Supporting Information

**I$_2$/TBHP-Promoted Approach to α-Ketoesters from Trifluoromethyl β-Diketones and Alcohols via C-C Bond Cleavage**

Tongle Shao$^a$, Xiang Fang$^*$, Jun Zhou$^a$, Chen Jin$^a$, Xueyan Yang$^*$, Fanhong Wu$^b$

$^a$ Laboratory for Advanced Material and Institute of Fine Chemicals, School of Chemistry and Molecular Engineering, East China University of Science and Technology, 130 Meilong Road, Shanghai 200237, China

$^b$ School of Chemical and Environmental Engineering, Shanghai Institute of Technology, 120 Caobao Road, Shanghai 200235, China

E-mail: fangxiang@ecust.edu.cn, yxy@ecust.edu.cn

1. General experimental methods

   All reactions were carried out in oven-dried glassware under the air. Trifluoromethyl β-diketones were obtained by trifluoroacetylation of methyl ketones.\(^1\) All the other reagents and solvents were purchased from commercial supplies and used without further purification. Flash column chromatography was performed on silica gel (300-400 mesh). Thin-layer chromatography (TLC) was performed on silica gel HSGF 254 plates and visualized by UV light (254 nm). $^1$H, $^{13}$C, $^{19}$F NMR spectra were recorded in CDCl$_3$ on a spectrometer operating at 400, 101 and 376 MHz, respectively. Chemical shifts (δ) are given in ppm and coupling constants (J) are given in Hz.

2. General experimental procedure for the synthesis of α-ketoesters

   To a mixture of trifluoromethyl β-diketones 1 (0.5 mmol, 1.0 equiv), alcohols 2 (1.5 mmol, 3.0 equiv), I$_2$
(0.55 mmol, 1.1 equiv), tert-butyl hydroperoxide (1.25 mmol, 2.5 equiv) and Na₂CO₃ (0.5 mmol, 1.0 equiv) was added 1,2-dichloroethane (1.5 mL) at room temperature. The reaction mixture was then stirred at 60 °C for 7.0 h. When the reaction was completed (monitored by TLC), the reaction was quenched with 2 mL of saturated NH₄Cl aqueous and 4 mL of saturated Na₂S₂O₃ aqueous. After extraction with EtOAc and drying with Na₂SO₄, the organic layer was concentrated under reduced pressure and the residue was purified by column chromatography on silica gel using hexanes/EtOAc (100:1 to 50:1) as eluent to afford the desired products 3.

3. Characterization data of products

**Methyl 2-oxo-2-phenylacetate (3aa)** Colorless liquid (76 mg, 93% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.02 (d, J = 8.0 Hz, 2H), 7.67 (t, J = 8.0 Hz, 1H), 7.52 (t, J = 8.0 Hz, 2H), 3.98 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 186.0, 164.0, 134.9, 132.4, 130.1, 128.9, 52.8.

**Methyl 2-oxo-2-(p-tolyl)acetate (3ab)** Colorless liquid (74 mg, 83% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.91 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 3.97 (s, 3H), 2.44 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 185.7, 164.2, 146.3, 130.2, 129.9, 129.6, 52.7, 21.8.

**Methyl 2-oxo-2-(o-tolyl)acetate (3ac)** Colorless liquid (68 mg, 76% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.68 (d, J = 8.0 Hz, 1H), 7.51-7.47 (m, 1H), 7.31 (t, J = 8.0 Hz, 2H), 3.96 (s, 3H), 2.60 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 188.4, 164.9, 141.3, 133.7, 132.3, 132.2, 131.2, 125.9, 52.7, 21.4.

**Methyl 2-(4-methoxyphenyl)-2-oxoacetate (3ad)** White solid (56 mg, 58% yield). m.p.: 50.9-51.4 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.01 (d, J = 8.0 Hz, 2H), 6.97 (d, J = 8.0 Hz, 2H), 3.96 (s, 3H), 3.89 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 184.4, 165.0, 164.3, 132.5, 125.3, 114.2,
Methyl 2-(4-fluorophenyl)-2-oxoacetate (3ae) White solid (81 mg, 89% yield). m.p.: 55.1-56.2 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.12-8.07 (m, 2H), 7.24-7.17 (m, 2H), 3.98 (s, 3H). $^{19}$F NMR (CDCl$_3$, 376 MHz) δ -100.95 - -100.02 (m, 1F). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 184.1, 166.8 (d, $J = 259.6$ Hz), 163.6, 132.9 (d, $J = 9.1$ Hz), 128.9 (d, $J = 2.0$ Hz), 116.2 (d, $J = 23.2$ Hz), 52.9.

Methyl 2-(4-chlorophenyl)-2-oxoacetate (3af) White solid (82 mg, 83% yield). m.p.: 55.9-56.9 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.01-7.99 (m, 2H), 7.50-7.48 (m, 2H), 3.98 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 184.4, 163.4, 141.7, 131.5, 130.8, 129.3, 52.9.

Methyl 2-(4-bromophenyl)-2-oxoacetate (3ag) White solid (109 mg, 90% yield). m.p.: 53.9-54.8 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.93-7.90 (m, 2H), 7.68-7.65 (m, 2H), 3.98 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 184.6, 163.3, 132.2, 131.4, 131.1, 130.5, 129.3, 52.9.

Methyl 2-(1,1'-biphenyl-4-yl)-2-oxoacetate (3ah) White solid (54 mg, 45% yield). m.p.: 44.1-45.2 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.11 (d, $J = 8.0$ Hz, 2H), 7.74 (d, $J = 8.0$ Hz, 2H), 7.64 (d, $J = 8.0$ Hz, 2H), 7.49 (t, $J = 8.0$ Hz, 2H), 7.43 (t, $J = 8.0$ Hz, 1H), 4.01 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 185.5, 163.9, 147.6, 139.3, 131.1, 130.7, 129.0, 128.6, 127.4, 127.3, 52.8.

Methyl 2-oxo-2-(4-(2,2,2-trifluoroethoxy)phenyl)acetate (3ai) White solid (63 mg, 48% yield). m.p.: 56.3-57.8 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.06 (d, $J = 8.0$ Hz, 2H), 7.03 (d, $J = 8.0$ Hz, 2H), 4.44 (q, $J = 8.0$ Hz, 2H), 3.97 (s, 3H). $^{19}$F NMR (CDCl$_3$, 376 MHz) δ -73.74 (t, $J = 7.5$ Hz, 3F). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 184.1, 163.9, 162.2, 132.7, 122.9 (q, $J = 278.7$ Hz), 114.8, 65.43 (q, $J = 36.4$ Hz), 52.8. EI-MS (m/z): 64, 83, 92, 111, 127, 175, 203 (100), 204, 219, 262. HRMS calcd for [C$_{11}$H$_6$F$_3$O$_4$]$^+$: 262.0453, found 262.0452.
Methyl 2-(naphthalen-1-yl)-2-oxoacetate (3aj) Yellow oil (79 mg, 74% yield). $^1$H NMR (400 MHz, CDCl$_3$) δ 9.03 (d, $J = 8.0$ Hz, 1H), 8.12 (d, $J = 8.0$ Hz, 1H), 7.99-7.97 (m, 1H), 7.92 (d, $J = 8.0$ Hz, 1H), 7.72-7.67 (m, 1H), 7.62-7.53 (m, 2H), 4.01 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 188.4, 164.8, 135.9, 133.9, 133.8, 130.8, 129.2, 128.7, 128.0, 126.9, 125.5, 124.2, 52.8. EI-MS (m/z): 51, 77, 101, 126, 127, 128, 155 (100), 156, 178, 214. HRMS calcd for [C$_{13}$H$_{10}$O$_3$]$^+$: 214.0630, found 214.0631.

Methyl 2-(3,4-difluorophenyl)-2-oxoacetate (3ak) White solid (99 mg, 99% yield). m.p.: 38.7-40.2 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.96-7.91 (m, 1H), 7.90-7.86 (m, 1H), 7.34-7.28 (m, 1H), 3.99 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 182.9, 162.9, 154.8 (dd, $J_1 = 261.6$ Hz, $J_2 = 13.1$ Hz), 150.5 (dd, $J_1 = 253.5$ Hz, $J_2 = 13.1$ Hz), 129.5 (t, $J = 4.0$ Hz), 127.7 (dd, $J_1 = 8.1$ Hz, $J_2 = 4.0$ Hz), 119.3 (dd, $J_1 = 18.2$ Hz, $J_2 = 2.0$ Hz), 117.9 (d, $J = 18.2$ Hz). $^{19}$F NMR (CDCl$_3$, 376 MHz) δ -125.53 - -125.65 (m, 1F), -134.76 - -134.87 (m, 1F). EI-MS (m/z): 63, 93, 113, 141 (100), 142, 153, 172, 184, 200. HRMS calcd for [C$_9$H$_6$F$_2$O$_3$]$^+$: 200.0285, found 200.0287.

Ethyl 2-oxo-2-phenylacetate (3ba) Colorless liquid (85 mg, 95% yield). $^1$H NMR (400 MHz, CDCl$_3$) δ 8.01 (d, $J = 8.0$ Hz, 2H), 7.66 (t, $J = 8.0$ Hz, 1H), 7.51 (t, $J = 8.0$ Hz, 2H), 4.46 (q, $J = 8.0$ Hz, 2H), 1.42 (t, $J = 48.0$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 186.4, 163.8, 134.8, 132.4, 129.9, 128.8, 62.3, 14.0.

Propyl 2-oxo-2-phenylacetate (3ca) Colorless liquid (86 mg, 90% yield). $^1$H NMR (400 MHz, CDCl$_3$) δ 8.00 (m, 2H), 7.66 (t, $J = 8.0$ Hz, 1H), 7.51 (t, $J = 8.0$ Hz, 2H), 4.35 (t, $J = 8.0$ Hz, 2H), 1.85-1.76 (m, 2H), 1.01 (t, $J = 8.0$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 186.4, 163.9, 134.8, 132.4, 129.9, 128.8, 67.7, 21.8, 10.2.

Butyl 2-oxo-2-phenylacetate (3da) Colorless liquid (94 mg, 91% yield). $^1$H NMR (400 MHz,
CDCl₃ δ 8.01-7.99 (m, 2H), 7.68-7.64 (m, 1H), 7.51 (t, J = 8.0 Hz, 2H), 4.39 (t, J = 8.0 Hz, 2H), 1.80-1.73 (m, 2H), 1.51-1.40 (m, 2H), 0.96 (t, J = 8.0 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 186.4, 163.9, 134.8, 132.4, 129.9, 128.8, 65.9, 30.4, 18.9, 13.5.

**Pentyl 2-oxo-2-phenylacetate (3ea)** Colorless liquid (103 mg, 94% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.00 (m, 2H), 7.66 (t, J = 8.0 Hz, 1H), 7.51 (t, J = 8.0 Hz, 2H), 4.38 (t, J = 8.0 Hz, 2H), 1.82-1.75 (m, 2H), 1.42-1.33 (m, 4H), 0.92 (t, J = 8.0 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 186.4, 163.9, 134.8, 132.4, 129.9, 128.8, 66.3, 28.0, 27.8, 22.1, 13.8.

**Octyl 2-oxo-2-phenylacetate (3fa)** Colorless liquid (117 mg, 89% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.00 (d, J = 8.0 Hz, 2H), 7.66 (t, J = 8.0 Hz, 1H), 7.51 (t, J = 8.0 Hz, 2H), 4.38 (t, J = 8.0 Hz, 2H), 1.81-1.74 (m, 2H), 1.45-1.37 (m, 2H), 1.35-1.24 (m, 8H), 0.88 (t, J = 8.0 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 186.5, 163.9, 134.8, 132.4, 129.9, 128.8, 66.3, 31.7, 29.0, 28.4, 25.7, 22.6, 14.0. EI-MS (m/z): 41, 51, 57, 77, 105 (100), 106, 123, 141, 157, 175, 203, 234, 262. HRMS caleed for [C₁₆H₂₂O₃]⁺: 262.1569, found 262.1568.

**2-Bromoethyl 2-oxo-2-phenylacetate (3ga)** Colorless liquid (87 mg, 68% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.04 (d, J = 8.0 Hz, 2H), 7.68 (t, J = 8.0 Hz, 1H), 7.53 (t, J = 8.0 Hz, 2H), 4.70 (t, J = 8.0 Hz, 2H), 3.65 (t, J = 8.0 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 185.6, 163.1, 135.2, 132.2, 130.1, 128.9, 65.1, 27.6.

**Benzyl 2-oxo-2-phenylacetate (3ha)** Colorless liquid (96 mg, 80% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.98-7.96 (m, 2H), 7.65 (t, J = 8.0 Hz, 1H), 7.51-7.37 (m, 7H), 5.42 (s, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 186.0, 163.6, 134.9, 134.5, 132.4, 129.9, 128.9, 128.8, 128.7, 128.6, 67.7.

**Phenethyl 2-oxo-2-phenylacetate (3ia)** Colorless liquid (99 mg, 78% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.86 (d, J = 8.0 Hz, 2H), 7.63 (t, J = 8.0 Hz, 1H), 7.45 (t, J = 8.0 Hz, 2H), 7.32 (t, J = 8.0 Hz, 2H), 7.27-7.25 (m, 3H), 4.62 (t, J = 8.0 Hz, 2H), 3.09 (t, J = 8.0 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 186.3, 163.7, 136.9, 134.9, 132.3, 130.0, 128.9, 128.8, 128.7, 126.8, 66.4, 34.9.
(Tetrahydrofuran-2-yl)methyl 2-oxo-2-phenylacetate (3ja) Colorless liquid (105 mg, 90% yield). $^1$H NMR (400 MHz, CDCl$_3$, $\delta$ 8.11 (d, $J$ = 8.0 Hz, 1H), 8.02 (d, $J$ = 8.0 Hz, 1H), 7.67-7.59 (m, 1H), 7.53-7.46 (m, 2H), 4.45 (dd, $J_1$ = 8.0 Hz, $J_2$ = 4.0 Hz, 1H), 4.36 (dd, $J_1$ = 12.0 Hz, $J_2$ = 4.0 Hz, 1H), 4.29-4.23 (m, 1H), 3.94-3.89 (m, 1H), 3.85-3.80 (m, 1H), 2.11-2.01 (m, 1H), 2.00-1.87 (m, 2H), 1.76-1.67 (m, 1H). $^{13}$C NMR (101 MHz, CDCl$_3$, $\delta$ 186.2, 163.8, 134.9, 132.4, 130.1, 128.9, 76.0, 68.5, 67.5, 27.9, 25.7. EI-MS (m/z): 43, 51, 71, 77, 78, 84, 105 (100), 106, 129, 149, 176, 188, 202, 204, 223, 234. HRMS calcd for [C$_{13}$H$_{14}$O$_4$]$^+$: 234.0892, found 234.0891.

Isopropyl 2-oxo-2-phenylacetate (3ka) Colorless liquid (90 mg, 94% yield). $^1$H NMR (400 MHz, CDCl$_3$, $\delta$ 8.00 (d, $J$ = 8.0 Hz, 2H), 7.66 (t, $J$ = 8.0 Hz, 1H), 7.52 (t, $J$ = 8.0 Hz, 2H), 5.38-5.28 (m, 1H), 1.42 (s, 3H), 1.41 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$, $\delta$ 186.7, 163.6, 134.8, 132.5, 129.9, 128.9, 70.7, 28.1, 21.7.

Methyl 4-methoxybenzoate (4ad) White solid (27 mg, 32% yield). m.p.: 45.9-46.8 °C. $^1$H NMR (400 MHz, CDCl$_3$, $\delta$ 8.01-7.97 (m, 2H), 6.93-6.90 (m, 2H), 3.88 (s, 3H), 3.86 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$, $\delta$ 166.8, 163.3, 131.5, 122.5, 113.5, 55.3, 51.8.

Methyl [1,1'-biphenyl]-4-carboxylate (4ah) White solid (36 mg, 34% yield). m.p.: 95.7-97.2 °C. $^1$H NMR (400 MHz, CDCl$_3$, $\delta$ 8.12-8.10 (m, 2H), 7.68-7.62 (m, 4H), 7.49-7.45 (m, 2H), 7.41-7.38 (m, 1H), 3.94 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$, $\delta$ 166.9, 145.6, 139.9, 130.1, 128.9, 128.8, 128.1, 127.2, 126.9, 52.1.

Methyl 4-(2,2,2-trifluoroethoxy)benzoate (4ai) White solid (41 mg, 35% yield). m.p.: 50.4-51.5 °C. $^1$H NMR (400 MHz, CDCl$_3$, $\delta$ 8.03 (d, $J$ = 8.0 Hz, 2H), 6.97 (d, $J$ = 8.0 Hz, 2H), 4.41 (q, $J$ = 8.0 Hz, 2H), 3.90 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$, $\delta$ 166.4, 160.7, 131.8, 124.5 (q, $J$ = 277.8 Hz), 114.3, 65.5 (q, $J$ = 36.4 Hz), 52.0. $^{19}$F NMR (CDCl$_3$, 376 MHz) $\delta$ -73.82 (t, $J$ = 7.5 Hz, 3F).
4. Gram scale experimental procedure for the synthesis of 3aa

To a mixture of trifluoromethyl β-diketones 1a (2.5 mmol, 0.54 g), methanol 2 (1.5 mmol, 3.0 equiv, 0.24g), I₂ (0.55 mmol, 1.1 equiv, 0.699g), tert-butyl hydroperoxide (1.25 mmol, 2.5 equiv, 0.810g) and Na₂CO₃ (0.5 mmol, 1.0 equiv, 0.279g) was added 1,2-dichloroethane (10.0 mL). The reaction mixture was then stirred at 60 °C for 7.0 h. When the reaction was completed (monitored by TLC), the reaction was quenched with saturated NH₄Cl aqueous and then saturated Na₂S₂O₃ aqueous. After extraction with EtOAc and drying with Na₂SO₄, the organic layer was concentrated under reduced pressure and the residue was purified by column chromatography on silica gel using hexanes/EtOAc (100:1 to 50:1) as eluent to afford the desired products 3aa (0.479g, 87%).

5. References


6. Copies of NMR spectra
<table>
<thead>
<tr>
<th>ppm</th>
<th>3.04</th>
<th>2.00</th>
<th>2.01</th>
<th>1.00</th>
<th>1.97</th>
<th>1.41</th>
<th>1.42</th>
<th>1.44</th>
<th>4.43</th>
<th>4.45</th>
<th>4.46</th>
<th>4.48</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>CH₃</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **1H NMR**

![1H NMR spectrum of compound](image1)

- **13C NMR**

![13C NMR spectrum of compound](image2)
$\text{H}_2\text{C} = \text{O} \quad \text{O} - \text{C} - \text{CH}_3$

$\text{H}_2\text{C} = \text{O} \quad \text{O} - \text{C} - \text{CH}_3$

$\text{H}_2\text{C} = \text{O} \quad \text{O} - \text{C} - \text{CH}_3$

$\text{H}_2\text{C} = \text{O} \quad \text{O} - \text{C} - \text{CH}_3$