Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Development of a photoenzymatic one-pot hybrid system for the direct synthesis of 3, 3-disubstituted indole-2-ketone from *N*-methyl indole

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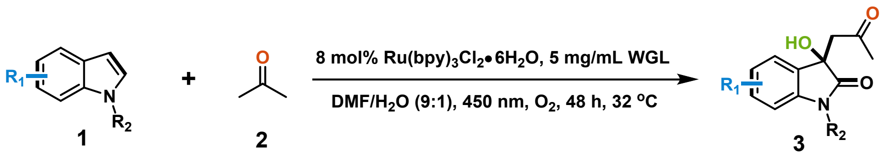
1. General information

All enzymes were purchased from Sigma-Aldrich Co. LLC (US), or Aladdin Co., Ltd. (Shanghai, China). All reagents were used without further purification unless otherwise noted. All the solvents were either HPLC or spectroscopic grade in the optical spectroscopic studies. The NMR spectra were obtained on an Agilent 400-MR DD2 spectrometer. The ^{1}HNMR (400 MHz) chemical shifts were measured relative to $CDCl_3$ as the internal reference ($CDCl_3$: δ=7.26 ppm). The ^{13}C NMR (100 MHz) chemical shifts were given using $CDCl_3$ as the internal standard ($CDCl_3$: δ=76.8~77.1 ppm). HPLC experiments were performed on an Agilent instrument using an OD-3 column with n-hexane/i-PrOH = 95:5 (v/v), 1.0 mL/min, λmax = 254 nm, and 30 °C. High-resolution mass spectra (HR-MS) were obtained with a Waters-Q-TOF-Premier (ESI). Absorption spectra were recorded on a Hitachi PharmaSpec UV-1900 UV-Visible Spectrophotometer. All reactions were performed on a PL-SX100A multichannel light reactor.

2. Experimental Procedure

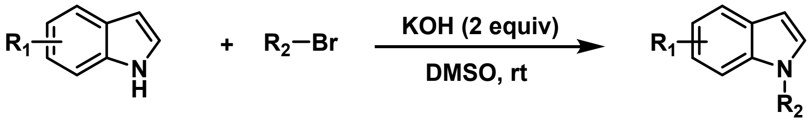
Photo-enzymatic indole oxidation-aldol reaction.



Indole (0.2 mmol), acetone (4 mmol), $Ru(bpy)_3Cl_2$•$6H_2O$ (8 mmol%), WGL (5 mg/mL) were dissolved in DMF/H_2O (1.8 mL/0.2 mL) stirred in a quartz tube irradiated by a 450 nm LED lamp (10 W) at 32 °C, O_2 atmosphere for 48 h. When the reaction was finished, the yields were determined by HPLC with the product sample.

3. Synthesis of substrates

General procedure for the synthesis of N-protected indoles from substituted indoles with alkyl bromides (iodomethane used for methyl-protected indoles).



A 50 mL round-bottom flask was charged with substituted indoles (5 mmol), KOH (10.0 mmol), 20 mL of DMSO, and alkyl bromides (10.0 mmol). The reaction mixture was stirred at room temperature and monitored by TLC. Upon completion, the reaction mixture was quenched with water (20 mL). The mixture was extracted with ethyl acetate (3×30 mL). The combined organic phases were dried over anhydrousMgSO4. The product was purified by silica gel chromatography with petroleumether/EtOAc.

4. The investigation of optimal conditions for the reaction

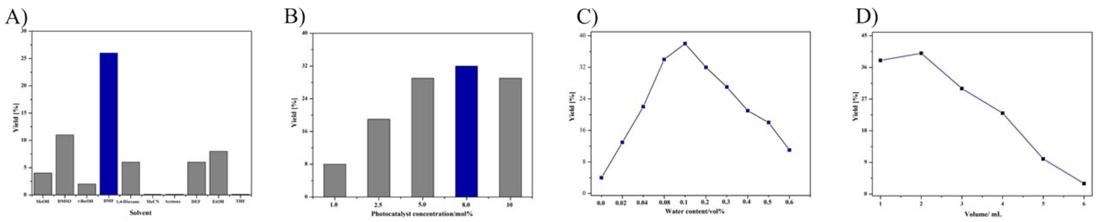
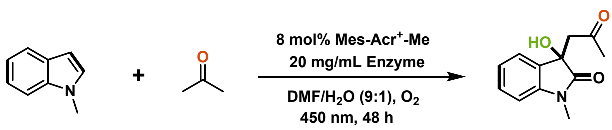


Figure S1 Influence of medium and the amount of photocatalyst on reaction system. A) **1a** (0.3 mmol), **2** (7 mmol), BSA (20 mg/mL), Mes-Acr$^+$-Me (8 mol%), in solvent/H_2O (v/v 9:1, 1 mL), 450 nm LED, O_2, 32 °C, 48 h. B) **1a** (0.3 mmol), **2** (7 mmol), BSA (20 mg/mL), Mes-Acr$^+$-Me (X mol%), in DMF/H_2O (v/v 9:1, 1 mL), 450 nm LED, O_2, 32 °C, 48 h. C) **1a** (0.3 mmol), **2** (7 mmol), BSA (20 mg/mL), Mes-Acr$^+$-Me (8 mol%), in DMF/H_2O (v/v, 1 mL), 450 nm LED, O_2, 32 °C, 48 h. D) **1a** (0.3 mmol), **2** (7 mmol), BSA (20 mg/mL), Mes-Acr$^+$-Me (8 mol%), in DMF/H_2O (v/v 9:1, X mL), 450 nm LED, O_2, 32 °C, 48 h.

Table S1 Enzyme screening [a]



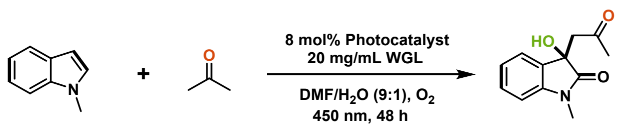
1a 2 3a

Entry	Enzyme	Yield (%) [b]
1	Bovine serum albumin (BSA)	40
2	Lipase from *porcine pancreas* (PPL)	8
3	Lipase from wheat germ (WGL)	55
4	Lipase from *Candida rugosa* (CRL)	49

5	Trypsin	39
6	Lipase B from *Candida* antarctica (CALB)	41
7	Lipase from *Mucor miehei* (MML)	8
8	Lipase from *Bacillus Pumilu* (BPL)	51

[a]Reaction conditions:**1a** (0.3 mmol), **2** (7 mmol), enzyme (20 mg/mL), Mes-Acr$^+$-Me (8 mol%), in DMF/H_2O (v/v 9:1, 2 mL), 450 nm LED, O_2, 32 °C, 48 h. [b]Determined by High Performance Liquid Chromatography (HPLC) with product sample.

Table S2 Photocatalyst screening [a]



1a 2 3a

Entry	Photocatalyst	Yield (%) [b]
1	4CzIPN	42
2	Eosin Y	65
3	SAS	17
4	Solvent Red 43	53
5	$Ru(bpy)_3Cl_2$•$6H_2O$	79
6	Mes-Acr$^+$-Ph	23
7	Mes-Acr$^+$-Me	52
8	Rose Bengal	15
9	Phloxine B	73
10	Rhodamine B	15

[a] Reaction conditions:**1a** (0.3 mmol), **2** (7 mmol), WGL (20 mg/mL), photocatalysts (8 mol%), in DMF/H_2O (v/v 9:1, 2 mL), 450 nm LED, O_2, 32 °C, 48 h. *[b]* Determined by High Performance Liquid Chromatography (HPLC) with product sample.

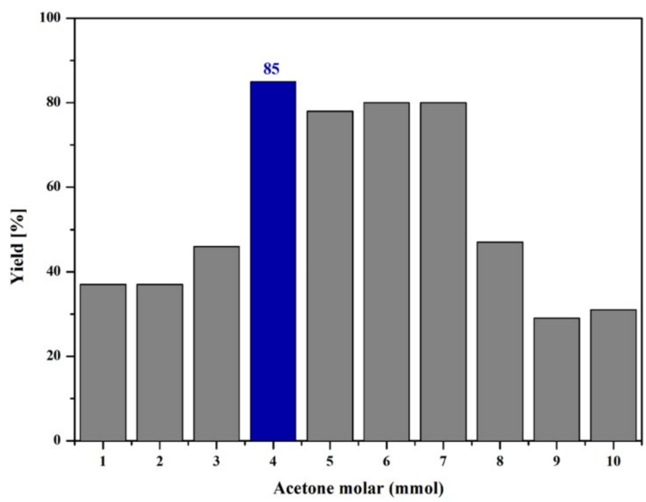


Figure S2 The effect of acetone molar on the reaction. Reaction conditions: **1a** (0.3 mmol), **2** (x mmol), WGL (5 mg/mL), $Ru(bpy)_3Cl_2$•$6H_2O$ (8 mol%), in DMF/H_2O (v/v 9:1, 2 mL), 450 nm LED, O_2, 32 °C, 48 h.

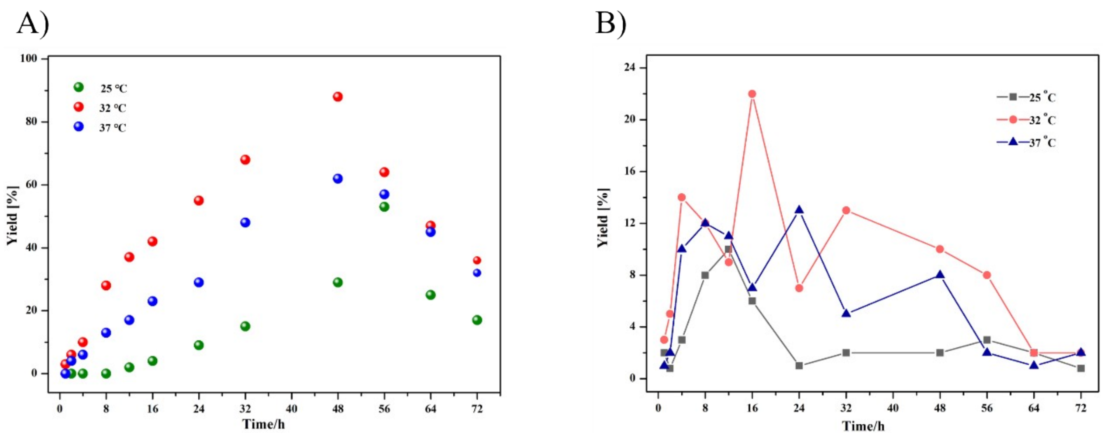
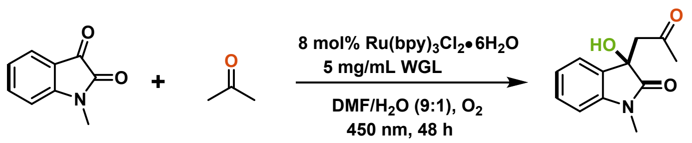


Figure S3 Time curve. A) Time curve of 3-acetonyl-3-hydroxy-2-oxindole; B) Time curve of N-methylisatin.

Table S3 *N*-methylisatin as starting material [a]

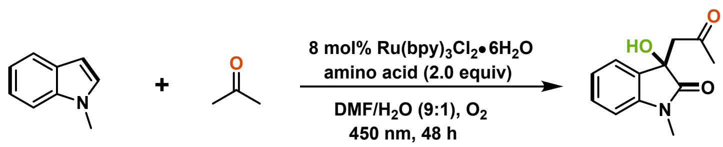


1a **2** **3a**

Entry	Variations from standard conditions	Yield (%) [b]
1	none	75
2	only light	37
3	no WGL	40
4	no PC	90

[a] Reaction conditions:**1a** (0.3 mmol), **2** (7 mmol), WGL (5 mg/mL), $Ru(bpy)_3Cl_2$•$6H_2O$ (8 mol%), in DMF/H_2O (v/v 9:1, 2 mL), 450 nm LED, O_2, 32 °C, 48 h. [b] Determined by High Performance Liquid Chromatography (HPLC) with product sample. PC = $Ru(bpy)_3Cl_2$•$6H_2O$.

Table S4 The effect of amino acids [a]



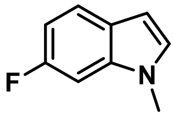
1a **2** **3a**

Entry	Conditions	Yield (%) [b]
1	Serine	<5%
2	Histidine	7%

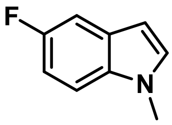
3	Aspartic acid	7%
4	Serine + Histidine	<5%
5	Serine + Aspartic acid	<5%
6	Histidine + Aspartic acid	5%
7	Serine + Histidine + Aspartic acid	<1%
8	WGL	85%

[a] Reaction conditions:**1a** (0.3 mmol), **2** (7 mmol), amino acid (2.0 equiv), $Ru(bpy)_3Cl_2•6H_2O$ (8 mol%), in DMF/H_2O (v/v 9:1, 2 mL), 450 nm LED, O_2, 32 °C, 48 h. [b] Determined by High Performance Liquid Chromatography (HPLC) with product sample.

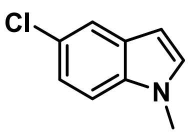
5. Experimental data for the substituted indoles



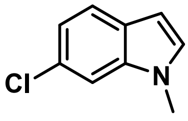
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53-7.49 (m, 1H), 7.02-6.97 (m, 2H), 6.86 (t, *J* = 12.0 Hz, 1H), 6.45 (s, 1H), 3.73 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.93, 158.57, 129.81, 121.44, 107.98 (d, J_{CF} = 25 Hz), 101.06, 95,54 (d, J_{CF} = 25 Hz), 32.92. The spectroscopic characterization corresponded with the data reported in the literature.[1]

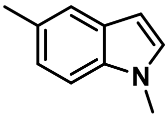


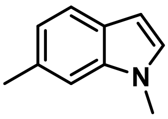
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8 Hz, 1H), 7.24-7.20 (m, 1H), 7.09 (s, 1H), 6.98 (t, *J* = 12 Hz, 1H), 6.44 (s, 1H), 3.77 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.00, 156.67, 133.37, 130.37, 128.57, 109.88 (d, J_{CF} = 15 Hz), 105.48 (d, J_{CF} = 24 Hz), 100.78, 33.04. The spectroscopic characterization corresponded with the data reported in the literature.[1]

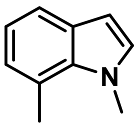


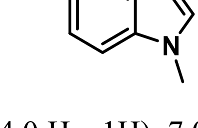
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (s, 1H), 7.23-7.15 (m, 2H), 7.06 (d, *J* = 4.0 Hz, 1H), 6.42 (d, *J* = 4.0 Hz, 1H), 3.76 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.06, 130.09, 129.37, 125.03, 121.73, 120.14, 110.18, 100.54, 33.00. The spectroscopic characterization corresponded with the data reported in the literature.[1]

 ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.0 Hz, 1H), 7.31 (s, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 7.03 (d, *J* = 4.0 Hz, 1H), 6.46 (d, *J* = 4 Hz, 1H), 3.73 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.08, 129.50, 127.49, 126.96, 121.66, 119.94, 109.24, 101.14, 32.86. The spectroscopic characterization corresponded with the data reported in the literature.[1]

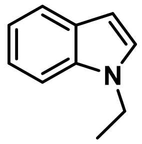
 ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.33 (d, *J* = 4 Hz, 1H), 7.19 (d, *J* = 8 Hz, 1H), 7.10 (d, *J* = 4 Hz, 1H), 6.53 (d, *J* = 4 Hz, 1H), 3.82 (s, 3H), 2.60 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.23, 128.95, 128.84, 128.49, 123.21, 120.60, 109.00, 100.36, 32.88, 21.57. The spectroscopic characterization corresponded with the data reported in the literature.[1]

 ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 4.0 Hz, 1H), 7.12 (s, 1H), 6.98-6.98-6.94 (m, 2H), 6.44 (d, *J* = 4.0 Hz, 1H), 3.75 (s, 3H), 2.50 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.03, 131.24, 128.18, 126.21, 121.01, 120.44, 109.15, 100.60, 32.72, 21.90. The spectroscopic characterization corresponded with the data reported in the literature.[1]

 ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.0 Hz, 1H), 6.99-6.90 (m, 3H), 6.44 (d, *J* = 4 Hz, 1H), 4.04 (s, 3H), 2.78 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.37, 130.37, 129.58, 124.11, 121.17, 119.54, 119.07, 100.86, 36.80, 19.77. The spectroscopic characterization corresponded with the data reported in the literature.[1]

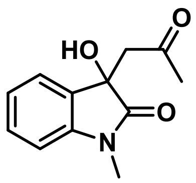
 ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.0 Hz, 1H), 7.11 (d, *J* = 4.0 Hz, 1H), 7.03 (d, *J* = 4.0 Hz, 1H), 6.91 (dd, *J* = 4.0 Hz, 8.0 Hz, 1H), 3.86 (s, 3H),

3.75 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.94, 132.08, 129.31, 128.73, 111.84, 109.93, 102.42, 100.34, 55.87, 32.98. The spectroscopic characterization corresponded with the data reported in the literature.[1]

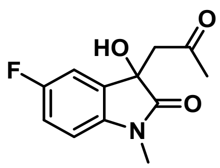


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.0 Hz, 1H), 7.35 (d, J = 8.0 Hz, 1H), 7.21 (t, J = 8.0 Hz, 1H), 7.12-7.08 (m, 2H), 4.18 (dd, J = 8.0 Hz, 12.0 Hz 2H), 1.46 (t, J = 8.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.62, 128.57, 126.97, 121.28, 120.93, 119.16, 109.23, 100.95, 40.93, 15.47. The spectroscopic characterization corresponded with the data reported in the literature.[1]

6. Experimental data for the 3-acetonyl-3-hydroxy-2-oxindoles derivatives

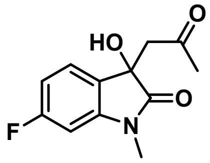


3a; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.35 (m, 2H), 7.07 (t, J = 8.0 Hz, 1H), 6.84 (d, J = 8.0 Hz, 1H), 4.41 (s, 1H), 3.20 (s, 3H), 3.02 (m, 2H), 2.18 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.50, 181.49, 143.49, 129.99, 129.69, 123.81, 123.10, 108.56, 74.18, 48.64, 31.38, 26.26. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{12}H_{13}NO_3Na^+$ 242.0788; Found 242.0785. The spectroscopic characterization corresponded with the data reported in the literature.[2]

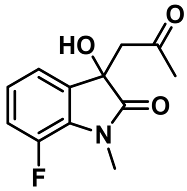


3b; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (d, J = 8.0 Hz,1H), 7.00 (t, J = 8.0 Hz, 1H), 6.75 (dd, J = 8.0, 4.0 Hz, 1H), 4.50 (dd, J = 4.0 Hz, 20.0 Hz, 1H), 3.19 (d, J = 16.0 Hz, 1H), 3.17 (s, 3H), 2.93 (d, J = 20.0 Hz, 1H), 2.16 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.28, 175.89, 160.60, 158.19, 135.34 (d, J_{CF} = 817.0 Hz),116.10 (d, J_{CF} = 12.5 Hz), 112.30 (d, J_{CF} = 25.0 Hz), 109.17 (d, J_{CF} = 8.0 Hz), 74.22, 48.74, 3.26, 26.43. ^{19}F (376 MHz, $CDCl_3$) δ -119.51 – -119.57 (m). HRMS

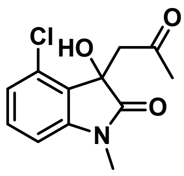
(ESI) m/z: [M + Na]$^+$ Calcd for $C_{12}H_{12}FNO_3Na^+$ 260.0693; Found 260.0694.



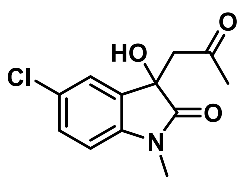
3c; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (q, J = 8.0 Hz, 1H), 6.75-6.70 (m, 1H), 6.59-6.56 (m, 1H), 4.27 (s, 1H), 3.19 (d, J = 20.0 Hz, 1H), 3.18 (s, 3H), 2.94 (d, J = 16.0 Hz, 1H), 2.17 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.40, 176.32, 165.32, 162.86, 125.21 (d, J_{CF} = 10.0 Hz), 109.19, 108.95, 97.54 (d, J_{CF} = 27.0 Hz), 73.71, 48.77, 31.30, 26.42. ^{19}F (376 MHz, $CDCl_3$) δ -109.24 – -109.30 (m). HRMS (ESI) m/z: [M + Na]$^+$ Calcd for $C_{12}H_{12}FNO_3Na^+$ 260.0693; Found 260.0696.



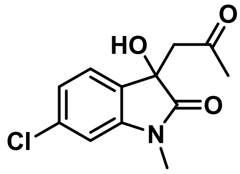
3d; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15-7.13 (m, 1H), 7.07-7.04 (m, 1H), 7.03-6.96 (m, 1H), 4.46 (s, 1H), 3.41 (d, J = 2.8 Hz, 3H), 3.19 (d, J = 16.0 Hz, 1H), 2.99 (d, J = 16.0 Hz, 1H), 2.16 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.21, 175.49, 149.07, 146.63, 132.54, 130.19, 119.60 (d, J_{CF} = 3.0 Hz), 118.12 (d, J_{CF} = 20.0 Hz), 74.10, 48.96, 31.28, 28.88. ^{19}F (376 MHz, $CDCl_3$) δ -135.89 (td, J = 7.52, 3.76 Hz). HRMS (ESI) m/z: [M + Na]$^+$ Calcd for $C_{12}H_{12}FNO_3Na^+$ 260.0693; Found 260.0686.



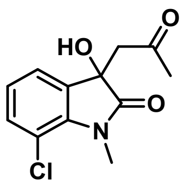
3e; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (t, J = 8.0 Hz, 1H), 6.99 (d, J = 8.0 Hz, 1H), 6.75 (d, J = 4.0 Hz, 1H), 3.81 (s, 1H), 3.66 (d, J = 20.0 Hz, 1H), 3.38 (d, J = 20 Hz,1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.03, 175.94, 145.98, 131.18, 131.01, 125.34, 123.96, 74.54, 47.49, 30.81, 26.51. HRMS (ESI) m/z: [M + Na]$^+$ Calcd for $C_{12}H_{12}ClNO_3Na^+$ 276.0398; Found 276.0396.



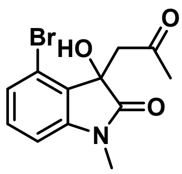
3f; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (s, 1H), 7.29 (d, J = 8.0 Hz, 1H), 6.76 (d, J = 8.0 Hz, 1H), 3.22 (d, J = 20.0 Hz, 1H), 3.17 (s, 3H), 3.01 (d, J = 16.0 Hz, 1H), 2.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.96, 175.94, 142.17, 131.31, 129.79, 128.46, 124.43, 109.59, 73.95, 48.98, 31.09, 26.42. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{12}H_{12}ClNO_3Na^+$ 276.0398; Found 276.0396.



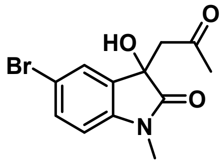
3g; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, J = 8.0 Hz, 1H), 7.03 (d, J = 8.0 Hz, 1H), 6.83 (s, 1H), 4.41 (s, 1H), 3.19 (d, J = 8.0 Hz, 1H), 3.18 (s, 3H), 2.96 (d, J = 20.0 Hz, 1H), 2.16 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.27, 176.09, 144.81, 135.83, 128.03, 124.83, 122.89, 109.39, 73.71, 48.80, 31.25, 26.40. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{12}H_{12}ClNO_3Na^+$ 276.0398; Found 276.0398. The spectroscopic characterization corresponded with the data reported in the literature.[3]



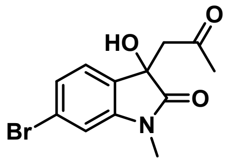
3h; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.23 (m, 2H), 6.97 (t, J = 8 MHz, 1H), 4.48 (s, 1H), 3.57 (s, 3H), 3.16 (d, J = 20.0 Hz, 1H), 2.98 (d, J = 16.0 Hz, 1H), 2.16 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.19, 176.58, 139.46, 132.43, 132.27, 123.94, 122.25, 116.03, 73.54, 48.91, 31.31, 29.74. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{12}H_{12}ClNO_3Na^+$ 276.0398; Found 276.0400.



