CHAPTER-5

Synthesis of 1,2,4,5-tetra substituted imidazole using secondary amine based ionic liquid and defective Keggin type heteropoly acid. A comparative study of the efficiency of the two catalysts

Introduction

The Chemistry of imidazole and its derivatives form an important topic in medicinal as well as in synthetic organic chemistry. The imidazole nucleus forms an important structure of some well-known components of human organism, i.e. the amino acid histidine, Vit-B<sub>12</sub>, a component of DNA base structure and purines, histamine and biotin (Figure 5.1). The well known microtubule stabilizing agents Eleutherobin and Sarcodictyin<sup>1</sup> are among the numerous other marine- and plant-derived natural products<sup>2</sup> which contain the imidazole ring. Highly substituted imidazoles and benzimidazoles are structural scaffolds which are the building blocks of many natural products having a wide spectrum of biological activities such as anti-inflamatory,<sup>3</sup> anti-allergic,<sup>4</sup> analgesic,<sup>5</sup> pesticides,<sup>6</sup> fungicides and herbicides,<sup>7</sup> sodium channel modulators,<sup>8</sup> plant growth regulators,<sup>9</sup> and glucagon receptor antagonism<sup>10</sup> and CB<sub>1</sub> cannabinoid receptor antagonists.<sup>11</sup> Lepidilines A and B, which contain the imidazole moiety, show micromolar cytotoxicity against several human cancer cell lines.<sup>12</sup> They are the key intermediate for the synthesis of Olmesartan medoxomil,<sup>13</sup> an angiotensin II receptor antagonist used for the treatment of high blood pressure. Other drug molecules which contain the tetrasubstituted imidazole scaffold are Omeprazole,<sup>14</sup> Losartan, Eprosartan, Pimobendan and Trifenagrel.<sup>15</sup> In recent years it is reported that the imidazole structural core are active in other advanced areas of research such as fluorescence labelling agents,<sup>16</sup> biological imaging<sup>17</sup> and chromophores for non-linear optic systems.<sup>18</sup> It is reported that many substituted imidazoles are also known inhibitors of P38 MAP kinase,<sup>19</sup> B-Raf kinase,<sup>20</sup> transforming growth factor β1 (TGF- β1) type
1 activin receptor-like kinase (ALK5),\textsuperscript{21} cyclooxygenase-2 (COX-2)\textsuperscript{22} and biosynthesis of interleukin-1 (IL-1)\textsuperscript{23} (one of the representative imidazole is shown in Figure 5.2). Besides these, they are found to be applicable in conjugated and functional polymers,\textsuperscript{24} in coordination complexes\textsuperscript{25} as important ligands in metalloenzymes\textsuperscript{26} and as precursors of stable carbene ligands.\textsuperscript{27} Recent development of green chemistry expands the role of imidazole, which is found to be an essential cationic part of most of ILs.

**Figure 5.1**

\begin{align*}
\text{Histamine} & \quad \text{Histidine} & \quad \text{Purine}
\end{align*}

**Figure 5.2**

This compound potently inhibited the mitogenactivated protein kinase p38 (p38 IC\textsubscript{50} = 0.218\textmu M) as well as the release of the proinflammatory cytokines interleukin -1\beta (IL-1\beta) and tumor necrosis factor α (TNF α) from human whole blood after stimulation with LPS.

The versatility of imidazole derivatives mentioned above has encouraged the synthetic organic chemists to develop several synthetic routes to the highly substituted imidazoles. There are many synthetic route to tetrasubstituted imidazoles and among them the one pot multicomponent condensation strategy attains greater
value as it obey the ‘economy of steps’ due to which the target molecules are often obtained in a single step rather than the multiple step process which consequently minimizes the tedious work-up procedures and the release of environmentally hazardous wastes. In 1858, Debus reported the reaction between glyoxal and ammonia, which is acknowledged as the pioneering method for the synthesis of imidazoles and even today, research in imidazole chemistry continues unabated. Some of the important methods are reviewed herein.

A novel synthetic approach to 2-substituted imidazole was done by D. J. Hlasta via imidazolium ylides. Diisopropylethyl amine is the base used for the reaction. It was observed that in the absence of the base, the yield of the desired product was found to be low and the method synthetically less important. The reaction is shown in Scheme 5.1.

**Scheme 5.1**

Tetrasubstituted imidazoles have been synthesized using different substrates and different procedure which includes N-alkylation of trisubstituted imidazoles, cyclization of sulphonamides with mesoionic 1,3-oxazolium-5-olates, condensation of β-carbonyl-N acyl-N-alkylamines with ammonium acetate in HOAc under reflux condition, conversion of N-(2-oxo)amides with ammonium trifluoroacetate under neutral conditions and others. Another important route is reported by B. Hu et al. for the synthesis of tetrasubstituted imidazole from 2-azido
The aza-Wittig reactions of iminophosphoranes have received increased attention considering their efficiency in the synthesis of nitrogen heterocyclic compounds.\textsuperscript{35} Y-B. Nie \textit{et al.} had arrived at the target product by a sequential Aza-Wittig/Michael/Isomerisation reaction.\textsuperscript{36} At first, carbodiimides was obtained from aza-Wittig reactions of iminophosphorane with arylisocyanates, then these carbodiimides reacted with secondary amines in presence of a catalytic amount of sodium alkoxide to give $1,2,4,5$-tetrasubstituted imidazoles in good yields.

