Synthesis of α-functionalized amide via Ritter reaction in the presence of NaHSO₄/SiO₂

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Supporting Information

Experimental Section

General
Melting points were determined on Büchi Melting Point B-540. NMR spectra were recorded on a JEOL ECX 400 spectrometer. Tetramethylsilane (δ = 0) was used as an internal standard for ¹H NMR and CDCl₃ (δ = 77.0) for ¹³C NMR. Mass analyses were performed on a Xevo G2-S QToF (Waters) Positive ESI. Elemental analyses were performed on a J Science Lab. micro corder JM-10. IR spectra were recorded on a FT/IR-6100 (JASCO).

Preparation of NaHSO₄/SiO₂: SiO₂ [Wakogel C-200 (Wako Pure Chemical Ind. Ltd.), 10 g] was added to a solution of NaHSO₄·H₂O (30 mmol, 4.14 g) in distilled water, and the mixture was stirred at room temperature for 0.5 h. The water was removed by rotary evaporator under reduced pressure, and the resulting reagent was dried in vacuo (10 mmHg) at 120 °C for 5 h.

Typical procedure: A mixture of alcohol 1 (2.0 mmol), nitrile 2 (3.0 mmol) and NaHSO₄/SiO₂ (2.1 mmol/g, 1.00 g) in DCE (10 mL) was stirred at 80 °C, and in MCB (10 mL) was stirred at 130 °C, and then the used supported reagent was removed by filtration. The filtrate was evaporated to leave crude product, which was purified by column chromatography (hexane/ethyl acetate) to obtain 3.

N-Diphenylmethyl-2-bromoacetamide ¹ [3aa]

\[
\begin{array}{c}
\text{HN} \\
\text{O} \\
\text{Br}
\end{array}
\]

White solid: m.p (n-hexane) 148-149°C (140-141°C)
IR (neat) 3189, 1645 cm⁻¹
¹H-NMR (400MHz, CDCl₃) δ 3.81 (2H, s), 6.17 (1H, d, J = 8.2 Hz), 7.20-7.34 (11H, m).
¹³C-NMR (100MHz, CDCl₃) δ 28.98, 57.42, 127.24, 127.61, 128.68, 140.65, 164.75.
HR-MS (ESI) m/z [M + Na]⁺ calcd for C₁₅H₁₄BrNONa: 326.0159; Found :326.0156

N-[(4-Chlorophenyl)phenylmethyl]-2-bromoacetamide [3ba]

\[
\begin{array}{c}
\text{Cl} \\
\text{HN} \\
\text{O} \\
\text{Br}
\end{array}
\]
White solid: m.p (n-hexane) 130-132 °C
IR (neat) 3284, 1661 cm⁻¹

¹H-NMR (400MHz, CDCl₃) δ 3.91 (2H, s), 6.17 (1H, d, J = 7.9 Hz), 7.08 (1H, d, J = 7.9 Hz), 7.16-7.37 (9H, m).
¹³C-NMR (100MHz, CDCl₃) δ 29.04, 56.99, 127.28, 128.00, 128.59, 128.91, 128.93, 133.57, 139.20, 140.15, 164.64.
HR-MS (ESI) m/z [M + Na]⁺ calcld for C₁₅H₁₃NOBrClNa: 359.9770; Found: 359.9767

**N-[Bis(4-chlorophenyl)methyl]-2-bromoacetamide [3ca]**

![Structural diagram]

White solid: m.p (n-hexane) 173-174 °C
IR (neat) 3282, 1652 cm⁻¹

¹H-NMR (400MHz, CDCl₃) δ 3.94 (2H, s), 6.14 (1H, d, J = 7.8 Hz), 7.02 (1H, d, J = 7.8 Hz), 7.13-7.34 (8H, m).
¹³C-NMR (100MHz, CDCl₃) δ 29.00, 56.44, 128.63, 129.12, 133.94, 138.66, 164.64.
HR-MS (ESI) m/z [M + Na]⁺ calcld for C₁₅H₁₃NOBrClNa: 393.9377; Found: 393.9377

