CHAPTER III

Lithium Hydroxide Mediated Michael Addition of Dicarboxylic Acid Esters to $\alpha, \beta$-Unsaturated Ketones
CHAPTER III

Lithium Hydroxide Mediated Michael Addition of Dicarboxylic Acid Esters to \(\alpha,\beta\)-Unsaturated Ketones

III.1 Results and Discussion

III.1.1 Lithium hydroxide mediated Michael addition of dialkyl malonate to \(\alpha,\beta\)-unsaturated ketone

III.1.1.1 Lithium hydroxide mediated Michael addition of dimethyl malonate

As reviewed in Chapter I Michael addition of dimethyl malonate, mediated either by an acid or a base, to \(\alpha,\beta\)-unsaturated ketone has been reported by others but the same in the presence of lithium hydroxide could not be traced. We have examined here the efficiency of lithium hydroxide as a catalyst in ten different Michael addition reactions of dimethyl malonate to \(\alpha,\beta\)-unsaturated ketone under three different sets of reaction conditions viz. (i) ambient temperature in methanol, (ii) refluxing temperature in methanol and (iii) microwave irradiation without solvent.

Results of the reactions at ambient temperature are summarized in Table III.1. Moderate to high yield (64 to 88\%) could be achieved in 40 to 60 h. At refluxing temperature in methanol yields achieved virtually remains same but the reaction time can be substantially reduced (by about 20-25\%). Interestingly, reaction time is drastically reduced to about 5 to 10 min under microwave irradiation against 30 to 50 h at refluxing temperature in methanol, isolated yields practically remaining same in both the cases. If the three sets of reaction conditions are compared it appears that microwave irradiation definitely has distinct advantages over the other two processes as the former requires no solvent and reaction time is quite short. Purity of the product is also high making
chromatography easier. Microwave option is distinctly the greener option (no solvent used and power consumption is low).

Table III.1: Michael addition of dimethyl malonate (DMM) at ambient temperature

\[
\begin{align*}
\text{X} & \quad & \text{R} & \quad & \text{Time (h)} & \quad & \text{Yield (mol\%)} & \quad & \text{Product} \\
1 & H & Me & 40 & 88 & & & III.3a \\
2 & \alpha-OMe & Me & 40 & 68 & & & III.3b \\
3 & m-OMe & Me & 40 & 70 & & & III.3c \\
4 & p-OMe & Me & 40 & 76 & & & III.3d \\
5 & p-Cl & Me & 40 & 75 & & & III.3e \\
6 & H & Ph & 60 & 76 & & & III.3f \\
7 & \alpha-OMe & Ph & 60 & 64 & & & III.3g \\
8 & m-OMe & Ph & 60 & 65 & & & III.3h \\
9 & p-OMe & Ph & 60 & 71 & & & III.3i \\
10 & p-Cl & Ph & 60 & 72 & & & III.3j
\end{align*}
\]
Table III.2: Michael addition of dimethyl malonate (DMM) at refluxing temperature

![Reaction Scheme]

<table>
<thead>
<tr>
<th>Entry</th>
<th>X</th>
<th>R</th>
<th>Time (h)</th>
<th>Yield (mol%)</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H</td>
<td>Me</td>
<td>30</td>
<td>85</td>
<td>III.3a</td>
</tr>
<tr>
<td>2</td>
<td>o-OMe</td>
<td>Me</td>
<td>30</td>
<td>64</td>
<td>III.3b</td>
</tr>
<tr>
<td>3</td>
<td>m-OMe</td>
<td>Me</td>
<td>30</td>
<td>65</td>
<td>III.3c</td>
</tr>
<tr>
<td>4</td>
<td>p-OMe</td>
<td>Me</td>
<td>30</td>
<td>73</td>
<td>III.3d</td>
</tr>
<tr>
<td>5</td>
<td>p-Cl</td>
<td>Me</td>
<td>30</td>
<td>70</td>
<td>III.3e</td>
</tr>
<tr>
<td>6</td>
<td>H</td>
<td>Ph</td>
<td>50</td>
<td>74</td>
<td>III.3f</td>
</tr>
<tr>
<td>7</td>
<td>o-OMe</td>
<td>Ph</td>
<td>50</td>
<td>65</td>
<td>III.3g</td>
</tr>
<tr>
<td>8</td>
<td>m-OMe</td>
<td>Ph</td>
<td>50</td>
<td>67</td>
<td>III.3h</td>
</tr>
<tr>
<td>9</td>
<td>p-OMe</td>
<td>Ph</td>
<td>50</td>
<td>72</td>
<td>III.3i</td>
</tr>
<tr>
<td>10</td>
<td>p-Cl</td>
<td>Ph</td>
<td>50</td>
<td>69</td>
<td>III.3j</td>
</tr>
</tbody>
</table>
Table III.3: Michael addition of dimethyl malonate (DMM) under microwave condition

\[
\begin{align*}
X-\text{CH} & \quad \xrightarrow{\text{DMM}} \quad \text{COOMe} \\
\text{LiOH, Microwave, 750W} & \quad \text{COOMe}
\end{align*}
\]

III (3a-3j)

<table>
<thead>
<tr>
<th>Entry</th>
<th>X</th>
<th>R</th>
<th>Time (min)</th>
<th>Yield (mol%)</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H</td>
<td>Me</td>
<td>5</td>
<td>87</td>
<td>III.3a</td>
</tr>
<tr>
<td>2</td>
<td>o-OMe</td>
<td>Me</td>
<td>7</td>
<td>72</td>
<td>III.3b</td>
</tr>
<tr>
<td>3</td>
<td>m-OMe</td>
<td>Me</td>
<td>7</td>
<td>70</td>
<td>III.3c</td>
</tr>
<tr>
<td>4</td>
<td>p-OMe</td>
<td>Me</td>
<td>7</td>
<td>79</td>
<td>III.3d</td>
</tr>
<tr>
<td>5</td>
<td>p-Cl</td>
<td>Me</td>
<td>6</td>
<td>79</td>
<td>III.3e</td>
</tr>
<tr>
<td>6</td>
<td>H</td>
<td>Ph</td>
<td>7</td>
<td>80</td>
<td>III.3f</td>
</tr>
<tr>
<td>7</td>
<td>o-OMe</td>
<td>Ph</td>
<td>10</td>
<td>68</td>
<td>III.3g</td>
</tr>
<tr>
<td>8</td>
<td>m-OMe</td>
<td>Ph</td>
<td>10</td>
<td>71</td>
<td>III.3h</td>
</tr>
<tr>
<td>9</td>
<td>p-OMe</td>
<td>Ph</td>
<td>10</td>
<td>73</td>
<td>III.3i</td>
</tr>
<tr>
<td>10</td>
<td>p-Cl</td>
<td>Ph</td>
<td>8</td>
<td>72</td>
<td>III.3j</td>
</tr>
</tbody>
</table>

Efforts were also made to improve yields and reduce reaction time by changing solvent and quantity of catalyst. As shown in Table III.4 methanol appears much better solvent as compared to other three viz. acetonitrile, toluene and THF. THF with low polarity and high volatility (low b.p) is the least suited for these reactions. Efforts to improve yield in less time by adding more catalyst were met with some success. Increase in catalyst load from 0.025 molar equivalent to 0.1 molar equivalent enhanced yields
from 49% to 88% (Table III.5) but increase in the catalyst load beyond 0.1 molar equivalent has no noticeable effect. Therefore, we consider that 0.1 molar equivalent of catalyst is the optimal.

**Table III.4: Effect of solvent on Michael addition of dimethyl malonate (DMM)**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Time (h)</th>
<th>Yield (mol%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Methanol</td>
<td>40</td>
<td>88</td>
</tr>
<tr>
<td>2</td>
<td>Acetonitrile</td>
<td>40</td>
<td>53</td>
</tr>
<tr>
<td>3</td>
<td>Toluene</td>
<td>40</td>
<td>41</td>
</tr>
<tr>
<td>4</td>
<td>Tetrahydrofuran</td>
<td>40</td>
<td>15</td>
</tr>
</tbody>
</table>

**Table III.5: Effect of catalyst to reactant mol ratio on Michael addition of dimethyl malonate (DMM)**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (equivalent)</th>
<th>Yield (mol %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.025</td>
<td>49</td>
</tr>
<tr>
<td>2</td>
<td>0.05</td>
<td>60</td>
</tr>
<tr>
<td>3</td>
<td>0.1</td>
<td>88</td>
</tr>
<tr>
<td>4</td>
<td>0.2</td>
<td>89</td>
</tr>
<tr>
<td>5</td>
<td>0.3</td>
<td>89</td>
</tr>
</tbody>
</table>
Finally, higher catalytic efficiency of LiOH as compared to a few other commonly used catalysts in Michael addition, is clearly evident from the results shown in Table III.6. In a coupling reaction of dimethyl malonate with chalcone in methanol at room temperature $\text{K}_2\text{CO}_3$ is nowhere close to LiOH in catalytic efficiency. $\text{K}_2\text{CO}_3$ results only 36 mol% of conversion against 76 mol% with LiOH. Yields with NaOEt is lower by about 8 mol% as compared to that with LiOH, and it also requires much longer time 96 h against 60 h for LiOH at room temperature. Even after 96 h of reaction time at room temperature no reaction is visible either with L-proline as indicated by TLC.

Table III.6: Comparison of catalytic efficiency of LiOH with some other reported catalysts

<table>
<thead>
<tr>
<th>Entry</th>
<th>Base</th>
<th>Time (h)</th>
<th>Yield (mol%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>LiOH</td>
<td>60</td>
<td>76</td>
</tr>
<tr>
<td>2</td>
<td>$\text{K}_2\text{CO}_3$</td>
<td>60</td>
<td>36</td>
</tr>
<tr>
<td>3</td>
<td>NaOEt</td>
<td>96</td>
<td>68</td>
</tr>
<tr>
<td>4</td>
<td>L-Proline</td>
<td>96</td>
<td>No reaction</td>
</tr>
</tbody>
</table>

All the products have been characterized by FT IR, NMR and mass spectra, and whenever possible melting point and gas chromatogram have also been recorded. All
these data are recorded in the experimental section, and only a few typical data are discussed below.

