96%; M.p.: 196°C (Lit. 197-198°C); IR (KBr) ν_max, cm⁻¹: 3410, 3315, 3191, 2192, 1645, 1599, 1489, 1401, 1044; ¹H NMR (300 MHz, DMSO-d₆): δ 12.06 (brs, 1H, NH), 7.13 (d, J = 7.5 Hz, 2H, Ar), 7.05 (d, J = 7.5 Hz, 2H, Ar), 6.80 (br s, 2H, NH₂), 4.54 (s, 1H, CH), 2.26 (s, 3H, CH₃, ArCH₃), 1.78 (s, 3H, CH₃).

6-Amino-3-methyl-4-(4-nitrophenyl)-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (IIIf, C₁₄H₁₁N₅O₃)
Pale Yellow; Yield: 96%; M.p.: 251°C (Lit. 251-252°C); IR (KBr) ν_max, cm⁻¹: 3477, 3229, 3119, 2196, 1651, 1595, 1516, 1493, 1049; ¹H NMR (300 MHz, DMSO-d₆): δ = 12.14 (s, 1H, NH), 8.19 (d, J = 8.4 Hz, 2H, Ar), 7.45 (d, J = 8.4 Hz, 2H, Ar), 6.96 (s, 2H, NH₂), 4.80 (s, 1H, CH), 1.78 (s, 3H, CH₃).

6-Amino-4-(4-methoxyphenyl)-3-methyl-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (IIIf, C₁₅H₁₄N₄O₂)
Pale Yellow; Yield: 94%; M.p.: 211°C (Lit. 212-213°C); IR (KBr) ν_max, cm⁻¹: 3483, 3257, 3115, 2192, 1642, 1599, 1493, 1392, 1260, 1030; ¹H NMR (300 MHz, DMSO-d₆): δ = 11.91 (brs, 1H, NH), 7.00 (d, J = 8.1 Hz, 2H, Ar), 6.79 (d, J = 8.1 Hz, 2H, Ar), 6.60 (s, 2H, NH₂), 4.45 (s, 1H, CH), 3.64 (s, 3H, OCH₃), 1.70 (s, 3H, CH₃).

6-Amino-3-methyl-4-(3-nitrophenyl)-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (IIIf, C₁₄H₁₁N₅O₃)
Pale Yellow; Yield: 85%; M.p.: 190°C (Lit. 188-190°C); IR (KBr) ν_max, cm⁻¹: 3474, 3224, 3110, 2195, 1655, 1598, 1518, 1491, 1403, 1349, 1041, 732; ¹H NMR (300 MHz, DMSO-d₆): δ = 12.18 (s, 1H, NH), 7.99-8.11 (m, 4H, Ar), 7.03 (s, 2H, NH₂), 4.85 (s, 1H, CH), 1.77 (s, 3H, CH₃).
6-Amino-4-(4-hydroxyphenyl)-3-methyl-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (IIIh, C_{14}H_{12}N_{4}O_{2})

Pale Yellow; Yield: 87%; M.p.: 224°C (Lit. 223-224°C);\textsuperscript{22} IR (KBr) \(\nu_{\text{max}}\), cm\(^{-1}\): 3435, 3390, 3139, 2176, 1648, 1599, 1493, 1408, 1194, 1045; \(^{1}\)H NMR (300 MHz, DMSO-d\(_6\)): \(\delta = 12.03\) (s, 1H, NH), 9.26 (s, 1H, OH), 6.96 (d, \(J = 7.5\) Hz, 2H, Ar), 6.76 (s, 2H, NH\(_2\)), 6.70 (d, \(J = 7.5\) Hz, 2H, Ar), 4.47 (s, 1H, CH), 1.78 (s, 3H, CH\(_3\)).

