Supplementary Information

Metal-free electrochemical synthesis of α-ketoamides via decarboxylative coupling of α-keto acids with isocyanides and water

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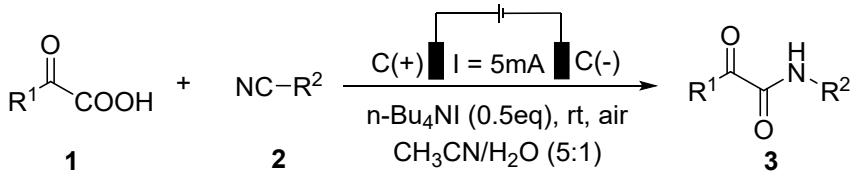
1. General information

All commercially available reagent grade chemicals were purchased from Aldrich, Acros, Bidepharm and Energy Chemical Company and used as received without further purification unless otherwise stated. ^{1}H NMR and ^{13}C NMR were recorded in $CDCl_3$ on a Bruker Avance III spectrometer with TMS as internal standard (500/400 MHz ^{1}H, 125/400 MHz ^{13}C) at room temperature, the chemical shifts (δ) were expressed in ppm and *J* values were given in Hz. The following abbreviations are used to indicate the multiplicity: singlet (s), doublet (d), triplet (t), quartet (q), doublet of doublets (dd), doublet of triplets (dt), and multiplet (m). All first order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted were designated as multiplet (m). Mass analyses and HRMS were obtained on a Finnigan-LCQDECA mass spectrometer and a Bruker Daltonics Bio-TOF-Q mass spectrometer by the ESI method, respectively. Column chromatography was performed on silica gel (200-300 mesh). The instrument for electrolysis is dual-display potentiostat (DJS-292B) (made in China), the carbon rod (d: 6 mm), Pt (1.5 x 1.5 cm x 2) was purchased from Xuzhou Xinke Instrument and Meter Co. LTD.

2. General procedure for electrochemical synthesis of α-ketoamides from α-oxocarboxylic acids, isocyanides and water.



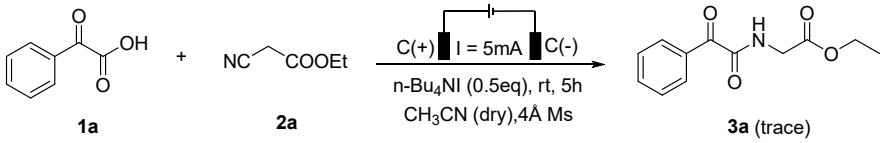
1 **2** **3**

In an oven-dried undivided three-necked flask (25 mL) equipped with a stir bar, α -oxocarboxylic acids **1** (0.2 mmol), isocyanide **2** (0.4 mmol), n-Bu_4NI (0.01 mmol) and CH_3CN/H_2O (5:1, 12 ml) were combined and added. The flask was equipped with graphite rod (d: 6.0 mm) anode and graphite rod cathode (distance between electrodes (5 - 10 mm)). The reaction mixture was stirred and electrolyzed at a constant current of 5 mA under room temperature for 5 h. After completion of the reaction, the solution was concentrated in vacuum. The residue was purified by flash column chromatography using a mixture of petroleum ether and ethyl acetate (10:1) as eluent to give the desired

product **3**.

3. Preliminary mechanistic studies

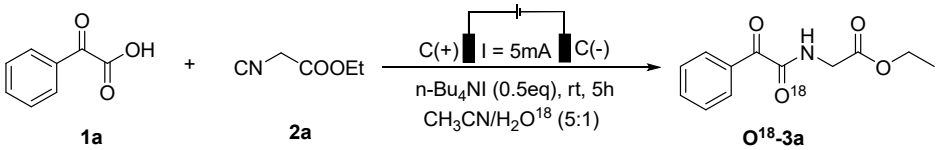
3.1 The reaction of 1a and 2a was carried out in the absence of H_2O.



1a **2a** **3a** (trace)

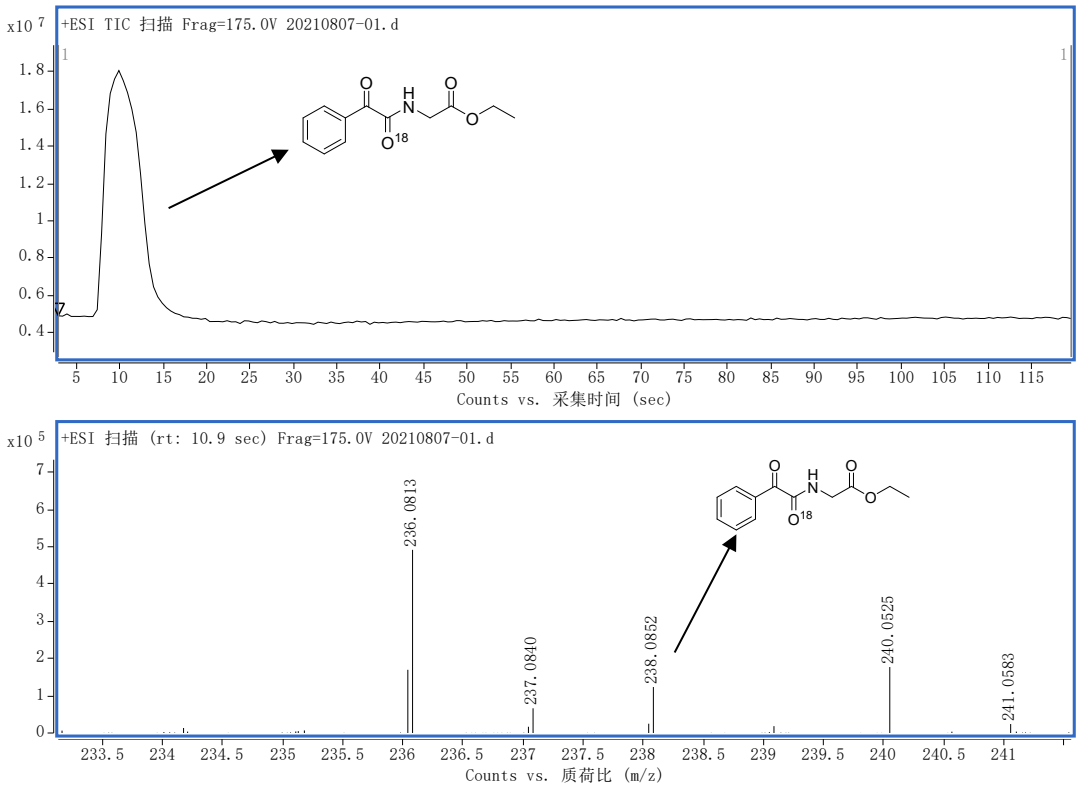
In an oven-dried undivided three-necked flask (25 mL) equipped with a stir bar, α-oxocarboxylic acid **1** (0.2 mmol), isocyanide **2** (0.4 mmol), n-Bu_4NI (0.01 mmol), 4Å Ms and CH_3CN (10 mL) were combined and added. The flask was equipped with graphite rod (d: 6.0 mm) anode and graphite rod cathode (distance between electrodes (5 - 10 mm)). The reaction mixture was stirred and electrolyzed at a constant current of 5 mA under room temperature for 5 h. After completion of the reaction, the solution was concentrated in vacuum, only a trace amount of the desired product **3a** was detected.

3.2 The reaction of 1a and 2a was carried out under H_2O^{18}.

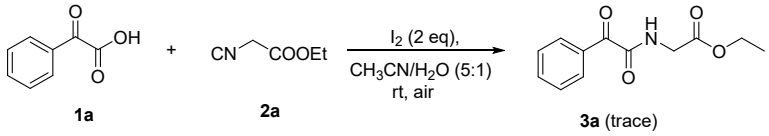


1a **2a** **O^{18}-3a**

In an oven-dried undivided three-necked flask (25 mL) equipped with a stir bar, α-oxocarboxylic acid **1a** (0.2 mmol), isocyanide **2a** (0.4 mmol), n-Bu_4NI (0.01 mmol), $CH_3CN/H_2{}^{18}O$ (5:1, 12 ml) were combined and added. The flask was equipped with graphite rod (d: 6.0 mm) anode and graphite rod cathode (distance between electrodes (5 - 10 mm)). The reaction mixture was stirred and electrolyzed at a constant current of 5 mA under room temperature for 5 h. After completion of the reaction, the solution was concentrated in vacuum. The residue was purified by flash column chromatography using a mixture of petroleum ether and ethyl acetate as eluent to give the desired product **^{18}O-3a** (33.1mg, 70%).

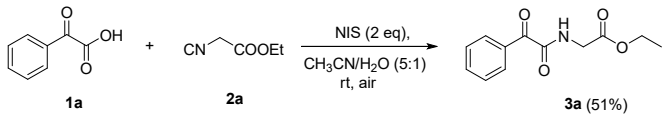


3.3 The reaction of 1a and 2a in the presence of I_2.



In an oven-dried undivided three-necked flask (25 mL) equipped with a stir bar, α-oxocarboxylic acid **1a** (0.2 mmol), isocyanide **2a** (0.4 mmol), I_2 (0.4 mmol), CH_3CN/H_2O (5:1, 2.4 ml) were combined and added. The reaction mixture was stirred at room temperature for 24 h. After completion of the reaction, the solution was concentrated in vacuum. Only a trace amount of product **3a** was detected.

3.4 The reaction of 1a and 2a in the presence of NIS.



In an oven-dried undivided three-necked flask (25 mL) equipped with a stir bar, α-oxocarboxylic acid **1a** (0.2 mmol), isocyanide **2a** (0.4 mmol), NIS (0.4 mmol), CH_3CN/H_2O (5:1, 2.4 ml) were combined and added. The reaction mixture was stirred at room temperature for 24 h. After completion of the reaction, the solution was

concentrated in vacuum. The residue was purified by flash column chromatography using a mixture of petroleum ether and ethyl acetate as eluent to give the desired product **3a** (23.8mg, 51%).

3.5 Cyclic voltammetry (CV) tests

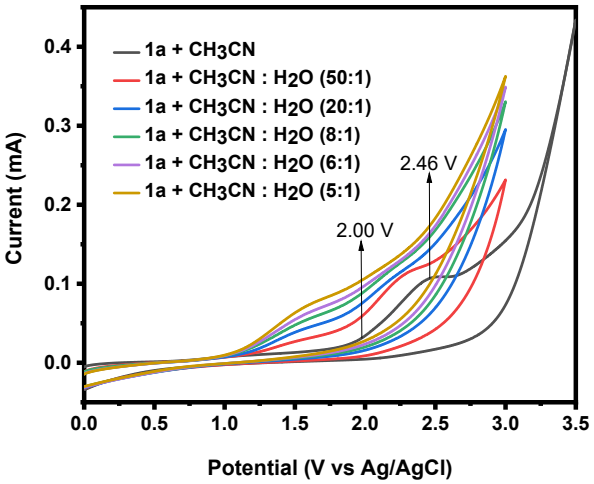


Figure S1. Conditions: glass carbon as work electrode, Pt plate (1.5 x 1.5 cm^2) as conter electrode Ag/AgCl (KCl) as reference electrode in 0.1 M $LiClO_4$ with different solvent under **1a** (0.2 mM), the mixed solvent of CH_3CN/H_2O, scan rate: 100 mV s^{-1}.

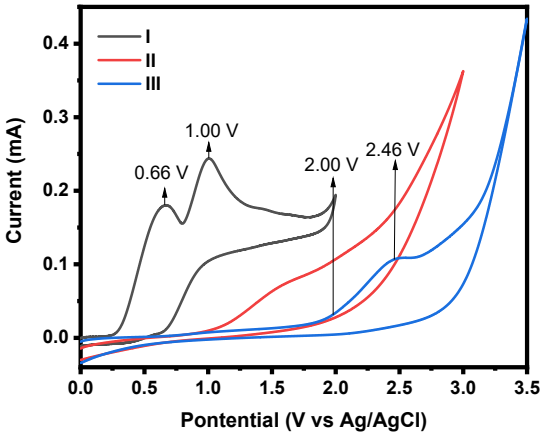


Figure S2. Conditions: glass carbon as work electrode, Pt plate (1.5 x 1.5 cm^2) as conter electrode and Ag/AgCl (KCl) as reference electrode in 0.1 M $LiClO_4$ at 100 mV s^{-1} : (I) 0.1 mM of n-Bu_4NI, anhydrous CH_3CN, (II) 0.2 mM of PhCOCOOH, CH_3CN/H_2O (5 : 1) and (III) 0.2 mM of PhCOCOOH, anhydrous CH_3CN.

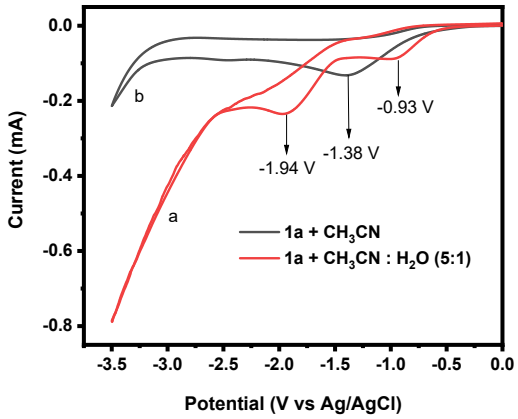
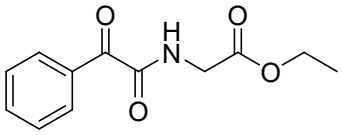


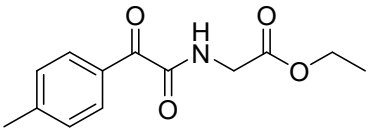
Figure S3. Cyclic voltammograms of 0.2 mM PhCOCOOH in 0.1 M $LiClO_4$ in (a) CH_3CN/H_2O (5 : 1), and (b) anhydrous CH_3CN using glass carbon as the working electrode, Pt plate (1.5 x 1.5 cm^2) and Ag/AgCl (KCl) as the counter and reference electrodes at 100 mV s^{-1}.

4. Characterization data of products 3a – 3u



ethyl (2-oxo-2-phenylacetyl)glycinate

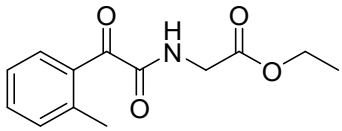
Compound **3a** was obtained in 78% yield (36.7 mg) according to the general procedure (petroleum ether/EtOAc, 10:1). Yellow oil. ^1H NMR ($CDCl_3$, 500 MHz, ppm): δ 8.32 (d, J = 8.3 Hz, 2H), 7.64 - 7.60 (m, 2H), 7.48 (t, J = 7.7 Hz, 2H), 4.26 (q, J = 7.1 Hz, 2H), 4.17 (d, J = 5.6 Hz, 2H), 1.31 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz, ppm): δ 186.9, 169.0, 161.9, 134.5, 133.1, 131.2, 128.5, 61.8, 41.2, 14.1; MS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{14}NO_4$ 236.0923; found 236.0856.



ethyl (2-oxo-2-(p-tolyl)acetyl)glycinate

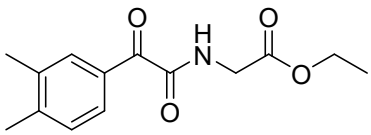
Compound **3b** was obtained in 71% yield (35.4 mg) according to the general procedure (petroleum ether/EtOAc, 5:1). Yellow solid. mp = 80.7 - 81.2 °C; ^1H NMR ($CDCl_3$, 500 MHz, ppm): δ 8.25 (d, J = 8.3 Hz, 2H), 7.56 (s, 1H), 7.28 (d, J = 8.3 Hz, 2H), 4.26 (q, J = 7.1 Hz, 2H), 4.16 (d, J = 5.6 Hz, 2H), 2.42 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz, ppm): δ 186.4, 169.0, 162.1, 145.8, 131.4, 130.7, 129.3, 61.8,

41.2, 21.9, 14.2; MS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{16}NO_4$ 250.1079; found 250.0975.



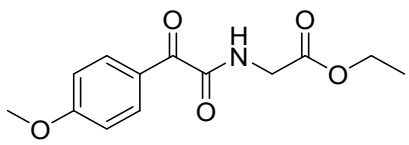
ethyl (2-oxo-2-(o-tolyl)acetyl)glycinate

Compound **3c** was obtained in 64% yield (31.9 mg) according to the general procedure (petroleum ether/EtOAc, 5:1). Yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 7.93 - 7.91 (m, 1H), 7.54 (s, 1H), 7.45 (t, J = 7.5 Hz, 1H), 7.30 - 7.27 (m, 2H), 4.26 (q, J = 7.1 Hz, 2H), 4.16 (d, J = 5.6 Hz, 2H), 2.51 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz, ppm): δ 190.4, 169.0, 162.3, 140.3, 132.9, 132.5, 132.1, 131.7, 125.4, 61.8, 41.4, 20.9, 14.2; MS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{16}NO_4$ 250.1079; found 250.1020.



ethyl (2-(3,4-dimethylphenyl)-2-oxoacetyl)glycinate

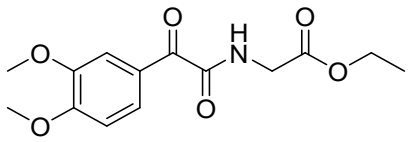
Compound **3d** was obtained in 76% yield (39.8 mg) according to the general procedure (petroleum ether/EtOAc, 10:1). Yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 8.10 - 8.08 (m, 2H), 7.56 (s, 1H), 7.23 (d, J = 8.4 Hz, 1H), 4.26 (q, J = 7.2 Hz, 2H), 4.16 (d, J = 5.6 Hz, 2H), 2.33 (s, 3H), 2.31 (s, 3H), 1.31 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz, ppm): δ 186.7, 169.0, 162.3, 144.6, 137.0, 132.0, 131.0, 129.9, 129.1, 61.8, 41.2, 20.3, 19.7, 14.2; MS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{16}NO_5$ 264.1236; found 264.1185.



ethyl (2-(4-methoxyphenyl)-2-oxoacetyl)glycinate

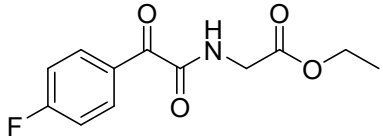
Compound **3e** was obtained in 75% yield (39.7 mg) according to the general procedure (petroleum ether/EtOAc, 5:1). Yellow solid. mp = 99.7 - 100.2 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 8.39 (d, J = 8.8 Hz, 2H), 7.61 (s, 1H), 6.95 (d, J = 8.8 Hz, 2H), 4.26

(q, J = 7.1 Hz, 2H), 4.15 (d, J = 5.6 Hz, 2H), 3.88 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz, ppm): δ 184.9, 169.0, 164.8, 162.5, 133.9, 126.2, 113.9, 61.7, 55.6, 41.2, 14.1; MS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{14}NO_4$ 266.1028; found 266.0972.



