Chapter-3

Construction of *bis*-nitrogen containing heterocycles like imidazoles, their bis-analogues, benzimidazoles and bis-benzimidazoles
Chapter 3 (Section-3A)
Room temperature synthesis of densely substituted imidazoles, their bis-analogues and the drug Trifenagrel catalysed by the heterogeneous solid catalyst mercaptopropyl silica (MPS) in aqueous methanol
3A.1 Introduction

This section deals with the synthesis of densely substituted imidazoles, their bis-analogues and the drug trifénagrel using solid mercaptopropylsilica (MPS) as catalyst at room temperature.

3A.1.1 Importance of the substituted imidazoles

Substituted imidazoles is a core molecule in many biological systems like biotin, histamine, histidine as well as active component in potential drug molecules like trifénagrel\(^1\) (Figure 3A.1.1.1) and several pesticides.\(^2\) Various substituted imidazoles possess anti-allergic,\(^3\) analgesic\(^4\) and anti-inflammatory activities.\(^5\) Of particular interest is the 4,5-diaryl imidazoles which act as potential inhibitors of p38 MAP kinase,\(^6\) B-Raf kinase, transforming growth factor β1 (TGF-β1), type 1 activin receptor-like kinase (ALK-5) and cyclooxygenase-2 (COX-2). This moiety is also a significant intermediate in the biosynthesis of interleukin-1 (IL-1)

![Figure 3A.1.1.1 Trifenagrel](image)

Recent advancements in organometallic catalysis and green chemistry have extended the applicability of substituted imidazoles as ionic liquids.\(^8\) Such wide applicability of substituted imidazoles, in particular the 4,5-diaryl ones, triggered me to undertake the synthesis of these systems. Before going into details about the synthesis of substituted imidazoles, I would like to present a brief review on the earlier syntheses of tri and tetrasubstituted imidazoles.

3A.1.2 A brief review on the synthesis of highly substituted imidazoles

Since it is not possible for me to give every details of the synthesis of substituted imidazoles, I have incorporated only those references which are closely related to my work.

Preparation of 2,4,5-triphenyl imidazole (Lophone) was first reported by Radziszewski and simultaneously by Japp and Robinson in 1882 and are synthesized by the reaction of benzil with aryl aldehyde in alcoholic ammonia solution.\(^9\)
The procedure was later modified by Cook and Jones by refluxing benzil with substituted aldehydes and ammonium acetate in glacial acetic acid.\textsuperscript{10}

C. F. Claiborne and his coworkers described the synthesis of tri- and tetra-substituted imidazoles from N-(2-oxo)-amides under neutral reaction conditions on treatment with neat ammonium trifluoroacetate.\textsuperscript{11}

S. Balalaie and A. Arabanian reported the four-component condensation reaction of benzil, aromatic aldehydes, primary amines and ammonium acetate catalysed by zeolite HY and silica gel without any solvent under microwave (MW) irradiation to yield tetrasubstituted imidazoles in high yields and purity.\textsuperscript{12}
Later, the same group synthesized the tetrasubstituted imidazoles in high yields by a one-pot, three-component condensation of benzonil, benzonitrile derivatives and primary amines on the surface of silica gel under solvent-free conditions and microwave (MW) irradiation.\textsuperscript{13}

\[
\begin{array}{c}
\text{Ph}^- + \text{Ar}^- + \text{PhCN} + \text{R-NH}_2 \rightarrow \text{Ph-N} \cdots \text{N} - \text{Ar}^+ \text{R}^-
\end{array}
\]

Scheme 3A.1.2.5

A. Ya et al. described the solvent-free microwave-assisted (MW) synthesis of 2,4,5-trisubstituted and 1,2,4,5-tetrasubstituted imidazoles. Imidazoles are obtained as a result of the condensation of a 1,2-dicarbonyl compound with an aldehyde and an amine using acidic alumina impregnated with ammonium acetate as the solid support.\textsuperscript{14}

\[
\begin{array}{c}
\text{R}^2\text{O} \cdots \text{O} \cdots \text{R}^2 + \text{R}^1\text{CHO} \rightarrow \text{NH}_4\text{OAc/Al}_2\text{O}_3 \rightarrow \text{NH}_4\text{OAc/Al}_2\text{O}_3 \rightarrow \text{R}^2\text{N} \cdots \text{H} \cdots \text{R}^1
\end{array}
\]

Scheme 3A.1.2.6

S. E. Wolkenberg and his coworkers described a simple, high-yielding synthesis of 2,4,5-trisubstituted imidazoles from 1,2-diketones and aldehydes in the presence of NH\textsubscript{4}OAc. Alkyl, aryl and heteroaryl substituted imidazoles are formed in yields ranging from 80 to 99\% under microwave (MW) irradiation. Short syntheses of lepidiline and trifeneagrel illustrate the utility of this approach.\textsuperscript{15}
S. Das et al. found InCl₃·3H₂O to be a mild and effective catalyst for the efficient, one-pot, three component synthesis of 2,4,5-trisubstituted imidazoles at room temperature. Moreover, the utility of this protocol was further explored conveniently for the one-pot, four component synthesis of 1,2,4,5-tetrasubstituted imidazoles in high yields.¹⁶

M. Adib and his coworkers described a one-pot, four-component synthesis of 1,2,4-trisubstituted-1H-imidazoles. Heating a mixture of a 2-bromoacetophenone, an aldehyde, a primary amine and ammonium acetate under solvent-free conditions afforded functionalized imidazoles in good to excellent yields.¹⁷

S. Samai et al. reported the synthesis of 2,4,5-trisubstituted imidazoles by three-component cyclocondensation of 1,2-dicarbonyl compound, aldehyde and ammonium
acetate using L-proline as a catalyst in methanol at moderate temperature. To explore the utility of this method 1,2,4,5-tetrasubstituted imidazoles were also synthesized. The key advantages of this process are high yields, cost effectiveness of catalyst, easy work-up and purification of products by non-chromatographic methods.\(^{18}\)

3A.2 Results and Discussion

Here a simple, mild and efficient synthesis of densely substituted imidazoles in excellent yields employing mercaptopropylsilica (MPS) as a heterogeneous solid catalyst at room temperature (25-30 °C) has been reported.

Application of solid catalysts in generating environmentally benign methodologies which prove highly advantageous for both academia and industry is a major area of research in recent organic synthesis.\(^{19}\) Although a number of solid catalysts have been developed for varieties of useful synthetic transformations, a majority of them possess several drawbacks such as long hours of reaction and rough reaction protocols. In addition, most of these methodologies are sensitive towards moisture and not recoverable. These problems can be easily overcome by switching over to a silica chain possessing covalently anchored organic spacer to produce organic-inorganic hybrid catalysts. In such catalysts, the reactive centres are highly mobile similar to homogeneous catalysts, in addition, possessing the recyclability like the heterogeneous catalysts. On this basis, I have decided to utilize a silica-bonded solid acid catalyst as a heterogeneous solid catalyst for the construction of the substituted imidazoles and bis-imidazoles at room temperature (25-30 °C).
Initially, the desired catalyst, mercaptopropylsilica (MPS) (2) (Scheme 3A.2.1) was prepared following a known procedure\textsuperscript{20} with slight modification and then it was employed for the synthesis of the tri / tetra substituted imidazoles and their corresponding bis-analogues in excellent yields at room temperature with easy regeneration and recyclability of the catalyst.

![Scheme 3A.2.1 Preparation of the catalyst: mercaptopropylsilica (MPS) (2) in water](image)

The prepared catalyst mercaptopropylsilica (MPS) (2) was characterized by comparing the solid state carbon-13 CP MAS NMR spectrum of the prepared catalyst mercaptopropylsilica (MPS) (2) and the normal solution phase carbon 13 NMR spectrum of 3-(mercaptopropyl)-trimethoxysilane (1). The normal solution phase carbon -13 NMR spectrum of (1) showed peaks at $\delta 50.3$ (OCH$_3$), 27.3 (b and c) and at 8.0 (a). When the catalyst was prepared, the peak at 50.3 vanished as the bonding took place through the methoxy groups while the remaining two peaks remained with slight deviations at $\delta 27.1$ (b,c) and 10.6 (a) [(scanned documents of $^{13}$C NMR spectra of 3-(mercaptopropyl)-trimethoxysilane (1) and solid state carbon-13 CP MAS NMR spectrum of mercaptopropylsilica (MPS) (2) are given in the experimental section, as Figure 3A.5.4.12)]. Thus, there is no ambiguity regarding structural proof of MPS (2). Earlier, the structure of MPS has never been confirmed by solid state carbon-13 NMR spectrum. The elemental analysis of MPS was also done which showed the carbon content to be 2.49%.

To optimize the amount of the catalyst per mmol of aldehyde, the synthesis of 2,4,5-triphenyl imidazole was chosen as a model reaction (Table 3A.2.1). The results show very well that MPS (1) is a highly effective catalyst for this transformation and in the absence of this catalyst the reaction only proceed in very trace amounts even after 24 hours. The optimum loading was 5 mg of MPS per mmol of aldehyde in terms of isolated yield and reaction time although a lower catalyst loading (1 mg of MPS) could be used to furnish the reaction in much lower yields.
Table 3A.2.1 Synthesis of 2,4,5-triphenyl imidazole in the presence of different amounts of MPS* at room temperature

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst loading (g)</th>
<th>Time (h)</th>
<th>Yield % (isolated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No catalyst</td>
<td>24</td>
<td>very trace</td>
</tr>
<tr>
<td>2</td>
<td>0.1</td>
<td>4</td>
<td>30</td>
</tr>
<tr>
<td>3</td>
<td>0.05</td>
<td>6</td>
<td>45</td>
</tr>
<tr>
<td>4</td>
<td>0.01</td>
<td>8</td>
<td>67</td>
</tr>
<tr>
<td>5</td>
<td>0.005</td>
<td>2</td>
<td>90</td>
</tr>
<tr>
<td>6</td>
<td>0.004</td>
<td>4</td>
<td>85</td>
</tr>
<tr>
<td>7</td>
<td>0.002</td>
<td>6</td>
<td>75</td>
</tr>
<tr>
<td>8</td>
<td>0.001</td>
<td>10</td>
<td>60</td>
</tr>
</tbody>
</table>

*Reaction conditions: benzaldehyde (1mmol), benzil (1mmol), ammonium acetate (3 mmol) in aqueous methanol (2 + 2 mL).

The model reaction was also studied in various other solvents in the presence of MPS (5 mg per mmol of aldehyde) (Table 3A.2.2). Using 50% aqueous methanol (Table 3A.2.2, entry 3), the yield of the reaction was highest and the reaction time shortest. The yield did not increase further on increasing the time in this optimized solvent (Table 3A.2.2, entries 4 and 5). Using only water as a solvent (Table 3A.2.2, entry 1), probably resulted in some solubility problems of the starting materials, while employing only methanol (Table 3A.2.2, entry 2), the yield was quite good. The addition of water surely has some positive effect on the yield of the reaction as it probably helps in the hydrolysis of ammonium acetate to ammonium hydroxide and acetic acids both of which are absolutely required for the completion of the reaction in addition to helping in product isolation.

Table 3A.2.2 Synthesis of 2,4,5 triphenyl imidazole with MPS (5 mg) in various solvents at room temperature

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent mixtures (mL)</th>
<th>Time (h)</th>
<th>Yield (% (isolated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>water (4)</td>
<td>2</td>
<td>30</td>
</tr>
<tr>
<td>2</td>
<td>methanol (4)</td>
<td>2</td>
<td>70</td>
</tr>
<tr>
<td>3</td>
<td>water + methanol (2+2)</td>
<td>2</td>
<td>90</td>
</tr>
<tr>
<td>4</td>
<td>water + methanol (2+2)</td>
<td>4</td>
<td>85</td>
</tr>
<tr>
<td>5</td>
<td>water + methanol (2+2)</td>
<td>6</td>
<td>85</td>
</tr>
<tr>
<td>6</td>
<td>iso-propanol (4)</td>
<td>7</td>
<td>35</td>
</tr>
<tr>
<td>7</td>
<td>tert-butanol (4)</td>
<td>6</td>
<td>42</td>
</tr>
<tr>
<td>8</td>
<td>dichloromethane (4)</td>
<td>8</td>
<td>60</td>
</tr>
</tbody>
</table>
Once the optimum conditions were standardized, several 2,4,5-trisubstituted imidazoles were synthesized (Scheme 3A.2.2, Table 3A.2.3) using this methodology in excellent yields.

Scheme 3A.2.2 Synthesis of 2,4,5-trisubstituted imidazoles with MPS at room temperature (25-30 °C).

Table 3A.2.3 Synthesis of 2,4,5-trisubstituted imidazoles at room temperature (25-30 °C)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Product no.</th>
<th>Product</th>
<th>Time (h)</th>
<th>Yield (%) (isolated)ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3A.2.2a</td>
<td><img src="image" alt="Product 1" /></td>
<td>2</td>
<td>(65)²¹</td>
</tr>
<tr>
<td>2</td>
<td>3A.2.2b</td>
<td><img src="image" alt="Product 2" /></td>
<td>2.5</td>
<td>61</td>
</tr>
<tr>
<td>3</td>
<td>3A.2.2c</td>
<td><img src="image" alt="Product 3" /></td>
<td>3</td>
<td>(92)²²</td>
</tr>
<tr>
<td>4</td>
<td>3A.2.2d</td>
<td><img src="image" alt="Product 4" /></td>
<td>3</td>
<td>90</td>
</tr>
</tbody>
</table>
Reaction conditions: aldehyde (1mmol), diketo compound (1mmol), ammonium acetate (3 mmol) and catalyst MPS (5 mg)

The methodology was then applied for the synthesis of 1,2,4,5-tetrasubstituted imidazoles (Scheme 3A.2.3) using structurally different aldehydes and primary amines (Table 3A.2.4).

Scheme 3A.2.3 Synthesis of 1,2,4,5-tetrasubstituted imidazoles
Table 3A.2.4 Synthesis of 1,2,4,5-tetrasubstituted imidazoles with MPS at room temperature (25-30 °C)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Product no.</th>
<th>Product</th>
<th>Time (h)</th>
<th>Yields (%) (isolated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3A.2.3a</td>
<td>![Image]</td>
<td>4</td>
<td>65</td>
</tr>
<tr>
<td>2</td>
<td>3A.2.3b</td>
<td>![Image]</td>
<td>4</td>
<td>68</td>
</tr>
<tr>
<td>3</td>
<td>3A.2.3c</td>
<td>![Image]</td>
<td>5</td>
<td>89</td>
</tr>
<tr>
<td>4</td>
<td>3A.2.3d</td>
<td>![Image]</td>
<td>5</td>
<td>89</td>
</tr>
<tr>
<td>5</td>
<td>3A.2.3e</td>
<td>![Image]</td>
<td>6</td>
<td>92</td>
</tr>
<tr>
<td>6</td>
<td>3A.2.3f</td>
<td>![Image]</td>
<td>7</td>
<td>91</td>
</tr>
</tbody>
</table>
The structure of one of the products (3A.2.3j, Table 3A.2.4, entry 10) has been confirmed by X-ray crystal structure analysis of its single crystal and is given below in Figure 3A.2.1

Figure 3A.2.1 ORTEP diagram of compound 3A.2.3j (Table 3A.2.4, entry 10) showing the crystallographic numbering (CCDC 715053)

Once the catalyst was successful towards the synthesis of various 2,4,5-tri and 1,2,4,5-tetrasubstituted imidazoles, synthesis of the corresponding bis-analogues were tried immediately. Various tetra-tri and tetra-tetra substituted bis-analogues were easily
synthesized by simply varying the mole ratio of the aromatic amines (Scheme 3A.2.4, Table 3A.2.5).

Scheme 3A.2.4 Synthesis of tetra-tri and tetra-tetra bis-imidazoles with MPS

Table 3A.2.5 Synthesis of tetra-tri and tetra-tetra substituted bis-imidazoles with MPS at room temperature (25-30 °C)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Product no.</th>
<th>Product</th>
<th>Time (h)</th>
<th>Yield (%) (isolated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3A.2.4a</td>
<td><img src="3A.2.4a.png" alt="Image" /></td>
<td>8</td>
<td>75</td>
</tr>
<tr>
<td>2</td>
<td>3A.2.4b</td>
<td><img src="3A.2.4b.png" alt="Image" /></td>
<td>8</td>
<td>74</td>
</tr>
<tr>
<td>3</td>
<td>3A.2.4c</td>
<td><img src="3A.2.4c.png" alt="Image" /></td>
<td>8</td>
<td>78</td>
</tr>
</tbody>
</table>
The final confirmation for the structure of a bis-analogue comes from the X-ray crystal structure analysis of a single crystal of compound 3A.2.4a (Table 3A.2.5, entry 1) and is given below in Figure 3A.2.2

Figure 3A.2.2 ORTEP diagram of compound 3A.2.4a (Table 3A.2.5, entry 1) showing the crystallographic numbering (CCDC 715054).
The synthetic utility of the present methodology was shown by the ready synthesis of the drug trifenagrel (Figure 3A.1.1.1) which is a chemically novel potent inhibitor of arachidonate and collagen induced aggregation of platelets, at room temperature (Scheme 3A.2.5).

