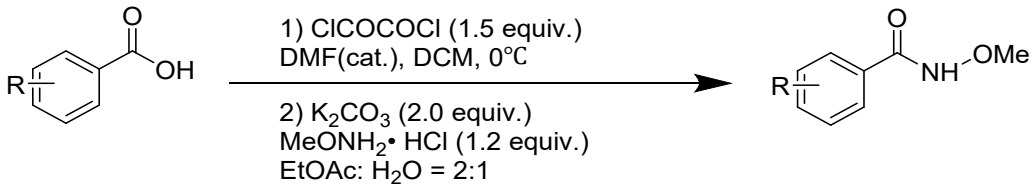
Electronic Supplementary Information

Isoindolinone synthesis through Rh/Cu-catalyzed Oxidative C-H/N-H Annulation of N-methoxy benzamides with Saturated Ketones

1. General comments

All other reagents were purchased from TCI, Alfa Aesar, Accela and Adamas used without further purification. 1,4-dioxane was distilled from sodium and benzophenone under nitrogen and stored over 4Å molecular sieves under nitrogen. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra were obtained on Bruker spectrometer with $CDCl_3$ as solvent and tetramethylsilane (TMS) as internal standard. Chemical shifts are reported in units (ppm) by assigning the TMS resonance in the ^{1}H NMR spectra as 0.00 ppm ($CDCl_3$, 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet), coupling constant (J values) in Hz and integration. Chemical shifts for the ^{13}C NMR spectra are recorded in ppm relative to tetramethylsilane using the central peak of $CDCl_3$ (77.05 ppm) as the internal standard. Flash column chromatography was performed using 300–400 mesh silica with the indicated solvent system according to standard techniques. Analytical thin layer chromatography (TLC) was performed on pre-coated, glass-backed silica gel plates. The yields of the products reported are the isolated yields and the average of two runs.

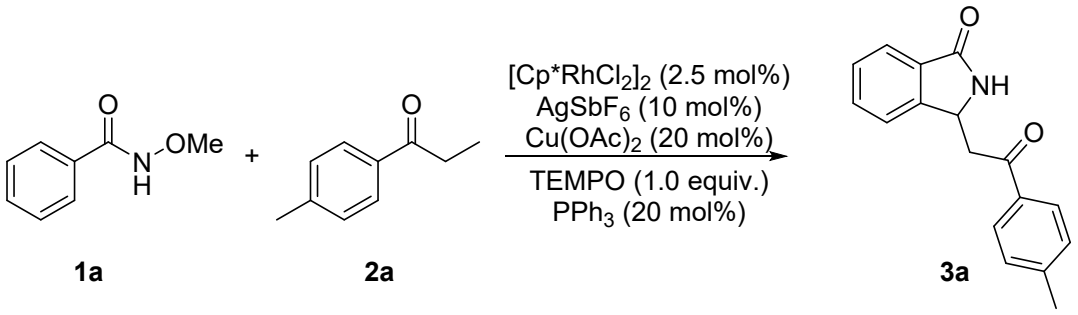
2. General procedure to prepare N-methoxybenzamides



A dried round-bottom flask was charged with acid (4.5 mmol), DCM (15 mL), and 2 drops of DMF. Then, oxalyl chloride (0.60 mL, 0.876 g, 6.9 mmol) was added dropwise within 5 min at 0 °C. The resulting mixture was stirred at room temperature for about 4h and then concentrated under reduced pressure. The residue was dissolved in EtOAc (40 mL) and K_2CO_3 (1.24 g, 9.0 mmol), $MeONH_2{\cdot}HCl$ (458 mg, 5.4 mmol), water (20 mL) were sequentially added. The resulting mixture was stirred for 12 h at room temperature and extracted with EtOAc (50 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ (15 mL × 2), brine (15 mL × 2), and dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was recrystallized (EtOAc) to afford the product. In the case of an oil, the crude product was purified by silica gel column chromatography, using EtOAc/ PE as the eluent.