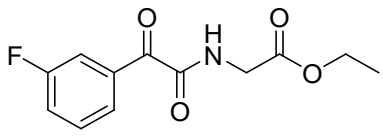
ethyl (2-(3,4-dimethoxyphenyl)-2-oxoacetyl)glycinate

Compound **3f** was obtained in 60% yield (35.4 mg) according to the general procedure (petroleum ether/EtOAc, 3:1). Yellow solid. mp = 81.5 - 81.9 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 8.24 - 8.21 (m, 1H), 7.85 (d, J = 1.9 Hz, 1H), 7.60 (s, 1H), 6.92 (d, J = 8.6 Hz, 1H), 4.26 (q, J = 7.2 Hz, 2H), 4.16 (d, J = 5.6 Hz, 2H), 3.97 (s, 3H), 3.95 (s, 3H), 1.31 (t, J = 7.4 Hz, 3H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz, ppm): δ 184.7, 169.0, 162.4, 154.8, 148.9, 127.4, 126.2, 112.5, 110.2, 61.8, 56.2, 56.0, 41.2, 14.2; MS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{18}NO_6$ 296.1134; found 296.1083.



ethyl (2-(4-fluorophenyl)-2-oxoacetyl)glycinate

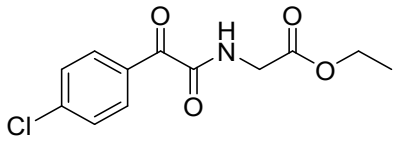
Compound **3g** was obtained in 66% yield (33.4 mg) according to the general procedure (petroleum ether/EtOAc, 10:1). Yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 8.44 - 8.41 (m, 2H), 7.64 (s, 1H), 7.17 - 7.14 (m, 2H), 4.29 - 4.24 (m, 2H), 4.16 (d, J = 5.7 Hz, 2H), 1.33 - 1.30 (m, 3H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz, ppm): δ 185.0, 168.9, 166.7 (d, J = 256.4 Hz), 134.2 (d, J = 9.6 Hz), 129.6 (d, J = 2.9 Hz), 115.8 (d, J = 21.8 Hz), 61.8, 41.2, 14.1; ^{19}F NMR ($CDCl_3$, 500 MHz): -101.9; MS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{13}FNO_4$ 254.0829; found 254.0765.



ethyl (2-(3-fluorophenyl)-2-oxoacetyl)glycinate

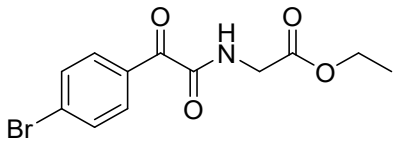
Compound **3h** was obtained in 62% yield (31.3 mg) according to the general procedure

(C/Pt, petroleum ether/EtOAc, 10:1). Yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 8.17 (d, J = 7.8 Hz, 1H), 8.06 - 8.04 (m, 1H), 7.59 (s, 1H), 7.49 - 7.45 (m, 1H), 7.36 - 7.32 (m, 1H), 4.27 (q, J = 7.2 Hz, 2H), 4.17 (d, J = 5.6 Hz, 2H), 1.32 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz, ppm): δ 185.5, 168.8, 162.4(d, J = 246.2 Hz), 161.3, 134.9 (d, J = 7.0 Hz), 130.2 (d, J = 7.5 Hz), 127.1(d, J = 3.3 Hz), 121.6 (d, J = 21.3 Hz), 117.8 (d, J = 23.1 Hz), 61.9, 41.3, 14.1; ^{19}F NMR ($CDCl_3$, 500 MHz): -111.5; MS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{13}FNO_4$ 254.0829; found 254.0766.



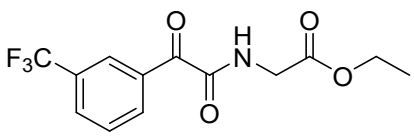
ethyl (2-(4-chlorophenyl)-2-oxoacetyl)glycinate

Compound **3i** was obtained in 70% yield (37.8 mg) according to the general procedure (petroleum ether/EtOAc, 10:1). Yellow solid. mp = 51.8 - 52.2 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 8.34 - 8.30 (m, 2H), 7.60 (s, 1H), 7.47 - 7.43 (m, 2H), 4.26 (q, J = 7.1 Hz, 2H), 4.16 (d, J = 5.6 Hz, 2H), 1.31 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz, ppm): δ 185.4, 168.8, 161.5, 141.3, 132.7, 131.5, 128.9, 61.9, 41.2, 14.2; MS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{13}ClNO_4$ 270.0533; found 270.0475.



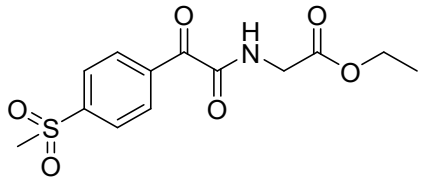
ethyl (2-(4-bromophenyl)-2-oxoacetyl)glycinate

Compound **3j** was obtained in 62% yield (28.3 mg) according to the general procedure (petroleum ether/EtOAc, 10:1). Yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 8.23 (m, J = 8.6 Hz, 2H), 7.64 - 7.62 (m, 3H), 4.26 (q, J = 7.2 Hz, 2H), 4.15 (d, J = 5.6 Hz, 2H), 1.31 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz, ppm): δ 185.7, 168.9, 161.4, 132.7, 131.9, 131.9, 130.3, 61.9, 41.2, 14.2; MS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{13}BrNO_4$ 314.0028; found 313.9967.



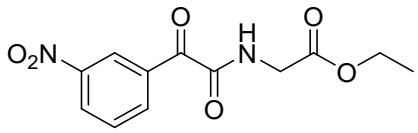
ethyl (2-oxo-2-(3-(trifluoromethyl)phenyl)acetyl)glycinate

Compound **3k** was obtained in 63% yield (38.1 mg) according to the general procedure (C/Pt, petroleum ether/EtOAc, 10:1). Yellow solid. mp = 50.8 - 51.0 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 8.63 (s, 1H), 8.56 (d, J = 7.7 Hz, 1H), 7.88 (t, J = 7.8 Hz, 1H), 7.65 - 7.62 (m, 2H), 4.27 (q, J = 7.1 Hz, 2H), 4.18 (d, J = 5.6 Hz, 2H), 1.32 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz, ppm): δ 185.4, 168.8, 161.1, 134.4, 133.7, 131.2 (d, J = 33.0 Hz), 130.8 (q, J = 3.6 Hz), 129.2, 128.1 (q, J = 3.8 Hz), 123.5 (d, J = 270.9 Hz), 61.9, 41.3, 14.1; ^{19}F NMR ($CDCl_3$, 500 MHz): -62.9; MS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{13}F_3NO_4$ 304.0797; found 304.0745.



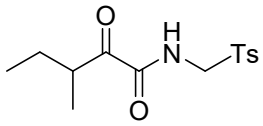
ethyl (2-(4-(methylsulfonyl)phenyl)-2-oxoacetyl)glycinate

Compound **3l** was obtained in 70% yield (43.7 mg) according to the general procedure (petroleum ether/EtOAc, 1:1). Yellow solid. mp = 112.1 - 112.5 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 7.98 - 7.97 (m, 4H), 7.11 (s, 1H), 4.29 - 4.23 (m, 4H), 3.08 (s, 3H), 1.32 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz, ppm): δ 169.8, 165.9, 143.1, 138.7, 128.3, 127.7, 61.8, 44.3, 41.9, 14.2; MS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{16}NO_6S$ 314.0698; found 314.0665.



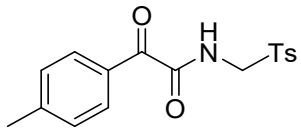
ethyl (2-(4-nitrophenyl)-2-oxoacetyl)glycinate

Compound **3m** was obtained in 41% yield (22.9 mg) according to the general procedure (petroleum ether/EtOAc, 10:1). Yellow solid. mp = 71.2 - 71.5 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 9.19 - 9.18 (m, 1H), 8.71 - 8.69 (m, 1H), 8.49 - 8.47 (m, 1H), 7.72 - 7.69 (m, 2H), 4.28 (q, J = 7.2 Hz, 2H), 4.19 (d, J = 5.7 Hz, 2H), 1.33 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz, ppm): δ 184.6, 168.7, 160.7, 148.2, 136.8, 134.3, 129.8, 128.5, 126.1, 62.0, 41.3, 14.1; MS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{13}N_2O_6$ 281.0774; found 281.0709.



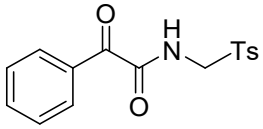
3-methyl-2-oxo-N-(tosylmethyl)pentanamide

Compound **3n** was obtained in 47% yield (27.8 mg) according to the general procedure (C/Pt, petroleum ether/EtOAc, 10:1). Yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 7.76 (d, J = 8.2 Hz, 2H), 7.72 (s, 1H), 7.34 (d, J = 8.2 Hz, 2H), 4.74 - 4.64 (m, 2H), 3.25 - 3.18 (m, 1H), 2.43 (s, 3H), 1.62 - 1.53 (m, 1H), 1.33 - 1.25 (m, 1H), 0.98 (d, J = 7.0 Hz, 3H), 0.81 (t, J = 7.5 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz, ppm): δ 200.3, 159.0, 145.7, 133.4, 130.0, 129.0, 60.0, 40.6, 25.2, 21.7, 14.8, 11.4; MS (ESI) m/z: [M + H]$^+$ Calcd for $C_{14}H_{20}NO_4S$ 298.1113; found 298.1052.



2-oxo-2-(p-tolyl)-N-(tosylmethyl)acetamide

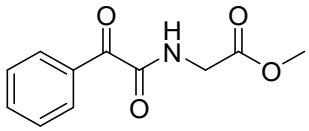
Compound **3o** was obtained in 71% yield (47.1 mg) according to the general procedure (petroleum ether/EtOAc, 5:1). Yellow solid. mp = 96.9 - 97.0 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 7.97 - 7.95 (m, 3H), 7.81 (d, J = 8.0 Hz, 2H), 7.32 (d, J = 7.8 Hz, 2H), 7.22 (d, J = 7.9 Hz, 2H), 4.78 (d, J = 7.0 Hz, 2H), 2.41 (d, J = 7.3 Hz, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz, ppm): δ 185.6, 161.2, 146.3, 145.6, 133.5, 131.2, 130.1, 130.1, 129.3, 129.1, 60.1, 21.9, 21.7; MS (ESI) m/z: [M + H]$^+$ Calcd for $C_{17}H_{18}NO_4S$ 332.0957; found 332.0903.



2-oxo-2-phenyl-N-(tosylmethyl)acetamide

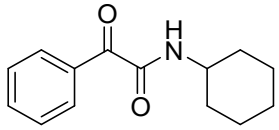
Compound **3p** was obtained in 72% yield (45.5 mg) according to the general procedure (petroleum ether/EtOAc, 5:1). White solid. mp = 99.0 - 99.4 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 7.99 - 7.97 (m, 2H), 7.81 (s, 1H), 7.74 (d, J = 8.3 Hz, 2H), 7.37 - 7.34 (m, 1H), 7.26 (d, J = 8.0 Hz, 2H), 4.71 (d, J = 7.0 Hz, 2H), 2.35 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz, ppm): δ 186.1, 160.8, 145.7, 134.9, 133.4, 132.5, 131.1, 130.1,

129.1, 128.6, 60.0, 21.7; MS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{16}NO_4S$ 318.0800; found 318.0744.



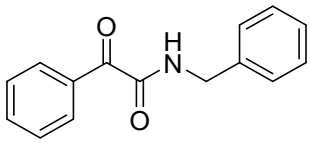
methyl (2-oxo-2-phenylacetyl)glycinate

Compound **3q** was obtained in 68% yield (30.1 mg) according to the general procedure (petroleum ether/EtOAc, 5:1). Yellow oil. ^1H NMR ($CDCl_3$, 500 MHz, ppm): δ 8.34 - 8.33 (m, 2H), 7.64 (t, J = 7.5 Hz, 1H), 7.55 (s, 1H), 7.47 (t, J = 7.8 Hz, 2H), 4.19 (d, J = 5.6 Hz, 2H), 3.81 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz, ppm): δ 186.8, 169.4, 161.8, 134.6, 133.1, 131.2, 128.6, 52.6, 41.1; MS (ESI) m/z: $[M + H]^+$ Calcd for $C_{11}H_{12}NO_4$ 222.0766; found 222.0694.



N-cyclohexyl-2-oxo-2-phenylacetamide

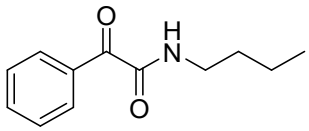
Compound **3r** was obtained in 55% yield (25.4 mg) according to the general procedure (C/Pt, petroleum ether/EtOAc, 10:1). Yellow solid. mp = 104.8 - 105.1 °C; ^1H NMR ($CDCl_3$, 500 MHz, ppm): δ 8.33 (d, J = 8.2 Hz, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.47 (t, J = 7.7 Hz, 2H), 6.97 (s, 1H), 3.88 - 3.83 (m, 1H), 1.99 (d, J = 11.9 Hz, 2H), 1.78 - 1.75 (m, 2H), 1.67 - 1.64 (m, 1H), 1.45 - 1.38 (m, 2H), 1.31 - 1.19 (m, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz, ppm): δ 188.1, 160.9, 134.3, 133.5, 131.2, 128.5, 48.5, 32.7, 25.4, 24.8; MS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{18}NO_2$ 232.1338; found 232.1286.



N-benzyl-2-oxo-2-phenylacetamide

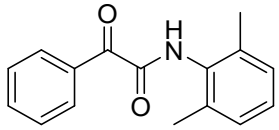
Compound **3s** was obtained in 86% yield (41.2 mg) according to the general procedure (petroleum ether/EtOAc, 15:1). Yellow solid. mp = 95.2 - 95.6 °C; ^1H NMR ($CDCl_3$, 500 MHz, ppm): δ 8.36 - 8.34 (m, 2H), 7.64 - 7.60 (m, 1H), 7.49 - 7.46 (m, 2H), 7.43(s, 1H), 7.37 - 7.28 (m, 5H), 4.57 (d, J = 6.1 Hz, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz,

ppm): δ 187.6, 161.6, 137.2, 134.5, 133.3, 131.3, 128.9, 128.5, 127.9, 127.9, 43.5; MS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{14}NO_2$ 240.1025; found 240.0951.



N-butyl-2-oxo-2-phenylacetamide

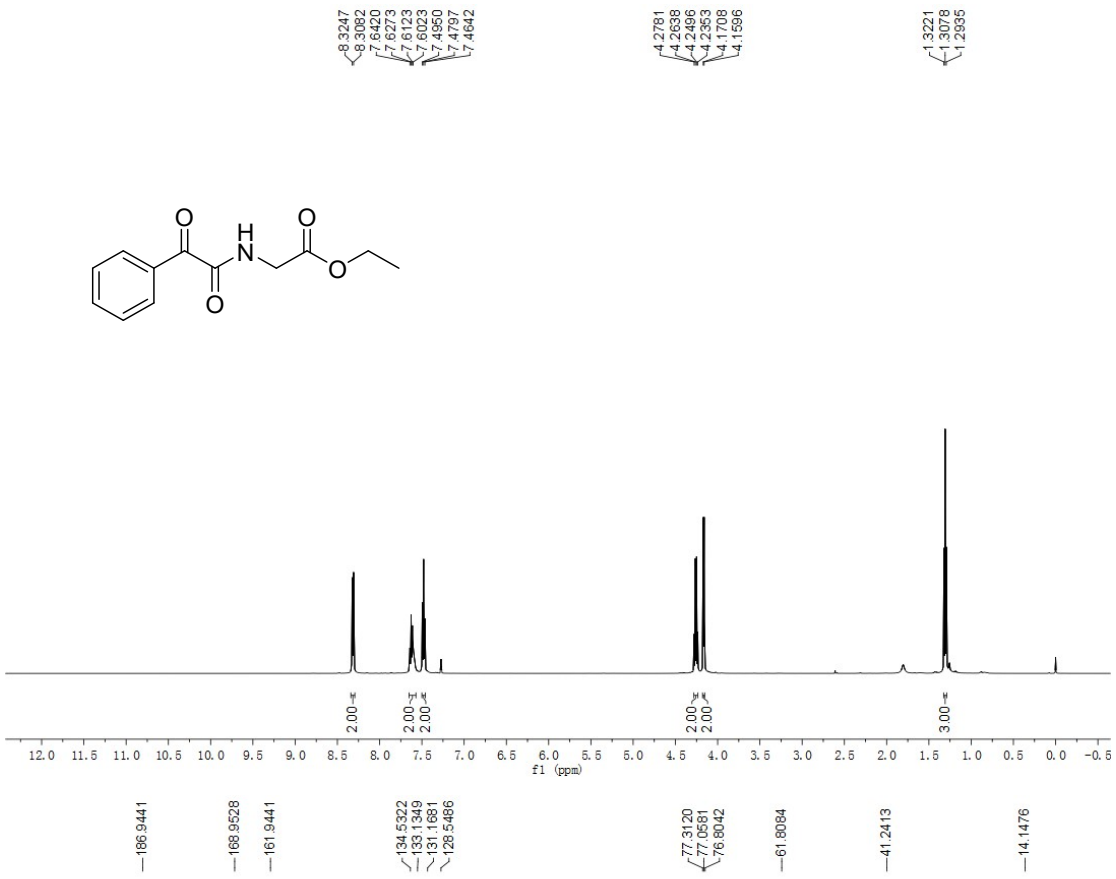
Compound **3u** was obtained in 71% yield (29.1 mg) according to the general procedure (petroleum ether/EtOAc, 15:1). Yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 8.34 - 8.32 (m, 2H), 7.64 - 7.60 (m, 1H), 7.49 - 7.45 (m, 2H), 7.14 - 7.11 (m, 1H), 3.40 (q, J = 6.9 Hz, 2H), 1.63 - 1.56 (m, 2H), 1.46 - 1.36 (m, 2H), 0.96 (t, J = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz, ppm): δ 187.9, 161.8, 134.3, 133.4, 131.2, 128.5, 39.2, 31.3, 20.1, 13.7; MS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{16}NO_2$ 206.1181; found 206.1112.



N-(2,6-dimethylphenyl)-2-oxo-2-phenylacetamide

Compound **3t** was obtained in 70% yield (35.4 mg) according to the general procedure (petroleum ether/EtOAc, 15:1). Yellow solid. mp = 111.0 - 111.3 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 8.41 - 8.40 (m, 3H), 7.65 (t, J = 7.8 Hz, 1H), 7.50 (t, J = 7.8 Hz, 2H), 7.18 - 7.11 (m, 3H), 2.29 (s, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz, ppm): δ 187.7, 159.9, 135.2, 134.7, 133.2, 132.5, 131.4, 128.7, 128.4, 127.8, 18.5; MS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{16}NO_2$ 254.1181; found 254.1123.

