

Supporting Information

Electrochemical Synthesis of α -Ketoamides under Catalyst-, Oxidant- and Electrolyte-free Conditions

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Total number of pages: 40

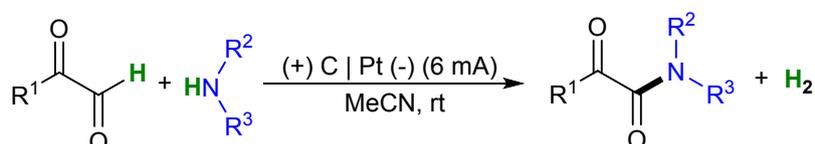
Total number of Figures: 58

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Graphical Abstract



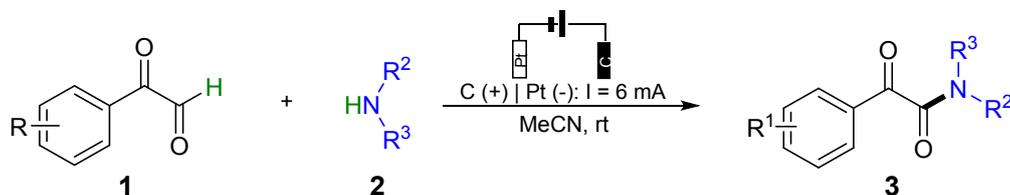
28 examples, 71-91%, >1 gram
H₂ as the sole byproduct
atom- and step-economy
Catalyst, Oxidant, Electrolyte-free

1. General Information

All glassware was oven dried at 110 °C for hours and cooled down under vacuum. Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. The instrument for electrolysis is dual display potentiostat (DJS-292B) (made in China). The anode electrode is graphite rod (Φ 4 mm) and cathode electrode is platinum electrode (15 mm \times 15 mm \times 0.3 mm), and all electrodes were purchased from Beijing instrument electric technologe co., LTD and used directly. All reagents were purchased from Energy Chemical (China) and used directly. The instrument for cyclic voltammetrys is ElectraSyn 2.0 (IKA, made in Germany), and the conditions are as follow: 3 mm diameter glassy carbon disc working electrode, Pt plate electrode, Ag wire reference electrode. 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 (boiling point is between 60-90 °C). Gradient flash chromatography was conducted eluting with a continuous gradient from petroleum to the indicated solvent. NMR spectra were recorded on a Bruker spectrometer at 500 MHz (^1H NMR), 125 MHz (^{13}C NMR). Tetramethylsilane was used as an internal standard. All ^1H NMR spectra were reported in delta (δ) units, parts per million (ppm) downfield from the internal standard. Coupling constants are reported in Hertz (Hz). Mass spectra (MS) were obtained using EI mass spectrometer.

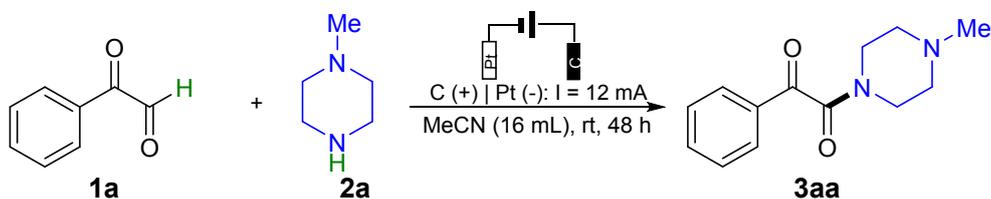
2. Experimental Section

General experimental procedures for 3aa-3ja



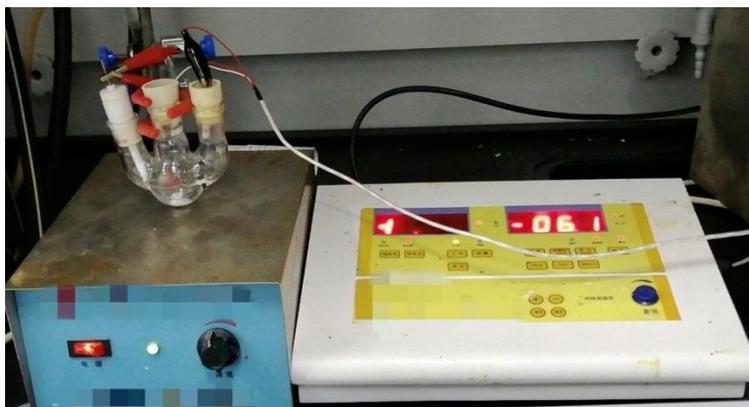
In an undivided three-necked flask (25 mL) equipped with a stir bar, α -ketoaldehydes **1** (0.5 mmol), amines **2** (0.5 mmol) and CH₃CN (8 mL) were added. The flask was equipped with platinum electrodes (15 mm x 15 mm x 0.3 mm) as cathode, graphite rod (Φ 4 mm) as the anode. The reaction mixture was stirred and electrolyzed at a constant current of 6.0 mA under room temperature for 23 h. The solvent was recycled with a rotary evaporator. The pure products **3** were obtained by flash chromatography on silica gel using petroleum ether and ethyl acetate as the eluent.

Larger-scale synthesis of 3aa

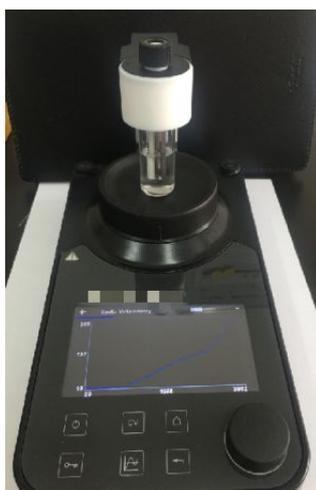


In an undivided three-necked flask (50 mL) equipped with a stir bar, 2-oxo-2-phenylacetaldehyde **1a** (10 mmol), 1-methylpiperazine **2a** (10 mmol) and CH₃CN (16 mL) were added. The flask was equipped with platinum electrodes (15 mm x 15 mm x 0.3 mm) as cathode, graphite rod (Φ 4 mm) as the anode. The reaction mixture was stirred and electrolyzed at a constant current of 12 mA under room temperature for 48 h. The solvent was recycled with a rotary evaporator. The pure products **3aa** was obtained by flash chromatography on silica gel using petroleum ether and ethyl acetate as the eluent (1.79 g, 79%).

Photographic depiction of the reaction setup:

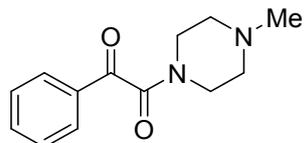


Photographic depiction of the cyclic voltammetry (CV) experiments:



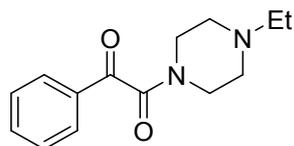
3. Characterization data of products

1-(4-methylpiperazin-1-yl)-2-phenylethane-1,2-dione (3aa)[†]



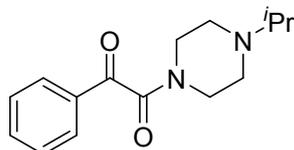
(Yellow solid, 104.5 mg, 90%); ¹H NMR (500 MHz, CDCl₃) δ 7.95 (d, *J* = 7.5 Hz, 2H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 2H), 3.80 (t, *J* = 5.0 Hz, 2H), 3.38 (t, *J* = 5.0 Hz, 2H), 2.52 (t, *J* = 5.0 Hz, 2H), 2.38 (t, *J* = 5.0 Hz, 2H), 2.32 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 191.5, 165.4, 134.8, 133.2, 129.7, 129.1, 54.9, 54.5, 46.0, 45.8, 41.2.

1-(4-ethylpiperazin-1-yl)-2-phenylethane-1,2-dione (3ab)



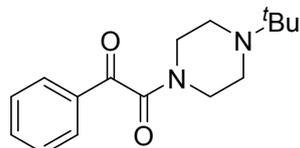
(Yellow solid, 105.9 mg, 86%); ¹H NMR (500 MHz, CDCl₃) δ 7.88 (d, *J* = 7.5 Hz, 2H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 2H), 3.73 (t, *J* = 5.0 Hz, 2H), 3.32 (t, *J* = 5.0 Hz, 2H), 2.49 (t, *J* = 5.0 Hz, 2H), 2.41-2.34 (m, 4H), 1.02 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 191.5, 165.4, 134.8, 133.2, 129.7, 129.0, 52.8, 52.2, 52.2, 45.9, 41.3, 11.8; HRMS (TOF) *m/z* [M+H]⁺ Calcd for C₁₄H₁₈N₂O₂ 247.1441 found 247.1442.

1-(4-isopropylpiperazin-1-yl)-2-phenylethane-1,2-dione (3ac)



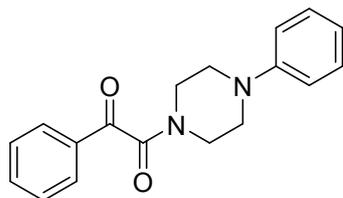
(Yellow solid, 114.5 mg, 88%). ¹H NMR (500 MHz, CDCl₃) δ 7.96 (d, *J* = 8.0 Hz, 2H), 7.65 (t, *J* = 8.0 Hz, 1H), 7.52 (t, *J* = 8.0 Hz, 2H), 3.79 (t, *J* = 6.0 Hz, 2H), 3.37 (t, *J* = 6.0 Hz, 2H), 2.75 (m, 1H), 2.63 (t, *J* = 6.0 Hz, 2H), 2.49 (t, *J* = 6.0 Hz, 2H), 1.04 (d, *J* = 8.0 Hz, 6H); ¹³C NMR (126 MHz, CDCl₃) δ 191.6, 165.3, 134.8, 133.2, 129.7, 129.1, 54.6, 48.8, 48.2, 46.3, 41.6, 18.3; HRMS (TOF) *m/z* [M+H]⁺ Calcd for C₁₅H₂₀N₂O₂ 261.1598 found 261.1601.

1-(4-(tert-butyl)piperazin-1-yl)-2-phenylethane-1,2-dione (3ad)



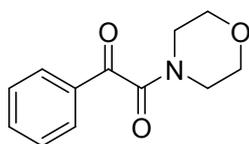
(Yellow solid, 97.4 mg, 71%). ¹H NMR (500 MHz, CDCl₃) δ 7.88 (d, *J* = 8.0 Hz, 2H), 7.57 (t, *J* = 8.0 Hz, 1H), 7.45 (t, *J* = 8.0 Hz, 2H), 3.71 (t, *J* = 4.5 Hz, 2H), 3.29 (t, *J* = 4.5 Hz, 2H), 2.61 (t, *J* = 4.5 Hz, 2H), 2.48 (d, *J* = 4.5 Hz, 2H), 1.01 (s, 9H); ¹³C NMR (126 MHz, CDCl₃) δ 191.6, 165.2, 134.7, 133.3, 129.7, 129.0, 54.3, 46.6, 46.2, 45.7, 42.0, 25.9; HRMS (TOF) *m/z* [M+H]⁺ Calcd for C₁₆H₂₂N₂O₂ 275.1754 found 275.1759.

1-phenyl-2-(4-phenylpiperazin-1-yl)ethane-1,2-dione (3ae)²



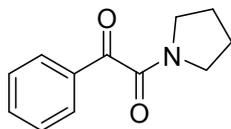
(Yellow solid, 122.2 mg, 83%). ¹H NMR (500 MHz, CDCl₃) δ 7.91 (d, *J* = 7.5 Hz, 2H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.22 (t, *J* = 7.5 Hz, 2H), 6.86 (d, *J* = 7.5 Hz, 3H), 3.87 (t, *J* = 5.0 Hz, 2H), 3.46 (t, *J* = 5.0 Hz, 2H), 3.23 (t, *J* = 5.0 Hz, 2H), 3.08 (t, *J* = 5.0 Hz, 2H); ¹³C NMR (126 MHz, CDCl₃) δ 191.4, 165.4, 150.8, 137.9, 134.9, 133.2, 132.4, 129.7, 129.3, 129.1, 121.0, 117.0, 49.9, 49.7, 45.9, 41.3.

1-morpholino-2-phenylethane-1,2-dione (3af)¹



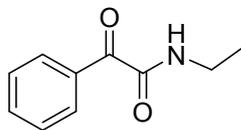
(Yellow solid, 94.3 mg, 86%); ¹H NMR (500 MHz, CDCl₃) δ 7.97 (d, *J* = 8.0 Hz, 2H), 7.66 (t, *J* = 8.0 Hz, 1H), 7.53 (t, *J* = 8.0 Hz, 2H), 3.80 (m, 4H), 3.66 (t, *J* = 5.0 Hz, 2H), 3.39 (t, *J* = 5.0 Hz, 2H); ¹³C NMR (126 MHz, CDCl₃) δ 191.2, 165.5, 134.9, 133.1, 129.7, 129.1, 66.8, 66.7, 46.3, 41.7.

1-phenyl-2-(pyrrolidin-1-yl)ethane-1,2-dione (3ag)²



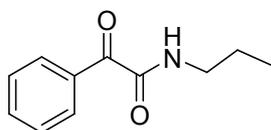
(Yellow oil, 79.3 mg, 78%); ¹H NMR (500 MHz, CDCl₃) δ 8.00 (d, *J* = 7.5 Hz, 2H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 2H), 3.67 (t, *J* = 6.5 Hz, 2H), 3.43 (t, *J* = 6.5 Hz, 2H), 1.98-1.93 (m, 4H); ¹³C NMR (126 MHz, CDCl₃) δ 191.6, 165.0, 134.6, 133.0, 129.9, 128.9, 46.7, 45.3, 25.9, 24.0.

N-ethyl-2-oxo-2-phenylacetamid (3ah)³



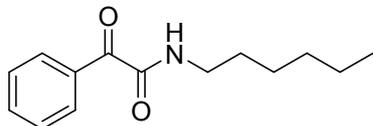
(Yellow oil, 79.7 mg, 90%); ¹H NMR (500 MHz, CDCl₃) δ 8.34 (d, *J* = 7.5 Hz, 2H), 7.62 (m, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.08 (s, 1H), 3.47-3.41 (m, 2H), 1.26 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 187.9, 161.7, 134.4, 133.4, 131.2, 128.5, 34.4, 14.5.

2-oxo-2-phenyl-N-propylacetamide (3ai)⁴



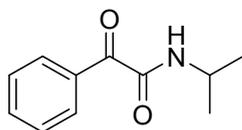
(Yellow oil, 85.1 mg, 89%); ^1H NMR (500 MHz, CDCl_3) δ 8.34 (d, $J = 7.5$ Hz, 2H), 7.62 (m, $J = 7.5$ Hz, 1H), 7.48 (t, $J = 7.5$ Hz, 2H), 7.12 (s, 1H), 3.39-3.34 (m, 2H), 1.66-1.62 (m, 2H), 0.99 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 188.0, 161.8, 134.4, 133.4, 131.2, 128.5, 41.1, 22.6, 11.4.

***N*-hexyl-2-oxo-2-phenylacetamide (3aj)⁴**



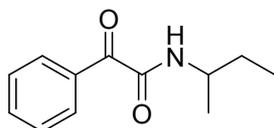
(Yellow oil, 94.4 mg, 81%); ^1H NMR (500 MHz, CDCl_3) δ 8.34 (d, $J = 7.5$ Hz, 2H), 7.62 (d, $J = 7.5$ Hz, 1H), 7.48 (d, $J = 7.5$ Hz, 2H), 7.08 (s, 1H), 3.41-3.37 (m, 2H), 1.64-1.58 (m, 2H), 1.36-1.26 (m, 6H), 0.90 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 187.9, 161.7, 134.3, 133.4, 131.2, 128.5, 39.5, 31.4, 29.3, 26.6, 22.5, 14.0.

***N*-isopropyl-2-oxo-2-phenylacetamide (3ak)¹**



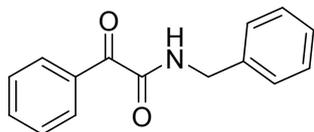
(Yellow oil, 85.0 mg, 89%); ^1H NMR (500 MHz, CDCl_3) δ 8.33 (d, $J = 7.5$ Hz, 2H), 7.62 (t, $J = 7.5$ Hz, 1H), 7.47 (t, $J = 7.5$ Hz, 2H), 6.92 (s, 1H), 4.19-4.14 (m, 1H), 1.27 (d, $J = 6.5$ Hz, 6H); ^{13}C NMR (126 MHz, CDCl_3) δ 188.0, 160.9, 134.3, 133.5, 131.2, 128.5, 41.7, 22.4.

***N*-(*sec*-butyl)-2-oxo-2-phenylacetamide (3al)⁵**



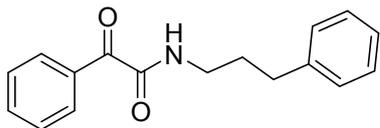
(Yellow oil, 88.3 mg, 86%); ^1H NMR (500 MHz, CDCl_3) δ 8.34 (t, $J = 7.5$ Hz, 2H), 7.62 (t, $J = 7.5$ Hz, 1H), 7.48 (t, $J = 7.5$ Hz, 2H), 6.87 (s, 1H), 4.03-3.97 (m, 1H), 1.61-1.55 (m, 2H), 1.24 (d, $J = 6.5$ Hz, 3H), 0.96 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 188.1, 161.2, 134.3, 133.5, 131.2, 128.5, 47.0, 29.5, 20.2, 10.3.

***N*-benzyl-2-oxo-2-phenylacetamide (3am)**



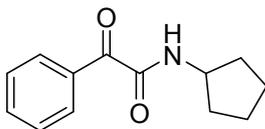
(Yellow solid, 89.7 mg, 75%); ^1H NMR (500 MHz, CDCl_3) δ 8.31 (s, 1H), 7.71-7.69 (m, 2H), 7.34-7.32 (m, 3H), 7.26-7.25 (m, 4H), 7.19-7.15 (m, 1H), 4.74 (d, $J = 1.5$ Hz, 2H); ^{13}C NMR (126 MHz, CDCl_3) δ 162.0, 139.3, 136.2, 130.8, 128.6, 128.5, 128.5, 128.3, 128.0, 127.0, 65.1; HRMS (TOF) m/z $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{15}\text{H}_{13}\text{NO}_2$ 240.0940 found 240.0949.

***2*-oxo-2-phenyl-*N*-(3-phenylpropyl)acetamide (3an)**



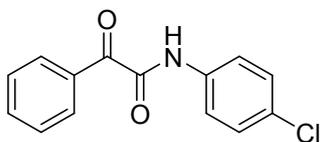
(Yellow solid, 106.9 mg, 80%). ^1H NMR (500 MHz, CDCl_3) δ 8.34-8.32 (m, 2H), 7.63-7.60 (m, 1H), 7.47 (m, 2H), 7.31-7.25 (m, 2H), 7.21-7.20 (m, 3H), 7.11 (s, 1H), 3.44-3.40 (m, 2H), 2.71 (t, $J = 8.0$ Hz, 2H), 1.98-1.92 (m, 2H); ^{13}C NMR (126 MHz, CDCl_3) δ 187.79, 161.8, 141.0, 134.4, 133.4, 131.2, 128.6, 128.5, 128.4, 126.2, 39.1, 33.2, 30.8; HRMS (TOF) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{17}\text{H}_{17}\text{NO}_2$ 268.1332 found 268.1337.

***N*-cyclopentyl-2-oxo-2-phenylacetamide (3ao)⁶**



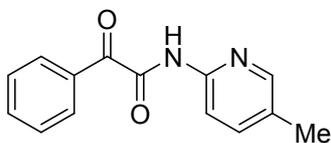
(Yellow oil, 85.8, 79%), ^1H NMR (500 MHz, CDCl_3) δ 8.34 (d, $J = 7.5$ Hz, 2H), 7.62 (t, $J = 7.5$ Hz, 1H), 7.48 (t, $J = 7.5$ Hz, 2H), 7.01 (s, 1H), 4.33-4.26 (m, 1H), 2.09-2.05 (m, 2H), 1.76-1.74 (m, 2H), 1.68-1.66 (m, 2H), 1.55-1.52 (m, 2H); ^{13}C NMR (126 MHz, CDCl_3) δ 188.0, 161.3, 134.3, 133.5, 131.2, 128.5, 51.2, 33.0, 23.8.

***N*-(4-chlorophenyl)-2-oxo-2-phenylacetamide (3ap)**



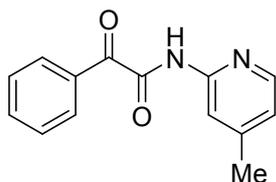
(Yellow solid, 103.9 mg, 80%); ^1H NMR (500 MHz, CDCl_3) δ 8.97 (s, 1H), 8.41 (m, 2H), 7.67 (m, 3H), 7.52 (m, 2H), 7.37 (m, 2H); ^{13}C NMR (126 MHz, CDCl_3) δ 187.1, 158.8, 135.2, 134.8, 133.0, 131.5, 130.4, 129.3, 128.6, 121.2; HRMS (TOF) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{14}\text{H}_{10}\text{ClNO}_2$ 260.0400 found 260.0402.

***N*-(5-methylpyridin-2-yl)-2-oxo-2-phenylacetamide (3aq)**



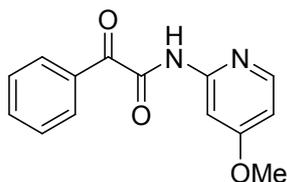
(Yellow solid, 90.1 mg, 75%); ^1H NMR (500 MHz, CDCl_3) δ 8.71 (s, 1H), 8.22 (d, $J = 8.5$ Hz, 1H), 7.98 (s, 1H), 7.85 (d, $J = 8.5$ Hz, 2H), 7.51-7.47 (m, 2H), 7.41 (t, $J = 7.5$ Hz, 2H), 2.23 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 165.6, 149.4, 147.7, 139.1, 134.4, 132.1, 129.3, 128.8, 127.2, 113.7, 17.8; HRMS (TOF) m/z $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{14}\text{H}_{12}\text{N}_2\text{O}_2\text{Na}$ 263.0791 found 263.0793.

***N*-(4-methylpyridin-2-yl)-2-oxo-2-phenylacetamide (3ar)**



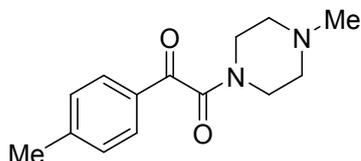
(Yellow solid, 87.7 mg, 75%); ^1H NMR (500 MHz, CDCl_3) δ 8.68 (s, 1H), 8.29 (d, $J = 8.5$ Hz, 1H), 8.08 (s, 1H), 7.92 (d, $J = 7.0$ Hz, 2H), 7.56 (t, $J = 8.0$ Hz, 2H), 7.49 (t, $J = 8.0$ Hz, 2H), 2.31 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 165.6, 149.4, 147.8, 139.0, 134.4, 132.1, 129.3, 128.8, 127.2, 113.7, 17.8; HRMS (TOF) m/z $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{14}\text{H}_{12}\text{N}_2\text{O}_2\text{Na}$ 263.0791 found 263.0794.

***N*-(4-methoxypyridin-2-yl)-2-oxo-2-phenylacetamide (3as)**



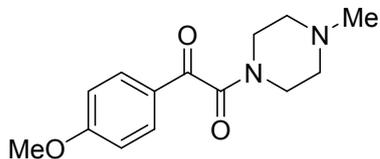
(Yellow solid, 101.2 mg, 79%); ^1H NMR (500 MHz, CDCl_3) δ 9.37 (s, 1H), 8.06 (d, $J = 2.5$ Hz, 1H), 7.93-7.91 (m, 2H), 7.88 (d, $J = 7.5$ Hz, 1H), 7.55 (t, $J = 7.5$ Hz, 1H), 7.47 (t, $J = 7.5$ Hz, 2H), 6.57-6.55 (m, 1H), 3.90 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 167.6, 166.2, 153.5, 148.4, 134.4, 132.2, 128.8, 127.4, 107.9, 98.9, 55.4; HRMS (TOF) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{14}\text{H}_{12}\text{N}_2\text{O}_3$ 257.0921 found 257.0923.