**N-[4-Methylphenyl)phenylmethyl]-2-bromoacetamide [3da]**

![Structural diagram]

White solid: m.p (n-hexane) 131-133 °C
IR (neat) 3236, 1644 cm⁻¹

¹H-NMR (400MHz, CDCl₃) δ 2.33 (3H, s), 3.87 (2H, s), 6.16 (1H, d, J = 8.2 Hz), 7.01-7.35 (10H, m).
¹³C-NMR (100MHz, CDCl₃) δ 21.03, 29.14, 57.24, 127.17, 127.21, 127.57, 128.69, 129.42, 137.43, 137.77, 140.85, 164.55.
HR-MS (ESI) m/z [M + Na]⁺ calcld for C₁₆H₁₆BrNO Na: 340.0315; Found: 340.0313
Anal. Calcd. for C₁₆H₁₆BrNO: C 60.39; H 5.07; N 4.40. Found: C 60.45; H 4.91; N 4.24.

**N-[Bis(4-methylphenyl)methyl]-2-bromoacetamide [3ea]**

![Structural diagram]

White solid: m.p (n-hexane) 153-154 °C
IR (neat) 3285, 1661 cm⁻¹

¹H-NMR (400MHz, CDCl₃) δ =2.33 (6H, s), 3.90 (2H, s), 6.13 (1H, d, J= 7.9 Hz), 7.08 (1H, d, J=7.9 Hz), 7.10-7.15 (8H, m).
¹³C-NMR (100MHz, CDCl₃) δ =21.04, 29.22, 57.02, 127.12, 129.39, 137.34, 137.93, 164.42.
HR-MS (ESI) m/z [M + Na]⁺ calcld for C₁₇H₁₈BrNO Na: 3554.0472; Found: 354.0469

**N-[(4-Methylphenyl)-(4-chlorophenyl)methyl]-2-bromoacetamide [3fa]**

![Structural diagram]

White solid: m.p (n-hexane) 151-153 °C
IR (neat) 3280, 1662 cm\(^{-1}\)

\(^1\)H-NMR (400MHz, CDCl\(_3\) δ=2.34 (3H, s), 3.89 (2H, s), 6.12 (1H, d, J=7.8 Hz), 7.10-7.32 (9H, m).

\(^13\)C-NMR (100MHz, CDCl\(_3\) δ=21.04, 29.04, 56.76, 127.22, 128.50, 128.83, 129.58, 133.43, 137.22, 137.81, 139.39, 164.62.

HR-MS (ESI) m/z [M + Na]^+ calcld for C\(_{16}\)H\(_{11}\)BrClNOna: 373.9926; Found :373.9923

Anal. Calcd. for C\(_{16}\)H\(_{11}\)BrClNO: C 54.49; H 4.29; N 3.97. Found: C 54.49; H 4.17; N 3.85.

\(N\)-t-Butyl-2-bromoacetamide \(^2\) [3ha]

\[
\begin{align*}
\text{O} \\
\text{Br}
\end{align*}
\]

White solid: m.p (n-hexane) 99-101 °C

IR (neat) 3304, 1646 cm\(^{-1}\)

\(^1\)H-NMR (400MHz, CDCl\(_3\) δ=1.38 (9H, s), 3.79 (2H, s), 6.29 (1H, s).

\(^13\)C-NMR (100MHz, CDCl\(_3\) δ=28.37, 29.86, 51.90, 164.36.

HR-MS (ESI) m/z [M + Na]^+ calcld for C\(_{4}\)H\(_{12}\)BrNO: 216.0004; Found :216.0000

\(N\)-Triphenylmethyl-2-bromoacetamide [3ka]

\[
\begin{align*}
\text{O} \\
\text{Br}
\end{align*}
\]

White solid: m.p (n-hexane) 204-211 °C

IR (neat) 3363, 1667 cm\(^{-1}\)

\(^1\)H-NMR (400MHz, CDCl\(_3\) δ=3.90 (2H,s), 7.19-7.33 (15H, m), 7.70 (1H, s).