5. Copies of NMR Spectra for 3a−3u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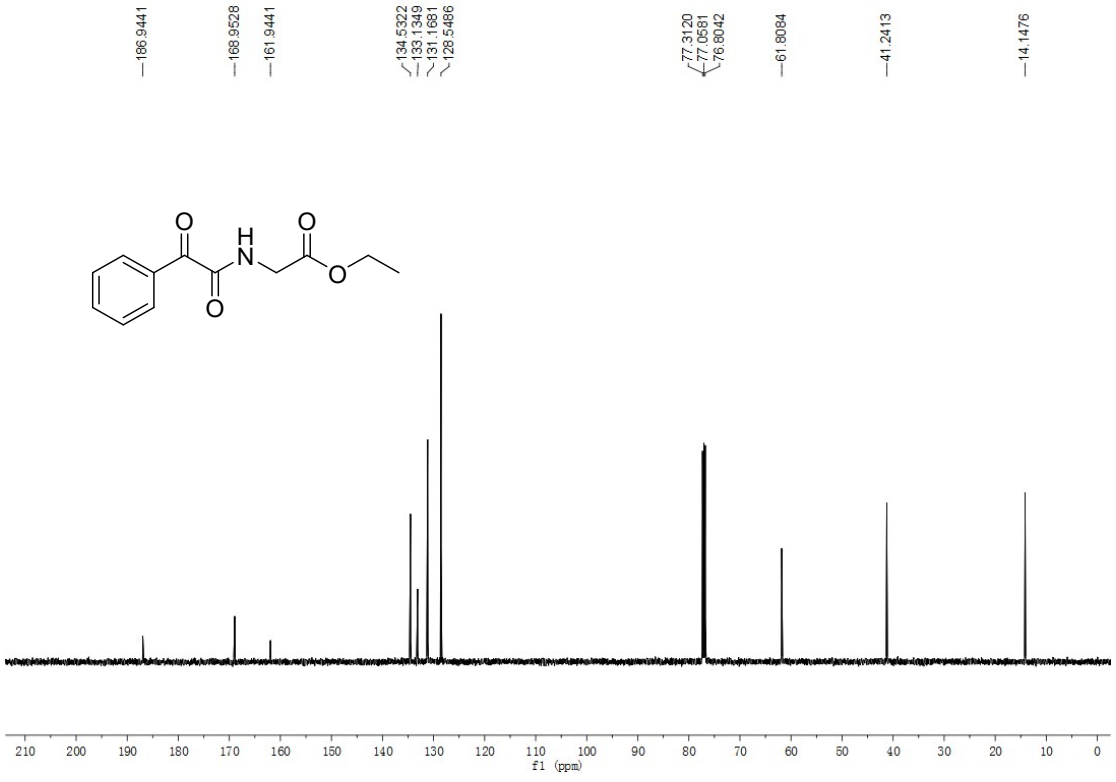
f1 (ppm)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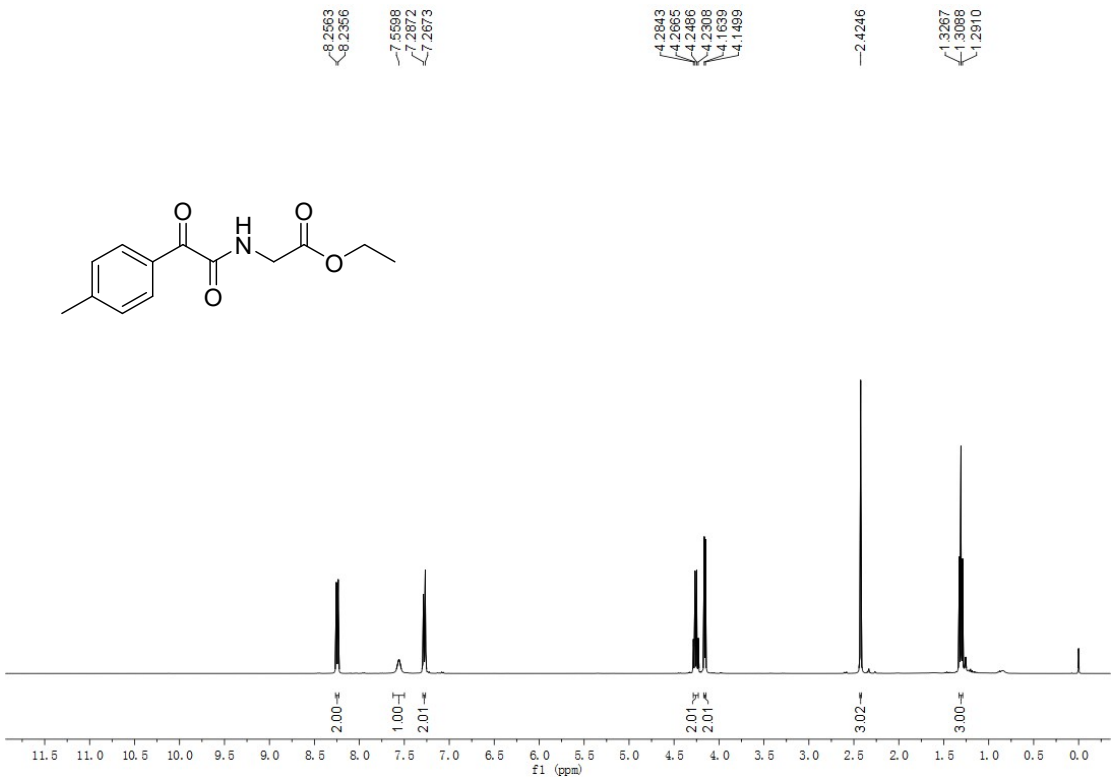
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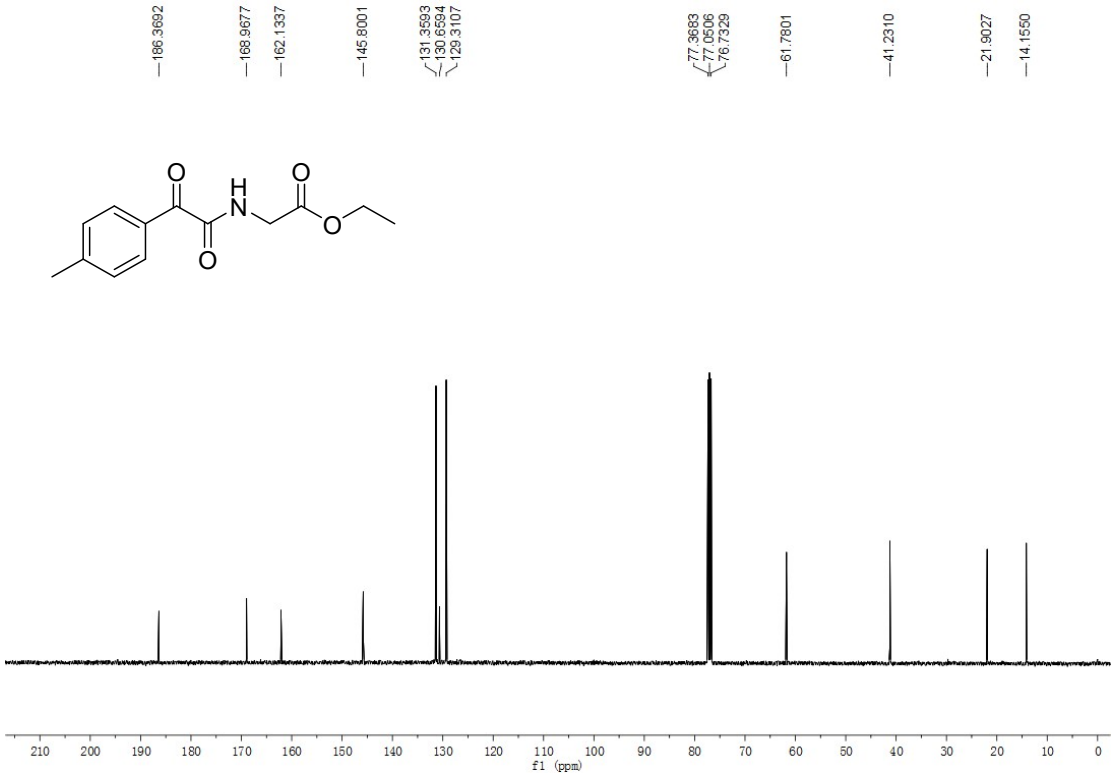
f1 (ppm)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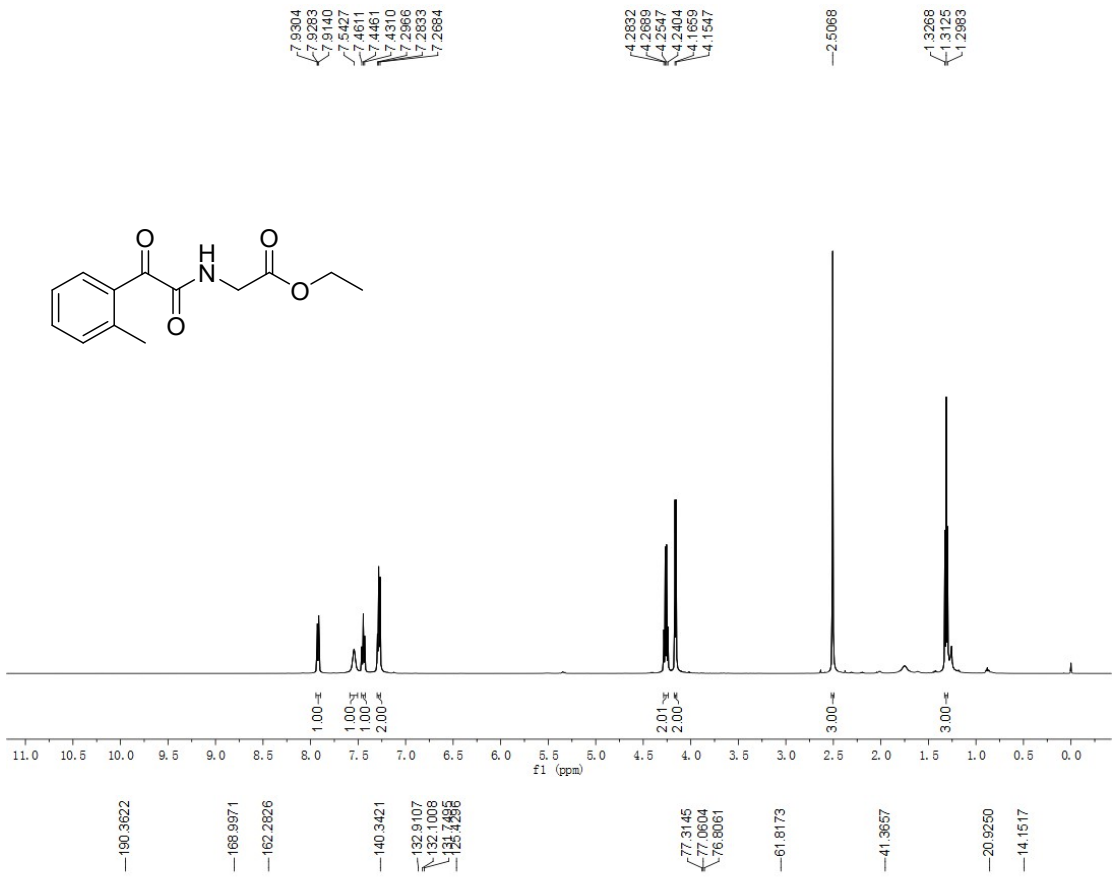
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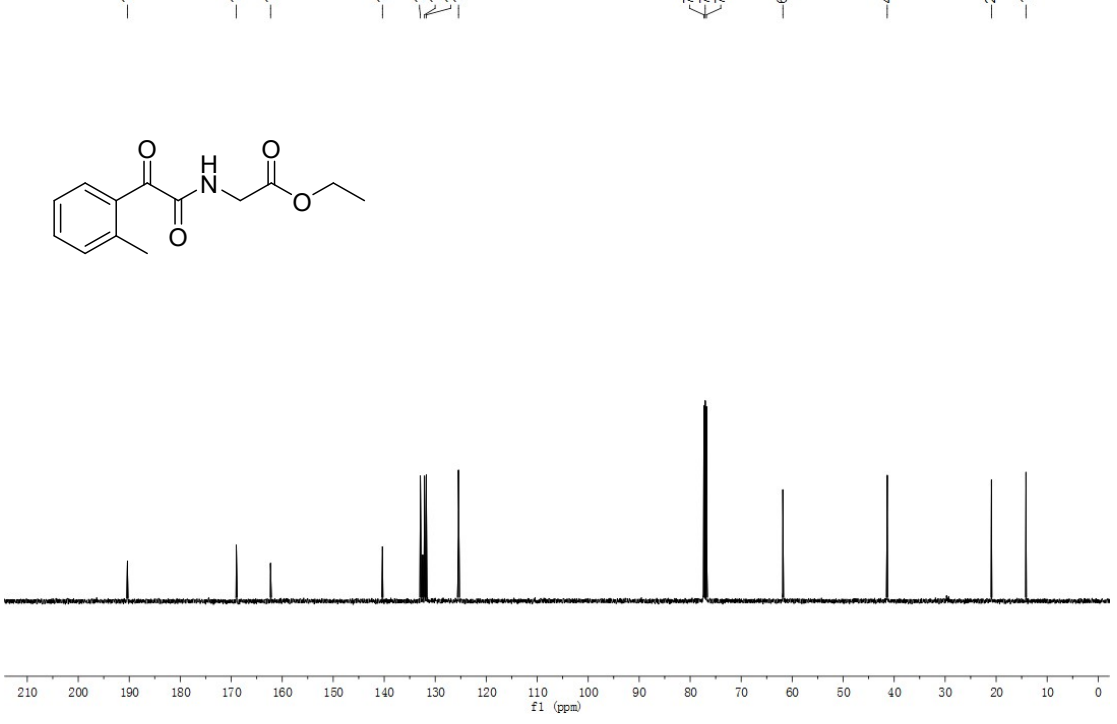
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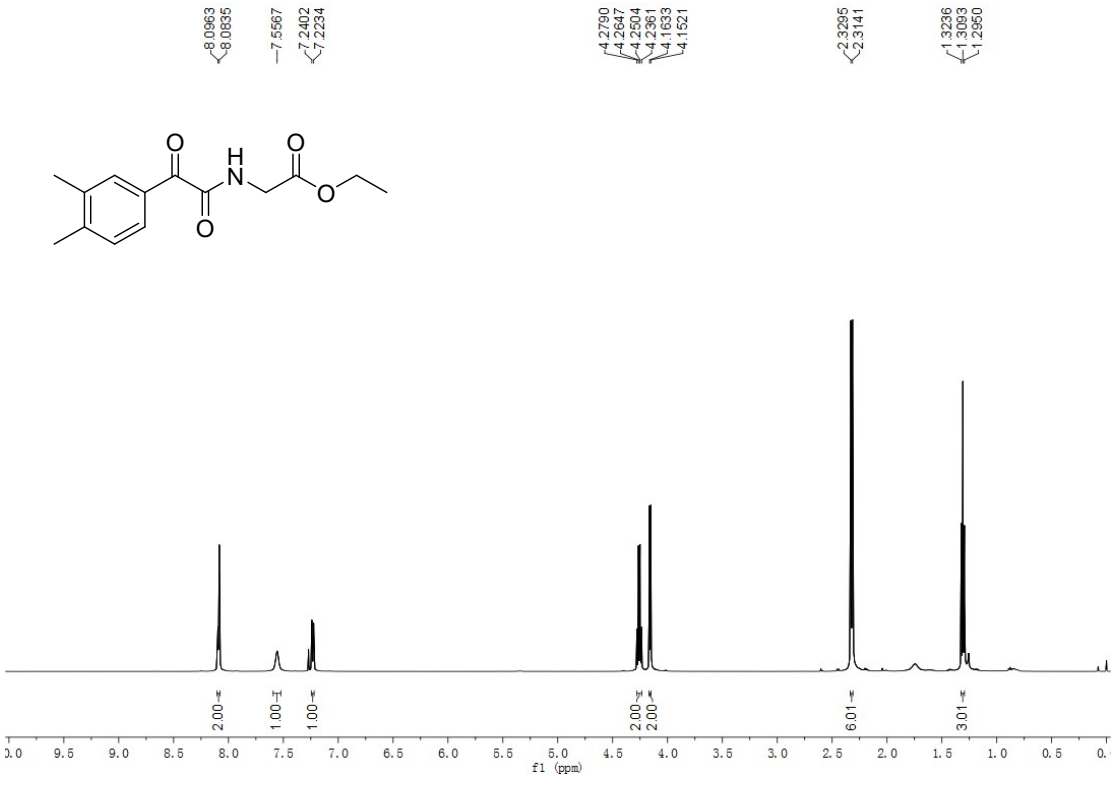
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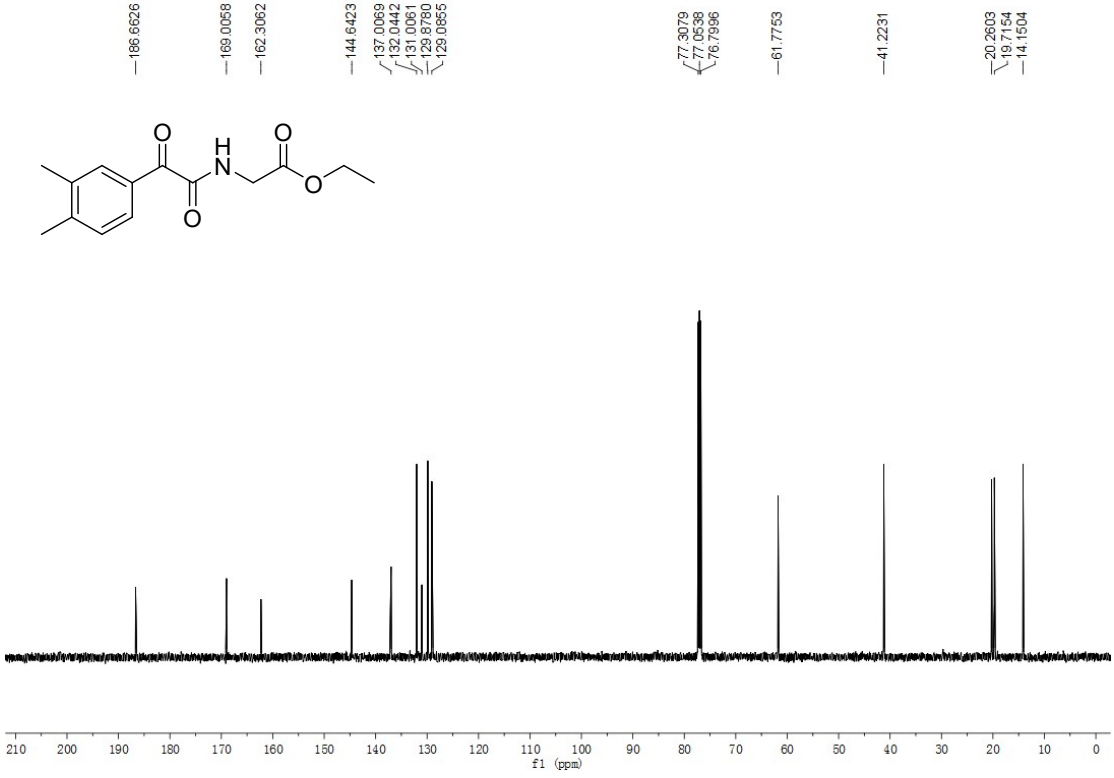
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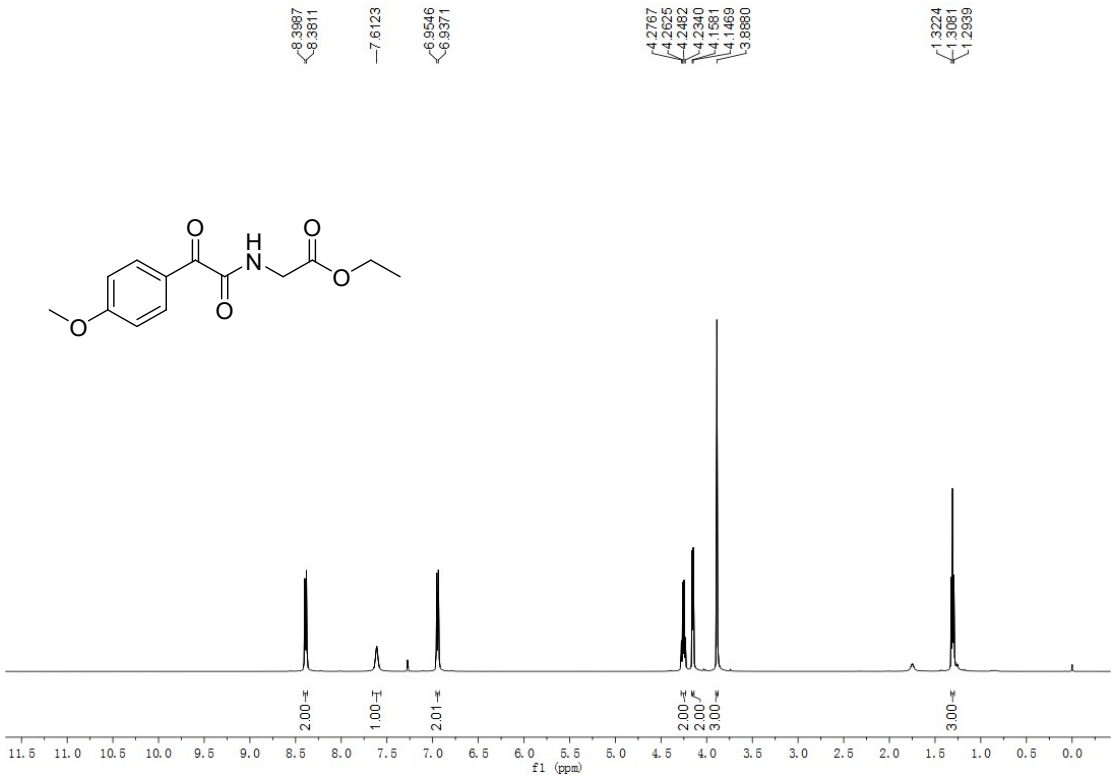
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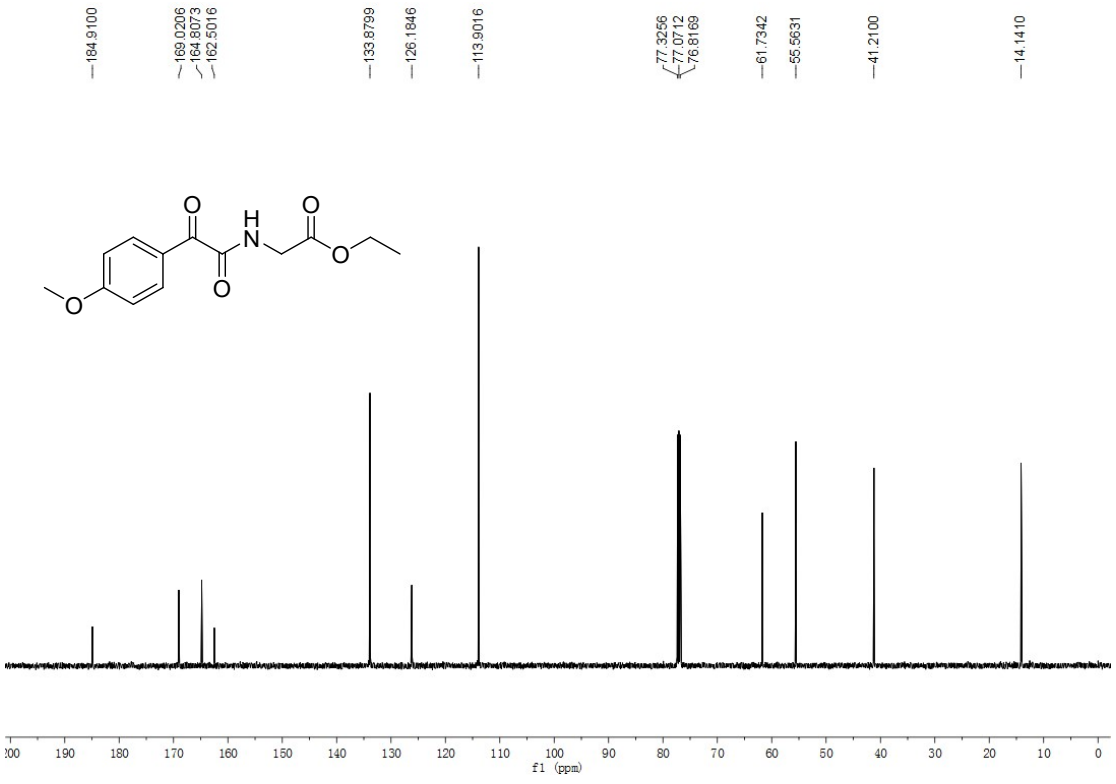
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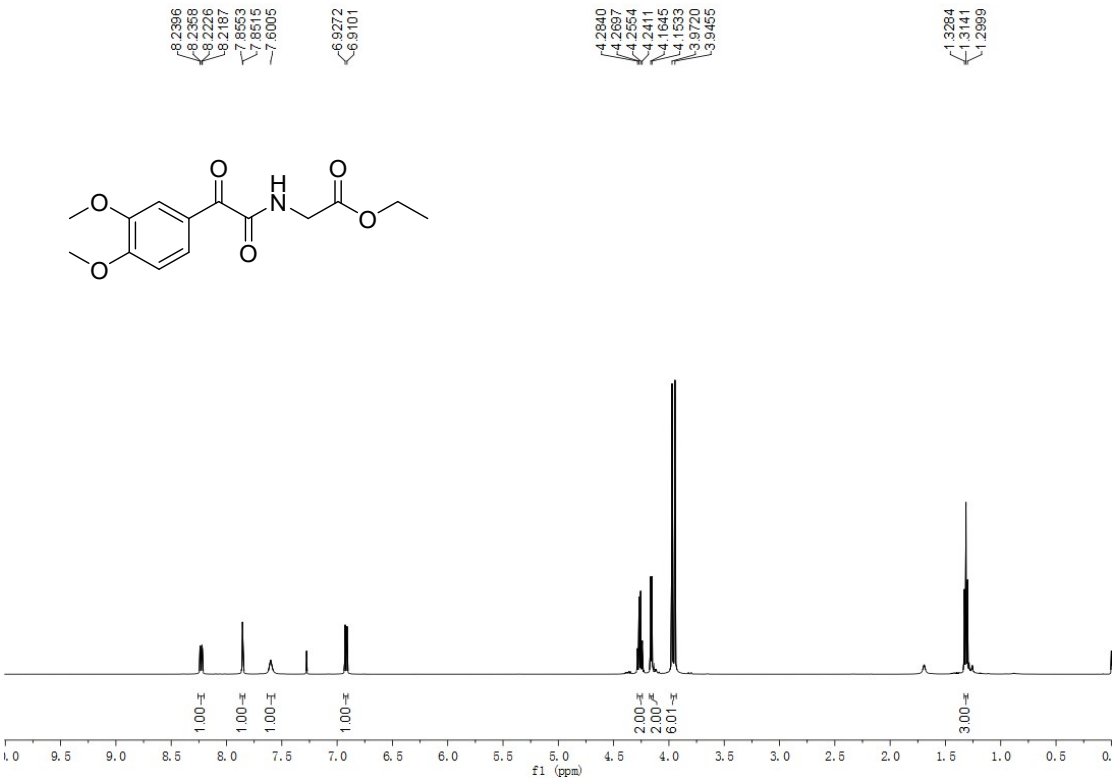
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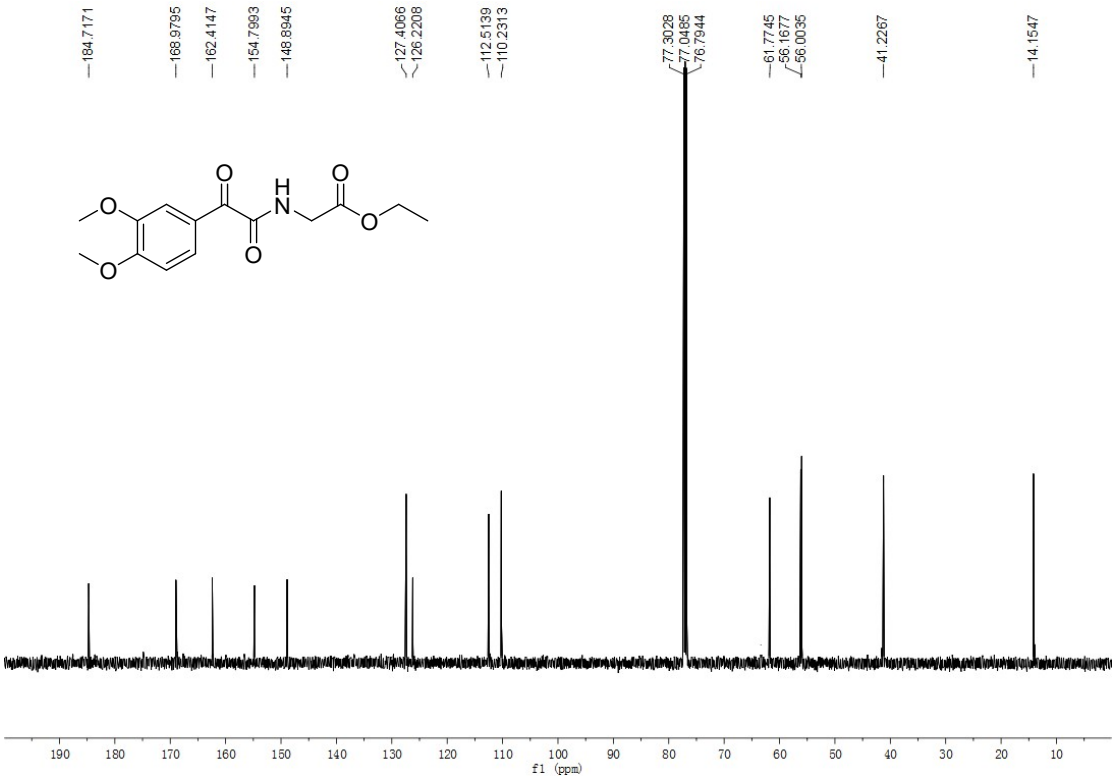
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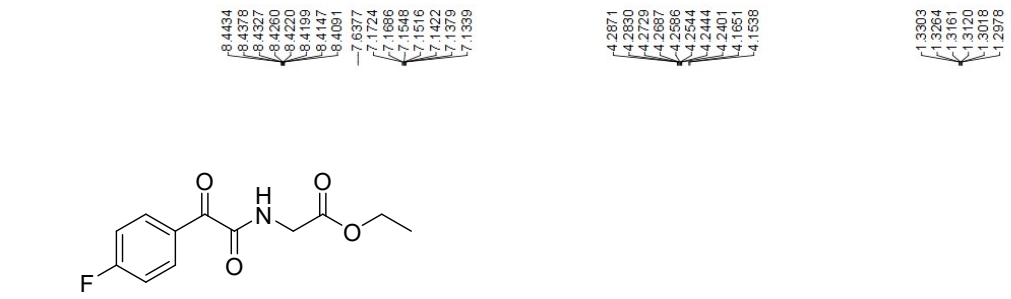
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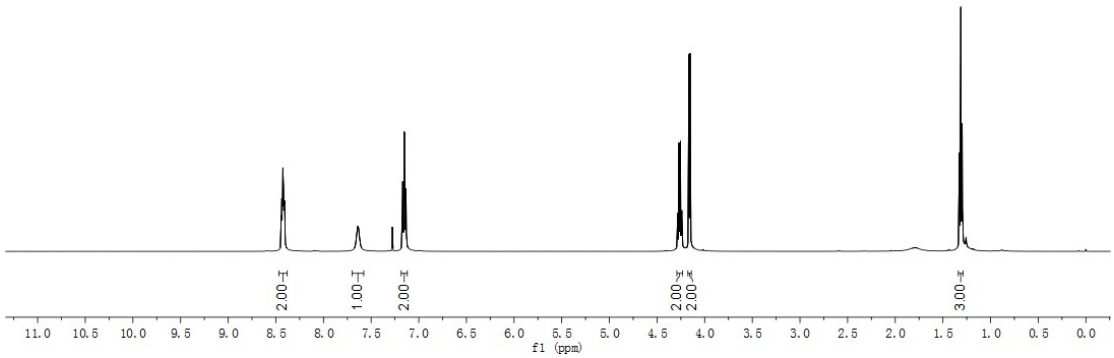
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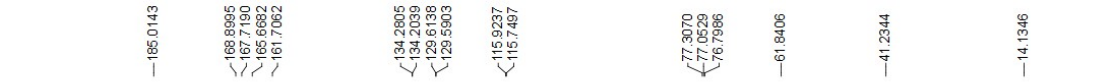
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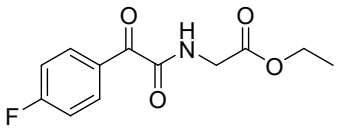
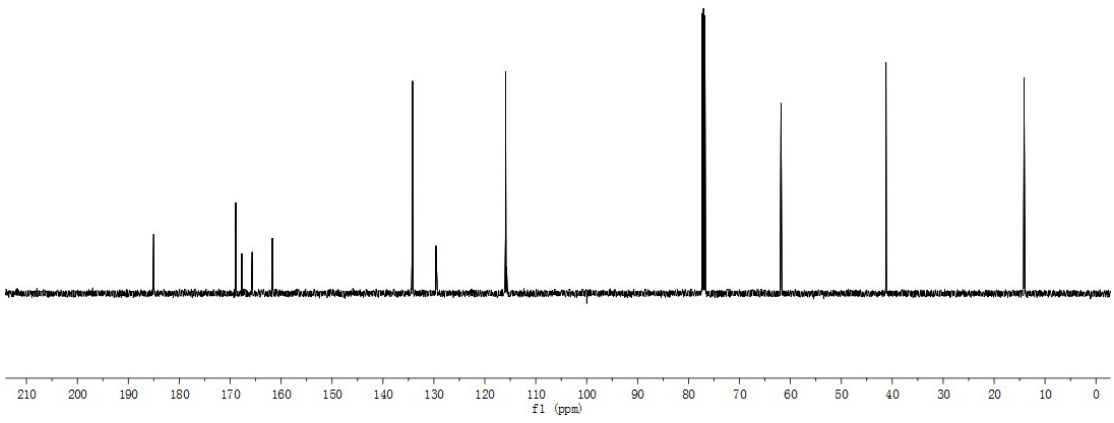
14.1346