The mechanism (Scheme 3A.2.6) of the formation of tri-substituted imidazoles involves protonation (probably due to proton exchange property of the SH group in the catalyst) of the aldehydic oxygen, diamine intermediate \([A]\) formation with two molecules of ammonia from ammonium acetate and condensation with one molecule of diketone compound to form intermediate \([B]\) which subsequently aromatized to produce the final products. In case of tetra-substituted imidazoles formation, the mechanism proceeds through the formation of the imine of the aromatic aldehydes with aromatic amines (as it is more stable than the imine of aldehydes and ammonia). This imine subsequently forms the diamine intermediate \([C]\) with ammonia and the rest of the mechanism remains same.
To rule out the contribution of homogeneous catalysts towards the synthesis of 2,4,5-triphenyl imidazole, the reaction of benzil, benzaldehyde and ammonium acetate was carried out at room temperature (25-30 °C) in the presence of MPS (2) until the conversion was 30% (by crude \(^1\)H NMR) and at that point, the solid was filtered off. The liquid phase in (H\(_2\)O:MeOH) (2 mL + 2 mL) was allowed to react, but no further conversion was observed. This proves that MPS (2) is the active catalyst for this reaction.

A recycling experiment was done for the synthesis of 2,4,5-triphenyl imidazole under the optimized conditions (Table 3A.2.6). Upon completion of the reaction, the solvent was removed under vacuum, the residue taken up in EtOAc and filtered to remove the catalyst. The catalyst was washed with EtOAc in order to separate the organic product from the catalyst, dried in air and used again. The recycled catalyst was reused ten times without any other treatment. No observation in the appreciable loss in the yield of the reaction was observed.
Table 3A.2.6 Recycling of the catalyst MPS (2) (5 mg) for the synthesis of 2,4,5-triphenyl imidazole at room temperature (25-30 °C)

<table>
<thead>
<tr>
<th>No. of runs</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isolated yield (%)</td>
<td>90</td>
<td>90</td>
<td>88</td>
<td>88</td>
<td>88</td>
<td>87</td>
<td>87</td>
<td>86</td>
<td>86</td>
<td>86</td>
</tr>
</tbody>
</table>

3A.3 Importance of the present methodology

a) Mercaptopropylsilica (MPS) has been prepared by a modified procedure using water as a solvent in a shorter reaction time.

b) Mercaptopropylsilica (MPS) has been used as a heterogeneous solid catalyst for the synthesis of 2,4,5-tri, 1,2,4,5-tetrasubstituted imidazoles and their bis analogues at room temperature (25-30 °C) for the first time. Example of the synthesis of tri and tetrasubstituted imidazoles at room temperature is rather rare.

c) This is the first report on the synthesis of substituted bis-imidazoles.

d) The solid catalyst mercaptopropylsilica (MPS) can be easily regenerated and recycled.

3A.4 Conclusion

Several tri and tetra-substituted imidazoles have been efficiently synthesized at room temperature (25-30 °C) using mercaptopropylsilica (MPS) as a heterogeneous catalyst. This methodology has been very efficiently extended towards the synthesis of the corresponding bis-analogues in addition to the drug trifenagrel.

Publication: This work has been published.


3A.5 Experimental

3A.5.1 Materials and instruments

General: Methanol was distilled before use. All the chemicals were purchased from Aldrich Chemical Company and Spectrochem, Pvt. Ltd. (Mumbai, India). Silica Gel G with binder
from Spectrochem, Pvt. Ltd. Mumbai, India was used for thin layer chromatography. $^1$H and $^{13}$C NMR spectra were obtained on Bruker 300 MHz instrument at 300 and 75 MHz respectively. CDCl$_3$ was purchased from Aldrich Chemical Company and D$_2$O-DMSO from CIL. Melting points were determined on an electrical melting point apparatus with an open capillary and are uncorrected. IR spectra were recorded on a Perkin Elmer Spectrophotometer RX / FT-IR system. The C-H-N analyses were carried out on a 2400 series II CHNS Analyzer, Perkin Elmer (USA).

3A.5.2 General experimental procedure for the preparation of solid catalyst MPS and for the synthesis of substituted imidazoles

3A.5.2.1 General experimental procedure for the preparation of solid catalyst MPS

Mesoporous amorphous silica gel (100-200 mesh) was initially activated by refluxing in sulfuric acid (6 M) for 24 hours and was washed thoroughly with water and dried. Activated silica gel (10 g) was then refluxed with 3-mercaptopropyltrimethoxysilane (5 mmol) in water for 10 hours. The mercaptopropylsilica was then filtered and washed several times with water and finally with ethanol. The catalyst was dried in oven at 110 °C overnight.

3A.5.2.2 General procedure for trisubstituted imidazole formation

To a mixture of aldehyde (1mmol), diketo compound (1mmol), ammonium acetate (3 mmol) in aqueous methanol (2 mL + 2 mL) was added MPS catalyst (5 mg) and the mixture was stirred at room temperature (25-30 °C) for the stipulated time mentioned in Table 3A.2.3. When the reaction was completed as monitored by TLC, the solvent was removed under vacuum, the residue taken up in EtOAc and filtered to remove the catalyst. The catalyst was washed with EtOAc (3 x 5 mL) in order to separate the organic product from the catalyst. The combined EtOAc parts were washed with water (2 x 10 mL) and dried over anhydrous Na$_2$SO$_4$. After removal of the solvent in vacuum, the obtained residue was recrystallized from ethanol. Trifenagrel was synthesized in the above manner by employing the aldehyde (10) (1mmol), benzil (3) (1mmol), ammonium acetate (5) (3 mmol) with MPS (5 mg) in aqueous methanol (2 mL + 2 mL) at room temperature (25-30 °C) for 3 hours.
3A.5.2.3 General procedure for tetrasubstituted imidazole formation

To a mixture of aldehyde (1mmol), diketo compound (1mmol), aromatic amine (1mmol), ammonium acetate (2mmol) in aqueous methanol (2 mL + 2 mL) was added MPS catalyst (5 mg) and the mixture was stirred at room temperature (25-30 °C) for the stipulated time mentioned in Table 3A.2.4. When the reaction was completed as monitored by TLC, the solvent was removed under vacuum, the residue taken up in EtOAc and filtered to remove the catalyst. The catalyst was washed with EtOAc (3 x 5 mL) in order to separate the organic product from the catalyst. The combined EtOAc parts were washed with water (2 x 10 mL) and dried over anhydrous Na$_2$SO$_4$. After removal of the solvent in vacuo, the obtained residue was recrystallized from ethanol.

3A.5.2.4 General procedure for bisimidazole formation

Bisimidazoles were prepared in a similar fashion as above employing aldehyde (1mmol), benzil (2mmol), aromatic amine [either 1 mmol for entries 1,2 (Table 3A.2.5) or 2 mmol for entries 3-5 (Table 3A.2.5)] ammonium acetate [either 4.5 mmol for entries 1,2 (Table 3A.2.5) or 3 mmol for entries 3-5 (Table 3A.2.5)] and catalyst MPS (10 mg) in (water + methanol) (2 + 2 mL) at room temperature (25-30 °C). The characteristic data of all the representative compounds are given below.

3A.5.3 Characteristic data of the representative compounds

4,5-Dimethyl-2-phenyl-1H-imidazole (3A.2.2a, Table 3A.2.3, entry 1): Pale yellow solid; mp 245-246 °C (MeOH) [lit.21 245-247 °C]; $^1$H NMR (300MHz, DMSO-d$_6$) δ 11.96 (br. s, 1H), 7.84 (d, J = 7.2 Hz, 2H), 7.38 (d, J =7.2 Hz, 2H), 7.27 (d, J=7.2 Hz, 1H), 2.11 (s, 6H).

2-(3',4'-Dimethoxyphenyl)-4,5-dimethyl-1H-imidazole (3A.2.2b, Table 3A.2.3, entry 2) Grey solid; mp 220 °C (MeOH); IR (KBr, cm$^{-1}$) 2903, 2838, 2751, 2031, 1616, 1544, 1505, 1455, 1261, 1228, 1123, 1026; $^1$H NMR (300MHz, CDCl$_3$) δ 7.52 (s, 1H, C$_2$-H), 7.43 (dd,
J=8.4 Hz, 1H, C6-H), 6.83 (d, J=8.4 Hz, 1H, C5-H), 3.83 (s, 3H, C4-OCH₃), 3.77 (s, 3H, C3-OCH₃), 2.18 (s, 6H, C4, C5-CH₃); 

^1^H-NMR (CDCl₃, 75 MHz) δ 148.7 and 148.5 (C3, C4), 143.6 (C2), 127.1 (C4, C5), 123.5 (C1), 117.0 (C2), 110.9 (C6), 108.3, (C5), 55.5 (C3 and C4-OCH₃), 10.3 (C6, C5-CH₃); Anal. calcd. for C₁₃H₁₆N₂O₂: C, 67.22; H, 6.94; N, 12.06%;

Found: C, 67.08; H, 7.06; N, 12.08%.

2-(4'-Nitrophenyl)-1H-phenanthro(9,10-d)imidazole (3A.2.2c, Table 3A.2.3, entry 3)
Yellow solid; mp > 300 °C (MeOH) [lit.²² > 300 °C]; 

^1^H NMR (300 MHz, DMSO-d₆) δ 13.82 (br. s, 1H), 8.87 (d, J = 7.2 Hz, 2H), 8.60-8.54 (m, 4H), 8.46 (d, J =7.8 Hz, 2H), 7.78-7.66 (m, 4H).

2-(2',5'-Dimethoxyphenyl)-1H-phenanthro(9,10-d)imidazole (3A.2.2d, Table 3A.2.3, entry 4): Brown solid; mp 224 °C (MeOH); IR (KBr, cm⁻¹) 3416, 2938, 2830, 2376, 2037, 1475, 1211, 1173, 1020, 752, 726 and 571; 

^1^H NMR (300 MHz, d₆-DMSO) δ 12.67 (br.s,1H, NH), 8.80 (dd, J=8.1, 8.1 Hz, 2H, C₄-H, C₅-H), 8.66 (d, J=7.8Hz, 1H, C₆-H), 8.59 (d, J=7.5Hz, 1H, C₇-H), 7.78 (d, J=3.0Hz, 1H, C₈-H), 7.68 (dd, J=7.5, 7.5 Hz, 2H, C₇-H,C₈-H), 7.59 (dd, J=7.5, 7.5 Hz, 2H, C₃-H,C₆-H), 7.14 (d, J=9.0Hz, 1H, C₉-H), 7.02 (dd, J=9.0 and 3.0Hz, 1H, C₄-H), 3.94 and 3.80 (2s, 2×3H, C₂-OCH₃ and C₅-OCH₃); 

^1^C NMR (75 MHz, d₆-DMSO) δ 153.3 (C₂), 150.8 (C₃), 146.8 (C₂ of imidazole ring), 136.3 (C₁₀), 127.7 (C₁₂), 127.6 (C₁₃), 127.1 (C₄/C₅), 127.0 (C₁₄/C₅), [125.3 and 125.2] (C₁/C₉), [(124.0 and 123.7) (C₂,C₇)], [(122.6 and 122.1) (C₃,C₆)], 122.5 (C₁₁), 119.6 (C₁), 116.2 (C₆), 114.6 (C₃), 113.2 (C₄), 56.3 (C₂-OCH₃), 55.7 (C₇-OCH₃). Anal. calcd. for C₂₃H₁₈N₂O₂: C, 77.95; H, 5.12; N, 7.90% Found: 77.80; H, 5.25; N, 7.92%
2-(4'-Cyanophenyl)-1H-phenanthro(9,10-d)imidazole (3A.2.2e, Table 3A.2.3, entry 5)
Brown solid; mp 314-316 °C (MeOH); IR (KBr, cm\(^{-1}\)) 3551, 3385, 3216, 3061, 2375, 2222, 1605, 1424, 842, 758, 723, 540; \(^1\)H NMR (300 MHz, \(d_6\)-DMSO) \(\delta\) 13.70 (br.s,1H, NH), 8.82 (dd, J=8.4, 8.4 Hz, 2H, C4-H and C5-H), 8.55 (d, J=6.9 Hz, 1H, C1-H/C8-H), 8.50 (d, J=7.8Hz, 1H, C1-H/C7-H), 8.43 (d, J=8.1Hz, 2H, C2-H and C6-H), 8.03 (d, J=8.4Hz, 2H, C2-H and C5-H), 7.76-7.61 (m, 4H, C4-H, C7-H, C2-H, C6-H); \(^13\)C NMR (75 MHz, \(d_6\)-DMSO) \(\delta\) 147.3 (C2 of imidazole ring), 137.5 (C10), 134.4 (C11), 131.1 (C3v,C5), 128.5 (C12), 128.2 (C13), 127.9 (C14,C9), [(127.4 and 127.3) (C4,C5)], 126.9 (C11), 126.6 (C2,C6), [(126.0 and 125.7) (C1,C8)], [(124.3 and 123.9) (C2,C7)], [(122.3 and 122.0) (C1,C9)], 118.9 (CN), 111.2 (C4); Anal. cald. for C\(_{52}\)H\(_{35}\)N\(_3\): C, 82.74; H, 4.10; N, 13.16% Found: C, 82.55; H, 4.26; N, 13.19%

2,4,5-Triphenyl-1H-imidazole (3A.2.2f, Table 3A.2.3, entry 6)
Pale yellow solid; mp 275-277 °C (MeOH) [lit.\(^{16}\) 275-276 °C]; \(^1\)H NMR (300MHz, DMSO-d6) \(\delta\) 12.59 (br. s, 1H), 7.52-7.24 (m, 13H), 8.05 (d, J = 7.5 Hz, 1H), 7.91 (d, J = 7.5 Hz, 1H).