6-Amino-4-(2-chlorophenyl)-3-methyl-2,4-dihydro-pyrano[2,3-c]pyrazole-5-carbonitrile (IIIi, C_{14}H_{11}ClN_{4}O)

Pale Yellow; Yield: 91%; M.p.: 246°C (Lit. 245-246°C);\textsuperscript{22} IR (KBr) \(\nu_{\text{max}}\), cm\(^{-1}\): 3391, 3356, 3166, 2190, 1654, 1611, 1490, 1408, 1051; \(^{1}\)H NMR (300 MHz, DMSO-d\(_6\)): \(\delta = 12.12\) (s, 1H, NH), 7.16-7.59 (m, 4H, Ar), 6.94 (s, 2H, NH\(_2\)), 5.06 (s, 1H, CH), 1.76 (s, 3H, CH\(_3\)).

6-Amino-3-methyl-4-(3,4,5-trimethoxyphenyl)-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (IIIj, C_{17}H_{18}N_{4}O_{4})

Pale Yellow; Yield: 84%; M.p.: 226°C (Lit. 228°C);\textsuperscript{73} IR (KBr) \(\nu_{\text{max}}\), cm\(^{-1}\): 3378, 3284, 3145, 2186, 1647, 1599, 1487, 1402, 1232, 1126; \(^{1}\)H NMR (300 MHz, DMSO-d\(_6\)): \(\delta = 11.95\) (brs, 1H, NH), 6.69 (brs, 2H, NH\(_2\)), 6.38 (s, 2H, Ar), 4.49 (s, 1H, CH), 3.63 (s, 6H, OCH\(_3\)), 3.56 (s, 3H, OCH\(_3\)), 1.79 (s, 3H, CH\(_3\)).

6-Amino-4-(4-fluorophenyl)-3-methyl-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (IIIk, C_{14}H_{11}FN_{4}O)

Pale Yellow; Yield: 86%; M.p.: 245°C (Lit. 247-248 °C);\textsuperscript{22} IR (KBr) \(\nu_{\text{max}}\), cm\(^{-1}\): 3480, 3232, 3119, 2195, 1648, 1596, 1493, 1398, 1230; \(^{1}\)H NMR (300 MHz, DMSO-d\(_6\)): \(\delta = 11.94\) (s, 1H, NH), 7.14-7.00 (m, 4H, Ar), 6.66 (s, 2H, NH\(_2\)), 4.54 (s, 1H, CH), 1.70 (s, 3H, CH\(_3\)).

6-Amino-4-(4-dimethylaminophenyl)-3-methyl-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (IIIl, C_{16}H_{17}N_{5}O)

Orange Solid; Yield: 95%; M.p.: 218°C (Lit. 219-220 °C);\textsuperscript{22} IR (KBr) \(\nu_{\text{max}}\), cm\(^{-1}\): 3385, 3305, 3172, 2189, 1644, 1598, 1488, 1397, 1050; \(^{1}\)H NMR (300 MHz, DMSO-d\(_6\)): \(\delta = \)
12.03 (s, 1H, NH), 6.97 (d, J = 7.5 Hz, 2H, Ar), 6.75 (s, 2H, NH$_2$), 6.67 (d, J = 7.5 Hz, 2H, Ar), 4.45 (s, 1H, CH), 2.85 (s, 6H, N(CH$_3$)$_2$), 1.79 (s, 3H, CH$_3$); MS (ESI) m/z = 295 [M$^+$].

6-Amino-4-(2-methoxyphenyl)-3-methyl-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (III_m, C$_{15}$H$_{14}$N$_4$O$_2$)

Pale Yellow; Yield: 92%; M.p.: 251°C (Lit. 252-253°C);$^{73}$ IR (KBr) $\nu$$_{max}$, cm$^{-1}$: 3376, 3340, 3159, 2194, 1657, 1612, 1488, 1404, 1048, 765; $^1$H NMR (300 MHz, DMSO-d$_6$): $\delta$ = 12.00 (s, 1H, NH), 7.22-6.87 (m, 4H, Ar), 6.79 (s, 2H, NH$_2$), 4.96 (s, 1H, CH), 3.77 (s, 3H, OCH$_3$), 1.78 (s, 3H, CH$_3$).