O
H
N
O
O
O
F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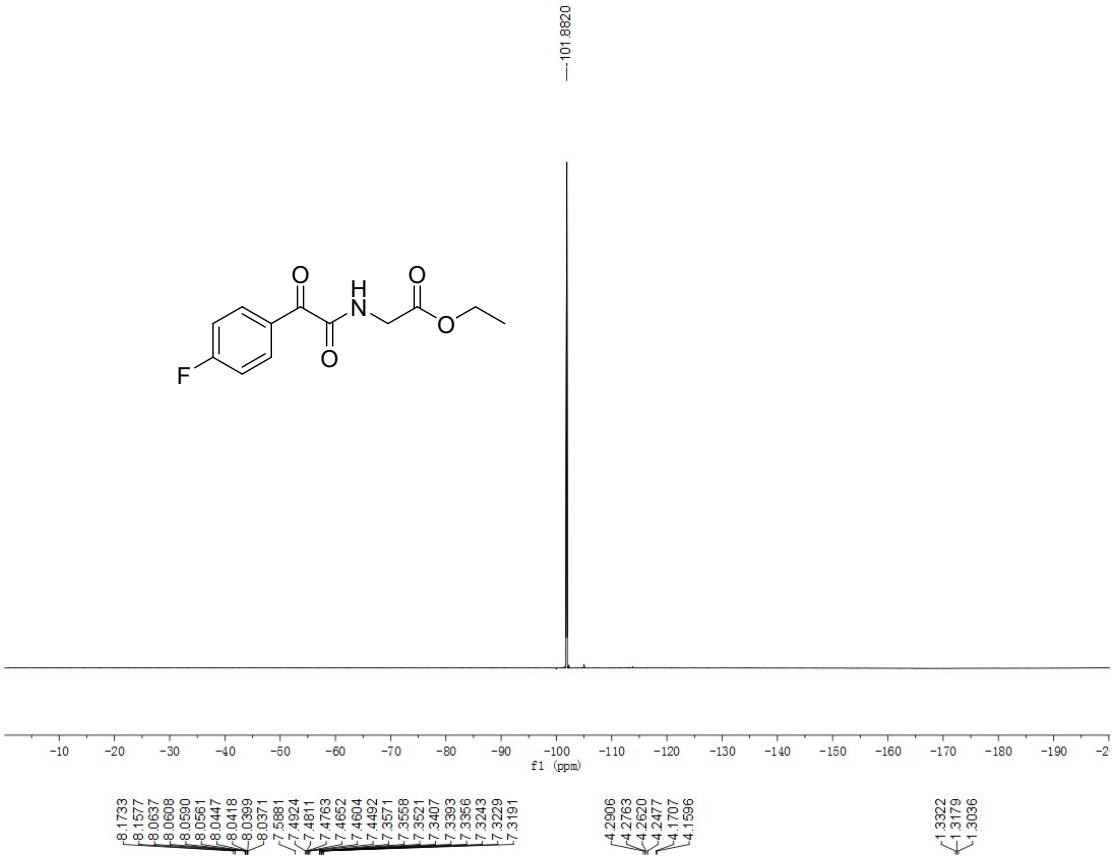
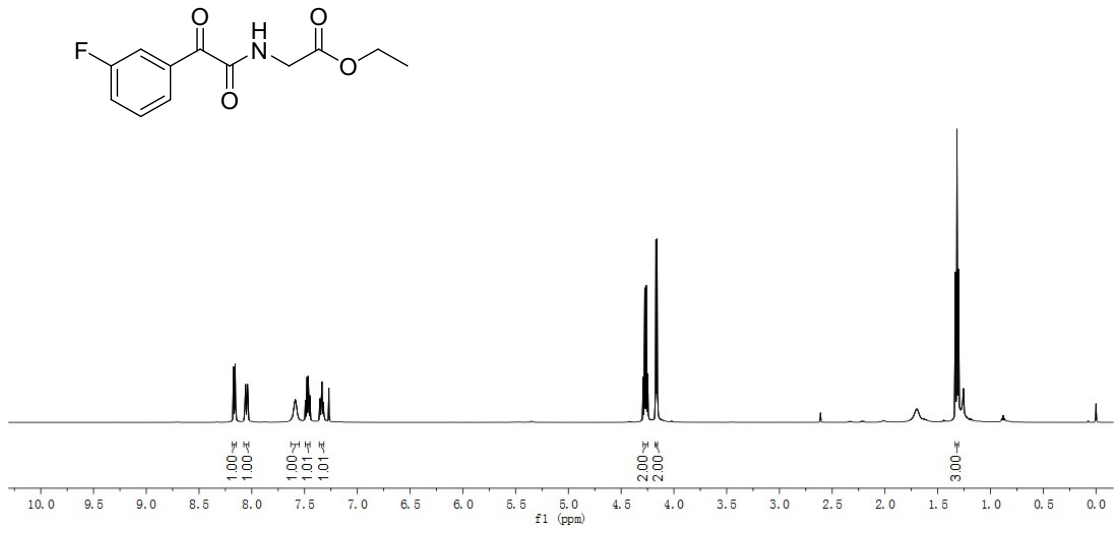
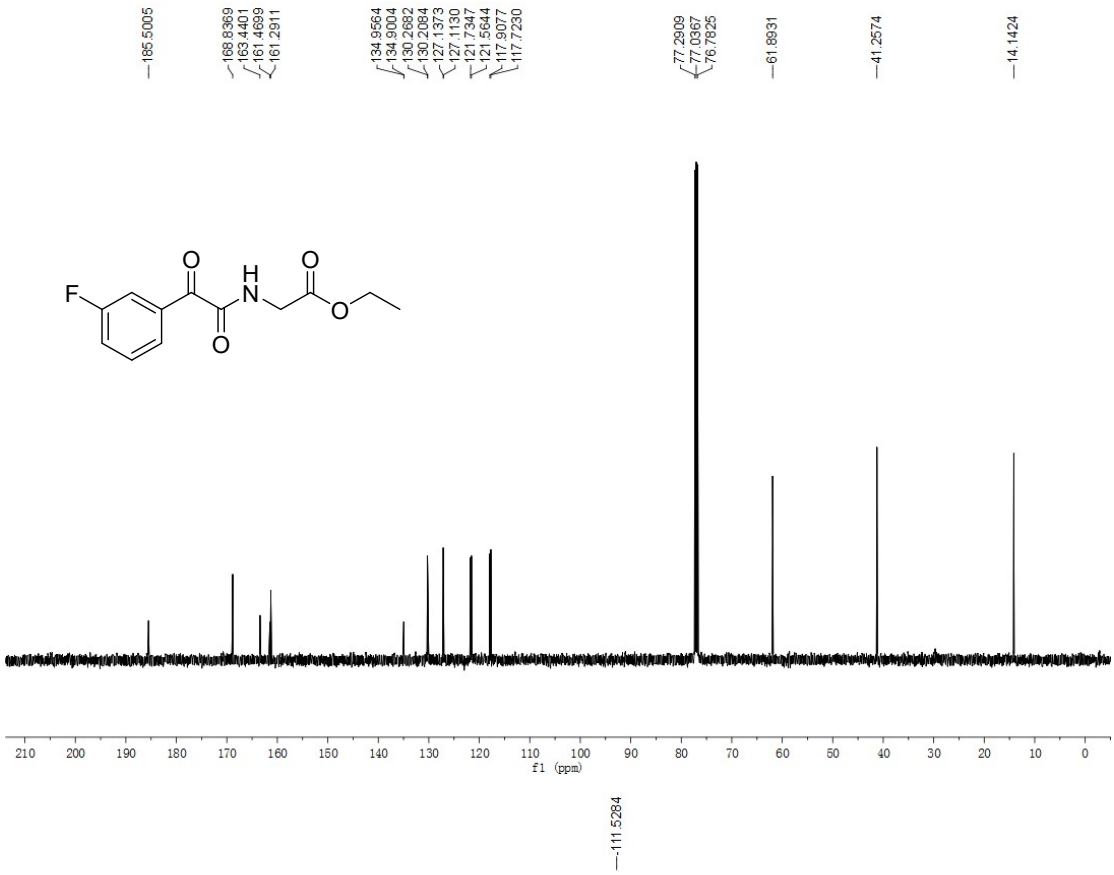
f1 (ppm)