### 5.1.1. Synthesis by four component condensation

Recent development in the synthesis of tetrasubstituted imidazoles inspired the scientist to perform the reaction by a one pot multicomponent condensation of substrates namely 1,2 dicarbonyl compounds, aldehydes, amines and a source of ammonia. The reactions were carried out under the influence of several catalysts. S. Narayana Murthy \textit{et al.} used DABCO (1,4-diazabicyclo[2.2.2]octane) as the basic catalyst to get the target molecules from benzil, benzaldehyde derivatives, primary amine and ammonium acetate.\textsuperscript{37} They have carried out the reactions in different solvent such as methanol, ethanol, iso-propanol and tert-butanol and found that tert-butanol is the most appropriate solvent in terms of high yield and lower reaction time. The other catalysts which are used in the four component condensation are
silica bonded propylpiperazine N-sulfamic acid, \(^{38}\) BF\(_3\).SiO\(_2\), \(^{39}\) HClO\(_4\)-SiO\(_2\), \(^{40}\) InCl\(_3\)-3H\(_2\)O, \(^{41}\) L-proline \(^{42}\) besides others. All the above mentioned reactions are carried out under mild conditions and recovered yields were comparatively high. Further, the use of inexpensive ecofriendly catalyst and reusability of some of the catalyst makes these methods attractive. In all the reactions ammonium acetate was used as a source of ammonia. These reactions are summarized in Scheme 5.3.

**Scheme 5.3**

In similar way, molecular iodine, a cheap and nontoxic catalyst also found to be efficient in the synthesis of 1,2,4,5-tetrasubstituted imidazole from benzoin, aromatic aldehyde, amine and ammonium acetate. \(^{43}\) The reaction is shown in Scheme 5.4.

**Scheme 5.4**
Recently, a new investigation for catalytic activity of different fluoroboric acids was carried out by D. Kumar et al. for the synthesis of trisubstituted and tetrasubstituted imidazoles from 1,2-diketone, aldehyde and ammonium salt and 1,2-diketone, aldehyde, amine and ammonium acetate respectively. They have carried out extensive analysis of the reaction using aqueous HBF$_4$, solid supported HBF$_4$, metal tetrafluoroborates (inorganic salt), solid supported metal tetrafluoroborates, and tetrafluoroborate based ILs as catalyst and concluded that HBF$_4$-SiO$_2$ is most effective catalyst followed by LiBF$_4$ and Zn(BF$_4$)$_2$ in comparison to the others. Analysis for best nitrogen source was also examined by considering different ammonium salts and results showed that ammonium acetate was found to be the best and most suitable.

5.1.2. Microwave assisted synthesis of highly substituted imidazoles

It is well established that microwaves (MW) enhance reaction rates and hence reduce the reaction time, increase selectivities and also the yields. Following the observation of these advantages found by the use of MW technique, this technique was used in a few reported publications for the synthesis of tetrasubstituted imidazoles. S. Balalaie et al. successfully applied zeolite HY and silica gel as the catalyst for the synthesis under MW irradiation with high yield. A comparative study showed that yields with zeolite HY were lower than silica gel because acidic sites on the surface of zeolite HY were weaker than that of silica gel and hence excess zeolite HY was found to be necessary. One of the most interesting applications of MW in the synthesis of highly substituted imidazole was reported by S. E. Wolkenberg and co-workers. They used this method for the preparation of imidazolium alkaloid lepidiline B and the platelet aggregation inhibitor trifenagrel along with the synthesis of other related 2,4,5-trisubstituted imidazole. These reactions are summerized in Scheme 5.5 and 5.6.
Different solid supports such as acidic, basic, neutral alumina, bentonite, montmorillonite K10, montmorillonite KSF, silica gel and florisil was tested by A. Ya et al. for the MW assisted synthesis of highly substituted imidazoles and found acidic alumina to be most efficient in comparison to the others.\textsuperscript{47}

### 5.1.3. Synthesis using ionic liquids and heteropoly acids as catalyst

Recently the concept of ILs received a great deal of attention in view of the fact that almost all the ILs are environmental favourable compound and most of the ILs are effective in all respects. The application of IL also examined in the synthesis of highly substituted imidazoles. S. A. Siddiqui et al. applied imidazolium based ILs
in the synthesis of trisubstituted imidazoles. The other ILs which are used in the synthesis of tetrasubstituted imidazoles are N-methyl-2-pyrrolidinium hydrogen sulphate, 1-Butyl-3-methylimidazolium bromide and a Bronsted acidic IL. In addition to the ILs, the HPAs have also emerged as versatile catalysts for performing a variety of organic synthesis starting from condensation reactions to oxidation and reduction reactions. The application of the HPAs as a catalyst for the synthesis of heterocyclic compounds is particularly important. The use of HPAs in organic synthesis have been reviewed by Kozhevakinov. In particular the tetrasubstituted imidazoles have been synthesized in a one pot procedure by Heravi et al using the Preyssler type HPA (H_{14}[NaP_5W_{30}O_{110}]).

