4.1 Introduction

In Chemistry, a multi-component reaction (or MCR), sometimes referred to as a "Multi-component Assembly Process" (or MCAP), is a chemical reaction where three or more compounds react to form a single product.\(^1\) By definition, multicomponent reactions are those reactions whereby more than two reactants combine in a sequential manner to give highly selective products that retain majority of the atoms of the starting material.

Multi-component and domino reactions are efficient and effective methods in the sustainable and diversity-oriented synthesis of heterocycles. In particular, transition metal-catalyzed multi-component sequences have recently gained considerable interest. Based upon the Sonogashira entry to alkynones, alkenones, and intermediate allenes, has opened new avenues to the one-pot synthesis of numerous classes of heterocyclic frameworks in an MCR fashion. This methodological approach has now found various applications in one-pot syntheses of functional chromophores, pharmaceutically active compounds, and marine alkaloids and derivatives.

Design of highly efficient chemical reaction sequences that provide maximum structural complexity and diversity with a minimum number of synthetic steps to assemble compounds with interesting properties is a major challenge of modern drug discovery. One step methods are more convenient as compared to multistep since they are requiring shorter reaction time and gives high yield with easy workup. Heterocycles are ubiquitous among pharmaceutical compounds. The heterocyclic compound so produced as a result of chemical reaction having interesting pharmacology activates such as antihypertensive, anticancer anti-HIV activities.

The present chapter covers the synthesis of 4H-pyran derivatives. Presence of these moieties in organic molecules imparts them with the extensive range of biological and pharmacological properties, such as spasmolytic, diuretic, anti-coagulant, anti-cancer, and anti-anaphylactic activities.\(^2\) They are also helpful for the treatment of neurodegenerative disorders, including Alzheimers disease, amyotrophic lateral sclerosis, Huntingtons disease, and Parkinsons disease.\(^3\) Moreover, these compounds are also useful as photoactive materials\(^4\) and occur in various natural products.\(^5\) Many of the methods
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reported for the synthesis of these compounds\textsuperscript{6-18} are associated with use of hazardous organic solvents, long reaction time, use of toxic amine-based catalysts, and lack of general applicability; particularly synthesis of 6-amino-5-cyano-2-methyl-4-aryl-4H-pyran-3-carboxylic acid ethyl ester\textsuperscript{19} was rarely addressed. Thus, development of a mild, neutral, and reusable catalyst for one-pot synthesis of 4H-pyran derivatives still remains an attractive goal for researchers.

2-Amino-4H-pyran derivatives often use in cosmetics and pigments, and utilized as potentially biodegradable agrochemicals\textsuperscript{2}. Polyfunctionalized 4H-pyrans also constitute a structural unit of many natural products\textsuperscript{21} and biologically interesting compounds which possess various pharmacological activities, such as antiallergic, antitumor and antibacterial\textsuperscript{20}

The typical procedure to synthesize pyran derivatives is usually a two-step reaction carried out between a Michael acceptor (arylidemalononitriles) and $\beta$-dicarbonyl compounds in the presence of a base as the catalyst (Mg-Al hydrotalcite) in ethanol/water solvent (1:1). A variety of methods have been used to prepare 4H-pyrans, which involve several catalysts viz; ionic liquids, hexadecyltrimethylammonium bromide, Mg/La mixed metal oxides, Cu(II) oxymetasilicate, organic bases, MgO, and rubidium fluoride, Bi(NO$_3$)$_3$.5H$_2$O, SrCl$_2$.6H$_2$O, hydrotalcite. In keeping with our interest in the application hydrotalcites in organic synthesis, we herein disclose a simple and efficient synthesis of 4H-pyran derivatives via a three-component cyclocondensation reaction of aldehydes, malononitrile, and ethyl acetoacetate using hydrotalcite as the catalyst.

