6.1 Introduction

Aza-Michael addition has tremendous potential in organic synthesis since it provides an easy route to $\beta$-amino carbonyl derivatives such as synthesis of $\beta$-amino ketones, esters, nitriles or amides. $\beta$-Amino carbonyl derivatives are versatile intermediates for the synthesis of a variety of biologically important natural products, antibiotics, $\beta$-amino alcohols and other nitrogen-containing molecules. Over the past years researchers many different synthetic strategies have been established by the researchers for the synthesis of these $\beta$-amino carbonyl derivatives. Among these, Mannich reaction is one of the most powerful tools for the synthesis of $\beta$-amino carbonyl compounds, although its utility is restricted due to several drawbacks like low yield, harsh reaction conditions, long reaction time etc. Aza-Michael addition is the most efficient method of synthesizing these $\beta$-amino carbonyl derivatives. Aza-Michael adducts are extensively used in the synthesis of pharmaceutical intermediates, peptide analogues, antibiotics and other biologically active molecules and drugs.

6.2 Results and Discussion

Preliminary experiments were directed to investigate the catalytic action of the water extract of the ash of banana trunk (WEABT) on aza-Michael addition reaction. Benzyl amine and acrylonitrile were chosen as template substrates to carry out the initial reactions. Formation of desired addition product in excellent yield was observed when 1:1 molar ratio of benzylamine and acrylonitrile were stirred at room temperature for 10 minutes by employing 3 mL of the extract. Several trial and error reactions were performed to standardize the reaction conditions by employing the ash of banana trunk (ABT) in different solvents such as acetonitrile, THF, toluene, DMF, DCM and without solvent. It was observed that 3 mL WEABT was enough for catalyzing the reaction in terms of yield and duration. The reaction proceeded very slowly in absence of the catalyst (Table 6.1).
Table 6.1: Reaction condition optimization

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Solvent</th>
<th>Time (min)</th>
<th>Yield(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ABT (20 wt%)</td>
<td>None</td>
<td>10</td>
<td>68</td>
</tr>
<tr>
<td>2</td>
<td>ABT (20 wt%)</td>
<td>Acetonitrile</td>
<td>10</td>
<td>30</td>
</tr>
<tr>
<td>3</td>
<td>ABT (20 wt%)</td>
<td>THF</td>
<td>10</td>
<td>25</td>
</tr>
<tr>
<td>4</td>
<td>ABT (20 wt%)</td>
<td>Toluene</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>5</td>
<td>ABT (20 wt%)</td>
<td>DMF</td>
<td>10</td>
<td>25</td>
</tr>
<tr>
<td>6</td>
<td>ABT (20 wt%)</td>
<td>Water</td>
<td>10</td>
<td>85</td>
</tr>
<tr>
<td>7</td>
<td>WEABT (3 mL)c</td>
<td>-</td>
<td>10</td>
<td>96</td>
</tr>
</tbody>
</table>

*Reaction conditions: benzyl amine (1 mmol), acrylonitrile (1 mmol), ABT(20 wt%) in 3 mL of the solvent or 3 mL of WEABT.\(^{b}\) Isolated yield.\(^{c}\) Refer section 6.4.2

The catalytic efficiency of WEABT was compared to common bases like K\(_2\)CO\(_3\), Na\(_2\)CO\(_3\) and Lewis acids such as FeCl\(_3\).6H\(_2\)O and SnCl\(_4\) with results as shown in Table 6.2. It was observed that WEABT shows better catalytic activity as compared to K\(_2\)CO\(_3\), Na\(_2\)CO\(_3\), FeCl\(_3\).6H\(_2\)O and SnCl\(_4\).

