Electrochemical Synthesis of α-Amino Amides via C(sp³)-H Bond Activation

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General information

All glassware was oven dried at 110 °C for hours and cooled down under vacuum. Unless otherwise noted, all reagents were purchased from commercial suppliers and used without further purification. The instrument for electrolysis was dual display potentiostat (DJS-292B) (made in China). Cyclic voltammograms were obtained on a CHI 605E potentiostat. The anodic electrode was graphite felt (1.5 cm×1.5 cm) and cathodic electrode was platinum sheet (1.5 cm×1.5 cm×0.3 mm). These electrodes were commercially available from GaossUnion and Huanqijinxin, China. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 200-300 mesh silica gel in petroleum (bp. 60-90 °C). GC-MS spectra were recorded on a Varian GC-MS 3900-2100T. The known compounds were characterized by 1H NMR, 13C NMR and 19F NMR. 1H, 19F and 13C NMR data were recorded with ADVANCE III 400 MHz with tetramethylsilane as an internal standard. High resolution mass spectra (HRMS) were measured with a Waters Micromass GCT instrument. All chemical shifts (δ) were reported in ppm and coupling constants (J) in Hz. All chemical shifts were reported relative to tetramethylsilane (0 ppm for 1H), Chloroform-d (77.16 ppm for 13C), respectively.

Experimental Section

1) General procedure for preparation electrochemical oxidative difunctionalization of isocyanides

In an oven-dried undivided three-necked bottle (25 mL) equipped with a stir bar and Bu₄NOAc (0.5 mmol) were combined and added. The bottle was equipped with carbon felt (1.5 cm×1.5 cm) as the anode and platinum plate (1.5 cm × 1.5 cm × 1 mm) as the cathode and was then charged with nitrogen. Under the protection of N₂, N,N-dimethylaniline (0.5 mmol), isocyanide (0.3 mmol), H₂O (50 μL), HOAc (0.5 mL) and MeCN (5.5 mL) were injected respectively into the tubes via syringes. The reaction mixture was stirred and electrolyzed at a constant current of 5 mA for 4 h at room temperature. When the reaction was finished, the pure product was purified by flash column chromatography (PE/EA/Et₃N) on silica gel.

2) Gram-scale experiments

In an oven-dried undivided three-necked bottle (100 mL) equipped with a stir bar and Bu₄NBF₄ (10 mmol) were combined and added. The bottle was equipped with carbon felt (1.5 cm×1.5 cm) as the anode and platinum plate (1.5 cm × 1.5 cm × 1 mm) as the cathode and was then charged with nitrogen. Under the protection of N₂, N,N-dimethylaniline (10 mmol), isocyanide (6 mmol), H₂O (1
mL), HOAc (7.5 mL) and MeCN (82.5 mL) were injected respectively into the tubes via syringes. The reaction mixture was stirred and electrolyzed at a constant current of 20 mA for 22.5 h at room temperature. When the reaction was finished, the pure product was purified by flash column chromatography (PE/EA/Et₃N) on silica gel.

3) **Screening of other cathode materials**

![Chemical Reaction](image)

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Conditions: \(^\text{a}\) (0.6 mmol), \(^\text{b}\) (0.3 mmol), \(^\text{a}\)Bu₄NOAc (0.5 mmol), H₂O (50 μL), HOAc (0.5 mL), MeCN (5.5 mL), carbon felt anode, Pt cathode, undivided cell, constant current = 5 mA, 4 h, rt, N₂, GC yield. \(^\text{b}\)isolated yield.

4) **Screening of other nucleophiles**

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S4
5) Control experiments

a) In an oven-dried undivided three-necked bottle (25 mL) equipped with a stir bar and \(^{15}\text{Bu}_4\text{NOAc} (0.5 \text{ mmol})\) were combined and added. The bottle was equipped with carbon felt (1.5 cm×1.5 cm) as the anode and platinum plate (1.5 cm×1.5 cm×1 mm) as the cathode and was then charged with nitrogen. Under the protection of \(\text{N}_2\), \(N,N\)-dimethylaniline (0.5 mmol), isocyanide (0.3 mmol), \(\text{H}_2^{18}\text{O} \) (50 μL), \(\text{HOAc} \) (0.5 mL) and \(\text{MeCN} \) (5.5 mL) were injected respectively into the tubes via syringes. The reaction mixture was stirred and electrolyzed at a constant current of 5 mA for 4 h at room temperature. When the reaction was finished, the pure product was purified by flash column chromatography (PE/EA/Et3N) on silica gel.

b) In an oven-dried undivided three-necked bottle (25 mL) equipped with a stir bar and \(^{15}\text{Bu}_4\text{NOAc} (0.5 \text{ mmol})\) were combined and added. The bottle was equipped with carbon felt (1.5 cm×1.5 cm) as the anode and platinum plate (1.5 cm×1.5 cm×1 mm) as the cathode and was then charged with nitrogen. Under the protection of \(\text{N}_2\), \(N,N\)-dimethylaniline (0.5 mmol), isocyanide (0.3 mmol), \(\text{H}_2^{18}\text{O} \) (50 μL), \(\text{HOAc} \) (0.5 mL) and \(\text{MeCN} \) (5.5 mL) were injected respectively into the tubes via syringes. The reaction mixture was stirred and electrolyzed at a constant current of 5 mA for 4 h at room temperature. When the reaction was finished, the pure product was purified by flash column chromatography (PE/EA/Et3N) on silica gel.
as the anode and platinum plate (1.5 cm × 1.5 cm × 1 mm) as the cathode and was then charged with nitrogen. Under the protection of N₂, N,N-dimethylaniline (0.5 mmol), isocyanide (0.3 mmol), D₂O (50 μL), HOAc (0.5 mL) and MeCN (5.5 mL) were injected respectively into the tubes via syringes. The reaction mixture was stirred and electrolyzed at a constant current of 5 mA for 4 h at room temperature. When the reaction was finished, the pure product was purified by flash column chromatography (PE/EA/Et₃N) on silica gel.

\[
\text{[M+H]}^+ 292.1423 \\
\text{detected by HRMS}
\]

In an oven-dried undivided three-necked bottle (25 mL) equipped with a stir bar and Bu₄NOAc (0.5 mmol) were combined and added. The bottle was equipped with carbon felt (1.5 cm × 1.5 cm) as the anode and platinum plate (1.5 cm × 1.5 cm × 1 mm) as the cathode and was then charged with nitrogen. Under the protection of N₂, N,N-dimethylaniline (0.5 mmol), isocyanide (0.3 mmol), HOAc (0.5 mL) and MeCN (5.5 mL) were injected respectively into the tubes via syringes. The reaction mixture was stirred and electrolyzed at a constant current of 5 mA for 4 h at room temperature.