\(^13\)C-NMR (100MHz, CDCl\(_3\) δ=29.99, 70.81, 127.26, 128.09, 128.47, 143.95, 164.30.

HR-MS (ESI) m/z [M + Na]^+ calcld for C\(_{21}\)H\(_{18}\)BrNO: 402.0471; Found :402.0469

Anal. Calcd. for C\(_{21}\)H\(_{18}\)BrNO: C 66.33; H 4.77; N 3.68. Found: C 66.26; H 4.79; N 3.77.

\(N\)-(Diphenylmethyl)-2-chloroacetamide \(^3\) [3ab]

\[
\begin{align*}
\text{O} \\
\text{Cl}
\end{align*}
\]

White solid: m.p(n-hexane) 129-132 °C

IR (neat) 3198, 1648 cm\(^{-1}\);

\(^1\)H-NMR (400MHz, CDCl\(_3\) δ 4.10 (2H, s), 6.25 (1H, d, J = 7.9 Hz), 7.20 (1H, d, J = 7.9 Hz), 7.23-7.37 (11H,m).

\(^13\)C-NMR (100MHz, CDCl\(_3\) δ 42.63, 57.16, 127.29, 127.72, 128.77, 140.68, 165.00.

HR-MS (ESI) m/z [M + Na]^+ calcld for C\(_{15}\)H\(_{14}\)ClNOna:282.0664; Found :282.0662

\(N\)-(Diphenylmethyl)-2-propenamide \(^4\) [3ac]

\[
\begin{align*}
\text{O} \\
\text{CH} = \\
\text{CH}
\end{align*}
\]

White solid: m.p (n-hexane) 180-182 °C

IR (neat) 3276, 1667 cm\(^{-1}\)

\(^1\)H-NMR (400MHz, CDCl\(_3\) δ 5.64-5.67 (1H, dd, J = 1.2, 10.3 Hz), 6.12-6.33 (4H, m), 7.22-7.34 (10H, m).

\(^13\)C-NMR (100MHz, CDCl\(_3\) δ 57.01, 127.20, 127.44, 127.49, 128.65, 130.45, 141.26, 164.55.

HR-MS (ESI) m/z [M + Na]^+ calcld for C\(_{16}\)H\(_{15}\)NOna:260.1053; Found :260.1051
**N-(Diphenylmethyl)-3-butenamide [3ad]**

![Structure](attachment:image.png)

White solid: m.p (n-hexane) 129-132 °C
IR (neat) 3299, 1644 cm⁻¹

1H-NMR (400MHz, CDCl₃) δ 3.04 (2H, d, J = 6.9), 5.20-5.24 (2H, m), 5.90-6.00 (1H, m) 6.24 (1H, d, J=7.8 Hz), 6.36 (1H, d, J=7.8 Hz), 7.20-7.31 (10H, m).

13C-NMR (100MHz, CDCl₃) δ 41.52, 56.73, 119.90, 127.30, 127.39, 128.59, 131.20, 141.39, 169.51.

HR-MS (ESI) m/z [M + Na]⁺ calcld for C₁₇H₁₇NO: 274.1211; Found: 274.1208
Ana. Calcd. for C₁₇H₁₇NO: C 81.24; H 6.82; N 5.57. Found: C 81.30; H 6.60; N 5.49.

**N-(Diphenylmethyl)-3-pentenamide [3ae]**

![Structure](attachment:image.png)

White solid: m.p (n-hexane) 143-145 °C
IR (neat) 3301, 1644 cm⁻¹

1H-NMR (400MHz, CDCl₃) δ 1.70 (3H, d, J = 6.0 Hz), 2.97 (2H, d, J = 6.4 Hz), 5.52-5.67 (2H, m), 6.24 (1H, d, J = 8.2) 6.39 (1H, d, J = 8.2), 7.19-7.33 (10H, m).

