Supporting Information

Ruthenium-Catalyzed Redox-Neutral [4+1] Annulation of Benzamides and Propargyl alcohols via C-H Bond Activation

Xiaowei Wu, Bao Wang, Shengbin Zhou, Yu Zhou,* Hong Liu*

CAS Key Laboratory of Receptor Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, 555 Zuchongzhi Road, Shanghai 201203, P. R. China.

*E-mail: hliu@simm.ac.cn; zhouyu@simm.ac.cn

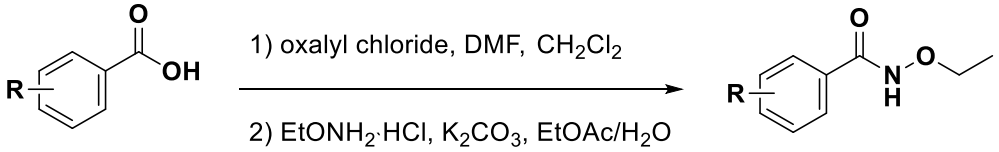
Table of Contents

(A) General Methods and Materials

The reagents (chemicals) were purchased from commercial sources (J&K, TCI, Sigma-Aldrich, Adamas-beta, etc.), and used without further purification. Analytical thin layer chromatography (TLC) was HSGF 254 (0.15-0.2 mm thickness). All products were characterized by their NMR and MS spectra. ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz, 500 MHz or 600MHz instrument. Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane. Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), doublet of doublets (dd) and broad (br). High-resolution mass spectra (HRMS) were measured on Micromass Ultra Q-TOF spectrometer. The determination of isomer ratio was performed via HPLC analysis using Agilent 1260 infinity series. The Agilent column was a 4.6 x 250 mm Eclipse XDB-C18 5 μm. The determination of purity was performed via HPLC analysis using Agilent 1100 series. The Agilent column was a 4.6 x 150 mm Eclipse XDB-C18 5 μm (H_2O/MeOH = 25/75, λ = 254 nm, 1.0 mL/min). The following substrates were prepared according to literature methods: Propargyl alcohols **2a**,[1] **2b,**[2] **2d,**[3] **2e,**[4] **2f,**[1] **2h,**[1] **2n**,[5] **2q**,[6] **2t**,[7] **2v**.[8] Propargyl alcohol **2p** and **2u** were commercial materials and α,β-unsaturated ketone **2y** was purchased from TCI; α,β-unsaturated ketone **2z** was prepared according to literature method.[9]

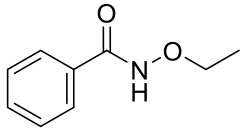
(B) General Procedures and Characterization of Substrates

General Procedure A for the Preparation of N-ethoxybenzamides 1a-1o.[10]



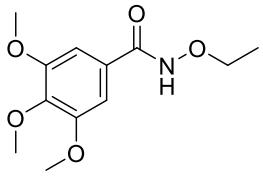
To a solution of the carboxylic acid (10 mmol) in CH_2Cl_2 (0.3 M) at room temperature was added dropwise oxalyl chloride (12 mmol) followed by a catalytic amount of DMF (2 drops). The reaction was allowed to stir at room temperature until completion . The solvent was then removed under reduce pressure to afford the corresponding crude acid chloride. Ethoxyamine hydrochloride (12 mmol) was added to a biphasic mixture of K_2CO_3 (20 mmol) in a 3:1 mixture of $EtOAc/H_2O$. The resulting solution was cooled to 0 ℃ followed by addition of a solution unpurified acid chloride in a minimum amount of EtOAc dropwise. The reaction was stirring for 4 h and slowly warmed up to room temperature. The two layers were separated and extracted with EtOAc (40 mL x 2). The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel.

Analytical data of benzamides 1a-1o



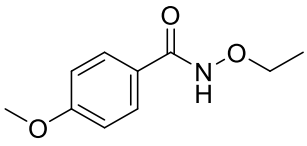
N-ethoxybenzamide (1a).

Following general procedure A, **1a** was obtained as white solid. m.p.: 57–58 ℃; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.76 – 7.72 (m, 2H), 7.54 – 7.49 (m, 1H), 7.46 – 7.39 (m, 2H), 4.09 (q, J = 7.0 Hz, 2H), 1.33 (t, J = 7.0 Hz, 3H) ppm. **^{13}C NMR (151 MHz, $CDCl_3$)** δ 132.08, 132.03, 128.79, 127.16, 72.45, 13.68 ppm. **HRMS (ESI) m/z:** calculated for $C_9H_{10}NO_2^-$ $[M–H]^-$: 164.0717, found: 164.0717.



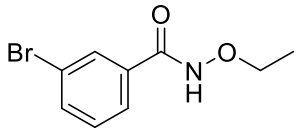
N-ethoxy-3,4,5-trimethoxybenzamide (1b)

Following general procedure A, **1b** was obtained as white solid. m.p.: 134–136 ℃; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 6.99 (s, 2H), 4.03 (q, J = 7.0 Hz, 2H), 3.85 - 3.79 (m, 9H), 1.26 (t, J = 7.0 Hz, 3H) ppm. **^{13}C NMR (151 MHz, $CDCl_3$)** δ 153.43, 141.39, 127.22, 104.52, 72.49, 61.06, 56.45, 13.72 ppm. **HRMS (ESI) m/z:** calculated for $C_{12}H_{16}NO_5^-$ $[M–H]^-$: 254.1034, found: 254.1036.



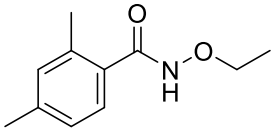
N-ethoxy-4-methoxybenzamide (1c)

Following general procedure A, **1c** was obtained as white solid. m.p.: 78–80 ℃; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.91 (br, 1H), 7.77 – 7.67 (m, 2H), 6.90 – 6.76 (m, 2H), 3.99 (q, J = 7.0 Hz, 2H), 3.77 (s, 3H), 1.22 (t, J = 7.0 Hz, 3H) ppm. **^{13}C NMR (151 MHz, $CDCl_3$)** δ 162.59, 129.08, 124.27, 113.92, 72.31, 55.49, 13.63 ppm. **HRMS (ESI) m/z:** calculated for $C_{10}H_{12}NO_3^-$ $[M–H]^-$: 194.0823, found: 194.0824.



3-bromo-N-ethoxybenzamide (1d)

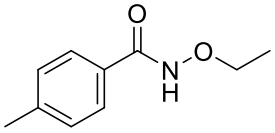
Following general procedure A, **1d** was obtained as white solid. m.p.: 89–90 ℃; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.89 (s, 1H), 7.70 – 7.60 (m, 2H), 7.30 (t, *J* = 7.9 Hz, 1H), 4.08 (q, *J* = 7.0 Hz, 2H), 1.32 (t, *J* = 7.0 Hz, 3H) ppm. **^{13}C NMR (151 MHz, $CDCl_3$)** δ 134.98, 133.91, 130.32, 125.78, 122.88, 72.48, 13.68 ppm. **HRMS (ESI) m/z:** calculated for $C_9H_9BrNO_2^-$ $[M–H]^-$: 241.9822, found: 241.9825.



N-ethoxy-2,4-dimethylbenzamide (1e)

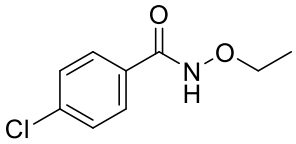
Following general procedure A, **1e** was obtained as white solid. m.p.: 58–60 ℃; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.33 (br, 1H), 7.07 (d, J = 7.7 Hz, 1H), 6.92 (s, 1H), 6.85 (d, J = 7.7 Hz, 1H), 3.97 – 3.86 (m, 2H),

2.25 (s, 6H), 1.21 (t, J = 6.8 Hz, 3H) ppm. **^{13}C NMR (151 MHz, $CDCl_3$)** δ 140.65, 136.97, 131.91, 129.96, 127.28, 126.28, 72.39, 21.36, 19.63, 13.58 ppm. **HRMS (ESI) m/z:** calculated for $C_{11}H_{16}NO_2^+$ $[M + H]^+$: 194.1176, found: 194.1176.



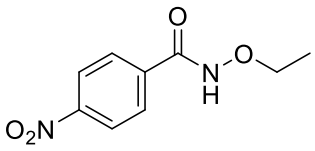
N-ethoxy-4-methylbenzamide (1f)

Following general procedure A, **1f** was obtained as white solid. m.p.: 96–97 ℃; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.62 (br, 1H), 7.65 (d, J = 8.2 Hz, 2H), 7.16 (d, J = 7.9 Hz, 2H), 4.02 (q, J = 7.0 Hz, 2H), 2.35 (s, 3H), 1.25 (t, J = 7.0 Hz, 3H) ppm. **^{13}C NMR (151 MHz, $CDCl_3$)** δ 142.44, 129.29, 129.09, 127.06, 72.28, 21.51, 13.55 ppm. **HRMS (ESI) m/z:** calculated for $C_{10}H_{14}NO_2^+$ $[M + H]^+$: 180.1019, found: 180.1021.



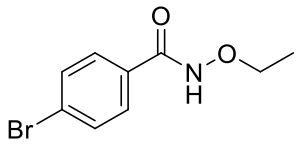
4-chloro-N-ethoxybenzamide (1g)

Following general procedure A, **1g** was obtained as white solid. m.p.: 105–107 ℃; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.68 (br, 1H), 7.69 (d, J = 8.5 Hz, 2H), 7.35 (d, J = 8.4 Hz, 2H), 4.03 (q, J = 7.0 Hz, 2H), 1.27 (t, J = 7.0 Hz, 3H) ppm. **^{13}C NMR (151 MHz, DMSO-d_6)** δ 163.13, 136.34, 131.14, 128.99, 128.56, 70.77, 13.52. **HRMS (ESI) m/z:** calculated for $C_9H_9ClNO_2^-$ $[M–H]^-$: 198.0327, found: 198.0325.



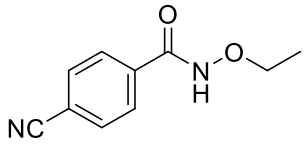
N-ethoxy-4-nitrobenzamide (1h)

Following general procedure A, **1h** was obtained as white solid. m.p.: 133–135 ℃; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.18 (br, 1H), 8.27 (d, *J* = 8.3 Hz, 2H), 7.95 (d, *J* = 8.3 Hz, 2H), 4.20 - 4.05 (m, 2H), 1.33 (t, *J* = 6.9 Hz, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 164.63, 150.03, 137.76, 128.58, 123.97, 72.93, 13.63 ppm. **HRMS (ESI) m/z:** calculated for $C_9H_9N_2O_4^-$ $[M–H]^-$: 209.0568, found: 209.0563.



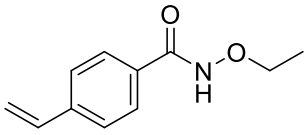
4-bromo-N-ethoxybenzamide (1i)

Following general procedure A, **1i** was obtained as white solid. m.p.: 109–112 ℃; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.68 (s, 1H), 7.65 – 7.53 (m, 4H), 4.13 – 4.03 (m, 2H), 1.33 (t, J = 7.0 Hz, 3H) ppm. **^{13}C NMR (151 MHz, $CDCl_3$)** δ 132.07, 130.74, 128.72, 126.79, 72.50, 13.72 ppm. **HRMS (ESI) m/z:** calculated for $C_9H_9BrNO_2^-$ [M–H]$^-$: 241.9822, found: 241.9825.



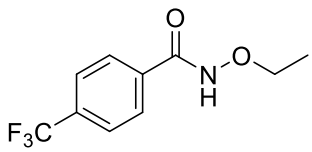
4-cyano-N-ethoxybenzamide (1j)

Following general procedure A, **1j** was obtained as gray solid. m.p.: 112–115 ℃; **^{1}H NMR (500 MHz, DMSO-d_6)** δ 7.93 (d, *J* = 8.1 Hz, 2H), 7.81 (d, *J* = 7.8 Hz, 2H), 3.86 (q, *J* = 6.9 Hz, 2H), 1.17 (t, *J* = 6.9 Hz, 3H). **^{13}C NMR (126 MHz, DMSO-d_6)** δ 161.25, 131.86, 127.61, 118.79, 111.79, 69.06, 14.06 ppm. **HRMS (ESI) m/z:** calculated for $C_{10}H_9N_2O_2^-$ [M–H]$^-$: 189.0670, found: 189.0672.



N-ethoxy-4-vinylbenzamide (1k)

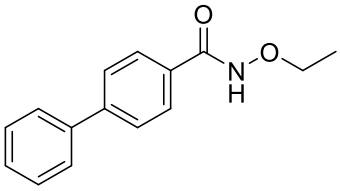
Following general procedure A, **1k** was obtained as white solid. m.p.: 94–95 ℃; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.70 (d, *J* = 8.2 Hz, 2H), 7.44 (d, *J* = 8.2 Hz, 2H), 6.72 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.83 (d, *J* = 17.6 Hz, 1H), 5.36 (d, *J* = 10.9 Hz, 1H), 4.09 (q, *J* = 7.0 Hz, 2H), 1.32 (t, *J* = 7.0 Hz, 3H) ppm. **^{13}C NMR (151 MHz, DMSO-d_6)** δ 163.82, 140.09, 135.84, 131.53, 127.42, 126.09, 116.39, 70.70, 13.54 ppm. **HRMS (ESI) m/z:** calculated for $C_{11}H_{12}NO_2^-$ [M–H]$^-$: 190.0874, found: 190.0871.



N-ethoxy-4-(trifluoromethyl)benzamide (**1l**)

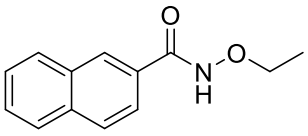
Following general procedure A, **1l** was obtained as white solid. m.p.: 114–116 ℃; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.56 (br, 1H), 7.86 (d, J = 8.1 Hz, 2H), 7.65 (d, J = 8.1 Hz, 2H), 4.09 (q, J = 7.0 Hz,

2H), 1.29 (t, J = 7.0 Hz, 3H) ppm. **^{13}C NMR (151 MHz, $CDCl_3$)** δ 165.22, 135.26, 127.66, 125.65, 124.47, 122.66, 72.59, 13.50 ppm. **^{19}F NMR (471 MHz, DMSO-d_6)** δ -61.48 ppm. **HRMS (ESI) m/z:** calculated for $C_{10}H_9F_3NO_2^-$ $[M–H]^-$: 232.0591, found: 232.0590.



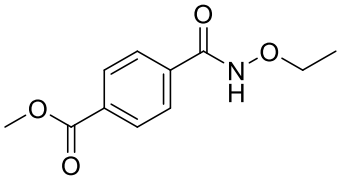
N-ethoxy-[1,1'-biphenyl]-4-carboxamide (1m)

Following general procedure A, **1l** was obtained as white solid. m.p.: 152–154 ℃; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.66 (br, 1H), 7.81 (d, J = 8.5 Hz, 2H), 7.66 (d, J = 8.5 Hz, 2H), 7.65 - 7.57 (m, 2H), 7.49 - 7.43 (m, 2H), 7.42 - 7.36 (m, 1H),, 4.12 (q, J = 7.0 Hz, 2H), 1.36 (t, J = 7.0 Hz, 3H) ppm. **^{13}C NMR (151 MHz, DMSO-d_6)** δ 163.89, 143.09, 139.08, 131.20, 129.08, 128.16, 127.76, 126.90, 126.68, 70.76, 13.58 ppm. **HRMS (ESI) m/z:** calculated for $C_{15}H_{14}NO_2^-$ $[M–H]^-$: 240.1030, found: 240.1032.



N-ethoxy-2-naphthamide (1n)

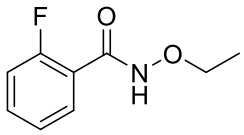
Following general procedure A, **1n** was obtained as white solid. m.p.: 106–108 ℃; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.32 (br, 1H), 8.25 (s, 1H), 7.88 – 7.74 (m, 4H), 7.58 – 7.47 (m, 2H), 4.12 (q, J = 7.0 Hz, 2H), 1.33 (t, J = 7.0 Hz, 3H) ppm. **^{13}C NMR (151 MHz, DMSO-d_6)** δ 164.04, 134.18, 132.13, 130.06, 128.83, 128.01, 127.66, 127.36, 126.80, 123.89, 70.59, 13.68 ppm. **HRMS (ESI) m/z:** calculated for $C_{13}H_{12}NO_2^-$ $[M–H]^-$: 214.0874, found: 214.0874.



Methyl 4-(ethoxycarbamoyl)benzoate (1o)

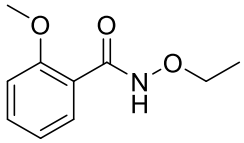
Following general procedure A, **1n** was obtained as white solid. m.p.: 126–128 ℃; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.03 (d, *J* = 8.2 Hz, 2H), 7.80 (d, *J* = 8.2 Hz, 2H), 4.07 (q, *J* = 7.0 Hz, 2H), 3.92 (s, 3H), 1.29 (t, *J* = 7.0 Hz, 3H) ppm. **^{13}C NMR (151 MHz, $CDCl_3$)** δ 166.41, 135.88,

133.04, 129.91, 127.22, 72.41, 52.58, 13.70 ppm. **HRMS (ESI) m/z:** calculated for $C_{11}H_{12}NO_4^-$ [M–H]$^-$: 222.0772, found: 222.0775.



N-ethoxy-2-fluorobenzamide (**1p**)

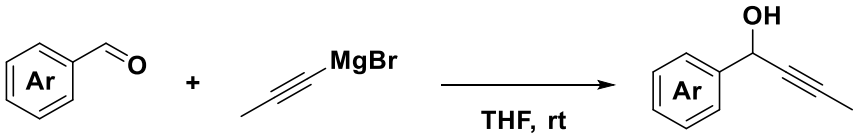
Following general procedure A, **1p** was obtained as white solid. m.p.: 53–55 ℃; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.19 (br, 1H), 8.10 (t, J = 7.4 Hz, 1H), 7.54 - 7.45 (m, 1H), 7.32 - 7.26 (m, 1H), 7.17 - 7.08 (m, 1H), 4.11 (q, J = 7.0 Hz, 2H), 1.34 (t, J = 7.0 Hz, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 162.07, 160.33 (d, J = 247.3 Hz), 133.91 (d, J = 9.1 Hz), 132.13, 125.18, 119.03 (d, J = 13.2 Hz), 116.09 (d, J = 24.7 Hz), 72.68, 13.59 ppm. **^{19}F NMR (471 MHz, CDCl3)** δ -110.47 ppm. **HRMS (ESI) m/z:** calculated for $C_9H_{11}FNO_2^+$ [M+H]$^+$: 184.0768, found: 184.0764.



N-ethoxy-2-methoxybenzamide (**1q**)

Following general procedure A, **1q** was obtained as oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.15 (s, 1H), 8.19 (dd, J = 7.8, 1.6 Hz, 1H), 7.49 – 7.44 (m, 1H), 7.16 – 7.03 (m, 1H), 6.97 (d, J = 8.3 Hz, 1H), 4.10 (q, J = 7.0 Hz, 2H), 3.97 (s, 3H), 1.33 (t, J = 7.0 Hz, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 164.28, 157.10, 133.30, 132.35, 121.71, 119.94, 111.39, 72.30, 56.20, 13.66 ppm. **HRMS (ESI) m/z:** calculated for $C_{10}H_{14}NO_3^+$ [M+H]$^+$: 196.0968, found: 196.0966.

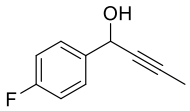
General Procedure B for the Preparation of Propargyl alcohols 2.[1]



To a solution of the corresponding aldehyde (1.0 eq.) in dry THF was added the Grignard reagent (1.2 eq., 0.5 M in THF) at 0 ℃. The reaction mixture was stirred at 0 ℃ for one hour and then another hour at room temperature. The completion of the reactions was confirmed by TLC, and a saturated solution of ammonium chloride was added slowly under cooling. The organic mixture was extracted using EtOAc, dried

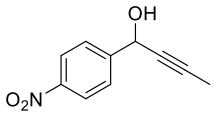
with anhydrous Na_2SO_4 and the solvent removed under vacuum. The crude product was purified by column chromatography on silica gel.

Analytical data of Propargyl alcohols 2.



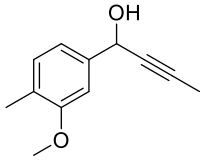
1-(4-fluorophenyl)but-2-yn-1-ol (2c)

Following general procedure B, **2c** was obtained as colorless oil. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.65 – 7.45 (m, 2H), 7.07 – 7.02 (m, 2H), 5.40 (d, *J* = 2.2 Hz, 1H), 2.25 (br, 1H), 1.91 (d, *J* = 2.2 Hz, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 162.72 (d, J = 246.5 Hz), 137.16 (d, J = 3.0 Hz), 128.54 (d, J = 8.3 Hz), 115.47 (d, J = 21.6 Hz), 83.50, 79.12, 64.24, 3.80 ppm. **^{19}F NMR (471 MHz, $CDCl_3$)** δ -114.12 ppm. **HRMS (EI) m/z:** calculated for $C_{10}H_9FO$ $[M]^+$: 164.0637, found: 164.0636.



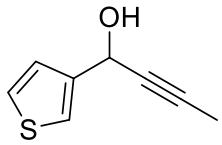
1-(4-nitrophenyl)but-2-yn-1-ol (2g)

Following general procedure B, **2g** was obtained as pale yellow crystalline solid. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.26 – 8.19 (m, 2H), 7.70 (d, *J* = 8.4 Hz, 2H), 5.52 (d, *J* = 2.1 Hz, 1H), 2.21 (br, 1H), 1.91 (d, *J* = 2.1 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 148.11, 147.76, 127.43, 123.86, 84.56, 78.24, 63.86, 3.82 ppm. **HRMS (ESI) m/z:** calculated for $C_{10}H_8NO_3^-$ $[M–H]^-$: 190.0510, found: 190.0512.



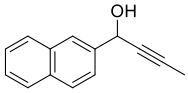
1-(3-methoxy-4-methylphenyl)but-2-yn-1-ol (2i)

Following general procedure B, **2i** was obtained as deep red oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.12 (d, *J* = 7.6 Hz, 1H), 7.03 - 6.97 (m, 2H), 5.39 (s, 1H), 3.85 (s, 3H), 2.31 - 2.17 (m, 4H), 1.91 (d, *J* = 1.8 Hz, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 157.97, 140.32, 130.65, 126.89, 118.39, 108.31, 82.93, 79.46, 64.99, 55.42, 16.12, 3.84 ppm. **HRMS (EI) m/z:** calculated for $C_{12}H_{14}O_2$ $[M]^+$: 190.0994, found: 190.0988.



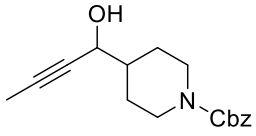
1-(thiophen-3-yl)but-2-yn-1-ol (2j)

Following general procedure B, **2j** was obtained as colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.40 - 7.35 (m, 1H), 7.33 - 7.28 (m, 1H), 7.22 - 7.17 (m, 1H), 5.46 (s, 1H), 2.19 (br, 1H), 1.91 (d, *J* = 1.9 Hz, 3H) ppm. **^{13}C NMR (151 MHz, $CDCl_3$)** δ 142.85, 126.53, 126.46, 122.50, 82.41, 79.14, 60.86, 3.79 ppm. **HRMS (EI) m/z:** calculated for C_8H_8OS $[M]^+$: 152.0296, found: 152.0298.



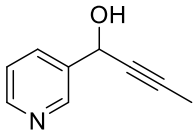
1-(naphthalen-2-yl)but-2-yn-1-ol (2k)

Following general procedure B, **2k** was obtained as colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.97 (s, 1H), 7.89 - 7.80 m, 3H), 7.65 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.56 – 7.44 (m, 2H), 5.59 (d, *J* = 2.2 Hz, 1H), 2.36 (br, 1H), 1.94 (d, *J* = 2.2 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 138.66, 133.30, 133.27, 128.58, 128.29, 127.78, 126.34, 126.31, 125.35, 124.74, 83.51, 79.28, 65.03, 3.90 ppm. **HRMS (EI) m/z:** calculated for $C_{14}H_{12}O$ $[M]^+$: 196.0888, found: 196.0891.



benzyl 4-(1-hydroxybut-2-yn-1-yl)piperidine-1-carboxylate (2l)

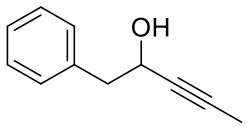
Following general procedure B, **2l** was obtained as colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.38 – 7.27 (m, 5H), 5.13 (s, 2H), 4.38 – 4.06 (m, 3H), 2.79 – 2.71 (m, 2H), 1.86 – 1.75 (m, 6H), 1.69 – 1.63 (m, 1H), 1.40 – 1.22 (m, 2H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 155.42, 137.02, 128.59, 128.06, 127.97, 82.59, 78.64, 67.14, 66.52, 43.96, 43.95, 42.74, 27.32, 3.67 ppm. **HRMS (EI) m/z:** calculated for $C_{17}H_{21}NO_3$ $[M]^+$: 287.1521, found: 287.1518.



1-(pyridin-3-yl)but-2-yn-1-ol (2m)

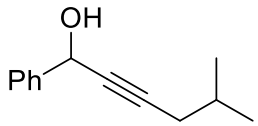
Following general procedure B, **2m** was obtained as dark brown oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.66 (d, *J* = 2.2 Hz, 1H), 8.44 (dd, *J* = 4.9, 1.7 Hz,

1H), 7.89 (dt, *J* = 7.9, 1.7 Hz, 1H), 7.30 - 7.27 (m, 1H), 5.47 (d, *J* = 2.2 Hz, 1H), 4.54 (br, 1H), 1.88 (d, *J* = 2.2 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 148.74, 147.99, 137.60, 134.90, 123.61, 83.58, 78.74, 62.26, 3.79 ppm. **HRMS (ESI) m/z:** calculated for $C_9H_{10}NO^+$ $[M+H]^+$: 148.0757, found: 148.0754.



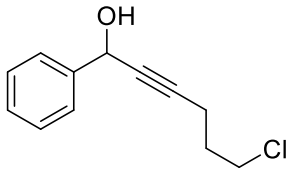
1-phenylpent-3-yn-2-ol (2o)

Following general procedure B, **2o** was obtained as colorless oil. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.35 – 7.26 (m, 5H), 4.64 – 4.47 (m, 1H), 3.03 – 2.93 (m, 2H), 1.90 – 1.82 (m, 4H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 137.02, 129.85, 128.49, 126.91, 82.07, 79.86, 63.51, 44.58, 3.67 ppm. **HRMS (EI) m/z:** calculated for $C_{11}H_{12}O$ $[M]^+$: 160.0888, found: 160.0895.



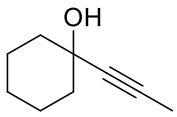
5-methyl-1-phenylhex-2-yn-1-ol (2r)

Following literature's method[8], **2r** was obtained as colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.59 – 7.53 (m, 2H), 7.41 – 7.29 (m, 3H), 5.47 (t, J = 2.0 Hz, 1H), 2.18 (dd, J = 6.6, 2.0 Hz, 2H), 2.11 (br, 1H), 1.90 – 1.80 (m, 1H), 1.00 (d, J = 6.6 Hz, 6H) ppm. **^{13}C NMR (151 MHz, $CDCl_3$)** δ 141.43, 128.65, 128.31, 126.76, 86.75, 80.96, 64.98, 28.12, 28.11, 22.15 ppm. **HRMS (EI) m/z:** calculated for $C_{13}H_{16}O$ $[M]^+$: 188.1201, found: 188.1199.



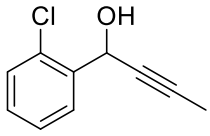
6-chloro-1-phenylhex-2-yn-1-ol (2s)

Following literature's method[8], **2s** was obtained as colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.56 – 7.50 (m, 2H), 7.42 – 7.30 (m, 3H), 5.45 (t, J = 2.0 Hz, 1H), 3.65 (t, J = 6.3 Hz, 2H), 2.48 (td, J = 6.9, 2.0 Hz, 2H), 2.18 (br, 1H), 2.05 – 1.95 (m, 2H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 141.13, 128.74, 128.46, 126.69, 85.60, 81.16, 64.90, 43.76, 31.32, 16.40 ppm. **HRMS (EI) m/z:** calculated for $C_{12}H_{13}ClO$ $[M]^+$: 208.0655, found: 208.0648.



1-(prop-1-yn-1-yl)cyclohexan-1-ol (2w)

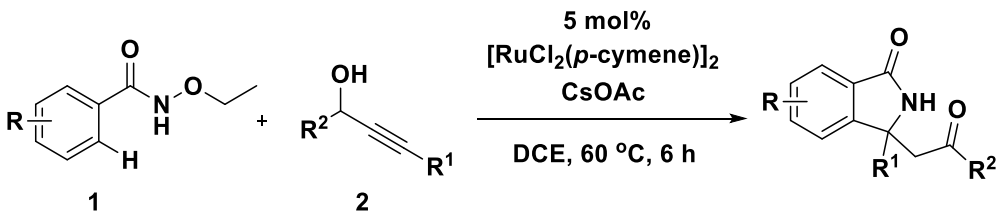
Following general procedure B, **2w** was obtained as colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 1.98 (s, 1H), 1.88 – 1.80 (m, 4H), 1.71 – 1.59 (m, 2H), 1.58 – 1.45 (m, 5H), 1.29 – 1.15 (m, 1H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 83.22, 80.08, 68.87, 40.30, 25.36, 23.44, 3.65 ppm. **HRMS (EI) m/z:** calculated for $C_9H_{14}O$ $[M]^+$: 138.1045, found: 138.1041.



1-(2-chlorophenyl)but-2-yn-1-ol (2x)

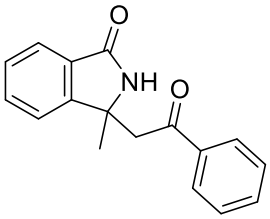
Following general procedure B, **2x** was obtained as colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.79 – 7.74 (m, 1H), 7.39 – 7.26 (m, 3H), 5.79 (q, J = 2.1 Hz, 1H), 2.22 (br, 1H), 1.96 – 1.85 (m, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 138.54, 132.80, 129.79, 129.63, 128.43, 127.32, 83.44, 78.08, 62.20, 3.88 ppm. **HRMS (EI) m/z:** calculated for $C_{10}H_9ClO$ $[M]^+$: 180.0342, found: 180.0333.

General Procedure C for C-H activation:



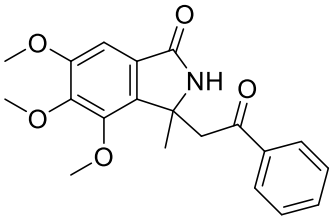
The dry sealed tube was charged with *N*-ethoxybenzamides **1** (0.3 mmol, 1 equiv), Propargyl alcohols **2** (0.6 mmol, 2 equiv), $[RuCl_2(p\text{-cymene})]_2$ (0.015 mmol, 0.05 equiv), CsOAc (0.3 mmol, 1 equiv) and 6 mL dry 1,2-dichloroethane. The mixture was heated at 60 ℃ for 1~6 h under Ar atmosphere. The resulting mixture was diluted with dichloromethane and washed by water. The combined organic layers were dried with Na_2SO_4, filtered, concentrated and purified by column chromatography on silica gel (PE/EA = 2/1 ~ 1/1, v/v) to give desired products**.**

(C) Analytical Characterization Data of Products



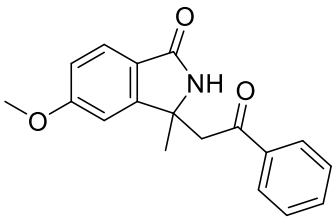
3-methyl-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3a)

Following general procedure C, **3a** was obtained as colorless oil in 78% yield. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.93 – 7.89 (m, 2H), 7.87 – 7.82 (m, 1H), 7.63 – 7.54 (m, 2H), 7.50 – 7.42 (m, 4H), 7.36 (br, 1H), 3.77 (d, *J* = 17.7 Hz, 1H), 3.01 (d, *J* = 17.7 Hz, 1H), 1.67 (s, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 198.08, 168.98, 152.24, 136.78, 133.86, 132.28, 130.87, 128.88, 128.67, 128.58, 128.07, 127.50, 124.38, 121.18, 59.45, 47.46, 24.90 ppm. HPLC purity: 98.4%, t_R = 2.16 min. **HRMS (ESI) m/z:** calculated for $C_{17}H_{16}NO_2^+$ $[M + H]^+$: 266.1176, found: 266.1173.



4,5,6-trimethoxy-3-methyl-3-(2-oxo-2-phenylethyl)-isoindolin-1-one (3b)

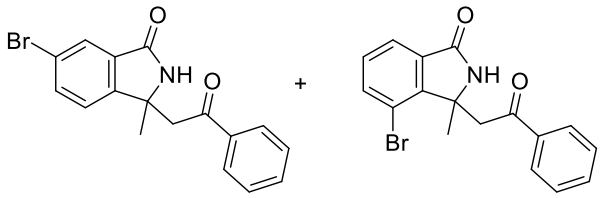
Following general procedure C, **3b** was obtained as colorless oil in 70% yield. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.98 – 7.87 (m, 2H), 7.60 – 7.53 (m, 1H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.31 (br, 1H), 7.12 (s, 1H), 4.11 (d, *J* = 17.8 Hz, 1H), 4.05 (s, 3H), 3.93 (s, 3H), 3.90 (s, 3H), 2.94 (d, *J* = 17.8 Hz, 1H), 1.68 (s, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 198.75, 168.51, 155.15, 148.36, 145.40, 136.96, 136.50, 133.70, 128.82, 128.07, 126.47, 101.97, 61.05, 61.03, 59.09, 56.44, 45.77, 23.68 ppm. HPLC purity: 95.6%, t_R = 6.88 min. **HRMS (ESI) m/z:** calculated for $C_{20}H_{21}NO_5^+$ $[M + H]^+$: 356.1492, found: 356.1484.



5-methoxy-3-methyl-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3c)

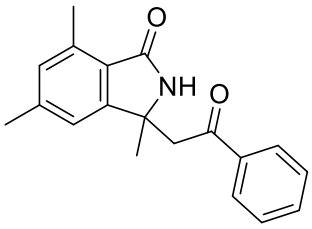
Following general procedure C, **3c** was obtained as colorless oil in 79% yield. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.90 – 7.85 (m, 2H), 7.72 (d, *J* = 8.3 Hz, 1H), 7.55 – 7.50 (m, 1H), 7.40 (t, *J* = 7.8

Hz, 2H), 7.28 (br, 1H), 6.98 – 6.90 (m, 2H), 3.87 (s, 3H), 3.70 (d, *J* = 17.7 Hz, 1H), 3.00 (d, *J* = 17.7 Hz, 1H), 1.62 (s, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 197.94, 168.88, 163.25, 154.46, 136.71, 133.70, 128.75, 127.98, 125.64, 123.20, 114.55, 106.44, 59.07, 55.75, 47.41, 24.90 ppm. HPLC purity: 96.7%, t_R = 6.16 min. **HRMS (ESI) m/z:** calculated for $C_{18}H_{18}NO_3^+$ $[M + H]^+$: 296.1281, found: 296.1277.



6-bromo-3-methyl-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3d) and 4-bromo-3-methyl-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3d')

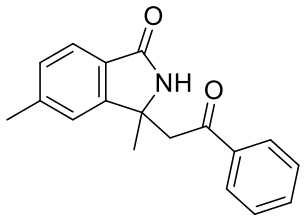
Following general procedure C, the products were obtained as colorless oil in 77% yield in a 2.3:1 ratio. The two isomers were inseparable under previous purification conditions. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.96 – 7.86 (m, 3H), 7.81 (dd, *J* = 7.4, 0.9 Hz, 1H), 7.72 (dd, *J* = 7.9, 0.8 Hz, 1H), 7.68 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.61 (br, 1H), 7.59 – 7.51 (m, 2H), 7.46 – 7.40 (m, 3H), 7.39 – 7.30 (m, 2H), 4.49 (d, *J* = 17.8 Hz, 1H, major), 3.74 (d, *J* = 17.8 Hz, 1H, minor), 3.05 – 2.95 (m, 2H, major + minor), 1.81 (s, 3H, major), 1.65 (s, 3H, minor) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 197.98, 197.66, 167.41, 167.10, 150.73, 148.91, 136.76, 136.59, 136.51, 135.12, 134.08, 133.88, 133.83, 133.03, 130.31, 128.84, 128.06, 128.04, 127.46, 123.55, 123.01, 122.53, 116.70, 60.92, 59.47, 47.11, 43.75, 24.84, 22.10 ppm. HPLC purity (combined): 96.4%, t_R = 2.52–2.61 min. **HRMS (ESI) m/z:** calculated for $C_{17}H_{15}BrNO_2^+$ $[M + H]^+$: 344.0281, found: 344.0285.



3,5,7-trimethyl-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3e)

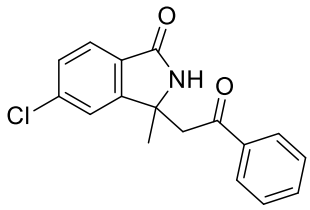
Following general procedure C, the product was obtained as colorless oil in 67% yield. **^{1}H NMR (500 MHz, $CDCl_3$)**

δ 7.94 – 7.89 (m, 2H), 7.60 – 7.54 (m, 1H), 7.49 – 7.43 (m, 2H), 7.08 (br, 1H), 7.04 (s, 1H), 7.01 (s, 1H), 3.71 (d, *J* = 17.7 Hz, 1H), 2.98 (d, *J* = 17.7 Hz, 1H), 2.67 (s, 3H), 2.43 (s, 3H), 1.62 (s, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 198.25, 169.97, 153.45, 142.41, 138.28, 136.90, 133.77, 131.42, 128.85, 128.06, 125.30, 119.07, 58.16, 47.80, 25.07, 21.91, 17.38 ppm. HPLC purity: 97.6%, t_R = 2.86 min. **HRMS (ESI) m/z:** calculated for $C_{19}H_{19}NO_2^+$ $[M + H]^+$: 294.1489, found: 294.1485.



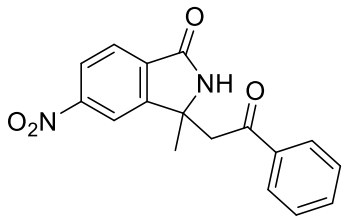
3,5-dimethyl-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3f)

Following general procedure C, the product was obtained as colorless oil in 89% yield. (EA/DCM = 1:1 v/v) for crystallization, needles, m.p.: 158–159 ℃. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.94 – 7.87 (m, 2H), 7.73 - 7.69 (m, 1H), 7.59 – 7.53 (m, 1H), 7.47 - 7.40 (m, 2H), 7.33 (br, 1H), 7.28 – 7.24 (m, 2H), 3.75 (d, *J* = 17.7 Hz, 1H), 2.99 (d, *J* = 17.7 Hz, 1H), 2.47 (s, 3H), 1.64 (s, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 198.06, 169.07, 152.60, 142.93, 136.74, 133.73, 129.46, 128.77, 128.17, 128.00, 124.04, 121.67, 59.18, 47.42, 24.84, 22.04 ppm. HPLC purity: 97.1%, t_R = 6.83 min. **HRMS (ESI) m/z:** calculated for $C_{18}H_{18}NO_2^+$ $[M + H]^+$: 280.1332, found: 280.1334.



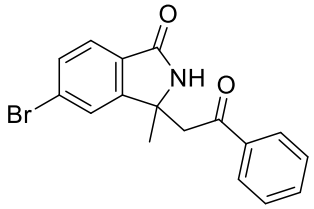
5-chloro-3-methyl-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3g)

Following general procedure C, the product was obtained as colorless oil in 73% yield. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.90 (d, *J* = 7.4 Hz, 2H), 7.76 (d, *J* = 8.1 Hz, 1H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.50 – 7.40 (m, 5H), 3.74 (d, *J* = 17.7 Hz, 1H), 3.03 (d, *J* = 17.7 Hz, 1H), 1.66 (s, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 197.62, 167.91, 153.71, 138.52, 136.59, 133.94, 129.42, 129.13, 128.88, 128.06, 125.66, 121.90, 59.32, 47.19, 24.86 ppm. HPLC purity: > 99%, t_R = 2.48 min. **HRMS (ESI) m/z:** calculated for $C_{17}H_{15}ClNO_2^+$ $[M + H]^+$: 300.0786, found: 300.0787.



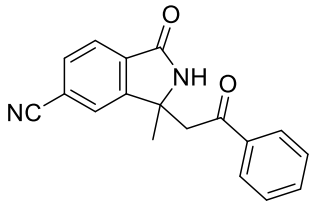
3-methyl-5-nitro-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3h)

Following general procedure C, the product was obtained as white solid in 33% yield. **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.39 (dd, *J* = 8.2, 1.9 Hz, 1H), 8.36 (d, *J* = 1.7 Hz, 1H), 8.03 (d, *J* = 8.2 Hz, 1H), 7.97 – 7.92 (m, 2H), 7.65 – 7.57 (m, 2H), 7.50 (t, *J* = 7.8 Hz, 2H), 3.88 (d, *J* = 17.7 Hz, 1H), 3.06 (d, *J* = 17.7 Hz, 1H), 1.75 (s, 3H) ppm. **^{13}C NMR (151 MHz, $CDCl_3$)** δ 197.42, 166.42, 153.03, 150.70, 136.48, 136.41, 134.29, 129.07, 128.17, 125.75, 124.44, 117.15, 59.85, 46.98, 24.93 ppm. HPLC purity: > 99%, t_R = 2.01 min. **HRMS (ESI) m/z:** calculated for $C_{17}H_{14}N_2O_4^+$ $[M + H]^+$: 311.1026, found: 311.1024.



5-bromo-3-methyl-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3i)

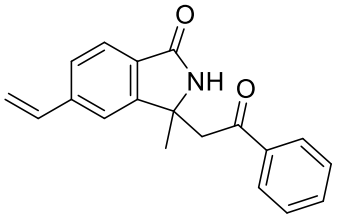
Following general procedure C, the product was obtained as colorless oil in 86% yield. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.94 – 7.89 (m, 2H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.65 – 7.55 (m, 3H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.38 (br, 1H), 3.75 (d, *J* = 17.7 Hz, 1H), 3.03 (d, *J* = 17.7 Hz, 1H), 1.67 (s, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 197.68, 167.93, 153.93, 136.60, 134.00, 132.05, 129.90, 128.93, 128.10, 126.95, 125.94, 124.85, 59.30, 47.24, 24.86 ppm. HPLC purity: 97.7%, t_R = 2.57 min. **HRMS (ESI) m/z:** calculated for $C_{17}H_{15}BrNO_2^+$ $[M + H]^+$: 344.0281, found: 344.0280.



3-methyl-1-oxo-3-(2-oxo-2-phenylethyl)isoindoline-5-carbonitrile (3j)

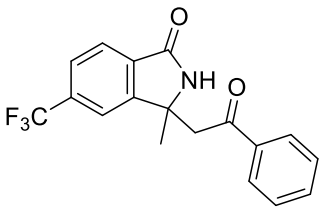
Following general procedure C, the product was obtained as colorless oil in 42% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.99 – 7.89 (m, 3H), 7.84 – 7.74 (m, 2H), 7.65 – 7.55 (m, 2H), 7.48 (t, *J* = 7.5 Hz, 2H), 3.80 (d, *J* = 17.8 Hz, 1H),

3.05 (d, *J* = 17.8 Hz, 1H), 1.71 (s, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 197.38, 166.84, 152.47, 136.50, 135.04, 134.20, 132.68, 129.03, 128.13, 125.54, 125.43, 118.20, 115.81, 59.76, 47.06, 24.93 ppm. HPLC purity: 96.9%, t_R = 2.07 min. **HRMS (ESI) m/z:** calculated for $C_{18}H_{15}N_2O_2^+$ $[M + H]^+$: 291.1128, found: 291.1130.



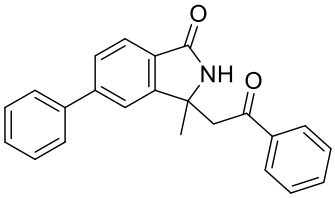
3-methyl-3-(2-oxo-2-phenylethyl)-5-vinylisoindolin-1-one (3k)

Following general procedure C, the product was obtained as colorless oil in 68% yield. **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.92 (d, *J* = 7.4 Hz, 2H), 7.80 (d, *J* = 7.8 Hz, 1H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.52 (d, *J* = 7.8 Hz, 1H), 7.46 (t, *J* = 7.8 Hz, 3H), 7.33 (br, 1H), 6.82 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.90 (d, *J* = 17.6 Hz, 1H), 5.42 (d, *J* = 10.9 Hz, 1H), 3.78 (d, *J* = 17.7 Hz, 1H), 3.03 (d, *J* = 17.7 Hz, 1H), 1.68 (s, 3H) ppm. **^{13}C NMR (151 MHz, $CDCl_3$)** δ 198.06, 168.73, 152.78, 141.77, 136.75, 136.32, 133.91, 130.24, 128.90, 128.10, 126.87, 124.61, 118.72, 116.64, 59.40, 47.50, 24.89 ppm. HPLC purity: 96.0%, t_R = 2.43 min. **HRMS (ESI) m/z:** calculated for $C_{19}H_{17}NO_2^+$ $[M + H]^+$: 292.1332, found: 292.1328.



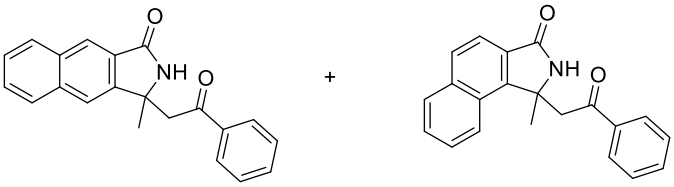
3-methyl-3-(2-oxo-2-phenylethyl)-5-(trifluoromethyl)isoindolin-1-one (3l)

Following general procedure C, the product was obtained as colorless oil in 64% yield. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.97 (d, *J* = 7.8 Hz, 1H), 7.95 – 7.90 (m, 2H), 7.78 – 7.72 (m, 2H), 7.62 – 7.56 (m, 2H), 7.47 (t, *J* = 7.8 Hz, 2H), 3.82 (d, *J* = 17.7 Hz, 1H), 3.05 (d, *J* = 17.7 Hz, 1H), 1.72 (s, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 197.62, 167.42, 152.47, 136.57, 134.32, 134.08, 128.96, 128.13, 126.00, 125.97, 125.13, 118.60, 118.57, 59.78, 47.16, 24.90 ppm. **^{19}F NMR (471 MHz, DMSO-d_6)** δ -60.60 ppm. HPLC purity: 98.2%, t_R = 2.47 min. **HRMS (ESI) m/z:** calculated for $C_{18}H_{14}F_3NO_2^+$ $[M + H]^+$: 334.1049, found: 334.1052.



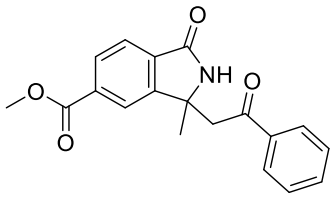
3-methyl-3-(2-oxo-2-phenylethyl)-5-phenylisoindolin-1-one (3m)

Following general procedure C, the product was obtained as colorless oil in 78% yield. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.95 – 7.90 (m, 3H), 7.71 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.67 – 7.62 (m, 3H), 7.62 – 7.57 (m, 1H), 7.53 – 7.41 (m, 5H), 7.29 (br, 1H), 3.83 (d, *J* = 17.7 Hz, 1H), 3.08 (d, *J* = 17.7 Hz, 1H), 1.74 (s, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 198.09, 168.78, 153.02, 145.77, 140.54, 136.83, 133.94, 129.79, 129.17, 128.95, 128.36, 128.14, 127.94, 127.66, 124.85, 119.93, 59.53, 47.63, 25.00 ppm. HPLC purity: > 99%, t_R = 3.18 min. **HRMS (ESI) m/z:** calculated for $C_{23}H_{20}NO_2^+$ $[M + H]^+$: 342.1489, found: 342.1487.



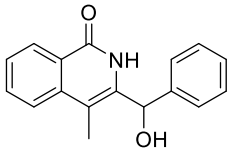
3-methyl-3-(2-oxo-2-phenylethyl)-2,3-dihydro-1H-benzo[f]isoindol-1-one (3n) and 1-methyl-1-(2-oxo-2-phenylethyl)-1,2-dihydro-3H-benzo[e]isoindol-3-one (3n')

Following general procedure C, the products were obtained as colorless oil in 75% yield in a 1.1:1 ratio. The two isomers were inseparable under previous purification conditions. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.40 (s, 1H), 8.11 – 7.87 (m, 11H), 7.72 – 7.52 (m, 7H), 7.50 – 7.44 (m, 4H), 7.39 (s, 1H), 4.25 (d, *J* = 17.8 Hz, 1H, major), 3.90 (d, *J* = 17.8 Hz, 1H, minor), 3.19 – 3.10 (m, 2H, major + minor), 1.97 (s, 3H, major), 1.78 (s, 3H, minor) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 197.59, 197.50, 168.31, 168.12, 148.52, 146.99, 136.22, 135.66, 134.89, 133.33, 132.63, 129.71, 129.51, 129.22, 128.62, 128.33, 127.58, 127.50, 126.82, 126.79, 126.60, 126.07, 124.35, 123.16, 119.86, 119.52, 59.90, 58.78, 47.67, 46.41, 25.14, 23.72 ppm. HPLC purity (combined): > 99%, t_R = 2.45 – 2.64 min. **HRMS (ESI) m/z:** calculated for $C_{21}H_{17}NO_2^+$ $[M + H]^+$: 316.1332, found: 316.1334.



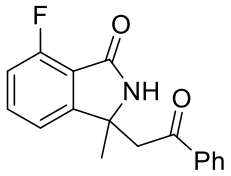
Methyl 3-methyl-1-oxo-3-(2-oxo-2-phenylethyl) isoindoline-5-carboxylate (3o)

Following general procedure C, the product was obtained as colorless oil in 61% yield. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.21 – 8.11 (m, 2H), 7.98 – 7.87 (m, 3H), 7.63 – 7.58 (m, 1H), 7.51 – 7.42 (m, 3H), 3.99 (s, 3H), 3.86 (d, *J* = 17.8 Hz, 1H), 3.00 (d, *J* = 17.8 Hz, 1H), 1.70 (s, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 197.92, 167.76, 166.50, 152.20, 136.67, 134.96, 134.07, 133.78, 130.14, 128.99, 128.15, 124.57, 122.68, 59.65, 52.77, 47.25, 24.90 ppm. HPLC purity: 97.6%, t_R = 2.06 min. **HRMS (ESI) m/z:** calculated for $C_{19}H_{17}NO_4^+$ $[M + H]^+$: 324.1230, found: 324.1230.



3-(hydroxy(phenyl)methyl)-4-methylisoquinolin-1(2H)-one (4a)

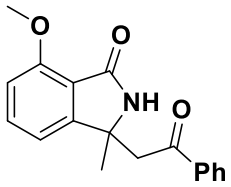
Following general procedure C, the **byproduct** was obtained as colorless oil in 2% yield. **^{1}H NMR (600 MHz, $CDCl_3$)** δ 9.72 (br, 1H), 8.34 (d, *J* = 7.8 Hz, 1H), 7.65 – 7.59 (m, 1H), 7.48 – 7.60 (m, 2H), 7.37 – 7.33 (m, 2H), 7.32 – 7.28 (m, 2H), 7.27 – 7.26 (m, 1H), 6.07 (s, 1H), 2.05 (s, 3H) ppm. **^{13}C NMR (151 MHz, $CDCl_3$)** δ 162.69, 140.47, 138.59, 136.60, 132.79, 128.98, 128.45, 127.64, 126.76, 126.40, 125.12, 123.24, 108.72, 69.92, 11.94 ppm. **LRMS (ESI) m/z:** calculated for $C_{17}H_{16}NO_2^+$ $[M + H]^+$: 266.1, found: 266.1.



7-fluoro-3-methyl-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3p)

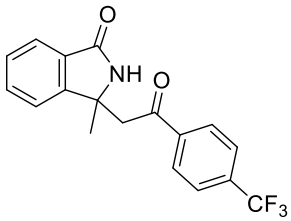
Following general procedure C, the product was obtained as colorless oil in 44% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.95 – 7.87 (m, 2H), 7.64 – 7.54 (m, 2H), 7.47 (t, J = 7.7 Hz, 2H), 7.24 (s, 1H), 7.11 (t, J = 8.7 Hz, 1H), 3.76 (d, J = 17.8 Hz, 1H), 3.03 (d, J = 17.8 Hz, 1H), 1.67 (s, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 197.73, 165.90, 159.43 (d, J = 261.3 Hz), 155.10 (d,

J = 2.4 Hz), 136.67, 134.42 (d, J = 7.6 Hz), 133.98, 128.94, 128.09, 118.17 (d, J = 13.3 Hz), 117.20 (d, J = 4.1 Hz), 115.92 (d, J = 19.6 Hz), 59.32, 47.44, 25.06 ppm. **^{19}F NMR (471 MHz, $CDCl_3$)** δ -117.11 (m) ppm. HPLC purity: 97.7%, t_R = 1.99 min. **HRMS (ESI) m/z:** calculated for $C_{17}H_{15}FNO_2^+$ $[M + H]^+$: 284.1081, found: 284.1082.



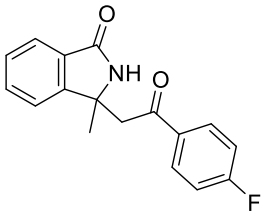
7-methoxy-3-methyl-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3q)

Following general procedure C, the product was obtained as colorless oil in 32% yield. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.90 (d, J = 7.4 Hz, 2H), 7.60 - 7.50 (m, 2H), 7.45 (t, J = 7.7 Hz, 2H), 7.09 (br, 1H), 7.01 (d, J = 7.5 Hz, 1H), 6.92 (d, J = 8.3 Hz, 1H), 3.98 (s, 3H), 3.70 (d, J = 17.7 Hz, 1H), 2.99 (d, J = 17.7 Hz, 1H), 1.63 (s, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 197.96, 167.97, 158.08, 155.27, 136.86, 134.12, 133.81, 128.88, 128.08, 117.91, 113.10, 110.62, 58.48, 56.09, 47.61, 25.03 ppm. HPLC purity: 94.7%, t_R = 1.86 min. **HRMS (ESI) m/z:** calculated for $C_{18}H_{18}NO_3^+$ $[M + H]^+$: 296.1281, found: 296.1279.



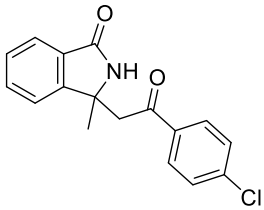
3-methyl-3-(2-oxo-2-(4-(trifluoromethyl)phenyl)ethyl)isoindolin-1-one (3r)

Following general procedure C, the product was obtained as colorless oil in 82% yield. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.01 (d, *J* = 8.2 Hz, 2H), 7.86 – 7.80 (m, 1H), 7.70 (d, *J* = 8.2 Hz, 2H), 7.64 – 7.56 (m, 1H), 7.52 – 7.45 (m, 2H), 7.40 (br, 1H), 3.77 (d, *J* = 17.8 Hz, 1H), 3.08 (d, *J* = 17.8 Hz, 1H), 1.68 (s, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 197.10, 169.11, 151.88, 139.36, 135.02 (q, *J* = 32.8 Hz), 132.39, 130.80, 128.72, 128.46, 125.95, 125.92, 124.42, 121.20, 59.35, 47.85, 24.95 ppm. **^{19}F NMR (471 MHz, $CDCl_3$)** δ -63.21 ppm. HPLC purity: 98.2%, t_R = 2.38 min. **HRMS (ESI) m/z:** calculated for $C_{18}H_{14}F_3NO_2^+$ $[M + H]^+$: 334.1049, found: 334.1042.



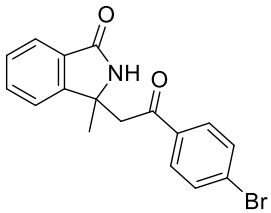
3-(2-(4-fluorophenyl)-2-oxoethyl)-3-methylisoindolin-1-one (3s)

Following general procedure C, the product was obtained as colorless oil in 78% yield. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.97 – 7.91 (m, 2H), 7.84 (d, *J* = 7.5 Hz, 1H), 7.60 (td, *J* = 7.5, 1.0 Hz, 1H), 7.51 – 7.43 (m, 2H), 7.33 (br, 1H), 7.15 – 7.08 (m, 2H), 3.73 (d, *J* = 17.7 Hz, 1H), 3.00 (d, *J* = 17.7 Hz, 1H), 1.67 (s, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 196.41, 168.97, 166.18 (d, *J* = 256.1 Hz), 152.13, 133.24 (d, *J* = 2.9 Hz), 132.31, 130.85, 130.78, 128.64, 124.43, 121.16, 116.05 (d, *J* = 22.0 Hz), 59.40, 47.43, 24.91 ppm. **^{19}F NMR (471 MHz, $CDCl_3$)** δ -103.72 ppm. HPLC purity: > 99%, t_R = 2.21 min. **HRMS (ESI) m/z:** calculated for $C_{17}H_{14}FNO_2^+$ $[M + H]^+$: 284.1081, found: 284.1088.



3-(2-(4-chlorophenyl)-2-oxoethyl)-3-methylisoindolin-1-one (3t)

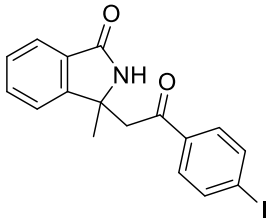
Following general procedure C, the product was obtained as colorless oil in 90% yield. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.85 – 7.80 (m, 3H), 7.60 – 7.56 (m, 1H), 7.49 – 7.43 (m, 2H), 7.43 – 7.37 (m, 3H), 3.72 (d, *J* = 17.7 Hz, 1H), 3.00 (d, *J* = 17.7 Hz, 1H), 1.66 (s, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 196.76, 169.02, 152.00, 140.30, 135.04, 132.28, 130.80, 129.48, 129.14, 128.59, 124.33, 121.19, 59.37, 47.42, 24.91 ppm. HPLC purity: > 99%, t_R = 2.30 min. **HRMS (ESI) m/z:** calculated for $C_{17}H_{14}ClNO_2^+$ $[M + H]^+$: 300.0786, found: 300.0783.



3-(2-(4-bromophenyl)-2-oxoethyl)-3-methylisoindolin-1-one (3u)

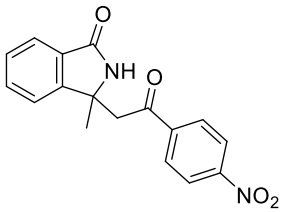
Following general procedure C, the product was obtained as colorless oil in 72% yield. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.84 (d, *J* = 7.5 Hz, 1H), 7.79 – 7.74 (m, 2H), 7.62 – 7.57 (m, 3H), 7.50 – 7.43 (m, 2H), 7.32 (br, 1H), 3.71 (d,

J = 17.8 Hz, 1H), 2.99 (d, *J* = 17.8 Hz, 1H), 1.67 (s, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 197.03, 169.05, 152.05, 135.46, 132.36, 132.22, 130.78, 129.58, 129.18, 128.69, 124.46, 121.16, 59.39, 47.46, 24.89 ppm. HPLC purity: > 99%, t_R = 1.94 min. **HRMS (ESI) m/z:** calculated for $C_{17}H_{15}BrNO_2^+$ $[M + H]^+$: 344.0281, found: 344.0282.



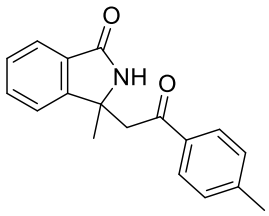
3-(2-(4-iodophenyl)-2-oxoethyl)-3-methylisoindolin-1-one (3v)

Following general procedure C, the product was obtained as colorless oil in 81% yield. **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.86 (d, *J* = 7.5 Hz, 1H), 7.85 – 7.82 (m, 2H), 7.64 – 7.59 (m, 3H), 7.50 (td, *J* = 7.5, 0.8 Hz, 1H), 7.46 (d, *J* = 7.5 Hz, 1H), 7.28 (br, 1H), 3.71 (d, *J* = 17.8 Hz, 1H), 2.99 (d, *J* = 17.8 Hz, 1H), 1.67 (s, 3H) ppm. **^{13}C NMR (151 MHz, $CDCl_3$)** δ 197.36, 168.99, 152.09, 138.27, 135.99, 132.40, 130.79, 129.43, 128.74, 124.53, 121.15, 102.11, 59.41, 47.43, 24.89 ppm. HPLC purity: 97.2%, t_R = 2.55 min. **HRMS (ESI) m/z:** calculated for $C_{17}H_{14}INO_2^+$ $[M + H]^+$: 392.0142, found: 392.0149.



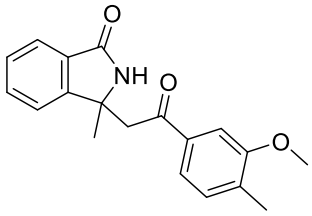
3-methyl-3-(2-(4-nitrophenyl)-2-oxoethyl)isoindolin-1-one (3w)

Following general procedure C, the product was obtained as colorless oil in 88% yield. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.28 – 8.24 (m, 2H), 8.06 (d, *J* = 8.7 Hz, 2H), 7.89 – 7.75 (m, 1H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.49 – 7.43 (m, 3H), 3.79 (d, *J* = 17.8 Hz, 1H), 3.14 (d, *J* = 17.8 Hz, 1H), 1.69 (s, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 196.54, 169.13, 151.65, 150.62, 141.05, 132.43, 130.74, 129.20, 128.76, 124.37, 124.02, 121.23, 59.33, 48.12, 25.02 ppm. HPLC purity: 97.1%, t_R = 1.92 min. **HRMS (ESI) m/z:** calculated for $C_{17}H_{14}N_2O_4^+$ $[M + H]^+$: 311.1026, found: 311.1021.



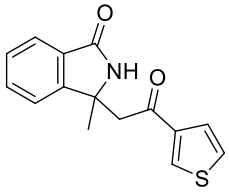
3-methyl-3-(2-oxo-2-(p-tolyl)ethyl)isoindolin-1-one (3x)

Following general procedure C, the product was obtained as colorless oil in 76% yield. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.64 – 7.60 (m, 1H), 7.60 – 7.56 (m, 2H), 7.39 – 7.35 (m, 1H), 7.24 (d, *J* = 7.5 Hz, 2H), 7.13 (br, 1H), 7.04 – 7.00 (m, 2H), 3.52 (d, *J* = 17.6 Hz, 1H), 2.74 (d, *J* = 17.6 Hz, 1H), 2.17 (s, 3H), 1.43 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 197.68, 168.98, 152.33, 144.84, 134.35, 132.24, 130.88, 129.55, 128.54, 128.20, 124.37, 121.17, 59.50, 47.28, 24.88, 21.79 ppm. HPLC purity: > 99%, t_R = 2.22 min. **HRMS (ESI) m/z:** calculated for $C_{18}H_{17}NO_2^+$ $[M + H]^+$: 280.1332, found: 280.1335.



3-(2-(3-methoxy-4-methylphenyl)-2-oxoethyl)-3-methylisoindolin-1-one (3y)

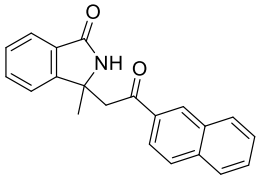
Following general procedure C, the product was obtained as colorless oil in 36% yield. **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.86 (d, *J* = 7.5 Hz, 1H), 7.61 (td, *J* = 7.5, 1.0 Hz, 1H), 7.50 – 7.45 (m, 2H), 7.41 (d, *J* = 1.3 Hz, 1H), 7.37 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.34 (br, 1H), 7.18 (d, *J* = 7.7 Hz, 1H), 3.89 (s, 3H), 3.76 (d, *J* = 17.6 Hz, 1H), 2.99 (d, *J* = 17.6 Hz, 1H), 2.26 (s, 3H), 1.67 (s, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 197.72, 169.01, 158.24, 152.34, 135.97, 134.09, 132.28, 130.90, 130.61, 128.59, 124.44, 121.20, 121.00, 108.31, 59.57, 55.60, 47.31, 24.91, 16.74 ppm. HPLC purity: 98.2%, t_R = 2.40 min. **HRMS (ESI) m/z:** calculated for $C_{19}H_{20}NO_3^+$ $[M + H]^+$: 310.1438, found: 310.1440.



3-methyl-3-(2-oxo-2-(thiophen-3-yl)ethyl)isoindolin-1-one (3z)

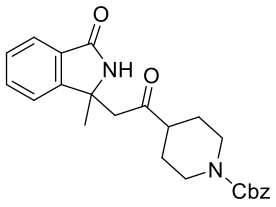
Following general procedure C, the product was obtained as colorless oil in 48% yield. **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.04 (dd, *J* = 2.9, 1.2 Hz, 1H), 7.86 (d, *J* = 7.5 Hz, 1H), 7.61 (td, *J* = 7.5, 1.0 Hz, 1H), 7.53 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.49 (td, *J* = 7.5, 0.7 Hz, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.34

(dd, *J* = 5.1, 2.9 Hz, 1H), 3.65 (d, *J* = 17.4 Hz, 1H), 2.95 (d, *J* = 17.4 Hz, 1H), 1.67 (s, 3H) ppm. **^{13}C NMR (151 MHz, $CDCl_3$)** δ 192.21, 168.94, 152.14, 142.13, 132.75, 132.31, 130.91, 128.65, 127.01, 126.81, 124.48, 121.14, 59.47, 48.64, 24.96 ppm. HPLC purity: > 99%, t_R = 1.85 min. **HRMS (ESI) m/z:** calculated for $C_{15}H_{13}NO_2S^+$ $[M + H]^+$: 272.0740, found: 272.0744.



3-methyl-3-(2-(naphthalen-2-yl)-2-oxoethyl)isoindolin-1-one (3za)

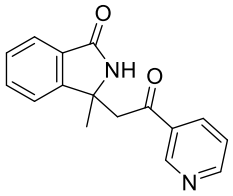
Following general procedure C, the product was obtained as colorless oil in 85% yield. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.38 (s, 1H), 7.96 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.91 (d, *J* = 8.1 Hz, 1H), 7.89 – 7.82 (m, 3H), 7.65 – 7.56 (m, 2H), 7.54 – 7.44 (m, 4H), 3.90 (d, *J* = 17.6 Hz, 1H), 3.11 (d, *J* = 17.6 Hz, 1H), 1.70 (s, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 197.94, 169.01, 152.26, 135.85, 134.07, 132.42, 132.27, 130.89, 129.97, 129.65, 128.94, 128.77, 128.56, 127.89, 127.10, 124.36, 123.47, 121.26, 59.55, 47.44, 24.93 ppm. HPLC purity: > 99%, t_R = 2.51 min. **HRMS (ESI) m/z:** calculated for $C_{21}H_{17}NO_2^+$ $[M + H]^+$: 316.1332, found: 316.1326.



benzyl 4-(2-(1-methyl-3-oxoisoindolin-1-yl)acetyl)piperidine-1-carboxylate (3zb)

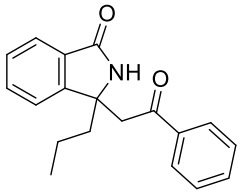
Following general procedure C, the product was obtained as colorless oil in 53% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.85 (d, *J* = 7.5 Hz, 1H), 7.62 – 7.56 (m, 1H), 7.51 – 7.45 (m, 1H), 7.41 – 7.30 (m, 6H), 7.23 (s, 1H), 5.13 (s, 2H), 4.32 – 4.10 (m, 2H), 3.23 (d, *J* = 17.9 Hz, 1H), 2.89 – 2.76 (m, 2H), 2.57 (d, *J* = 17.9 Hz, 1H), 2.51 – 2.42 (m, 1H), 1.87 – 1.73 (m, 2H), 1.64 – 1.48 (m, 5H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 210.24, 168.98, 155.19, 151.80, 136.71, 132.30, 130.74, 128.60, 128.16, 128.00, 124.36, 121.00, 67.31, 59.15, 49.41, 49.17, 43.36, 43.33, 27.29, 27.27, 24.81 ppm.

HPLC purity: > 99%, t_R = 2.53 min. **HRMS (ESI) m/z:** calculated for $C_{24}H_{27}N_2O_4^+$ $[M + H]^+$: 407.1965, found: 407.1969.



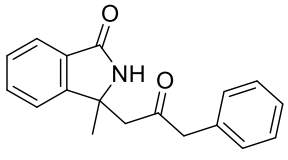
3-methyl-3-(2-oxo-2-(pyridin-3-yl)ethyl)isoindolin-1-one (3zc)

Following general procedure C, the product was obtained as colorless oil in 67% yield. **^{1}H NMR (600 MHz, $CDCl_3$)** δ 9.09 (s, 1H), 8.75 (d, *J* = 3.8 Hz, 1H), 8.18 (dt, *J* = 8.0, 1.9 Hz, 1H), 7.81 (d, *J* = 7.5 Hz, 1H), 7.58 (td, *J* = 7.6, 1.0 Hz, 1H), 7.51 – 7.43 (m, 3H), 7.39 (dd, *J* = 7.9, 4.8 Hz, 1H), 3.75 (d, *J* = 17.7 Hz, 1H), 3.08 (d, *J* = 17.7 Hz, 1H), 1.67 (s, 3H) ppm. **^{13}C NMR (151 MHz, $CDCl_3$)** δ 196.90, 169.09, 153.98, 151.75, 149.44, 135.46, 132.36, 132.08, 130.74, 128.67, 124.33, 123.86, 121.21, 59.31, 47.74, 25.02 ppm. HPLC purity: > 99%, t_R = 1.58 min. **HRMS (ESI) m/z:** calculated for $C_{16}H_{15}N_2O_2^+$ $[M + H]^+$: 267.1128, found: 267.1126.



3-(2-oxo-2-phenylethyl)-3-propylisoindolin-1-one (3zd)

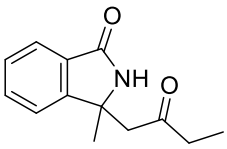
Following general procedure C, the product was obtained as colorless oil in 77% yield. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.92 (d, *J* = 7.4 Hz, 2H), 7.85 (d, *J* = 7.5 Hz, 1H), 7.63 – 7.56 (m, 2H), 7.52 – 7.41 (m, 4H), 7.16 (br, 1H), 3.81 (d, *J* = 17.7 Hz, 1H), 3.03 (d, *J* = 17.7 Hz, 1H), 2.29 – 2.21 (m, 1H), 1.89 – 1.81 (m, 1H), 1.28 – 1.20 (m, 1H), 0.84 – 0.67 (m, 4H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 198.21, 169.44, 150.60, 136.91, 133.88, 132.20, 131.88, 128.92, 128.56, 128.11, 124.33, 121.26, 62.64, 47.23, 38.94, 16.93, 14.10 ppm. HPLC purity: > 99%, t_R = 2.38 min. **HRMS (ESI) m/z:** calculated for $C_{19}H_{20}NO_2^+$ $[M + H]^+$: 294.1489, found: 294.1491.



3-methyl-3-(2-oxo-3-phenylpropyl)isoindolin-1-one (3ze)

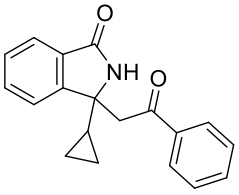
Following general procedure C, the product was obtained as colorless oil in 61% yield. **^{1}H NMR (500 MHz, $CDCl_3$)** δ

7.80 (d, *J* = 7.5 Hz, 1H), 7.53 (td, *J* = 7.5, 0.9 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.35 – 7.29 (m, 3H), 7.28 – 7.24 (m, 1H), 7.22 (br, 1H), 7.19 – 7.14 (m, 2H), 3.67 (s, 2H), 3.19 (d, *J* = 17.9 Hz, 1H), 2.55 (d, *J* = 17.9 Hz, 1H), 1.50 (s, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 206.54, 168.97, 151.74, 133.23, 132.23, 130.72, 129.41, 129.04, 128.52, 127.50, 124.28, 121.06, 59.17, 51.02, 50.41, 24.73 ppm. HPLC purity: 96.9%, t_R = 6.67 min. **HRMS (ESI) m/z:** calculated for $C_{18}H_{17}NO_2^+$ $[M + H]^+$: 280.1332, found: 280.1329.



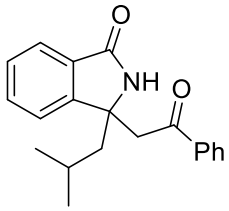
3-methyl-3-(2-oxobutyl)isoindolin-1-one (3zf)

Following general procedure C, the product was obtained as colorless oil in 70% yield. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.82 (d, *J* = 7.5 Hz, 1H), 7.56 (td, *J* = 7.5, 1.1 Hz, 1H), 7.45 (td, *J* = 7.5, 0.8 Hz, 1H), 7.37 (d, *J* = 7.6 Hz, 1H), 7.19 (br, 1H), 3.15 (d, *J* = 17.7 Hz, 1H), 2.52 (d, *J* = 17.7 Hz, 1H), 2.42 (q, *J* = 7.3 Hz, 2H), 1.57 (s, 3H), 1.05 (t, *J* = 7.3 Hz, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 209.64, 169.00, 151.97, 132.25, 130.79, 128.53, 124.33, 121.04, 59.23, 50.90, 37.07, 24.85, 7.69 ppm. HPLC purity: > 99%, t_R = 2.10 min. **HRMS (ESI) m/z:** calculated for $C_{13}H_{16}NO_2^+$ $[M + H]^+$: 218.1176, found: 218.1172.



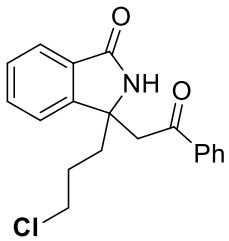
3-cyclopropyl-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3zg)

Following general procedure C, the product was obtained as colorless oil in 63% yield. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.97 – 7.93 (m, 2H), 7.85 – 7.81 (m, 1H), 7.63 – 7.55 (m, 2H), 7.50 – 7.45 (m, 4H), 7.17 (br, 1H), 3.99 (d, *J* = 16.8 Hz, 1H), 3.07 (d, *J* = 16.8 Hz, 1H), 1.54 – 1.45 (m, 1H), 0.54 – 0.40 (m, 1H), 0.35 – 0.11 (m, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 198.13, 169.76, 150.12, 137.25, 133.78, 132.07, 131.35, 128.91, 128.67, 128.24, 124.33, 121.64, 62.03, 46.77, 17.92, 3.59, 0.94 ppm. HPLC purity: > 99%, t_R = 1.70 min. **HRMS (ESI) m/z:** calculated for $C_{19}H_{18}NO_2^+$ $[M + H]^+$: 292.1332, found: 292.1334.



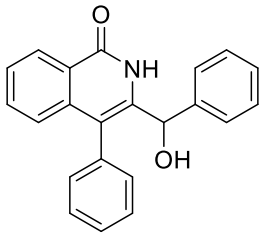
3-isobutyl-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3zh)

Following general procedure C, the product was obtained as colorless oil in 73% yield. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.92 – 7.82 (m, 3H), 7.62 – 7.53 (m, 2H), 7.50 – 7.41 (m, 4H), 7.29 (br, 1H), 3.76 (d, J = 17.7 Hz, 1H), 2.96 (d, J = 17.7 Hz, 1H), 2.28 (dd, J = 14.3, 6.2 Hz, 1H), 1.80 (dd, J = 14.3, 6.2 Hz, 1H), 1.30 – 1.24 (m, 1H), 0.86 (d, J = 6.7 Hz, 3H), 0.49 (d, J = 6.7 Hz, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 198.18, 169.38, 150.76, 136.89, 133.81, 132.05, 131.92, 128.85, 128.54, 128.05, 124.30, 121.60, 62.70, 48.34, 44.88, 24.51, 24.37, 24.24 ppm. HPLC purity: 97.3%, t_R = 2.04 min. **HRMS (ESI) m/z:** calculated for $C_{20}H_{22}NO_2^+$ $[M+H]^+$: 308.1645, found: 308.1649.



3-(3-chloropropyl)-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3zi)

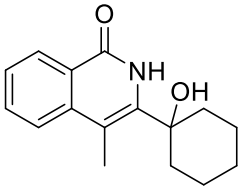
Following general procedure C, the product was obtained as colorless oil in 88% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.95 – 7.87 (m, 2H), 7.84 (d, J = 7.5 Hz, 1H), 7.64 – 7.52 (m, 2H), 7.50 – 7.41 (m, 5H), 3.81 (d, J = 17.9 Hz, 1H), 3.45 – 3.28 (m, 2H), 3.07 (d, J = 17.8 Hz, 1H), 2.50 – 2.41 (m, 1H), 2.15 – 2.04 (m, 1H), 1.72 – 1.60 (m, 1H), 1.20 – 1.04 (m, 1H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 197.97, 169.44, 149.79, 136.68, 133.90, 132.46, 131.76, 128.85, 128.79, 128.06, 124.35, 121.31, 62.14, 47.39, 44.83, 33.86, 26.58 ppm. HPLC purity: 97.6%, t_R = 2.26 min. **HRMS (ESI) m/z:** calculated for $C_{19}H_{19}ClNO_2^+$ $[M+H]^+$: 328.1099, found: 328.1093.



3-(hydroxy(phenyl)methyl)-4-phenylisoquinolin-1(2H)-one (4zj)

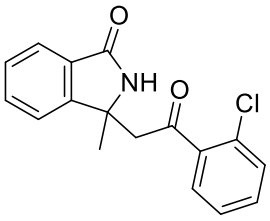
Following general procedure C, the product was obtained as white solid in 50% yield. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 9.13 (s, 1H), 8.33 (d, J = 7.8 Hz, 1H), 7.72 (d, J = 8.1 Hz, 1H), 7.55 - 7.28 (m, 11H), 7.26 - 7.21 (m, 1H), 6.06 (s, 1H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 142.96, 139.64, 136.19, 134.54, 132.36, 129.95, 129.27, 128.90, 128.56, 127.85, 127.18, 127.06,

126.73, 125.77, 114.79, 71.18 ppm. HPLC purity: 95.2%, t_R = 1.79 min. **HRMS (ESI) m/z:** calculated for $C_{22}H_{16}NO_2^-$ $[M-H]^-$: 326.1187, found: 326.1191.



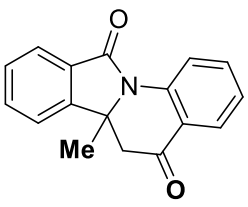
3-(1-hydroxycyclohexyl)-4-methylisoquinolin-1(2H)-one (4zm)

Following general procedure C, the product was obtained as light purple solid in 41% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.47 (br, 1H), 8.42 (d, J = 8.2 Hz, 1H), 7.76 – 7.64 (m, 2H), 7.50 – 7.43 (m, 1H), 2.46 (s, 3H), 2.26 – 2.15 (m, 2H), 1.90 – 1.74 (m, 7H), 1.45 – 1.26 (m, 1H).ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 162.22, 141.93, 140.33, 132.72, 128.78, 127.59, 126.03, 123.14, 106.53, 73.02, 35.50, 25.11, 21.91, 14.67 ppm. HPLC purity: > 99%, t_R = 2.21 min. **HRMS (ESI) m/z:** calculated for $C_{16}H_{20}NO_2^+$ $[M+H]^+$: 258.1489, found: 258.1495.



3-(2-(2-chlorophenyl)-2-oxoethyl)-3-methylisoindolin-1-one (3zn)

Following general procedure C, the product was obtained as colorless oil in 73% yield. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.83 (d, J = 7.6 Hz, 1H), 7.55 (td, J = 7.5, 0.9 Hz, 1H), 7.46 – 7.40 (m, 1H), 7.42 – 7.36 (m, 4H), 7.33 – 7.27 (m, 2H), 3.76 (d, J = 17.8 Hz, 1H), 3.04 (d, J = 17.8 Hz, 1H), 1.67 (s, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 201.45, 169.05, 151.64, 138.97, 132.35, 132.31, 130.80, 130.71, 128.89, 128.61, 127.26, 124.31, 121.19, 59.69, 51.82, 25.01 ppm. HPLC purity: 96.5%, t_R = 2.01 min. **HRMS (ESI) m/z:** calculated for $C_{17}H_{15}ClNO_2^+$ $[M+H]^+$: 300.0786, found: 300.0794.



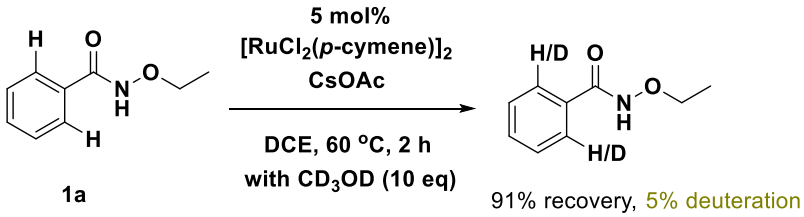
6a-methyl-6,6a-dihydroisoindolo[2,1-a]quinoline-5,11-dione (3zn-1)

The product was obtained as colorless oil in 38% yield. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.48 (d, J = 8.3 Hz, 1H), 8.09 (dd, J = 7.9, 1.6 Hz, 1H), 8.01 (d, J = 7.6 Hz, 1H), 7.74 – 7.65 (m, 2H), 7.60 – 7.56 (m, 1H), 7.49 (d, J = 7.6 Hz, 1H), 7.32 – 7.27 (m, 1H), 3.15 (d, J = 16.2 Hz, 1H), 2.75 (d, J =

16.2 Hz, 1H), 1.60 (s, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 192.44, 165.47, 149.90, 139.26, 135.75, 133.29, 130.66, 129.30, 127.48, 125.14, 124.56, 122.39, 121.81, 120.99, 64.36, 48.77, 24.05 ppm. HPLC purity: 96.8%, t_R = 2.42 min. **HRMS (ESI) m/z:** calculated for $C_{17}H_{14}NO_2^+$ $[M+H]^+$: 264.1019, found: 264.1022.

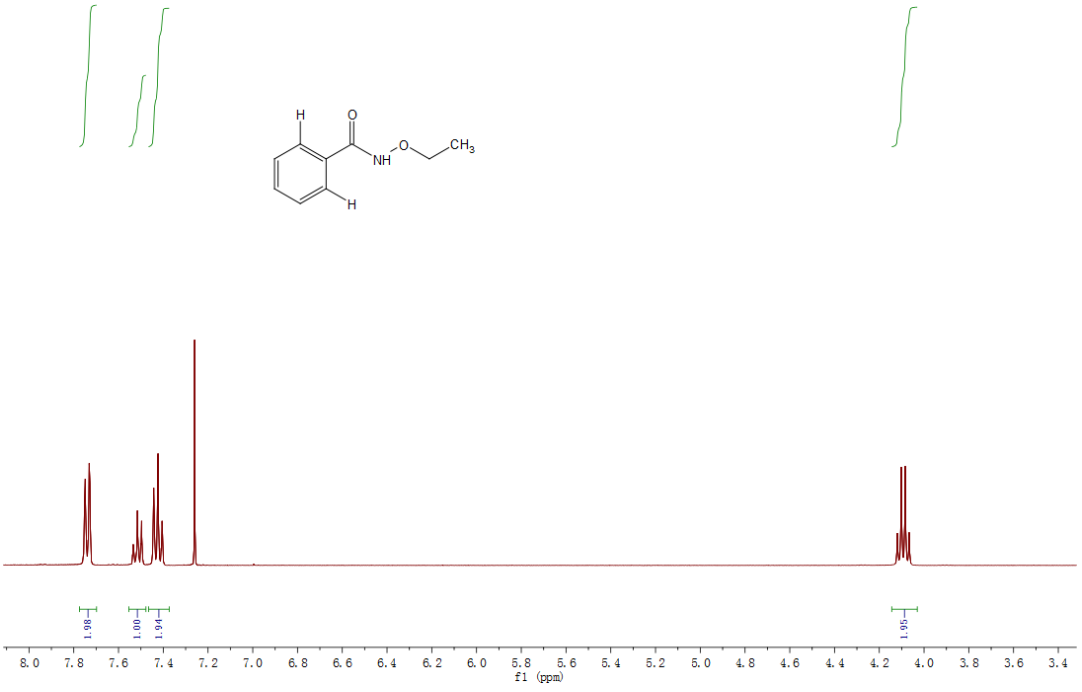
(D) MECHANISTIC EXPERIMENTS

Deuterium Incorporation Experiments A:

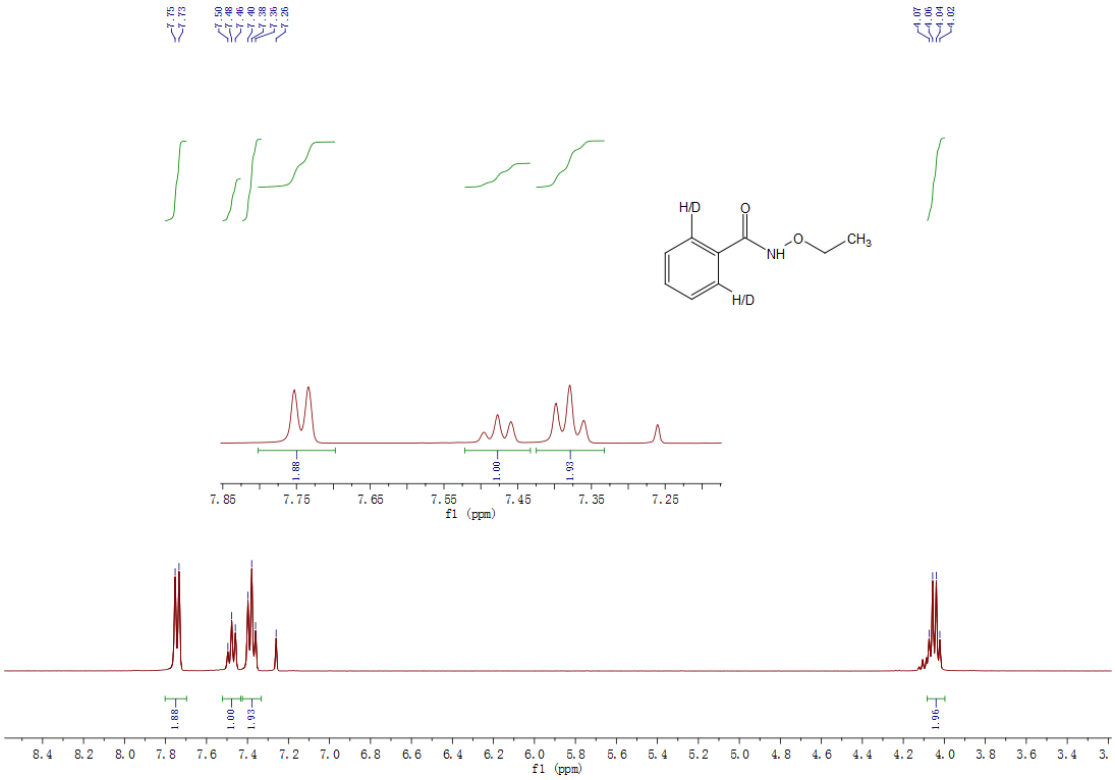


A mixture of N-ethoxybenzamide (**1a**, 0.2 mmol), 5 mol% $[RuCl_2(p\text{-cymene})]_2$ and CsOAc (0.2 mmol, 1 equiv) were added to a dry tube. Dry DCE (2 mL) and CD_3OD (2 mmol, 10 equiv) was added and the mixture was stirred at 60 ℃ for 2 h under Ar atmosphere. The resulting mixture was diluted with dichloromethane and washed by water. The combined organic layers were dried with Na_2SO_4, concentrated and purified by column chromatography on silica gel. *Found about 5% deuterium incorporation at the ortho position of the hydroxamic acid* (see below).

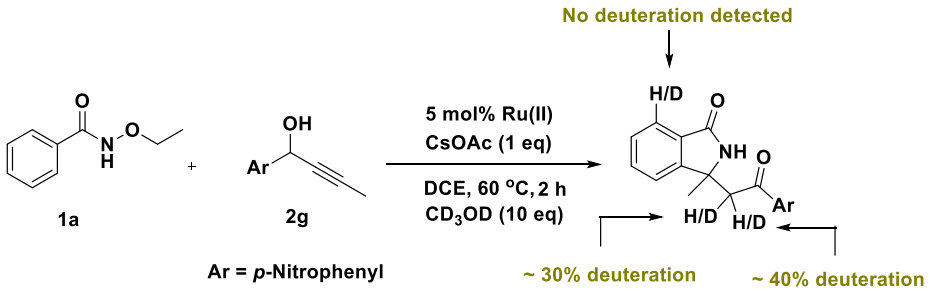
1) ^{1}H NMR of starting material **1a**



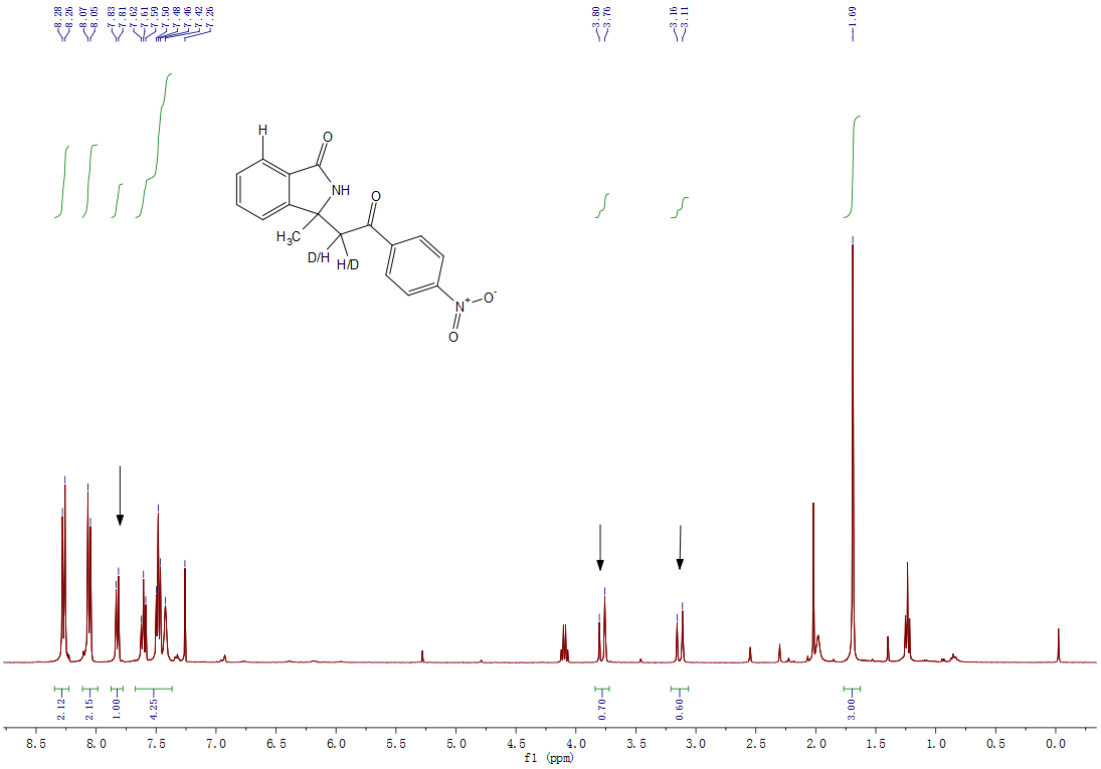
2) ^{1}H NMR of starting material **1a**-recovered (5% deuteration)



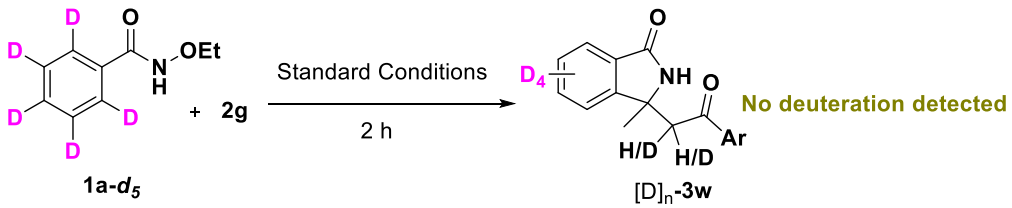
Deuterium Incorporation Experiments B:



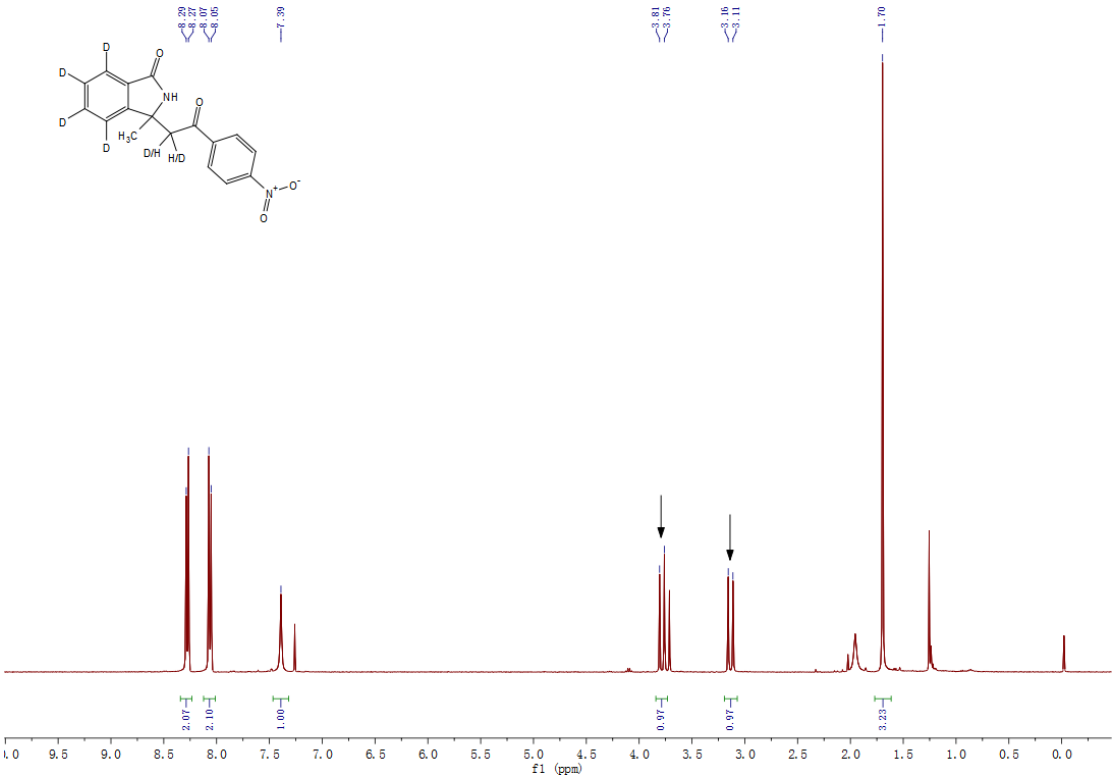
1a (17.0 mg, 0.1 mmol) was allowed to react with **2g** (39.0 mg, 0.2 mmol) in dry DCE (1 mL) in the presence of CsOAc (1 equiv), 5 mol% $[RuCl_2(p\text{-cymene})]_2$ and CD_3OD (1 mmol, 10 equiv). The mixture was stirred at 60 ℃ under Ar atmosphere. The reaction was stopped after 2 h, and the resulting mixture was diluted with dichloromethane and washed by water. The combined organic layers were dried with Na_2SO_4, concentrated and purified by column chromatography on silica gel to give the crude product. *About 30% deuteration and 40% deuteration on both methylene protons of the product based on ^{1}H NMR* (see below).



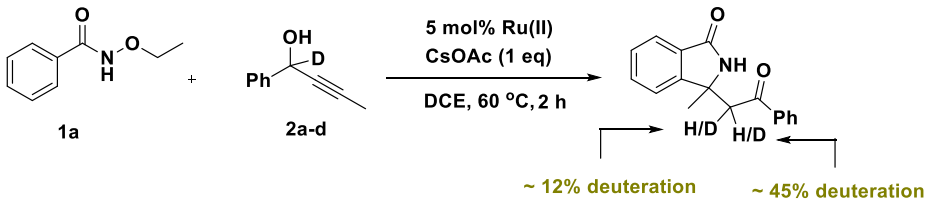
Deuterium Incorporation Experiments C:



A mixture of N-ethoxybenzamide (**1a-*d*$_5$**, 0.2 mmol), **2g** (0.4 mmol, 2 equiv.), 5 mol% $[RuCl_2(p\text{-cymene})]_2$ and CsOAc (0.2 mmol, 1 equiv) were added to a dry tube. Dry DCE (2 mL) was added and the mixture was stirred at 60 ℃ for 2 h under Ar atmosphere. The resulting mixture was diluted with dichloromethane and washed by water. The combined organic layers were dried with Na_2SO_4, concentrated and purified by column chromatography on silica gel to give the product. *No deuterium incorporation was observed on both methylene protons of the product based on* ^1H *NMR (see below).*



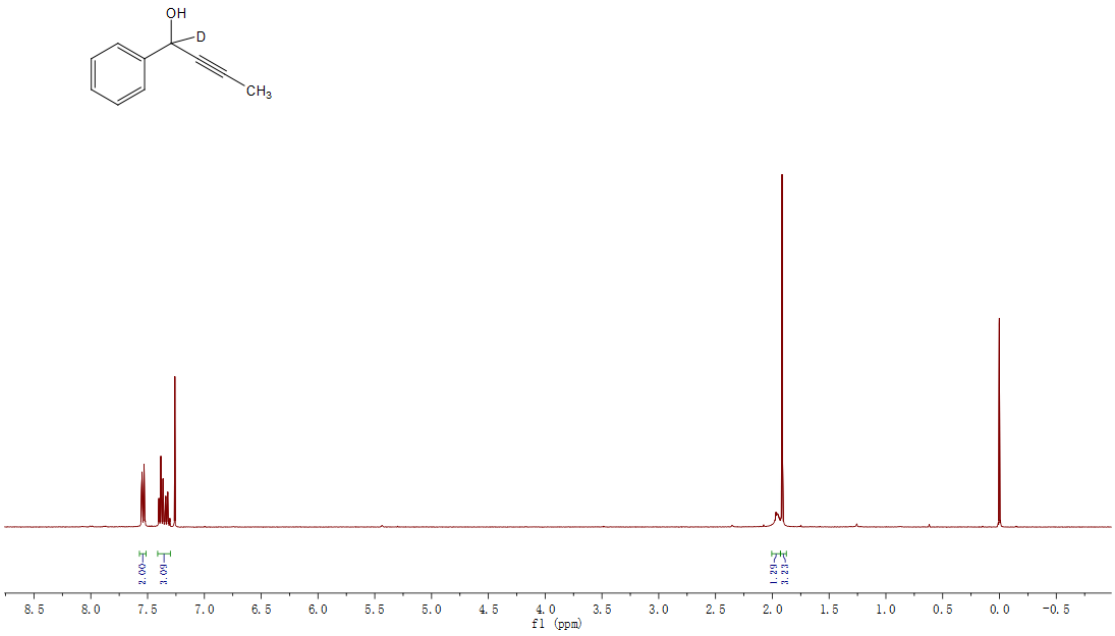
Deuterium Incorporation Experiments D:



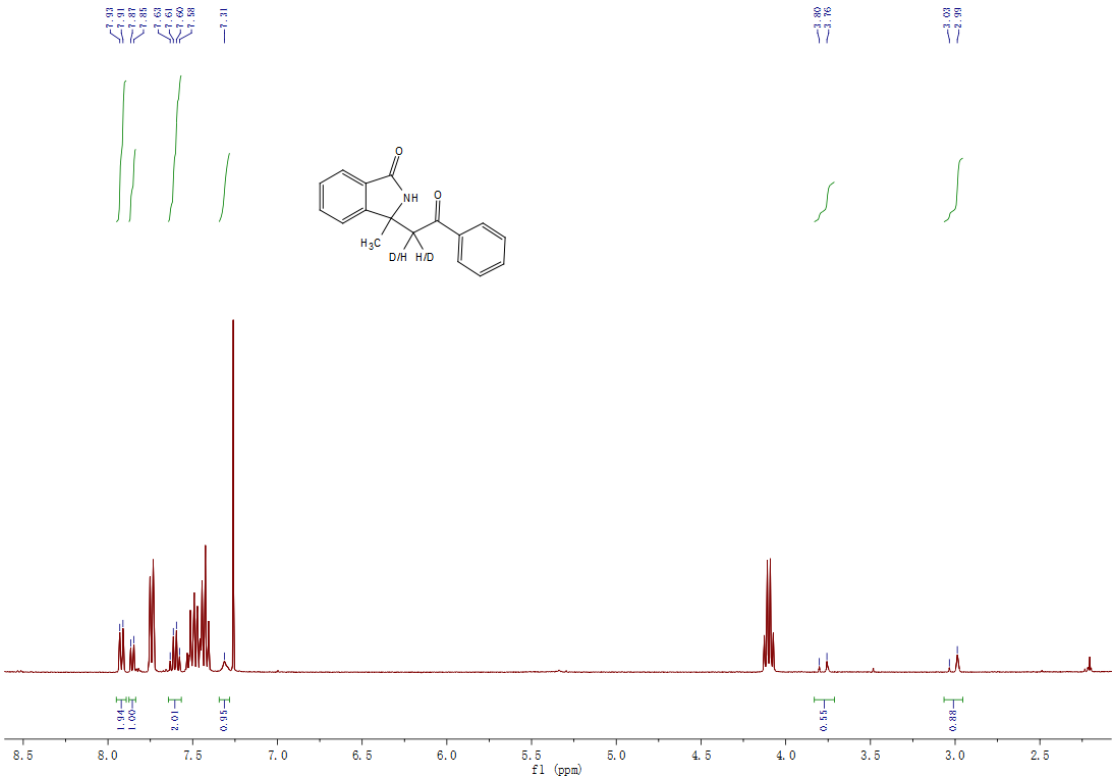
Synthesis of compound **2a-d**. To a solution of **2a** (0.5 mmol, 1 eq.) in dry THF was added $NaBD_4$ (1 mmol, 2 eq.). The mixture was stirred for 1h at room temperature, then saturated NH_4Cl aqueous solution was added. The resulting mixture was diluted with dichloromethane and washed by water. The combined organic layers were dried with Na_2SO_4, concentrated and purified by column chromatography on silica gel to give the product **2a-d**.

1a (17.0 mg, 0.1 mmol) was allowed to react with **2a-d** (0.2 mmol) in dry DCE (2 mL) in the presence of CsOAc (1 equiv), 5 mol% $[RuCl_2(p\text{-cymene})]_2$. The mixture was stirred at 60 ℃ under Ar atmosphere. The reaction was stopped after 2 h, and the resulting mixture was concentrated and directly purified by column chromatography on silica gel to give the crude product. *About 12% deuteration and 45% deuteration*

on both methylene protons of the product based on ^1H NMR (see below).

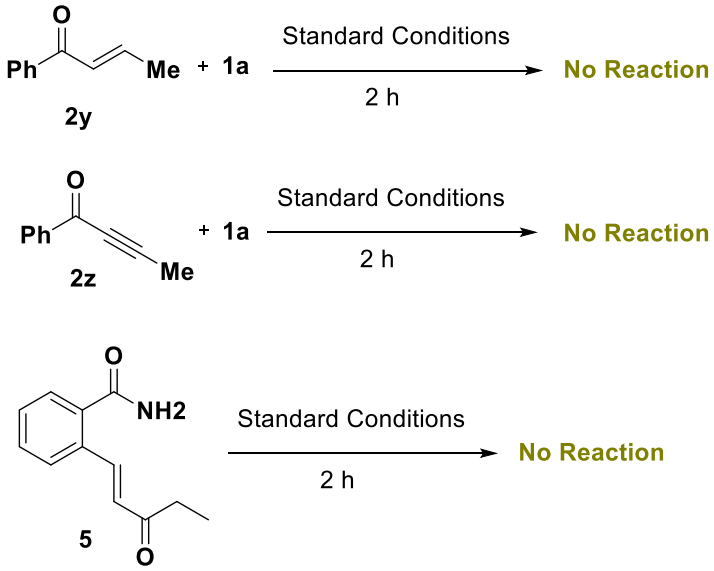


^{1}H-NMR of **2a-d**



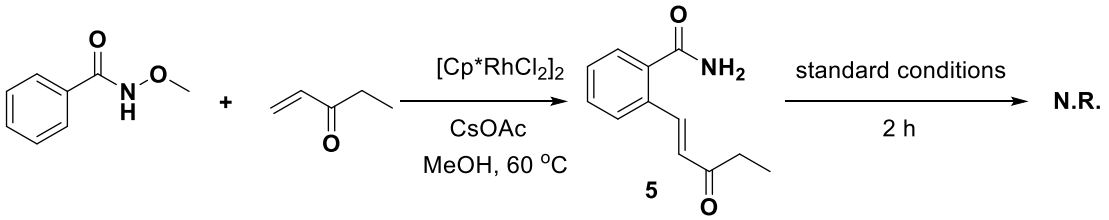
^{1}H-NMR of the crude products

Control experiments:



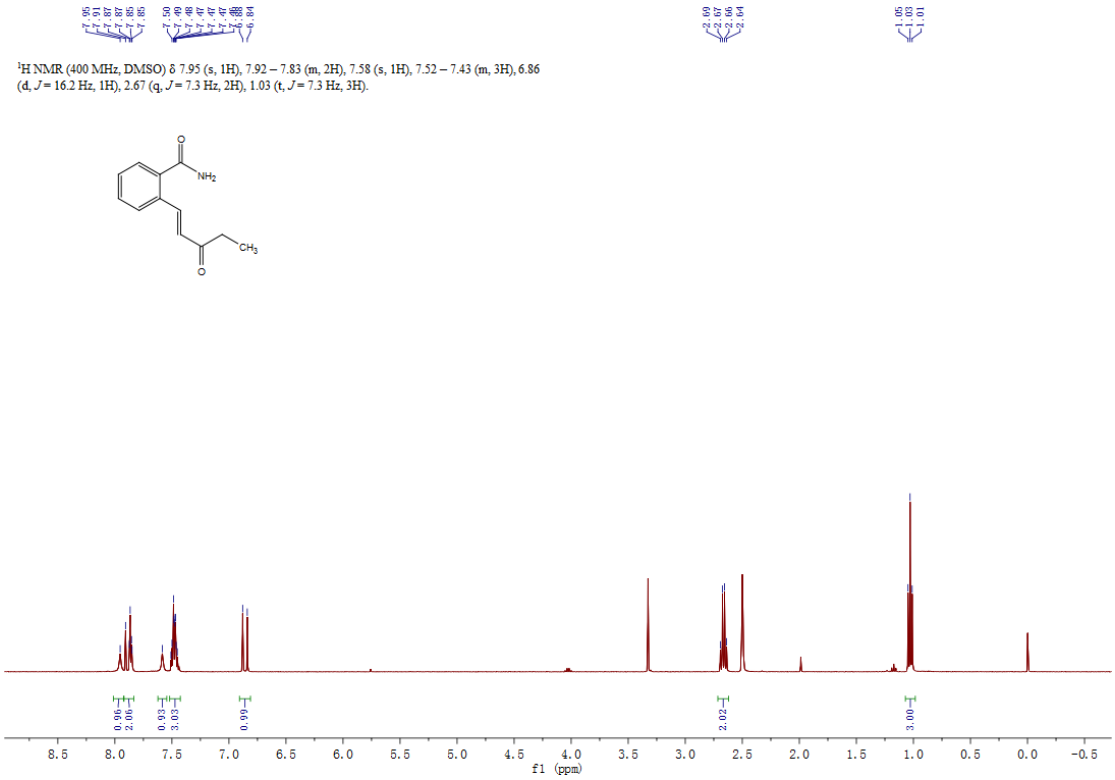
1a (17.0 mg, 0.1 mmol) was allowed to react with **2y** (0.2 mmol) in dry DCE (2 mL) in the presence of CsOAc (1 equiv), 5 mol% $[RuCl_2(p\text{-cymene})]_2$. The mixture was stirred at 60 ℃ under Ar atmosphere. The reaction was stopped after 2 h, we found the reaction didn't proceed by analyzing TLC.

Additionally, **1a** (17.0 mg, 0.1 mmol) was allowed to react with **2z** (0.2 mmol) in dry DCE (2 mL) in the presence of CsOAc (1 equiv), 5 mol% $[RuCl_2(p\text{-cymene})]_2$. The mixture was stirred at 60 ℃ under Ar atmosphere. The reaction was stopped after 2 h, we found the reaction didn't proceed by analyzing TLC.



Synthesis of compound **5**. *N*-methoxybenzamide (0.1 mmol) was allowed to react with pent-1-en-3-one (0.2 mmol) in dry MeOH (4 mL) in the presence of CsOAc (0.5 equiv), 5 mol% $[Cp^*RhCl_2]_2$. The mixture was stirred at 60 ℃ under Ar atmosphere. The reaction was stopped after 5 h, and the resulting mixture was concentrated and directly purified by column chromatography on silica gel to give the product **5**. Then, compound **5** was allowed to react in dry DCE (2 mL) in the presence of CsOAc (1

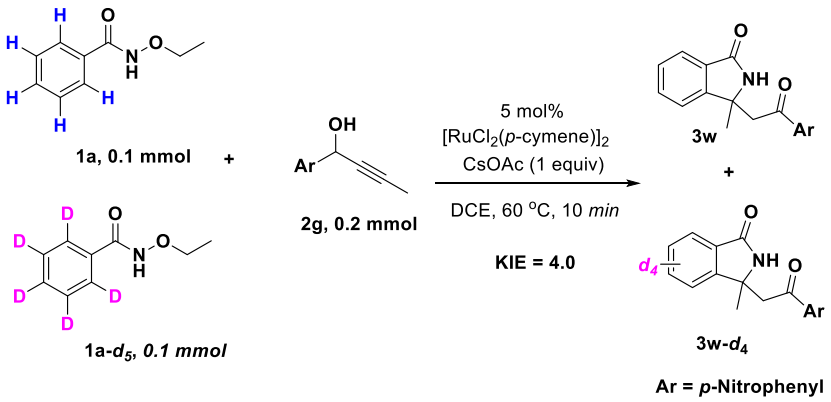
equiv), 5 mol% $[RuCl_2(p\text{-cymene})]_2$. The mixture was stirred at 60 ℃ under Ar atmosphere. The reaction was stopped after 2 h, we found the reaction didn't proceed by analyzing TLC and ^{1}H-NMR.



^{1}H-NMR of compound **5**

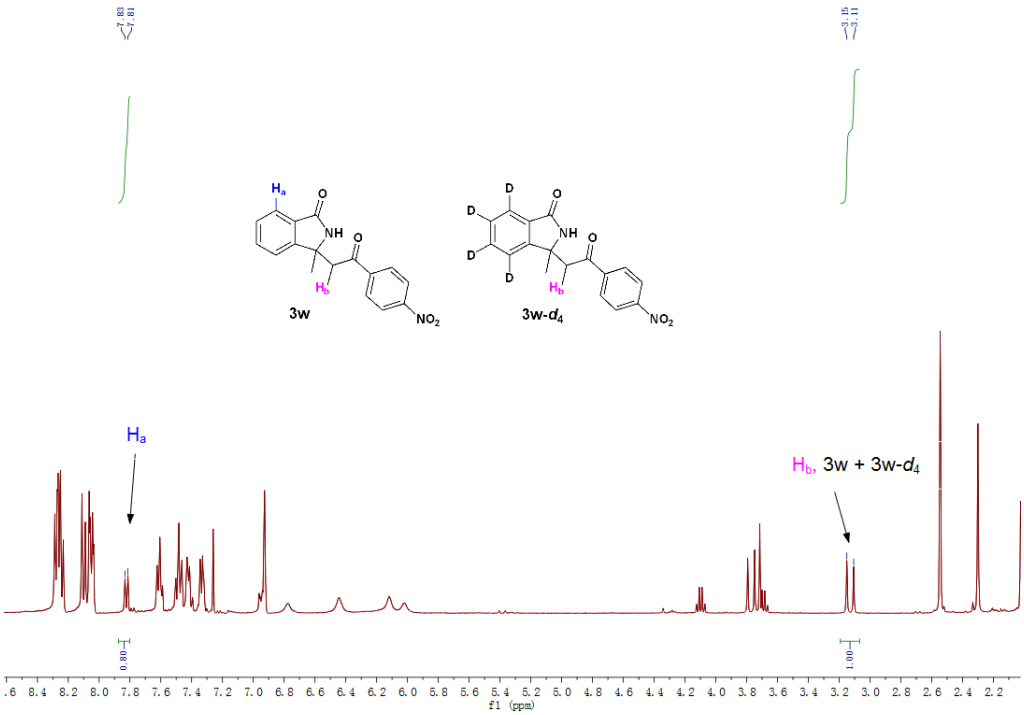
Determination of the KIE:

1) The intermolecular Competition experiment

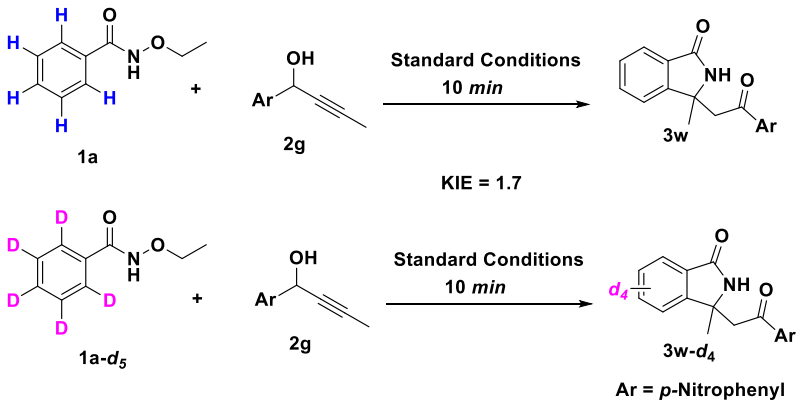


An equimolar mixture of **1a** and **1a**-d_5 were allowed to react with **2g** (1:1:2 ratio) in dry DCE (1 mL) in the presence of CsOAc (1 equiv) and 5 mol% $[RuCl_2(p\text{-cymene})]_2$.

The mixture was stirred at 60 ℃ under Ar atmosphere. The reaction was stopped after 10 min, and the crude product was isolated by using column chromatography on silica gel and was analyzed by ^{1}H NMR spectroscopy ($CDCl_3$, 400 MHz). The KIE value (approx. 4.0) was obtained by integrating the H_a of **3w** and the H_b of **3w** and **3w-*d*$_4$**. The conversion (approx. 32%) was determined based on the starting material (**1a** and **1a- *d*$_5$**) recovered. The crude products were further purified by preparative thin layer chromatography (DCM/MeOH = 50/1 v/v) to give a mixture of **3w** and **3w-*d*$_4$** (16.0 mg, 29% yield).



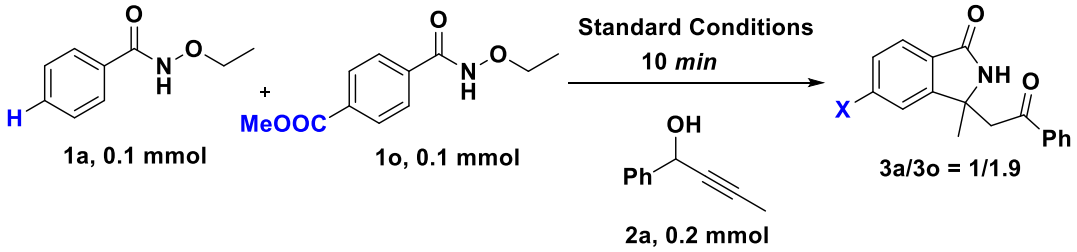
2) Two parallel reactions for KIE value measurement



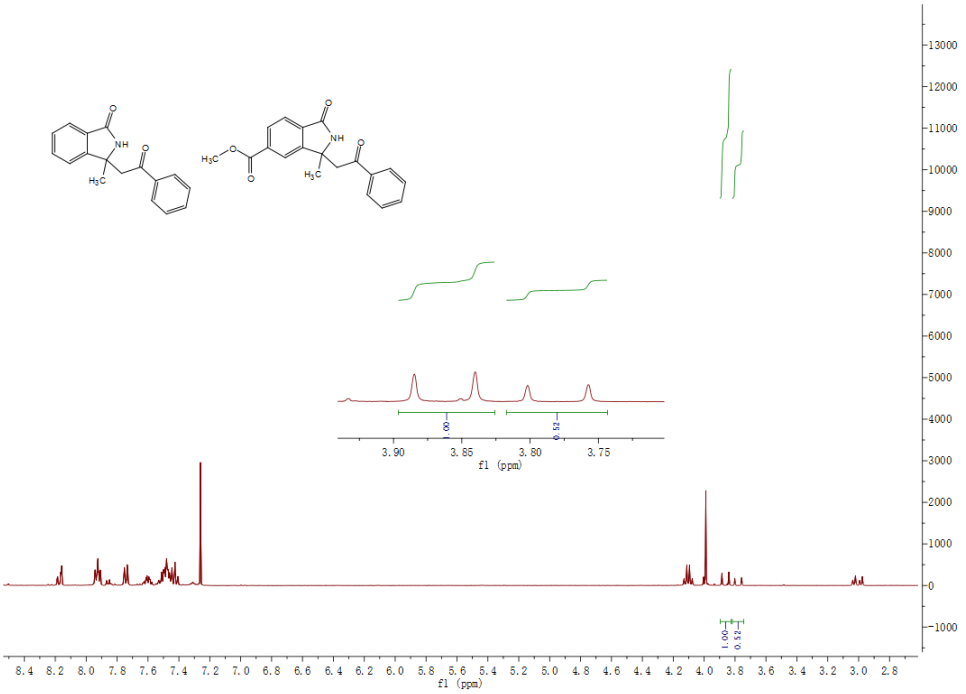
1a (17.0 mg, 0.1 mmol) or **1a**-d_5 (17.5 mg, 0.1 mmol) was allowed to react with **2g**

(39.0 mg, 0.2 mmol) in dry DCE (1 mL) in the presence of CsOAc (1 equiv) and 5 mol% $[RuCl_2(p\text{-cymene})]_2$. The mixture was stirred at 60 ℃ under Ar atmosphere. The reaction was stopped after 10 min, and the desired product was isolated by using column chromatography on silica gel. The value of KIE (approx. 1.7) was determined by moles of **3w** (11.0 mg, 40% yield) and **3w-*d*$_4$** (6.6 mg, 24% yield).

Intermolecular Competition Experiments with Benzamides 1a and 1o

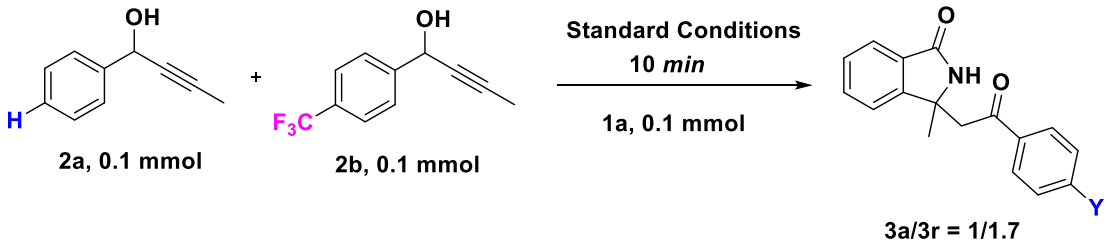


An equimolar mixture of **1a** and **1o** were allowed to react with **2a** (1:1:2 ratio) in dry DCE (2 mL) in the presence of CsOAc (1 equiv) and 5 mol% $[RuCl_2(p\text{-cymene})]_2$. The mixture was stirred at 60 ℃ under Ar atmosphere. The reaction was stopped after 10 min, and the ratio of **3a/3o** in the crude mixture of products was determined to be **1/1.9** by ^{1}H NMR (see below).

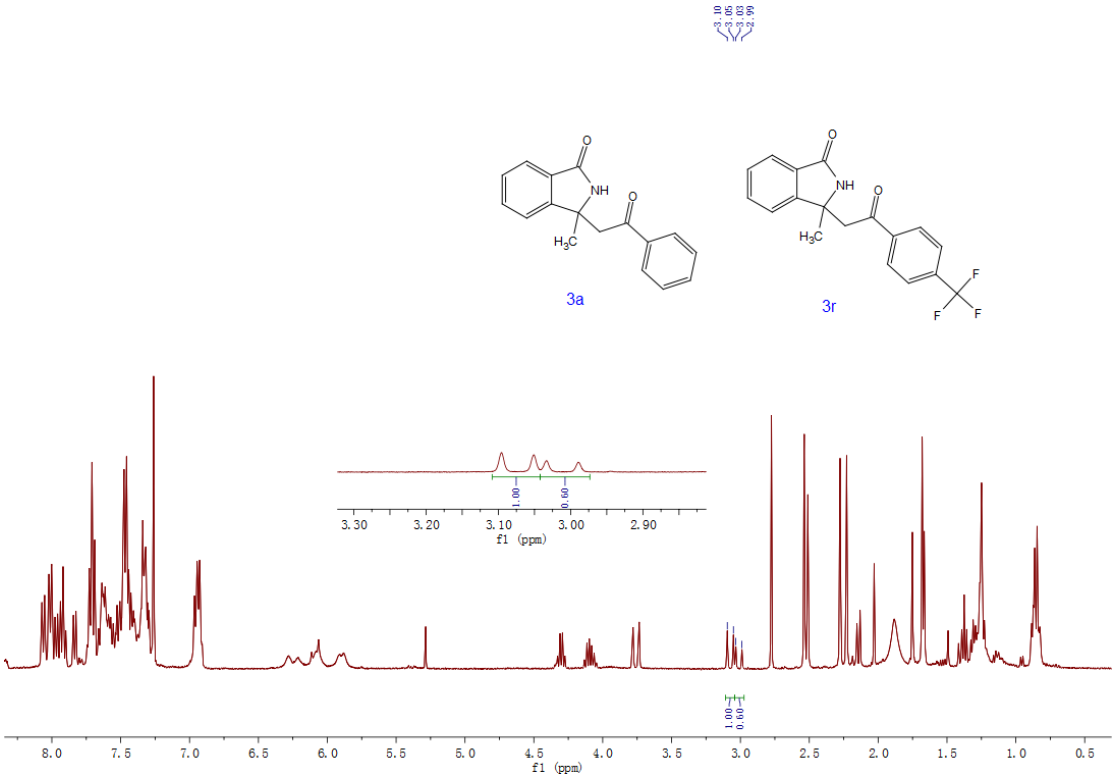


^{1}H NMR of the ratio of **3a/3o** in the crude mixture of products.

Intermolecular Competition Experiments with Propargyl alcohols 2a and 2b.

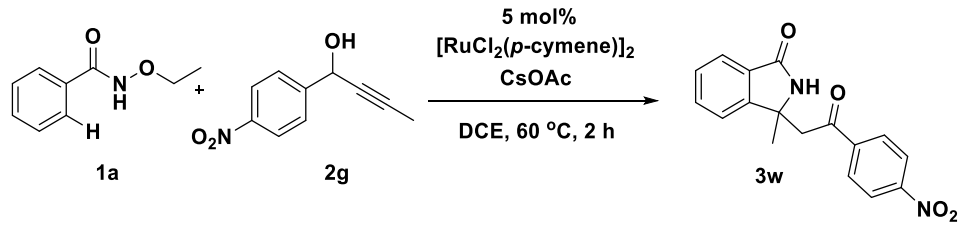


An equimolar mixture of **2a** and **2b** were allowed to react with **1a** (1:1:1 ratio) in dry DCE (1 mL) in the presence of CsOAc (1 equiv) and 5 mol% $[RuCl_2(p\text{-cymene})]_2$. The mixture was stirred at 60 ℃ under Ar atmosphere. The reaction was stopped after 10 min, and the ratio of **3a/3r** in the crude mixture of products was determined to be **1/1.7** by ^{1}H NMR (see below).



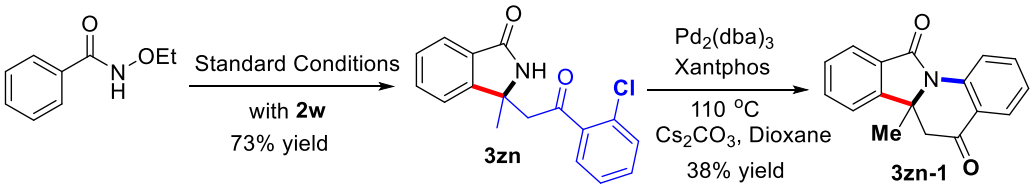
^{1}H NMR of the ratio of **3a/3r** in the crude mixture of products.

(E) Gram-Scale Preparation of 3w



The dry sealed tube was charged with N-ethoxybenzamides **1a** (0.66 g, 4 mmol, 1 equiv), Propargyl alcohols **2g** (1.53 g, 8 mmol, 2 equiv), $[RuCl_2(p\text{-cymene})]_2$ (0.2 mmol, 0.05 equiv), CsOAc (4 mmol, 1 equiv) and 40 mL dry 1,2-dichloroethane. The mixture was heated at 60 ℃ for 2 h under Ar atmosphere. The resulting mixture was diluted with dichloromethane and washed by water. The combined organic layers were dried with Na_2SO_4, filtered, concentrated and purified by column chromatography on silica gel (PE/EA = 2/1 ~ 1/1, v/v) to give the desired product **3w** (1.08 g, 82% yield)**.**

A rapid entry to isoindolo[2,1-a]quinoline scaffold



The dry sealed tube was charged with N-ethoxybenzamides **1a** (0.6 g, 3.63 mmol, 1 equiv), Propargyl alcohols **2w** (1.31 g, 7.26 mmol, 2 equiv), $[RuCl_2(p\text{-cymene})]_2$ (0.18 mmol, 0.05 equiv), CsOAc (3.63 mmol, 1 equiv) and 35 mL dry 1,2-dichloroethane. The mixture was heated at 60 ℃ for 2 h under Ar atmosphere. The resulting mixture was diluted with dichloromethane and washed by water. The combined organic layers were dried with Na_2SO_4, filtered, concentrated and purified by column chromatography on silica gel (PE/EA = 4/1 ~ 2/1, v/v) to give the compound **3zn** (790 mg, 73% yield)**.**

A mixture of the compound **3zn** (30.0 mg, 0.1 mmol, 1 eq.), $Pd_2(dba)_3$ (9.2 mg, 0.1 eq), Xantphos (11.6 mg, 0.2 eq.) and Cs_2CO_3 (48.9 mg, 1.5 eq.) in 2 mL dry

1,4-dioxane was stirred and heated at 110 ^{o}C for 24 h under Ar atmosphere. The resulting mixture was diluted with dichloromethane and washed by water. The combined organic layers were dried with Na_2SO_4, filtered, concentrated and purified by preparative thin layer chromatography (PE/EA = 10/1 v/v) to give the product **3zn-1** (10 mg, 38% yield)**.**

(F) The Single Crystal Stucture of 3f.

X-ray Single Crystal Stucture Analysis of **3f**:

X-ray crystallographic data of **3f** were solutions at T = 173 K. $C_{18}H_{17}NO_2$, triclinic. Space group P1, a = 7.3719 (3) Å, b = 8.0356 (3) Å, c = 12.4786 (5) Å, α = 82.255 (2) °, β = 78.930 (2) °, γ = 86.099 (2) °, V = 718.16 (5) Å^3, Z = 2.

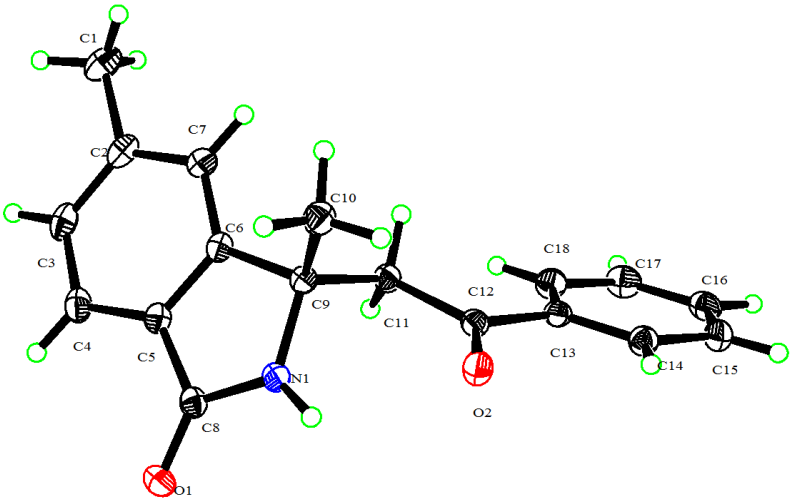


Figure S1: The crystal structure of **3f** by X-ray analysis.

These data can be obtained free of charge from the Cambridge Crystallographic Data Centre *via www.ccdc.cam.ac.uk/data_request/cif*, the CCDC number is 1499534.

(G) HPLC spectra for isomer ratio (3a/4a) determination.

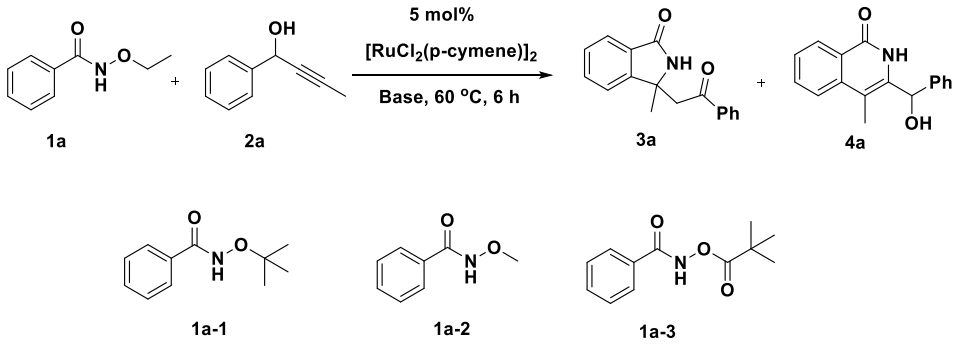


Table S1. Optimization of reaction conditions.

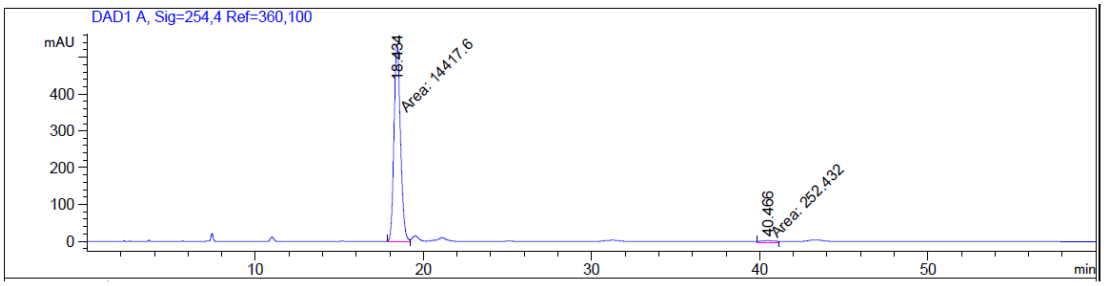
NO.	Cat.	Solvent	Base	**3a** Yield (%)[b]	**3a/4a** ratio[c]
1	$[RuCl_2(p\text{-cymene})]_2$	MeOH	CsOAc	0	-
2	$[RuCl_2(p\text{-cymene})]_2$	CH_3CN	CsOAc	Trace	-
3	$[RuCl_2(p\text{-cymene})]_2$	Dioxane	CsOAc	10	-
4	$[RuCl_2(p\text{-cymene})]_2$	THF	CsOAc	71	98:2
5	$[RuCl_2(p\text{-cymene})]_2$	DCE	CsOAc	82 (78)	98:2
6	$[RuCl_2(p\text{-cymene})]_2$	DCE	Na_2CO_3	0	-
7	$[RuCl_2(p\text{-cymene})]_2$	DCE	KOAc	55	95:5
8	$[RuCl_2(p\text{-cymene})]_2$	DCE	NaOAc	59	95:5
9[d]	$[RuCl_2(p\text{-cymene})]_2$	DCE	CsOAc	50	96:4
10[e]	$[RuCl_2(p\text{-cymene})]_2$	DCE	CsOAc	69	94:6
11[f]	$[RuCl_2(p\text{-cymene})]_2$	DCE	CsOAc	Trace	-
12	$[RuCl_2(p\text{-cymene})]_2$	DCE	-	0	-
13	-	DCE	CsOAc	0	-
14	$[RuCl_2(p\text{-cymene})]_2$	DCE	KOH	0	-
15	$[RuCl_2(p\text{-cymene})]_2$	DCE	NaOH	0	-
16	$[RuCl_2(p\text{-cymene})]_2$	DCE	K_2CO_3	0	-
17	$[RuCl_2(p\text{-cymene})]_2$	DCE	LiOAc	0	-
18[g]	$[RuCl_2(p\text{-cymene})]_2$	DCE	CsOAc	60	-
19[h]	$[RuCl_2(p\text{-cymene})]_2$	DCE	CsOAc	75	-
20[i]	$[RuCl_2(p\text{-cymene})]_2$	DCE	CsOAc	trace	-
21[j]	$[RuCl_2(p\text{-cymene})]_2$	DCE	CsOAc	76	-
22	$RuCl_3$	DCE	CsOAc	0	-
23	$CpRu(Ph_3P)_2Cl$	DCE	CsOAc	0	-

24	$Ru_3(CO)_{12}$	DCE	CsOAc	trace	-
25	$Ru(OAc)_2$[(R)-BINAP]	DCE	CsOAc	0	-
26	[RuCl(p-cymene)((R)-BINAP)]Cl	DCE	CsOAc	0	-
27[k]	$[RuCl_2(p\text{-cymene})]_2$/(R)-BINAP	DCE	CsOAc	71(ee < 2%)	-
28[l]	$[RuCl_2(p\text{-cymene})]_2$/37002-48-5 (CAS)	DCE	CsOAc	73(ee < 2%)	-

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), Catalyst (5 mol %), Base (1 equiv) in Solvent (4 mL) at 60 °C. [b]NMR yields using CH_2Br_2 as an internal standard, isolated yields in parentheses. [c]Determined by HPLC analysis of the crude mixture. [d]**1a-1** instead of **1a**. [e]**1a-2** instead of **1a**. [f]**1a-3** instead of **1a**. [g]**2a** (0.26 mmol) was used. [h]80 °C. [i]30 °C. [j]12 h. [k](R)-BINAP (10 mol %) was added. [l]37002-48-5 (10 mol %) was added. ee = enantiomeric excess.

(1) Table S1, Entry 4

The isomer ratio **(3a/4a)** was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 250 mm) (H_2O/MeOH = 50/50, λ = 254 nm, 1.0 mL/min). t_R (major) = 18.434 min, t_R (minor) = 40.466 min, 98:2 ratio.



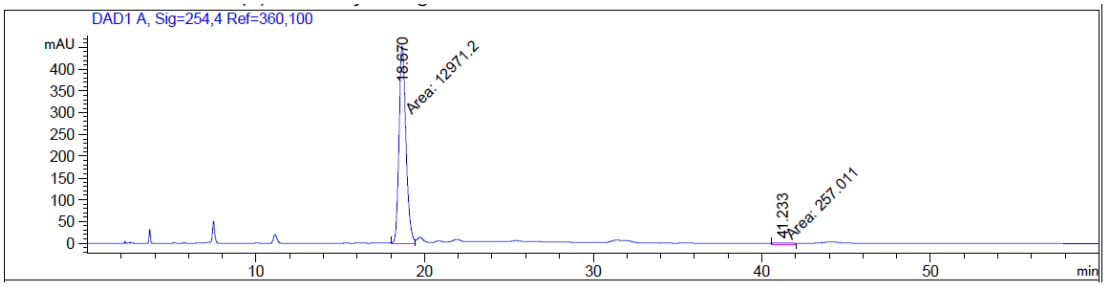
Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.434	MM	0.4487	1.44176e4	535.47418	98.2793
2	40.466	MM	1.0485	252.43201	4.01243	1.7207
Totals :				1.46701e4	539.48661	

(2) Table S1, Entry 5

The isomer ratio **(3a/4a)** was determined by HPLC with an Eclipse XDB-C18 column

(5 μm, 4.6 × 250 mm) (H_2O/MeOH = 50/50, λ = 254 nm, 1.0 mL/min). t_R (major) = 18.670 min, t_R (minor) = 41.233 min, 98:2 ratio.

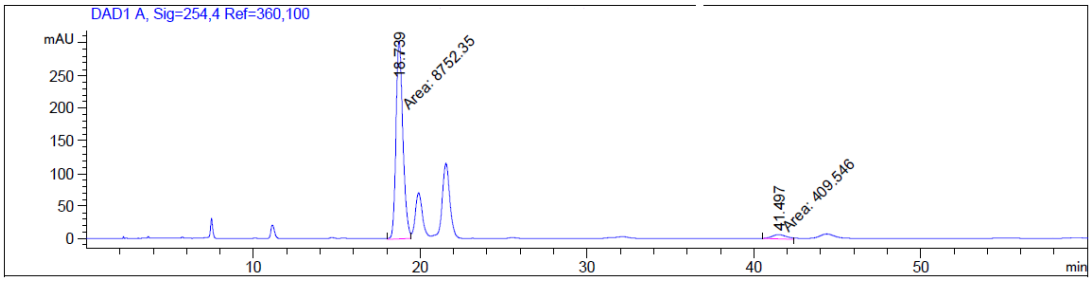


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.670	MM	0.4776	1.29712e4	452.64777	98.0571
2	41.233	MM	1.3530	257.01062	3.16605	1.9429
Totals :				1.32282e4	455.81382	

(3) Table S1, Entry 7

The isomer ratio **(3a/4a)** was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 250 mm) (H_2O/MeOH = 50/50, λ = 254 nm, 1.0 mL/min). t_R (major) = 18.739 min, t_R (minor) = 41.497 min, 95:5 ratio.

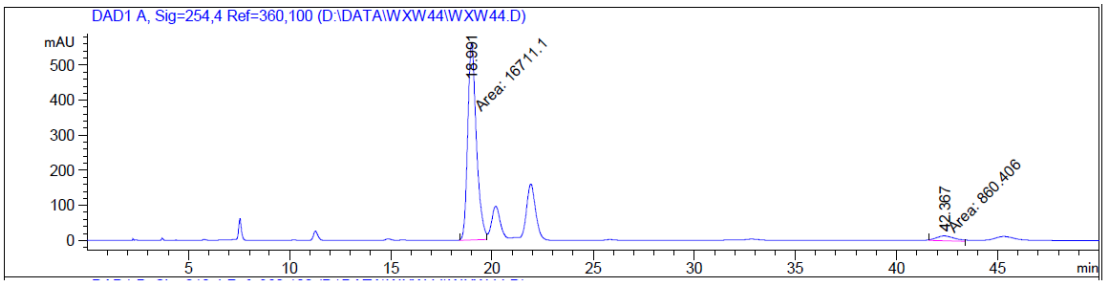


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.739	MM	0.4818	8752.34766	302.76288	95.5299
2	41.497	MM	1.0422	409.54642	6.54941	4.4701
Totals :				9161.89407	309.31229	

(4) Table S1, Entry 8

The isomer ratio **(3a/4a)** was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 250 mm) (H_2O/MeOH = 50/50, λ = 254 nm, 1.0 mL/min). t_R (major) = 18.991 min, t_R (minor) = 42.367 min, 95:5 ratio.



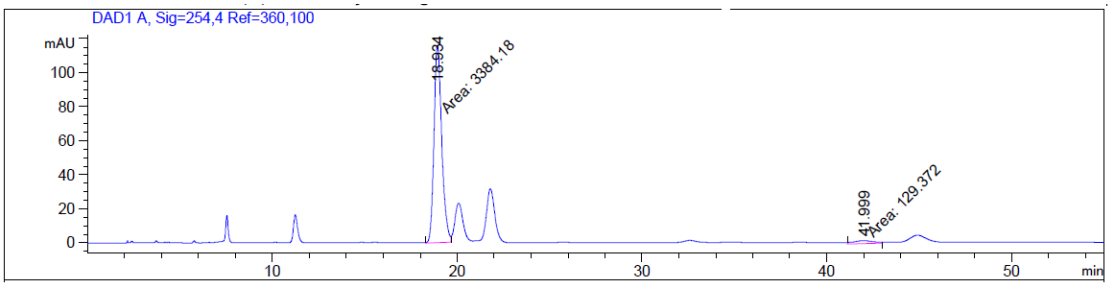
Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.991	MM	0.4966	1.67111e4	560.81329	95.1034
2	42.367	MM	1.0309	860.40643	13.91067	4.8966
Totals :				1.75716e4	574.72396	

(5) Table S1, Entry 9

The isomer ratio **(3a/4a)** was determined by HPLC with an Eclipse XDB-C18 column

(5 μm, 4.6 × 250 mm) (H_2O/MeOH = 50/50, λ = 254 nm, 1.0 mL/min). t_R (major) = 18.934 min, t_R (minor) = 41.999 min, 96:4 ratio.

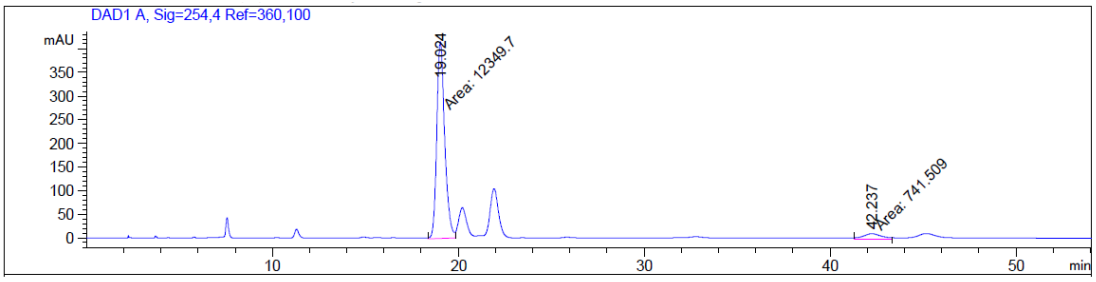


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.934	MM	0.4863	3384.18091	115.99490	96.3179
2	41.999	MM	1.2695	129.37183	1.69843	3.6821
Totals :				3513.55273	117.69333	

(6) Table S1, Entry 10

The isomer ratio **(3a/4a)** was determined by HPLC with an Eclipse XDB-C18 column (5 μm, 4.6 × 250 mm) (H_2O/MeOH = 50/50, λ = 254 nm, 1.0 mL/min). t_R (major) = 19.024 min, t_R (minor) = 42.237 min, 94:6 ratio.

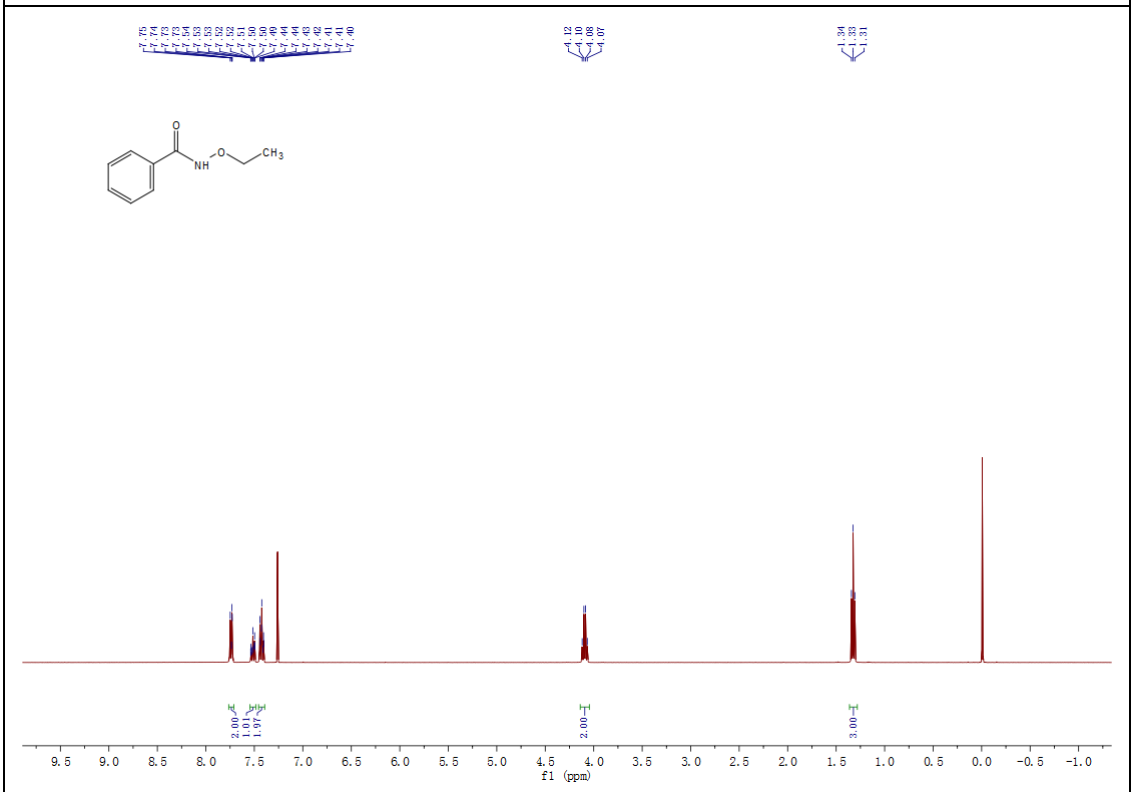


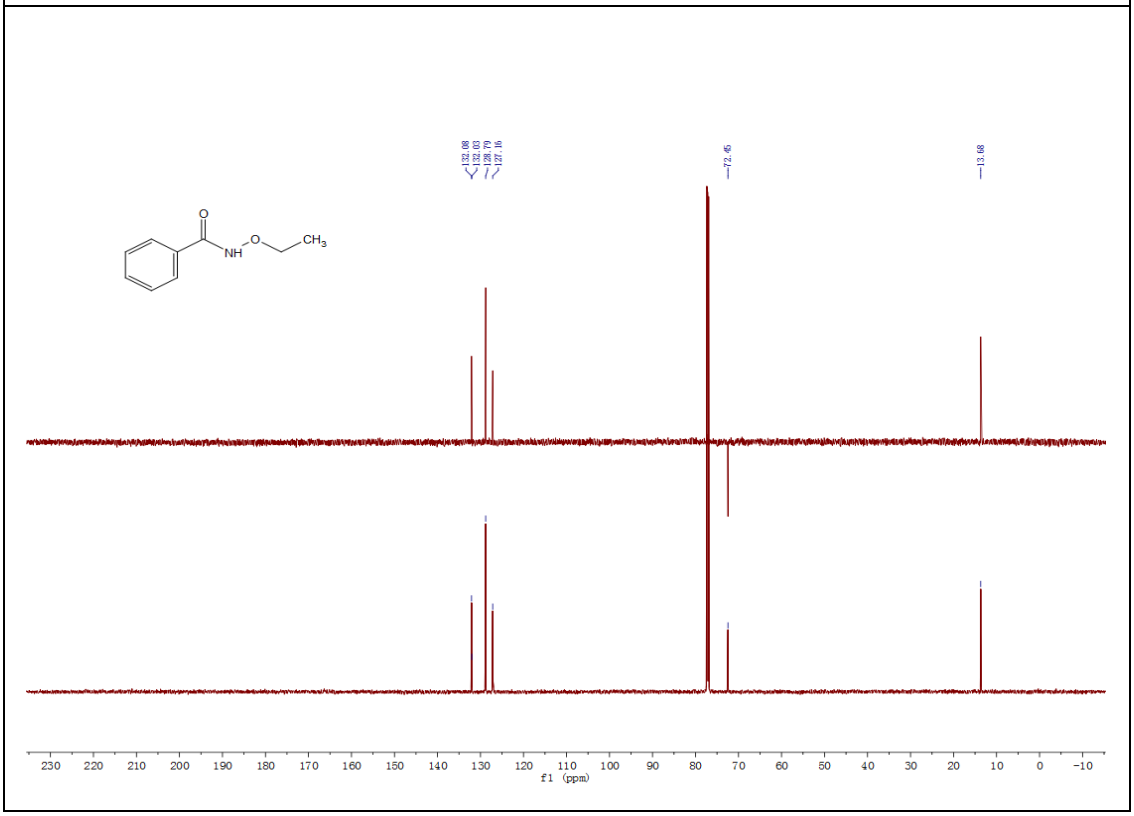
Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.024	MM	0.4953	1.23497e4	415.56857	94.3358
2	42.237	MM	1.1674	741.50897	10.58601	5.6642
Totals :				1.30912e4	426.15458	

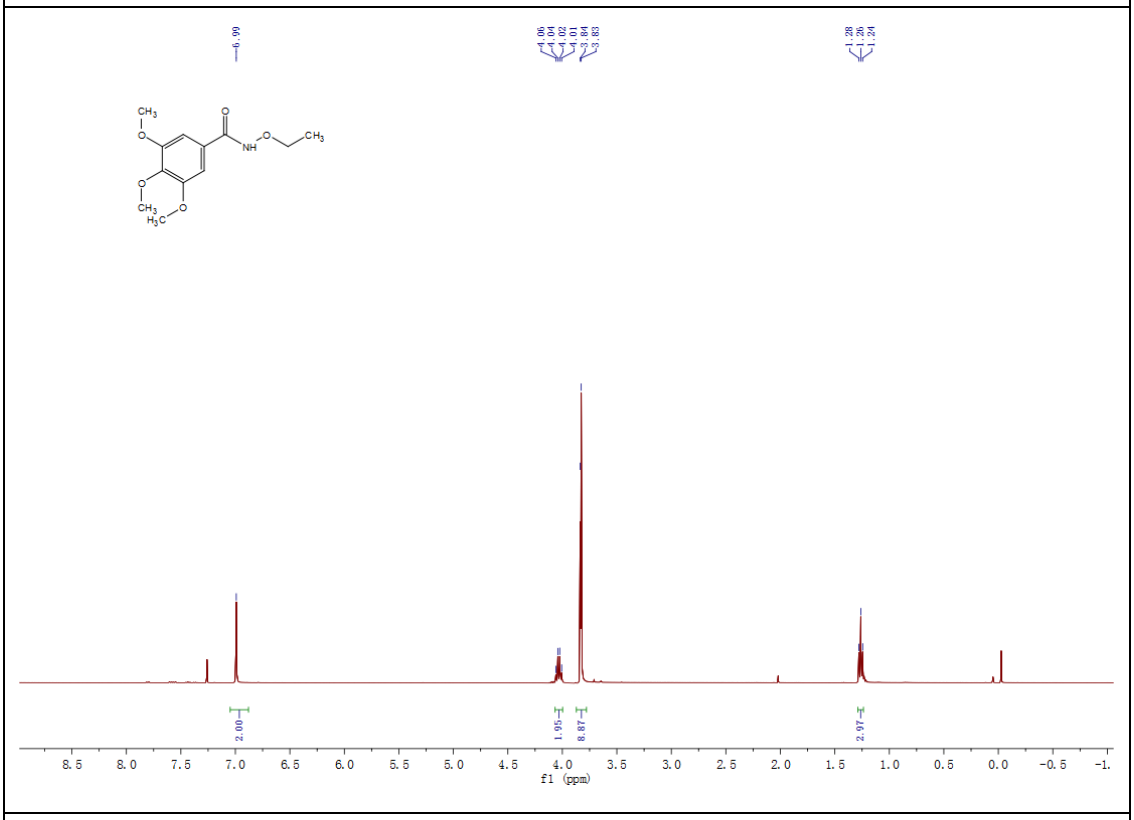
(H) Copies of ^{1}H NMR, ^{19}F NMR, and ^{13}C NMR Spectra for the Substrates and Products.

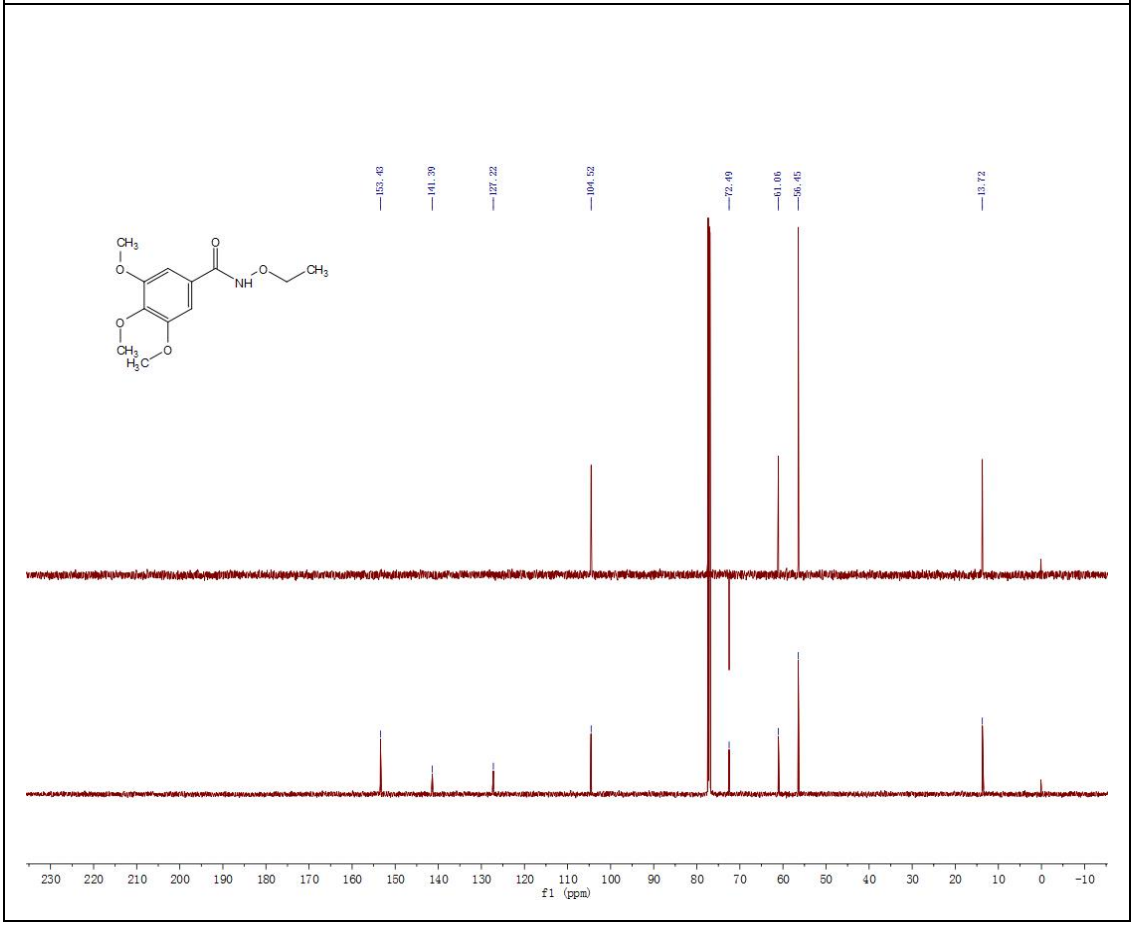
N-ethoxybenzamide (1a):



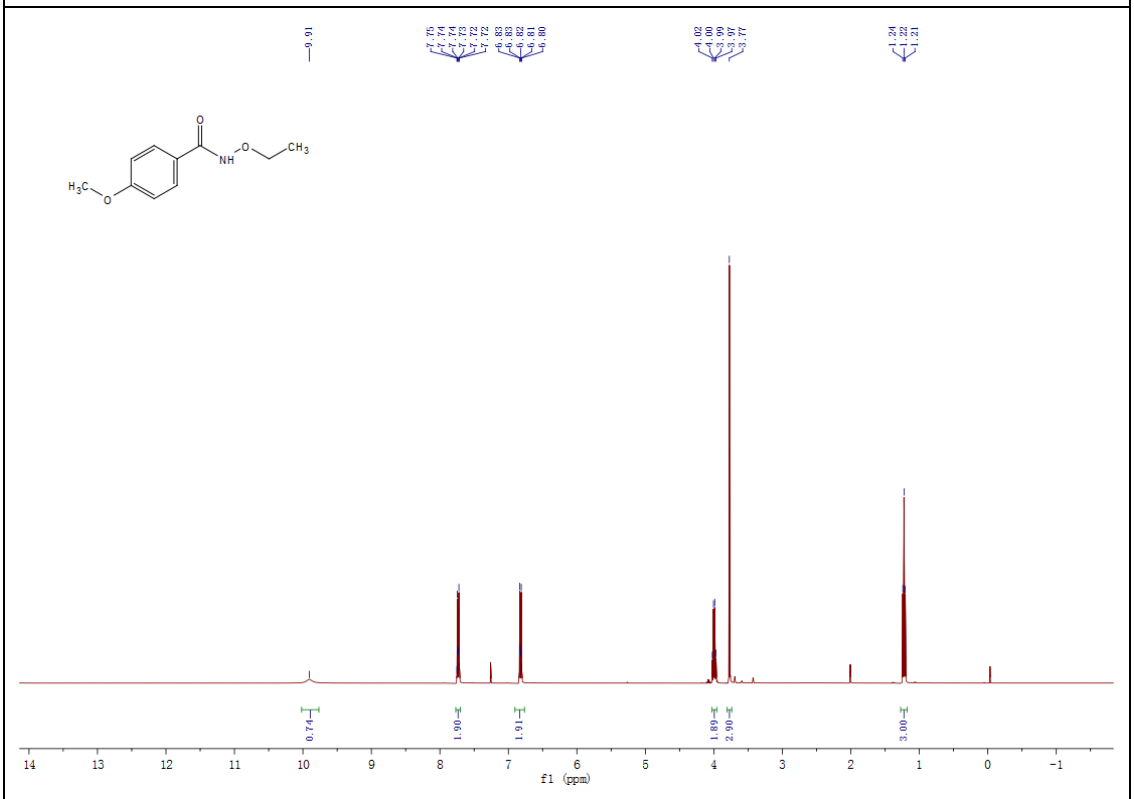


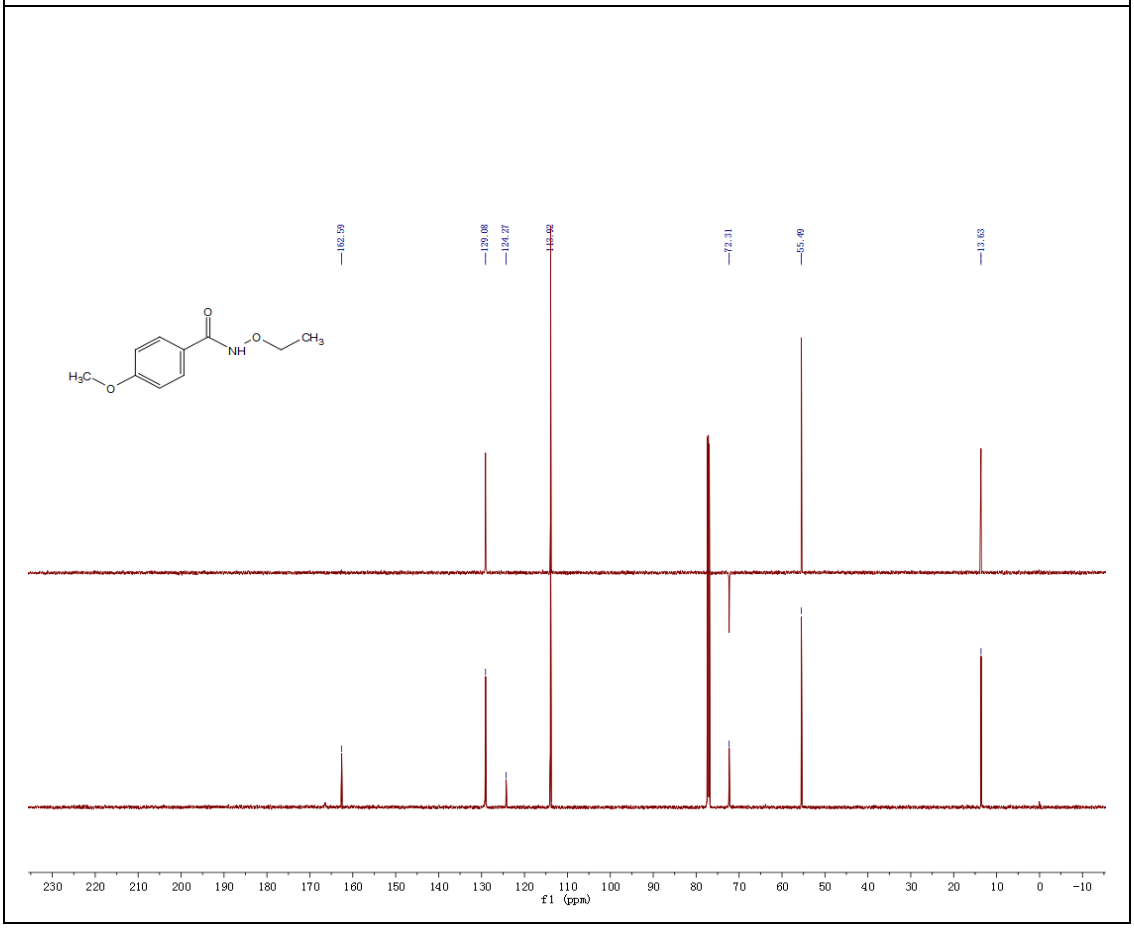
N-ethoxy-3,4,5-trimethoxybenzamide (1b):



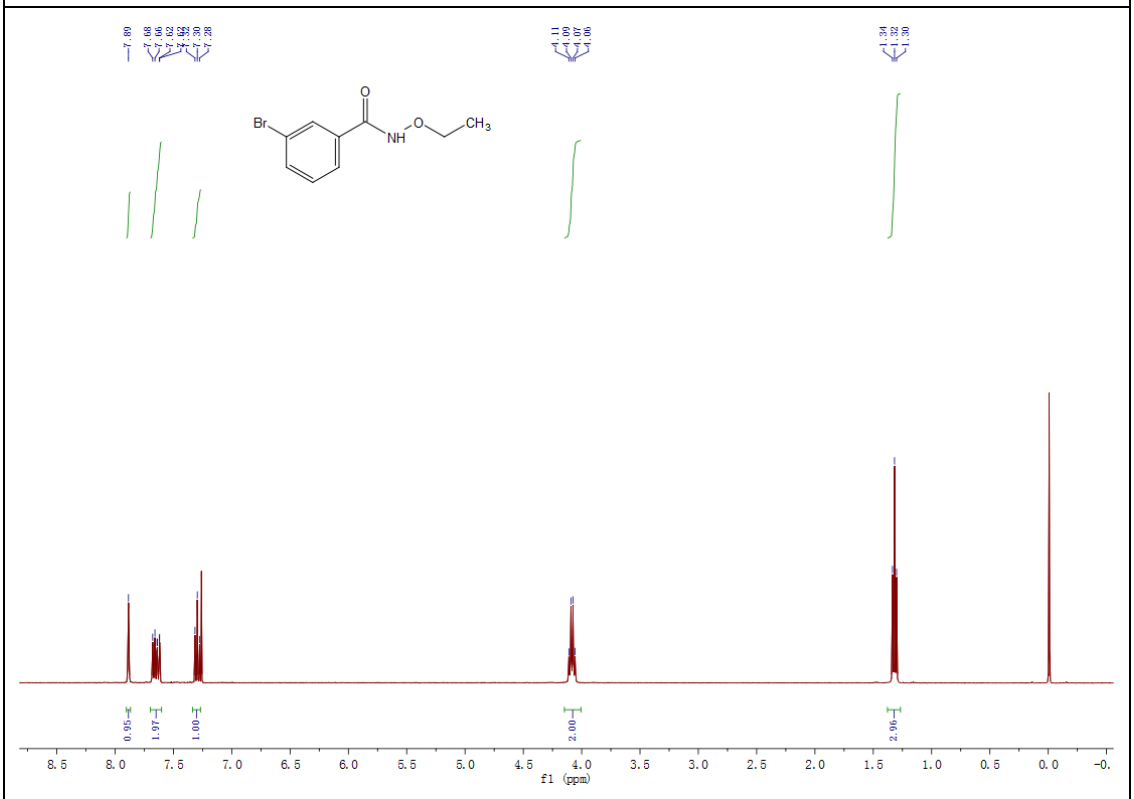


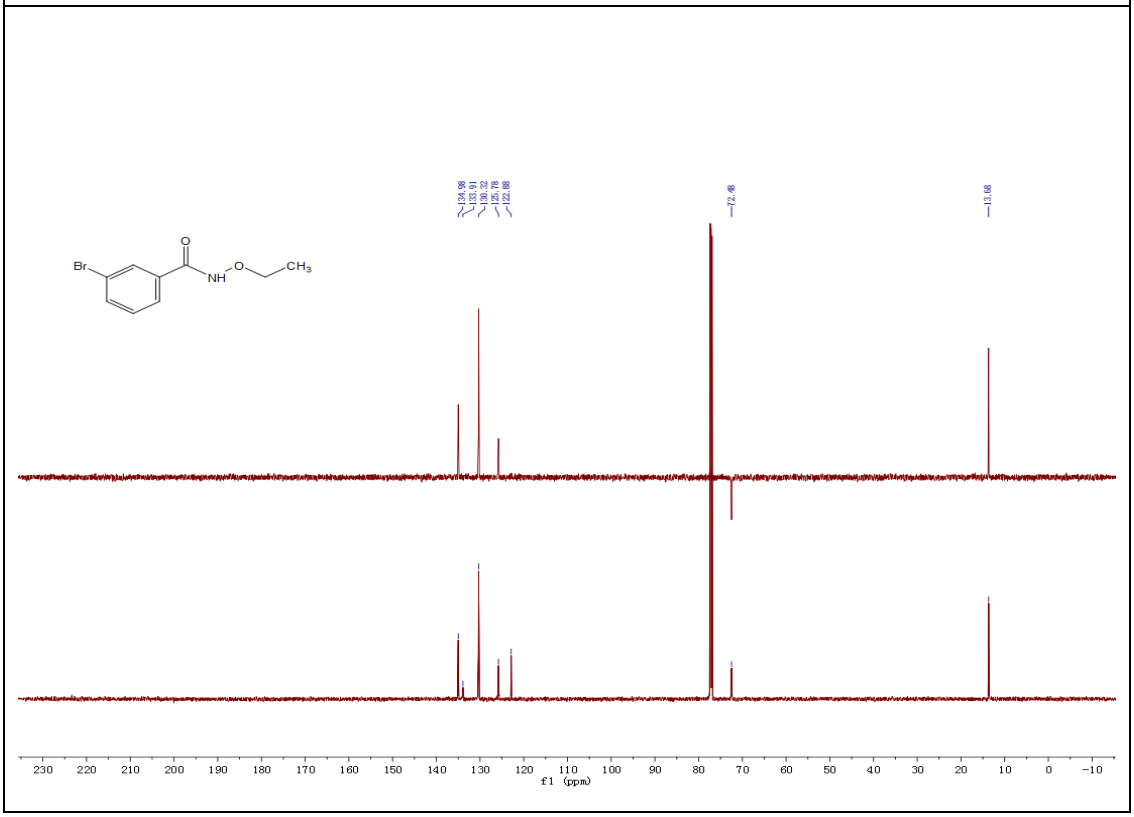
N-ethoxy-4-methoxybenzamide (1c):



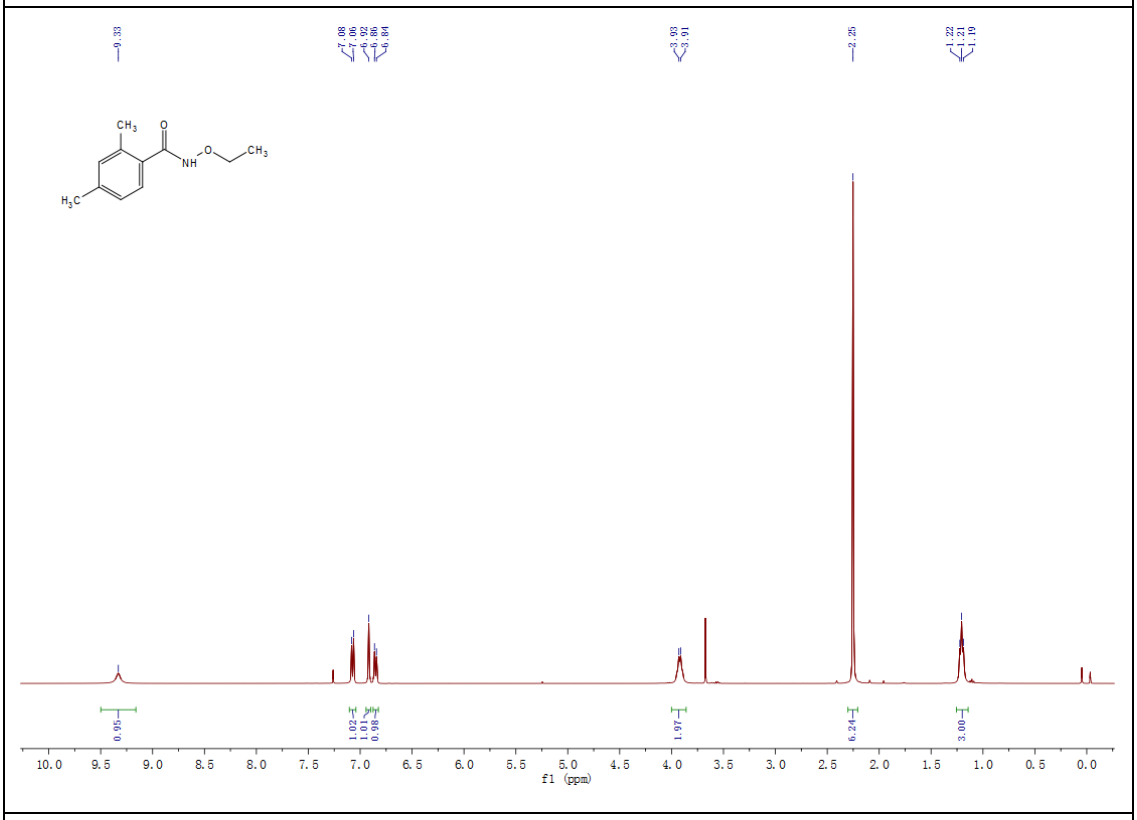


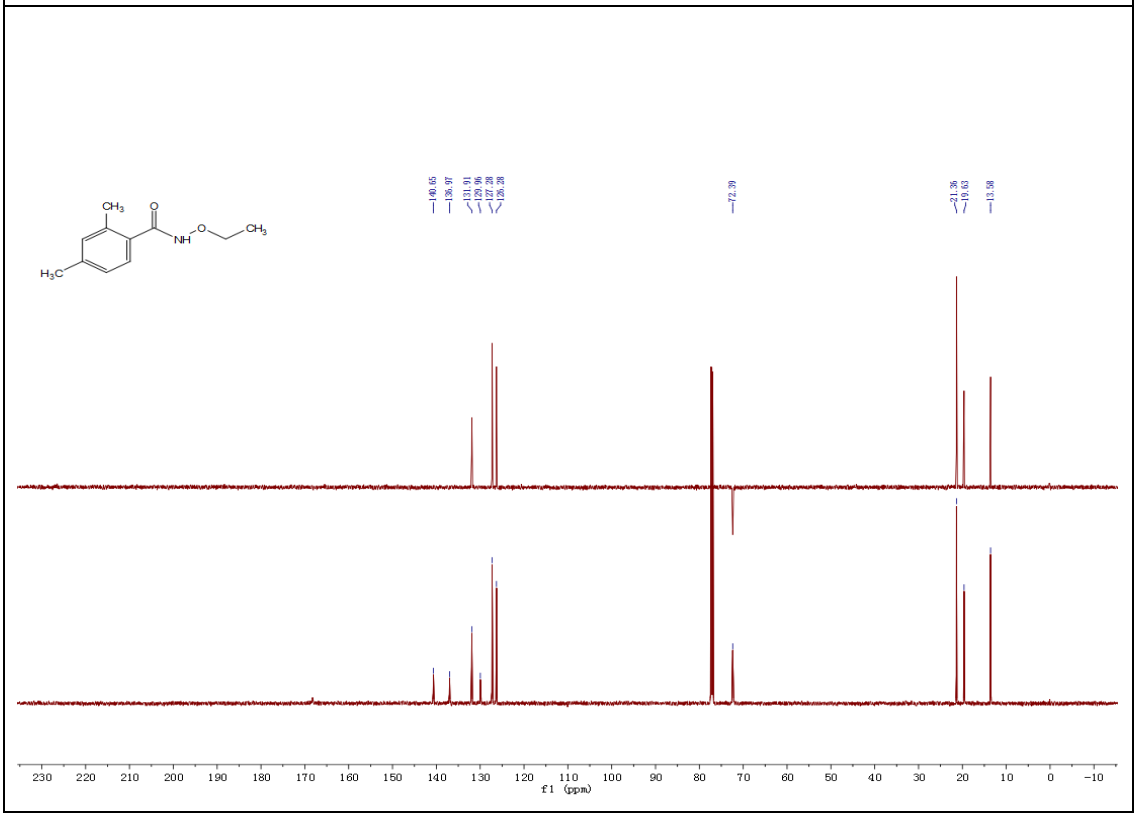
3-bromo-N-ethoxybenzamide (1d):



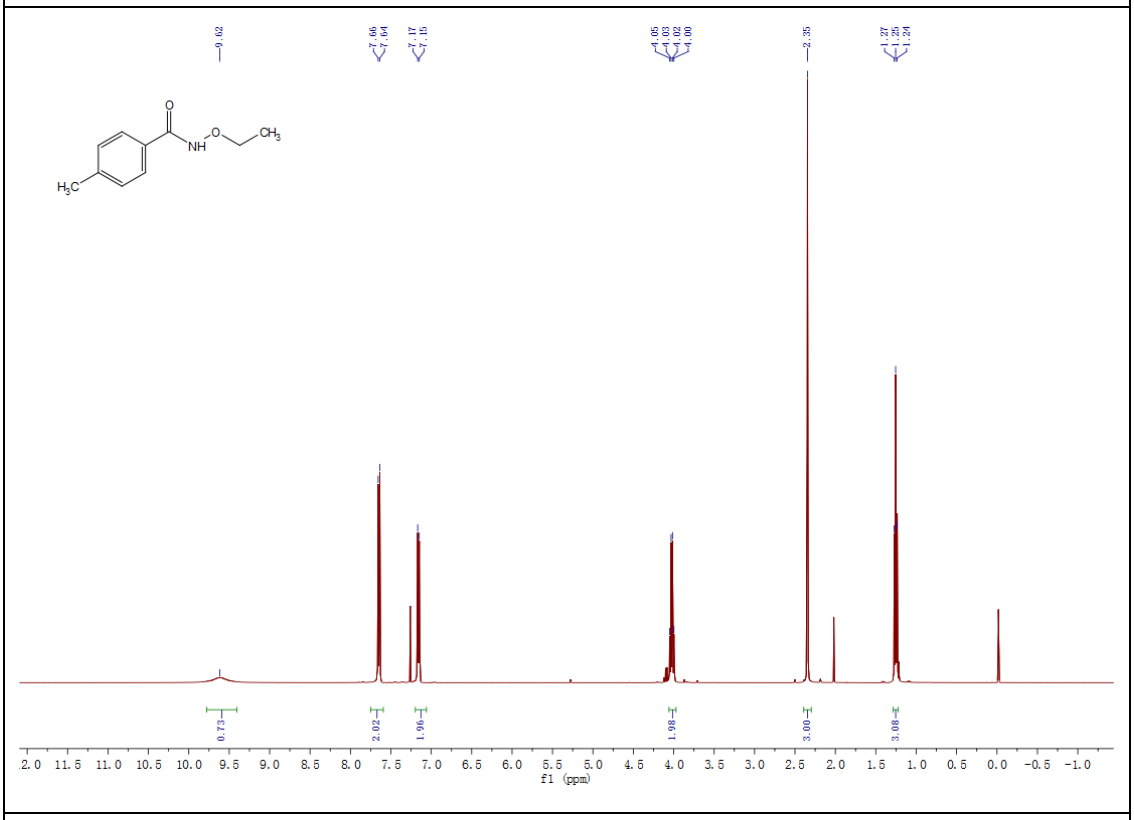


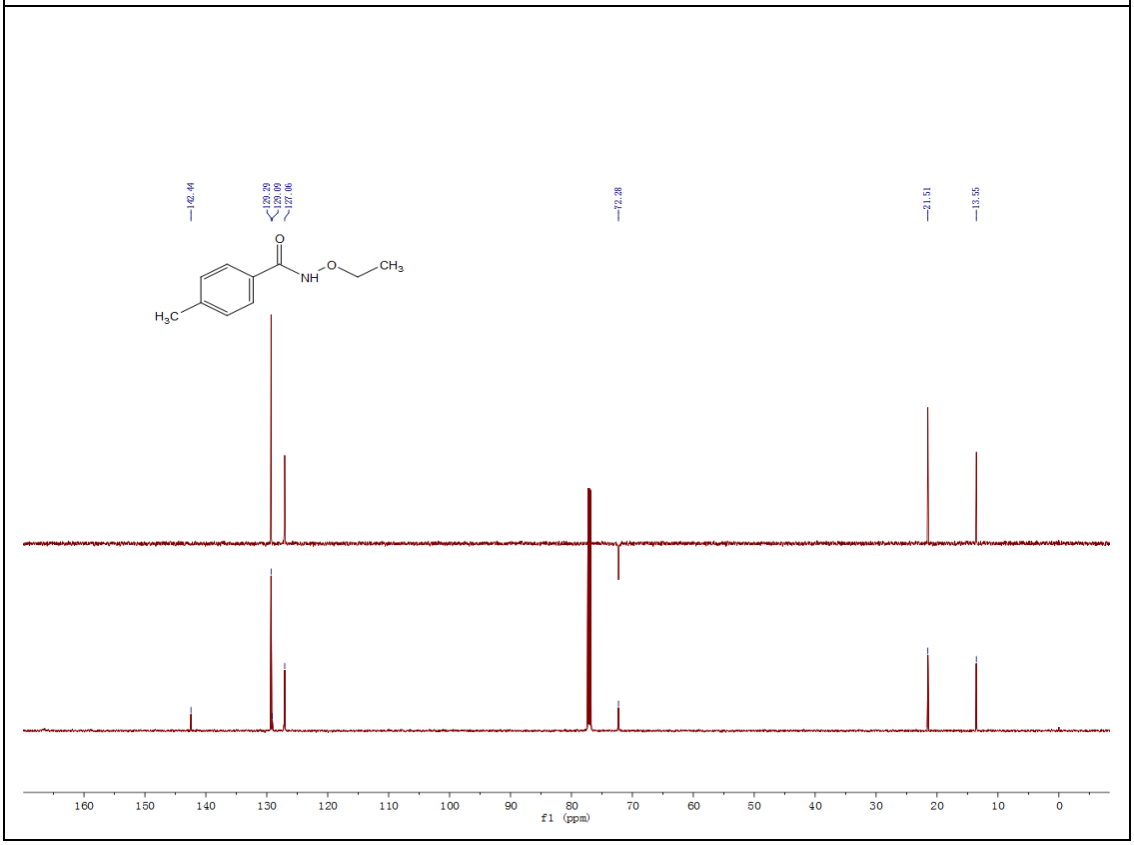
N-ethoxy-2,4-dimethylbenzamide (1e):



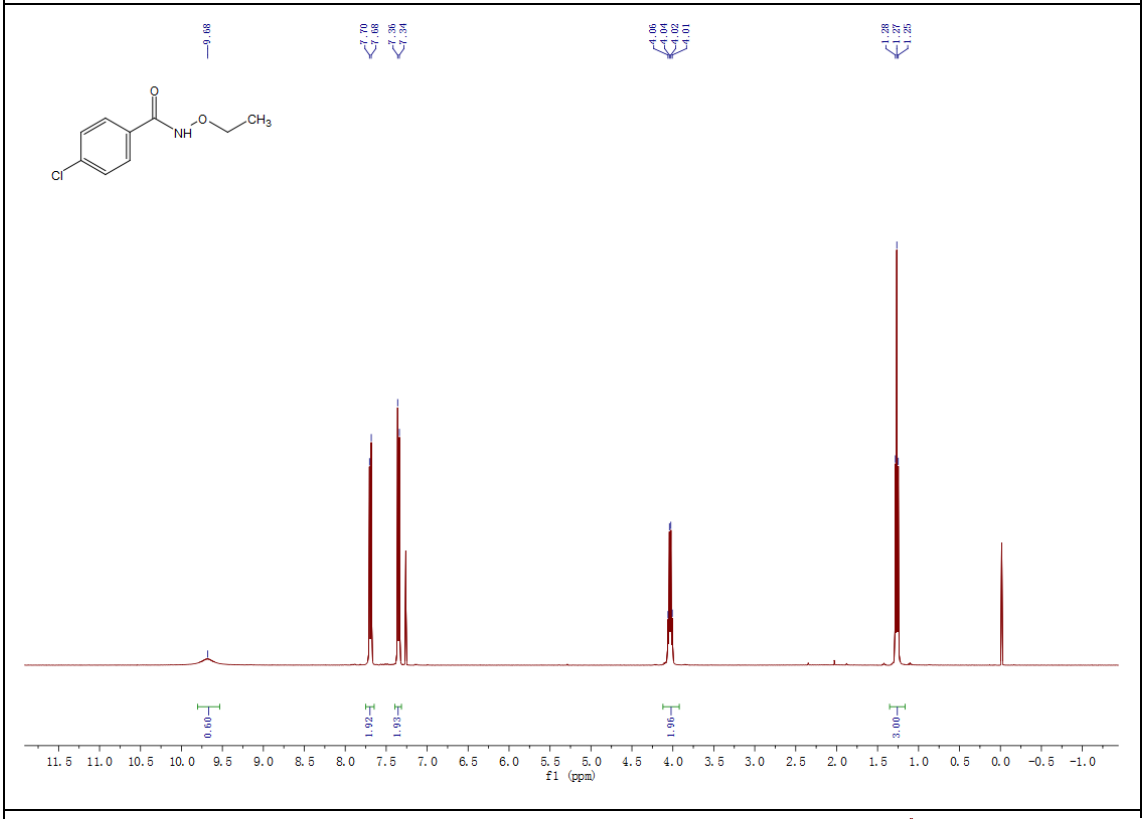


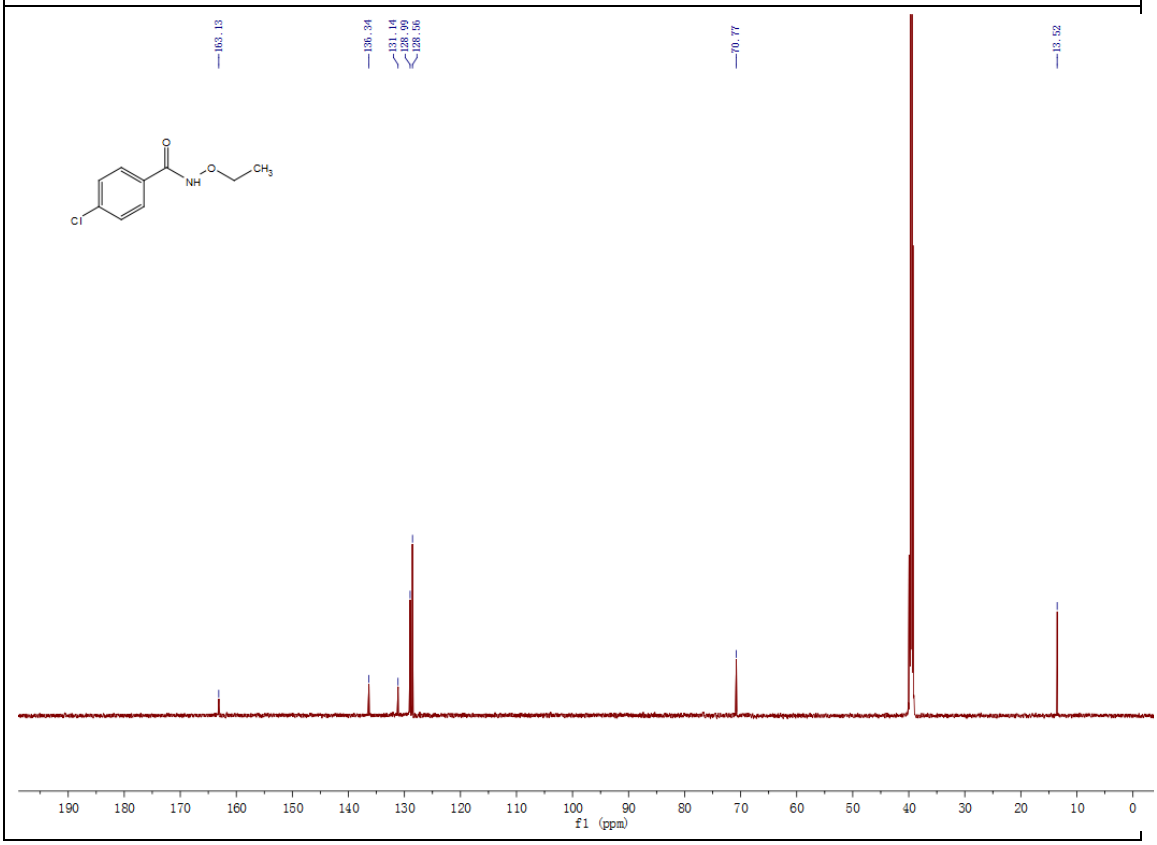
N-ethoxy-4-methylbenzamide (1f):



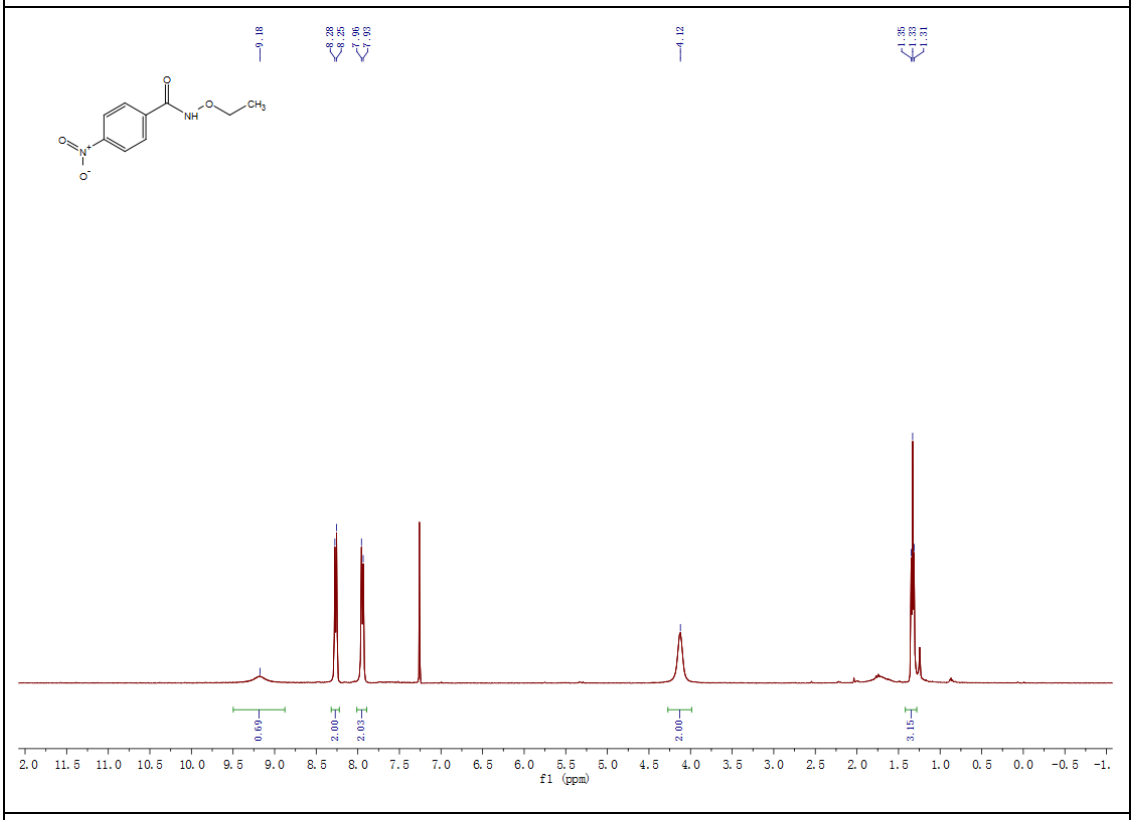


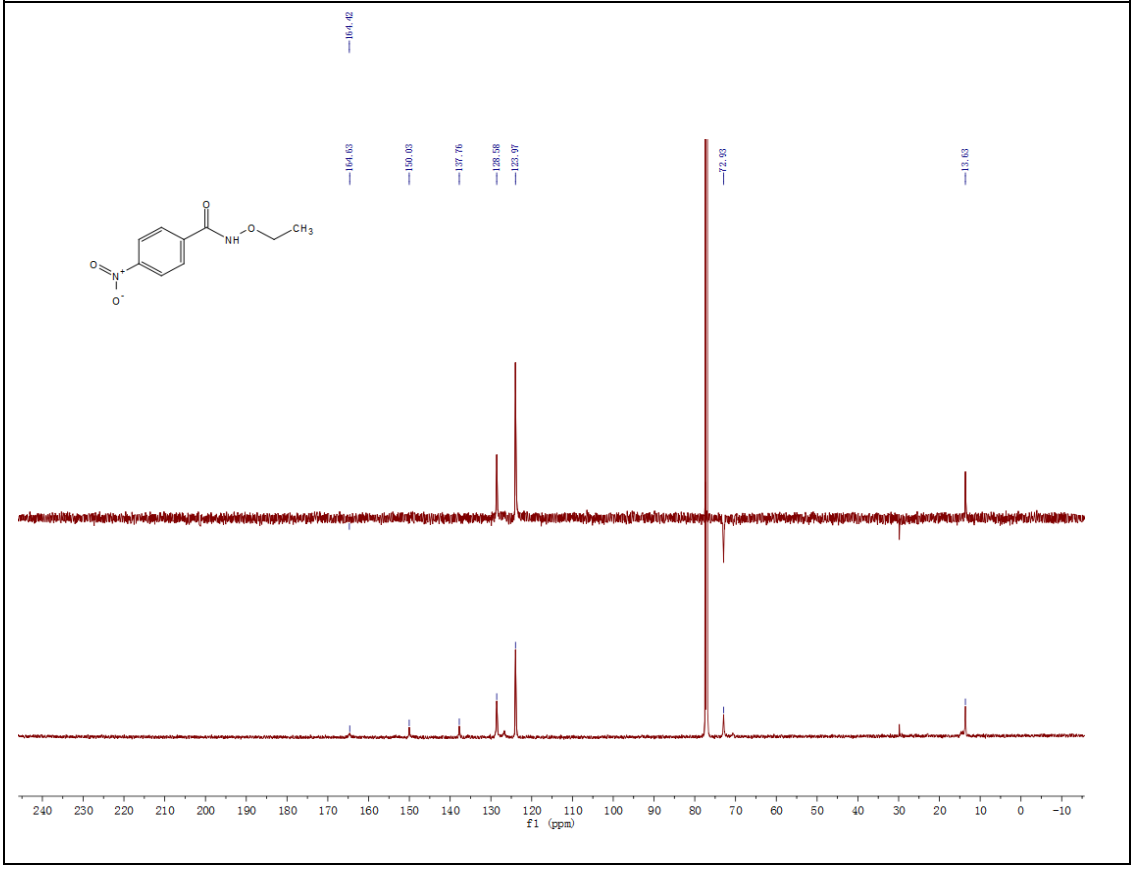
4-chloro-N-ethoxybenzamide (1g):



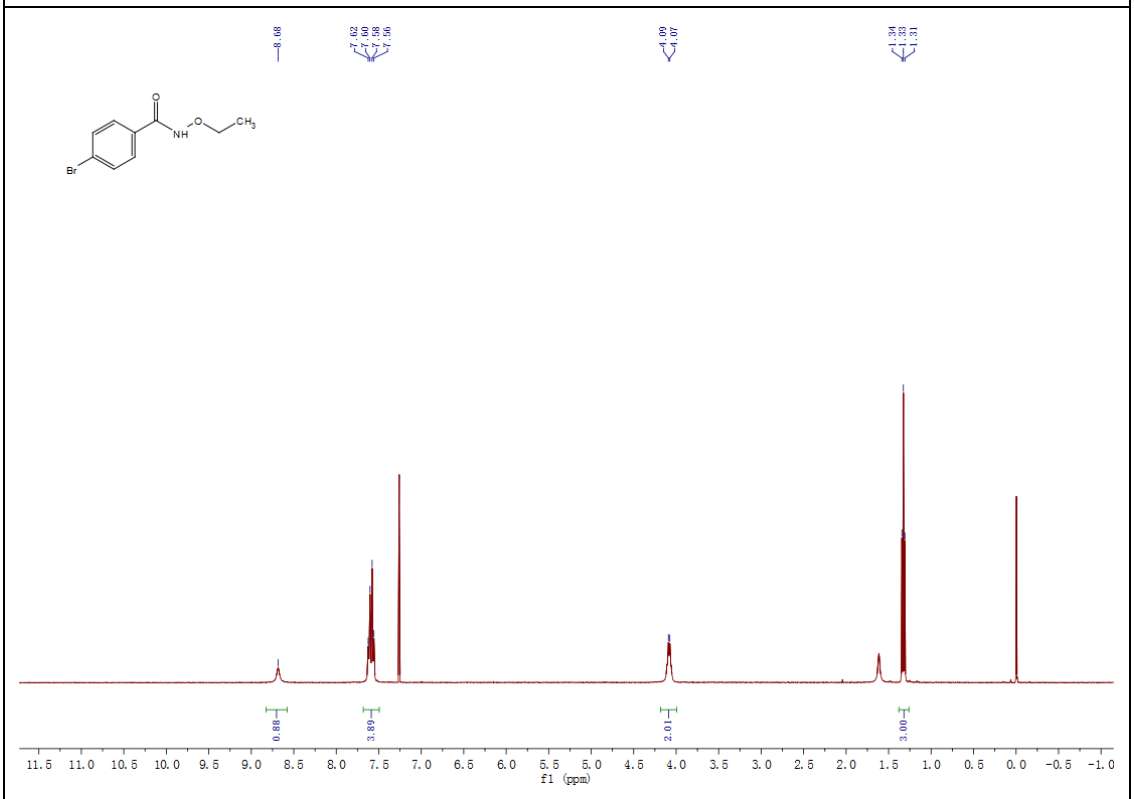


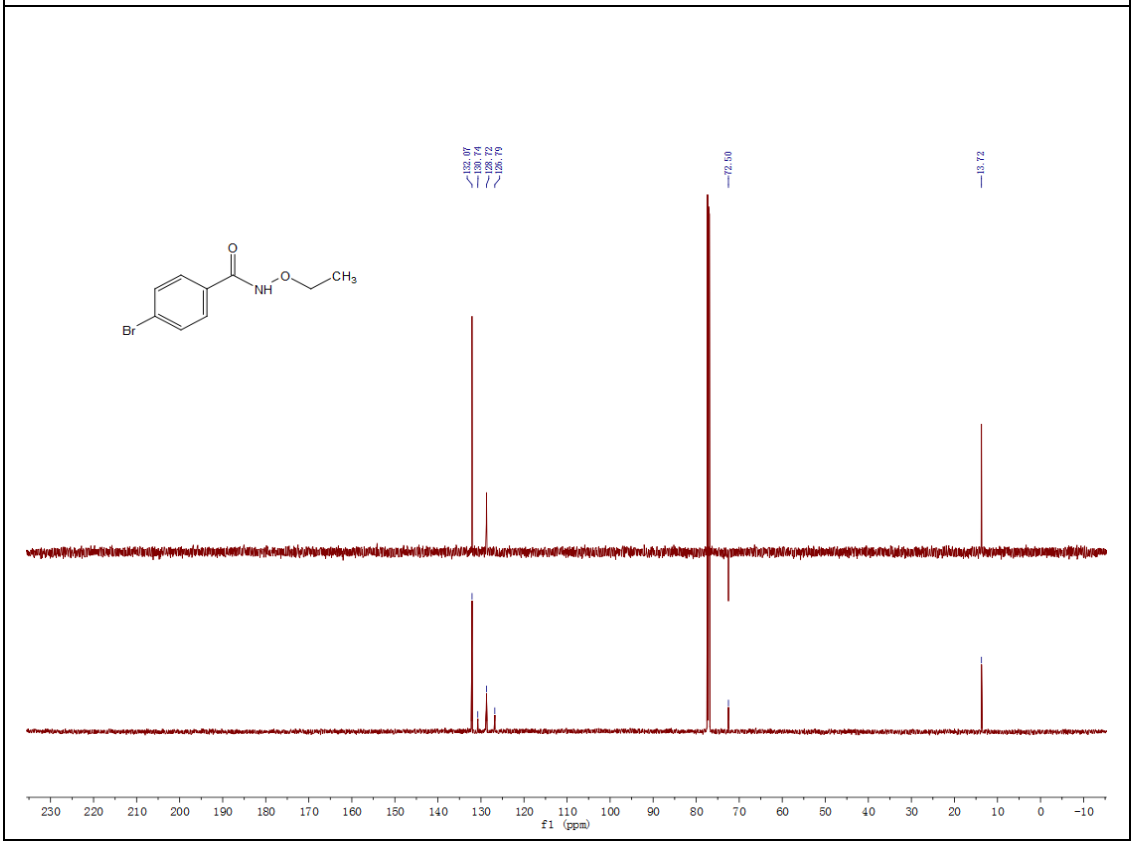
N-ethoxy-4-nitrobenzamide (1h):



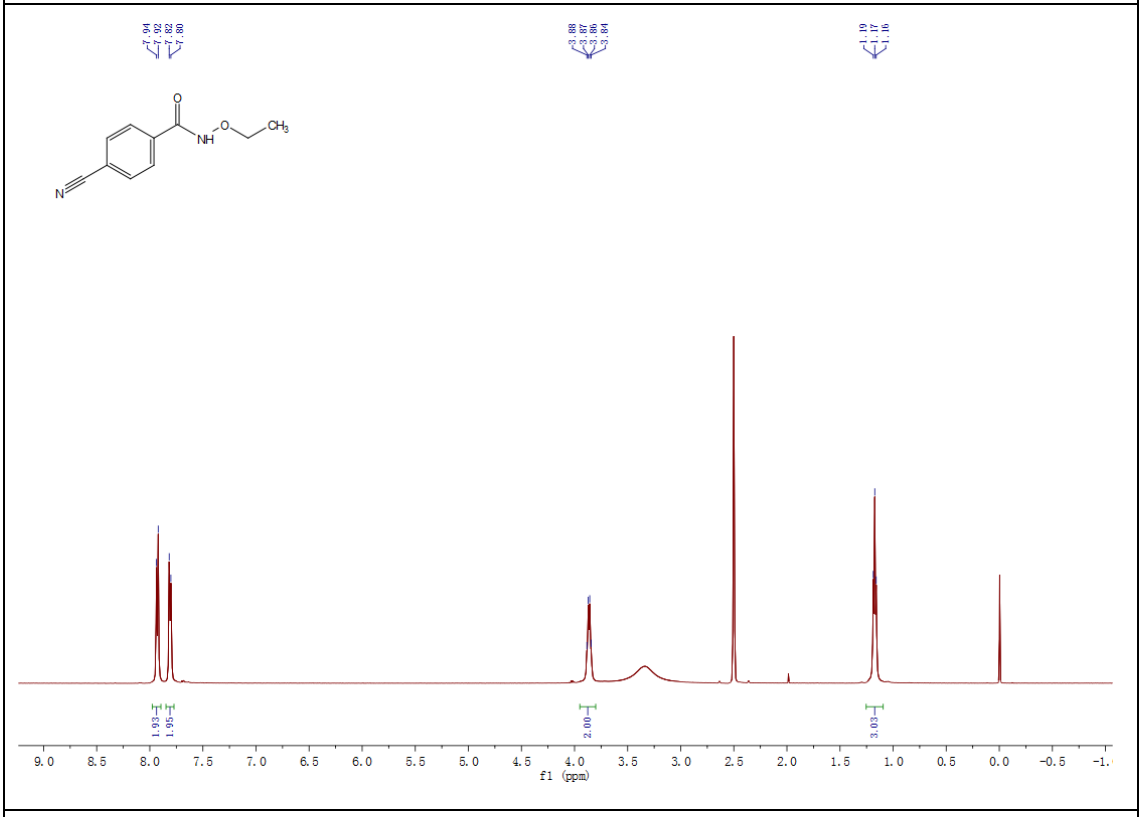


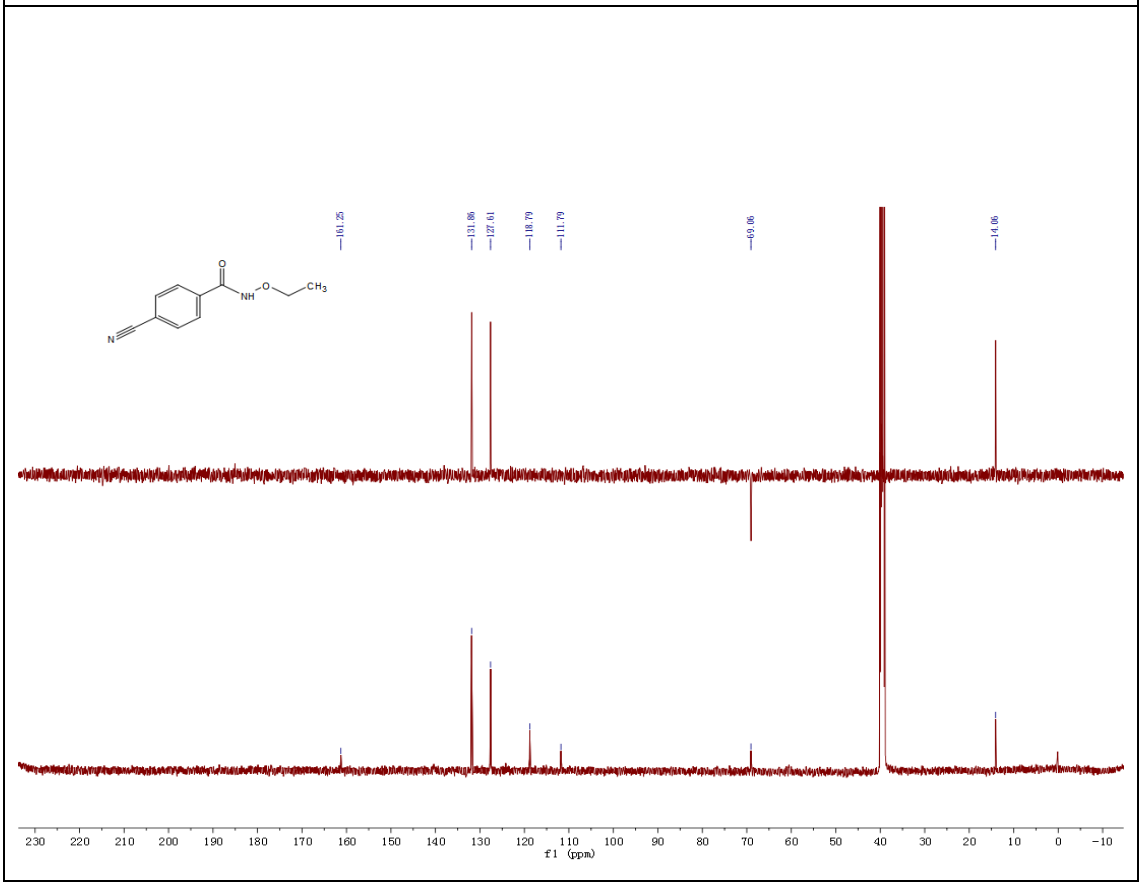
4-bromo-N-ethoxybenzamide (1i):



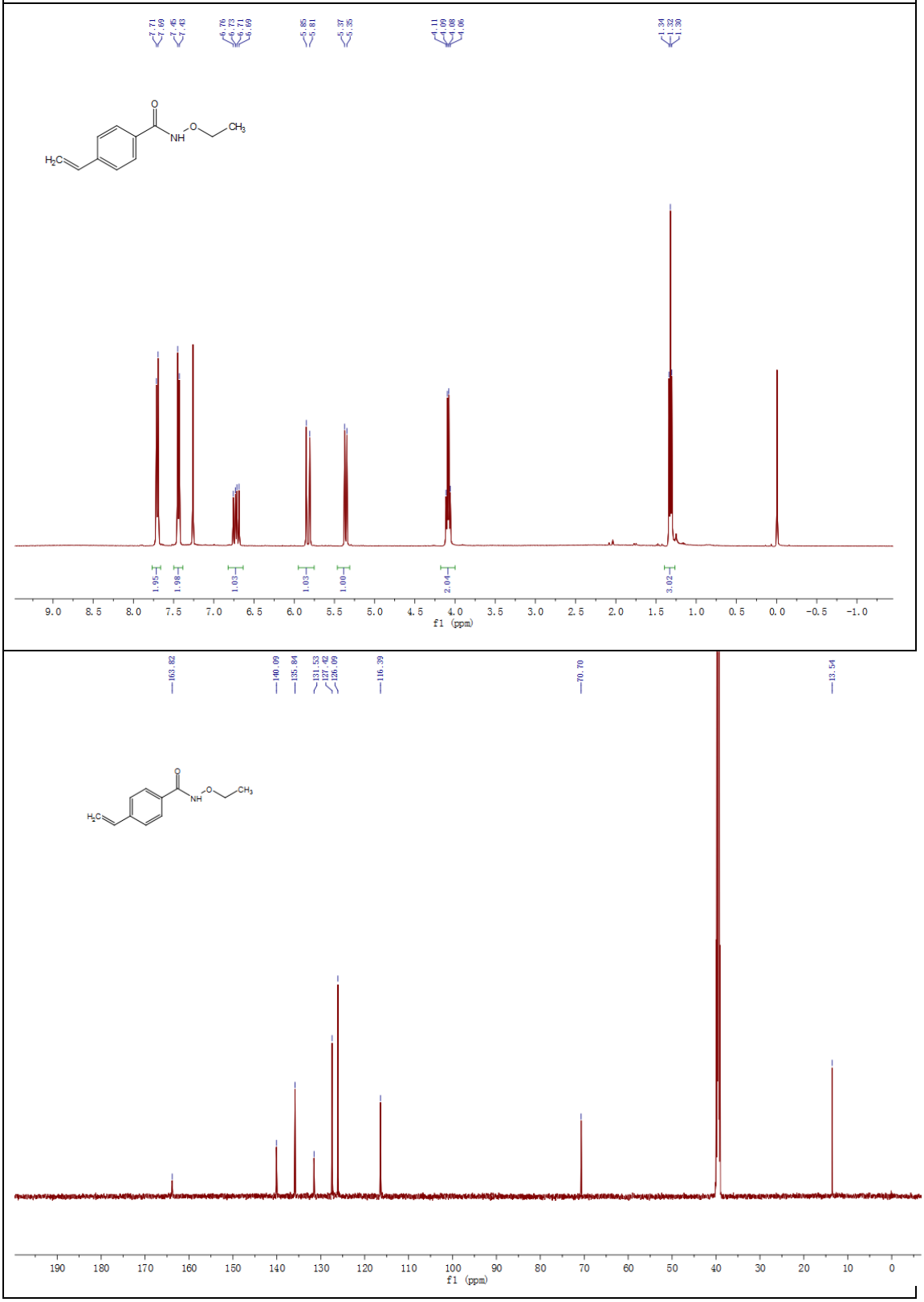


4-cyano-N-ethoxybenzamide (1j):

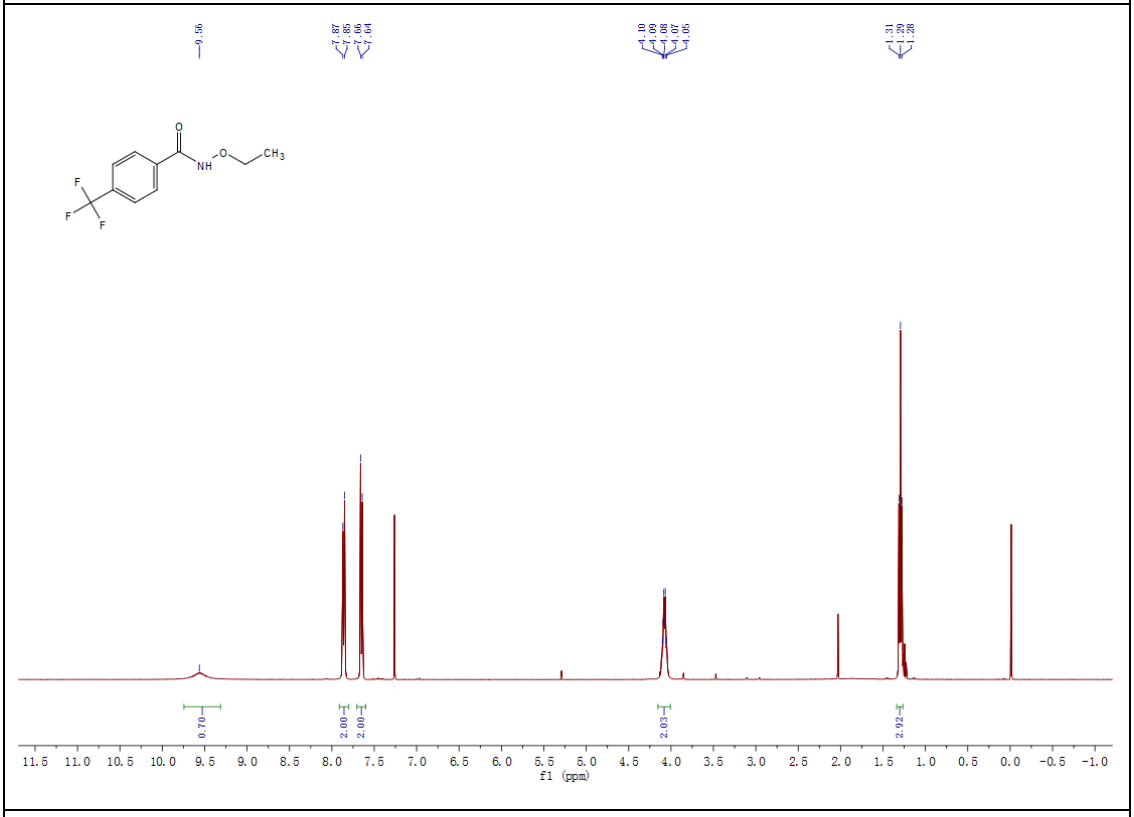


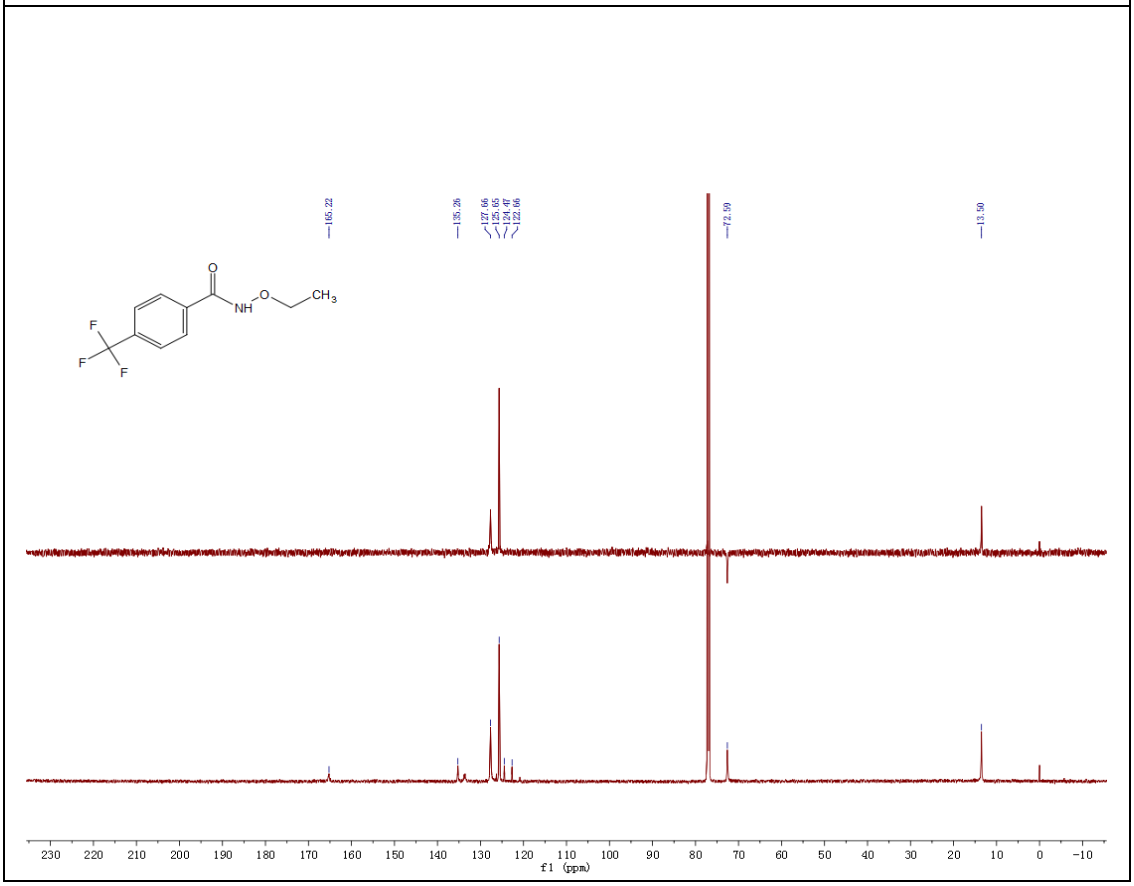


N-ethoxy-4-vinylbenzamide (1k):

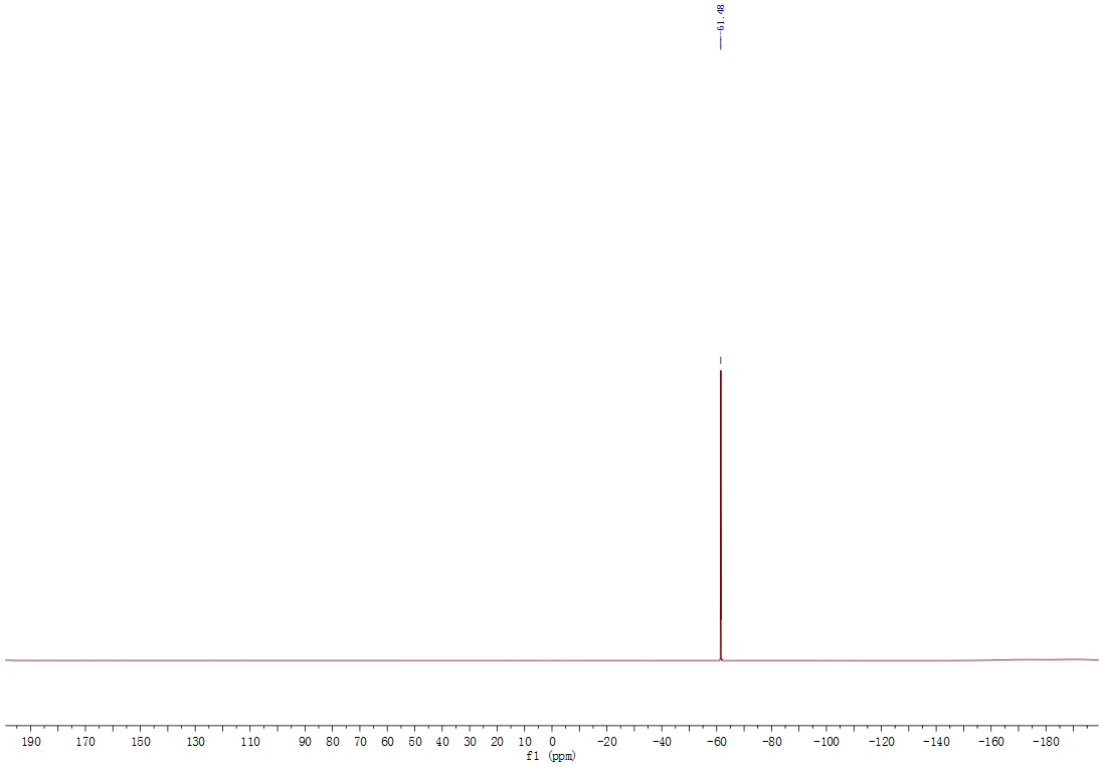


N-ethoxy-4-(trifluoromethyl)benzamide (1l):

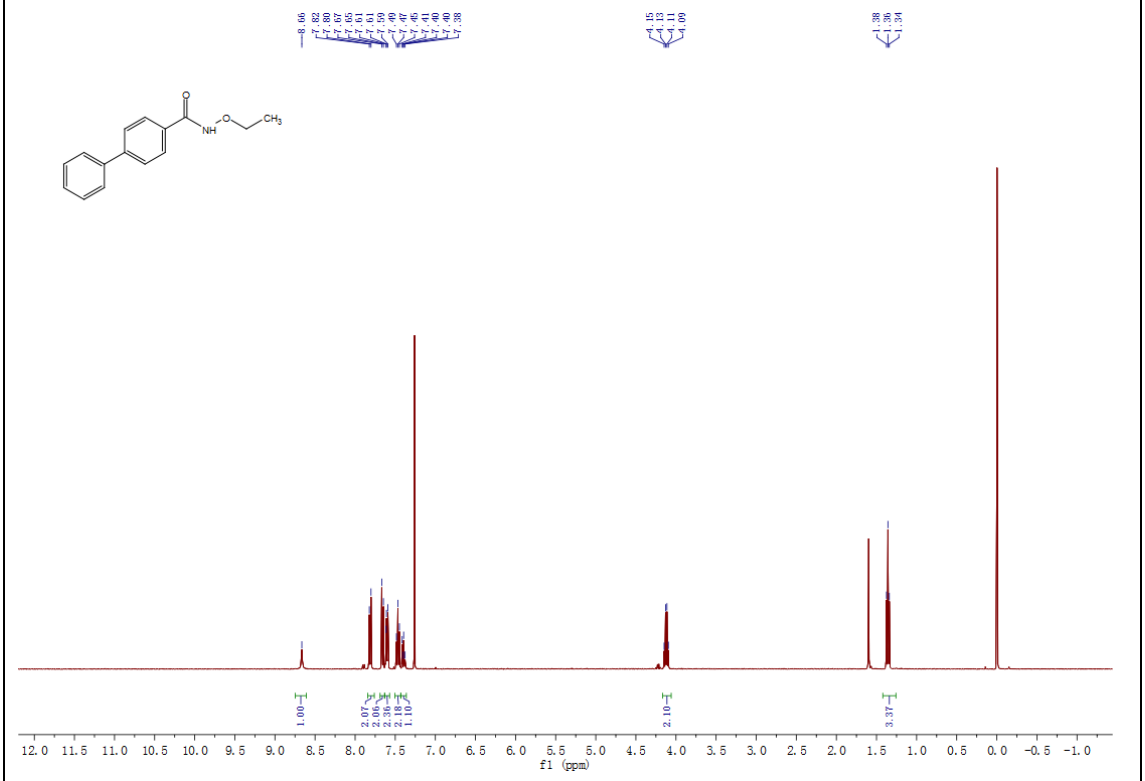


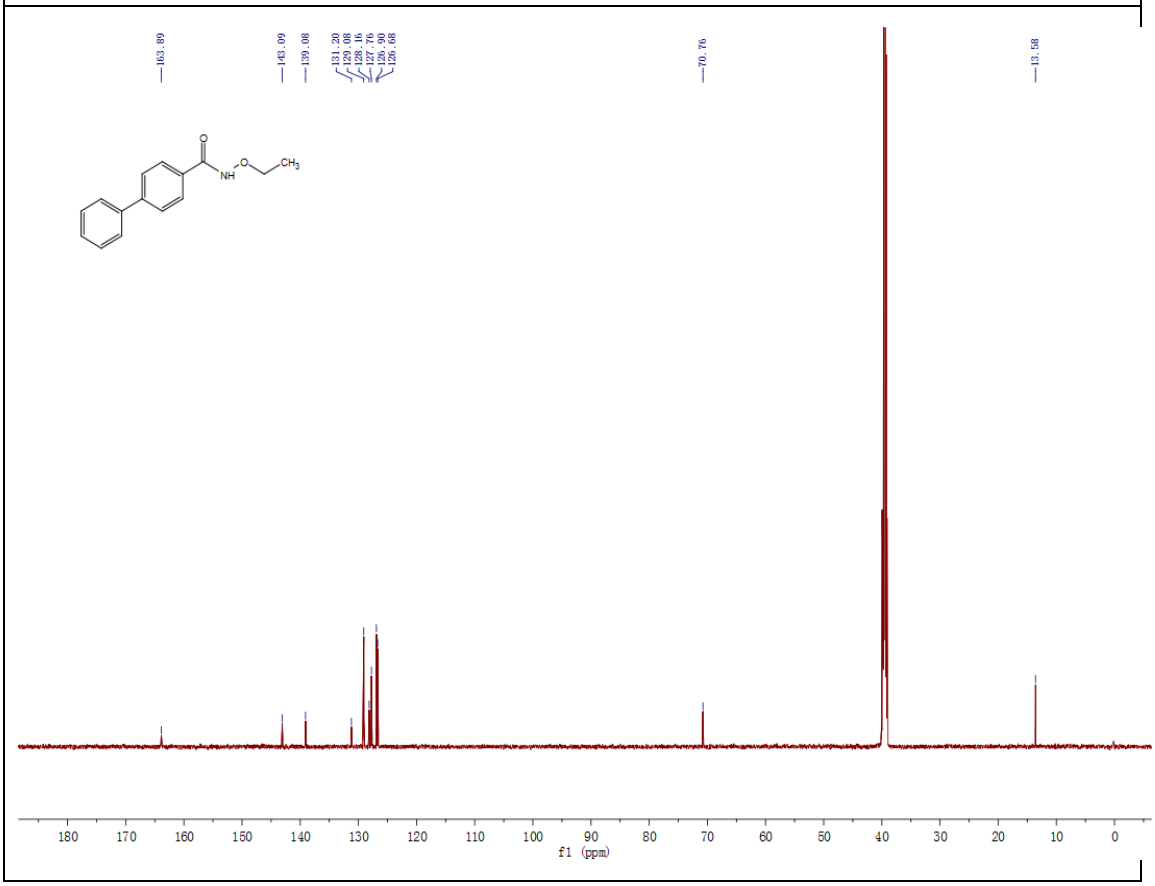


^{19}F NMR of *N*-ethoxy-4-(trifluoromethyl)benzamide (1l):

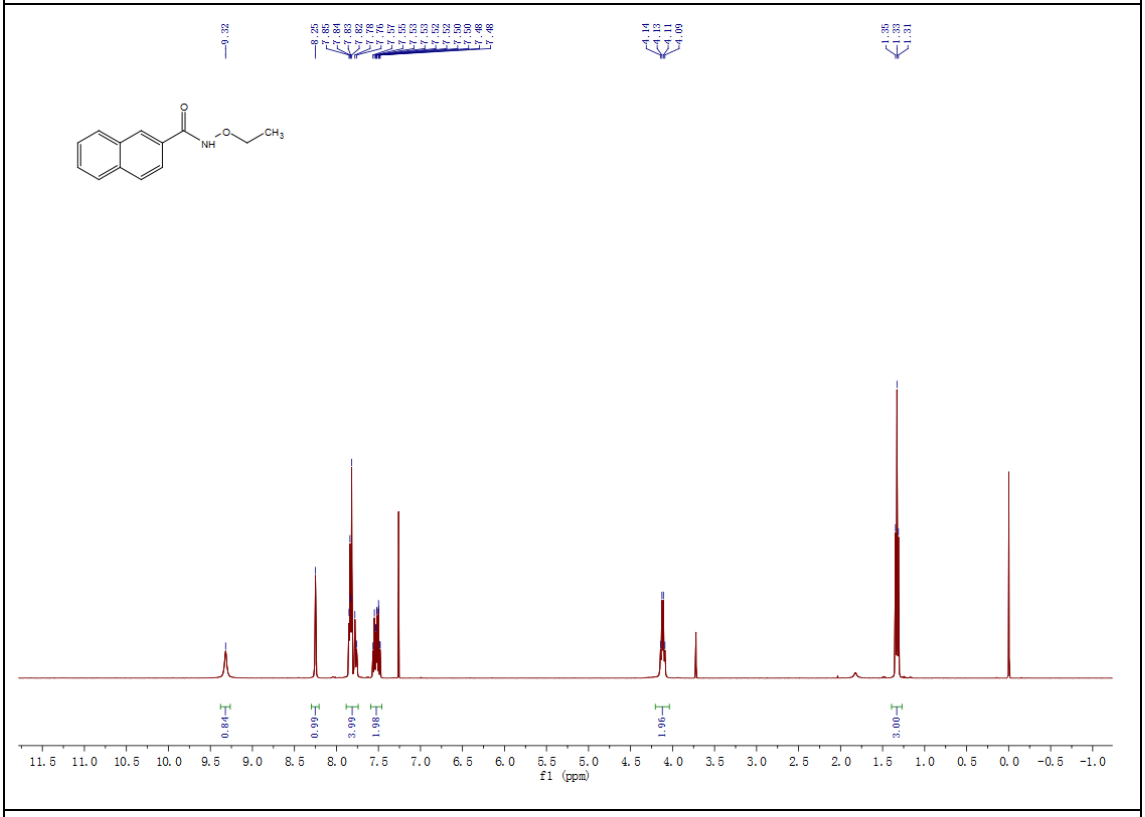


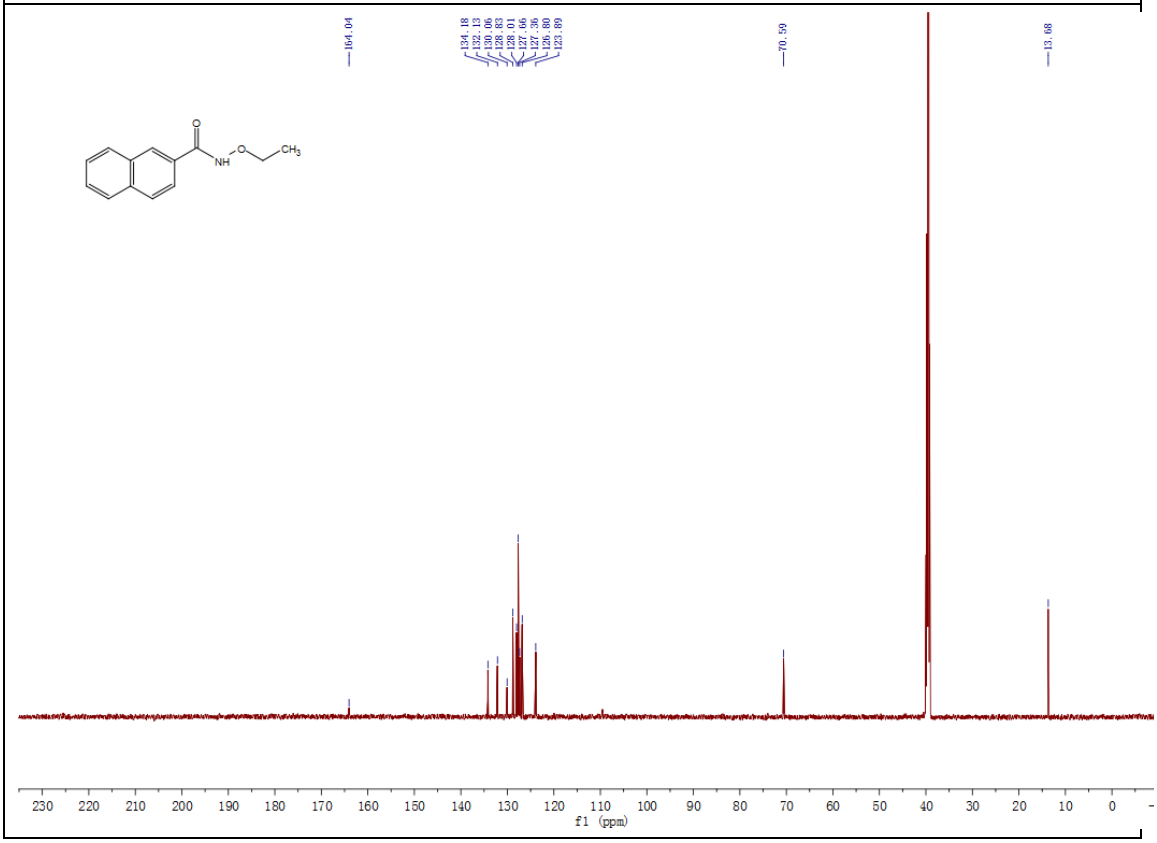
_N_-ethoxy-[1,1'-biphenyl]-4-carboxamide (1m):



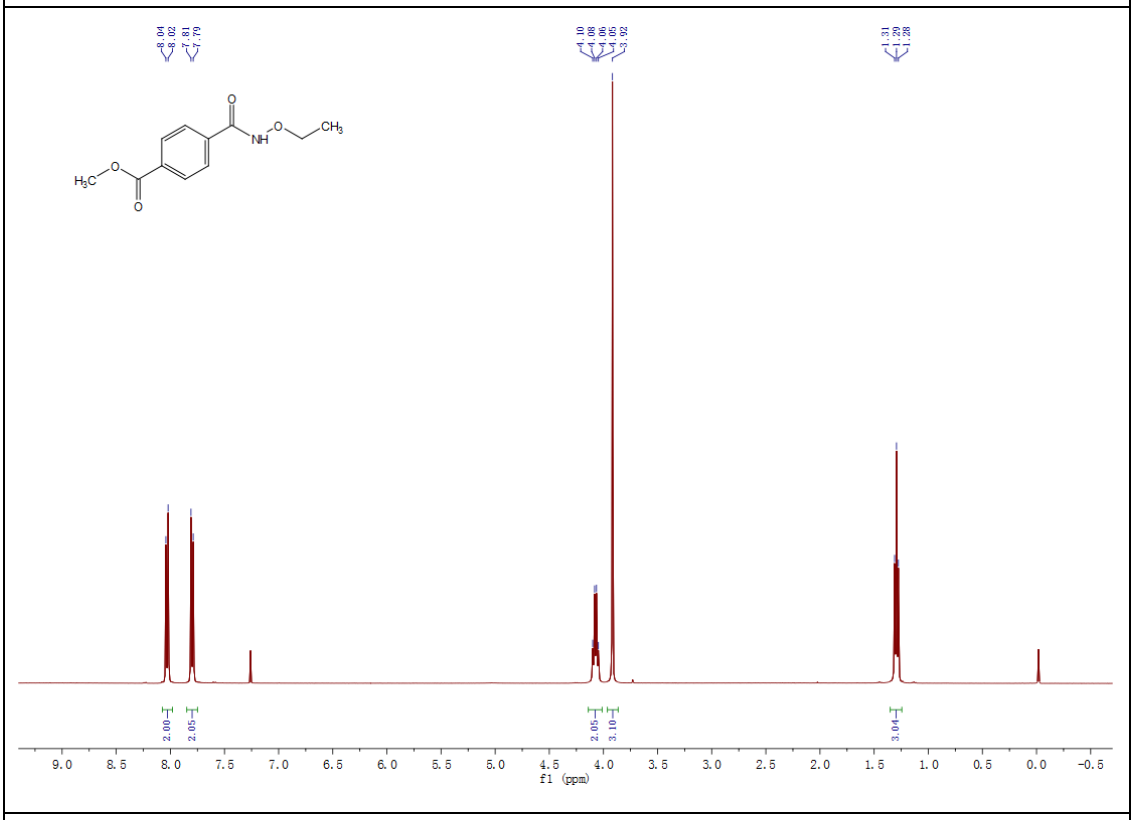


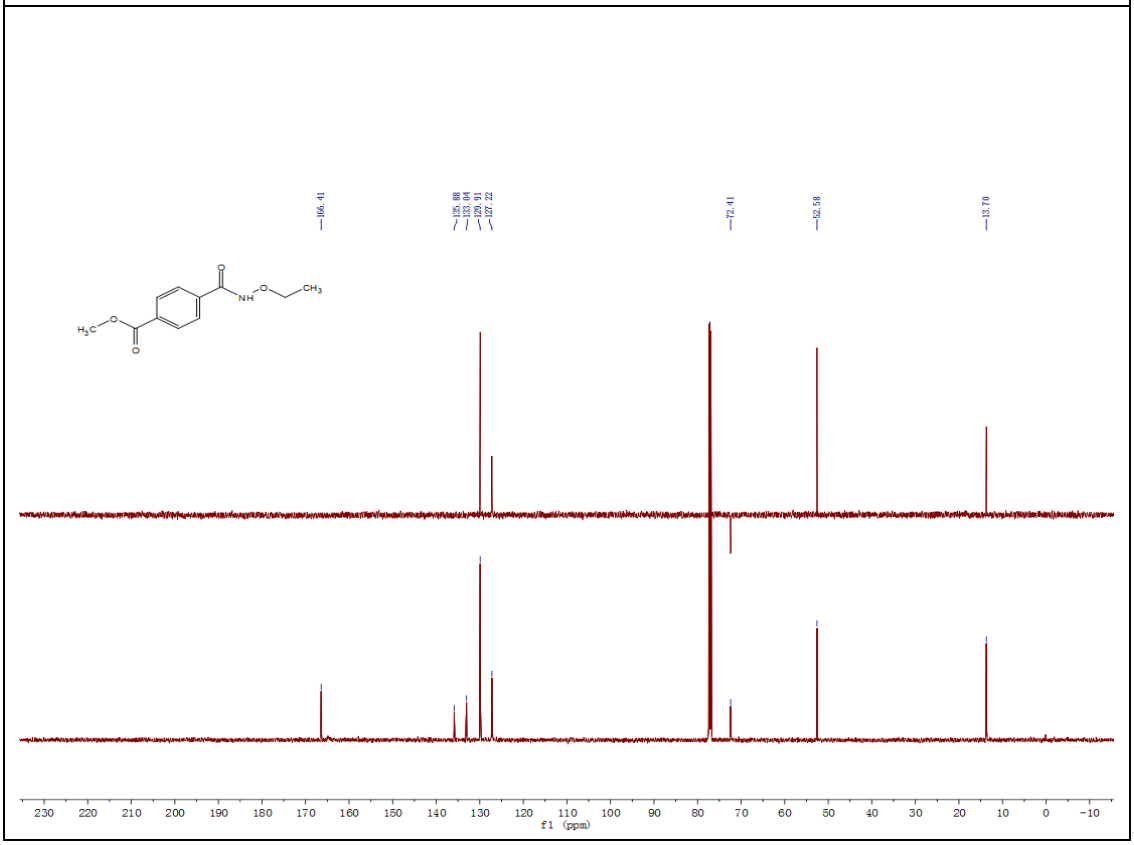
N-ethoxy-2-naphthamide (1n):



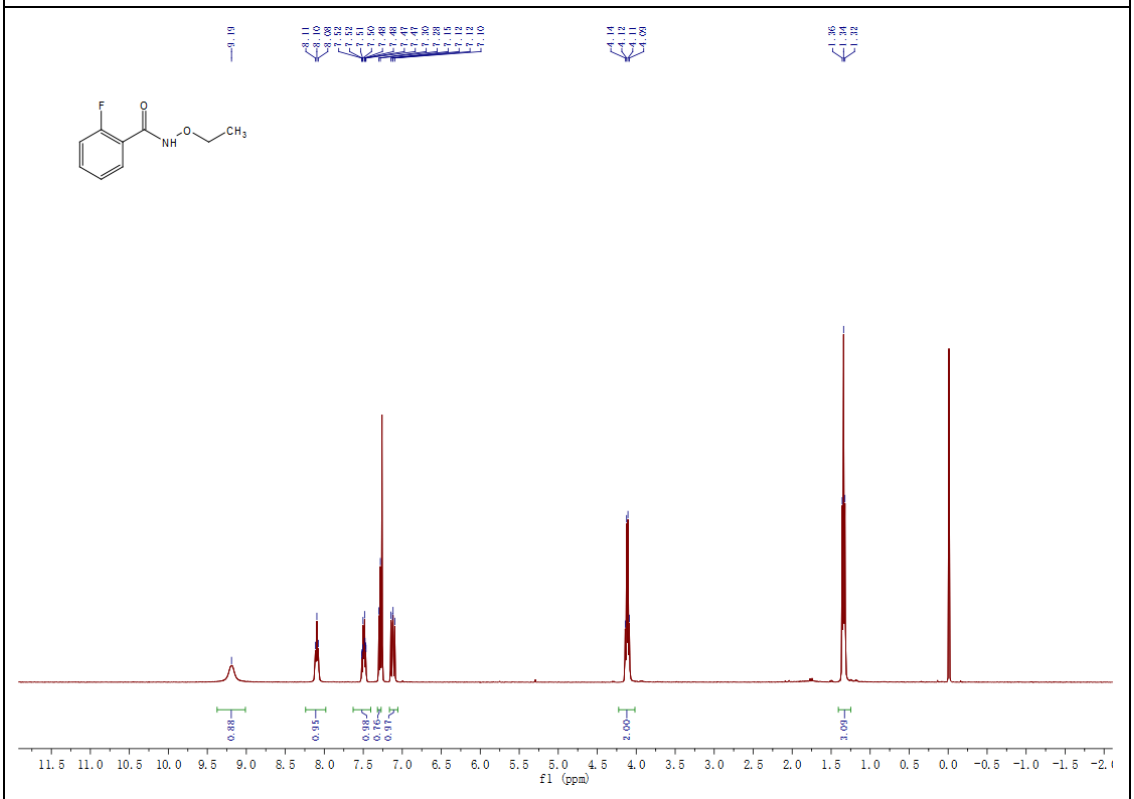


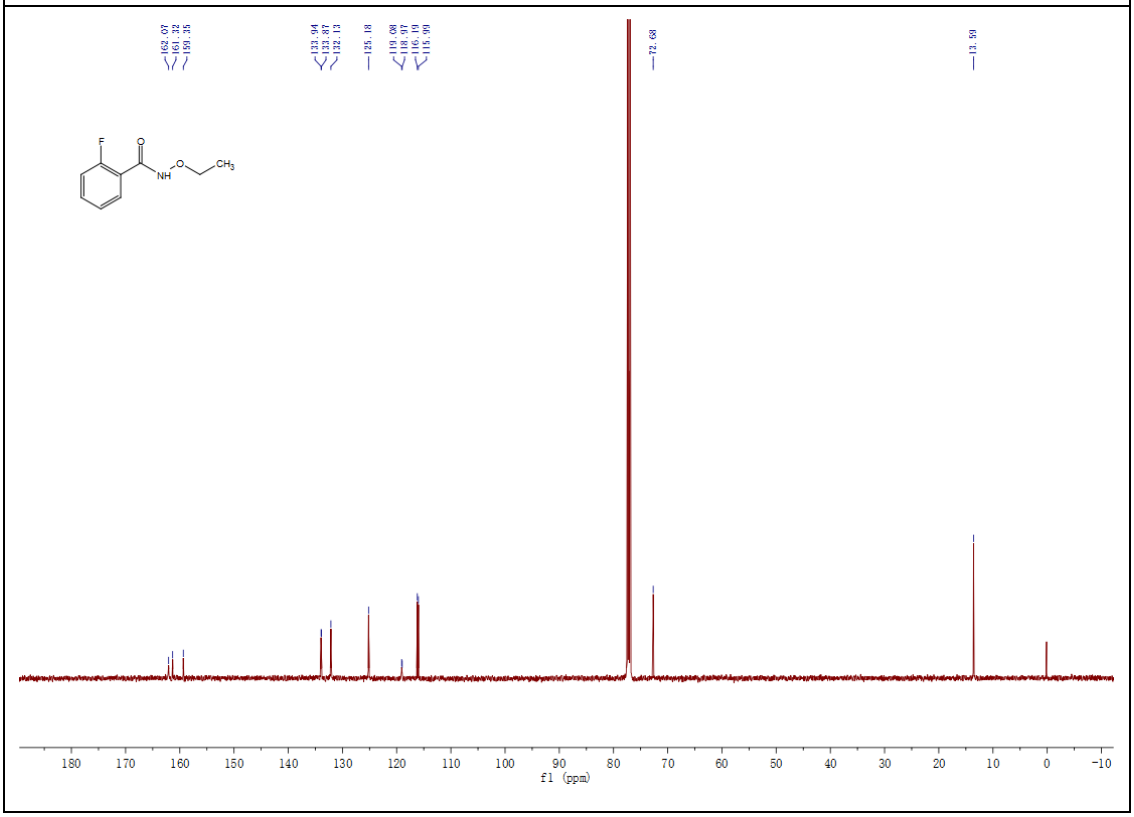
Methyl 4-(ethoxycarbamoyl)benzoate (1o):



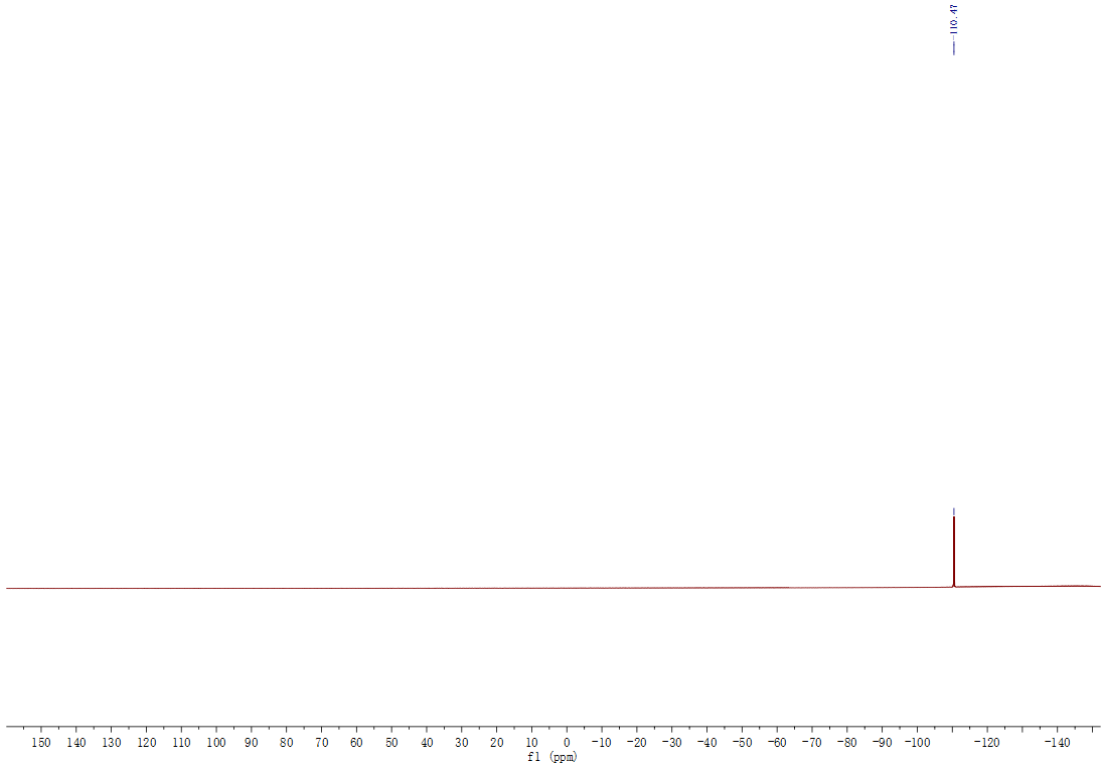


_N_-ethoxy-2-fluorobenzamide (1p):

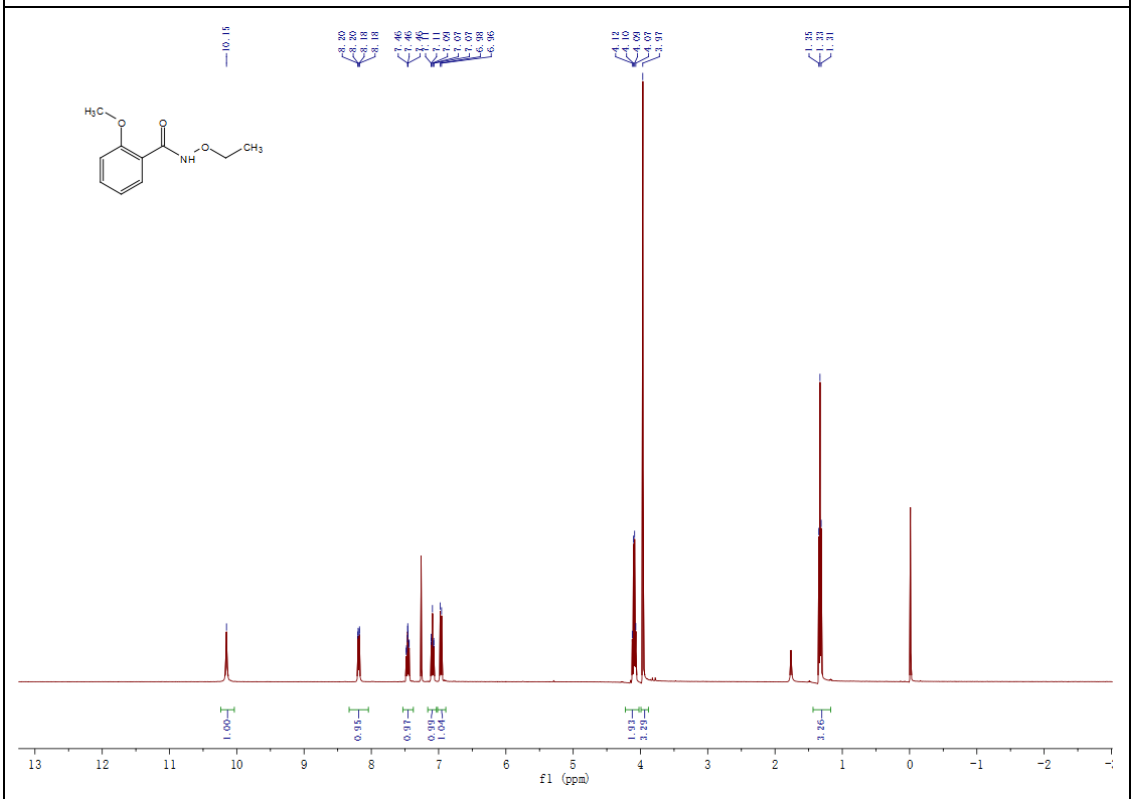


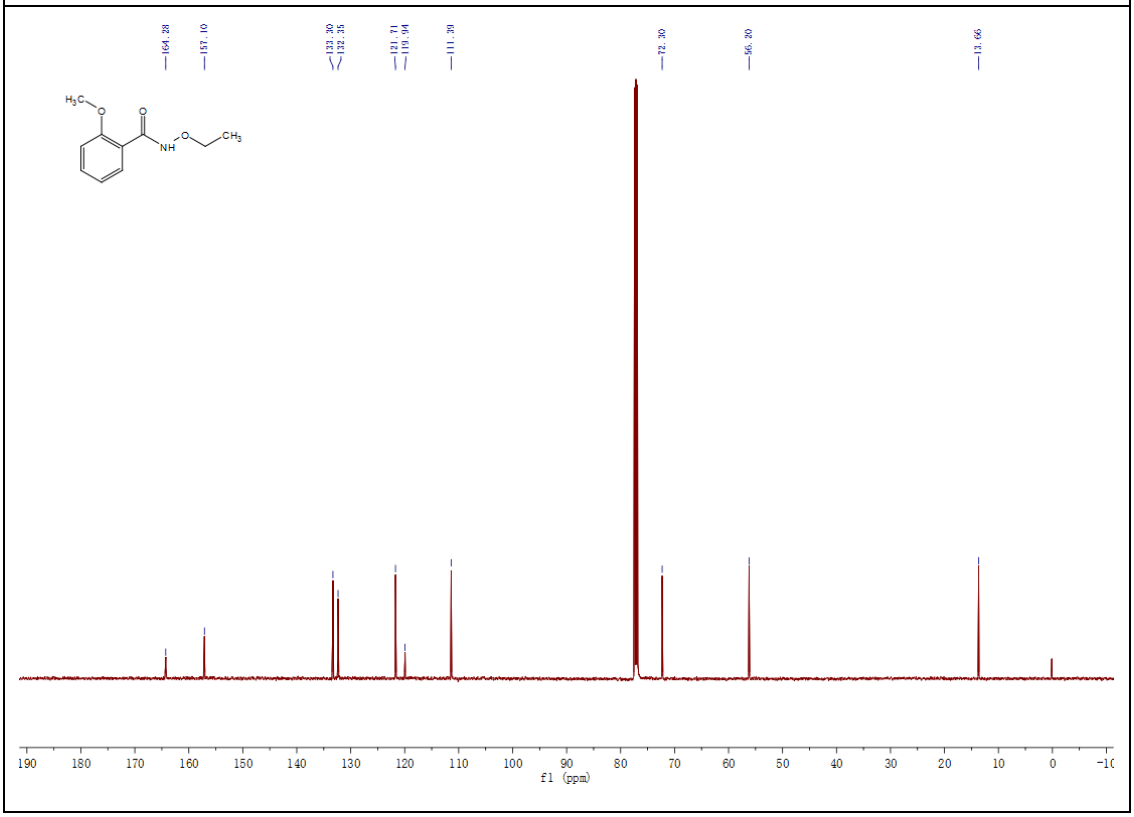


^{19}F NMR of *N*-ethoxy-2-fluorobenzamide (1p):

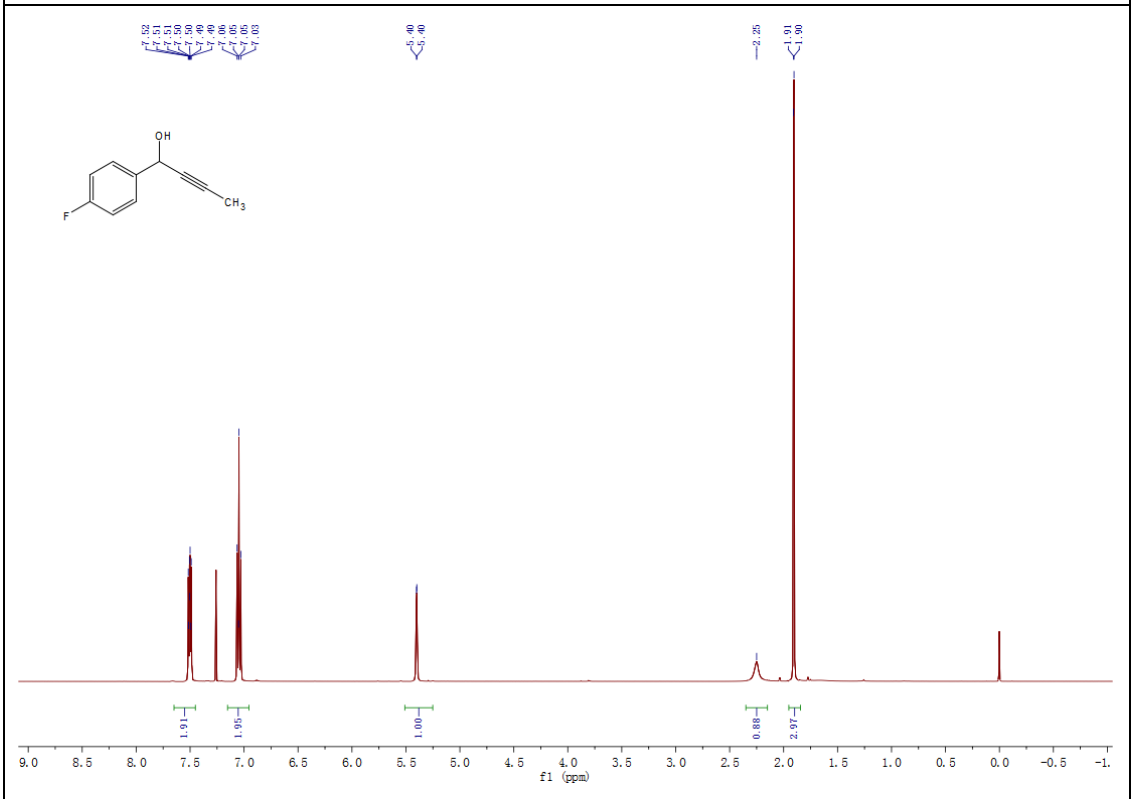


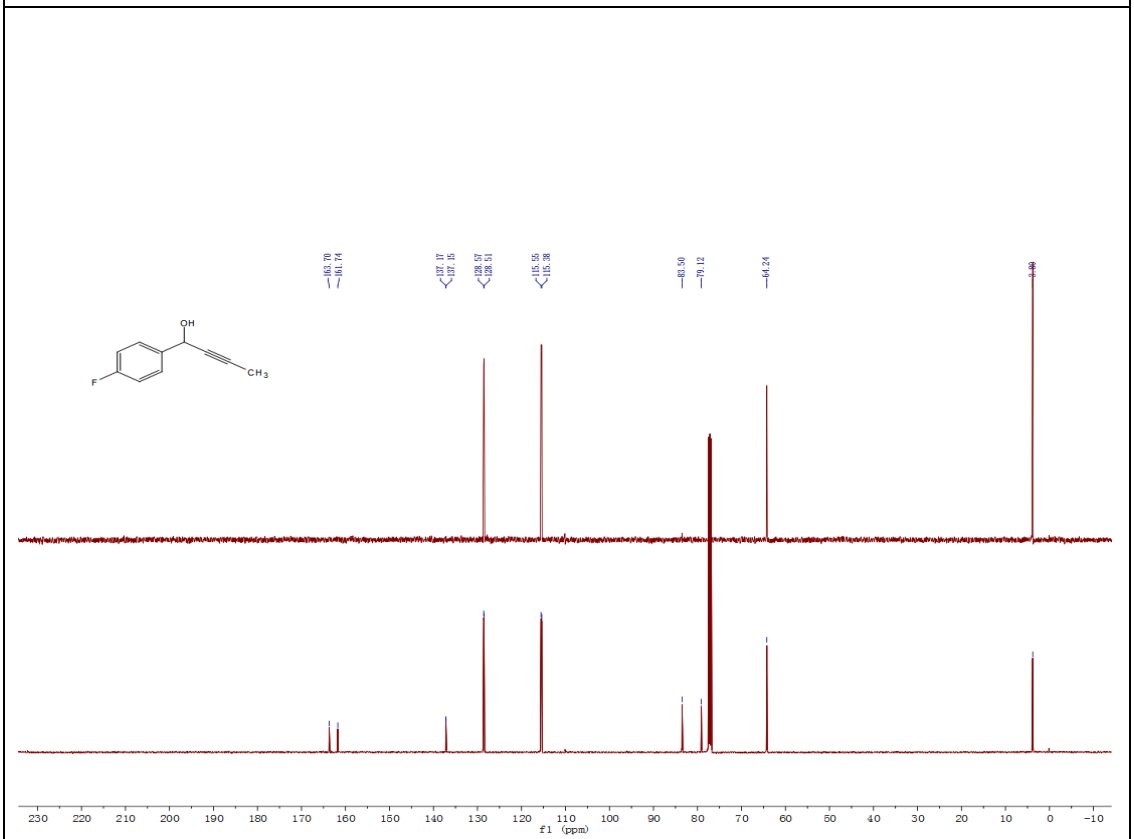
N-ethoxy-2-methoxybenzamide (1q):



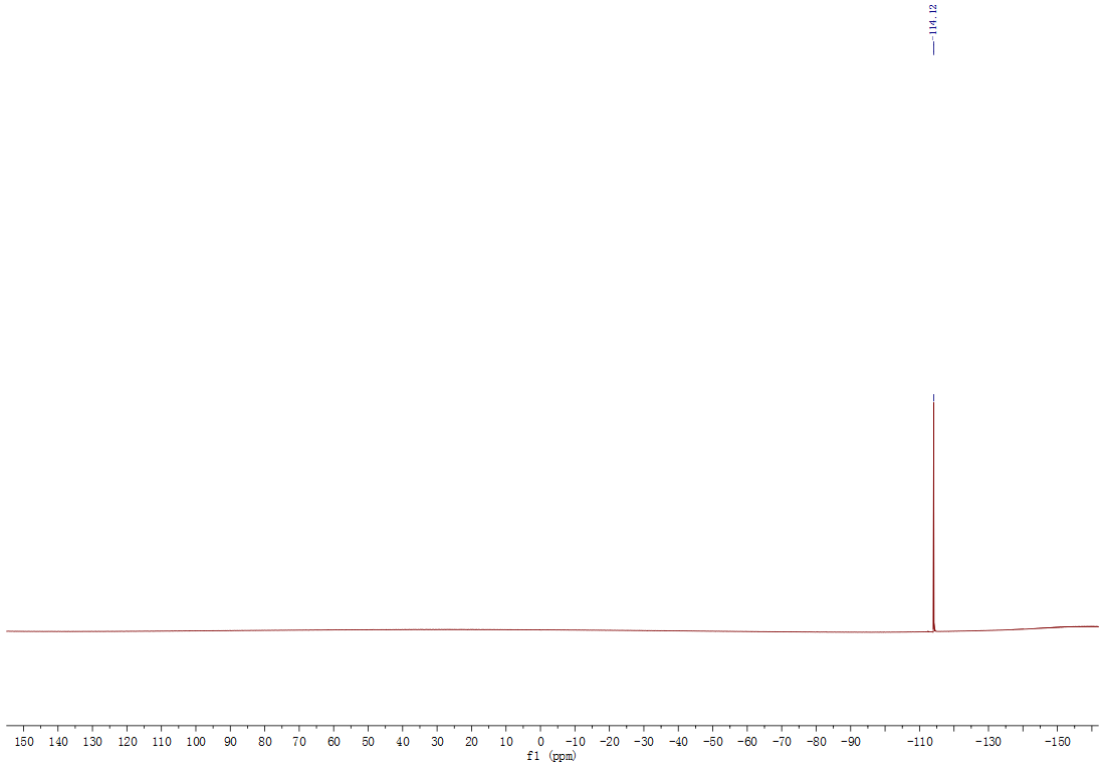


1-(4-fluorophenyl)but-2-yn-1-ol (2c)：

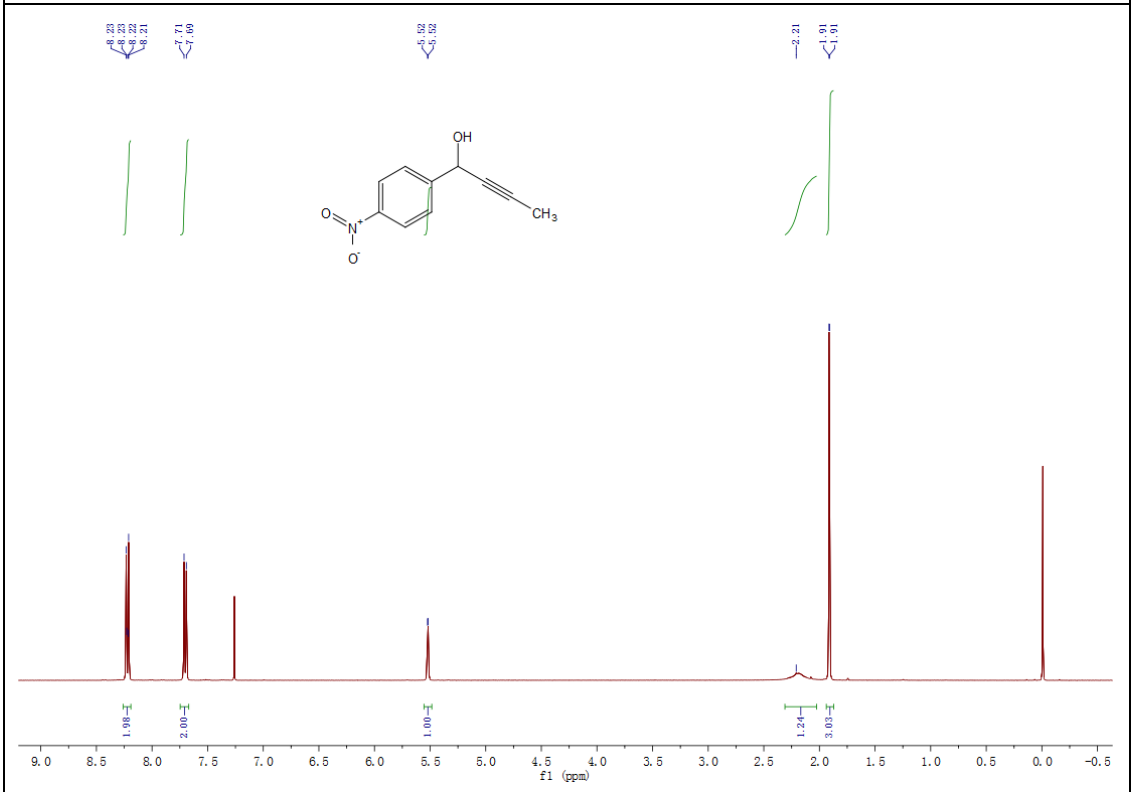


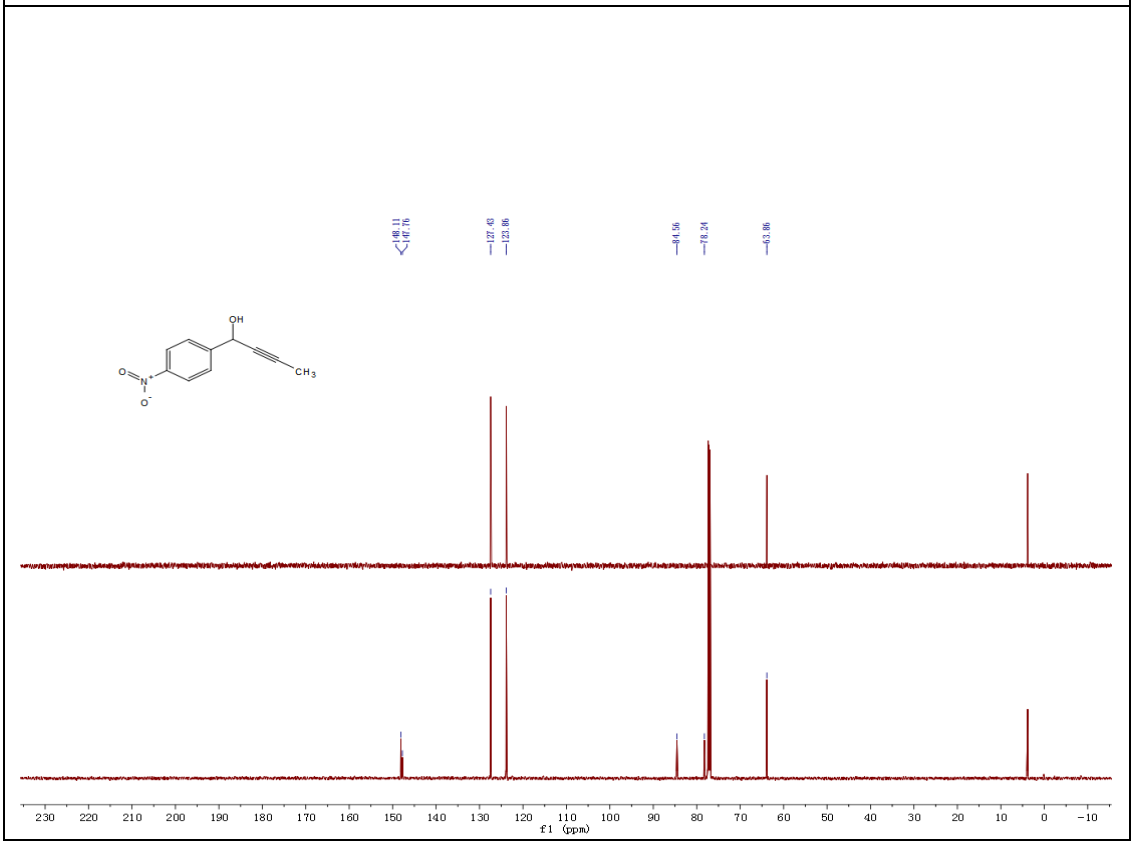


^{19}F NMR of 1-(4-fluorophenyl)but-2-yn-1-ol (2c):

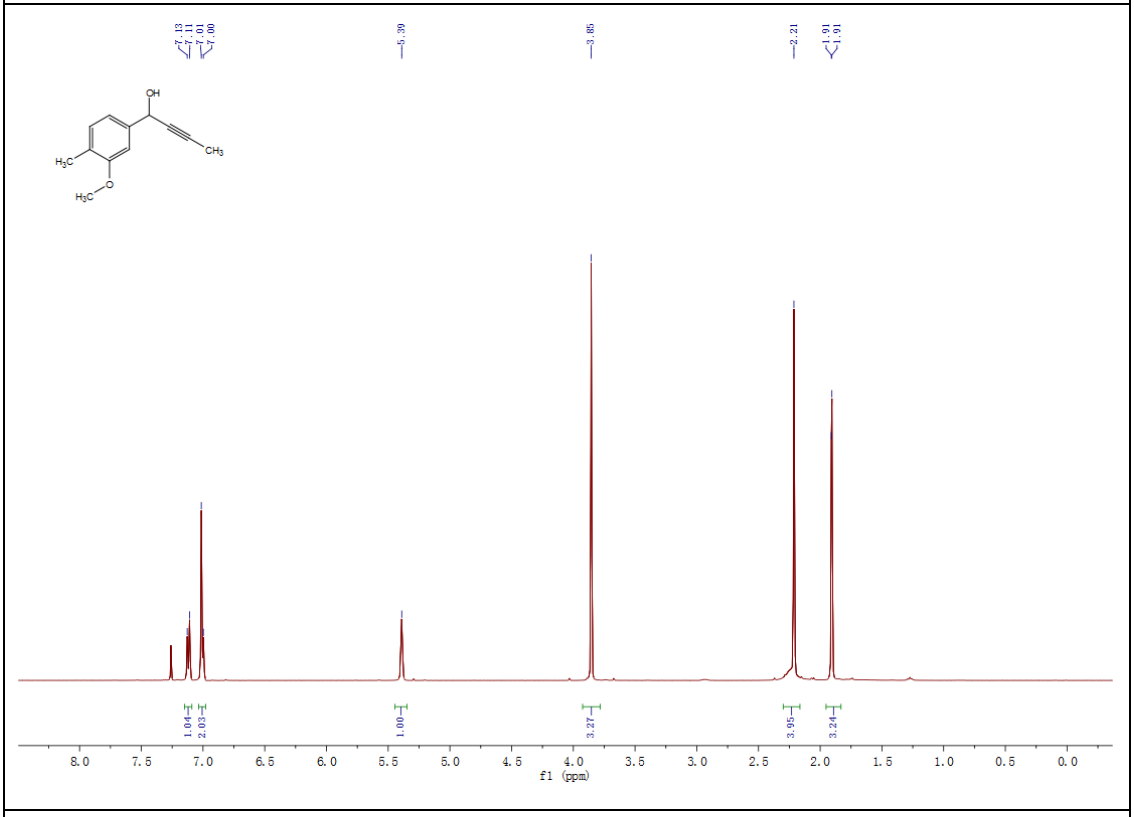


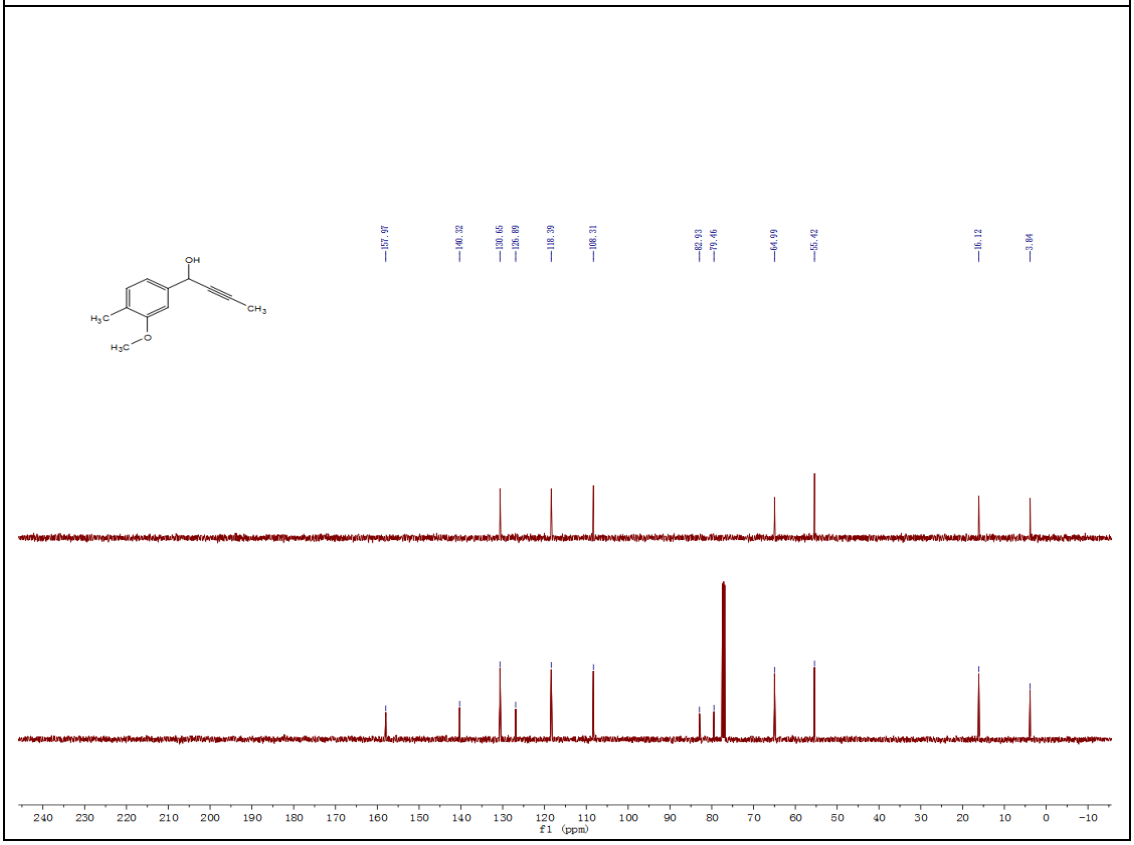
1-(4-nitrophenyl)but-2-yn-1-ol (2g):



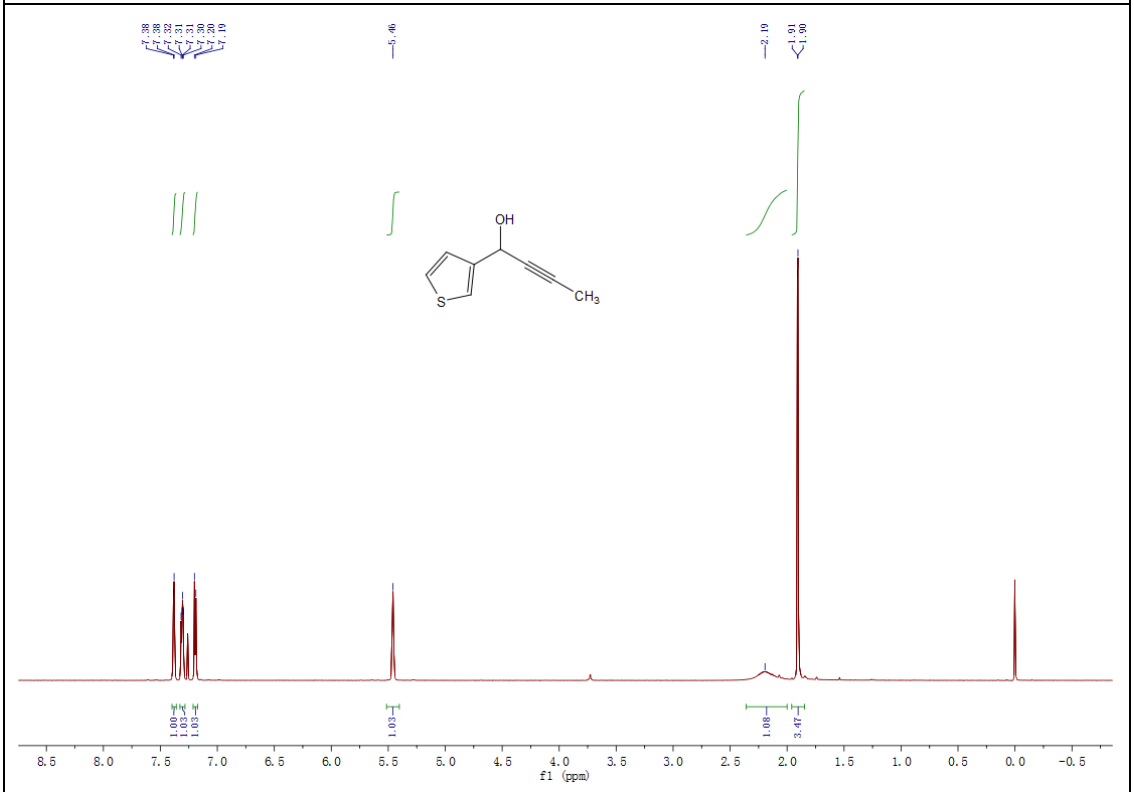


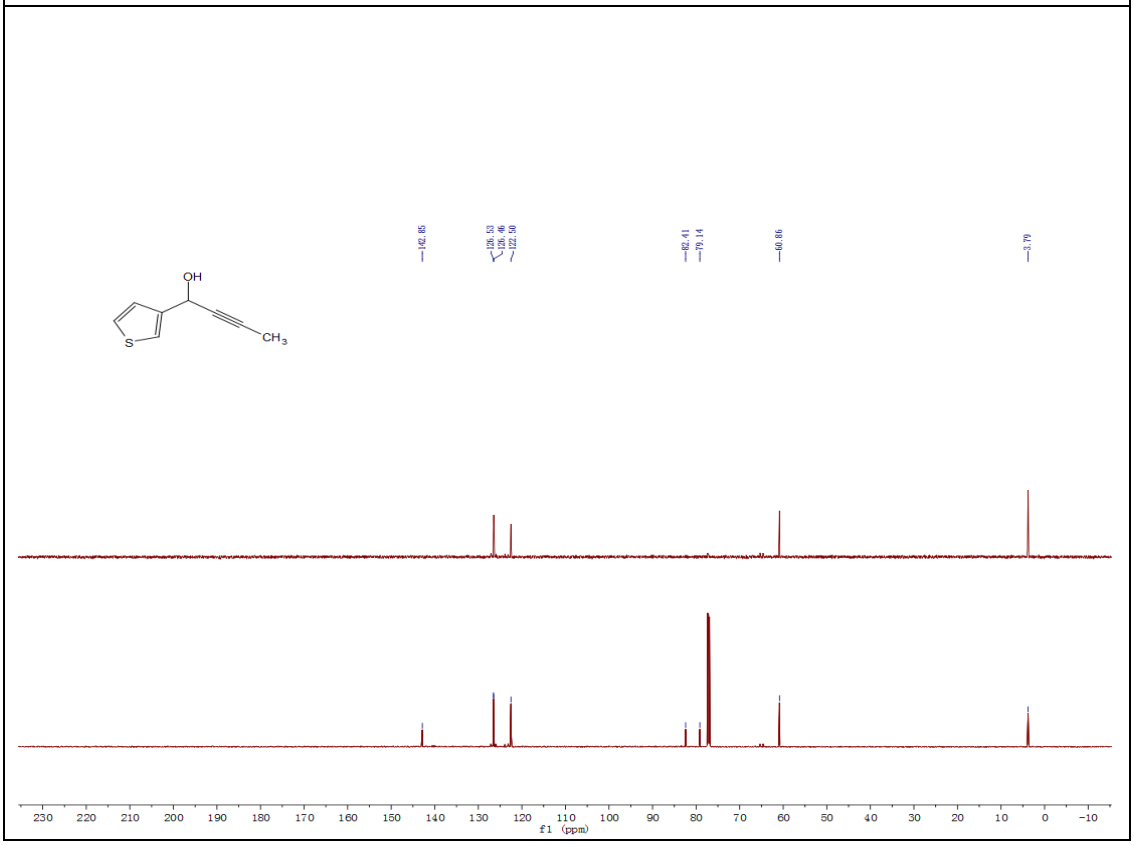
1-(3-methoxy-4-methylphenyl)but-2-yn-1-ol (2i):



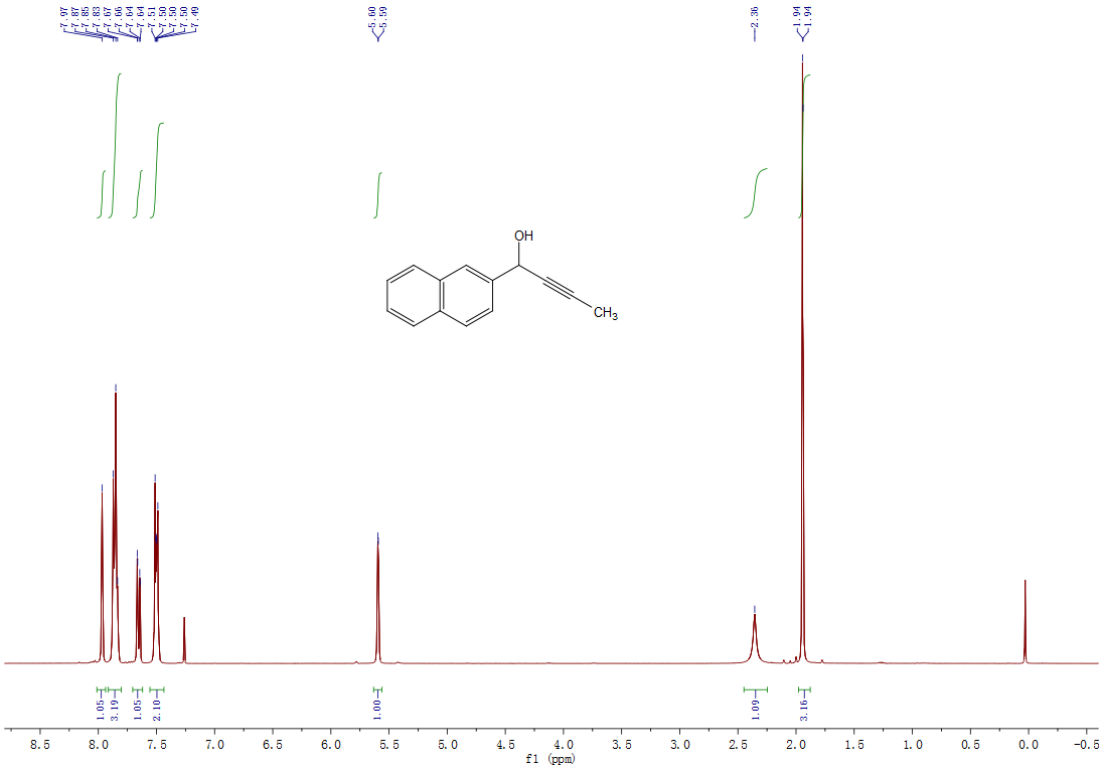


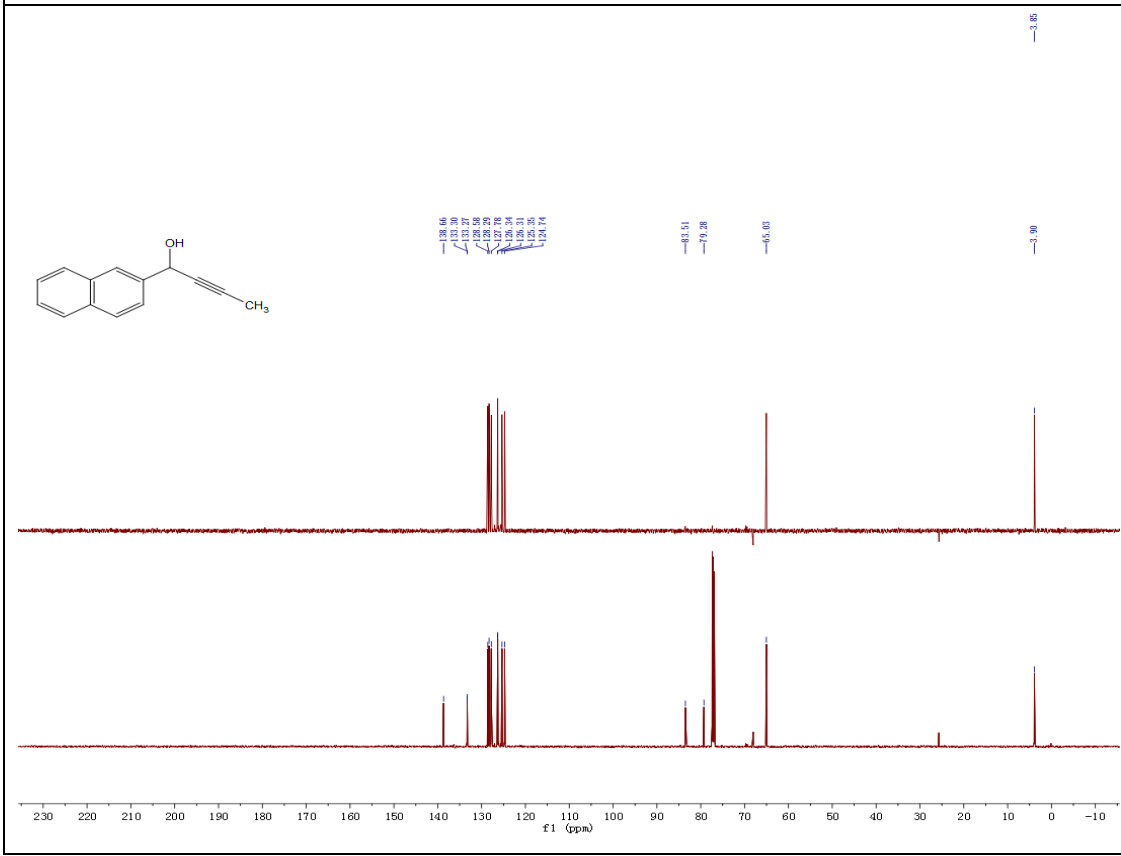
1-(thiophen-3-yl)but-2-yn-1-ol (2j):



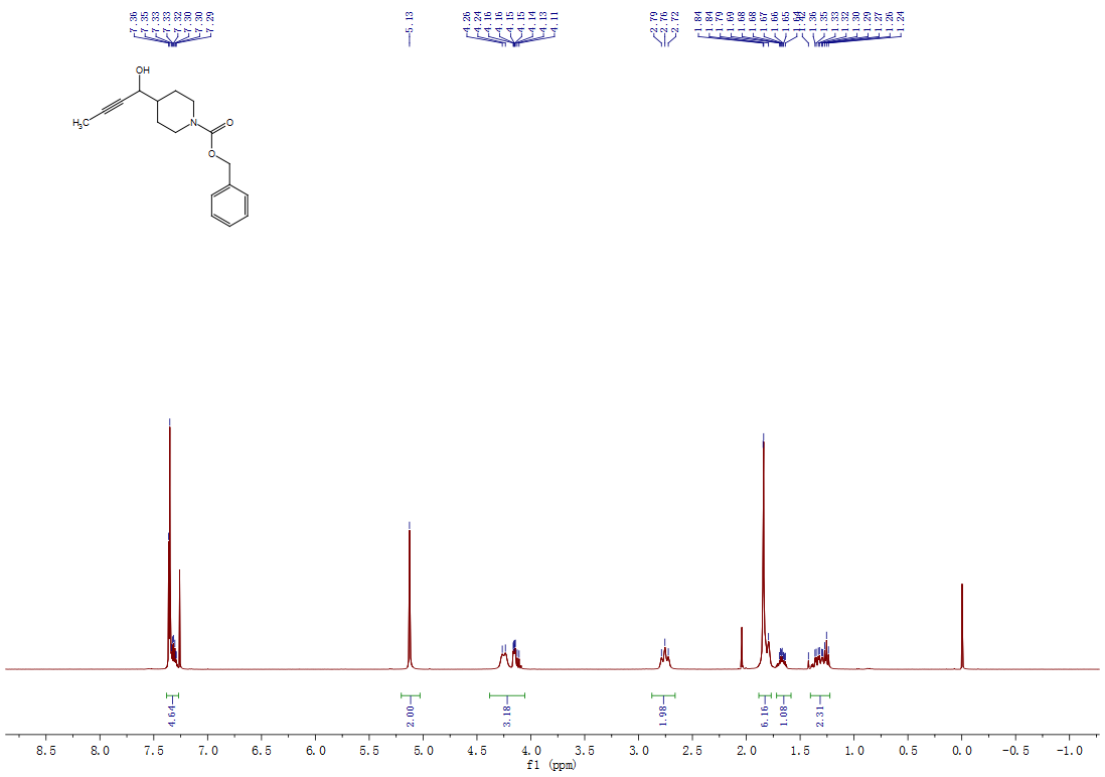


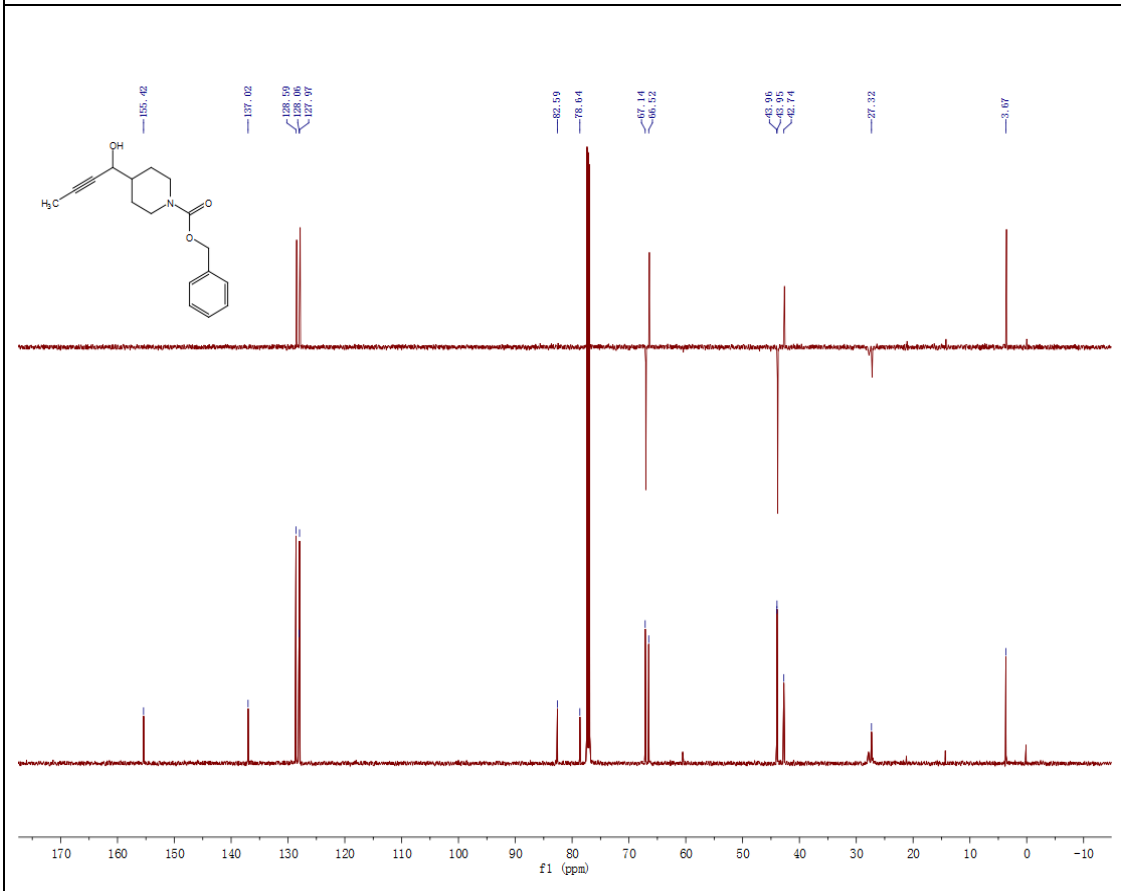
1-(naphthalen-2-yl)but-2-yn-1-ol (2k):



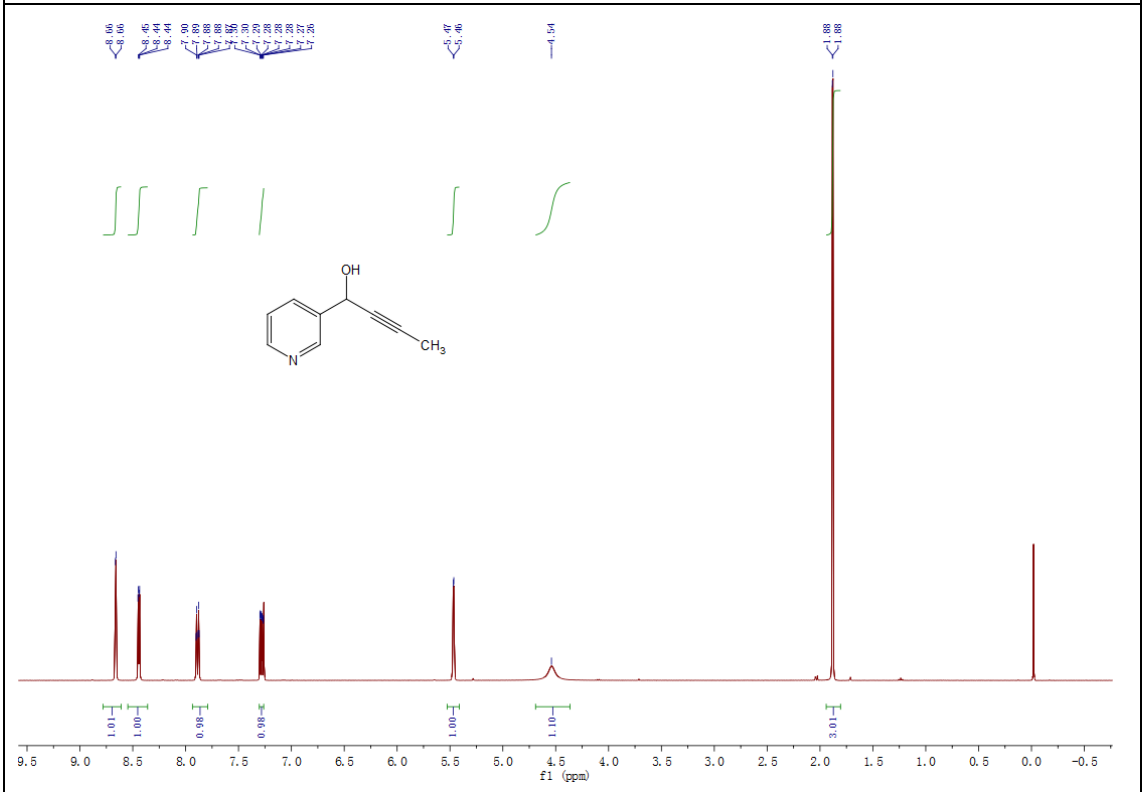


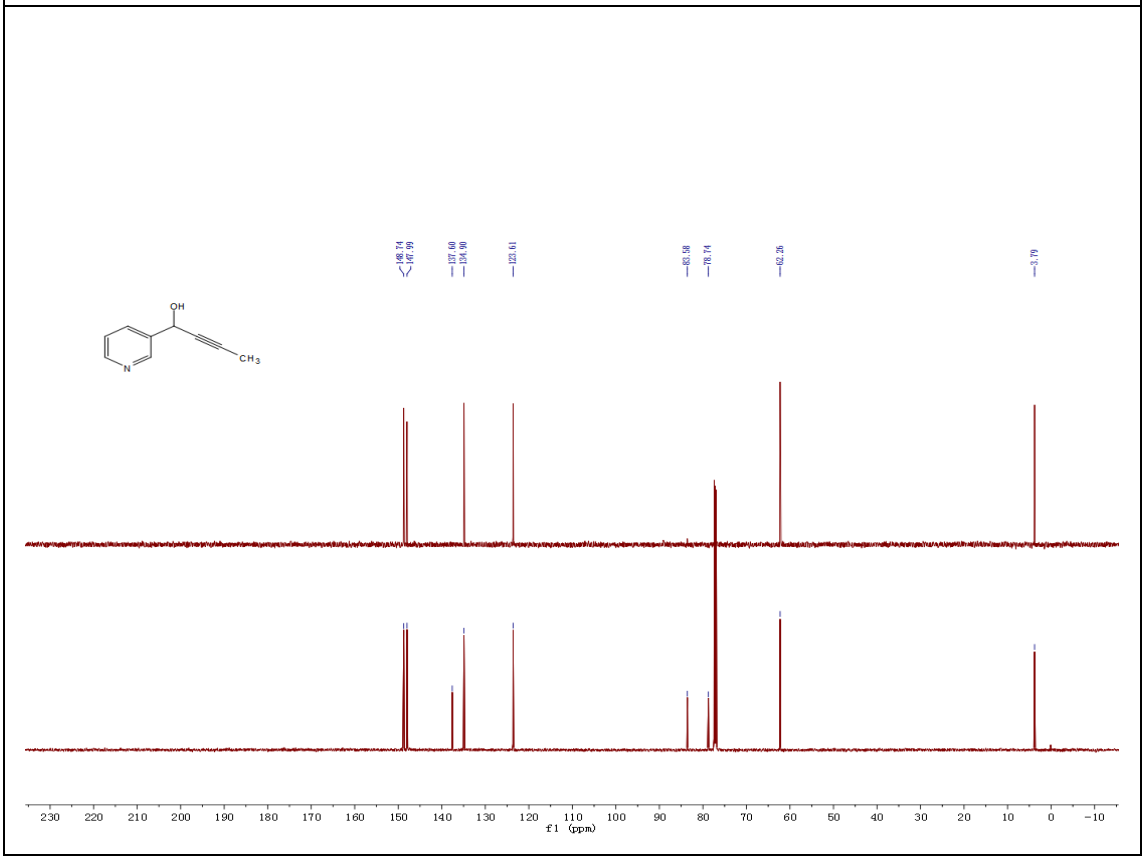
benzyl 4-(1-hydroxybut-2-yn-1-yl)piperidine-1-carboxylate (2l)



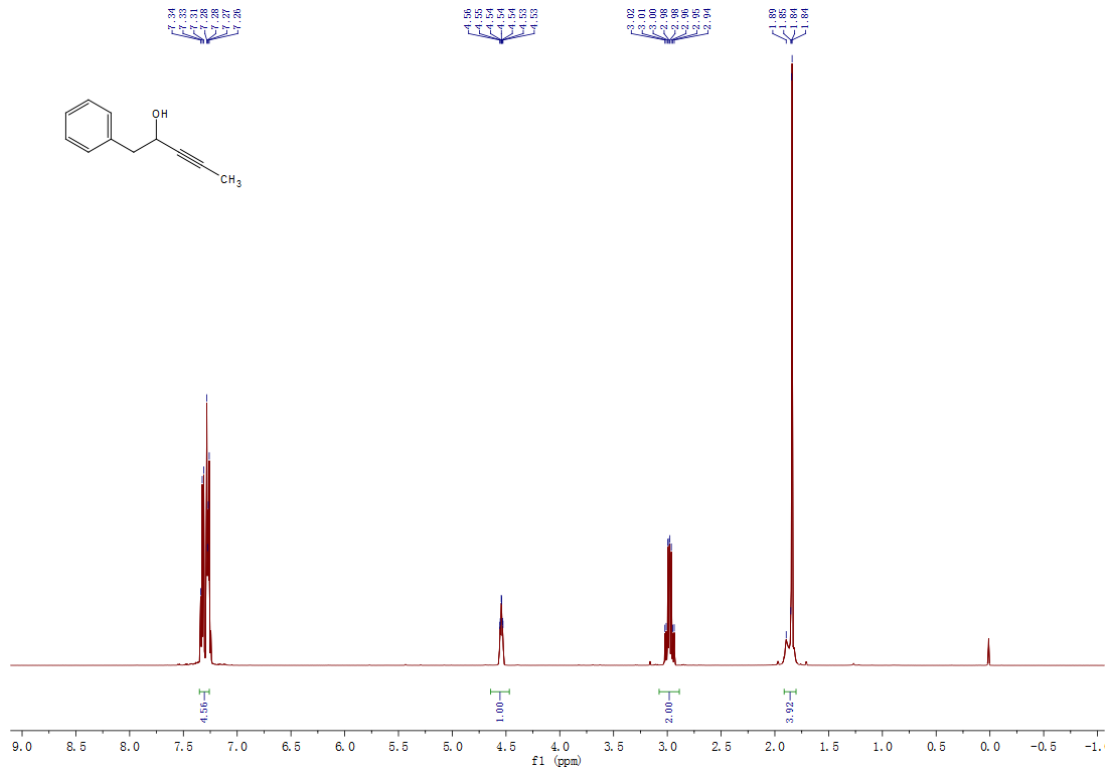


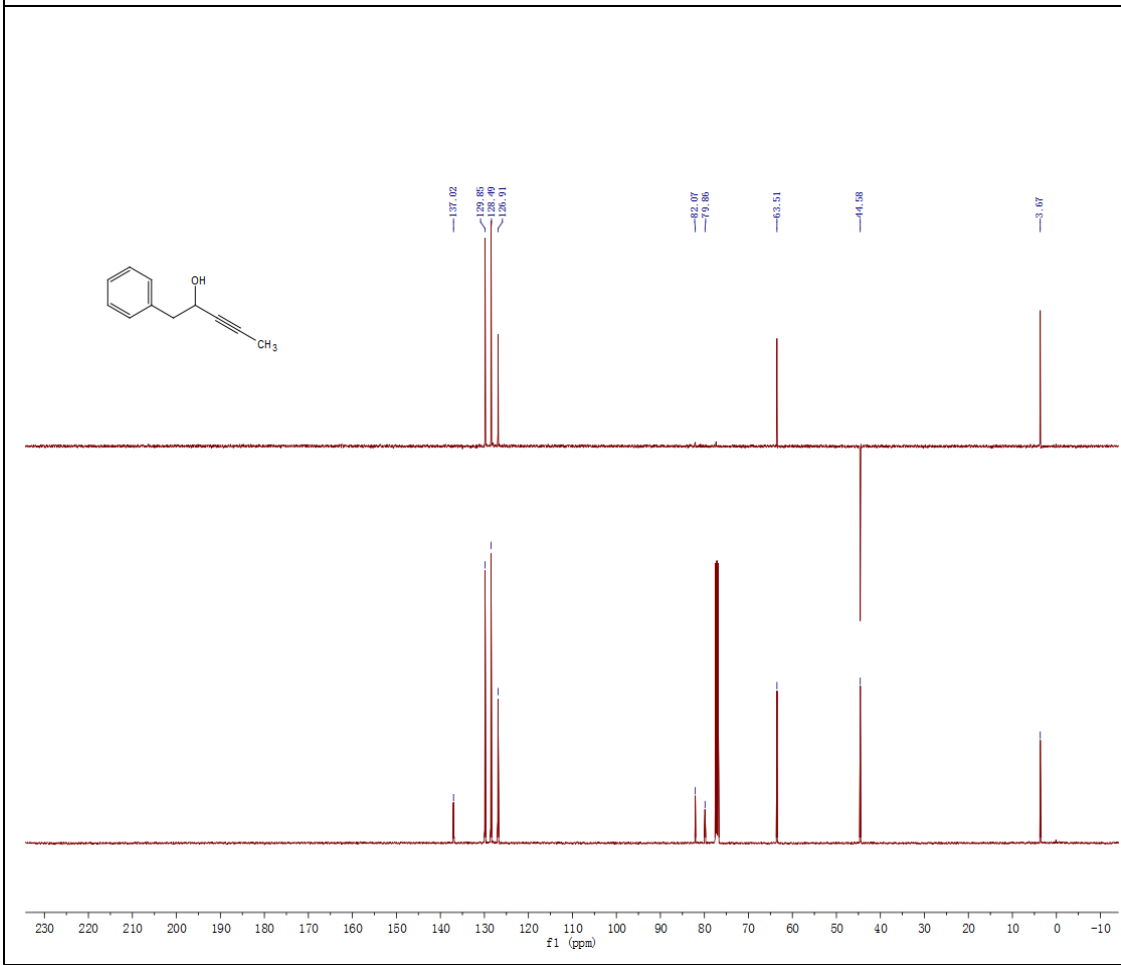
1-(pyridin-3-yl)but-2-yn-1-ol (2m):



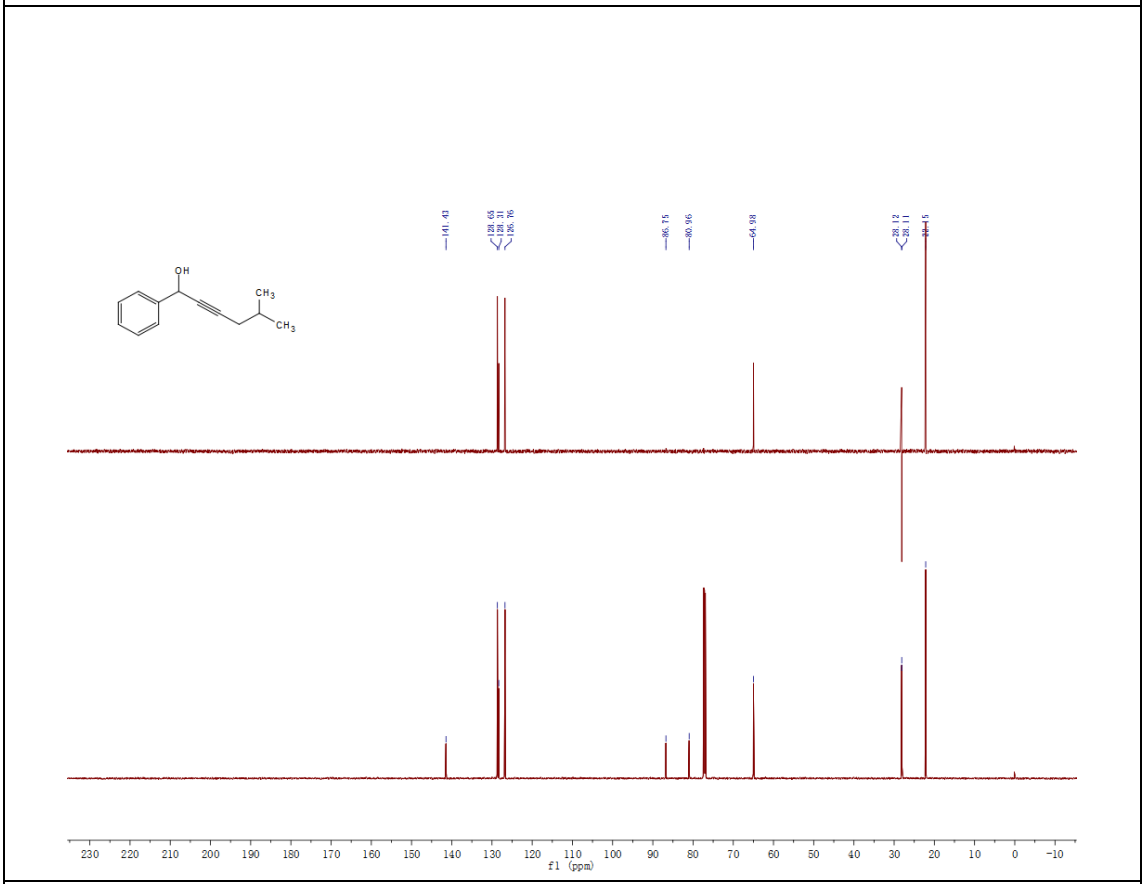


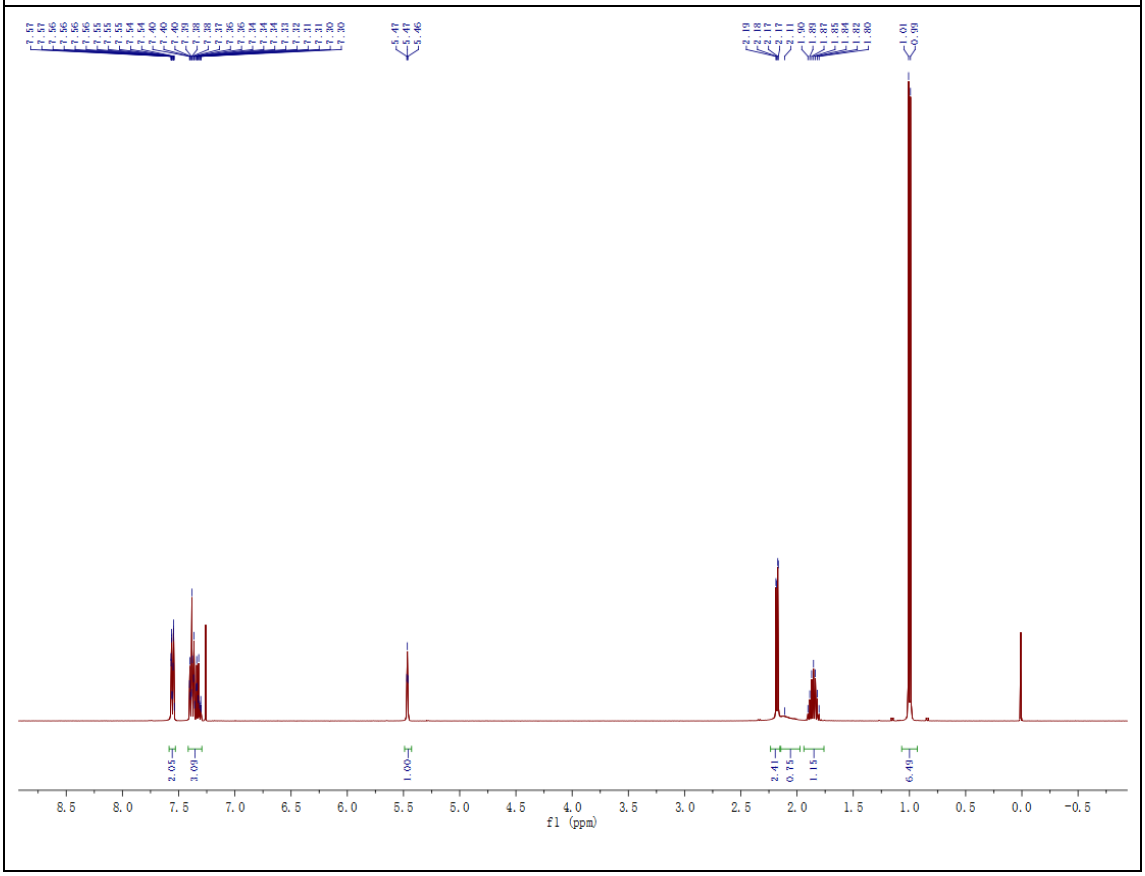
1-phenylpent-3-yn-2-ol (2o):



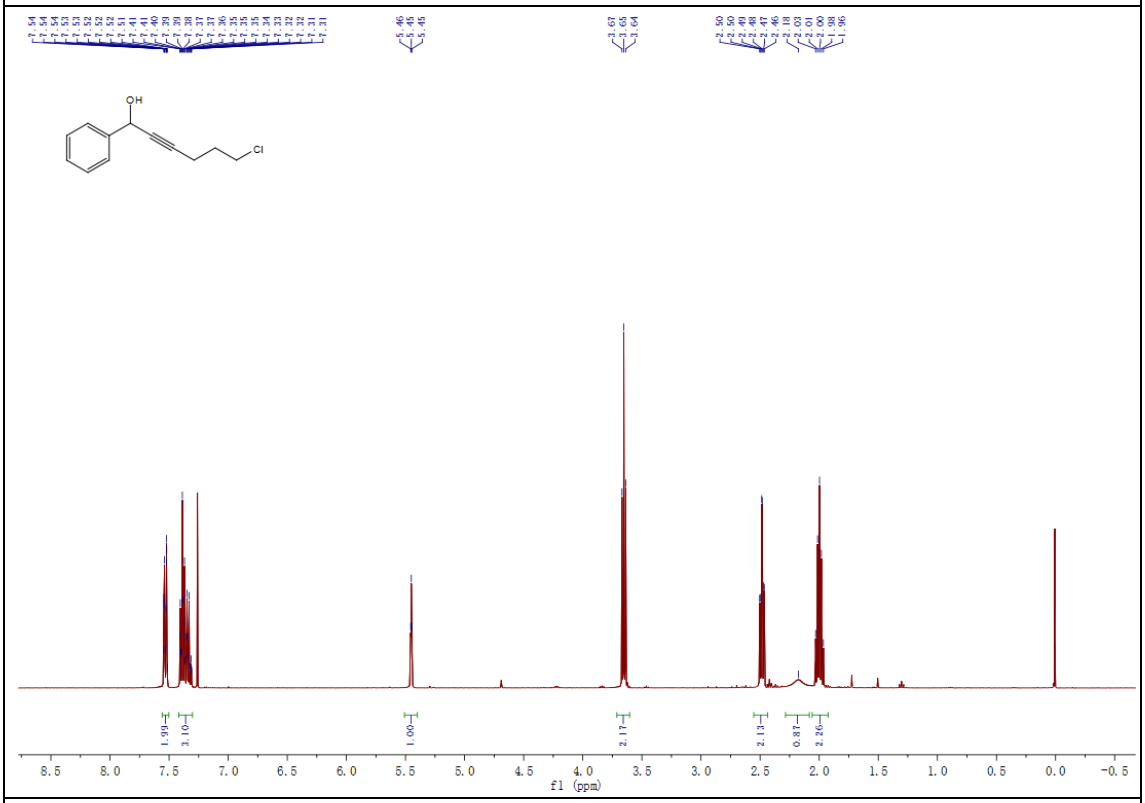


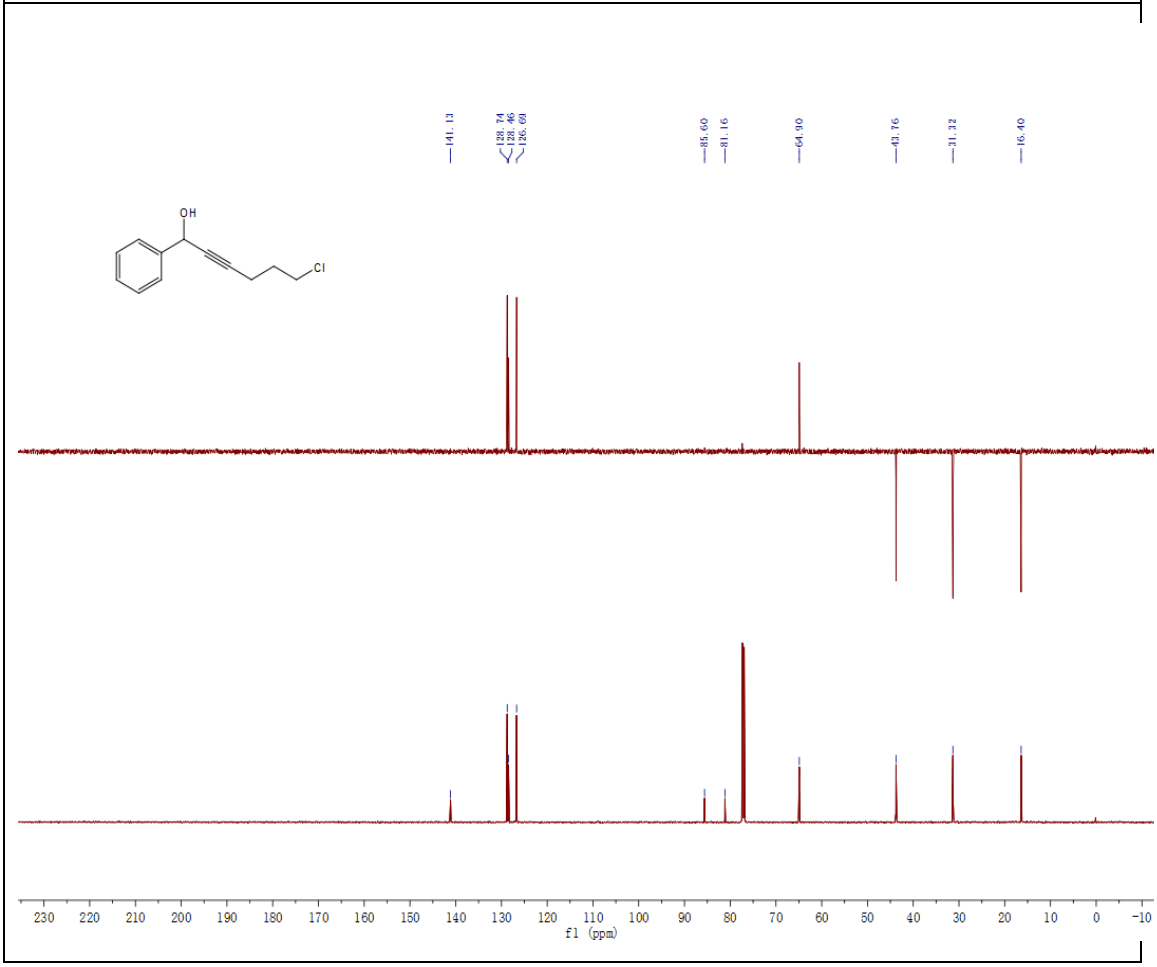
5-methyl-1-phenylhex-2-yn-1-ol (2r)



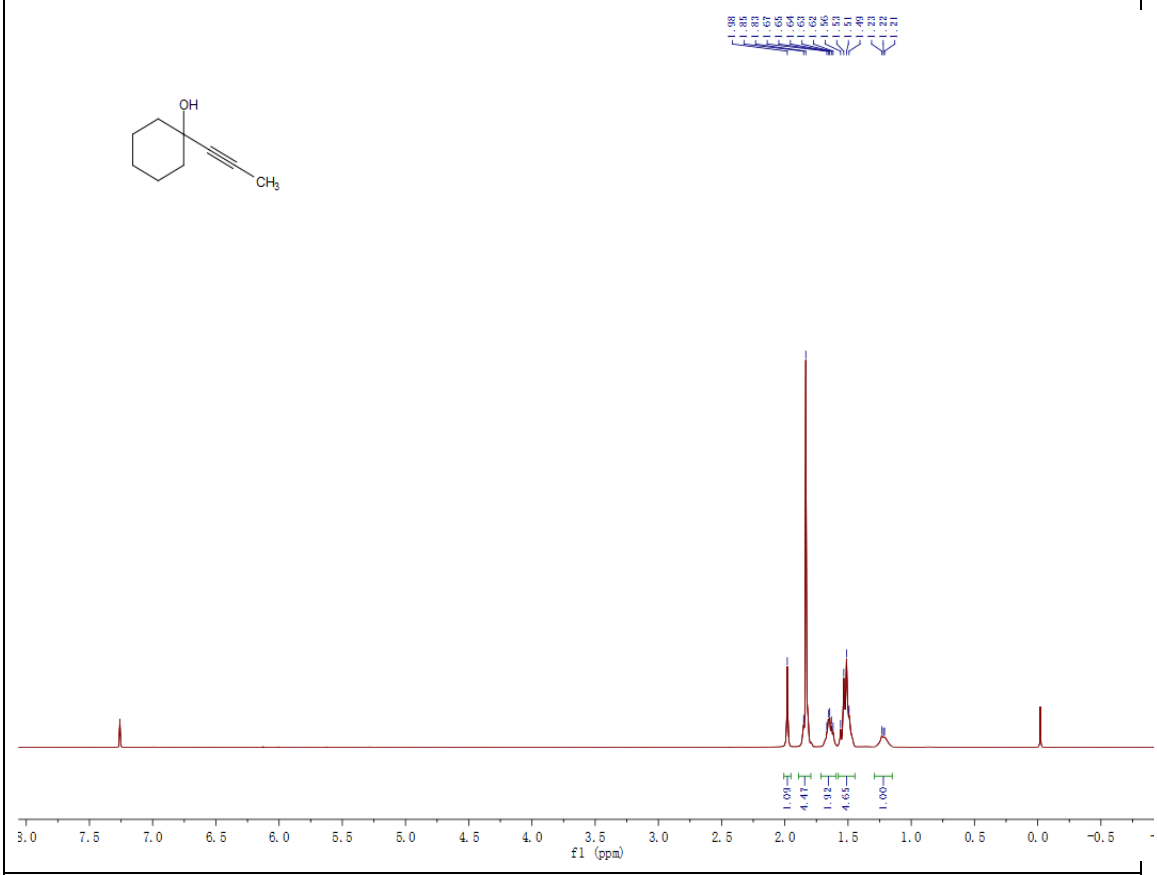


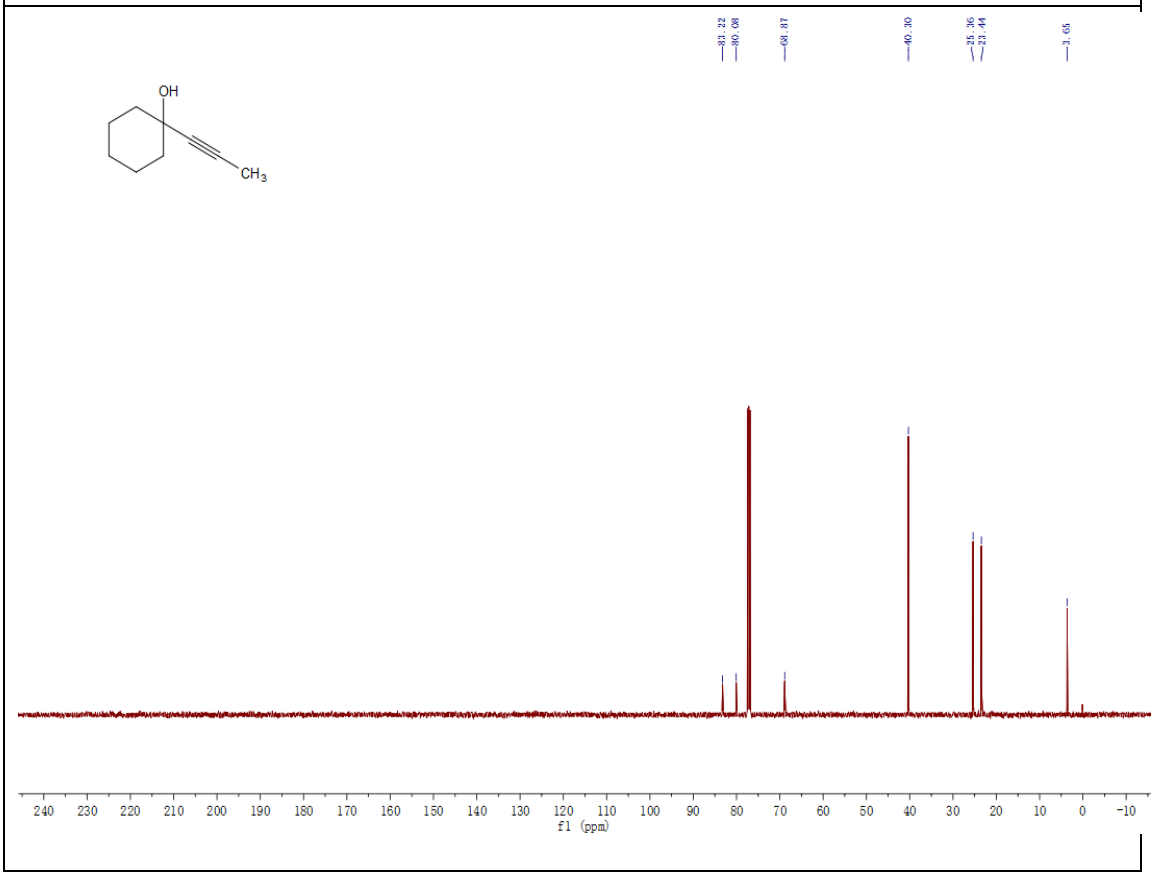
6-chloro-1-phenylhex-2-yn-1-ol (2s)



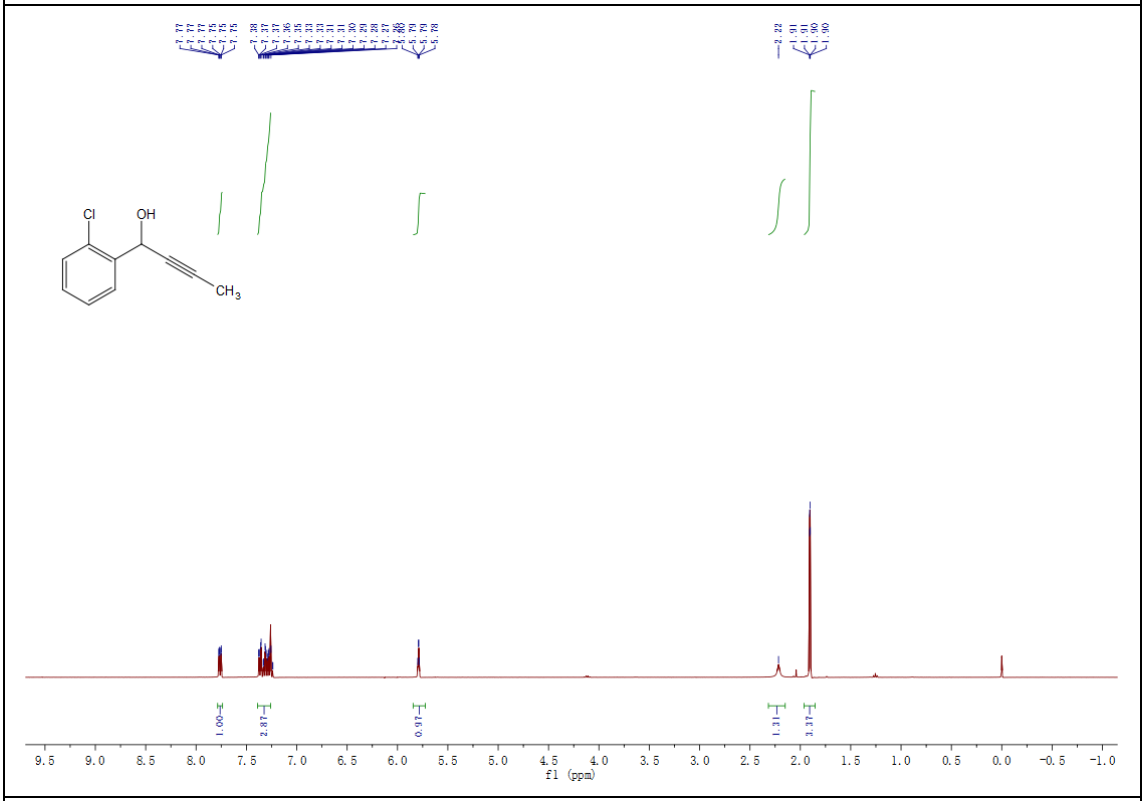


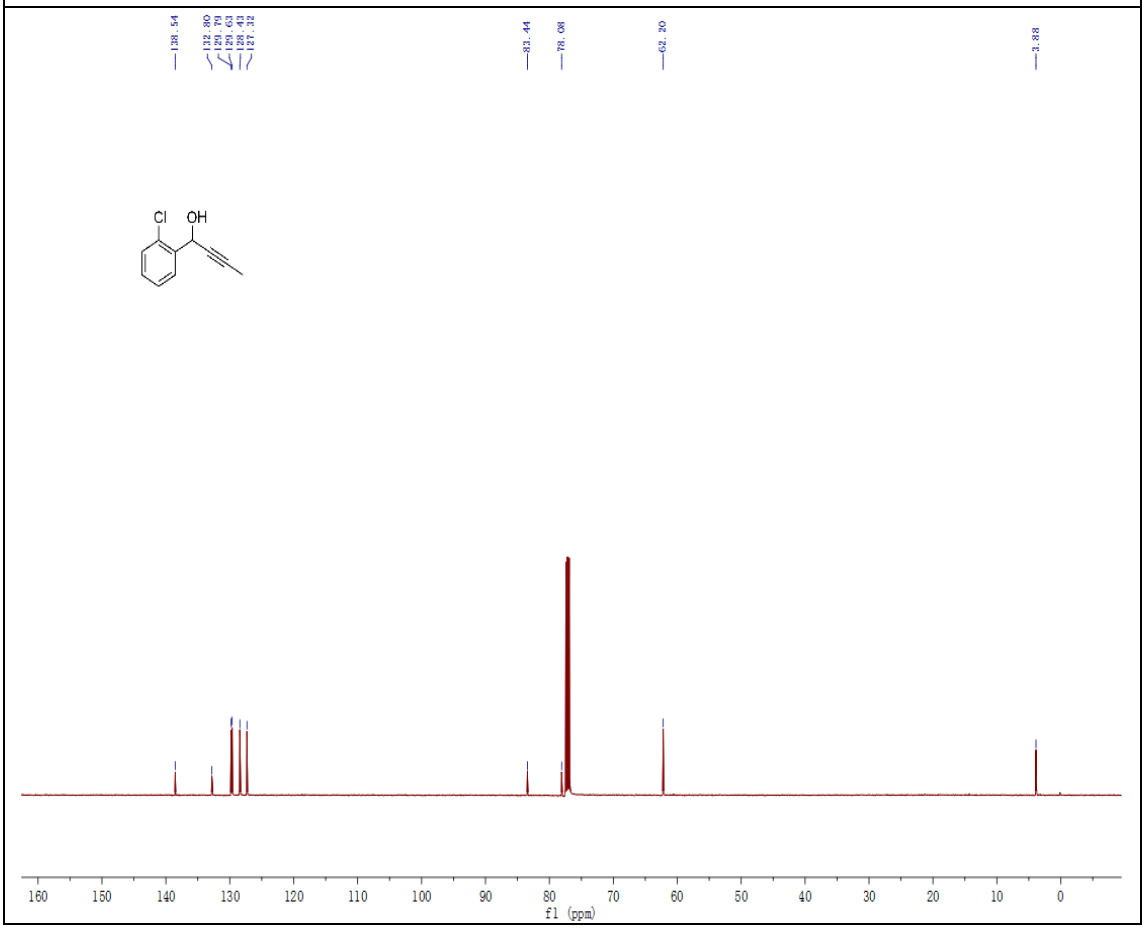
1-(prop-1-yn-1-yl)cyclohexan-1-ol (2w)



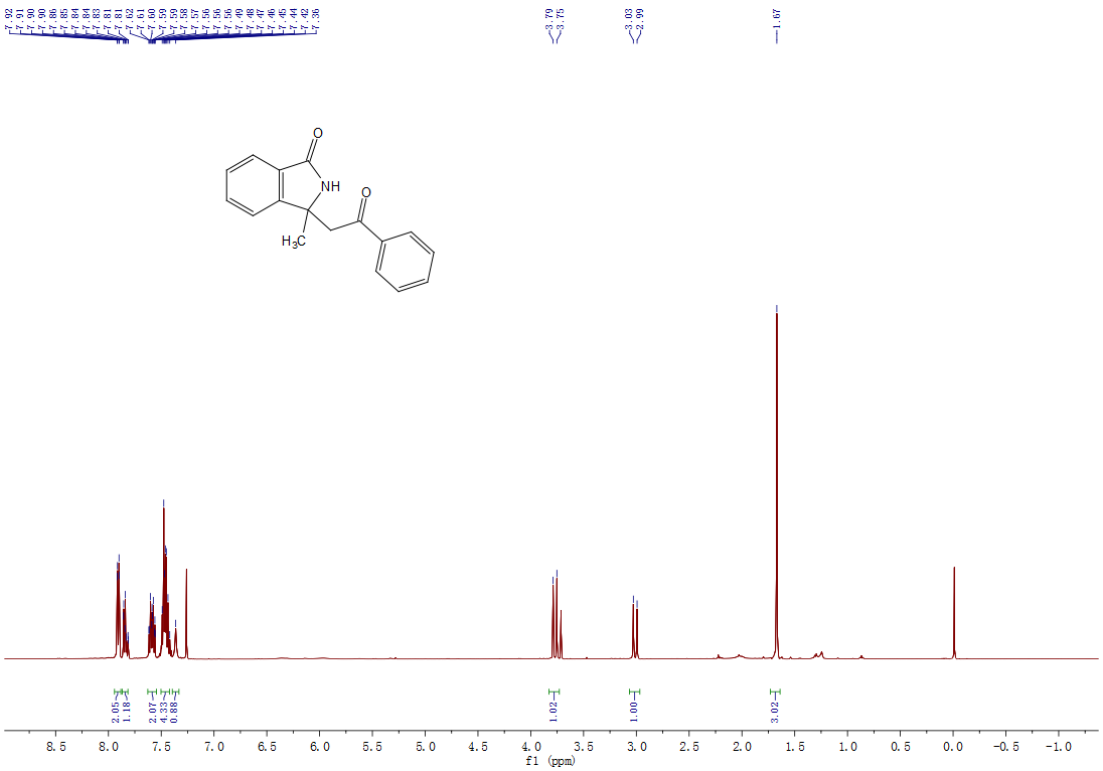


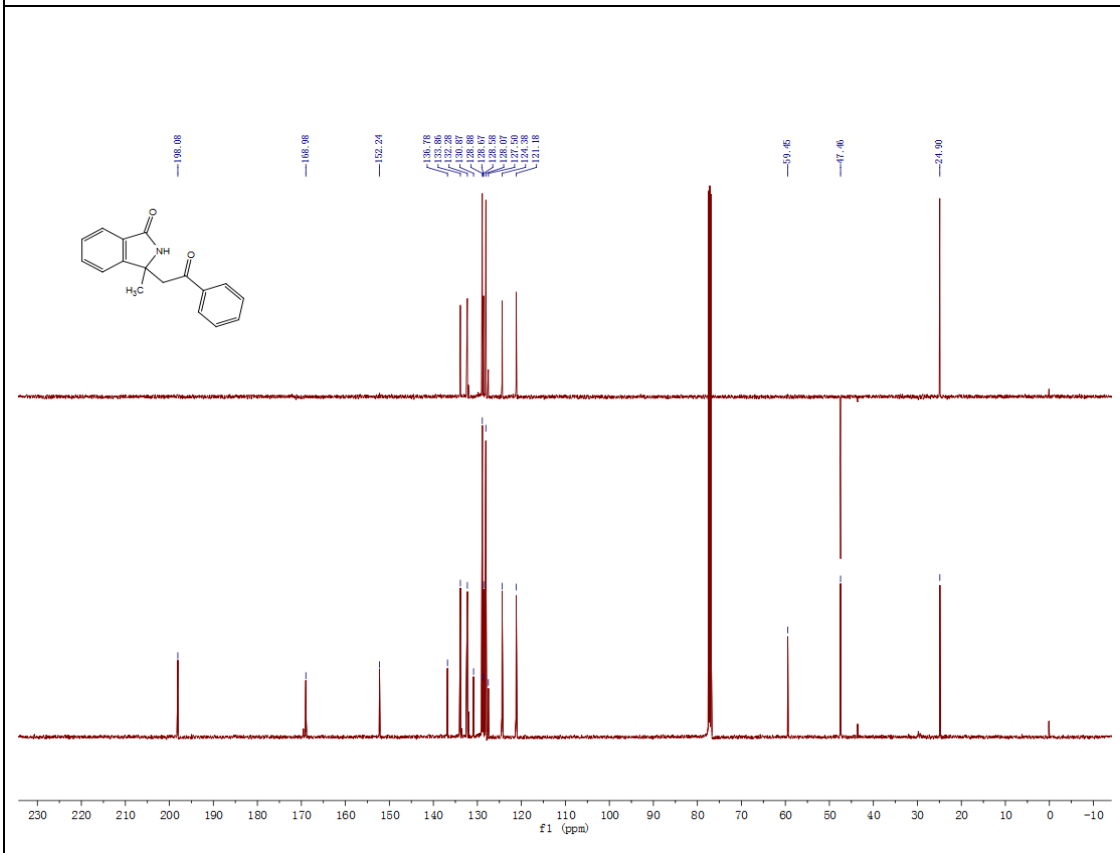
1-(2-chlorophenyl)but-2-yn-1-ol (2x)



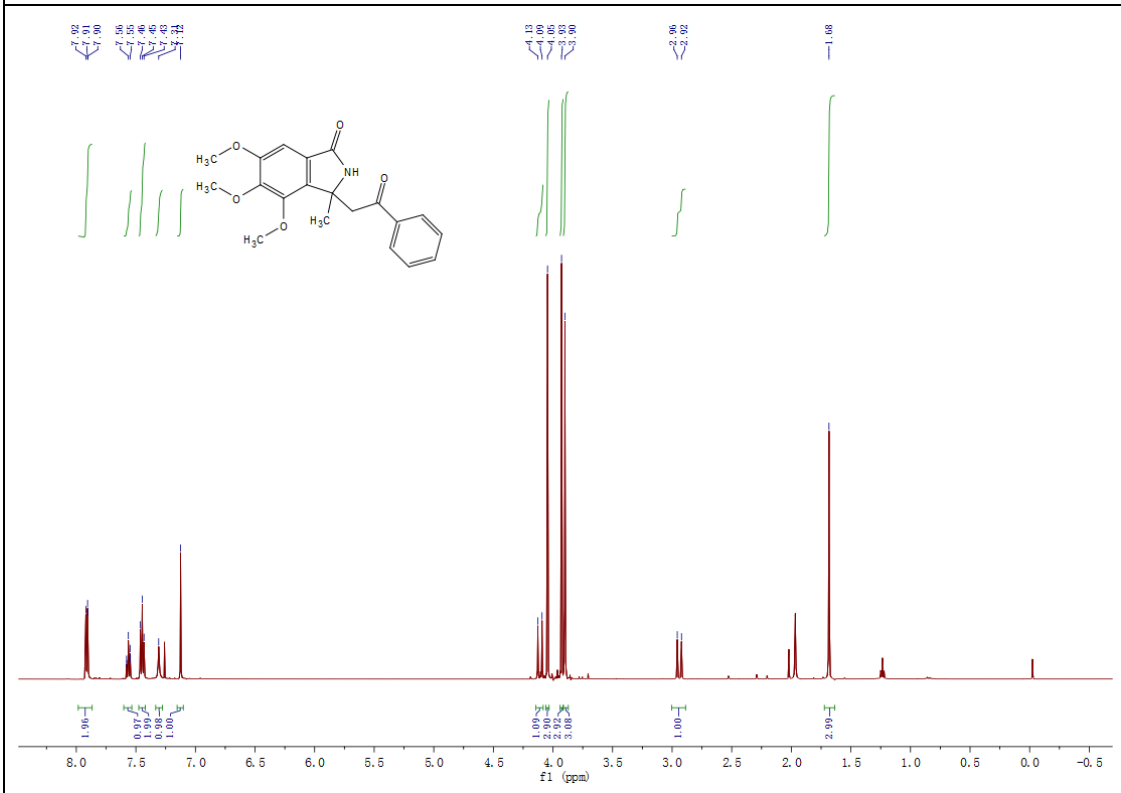


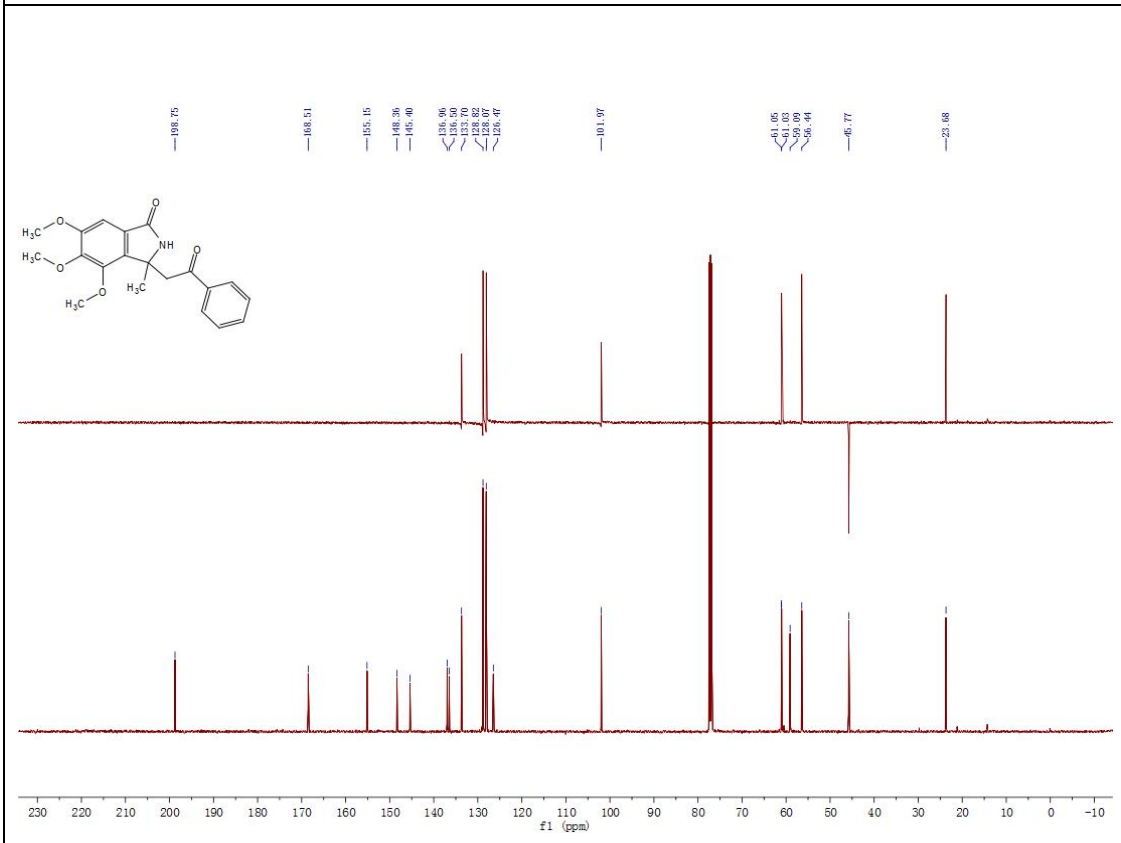
3-methyl-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3a):



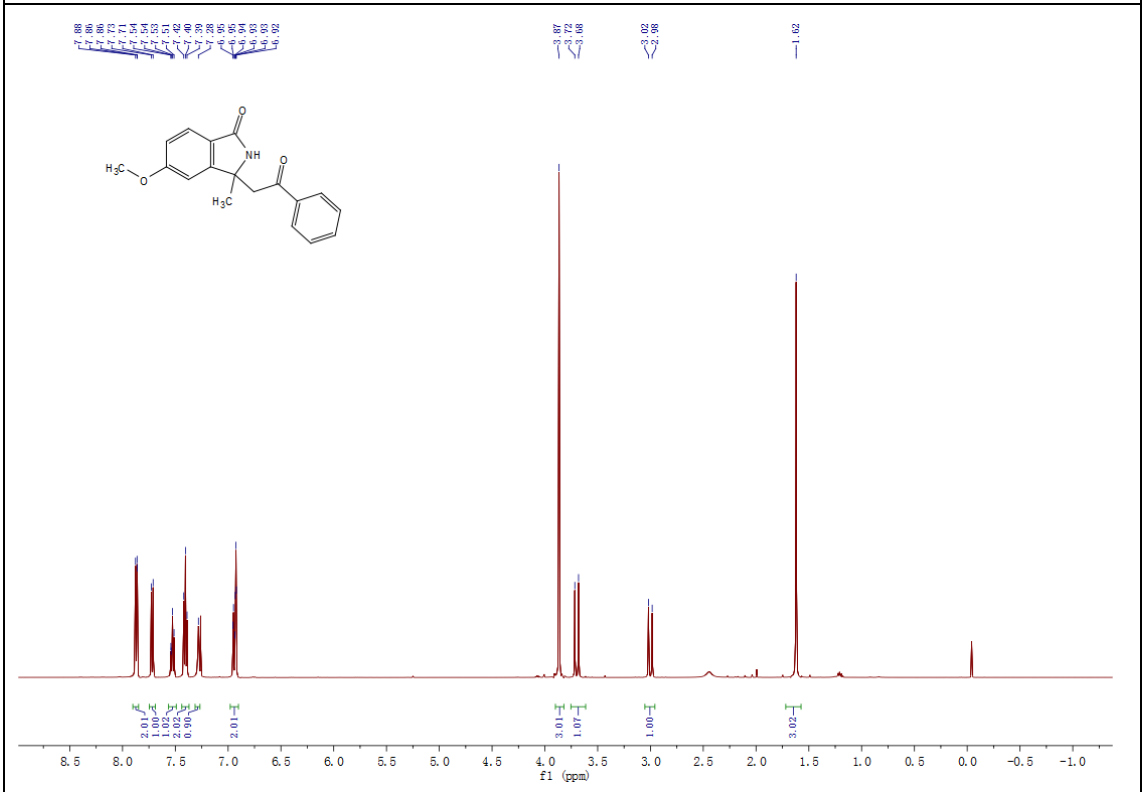


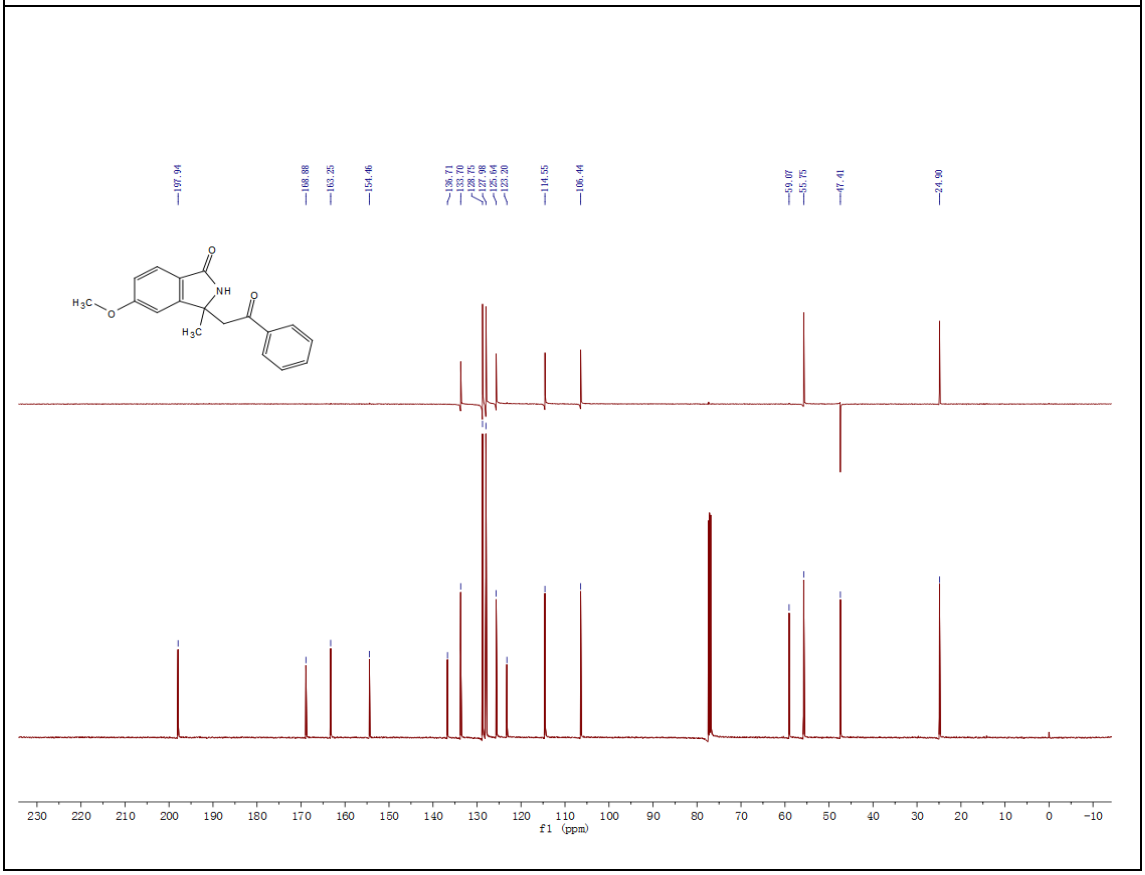
4,5,6-trimethoxy-3-methyl-3-(2-oxo-2-phenylethyl)-isoindolin-1-one (3b):





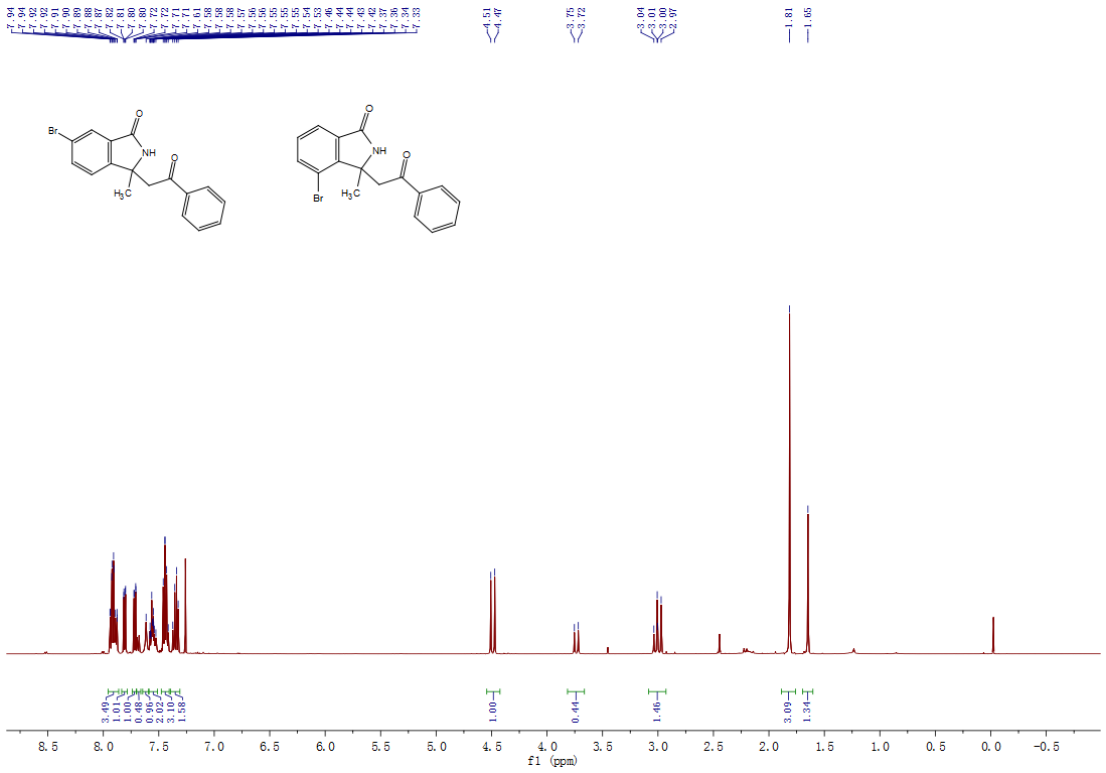
5-methoxy-3-methyl-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3c):

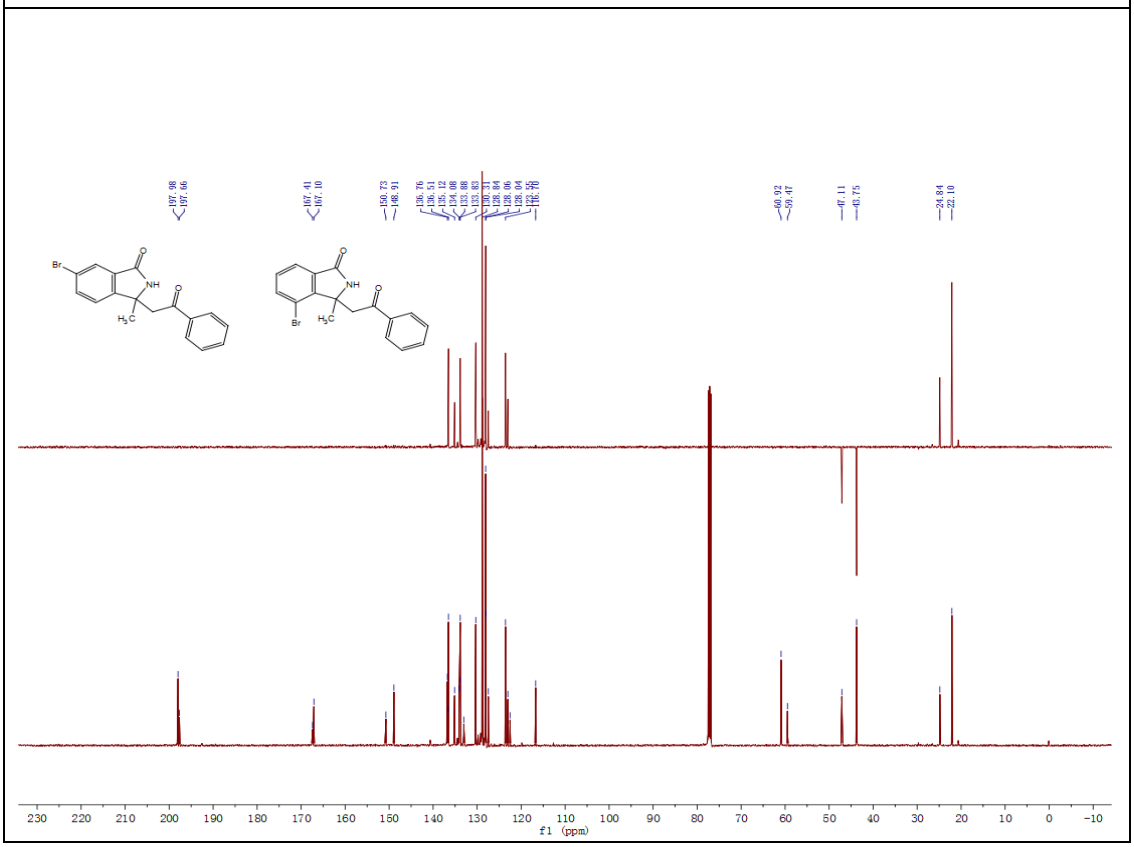




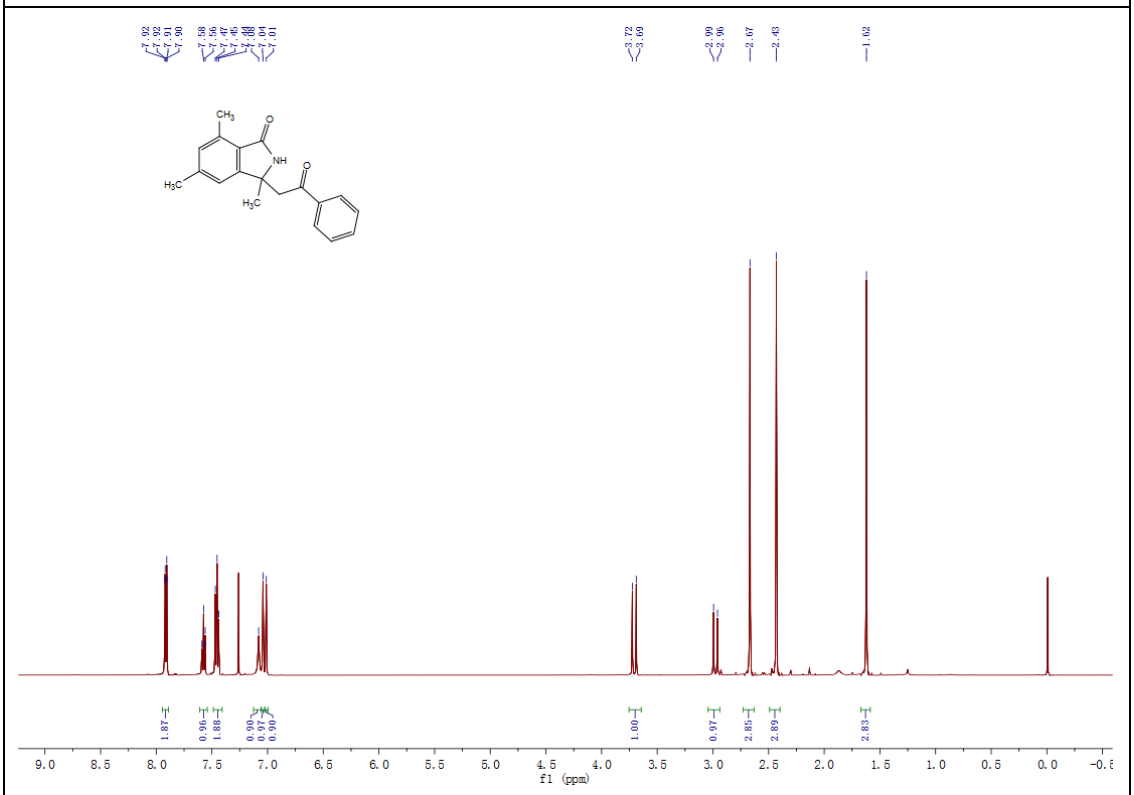
6-bromo-3-methyl-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3d) and

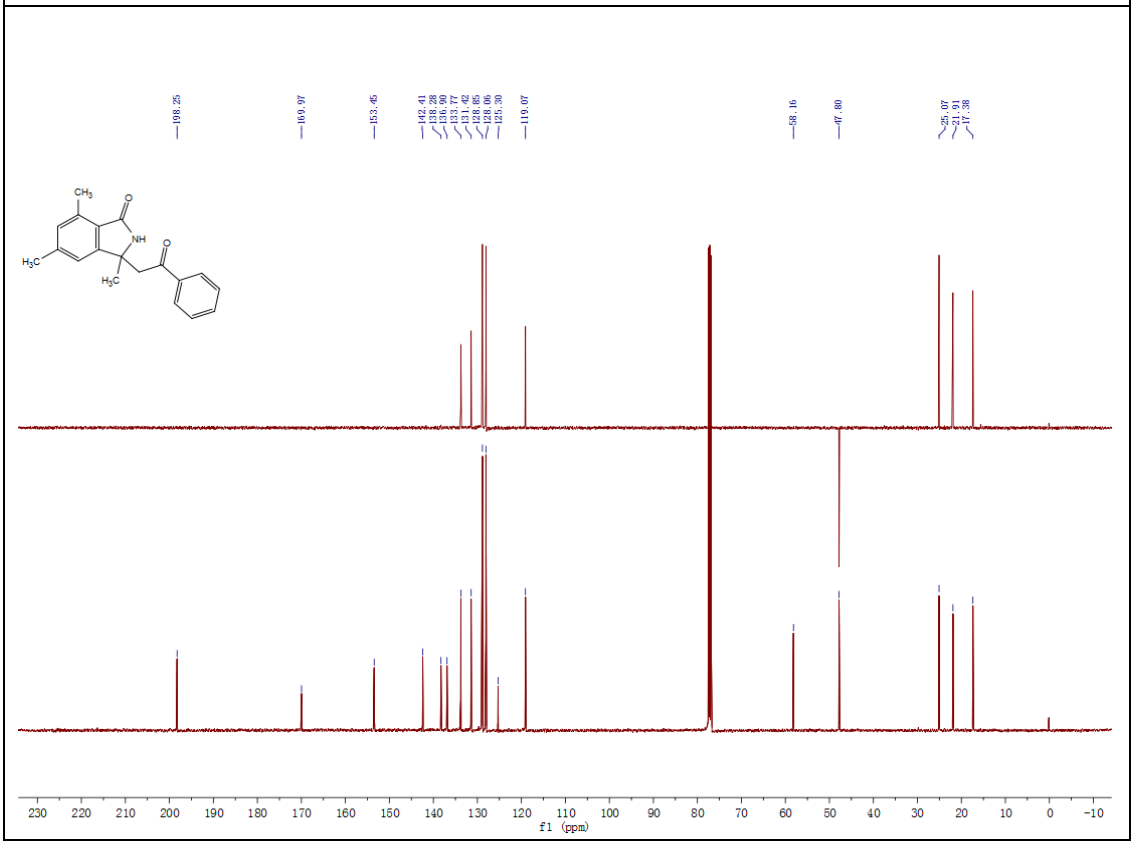
4-bromo-3-methyl-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3d'):



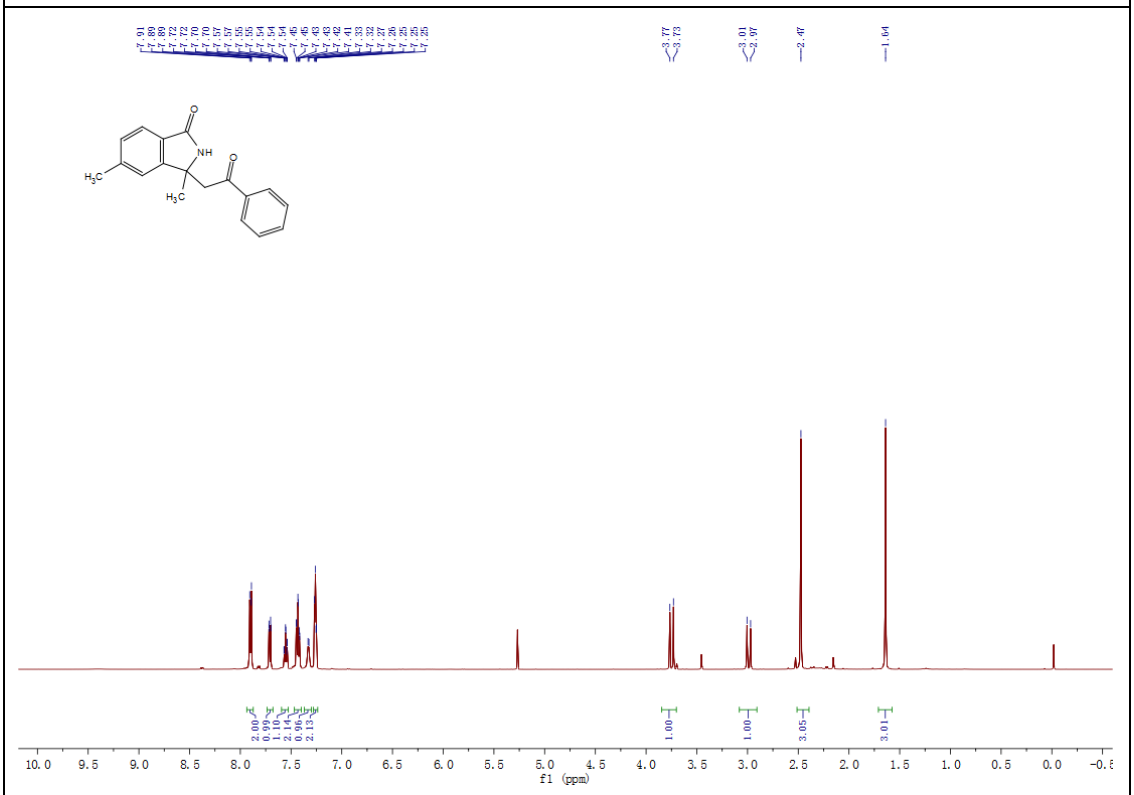


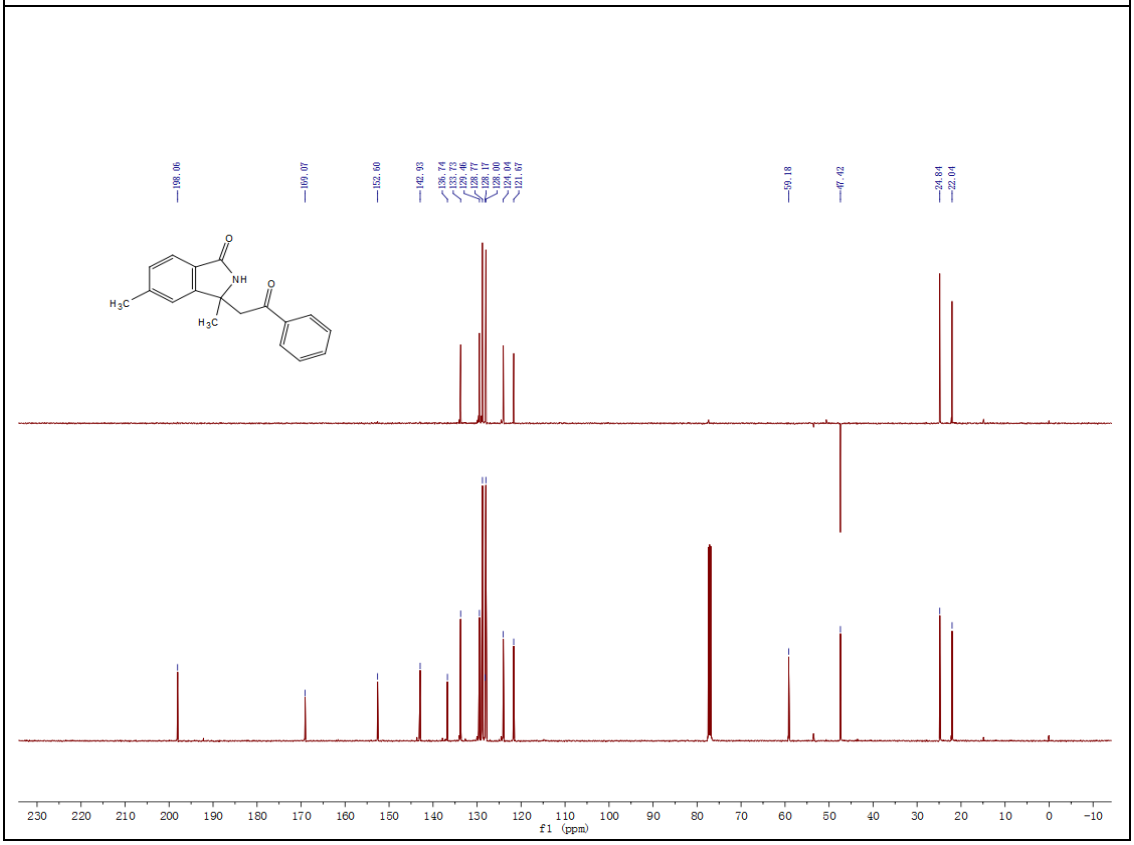
3,5,7-trimethyl-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3e):



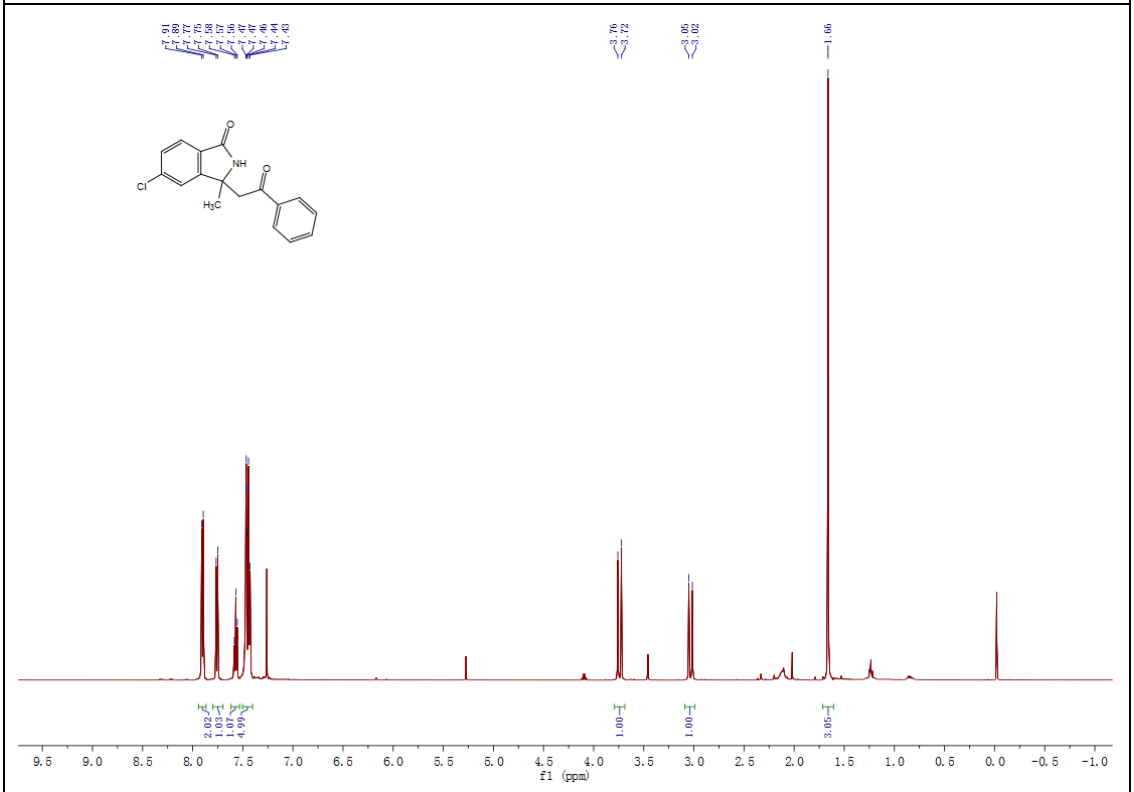


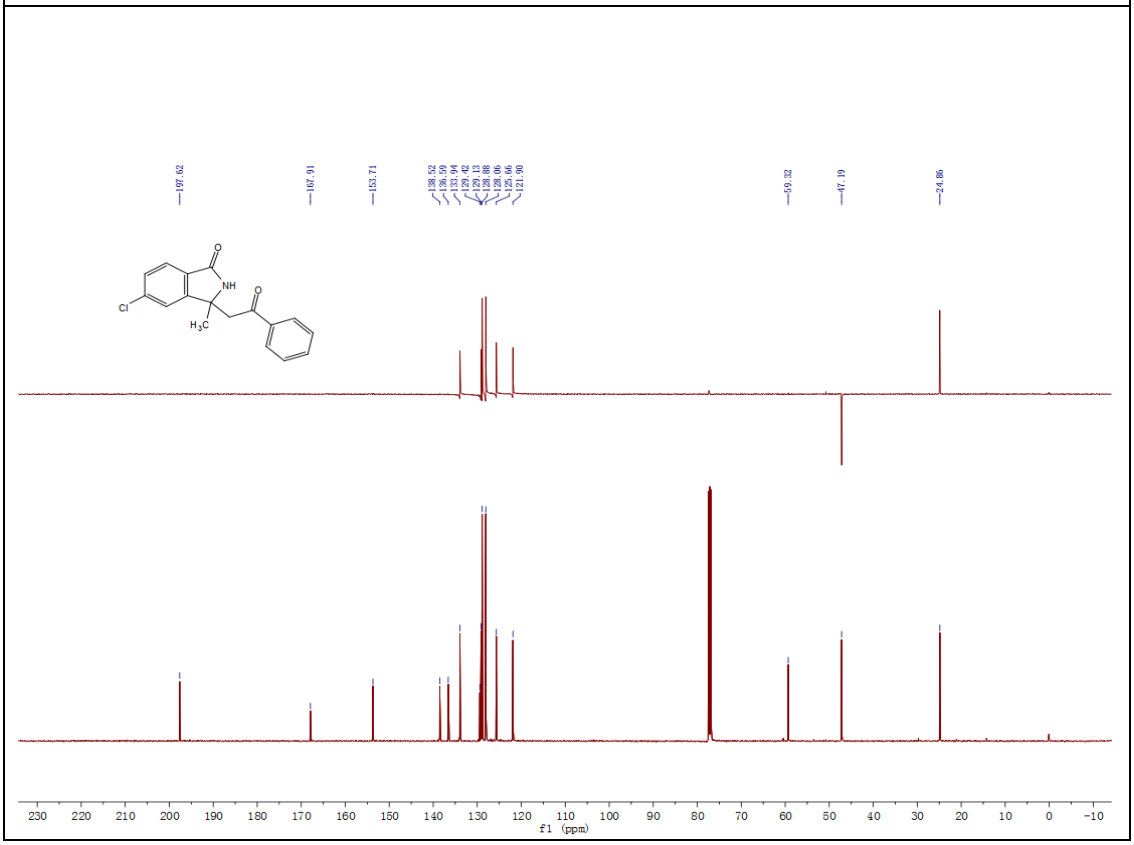
3,5-dimethyl-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3f):



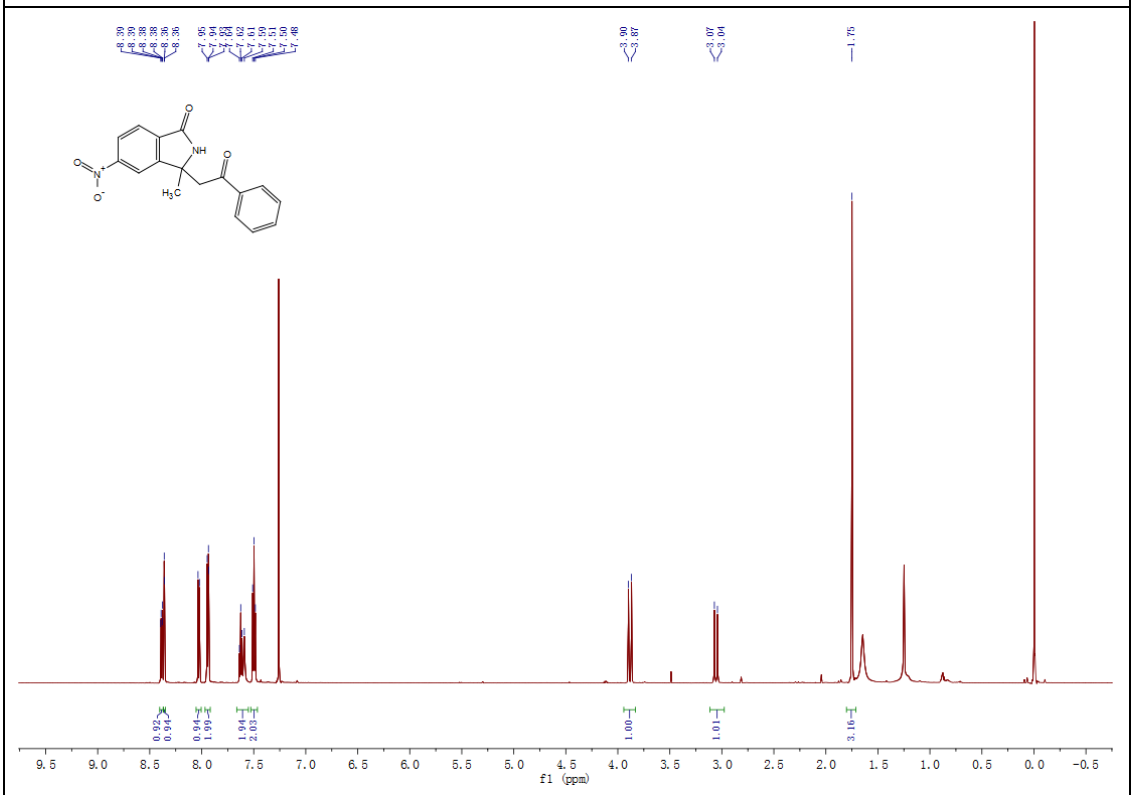


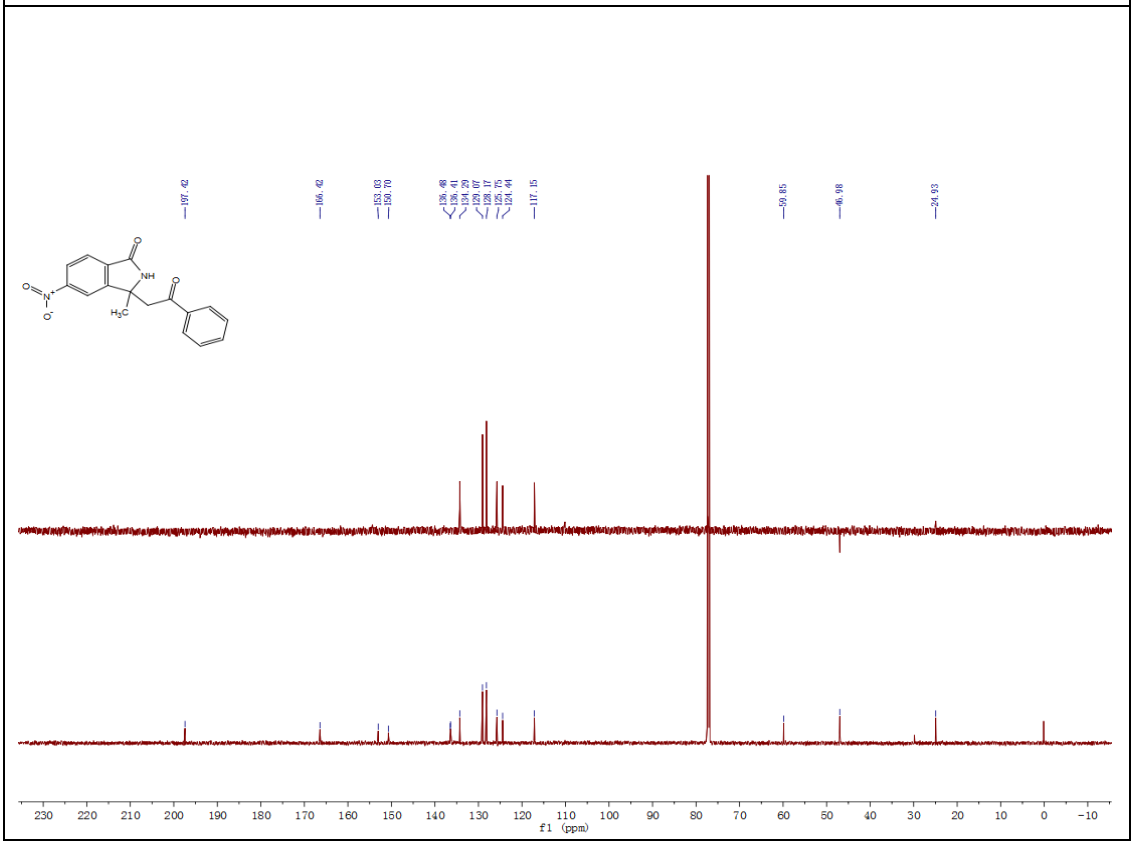
5-chloro-3-methyl-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3g):



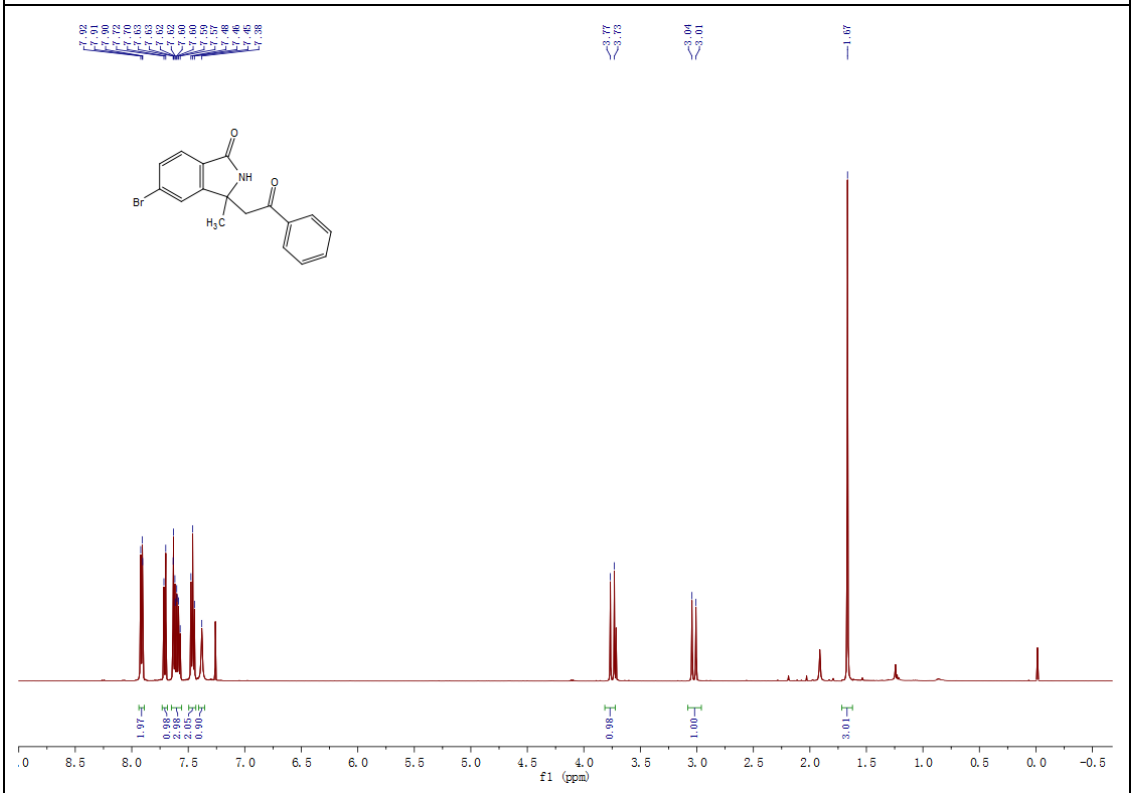


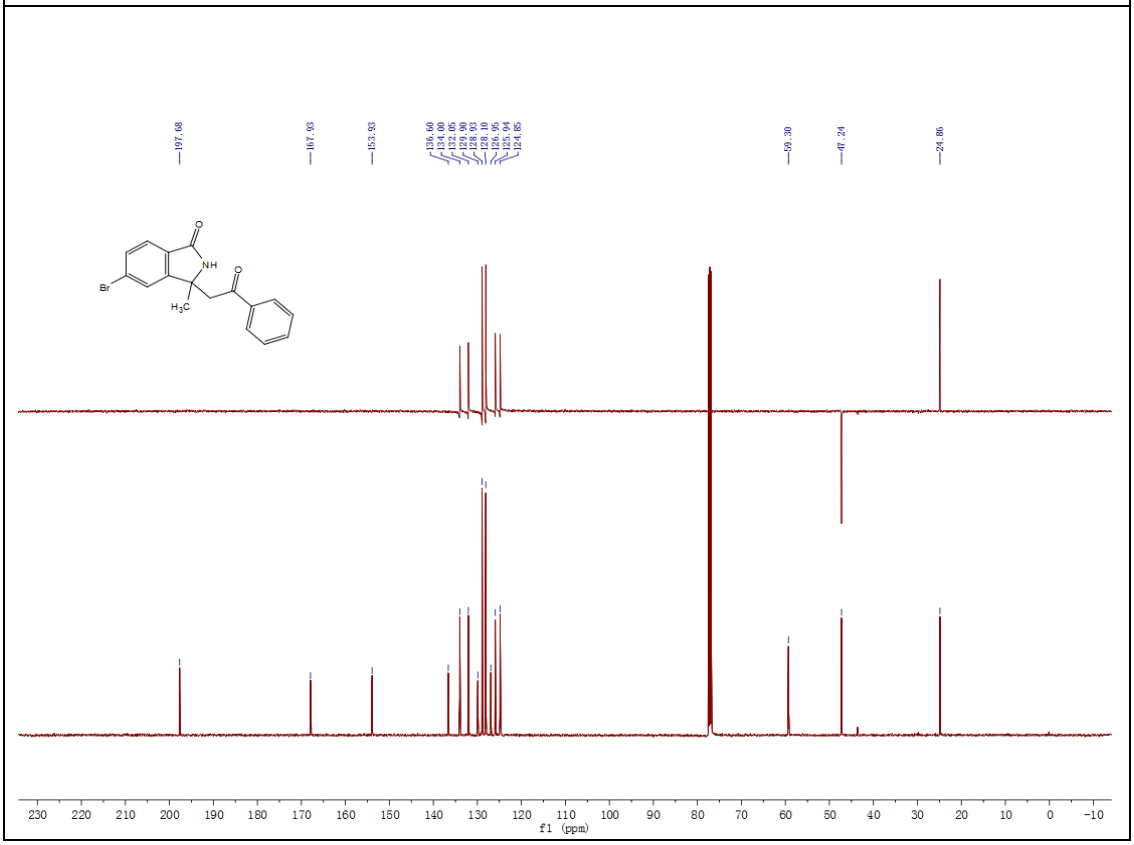
3-methyl-5-nitro-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3h):



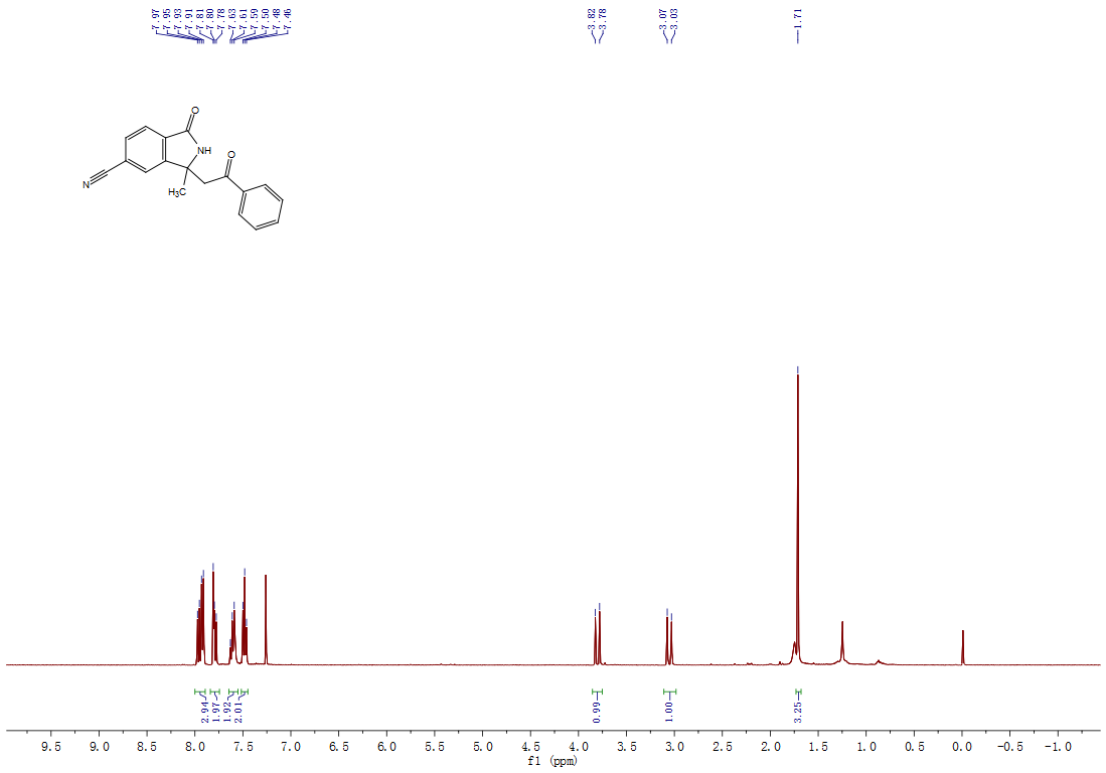


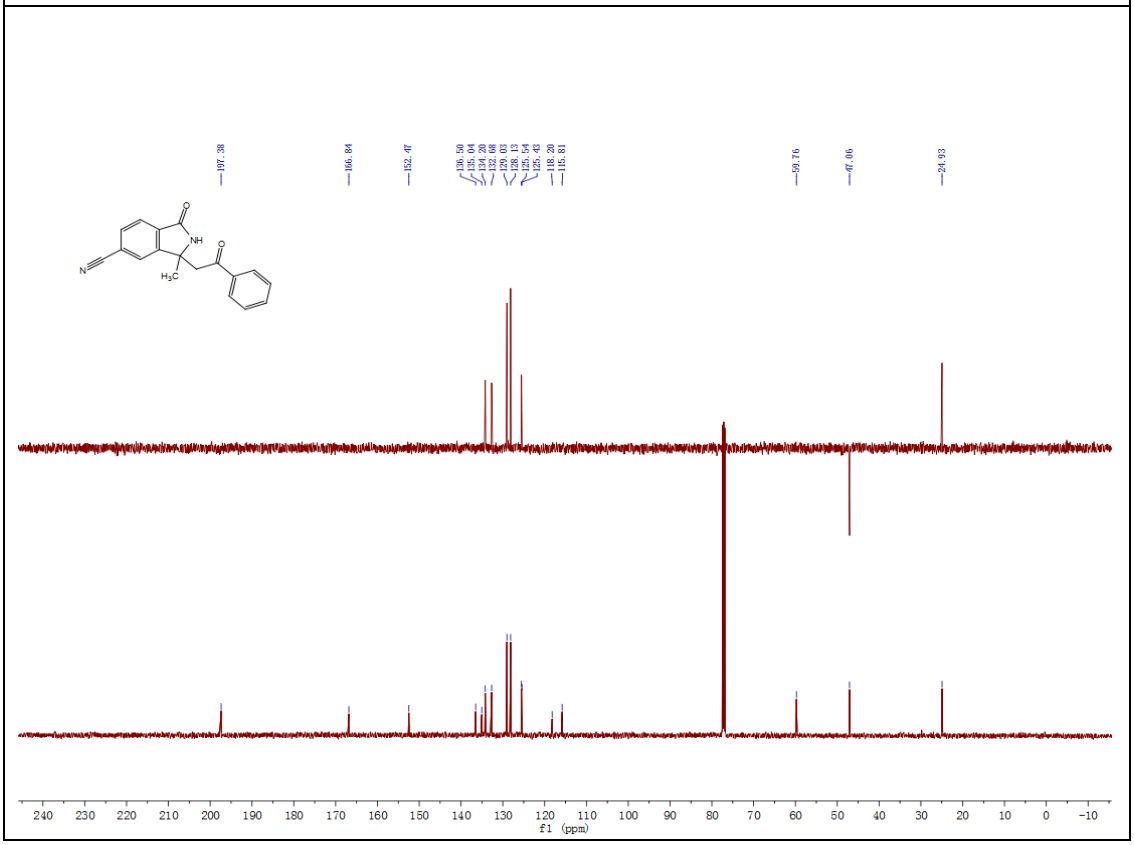
5-bromo-3-methyl-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3i):



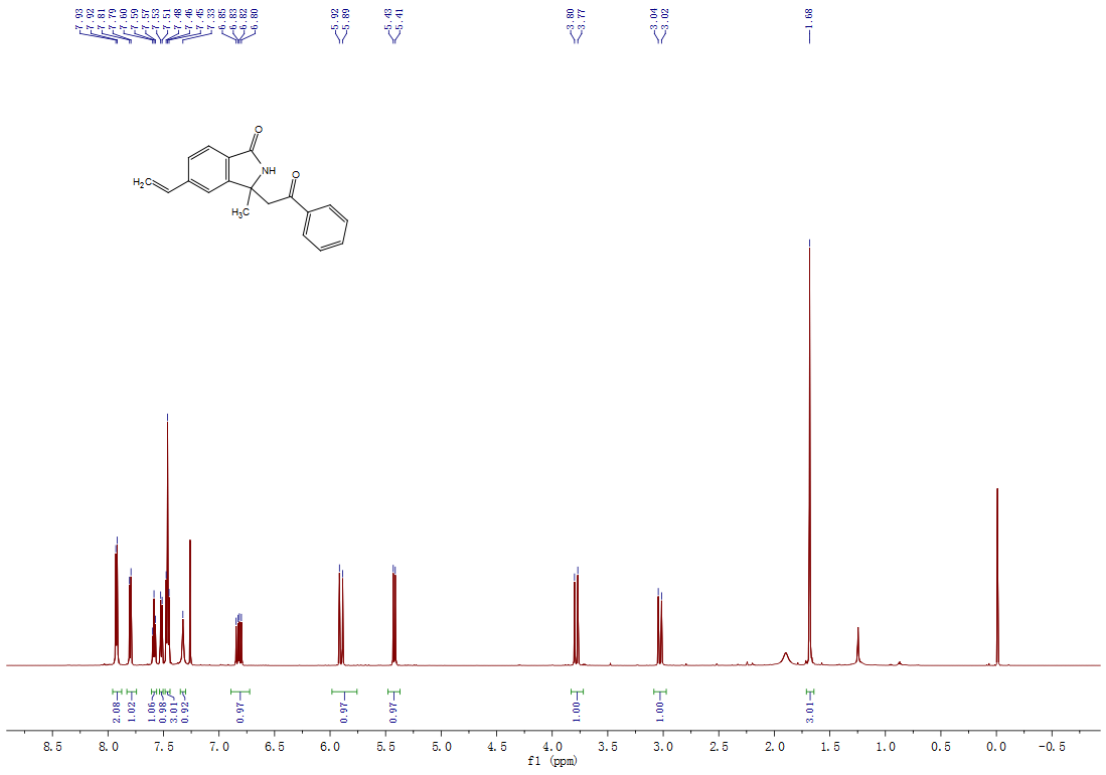


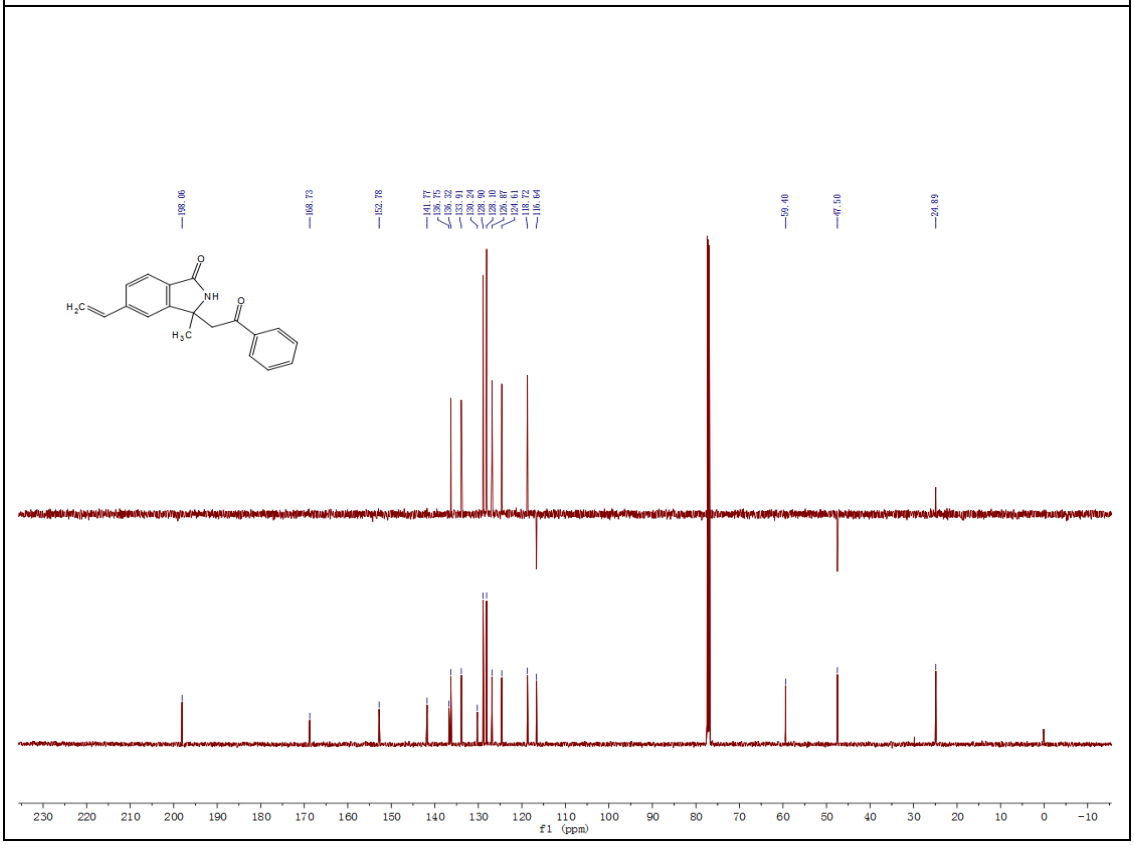
3-methyl-1-oxo-3-(2-oxo-2-phenylethyl)isoindoline-5-carbonitrile (3j):



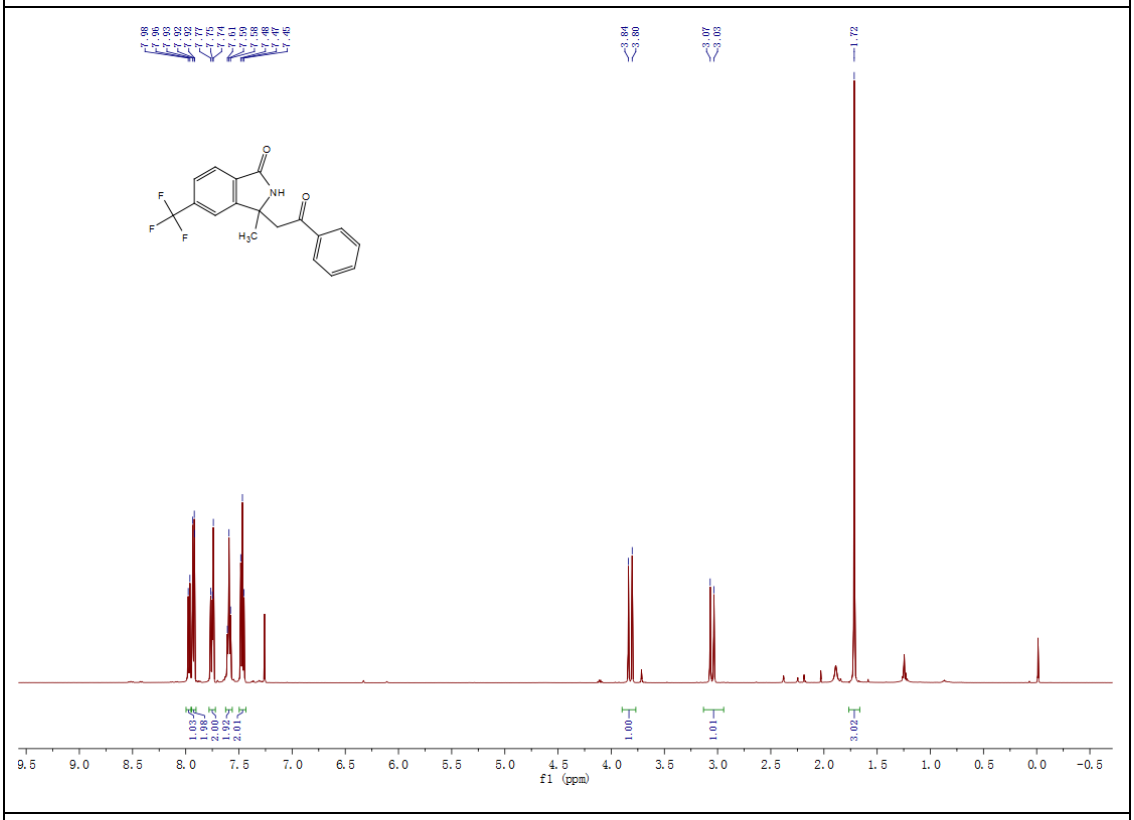


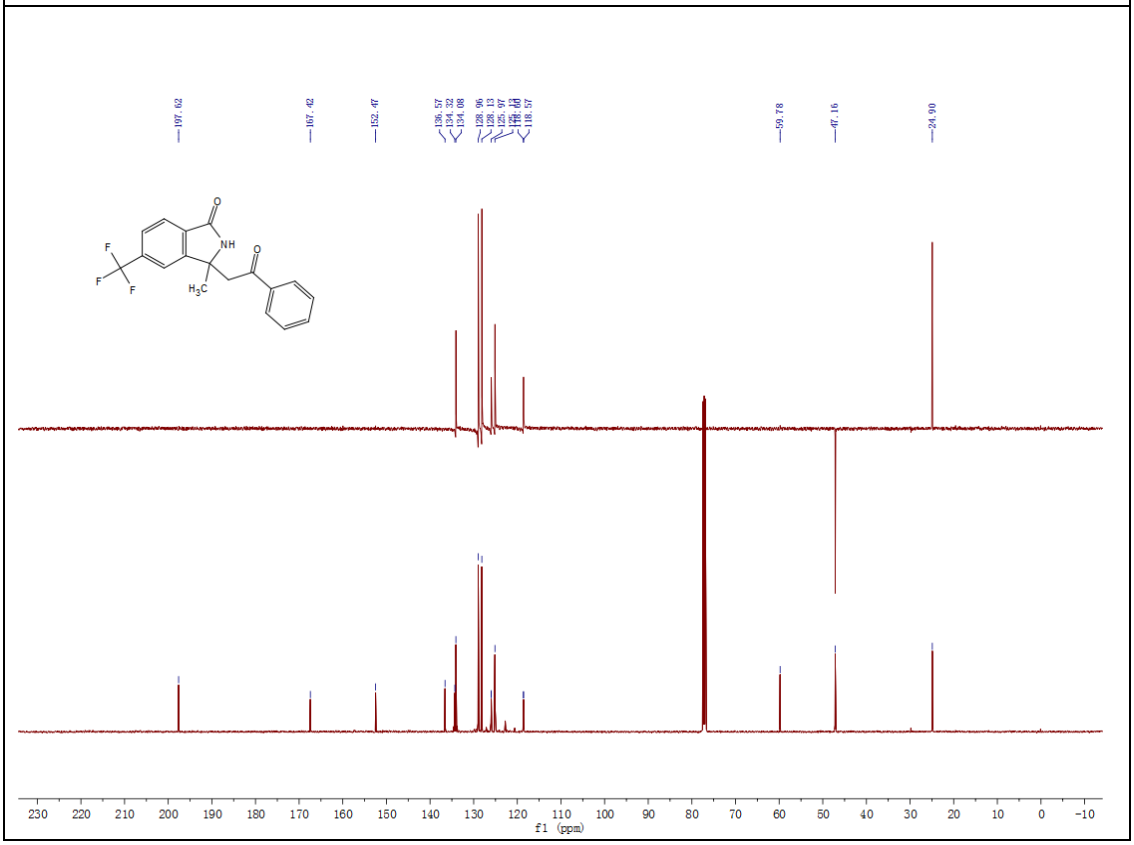
3-methyl-3-(2-oxo-2-phenylethyl)-5-vinylisoindolin-1-one (3k):





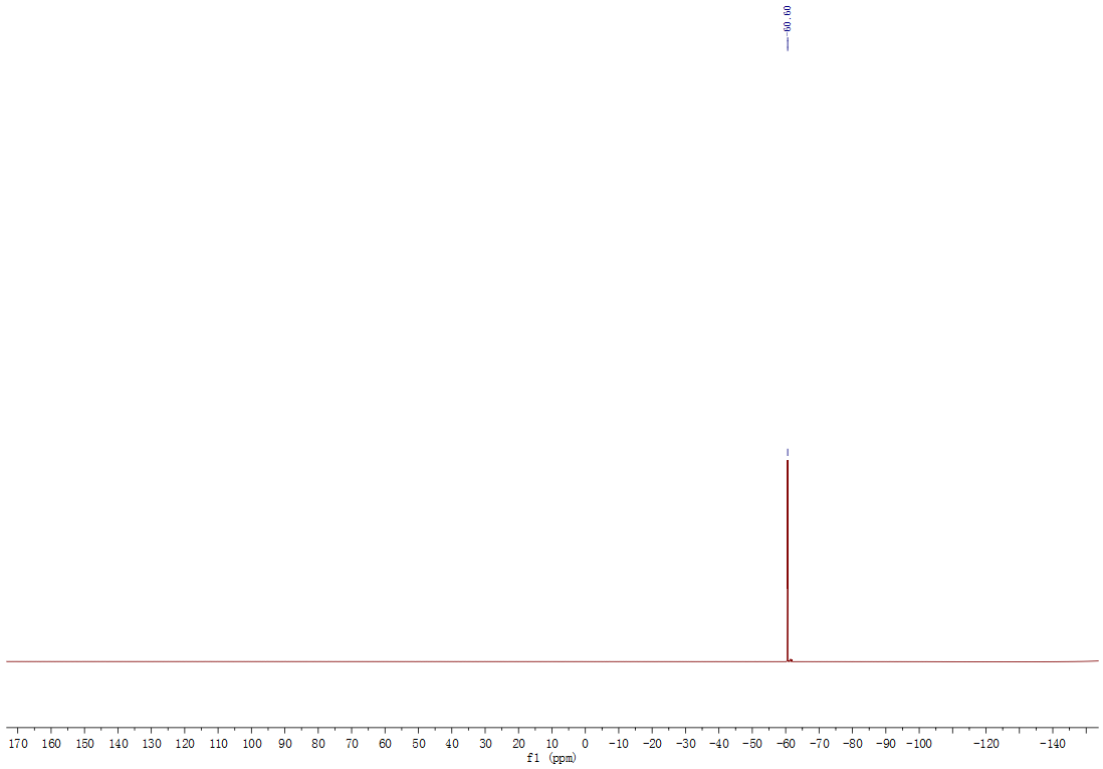
3-methyl-3-(2-oxo-2-phenylethyl)-5-(trifluoromethyl)isoindolin-1-one (3l):



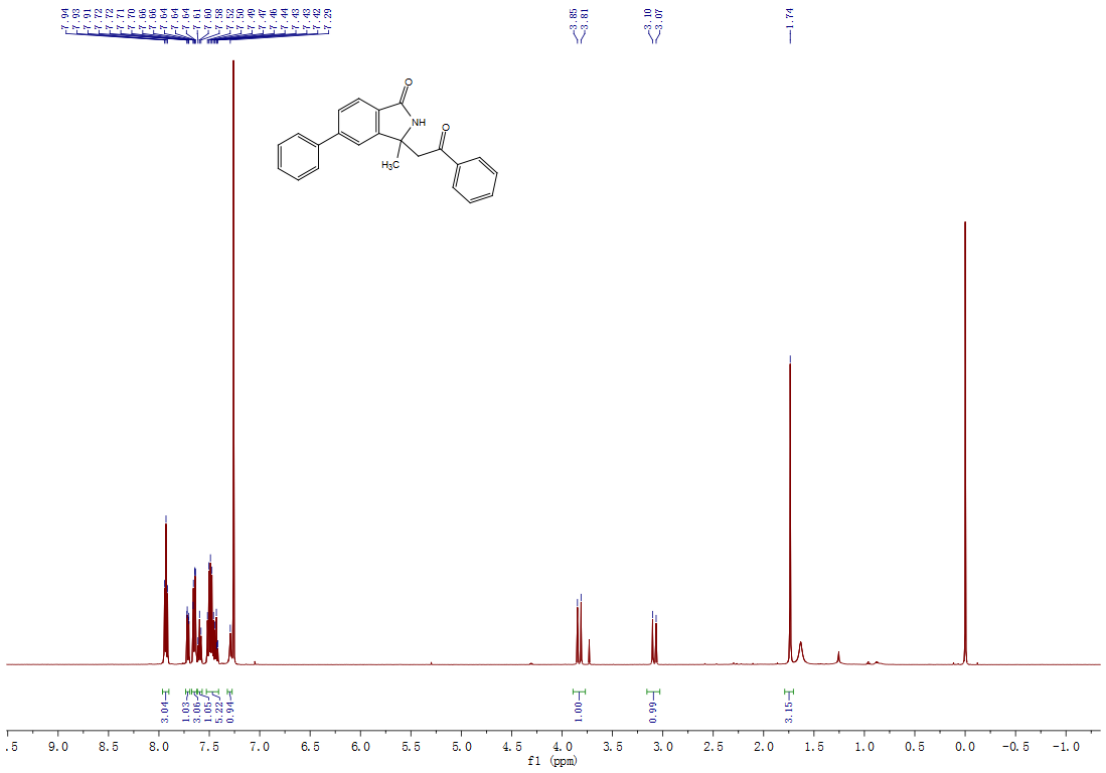


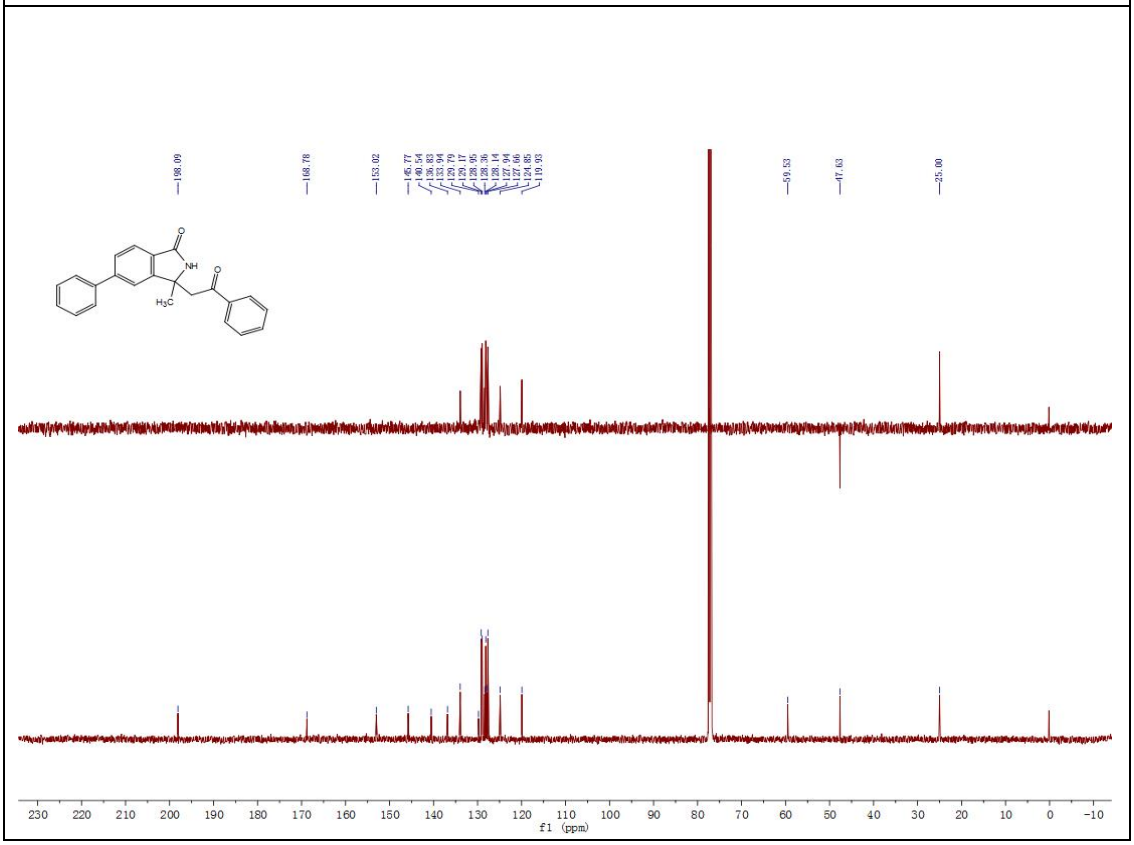
^{19}F NMR of

3-methyl-3-(2-oxo-2-phenylethyl)-5-(trifluoromethyl)isoindolin-1-one (3l):

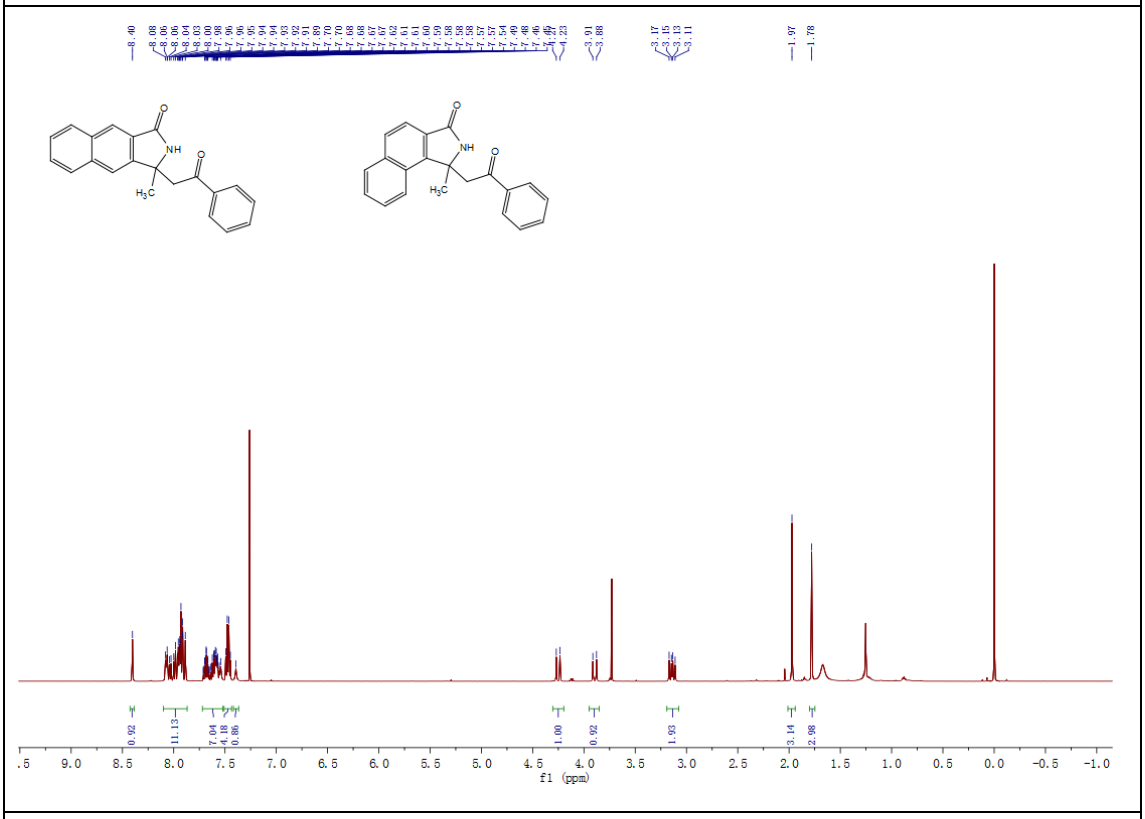


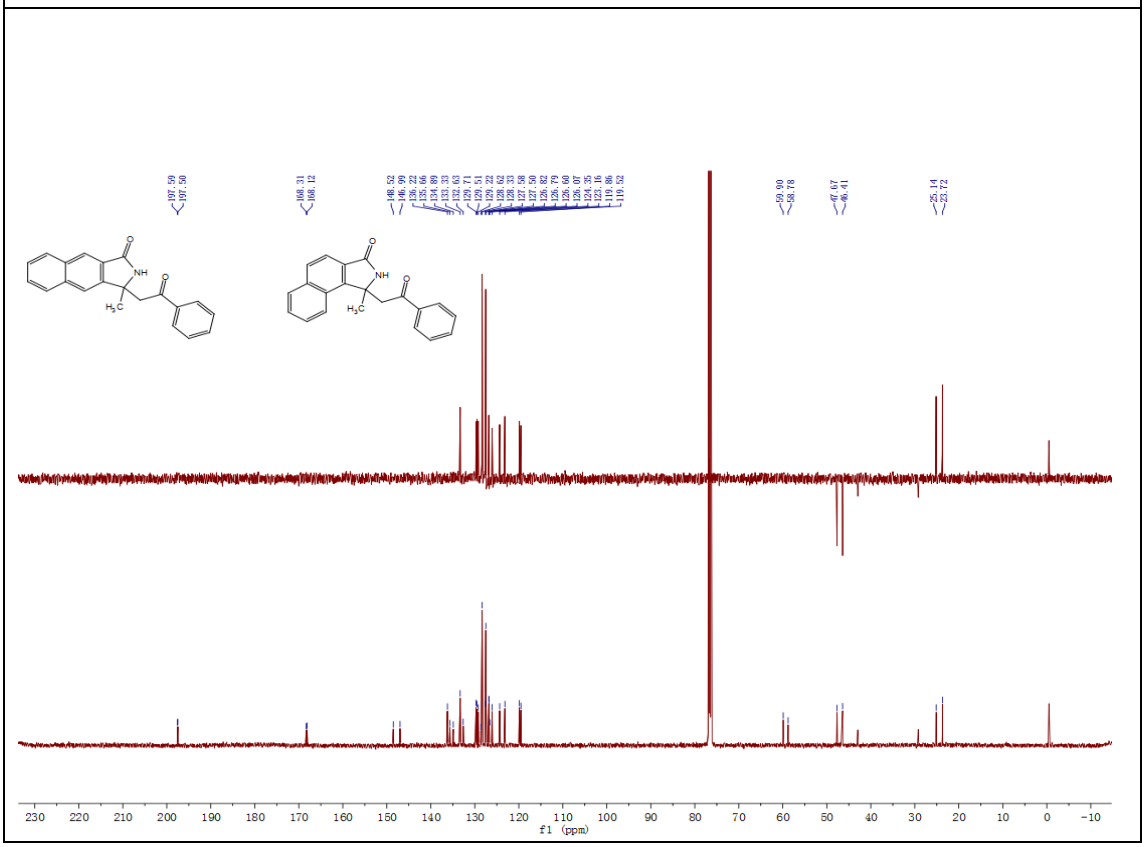
3-methyl-3-(2-oxo-2-phenylethyl)-5-phenylisoindolin-1-one (3m):



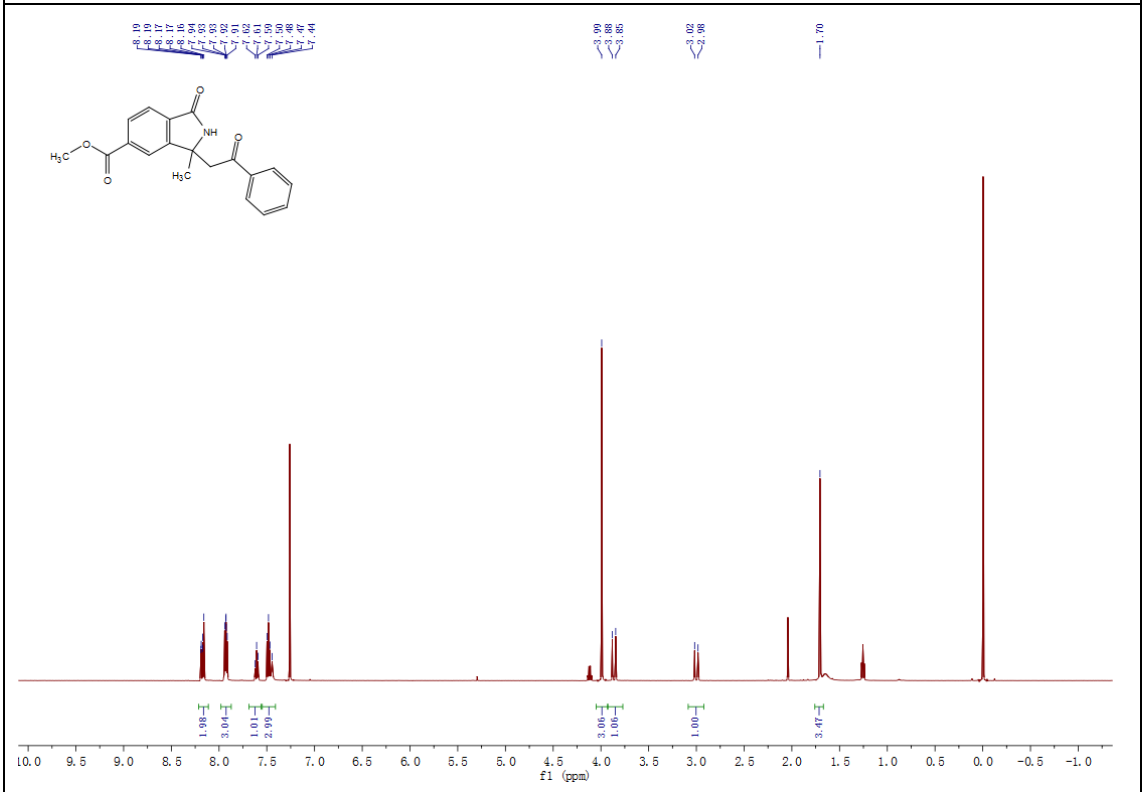


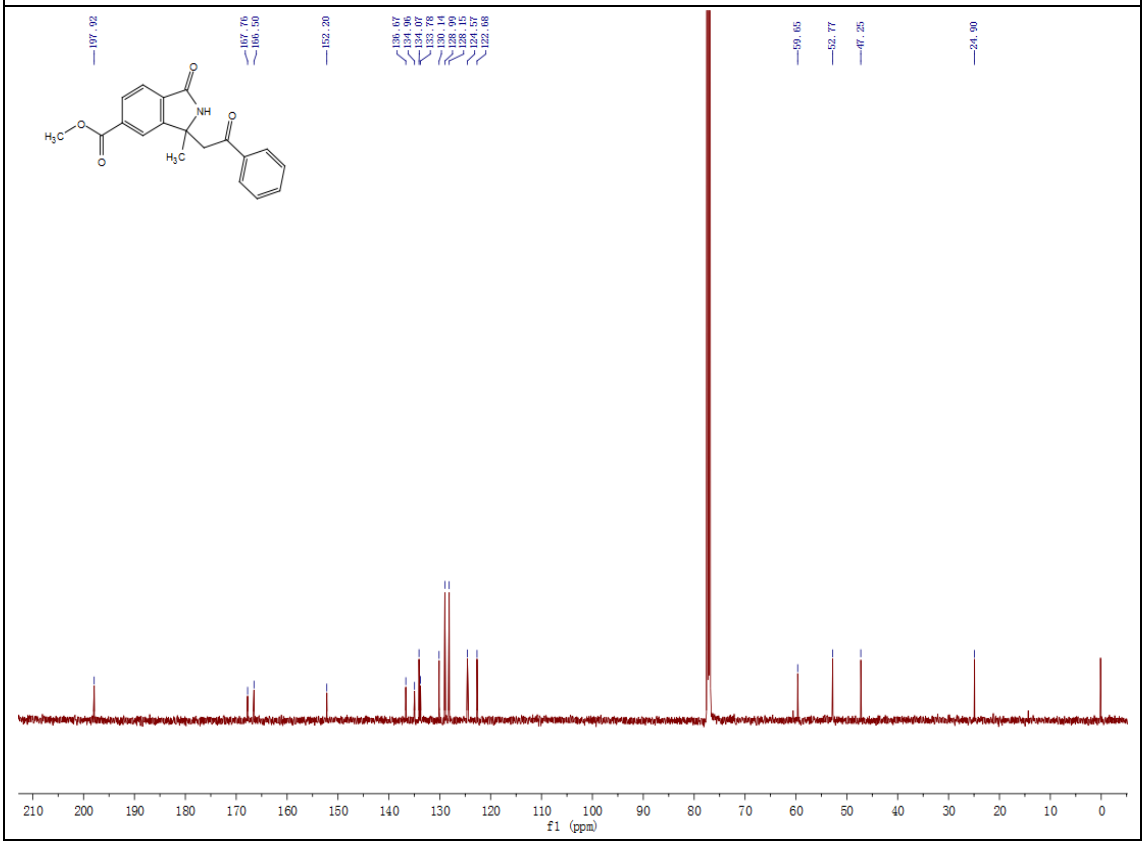
3-methyl-3-(2-oxo-2-phenylethyl)-2,3-dihydro-1H-benzo[f]isoindol-1-one (3n) and 1-methyl-1-(2-oxo-2-phenylethyl)-1,2-dihydro-3H-benzo[e]isoindol-3-one (3n'):



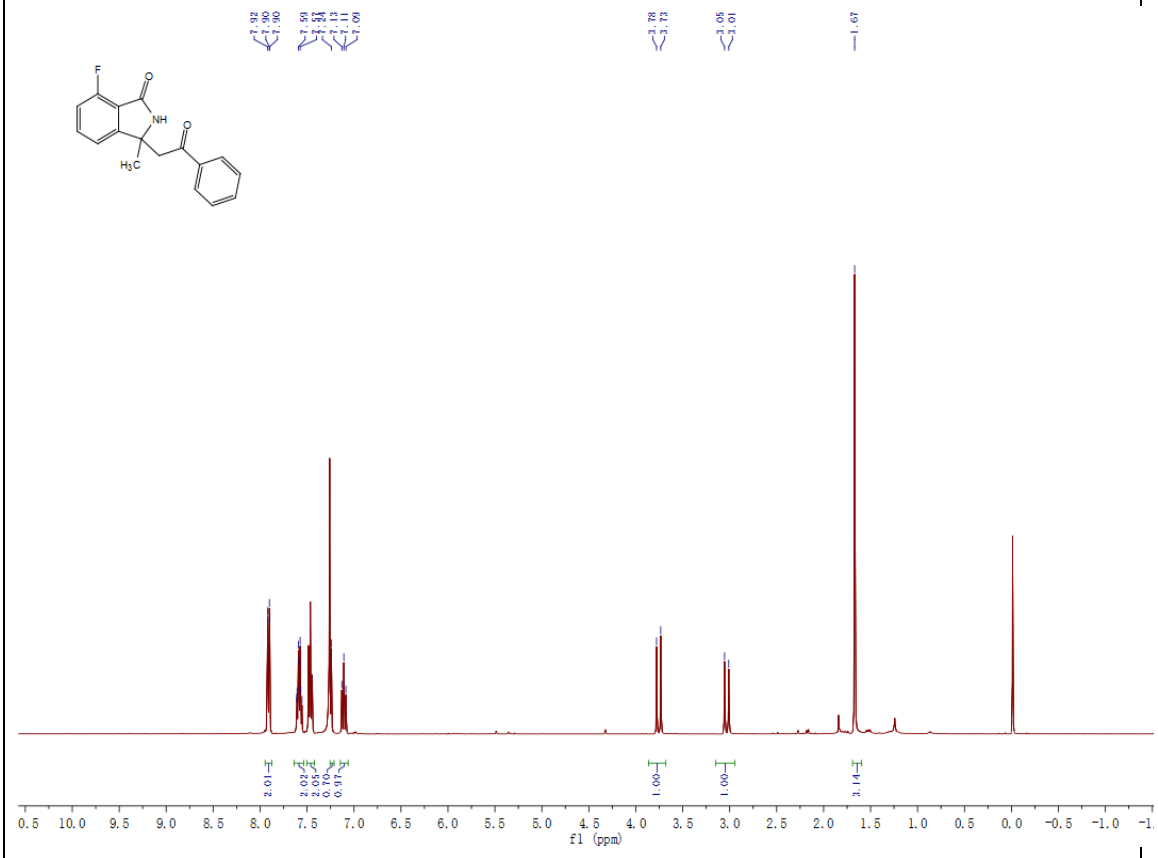


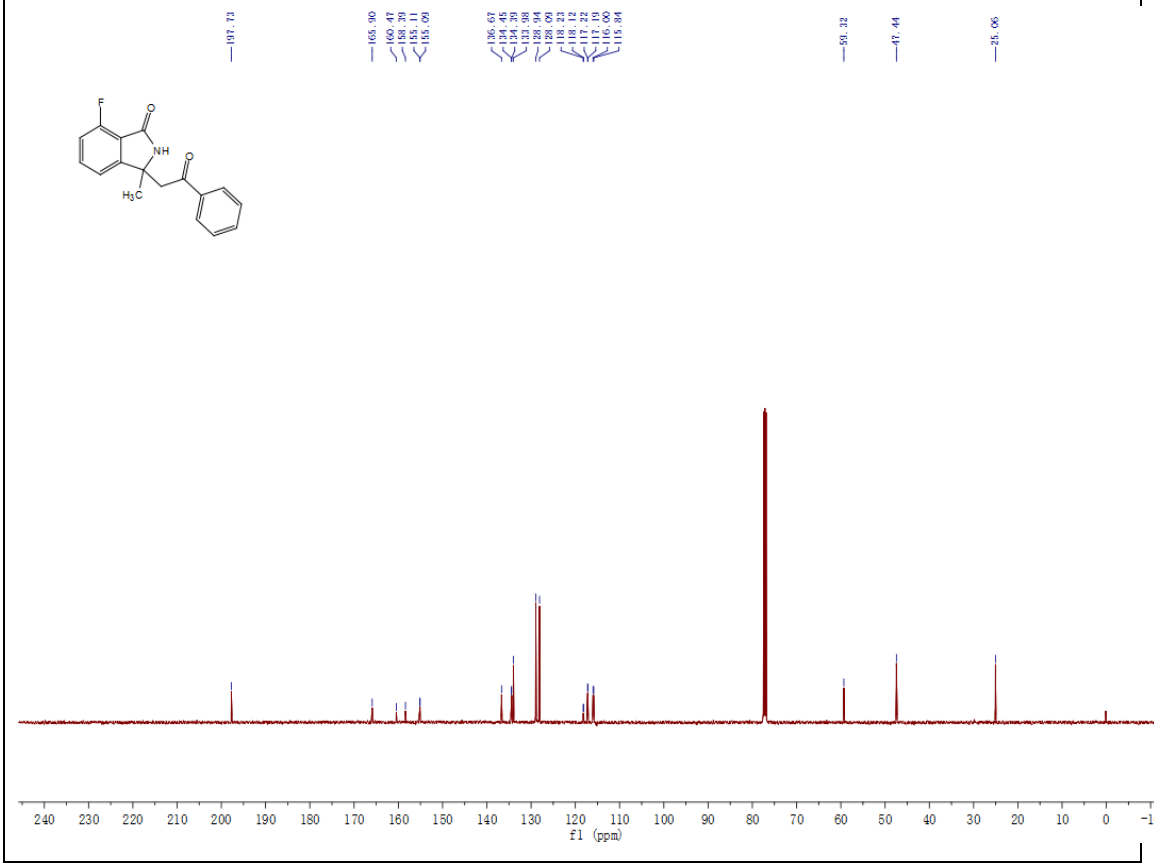
Methyl 3-methyl-1-oxo-3-(2-oxo-2-phenylethyl) isoindoline-5-carboxylate (3o):



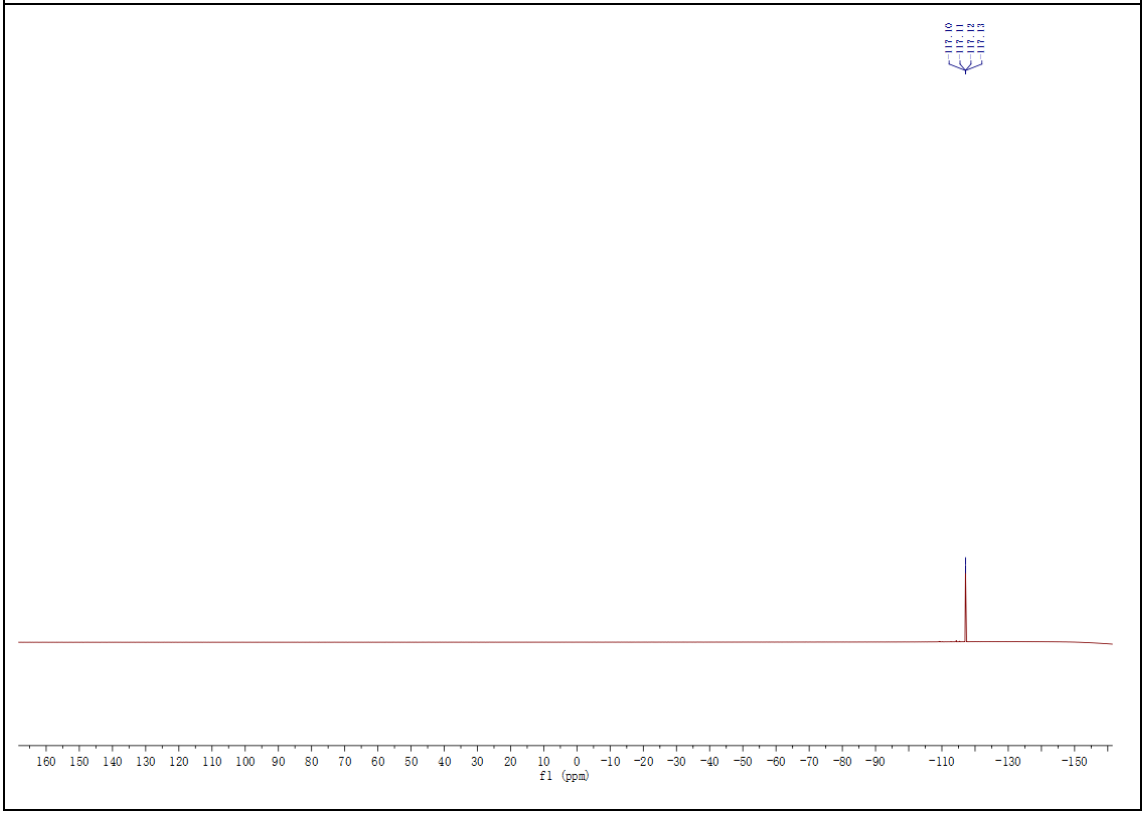


7-fluoro-3-methyl-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3p):

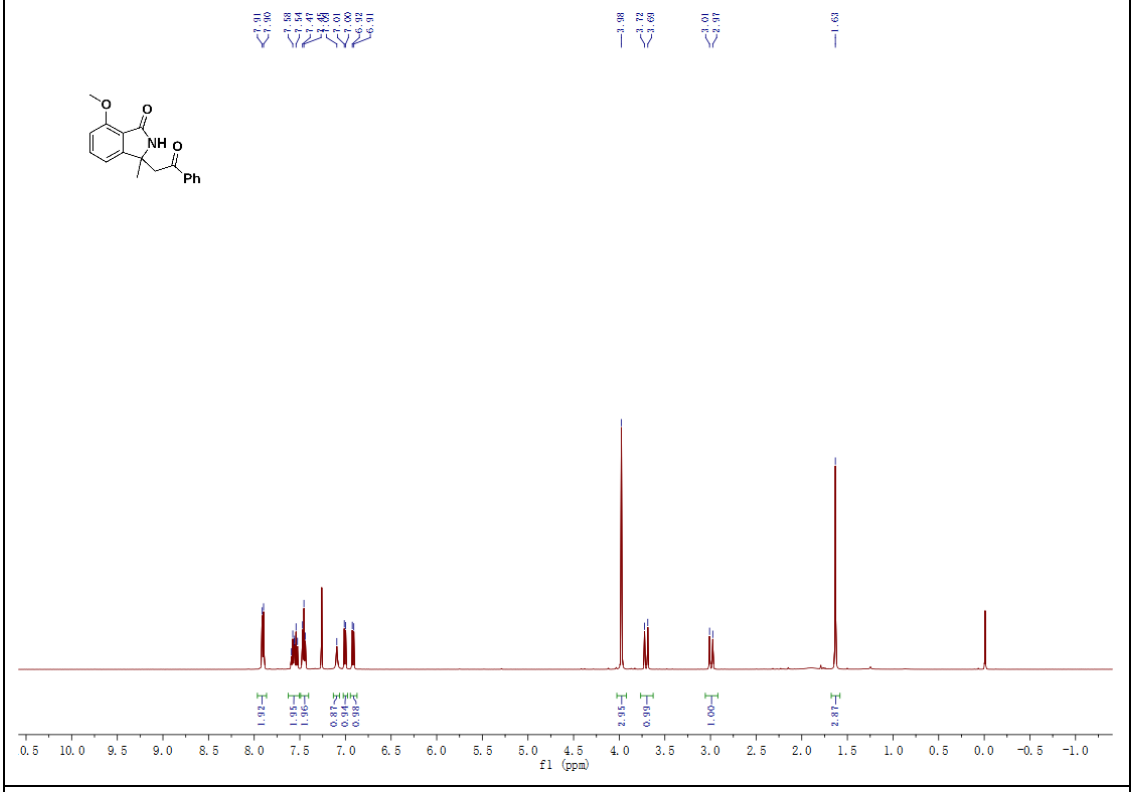


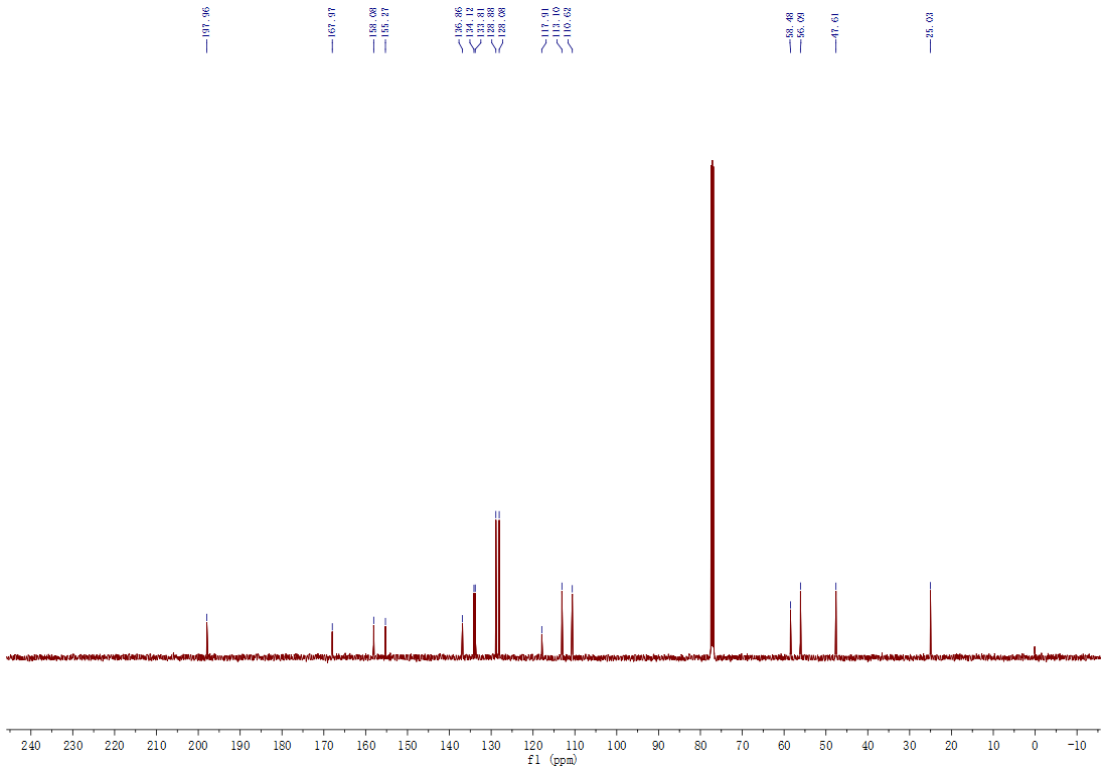


^{19}F NMR of 7-fluoro-3-methyl-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3p):

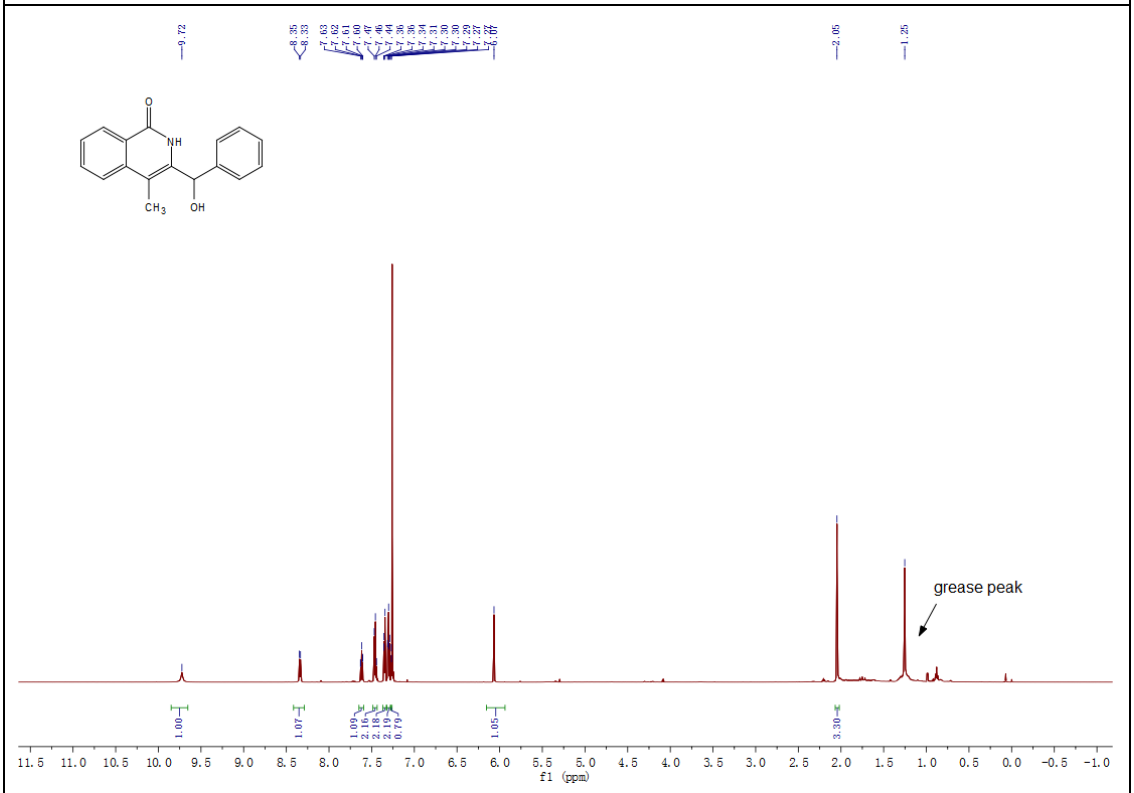


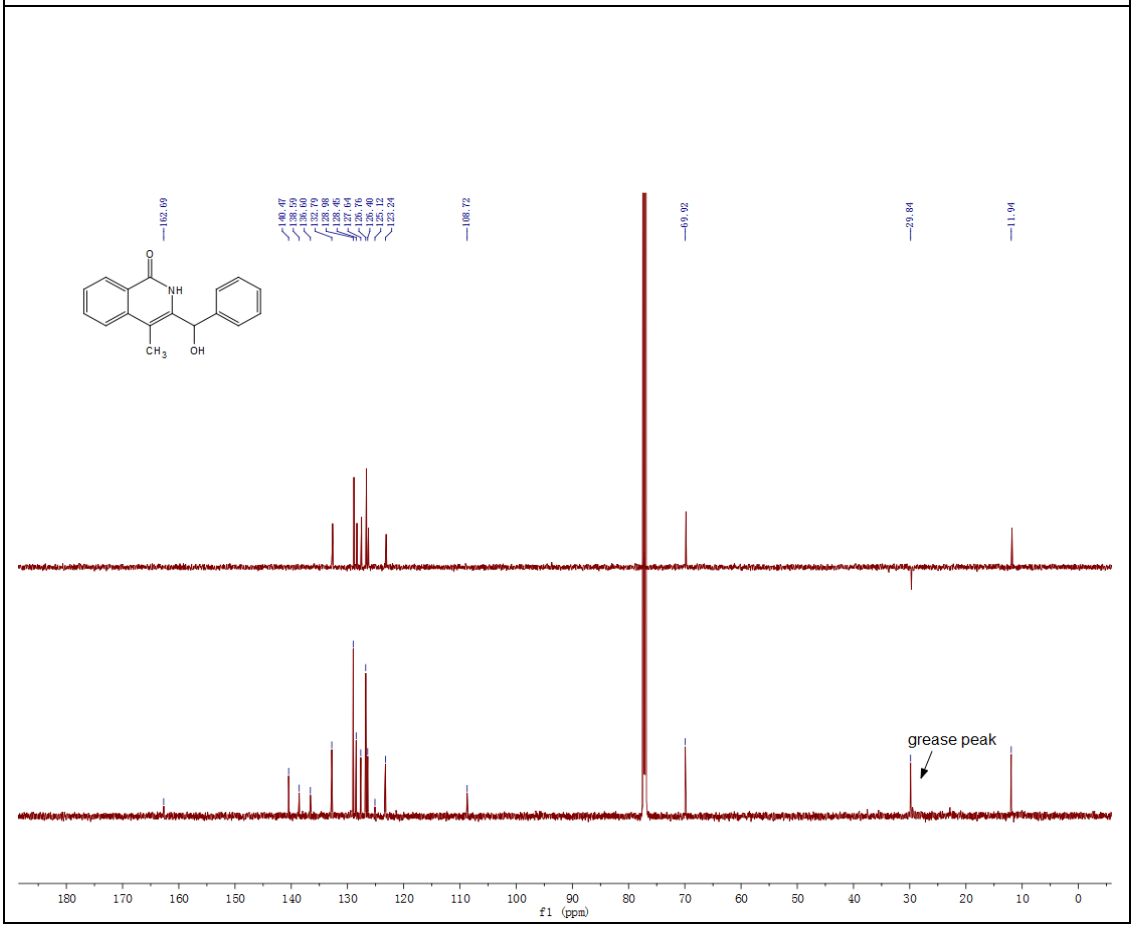
7-methoxy-3-methyl-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3q):



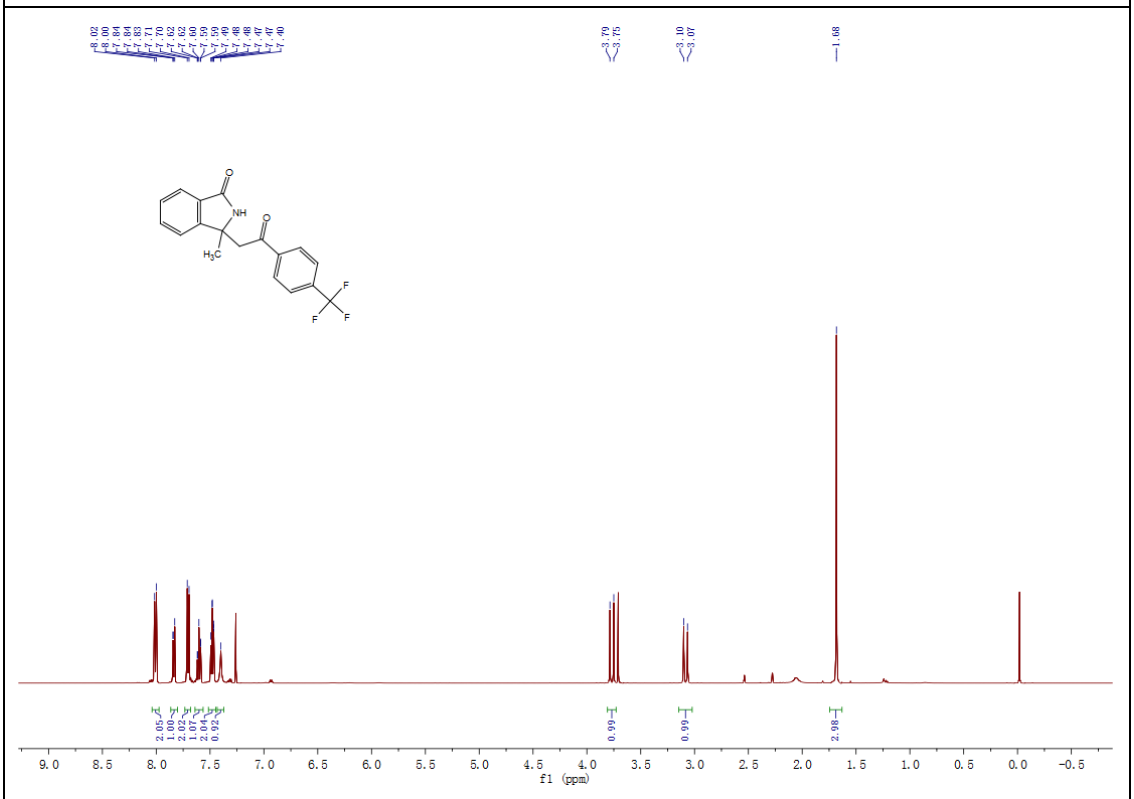


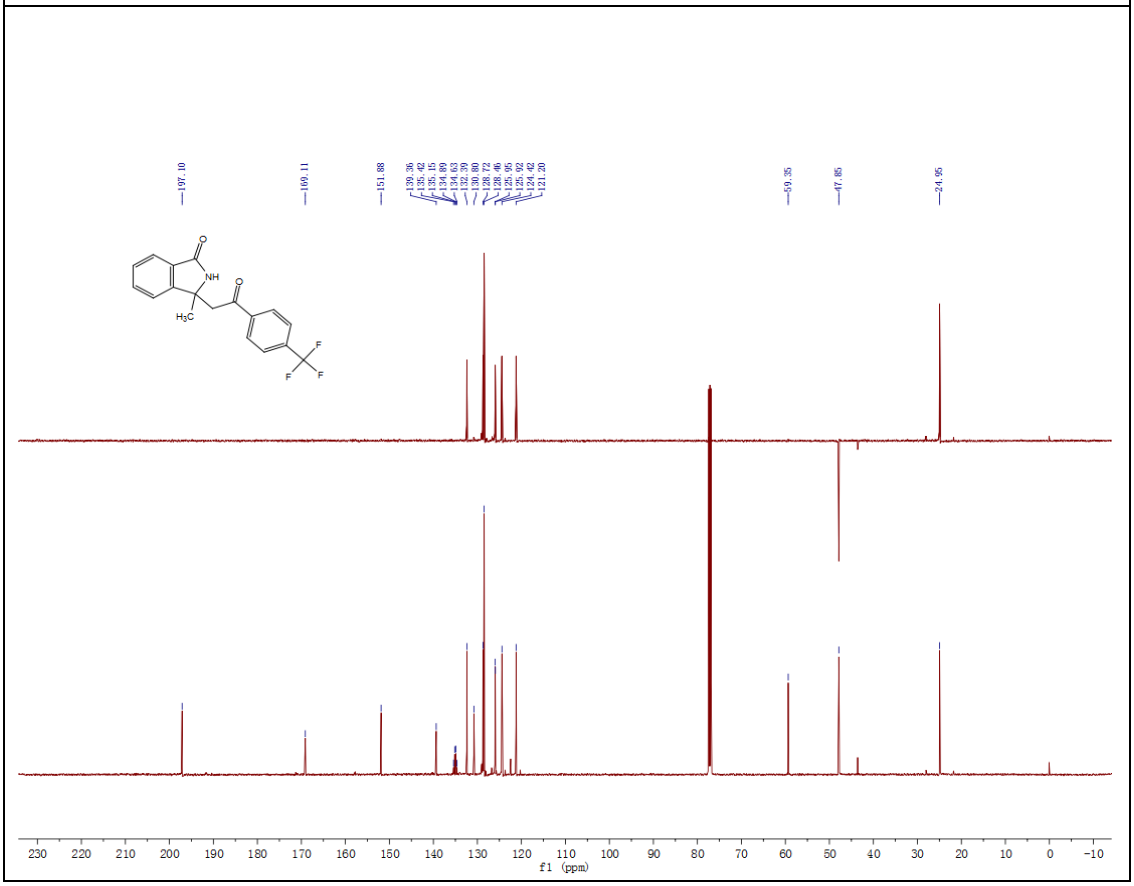
3-(hydroxy(phenyl)methyl)-4-methylisoquinolin-1(2H)-one (4a):





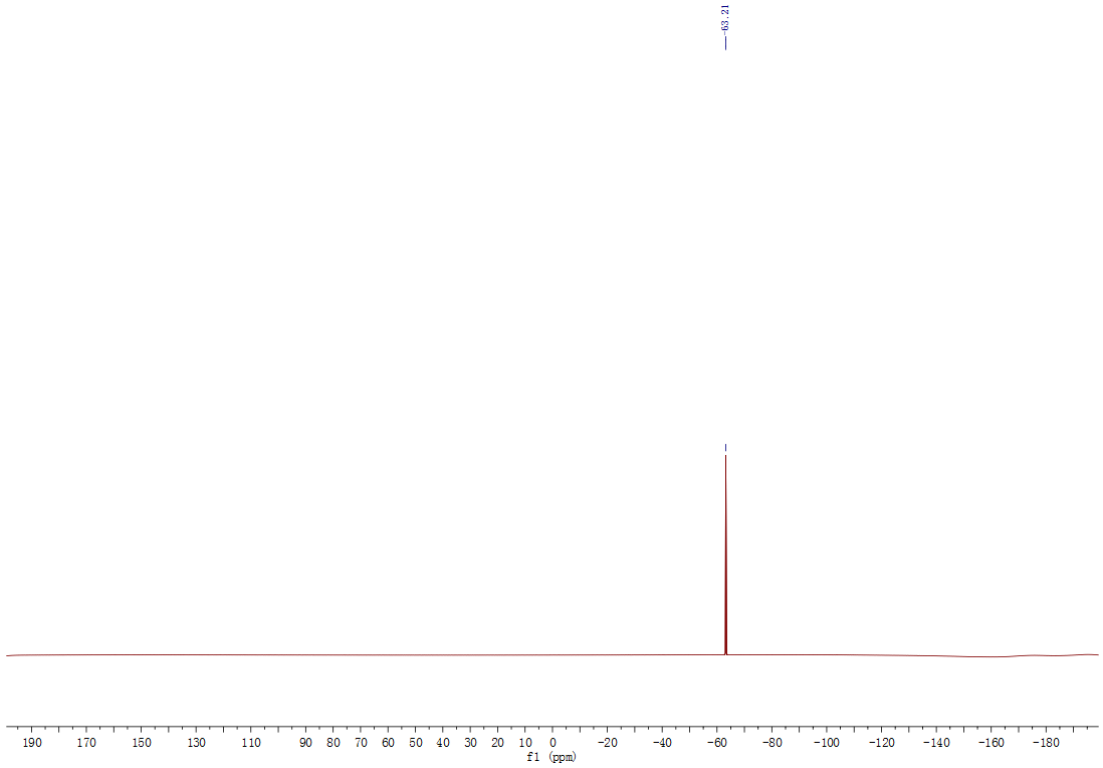
3-methyl-3-(2-oxo-2-(4-(trifluoromethyl)phenyl)ethyl)isoindolin-1-one (3r):



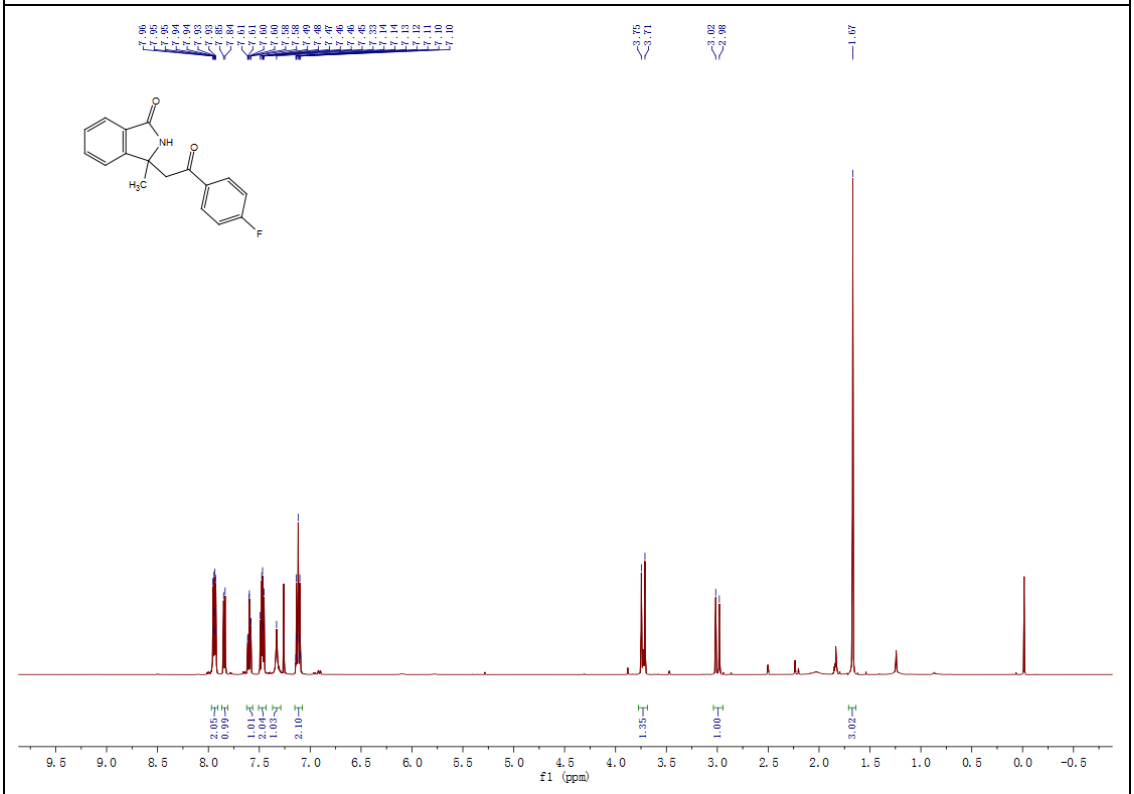


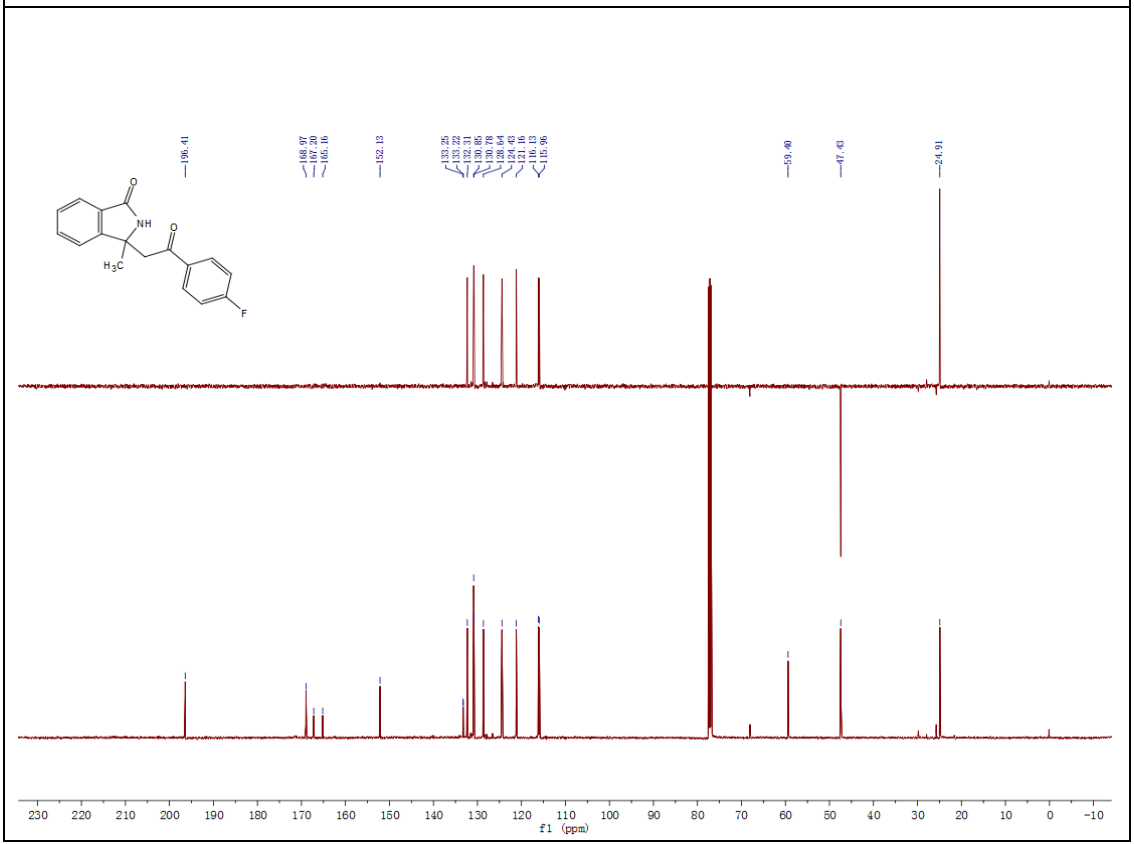
^{19}F NMR of

3-methyl-3-(2-oxo-2-(4-(trifluoromethyl)phenyl)ethyl)isoindolin-1-one (3r):

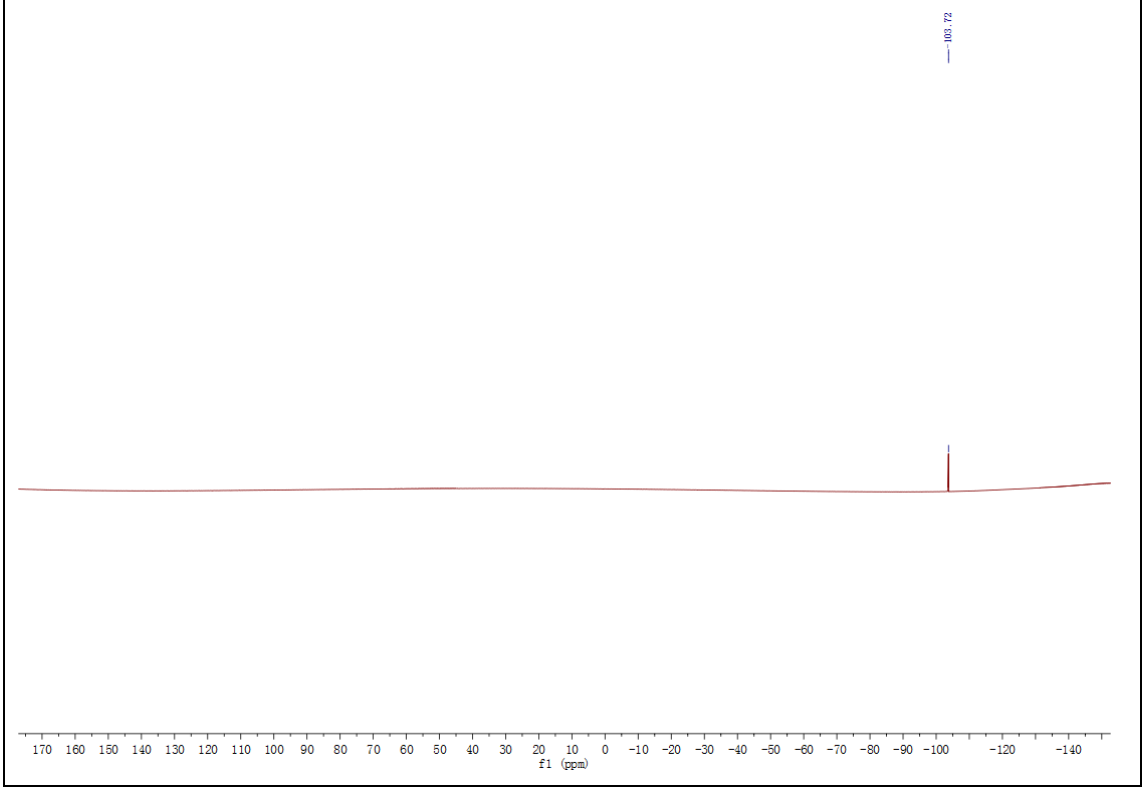


3-(2-(4-fluorophenyl)-2-oxoethyl)-3-methylisoindolin-1-one (3s):

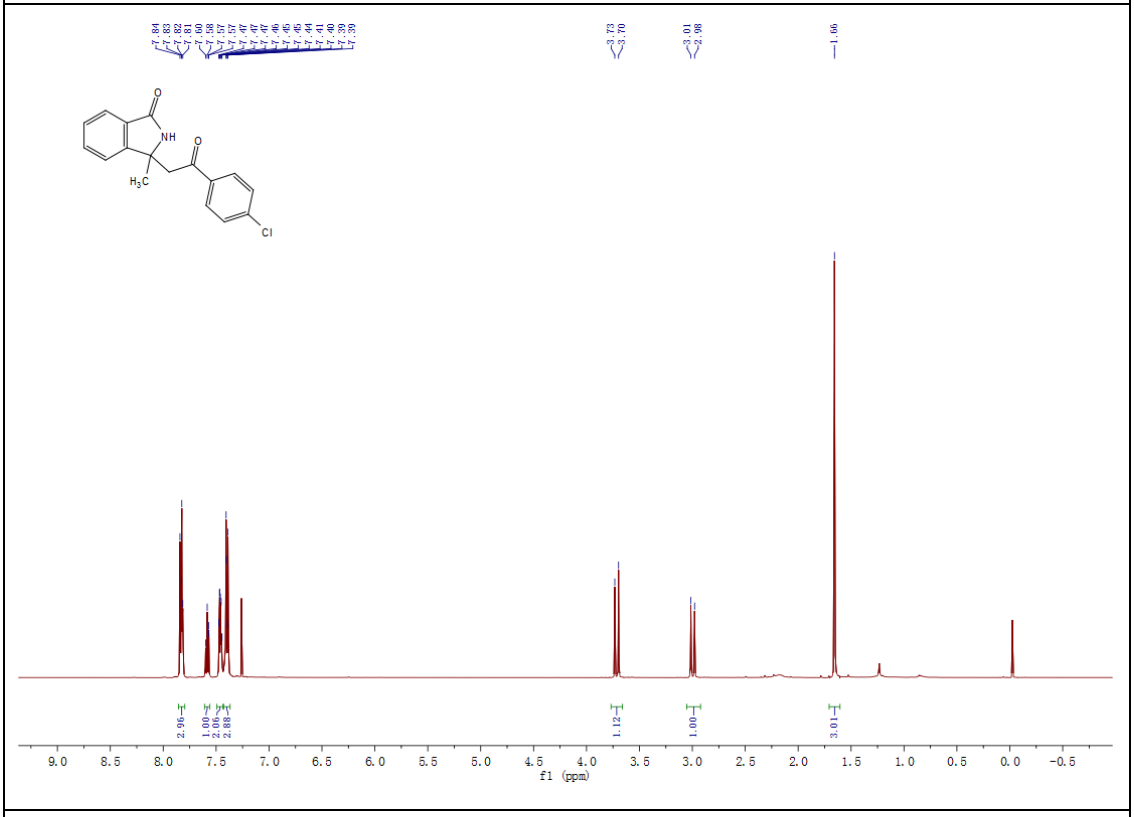


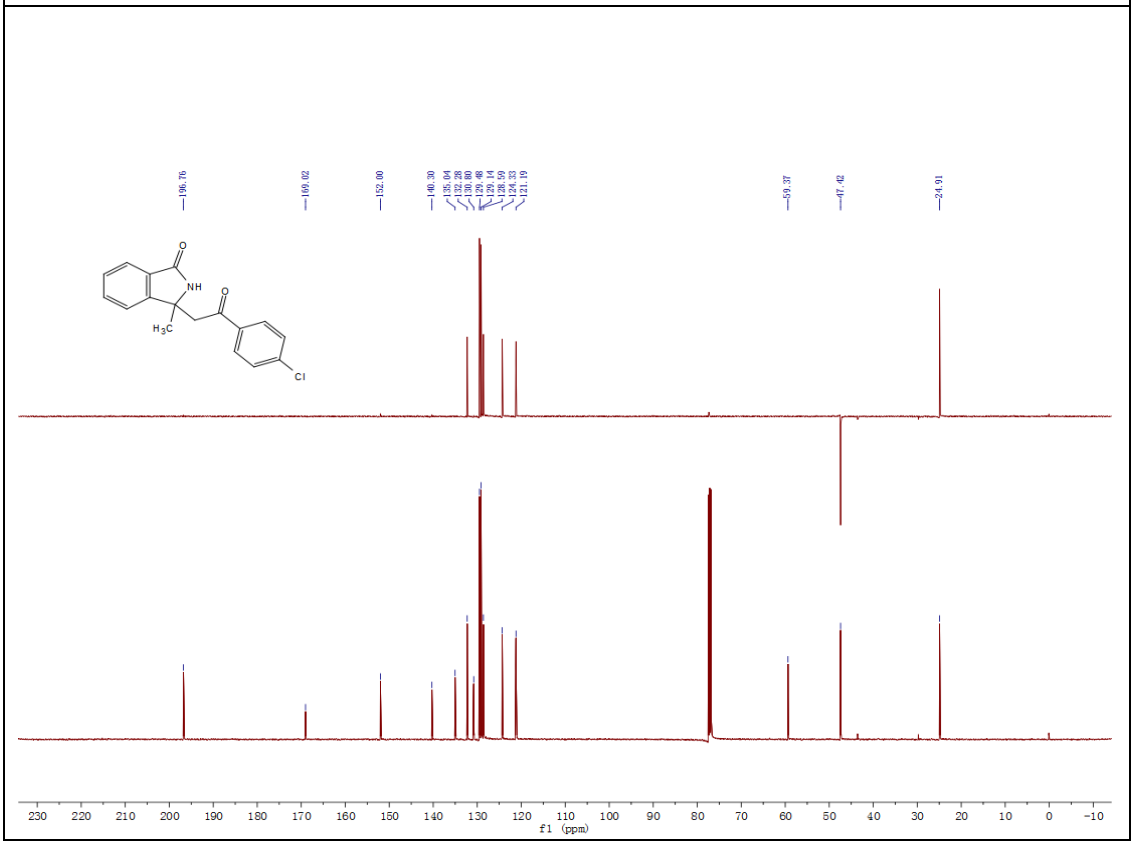


^{19}F NMR of 3-(2-(4-fluorophenyl)-2-oxoethyl)-3-methylisoindolin-1-one (3s):

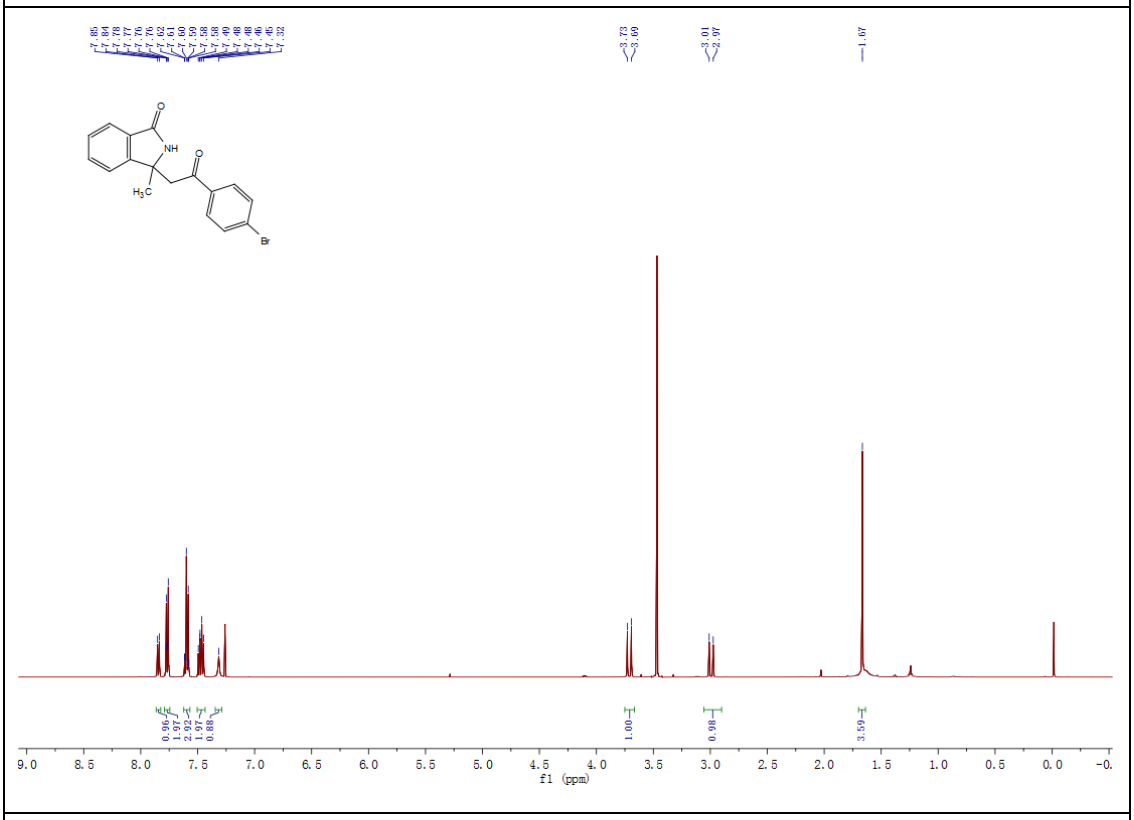


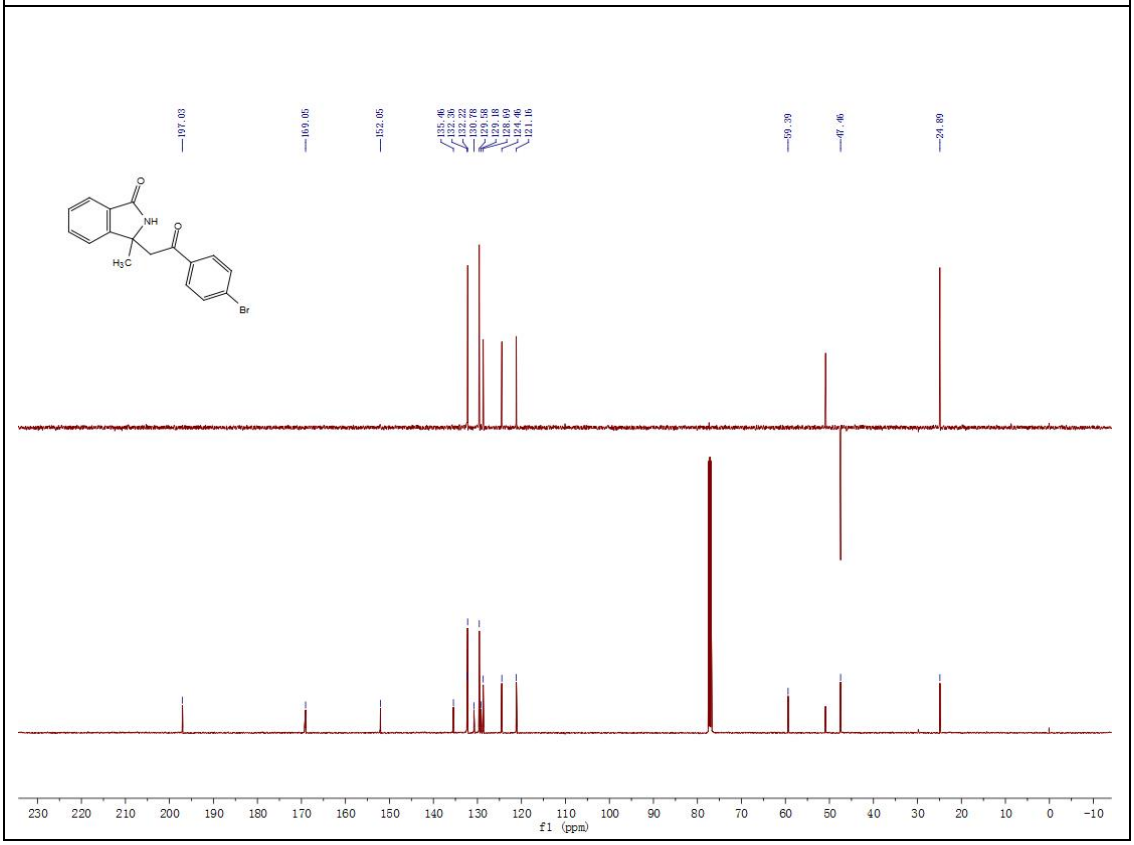
3-(2-(4-chlorophenyl)-2-oxoethyl)-3-methylisoindolin-1-one (3t):



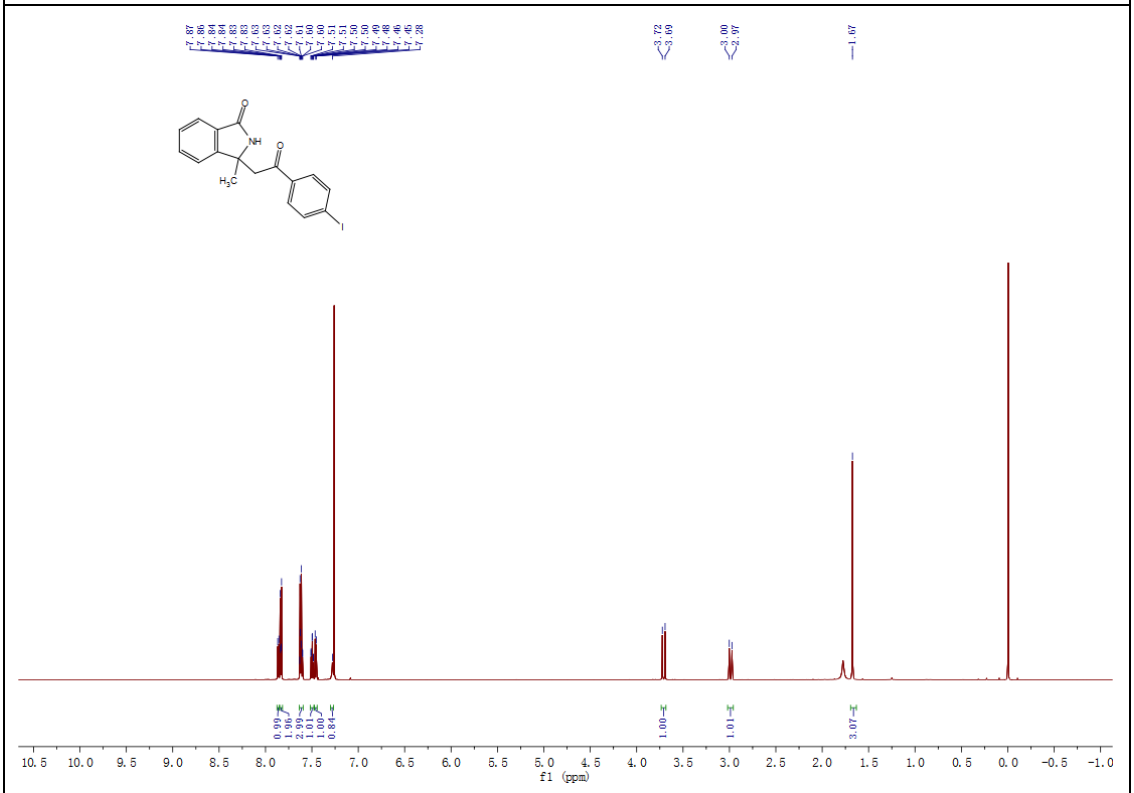


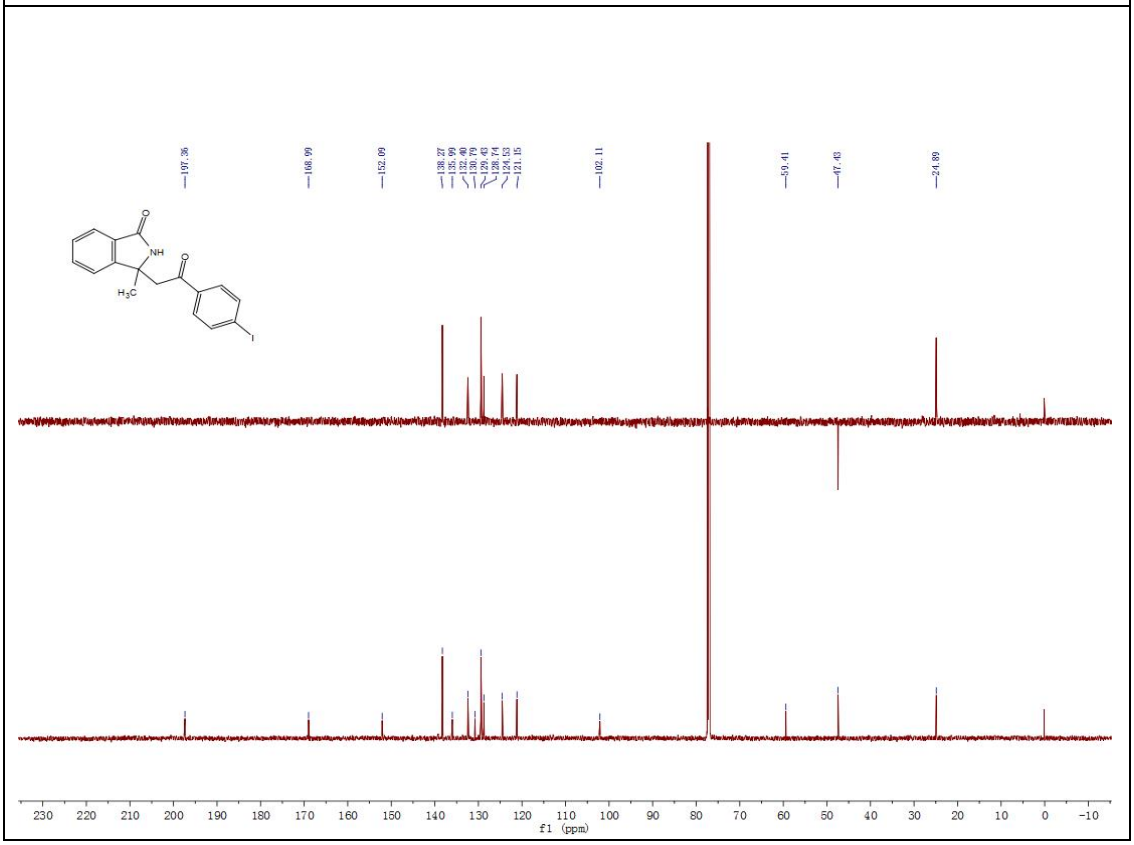
3-(2-(4-bromophenyl)-2-oxoethyl)-3-methylisoindolin-1-one (3u):



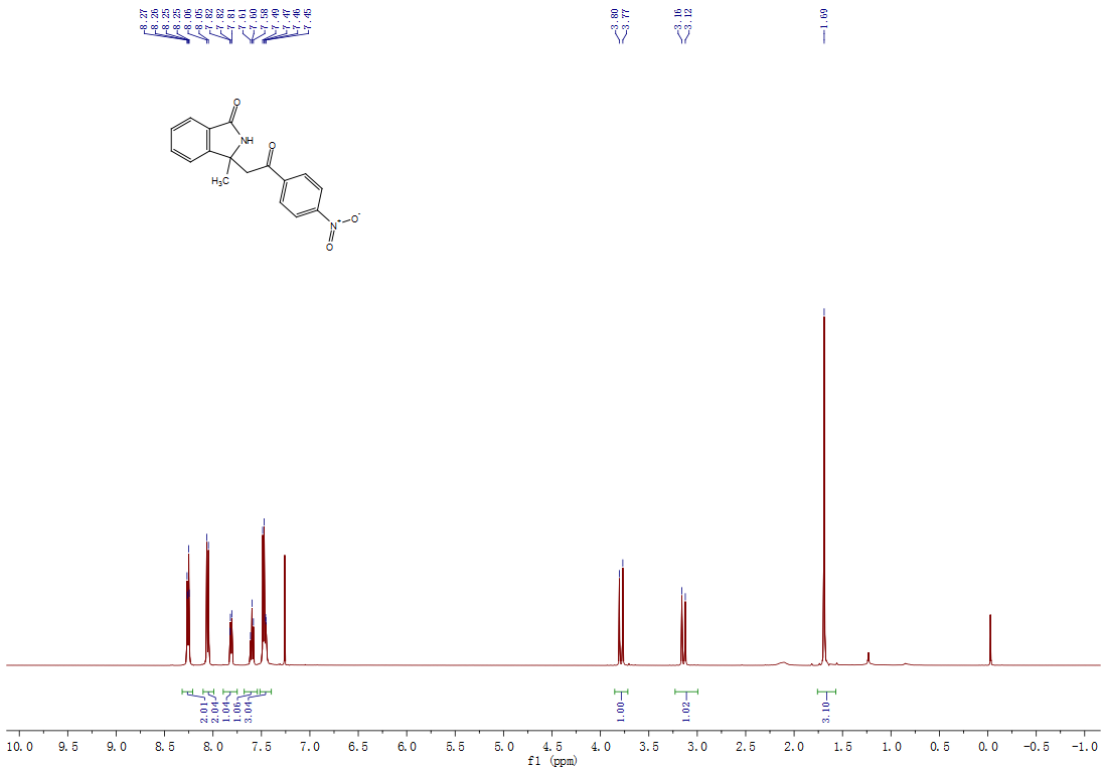


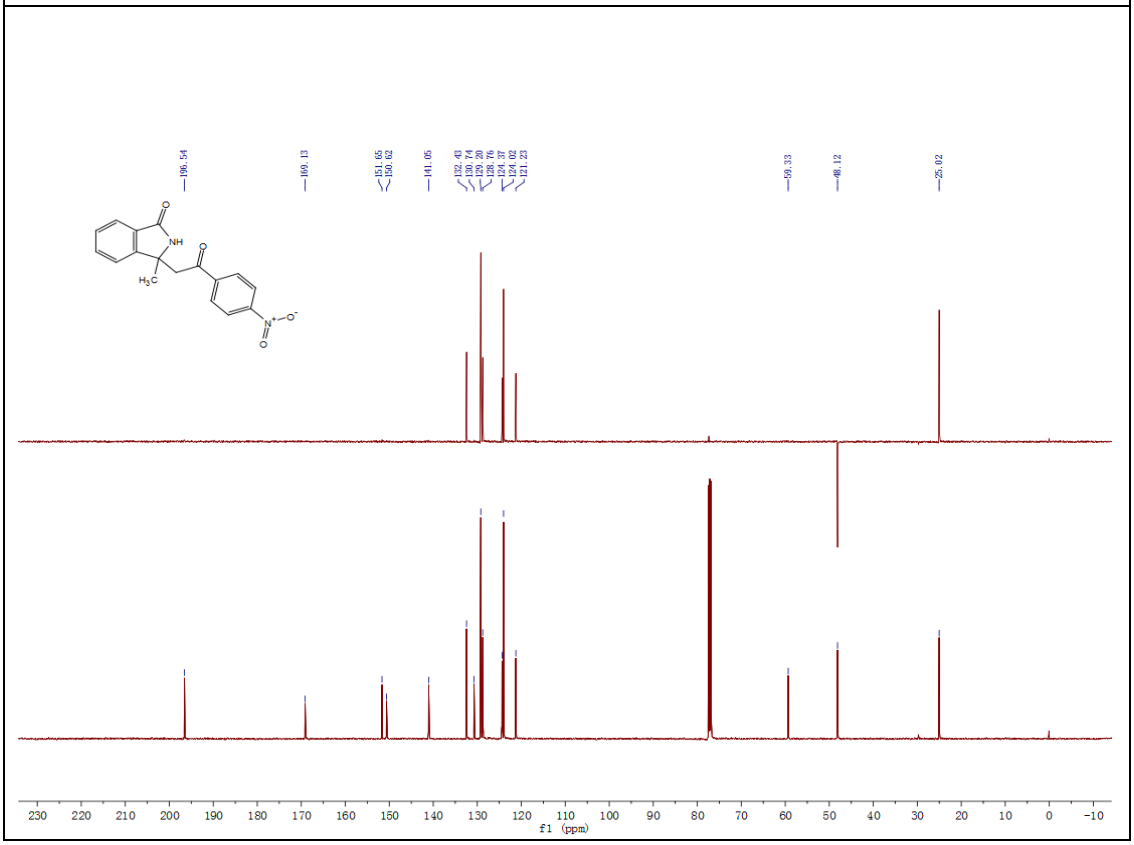
3-(2-(4-iodophenyl)-2-oxoethyl)-3-methylisoindolin-1-one (3v):



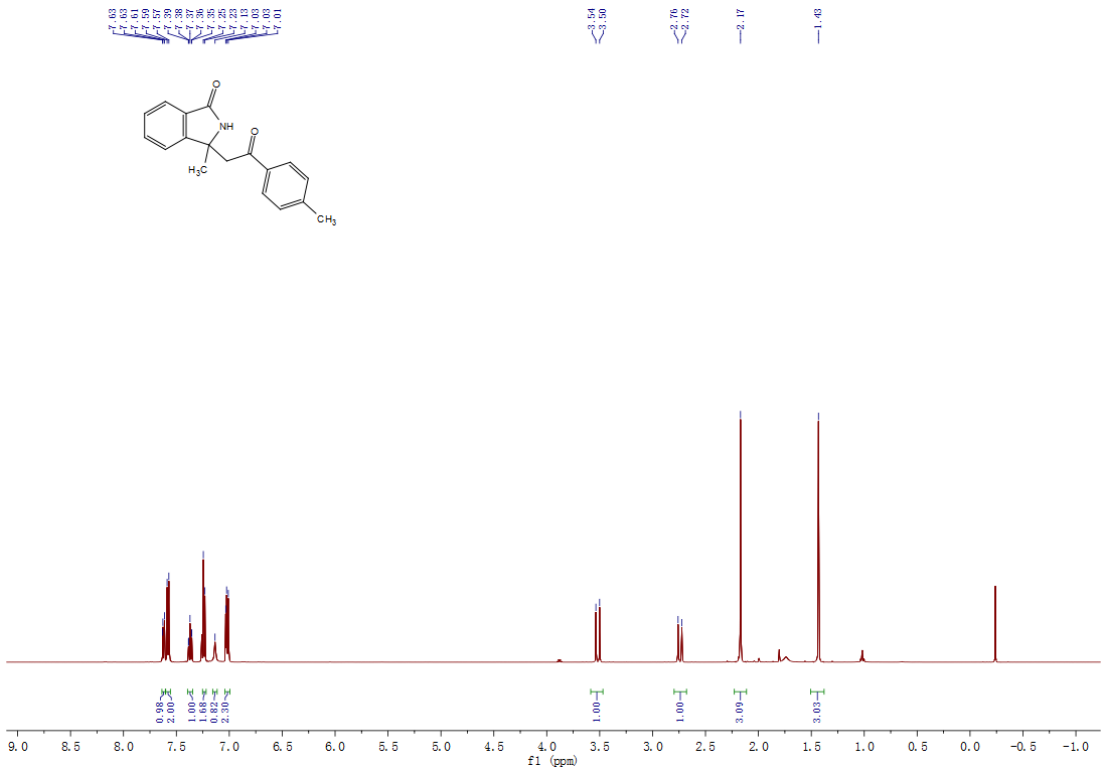


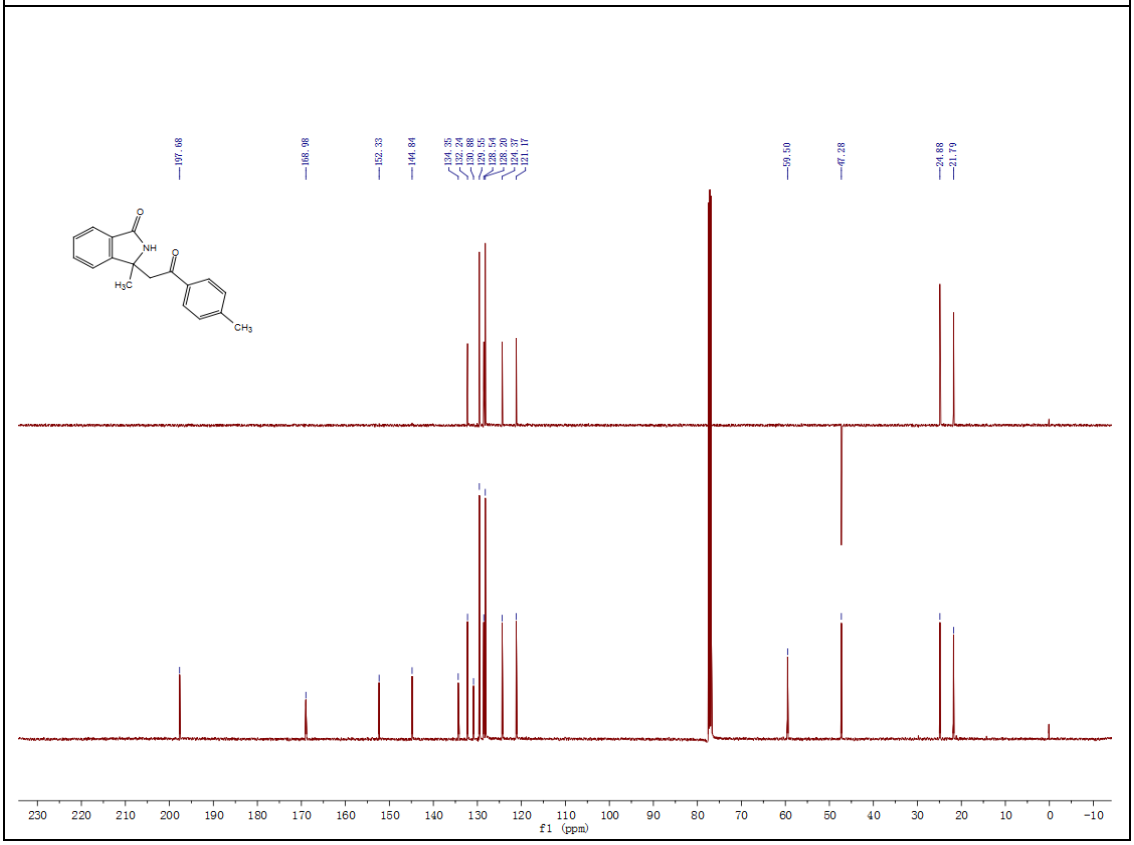
3-methyl-3-(2-(4-nitrophenyl)-2-oxoethyl)isoindolin-1-one (3w):



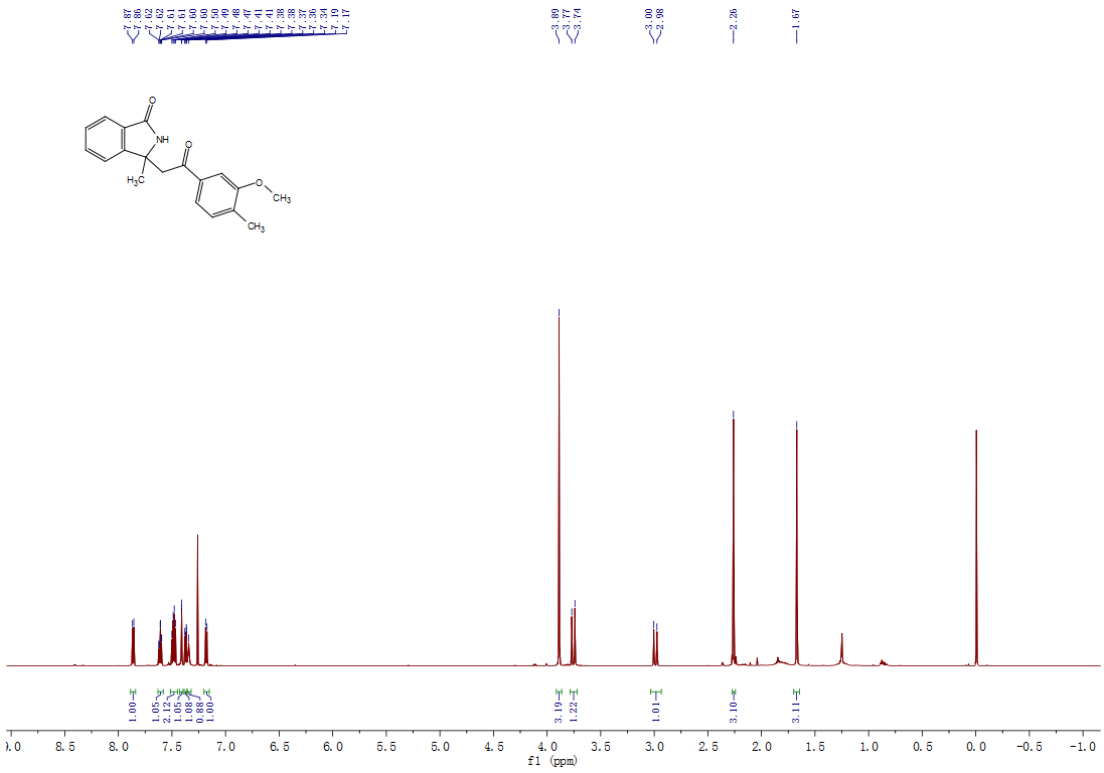


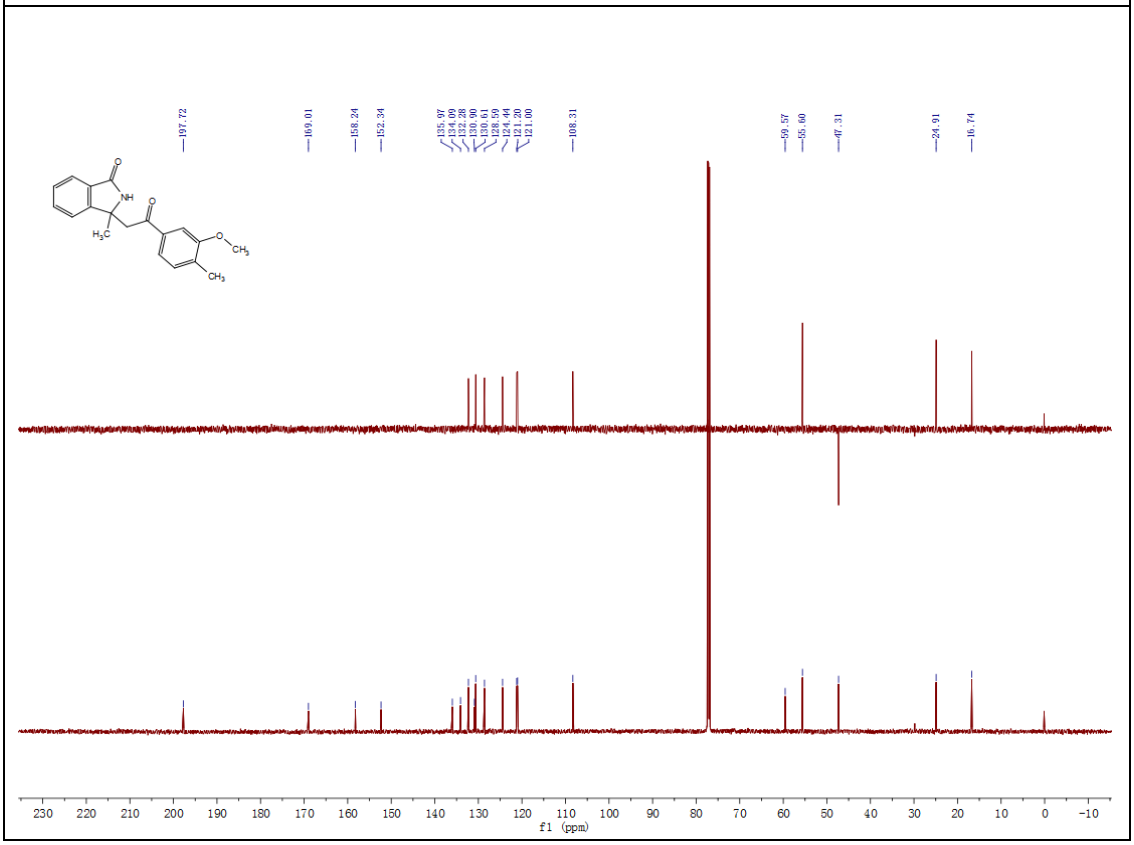
3-methyl-3-(2-oxo-2-(p-tolyl)ethyl)isoindolin-1-one (3x):



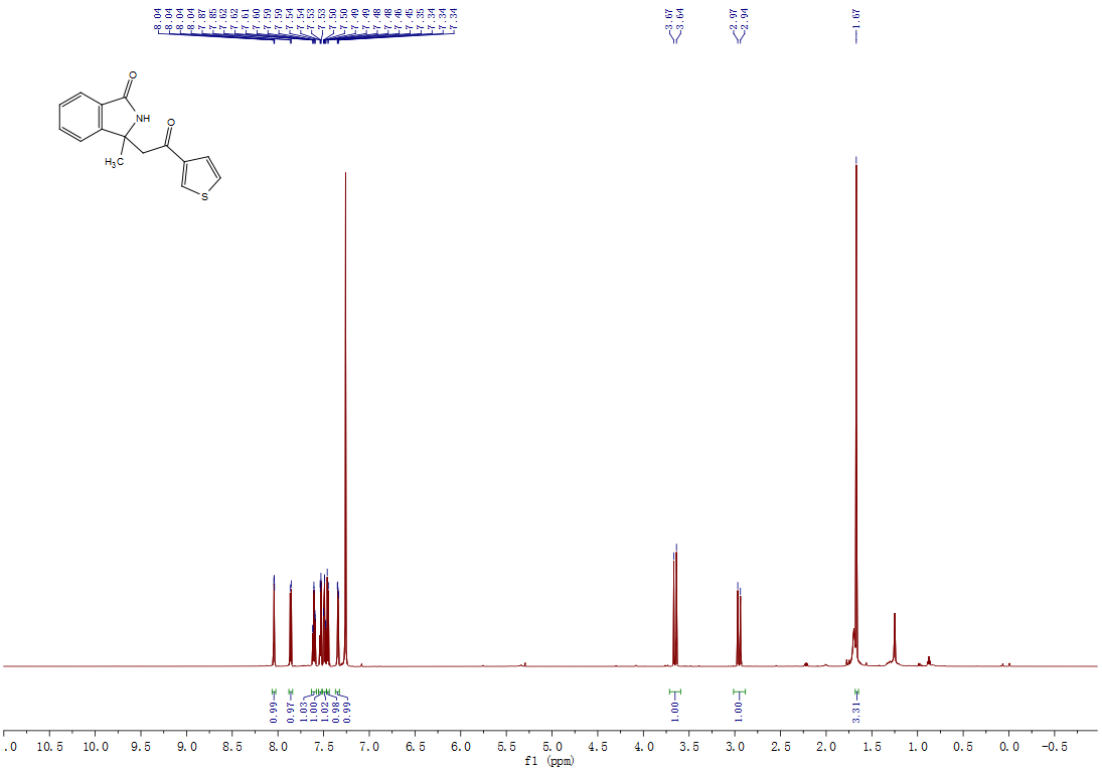


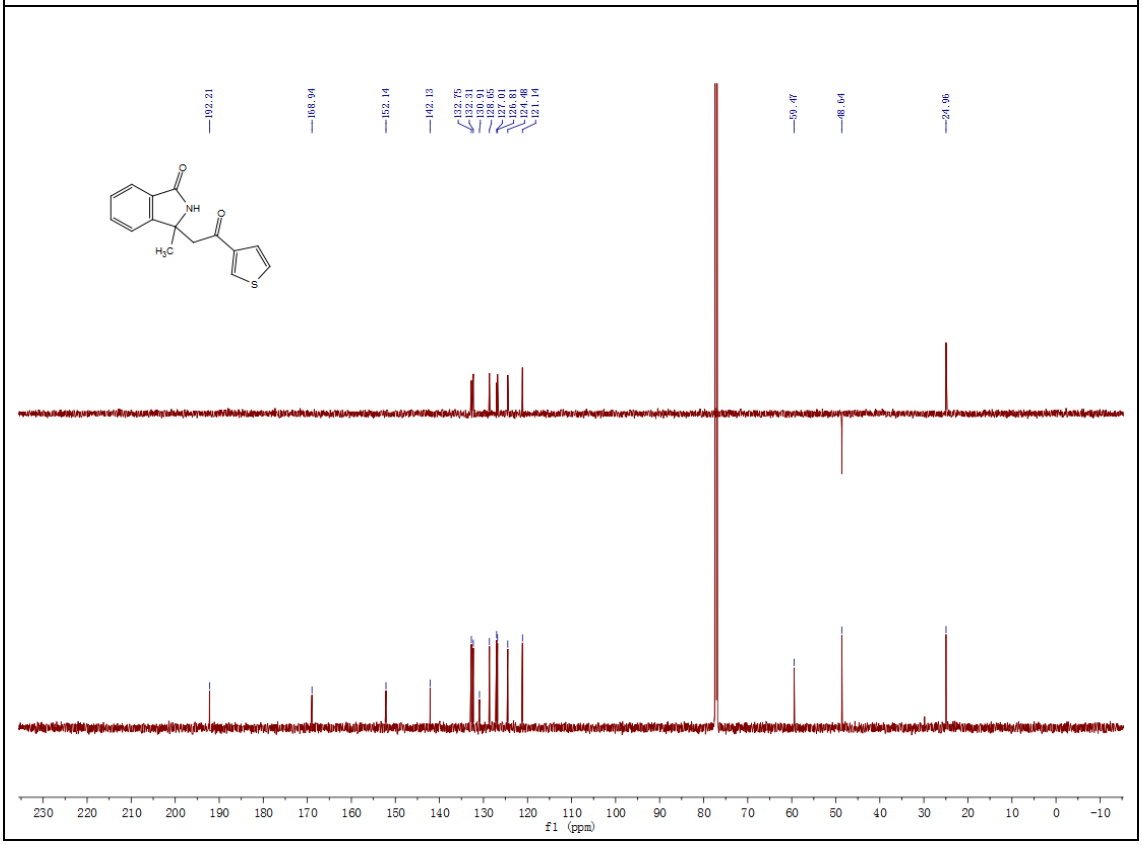
3-(2-(3-methoxy-4-methylphenyl)-2-oxoethyl)-3-methylisoindolin-1-one (3y):



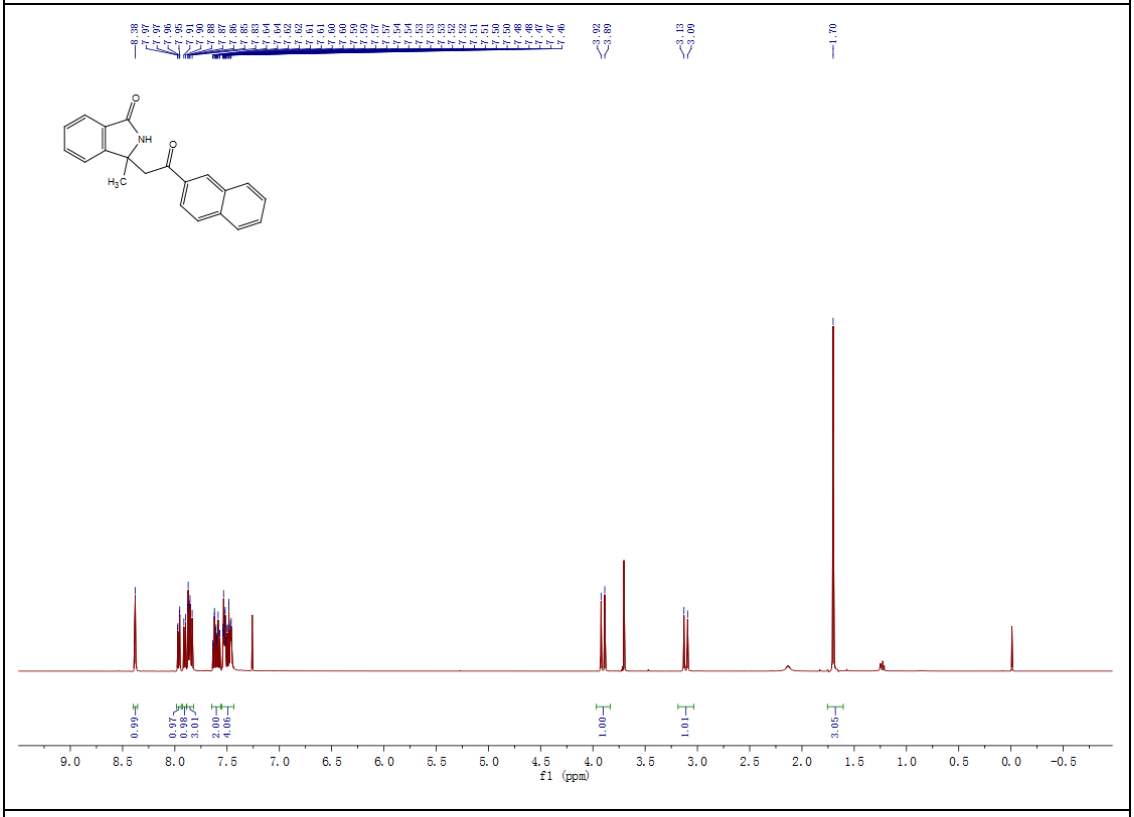


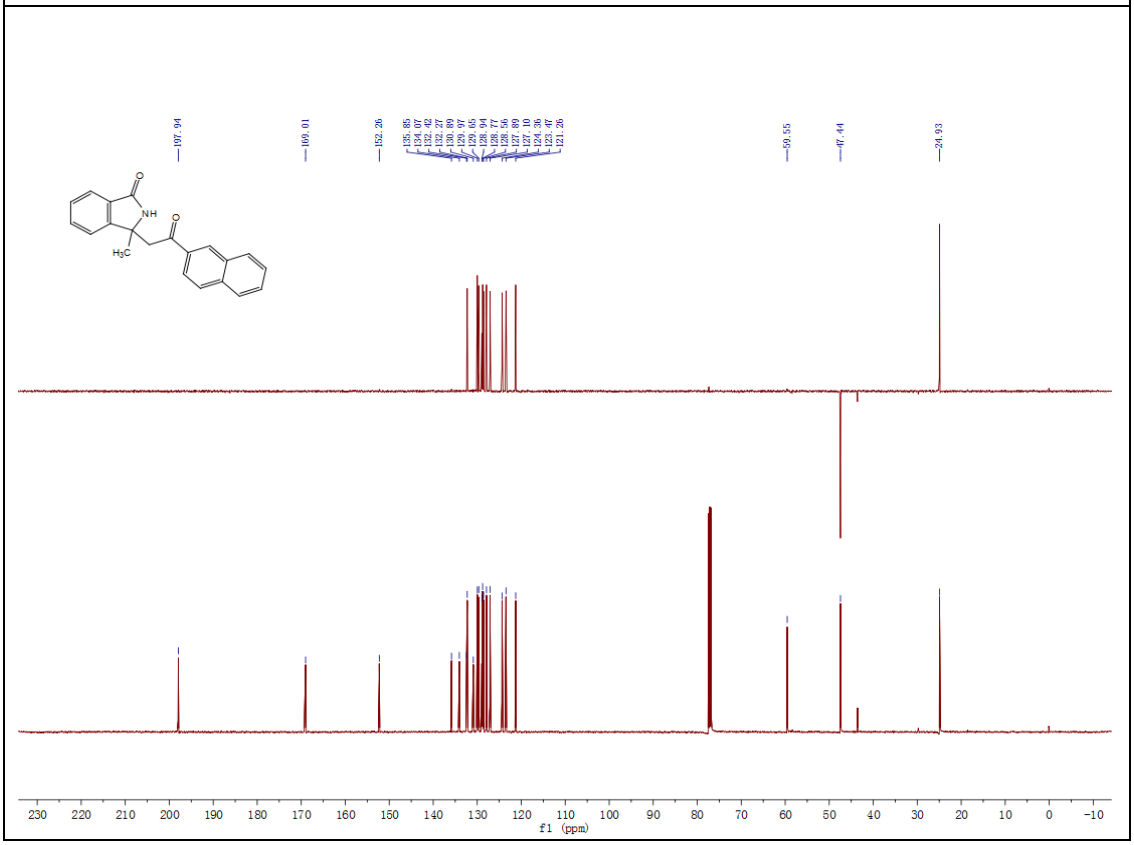
3-methyl-3-(2-oxo-2-(thiophen-3-yl)ethyl)isoindolin-1-one (3z):



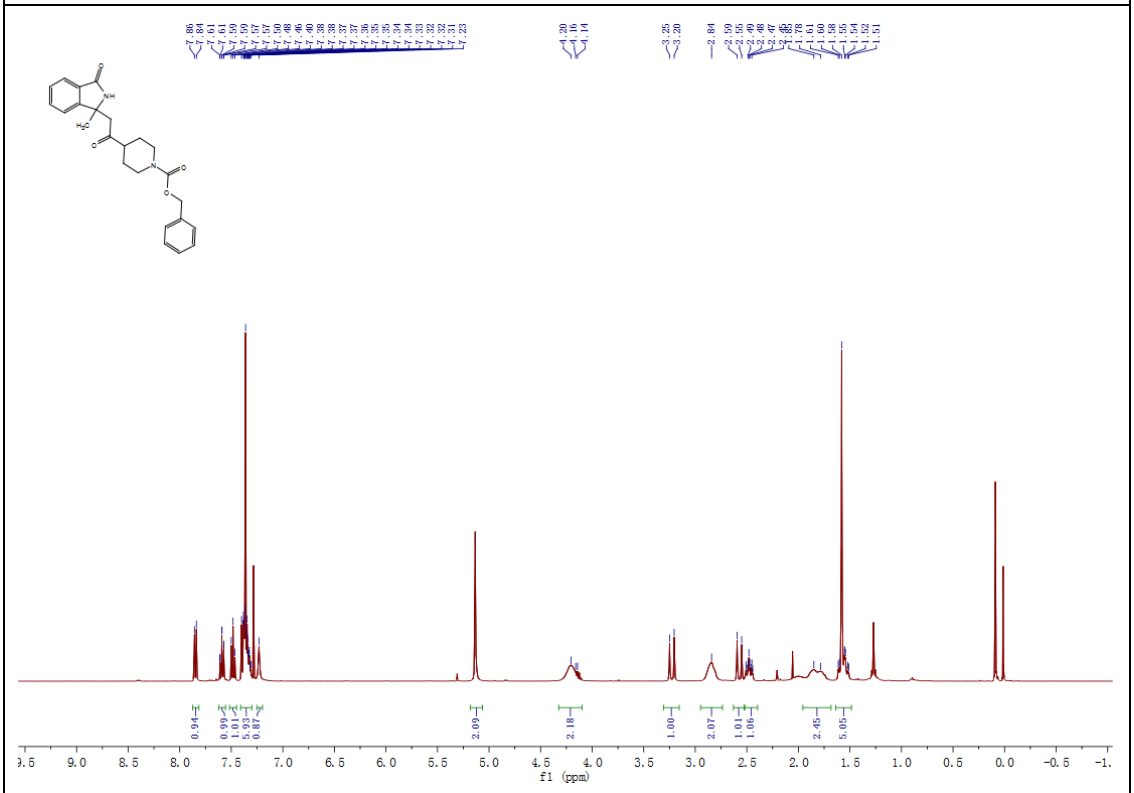


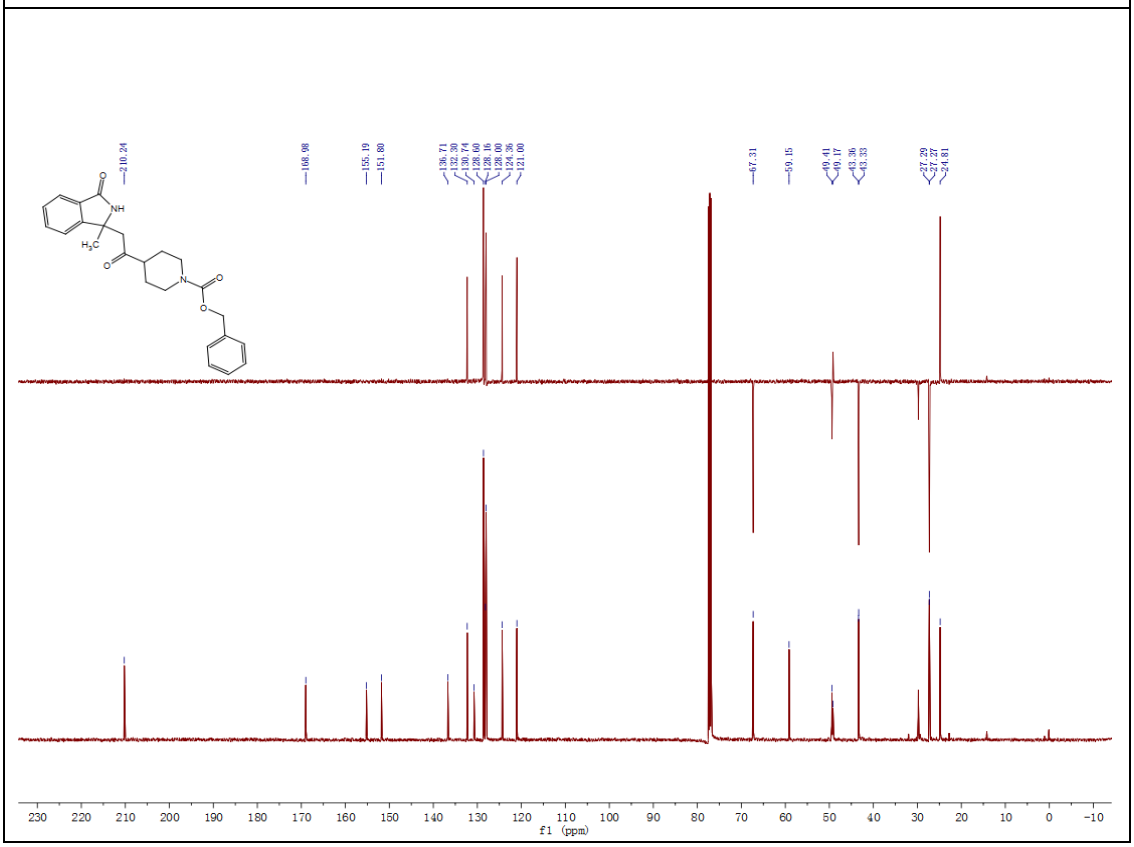
3-methyl-3-(2-(naphthalen-2-yl)-2-oxoethyl)isoindolin-1-one (3za):



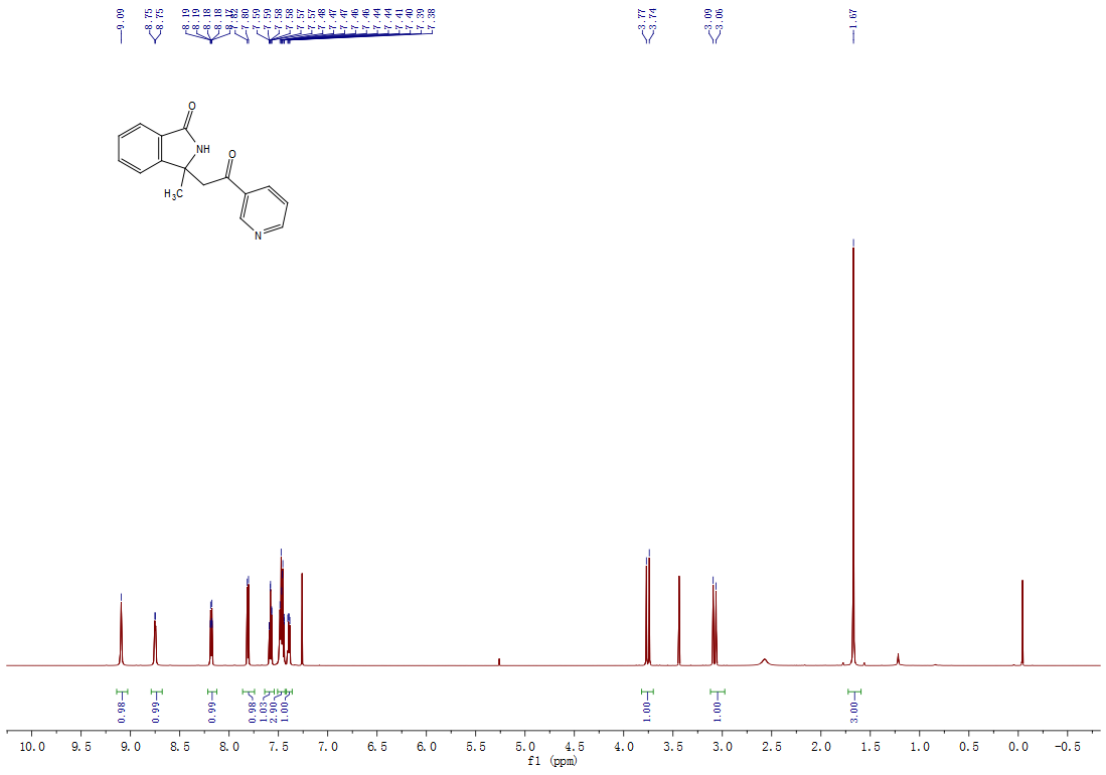


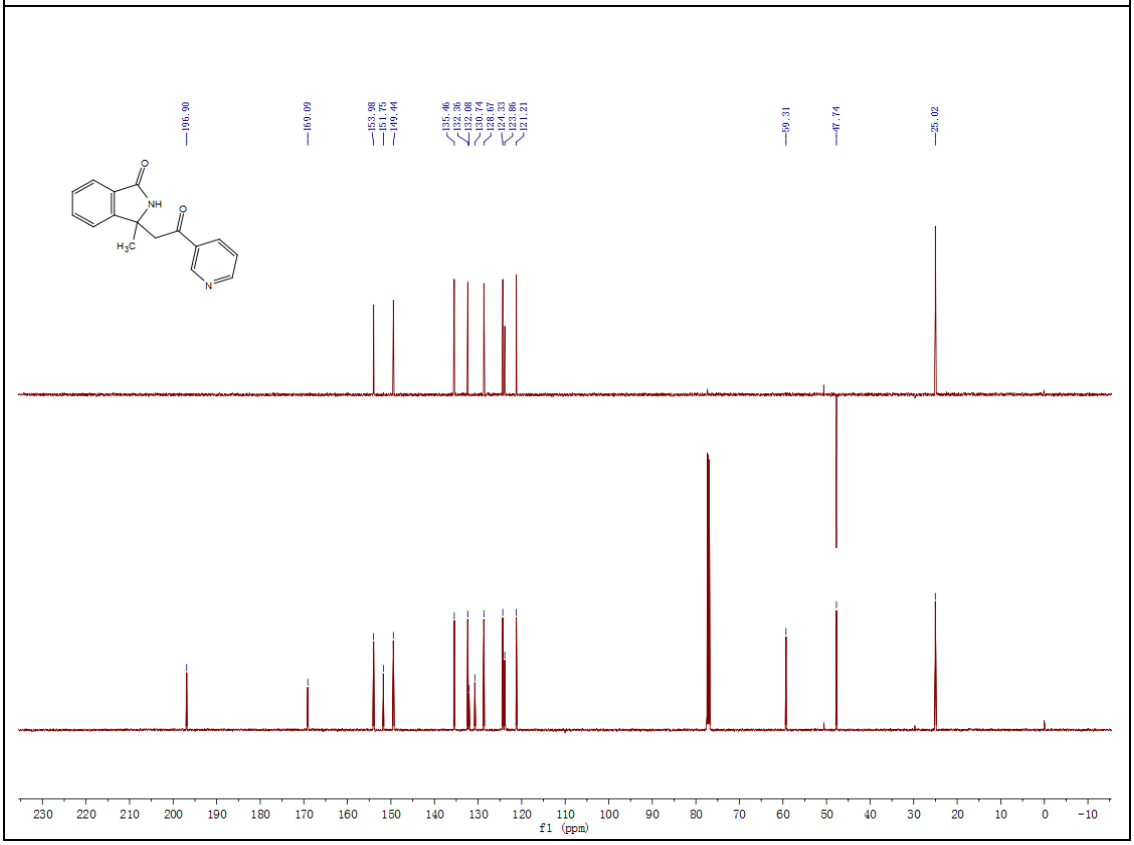
benzyl 4-(2-(1-methyl-3-oxoisoindolin-1-yl)acetyl)piperidine-1-carboxylate (3zb):



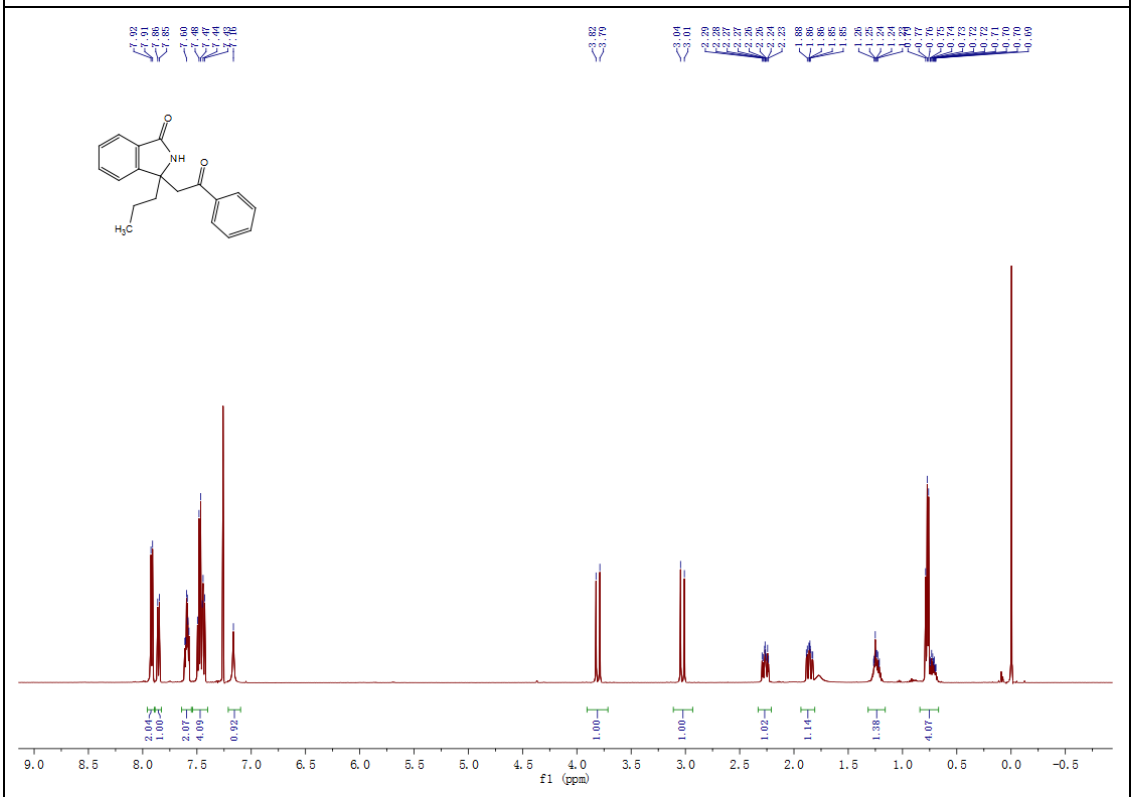


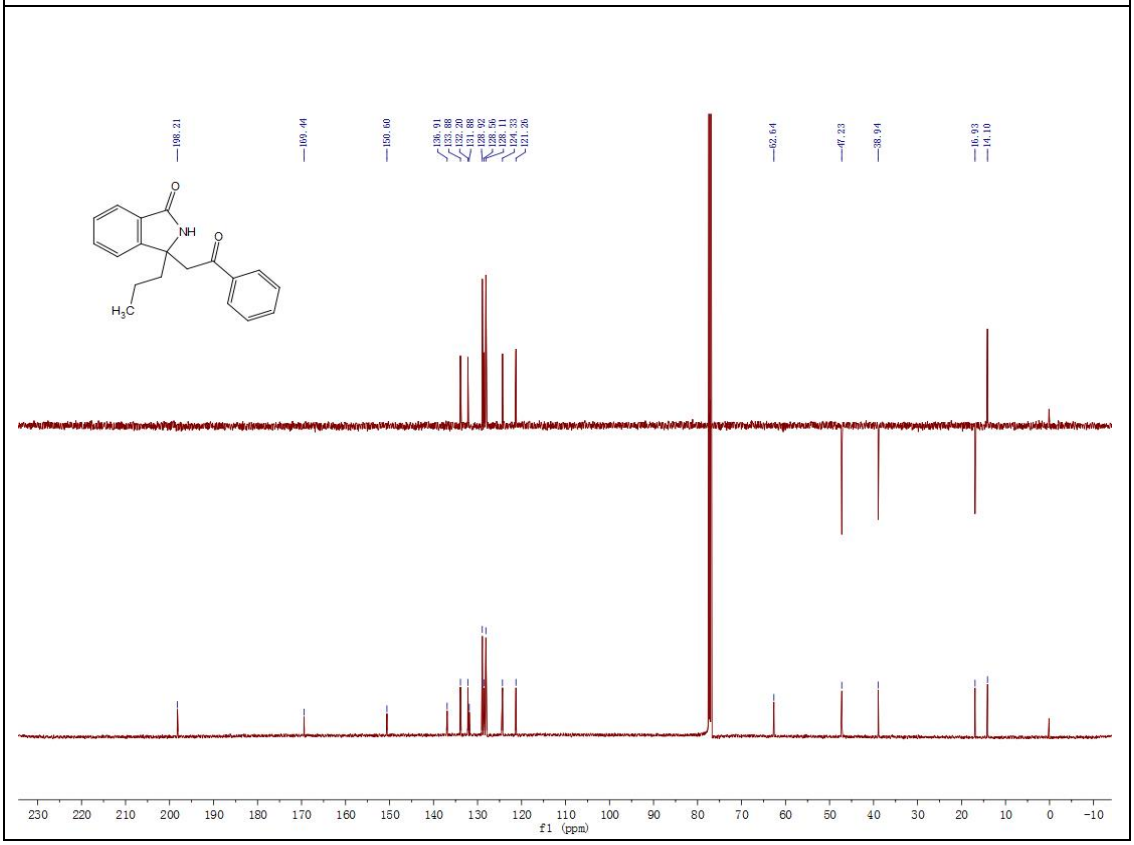
3-methyl-3-(2-oxo-2-(pyridin-3-yl)ethyl)isoindolin-1-one (3zc):



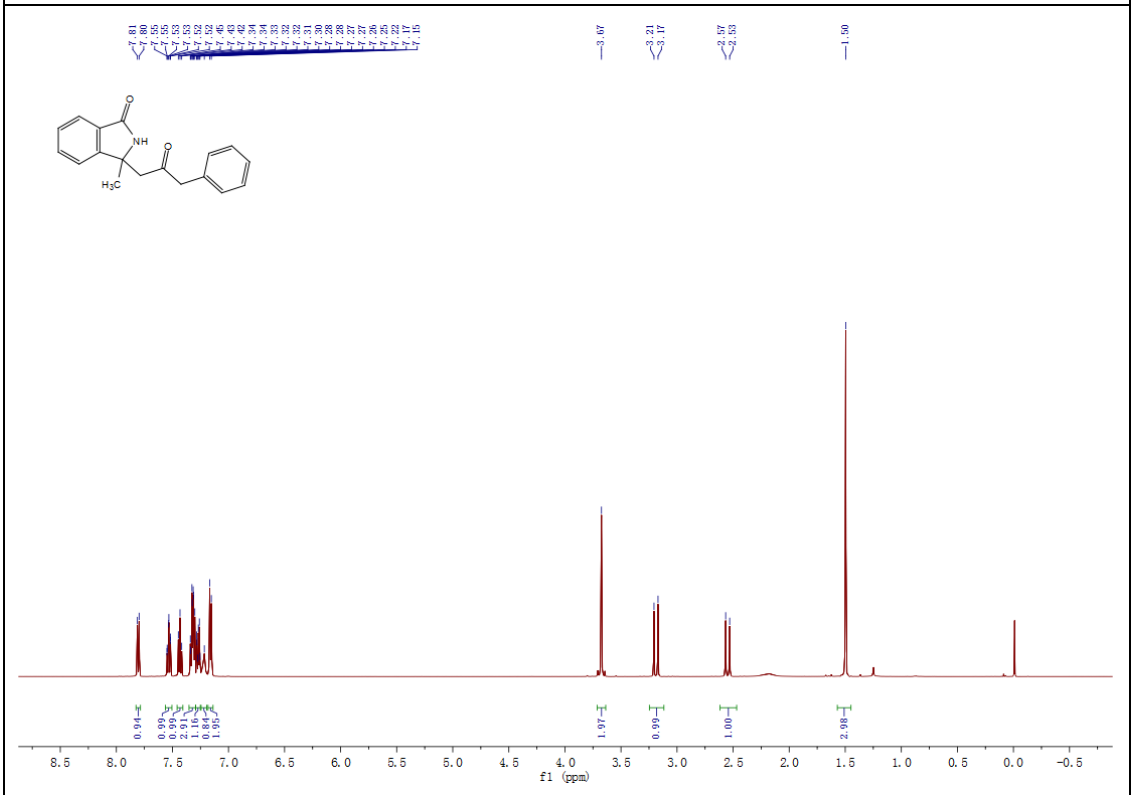


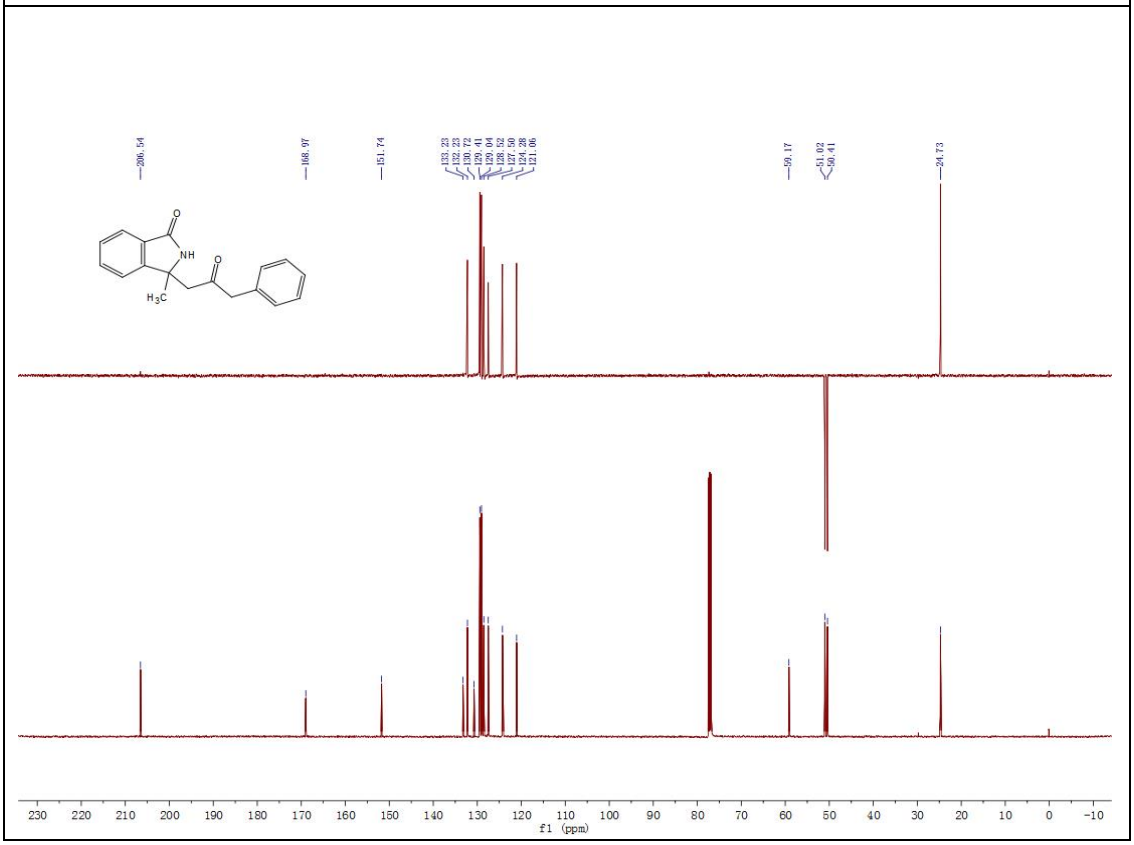
3-(2-oxo-2-phenylethyl)-3-propylisoindolin-1-one (3zd):



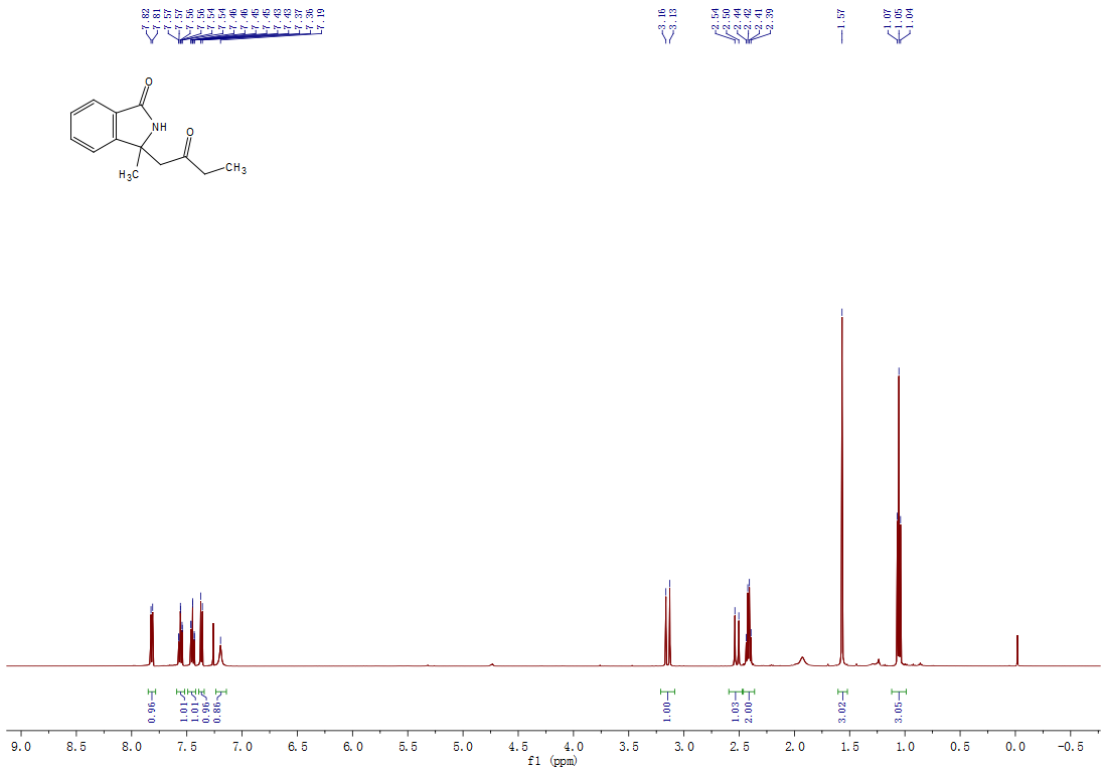


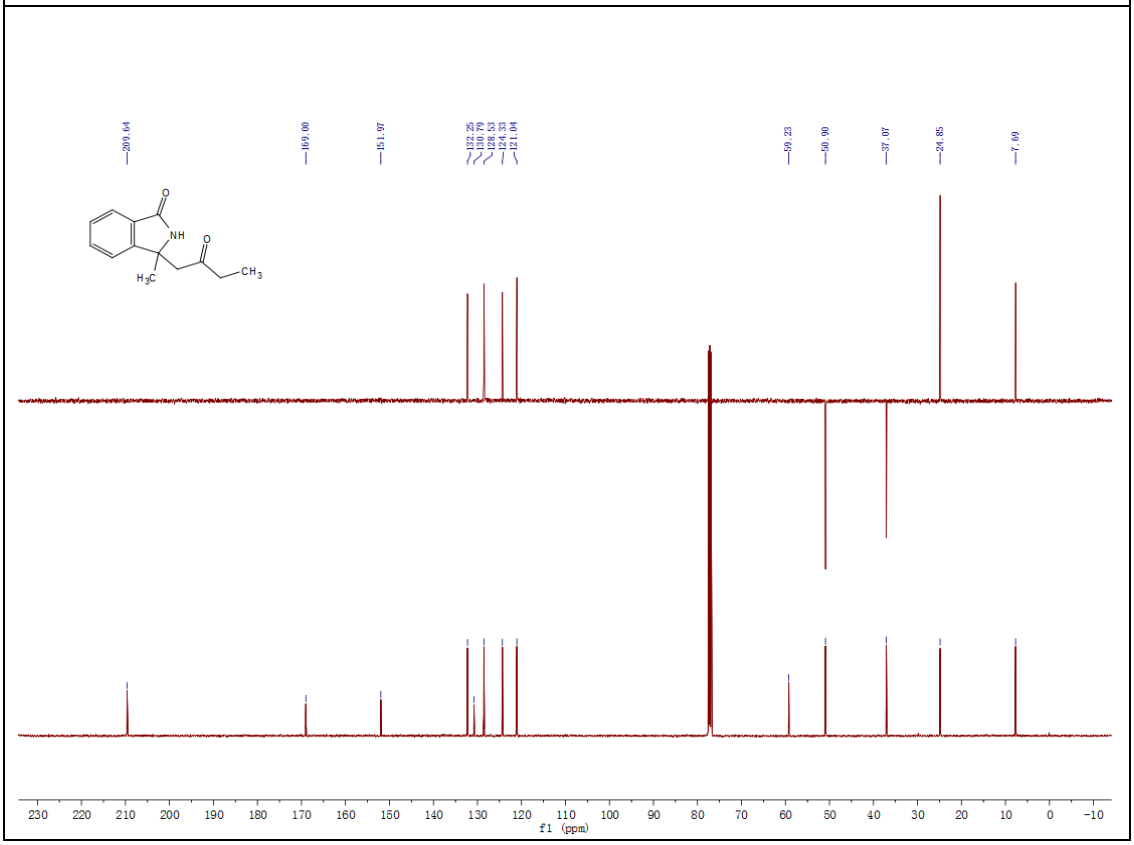
3-methyl-3-(2-oxo-3-phenylpropyl)isoindolin-1-one (3ze):



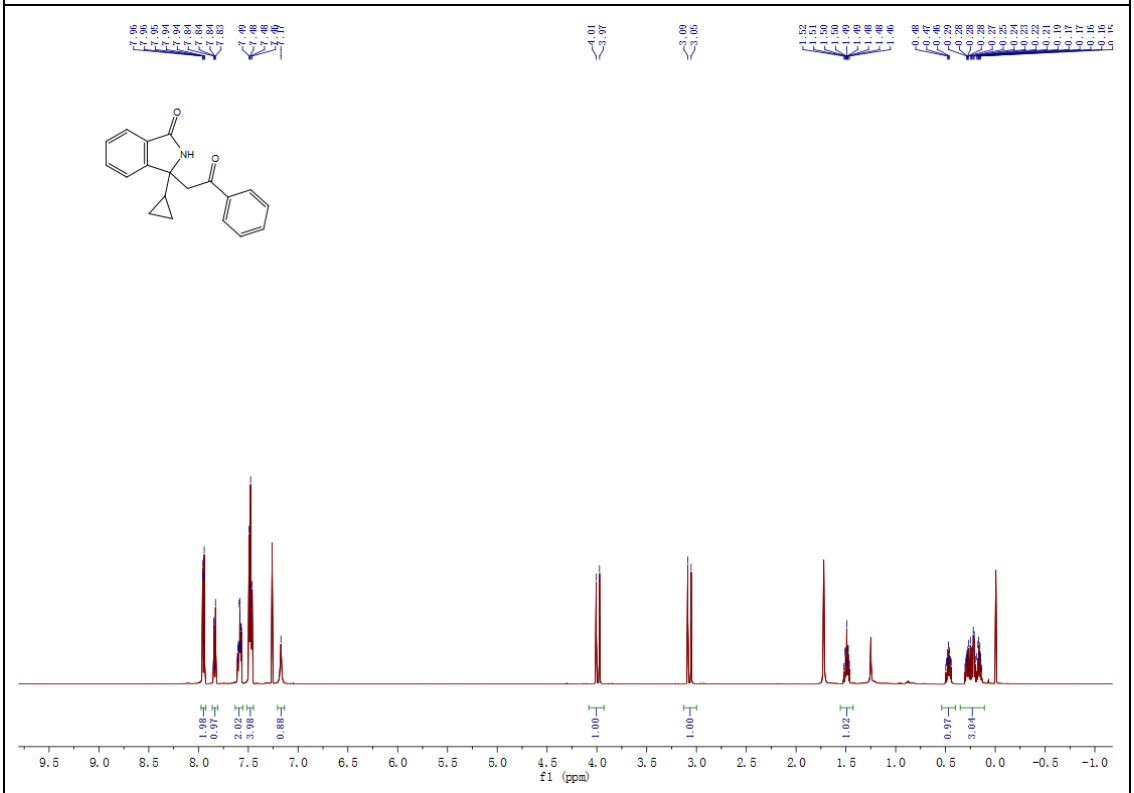


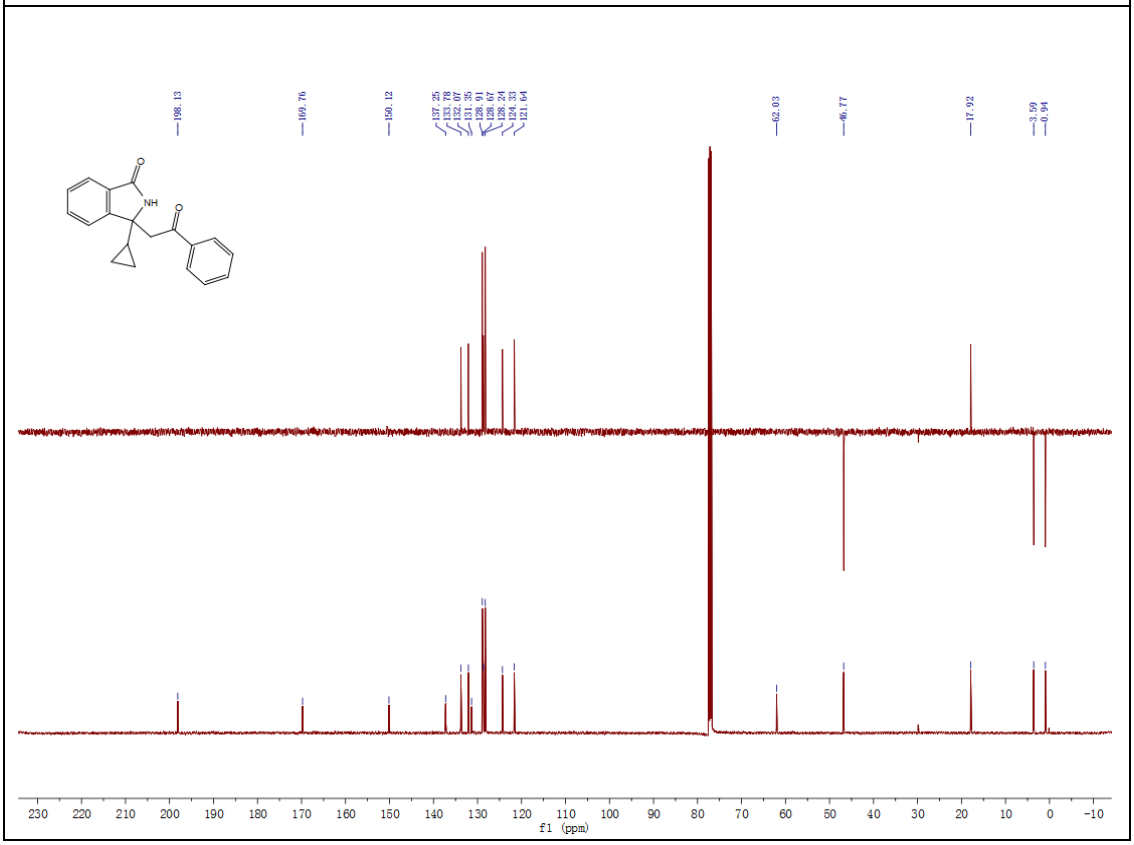
3-methyl-3-(2-oxobutyl)isoindolin-1-one (3zf):



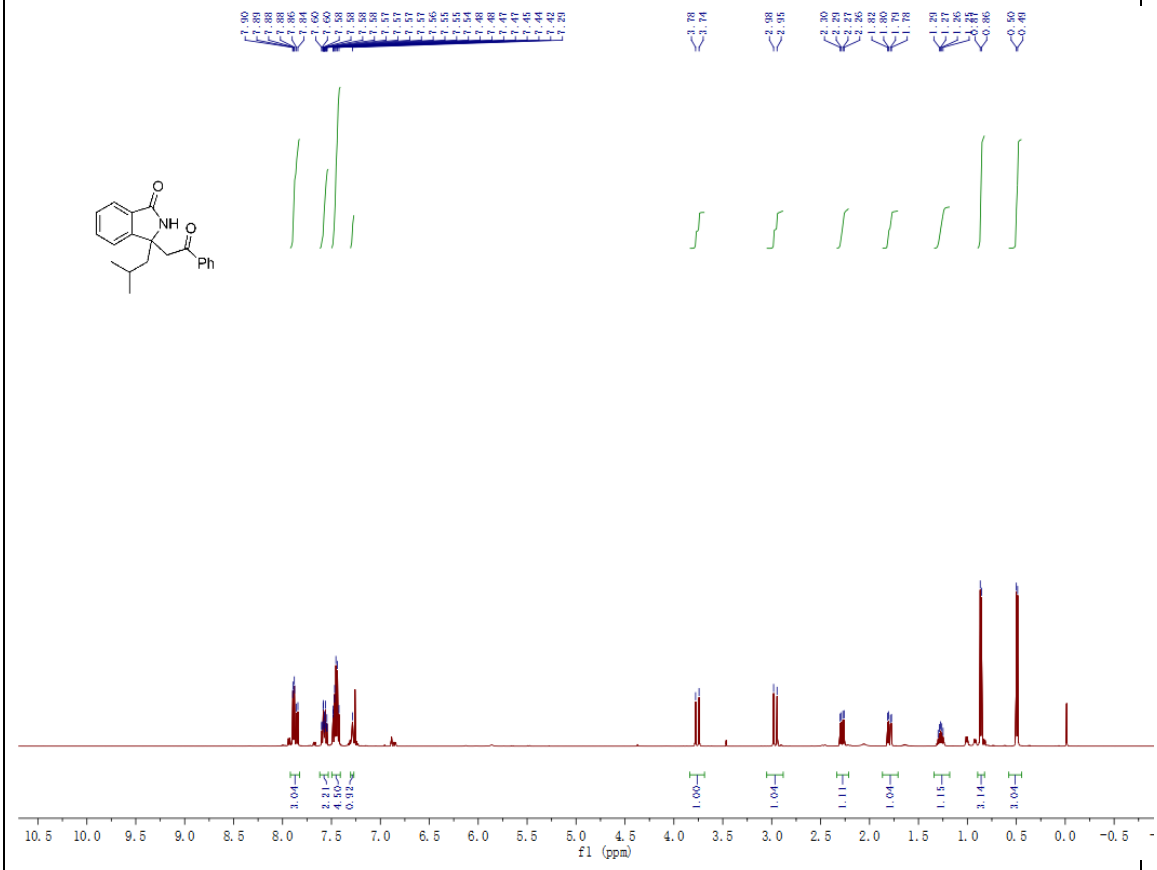


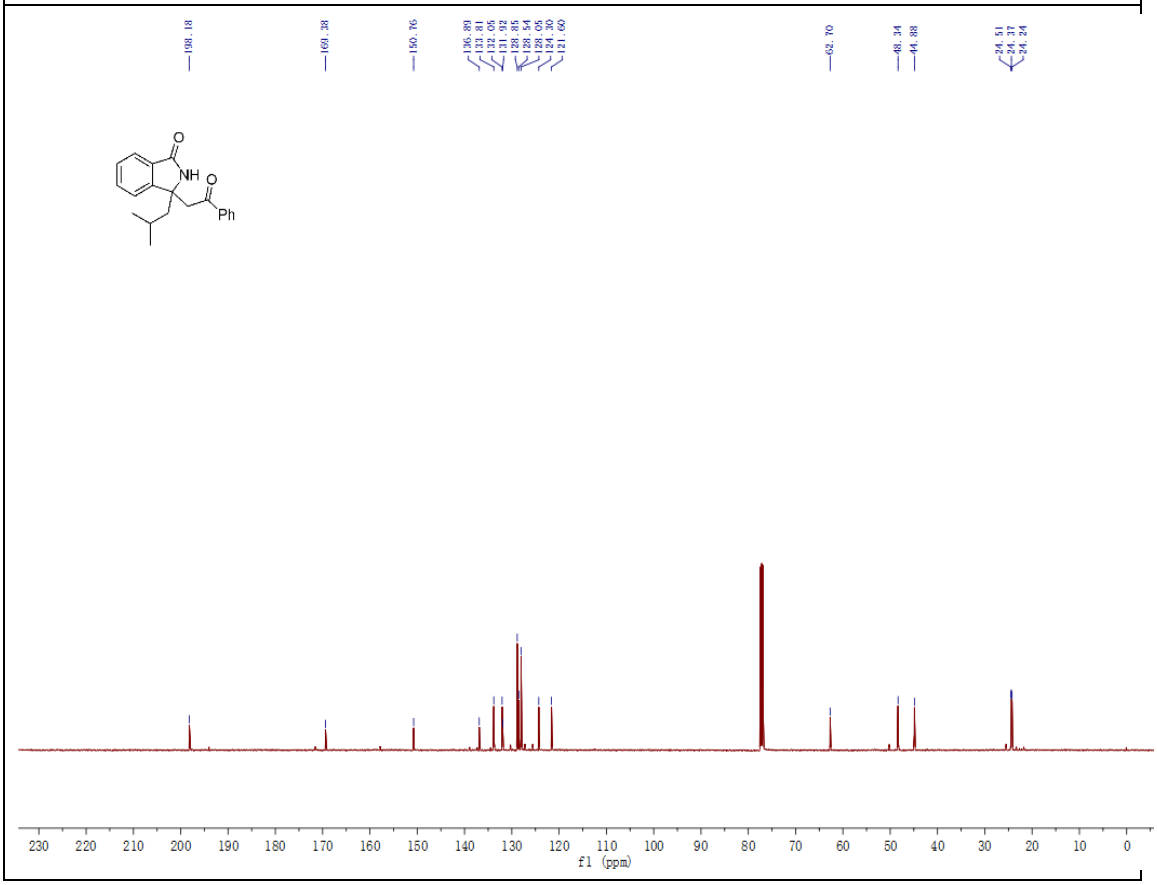
3-cyclopropyl-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3zg):



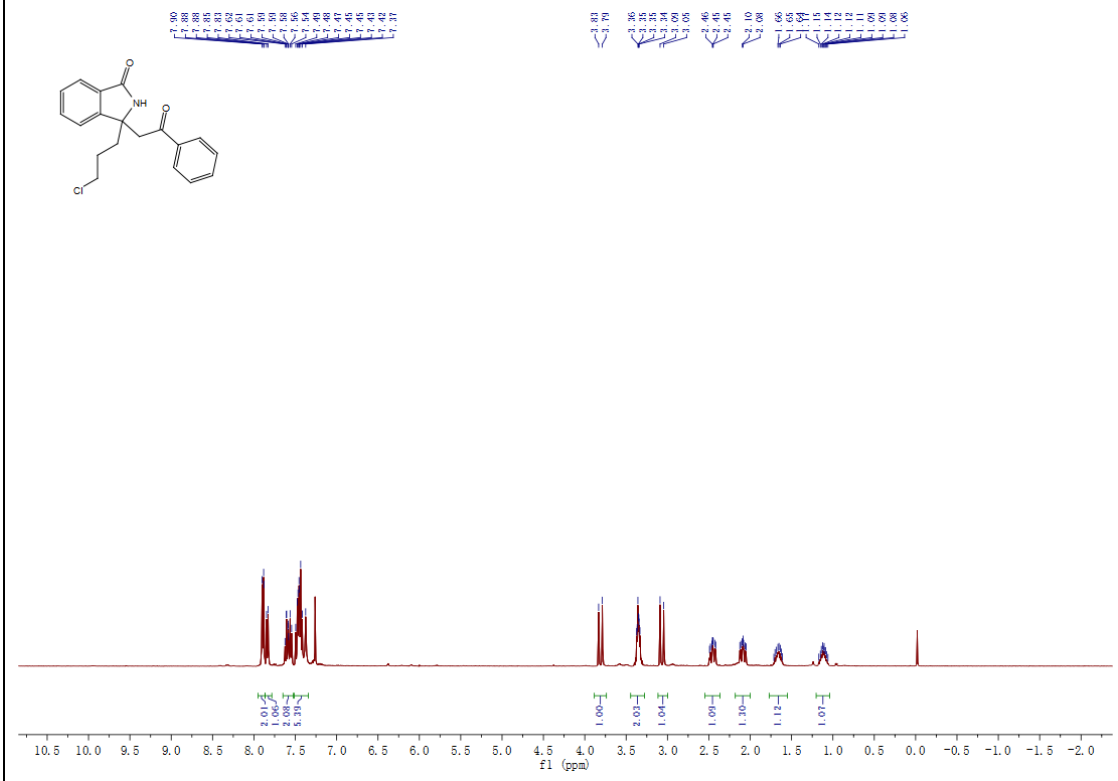


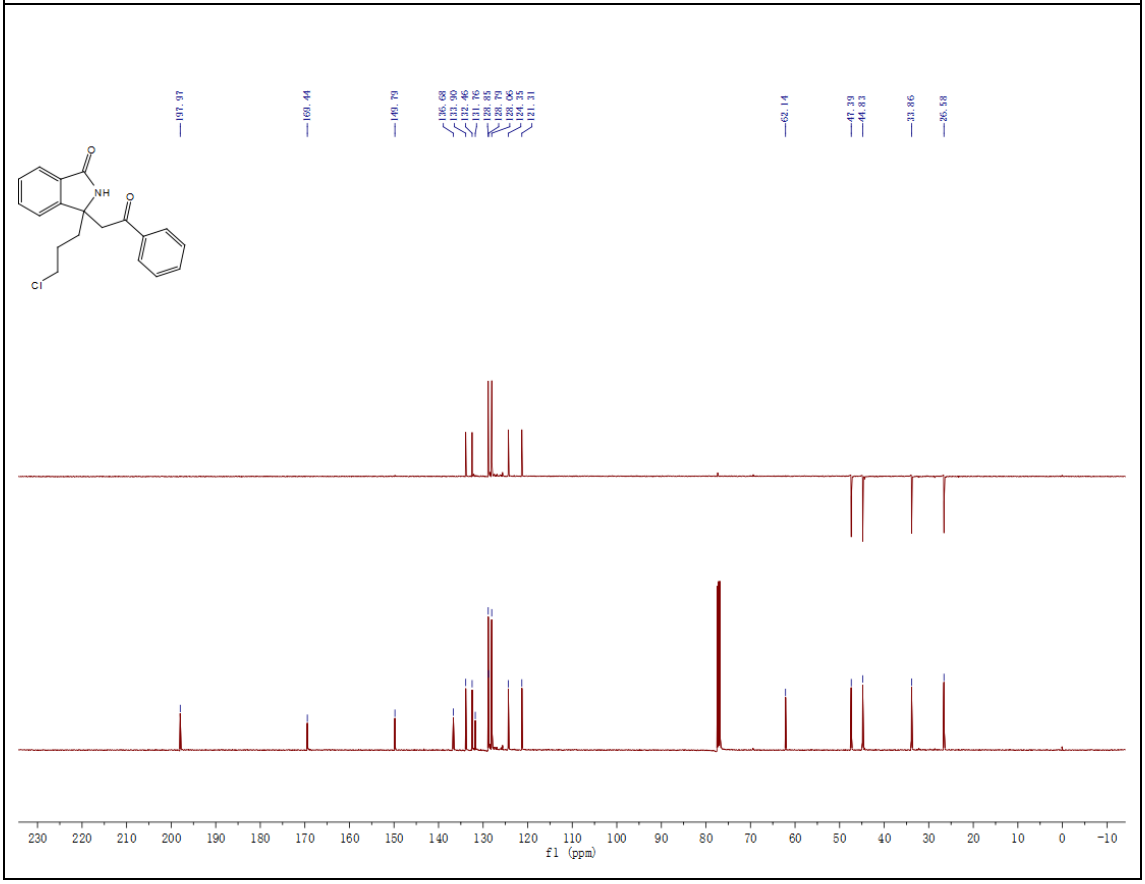
3-isobutyl-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3zh):



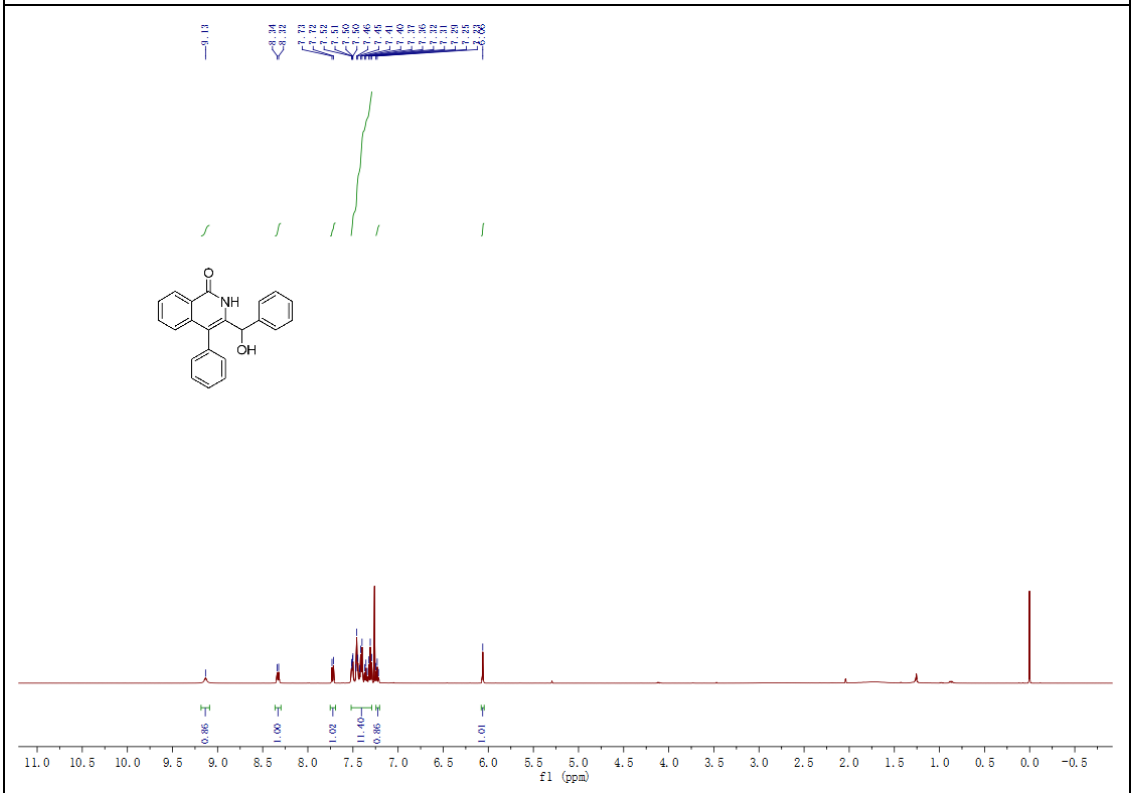


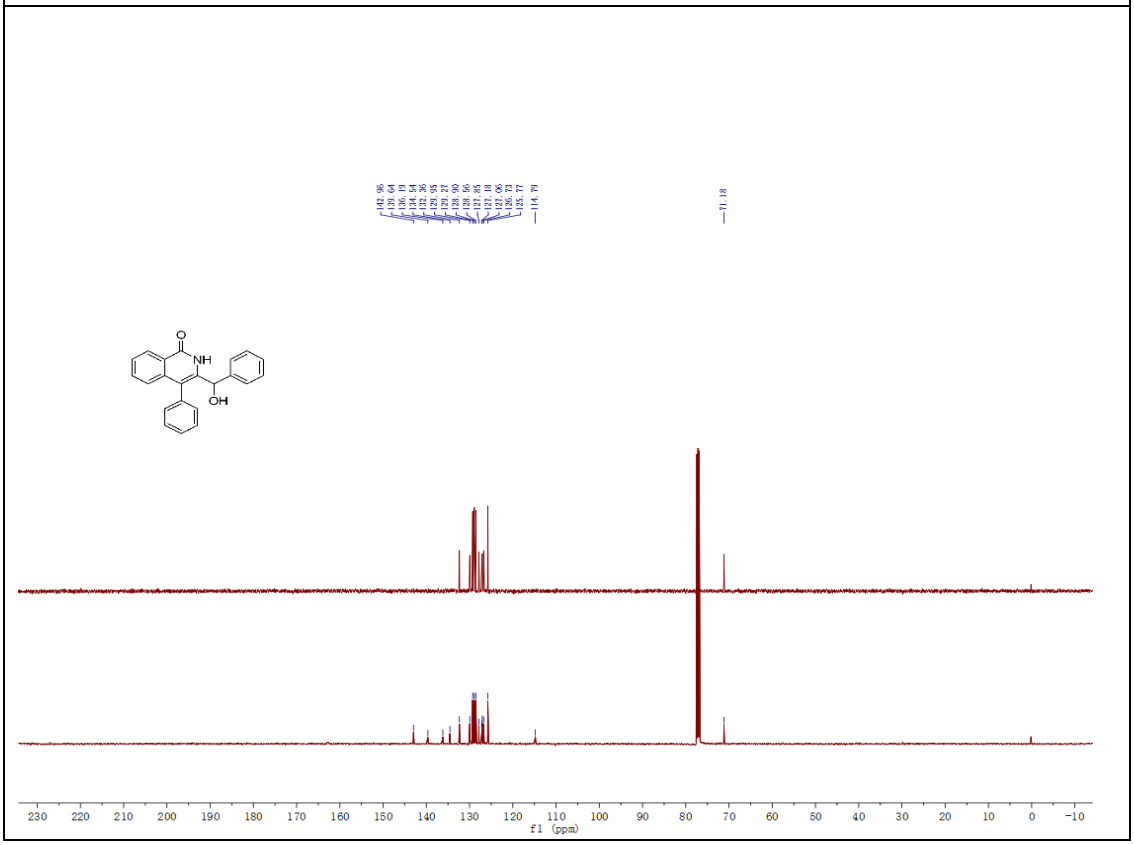
3-(3-chloropropyl)-3-(2-oxo-2-phenylethyl)isoindolin-1-one (3zi):



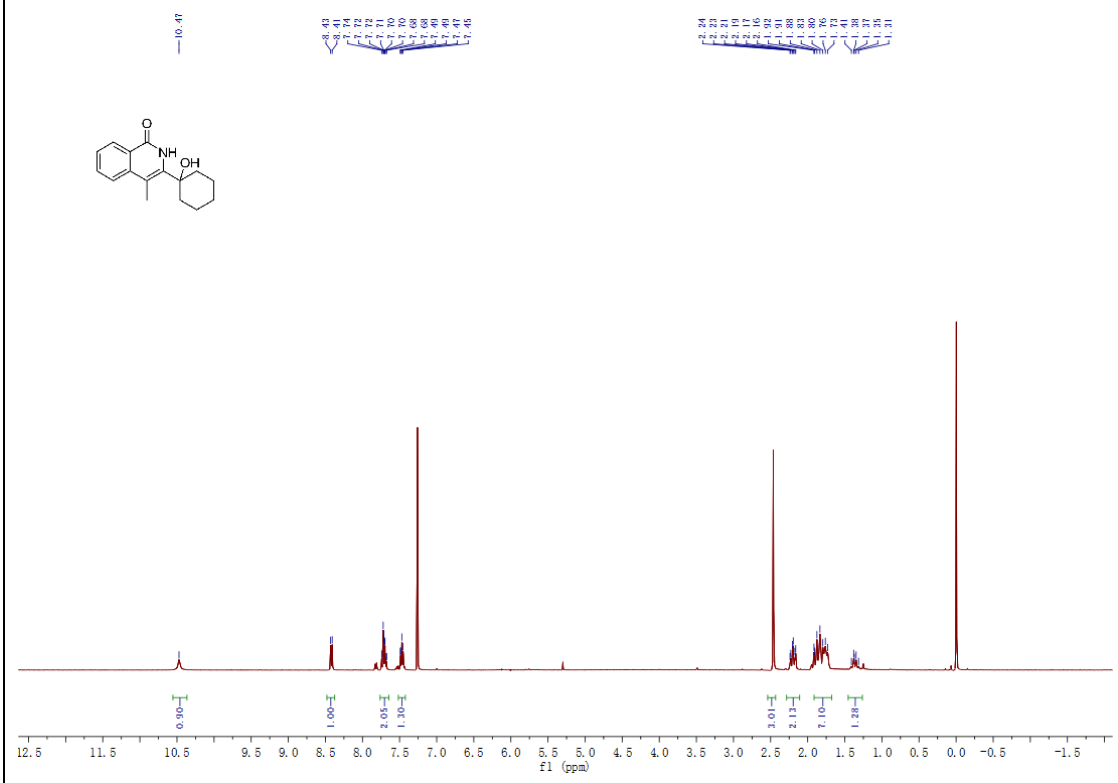


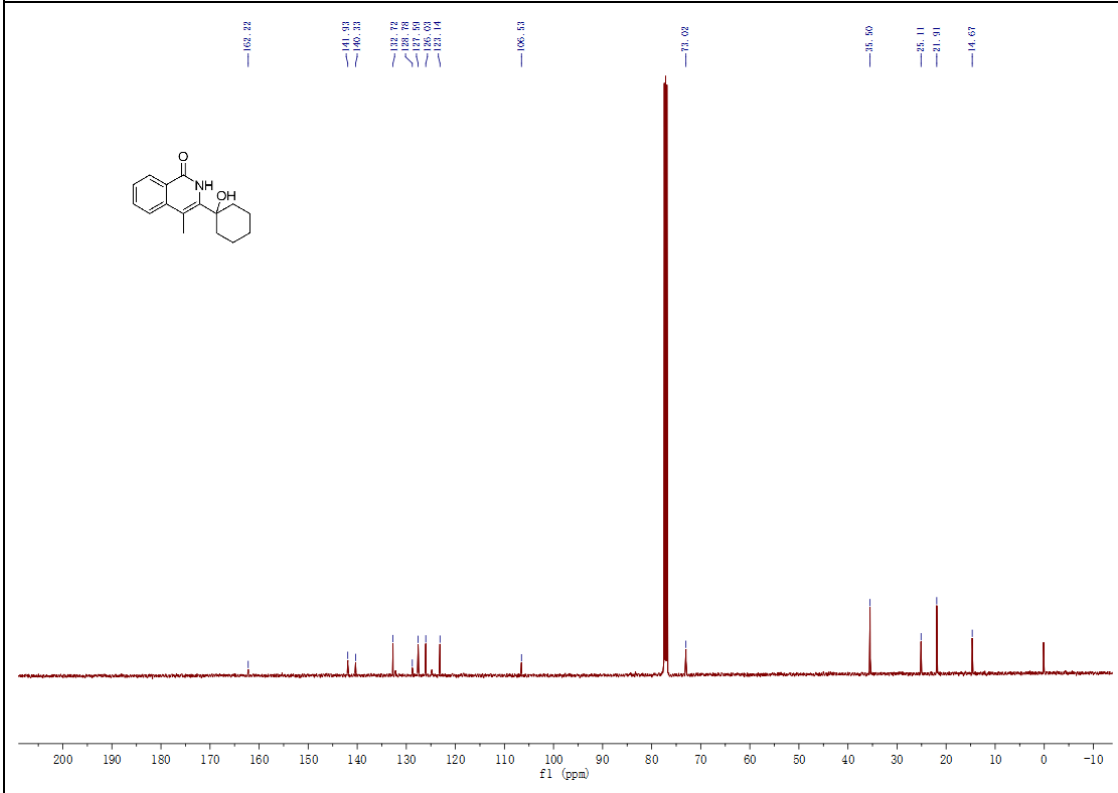
3-(hydroxy(phenyl)methyl)-4-phenylisoquinolin-1(2H)-one (4zj):



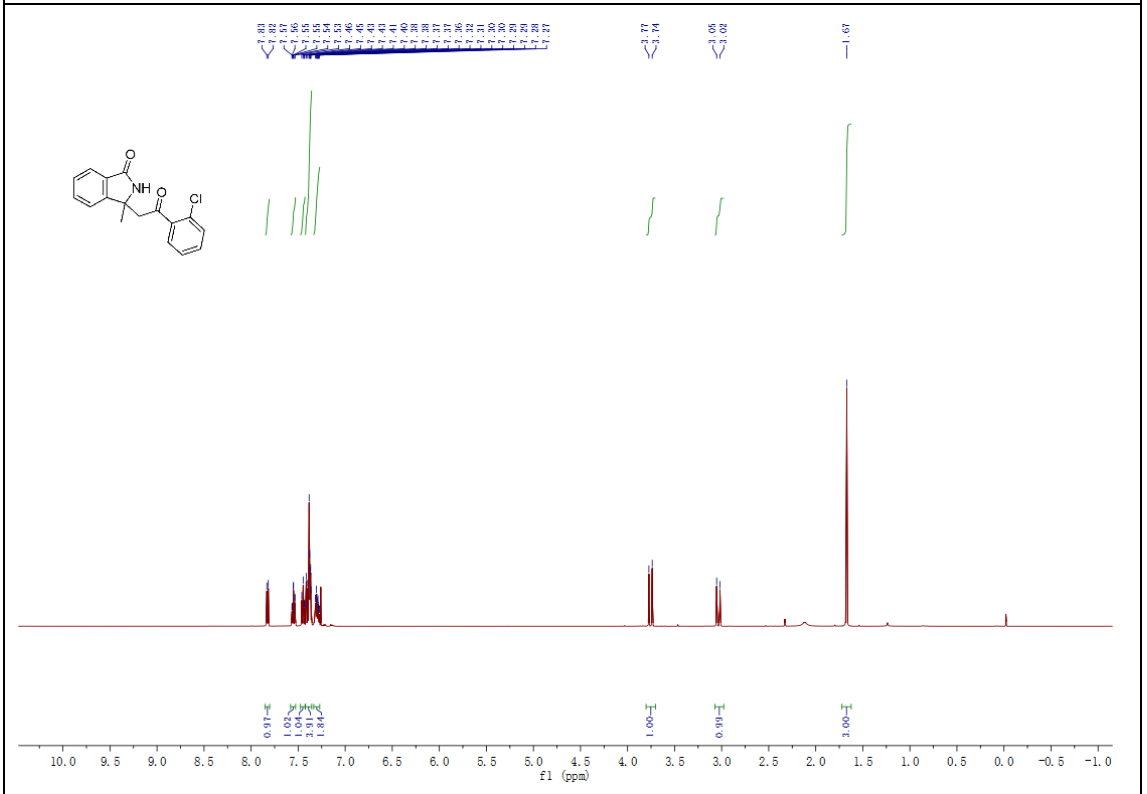


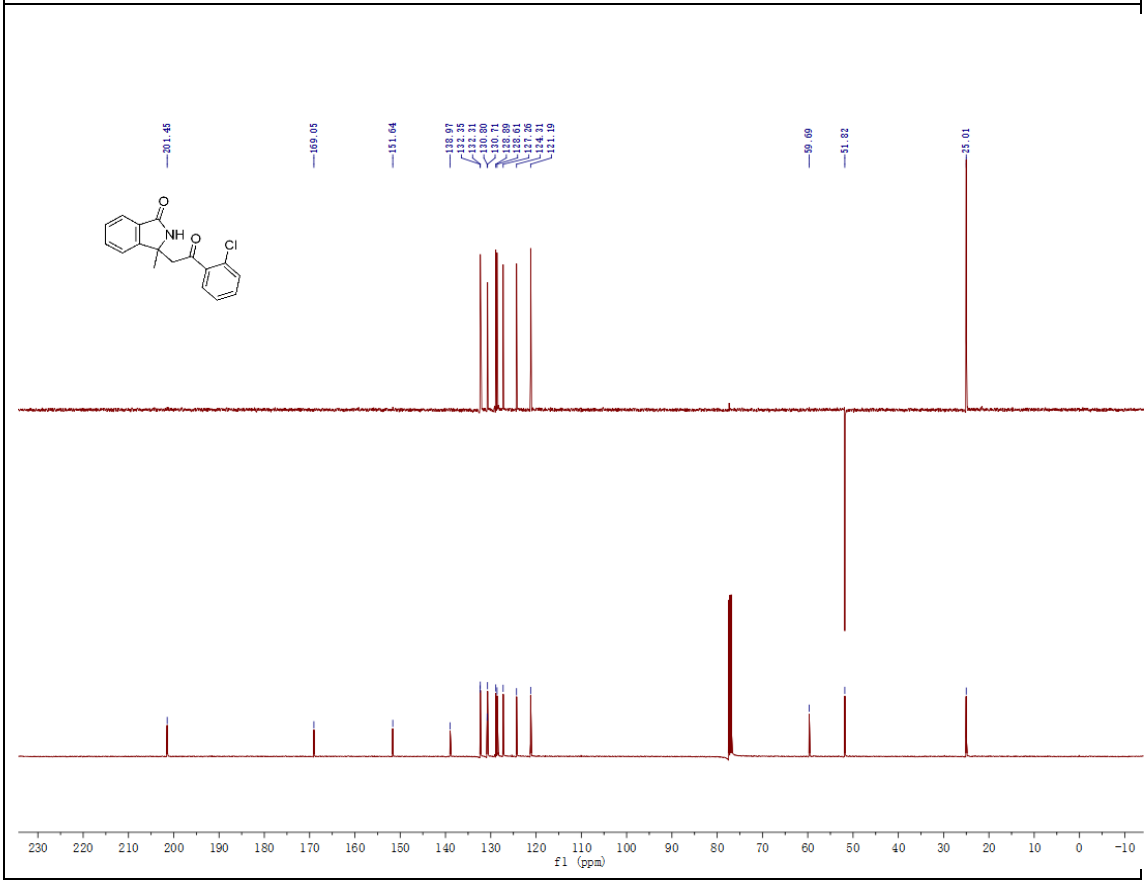
3-(1-hydroxycyclohexyl)-4-methylisoquinolin-1(2H)-one (4zm):



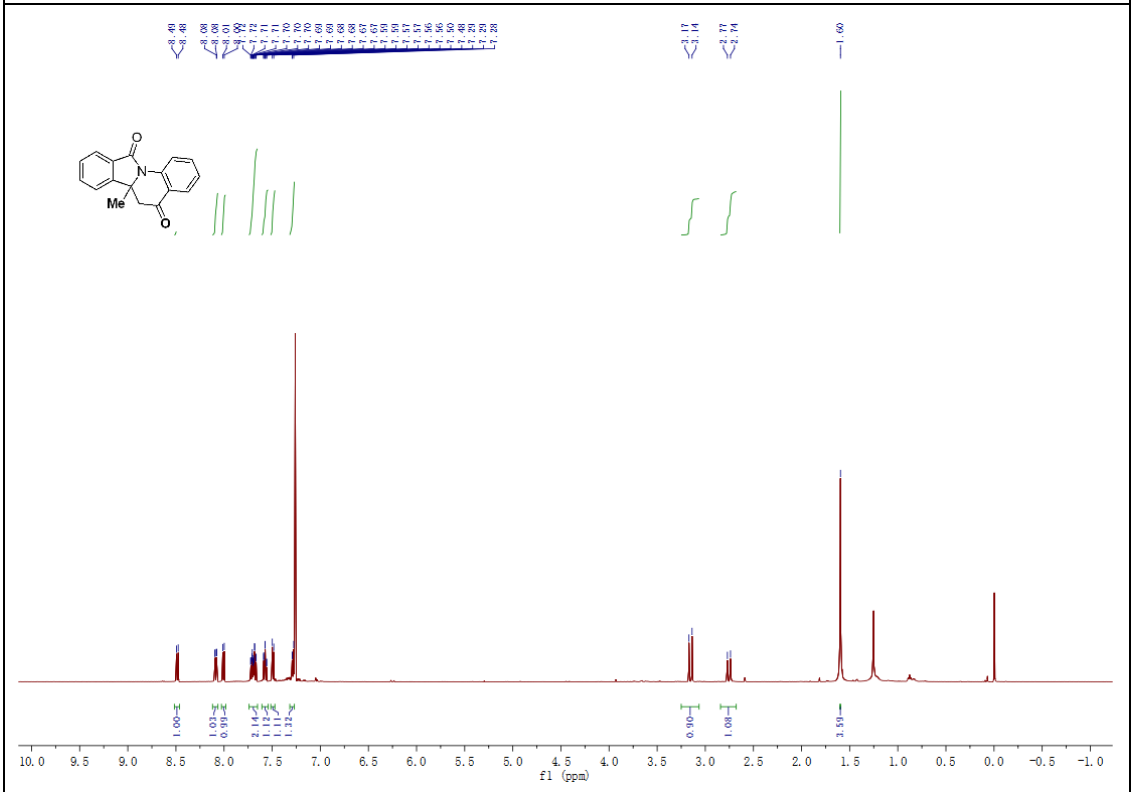


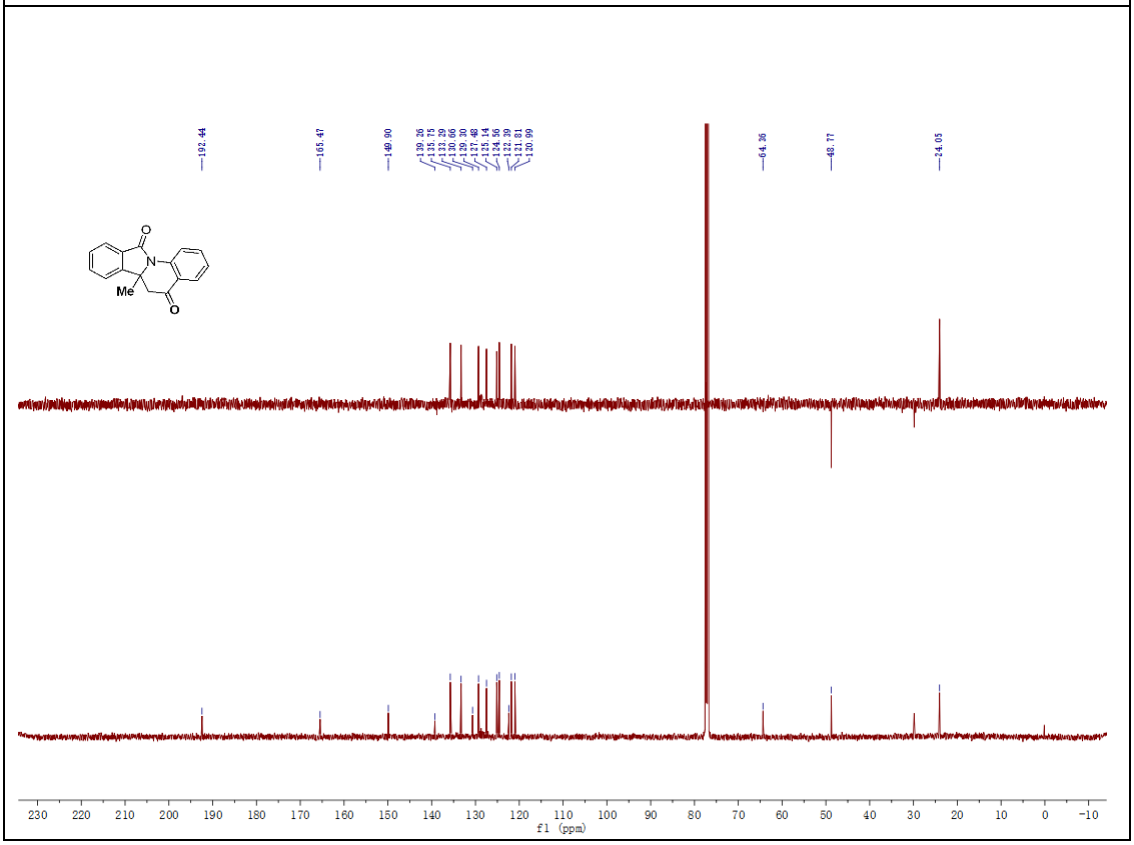
3-(2-(2-chlorophenyl)-2-oxoethyl)-3-methylisoindolin-1-one (3zn):





6a-methyl-6,6a-dihydroisoindolo[2,1-a]quinoline-5,11-dione (3zn-1):





(I) Reference

(1) Jaimes, M. C. B.; Ahrens, A.; Rudolph, M.; Hashmi, A. S. K. *Chem. Eur. J.* **2015**, *21*, 427−433.

(2) P. Lenden, D. A. Entwistle, M. C. Willis, *Angew. Chem. Int. Ed.* **2011**, *50*, 10657−10660.

(3) Alyson, E. G.; Alexandra, D. B.; Kristine, A. N. *Tetrahedron Lett.* **2013**, *54*, 459−461.

(4) Fernández-Salas, J. A.; Eberhart, A. J.; Procter, D. J. *J. Am. Chem. Soc.* **2016**, *138*, 790−793.

(5) Schwier, T.; Rubin, M.; Gevorgyan, V. *Org. Lett.* **2004**, *6*, 1999−2001.

(6) Yan, W.; Wang, Q.; Chen, Y.; Petersen, J. L.; Shi, X. *Org. Lett.* **2010**, *12*, 3308−3311.

(7) Cheng, X.; Yu, Y.; Mao, Z.; Chen, J.; Huang, X. *Org. Biomol. Chem.* **2016**, *14*, 3878−3882.

(8) Hu, G.; Shan, C.; Chen, W.; Xu, P.; Gao, Y.; Zhao, Y. *Org. Lett.* **2016**, *18*, 6066−6069.

(9) Herrero, M. T.; Tellitu, I.; Domínguez, E.; Hernández, S.; Moreno, I.; SanMartín, R. *Tetrahedron*. **2002**, *58*, 8581−8589.

(10) Zhang, N.; Yu, Q.; Chen, R.; Huang, J.; Xia, Y.; Zhao, K. *Chem. Commun.* **2013**, *49*, 9464−9466.