-101.8820
f1 (ppm)


f1 (ppm)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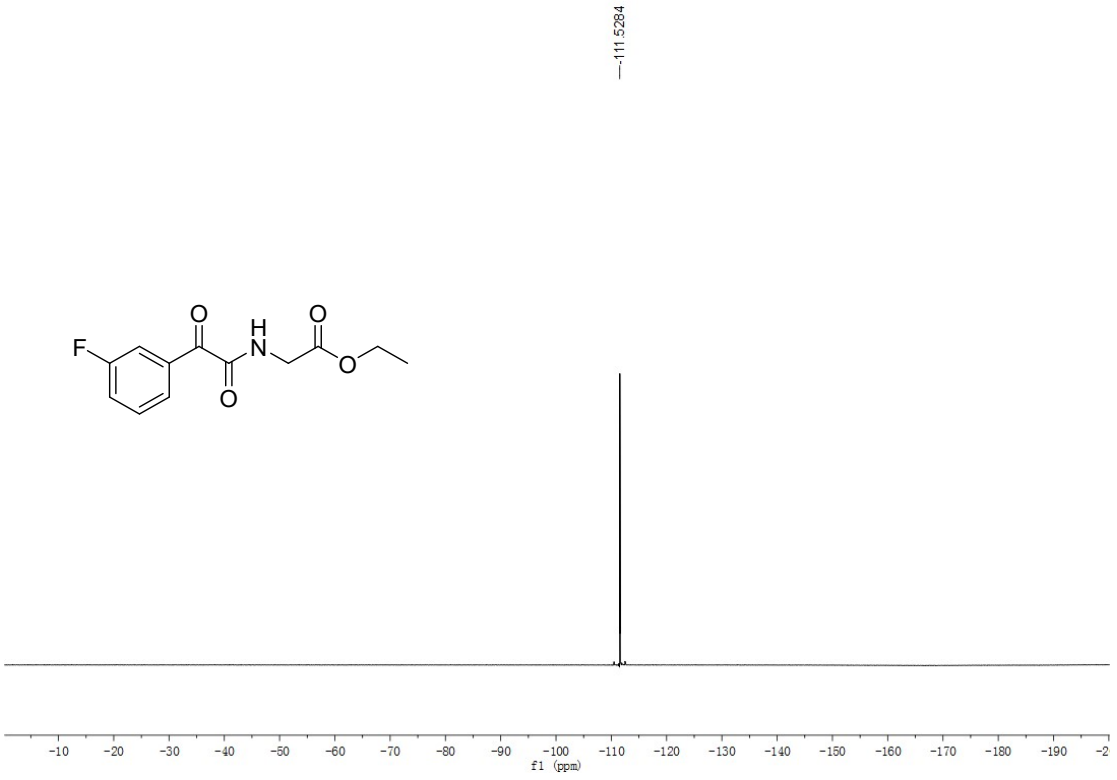
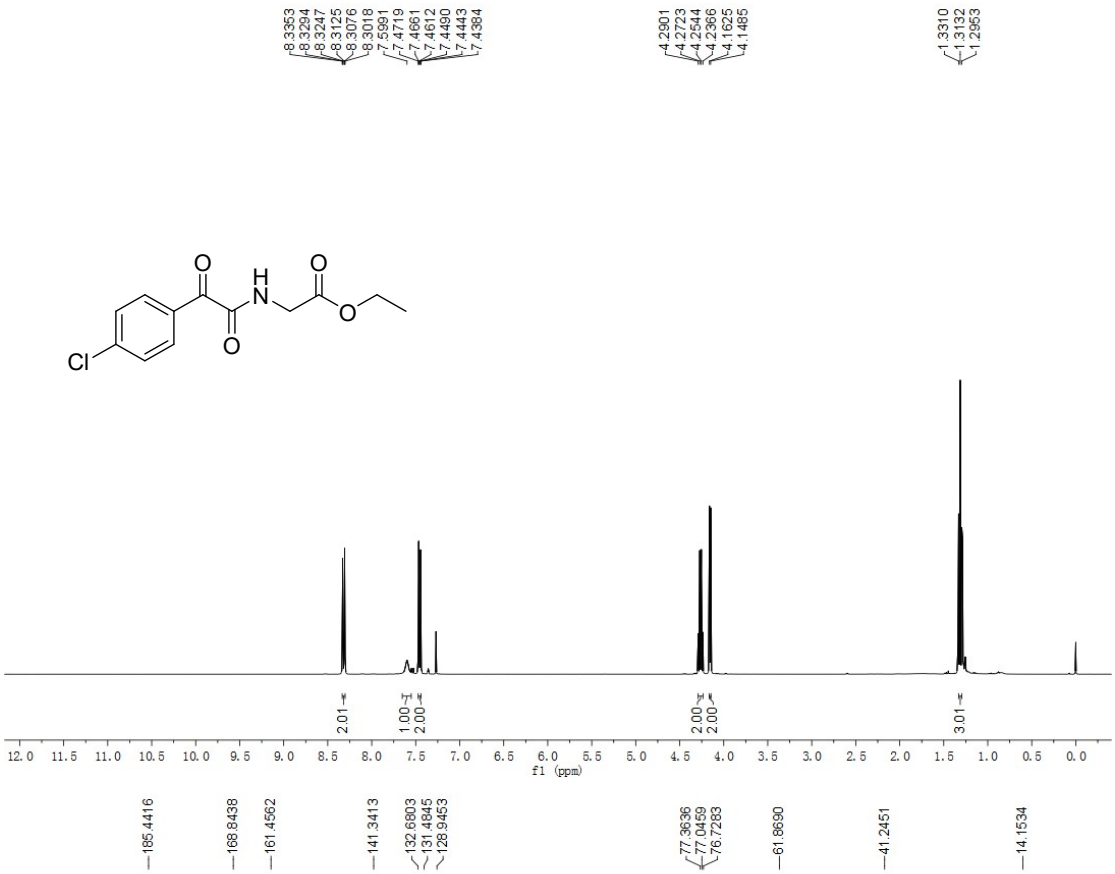
163.4401
161.4699
161.2911
134.9564
134.9004
130.2682
130.2084
127.1373
127.1130
121.7347
121.5644
117.9077
117.7230
77.2909
77.0367
76.7825
61.8931
41.2574
14.1424
F
O
H
N
O
O
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-111.5284
F
O
H
N
O
O
O
-10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -2
f1 (ppm)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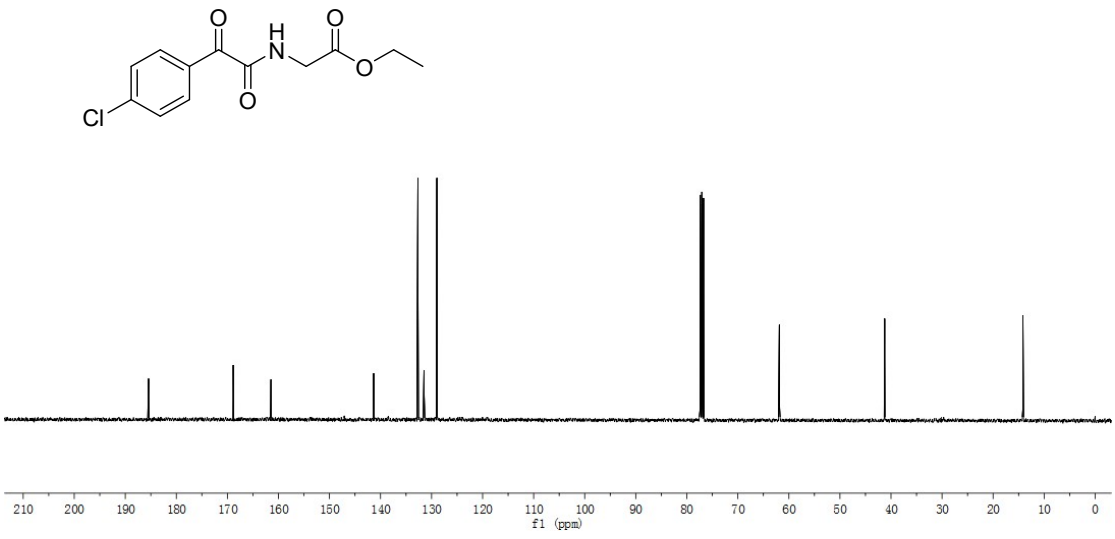
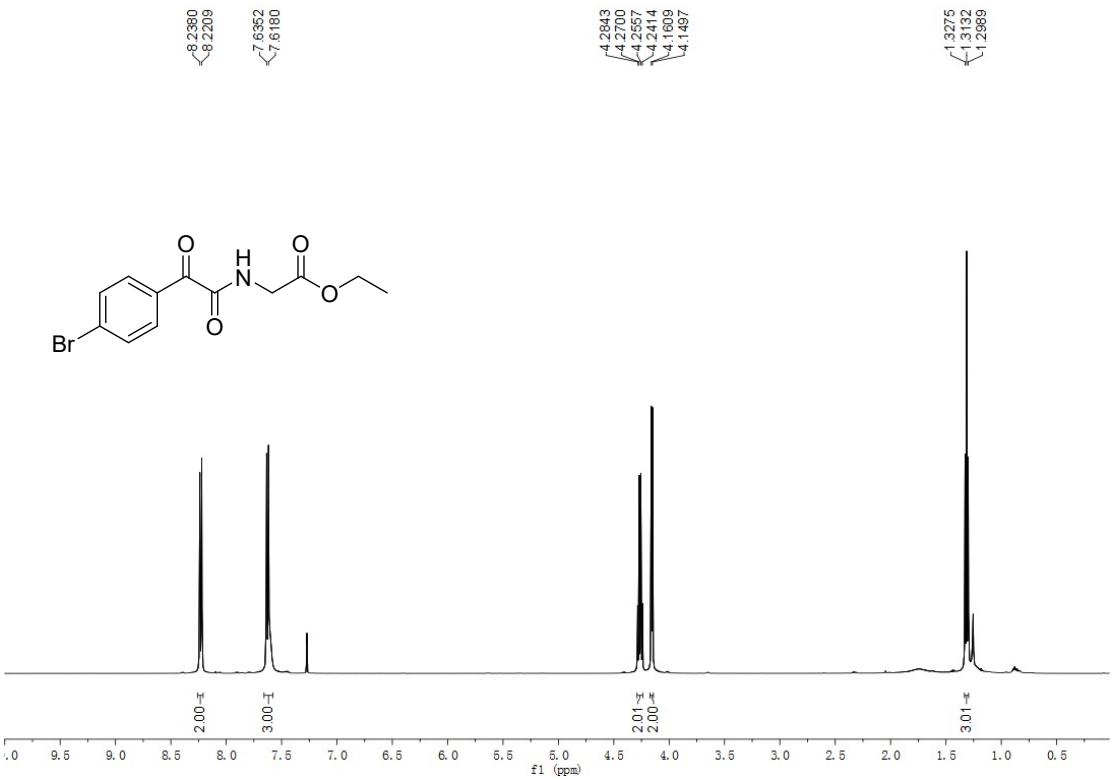
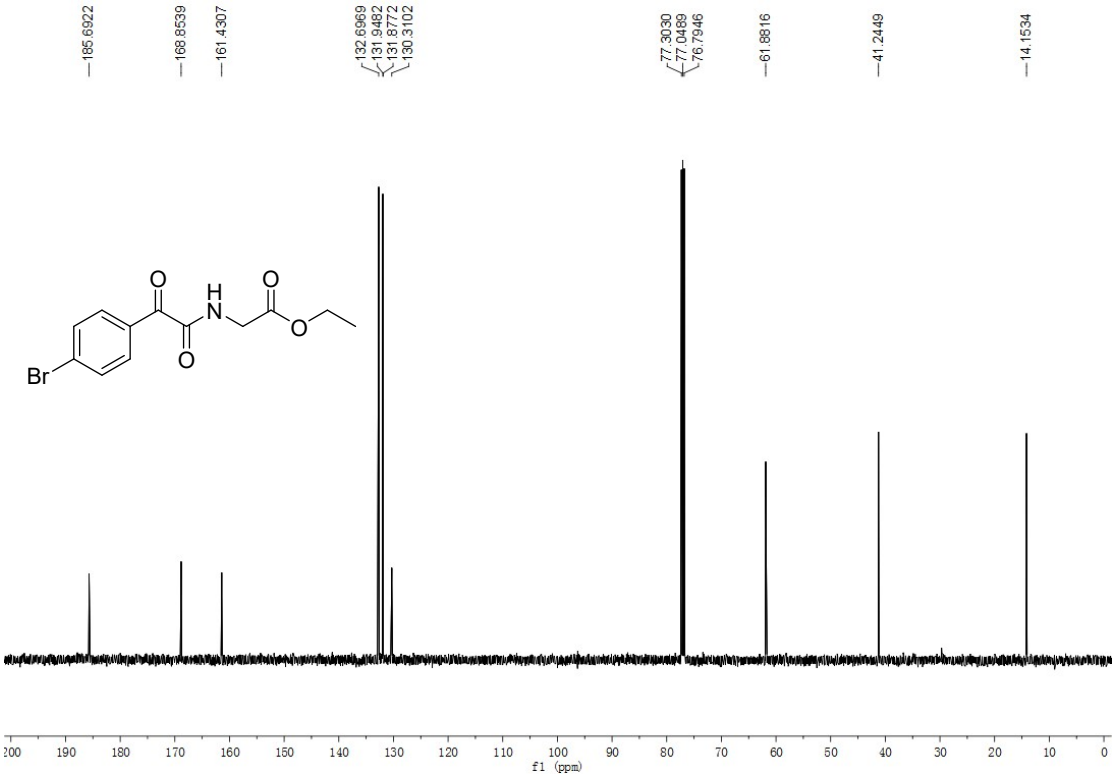
8.3247
8.3125
8.3076
8.3018
7.5991
7.4719
7.4661
7.4612
7.4490
7.4443
7.4384
4.2901
4.2723
4.2544
4.2366
4.1625
4.1485
1.3310
1.3132
1.2953
Cl
2.01
1.00
2.00
2.00
2.00
3.01
f1 (ppm)


185.4416
168.8438
161.4562
141.3413
132.6803
131.4845
129.9453
77.3636
77.0459
76.7283
61.8690
41.2451
14.1534
Cl
f1 (ppm)


8.2380
8.2209
7.6352
7.6180
4.2843
4.2700
4.2557
4.2414
4.1609
4.1497
1.3275
1.3132
1.2989
Br
2.00
3.00
2.01
2.00
3.01
f1 (ppm)