Table 6.2: Effect of various catalysts on the model reaction of benzyl amine and acrylonitrile

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Yield(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>K(_2)CO(_3)</td>
<td>60</td>
</tr>
<tr>
<td>2</td>
<td>Na(_2)CO(_3)</td>
<td>52</td>
</tr>
<tr>
<td>3</td>
<td>FeCl(_3).6H(_2)O</td>
<td>55</td>
</tr>
<tr>
<td>4</td>
<td>SnCl(_4)</td>
<td>55</td>
</tr>
<tr>
<td>5</td>
<td>WEABT</td>
<td>96</td>
</tr>
</tbody>
</table>

*Reaction conditions: Benzylamine (1 mmol), acrylonitrile (1 mmol) and catalyst (20 wt%) of benzylamine in 3 mL water or 3 mL WEABT was stirred at room temperature for 10 minutes.\(^b\) Isolated yield
Scope and generality of the standard protocol was studied by performing reaction of various nitrogen nucleophiles such as primary, secondary and aromatic amines with a good number of electrophiles including Baylis-Hillman adducts (prepared according to the established protocol), the results are shown in Table 6.3. Both the primary and the secondary amines were transformed to the Michael product at room temperature with excellent yields. However, there was wide variation in the reaction time depending on the reactivity of the \( \alpha,\beta \)-unsaturated compounds. It was observed that when primary amine and alkene were taken in 1:2 molar ratio, bis-addition product was obtained along with mono-addition product. Weakly nucleophilic imidazole also participated in the reaction at room temperature giving satisfactory yield of the product. All alkenes including Baylis-Hillman adducts (Entry 6, 7, 13-6, 18-20, Table 6.3) reacted efficiently with the amines; however the steric effect of the substituted alkenes has an important role on the rate of the reaction. Chalcone reacted slowly than the unsubstituted alkene. Baylis-Hillman adducts having electron withdrawing group reacted faster than the adducts having electron releasing group. All the products were characterized by \(^1\text{H}, \, ^{13}\text{C-NMR} \) and mass spectral analysis.

**Table 6.3:** Aza-Michael addition of amines to various alkenes catalyzed by WEABT

<table>
<thead>
<tr>
<th>Entry</th>
<th>Amines (A)</th>
<th>( \alpha,\beta )-unsaturated compounds (B)</th>
<th>Product</th>
<th>Time (min)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>HO( \text{CH}_2\text{CH}_2\text{NH}_2 )</td>
<td>( \text{O} = \text{Me} )</td>
<td>HO( \text{CH}_2\text{CH}_2\text{NH} ) ( \text{O} = \text{Me} )</td>
<td>5</td>
<td>87</td>
</tr>
<tr>
<td></td>
<td>Chemical Structure</td>
<td>(CH₂=CHCH₂)₂NH</td>
<td>(H₂C=CHCH₂)₂N</td>
<td>Products</td>
<td>Yield (%)</td>
</tr>
<tr>
<td>---</td>
<td>--------------------</td>
<td>-----------------</td>
<td>----------------</td>
<td>----------</td>
<td>-----------</td>
</tr>
<tr>
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<td><img src="image2" alt="Structure" /></td>
<td><img src="image3" alt="Structure" /></td>
<td><img src="image4" alt="Structure" /></td>
<td>15 90</td>
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<tr>
<td>3</td>
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<td><img src="image6" alt="Structure" /></td>
<td><img src="image7" alt="Structure" /></td>
<td><img src="image8" alt="Structure" /></td>
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<tr>
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<td><img src="image10" alt="Structure" /></td>
<td><img src="image11" alt="Structure" /></td>
<td><img src="image12" alt="Structure" /></td>
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<td><img src="image18" alt="Structure" /></td>
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<td>8</td>
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<td><img src="image26" alt="Structure" /></td>
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<td>10 89</td>
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<tr>
<td>9</td>
<td><img src="image29" alt="Structure" /></td>
<td><img src="image30" alt="Structure" /></td>
<td><img src="image31" alt="Structure" /></td>
<td><img src="image32" alt="Structure" /></td>
<td>10 92</td>
</tr>
</tbody>
</table>
Chapter 6

10  
\[
\begin{array}{c}
\text{NH} \\
\text{H}
\end{array}
\quad
\begin{array}{c}
\text{O} \\
\text{Me}
\end{array}
\quad
\begin{array}{c}
\text{N} \\
\text{Me}
\end{array}
\quad
15 \\
90
\]