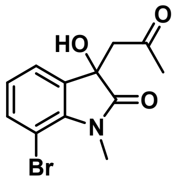
3i; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (q, J = 8 Hz, 2H), 6.78 (d, J = 8.0 Hz, 1H), 4.01 (s, 1H), 3.76 (d, J = 20.0 Hz, 1H), 3.35 (d, J = 16.0 Hz, 1H), 3.19 (s, 3H), 2.11 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.86, 176.11, 146.23, 131.30, 127.14, 126.97, 118.92, 107.68, 75.07, 47.60, 30.73, 26.44. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{12}H_{12}BrNO_3Na^+$ 319.9893; Found 319.9895.



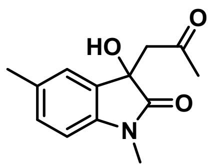
3j; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (t, *J* = 8.0 Hz, 2H), 6.72 (d, *J* = 8.0 Hz, 1H), 4.45 (s, 1H), 3.20 (d, *J* = 16.0 Hz, 1H), 3.18 (s, 3H), 2.97 (d, *J* = 16.0 Hz, 1H), 2.18 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.24, 175.57, 142.63, 132.76, 131.64, 127.22, 115.74, 110.07, 73.98, 48.72, 31.19, 26.39. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{12}H_{12}BrNO_3Na^+$ 319.9893; Found 319.9880.



3k; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (q, *J* = 8.0 Hz, 2H), 6.99 (s, 1H), 4.37 (s, 1H), 3.19 (d, *J* = 16.0 Hz, 1H), 3.18 (s, 3H), 2.95 (d, *J* = 16.0 Hz, 1H), 2.17 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.30, 175.93, 144.88, 128.56, 125.87, 125.61, 123.71, 112.17, 109.99, 73.77, 48.69, 31.25, 26.40. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{12}H_{12}BrNO_3Na^+$ 319.9893; Found 319.9887.

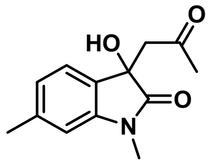


3l; ^{1}H NMR (400 MHz, $CDCl_3$) 7.42 (d, *J* = 8.0 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 6.90 (t, *J* = 8.0 Hz, 1H), 4.46 (s, 1H), 3.58 (3H), 3.16 (d, *J* = 16.0 Hz, 1H), 2.98 (d, *J* = 16.0 Hz, 1H), 2.16 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.13, 176.83, 140.97, 135.62, 132.82, 124.32, 122.81, 102.90, 73.49, 48.98, 31.29, 29.97. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{12}H_{12}BrNO_3Na^+$ 319.9893; Found 319.9877.

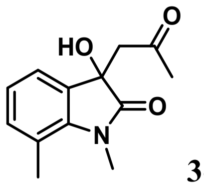


3m; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (s, 1H), 7.11 (d, *J* = 8.0 Hz, 1H), 6.72 (d, *J* = 8.0 Hz, 1H), 4.49 (s, 1H), 3.17 (d, *J* = 16.0 Hz, 1H), 3.17 (s, 3H), 2.94 (d, *J* = 16.0 Hz, 1H), 2.31 (s, 3H), 2.17 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.72, 176.08, 141.05, 132.77, 130.17, 129.65, 124.63, 108.34, 74.29, 48.72, 31.40, 26.30, 21.05. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{13}H_{15}NO_3Na^+$ 256.0944; Found

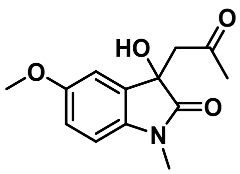
256.0946.



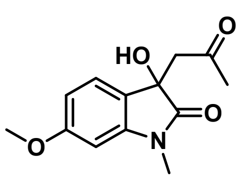
3n; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.0 Hz, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.65 (s, 1H), 3.18 (d, *J* = 20.0 Hz, 1H), 3.17 (s, 3H), 2.94 (d, *J* = 16.0 Hz, 1H).36 (s, 3H), 2.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.57, 176.50, 143.63, 140.40, 126.79, 123.57, 109.55, 74.04, 48.93, 31.37, 26.25, 21.90. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{13}H_{15}NO_3Na^+$ 256.0944; Found 256.0942.



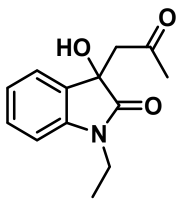
3o; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (d, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 1H), 6.94 (t, *J* = 8.0 Hz, 1H), 4.46 (s, 1H), 3.47 (s, 3H), 3.14 (d, *J* = 16.0 Hz, 1H), 2.97 (d, *J* = 20.0 Hz, 1H), 2.55 (s, 3H), 2.14 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.45, 177.07, 141.15, 133.74, 130.27, 123.08, 121.57, 120.27, 73.47, 49.05, 31.42, 29.71, 18.97. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{13}H_{15}NO_3Na^+$ 256.0944; Found 256.0944.



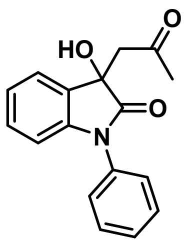
3p; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.00 (s, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 6.74 (d, *J* = 8.0 Hz, 1H), 4.48 (s, 1H), 3.78 (s, 3H), 3.17 (d, *J* = 16.0 Hz, 1H), 3.17 (s, 3H), 2.93 (d, *J* = 16.0 Hz, 1H), 2.18 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.69, 175.77, 156.31, 136.78, 130.86, 114.20, 111.29, 109.01, 74.55, 55.82, 48.66, 31.42, 26.36. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{13}H_{15}NO_4Na^+$ 272.0893; Found 272.0896.



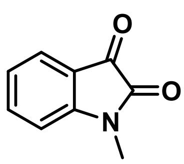
3q; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.0 Hz, 1H), 6.52 (d, *J* = 8.0 Hz, 1H), 4.32 (s, 1H), 3.81 (s, 3H), 3.17 (d, *J* = 16.0 Hz, 1H), 3.16 (s, 3H), 2.93 (d, J = 16.0 Hz, 1H), 2.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.59, 176.66, 161.47, 144.99, 124.71, 121.68, 106.48, 96.70, 73.82, 55.53, 48.95, 31.37, 26.28. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{13}H_{15}NO_4Na^+$ 272.0893; Found 272.0895.



3r; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, J = 8.0 Hz, 1H), 7.32 (t, J = 8.0 Hz, 1H), 7.05 (t, J = 8.0 Hz, 1H), 6.86 (d, J = 8.0 Hz, 1H), 4.23 (s, 1H), 3.81-3.68 (m), 3.19 (d, J = 12 Hz, 1H), 2.95 (d, J = 12.0 Hz, 1H), 1.29 (t, J = 4.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.45, 175.62, 142.65, 129.90, 124.01, 122.90, 109.99, 108.72, 74.13, 48.83, 34.79, 31.35, 12.34. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{13}H_{15}NO_3Na^+$ 256.0944; Found 256.0946.



3s; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (t, J = 8.0 Hz, 2H), 7.46-7.40 (m, 4H), 7.26 (t, J = 4.0 Hz, 1H), 7.09 (t, J = 4.0 Hz, 1H), 6.80 (d, J = 8.0 Hz, 1H), 3.34 (d, J = 16.0 Hz, 1H), 3.16 (d, J = 16.0 Hz, 1H), 2.17 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.89, 175.85, 143.91, 134.04, 129.98, 129.68,129.26, 128.29, 126.53, 123.97, 123.53, 109.92, 74.14, 49.72, 31.18. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{15}NO_3Na^+$ 309.0944; Found 304.0945. The spectroscopic characterization corresponded with the data reported in the literature.[4]



1a'; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62-7.58 (m, 2H), 7.12 (t, J = 8.0 Hz, 1 H), 6.89 (d, J = 8 Hz), 3.25 (s, 3H). ^{13}C δ 183.39, 158.24, 151.45, 138.50, 125.36, 123.93, 117.41, 110.00, 26.23. The spectroscopic characterization corresponded with the data reported in the literature.[5]

7. References

1 X. Li, X.-Y. Gu, Y.-J. Li and P.-X. Li, Aerobic Transition-Metal-Free Visible-Light Photoredox Indole C-3 Formylation Reaction, *ACS Catal.,* 2014, **4**, 1897-1900.

2 Q.-B. Zhang, W.-L. Jia, Y.-J. Ban, Y. Zheng, Q. Liu and L.-Z. Wu, Autoxidation/Aldol Tandem Reaction of 2-Oxindoles with Ketones: A Green Approach for the Synthesis of 3-Hydroxy-2-Oxindoles, *Chem-Eur. J.,* 2016, **22**, 2595-2598.

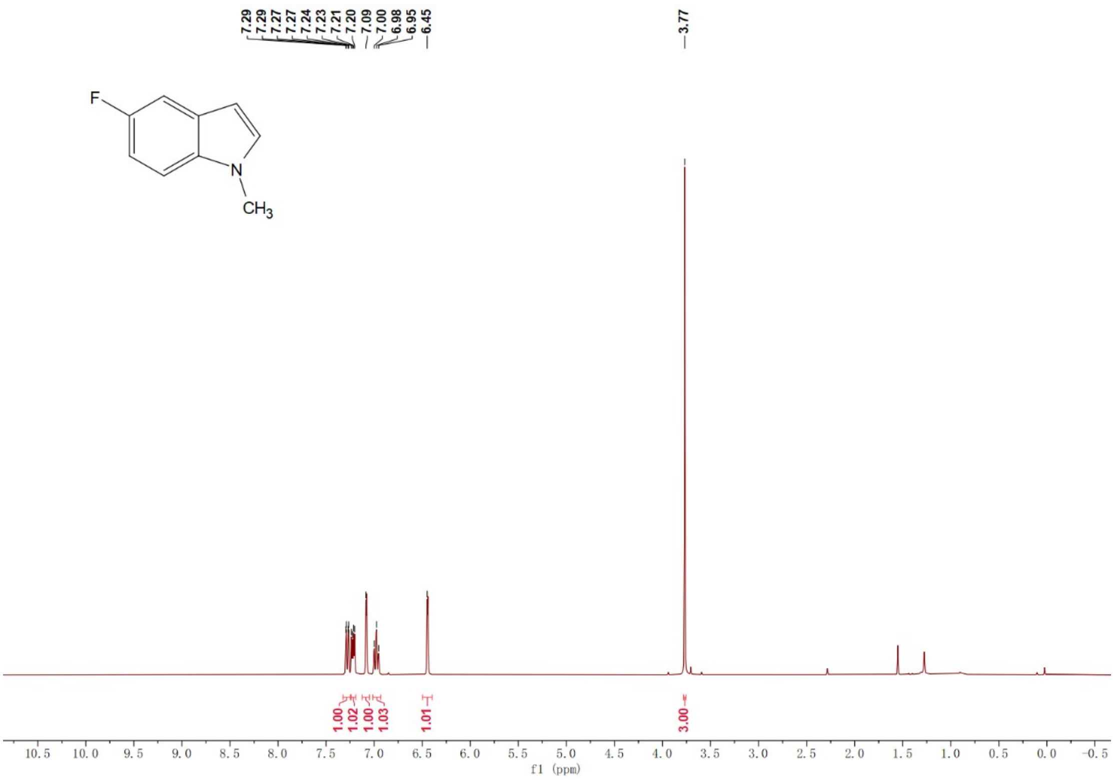
3 P.-J. Liu, J.-J. Guo, W.-T. Wei, X.-Z. Liu and P.-H. Sun, Iodine-Catalyzed Oxidation of N-Substituted Indoles by using Chloramine-B: A Facile and Practical Approach to Isatins, *Eur. J. Chem.,* 2016, **2016**, 2105-2109.

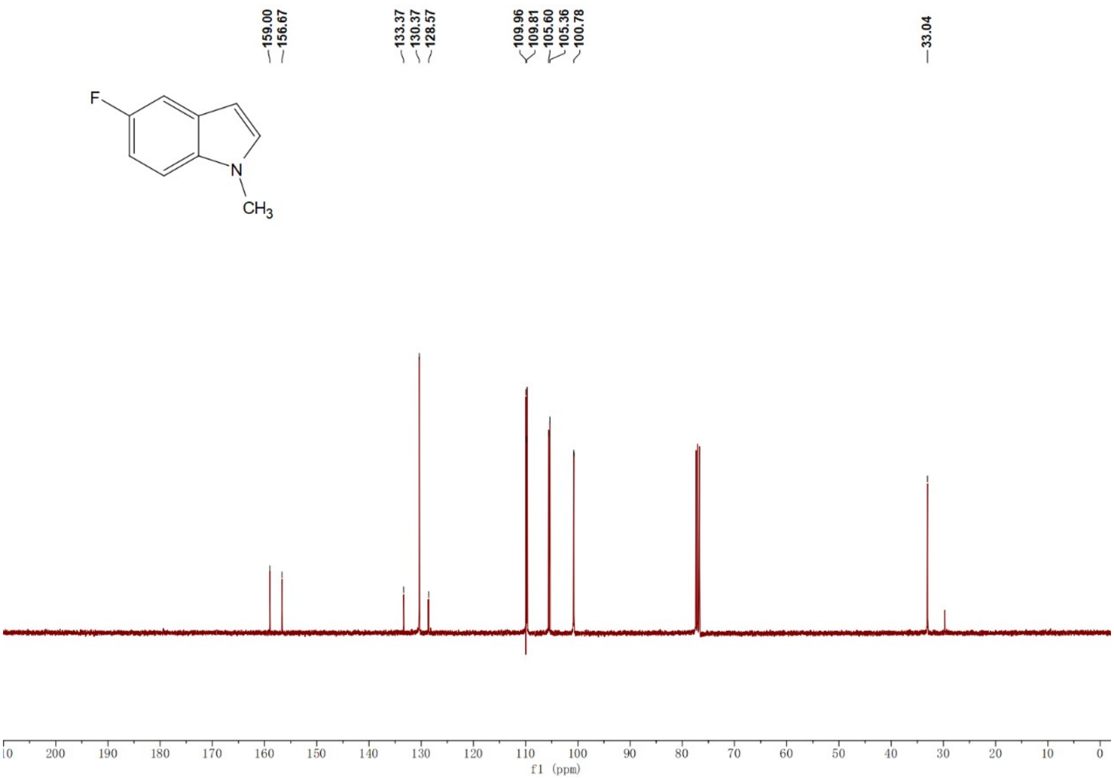
4 G. Gentile, M. Mamone, C. Rosso, F. Amato, C. Lanfrit, G. Filippini and M. Prato, Tailoring the Chemical Structure of Nitrogen-Doped Carbon Dots for Nano-Aminocatalysis in Aqueous Media, *ChemSusChem,* 2023, **16**, e202202399.

5 A. Paul, A. Segupta and S. Yadav, Visible-Light Driven Acetoxylation and Dioxygenation of Indoles via Electron Donor-Acceptor Complex, *Chem. Commun.*, 59, 7455-7458.

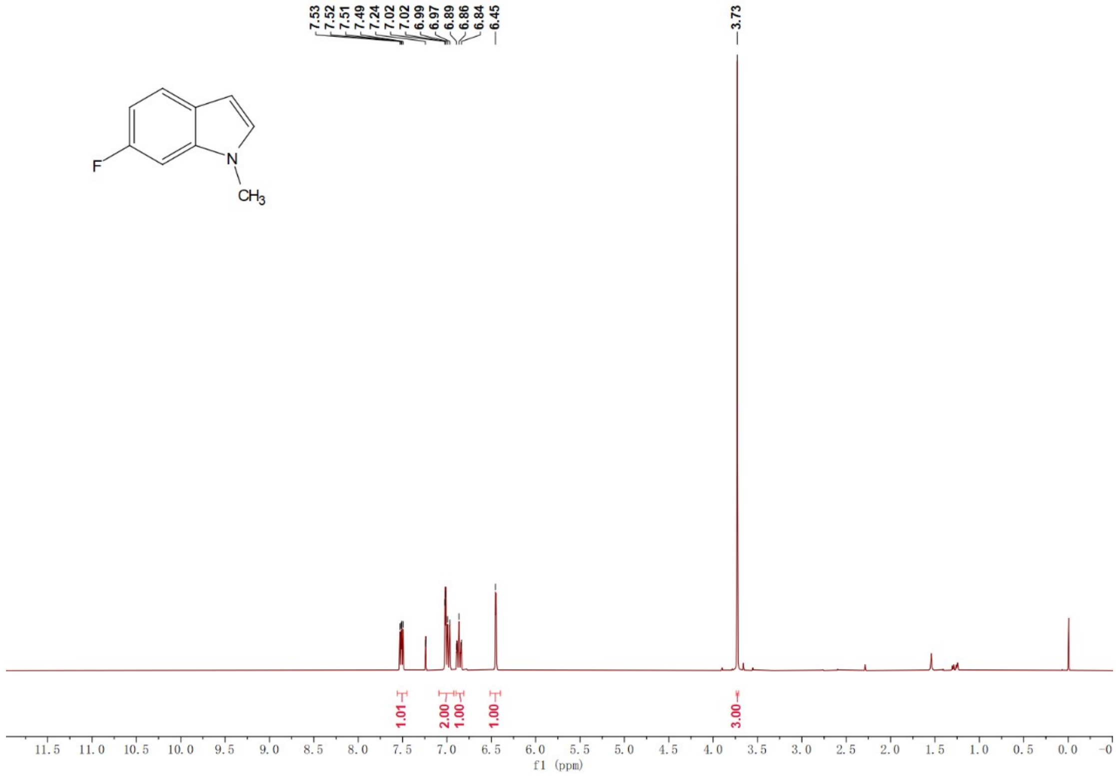
8. Spectral data.