4.2 Experimental Section

4.2.1 Characterization Techniques

The $^1$H NMR spectra was measured by Bruker Avance II 500 NMR spectrometer with tetramethylsilane as an internal standard $^1$H NMR data has been reported as follows; Chemical shift (ppm), integration, multiplicity, (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet and Br broad), Coupling constant (Hz). IR spectra were recorded by SHIMADZU IR spectrometer by sample dispersed in KBr pellet and is reported in terms of frequency of absorption (cm$^{-1}$). E-Merck Pre-coated TLC plates, Rankem silica gel G
were used for thin layer liquid chromatography. Melting points were determined in open capillaries and are uncorrected.

4.2.2 Chemicals used

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethyl acetoacetate</td>
<td>Rankem</td>
</tr>
<tr>
<td>Malanenitrile</td>
<td>CDH</td>
</tr>
<tr>
<td>Benzaldehyde</td>
<td>Rankem</td>
</tr>
<tr>
<td>Aluminum hydroxide</td>
<td>Rankem</td>
</tr>
<tr>
<td>Magnesium hydroxide</td>
<td>Merck</td>
</tr>
<tr>
<td>Sodium hydroxide</td>
<td>Fisher Scientific</td>
</tr>
<tr>
<td>Sodium carbonate</td>
<td>Rankem</td>
</tr>
<tr>
<td>m-Tolualdehyde</td>
<td>Himedia</td>
</tr>
<tr>
<td>3-Chlorobenzaldehyde</td>
<td>Himedia</td>
</tr>
<tr>
<td>o-nitrobenzaldehyde</td>
<td>Himedia</td>
</tr>
<tr>
<td>2,4 dichlorobenzaldehyde</td>
<td>Himedia</td>
</tr>
<tr>
<td>4-methoxybenzaldehyde</td>
<td>Himedia</td>
</tr>
<tr>
<td>Crotonoaldehyde</td>
<td>Himedia</td>
</tr>
<tr>
<td>3-Hydroxybenzaldehyde</td>
<td>Himedia</td>
</tr>
<tr>
<td>P-hydroxybenzaldehyde</td>
<td>Himedia</td>
</tr>
</tbody>
</table>

4.2.3 Preparation of Hydrotalcites

Al-Mg-CO$_3$ was prepared by one pot co-precipitation reaction at 100 $^\circ$C for 30 minutes and autogenous pressure in aqueous media to obtain small and high surface area particles. In a typical reaction Zn and Al chloride (metallic ratio 3:1) were taken and corresponding ratio of sodium bicarbonate were added and pH was maintained at 8.5. After aging the slurry for 12 h. white precipitate obtained were dried. The detailed procedure and characterization of different hydrotalcites used in this chapter has been reported in chapter-2.
4.2.4 Typical procedure for preparation of 4H-pyran derivatives using hydrotalcites as catalyst

A mixture of aldehyde (0.005 mol), malononitrile (0.005 mol) and ethyl acetoacetate was added in presence of Mg-Al-CO$_3$ hydrotalcite (Water/EtOH 1:1). The content stirred at room temperature (30°C). The reaction was monitored by TLC. After completion the reaction mixture was then filtered. The product was purified in column chromatography with ethyl acetate/Hexane (7:3). The solid was recrystallized by ethanol. The derivatives of 4-H pyran were collected as white crystals.

4.2.5 Synthesis of intermediate

A mixture of benzaldehyde (0.005 mol) and malononitrile (0.005 mol) was added at 50-60°C in solvent (water/ethanol) using as a catalyst of Mg-Al-CO$_3$ hydrotalcite as catalyst. The reaction was monitored by TLC (ethyl acetate/hexane 7:3). After completion of reaction solvent was evaporated and product was purified by column chromatography using hexane and ethyl acetate (7:3). The solid was recrystallized by ethanol and methanol. The product was characterized by NMR, MS and FT-IR.