5.2. Materials and methods

From the review mentioned above it can be concluded that although a variety of catalysts have been used for the synthesis of tetrasubstituted imidazoles, giving good to excellent yields of the desired products, the nature of the catalysts used and the experimental procedures involved are neither cost effective nor benign to the environment. Additional drawbacks associated with these procedures are the laborious and complex work-up and purification procedures involved, which results in generation of a significant amounts of waste materials. Low selectivity, occurrence of side reactions, and the necessity of strong acidic conditions leaves a lot to be desired. Moreover high temperature and long reaction time make the procedures unacceptable from the point of view of energy economy which is an important tenet of green chemistry. The use of volatile organic solvents in some of the synthetic methods makes the procedures cumbersome and hazardous.

It may be mentioned that the ILs are a group of non volatile solvents that can be used as an alternative to the usual volatile organic compounds (solvents) in order to reduce hazards due to exposure. The aim of this work is to examine whether the simple acidic ILs could be used as catalyst for the synthesis of important heterocycles such as the tetra substituted imidazoles. With this aim in view the
classical and cheap IL namely di-\textit{n}-propylammonium hydrogensulphate was prepared from easily available starting material and used for the synthesis of the target molecule. Experiments have also been carried out to synthesize the target tetrasubstituted imidazole using a particular HPA namely the defective Keggin type HPA, \( \text{H}_6\text{PAI}_{11}\text{Mo}_{40} \) which was prepared by a novel green procedure from easily available starting materials. The time required for the preparation of this HPA under conventional heating (80°C) is 6 hours whereas, under MW irradiation it takes only 10 minutes. A comparison of the efficiency of the IL and the HPA on the synthesis was examined. The synthesis using both the IL as well as the HPA as the catalyst was promoted by MW.

Di-\textit{n}-propylammonium hydrogensulphate, a quaternary ammonium IL was prepared by simple addition of conc. sulphuric acid in di-\textit{n}-propylamine. The detail of preparation procedure is described in Chapter 2. Using this IL as catalyst the target tetrasubstituted imidazoles were prepared from 1,2-diketone, aldehydes, alkyl or arylamines and ammonium acetate or urea under the influence of MW. A major improvement over other established procedures was the observation that urea could be used as an alternative to ammonium acetate as a source of ammonia. In earlier reports on the synthesis of 1,2,4,5-tetrasubstituted imidazoles, the use of urea as a nitrogen source have not be explored. This study conclusively indicates that urea can indeed be used as an alternative nitrogen source thus reducing the overall cost of the conversion. In a typical procedure, a mixture of the 1,2 diketone, the aldehyde, the alkyl/aryl amine, urea/ammonium acetate and the di-\textit{n}-propylammonium hydrogen sulphate IL was exposed to MW irradiation for short time to arrive at the target 1,2,4,5-tetrasubstituted imidazoles in almost pure form. Side products have been found to be absent. The reaction is completed within 2-5 minutes and the recovered yields are good to high. Isolation of the pure products involved only recrystallization of the recovered crude in ethanol. The usual tedious work up procedure and other chromatographic purification procedures were found unnecessary. It has also been observed that the IL could be recovered and reused for further reaction without appreciable depletion in activity. When the reaction mixture was extracted with DCM the IL remained in the reaction vessel being insoluble in DCM. The same IL
could be reused for another run of the reaction with comparable efficiency. Another important feature of the use of the di-\textit{n}-propylammonium hydrogensulphate is the observation that both the aromatic amines as well as the aliphatic amines gave good yields of the product. The synthesis was studied using NaHSO$_4$ instead of the di-\textit{n}-propylammonium hydrogensulphate. It was observed that NaHSO$_4$ did catalyze the reaction but the observed yield was not more than 40%. The reaction was also studied in the presence of a phase transfer catalyst, tetrapropylammonium bromide, instead of the IL used it was observed that the reaction did not proceed at all. The details of the study carried out are given in the experimental section of this chapter.

In an additional study, the defective Keggin type HPA was prepared and used for the synthesis of the tetra substituted imidazole. A comparison of the reaction time and the yield obtained, with both the IL as well as the HPA under consideration were examined and the results indicate that both the di-\textit{n}-propylammonium hydrogensulphate and the defective Keggin type HPA are efficient catalysts for this conversion.