***1*-(4-methylpiperazin-1-yl)-2-(*p*-tolyl)ethane-1,2-dione (3ba)**



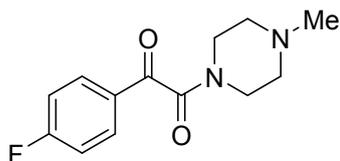
(Yellow solid, 106.0 mg, 86%); ^1H NMR (500 MHz, CDCl_3) δ 7.77 (d, $J = 8.0$ Hz, 2H), 7.25 (d, $J = 8.0$ Hz, 2H), 3.77 (t, $J = 5.0$ Hz, 2H), 3.35 (t, $J = 5.0$ Hz, 2H), 2.52 (t, $J = 5.0$ Hz, 2H), 2.38 (t, $J = 5.0$ Hz, 2H), 2.31 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 191.1, 165.6, 146.2, 130.7, 129.8, 129.8, 54.7, 54.3, 45.7, 45.4, 40.8, 21.9; HRMS (TOF) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{14}\text{H}_{18}\text{N}_2\text{O}_2$ 247.1441 found 247.1446.

***1*-(4-methoxyphenyl)-2-(4-methylpiperazin-1-yl)ethane-1,2-dione (3ca)⁷**



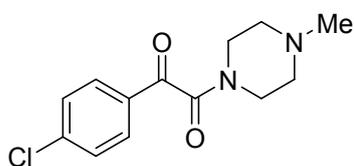
(Yellow solid, 108.8 mg, 83%); ^1H NMR (500 MHz, CDCl_3) δ 7.84 (d, $J = 8.5$ Hz, 2H), 6.90 (d, $J = 8.5$ Hz, 2H), 3.82 (s, 3H), 3.71 (t, $J = 5.0$ Hz, 2H), 3.31 (t, $J = 5.0$ Hz, 2H), 2.44 (t, $J = 5.0$ Hz, 2H), 2.30 (t, $J = 5.0$ Hz, 2H), 2.25 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 190.2, 165.3, 164.9, 132.1, 126.3, 114.4, 55.7, 55.0, 54.5, 46.0, 45.8, 41.1.

***1*-(4-fluorophenyl)-2-(4-methylpiperazin-1-yl)ethane-1,2-dione (3da)**



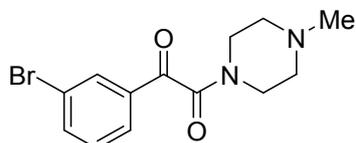
(Yellow solid, 107.6 mg, 86%); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 8.02-7.98 (m, 2H), 7.20 (t, $J = 10.5$ Hz, 2H), 3.79 (t, $J = 6.5$ Hz, 2H), 3.39 (t, $J = 6.5$ Hz, 2H), 2.52 (t, $J = 6.5$ Hz, 2H), 3.39 (t, $J = 6.5$ Hz, 2H), 2.33 (s, 3H); $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 189.8, 168.0, 165.5 (d, $J_{\text{C-F}} = 51.5$ Hz), 132.6 (d, $J_{\text{C-F}} = 12.3$ Hz), 129.7, 116.4 (d, $J_{\text{C-F}} = 27.6$ Hz), 55.0, 54.5, 46.0, 45.8, 41.3; HRMS (TOF) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{13}\text{H}_{15}\text{FN}_2\text{O}_2$ 251.1190 found 251.1192.

1-(4-chlorophenyl)-2-(4-methylpiperazin-1-yl)ethane-1,2-dione (3ea)



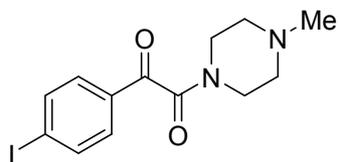
(Yellow solid, 112.0 mg, 84%); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 8.83 (d, $J = 8.5$ Hz, 2H), 7.42 (d, $J = 8.5$ Hz, 2H), 7.72 (t, $J = 5.0$ Hz, 2H), 3.31 (t, $J = 5.0$ Hz, 2H), 2.45 (t, $J = 5.0$ Hz, 2H), 2.32 (t, $J = 5.0$ Hz, 2H), 2.26 (s, 3H); $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 190.0, 164.9, 141.5, 131.6, 131.0, 129.5, 54.9, 54.4, 46.0, 45.8, 41.2; HRMS (TOF) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{13}\text{H}_{15}\text{ClN}_2\text{O}_2$ 267.0895 found 267.0899.

1-(3-bromophenyl)-2-(4-methylpiperazin-1-yl)ethane-1,2-dione (3fa)



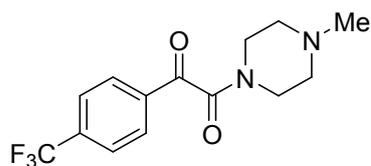
(Yellow solid, 129.1 mg, 83%); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 8.09 (s, 1H), 7.87 (d, $J = 7.5$ Hz, 1H), 7.76 (d, $J = 7.5$ Hz, 1H), 7.39 (t, $J = 7.5$ Hz, 1H), 3.79 (t, $J = 5.0$ Hz, 2H), 3.38 (t, $J = 5.0$ Hz, 2H), 2.52 (t, $J = 5.0$ Hz, 2H), 2.4 (t, $J = 5.0$ Hz, 2H), 2.33 (s, 3H); $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 187.8, 164.6, 137.6, 135.0, 132.4, 130.6, 128.3, 123.3, 54.9, 54.4, 46.0, 45.8, 41.3; HRMS (TOF) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{13}\text{H}_{15}\text{BrN}_2\text{O}_2$ 311.0390 found 311.0396.

1-(4-iodophenyl)-2-(4-methylpiperazin-1-yl)ethane-1,2-dione (3ga)



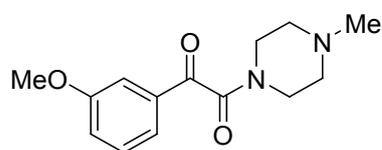
(Yellow solid, 155.8 mg, 87%); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.82 (d, $J = 8.5$ Hz, 2H), 7.58 (d, $J = 8.5$ Hz, 2H), 3.72 (t, $J = 5.0$ Hz, 2H), 3.30 (t, $J = 5.0$ Hz, 2H), 2.45 (t, $J = 5.0$ Hz, 2H), 2.32 (t, $J = 5.0$ Hz, 2H), 2.26 (s, 3H); $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 190.6, 164.8, 138.5, 132.5, 130.8, 103.4, 54.9, 54.4, 46.0, 45.8, 41.2; HRMS (TOF) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{13}\text{H}_{15}\text{IN}_2\text{O}_2$ 359.0251 found 359.0250.

1-(4-methylpiperazin-1-yl)-2-(4-(trifluoromethyl)phenyl)ethane-1,2-dione (3ha)



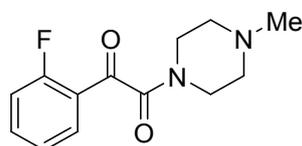
(Yellow solid, 112.6 mg, 75%); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 8.07 (d, $J = 8.0$ Hz, 2H), 7.77 (d, $J = 8.0$ Hz, 2H), 3.79 (t, $J = 5.0$ Hz, 2H), 3.38 (t, $J = 5.0$ Hz, 2H), 2.51 (t, $J = 5.0$ Hz, 2H), 2.39 (t, $J = 5.0$ Hz, 2H), 2.32 (s, 3H); $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 190.0, 164.5, 135.9 (t, $J_{\text{C-F}} = 8.4$ Hz), 130.0, 126.1 (q, $J_{\text{C-F}} = 3.75$ Hz), 124.4, 122.3, 55.0, 54.5, 46.0, 45.8, 41.4; HRMS (TOF) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{14}\text{H}_{15}\text{F}_3\text{N}_2\text{O}_2$ 300.1086 found 300.1088.

1-(3-methoxyphenyl)-2-(4-methylpiperazin-1-yl)ethane-1,2-dione (3ia)



(Yellow solid, 108.8 mg, 83%); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.43-7.42 (m, 2H), 7.35 (t, $J = 8.0$ Hz, 1H), 7.14-7.11 (m, 1H), 3.80 (s, 3H), 3.76-3.74 (t, $J = 5.0$ Hz, 2H), 3.33 (t, $J = 5.0$ Hz, 2H), 2.50 (t, $J = 5.0$ Hz, 2H), 2.37 (t, $J = 5.0$ Hz, 2H), 2.30 (s, 3H); $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 191.3, 165.4, 160.2, 134.5, 130.1, 122.9, 121.8, 112.8, 55.6, 54.8, 54.4, 45.8, 45.6, 41.0; HRMS (TOF) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{14}\text{H}_{18}\text{N}_2\text{O}_3$ 263.1290 found 263.1394.

1-(2-fluorophenyl)-2-(4-methylpiperazin-1-yl)ethane-1,2-dione (3ja)

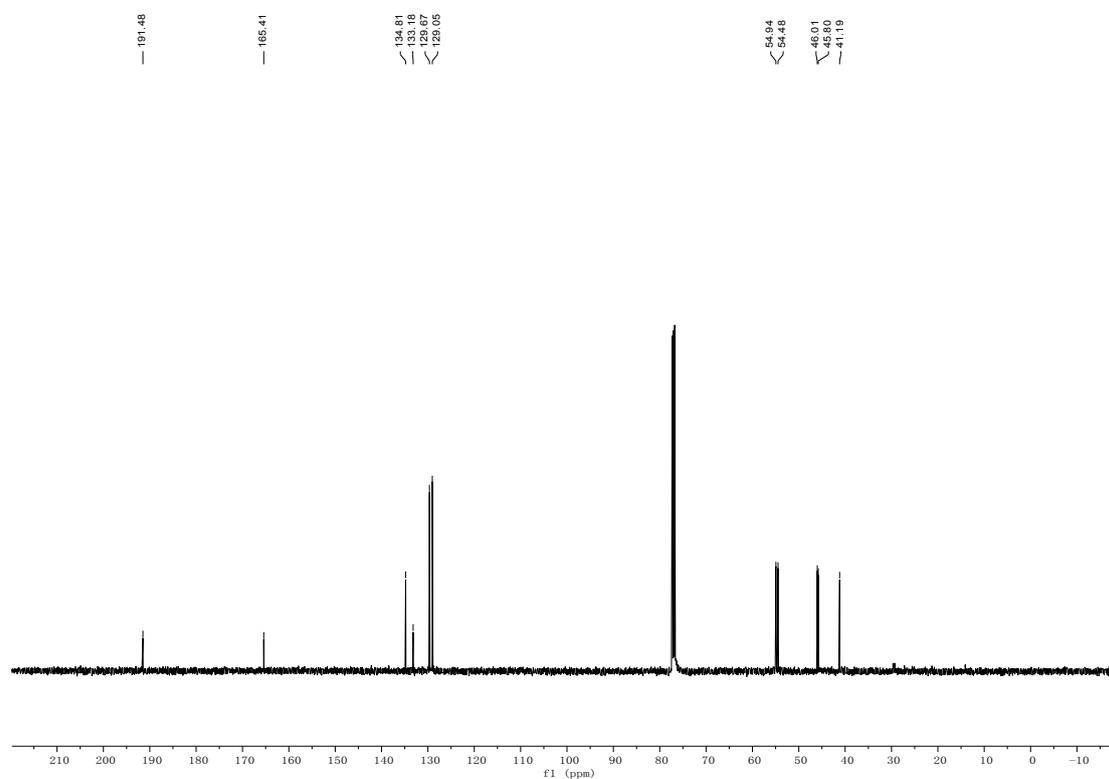
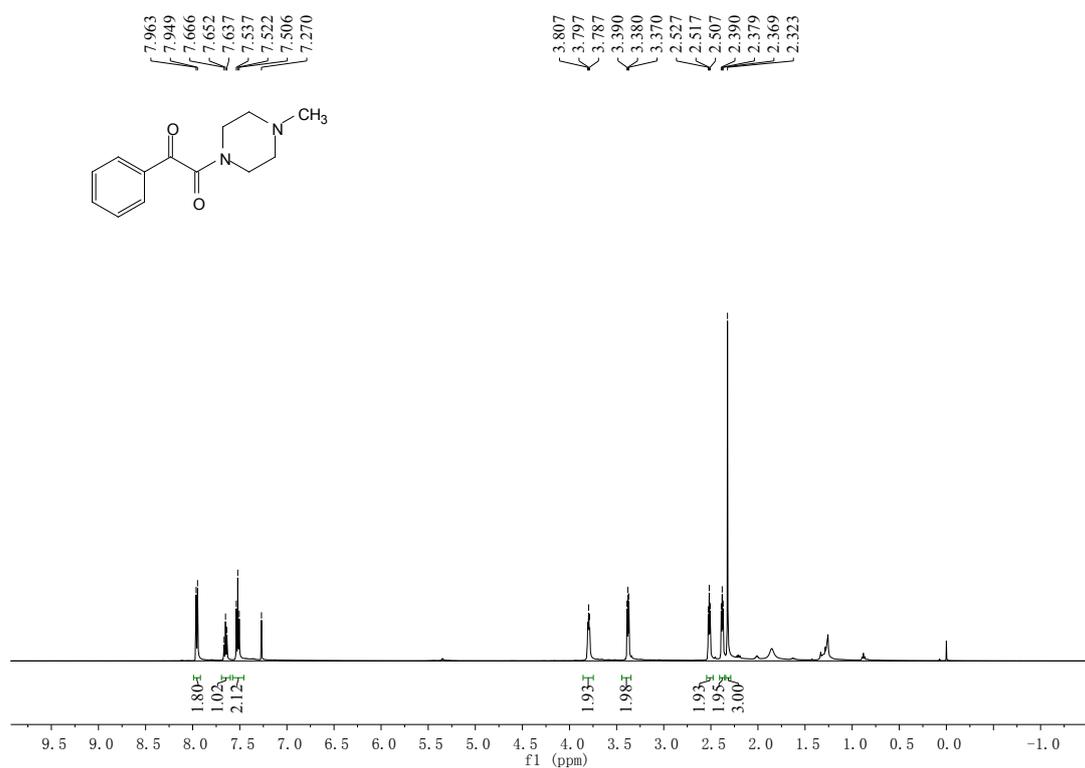


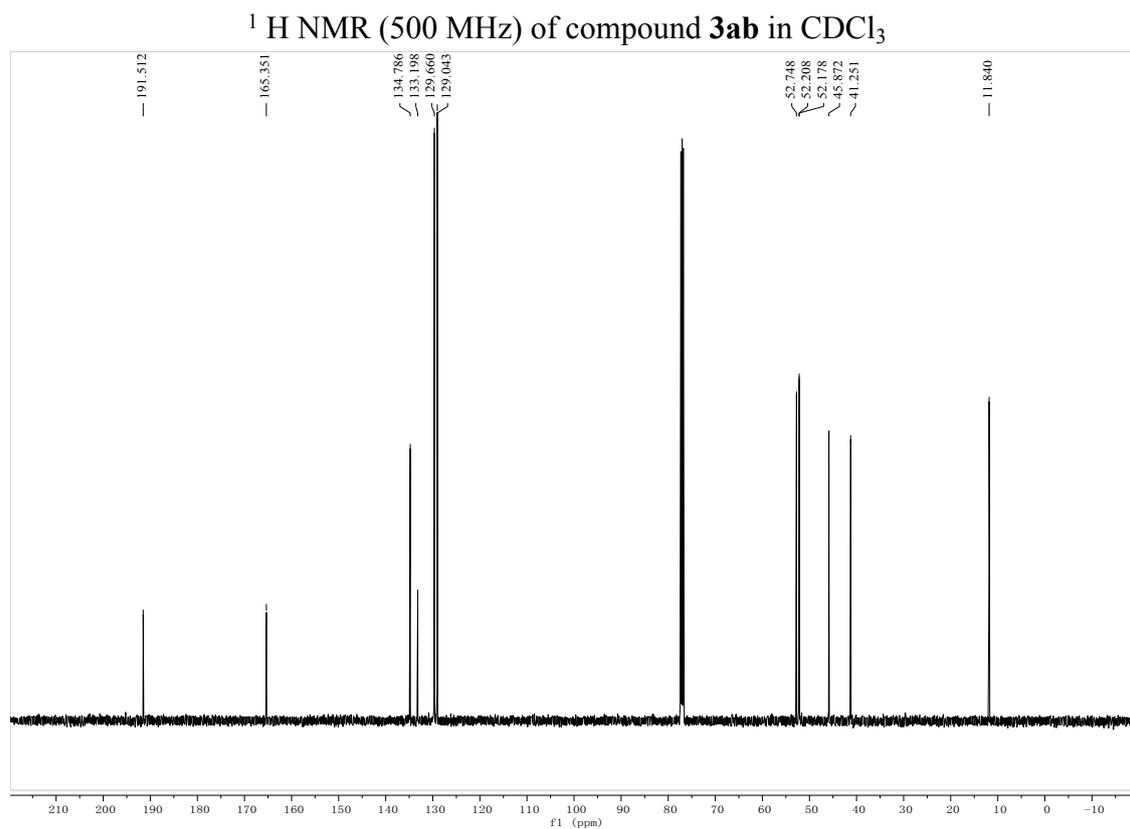
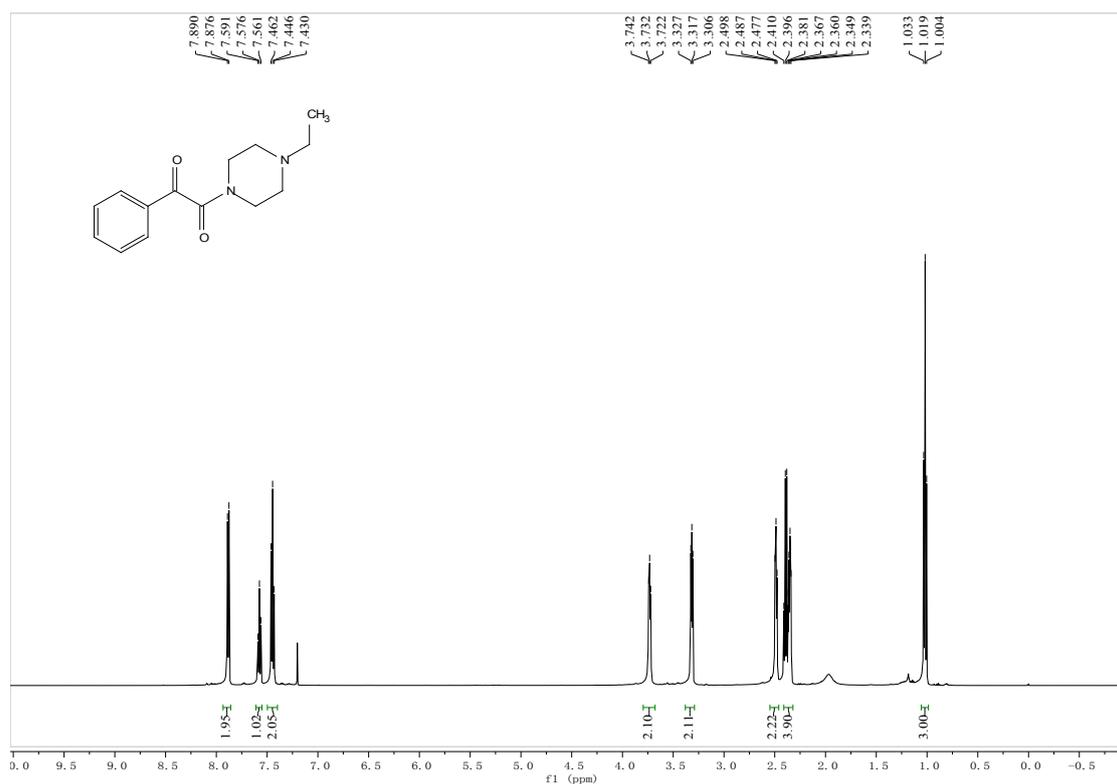
(Yellow solid, 101.4 mg, 81%); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.90-7.86 (m, 1H), 7.57-7.52 (m, 1H), 7.24-7.21 (m, 1H), 7.10-7.06 (m, 1H), 3.67 (t, $J = 5.0$ Hz, 2H), 3.36 (t, $J = 5.0$ Hz, 2H), 2.43 (t, $J = 5.0$ Hz, 2H), 2.35 (t, $J = 5.0$ Hz, 2H), 2.25 (s, 3H); $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 187.9, 165.8, 162.6 (d, $J_{\text{C-F}} = 256.6$ Hz), 136.6 (d, $J_{\text{C-F}} = 9.1$ Hz), 131.0 (d, $J_{\text{C-F}} = 27.6$ Hz), 124.9 (d, $J_{\text{C-F}} = 3.5$ Hz), 122.4 (d, $J_{\text{C-F}} = 10.0$ Hz), 116.7 (d, $J_{\text{C-F}} = 21.5$ Hz), 54.5, 54.1, 46.0, 45.6, 41.2; HRMS (TOF) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{13}\text{H}_{15}\text{FN}_2\text{O}_2$ 251.1190 found 251.1193.

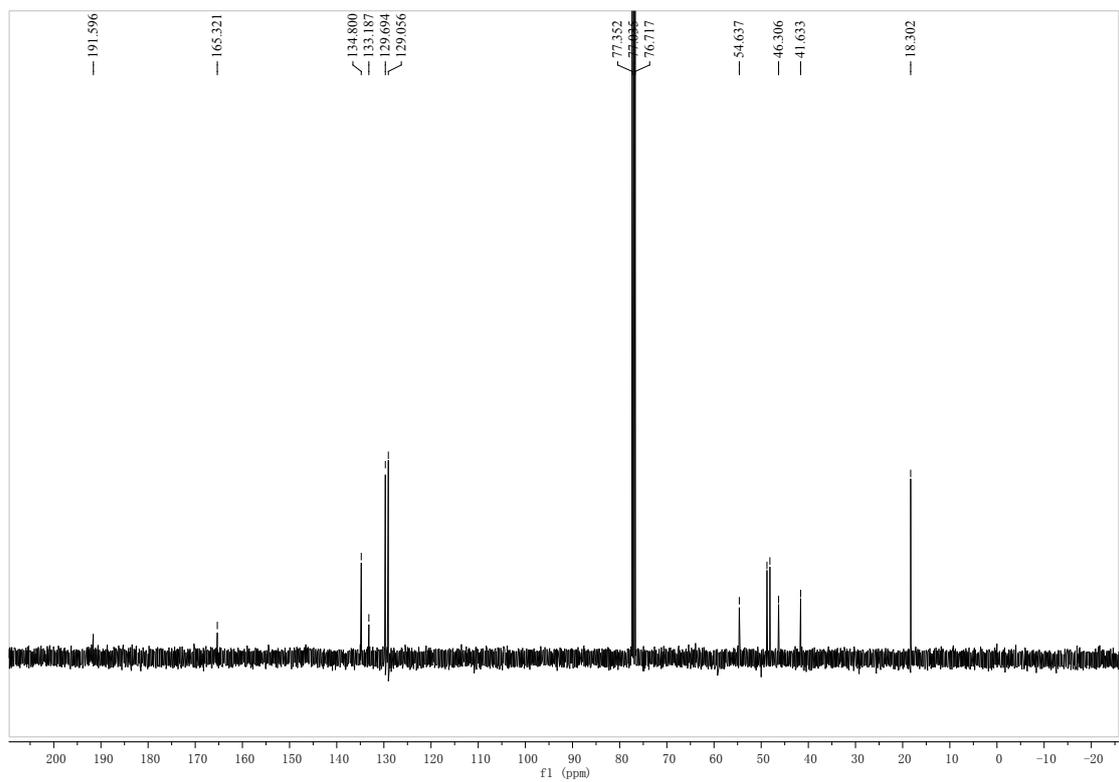
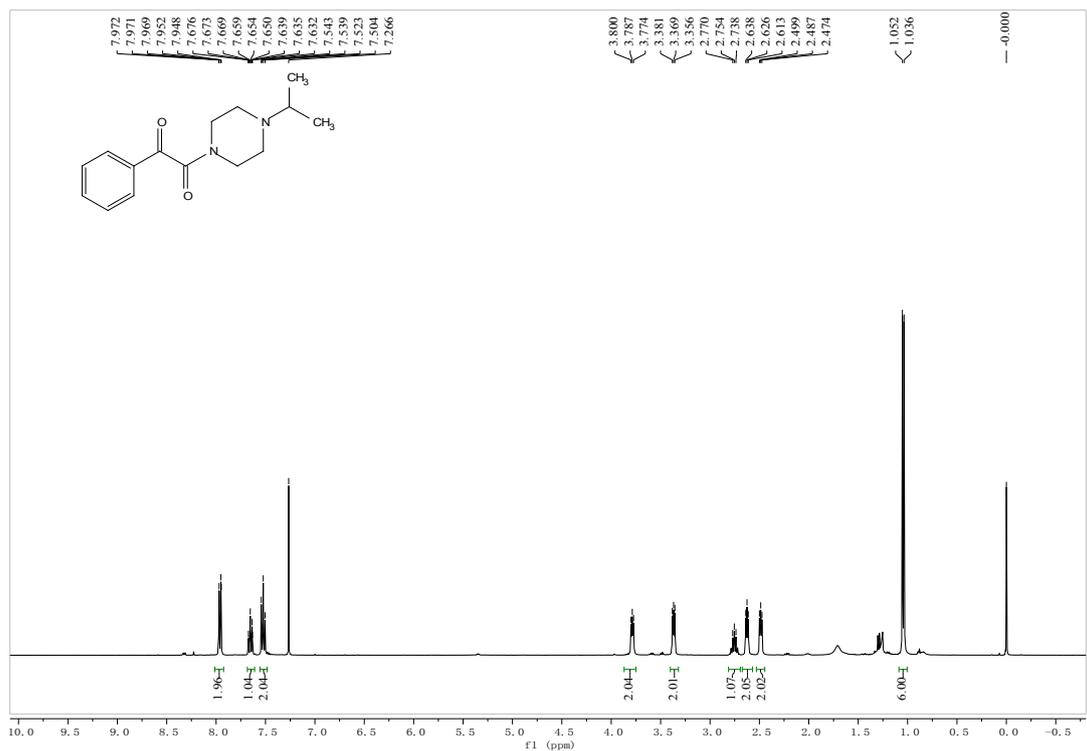
4. References