11  
\[
\begin{array}{c}
\text{NH} \\
\text{H}
\end{array}
\quad
\begin{array}{c}
\text{CN}
\end{array}
\quad
\begin{array}{c}
\text{N} \\
\text{Me}
\end{array}
\quad
10 \\
94
\]

12  
\[
\begin{array}{c}
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\end{array}
\quad
\begin{array}{c}
\text{CN}
\end{array}
\quad
\begin{array}{c}
\text{O}
\end{array}
\quad
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90
\]

13  
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\begin{array}{c}
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\quad
\begin{array}{c}
\text{OH} \\
\text{Me}
\end{array}
\quad
\begin{array}{c}
\text{OH} \\
\text{Me}
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\quad
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\]

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\text{OH} \\
\text{Me}
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\text{Me}
\end{array}
\quad
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90
\]

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\begin{array}{c}
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\text{OH}
\end{array}
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\begin{array}{c}
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\text{OH}
\end{array}
\quad
75 \\
89
\]

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\[
\begin{array}{c}
\text{N}
\end{array}
\quad
\begin{array}{c}
\text{Cl} \\
\text{OH}
\end{array}
\quad
\begin{array}{c}
\text{Cl} \\
\text{OH}
\end{array}
\quad
90 \\
90
\]
**Reaction conditions:** Amine (1 mmol) and Alkene (1 mmol) in 3 mL of WEABT were stirred at room temperature for the specified time.

\^Isolated yields.

The recyclability and reusability of WEABT under the standard protocol was also investigated by reacting benzylamine and acrylonitrile at room temperature. It was observed that WEABT can be reused up to 3\(^{rd}\) consecutive runs without significant loss in catalytic activity (Table 6.4). After the 1\(^{st}\) run, the reaction mixture was extracted with ethyl acetate and then the aqueous phase was separated and washed carefully with ethyl acetate. The aqueous phase was then reused for the 2\(^{nd}\) run. The yield of the product was found to be unchanged after 2\(^{nd}\) run. The same procedure was repeated for the consecutive runs as well. A visible deterioration in the yield was observed after 4\(^{th}\) run (Table 6.4).
Table 6.4 Recyclability of WEABT in aza-Michael addition

![Diagram of aza-Michael addition]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Run&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Time (min)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1&lt;sup&gt;st&lt;/sup&gt;</td>
<td>10</td>
<td>95</td>
</tr>
<tr>
<td>2</td>
<td>2&lt;sup&gt;nd&lt;/sup&gt;</td>
<td>10</td>
<td>92</td>
</tr>
<tr>
<td>3</td>
<td>3&lt;sup&gt;rd&lt;/sup&gt;</td>
<td>10</td>
<td>85</td>
</tr>
<tr>
<td>4</td>
<td>4&lt;sup&gt;th&lt;/sup&gt;</td>
<td>10</td>
<td>68</td>
</tr>
</tbody>
</table>

<sup>a</sup>Reaction conditions: Mixture of benzyl amine (1mmol), acrylonitrile (1 mmol) and WEABT was stirred at room temperature for 10 minutes.

<sup>b</sup>After completion of the reaction, the mixture was extracted with ethyl acetate and the aqueous phase thus obtained was used in the next run. Isolated yield

6.3 Conclusion

In conclusion, the present procedures provide efficient protocols for the synthesis of β-aminocarbonyl compounds via aza-Michael reaction. The notable features offered by these protocols are simple operation, mild, non-toxic and environment friendly reaction conditions, high yields of products and cost effectiveness.