Single crystal X-ray analysis of one of the new product namely 1-ethyl-2-(2', 6'-dichlorophenyl)-4, 5-di(4'-methylphenyl)-imidazole (1p) confirms the structure (Figure 5.3). Crystals were obtained from ethanol in which case the results indicate the presence of residual solvent in the crystal. Attempt to remove the solvent destroyed crystallinity of the product and no worthwhile data could be obtained. All products obtained were characterized by spectroscopic method such as IR, $^1$H-NMR, $^{13}$C NMR, Mass spectrometry and by comparing their melting points with those reported in literature. $^1$H and $^{13}$C NMR spectra of two compounds are shown in Figure 5.(4-7). The experimental results are summerized in Table 5.1 and the reaction carried out is shown in Scheme 5.7. The crystallographic parameters are summarized in Table 5.2.
Scheme 5.7

![Scheme 5.7](image)

(Yield= IL/83-92%, HPA/85-93%)  \( \text{I(a-s)} \)

\( R = \text{Phenyl, p-tolyl} \)

\( R_1 = \text{C}_6\text{H}_5^-, \text{C}_6\text{H}_5\text{CH}_2^-, 4-\text{NO}_2\text{C}_6\text{H}_4^-, \text{C}_3\text{H}_5^-, \text{CH}_3^- \)

\( \text{IL= [n-Pr}_2\text{NH}_2][\text{HSO}_4] \)

Table 5.1: Solvent free MW induced one pot synthesis of 1, 2, 4, 5-tetrasubstituted imidazole promoted by [n-Pr\(_2\)NH\(_2\)][HSO\(_4\)] and defective keggin HPA using ammonium acetate as nitrogen source.

<table>
<thead>
<tr>
<th>Product</th>
<th>R</th>
<th>Ar</th>
<th>( R_1 )</th>
<th>Reaction with IL</th>
<th>Reaction with HPA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Time (min)</td>
<td>Yield (%)(^{a})</td>
</tr>
<tr>
<td>Ia</td>
<td>Ph</td>
<td>C(_6)H(_5)</td>
<td>C(_6)H(_5)CH(_2)</td>
<td>2</td>
<td>85</td>
</tr>
<tr>
<td>Ib</td>
<td>Ph</td>
<td>4-CH(_3)C(_6)H(_4)</td>
<td>C(_6)H(_5)CH(_2)</td>
<td>2</td>
<td>87</td>
</tr>
<tr>
<td>Ic</td>
<td>Ph</td>
<td>2-CH(_3)OC(_6)H(_4)</td>
<td>C(_6)H(_5)CH(_2)</td>
<td>2</td>
<td>87</td>
</tr>
<tr>
<td>Id</td>
<td>Ph</td>
<td>3,4-(OCH(_3))(_2)C(_6)H(_3)</td>
<td>C(_6)H(_5)CH(_2)</td>
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<td>Ie</td>
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<td>4-ClC(_6)H(_4)</td>
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<tr>
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<td>C(_6)H(_5)CH(_2)</td>
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<tr>
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<td>Ph</td>
<td>3-BrC(_6)H(_4)</td>
<td>C(_6)H(_5)CH(_2)</td>
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<td>85</td>
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<tr>
<td>Ih</td>
<td>Ph</td>
<td>4-NO(_2)C(_6)H(_4)</td>
<td>C(_6)H(_5)CH(_2)</td>
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<tr>
<td>If(^b)</td>
<td>Ph</td>
<td>2,5-(CH(_3))(_2)C(_6)H(_4)</td>
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<td>Ph</td>
<td>C(_6)H(_5)</td>
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<tr>
<td>-------</td>
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<td>-----------------</td>
<td>------------------</td>
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<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Time(min)</td>
<td>Yield(%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Time(min)</td>
<td>Yield(%)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>1</td>
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<td>87</td>
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<tr>
<td>8</td>
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<td>3</td>
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<td>10</td>
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<td>3</td>
<td>85</td>
<td>13</td>
<td>86</td>
</tr>
</tbody>
</table>

<sup>a</sup>Yields refers to the pure isolated products; <sup>b</sup>New compound.

**Table 5.2**: Solvent free MW assisted one pot synthesis of 1, 2, 4, 5-tetrasubstituted imidazole promoted by [n-Pr<sub>2</sub>NH<sub>2</sub>][HSO<sub>4</sub>] and HPA using urea as nitrogen source
Table 5.3: Effect of catalyst on the solvent free one pot four component synthesis of tetra substituted imidazole 1c with the usual reactants and urea

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst(^b)</th>
<th>Time(min)</th>
<th>Yield(%)(^a)</th>
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<tr>
<td>1</td>
<td>HPA</td>
<td>10</td>
<td>95</td>
</tr>
<tr>
<td>2</td>
<td>[n-Pr(_2)NH(_2)][HSO(_4)]</td>
<td>2</td>
<td>87</td>
</tr>
<tr>
<td>3</td>
<td>NaHSO(_4)</td>
<td>10</td>
<td>40</td>
</tr>
<tr>
<td>4</td>
<td>n-Pr(_4)NBr</td>
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<tr>
<td>5</td>
<td>Catalyst free</td>
<td>10</td>
<td>-</td>
</tr>
</tbody>
</table>

\(^a\)Yields refers to the pure isolated product; \(^b\) 10 mol% amount of catalysts were used.