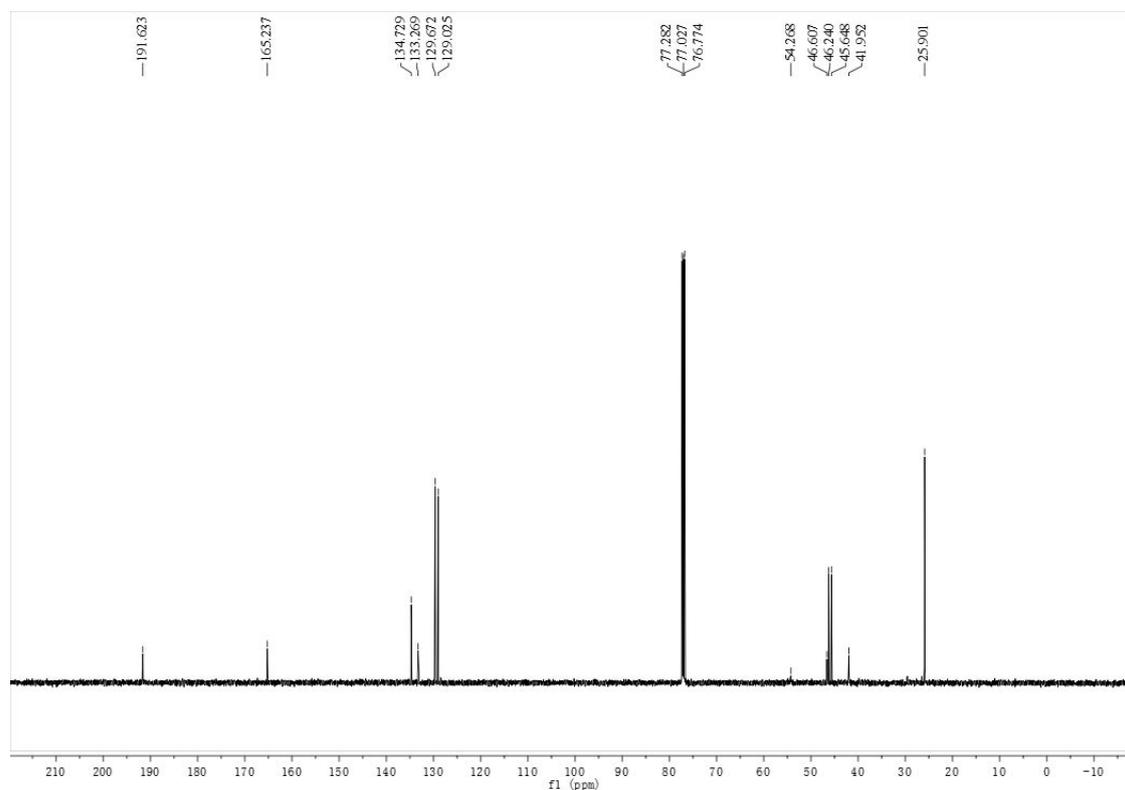
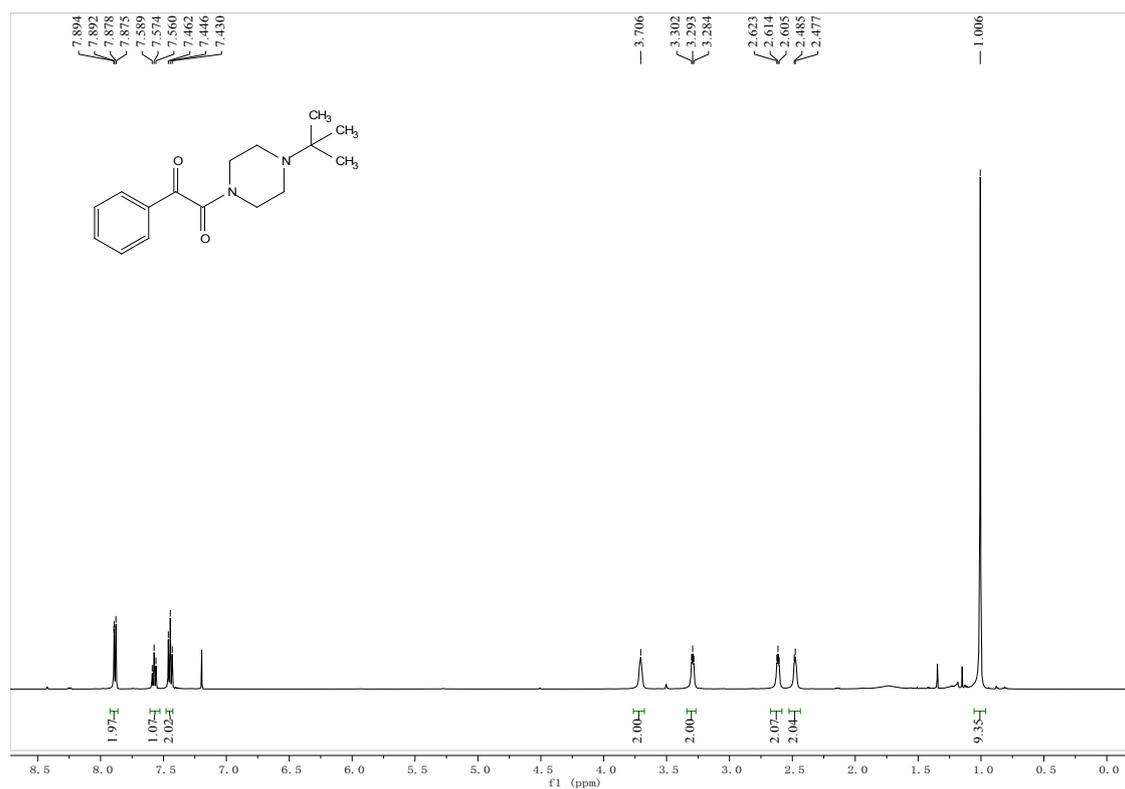
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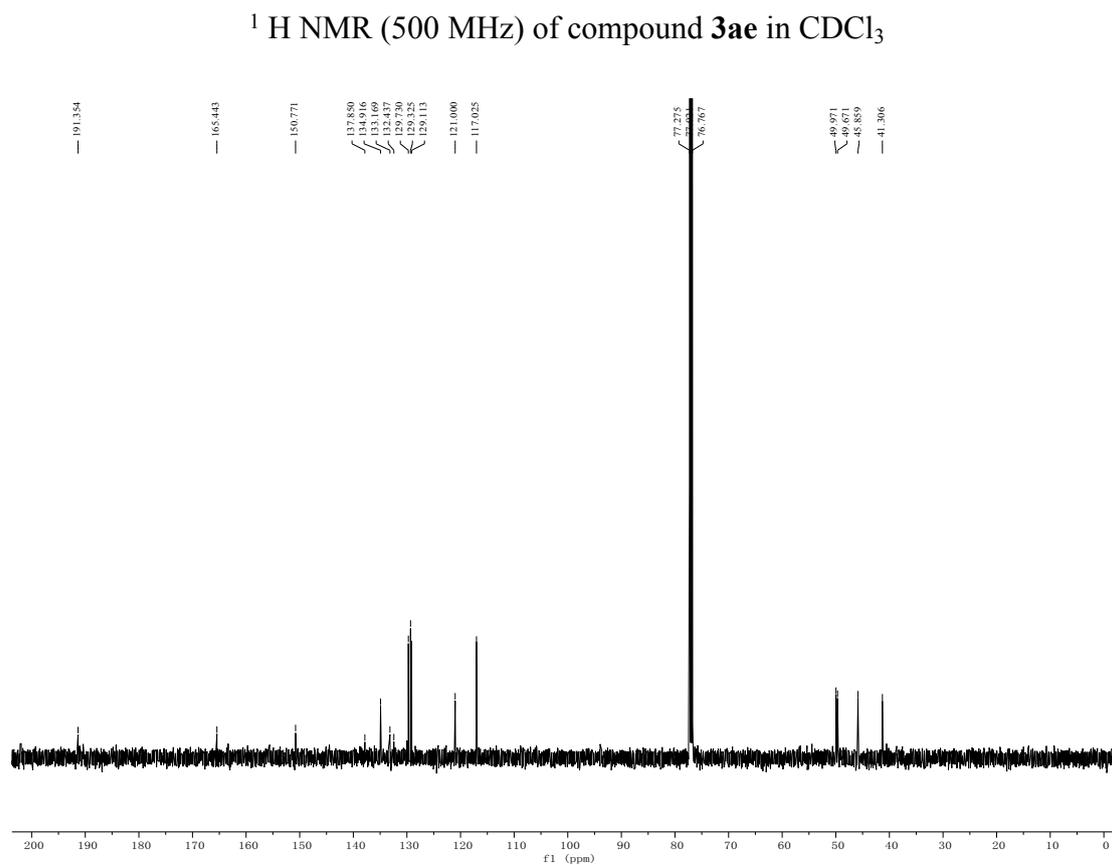
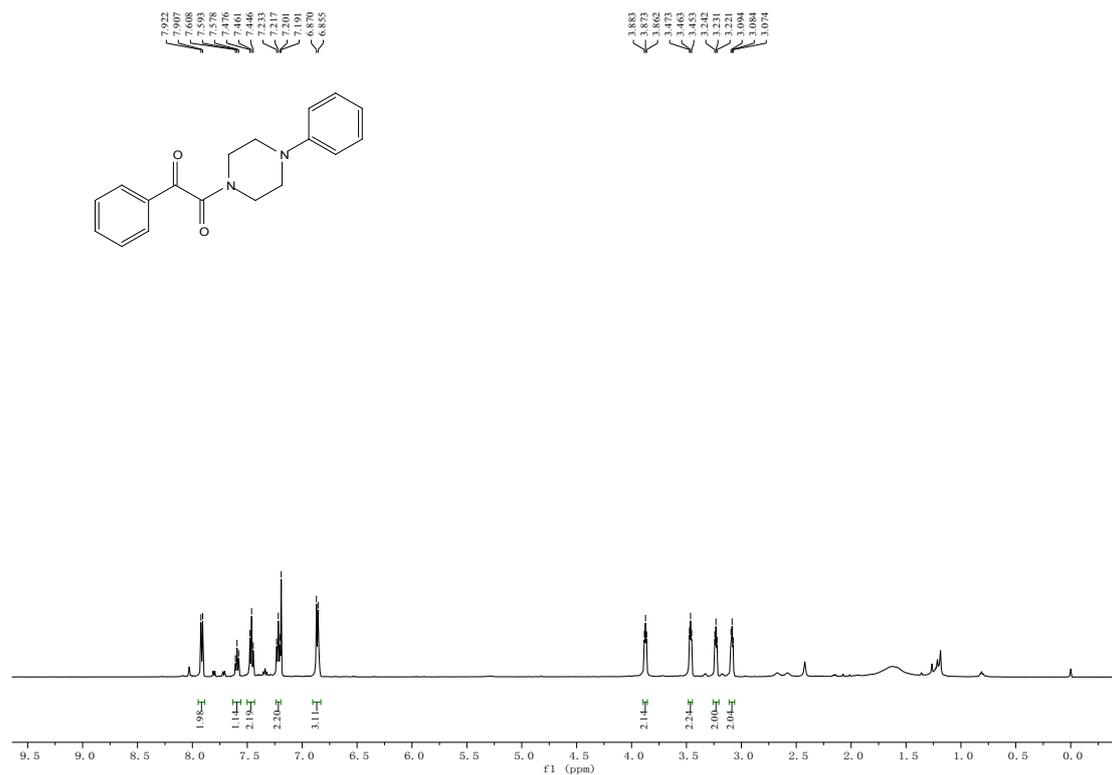
5. ^1H and ^{13}C NMR spectra of products

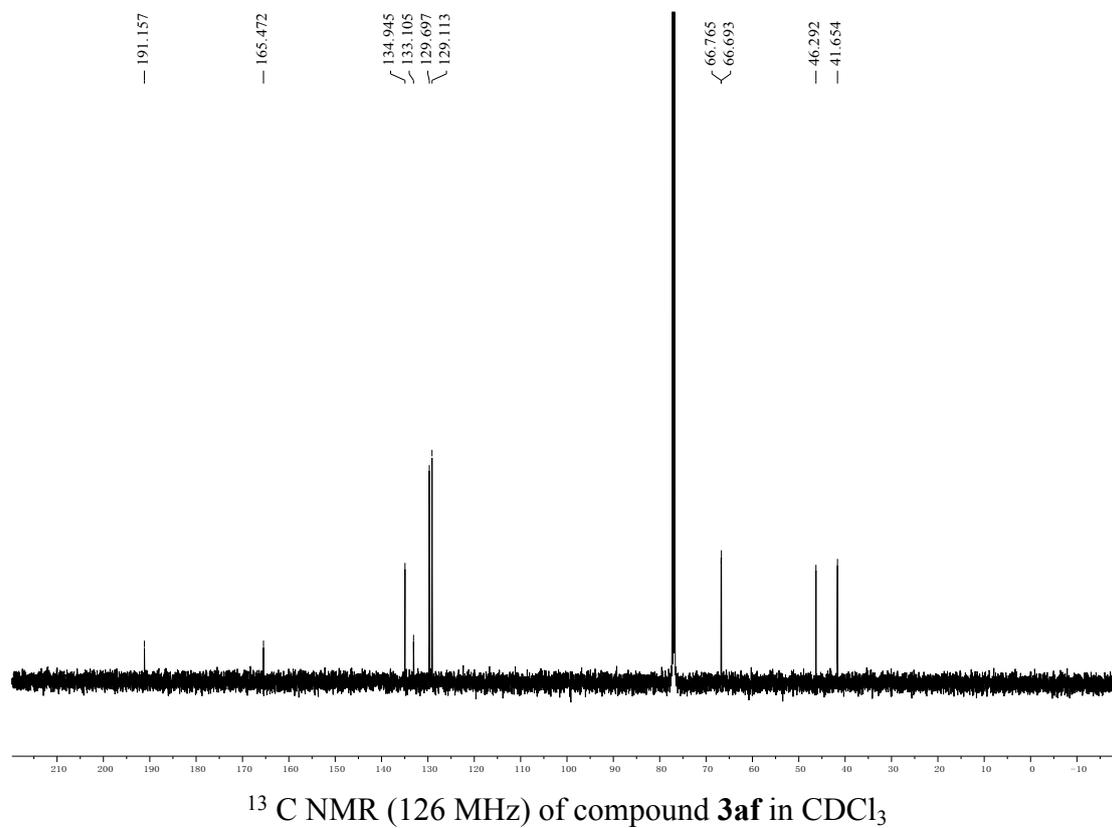
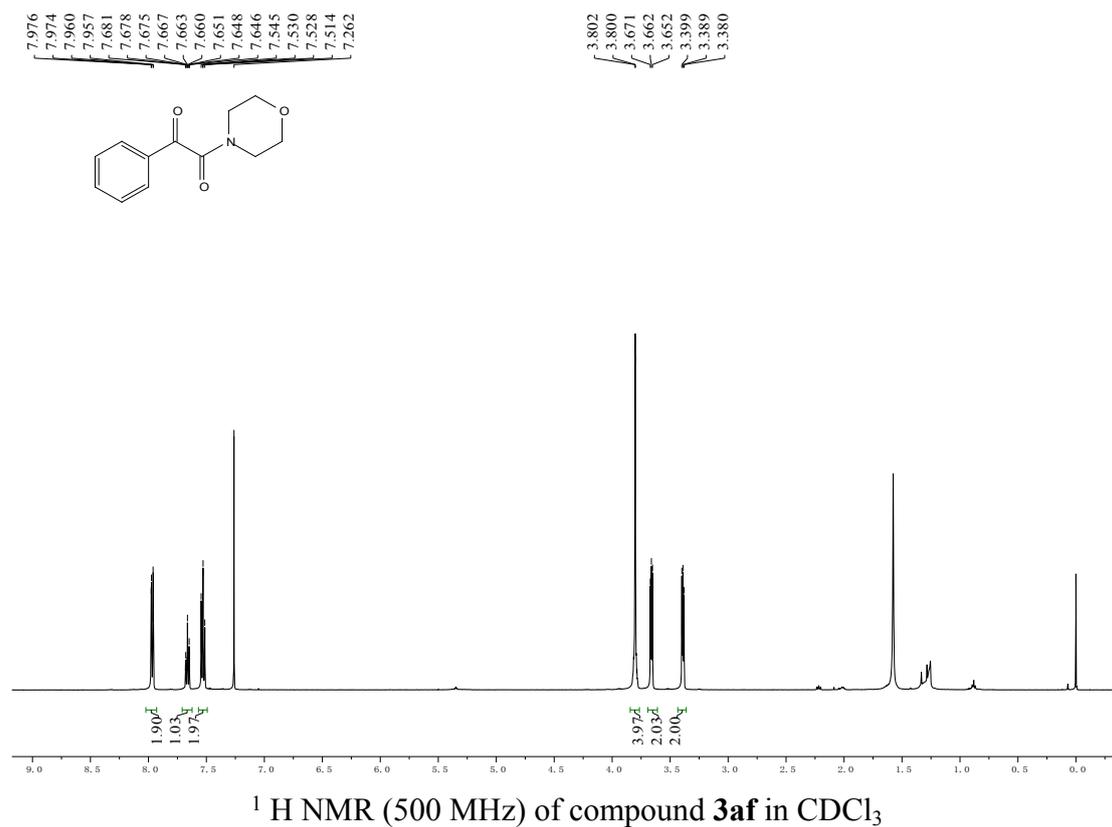


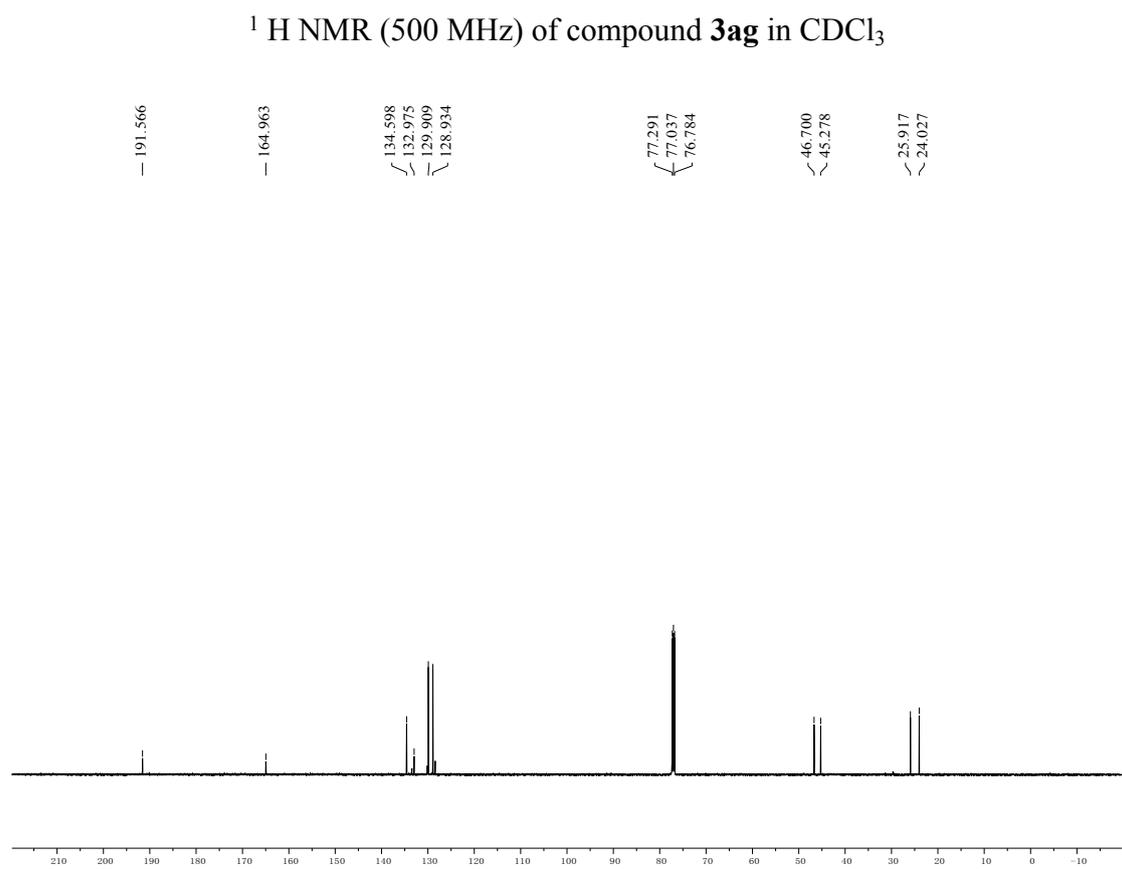
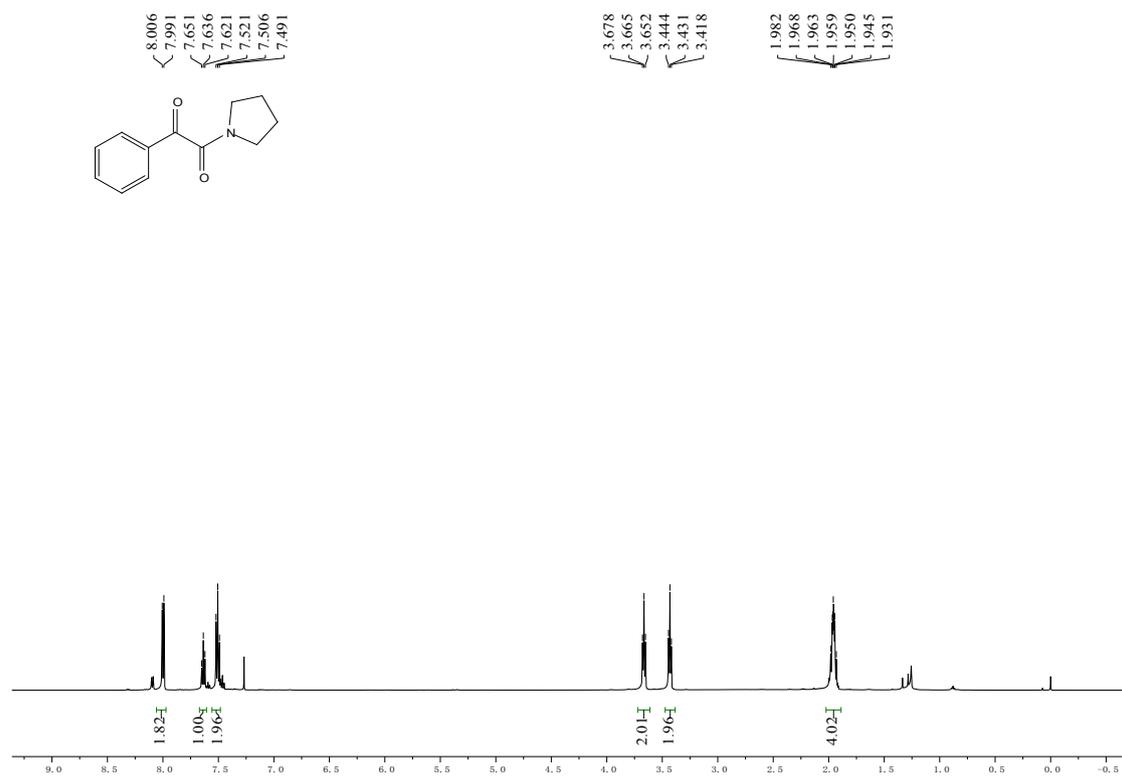