6.4 Experimental

6.4.1 General information

All the commercially available reagents were used as received. IR spectra were recorded on a SHIMADZU infrared spectrometer as KBr pellets and the absorption expressed in cm<sup>-1</sup>. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded in CDCl<sub>3</sub> on 300 MHz Bruker NMR spectrometer at ≈ 25 °C using tetramethylsilane (TMS) as the internal standard, and resonances (δ) are given in ppm. Data are reported as follows: chemical shift (δ), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet signal), coupling constants (Hz) and integration. MS were obtained on Waters ZQ 4000 equipped with ESI source.
Melting points were determined using Veego VMP-D and uncorrected. All experiments were monitored on thin layer chromatography (TLC). TLC was performed on pre-coated silica gel G plates. After elution, plate was visualized under UV illumination or in iodine chamber. Column chromatography was performed on silica gel (60–120 mesh) using ethyl acetate:petroleum ether as the eluent.

6.4.2 Preparation of WEABT

In a beaker, 50g of ash of banana trunk (ABT) was taken in 500 mL of distilled water and the mixture was stirred at room temperature for 15 minutes. After 15 minutes, the resultant mixture was filtered and the filtrate was termed as Water Extract of Ash of Banana Trunk (WEABT).

6.4.3 General procedure for aza-Michael reaction using WEABT catalyst

In a round bottomed flask, a mixture of amine (1 mmol) and alkene (1 mmol) in 3 mL of WEABT with the heterogeneous catalyst was stirred at room temperature for the specified time. After completion of the reaction, the reaction mixture was extracted with ethyl acetate. The organic phase was separated, washed with brine and dried over anhydrous MgSO₄. The ethyl acetate extract was evaporated and the crude product thus obtained was purified by column chromatography or preparative TLC using ethyl acetate:petroleum ether as the eluent.

6.4.4 Spectral data of products

**Compound (Entry1, Table 6.3): 3-(2-Hydroxyethylamino)propionic acid methyl ester**

\[
\text{HOH-CH₂-CHN-OOME}
\]

Yield 87%; oily liquid; ¹H NMR (CDCl₃, 300 MHz) δH 3.70 (s, 3H), 3.64 (t, J = 5 Hz, 2H), 2.92 (t, J = 6.5 Hz, 2H), 2.80 (t, J = 5 Hz, 2H), 2.53 (t, J = 6.5 Hz, 2H), 2.08 (br s, 1H); ¹³C NMR (CDCl₃, 75 MHz) δC 172.0, 63.1, 52.6, 50.5, 44.3, 33.8; IR (thin film on KBr, cm⁻¹) 1439, 1626, 1732, 2954; MS (ESI, m/z) 148.2 (M⁺+1).
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Compound (Entry 2, Table 6.3): 3-(Benzy lamino)propanoic acid methyl ester

Yield 90%; colorless oily compound; $^1$H NMR (CDCl$_3$, 300 MHz) δ$_H$ 6.98-7.60 (m, 5H), 3.80 (s, 2H); 3.67 (s, 3H), 2.89 (t, J = 6.5 Hz, 2H); 2.57 (t, J = 9 Hz, 2H), 2.31 (brs, 1H); $^{13}$C NMR (CDCl$_3$, 75 MHz) δ$_C$ 172.9, 139.51, 128.15, 127.83, 126.75, 53.39, 51.37, 44.03, 34.08; IR (thin film on KBr, cm$^{-1}$) 772, 1173, 1197; 1454, 1735, 2952, 3027, 3418, 3027; MS (ESI, m/z: 194.3 (M$^+$+1)).

Compound (Entry 3, Table 6.3):

3-[Benzy(2-methoxylcarbonylylethyl)amino]propanoic acid methyl ester

Yield 87%; gummy compound; $^1$H NMR (CDCl$_3$, 300 MHz) δ$_H$ 3.64 (s, 6H), 3.80 (s, 2H), 2.79 (t, J = 7.1 Hz, 4H), 2.49 (t, J = 7.2 Hz, 4H); $^{13}$C NMR (CDCl$_3$, 75 MHz, CDCl$_3$) δ$_C$ 172.67, 138.67, 128.41, 127.91, 126.74, 57.98, 51.27, 48.83, 32.27; IR (thin film on KBr, cm$^{-1}$) 772, 1173, 1200, 1218, 1454, 1737, 2847, 2951, 3027; MS (ESI, m/z: 280.1 (M$^+$+1)).