Figure 5.3: ORTEP diagram of 1p
### Table 5.4

Crystallographic parameter of compound 1p

<table>
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<th>Property</th>
<th>Value</th>
</tr>
</thead>
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<td>empirical formula</td>
<td>C_{25}H_{22}Cl_{2}N_{2}. C_{2}H_{5}OH</td>
</tr>
<tr>
<td>formula weight</td>
<td>467.43</td>
</tr>
<tr>
<td>crystal system</td>
<td>Monoclinic</td>
</tr>
<tr>
<td>space group</td>
<td>P 2(1)/n</td>
</tr>
<tr>
<td>T(K)</td>
<td>298</td>
</tr>
<tr>
<td>a/lÅ</td>
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</tr>
<tr>
<td>b/lÅ</td>
<td>15.5380(12)</td>
</tr>
<tr>
<td>c/lÅ</td>
<td>13.9410(12)</td>
</tr>
<tr>
<td>α/deg</td>
<td>90.00</td>
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<tr>
<td>β/deg</td>
<td>95.289(5)</td>
</tr>
<tr>
<td>γ/deg</td>
<td>90.00</td>
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<tr>
<td>V / Å³</td>
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<tr>
<td>D\text{calc} (g cm(^{-3}))</td>
<td>1.223</td>
</tr>
<tr>
<td>μ (mm(^{-1}))</td>
<td>0.271</td>
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<td>unique reflns</td>
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<td>wR2(all)</td>
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<td>goodness-of-fit</td>
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<td>Diffractometer</td>
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</tbody>
</table>

144
Figure 5.4

$^1$H NMR Spectrum of 1-Benzyl-2-(3', 4'-dimethoxyphenyl)-4,5-diphenylimidazole

Figure 5.5

$^{13}$C NMR NMR Spectrum of 1-Benzyl-2-(3', 4'-dimethoxyphenyl)-4, 5-diphenylimidazole
Figure 5.6

$^1$H NMR Spectrum of 1-Ethyl-2-(2’-methoxyphenyl)-4, 5-diphenylimidazole

Figure 5.7

$^{13}$C NMR NMR Spectrum of 1-Ethyl-2-(2’-methoxyphenyl)-4, 5-diphenylimidazole
5.3. Conclusion

In conclusion, a one pot solvent free multicomponent reaction (MCR) promoted by the synergic use of MW and simple IL on one hand and MW and the HPA on the other, for the synthesis of the tetrasubstituted imidazole have been carried out under simplified reaction conditions. The reaction conditions are simple and product recovery easy. The study also indicated that the both the catalysts used herein is much more efficient than those used earlier. The added advantage of both the procedures is the reusability of the catalysts for further use.

5.4. Experimental section

Melting points were recorded in a VMP-D model Melting point apparatus and are uncorrected. $^1$H-NMR and $^{13}$C-NMR spectra were recorded in a Bruker Advance digital 300 MHz spectrometer in CDCl$_3$. In both the recordings TMS was used as the internal standard. IR spectra was recorded in a Perkin Elmer 1600 FT IR spectrometer using KBr pallets. Mass spectra were recorded in a Waters Micromass ZQ™ 400 mass spectrometer. Microwave irradiation was done in a MW reactor procured from Catalyst™ System. All reagents were purified by standard literature procedure.

5.4.1. Preparation of di-$n$-propylammonium hydrogensulphate

The preparation and characterization is given in Chapter 2.

5.4.2. Preparation of defective Keggin heteropoly acid $\text{H}_6\text{PAI}_{11}\text{O}_{40}$

A stoichiometric mixture of $\text{H}_3\text{PO}_4$ 85% (0.58 g., 0.01 mol), $\text{Al}_2\text{O}_3.6\text{H}_2\text{O}$ (1.21 g., 0.005 mol) and $\text{MoO}_3$ (14.4 g.,11 mol) was suspended in 150 mL of distilled water in RBF and irradiated with MW for 10 minutes (560W). On cooling
the mixture to room temperature the unreacted MoO₃ precipitated and recovered by filtration. Reduced pressure removal of water and drying at 85°C for 24 hours gave dark green crystals of composition H₆PAlMo₁₁O₄₀ identical to that obtained earlier. The metal composition was established by powder X-ray diffraction studies. IR cm⁻¹ 1074, 98.2, 875, 765, 362 and 345.