In IR spectra two C=O stretching frequencies are clearly visible - one for the two ester carbonyl at 1730 to 1741 cm\(^{-1}\) and the other for keto carbonyl at 1630 to 1680 cm\(^{-1}\), ester carbonyl always absorbing at a higher frequency by about 50-80 units than the corresponding keto carbonyl in the same compound. Aromatic ring C=C stretching with higher intensity in case of adducts from chalcones (III.3f to III.3j), is observed at 1595 to 1600 cm\(^{-1}\). In Table III.7, C=O and C=C ring stretching frequencies of all the ten Michael adducts are compared. IR spectrum of adduct III.3a are shown in Fig. III.1.

In \(^1\)H NMR the methylene protons (CH\(_2\)) of the adducts absorb at different frequencies and appear as dds due to hindered free rotation about \(\sigma\)-bond of CH\(_2\)-CH. The two dds appear at close frequencies, along with a singlet responsible for one of the two COCH\(_3\) group at about \(\delta \) 3.50 ppm (Fig. III.3 for compound III.3a). Methine proton of COCHCO fragment appears as a clear doublet at about \(\delta \) 3.85 ppm with \(^3J = 9\) Hz. Methine proton of ArCH fragment appears as a multiplet around \(\delta \) 4.10 ppm due to simultaneous coupling with three protons, two from methylene group and the other from COCHCO fragment. As expected keto methyl and ester methyl groups appear as singlets. Keto methyl protons appear at \(\delta \) 2.60-2.80 ppm while two ester methyl groups show up independently as singlet at 3.50 and 3.70 ppm. Incidentally CH\(_3\)O protons of CH\(_3\)OAr moiety (III.3b, 3c, 3d, 3g, 3h & 3i) always appear along with one of the two ester CH\(_3\)O groups. Aromatic protons, as expected, appear as multiplets at \(\delta \) 7 to 8 ppm.
Table III.7: Characteristic IR absorptions by Michael adducts III (3a-3j)

<table>
<thead>
<tr>
<th>Entry</th>
<th>X</th>
<th>R</th>
<th>$\nu$ cm$^{-1}$</th>
<th>$\nu$ cm$^{-1}$</th>
<th>$\nu$ cm$^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>C=O ester</td>
<td>C=O ketone</td>
<td>Ar ring C=C</td>
</tr>
<tr>
<td>1</td>
<td>H</td>
<td>Me</td>
<td>1731</td>
<td>1680</td>
<td>1596</td>
</tr>
<tr>
<td>2</td>
<td>o-OMe</td>
<td>Me</td>
<td>1734</td>
<td>1671</td>
<td>1596</td>
</tr>
<tr>
<td>3</td>
<td>m-OMe</td>
<td>Me</td>
<td>1739</td>
<td>1660</td>
<td>1600</td>
</tr>
<tr>
<td>4</td>
<td>p-OMe</td>
<td>Me</td>
<td>1741</td>
<td>1661</td>
<td>1597</td>
</tr>
<tr>
<td>5</td>
<td>p-Cl</td>
<td>Me</td>
<td>1731</td>
<td>1680</td>
<td>1595</td>
</tr>
<tr>
<td>6</td>
<td>H</td>
<td>Ph</td>
<td>1731</td>
<td>1679</td>
<td>1595</td>
</tr>
<tr>
<td>7</td>
<td>o-OMe</td>
<td>Ph</td>
<td>1739</td>
<td>1656</td>
<td>1566</td>
</tr>
<tr>
<td>8</td>
<td>m-OMe</td>
<td>Ph</td>
<td>1738</td>
<td>1631</td>
<td>1596</td>
</tr>
<tr>
<td>9</td>
<td>p-OMe</td>
<td>Ph</td>
<td>1729</td>
<td>1678</td>
<td>1596</td>
</tr>
<tr>
<td>10</td>
<td>p-Cl</td>
<td>Ph</td>
<td>1732</td>
<td>1680</td>
<td>1596</td>
</tr>
</tbody>
</table>

Only one peak can be seen in gas chromatogram at about $R_T = 4-8$ min thus indicating high purity of the isolated adduct. Mass spectra of the adducts show either RCO or ArCO fragment as one of the dominating species. MeCO fragment appears at $m/z = 43$ as the base peak (100%) and PhCO fragment appears at $m/z = 105$ as the base peak (100%). Other major characteristic fragment is XCH$_2$CH$_2$COR which differs in
its m/z value from adduct to adduct depending on X and R. Ph, as expected, is also seen as one of the major fragments in some of the mass spectra.

IR, $^1$H NMR and mass spectra of some of the adducts are shown in Fig III.1 to Fig III.13.

Fig III.1 : IR spectrum of 2-(3-oxo-1-phenylbutyl)malonate

Fig III.2 : Mass spectrum of 2-(3-oxo-1-phenylbutyl)malonate
Fig III.3: $^1$H NMR spectrum of 2-(3-oxo-1-phenylbutyl)malonate

Fig III.4: $^1$H NMR spectrum of dimethyl 2-(1-o-methoxyphenyl-3-oxobutyl)malonate
Chapter III

Fig III.5: $^1$H NMR spectrum of dimethyl 2-(1-p-chlorophenyl-3-oxobutyl)malonate

Fig III.6: Mass spectrum of dimethyl 2-(1-p-chlorophenyl-3-oxobutyl)malonate
Fig III.7: IR spectrum of dimethyl 2-(3-oxo-1,3-diphenylpropyl)malonate

Fig III.8: $^1$H NMR spectrum of dimethyl 2-(3-oxo-1,3-diphenylpropyl)malonate
Fig III.9: Mass spectrum of dimethyl 2-(3-oxo-1,3-diphenylpropyl)malonate

Fig III.10: IR spectrum of dimethyl 2-(1-o-methoxyphenyl-3-oxo-3-phenyl(propyl)malonate
Fig III.11: $^1\text{H}$ NMR spectrum of dimethyl 2-(1-o-methoxyphenyl-3-oxo-3-phenylpropyl)malonate

Fig III.12: $^1\text{H}$ NMR spectrum of dimethyl 2-(1-p-chlorophenyl-3-oxo-3-phenylpropyl)malonate
III.1.1.2 Lithium hydroxide mediated Michael addition of diethyl malonate

Like dimethyl malonate, diethyl malonate also undergo Michael addition to α,β-unsaturated ketones to yield moderate to high yield. Microwave process, being greener and quicker, has been adopted to examine Michael addition of diethyl malonate to benzylideneacetone and chalcone. Diethyl malonate reacts with benzylideneacetone and chalcone to give almost equal yields, 82% and 84% respectively (Table III.8, Entry 1 & 4); however, chromatographic isolation of the product is somewhat easier with the one obtained from chalcone (Product III.3n).
Table III.8: Michael addition of dialky malonate to \(\alpha,\beta\)-unsaturated ketones

\[
\text{RCOOR} + \text{LCOO}^+ \rightarrow \text{RCOOR} + \text{LiOH}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>(\text{R'})</th>
<th>(\text{R})</th>
<th>Time (min)</th>
<th>Yield (mol %)</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Me</td>
<td>Et</td>
<td>6</td>
<td>82</td>
<td>III.3k</td>
</tr>
<tr>
<td>2</td>
<td>Me</td>
<td>(n)-Pr</td>
<td>6</td>
<td>79</td>
<td>III.3l</td>
</tr>
<tr>
<td>3</td>
<td>Me</td>
<td>(n)-Bu</td>
<td>4</td>
<td>72*</td>
<td>III.3m</td>
</tr>
<tr>
<td>4</td>
<td>Ph</td>
<td>Et</td>
<td>7</td>
<td>84</td>
<td>III.3n</td>
</tr>
<tr>
<td>5</td>
<td>Ph</td>
<td>(n)-Pr</td>
<td>7</td>
<td>67</td>
<td>III.3o</td>
</tr>
<tr>
<td>6</td>
<td>Ph</td>
<td>(n)-Bu</td>
<td>4</td>
<td>82</td>
<td>III.3p</td>
</tr>
</tbody>
</table>

* estimated from gas chromatography

In IR spectra, \(C=O\) stretching frequencies of products III.3k (from benzylideneacetone) and III.3n (from chalcone) appear at 1715 cm\(^{-1}\) and 1733 cm\(^{-1}\) respectively showing higher force constant for \(C=O\) in III.3n as expected. Ester \(C=O\) stretching frequency in III.3n (1662 cm\(^{-1}\)) is also higher as compared to that in III.3k (1650 cm\(^{-1}\)). However aryl \(C=C\) stretching frequencies in both the adducts are virtually same (1606 cm\(^{-1}\) & 1603 cm\(^{-1}\)).

The two ethyl groups in malonate moiety of the adducts III.3k and III.3n display separate signals indicating hindered rotation about CH-CH bond (Fig. III.14 & Fig III.16). Methyl protons of ethyl groups appear as triplets at \(\delta 0.99\) and 1.26 ppm and methylene protons at \(\delta 3.96\) and 4.08 ppm. Methine proton of CO\(_2\)CHCO\(_2\) moiety appears at \(\delta 3.69\)
ppm as a doublet and the methine proton of PhCH moiety appears at 3.96 ppm superimposed on the methylene quartet of one of the ester functionality. The methylene protons in COCH$_2$ moiety appear as unresolved and uneven multiplets at $\delta$ 2.82 ppm indicating that the two protons are not magnetically equivalent. The singlet at $\delta$ 2.01 ppm represents the methyl protons of CH$_3$CO moiety. In the adduct III.3n the methylene proton of COCH$_2$ moiety are better resolved in proton NMR due to higher degree of hindered rotation by virtue of the presence of the two phenyl groups. The methine protons of PhCH & CO$_2$CHCO$_2$ moieties also appear more down field as compared to the respective groups in III.3k.

In $^{13}$C NMR spectra (Fig III.15 & Fig III.17) each and every aliphatic carbon of adducts III.3k & III.3n gives separate signals. This again reaffirms that free rotation around C-C sigma bonds are hindered resulting all the aliphatic carbons magnetically non-equivalent.

