Supporting Information

Iron-Catalyzed Hydroalkylation Reaction of $\alpha,\beta$-Unsaturated Ketones with Ethers

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I. General Information.

Unless otherwise noted, all reactions were set up on the bench top and enforced under an nitrogen atmosphere. Diiron nonacarbonyl and 2,2,2-trifluoroethanol were purchased from Energy Chemical and used as received. All other solvents were purified and dried by passage through alumina and Q5 reactant-packed columns on a solvent purification system. Tert-butyl peroxide was purchased from Aladdin China and stored between 0 °C and 4 °C. Other commercial reagents were bought from Adamas-beta, TCI, J&K Chemical, Alfa Aesar or Energy Chemical and were used as received.

Thin layer chromatography was used to monitor the reaction on Merck 60 F254 precoated silica gel plate (0.2 mm thickness). TLC spots were visualized by UV-light irradiation on Spectroline Model ENF-24061/F 254 nm. Other visualization method was staining with a basic solution of potassium permanganate, bromocresol green or acidic solution of ceric molybdate, followed by heating. Flash column chromatography was performed using Merck silica gel 60 with analytical grade solvents as eluents.

All compounds including starting materials and products were characterized by \(^1\)H NMR, \(^{13}\)C NMR, and high resolution mass spectrometry. \(^1\)H NMR and \(^{13}\)C NMR spectra were recorded using Bruker Avance 400 MHz spectrometers. Corresponding chemical shifts are reported in ppm downfield relative to TMS and were referenced to the signal of chloroform-\(d\) (\(\delta=7.26\), singlet). Multiplicities were given as: s = single, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet, td = triplet of doublet. Values of coupling constant are reported as \(J\) in Hz. HRMS spectra were recorded on a Waters Q–Tof Permier Spectrometer.

**CAUTION:** We have never encountered any safety issue in working with or handling the compounds described in this work. Nonetheless, extra precaution should be taken when working with mixture of peroxides and metal salts or metals will cause explosion. It is noteworthy to avoid exposing neat peroxides with heating, too.
II. Optimization of Reaction Conditions.

Table 1. Effect of solvent on the reaction of (E)-1-phenylbut-2-en-1-one with 1,4-dioxane<sup>a,b</sup>

<table>
<thead>
<tr>
<th>entry</th>
<th>solvent</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1&lt;sup&gt;c&lt;/sup&gt;</td>
<td>neat</td>
<td>46</td>
</tr>
<tr>
<td>2</td>
<td>dioxane/benzene (4:1)</td>
<td>trace</td>
</tr>
<tr>
<td>3</td>
<td>dioxane/MeCN (4:1)</td>
<td>N.D.</td>
</tr>
<tr>
<td>4</td>
<td>dioxane/DCM (4:1)</td>
<td>N.D.</td>
</tr>
<tr>
<td>5</td>
<td>dioxane/DMF (4:1)</td>
<td>N.D.</td>
</tr>
</tbody>
</table>

<sup>a</sup>Unless otherwise noted, typical reaction conditions: α,β-unsaturated ketone (0.5 mmol), Fe<sub>2</sub>(CO)<sub>9</sub> (0.05 mmol), DTBP (1.5 mmol), solvent (2.5 mL), 120 °C, under N<sub>2</sub>.  
<sup>b</sup>Isolated yields.

Table 2. Effect of amount of DTBP and Fe<sub>2</sub>(CO)<sub>9</sub> on the reaction of (E)-1-phenylbut-2-en-1-one with 1,4-dioxane<sup>a,b</sup>

<table>
<thead>
<tr>
<th>entry</th>
<th>1,4-dioxane (mL)</th>
<th>Fe&lt;sub&gt;2&lt;/sub&gt;(CO)&lt;sub&gt;9&lt;/sub&gt; (%)</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.0</td>
<td>5</td>
<td>21</td>
</tr>
<tr>
<td>2</td>
<td>2.0</td>
<td>10</td>
<td>47</td>
</tr>
<tr>
<td>3</td>
<td>2.0</td>
<td>15</td>
<td>43</td>
</tr>
<tr>
<td>4</td>
<td>1.0</td>
<td>10</td>
<td>31</td>
</tr>
<tr>
<td>5</td>
<td>1.5</td>
<td>10</td>
<td>39</td>
</tr>
<tr>
<td>6</td>
<td>2.5</td>
<td>10</td>
<td>45</td>
</tr>
</tbody>
</table>

<sup>a</sup>Unless otherwise noted, typical reaction conditions: α,β-unsaturated ketone (0.5 mmol), DTBP (1.5 mmol), 1,4-dioxane (2.0 mL), 120 °C, under N<sub>2</sub>.  
<sup>b</sup>Isolated yields.

Table 3. Effect of ligand and temperature on the reaction of (E)-1-phenylbut-2-en-1-one with 1,4-dioxane<sup>a,b</sup>

<table>
<thead>
<tr>
<th>entry</th>
<th>ligand, solvent</th>
<th>Fe&lt;sub&gt;2&lt;/sub&gt;(CO)&lt;sub&gt;9&lt;/sub&gt;, DTBP</th>
<th>yield (%)</th>
</tr>
</thead>
</table>

<sup>a</sup>Unless otherwise noted, typical reaction conditions: α,β-unsaturated ketone (0.5 mmol), Fe<sub>2</sub>(CO)<sub>9</sub> (0.05 mmol), DTBP (1.5 mmol), 1,4-dioxane (2.0 mL), 120 °C, under N<sub>2</sub>.  
<sup>b</sup>Isolated yields.
<table>
<thead>
<tr>
<th>entry</th>
<th>ligand</th>
<th>solvent</th>
<th>temp (°C)</th>
<th>time (h)</th>
<th>yield (%)</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>L1</td>
<td>dioxane</td>
<td>120</td>
<td>6</td>
<td>54</td>
</tr>
<tr>
<td>2</td>
<td>L2</td>
<td>dioxane</td>
<td>120</td>
<td>6</td>
<td>60</td>
</tr>
<tr>
<td>3</td>
<td>L3</td>
<td>dioxane</td>
<td>120</td>
<td>6</td>
<td>52</td>
</tr>
<tr>
<td>4</td>
<td>L4</td>
<td>dioxane</td>
<td>120</td>
<td>6</td>
<td>trace</td>
</tr>
<tr>
<td>5&lt;sup&gt;c&lt;/sup&gt;</td>
<td>L2</td>
<td>TFE/dioxane (1:2)</td>
<td>120</td>
<td>6</td>
<td>65</td>
</tr>
<tr>
<td>6&lt;sup&gt;c&lt;/sup&gt;</td>
<td>L2</td>
<td>TFE/dioxane (1:2)</td>
<td>105</td>
<td>24</td>
<td>trace</td>
</tr>
<tr>
<td>7&lt;sup&gt;c&lt;/sup&gt;</td>
<td>L2</td>
<td>TFE/dioxane (1:2)</td>
<td>110</td>
<td>24</td>
<td>trace</td>
</tr>
<tr>
<td>8&lt;sup&gt;c&lt;/sup&gt;</td>
<td>L2</td>
<td>TFE/dioxane (1:2)</td>
<td>115</td>
<td>12</td>
<td>69</td>
</tr>
</tbody>
</table>

<sup>a</sup>Unless otherwise noted, typical reaction conditions: α,β-unsaturated ketone (0.5 mmol), Fe<sub>2</sub>(CO)<sub>9</sub> (0.05 mmol, 10 mol%), ligand (0.15 mmol, 30 mol%), DTBP (1.5 mmol, 3 equiv), 1,4-dioxane (2.0 mL), under N<sub>2</sub>.  
<sup>b</sup>Isolated yields.  
<sup>c</sup>Reaction conditions: α,β-unsaturated ketone (0.5 mmol), Fe<sub>2</sub>(CO)<sub>9</sub> (0.05 mmol, 10 mol%), ligand (0.15 mmol, 30 mol%), DTBP (1.5 mmol, 3 equiv), solvent (3.0 mL), under N<sub>2</sub>.  

### III. Fe-catalyzed Direct Coupling of Alkanes with α,β-Unsaturated Ketones.

**General Procedure (A) for the Fe-catalyzed Direct Coupling of sp<sup>3</sup> Carbon of Ethers with β-Substituted α,β-Unsaturated Ketones.** To an over-dried 10 mL Schlenk tube equipped with a magnetic stir bar was added Fe<sub>2</sub>(CO)<sub>9</sub> (18.2 mg, 0.05 mmol, 10 mol%). The vial was sealed with a teflon-lined screw cap, evacuated, and backfilled with nitrogen by connecting with a tube attached to a Schlenk line. The cycle was repeated three times and followed by addition of α,β-unsaturated ketone (0.5 mmol, 1.0 equiv), 2,2,2-trifluoroethanol (1.0 mL), N,N,N',N'-tetramethylethylenediamine (30 mol%), di-tert-butyl peroxide (219 mg, 1.5 mmol, 3.0 equiv) and anhydrous ether (2.0 mL) via syringe. The mixture was stirred at 115 °C for 12 h. After the reaction was completed, the reaction mixture was allowed to cool to room temperature. And the crude product was afforded after evaporation of the solvent under reduced pressure and ready to be purified by silica gel column chromatography with ethyl acetate/petroleum ether.
General Procedure (B) for the Fe-catalyzed Direct Coupling of \(sp^3\) Carbon of Ethers with \(\alpha\)-Substituted \(\alpha,\beta\)-Unsaturated Ketones. To an over-dried 10 mL Schlenk tube equipped with a magnetic stir bar was added \(\text{Fe}_2(\text{CO})_9\) (18.2 mg, 0.05 mmol, 10 mol%). The vial was sealed with a teflon-lined screw cap, evacuated, and backfilled with nitrogen by connecting with a tube attached to a Schlenk line. The cycle was repeated three times and followed by addition of \(\alpha,\beta\)-unsaturated ketone (0.5 mmol, 1.0 equiv), HOAc (1.0 mmol, 2.0 equiv), \(N,N',N'\)-tetramethylethlenediamine (30 mol%), di-tert-butyl peroxide (292 mg, 2.0 mmol, 4.0 equiv) and anhydrous ether (2.0 mL) via syringe. The mixture was stirred at 115 °C for 24 h. After the reaction was complete, the reaction mixture was allowed to cool to room temperature, t

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\text{1} + \text{2} \rightarrow \text{3}
\]

\(1\) \(\text{2.0 mL}\) \(\text{HOAc (2.0 equiv)}\) \(10 \text{ mol\%} \text{Fe}_2(\text{CO})_9\) \(30 \text{ mol\%} \text{TEMED} \) \(\text{DTBP (4.0 equiv)}\)

3-(1,4-dioxan-2-yl)-1-phenylbutan-1-one (Table 2, entry 3a). From (E)-1-phenylbut-2-en-1-one (73 mg, 0.5 mmol), the title compound was prepared following the general procedure A using 1, 4-dioxane (2.0 mL). The residue was purified by silica gel flash column chromatography (10% EtOAc in petroleum ether) to provide the title compound as a pale yellow oil (81 mg, 69%). \(^1\)H NMR (400 MHz, Chloroform-\(d\), 2 diastereomers): \(\delta\) 7.97 (m, 2H), 7.60 – 7.50 (m, 1H), 7.45 (m, 2H), 3.90 – 3.84 (m, 0.50H, 1 diastereomer), 3.81 – 3.62 (m, 3.50H), 3.61 – 3.43 (m, 2H), 3.41 – 3.30 (m, 1.5H), 3.19 (dd, \(J = 16.6, 5.5\) Hz, 1H, 1 diastereomer), 2.80 (dd, \(J = 16.6, 7.9\) Hz, 0.5H, 1 diastereomer), 2.70 (dd, \(J = 16.5, 8.7\) Hz, 0.5H, 1 diastereomer), 2.42 – 2.22 (m, 1H), 0.99 (d, \(J = 7.0\) Hz, 1.5H, 1 diastereomer), 0.94 (d, \(J = 7.0\) Hz, 1.5H, 1 diastereomer); \(^{13}\)C NMR (101 MHz, Chloroform-\(d\), 2 diastereomers): \(\delta\) 199.84, 199.50, 137.46, 137.32, 133.08, 132.90, 128.64, 128.58, 128.16, 79.06, 78.26, 69.98, 69.12, 67.20, 67.05, 66.63, 66.49, 41.90, 41.58, 31.88, 31.20, 16.40, 15.11; HRMS (ESI): calcd. for \(\text{C}_{14}\text{H}_{18}\text{O}_3\) [M+Na]+ \(m/z\) 257.1154, found 257.1157.

1-phenyl-3-(tetrahydro-2H-pyran-2-yl)butan-1-one (Table 2, entry 3b). From (E)-1-phenylbut-2-en-1-one (73 mg, 0.5 mmol), the title compound was prepared following the general procedure A using tetrahydro-2H-pyran (2.0 mL). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a pale yellow oil (70 mg, 60%). \(^1\)H NMR (400 MHz, Chloroform-\(d\), 2 diastereomers): \(\delta\) 7.95 – 7.86 (m, 2H), 7.50 – 7.42 (m, 1H), 7.40 – 7.32 (m, 2H), 3.94 – 3.81 (m, 1H), 3.39 – 3.21 (m, 1.5H),
3.21 – 3.11 (m, 1H), 3.14 (ddd, J = 11.0, 7.1, 2.1 Hz, 0.5H, 1 diastereomer), 2.67 (dd, J = 16.2, 8.1 Hz, 0.5H, 1 diastereomer), 2.60 (dd, J = 16.1, 8.8 Hz, 1H, 1 diastereomer), 2.30 – 2.10 (m, 1H), 1.84 – 1.70 (m, 1H), 1.65 – 1.55 (m, 0.5H, 1 diastereomer), 1.56 – 1.28 (m, 4H), 1.25 – 1.11 (m, 0.5H, 1 diastereomer), 0.89 (d, J = 6.8 Hz, 1.5H, 1 diastereomer), 0.89 (d, J = 6.6 Hz, 1.5H, 1 diastereomer); $^{13}$C NMR (101 MHz, Chloroform-$d$, 2 diastereomers): δ 200.60, 200.53, 137.68, 137.58, 132.91, 132.75, 128.58, 128.54, 128.26, 128.24, 81.86, 80.82, 68.85, 68.73, 42.13, 42.05, 35.49, 34.58, 29.24, 28.25, 26.39, 26.26, 23.84, 23.70, 16.67, 15.02; HRMS (ESI): calcd. for $C_{15}H_{32}O_2$ [M+Na]$^+$ m/z 255.1361, found 255.1366.

3-(2,2-dimethyl-1,3-dioxolan-4-yl)-1-phenylbutan-1-one (Table 2, entry 3c). From (E)-1-phenylbutan-2-ene-1-one (73 mg, 0.5 mmol), the title compound was prepared following the general procedure A using 2,2-dimethyl-1,3-dioxolane (2.0 mL). The residue was purified by silica gel flash column chromatography (10% EtOAc in petroleum ether) to provide the title compound as a pale yellow oil (108 mg, 87%). $^1$H NMR (400 MHz, Chloroform-$d$, 2 diastereomers): δ 7.94 – 7.86 (m, 2H), 7.53 – 7.44 (m, 1H), 7.42 – 7.35 (m, 2H), 4.11 – 3.98 (m, 1.5H), 3.86 (dt, J = 8.1, 6.6 Hz, 0.5H, 1 diastereomer), 3.64 (dd, J = 8.1, 7.0 Hz, 0.5H, 1 diastereomer), 3.59 (dd, J = 8.1, 7.1 Hz, 1H, 1 diastereomer), 3.28 (dd, J = 16.4, 3.5 Hz, 1H, 1 diastereomer), 3.04 (dd, J = 16.5, 4.9 Hz, 1H, 1 diastereomer), 2.75 (dd, J = 13.9, 9.0 Hz, 0.5H, 1 diastereomer), 2.71 (dd, J = 13.9, 8.9 Hz, 0.5H, 1 diastereomer), 2.45 – 2.19 (m, 1H), 1.31 (4 s, 6H), 0.94 (d, J = 6.8 Hz, 1.5H, 1 diastereomer), 0.86 (d, J = 6.8 Hz, 1.5H, 1 diastereomer); $^{13}$C NMR (101 MHz, Chloroform-$d$, 2 diastereomers): δ 199.73, 199.46, 137.43, 137.36, 133.18, 133.06, 128.73, 128.67, 128.29, 128.26, 109.16, 109.05, 80.00, 79.04, 68.30, 66.87, 42.36, 41.69, 34.01, 31.99, 28.80, 26.49, 25.74, 25.29, 16.45, 15.32; HRMS (ESI): calcd. for $C_{15}H_{20}O_3$ [M+Na]$^+$ m/z 271.1310, found 271.1310.

3-methyl-1-phenyl-4-propanoylhexan-1-one (Table 2, entry 3d). From (E)-1-phenylbutan-2-ene-1-one (73 mg, 0.5 mmol), the title compound was prepared following the general procedure A using 1-propoxypropane (2.0 mL). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a pale yellow oil (96 mg, 77%). $^1$H NMR (400 MHz, Chloroform-$d$, 2 diastereomers): δ 8.02 – 7.95 (m, 2H), 7.60 – 7.51 (m, 1H), 7.51 – 7.40 (m, 2H), 3.53 – 3.31 (m, 2H), 3.22 (dd, J = 6.2, 4.3 Hz, 0.5H, 1 diastereomer), 3.18 (dd, J = 6.2, 4.4 Hz, 0.5H, 1 diastereomer), 3.13 – 3.02 (m, 1H), 2.73 (dd, J = 16.1, 8.9 Hz, 0.5H, 1 diastereomer), 2.72 (dd, J = 16.2, 8.9 Hz, 0.5H, 1 diastereomer), 2.56 – 2.37 (m, 1H), 1.63 – 1.56 (m, 2H), 1.55 – 1.48 (m, 2H), 0.99 – 0.88 (m, 9H); $^{13}$C NMR (101 MHz, Chloroform-$d$, 2 diastereomers): δ 200.67, 200.55, 137.62, 137.59, 132.97, 132.92, 128.65, 128.29, 128.25, 84.56, 84.50, 71.95, 71.81, 41.91, 41.32, 32.61, 31.88, 29.85, 23.60, 23.55, 23.42, 23.40, 16.57, 15.38, 10.94, 10.91, 9.65; HRMS (ESI): calcd. for $C_{16}H_{24}O_2$ [M+Na]$^+$ m/z 271.1674, found 271.1675.
3-(3,3-dimethyloxetan-2-yl)-1-phenylbutan-1-one (Table 2, entry 3e). From (E)-1-phenylbut-2-en-1-one (73 mg, 0.5 mmol), the title compound was prepared following the general procedure A using 3,3-dimethyloxetane (2.0 mL). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a pale yellow oil (81 mg, 70%). \( ^1 \)H NMR (400 MHz, Chloroform-\( d \), 2 diastereomers): \( \delta \) 8.00 – 7.92 (m, 2H), 7.61 – 7.51 (m, 1H), 7.50 – 7.41 (m, 2H), 4.30 (d, \( J = 5.8 \) Hz, 1H, 1 diastereomer), 4.19 (d, \( J = 9.9 \) Hz, 0.4H, 1 diastereomer), 4.10 (d, \( J = 10.5 \) Hz, 0.6H, 1 diastereomer), 4.02 (d, \( J = 5.8 \) Hz, 1H), 3.29 (dd, \( J = 16.0, 2.7 \) Hz, 0.6H, 1 diastereomer), 2.74 – 2.58 (m, 1.7H), 2.52 (dd, \( J = 16.0, 9.9 \) Hz, 0.6H, 1 diastereomer), 1.27 (4 s, 6H), 0.96 (d, \( J = 6.1 \) Hz, 1H), 0.83 (d, \( J = 6.4 \) Hz, 2H); \( ^{13} \)C NMR (101 MHz, Chloroform-\( d \), 2 diastereomers): \( \delta \) 199.80, 198.54, 137.43, 137.40, 133.19, 132.93, 128.72, 128.60, 128.21, 128.10, 93.94, 93.80, 80.20, 80.17, 80.41, 80.34, 38.40, 32.20, 31.78, 27.22, 27.07, 21.33, 21.10, 15.49, 15.10; HRMS (ESI): calcd. for \( \text{C}_{15}\text{H}_{20}\text{O}_{2} \) [M+Na]\(^+\) m/z 255.1361, found 255.1363.

1-phenyl-3-(1,3,5-trioxan-2-yl)butan-1-one (Table 2, entry 3f). From (E)-1-phenylbut-2-en-1-one (73 mg, 0.5 mmol), the title compound was prepared following the general procedure A using 1,3,5-trioxane (2.25 g, 25.0 mmol, 50.0 equiv). The residue was purified by silica gel flash column chromatography (15% EtOAc in petroleum ether) to provide the title compound as a pale yellow oil (57 mg, 48%). \( ^1 \)H NMR (400 MHz, Chloroform-\( d \)): \( \delta \) 8.06 – 7.92 (m, 2H), 7.59 – 7.51 (m, 1H), 7.51 – 7.41 (m, 2H), 5.22 (ddd, \( J = 13.5, 6.1, 1.2 \) Hz, 2H), 5.09 (dd, \( J = 6.2, 4.4 \) Hz, 2H), 4.90 (d, \( J = 3.9 \) Hz, 1H), 3.34 (ddd, \( J = 17.1, 4.7 \) Hz, 1H), 2.85 (dd, \( J = 17.1, 8.3 \) Hz, 1H), 2.65 – 2.46 (m, 1H), 1.06 (d, \( J = 7.0 \) Hz, 3H); \( ^{13} \)C NMR (101 MHz, Chloroform-\( d \)): \( \delta \) 199.33, 137.27, 133.07, 128.63, 128.21, 103.99, 93.45, 93.36, 39.50, 33.67, 14.44; HRMS (ESI): calcd. for \( \text{C}_{13}\text{H}_{16}\text{O}_{4} \) [M+Na]\(^+\) m/z 259.0946, found 259.0947.

1-phenyl-3-(2,4,6-trimethyl-1,3,5-trioxan-2-yl)butan-1-one (Table 2, entry 3g). From (E)-1-phenylbut-2-en-1-one (73 mg, 0.5 mmol), the title compound was prepared following the general procedure A using 1,3,5-trioxane (2.0 mL). The residue was purified by silica gel flash column chromatography (15% EtOAc in petroleum ether) to provide the title compound as a pale yellow oil (63 mg, 45%). \( ^1 \)H NMR (400 MHz, Chloroform-\( d \)): \( \delta \) 7.96 (d, \( J = 7.3 \) Hz, 2H), 7.58 (t, \( J = 7.4 \) Hz, 1H), 7.48 (t, \( J = 7.6 \) Hz, 2H), 5.34 (dq, \( J = 22.6, 5.1 \) Hz, 2H), 3.58 – 3.47 (m, 1H), 3.15 (dd, \( J = 16.9, 3.4 \) Hz, 1H), 2.79 (dd, \( J = 16.9, 9.1 \) Hz, 1H), 1.37 (s, 3H), 1.36 (d, \( J = 5.1 \) Hz, 3H), 1.26 (d, \( J = 5.0 \) Hz, 3H), 1.00 (d, \( J = 6.8 \) Hz, 3H); \( ^{13} \)C NMR (101 MHz, Chloroform-\( d \)): \( \delta \) 199.23,
3-methyl-4-phenoxy-1-phenylpentan-1-one (Table 2, entry 3h). From (E)-1-phenylbut-2-en-1-one (73 mg, 0.5 mmol), the title compound was prepared following the general procedure A using ethoxybenzene (2.0 mL). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a pale yellow oil (54 mg, 40%). 1H NMR (400 MHz, Chloroform-d, 2 diastereomers): δ 8.05 – 7.87 (m, 2H), 7.58 – 7.48 (m, 1H), 7.48 – 7.35 (m, 2H), 7.30 – 7.21 (m, 2H), 6.95 – 6.84 (m, 3H), 4.45 (qd, J = 6.2, 3.6 Hz, 0.4H, 1 diastereomer), 4.30 (qd, J = 6.2, 3.6 Hz, 0.6H, 1 diastereomer), 3.32 (dd, J = 4.8, 3.2 Hz, 0.4H, 1 diastereomer), 3.27 (dd, J = 4.8, 3.2 Hz, 0.6H, 1 diastereomer), 2.84 (dd, J = 16.3, 8.5 Hz, 0.4H, 1 diastereomer), 2.83 (dd, J = 16.4, 8.4 Hz, 0.6H, 1 diastereomer), 2.66 – 2.46 (m, 1H), 1.30 (d, J = 6.3 Hz, 1.2H, 1 diastereomer), 1.29 (d, J = 6.3 Hz, 1.8H, 1 diastereomer), 1.08 (d, J = 6.9 Hz, 1.2H), 1.05 (d, J = 6.8 Hz, 1.8H); 13C NMR (101 MHz, Chloroform-d, 2 diastereomers): δ 200.07, 199.92, 158.12, 158.10, 137.38, 137.28, 133.03, 129.61, 129.60, 128.67, 128.63, 128.26, 128.23, 120.79, 120.75, 116.09, 115.98, 76.97, 76.18, 41.92, 41.39, 35.16, 34.27, 16.80, 16.34, 16.06, 15.10; HRMS (ESI): calcd. for C18H20O3 [M+Na]+ m/z 301.1416, found 301.1417.

1-phenyl-3-(tetrahydrofuran-2-yl)butan-1-one (Table 2, entry 3i). From (E)-1-phenylbut-2-en-1-one (73 mg, 0.5 mmol), the title compound was prepared following the general procedure A using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a pale yellow oil (94 mg, 86%). 1H NMR (400 MHz, Chloroform-d, 2 diastereomers): δ 7.93 – 7.86 (m, 2H), 7.53 – 7.42 (m, 1H), 7.42 – 7.32 (m, 2H), 3.85 – 3.60 (m, 2.5H), 3.55 (td, J = 8.0, 6.5 Hz, 0.5H, 1 diastereomer), 3.30 (dd, J = 16.1, 4.0 Hz, 0.5H, 1 diastereomer), 3.04 (dd, J = 16.0, 4.7 Hz, 0.5H, 1 diastereomer), 2.66 (dd, J = 16.0, 8.8 Hz, 1H), 2.40 – 2.29 (m, 0.5H, 1 diastereomer), 2.40 – 2.29 (m, 0.5H, 1 diastereomer), 2.24 – 2.09 (m, 0.5H, 1 diastereomer), 1.97 – 1.84 (m, 1H), 1.84 – 1.72 (m, 2H), 1.58 – 1.42 (m, 1H), 0.91 (d, J = 6.8 Hz, 1.5H), 0.86 (d, J = 6.8 Hz, 1.5H); 13C NMR (101 MHz, Chloroform-d, 2 diastereomers): δ 200.27, 200.06, 137.55, 137.45, 132.94, 132.83, 128.63, 128.57, 128.23, 83.49, 82.78, 68.29, 67.85, 42.91, 42.13, 35.36, 33.86, 29.71, 28.24, 26.16, 26.07, 16.80, 15.66; HRMS (ESI): calcd. for C14H18O2 [M+Na]+ m/z 241.1204, found 241.1209.

1-(4-(benzyloxy)phenyl)-3-(tetrahydrofuran-2-yl)butan-1-one (Table 3, entry 3j). From
**(E)-1-(4-(benzyloxy)phenyl)but-2-en-1-one** (126 mg, 0.5 mmol), the title compound was prepared following the general procedure A using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (10% EtOAc in petroleum ether) to provide the title compound as a pale yellow oil (107 mg, 66%). $^1$H NMR (400 MHz, Chloroform-d, 2 diastereomers): 6.810 – 7.85 (m, 2H), 7.50 – 7.28 (m, 5H), 7.10 – 6.86 (m, 2H), 5.11 (s, 2H), 3.90 – 3.76 (m, 1.5H), 3.77 – 3.67 (m, 1H, 1 diastereomer), 3.66 – 3.58 (m, 0.5H, 1 diastereomer), 3.32 (dd, $J$ = 15.9, 3.9 Hz, 0.5H, 1 diastereomer), 3.05 (dd, $J$ = 15.7, 4.6 Hz, 0.5H, 1 diastereomer), 2.71 (dd, $J$ = 15.7, 8.9 Hz, 0.5H, 1 diastereomer), 2.64 (dd, $J$ = 15.9, 9.3 Hz, 0.5H, 1 diastereomer), 2.49 – 2.14 (m, 1H), 2.06 – 1.78 (m, 3H), 1.72 – 1.45 (m, 1H), 0.97 (d, $J$ = 6.8 Hz, 1.5H, 1 diastereomer), 0.93 (d, $J$ = 6.7 Hz, 1.5H, 1 diastereomer); $^{13}$C NMR (101 MHz, Chloroform-d, 2 diastereomers): δ 198.91, 198.71, 162.63, 162.54, 136.42, 136.38, 130.90, 130.82, 130.60, 130.57, 128.82, 128.35, 128.33, 127.60, 114.67, 114.62, 83.59, 82.92, 70.27, 70.25, 68.35, 67.92, 42.59, 41.90, 35.51, 34.12, 29.70, 28.34, 26.22, 26.12, 16.81, 15.69; HRMS (ESI): calcd. for C$_{17}$H$_{22}$O$_3$ [M+Na]$^+$ m/z 347.1623, found 347.1620.

![Structure of (E)-1-(4-(benzyloxy)phenyl)but-2-en-1-one](image)

**1-[(1,1'-biphenyl)-4-yl]-3-(tetrahydrofuran-2-yl)butan-1-one** (Table 3, entry 3k). From **(E)-1-[(1,1'-biphenyl)-4-yl]but-2-en-1-one** (95 mg, 0.5 mmol), the title compound was prepared following the general procedure A using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (25% EtOAc in petroleum ether) to provide the title compound as a pale yellow oil (80 mg, 61%). $^1$H NMR (400 MHz, Chloroform-d, 2 diastereomers): δ 7.91 (d, $J$ = 2.3 Hz, 1H, 1 diastereomer), 7.89 (d, $J$ = 2.3 Hz, 1H, 1 diastereomer), 6.64 (d, $J$ = 9.0 Hz, 2H), 3.90 – 3.82 (m, 1H, 1 diastereomer), 3.82 – 3.70 (m, 1.5H), 3.68 – 3.59 (m, 0.5H, 1 diastereomer), 3.26 (dd, $J$ = 15.4, 3.8 Hz, 0.5H, 1 diastereomer), 3.03 (2 s, 6H), 3.00 (dd, $J$ = 15.2, 4.5 Hz, 0.5H, 1 diastereomer), 2.68 (dd, $J$ = 15.2, 9.0 Hz, 0.5H, 1 diastereomer), 2.62 (dd, $J$ = 15.4, 9.6 Hz, 0.5H, 1 diastereomer), 2.43 – 2.15 (m, 1H), 2.04 – 1.79 (m, 3H), 1.67 – 1.50 (m, 1H), 0.97 (d, $J$ = 6.7 Hz, 1.5H, 1 diastereomer), 0.92 (d, $J$ = 6.7 Hz, 1.5H, 1 diastereomer); $^{13}$C NMR (101 MHz, Chloroform-d, 2 diastereomers): δ 198.37, 198.13, 153.34, 153.28, 130.43, 130.40, 125.54, 125.48, 110.67, 110.66, 83.54, 83.06, 68.19, 67.83, 41.99, 41.47, 40.03, 35.54, 34.46, 29.42, 28.45, 26.13, 26.05, 16.57, 15.70; HRMS (ESI): calcd. for C$_{18}$H$_{23}$NO$_2$ [M+Na]$^+$ m/z 284.1626, found 284.1629.

![Structure of 1-[(1,1'-biphenyl)-4-yl]-3-(tetrahydrofuran-2-yl)butan-1-one](image)

**S9**
(m, 0.5H, 1 diastereomer), 3.41 (dd, J = 15.4, 3.8 Hz, 0.5H, 1 diastereomer), 3.14 (dd, J = 15.9, 4.6 Hz, 0.5H, 1 diastereomer), 2.80 (dd, J = 15.9, 8.8 Hz, 0.5H, 1 diastereomer), 2.72 (dd, J = 16.0, 9.1 Hz, 0.5H, 1 diastereomer), 2.51 – 2.20 (m, 1H), 2.03 – 1.92 (m, 1H), 1.92 – 1.81 (m, 2H), 1.68 – 1.50 (m, 1H), 1.00 (d, J = 6.8 Hz, 1.5H, 1 diastereomer), 0.96 (d, J = 6.7 Hz, 1.5H, 1 diastereomer); $^{13}$C NMR (101 MHz, Chloroform-$d$, 2 diastereomers): $\delta$ 199.77, 199.57, 145.55, 145.42, 139.99, 139.94, 136.19, 136.08, 128.97, 128.95, 128.81, 128.79, 128.20, 128.16, 127.28, 127.21, 127.17, 83.47, 82.74, 68.25, 67.80, 42.91, 42.13, 35.42, 33.90, 29.69, 28.20, 26.13, 26.04, 16.78, 15.64; HRMS (ESI): calcd. for $C_{20}H_{20}O_3$ [M+Na]$^+$ m/z 317.1517, found 317.1524.

1-(3-methoxyphenyl)-3-(tetrahydrofuran-2-yl)butan-1-one (Table 3, entry 3m). From (E)-1-(3-methoxyphenyl)but-2-en-1-one (88 mg, 0.5 mmol), the title compound was prepared following the general procedure A using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (20% EtOAc in petroleum ether) to provide the title compound as a pale yellow oil (90 mg, 72%). $^1$H NMR (400 MHz, Chloroform-$d$, 2 diastereomers): $\delta$ 8.02 – 7.91 (m, 2H), 6.98 – 6.87 (m, 2H), 3.86 (2 s, 3H), 3.84 – 3.78 (m, 1.5H), 3.77 – 3.69 (m, 1H), 3.67 – 3.58 (m, 0.5H, 1 diastereomer), 3.33 (dd, J = 15.8, 3.8 Hz, 0.5H, 1 diastereomer), 3.06 (dd, J = 15.7, 4.6 Hz, 0.5H, 1 diastereomer), 2.72 (dd, J = 15.7, 8.9 Hz, 0.5H, 1 diastereomer), 2.65 (dd, J = 15.8, 9.3 Hz, 1H, 1 diastereomer), 2.46 – 2.34 (m, 0.5H, 1 diastereomer), 2.28 – 2.15 (m, 0.5H, 1 diastereomer), 2.02 – 1.95 (m, 0.5H, 1 diastereomer), 1.94 – 1.81 (m, 2.5H), 1.68 – 1.50 (m, 1H), 0.97 (d, J = 6.8 Hz, 1.5H, 1 diastereomer), 0.93 (d, J = 6.7 Hz, 1.5H, 1 diastereomer); $^{13}$C NMR (101 MHz, Chloroform-$d$, 2 diastereomers): $\delta$ 198.85, 198.65, 163.43, 163.34, 130.65, 130.58, 130.53, 130.51, 113.76, 113.70, 83.54, 82.87, 68.29, 67.87, 55.53, 55.52, 42.53, 41.84, 35.48, 34.09, 29.66, 28.31, 26.17, 26.08, 16.75, 15.65; HRMS (ESI): calcd. for $C_{15}H_{16}O_3$ [M+Na]$^+$ m/z 271.1310, found 271.1312.

1-(3-methoxyphenyl)-3-(tetrahydrofuran-2-yl)butan-1-one (Table 3, entry 3n). From (E)-1-(3-methoxyphenyl)but-2-en-1-one (88 mg, 0.5 mmol), the title compound was prepared following the general procedure A using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (15% EtOAc in petroleum ether) to provide the title compound as a pale yellow oil (94 mg, 76%). $^1$H NMR (400 MHz, Chloroform-$d$, 2 diastereomers): $\delta$ 7.59 – 7.53 (m, 1H), 7.52 – 7.46 (m, 1H), 7.38 – 7.31 (m, 1H), 7.12 – 7.05 (m, 1H), 3.84 (2 s, 3H), 3.91 – 3.77 (m, 1.5H), 3.77 – 3.68 (m, 1H, 1 diastereomer), 3.67 – 3.58 (m, 0.5H, 1 diastereomer), 3.37 (dd, J = 16.1, 4.0 Hz, 0.5H, 1 diastereomer), 3.10 (dd, J = 16.0, 4.6 Hz, 0.5H, 1 diastereomer), 2.76 (dd, J = 16.0, 8.8 Hz, 0.5H, 1 diastereomer), 2.68 (dd, J = 16.1, 9.1 Hz, 0.5H, 1 diastereomer), 2.49 – 2.16 (m, 1H), 2.03 – 1.95 (m, 0.5H, 1 diastereomer), 1.95 – 1.79 (m, 2H), 1.69 – 1.47 (m, 1H), 0.98 (d, J = 6.8 Hz, 1.5H, 1 diastereomer), 0.94 (d, J = 6.7 Hz, 1.5H, 1 diastereomer); $^{13}$C NMR (101 MHz, Chloroform-$d$, 2 diastereomers): $\delta$ 199.90, 199.71, 159.81, 159.77, 138.82, 138.72, 129.51, 129.46, 120.80, 120.80, 119.33, 119.25, 112.39, 112.36,
1-(2-methoxyphenyl)-3-(tetrahydrofuran-2-yl)butan-1-one (Table 3, entry 3o). From (E)-1-(2-methoxyphenyl)but-2-en-1-one (88 mg, 0.5 mmol), the title compound was prepared following the general procedure A using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (15% EtOAc in petroleum ether) to provide the title compound as a pale yellow oil (88 mg, 71%). ^1H NMR (400 MHz, Chloroform-d, 2 diastereomers): δ 7.57 – 7.50 (m, 1H), 7.37 – 7.29 (m, 1H), 6.95 – 6.81 (m, 2H), 3.80 (2 s, 3H), 3.76 – 3.67 (m, 1H, 1 diastereomer), 3.67 – 3.59 (m, 1.5H), 3.57 – 3.49 (m, 0.5H, 1 diastereomer), 3.18 (dd, J = 16.5, 4.7 Hz, 0.5H, 1 diastereomer), 2.99 (dd, J = 16.3, 4.9 Hz, 0.5H, 1 diastereomer), 2.72 (dd, J = 12.9, 8.7 Hz, 0.5H, 1 diastereomer), 2.68 (dd, J = 13.1, 8.7 Hz, 0.5H, 1 diastereomer), 2.30 – 2.06 (m, 1H), 1.90 – 1.68 (m, 3H), 1.55 – 1.39 (m, 1H), 0.88 (d, J = 6.8 Hz, 1.5H, 1 diastereomer), 0.83 (d, J = 6.7 Hz, 1.5H, 1 diastereomer); ^13C NMR (101 MHz, Chloroform-d, 2 diastereomers): δ 202.96, 202.59, 158.14, 158.14, 133.07, 132.90, 130.16, 130.08, 129.34, 129.11, 120.67, 120.60, 111.51, 111.49, 83.39, 83.08, 68.08, 67.76, 55.49, 48.03, 47.43, 34.98, 34.06, 29.26, 28.54, 26.06, 16.53, 16.05; HRMS (ESI): calcd. for C_{15}H_{20}O_3 [M+Na]^+ m/z 271.1310, found 271.1309.

1-(3-fluorophenyl)-3-(tetrahydrofuran-2-yl)butan-1-one (Table 3, entry 3p). From (E)-1-(3-fluorophenyl)but-2-en-1-one (82 mg, 0.5 mmol), the title compound was prepared following the general procedure A using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a pale yellow oil (79 mg, 67%). ^1H NMR (400 MHz, Chloroform-d, 2 diastereomers): δ 7.79 – 7.72 (m, 1H), 7.69 – 7.62 (m, 1H), 7.47 – 7.38 (m, 1H), 7.29 – 7.19 (m, 1H), 3.90 – 3.77 (m, 1.5H), 3.76 – 3.68 (m, 1H, 1 diastereomer), 3.67 – 3.56 (m, 0.5H, 1 diastereomer), 3.36 (dd, J = 16.3, 4.2 Hz, 0.5H, 1 diastereomer), 3.10 (dd, J = 16.1, 4.8 Hz, 0.5H, 1 diastereomer), 2.76 (dd, J = 16.1, 8.7 Hz, 0.5H, 1 diastereomer), 2.67 (dd, J = 16.2, 8.9 Hz, 0.5H, 1 diastereomer), 2.49 – 2.16 (m, 1H), 2.05 – 1.95 (m, 0.5H, 1 diastereomer), 1.95 – 1.84 (m, 2.5H), 1.67 – 1.49 (m, 1H), 0.98 (d, J = 6.8 Hz, 1.5H, 1 diastereomer), 0.95 (d, J = 6.7 Hz, 1.5H, 1 diastereomer); ^13C NMR (101 MHz, Chloroform-d, 2 diastereomers): δ 198.80 (d, J = 2.1 Hz), 198.61 (d, J = 2.1 Hz), 162.83 (d, J = 247.7 Hz), 162.81 (d, J = 247.5 Hz), 139.57 (d, J = 6.1 Hz), 139.45 (d, J = 6.0 Hz), 130.16 (d, J = 7.3 Hz), 130.08 (d, J = 7.3 Hz), 123.88 (d, J = 1.7 Hz), 123.85 (d, J = 1.5 Hz), 119.81 (d, J = 21.5 Hz), 119.66 (d, J = 21.6 Hz), 114.83 (d, J = 22.1 Hz), 83.33, 82.48, 68.18, 67.69, 43.00, 42.09, 35.38, 33.62, 29.70, 27.97, 26.02, 25.94, 16.73, 15.48; HRMS (ESI): calcd. for C_{14}H_{17}FO_2 [M+Na]^+ m/z 259.1110, found 259.1112.
3-({tetrahydrofuran-2-yl})-1-(thiophen-2-yl)butan-1-one (Table 3, entry 3q). From (E)-1-(thiophen-2-yl)but-2-en-1-one (76 mg, 0.5 mmol), the title compound was prepared following the general procedure A using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a pale yellow oil (80 mg, 71%). \(^1\)H NMR (400 MHz, Chloroform-d, 2 diastereomers): \(\delta 7.76 – 7.71\) (m, 1H), 7.64 – 7.58 (m, 1H), 7.14 – 7.08 (m, 1H), 3.92 – 3.76 (m, 1.5H), 3.76 – 3.68 (m, 1H, 1 diastereomer), 3.68 – 3.57 (m, 0.5H, 1 diastereomer), 3.28 (dd, \(J = 15.5, 4.2\) Hz, 0.5H, 1 diastereomer), 3.03 (dd, \(J = 15.4, 4.8\) Hz, 0.5H, 1 diastereomer), 2.72 (dd, \(J = 15.3, 8.8\) Hz, 0.5H, 1 diastereomer), 2.66 (dd, \(J = 15.5, 9.1\) Hz, 0.5H, 1 diastereomer), 2.46 – 2.17 (m, 1H), 2.04 – 1.92 (m, 1H), 1.92 – 1.85 (m, 2H), 1.67 – 1.51 (m, 1H), 0.99 (d, \(J = 6.8\) Hz, 1.5H, 1 diastereomer), 0.96 (d, \(J = 6.7\) Hz, 1.5H, 1 diastereomer); \(^{13}\)C NMR (101 MHz, Chloroform-d, 2 diastereomers): \(\delta 193.15, 192.97, 145.08, 144.98, 133.54, 133.32, 132.06, 131.93, 128.16, 128.11, 83.37, 82.67, 68.31, 67.87, 43.58, 43.05, 35.76, 34.42, 29.69, 28.33, 26.15, 26.06, 16.75, 15.58; HRMS (ESI): calcd. for C_{12}H_{18}SO_2 [M+Na]^+ m/z 247.0769, found 247.0775.

1-(1-methyl-1H-imidazol-2-yl)-3-({tetrahydrofuran-2-yl})butan-1-one (Table 3, entry 3r). From (E)-1-(thiophen-2-yl)but-2-en-1-one (76 mg, 0.5 mmol), the title compound was prepared following the general procedure A using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a pale yellow oil (67 mg, 60%). \(^1\)H NMR (400 MHz, Chloroform-d, 2 diastereomers): \(\delta 7.14 – 7.10\) (m, 1H), 7.04 – 6.98 (m, 1H), 3.99 (2 s, 3H), 3.82 – 3.72 (m, 1.5H), 3.72 – 3.62 (m, 1.5H), 3.33 (dd, \(J = 16.0, 5.6\) Hz, 0.5H, 1 diastereomer), 3.14 (dd, \(J = 15.9, 5.2\) Hz, 0.5H, 1 diastereomer), 2.99 (dd, \(J = 16.0, 10.5\) Hz, 0.5H, 1 diastereomer), 2.97 (dd, \(J = 16.0, 10.0\) Hz, 0.5H, 1 diastereomer), 2.51 – 2.28 (m, 1H), 1.97 – 1.79 (m, 3H), 1.68 – 1.55 (m, 1H), 1.00 (d, \(J = 6.8\) Hz, 1.5H, 1 diastereomer), 0.94 (d, \(J = 6.8\) Hz, 1.5H, 1 diastereomer); \(^{13}\)C NMR (101 MHz, Chloroform-d, 2 diastereomers): \(\delta 192.85, 192.56, 143.66, 143.52, 128.88, 128.85, 126.80, 126.69, 83.43, 83.05, 68.09, 67.76, 43.47, 42.01, 36.22, 36.19, 35.05, 34.14, 29.12, 28.13, 26.04, 26.00, 16.63, 16.49; HRMS (ESI): calcd. for C_{12}H_{18}N_2O_2 [M+Na]^+ m/z 245.1266, found 245.1269.

2-oxo-4-({tetrahydrofuran-2-yl})pentyl pivalate (Table 3, entry 3s). From (E)-2-oxopent-3-en-1-yl pivalate (92 mg, 0.5 mmol), the title compound was prepared following the general procedure A using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (15% EtOAc in petroleum ether) to provide the title compound as a pale
yellow oil (78 mg, 61%). $^1$H NMR (400 MHz, Chloroform-$d$, 2 diastereomers): $\delta$ 4.72 – 4.56 (m, 2H), 3.85 – 3.77 (m, 0.5H, 1 diastereomer), 3.77 – 3.64 (m, 2H), 3.57 – 3.48 (m, 0.5H, 1 diastereomer), 2.69 (dd, $J$ = 15.7, 5.2 Hz, 0.5H, 1 diastereomer), 2.69 (dd, $J$ = 15.4, 4.6 Hz, 0.5H, 1 diastereomer), 2.36 – 2.15 (m, 1.5H), 2.15 – 2.04 (m, 0.5H), 2.00 – 1.92 (m, 0.5H), 1.90 – 1.80 (m, 2.5H), 1.58 – 1.46 (m, 1H), 1.27 (2 s, 9H), 0.94 (d, $J$ = 6.5 Hz, 1.5H, 1 diastereomer), 0.91 (d, $J$ = 6.6 Hz, 1.5H, 1 diastereomer); $^{13}$C NMR (101 MHz, Chloroform-$d$, 2 diastereomers): $\delta$ 203.89, 203.64, 177.95, 177.94, 83.48, 82.27, 68.36, 68.31, 68.26, 67.76, 43.24, 42.27, 38.81, 35.26, 33.05, 29.88, 27.89, 27.28, 27.27, 26.09, 25.98, 17.02, 15.62; HRMS (ESI): calcd. for C$_{14}$H$_{22}$O$_4$ [M+Na]$^+$ m/z 279.1572, found 279.1574.

**1-phenyl-3-(tetrahydrofuran-2-yl)pentan-1-one** (Table 3, entry 3t). From (E)-1-phenylpent-2-en-1-one (80 mg, 0.5 mmol), the title compound was prepared following the general procedure A using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a pale yellow oil (76 mg, 65%). $^1$H NMR (400 MHz, Chloroform-$d$, 2 diastereomers): $\delta$ 8.00 – 7.94 (m, 2H), 7.58 – 7.50 (m, 1H), 7.48 – 7.40 (m, 2H), 3.94 – 3.85 (m, 0.5H, 1 diastereomer), 3.84 – 3.72 (m, 1.5H), 3.72 – 3.60 (m, 1H, 1 diastereomer), 3.18 (dd, $J$ = 16.6, 5.5 Hz, 0.5H, 1 diastereomer), 3.06 (dd, $J$ = 16.0, 5.7 Hz, 0.5H, 1 diastereomer), 2.86 (dd, $J$ = 16.6, 6.9 Hz, 0.5H, 1 diastereomer), 2.79 (dd, $J$ = 16.0, 7.2 Hz, 0.5H, 1 diastereomer), 2.45 – 2.18 (m, 1H), 2.01 – 1.92 (m, 0.5H, 1 diastereomer), 1.92 – 1.82 (m, 2.5H), 1.64 – 1.40 (m, 2.5H), 1.40 – 1.27 (m, 0.5H, 1 diastereomer), 0.93 (dd, $J$ = 7.5, 4.3 Hz, 1.5H, 1 diastereomer), 0.91 (dd, $J$ = 7.5, 4.3 Hz, 1.5H, 1 diastereomer); $^{13}$C NMR (101 MHz, Chloroform-$d$, 2 diastereomers): $\delta$ 200.55, 200.39, 137.74, 137.52, 132.83, 132.70, 128.59, 128.53, 128.21, 128.17, 81.63, 81.23, 67.98, 67.63, 41.02, 40.02, 39.60, 39.22, 29.75, 27.70, 26.05, 24.48, 23.96, 11.71, 11.31; HRMS (ESI): calcd. for C$_{15}$H$_{22}$O$_4$ [M+Na]$^+$ m/z 255.1361, found 255.1362.

**1-phenyl-3-(tetrahydrofuran-2-yl)octan-1-one** (Table 3, entry 3u). From (E)-1-phenyloct-2-en-1-one (101 mg, 0.5 mmol), the title compound was prepared following the general procedure A using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a pale yellow oil (87 mg, 63%). $^1$H NMR (400 MHz, Chloroform-$d$, 2 diastereomers): $\delta$ 8.01 – 7.93 (m, 2H), 7.57 – 7.48 (m, 1H), 7.48 – 7.40 (m, 2H), 3.94 – 3.85 (m, 0.5H, 1 diastereomer), 3.84 – 3.72 (m, 1.5H), 3.72 – 3.61 (m, 1H, 1 diastereomer), 3.17 (dd, $J$ = 16.6, 5.6 Hz, 0.5H, 1 diastereomer), 3.09 (dd, $J$ = 16.0, 5.8 Hz, 0.5H, 1 diastereomer), 2.85 (dd, $J$ = 16.6, 6.6 Hz, 0.5H, 1 diastereomer), 2.77 (dd, $J$ = 16.0, 7.1 Hz, 0.5H, 1 diastereomer), 2.51 – 2.22 (m, 1H), 2.01 – 1.92 (m, 0.5H, 1 diastereomer), 1.92 – 1.75 (m, 2.5H), 1.64 – 1.50 (m, 1H), 1.49 – 1.38 (m, 1H), 1.38 – 1.16 (m, 7H), 0.89 – 0.81 (m, 3H); $^{13}$C NMR (101 MHz, Chloroform-$d$, 2 diastereomers): $\delta$ 200.55, 200.45, 137.80, 137.58, 132.82, 132.70, 128.60, 128.55, 128.24, 128.19, 81.97, 81.51,
3-(1,4-dioxan-2-yl)-(4-methoxyphenyl)butan-1-one (Table 3, entry 3v). From (E)-1-(4-methoxyphenyl)but-2-en-1-one (88 mg, 0.5 mmol), the title compound was prepared following the general procedure A using 1,4-dioxane (2.0 mL). The residue was purified by silica gel flash column chromatography (20% EtOAc in petroleum ether) to provide the title compound as a pale yellow oil (86 mg, 65%). 1H NMR (400 MHz, Chloroform-d, 2 diastereomers): δ 8.01 – 7.90 (m, 2H), 6.98 – 6.88 (m, 2H), 3.94 – 3.78 (m, 1H), 3.86 (2 s, 3H), 3.78 – 3.72 (m, 1H), 3.72 – 3.64 (m, 2H), 3.61 – 3.44 (m, 2H), 3.39 – 3.26 (m, 1.5H), 3.13 (dd, J = 16.3, 5.5 Hz, 0.5H, 1 diastereomer), 2.74 (dd, J = 16.3, 8.0 Hz, 0.5H, 1 diastereomer), 2.65 (dd, J = 16.2, 8.9 Hz, 0.5H, 1 diastereomer), 2.39 – 2.30 (m, 0.5H, 1 diastereomer), 2.30 – 2.21 (m, 0.5H, 1 diastereomer), 0.98 (d, J = 6.9 Hz, 1.5H, 1 diastereomer), 0.94 (d, J = 6.8 Hz, 1.5H, 1 diastereomer); 13C NMR (101 MHz, Chloroform-d, 2 diastereomers): δ 198.44, 198.11, 163.52, 163.39, 130.52, 130.47, 130.45, 130.43, 113.77, 113.72, 79.10, 78.34, 69.97, 69.17, 67.21, 67.08, 66.63, 66.50, 55.53, 55.51, 41.54, 41.18, 32.01, 31.39, 16.37, 15.14; HRMS (ESI): calcd. for C15H16O2 [M+Na]+ m/z 287.1259, found 287.1260.

2-methyl-1-phenyl-3-(tetrahydrofuran-2-yl)propan-1-one (Table 3, entry 3w). From 2-methyl-1-phenylprop-2-en-1-one (73 mg, 0.5 mmol), the title compound was prepared following the general procedure B using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a colorless oil (76 mg, 70%). 1H NMR (400 MHz, Chloroform-d, 2 diastereomers): δ8.04 – 7.96 (m, 2H), 7.60 – 7.51 (m, 1H), 7.50 – 7.40 (m, 2H), 3.99 (dtd, J = 10.3, 6.8, 3.6 Hz, 0.5H, 1 diastereomer), 3.85 – 3.60 (m, 3.5H), 2.15 (ddd, J = 13.4, 9.5, 3.6 Hz, 0.5H, 1 diastereomer), 2.05 – 1.93 (m, 1.5H), 1.91 – 1.76 (m, 2H), 1.64 – 1.52 (m, 1H), 1.52 – 1.38 (m, 1H), 1.23 (d, J = 6.8 Hz, 1.5H, 1 diastereomer), 1.21 (d, J = 7.1 Hz, 1.5H, 1 diastereomer); 13C NMR (101 MHz, Chloroform-d, 2 diastereomers): δ 204.72, 204.18, 137.03, 136.46, 132.95, 132.82, 128.68, 128.66, 128.52, 128.47, 77.58, 76.73, 67.68, 67.55, 39.82, 39.48, 38.17, 38.02, 32.00, 31.86, 25.78, 25.71, 19.12, 16.78; HRMS (ESI): calcd. for C14H16O2 [M+Na]+ m/z 241.1204, found 241.1204.

1-(4-bromophenyl)-2-methyl-3-(tetrahydrofuran-2-yl)propan-1-one (Table 3, entry 3x). From 1-(4-bromophenyl)-2-methylprop-2-en-1-one (112 mg, 0.5 mmol), the title compound was
prepared following the general procedure B using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a colorless oil (110 mg, 74%). $^1$H NMR (400 MHz, Chloroform-d, 2 diastereomers): δ 7.95 – 7.82 (m, 2H), 7.61 (d, J = 2.3 Hz, 1H, 1 diastereomer), 7.58 (d, J = 2.3 Hz, 1H, 1 diastereomer), 4.04 – 3.93 (m, 0.5H, 1 diastereomer), 3.85 – 3.76 (m, 1H), 3.76 – 3.59 (m, 2.5H), 2.13 (ddd, J = 13.4, 9.7, 3.4 Hz, 0.5H, 1 diastereomer), 2.05 – 1.93 (m, 1.5H), 1.91 – 1.77 (m, 2H), 1.63 – 1.50 (m, 1H), 1.50 – 1.37 (m, 1H), 1.22 (d, J = 6.8 Hz, 1.5H, 1 diastereomer), 1.20 (d, J = 7.0 Hz, 1.5H, 1 diastereomer); $^{13}$C NMR (101 MHz, Chloroform-d, 2 diastereomers): δ 203.79, 203.11, 135.78, 135.17, 131.97, 131.95, 130.11, 130.05, 128.12, 127.92, 77.37, 76.72, 67.71, 67.55, 39.88, 39.56, 38.12, 38.09, 31.99, 31.85, 25.78, 25.70, 19.03, 16.65; HRMS (ESI): calcd. for C$_{16}$H$_{13}$BrO$_2$ [M+Na]$^+$ m/z 319.0310, found 319.0308.

**4-(2-methyl-3-(tetrahydrofuran-2-yl)propanoyl)benzonitrile** (Table 3, entry 3y). From 4-methacryloylbenzonitrile (86 mg, 0.5 mmol), the title compound was prepared following the general procedure B using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (25% EtOAc in petroleum ether) to provide the title compound as a colorless oil (84 mg, 69%). $^1$H NMR (400 MHz, Chloroform-d, 2 diastereomers): δ 8.15 – 8.04 (m, 2H), 7.82 – 7.74 (m, 2H), 4.05 – 3.95 (m, 0.5H, 1 diastereomer), 3.82 – 3.73 (m, 1.5H), 3.73 – 3.61 (m, 2H), 2.14 (ddd, J = 13.4, 9.7, 3.3 Hz, 1H, 1 diastereomer), 2.05 – 1.76 (m, 4H), 1.66 – 1.54 (m, 1H), 1.52 – 1.38 (m, 1H), 1.24 (d, J = 6.8 Hz, 1.5H, 1 diastereomer), 1.21 (d, J = 6.8 Hz, 1.5H, 1 diastereomer); $^{13}$C NMR (101 MHz, Chloroform-d, 2 diastereomers): δ 203.59, 202.76, 140.21, 139.70, 132.53, 132.50, 128.88, 128.82, 118.12, 118.09, 116.09, 115.94, 77.05, 76.74, 67.71, 67.45, 39.78, 39.64, 38.65, 38.42, 31.90, 31.76, 25.72, 25.65, 18.70, 16.59; HRMS (ESI): calcd. for C$_{15}$H$_{12}$NO$_2$ [M+Na]$^+$ m/z 266.1157, found 266.1155.

**2-methyl-3-(tetrahydrofuran-2-yl)-1-(4-(trifluoromethyl)phenyl)propan-1-one** (Table 3, entry 3z). From 2-methyl-1-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (107 mg, 0.5 mmol), the title compound was prepared following the general procedure B using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (15% EtOAc in petroleum ether) to provide the title compound as a colorless oil (100 mg, 70%). $^1$H NMR (400 MHz, Chloroform-d, 2 diastereomers): δ 8.11 (d, J = 8.1 Hz, 2H), 7.77 – 7.70 (m, 2H), 4.06 – 3.96 (m, 0.5H, 1 diastereomer), 3.86 – 3.74 (m, 1.5H), 3.74 – 3.68 (m, 1.5H), 3.68 – 3.60 (m, 0.5H, 1 diastereomer), 2.16 (ddd, J = 13.9, 9.7, 3.4 Hz, 0.5H, 1 diastereomer), 2.06 – 1.93 (m, 1.5H), 1.93 – 1.79 (m, 2H), 1.68 – 1.53 (m, 1H), 1.53 – 1.39 (m, 1H), 1.24 (d, J = 6.8 Hz, 1.5H, 1 diastereomer), 1.22 (d, J = 7.1 Hz, 1.5H, 1 diastereomer); $^{13}$C NMR (101 MHz, Chloroform-d, 2 diastereomers): δ 203.82, 203.04, 139.49 (d, J = 56.7 Hz, 1 diastereomer), 139.48 (d, J = 56.3 Hz, 1 diastereomer), 134.10 (q, J = 32.7 Hz, 1 diastereomer), 133.96 (q, J = 32.5 Hz, 1 diastereomer), 128.70 (d, J = 5.5 Hz), 125.18 (q, J = 3.8 Hz, 1 diastereomer), 125.58 (q, J = 3.7 Hz, 1
diastereomer), 123.66 (q, J = 272.6 Hz, 1 diastereomer), 123.64 (q, J = 272.7 Hz, 1 diastereomer), 77.29, 76.79, 67.62, 67.41, 39.70, 39.48, 38.48, 38.38, 31.86, 31.71, 25.65, 25.58, 18.72, 16.48; HRMS (ESI): calcd. for C_{15}H_{14}FO_2 [M+Na]^+ m/z 309.1078, found 309.1077.

1-(4-methoxyphenyl)-2-methyl-3-(tetrahydrofuran-2-yl)propan-1-one (Table 3, entry 3aa). From 1-(4-methoxyphenyl)-2-methylprop-2-en-1-one (88 mg, 0.5 mmol), the title compound was prepared following the general procedure B using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (10% EtOAc in petroleum ether) to provide the title compound as a colorless oil (96 mg, 77%). 1H NMR (400 MHz, Chloroform-d, 2 diastereomers): δ 8.06 – 7.95 (m, 2H), 6.99 – 6.89 (m, 2H), 4.03 – 3.93 (m, 0.5H, 1 diastereomer), 3.86 (2 s, 3H), 3.84 – 3.78 (m, 1H), 3.77 – 3.58 (m, 2.5H), 2.13 (ddd, J = 13.5, 9.7, 3.5 Hz, 0.5H, 1 diastereomer), 2.03 – 1.92 (m, 1.5H), 1.92 – 1.74 (m, 2H), 1.66 – 1.51 (m, 1H), 1.51 – 1.34 (m, 1H), 1.22 (d, J = 6.9 Hz, 1H, 1 diastereomer), 1.20 (d, J = 7.0 Hz, 1H, 1 diastereomer); 13C NMR (101 MHz, Chloroform-d, 2 diastereomers): δ 203.20, 202.70, 163.45, 163.31, 130.73, 130.72, 129.96, 129.30, 113.78, 113.77, 77.59, 76.71, 67.61, 67.53, 55.48, 55.47, 39.97, 39.56, 37.66, 37.52, 31.96, 31.82, 25.75, 25.66, 19.25, 16.79; HRMS (ESI): calcd. for C_{15}H_{20}O_3 [M+Na]^+ m/z 271.1310, found 271.1311.

1-(3-chlorophenyl)-2-methyl-3-(tetrahydrofuran-2-yl)propan-1-one (Table 3, entry 3ab). From 1-(3-chlorophenyl)-2-methylprop-2-en-1-one (90 mg, 0.5 mmol), the title compound was prepared following the general procedure B using tetrahydrofuran, (2.0 mL). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a colorless oil (89 mg, 71%). 1H NMR (400 MHz, Chloroform-d, 2 diastereomers): δ 8.00 – 7.96 (m, 1H), 7.88 (2 s, 1H), 7.54 – 7.48 (m, 1H), 7.44 – 7.36 (m, 1H), 4.05 – 3.94 (m, 0.5H, 1 diastereomer), 3.85 – 3.76 (m, 1H), 3.76 – 3.58 (m, 2.5H), 2.21 – 2.08 (m, 0.5H, 1 diastereomer), 2.03 – 1.93 (m, 1.5H), 1.92 – 1.74 (m, 2H), 1.67 – 1.51 (m, 1H), 1.51 – 1.35 (m, 1H), 1.23 (d, J = 6.6 Hz, 1.5H, 1 diastereomer), 1.21 (d, J = 6.9 Hz, 1.5H, 1 diastereomer); 13C NMR (101 MHz, Chloroform-d, 2 diastereomers): δ 203.42, 202.75, 138.63, 138.07, 134.99, 134.95, 132.82, 132.68, 129.98, 129.96, 128.65, 128.55, 126.56, 126.52, 77.31, 76.68, 67.68, 67.49, 39.73, 39.52, 38.32, 31.96, 31.81, 25.76, 25.68, 18.97, 16.67; HRMS (ESI): calcd. for C_{15}H_{16}ClO_2 [M+Na]^+ m/z 275.0815, found 275.0819.

1-(2-chlorophenyl)-2-methyl-3-(tetrahydrofuran-2-yl)propan-1-one (Table 3, entry 3ac). From 1-(2-chlorophenyl)-2-methylprop-2-en-1-one (90 mg, 0.5 mmol), the title compound was prepared following the general procedure B using tetrahydrofuran, (2.0 mL). The residue was
purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a colorless oil (86 mg, 68%). \(^1\)H NMR (400 MHz, Chloroform-\(d\), 2 diastereomers): \(\delta\) 7.54 – 7.25 (m, 4H), 3.99 – 3.90 (m, 0.5H, 1 diastereomer), 3.90 – 3.72 (m, 1.5H), 3.68 (td, \(J = 8.0, 6.4\) Hz, 1H), 3.56 – 3.41 (m, 1H), 2.08 (ddd, \(J = 13.8, 8.4, 4.2\) Hz, 0.5H, 1 diastereomer), 2.04 – 1.94 (m, 1.5H), 1.93 – 1.77 (m, 2H), 1.63 – 1.51 (m, 1H), 1.51 – 1.38 (m, 1H), 1.22 (d, \(J = 7.1\) Hz, 1.5H, 1 diastereomer), 1.20 (d, \(J = 7.3\) Hz, 1.5H, 1 diastereomer); \(^{13}\)C NMR (101 MHz, Chloroform-\(d\), 2 diastereomers): \(\delta\) 207.12, 206.97, 139.78, 139.65, 131.34, 131.29, 131.03, 130.93, 130.46, 128.99, 128.90, 126.80, 126.75, 77.43, 76.60, 67.70, 67.50, 43.07, 42.90, 38.82, 38.49, 31.89, 31.85, 25.68, 17.43, 16.04; HRMS (ESI): calcd. for \(\text{C}_{14}\text{H}_{17}\text{ClO}_2\) [M+Na]\(^+\) \(m/z\) 275.0815, found 275.0815.

![Chemical structure](image)

1-(3-chlorophenyl)-3-(1,4-dioxan-2-yl)-2-methylpropan-1-one (Table 3, entry 3ad). From 1-(3-chlorophenyl)-2-methylprop-2-en-1-one (90 mg, 0.5 mmol), the title compound was prepared following the general procedure B using 1,4-dioxane (2.0 mL). The residue was purified by silica gel flash column chromatography (15% EtOAc in petroleum ether) to provide the title compound as a colorless oil (85 mg, 63%). \(^1\)H NMR (400 MHz, Chloroform-\(d\), 2 diastereomers): \(\delta\) 8.04 – 7.97 (m, 1H), 7.94 – 7.86 (m, 1H), 7.62 – 7.53 (m, 1H), 7.50 – 7.42 (m, 1H), 3.81 – 3.67 (m, 5H), 3.65 – 3.52 (m, 1.5H), 3.48 – 3.39 (m, 0.5H, 1 diastereomer), 3.36 – 3.24 (m, 1H), 2.00 – 1.85 (m, 1H), 1.57 – 1.41 (m, 1H), 1.25 (d, \(J = 6.3\) Hz, 1.5H, 1 diastereomer), 1.24 (d, \(J = 6.3\) Hz, 1.5H, 1 diastereomer); \(^{13}\)C NMR (101 MHz, Chloroform-\(d\), 2 diastereomers): \(\delta\) 203.21, 202.70, 138.61, 138.04, 135.07, 133.07, 132.88, 130.09, 130.05, 128.67, 126.60, 126.52, 73.47, 73.30, 71.53, 71.43, 66.91, 66.77, 66.59, 66.54, 36.70, 36.48, 35.50, 34.91, 19.05, 17.00; HRMS (ESI): calcd. for \(\text{C}_{14}\text{H}_{17}\text{ClO}_2\) [M+Na]\(^+\) \(m/z\) 291.0764, found 291.0765.

![Chemical structure](image)

2-methyl-1-(naphthalen-2-yl)-3-(tetrahydrofuran-2-yl)propan-1-one (Table 3, entry 3ae). From 2-methyl-1-(naphthalen-2-yl)prop-2-en-1-one (98 mg, 0.5 mmol), the title compound was prepared following the general procedure B using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a colorless oil (113 mg, 84%). \(^1\)H NMR (400 MHz, Chloroform-\(d\), 2 diastereomers): \(\delta\) 8.56 (2 s, 1H), 8.06 (d, \(J = 8.6\) Hz, 1H), 7.96 (d, \(J = 8.0\) Hz, 1H), 7.87 (d, \(J = 8.9\) Hz, 2H), 7.62 – 7.48 (m, 2H), 4.09 – 3.99 (m, 0.5H, 1 diastereomer), 3.99 – 3.87 (m, 1H), 3.87 – 3.79 (m, 1H), 3.79 – 3.70 (m, 1H), 3.67 – 3.58 (m, 0.5H, 1 diastereomer), 2.21 (ddd, \(J = 13.4, 9.6, 3.5\) Hz, 0.5H, 1 diastereomer), 2.11 – 1.93 (m, 1.5H), 1.91 – 1.76 (m, 2H), 1.68 – 1.57 (m, 1H), 1.53 – 1.39 (m, 1H), 1.30 (d, \(J = 7.3\) Hz, 1.5H, 1 diastereomer), 1.28 (d, \(J = 7.5\) Hz, 1.5H, 1 diastereomer); \(^{13}\)C NMR (101 MHz, Chloroform-\(d\), 2 diastereomers): \(\delta\) 204.68, 204.12, 135.63, 135.56, 134.32, 133.68, 132.72, 130.09, 130.04, 129.74, 129.68, 128.47, 128.42, 128.35, 127.78, 126.72, 126.69, 124.51, 124.37, 77.62, 76.78, 67.69, 67.58, 39.98, 39.63, 38.20, 38.07, 32.02, 31.87, 25.80, 25.70, 19.34, 16.90; HRMS (ESI): calcd. for \(\text{C}_{18}\text{H}_{22}\text{O}_2\) [M+Na]\(^+\) \(m/z\) 291.1361, found
1-(2-methoxyphenyl)-3-(tetrahydrofuran-2-yl)butan-1-one (Table 3, entry 3af). From 2-methyl-1-(thiophen-2-yl)prop-2-en-1-one (76 mg, 0.5 mmol), the title compound was prepared following the general procedure B using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (10% EtOAc in petroleum ether) to provide the title compound as a colorless oil (75 mg, 67%). $^1$H NMR (400 MHz, Chloroform-\(d\), 2 diastereomers): δ 7.80 (dd, \(J = 3.8, 1.2\) Hz, 1H), 7.63 (dd, \(J = 4.9, 1.1\) Hz, 1H), 7.16 – 7.11 (m, 1H), 4.02 – 3.92 (m, 0.5H, 1 diastereomer), 3.86 – 3.78 (m, 1H), 3.74 – 3.63 (m, 1.5H), 3.63 – 3.49 (m, 1H), 2.12 (ddd, \(J = 13.6, 9.8, 3.5\) Hz, 0.5H, 1 diastereomer), 2.02 – 1.94 (m, 1.5H), 1.93 – 1.77 (m, 2H), 1.66 – 1.54 (m, 1H), 1.50 – 1.36 (m, 1H), 1.27 (d, \(J = 2.0\) Hz, 1.5H, 1 diastereomer), 1.25 (d, \(J = 2.1\) Hz, 1.5H, 1 diastereomer); $^{13}$C NMR (101 MHz, Chloroform-\(d\), 2 diastereomers): δ 197.46, 197.10, 144.54, 143.97, 133.87, 133.55, 132.18, 131.88, 128.23, 128.16, 77.41, 76.62, 67.66, 67.54, 40.05, 40.00, 39.84, 39.68, 31.92, 31.78, 25.74, 25.69, 19.36, 17.06; HRMS (ESI): calcd. for C_{12}H_{16}SO_{2} [M+Na]$^+$ m/z 247.0769, found 247.0772.

2-methyl-1-(1-methyl-1H-imidazol-2-yl)-3-(tetrahydrofuran-2-yl)propan-1-one (Table 3, entry 3ag). From 2-methyl-1-(1-methyl-1H-imidazol-2-yl)prop-2-en-1-one (75 mg, 0.5 mmol), the title compound was prepared following the general procedure B using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (70% EtOAc in petroleum ether) to provide the title compound as a colorless oil (84 mg, 76%). $^1$H NMR (400 MHz, Chloroform-\(d\), 2 diastereomers): δ 7.13 (d, \(J = 1.4\) Hz, 1H), 7.03 (d, \(J = 1.3\) Hz, 1H), 4.08 – 3.97 (m, 0.5H, 1 diastereomer), 3.99 (2 s, 3H), 3.90 – 3.82 (m, 1H), 3.80 – 3.56 (m, 2.5H), 2.12 – 2.01 (m, 1H), 1.99 – 1.90 (m, 1H), 1.89 – 1.77 (m, 2H), 1.75 – 1.68 (m, 0.5H, 1 diastereomer), 1.58 – 1.43 (m, 1.5H), 1.24 (d, \(J = 5.6\) Hz, 1.5H, 1 diastereomer), 1.22 (d, \(J = 5.5\) Hz, 1.5H, 1 diastereomer); $^{13}$C NMR (101 MHz, Chloroform-\(d\), 2 diastereomers): δ 196.84, 196.72, 143.04, 142.89, 129.02, 128.98, 127.00, 126.95, 77.58, 77.51, 67.75, 67.40, 39.60, 39.12, 39.02, 38.82, 36.30, 31.69, 31.55, 25.78, 25.68, 18.11, 18.06; HRMS (ESI): calcd. for C_{12}H_{18}N_{2}O_{2} [M+Na]$^+$ m/z 245.1266, found 245.1267.

2-benzyl-1-phenyl-3-(tetrahydrofuran-2-yl)propan-1-one (Table 3, entry 3ah). From 2-benzyl-1-phenylprop-2-en-1-one (111 mg, 0.5 mmol), the title compound was prepared following the general procedure B using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a colorless oil (120 mg, 82%). $^1$H NMR (400 MHz, Chloroform-\(d\), 2 diastereomers):
δ 8.04 – 7.80 (m, 2H), 7.55 – 7.45 (m, 1H), 7.44 – 7.33 (m, 2H), 7.25 – 7.07 (m, 5H), 4.10 – 3.99 (m, 0.5H), 3.99 – 3.86 (m, 1H), 3.81 – 3.52 (m, 2.5H), 3.09 (dd, J = 13.6, 8.0 Hz, 0.5H, 1 diastereomer), 3.05 (dd, J = 13.7, 7.2 Hz, 0.5H, 1 diastereomer), 2.83 (dd, J = 13.6, 6.2 Hz, 0.5H, 1 diastereomer), 2.76 (dd, J = 13.6, 7.2 Hz, 0.5H, 1 diastereomer), 2.15 – 2.00 (m, 1H), 1.96 – 1.73 (m, 3H), 1.71 – 1.60 (m, 1H), 1.49 – 1.30 (m, 1H); ¹³C NMR (101 MHz, Chloroform-d, 2 diastereomers): δ 204.65, 203.34, 139.83, 139.35, 137.94, 137.32, 132.89, 132.72, 129.18, 129.14, 128.56, 128.54, 128.42, 128.41, 128.38, 126.29, 126.24, 77.18, 77.14, 67.58, 67.38, 45.88, 45.30, 39.77, 38.31, 38.29, 38.04, 31.93, 31.70, 25.68, 25.63; HRMS (ESI): calcd. for C₂₀H₂₂O₂ [M+Na]⁺ m/z 317.1517, found 317.1520.

**1-phenyl-2-((tetrahydrofuran-2-yl)methyl)hexan-1-one** (Table 3, entry 3ai). From 2-methylene-1-phenylhexan-1-one (94 mg, 0.5 mmol), the title compound was prepared following the general procedure B using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a colorless oil (106 mg, 81%). ¹H NMR (400 MHz, Chloroform-d, 2 diastereomers): δ 8.07 – 7.95 (m, 2H), 7.59 – 7.52 (m, 1H), 7.49 – 7.41 (m, 2H), 4.01 – 3.88 (m, 0.5H, 1 diastereomer), 3.82 – 3.73 (m, 1H), 3.67 – 3.58 (m, 1.5H), 2.10 (ddd, J = 13.8, 10.4, 3.3 Hz, 0.5H, 1 diastereomer), 2.02 – 1.91 (m, 1.5H), 1.89 – 1.70 (m, 3H), 1.68 – 1.54 (m, 2.5H), 1.52 – 1.36 (m, 1.5H), 1.33 – 1.17 (m, 4H), 0.87 – 0.77 (m, 3H); ¹³C NMR (101 MHz, Chloroform-d, 2 diastereomers): δ 205.29, 204.09, 138.02, 137.41, 132.90, 132.74, 129.14, 128.75, 77.39, 67.59, 67.38, 43.43, 43.31, 38.49, 38.32, 33.77, 31.97, 31.80, 31.70, 29.68, 29.56, 25.68, 25.66, 22.98, 22.89, 13.97, 13.94; HRMS (ESI): calcd. for C₂₁H₂₄O₂ [M+Na]⁺ m/z 283.1674, found 283.1676.

**1-cyclohexyl-2-methyl-3-(tetrahydrofuran-2-yl)propan-1-one** (Table 3, entry 3aj). From 1-cyclohexyl-2-methylprop-2-en-1-one (76 mg, 0.5 mmol), the title compound was prepared following the general procedure B using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a colorless oil (56 mg, 50%). ¹H NMR (400 MHz, Chloroform-d, 2 diastereomers): δ 3.84 – 3.66 (m, 1.5H), 3.65 – 3.57 (m, 1H), 3.57 – 3.49 (m, 0.5H, 1 diastereomer), 2.90 (ddd, J = 9.5, 7.0, 4.3 Hz, 0.5H, 1 diastereomer), 2.85 – 2.75 (m, 0.5H, 1 diastereomer), 2.48 – 2.35 (m, 1H), 1.95 – 1.82 (m, 2H), 1.81 – 1.67 (m, 6H), 1.63 – 1.57 (m, 1H), 1.38 – 1.29 (m, 2H), 1.28 – 1.10 (m, 5H), 1.01 (d, J = 2.6 Hz, 1.5H, 1 diastereomer), 0.99 (d, J = 2.7 Hz, 1.5H, 1 diastereomer); ¹³C NMR (101 MHz, Chloroform-d, 2 diastereomers): δ 217.93, 217.52, 77.56, 76.97, 67.66, 67.46, 50.43, 50.17, 41.91, 41.83, 39.33, 39.11, 31.94, 31.81, 28.79, 28.57, 28.47, 28.41, 26.00, 25.93, 25.91, 25.79, 25.74, 25.69, 25.68, 18.18, 16.73; HRMS (ESI): calcd. for C₁₄H₂₄O₂ [M+Na]⁺ m/z 247.1674, found 247.1678.
7-chloro-2-methyl-1-(tetrahydrofuran-2-yl)heptan-3-one (Table 3, entry 3ak). From 7-chloro-2-methylhept-1-en-3-one (80 mg, 0.5 mmol), the title compound was prepared following the general procedure B using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a colorless oil (60 mg, 52%). $^1$H NMR (400 MHz, Chloroform-d, 2 diastereomers): δ 3.92 – 3.74 (m, 1.5H), 3.74 – 3.63 (m, 1.5H), 3.54 (t, J = 6.4 Hz, 2H), 2.85 – 2.75 (m, 0.5H, 1 diastereomer), 2.75 – 2.67 (m, 0.5H, 1 diastereomer), 2.57 – 2.48 (m, 2H), 2.00 – 1.81 (m, 4H), 1.80 – 1.68 (m, 4H), 1.52 – 1.36 (m, 2H), 1.10 (d, J = 4.2 Hz, 1.5H, 1 diastereomer), 1.09 (d, J = 4.1 Hz, 1.5H, 1 diastereomer); $^{13}$C NMR (101 MHz, Chloroform-d, 2 diastereomers): δ 214.14, 213.96, 77.30, 77.14, 67.77, 67.49, 44.85, 44.81, 43.97, 43.40, 40.75, 40.28, 39.13, 39.07, 32.11, 31.83, 31.82, 25.71, 25.71, 21.02, 21.00, 17.75, 16.73; HRMS (ESI): calcd. for C_{12}H_{21}ClO_2 [M+Na]^+ m/z 255.1128, found 255.1128.

7-chloro-2-methyl-1-(tetrahydrofuran-2-yl)heptan-3-one (Table 3, entry 3al). From 7-chloro-2-methylhept-1-en-3-one (80 mg, 0.5 mmol), the title compound was prepared following the general procedure B using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a colorless oil (62 mg, 58%). $^1$H NMR (400 MHz, Chloroform-d, 2 diastereomers): δ 3.93 – 3.75 (m, 1.5H), 3.74 – 3.61 (m, 1.5H), 2.86 – 2.76 (m, 0.5H, 1 diastereomer), 2.76 – 2.66 (m, 0.5H, 1 diastereomer), 2.54 – 2.39 (m, 2H), 2.04 – 1.77 (m, 4H), 1.63 – 1.51 (m, 2H), 1.50 – 1.38 (m, 2H), 1.35 – 1.23 (m, 4H), 1.10 (d, J = 1.5 Hz, 1.5H, 1 diastereomer), 1.08 (d, J = 1.4 Hz, 1.5H, 1 diastereomer), 0.89 (t, J = 7.0 Hz, 3H); $^{13}$C NMR (101 MHz, Chloroform-d, 2 diastereomers): δ 215.03, 214.84, 77.46, 76.99, 67.72, 67.51, 43.77, 43.44, 41.87, 41.29, 39.06, 38.90, 31.86, 31.82, 31.57, 31.55, 25.71, 23.47, 23.39, 22.60, 17.79, 16.54, 14.03; HRMS (ESI): calcd. for C_{13}H_{24}O_2 [M+Na]^+ m/z 235.1674, found 235.1677.

2-methyl-7-(naphthalen-1-yloxy)-1-(tetrahydrofuran-2-yl)heptan-3-one (Table 3, entry 3am). From 2-methyl-7-(naphthalen-1-yloxy)hept-1-en-3-one (134 mg, 0.5 mmol), the title compound was prepared following the general procedure B using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (20% EtOAc in petroleum ether) to provide the title compound as a colorless oil (93 mg, 55%). $^1$H NMR (400 MHz, Chloroform-d, 2 diastereomers): δ 8.28 (d, J = 2.2 Hz, 1H), 7.89 – 7.70 (m, 1H), 7.56 – 7.42 (m, 2H), 7.42 – 7.28 (m, 2H), 6.77 (d, J = 1.2 Hz, 1H), 4.19 – 4.03 (m, 2H), 3.90 – 3.55 (m, 3H), 2.86 – 2.76 (m, 0.5H, 1 diastereomer), 2.76 – 2.67 (m, 0.5H, 1 diastereomer), 2.66 – 2.50 (m, 2H), 2.01 – 1.69 (m, 8H), S20.
1.55 – 1.30 (m, 2H), 1.11 (d, J = 3.5 Hz, 1.5H, 1 diastereomer), 1.09 (d, J = 3.3 Hz, 1.5H, 1 diastereomer); ^13^C NMR (101 MHz, Chloroform-^d_, 2 diastereomers): δ 214.45, 214.27, 154.82, 154.80, 134.56, 127.47, 126.38, 125.96, 125.78, 125.13, 122.15, 120.12, 120.10, 104.61, 77.34, 77.06, 67.86, 67.83, 67.72, 67.47, 43.92, 43.44, 41.35, 40.85, 39.08, 39.05, 31.82, 31.79, 28.90, 25.68, 20.54, 20.51, 17.76, 16.66; HRMS (ESI): calcd. for C_{22}H_{28}O_3 [M+Na]^+ m/z 363.1936, found 363.1940.

2-methyl-1-{(tetrahydrofuran-2-yl)trideca-12-en-3-one} (Table 3, entry 3an). From 2-methyltrideca-1,12-dien-3-one (104 mg, 0.5 mmol), the title compound was prepared following the general procedure B using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a colorless oil (94 mg, 67%). ^1H NMR (400 MHz, Chloroform-^d_, 2 diastereomers): δ 5.86 – 5.73 (m, 1H), 5.05 – 4.87 (m, 2H), 3.92 – 3.83 (m, 0.5H, 1 diastereomer), 3.83 – 3.74 (m, 1H, 3.74 – 3.61 (m, 1.5H), 2.89 – 2.61 (m, 1H), 2.55 – 2.36 (m, 2H), 2.07 – 2.01 (m, 2H), 1.99 – 1.92 (m, 1H), 1.91 – 1.81 (m, 2H), 1.61 – 1.50 (m, 2H), 1.50 – 1.42 (m, 1.5H), 1.41 – 1.33 (m, 2.5H), 1.28 (m, 9H), 1.10 (d, J = 1.6 Hz, 1.5H, 1 diastereomer), 1.08 (d, J = 1.5 Hz, 1.5H, 1 diastereomer); ^13^C NMR (101 MHz, Chloroform-^d_, 2 diastereomers): δ 214.91, 214.70, 139.21, 114.19, 77.43, 76.98, 67.70, 67.48, 43.76, 43.42, 41.87, 41.30, 39.07, 38.91, 33.86, 31.85, 31.81, 29.48, 29.40, 29.35, 29.34, 29.15, 28.98, 25.70, 23.76, 23.68, 17.78, 16.53; HRMS (ESI): calcd. for C_{18}H_{32}O_3 [M+Na]^+ m/z 303.2300, found 303.2309.

2-methyl-5-phenyl-1-{(tetrahydrofuran-2-yl)pentan-3-one} (Table 3, entry 3ao). From 2-methyl-5-phenylpent-1-en-3-one (87 mg, 0.5 mmol), the title compound was prepared following the general procedure B using tetrahydrofuran (2.0 mL). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a colorless oil (72 mg, 59%). ^1H NMR (400 MHz, Chloroform-^d_, 2 diastereomers): δ 7.30 – 7.23 (m, 2H), 7.22 – 7.13 (m, 3H), 3.89 – 3.70 (m, 1.5H), 3.70 – 3.57 (m, 1.5H), 2.93 – 2.84 (m, 2H), 2.84 – 2.77 (m, 2H), 2.76 – 2.65 (m, 1H), 2.05 – 1.70 (m, 4H), 1.53 – 1.27 (m, 2H), 1.07 (d, J = 1.7 Hz, 1.5H, 1 diastereomer), 1.05 (d, J = 1.7 Hz, 1.5H, 1 diastereomer); ^13^C NMR (101 MHz, Chloroform-^d_, 2 diastereomers): δ 213.70, 213.55, 141.54, 141.45, 128.46, 128.45, 126.04, 126.01, 77.25, 76.99, 67.71, 67.47, 44.04, 43.58, 43.31, 42.91, 39.02, 38.97, 31.78, 31.76, 29.83, 29.72, 25.68, 17.54, 16.49; HRMS (ESI): calcd. for C_{16}H_{20}O_3 [M+Na]^+ m/z 269.1517, found 269.1523.

3-(1,4-dioxan-2-yl)-2-methyl-1-phenylpropan-1-one (Table 3, entry 3ap). From
2-methyl-1-phenylprop-2-en-1-one (73 mg, 0.5 mmol), the title compound was prepared following the general procedure B using 1,4-dioxane (2.0 mL). The residue was purified by silica gel flash column chromatography (15% EtOAc in petroleum ether) to provide the title compound as a colorless oil (102 mg, 87%). 1H NMR (400 MHz, Chloroform-d, 2 diastereomers): δ 8.02 – 7.95 (m, 2H), 7.63 – 7.52 (m, 1H), 7.53 – 7.42 (m, 2H), 3.82 (ddd, J = 10.6, 7.1, 3.7 Hz, 0.5H, 1 diastereomer), 3.77 – 3.62 (m, 4.5H), 3.62 – 3.51 (m, 1H), 3.57 – 3.39 (m, 0.5H, 1 diastereomer), 3.31 – 3.21 (m, 1H), 2.05 – 1.82 (m, 1H), 1.55 – 1.36 (m, 1H), 1.21 (d, 5.6 Hz, 3H); 13C NMR (101 MHz, Chloroform-d, 2 diastereomers): δ 204.34, 203.96, 136.93, 136.35, 133.13, 132.95, 128.74, 128.71, 128.52, 128.47, 73.69, 73.28, 71.59, 71.48, 66.92, 66.77, 66.58, 66.53, 36.34, 36.32, 35.46, 34.94, 19.21, 16.98; HRMS (ESI): calcd. for C14H14O3 [M+Na]⁺ m/z 257.1154, found 257.1151.

\[ \text{Structure of 2-methyl-1-phenylprop-2-en-1-one} \]

2-methyl-4-phenoxy-1-phenylpentan-1-one (Table 3, entry 3aq). From 2-methyl-1-phenylprop-2-en-1-one (73 mg, 0.5 mmol), the title compound was prepared following the general procedure B using ethoxybenzene (2.0 mL). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a colorless oil (100 mg, 75%). 1H NMR (400 MHz, Chloroform-d, 2 diastereomers): δ 8.09 – 7.96 (m, 1H), 7.94 – 7.83 (m, 1H), 7.59 – 7.42 (m, 2H), 7.40 – 7.31 (m, 1H), 7.30 – 7.25 (m, 1H), 7.21 – 7.11 (m, 1H), 6.97 – 6.81 (m, 2H), 6.78 – 6.69 (m, 1H), 4.56 – 4.45 (m, 0.5H, 1 diastereomer), 4.56 – 4.45 (m, 0.5H, 1 diastereomer), 4.36 – 4.24 (m, 0.5H, 1 diastereomer), 3.90 – 3.81 (m, 0.5H, 1 diastereomer), 3.80 – 3.71 (m, 0.5H, 1 diastereomer), 2.31 (ddd, J = 14.3, 9.0, 5.5 Hz, 1H, 1 diastereomer), 2.22 (ddd, J = 14.3, 9.0, 5.5 Hz, 1H, 1 diastereomer), 1.76 (ddd, J = 13.9, 9.4, 4.1 Hz, 0.5H, 1 diastereomer), 1.76 (ddd, J = 13.9, 9.4, 4.1 Hz, 0.5H, 1 diastereomer), 1.28 (d, J = 6.0 Hz, 3H), 1.23 (d, J = 7.0 Hz, 3H); 13C NMR (101 MHz, Chloroform-d, 2 diastereomers): δ 204.71, 203.94, 158.06, 158.00, 136.82, 136.33, 133.03, 133.01, 129.66, 129.52, 128.77, 128.68, 128.60, 128.41, 120.83, 120.78, 116.08, 115.84, 72.16, 71.46, 41.24, 40.62, 37.25, 20.31, 20.18, 19.04, 17.29; HRMS (ESI): calcd. for C18H20O2 [M+Na]⁺ m/z 291.1361, found 291.1363.

\[ \text{Structure of 2-methyl-4-phenoxy-1-phenylpentan-1-one} \]

3-(2,2-dimethyl-1,3-dioxolan-4-yl)-2-methyl-1-phenylpropan-1-one (Table 3, entry 3ar). From 2-methyl-1-phenylprop-2-en-1-one (73 mg, 0.5 mmol), the title compound was prepared following the general procedure B using 2,2-dimethyl-1,3-dioxolan (2.0 mL). The residue was purified by silica gel flash column chromatography (10% EtOAc in petroleum ether) to provide the title compound as a colorless oil (97 mg, 78%). 1H NMR (400 MHz, Chloroform-d, 2 diastereomers): δ 8.09 – 7.94 (m, 2H), 7.60 – 7.52 (m, 1H), 7.52 – 7.41 (m, 2H), 4.24 (dd, J = 9.1, 7.0, 6.0, 3.9 Hz, 1H, 1 diastereomer), 4.06 (dd, J = 8.0, 6.0 Hz, 1H, 1 diastereomer), 4.03 – 3.95 (m, 1H), 3.83 – 3.65 (m, 1H), 3.58 – 3.46 (m, 1H), 2.27 – 2.13 (m, 0.5H, 1 diastereomer), 2.11 – 2.02 (m, 0.5H, 1 diastereomer), 1.73 – 1.55 (m, 1H), 1.47 – 1.32 (m, 4.5H, 1
2-methyl-1-phenyl-4-propoxyhexan-1-one (Table 3, entry 3as). From 2-methyl-1-phenylprop-2-en-1-one (73 mg, 0.5 mmol), the title compound was prepared following the general procedure B using 1-propoxypropane (2.0 mL). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a colorless oil (89 mg, 72%). $^1$H NMR (400 MHz, Chloroform-$d$, 2 diastereomers): $\delta$ 8.08 – 7.93 (m, 2H), 7.60 – 7.51 (m, 1H), 7.51 – 7.41 (m, 2H), 3.87 – 3.77 (m, 0.5H, 1 diastereomer), 3.77 – 3.64 (m, 0.5H, 1 diastereomer), 3.49 (ddd, $J = 13.2, 6.6, 6.6$ Hz, 0.5H, 1 diastereomer), 3.37 – 3.23 (m, 1.5H), 3.15 – 3.06 (m, 0.5H), 3.01 (ddd, $J = 13.5, 6.7, 6.7$ Hz, 0.5H, 1 diastereomer), 2.15 – 1.95 (m, 1H), 1.65 – 1.38 (m, 5H), 1.21 (d, $J = 4.9$ Hz, 1.5H, 1 diastereomer), 1.20 (d, $J = 5.2$ Hz, 1.5H, 1 diastereomer). 0.98 – 0.78 (m, 6H); $^{13}$C NMR (101 MHz, Chloroform-$d$, 2 diastereomers): $\delta$ 203.79, 203.26, 135.48, 131.91, 131.80, 127.65, 127.63, 127.56, 127.35, 77.46, 77.41, 69.84, 69.65, 37.19, 37.13, 36.18, 35.90, 25.74, 25.69, 22.50, 22.39, 18.09, 15.99, 9.89, 9.76, 8.43, 8.22; HRMS (ESI): calcd. for C$_{16}$H$_{24}$O$_2$ [M+Na]$^+$ $m/z$ 271.1364, found 271.1364.

2-methyl-1-phenyl-3-(tetrahydro-2H-pyran-2-yl)propan-1-one (Table 3, entry 3at). From 2-methyl-1-phenylprop-2-en-1-one (73 mg, 0.5 mmol), the title compound was prepared following the general procedure B using tetrahydro-2H-pyran (2.0 mL). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a colorless oil (77 mg, 66%). $^1$H NMR (400 MHz, Chloroform-$d$, 2 diastereomers): $\delta$ 8.04 – 7.96 (m, 2H), 7.60 – 7.50 (m, 1H), 7.50 – 7.40 (m, 2H), 3.99 – 3.79 (m, 1.5H), 3.80 – 3.68 (m, 0.5H, 1 diastereomer), 3.43 – 3.30 (m, 1H), 3.18 (td, $J = 11.6, 2.5$ Hz, 0.5H, 1 diastereomer), 3.15 – 3.03 (m, 0.5H, 1 diastereomer), 2.06 – 1.91 (m, 1H), 1.87 – 1.71 (m, 1H), 1.62 – 1.35 (m, 5H), 1.31 – 1.23 (m, 1H), 1.20 (d, $J = 6.8$ Hz, 1H, 1 diastereomer), 1.17 (d, $J = 7.0$ Hz, 1H, 1 diastereomer); $^{13}$C NMR (101 MHz, Chloroform-$d$, 2 diastereomers): $\delta$ 205.30, 204.53, 137.32, 136.60, 132.95, 132.72, 128.63, 128.60, 128.52, 128.45, 75.86, 75.45, 68.52, 68.36, 41.10, 40.25, 36.89, 36.63, 32.56, 32.48, 26.16, 26.13, 23.65, 23.47, 19.05, 16.81; HRMS (ESI): calcd. for C$_{16}$H$_{24}$O$_2$ [M+Na]$^+$ $m/z$ 255.1361, found 255.1363.

4-isopropoxy-2,4-dimethyl-1-phenylpentan-1-one (Table 3, entry 3au). From
2-methyl-1-phenylprop-2-en-1-one (73 mg, 0.5 mmol), the title compound was prepared following the general procedure B using 2-isopropanoylpropane (2.0 mL). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a colorless oil (87 mg, 70%). $^1$H NMR (400 MHz, Chloroform-d): δ 7.99 – 7.88 (m, 2H), 7.51 – 7.42 (m, 1H), 7.42 – 7.34 (m, 2H), 3.76 – 3.66 (m, 1H), 3.66 – 3.60 (m, 1H), 2.29 (dd, $J = 14.2, 8.7$ Hz, 1H), 1.43 (dd, $J = 14.2, 2.8$ Hz, 1H), 1.10 (d, $J = 7.2$ Hz, 3H), 1.08 (s, 3H), 0.94 (s, 3H), 0.93 (d, $J = 6.2$ Hz, 3H), 0.90 (d, $J = 6.1$ Hz, 3H); $^{13}$C NMR (101 MHz, Chloroform-d): δ 204.77, 136.96, 132.73, 128.60, 128.52, 74.71, 63.30, 45.62, 35.93, 26.72, 26.41, 25.19, 24.91, 20.38; HRMS (ESI): calcd. for C_{16}H_{24}O_{4} [M+Na]$^+$ m/z 271.1674, found 271.1672.

![2-methyl-1-phenylprop-2-en-1-one](image)

2-methyl-1-phenyl-3-(1,3,5-trioxan-2-yl)propan-1-one (Table 3, entry 3av). From 2-methyl-1-phenylprop-2-en-1-one (73 mg, 0.5 mmol), the title compound was prepared following the general procedure B using 1,3-dioxolane (2.25 g, 25.0 mmol, 50.0 equiv). The residue was purified by silica gel flash column chromatography (10% EtOAc in petroleum ether) to provide the title compound as a colorless oil (56 mg, 47%). $^1$H NMR (400 MHz, Chloroform-d): δ 7.99 (d, $J = 7.4$ Hz, 2H), 7.57 (t, $J = 7.3$ Hz, 1H), 7.47 (t, $J = 7.6$ Hz, 2H), 5.21 (d, $J = 6.2$ Hz, 1H), 5.12 (d, $J = 6.2$ Hz, 1H), 5.05 (d, $J = 6.2$ Hz, 1H), 4.98 (d, $J = 6.3$ Hz, 1H), 4.96 (dd, $J = 10.7, 5.7$ Hz, 1H), 3.85 – 3.71 (m, 1H), 2.35 (ddd, $J = 13.7, 8.4, 4.6$ Hz, 1H), 2.35 (ddd, $J = 14.0, 5.6, 5.6$ Hz, 1H), 1.23 (d, $J = 7.1$ Hz, 3H); $^{13}$C NMR (101 MHz, Chloroform-d): δ 203.64, 136.34, 133.14, 128.77, 128.58, 100.49, 93.38, 93.34, 37.74, 35.30, 18.52; HRMS (ESI): calcd. for C_{13}H_{24}O_{4} [M+Na]$^+$ m/z 259.0946, found 259.0950.

![2-methyl-1-phenyl-3-(1,3,5-trioxan-2-yl)propan-1-one](image)

2-methyl-1-phenyl-3-(2,4,6-trimethyl-1,3,5-trioxan-2-yl)propan-1-one (Table 3, entry 3aw). From 2-methyl-1-phenylprop-2-en-1-one (73 mg, 0.5 mmol), the title compound was prepared following the general procedure B using 1,3-dioxolane (2.0 mL). The residue was purified by silica gel flash column chromatography (10% EtOAc in petroleum ether) to provide the title compound as a pale yellow oil (114 mg, 82%). $^1$H NMR (400 MHz, Chloroform-d): δ 8.00 – 7.91 (m, 2H), 7.62 – 7.54 (m, 1H), 7.53 – 7.44 (m, 2H), 5.37 (q, $J = 5.0$ Hz, 1H), 5.11 (q, $J = 5.1$ Hz, 1H), 3.80 – 3.56 (m, 1H), 3.10 (dd, $J = 14.5, 9.1$ Hz, 1H), 1.71 (dd, $J = 14.5, 3.1$ Hz, 1H), 1.43 (s, 3H), 1.33 (d, $J = 5.6$ Hz, 3H), 1.22 (d, $J = 7.1$ Hz, 3H), 1.05 (d, $J = 5.1$ Hz, 3H); $^{13}$C NMR (101 MHz, Chloroform-d): δ 203.83, 136.58, 133.21, 128.85, 128.35, 100.53, 92.74, 92.19, 36.44, 36.21, 28.10, 21.19, 20.78, 20.05; HRMS (ESI): calcd. for C_{16}H_{24}O_{4} [M+Na]$^+$ m/z 301.1416, found 301.1414.
IV. Application of the Novel Approach

Derivative Reactions of 3r to Form Other Functional Carbonyl and Carboxyl Compounds.

3-(tetrahydrofuran-2-yl)butanoic acid (4). From 1-(1-methyl-1H-imidazol-2-yl)-3-(tetrahydrofuran-2-yl)butan-1-one.\(^1\)

To an over-dried sealed vial containing 3r (111 mg, 0.5 mmol, 1.0 equiv) and a magnetic stirring bar was added DMF (300 \(\mu\)L) and methyl iodide (710 mg, 5.0 mmol, 10.0 equiv) at room temperature. After 24 h of stirring at 65 °C, the resulting yellow mixture was concentrated under reduced pressure to remove excess methyl iodide. To the reaction mixture in DMF was added distilled water (300 \(\mu\)L) and DBU (228 mg, 1.5 mmol, 3.0 equiv) at room temperature. After 2 h of stirring at room temperature, the reaction mixture was quenched with 1N HCl (30 mL) and extracted with EtOAc (3x). The combined organic layers were dried over anhydrous Na\(_2\)SO\(_4\), filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (25% EtOAc in petroleum ether) to give the title compound as a colorless liquid (62 mg, 78%).\(^1\) H NMR (400 MHz, Chloroform-\(d\), 2 diastereomers): \(\delta\) 11.37 (s, 1H), 3.91 – 3.69 (m, 2.5H), 3.91 – 3.69 (m, 0.5H, 1 diastereomer), 2.66 (dd, \(J = 15.3, 4.9\) Hz, 0.5H, 1 diastereomer), 2.47 (dd, \(J = 13.8, 3.6\) Hz, 0.5H, 1 diastereomer), 2.28 – 2.12 (m, 1.5H), 2.09 – 1.93 (m, 1.5H), 1.93 – 1.82 (m, 2H), 1.66 – 1.47 (m, 1H), 1.01 (dd, \(J = 6.2, 1.5\) Hz, 1 diastereomer), 0.96 (dd, \(J = 6.8, 1.5\) Hz, 1 diastereomer); \(^13\)C NMR (101 MHz, Chloroform-\(d\), 2 diastereomers): \(\delta\) 178.73, 178.63, 83.34, 82.54, 68.31, 68.00, 38.94, 37.82, 35.64, 34.40, 29.81, 29.72, 28.10, 26.08, 26.01, 16.66, 15.88; HRMS (ESI): calcd. for C\(_8\)H\(_{14}\)O\(_3\) [M+H]\(^+\) m/z 159.1021, found 159.1020.

3-(tetrahydrofuran-2-yl)butanal (5). From 1-(1-methyl-1H-imidazol-2-yl)-3-(tetrahydrofuran-2-yl)butan-1-one.\(^1,2\) To an over-dried 15 mL Schlenk tube under N\(_2\) was added 3r (111 mg, 0.5 mmol, 1.0 equiv), MeOH (2.5 mL), and NaBH\(_4\) (48 mg, 1.25 mmol, 2.5 equiv). The reaction was stirred at room temperature for 1.5 h before being quenched with H\(_2\)O (1.0 mL). The resulting solution was diluted with EtOAc (25 mL) and sat. Na\(_2\)CO\(_3\) (25 mL). The organic layer was removed and the resulting aqueous layer was extracted EtOAc (2x). The combined organic layers were dried over Na\(_2\)SO\(_4\), filtered and concentrated under reduced pressure. The residue in a 15 mL over-dried sealed vial was dissolved in EtOAc (2.5 mL) before Mel (500 mg, 3.5 mmol,
7.0 equiv) was added. After stirring at 50°C for 14 h, Mel and EtOAc were removed under reduced pressure, followed by addition of toluene (3 mL), glycine (150 mg, 2.0 mmol, 4.0 equiv), and 2 M NaOH solution (2.3 mL, 4.6 mmol, 9.2 equiv). The reaction mixture was heated at 80°C for 5 h. At 80°C, 1 M HCl solution (4.6 mL, 4.6 mmol, 9.2 equiv) was added and the mixture was stirred until lightening of the aqeous phase. Then the mixture was cooled down to room temperature and EtOAc (50 mL) was added. The organic layer was washed with an aqueous solution of 1 M HCl (20 mL) and brine (20 mL), dried over Na2SO4 filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (20% EtOAc in petroleum ether) to provide the title compound as a colorless oil (58 mg, 82%).

N-benzyl-3-(tetrahydrofuran-2-yl)butanamide (6). From 1-(1-methyl-1H-imidazol-2-yl)-3-(tetrahy drofuran -2-yl)butan-1-one. To an over-dried sealed vial containing 3r (111 mg, 0.5 mmol, 1.0 equiv) and a magnetic stirring bar was added DMF (300 µL) and methyl iodide (710 mg, 5.0 mmol, 10.0 equiv) at room temperature. After 24 h of stirring at 65 °C, the resulting yellow mixture was concentrated under reduced pressure to remove excess methyl iodide. To the reaction mixture in DMF was added benzylamine (268 mg, 2.5 mmol) and DBU (228 mg, 1.5 mmol, 3.0 equiv) at room temperature. After 2 h of stirring, the reaction mixture was diluted with EtOAc (50 mL) and washed with 1N HCl (20 mL) and brine (20 mL). The organic layer was dried over anhydrous Na2SO4 filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (20% EtOAc in petroleum ether) to give the title compound as a pale yellow solid (116 mg, 94%).

1H NMR (400 MHz, Chloroform-d, 2 diastereomers): δ 7.44 – 7.12 (m, 5H), 6.40 (s, 1H), 4.41 (d, J = 5.7 Hz, 2H), 3.84 – 3.59 (m, 2.5H), 3.56 – 3.46 (m, 0.5H, 1 diastereomer), 2.50 (dd, J = 13.6, 4.4 Hz, 0.5H, 1 diastereomer), 2.41 – 2.26 (m, 1H), 2.24 – 2.13 (m, 0.5H, 1 diastereomer), 2.11 – 1.90 (m, 2H), 1.89 – 1.79 (m, 2H), 1.60 – 1.41 (m, 1H), 0.96 (d, J = 3.9 Hz, 1.5H, 1 diastereomer), 0.94 (d, J = 4.0 Hz, 1.5H, 1 diastereomer); 13C NMR (101 MHz, Chloroform-d, 2 diastereomers): δ 172.55, 172.39, 138.66, 138.53, 128.66, 128.64, 127.79, 127.78, 127.41, 127.36, 83.47, 82.30, 68.17, 67.80, 43.57, 43.54, 41.13, 40.77, 36.29, 34.88, 29.83, 28.24, 26.06, 25.91, 16.91, 15.35; HRMS (ESI): calcd. for C15H21NO2 [M+Na]+ m/z 270.1470, found 270.1470.

p-OMeC₆H₄
4-methoxyphenethyl 3-(tetrahydrofuran-2-yl)butanoate \((7)\). From 1-(1-methyl-1H-imidazol-2-yl)-3-(tetrahydrofuran-2-yl)butan-1-one.\(^1\) To an over-dried sealed vial containing 3r (111 mg, 0.5 mmol, 1.0 equiv) and a magnetic stirring bar was added DMF (300 µL) and methyl iodide (710 mg, 5.0 mmol, 10.0 equiv) at room temperature. After 24 h of stirring at 65 °C, the resulting yellow mixture was concentrated under reduced pressure to remove excess methyl iodide and DMF, and followed by addition of \(\text{CH}_2\text{Cl}_2\) (1 mL), \(p\)-methoxyphenethyl alcohol (375 mg, 2.5 mmol, 5.0 equiv) and DBU (228 mg, 1.5 mmol, 3.0 equiv) at room temperature. After 2 h of stirring at room temperature, the reaction mixture was diluted with EtOAc (50 mL) and washed with \(\text{H}_2\text{O}\) (2x). The organic layer was dried over anhydrous \(\text{Na}_2\text{SO}_4\), filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (10% EtOAc in petroleum ether) to give 41 as a pale yellow oil (126 mg, 86%). \(^1\)H NMR (400 MHz, Chloroform-\(d\), 2 diastereomers): \(\delta\) 7.13 (d, \(J = 7.9\) Hz, 2H), 6.83 (d, \(J = 8.6\) Hz, 2H), 4.25 (t, \(J = 7.1\) Hz, 2H), 3.84 – 3.74 (m, 1H), 3.78 (s, 3H), 3.75 – 3.63 (m, 1.5H), 3.58 – 3.48 (m, 0.5H, 1 diastereomer), 2.87 (t, \(J = 7.1\) Hz, 2H), 2.60 (dd, \(J = 14.8, 4.8\) Hz, 0.5H, 1 diastereomer), 2.40 (dd, \(J = 13.2, 3.3\) Hz, 0.5H, 1 diastereomer), 2.17 – 2.05 (m, 1.5H), 2.03 – 1.93 (m, 1H), 1.92 – 1.78 (m, 2.5H), 1.59 – 1.44 (m, 1H), 0.94 (d, \(J = 6.4\) Hz, 1.5H, 1 diastereomer), 0.88 (d, \(J = 6.6\) Hz, 1.5H, 1 diastereomer). \(^{13}\)C NMR (101 MHz, Chloroform-\(d\), 2 diastereomers): \(\delta\) 173.28, 173.07, 158.31, 158.29, 129.97, 129.91, 129.89, 113.92, 113.90, 83.05, 82.47, 68.15, 67.85, 65.07, 64.99, 55.27, 38.87, 38.01, 35.73, 34.68, 34.29, 29.47, 28.22, 26.05, 25.98, 16.38, 15.86; HRMS (ESI): calcd. for \(\text{C}_{17}\text{H}_{24}\text{O}_4\) [M+Na]+ \(m/z\) 315.1572, found 315.1575.

![Derivative Reactions of 3q and 3c to Form 1,4-Diketone and 1,2,5-Triol Products](image)

3-methyl-1-phenylpentane-1,4-dione \((8)\) From 2-methyl-1-phenyl-3-(2,4,6-trimethyl-1,3,5-trioxa n-2-yl)propan-1-one 3q. To the compound 3q (139 mg, 0.5 mmol) was added a solution of acetic acid (2.25 mL) and water (0.25 mL), and the reaction mixture was stirred at 60 °C for 3 h. After cooling to room temperature, the reaction mixture was neutralized with saturated aq. \(\text{NaHCO}_3\) and extracted with \(\text{CH}_2\text{Cl}_2\) (3x). The combined organic layers were dried over anhydrous \(\text{Na}_2\text{SO}_4\), filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (3%
EtOAc in petroleum ether) to give 41 as a colorless oil (89 mg, 93%). $^1$H NMR (400 MHz, Chloroform-d): $\delta$ 8.04 – 7.90 (m, 2H), 7.58 – 7.51 (m, 1H), 7.49 – 7.41 (m, 2H), 4.06 – 3.88 (m, 1H), 3.16 (dd, $J = 18.1, 8.5$ Hz, 1H), 2.55 (dd, $J = 18.1, 5.0$ Hz, 1H), 2.16 (s, 3H), 1.17 (d, $J = 7.2$ Hz, 3H); $^{13}$C NMR (101 MHz, Chloroform-d): $\delta$ 207.03, 203.20, 136.00, 132.95, 128.63, 128.44, 46.82, 36.22, 30.05, 17.76; HRMS (ESI): calcd. for C$_{12}$H$_{14}$O$_2$ [M+Na]$^+$ m/z 213.0891, found 213.0891.

3-methyl-5,5-diphenylpentane-1,2,5-triol (10) From 3-(2,2-dimethyl-1,3-dioxolan-4-yl)-1-phenyl butan-1-one 3c. To a solution of ketone 3c (124 mg, 0.5 mmol) in THF (1 mL) was added phenyl magnesium bromide solution (1 N, 0.6 mL, 0.6 mmol) at 0 °C under the atmosphere of argon. After stirring for 10 min at 0 °C, the reaction mixture was allowed to warm up to room temperature and stirred for another 2 hours. The mixture was quenched with saturated aq. NH$_4$Cl at 0 °C, and the organic layer was separated and aqueous layer was extracted with Et$_2$O (3×). The combined organic layers were washed with brine and dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The residue was used in next step without further purification.

To the resulting material was added a solution of acetic acid (2.25 mL) and water (0.25 mL), and the reaction mixture was stirred at 60 °C for 3 h. After cooling to room temperature, the reaction mixture was neutralized with saturated aq. NaHCO$_3$ and extracted with CH$_2$Cl$_2$ (3×). The combined organic layers were dried over anhydrous Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (15% EtOAc in petroleum ether) to give 41 as a pale yellow oil (111 mg, 78%). $^1$H NMR (400 MHz, Chloroform-d, 2 diastereomers): $\delta$ 7.50 – 7.36 (m, 4H), 7.32 – 7.22 (m, 4H), 7.21 – 7.12 (m, 2H), 4.28 – 4.18 (m, 0.5H, 1 diastereomer), 3.87 – 3.74 (m, 1H), 3.70 – 3.52 (m, 1.5H), 2.97 (dd, $J = 9.2, 4.4$ Hz, 0.5H, 1 diastereomer), 2.79 (dd, $J = 11.7, 6.4$ Hz, 0.5H, 1 diastereomer), 2.46 – 2.32 (m, 0.5H, 1 diastereomer), 2.31 – 2.03 (m, 2H), 1.03 (d, $J = 6.9$ Hz, 1.5H, 1 diastereomer), 0.99 (d, $J = 5.6$ Hz, 1.5H, 1 diastereomer); $^{13}$C NMR (101 MHz, Chloroform-d, 2 diastereomers): $\delta$ 147.58, 147.07, 146.83, 146.76, 128.35, 128.25, 128.22, 128.19, 126.90, 126.88, 126.69, 126.65, 125.80, 125.75, 125.69, 125.46, 87.62, 87.50, 86.91, 80.94, 63.59, 63.07, 48.18, 46.86, 34.97, 34.50, 16.43, 13.42; HRMS (ESI): calcd. for C$_{19}$H$_{32}$O$_3$Si [M+H]$^+$ m/z 287.1647, found 287.1648.
V. Kinetic Isotope Effect Research.

![Kinetic Isotope Effect Reaction](image)

2-methyl-1-phenyl-3-(tetrahydrofuran-2-yl)propan-1-one
and
2-methyl-1-phenyl-3-(tetrahydrofuran-2-yl)propan-1-one (Scheme 4). From 2-methyl-1-phenylprop-2-en-1-one (73 mg, 0.5 mmol), the title compound was prepared following the general procedure B using tetrahydrofuran-$d_8$ and tetrahydrofuran (2.0 mL, 1:1). The residue was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound as a colorless oil (76 mg, 70%).

$^1$H NMR (400 MHz, Chloroform-$d$, 2 diastereomers): δ 8.01 (d, $J = 8.2$ Hz, 2H), 7.58 – 7.50 (m, 1H), 7.50 – 7.41 (m, 2H), 4.04 – 3.94 (m, 0.42H, 1 diastereomer), 3.86 – 3.77 (m, 1H), 3.77 – 3.68 (m, 1.63H), 3.68 – 3.59 (m, 0.43H, 1 diastereomer), 2.20 – 2.10 (m, 0.5H, 1 diastereomer), 2.05 – 1.94 (m, 1.44H), 1.94 – 1.73 (m, 1.68H), 1.63 – 1.52 (m, 1H), 1.50 – 1.37 (m, 0.85H), 1.23 (d, $J = 7.0$ Hz, 1.5H, 1 diastereomer), 1.21 (d, $J = 7.3$ Hz, 1.5H, 1 diastereomer); $^{13}$C NMR (101 MHz, Chloroform-$d$, 2 diastereomers): δ 204.65, 204.10, 136.99, 136.42, 132.90, 132.77, 128.63, 128.61, 128.47, 128.42, 77.52, 76.69, 67.63, 67.49, 39.77, 39.45, 38.11, 37.97, 31.95, 31.81, 25.73, 25.66, 19.06, 16.73.

VI. Preparation of Substrates.

General procedure (C) for the synthesis of enone $1a$, $1l$, $1q$, $1t$:

![General procedure (C) for the synthesis of enone](image)

To a solution of 1-phenylalkan-1-one (1.0 equiv) in DMSo (0.3 M with respect to IBX) was added IBX (6.0 equiv) and $p$-TsOH (0.3 equiv). The solution was heated to 85 °C, and the reaction was monitored by TLC (thin layer chromatography) until complete consumption of starting material was observed (8-12 h). The reaction mixture was cooled to room temperature and diluted with Et,O. The organic layer was washed with 5% NaHCO$_3$, H$_2$O (1×), and dried over Na$_2$SO$_4$. filtered, and the solution was concentrated under reduced pressure to furnish corresponding (E)-1-phenylalk-2-en-1-one which was purified by silica gel flash column chromatography.

(E)-1-phenylbut-2-en-1-one ($1a$). Prepared following general procedure C using
1-phenylbutan-1-one (2.96 g, 20.0 mmol). The crude reaction mixture was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound (2.46 g, 83% yield) as a pale yellow oil. \(^1\)H NMR (400 MHz, Chloroform-\(d\)): \(\delta\) 7.98 – 7.87 (m, 2H), 7.60 – 7.52 (m, 1H), 7.50 – 7.43 (m, 2H), 7.08 (dq, \(J = 15.3, 6.8\) Hz, 1H), 6.97 – 6.85 (m, 1H), 2.00 (dd, \(J = 6.8, 1.6\) Hz, 3H); \(^{13}\)C NMR (101 MHz, Chloroform-\(d\)): \(\delta\) 190.93, 145.17, 138.07, 132.71, 128.64, 127.70, 18.73; HRMS (ESI): calcd. for \(C_{10}H_{12}O\) [M+Na]\(^+\) \(m/z\) 169.0629, found 169.0636.

\((E)-1-[(1,1'-biphenyl)-4-yl]but-2-en-1-one (1l)\). Prepared following general procedure C using 1-[(1,1'-biphenyl)-4-yl]butan-1-one (1.12 g, 5.0 mmol). The crude reaction mixture was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound (933 mg, 84% yield) as a pale yellow oil. \(^1\)H NMR (400 MHz, Chloroform-\(d\)): \(\delta\) 8.01 (d, \(J = 8.3\) Hz, 2H), 7.68 (d, \(J = 8.2\) Hz, 2H), 7.68 (d, \(J = 7.2\) Hz, 2H), 7.46 (t, \(J = 7.5\) Hz, 2H), 7.39 (dd, \(J = 8.3, 6.4\) Hz, 1H), 7.11 (dq, \(J = 15.2, 6.8\) Hz, 1H), 6.95 (dq, \(J = 15.3, 1.5\) Hz, 1H), 2.00 (dd, \(J = 6.8, 1.5\) Hz, 3H); \(^{13}\)C NMR (101 MHz, Chloroform-\(d\)): \(\delta\) 190.23, 145.42, 145.02, 140.06, 136.68, 129.21, 129.03, 128.24, 127.52, 127.35, 127.27, 18.73; HRMS (ESI): calcd. for \(C_{16}H_{14}O\) [M+Na]\(^+\) \(m/z\) 245.0942, found 245.0944.

\((E)-1-((thiophen-2-yl)but-2-en-1-one (1q)\). Prepared following general procedure C using 1-((thiophen-2-yl)butan-1-one (771 mg, 5.0 mmol). The crude reaction mixture was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound (586 mg, 77% yield) as a pale yellow oil. \(^1\)H NMR (400 MHz, Chloroform-\(d\)): \(\delta\) 7.75 (dd, \(J = 3.8, 1.1\) Hz, 1H), 7.63 (dd, \(J = 4.9, 1.1\) Hz, 1H), 7.21 – 7.05 (m, 2H), 6.83 (dq, \(J = 15.2, 1.6\) Hz, 1H), 1.98 (dd, \(J = 6.9, 1.7\) Hz, 3H); \(^{13}\)C NMR (101 MHz, Chloroform-\(d\)): \(\delta\) 182.20, 145.14, 144.23, 133.67, 131.84, 128.19, 126.97, 18.47; HRMS (ESI): calcd. for \(C_{8}H_{8}SO\) [M+Na]\(^+\) \(m/z\) 175.0194, found 175.0192.

\((E)-1-phenylpent-2-en-1-one (1t)\). Prepared following general procedure C using 1-phenylbutan-1-one (741 mg, 5.0 mmol). The crude reaction mixture was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound (648 mg, 81% yield) as a pale yellow oil. \(^1\)H NMR (400 MHz, Chloroform-\(d\)): \(\delta\) 7.93 (d, \(J = 7.2\) Hz, 2H), 7.55 (t, \(J = 7.4\) Hz, 1H), 7.46 (t, \(J = 7.7\) Hz, 2H), 7.11 (dt, \(J = 15.3, 6.3\) Hz, 1H), 6.87 (dt, \(J = 15.4, 1.8\) Hz, 1H), 2.41 – 2.28 (m, 2H), 1.14 (t, \(J = 7.4\) Hz, 3H); \(^{13}\)C NMR (101 MHz, Chloroform-\(d\)): \(\delta\) 191.19, 151.40, 138.15, 132.67, 128.62, 128.60, 125.12, 26.03, 12.46; HRMS (ESI): calcd. for \(C_{13}H_{12}O\) [M+Na]\(^+\) \(m/z\) 183.0786, found 183.0783.
General procedure (D) for the synthesis of enone 1j-1k, 1m-1p.

\[
\begin{align*}
\text{OCl} & \quad \text{Me}^\text{N-O\text{Me}} \\
\text{CH}_2\text{Cl}_2, 0\rightarrow 25^\circ\text{C} & \quad \text{ArMgBr} \\
\text{THF, } 0\rightarrow 25^\circ\text{C}
\end{align*}
\]

To a suspension of over-dried magnesium turnings (1.4 equiv) and iodine (2 mol%) in dry THF (5 mL) was added bromoarene (1.0 equiv, 0.5 M in THF) dropwise over 20 min to maintain a steady reflux. Some initial heating of the suspension was required to begin the reaction. After which the reaction was heated to reflux and stirred for additional 2 h. On cooling to ambient temperature this gave a brown solution of the Grignard reagent, which was used immediately in the next reaction.

To a stirred suspension of N-methoxy methylamine hydrochloride salt (1.1 equiv) in DCM (0.2 M acylhalide) at 0 °C was slowly added triethylamine (2.1 equiv). (E)-but-2-enoyl chloride (1.0 equiv) was then added dropwise to the solution. The temperature was monitored at all stages and kept at 0°C. The solution was then allowed to warm to room temperature and stirred for 3 h before quenching with HCl (aq., 1.0 N). The phases were separated and the aqueous layer was extracted with CH₂Cl₂ (3 x). The combined organic phases were dried over Na₂SO₄, filtered and then the solvent was removed in vacuo to afford the Weinreb amide. This crude amide was used in next step without further purification.

To a stirred solution of Weinreb amide (1.0 equiv) in dry THF (0.2 M Weinreb amide) was added dropwise the Grignard reagent (1.2 equiv) synthesized above for 15 min at 0 °C under atmosphere of argon. After stirred at 0°C for 10 min, the reaction mixture was allowed to warm up to room temperature and stirred for 2 h. The reaction mixture was quenched with HCl (aq., 1.0 N), and extracted with diethyl ether (3x). The combined organic layers were dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with EtOAc/PE to afford corresponding (E)-1-arylbut-2-en-1-one.

(E)-1-(4-(benzyloxy)phenyl)but-2-en-1-one (1j). Prepared following general procedure D using 1-(benzyloxy)-4-bromobenzene (3.16 g, 12.0 mmol). The crude reaction mixture was purified by silica gel flash column chromatography (10% EtOAc in petroleum ether) to provide the title compound (1.33 g, 53% yield) as a pale yellow oil. \(^1\)H NMR (400 MHz, Chloroform-d): δ 8.00 – 7.88 (m, 2H), 7.49 – 7.31 (m, 5H), 7.12 – 6.97 (m, 3H), 6.91 (dq, J = 15.2, 1.6 Hz, 1H), 5.14 (s, 2H), 1.99 (dd, J = 6.8, 1.5 Hz, 3H); \(^13\)C NMR (101 MHz, Chloroform-d): δ 189.05, 162.50, 144.10, 136.31, 131.00, 130.88, 128.75, 128.28, 127.55, 127.20, 114.67, 70.19, 18.62; HRMS (ESI): calcd. for C₁₇H₁₆O₂ [M+Na]^+ m/z 275.1048, found 275.1045.
**(E)-1-(4-(dimethylamino)phenyl)but-2-en-1-one (1k)**. Prepared following general procedure D using 4-bromo-N,N-dimethylaniline (2.40 g, 12.0 mmol). The crude reaction mixture was purified by silica gel flash column chromatography (15% EtOAc in petroleum ether) to provide the title compound (1.12 g, 59% yield) as a pale yellow oil. $^1$H NMR (400 MHz, Chloroform-$d$): $\delta$ 7.91 ($d$, $J = 9.1$ Hz, 2H), 7.10 – 6.89 (m, 2H), 6.66 ($d$, $J = 9.0$ Hz, 2H), 3.05 ($s$, 6H), 1.97 ($dd$, $J = 6.4$, 1.1 Hz, 3H); $^{13}$C NMR (101 MHz, Chloroform-$d$): $\delta$ 188.26, 153.40, 142.26, 130.87, 127.27, 125.70, 110.86, 40.13, 18.58; HRMS (ESI): calcd. for C$_{12}$H$_{15}$NO $[M+Na]^+$ m/z 212.1051, found 212.1050.

**Preparation of (E)-1-(4-methoxyphenyl)but-2-en-1-one (1m)**. Prepared following general procedure D using 1-bromo-4-methoxybenzene (2.24 g, 12.0 mmol). The crude reaction mixture was purified by silica gel flash column chromatography (10% EtOAc in petroleum ether) to provide the title compound (1.18 g, 67% yield) as a pale yellow oil. $^1$H NMR (400 MHz, Chloroform-$d$): $\delta$ 7.99 ($d$, $J = 8.9$ Hz, 2H), 7.17 – 7.04 (m, 1H), 7.03 – 6.89 (m, 3H), 3.91 ($s$, 3H), 2.03 ($dd$, $J = 6.7$, 1.1 Hz, 3H); $^{13}$C NMR (101 MHz, Chloroform-$d$): $\delta$ 189.14, 163.39, 144.08, 130.91, 130.84, 127.25, 113.84, 55.55, 18.65; HRMS (ESI): calcd. for C$_{11}$H$_{12}$O$_2$ $[M+Na]^+$ m/z 199.0735, found 199.0735.

**Preparation of (E)-1-(3-methoxyphenyl)but-2-en-1-one (1n)**. Prepared following general procedure D using 1-bromo-3-methoxybenzene (2.24 g, 12.0 mmol). The crude reaction mixture was purified by silica gel flash column chromatography (10% EtOAc in petroleum ether) to provide the title compound (1.07 g, 61% yield) as a pale yellow oil. $^1$H NMR (400 MHz, Chloroform-$d$): $\delta$ 7.46 – 7.33 (m, 2H), 7.27 ($t$, $J = 7.9$ Hz, 1H), 7.07 – 6.91 (m, 2H), 6.80 ($dq$, $J = 15.3$, 1.6 Hz, 1H), 3.76 ($s$, 3H), 1.90 ($dd$, $J = 6.8$, 1.6 Hz, 3H); $^{13}$C NMR (101 MHz, Chloroform-$d$): $\delta$ 190.45, 159.85, 145.09, 139.34, 129.50, 127.58, 121.11, 119.15, 112.89, 55.46, 18.63; HRMS (ESI): calcd. for C$_{11}$H$_{12}$O$_2$ $[M+Na]^+$ m/z 199.0735, found 199.0731.

**Preparation of (E)-1-(2-methoxyphenyl)but-2-en-1-one (1o)**. Prepared following general procedure D using 1-bromo-2-methoxybenzene (2.24 g, 12.0 mmol). The crude reaction mixture was purified by silica gel flash column chromatography (10% EtOAc in petroleum ether) to provide the title compound (1.14 g, 65% yield) as a pale yellow oil. $^1$H NMR (400 MHz, Chloroform-$d$): $\delta$ 7.40 ($dd$, $J = 7.6$, 1.8 Hz, 1H), 7.33 ($ddd$, $J = 8.3$, 7.4, 1.8 Hz, 1H), 6.94 – 6.84 (m, 2H), 6.82 – 6.73 (m, 1H),
6.60 (dq, J = 15.5, 1.6 Hz, 1H), 3.77 (s, 3H), 1.85 (dq, J = 6.8, 1.6 Hz, 3H); $^{13}$C NMR (101 MHz, Chloroform-d): δ 193.61, 157.84, 144.25, 132.45, 132.33, 130.00, 129.27, 120.59, 111.60, 55.72, 18.46; HRMS (ESI): calcd. for C$_{11}$H$_{12}$O$_2$ [M+Na]$^+$ m/z 199.0735, found 199.0732.

(E)-1-(3-fluorophenyl)but-2-en-1-one (1p). Prepared following general procedure D using 1-bromo-3-fluorobenzene (2.10 g, 12.0 mmol). The crude reaction mixture was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound (607 mg, 37% yield) as a pale yellow oil. $^1$H NMR (400 MHz, Chloroform-d): δ 7.63 (dt, J = 7.7, 1.3 Hz, 1H), 7.53 (ddd, J = 9.5, 2.6, 1.5 Hz, 1H), 7.37 (td, J = 8.0, 5.5 Hz, 1H), 7.21 – 7.15 (m, 1H), 7.03 (dq, J = 15.3, 6.9 Hz, 1H), 6.79 (dq, J = 15.2, 1.6 Hz, 1H), 1.94 (dd, J = 6.9, 1.7 Hz, 3H); $^{13}$C NMR (101 MHz, Chloroform-d): δ 188.32, 161.77 (d, J = 247.7 Hz), 144.93, 139.02 (d, J = 6.2 Hz), 129.12 (d, J = 7.7 Hz), 126.13, 123.14 (d, J = 3.1 Hz), 118.55 (d, J = 21.5 Hz), 114.27 (d, J = 22.3 Hz), 17.63; HRMS (ESI): calcd. for C$_{10}$H$_9$FO [M+Na]$^+$ m/z 187.0535, found 187.0536.

1s$^1$, 1ah-1ai$^{5,6}$ was synthetized following reported method.

**General procedure (E) for the synthesis of enone 1ak, 1an$^7$.**

R=Alkyl group or Aryl group

To a stirred suspension of N-methoxy methylanime hydrochloride salt (1.1 equiv) in DCM (0.2 M acylhalide) at 0 °C was slowly added triethylamine (2.1 equiv). acylhalide (1.0 equiv) was then added dropwise to the solution. The temperature was monitored at all stages and kept at 0°C. The solution was then allowed to warm to room temperature and stirred for 3 h before quenching with HCl (aq., 1.0 N). The phases were separated and the aqueous layer was extracted with CH$_2$Cl$_2$ (3 x). The combined organic phases were dried over Na$_2$SO$_4$, filtered, and then the solvent was removed in vacuo to afford the Weinreb amide. This crude amide was used in next step without further purification.

To a stirred solution of Weinreb amide (1.0 equiv) in dry THF (0.2 M Weinreb amide) was added dropwise isopropenylmagnesium bromide (1.2 equiv) for 15 min at 0 °C under atmosphere of argon. After stirred at 0°C for 10 min, the reaction mixture was allowed to warm up to room temperature and stirred for 2 h. The reaction mixture was quenched with HCl (aq., 1.0 N), and extracted with diethyl ether (3 x). The combined organic layer was dried over Na$_2$SO$_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with EtOAc/PE to afford corresponding α,β-unsaturated ketone.
7-chloro-2-methylhept-1-en-3-one (1ak). Prepared following general procedure E using thiophene-2-carbonyl chloride (1.55 g, 10.0 mmol). The crude reaction mixture was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound (1.06 g, 66% yield) as a pale yellow oil. 1H NMR (400 MHz, Chloroform-d): δ 5.89 (d, J = 1.2 Hz, 1H), 5.71 (t, J = 1.9 Hz, 1H), 3.48 (t, J = 6.2 Hz, 2H), 2.66 (t, J = 6.9 Hz, 2H), 1.80 (s, 3H), 1.77 – 1.66 (m, 4H); 13C NMR (101 MHz, Chloroform-d): δ 201.39, 144.50, 124.60, 44.76, 36.48, 32.11, 21.78, 17.66; HRMS (ESI): calcd. for C14H13ClO [M+Na]+ m/z 231.1731, found 231.1731.

7-chloro-2-methylhept-1-en-3-one (1an). Prepared following general procedure E using undec-10-enoyl chloride (2.02 g, 10.0 mmol). The crude reaction mixture was purified by silica gel flash column chromatography (5% EtOAc in petroleum ether) to provide the title compound (1.60 g, 77% yield) as a pale yellow oil. 1H NMR (400 MHz, Chloroform-d): δ 5.87 (s, 1H), 5.81 – 5.67 (m, 1H), 5.68 (s, 1H), 4.97 – 4.80 (m, 2H), 2.60 (t, J = 7.2 Hz, 2H), 2.65 – 2.54 (m, 3H), 1.96 (q, J = 6.9 Hz, 3H), 1.80 (s, 3H), 1.57 – 1.47 (m, 2H), 1.34 – 1.26 (m, 2H), 1.26 – 1.17 (m, 8H); 13C NMR (101 MHz, Chloroform-d): δ 202.45, 144.70, 139.26, 114.23, 37.60, 33.90, 29.52, 29.45, 29.19, 29.02, 24.74, 17.77; HRMS (ESI): calcd. for C14H22O [M+Na]+ m/z 231.1725, found 231.1731.

Reaction procedure for the synthesis of enone 1am.

7-chloro-2-methylhept-1-en-3-one (482 mg, 3.0 mmol, 1.0 equiv) was added to a slurry of 1-naphthol (649 mg, 4.5 mmol, 1.5 equiv) and K2CO3 (2.49 g, 18 mmol, 6.0 equiv) in dry DMF (40 mL) and the mixture was stirred at 80 °C under N2 for 16 h. The crude reaction mixture was partitioned between ethyl acetate (100 mL) and an aqueous solution of NH4Cl (1 M, 80 mL). The organic layer was washed with aqueous NH4Cl (1 M, 1x), H2O (2x), brine (1x), and then dried over Na2SO4, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (5% EtOAc in petroleum ether) to afford the title compound (819 mg, 61% yield) as a colorless oil. 1H NMR (400 MHz, Chloroform-d): δ 8.36 – 8.19 (m, 1H), 7.78 (dd, J = 6.8, 2.4 Hz, 1H), 7.51 – 7.42 (m, 2H), 7.42 – 7.32 (m, 2H), 6.79 (d, J = 7.4 Hz, 1H), 5.96 (s, 1H), 5.76 (s, 1H), 4.15 (t, J = 5.8 Hz, 2H), 2.82 (t, J = 6.9 Hz, 2H), 2.04 – 1.89 (m, 4H), 1.88 (s, 3H); 13C NMR (101 MHz, Chloroform-d): δ 201.89, 154.84, 144.65, 134.63, 127.55, 126.46, 126.00, 125.83, 125.20, 124.60, 122.17, 120.21, 104.66, 67.89, 37.16, 28.99, 21.47, 17.78; HRMS (ESI): calcd. for C18H18O2 [M+Na]+ m/z 291.1361, found 291.1362.

General procedure (G) for the synthesis of enone 1r, 1ag2,8
To a stirred suspension of N-methoxy methylamine hydrochloride salt (2.15 g, 22.0 mmol, 1.1 equiv) in DCM (100 mL) at 0 °C was slowly added triethylamine (4.25 g, 42.0 mmol, 2.1 equiv). Acylhalide (20.0 mmol, 1.0 equiv) was then added dropwise to the solution. The temperature was monitored at all stages and kept at 0°C. The solution was then allowed to warm to room temperature and stirred for 3 h before quenching with HCl (aq., 1.0 N). The organic layer was separated and the aqueous layer was extracted with CH$_2$Cl$_2$ (3x). The combined organic layers were dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford corresponding Weinreb amide.

To a solution of N-methylimidazole (1.48 g, 18.0 mmol, 1.2 equiv) in THF (50 mL) at -78 °C under the atmosphere of Ar was added n-BuLi (2.5 M in hexane, 7.2 mL, 18.0 mmol, 1.2 equiv) dropwise. The reaction mixture was stirred at -78 °C for 10 min, then stirred at room temperature for 30 min. The solution of weinreb amide (15.0 mmol, 1.0 equiv) in THF (5 mL) was added dropwise to the flask after the reaction was cooled back down to -78 °C. After stirring for another 5 h, the reaction was quenched with a saturated aqueous solution of Na$_2$CO$_3$ (30 mL) and extracted with EtOAc (3x). The combined organic layers were dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to give the corresponding ketones.

(1R)-1-(1-methyl-1H-imidazol-2-yl)but-2-en-1-one (1r). Prepared following general procedure G using (E)-but-2-enoyl chloride (2.09 g, 20.0 mmol). The crude Weinreb amide was purified by silica gel column chromatography (40% EtOAc in petroleum ether) to provide the pure one (2.50 g, 96% yield) as a colorless oil. In the second step, the residue was purified by silica gel column chromatography (40% EtOAc in petroleum ether) to give the title compound as a pale yellow oil (1.69 g, 75%). $^1$H NMR (400 MHz, Chloroform-d): δ 7.42 (dq, J = 15.6, 1.6 Hz, 1H), 7.19 – 7.07 (m, 2H), 7.06 (d, J = 1.0 Hz, 1H), 4.03 (s, 3H), 1.98 (dd, J = 6.9, 1.7 Hz, 3H); $^{13}$C NMR (101 MHz, Chloroform-d): δ 180.42, 143.60, 143.52, 128.97, 127.78, 126.97, 36.09, 18.30; HRMS (ESI): calcd. for C$_8$H$_{10}$N$_2$O [M+H]$^+$ m/z 151.0871, found 151.0875.

2-methyl-1-(1-methyl-1H-imidazol-2-yl)prop-2-en-1-one (1a). Prepared following general procedure G using methacryloyl chloride (2.09 g, 20.0 mmol). The crude Weinreb amide was purified by silica gel column chromatography (40% EtOAc in petroleum ether) to provide the pure one (2.43 g, 95% yield) as a colorless oil. In the second step, the residue was purified by...
silica gel column chromatography (40% EtOAc in petroleum ether) to give the title compound as a pale yellow oil (946 mg, 42%). $^1$H NMR (400 MHz, Chloroform-$d$): $\delta$ 7.13 (d, $J = 1.0$ Hz, 1H), 7.04 (d, $J = 1.0$ Hz, 1H), 6.49 (s, 1H), 6.01 (s, 1H), 3.97 (s, 3H), 2.06 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-$d$): $\delta$ 186.21, 143.09, 142.96, 129.36, 128.90, 126.49, 36.21, 18.69; HRMS (ESI): calcd. for C$_8$H$_{10}$N$_2$O [M+H]$^+$ m/z 151.0871, found 151.0872.

VII. References

VIII. NMR Spectrum