Compound (Entry 4, Table 6.3): 3-(Benzy lamino)propanenitrile

Yield 96%; white solid; mp 47 °C; $^1$H NMR (CDCl$_3$, 300 MHz) δ$_H$ 7.34 (m, 5H), 3.85 (s, 2H), 2.97 (t, J = 6.3 Hz, 2H), 2.58 (t, J = 6.27 Hz, 2H), 1.69 (br s, 1H); $^{13}$C NMR (CDCl$_3$, 75 MHz) δ$_C$ 139.35, 128.59, 128.09, 127.33, 118.74, 53.18, 44.30, 18.78; IR (thin film on KBr, cm$^{-1}$) 772, 1173, 1197, 1454, 2420, 2952, 3027, 3418; MS (ESI, m/z) 161.8 (M$^+$+1).
Compound (Entry 5, Table 6.3): 3-(benzylamino)-1,3-diphenylpropan-1-one

Yield 84%; white solid; mp 47 °C; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta_H$ 8.41 (s, 1H), 7.80 (m, 15 H), 4.8 (s, 2H), 4.45 (t, $J = 6.27$ Hz, 1H), 3.9 (m, 2H); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta_C$ 195.53, 136.62, 136.09, 134.83, 133.90, 132.88, 130.63, 129.00, 128.88, 128.53, 128.50, 126.65, 56.51, 55.76, 44.24; IR (thin film on KBr, cm$^{-1}$) 772, 1173, 1197, 1454, 2420, 2952, 3027, 3418; MS (ESI, m/z) 316.13 (M$^+$+1).

Compound (Entry 6, Table 6.3):

2-(Benzylaminomethyl)-3-hydroxy-3-phenylpropanoic acid methyl ester

Yield 90%; white solid; mp 45 °C; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta_H$ 7.33-7.27 (m, 10H), 5.11 (d, $J = 6.3$ Hz, 1H), 3.8-3.7 (m, 1H), 3.75 (d, $J = 3.9$ Hz, 1H), 3.62 (s, 3H), 3.00-3.06 (m, 1H), 2.9 (s, 2H); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta_C$ 173.61, 141.75, 139.39, 128.54, 128.32, 124.24, 128.03, 127.63, 127.25, 74.98, 53.82, 51.76, 48.34; IR (thin film on KBr, cm$^{-1}$) 3425, 3313, 3066, 2912, 1728, 1597, 1446, 1269, 1026; MS (ESI, m/z) 299 (M$^+$).

Compound (Entry 7, Table 6.3):

2-(Benzylaminomethyl)-3-hydroxy-3-(p-nitrophenyl)propanoic acid methyl ester

Yield 92%; gummy semi solid; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta_H$ 8.06-8.19 (m, 4H), 7.25-7.57 (m, 5H), 5.68 (br s, 1H), 5.31 (d, $J = 4.2$ Hz, 1H), 3.4-3.8 (complex m, 8H); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta_C$ 171.97, 147.38, 138.65, 128.92, 128.79, 128.54, 128.49, 127.75, 73.05, 53.02, 52.40, 51.79; IR (thin film on KBr, cm$^{-1}$) 833, 1033, 1080, 1226, 1411, 1670, 3109, 3143, 3387; MS (ESI, m/z) 345 (M$^+$+1).
Compound (Entry 8, Table 6.3): 3-(Diallylamino)propionic acid methyl ester

![Image of 3-(Diallylamino)propionic acid methyl ester]

Yield 89%; colorless oil; \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta_H 5.77-5.83\) (m, 2H), 5.06-5.21 (t, \(J=6\) Hz, 2H), 3.67 (s, 3H), 3.11 (d, \(J=6\) Hz, 4H), 2.88 (t, \(J=6\) Hz, 2H), 2.38 (t, \(J=7.21\) Hz, 2H); \(^1^3\)C NMR (CDCl\(_3\), 75 MHz) \(\delta_C 172.79, 135.05, 117.36, 56.47, 51.28, 48.18, 31.95\); IR (thin film on KBr, cm\(^{-1}\)) 919, 1192, 1437, 1643, 1741, 2808, 2978, 3078; MS (ESI, m/z) 184.5 (M\(^+1\)).