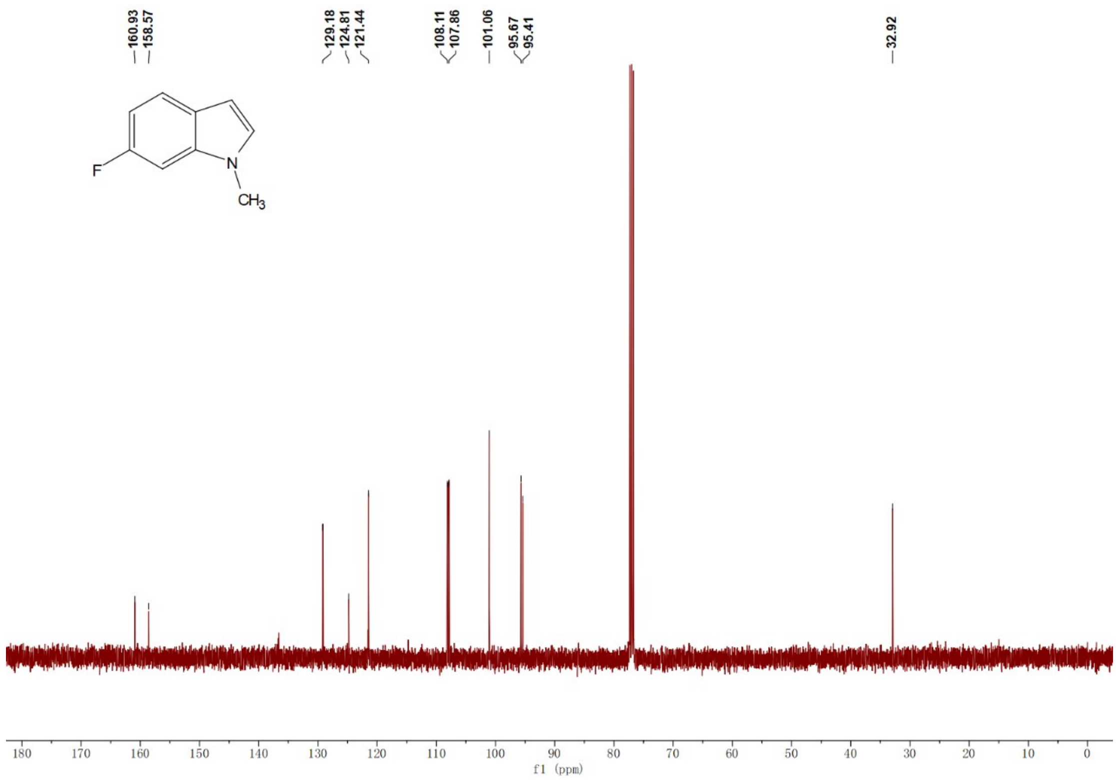
5-fluoro-N-methyl-indole



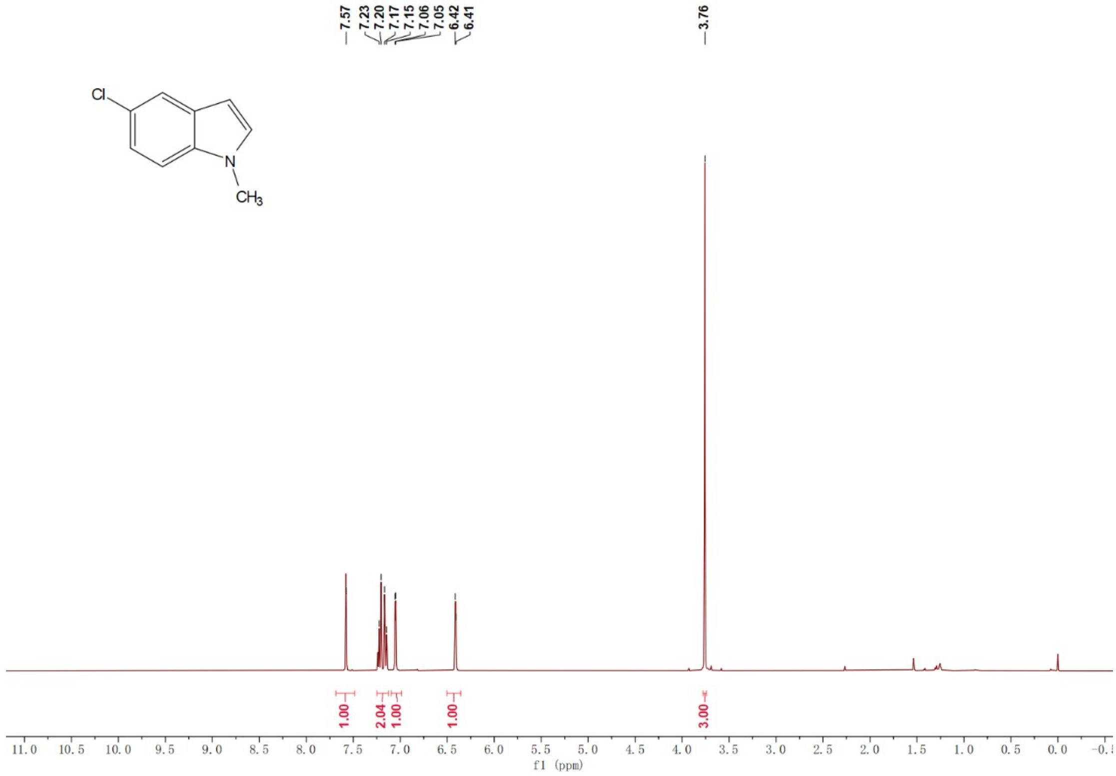


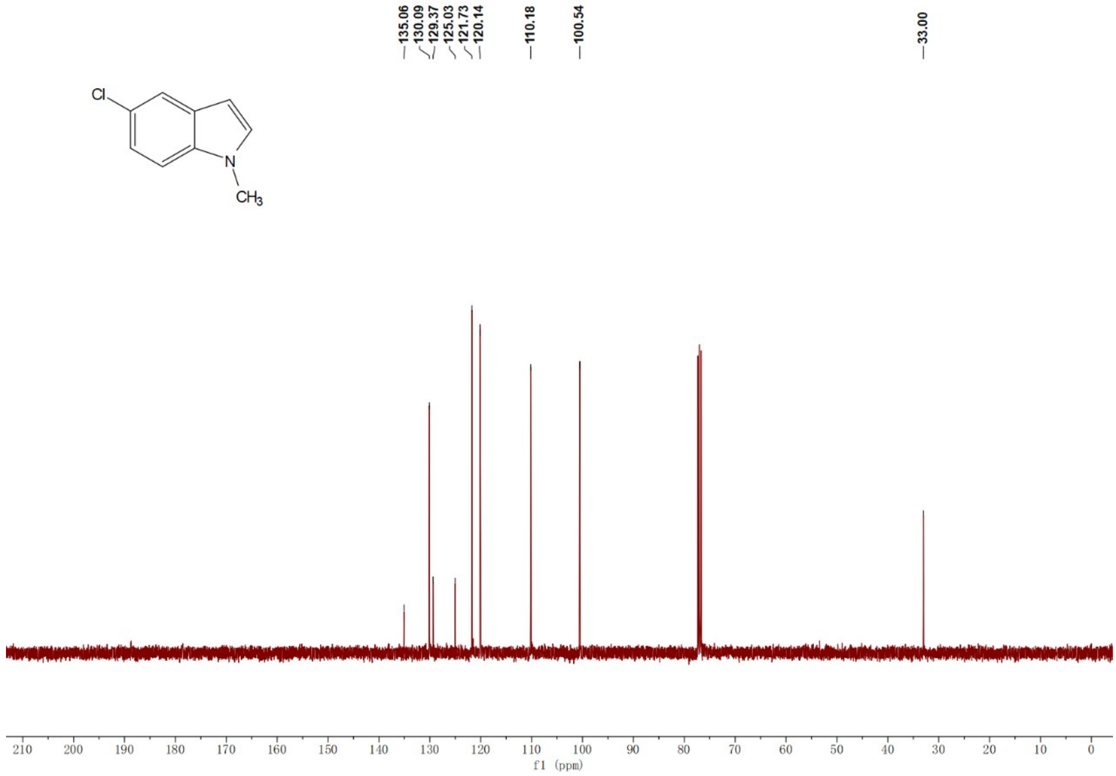
6-fluoro-N-methyl-indole



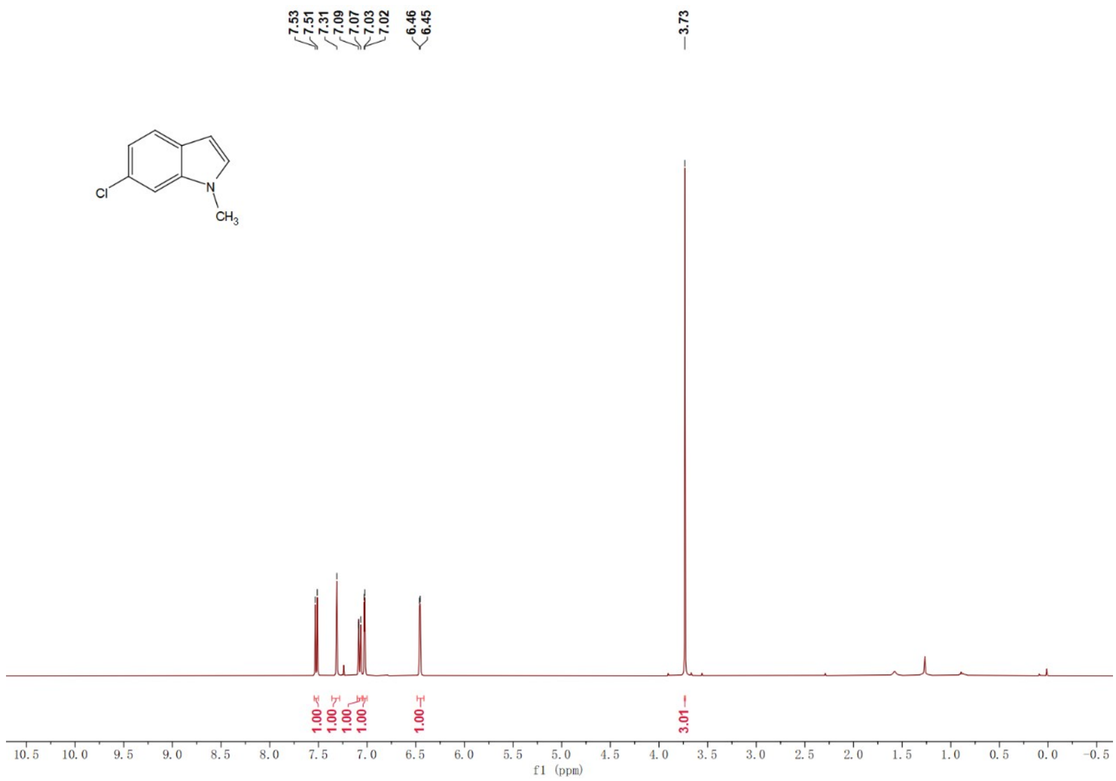


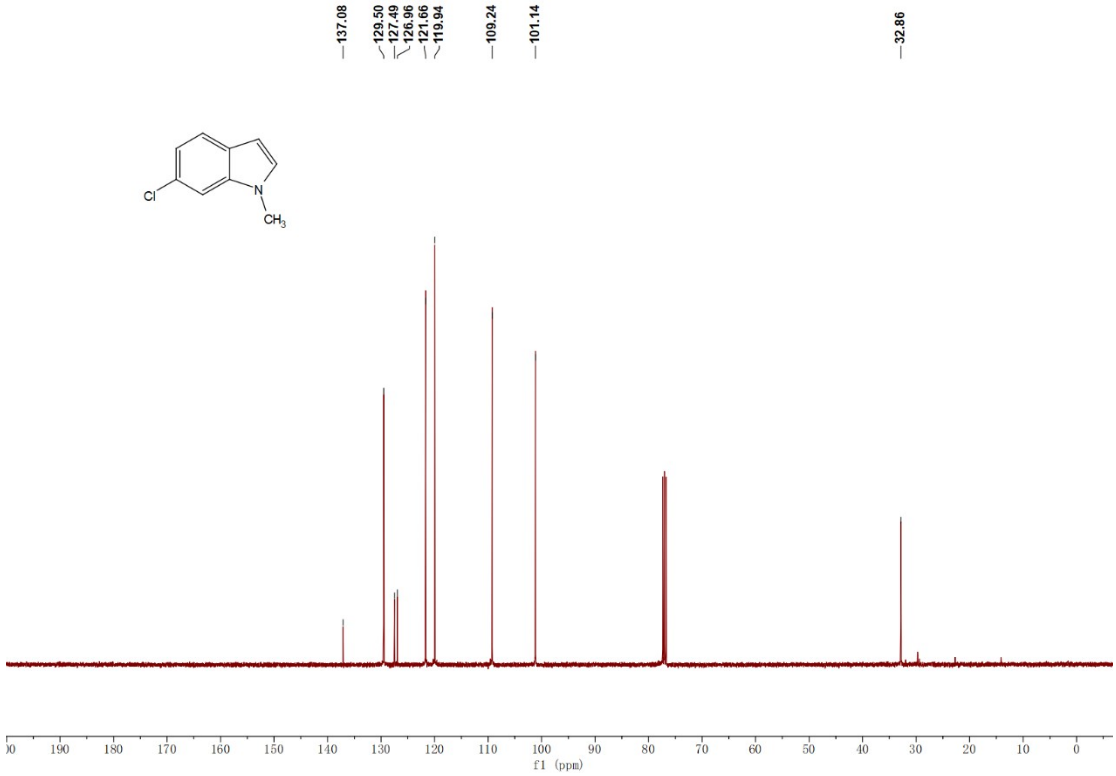
5-chloro-N-methyl-indole



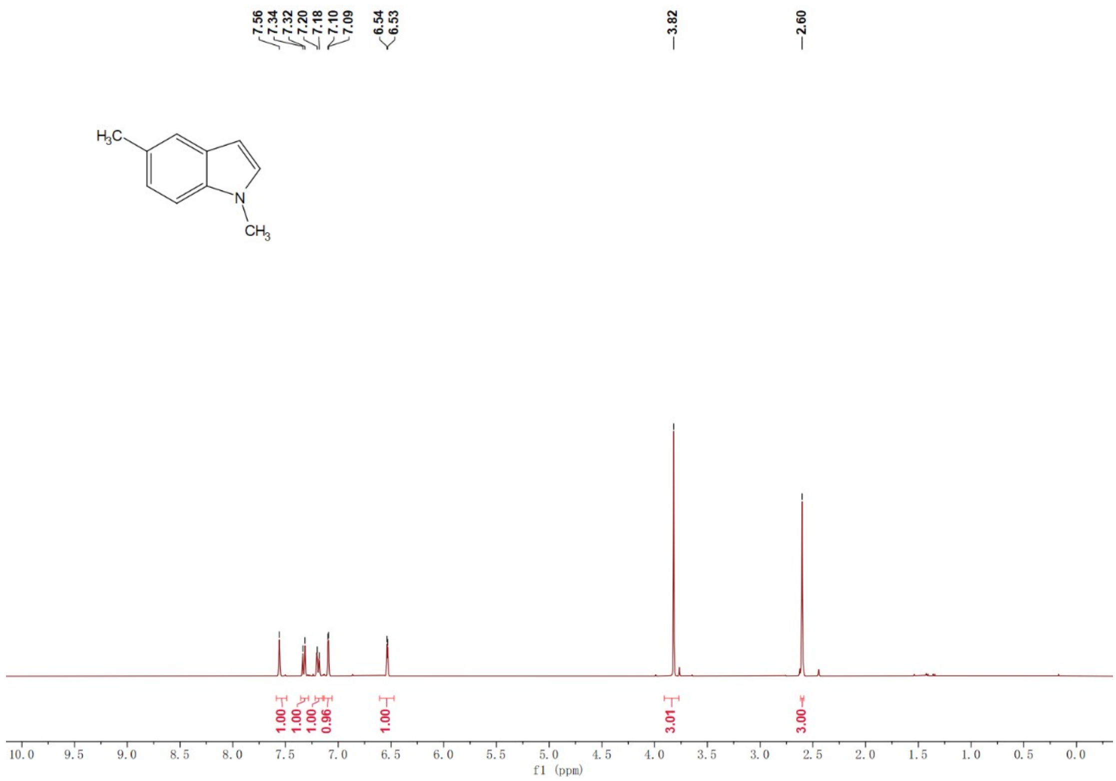


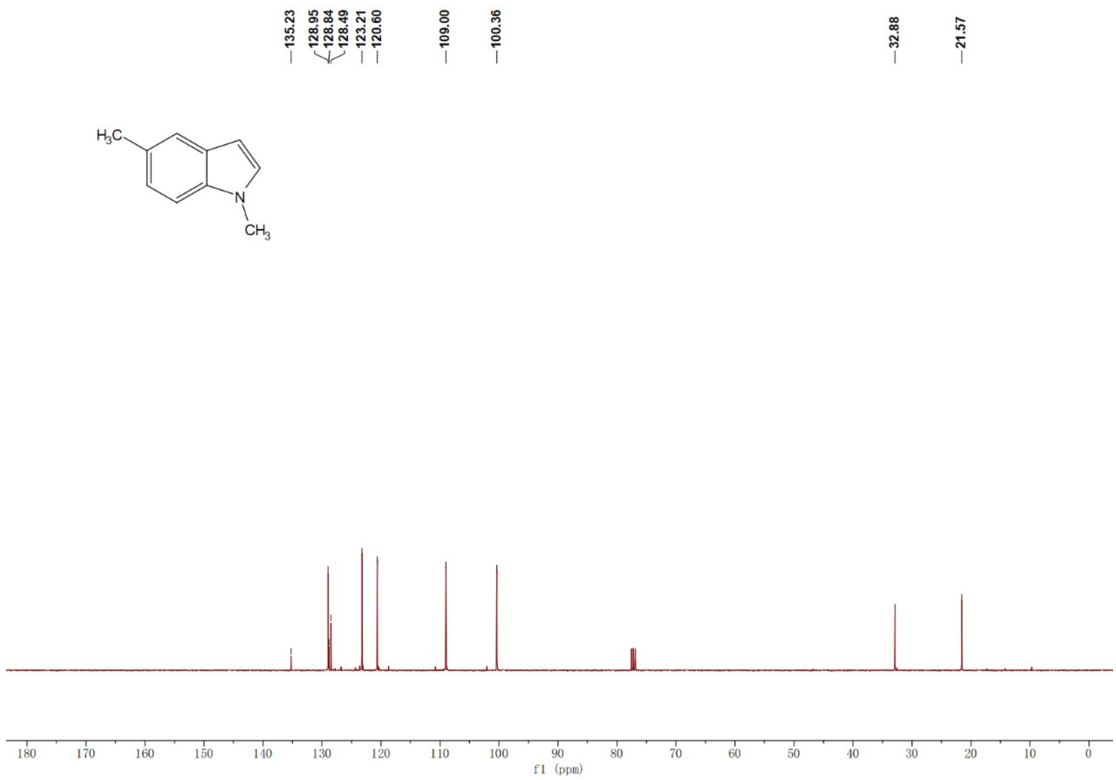
6- chloro-N-methyl-indole



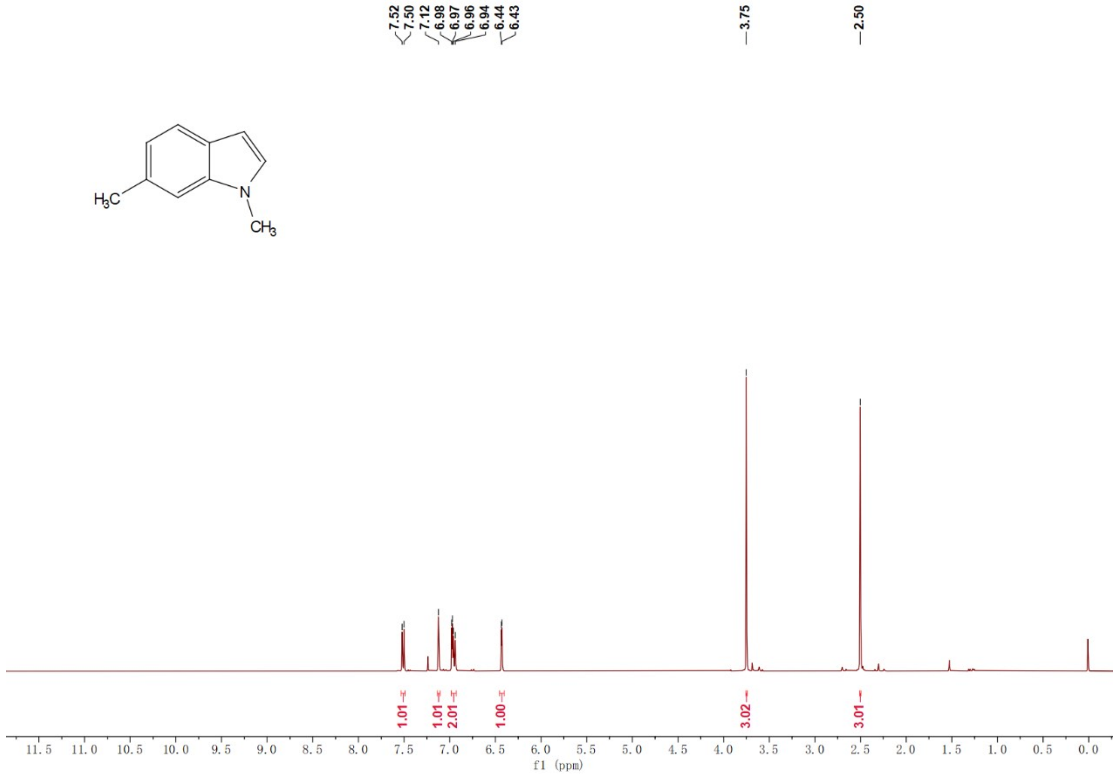


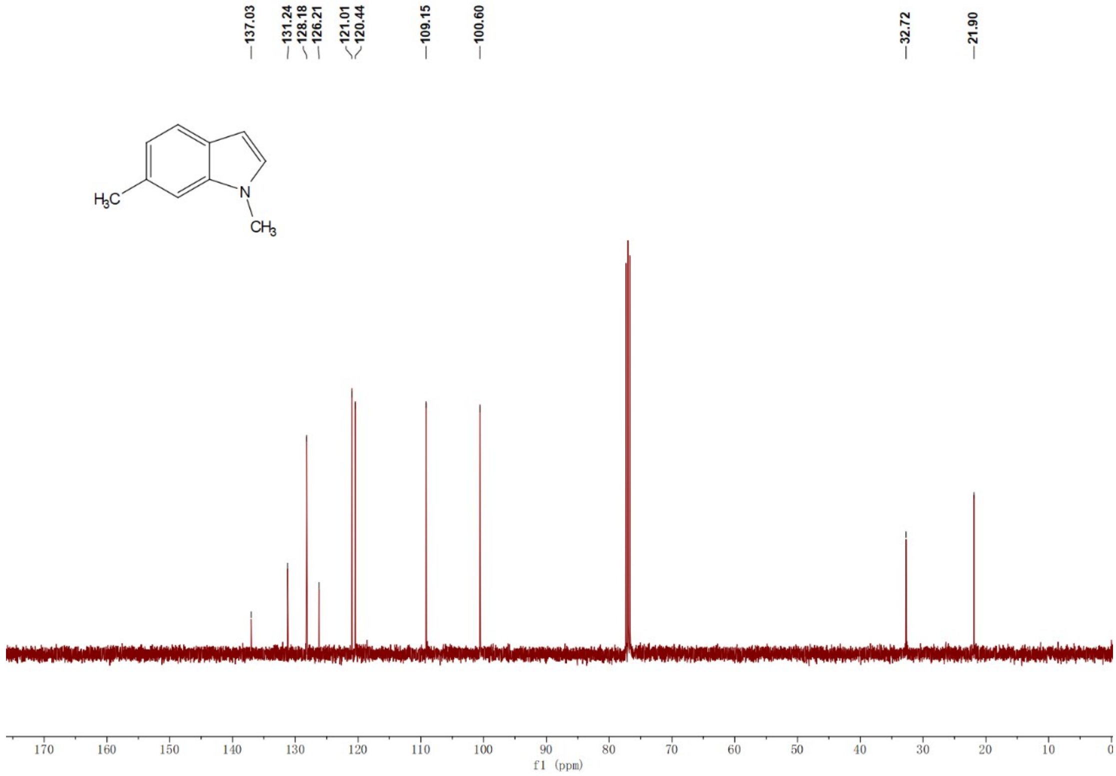
5- methyl-N-methyl-indole



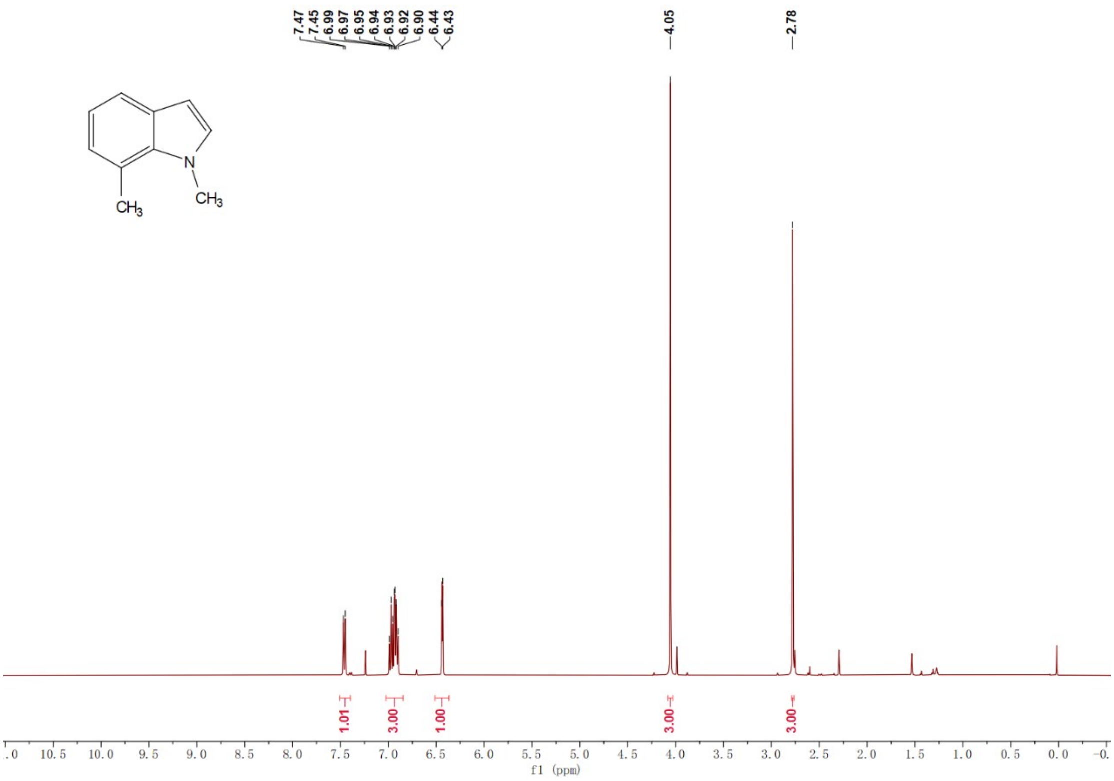


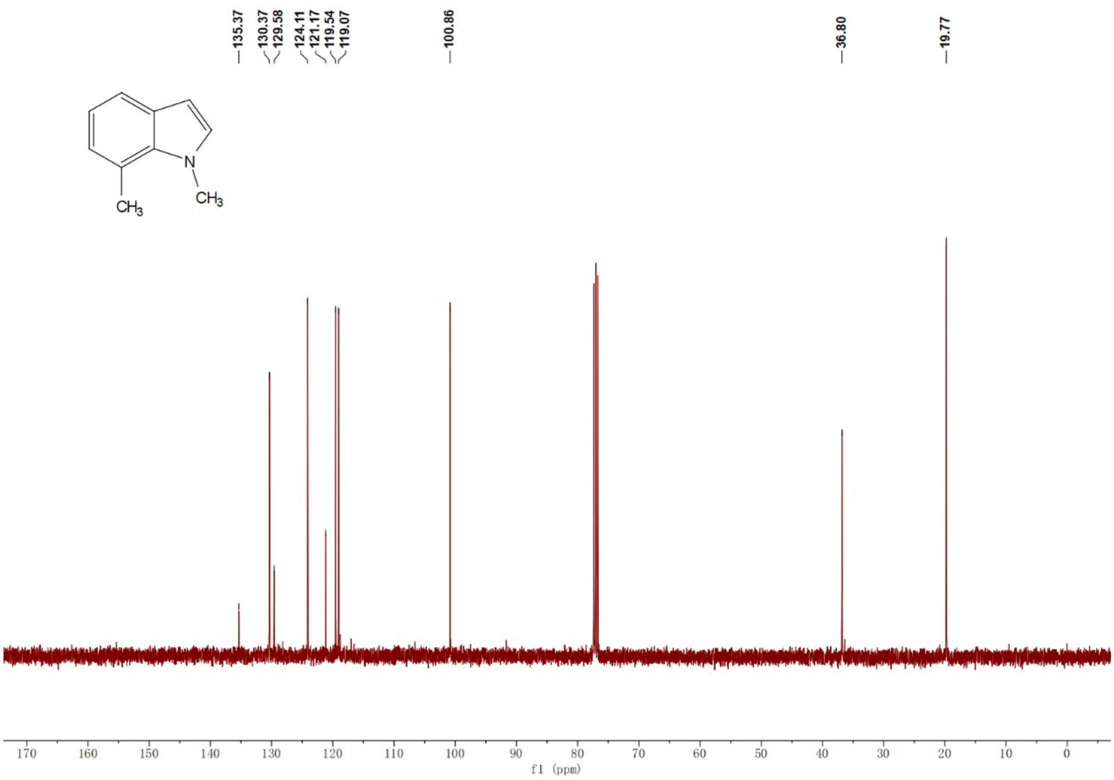
6- methyl-N-methyl-indole



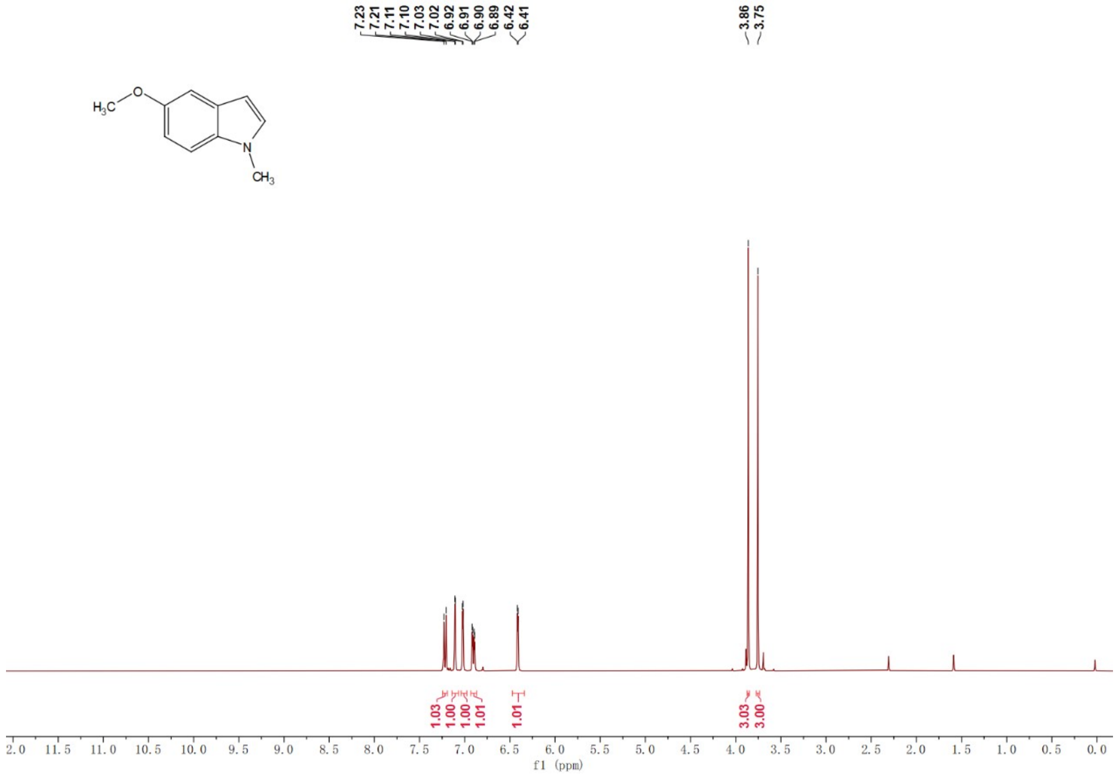


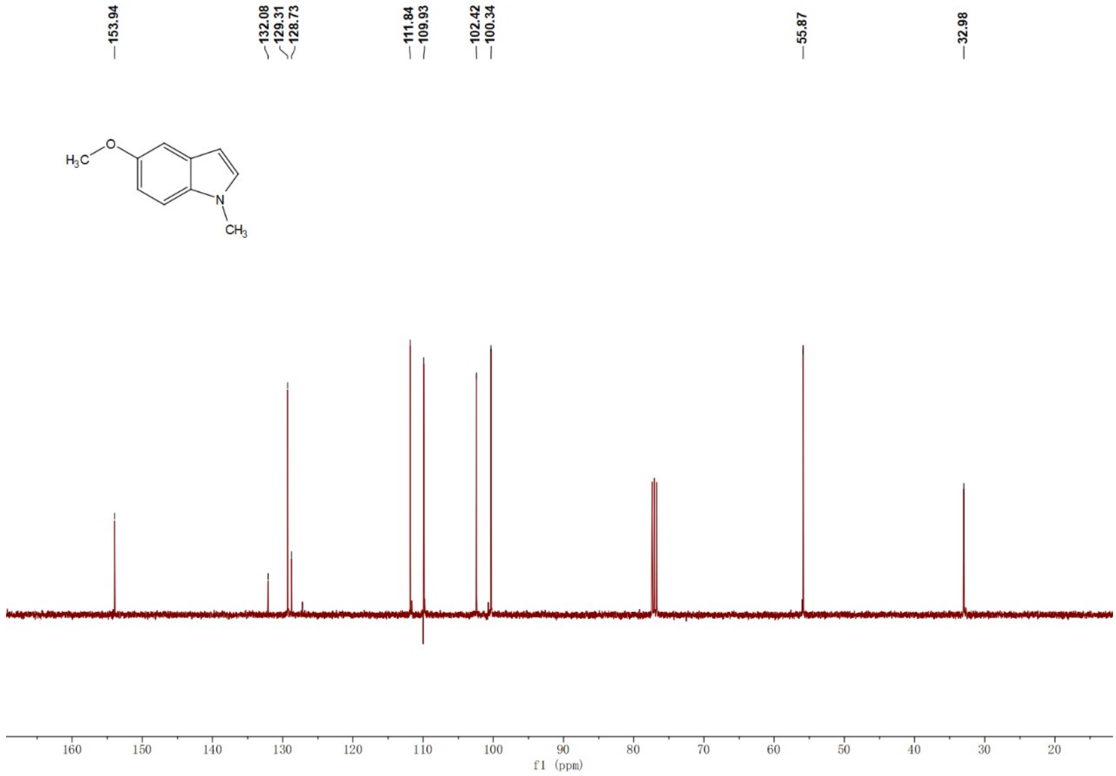
7- methyl-N-methyl-indole



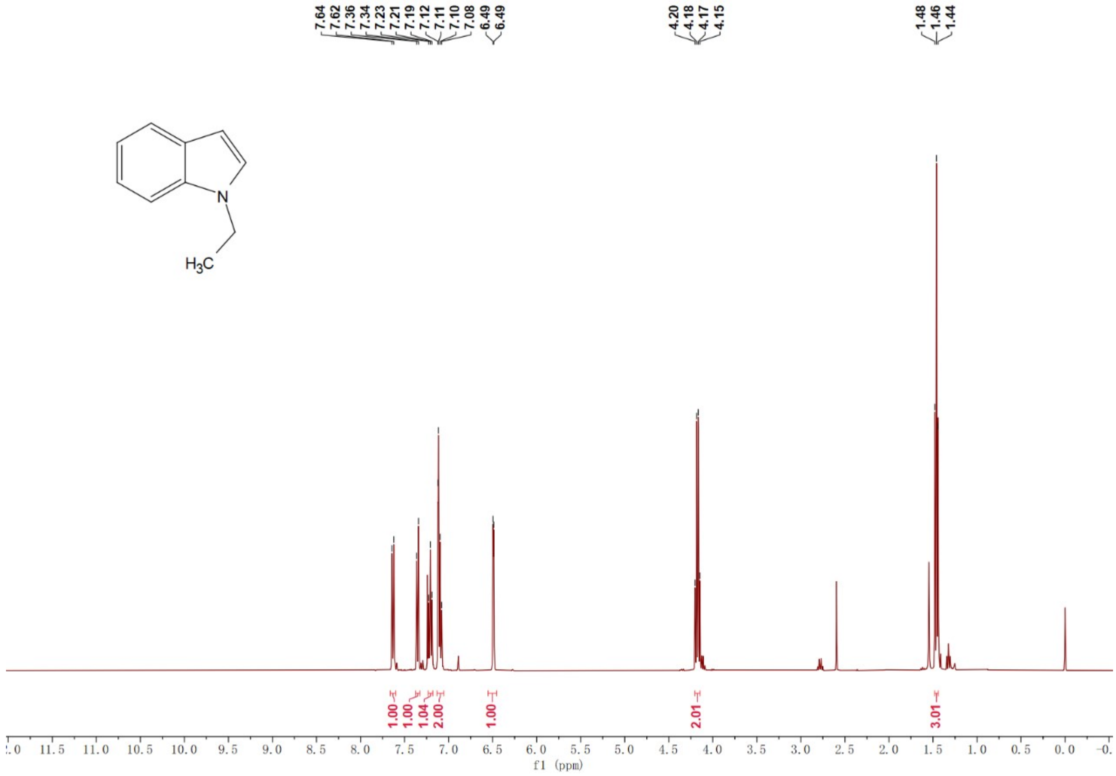


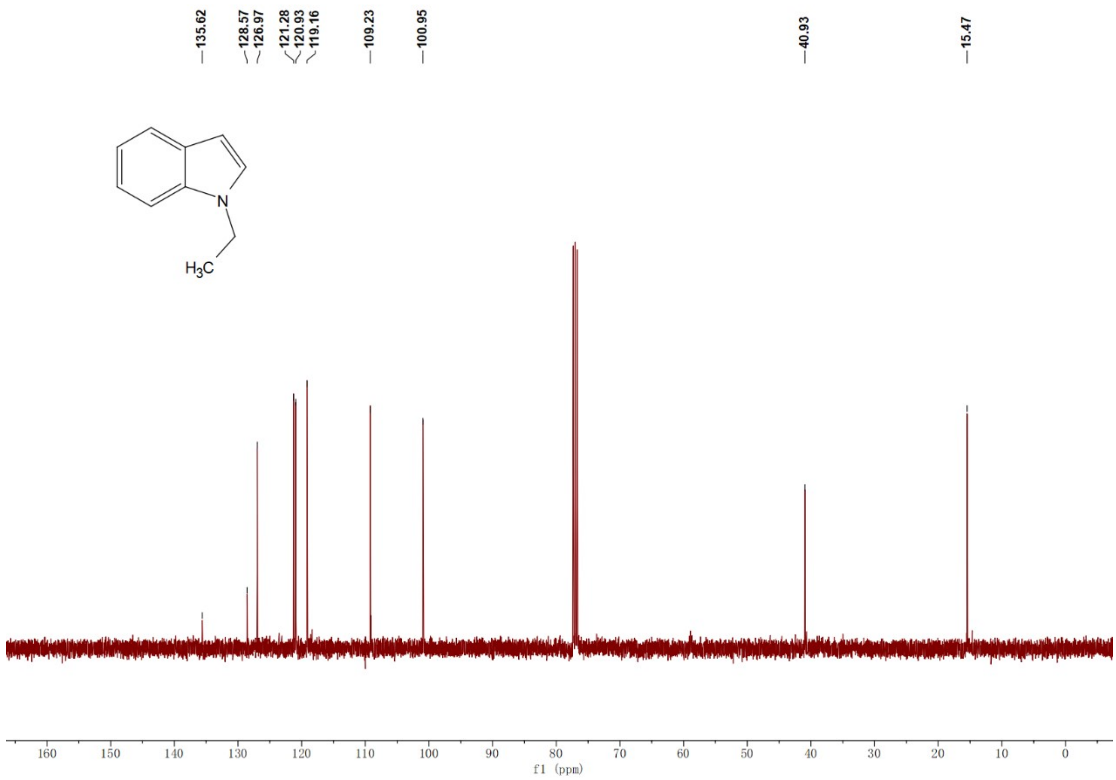
5-methoxy- N-methyl-indole