2-[2-(4,5-Diphenyl-1H-imidazol-2-yl)-phenoxy]-ethanol (3A.2.2g, Table 3A.2.3, entry 7)
White crystalline solid; mp 184-186 °C (MeOH); IR (KBr, cm\(^{-1}\)) 3349, 3208, 3054, 2944, 2377, 1593, 1470, 1245, 1081, 758, 689; \(^1\)H NMR (300MHz, \(d_6\)-DMSO): \(\delta\) 11.95 (s, 1H, NH), 8.12 (dd, J=7.7 Hz and 1.5 Hz, 1H, C6-H), 7.56 (d, J=7.2Hz, 2H, C4, C5-phenyl protons), 7.47 (d, J=7.2Hz, 2H, C4,C5-phenyl protons), 7.40-7.17 (m, 8H, C3-H, C4-H, C4,
Cs-phenyl protons), 7.08 (t, J=7.5Hz, 1H, C5-H), 5.56 (s, 1H, -OH), 4.22 (t, J=4.5Hz, 2H, -OCH2), 3.82 (br.s, 2H, -CH2); 13C NMR (75MHz, d6-DMSO): δ 155.4, 143.4, 136.8, 135.4, 130.9, 129.8, 128.8, 128.4, 128.3, 127.8, 127.5, 127.2, 126.7, 121.6, 119.6, 114.6, 70.8, 59.6. Anal. cald. for C23H20N2O2: C, 77.51%; H, 5.66%; N, 7.86% Found C, 77.38%; H, 5.78%; N, 7.87%

4,5-Diphenyl-2-methyl-1H-imidazole (3A.2.2h, Table 3A.2.3, entry 8)
Pale yellow solid; mp 241-242 °C (MeOH) [lit.18 241-242 °C]; 1H NMR (300MHz, DMSO-d6) δ 12.07 (s, 1H), 8.11-7.25 (m, 10H), 2.34 (s, 3H)

2-(4'-Bromophenyl)-1-(4a-chlorophenyl)-4,5-dimethyl-1H-imidazole (3A.2.3a, Table 3A.2.4, entry 1): Grey solid; mp 134-136 °C (EtOAc); IR (KBr, cm⁻¹) 3043, 2920, 2376, 2255, 1638, 1493, 1006, 825; 1H NMR (300MHz, CDCl3) δ 7.43 (d, J=8.4Hz, 2H, C2a-H, C6a-H), 7.34 (d, J=8.7Hz, 2H, C2-H, C6-H), 7.17 [d, J=8.7Hz, 2H, (C3a-H, C5a-H) / (C3-H, C5-H)], 7.10 [d, J=8.7Hz, 2H, (C3a-H, C5a-H) / (C3-H, C5-H)], 2.27 (s, 3H, C4-CH3), 2.01 (s, 3H, C5-CH3); 13C NMR (CDCl3, 75MHz) δ 144.1 (C2), 136.1 (C1a), 134.7 (C3), 134.2 (C4), 131.4 (C2a, C6a), 130.0 (C2', C6'), 129.4 (C4a), 129.5 [(C3a, C5a) or (C3, C5)], 129.1 [(C3a, C5a) or (C3, C5)], 125.7 (C4), 124.1 (C1), 126 and 9.5 (C4, C5-CH3); Anal. cald. for C17H14BrClN2: C, 56.46%; H, 3.90%; N, 7.75% Found C, 56.31%; H, 4.02%; N, 7.78%
2-(4′-Bromophenyl)-1-(4α-methylphenyl)-4,5-dimethyl-1H-imidazole (3A.2.3b, Table 3A.2.4, entry 2): Grey solid; mp 120 °C (EtOAc); IR (KBr, cm⁻¹) 3028, 2916, 2860, 2375, 1588, 1509, 1416, 828; ¹H NMR (300 MHz, CDCl₃) δ 7.31 (d, J=9.0 Hz, 2H, C₂a-H, C₅a-H), 7.27-7.17 (m, 4H, C₂-H, C₆-H, C₇-H, C₅-H), 7.04 (d, J=9.0 Hz, 2H, C₃a-H, C₅a-H), 2.39 (s, 3H, C₄a-CH₃), 2.27 (s, 3H, C₄-CH₃), 2.00 (s, 3H, C₅-CH₃); ¹³C NMR (CDCl₃, 75 MHz) δ 144.0 (C₂), 138.7 (C₁α), 135.1 (C₅), 133.7 (C₄), 131.2 (C₂, C₆), 130.3 (C₆a, C₉a), 129.9 (C₄a), 129.4 (C₃a, C₅a), 127.6 (C₇, C₅), 125.9 (C₆), 121.8 (C₇), 21.2 (C₄a-CH₃), [(12.1 and 9.5) (C₄, C₅-CH₃)]; Anal. calcd. for C₂₇H₂₃BrN₂: C, 63.35; H, 5.02; N, 8.21% Found C, 63.22; H, 5.13; N, 8.23%

1,2-Bis-(4-chlorophenyl)-1H-phenanthro(9,10-d)imidazole (3A.2.3c, Table 3A.2.4, entry 3): White solid; mp 230 °C (EtOAc); IR (KBr, cm⁻¹) 3058, 2377, 1902, 1609, 1484, 1377, 1088, 753, 726; ¹H NMR (300 MHz, CDCl₃) δ 8.79 (d, J=7.8 Hz, 1H, C₇-H), 8.67 (d, J=8.1 Hz, 1H, C₄-H), 8.60 (d, J=8.4 Hz, 1H, C₅-H), 7.67 (t, J=7.3 Hz, 1H, C₃-H), 7.58 (t, J=7.5 Hz, 1H, C₆-H), 7.54-7.43 (m, 3H, C₂a-H, C₆a-H, C₇-H), 7.40 (d, J=8.4 Hz, 2H, C₂-H, C₅-H), 7.34 (d, J=8.3 Hz, 2H, C₃-H, C₅-H), 7.28-7.16 (m, 3H, C₂-H, C₃a-H, C₅a-H), 7.11 (d, J=8.2 Hz, 1H, C₁-H); ¹³C NMR (75 MHz, CDCl₃) δ 149.5 (C₂ of imidazole ring) 136.9 (C₁a), 136.8 (C₁₀), 136.0 (C₄a), 135.4 (C₄), 130.6 (C₂a, C₆a), 130.5 (C₂, C₆), 130.3 (C₇, C₅), 129.4 (C₁₂), 128.6 (C₃a, C₅a), 128.3 (C₁₃), 128.1 (C₁₄), 127.9 (C₉), 127.4 (C₇), 126.5 (C₄₆), 126.4 (C₂), 125.9 (C₆), 125.3 (C₃), 124.2 (C₉), 123.1 (C₃), 122.8 (C₈), 122.5 (C₁), 120.6 (C₁); Anal. calcd. for C₂₉H₁₆Cl₂N₂: C, 73.81; H, 3.67; N, 6.38% Found: C, 73.62; H, 3.80; N, 6.44%
2-(4'-Bromophenyl)-1-(4a-chlorophenyl)-1H-phenanthro[9,10-d]imidazole (3A.2.3d, Table 3A.2.4, entry 4): Green solid; mp 236 °C (EtOAc); IR (KBr, cm⁻¹) 3056, 2926, 2374, 1492, 1466, 1376, 1090, 1009, 831, 755, 724; ¹H NMR (300 MHz, CDCl₃) δ 8.84 (d, J=7.5Hz, 1H, C₈-H), 8.75 (d, J=8.1Hz, 1H, C₄-H), 8.68 (d, J=8.1Hz, 1H, C₅-H), 7.74 (t, J=7.2Hz, 1H, C₇-H), 7.65 (t, J=7.5Hz, 1H, C₆-H), 7.60-7.50 (m, 3H, C₃-H, C₂a-H, C₆a-H), 7.49-7.35 (m, 6H, C₂-H, C₃-H, C₅-H, C₆-H, C₃a-H, C₅a-H), 7.33-7.26 (m, 1H, C₂-H), 7.18 (d, J=8.1Hz, 1H, C₁-H); ¹³C NMR (75MHz, CDCl₃) δ 149.6 (C₂ of imidazole ring), 137.3 (C₁₆), 136.9 (C₁₀), 136.0 (C₆α), 131.6 (C₂α, C₆α), 130.8 (C₂, C₆), 130.5 (C₃, C₉), 130.3 (C₃α, C₅α), 129.4 (C₁₂), 128.9 (C₁₃), 128.3 (C₁₄), 128.0 (C₉), 127.4 (C₇), 126.8 (C₁₁), 126.4 (C₂), 125.9 (C₆), 125.2 (C₉), 124.2 (C₄), 123.7 (C₄), 123.1 (C₃), 122.7 (C₈), 122.6 (C₉), 120.6 (C₁); Anal. calcd. for C₂₇H₁₆BrClN₂: C, 67.03; H, 3.33; N, 5.79% Found: C, 66.83; H, 3.50; N, 5.82%

1-(4a-Chlorophenyl)-2-(4'-N,N-dimethylaminophenyl)-1H-phenanthro[9,10-d]imidazole (3A.2.3e, Table 3A.2.4, entry 5): Light yellow solid; mp 224-226 °C (EtOAc); IR (KBr, cm⁻¹): 3049, 2888, 2803, 2375, 1898, 1607, 1483, 1360, 1194, 1089, 946, 816, 740; ¹H NMR (300 MHz, CDCl₃) δ 8.93 (d, J=7.8Hz, 1H, C₈-H), 8.74 (d, J=8.4Hz, 1H, C₅-H), 8.67 (d, J=8.4Hz, 1H, C₅-H), 7.74 (t, J=7.5Hz, 1H, C₇-H), 7.63 (t, J=8.3Hz, 1H, C₆-H), 7.56 (d, J=7.5Hz, 2H, C₂a-H,C₆α-H), 7.51-7.41 (m, 5H, C₃-H, C₂-H, C₆-H, C₃a-H, C₅a-H), 7.29 (t, J=7.7Hz, 1H, C₂-H), 7.17 (d, J=8.1Hz, 1H, C₁-H), 6.58 (d, J=9.0Hz, 2H, C₃-H, C₅-H), 2.94 [s, 6H, -N(CH₃)₂]; ¹³C NMR (75 MHz, CDCl₃) δ 151.6 (C₂ of imidazole ring), 150.5 (C₄), 137.6 (C₁₆), 136.9 (C₁₀), 135.5 (C₄α), 130.6 (C₂α, C₆α), [130.3 and 130.3 (C₃α, C₅α, C₂, C₆)], 128.9 (C₁₄), 128.1 (C₁₃), 127.4 (C₁₂), 127.2 (C₇), 126.8 (C₁₁), 126.2 (C₂),
125.5 (Ca), 124.6 (C3), 124.1 (C4), 123.0 (C5), 122.9 (C6), 122.7 (C9), 120.4 (C2), 116.9 (C1), 111.5 (C3a,C5a), 40.0 [N(CH3)2]; Anal. cald. for C29H21ClN2O2: C, 77.76; H, 4.95; N, 9.38% Found: C, 77.61; H, 5.09; N, 9.39%

1-(4a-chlorophenyl)-2-(3',4'-dimethoxyphenyl)-1H-phenanthro[9,10-d]imidazole
(3A.2.3f, Table 3A.2.4, entry 6): White solid; mp 164-166 °C (EtOAc); IR (KBr, cm⁻¹): 3058, 2987, 2931, 2836, 1600, 1485, 1446, 1256, 1021; ¹H NMR (300 MHz, CDCl₃) δ 8.91 (d, J=7.5Hz, 1H, Cg-H), 8.75 (d, J=8.4Hz, 1H, C4-H), 8.68 (d, J=8.1Hz, 1H, C5-H), 7.73 (t, J=7.4Hz, 1H, C7-H), 7.65 (t, J=7.8Hz, 1H, C6-H), 7.59 (d, J=8.7Hz, 2H, C2a-H, C6a-H), 7.54-7.44 (m, 3H, C3a-H, C5a-H, C3-H), 7.31 (t, J=7.7Hz, 1H, C2-H), 7.22-7.16 (m, 2H, C1-H, C2-H), 7.03 (dd, J=8.4 and 1.8Hz, 1H, C6-H), 6.76 (d, J=8.4Hz, 1H, C2-H), 3.87 (s, 3H, C4-OCH₃), 3.79 (s, 3H, C3-OCH₃); ¹³C NMR (75MHz, CDCl₃) δ 150.4 (C₂ of imidazole ring), 150.1 (C₄), 148.6 (C₇), 137.0 (C₁₅), 136.0 (C₄₆,C₁₀), 130.5 (C₂₆, C₃₄, C₅₆, C₆₆), 129.3 (C₁₂), 128.3 (C₁₃), 127.4 (C₇), 126.5 (C₂), 126.1 (C₁₄,C₉), 126.0 (C₆), 125.2 (C₃), 124.2 (C₄), 123.1 (C₅), 123.0 (C₆a), 122.6 (C₁), 122.4 (C₁₁), 121.4 (C₁₇), 120.6 (C₂), 112.7 (C₇), 110.8 (C₃), 55.8 (C₄-OCH₃, C₃-OCH₃); Anal. cald. for C₂₉H₂₁ClN₂O₂: C, 74.91; H, 4.55; N, 6.03% Found: C, 77.77; H, 4.65; N, 6.07%

2-(3',4'-Dimethoxyphenyl)-1-(4a-methoxyphenyl)-1H-phenanthro[9,10-d]imidazole
(3A.2.3g, Table 3A.2.4, entry 7): White solid; mp 166-168 °C (EtOAc); IR (KBr, cm⁻¹): 2935, 2047, 1602, 1512, 1486, 1449, 1247, 1027, 761, 727; ¹H NMR (300 MHz,CDCl₃) δ 8.90 (d, J=7.5Hz, 1H, Cg-H), 8.68 (d, J=8.4Hz, 1H, C₄-H), 8.63 (d, J=8.4Hz, 1H, C₅-H), 7.71 (t, J=7.4Hz, 1H, C₇-H), 7.58 (t, J=8.1Hz, 1H, C₆-H), 7.43 (t, J=8.3Hz, 1H, C₃-H), 7.33 (d,
J=9.0Hz, 2H, C\textsubscript{2a}-H, C\textsubscript{6a}-H), 7.26-7.16 (m, 3H, C\textsubscript{2}-H, C\textsubscript{1}-H, C\textsubscript{2}-H), 7.09 (dd, J=8.4, and 1.8Hz, 1H, C\textsubscript{5}-H), 7.01 (d, J=9.0Hz, 2H, C\textsubscript{3a}-H, C\textsubscript{5a}-H), 6.70 (d, J=8.7Hz, 1H, C\textsubscript{7}-H), 3.85 (s, 3H, C\textsubscript{4a}-OCH\textsubscript{3}), 3.80 (s, 3H, C\textsubscript{4}-OCH\textsubscript{3}), 3.73 (s, 3H, C\textsubscript{3}-OCH\textsubscript{3}); \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}) \delta 160.2 (C\textsubscript{4a}), 150.7 (C\textsubscript{2} of imidazole ring), 149.5 (C\textsubscript{4}), 148.3 (C\textsubscript{3}), 136.5 (C\textsubscript{1a},C\textsubscript{10}), 131.2 (C\textsubscript{12}), 130.0 (C\textsubscript{2a}C\textsubscript{6a}), 129.0 (C\textsubscript{13}), 128.1 (C\textsubscript{14}), 127.9 (C\textsubscript{6}), 127.1 (C\textsubscript{7}), 126.8 (C\textsubscript{11}), 126.2 (C\textsubscript{2}), 125.4 (C\textsubscript{3}), 124.7 (C\textsubscript{3}), 123.9 (C\textsubscript{4}), 123.0 (C\textsubscript{5}), 122.9 (C\textsubscript{1}), 122.7 (C\textsubscript{8}), 122.2 (C\textsubscript{1}), 120.6 (C\textsubscript{2}), 115.1 (C\textsubscript{3a}C\textsubscript{5a}), 112.4 (C\textsubscript{9}), 110.6 (C\textsubscript{5}), 55.7 (C\textsubscript{4a}-OCH\textsubscript{3}), 55.6 (C\textsubscript{4}-OCH\textsubscript{3}), 55.5 (C\textsubscript{3}-OCH\textsubscript{3}); Anal. calcd. for C\textsubscript{30}H\textsubscript{24}N\textsubscript{2}O\textsubscript{3}: C, 78.24; H, 5.25; N, 6.08% Found: C, 78.02; H, 5.45; N, 6.10%
1-(4a-Methylphenyl)-2-(4'-N,N-dimethylaminophenyl)-1H-phenanthro[9,10-d]imidazole (3A.2.3i, Table 3A.2.4, entry 9): Grey solid; mp 226 °C (EtOAc); IR (KBr, cm⁻¹) 3035, 2887, 2375, 1605, 1444, 1358, 1192, 742; ¹H NMR (300 MHz, CDCl₃) δ 8.88 (dd, J=8.0 and 1.2 Hz, 1H, C₈-H), 8.74 (d, J=8.1Hz, 1H, C₄-H), 8.69 (d, J=8.1Hz, 1H, C₅-H), 7.72 (t, J=7.4Hz, 1H, C₇-H), 7.61 (t, J=7.4Hz, 1H, C₅-H), 7.48 (br.d, J=9.0Hz, 3H, C₂-H, C₆-H, C₇-H), 7.38 (br.s, 4H, C₁⁻H, C₃⁻H, C₃a-H, C₅a-H), 7.28-7.18 (m, 2H, C₁⁻H, C₂⁻H), 6.57 (d, J=9.0Hz, 2H, C₃⁻H, C₅⁻H), 2.94 [s, 6H, -N(CH₃)₂], 2.53 (s, 3H, -CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 151.8 (C₂ of imidazole ring), 150.4 (C₄), 139.6 (C₁a), 137.1 (C₁₀), 136.5 (C₄a), 130.7 (C₂a,C₆a), 130.2 (C₃a,C₅a), 128.9 (C₇,C₉), 128.1 (C₁₂), 127.8 (C₁₃), 127.2 (C₁₄), 127.1 (C₇), 126.1 (C₂), 125.2 (C₆), 124.3 (C₃), 124.0 (C₄), 123.2 (C₁₁,C₅), 123.0 (C₅), 122.8 (C₈), 120.7 (C₁), 118.0 (C₇,C₉), 40.1 [-N(CH₃)₂], 21.5 (-CH₃); Anal. cald. for C₃₉H₂₅N₃: C, 84.28; H, 5.89; N, 9.83% Found: C, 84.09; H, 6.05; N, 9.86%

2-(4'-Bromophenyl)-1-(4a-chlorophenyl)-4,5-diphenyl-1H-imidazole (3A.2.3j, Table 3A.2.4, entry 10): White crystalline solid; mp 218 °C (EtOAc); IR (KBr, cm⁻¹): 3434, 3061, 2377, 1895, 1486, 1407, 1086, 833 and 697; ¹H NMR (300 MHz, CDCl₃) δ: 7.61 (d, J=6.9 Hz, 2H, C₄⁻, C₅⁻phenyl protons), 7.42 (d, J=8.7 Hz, 2H, C₂⁻H and C₆⁻H), 7.32 (d, J=8.7 Hz, 2H, C₃⁻H and C₇⁻H), 7.32-7.18 (m, 8H, C₄⁻, C₅⁻phenyl protons), 7.13 (d, J=7.1Hz, 2H, C₂⁻H and C₆⁻H), 6.97 (d, J=8.4 Hz, 2H, C₃a⁻H and C₅a⁻H); ¹³C NMR (75 MHz, CDCl₃) δ: 145.5 (C₂), 138.3 (C₄), 135.2 (C₅), 134.4 (C₁a), 133.7 (C₆a), 131.4 (2C, C₄⁻, C₅⁻phenyl carbons), 130.9 (C₂, C₆)}, 130.3 (C₂a,C₆a), 129.9 (2C, ipso to C₄ and C₃), 129.4 (4C, C₅, C₇, C₃a, C₅a), 128.8 (C₁), 128.5 (2C, C₄, C₅-phenyl carbons), 128.3 (C₄⁻ or C₅-phenyl carbon), 128.1 (2C, C₄, C₅-phenyl carbons), 127.2 (2C, C₄, C₅-phenyl carbons), 126.8 (C₄ or C₅-
phenyl carbon), 122.9 (C₄); MS: m/z (%): 376.9 (6), 484.8 (M-1) (74), 486.8 (M+1) (100),
487.9 (M+2) (30), 489.8 (M+4) (8); Anal. calcd. for C₂₇H₁₈N₂ClBr; C: 66.75, H: 3.73, N: 5.77% . Found: C: 66.64, H: 3.81, N: 5.94%.