![Scheme 4.2 Synthesis of intermediate 2-benzylidemalalonitrile using Mg-Al-CO$_3$ hydrotalcite](image)

4.2.6 Recycling of the Catalyst

At the end of the reaction, the catalyst could be recovered by simple filtration. The recycled catalyst was washed with ethanol and subjected to a second run of the reaction.
process. The comparisons of efficiency of this catalyst in synthesis of 4H-pyran after three times show a slight reduction in the yield.

4.3 Results and Discussion

One-pot three component reaction of malonitrile, aldehyde and ethyl acetoacetate using various catalyst in water/ethanol as a solvent at 30°C has been studied.

4.3.1 Effect of catalyst

The reaction shows (Table 4.1) that yield of the product is dependent on the nature of catalyst. Highest yield (97%) was obtained with Mg-Al-CO$_3$, It was followed by Ca-Al-CO$_3$ giving 75% yield and lowest yield was obtained with Zn-Al-CO$_3$. This suggested that M$^{2+}$ions play an important role.

Table 4.1. Optimization of reaction conditions using various hydrotalcites

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Time(minutes)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Zn-Al-CO$_3$ (1:3)</td>
<td>30</td>
<td>40</td>
</tr>
<tr>
<td>2</td>
<td>Mg-Al-CO$_3$ (1:3)</td>
<td>5</td>
<td>97</td>
</tr>
<tr>
<td>3</td>
<td>Ca-Al-CO$_3$ (1:3)</td>
<td>40</td>
<td>75</td>
</tr>
<tr>
<td>4</td>
<td>Mn-Al-CO$_3$ (1:3)</td>
<td>720</td>
<td>60</td>
</tr>
<tr>
<td>5</td>
<td>Ce-Ni-CO$_3$ (1:3)</td>
<td>15</td>
<td>45</td>
</tr>
</tbody>
</table>

Reaction conditions: Benzaldehyde (0.005mmol), malononitrile (10.005mmol), ethyl acetoacetate (0.005mmol) and Mg-Al-CO$_3$ hydrotalcite (0.1g) in ethanol/water (1:1) at room temperature (30°C±2°C).
4.3.2 Effect of solvent

The reaction using malononitrile (0.005 mol), benzaldehyde (0.005 mol) and ethyl acetoacetate (0.005 mol) was carried out in presence of Mg-Al-CO$_3$ hydrotalcite at 30°C with water (5 ml) as solvents. The reaction was very sensitive to the nature of the solvent employed (Table 4.2). No product was obtained where hexane and toluene was used as solvent. Acetonitrile gave 45% yield while ethanol and methanol gave 64 and 69% respectively (Table 4.2) with pure water, the yield was 57%. Highest yield 97% was obtained when water-ethanol mixture was used.

Table 4.2 Optimization of reaction condition using various solvents.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Methanol</td>
<td>69</td>
</tr>
<tr>
<td>2</td>
<td>Ethanol</td>
<td>64</td>
</tr>
<tr>
<td>3</td>
<td>Acetonitrile</td>
<td>45</td>
</tr>
<tr>
<td>4</td>
<td>Toluene</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>Water</td>
<td>57</td>
</tr>
<tr>
<td>6</td>
<td>Hexane</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>Water/Ethanol (1:1)</td>
<td>97</td>
</tr>
</tbody>
</table>

Reaction conditions: benzaldehyde (0.005 mmol), malononitrile (10.005 mmol), ethyl acetoacetate (0.005 mmol) and Mg-Al-CO$_3$ hydrotalcite (0.1 g) in ethanol/water (1:1) at room temperature (30°C) for 5 minutes.

4.3.4 Effect of catalyst concentration

The effect of different concentration of catalyst was also studied (table 4.3) which indicated that 0.01 g of Mg-Al-CO$_3$ was sufficient enough to catalyze the reaction. Further, increase in concentration of catalyst did not show any improvement in yield of the
product. Owning to unique and novel characteristics properties like polar surface, non-
corrosiveness and ability to generate product, hydrotalcites (Mg-Al-CO$_3$) can be reused
after catalytic reaction.

