3.1 Introduction

Present day synthetic organic chemistry prefers and even demands certain regulations and guidelines in developing any operationally simple, useful and practical carbon-carbon bond forming reaction keeping the protection of the environment as a major concern. Thus, in addition to the concept of atom economy, other aspects such as solvent free reaction media and use of microwave have received utmost attention from synthetic chemists. The Michael reaction is one such reaction that is well equipped with the important concept of atom economy thus creating a special place for itself in the history of named and unnamed organic reactions.\(^1\)\(^2\) It is a reaction, in the present day version, an atom-economic carbon-carbon bond-forming reaction between the \(\beta\)-position of an activated alkenes/alkynes and carbon nucleophile under the influence of a catalyst or a catalytic system providing polysubstituted carbonyl compounds. The Michael addition adducts have wide applications in organic synthesis\(^3\) and biosynthesis.\(^4\)

3.2 Results and Discussion:

We initiated our investigation by considering dimethyl malonate and chalcone as model substrates. A mixture of dimethylmalonate and chalcone was irradiated under microwave at 500 W in the presence of 5mol% \(\text{In(OTf)}_3\) and no solvent. The reaction was very clean and proceeded smoothly in a short timewith excellent yield. Several experiments were performed to optimize the yield and quantify the catalyst (Table 3.1). It was found that 5 mol% \(\text{In(OTf)}_3\) was enough to achieve the optimum yield. Catalyst more than 5 mol% (up to 10 mol%) did not bring any change in the reaction time and yield. Experiments with various solvents such as acetonitrile, THF, water, methanol and no solvent under identical set of reaction conditions revealed “no solvent” to be the best choice for this transformation.

Table 3.1: Optimization of reaction condition for Michael addition\(^a\)

\[
\begin{array}{c|c}
\text{MeO} & \text{MeO} \\
\hline
\text{CO} & \text{CO} \\
\text{O Me} & \text{O Me} \\
\end{array}
\begin{array}{c|c}
\text{In(OTf)}_3 & \text{In(OTf)}_3 \\
\end{array}
\begin{array}{c|c}
\text{MeOOC} & \text{MeOOC} \\
\text{COOMe} & \text{COOMe} \\
\end{array}
\]
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Reaction conditions: dimethyl malonate (1mmol), chalcone (1 mmol) and In(OTf)$_3$ in varying amounts either in 4 mL solvents or no solvent.

Isolated yields

The catalytic efficiency of In(OTf)$_3$ was compared to a few other commonly used Lewis acids as shown in Table 3.2. It was observed that under microwave irradiation In(OTf)$_3$ gives 97% of conversion in 5 minutes against 60% with FeCl$_3$·6H$_2$O, 63% with I$_2$, 55% with SnCl$_4$ and 50% with CuCl$_2$·2H$_2$O. Thus In(OTf)$_3$ was considered best among the Lewis acid catalysts examined.

Table 3.2: Effect of different catalysts on the model reaction of dimethylmalonate and chalcone

<table>
<thead>
<tr>
<th>Entry</th>
<th>In(OTf)$_3$ (mol%)</th>
<th>Conditions</th>
<th>Time</th>
<th>Yield (%)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>MW/ Neat</td>
<td>5 min</td>
<td>68</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>MW/ Neat</td>
<td>5 min</td>
<td>97</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>MW/ Neat</td>
<td>5 min</td>
<td>97</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>rt/ Neat</td>
<td>24 h</td>
<td>70</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>MW/CH$_3$CN</td>
<td>5 min</td>
<td>85</td>
</tr>
<tr>
<td>6</td>
<td>5</td>
<td>MW/MeOH</td>
<td>5 min</td>
<td>90</td>
</tr>
<tr>
<td>7</td>
<td>5</td>
<td>MW/H$_2$O</td>
<td>5 min</td>
<td>65</td>
</tr>
<tr>
<td>8</td>
<td>5</td>
<td>MW/THF</td>
<td>5 min</td>
<td>49</td>
</tr>
</tbody>
</table>

$^a$Reaction conditions: dimethyl malonate (1mmol), chalcone (1 mmol) and In(OTf)$_3$ in varying amounts either in 4 mL solvents or no solvent.

$^b$Isolated yields

Entry | Catalyst (5 mol%) | Time (min) | Yield (%)$^b$
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MeOOC$\text{COOMe}$</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


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The scope and limitations of the addition reaction under the optimized protocol were explored by reacting dimethyl malonate to various $\alpha,\beta$-unsaturated compounds as shown in Table 3.3. It was observed that all the reactions afforded the desired products in excellent yields. It was also observed that electron withdrawing substituents accelerated the rate of the reaction as compared to that with electron releasing substituents. All the products were characterized by IR, $^1$H NMR, $^{13}$C NMR and GCMS spectra.

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**Table 3.3:** Michael addition of dimethyl malonate to various $\alpha,\beta$-unsaturated compounds catalyzed by In(OTf)$_3$.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reactant</th>
<th>Product</th>
<th>Time (min)</th>
<th>Yield (%)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td>5</td>
<td>97</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td>5</td>
<td>96</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td>5</td>
<td>97</td>
</tr>
</tbody>
</table>
**Reaction condition:** dimethyl malonate (1 mmol), $\alpha,\beta$-unsaturated compound (1 mmol), 5 mol% In(OTf)$_3$, microwave irradiation (500 W) and no solvent

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Isolated Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dimethyl Malonate</td>
<td>97</td>
</tr>
<tr>
<td>Chlorine Compound</td>
<td>95</td>
</tr>
<tr>
<td>MeO Compound</td>
<td>92</td>
</tr>
<tr>
<td>Hydroxy Compound</td>
<td>90</td>
</tr>
</tbody>
</table>

The effect of the alkyl group present in different malonates in the conjugate addition reaction was also investigated by reacting with chalcone under the optimized conditions. It was observed that the bulkiness of the alkyl group did not have much effect on the overall yield of the reaction and satisfactory yields were obtained for all malonates (Table 3.4).
Table 3.4: Michael addition with different malonates

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Time (min)</th>
<th>Yield(%)^b</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Me (1a)</td>
<td>5</td>
<td>97 (3a)</td>
</tr>
<tr>
<td>2</td>
<td>Et (1b)</td>
<td>5</td>
<td>97 (3x)</td>
</tr>
<tr>
<td>3</td>
<td>n-Pr (1c)</td>
<td>5</td>
<td>94 (3y)</td>
</tr>
<tr>
<td>4</td>
<td>n-Bu (1d)</td>
<td>5</td>
<td>92 (3z)</td>
</tr>
</tbody>
</table>

^a Reaction condition: dialkylmalonate (1 mmol), chalcone (1 mmol), 5 mol% In(OTf)_3 under no solvent and microwave irradiation (500 W) and no solvent

^b Isolated yields

The probable mechanism of the In(OTf)_3 catalysed reaction is shown in Scheme 3.1

Scheme 3.1: Mechanism of the In(OTf)_3 catalysed Michael addition reaction of dialkylmalonate to chalcone
3.3 Conclusion

In conclusion, a mild and efficient route for the synthesis of polysubstituted carbonyl compounds utilizing indium triflate as the catalyst is described. This new method of carbon-carbon bond formation under microwave irradiation and no use of solvent offer significant improvement over the existing procedures and thus helps facile entry into a host of Michael adducts of potentially high synthetic utility. Also this simple and easily reproducible protocol affords various adducts in shorter reaction time, with excellent yields and without involvement of any toxic material and formation of any undesirable side products.

3.4 Experimental Section

3.4.1 General information

All the reagents from commercial source were used as received. Infrared spectra were recorded as a thin film on KBr plates with a Perkin Elmer RX I FT-IR instrument. $^1$H and $^{13}$C NMR spectra were recorded in CDCl$_3$ on 300 MHz Bruker NMR spectrometer using tetramethylsilane (TMS) as the internal standard, and resonances (δ) are given in ppm. GCMS were obtained on Waters ZQ 4000 equipped with ESI source. Melting points were measured using Veego VMP-D melting point apparatus and are uncorrected. All experiments were monitored by TLC (thin layer chromatography). Pre-coated silica gel G plates were used to perform TLC. UV illumination or iodine chamber was used to view the eluted TLC plates. Column chromatography was accomplished on silica gel (60–120 mesh) taking ethyl acetate:petroleum ether as the eluent. Catalyst™ System microwave reactor was used for microwave irradiation.

3.5.2 General procedure for synthesis of α,β-unsaturated ketone

A paste of dialkyldmalonate (1 mmol), α,β-unsaturated ketone(0.7 mmol) and In(OTf)$_3$ (0.05 mmol) was placed in a reaction vessel and allowed to react under microwave irradiation (500 W) for the specified time. The reaction mixture was allowed to cool to room temperature and then added ice cold methanol. The catalyst was filtered off and the filtrate was evaporated to get the crude product. The crude product thus obtained was
purified by column chromatography or preparative TLC using ethylacetate/petroleum ether as an eluent.

3.5.3 Spectral data of products

**Compound 3a (Entry 1, Table 3.3) Dimethyl 2-(3-oxo-1,3-diphenylpropyl)malonate**

![Compound 3a structure](image)

Yield 97%; white solid; mp 85-86 °C; \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta_H\) 7.51-7.56 (m, 2H, aromatic), 7.40-7.45, (m, 3H, aromatic), 7.16-7.25 (m, 5H, aromatic), 4.16-4.22 (m, 1H, PhCH), 3.84 (d, \(J = 9.3\) Hz, 1H, COCHCO), 3.73 (s, 1H, OCH\(_3\)), 3.49-3.57 (complex m, 5H, OCH\(_3\) & COCH\(_2\)); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \(\delta_C\) 197.41, 168.59, 168.12, 140.43, 136.71, 133.00, 125.54, 128.40, 128.04, 127.13, 57.21, 52.63, 52.34, 42.26, 40.71; IR (thin film on KBr, cm\(^{-1}\)) 543, 566, 687, 748, 764, 868, 925, 960, 980, 1024, 1095, 1161, 1238, 1310, 1367; 1451, 1490, 1596, 1681, 1732, 2842, 2901, 2954, 3045; MS (GCMS, \(m/z\))

**Compound 3b (Entry 2, Table 3.3)**

**Dimethyl 2-[1-(4-chlorophenyl)-3-oxo-3-phenylpropyl]malonate**

![Compound 3b structure](image)

Yield 96%; white solid; mp 84-86 °C; \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta_H\) 7.89 (d, \(J = 7.8\) Hz, 2H, aromatic), 7.55 (t, \(J = 7.8\) Hz, 1H, aromatic), 7.44 (t, \(J = 7.8\) Hz, 2H, aromatic), 7.22 (s, 5H, aromatic), 4.13-4.21 (m, 1H, PhCH), 3.83 (d, \(J = 9.2\) Hz, 1H, COCHCO), 3.74 (s, 3H, OCH\(_3\)), 3.41-3.54 (complex m, 5H, OCH\(_3\) & CH\(_2\)); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \(\delta_C\) 197.16, 168.47, 167.92, 138.86, 136.45, 133.23, 132.90, 129.45, 128.59, 127.99, 56.95, 52.74, 52.52, 42.06, 40.00; IR (thin film on KBr, cm\(^{-1}\)) 561, 621, 688, 750, 867, 963, 1022, 1062, 1162, 1238, 1303, 1354, 1434, 1494, 1596, 1681, 1731, 2840, 2951, 2990; MS (GCMS, \(m/z\)) 374 [M]\(^+\).
Compound 3c (Entry 3, Table 3.3)

Dimethyl 2-[1-(4-bromophenyl)-3-oxo-3-phenylpropyl]malonate

Yield 97%; cream colored solid; mp 86-87 °C; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta_H$ 7.88 (d, $J = 6.9$ Hz, 2H, aromatic), 7.54 (t, $J = 8.2$ Hz, 1H, aromatic), 7.35-7.42 (complex m, 2H, aromatic), 7.15 (d, $J = 8.4$ Hz, 5H, aromatic), 4.10-4.19 (m, 1H, PhCH), 3.82 (d, $J = 9.9$ Hz, 1H, COCHCO), 3.74 (s, 3H, OCH$_3$), 3.40-3.52 (complex m, 5H, OCH$_3$ & CH$_2$); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta_C$ 197.20, 168.52, 167.97, 139.48, 136.51, 131.65, 129.96, 128.66, 128.08, 121.17, 56.95, 52.79, 52.52, 52.62, 42.07, 40.12; IR (thin film on KBr, cm$^{-1}$) 594, 682, 745, 800, 976, 1072, 1151, 1238, 1357, 1354, 1431, 1529, 1588, 1668, 1737, 2341, 2947; MS (GCMS, m/z) 418 [M]$^+$.  

Compound 3d (Entry 4, Table 3.3)

Dimethyl 2-[1-(4-fluorophenyl)-3-oxo-3-phenylpropyl]malonate

Yield 97%; white solid; mp 81-83 °C; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta_H$ 7.87 (d, $J = 8.1$ Hz, 2H, aromatic), 7.55-7.56 (m, 1H, aromatic), 7.51-7.53 (m, 2H, aromatic), 7.21-7.39 (m, 2H, aromatic), 6.90-6.96 (m, 2H, aromatic) 4.15-4.22 (m, 1H, PhCH), 3.83 (d, $J = 9.3$ Hz, 1H, COCHCO), 3.72 (s, 3H, OCH$_3$), 3.39-3.50 (complex m, 5H, OCH$_3$ & CH$_2$); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta_C$ 197.36, 168.60, 168.06, 163.40, 160.14, 136.58, 136.09, 136.05, 133.25, 129.79, 129.68, 128.63, 128.06, 115.49, 115.21, 57.24, 52.76, 52.50, 42.36, 40.04; IR (thin film on KBr, cm$^{-1}$) 678, 744, 877, 983, 1082, 1151, 1237, 1307, 1359, 1435, 1523, 1593, 1672, 1738, 2351, 2951; MS (GCMS, m/z) 358 [M]$^+$.  

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Compound 3e (Entry 5, Table 3.3)

**Dimethyl 2-[1-(4-methoxyphenyl)-3-oxo-3-phenylpropyl]malonate**

Yield 94%; white solid; mp 80-82 °C; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$H 7.90 (d, $J$ = 7.8 Hz, 2H, aromatic), 7.54 ($J$ = 7.8 Hz, 1H, aromatic), 7.43 (t, $J$ = 7.8 Hz, 2H, aromatic), 7.17 (t, $J$ = 7.8 Hz, 1H, aromatic), 6.70-6.86 (m, 3H, aromatic), 4.13-4.21 (m, 1H, PhCH), 3.85 (d, $J$ = 9.3 Hz, COCHCO), 3.75 (s, 3H, PhOCH$_3$), 3.72 (s, 3H, OCH$_3$), 3.48-3.57 (complex m, 5H, OCH$_3$ & CH$_2$); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$C 197.47, 168.68, 168.10, 159.42, 142.02, 136.64, 133.07, 129.43, 128.51, 128.04, 120.16, 113.88, 112.42, 57.14, 55.09, 52.67, 52.46, 42.17, 40.61; IR (thin film on KBr, cm$^{-1}$) 433, 532, 740, 835, 896, 1029, 1122, 1175, 1242, 1368, 1442, 1514, 1610, 1668, 1738, 2870, 2961, 3056; MS 370 (GCMS, m/z).

Compound 3f (Entry 6, Table 3.3)

**Dimethyl 2-[1-(3-bromophenyl)-3-oxo-3-phenylpropyl]malonate**

Yield 95%; light yellow solid; mp 90-91°C; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$H 7.90 (d, $J$ = 7.8 Hz, 2H, aromatic), 7.55 (t, $J$ = 7.8 Hz, 1H, aromatic), 7.43 (t, $J$ = 7.8 Hz, 3H, aromatic), 7.33 (d, $J$ = 7.8 Hz, 1H, aromatic), 7.23 (d, $J$ = 7.8 Hz, 1H, aromatic), 7.10-7.15 (m, 1H, aromatic), 4.13-4.20 (m, 1H, PhCH), 3.82 (d, $J$ = 9.2 Hz, 1H, COCHCO), 3.72 (s, 3H, OCH$_3$), 3.48-3.59 (complex m, 5H, OCH$_3$ & CH$_2$); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$C 196.98, 168.41, 167.87, 142.87, 136.44, 133.23, 131.02, 130.33, 129.99, 128.57, 127.99, 126.93, 122.38, 56.84, 52.72, 52.52, 41.84, 40.09; IR (thin film on KBr, cm$^{-1}$) MS 418 (GCMS, m/z).
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Compound 3g (Entry 7, Table 3.3)

**Dimethyl 2-[1-(3-fluorophenyl)-3-oxo-3-phenylpropyl]malonate**

Yield 93%; white solid; mp 79-80 °C; \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta_H\) 7.90 (d, \(J = 7.2\) Hz, 2H, aromatic), 6.86-7.89, (complex m, 7H, aromatic), 4.18-4.21 (m, 1H, PhCH), 3.84 (d, \(J = 9.3\) Hz, 1H, COCHCO), 3.73 (s, 1H, OCH\(_3\)), 3.49-3.57 (complex m, 5H, OCH\(_3\)& COCH\(_2\)); \(^13\)C NMR (CDCl\(_3\), 75 MHz) \(\delta_C\) 197.10, 168.46, 167.93, 164.25, 160.99, 143.07, 142.98, 136.51, 133.22, 130.00, 129.89, 128.59, 128.01, 123.83, 123.80, 115.17, 114.89, 114.31, 114.03, 56.93, 54.56, 54.00, 52.74, 52.52, 41.97, 40.24; IR (thin film on KBr, cm\(^{-1}\)) 460, 511, 678, 744, 877, 1082, 1151, 1237, 1359, 1435, 1523, 1593, 1672, 1733, 2351, 2951, 3448; MS 358 (GCMS, m/z).

**Compound 3h (Entry 8, Table 3.3)**

**Dimethyl 2-[1-(3-chlorophenyl)-3-oxo-3-phenylpropyl]malonate**

Yield 94%; pale yellow solid; mp 87 °C; \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta_H\) 7.91 (d, \(J = 7.5\) Hz, 2H, aromatic), 7.55 (t, \(J = 7.2\) Hz, 1H, aromatic), 7.44 (t, \(J = 7.2\) Hz, 2H, aromatic), 7.18-7.26 (m, 4H, aromatic), 4.10-4.21 (m, 1H, PhCH), 3.82 (d, \(J = 9.0\) Hz, 1H, COCHCO), 3.75 (s, 1H, OCH\(_3\)), 3.48-3.59 (complex m, 5H, OCH\(_3\)& COCH\(_2\)); \(^13\)C NMR (CDCl\(_3\), 75 MHz) \(\delta_C\) 197.03, 168.45, 167.91, 142.58, 136.48, 134.17, 133.25, 129.71, 129.59, 128.15, 128.02, 127.44, 126.46, 60.39, 56.88, 52.74, 52.54, 41.88, 40.16; IR (thin film on KBr, cm\(^{-1}\)) 560, 621, 693, 752, 867, 963, 1021, 1065, 1165, 1241, 1305, 1364, 1431, 1494, 1596, 1684, 1732, 2840, 2951, 2991; MS 374 (GCMS, m/z).
**Compound 3i (Entry 9, Table 3.3)**

**Dimethyl 2-[1-(3-nitrophenyl)-3-oxo-3-phenylpropyl]malonate (Entry 9, Table 3.3)**

![Chemical Structure of Compound 3i](image)

Yield 96%; light yellow solid; mp121-123 ºC; \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta_H\) 7.42-8.16 (m, 9H, aromatic), 4.28-4.36 (m, 1H, PhCH), 3.88 (d, \(J = 8.7\) Hz, 1H, COCHCO), 3.76 (s, 3H, OCH\(_3\)), 3.56-3.60 (complex m, 5H, OCH\(_3\) & CH\(_2\)); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \(\delta_C\) 196.67, 168.18, 167.71, 148.14, 142.74, 136.21, 135.18, 133.47, 129.34, 128.66, 127.98, 122.71, 122.35, 60.38, 56.53, 52.89, 52.67, 41.68, 39.99; IR (thin film on KBr, cm\(^{-1}\)) 682, 961, 1098, 1149, 1276, 1445, 1531, 1639, 1735, 2353, 2939; MS (GCMS, \(m/z\)) 385 [M]\(^+\).

**Compound 3j (Entry 10, Table 3.3)**

**Dimethyl 2-[1-(2-nitrophenyl)-3-oxo-3-phenylpropyl]malonate**

![Chemical Structure of Compound 3j](image)

Yield 94%; thick liquid; \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta_H\) 7.41-8.16 (complex m, 9H, aromatic), 4.30-4.33 (m, 1H, PhCH), 3.86 (d, \(J = 9.2\) Hz, 1H, COCHCO), 3.72 (s, 3H, OCH\(_3\)), 3.55-3.64 (complex m, 5H, OCH\(_3\) & CH\(_2\)); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \(\delta_C\) 196.66, 168.16, 167.69, 148.12, 142.74, 136.19, 135.16, 133.45, 129.33, 128.65, 127.96, 122.72, 122.33; IR (thin film on KBr, cm\(^{-1}\)) 413, 757, 803, 1024, 1151, 1249, 1352, 1439, 1490, 1598, 1666, 1734, 2852, 2952; MS (GCMS, \(m/z\)) 385 [M]\(^+\).
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Compound 3k (Entry 11, Table 3.3)
Dimethyl 2-[1-(2-methoxyphenyl)-3-oxo-3-phenylpropyl]malonate

Yield 90%; thick brown liquid; \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta_H\) 7.36-7.70 (complex m, 9H, aromatic), 4.33-4.97 (m, 1H, PhCH), 3.95 (d, \(J = 9.3\) Hz, 1H, COCHCO), 3.65 (s, 3H, OCH\(_3\)), 3.21-3.54 (complex m, 8H, 2OCH\(_3\) & CH\(_2\)); \(^13\)C NMR (CDCl\(_3\), 75 MHz) \(\delta_C\) 197.46, 168.56, 168.07, 159.45, 142.03, 136.69, 133.04, 129.40, 128.47, 128.01, 120.18, 113.88, 112.43, 57.17, 55.19, 52.77, 52.64, 42.19, 40.60; IR (thin film on KBr, cm\(^{-1}\)) 576, 701, 739, 801, 904, 1023, 1090, 1161, 1257, 1340, 1437, 1565, 1656, 1739, 2354, 2956; MS (GCMS, \(m/z\)) 370 [M]+.

Compound 3l (Entry 12, Table 3.3)
Dimethyl 2-[3-oxo-3-phenyl-1-(thiophen-2-yl)propyl]malonate

Yield 95%; light brown solid; mp 66-68°C; \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta_H\) 7.93 (d, \(J = 7.5\) Hz, 2H, aromatic), 7.55 (t, \(J = 7.5\) Hz, 1H, aromatic), 7.44 (t, \(J = 7.5\) Hz, 2H, aromatic), 6.87-7.13 (complex m, 3H, aromatic), 4.50-4.57 (m, 1H, PhCH), 3.92 (d, \(J = 8.1\) Hz, 1H, COCHCO), 3.73 (s, 1H, OCH\(_3\)), 3.56-3.61 (complex m, 5H, OCH\(_3\) & COCH\(_2\)); \(^13\)C NMR (CDCl\(_3\), 75 MHz) \(\delta_C\) 197.11, 168.41, 168.01, 143.49, 142.98, 136.55, 133.20, 128.57, 128.06, 126.60, 125.68, 124.22, 57.48, 52.68, 52.60, 42.91, 35.83; IR (thin film on KBr, cm\(^{-1}\)) 449, 540, 684, 750, 823, 972, 1066, 1163, 1257, 1363, 1433, 1537, 1581, 1676, 1747, 2360, 2902, 3435; MS 346 (GCMS, \(m/z\)).
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Compound 3m (Entry 13, Table 3.3) Dimethyl 2-(3-oxo-1-phenylbutyl)malonate

Yield 97%; low melting solid; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta_H$ 7.50 (t, 1H, aromatic), 7.42 (t, 2H, aromatic), 7.20-7.25 (m, 2H, aromatic), 4.16-4.20 (m, 1H, PhCH), 3.85 (d, 1H, COCHCO), 3.65 (s, 3H, OCH$_3$), 3.50 (complex m, OCH$_3$& CH$_2$), 2.95 (s, 3H, -COCH$_3$); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta_C$ 207.21, 168.98, 168.42, 140.24, 128.03, 127.61, 127.23, 57.12, 52.41, 51.93, 47.09, 40.98, 30.74; IR (thin film on KBr, cm$^{-1}$) 573, 697, 753, 867, 981, 1024, 1094, 1160, 1240, 1299, 1368, 1441, 1598, 1682, 1732, 2957, 3044; MS (GCMS, m/z) 278 [M$^+$].

Compound 3n (Entry 14, Table 3.3)

Dimethyl 2-(1-4-chlorophenyl-3-oxo-butyl)malonate

Yield 95%; brown liquid; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta_H$ 7.18-7.60 (complex m, 4H aromatic), 4.23-4.31 (m, 1H, PhCH), 3.81 (d, $J = 9.2$ Hz, 1H, COCHCO), 3.71 (s, 3H, OCH$_3$), 3.58-3.64 (complex m, 5H, OCH$_3$& CH$_2$), 3.02 (s, 3H, -COCH$_3$); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta_C$ 205.66, 167.95, 167.45, 139.07, 132.92, 129.56, 128.60, 57.03, 52.49, 52.04, 47.10, 40.03, 30.25; IR (thin film on KBr, cm$^{-1}$) 563, 687, 866, 923, 1025, 1065, 1096, 1161, 1235, 1310, 1371, 1437, 1446, 1596, 1681, 1732, 2833, 2892, 2951, 3048; MS 312 (GCMS, m/z).
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Compound 3o (Entry 15, Table 3.3)

**Dimethyl 2-(1- 4-methoxyphenyl-3-oxo-butyl)malonate**

![Structural formula of Compound 3o]

Yield 92%; brown liquid; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta_H$ 7.0-7.6 (complex m, 4H, aromatic), 4.08-4.13 (m, 1H, PhCH), 3.86 (d, $J = 9.2$ Hz, 1H, COCHCO), 3.70 (s, 6H, 2OCH$_3$), 3.45-3.57 (complex m, 5H, OCH$_3$ & CH$_2$), 2.51 (s, 3H, -COCH$_3$); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta_C$ 206.16, 168.19, 167.64, 158.57, 132.28, 129.14, 113.78, 57.58, 55.09, 52.67, 52.17, 47.55, 39.78, 30.23; IR (thin film on KBr, cm$^{-1}$) 558, 644, 695, 806, 1022, 1163, 1209, 1273, 1362, 1440, 1596, 1662, 1741, 2852, 2955, 2998; MS 309 (GCMS, m/z)

Compound 3p (Entry 16, Table 3.3)

**Dimethyl 2-(1- 4-hydroxyphenyl-3-oxo-butyl)malonate**

![Structural formula of Compound 3p]

Yield 93%; brown thick liquid; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta_H$ 7.04 (d, $J = 7.2$ Hz, 2H, aromatic), 6.65 (d, $J = 7.2$ Hz, 2H, aromatic), 3.87-3.89 (m, 1H, PhCH), 3.44-3.77 (m, 8H, 2CO$_2$CH$_3$, COCHCO & PhOH), 2.88-2.92 (m, 2H, COCH$_2$), 2.04 (s, 3H, -COCH$_3$); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta_C$ 208.31, 168.74, 168.43, 155.75, 131.48, 129.57, 113.78, 57.58, 55.09, 52.63, 52.16, 48.19, 40.42, 30.61; IR (thin film on KBr, cm$^{-1}$) 536, 698, 747, 856, 1076, 1107, 1166, 1351, 1520, 1601, 1664, 1704, 2853, 2921, 3449; MS 294 (GCMS, m/z)
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Compound 3q (Entry 17, Table 3.3)
Dimethyl 2-(1-4-methylphenyl-3-oxo-buty1)malonate

\[
\begin{align*}
\text{MeOOC} & \quad \text{COOMe} \\
\text{Me} & \quad \text{Me}
\end{align*}
\]

Yield 93%; colorless liquid; \(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta_H\) 7.03-7.17 (m, 4H, aromatic), 3.89-3.96 (m, 1H, PhCH), 3.74 (d, \(J = 8.8\) Hz, 1H, COCHCO), 3.61 (s, 3H, OCH\(_3\)), 3.43-3.51 (m, 5H, OCH\(_3\)& COCH\(_2\)), 3.15 (s, 3H, PhCH\(_3\)), 3.05 (s, 3H, -COCH\(_3\)); IR (thin film on KBr, cm\(^{-1}\)) 497, 518, 699, 814, 1024, 1093, 1161, 1262, 1354, 1412, 1445, 1518, 1604, 1657, 1714, 2859, 2920, 2955; MS 292 (GCMS, m/z).

Compound 3x (Entry 2, Table 3.4)
Diethyl 2-(3-oxo-1,3-diphenylpropyl)malonate

\[
\begin{align*}
\text{CH}_2\text{COOEt} & \quad \text{OEtOOC} \\
\text{Et} & \quad \text{Ph}
\end{align*}
\]

Yield 97%; white solid; mp 62-65 °C; \(^1\)H NMR (CDCl\(_3\), 300 MH) \(\delta_H\) 7.90 (d, \(J = 7.8\) Hz, 2H, aromatic), 7.39-7.54, (complex m, 3H, aromatic), 7.16-7.28, (complex m, 5H, aromatic), 4.15-4.25 (complex m, 3H, OCH\(_2\)CH\(_2\)&PhCH), 3.96 (m, 2H, OCH\(_2\)CH\(_3\)), 3.83 (d, \(J = 9.6\) Hz, 1H, CHCOCH), 3.47-3.57 (complex m, 2H, PhCOCH\(_2\)), 1.24 (t, \(J = 7.2\) Hz, 3H, CH\(_3\)CH\(_3\)), 1.00 (t, \(J = 7.2\) Hz, 3H, CH\(_2\)CH\(_3\)) ; \(^13\)C NMR (CDCl\(_3\), 75 MHz) \(\delta_C\) 197.46, 168.26, 167.65, 140.38, 136.73, 132.93, 128.44, 128.29, 128.15, 127.99, 127.03, 61.56, 61.24, 57.49, 42.54, 40.73, 13.92, 13.65; IR (thin film on KBr, cm\(^{-1}\)) 559, 698, 751, 861, 1031, 1095 1155, 1257, 1368, 1443, 1490, 1662, 1732, 2922, 3058; MS (GCMS, m/z) 368 [M\(^+\)].
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Compound 3y (Entry 3, Table 3.4)
Di-n-propyl 2-(3-oxo-1,3-diphenylpropyl)malonate

Yield 94%; white solid; mp 52-55 °C; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$H 7.90 (d, $J$= 8.1 Hz, 2H, aromatic), 7.17-7.52 (complex m, 8H, aromatic), 4.09-4.20 (complex m, 3H, OCH$_2$CH$_2$CH$_3$&PhCH), 3.83-3.87 (complex m, 3H, OCH$_2$CH$_2$CH$_3$& COCHCO), 3.48-3.53 (complex m, 2H, PhCOCH$_2$), 1.60-1.67 (m, 2H, CH$_2$CH$_2$CH$_3$), 1.42-1.46 (m, 2H, CH$_2$CH$_2$CH$_3$), 0.90 (t, $J$= 7.2 Hz, 3H, CH$_2$CH$_2$CH$_3$), 0.77 (t, $J$= 7.2 Hz, 3H, CH$_2$CH$_2$CH$_3$); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$C 197.65, 168.21, 167.64, 140.38, 136.73, 132.93, 128.44, 128.29, 128.15, 127.99, 127.03, 61.56, 61.24, 57.49, 42.54, 40.73, 13.92, 13.65, 10.35, 9.97; IR (thin film on KBr, cm$^{-1}$) 686, 752, 803, 1083, 1163, 1226, 1307, 1462, 1521, 1595, 1674, 1733, 2318, 2953; MS (GCMS, m/z) 396 [M]$^+$.

Compound 3z (Entry 4, Table 3.4)
Di-n-butyl 2-(3-oxo-1,3-diphenylpropyl)malonate

Yield 92%; white solid; mp 38-40 °C; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$H 7.89 (d, $J$= 7.5 Hz, 2H, aromatic), 7.52 (t, $J$= 6.9 Hz, 1H, aromatic), 7.41 (t, $J$= 7.2 Hz, 2H, aromatic), 7.16-7.23 (complex m, 5H, aromatic), 4.11-4.20 (complex m, 3H, OCH$_2$CH$_2$CH$_2$CH$_3$&PhCH), 3.83-3.92 (complex m, 3H, OCH$_2$CH$_2$CH$_2$CH$_3$& COCHCO), 3.48-3.53 (complex m, 2H, PhCOCH$_2$), 1.14-1.62 (m, 8H, 2CH$_2$CH$_2$CH$_3$CH$_3$), 0.90 (t, $J$= 7.5 Hz, 3H, CH$_2$CH$_2$CH$_2$CH$_3$), 0.82 (t, $J$= 6.6 Hz, 3H, CH$_2$CH$_2$CH$_2$CH$_3$); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$C 197.10, 168.41, 167.79, 140.37, 136.67, 132.98, 128.46, 128.34, 128.11, 128.01, 127.09, 65.44, 65.15, 57.53, 42.52, 40.66, 30.45, 30.34, 18.93, 18.81; IR (thin film on KBr, cm$^{-1}$) 696, 752, 1056, 1159, 1257, 1375, 1454, 1529, 1685, 1735, 2877, 2954; MS (GCMS, m/z) 424 [M]$^+$.
Fig 3.1: $^1$H NMR spectra of Dimethyl 2-(1-(3-chlorophenyl)-3-oxo-3-phenylpropyl)malonate (Entry 8, Table 3.3)

![H NMR spectra of Dimethyl 2-(1-(3-chlorophenyl)-3-oxo-3-phenylpropyl)malonate (Entry 8, Table 3.3)](image)

Fig 3.1: $^{13}$C NMR spectra of Dimethyl 2-(1-(3-chlorophenyl)-3-oxo-3-phenylpropyl)malonate (Entry 8, Table 3.3)

![C NMR spectra of Dimethyl 2-(1-(3-chlorophenyl)-3-oxo-3-phenylpropyl)malonate (Entry 8, Table 3.3)](image)
Figure 3.2: $^1$H NMR spectra of Dimethyl 2-(3-oxo-3-phenyl-1-(thiophen-2-yl)propyl)malonate

Fig3.2: $^{13}$C NMR spectra of Dimethyl 2-(3-oxo-3-phenyl-1-(thiophen-2-yl)propyl)malonate
Fig 3.3: $^1$H NMR spectra of Di-$n$-butyl 2-(3-oxo-1,3-diphenylpropyl)malonate (Entry 4, Table 3.4)

Fig 3.3: $^{13}$C NMR spectra of Di-$n$-butyl 2-(3-oxo-1,3-diphenylpropyl)malonate (Entry 4, Table 3.4)
References