6-Amino-4-(3-bromophenyl)-3-methyl-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (IIIn, C$_{14}$H$_{11}$BrN$_4$O)

Pale Yellow; Yield: 94%; M.p.: 222°C (Lit. 223-224°C);$^{72}$ IR (KBr) $\nu$$_{max}$, cm$^{-1}$: 3369, 3254, 3171, 2192, 1653, 1595, 1492, 1409, 1040; $^1$H NMR (300 MHz, DMSO-d$_6$): $\delta$ = 12.01 (brs, 1H, NH), 7.30-7.24 (m, 4H, Ar), 6.77 (brs, 2H, NH$_2$), 4.55 (s, 1H, CH), 1.72 (s, 3H, CH$_3$).

6-Amino-3-methyl-4-(2-nitrophenyl)-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (III_o, C$_{14}$H$_{11}$N$_5$O$_3$)

Pale Yellow; Yield: 87%; M.p.: 241°C (Lit. 242-243°C);$^{73}$ IR (KBr) $\nu$$_{max}$, cm$^{-1}$: 3415, 3374, 3173, 2187, 1655, 1596, 1529, 1492, 1413, 1349, 1049; $^1$H NMR (300 MHz, DMSO-d$_6$): $\delta$ = 12.23 (s, 1H, NH), 7.86 (d, J = 8.1 Hz, 1H, Ar), 7.69 (t, J = 7.5 Hz, 1H, Ar), 7.51 (t, J = 7.5 Hz, 1H, Ar), 7.33 (d, J = 7.5 Hz, 1H, Ar), 7.05 (s, 2H, NH$_2$), 5.09 (s, 1H, CH), 1.76 (s, 3H, CH$_3$).

6-Amino-4-(furan-2-yl)-3-methyl-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (III_p, C$_{12}$H$_{10}$N$_4$O$_2$)

Pale Yellow; Yield: 93%; M.p.: 232°C (Lit. 233-234°C);$^{73}$ IR (KBr) $\nu$$_{max}$, cm$^{-1}$: 3355, 3250, 3172, 2187, 1649, 1601, 1493, 1405, 1043; $^1$H-NMR (300 MHz, DMSO-d$_6$): $\delta$ 12.11 (s, 1H, NH), 7.50 (s, 1H, Ar), 6.89 (s, 2H, NH$_2$), 6.34 (s, 1H, Ar), 6.16 (s, 1H, Ar), 4.75 (s, 1H, CH), 1.96 (s, 3H, CH$_3$).
6-Amino-3-methyl-4-(1-naphthyl)-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (IIIq, C$_{18}$H$_{14}$N$_{4}$O)

Pale Yellow; Yield: 86%; M.p.: 226-228°C (Lit. 226-228°C); $^{55}$ IR (KBr) $\nu_{\text{max}}$, cm$^{-1}$: 3402, 3344, 3160, 2192, 1655, 1610, 1486, 1407, 1050, 791, 774; $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ = 12.08 (s, 1H, NH), 8.2 (brs, 1H, Ar), 7.38-7.96 (m, 6H, Ar), 6.91 (s, 2H, NH$_2$), 5.43 (s, 1H, CH), 1.54 (s, 3H, CH$_3$).

**General procedure for the synthesis of 4$H$-benzo[g]chromene derivatives (IVa-IVm)**

A mixture of aldehyde (1.0 mmol), malononitrile (1.0 mmol), 2-hydroxy-1,4-naphthoquinone (1.0 mmol) and [bmim]OH (20 mol%) was stirred magnetically in a 50 mL round bottomed flask maintained at 50-60°C in an oil-bath for an appropriate time as mentioned in Table II.4. After completion of the reaction as monitored by TLC using ethyl acetate: petroleum ether (30:70, v/v) as eluent, the reaction mixture was allowed to cool to room temperature and quenched with water (~5 mL). The solid product obtained was filtered at pump, washed with water and dried. The crude product was washed well with hot ethanol to yield pure 4$H$-benzo[g]chromene derivatives.