3. Optimization details for the reaction conditions

Table S1. Optimization of silver salts [a]

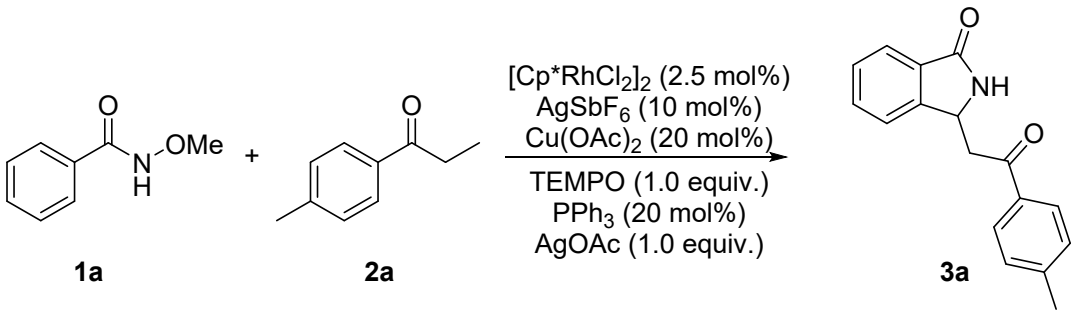


1a **2a** **3a**

Entry	Silver salts (equiv.)	Yield (%)
1	Ag_2CO_3 (1.0)	43
2	AgOAc (2.0)	46
3	Ag_2O (1.0)	30
4	$AgNO_3$ (2.0)	trace
5	Ag_2SO_4 (1.0)	17
6	AgOAc (1.5)	50
7	**AgOAc (1.0)**	**53**

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.6 mmol), 1,2-Diethoxyethane (2.0 mL), N_2, 22 h, isolated yield.

Table S2. Optimization of solvents [a]

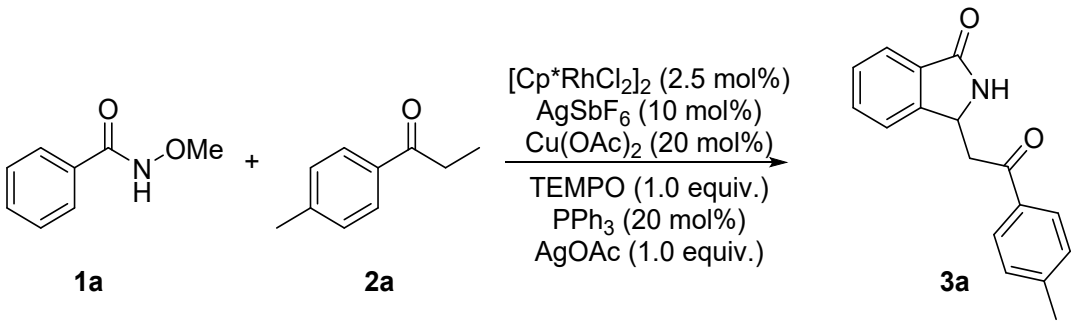


1a **2a** **3a**

Entry	Solvent (mL)	Yield (%)
1	1,2-diethoxyethane (2.0)	53
2	1,4-dioxane (2.0)	59
3	Toluene (2.0)	45
4	1,2-DCB (2.0)	41
5	TFE (2.0)	0
6	HFIP (2.0)	0
7	MeCN (2.0)	0
8	**1,4-dioxane (1.5)**	**65**

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.6 mmol), 120 °C, N_2, 22 h, isolated yield.

Table S3. Optimization of reaction temperature. [a]



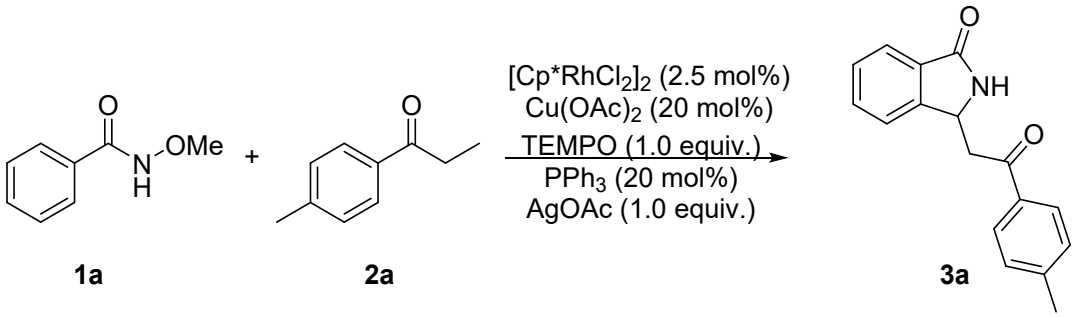
1a **2a** **3a**

Entry	Temp. (℃)	Yield (%)
1	120	65
2	**110**	**78**

3	100	67

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.6 mmol), 1,4-dioxane (1.5 mL), N_2, 22 h, isolated yield.