1-(4a-Chlorophenyl)-2-(2'-chlorophenyl)-4,5-diphenyl-1H-imidazole (3A.2.3k, Table 3A.2.4, entry 11): White crystalline solid; mp 210-212 °C (EtOAc); IR (KBr, cm⁻¹): 3435, 3061, 2380, 1493, 1434, 1394, 1090, 751 and 699; ¹H NMR (300 MHz, CDCl₃) δ:
7.61 (dd, J=8.1 and 1.8 Hz, 2H, C₄, C₅-phenyl protons), 7.55 (d, J=6.6 Hz, 1H, C₆-H), 7.37-
7.15 (m, 11H, eight from C₄, C₅-phenyl protons, C₃-H, C₄-H and C₅-H), 7.12 (d, J=8.7 Hz,
2H, C₂a-H and C₃a-H), 6.90 (d, J=8.7 Hz, 2H, C₃a-H and C₅a-H); ¹³C NMR (75 MHz, 
CDCl₃) δ: 144.6 (C₂), 137.1 (C₄), 134.6 (C₅ and C₂), 134.2 and 134.17 (C₁₈, C₄a), 132.9
(C₉), 131.2 (C₆), 130.9 (2C, C₄, C₅-phenyl carbons), 129.7 (2C, ipso to C₄ and C₅), 129.6
(C₃), 129.5 (C₁₇), [(128.9 and 128.7) (6C, C₂a, C₃a, C₅a, C₆a and two others from C₄, C₅-
phenyl carbons)], 128.5 (C₄ or C₅-phenyl carbon), 128.2 (2C, C₄, C₅-phenyl carbons), 127.6
(2C, C₄, C₅-phenyl carbons), 127.2 (C₉), 126.7 (C₄ or C₅-phenyl carbon); Anal. calcd. for 
C₂₇H₁₈N₂Cl₂; C: 73.48, H: 4.11, N: 6.35% Found: C: 73.29, H: 4.27, N: 6.54%.

1-(4a-Chlorophenyl)-2-(3'-nitrophenyl)-4,5-diphenyl-1H-imidazole (3A.2.3l, Table 3A.2.4, entry 12): Light yellow crystalline solid; mp 238-240 °C (EtOAc); IR (KBr): 3060, 
2374, 1735, 1601, 1728, 1492, 1347, 1087 and 701 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ:
8.33 (s, 1H, C₂-H), 8.15 (d, J=7.4 Hz, 1H, C₅-H), 7.81 (d, J=7.2 Hz, 1H, C₆-H), 7.61 (d,
J=6.6 Hz, 2H, C₄, C₅-phenyl protons), 7.47 (t, J=7.8 Hz, 1H, C₉-H), 7.32-7.21 (m, 8H, C₄,
C₅-phenyl protons), 7.16 (d, J=6.0 Hz, 2H, C₃a-H and C₅a-H), 7.05 (d, J=8.4 Hz, 2H, C₃a-H 
and C₅a-H); ¹³C NMR (75MHz, CDCl₃) δ: 148.0 (C₉), 144.1 (C₂), 138.7 (C₄), 134.9 and
134.8 (C_{1a} and C_{5}), 134.1 (C_{5}), 133.4 (C_{4a}), 131.7 (ipso to C_{4}), 131.6 (ipso to C_{5}), 130.9 (2C, C_{4}, C_{5}-phenyl carbons), 129.7 (C_{2a}, C_{6a}), 129.6 (C_{1}), 129.4 (C_{3a}, C_{5a}), 129.2 (C_{2}), 128.6 (2C, C_{4}, C_{5}-phenyl carbons), 128.5 (C_{4} or C_{5}-phenyl carbon), 128.2 (2C, C_{4}, C_{5}-phenyl carbons), 127.1 (2C, C_{4}, C_{5}-phenyl carbons), 127.0 (C_{4} or C_{5}-phenyl carbon), 123.5 and 122.9 (2C, C_{2}, C_{4}); Anal. calcd. for C_{27}H_{18}N_{3}O_{2}Cl; C: 71.76, H: 4.01, N: 9.30% Found: C: 71.59, H: 4.18, N: 9.52%.

1-(4a-Chlorophenyl)-2-(4'-nitrophenyl)-4,5-diphenyl-1H-imidazole (3A.2.3m, Table 3A.2.4, entry 13): Yellow crystalline solid; mp 236-238 °C (EtOAc); IR (KBr): 3067, 2373, 1599, 1509, 1344, 1095, 853 and 694 cm^{-1}; ^{1}H NMR (300 MHz, CDCl_{3}) δ: 8.10 (d, J=8.7 Hz, 2H, C_{3}-H and C_{5}-H), 7.62 (d, J=8.7 Hz, 2H, C_{2}-H and C_{6}-H), 7.56 (dd, J=8.1, 2.1 Hz, 2H, C_{3a}-H and C_{5a}-H); ^{13}C NMR (75MHz, CDCl_{3}) δ: 147.2 (C_{4}), 144.1 (C_{2}), 139.0 (C_{4}), 135.6 (C_{5}), 135.1 (C_{1a}), 134.8 (C_{4a}), [(133.1 and 132.21) (3C, C_{1} and ipso to C_{4} and C_{5})], 130.9 (2C, C_{4}, C_{5}-phenyl carbons), 129.8 (2C, C_{2a} and C_{6a}), 129.4 (2C, C_{2} and C_{6}), 129.2 (2C, C_{3a} and C_{5a}), 128.7 (2C, C_{4}, C_{5}-phenyl carbons), 128.3 (2C, C_{4}, C_{5}-phenyl carbons), 127.3 (2C, C_{4}, C_{5}-phenyl carbons), 127.2 (2C, C_{4}, C_{5}-phenyl carbons), 123.5 (2C, C_{3} and C_{5}); Anal. calcd. for C_{27}H_{18}N_{3}O_{2}Cl; C: 71.76, H: 4.01 , N: 9.30% Found: C: 71.67, H: 4.24, N: 9.45%.

1-(4a-Chlorophenyl)-2-(4'-N,N-dimethylanilinophenyl)-4,5-diphenyl-1H-imidazole (3A.2.3n, Table 3A.2.4, entry 14): Off white crystalline solid; mp 236-238 °C (EtOAc); IR (KBr): 3434, 3049, 2897, 2377, 1609, 1487, 1365, 1200, 1091, 818 and 699 cm^{-1}; ^{1}H NMR (300 MHz, CDCl_{3}) δ: 7.63 (d, J=7.5 Hz, 2H, C_{4}-, C_{5}-phenyl protons), 7.32 (d, J=8.7 Hz, 2H,
C2-H and C6-H), 7.26-7.20 (m, 8H, C4-, C5-phenyl protons), 7.13 (br.d, J=5.4 Hz, 2H, C2a-H and Cfa-H), 7.00 (d, J=8.4 Hz, 2H, C3a-H and C5a-H), 6.61 (d, J=8.7 Hz, 2H, C3-, C5-H), 2.96 [s, 6H, -N(CH3)2]; 13C NMR (75MHz, CDCl3) δ: 150.3 (C4), 147.5 (C2), 137.5 (C4), 135.9 (C3), 137.9 (C1a, C4a), 131.1 (2C, C4-, C5-phenyl carbons), 130.4 (ipso to C4), 130.0 (2C, C2-, C6), 129.8 (ipso to C3), 129.7 (2C, C2a, C6a), 129.2 (2C, C3a, C5a), 128.4 (2C, C4-, C5-phenyl carbons), 128.1 (2C, C4-, C5-phenyl carbons), 128.0 (C4- or C3-phenyl carbon), 127.5 (2C, C4-, C5-phenyl carbons), 126.6 (C4- or C5-phenyl carbon), 117.1 (C1), 111.5 (2C, C3, C5), 40.1 [2C, -N(CH3)2]; Anal. calcd. for C29H24N3Cl: C: 77.41, H: 5.38, N: 9.34%. Found: C: 77.34, H: 5.49, N: 9.53%.

1-(4a-Chlorophenyl)-2-(3'-formylphenyl)-4,5-diphenyl-1H-imidazole (3A.2.3o, Table 3A.2.4, entry 15): White crystalline solid; mp 154-156 °C (EtOAc); IR (KBr): 3386, 3058, 2834, 2733, 2376, 2245, 1697, 1584, 1489, 1400, 1202, 1088, 911 and 721 cm⁻¹; 1H NMR (300 MHz, CDCl3) δ: 9.94 (s, 1H, -CHO), 8.07 (s, 1H, C2-II), 7.83 (d, J=7.5 Hz, 1H, C4-H), 7.65 (d, J=6.9 Hz, 3H, C6-H and two from C4, C5-phenyl protons), 7.43 (t, J=7.5 Hz, 1H, C3-H), 7.36-7.16 (m, 10H, C2a-H, Cfa-H and eight from C4, C5-phenyl protons), 7.03 (d, J=8.7Hz, 2H, C3a-H and C5a-H); 13C NMR (75MHz, CDCl3) δ: 191.3 (-CHO), 145.1 (C2), 138.4 (C4), 136.2 (C3), 135.0 (C1a), 134.4 (C4a), 134.0 (C2), 133.6 (C5), [131.1 and 130.9 (2C, ipso to C4 and C5)], 130.8 (2C, C4, C5-phenyl carbons), 130.6 (C4), 129.7 (C1), 129.4 (4C, C2a, C6a and two from C4, C5-phenyl carbons), 128.8 (C6), 128.6 (C3), 128.4 (2C, C3a, C5a), 128.3 (one carbon from C4, C5-phenyl carbons), 128.1 (2C, C4, C5-phenyl carbons), 127.1 (2C, C4, C5-phenyl carbons), 126.8 (C4 or C5-phenyl carbon); Anal. calcd. for C29H24N3O2Cl: C: 77.33, H: 4.40, N: 6.44% Found: C: 77.19, H: 4.57, N: 6.59%.
1-(4a-Chlorophenyl)-2-[3'(4,5-diphenyl-1H-imidazol-2-yl)-phenyl]-4,5-diphenyl-1H-imidazole (3A.2.4a, Table 3A.2.5, entry 1): White solid; mp >320 °C (MeOH); IR (KBr, cm\(^{-1}\)) 3056, 2831, 2376, 1596, 1489, 1369, 1196, 1089, 779, 696; \(^1\)H NMR (CDCl\(_3\), 300 MHz) δ 8.45 (s, 1H, C2-H), 8.11 (d, J=7.5Hz, 1H, C6-H), 7.50-7.44 (m, 6H, C4, C5-phenyl protons), 7.36-7.21 (m, 9H, C4-H, C4, C5-phenyl protons), 7.20-7.14 (m, 6H, C4, C5-phenyl protons), 7.09 (dd, J=7.8 and 1.5Hz, 2H, C2a-H, C6a-H), 6.87 (d, J=8.4Hz, 2H, C3a-H, C5a-H), 6.80 (d, J=7.8Hz, 1H, C7-H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) δ 147.2, 145.2, 138.0, 134.7, 134.5, 133.2, 131.0, 130.8, 130.0, 129.6, 129.5, 129.4, 129.2, 128.6, 128.5, 128.3, 128.2, 128.0, 127.5, 127.1, 126.9, 126.2; Anal. cald. for C\(_{42}\)H\(_{29}\)ClN\(_4\): C, 80.69; H, 4.68; N, 8.96% Found: C, 80.51; H, 4.85; N, 8.97%

1-(4a-Methylphenyl)-2-[4'(4,5-diphenyl-1H-imidazol-2-yl)-phenyl]-4,5-diphenyl-1H-imidazole (3A.2.4b, Table 3A.2.5, entry 2): Light yellow solid; mp 214-216 °C (MeOH); IR (KBr, cm\(^{-1}\)) 3041, 2924, 2860, 1601, 1502, 1444, 1386, 840, 766, 695; \(^1\)H NMR (CDCl\(_3\), 300 MHz) δ: 7.85 (s, 2H, C3-H, C5-H), 7.64-7.42 (m, 6H, C2-H, C6-H and four other from C4, C5-phenyl protons), 7.40-7.14 (m, 16H, C4, C5-phenyl protons), 7.03 (d, J=8.1Hz, 2H, C2a-H, C6a-H), 6.90 (d, J=8.1Hz, 2H, C3a-H, C5a-H), 2.30 [s, 3H, (-CH\(_3\))]; \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) δ: 146.4, 145.3, 138.6, 133.8, 131.2, 131.1, 130.1, 129.8, 129.1, 128.8, 128.4, 128.2, 128.1, 128.0, 127.5, 126.8, 125.6, 21.1; Anal. cald. for C\(_{43}\)H\(_{32}\)N\(_4\): C, 85.40; H, 5.33; N, 9.26% Found: C, 85.25; H, 5.47; N, 9.27%
1-(4a-Methylphenyl)-2-[3'-{1-(4a'-methylphenyl-4,5-diphenylimidazolyi)}]-4,5-
diphenylimidazole (3A.2.4c, Table 3A.2.5, entry 3): White solid; mp 324-326 °C (EtOAc);
IR (KBr, cm⁻¹) 3056, 2934, 2835, 2375, 1599, 1507, 1447, 1247, 1170, 1029, 770, 694; ¹H
NMR (CDCl₃, 300 MHz) δ: 7.90 (t, J=1.5Hz, 1H, C₂-H), 7.63-7.55 (m, 4H, C₄, C₅-phenyl
protons), 7.34-7.11 (m, 19H, C₄-H, C₅-H, C₆-H and 16 from C₄, C₅-phenyl protons), 7.07
(d, J=8.1Hz, 4H, C2a-H, C6a-H, C3a-H, C3a-H), 6.91 (d, J=8.4Hz, 4H, C3a-H, C5a-H, C3a-H,
C5a-H), 2.33 [s, 6H, 2-(CH₃)]; ¹³C NMR (CDCl₃, 75 MHz) δ: 146.4, 138.2, 138.0, 134.5, 134.3,
131.2, 131.1, 131.0, 130.8, 130.6, 130.0, 129.7, 128.4, 128.4, 128.3, 128.1, 128.0,
127.9, 127.8, 127.6, 127.3, 127.1, 126.4, 21.1; Anal. cald. for C₅₀H₃₈N₄: C, 86.42; H, 5.51;
N, 8.06% Found: C, 86.30; H 5.62; N, 8.07%