\[
\text{detected by GC-MS}
\]

In an oven-dried undivided three-necked bottle (25 mL) equipped with a stir bar and TEMPO (0.6 mmol), Bu₄NOAc (0.5 mmol) were combined and added. The bottle was equipped with carbon felt (1.5 cm × 1.5 cm) as the anode and platinum plate (1.5 cm × 1.5 cm × 1 mm) as the cathode and was then charged with nitrogen. Under the protection of N₂, N,N-dimethylaniline (0.5 mmol), isocyanide (0.3 mmol), H₂O (50 μL), HOAc (0.5 mL) and MeCN (5.5 mL) were injected respectively into the tubes via syringes. The reaction mixture was stirred and electrolyzed at a constant current of 5 mA for 4 h at room temperature.

\[
\text{detected by GC-MS}
\]

In an oven-dried undivided three-necked bottle (25 mL) equipped with a stir bar and BHT (0.6 mmol), Bu₄NOAc (0.5 mmol) were combined and added. The bottle was equipped with carbon felt (1.5 cm × 1.5 cm) as the anode and platinum plate (1.5 cm × 1.5 cm × 1 mm) as the cathode and was then charged with nitrogen. Under the protection of N₂, N,N-dimethylaniline (0.5 mmol), isocyanide (0.3 mmol), H₂O (50 μL), HOAc (0.5 mL) and MeCN (5.5 mL) were injected respectively into the
tubes via syringes. The reaction mixture was stirred and electrolyzed at a constant current of 5 mA for 4 h at room temperature.

6) **General procedure of cyclic voltammetry (CV) experiment**

Cyclic voltammetry was performed in a three electrode cell connected to a schlenk line under nitrogen at room temperature. The working electrode was a glassy carbon electrode, the counter electrode was a platinum wire. The reference electrode was an Ag/AgCl electrode submerged in saturated aqueous KCl solution, and separated from reaction by a salt bridge. 0.2 mmol 1,10 mL of CH$_3$CN containing 1.0 mmol $^\text{t}$Bu$_4$NOAc were poured into the electrochemical cell in all experiments. The scan rate is 0.1 V/s, ranging from 0 V to 2.0 V. The peak potentials vs. Ag/AgCl for used. The oxidation peak of 1 in acetonitrile was obtained at 1.15 V and 1.6 V. After 1 mL acetic acid was added to the reaction mixture (9 mL CH$_3$CN), the oxidation peak of 1 decreased to 1.0 V and 1.47 V.
Detail descriptions for products

**ethyl N-methyl-N-phenylglycylglycinate (3).** White solid was obtained in 83% isolated yield. $^1$H NMR (400 MHz, Chloroform-)$d$ δ 7.34 – 7.24 (m, 2H), 7.14 – 6.98 (m, 1H), 6.85 (t, $J = 7.4$ Hz, 1H), 6.80 – 6.74 (m, 2H), 4.18 (q, $J = 7.1$ Hz, 2H), 4.06 (d, $J = 5.7$ Hz, 2H), 3.91 (s, 2H), 3.04 (s, 3H), 1.26 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 171.09, 169.65, 149.44, 129.49, 118.90, 113.45, 61.61, 58.89, 41.06, 39.82, 14.24.

**ethyl N-(4-chlorophenyl)-N-methylglycylglycinate (4).** White solid was obtained in 76% isolated yield. $^1$H NMR (400 MHz, Chloroform-)$d$ δ 7.24 – 7.17 (m, 2H), 7.02 (t, $J = 5.7$ Hz, 1H), 6.71 – 6.64 (m, 2H), 4.18 (q, $J = 7.1$ Hz, 2H), 4.04 (d, $J = 5.7$ Hz, 2H), 3.87 (s, 2H), 3.03 (s, 3H), 1.26 (t, $J = 7.2$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 170.62, 169.59, 147.92, 129.20, 123.75, 114.49, 113.49, 61.63, 58.69, 41.00, 39.98, 14.18.

**ethyl N-(4-bromophenyl)-N-methylglycylglycinate (5).** White solid was obtained in 75% isolated yield. $^1$H NMR (400 MHz, Chloroform-)$d$ δ 7.39 – 7.32 (m, 2H), 7.01 (t, $J = 5.8$ Hz, 1H), 6.73 – 6.59 (m, 2H), 4.19 (q, $J = 7.2$ Hz, 2H), 4.05 (d, $J = 5.7$ Hz, 2H), 3.88 (s, 2H), 3.04 (s, 3H), 1.28 (t, $J = 7.2$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 170.55, 169.58, 148.30, 132.10, 114.92, 110.94, 61.64, 58.56, 41.01, 39.92, 14.19. HRMS (ESI) calculated for C$_{13}$H$_{18}$BrN$_2$O$_3$+[M+H]$^+$ 329.0495 found 329.0495.

**ethyl N-(4-iodophenyl)-N-methylglycylglycinate (6).** White solid was obtained in 68% isolated yield. $^1$H NMR (400 MHz, Chloroform-)$d$ δ 7.52 (d, $J = 8.9$ Hz, 2H), 6.98 (t, $J = 5.7$ Hz, 2H), 6.54 (d, $J = 9.0$ Hz, 1H), 4.19 (q, $J = 7.2$ Hz, 2H), 4.04 (d, $J = 5.7$ Hz, 2H), 3.88 (s, 2H), 3.03 (s, 3H), 1.27 (t, $J = 7.2$ Hz,
ethyl N-methyl-N-(p-toly)glycylglycinate (7). White solid was obtained in 76% isolated yield. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.17 (t, $J = 5.8$ Hz, 1H), 7.11 – 7.05 (m, 2H), 6.72 – 6.65 (m, 2H), 4.18 (q, $J = 7.1$ Hz, 2H), 4.07 (d, $J = 5.7$ Hz, 2H), 3.81 (s, 2H), 3.77 (s, 3H), 2.96 (s, 3H), 1.27 (t, $J = 7.2$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 171.37, 169.74, 153.29, 144.17, 115.55, 114.86, 61.61, 55.80, 41.04, 40.70, 14.25. HRMS (ESI) calculated for C$_{14}$H$_{21}$N$_{2}$O$_{4}$ $[M+H]^+$ 281.1496 found 281.1498.

ethyl N-(4-methoxyphenyl)-N-methylglycylglycinate (8). White solid was obtained in 78% isolated yield. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.28 (t, $J = 5.8$ Hz, 1H), 6.89 – 6.83 (m, 2H), 6.80 – 6.72 (m, 2H), 4.19 (q, $J = 7.1$ Hz, 2H), 4.07 (d, $J = 5.7$ Hz, 2H), 3.81 (s, 2H), 3.77 (s, 3H), 2.96 (s, 3H), 1.27 (t, $J = 7.2$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 171.37, 169.74, 153.29, 144.17, 115.55, 114.86, 61.61, 55.80, 41.04, 40.70, 14.25. HRMS (ESI) calculated for C$_{14}$H$_{21}$N$_{2}$O$_{4}$ $[M+H]^+$ 281.1496 found 281.1498.

ethyl N-(4-acetoxyphenyl)-N-methylglycylglycinate (9). White solid was obtained in 76% isolated yield. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.12 (t, $J = 5.8$ Hz, 1H), 6.98 (d, $J = 9.0$ Hz, 1H), 6.74 (d, $J = 9.1$ Hz, 1H), 4.18 (q, $J = 7.1$ Hz, 2H), 4.04 (d, $J = 5.8$ Hz, 2H), 3.88 (s, 2H), 3.02 (s, 3H), 2.27 (s, 3H), 1.26 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 170.85, 170.14, 169.54, 147.34, 143.01, 122.27, 113.94, 61.53, 58.98, 40.97, 40.05, 21.09, 14.16. HRMS (ESI) calculated for C$_{15}$H$_{22}$N$_{2}$O$_{4}$ $[M+H]^+$ 309.1445 found 309.1447.

ethyl N-methyl-N-(m-toly)glycylglycinate (10). White solid was obtained in 66% isolated yield. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.20 – 7.13 (m, 1H), 7.08 (d, $J = 6.4$ Hz, 1H), 6.71 – 6.65 (m, 1H), 3.97, 14.19. HRMS (ESI) calculated for C$_{13}$H$_{18}$IN$_{2}$O$_{3}$ $[M+H]^+$ 377.0357 found 377.0355.
6.59 (d, \( J = 6.6 \, \text{Hz}, \, 2\, \text{H} \)), 4.18 (q, \( J = 7.1 \, \text{Hz}, \, 2\, \text{H} \)), 4.06 (d, \( J = 5.7 \, \text{Hz}, \, 2\, \text{H} \)), 3.89 (s, 2H), 3.02 (s, 3H), 2.33 (s, 3H), 1.26 (t, \( J = 7.2 \, \text{Hz}, \, 3\, \text{H} \)). \(^{13}\text{C} \, \text{NMR} \) (101 MHz, CDCl\(_3\)) \( \delta 171.22, \, 169.64, \, 149.52, \, 139.34, \, 129.34, \, 119.81, \, 114.22, \, 110.60, \, 61.61, \, 58.92, \, 41.05, \, 39.83, \, 21.94, \, 14.25 \). HRMS (ESI) calculated for C\(_{14}\)H\(_{20}\)N\(_2\)O\(_3\)\([\text{M+Na}]^+\) 287.1366 found 287.1368.

**ethyl N-(2-bromophenyl)-N-methylglycylglycinate (11).** White solid was obtained in 62% isolated yield. \(^{1}H \, \text{NMR} \) (400 MHz, Chloroform-d) \( \delta 7.89 \) (t, \( J = 5.8 \, \text{Hz}, \, 1\, \text{H} \)), 7.59 (dd, \( J = 7.9, \, 1.5 \, \text{Hz}, \, 1\, \text{H} \)), 7.31 (td, \( J = 7.7, \, 1.5 \, \text{Hz}, \, 1\, \text{H} \)), 7.18 (dd, \( J = 8.0, \, 1.6 \, \text{Hz}, \, 1\, \text{H} \)), 7.00 (td, \( J = 7.7, \, 1.6 \, \text{Hz}, \, 1\, \text{H} \)), 4.23 (q, \( J = 7.1 \, \text{Hz}, \, 2\, \text{H} \)), 4.14 (d, \( J = 5.7 \, \text{Hz}, \, 2\, \text{H} \)), 3.66 (s, 2H), 2.81 (s, 3H), 1.30 (t, \( J = 7.1 \, \text{Hz}, \, 3\, \text{H} \)). \(^{13}\text{C} \, \text{NMR} \) (101 MHz, CDCl\(_3\)) \( \delta 170.39, \, 169.80, \, 150.26, \, 128.64, \, 125.83, \, 122.64, \, 120.51, \, 61.55, \, 60.70, \, 42.65, \, 41.10, \, 14.29 \). HRMS (ESI) calculated for C\(_{13}\)H\(_{17}\)BrN\(_2\)O\(_3\)\([\text{M+Na}]^+\) 351.0315 found 351.0315.

**ethyl N-(3-bromophenyl)-N-methylglycylglycinate (12).** White solid was obtained in 70% isolated yield. \(^{1}H \, \text{NMR} \) (400 MHz, Chloroform-d) \( \delta 7.12 \) (t, \( J = 8.1 \, \text{Hz}, \, 1\, \text{H} \)), 6.99 – 6.87 (m, 3H), 6.66 (m, 1H), 4.19 (q, \( J = 7.1 \, \text{Hz}, \, 2\, \text{H} \)), 4.06 (d, \( J = 5.6 \, \text{Hz}, \, 2\, \text{H} \)), 3.91 (s, 2H), 3.04 (s, 3H), 1.27 (t, \( J = 7.2 \, \text{Hz}, \, 3\, \text{H} \)). \(^{13}\text{C} \, \text{NMR} \) (101 MHz, CDCl\(_3\)) \( \delta 170.39, \, 169.59, \, 150.51, \, 130.72, \, 123.62, \, 121.63, \, 116.10, \, 111.89, \, 61.72, \, 58.37, \, 41.10, \, 14.25 \). HRMS (ESI) calculated for C\(_{13}\)H\(_{17}\)BrN\(_2\)O\(_3\)\([\text{M+Na}]^+\) 351.0319 found 351.0315.

**ethyl N-methyl-N-(2-phenoxophenyl)glycylglycinate (13).** White solid was obtained in 72% isolated yield. \(^{1}H \, \text{NMR} \) (400 MHz, Chloroform-d) \( \delta 7.31 – 7.23 \) (m, 2H), 7.18 – 7.08 (m, 2H), 7.06 – 6.98 (m, 3H), 6.91 – 6.86 (m, 2H), 6.82 (d, \( J = 6.9 \, \text{Hz}, \, 1\, \text{H} \)), 4.14 (q, \( J = 7.1 \, \text{Hz}, \, 2\, \text{H} \)), 3.73 (d, \( J = 6.0 \, \text{Hz}, \, 2\, \text{H} \)), 3.69 (s, 2H), 2.83 (s, 3H), 1.25 (t, \( J = 7.1 \, \text{Hz}, \, 3\, \text{H} \)). \(^{13}\text{C} \, \text{NMR} \) (101 MHz, CDCl\(_3\)) \( \delta 170.75, \, 169.59, \, 157.81, \, 147.95, \, 143.93, \, 129.79, \, 125.30, \, 123.71, \, 122.45, \, 122.13, \, 116.62, \, 61.31, \, 59.92, \, 41.12, \, 40.89, \, 14.25 \). HRMS (ESI) calculated for C\(_{19}\)H\(_{23}\)N\(_2\)O\(_4\)\([\text{M+H}]^+\) 343.1652 found 343.1650.

**ethyl N-(2,4-dimethylphenyl)-N-methylglycylglycinate (14).** White solid was obtained in 78% isolated yield. \(^{1}H \, \text{NMR} \) (400 MHz, Chloroform-d) \( \delta 7.94 \) (t, \( J = 5.5 \, \text{Hz}, \, 1\, \text{H} \)), 7.06 – 6.96 (m, 3H), 4.25 (q, \( J =
7.1 Hz, 2H), 4.16 (d, J = 5.3 Hz, 2H), 3.73 (s, 2H), 2.79 (s, 3H), 2.40 (s, 6H), 1.31 (t, J = 7.2 Hz, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 171.79, 169.95, 148.92, 136.25, 129.60, 126.13, 61.60, 60.60, 41.47, 41.20, 19.76, 14.26. HRMS (ESI) calculated for C$_{15}$H$_{23}$N$_2$O$_3$+ [M+H]$^+$ 279.1703 found 279.1703.

<chemical formula>

**ethyl N-(3,5-dimethylphenyl)-N-methylglycylglycinate (15).** White solid was obtained in 78% isolated yield. $^1$H NMR (400 MHz, Chloroform-d) δ 7.10 (t, J = 5.8 Hz, 1H), 6.51 (s, 1H), 6.41 (s, 2H), 4.18 (q, J = 7.1 Hz, 2H), 4.05 (d, J = 5.8 Hz, 2H), 3.88 (s, 2H), 3.01 (s, 3H), 2.28 (s, 6H), 1.26 (t, J = 7.2 Hz, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 171.32, 169.61, 149.60, 139.15, 120.81, 111.38, 61.54, 58.90, 41.02, 39.79, 21.77, 14.22. HRMS (ESI) calculated for C$_{15}$H$_{23}$N$_2$O$_3$+ [M+H]$^+$ 279.1703 found 279.1705.

<chemical formula>

**ethyl N-(3,5-dichlorophenyl)-N-methylglycylglycinate (16).** White solid was obtained in 72% isolated yield. $^1$H NMR (400 MHz, Chloroform-d) δ 6.81 (m, 1H), 6.76 (d, J = 5.7 Hz, 1H), 6.60 (d, J = 1.7 Hz, 2H), 4.21 (q, J = 7.1 Hz, 2H), 4.07 (d, J = 5.6 Hz, 2H), 3.92 (s, 2H), 3.05 (s, 3H), 1.27 (t, J = 7.1 Hz, 3H), $^{13}$C NMR (101 MHz, CDCl$_3$) δ 169.69, 169.56, 150.76, 135.93, 118.53, 111.51, 61.83, 57.93, 41.19, 39.83, 14.26. HRMS (ESI) calculated for C$_{13}$H$_{17}$Cl$_2$N$_2$O$_3$+ [M+H]$^+$ 319.0611 found 319.0618.

<chemical formula>

**ethyl N-octyl-N-(p-toly)glycylglycinate (17).** White solid was obtained in 70% isolated yield. $^1$H NMR (400 MHz, Chloroform-d) δ 7.09 – 7.02 (m, 3H), 6.68 – 6.61 (m, 2H), 4.17 (q, J = 7.1 Hz, 2H), 4.02 (d, J = 5.7 Hz, 2H), 3.87 (s, 2H), 2.25 (s, 3H), 1.61 (t, J = 7.7 Hz, 2H), 1.34 – 1.21 (m, 13H), 0.95 – 0.84 (m, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 171.39, 169.55, 145.76, 130.00, 127.62, 113.53, 61.51, 56.59, 52.51, 41.04, 31.87, 29.49, 29.36, 27.18, 26.59, 22.73, 20.31, 14.20. HRMS (ESI) calculated for C$_{21}$H$_{35}$N$_2$O$_3$+ [M+H]$^+$ 363.2642 found 362.2645.
**ethyl N-(4-fluorophenyl)-N-octylglycylglycinate (18).** White solid was obtained in 67% isolated yield.

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.04 (t, $J = 5.6$ Hz, 1H), 6.99 – 6.91 (m, 2H), 6.71 – 6.62 (m, 2H), 4.18 (q, $J = 7.1$ Hz, 2H), 4.03 (d, $J = 5.6$ Hz, 2H), 3.85 (s, 2H), 3.36 – 3.27 (m, 2H), 1.60 (t, $J = 7.8$ Hz, 2H), 1.33 – 1.24 (m, 13H), 0.92 – 0.85 (m, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 171.04, 169.59, 156.44 (d, $J = 237.7$ Hz), 144.60, 115.96 (d, $J = 22.1$ Hz), 114.93 (d, $J = 7.4$ Hz), 77.48, 77.16, 76.84, 61.62, 57.00, 53.13, 41.10, 31.89, 29.50, 29.37, 27.19, 26.67, 22.75, 14.23, 14.21. $^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -126.74. HRMS (ESI) calculated for $\text{C}_{20}\text{H}_{32}\text{FN}_2\text{O}_3$ $[\text{M+H}]^+$ 367.2391 found 367.2392.

![Structure of ethyl N-(4-fluorophenyl)-N-octylglycylglycinate (18).]

**ethyl N-(4-phenylbutyl)-N-(p-tolyl)glycylglycinate (19).** White solid was obtained in 66% isolated yield. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.31 – 7.23 (m, 2H), 7.18 (m, 3H), 7.04 (m, 2H), 6.62 (d, $J = 8.6$ Hz, 2H), 4.16 (q, $J = 7.2$ Hz, 2H), 4.00 (d, $J = 5.7$ Hz, 2H), 3.85 (s, 2H), 3.41 – 3.30 (m, 2H), 2.69 – 2.56 (m, 2H), 2.25 (s, 3H), 1.66 (p, $J = 3.5$ Hz, 4H), 1.24 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 171.27, 169.56, 145.72, 142.06, 130.04, 128.46, 128.44, 127.81, 125.97, 113.66, 61.53, 56.60, 52.40, 41.06, 35.73, 28.95, 26.29, 20.33, 14.22. HRMS (ESI) calculated for $\text{C}_{23}\text{H}_{31}\text{N}_2\text{O}_3$ $[\text{M+H}]^+$ 383.2329 found 383.2331.

![Structure of ethyl N-(4-phenylbutyl)-N-(p-tolyl)glycylglycinate (19).]

**ethyl N-(cyclobutylmethyl)-N-(p-tolyl)glycylglycinate (20).** White solid was obtained in 66% isolated yield. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.05 (m, 3H), 6.66 (d, $J = 8.3$ Hz, 2H), 4.17 (q, $J = 7.1$ Hz, 2H), 4.01 (d, $J = 5.7$ Hz, 2H), 3.87 (s, 2H), 3.36 (d, $J = 7.0$ Hz, 2H), 2.69 (p, $J = 3.5$ Hz, 4H), 2.26 (s, 3H), 2.14 – 2.02 (m, 2H), 1.97 – 1.82 (m, 2H), 1.77 (m, 2H), 1.25 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 172.11, 169.69, 145.54, 130.01, 127.86, 113.52, 70.04, 61.54, 58.59, 57.15, 41.12, 34.13, 27.27, 20.36, 18.76, 14.22. HRMS (ESI) calculated for $\text{C}_{18}\text{H}_{27}\text{N}_2\text{O}_4$ $[\text{M+H}]^+$ 319.2016 found 319.2017.

![Structure of ethyl N-(cyclobutylmethyl)-N-(p-tolyl)glycylglycinate (20).]

**ethyl N-(2-methoxyethyl)-N-(p-tolyl)glycylglycinate (21).** White solid was obtained in 47% isolated yield. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.80 (s, 1H), 7.11 – 7.02 (m, 2H), 6.64 (d, $J = 8.6$ Hz, 2H), 4.17 (q, $J = 7.2$ Hz, 2H), 4.01 (d, $J = 5.8$ Hz, 2H), 3.95 (s, 2H), 3.72 – 3.57 (m, 3H), 3.35 (s, 3H), 2.26 (s, 3H), 1.25 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 172.11, 169.69, 145.54, 130.01, 127.86, 113.52, 70.04, 61.41, 58.98, 58.63, 52.54, 41.29, 20.37, 14.26. HRMS (ESI) calculated for $\text{C}_{16}\text{H}_{23}\text{N}_2\text{NaO}_4$ $[\text{M+Na}]^+$ 331.1628 found 331.1630.

S12
ethyl N-(2-(1,3-dioxolan-2-yl)ethyl)-N-(p-tolyl)glycylglycinate (22). White solid was obtained in 72% isolated yield. \(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 7.12 (t, \(J = 5.6\) Hz, 1H), 7.06 (d, \(J = 8.3\) Hz, 2H), 6.72 – 6.59 (m, 2H), 4.63 (t, \(J = 4.7\) Hz, 1H), 4.16 (q, \(J = 7.1\) Hz, 2H), 4.13 – 4.06 (m, 2H), 4.00 (d, \(J = 5.7\) Hz, 2H), 3.87 (s, 2H), 3.75 (m, 2H), 3.53 (t, \(J = 7.2\) Hz, 2H), 2.25 (s, 3H), 1.92 (m, 2H), 1.24 (t, \(J = 7.1\) Hz, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 171.35, 169.58, 145.52, 130.05, 127.76, 113.62, 100.47, 67.01, 61.53, 56.62, 47.22, 41.15, 32.38, 25.79, 20.36, 14.23. HRMS (ESI) calculated for C\(_{18}\)H\(_{27}\)N\(_2\)O\(_5\)+ [M+H]\(^+\) 351.1914 found 351.1912.

ethyl N-(4-acetoxybutyl)-N-(p-tolyl)glycylglycinate (23). White solid was obtained in 73% isolated yield. \(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 7.09 – 7.05 (m, 2H), 7.04 (t, \(J = 5.9\) Hz, 1H), 6.67 – 6.63 (m, 2H), 4.17 (q, \(J = 7.2\) Hz, 2H), 4.11 – 4.07 (m, 2H), 4.02 (d, \(J = 5.6\) Hz, 2H), 3.88 (s, 2H), 3.42 – 3.35 (m, 2H), 2.26 (s, 3H), 2.05 (s, 3H), 1.71 – 1.66 (m, 4H), 1.25 (t, \(J = 7.1\) Hz, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 171.27, 171.18, 169.60, 145.57, 130.11, 128.10, 113.78, 64.10, 61.58, 56.64, 52.14, 41.06, 26.22, 23.25, 21.10, 20.35, 14.22. HRMS (ESI) calculated for C\(_{19}\)H\(_{29}\)N\(_2\)O\(_5\) [M+H]\(^+\) 365.2071 found 365.2075.

ethyl N-(3-cyanopropyl)-N-phenylglycylglycinate (24). White solid was obtained in 44% isolated yield. \(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 7.10 (d, \(J = 8.2\) Hz, 2H), 6.98 (t, \(J = 5.6\) Hz, 1H), 6.71 (d, \(J = 8.5\) Hz, 2H), 4.18 (q, \(J = 7.1\) Hz, 2H), 4.03 (d, \(J = 5.6\) Hz, 2H), 3.88 (s, 2H), 3.49 (dd, \(J = 8.4, 6.4\) Hz, 2H), 2.44 (t, \(J = 6.9\) Hz, 2H), 2.27 (s, 3H), 1.98 (p, \(J = 7.1\) Hz, 2H), 1.26 (t, \(J = 7.1\) Hz, 4H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 170.63, 169.70, 145.24, 130.33, 129.32, 119.17, 114.70, 61.70, 57.19, 51.36, 41.10, 22.81, 20.43, 15.02, 14.25. HRMS (ESI) calculated for C\(_{17}\)H\(_{20}\)N\(_3\)O\(_3\) [M+H]\(^+\) 318.1812 found 318.1811.
ethyl N-(4-chlorobutyl)-N-(p-tolyl)glycylglycinate (25). White solid was obtained in 53% isolated yield. \( ^1 \text{H NMR (400 MHz, Chloroform-d)} \) \( \delta \) 7.32 – 7.23 (m, 2H), 7.18 (m, 2H), 7.04 (dd, \( J = 10.7 \), 8.3 Hz, 3H), 6.67 – 6.52 (m, 2H), 4.16 (q, \( J = 7.2 \) Hz, 2H), 4.00 (d, \( J = 5.7 \) Hz, 2H), 3.85 (s, 2H), 3.40 – 3.30 (m, 2H), 2.70 – 2.59 (m, 2H), 2.25 (s, 3H), 1.66 (p, \( J = 3.5 \) Hz, 4H), 1.24 (t, \( J = 7.1 \) Hz, 3H). \( ^{13} \text{C NMR (101 MHz, CDCl}_3 \) \( \delta \) 171.14, 169.55, 168.46, 145.62, 134.04, 132.11, 130.04, 128.46, 128.44, 127.81, 125.97, 113.66, 61.53, 56.60, 52.40, 41.06, 35.73, 28.95, 26.29, 20.33, 14.22. HRMS (ESI) calculated for C\(_{17}\)H\(_{26}\)ClN\(_2\)O\(_3\)\([M+H]^+\) 341.1626 found 341.1628.

![ethyl N-(4-chlorobutyl)-N-(p-tolyl)glycylglycinate (25)](image)

ethyl N-(4-(1,3-dioxoisodolin-2-yl)butyl)-N-(p-tolyl)glycylglycinate (26). \( ^1 \text{H NMR (400 MHz, Chloroform-d)} \) \( \delta \) 7.86 (dd, \( J = 5.5 \), 3.1 Hz, 2H), 7.74 (dd, \( J = 5.5 \), 3.1 Hz, 2H), 7.11 – 7.03 (m, 3H), 6.67 (d, \( J = 8.2 \) Hz, 2H), 4.15 (q, \( J = 7.2 \) Hz, 2H), 4.04 (d, \( J = 5.7 \) Hz, 2H), 3.88 (s, 2H), 3.73 (t, \( J = 6.9 \) Hz, 2H), 3.41 (t, \( J = 7.4 \) Hz, 2H), 2.26 (s, 3H), 1.83 – 1.63 (m, 4H), 1.25 (t, \( J = 7.1 \) Hz, 3H). \( ^{13} \text{C NMR (101 MHz, CDCl}_3 \) \( \delta \) 171.14, 169.55, 168.46, 145.62, 134.04, 132.11, 130.04, 128.08, 123.32, 113.94, 61.45, 56.78, 52.05, 41.06, 37.58, 26.19, 23.98, 20.32, 14.19. HRMS (ESI) calculated for C\(_{22}\)H\(_{34}\)ClN\(_2\)O\(_5\)\([M+H]^+\) 407.1710 found 407.1709.

![ethyl N-(4-(1,3-dioxoisodolin-2-yl)butyl)-N-(p-tolyl)glycylglycinate (26)](image)

ethyl N-(pent-4-en-1-yl)-N-(p-tolyl)glycylglycinate (27). White solid was obtained in 75% isolated yield. \( ^1 \text{H NMR (400 MHz, Chloroform-d)} \) \( \delta \) 7.13 – 6.96 (m, 3H), 6.70 – 6.60 (m, 2H), 5.82 (m, 1H), 5.09 – 4.95 (m, 2H), 4.17 (q, \( J = 7.1 \) Hz, 2H), 4.02 (d, \( J = 5.6 \) Hz, 2H), 3.87 (s, 2H), 3.41 – 3.31 (m, 2H), 2.26 (s, 3H), 2.17 – 2.07 (m, 2H), 1.81 – 1.66 (m, 2H), 1.25 (t, \( J = 7.2 \) Hz, 3H). \( ^{13} \text{C NMR (101 MHz, CDCl}_3 \) \( \delta \) 171.30, 169.60, 145.69, 137.70, 130.09, 127.89, 115.58, 113.69, 61.58, 56.68, 51.99, 41.10, 31.22, 25.67, 20.36, 14.24. HRMS (ESI) calculated for C\(_{19}\)H\(_{32}\)N\(_2\)O\(_4\)\([M+H]^+\) 319.2016 found 319.2018.

![ethyl N-(pent-4-en-1-yl)-N-(p-tolyl)glycylglycinate (27)](image)

ethyl N-(but-3-yn-1-yl)-N-(p-tolyl)glycylglycinate (28). White solid was obtained in 71% isolated yield. \( ^1 \text{H NMR (400 MHz, Chloroform-d)} \) \( \delta \) 7.15 (t, \( J = 5.7 \) Hz, 1H), 7.08 (d, \( J = 8.4 \) Hz, 2H), 6.69 (d, \( J = 8.6 \) Hz, 2H), 4.17 (q, \( J = 7.2 \) Hz, 2H), 4.01 (d, \( J = 5.7 \) Hz, 2H), 3.94 (s, 2H), 3.58 (t, \( J = 7.0 \) Hz, 2H), 2.51 (td, \( J = 7.0, 2.7 \) Hz, 2H), 2.26 (s, 3H), 2.03 (t, \( J = 2.7 \) Hz, 1H), 1.25 (t, \( J = 7.2 \) Hz, 3H). \( ^{13} \text{C NMR (101 MHz, CDCl}_3 \) \( \delta \) 171.30, 169.60, 145.69, 137.70, 130.09, 127.89, 115.58, 113.69, 61.58, 56.68, 51.99, 41.10, 31.22, 25.67, 20.36, 14.24. HRMS (ESI) calculated for C\(_{18}\)H\(_{24}\)N\(_2\)O\(_4\)\([M+H]^+\) 319.2016 found 319.2018.
MHz, CDCl$_3$) $\delta$ 170.95, 169.53, 145.07, 130.17, 128.76, 114.21, 81.85, 70.51, 61.54, 57.18, 51.57, 41.07, 20.38, 17.18, 14.22. HRMS (ESI) calculated for C$_{13}$H$_{17}$N$_2$O$_3$[M+H]$^+$ 303.1703 found 303.1708.

**ethyl N-isopropyl-N-phenylglycylglycinate (29).** White solid was obtained in 79% isolated yield. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.31 – 7.23 (m, 2H), 7.17 (t, $J$ = 5.9 Hz, 1H), 6.87 – 6.75 (m, 3H), 4.17 (p, $J$ = 6.8 Hz, 3H), 4.04 (d, $J$ = 5.8 Hz, 2H), 3.78 (s, 2H), 1.32 – 1.18 (m, 9H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 171.88, 169.59, 148.69, 129.50, 118.76, 114.22, 61.50, 49.77, 48.36, 40.98, 19.41, 14.19. HRMS (ESI) calculated for C$_{15}$H$_{23}$N$_2$O$_3$[M+H]$^+$ 279.1703 found 279.1701.

**ethyl N-sec-butyl-N-(p-tolyl)glycylglycinate (30).** White solid was obtained in 67% isolated yield. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.14 (t, $J$ = 5.6 Hz, 1H), 7.09 – 7.03 (m, 2H), 6.77 – 6.69 (m, 2H), 4.16 (q, $J$ = 7.1 Hz, 2H), 4.00 (d, $J$ = 5.7 Hz, 2H), 3.80 (dt, $J$ = 8.1, 6.2 Hz, 1H), 3.74 (s, 2H), 2.26 (s, 3H), 1.73 – 1.60 (m, 1H), 1.52 – 1.37 (m, 1H), 1.24 (t, $J$ = 7.1 Hz, 3H), 1.16 (d, $J$ = 6.6 Hz, 3H), 0.98 (t, $J$ = 7.4 Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 171.82, 169.57, 146.63, 129.99, 128.37, 115.04, 61.48, 56.07, 49.87, 41.09, 27.16, 20.34, 16.79, 14.20, 11.74. HRMS (ESI) calculated for C$_{17}$H$_{27}$N$_2$O$_3$[M+H]$^+$ 307.2016 found 307.2018.

**ethyl N-cyclohexyl-N-phenylglycylglycinate (31).** White solid was obtained in 79% isolated yield. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.30 – 7.22 (m, 2H), 7.14 (t, $J$ = 5.8 Hz, 1H), 6.86 – 6.72 (m, 3H), 4.16 (q, $J$ = 7.1 Hz, 2H), 4.03 (d, $J$ = 5.7 Hz, 2H), 3.82 (s, 2H), 3.69 (m, 1H), 1.98 – 1.82 (m, 4H), 1.77 – 1.64 (m, 1H), 1.49 – 1.28 (m, 5H), 1.25 (t, $J$ = 7.1 Hz, 3H), 1.20 – 1.07 (m, 1H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 171.95, 169.58, 148.59, 129.49, 118.61, 114.04, 61.50, 57.27, 50.90, 41.03, 29.92, 26.02, 25.77, 14.19. HRMS (ESI) calculated for C$_{18}$H$_{25}$N$_2$O$_3$[M+H]$^+$ 319.2016 found 319.2017.
ethyl diphenylglycylglycinate (32). White solid was obtained in 50% isolated yield. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.35 – 7.28 (m, 4H), 7.11 (t, $J$ = 5.5 Hz, 1H), 7.07 – 7.01 (m, 6H), 4.37 (s, 2H), 4.18 (q, $J$ = 7.1 Hz, 2H), 4.05 (d, $J$ = 5.4 Hz, 2H), 1.25 (t, $J$ = 7.1 Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 170.64, 169.55, 147.50, 129.78, 122.87, 120.83, 61.66, 57.52, 41.32, 14.23. HRMS (ESI) calculated for C$_{18}$H$_{21}$N$_2$O$_3$+$[M+H]^+$ 313.1547 found 313.1545.

ethyl N-phenyl-N-(p-tolyl)glycylglycinate (33). White solid was obtained in 49% isolated yield. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.29 – 7.22 (m, 2H), 7.14 (t, $J$ = 8.3 Hz, 3H), 7.05 – 6.99 (m, 2H), 6.98 – 6.89 (m, 3H), 4.33 (s, 2H), 4.17 (q, $J$ = 7.1 Hz, 2H), 4.04 (d, $J$ = 5.4 Hz, 2H), 2.33 (s, 3H), 1.25 (t, $J$ = 7.1 Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 170.75, 169.55, 147.97, 144.95, 133.57, 130.50, 129.56, 122.74, 121.58, 118.81, 61.62, 57.68, 41.33, 20.87, 14.22. HRMS (ESI) calculated for C$_{19}$H$_{23}$N$_2$O$_3$+$[M+H]^+$ 327.1703 found 327.1709.

ethyl N-ethyl-N-phenylalanylglycinate (34). White solid was obtained in 43% isolated yield. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.30 – 7.23 (m, 2H), 7.16 (s, 1H), 6.89 – 6.80 (m, 3H), 4.27 – 4.07 (m, 4H), 3.97 (dd, $J$ = 18.2, 5.2 Hz, 1H), 3.32 (dp, $J$ = 21.8, 7.2 Hz, 2H), 1.42 (d, $J$ = 7.1 Hz, 3H), 1.27 (t, $J$ = 7.1 Hz, 3H), 1.20 (t, $J$ = 7.0 Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 174.05, 169.91, 147.52, 129.37, 119.50, 116.82, 61.56, 61.21, 42.51, 41.44, 14.28, 13.69, 13.43. HRMS (ESI) calculated for C$_{15}$H$_{23}$N$_2$O$_3$+$[M+H]^+$ 279.1703 found 279.1707.
ethyl phenylprolylglycinate (35). White solid was obtained in 69% isolated yield. $^1$H NMR (400 MHz, Chloroform-$d$) δ 7.30 – 7.21 (m, 2H), 7.04 (t, $J = 5.8$ Hz, 1H), 6.81 (tt, $J = 7.4$, 1.1 Hz, 1H), 6.72 – 6.61 (m, 2H), 4.22 – 4.10 (m, 3H), 4.05 (dd, $J = 8.4$, 3.2 Hz, 1H), 3.82 (dd, $J = 18.1$, 4.9 Hz, 1H), 3.72 – 3.58 (m, 1H), 3.23 (q, $J = 8.8$ Hz, 1H), 2.34 – 2.19 (m, 2H), 2.12 – 1.99 (m, 2H), 1.24 (t, $J = 7.2$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 174.42, 169.64, 147.49, 129.38, 118.24, 113.19, 64.33, 61.47, 49.72, 41.04, 31.57, 24.19, 14.18. HRMS (ESI) calculated for C$_{15}$H$_{21}$N$_2$O$_3$ $\text{[M+H]}^+$ 277.1547 found 277.1547.

ethyl (1-phenylpiperidine-2-carbonyl)glycinate (36). White solid was obtained in 58% isolated yield. $^1$H NMR (400 MHz, Chloroform-$d$) δ 7.27 (t, $J = 7.9$ Hz, 2H), 7.01 (t, $J = 5.8$ Hz, 1H), 6.96 (d, $J = 8.1$ Hz, 2H), 6.87 (t, $J = 7.3$ Hz, 1H), 4.24 – 4.05 (m, 4H), 3.79 (dd, $J = 18.2$, 4.8 Hz, 1H), 3.46 – 3.25 (m, 2H), 2.19 (m, 1H), 1.84 (m, 1H), 1.64 (m, 4H), 1.25 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 173.35, 169.91, 150.66, 129.49, 120.11, 116.87, 77.48, 77.16, 76.84, 61.46, 47.92, 41.17, 26.09, 23.92, 21.32, 14.22. HRMS (ESI) calculated for C$_{16}$H$_{23}$N$_2$O$_3$ $\text{[M+H]}^+$ 291.1703 found 291.1704.

methyl $N$-methyl-$N$-($p$-tolyl)glycylglycinate (37). White solid was obtained in 91% isolated yield. $^1$H NMR (400 MHz, Chloroform-$d$) δ 7.19 (t, $J = 5.8$ Hz, 1H), 7.11 (d, $J = 8.3$ Hz, 2H), 6.72 (d, $J = 8.7$ Hz, 1H), 4.09 (d, $J = 5.8$ Hz, 2H), 3.88 (s, 2H), 3.76 (s, 3H), 3.03 (s, 3H), 2.30 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 171.41, 170.14, 147.39, 129.93, 128.30, 113.73, 59.19, 52.42, 40.86, 40.07, 20.36. HRMS (ESI) calculated for C$_{16}$H$_{23}$N$_2$O$_3$ $\text{[M+H]}^+$ 251.1390 found 251.1392.

$N$-benzyl-2-(methyl($p$-tolyl)amino)acetamide (38). White solid was obtained in 72% isolated yield. $^1$H NMR (400 MHz, Chloroform-$d$) δ 7.35 – 7.15 (m, 7H), 6.93 (s, 1H), 6.84 (td, $J = 7.3$, 1.0 Hz, 1H), 6.73 (dt, $J = 7.8$, 1.1 Hz, 2H), 4.48 (d, $J = 6.0$ Hz, 2H), 3.91 (s, 2H), 2.99 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 170.50, 149.36, 138.12, 129.49, 128.77, 127.60, 127.56, 118.86, 113.36, 59.10, 43.21, 40.01.
2-(methyl(phenyl)amino)-N-(tosylmethyl)acetamide (39).  White solid was obtained in 51% isolated yield. \(^1^H\) NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 7.63 (d, \(J = 8.1\) Hz, 2H), 7.33 (t, \(J = 6.9\) Hz, 1H), 7.28 – 7.15 (m, 4H), 6.80 (t, \(J = 7.3\) Hz, 1H), 6.58 (d, \(J = 8.1\) Hz, 2H), 4.58 (d, \(J = 6.9\) Hz, 2H), 3.66 (s, 2H), 2.90 (s, 3H), 2.37 (s, 3H). \(^1^C\) NMR (101 MHz, CDCl\(_3\)) \(\delta\) 170.43, 149.06, 145.60, 133.81, 130.00, 129.50, 128.91, 119.18, 113.43, 59.93, 58.51, 40.07, 21.87.

\[
\begin{align*}
\text{N-cyclohexyl-2-(methyl(phenyl)amino)acetamide (40).} & \text{ White solid was obtained in 81\% isolated yield.} \\
\end{align*}
\]

\(^1^H\) NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 7.33 – 7.22 (m, 2H), 6.84 (t, \(J = 7.3\) Hz, 1H), 6.78 – 6.69 (m, 2H), 6.54 – 6.36 (m, 1H), 3.82 (m, 3H), 2.99 (s, 3H), 1.92 – 1.82 (m, 2H), 1.70 – 1.51 (m, 3H), 1.34 (m, 3H). \(^1^C\) NMR (101 MHz, CDCl\(_3\)) \(\delta\) 169.34, 149.57, 129.45, 118.78, 113.37, 59.30, 47.93, 39.82, 33.13, 25.53, 24.88.

\[
\begin{align*}
\text{N-(tert-butyl)-2-(methyl(p-tolyl)amino)acetamide (41).} & \text{ White solid was obtained in 69\% isolated yield.} \\
\end{align*}
\]

\(^1^H\) NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 7.08 (d, \(J = 8.4\) Hz, 2H), 6.72 – 6.62 (m, 2H), 6.49 (s, 1H), 3.67 (s, 2H), 2.94 (s, 3H), 2.27 (s, 3H), 1.33 (s, 8H). \(^1^C\) NMR (101 MHz, CDCl\(_3\)) \(\delta\) 169.84, 147.61, 129.88, 128.20, 113.75, 60.34, 50.95, 40.11, 28.81, 20.38.

\[
\begin{align*}
\text{2-(methyl(phenyl)amino)-N-(2,4,4-trimethylpentan-2-yl)acetamide (42).} & \text{ White solid was obtained in 75\% isolated yield.} \\
\end{align*}
\]

\(^1^H\) NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 7.32 – 7.23 (m, 2H), 6.84 (m, 1H), 6.77 – 6.71 (m, 2H), 6.56 (s, 1H), 3.72 (s, 2H), 2.97 (s, 3H), 1.66 (s, 2H), 1.40 (s, 6H), 1.04 (s, 9H). \(^1^C\) NMR (101 MHz, CDCl\(_3\)) \(\delta\) 169.30, 149.50, 129.37, 118.77, 113.41, 60.12, 54.98, 52.66, 39.89, 31.70, 31.52, 28.88. HRMS (ESI) calculated for C\(_{17}\)H\(_{29}\)N\(_2\)O\([\text{M+H]}^+\) 277.2274 found 277.2274.

\[
\begin{align*}
\text{N-(2,6-dimethylphenyl)-2-(methyl(p-tolyl)amino)acetamide (43).} & \text{ White solid was obtained in 33\% isolated yield.} \\
\end{align*}
\]

\(^1^H\) NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 7.21 (m, 3H), 7.14 (m, 2H), 6.76 – 6.64 (m, 3H),
4.44 (s, 2H), 3.01 (s, 3H), 2.16 (m, 9H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 173.10, 172.59, 149.12, 136.62, 135.67, 129.28, 129.24, 117.33, 112.36, 58.55, 39.52, 25.86, 18.09. HRMS (ESI) calculated for C$_{18}$H$_{23}$N$_2$O$^+[M+H]^+$ 283.1805 found 283.1804.
Reference:


Aromatic NMR spectrum of a compound with the following features:

- Protons at 7.29, 7.13, 6.98, and 6.75 ppm.
- Carbon atoms with chemical shifts at 170.85, 170.34, 147.34, and 113.94 ppm.

The molecule contains an acetate group (AcO) and is connected to a carboxylic acid group (CO₂Et).