**Table 4.3: The effect of catalyst concentration on the synthesis of methyl 6-amino-5-
cyano-2-methyl-4-phenyl-4H-pyran-3-carboxylate**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (mg)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Free</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
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<tr>
<td>3</td>
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<td>35</td>
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<tr>
<td>4</td>
<td>50</td>
<td>87</td>
</tr>
<tr>
<td>5</td>
<td>100</td>
<td>97</td>
</tr>
</tbody>
</table>

A reaction conditions: Benzaldehyde (1 mmol, 0.106 g), ethylacetoacetate (0.005 mmol),
malononitrile (0.005 mmol) and Mg-Al-CO$_3$ (0.1 g) in ethanol/water (6 mL, 1:1) at room
temperature (30°C).

![Fig.4.1. Effect of catalyst amount on yield](image)
4.4.4 Effect of substitution in aldehyde

Various aromatic aldehydes containing electron withdrawing and electron donating substituted at ortho, meta and para position show equal ease towards the product formation high yields suggesting that electronic effect is not operational in rate determining step. This method has the ability to tolerate a variety of other functional groups such as hydroxyl, methyl, nitro, and chloro under the reaction conditions. Both, the electron-rich and electron-deficient aldehydes worked well, leading to high yields of products. In a series of reactions, ethyl acetate was employed under reaction condition to give the corresponding or 2-amino-tetrahydro-4H-chromenes. In these cases, the reactions were then evaluated using a variety of structurally diverse aldehydes. Three component condensation of ethyl acetoacetate with various aromatic aldehydes bearing electron withdrawing groups such as nitro or electron releasing groups such as methyl and malononitrile was carried out in the presence of Mg-Al-CO$_3$ as a catalyst. The yields obtained were good-to-excellent.

After optimization the reaction condition such as reaction time water and ethanol solvent system, the work has been extended to the synthesis of 4-H pyran derivatives of hydrotalcite using substituted aldehyde, malononitrile and ethyl acetoacetate in water /EtOH solvent as 30$^\circ$C.

When a β-ketoester (e.g., ethyl acetoacetate) was used, the reaction led to 6-amino-5-cyano-2-methyl-4-aryl-4H-pyran-3-carboxylic acid ethyl ester (2). The experimental procedure is very simple. Briefly, a mixture of an aromatic aldehyde (0.005 mmol), malononitrile (0.005 mmol), and ethyl acetoacetate (0.005 mmol), and 0.1g of Mg-Al-CO$_3$hydrotalcite was stirred in 1 mL ethanol/water (1:1) at 30$^\circ$C until the completion of reaction (TLC). The reaction mixture was kept up at room temperature then filtered using filter paper to separate the catalyst and the filtrate was solidified after cooling at room temperature. The solid product was consequentially washed with water (3 mL) and dried in air. The reaction products were identified by their melting points and NMR-data. Differently substituted aromatic aldehydes readily underwent the reaction, which proceeded with excellent yields (97%, Table 4.4).
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Scheme 4.3 proposed reaction using Mg-Al-CO₃ hydrotalcite

The results obtained in the current method are illustrated in Table 4.4. In each case, the reaction profile is clean and this one-pot three-component procedure presents some improvements and advantages over existing methods. One of the major advantages of this protocol is the isolation and purification of the products, which have been achieved by simple washing and crystallization of the crude products. All the products were identified by comparison of analytical data with those of authentic samples.

Table 4.4 Synthesis of 4H-pyrans using Mg-Al-CO₃ hydrotalcites.