185.6922
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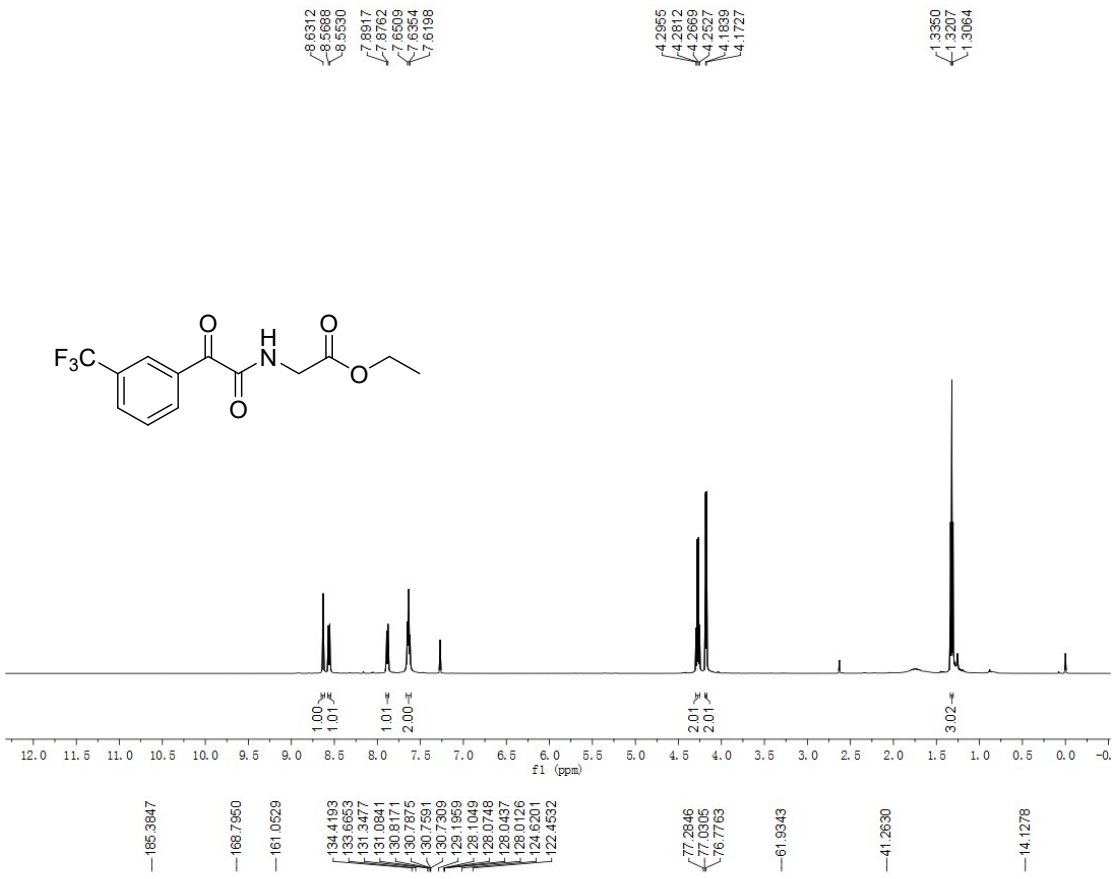
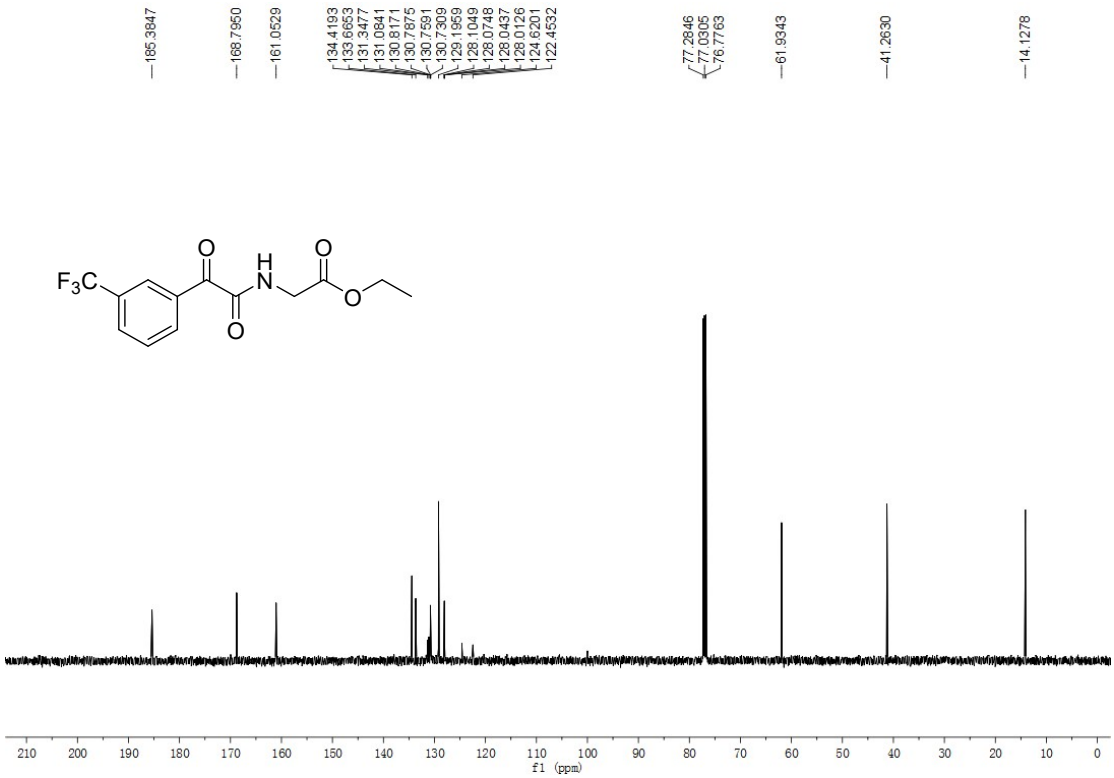
161.4307
132.6969
131.9482
131.8772
130.3102
77.3030
77.0489
76.7946
61.8816
41.2449
14.1534
Br
f1 (ppm)


8.6312
8.5688
8.5530
7.8917
7.8762
7.6509
7.6354
7.6198
4.2955
4.2812
4.2669
4.2527
4.1839
4.1727
1.3350
1.3207
1.3064
F3C
O
H
N
O
O
O
1.00
1.01
1.01
2.00
2.01
2.01
3.02
f1 (ppm)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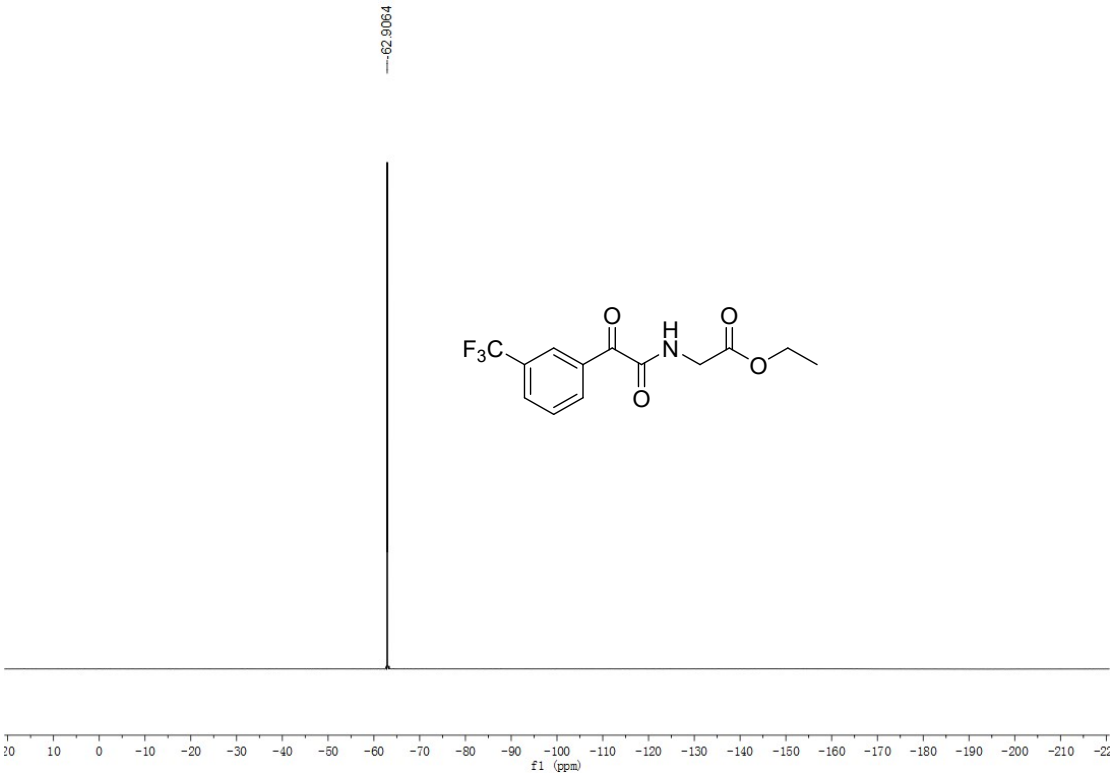
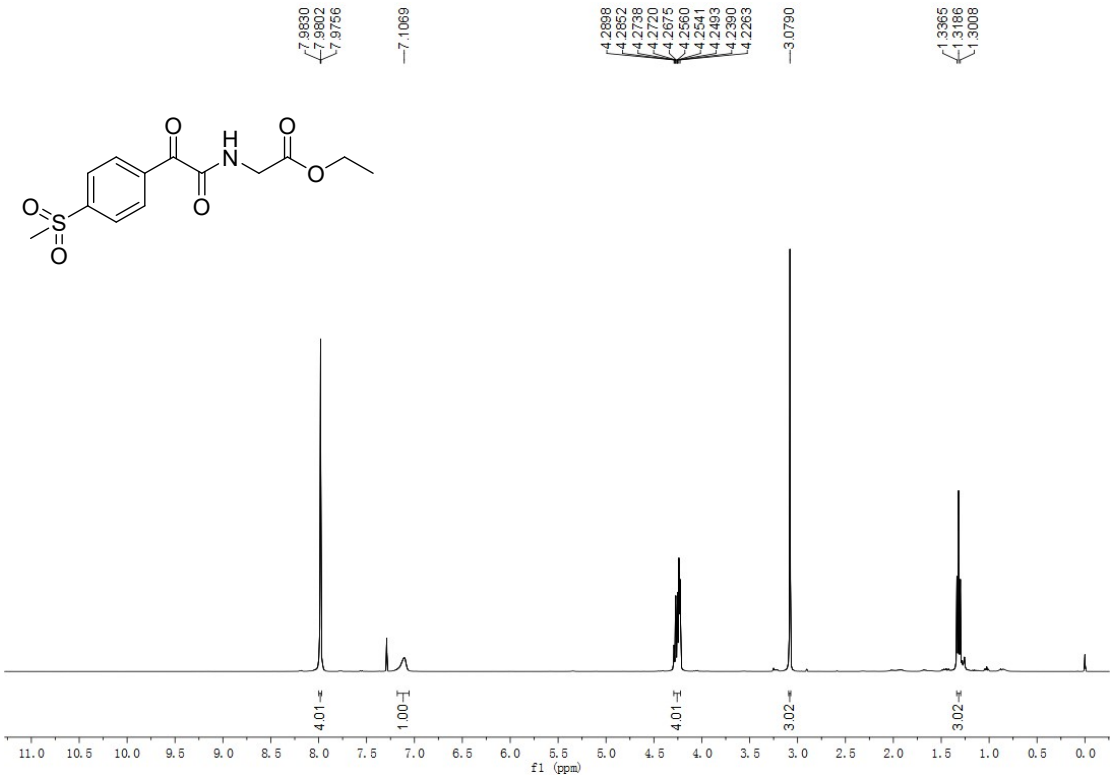
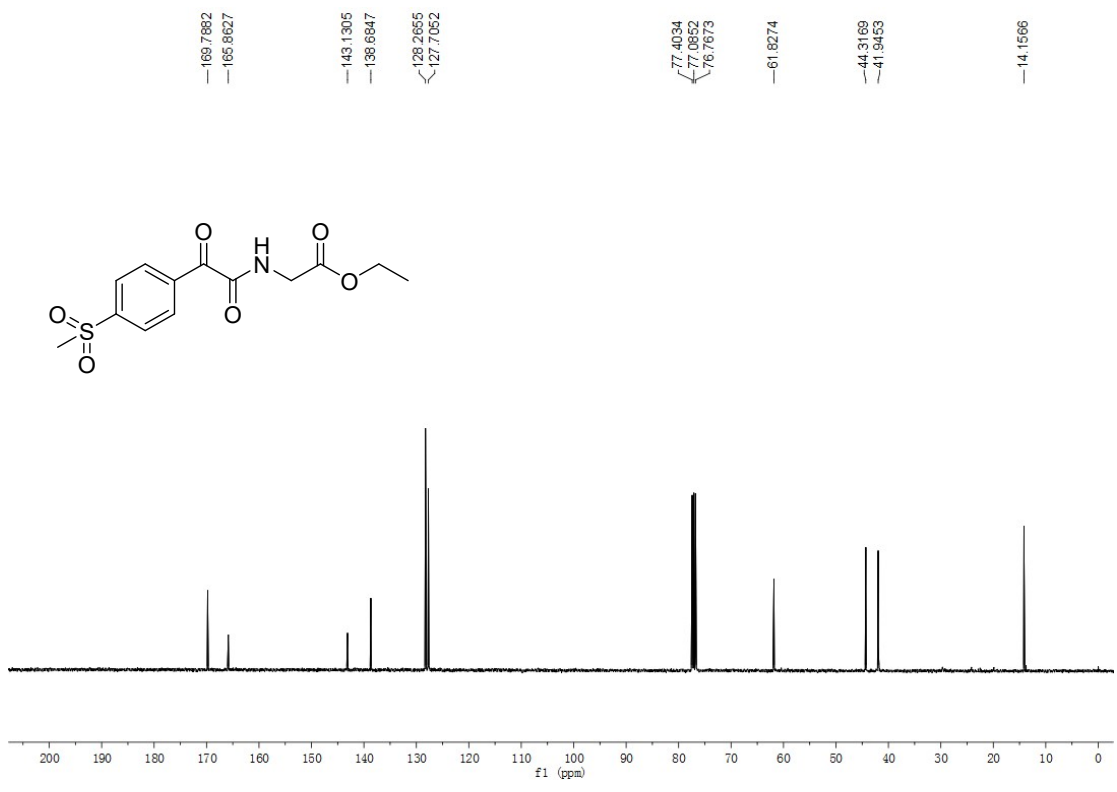
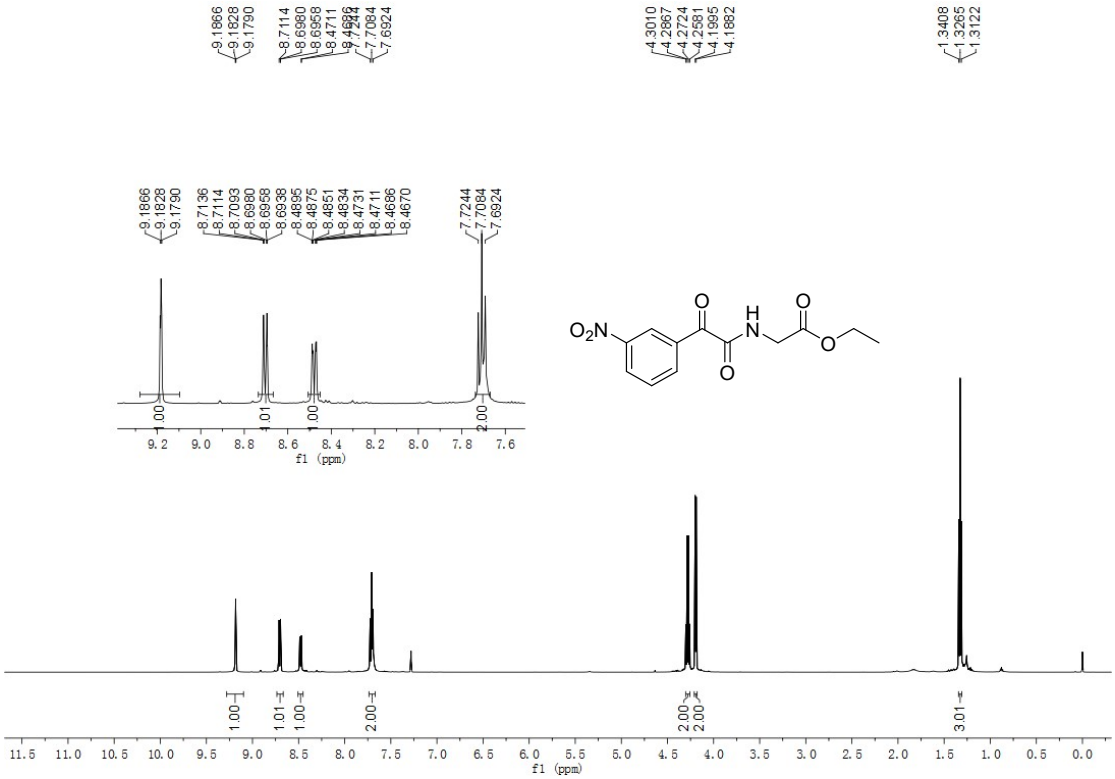
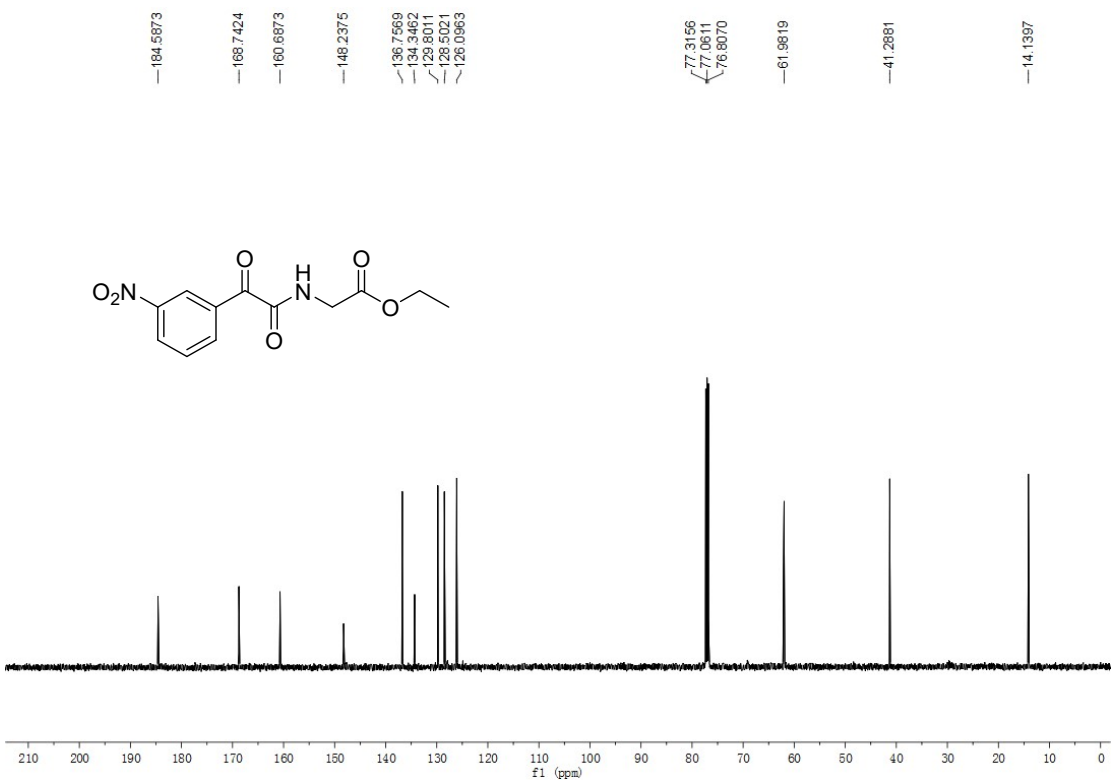
161.0529
134.4193
133.6653
131.3477
131.0641
130.8171
130.7875
130.7591
130.7309
129.1959
128.1049
128.0748
128.0437
128.0126
124.6201
122.4532
77.2846
77.0305
76.7763
61.9343
41.2630
14.1278
F3C
O
H
N
O
O
O
f1 (ppm)


-62.9064
F3C
O
H
N
O
O
O
f1 (ppm)


7.9830
7.9802
7.9756
7.1069
4.2898
4.2852
4.2738
4.2720
4.2675
4.2560
4.2541
4.2493
4.2390
4.2263
3.0790
1.3365
1.3186
1.3008
4.01
1.00
4.01
3.02
3.02
f1 (ppm)


169.7882
165.8627
143.1305
138.6847
128.2655
127.7052
77.4034
77.0852
76.7673
61.8274
44.3169
41.9453
14.1566
f1 (ppm)