2-Amino-4-(4-bromophenyl)-5,10-dioxo-5,10-dihydro-4$H$-benzo[g]chromene-3-carbonitrile (IVa, C$_{20}$H$_{11}$BrN$_2$O$_3$)

Orange solid; Yield: 90%; M.p.: 254-256°C (Lit. 253-255°C); $^{68}$ IR (KBr) $\nu_{\text{max}}$, cm$^{-1}$: 3407, 3330, 3197, 2925, 2205, 1669, 1606; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ = 8.04-8.02 (m, 1H, Ar), 7.87-7.79 (m, 3H, Ar), 7.49 (d, $J$ = 8.8 Hz, 2H, Ar), 7.38 (s, 2H, NH$_2$), 7.30 (d, $J$ = 8.1 Hz , 2H, Ar), 4.61 (s, 1H, CH); $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ = 182.55, 176.79, 158.29, 149.07, 143.06, 134.52, 134.15, 131.40, 130.97, 130.66, 130.04, 126.05, 125.78, 121.23, 120.21, 119.20, 56.91, 36.03.

2-Amino-4-(4-chlorophenyl)-5,10-dioxo-5,10-dihydro-4$H$-benzo[g]chromene-3-carbonitrile (IVb, C$_{20}$H$_{11}$ClN$_2$O$_3$)

Red Solid; Yield: 91%; M.p.: 278-280°C (Lit. 278-280°C); $^{69}$ IR (KBr) $\nu_{\text{max}}$, cm$^{-1}$: 3407, 3324, 3208, 3194, 2210, 1667, 1635, 1594; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ = 8.06-8.04 (m, 1H, Ar), 7.88-7.83 (m, 3H, Ar), 7.36 (t, $J$=5.6 Hz, 2H, Ar), 7.35 (s, 2H, NH$_2$), 7.10 (t, $J$ = 8.8 Hz, 2H, Ar), 4.65 (s, 1H, CH).
2-Amino-4-(3-chlorophenyl)-5,10-dioxo-5,10-dihydro-4H-benzo[g]chromene-3-carbonitrile (IVc, C$_{20}$H$_{11}$ClN$_{2}$O$_{3}$)

Orange Solid; Yield: 91%; M.p.: 252-254°C; IR (KBr) $\nu_{\text{max}}$ cm$^{-1}$: 3392, 3322, 3193, 2920, 2202, 1666, 1605; $^1$H NMR (300 MHz, CDCl$_3$ + DMSO-d$_6$): $\delta$ = 8.12-7.22 (m, 8H, Ar), 6.32 (s, 2H, NH$_2$), 4.75 (s, 1H, CH); $^{13}$C NMR (75 MHz, CDCl$_3$ + DMSO-d$_6$): $\delta$ = 181.82, 176.39, 158.31, 147.87, 144.00, 134.04, 133.69, 133.41, 130.61, 129.74, 129.43, 127.30, 127.04, 125.87, 125.72, 122.11, 118.29, 57.64, 35.80; MS (ESI) m/z calcd. for C$_{20}$H$_{11}$ClN$_{2}$O$_{3}$: 362, found: 363 [M$^+$+H], 365 [(M$^+$+2)+H].

2-Amino-5,10-dioxo-5,10-dihydro-4-phenyl-4H-benzo[g]chromene-3-carbonitrile (IVd, C$_{20}$H$_{12}$N$_2$O$_3$)

Orange Solid, Yield: 86%; M.p.: 260-262°C (Lit. 261-262°C); IR (KBr) $\nu_{\text{max}}$ cm$^{-1}$: 3401, 3325, 3192, 2924, 2199, 1670, 1602; $^1$H NMR (300 MHz, CDCl$_3$ + DMSO-d$_6$): $\delta$ = 8.11-7.23 (m, 9H, Ar), 6.21 (s, 2H, NH$_2$), 4.54 (s, 1H, CH).