Table S4. Optimization of the amount of $AgSbF_6$. [a]

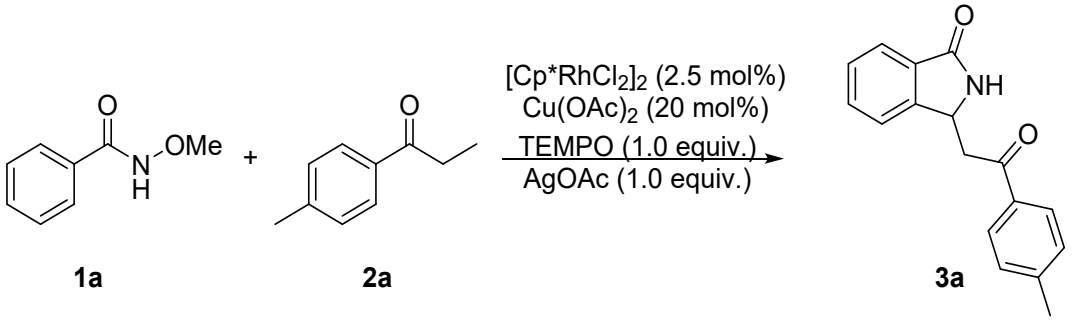


1a **2a** **3a**

Entry	$AgSbF_6$ (equiv.)	Yield (%)
1	**0.1**	**78**
2	0.05	47
3	0	42

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.6 mmol), 1,4-dioxane (1.5 mL), 110 °C, N_2, 22 h, isolated yield.

Table S5. Optimization of the amount of PPh_3. [a]

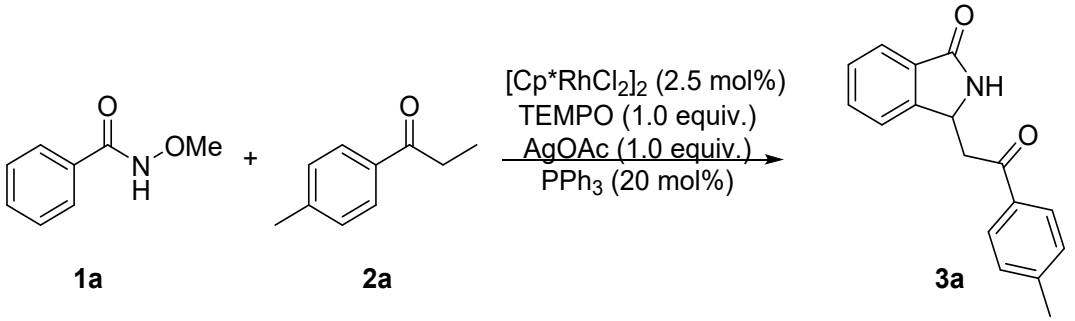


1a **2a** **3a**

Entry	PPh_3 (equiv.)	Yield (%)
1	**0.2**	**78**
2	0.1	67
3	0.05	54

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.6 mmol), 1,4-dioxane (1.5 mL), 110 °C, N_2, 22 h, isolated yield.

Table S6. Optimization of the amount of $Cu(OAc)_2$. [a]



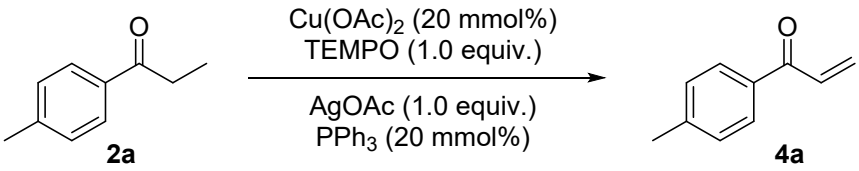
1a **2a** **3a**

Entry	$Cu(OAc)_2$ (equiv.)	Yield (%)
1	**0.2**	**78**
2	0.1	69
3	0	0

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.6 mmol), 1,4-dioxane (1.5 mL), 110 °C, N_2, 22 h, isolated yield.