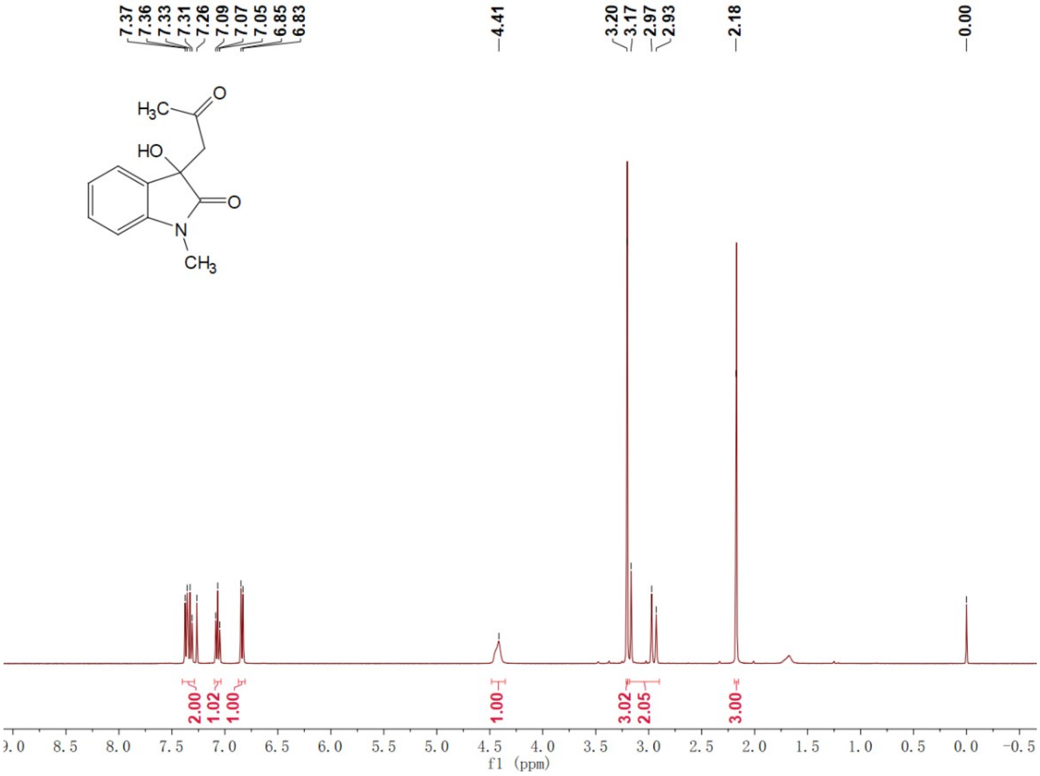


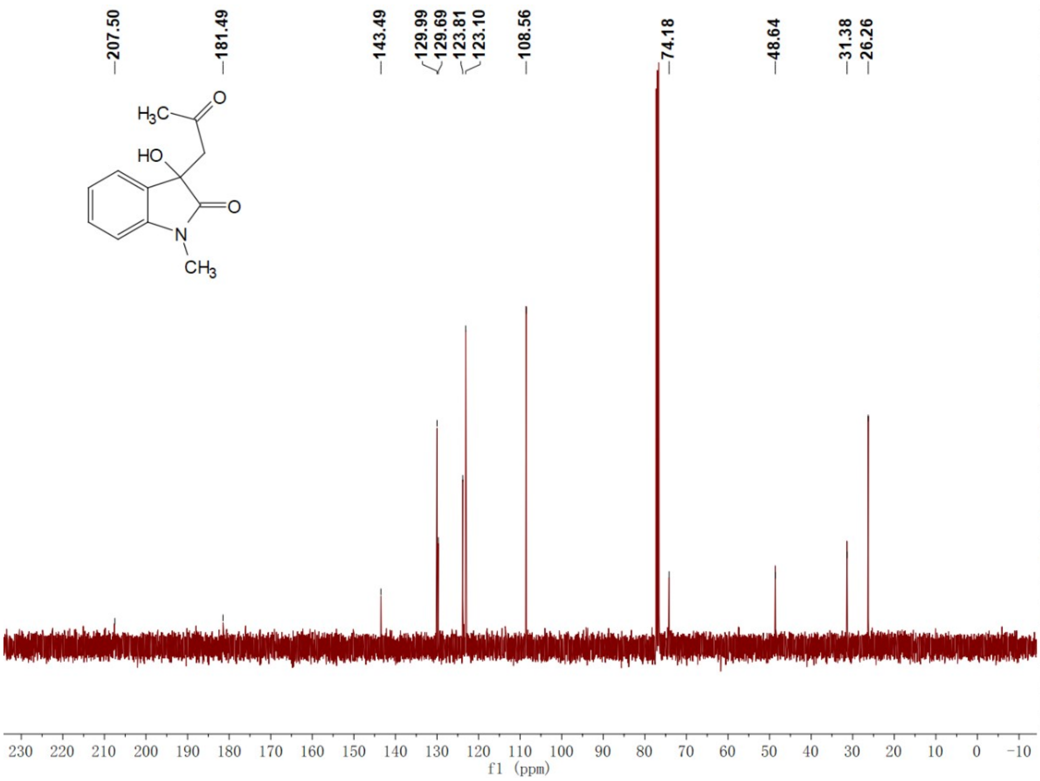
N-ethly-indole



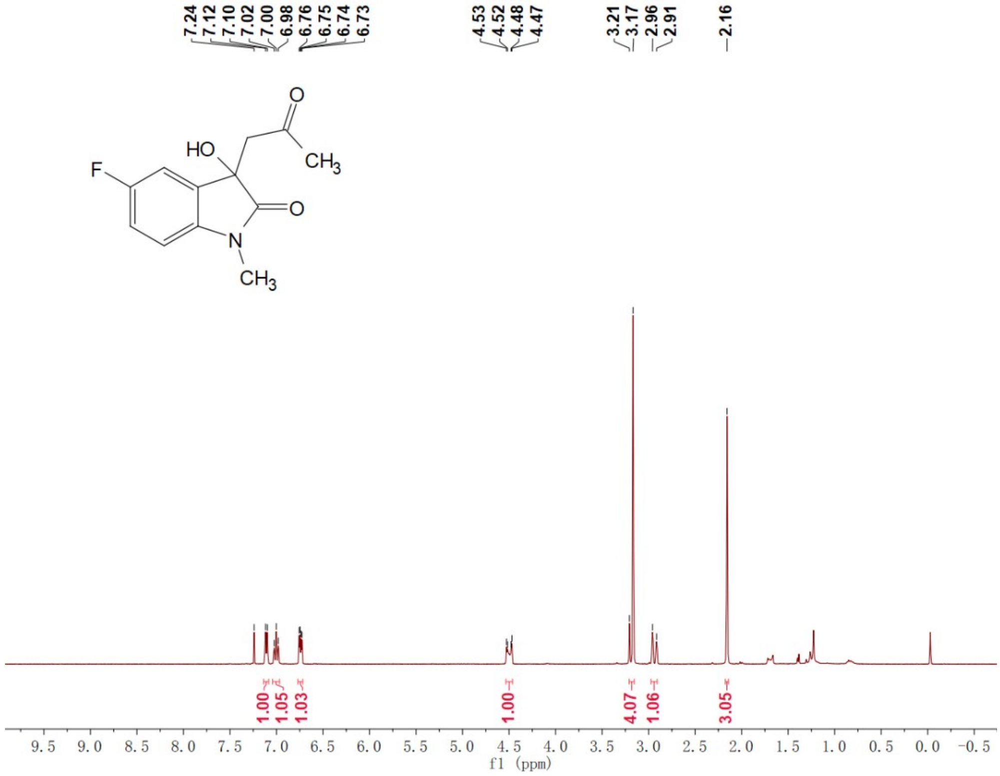


3-hydroxy-1-methyl-3-(2-oxopropyl)indolin-2-one (3a)





5-fluoro-3-hydroxy-1-methyl-3-(2-oxopropyl)indolin-2-one (3b)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4.47
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2.96
2.91
2.16
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1.03
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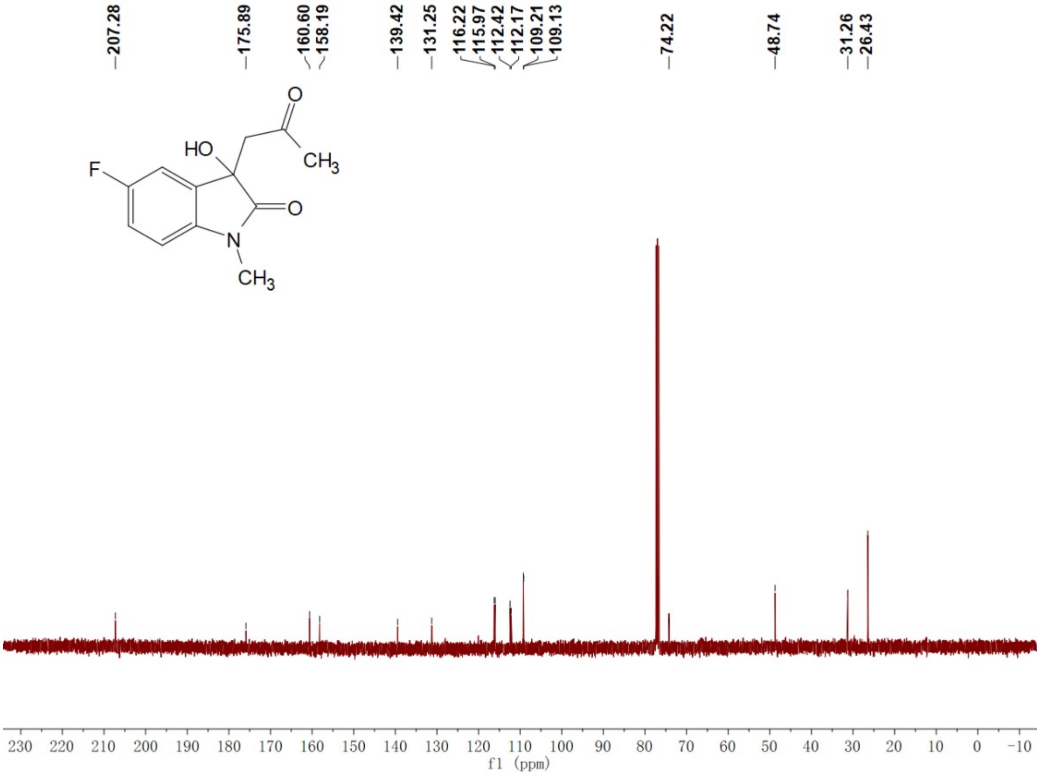
4.07
1.06
3.05
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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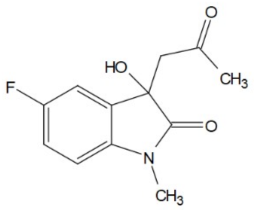
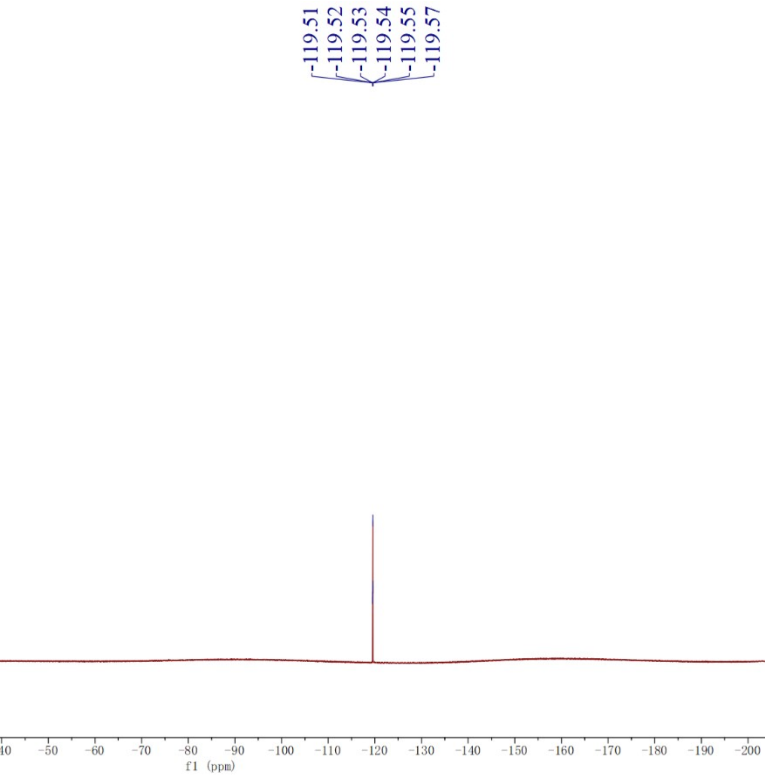
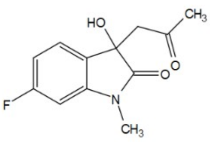
48.74
31.26
26.43
HO
O
CH3
F
O
N
CH3
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