1-(4a-Methoxyphenyl)-2-[3'-{1-(4a'-methoxyphenyl-4,5-diphenylimidazolyi)}]-4,5-
diphenylimidazole (3A.2.4d, Table 3A.2.5, entry 4): White solid; mp 284-286 °C (EtOAc);
IR (KBr, cm⁻¹) 3035, 2920, 2375, 1599, 1503, 1444, 1366, 767, 694; ¹H NMR (CDCl₃, 300
MHz) δ: 7.94 (s, 1H, C₂-H), 7.60 (d, J=6.0Hz, 4H, C₄, C₅-phenyl protons), 7.26-7.07 (m,
19H, C₄-H, C₅-H, C₆-H and 16 from C₄, C₅-phenyl protons), 6.97 (d, J=7.5Hz, 4H, C2a-H,
C6a-H, C3a-H, C3a-H), 6.79 (d, J=7.5Hz, 4H, C3a-H, C5a-H, C3a-H, C5a-H), 3.75 [s, 6H,
2-(OCH₃)]; ¹³C NMR (CDCl₃, 75 MHz) δ 159.2, 146.5, 137.9, 134.5, 131.2, 130.8, 130.7,
129.8, 129.7, 129.5, 128.3, 128.0, 127.9, 127.7, 127.1, 126.4, 114.2, 55.3; Anal. cald. for
C₅₀H₃₈N₄O₂: C, 82.62; H, 5.27; N, 7.71% Found: C, 82.50; H, 5.37; N, 7.73%
1-(4a-ChlorophenyI)-2-[3"-(1-4a'-chlophenyl)-phenanthro-9',10'-d-imidazolyl]-phenanthro-9,10-d-imidazole (3A.2.4e, Table 3A.2.5, entry 5): White solid; mp 324-326 °C (EtOAc); IR (KBr, cm⁻¹) 3065, 2922, 2368, 1491, 1088, 750, 722; ^1H NMR (300 MHz, CDCl₃) δ: 8.77 (d, J=7.6Hz, 2H, C₈-H and C₉-H), 8.64 (d, J=8.0Hz, 2H, C₄-H, C₅-H), 8.60 (d, J=8.2Hz, 2H, C₅-H and C₆-H), 8.03 (s, 1H, C₂-H), 7.64 (t, J=7.1Hz, 2H, C₇-H and C₈-H), 7.54 (t, J=7.7Hz, 2H, C₆-H, C₇-H), 7.51 (d, J=8.2Hz, 4H, C₈-H, C₉-H, C₂-H, C₃-H), 7.42 (t, J=7.1Hz, 2H, C₂-H, C₃-H), 7.36 (d, J=8.4Hz, 4H, C₄-H, C₅-H, C₆-H, C₇-H), 7.28 (d, J=7.5Hz, 2H, C₃-H, C₄-H), 7.21 (t, J=7.1Hz, 2H, C₂-H, C₃-H), 7.09 (m, 3H, C₄-H, C₅-H, C₆-H); ^13C NMR (75 MHz, CDCl₃) δ: 149.5, 136.5, 136.3, 131.7, 130.6, 130.4, 130.0, 129.5, 128.4, 128.3, 127.8, 127.6, 126.6, 126.2, 125.5, 124.3, 123.1, 122.4, 120.7; Anal. cald. for C₄₈H₂₈Cl₂N₄: C, 78.79; H, 3.86; N, 7.66% Found: C, 78.58; H, 4.06; N, 7.67%

TRIFENAGREL: White crystalline solid; mp 132-134 °C (EtOAc); IR (KBr): 3287, 3067, 2941, 2871, 2813, 1591, 1465, 1245, 764 and 693 cm⁻¹; ^1H NMR (300 MHz, CDCl₃) δ: 12.27 (brs, 1H, NH), 8.46 (dd, J=7.8 Hz and 1.2 Hz, 1H, C₆-H), 7.56 (brs, 4H, C₄, C₅-phenyl protons), 7.33-7.21 (m, 7H, six from C₄, C₅-phenyl protons and C₆-H), 7.09 (dt, J=7.8 Hz and 0.9 Hz, 1H, C₅-H), 6.95 (d, J=8.1 Hz, 1H, C₃-H), 4.15 (t, J=5.4 Hz, 2H, -OCH₂), 2.59 (t, J=5.4 Hz, 2H, -NCH₂), 1.92 [brs, 6H, -N(CH₃)₂]; ^13C NMR (75MHz, CDCl₃) δ: 155.0 (C₂), 143.6 (3C, C₃, C₄ and C₅), 129.0 (C₆), 128.7 (C₇), [(128.2 and 126.9) (12C, C₈, C₉-phenyl carbons)], 122.0 (C₁₀), 120.2 (C₁₁), 113.5 (C₁₂), 65.5 (-OCH₂), 57.8 (-NCH₂), 44.3 [2C, -N(CH₃)₂].
3A.5.4 Few representative spectra of previously unknown products

Figure 3A.5.4.1 a) $^1$H NMR and b) $^{13}$C NMR spectra of product [3A.2.2b] (Table 3A.2.3, entry 2)
Figure 3A.5.4.2 a) $^1$H NMR and b) $^{13}$C NMR spectra of product [3A.2.2d] (Table 3A.2.3, entry 4)
Figure 3A.5.4.3 a) $^1$H NMR and b) $^{13}$C NMR spectra of product [3A.2.2g] (Table 3A.2.3, entry 7)
Figure 3A.5.4.4 a) $^1$H NMR and b) $^{13}$C NMR spectra of product [3A.2.3b] (Table 3A.2.4, entry 2)
Figure 3A.5.4.5 a) $^1$H NMR and b) $^{13}$C NMR spectra of product [3A.2.3e] (Table 3A.2.4, entry 5)
Figure 3A.5.4.6  a) $^1$H NMR and b) $^{13}$C NMR spectra of product [3A.2.3j] (Table 3A.2.4, entry 10)
Figure 3A.5.4.7 a) $^1$H-$^1$H homonuclear and b) $^1$H-$^{13}$C heteronuclear coupling spectra of product [3A.2.3h] (Table 3A.2.4, entry 8)
Figure 3A.5.4.8 a) $^1$H NMR in d$_6$-DMSO and b) $^1$H NMR spectra in CDCl$_3$ of product [3A.2.4a] (Table 3A.2.5, entry 1)
Figure 3A.5.4.9 a) $^{13}$C NMR spectra in CDCl$_3$ of product [3A.2.4a] (Table 3A.2.5, entry 1)
Figure 3A.5.4.10 a) $^1$H NMR and b) $^{13}$C NMR spectra of product [3A.2.4e] (Table 3A.2.5, entry 5)
Figure 3A.5.4.11 a) $^1$H NMR and b) $^{13}$C NMR spectra of trifenagrel
Figure 3A.5.4.12 a) $^{13}$C NMR spectra of 3-(Mercaptopropyl)-trimethoxysilane in CDCl$_3$ b) Solid state carbon-13 CP MAS NMR spectrum of MPS
3A.5.5 Detailed analysis data of the X-ray crystal structures (ORTEP diagrams given in Figure 3A.2.1 and 3A.2.2 respectively)

Compound 3A.2.3j: Empirical formula C27 H18 Br Cl N2, M = 485.79, white needle shaped crystal, Crystal size 0.30 x 0.05 x 0.05 mm³, a = 9.8597(12) Å, b = 10.616(3) Å, c = 20.849(8) Å, Crystal system orthorhombic, α = β = γ = 90°, Volume = 2182.3(11) Å³, ρcalc = 1.479 Mg/m³, μ = 2.023 mm⁻¹, Z = 4, Space group P212121, λ = 0.71073 Å, T = 150(2) K, Reflections collected 10807, Independent reflections 6170 [R(int) = 0.0785], F(000) = 984, Theta range for data collection 5.00 to 60.00°, Index ranges -13≤h≤13, -6≤k≤14, -29≤l≤26, Completeness to theta = 30.00° 100.0 %, Absorption correction Semi-empirical from equivalents, Refinement method Full-matrix least-squares on F², Data / restraints / parameters 6170 / 0 / 280, Goodness-of-fit on F² 0.844, Final R indices [I>2sigma(I)] R1 = 0.0631, wR2 = 0.1200, R indices (all data) R1 = 0.1280, wR2 = 0.1338, Largest diff. peak and hole 1.110 and -0.594 e Å⁻³, CCDC 715053 contains the crystallographic data of compound 3A.2.3j.

Compound 3A.2.4a: Empirical formula C43 H33 Cl N4 O, M = 657.18, white needle shaped crystal, Crystal size 0.30 x 0.05 x 0.05 mm³, a = 11.7389(2) Å, b = 18.0645(3) Å, c = 16.5191(4) Å, Crystal system monoclinic, α =90.00 β = 103.931(2) γ = 90°, Volume = 3399.96(12) Å³, ρcalc = 1.284 Mg/m³, μ = 0.153 mm⁻¹, Z = 4, Space group P21/n, λ = 0.71073 Å, T = 150(2) K, Reflections collected 23506, Independent reflections 9860 [R(int) = 0.0305], F(000) = 1376, Theta range for data collection 4.50 to 60.00°, Index ranges -14≤h≤16, -25≤k≤25, -23≤l≤22, Completeness to theta = 30.00° 100.0 %, Absorption correction Semi-empirical from equivalents, Refinement method Full-matrix least-squares on F², Data / restraints / parameters 9860 / 0 / 444, Goodness-of-fit on F² 0.730, Final R indices [I>2sigma(I)] R1 = 0.0578, wR2 = 0.1638, R indices (all data) R1 = 0.0966, wR2 = 0.1895, Largest diff. peak and hole 0.392 and -0.375 e Å⁻³, CCDC 715054 contains the crystallographic data of compound 3A.2.4a.
3A.6 References

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15. S. E. Wolkenberg, D. D. Wisnoski, W. H. Leister, Y. Wang, Z. Zhao and C. W.
    3263.
Chapter-3 [Section-3B]

Synthesis of 2-substituted benzimidazoles and bis-benzimidazoles by an expeditious phase-transfer catalyst PEG-400 under solvent-free conditions
3B.1 Introduction
This section deals with the synthesis of 2-substituted benzimidazoles and bis-benzimidazoles using PEG-400 under solvent-free conditions.

3B.1.1 Importance of the benzimidazoles and bis-benzimidazoles
Benzimidazoles are present in various bioactive compounds possessing antiviral, anti-hypertension and anticancer properties.\textsuperscript{1,2} Compounds possessing the benzimidazole moiety express significant activity against several viruses such as HIV,\textsuperscript{3} Herpes (HSV-1),\textsuperscript{4} human cytomegalovirus (HCMV)\textsuperscript{3} and influenza.\textsuperscript{5} Bis-benzimidazoles are DNA-minor groove binding agents possessing anti-tumor activity.\textsuperscript{6} Such wide range of pharmaceutical activities inspired me to undertake the synthesis of 2-substituted benzimidazoles as well as their bis-analouges. Before going into further details about their synthesis, I would just like to present a brief review on the synthesis of substituted benzimidazoles.

3B.1.2 A brief review on the synthesis of benzimidazoles
As it is not possible for me to discuss the synthesis of 2-substituted benzimidazoles in details, I have incorporated only those references which are closely related to my work.

It was R. Walther and his coworkers, who for the first time, synthesized several 2-arylbenzimidazoles by heating a reaction mixture containing 1,2-phenylenediamines and benzoic acids at 210-220 °C in an oil bath for one hour.\textsuperscript{7}

\[
\begin{array}{c}
\text{O}_2\text{N} \quad \text{NH}_2 \\
\text{NH}_2 \\
\text{COOH} \\
\text{X=Cl, Br, I}
\end{array}
\xrightarrow{210 ^\circ \text{C}; 1h}
\begin{array}{c}
\text{O}_2\text{N} \\
\text{N} \\
\text{H} \\
\text{X}
\end{array}
\]

Scheme 3B.1.2.1

D. W. Hein et al. described the formation of 2-aryl- and 2-alkyl-substituted benzimidazoles, benzoazoles and benzothiazoles by the polyphosphoric acid-catalysed condensation of a carboxylic acid, ester, amide or nitrile with an ortho-amino, ortho-hydroxy or ortho-mercapto-arylamine.\textsuperscript{8}
J. J. Vanden Eynde et al. developed a methodology that enables the preparation of 1H-benzimidazoles from benzene-1,2-diamines and aldehydes, without the necessity of isolating the intermediate imines.9

A. B. Alloum and his coworkers developed chemoselective synthesis of benzimidazoles by the condensation of ortho-phenylenediamine with aldehydes by silica-supported thionyl chloride in dichloromethane at ambient temperature.10

L. M. Dudd et al. described the synthesis of benzimidazoles by the cyclocondensation of 1,2-phenylenediamines and benzoic acids in high temperature water in batch-type autoclave.11
Benzimidazoles have been efficiently synthesized in high yields by B. Das et al. using (bromodimethyl)sulfonium bromide at room temperature by treatment of 1,2-phenylenediamine with aldehydes.\textsuperscript{12}

\[
\begin{array}{c}
\text{NH}_2 \quad \text{NH}_2 \\
\text{R} + \text{CHO} \\
\text{Me}_2\text{SBrBr}^{-} \quad \text{MeCN} \\
\text{room temp, 4-8 h} \\
\end{array}
\]

Scheme 3B.1.2.6

P. Gogoi et al. showed that the system, \(\text{I}_2/\text{KI}/\text{K}_2\text{CO}_3/\text{H}_2\text{O}\), oxidizes carbon-nitrogen bonds for the synthesis of imidazolines and benzimidazoles from aldehydes and diamines under an aerobic conditions in water at 90 °C with excellent yields. The process is green, mild and inexpensive.\textsuperscript{13}

\[
\begin{array}{c}
\text{H}_2\text{N} \quad \text{NH}_2 \\
\text{R} \quad \text{CHO} \\
\text{I}_2/\text{KI}/\text{K}_2\text{CO}_3/\text{H}_2\text{O} \\
\text{R=alkyl, aryl, CHO} \\
\end{array}
\]

Scheme 3B.1.2.7

A new, convenient method for the syntheses of 2-substituted benzimidazole and benzothiazole has been described by K. Bahrami et al. Short reaction time, large-scale synthesis, easy and quick isolation of the products, excellent chemoselectivity, and excellent yields are the main advantages of this procedure.\textsuperscript{14}

\[
\begin{array}{c}
\text{NH}_2 \quad \text{NH}_2 \\
\text{R} \quad \text{Ar-CHO} \\
\text{X=NH, S} \\
\text{R= H, Me, NO}_2 \\
\text{H}_2\text{O}_2/\text{CAN} \\
\text{solvent-free, 50 °C} \\
\end{array}
\]

Scheme 3B.1.2.8
VO(acac)$_2$-CeCl$_3$ combo catalyst has been developed by D. K. Maity and his coworkers for chemoselective cyclocondensation cum oxidation under mild reaction conditions toward synthesis of a new class of optically pure glycal based chiral benzimidazoles.\textsuperscript{15}

\begin{align*}
&\text{RO} \quad \text{CHO} \quad \text{R'} \quad \text{NH}_2 \quad \text{NH}_2 \\
&\text{OR} \quad \text{OR} \quad \text{X=CH, N} \quad \text{RO} \quad \text{R'} \quad \text{NH}_2 \\
&\text{RO} \quad \text{R'} \quad \text{NH}_2 \quad \text{NH}_2
\end{align*}

\begin{align*}
&\text{THF, O}_2 \text{ (air), MgSO}_4, 9-20 \text{ h} \\
&\text{VO(acac)$_2$-CeCl$_3$ Ti(OBu)$_4$ (10 mol\%)}
\end{align*}

Scheme 3B.1.2.9

A practical and convenient synthetic method has been developed by K. Bahrami et al. for the facile synthesis of 1,2-disubstituted benzimidazoles, 2-substituted benzimidazoles and 2-substituted benzothiazoles.\textsuperscript{16}

\begin{align*}
&\text{Y=NH, S} \\
&R= \text{alkyl, aryl, heteroaryl}
\end{align*}

\begin{align*}
&\text{NH}_2 \\
&\text{X=NH, S} \\
&\text{R= alkyl, aryl, heteroaryl}
\end{align*}

\begin{align*}
&\text{Y} \quad \text{NH}_2 \quad \text{R} \\
&\text{X} \\
&\text{Y} \quad \text{NH}_2 \\
&\text{R}
\end{align*}

Scheme 3B.1.2.10

\textbf{3B.2 Results and Discussion}

Here a simple, mild and efficient synthesis of 2-substituted benzimidazoles using PEG-400 under solvent-free conditions has been reported.

Organic synthesis in PEG under solvent-less conditions is an area of very high significance in modern organic synthesis\textsuperscript{17,18} as it is inexpensive, non-toxic, possesses high

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thermal stability, recyclability and helps in maintaining a neutral reaction medium. For these reasons, I examined the synthesis of benzimidazoles in PEG-400.