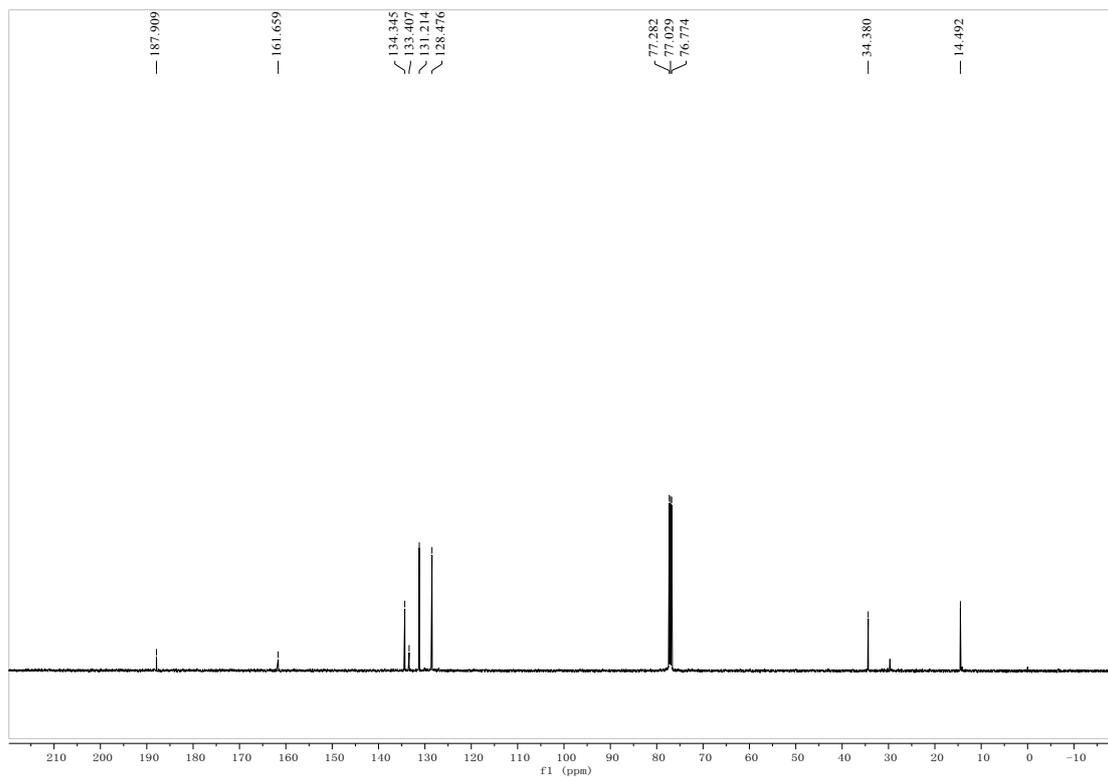
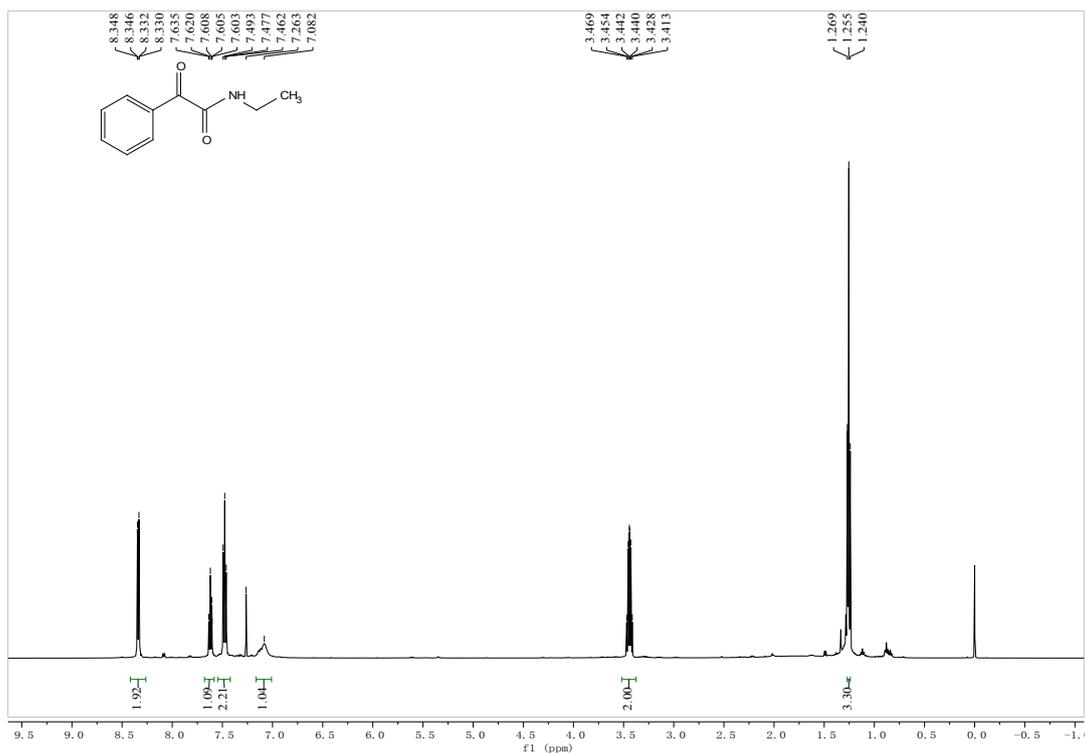


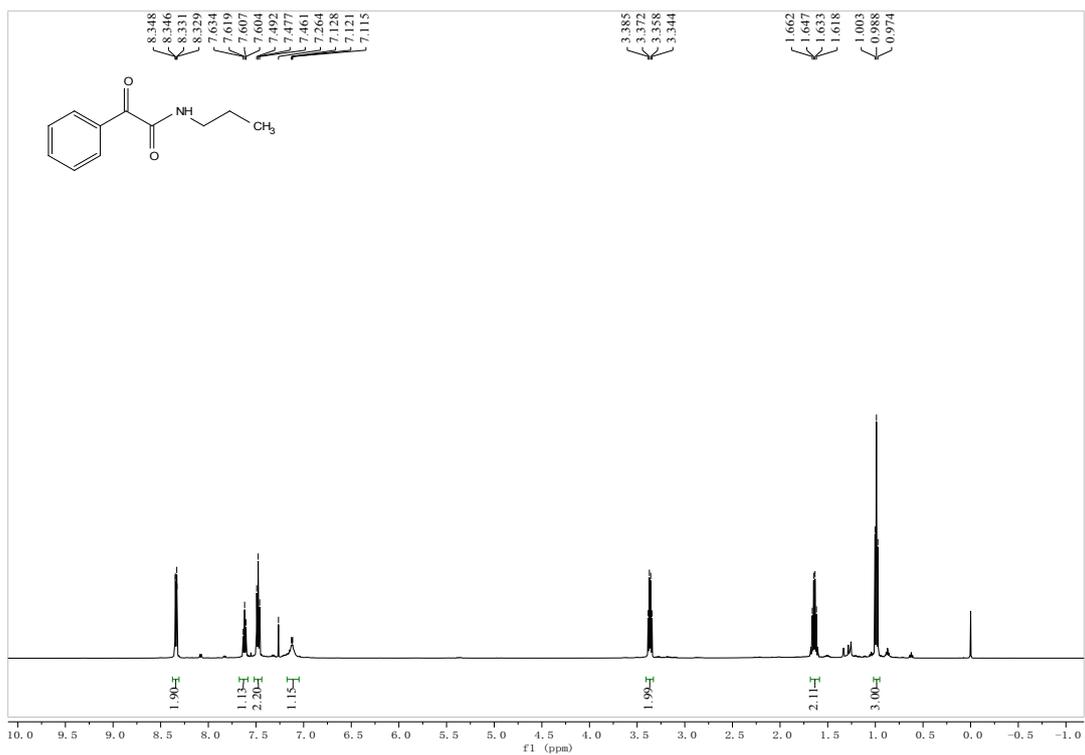




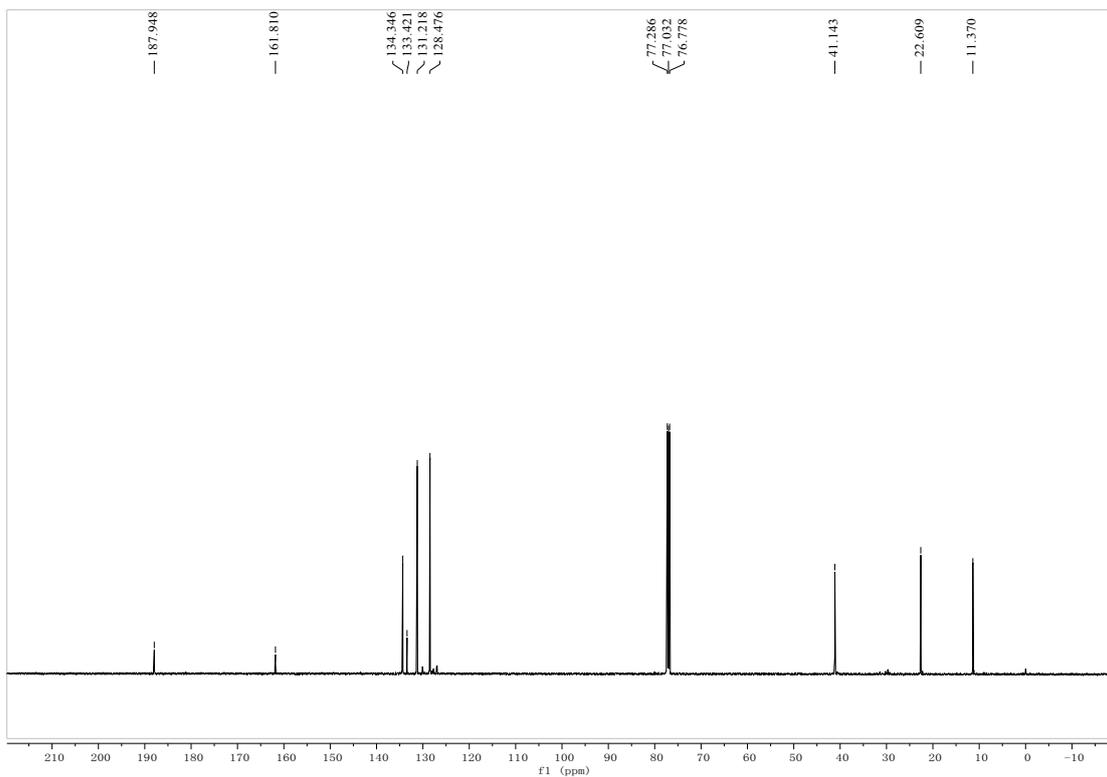




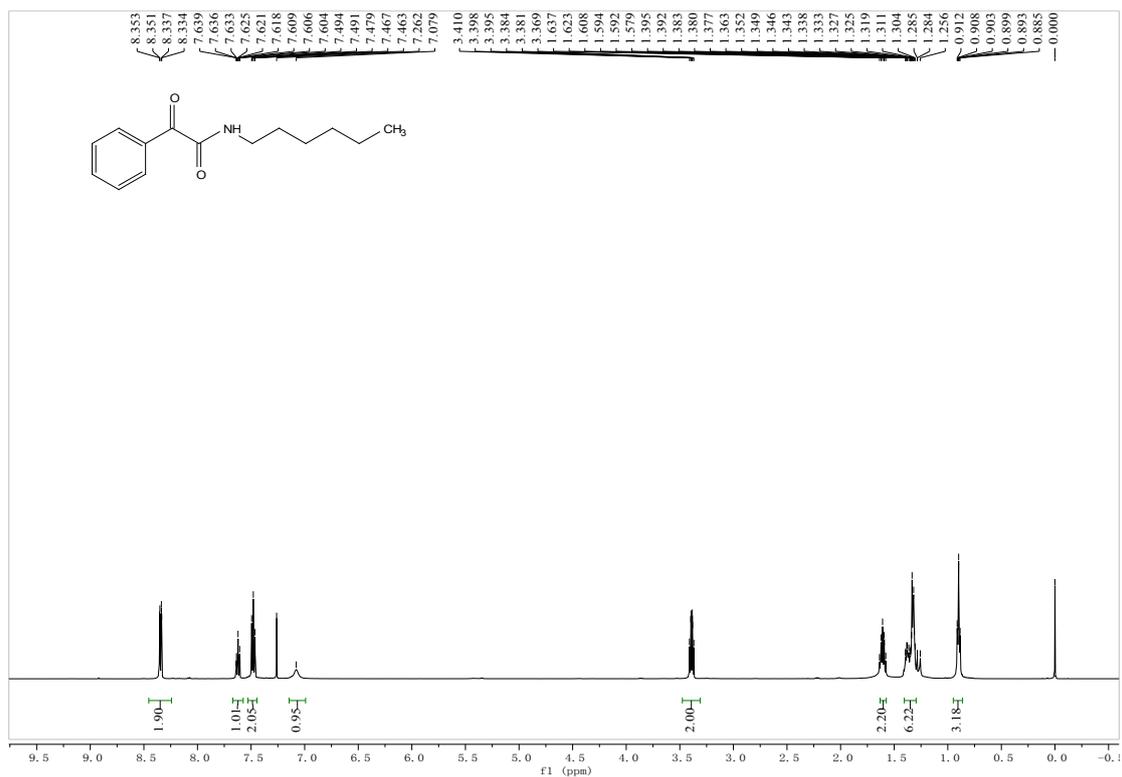




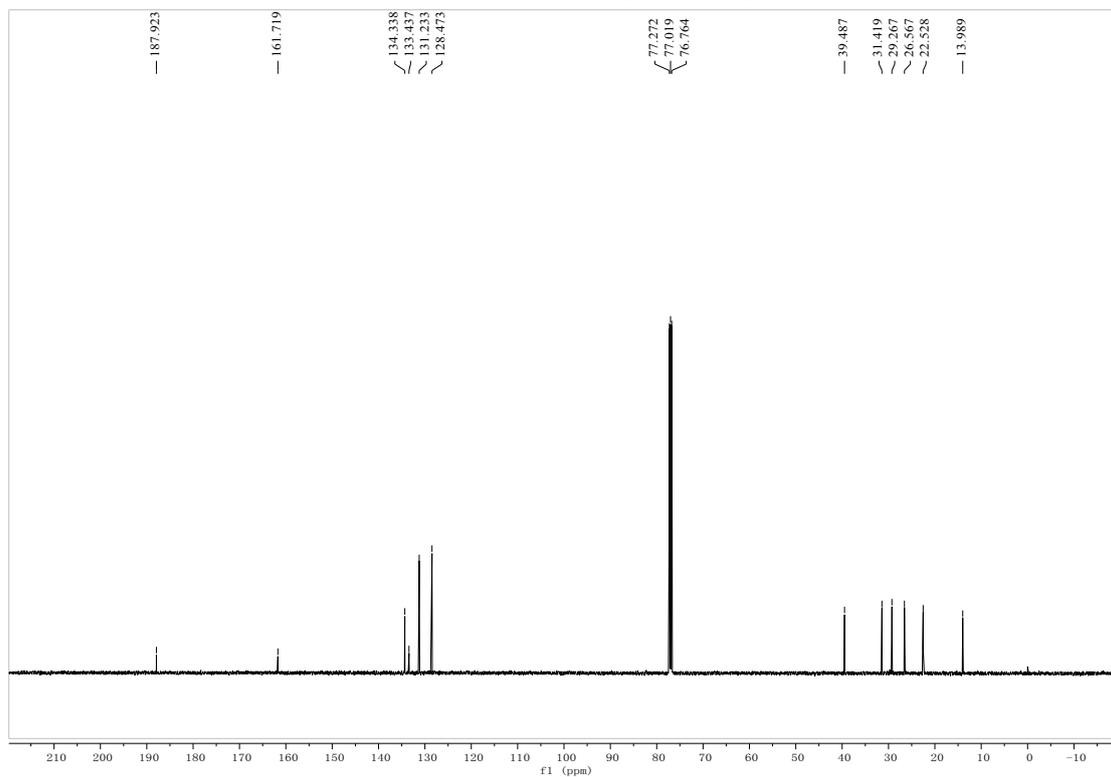
¹H NMR (500 MHz) of compound **3ai** in CDCl₃



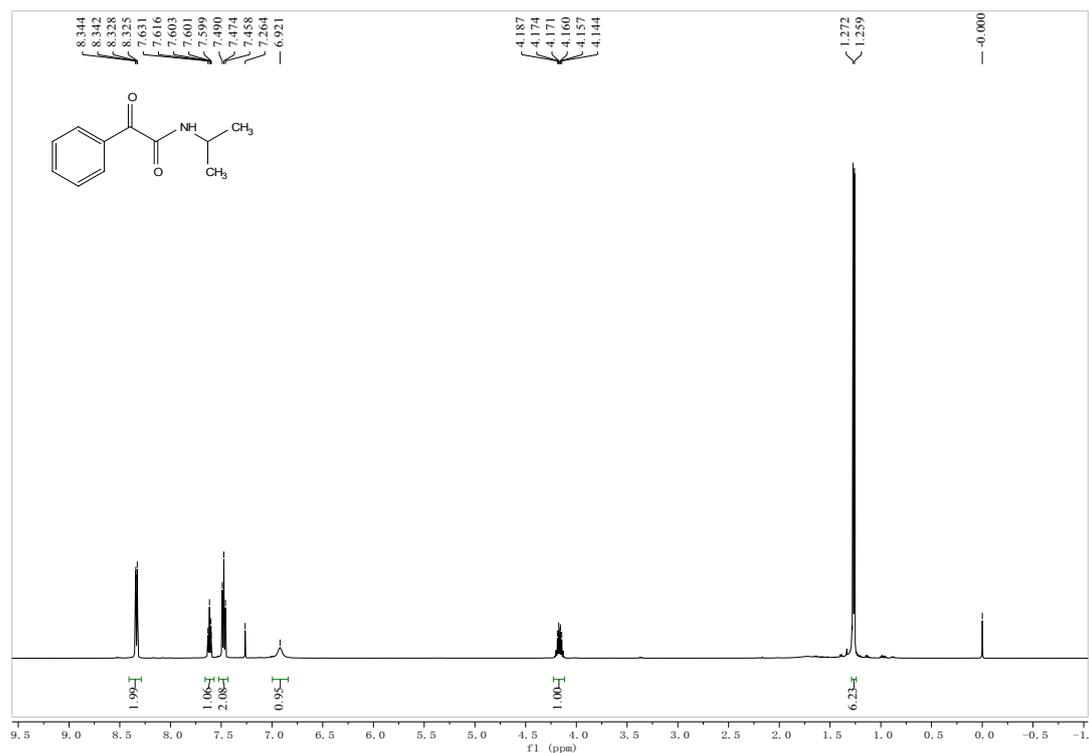
¹³C NMR (126 MHz) of compound **3ai** in CDCl₃



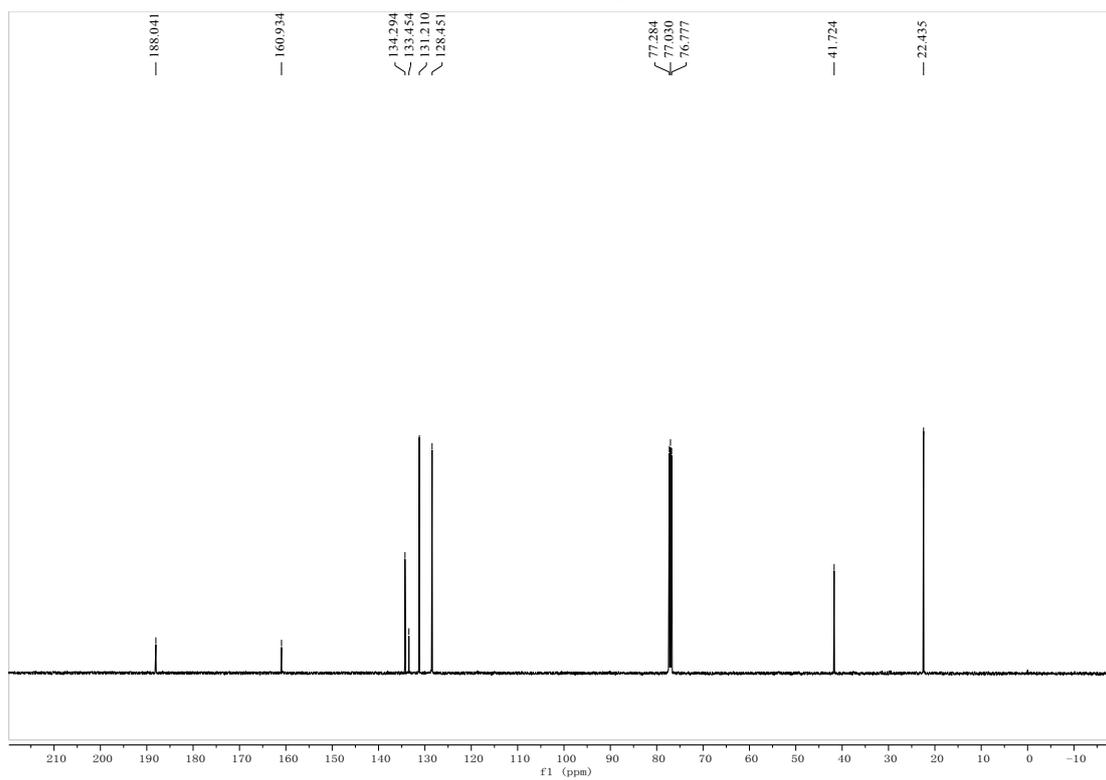
¹H NMR (500 MHz) of compound **3aj** in CDCl₃



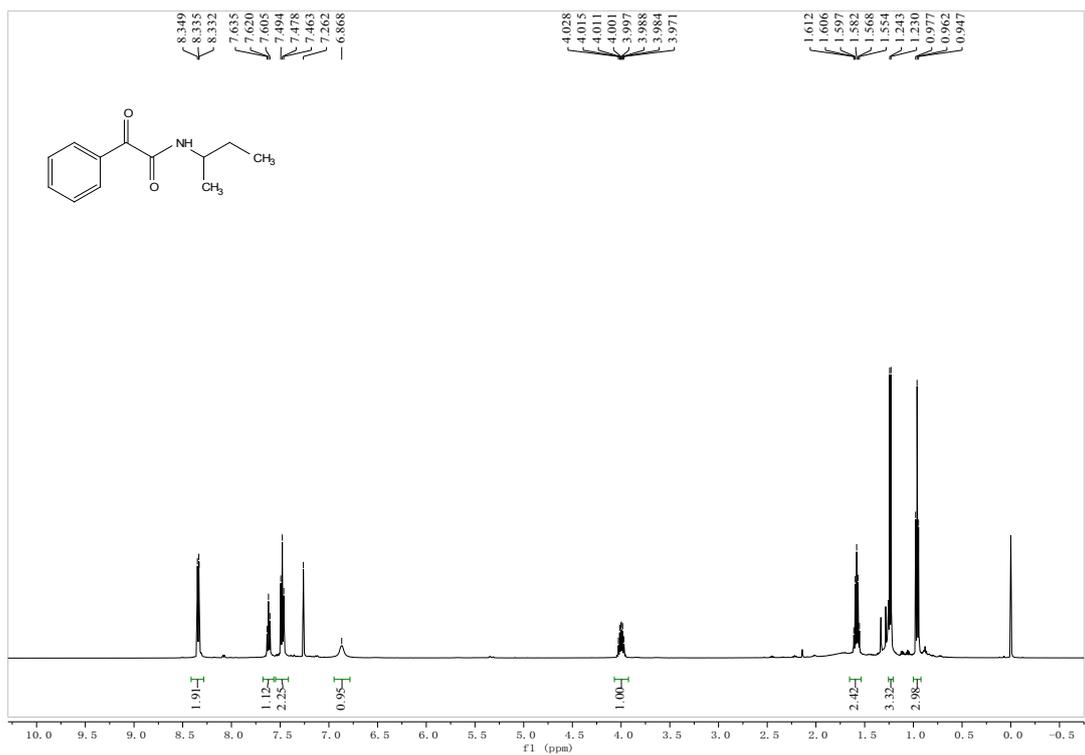
¹³C NMR (126 MHz) of compound **3aj** in CDCl₃