4. Mechanistic studies

Table S7. Dehydrogenation control experiments. [a]



2a **4a**

Entry	AgOAc (equiv.)	PPh_3 (equiv.)	GC-Yield (%)
1	1.0	0.2	70
2	0	0.2	30
3	1.0	0	34
4	0	0	6

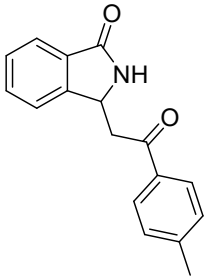
[a] Reaction conditions: **2a** (0.2 mmol), 1,4-dioxane (1.5 mL), 110 °C, N_2, 22 h.

5. General experimental procedures for the synthesis of isoindolinones

In a glove box, a 35 mL Schlenk tube equipped with a stir bar was charged with N-Methoxybenzamides **1** (0.2 mmol) $Cu(OAc)_2$ (20 mol%), TEMPO (1.0 equiv.), $AgSbF_6$ (10 mol %), Cp*$RhCl_2$ (2.5 mol%), AgOAc (1.0 equiv.), PPh_3 (20 mol%). The tube was fitted with a rubber septum, and removed out from the glove box. Then propiophenone **2** (3.0 equiv.) were added through the rubber septum using syringe under the atmosphere of N_2. Dioxane (1.5 mL) was added to the Schlenk tube through the rubber septum using a syringe. The septum was replaced by a Teflon screwcap under N_2 flow. The mixture was stirred at 110 °C (preheated to 110 °C) for 22 h. After cooling, the mixture was diluted with ethyl acetate (10 mL), filtered through a pad of silica gel, followed by washing the pad of the silica gel with the ethyl acetate (10 mL). The organic phase was concentrated under reduced pressure. The residue was then purified by chromatography on silica gel to provide the corresponding product **3**.

6. Characterization for products

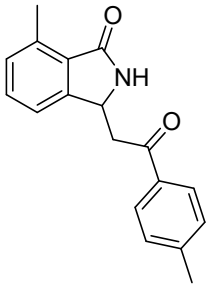
3-(2-Oxo-2-(*p*-tolyl)ethyl)isoindolin-1-one (**3a**) [1]



3a

41.4 mg (78%); white solid (R_f = 0.4, V_{THF}/V_{PE} = 40:60), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 12.5, 7.9 Hz, 3H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.49 (dd, *J* = 12.4, 7.5 Hz, 2H), 7.27 (d, *J* = 8.5 Hz, 2H), 6.94 (s, 1H), 5.13 (d, *J* = 12.5 Hz, 1H), 3.70 (dd, *J* = 18.0, 3.1 Hz, 1H), 3.07 (dd, *J* = 18.0, 10.3 Hz, 1H), 2.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.3, 169.9, 164.1, 146. 7, 131.9, 130.4, 129.1, 128.5, 124.1, 122.4, 114.0, 55.6, 52.6, 43.7.

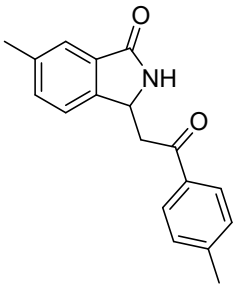
7-Methyl-3-(2-oxo-2-(*p*-tolyl)ethyl)isoindolin-1-one (**3b**) [2]



3b

43.1mg (77%); white solid (R_f = 0.4, V_{THF}/V_{PE} = 15:85), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.1 Hz, 2H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.28 – 7.26 (m, 3H), 7.22 (d, *J* = 7.5 Hz, 1H), 6.83 (s, 1H), 5.05 (d, *J* = 9.3 Hz, 1H), 3.66 (dd, *J* = 18.0, 2.8 Hz, 1H), 3.04 (dd, *J* = 18.0, 10.3 Hz, 1H), 2.73 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.7, 170.9, 147.3, 144.8, 138.4, 133.7, 131.5, 130.4, 129.5, 129.0, 128.2, 119.7, 51.7, 44.2, 21.7, 17.3.

6-Methyl-3-(2-oxo-2-(*p*-tolyl)ethyl)isoindolin-1-one (**3c**)

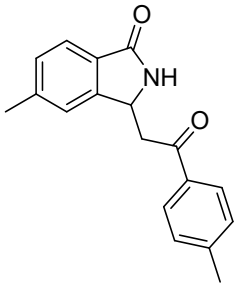


3c

40.2 mg (72%); white solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.1 Hz, 2H), 7.68 (s, 1H), 7.38 (dd, *J* = 17.4, 7.7 Hz, 2H), 7.28 – 7.26 (m, 2H), 6.99 (s, 1H), 5.10 – 5.08 (m, 1H), 3.67 (dd, *J* = 18.0, 3.2 Hz, 1H), 3.05 (dd, *J* = 18.0, 10.1 Hz, 1H), 2.45 (s, 3H), 2.42 (s, 3H). ^{13}C

NMR (101 MHz, $CDCl_3$) δ 197.6, 170.1, 144.8, 143.9, 138.6, 133.6, 132.9, 132.1, 129.5, 128.2, 124.3, 122.1, 52.3, 44.0, 21.7, 21.3. HRMS (ESI): Calcd for $C_{18}H_{17}NO_2$ [M +Na]$^+$: 302.1157, found:302.1165.