In mass spectrum of III.3k the base peak at m/z = 43 indicates CH$_3$CO as the dominating fragment while in mass spectrum of III.3n, the peak at m/z = 105 (~90%) indicates PhCO as one of the dominating species. In both the cases molecular ion peaks are easily visible albeit in low intensity.
Chapter III

Fig III.14: $^1$H NMR spectrum of diethyl 2-(3-oxo-1-phenylbutyl)malonate

Fig III.15: $^{13}$C NMR spectrum of diethyl 2-(3-oxo-1-phenylbutyl)malonate
Fig III.16: $^1$H NMR spectrum of diethyl 2-(3-oxo-1,3-diphenylpropyl)malonate

Fig III.17: $^{13}$C NMR spectrum of diethyl 2-(3-oxo-1,3-diphenylpropyl)malonate
III.1.1.3 Lithium hydroxide mediated Michael addition of di-n-propyl malonate

Michael addition of di-n-propyl malonate to benzylideneacetone and chalcone proceeds smoothly under microwave irradiation resulting near about 70% yield. The adduct from chalcone and benzylideneacetone could easily be separated from the unreacted malonate by column chromatography. In IR of the adduct III.31, the absorptions at 1733 cm\(^{-1}\) and 1687 cm\(^{-1}\) correspond to the ester C=O and keto C=O stretching frequency respectively. Aryl C=C stretching frequency appears at 1597 cm\(^{-1}\). In IR of the adduct from chalcone, III.30, the absorptions at 1735 cm\(^{-1}\) and 1685 cm\(^{-1}\) correspond to the ester C=O and keto C=O stretching frequency respectively. Aromatic C=C stretching frequency appears at 1592 cm\(^{-1}\).

The proton NMR of adduct III.31 (Fig III.18) is similar to III.30 except a singlet at 8 2.02 ppm in III.31. The proton NMR of adduct III.30 is quite similar with that of III.3n expect one extra multiplet at 8 1.61-1.80 ppm due to additional methylene protons present in propyl moiety as compared to ethyl moiety.

In \(^{13}\)C NMR of III.31, all the ten aliphatic carbons are clearly visible although some of them are very closely placed.

In mass spectra of III.30, PhCO fragment at m/z = 105 appears as the major peak (100%). But in mass spectra of III.31, CH(CO\(_2\)Pr)\(_2\) fragment at m/z = 187 appears as the major fragment (100%) along with CH\(_3\)CO at m/z = 43 as another major fragment.
Fig III.18: $^1$H NMR spectrum of di-$n$-propyl 2-(3-oxo-1-phenylbutyl)malonate

Fig III.19: $^{13}$C NMR spectrum of di-$n$-propyl 2-(3-oxo-1-phenylbutyl)malonate
III.1.1.4 Lithium hydroxide mediated Michael addition of di-n-butyl malonate

Michael addition of di-n-butyl malonate to benzylideneacetone and chalcone proceeds smoothly under microwave irradiation resulting near about 80% yield. The adduct with chalcone could easily be separated from the unreacted malonate by column chromatography but the separation of the adduct with benzylideneacetone from unreacted ester could not be carried out. However, the yield of the reaction could be estimated from gas chromatogram.

In IR of the adduct with chalcone (III.3p), the absorptions at 1735 cm\(^{-1}\) and 1685 cm\(^{-1}\) correspond to the ester C=O and keto C=O stretching frequency respectively. These values are quite close to corresponding values for the adduct III.3o (Section III.1.1.3. Aromatic C=C stretching frequency appears at 1592 cm\(^{-1}\) against 1593 cm\(^{-1}\) for III.3o.

In proton NMR of adduct III.3p the two methyl groups from the two butyl moieties appear separately as triplets at \(\delta\) 0.82 & 0.89 ppm. Other butyl protons (total eight) excluding those from OCH\(_2\) groups appear as three closely placed multiplets in between \(\delta\) 1.0 to 1.8 ppm. Like in adduct III.3o, methylene protons of the PhCOCH\(_2\) moiety in III.3p appears as a multiplet indicating their magnetically non-equivalent character. But unlike in adduct III.3o, the doublet expected from COCHCO moiety of III.3p is merged into one of the triplets due to OCH\(_2\) protons at \(\delta\) 3.82 to 3.91 ppm. The multiplet expected from methylene proton of the PhCH moiety is also merged into the other triplet at \(\delta\) 4.09 to 4.21 ppm arising from the second OCH\(_2\) group of the ester functionality.

In \(^{13}\)C NMR of III.3p, all the eleven aliphatic carbons are clearly visible although some of them are very closely placed.
In mass spectrum of III.3p, the major dominating species is PhCO showing up at 
m/z = 105 (100%), as expected and usually observed in case of the other adducts with chalcone. Similarly, in mass spectrum of III.3m the dominating species showed up at m/z = 43 (100%) as was expected and is usually observed in mass spectra of Michael adducts with benzylideneacetone.

Fig : III.20 : $^1$H NMR spectrum of di-$n$-butyl 2-(3-oxo-1-phenylbutyl)malonate

III.1.2 Lithium hydroxide mediated Michael addition of dimethyl succinate to $\alpha,\beta$-unsaturated ketones

Succinic acid occurs naturally in plant and animal tissues. It is a colourless crystalline solid with a melting point of 185-187 °C. It is considerably soluble in water, slightly in ethanol, ether, acetone and glycerine, and sparingly in benzene, carbon sulfide, carbon tetrachloride and oil ether. Dimethyl succinate is used in preparing
pharmaceuticals, agrochemicals and perfumery products. It is also used in manufacturing additives, plastics and other organic compounds. It is useful in a variety of industrial applications including plasticizer for polymers, biodegradable solvents and lubricants, engineering plastics, epoxy curing agent, adhesive and powder coating, corrosion inhibitor, etc.

Unlike the chemistry of dimethyl malonate, the chemistry of dimethyl succinate is not well explored. Michael addition of dimethyl succinate could not be traced in literature. Michael addition of dimethyl succinate to α,β-unsaturated ketones generates a multifunctional compound with two new chiral centres. We therefore believe that such molecules should be useful as intermediates in the synthesis of naturally occurring bioactive molecules.

We did attempt lithium hydroxide mediated Michael addition of dimethyl succinate to α,β-unsaturated ketone at ambient as well as refluxing temperature in methanol. However, reaction at ambient temperature was extremely sluggish and therefore abandoned. Results of the reaction of dimethyl succinate with six different benzylideneacetones under refluxing condition are shown in Table III.9. In all the reactions moderately high yield (56 to 71 mol%) was achieved but reaction time was somewhat long (40 to 50 h). In an attempt to reduce reaction time we resorted to microwave irradiation, and were successful. As shown in Table III.10 microwave irradiation reduced reaction time drastically (10 to 15 min only) but yield practically remained same as with refluxing condition. Microwave irradiation has distinct advantage over the other two processes with respect to time and purity of the product. In microwave assisted reactions no solvent was needed and yields could be obtained just in a few
minutes. Further, microwave assisted process was much cleaner as compared to ambient and refluxing conditions in the sense that no side products were formed, and chromatographic separations were easier.

Michael additions of dimethyl succinate to chalcone were tried both at refluxing temperature and under microwave irradiation but without success. Even after 100 h of refluxing time dimethyl succinate did not show any sign of reaction with chalcone. Under microwave irradiation we allowed 30 min time (double the time allowed with benzylideneacetones) but met with no success.

Table III.9 : Michael addition of dimethyl succinate (DMS) at refluxing temperature

<table>
<thead>
<tr>
<th>Entry</th>
<th>X</th>
<th>R</th>
<th>Time (h)</th>
<th>Yield (mol %)</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H</td>
<td>Me</td>
<td>40</td>
<td>71</td>
<td>III.5a</td>
</tr>
<tr>
<td>2</td>
<td>o-OMe</td>
<td>Me</td>
<td>50</td>
<td>61</td>
<td>III.5b</td>
</tr>
<tr>
<td>3</td>
<td>m-OMe</td>
<td>Me</td>
<td>50</td>
<td>56</td>
<td>III.5c</td>
</tr>
<tr>
<td>4</td>
<td>p-OMe</td>
<td>Me</td>
<td>50</td>
<td>69</td>
<td>III.5d</td>
</tr>
<tr>
<td>5</td>
<td>p-Cl</td>
<td>Me</td>
<td>50</td>
<td>68</td>
<td>III.5e</td>
</tr>
<tr>
<td>6</td>
<td>p-CH₃</td>
<td>Me</td>
<td>40</td>
<td>71</td>
<td>III.5f</td>
</tr>
<tr>
<td>7</td>
<td>H</td>
<td>Ph</td>
<td>100</td>
<td>No reaction</td>
<td>-</td>
</tr>
</tbody>
</table>
Table III.10: Michael addition of dimethyl succinate (DMS) under microwave

```
<table>
<thead>
<tr>
<th>Entry</th>
<th>X</th>
<th>R</th>
<th>Time (min)</th>
<th>Yield (mol %)</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H</td>
<td>Me</td>
<td>10</td>
<td>64</td>
<td>III.5a</td>
</tr>
<tr>
<td>2</td>
<td>o-OMe</td>
<td>Me</td>
<td>15</td>
<td>54</td>
<td>III.5b</td>
</tr>
<tr>
<td>3</td>
<td>m-OMe</td>
<td>Me</td>
<td>15</td>
<td>55</td>
<td>III.5c</td>
</tr>
<tr>
<td>4</td>
<td>p-OMe</td>
<td>Me</td>
<td>15</td>
<td>57</td>
<td>III.5d</td>
</tr>
<tr>
<td>5</td>
<td>p-Cl</td>
<td>Me</td>
<td>12</td>
<td>68</td>
<td>III.5e</td>
</tr>
<tr>
<td>6</td>
<td>p-CH₃</td>
<td>Me</td>
<td>12</td>
<td>70</td>
<td>III.5f</td>
</tr>
<tr>
<td>7</td>
<td>H</td>
<td>Ph</td>
<td>30</td>
<td>No rxn</td>
<td>-</td>
</tr>
</tbody>
</table>
```

All the six products (III.5a to III.5f) could be easily purified by column chromatography, and were characterized by IR, NMR and mass spectra. In IR spectra two C=O stretching frequencies are clearly visible - one for the ester carbonyl and the other for the keto carbonyl. The ester carbonyl stretching frequency absorbs at about the same frequency (1711 cm⁻¹) irrespective of some variation in the structure. Keto carbonyl stretching frequency absorbs in the range 1632 to 1669 cm⁻¹. Aromatic C=C stretching frequency also absorbs at about the same frequency (1598 to 1603 cm⁻¹) irrespective of the variation, albeit minor, in the structure of the compounds. Characteristic IR absorptions are compared in Table III.11.
Table III.11: Characteristic IR absorptions by Michael adducts III (5a-5f)

<table>
<thead>
<tr>
<th>Entry</th>
<th>X</th>
<th>$\nu$ cm$^{-1}$ C=O ester</th>
<th>$\nu$ cm$^{-1}$ C=O ketone</th>
<th>$\nu$ cm$^{-1}$ Ar ring C=C</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H</td>
<td>1711</td>
<td>1642</td>
<td>1602</td>
</tr>
<tr>
<td>2</td>
<td>$o$-OMe</td>
<td>1711</td>
<td>1636</td>
<td>1599</td>
</tr>
<tr>
<td>3</td>
<td>$m$-OMe</td>
<td>1711</td>
<td>1656</td>
<td>1603</td>
</tr>
<tr>
<td>4</td>
<td>$p$-OMe</td>
<td>1711</td>
<td>1646</td>
<td>1599</td>
</tr>
<tr>
<td>5</td>
<td>$p$-Cl</td>
<td>1713</td>
<td>1669</td>
<td>1601</td>
</tr>
<tr>
<td>6</td>
<td>$p$-CH$_3$</td>
<td>1707</td>
<td>1661</td>
<td>1598</td>
</tr>
</tbody>
</table>

In $^1$H NMR of III.5a (Fig III.21) the singlet at $\delta$ 1.66 ppm represents the methyl protons of CH$_3$CO moiety. The two ester methyl groups absorb at different frequencies one at $\delta$ 2.62 ppm and the other at $\delta$ 3.66 ppm. Two methylene protons – one from each methylene group – appear as a complex multiplet in the range $\delta$ 2.62-2.75 ppm. The other two methylene protons appear as dds – one at $\delta$ 2.98 ppm and the other at $\delta$ 3.17 ppm. The two methine protons (CHCO$_2$CH$_3$ & PhCH) appear in the range $\delta$ 3.42 to 3.62 ppm as a combination of multiplets. Aromatic protons are observed as a combination of multiplets in the range $\delta$ 7.08 to 7.53 ppm. Mass spectrum of III.5a (Scheme III.1) shows following fragmentations as the major ones.
*H NMR spectrum of the product III.5b is shown in Fig III.23. As expected, CH$_3$CO protons appear at δ 1.68 ppm as a singlet and the protons of the CH$_3$O group in the aromatic ring appear at δ 3.31 ppm also as a singlet. All the six protons from the two ester CH$_3$O group absorb at the same frequency and appear as a singlet at δ 3.72 ppm. Absorption frequencies of the remaining protons virtually remain same with corresponding frequencies of the compound III.5a in respect of both position and multiplicity.

*H NMR spectrum of the adduct III.5c, as far the aliphatic signals are concerned, virtually remain same with those of III.5b but there is clear change in the features of the aromatic signals. Aromatic signals of the adduct III.5b occupy wider range (~0.6 ppm) against a very narrow range in case of the adduct III.5c (~0.3 ppm). Fragmentation pattern of III.5c in mass spectroscopy is not substantially different from that of III.5a (Scheme III.1) and is shown below in Scheme III.2.
In $^1$H NMR spectrum of the adduct III.5d all the four methylene protons appear as a doublet of doublets, and well resolved. CH$_3$O protons are seen as a singlet at $\delta$ 1.70 ppm, and ring methoxy protons at $\delta$ 3.58 ppm, also as a singlet. All the six ester methoxy protons appear as a singlet $\delta$ 3.84 ppm. The two methine protons appear as a set of three multiplets in the range $\delta$ 3.64 to 3.89 ppm. Aromatic protons are seen as a set of signals in the range $\delta$ 6.75 to 7.24 ppm. Fragmentation pattern of III.5d in mass spectroscopy is similar with that of III.5e (Scheme III.2).

$^1$H NMR spectrum of the product III.5e (the only adduct with chloro substituent in the aromatic ring) shows similar appearance of aliphatic signals both in position and multiplicity with corresponding signals of adduct III.5a (the only adduct having no substituent in the aromatic ring). Aromatic signals of III.5e appear over a wider range ($\delta$ 6.92-8.02 ppm) as compared to that of III.5a ($\delta$ 7.08-7.53 ppm). Fragmentation pattern of III.5e in mass spectroscopy is comparable to that of III.5c (Scheme III.2).
In $^1$H NMR spectrum of III.5f it is observed that aliphatic signals are relatively less resolved when compared with those of adducts III.5a to III.5e. CH$_3$CO, ArCH$_3$ and ester CH$_3$CO protons appear as singlets at $\delta$ 1.61, 2.40 and 3.72 ppm respectively. Out of the four methylene protons two appear as a multiplet at $\delta$ 2.62-2.69 ppm. The other two methylene protons appear as dds - one at $\delta$ 2.96 ppm and the other at $\delta$ 3.12 ppm. Two methine protons appear as a complex multiplet in the range of $\delta$ 3.37 to 3.57 ppm unlike those in other adducts where three or four multiplets were usually observed. Aromatic protons are found in the range $\delta$ 6.89 to 7.24 ppm as a complex multiplet. Mass spectrum of III.5f shows following fragments as the major ones (Scheme III.3).

\begin{center}
\includegraphics[width=\textwidth]{scheme_iii3.png}
\end{center}

Scheme III.3
Fig III.21: $^1$H NMR spectrum of dimethyl 2-(3-oxo-1-phenylbutyl)succinate

Fig III.22: Mass spectrum of dimethyl 2-(3-oxo-1-phenylbutyl)succinate
Fig III.23: $^1$H NMR spectrum of dimethyl 2-(1-o-methoxyphenyl-3-oxobutyl)succinate

Fig III.24: Mass spectrum of dimethyl 2-(1-p-methoxyphenyl-3-oxobutyl)succinate
Fig III.25: IR spectrum of dimethyl 2-(1-p-chlorophenyl-3-oxobutyl)succinate

Fig III.26: Mass spectrum of dimethyl 2-(1-p-chlorophenyl-3-oxobutyl)succinate
Chapter III

III.2 Experimental Section

The olefins and esters used were prepared in the laboratory as described in Chapter II. Lithium hydroxide (Merck) was procured from commercial sources and used as such. All the Michael reactions were carried out under nitrogen atmosphere, products were purified using column chromatography and were characterized using melting point FT IR, $^1$H NMR, GC-MS analysis. Melting points were recorded in a melting point apparatus (Scientific Device, India, Type MP-D in open capillary) and were uncorrected. IR spectra were recorded with a FT IR instrument (Model Perkin Elmer spectrum RX I FT-IR system) either as a thin film on KBr plate or as a KBr pellet. All $^1$H NMR spectra were recorded on Bruker 400 MHz spectrometer in CDCl$_3$ as the solvent using TMS as the internal reference. All GC-MS spectra were recorded on Perkin Elmer Clarus 600 Spectrometer with Elite 5 MS column with dimension 30 m x 250 μm. The injection temperature was fixed at 290 °C. The oven temperature was initially held at 250 °C for 2 min, increased to 280 °C at 3 °C/min and held at 280 °C for 5 min. Helium was used as the carrier gas.

III.2.1 Lithium hydroxide mediated Michael addition of dimethyl malonate to α,β-unsaturated ketones.

Typical procedure for Michael addition

(a) Procedure at ambient and refluxing temperature:

To a stirred solution of dimethyl malonate (1.2 mmol) in a round bottom flask at room temperature, LiOH (0.1 mmol) and MeOH (7 ml) were added and stirring was continued. After 15 min, α,β-unsaturated carbonyl compound (1 mmol) was added to the reaction mixture and was stirred either at ambient or refluxing temperature for several
hours until the reaction was completed or appeared to have reached equilibrium (monitored by TLC). Reaction was then quenched with water and the mixture partitioned thrice between water and ethyl acetate. The combined organic phase was washed with brine, dried over anhydrous sodium sulfate, filtered and the solvent removed under vacuum to yield the crude product. The crude product was purified by column chromatography over silica gel (60 to 120 mesh) using a mixture of ethyl acetate and petroleum ether 40°- 60 °C as the eluent. Purified products were characterized by melting point, FT IR, 1H NMR and GC-MS.

(b) Procedure for microwave irradiation : 

A mixture of α,β-unsaturated carbonyl compounds (1 mmol), LiOH (0.1 mmol) and dimethyl malonate (1.2 mmol) taken in a cylindrical glass vessel was irradiated with microwave radiation. Progress of the reaction was monitored by TLC. When the reaction appeared complete or to have reached equilibrium, the mixture was partitioned thrice between ethyl acetate and water. The combined organic phase was washed with 10% brine solution, dried over anhydrous Na2SO4 and solvent removed under vacuum to yield the crude product. The crude product was purified by column chromatography over silica gel (60-120 mesh) using petroleum ether (40-60 °C) and ethyl acetate as the eluent.
Characterization of Products

(i) Dimethyl 2-(3-oxo-1-phenylbutyl)malonate (III.3a)

Formula & Formula weight: C_{15}H_{18}O_5, 278

State: low melting solid

Olefin used: (E)-4-phenylbut-3-en-2-one

Ester used: dimethyl malonate

Reaction at ambient temperature: 40 h

Yield (mol%): 88

Reaction at refluxing temperature: 30 h

Yield (mol%): 85

Reaction under microwave irradiation: 5 min

Yield (mol%): 87

IR (thin film on KBr), ν cm⁻¹: 563, 689, 746, 863, 978, 1022, 1091, 1159, 1237, 1298, 1370, 1436, 1596, 1680, 1731, 2955, 3048.

¹H NMR (400 MHz, CDCl₃, TMS) δ: 2.95 (s, 3H, -COCH₃), 3.50 (complex m, 5H, OCH₃ & CH₂), 3.65 (s, 3H, OCH₃), 3.85 (d, 3J=9.2 Hz, 1H, COCHCO), 4.16-4.20 (m, 1H, PhCH), 7.25 (unresolved, 2H, aromatic ortho), 7.40 (t, 2H, aromatic meta), 7.50 (t, 1H, aromatic para).
MS (EI) m/z : 18, 28, 43 (100%), 59, 77, 91, 103, 115, 121, 131, 144, 145, 147, 158, 171, 176, 187, 215, 221, 246, 278 (M+, ~5%).

(ii) Dimethyl 2-(1-m-methoxyphenyl-3-oxobutyl)malonate (III.3b)

\[
\text{OMe} \quad \text{COOMe} \\
\text{COOMe}
\]

Formula & Formula weight : C_{16}H_{21}O_{6}, 309
State : thick brown liquid
Olefin used : (E)-4-(o-methoxyphenyl)but-3-en-2-one
Ester used : dimethyl malonate
Reaction at ambient temperature : 40 h
Yield (mol%) : 68
Reaction at refluxing temperature : 30 h
Yield (mol%) : 64
Reaction under microwave irradiation: 5 min
Yield (mol%) : 72

IR (thin film on KBr), ν cm\(^{-1}\) : 507, 571, 693, 751, 801, 1022, 1258, 1444, 1489, 1596, 1671, 1734, 2851, 2924, 2989.

\(^1\)H NMR (400 MHz, CDCl\(_3\), TMS) δ : 2.52 (s, 3H, -COCH\(_3\)), 3.46-3.58 (complex m. 5H, OCH\(_3\) & CH\(_2\)), 3.71 (s, 6H, 2OCH\(_3\)), 3.85 (d. 3J= 9.2 Hz, 1H, COCHCO), 4.09-4.14 (m. 1H.}

\[^{1}\hphantom{1}\)NMR (400 MHz, CDCl\(_3\), TMS) δ : 2.52 (s, 3H, -COCH\(_3\)), 3.46-3.58 (complex m. 5H, OCH\(_3\) & CH\(_2\)), 3.71 (s, 6H, 2OCH\(_3\)), 3.85 (d. 3J= 9.2 Hz, 1H, COCH\(_2\)).
ArCH, 7.0-7.6 (complex m, 4H, aromatic).

MS (EI) m/z : 28, 32, 43 (100%), 44, 59, 65, 69, 77, 78, 89, 91, 102, 105, 119, 131, 132, 145, 151, 161, 174, 175, 177, 178, 201, 206, 217, 219, 233, 244, 248, 277, 308, 309 (M+, ~5%).

(iii) Dimethyl 2-(1-m-methoxyphenyl-3-oxobutyl)malonate (III.3c)

![Chemical Structure]

**Formula & Formula weight** : C_{16}H_{19}O_{6}, 309

**State** : thick brown liquid

**Olefin used** : (E)-4-(m-methoxyphenyl)but-3-en-2-one

**Ester used** : dimethyl malonate

**Reaction at ambient temperature** : 40 h

**Yield (mol%)** : 70

**Reaction at refluxing temperature** : 30 h

**Yield (mol%)** : 65

**Reaction under microwave irradiation**: 7 min

**Yield (mol%)** : 70

**IR (thin film on KBr), v cm^{-1}** : 503, 559, 756, 988, 1024, 1106, 1167, 1250, 1358, 1439, 1600, 1660, 1739, 2832, 2953, 2999.

**{H NMR (400 MHz, CDCl₃, TMS) δ : 2.60 (s, 3H, -COCH₃), 3.56-3.68 (complex m, 5H,
OCH₃ & CH₂), 3.78 (s, 6H, 2OCH₃), 3.86 (d, 3\(^3\)J=9.6 Hz, 1H, COCHCO), 4.20-4.29 (m, 1H, ArCH), 7.2-7.6 (complex m, 4H, aromatic).

**MS (EI) m/z**

: 28, 39, 43 (100%), 59, 65, 77, 78, 91, 102, 103, 104, 115, 122, 131, 132, 134, 135, 145, 147, 161, 174, 177, 187, 188, 210, 206, 217, 219, 233, 244, 245, 247, 276, 308, 309 (M⁺, ~5%).

(iv) **Dimethyl 2-(1-p-methoxyphenyl-3-oxobutyl)malonate (III.3d)**

![Chemical structure of dimethyl 2-(1-p-methoxyphenyl-3-oxobutyl)malonate](image)

**Formula & Formula weight**

: C₁₆H₂₁O₆, 309

**State**

: thick brown liquid

**Olefin used**

: (E)-4-(p-methoxyphenyl)but-3-en-2-one

**Ester used**

: dimethyl malonate

**Reaction at ambient temperature**

: 40 h

**Yield (mol%)**

: 76

**Reaction at refluxing temperature**

: 30 h

**Yield (mol%)**

: 73

**Reaction under microwave irradiation:** 7 min

**Yield (mol%)**

: 79

**IR (thin film on KBr), v cm⁻¹**

: 559, 645, 699, 802, 846, 1001, 1027, 1163, 1209,
1H NMR (400 MHz, CDCl3, TMS) δ : 2.95 (s, 3H, -CH3), 3.4-3.6 (complex m, 5H, \( \text{OCH}_3 \) & \( \text{CH}_2 \)), 3.68 (s, 6H, \( \text{OCH}_3 \)), 3.80 (d, \( J=9.0 \text{ Hz} \), 1H, \( \text{COCHCO} \)), 3.94-4.2 (m, 1H, \( \text{ArCH} \)), 7.0-7.6 (complex m, 4H, aromatic).

MS (El) m/z : 28, 43, 51, 59, 77, 78, 91, 102, 103, 104, 115, 117, 121, 131 (100%), 132, 145, 146, 157, 176, 203, 216, 234, 235, 248, 277, 308, 309 (M⁺, ~5%).

(v) Dimethyl 2-(1-p-chlorophenyl-3-oxobuty)malonate (III.3e)

![Chemical Structure](image)

Formula & Formula weight : C_{16}H_{21}O_{6}, 312
State : thick brown liquid
Olefin used : (E)-4-(p-chlorophenyl)but-3-en-2-one
Ester used : dimethyl malonate
Reaction at ambient temperature : 40 h
Yield (mol%) : 75
Reaction at refluxing temperature : 30 h
Yield (mol%) : 70
Reaction under microwave irradiation: 6 min
Yield (mol%) : 79

IR (thin film on KBr), v cm⁻¹:
564, 6888, 746, 869, 924, 978, 1024, 1062, 1094, 1160, 1238, 1309, 1368, 1435, 1449, 1595, 1680, 1731, 2832, 2891, 2950, 3048.

³H NMR (400 MHz, CDCl₃, TMS) δ:
3.01 (s, 3H, -COCH₃), 3.59-3.65 (complex m, 5H, OCH₃ & CH₂), 3.7 (s, 3H, OCH₃), 3.8 (d, ³J=9.2 Hz, 1H, COCHCO), 4.24-4.30 (m, 1H, ArCH), 7.1-7.6 (complex m, 4H, aromatic).

MS (El) m/z:
28, 43 (100%), 59, 69, 75, 101, 102, 103, 115, 132, 137, 138, 155, 165, 179, 181, 183, 192, 205, 210, 221, 225, 235, 249, 255, 281, 312 (M⁺ - 75). (vi) Dimethyl 2-(3-oxo-1,3-diphenylpropyl)malonate² (III.3f)

Formula & Formula weight: C₂₀H₂₀O₅, 340

State: white solid

m.p.: 80-82 °C

Olefin used: chalcone

Ester used: dimethyl malonate

Reaction at ambient temperature: 60 h

Yield (mol%): 76
Chapter III

Reaction at refluxing temperature : 50 h
Yield (mol%) : 74

Reaction under microwave irradiation: 7 min
Yield (mol%) : 80

IR (thin film on KBr), v cm\(^{-1}\) : 563, 596, 691, 746, 866, 924, 978, 1024, 1091, 1159, 1239, 1309, 1367, 1440, 1595, 1680, 1731, 2842, 2901, 2950, 3048.

\(^{1}\)H NMR (400 MHz, CDCl\(_3\), TMS) \(\delta\) : 3.4-3.6 (complex m, 5H, OCH\(_2\) & CH\(_2\)), 3.7 (s, 3H, CH), 3.85 (d, \(^3\)\(J\)=9.2 Hz, 1H, COCHCO).

4.14-4.20 (m, 1H, ArCH), 7.1-7.3 (complex m, 5H, aromatic), 7.4 (t, 2H, aromatic), 7.5 (t, 1H, aromatic), 7.87 (d, 2H, aromatic).

MS (EI) m/z : 28, 39, 51, 59, 77, 78, 103, 105 (100%), 115, 131, 144, 157, 171, 189, 207, 209, 221, 231, 249, 263, 277, 309, 340 (M\(^+\), ~5%).

(vii) Dimethyl 2-[(1-o-methoxyphenyl)-3-oxo-3-phenylpropyl]malonate (III.3g)

Formula & Formula weight : C\(_{21}\)H\(_{22}\)O\(_6\), 370
State : thick brown liquid
Olefin used : (E)-3-(o-methoxyphenyl)-1-phenylprop-2-en-1-one
Ester used : dimethyl malonate

Reaction at ambient temperature : 60 h
Yield (mol%) : 64

Reaction at refluxing temperature : 50 h
Yield (mol%) : 65

Reaction under microwave irradiation: 10 min
Yield (mol%) : 68

IR (thin film on KBr), $\nu$ cm$^{-1}$ : 577, 702, 740, 802, 905, 1024, 1091, 1160, 1258, 1341, 1437, 1566, 1656, 1739, 2852, 2956, 3029.

$^1$H NMR (400 MHz, CDCl$_3$, TMS) $\delta$ : 3.2-3.5 (complex m, 8H, 2OCH$_3$ & CH$_2$), 3.65 (s, 3H, OCH$_3$), 3.95 (d, $^2J$=9.8 Hz, 1H, COCHCO), 4.33-5.27 (m, 1H, ArCH), 7.3-7.8 (complex m, 9H, aromatic).


(viii) Dimethyl 2-(1-m-methoxyphenyl-3-oxo-3-phenylpropyl)malonate (III.3h)

Formula & Formula weight : C$_{21}$H$_{22}$O$_6$, 370
State : brown solid
m.p. : 61-63 °C

Olefin used : (E)-3-(m-methoxyphenyl)-1-phenylprop-2-en-1-one

Ester used : dimethyl malonate

Reaction at ambient temperature : 60 h
Yield (mol%) : 65

Reaction at refluxing temperature : 50 h
Yield (mol%) : 67

Reaction under microwave irradiation: 10 min
Yield (mol%) : 71

IR (thin film on KBr), v cm\(^{-1}\) : 571, 645, 748, 802, 847, 1001, 1027, 1163, 1214, 1273, 1327, 1361, 1439, 1596, 1631, 1738, 2842, 2956, 3009.

\(^1\)H NMR (400 MHz, CDCl\(_3\), TMS) \(\delta\): 3.4-3.58 (complex m, 8H, 2OCH\(_3\) & CH\(_3\)), 3.7 (s, 3H, CH\(_3\)), 3.84 (d, \(^3\)J=9.2 Hz, 1H, COCHCO), 4.06-4.17 (m, 1H, CH), 7.0-7.8 (complex m, 9H aromatic)

MS (El) m/z : 17, 18, 28, 45, 51, 59, 77, 78, 91, 105 (100%), 106, 119, 131, 145, 151, 161, 197, 207, 219, 220, 239, 250, 251, 279, 280, 306, 311, 338, 370, 372 (M\(^+\), ~3%).
(ix) Dimethyl 2-(1-p-methoxyphenyl-3-oxo-3-phenylpropyl)malonate (III.3i)

Formula & Formula weight: $C_{21}H_{22}O_6$, 370

State: brown solid

m.p.: 80-82 °C

Olefin used: $(E)$-3-($p$-methoxyphenyl)-1-phenylprop-2-en-1-one

Ester used: dimethyl malonate

Reaction at ambient temperature: 60 h

Yield (mol%): 71

Reaction at refluxing temperature: 50 h

Yield (mol%): 72

Reaction under microwave irradiation: 10 min

Yield (mol%): 73

IR (thin film on KBr), $\nu$ cm$^{-1}$: 560, 620, 688, 748, 826, 866, 924, 1021, 1062, 1096, 1161, 1239, 1302, 1359, 1435, 1493, 1596, 1678, 1729, 2832, 2950.

$^1$H NMR (400 MHz, CDCl$_3$, TMS) $\delta$: 3.4-3.58 (complex m, 8H, 2OCH$_3$ & CH$_2$), 3.7 (s, 3H, OCH$_3$), 3.84 (d, $^3J=9.6$ Hz, 1H, COCHCO), 4.17-4.20 (m, 1H, ArCH), 7.1-7.3 (complex m, 5H, aromatic), 7.4 (t, 1H, aromatic), 7.5 (t, 1H, aromatic), 7.87 (d, 2H, aromatic).
(x) Dimethyl 2-(1-p-chlorophenyl-3-oxo-3-phenylpropyl)malonate (III.3j)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>Formula &amp; Formula weight</strong></td>
<td>C_{21}H_{22}O_{6}, 374</td>
</tr>
<tr>
<td><strong>State</strong></td>
<td>white solid</td>
</tr>
<tr>
<td><strong>m.p.</strong></td>
<td>85-87°C</td>
</tr>
<tr>
<td><strong>Olefin used</strong></td>
<td>(E)-3-(p-chlorophenyl)-1-phenylprop-2-en-1-one</td>
</tr>
<tr>
<td><strong>Ester used</strong></td>
<td>dimethyl malonate</td>
</tr>
<tr>
<td><strong>Reaction at ambient temperature</strong></td>
<td>60 h</td>
</tr>
<tr>
<td><strong>Yield (mol%)</strong></td>
<td>72</td>
</tr>
<tr>
<td><strong>Reaction at refluxing temperature</strong></td>
<td>50 h</td>
</tr>
<tr>
<td><strong>Yield (mol%)</strong></td>
<td>69</td>
</tr>
<tr>
<td><strong>Reaction under microwave irradiation: 8 min</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Yield (mol%)</strong></td>
<td>72</td>
</tr>
<tr>
<td><strong>IR (thin film on KBr), v cm^{-1}</strong></td>
<td>560, 620, 687, 751, 828, 866, 924, 964, 1022, 1062, 1091, 1162, 1238, 1302, 1355, 1434, 1494, 1596, 1680, 1732, 2842, 2950, 2989.</td>
</tr>
<tr>
<td><strong>^1H NMR (400 MHz, CDCl₃, TMS) δ</strong></td>
<td>3.4-3.58 (complex m, 5H, OCH₃ &amp; CH₂), 3.71 (s, 3H, OCH₃), 3.85 (d, J=9.2 Hz, 1H, COCHCO), 4.18-4.21 (m, 1H, ArCH), 7.1-7.28 (complex m, 4H, aromatic), 7.4 (t, 2H, aromatic), 7.5 (t, 1H, aromatic), 7.87 (d, 2H, aromatic).</td>
</tr>
</tbody>
</table>
III.2.2 Lithium hydroxide mediated Michael addition reaction of dicarboxylic acid esters with chalcone or benzylideneacetone under microwave irradiation.

Typical procedure for Michael addition

In case of microwave assisted reaction, dimethyl malonate (1.2 mmol), chalcone / benzylideneacetone (1 mmol) and LiOH (0.1 mmol) were mixed together in a cylindrical vessel, and irradiated with microwave radiation with 750 W. The progress of the reaction was monitored by TLC. After completion, reaction was extracted with ethyl acetate. The organic layer was washed with brine, dried (sodium sulfate), filtered and evaporated to give a residue which was further purified by column chromatography using ethyl acetate and petroleum ether 40°- 60 °C as the eluent. The isolated products were characterized by melting point, FT IR, ¹H NMR, GC-MS and compared with literature data.
(i) Dimethyl 2-(3-oxo-1-phenylbutyl)malonate (III.3k)

![Structure of dimethyl 2-(3-oxo-1-phenylbutyl)malonate](image)

**Formula & Formula weight**: \(C_{17}H_{22}O_5\), 306

**State**: colorless liquid

**Olefin used**: (E)-4-phenylbut-3-en-2-one

**Esters used**: diethyl malonate

**Reaction under microwave irradiation**: 6 min

**Yield (mol%)**: 82

**IR (thin film on KBr), \(\nu\) cm\(^{-1}\)**: 522, 702, 748, 1033, 1102, 1170, 1261, 1362, 1455, 1606, 1650, 1715, 2862, 3028.

**\(^1\)H NMR (400 MHz, CDCl\(_3\), TMS) \(\delta\)**: 0.99 (t, \(J=7.2\) Hz, 3H, CH\(_2\)CH\(_3\)), 1.26 (t, \(J=7.2\) Hz, 3H, CH\(_2\)CH\(_3\)), 2.01 (s, 3H, COCH\(_3\)), 2.82 (m, 2H, COCH\(_2\)), 3.69 (d, \(J=9.6\) Hz, 1H, COCH\(_2\)CO), 3.96 (q, \(J=7.2\) Hz, 2H, CH\(_2\)CH\(_3\)), 4.08 (q, \(J=7.2\) Hz, 2H, CH\(_2\)CH\(_3\)), 7.26-7.25 (m, 5H, aromatic).

**MS (El) m/z**: 27, 29, 39, 43 (100%), 51, 65, 69, 77, 78, 86, 91, 102, 103, 104, 115, 117, 118, 131, 133, 135, 145, 147, 148, 158, 160, 161, 171, 187, 190, 203, 215, 236, 249, 261, 263, 288, 306 (M\(^+\)~9%).
(ii) Di-n-propyl 2-(3-oxo-1-phenylbutyl)malonate (III.3I)

\[ \text{Me} \quad \text{COOPr} \]
\[ \text{COOPr} \]

Formula & Formula weight : \( C_{19}H_{28}O_5 \), 334
State : colorless liquid
Olefin used : (E)-4-phenylbut-3-en-2-one
Esters used : di-n-propyl malonate

Reaction under microwave irradiation: 6 min

Yield (mol%) : 79

IR (thin film on KBr), \( \nu \ \text{cm}^{-1} \) : 549, 695, 751, 978, 1023, 1067, 1165, 1256, 1359, 1420, 1449, 1597, 1687, 1733, 2871, 3048.

\(^1\)H NMR (400 MHz, CDCl\(_3\), TMS) \( \delta \) : 0.73 (t, \( ^3J=7.5 \text{ Hz} \), 3H, CH\(_2\)CH\(_2\)CH\(_3\)), 0.83 (t, \( ^3J=7.2 \text{ Hz} \), 3H, CH\(_2\)CH\(_3\)), 1.32-1.65 (m, 4H, 2CH\(_2\)CH\(_2\)CH\(_3\)), 2.02 (s, 3H, OCH\(_3\)), 2.89-2.93 (complex m, 2H, PhCOCH\(_2\)), 3.71 (d, \( ^3J=9.9 \text{ Hz} \), 1H, COCH\(_2\)CO), 3.81 (t, \( ^3J=6.7 \text{ Hz} \), 2H, CH\(_2\)CH\(_2\)CH\(_3\)), 3.93-4.04 (complex m, 3H, CH\(_2\)CH\(_2\)CH\(_3\) & PhCH), 8.00-8.07 (complex m, 4H, aromatic).

\(^1^3\)C NMR (100 MHz, CDCl\(_3\), TMS) \( \delta \) : 9.98, 10.06, 21.41, 21.60, 29.48, 30.10, 40.25.
MS (El) m/z : 27, 29, 39, 41, 43, 44, 77, 78, 87, 91, 103, 104, 105, 115, 129, 131, 144, 147, 148, 158, 162, 171, 187 (100%), 188, 204, 214, 215, 217, 229, 247, 275, 277, 299, 334 (M+−3%), 335.

(iii) di-n-butyl 2-(3-oxo-1-phenylbutyl)malonate (III.3m)

\[
\begin{align*}
\text{Formula & Formula weight} & : C_{21}H_{30}O_5, 362 \\
\text{State} & : \text{colorless liquid (mixture)} \\
\text{Olefin used} & : (E)-4-phenylbut-3-en-2-one \\
\text{Esters used} & : \text{di-n-butyl malonate} \\
\text{Reaction under microwave irradiation:} & 4 \text{ min} \\
\text{Yield (mol\%)} & : 72 \\
\text{IR (thin film on KBr), } \nu \text{ cm}^{-1} & : 493, 675, 808, 1013, 1170, 1254, 1356, 1405, 1454, 1489, 1610, 1655, 1734, 2852, 2925. \\
\text{MS (El) m/z} & : 27, 29, 39, 41, 43 (100%), 57, 77, 87, 91, 103, 104, 105, 115, 131, 144, 146, 147, 158, 161, 162, 171, 175, 187, 188, 214, 215, 218, 231, 243, 261, 289, 305, 319, 362 (M+−3%), 363.
\end{align*}
\]
(iv) Diethyl 2-(3-oxo-1,3-diphenylpropyl)malonate (III.3n)

\[
\begin{align*}
\text{Formula & Formula weight} & : \text{C}_{22}\text{H}_{24}\text{O}_5, \text{368} \\
\text{State} & : \text{white solid} \\
\text{m.p.} & : 62-64 \degree \text{C} \\
\text{Olefin used} & : \text{chalcone} \\
\text{Esters used} & : \text{diethyl malonate} \\
\text{Reaction at refluxing temperature} & : 50 \text{ h} \\
\text{Yield (mol\%)} & : 85 \\
\text{Reaction under microwave irradiation: 7 min} \\
\text{Yield (mol\%)} & : 84 \\
\text{IR (thin film on KBr), v cm}^{-1} & : 576, 687, 771, 846, 983, 1018, 1042, 1160, 1214, 1256, 1322, 1450, 1484, 1603, 1662, 1733, 2532, 2963, 3058. \\
^{1}\text{H NMR (400 MHz, CDCl}_3, \text{TMS) } \delta : 1.00 \text{ (t, } ^{3}J=7.2 \text{ Hz, 3H, } \text{CH}_2\text{CH}_3), 1.26 \text{ (t, } ^{3}J=7.2 \text{ Hz, 3H, } \text{CH}_2\text{CH}_3), 3.47-3.53 \text{ (complex m, 2H, PhCOCH}_2), 3.82 \text{ (d, } ^{3}J=9.7 \text{ Hz, 1H, COCHCO), 3.93 \text{ (q, } ^{3}J=7.1 \text{ Hz, 2H, } \text{CH}_2\text{CH}_3), 4.14-4.22 \text{ (complex m, 3H, } \text{CH}_2\text{CH}_3 \& \text{PhCH), 7.16-7.27 \text{ (complex m, 5H, aromatic), 7.39-7.44 \text{ (complex m, 2H, aromatic), 7.50-7.53 \text{ (complex m, 1H,}}}
\end{align*}
\]
aromatic), 7.88-7.91 (m, 2H, aromatic).

\[ \text{\textsuperscript{13}C NMR (100 MHz, CDCl}_3\text{) \delta : 13.77, 14.04, 29.72, 40.81, 42.65, 57.59, 61.37, 61.69, 127.16, 128.11, 128.25, 128.41, 128.56, } \\
\text{133.06, 136.79, 140.44, 167.77, 168.38, 197.57.} \]

\[ \text{MS (EI) m/z : 27, 29, 39, 51, 76, 77 (100\%), 78, 91, 103, 104, } \\
\text{105, 115, 131, 135, 145, 160, 171, 203, 209, 210, } \\
\text{249, 250, 276, 277, 295, 323, 350, 368 (M^+, ~5\%).} \]

(v) \text{Di-}n\text{-propyl 2-(3-oxo-1,3-diphenylpropyl)malonate}^1 \text{ (III.30)}

\[
\text{\begin{center}
\begin{tikzpicture}
\filldraw[black] (0,0) circle (0.1) node[above] {Ph};
\filldraw[black] (0.5,0) circle (0.1) node[above] {COOPr};
\filldraw[black] (1.5,0) circle (0.1) node[above] {COOPr};
\end{tikzpicture}
\end{center}}
\]

Formula & Formula weight : \text{C}_{24}\text{H}_{28}\text{O}_5, 396

State : white solid

m.p. : 52-55 °C

Olefin used : chalcone

Esters used : di-\text{n}-propyl malonate

Reaction under microwave irradiation: 7 min

Yield (mol\%) : 67

IR (thin film on KBr), \nu \text{ cm}^{-1} : 400, 561, 697, 751, 802, 1023, 1067, 1156, 1258, \\
1381, 1455, 1489, 1533, 1593, 1687, 1733, 2872, \\
2961, 3058.

\[ \text{\textsuperscript{1}H NMR (400 MHz, CDCl}_3, \text{TMS) \delta : 1.02 (t, }^3J=6.8 \text{ Hz, 3H, CH}_2\text{CH}_2\text{CH}_3, 1.26 (t,} \]
Chapter III

3\text{J}=8.6 \text{Hz}, \, 3\text{H}, \, \text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3), \, 1.61-1.80 \text{ (m, 4H).}

2\text{CH}_2\text{CH}_2\text{CH}_3), \, 3.48-3.53 \text{ (complex m, 2H).}

\text{PhCOCH}_2\text{H}, \, 3.84 \text{ (d, } 3\text{J}=12.7 \text{Hz, 1H, COCH(CO)}

3.95 \text{ (t, } 3\text{J}=10.7 \text{Hz, 2H, } \text{CH}_2\text{CH}_2\text{CCH}_2), \, 4.15-4.23

\text{(complex m, 3H, } \text{CH}_2\text{CH}_2\text{CH}_3 & \text{PhCCH)} \, 7.16-7.28

\text{(complex m, 5H, aromatic), 7.39-7.44 \text{ (complex m).}}

2\text{H, aromatic), 7.50-7.52 \text{ (complex m, 1H).}

\text{aromatic), 7.88-7.91 \text{ (m, 2H, aromatic).}}

\text{MS (El) m/z : 27, 28, 41, 43, 51, 77, 78, 103, 105 (100\%). 106.}

115, 131, 147, 171, 207, 209, 217, 220, 221, 231.

249, 250, 276, 277, 291, 292, 309, 337, 396

\text{(M$^+$~3%).}

\text{(vi) Di-n-butyl 2-(3-oxo-1,3-diphenylpropyl)malonate (III.3p)}

\begin{center}
\includegraphics[width=0.5\textwidth]{structure.png}
\end{center}

\text{Formula & Formula weight : C}_{26}\text{H}_{32}\text{O}_5, 424

\text{State : white solid}

\text{m.p. : 38-40 °C}

\text{Olefin used : chalcone}

\text{Esters used : di-n-butyl malonate}

\text{Reaction at refluxing temperature : 40 h}
Chapter III

Yield (mol%) : 83

Reaction under microwave irradiation: 4 min

Yield (mol%) : 82

IR (thin film on KBr), ν cm⁻¹ :
- 400, 697, 748, 1057, 1156, 1261, 1381, 1455, 1592, 1685, 1735, 2882, 2968, 3058.

¹H NMR (400 MHz, CDCl₃, TMS) δ :
- 0.82 (t, J=7.6 Hz, 3H, CH₂CH₂CH₂CH₃), 0.89 (t, J=7.2 Hz, 3H, CH₂CH₂CH₂CH₃), 1.13 (t, J=6.4 Hz, 3H, CH₂CH₂CH₂CH₃), 3.43-3.57 (complex m, 8H, 2CH₂CH₂CH₃), 3.82-3.91 (complex m, 3H, COCH₂ & CH₂CH₂CH₃), 4.09-4.21 (complex m, 3H, CH₂CH₂CH₂CH₃ & PhCH₂).
- 7.14-7.27 (complex m, 5H, aromatic), 7.40-7.44 (complex m, 2H, aromatic), 7.51-7.55 (complex m, 1H, aromatic), 7.88-7.90 (m, 2H, aromatic).

¹³C NMR (75 MHz, CDCl₃) :
- 13.98, 13.53, 18.77, 18.89, 30.16, 30.31, 40.63, 42.48, 57.50, 65.11, 65.40, 127.00, 127.97, 128.07, 128.29, 128.42, 132.92, 136.62, 167.80, 168.36, 197.44.

MS (EI) m/z :
- 27, 28, 29, 39, 41, 42, 56, 57, 77, 78, 87, 103, 105 (100%), 131, 143, 161, 179, 207, 209, 210, 231, 249, 250, 305, 306, 351, 424 (M⁺~2%).
Chapter III 160

III.2.3 Lithium hydroxide mediated Michael addition reaction of dimethyl succinate with α,β-unsaturated ketones

Typical procedure for Michael addition

In a typical procedure dimethyl malonate (1.2 mmol) was placed in a double neck round bottom flask. To it was added LiOH (0.1 mmol) and MeOH (8 ml) under nitrogen atmosphere, and the solution was stirred for 15 min. To the stirred solution α,β-unsaturated ketone (1 mmol) was added and the mixture was refluxed for several hours until completion of reaction (monitored by TLC). After completion, the reaction mixture was extracted with ethyl acetate (thrice). The combined organic phase was washed with brine, dried (sodium sulfate), filtered and evaporated to give a residue which was further purified by column chromatography using ethyl acetate and petroleum ether 40°- 60 °C as the eluent. A range of α,β-unsaturated ketone were reacted with dimethyl succinate under similar conditions to give the respective Michael adduct. The isolated and purified products were characterized by melting point, FT IR, 1H NMR, GC-MS and compared with literature data.

(i) Dimethyl 2-(3-oxo-1-phenylbutyl)succinate (III.5a)

\[
\begin{align*}
\text{Formula & Formula weight} & : C_{16}H_{26}O_{5}, 292 \\
\text{State} & : \text{thick brown liquid} \\
\text{Olefin used} & : (E)-4-phenylbut-3-en-2-one \\
\text{Ester used} & : \text{dimethyl succinate}
\end{align*}
\]
Chapter III

Reaction at refluxing temperature: 40 h
Yield (mol%): 71

Reaction under microwave irradiation: 10 min
Yield (mol%): 64

IR (thin film on KBr), $\nu$ cm$^{-1}$: 513, 702, 738, 1043, 1077, 1165, 1243, 1266, 1352, 1452, 1495, 1602, 1642, 1711, 2862, 2924, 3058.