5.4.3. General procedure for the synthesis of tetrasubstituted imidazole with di-\textit{n}-propylammonium hydrogen sulphate

A mixture of 1, 2 diketone (1 mmol), aldehydes (1 mmol), primary amines (1 mmol), ammonium acetate (or urea) (1.5 mmol) and di-\textit{n}-propylammonium hydrogensulphate (10 mol%) was irradiated with MW (560 W) with stirring for 1-3 minute as mentioned in Table 4.1 and Table 4.2. On completion of the reaction monitored by TLC using 20% ethyl acetate in petroleum ether (60-80°C), the reaction mixture was extracted with DCM (5 mL x 3), washed with water, dried with anhydrous Na₂SO₄ and solvent removed under reduced pressure. The crude products were purified by recrystallization from ethanol.

5.4.4. General procedure for the synthesis of tetrasubstituted imidazole using defective Keggin heteropoly acid H₆PAlMo₁₁O₄₀

A mixture of 1,2-diketone (1 mmol), aldehydes (1 mmol), primary amines (1 mmol), ammonium acetate (or urea) (1.5 mmol) and HPA (5 mol%) was irradiated with MW (560 W) with stirring for 10-13 min. as mentioned in Table 5.1 and Table 5.2. On completion of the reaction determined by TLC, the reaction mixture was extracted with DCM (5 mL x 3), washed with water, dried with anhydrous Na₂SO₄. The combined extract was evaporated under reduced pressure to obtain the crude product which was purified by recrystallization from ethanol. The results are summarized in the Table 5.1 and Table 5.2.
5.4.5. Synthesis of compounds 1(k-p)

The synthesis was carried out as per the general procedure with 0.5 mL of aliphatic amines (methyl amine and ethyl amine).
5.4.6. Spectral data of reported compounds

1-Benzyl-2,4,5-triphenylimidazole (1a)

Mp: 159-161°C (EtOH).

IR (KBr): υ 2890 (CH), 1590 (CN), 1480 cm⁻¹.

¹H NMR (300MHz, CDCl₃): δppm 7.58-6.82 (m, 20H, Ar), 5.12 (s, 2H, CH₂).

¹³C NMR (75MHz, CDCl₃): δ ppm 148.08, 138.07, 137.56, 134.46, 131.08, 131.02, 130.94, 130.05, 129.08, 128.92, 128.81, 128.61, 128.59, 128.09, 127.36, 126.78, 126.37, 126.02, 48.28.

1-Benzyl-2-(4’-methylphenyl)-4,5-diphenylimidazole (1b)

Mp: 164-166 °C (EtOH).

IR (KBr): υ 2885 (CH), 1580 (CN), 1482 cm⁻¹.

¹H NMR (300MHz, CDCl₃): δppm 7.58-6.81 (m, 19H, Ar), 5.11 (s, 2H, CH₂), 2.38 (s, 3H, CH₃).

¹³C NMR (75MHz, CDCl₃): δ ppm 148.21, 138.84, 137.67, 134.52, 131.07, 129.28, 128.94, 128.75, 128.55, 128.06, 126.78, 125.99, 48.24, 21.36.

1-Benzyl-2-(2’-methoxyphenyl)-4,5-diphenylimidazole (1c)

Mp: 188-190°C (EtOH).

IR(KBr): ν 2823 (CH), 1593 (CN), 1460 (CC), 1250 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δppm 7.59-6.82 (m, 19H,
Ar), 5.09 (s, 2H, CH₂), 3.83 (s, 3H, OCH₃).

¹³C NMR (75 MHz, CDCl₃): δ ppm 160.04, 147.94, 137.61, 131.02, 130.37, 128.72, 128.53, 128.02, 127.27, 126.72, 126.25, 125.92, 123.29, 113.95, 55.27, 48.16.

HRMS (ESI): m/z= 416.1889 ([M⁺]).

1-Benzyl-2-(3',4'-dimethoxyphenyl)-4,5-diphenylimidazole (1d)

Mp: 163-165 °C (EtOH).

IR (KBr): ν 2835 (CH), 1600 (CN) cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δH ppm 7.64-6.89 (m, 18H, Ar), 5.10 (s, 2H, CH₂), 3.89 (s, 3H, OCH₃), 3.69 (s, 3H, OCH₃).

¹³C NMR (75 MHz, CDCl₃): δ ppm 149.63, 148.80, 137.99, 134.52, 131.10, 128.89, 128.75, 128.16, 127.42, 126.90, 126.42, 125.96, 121.65, 112.24, 110.99, 55.96, 55.69, 48.28.

1-Benzyl-2-(4'-chlorophenyl)-4,5-diphenylimidazole (1e)

Mp: 163-165 °C (EtOH).

IR (KBr): ν 2832 (CH), 1598 (CN) cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δH ppm 8.00-6.82 (m, 19H, Ar), 5.09 (s, 2H, CH₂).