To standardize the reaction, 4-chlorobenzaldehyde (4 mmol) and 1,2-phenylenediamine (4.5 mmol) were initially heated in an oil-bath at 110 °C for 20 h under solvent-less and catalyst-free conditions which yielded only the imine of the aldehyde and diamine but not the desired benzimidazole. After a thorough screening with different amounts of PEG-400, at various temperatures, the best result was obtained with 0.1 mL of PEG-400 under solvent-free conditions (Table 3B.2.1, entry 4). It was also found that the reaction proceeded best under solvent-less conditions rather than using solvents. Employing more than 0.1 mL of PEG-400 did not improve the yield of the product, and at the same time, no reaction took place in the absence of PEG-400. Thus, the use of PEG is absolutely essential in this reaction. Since only 0.1 mL of PEG-400 is used, it cannot act as a solvent. Therefore, PEG-400 is the promoter for the reaction without requiring any additional acid catalyst. No formation of benzimidazole took place under argon atmosphere (the reaction stopping at the imine stage) indicating that the aerial oxygen is absolutely necessary for the oxidation step. Investigation of the same reaction with various PEGs with molecular weights 200, 400, 4000, 6000 and 9000 (0.01 mol % each) was also done. The reaction occurred giving excellent yields of the product (95–88%) with low as well as high molecular weight PEGs. The yields remain quite excellent in all the cases using aromatic aldehydes containing both electron donating and electron withdrawing groups but with aliphatic aldehydes, as expected the yields are little bit lower (Table 3B.2.2, entries 28-31). For compounds 3B.2.1g to 3B.2.1m (Table 3B.2.2, entries 7-13), two different isomers are possible (tautomers). Surprisingly, only one isomer is forming absolutely in the present methodology. The previous reports are also in accordance with this observation. The structure of these products have been confirmed by comparing the analytical data of these compounds with the previous reports. The complete optimization table is given below (Table 3B.2.1).
Table 3B.2.1 Optimization of the reaction of 4-chlorobenzaldehyde (4 mmol) and 1,2-phenylenediamine (4.5 mmol).

<table>
<thead>
<tr>
<th>Entry</th>
<th>PEG-400 (mL)</th>
<th>Solvent (mL)</th>
<th>Temperature (°C)</th>
<th>Time (h)</th>
<th>Yield (%) (isolated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-</td>
<td>-</td>
<td>110</td>
<td>20</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>0.05</td>
<td>-</td>
<td>99</td>
<td>20</td>
<td>35</td>
</tr>
<tr>
<td>3</td>
<td>0.05</td>
<td>-</td>
<td>110</td>
<td>15</td>
<td>50</td>
</tr>
<tr>
<td>4</td>
<td>0.1</td>
<td>-</td>
<td>110</td>
<td>4</td>
<td>95</td>
</tr>
<tr>
<td>5</td>
<td>0.2</td>
<td>-</td>
<td>110</td>
<td>4</td>
<td>90</td>
</tr>
<tr>
<td>6</td>
<td>0.4</td>
<td>-</td>
<td>110</td>
<td>4</td>
<td>80</td>
</tr>
<tr>
<td>7</td>
<td>0.1</td>
<td>-</td>
<td>99</td>
<td>20</td>
<td>35</td>
</tr>
<tr>
<td>8</td>
<td>0.1</td>
<td>EtOH (5)</td>
<td>reflux</td>
<td>20</td>
<td>30</td>
</tr>
<tr>
<td>9</td>
<td>0.1</td>
<td>DMF (5)</td>
<td>reflux</td>
<td>20</td>
<td>42</td>
</tr>
<tr>
<td>10</td>
<td>0.1</td>
<td>THF (5)</td>
<td>reflux</td>
<td>20</td>
<td>38</td>
</tr>
<tr>
<td>11</td>
<td>0.1</td>
<td>CH₃CN (5)</td>
<td>reflux</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td>12</td>
<td>0.1</td>
<td>any above</td>
<td>reflux</td>
<td>50-55</td>
<td>-</td>
</tr>
<tr>
<td>13</td>
<td>0.1</td>
<td>-</td>
<td>MW, 110 °C, 600 W</td>
<td>1</td>
<td>70</td>
</tr>
</tbody>
</table>

After standardizing the reaction, variety of aldehydes [aliphatic, aromatic (possessing both electron-donating and electron-withdrawing groups and heteroaromatic] were employed for benzimidazole formation. In all the cases the yields were excellent (Scheme 3B.2.1, Table 3B.2.2). Five different ortho-phenylenediamines (Scheme 3B.2.1, Table 3B.2.2) were employed and all of them reacted smoothly under the reaction conditions.

Scheme 3B.2.1 Synthesis of 2-substituted benzimidazoles
Table 3B.2.2 Synthesis of 2-substituted benzimidazoles with PEG-400 (0.1 mL) under solvent-less conditions in an oil-bath at 110 °C

<table>
<thead>
<tr>
<th>Entry</th>
<th>Product no.</th>
<th>Product</th>
<th>Time (h)</th>
<th>Yield (%) (isolated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3B.2.1a</td>
<td><img src="image1" alt="Product" /></td>
<td>6</td>
<td>(90)^12</td>
</tr>
<tr>
<td>2</td>
<td>3B.2.1b</td>
<td><img src="image2" alt="Product" /></td>
<td>7</td>
<td>(92)^19</td>
</tr>
<tr>
<td>3</td>
<td>3B.2.1c</td>
<td><img src="image3" alt="Product" /></td>
<td>5</td>
<td>(92)^20</td>
</tr>
<tr>
<td>4</td>
<td>3B.2.1d</td>
<td><img src="image4" alt="Product" /></td>
<td>8</td>
<td>(90)^21</td>
</tr>
<tr>
<td>5</td>
<td>3B.2.1e</td>
<td><img src="image5" alt="Product" /></td>
<td>4</td>
<td>(95)^12</td>
</tr>
<tr>
<td>6</td>
<td>3B.2.1f</td>
<td><img src="image6" alt="Product" /></td>
<td>9</td>
<td>(87)^22</td>
</tr>
<tr>
<td>7</td>
<td>3B.2.1g</td>
<td><img src="image7" alt="Product" /></td>
<td>6</td>
<td>(89)^23</td>
</tr>
<tr>
<td>8</td>
<td>3B.2.1h</td>
<td><img src="image8" alt="Product" /></td>
<td>8</td>
<td>(93)^24</td>
</tr>
<tr>
<td>9</td>
<td>3B.2.1i</td>
<td><img src="image9" alt="Product" /></td>
<td>8</td>
<td>(88)^25</td>
</tr>
<tr>
<td>No.</td>
<td>Formula</td>
<td>Structure</td>
<td>Log P</td>
<td>Ref.</td>
</tr>
<tr>
<td>-----</td>
<td>---------</td>
<td>-----------</td>
<td>-------</td>
<td>------</td>
</tr>
<tr>
<td>10</td>
<td>3B.2.1j</td>
<td><img src="image" alt="Structure 3B.2.1j" /></td>
<td>4</td>
<td>(91)²⁶</td>
</tr>
<tr>
<td>11</td>
<td>3B.2.1k</td>
<td><img src="image" alt="Structure 3B.2.1k" /></td>
<td>6</td>
<td>(90)²⁵</td>
</tr>
<tr>
<td>12</td>
<td>3B.2.1l</td>
<td><img src="image" alt="Structure 3B.2.1l" /></td>
<td>8</td>
<td>(93)²⁶</td>
</tr>
<tr>
<td>13</td>
<td>3B.2.1m</td>
<td><img src="image" alt="Structure 3B.2.1m" /></td>
<td>4</td>
<td>89</td>
</tr>
<tr>
<td>14</td>
<td>3B.2.1n</td>
<td><img src="image" alt="Structure 3B.2.1n" /></td>
<td>9</td>
<td>(86)²⁷</td>
</tr>
<tr>
<td>15</td>
<td>3B.2.1o</td>
<td><img src="image" alt="Structure 3B.2.1o" /></td>
<td>7</td>
<td>87</td>
</tr>
<tr>
<td>16</td>
<td>3B.2.1p</td>
<td><img src="image" alt="Structure 3B.2.1p" /></td>
<td>4</td>
<td>92</td>
</tr>
<tr>
<td>17</td>
<td>3B.2.1q</td>
<td><img src="image" alt="Structure 3B.2.1q" /></td>
<td>3</td>
<td>87</td>
</tr>
<tr>
<td>18</td>
<td>3B.2.1r</td>
<td><img src="image" alt="Structure 3B.2.1r" /></td>
<td>5</td>
<td>88</td>
</tr>
<tr>
<td>19</td>
<td>3B.2.1s</td>
<td><img src="image" alt="Structure 3B.2.1s" /></td>
<td>2</td>
<td>88</td>
</tr>
</tbody>
</table>

²⁶<sup>26</sup>²⁵<sup>25</sup>²⁷<sup>27</sup>
<table>
<thead>
<tr>
<th>No.</th>
<th>Code</th>
<th>Structure</th>
<th>N</th>
<th>R</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>3B.2.1t</td>
<td><img src="image" alt="Structure 1" /></td>
<td>5</td>
<td>89</td>
</tr>
<tr>
<td>21</td>
<td>3B.2.1u</td>
<td><img src="image" alt="Structure 2" /></td>
<td>4</td>
<td>90</td>
</tr>
<tr>
<td>22</td>
<td>3B.2.1v</td>
<td><img src="image" alt="Structure 3" /></td>
<td>4</td>
<td>87</td>
</tr>
<tr>
<td>23</td>
<td>3B.2.1w</td>
<td><img src="image" alt="Structure 4" /></td>
<td>5</td>
<td>83</td>
</tr>
<tr>
<td>24</td>
<td>3B.2.1x</td>
<td><img src="image" alt="Structure 5" /></td>
<td>9</td>
<td>82</td>
</tr>
<tr>
<td>25</td>
<td>3B.2.1y</td>
<td><img src="image" alt="Structure 6" /></td>
<td>7</td>
<td>85</td>
</tr>
<tr>
<td>26</td>
<td>3B.2.1z</td>
<td><img src="image" alt="Structure 7" /></td>
<td>8</td>
<td>87</td>
</tr>
<tr>
<td>27</td>
<td>3B.2.1a'</td>
<td><img src="image" alt="Structure 8" /></td>
<td>6</td>
<td>93</td>
</tr>
<tr>
<td>28</td>
<td>3B.2.1b'</td>
<td><img src="image" alt="Structure 9" /></td>
<td>5</td>
<td>(75)₂⁸</td>
</tr>
<tr>
<td>29</td>
<td>3B.2.1c'</td>
<td><img src="image" alt="Structure 10" /></td>
<td>6</td>
<td>(79)₂⁹</td>
</tr>
<tr>
<td>30</td>
<td>3B.2.1d'</td>
<td><img src="image" alt="Structure 11" /></td>
<td>6</td>
<td>(77)₃₀</td>
</tr>
</tbody>
</table>
Reaction conditions: aldehyde (4 mmol), substituted ortho-phenylenediamine (4.5 mmol)

The structure of one of the products (3B.2.1v, Table 3B.2.2, entry 22) has been confirmed by X-ray crystal structure analysis of its single crystal and is given below in Figure 3B.2.1

As bis-benzimidazoles are important medicinal scaffolds, I turned my attention to the synthesis of the bis-benzimidazoles starting from benzene dialdehydes. For this purpose, two benzene dialdehydes 1,4 and 1,3 were chosen and applying the mentioned methodology at 140 °C in an oil-bath, the bis-benzimidazoles were synthesized (Scheme 3B.2.2) in excellent yields as summarized in Table 3B.2.3.
Scheme 3B.2.2 Synthesis of bis-benzimidazoles

Table 3B.2.3 Synthesis of bis-benzimidazoles mediated by PEG-400 (0.1 mL) at 140°C

<table>
<thead>
<tr>
<th>Entry</th>
<th>Product no.</th>
<th>Product</th>
<th>Time (h)</th>
<th>Yields (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3B.2.2a</td>
<td><img src="image1" alt="Image" /></td>
<td>7</td>
<td>(85)²⁶</td>
</tr>
<tr>
<td>2</td>
<td>3B.2.2b</td>
<td><img src="image2" alt="Image" /></td>
<td>8</td>
<td>(83)³²</td>
</tr>
<tr>
<td>3</td>
<td>3B.2.2c</td>
<td><img src="image3" alt="Image" /></td>
<td>9</td>
<td>80</td>
</tr>
<tr>
<td>4</td>
<td>3B.2.2d</td>
<td><img src="image4" alt="Image" /></td>
<td>6</td>
<td>(86)³³</td>
</tr>
</tbody>
</table>
The mechanism of the benzimidazole formation is shown below. The initial formation is of the imine normally with trans stereochemistry. The imine obtained from the reaction of 4,5-dichloro-1,2-phenylenediamine and 4-cyanobenzaldehyde (Table 3B.2.2, entry 24) was isolated, purified and characterized (characteristic data of the isolated imine is given in section 3B.5.3). The imine then cyclizes, followed by oxidation and dehydration to form the final product.

Scheme 3B.2.3 Proposed mechanism for the synthesis of 2- substituted benzimidazoles.

**3B.3 Importance of the present methodology**

On directly comparing my methodology with some very recent solvent-free techniques for the benzimidazole formation\textsuperscript{24,34-37} (i) this methodology succeeded with a wide variety of substrates (ii) synthesis of benzimidazoles from 4,5-dichloro-\textit{ortho}-phenylenediamine produced a number of previously unknown benzimidazoles (Table 3B.2.2, entries 22–27), (iii) no catalyst was required and (iv) this green methodology was readily applicable to the synthesis of bis-benzimidazoles.
3B.4 Conclusion
Thus PEG-400 has proved to be a very efficient 'green' promoter for the construction of a wide variety of 2-substituted benzimidazoles and particularly bis-benzimidazoles under catalyst-free and solvent-less conditions at 110 °C (or 140 °C) in excellent yields. This methodology worked equally well with both low and high molecular weight PEGs and therefore was a very general and environmentally benign eco-friendly procedure, which would prove beneficial to both academia and industry.

Publication: This work has been published.
"PEG-mediated catalyst-free expeditious synthesis of 2-substituted benzimidazoles and bis-benzimidazoles under solvent-less conditions", Chhanda, Mukhopadhyay and Pradip Kumar Tapaswi, Tetrahedron Letters (2008), 49(43), 6237-6240.

3B.5 Experimental
3B.5.1 Materials and instruments
General: Methanol was distilled before use. All the chemicals were purchased from Aldrich Chemical Company and Spectrochem, Pvt. Ltd. (Mumbai, India). Silica Gel G with binder from Spectrochem, Pvt. Ltd. Mumbai, India was used for thin layer chromatography. $^1$H and $^{13}$C NMR spectra were obtained on Bruker 300 MHz instrument at 300 and 75 MHz respectively. CDCl$_3$ was purchased from Aldrich Chemical Company and d$_6$-DMSO from CIL. Melting points were determined on an electrical melting point apparatus with an open capillary and are uncorrected. IR spectra were recorded on a Perkin Elmer Spectrophotometer RX / FT-IR system. The C-H-N analyses were carried out on a 2400 series II CHNS Analyzer, Perkin Elmer (USA).

3B.5.2 General experimental procedure for 2-substituted benzimidazole formation
A mixture of an aldehyde (4 mmol), substituted ortho-phenylenediamine (4.5 mmol) and PEG-400 (0.1 mL) were taken in a dry round-bottomed flask (10 mL). The flask was placed on an oil-bath at a temperature of 110 °C fitted with a condenser. The reaction mixture was heated for the specified time (Tables 3B.2.2) and was monitored by TLC till the disappearance of the starting aldehyde. On cooling to room temperature (25 °C), the reaction mixture solidified and product was directly recrystallized from hot methanol to afford the pure benzimidazoles. The mother liquor was concentrated further to obtain some more products and thus the total yield was calculated. For the synthesis of the bis-benzimidazoles,
the dialdehyde (4 mmol) was mixed with substituted 1,2-phenylenediamines (9 mmol) and heated at 140 °C with PEG-400 (0.1 mL) by the application of the same methodology carried out for the benzimidazoles for the time period as mentioned in Table 3B.2.3. The characteristic data of all the representative compounds are given below.