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Product</th>
<th>Time (Minutes)</th>
<th>Yield</th>
<th>M.P.(°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="CHO.png" alt="CHO" /></td>
<td><img src="Product1.png" alt="Product 1" /></td>
<td>5</td>
<td>53</td>
<td>190-192</td>
</tr>
<tr>
<td>2</td>
<td>![CHO NO₂](CHO NO₂.png)</td>
<td><img src="Product2.png" alt="Product 2" /></td>
<td>60</td>
<td>78</td>
<td>178-180</td>
</tr>
<tr>
<td>3</td>
<td><img src="image1" alt="Chemical Structure" /></td>
<td><img src="image2" alt="Chemical Structure" /></td>
<td>98</td>
<td>40</td>
<td>120-122</td>
</tr>
<tr>
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</tr>
<tr>
<td>4</td>
<td><img src="image3" alt="Chemical Structure" /></td>
<td><img src="image4" alt="Chemical Structure" /></td>
<td>22</td>
<td>56</td>
<td>182-184</td>
</tr>
<tr>
<td>5</td>
<td><img src="image5" alt="Chemical Structure" /></td>
<td><img src="image6" alt="Chemical Structure" /></td>
<td>180</td>
<td>65</td>
<td>130-131</td>
</tr>
<tr>
<td>6</td>
<td><img src="image7" alt="Chemical Structure" /></td>
<td><img src="image8" alt="Chemical Structure" /></td>
<td>2</td>
<td>75</td>
<td>170-172</td>
</tr>
</tbody>
</table>
4.5 Mechanism

Mechanistically, the initial condensation of aromatic aldehyde with malononitrile in the presence of Mg-Al-CO$_3$ Hydrotalcite leads to the formation of arylidenemalononitrile 2 with the loss of a water molecule.\cite{27} The nucleophilic addition of the enolizable ethyl acetoacetate to arylidenemalononitrile 2 followed by intramolecular cyclization of the resulting species A produce the 2-amino-4H-pyran 3 (Scheme 4.4).

To prove the mechanism of one-pot three component reaction we have studied, three set of reaction of malanonitrile, benzaldehyde and ethyl acetoacetate under experimental condition; Under the present condition intermediate has been isolated and characterized by IR, $^1$H NMR, $^{13}$C NMR and mass spectra. The intermediate was subsequently reacted with third component. It was found that the intermediate gave the target molecule with 80% yield i.e reaction proceeds in two step first condensation of benzaldehyde 1 and malanonitrile 2 according to Knoevenagel type reaction takes place leading to intermediate 3 which then react with ethyl acetoacetate to give product (Scheme 4.4).
Scheme 4.4 proposed reaction mechanism using Mg-Al-CO$_3$ hydrotalcite

4.6 Characterization of product(4-H pyran derivatives)

Synthesis of Ethyl 6-amino-5-cyano-2-methyl-4-phenyl-4H-pyran-3-carboxylate.

In the mass spectra of compound (h). The molecular peak is obtained at 284 m/z which matches to the calculated molecular ion weight of the molecule having assigned structure as follows.

R= H

**Fig. 4.2 Ethyl 6-amino-5-cyano-2-methyl-4-phenyl-4H-pyran-3-carboxylate**
In the IR spectra of compound (h) the bands due to \( \nu \) (CN) and \( \nu \) NH\textsubscript{2} appeared at 2208 and 3360 cm\(^{-1}\) respectively.\(^{22}\)

The band due to \( \nu \) C=O stretching vibration was observed at 1681 cm\(^{-1}\). The other characteristics group \( \nu \) C-H, \( \nu \) C-C and \( \nu \) C-O appeared at 3452, 1600 and 1217 cm\(^{-1}\) respectively.

In the \(^1\)H NMR spectra of compound (h), one triplet appearing at 1.02 ppm was assigned to CH\textsubscript{3}. A singlet and a multiplet at 2.30 and 3.94-3.97 ppm were due to CH\textsubscript{3} and CH\textsubscript{2} respectively.\(^{23}\) Two singlets appearing at 4.28 and 5.01 ppm were due to heterocyclic ring proton and NH\textsubscript{2} proton respectively. The signal due to aromatic proton appeared as expected and found in the range 7.12-7.32 ppm.