¹³C NMR (75 MHz, CDCl₃): δ ppm 146.92, 137.37, 135.06, 131.08, 130.31, 129.98, 129.11, 128.92, 128.79, 128.20, 126.85, 125.92, 48.34.
1-Benzyl-2-(4'-ethylphenyl)-4,5-diphenylimidazole (1f)

Mp: 138-140 °C (EtOH).

IR (KBr): ν 2958 (CH), 1597 (CN), 1492 (CC), 1446, 1388 cm⁻¹

¹H NMR (300 MHz, CDCl₃): δ_H ppm 7.59-6.83 (m, 19H, Ar), 5.11 (s, 2H, CH₂), 2.67 (q, 2H, J = 6 Hz, CH₂), 1.24 (t, 3H, J = 6 Hz, CH₃).

¹³C NMR (75 MHz, CDCl₃): δ ppm 148.20, 145.13, 137.88, 137.63, 131.04, 128.97, 128.70, 128.51, 128.08, 128.02, 126.73, 126.26, 125.98, 48.22, 28.66, 15.41.

HRMS (ESI): m/z = 414.2098 ([M]+).

1-Benzyl-2-(3'-bromophenyl)-4,5-diphenylimidazole (1g)

Mp: 148-150 °C (EtOH).

IR (KBr): ν 2949 (CH), 1601(CN) cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ_H ppm 7.66-6.82 (m, 19H, Ar), 5.11 (s, 2H, CH₂).

¹³C NMR (75 MHz, CDCl₃): δ ppm 132.17, 131.86, 130.99, 130.00, 129.04, 128.86, 128.77, 128.69, 128.57, 128.11, 127.51, 127.22, 126.75, 126.51, 125.98, 125.90, 48.31.

1-Benzyl-2-(4'-nitrophenyl)-4,5-diphenylimidazole (1h)

Mp: 170-172 °C (EtOH).

IR (KBr): ν 2963 (CH), 1608 (CN) cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ_H ppm 8.12-6.73 (m, 19H, Ar), 4.88 (s, 2H, CH₂).
$^{13}$C NMR (CDCl$_3$): $\delta$ ppm 148.92, 143.00, 136.57, 133.23, 131.10, 128.93, 128.79, 128.38, 128.05, 126.64, 126.48, 126.41, 124.65, 48.27.

2-(2', 5'-Dimethylphenyl)-1,4,5-triphenylimidazole (1i)

Mp: 173-175 °C (EtOH).

IR (KBr): $\nu$ 2942 (CH), 1598 (CN), 1492 (CC) cm$^{-1}$.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta_H$ ppm 7.61-6.87 (m, 18H, ArH), 2.23 (s, 3H, CH$_3$), 2.10 (s, 3H, CH$_3$).

$^{13}$C NMR (75MHz, CDCl$_3$): $\delta$ ppm 147.59, 137.64, 136.50, 134.74, 134.64, 134.51, 131.79, 130.94, 130.78, 130.40, 129.83, 129.73, 129.07, 128.46, 128.37, 128.05, 127.78, 127.71, 127.49, 127.41, 126.44, 20.73, 19.67.

HRMS (ESI): m/z = 400.1939 ([M]$^+$).

1-methyl-2-(4'-chlorophenyl)-4,5-diphenylimidazole (1k)

Mp: 192-194 °C (EtOH).

IR(KBr): $\nu$ 2925 (CH), 1604 (CN), 1483 (CC), 735 (CCl) cm$^{-1}$

$^1$H NMR (300 MHz, CDCl$_3$): $\delta_H$ ppm 7.71-7.18 (m, 14H, ArH), 3.50 (s, 3H, NCH$_3$).

$^{13}$C NMR (75MHz, CDCl$_3$): $\delta$ ppm 146.79, 137.98, 134.90, 134.44, 130.97, 130.89, 130.84, 130.32, 129.38, 129.15, 129.05, 128.92, 128.77, 128.20, 127.01, 126.54, 33.29.

1-methyl-2-(4'-ethylphenyl)-4, 5-diphenylimidazole (II)

Mp: 127-130 °C (EtOH).

IR (KBr): ν 2920 (CH), 1597 (CN), 1480 (CC) cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δH ppm 7.67-7.19 (m, 14H, ArH), 3.51 (s, 3H, NCH₃), 2.73 (q, 2H, J = 6 Hz, CH₂), 1.29 (t, 3H, J = 6 Hz, CH₃).

¹³C NMR (75MHz, CDCl₃): δ ppm 134.84, 130.79, 129.84, 128.95, 128.43, 128.00, 127.97, 126.87, 33.06, 28.65, 15.40.

HRMS (ESI): m/z = 338.1786 ([M]+).

1-Ethyl-2-(2'-methoxyphenyl)-4,5-diphenylimidazole (1m)

Mp: 123-125°C (EtOH).

IR(KBr): ν 2924 (CH), 1600 (CN), 1462 (CC), 1260 (CO) cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δH ppm 7.57-7.09 (14H, m, ArH), 3.85 (3H, s, OCH₃), 3.77 (2H, q, J = 6 Hz, CH₂), 0.90 (3H, t, J = 6 Hz, CH₃).