$^1$H NMR (400 MHz, CDCl$_3$, TMS) $\delta$: 1.66 (s, 3H, $CH_3CO$), 2.62 (s, 3H, Co$_2$CH$_3$), 2.62-2.75 (complex m, 2H, CH$_2$CO$_2$Me & CH$_2$COCH$_3$), 2.98 (dd, $^2J=6$ Hz, $^3J=16$ Hz, 1H, CH$_2$CO$_2$Me or CH$_2$COCH$_3$), 3.17 (dd, $^2J=10.4$ Hz, $^3J=15.6$ Hz, 1H, CH$_2$CO$_2$Me or CH$_2$COCH$_3$), 3.42-3.62 (complex m, 2H, CH$_2$CO$_2$Me & PhCH), 3.66 (s, 6H, 2CO$_2$CH$_3$), 7.08-7.53 (complex m, 5H, aromatic).

MS (EI) m/z: 28, 32, 39, 43, 51, 55, 65, 77, 78, 91, 102, 103, 104, 105, 115, 117, 128, 131, 145, 146, 159, 160, 178, 187 (100%), 188, 193, 205, 231, 235, 249, 259, 273, 277, 292 (M$^+$, ~5%)
(ii) Dimethyl 2-(1-<o-methoxyphenyl>-3-oxobutylsuccinate (III.5b)

```
O
Me
C=O

OMe
COOMe

Me
```

Formula & Formula weight: C₁₇H₂₂O₆, 322
State: thick brown liquid
Olefin used: (E)-4-(o-methoxyphenyl)but-3-en-2-one
Ester used: dimethyl succinate
Reaction at refluxing temperature: 50 h
Yield (mol%): 61
Reaction under microwave irradiation: 15 min
Yield (mol%): 54
IR (thin film on KBr), v cm⁻¹: 582, 691, 737, 809, 905, 1070, 1168, 1259, 1313, 1430, 1531, 1599, 1636, 1711, 2928, 3078.

¹H NMR (400 MHz, CDCl₃, TMS) δ: 1.68 (s, 3H, CH₂CO), 2.65-2.77 (complex m, 2H, CH₂C=O₂Me & CH₂HCOCH₃), 3.02 (dd, ²J=6 Hz, ³J=16 Hz, 1H, CHHCO₂Me or CHHCOCH₃), 3.20 (dd, ²J=10 Hz, ³J=15 Hz, 1H, CHHCO₂Me or CHHCOCH₃), 3.31 (s, 3H, ArOCH₃), 3.43-3.63 (complex m, 2H, CHHCO₂Me & PhCH), 3.72 (s, 6H, 2CO₂CH₃), 6.69-7.31 (complex m, 4H, aromatic).

MS (EI) m/z: 27, 28 (100%), 29, 43, 55, 65, 77, 91, 105, 115, 121, 134, 145, 159, 201, 217, 231, 279, 295, 309,
(iii) Dimethyl 2-(1-m-methoxyphenyl-3-oxobutyI)succinate (III.5c)

Formula & Formula weight : C_{17}H_{22}O_{6}, 322

State : white solid

m.p. : 127-130 °C

Olefin used : (E)-4-(m-methoxyphenyl)but-3-en-2-one

Ester used : dimethyl succinate

Reaction at refluxing temperature : 50 h

Yield (mol%) : 56

Reaction under microwave irradiation: 15 min

Yield (mol%) : 55

IR (thin film on KBr), ν cm⁻¹ : 699, 757, 974, 1033, 1078, 1170, 1261, 1350, 1451, 1495, 1603, 1656, 1711, 2911, 2960, 3058.

¹H NMR (400 MHz, CDCl₃, TMS) δ : 1.78 (s, 3H, CH₂CO), 2.81-2.91 (complex m, 2H, CH₃CO₂Me & CH₂CO₂Me), 3.17 (dd, ²J=5.2 Hz, ³J=16 Hz, 1H, CH₂CO₂Me or CH₂CO₂Me), 3.35 (dd, ²J=10 Hz, ³J=15.2 Hz, 1H, CH₂CO₂Me or CH₂CO₂Me), 3.46 (s, 3H, ArOCH₃), 3.58-3.78 (complex m, 2H, CH₂CO₂Me & PhCH), 3.84 (s, 6H,
Chapter III

2\textsubscript{CO}_2\textsubscript{CH}_3), \textit{7.03-7.36 (complex m. 4H, aromatic}).

\textbf{MS (El) m/z}:

\begin{itemize}
  \item 28 (100\%), 40, 43, 77, 89, 91, 105, 115, 121, 134.
  \item 145, 147, 159, 161, 175, 190, 175, 190, 217, 218.
  \item 231, 279, 309, 321, 322 ((M\textsuperscript{+}, ~2\%).
\end{itemize}

(iv) \textit{Dimethyl 2-(1-p-methoxyphenyl-3-oxobutyl)succinate (III.5d)}

\textbf{Formula & Formula weight}:

\begin{itemize}
  \item \text{C\textsubscript{17}H\textsubscript{22}O\textsubscript{6}, 322}
\end{itemize}

\textbf{State}:

\begin{itemize}
  \item thick brown liquid
\end{itemize}

\textbf{Olefin used}:

\begin{itemize}
  \item (E)-4-(p-methoxyphenyl)but-3-en-2-one
\end{itemize}

\textbf{Ester used}:

\begin{itemize}
  \item dimethyl succinate
\end{itemize}

\textbf{Reaction at refluxing temperature}:

\begin{itemize}
  \item 50 h
  \item Yield (mol\%) : 69
\end{itemize}

\textbf{Reaction under microwave irradiation: 15 min}

\textbf{Yield (mol\%)}:

\begin{itemize}
  \item 57
\end{itemize}

\textbf{IR (thin film on KBr), v cm\textsuperscript{-1}}:

\begin{itemize}
  \item 464, 562, 701, 782, 866, 1043, 1158, 1264, 1353.
  \item 1435, 1491, 1599, 1646, 1711, 2833, 2941.
\end{itemize}

\textbf{\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}, TMS)} \delta:

\begin{itemize}
  \item 1.70 (s, 3H, \textit{CH}_3\textit{CO}), 2.48 (dd, \textit{J}=4.4 Hz, \textit{J}=15.6 Hz, 1H, CH\textit{HCO}_2\textit{Me or CH\textit{HCOCH}_3}). 2.75 (dd.
  \item \textit{J}=6 Hz, \textit{J}=16 Hz, 1H, CH\textit{HCO}_2\textit{Me or CH\textit{HCOCH}_3}). 2.92 (dd, \textit{J}=6.4 Hz, \textit{J}=16 Hz, 1H.
\end{itemize}
Chapter III

(CHHCO₂Me or CHHCOCH₃), 3.25 (dd, 3J=11.6 Hz, 3J=15.6 Hz, 1H, CHHCO₂Me or CHHCOCH₃). 3.45 (dd, 3J=7.2 Hz & 6.8 Hz), 3.58 (s, 3H, ArOC₃H₃), 3.64 (t, J=5 Hz), 3.77 (dt, 1J=4.6 Hz & 11.6 Hz), 3.84 (s, 6H, 2CO₂CH₃), 3.86-3.89 (m), 6.75-7.24 (complex m, 4H, aromatic).

MS (El) m/z : 27, 28, 32, 39, 43, 51, 55, 65, 76, 77, 89, 91, 105, 115, 121, 131, 134, 135, 145, 147, 159, 161, 173, 176, 190, 201, 217 (100%), 218, 231, 253, 279, 295, 309, 321, 322 (M⁺, ~2%).

(v) Dimethyl 2-(1-p-chlorophenyl-3-oxobutyl)succinate (III.5e)

Formula & Formula weight : C₁₆H₁₉O₅Cl, 326
State : brown solid
m.p. : 70-72 °C
Olefin used : (E)-4-(p-chlorophenyl)but-3-en-2-one
Ester used : dimethyl succinate
Reaction at refluxing temperature : 50 h
Yield (mol%) : 68
Reaction under microwave irradiation: 12 min
Yield (mol%) : 68
IR (thin film on KBr), v cm$^{-1}$: 521, 827, 974, 1013, 1093, 1169, 1228, 1355, 1412, 1601, 1669, 1713, 2882, 2981, 3048.

$^1$H NMR (400 MHz, CDCl$_3$, TMS) δ: 1.70 (s, 3H, CH$_3$CO), 2.61 (s, 3H, CO$_2$CH$_3$), 2.62-2.70 (complex m, 2H, CH$_2$C$_6$H$_4$CO$_2$Me & CH$_2$COCH$_3$), 2.96 (dd, $^2$J=6 Hz, $^3$J=16 Hz, 1H, CHHCO$_2$Me or CHHCOCH$_3$), 3.16 (dd, $^2$J=10 Hz, $^3$J=14.8 Hz, 1H, CHHCO$_2$Me or CHHCOCH$_3$), 3.35 (t, $^2$J=6 Hz), 3.46 (m), 3.56 (dd, $^2$J=6.4 & 6.2 Hz), 3.64 (s, 3H, CO$_2$CH$_3$), 6.92-8.02 (complex m, 4H, aromatic).


(vi) Dimethyl 2-(3-oxo-1-p-tolylbutyl)succinate (III.5f)

![Chemical structure](image)

Formula & Formula weight : C$_{17}$H$_{22}$O$_5$, 306
State : thick brown liquid
Olefin used : (E)-4-p-tolylbut-3-en-2-one
Chapter III

Ester used: dimethyl succinate

Reaction at refluxing temperature: 40 h
Yield (mol%): 71

Reaction under microwave irradiation: 12 min
Yield (mol%): 70

IR (thin film on KBr), $\nu$ cm$^{-1}$: 709, 739, 800, 1028, 1170, 1296, 1357, 1461, 1490, 1598, 1661, 1707, 2851, 2924, 3054

$^1$H NMR (400 MHz, CDCl$_3$, TMS) $\delta$: 1.61 (s, 3H, CH$_3$CO), 2.40 (s, 3H, ArCH$_2$), 2.69 (complex m, 2H, CH/HCO$_2$Me & CH/HCOCH$_3$), 2.96 (dd, $^2$$J$=6 Hz, $^3$$J$=5.6 Hz.
1H, CH/HCO$_2$Me or CH/HCOCH$_3$), 3.12 (dd, $^2$$J$=10 Hz, $^3$$J$=16 Hz, 1H, CH/HCO$_2$Me or CH/HCOCH$_3$).
3.37-3.57 (complex m, 2H, CH/HCO$_2$Me & PhCH$_2$).
3.72 (s, 6H, 2CO$_2$CH$_3$), 6.89-7.24 (complex m, 4H, aromatic).

References