13C-NMR (100MHz, CDCl₃) δ 17.98, 40.36, 56.62, 123.51, 127.30 (over rap), 128.55, 130.96, 141.46, 170.34.

HR-MS (ESI) m/z [M + Na]⁺ calcld for C₁₈H₁₉NONa: 288.1365; Found: 288.1364
Ana. Calcd. for C₁₈H₁₉NO: C 81.47; H 7.22; N 5.28. Found: C 81.47; H 7.03; N 5.16.

**N-(Diphenylmethyl)-2-butenamide [3af E-isomer]**

![Structure](attachment:image.png)

White solid: m.p (n-hexane) 169-170 °C
IR (neat) 3255, 1667 cm⁻¹

1H-NMR (400MHz, CDCl₃) δ 1.81 (3H, dd, J = 6.9, 1.6 Hz), 5.86 (1H, dd, J = 15.1, 1.6 Hz), 6.29 (2H, s), 6.80-6.89(1H, m), 7.20-7.30 (10H, m).

13C-NMR (100MHz, CDCl₃) δ 17.74, 56.83, 124.70, 127.39, 127.44, 128.60, 140.75, 141.52, 164.95.

HR-MS (ESI) m/z [M + Na]⁺ calcld for C₁₇H₁₉NONa: 274.1211; Found: 274.1208
Ana. Calcd. for C₁₇H₁₇NO: C 81.24; H 6.82; N 5.57. Found: C 81.27; H 6.80; N 5.42.

**N-(Diphenylmethyl)-2-butenamide [3af Z-isomer]**

![Structure](attachment:image.png)

White solid: m.p (n-hexane) 155-157 °C
IR (neat) 3303, 1654 cm⁻¹

1H-NMR (400MHz, CDCl₃) δ 2.14 (3H, d, J = 7.3 Hz), 5.77 (1H, d, J = 11.5 Hz), 6.29 (1H, d, J = 7.8 Hz), 6.85-6.94 (1H, m), 6.28-6.33 (1H, m), 7.22-7.35 (10H, m).

13C-NMR (100MHz, CDCl₃) δ 17.76, 56.87, 124.68, 127.44, 141.50, 164.92.

HR-MS (ESI) m/z [M + Na]⁺ calcld for C₁₇H₁₉NONa: 274.12101; Found: 274.1208
Ana. Calcd. for C₁₇H₁₇NO: C 81.24; H 6.82; N 5.57. Found: C 81.08; H 6.65; N 5.45.
**N-(Diphenylmethyl)malonic acid ethyl ester [3ag]**

![Chemical Structure](attachment:chemical_structure.png)

White solid: m.p (n-hexane) 93-95 °C
IR (neat) 3235, 1664 1548 cm⁻¹

¹H-NMR (400MHz, CDCl₃) δ 1.27 (3H, t, J = 7.3 Hz), 3.36 (2H, s), 4.19 (2H, q, J = 7.3 Hz), 6.27 (1H, d, J = 7.9 Hz), 7.22-7.33 (10H, m), 7.92 (1H, d, J = 7.9 Hz).

¹³C-NMR (100MHz, CDCl₃) δ 14.01, 40.98, 56.86, 61.66, 127.28, 127.44, 128.67, 141.37, 164.02, 169.70.
HR-MS (ESI) m/z [M+Na]+ calcd for C₁₈H₁₉NO₃Na: 320.1265; Found: 320.1263
Anal. Calcd. for C₁₈H₁₉NO₃: C 72.71; H 6.44; N 4.71. Found: C 72.51; H 6.44; N 4.54.