2-Amino-5,10-dioxo-5,10-dihydro-4-(4-methylphenyl)-4H-benzo[g]chromene-3-carbonitrile (IVe, C$_{21}$H$_{14}$N$_2$O$_3$)

Orange Solid; Yield: 86%; M.p.: 241-243°C (Lit. 242-244°C); IR (KBr) $\nu_{\text{max}}$ cm$^{-1}$: 3405, 3326, 3195, 2923, 2200, 1661, 1604; $^1$H NMR (300 MHz, CDCl$_3$ + DMSO-d$_6$): $\delta$ = 8.12-7.10 (m, 8H, Ar and NH$_2$), 6.21 (s, 2H, NH$_2$), 4.73 (s, 1H, CH), 2.29 (s, 3H, CH$_3$).

2-Amino-4-(2,4-dichlorophenyl)-5,10-dioxo-5,10-dihydro-4H-benzo[g]chromene-3-carbonitrile (IVf, C$_{20}$H$_{10}$Cl$_2$N$_2$O$_3$)

Orange Solid; Yield: 89%; M.p.: 257-258°C (Lit. 293-295°C); IR (KBr) $\nu_{\text{max}}$ cm$^{-1}$: 3466, 3340, 2924, 2201, 1670, 1591; $^1$H NMR (300 MHz, CDCl$_3$ + DMSO-d$_6$): $\delta$ = 8.11-6.64 (m, 9H, Ar and NH$_2$), 5.23 (s, 1H, CH).

2-Amino-5,10-dioxo-5,10-dihydro-4-(4-nitrophenyl)-4H-benzo[g]chromene-3-carbonitrile (IVg, C$_{20}$H$_{11}$N$_3$O$_5$)

Orange Solid; Yield: 90%; M.p.: 232-234°C (Lit. 234-235°C); IR (KBr) $\nu_{\text{max}}$ cm$^{-1}$: 3458, 3354, 3190, 2925, 2199, 1664, 1594; $^1$H NMR (300 MHz, CDCl$_3$ + DMSO-d$_6$): $\delta$ = 8.36-7.54 (m, 8H, Ar), 6.55 (s, 2H, NH$_2$), 4.90 (s, 1H, CH).
2-Amino-5,10-dioxo-5,10-dihydro-4-(4-methoxyphenyl)-4H-benzo[g]chromene-3-carbonitrile (IVh, C_{21}H_{14}N_{2}O_{4})

Orange Solid; Yield: 88%; M.p.: 247-248°C (Lit. 247-248°C); IR (KBr) \( \nu_{\text{max}} \, \text{cm}^{-1} \): 3407, 3327, 3210, 2926, 2194, 1660, 1603; \(^1\)H NMR (300 MHz, CDCl\(_3\) + DMSO-d\(_6\)): \( \delta = 8.11-6.81 \) (m, 8H, Ar), 6.28 (s, 2H, NH\(_2\)), 4.72 (s, 1H, CH), 3.76 (s, 3H, OCH\(_3\)).

2-Amino-4-(4-hydroxyphenyl)-5,10-dioxo-5,10-dihydro-4H-benzo[g]chromene-3-carbonitrile (IVi, C_{20}H_{12}N_{2}O_{4})

Orange Solid; Yield: 87%; M.p.: 258-260°C (Lit. 258-260°C); IR (KBr) \( \nu_{\text{max}} \, \text{cm}^{-1} \): 3399, 3327, 3188, 2202, 1668, 1596; \(^1\)H NMR (300 MHz, DMSO-d\(_6\)): \( \delta = 9.34 \) (s, 1H, OH), 8.05-6.66 (m, 10H, Ar and NH\(_2\)), 4.49 (s, 1H, CH).

