CHAPTER: 4

APPLICATIONS:
ORGANIC TRANSFORMATION REACTIONS
CHAPTER: 4

Section-I

Synthesis of 3,4-dihydro-pyrimidone derivatives by using carbon doped MoO$_3$ with PEG-400

Work reported in this section has been published in the Journal “CHINESE JOURNAL OF CHEMISTRY, (2011), 29, 2049-2056”
4.1.1 Introduction:

Acid-catalyzed organic reactions are numerous and the usage of solid acid catalysts is very important in several industrial and environmental processes [1-5]. It can be said that solid acids are the most important heterogeneous catalysts used today, considering in terms of both the total amounts used and the final economic impact [6]. It clearly indicates the significance of these materials and the scope of their commercial exploitation.

The use of conventional liquid acids and Lewis acids has significant risks in handling, containment, disposal and regeneration due to their toxic and corrosive nature. Thus, there is need in the development of strong solid acid catalysts which must be stable, regenerable and active at moderate temperatures. Solid acids are such as clays, zeolites, heteropolyacids and ion exchange resins, due to their superior catalytic activity for hydrocarbon conversions [7-9]. Over the past few years, the preparation and characterization of Molybdenum based solid acids has been receiving much attention. The MoO$_3$, were particularly interesting due to their potential applications. It has been extensively investigated as a key material for fundamental research and technological applications in optical devices, smart windows, catalysts, sensors, lubricants, electrochemical storage batteries, information displays and optical filters. Molybdenum oxides and molybdenum oxide based materials are of great technical interest [10-14].

4.1.1.1 Literature review:

The Biginelli reaction is one of the most important multi-component reaction for the synthesis of dihydropyrimidinones. Dihydropyrimidinones are known to exhibit a wide range of biological and their therapeutic activities such as antiviral, antitumor, antibacterial, and anti-inflammatory, analgesic, blood
platelets aggregation inhibitors, cardiovascular properties [15]. The classical Biginelli reaction requires long reaction times (20 h) and often suffers from low yields of products in case of substituted aromatic and aliphatic aldehydes [16]. Multi-step synthesis [17] produces somewhat higher yields but lacks the simplicity of original one-pot Biginelli protocol, hence the Biginelli reaction continues to attract the attention of organic chemists interested in finding milder and more efficient procedures for the synthesis of dihydropyrimidinones.

Recently several methods have been reported for preparing dihydropyrimidines using different Lewis acids such as BF$_3$.OEt$_2$, LaCl$_3$, Yb(OTF)$_3$ [18-20], as well as protic acids such as H$_2$SO$_4$, HCl [21-24] as promoters. Many other methods including microwave irradiations, ionic liquids and clay [25] are also reported.

Adib et al [26], described the cerium(III) nitrate hexahydrate efficiently catalyzes the three-component Biginelli reaction under solvent-free conditions of an aldehyde, a $\beta$-keto ester or $\beta$-diketone and urea or thiourea to afford the corresponding 3,4-dihydropyrimidin-2(1H)-ones or -thiones for 90-97% yield in 10-40 min. (Scheme 4.1.1).

![Scheme 4.1.1](image)

Li et al [27], synthesis dihydropyrimidinones using NH$_2$SO$_3$H catalyzed condensation of aldehydes, $\beta$-keto esters and urea in ethanol under ultrasound irradiation to afford 97% yields in 40 min. (Scheme 4.1.2).

![Scheme 4.1.2](image)
Sabitha et al. [28], carried out the synthesis of dihydropyrimidinones using $\text{VCl}_3$ as catalyst, from aldehyde, a $\beta$-keto ester and urea (thiourea) in acetonitrile reflux in 2h (Scheme 4.1.3).

Su, et al. [29], carried out the synthesis of dihydropyrimidiones using strontium(II) triflate [$\text{Sr(OTf)}_2$] as catalyst, was heated at 70 °C under stirring to afford 86-97% yields in 4 h (Scheme 4.1.4).

Debache, et al. [30], developed triphenylphosphine (TPP) catalyzed one-pot Biginelli reaction of $\beta$-ketoesters, aldehydes and urea (or thiourea) to afford the corresponding dihydropyrimidinones/thiones to give 42-70% yields in 10 h (Scheme 4.1.5).
However, some of these methods are plagued by one or many drawbacks such as long reaction time, use of volatile solvents, low yields and harsh reaction conditions. Therefore, it is necessary to develop an improved route for the synthesis of 3,4-dihydropyrimidinones (DHPMs) under mild reaction conditions.

### 4.1.1.2 Present work:

The motivation for this work was the investigation of novel synthetic route to prepare realistic solid acid catalytic model system based on molybdenum oxide by using PEG-400 and natural carbon. The prepared catalytic material was tested on the synthesis of 3,4-dihydropyrimidones via the Biginelli-type condensation reaction. The short reaction time, clean reaction condition, consistent yield and minimum environmental effect are important features of the reaction. **(Scheme 4.1.6)**.
4.1.2 Experimental:

4.1.2.1 General procedure for the synthesis substituted 3,4 dihydropyrimidotiones:

As shown in Scheme 4.1.6, a mixture of aldehydes (1 mmol), ethyl acetoacetate (1.2 mmol) and urea/thiourea (1.2 mmol) in the presence of series of carbon-doped MoO$_3$ with and without PEG-400 (0.1 g) in acetonitrile as solvent reflux at 70–80° C for appropriate time gave 3,4-dihydropyrimidinone. After completion of the reaction monitored by TLC (hexane/ethyl acetate 8:2), the reaction mixture was brought to room temperature and washed by cold water to remove excess urea or thiourea and then filtered. The remaining solid material was washed with hot ethyl acetate. The filtrate was concentrated and the solid product was recrystallized from ethanol to give the pure product. The structure of all the products was confirmed by comparing melting point and spectral data by taking IR, $^1$H NMR, and mass analysis.

4.1.2.2 Spectroscopic data of representative compound (4 a-i):

Ethyl1,2,3,4-tetrahydro-4-methyl-2-oxo-6-phenylpyrimidine-5-
carboxylate (a): $^1$H NMR (CDCl$_3$, 300MHz) $\delta$: 8.40 (s, 1H), 8.07(s, 1H), 7.28 (m, 5H), 5.45 (d, 1H), 4.08 (q, 2H), 2.36 (s, 3H), 1.19 (t, 3H); FTIR (KBr) $\nu_{\text{max}}$/cm$^{-1}$: 3240, 1725, 1638; Mass: m/z 260 (M+1).

Ethyl1,2,3,4-tetrahydro-4-methyl-2-oxo-6-p-tolylpyrimidine-5-
carboxylate (b): $^1$H NMR (CDCl$_3$, 300MHz) $\delta$: 8.10 (s, 1H), 7.94(s, 1H), 7.28 (m, 5H), 5.35 (d, 1H), 4.11 (q, 2H), 2.35 (s, 3H), 1.71 (s, 3H), 1.19 (t, 3H); FTIR (KBr) $\nu_{\text{max}}$/cm$^{-1}$: 3240, 1722, 1638;

Ethyl4-(4-chlorophenyl)-1,2,3,4-tetrahydro-4-methyl-2-oxopyrimidine-
5-carboxylate (c): $^1$H NMR (CDCl$_3$, 300MHz) $\delta$: 8.08 (s, 1H), 7.85(s, 1H), 7.58 (d, 2H), 7.32 (d, 2H), 4.38 (d, 1H), 4.12 (q, 2H), 2.37 (s, 3H), 1.28 (t, 3H); FTIR (KBr) $\nu_{\text{max}}$/cm$^{-1}$: 3225, 1720, 1615;

Ethyl4-(3-nitrophenyl)-1,2,3,4-tetrahydro-4-methyl-2-oxopyrimidine-
5-carboxylate (d): $^1$H NMR (CDCl$_3$, 300MHz) $\delta$: 8.38 (s, 1H), 8.15(s, 1H),
7.75 (d, 2H), 7.48 (d, 2H), 5.05 (d, 1H), 3.97 (q, 2H), 2.42 (s, 3H), 1.30 (t, 3H);

Ethyl4-(2-chlorophenyl)-1,2,3,4-tetrahydro-4-methyl-2-oxopyrimidine-5-carboxylate (e): \( ^1H \) NMR (CDCl\(_3\), 300MHz) \( \delta \): 8.38 (s, 1H), 8.11(s, 1H), 7.35 (d, 2H), 7.08 (d, 2H), 5.45 (d, 1H), 4.08 (q, 2H), 2.36 (s, 3H), 1.19 (t, 3H);

FTIR (KBr) \( \nu_{\text{max}}/\text{cm}^{-1} \): 3232, 1724, 1631;

Ethyl4-(4-fluorophenyl)-1,2,3,4-tetrahydro-4-methyl-2-oxopyrimidine-5-carboxylate (f): \( ^1H \) NMR (CDCl\(_3\), 300MHz) \( \delta \): 8.08 (s, 1H), 7.85(s, 1H), 7.65 (d, 2H), 7.28 (d, 2H), 5.45 (d, 1H), 4.11 (q, 2H), 2.37 (s, 3H), 1.28 (t, 3H);

FTIR (KBr) \( \nu_{\text{max}}/\text{cm}^{-1} \): 3232, 1724, 1631;

Ethyl1,2,3,4-tetrahydro-4-methyl-6-phenyl-2-thioxopyrimidine-5-carboxylate (g): \( ^1H \) NMR (CDCl\(_3\), 300MHz) \( \delta \): 8.05 (s, 1H), 7.75 (s, 1H), 7.28 (m, 4H), 5.35 (d, 1H), 4.21 (q, 2H), 2.45 (s, 3H), 1.31 (s, 3H), 0.90 (t, 3H);