¹³C NMR (75MHz, CDCl₃): δ ppm 157.53, 144.69, 137.57, 134.76, 132.66, 131.77, 130.92, 130.81, 128.93, 128.68, 128.40, 127.88, 126.72, 125.91, 120.88, 120.66, 110.85, 55.47, 39.47, 15.85.

1-Ethyl-2(4'-chlorophenyl)-4,5-diphenylimidazole (1n)

Mp: 311-313 °C (EtOH).

IR (KBr): ν 2930 (CH), 1596 (CN) cm⁻¹.

¹H NMR (300MHz, CDCl₃): δ H ppm 7.68-7.16 (14H, m, ArH), 3.94 (2H, q, J = 6 Hz, CH₂), 1.03 (3H, t, J = 6 Hz, CH₃).

¹³C NMR (75MHz, CDCl₃): δ ppm 194.57, 146.04, 137.95, 134.90, 134.33, 132.91, 131.26, 130.98, 130.34, 129.89, 129.82, 129.66, 129.08, 129.01, 128.87, 128.76, 128.05, 126.70, 126.30, 39.65, 16.22.

1-Ethyl-2-(3',4'-dimethoxyphenyl)-4,5-diphenylimidazole (1o)

Mp: 173-175 °C (EtOH).

IR(KBr): ν 2928 (CH), 1608 (CN), 1482(CC), 1258 (CO) cm⁻¹.

¹H NMR (300MHz, CDCl₃): δ H ppm 7.54-6.98 (13H, m, ArH), 3.96-3.90 (8H, m, 2OCH₃ and CH₂), 1.02 (3H, t, J = 6 Hz, CH₃).

¹³C NMR (75MHz, CDCl₃): δ ppm 149.64, 149.04, 137.54, 134.63, 131.66, 131.08, 129.21, 129.08, 128.66, 128.04, 126.77, 126.18, 124.11, 121.51, 112.72, 110.98, 56.04, 55.99, 39.65, 16.28.

1-Ethyl-2-(2', 6'-dichlorophenyl)-4, 5-di(4'-methylphenyl)imidazole (1p)

Mp: 135-137 °C (EtOH).

IR (KBr): \( \nu \) 2924 (CH), 1605 (CN), 1450 (CC), 738 (CCl) cm\(^{-1}\)

\(^1\)H NMR (300MHz, CDCl\(_3\)): \( \delta \) ppm 7.46-7.00 (11H, m, ArH), 3.66 (2H, q, \( J = 6 \) Hz, NCH\(_2\)), 2.45 (3H, s, CH\(_3\)), 2.28 (3H, s, CH\(_3\)), 1.00 (3H, t, \( J = 6 \) Hz, CH\(_3\)).

\(^{13}\)C NMR (75MHz, CDCl\(_3\)): \( \delta \) ppm 141.10, 138.43, 137.28, 135.59, 131.78, 131.22, 130.86, 129.72, 128.65, 128.22, 128.08, 126.54, 39.32, 21.40, 21.10, 15.88.

HRMS (ESI): \( m/z = 420.1160 ([M]^+) \).

1-(4'-nitrophenyl)-2-(4'-chlorophenyl)-4,5-diphenylimidazole (1q)

Mp: 122-124 °C (EtOH).

IR (KBr): \( \nu \) 2928 (CH), 1590 (CN), 1489 (CC), 1351 (C-NO\(_2\)), 739 (CCl) cm\(^{-1}\).

\(^1\)H NMR (300MHz, CDCl\(_3\)): \( \delta \) ppm 8.05-7.03 (18H, m, ArH).

\(^{13}\)C NMR (75MHz, CDCl\(_3\)): \( \delta \) ppm 194.66, 152.50, 134.94, 132.87, 129.88, 129.02, 128.60, 127.77, 127.54, 126.47, 126.33, 113.31.

HRMS (ESI): \( m/z = 451.1089 ([M]^+) \).
1-(4'-Nitrophenyl)-2-(3',4'-dimethoxyphenyl)-4,5-diphenylimidazole (1r)

Mp: 125-126 °C (EtOH).

IR (KBr): ν 2939 (CH), 1597 (CN), 1489 (CC), 1346 (C-NO2), 1246 (CO) cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δH ppm 8.14-8.11 (m, 2H, ArH), 7.59-7.56 (m, 2H, ArH), 7.30-7.12 (m, 12H, ArH), 6.70 (s, 1H, ArH), 3.86 (s, 3H, OCH₃), 3.78 (s, 3H, OCH₃).

¹³C NMR (75MHz, CDCl₃): δ ppm 149.60, 133.72, 131.02, 129.90, 129.18, 128.78, 128.56, 128.24, 127.40, 126.99, 124.36, 121.91, 112.28, 110.63, 55.83.

HRMS (ESI): m/z = 477.1689 ([M⁺]).
References