2-Amino-4-(2-chlorophenyl)-5,10-dioxo-5,10-dihydro-4H-benzo[g]chromene-3-carbonitrile (IVj, C_{20}H_{11}ClN_{2}O_{3})

Red Solid; Yield: 92%; M.p.: >300°C (Lit. >300°C); IR (KBr) \( \nu_{\text{max}} \, \text{cm}^{-1} \): 3434, 3327, 3184, 2192, 1663, 1635, 1595; \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): \( \delta = 8.08-8.06 \) (m, 1H, Ar), 7.87-7.84 (m, 3H, Ar), 7.45-7.40 (m, 2H, Ar), 7.37 (s, 2H, NH\(_2\)), 7.26-7.24 (m, 2H, Ar), 5.15 (s, 1H, CH).

2-Amino-5,10-dioxo-5,10-dihydro-4-(4-fluorophenyl)-4H-benzo[g]chromene-3-carbonitrile (IVk, C_{20}H_{11}FN_{2}O_{3})

Orange Solid; Yield: 90%; M.p.: 252-254°C (Lit. 286-288°C); IR (KBr) \( \nu_{\text{max}} \, \text{cm}^{-1} \): 3419, 3328, 3189, 2925, 2207, 1668, 1604; \(^1\)H NMR (300 MHz, CDCl\(_3\) + DMSO-d\(_6\)): \( \delta = 8.11-6.71 \) (m, 10H, Ar and NH\(_2\)), 4.74 (s, 1H, CH).

2-Amino-4-(3-bromophenyl)-5,10-dioxo-5,10-dihydro-4H-benzo[g]chromene-3-carbonitrile (IVl, C_{20}H_{11}BrN_{2}O_{3})

Orange Solid; Yield: 88%; M.p.: 255-256°C (Lit. 253-255°C); IR (KBr) \( \nu_{\text{max}} \, \text{cm}^{-1} \): 3399, 3327, 3214, 2187, 1668, 1591, 1488; \(^1\)H NMR (300 MHz, DMSO-d\(_6\)): \( \delta = 4.61 \) (s, 1H, CH), 8.04-7.28 (m, 10H, Ar and NH\(_2\)).
2-Amino-5,10-dioxo-5,10-dihydro-4-(2-naphthyl)-4H-benzo[g]chromene-3-carbonitrile (IVm, C$_{24}$H$_{14}$N$_2$O$_3$)

Orange Solid; Yield: 92%; M.p.: 244-246°C; IR (KBr) $\nu_{\text{max}}$, cm$^{-1}$: 3397, 3320, 3195, 2925, 2199, 1662, 1606; $^1$H NMR (300 MHz, CDCl$_3$ + DMSO-d$_6$): $\delta = 8.37$-$7.31$ (m, 11H, Ar), 6.75 (s, 2H, NH$_2$), 4.96 (s, 1H, CH); $^{13}$C NMR (75 MHz, CDCl$_3$ + DMSO): $\delta =$ 187.40, 181.94, 163.72, 145.02, 139.40, 138.79, 138.03, 137.40, 136.13, 135.26, 133.37, 132.69, 132.35, 131.55, 131.18, 131.11, 130.86, 130.65, 127.96, 124.02, 63.36, 41.73. MS (ESI) calcd. for C$_{24}$H$_{14}$N$_2$O$_3$: 378.10, found: $m/z = 379$ [M$^+$+H].
Chapter II

Figure II.4: IR Spectra of Compound IIh
Figure II.5: $^1$H Spectra of Compound IIh
Figure II.6: $^{13}$C Spectra of Compound IIIh
Figure II.7: IR Spectra of Compound IIIa
Figure II.8: $^1$H Spectra of Compound IIIa
Figure II.9: $^{13}$C Spectra of Compound IIIa
Figure II.10: IR Spectra of Compound IVa
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Figure II.11: $^1H$ Spectra of Compound IVa
Figure II.12: $^{13}$C Spectra of Compound IVa
II.4: REFERENCES