FTIR (KBr) \( \nu_{\text{max}}/\text{cm}^{-1} \): 3240, 1722, 1638;

Ethyl1,2,3,4-tetrahydro-4-methyl-6-(3-nitrophenyl)-2-thioxopyrimidine-5-carboxylate (h): \( ^1H \) NMR (CDCl\(_3\), 300MHz) \( \delta \): 8.15 (s, 1H), 8.08(s, 1H), 7.25 (d, 2H), 7.18 (d, 2H), 5.45 (d, 1H), 4.17 (q, 2H), 1.88 (s, 3H), 1.19 (t, 3H); FTIR(KBr) \( \nu_{\text{max}}/\text{cm}^{-1} \): 3240, 1741, 1654;

Ethyl4-(4-chlorophenyl)-1,2,3,4-tetrahydro-4-methyl-2-thioxopyrimidine-5-carboxylate (i): \( ^1H \) NMR (CDCl\(_3\), 300MHz) \( \delta \): 8.75 (s, 1H), 8.51(s, 1H), 8.25 (d, 2H), 7.88 (d, 2H), 5.45 (d, 1H), 4.32 (q, 2H), 1.71 (s, 3H), 1.32 (t, 3H ); FTIR (KBr) \( \nu_{\text{max}}/\text{cm}^{-1} \): 3245, 1725, 1632, 1575, 1545;

4.1.3 Results and discussion:

In order to get best experimental results, we have considered the model reaction of Biginelli’s one-pot condensation reaction. In that the reaction of benzaldehyde (1.0 mmol) with urea (1.2 mmol) and ethyl acetoacetate (1.2 mmol) using 0.1 g of catalyst in acetonitrile (10 mL) as solvent at ambient temperature. The reaction is very fast and 93% conversion is observed in 90-180 min. In this study, the effect of different solvent was investigated and given in Table 4.1.1. The choice of solvent proved critical. The best result
was found to be with 0.1 g of CMP-3 catalyst proved the optimized reaction condition, affording 93% yield of product. It was observed that the acetonitrile is a much better solvent in terms of yield (93%) than all other tested solvents such as methanol, dichloromethane, THF, water, H₂O-THF, toluene [31].

Table 4.1.1: Comparative study of different solvent system

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Time (min.)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>EtOH</td>
<td>180</td>
<td>35</td>
</tr>
<tr>
<td>2</td>
<td>Acetic acid</td>
<td>180</td>
<td>40</td>
</tr>
<tr>
<td>3</td>
<td>CH₃CN</td>
<td>90</td>
<td>93</td>
</tr>
<tr>
<td>4</td>
<td>CH₃OH</td>
<td>120</td>
<td>82</td>
</tr>
<tr>
<td>5</td>
<td>CH₂Cl₂</td>
<td>120</td>
<td>76</td>
</tr>
<tr>
<td>6</td>
<td>THF</td>
<td>180</td>
<td>65</td>
</tr>
<tr>
<td>7</td>
<td>H₂O</td>
<td>180</td>
<td>40</td>
</tr>
<tr>
<td>8</td>
<td>H₂O-THF</td>
<td>180</td>
<td>70</td>
</tr>
<tr>
<td>9</td>
<td>Toluene</td>
<td>180</td>
<td>60</td>
</tr>
</tbody>
</table>

*aReaction condition: Benzaldehyde (1.0 mmol) with Ethyl acetoacetate (1.2 mmol) and Urea (1.2 mmol) using 0.1 gm of CMP-3 catalyst in 10 ml solvent in reflux, \(^ {b}\) isolated yields.

The results obtained are summarized in Table 4.1.2. From obtained results, it is observed that, the pure MoO₃ (CM-0) and increases in carbon doping (0, 1, 2, 3 wt. %) with PEG-400 increases the catalytic activity in terms of time and yields of the product. Among the various carbon doping with CMP-3, the catalytic material have shown very good catalytic activity during the synthesis of substituted 3,4 dihydropyrimidinones with excellent to high yield in a very shorter reaction time, which might be due to small particle size and high porosity. The possible mechanism for the preparation of substituted 3,4 dihydro pyrimidinones by using CMP-3 catalyst are presented in Scheme 4.1.7.
Table 4.1.2: Effect of variation in % carbon and PEG-400 in the catalyst

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Time (min)</th>
<th>Yield (%)b</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CM-0</td>
<td>180</td>
<td>51</td>
</tr>
<tr>
<td>2</td>
<td>CM-1</td>
<td>120</td>
<td>62</td>
</tr>
<tr>
<td>3</td>
<td>CM-2</td>
<td>120</td>
<td>65</td>
</tr>
<tr>
<td>4</td>
<td>CM-3</td>
<td>90</td>
<td>76</td>
</tr>
<tr>
<td>5</td>
<td>CMP-0</td>
<td>120</td>
<td>55</td>
</tr>
<tr>
<td>6</td>
<td>CMP-1</td>
<td>120</td>
<td>70</td>
</tr>
<tr>
<td>7</td>
<td>CMP-2</td>
<td>90</td>
<td>82</td>
</tr>
<tr>
<td>8</td>
<td>CMP-3</td>
<td>90</td>
<td>93, 91, 91c</td>
</tr>
</tbody>
</table>

aReaction condition: Benzaldehyde (1.0 mmol) with Ethyl acetoacetate (1.2 mmol) and Urea (1.2 mmol) using 0.1 g of catalyst in 10 mL acetonitrile solvent in reflux. b isolated Yield, c yield of product with catalyst reused up to three times.

Scheme 4.1.7: Possible mechanism for the preparation of substituted 3, 4 dihydropyrimidinones by using CMP-3 catalyst

Scheme 4.1.7

In order to strengthen the novelty of the present method, we have compared our results with some reported procedures using some other catalysts such as Cu(NH₂SO₄)₂, Bi(NO₃)₃, Pb(NO₃)₂, Zn(BF₄)₂, H₂SO₄/SiO₂ [32,33]. It has been observed that CMP-3
catalytic materials gave high yield within very short reaction time in comparison with earlier reported methods.

Therefore, the CMP-3 catalytic material in acetonitrile solvent system under refluxing condition was used for the preparation of different derivatives of 3, 4 dihydropyrimidinones with electron donating as well as withdrawing substituent gave the desired product. Similarly, we have studied the tolerance of various functional groups such as methyl, chlorides, nitro and fluorides, etc. to the reaction conditions. Aromatic aldehyde with these functional groups reacted smoothly and produced the corresponding dihydropyrimidinones in high yields and with required purity. Thiourea has been used with similar success to provide corresponding S-dihydropyrimidinones analogues, which are also of interest due to their biological activities (Table 4.1.3).

The catalyst was recovered by filtration of reaction mixture under hot condition. The recovered catalyst was washed several times with acetone and dried at 100°C. The separated catalyst was again reused for the same reaction. In these cases the yield of product is 93, 91, 91 % in successive three-time use. Thus the activity of catalyst is found to be diminished to some extent after its recyclability.

The reaction proceeds efficiently under these conditions and the dihydropyrimidinones are produced in excellent yields (93%) in short reaction times (90 min). The CMP-3 catalytic material shows highest activity for the synthesis of dihydropyrimidinones. It offers several advantages including mild reaction conditions, greater selectivity, high product yields as well as simple experimental and isolation procedure, which makes it useful and attractive process for large scale synthesis of these compounds.
**Table 4.1.3: Preparation of different derivatives of 3,4dihydropyrimidinones**

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>X</th>
<th>Time (min.)</th>
<th>Yield (%)</th>
<th>M.P. °C Reported</th>
<th>M.P. °C Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>H</td>
<td>O</td>
<td>90</td>
<td>93</td>
<td>202-203 [34]</td>
<td>206-208</td>
</tr>
<tr>
<td>4b</td>
<td>4 -CH₃</td>
<td>O</td>
<td>135</td>
<td>88</td>
<td>213-214 [34]</td>
<td>212-214</td>
</tr>
<tr>
<td>4c</td>
<td>4 -Cl</td>
<td>O</td>
<td>120</td>
<td>90</td>
<td>213-214 [34]</td>
<td>215-216</td>
</tr>
<tr>
<td>4d</td>
<td>3 -NO₂</td>
<td>O</td>
<td>150</td>
<td>90</td>
<td>227-229 [35]</td>
<td>227-229</td>
</tr>
<tr>
<td>4e</td>
<td>2 -Cl</td>
<td>O</td>
<td>140</td>
<td>81</td>
<td>215-218 [36]</td>
<td>215-218</td>
</tr>
<tr>
<td>4f</td>
<td>4 -F</td>
<td>O</td>
<td>125</td>
<td>89</td>
<td>182-184 [35]</td>
<td>178-180</td>
</tr>
<tr>
<td>4g</td>
<td>4 -CH₃</td>
<td>S</td>
<td>160</td>
<td>87</td>
<td>193-195 [34]</td>
<td>192-194</td>
</tr>
<tr>
<td>4h</td>
<td>3 -NO₂</td>
<td>S</td>
<td>140</td>
<td>91</td>
<td>205-207 [35]</td>
<td>205-207</td>
</tr>
<tr>
<td>4i</td>
<td>4 -Cl</td>
<td>S</td>
<td>145</td>
<td>90</td>
<td>192-194 [34]</td>
<td>236-238</td>
</tr>
</tbody>
</table>

*Reaction condition:* aldehyde (1.0 mmol) with Ethyl acetoacetate (1.2 mmol) and Urea or thiourea (1.2 mmol) using 0.1 g of CPM-3 in 10 mL acetonitrile solvent in reflux, *b* isolated yields