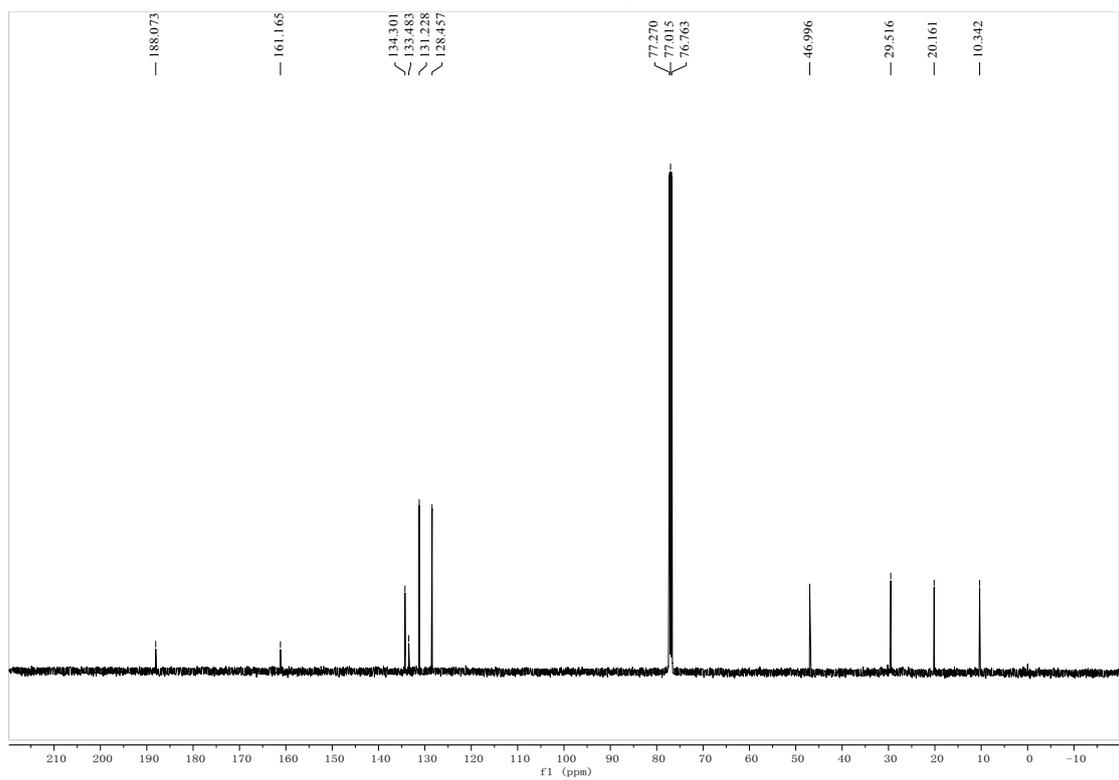
¹H NMR (500 MHz) of compound **3ak** in CDCl₃



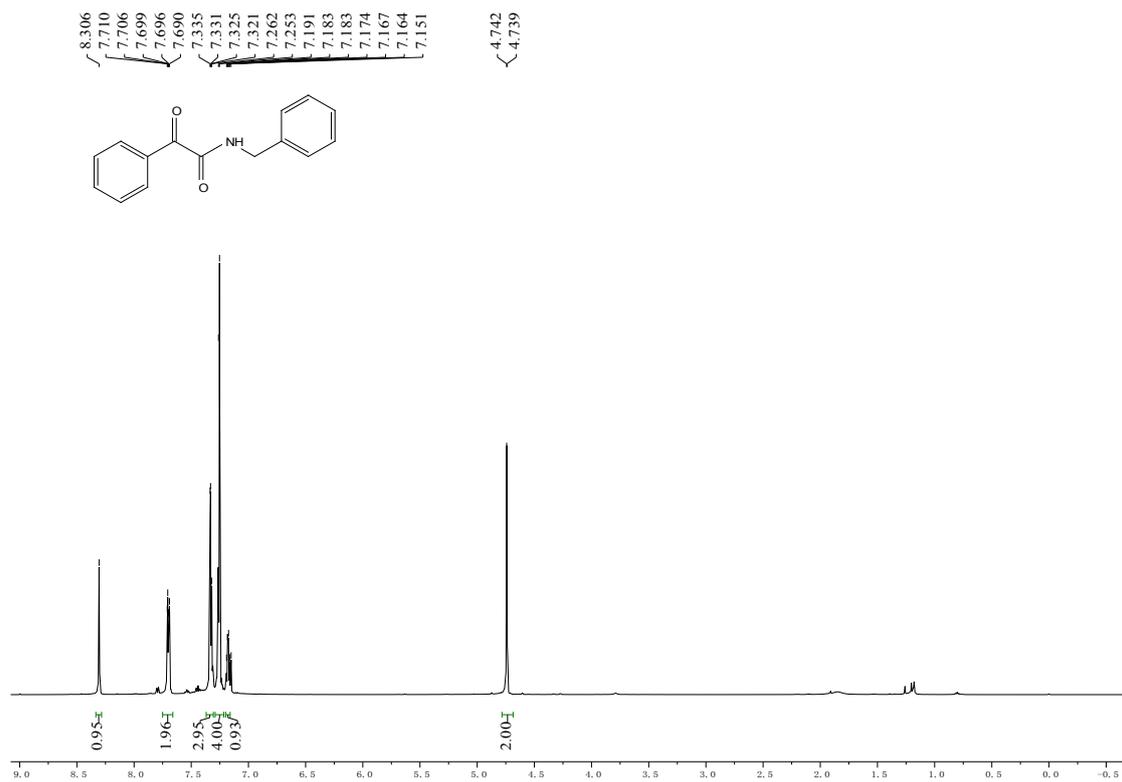
¹³C NMR (126 MHz) of compound **3ak** in CDCl₃



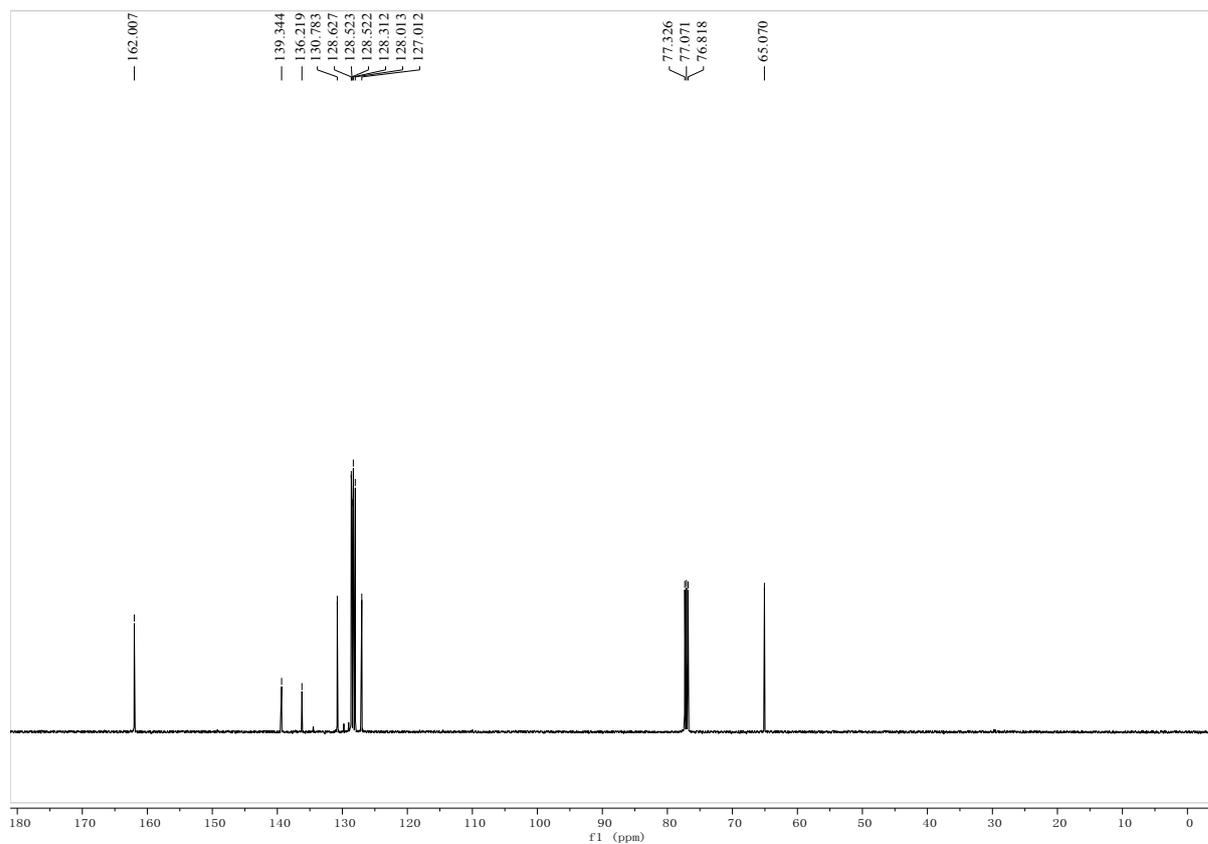
¹H NMR (500 MHz) of compound **3al** in CDCl₃



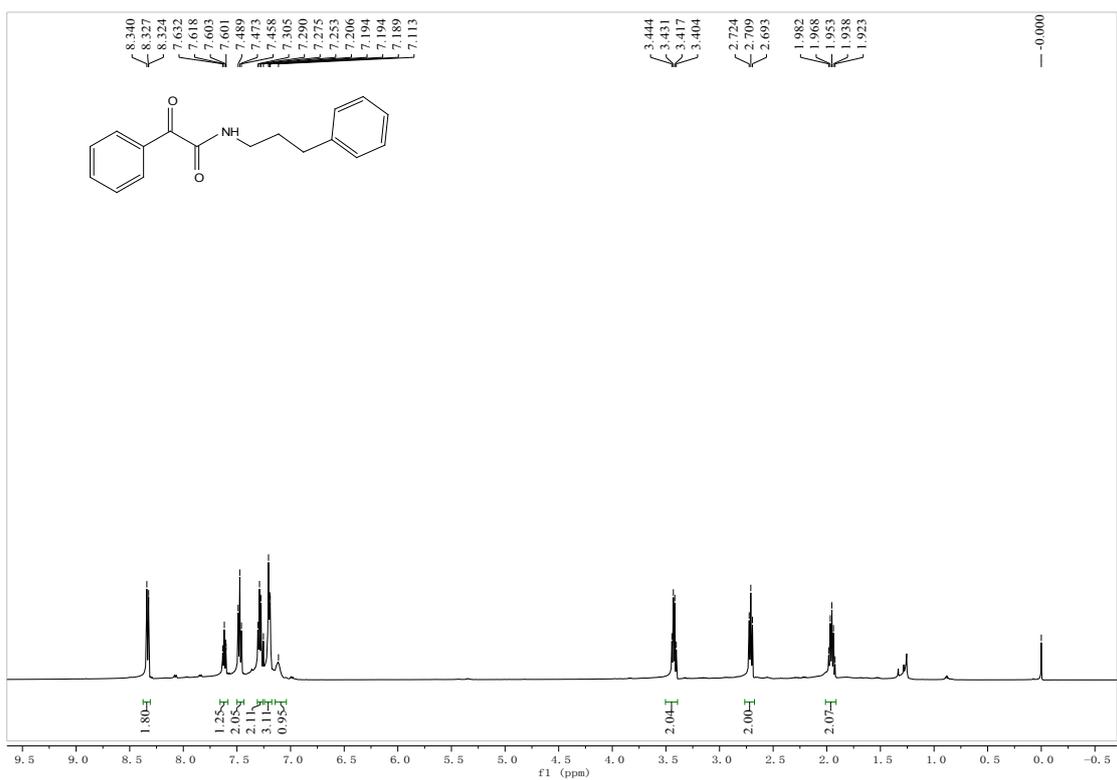
¹³C NMR (126 MHz) of compound **3al** in CDCl₃



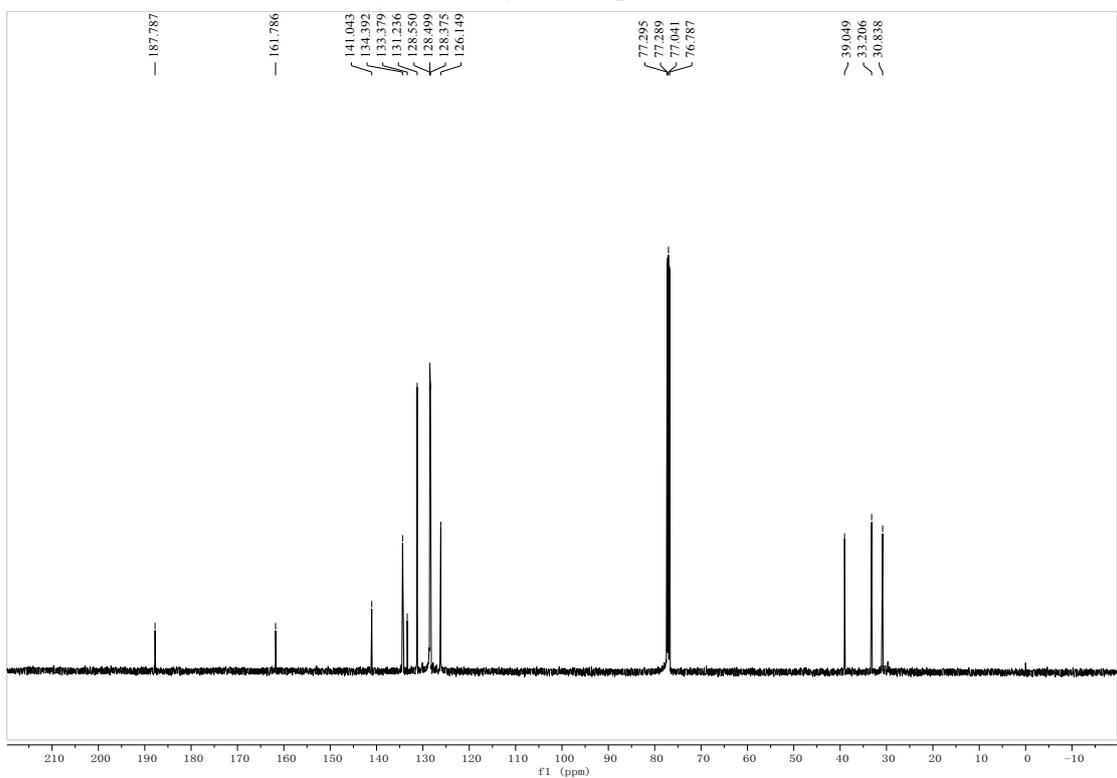
¹H NMR (500 MHz) of compound **3am** in CDCl₃



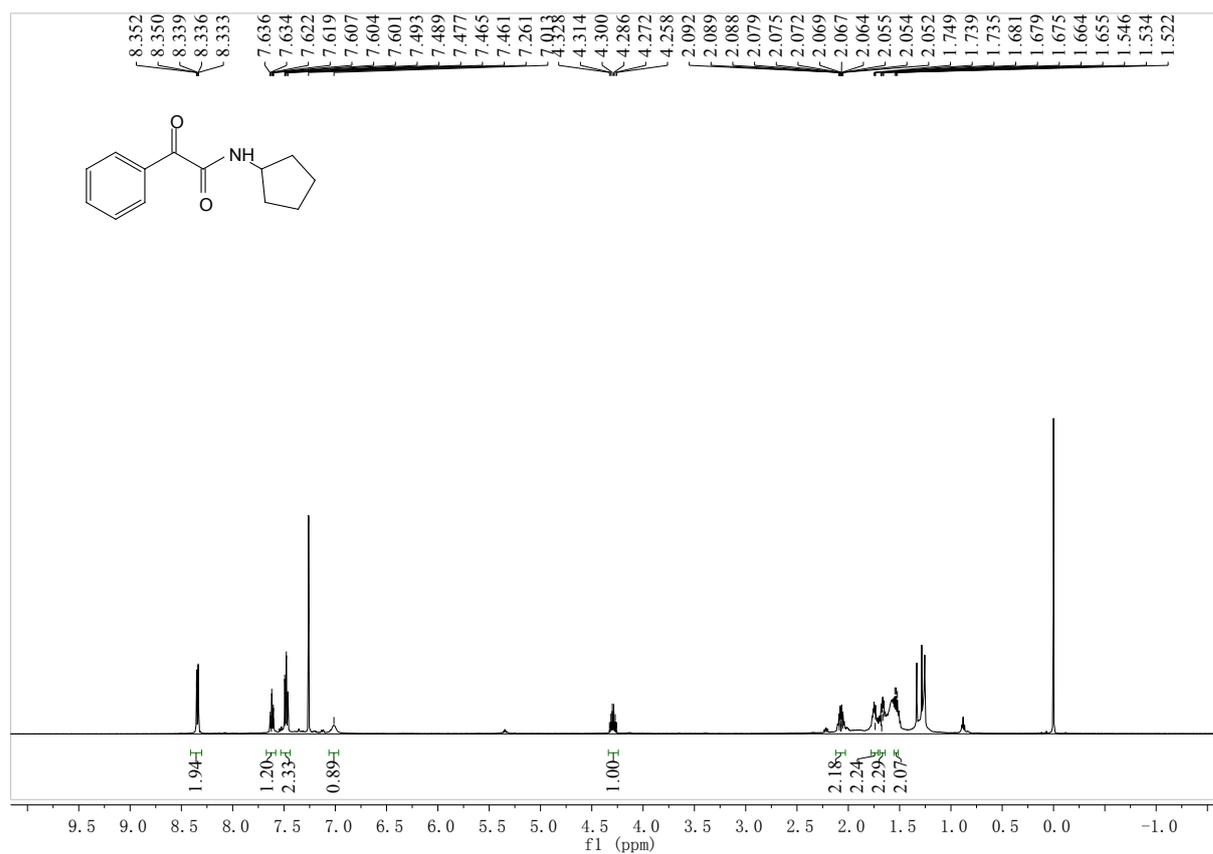
¹³C NMR (126 MHz) of compound **3am** in CDCl₃



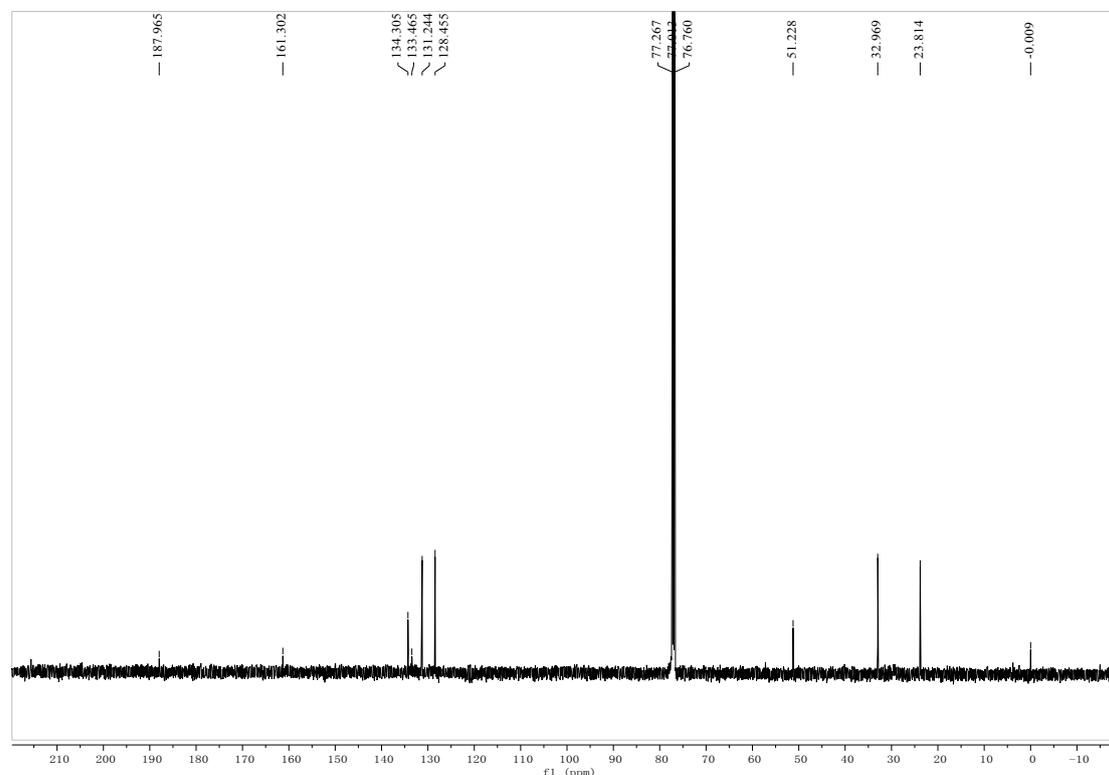
¹H NMR (500 MHz) of compound **3an** in CDCl₃



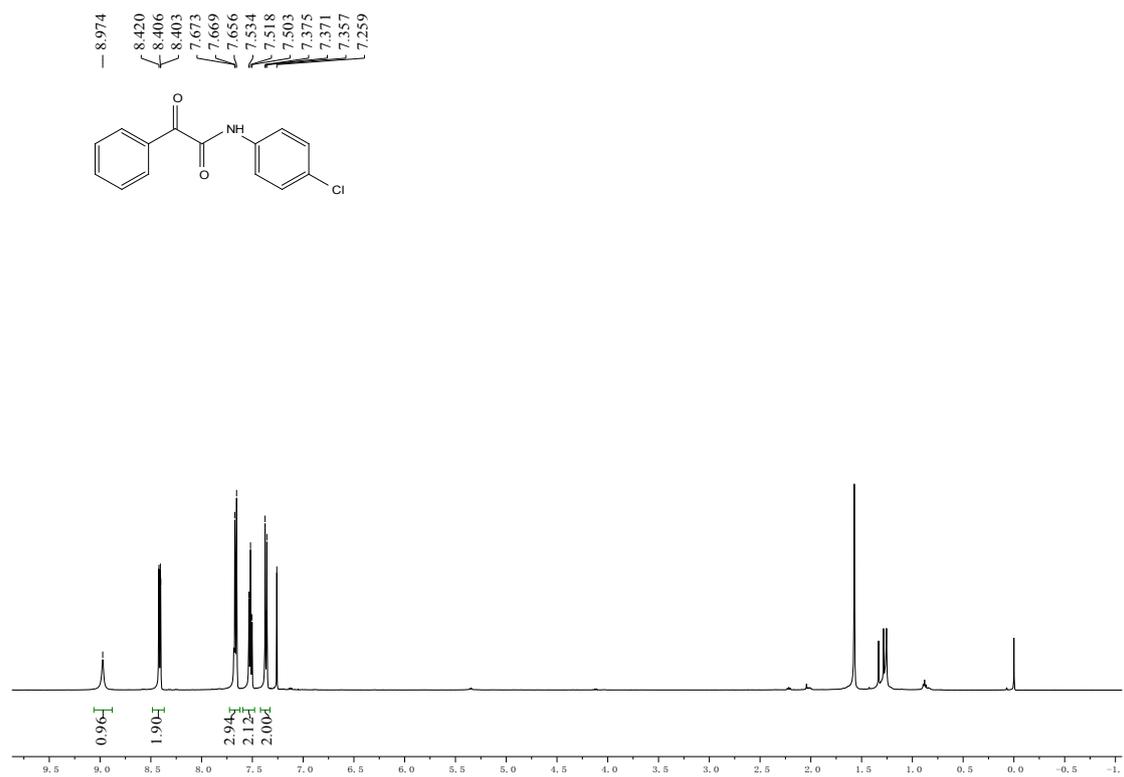
¹³C NMR (126 MHz) of compound **3an** in CDCl₃