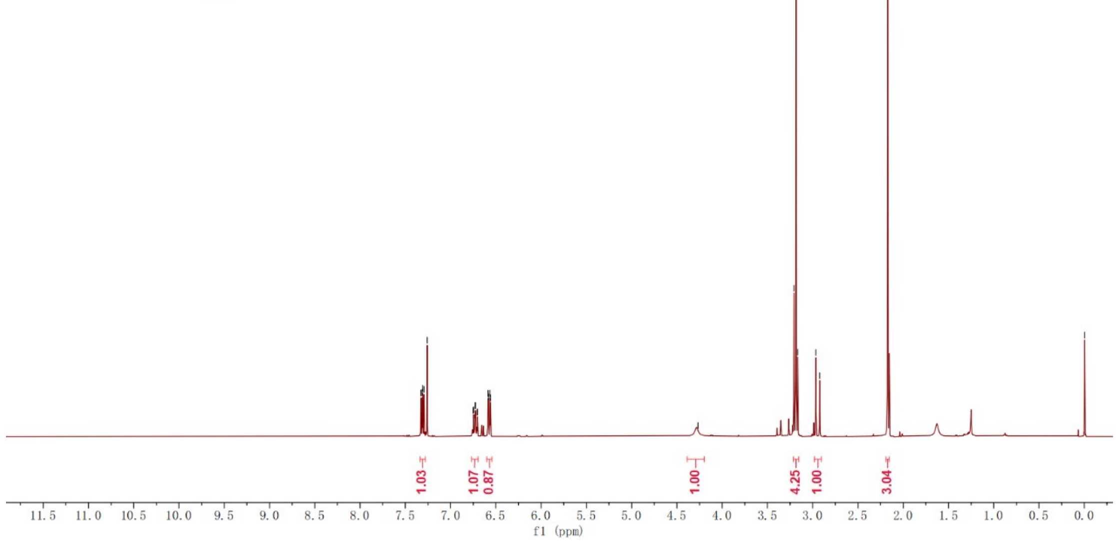
FLUORINE_01

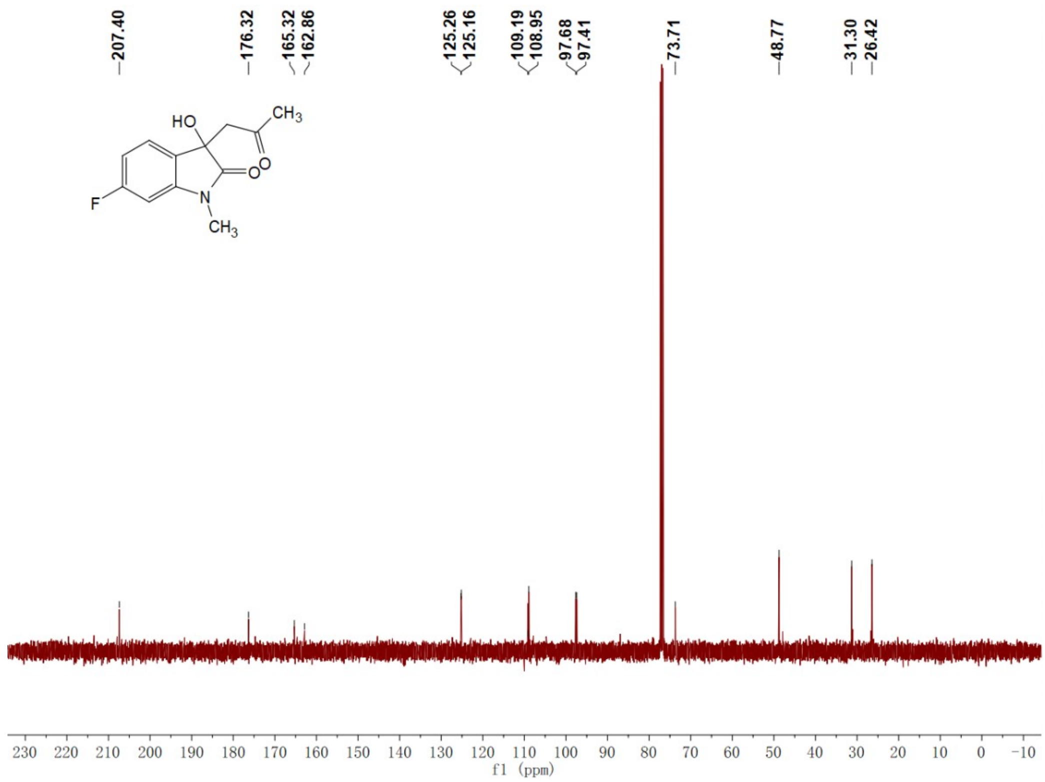




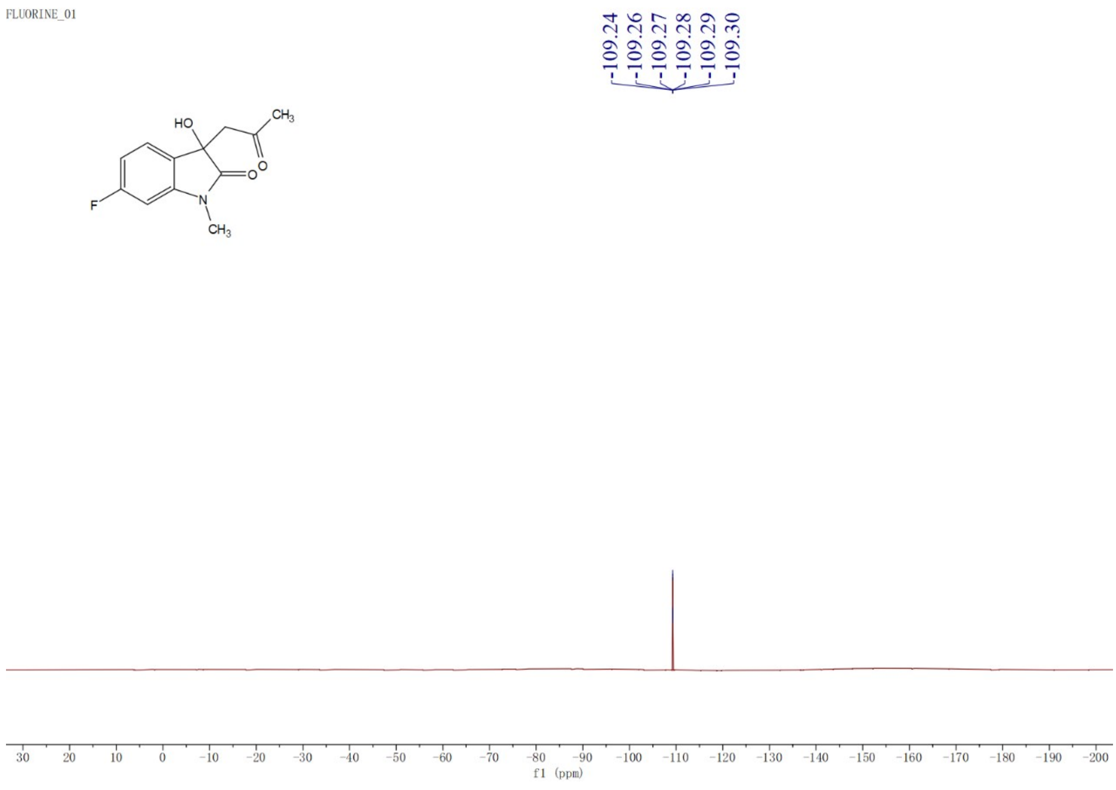
6-fluoro-3-hydroxy-1-methyl-3-(2-oxopropyl)indolin-2-one (3c)





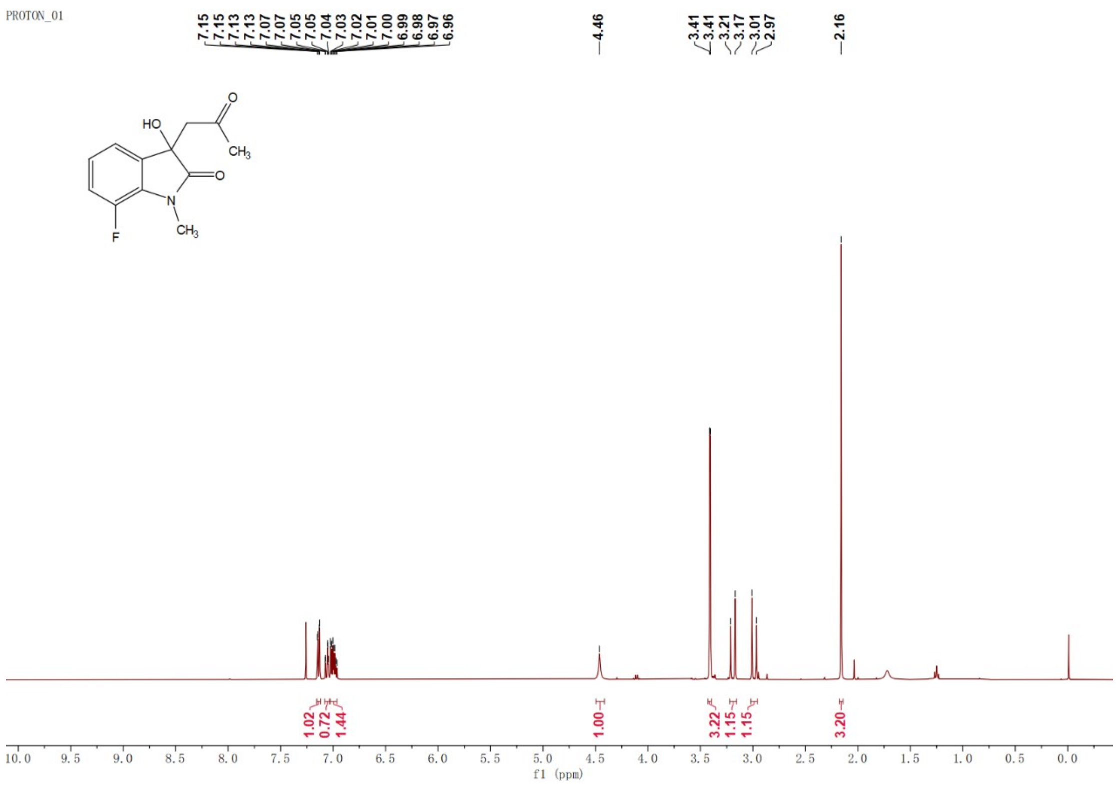


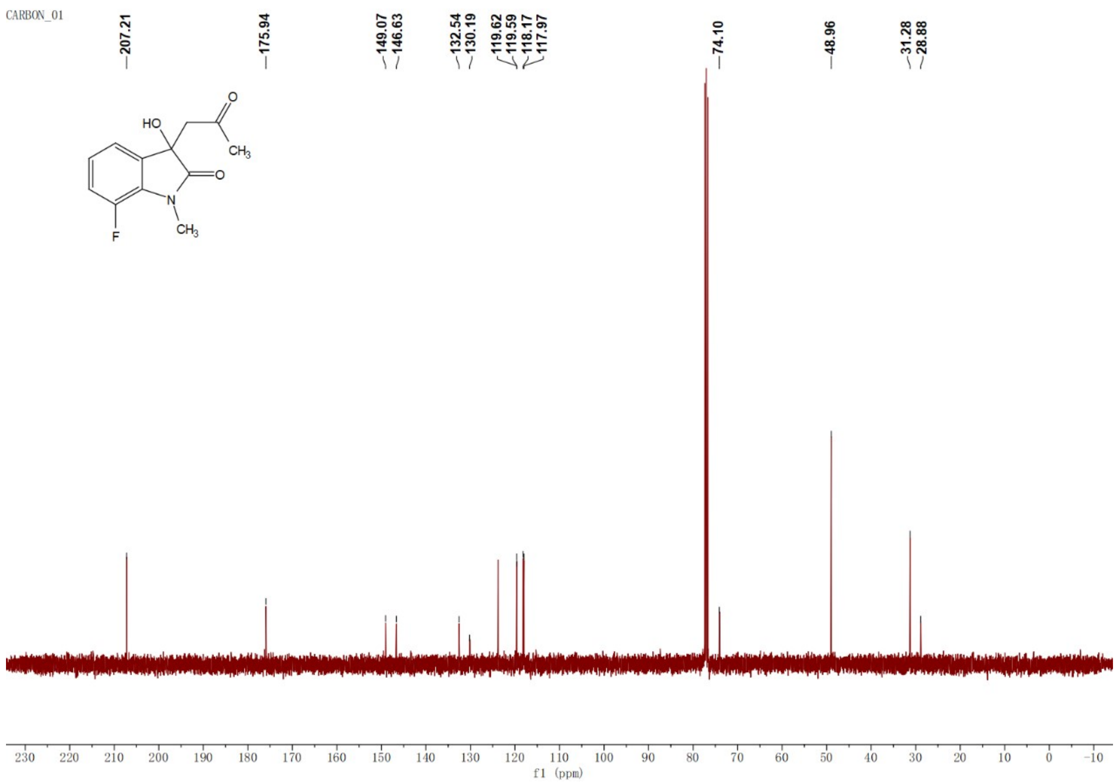
207.40
176.32
165.32
162.86
125.26
125.16
109.19
108.95
97.68
97.41
73.71
48.77
31.30
26.42
HO
CH3
O
O
F
N
CH3
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

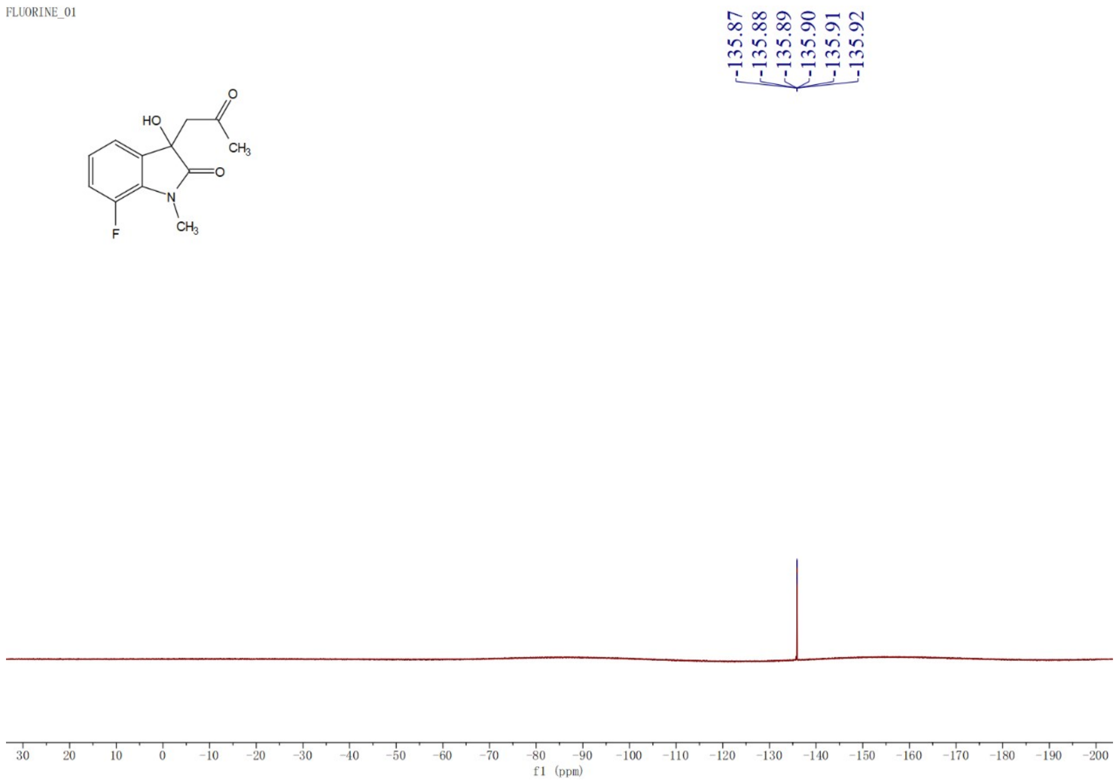


FLUORINE_01
-109.24
-109.26
-109.27
-109.28
-109.29
-109.30
HO
CH3
O
O
F
N
CH3
30 20 10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200
f1 (ppm)

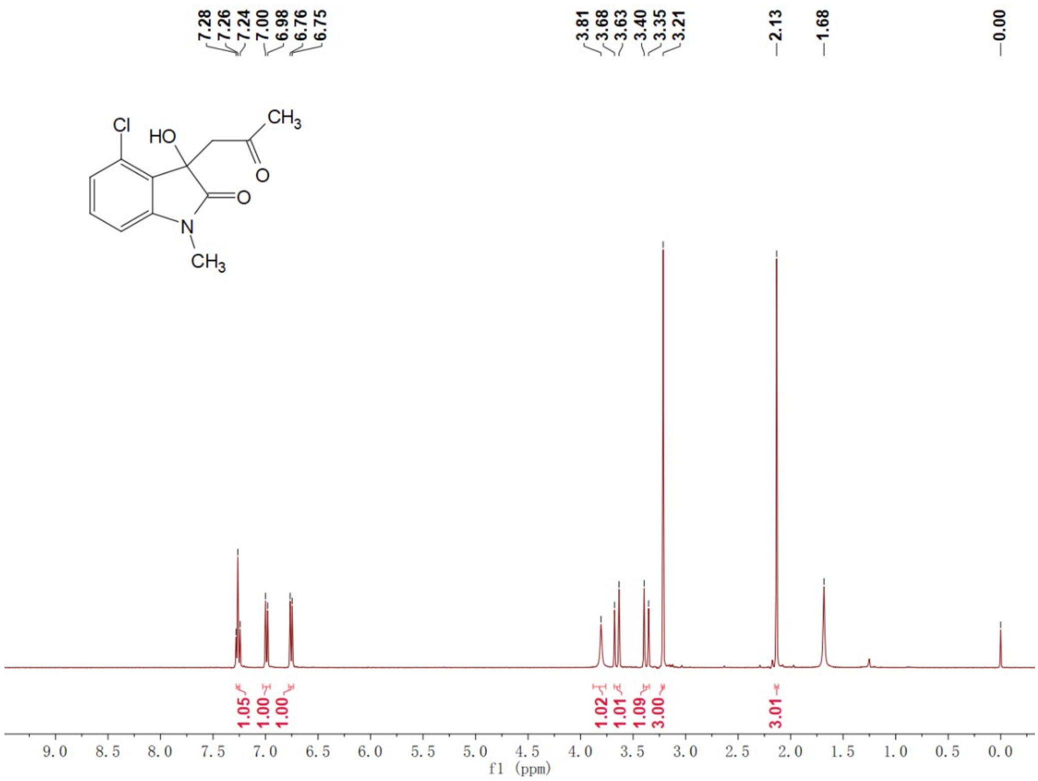
7-fluoro-3-hydroxy-1-methyl-3-(2-oxopropyl)indolin-2-one (3d)

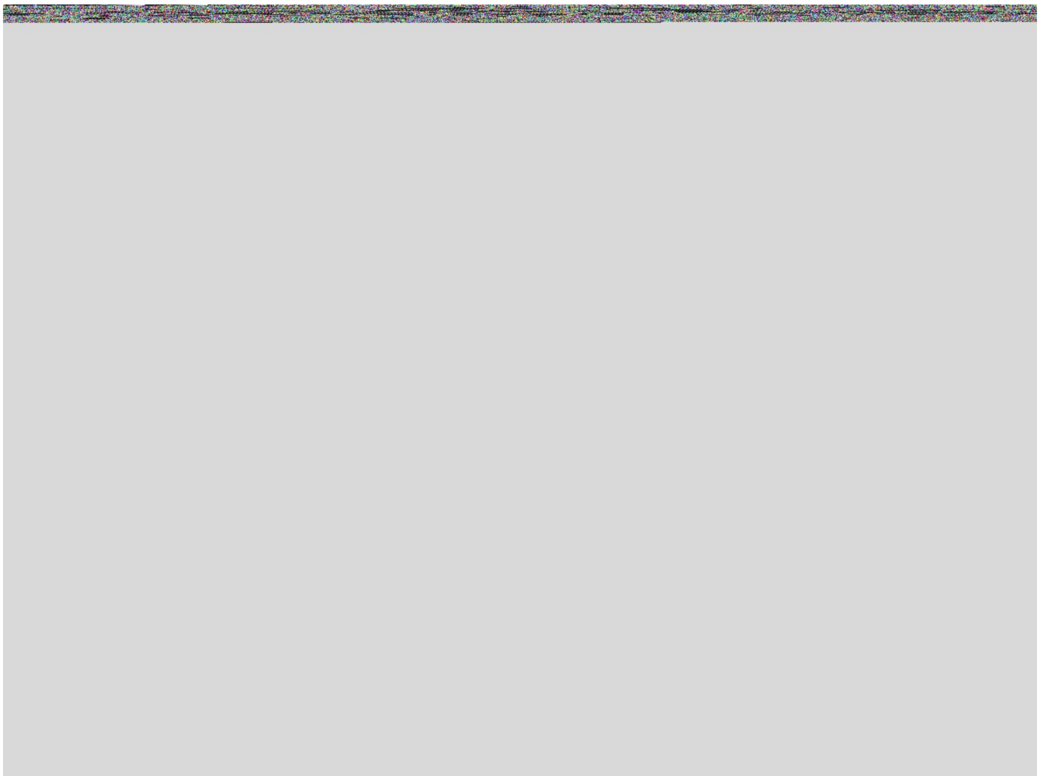




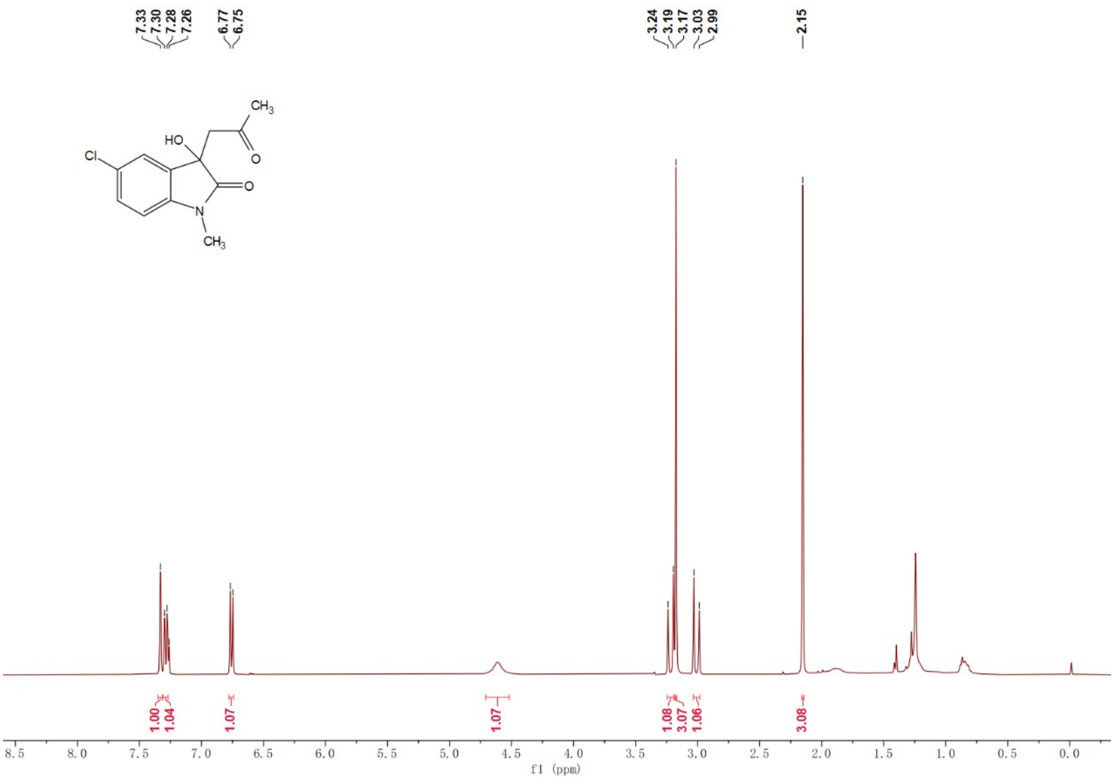


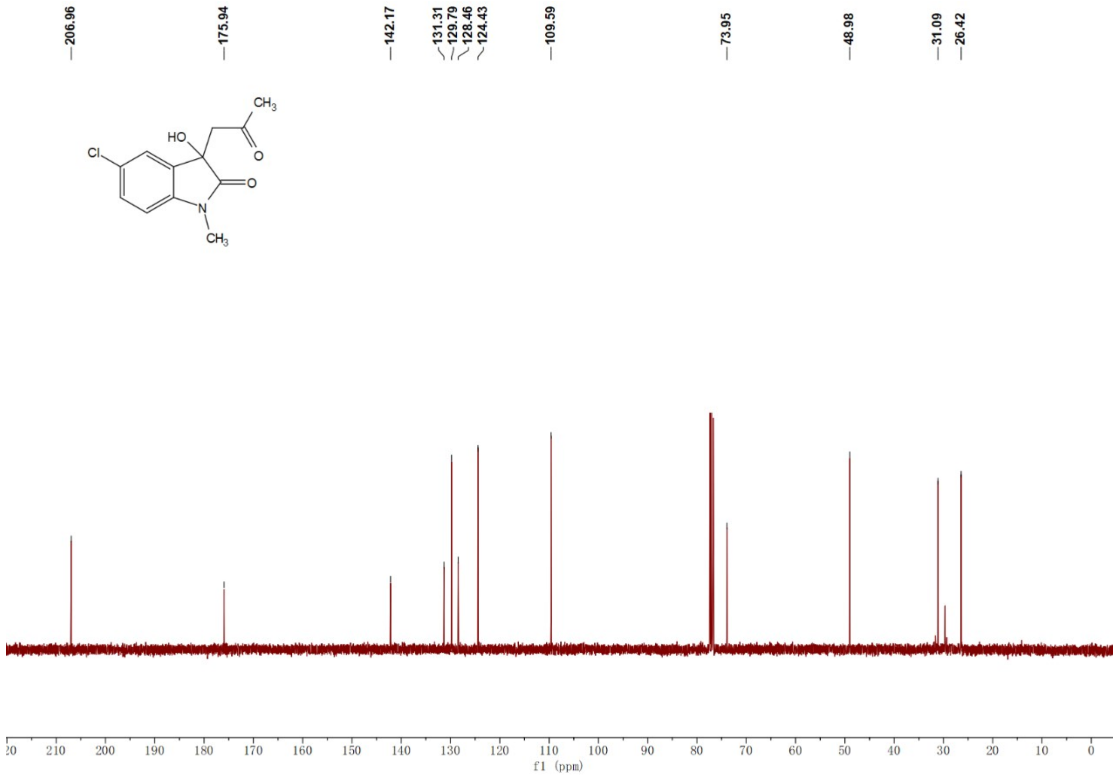
4-chloro-3-hydroxy-1-methyl-3-(2-oxopropyl)indolin-2-one (3e)