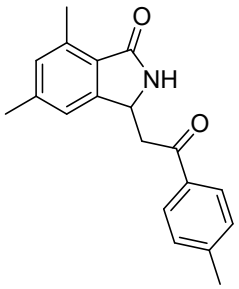
5-Methyl-3-(2-oxo-2-(*p*-tolyl)ethyl)isoindolin-1-one (**3d**)



3d

33.5 mg (60%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 7.7 Hz, 2H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.28 (d, *J* = 14.1 Hz, 4H), 6.92 (s, 1H), 5.07 (d, *J* = 9.1 Hz, 1H), 3.69 – 3.64 (m, 1H), 3.05 (dd, *J* = 17.9, 10.1 Hz, 1H), 2.46 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.6, 170.1, 147.1, 144.8, 142. 7, 133.6, 129.5, 129.5, 129.2, 128.2, 123.9, 122.8, 52.3, 44.0, 22.0, 21.7. HRMS (ESI): Calcd for $C_{18}H_{18}NO_2$ [M +H]$^+$: 280.1332, found: 280.1335.

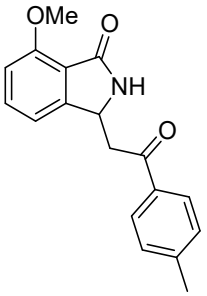
5,7-Dimethyl-3-(2-oxo-2-(*p*-tolyl)ethyl)isoindolin-1-one (**3e**)



3e

41.1 mg (70%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 7.0 Hz, 2H), 7.04 (d, *J* = 9.7 Hz, 2H), 6.68 (s, 1H), 5.00 (d, *J* = 9.4 Hz, 1H), 3.64 (dd, *J* = 18.0, 2.8 Hz, 1H), 3.02 (dd, *J* = 18.0, 10.4 Hz, 1H), 2.67 (s, 3H), 2.42 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.7, 171.0, 147.7, 144.8, 142.1, 138.0, 133.7, 131.4, 129.5, 128.2, 126.5, 120.2, 51.5, 44.3, 21.8, 21.7, 17.2. HRMS (ESI): Calcd for $C_{19}H_{20}NO_2$ [M +H]$^+$: 294.1489, found: 294.1488.

7-Methoxy-3-(2-oxo-2-(*p*-tolyl)ethyl)isoindolin-1-one (**3f**)

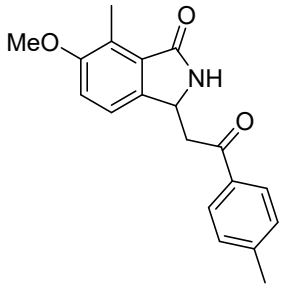


3f

39.6 mg (67%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* =

8.1 Hz, 2H), 7.53 (t, *J* = 7.9 Hz, 1H), 7.27 – 7.25 (m, 2H), 7.12 (s, 1H), 7.02 (d, *J* = 7.5 Hz, 1H), 6.92 (d, *J* = 8.3 Hz, 1H), 5.07 (d, *J* = 8.3 Hz, 1H), 4.00 (d, *J* = 18.4 Hz, 3H), 3.62 (dd, *J* = 18.0, 3.1 Hz, 1H), 3.08 (dd, *J* = 18.0, 9.9 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.4, 158.0, 149.7, 144.9, 134.0, 133.6, 129.5, 128.3, 114.4, 110.6, 56.0, 52.2, 44.0, 21.7. HRMS (ESI): Calcd for $C_{18}H_{18}NO_3$ [M +H]$^+$: 296.1281, found: 296.1273.