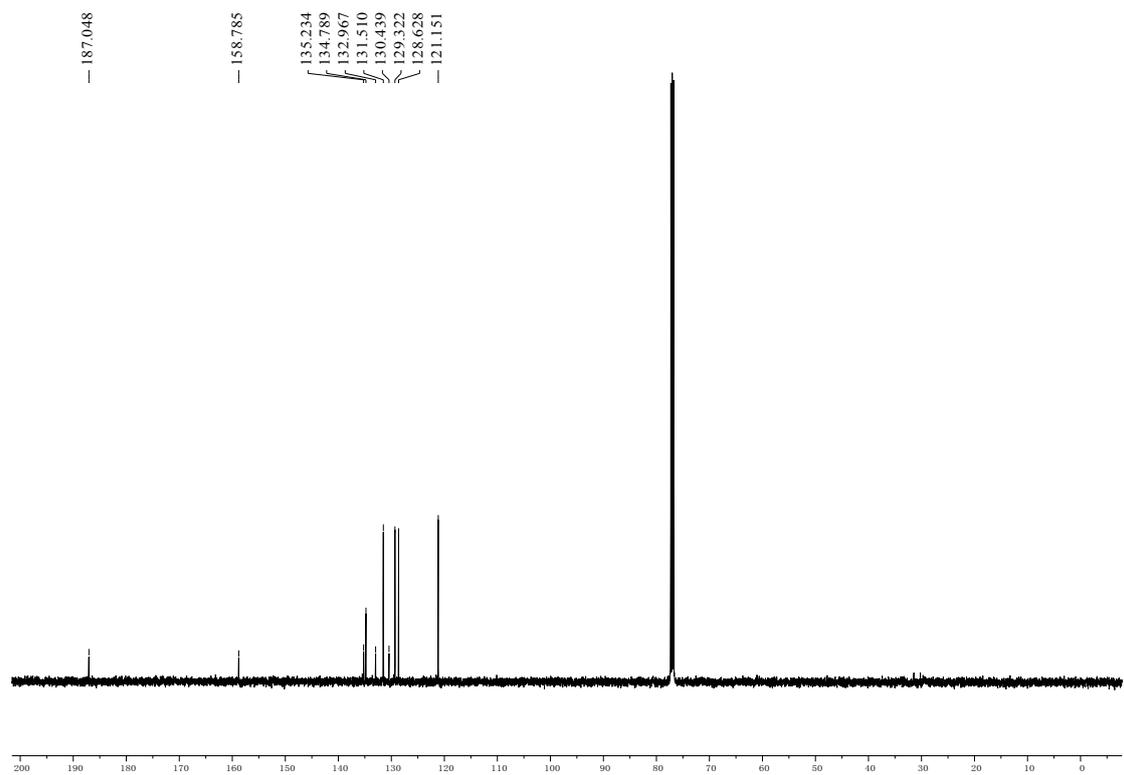
¹H NMR (500 MHz) of compound 3ao in CDCl₃



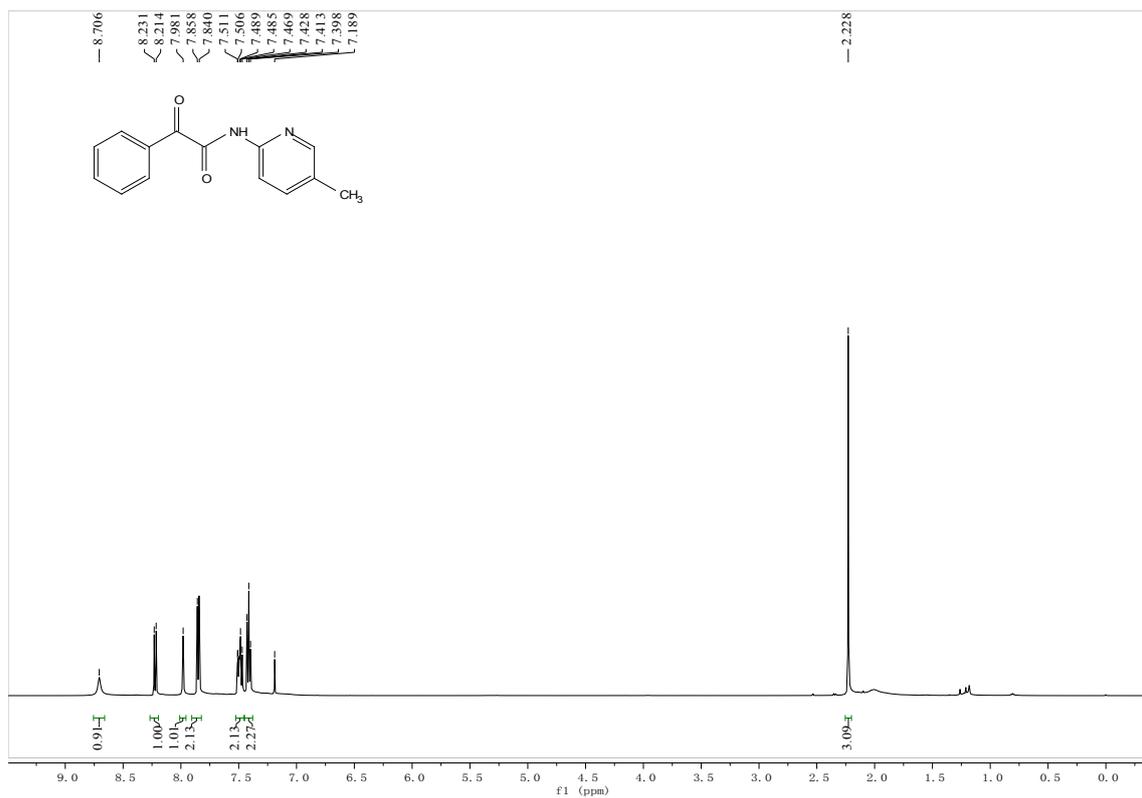
¹³C NMR (126 MHz) of compound 3ao in CDCl₃



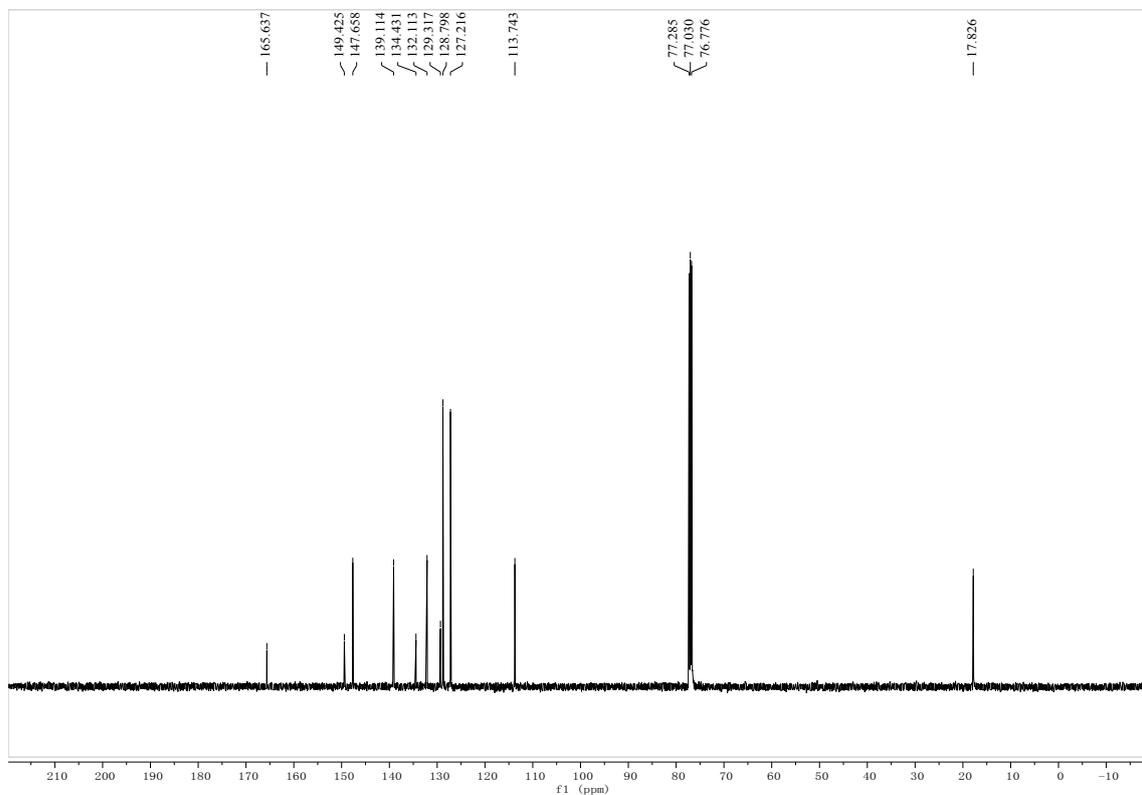
^1H NMR (500 MHz) of compound **3ap** in CDCl_3



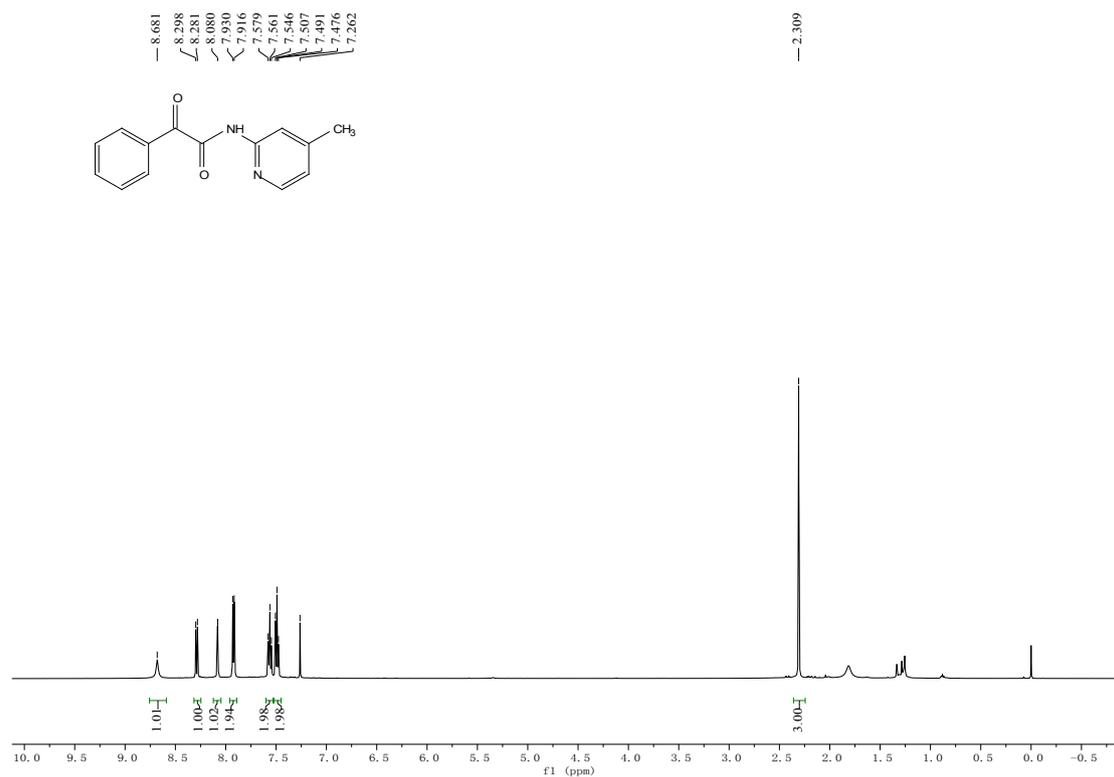
^{13}C NMR (126 MHz) of compound **3ap** in CDCl_3



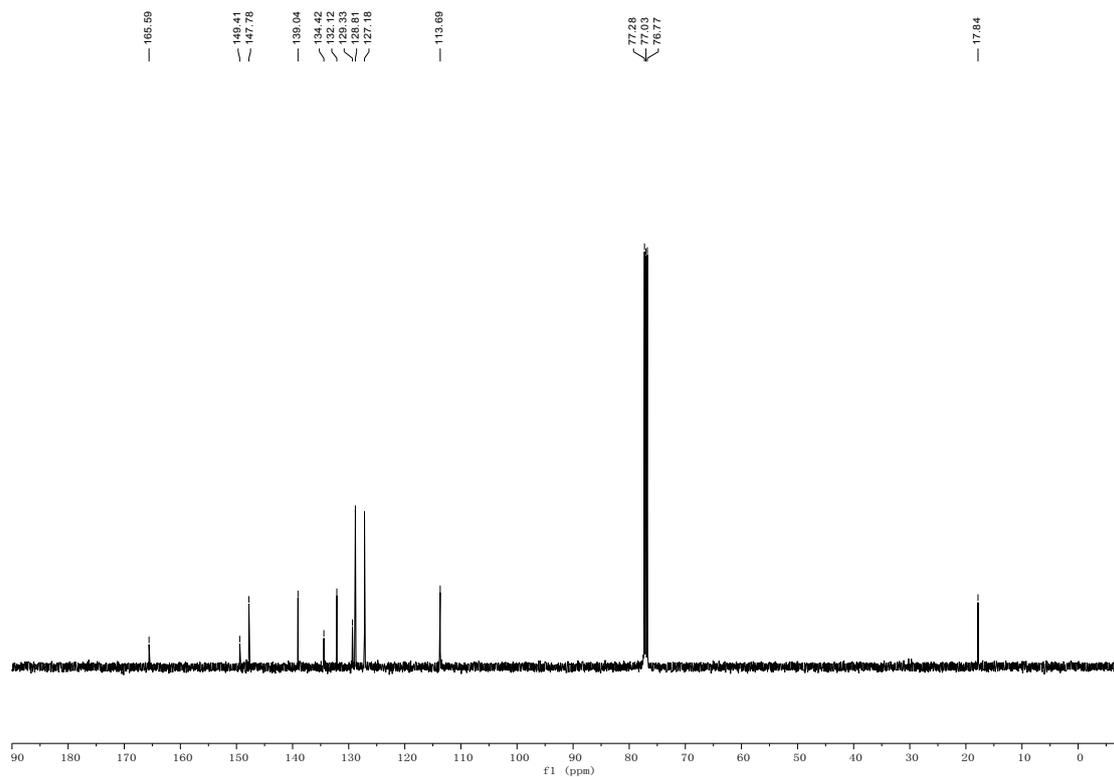
¹H NMR (500 MHz) of compound **3aq** in CDCl₃



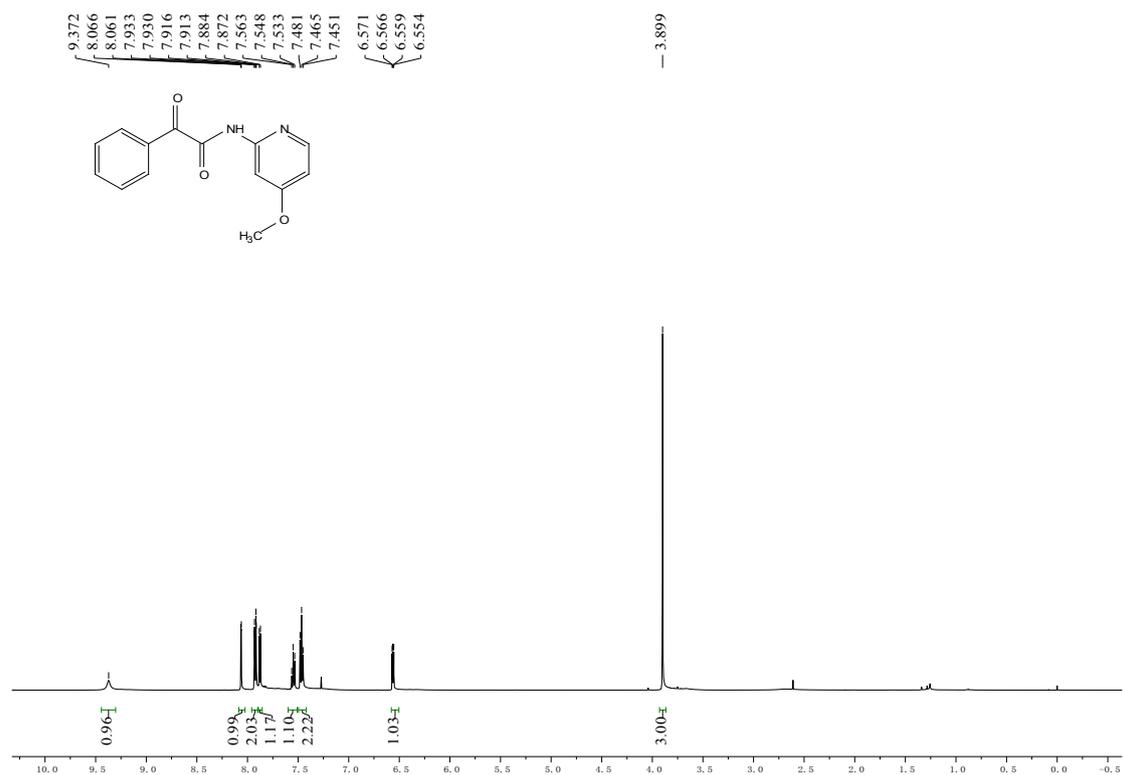
¹³C NMR (126 MHz) of compound **3aq** in CDCl₃



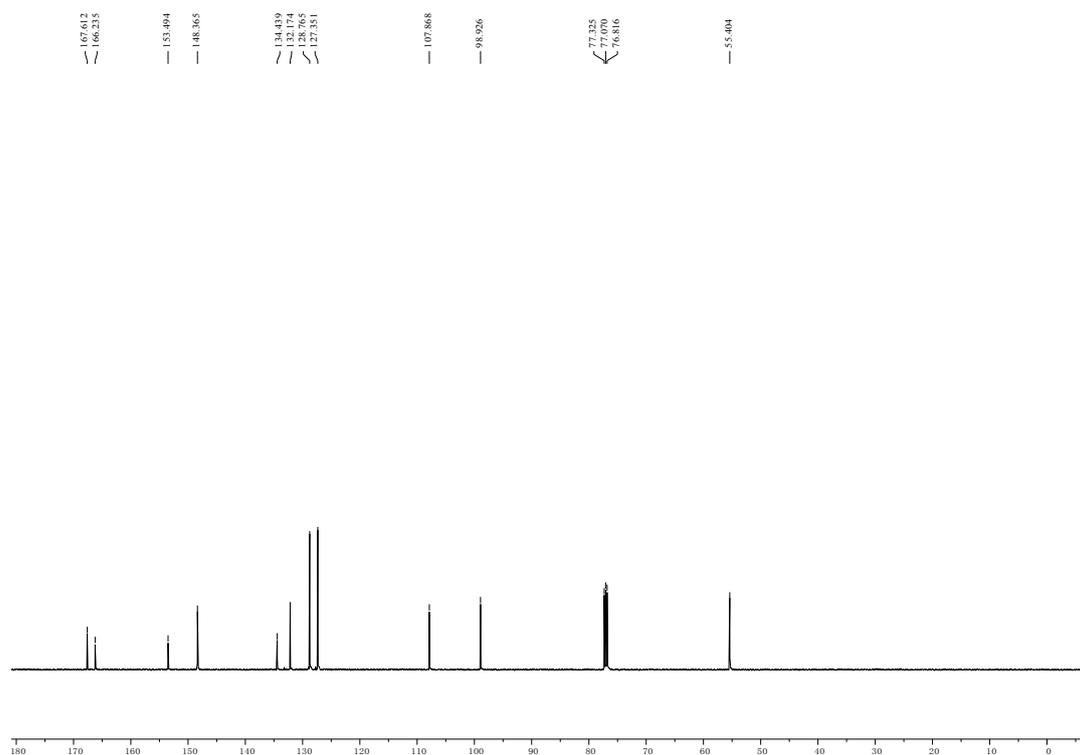
^1H NMR (500 MHz) of compound **3ar** in CDCl_3



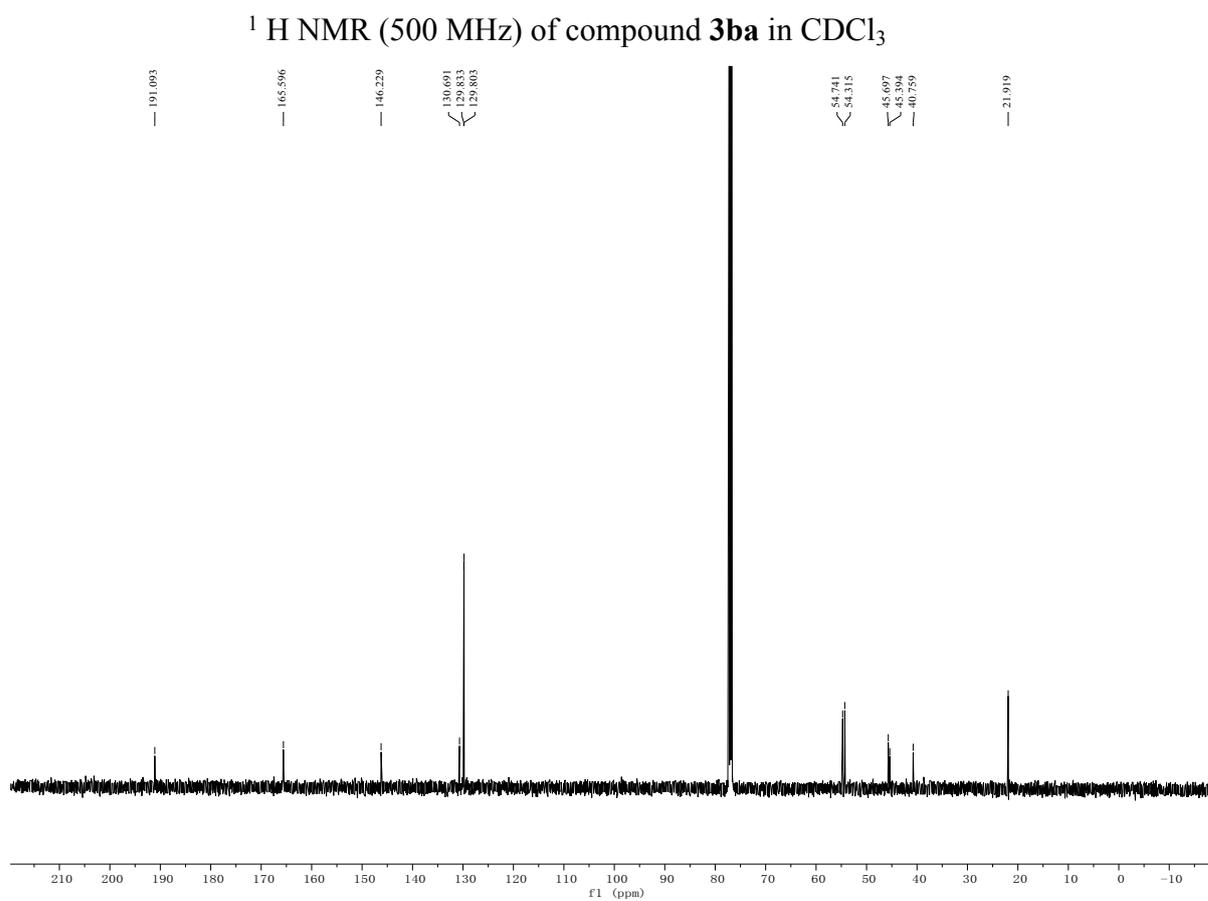
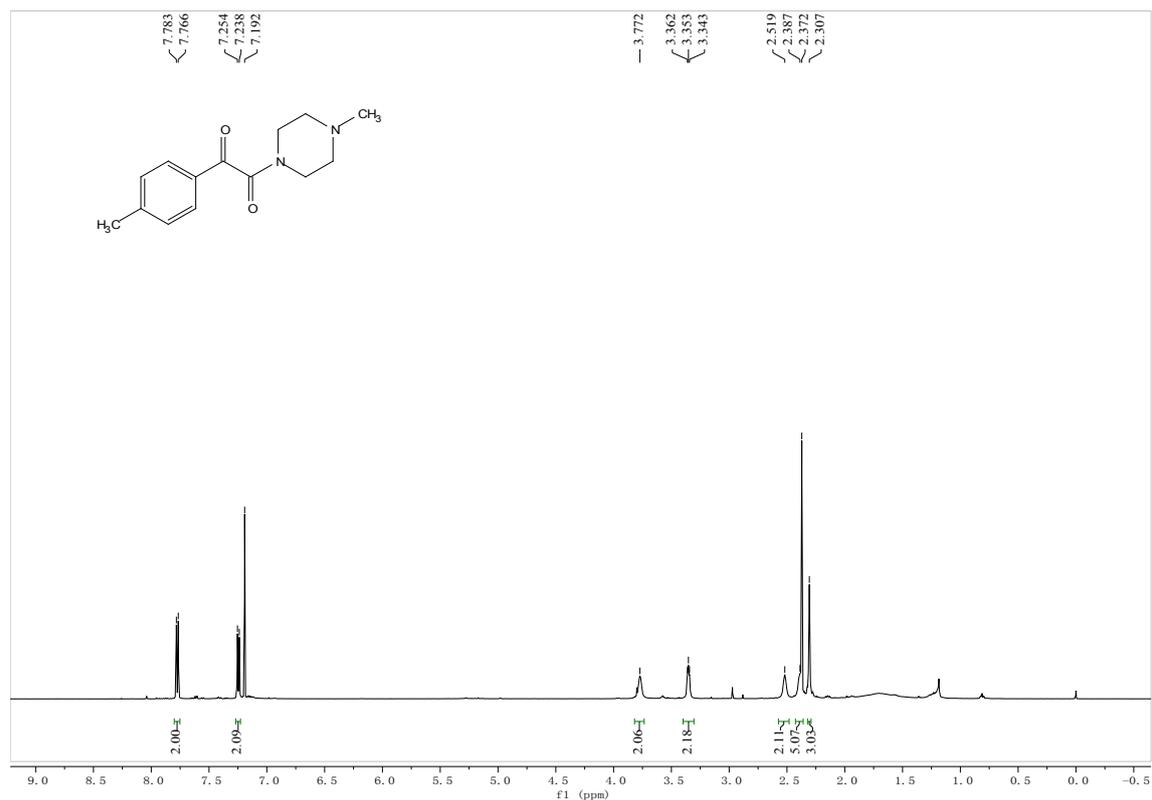
^{13}C NMR (126 MHz) of compound **3ar** in CDCl_3