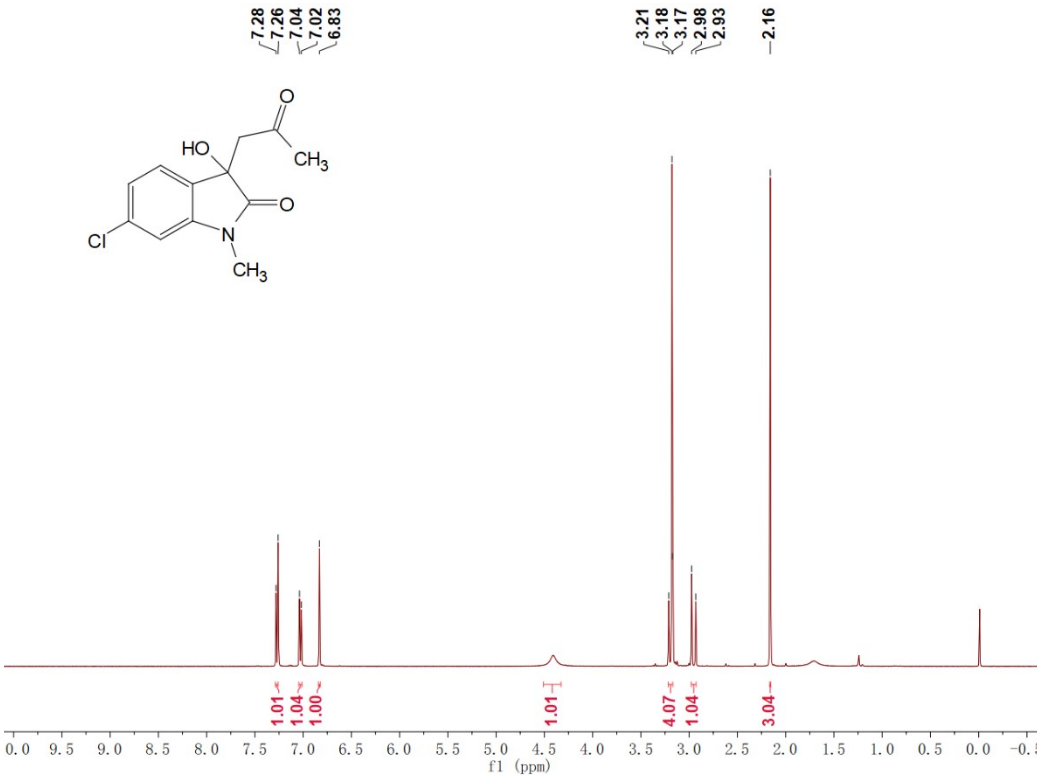


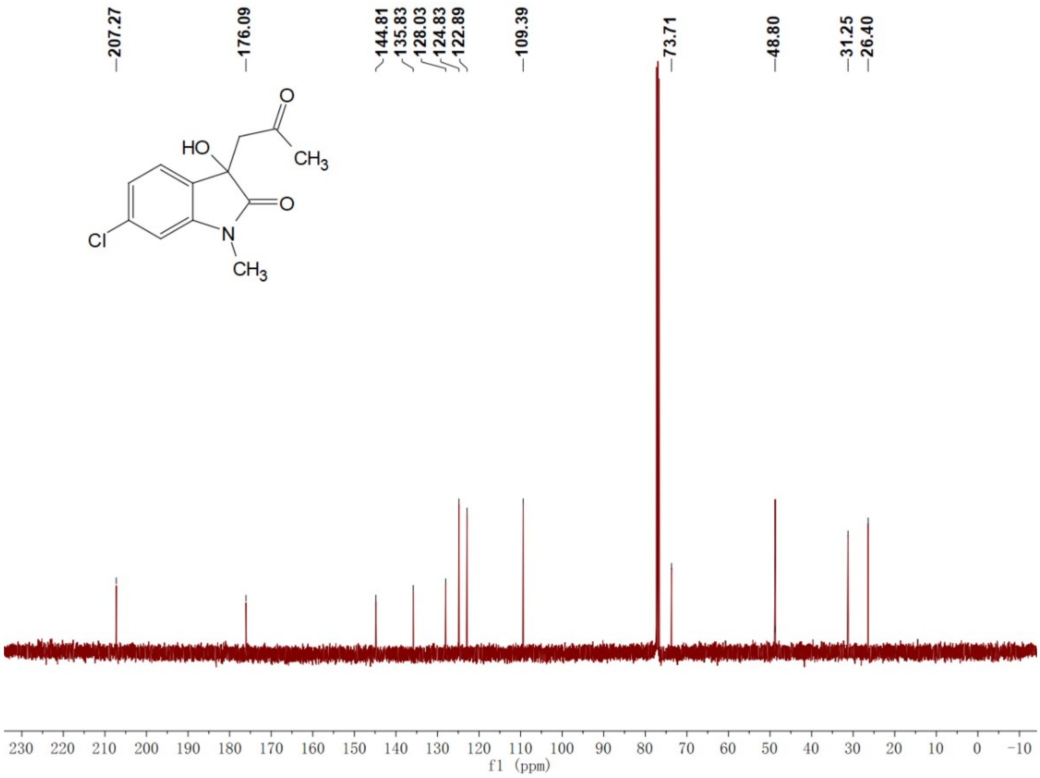
5-chloro-3-hydroxy-1-methyl-3-(2-oxopropyl)indolin-2-one (3f)



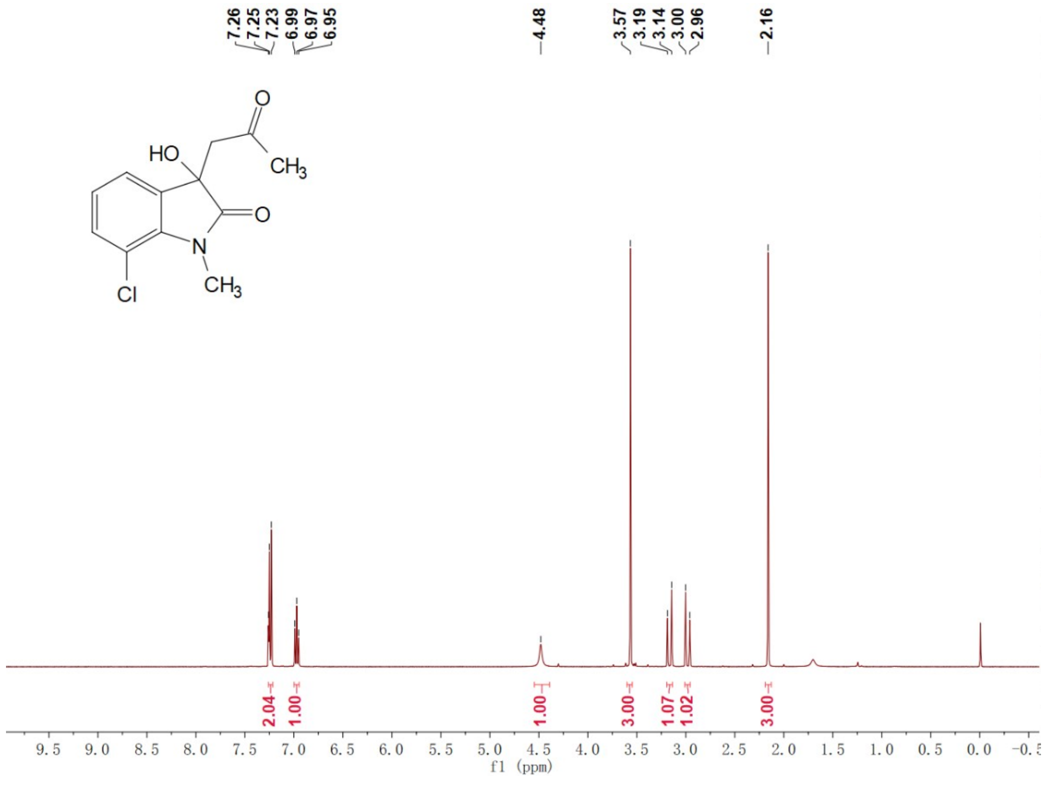


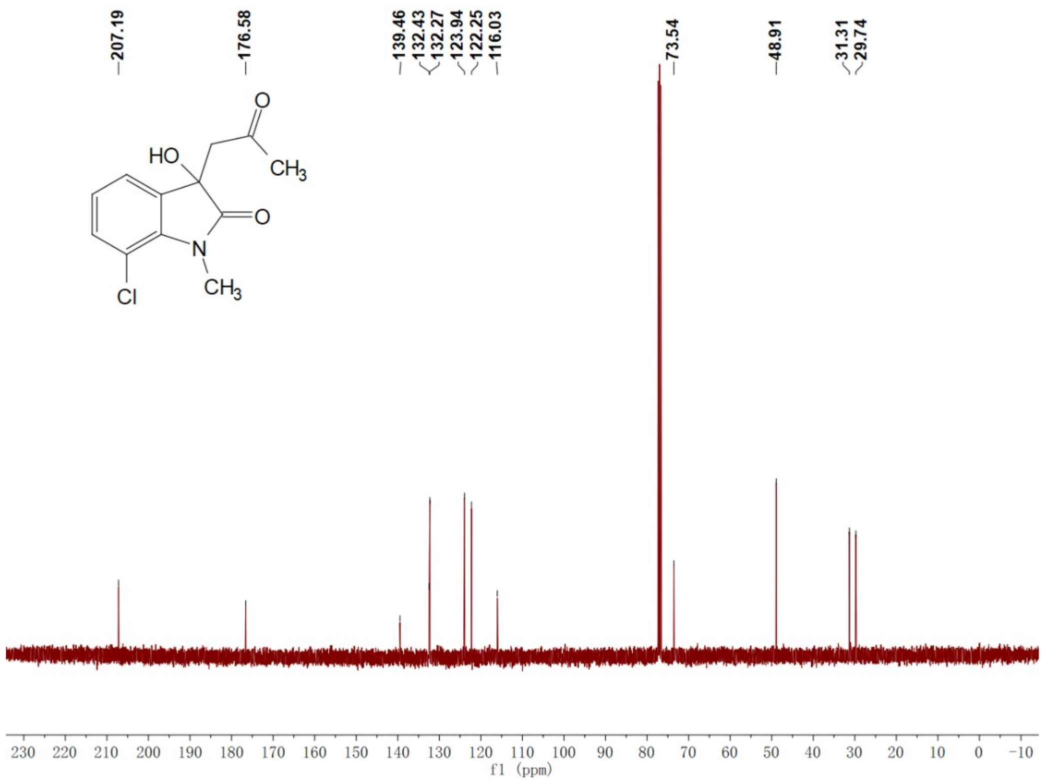
6-chloro-3-hydroxy-1-methyl-3-(2-oxopropyl)indolin-2-one (3g)



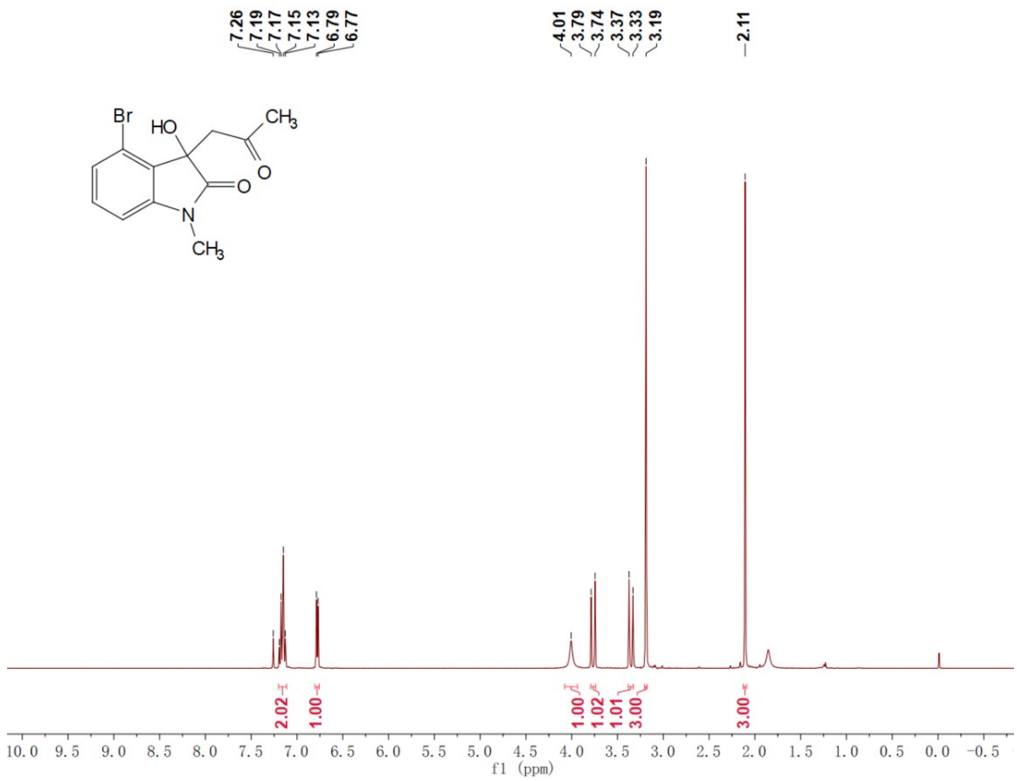


7-chloro-3-hydroxy-1-methyl-3-(2-oxopropyl)indolin-2-one (3h)

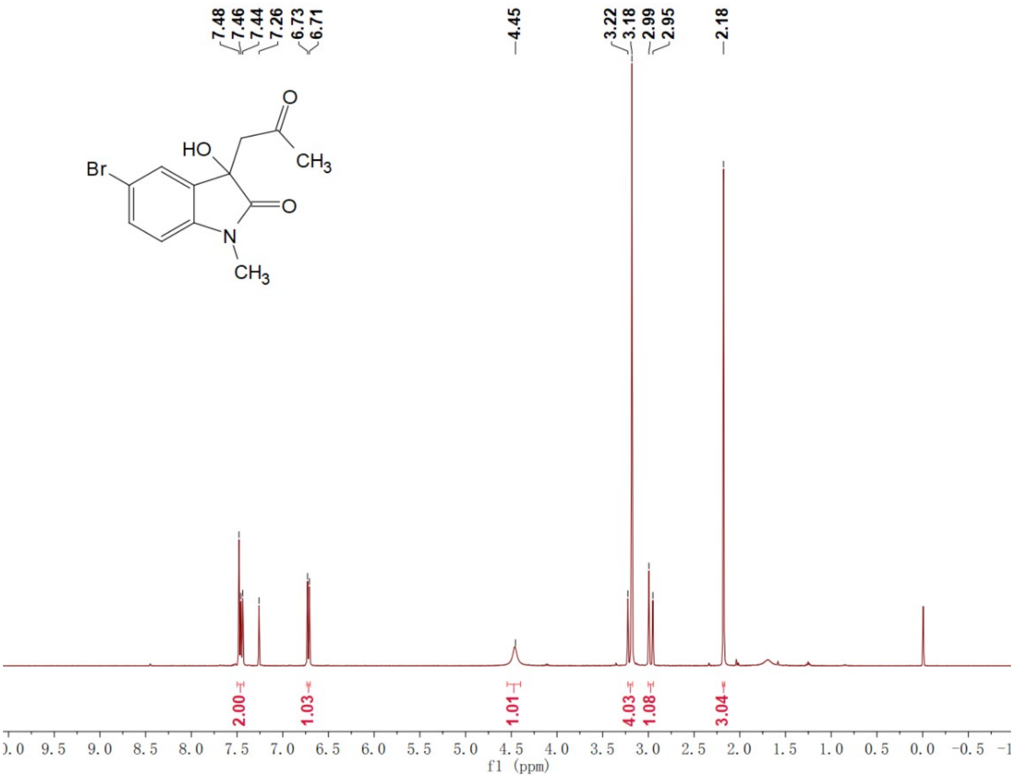


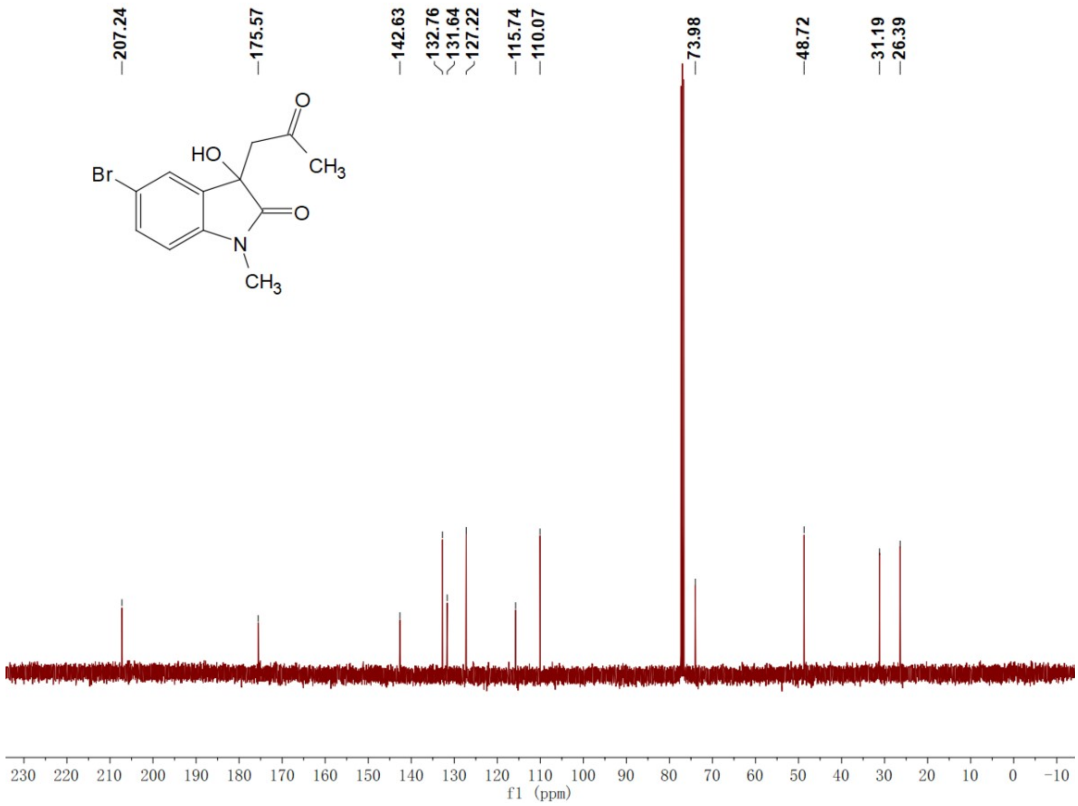


4-bromo-3-hydroxy-1-methyl-3-(2-oxopropyl)indolin-2-one (3i)

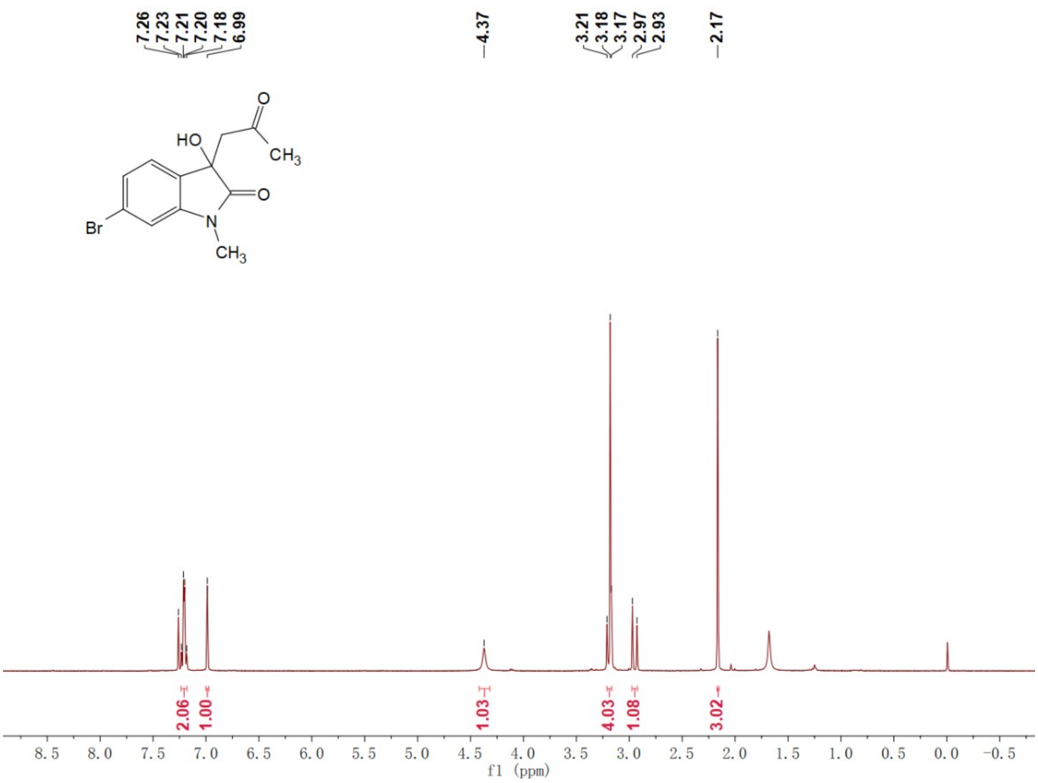


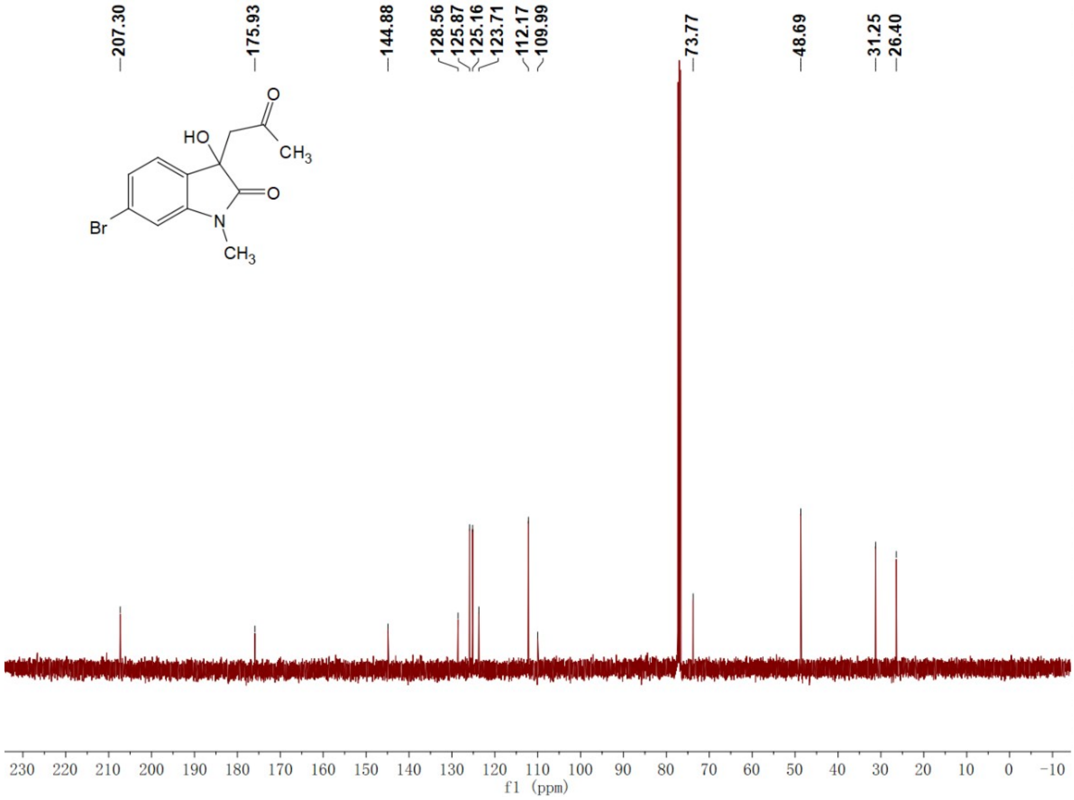
5-bromo-3-hydroxy-1-methyl-3-(2-oxopropyl)indolin-2-one (3j)



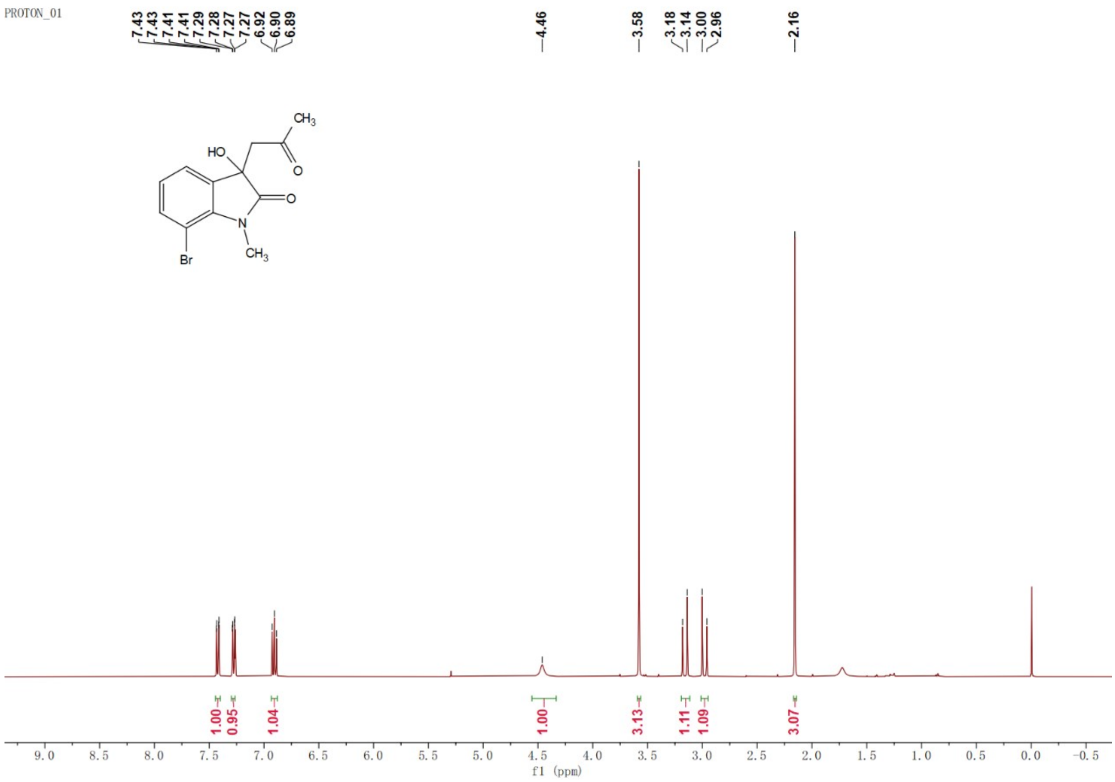


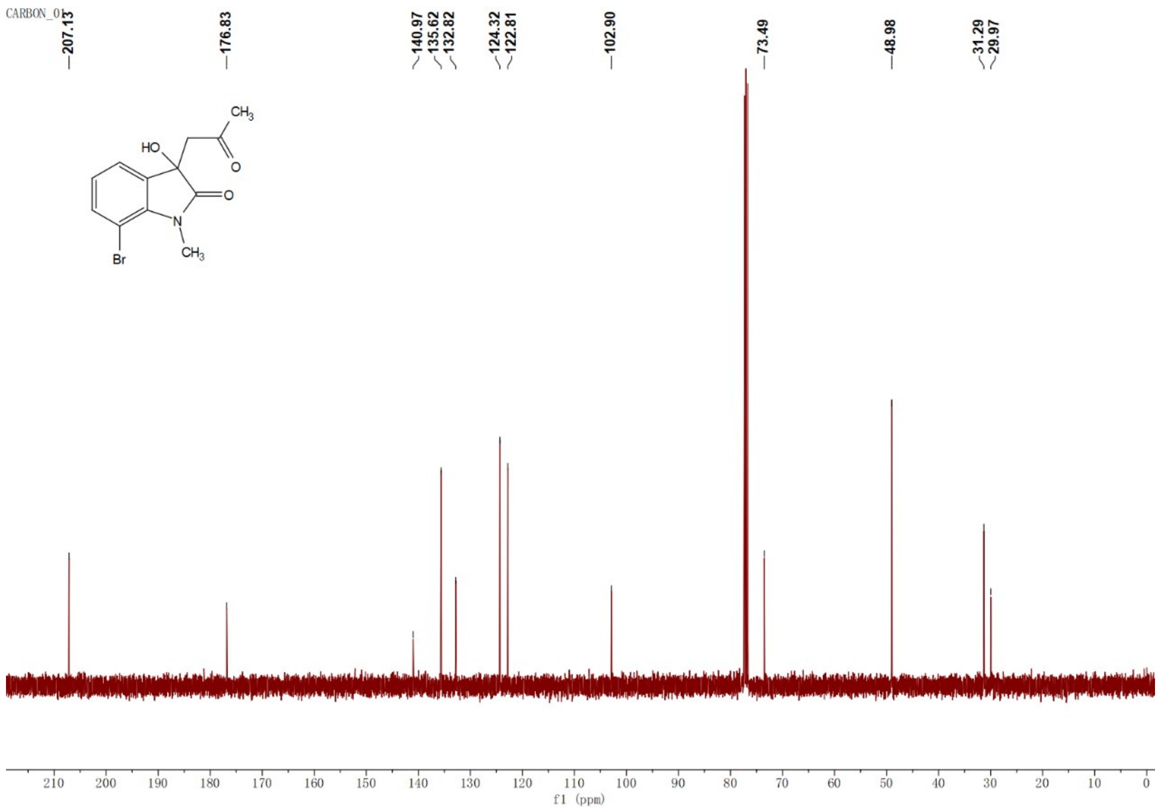
6-bromo-3-hydroxy-1-methyl-3-(2-oxopropyl)indolin-2-one (3k)



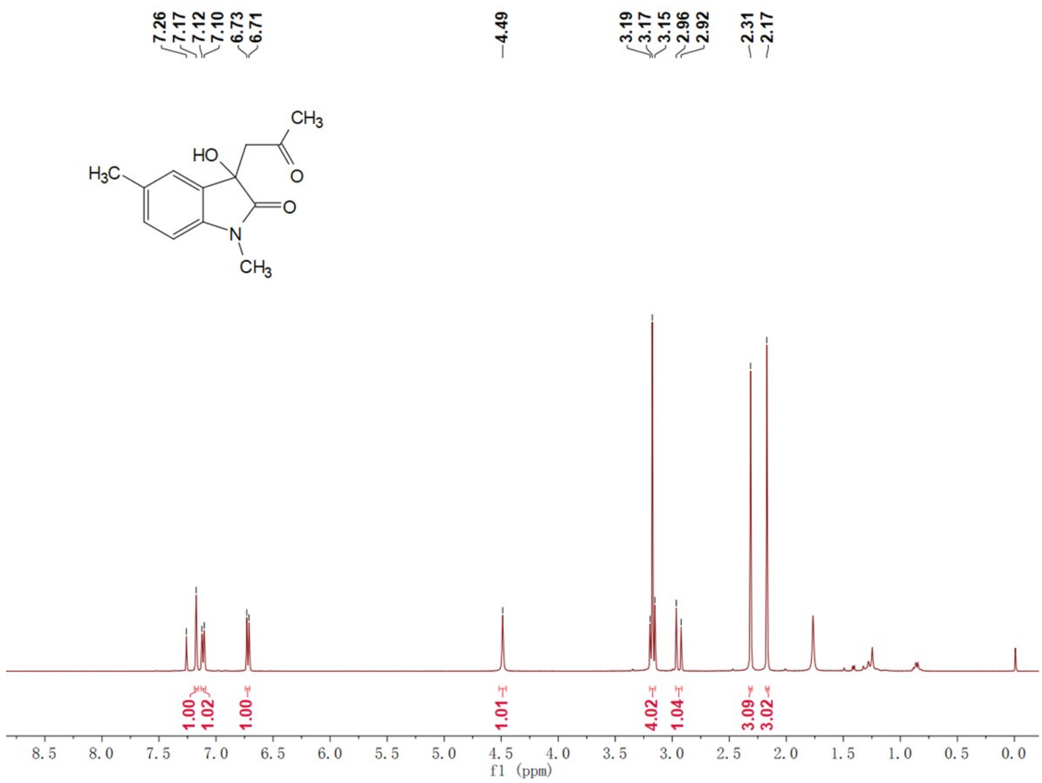


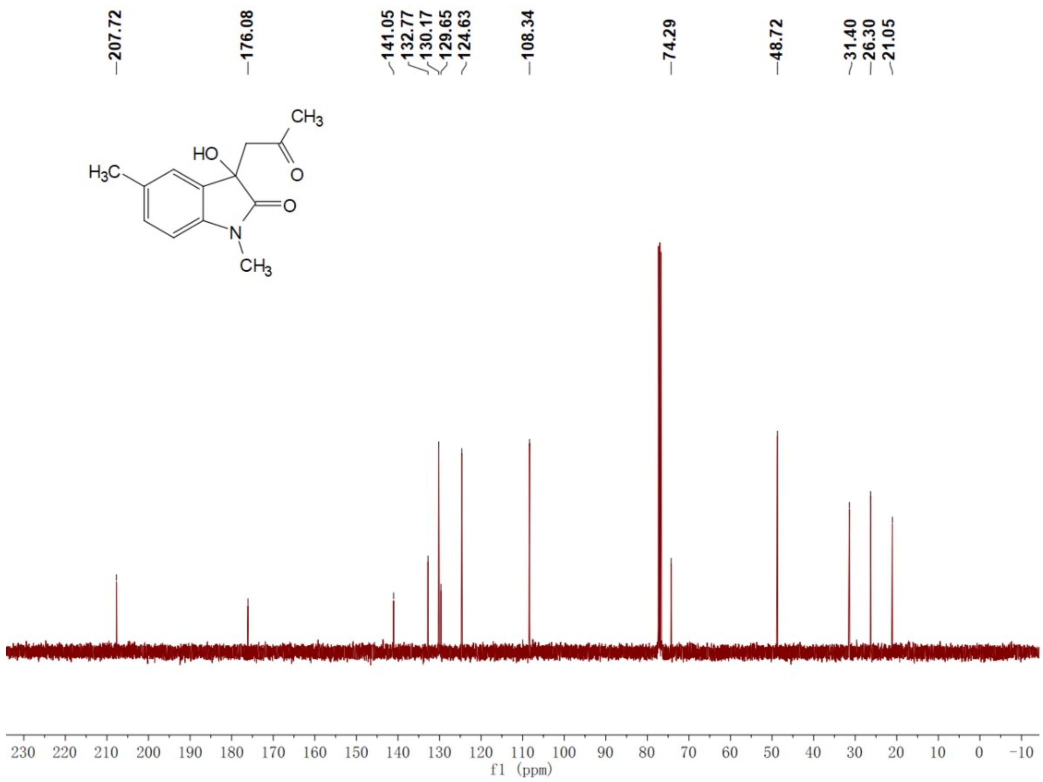
7-bromo-3-hydroxy-1-methyl-3-(2-oxopropyl)indolin-2-one (3l)



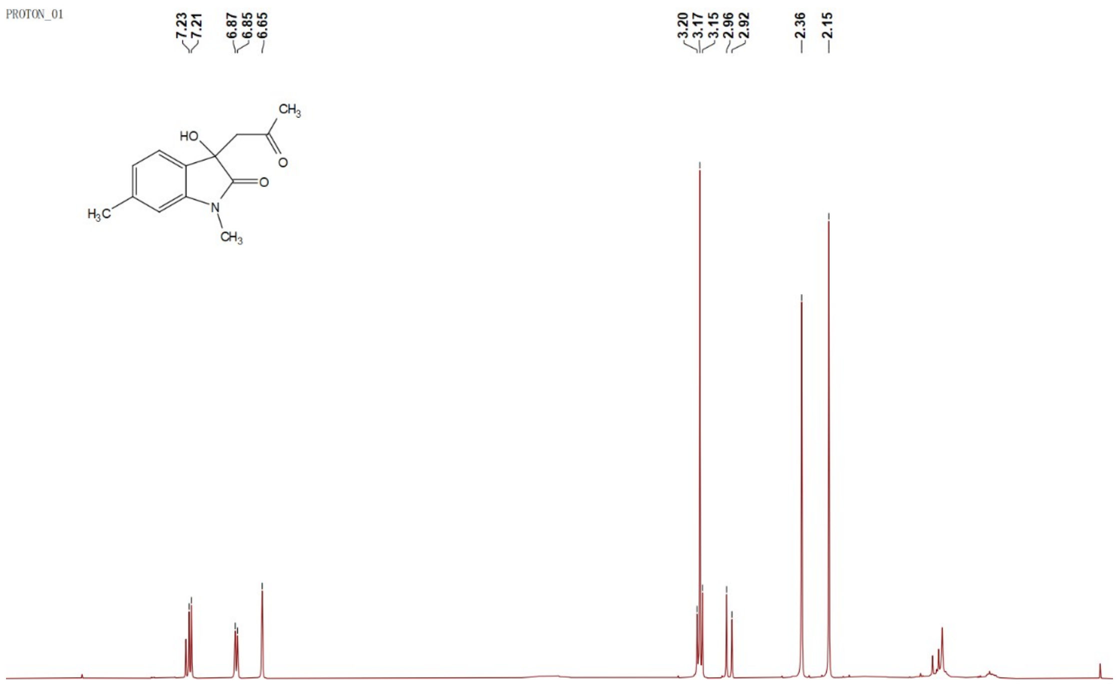


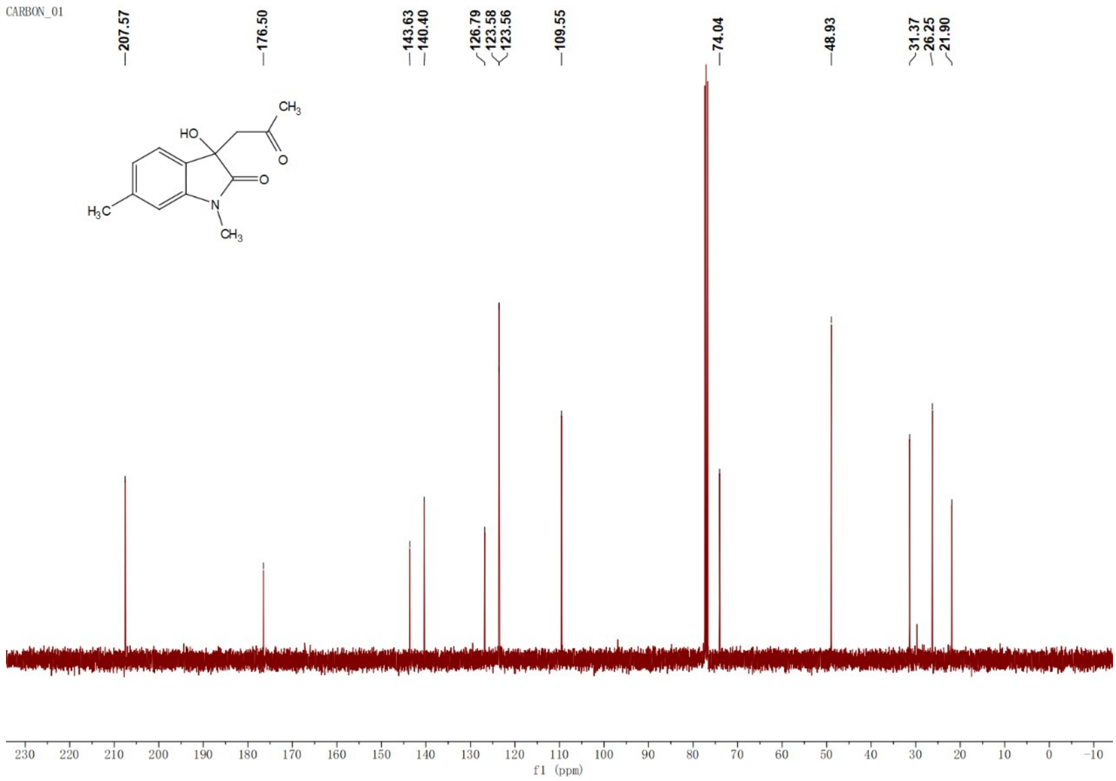
hydroxy-1,5-dimethyl-3-(2-oxopropyl)indolin-2-one (3m)



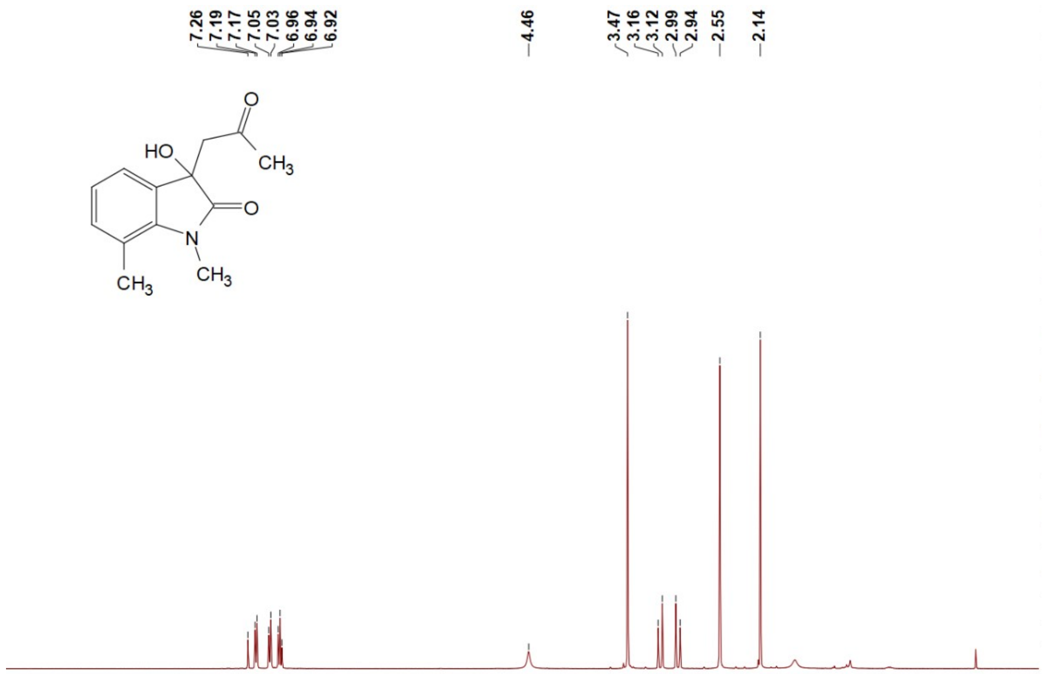


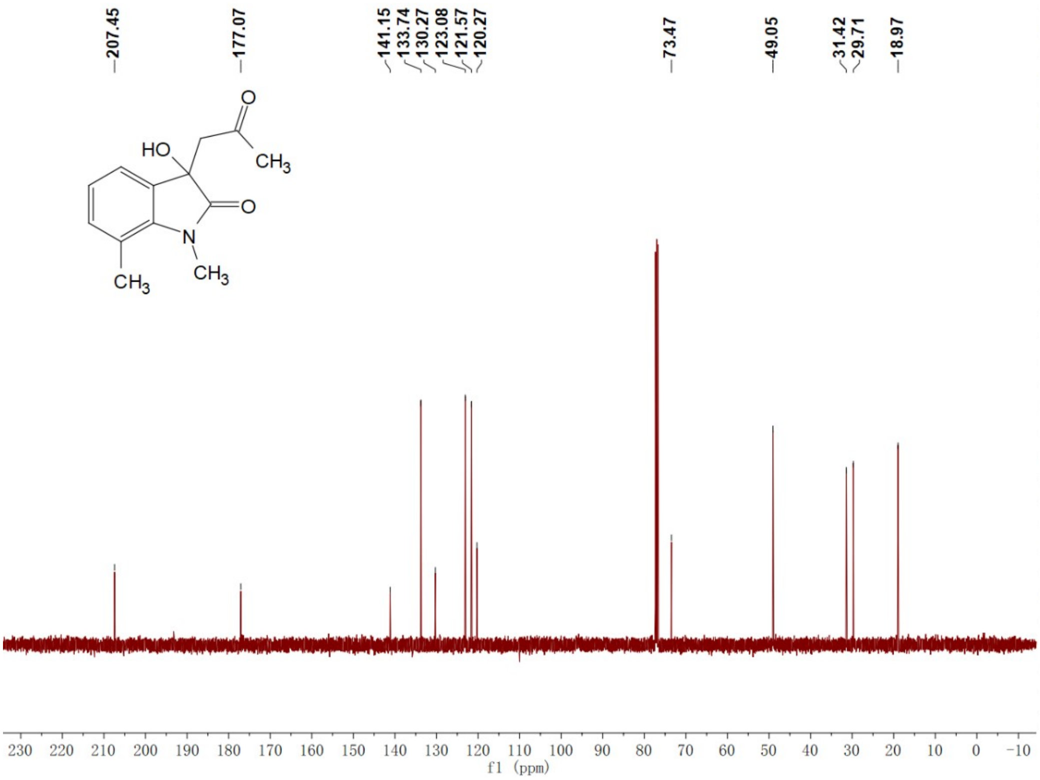
3-hydroxy-1,6-dimethyl-3-(2-oxopropyl)indolin-2-one (3n)



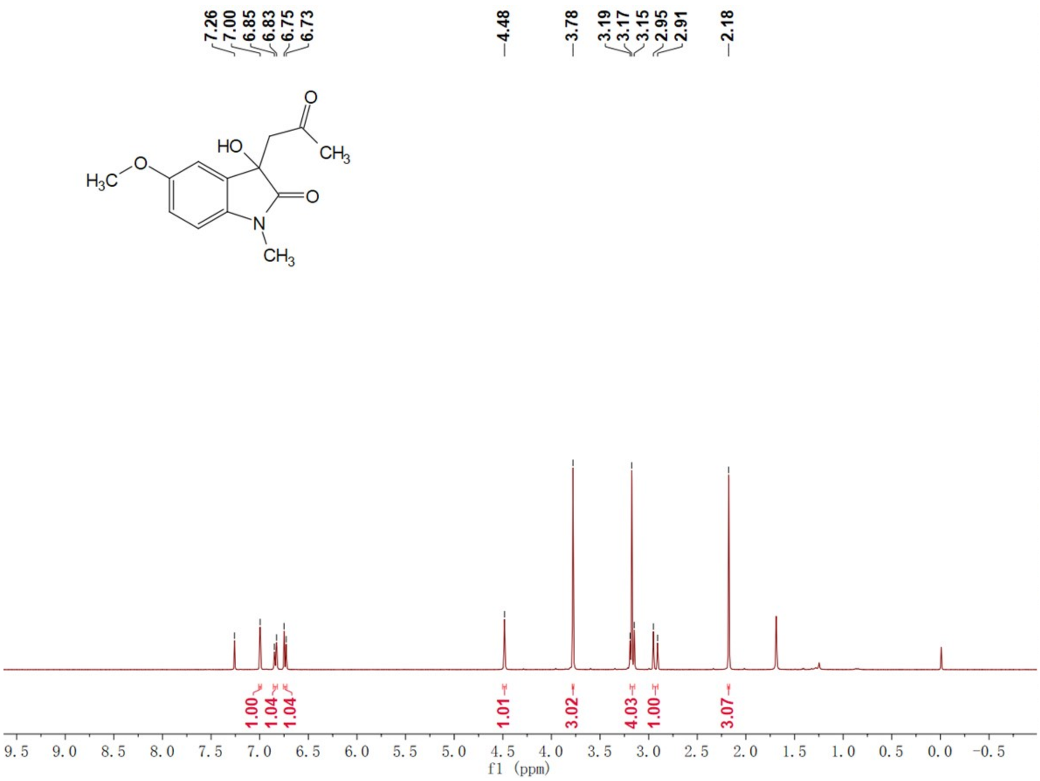


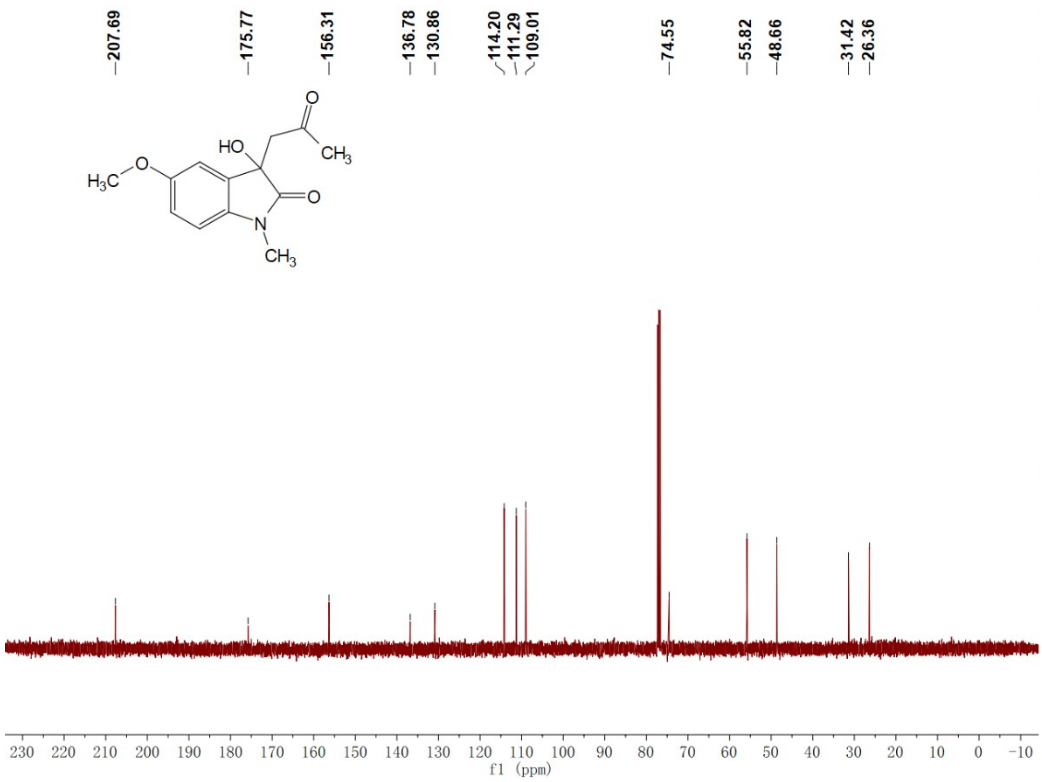
3-hydroxy-1,7-dimethyl-3-(2-oxopropyl)indolin-2-one (3o)



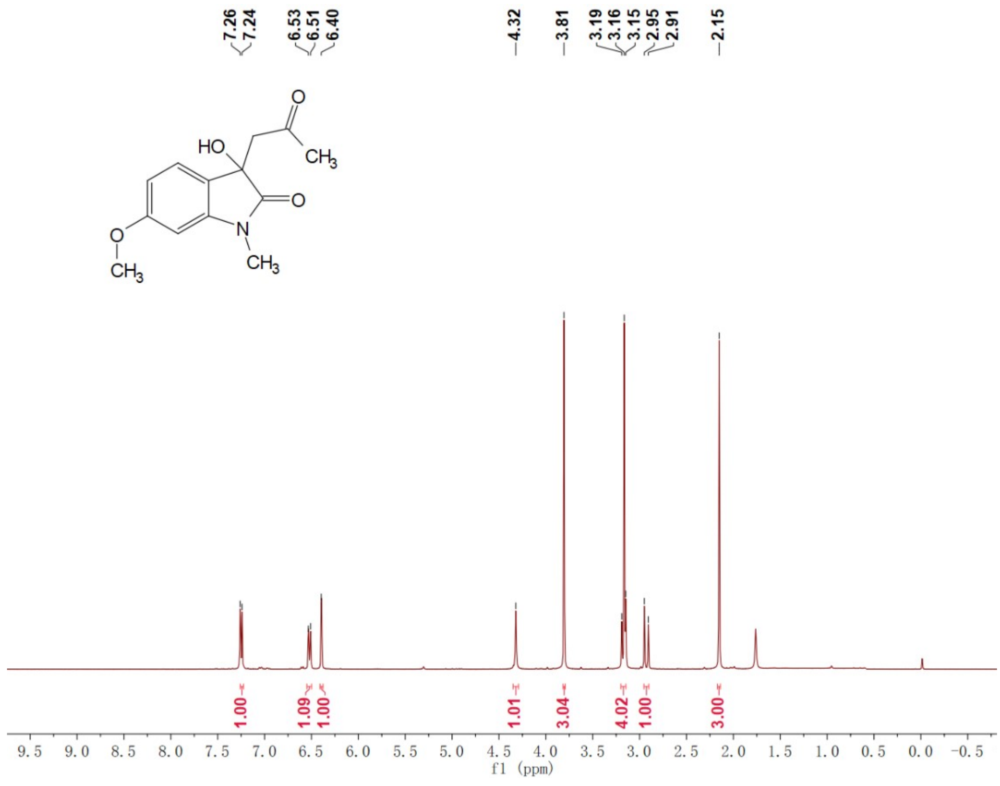


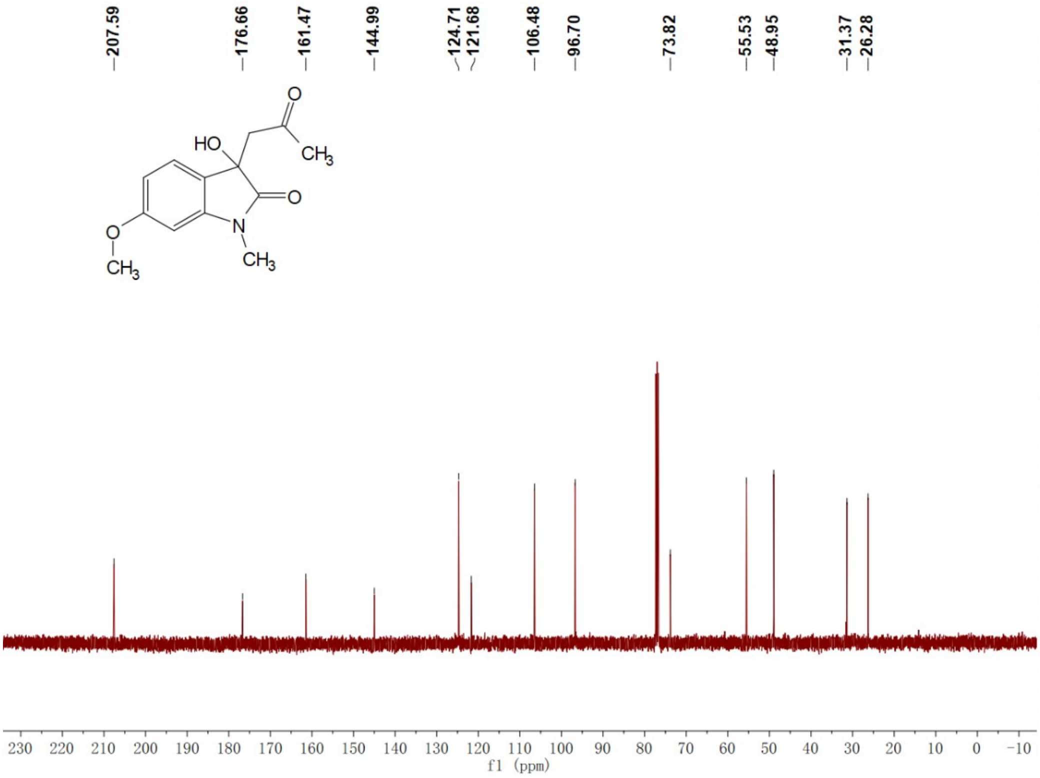
3-hydroxy-5-methoxy-1-methyl-3-(2-oxopropyl)indolin-2-one (



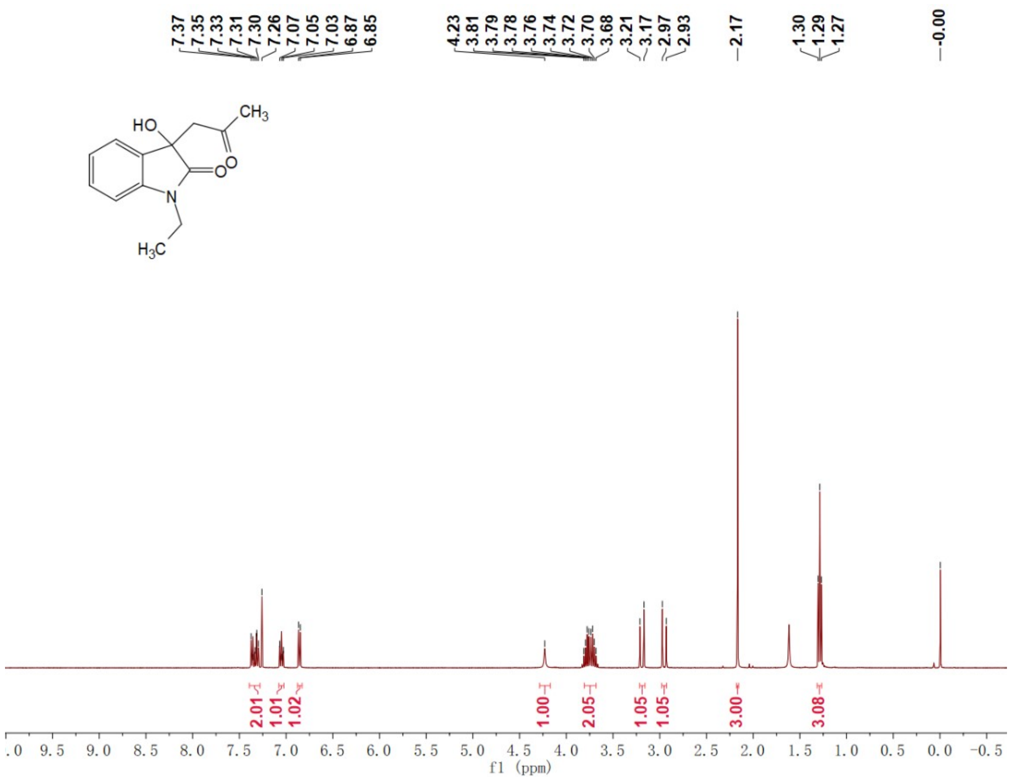


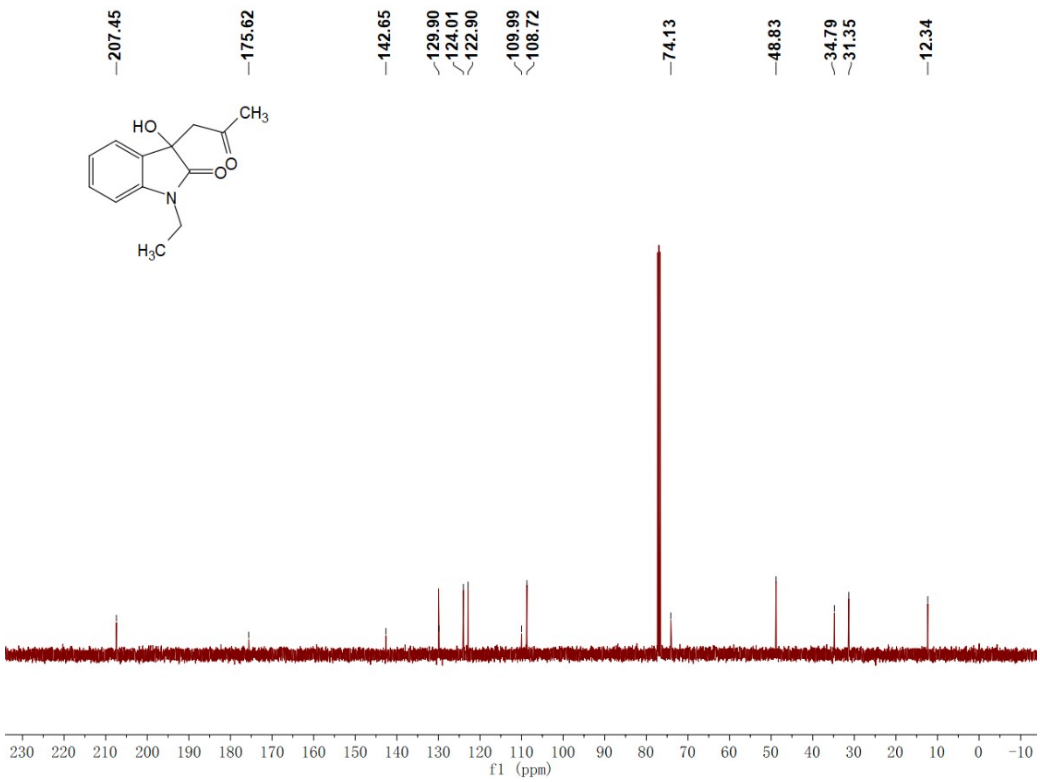
3-hydroxy-5-methoxy-1-methyl-3-(2-oxopropyl)indolin-2-one (3q)



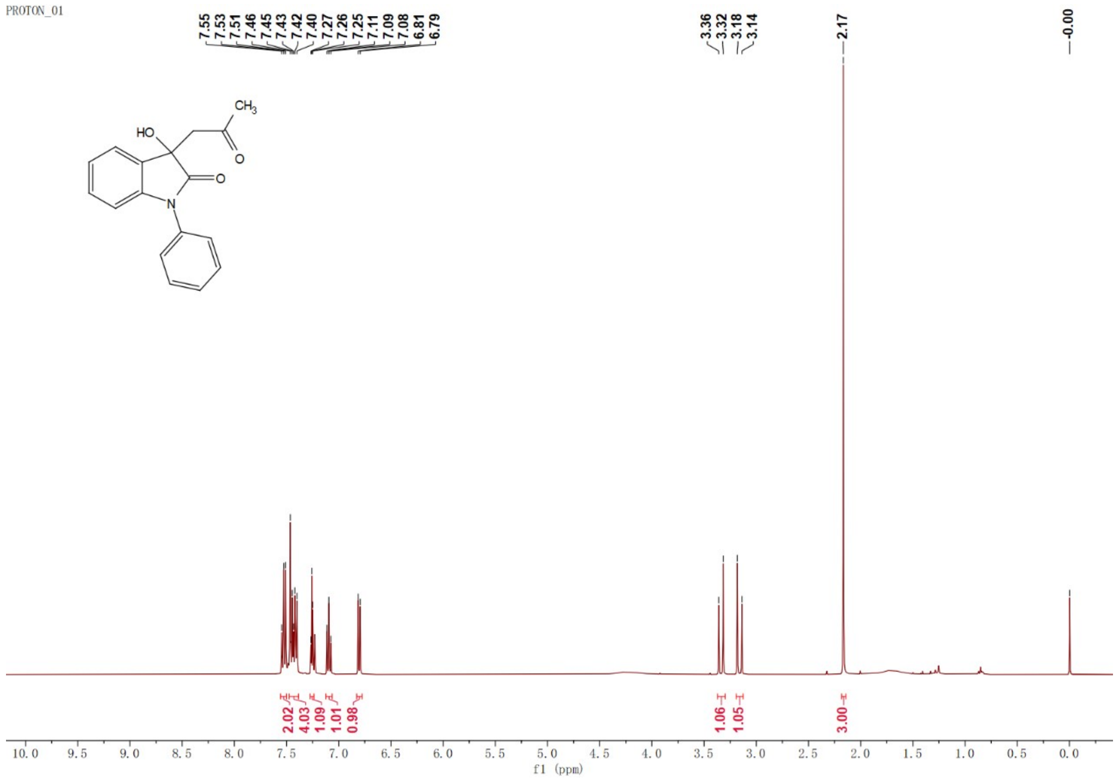


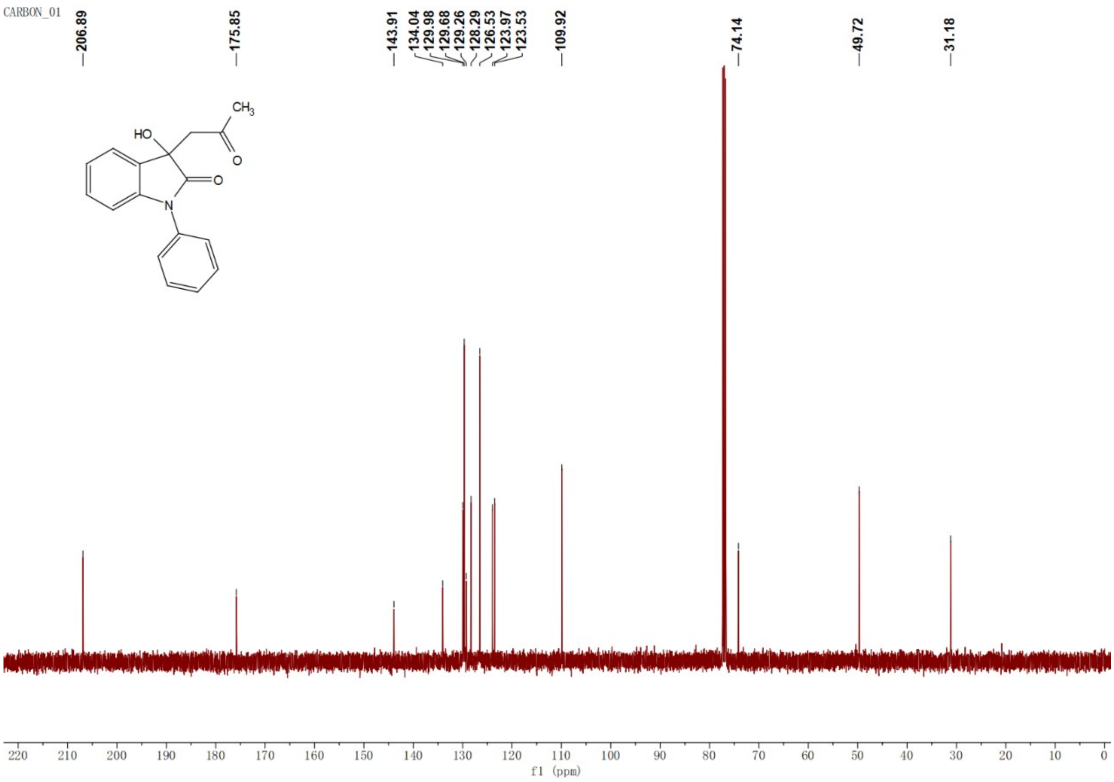
1-ethyl-3-hydroxy-3-(2-oxopropyl)indolin-2-one (3r)



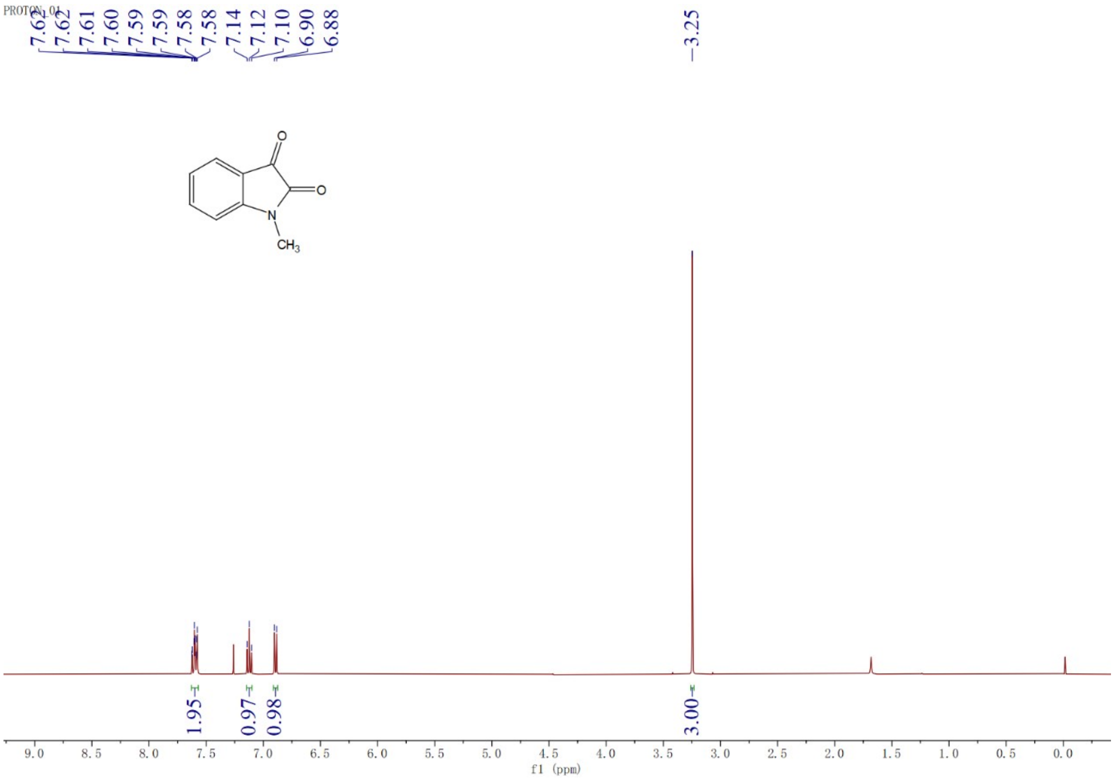


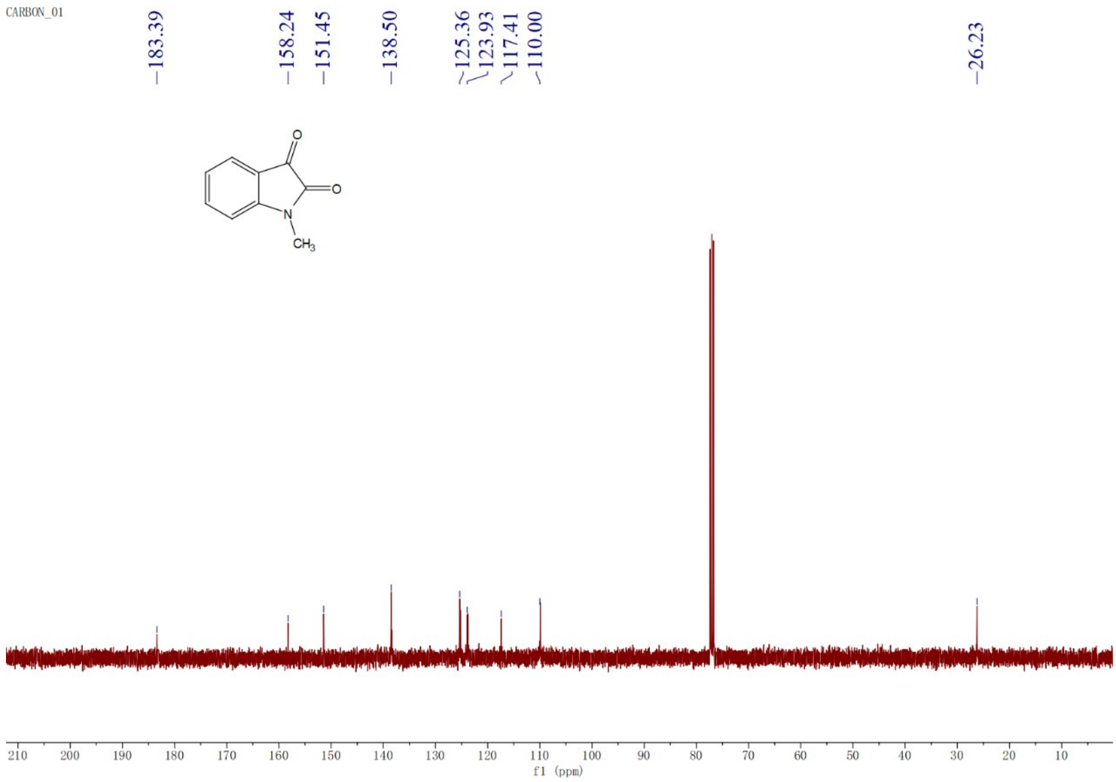
3-hydroxy-3-(2-oxopropyl)-1-phenylindolin-2-one (3s)





N-methyl isatin (1a')




CARBON_01
183.39
158.24
151.45
138.50
125.36
123.93
117.41
110.00
26.23
O
O
N
CH3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)