9.1866
9.1828
9.1790
8.7136
8.7114
8.7093
8.6980
8.6958
8.6938
8.4895
8.4875
8.4851
8.4834
8.4731
8.4711
8.4686
8.4670
7.7244
7.7084
7.6924
4.3010
4.2867
4.2724
4.2581
4.1995
4.1882
1.3408
1.3265
1.3122
O2N
H
N
O
f1 (ppm)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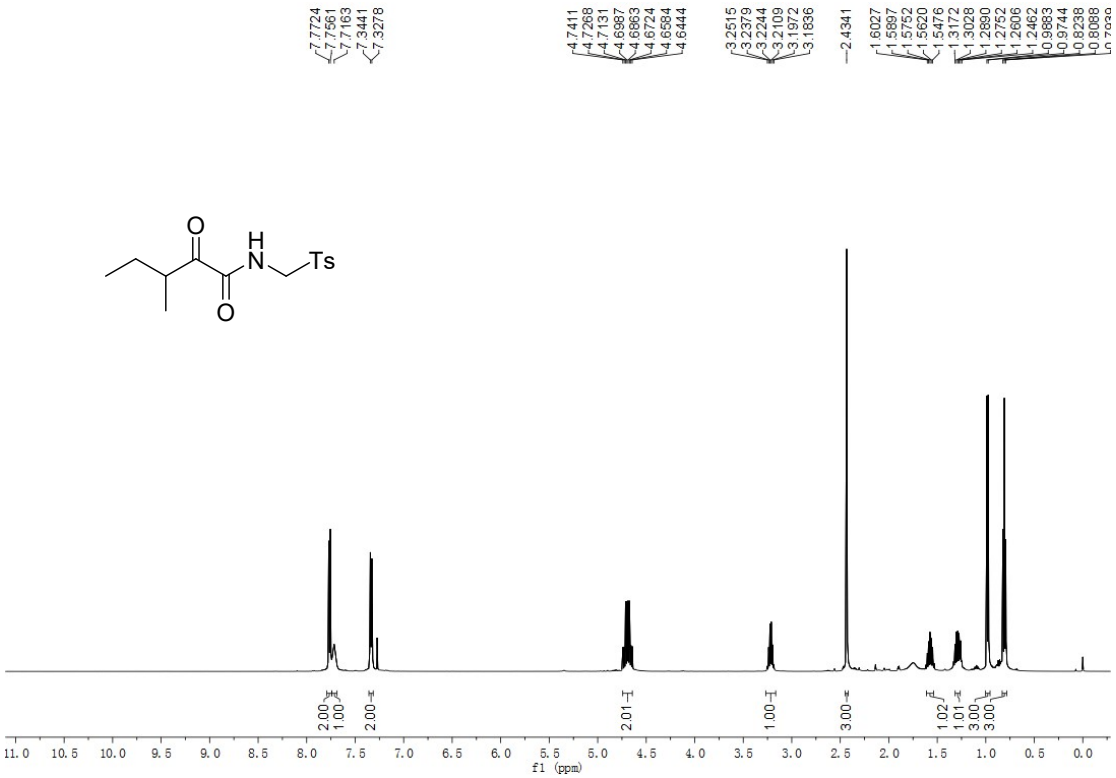
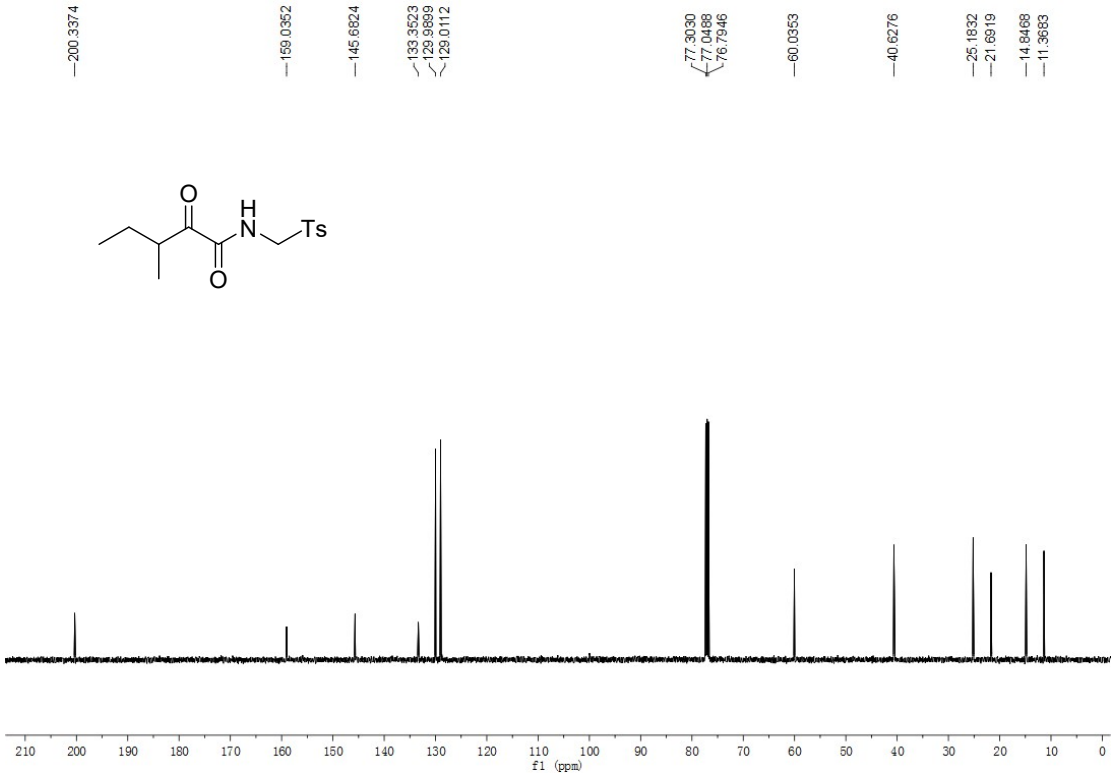
160.6873
149.2375
136.7569
134.3462
129.8011
128.5021
126.0963
77.3156
77.0611
76.8070
61.9819
41.2681
14.1397
O2N
H
N
O
f1 (ppm)


7.7724
7.7561
7.7163
7.3441
7.3278
4.7411
4.7268
4.7131
4.6987
4.6863
4.6724
4.6584
4.6444
3.2515
3.2379
3.2244
3.2109
3.1972
3.1836
2.4341
1.6027
1.5897
1.5752
1.5620
1.5476
1.3172
1.3028
1.2890
1.2752
1.2606
1.2462
0.9883
0.9744
0.8238
0.8088
O
H
N
Ts
O
2.00
1.00
2.00
2.01
1.00
3.00
1.02
1.01
3.00
3.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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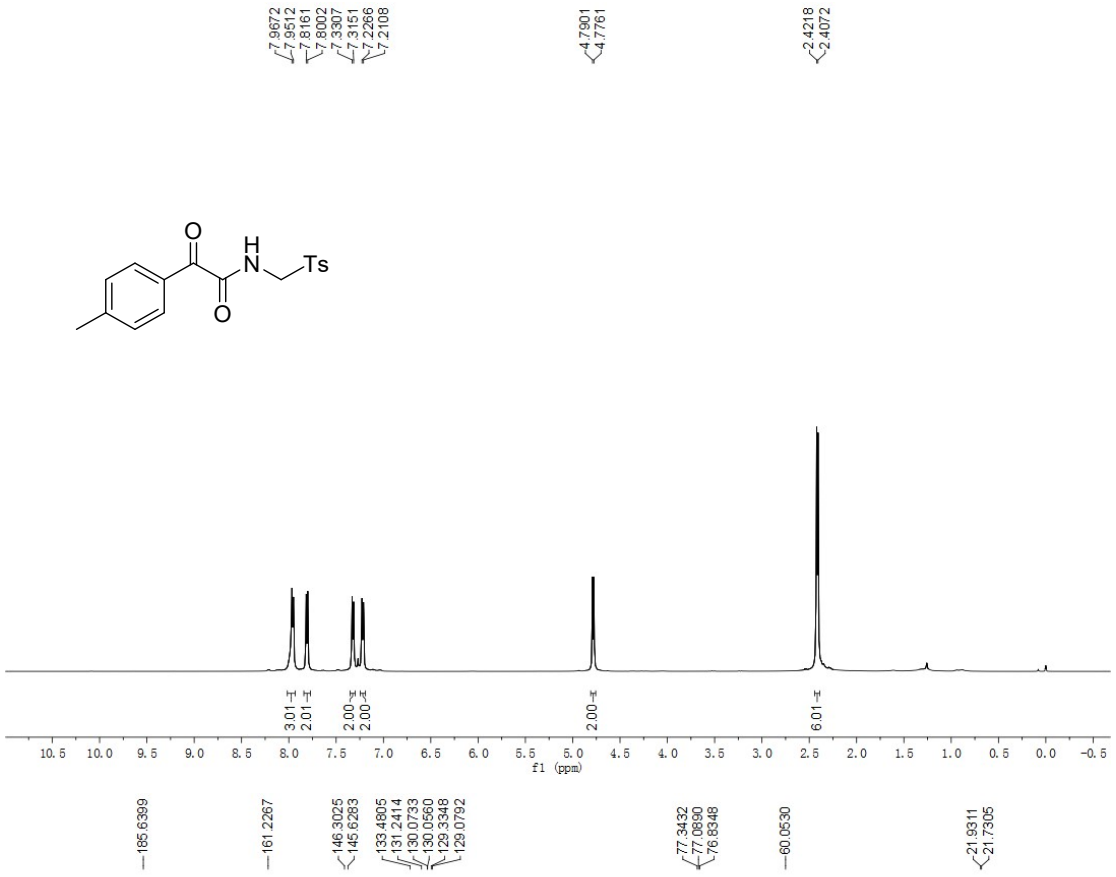
145.6824
133.3523
129.9899
129.0112
77.3030
77.0488
76.7946
60.0353
40.6276
25.1832
21.6919
14.8468
11.3683
O
H
N
Ts
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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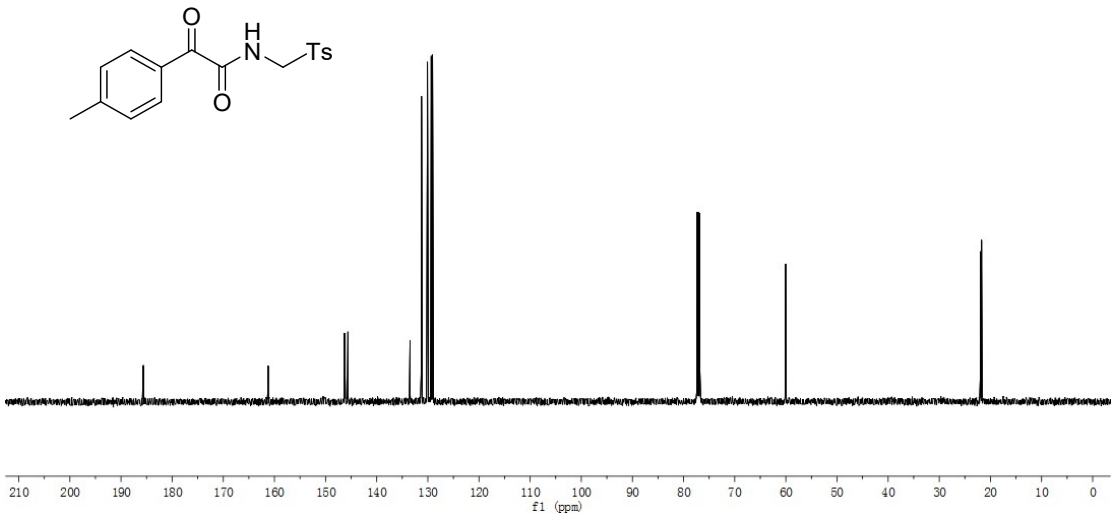
7.9512
7.8161
7.8002
7.3307
7.3151
7.2266
7.2108
4.7901
4.7761
2.4218
2.4072
O
H
N
Ts
O
3.01
2.01
2.00
2.00
2.00
6.01
f1 (ppm)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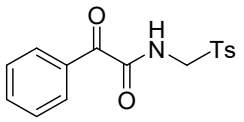
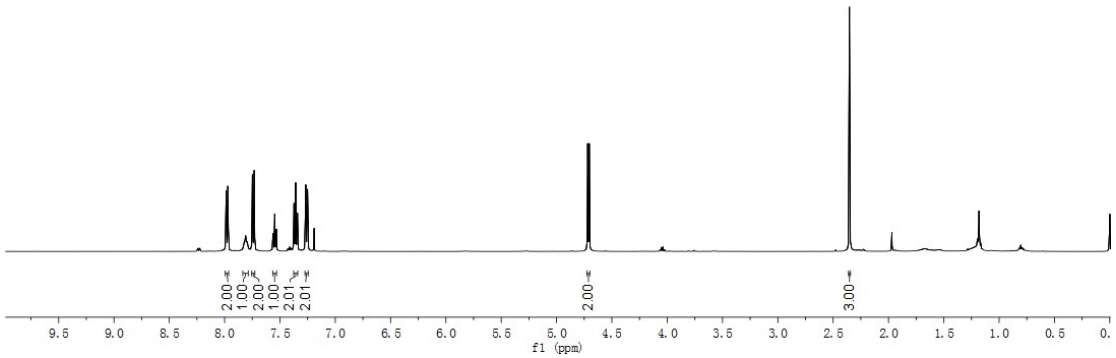
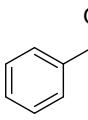
161.2267
146.3025
145.6283
133.4805
131.2414
130.0733
130.0560
129.3348
129.0792
77.3432
77.0890
76.8348
60.0530
21.9311
21.7305
O
H
N
Ts
O
f1 (ppm)


7.9875
7.9853
7.9709
7.9684
7.8223
7.8096
7.7967
7.7489
7.7324
7.5623
7.5600
7.5474
7.5349
7.5326
7.5302
7.3732
7.3578
7.3570
7.3417
7.2667
7.2507
7.1908
4.7185
4.7045
2.3530

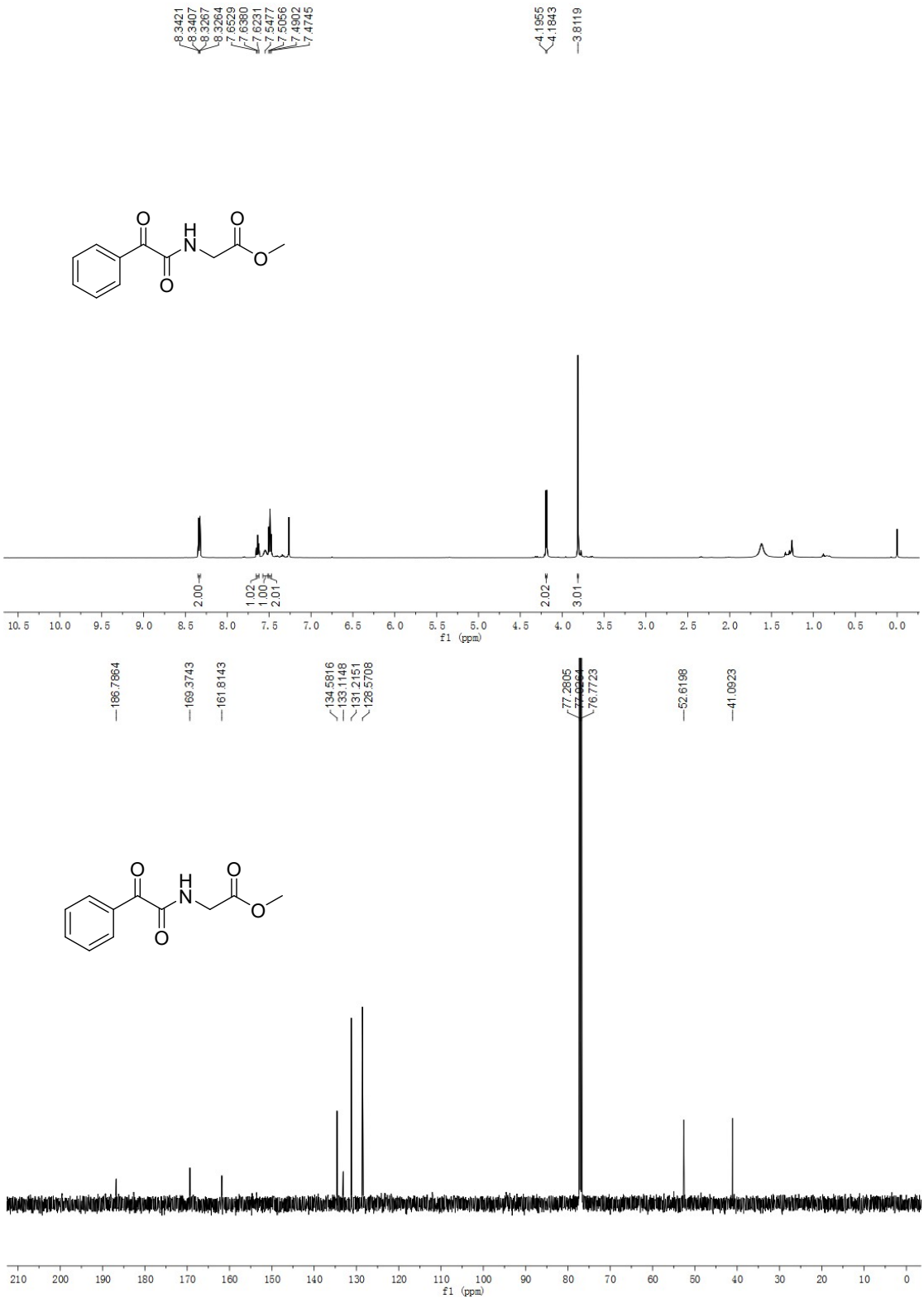

O
H
N
Ts
O


2.00
1.00
2.00
1.00
2.01
2.01
2.00
3.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)


186.0561
160.8426
145.7009
134.9268
133.4349
132.5096
131.0909
130.1068
129.0822
128.5879
77.3136
77.0595
76.8052
60.0094
21.7361