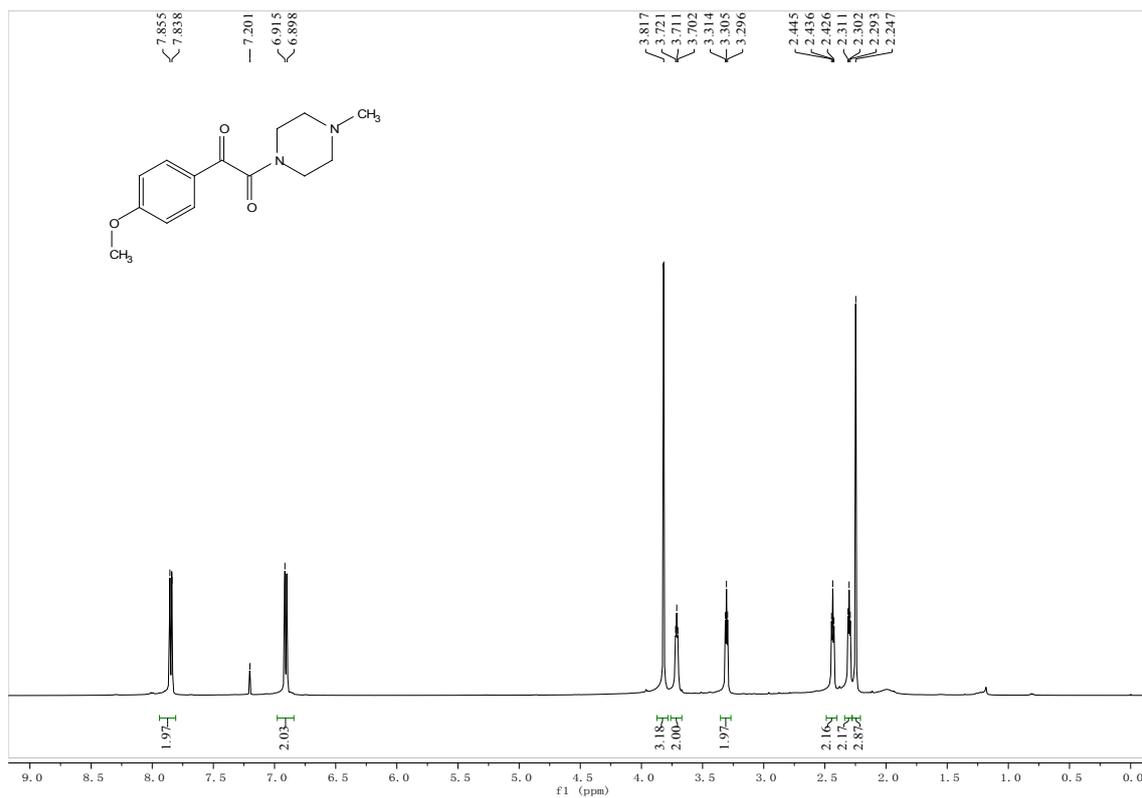
$^1\text{H NMR}$ (500 MHz) of compound **3as** in CDCl_3



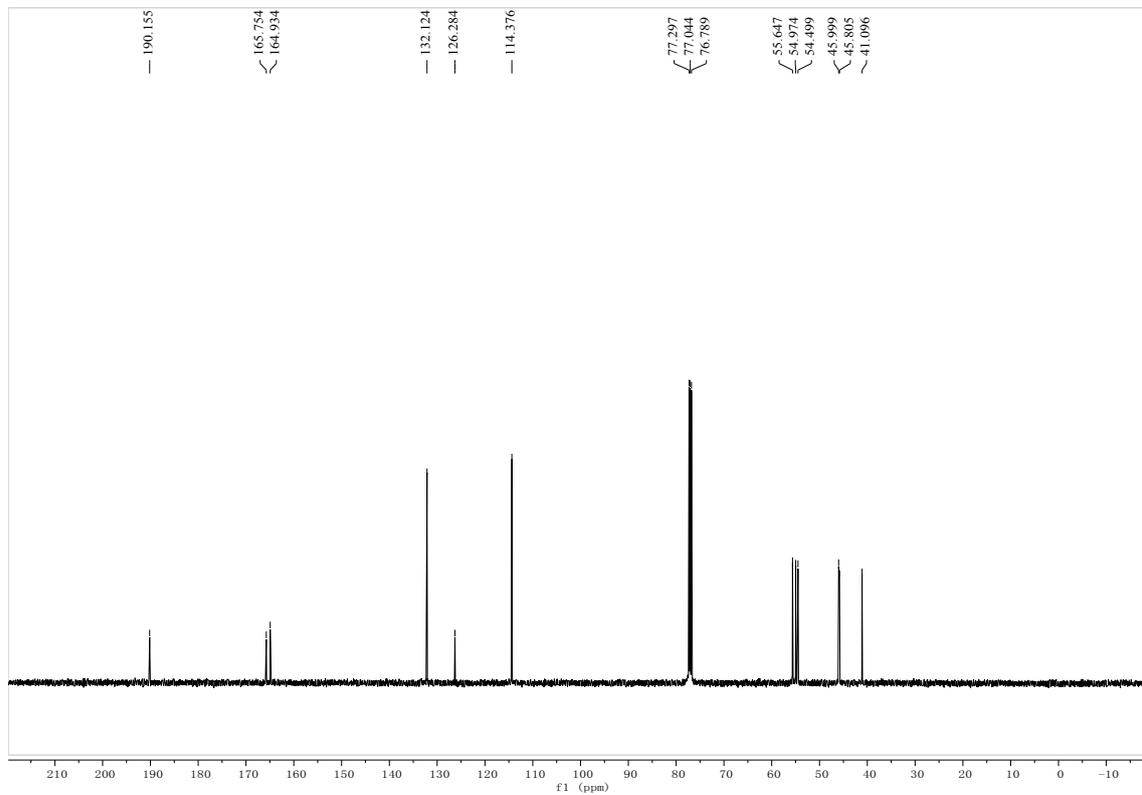
$^{13}\text{C NMR}$ (126 MHz) of compound **3as** in CDCl_3



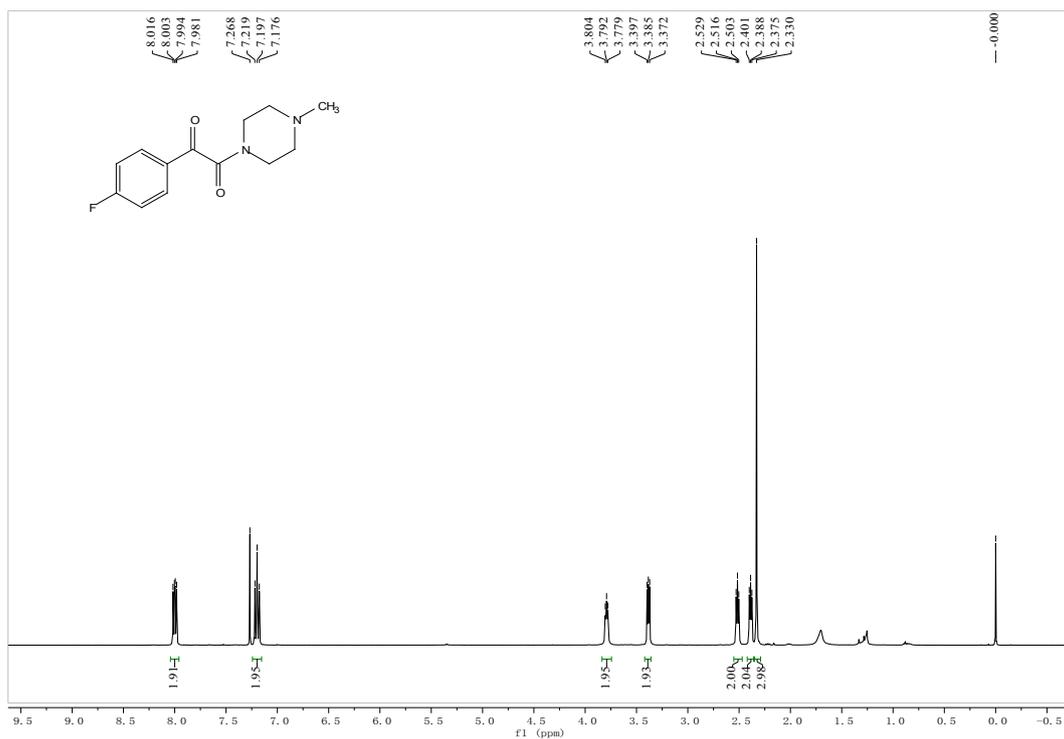
¹³C NMR (126 MHz) of compound **3ba** in CDCl₃



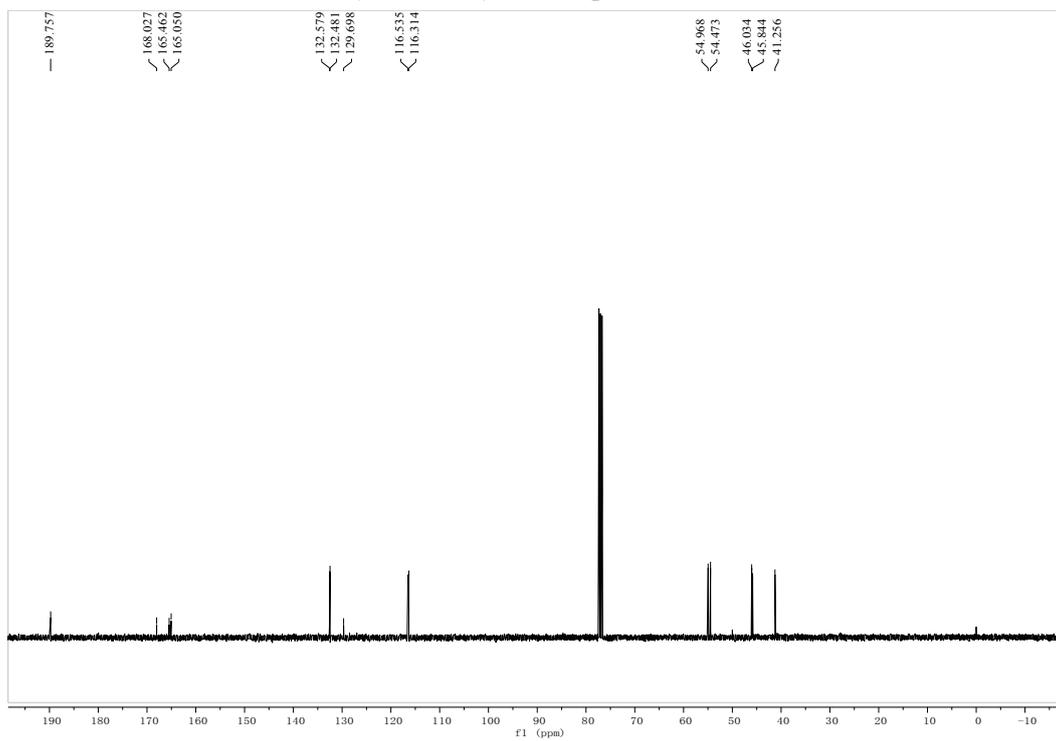
¹H NMR (500 MHz) of compound **3ca** in CDCl₃



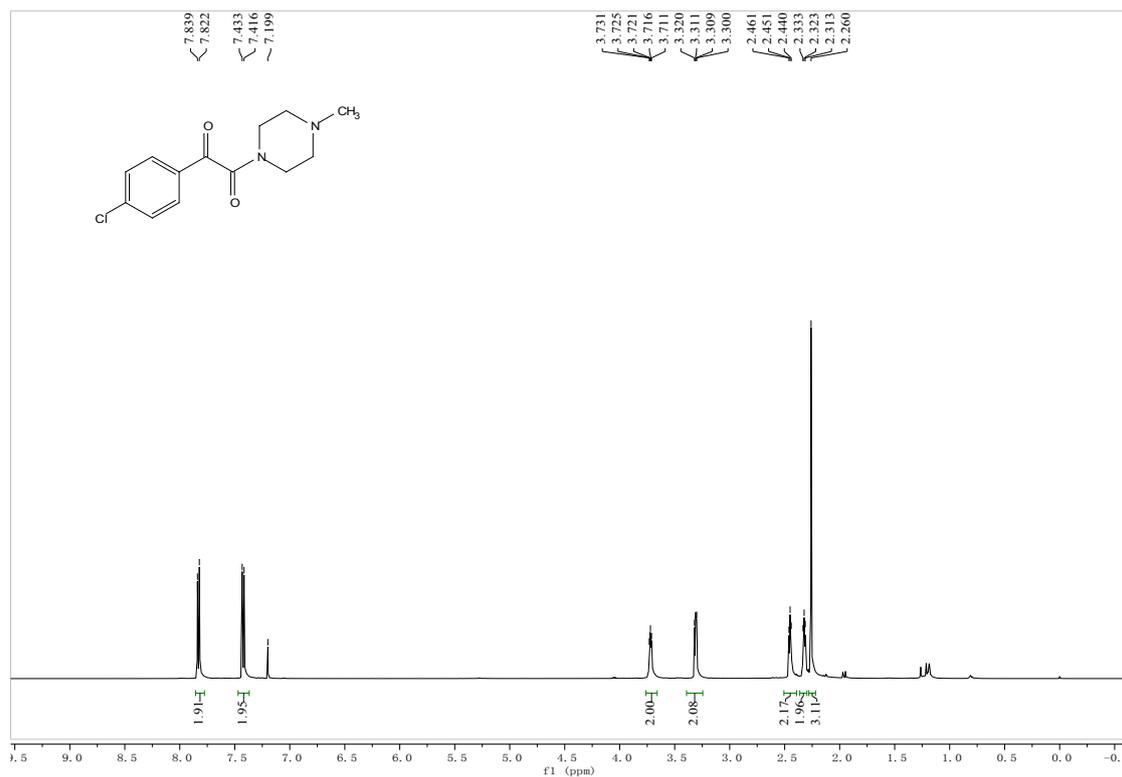
¹³C NMR (126 MHz) of compound **3ca** in CDCl₃



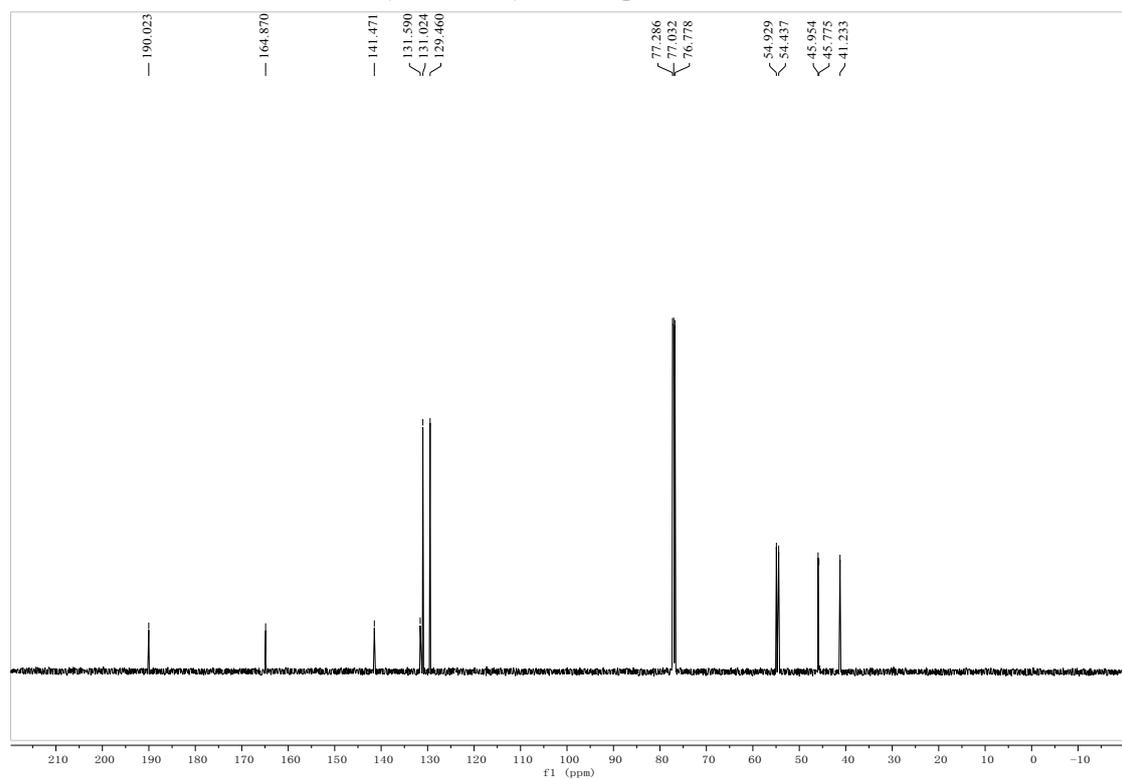
¹H NMR (500 MHz) of compound **3da** in CDCl₃



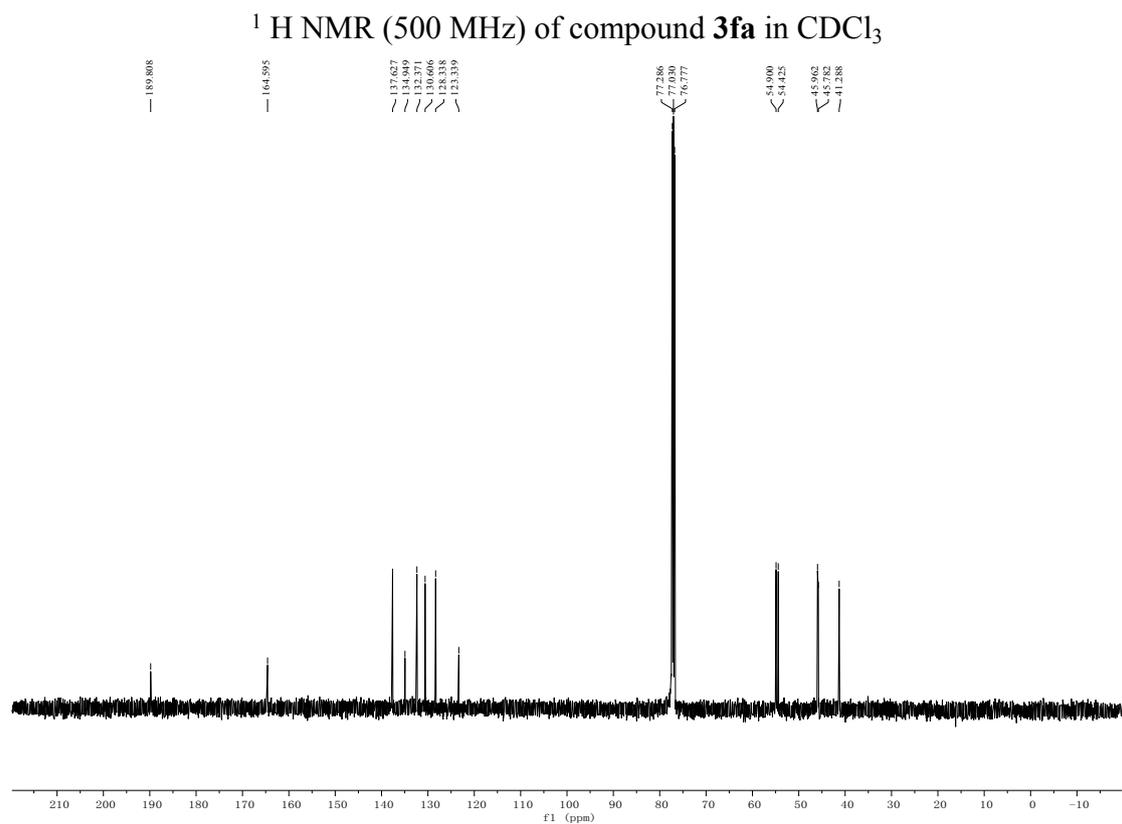
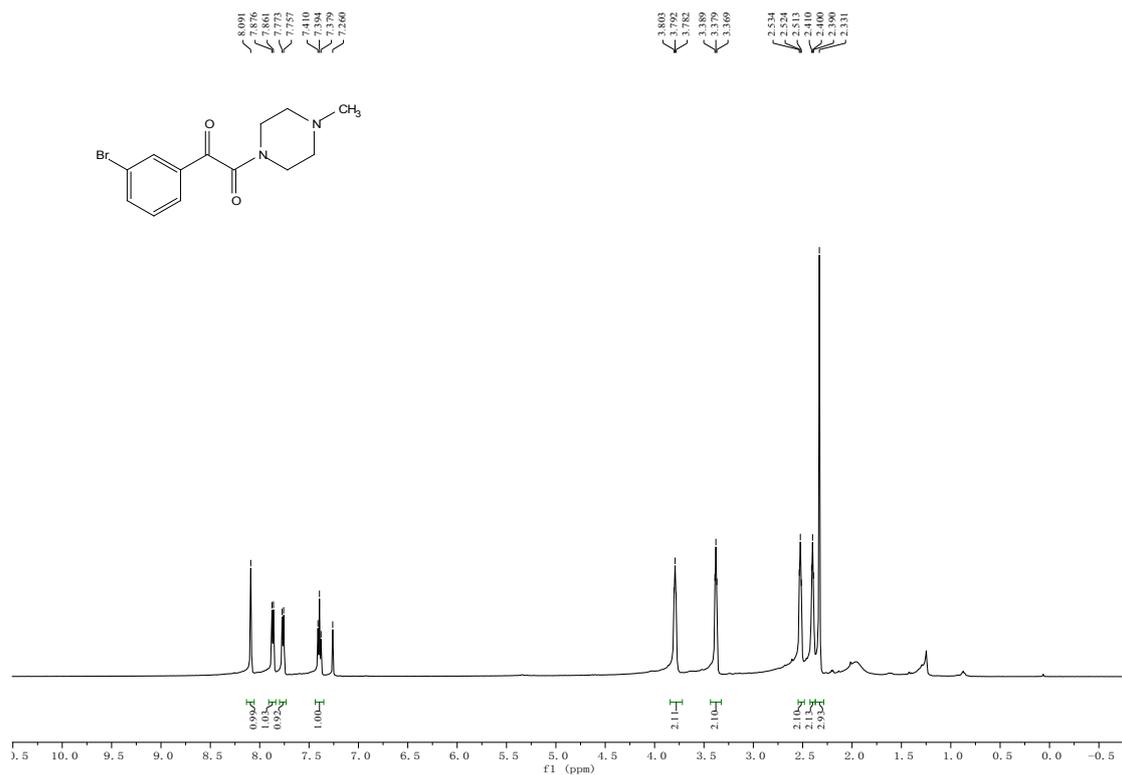
¹³C NMR (126 MHz) of compound **3da** in CDCl₃