Compound (Entry 9, Table 6.3): 3-(Diallylamino)propanenitrile

![Image of 3-(Diallylamino)propanenitrile]

Yield 92%; white solid; mp 49.5 °C; \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta_H 2.70\) (m, 2H), 2.54 (m, 4H), 1.59 (m, 4H), 1.47 (m, 2H); \(^1^3\)C NMR (CDCl\(_3\), 75 MHz) \(\delta_C 118.74, 57.98, 51.27, 48.83, 32.27, 18.78\); IR (thin film on KBr, cm\(^{-1}\)) 740, 1033, 1118, 1265, 1446, 2249, 2854, 2935; MS (ESI, m/z) 139 (M\(^+1\)).

Compound (Entry 10, Table 6.3): 3-(Piperidin-1-yl)propionic acid methyl ester

![Image of 3-(Piperidin-1-yl)propionic acid methyl ester]

Yield 90%; white solid; mp 106 °C; \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta_H 3.68\) (s, 3H), 2.70 (m, 2H), 2.55 (m, 2H), 40 (m, 4H), 1.60 (m, 6H); \(^1^3\)C NMR (CDCl\(_3\), 75 MHz) \(\delta_C 172.85, 53.90, 3.87, 51.35, 31.81, 25.48, 23.86\); IR (thin film on KBr, cm\(^{-1}\)) 775, 1026, 1190, 1247, 1600, 1745, 2924, 2950; MS (ESI, m/z) 172 (M\(^+1\)).

Compound (Entry 11, Table 6.3): 3-(Piperidin-1-yl)propanenitrile

![Image of 3-(Piperidin-1-yl)propanenitrile]

Yield 94%; white solid; mp 49.5 °C; \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta_H 2.70\) (m, 2H), 2.54 (m, 2H), 2.44 (m, 4H), 1.59 (m, 4H), 1.47 (m, 2H); \(^1^3\)C NMR (CDCl\(_3\), 75 MHz) \(\delta_C 118.74, 53.90, 3.87, 51.35, 31.81, 25.48, 23.86\); IR (thin film on KBr, cm\(^{-1}\)) 775, 1026, 1190, 1247, 1600, 1745, 2924, 2950; MS (ESI, m/z) 172 (M\(^+1\)).
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57.98, 51.27, 48.83, 32.27, 18.78; IR (thin film on KBr, cm\(^{-1}\)): 740, 1033, 1118, 1265, 1446, 2249, 2854, 2935; MS (ESI, m/z) 139 (M\(^+\)+1).

Compound (Entry 12, Table 6.3): 1,3-Diphenyl-3-(piperidin-1-yl)propan-1-one

![Structural formula](image)

Yield 90%; colorless oil; \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta_H 8.04-6.90\) (m, 10H), 3.76-4.01 (m, 2H), 2.56-2.67 (m, 2H), 1.90-2.18 (m, 4H), 1.61-1.99 (m, 6H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \(\delta_C 190.56, 139.35, 128.59, 127.3353.18, 44.30, 37.11, 25.52\); IR (thin film on KBr, cm\(^{-1}\)): 809, 1033, 1240, 1259, 1444, 1703, 2833, 2946, 3033; MS (ESI, m/z) 277 (M\(^+\)).

Compound (Entry 13, Table 6.3):

3-Hydroxy-3-phenyl-2-(piperidin-1-ylmethyl)propanoic acid methyl ester

![Structural formula](image)

Yield 87%; gummy semi solid; \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta_H 7.18-7.33\) (m, 5H), 4.95 (d, \(J= 9.3\) Hz, 1H), 3.64-3.67 (m, 1H), 3.35 (s, 3H), 2.95-3.08 (m, 2H), 2.5-2.7 (m, 4H), 1.4-1.7 (m, 5H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \(\delta_C 172.00, 128.16, 127.79, 127.71, 127.48, 72.85, 54.87, 49.86, 25.94, 25.85, 24.05\); IR (thin film on KBr, cm\(^{-1}\)): 819, 1040, 1195, 1302, 1436, 1736, 2851, 2930, 3396; MS (ESI, m/z) 277 (M\(^+\)).