O
H
N
Ts
O

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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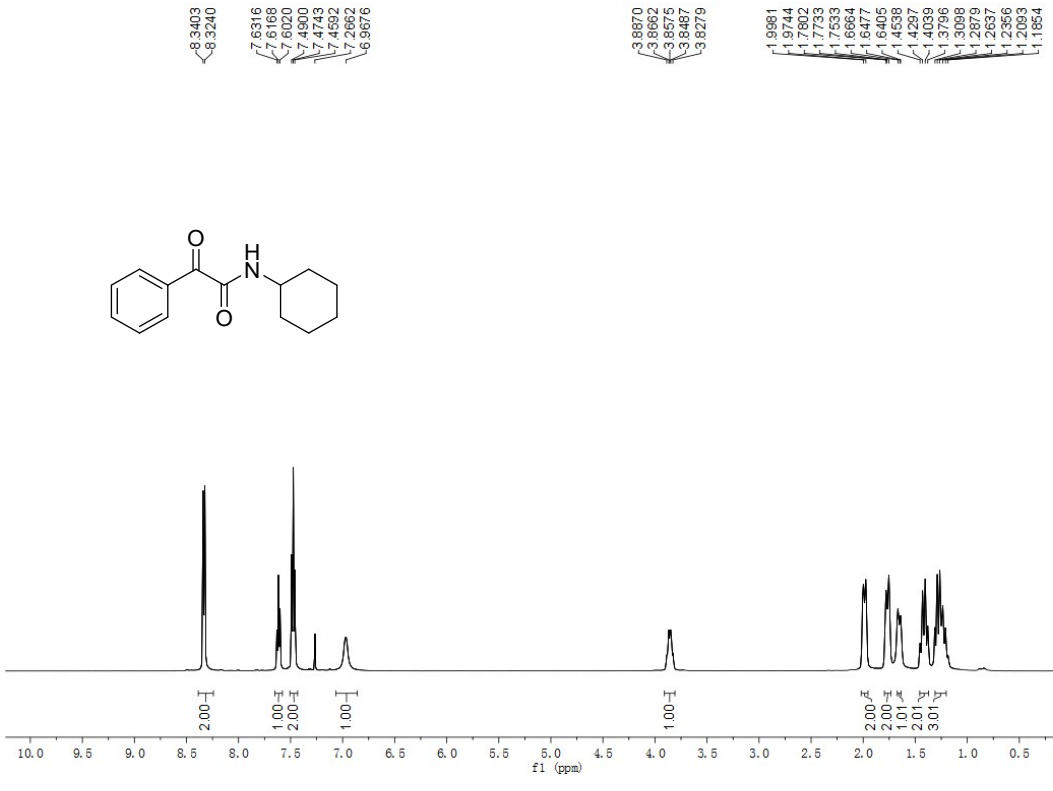
8.3267
8.3264
7.6529
7.6380
7.6231
7.5477
7.5056
7.4902
7.4745
4.1955
4.1843
3.8119
2.00
1.02
1.00
2.01
2.02
3.01
f1 (ppm)
186.7864
169.3743
161.8143
134.5816
133.1148
131.2151
128.5708
77.2805
77.0264
76.7723
52.6198
41.0923
f1 (ppm)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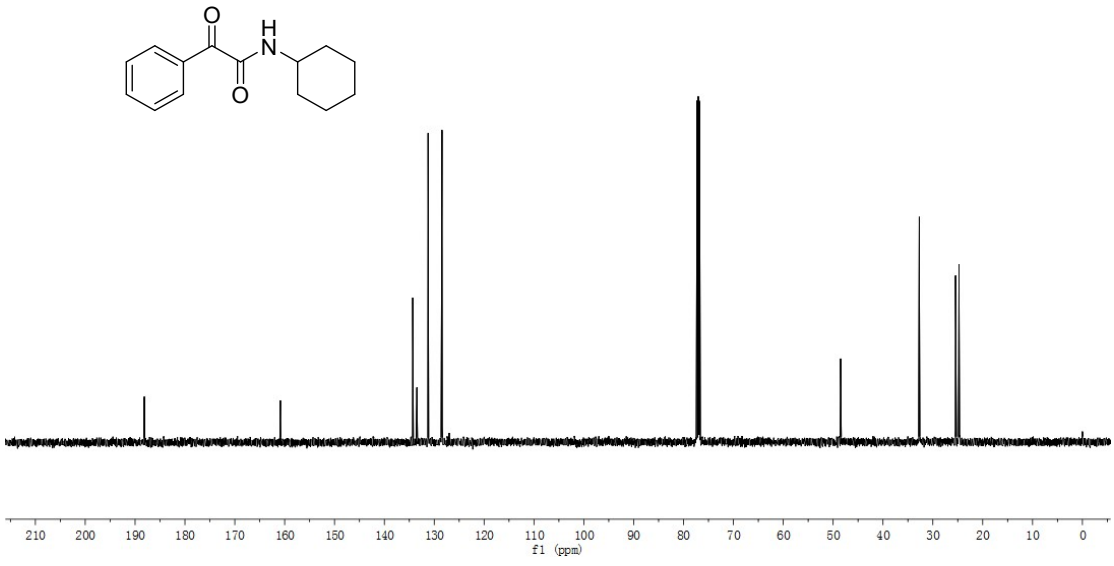
7.6316
7.6168
7.6020
7.4900
7.4743
7.4592
7.2662
6.9676
3.8870
3.8662
3.8575
3.8487
3.8279
1.9981
1.9744
1.7802
1.7733
1.7533
1.6664
1.6477
1.6405
1.4538
1.4297
1.4039
1.3796
1.3098
1.2879
1.2637
1.2356
1.2093
1.1854
2.00
1.00
2.00
1.00
1.00
2.00
2.00
1.01
2.01
3.01
f1 (ppm)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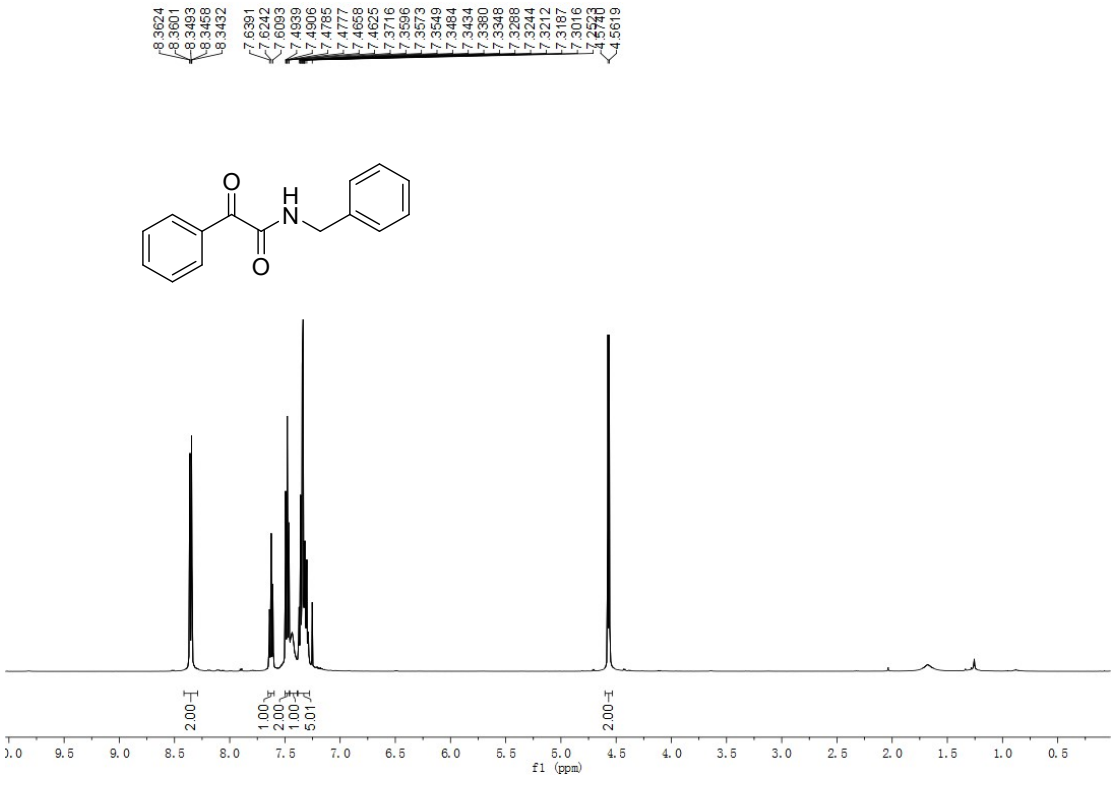
160.8698
134.3001
133.4715
131.2211
128.4552
77.2959
77.0418
76.7876
48.4843
32.7240
25.4316
24.7517
f1 (ppm)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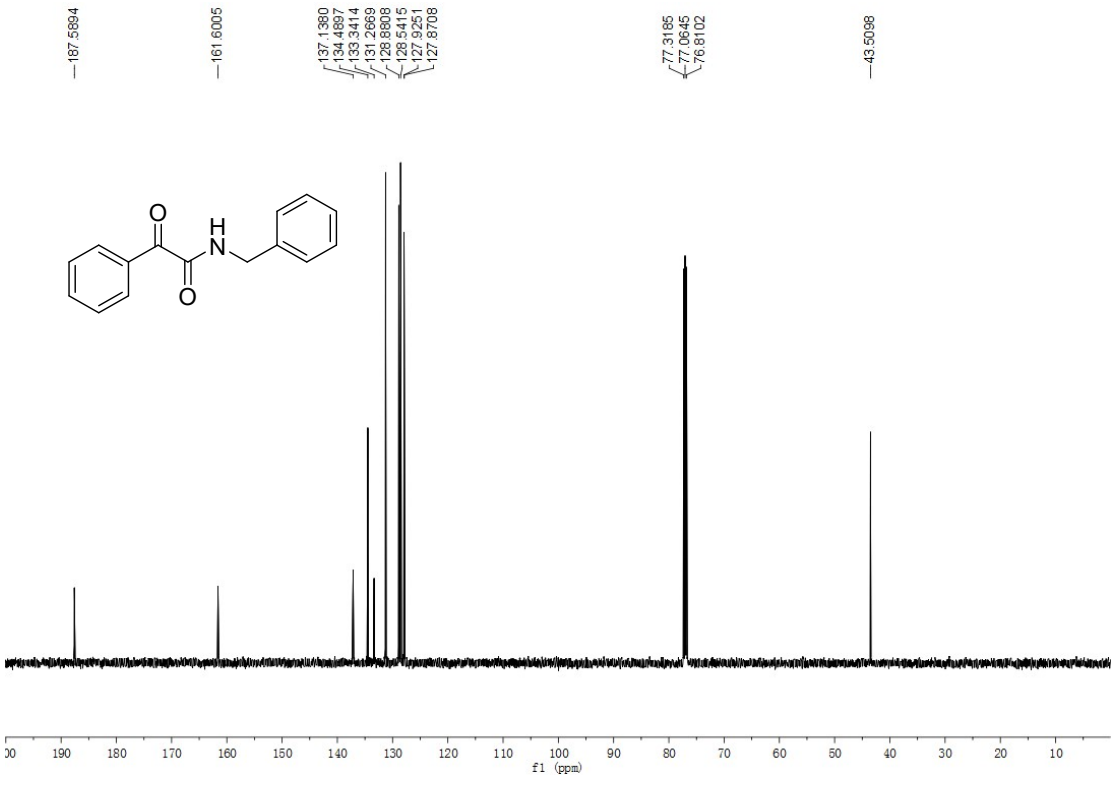
8.3601
8.3493
8.3458
8.3432
7.6391
7.6242
7.6093
7.4939
7.4906
7.4785
7.4777
7.4658
7.4625
7.3716
7.3596
7.3573
7.3549
7.3484
7.3434
7.3380
7.3348
7.3288
7.3244
7.3212
7.3187
7.3016
4.5619
2.00
1.00
2.00
1.00
5.01
2.00
f1 (ppm)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137.1380
134.4697
133.3414
131.2669
128.8808
128.5415
127.9251
127.8708
77.3185
77.0645
76.8102
43.5098
f1 (ppm)


8.3489
8.3462
8.3327
8.3283
8.3249
7.6169
7.4932
7.4734
7.1410
7.1347
7.1195
7.1133
3.4209
3.4033
3.3878
3.3700
1.6320
1.6141
1.6079
1.5956
1.5898
1.5776
1.5585
1.4550
1.4366
1.4178
1.3984
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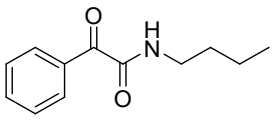
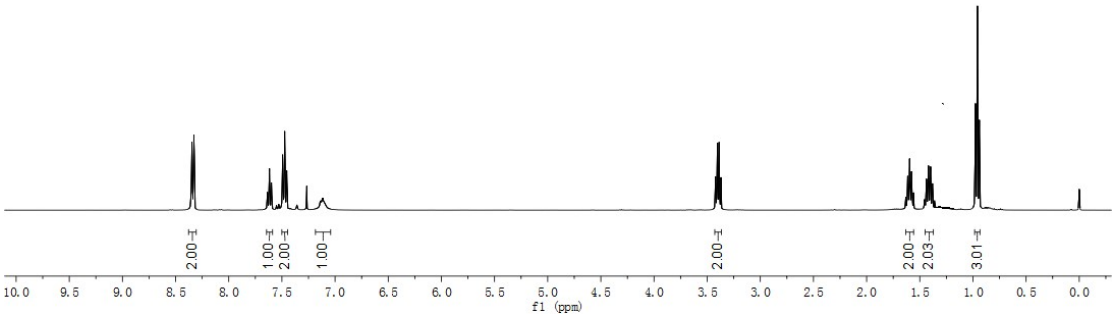
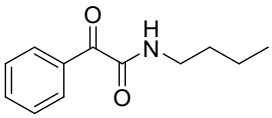
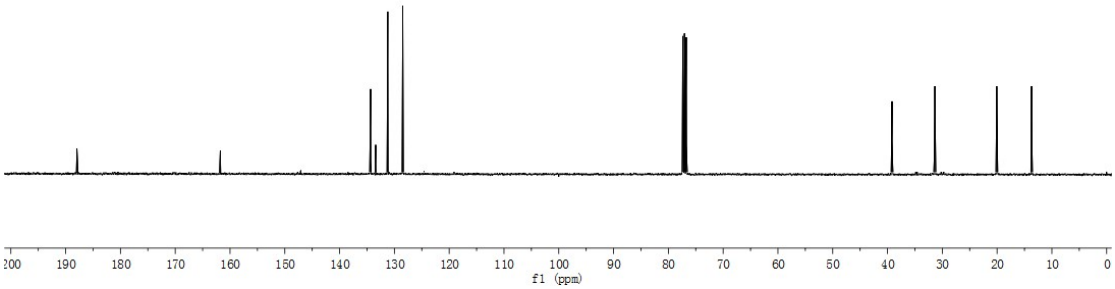
0.9579
0.9396


O
H
N
O


2.00
1.00
2.00
1.00
2.00
2.00
2.03
3.01
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


187.9444
161.7712
134.3460
133.4160
131.2197
128.4751
39.1742
31.3460
20.0703
13.7048


O
H
N
O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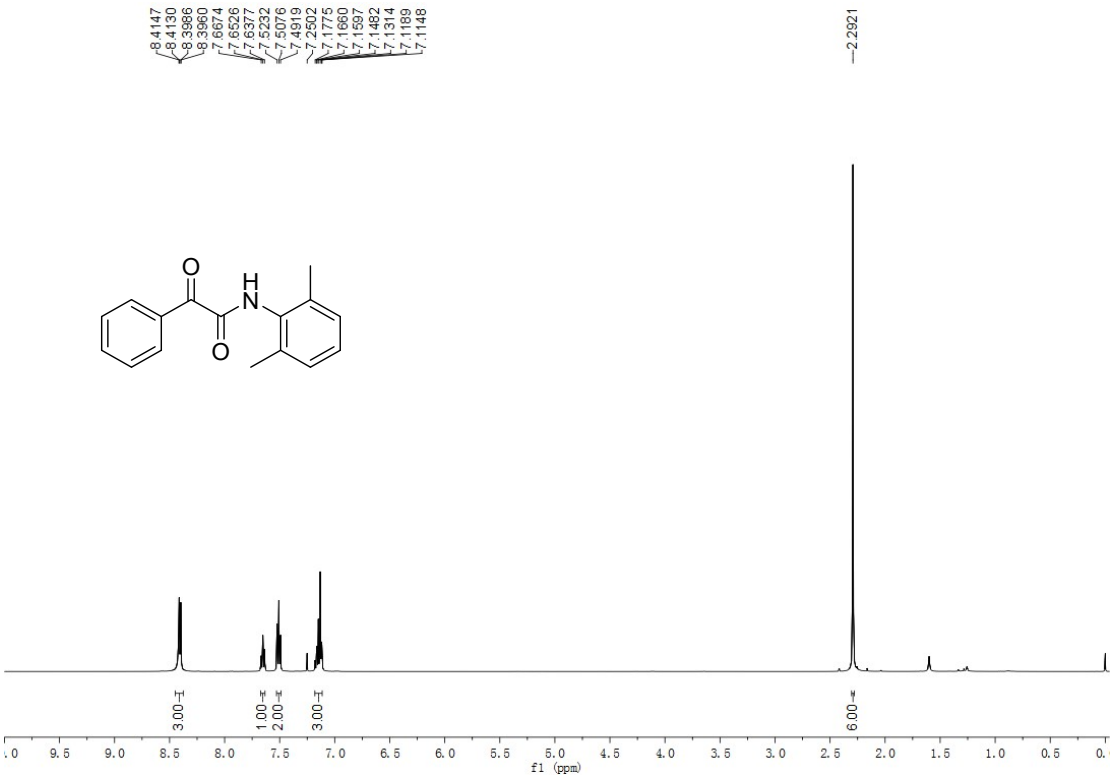
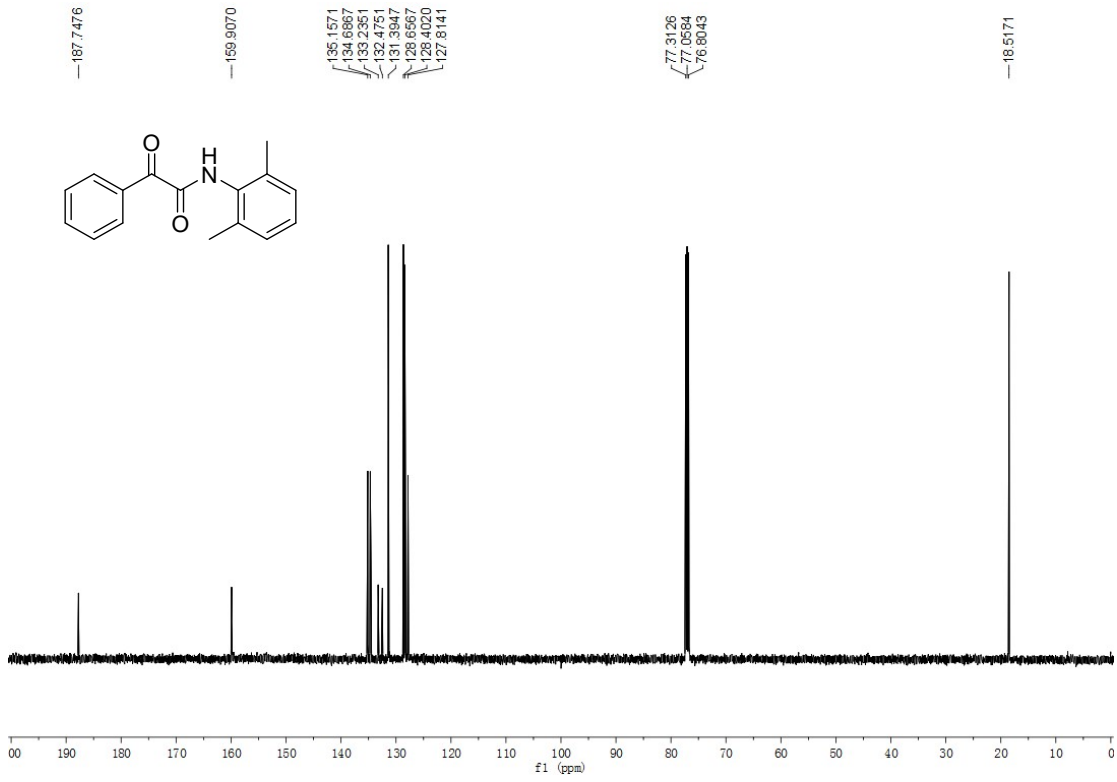
f1 (ppm)


8.4147
8.4130
8.3986
8.3960
7.6674
7.6526
7.6377
7.5232
7.5076
7.4919
7.2502
7.1775
7.1660
7.1597
7.1482
7.1314
7.1189
7.1148
2.2921
O
H
N
O
3.00
1.00
2.00
3.00
6.00
f1 (ppm)


187.7476
159.9070
135.1571
134.6867
133.2351
132.4751
131.3947
128.6567
128.4020
127.8141
77.3126
77.0584
76.8043
18.5171
O
H
N
O
f1 (ppm)