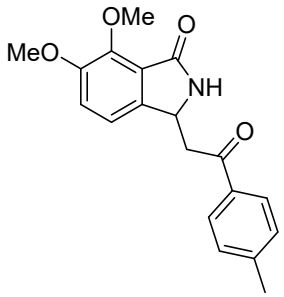
6-Methoxy-7-methyl-3-(2-oxo-2-(*p*-tolyl)ethyl)isoindolin-1-one (**3g**)



3g

42.7 mg (68%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 9.2 Hz, 3H), 7.21 (d, *J* = 8.2 Hz, 1H), 7.03 (d, *J* = 8.2 Hz, 1H), 6.71 (s, 1H), 4.99 (d, *J* = 10.4 Hz, 1H), 3.88 (s, 3H), 3.63 (dd, *J* = 17.9, 2.9 Hz, 1H), 3.01 (dd, *J* = 18.0, 10.3 Hz, 1H), 2.62 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.9, 170.9, 158.1, 144.8, 138.7, 133.8, 129.9, 129.5, 128.2, 127.3, 119.7, 113.6, 56.2, 50.9, 44.6, 21.8, 9.6. HRMS (ESI): Calcd for $C_{19}H_{20}NO_3$ [M +Na]$^+$: 310.1438, found: 310.1434.

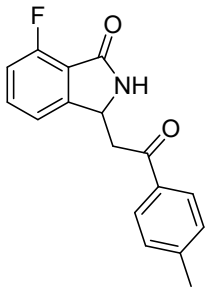
6,7-Dimethoxy-3-(2-oxo-2-(*p*-tolyl)ethyl)isoindolin-1-one(**3h**)



3h

42.9 mg (66%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 40:60), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.1 Hz, 2H), 7.25 (d, *J* = 7.6 Hz, 2H), 7.10 (q, *J* = 8.2 Hz, 2H), 6.86 (s, 1H), 4.99 (dd, *J* = 9.8, 2.5 Hz, 1H), 4.07 (s, 3H), 3.89 (s, 3H), 3.60 (dd, *J* = 17.9, 3.3 Hz, 1H), 3.05 (dd, *J* = 18.0, 10.0 Hz, 1H), 2.40 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.6, 168.3, 152.6, 147.8, 144.8, 140.1, 133.7, 129.5, 128.2, 124.1, 117.3, 117.0, 62.5, 56.8, 51.3, 44.4, 21.7. HRMS (ESI): Calcd for $C_{19}H_{20}NO_4$ [M +H]$^+$: 326.1387, found: 326.1392.

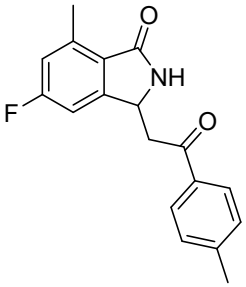
7-Fluoro-3-(2-oxo-2-(*p*-tolyl)ethyl)isoindolin-1-one (**3i**)



3i

36.3 mg (64%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^{1}H NMR (400 MHz, DMSO) δ 8.60 (s, 1H), 7.90 (d, *J* = 8.2 Hz, 2H), 7.61 (td, *J* = 7.9, 4.9 Hz, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.23 (t, *J* = 9.2 Hz, 1H), 5.10 (dd, *J* = 7.6, 4.6 Hz, 1H), 3.68 (dd, *J* = 17.9, 4.6 Hz, 1H), 3.39 – 3.33 (m, 1H), 2.37 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 197.0, 166.2 (d, *J* = 2.0 Hz), 158.2 (d, *J* = 257.4 Hz), 150.9 (d, *J* = 3.1 Hz), 144.0, 134.0 (d, *J* = 7.6 Hz), 133.9, 129.4, 128.3, 119.7 (d, *J* = 3.8 Hz), 119.3 (d, *J* = 13.4 Hz), 115.1 (d, *J* = 19.4 Hz), 52.1, 43.3, 21.2. HRMS (ESI): Calcd for $C_{17}H_{15}FNO_2$ $[M+H]^+$: 284.1081, found: 284.1081.