In the \(^{13}\)C NMR spectra of compound (h) signals due to CN, CH\textsubscript{3}, CH\textsubscript{2} aromatic and heterocyclic ring carbons appeared as expected (Fig 4.7).\(^{24}\)

Peak obtained from \(^{13}\)C NMR spectra further authenticates the finding of IR, \(^1\)HNMR and mass spectra.

### 4.7 Conclusion

In continuation of our efforts to develop efficiently environmentally benign protocol for the synthesis of various heterocycles, we report herein our result with Mg-Al-CO\textsubscript{3} hydrotalcite that efficiently catalyzed three component of aromatic aldehyde, malononitrile and ethyl acetoacetate in solvent (water/ethanol) giving good yield. The reaction shows that yields of the product are depend on the nature of catalyst. Highest yield (97%) was obtained with Mg-Al-CO\textsubscript{3}, It was followed by Ca-Al-CO\textsubscript{3} giving 75% yield. Acetonitrile gave 45% yields. No yield was obtained when reaction was carried out in hexane and toluene.
Spectral data

**Ethyl 6-amino-5-cyano-2-methyl-4-phenyl-4H-pyran-3-carboxylate (h):** IR (KBr), \( \nu (\text{cm}^{-1}) \): 3452, 3398 (NH\(_2\)), 2208 (CN), 1681 (C=O), 1217 (C-O), 1600 (C-C). \(^{1}\)HNMR (CDCl\(_3\), 500 MHz) \( \delta \) ppm: 7.12-7.32 (m, 5H), 5.01(s, 2H), 4.28 (s, 1H), 3.94-3.97 (m, 2H), 2.30 (s, 3H), 1.02 (t, 3H). \(^{13}\)CNMR (CDCl\(_3\), 500 MHz) \( \delta \) ppm: 165.55, 156.62, 144.91, 136.94, 131.84, 128.32, 127.22, 126.84, 119.85, 107.58, 60.16, 38.83, 18.15, 13.80, MS (El) m/z (%): 284 (M\(^+\)).

**Ethyl 5-amino-4-(2-nitrophenyl)-6-cyano-2-methyl-4H-pyran-3-carboxylate (i):** IR (KBr), \( \nu (\text{cm}^{-1}) \): 3448, 3385 (NH\(_2\)), 2208 (CN), 1681 (C=O), 1219 (C-O). \(^{1}\)HNMR (CDCl\(_3\), 500 MHz) \( \delta \) ppm: 7.08-7.92 (d, 1H), 7.37-7.54 (t, 1H), 7.36-7.34 (d, 2H), 5.25 (s, 2H), 4.66 (s, 1H), 3.94-3.95 (m, 2H), 2.39 (s, 3H), 0.99 (t, 3H). \(^{13}\)CNMR (CDCl\(_3\), 500 MHz) \( \delta \) ppm: 165.17, 158.19, 149.20, 139.28, 133.28, 130.74, 128.30, 124.18, 118.34, 107.40, 61.07, 33.06, 18.59, 13.79, MS (El) m/z (%): 329 (M\(^+\)).

**Ethyl 5-amino-4-(4-methoxyphenyl)-5-cyano-2-methyl-4H-pyran-3-carboxylate (j):** IR (KBr), \( \nu (\text{cm}^{-1}) \): 3450, 3316 (NH\(_2\)), 2208 (CN), 1691 (C=O), 1216 (C-O), 1602 (C-C). \(^{1}\)HNMR (CDCl\(_3\), 500 MHz) \( \delta \) ppm: 7.84 (m, J\(_{HH}=8.5\), 2H), 7.38 (m, J\(_{HH}=8.0\), 2H), 4.46 (s, 2H), 4.39 (s, 1H), 4.13-4.20 (m, 2H), 3.89 (s, 3H) 2.35 (s, 3H), 1.11 (t, J\(_{HH}=7.0\)Hz, 3H). \(^{13}\)CNMR (CDCl\(_3\), 500 MHz) \( \delta \) ppm: 166.10, 158.79, 156.46, 132.15, 130.07, 128.74, 126.30, 119.12, 108.34, 62.76, 60.38, 18.52, 14.35, MS (El) m/z (%): 314 (M\(^+\)).

**Ethyl 6-amino-4-(2-chlorophenyl)-5-cyano-2-methyl-4H-pyran-3-carboxylate (k):** IR (KBr) \( \nu (\text{cm}^{-1}) \): 3450, 3380 (NH\(_2\)), 2208 (CN), 1681 (C=O), 1244 (C-O), 1600 (C-C). \(^{1}\)HNMR (CDCl\(_3\), 500 MHz) \( \delta \) ppm: 7.14-7.21 (m, 2H), 6.73-6.81 (m, 2H), 4.42 (s, 2H), 4.02-4.04 (m, 3H), 3.79 (s, 1H), 2.37 (s, 3H), 1.11 (t, 3H). \(^{13}\)CNMR (CDCl\(_3\), 500 MHz) \( \delta \) ppm: 165.72, 157.97, 141.23, 133.12, 131.14, 130.70, 128.47, 127.42, 118.65, 107.02, 61.28, 35.48, 18.46, 13.86, MS (El) m/z (%): 318 (M\(^+\)).

**Ethyl 5-amino-4-(3-methoxyphenyl)-6-cyano-2-methyl-4H-pyran-3-carboxylate (l):** IR (KBr) \( \nu (\text{cm}^{-1}) \): 3421, 3385 (NH\(_2\)), 2200 (CN), 1672 (C=O), 1247 (C-O), 1602 (C-C). \(^{1}\)HNMR
(CDCl₃, 500 MHz) δ ppm: 7.13-7.32 (m, 4H), 5.06 (s, 2H), 4.47 (s, 1H), 3.96-4.02 (m, 5H, CH₂, OCH₃), 2.40 (s, 3H), 1.04 (t, 2H), 314 (m= ±1)m/z.

**Ethyl 5-amino-4-(2,4-chlorophenyl)-6-cyano-2-methyl-4H-pyran-3-carboxylate (m):** IR (KBr) ν (cm⁻¹): 3473, 3325 (NH₂), 2200 (CN), 1681 (C=O), 1244 (C-O). ¹HNMR (CDCl₃, 500 MHz) δ ppm: 7.11-7.23 (m, 3H), 5.01 (s, 2H), 4.52 (m, 1H), 4.00-4.08 (m, 3H), 2.45 (s, 3H), 0.99 (t, 2H), MS (EI) m/z (%) : 353 (M⁺).

**Ethyl 5-amino-4-(4-nitrophenyl)-6-cyano-2-methyl-4H-pyran-3-carboxylate (n):** IR (KBr), ν (cm⁻¹) : 3450, 3315 (NH₂), 2200 (CN), 1681 (C=O), 1244 (C-O), 1600 (C-C). ¹HNMR (CDCl₃, 500 MHz) δ ppm: 8.18 (d, Jₖₖ =10Hz, 2H), 7.38 (d, Jₖₖ =10Hz, 2H), 4.85 (s, 2H), 4.57 (s, 1H), 4.02-4.07 (m, 2H), 2.42 (s, 3H), 1.10 (t, 3H), MS (EI) m/z (%) : 329 (M⁺).

**Mass spectra of intermediate compound**

**2-benzalidenemalanonitrile (3) IR (KBr / cm⁻¹):** 3100, 2222 (CN), 1591 (C=O), 1217 (C-O). MS (EI) m/z (%) : 154 (M⁺).

**Fig.4.3 Mass spectra of 2-benzalidenemalanonitrile**
Fig. 4.4 FT-IR spectra of 2-benzalidenemalononitrile

Fig. 4.5 Mass spectra of Ethyl 6-amino-5-cyano-2-methyl-4-phenyl-4H-pyran-3-carboxylate
Fig. 4.6. FT-IR spectra of Ethyl 6-amino-5-cyano-2-methyl-4-phenyl-4H-pyran-3-carboxylate

Fig. 4.7. $^1$H NMR spectra of Ethyl 6-amino-5-cyano-2-methyl-4-phenyl-4H-pyran-3-carboxylate
Fig. 4.8. $^{13}$C NMR spectra of Ethyl 6-amino-5-cyano-2-methyl-4-phenyl-4H-pyran-3-carboxylate

Compound (i)

Fig. 4.9 Mass spectra of Ethyl 5-amino-4-(2-nitrophenyl)-6-cyano-2-methyl - 4H-pyran-3-carboxylate
Fig. 4.10 FT-IR spectra of Ethyl 5-amino-4-(2-nitrophenyl)-6-cyano-2-methyl - 4H-pyran-3-carboxylate

Fig. 4.11 $^1$H NMR spectra of Ethyl 5-amino-4-(2-nitrophenyl)-6-cyano-2-methyl - 4H-pyran-3-carboxylate
Fig. 4.12 $^{13}$C NMR spectra of Ethyl 5-amino-4-(2-nitrophenyl)-6-cyano-2-methyl -4H-pyran-3-carboxylate

Compound (j)

Fig. 4.13 Mass spectra of Ethyl 5-amino-4-(4-methoxyphenyl)-5-cyano-2-methyl -4H- pyran-3-carboxylate
Fig. 4.14 FT-IR spectra of Ethyl 5-amino-4-(4-methoxyphenyl)-5-cyano-2-methyl-4H-pyran-3-carboxylate

Fig. 4.15 $^{13}$C NMR spectra of Ethyl 5-amino-4-(4-methoxyphenyl)-5-cyano-2-methyl-4H-pyran-3-carboxylate
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Compound (k)

Fig.4.16 Mass spectra of Ethyl 6-amino-4-(2-chlorophenyl)-5-cyano-2-methyl- 4H-pyran-3-carboxylate

Fig.4.17 FT-IR spectra of Ethyl 6-amino-4-(2-chlorophenyl)-5-cyano-2-methyl- 4H-pyran-3-carboxylate
Fig. 4.18 $^1$H NMR spectra of Ethyl 6-amino-4-(2-chlorophenyl)-5-cyano-2-methyl-4H-pyran-3-carboxylate

Fig. 4.19 $^{13}$C NMR spectra of Ethyl 6-amino-4-(2-chlorophenyl)-5-cyano-2-methyl-4H-pyran-3-carboxylate
Compound (I)

Fig. 4.20 Mass spectra of Ethyl 5-amino-4-(3-methoxyphenyl)-6-cyano-2-methyl-4H-pyran-3-carboxylate

Fig. 4.21 FT-IR spectra of Ethyl 5-amino-4-(3-methoxyphenyl)-6-cyano-2-methyl-4H-pyran-3-carboxylate
Fig.4.22 ¹H NMR spectra of Ethyl 5-amino-4-(3-methoxyphenyl)-6-cyano-2-methyl-4H-pyran-3-carboxylate

Fig.4.23 Mass spectra of Ethyl 5-amino-4-(2, 4-dichlorophenyl)-6-cyano-2-methyl-4H-pyran-3-carboxylate
Fig. 4.24 FT-IR spectra of Ethyl 5-amino-4-(2,4-dichlorophenyl)-6-cyano-2-methyl-4H-pyran-3-carboxylate

Compound (n)

Fig. 4.25 Mass spectra of Ethyl 5-amino-4-(4-nitrophenyl)-6-cyano-2-methyl-4H-pyran-3-carboxylate
Fig. 4.26 FT-IR spectra of Ethyl 5-amino-4-(4-nitrophenyl)-6-cyano-2-methyl-4H-pyran-3-carboxylate

Fig. 4.27 $^1$H NMR spectra of Ethyl 5-amino-4-(4-nitrophenyl)-6-cyano-2-methyl-4H-pyran-3-carboxylate
4.8. Reference