**N-[(4-Chlorophenyl)phenylmethyl]malonic acid ethyl ester [3bg]**

![Chemical Structure](attachment:chemical_structure.png)

White solid: m.p (n-hexane) 96-100°C
IR (neat) 3232, 1734, 1664 cm⁻¹

¹H-NMR (400MHz, CDCl₃) δ 1.28 (3H, t, J = 7.3 Hz), 3.36 (2H, s), 4.20 (2H, q, J = 7.3 Hz), 6.23 (1H, d, J = 7.8 Hz), 7.18-7.35(9H, m), 7.99(1H, d, J = 7.8 Hz).

¹³C-NMR (100MHz, CDCl₃) δ 14.00, 40.81, 56.31, 61.71, 127.26, 127.71, 128.61, 128.76, 128.80, 133.23, 139.91, 140.78, 164.19, 169.65.
HR-MS (ESI) m/z [M+Na]+ calcd for C₁₈H₁₈ClNO₃Na: 354.0872; Found : 354.0873
Anal. Calcd. for C₁₈H₁₈ClNO₃: C 65.16; H 5.47; N 4.22. Found: C 65.18; H 5.42; N 4.16.

**N-[Bis(4-chlorophenyl)methyl]malonic acid ethyl ester [3cg]**

![Chemical Structure](attachment:chemical_structure.png)

White solid: m.p(n-hexane) 130-133 °C
IR (neat) 3257, 1730 1642 cm⁻¹

¹H-NMR (400MHz, CDCl₃) δ 1.29 (3H, t, J = 7.3 Hz), 3.35 (2H, s), 4.20 (2H, q, J = 7.3 Hz), 6.20 (1H, d, J = 7.8 Hz), 7.15-7.31 (8H, m), 8.02 (1H, d, J = 7.8 Hz).

¹³C-NMR (100MHz, CDCl₃) δ 13.98, 40.69, 55.70, 61.76, 128.611, 128.91, 133.53, 139.34, 164.27, 169.63.
HR-MS (ESI) m/z [M+Na]+ calcd for C₁₉H₁₇Cl₂NO₃ Na: 388.0481; Found: 388.0483
Anal. Calcd. for C₁₉H₁₇Cl₂NO₃: C 59.03; H 4.68; N 3.82. Found: C 59.23; H 4.45; N 3.87.

**N-[(4-Methylphenyl)phenylmethyl]malonic acid ethyl ester [3dg]**

![Chemical Structure](attachment:chemical_structure.png)

White solid: m.p(n-hexane) 96-99 °C
IR (neat) 3236, 1738 1640 cm⁻¹

¹H-NMR (400MHz,CDCl₃) δ 1.27 (3H, t, J = 7.3 Hz), 2.32 (3H, s), 3.34 (2H, s), 4.19 (2H, q, J = 7.3 Hz), 6.23(1H, d, J = 8.2 Hz), 7.11 -7.33 (9H, m), 7.94 (1H, d, J = 8.2 Hz).

¹³C-NMR (100MHz,CDCl₃) δ 13.98, 21.00, 40.98, 56.58, 61.57, 127.15, 127.18, 127.29, 128.56, 129.30, 137.08,
138.42, 141.50, 164.01, 169.58.
HR-MS (ESI) m/z [M+Na]+ calcld for C_{19}H_{21}NO_{3}Na: 334.1420; Found: 334.1419
Anal. Calcld. for C_{19}H_{21}NO_{3}: C 73.29; H 6.80; N 4.50. Found: C 73.13; H 6.69; N 4.46.

\[ \text{N-[Bis(4-methylphenyl)methyl]malonamic acid ethyl ester [3eg]} \]

\[
\text{\begin{tikzpicture}
  \draw[thick,->] (0,0) -- (1,0) node[above] {\text{COOEt}};
  \draw[thick,->] (0,0) -- (0,1) node[right] {\text{H}};
  \draw[thick,->] (0,1) -- (1,1) node[above] {\text{H}};
  \draw[thick,->] (1,1) -- (1,0) node[right] {\text{H}};
  \draw[thick,->] (1,0) -- (0,0) node[below] {\text{H}};
\end{tikzpicture}}
\]

White solid: m.p(n-hexane) 100-104 °C
IR (neat) 3245, 1738 1640 cm\(^{-1}\)
\( ^1\text{H-NMR (400MHz,CDCl}_3\) \( \delta \) 1.28 (3H, t, \( J = 7.3 \text{ Hz} \)), 2.32 (6H, s), 3.35 (2H, s) 4.20 (2H, q, \( J = 7.3 \text{ Hz} \)), 6.19 (1H, d, \( J = 7.9 \text{ Hz} \)), 7.10-7.15 (8H, m), 7.88 (1H, d, \( J = 7.9 \text{ Hz} \)).
\( ^{13}\text{C-NMR (100MHz,CDCl}_3\) \( \delta \) 13.99, 21.00, 41.03, 56.38, 61.58, 127.10, 129.27, 136.98, 138.57, 163.99, 169.60.
HR-MS (ESI) m/z [M+Na]+ calcld for C_{20}H_{23}NO_{3}Na: 348.1577; Found: 348.1576
Anal. Calcld. for C_{20}H_{23}NO_{3}: C 73.82; H 7.12; N 4.30. Found: C 73.55; H 7.12; N 4.24.

\[ \text{N-(Diphenylmethyl)-acetamide [5]} \]

\[
\text{\begin{tikzpicture}
  \draw[thick,->] (0,0) -- (1,0) node[above] {\text{COOH}};
  \draw[thick,->] (0,0) -- (0,1) node[right] {\text{H}};
  \draw[thick,->] (0,1) -- (1,1) node[above] {\text{H}};
  \draw[thick,->] (1,1) -- (1,0) node[right] {\text{H}};
  \draw[thick,->] (1,0) -- (0,0) node[below] {\text{H}};
\end{tikzpicture}}
\]

White solid: m.p (n-hexane) 142-146°C (144-146°C)
IR (neat) 3257, 1642 cm\(^{-1}\)
\( ^1\text{H-NMR (400MHz,CDCl}_3\) \( \delta \) 2.05 (3H, s), 6.12 (1H, d, \( J = 7.5 \text{ Hz} \)), 6.25 (1H, d, \( J = 7.5 \text{ Hz} \)), 7.21-7.34 (10H, m).
\( ^{13}\text{C-NMR (100MHz,CDCl}_3\) \( \delta \) 23.36, 56.98, 127.39, 127.46, 128.65, 141.48, 169.05.
HR-MS (ESI) m/z [M+H]+ calcld for C_{13}H_{18}NO: 226.1231; Found :226.1235

X : parts per Million : 1H
The diagram shows a structure labeled [3ba] with peaks at various parts per million (ppm) values on the X-axis. The Y-axis represents abundance. The ppm values are marked at 164.642, 140.148, 139.204, 133.569, 128.925, 128.906, 128.592, 128.000, and 127.276. The abundance values are indicated at 77.315, 77.000, 76.676, 56.987, and 29.041.
The image shows a graph with labels for parts per Million (13C) and abundance on the y-axis. The x-axis is labeled with values in parts per Million, ranging from 0 to 170.0. The graph contains a spectrum with several peaks, labeled with values such as 164.699, 138.651, 133.912, 129.087, 128.620, 77.315, 77.000, 76.685, 56.424, and 28.955. The structure labeled [3ca] is also present in the image.
X: parts per Million: 13C

[Chemical Structures and Diagrams]
X: parts per Million: 13C
X : parts per Million : 13C

[3ab]
X: parts per Million: 1H

[Chemical Structure Image]

[Plot Image]
$X$ : parts per Million : 13C
[3ae]

X : parts per Million : 13C
X : parts per Million : 1H
[3bg]
abundance

X : parts per Million : 1H
X: parts per Million: 13C

[Chemical Structure]
X : parts per Million : 1H
X : parts per Million : 13C