Direct Synthesis of $\beta,\gamma$-Unsaturated $\alpha$-Keto Esters from Aldehyde and Pyruvate

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Table of Contents

General S2
General procedure A and B S2
Characterization data for compounds 1 S3
References S8
NMR Spectrum for compounds 1 S9
General

All chemicals and solvents were used without further purification as commercially available. Thin-layer chromatography (TLC) was performed on silica gel plates (60F-254) using UV-light (254 and 365 nm). Flash chromatography was conducted on silica gel (200–300 mesh). NMR spectra were recorded in CDCl3 on a Bruker ACF400 spectrometer. Chemical shifts were reported in parts per million (ppm). All the products 1\(^{[1-9]}\) were known compounds.

General procedure A

\[
\begin{align*}
\text{R-CHO} + \text{CO}_2\text{R}^1 \xrightarrow{\text{BF}_3\cdot\text{Et}_2\text{O 0.5 equiv.} \, \text{Ac}_2\text{O 1.5 equiv.}} \text{Toluene, 40 °C, 48h} & \rightarrow \text{R-\text{CO}_2\text{R}^1} \\
\end{align*}
\]

To the solution of aldehyde (2 mmol) and pyruvate (2.4 mmol) in toluene (10 mL) was added BF\(_3\)·Et\(_2\)O (1 mmol) and Ac\(_2\)O (3 mmol). After stirred for 48 h at 40 °C, the mixture was poured into 20 mL saturated NaHCO\(_3\) aqueous solution. The separated aqueous phase was extracted with 20 mL ethyl acetate, and the combined organic phase was washed by brine (20 mL), dried by Na\(_2\)SO\(_4\), filtrated and concentrated in vacuum. The residue was filtrated through a short pad of silica gel with petroleum ether: Ethyl acetate 10:1 as elute to get a crud product, which was detected by \(^1\)HNMR to calculate the E/Z ratio. Further purification was carried out by column chromatography on silica gel with petroleum ether: Ethyl acetate 20:1 as elute to afford the products 1.

General procedure B

\[
\begin{align*}
\text{R-CHO} + \text{CO}_2\text{Et} \xrightarrow{\text{Ti(OEt)}_4 1.2 equiv.} \text{Toluene, 40 °C, 3 days} & \rightarrow \text{R-\text{CO}_2\text{Et}} \\
\end{align*}
\]

To the solution of aldehyde (2 mmol) and pyruvate (2.4 mmol) in toluene (10 mL) was added Ti(OEt)_4 (2.4 mmol). After stirred for 72 h at 40 °C, the mixture was diluted by 40 mL Ea and quenched by 1 mL water. After stirred for 0.5 h at room temperature, the mixture was dried by Na\(_2\)SO\(_4\), filtrated and concentrated in vacuum. The residue was filtrated through a short pad of silica gel with petroleum ether: Ethyl acetate 10:1 as elute to get a crud product, which was detected by \(^1\)HNMR to calculate the E/Z ratio. Further purification was carried out by column chromatography on silica gel with petroleum ether: Ethyl acetate 20:1 as elute to afford the products 1.
Characterization data for compounds 1

Ethyl (E)-2-oxo-4-phenylbut-3-enoate 1a

![Structure](image1)

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.85 (d, $J = 16.1$ Hz, 1H), 7.64 – 7.60 (m, 2H), 7.46 – 7.38 (m, 3H), 7.36 (d, $J = 16.1$ Hz, 1H), 4.38 (q, $J = 7.1$ Hz, 2H), 1.40 (t, $J = 7.1$ Hz, 3H).

Methyl (E)-2-oxo-4-phenylbut-3-enoate 1b

![Structure](image2)

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.89 (d, $J = 16.1$ Hz, 1H), 7.64 (dd, $J = 7.7$, 1.4 Hz, 2H), 7.49 – 7.38 (m, 3H), 7.38 (d, $J = 16.2$ Hz, 1H), 3.94 (s, 3H).

Isopropyl (E)-2-oxo-4-phenylbut-3-enoate 1c

![Structure](image3)

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.79 (d, $J = 16.2$ Hz, 1H), 7.57 (dd, $J = 7.6$, 1.6 Hz, 2H), 7.42 – 7.34 (m, 3H), 7.30 (d, $J = 16.1$ Hz, 1H), 5.19 (hept, $J = 6.3$ Hz, 1H), 1.35 (d, $J = 6.3$ Hz, 6H).

Ethyl (E)-2-oxo-4-(o-tolyl)but-3-enoate 1d

![Structure](image4)

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.19 (d, $J = 16.0$ Hz, 1H), 7.69 (d, $J = 7.8$ Hz, 1H), 7.37 – 7.32 (m, 1H), 7.30 (d, $J = 15.9$ Hz, 1H), 7.24 (t, $J = 6.8$ Hz, 1H), 4.40 (q, $J = 7.1$ Hz, 2H), 2.48 (s, 3H), 1.42 (t, $J = 7.1$ Hz, 3H).

Ethyl (E)-2-oxo-4-(m-tolyl)but-3-enoate 1e

![Structure](image5)

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.83 (d, $J = 16.1$ Hz, 1H), 7.44 (s, 1H), 7.43 (d, $J = 7.1$ Hz, 1H), 7.34 (d, $J = 16.1$ Hz, 1H), 7.32 – 7.22 (m, 2H), 4.39 (q, $J = 7.1$ Hz, 2H), 2.38 (s, 3H), 1.41 (t, $J = 7.1$ Hz, 3H).
Ethyl (E)-2-oxo-4-(p-tolyl)but-3-enoate **1f**

\[
\begin{align*}
\text{Me} & \quad \text{CO}_2\text{Et} \\
\end{align*}
\]

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.73 (d, $J = 16.1$ Hz, 1H), 7.42 (d, $J = 7.9$ Hz, 2H), 7.21 (d, $J = 16.1$ Hz, 1H), 7.12 (d, $J = 7.9$ Hz, 2H), 4.31 (q, $J = 7.1$ Hz, 2H), 2.29 (s, 3H), 1.33 (t, $J = 7.1$ Hz, 3H).

Ethyl (E)-4-(4-methoxyphenyl)-2-oxobut-3-enoate **1g**

\[
\begin{align*}
\text{MeO} & \quad \text{CO}_2\text{Et} \\
\end{align*}
\]

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.82 (d, $J = 16.0$ Hz, 1H), 7.59 (d, $J = 8.7$ Hz, 2H), 7.22 (d, $J = 16.0$ Hz, 1H), 6.93 (d, $J = 8.8$ Hz, 2H), 4.38 (q, $J = 7.1$ Hz, 2H), 3.85 (s, 3H), 1.40 (t, $J = 7.1$ Hz, 3H).

Ethyl (E)-4-(4-fluorophenyl)-2-oxobut-3-enoate **1h**

\[
\begin{align*}
\text{F} & \quad \text{CO}_2\text{Et} \\
\end{align*}
\]

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.83 (d, $J = 16.1$ Hz, 1H), 7.67 – 7.60 (m, 2H), 7.30 (d, $J = 16.1$ Hz, 1H), 7.15 – 7.09 (t, $J = 8.6$ Hz, 1H), 4.40 (q, $J = 7.1$ Hz, 1H), 1.41 (t, $J = 7.1$ Hz, 1H).

Ethyl (E)-4-(2-chlorophenyl)-2-oxobut-3-enoate **1i**

\[
\begin{align*}
\text{Cl} & \quad \text{CO}_2\text{Et} \\
\end{align*}
\]

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.19 (d, $J = 16.2$ Hz, 1H), 7.67 (dd, $J = 7.7$, 1.5 Hz, 1H), 7.36 (dd, $J = 7.9$, 1.2 Hz, 1H), 7.32 – 7.22 (m, 3H), 4.34 (q, $J = 7.1$ Hz, 2H), 1.35 (t, $J = 7.2$ Hz, 3H).

Ethyl (E)-4-(3-chlorophenyl)-2-oxobut-3-enoate **1j**

\[
\begin{align*}
\text{Cl} & \quad \text{CO}_2\text{Et} \\
\end{align*}
\]

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.71 (d, $J = 16.1$ Hz, 1H), 7.55 (s, 1H), 7.44 (d, $J = 7.4$ Hz, 1H), 7.38 – 7.28 (m, 3H), 4.35 (q, $J = 7.1$ Hz, 2H), 1.37 (t, $J = 7.1$ Hz, 3H).
Ethyl (E)-4-(2,4-dichlorophenyl)-2-oxobut-3-enoate **1k**

![](https://via.placeholder.com/150)

\[ ^1H \text{ NMR (400 MHz, CDCl}_3 \text{)} \delta 8.14 (d, J = 16.2 Hz, 1H), 7.64 (d, J = 8.5 Hz, 1H), 7.41 (d, J = 1.9 Hz, 1H), 7.27 (d, J = 16.1 Hz, 1H), 7.27 – 7.24 (m, 1H), 4.36 (q, J = 7.1 Hz, 2H), 1.37 (t, J = 7.1 Hz, 3H). \]

Ethyl (E)-4-(2-bromophenyl)-2-oxobut-3-enoate **1l**

![](https://via.placeholder.com/150)

\[ ^1H \text{ NMR (400 MHz, CDCl}_3 \text{)} \delta 8.24 (d, J = 16.1 Hz, 1H), 7.73 (dd, J = 7.8, 1.6 Hz, 1H), 7.64 (dd, J = 8.0, 1.2 Hz, 1H), 7.40 – 7.33 (m, 1H), 7.31 – 7.23 (m, 2H), 4.40 (q, J = 7.1 Hz, 2H), 1.42 (t, J = 7.1 Hz, 3H). \]

Ethyl (E)-4-(4-bromophenyl)-2-oxobut-3-enoate **1m**

![](https://via.placeholder.com/150)

\[ ^1H \text{ NMR (400 MHz, CDCl}_3 \text{)} \delta 7.79 (d, J = 16.1 Hz, 1H), 7.56 (d, J = 8.5 Hz, 1H), 7.49 (d, J = 8.6 Hz, 1H), 7.35 (d, J = 16.1 Hz, 1H), 4.39 (q, J = 7.1 Hz, 1H), 1.41 (t, J = 7.1 Hz, 1H). \]

Ethyl (E)-4-(3-nitrophenyl)-2-oxobut-3-enoate **1n**

![](https://via.placeholder.com/150)

\[ ^1H \text{ NMR (400 MHz, CDCl}_3 \text{)} \delta 8.48 (t, J = 1.7 Hz, 1H), 8.29 (dd, J = 8.2, 1.3 Hz, 1H), 7.93 (d, J = 7.8 Hz, 1H), 7.88 (d, J = 16.2 Hz, 1H), 7.63 (t, J = 8.0 Hz, 1H), 7.49 (d, J = 16.2 Hz, 1H), 4.41 (q, J = 7.1 Hz, 2H), 1.42 (t, J = 7.1 Hz, 3H). \]

Ethyl (E)-4-(4-nitrophenyl)-2-oxobut-3-enoate **1o**

![](https://via.placeholder.com/150)

\[ ^1H \text{ NMR (400 MHz, CDCl}_3 \text{)} \delta 8.25 (d, J = 8.7 Hz, 2H), 7.85 (d, J = 16.2 Hz, 1H), 7.78 (d, J = 8.7 Hz, 2H), 7.47 (d, J = 16.2 Hz, 1H), 4.39 (q, J = 7.1 Hz, 2H), 1.40 (t, J = 7.1 Hz, 3H). \]
Ethyl (E)-4-(naphthalen-1-yl)-2-oxobut-3-enoate **1p**

\[
\text{\begin{center}
\includegraphics[width=0.1\textwidth]{image}
\end{center}}
\]

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.76 (d, \(J = 15.9\) Hz, 1H), 8.23 (d, \(J = 8.4\) Hz, 1H), 7.97 (d, \(J = 8.2\) Hz, 1H), 7.94 (d, \(J = 7.3\) Hz, 1H), 7.90 (d, \(J = 7.9\) Hz, 1H), 7.64 – 7.59 (m, 1H), 7.58 – 7.50 (m, 2H), 7.48 (d, \(J = 15.9\) Hz, 1H), 4.43 (q, \(J = 7.1\) Hz, 2H), 1.44 (t, \(J = 7.1\) Hz, 3H).

Ethyl (E)-4-(furan-2-yl)-2-oxobut-3-enoate **1q**

\[
\text{\begin{center}
\includegraphics[width=0.1\textwidth]{image}
\end{center}}
\]

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.62 (d, \(J = 15.7\) Hz, 1H), 7.59-7.57 (m, 1H), 7.23 (d, \(J = 15.7\) Hz, 1H), 6.82 (d, \(J = 3.5\) Hz, 1H), 6.54 (dd, \(J = 3.5, 1.8\) Hz, 1H), 4.38 (q, \(J = 7.1\) Hz, 2H), 1.41 (t, 3H).

Ethyl (E)-2-oxo-4-(thiophen-2-yl)but-3-enoate **1r**

\[
\text{\begin{center}
\includegraphics[width=0.1\textwidth]{image}
\end{center}}
\]

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.99 (d, \(J = 15.7\) Hz, 1H), 7.51 (d, \(J = 5.1\) Hz, 1H), 7.42 (d, \(J = 3.6\) Hz, 1H), 7.15 (d, \(J = 15.8\) Hz, 1H), 7.11 (dd, \(J = 5.0, 3.8\) Hz, 1H), 4.38 (q, \(J = 7.1\) Hz, 2H), 1.41 (t, \(J = 7.1\) Hz, 3H).

Ethyl (E)-2-oxohept-3-enoate **1s**

\[
\text{\begin{center}
\includegraphics[width=0.1\textwidth]{image}
\end{center}}
\]

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.18 (dt, \(J = 15.8, 6.9\) Hz, 1H), 6.64 (d, \(J = 15.9\) Hz, 1H), 6.64 (d, \(J = 15.9\) Hz, 1H), 4.34 (q, \(J = 7.1\) Hz, 2H), 2.29 (td, \(J = 8.0, 1.0\) Hz, 2H), 1.59 – 1.47 (m, 2H), 1.37 (t, \(J = 7.1\) Hz, 3H), 0.95 (t, \(J = 7.4\) Hz, 3H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 183.5, 162.4, 154.9, 125.3, 62.30, 35.1, 21.1, 14.0, 13.7.

Ethyl (E)-5-methyl-2-oxohex-3-enoate **1t**

\[
\text{\begin{center}
\includegraphics[width=0.1\textwidth]{image}
\end{center}}
\]

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.10 (dd, \(J = 16.0, 6.6\) Hz, 1H), 6.56 (dd, \(J = 16.0, 1.3\) Hz, 1H), 4.30 (q, \(J = 7.1\) Hz, 2H), 2.56 – 2.47 (m, 1H), 1.33 (t, \(J = 7.2\) Hz, 3H), 1.06 (d, \(J = 6.8\) Hz, 6H).

56
Ethyl (E)-4-cyclohexyl-2-oxobut-3-enoate **1u**

\[
\begin{align*}
\text{CO}_2\text{Et} \\
\text{C} & \text{H} \\
\end{align*}
\]

\[^{1}H\text{ NMR (400 MHz, CDCl}_3\left) \delta 7.09 \text{ (dd, } J = 16.0, 6.8 \text{ Hz, 1H}), 6.57 \text{ (dd, } J = 16.0, 1.1 \text{ Hz, 1H}), 4.31 \text{ (q, } J = 7.1 \text{ Hz, 2H)}, 2.29 - 2.13 \text{ (m, 1H)}, 1.78 - 1.64 \text{ (m, 5H)}, 1.35 \text{ (t, } J = 7.1 \text{ Hz, 3H)}, 1.31 - 1.08 \text{ (m, 5H)};\]

\[^{13}C\text{ NMR (101 MHz, CDCl}_3\left) \delta 183.8, 162.5, 159.6, 122.7, 62.2, 41.2, 31.4, 25.8, 25.6, 14.0.\]

Ethyl (E)-2-oxo-6-phenylhex-3-enoate **1v**

\[
\begin{align*}
\text{CO}_2\text{Et} \\
\text{Ph} \\
\end{align*}
\]

\[^{1}H\text{ NMR (400 MHz, CDCl}_3\left) \delta 7.30 \text{ (t, } J = 7.4 \text{ Hz, 2H}), 7.24 - 7.17 \text{ (m, 3H)}, 6.68 \text{ (d, } J = 15.9 \text{ Hz, 1H)}, 4.34 \text{ (q, } J = 7.1 \text{ Hz, 2H)}, 2.83 \text{ (t, } J = 7.7 \text{ Hz, 2H)}, 2.69 - 2.57 \text{ (m, 2H)}, 1.37 \text{ (t, } J = 7.1 \text{ Hz, 3H});\]

\[^{13}C\text{ NMR (101 MHz, CDCl}_3\left) \delta 183.3, 162.3, 153.5, 140.3, 128.6, 128.3, 126.4, 125.6, 62.4, 34.7, 34.0, 14.0.\]

Ethyl (3E,5E)-2-oxo-6-phenylhexa-3,5-dienoate **1w**

\[
\begin{align*}
\text{CO}_2\text{Et} \\
\text{Ph} \\
\end{align*}
\]

\[^{1}H\text{ NMR (400 MHz, CDCl}_3\left) \delta 7.65 \text{ (dd, } J = 15.3, 10.8 \text{ Hz, 1H}), 7.51 \text{ (dd, } J = 7.7, 1.4 \text{ Hz, 1H}), 7.42 - 7.33 \text{ (m, 3H)}, 7.09 \text{ (d, } J = 15.5 \text{ Hz, 1H}), 6.98 \text{ (dd, } J = 15.5, 10.9 \text{ Hz, 1H}), 6.88 \text{ (d, } J = 15.3 \text{ Hz, 1H)}, 4.38 \text{ (q, } J = 7.1 \text{ Hz, 2H)}, 1.40 \text{ (t, } J = 7.1 \text{ Hz, 3H)};\]

Ethyl (E)-3-(1-benzyl-2-oxoindolin-3-ylidene)-2-oxopropanoate **1x**

\[
\begin{align*}
\text{CO}_2\text{Et} \\
\text{Bn} \\
\end{align*}
\]

\[^{1}H\text{ NMR (400 MHz, CDCl}_3\left) \delta 8.68 \text{ (d, } J = 7.7 \text{ Hz, 1H}), 7.91 \text{ (s, 1H)}, 7.35 - 7.26 \text{ (m, 6H)}, 7.03 \text{ (t, } J = 7.7 \text{ Hz, 1H}), 6.70 \text{ (d, } J = 7.8 \text{ Hz, 1H)}, 4.94 \text{ (s, 2H)}, 4.43 \text{ (q, } J = 7.1 \text{ Hz, 2H)}, 1.43 \text{ (t, } J = 7.1 \text{ Hz, 3H)};\]

\[^{13}C\text{ NMR (100 MHz, CDCl}_3\left) \delta 182.9, 167.6, 161.0, 146.3, 140.3, 135.2, 134.4, 129.2, 128.9, 127.9, 127.3, 123.1, 121.9, 120.3, 109.4, 63.0, 44.0, 14.1.\]
References

S22