**3B.5.3 Characteristic data of the representative compounds**

**3B.5.3.1 Characteristic data of the previously unknown compounds**

![Representative compound structure](image)

**2-(2',5'-Dimethoxyphenyl)-5-methyl-1H-benzimidazole** (3B.2.1m, Table 3B.2.2, entry 13)

Pale yellow solid; mp 170–172 °C (EtOAc); IR (KBr): 3227, 2932, 1612, 1489, 1433, 1212, 1041, 807 and 736 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ: 10.67 (br s, 1H, −NH), 8.10 (d, J = 1.5 Hz, 1H, C₆–H), 7.78–7.55 (br d, 1H, C₇–H), 7.43–7.28 (br d, 1H, C₄–H), 7.09 (d, J = 8.1 Hz, 1H, C₅–H), 7.02–6.90 (m, 2H, C₂–H and C₄–H), 4.01 (s, 3H, C₂-OCH₃), 3.88 (s, 3H, C₆-OCH₃), 2.49 (s, 3H, −CH₃); ¹³C NMR (75 MHz, CDCl₃) δ: 154.2 (C₂ and C₆), 151.1 (C₂), 149.7 (C₃a and C₇a), 131.5 (C₇), 124.1 (C₉), 118.5 (C₃), 118.0 (C₇ and C₈), 113.1 (C₆), 113.0 (C₅), 111.1 (C₄), 56.4 (C₂-OCH₃), 56.0 (C₆-OCH₃), 21.7 (−CH₃); Anal. Calcd for C₁₆H₁₈N₂O₂; C: 71.62%, H: 6.01%, N: 10.44%; Found: C: 71.81%, H: 6.23%, N: 10.25%.

![Representative compound structure](image)

**2-(2'-Methoxyphenyl)-5,6-dimethyl-1H-benzimidazole** (3B.2.1o, Table 3B.2.2, entry 15)

Pale yellow solid; mp 214–216 °C (EtOAc); IR (KBr): 3258, 2931, 2371, 1585, 1468, 1443, 1384, 1312, 1243, 1023, 857 and 752 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ: 10.48 (br s, 1H, −NH), 8.55 (dd, J = 8.1 Hz and 1.7 Hz, 1H, C₆–H), 7.37 (one dd and one d merged together, J = 8.6 Hz and 1.8 Hz, 2H, C₃–H and C₄–H), 7.11 (two doublets merged together as a triplet with a small meta coupling, J = 7.5 Hz and 1.8 Hz, 1H, C₅–H), 7.03 and 7.00 (two singlets merged together to form a doublet, 2H, C₄–H and C₇–H), 4.02 (s, 3H, OCH₃), 2.37 [s, 6H, 2
2-(4'-Chlorophenyl)-5,6-dimethyl-1H-benzimidazole (3B.2.1p, Table 3B.2.2, entry 16)
White crystalline solid; mp 262-264 °C (MeOH); IR (KBr): 2924, 2374, 1590, 1438, 1091, 1011, 834, 726 and 534 cm⁻¹; ¹H NMR (300 MHz, DMSO-δ6) δ: 12.67 (s, 1H, -NH), 8.10 (d, J=8.7 Hz, 2H, C₂-H and C₆-H), 7.55 (d, J=8.4 Hz, 2H, C₃-H and C₅-H), 7.39 (s, 1H, C₄-H), 7.25 (s, 1H, C₇-H), 2.28 [s, 6H, 2 ×(-CH₃)]; ¹³C NMR (75 MHz, DMSO-δ6) δ: 149.3, 142.5, 134.1, 133.6, 131.5, 130.2, 129.4, 129.0 (two carbons), 128.0 (two carbons), 119.1, 111.4, 20.1 (two carbons); Anal. calcd. for C₁₅H₁₃N₂Cl; C: 70.18, H: 5.10, N: 10.91%. Found: C: 70.25, H: 5.05, N: 10.79%.

2-(4'-Bromophenyl)-5,6-dimethyl-1H-benzimidazole (3B.2.1q, Table 3B.2.2, entry 17)
Pale yellow crystalline solid; mp 272-274°C (MeOH); IR (KBr): 2935, 2373, 1578,1438, 1010, 819, 717 and 524 cm⁻¹; ¹H NMR (300 MHz, DMSO-δ6) δ: 12.67 (s, 1H, -NH), 8.03 (d, J=8.4 Hz, 2H, C₂-H and C₆-H), 7.69 (d, J=8.4Hz, 2H, C₃-H and C₅-H), 7.39 (s, 1H, C₄-H), 7.25 (s, 1H, C₇-H), 2.26 [s, 6H, 2 ×(-CH₃)]; ¹³C NMR (75 MHz, DMSO-δ6) δ: 149.4, 142.5, 133.6, 131.9 (two carbons), 131.6, 130.3, 129.8, 128.2 (two carbons), 122.9, 119.1, 111.5, 28.5 (two carbons); Anal. calcd. for C₁₅H₁₃N₂Br; C: 59.82, H: 4.35 , N: 9.30% Found: C: 59.63, H: 4.42, N: 9.25%. 

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2-(2',5'-Dimethoxyphenyl)-5,6-dimethyl-1H-benzimidazole (3B.2.1r, Table 3B.2.2, entry 18): Pale yellow crystalline solid; mp 246-248 °C (MeOH); IR(KBr): 2925, 2375, 1523, 1345, 1129, 851 and 698 cm⁻¹; ¹H NMR (300 MHz, DMSO-d₆) δ: 11.85 (s, 1H, NH), 7.81 (d, J=2.7 Hz, 1H, C₆-H), 7.38 (s, 1H, C₄-H), 7.33 (s, 1H, C₇-H), 7.11 (d, J=9.0 Hz, 1H, C₄-H), 6.98 (d, J=9.0Hz, 1H, C₃-H), 3.92 (s, 3H, C₂-OMe), 3.75 (s, 3H, C₃-OMe), 2.29 and 2.27 [two merged singlets, 6H, 2 x (-CH₃)]; ¹³C NMR (75 MHz, DMSO-d₆) δ: 153.3, 151.0, 147.9, 141.4, 133.4, 130.8, 129.9, 118.9, 118.6, 116.8, 113.5, 113.4, 112.1, 56.2, 55.6, 20.3, 20.1; Anal. calcd. for C₁₉H₁₈N₂O₂; C: 72.32, H: 6.43, N: 9.92% Found: C: 72.19, H: 6.54, N: 9.75%.

2-(3'-Bromophenyl)-5,6-dimethyl-1H-benzimidazole (3B.2.1s, Table 3B.2.2, entry 19)
Pale yellow crystalline solid; mp 226-228 °C (MeOH); IR (KBr): 2904, 2856, 2371, 1586, 1446, 1315, 852 and 714 cm⁻¹; ¹H NMR (300 MHz, DMSO-d₆) δ: 12.73 (brs, 1H, NH), 8.31 (s, 1H, C₂-H), 8.12 (d, J=7.8 Hz, 1H, C₆-H), 7.58 (d, J=8.1 Hz, 1H, C₄-H), 7.47-7.38 [m (containing a singlet for C₄-H and two merged doublets with J=7.9 ,7.8 Hz respectively for C₅-H), 2H], 7.27 (s, 1H, C₇-H), 2.27 [s, 6H, 2 x (-CH₃)]; ¹³C NMR (75 MHz, DMSO-d₆) δ: 148.8, 142.5, 133.6, 132.8, 132.0, 131.8, 131.1, 130.4, 128.7, 125.2, 122.3, 119.1, 111.5, 20.1 (two carbons) Anal. calcd. for C₁₅H₁₃N₂Br; C: 59.82, H: 4.35, N: 9.30%. Found: C: 59.98, H: 4.28, N: 9.40%.

2-(3',4'-Dimethoxyphenyl)-5,6-dimethyl-1H-benzimidazole (3B.2.1t, Table 3B.2.2, entry 20): Pale yellow solid; mp 258-260 °C (MeOH); IR (KBr): 3399, 2931, 1435, 1260, 1030 and 850 cm⁻¹; ¹H NMR (300 MHz, DMSO-d₆) δ: 12.45 (s, 1H, NH), 7.68 (dd, J=6.9 ,1.8 Hz, 1H, C₆-H), 7.64 (d, J=1.8 Hz,1H, C₂-H), 7.35 (s, 1H, C₄-H), 7.22 (s, 1H, C₇-H), 7.06 (d,
J=8.4Hz, 1H, C3-H), 3.83 (s, 3H, -OMe), 3.78 (s, 3H, -OMe), 2.27 [s, 6H, 2 x(-CH3)]; 13C NMR (75 MHz, DMSO-d6) δ: 150.7, 150.1, 149.0, 142.6, 133.5, 130.7, 129.7, 123.2, 119.1, 118.7, 111.9, 111.7, 109.7, 55.7 (two carbons), 20.1 (two carbons); Anal. calcd. for C17H18N2O2; C: 72.32, H: 6.43, N: 9.92% Found: C: 72.51, H: 6.27, N: 9.81%.

5,6-Dimethyl-2-(3’-nitrophenyl)-1H-benzimidazole (3B.2.1u, Table 3B.2.2, entry 21)
Yellow crystalline solid; mp 282-284 °C (MeOH); IR (KBr): 2928, 2376, 1488, 1431, 1209,1042, 737 and 574 cm⁻¹; ¹H NMR (300 MHz, DMSO-d6) δ: 12.93 (s, 1H, NH), 8.89 (s, 1H, C2-H), 8.50 (d, J=7.5 Hz, 1H, C4-H), 8.21 (d, J=7.8 Hz, 1H, C6-H), 7.74 (dd, J=8.1, 7.8 Hz, 1H, C5-H), 7.40 and 7.27 (two singlets merged together, 2H, C4-H and C7-H), 2.27 [s, 6H, 2 x(-CH3)]; ¹3C NMR (75 MHz, DMSO-d6) δ: 148.4, 148.2, 142.4, 133.7, 132.3 (two carbons), 132.1, 130.6, 123.8, 120.6 (two carbons), 119.2, 111.7, 20.1 (two carbons); Anal. calcd. for C15H13N3O2; C: 67.40, H: 4.90, N: 15.72% Found: C: 67.32, H: 4.97, N: 15.57%.

2-(4’-Bromophenyl)-5,6-dichloro-1H-benzimidazole (3B.2.1v, Table 3B.2.2, entry 22)
Pale yellow crystalline solid; mp 285 °C (MeOH); IR (KBr): 3035, 2950, 2296, 1591, 1442, 1407, 1292, 1099, 1017, 836 and 723 cm⁻¹; ¹H NMR (300 MHz, DMSO-d6) δ: 13.29 (br s, 1H, NH), 8.05 (d, J = 8.4, 2H, C2-H, and C6-H), 7.81 (s, 2H, C4-H, and C7-H), 7.74 (d, J = 8.7, 2H, C3-H, and C5-H); ¹3C NMR (75 MHz, DMSO-d6) δ: 152.9, 132.2, 128.7, 128.6, 124.8, 124.1; Anal. Calcd. for C13H7N2Cl2Br; C: 45.65, H: 2.06, N: 8.19%. Found: C: 45.49, H: 2.23, N: 8.06.
5,6-Dichloro-2-(2',5'-dimethoxyphenyl)-1H-benzimidazole (3B.2.1w, Table 3B.2.2, entry 23): Pale yellow solid; mp 196 °C (EtOAc); IR (KBr): 3406, 2941, 2365, 1488, 1448, 1222, 1176, 1042, 858, 804 and 737 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ: 10.63 (brs, 1H, NH), 8.01 (brs with a small meta coupling, J= 2.1 Hz, 1H, C₆-H), 7.71 (s, 2H, C₄-H and C₇-H), 7.01 (dd, J=9.2, 2.3 Hz, 2H, C₃-H and C₄-H), 4.02 (s, 3H, C₂-OCH₃), 3.87 (s, 3H, C₅-OCH₃); ¹³C NMR (75 MHz, CDCl₃) δ: 154.3 (two carbons), 151.8, 151.3 (two carbons), 126.5 (two carbons), 118.9 (two carbons), 117.3, 113.2, 113.0 (two carbons), 56.5, 56.0; Anal. calcd. for C₁₅H₁₀N₂O₂Cl₂; C: 55.75, H: 3.74, N: 8.67%. Found: C: 55.59, H: 3.83, N: 8.55 %.

2-(4'-Cyanophenyl)-5,6-dichloro-1H-benzimidazole (3B.2.1x, Table 3B.2.2, entry 24)
Pale yellow solid; mp >320 °C (MeOH); IR (KBr): 3294, 2232, 1610, 1440, 1414, 1291, 1100 and 846 cm⁻¹; ¹H NMR [300 MHz, (0.4 mL CDCl₃ and 0.1 mL DMSO-d₆)] δ: 12.91 (br s, 1H, –NH), 8.30 (d, J = 8.4 Hz, 2H, C₃-H and C₅-H), 7.90–7.73 [a br s (for C₄-H) and a doublet (J = 8.4 Hz for C₂-H and C₆-H) merged together, 3H], 7.61 (br s, 1H, C₇-H); ¹³C NMR [75 MHz, (0.4 mL CDCl₃ and 0.1 mL DMSO-d₆)] δ: 150.6 (C₂, C₃a and C₇a), 132.5 (C₅, C₆ and C₁), 131.3 (C₄, C₅a and C₄a), 126.2 (C₂, C₆ and C₇), 117.0 (CN), 111.8 (C₉); Anal. Calcd for C₁₄H₇N₂Cl₂; C: 58.36, H: 2.45, N: 14.58% Found: C: 58.49, H: 2.53, N: 14.66%.

5,6-Dichloro-2-(3',4'-dimethoxyphenyl)-1H-benzimidazole (3B.2.1y, Table 3B.2.2, entry 25): Pale yellow solid; mp 271 °C (MeOH); IR (KBr): 3432, 2935, 2376, 1606, 1498, 1449, 1264, 1028 and 855 cm⁻¹; ¹H NMR (300 MHz, DMSO-d₆) δ: 13.05 (brs, 1H, NH), 7.95–7.65 (m, 4H, C₂-H, C₆-H, C₄-H and C₇-H), 7.11 (d, J = 9.0 Hz, 1H, C₅-H), 3.80 (s, 3H,
5,6-Dichloro-2-((3'-hydroxy-4'-methoxyphenyl)-1H-benzimidazole (3B.2.1z, Table 3B.2.2, entry 26): Pale yellow solid; mp 194 °C (EtOAc); IR (KBr): 3442, 3107, 2364, 1605, 1498, 1451, 1282, 1229, 1029 and 773 cm⁻¹; ¹H NMR [300 MHz, (0.4 mL CDCl₃ + 0.1 mL DMSO-d₆)] δ: 12.21 (brs, 1H, NH), 7.74 (d, J = 1.7 Hz, 1H, C₂-H), 7.66 (brs, 2H, C₄-H and C₇-H), 7.58 (dd, J = 8.3 Hz and 1.8 Hz, 1H, C₆-H), 6.98 (d, J = 8.3 Hz, 1H, C₅-H), 3.89 (s, 3H, C₄-OCH₃); ¹³C NMR [75 MHz (0.4mL CDCl₃ + 0.1mL DMSO-d₆)] δ: 154.4 (two carbons), 148.4, 147.4 (two carbons), 125.6 (two carbons), 116.3 (two carbons), 112.6 and 111.9; Anal. calcd. for C₁₁H₉N₂O₂Cl₂; C: 54.39, H: 3.26, N: 9.06% Found: C: 54.59, H: 3.15, N: 9.25%.

5,6-Dichloro-2-((furanyl)-1H-benzimidazole (3B.2.1a', Table 3B.2.2, entry 27)
Pale yellow solid; mp 274 °C (MeOH); IR (KBr): 3438, 3116, 2369, 1631, 1522, 1423, 1378, 1295, 1017 and 752 cm⁻¹; ¹H NMR (300 MHz, DMSO-d₆) δ: 7.94 (d, J = 1.1 Hz, 1H, C₄-H), 7.75 (s, 2H, C₄-H and C₇-H), 7.23 (d, J = 3.2Hz, 1H, C₂-H), 6.71 (dd, J = 3.4, 1.7 Hz, 1H, C₃-H); ¹³C NMR (75 MHz, DMSO-d₆) δ: 146.2, 145.4, 144.3, 138.7 (two carbons), 124.6 (two carbons), 116.3 (two carbons), 112.6 and 111.9; Anal. calcd. for C₁₁H₉N₂OCl₂; C: 52.20, H: 2.39, N: 11.07% Found: C: 52.39, H: 2.44, N: 11.15%.
5,6-Dimethyl-2-[3'-{(5,6-dimethyl-1H-benzimidazol-2-yl)phenyl]-1H-benzimidazole
(3B.2.2c, Table 3B.2.3, entry 3): Pale yellow solid; mp 230 °C (MeOH); IR (KBr): 3376, 3166, 2926, 2373, 1634, 1579, 1453, 1291, 1003, 858 and 690 cm⁻¹; ¹H NMR (300 MHz, DMSO-d₆) δ: 12.80 [brs, 2H, 2 x (-NH)], 8.92 (s, 1H, C₂-H), 8.15 (dd, J = 7.7 , 1.1 Hz, 2H, C₄-H and C₆-H), 7.64 (t, J = 7.8 Hz, 1H, C₅-H), 7.36 [brs, 4H, (2 x C₄-H) and (2 x C₅-H)], 2.30 [s, 12H, (2 x C₅-Me) and (2 x C₆-Me)]; ¹³C NMR (75 MHz, DMSO-d₆) δ: 150.0, 131.3, 129.5, 127.0, 124.3, 118.7, 110.7, 20.2; Anal. calcd. for C₂₄H₂₂N₄: C: 78.66, H: 6.05, N: 15.29%. Found: C: 78.49, H: 6.24, N: 15.15 %.

5,6-Dichloro-2-[3'-(5,6-dichloro-1H-benzimidazol-2-yl)phenyl]-1H-benzimidazole
(3B.2.2e, Table 3B.2.3, entry 5): Pale yellow solid; mp >320 °C (MeOH); IR (KBr): 3409, 2925, 2856, 2197,1448, 1298, 1098 and 864 cm⁻¹; ¹H NMR (300 MHz, DMSO-d₆) δ: 13.43 [br s, 2H, 2 X (−NH)], 8.96 (s, 1H, C₂-H), 8.22 (d, J = 7.7 Hz, 2H, C₄-H and C₆-H), 8.00-7.62 [m, 5H, (2 X C₄-H), (2 X C₅-H) and C₅-H]; ¹³C NMR (75 MHz, DMSO-d₆) δ: 153.2 (two carbons), 143.4 (two carbons), 134.4 (two carbons), 130.2 (two carbons), 129.9, 128.4 (two carbons), 125.3, 125.0 (two carbons), 124.6 (two carbons), 120.1 (two carbons), 113.0 (two carbons). Anal. Calcd for C₂₀H₁₀N₄Cl₄: C: 57.18, H: 2.40, N: 6.67%. Found: C: 57.39, H: 2.44, N: 6.45%.
3B.5.3.1 Characteristic data of the previously known compounds

2-Phenylbenzimidazole (3B.2.1a, Table 3B.2.2, entry 1)
White powder; mp 290-292 °C (MeOH) [lit.12 289-291 °C]; \(^1\)H NMR (300 MHz, DMSO-\(d_6\)) \(\delta\): 12.90 (s, 1H, -NH), 8.17 (d, \(J = 8.1\) Hz, 2H, Ar-H), 7.66 (d, 1H, Ar-H), 7.49–7.57 (m, 4H, Ar-H), 7.17–7.24 (m, 2H, Ar-H).

2-(4'-Hydroxyphenyl)-1H-benzimidazole (3B.2.1b, Table 3B.2.2, entry 2)
Pale yellow solid; mp 229-230 °C (MeOH) [lit.19 229-231 °C]; \(^1\)H NMR (300 MHz, DMSO-\(d_6\)) \(\delta\): 7.58–7.65 (m, 3H, Ar-H), 7.43 (d, 1H, Ar-H), 7.21 (d, 1H, \(J = 8.2\) Hz, Ar-H), 6.91 (s, 2H, Ar-H), 6.67 (s, 1H, Ar-H), 5.43 (s, 1H, OH).

2-(2'-Methoxyphenyl)-1H-benzimidazole (3B.2.1c, Table 3B.2.2, entry 3)
White powder; mp 157-158 °C (MeOH) [lit.20 155-158 °C]; \(^1\)H NMR (300 MHz, DMSO-\(d_6\)) \(\delta\): 12.11 (s, 1H), 8.32 (m, 1H), 7.62 (m, 2H), 7.48 (m, 1H), 7.18 (m, 4H), 4.03 (s, 3H).

2-(4'-Cyanophenyl)-1H-benzimidazole (3B.2.1d, Table 3B.2.2, entry 4)
Pale yellow solid; mp 261-262 °C (MeOH) [lit.12 262 °C (EtOH-water)]; \(^1\)H NMR (300 MHz, DMSO-\(d_6\)) \(\delta\): 13.17 (br s, 1H, -NH), 8.30 (d, \(J = 8.4\) Hz, 2H), 7.95 (d, \(J = 8.2\) Hz, 2H), 7.61 (br s, 2H), 7.21 (m, 2H).
2-(4'-Chlorophenyl)-1H-benzimidazole (3B.2.1e, Table 3B.2.2, entry 5)
White crystalline solid; mp 292-294 °C (MeOH) [lit.28 294 °C (EtOH-water)]; \(^1\)H NMR (300 MHz, DMSO-\(d_6\)) \(\delta\): 12.97 (s, 1H), 8.15 (d, \(J = 8.4\) Hz, 2H), 7.70-7.51 (m, 4H), 7.18 (br.d, \(J = 4.8\) Hz, 2H).

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\begin{array}{c}
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2-(2'-Hydroxyphenyl)-1H-benzimidazoles (3B.2.1f, Table 3B.2.2, entry 6)
White powder, mp 250-252 °C (MeOH) [lit.22 251-252 °C]; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\): 13.09 (s, 1H, OH), 9.41 (s, 1H, -NH), 7.75 (brs, 2H), 7.58 (d, \(J = 7.32\) Hz, 2H), 7.31-7.39 (m, 2H), 7.13 (d, \(J = 7.96\) Hz, 1H), 6.96 (t, \(J = 7.08\) Hz, 1H).

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4-Methyl-(2-phenyl)-1H-benzimidazole (3B.2.1g, Table 3B.2.2, entry 7)
Brown solid; mp 248-249 °C (MeOH) [lit.23 246-247 °C]; \(^1\)H NMR (300 MHz, DMSO-\(d_6\)) \(\delta\): 12.27 (s, 1H, -NH), 8.21 (br s, 2H), 7.47-7.53 (m, 4H), 7.07 (t, \(J = 7.5\) Hz, 1H), 6.96 (d, \(J = 7.1\) Hz, 1H), 2.56 (s, 3H).

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\begin{array}{c}
\text{N} \\
\text{Cl}
\end{array}
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2-(4'-Cyanophenyl)-4-methyl-1H-benzimidazole (3B.2.1h, Table 3B.2.2, entry 8)
Clourless solid; mp > 300 °C (MeOH) [lit.26 > 300 °C]; \(^1\)H NMR (300 MHz, DMSO-\(d_6\)) \(\delta\): 8.15-8.21 (m, 2H), 7.76-7.81 (m, 2H), 7.44-7.47 (m, 1H), 7.21 (d, \(J = 7.1\) Hz, 1H), 7.02-7.06 (m, 1H), 2.62 (s, 3H).
2-(4'-Hydroxyphenyl)-5-methyl-1H-benzimidazole (3B.2.1i, Table 3B.2.2, entry 9)
Clourless solid; mp 300-301 °C (MeOH) [lit.25 300-302 °C (EtOH-water)]; $^1$H NMR (300 MHz, DMSO-d$_6$) $\delta$: 14.82 (br s, 1H), 10.75 (s, 1H), 8.15 (d, J = 8.8, 2H), 7.69 (d, J = 8.3, 1H), 7.59 (s, 1H), 7.37 (d, J = 8.5, 1H), 7.11 (d, J = 8.8, 2H), 2.54 (s, 3H).

5-Methyl-2-(3'-nitrrophenyl)-1H-benzimidazole (3B.2.1j, Table 3B.2.2, entry 10)
Yellow solid; mp 121-123 °C (MeOH) [lit26 120-122 °C (EtOH-water)]; $^1$H NMR (300 MHz, DMSO-d$_6$) $\delta$: 12.20 (br s, 1H), 8.62-6.16 (m, 7H), 2.05 (s, 3H).

5-Methyl-2-(4'-N,N-dimethylaminophenyl)-1H-benzimidazole (3B.2.1k, Table 3B.2.2, entry 11): White crystalline solid; mp 250 °C (MeOH) [lit.25 249-251 °C (EtOH-water)]; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$: 8.40 (br s, 1H), 7.82-7.79 (m, 2H), 6.96-6.85 (m, 1H), 6.74 (d, J = 8.2 Hz, 2H), 6.60-6.55 (m, 1H), 4.23 (s, 1H), 3.06 (s, 6H), 2.29 (s, 3H).

2-(3'-Chlorophenyl)-5-methyl-1H-benzimidazole (3B.2.1l, Table 3B.2.2, entry 12)
White crystalline solid; mp 140 °C (MeOH) [lit.26 139-140 °C (EtOH-water)]; $^1$H NMR (300 MHz, DMSO-d$_6$) $\delta$: 12.20 (br s, 1H), 7.90-6.31 (m, 7H), 2.05 (s, 3H).
2-(4'-Cyanophenyl)-5,6-dimethyl-1H-benzimidazole (3B.2.1n, Table 3B.2.2, entry 14)
Light yellow solid; mp 199-202 °C (EtOAc) [lit. 27 200-202 °C]; ¹H NMR (300 MHz, CDCl₃) δ: 8.30 (d, J = 7.8 Hz, 2H), 7.79 (d, J = 7.8 Hz, 2H), 7.38 (s, 2H), 2.36 (s, 6H).

2-Methyl-1H-benzimidazole (3B.2.1b', Table 3B.2.2, entry 28)
Pale yellow solid; mp 178 °C (MeOH) [lit. 28 178 °C]; ¹H-NMR (300 MHz, DMSO-d₆) δ: 10.98 (bs, 1H), 7.70 - 7.62 (m, 1H), 7.33 - 7.30 (m, 1H), 7.22 - 7.18 (m, 2H), 2.66 (s, 3H).

2,5,6-Trimethyl-1H-benzimidazole (3B.2.1c', Table 3B.2.2, entry 29)
Pale yellow solid; mp 239-241 °C (MeOH) [lit. 29 240-242 °C]; ¹H-NMR (300 MHz, DMSO-d₆) δ: 11.91 (bs, 1H), 7.20 (bs, 2H), 2.42 (s, 3H), 2.27 (s, 6H).

5,6-Dichloro-2-ethyl-1H-benzimidazole (3B.2.1d', Table 3B.2.2, entry 30)
Pale yellow solid; mp > 310 °C (MeOH) [lit. 26 > 310 °C]; ¹H-NMR (300 MHz, DMSO-d₆) δ: 7.72 (bs, 2H), 2.84 (q, J = 7.58 Hz, 2H), 1.31 (t, J = 7.58 Hz, 3H).

5,6-Dichloro-2-propyl-1H-benzimidazole (3B.2.1e', Table 3B.2.2, entry 31)
Pale yellow solid; mp > 310 °C (MeOH) [lit. 26 > 310 °C]; ¹H-NMR (300 MHz, DMSO-d₆) δ: 7.77 (s, 1H), 7.68 (s, 1H), 2.78 (t, 2H, J = 7.5), 1.77 (q, 2H, J = 7.5), 0.92 (t, 3H, J = 7.5).
2-[4'-({1H-benzimidazol-2-yl} phenyl]-1H-benzimidazole (3B.2.2a, Table 3B.2.3, entry 1)
Pale yellow solid; mp > 310 °C (MeOH) [lit.26 > 310 °C]; \(^1\)H NMR (300 MHz, DMSO-\(d_6\)) \(\delta\): 13.00 (br s, 2H), 8.34 (s, 4H), 7.70-7.55 (m, 4H), 7.30-7.16 (m, 4H).

2-[3'-({1H-benzimidazol-2-yl} phenyl]-1H-benzimidazole (3B.2.2b, Table 3B.2.3, entry 2)
Pale yellow solid; mp 310-312 °C (MeOH) [lit.32 311-312 °C]; \(^1\)H NMR (300 MHz, DMSO-\(d_6\)) \(\delta\): 13.11 (s, 2H), 9.03 (s, 1H), 8.23 (d, \(J = 7.8 \text{ Hz}\), 2H), 7.73-7.61 (m, 5H), 7.22-7.18 (m, 4H).

5-Methyl-2-[3'-(5-methyl-{1H-benzimidazol-2-yl} phenyl]-1H-benzimidazole (3B.2.2d, Table 3B.2.3, entry 4): Pale yellow solid; mp 126 °C (decomp) (MeOH) [lit.33 126 °C (decomp)]; \(^1\)H NMR (300 MHz, DMSO-\(d_6\)) \(\delta\): 8.93 (s, 2H), 8.66 (d, \(J = 8.2 \text{ Hz}\), 2H), 8.16 (d, \(J = 8.2 \text{ Hz}\), 2H), 7.93 (t, \(J = 7.9 \text{ Hz}\), 2H), 6.96 (d, \(J = 8.2 \text{ Hz}\), 2H), 6.24 (br.s, 2H), 2.41 (s, 3H), 2.36 (s, 3H).
1-(4'-Cyanophenyliminyl)-4,5-dichloroaniline

Pale yellow solid; mp 300–302 °C (EtOAc); IR (KBr): 3466, 3370, 2926, 2373, 2222, 1610, 1477, 1267, 1129, 957 and 831 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ: 8.53 (s, 1H, –CH=N), 8.00 (d, J = 8.4 Hz, 2H, C₃–H and C₅–H), 7.76 (d, J = 8.4 Hz, 2H, C₂–H and C₆–H), 7.24 (s, 1H, C₆–H), 6.87 (s, 1H, C₃–H), 4.36 (br s, 2H, –NH₂); ¹³C NMR (75 MHz, CDCl₃) δ: 155.7 (–CH=N), 142.4 (C₁), 139.6 (C₂), 134.9 (C₄ and C₅), 132.6 (C₃ and C₆), 132.0 (C₇), 129.06 (C₈ and C₁₀), 120.96 (CN), 118.33 (C₉), 116.37 (C₃), 114.62 (C₄); Anal. Calcd for C₁₄H₉N₃Cl₂: C: 57.95, H: 3.13, N: 14.48% Found: C: 58.09, H: 3.03, N: 14.56%
Figure 3B.5.4.1 a) $^1$H NMR and b) $^{13}$C NMR spectra of product [3B.2.1p] (Table 3B.2.2, entry 16)
Figure 3B.5.4.2 a) $^1$H NMR and b) $^{13}$C NMR spectra of product [3B.2.1r] (Table 3B.2.2, entry 18)
Figure 3B.5.4.3 a) $^1$H NMR and b) $^{13}$C NMR spectra of product [3B.2.1v] (Table 3B.2.2, entry 22)
Figure 3B.5.4.4 a) $^1$H NMR and b) $^{13}$C NMR spectra of product [3B.2.1x] (Table 3B.2.2, entry 24)
Figure 3B.5.4.5 a) $^1$H NMR and b) $^{13}$C NMR spectra of product [3B.2.2e] (Table 3B.2.3, entry 5)
3B.5.5 Detailed analysis data of the X-ray crystal structure (ORTEP diagram given in Figure 3B.2.1)

Compound 3B.2.1v: Empirical formula C15 H13 Br Cl2 N2 O S, M = 420.14, pale yellow crystal, Crystal size 0.54 x 0.48 x 0.24 mm³, a = 7.9139(6) Å, b = 10.6279(8) Å, c = 11.2603(6) Å, Crystal system Triclinic, α = 104.140(5)° β = 109.812(6)° γ = 102.602(6)°, Volume = 815.65(10) Å³, ρcalc = 1.711 Mg/m³, μ = 2.977 mm⁻¹, Z = 2, Space group P -1, λ = 0.71073 Å, T = 200(2) K, Reflections collected 13510, 6369 [R(int) = 0.0292], F(000) = 420, Theta range for data collection 4.60 to 34.67°, Index ranges -11<=h<=12, -15<=k<=16, -17<=l<=17, Completeness to theta = 25.00° 99.0 %, Absorption correction Semi-empirical from equivalents, Max. and min. transmission 1.00000 and 0.63854, Refinement method Full-matrix least-squares on F², Data / restraints / parameters 6369 / 0 / 201, Goodness-of-fit on F² 0.911, Final R indices [I>2sigma(I)] R1 = 0.0344, wR2 = 0.0731, R indices (all data) R1 = 0.0758, wR2 = 0.0792, Largest diff. peak and hole 0.580 and -0.633 e.Å⁻³. CCDC 695339 contains the crystallographic data of compound 3B.2.1v.
3B.6 References


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