Compound (Entry 14, Table 6.3):

3-Hydroxy-2-(piperidin-1-ylmethyl)-3-p-tolylpropanoic acid methyl ester

![Structural formula](image)

Yield 90%; yellowish solid; mp 70 °C; \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta_H 7.10-7.26\) (m, 4H), 4.92 (d, \(J=6\) Hz, 1H), 4.3 (m, 1H), 3.4 (s, 3H), 2.4-3.2 (complex m, 13H), 2.0 (s,
3H); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$C172.71, 137.39, 133.07, 129.64, 124.19, 69.14, 68.24, 58.10, 57.96, 55.10, 54.40, 50.38, 25.93, 25.13, 24.19; IR (thin film on KBr, cm$^{-1}$): 3439, 3112, 2946, 1743, 1636, 1443, 1229, 1240, 1033, 822, 809; MS (ESI, m/z) 292 (M$^+$+1).

**Compound (Entry15, Table 6.3):**

3-Hydroxy-3-(m-nitrophenyl)-2-(piperidin-1-ylmethyl)-propanoic acid methyl ester

![Chemical Structure](image1.png)

Yield 89%; gummy semi solid; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$h 8.28 (s, 1H), 8.17 (d, J=8.7 Hz, 1H), 7.71 (d, J=6.9 Hz, 1H), 7.53 (m, 1H), 5.04 (d, J=7.8 Hz, 1H), 4.61 (m, 1H), 4.35 (m, 2H), 3.51 (s, 3H), 3.5-3.0 (m, 8H), 3.04 (m, 4H), 0.88-0.82 (m, 6H); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$C172.71, 148.74, 137.39, 133.07, 129.64, 190.00, 124.19, 69.14, 51.78, 51.26, 25.93, 24.19; IR (thin film on KBr, cm$^{-1}$): 756, 1194, 1246, 1353, 1439, 1528, 1634, 1732, 2854, 2937, 3444; MS (ESI, m/z) 223 (M$^+$+1).

**Compound (Entry16, Table 6.3):**

3-(2,4-Dichlorophenyl)-3-hydroxy-2-(piperidin-1-ylmethyl)propanoic acid methyl ester

![Chemical Structure](image2.png)

Yield 90%; white solid; mp 110°C; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$h 7.25-7.52 (m, 3H), 5.44 (d, J=7.5 Hz, 1H), 3.53 (s, 3H), 3.38 (m, 1H), 3.2-2.4 (m, 7H); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$C172.71, 148.74, 137.39, 133.07, 129.64, 124.19, 58.10, 51.78, 51.26, 25.93, 24.19; IR (thin film on KBr, cm$^{-1}$): 756, 882, 1194, 1246, 1353, 1439, 1528, 1634, 1745, 2854, 2937, 3444; MS (ESI, m/z) 332 (M$^+$+1).
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Compound (Entry 17, Table 6.3): 3-(Imidazol-1-yl)-1,3-diphenylpropan-1-one

Yield 92%; white solid; mp 85 °C; \( ^1H \) NMR (CDCl\(_3\), 300 MHz) \( \delta \) 6.98-8.04 (complex m, 3H), 6.10 (t, \( J=6.32 \) Hz, 1H), 3.76-4.01 (m, 2H); \( ^{13}C \) NMR (CDCl\(_3\), 75 MHz) \( \delta \) 195.53, 144.95, 144.09, 139.35, 138.17, 136.62, 134.83, 133.90, 132.88, 126.65, 122.04, 56.51, 44.24; IR (thin film on KBr, cm\(^{-1}\)): 756, 833, 1080, 1226, 1273, 1411, 1454, 1710, 2924, 3055; MS (ESI, m/z) 277 (M\(^+\)+1).

Compound (Entry 18, Table 6.3):

3-Hydroxy-2-(imidazol-1-ylmethyl)-3-(4-nitrophenyl)propanoic acid methyl ester

Yield 89%; white solid; mp 168 °C; \( ^1H \) NMR (CDCl\(_3\), 300 MHz) \( \delta \) 8.12 (d, \( J=3.6 \) Hz, 2H), 8.09 (m, 3H), 6.87 (m, 2H), 6.75 (s, 1H) 4.89 (d, \( J=7.2 \) Hz, 1H), 4.44-4.12 (m, 3H), 4.20 (d, \( J=3.3 \) Hz, 2H), 3.11 (s, 3H); \( ^{13}C \) NMR (CDCl\(_3\), 75 MHz) \( \delta \) 175.76, 152.79, 132.04, 131.77, 128.24, 123.96, 59.54, 56.70, 44.99, 44.16; IR (thin film on KBr, cm\(^{-1}\)): 757, 856, 1080, 1223, 1244, 1353, 1446, 1514, 1514, 1634, 1737, 2851, 2959, 3112, 3426; MS (ESI, m/z) 305.99 (M\(^+\)+1).

Compound (Entry 19, Table 6.3):

3-(p-Chlorophenyl)-3-hydroxy-2-(imidazol-1-ylmethyl)propanoic acid methyl ester
Yield 88%; white solid; mp 136 °C; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$H 7.3-7.4 (m, 4H), 7.27 (m, 1H), 6.88-6.97 (m, 2H), 6.82 (d, $J$=12 Hz, 1H) 4.98 (d, $J$=6.72 Hz, 1H); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$C 175.76, 152.79, 132.04, 131.77, 128.24, 123.96, 59.54, 45.27, 44.99, 44.16; IR (thin film on KBr, cm$^{-1}$): 771, 826, 1089, 1209, 1334, 1437, 1490, 1509, 1732, 2849, 2952, 3119, 3391; MS (ESI, m/z) 295 (M$^+$+1).

**Compound (Entry 20, Table 6.3):** 3-(2,4-Dichlorophenyl)-3-hydroxy-2-(imidazol-1-ylmethyl) propanoic acid methyl ester

Yield 89%; white solid; mp 123 °C; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$H 6.88-7.92 (m, 6H), 5.44 (d, $J$=4.8 Hz, 1H), 5.14 (d, $J$= 4.7 Hz, 2H), 4.44-4.52 (m, 1H), 2.69-4.33 (m, 1H), 3.60 (s, 3H); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$C 171.35, 140.32, 137.93, 137.77, 137.09, 134.09, 133.45, 131.78, 129.22, 127.32, 68.86, 52.51, 52.07, 45.53; IR (thin film on KBr, cm$^{-1}$): 771, 826, 1089, 1209, 1334, 1437, 1490, 1509, 1732, 2849, 2952, 3119, 3391; MS (ESI, m/z) 328.9 (M$^+$+1).
Fig 6.1: $^1$H NMR spectra of 3-(Benzylamino)propanenitrile (Entry 2, Table 6.3)

Fig 6.2: $^{13}$C NMR spectra of 3-(Benzylamino)propanenitrile (Entry 2, Table 6.3)
Fig 6.2: $^1$H NMR spectra of 2-(Benzylaminomethyl)-3-hydroxy-3-phenylpropanoic acid methyl ester (Entry 6, Table 6.3)
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Figure 6.2: $^{13}$C NMR spectra of 2-(Benzylaminomethyl)-3-hydroxy-3-phenylpropanoic acid methyl ester (Entry 6, Table 6.3)

Fig 6.3: $^1$H NMR spectra of 3-Hydroxy-2-(imidazol-1-ylmethyl)-3-(4-nitrophenyl) propanoic acid methyl ester (Entry 18, Table 6.3)
Figure 6.3: $^{13}$C NMR spectra of 3-Hydroxy-2-(imidazol-1-ylmethyl)-3-(4-nitrophenyl) propanoic acid methyl ester (Entry 18, Table 6.3)

References: