SECTION-I

SOLID-SUPPORTED MULTICOMPONENT CONDENSATION:
SYNTHESIS OF HIGHLY FUNCTIONALIZED PIPERIDINES ON THE
SURFACE OF SILICA GEL
II.1.1 INTRODUCTION

The highly functionalized piperidines are widely distributed in many natural products, biologically active molecules and organic fine chemicals. Compounds containing piperidine structural motif exhibit anti-hypertensive, anti-bacterial, anticonvulsant and anti-inflammatory activities. They are also involved in mono-amino oxidase (MAO) based mechanism in Parkinson’s disease, and as inhibitors of farnesyl transferase, and dihydroorotate Dehydrogenase. Recently, piperidine scaffolds are also important as part of the active ingredient in a number of commercially available drugs such as donepezil (used for the treatment of Alzheimer’s disease), Naratriptan (used for the treatment of migraine headaches), Sertindole and Risperidone (both used for the treatment of schizophrenia) (Fig 1).

![Chemical structures of established drugs](image)

**Fig 1.** Established drugs containing 1,4-disustituted piperidine framework.

Thus, enormous uses of this scaffold have prompted significant efforts towards the synthesis of functionalized piperidines. A brief review on the preparation of highly functionalized piperidines is discussed below.
II.1.2 SYNTHESIS OF HIGHLY FUNCTIONALIZED PIPERIDINES: A BRIEF REVIEW

In literature, various conventional multistep and low yielding methods have been reported for the synthesis of highly functionalized piperidines such as imino Diels–Alder reactions,\textsuperscript{19} intramolecular Michael reaction,\textsuperscript{20} intramolecular Mannich reactions ontoiminium ions,\textsuperscript{21} tandem cyclopropane ring-opening/Conia-ene cyclizations\textsuperscript{22} and aza-Prins-cyclization.\textsuperscript{23} Recently, a few one-pot syntheses of polysubstituted 1,2,5,6-tetrahydropyridines by the component condensation reaction of aromatic aldehyde, amine (both aliphatic and aromatic) and $\beta$-keto ester using MCRs strategy has been reported.

In 2007, Paul A. Clarke \textit{et al}\textsuperscript{24} developed a five-component condensation reaction for the formation of highly substituted piperidines. The procedure involves mixing methyl acetoacetate, 2 equiv of aldehyde and 2 equiv of aniline together in the presence of InCl$_3$ under acetonitrile solvent at room temperature (scheme 1).

\begin{center}
\begin{tikzpicture}
\node (A) at (0,0) {CHO};
\node (B) at (1,0) {NH$_2$};
\node (C) at (2,0) {O \hspace{0.5cm} OR};
\node (D) at (3,0) {InCl$_3$ (15 mol\%)};
\draw (A) -- (B);
\draw (B) -- (C);
\draw (C) -- (D);
\end{tikzpicture}
\end{center}

\textbf{Scheme 1}

They have studied the relative stereochemistry of the 2,6-phenyl groups in piperidine and it was confirmed as \textit{trans} by single crystal X-ray analysis. They have investigated the scope of the reaction and brief results are displayed in Table 1. Aliphatic aldehydes and benzylamine did not afford the corresponding piperidines under the present reaction conditions.
Table 1. Synthesis of functionalized piperidines by InCl$_3$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar$^1$CHO</th>
<th>Ar$^2$NH$_2$</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4-CH$_3$C$_6$H$_4$</td>
<td>4-MeOC$_6$H$_4$</td>
<td>45</td>
</tr>
<tr>
<td>2</td>
<td>2-CH$_3$C$_6$H$_4$</td>
<td>4-MeOC$_6$H$_4$</td>
<td>27</td>
</tr>
<tr>
<td>3</td>
<td>4-CH$_3$C$_6$H$_4$</td>
<td>Ph</td>
<td>50</td>
</tr>
<tr>
<td>4</td>
<td>Ph</td>
<td>Ph</td>
<td>60</td>
</tr>
<tr>
<td>5</td>
<td>2-CH$_3$C$_6$H$_4$</td>
<td>Ph</td>
<td>16</td>
</tr>
<tr>
<td>6</td>
<td>4-MeOC$_6$H$_4$</td>
<td>4-ClC$_6$H$_4$</td>
<td>52</td>
</tr>
</tbody>
</table>

In 2008, Abu T. Khan and his co-workers$^{25}$ demonstrated a multicomponent reaction for the synthesis of highly functionalized piperidines mediated by bromodimethylsulfonium bromide at room temperature. Aromatic aldehydes bearing substituents such as Cl, Me, and OMe as well as NO$_2$ were treated with aniline and methyl acetoacetate under the standard reaction conditions and the corresponding products were obtained in good to moderate yields. Benzyl amine and butyl amine took part in this multicomponent reaction to provide the corresponding piperidine derivatives in low to moderate yields (scheme 2).

Scheme 2

Rama Pati Tripathi et al$^{26}$ developed a metal free, atom economic organocatalytic multicomponent synthesis of highly functionalized piperidines. The method consists of the reaction of aromatic aldehydes, anilines, and a $\beta$-keto ester under the influence of L-proline/TFA (20 mol% each) as organocatalyst under acetonitrile as solvent (scheme 3).

Scheme 3
The synthesized compounds were screened against Plasmodium falciparum in vitro and they have showed antimalarial activity with MIC as low as 0.09 lg/mL.

The most probable reaction mechanism (Fig 2) they explained, involves the initial formation of an imine A and a Knoevenagel adduct C formed through proline catalysed enamine B mediated reaction. Mannich type reaction of aniline with Knoevenagel adduct C results an intermediate enamine D which undergoes Aza Diels-Alder cyclization with imine A and results the desired piperidine E.
In 2010, Abu T. Khan and his group used Tetrabutylammonium tribromide (TBATB) as catalyst for the one-pot synthesis of highly substituted piperidines through a combination of 1,3-dicarbonyl compounds, aromatic aldehydes, and various amines in ethanol at room temperature (scheme 4).

Several solvents were screened prior to concluding ethanol as the best solvent as shown in Table 2.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Catalyst</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CH₃CN</td>
<td>No catalyst</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>CH₃CN</td>
<td>5</td>
<td>12</td>
<td>52</td>
</tr>
<tr>
<td>3</td>
<td>CH₃CN</td>
<td>10</td>
<td>12</td>
<td>72</td>
</tr>
<tr>
<td>4</td>
<td>CH₃CN</td>
<td>20</td>
<td>12</td>
<td>69</td>
</tr>
<tr>
<td>5</td>
<td>CH₂Cl₂</td>
<td>10</td>
<td>12</td>
<td>60</td>
</tr>
<tr>
<td>6</td>
<td>C₂H₅OH</td>
<td>10</td>
<td>10</td>
<td>78</td>
</tr>
<tr>
<td>7</td>
<td>CH₃OH</td>
<td>10</td>
<td>8</td>
<td>84</td>
</tr>
<tr>
<td>8</td>
<td>EtOAc</td>
<td>10</td>
<td>12</td>
<td>62</td>
</tr>
<tr>
<td>9</td>
<td>Neat</td>
<td>10</td>
<td>12</td>
<td>48</td>
</tr>
</tbody>
</table>

Various aromatic aldehydes containing substituents in the aromatic ring such as OMe, Cl, Br, and NO₂ and Several aliphatic and aromatic amines were examined to study the generality and scope of the present protocol. All these reactions underwent to provide the corresponding piperidine derivatives in moderate to good yields. Some of the aldehydes such as β-naphthaldehyde and n-butanal did not give their corresponding functionalized piperidines under the present reaction conditions.
In the same year, Abu T. Khan et al\textsuperscript{28} again reported a one-pot multicomponent reaction (MCR) for the synthesis of highly functionalized piperidines catalyzed by molecular iodine. This strategy demonstrated five-component reactions of 1,3-dicarbonyl compounds, amines and aromatic aldehydes in methanol using 10 mol \% of iodine at room temperature. Various types of \( \beta \)-keto ester such as methyl acetoacetate, ethyl acetoacetate, \textit{tert}-butyl acetoacetate and allyl acetoacetate reacted to provide the corresponding piperidine derivatives in good yields under the present reaction conditions. From these observations, they have concluded that the alkoxy (-OR) moiety present in the \( \beta \)-keto ester does not have any significant role in determining the course of the reaction (scheme 5).

\textbf{Scheme 5}

An one-pot synthesis of functionalized tetrahydropyridines by a multicomponent condensation reaction of \( \beta \)-keto ester, two equivalents of aromatic aldehyde, and two equivalents of amine in the presence of a catalytic amount of cerium ammonium nitrate (CAN) was reported by Zhan-Hui Zhang et al\textsuperscript{29} (scheme 6).

\textbf{Scheme 6}

Various potential catalysts were tested for the direct synthesis of tetrahydropyridines by the model reaction of 4-methylbenzaldehyde (2 mmol), aniline (2 mmol), and methyl acetoacetate (1 mmol) in acetonitrile at room temperature, with results listed in Table 3. CAN was proved to be superior catalyst.
Table 3. Effect of different catalysts

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Reaction Time(h)</th>
<th>Yield(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>none</td>
<td>30</td>
<td>trace</td>
</tr>
<tr>
<td>2</td>
<td>HClO₄/SiO₂</td>
<td>50</td>
<td>60</td>
</tr>
<tr>
<td>3</td>
<td>p-toluenesulfonic acid</td>
<td>50</td>
<td>58</td>
</tr>
<tr>
<td>4</td>
<td>phosphotungstic acid</td>
<td>50</td>
<td>65</td>
</tr>
<tr>
<td>5</td>
<td>(NH₄)₃PMo₁₂O₄₀.6H₂O</td>
<td>50</td>
<td>41</td>
</tr>
<tr>
<td>6</td>
<td>Mg(ClO₄)₂</td>
<td>50</td>
<td>40</td>
</tr>
<tr>
<td>7</td>
<td>LiClO₄.3H₂O</td>
<td>50</td>
<td>35</td>
</tr>
<tr>
<td>8</td>
<td>ZrOCl₂.8H₂O</td>
<td>50</td>
<td>45</td>
</tr>
<tr>
<td>9</td>
<td>ZrO(NO₃)₂</td>
<td>50</td>
<td>72</td>
</tr>
<tr>
<td>10</td>
<td>Co(NO₃)₂.6H₂O</td>
<td>50</td>
<td>68</td>
</tr>
<tr>
<td>11</td>
<td>(NH₄)₄Ce(SO₄)₄.2H₂O</td>
<td>50</td>
<td>42</td>
</tr>
<tr>
<td>12</td>
<td>CAN</td>
<td>50</td>
<td>85</td>
</tr>
</tbody>
</table>

Model reaction: 4-Methylbenzaldehyde, Aniline, and Methyl Acetoacetate

The scope and limitations of this five-component reaction under optimized conditions were explored using a variety of aldehydes, amines, and β-keto esters.

ZrOCl₂.8H₂O catalyzed highly diastereoselective efficient one-pot synthesis of functionalized piperidines from reactions of aromatic aldehydes, amines, and acetoacetic esters in refluxing ethanol have been described by S. Mishra and R. Ghosh in 2011. ZrOCl₂.8H₂O was recovered from the reaction mixture and was reused for subsequent reactions (scheme 7).

\[
\begin{align*}
\text{CHO} + \text{NH}_2 + \text{O} \xrightarrow{\text{ZrOCl}_2, 8 \text{H}_2\text{O}} \text{OR} \\
\text{EtOH, Reflux 3-7 hrs}
\end{align*}
\]

Scheme 7

In the same year, C. Mukhopadhyay and her group reported the formation of a syn-diastereoisomer in the diastereoselective synthesis of highly functionalized piperidines catalysed by wet picric acid via a one-pot condensation of aromatic aldehydes, 1,3-dicarboxylic esters.
compounds and aromatic amines. They established the conditions for getting pure anti and pure syn compounds. After DFT calculation, they have showed that anti isomers are more stable compared to the syn. A variety of solvents were tested to find out the best solvent for this transformation. Among dichloromethane, acetonitrile, methanol and water, the use of a mixture of methanol–water (60:40) (v/v) was found to give the best result (scheme 8).

The syn–anti ratio of the products depends on the temperature and the nature of substitution on both the aromatic aldehydes and aromatic amines as shown in Table 4.

### Table 4. Results for the reactions among aromatic amines, aromatic aldehydes, and b-dicarbonyl compounds with picric acid

<table>
<thead>
<tr>
<th>Entry</th>
<th>R₁</th>
<th>R₂</th>
<th>R₃</th>
<th>syn:anti at 5–8°C</th>
<th>syn:anti at 25–28°C</th>
<th>syn:anti at 65–70°C</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4-Cl</td>
<td>H</td>
<td>OEt</td>
<td>100:0</td>
<td>46:54</td>
<td>0:100</td>
</tr>
<tr>
<td>2</td>
<td>4-Br</td>
<td>H</td>
<td>OMe</td>
<td>67:33</td>
<td>10:90</td>
<td>0:100</td>
</tr>
<tr>
<td>3</td>
<td>4-Br</td>
<td>H</td>
<td>OEt</td>
<td>42:58</td>
<td>24:76</td>
<td>0:100</td>
</tr>
<tr>
<td>4</td>
<td>3-NO₂</td>
<td>H</td>
<td>OEt</td>
<td>100:0</td>
<td>77:33</td>
<td>0:100</td>
</tr>
<tr>
<td>5</td>
<td>4-Br</td>
<td>H</td>
<td>O-allyl</td>
<td>80:20</td>
<td>31:69</td>
<td>0:100</td>
</tr>
<tr>
<td>6</td>
<td>4-NO₂</td>
<td>H</td>
<td>OMe</td>
<td>95:5</td>
<td>65:35</td>
<td>0:100</td>
</tr>
<tr>
<td>7</td>
<td>4-CN</td>
<td>H</td>
<td>OMe</td>
<td>67:33</td>
<td>10:90</td>
<td>0:100</td>
</tr>
<tr>
<td>8</td>
<td>3-NO₂</td>
<td>H</td>
<td>O-allyl</td>
<td>100:0</td>
<td>46:54</td>
<td>0:100</td>
</tr>
<tr>
<td>9</td>
<td>2-NO₂</td>
<td>H</td>
<td>OMe</td>
<td>20:80</td>
<td>5:95</td>
<td>0:100</td>
</tr>
<tr>
<td>10</td>
<td>4-Cl</td>
<td>4-Me</td>
<td>OEt</td>
<td>5:95</td>
<td>0:100</td>
<td>0:100</td>
</tr>
</tbody>
</table>
Bir Sain et al$^{32}$ presented a catalytic protocol for the synthesis of functionalized piperidines by the one-pot coupling of aldehyde, amine and β-keto ester with PEG-wrapped potassium tribromide ([K$^+$PEG]Br$^-_3$) as a recyclable catalyst. At the end of the reaction the [K$^+$PEG]Br$^-_3$ was readily regenerated from the reaction mixture by treating the residue containing [K$^+$PEG]Br$^-_3$ with molecular bromine (scheme 9).

![Scheme 9](image)

First time they have synthesized PEG-embedded tribromide through the concept of host–guest complexation$^{33}$ of PEGs with alkali metal cations, as shown in scheme 10. The developed catalyst (3) was readily prepared by the mixing of equimolar amounts of PEG-400 (1) and KBr to give [K$^+$PEG]Br$^-_3$ (2), which on subsequent reaction with Br$_2$ resulted in a dark orange-red colored viscous liquid. The liquid was dried under vacuum and used as such for the present synthesis. Poly(ethylene)glycols are well known to have similar structures to crown ethers and therefore they have assumed the structure of the [K+PEG]Br$^-_3$ as being similar to [18-crown-6]KBr$_3$.$^{34}$

![Scheme 10](image)

In 2012, G. Brahmachari et al$^{35}$ used Bi(NO$_3$)$_3$, 5H$_2$O as a catalyst for one-pot synthesis of functionalized piperidine derivatives via tandem reactions of 1,3-dicarbonyl compounds, aromatic aldehydes, and various amines in ethanol at room temperature (scheme 11).
Very recently, M. Alla and his group developed an efficient MCR protocol for the construction of polysubstituted THPs starting from aromatic aldehydes, substituted aromatic amines, and β-keto esters, and catalyzed by ZrCl₄ in ethanol at room temperature. They also have synthesized piperidin-4-one-3-carboxylates from the corresponding polysubstituted THPs by simple enamine hydrolysis under acidic conditions at ambient temperature with acetone as the solvent (scheme 12).

The reaction conditions have been optimized by using different solvents and catalyst loading and the results suggest that ethanol is the best solvent and 15 mol% ZrCl₄ is the ideal catalyst concentration required for effective conversion.
They also studied the antiproliferative activity of various THPs and piperidin-4-one-3-carboxylates in four human cancer cell lines: A549 (human epithelial lung carcinoma), DU145 (human prostate cancer), HeLa (human epithelial cervical cancer), and SK-N-SH (human neuroblastoma) and they have showed that Piperidin-4-one-3-carboxylates have better efficacy against four cancer cell lines relative to the THPs.

II.1.3 CONCLUSION

From the above short review of the projected synthesis, it is cleared that the synthesis of highly functionalized piperidines attracted considerable interest among the synthetic organic chemist even in recent year. All the reported methods have described their own advantages but most of these methodologies are not satisfactory in view of green chemistry by means of using large amounts of volatile solvents, toxic and less available catalysts, longer reaction times and lower yields. Thus we can claim that though, a variety of procedures have been developed for functionalized piperidines synthesis our observation in this area is also important and are discussed below.

II.1.4 OUR ADOPTED METHODOLOGY

During the last two decades, silica gel has been used in a number of useful synthetic transformations because of its improved efficiency (higher surface to volume ratio) under mild and environmentally benign conditions in the context of green chemistry. In continuation of our interest to develop environmentally benign surface-mediated methodologies under solvent-free and catalyst-free conditions, we became involved in developing a greener methodology for the synthesis of diastereospecific functionalized piperidines using various aldehydes, aromatic amines and β-keto esters on a solid surface of silica gel at room temperature (scheme 13).
To demonstrate the generality of this method, we examined the substrate scope of this reaction under the present reaction conditions which are summarized in Table 5. A wide range of substituted aldehydes and amines underwent condensation with the \( \beta \)-keto ester to produce diastereospecific functionalized piperidenes with complete \textit{anti}-configuration in an equimolecular mixture of two enantiomers. The relative stereochemistry of 2,6-aryl substituents in these products being \textit{trans} to each other was confirmed by comparing the spectroscopic data of the known compounds those reported earlier.\textsuperscript{24,25,26,31} Generally, it is found that NH proton of the \textit{anti} isomer appears at \( \delta \) 10.20 – 10.35 ppm whereas \textit{syn} isomer appears at \( \sim \) \( \delta \) 10.70 ppm.\textsuperscript{31} In addition, C\(_6\)-H proton of \textit{anti} and \textit{syn} isomer appears at \( \sim \) \( \delta \) 5.1 and 4.6 ppm respectively. Coupling constants of two C\(_5\)-H protons for \textit{anti} and \textit{syn} isomers are also different. Several sensitive functionalities such as -NO\(_2\), -OMe, halogen (Cl, Br) are unaffected under the present reaction conditions. The present method is also efficient for aliphatic amines (4n & 4o). Not only the methyl acetoacetate and ethyl acetoacetate but also tert-butyl acetoacetate (4s) reacted smoothly in this procedure to furnish the desired product. However, aliphatic aldehydes such as cyclohexanecarboxaldehyde and \( n \)-butyraldehyde were not productive under the present reaction conditions. These aldehydes produced a mixture of products whose identities are yet to be established. The methodology is also effective for large scale synthesis (87% for 4i; 50 mmol scale).

Recyclability of the silica was also studied and that is recyclable without loss of significant catalytic activity. After completion of the reaction, the reaction mixture was extracted with ethanol and the silica gel kept in the round bottom flask was washed with methanol and dried under vacuum and was reused for the subsequent reaction. In a typical experiment the silica was reused for three times (recovery amount, 98% and yield, 82% after 4\textsuperscript{th} run for 4a, Table 5).
### Table 5. Synthesized Products

<table>
<thead>
<tr>
<th>Compound</th>
<th>Reaction Time</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>2.5h</td>
<td>86%</td>
</tr>
<tr>
<td>4d</td>
<td>2.5h</td>
<td>84%</td>
</tr>
<tr>
<td>4e</td>
<td>3h</td>
<td>82%</td>
</tr>
<tr>
<td>4f</td>
<td>3.5h</td>
<td>83%</td>
</tr>
<tr>
<td>4g</td>
<td>4h</td>
<td>68%</td>
</tr>
<tr>
<td>4h</td>
<td>2h</td>
<td>91%</td>
</tr>
<tr>
<td>4i</td>
<td>2.5h</td>
<td>87%</td>
</tr>
<tr>
<td>4j</td>
<td>3.5h</td>
<td>85%</td>
</tr>
<tr>
<td>4k</td>
<td>2h</td>
<td>74%</td>
</tr>
<tr>
<td>4l</td>
<td>4h</td>
<td>75%</td>
</tr>
<tr>
<td>4m</td>
<td>2.5h</td>
<td>77%</td>
</tr>
<tr>
<td>4n</td>
<td>4h</td>
<td>79%</td>
</tr>
<tr>
<td>4o</td>
<td>7h</td>
<td>68%</td>
</tr>
<tr>
<td>4p</td>
<td>2.5h</td>
<td>87%</td>
</tr>
<tr>
<td>4q</td>
<td>2.5h</td>
<td>84%</td>
</tr>
<tr>
<td>4r</td>
<td>3h</td>
<td>85%</td>
</tr>
<tr>
<td>4s</td>
<td>3.5h</td>
<td>82%</td>
</tr>
</tbody>
</table>
A plausible mechanism for the formation of piperidines is outlined in Fig 3. Initially imine and enamine are formed by the coupling of amine with aldehyde and β-keto ester respectively on the surface of silica\textsuperscript{40}. Through intermolecular Mannich-type reaction imine and enamine gives intermediate 7 which reacts with another molecule of aldehyde and gives intermediate 8. Due to the intramolecular hydrogen bonding intermediate 8 is in tautomerization with 9 or 10. The tautomer 10 readily gives intermediate 11 by intramolecular Mannich-type reaction. Intermediate 11 forms the highly substituted piperidine through tautomerization because of the presence of a conjugated double bond with the ester group. The vital role of silica gel may be explained in the way that the presence of microscopic pores provides a typical surface area to the starting materials to come in close contact to interact each other very well and thus enhance the rate of the reaction. Generally the silica gel is weakly acidic in nature\textsuperscript{41} due to the presence of water in it as a form of silicic acid. Surprisingly the reaction did not proceed at all in absence of silica gel which supports our observations on the mechanism.
Fig 3
II.1.5 CONCLUSION

In summary, a very convenient and efficient procedure has been developed for the synthesis of functionalized piperidines on the surface of silica gel. Absence of unwanted products, general applicability, reusability of the silica gel, non chromatographic purification procedure, green synthesis avoiding toxic reagents and solvent, improved and operational simplicity make this protocol a useful, greener, cost effective and practical for both academic as well as industrial purposes.

II.1.6 EXPERIMENTAL

General: Melting points were determined on a glass disk with an electrical bath and are uncorrected. $^1$H NMR (400 MHz) and $^{13}$C NMR (100 MHz) spectra were run in CDCl$_3$ solutions. Coupling constants are given in Hz and the signals were reported as s (singlet), d (doublet), t (triplet), m (multiplet). IR spectra were taken as KBr plates in a Shimadzu 8400S FTIR. All liquid reagents were distilled before use. Thin layer chromatography was done on silica gel coated glass slide (Merck, Silica gel G for TLC). Commercially available substrates were freshly distilled before the reaction. Solvents, reagents and chemicals were purchased from Aldrich, Fluka, Merck, SRL, Spectrochem and Process Chemicals. All reactions involving moisture sensitive reactants were executed using oven dried glassware. All reactions were carried out in oven-dried glassware with magnetic stirring.

General procedure for the synthesis of piperidine: To an commercially available silica gel (for TLC, 2 g), amine (2 mmol), $\beta$-ketoester (1 mmol) and followed by aldehyde (2 mmol) were added successively. The mixture was stirred at room-temperature for 2-7 hours. After completion of the reaction (TLC), the reaction mixture was eluted with ethanol. Evaporation of solvent furnished the crude product which was recrystallized from hot ethanol to obtain the pure product as crystalline solid. Here the spectral data, mp of piperidine derivatives presented in order of their entries in Table 5 are provided below for the ready references.
1-Phenyl-4-phenylamino-2,6-di-\textit{p}-tolyl-1,2,5,6-tetrahydro-pyridine-3-carboxylic acid methyl ester (4a):

![Chemical structure of 1-Phenyl-4-phenylamino-2,6-di-\textit{p}-tolyl-1,2,5,6-tetrahydro-pyridine-3-carboxylic acid methyl ester (4a)](image)

White solid; m.p. 211-213 °C;

IR (KBr): 1259, 1515, 1593, 1652, 2363, 2867, 3203, 3261 cm\(^{-1}\);

\( ^1\text{H} \) NMR (400 MHz, CDCl\(_3\)): \( \delta \) 2.34 (s, 3H), 2.36 (s, 3H), 2.78 (dd, \( J = 15.2, 2.4 \) Hz, 1H), 2.89 (dd, \( J = 14.8, 5.6 \) Hz, 1H), 3.95 (s, 3H), 5.13 (s, 1H), 6.33 (d, \( J = 8.0 \) Hz, 2H), 6.34 (s, 1H), 6.55 (d, \( J = 8.4 \) Hz, 2H), 6.61 (t, \( J = 7.2 \) Hz, 1H), 7.05-7.14 (m, 11H), 7.22 (d, \( J = 8.0 \) Hz, 2H), 10.27 (s, 1H);

\( ^{13}\text{C} \) NMR (100 MHz, CDCl\(_3\)): \( \delta \) 20.9, 21.0, 33.6, 50.9, 54.9, 57.8, 98.0, 112.8, 115.9, 125.6, 125.7, 126.2, 126.5, 128.7, 128.8, 128.9, 129.2, 135.7, 136.5, 137.9, 139.6, 140.9, 147.0, 156.2, 168.5.

2,6-Bis-(4-methoxy-phenyl)-1-phenyl-4-phenylamino-1,2,5,6-tetrahydro-pyridine-3 carboxylic acid methyl ester (4b):

![Chemical structure of 2,6-Bis-(4-methoxy-phenyl)-1-phenyl-4-phenylamino-1,2,5,6-tetrahydro-pyridine-3 carboxylic acid methyl ester (4b)](image)

White crystalline solid; m.p. 179-180 °C;

IR (KBr): 1253, 1443, 1507, 1599, 1655, 2369, 2917, 3424 cm\(^{-1}\);

\( ^1\text{H} \) NMR (400 MHz, CDCl\(_3\)): \( \delta \) 2.79 (dd, \( J = 15.2, 2.4 \) Hz, 1H), 2.88 (dd, \( J = 15.2, 5.6 \) Hz, 1H), 3.80 (s, 3H), 3.82 (s, 3H), 3.95 (s, 3H), 5.11 (s, 1H), 6.38-6.40 (m, 3H), 6.55-6.65 (m, 3H), 6.83-6.85 (m, 4H), 7.07-7.17 (m, 6H), 7.23-7.28 (m, 2H), 10.30 (s, 1H);
\[ ^{13} \text{C NMR (100 MHz, CDCl}_3 \text{): } \delta 33.6, 50.9, 54.7, 55.2, 57.4, 98.0, 112.8, 113.5, 113.9, 115.9, 125.6, 125.7, 127.3, 127.6, 128.8, 134.5, 135.7, 137.8, 146.9, 156.3, 157.9, 158.6, 168.5. \]

2,6-Bis-(4-chloro-phenyl)-1-phenyl-4-phenylamino-1,2,5,6-tetrahydro-pyridine-3-carboxylic acid methyl ester (4c)²⁹:

Light yellow solid; m.p. 220-222 °C;
IR (KBr): 1251, 1449, 1499, 1593, 1658, 3440 cm⁻¹;
\[ ^1 \text{H NMR (400 MHz, CDCl}_3 \text{): } \delta 2.78 (dd, J = 15.2, 2.4 Hz, 1H), 2.85 (d, J = 5.6 Hz, 1H), 3.96 (s, 3H), 5.13 (s, 1H), 5.40 (d, J = 8.4 Hz, 2H), 5.68 (t, J = 7.2 Hz, 1H), 7.08-7.22 (m, 7H), 7.26-7.27 (m, 6H), 10.2 (s, 1H); \]
\[ ^{13} \text{C NMR (100 MHz, CDCl}_3 \text{): } \delta 33.6, 51.1, 54.6, 57.3, 97.4, 112.8, 116.7, 125.7, 126.0, 127.7, 127.9, 128.3, 128.7, 128.9, 132.0, 132.8, 137.5, 140.8, 142.2, 146.3, 155.9, 168.2. \]

2,6-Bis-(4-bromo-phenyl)-1-phenyl-4-phenylamino-1,2,5,6-tetrahydro-pyridine-3-carboxylic acid methylester (4d)²⁷:

Light yellow solid; m.p. 242-244 °C;
IR (KBr): 1246, 1450, 1493, 1592, 1657, 3441 cm⁻¹;
\[ ^1 \text{H NMR (400 MHz, CDCl}_3 \text{): } \delta 2.79 (d, J = 2.4 Hz, 1H), 2.84 (dd, J = 5.6 Hz, 1H), 3.95 (s, 3H), 5.10 (s, 1H), 6.37 (s, 1H), 6.43 (d, J = 6.8 Hz, 2H), 6.48 (d, J = 8.4 Hz, 2H), 6.67 (t, J = 7.2 Hz, 1H), 7.02 (d, J = 8.4 Hz, 2H), 7.09-7.28 (m, 6H), 7.40-7.43 (m, 4H), 10.27 (s, 1H); \]
13C NMR (100 MHz, CDCl$_3$): δ 33.5, 51.1, 54.7, 57.3, 97.3, 112.8, 116.7, 117.2, 120.2, 120.9, 125.7, 126.0, 128.0, 128.3, 128.3, 128.6, 128.7, 128.9, 129.0, 131.3, 131.3, 131.6, 131.7, 137.5, 141.3, 142.8, 146.3, 155.9, 168.2.

2,6-Bis-(4-fluoro-phenyl)-1-phenyl-4-phenylamino-1,2,5,6-tetrahydro-pyridine-3-carboxylic acid methyl ester (4e)$^{27}$:

![Chemical Structure](image)

White solid; m.p. 192-194 °C;
IR (KBr): 1249, 1451, 1495, 1590, 1661, 3446 cm$^{-1}$;
$^1$H NMR (400 MHz, CDCl$_3$): δ 2.78 (dd, $J = 15.2, 2.4$ Hz, 1H), 2.86 (dd, $J = 15.2, 5.6$ Hz, 1H), 5.14 (s, 1H), 6.41-6.43 (m, 3H), 6.51 (d, $J = 8.4$ Hz, 2H), 6.67 (t, $J = 7.2$ Hz, 1H), 6.99 (t, $J = 8.8$ Hz, 4H), 7.09 -7.20 (m, 7H), 7.27-7.31 (m, 2H), 10.3 (s, 1H);
$^{13}$C NMR (100 MHz, CDCl$_3$): δ 33.7, 51.0, 54.5, 57.2, 97.7, 112.9, 114.8, 115.0, 115.3, 115.5, 116.5, 125.6, 125.9, 127.8, 128.0, 128.1, 128.9, 137.6, 138.0, 139.3, 146.5, 156.0, 160.7, 163.1, 168.3.

2,6-Bis-(3-nitro-phenyl)-1-phenyl-4-phenylamino-1,2,5,6-tetrahydro-pyridine-3-carboxylic acid methylester (4f)$^{27}$:

![Chemical Structure](image)

Light yellow solid; m.p. 183-184 °C;
IR (KBr): 1255, 1346, 1385, 1502, 1594, 1656, 3436 cm$^{-1}$;
**Chapter II**

**Section I**

$^1$H NMR (400 MHz, CDCl$_3$): δ 2.86 (d, $J = 5.6$ Hz, 2H), 4.00 (s, 3H), 5.35 (t, $J = 4.0$ Hz, 1H), 6.41-6.51 (m, 5H), 6.71 (t, $J = 7.2$ Hz, 1H), 7.08-7.18 (m, 5H), 7.43-7.53 (m, 3H), 7.68 (d, $J = 7.6$ Hz, 1H), 7.96 (s, 1H), 8.10-8.16 (m, 2H), 8.24 (s, 1H), 10.31 (s, 1H);

$^{13}$C NMR (100 MHz, CDCl$_3$): δ 33.7, 51.4, 55.8, 57.0, 96.7, 100.7, 113.0, 117.7, 121.4, 121.7, 121.8, 122.4, 122.5, 125.6, 126.5, 129.3, 129.6, 129.7, 132.9, 137.1, 144.4, 145.7, 146.2, 148.5, 148.6, 155.4, 167.9.

2,6-Bis-(4-nitro-phenyl)-1-phenyl-4-phenylamino-1,2,5,6-tetrahydro-pyridine-3-carboxylic acid methyl ester (4g)$^{27}$:

Yellow solid; m.p. 240-242 °C;

IR (KBr): 1253, 1349, 1381, 1502, 1593, 1660, 3356 cm$^{-1}$;

$^1$H NMR (400 MHz, CDCl$_3$): δ 2.88 (d, $J = 4.4$ Hz, 2H), 3.98 (s, 3H), 5.28-5.29 (m, 1H), 6.41-6.47 (m, 4H), 6.50 (s, 1H), 6.71 (t, $J = 6.8$ Hz, 1H), 7.06-7.09 (m, 2H), 7.18-7.22 (m, 3H), 7.30-7.32 (m, 2H), 7.52 (d, $J = 8.4$ Hz, 2H), 8.13-8.19 (m, 4H), 10.29 (s, 1H);

$^{13}$C NMR (100 MHz, CDCl$_3$): δ 33.7, 51.6, 55.3, 57.5, 96.8, 113.0, 117.8, 123.9, 124.1, 125.6, 126.6, 127.5, 127.7, 129.3, 129.5, 137.2, 145.9, 147.1, 147.4, 149.8, 151.6, 155.6, 168.0.

1-(4-Methyl-phenyl)-4-(4-methyl-phenylamino)-2,6-diphenyl-1,2,5,6-tetrahydro-pyridine-3-carboxylic acid methyl ester (4h)$^{29}$:

White solid; m.p. 218-219 °C;
IR (KBr): 1257, 1516, 1592, 1654, 2363, 3257 cm\(^{-1}\);

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 2.18 (s, 3H), 2.29 (s, 3H), 2.76 (dd, \(J = 15.2, 2.0\) Hz, 1H), 2.86 (dd, \(J = 15.2, 5.6\) Hz, 1H), 3.95 (s, 3H), 5.14 (s, 1H), 6.18 (d, \(J = 8.0\) Hz, 2H), 6.44-6.47 (m, 3H), 6.90 (t, \(J = 8.0\) Hz, 4H), 7.19-7.24 (m, 3H), 7.27-7.36 (m, 7H), 10.2 (br, 1H),

\(^1^3\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 20.0, 20.8, 33.5, 50.8, 55.1, 58.1, 97.4, 112.8, 125.0, 125.9, 126.1, 126.4, 126.6, 127.0, 128.1, 128.5, 129.4, 135.1, 135.6, 143.0, 144.2, 144.7, 156.6, 168.5.

2,6-Bis-(4-chloro-phenyl)-1-\(p\)-tolyl-4-\(p\)-tolylamino-1,2,5,6-tetrahydro-pyridine-3-carboxylic acid methyl ester (4i):

![Chemical Structure](image)

White solid; m.p. 210-212 °C;

IR (KBr): 1240, 1437, 1520, 1588, 1647, 2940, 3249 cm\(^{-1}\);

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 2.20 (s, 3H), 2.31 (s, 3H), 2.72-2.80 (m, 2H), 3.94 (s, 3H), 5.09 (s, 1H), 6.31 (d, \(J = 8.0\) Hz, 2H), 6.35 (s, 1H), 6.40 (d, \(J = 8.4\) Hz, 2H), 6.91 (d, \(J = 8.4\) Hz, 2H), 6.98 (d, \(J = 8.0\) Hz, 2H), 7.09 (d, \(J = 8.4\) Hz, 2H), 7.26-7.28 (m, 6H), 10.29 (s, 1H);

\(^1^3\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 20.2, 21.0, 33.7, 51.1, 54.9, 57.4, 97.1, 113.0, 125.8, 125.9, 127.9, 128.2, 128.4, 128.8, 129.7, 132.1, 132.8, 135.0, 136.0, 141.3, 142.8, 144.4, 156.4, 168.4
Chapter II

Section I

1-(4-Methoxy-phenyl)-4-(4-methoxy-phenylamino)-2,6-bis-(4-nitro-phenyl)-1,2,5,6-tetrahydro-pyridine-3-carboxylic acid methyl ester (4j):

Light yellow solid; m.p. 197-198 °C;
IR (KBr): 1246, 1462, 1512, 1597, 1660, 2949, 3224 cm\(^{-1}\);
Yield: 85%; \(^{1}\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 2.77-2.79 (m, 2H), 3.68 (s, 3H), 3.78 (s, 3H), 3.93 (s, 3H), 5.15 (t, \(J = 8.0\) Hz, 1H), 6.34-6.41 (m, 5H), 6.67-6.71 (m, 4H), 7.31 (d, \(J = 8.8\) Hz, 2H), 7.48 (d, \(J = 8.8\) Hz, 2H), 8.15 (dd, \(J = 8.8, 2.8\) Hz, 4H), 10.15 (br, 1H);
\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 33.5, 51.2, 55.4, 55.5, 56.1, 57.2, 98.5, 114.2, 114.7, 123.6, 123.8, 127.5, 127.5, 129.8, 140.1, 146.7, 147.2, 150.1, 151.7, 152.0, 156.0, 158.2, 168.0.

1-(4-Chloro-phenyl)-4-(4-chloro-phenylamino)-2,6-diphenyl-1,2,5,6-tetrahydro-pyridine-3-carboxylic acid methyl ester (4k):

White solid; m.p. 208-210 °C;
\(^{1}\)H NMR (400MHz, CDCl\(_3\)): 2.73 (dd, \(J = 14.8, 4.8\) Hz, 1H), 2.89 (dd, \(J = 15.1, 6.0\) Hz, 1H), 3.97 (s, 3H), 5.14 (s, 1H), 6.20 (d, \(J = 8.8\) Hz, 2H), 6.41 (s, 1H), 6.46 (d, \(J = 9.2\) Hz, 2H), 7.02 (d, \(J = 9.2\) Hz, 2H), 7.09 (d, \(J = 6.8\) Hz, 2H), 7.18 (d, \(J = 7.6\) Hz, 2H), 7.25-7.35 (m, 8H), 10.2 (s, 1H);
\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 33.4, 51.1, 55.2, 58.2, 98.4, 113.9, 121.2, 126.2, 126.4, 126.5, 127.0, 127.4, 128.3, 128.7, 128.8, 129.0, 131.4, 136.3, 142.2, 143.1, 145.4, 155.5, 168.4.

**1-(4-Bromo-phenyl)-4-(4-bromo-phenylamino)-2,6-di-p-tolyl-1,2,5,6-tetrahydro-pyridine-3-carboxylic acid ethyl ester (4l)**

White solid; m.p. 232-233 °C;
IR (KBr): 1253, 1489, 1587, 1607, 1655, 2949, 3241 cm\(^{-1}\);
\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 2.34 (s, 3H), 2.37 (s, 3H), 2.73 (dd, \(J = 15.2, 2.4\) Hz, 1H), 2.88 (dd, \(J = 15.2, 5.6\) Hz, 1H), 3.95 (s, 3H), 5.08 (d, \(J = 4.0\) Hz, 1H), 6.16 (d, \(J = 8.8\) Hz, 2H), 6.34 (s, 1H), 6.41 (d, \(J = 8.8\) Hz, 2H), 7.05 (d, \(J = 8.0\) Hz, 2H), 7.10-7.18 (m, 8H), 7.23 (d, \(J = 8.4\) Hz, 2H), 10.21 (s, 1H);
\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 20.9, 21.0, 33.4, 51.1, 55.0, 57.9, 98.6, 108.2, 114.5, 119.0, 126.1, 126.3, 127.2, 129.0, 129.4, 131.5, 131.9, 136.1, 136.9, 137.0, 139.0, 140.0, 145.9, 155.3, 168.4.

**1-(4-Chloro-phenyl)-4-(4-chloro-phenylamino)-2,6-bis-(4-methoxy-phenyl)-1,2,5,6-tetrahydro-pyridine-3-carboxylic acid methyl ester (4m)**

White solid; m.p. 198-200 °C;
IR (KBr): 1215, 1434, 1505, 1601, 1654, 2363, 2953, 3022, 3402 cm\(^{-1}\); 
\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 2.70 (dd, \(J = 15.2, 2\) Hz, 1H), 2.85 (dd, \(J = 15.2, 5.6\) Hz, 1H), 3.80 (s, 3H), 3.82 (s, 3H), 3.95 (s, 3H), 5.06 (s, 1H), 6.27-6.31 (m, 3H), 6.45 (d, \(J = 9.2\) Hz, 2H), 6.82-6.86 (m, 4H), 7.00-7.11 (m, 6H), 7.10 (d, \(J = 8.8\) Hz, 2H), 10.2 (s, 1H); 
\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 33.7, 51.2, 54.9, 55.3, 55.4, 57.7, 98.7, 113.8, 114.2, 114.3, 121.2, 127.1, 127.5, 127.7, 128.8, 129.1, 131.4, 134.1, 135.2, 136.6, 145.6, 155.8, 158.3, 159.0, 168.6.

1-Benzyl-4-benzylamino-2,6-di-\(p\)-tolyl-1,2,5,6-tetrahydro-pyridine-3-carboxylic acid methyl ester (4n)\(^27\):

![Chemical Structure](image)

Light yellow solid; m.p. 169-171 °C;
IR (KBr): 1229, 1453, 1599, 1649, 2945, 3024, 3278 cm\(^{-1}\);
\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 2.31 (s, 3H), 2.33 (s, 3H), 2.63-2.67 (m, 1H), 2.72-2.75 (m, 1H), 3.36 (d, \(J = 6.4\) Hz, 2H), 3.48 (s, 3H), 4.05 (dd, \(J = 11.2, 4.8\) Hz), 4.62 (m, 2H), 4.76 (s, 1H), 7.10 (t, \(J = 8.4\) Hz, 4H), 7.22-7.28 (m, 5H), 7.31-7.42 (m, 9H), 9.68 (t, \(J = 6.0\) Hz, 1H); 
\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 21.0, 21.0, 25.4, 46.1, 49.5, 50.3, 52.1, 58.0, 89.3, 126.6, 126.8, 127.1, 127.4, 128.0, 128.2, 128.6, 128.8, 128.9, 135.6, 136.5, 138.5, 138.9, 141.6, 158.7, 171.0.
1-Butyl-4-butylamino-2,6-di-p-tolyl-1,2,5,6-tetrahydro-pyridine-3-carboxylic acid methyl ester (4o)\(^27\):

![Chemical Structure](image)

Light Yellow solid; m.p. 160-162 °C;
IR (KBr): 1119, 1247, 1455, 1597, 1647, 2933, 3264 cm\(^{-1}\);
\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 0.81 (t, \(J = 7.2\) Hz, 3H), 1.00 (t, \(J = 7.2\) Hz, 3H), 1.10-1.30 (m, 1H), 1.30-1.40 (m, 1H), 1.47-1.69 (m, 6H), 2.14-2.15 (m, 1H), 2.31-2.35 (m, 7H), 2.54-2.62 (m, 2H), 3.29-3.37 (m, 2H), 3.57 (s, 1H), 3.87-3.89 (m, 1H), 4.95 (s, 1H), 7.08-7.12 (m, 4H), 7.19 (d, \(J = 8.0\) Hz, 2H), 7.33 (d, \(J = 8.0\) Hz, 2H), 9.23 (s, 1H);
\(^13\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 13.8, 14.0, 20.2, 20.3, 21.0, 25.3, 30.8, 32.3, 41.8, 44.5, 50.3, 52.2, 58.3, 87.8, 127.1, 128.2, 128.6, 128.7, 135.4, 136.1, 139.1, 142.2, 159.4, 171.1.

1,2,6-Triphenyl-4-phenylamino-1,2,5,6-tetrahydro-pyridine-3-carboxylic acid ethyl ester (4p)\(^25\):

![Chemical Structure](image)

White solid; m.p. 173-175 °C;
IR (KBr): 1250, 1065, 1501, 1593, 1653, 2982, 3052, 3244 cm\(^{-1}\);
\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.52 (d, \(J = 6.8\) Hz, 3H), 2.82 (d, \(J = 14.8\) Hz, 1H), 2.93 (dd, \(J = 15.2, 7.2\) Hz, 1H), 4.36-4.41 (m, 1H), 4.49-4.54 (m, 1H), 5.20 (s, 1H), 6.33 (d, \(J = 7.6\) Hz,
2H), 6.52 (s, 1H), 6.58 (d, \( J = 7.6 \text{ Hz} \), 2H), 6.66 (t, \( J = 7.2 \text{ Hz} \), 1H), 7.09-7.14 (m, 5H), 7.21-7.23 (m, 2H), 7.25-7.28 (m, 1H), 7.31-7.35 (m, 5H), 7.40 (d, \( J = 8.0 \text{ Hz} \), 2H), 10.35 (br, 1H);

\(^{13}\text{C} \text{ NMR} (100 \text{ MHz, CDCl}_3): \delta 14.7, 33.5, 55.0, 58.1, 59.6, 98.1, 112.9, 116.0, 125.6, 125.7, 126.2, 126.3, 126.5, 127.0, 128.1, 128.5, 128.7, 128.8, 137.8, 142.7, 143.9, 146.9, 156.0, 168.2

1-Phenyl-4-phenylamino-2,6-di-\( p \)-tolyl-1,2,5,6-tetrahydro-pyridine-3-carboxylic acid ethyl ester (4q)\(^{29}\):

![Structure of 1-Phenyl-4-phenylamino-2,6-di-\( p \)-tolyl-1,2,5,6-tetrahydro-pyridine-3-carboxylic acid ethyl ester (4q)]

White solid; m.p. 228-231 °C;

IR (KBr): 1247, 1503, 1597, 1653, 2979, 3241 cm\(^{-1}\);

\(^1\text{H} \text{ NMR (400 MHz, CDCl}_3): \delta 1.47-1.51 (m, 3H), 2.35 (s, 3H), 2.37 (s, 3H), 2.79 (dd, \( J = 14.8, 2.0 \text{ Hz} \), 1H), 2.90 (dd, \( J = 15.2, 5.6 \text{ Hz} \), 1H), 4.33-4.38 (m, 1H), 4.46-4.51 (m, 1H), 5.14 (s, 1H), 6.34 (d, \( J = 7.6 \text{ Hz} \), 2H), 6.44 (s, 1H), 6.56 (d, \( J = 8.0 \text{ Hz} \), 2H), 6.62 (t, \( J = 7.6 \text{ Hz} \), 1H), 7.07-7.15 (m, 11H), 7.25 (d, \( J = 8.0 \text{ Hz} \), 2H), 10.32 (s, 1H);

\(^{13}\text{C} \text{ NMR (100 MHz, CDCl}_3): \delta 14.7, 20.9, 21.0, 33.6, 54.8, 57.9, 59.5, 98.3, 112.8, 115.9, 125.4, 125.6, 126.2 126.5, 128.7, 128.8, 128.9, 139.2, 135.7, 136.5, 137.9, 139.6, 141.0, 147.0, 156.0, 168.2.

2,6-Diphenyl-1-\( p \)-tolyl-4-\( p \)-tolylamino-1,2,5,6-tetrahydro-pyridine-3-carboxylic acid ethyl ester (4r)\(^{36}\):

![Structure of 2,6-Diphenyl-1-\( p \)-tolyl-4-\( p \)-tolylamino-1,2,5,6-tetrahydro-pyridine-3-carboxylic acid ethyl ester (4r)]

White solid; m.p. 182-184 °C;
IR (KBr): 1243, 1595, 1649, 2358, 2977, 3417 cm⁻¹;

¹H NMR (400 MHz, CDCl₃): δ 1.38 (s, 3H), 2.24 (s, 3H), 2.25 (s, 3H), 2.70 (d, J = 2.4 Hz, 1H), 2.77 (d, J = 5.6 Hz, 1H), 4.24 (q, J = 8.0, 7.2 Hz, 1H), 4.37 (q, J = 7.2, 7.2 Hz, 1H), 5.03 (br, 1H), 6.21-6.23 (m, 2H), 6.33 (s, 1H), 6.44-6.46 (m, 2H), 6.96-7.03 (m, 12H), 7.13-7.15 (m, 2H), 10.21 (br, 1H);

¹³C NMR (100 MHz, CDCl₃): δ 14.8, 20.9, 21.0, 33.6, 54.8, 57.9, 59.6, 98.4, 112.9, 115.9, 125.5, 125.7, 126.3, 126.5, 128.7, 128.8, 128.9, 129.2, 135.7, 136.6, 138.0, 139.7, 141.0, 147.0, 156.0, 168.2.

1-Phenyl-4-phenylamino-2,6-di-p-tolyl-1,2,5,6-tetrahydro-pyridine-3-carboxylic acid tert-butyl ester (4s):**

![Structure](image)

White solid; m.p. 102-104 °C;

IR (KBr): 1252, 1501, 1593, 1650, 2924, 2977, 3245 cm⁻¹;

¹H NMR (400 MHz, CDCl₃): δ 1.68 (s, 9H), 2.35 (s, 6H), 2.79-2.84 (m, 2H), 5.12 (s, 1H), 6.33-6.39 (m, 3H), 6.55-6.62 (m, 3H), 7.00-7.30 (m, 13H), 10.29 (br, 1H);

¹³C NMR (100 MHz, CDCl₃): δ 20.9, 21.0, 28.7, 33.5, 55.2, 57.9, 79.8, 99.9, 112.8, 115.8, 125.1, 125.5, 126.3, 126.4, 128.6, 128.8, 129.1, 135.6, 136.5, 138.2, 139.7, 141.2, 147.1, 155.0, 168.1.
SOME IMPORTANT $^1$H & $^{13}$C NMR SPECTRA
REFERENCES


