Electronic Supporting Information

sp³C-H bond alkylation of ketones with alkenes via ruthenium(II) catalysed dehydrogenation of alcohols

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1- Optimisation studies for the alkylation of 2-phenyl-1-pyridyl ethanol with ruthenium catalyst

Table S1 Optimisation study of additives for $sp^3$ C-H alkylation of 2-phenyl-1-pyridyl ethanol 1a with methyl acrylate and $[\text{RuCl}_2(\text{p-cymene})]_2$ as the catalyst.\(^a\)

![Chemical structure of 1a, 2a, and 3a](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Additive</th>
<th>Conv. (%)(^b)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>AgSbF$_6$</td>
<td>20</td>
</tr>
<tr>
<td>2</td>
<td>KOAc</td>
<td>36</td>
</tr>
<tr>
<td>3</td>
<td>C$_6$H$_5$CO$_2$H</td>
<td>52</td>
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<tr>
<td>4</td>
<td>BNPAH</td>
<td>7</td>
</tr>
<tr>
<td>5</td>
<td>KPF$_6$</td>
<td>15</td>
</tr>
<tr>
<td>6</td>
<td>KOPiv</td>
<td>50</td>
</tr>
<tr>
<td>7</td>
<td>C$_6$H$_5$CO$_2$K</td>
<td>57</td>
</tr>
<tr>
<td>8</td>
<td>---</td>
<td>53</td>
</tr>
<tr>
<td>9</td>
<td>CF$_3$C$_6$H$_5$CO$_2$H</td>
<td>34</td>
</tr>
<tr>
<td>10</td>
<td>(CH$_3$)$_2$C$_6$H$_5$CO$_2$H</td>
<td>50</td>
</tr>
<tr>
<td>11</td>
<td>2,6-(OMe)$_2$-C$_6$H$_5$CO$_2$H</td>
<td>54</td>
</tr>
<tr>
<td>12(^c)</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>13(^d)</td>
<td>---</td>
<td>---</td>
</tr>
</tbody>
</table>

\(^a\)2-Phenyl-1-pyridyl ethanol (0.25 mmol), methyl acrylate (4 equiv.), $[\text{RuCl}_2(\text{p-cymene})]_2$ (5 mol%), additive (20 mol%), Cu(OAc)$_2$.H$_2$O (1 equiv.), 1,2-dichloroethane (DCE) (2 mL), 120 °C, 20 h. \(^b\)Determined by GC. \(^c\)Without Cu(OAc)$_2$.H$_2$O. \(^d\)Without Ru catalyst.
Table S2 Optimisation study of solvents and amount of Cu(OAc)$_2$.H$_2$O for sp$^3$ C-H alkylation of 2-phenyl-1-pyridyl ethanol 1a with methyl acrylate 2a with [RuCl$_2$(p-cymene)]$_2$ as the catalyst.$^a$

![Chemical structure of the reaction](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Amount of 2a (equiv.)</th>
<th>Cu(OAc)$_2$.H$_2$O (equiv.)</th>
<th>Solvent</th>
<th>Temperature (°C)</th>
<th>Conv. (%)$^b$</th>
</tr>
</thead>
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<tr>
<td>1</td>
<td>2.0</td>
<td>0.2</td>
<td>DCE</td>
<td>120</td>
<td>18</td>
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<tr>
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<td>2.0</td>
<td>0.5</td>
<td>DCE</td>
<td>120</td>
<td>47</td>
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<tr>
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<td>0.8</td>
<td>DCE</td>
<td>120</td>
<td>53</td>
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<tr>
<td>4</td>
<td>2.0</td>
<td>1.0</td>
<td>DCE</td>
<td>120</td>
<td>56</td>
</tr>
<tr>
<td>5</td>
<td>2.0</td>
<td>1.2</td>
<td>DCE</td>
<td>120</td>
<td>29</td>
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<tr>
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<td>2.0</td>
<td>0.8</td>
<td>toluene</td>
<td>140</td>
<td>57</td>
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<td>0.8</td>
<td>DMF</td>
<td>140</td>
<td>13</td>
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<tr>
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<td>2.0</td>
<td>0.8</td>
<td>xylene</td>
<td>140</td>
<td>7</td>
</tr>
<tr>
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<td>2.0</td>
<td>0.8</td>
<td>CH$_3$CN</td>
<td>100</td>
<td>12</td>
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<td>4.0</td>
<td>0.8</td>
<td>DCE</td>
<td>120</td>
<td>69(46)</td>
</tr>
<tr>
<td>11$^c$</td>
<td>4.0</td>
<td>0.8</td>
<td>DCE</td>
<td>120</td>
<td>9</td>
</tr>
<tr>
<td>12</td>
<td>6.0</td>
<td>0.8</td>
<td>DCE</td>
<td>120</td>
<td>72</td>
</tr>
<tr>
<td>13$^d$</td>
<td>4.0</td>
<td>0.8</td>
<td>DCE</td>
<td>120</td>
<td>75</td>
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<tr>
<td>14$^e$</td>
<td>4.0</td>
<td>0.8</td>
<td>DCE</td>
<td>120</td>
<td>80(68)</td>
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<tr>
<td>15</td>
<td>4.0</td>
<td>0.8</td>
<td>toluene</td>
<td>150</td>
<td>74(54)</td>
</tr>
</tbody>
</table>

$^a$2-phenyl-1-pyridyl ethanol (0.25 mmol), methyl acrylate (2-6 equiv.), [RuCl$_2$(p-cymene)]$_2$ (5 mol%), Cu(OAc)$_2$.H$_2$O (0.2-1.2 equiv.), DCE (2 mL), 20 h. $^b$Determined by GC, in parenthesis, isolated yields of purified alkylated product 3a. $^c$Under air. $^d$7.5 mol% of [RuCl$_2$(p-cymene)]$_2$. $^e$Run in 0.5 mmol scale, 36 h.
Table S3 Optimisation study of ruthenium catalysts for the sp³ C-H alkylation of 2-phenyl-1-pyridyl ethanol 1a with methyl acrylate 2a

\[
\text{RuCl}_2(\text{mesitylene})_2 (5) \quad 56 \\
\text{RuCl}_2(\text{hmb})_2 (5) \quad 14 \\
\text{RuCl}_2(1,2,4,5-\text{tetramethylbenzene})_2 (5) \quad 47 \\
\text{RuCl}_2(p\text{-cymene})_2 (5) \quad 69(46) \\
\text{RuCl}_2(p\text{-cymene})(\text{PPh}_3)_2 (10) \quad 22 \\
\text{CpRuCl}(_2\text{PPh}_3)_2 (10) \quad 2 \\
\text{Ru(OAc)}_2(p\text{-cymene})_2 (10) \quad 60
\]

\(^a\)2-phenyl-1-pyridyl ethanol (0.25 mmol), methyl acrylate (4 equiv.), [Ru], Cu(OAc)_2·H_2O (0.8 equiv.), DCE (2 mL), 120 °C, 20 h. \(^b\) Determined by GC, in parenthesis, isolated yields of purified alkylated product 3a. hmb = hexamethylbenzene.

Scheme S1 Ru(II)-catalyzed sp³ C-H alkylation of pyridyl ketone 5 with methyl acrylate 2a in DCE
Scheme S2. Influence of [RuCl$_2$(p-cymene)]$_2$ and Cu(OAc)$_2$ on the dehydrogenation of alcohol 1a into ketone 5.

with Cu(OAc)$_2$·H$_2$O (0.8 equiv.), conv > 98%, 3j is the unique product obtained. without Cu(OAc)$_2$·H$_2$O (0.8 equiv.), conv = 90%, a mixture of products is obtained, including 3j (30%) and the ketone Pyr·CO·CH$_2$·C$_6$H$_4$·pF (10 %).

Scheme S3- Influence Cu(OAc)$_2$·H$_2$O on $sp^3$ C-H alkylation of 2-phenyl-1-pyridyl ethanol 1a with methyl acrylate 2a catalysed by [Ru(OAc)$_2$(p-cymene)]
2- Deuterated experiments

Notably in the presence of either the ruthenium catalyst or the copper acetate, no reaction occurred.
The reaction of the ketone 5 with 4 equiv. of methyl acrylate 2a in the presence of 
\( \text{Ru(OAc)}_2(p\text{-cymene}) \) (10 mol%) without addition of \( \text{Cu(OAc)}_2 \) gave the compound 3a in only 10% GC-yield. The similar reaction in the presence of both 5 mol% of 
\( [\text{RuCl}_2(p\text{-cymene})]_2 \) and 0.8 equiv. of \( \text{Cu(OAc)}_2 \) only led to 10% of 3a. The presence of the alcohol functionality in 1a appears to play a key role to generate an active catalyst able to perform the alkylation of 5 with 2a without an additional base. (see also Scheme S1)
Starting from the alcohol 1a, the enolate formation under the conditions described in Table 1, entry 12, but without addition of the alkene 2 was shown to occur by H/D exchange at the \( \alpha \)-position as after 20 h of reaction, 80% of deuterium incorporation took place at the \( \alpha \) C-H bonds of the ketone 5. Similarly, starting from 5 under similar catalytic conditions, the same amount of deuterium incorporation was observed, indicating that the ketone 5 may be an intermediate in the sequential reaction. (Scheme S2)

![Scheme S4. Deuterium incorporation studies.](image)

The intermediate enolate formation is supported as both 1a and 5 under the reaction conditions in the presence of \( \text{D}_2\text{O} \) led to 80% deuterium incorporation at the carbonyl a carbon of 5 (Scheme S4).
3- General remarks

All reagents were obtained from commercial sources and used as received. 1,2-Dichloroethane (DCE), was distilled under conventional methods (sodium, benzophenone), and stored under an argon atmosphere. Toluene was dried over Braun MB-SPS-800 solvent purification system, and stored under an argon atmosphere. Technical grade petroleum ether (40-60 °C bp.) and ethyl acetate were used for chromatography column.

$^1$H NMR spectra were recorded in CDCl$_3$ at ambient temperature on AVANCE I 300, AVANCE III 400 spectrometers at 300.1 MHz and 400.1 MHz, respectively, using the solvent as internal standard (7.26 ppm). $^{13}$C NMR spectra were obtained at 75 or 100 MHz and referenced to the internal solvent signals (central peak is 77.2 ppm). Chemical shift ($\delta$) and coupling constants ($J$) are given in ppm and in Hz, respectively. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet, and br. for broad.

GC analyses were performed with GC-2014 (Shimadzu) 2010 equipped with a 30-m capillary column (Supelco, SPBTM-20, fused silica capillary column, 30 M×0.25 mm×0.25 mm film thickness), was used with N$_2$/air as vector gas. GCMS were measured by GCMS-QP2010S (Shimadzu) with GC-2010 equipped with a 30-m capillary column (Supelco, SLBTM-5ms, fused silica capillary column, 30 M×0.25 mm×0.25 mm film thickness), was used with helium as vector gas. The following GC conditions were used: initial temperature 100 °C for 2 minutes, then rate 10 °C/min until 250 °C and 250 °C for 20 minutes.

Melting points were performed on a LEICA VMHB Kofler system are uncorrected.

HRMS analyses were performed on a Thermo Fischer Scientific Q-Exactive apparatus in the CRMPO center, Rennes, France.

Pyridyl ethanol derivatives were synthesized by known method$^1$.

General procedure for [RuCl$_2$(p-cymene)]$_2$, catalyzed alkylation of 2-phenyl-1-pyridyl ethanol derivatives with functional alkenes

[RuCl$_2$(p-cymene)]$_2$ (0.025 mmol, 15.3 mg), functional alkene (2.0 mmol), 2-phenyl-1-pyridyl ethanol derivative (0.5 mmol), Cu(OAc)$_2$.H$_2$O (0.4 mmol, 80 mg), and DCE (2 mL) were introduced in a Schlenck tube under argon, equipped with a magnetic stirring bar and was stirred at 120 °C for 36 h. When the reaction was completed, the conversion of the reaction was analyzed by gas chromatography. The solvent was then evaporated under vacuum and the desired product was purified by silica gel chromatography column (0.5 mol% Et$_3$N) and a mixture of petrol ether/ethyl acetate as the eluent.
4- Characterization data of products

**Methyl 5-oxo-4-phenyl-5-(2'-pyridyl) pentanoate (3a)**

![Chemical Structure](image)

Light yellow oil, yield = 68%, 97 mg. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 8.66 (m, 1H), 8.02-8.00 (m, 1H), 7.77 (dt, 1H, $J$ = 1.8 Hz, $J$ = 7.5 Hz), 7.42-7.38 (m, 3H), 7.30-7.24 (m, 2H), 7.21-7.16 (m, 1H), 5.41 (dd, 1H, $J$ = 7.8 Hz, $J$ = 1.8 Hz), 3.65 (s, 3H), 2.51-2.43 (m, 1H), 2.36-2.23 (m, 3H). $^{13}$C($^1$H) NMR (75 MHz, CDCl$_3$): $\delta$ = 200.8, 173.8, 153.0, 149.0, 138.5, 136.9, 129.1, 128.8, 127.2, 127.1, 122.9, 51.7, 50.1, 32.2, 28.0. GC: $t_R$ = 17.0 min. MS (EI): m/z: 283 (M$^+$, 20), 210 (50), 117 (100), 106 (40), 91 (25), 78 (80), 51 (20).

**Ethyl 5-oxo-4-phenyl-5-(2'-pyridyl) pentanoate (3b)**

![Chemical Structure](image)

Light yellow oil, yield = 56%, 83 mg. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 8.66-8.64 (m, 1H), 7.76 (dt, 1H, $J$ = 1.5 Hz, $J$ = 7.8 Hz), 7.41-7.37 (m, 3H), 7.29-7.16 (m, 3H), 5.43 (dd, 1H, $J$ = 7.8 Hz, $J$ = 2.7 Hz), 4.15-4.07 (q, 2H, $J$ = 7.2 Hz), 2.51-2.43 (m, 1H), 2.32-2.23 (m, 3H), 1.23 (t, 3H, $J$ = 6.9 Hz). $^{13}$C($^1$H) NMR (75 MHz, CDCl$_3$): $\delta$ = 200.9, 173.4, 153.0, 149.0, 136.9, 129.1, 128.7, 127.2, 127.1, 122.8, 60.5, 50.1, 32.4, 28.1, 14.4. GC: $t_R$ = 17.5 min. MS (EI): m/z: 297 (M$^+$, 30), 252 (20), 210 (60), 117 (100), 106 (40), 91 (25), 78 (80), 51 (15).

**n-Butyl 5-oxo-4-phenyl-5-(2'-pyridyl) pentanoate (3c)**

![Chemical Structure](image)

Light yellow oil, yield = 55%, 90 mg. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 8.65-8.64 (m, 1H), 8.02-7.99 (m, 1H), 7.75 (dt, 1H, $J$ = 1.5 Hz, $J$ = 7.5 Hz), 7.41-7.36 (m, 3H), 5.43 (dd, 1H, $J$ = 7.8 Hz, $J$ = 2.4 Hz), 4.06 (t, 2H, $J$ = 6.6 Hz), 2.51-2.43 (m, 1H), 2.35-2.22 (m, 3H), 1.63-1.54 (m, 2H), 1.42-1.32 (m, 2H), 0.92 (t, 3H, $J$ = 7.2 Hz). $^{13}$C($^1$H) NMR (75 MHz, CDCl$_3$): $\delta$ = 200.8, 173.4, 153.0, 149.0, 138.5, 136.9, 129.1, 128.7, 127.2, 127.1, 122.8, 64.4, 50.0, 32.4, 30.8, 28.1, 19.3, 13.9. GC: $t_R$ = 20.5 min. MS (EI): m/z: 325 (M$^+$, 25), 252 (20), 210 (75), 117 (100), 106 (50), 91 (25), 78 (98), 51 (20). HRMS (ESI): m/z calcd for C$_{23}$H$_{22}$NO$_3$ [M+H]$^+$ 360.1594, found 360.1596.
Benzyl 5-oxo-4-phenyl-5-(2’-pyridyl) pentanoate (3d)

\[
\begin{align*}
&\text{Light yellow solid, yield = 51%, 92 mg, M. p.: 53-55 °C. } \^1\text{H NMR (300 MHz, CDCl}_3\text{): } \delta = 8.66-8.64 (m, 1H), 8.01 (d, 1H, } J = 7.8 \text{ Hz), 7.75 (dt, 1H, } J = 1.5 \text{ Hz, } J = 7.8 \text{ Hz), 7.41-7.32 (m, 8H), 7.29-7.16 (m, 3H), 5.46 (t, 1H, } J = 7.8 \text{ Hz), 5.12 (d, } J = 1.5 \text{ Hz), 2.55-2.46 (m, 1H), 2.42-2.27 (m, 3H). } \\
&\text{13}^\text{C}{\{\text{1H}} \text{ NMR (75 MHz, CDCl}_3\text{): } \delta = 200.8, 173.1, 152.9, 149.0, 138.5, 136.9, 136.1, 129.1, 128.7, 128.6, 128.3, 128.2, 127.2, 127.1, 122.8, 66.3, 50.0, 32.4, 28.0. } \\
&\text{GC: } t_R = 21.9 \text{ min. MS (EI): m/z: 359 (M}^+\text{, 10), 268 (20), 210 (15), 117 (5), 106 (30), 91 (100), 78 (40), 51 (10). }
\end{align*}
\]

5-oxo-4-phenyl-5-(2’-pyridyl) pentanitrile (3e)

\[
\begin{align*}
&\text{Light yellow solid, yield = 57%, 71 mg, M. p.: 64-66 °C. } \^1\text{H NMR (300 MHz, CDCl}_3\text{): } \delta = 8.67-8.65 (m, 1H), 8.02-8.00 (m, 1H), 7.77 (dt, 1H, } J = 1.8 \text{ Hz, } J = 7.8 \text{ Hz), 7.43-7.39 (m, 3H), 7.33-7.19 (m, 3H), 5.56-5.51 (m, 1H), 2.53-2.23 (m, 4H). } \\
&\text{13}^\text{C}{\{\text{1H}} \text{ NMR (75 MHz, CDCl}_3\text{): } \delta = 199.9, 152.5, 149.1, 137.2, 137.0, 129.1, 129.0, 127.7, 127.4, 122.9, 119.5, 49.8, 28.3, 15.4. } \\
&\text{GC: } t_R = 16.6 \text{ min. MS (EI): m/z: 250 (M}^+\text{, 5), 210 (35), 106 (50), 91 (10), 78 (100), 57 (20). }
\end{align*}
\]

N’-isopropyl 5-oxo-4-phenyl-5-(2’-pyridyl) pentanamide (3f)

\[
\begin{align*}
&\text{Light yellow solid, yield = 50%, 77 mg, M. p.: 137-139 °C. } \^1\text{H NMR (300 MHz, CDCl}_3\text{): } \delta = 8.67-8.65 (m, 1H), 8.01-7.98 (m, 1H), 7.77 (dt, 1H, } J = 1.8 \text{ Hz, } J = 7.5 \text{ Hz), 7.43-7.37 (m, 3H), 7.30-7.18 (m, 3H), 5.43 (t, 1H, } J = 7.5 \text{ Hz), 5.36 (brs, 1H), 4.12-4.03 (m, 1H), 2.51-2.42 (m, 1H), 2.28-2.19 (m, 1H), 2.15-2.07 (m, 2H), 1.16-1.11 (m, 6H). } \\
&\text{13}^\text{C}{\{\text{1H}} \text{ NMR (75 MHz, CDCl}_3\text{): } \delta = 201.1, 171.5, 153.1, 149.0, 138.7, 137.0, 129.1, 128.7, 127.2, 127.1, 122.9, 50.2, 41.4, 34.9, 29.0, 23.0, 22.9. } \\
&\text{GC: } t_R = 21.9 \text{ min. MS (EI): m/z: 310 (M}^+\text{, 10), 251 (40), 210 (50), 106 (45), 91 (50), 78 (100), 57 (20). } \\
&\text{HRMS (ESI): m/z calcd for C}_{21}\text{H}_{26}\text{NO}_2 [M + H}^+\text{] 324.1958. } \\
&\text{found 324.1961.}
\end{align*}
\]

3,6,6-trimethyl-2-phenyl-1-(2’-pyridyl)hepta-1,5-dione (3h)

\[
\begin{align*}
&\text{Light yellow oild, yield = 70%, 112 mg, M. p.: 87-89 °C. } \^1\text{H NMR (300 MHz, CDCl}_3\text{): } \text{major stereoisomer: } \delta = 8.67 (s, 1H), 7.74 (t, 1H, } J = 7.5 \text{ Hz), 7.45-7.13 (m, 6H), 5.42 (d, } J = 10.8
\end{align*}
\]
(Hz), 3.16-3.00 (m, 1H), 2.55-2.20 (m, 2H), 1.00-0.97 (m, 7H); minor stereoisomer: δ = 8.67 (s, 1H), 7.99 (t, 1H, J = 8.1 Hz), 7.45-7.13 (m, 6H), 5.32 (d, 1H, J = 10.5 Hz), 3.16-3.00 (m, 1H), 2.55-2.20 (m, 2H), 1.08 (s, 3.8H), 0.76 (d, 1.2H, J = 6.9 Hz).

\[^{13}\]C{\[^1\]H} NMR (75 MHz, CDCl\(_3\)):

major stereoisomer: δ = 215.13, 201.34, 153.42, 148.91, 137.87, 136.96, 129.70, 128.65, 127.15, 127.09, 122.69, 55.78, 44.32, 41.00, 32.23, 26.33, 23.63, 19.03; minor stereoisomer: δ = 214.73, 201.34, 153.40, 148.93, 137.81, 136.94, 129.72, 128.56, 127.15, 127.04, 122.72, 55.33, 44.36, 42.10, 31.87, 26.40, 17.92.

GC: t\(_R\) = 18.8 min. MS (EI): m/z: 323 (M\(^{+}\), 15), 248 (25), 224 (35), 198 (25), 106 (25), 91 (10), 78 (45), 57 (100).

Methyl 5-oxo-5-(2'-pyridyl)-4-(p-tolyl) pentanoate (3i)

Light yellow oil, yield = 67%, 100 mg. \(^1\)H NMR (300 MHz, CDCl\(_3\)); δ = 8.66-8.63 (m, 1H), 8.01-7.98 (m, 1H), 7.74 (dt, 1H, J = 1.8 Hz, J = 7.5 Hz), 7.40-7.35 (m, 1H), 7.29-7.26 (m, 2H), 7.09-7.03 (m, 2H), 5.38 (t, 1H, J = 7.8 Hz), 3.64 (s, 3H), 2.49-2.41 (m, 1H), 2.35-2.21 (m, 6H).

\[^{13}\]C{\[^1\]H} NMR (75 MHz, CDCl\(_3\)): δ = 200.8, 173.8, 153.0, 149.0, 136.9, 136.8, 135.4, 129.5, 129.0, 127.0, 122.8, 51.6, 49.7, 32.1, 28.0, 21.1 ppm. GC: t\(_R\) = 18.5 min. MS (EI): m/z: 297 (M\(^{+}\), 20), 224 (35), 131 (100), 106 (20), 91 (30), 78 (50), 51 (15).

Methyl 5-oxo-5-(2'-pyridyl)-4-(p-fluorophenyl) pentanoate (3j)

Light yellow oil, yield = 71%, 107 mg. \(^1\)H NMR (300 MHz, CDCl\(_3\)); δ = 8.66-8.64 (m, 1H), 8.01 (d, 1H, J = 7.8 Hz), 7.78 (dt, 1H, J = 1.5 Hz, J = 7.5 Hz), 7.43-7.34 (m, 3H), 6.98-6.93 (m, 2H), 5.42 (t, 1H, J = 7.8 Hz), 3.64 (s, 3H), 2.49-2.41 (m, 1H), 2.35-2.21 (m, 6H).

\[^{13}\]C{\[^1\]H} NMR (75 MHz, CDCl\(_3\)): δ = 200.6, 173.7, 162.1 (d, J\(_{CF}\) = 245.5 Hz), 152.8, 149.0, 137.0, 134.2 (d, J\(_{CF}\) = 3.8 Hz), 130.7 (d, J\(_{CF}\) = 8.0 Hz), 127.3, 122.9, 115.6 (d, J\(_{CF}\) = 21.2 Hz), 51.7, 49.2, 32.1, 28.1 ppm. GC: t\(_R\) = 16.8 min. MS (EI): m/z: 301 (M\(^{+}\), 20), 228 (45), 135 (100), 106 (40), 78 (80), 51 (20).

Methyl 5-oxo-5-(2'-pyridyl)-4-(o-fluorophenyl) pentanoate (3k)

Light yellow oil, yield = 56%, 84 mg. \(^1\)H NMR (300 MHz, CDCl\(_3\)); δ = 8.62-8.61 (m, 1H), 8.02 (d, 1H, J = 8.1 Hz), 7.77 (dt, 1H, J = 1.8 Hz, J = 7.8 Hz), 7.41-7.37 (m, 1H), 7.30-7.24 (m, 1H), 7.18-7.14 (m, 1H), 7.07-6.99 (m, 2H), 5.65-5.60 (m, 1H), 3.65 (s, 3H), 2.52-2.45 (m, 1H), 2.41-2.30 (m, 2H), 2.27-2.17 (m, 1H).

\[^{13}\]C{\[^1\]H} NMR (75 MHz, CDCl\(_3\)): δ = 200.3, 173.6, 161.0 (d, J\(_{CF}\) = 247.0 Hz), 152.8, 149.2, 136.9, 129.6 (d, J\(_{CF}\) = 3.9 Hz), 128.8 (d, J\(_{CF}\) = 8.2 Hz), 127.2, 126.0 (d, J\(_{CF}\) = 15.2 Hz), 124.4 (d, J\(_{CF}\) = 3.6 Hz) 122.7, 115.8 (d, J\(_{CF}\) = 22.5 Hz), 51.7, 43.3 (d, J\(_{CF}\) = 1.8 Hz), 32.0, 27.4. \(^{19}\)F NMR (376 MHz, CDCl\(_3\)); δ = -117.0 ppm. GC: t\(_R\) = 17.3 min. MS (EI): m/z: 301 (M\(^{+}\), 15), 228 (35), 135 (60), 106 (50), 78 (100), 51 (20).
Methyl 4-benzyl-5-oxo-5-(2'-pyridyl) pentanoate (3l)

Light yellow oil, yield = 66%, 98 mg. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 8.69-8.67 (m, 1H), 8.02 (d, 1H, $J = 7.8$ Hz), 7.80 (dt, 1H, $J = 1.8$ Hz, $J = 7.8$ Hz), 7.45-7.42 (m, 1H), 7.25-7.13 (m, 5H), 4.58-4.49 (m, 1H), 3.60 (s, 3H), 3.16 (dd, 1H, $J = 6.6$ Hz, $J = 13.8$ Hz), 2.74 (dd, 1H, $J = 7.5$ Hz, $J = 13.8$ Hz), 2.35-2.21 (m, 2H), 2.16-2.06 (m, 1H), 1.98-1.90 (m, 1H). $^{13}$C($^1$H) NMR (75 MHz, CDCl$_3$): $\delta$ = 203.9, 173.7, 153.2, 149.1, 139.6, 137.0, 129.2, 128.4, 127.2, 126.3, 122.4, 51.6, 45.5, 37.9, 31.9, 26.2.

GC: $t_R$ = 18.3 min. MS (EI): m/z: 297 (M$^+$, 5), 210 (20), 182 (25), 106 (30), 91 (45), 79 (100), 51 (10).

Methyl 4-tert-butyl-5-oxo-5-(2'-pyridyl) pentanoate (3m)

Light yellow oil, yield = 25%, 34 mg. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 8.70-8.68 (m, 1H), 8.04 (d, 1H, $J = 7.8$ Hz), 7.83 (dt, 1H, $J = 1.8$ Hz, $J = 7.8$ Hz), 7.48-7.43 (m, 1H), 4.33-4.28 (m, 1H), 3.61 (s, 3H), 2.19-2.09 (m, 3H), 2.06-1.97 (m, 1H), 0.96 (s, 9H). $^{13}$C($^1$H) NMR (75 MHz, CDCl$_3$): $\delta$ = 206.4, 173.9, 155.2, 148.9, 137.1, 127.0, 121.8, 51.6, 50.8, 34.6, 33.0, 28.2, 23.9.

GC: $t_R$ = 13.4 min. MS (EI): m/z: 263 (M$^+$, 20), 248 (35), 190 (50), 134 (75), 106 (70), 78 (100), 55 (40).

Methyl 4-methyl-5-oxo-5-(2'-pyridyl) pentanoate (3n)

Light yellow oil, yield = 40%, 48 mg. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 8.64-8.61 (m, 1H), 7.91-7.88 (m, 1H), 7.80 (dt, 1H, $J = 1.8$ Hz, $J = 7.5$ Hz), 7.42-7.37 (m, 1H), 3.63 (s, 3H), 2.43-2.38 (m, 2H), 2.28-2.22 (m, 2H), 1.43 (s, 6H). $^{13}$C($^1$H) NMR (75 MHz, CDCl$_3$): $\delta$ = 205.9, 174.3, 154.8, 148.0, 136.9, 137.1, 53.1, 31.1, 30.2, 25.5. GC: $t_R$ = 12.3 min. MS (EI): m/z: 235 (M$^+$, 2), 162 (15), 134 (30), 107 (20), 79 (100), 55 (15). HRMS (ESI): m/z calcd for C$_{13}$H$_{18}$NO$_3$ [M + H]$^+$ 236.1281, found 236.1280.

(1-phenyl-3-formyl lyllohex-3-en-1-yl) (2'-pyridyl) ketone (4a)

White solid, yield = 68%, 99 mg. M. p.: 116-118 °C. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 9.54 (s, 1H), 8.41-8.38 (m, 1H), 7.86-7.83 (m, 1H), 7.67 (dt, 1H, $J = 1.8$ Hz, $J = 7.8$ Hz), 7.28-7.14 (m, 6H), 6.83-6.80 (m, 1H), 3.37 (d, 1H, $J = 17.7$ Hz), 2.99 (d, 1H, $J = 17.7$ Hz), 2.82-2.74 (m, 1H), 2.41-2.30 (m, 2H), 2.18-2.05 (m, 1H). $^{13}$C($^1$H) NMR (75 MHz, CDCl$_3$): $\delta$ = 201.1, 193.7, 153.2, 150.7, 148.3, 141.8, 140.4, 136.5, 128.5, 126.6, 126.5, 126.1, 123.9, 53.1, 31.1, 30.3, 24.4. GC: $t_R$ = 20.6 min. MS (EI): m/z: 291 (M$^+$, 15), 155 (20), 107 (30), 91 (75), 79 (100), 51 (20). HRMS (ESI): m/z calcd for C$_{19}$H$_{17}$NO$_3$ [M + H]$^+$ 292.1332, found 292.1332.
[1-(p-tolyl)-3-formyl lylohex-3-en-1-yl] (2'-pyridyl)ketone (4b)

Light yellow oil, yield = 57%, 86 mg. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 9.53 (s, 1H), 8.43-8.41 (m, 1H), 7.81 (d, 1H, $J$ = 8.1 Hz), 7.66 (dt, 1H, $J$ = 1.8 Hz, $J$ = 7.8 Hz), 7.25-7.21 (m, 1H), 7.17 (d, 2H, $J$ = 8.1 Hz), 7.06 (d, 2H, $J$ = 8.4 Hz), 6.80-6.79 (m, 1H), 3.35 (d, 1H, $J$ = 17.7 Hz), 2.99 (d, 1H, $J$ = 17.7 Hz), 2.78-2.71 (m, 1H), 2.39-2.15 (m, 6H).

$^{13}$C{$_^1$H} NMR (75 MHz, CDCl$_3$): $\delta$ = 201.2, 193.7, 153.4, 150.8, 148.3, 140.4, 138.5, 136.5, 136.2, 129.2, 126.5, 126.0, 123.9, 52.8, 31.1, 30.2, 24.4, 21.1. GC: t$_R$ = 22.2 min. MS (EI): m/z: 305 (M$^+$, 15), 199 (30), 105 (80), 91 (15), 79 (100), 51 (20).

[1-(p-fluorophenyl)-3-formyl lylohex-3-en-1-yl] (2'-pyridyl)ketone (4c)

Light yellow oil, yield = 66%, 102 mg. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 9.54 (s, 1H), 8.42-8.40 (m, 1H), 7.88 (d, 1H, $J$ = 8.1 Hz), 7.70 (dt, 1H, $J$ = 1.8 Hz, $J$ = 7.8 Hz), 7.27-7.21 (m, 3H), 7.00-6.91 (m, 2H), 6.82-6.81 (m, 1H), 3.37 (d, 1H, $J$ = 17.7 Hz), 2.98 (d, 1H, $J$ = 17.7 Hz), 2.80-2.73 (m, 1H), 2.42-2.30 (m, 2H), 2.18-2.05 (m, 1H).

$^{13}$C{$_^1$H} NMR (75 MHz, CDCl$_3$): $\delta$ = 200.8, 193.7, 161.6 (d, $J$$_{CF}$ = 245.3 Hz), 153.0, 150.6, 148.3, 140.2, 137.5 (d, $J$$_{CF}$ = 3.2 Hz), 136.6, 128.3 (d, $J$$_{CF}$ = 7.9 Hz), 126.3, 124.0, 115.3 (d, $J$$_{CF}$ = 21.2 Hz), 52.6, 31.1, 30.4, 24.3. $^{19}$F NMR (376 MHz, CDCl$_3$): $\delta$ = -116.4 ppm. GC: t$_R$ = 20.4 min. MS (EI): m/z: 309 (M$^+$, 10), 203 (10), 109 (75), 79 (100), 51 (20).

[1-(o-fluorophenyl)-3-formyl lylohex-3-en-1-yl] (2'-pyridyl)ketone (4d)

Light yellow solid, yield = 58%, 90 mg, M. p.: 115-117 $^\circ$C. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 9.59 (s, 1H), 8.27 (d, 1H, $J$ = 4.5 Hz), 7.98 (d, 1H, $J$ = 7.8 Hz), 7.72 (dt, 1H, $J$ = 1.5 Hz, $J$ = 7.5 Hz), 7.32-7.21 (m, 2H), 7.14-7.04 (m, 2H), 6.89-6.76 (m, 2H), 3.51 (d, 1H, $J$ = 18.0 Hz), 2.84-2.65 (m, 2H), 2.44-2.35 (m, 2H), 2.07-1.95 (m, 1H). $^{13}$C{$_^1$H} NMR (75 MHz, CDCl$_3$): $\delta$ = 201.1, 193.6, 160.3 (d, $J$$_{CF}$ = 245.4 Hz), 153.1 (d, $J$$_{CF}$ = 1.5 Hz), 150.5, 147.8, 140.2, 136.6, 130.4 (d, $J$$_{CF}$ = 12.6 Hz), 128.4 (d, $J$$_{CF}$ = 3.7 Hz), 128.3 (d, $J$$_{CF}$ = 3.7 Hz), 126.3, 124.0 (d, $J$$_{CF}$ = 3.2 Hz), 133.6, 115.6 (d, $J$$_{CF}$ = 22.6 Hz), 50.4 (d, $J$$_{CF}$ = 1.7 Hz), 30.3, 28.7 (d, $J$$_{CF}$ = 2.3 Hz), 24.0. $^{19}$F NMR (376 MHz, CDCl$_3$): $\delta$ = -114.3 ppm. GC: t$_R$ = 20.4 min. MS (EI): m/z: 309 (M$^+$, 10), 203 (5), 109 (85), 79 (100), 51 (20). HRMS (ESI): m/z calcd for C$_{19}$H$_{17}$NO$_2$ [M + H]$^+$ 310.1238, found 310.1238.
[1-benyl-3-formyl llylohex-3-en-1-yl] (2'-pyridyl)ketone (4e)

Colorless oil, yield = 37%, 60 mg. $^1$H NMR (300 MHz, CDCl$_3$): $\delta = 9.42$ (s, 1H), 8.75-8.72 (m, 1H), 7.88-7.80 (m, 2H), 7.49-7.45 (m, 1H), 7.21-7.16 (m, 3H), 7.01-6.96 (m, 2H), 6.72-6.71 (m, 1H), 3.65-3.54 (m, 2H), 3.18 (d, 1H, $J = 17.1$ Hz), 2.84-2.78 (m, 1H), 2.51-2.28 (m, 3H), 1.87-1.77 (m, 1H). $^{13}$C$^1$H NMR (75 MHz, CDCl$_3$): $\delta = 203.1$, 193.7, 154.6, 149.7, 148.1, 140.6, 137.4, 137.1, 130.3, 128.2, 126.6, 126.5, 124.0, 51.5, 43.8, 29.9, 29.6, 24.9. GC: $t_R = 23.5$ min. MS (EI): m/z: 305 (M$^+$, 5), 214 (10), 106 (20), 91 (50), 79 (100), 51 (15).

6- References

### 7- Table of crystallographic data for 4a.

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8. $^1H$ and $^{13}C$ NMR Spectra of alkylated products
Methyl 5-oxo-4-phenyl-5-(2’-pyridyl) pentanoate (3a)

![NMR Spectra](image-url)
Ethyl 5-oxo-4-phenyl-5-(2'-pyridyl) pentanoate (3b)
n-Butyl 5-oxo-4-phenyl-5-(2'-pyridyl) pentanoate (3c)
Benzyl 5-oxo-4-phenyl-5-(2'-pyridyl) pentanoate (3d)
5-oxo-4-phenyl-5-(2’-pyridyl) pentanitrile (3e)
N’-isopropyl 5-oxo-4-phenyl-5-(2’-pyridyl) pentanamide (3f)
3,6,6-trimethyl-2-phenyl-1-(2'-pyridyl)hepta-1,5-dione (3h)
Methyl 5-oxo-5-(2’-pyridyl)-4-(p-tolyl) pentanoate (3i)
Methyl 5-oxo-5-(2’-pyridyl)-4-(p-fluorophenyl) pentanoate (3j)

\[
\begin{align*}
\text{O} & \quad \text{F} \\
\text{CO}_2\text{Me} &
\end{align*}
\]
Methyl 5-oxo-5-(2’-pyridyl)-4-(o-fluorophenyl) pentanoate (3k)

\[
\begin{align*}
\text{O} & \quad \text{F} \\
\text{CO}_2\text{Me} & \\
\end{align*}
\]
Methyl 4-benzyl-5-oxo-5-(2'-pyridyl) pentanoate (3l)

\[
\begin{array}{c}
\text{\chem{Methyl 4-benzyl-5-oxo-5-(2'-pyridyl) pentanoate (3l)}} \\
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Methyl 4-tert-butyl-5-oxo-5-(2'-pyridyl) pentanoate (3m)
Methyl 4-methyl-5-oxo-5-(2'-pyridyl) pentanoate (3n)
(1-phenyl-3-formyl llyllohex-3-en-1-yl) (2'-pyridyl)ketone (4a)
[1-(p-tolyl)-3-formyl lyllohex-3-en-1-yl] (2'-pyridyl)ketone (4b)
[1-(p-fluorophenyl)-3-formyl lyllohex-3-en-1-yl] (2'-pyridyl)ketone (4c)
[1-(o-fluorophenyl)-3-formyl lyllohex-3-en-1-yl] (2'-pyridyl)ketone (4d)
[1-benyl-3-formyl lylohex-3-en-1-yl] (2'-pyridyl)ketone (4e)