**4.1.4 Conclusions:**

In summary, carbon doped MoO₃ with PEG-400 as an efficient catalytic system has been developed. Present catalytic system offers remarkable advantages such as non-toxic, non-corrosive and an inexpensive. Simply recovery and reusability of the catalyst makes the reaction successful under environmental benign conditions. The prepared catalytic material were successfully tested on the synthesis of 3,4-dihydropyrimidones via the Biginelli-type condensation reaction.
$^1H$ NMR spectrum of Ethyl 1,2,3,4-tetrahydro-4-methyl-2-oxo-6-phenylpyrimidine-5-carboxylate (4.1.2.2 a)

FT-IR spectrum of Ethyl 1,2,3,4-tetrahydro-4-methyl-2-oxo-6-phenylpyrimidine-5-carboxylate (4.1.2.2 a)
Mass spectrum of Ethyl 1,2,3,4-tetrahydro-4-methyl-2-oxo-6-phenylpyrimidine-5-carboxylate (4.1.2.2 a)
CHAPTER: 4

Section-II

Synthesis of 2-Aryl 1-arylmethyl-1H-benzimidazole derivatives by using carbon doped MoO$_3$
4.2.1 Introduction:

The Acid-catalysed organic reactions are numerous and the usage of solid acid catalysts is very important in several industrial and environmental processes [1-6]. In recent years, inorganic solid acid-catalyzed organic transformations are gaining much attention due to proven advantage of heterogeneous catalysts, like easy product isolation, mild reaction conditions, high selectivity, and ease in recovery and recyclability of the catalysts and substantial reduction in the generation of waste materials [37-39].

Various solid acids such as zeolites, mesoporous materials, supported and unsupported metal oxides have been used as catalysts for variety of reactions. [40, 41]. Interestingly, modified molybdenum oxide exhibits excellent activity for a wide range of organic synthetic and transformation reactions. It has been receiving much attention, amongst other solid acid catalysts, due to its superior catalytic activity which possesses both strong Lewis and Bronsted acidity [7, 8, 11, 42-46].

4.2.1.1 Literature review:

Interest in benzimidazole containing structures stems from their widespread occurrence in molecules that exhibit significant activity against several viruses such as HIV, herpes (HSV-1), RNA, influenza and human cytomegalovirus (HCMV) [47]. Substituted benzimidazole derivatives have found commercial applications in veterinarian medicine as anthelmintic agents and in diverse human therapeutic areas such as treatment of ulcers and as antihistamines [48, 49].

The traditional synthesis of benzimidazoles involves the reaction between o-phenylenediamine and a carboxylic acid or its derivatives (nitriles, amidates, orthoesters) under harsh dehydrating conditions [50]. Benzimidazoles have also been prepared on solid-phase to provide a combinatorial approach [51]. However, many of
these methods have several drawbacks such as low yields, use of expensive reagents, and a special oxidation process or long reaction times, tedious work-up procedures, co-occurrence of several side reactions and poor selectivity. Therefore, the search continues for a better catalyst for the synthesis of 2-Aryl-1-arylmethyl-1H-benzimidazoles in terms of operational simplicity, economic viability and in particular, with greater selectivity.

Shingare and co-workers [52], have developed new route to synthesize benzimidazole and 2-substituted benzimidazoles using ionic liquid as a catalyst under microwave irradiation. This method afford 87-96% yield of the products in 5-8 min. (Scheme 4.2.1).

\[
\begin{align*}
\text{NH}_2 \quad \text{NH}_2 + 2\text{ArCHO} & \rightarrow \text{[bnmim]HSO}_4 \\
& \rightarrow \text{Ar}\text{N} \quad \text{Ar} \\
\end{align*}
\]

**Scheme 4.2.1**

Niknam et al [53], prepared 2-substituted benzimidazoles and bis-benzimidazoles using o-phenylenediamine and acids in the presence of alumina and methyl sulphonic acid in microwave; to give 74-87% yield of the products and required 8-18 min. for completion of reaction (Scheme 4.2.2).

\[
\begin{align*}
\text{NH}_2 \quad \text{NH}_2 + \text{HOOC-Y-COOH} & \rightarrow \text{AMA} \quad \text{MW} \\
& \rightarrow \text{N} \quad \text{Y} \quad \text{N} \\
\end{align*}
\]

**Scheme 4.2.2**

Varala et al [54], used L-proline- as a catalyst for the synthesis of 2-aryl-1-arylmethyl-1H-benzimidazoles from a wide range of substituted o-phenylenediamines and aldehydes in moderate to excellent yield 32–95% under mild conditions using chloroform as a solvent at ambient temperature (Scheme 4.2.3).
**Scheme 4.2.3**

Salehi *et al* [55], reported the synthesis of 2-aryl-1-arylmethyl-1H-1,3-benzimidazoles from the reaction of o-phenylenediamines and aromatic aldehydes in the presence of silica sulfuric acid. The reactions were performed in ethanol or water and the catalyst reused for several runs (**Scheme 4.2.4**).

**Scheme 4.2.4**

Sharma *et al* [56], have developed new method for the formation of biologically significant 2-aryl-1-arylmethyl-1H-benzimidazoles under the heterogeneous catalysis of Amberlite IR-120 in aqueous media gives excellent yields. The catalyst is recyclable without loss of activity (**Scheme 4.2.5**).

**Scheme 4.2.5**
4.2.1.2 Present work:

Thus, taking into considerations of above points in present article we report here the improvement in structural and catalytic properties of MoO$_3$ by the addition of carbon and PEG-400 as a surface directing agents. The carbon substrate was prepared and utilized from natural sources like Acacia Arabica plant. The synthesized catalyst was tested on the synthesis of 2-Aryl-1-arylmethyl-1$H$-benzimidazole derivatives Scheme 4.2.6.

\[ \text{Scheme 4.2.6} \]

4.2.2 Experimental:

4.2.2.1 Procedure for the synthesis of substituted 2-aryl-1-arylmethyl-1$H$-benzimidazoles:

A mixture of aromatic aldehydes (2 mmol), o-phenylenediamines (1 mmol) in the presence of carbon-doped MoO$_3$ with PEG-400 (0.1 g) was refluxed in Ethanol: Water (2:1) for the various time mentioned in Table 3. The progress of the reaction was monitored by thin layer chromatography using pet ether: ethyl acetate as a solvent system. After completion of the reaction, the reaction mass was filtered, and the filtrate was concentrated under reduced pressure, the crude product obtained was recrystallized from ethanol to afford pure products. The structure of all the products was confirmed by comparing melting point and spectral data (IR, $^1$H NMR, and mass analysis).
4.2.2.2 Spectroscopic data of representative compound (3 a-g):

1-benzyl-2-phenyl-1H-benzo[d]imidazole (a): \( ^1 \text{H} \) NMR (CDCl\(_3\), 300MHz) \( \delta \): 8.15-7.15 (m, 10H), 6.58 (dd, 2H), 6.25 (dd, 2H), 5.45 (s, 2H); FTIR (KBr) \( v_{\text{max}}/\text{cm}^{-1} \): 3059, 1599, 1489, 1394; Mass: m/z 284 (M+1).

1-(2-chlorobenzyl)-2-(2-chlorophenyl)-1H-benzo[d]imidazole (b): \( ^1 \text{H} \) NMR (CDCl\(_3\), 300MHz) \( \delta \): 7.55-7.25 (m, 8H), 7.06 (d, 2H), 6.65 (dd, 2H), 5.38 (s, 2H); FTIR (KBr) \( v_{\text{max}}/\text{cm}^{-1} \): 3059, 1591, 1442, 1400, 746, 727.

1-(4-fluorobenzyl)-2-(4-fluorophenyl)-1H-benzo[d]imidazole (c): \( ^1 \text{H} \) NMR (CDCl\(_3\), 300MHz) \( \delta \): 7.65 (m, 2H), 7.58-7.46 (m, 4H), 7.28-7.15 (m, 4H), 6.95 (dd, 2H), 5.41 (s, 2H); FTIR (KBr) \( v_{\text{max}}/\text{cm}^{-1} \): 3070, 1593, 1489, 1402, 744.

1-(3-nitrobenzyl)-2-(3-nitrophenyl)-1H-benzo[d]imidazole (d): \( ^1 \text{H} \) NMR (CDCl\(_3\), 300MHz) \( \delta \): 8.85 (s, 1H), 8.52 (d, 1H), 8.25 (d, 1H), 8.05 (s, 1H), 7.92 (d, 1H), 7.71 (dd, 2H), 7.55 (dd, 1H); 7.45-7.25 (m, 4H), 5.61 (s, 2H); FTIR (KBr) \( v_{\text{max}}/\text{cm}^{-1} \): 3055, 1521, 1475, 1315, 752.

1-(4-bromobenzyl)-2-(4-bromophenyl)-1H-benzo[d]imidazole (e): \( ^1 \text{H} \) NMR (CDCl\(_3\), 300MHz) \( \delta \): 7.92 (m, 2H), 7.65-7.42 (m, 4H), 7.38-7.21 (m, 4H); 6.95 (m, 2H), 5.40 (s, 2H); FTIR (KBr) \( v_{\text{max}}/\text{cm}^{-1} \): 3076, 1506, 1479, 748, 609.

1-(4-chlorobenzyl)-2-(4-chlorophenyl)-1H-benzo[d]imidazole (f): \( ^1 \text{H} \) NMR (CDCl\(_3\), 300MHz) \( \delta \): 7.92 (m, 2H), 7.65-7.42 (m, 4H), 7.45 (m, 2H), 7.25 (m, 2H), 7.02 (m, 2H), 5.45 (s, 2H); FTIR (KBr) \( v_{\text{max}}/\text{cm}^{-1} \): 3053, 1600, 1429, 831, 744.

1-(2-chlorobenzyl)-2-(2-chlorophenyl)-5-methyl-1H-benzo[d]imidazole (g): \( ^1 \text{H} \) NMR (CDCl\(_3\), 300MHz) \( \delta \): 8.10 (s, 1H), 7.70 (m, 1H), 7.6-7.45 (m, 4H), 7.40-7.15 (m, 4H), 7.05 (dd, 1H), 5.45 (s, 2H), 2.45 (s, 3H); FTIR (KBr) \( v_{\text{max}}/\text{cm}^{-1} \): 3059, 1537, 1452, 1365, 800, 709.
4.2.3 Results and Discussion:

In order to get best results of synthesized catalytic material, we have carried out the model reaction of o-phenylenediamine and benzaldehyde in presence of series of carbon-doped MoO$_3$ with PEG-400 (0.1 g) by refluxing in Ethanol: Water (2:1). To examine the solvent effect from this study, the reactions were carried out in various solvents such as water, Methanol (MeOH), Acetonitrile (MeCN), Tetrahydrofuran (THF), Ethanol (EtOH) and Ethanol: Water (EtOH:H$_2$O). From the results, it is observed that Ethanol: Water (2:1) found to be the best solvent medium to carry out the synthesis of desired compounds shown in Table 4.2.1.

**Table 4.2.1: Comparative study of synthesis of benzimidazole with different solvent with CMP-3 catalyst**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Time (Minute)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H$_2$O</td>
<td>180</td>
<td>65</td>
</tr>
<tr>
<td>2</td>
<td>EtOH</td>
<td>150</td>
<td>85</td>
</tr>
<tr>
<td>3</td>
<td>MeOH</td>
<td>210</td>
<td>82</td>
</tr>
<tr>
<td>4</td>
<td>MeCN</td>
<td>240</td>
<td>63</td>
</tr>
<tr>
<td>5</td>
<td>THF</td>
<td>240</td>
<td>60</td>
</tr>
<tr>
<td>6</td>
<td>EtOH:H$_2$O (1:1)</td>
<td>120</td>
<td>84</td>
</tr>
<tr>
<td>7</td>
<td>EtOH:H$_2$O (2:1)</td>
<td><strong>120</strong></td>
<td><strong>89</strong></td>
</tr>
</tbody>
</table>

*aReaction conditions: o-phenylenediamine (1 mmol), benzaldehyde (2 mmol) and 0.1 g catalyst and EtOH: H$_2$O (2:1) under reflux condition.*

*bIsolated Yields.*

After optimization of solvent effect, we also studied the effect of catalyst. Interestingly, it was observed that catalytic activities were increases with increasing amount of carbon in MoO$_3$. The CMP-0, CMP-1 and CMP-2 furnish the moderate amount of yields of the products, while CMP-3 catalyst gives excellent yield (89%) within 120 min. listed in Table 4.2.2.
**Table 4.2.2: Comparative study of synthesis of benzimidazole with different catalyst**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Time (Min.)</th>
<th>Yield (%)$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CM-0</td>
<td>120</td>
<td>71</td>
</tr>
<tr>
<td>2</td>
<td>CMP-0</td>
<td>120</td>
<td>72</td>
</tr>
<tr>
<td>3</td>
<td>CMP-1</td>
<td>120</td>
<td>81</td>
</tr>
<tr>
<td>4</td>
<td>CMP-2</td>
<td>120</td>
<td>86</td>
</tr>
<tr>
<td>5</td>
<td><strong>CMP-3</strong></td>
<td><strong>120</strong></td>
<td><strong>89</strong></td>
</tr>
</tbody>
</table>

$^a$isolated yields.

To test the generality of this reaction, a series of aromatic aldehydes and o-phenylenediamines were subjected to the optimal reaction conditions. Almost all substrates could gave corresponding 1,2-disubstituted benzimidazoles exclusively as a single product. The results are documented in Table 4.2.3. Therefore, under optimized conditions, the method was further employed to synthesize variety of 2-Aryl-1-aryl methyl-1$H$-benzimidazoles and found that electron withdrawing and donating aldehydes reacts without any significant loss in activity to give the desired products in good.

The catalyst was recovered by filtration under hot condition. The recovered catalyst was washed several times with acetone and dried at 100°C and again reused for the fresh reaction. In these cases the yield of product is found to be 89, 89, 88 and 88% in successive time use. Thus, the activity of catalyst was found to be diminished to some extent after several runs.
Table 4.2.3: Synthesis of benzimidazole derivatives

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>R₁</th>
<th>Time (Minute)</th>
<th>Yield (%)</th>
<th>M.P. (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>H</td>
<td>H</td>
<td>120</td>
<td>89(89,88,88)</td>
<td>130</td>
</tr>
<tr>
<td>3b</td>
<td>H</td>
<td>2-Cl</td>
<td>150</td>
<td>85</td>
<td>160</td>
</tr>
<tr>
<td>3c</td>
<td>H</td>
<td>4-F</td>
<td>210</td>
<td>82</td>
<td>113</td>
</tr>
<tr>
<td>3d</td>
<td>H</td>
<td>3-NO₂</td>
<td>240</td>
<td>63</td>
<td>155</td>
</tr>
<tr>
<td>3e</td>
<td>H</td>
<td>4-Br</td>
<td>240</td>
<td>60</td>
<td>159</td>
</tr>
<tr>
<td>3f</td>
<td>H</td>
<td>4-Cl</td>
<td>120</td>
<td>84</td>
<td>135</td>
</tr>
<tr>
<td>3g</td>
<td>CH₃</td>
<td>2-Cl</td>
<td>120</td>
<td>89</td>
<td>164</td>
</tr>
</tbody>
</table>

*Reaction conditions: o-phenylenediamine (1 mmol), aromatic aldehydes (2 mmol) and 0.1 g CMP-3 catalyst and EtOH: H₂O (2:1) solvent under reflux condition. bIsolated Yield, cAfter consecutive run.*

The synthetic protocol described herein allows exclusively biologically significant benzimidazoles under the heterogeneous catalysis using carbon-doped MoO₃ with PEG-400 as a catalyst. This synthetic procedure offers several advantages including mild reaction conditions, greater selectivity, high product yields as well as simple experimental and isolation procedure, which makes it useful and attractive process for large scale synthesis of these compounds.

4.2.4 Conclusions:

In summary the present paper describes a new, efficient and eco-friendly route for the synthesis of 2-Aryl-1-arylmethyl-1H-benzimidazoles. We have also compared the time required and product yields for the synthesis of benzimidazole by the addition of amount of carbon in MoO₃. The 3 wt % carbon doped MoO₃ with PEG-400 (CMP-3) catalyst exhibits excellent catalytic activity. The prepared catalyst is reusable and non-hazardous. A simple procedure combined with low toxicity, short reaction time, consistence yield and easy work up of the product, provides an economic and waste-free chemical method for the synthesis of 2-Aryl-1-arylmethyl-1H-benzimidazoles.
$^1$H NMR spectrum of 2-Aryl 1-arylmethyl-1H-benzimidazole (4.2.2.2 a)

FTIR spectrum of 2-Aryl 1-arylmethyl-1H-benzimidazole (4.2.2.2 a)
Mass spectrum of 2-Aryl 1-arylmethyl-1H-benzimidazole (4.2.2.2 a)
CHAPTER: 4

Section-III

One-pot synthesis of 1,8 dioxo-decahydroacridines catalyzed by Carbon doped MoO$_3$
4.3.1 Introduction:

1,8-Dioxo-decahydroacridines and their derivatives are poly-functionalized 1,4-dihydropyridine derivatives. In recent years, 1,4-dihydropyridines and their derivatives have attracted strong interest for the treatment of cardiovascular diseases, such as angina pectoris and hypertension [57, 58]. Acridine derivatives have been used to synthesize labelled conjugates with medicinals, peptides, proteins, and nucleic acids that exhibit antitumor and DNA-binding properties [59-61]. The 1,4-dihydropyridine derivatives are very important compounds because of their pharmacological properties [62]. Many members of this family are nowadays used for the treatment of platelet anti aggregatory activity, Alzheimer's disease, tumours, cardiovascular diseases including hypertension and diabetes [63-67]. These compounds can also be used as dyes [68-70].

The ultrasonic irradiation gives an idea about the great potential of the method because of its simplicity and efficiency. The sonochemical organic synthesis as a green synthetic approach has an interesting role compared with other traditional methods. The application of sonochemistry allows good yields, high crystallinity of the products; it is more efficient and homogeneous. It also affords an immense reduction of the reaction time, from days to minutes [71-73].

4.3.1.1 Literature review:

Some methods are available in the literature for the synthesis of acridine derivatives containing 1,4-dihydropyridines, from dimedone, aldehyde and different nitrogen sources like urea [74], methyl amine [75] and different anilines or ammonium acetate [76] via traditional heating in organic solvents, in the presence of triethyl benzylammonium chloride (TEBAC) [77], p-
dodecylbenzenesulfonic acid (DBSA) [78], Proline [79], Amberlyt-15 [80], ammonium chloride or Zn(OAc)$_2$·2H$_2$O or L-proline [81].

Ghorbani-Vaghei et al [82], described the application of $N,N'$-dibromo-$N,N'$-1,2-ethanediyl bis($p$-toluenesulfonamide) [BNBTS], in the preparation of acridines from naphthalen-1-amine, dimedone and various aldehydes solvent-free conditions at 90°C temperature for 25 min. **(Scheme 4.3.1).**

![Scheme 4.3.1](image)

**Scheme 4.3.1**

Dhruva Kumar et al [83], carried out the LiBr as catalyst for the synthesis of hexahydroacridine-1,8-diones under MW for 1–3 min. at solvent free condition to give 75–91% yield **(Scheme 4.3.2).**

![Scheme 4.3.2](image)

**Scheme 4.3.2**

Das et al [84], developed a new method for the synthesis of 1,8-dioxo-decahydroacridines in high yield employing Amberlyst-15 as a heterogeneous solid acid. The application of an inexpensive, easily available and reusable catalyst makes this method simple, clean, practical and economically viable. The method is an easy access to functionalized acridines. **(Scheme 4.3.3).**
Rashedian et al [85], reports silica-bonded N-propyl sulfamic acid (SBNPSA) as catalyst for the synthesis of 1,8-dioxo-decahydroacridines by the reaction of dimedone with aromatic aldehydes and aryl amines in ethanol under reflux conditions (Scheme 4.3.4).

Ziarani et al [86], reported a facile, efficient, and practical method for the preparation of 1,8-dioxo-decahydroacridines in excellent yield using silica-based sulfonic acid as a heterogeneous solid acid catalyst, which makes this reaction clean, safe and high-yielding process. The reaction was carried out under solvent free conditions at 120°C for 2 h by taking a 1:1.2:2 mol ratio mixture of an aromatic aldehyde, an amine and 5,5-dimethyl-1,3-cyclohexanedione to give the desired products (Scheme 4.3.5).
4.3.1.1 **Present Study:**

In connection with our studies on the preparation and applications of solid heterogeneous catalyst in organic transformations [87], we were interested in finding a simple and efficient method for the synthesis of acridine derivatives under mild conditions using carbon doped MoO$_3$ as a catalyst under ultrasonication method were shown in **Scheme 4.3.6**.

![Scheme 4.3.6](image)

4.3.2 **Experimental:**

4.3.2.1 **General procedure for preparation of 1,8 dioxodecahydroacridine and its derivatives:**

A mixture of dimedone (2 mmol), benzaldehyde (1 mmol), aniline (1 mmol) and catalyst (0.1 g) were taken in ethanol: water (3:1) 20 ml and the resulting mixture was taken in single neck round bottom flask and afterwards, the flask with the reaction mixture was immersed into the water bath of an ultrasonic cleaner where the mixture was exposed to high-intensity ultrasonic irradiation (600 W, 20 kHz) for the prescribed time.

The progress of the reaction was monitored on TLC using pet ether, and ethyl acetate as solvent system. After completion of the reaction, the reaction mixture was heated, the product dissolves in ethanol and the catalyst was separated easily from the reaction mixture by simple filtration. Finally the crude product obtained was
crystallized from ethanol to afford pure product. The derivatives were confirmed by comparisons with authentic sample, melting points, IR, and $^1\text{H}$ NMR.

4.3.2.2 Physical and spectroscopic data of derivatives (4 a–k):

$3,4,6,7$-tetrahydro-$3,3,6,6$-tetramethyl-$9,10$-diphenylacridine-$1,8(2\text{H},5\text{H},9\text{H},10\text{H})$-dione (a): $^1\text{H}$ NMR (300 MHz, CDCl$_3$): δ = 7.54–7.42 (m, 5H), 7.32–7.09 (m, 5H), 4.74 (s, 1H), 2.45 (d, 4H), 2.18 (d, 4H), 1.09 (s, 6H), 0.98 (s, 6H); FTIR (KBr) $\nu_{\text{max}}$/cm$^{-1}$: 2953, 1662, 1488, 1366, 1201, 955, 833, 740, 698;

$3,4,6,7$-tetrahydro-$3,3,6,6$-tetramethyl-$9$-(3-nitrophenyl)-10-phenylacridine-$1,8(2\text{H},5\text{H},9\text{H},10\text{H})$-dione (b): $^1\text{H}$ NMR (300 MHz, CDCl$_3$): δ = 8.38 (s, 1H), 7.48 (s, 1H), 7.33 (s, 2H), 6.72–6.59 (m, 5H), 4.72 (s, 1H), 2.44 (d, 4H), 2.20 (d, 4H), 1.08 (s, 6H), 0.99 (s, 6H); FTIR (KBr) $\nu_{\text{max}}$/cm$^{-1}$: 3292, 2953, 1589, 1367, 1261, 1201, 1145, 987, 817, 691, 574;

$9$-(4-chlorophenyl)-$3,4,6,7$-tetrahydro-$3,3,6,6$-tetramethyl-$10$-phenylacridine-$1,8(2\text{H},5\text{H},9\text{H},10\text{H})$-dione (c): $^1\text{H}$ NMR (300 MHz, CDCl$_3$): δ = 7.85 (s, 2H), 7.45 (s, 2H), 7.26–7.16 (m, 5H), 4.71 (s, 1H), 2.46 (d, 4H), 2.21 (d, 4H), 1.10 (s, 6H), 0.98 (s, 6H); FTIR (KBr) $\nu_{\text{max}}$/cm$^{-1}$: 3202, 2953, 1472, 1356, 1198, 1102, 997, 859, 711, 658, 699, 574;

$3,4,6,7$-tetrahydro-$3,3,6,6$-tetramethyl-$9$-(3-nitrophenyl)-10-phenylacridine-$1,8(2\text{H},5\text{H},9\text{H},10\text{H})$-dione (d): $^1\text{H}$ NMR (300 MHz, CDCl$_3$): δ = 7.47 (m, 1H), 7.37–7.25 (m, 3H), 7.13–7.08 (m, 5H), 4.87 (s, 1H), 2.45 (d, 4H), 2.33 (d, 4H), 1.11 (s, 6H), 0.94 (s, 6H); FTIR (KBr) $\nu_{\text{max}}$/cm$^{-1}$: 3397, 2953, 1726, 1610, 1472, 1378, 1240, 1134, 1071, 987, 859, 754, 648, 699, 574;

$3,4,6,7$-tetrahydro-$3,3,6,6$-tetramethyl-$10$-phenyl-$9$-p-tolylacridine-$1,8(2\text{H},5\text{H},9\text{H},10\text{H})$-dione (e): $^1\text{H}$ NMR (300 MHz, CDCl$_3$): δ = 7.85 (m, 1H), 7.16-7.00 (m, 4H), 4.71 (s, 1H), 2.46 (d, 4H), 2.24 (d, 4H), 1.25 (s, 3H), 1.09 (s, 6H), 0.99 (s, 6H); FTIR (KBr) $\nu_{\text{max}}$/cm$^{-1}$: 3321, 2963, 1716, 1610, 1472, 1378, 1240, 1134, 1071, 987, 859, 754, 648, 699, 574;

$9$-(2-chlorophenyl)-$3,4,6,7$-tetrahydro-$3,3,6,6$-tetramethyl-$10$-phenylacridine-$1,8(2\text{H},5\text{H},9\text{H},10\text{H})$-dione (f): $^1\text{H}$ NMR (300 MHz, CDCl$_3$): δ = 7.26–7.18 (m, 5H), 7.16–7.00 (m, 4H), 4.71 (s, 1H), 2.45 (d, 4H), 2.24 (d, 4H), 1.25 (s, 3H), 1.09 (s, 6H), 0.99 (s, 6H); FTIR (KBr) $\nu_{\text{max}}$/cm$^{-1}$: 3202, 2953, 1472, 1356, 1198, 1102, 997, 859, 711, 658, 699, 574;

$3,4,6,7$-tetrahydro-$3,3,6,6$-tetramethyl-$9$-(3-hydroxyphenyl)-10-p-tolylacridine-$1,8(2\text{H},5\text{H},9\text{H},10\text{H})$-dione (g): $^1\text{H}$ NMR (300 MHz, CDCl$_3$): δ

198
= 8.02 (m, 1H), 7.97 (m, 1H), 7.79 (m, 2H), 7.42-7.29 (m, 4H), 5.37 (s, 1H),
4.83 (s, 1H), 2.50 (d, 4H), 2.18 (d, 4H), 1.24 (s, 3H), 1.11 (s, 6H), 0.99 (s,
6H); FTIR (KBr) ν_max/cm⁻¹: 3312, 2963, 1663, 1526, 1463, 1356, 1198,
1134, 997, 817, 732, 691, 699, 574;

3,4,6,7-tetrahydro-9-(4-methoxyphenyl)-3,3,6,6-tetramethyl-10-
phenyl acridine-1,8(2H,5H,9H,10H)-dione (g): H NMR (300 MHz, CDCl₃):
δ = 7.30 (m, 2H), 7.18-7.23 (m, 2H), 7.16-7.07 (m, 5H), 4.75 (s, 1H), 2.46
(d, 4H), 2.21 (d, 4H), 1.54 (s, 3H), 1.10 (s, 6H), 0.99 (s, 6H); FTIR (KBr)
ν_max/cm⁻¹: 3309, 2956, 1662, 1595, 1452, 1361, 1199, 1141, 1003, 840,
742, 698, 572, 524;

3,4,6,7-tetrahydro-3,3,6,6-tetramethyl-9-(3-nitrophenyl)-10-p-
tolylacridine-1,8(2H,5H,9H,10H)-dione (h): H NMR (300 MHz, CDCl₃):
δ = 8.01 (s, 1H), 8.00 (s, 1H), 7.81 (s, 2H), 7.40-7.25 (m, 4H), 4.83 (s, 1H),
2.50 (d, 4H), 2.22 (d, 4H), 1.24 (s, 3H), 1.11 (s, 6H), 0.99 (s, 6H); FTIR
(KBr) ν_max/cm⁻¹: 3312, 2963, 1662, 1595, 1452, 1361, 1199, 1145, 997, 807,
699, 572, 524;

9-(4-chlorophenyl)-3,4,6,7-tetrahydro-3,3,6,6-tetramethyl-10-p-
tolylacridine-1,8(2H,5H,9H,10H)-dione (i): H NMR (300 MHz, CDCl₃):
δ = 7.85 (s, 2H), 7.45 (s, 2H), 7.26-7.15 (m, 4H), 4.71 (s, 1H), 2.46 (d, 4H),
2.21 (d, 4H), 1.25 (s, 3H), 1.10 (s, 6H), 0.99 (s, 6H); FTIR (KBr) ν_max/cm⁻¹
3312, 2953, 1663, 1472, 1356, 1198, 1092, 997, 849, 711, 606, 699,
521;

3,4,6,7-tetrahydro-3,3,6,6-tetramethyl-9,10-dip-tolylacridine-
1,8(2H,5H,9H,10H)-dione (j): H NMR (300 MHz, CDCl₃): δ = 7.18-7.00
(m, 8H), 4.71 (s, 1H), 2.45 (d, 4H), 2.24 (d, 4H), 1.25 (s, 6H), 1.09 (s, 6H),
0.99 (s, 6H); FTIR (KBr) ν_max/cm⁻¹: 3302, 2963, 1663, 1463, 1356, 1198,
1102, 997, 882, 700, 658, 699, 574;

9-(2-chlorophenyl)-3,4,6,7-tetrahydro-3,3,6,6-tetramethyl-10-p-
tolylacridine-1,8(2H,5H,9H,10H)-dione (k): H NMR (300 MHz, CDCl₃): δ
= 7.37 (m, 1H), 7.34-7.25 (m, 3H), 7.16-7.06 (m, 4H), 4.87 (s, 1H), 2.45 (d,
4H), 2.30 (d, 4H), 1.25 (s, 3H), 1.11 (s, 6H), 0.94 (s, 6H); FTIR (KBr)
ν_max/cm⁻¹: 3397, 2963, 1663, 1472, 1356, 1198, 1134, 1007, 839, 732,
617, 699, 574;
4.3.3 Results and discussion:

In order to get best experimental results, we have considered the model reaction of 1,8-dioxo-decahydroacridines in excellent yields using carbon doped MoO$_3$ with PEG-400 as a heterogeneous solid acid catalyst, which makes this reaction clean, safe and high-yielding process. The reaction was carried out under ultrasonication in EtOH: H$_2$O (3:1) by taking the mixture of dimedone (2 mmol), benzaldehyde (1 mmol) and aniline (2 mmol), to give the desired products.

The choice of solvent proved critical. The results showed that the examined solvents were not suitable separately. The reactions in C$_6$H$_6$, CH$_2$Cl$_2$, CH$_3$OH and CH$_3$CN gave low to moderate yield of products. When solvents such as EtOH and H$_2$O were used, it gave satisfactory results. The best ratio of EtOH:H$_2$O (v/v) was found to be 3:1 with 0.1 g of the CMP-3 catalyst proved to be the optimized reaction condition, affording highest yield of product shown in Table 4.3.1. While the other catalysts like CM-0, CMP-0, CMP-1 and CMP-2 shows less activity with same reaction condition. The CMP-3 shows highest catalytic activity i.e. 91% yield within short reaction time 10 minute shown in Table 4.3.2. It might be due to small particle size and high porosity with increase in amount of carbon addition supported by XRD, SEM, TEM and BET surface analysis.

The sonochemical techniques have been recently developed for the fast synthesis. It is expected that reaction in presence of sonochemical approach may gave high yield in short time by CMT-3 catalytic materials.
Table 4.3.1: Comparative study of 1,8 dioxo-decahydroacridine with different solvents, reaction was carried out in presence of CMP-3 under ultra-sonication

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Time (min)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C₆H₆</td>
<td>60</td>
<td>35</td>
</tr>
<tr>
<td>2</td>
<td>CH₂Cl₂</td>
<td>60</td>
<td>40</td>
</tr>
<tr>
<td>3</td>
<td>CH₃OH</td>
<td>60</td>
<td>56</td>
</tr>
<tr>
<td>4</td>
<td>CH₃CN</td>
<td>60</td>
<td>76</td>
</tr>
<tr>
<td>5</td>
<td>H₂O</td>
<td>60</td>
<td>72</td>
</tr>
<tr>
<td>6</td>
<td>EtOH</td>
<td>60</td>
<td>77</td>
</tr>
<tr>
<td>7</td>
<td>EtOH/H₂O (1:1)</td>
<td>30</td>
<td>79</td>
</tr>
<tr>
<td>8</td>
<td>EtOH/H₂O (3:1)</td>
<td>30</td>
<td>82</td>
</tr>
<tr>
<td>9</td>
<td>EtOH/H₂O (3:1) Ultra-sonication</td>
<td>10</td>
<td>91</td>
</tr>
</tbody>
</table>

b isolated yield

Table 4.3.2: Effect of various amount of catalyst

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Time (min)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No catalyst</td>
<td>300</td>
<td>51</td>
</tr>
<tr>
<td>2</td>
<td>only Ultra sonication</td>
<td>120</td>
<td>62</td>
</tr>
<tr>
<td>3</td>
<td>CM-0</td>
<td>30</td>
<td>65</td>
</tr>
<tr>
<td>4</td>
<td>CMP-1</td>
<td>30</td>
<td>84</td>
</tr>
<tr>
<td>5</td>
<td>CMP-2</td>
<td>20</td>
<td>85</td>
</tr>
<tr>
<td>6</td>
<td>CMP-3 Ultra-sonication</td>
<td>10</td>
<td>91</td>
</tr>
</tbody>
</table>

b isolated yield

The electron-withdrawing or electron-donating groups present in the aromatic ring of the aldehydes have the same effect on the products. Also both aniline and p-toluidine equally underwent the conversion well. The reaction mechanism is shown in Scheme 4.3.7. The structure of all derivatives is confirmed by IR, ¹H NMR and Mass data shown in Table 4.3.3.
### Table 4.3.3: Synthesis of 1,8 dioxo-decahydroacridine derivatives \(^a\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>(R_1)</th>
<th>(R_2)</th>
<th>Time (min.)</th>
<th>Yield (%)(^b)</th>
<th>M.P. (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>H</td>
<td>H</td>
<td>10</td>
<td>91</td>
<td>254-255</td>
</tr>
<tr>
<td>4b</td>
<td>3-NO(_2)</td>
<td>H</td>
<td>30</td>
<td>94</td>
<td>285-287</td>
</tr>
<tr>
<td>4c</td>
<td>4-Cl</td>
<td>H</td>
<td>20</td>
<td>74</td>
<td>271-272</td>
</tr>
<tr>
<td>4d</td>
<td>4-CH(_3)</td>
<td>H</td>
<td>30</td>
<td>87</td>
<td>290-292</td>
</tr>
<tr>
<td>4e</td>
<td>2-Cl</td>
<td>H</td>
<td>30</td>
<td>81</td>
<td>180-182</td>
</tr>
<tr>
<td>4f</td>
<td>3-OH</td>
<td>4-CH(_3)</td>
<td>25</td>
<td>82</td>
<td>281-283</td>
</tr>
<tr>
<td>4g</td>
<td>4-OCH(_3)</td>
<td>H</td>
<td>30</td>
<td>93</td>
<td>222-224</td>
</tr>
<tr>
<td>4h</td>
<td>3-NO(_2)</td>
<td>4-CH(_3)</td>
<td>30</td>
<td>77</td>
<td>150-151</td>
</tr>
<tr>
<td>4i</td>
<td>4-Cl</td>
<td>4-CH(_3)</td>
<td>25</td>
<td>74</td>
<td>220-221</td>
</tr>
<tr>
<td>4j</td>
<td>4-CH(_3)</td>
<td>4-CH(_3)</td>
<td>30</td>
<td>87</td>
<td>194-196</td>
</tr>
<tr>
<td>4k</td>
<td>2-Cl</td>
<td>4-CH(_3)</td>
<td>20</td>
<td>81</td>
<td>188-190</td>
</tr>
</tbody>
</table>

\(^a\) Reaction condition: dimedone (2 mmol), benzaldehyde (1 mmol) and aniline (1 mmol) in CMT-3 catalyst (0.1 g) under ultra-sonication in EtOH/H\(_2\)O (3:1, 20 ml).\(^b\): Isolated yields.

We examined the recycling performance of CMP-3. It was investigated using the same model reaction. After the separation of products, the catalyst was washed with \(n\)-hexane, dried at 80°C and reused for next run. The data listed in Table 4.3.4 which shows that the CMP-3 could be reused at least three times without significant loss in catalytic activity. The catalyst having easy recycling performance is also an attractive property for the environmental protection and economic reasons.

### Table 4.3.4: Reusability of CMP-3 under ultra-sonication in ethanol: water (3:1) solvent system for the synthesis of 1,8 dioxo-decahydroacridine \(^a\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cycle</td>
<td>Fresh</td>
<td>First</td>
<td>Second</td>
<td>Third</td>
</tr>
<tr>
<td>Yield (%)</td>
<td>91</td>
<td>90</td>
<td>90</td>
<td>89</td>
</tr>
</tbody>
</table>

\(^a\) Reaction condition: dimedone (2 mmol), benzaldehyde (1 mmol) and aniline (1 mmol) in CMT-3 catalyst (0.1 g) under ultra-sonication in EtOH/H\(_2\)O (3:1, 20 ml).\(^b\): Isolated yields.
Scheme 4.3.7: proposed mechanism for the synthesis of 1,8 dioxo-decahydroacridine
4.3.4 Conclusions:

The present study provides a new methodology for the preparation of 1,8 dioxo-decahydroacridine and its derivatives from dimedone, benzaldehyde and aniline in the presence of carbon-doped MoO$_3$ in EtOH:H$_2$O (3:1) solvent system under the ultrasonication method. The catalyst was recovered and reused without any noticeable loss of reactivity. The mild reaction conditions and simplicity of the procedure offers improvements over many existing methods. The advantages of this method are extremely short reaction time, high yield, simple experimental procedure and efficient.
$^1H$ NMR spectrum of 1,8 dioxo-decahydroacridine (4.3.2.2 a)

FTIR spectrum of 1,8 dioxo-decahydroacridine (4.3.2.2 a)
CHAPTER: 4

Section-IV

Synthesis of Quinoxaline derivatives catalyzed by Carbon doped MoO$_3$-TiO$_2$

Work reported in this section has been published in the Journal JOURNAL OF INDUSTRIAL AND ENGINEERING CHEMISTRY, (2012), 18, 277-282
4.4.1 Introduction:

Nanocrystalline supported molybdenum oxide catalysts are extremely important for industrial applications. These systems are active for various reactions, such as partial oxidation of hydrocarbons and alcohols [88, 89], hydrogenation of benzene [90] and cracking of hydrocarbons [91]. Usually the supports are alumina or silica, but considerable interest is now devoted to other supports such as TiO$_2$, Nb$_2$O$_5$ and ZrO$_2$ [92-94]. The supported MoO$_3$ has been applied to a wide range of applications such as their unique redox chemistry resulting from its high reduction potential [95]. The MoO$_3$ is known to be an important catalyst or a catalyst precursor in a number of industrially relevant reactions [96-98].

The ultrasonic irradiation gave an idea about the great potential of the method because of its simplicity and efficiency. The sonochemical organic synthesis as a green synthetic approach has an interesting feature compared with other traditional methods. It was natural that the non-aqueous process would be extended and performed by using ultrasonic waves. The application of sonochemistry allows good yields, high crystallinity of the products; it is more efficient and homogeneous. Sonochemistry affords an immense reduction of the reaction time, from days to minutes [71-73].

4.4.1.1 Literature review:

Among the various classes of nitrogen containing heterocyclic compounds, quinoxalines are important components of several pharmacologically active compounds associated with a wide spectrum of biological activities [99]. Although rarely described in nature, synthetic quinoxaline ring is a part of a number of antibiotics which is known to inhibit the growth of Gram-positive bacteria and also active against various transplantable tumors [100]. Moreover, they are well known for their application in dyes
efficient electroluminescent materials [102], organic semiconductors [103] and building blocks for the synthesis of anion receptors [104], cavitands [105], dehydroannulenes [106], and DNA cleaving agents [107].

It is worth noting that the methods that have been established for the preparation of quinoxaline derivatives are associated with one or more of the following drawbacks such as unsatisfactory yields, long reaction times and harsh reaction conditions. Thus, it seems highly desirable to find a more efficient and milder protocol for the synthesis of quinoxalines [108-112].

Islami et al [113], proposed the synthesis of quinoxalines by the condensation of benzil or benzoin and 1,2-diaminobenzene in acetic acid at reflux temperature for 2 h to give 85-92% yield of the products (Scheme 4.4.1).

![Scheme 4.4.1](image)

Kumar et al [114], have carried out the synthesis of quinoxaline derivatives catalyzed by Ni-nanoparticles by the condensation of glyoxal and 1,2-diamine at 25°C under N₂ atmosphere in acetonitrile to give 62-98% yield of the products within 10-50 min. (Scheme 4.4.2).

![Scheme 4.4.2](image)

Bhosale et al [115], have carried out the molecular iodine as the catalyst for one-pot synthesis of quinoxaline derivatives at room
temperature in DMSO to give 85-95% yields in 35-75 min. (Scheme 4.4.3).

**Scheme 4.4.3**

Heravi et al [116], have introduced the Zn\[L-proline] as the catalyst for a one-pot synthesis of quinoxaline derivatives at room temperature in acetic acid to afford 92-96% yields in 5-20 min. (Scheme 4.4.4).

**Scheme 4.4.4**

Srinivas et al [117], carried out the polyaniline-sulfate salt catalyst for the synthesis of quinoxaline derivatives at room temperature in 1,2-dichloro ethane to give 75-95% yields in 2 h (Scheme 4.4.5).

**Scheme 4.4.5**
4.4.1.2 Present work:

In this section we have reported the synthesis of quinoxaline derivatives from cyclocondensation reaction of benzils and 1,2-diamines in the presence of 3 wt% carbon-doped MoO$_3$–TiO$_2$ (CMT-3) as a catalyst in EtOH/H$_2$O (3:1) medium, at 40°C under ultrasonication (Scheme 4.4.6).

![Scheme 4.4.6](image)

4.4.2 Experimental:

4.4.2.1 General procedure for preparation of quinoxaline and its derivatives:

A mixture of 1,2-diamine (1.2 mmol), benzil (1 mmol), and catalytic amount of CMT (0.1 g) were taken in ethanol: water (3:1) 20 ml and the resulting mixture was taken in single neck round bottom flask and afterwards, the flask with the reaction mixture was immersed into the water bath of an ultrasonic cleaner where the mixture was exposed to high-intensity ultrasonic irradiation (600 W, 20 kHz) at 40°C for the prescribed time. The progress of the reaction was monitored on TLC using pet ether: ethyl acetate as solvent system. After completion of the reaction, the reaction mixture was heated, the product dissolves in ethanol and the catalyst was separated easily from the reaction mixture by simple filtration. Finally the crude product obtained was crystallized from ethanol to afford pure products. The products were confirmed by
comparisons with authentic samples, melting points, IR, Mass and $^1$H NMR.

### 4.4.2.2 Physical and spectroscopic data (3a–h):

2,3-Diphenylquinoxaline (a): $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 8.18 (m, 2H), 7.78 (m, 2H), 7.48 (m, 4H), 7.34 (m, 6H); FTIR (KBr) $\nu_{\text{max}}$/cm$^{-1}$: 3057, 1602, 1442, 1346, 1246, 852, 767, 698; Mass: m/z 284.09 (M+1).

6-Nitro-2,3-diphenylquinoxaline (b): $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 9.08 (s, 1H), 8.54 (d, 1H), 8.31 (d, 1H), 7.66 (m, 4H), 7.52 (m, 4H), 7.40 (m, 2H); FTIR (KBr) $\nu_{\text{max}}$/cm$^{-1}$: 3439, 3063, 1614, 1521, 1446, 1340, 1246, 850, 767, 698; Mass: m/z 328.05 (M-H).

6-Methyl-2,3-diphenylquinoxaline (c): $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 8.08 (d, 1H), 8.00 (s, 1H), 7.68 (d, 1H), 7.52 (m, 4H), 7.30 (m, 6H), 2.65 (s, 3H); FTIR (KBr) $\nu_{\text{max}}$/cm$^{-1}$: 3057, 2941, 1618, 1446, 1342, 1246, 817, 773, 702; Mass: m/z 296.53 (M-H).

6-Chloro-2,3-diphenylquinoxaline (d): $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 8.17 (s, 1H), 8.11 (d, 1H), 7.98 (d, 1H), 7.68 (m, 4H), 7.51 (m, 4H), 7.34 (m, 2H); FTIR (KBr) $\nu_{\text{max}}$/cm$^{-1}$: 3059, 2941, 1618, 1446, 1342, 1246, 817, 773, 702; Mass: m/z 316.08 (M-H).

2,3-Bis(4-methoxyphenyl)quinoxaline (e): $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 8.12 (m, 2H), 7.72 (m, 2H), 7.48 (d, 4H), 6.92 (d, 4H), 3.85 (s, 6H); FTIR (KBr) $\nu_{\text{max}}$/cm$^{-1}$: 2958, 1602, 1458, 1394, 1344, 1294, 1174, 835, 759, 698; Mass: m/z 341.09 (M-H).

2,3-Bis(4-methoxyphenyl)-6-nitroquinoxaline (f): $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 7.95 (d, 1H), 7.92 (s, 1H), 7.25 (d, 1H), 6.97 (d, 4H), 6.94 (m, 4H), 3.81 (s, 6H); FTIR (KBr) $\nu_{\text{max}}$/cm$^{-1}$: 3437, 3066, 2956, 1599, 1510, 1460, 1371, 1313, 1255, 1166, 833, 750, 698; Mass: m/z 394.03 (M-H).

2,3-Bis(4-methoxyphenyl)-6-methylquinoxaline (g): $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 8.00 (d, 1H), 7.93 (s, 1H), 7.49 (d, 1H), 7.35 (m, 4H), 6.96 (m, 4H), 3.95 (s, 6H), 2.65 (s, 3H); FTIR (KBr) $\nu_{\text{max}}$/cm$^{-1}$: 2953, 2848, 1597, 1425, 1373, 1311, 1259, 1159, 833, 750, 698; Mass: m/z 377.08 (M-H).

2,3-Bis(4-methoxyphenyl)-6-chloro quinoxaline (h): $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 7.96 (s, 1H), 7.93 (d, 1H), 7.48 (d, 1H), 6.97 (d, 4H), 6.86 (m, 4H), 3.82 (s, 6H); FTIR (KBr) $\nu_{\text{max}}$/cm$^{-1}$: 2955, 1599, 1464, 1313, 1257, 1163, 835, 750, 698; Mass: m/z 396.09 (M-H).
4.4.3 Results and discussion:

In order to get best experimental results, we have considered the model reaction of 1,2-diamine (1.2 mmol) and benzil (1 mmol) in different solvents as well as different catalyst amount. In this study, the effect of different solvent was investigated and given in Table 4.4.1. The choice of solvent proved critical. The results showed that the examined solvents were not suitable separately. Reactions in C₆H₆, CH₂Cl₂, CH₃OH and CH₃CN gave low to moderate yield of products. The satisfactory results were obtained when a mixture of EtOH and H₂O was used as solvent. The best ratio of EtOH:H₂O was found to be 3:1 with 0.1 g of series of catalyst i.e. CM-0, CMT-0, CMT-1, CMT-2 and CMT-3 proved to be the optimized reaction condition, affording maximum yield of product listed in Table 4.4.2.

The effect of the catalyst composition on the synthesis of quinoxalines, pure MoO₃ exhibits moderate catalytic activity. After optimizing the addition of carbon in the MoO₃-TiO₂, it was observed that CMT-3 catalytic material is sufficient to carry out the reaction smoothly under ultra-sonication in short time (4 minute) with excellent yields (91%). That might be due to small particle size and high porosity with increases in amount of carbon addition.
Table 4.4.1: Comparative study of quinoxalines with different catalyst, reaction was carried out in presence of CMT-3 ultra-sonication at 40°C and without ultra-sonication at RT. 

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Time (min.)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C₆H₆</td>
<td>90</td>
<td>35</td>
</tr>
<tr>
<td>2</td>
<td>CH₂Cl₂</td>
<td>120</td>
<td>40</td>
</tr>
<tr>
<td>3</td>
<td>CH₃OH</td>
<td>50</td>
<td>56</td>
</tr>
<tr>
<td>4</td>
<td>CH₃CN</td>
<td>20</td>
<td>76</td>
</tr>
<tr>
<td>5</td>
<td>H₂O</td>
<td>120</td>
<td>72</td>
</tr>
<tr>
<td>6</td>
<td>EtOH</td>
<td>120</td>
<td>77</td>
</tr>
<tr>
<td>7</td>
<td>EtOH/H₂O (1:1)</td>
<td>60</td>
<td>79</td>
</tr>
<tr>
<td>8</td>
<td>EtOH/H₂O (3:1)</td>
<td>15</td>
<td>82</td>
</tr>
<tr>
<td>9</td>
<td>EtOH/H₂O (3:1) Ultra-sonication</td>
<td>4</td>
<td>91</td>
</tr>
</tbody>
</table>

*Reaction condition: 1,2-diamine (1.2 mmol) with benzil (1 mmol) in catalyst (0.1 g) and in various solvents.; b: Isolated yields.

Table 4.4.2: Effect of various amount of catalyst 

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Time (min.)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No catalyst</td>
<td>15</td>
<td>51</td>
</tr>
<tr>
<td>2</td>
<td>CM-0</td>
<td>10</td>
<td>62</td>
</tr>
<tr>
<td>3</td>
<td>CMT-0</td>
<td>6</td>
<td>65</td>
</tr>
<tr>
<td>4</td>
<td>CMT-1</td>
<td>7</td>
<td>84</td>
</tr>
<tr>
<td>5</td>
<td>CMT-2</td>
<td>5</td>
<td>85</td>
</tr>
</tbody>
</table>

*Reaction condition: 1,2-diamine (1.2 mmol) with benzil (1 mmol) in catalyst (0.1 g) and EtOH/H₂O (3:1, 20 ml).; b: Isolated yields.

In order to strengthen the novelty of present method, we have compared our results with some reported procedures carried out in absence of ultra-sonication using some other catalysts such as (NH₄)₆Mo₇O₂₄.4H₂O, ZnCl₂, CoCl₂, I₂/DMSO, CuSO₄.5H₂O/CH₃COOH and ZnO-beta/EtOH. The results are summarized in Table 4.4.3. From this Table, it was observed that CMT-3 catalytic materials give the high yield within very short reaction time in comparison with earlier reported methods.

Table 4.4.3: Comparative study of quinoxalines with different catalysts; b Present methodology; c Conventional method; a isolated yield
<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Methodology</th>
<th>Solvent</th>
<th>Time (min)</th>
<th>Yielda (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(NH4)6Mo7O24.4H2O</td>
<td>[c]</td>
<td>-</td>
<td>15</td>
<td>95 [117]</td>
</tr>
<tr>
<td>2</td>
<td>ZnCl2</td>
<td>[c]</td>
<td>-</td>
<td>300</td>
<td>80 [117]</td>
</tr>
<tr>
<td>3</td>
<td>CoCl2</td>
<td>[c]</td>
<td>-</td>
<td>300</td>
<td>59 [117]</td>
</tr>
<tr>
<td>4</td>
<td>I2</td>
<td>[c]</td>
<td>DMSO</td>
<td>35</td>
<td>95 [118]</td>
</tr>
<tr>
<td>5</td>
<td>CuSO4.5H2O</td>
<td>[c]</td>
<td>CH3COOH</td>
<td>10</td>
<td>95 [118]</td>
</tr>
<tr>
<td>6</td>
<td>ZnO-beta</td>
<td>[c]</td>
<td>EtOH</td>
<td>8</td>
<td>98 [118]</td>
</tr>
<tr>
<td>7</td>
<td>CMT-3</td>
<td>[c]</td>
<td>EtOH:H2O (3:1)</td>
<td>15</td>
<td>82 [b]</td>
</tr>
<tr>
<td>8</td>
<td>CMT-3</td>
<td>Sonication</td>
<td>EtOH:H2O (3:1)</td>
<td>4</td>
<td>91 [b]</td>
</tr>
</tbody>
</table>

Therefore, the CMT-3 catalytic material in ethanol: water (3:1) solvent system was used for the preparation of different derivatives of quinoxalines with electron donating as well as withdrawing substituent gave the desired product in good to excellent yield reported in Table 4.4.4.

Table 4.4.4: Synthesis of quinoxaline derivatives catalyzed by CMT-3 under ultra-sonication in ethanol: water (3:1) solvent system. 

<table>
<thead>
<tr>
<th>Entry</th>
<th>R1</th>
<th>R2</th>
<th>Time (min)</th>
<th>Yieldb (%)</th>
<th>M.P. (°C)</th>
<th>M.P. (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>(Observed)</td>
<td>(Literature)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3a</td>
<td>H</td>
<td>H</td>
<td>4</td>
<td>91</td>
<td>129–131</td>
<td>126–127</td>
</tr>
<tr>
<td>3b</td>
<td>H</td>
<td>NO2</td>
<td>12</td>
<td>68</td>
<td>189–191</td>
<td>193–194</td>
</tr>
<tr>
<td>3c</td>
<td>H</td>
<td>CH3</td>
<td>12</td>
<td>74</td>
<td>116–118</td>
<td>116–117</td>
</tr>
<tr>
<td>3d</td>
<td>H</td>
<td>Cl</td>
<td>18</td>
<td>87</td>
<td>114–116</td>
<td>115–116</td>
</tr>
<tr>
<td>3e</td>
<td>OCH3</td>
<td>H</td>
<td>12</td>
<td>81</td>
<td>151–152</td>
<td>151–152</td>
</tr>
<tr>
<td>3f</td>
<td>OCH3</td>
<td>NO2</td>
<td>14</td>
<td>82</td>
<td>190–191</td>
<td>192–194</td>
</tr>
<tr>
<td>3g</td>
<td>OCH3</td>
<td>CH3</td>
<td>18</td>
<td>83</td>
<td>128–130</td>
<td>125–127</td>
</tr>
<tr>
<td>3h</td>
<td>OCH3</td>
<td>Cl</td>
<td>22</td>
<td>97</td>
<td>149–151</td>
<td>150–151</td>
</tr>
</tbody>
</table>

*aReaction condition: 1,2-diamine (1.2 mmol) with benzil (1 mmol) in catalyst (0.1 g) and EtOH/H2O (3:1, 20 ml).; b: Isolated yields.*
Table 4.4.5: Reusability of CMT-3 under ultra-sonication in ethanol: water (3:1) solvent system for the synthesis of quinoxaline.

<table>
<thead>
<tr>
<th>Entry</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cycle</td>
<td>Fresh</td>
<td>First</td>
<td>Second</td>
<td>Third</td>
</tr>
<tr>
<td>Yield (%)</td>
<td>91</td>
<td>90</td>
<td>90</td>
<td>89</td>
</tr>
</tbody>
</table>

*aReaction condition: 1,2-diamine (1.2 mmol) with benzil (1 mmol) in catalyst (0.1 g) and EtOH/H₂O (3:1, 20 ml); b: Isolated yields.*

We examined the recycling performance of CMT-3. It was investigated using the same model reaction. After the separation of products, the catalyst was washed with n-hexane, dried at 80°C and reused for next run. The data listed in Table 4.4.5 which shows that the CMT-3 could be reused at least three times without significant loss in catalytic activity. The catalyst having easy recycling performance is also an attractive property for the environmental protection and economic reasons.

4.4.4 Conclusions:

In the present investigations, we have introduced for the first time carbon substrate obtained from the *Acacia Arabica* wood plant as natural source and it was used for the preparation of carbon-doped MoO₃–TiO₂ nanocomposite material. This study also provides a new methodology for the preparation of quinoxaline and its derivatives from benzil and ortho-1,2-diamine in the presence of carbon-doped MoO₃–TiO₂ in EtOH:H₂O (3:1) solvent system at 40°C by using ultra-sonication method. The CMT-3 material shows highest catalytic activity for preparation of quinoxalines. The advantages of this method are extremely mild reaction conditions, short reaction time, high yield, simple experimental procedure and efficient, environmentally benign, green synthetic methodologies using ecofriendly conditions.
$^1$H NMR spectrum of 2,3-diphenylquinoxaline (4.4.2.2 a)

FT-IR spectrum of 2,3-diphenylquinoxaline (4.4.2.2 a)
Mass spectrum of 2,3 diphenyl quinoxaline (4.4.2.2 a)
References:

Section I:


Section II:


Section III:


Section IV:


