

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

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Supporting Information

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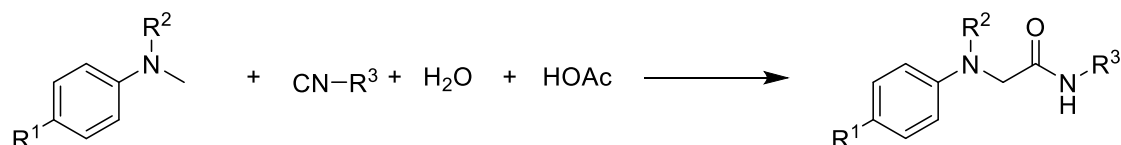
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General information

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 Huanqiuixin, 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.

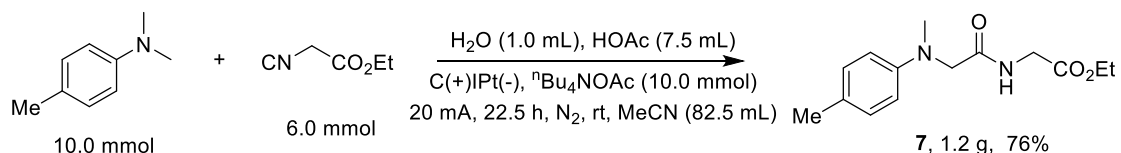
Experimental Section

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 ⁿBu₄NOAc (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.

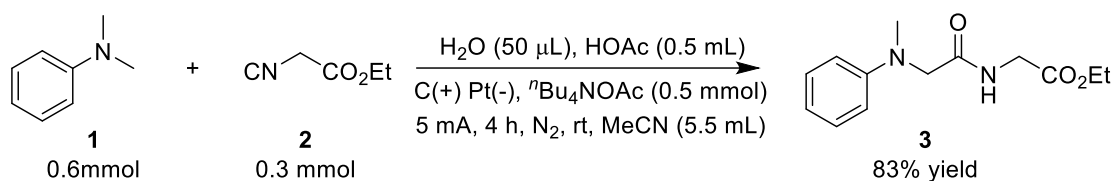
2) Gram-scale experiments



In an oven-dried undivided three-necked bottle (100 mL) equipped with a stir bar and ⁿBu₄NBF₄ (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.

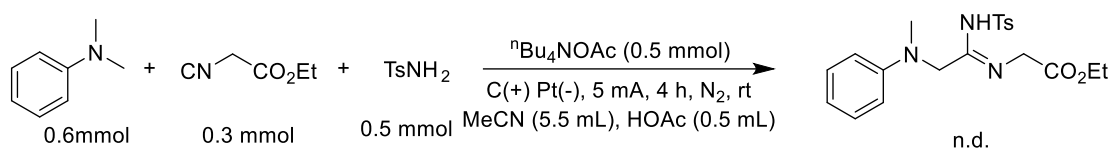
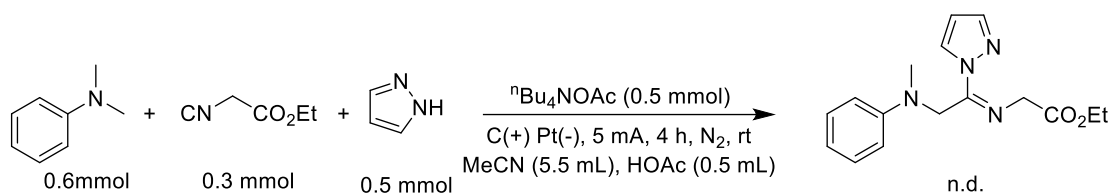
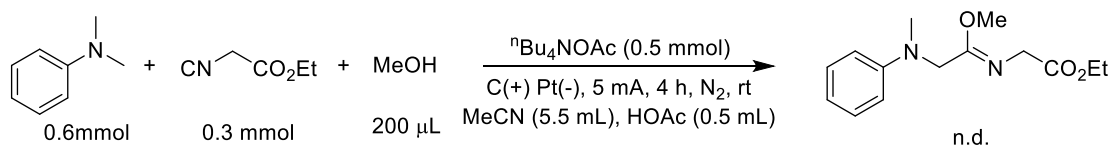
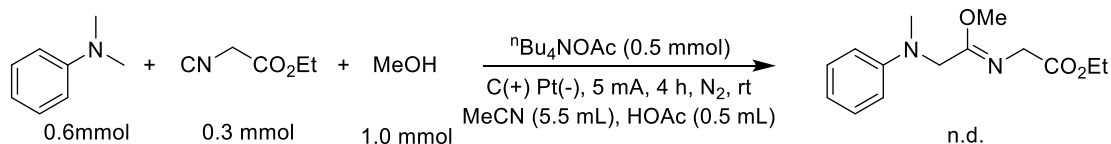
3) Screening of other cathode materials



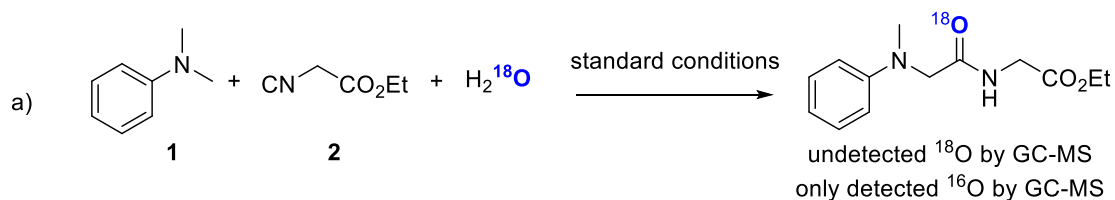
Entry	variation from standard conditions	Yield/% ^a
1	none	83 ^b
2	C felt (+) C felt (-)	55
3	C felt (+) C rod (-)	48
4	C felt (+) Ni (-)	56
5	C felt (+) Stainless steel (-)	60
6	C felt (+) C cloth (-)	59
7	C felt (+) Ni foam (-)	36
8	C felt (+) Cu foam(-)	49
9	C felt (+) Cu (-)	79

Conditions: ^a**1** (0.6 mmol), **2** (0.3 mmol), ⁿBu₄NOAc (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. ^bisolated yield.

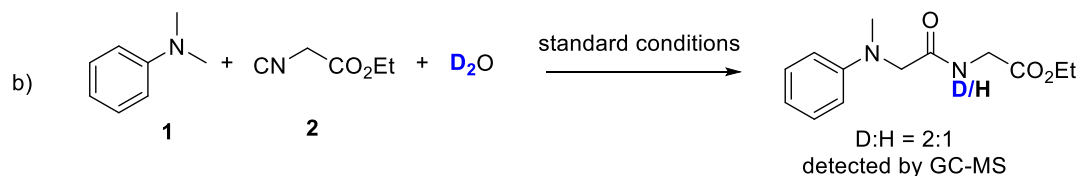
4) Screening of other nucleophiles



5) Control experiments

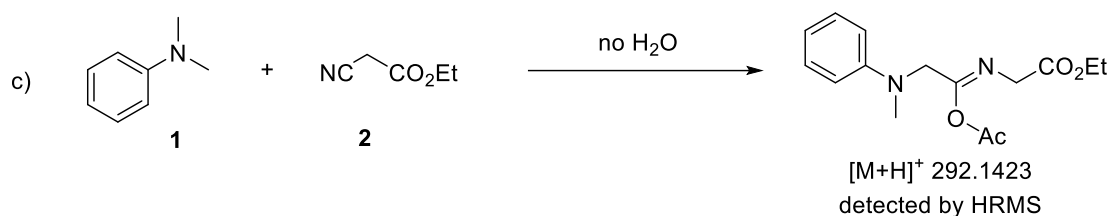


In an oven-dried undivided three-necked bottle (25 mL) equipped with a stir bar and $n\text{Bu}_4\text{NOAc}$ (0.5 mmol) were combined and added. The bottle was equipped with carbon felt (1.5 cm × 1.5 cm) as the anode and platinum plate (1.5 cm × 1.5 cm × 1 mm) as the cathode and was then charged with nitrogen. Under the protection of N_2 , N,N -dimethylaniline (0.5 mmol), isocyanide (0.3 mmol), H_2^{18}O (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/ Et_3N) on silica gel.

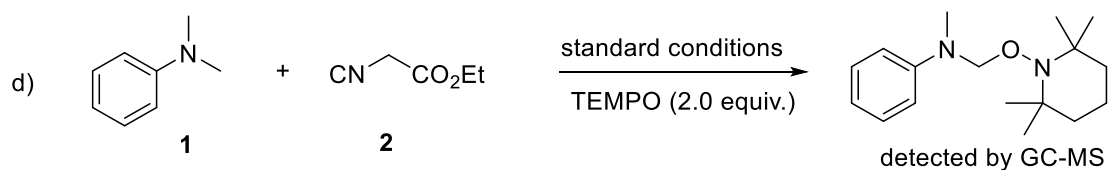


In an oven-dried undivided three-necked bottle (25 mL) equipped with a stir bar and $n\text{Bu}_4\text{NOAc}$ (0.5 mmol) were combined and added. The bottle was equipped with carbon felt (1.5 cm × 1.5 cm)

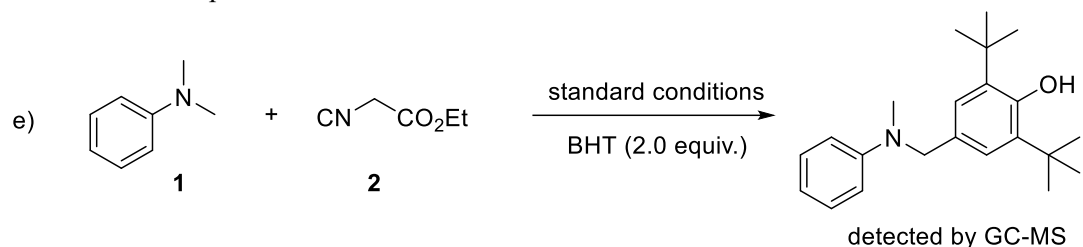
as the anode and platinum plate (1.5 cm × 1.5 cm × 1 mm) as the cathode and was then charged with nitrogen. Under the protection of N₂, *N,N*-dimethylaniline (0.5 mmol), isocyanide (0.3 mmol), D₂O (50 μL), HOAc (0.5 mL) and MeCN (5.5 mL) were injected respectively into the tubes via syringes. The reaction 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.



In an oven-dried undivided three-necked bottle (25 mL) equipped with a stir bar and ^tBu₄NOAc (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.



In an oven-dried undivided three-necked bottle (25 mL) equipped with a stir bar and TEMPO (0.6 mmol), ^tBu₄NOAc (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.



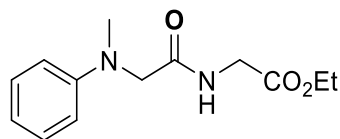
In an oven-dried undivided three-necked bottle (25 mL) equipped with a stir bar and BHT (0.6 mmol), ^tBu₄NOAc (0.5 mmol) were combined and added. The bottle was equipped with carbon felt (1.5 cm×1.5 cm) as the anode and platinum plate (1.5 cm × 1.5 cm × 1 mm) as the cathode and was then charged with 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.

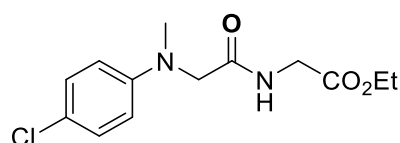
6) General procedure of cyclic voltammetry (CV) experiment

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 CH₃CN containing 1.0 mmol ⁿBu₄NOAc 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 CH₃CN), the oxidation peak of **1** decreased to 1.0 V and 1.47 V.

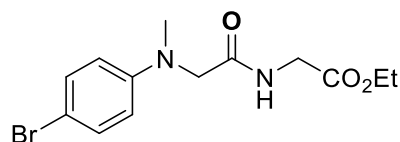
Detail descriptions for products



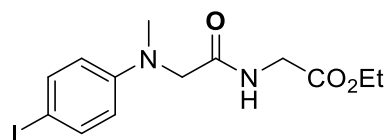
ethyl *N*-methyl-*N*-phenylglycylglycinate (3). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.34 – 7.24 (m, 2H), 7.14 – 6.98 (m, 1H), 6.85 (t, $J = 7.4$ Hz, 1H), 6.80 – 6.74 (m, 2H), 4.18 (q, $J = 7.1$ Hz, 2H), 4.06 (d, $J = 5.7$ Hz, 2H), 3.91 (s, 2H), 3.04 (s, 3H), 1.26 (t, $J = 7.1$ Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) 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). ¹H 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). ¹³C NMR (101 MHz, CDCl₃) δ 170.62, 169.59, 147.92, 129.20, 123.75, 114.49, 61.63, 58.69, 41.00, 39.98, 14.18.

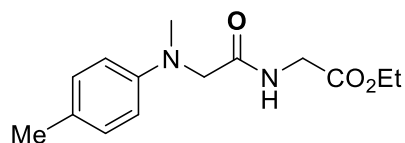


ethyl *N*-(4-bromophenyl)-*N*-methylglycylglycinate (5). White solid was obtained in 75% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.32 (m, 2H), 7.01 (t, $J = 5.8$ Hz, 1H), 6.73 – 6.59 (m, 2H), 4.19 (q, $J = 7.2$ Hz, 2H), 4.05 (d, $J = 5.7$ Hz, 2H), 3.88 (s, 2H), 3.04 (s, 3H), 1.28 (t, $J = 7.2$ Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) 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 C₁₃H₁₈BrN₂O₃⁺[M+H]⁺ 329.0495 found 329.0495.

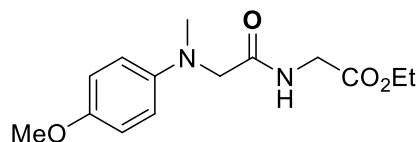


ethyl *N*-(4-iodophenyl)-*N*-methylglycylglycinate (6). White solid was obtained in 68% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.52 (d, $J = 8.9$ Hz, 2H), 6.98 (t, $J = 5.7$ Hz, 2H), 6.54 (d, $J = 9.0$ Hz, 1H), 4.19 (q, $J = 7.2$ Hz, 2H), 4.04 (d, $J = 5.7$ Hz, 2H), 3.88 (s, 2H), 3.03 (s, 3H), 1.27 (t, $J = 7.2$ Hz,

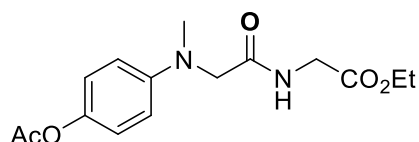
3H). ^{13}C NMR (101 MHz, CDCl_3) δ 170.45, 169.53, 148.83, 137.95, 115.43, 80.28, 61.60, 58.33, 41.00, 39.76, 14.19. HRMS (ESI) calculated for $\text{C}_{13}\text{H}_{18}\text{N}_2\text{O}_3^+$ $[\text{M}+\text{H}]^+$ 377.0357 found 377.0355.



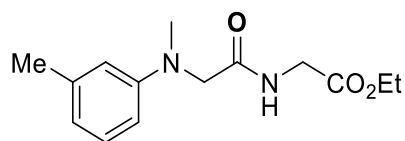
ethyl *N*-methyl-*N*-(*p*-tolyl)glycylglycinate (7).² White solid was obtained in 76% isolated yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.17 (t, $J = 5.8$ Hz, 1H), 7.11 – 7.05 (m, 2H), 6.72 – 6.65 (m, 2H), 4.18 (q, $J = 7.1$ Hz, 2H), 4.04 (d, $J = 5.8$ Hz, 2H), 3.85 (s, 2H), 2.99 (s, 3H), 2.26 (s, 3H), 1.26 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 171.31, 169.63, 147.36, 129.90, 128.20, 113.66, 61.53, 59.16, 40.98, 40.00, 20.34, 14.19.



ethyl *N*-(4-methoxyphenyl)-*N*-methylglycylglycinate (8). White solid was obtained in 78% isolated yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 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) δ 171.37, 169.74, 153.29, 144.17, 115.55, 114.86, 61.61, 59.96, 55.80, 41.04, 40.70, 14.25. HRMS (ESI) calculated for $\text{C}_{14}\text{H}_{21}\text{N}_2\text{O}_4^+$ $[\text{M}+\text{H}]^+$ 281.1496 found 281.1498.

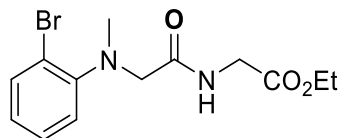


ethyl *N*-(4-acetoxyphenyl)-*N*-methylglycylglycinate (9). White solid was obtained in 76% isolated yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.12 (t, $J = 5.8$ Hz, 1H), 6.98 (d, $J = 9.0$ Hz, 1H), 6.74 (d, $J = 9.1$ Hz, 1H), 4.18 (q, $J = 7.1$ Hz, 2H), 4.04 (d, $J = 5.8$ Hz, 2H), 3.88 (s, 2H), 3.02 (s, 3H), 2.27 (s, 3H), 1.26 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 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 $\text{C}_{15}\text{H}_{21}\text{N}_2\text{O}_5^+$ $[\text{M}+\text{H}]^+$ 309.1445 found 309.1447.

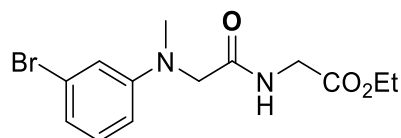


ethyl *N*-methyl-*N*-(*m*-tolyl)glycylglycinate (10). White solid was obtained in 66% isolated yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.20 – 7.13 (m, 1H), 7.08 (d, $J = 6.4$ Hz, 1H), 6.71 – 6.65 (m, 1H),

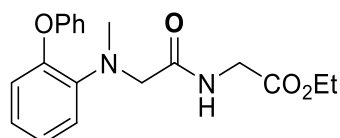
6.59 (d, $J = 6.6$ Hz, 2H), 4.18 (q, $J = 7.1$ Hz, 2H), 4.06 (d, $J = 5.7$ Hz, 2H), 3.89 (s, 2H), 3.02 (s, 3H), 2.33 (s, 3H), 1.26 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 171.22, 169.64, 149.52, 139.34, 129.34, 119.81, 114.22, 110.60, 61.61, 58.92, 41.05, 39.83, 21.94, 14.25. HRMS (ESI) calculated for $\text{C}_{14}\text{H}_{20}\text{N}_2\text{NaO}_3^+[\text{M}+\text{Na}]^+$ 287.1366 found 287.1368.



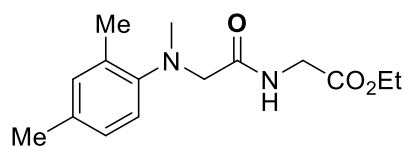
ethyl *N*-(2-bromophenyl)-*N*-methylglycylglycinate (11). White solid was obtained in 62% isolated yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.89 (t, $J = 5.8$ Hz, 1H), 7.59 (dd, $J = 7.9, 1.5$ Hz, 1H), 7.31 (td, $J = 7.7, 1.5$ Hz, 1H), 7.18 (dd, $J = 8.0, 1.6$ Hz, 1H), 7.00 (td, $J = 7.7, 1.6$ Hz, 1H), 4.23 (q, $J = 7.1$ Hz, 2H), 4.14 (d, $J = 5.7$ Hz, 2H), 3.66 (s, 2H), 2.81 (s, 3H), 1.30 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 170.39, 169.80, 150.26, 133.83, 128.64, 125.83, 122.64, 120.51, 61.55, 60.70, 42.65, 41.10, 14.29. HRMS (ESI) calculated for $\text{C}_{13}\text{H}_{17}\text{BrN}_2\text{NaO}_3^+[\text{M}+\text{Na}]^+$ 351.0315 found 351.0315.



ethyl *N*-(3-bromophenyl)-*N*-methylglycylglycinate (12). White solid was obtained in 70% isolated yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.12 (t, $J = 8.1$ Hz, 1H), 6.99 – 6.87 (m, 3H), 6.66 (m, 1H), 4.19 (q, $J = 7.1$ Hz, 2H), 4.06 (d, $J = 5.6$ Hz, 2H), 3.91 (s, 2H), 3.04 (s, 3H), 1.27 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 170.39, 169.59, 150.51, 130.72, 123.62, 121.63, 116.10, 111.89, 61.72, 58.37, 41.10, 39.78, 14.25. HRMS (ESI) calculated for $\text{C}_{13}\text{H}_{17}\text{BrN}_2\text{NaO}_3^+[\text{M}+\text{Na}]^+$ 351.0315 found 351.0319.

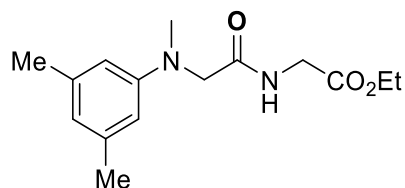


ethyl *N*-methyl-*N*-(2-phenoxyphenyl)glycylglycinate (13). White solid was obtained in 72% isolated yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.23 (m, 2H), 7.18 – 7.08 (m, 2H), 7.06 – 6.98 (m, 3H), 6.91 – 6.86 (m, 2H), 6.82 (d, $J = 6.9$ Hz, 1H), 4.14 (q, $J = 7.1$ Hz, 2H), 3.73 (d, $J = 6.0$ Hz, 2H), 3.69 (s, 2H), 2.83 (s, 3H), 1.25 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 170.75, 169.59, 157.81, 147.95, 143.93, 129.79, 125.30, 123.71, 122.45, 122.13, 120.00, 116.62, 61.31, 59.92, 41.12, 40.89, 14.25. HRMS (ESI) calculated for $\text{C}_{19}\text{H}_{23}\text{N}_2\text{O}_4^+[\text{M}+\text{H}]^+$ 343.1652 found 343.1650.

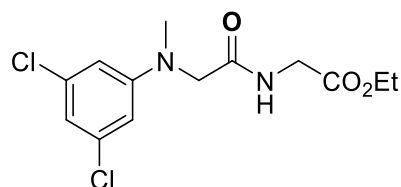


ethyl *N*-(2,4-dimethylphenyl)-*N*-methylglycylglycinate (14). White solid was obtained in 78% isolated yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.94 (t, $J = 5.5$ Hz, 1H), 7.06 – 6.96 (m, 3H), 4.25 (q, $J =$

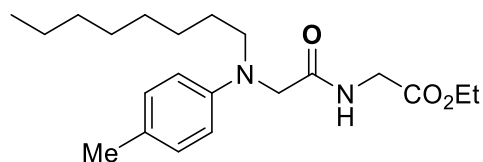
7.1 Hz, 2H), 4.16 (d, $J = 5.3$ Hz, 2H), 3.73 (s, 2H), 2.79 (s, 3H), 2.40 (s, 6H), 1.31 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 171.79, 169.95, 148.92, 136.25, 129.60, 126.13, 61.60, 60.60, 41.47, 41.20, 19.76, 14.26. HRMS (ESI) calculated for $\text{C}_{15}\text{H}_{23}\text{N}_2\text{O}_3^+[\text{M}+\text{H}]^+$ 279.1703 found 279.1703.



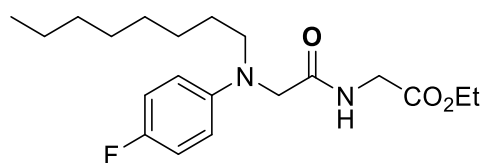
ethyl *N*-(3,5-dimethylphenyl)-*N*-methylglycylglycinate (15). White solid was obtained in 78% isolated yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.10 (t, $J = 5.8$ Hz, 1H), 6.51 (s, 1H), 6.41 (s, 2H), 4.18 (q, $J = 7.1$ Hz, 2H), 4.05 (d, $J = 5.8$ Hz, 2H), 3.88 (s, 2H), 3.01 (s, 3H), 2.28 (s, 6H), 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 $\text{C}_{15}\text{H}_{23}\text{N}_2\text{O}_3^+[\text{M}+\text{H}]^+$ 279.1703 found 279.1705.



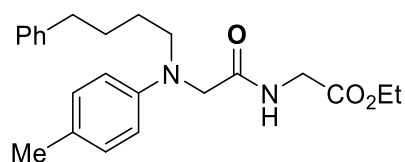
ethyl *N*-(3,5-dichlorophenyl)-*N*-methylglycylglycinate (16). White solid was obtained in 72% isolated yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 6.81 (m, 1H), 6.76 (d, $J = 5.7$ Hz, 1H), 6.60 (d, $J = 1.7$ Hz, 2H), 4.21 (q, $J = 7.1$ Hz, 2H), 4.07 (d, $J = 5.6$ Hz, 2H), 3.92 (s, 2H), 3.05 (s, 3H), 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 $\text{C}_{13}\text{H}_{17}\text{Cl}_2\text{N}_2\text{O}_3^+[\text{M}+\text{H}]^+$ 319.0611 found 319.0618.



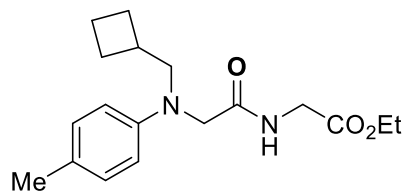
ethyl *N*-octyl-*N*-(*p*-tolyl)glycylglycinate (17). White solid was obtained in 70% isolated yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.09 – 7.02 (m, 3H), 6.68 – 6.61 (m, 2H), 4.17 (q, $J = 7.1$ Hz, 2H), 4.02 (d, $J = 5.7$ Hz, 2H), 3.87 (s, 2H), 2.25 (s, 3H), 1.61 (t, $J = 7.7$ Hz, 2H), 1.34 – 1.21 (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 $\text{C}_{21}\text{H}_{35}\text{N}_2\text{O}_3^+[\text{M}+\text{H}]^+$ 362.2642 found 362.2645.



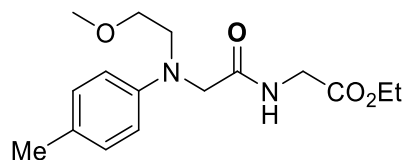
ethyl *N*-(4-fluorophenyl)-*N*-octylglycylglycinate (18). White solid was obtained in 67% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.04 (t, $J = 5.6$ Hz, 1H), 6.99 – 6.91 (m, 2H), 6.71 – 6.62 (m, 2H), 4.18 (q, $J = 7.1$ Hz, 2H), 4.03 (d, $J = 5.6$ Hz, 2H), 3.85 (s, 2H), 3.36 – 3.27 (m, 2H), 1.60 (t, $J = 7.8$ Hz, 2H), 1.33 – 1.24 (m, 13H), 0.92 – 0.85 (m, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 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. $^{19}\text{F NMR}$ (377 MHz, CDCl_3) δ -126.74. HRMS (ESI) calculated for $\text{C}_{20}\text{H}_{32}\text{FN}_2\text{O}_3^+[\text{M}+\text{H}]^+$ 367.2391 found 367.2392.



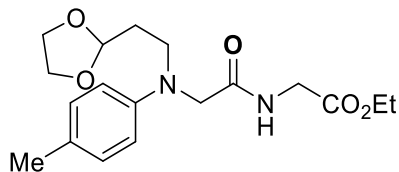
ethyl *N*-(4-phenylbutyl)-*N*-(*p*-tolyl)glycylglycinate (19). White solid was obtained in 66% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.31 – 7.23 (m, 2H), 7.18 (m, 3H), 7.04 (m, 2H), 6.62 (d, $J = 8.6$ Hz, 2H), 4.16 (q, $J = 7.2$ Hz, 2H), 4.00 (d, $J = 5.7$ Hz, 2H), 3.85 (s, 2H), 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). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 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 $\text{C}_{23}\text{H}_{31}\text{N}_2\text{O}_3^+[\text{M}+\text{H}]^+$ 383.2329 found 383.2331.



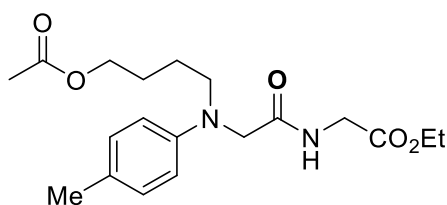
ethyl *N*-(cyclobutylmethyl)-*N*-(*p*-tolyl)glycylglycinate (20). White solid was obtained in 66% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.05 (m, 3H), 6.66 (d, $J = 8.3$ Hz, 2H), 4.17 (q, $J = 7.1$ Hz, 2H), 4.01 (d, $J = 5.7$ Hz, 2H), 3.87 (s, 2H), 3.36 (d, $J = 7.0$ Hz, 2H), 2.69 (p, $J = 7.6$ Hz, 1H), 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). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 171.38, 169.54, 146.37, 129.96, 128.09, 114.08, 61.54, 58.59, 57.15, 41.12, 34.13, 27.27, 20.36, 18.76, 14.22. HRMS (ESI) calculated for $\text{C}_{18}\text{H}_{27}\text{N}_2\text{O}_3^+[\text{M}+\text{H}]^+$ 319.2016 found 319.2017.



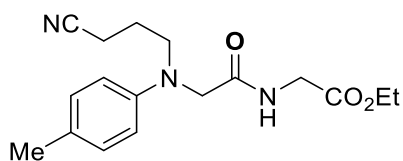
ethyl *N*-(2-methoxyethyl)-*N*-(*p*-tolyl)glycylglycinate (21). White solid was obtained in 47% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.80 (s, 1H), 7.11 – 7.02 (m, 2H), 6.64 (d, $J = 8.6$ Hz, 2H), 4.17 (q, $J = 7.2$ Hz, 2H), 4.01 (d, $J = 5.8$ Hz, 2H), 3.95 (s, 2H), 3.72 – 3.57 (m, 3H), 3.35 (s, 3H), 2.26 (s, 3H), 1.25 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 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 $\text{C}_{16}\text{H}_{24}\text{N}_2\text{NaO}_4^+[\text{M}+\text{Na}]^+$ 331.1628 found 331.1630.



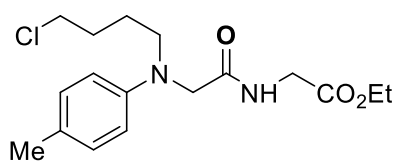
ethyl *N*-(2-(1,3-dioxolan-2-yl)ethyl)-*N*-(*p*-tolyl)glycylglycinate (22). White solid was obtained in 72% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.12 (t, $J = 5.6$ Hz, 1H), 7.06 (d, $J = 8.3$ Hz, 2H), 6.72 – 6.59 (m, 2H), 4.63 (t, $J = 4.7$ Hz, 1H), 4.16 (q, $J = 7.1$ Hz, 2H), 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). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 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 $\text{C}_{18}\text{H}_{27}\text{N}_2\text{O}_5^+[\text{M}+\text{H}]^+$ 351.1914 found 351.1912.



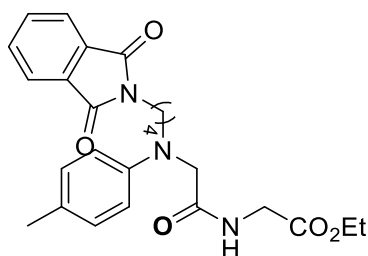
ethyl *N*-(4-acetoxybutyl)-*N*-(*p*-tolyl)glycylglycinate (23). White solid was obtained in 73% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.09 – 7.05 (m, 2H), 7.04 (t, $J = 5.9$ Hz, 1H), 6.67 – 6.63 (m, 2H), 4.17 (q, $J = 7.2$ Hz, 2H), 4.11 – 4.07 (m, 2H), 4.02 (d, $J = 5.6$ Hz, 2H), 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). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 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 $\text{C}_{19}\text{H}_{29}\text{N}_2\text{O}_5^+[\text{M}+\text{H}]^+$ 365.2071 found 365.2075.



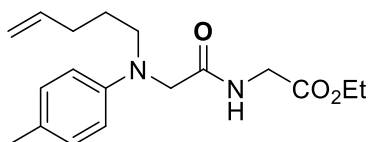
ethyl *N*-(3-cyanopropyl)-*N*-phenylglycylglycinate (24). White solid was obtained in 44% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.10 (d, $J = 8.2$ Hz, 2H), 6.98 (t, $J = 5.6$ Hz, 1H), 6.71 (d, $J = 8.5$ Hz, 2H), 4.18 (q, $J = 7.1$ Hz, 2H), 4.03 (d, $J = 5.6$ Hz, 2H), 3.88 (s, 2H), 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). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 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 $\text{C}_{17}\text{H}_{24}\text{N}_3\text{O}_3^+[\text{M}+\text{H}]^+$ 318.1812 found 318.1811.



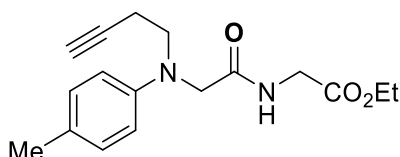
ethyl *N*-(4-chlorobutyl)-*N*-(*p*-tolyl)glycylglycinate(25) White solid was obtained in 53% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.32 – 7.23 (m, 2H), 7.18 (m, 2H), 7.04 (dd, $J = 10.7, 8.3$ Hz, 3H), 6.67 – 6.52 (m, 2H), 4.16 (q, $J = 7.2$ Hz, 2H), 4.00 (d, $J = 5.7$ Hz, 2H), 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) δ 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 $\text{C}_{17}\text{H}_{26}\text{ClN}_2\text{O}_3^+[\text{M}+\text{H}]^+$ 341.1626 found 341.1628.



ethyl *N*-(4-(1,3-dioxisoindolin-2-yl)butyl)-*N*-(*p*-tolyl)glycylglycinate (26). $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 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) δ 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 $\text{C}_{22}\text{H}_{24}\text{N}_3\text{O}_5^+[\text{M}+\text{H}]^+$ 407.1710 found 407.1709.

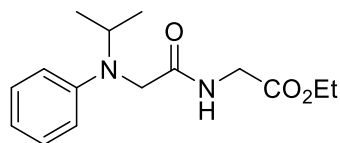


ethyl *N*-(pent-4-en-1-yl)-*N*-(*p*-tolyl)glycylglycinate (27). White solid was obtained in 75% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.13 – 6.96 (m, 3H), 6.70 – 6.60 (m, 2H), 5.82 (m, 1H), 5.09 – 4.95 (m, 2H), 4.17 (q, $J = 7.1$ Hz, 2H), 4.02 (d, $J = 5.6$ Hz, 2H), 3.87 (s, 2H), 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) δ 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 $\text{C}_{18}\text{H}_{27}\text{N}_2\text{O}_3^+[\text{M}+\text{H}]^+$ 319.2016 found 319.2018.

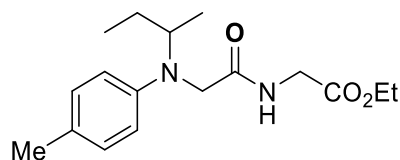


ethyl *N*-(but-3-yn-1-yl)-*N*-(*p*-tolyl)glycylglycinate (28). White solid was obtained in 71% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.15 (t, $J = 5.7$ Hz, 1H), 7.08 (d, $J = 8.4$ Hz, 2H), 6.69 (d, $J = 8.6$ Hz, 2H), 4.17 (q, $J = 7.2$ Hz, 2H), 4.01 (d, $J = 5.7$ Hz, 2H), 3.94 (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

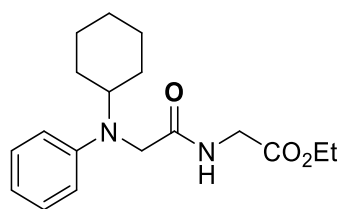
MHz, CDCl₃) δ 170.95, 169.53, 145.07, 130.17, 128.76, 114.21, 81.85, 70.51, 61.54, 57.18, 51.57, 41.07, 20.38, 17.18, 14.22. HRMS (ESI) calculated for C₁₃H₁₇N₂O₃⁺[M+H]⁺ 303.1703 found 303.1708.



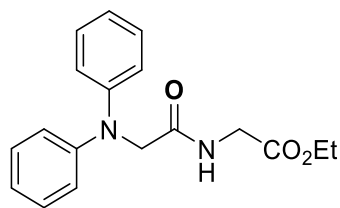
ethyl *N*-isopropyl-*N*-phenylglycylglycinate (29). White solid was obtained in 79% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.23 (m, 2H), 7.17 (t, *J* = 5.9 Hz, 1H), 6.87 – 6.75 (m, 3H), 4.17 (p, *J* = 6.8 Hz, 3H), 4.04 (d, *J* = 5.8 Hz, 2H), 3.78 (s, 2H), 1.32 – 1.18 (m, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 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 C₁₅H₂₃N₂O₃⁺[M+H]⁺ 279.1703 found 279.1701.



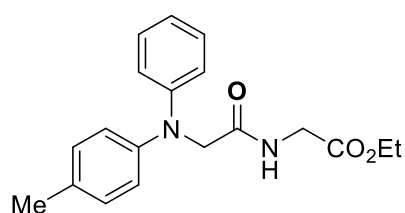
ethyl *N*-(*sec*-butyl)-*N*-(*p*-tolyl)glycylglycinate (30). White solid was obtained in 67% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.14 (t, *J* = 5.6 Hz, 1H), 7.09 – 7.03 (m, 2H), 6.77 – 6.69 (m, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 4.00 (d, *J* = 5.7 Hz, 2H), 3.80 (dt, *J* = 8.1, 6.2 Hz, 1H), 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). ¹³C NMR (101 MHz, CDCl₃) δ 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 C₁₇H₂₇N₂O₃⁺[M+H]⁺ 307.2016 found 307.2018.



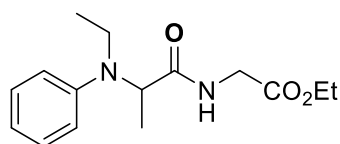
ethyl *N*-cyclohexyl-*N*-phenylglycylglycinate (31). White solid was obtained in 79% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.30 – 7.22 (m, 2H), 7.14 (t, *J* = 5.8 Hz, 1H), 6.86 – 6.72 (m, 3H), 4.16 (q, *J* = 7.1 Hz, 2H), 4.03 (d, *J* = 5.7 Hz, 2H), 3.82 (s, 2H), 3.69 (m, 1H), 1.98 – 1.82 (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). ¹³C NMR (101 MHz, CDCl₃) δ 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 C₁₈H₂₇N₂O₃⁺[M+H]⁺ 319.2016 found 319.2017.



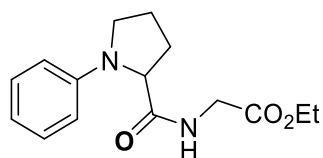
ethyl diphenylglycylglycinate (32). White solid was obtained in 50% isolated yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.35 – 7.28 (m, 4H), 7.11 (t, J = 5.5 Hz, 1H), 7.07 – 7.01 (m, 6H), 4.37 (s, 2H), 4.18 (q, J = 7.1 Hz, 2H), 4.05 (d, J = 5.4 Hz, 2H), 1.25 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 170.64, 169.55, 147.50, 129.78, 122.87, 120.83, 61.66, 57.52, 41.32, 14.23. HRMS (ESI) calculated for $\text{C}_{18}\text{H}_{21}\text{N}_2\text{O}_3^+[\text{M}+\text{H}]^+$ 313.1547 found 313.1545.



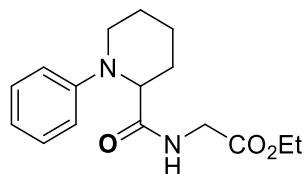
ethyl *N*-phenyl-*N*-(*p*-tolyl)glycylglycinate (33). White solid was obtained in 49% isolated yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.29 – 7.22 (m, 2H), 7.14 (t, J = 8.3 Hz, 3H), 7.05 – 6.99 (m, 2H), 6.98 – 6.89 (m, 3H), 4.33 (s, 2H), 4.17 (q, J = 7.1 Hz, 2H), 4.04 (d, J = 5.4 Hz, 2H), 2.33 (s, 3H), 1.25 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 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 $\text{C}_{19}\text{H}_{23}\text{N}_2\text{O}_3^+[\text{M}+\text{H}]^+$ 327.1703 found 327.1709.



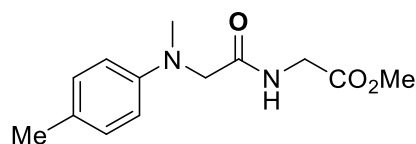
ethyl *N*-ethyl-*N*-phenylalanylglycinate (34). White solid was obtained in 43% isolated yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.30 – 7.23 (m, 2H), 7.16 (s, 1H), 6.89 – 6.80 (m, 3H), 4.27 – 4.07 (m, 4H), 3.97 (dd, J = 18.2, 5.2 Hz, 1H), 3.32 (dp, J = 21.8, 7.2 Hz, 2H), 1.42 (d, J = 7.1 Hz, 3H), 1.27 (t, J = 7.1 Hz, 3H), 1.20 (t, J = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 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 $\text{C}_{15}\text{H}_{23}\text{N}_2\text{O}_3^+[\text{M}+\text{H}]^+$ 279.1703 found 279.1707.



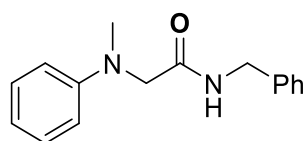
ethyl phenylprolylglycinate (35). White solid was obtained in 69% isolated yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.30 – 7.21 (m, 2H), 7.04 (t, $J = 5.8$ Hz, 1H), 6.81 (tt, $J = 7.4, 1.1$ Hz, 1H), 6.72 – 6.61 (m, 2H), 4.22 – 4.10 (m, 3H), 4.05 (dd, $J = 8.4, 3.2$ Hz, 1H), 3.82 (dd, $J = 18.1, 4.9$ 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 $\text{C}_{15}\text{H}_{21}\text{N}_2\text{O}_3^+[\text{M}+\text{H}]^+$ 277.1547 found 277.1547.



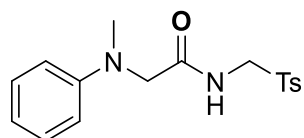
ethyl (1-phenylpiperidine-2-carbonyl)glycinate (36). White solid was obtained in 58% isolated yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.27 (t, $J = 7.9$ Hz, 2H), 7.01 (t, $J = 5.8$ Hz, 1H), 6.96 (d, $J = 8.1$ Hz, 2H), 6.87 (t, $J = 7.3$ Hz, 1H), 4.24 – 4.05 (m, 4H), 3.79 (dd, $J = 18.2, 4.8$ Hz, 1H), 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 $\text{C}_{16}\text{H}_{23}\text{N}_2\text{O}_3^+[\text{M}+\text{H}]^+$ 291.1703 found 291.1704.



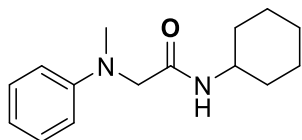
methyl N-methyl-N-(*p*-tolyl)glycylglycinate (37). White solid was obtained in 91% isolated yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.19 (t, $J = 5.8$ Hz, 1H), 7.11 (d, $J = 8.3$ Hz, 2H), 6.72 (d, $J = 8.7$ Hz, 1H), 4.09 (d, $J = 5.8$ Hz, 2H), 3.88 (s, 2H), 3.76 (s, 3H), 3.03 (s, 3H), 2.30 (s, 3H). ^{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 $\text{C}_{16}\text{H}_{23}\text{N}_2\text{O}_3^+[\text{M}+\text{H}]^+$ 251.1390 found 251.1392.



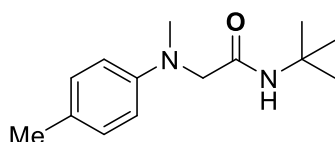
N-benzyl-2-(methyl(*p*-tolyl)amino)acetamide (38).³ White solid was obtained in 72% isolated yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.35 – 7.15 (m, 7H), 6.93 (s, 1H), 6.84 (td, $J = 7.3, 1.0$ Hz, 1H), 6.73 (dt, $J = 7.8, 1.1$ Hz, 2H), 4.48 (d, $J = 6.0$ Hz, 2H), 3.91 (s, 2H), 2.99 (s, 3H). ^{13}C 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.



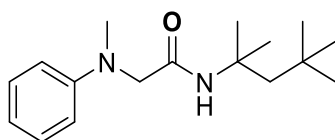
2-(methyl(phenyl)amino)-*N*-(tosylmethyl)acetamide (39).¹ White solid was obtained in 51% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.63 (d, J = 8.1 Hz, 2H), 7.33 (t, J = 6.9 Hz, 1H), 7.28 – 7.15 (m, 4H), 6.80 (t, J = 7.3 Hz, 1H), 6.58 (d, J = 8.1 Hz, 2H), 4.58 (d, J = 6.9 Hz, 2H), 3.66 (s, 2H), 2.90 (s, 3H), 2.37 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 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.



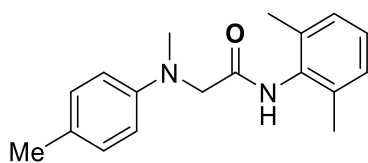
***N*-cyclohexyl-2-(methyl(phenyl)amino)acetamide (40).**¹ White solid was obtained in 81% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.33 – 7.22 (m, 2H), 6.84 (t, J = 7.3 Hz, 1H), 6.78 – 6.69 (m, 2H), 6.54 – 6.36 (m, 1H), 3.82 (m, 3H), 2.99 (s, 3H), 1.92 – 1.82 (m, 2H), 1.70 – 1.51 (m, 3H), 1.34 (m, 2H), 1.08 (m, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 169.34, 149.57, 129.45, 118.78, 113.37, 59.30, 47.93, 39.82, 33.13, 25.53, 24.88.



***N*-(*tert*-butyl)-2-(methyl(*p*-tolyl)amino)acetamide (41).**¹ White solid was obtained in 69% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 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). ¹³C NMR (101 MHz, CDCl₃) δ 169.84, 147.61, 129.88, 128.20, 113.75, 60.34, 50.95, 40.11, 28.81, 20.38.



2-(methyl(phenyl)amino)-*N*-(2,4,4-trimethylpentan-2-yl)acetamide (42). White solid was obtained in 75% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 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), 0.94 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 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 C₁₇H₂₉N₂O⁺[M+H]⁺ 277.2274 found 277.2274.

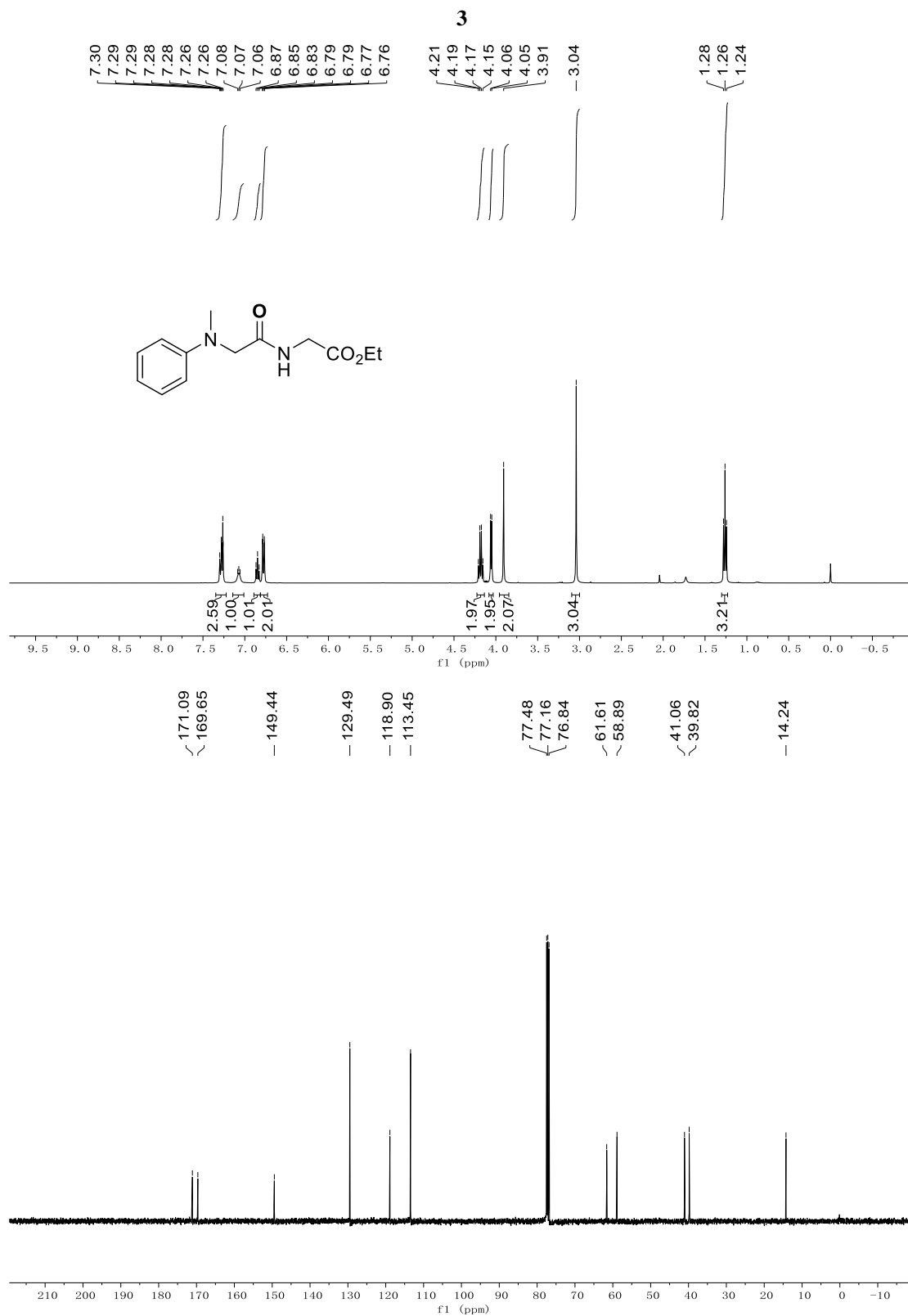


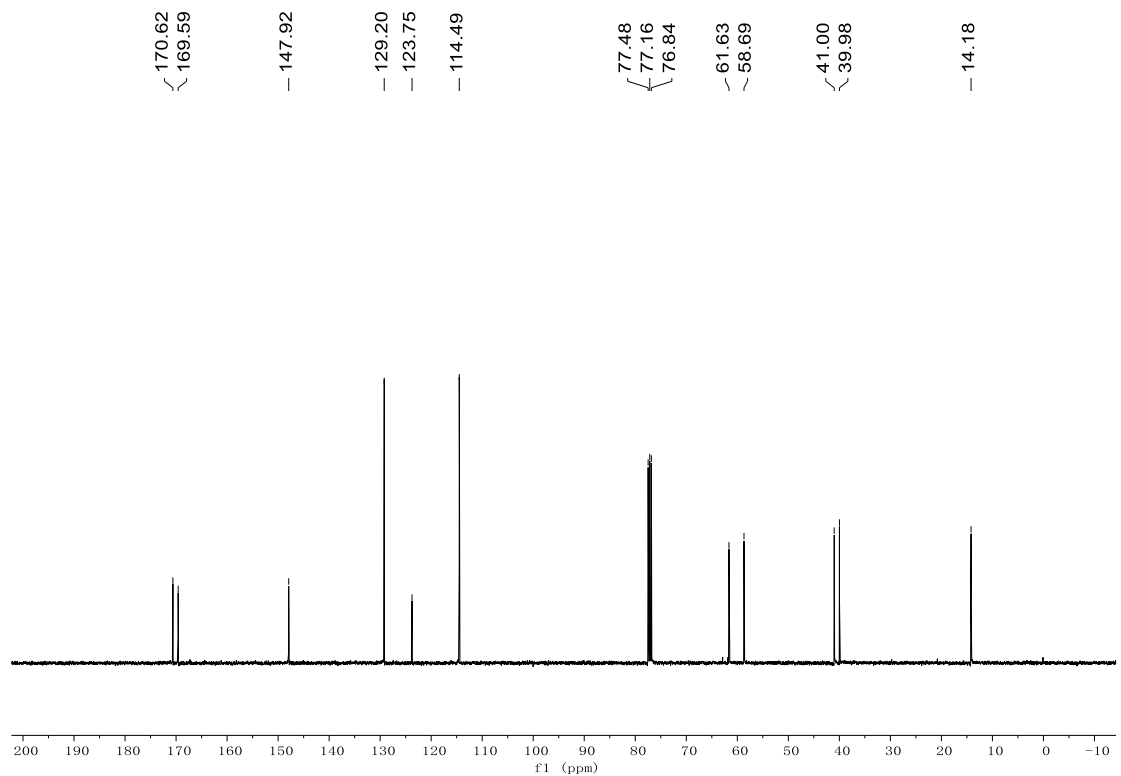
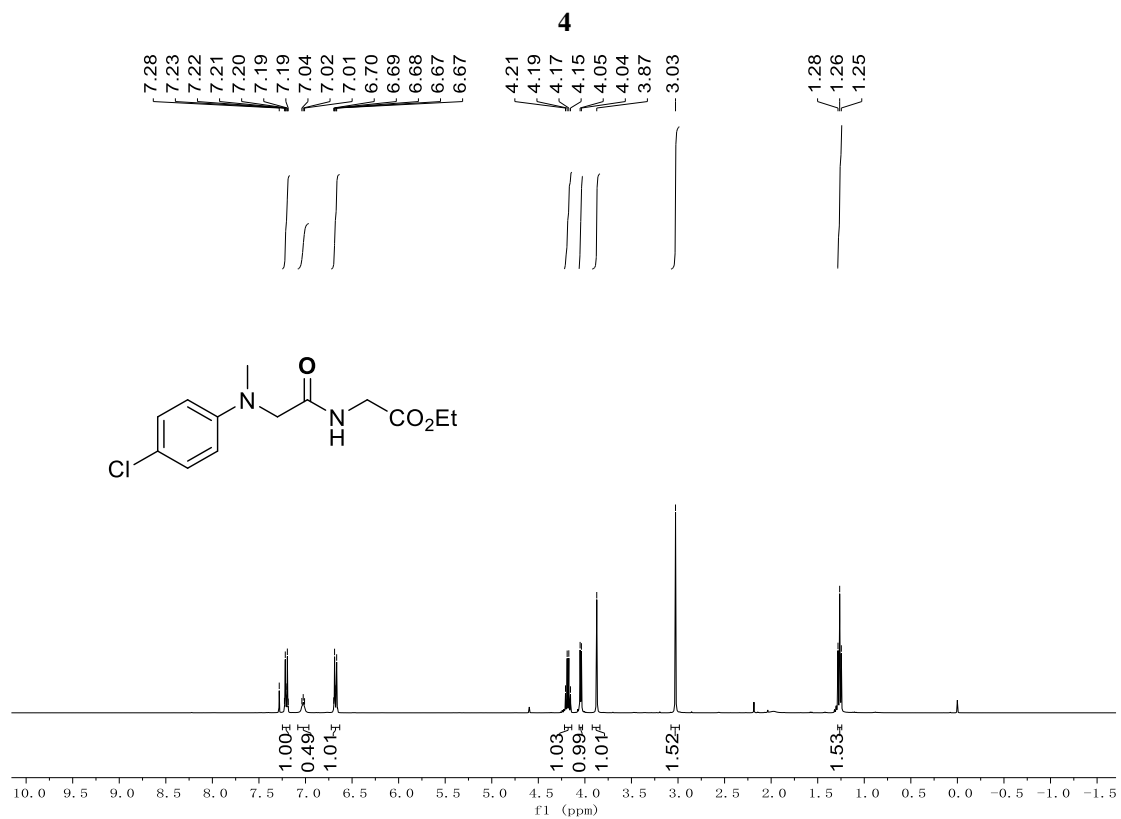
***N*-(2,6-dimethylphenyl)-2-(methyl(*p*-tolyl)amino)acetamide (43).** White solid was obtained in 33% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.21 (m, 3H), 7.14 (m, 2H), 6.76 – 6.64 (m, 3H),

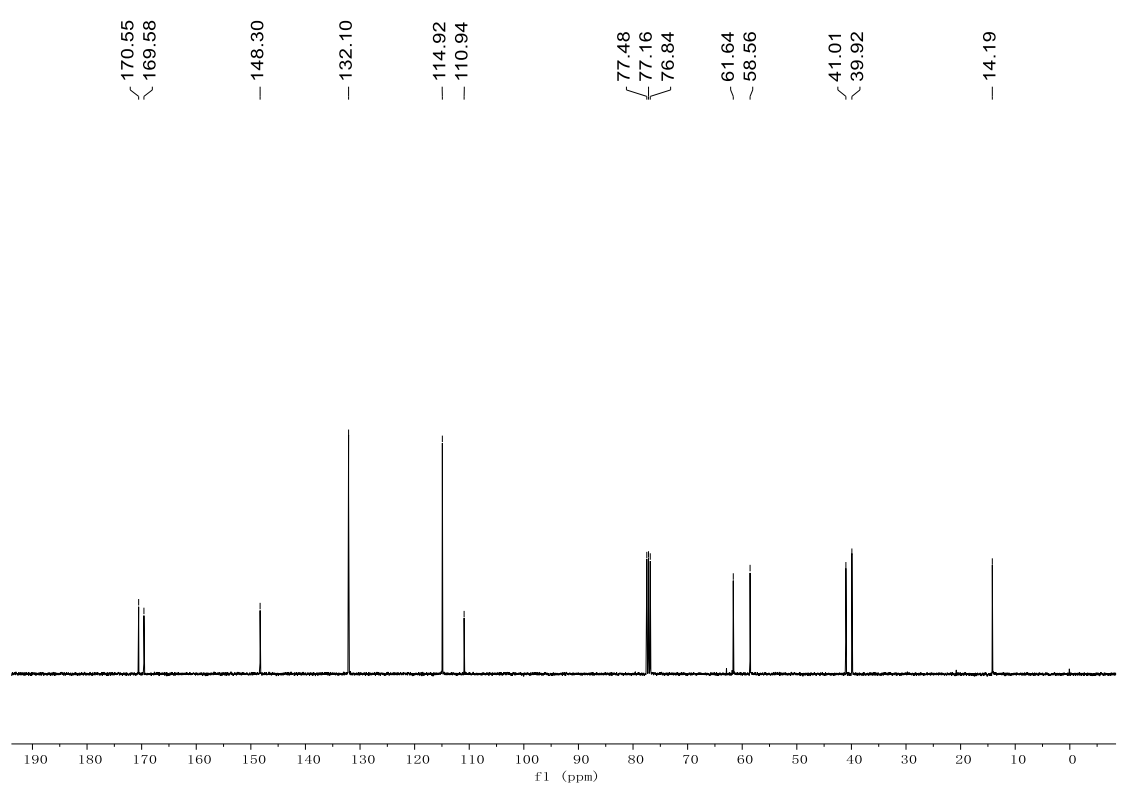
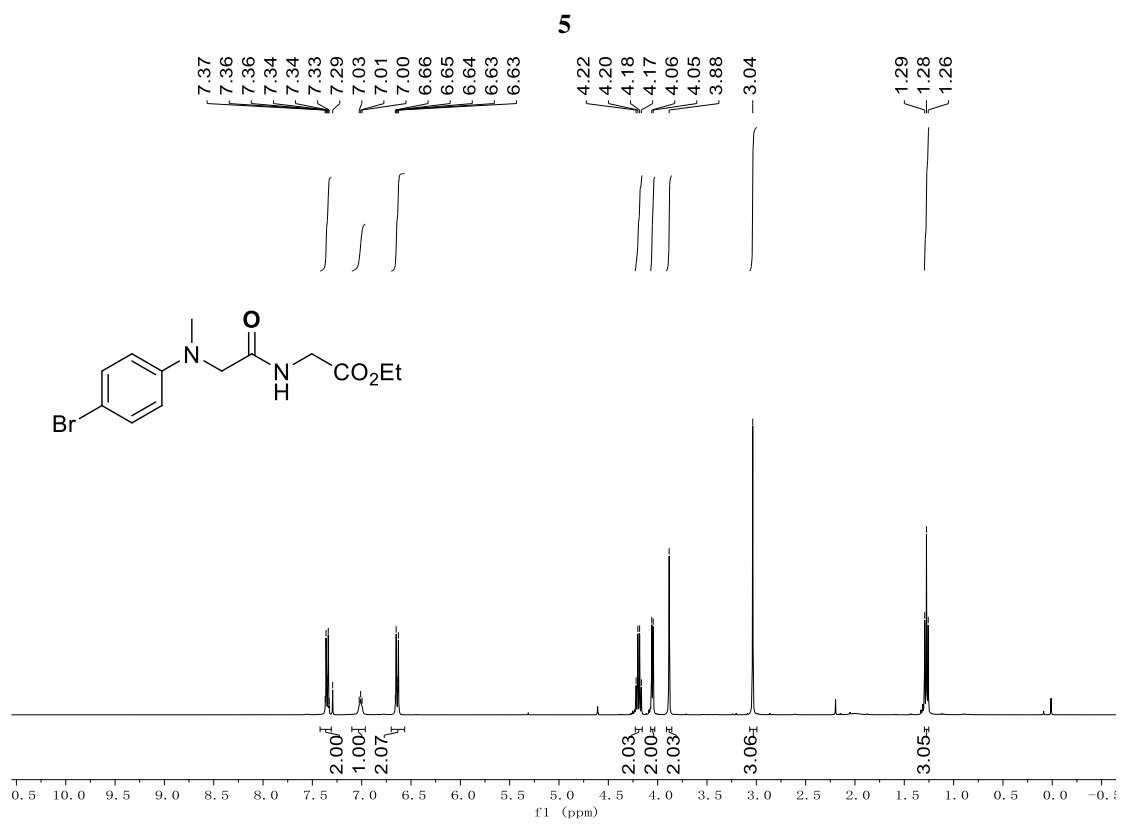
4.44 (s, 2H), 3.01 (s, 3H), 2.16 (m, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 173.10, 172.59, 149.12, 136.62, 135.67, 129.28, 129.24, 117.33, 112.36, 58.55, 39.52, 25.86, 18.09. HRMS (ESI) calculated for C₁₈H₂₃N₂O⁺[M+H]⁺ 283.1805 found 283.1804.

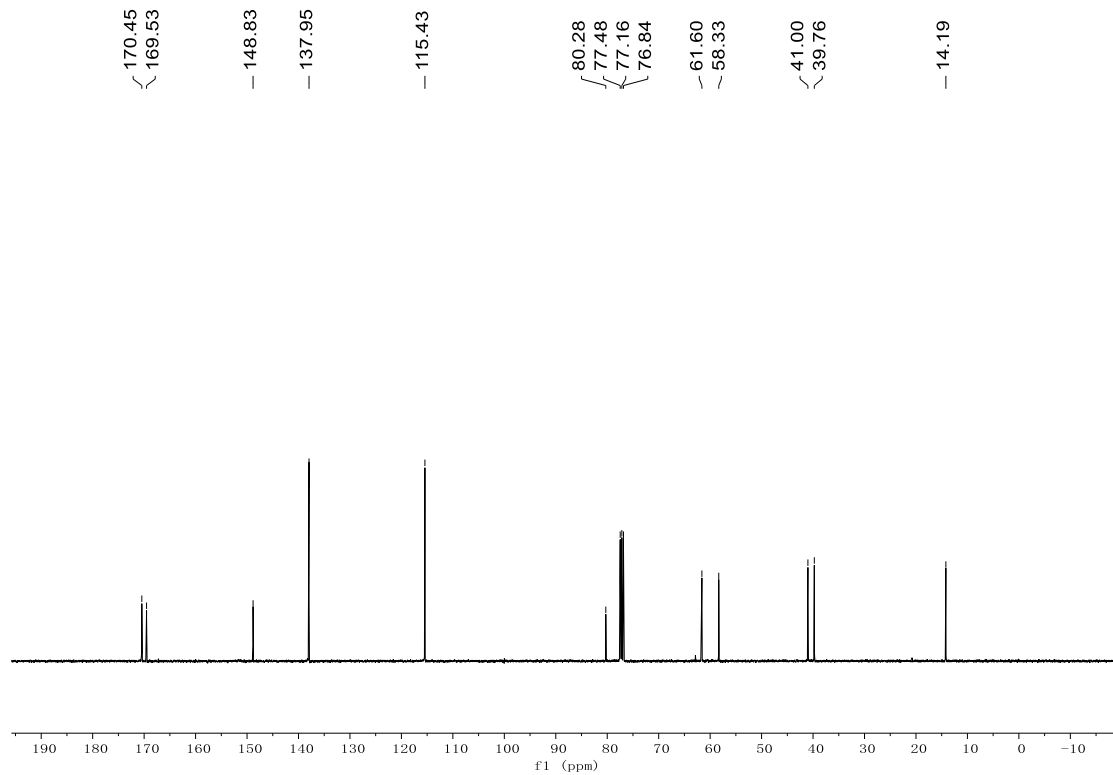
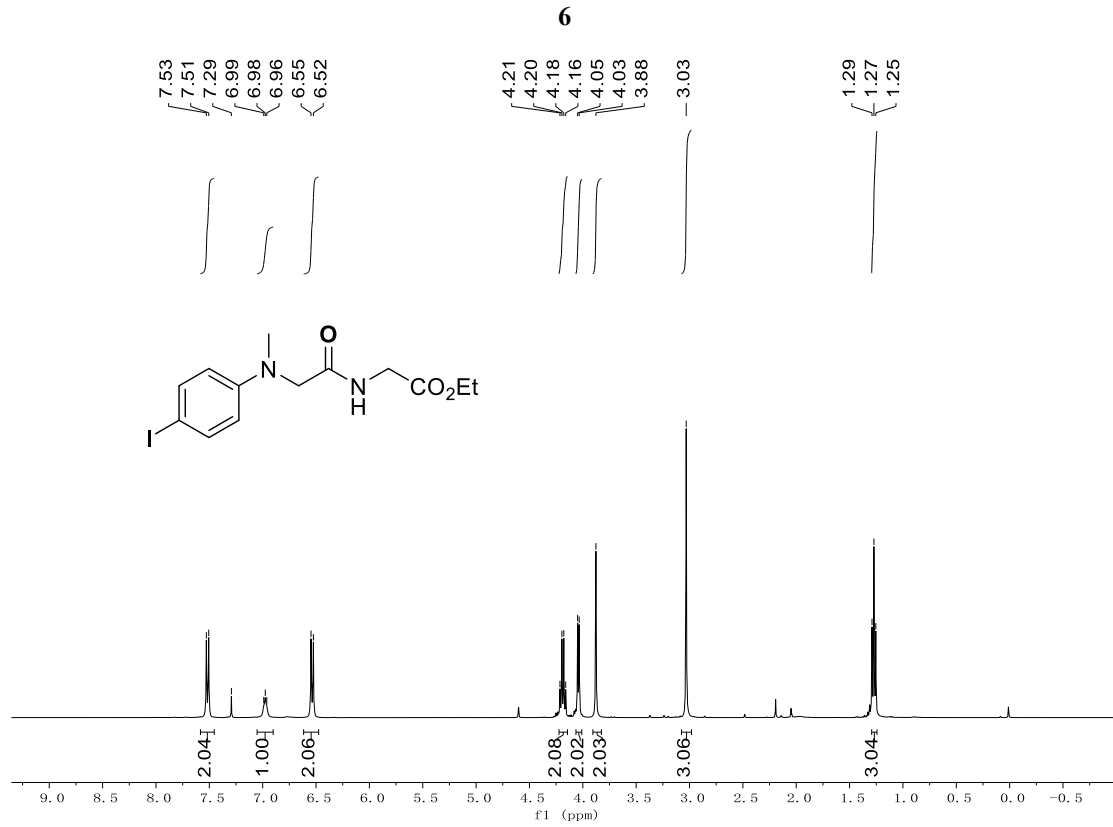
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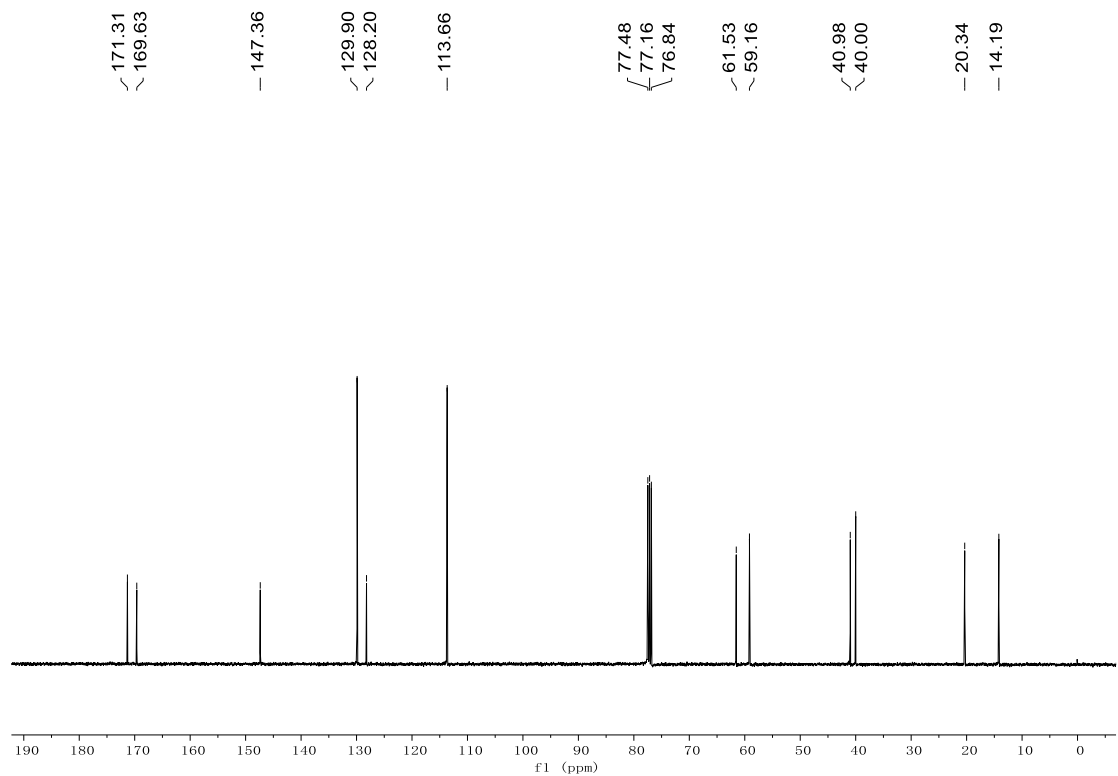
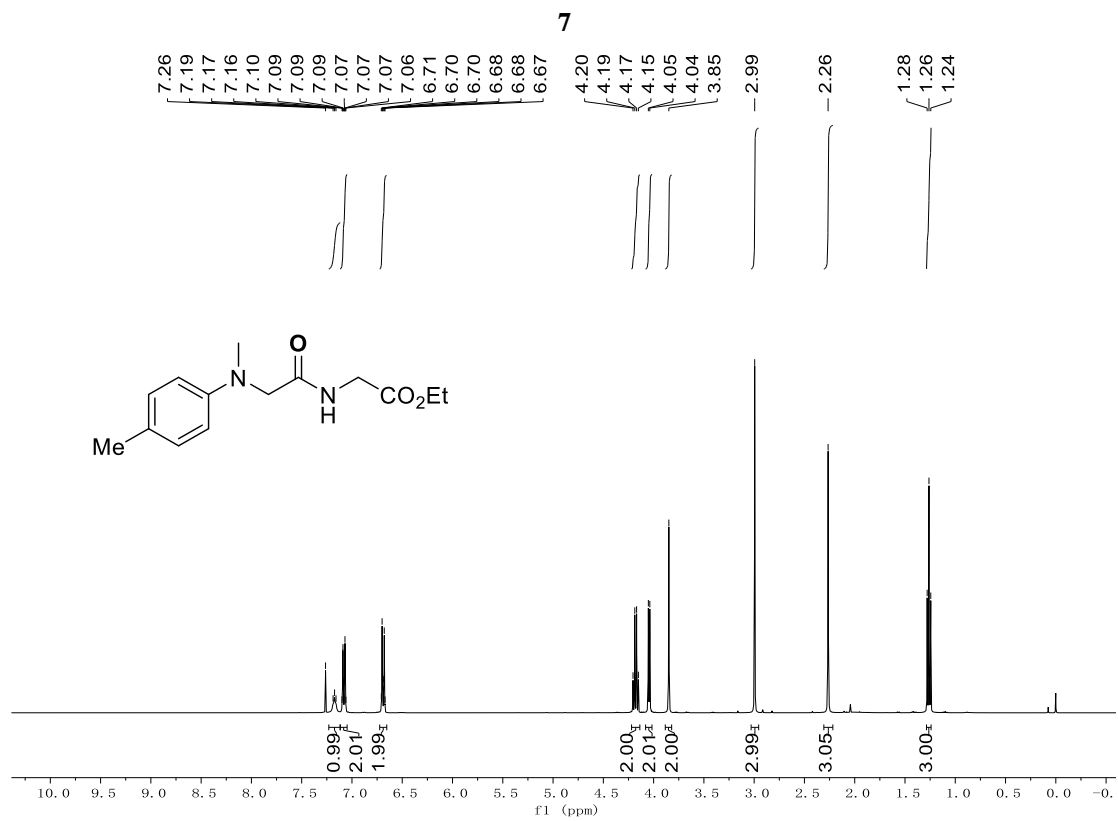
- (1) Guerrero, I.; San Segundo, M.; Correa, A., Iron-catalyzed C(sp³)-H functionalization of N,N-dimethylanilines with isocyanides. *Chem. Commun.* **2018**, *54*, 1627-1630.
- (2) Li, D.; Shen, X.; Lei, J., Metal-Free Iodine/TEMPO-Mediated Aerobic Oxidative Ugi-Type Multicomponent Reactions with Tertiary Amines. *J. Org. Chem.* **2020**, *85*, 2466-2475.
- (3) Chanthamath, S.; Thongjareun, S.; Shibatomi, K.; Iwasa, S., Ru(II)-Pheox catalyzed N-H insertion reaction of diazoacetamides: synthesis of N-substituted α -aminoamides. *Tetrahedron Lett.* **2012**, *53*, 4862-4865.

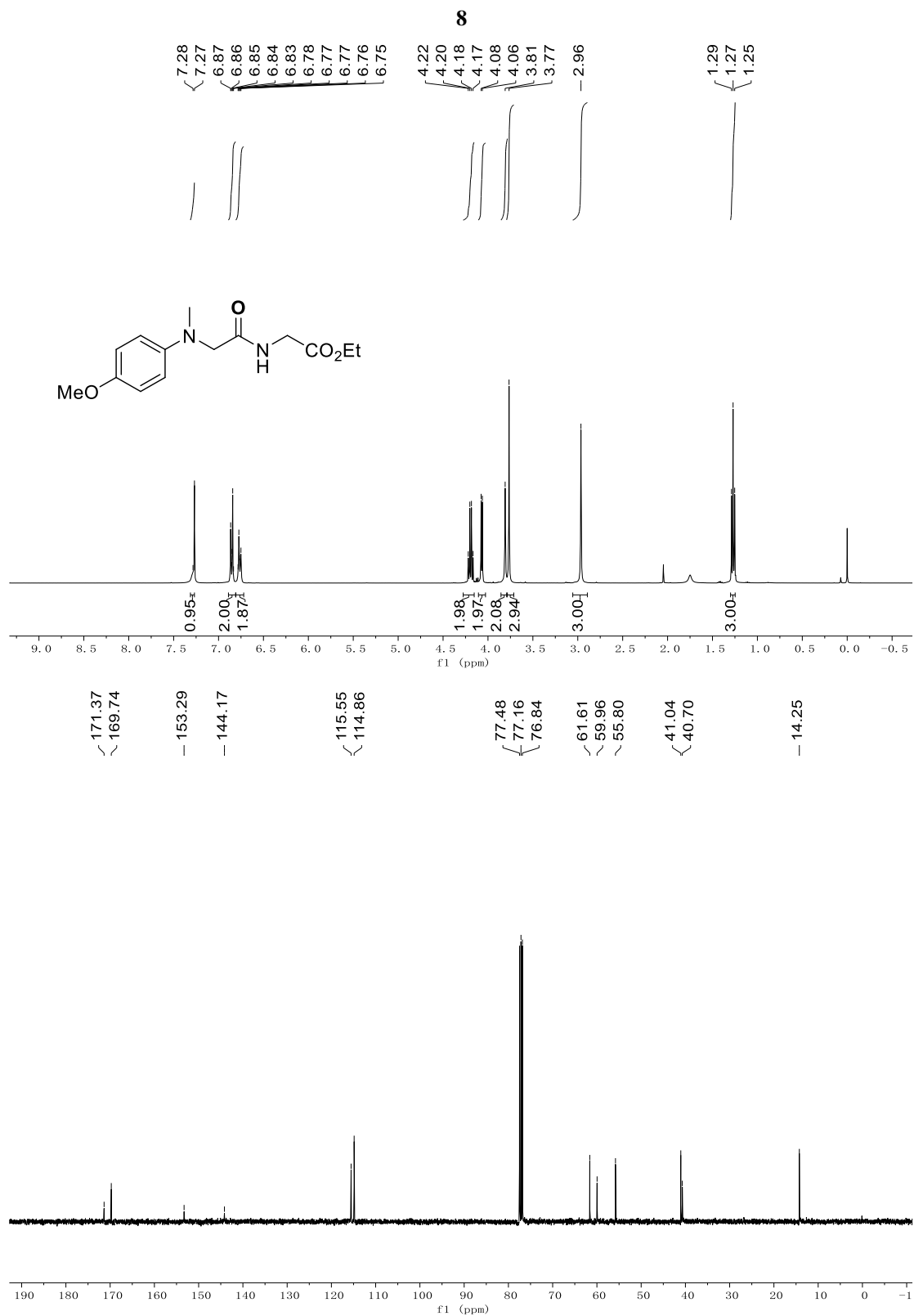


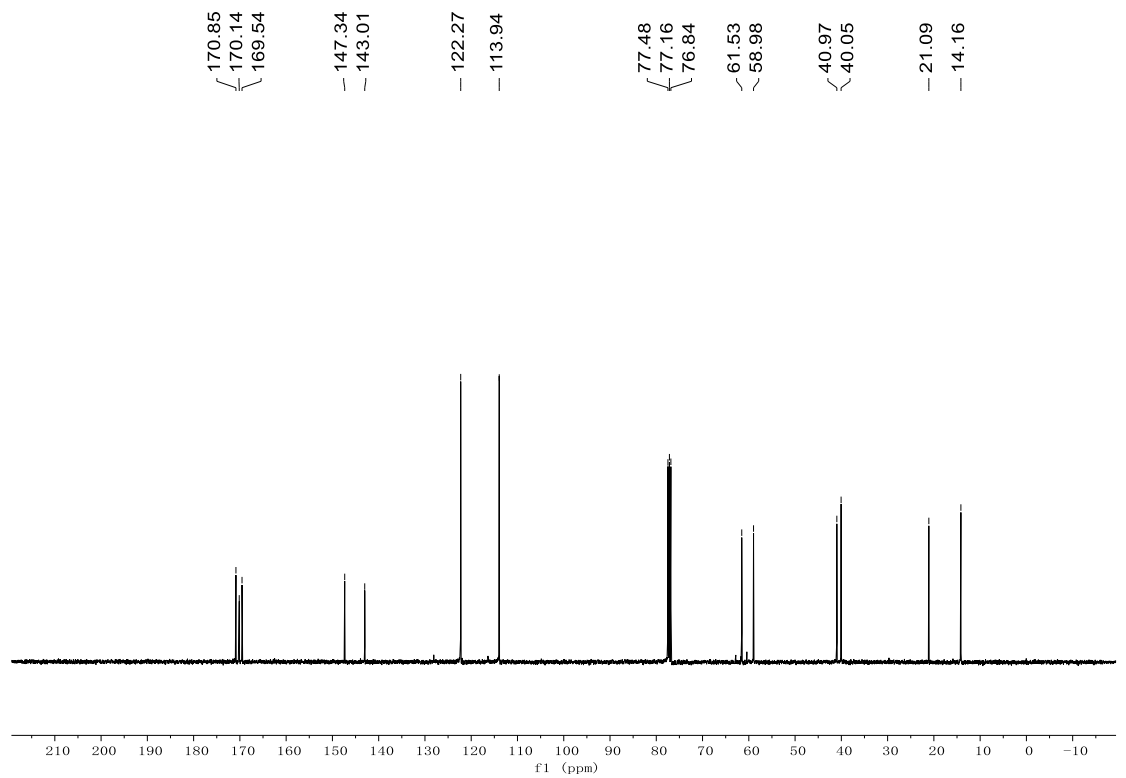
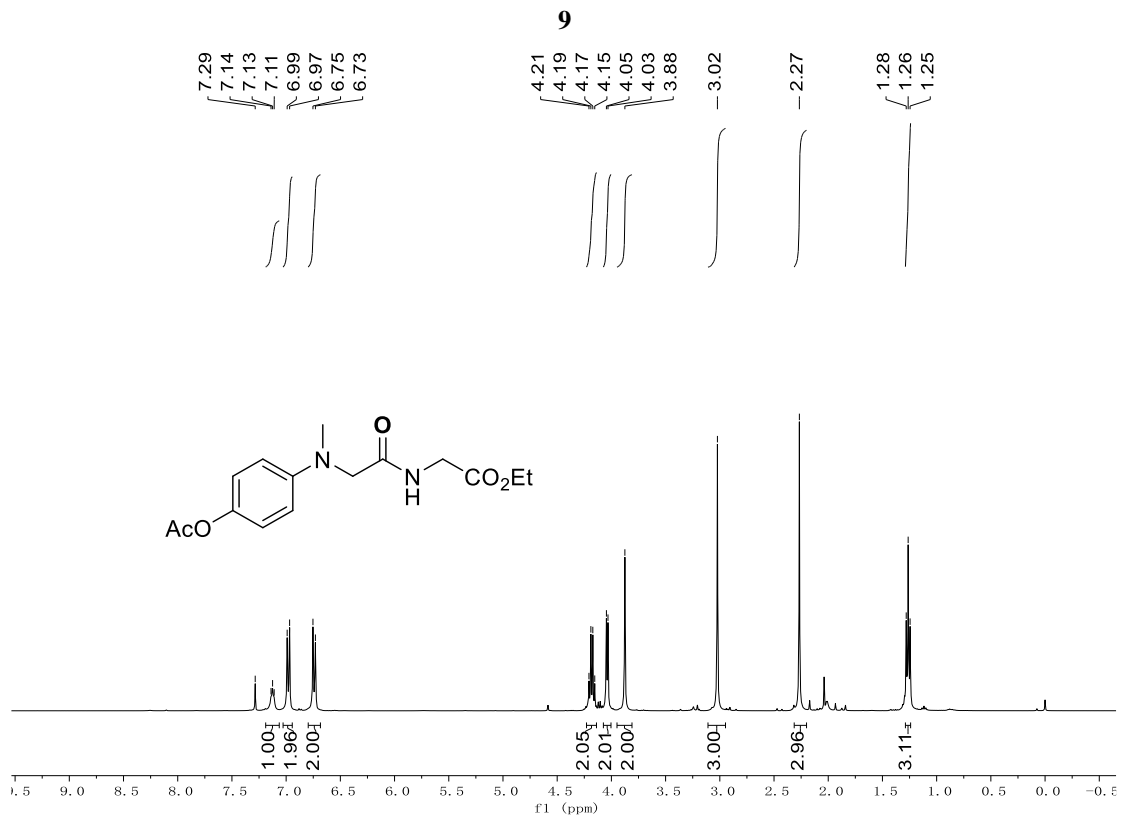


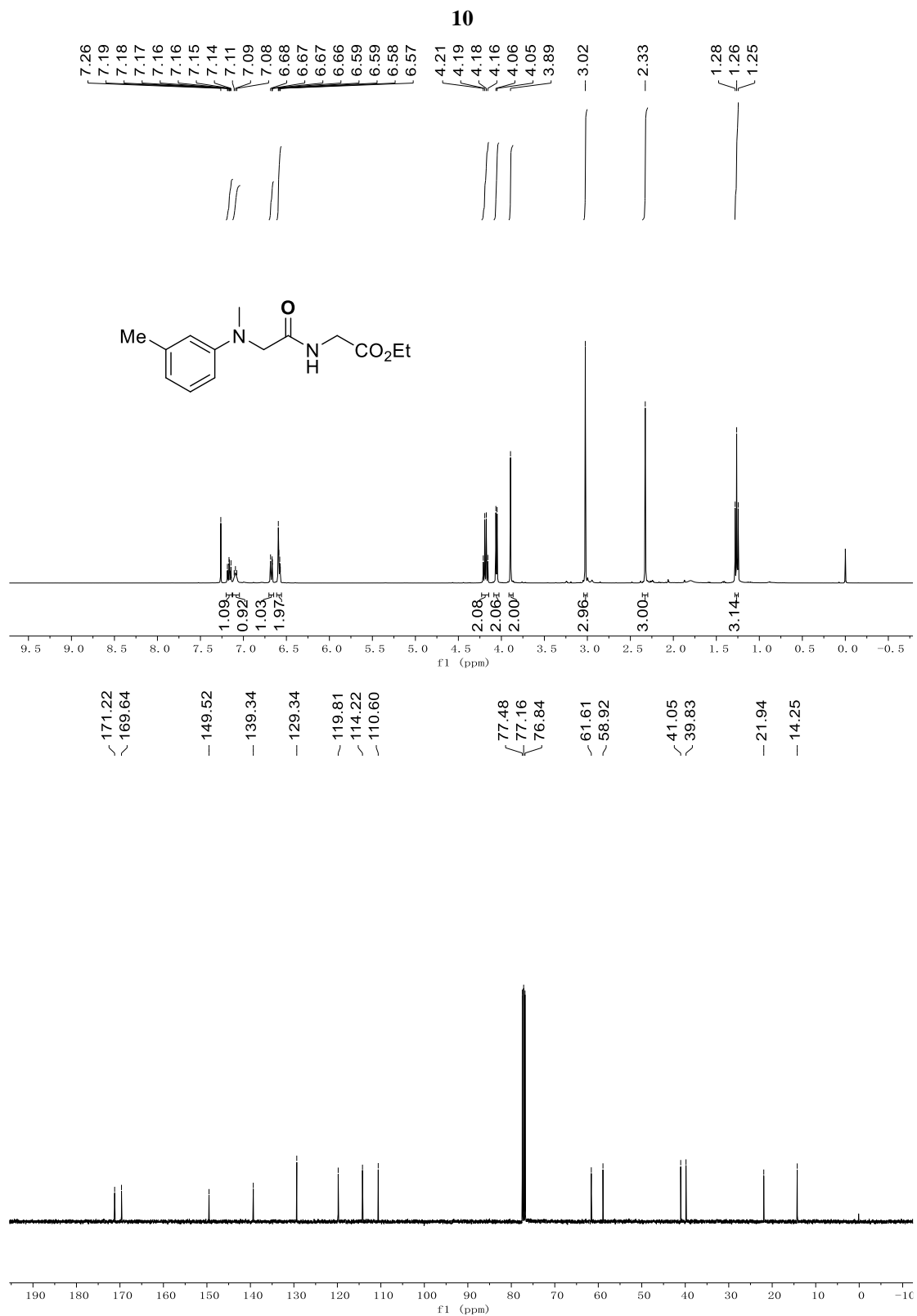




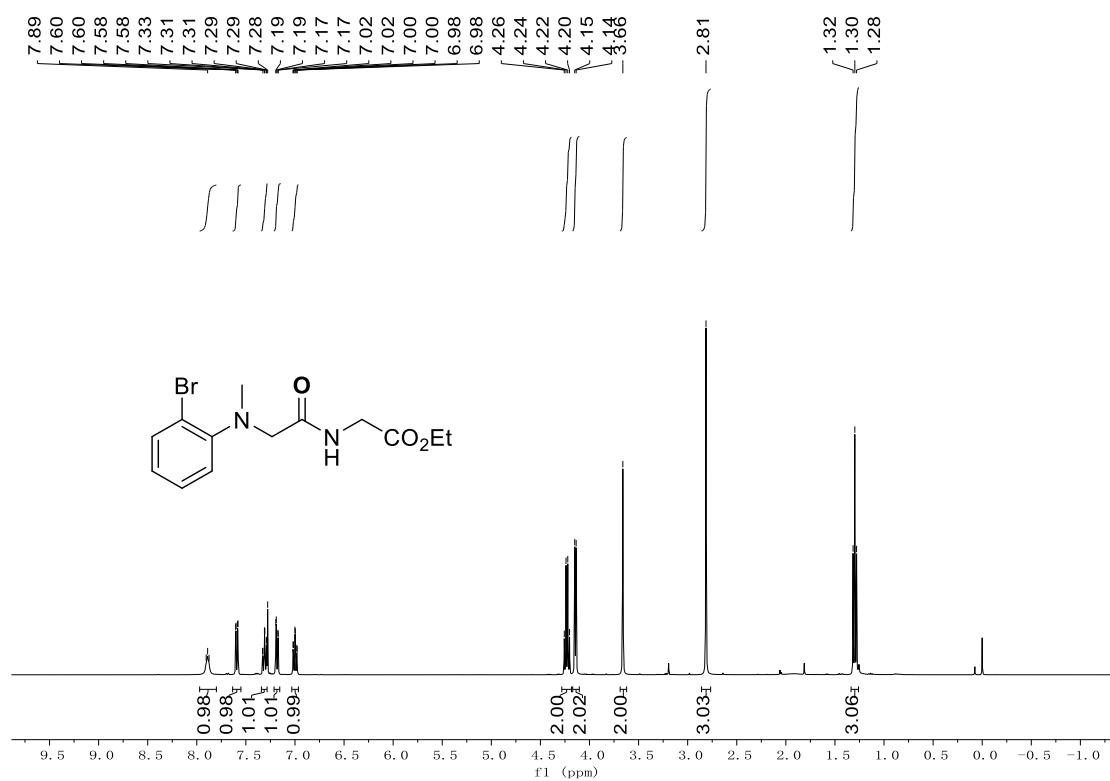




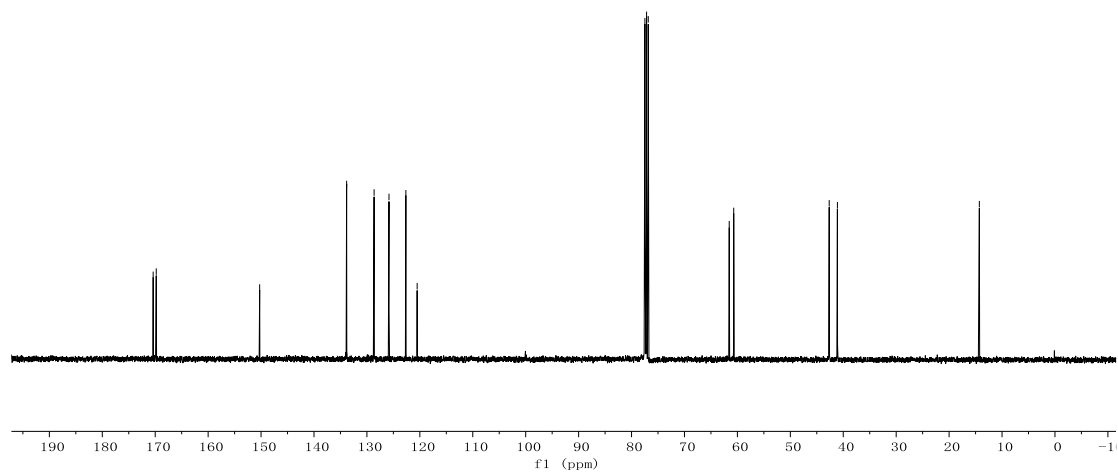




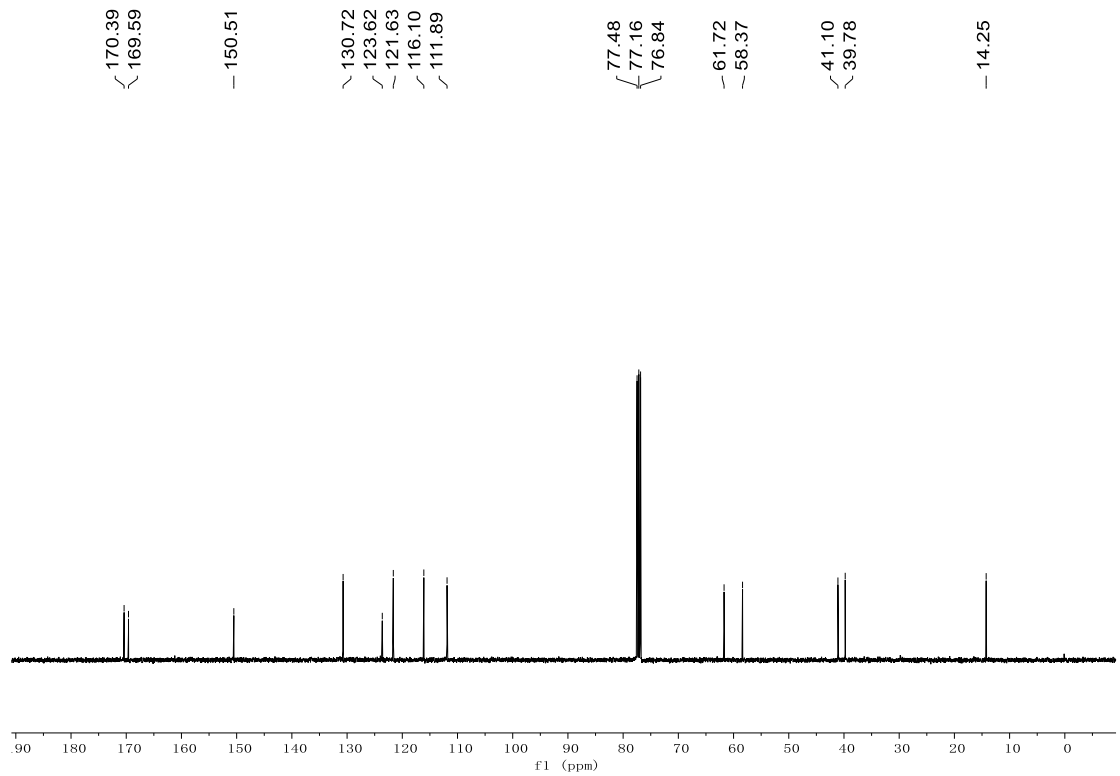
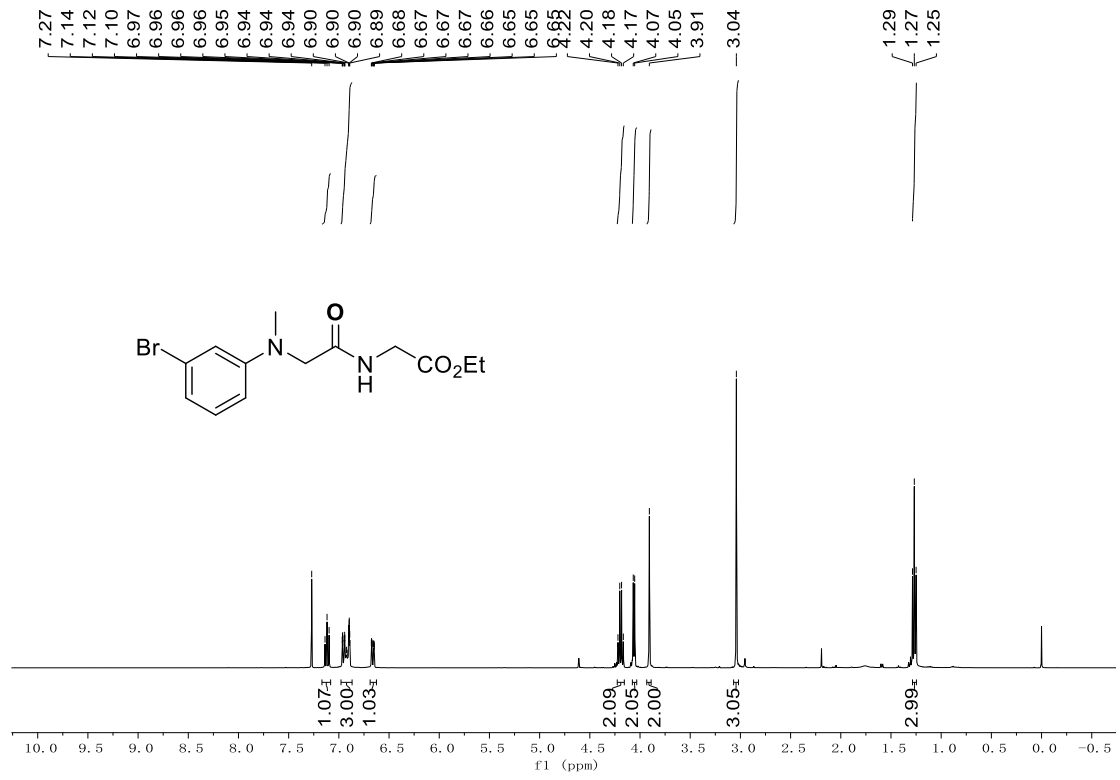
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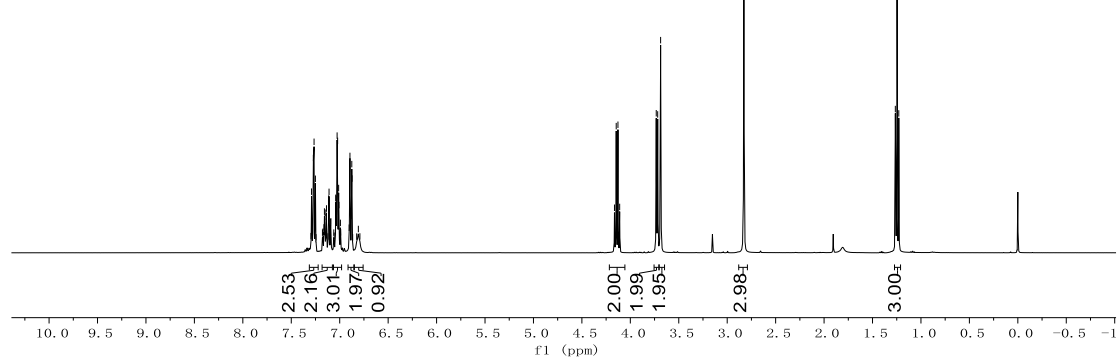
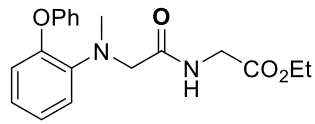
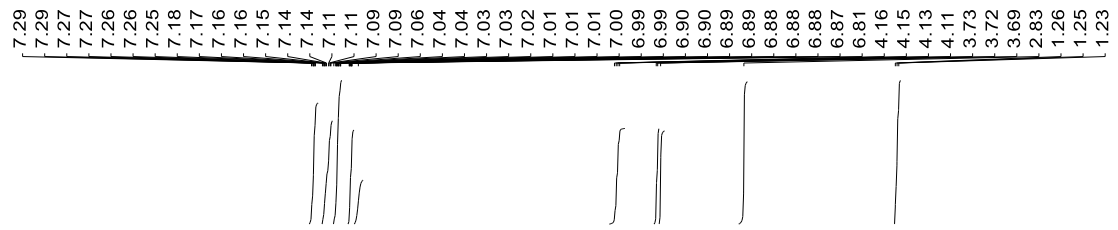
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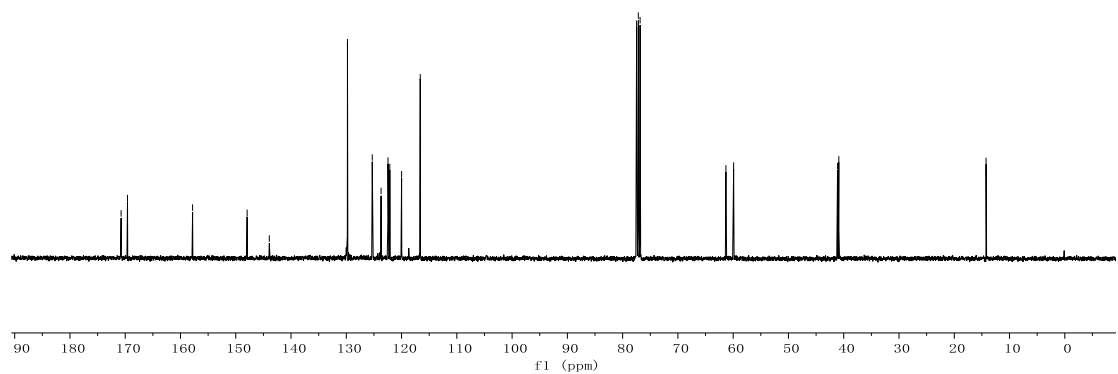
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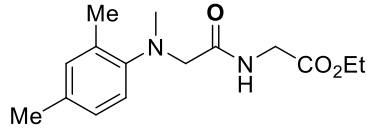
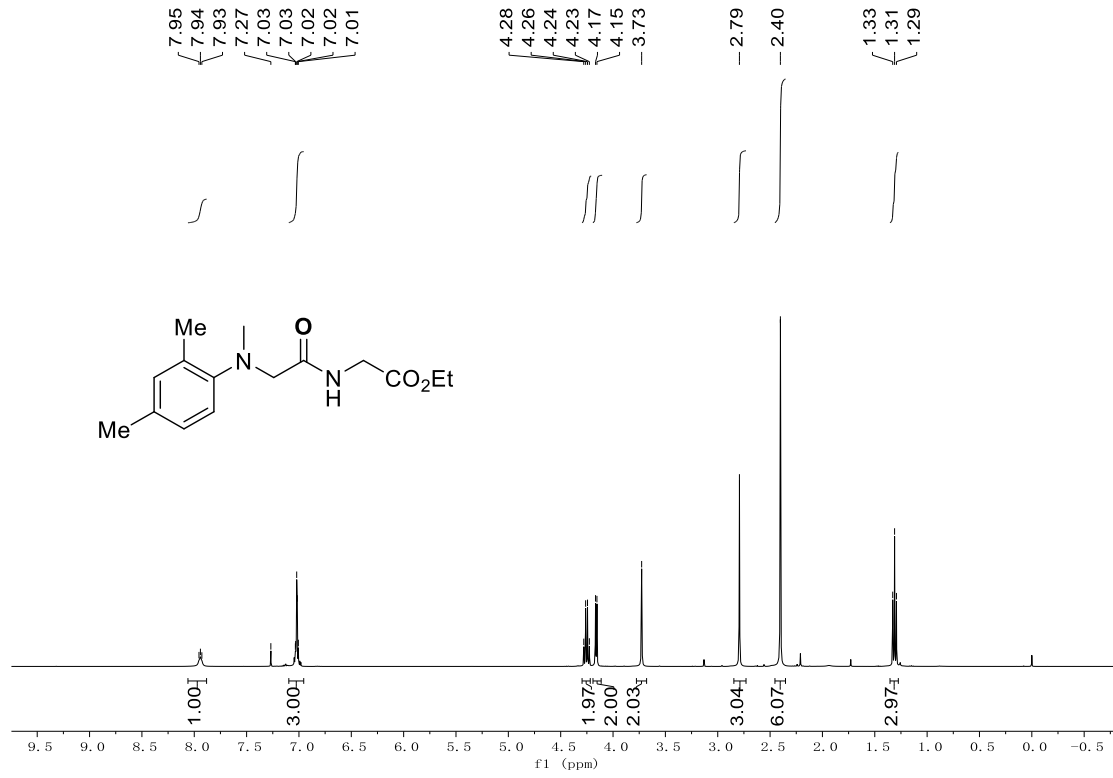
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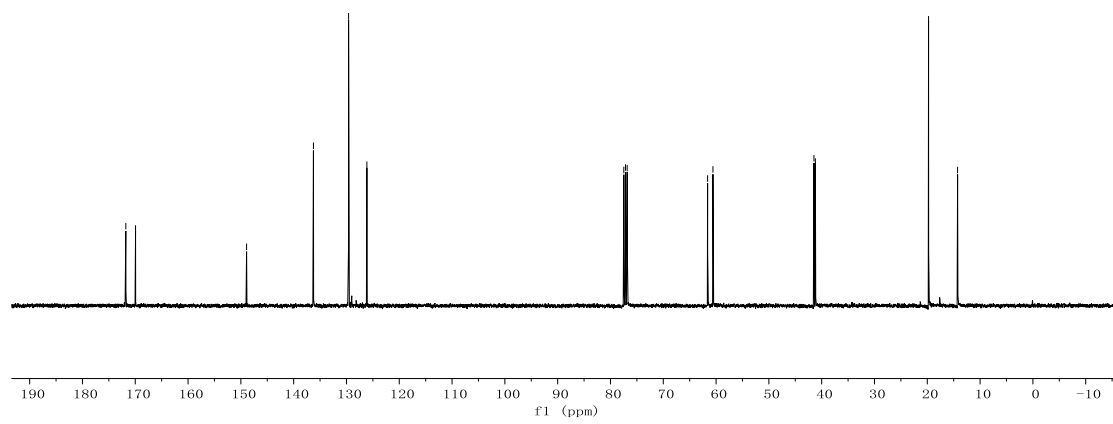
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- 14.25



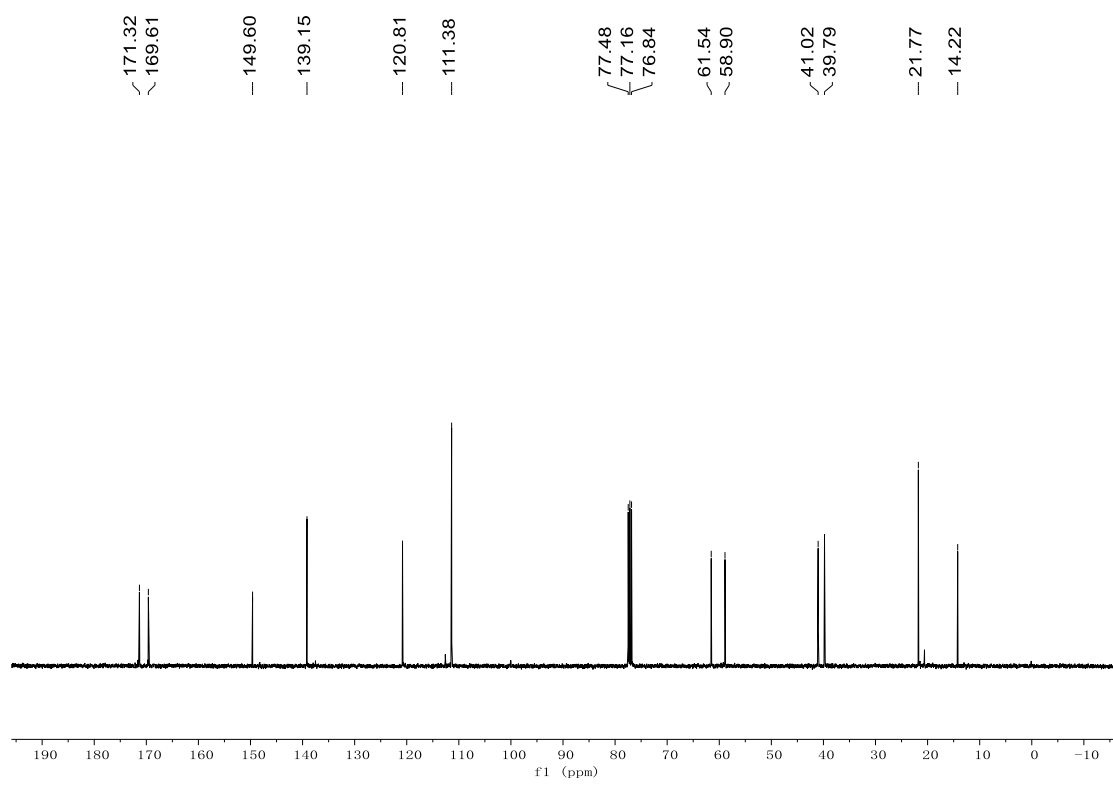
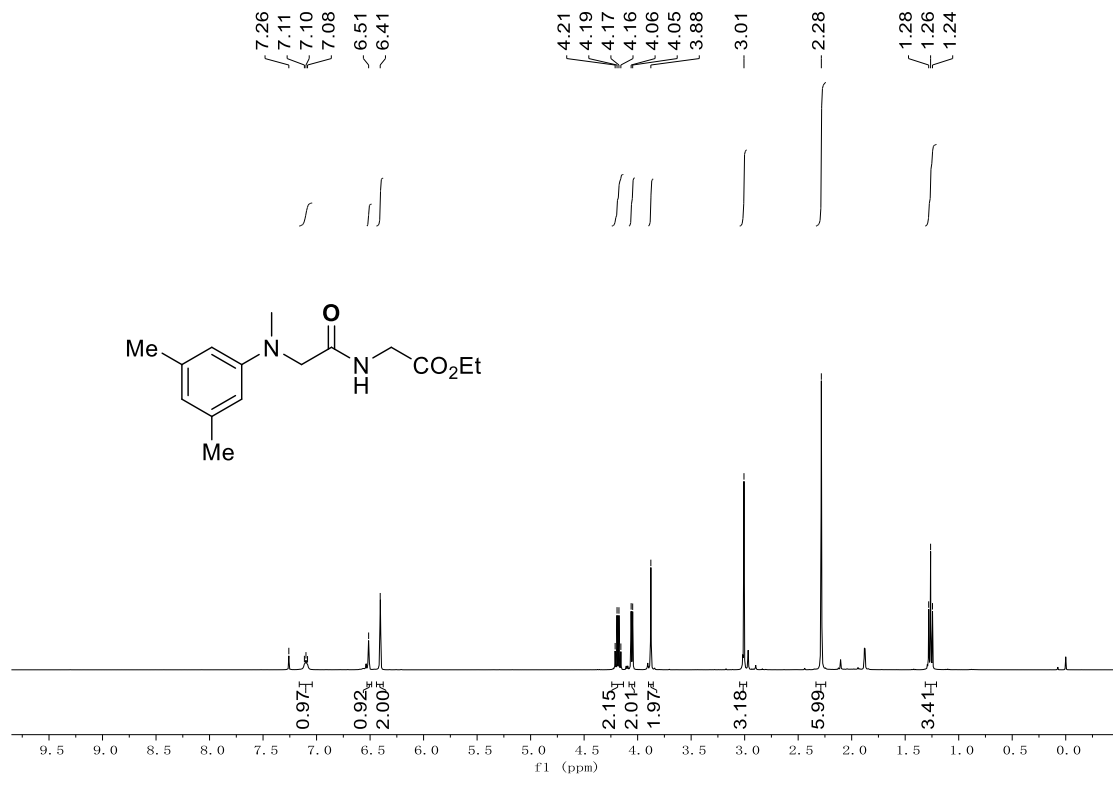
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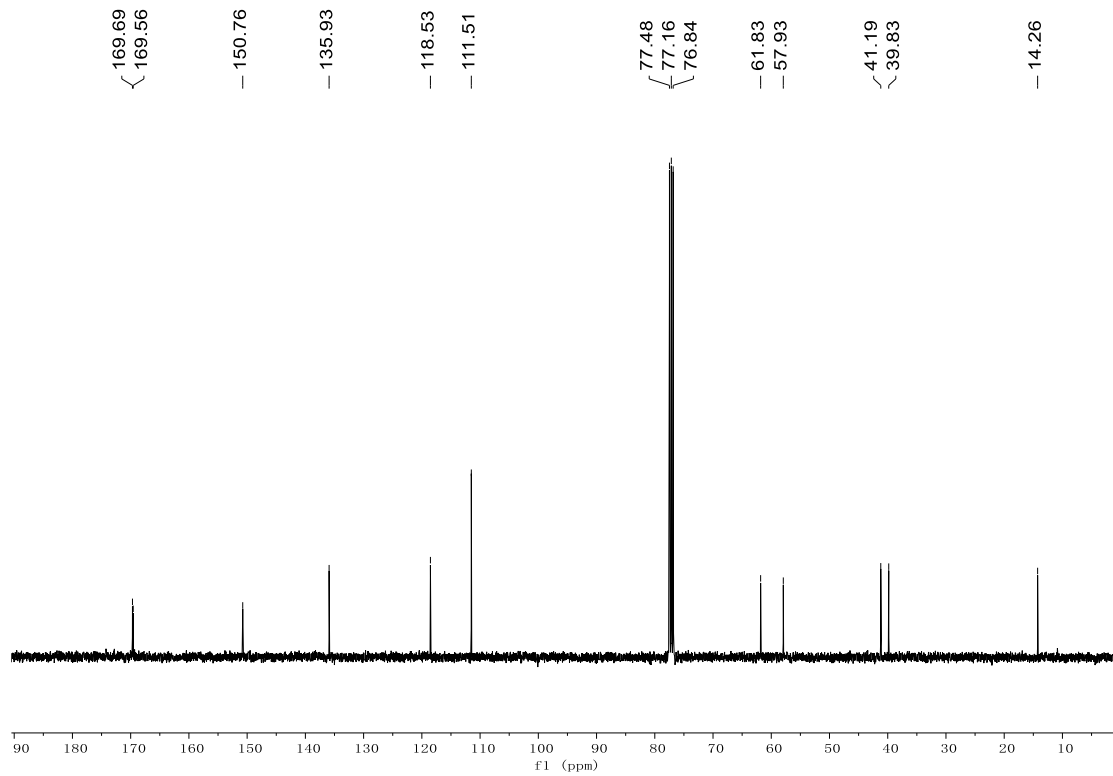
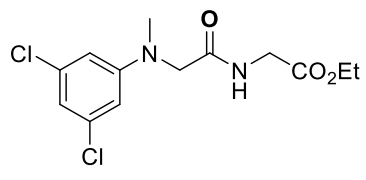
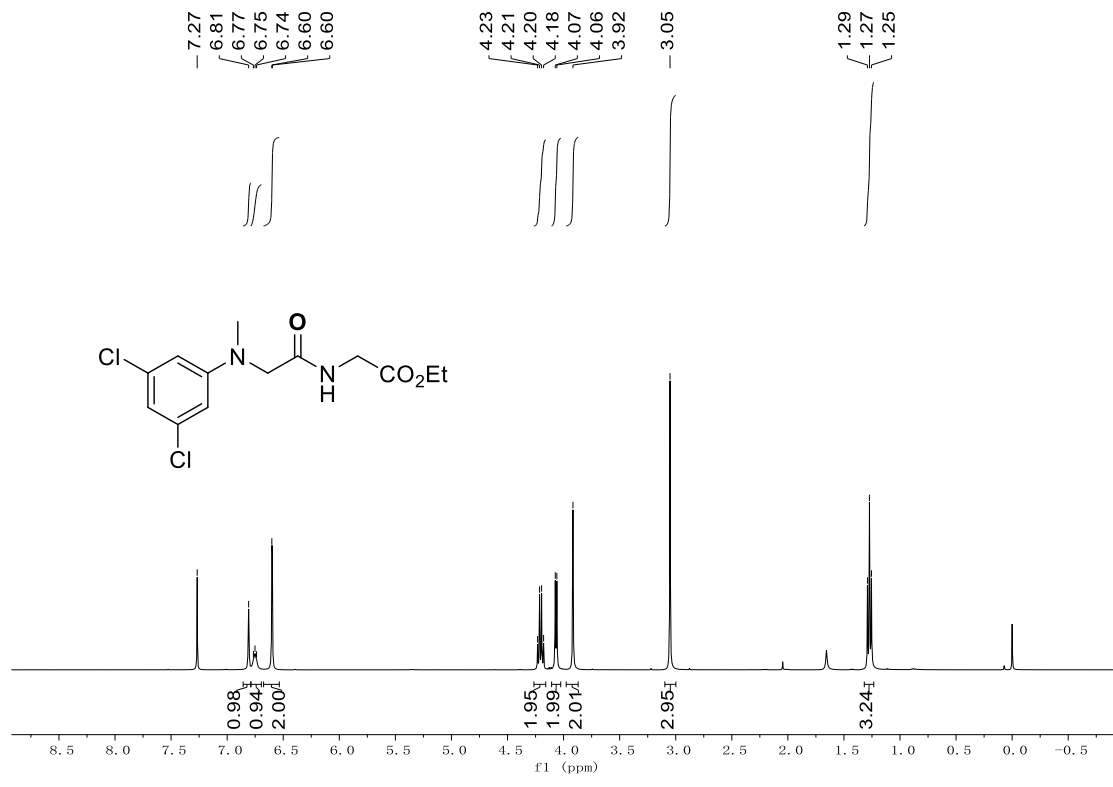
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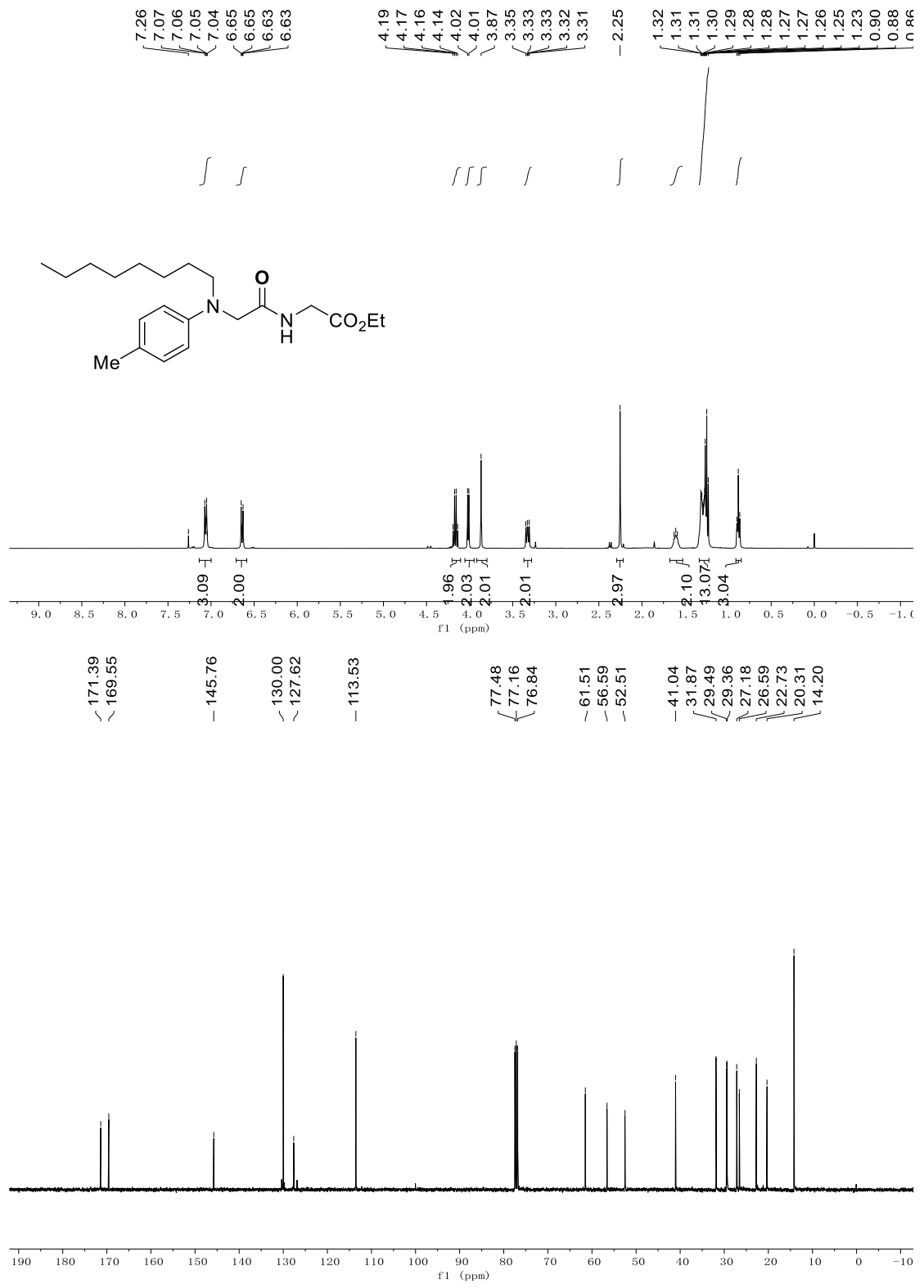
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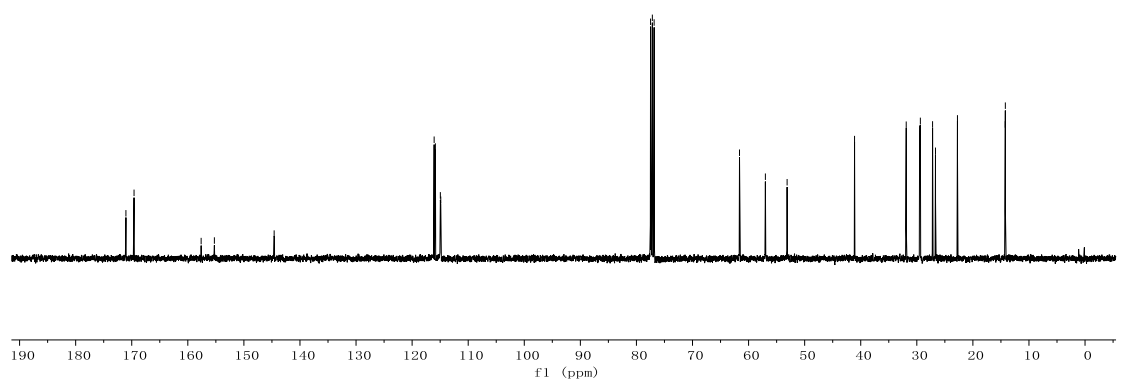
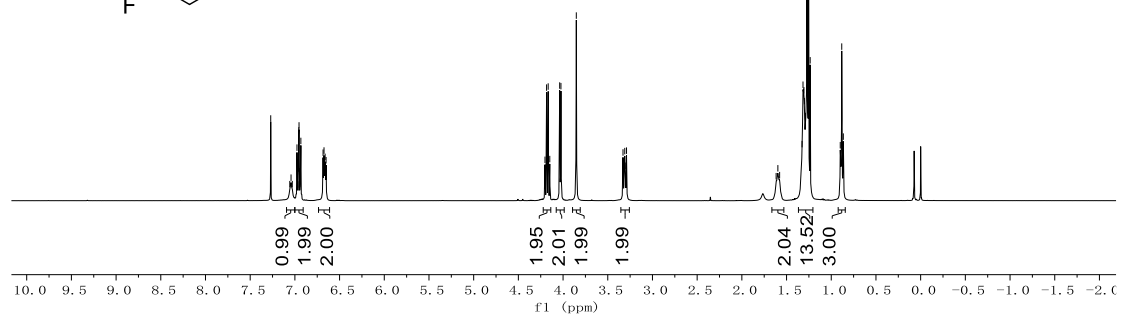
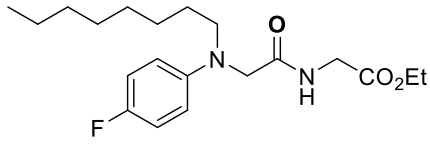
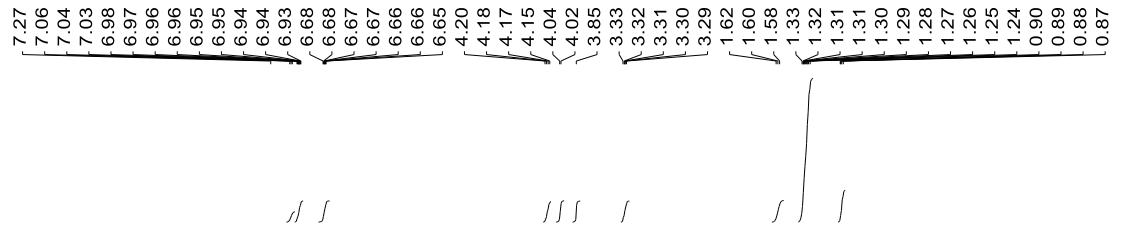
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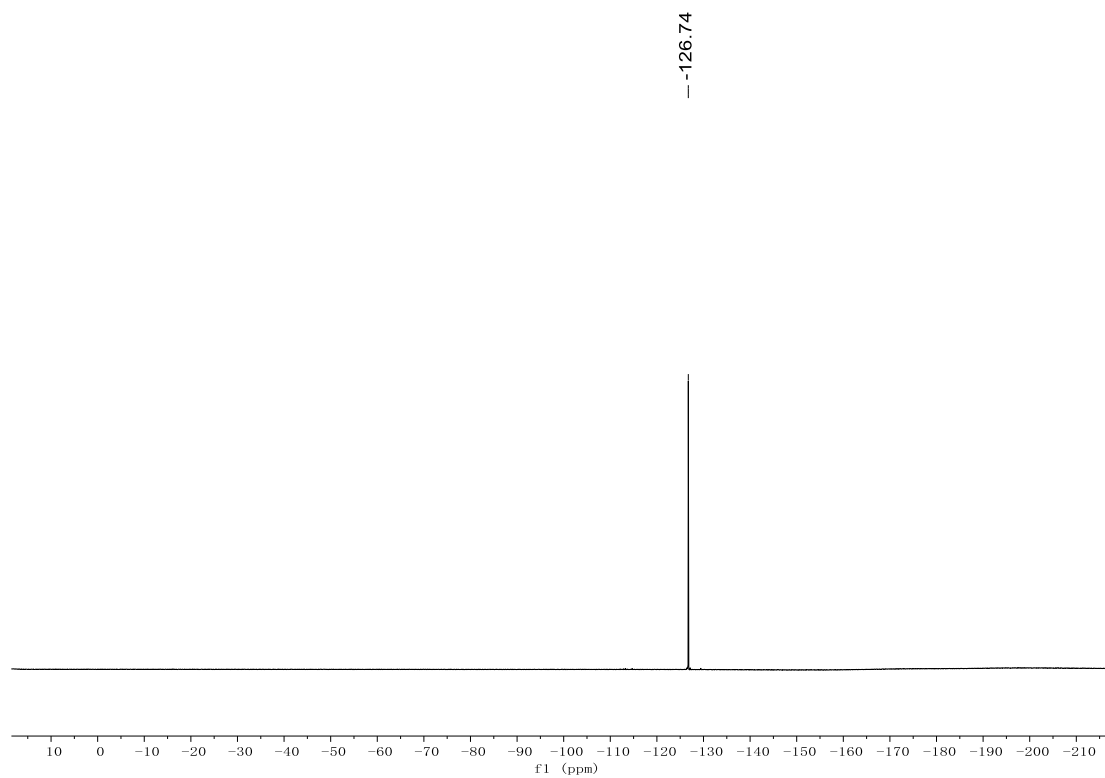


17

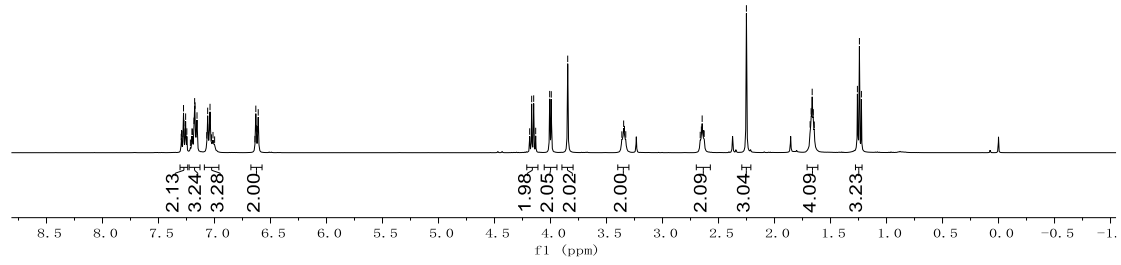
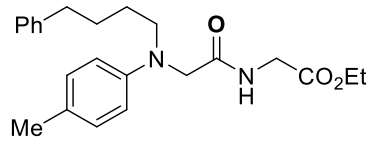
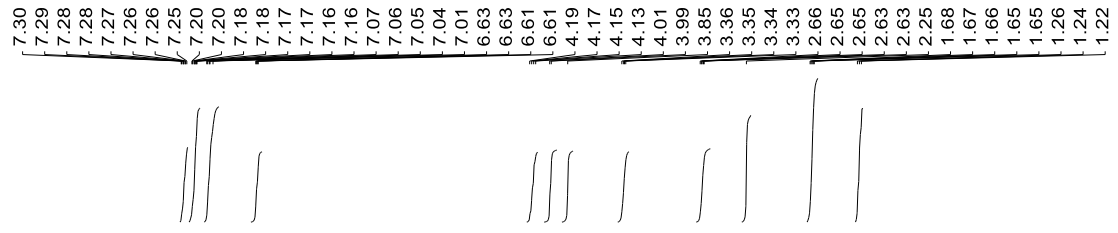


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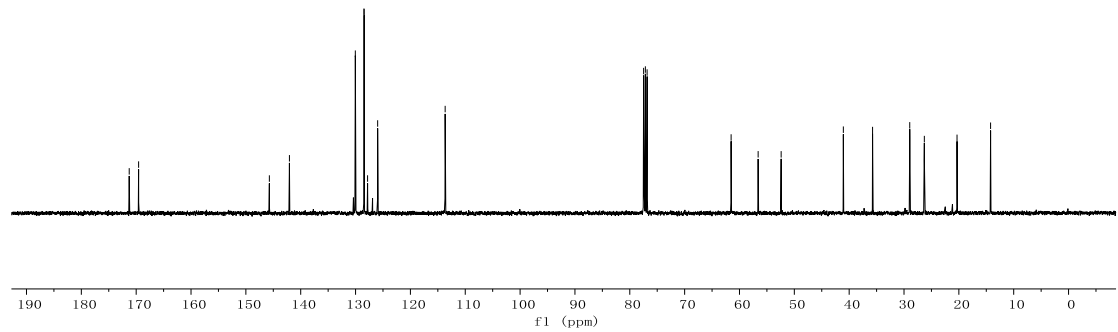




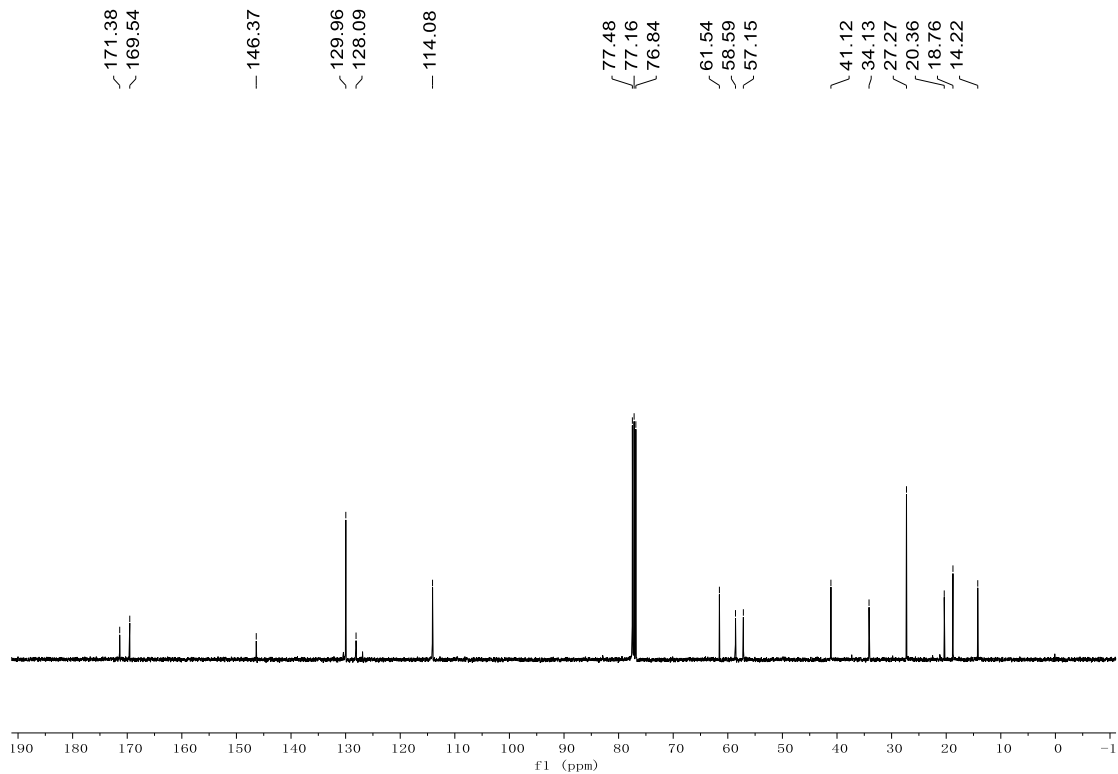
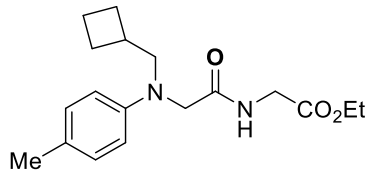
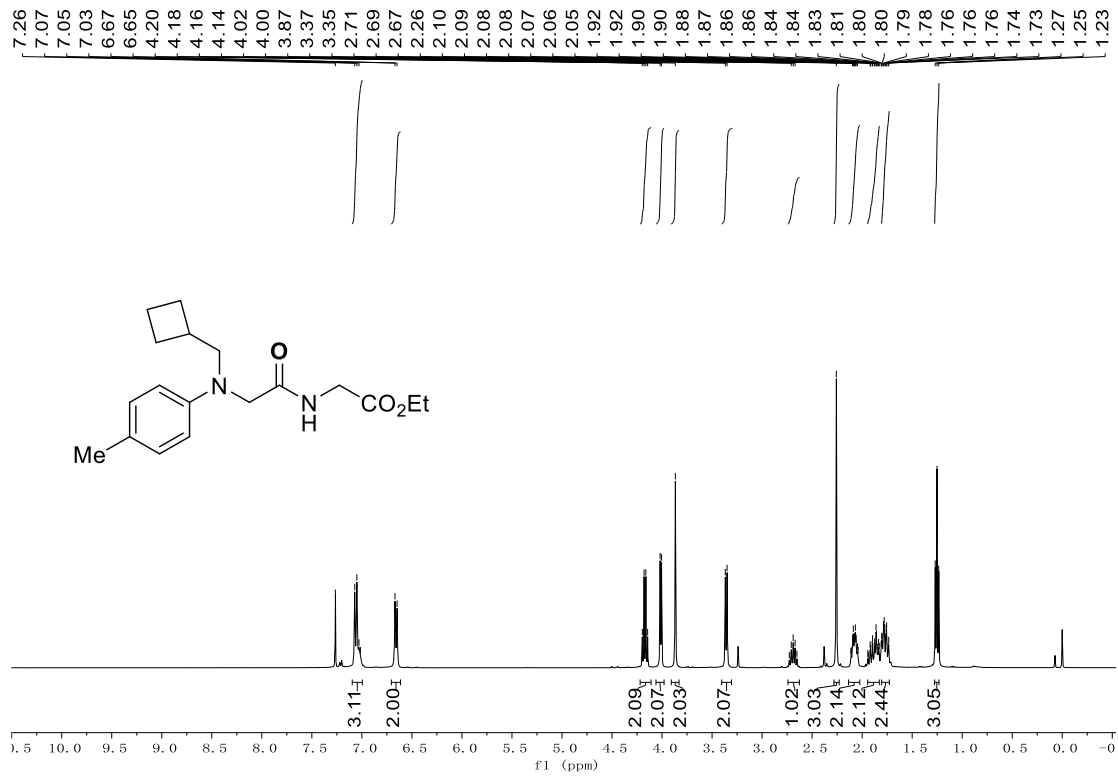
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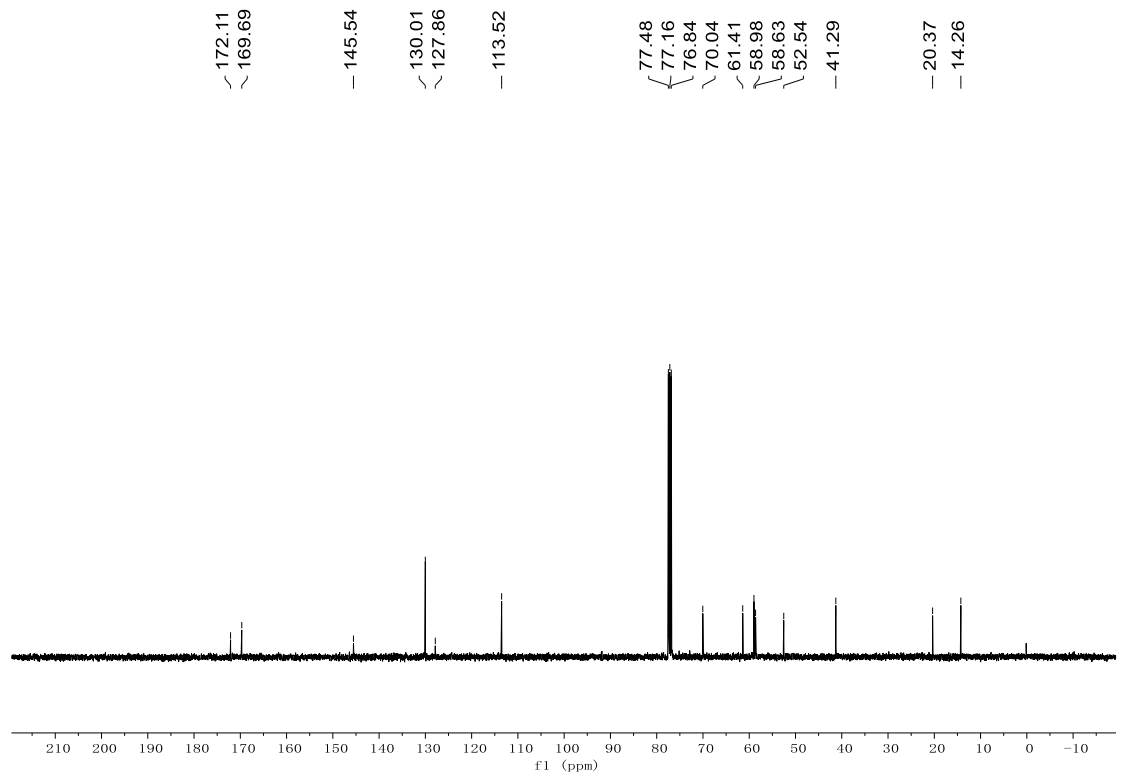
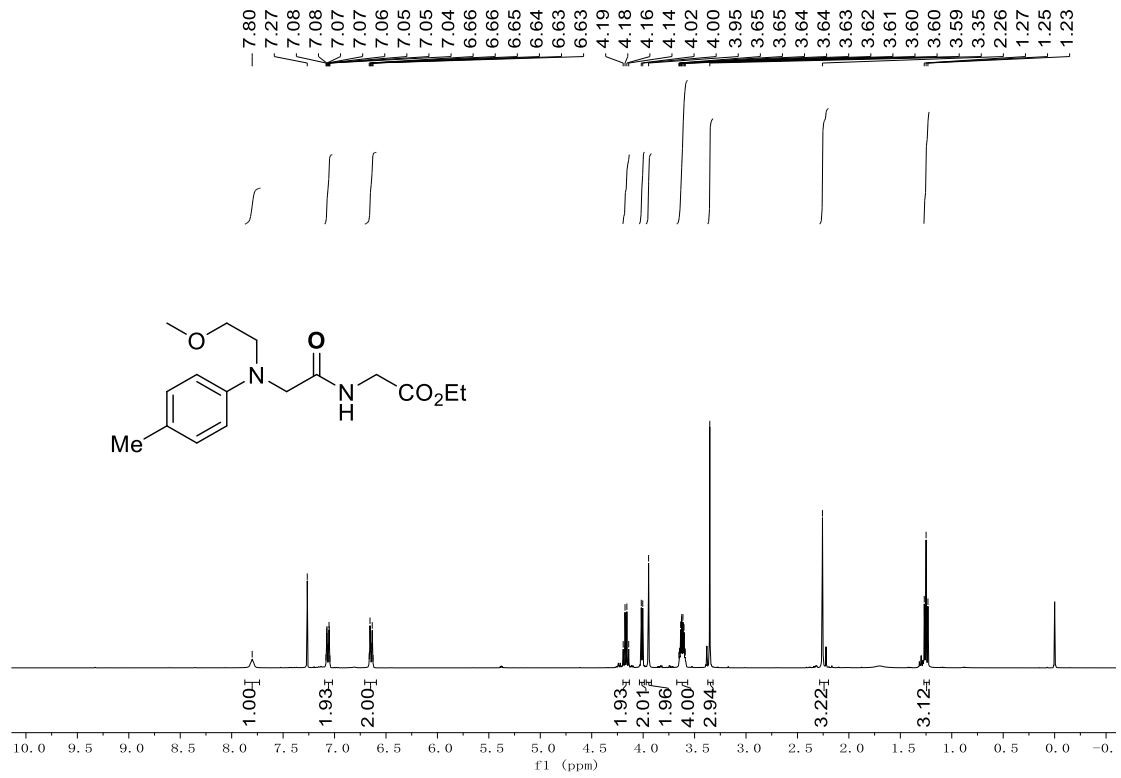
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- 41.06
- 35.73
- 28.95
- 26.29
- 20.33
- 14.22



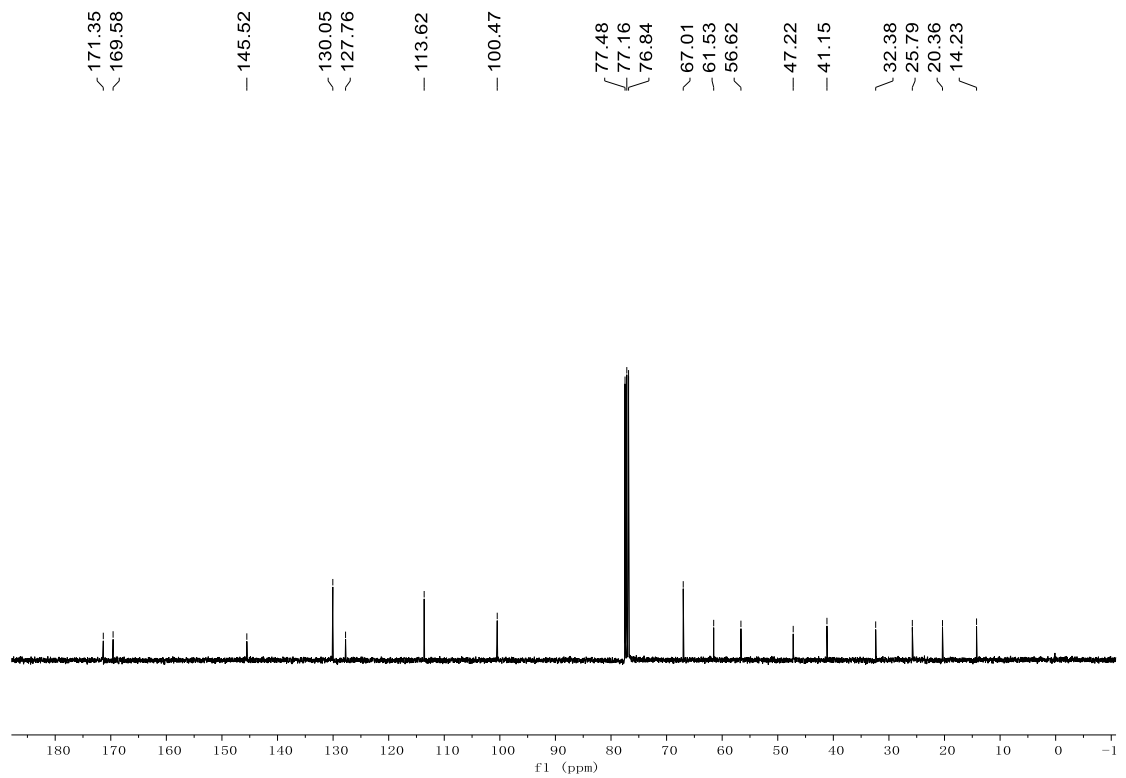
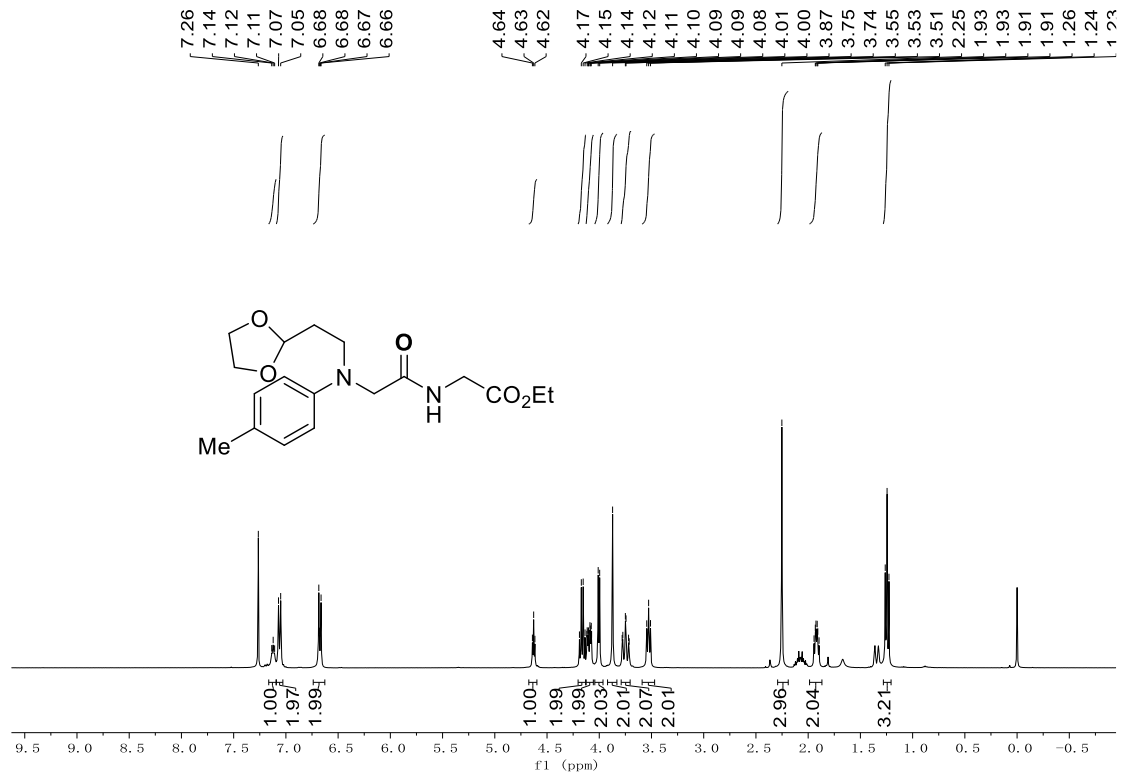
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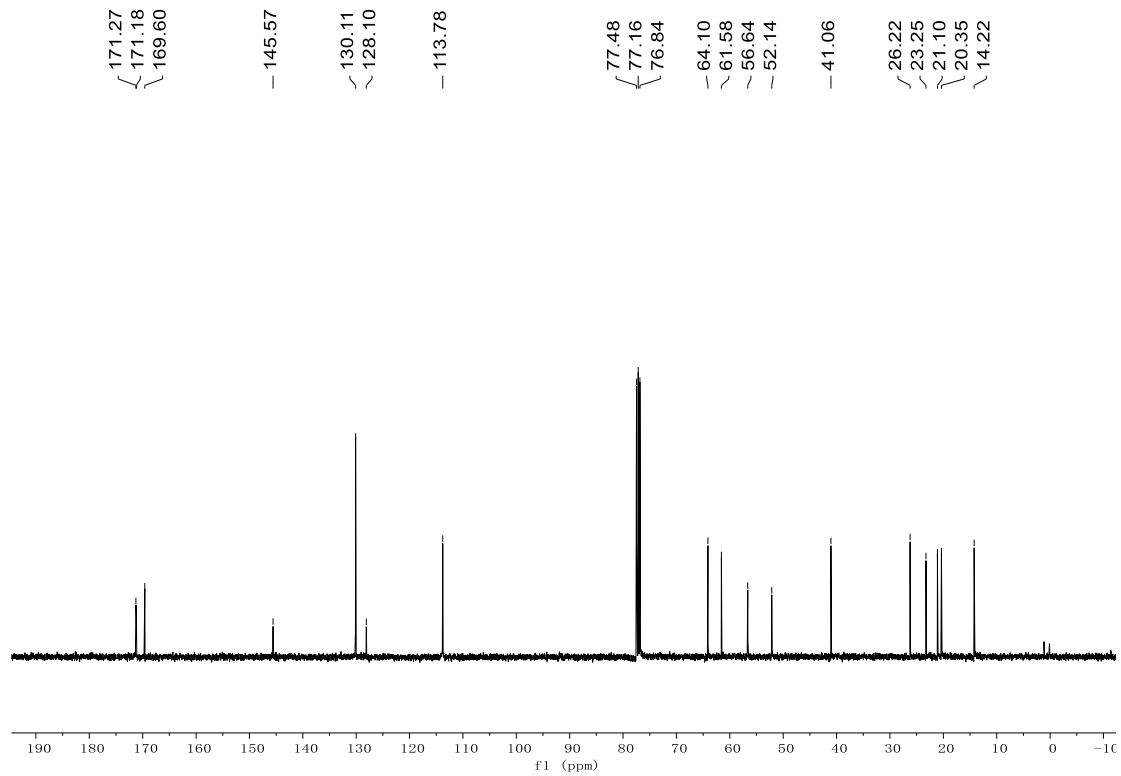
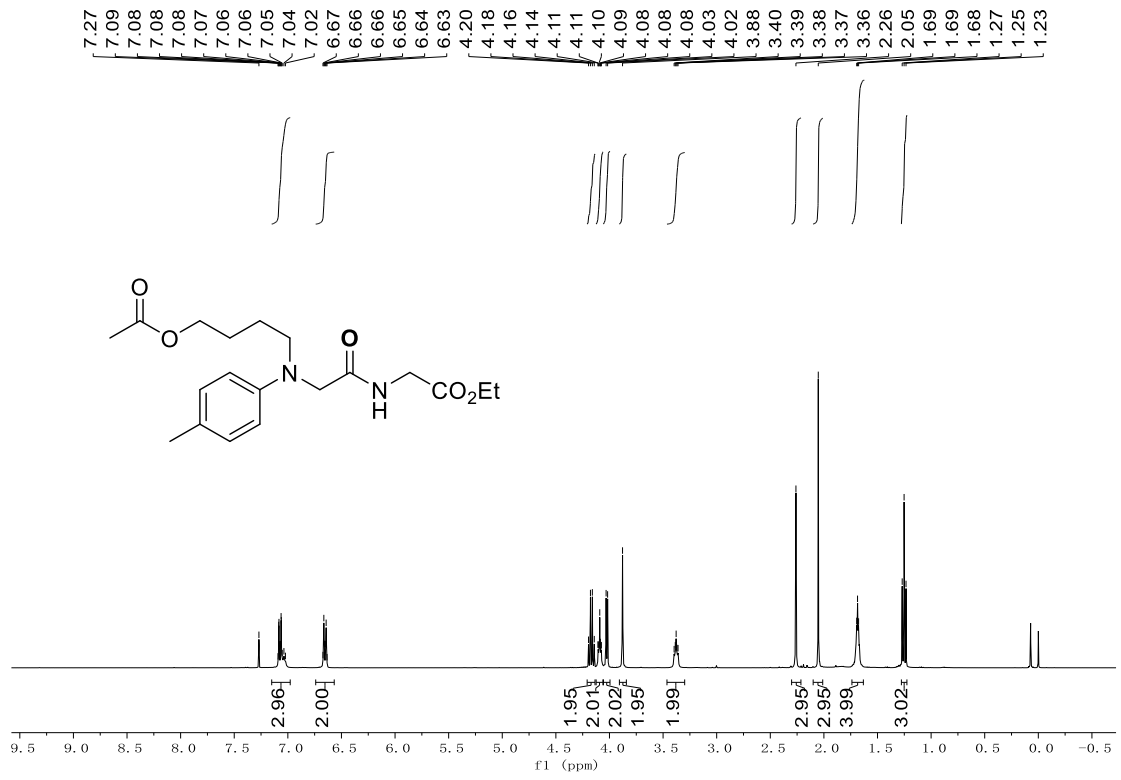
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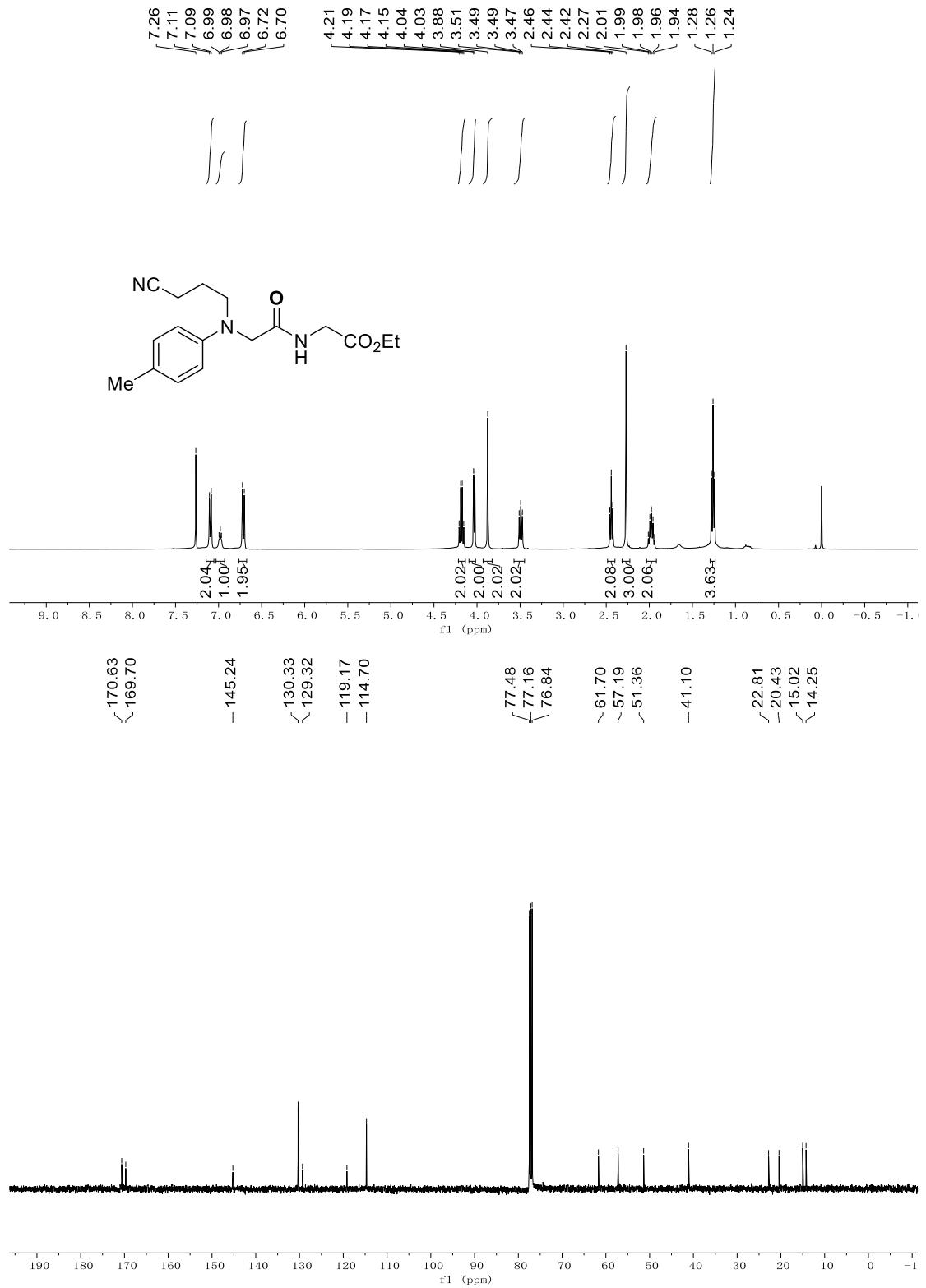
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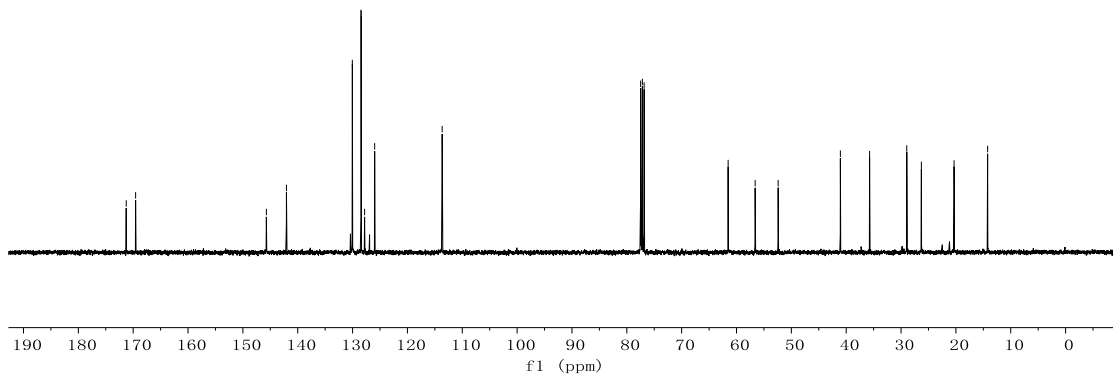
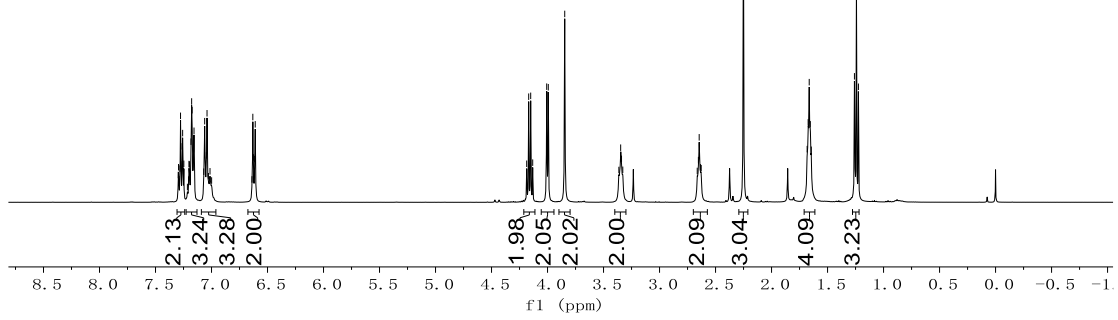
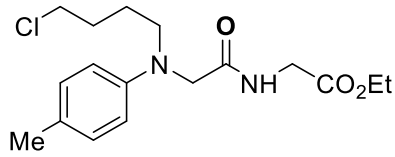
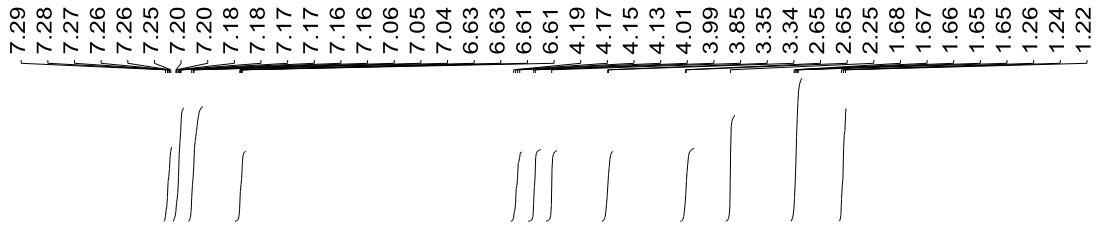
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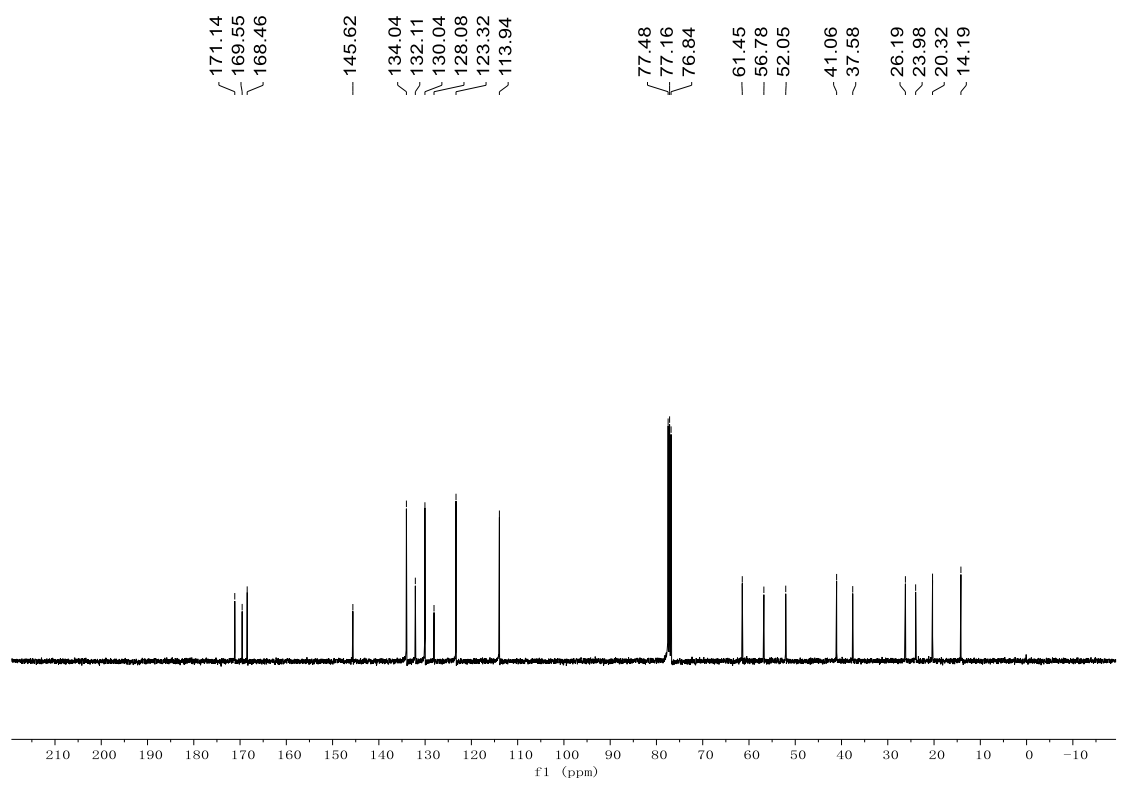
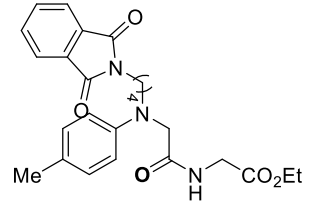
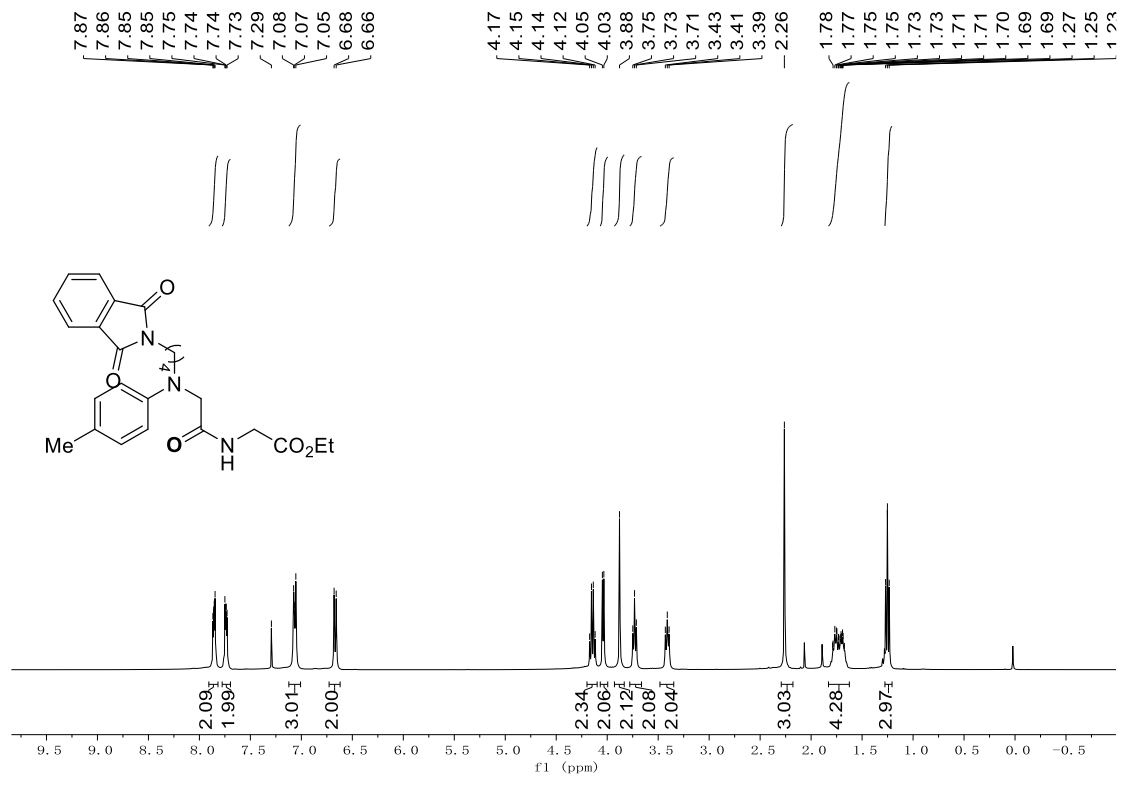
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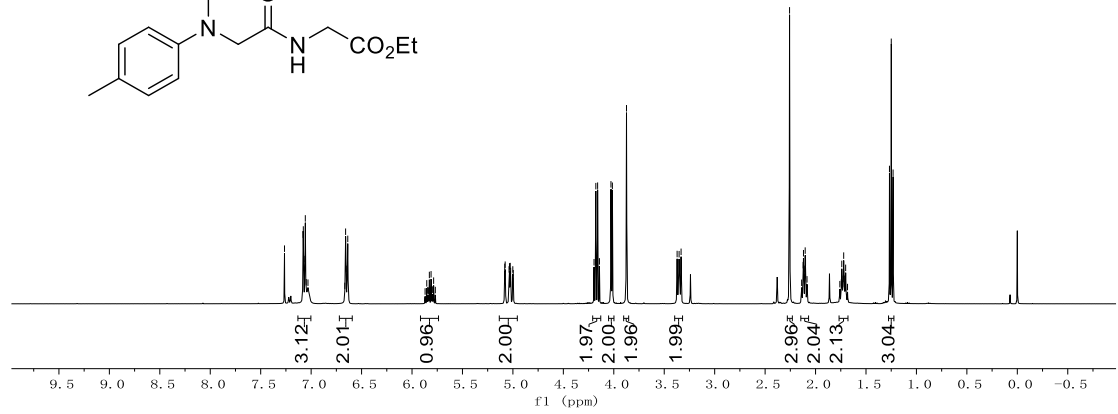
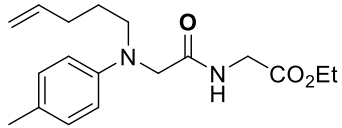
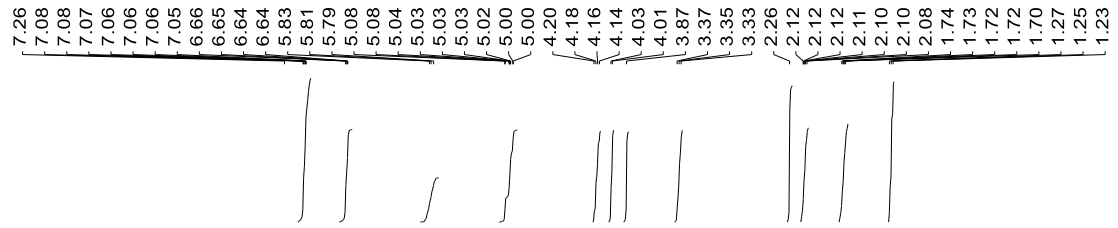
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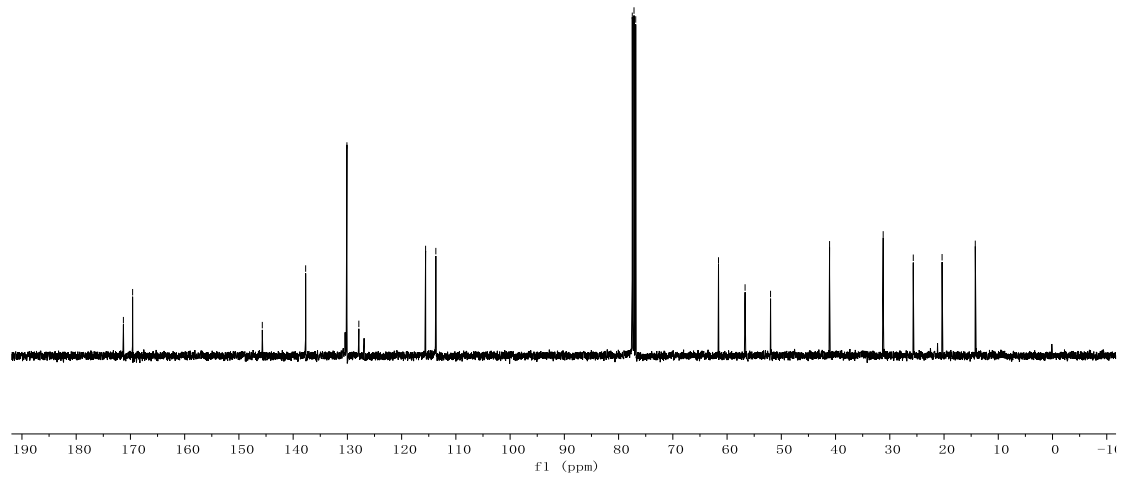
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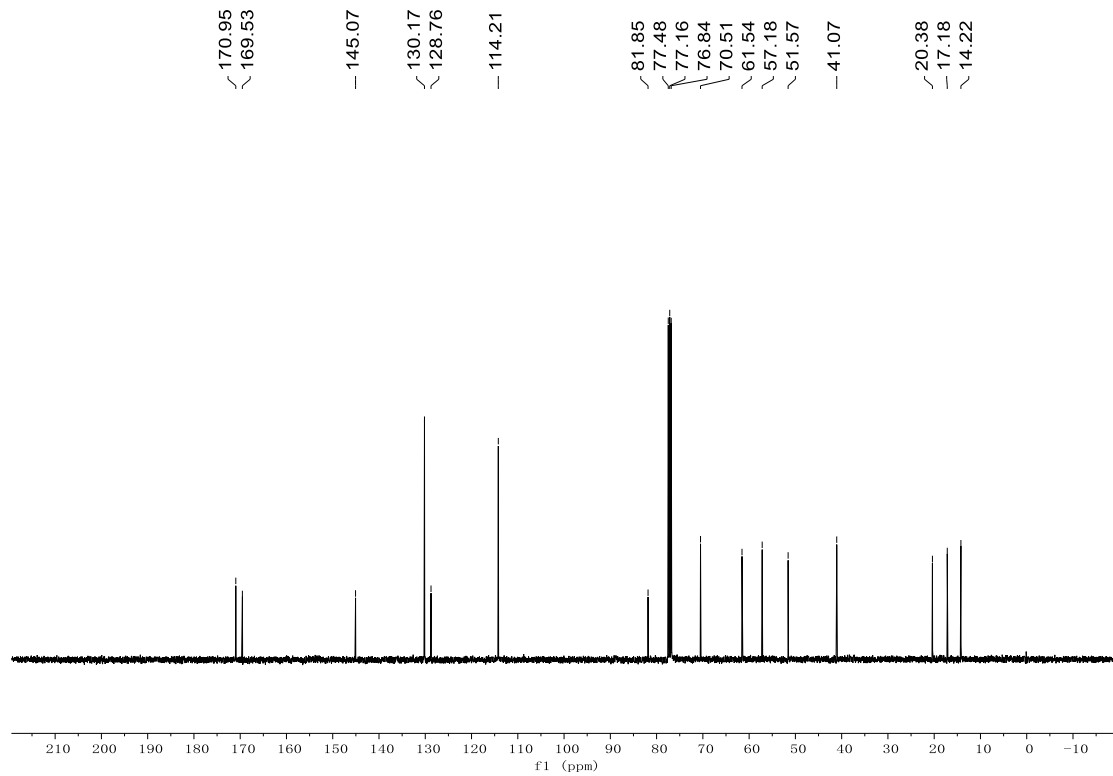
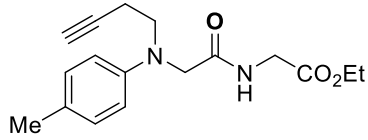
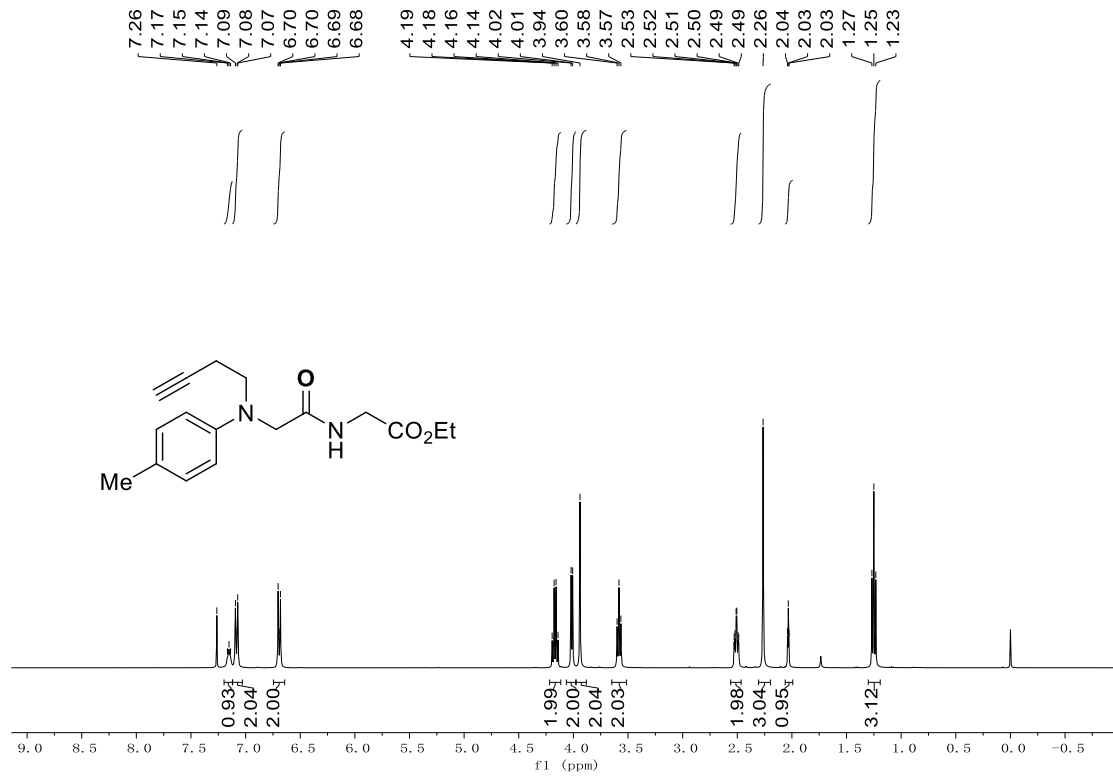
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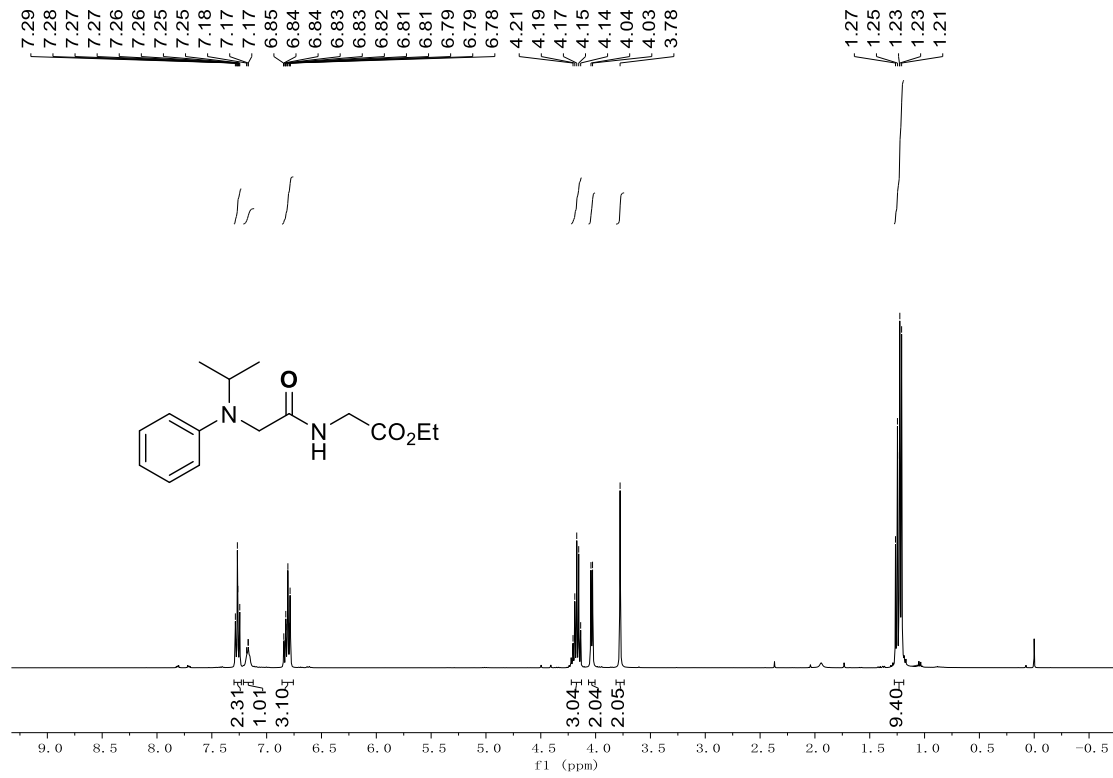
- ~ 171.30
- ~ 169.60
- ~ 145.69
- ~ 137.70
- ~ 130.09
- ~ 127.89
- ~ 115.58
- ~ 113.69
- ~ 77.48
- ~ 77.16
- ~ 76.84
- ~ 61.58
- ~ 56.68
- ~ 51.99
- ~ 41.10
- ~ 31.22
- ~ 25.67
- ~ 20.36
- ~ 14.24



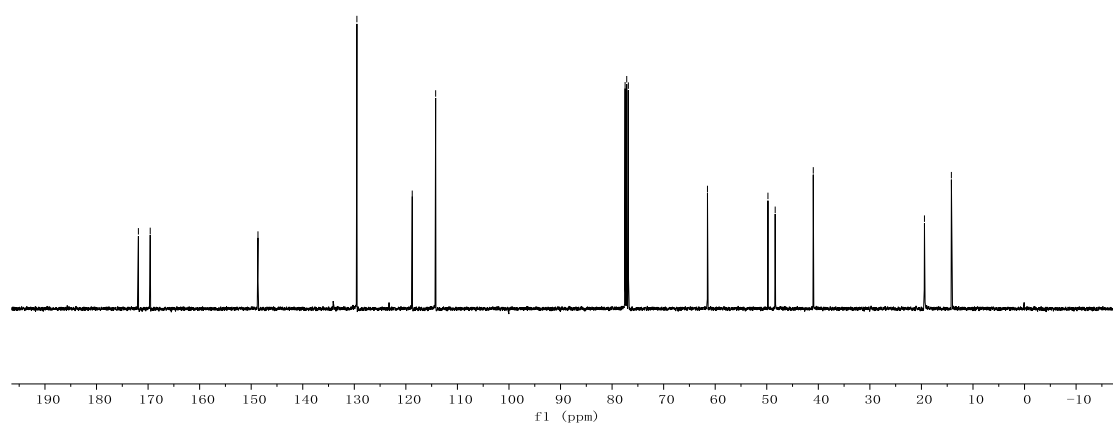
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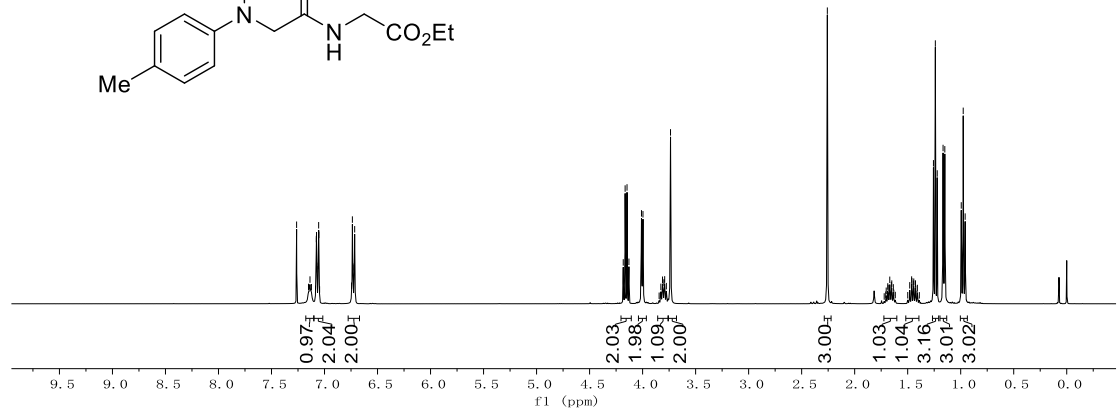
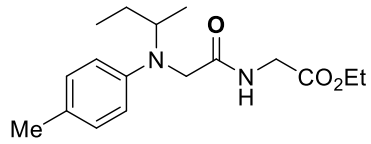
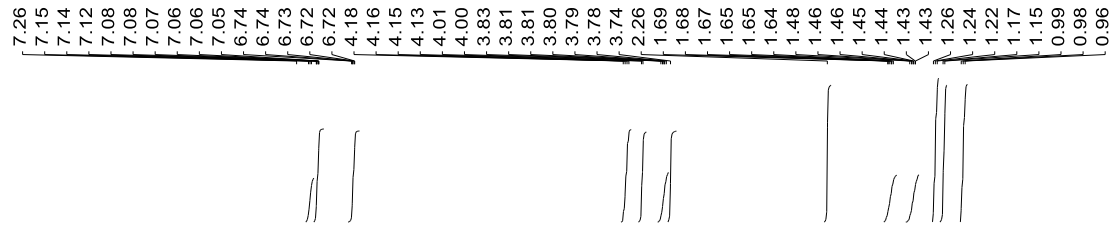
29



- 171.88
- 169.59
- 148.69
- 129.50
- 118.76
- 114.22
- 77.48
- 77.16
- 76.84
- 61.50
- 49.77
- 48.36
- 40.98
- 19.41
- 14.19



30



~ 171.82
~ 169.57

- 146.63

~ 129.99
~ 128.37

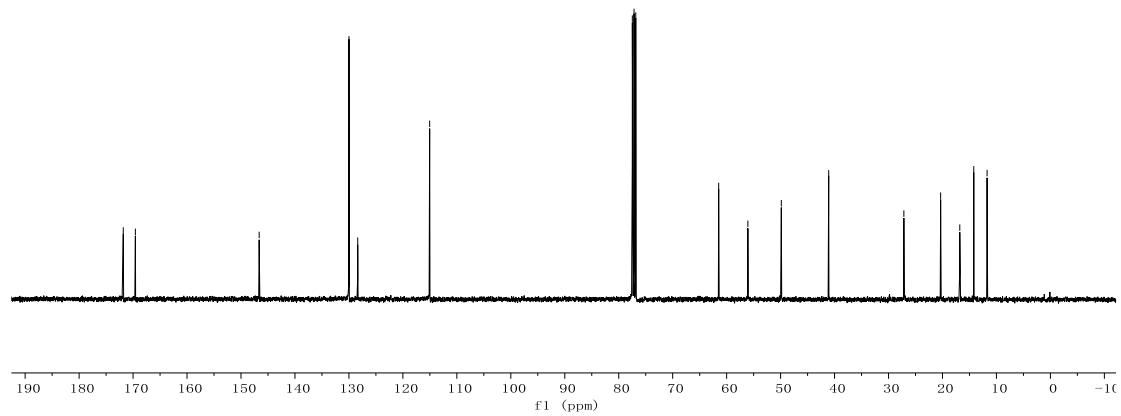
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{ 77.48
77.16
76.84

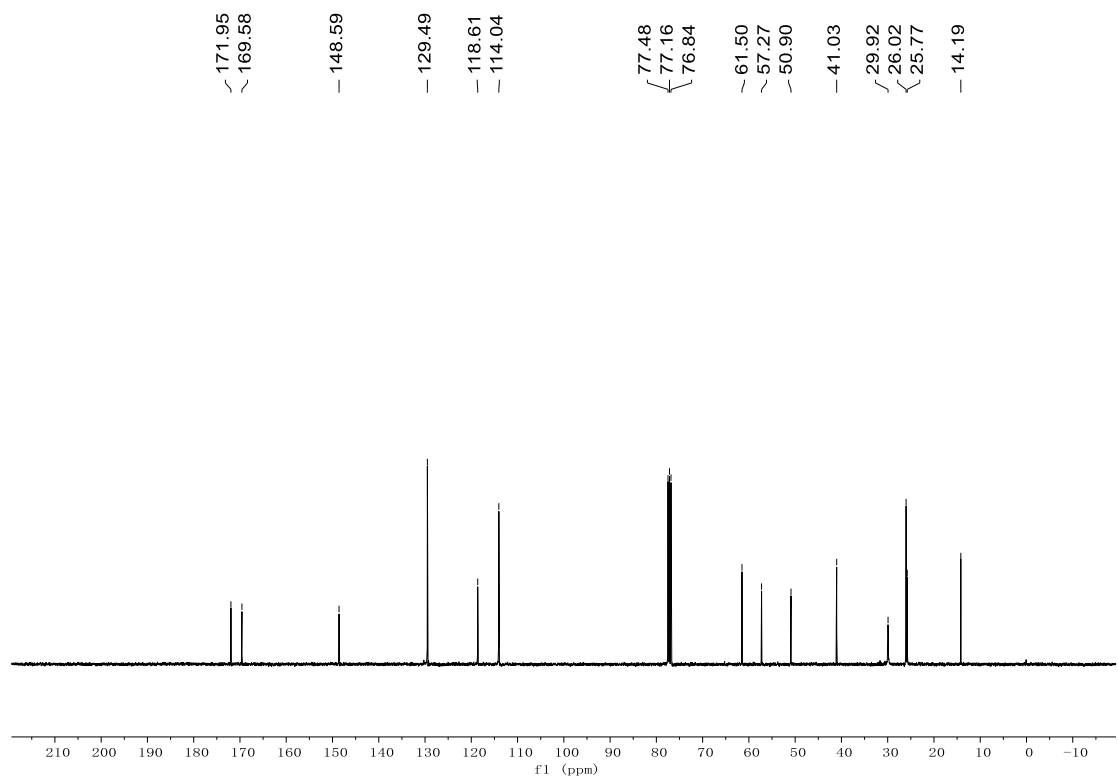
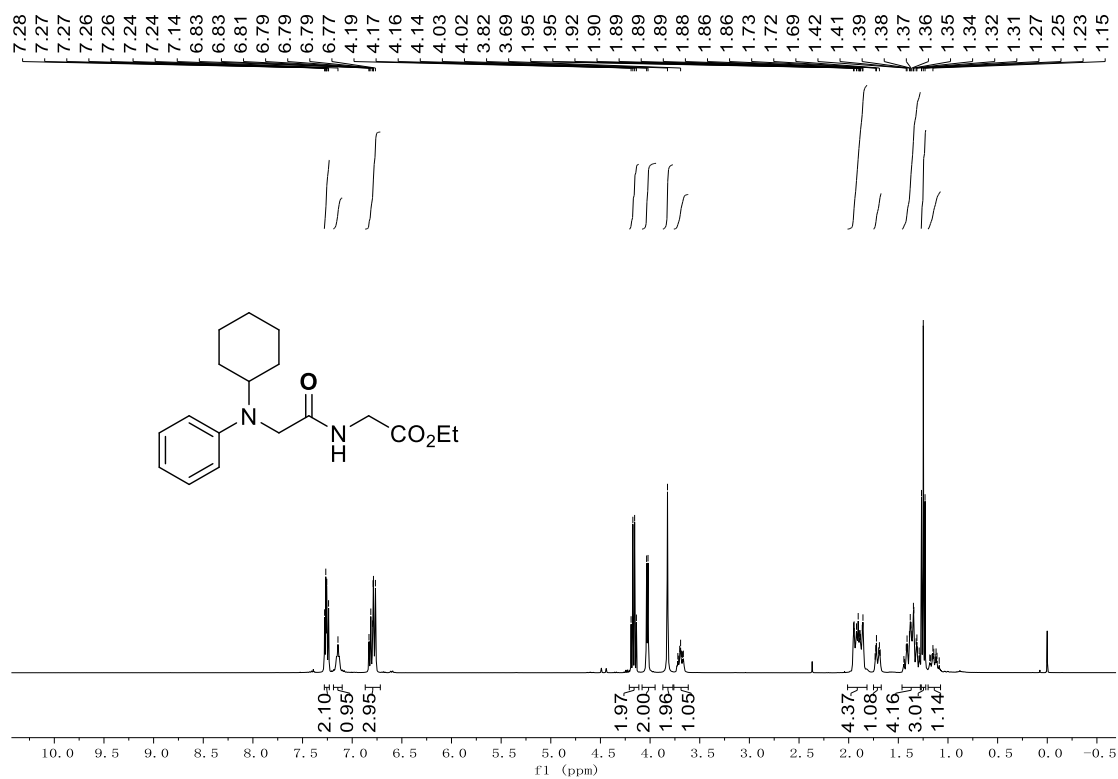
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~ 56.07
~ 49.87

- 41.09

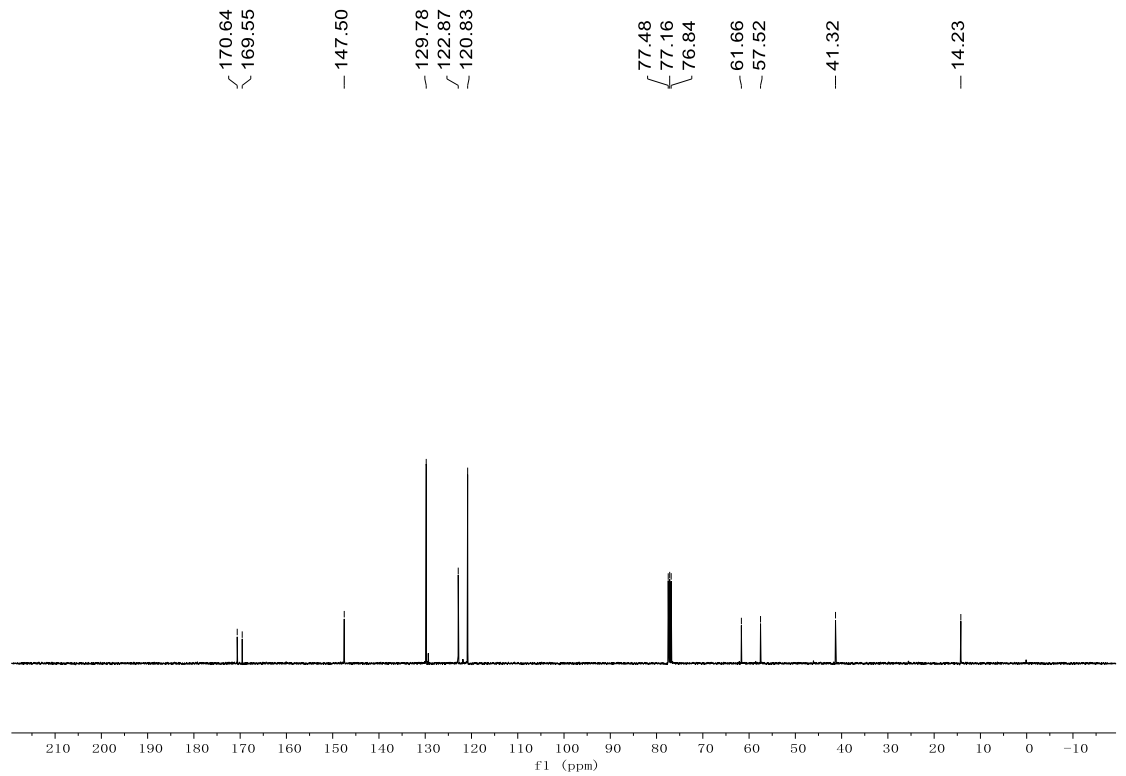
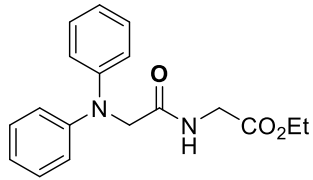
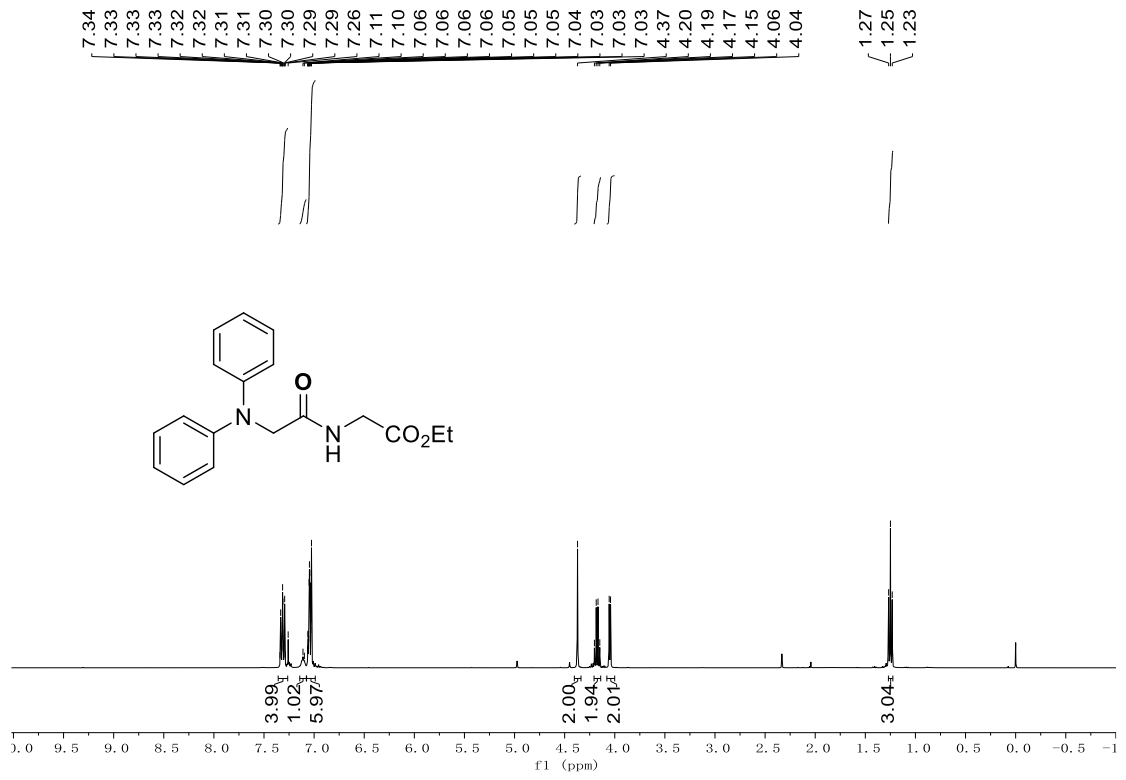
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/ 20.34
/ 16.79
/ 14.20
~ 11.74



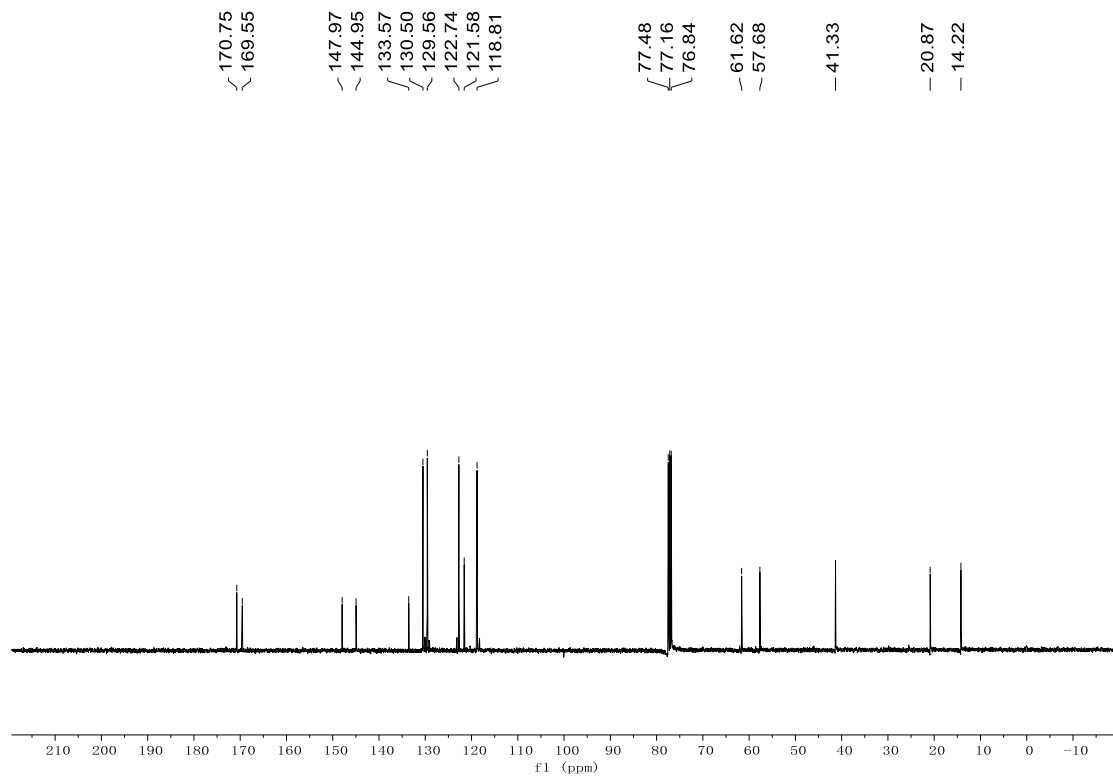
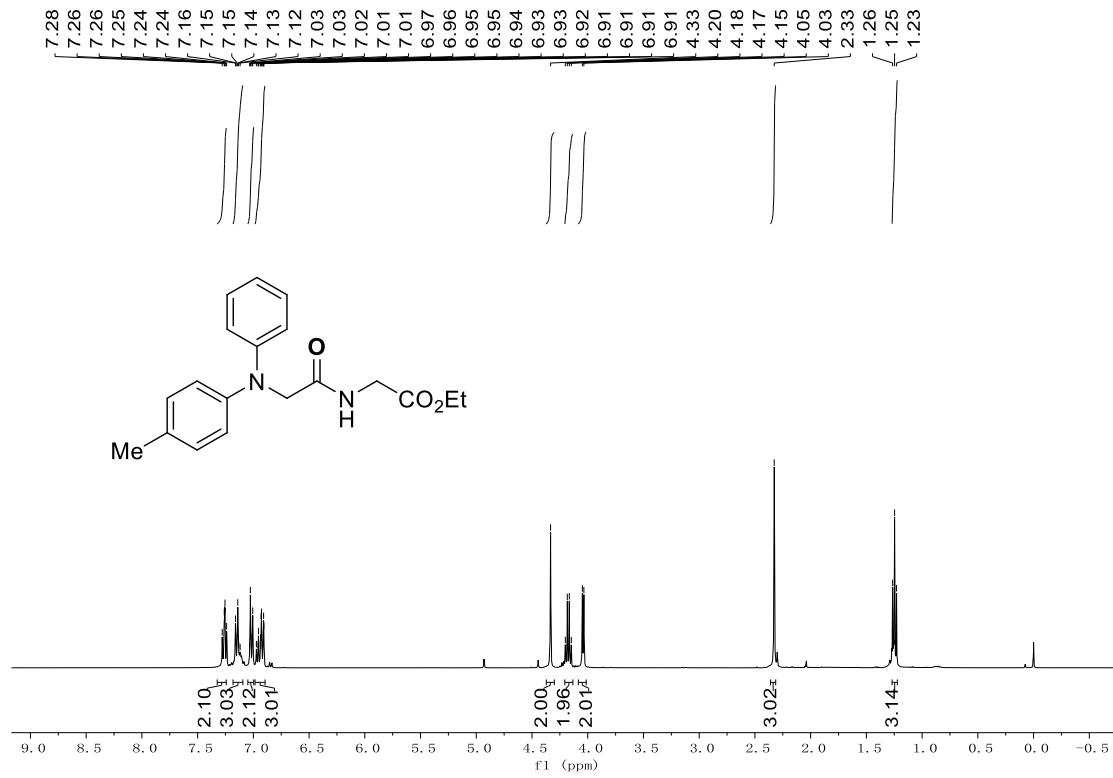
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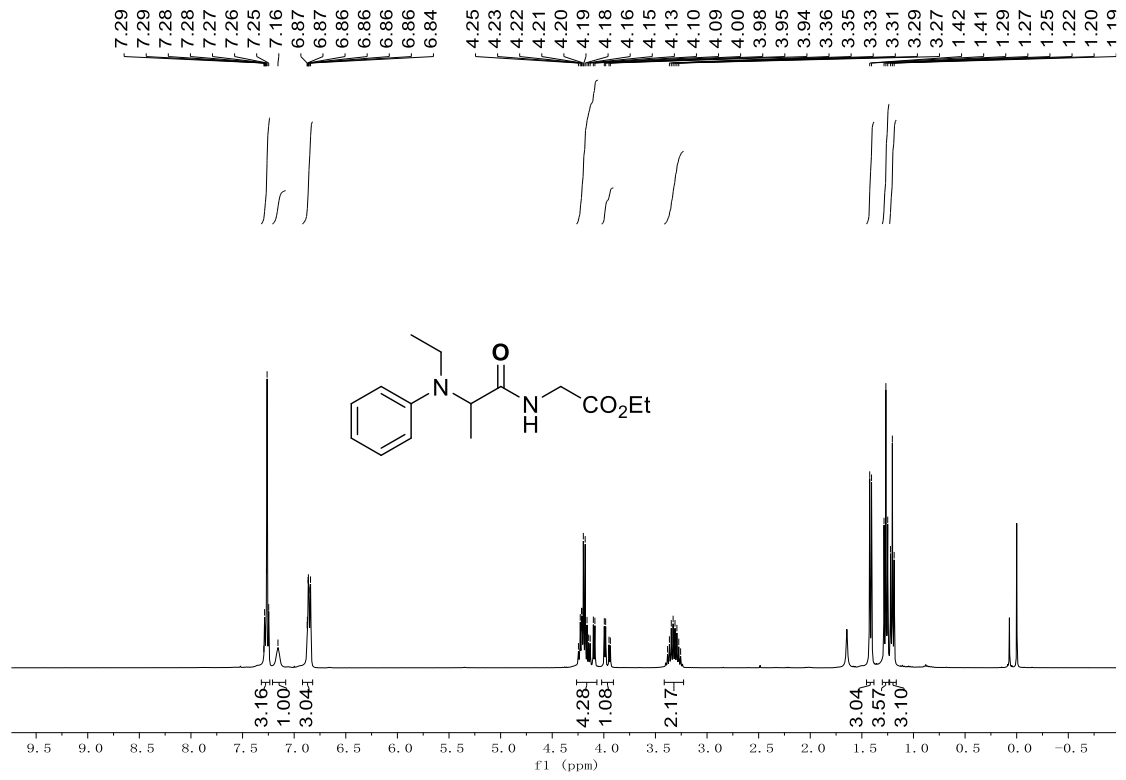
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33



34



- 174.05
- 169.91

- 147.52

- 129.37

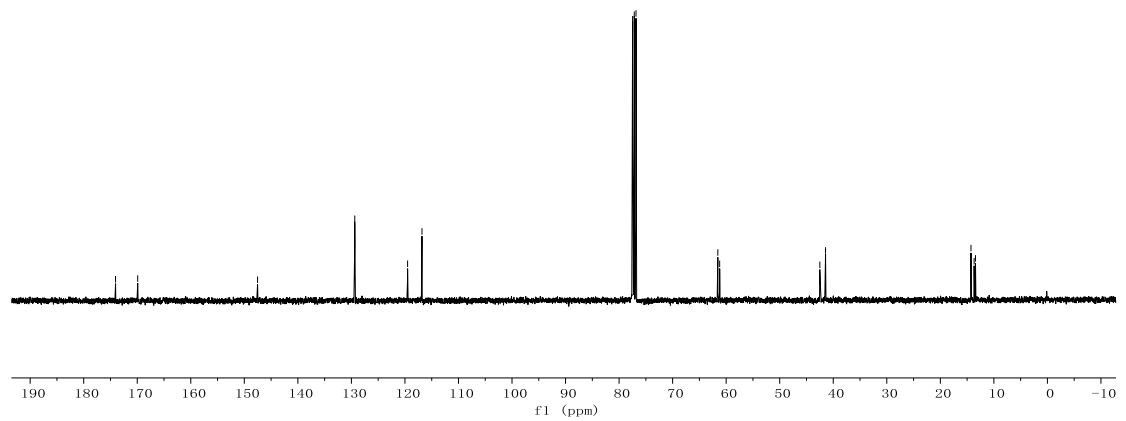
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- 116.82

{ 77.48
{ 77.16
{ 76.84

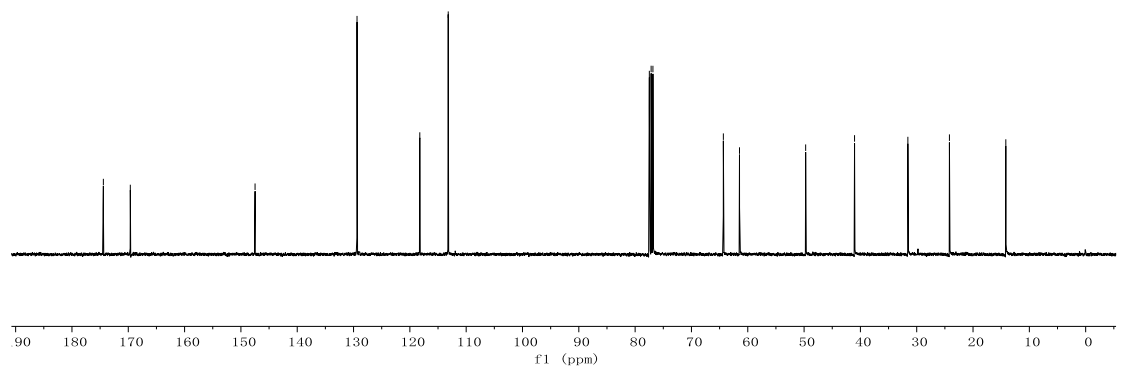
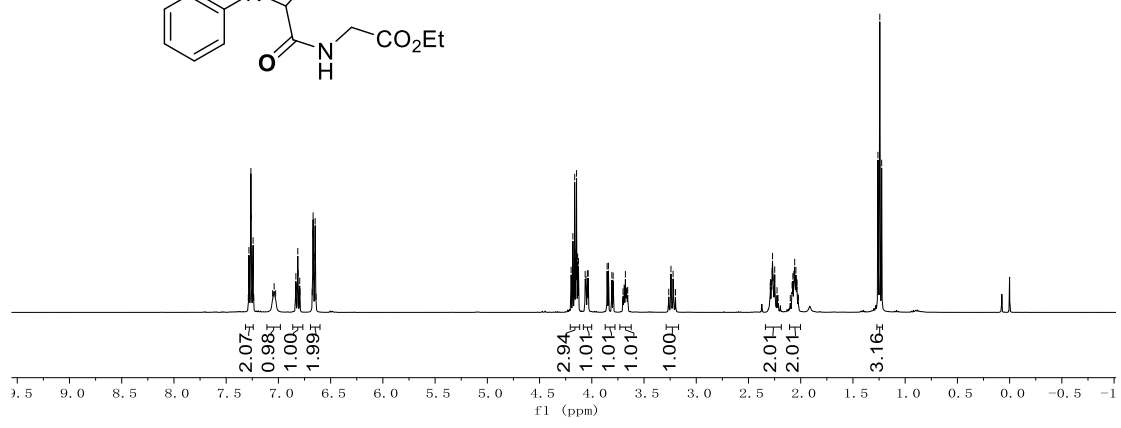
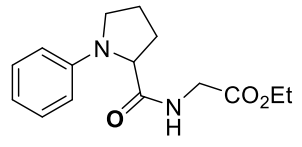
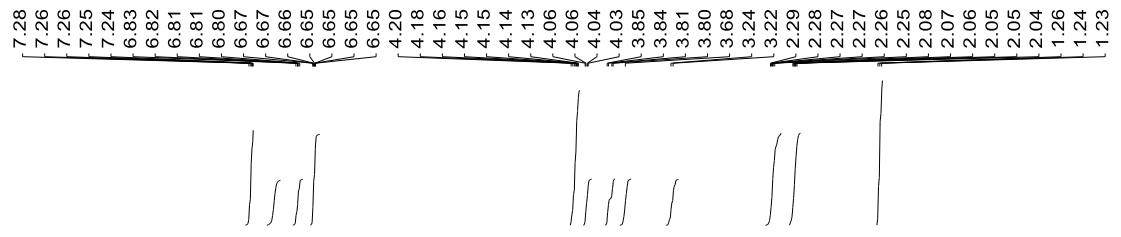
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{ 42.51
{ 41.44

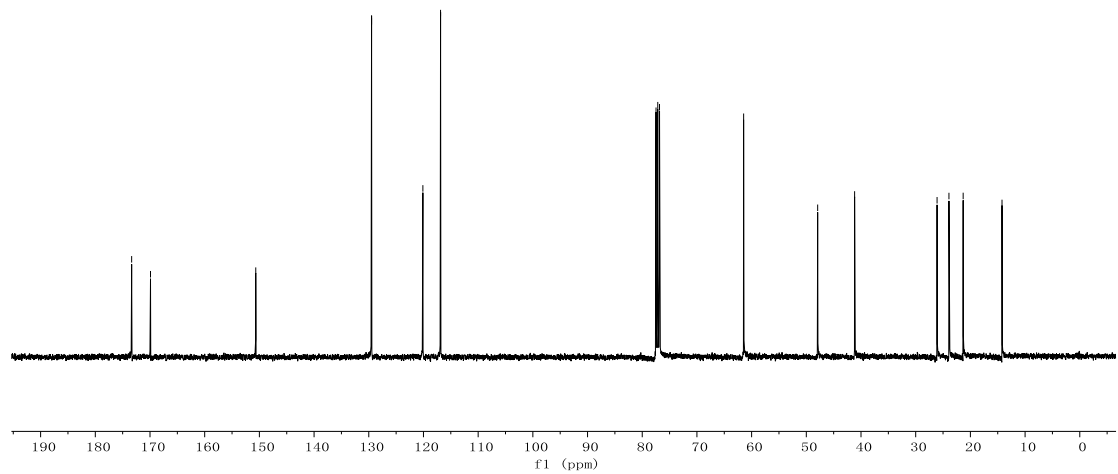
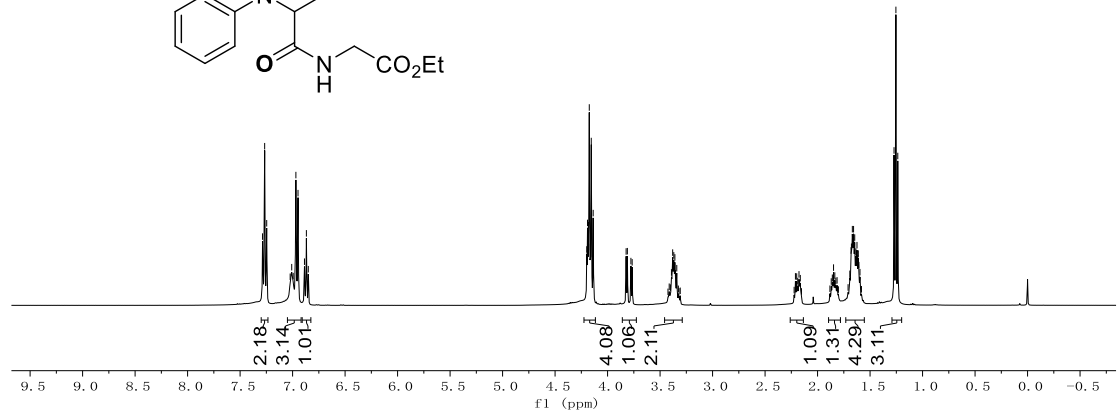
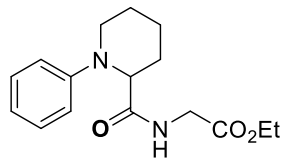
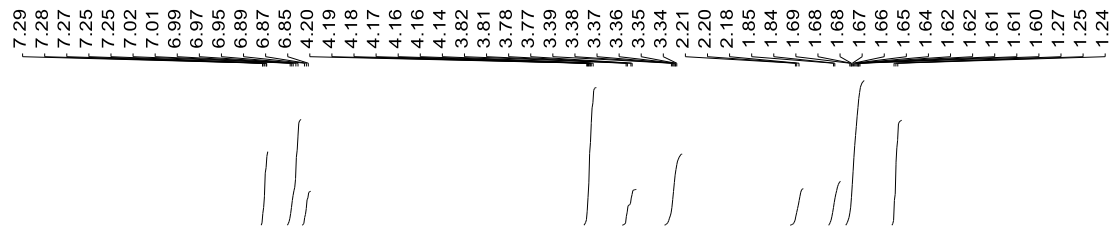
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{ 13.43



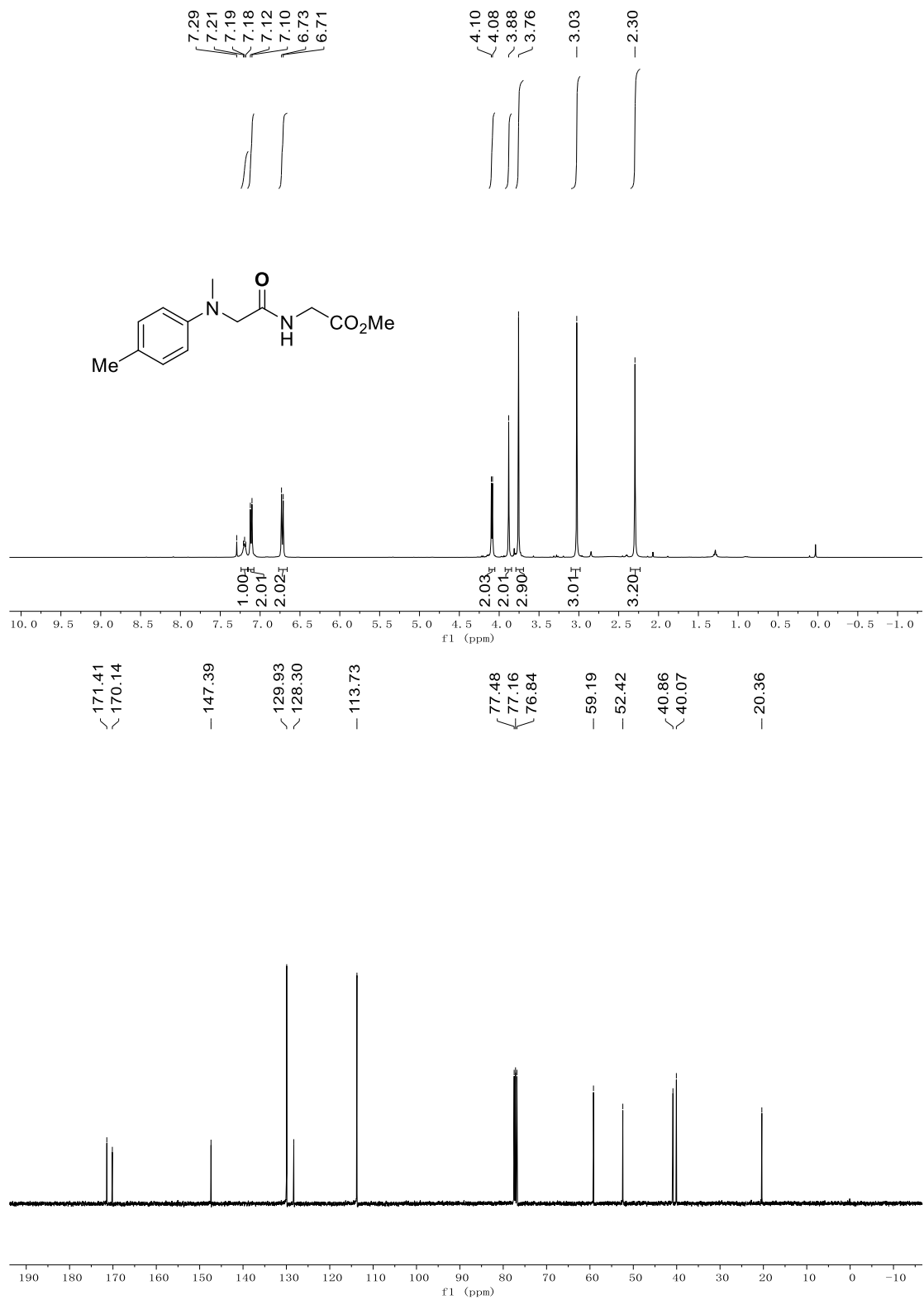
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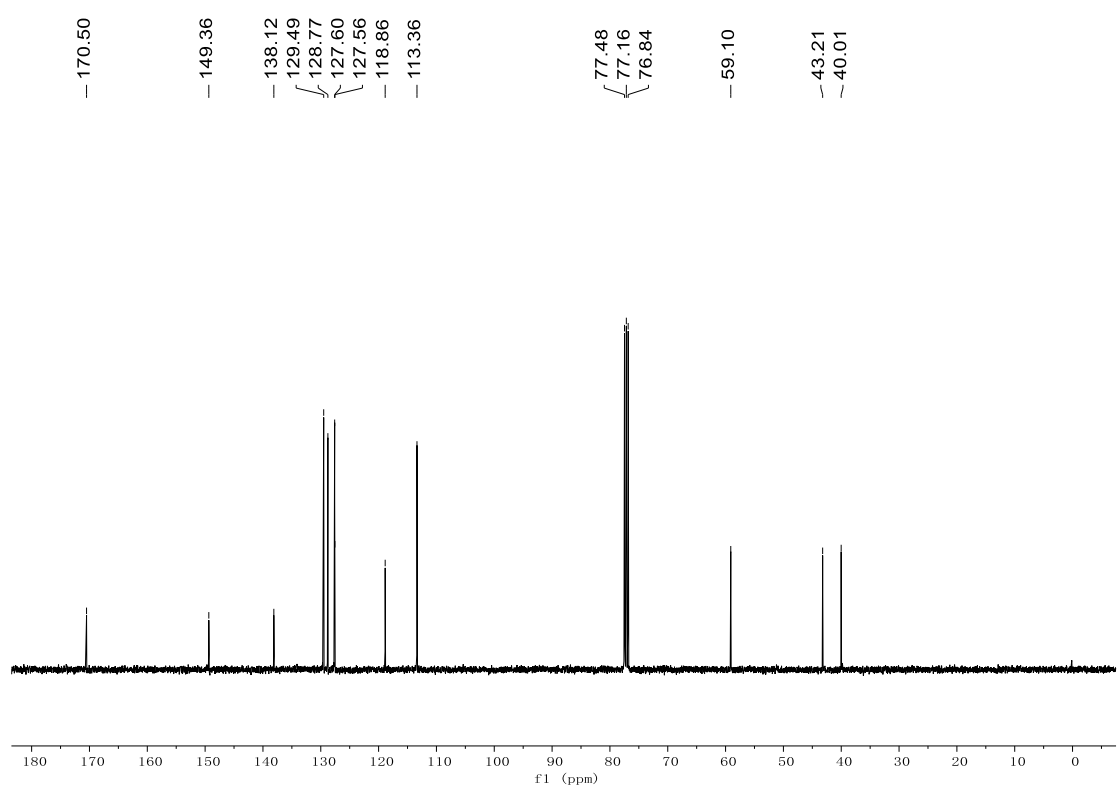
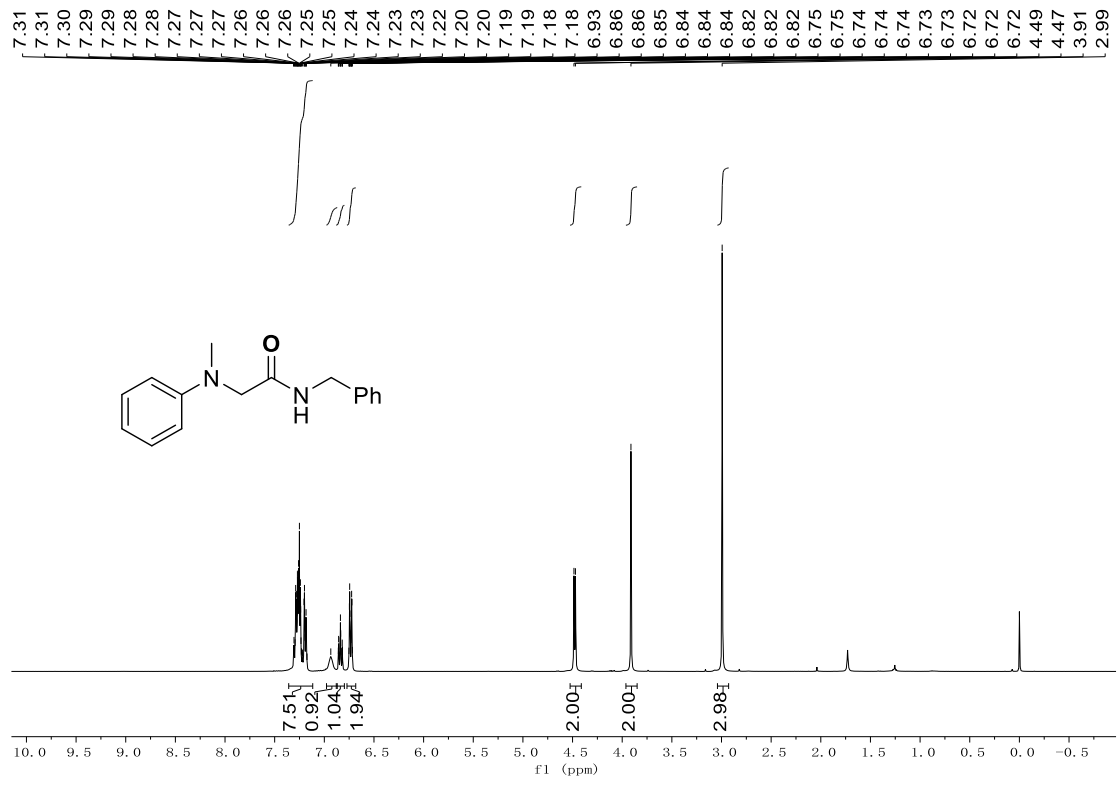
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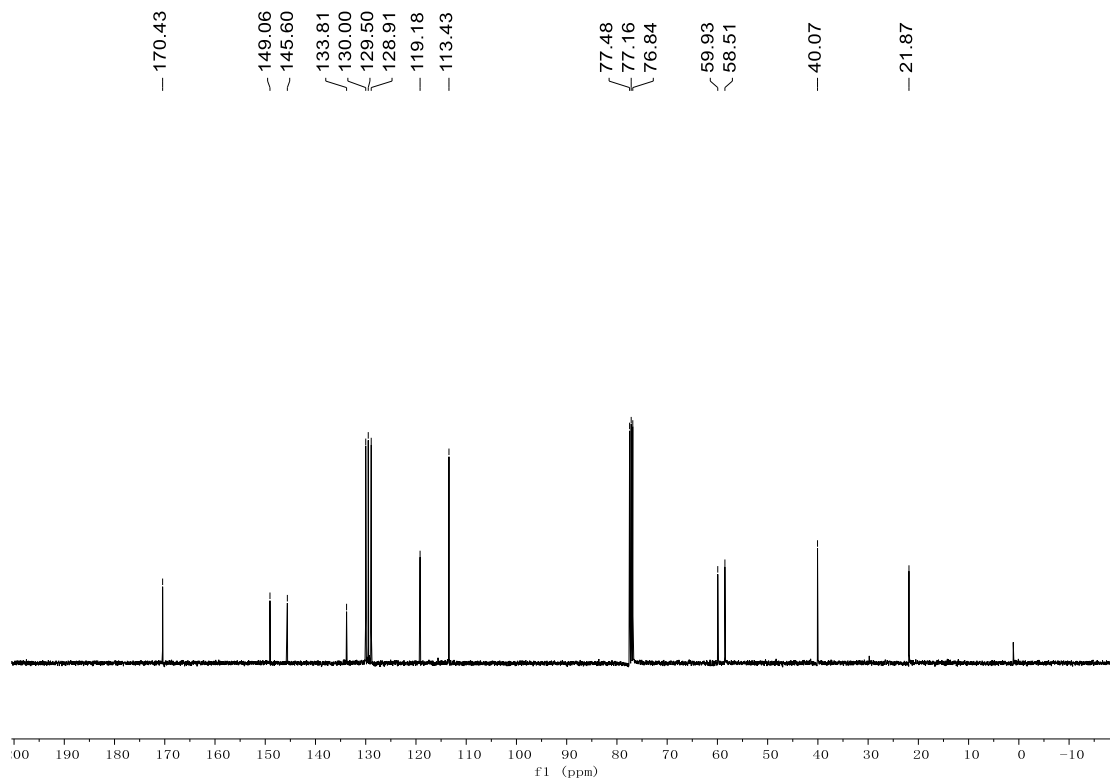
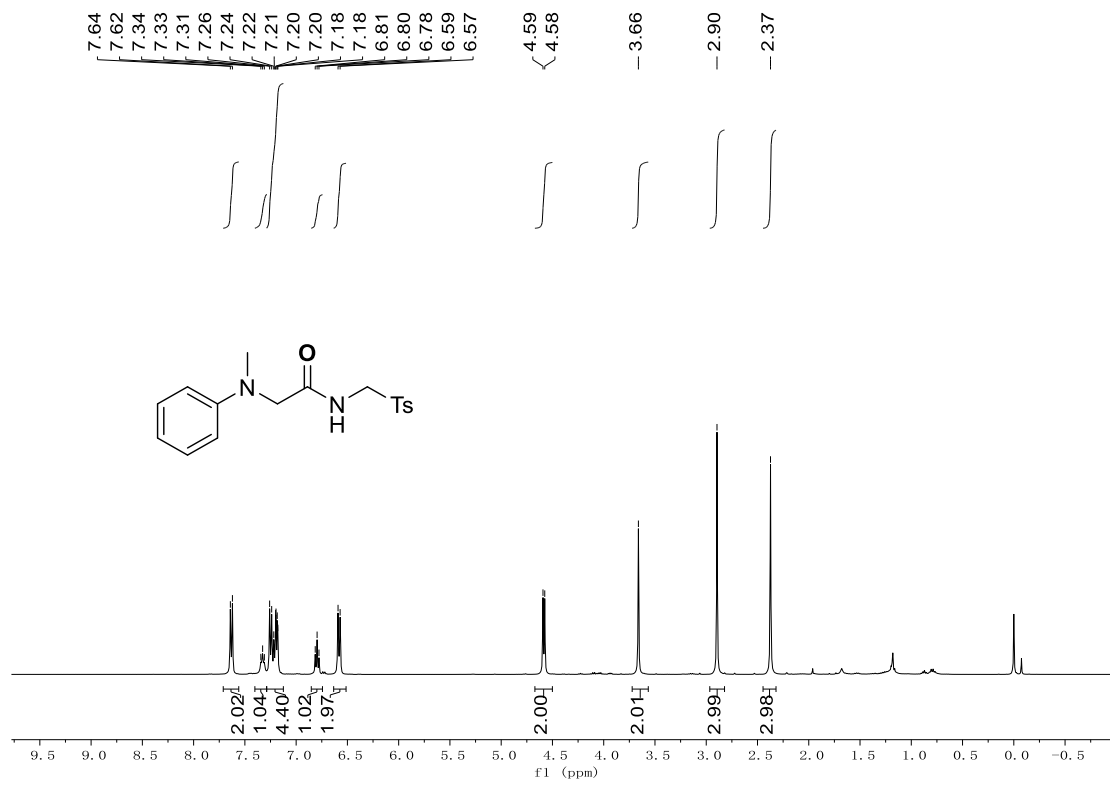
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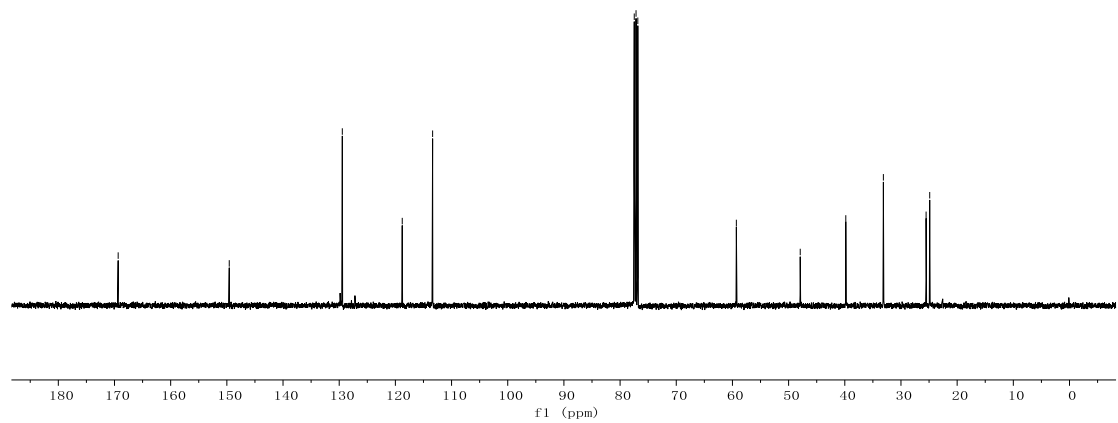
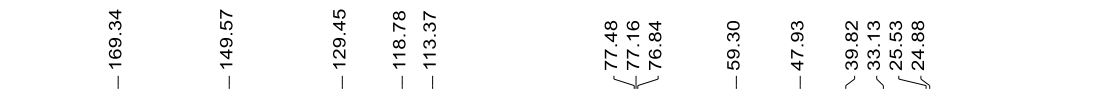
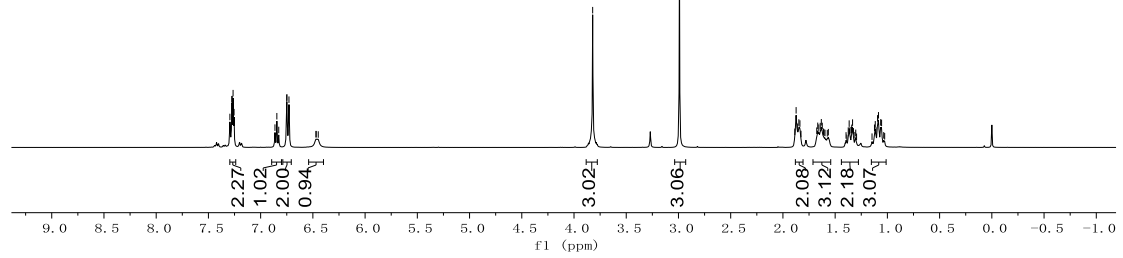
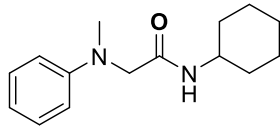
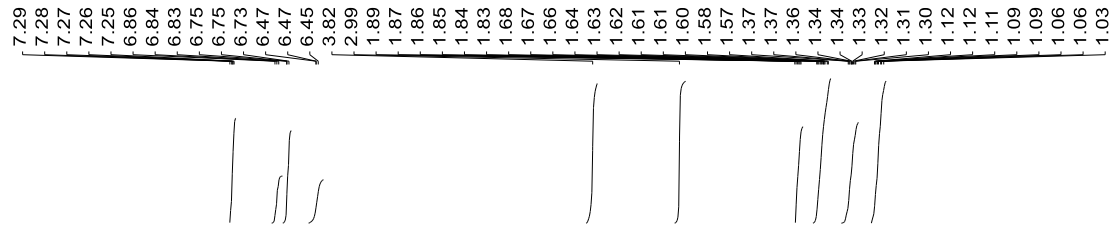
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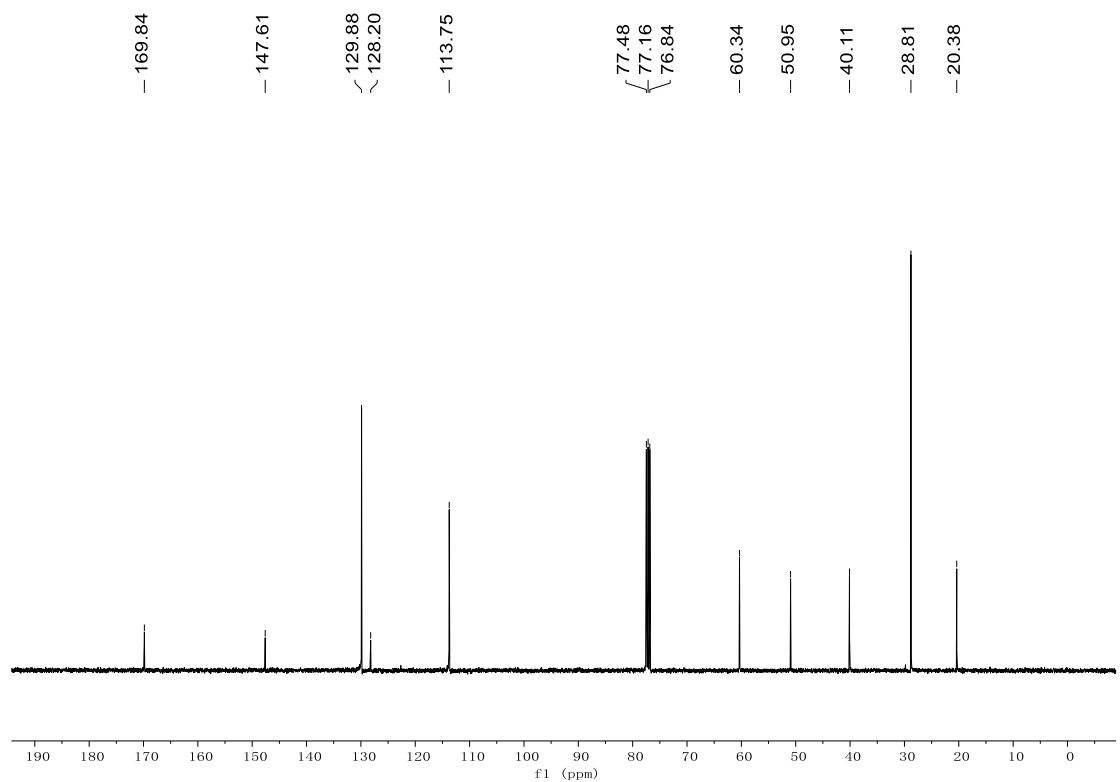
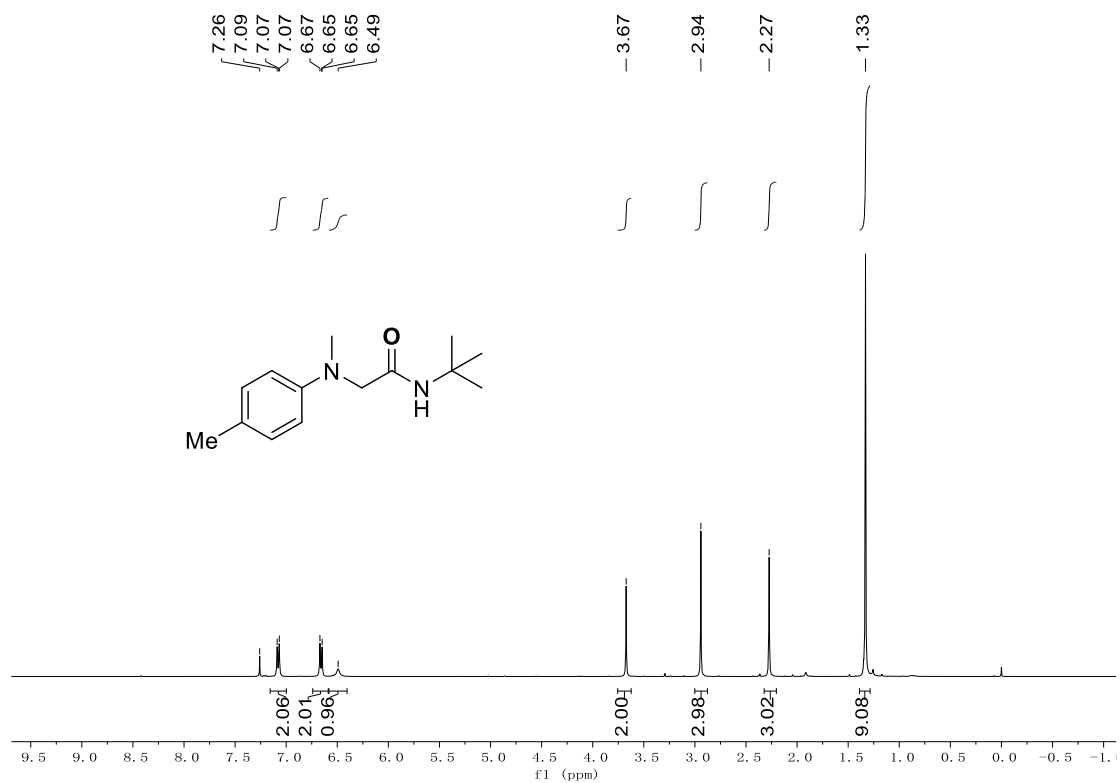
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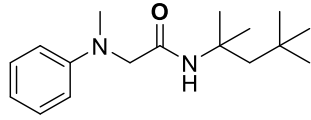
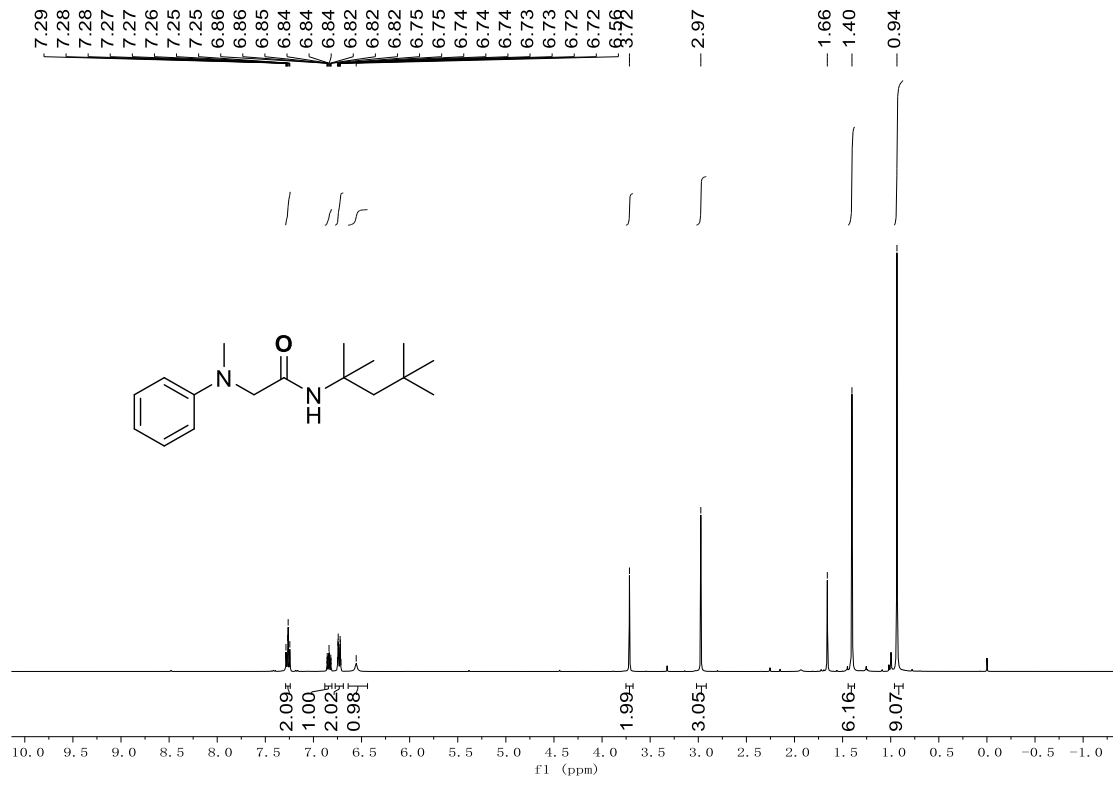
40



41



42



— 169.30

— 149.50

— 129.37

— 118.77

— 113.41

77.48

77.16

76.84

— 60.12

— 54.98

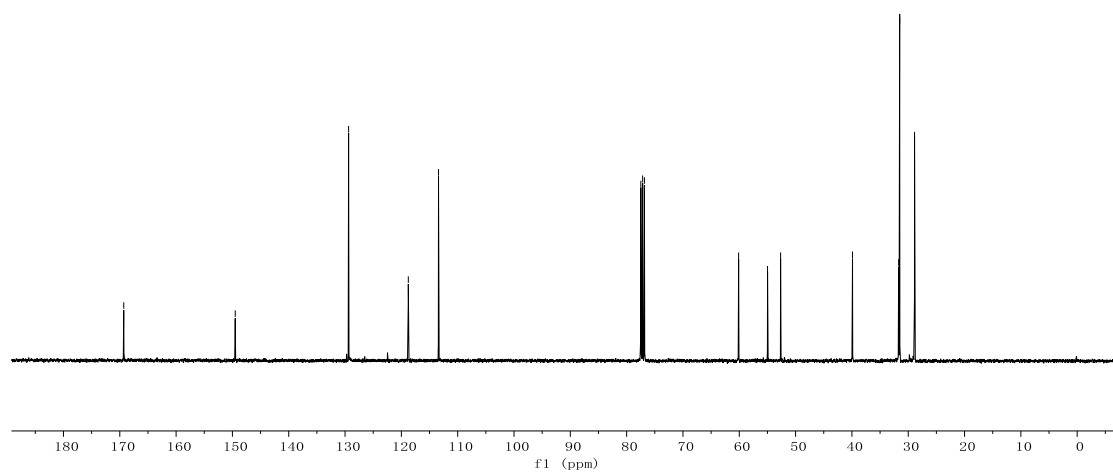
— 52.66

— 39.89

31.70

31.52

28.88



43