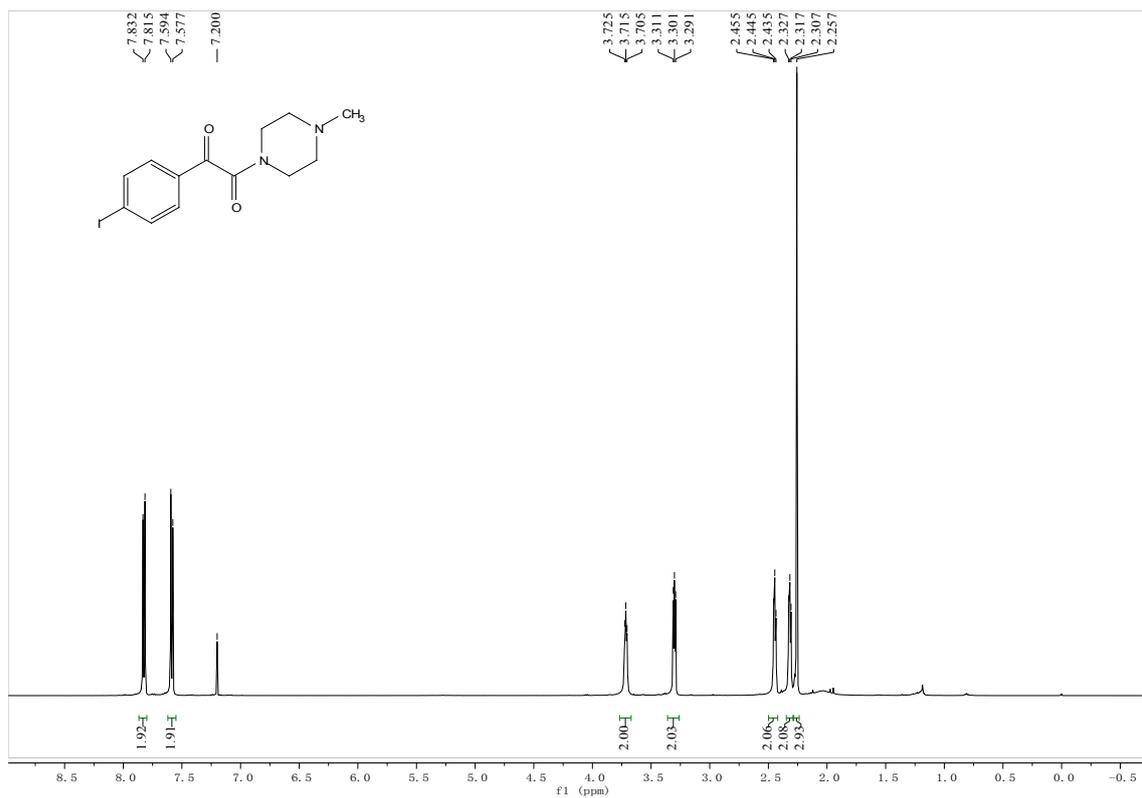


¹H NMR (500 MHz) of compound **3ea** in CDCl₃

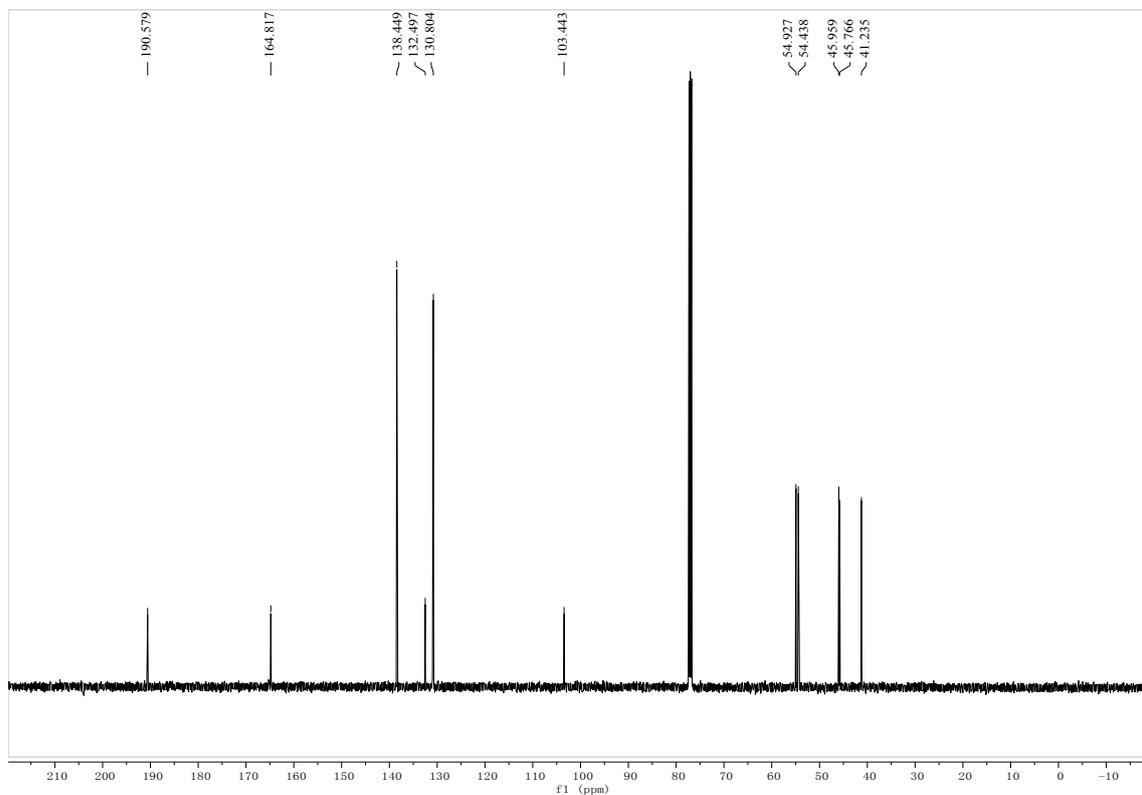


¹³C NMR (126 MHz) of compound **3ea** in CDCl₃

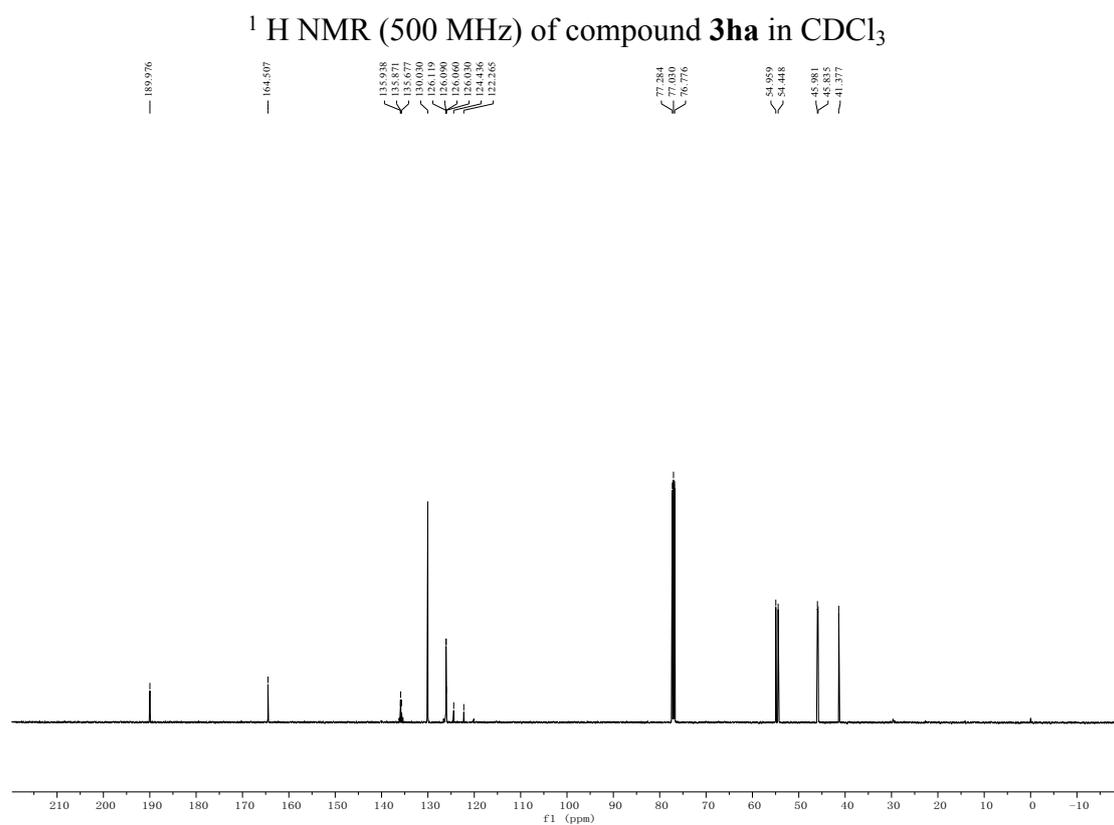
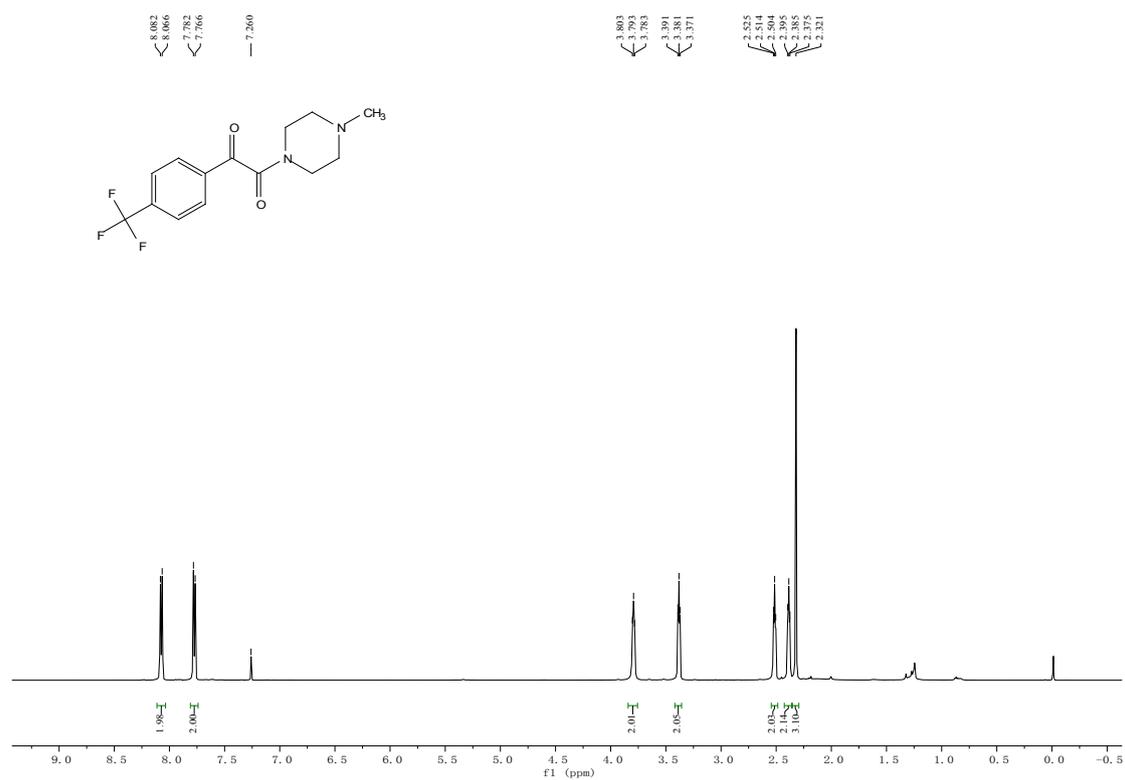


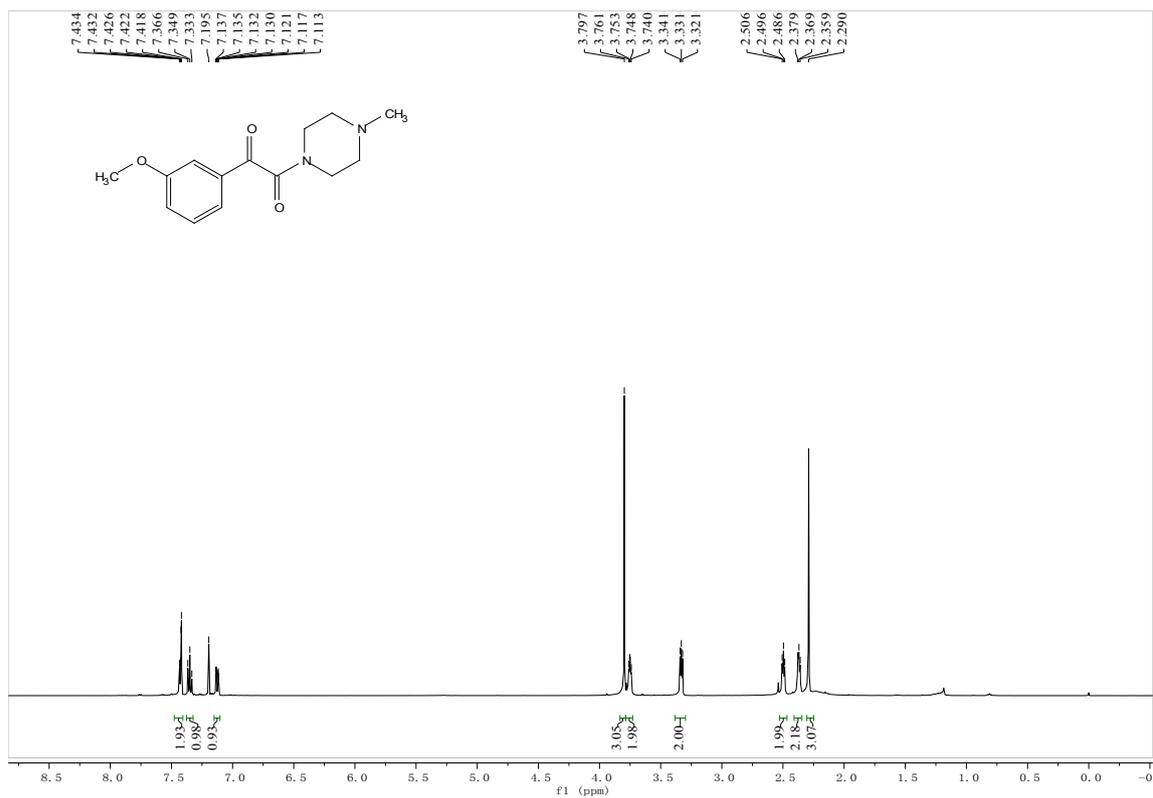


¹H NMR (500 MHz) of compound **3ga** in CDCl₃

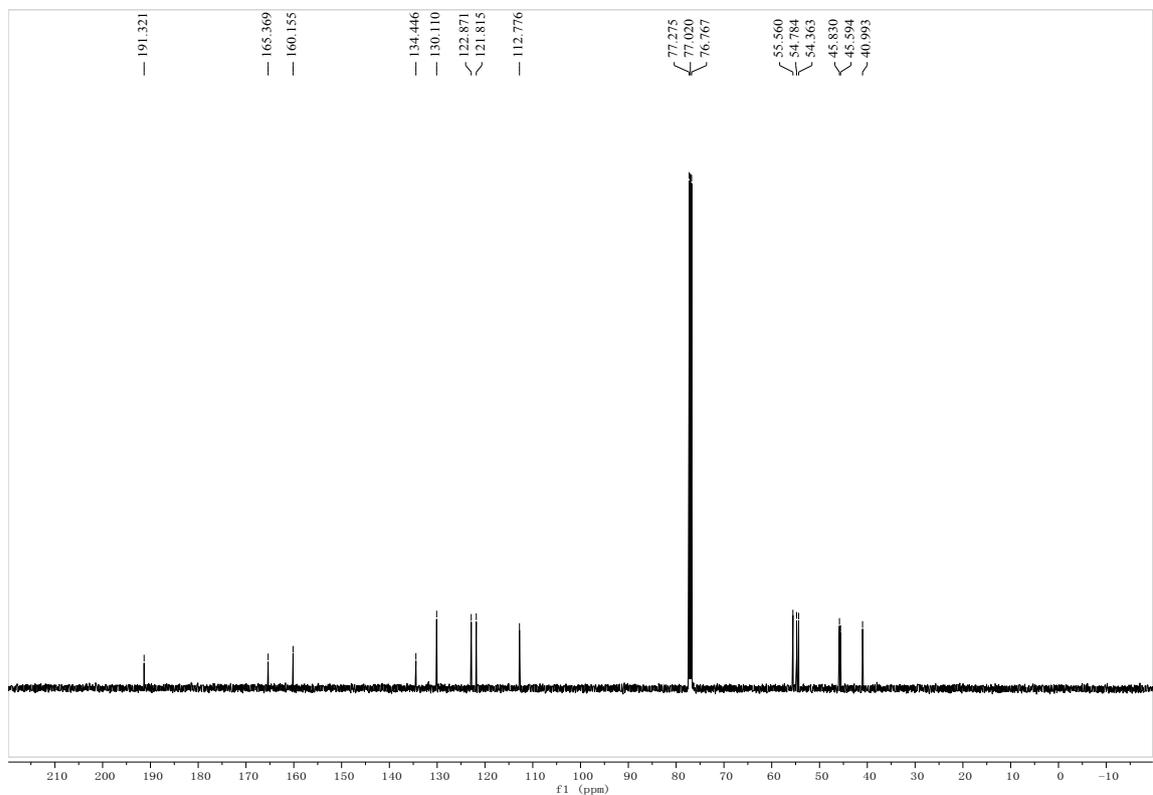


¹³C NMR (126 MHz) of compound **3ga** in CDCl₃

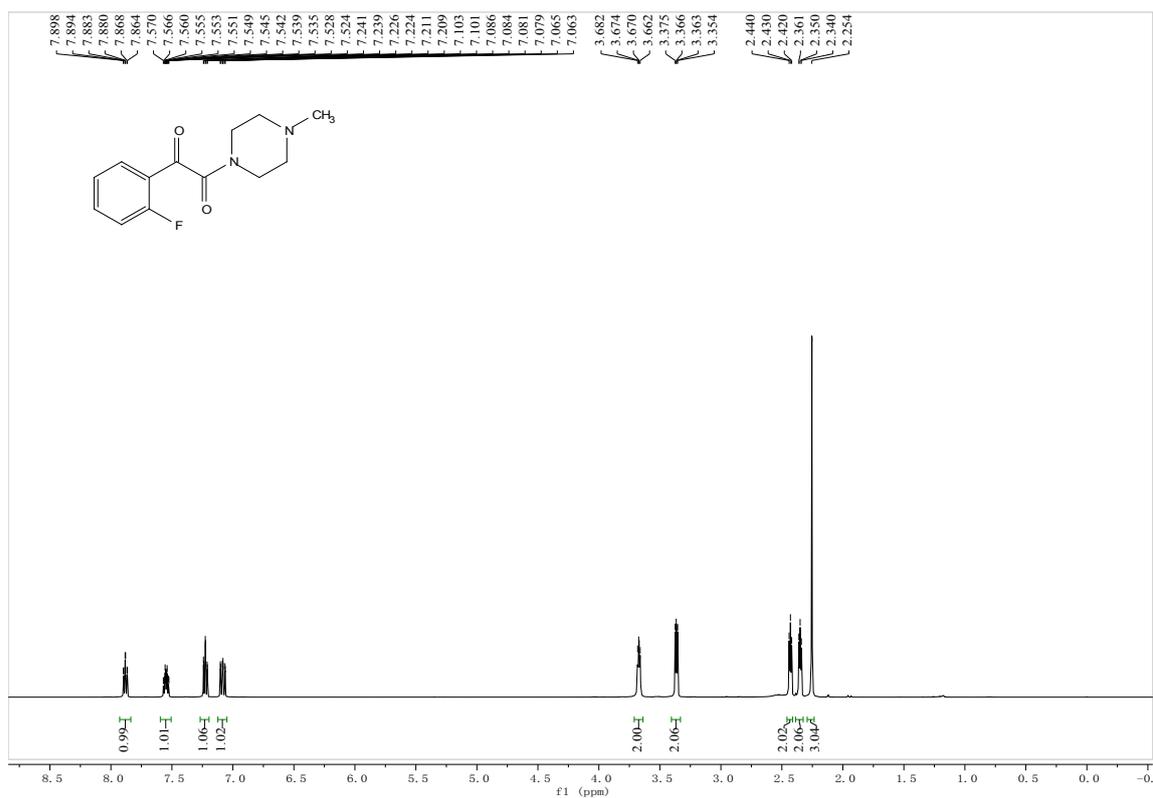




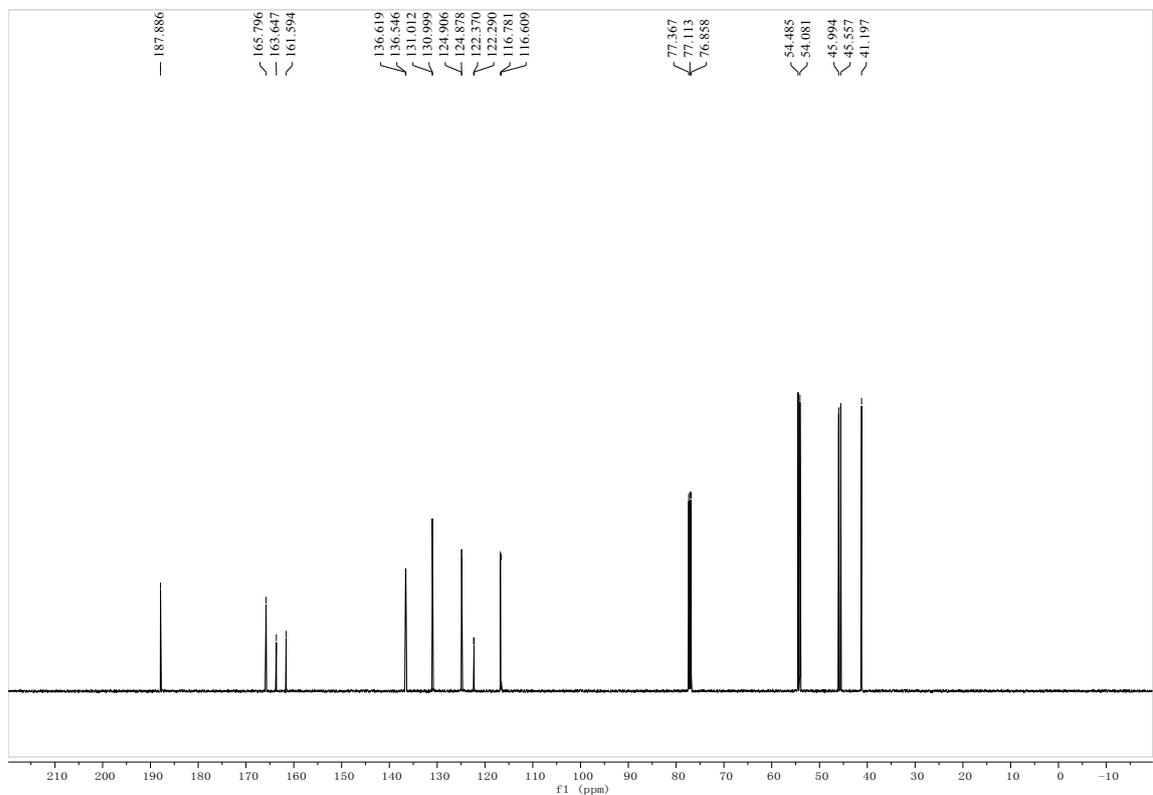
¹H NMR (500 MHz) of compound **3ia** in CDCl₃



¹³C NMR (126 MHz) of compound **3ia** in CDCl₃



¹H NMR (500 MHz) of compound **3ja** in CDCl₃



¹³C NMR (126 MHz) of compound **3ja** in CDCl₃