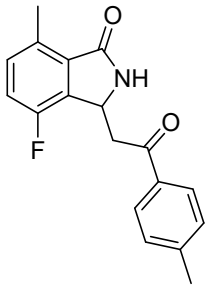
5-Fluoro-7-methyl-3-(2-oxo-2-(*p*-tolyl)ethyl)isoindolin-1-one (**3j**)



3j

41.6 mg (70%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 7.6 Hz, 2H), 7.27 (d, *J* = 6.9 Hz, 2H), 6.96 – 6.91 (m, 2H), 6.84 (s, 1H), 5.03 (d, *J* = 8.9 Hz, 1H), 3.63 – 3.58 (m, 1H), 3.07 (dd, *J* = 17.9, 10.1 Hz, 1H), 2.70 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.3, 169.9, 164.7 (d, *J* = 252.5 Hz), 149.8 (d, *J* = 10.1 Hz), 144.9, 141.3 (d, *J* = 9.5 Hz), 133.6, 129.5, 128.2, 125.2, 117.7 (d, *J* = 22.5 Hz), 107.3 (d, *J* = 24.0 Hz), 51.6 (d, *J* = 2.7 Hz), 44.1, 21.7, 17.4. HRMS (ESI): Calcd for $C_{18}H_{17}FNO_2$ $[M+H]^+$: 298.1238, found: 298.1243.

4-Fluoro-7-methyl-3-(2-oxo-2-(*p*-tolyl)ethyl)isoindolin-1-one (**3k**)

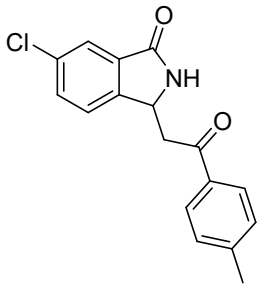


3k

38.1 mg (64%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.2 Hz, 2H), 7.26 – 7.25 (m, 2H), 6.93 (dd, *J* = 13.4, 9.0 Hz, 2H), 6.86 (s, 1H), 5.03 (dd, *J* = 9.9, 2.7 Hz,

1H), 3.59 (dd, *J* = 17.9, 3.3 Hz, 1H), 3.08 (dd, *J* = 17.9, 10.0 Hz, 1H), 2.70 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.3, 169.9, 167.7 (d, *J* = 252.5 Hz), 149.8 (d, *J* = 10.1 Hz), 144.9, 141.2 (d, *J* = 10.1 Hz), 133.6, 129.5, 128.2, 125.2 (d, *J* = 2.0 Hz), 117.6 (d, *J* = 22.2 Hz), 107.1 (d, *J* = 23.2 Hz), 51.6, 51.6, 44.1, 21.7, 17.4. HRMS (ESI): Calcd for $C_{18}H_{17}FNO_2$ [M +Na]$^+$: 320.1063, found: 320.1066.

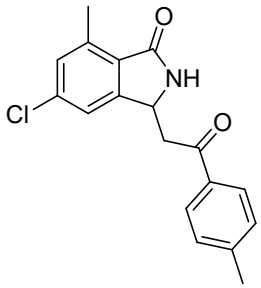
6-Chloro-3-(2-oxo-2-(*p*-tolyl)ethyl)isoindolin-1-one (**3l**)



3l

40.2 mg (67%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.3 Hz, 3H), 7.54 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.42 (d, *J* = 8.1 Hz, 1H), 7.27 (d, *J* = 7.4 Hz, 2H), 7.15 (s, 1H), 5.12 (dd, *J* = 9.7, 2.7 Hz, 1H), 3.65 (dd, *J* = 18.0, 3.2 Hz, 1H), 3.09 (dd, *J* = 18.0, 9.9 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.2, 168.6, 145.0, 144.8, 134.8, 133.5, 132.1, 131.3, 130.3, 129.6, 129.3, 128.2, 124.3, 123.8, 52.4, 43.7, 21.7. HRMS (ESI): Calcd for $C_{17}H_{15}ClNO_2$ [M +Na]$^+$: 322.0611, found: 322.0619.

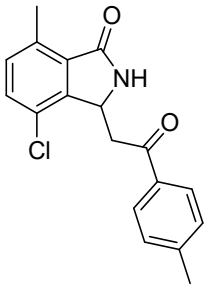
5-Chloro-7-methyl-3-(2-oxo-2-(*p*-tolyl)ethyl)isoindolin-1-one (**3m**)



3m

41.8 mg (67%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.2 Hz, 2H), 7.27 (d, *J* = 9.6 Hz, 3H), 7.22 (s, 1H), 6.87 (s, 1H), 5.03 (dd, *J* = 10.0, 1.9 Hz, 1H), 3.63 (dd, *J* = 18.0, 3.1 Hz, 1H), 3.06 (dd, *J* = 18.0, 10.3 Hz, 1H), 2.69 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.3, 169.9, 148.9, 145.0, 140.1, 137.6, 133.5, 130.6, 129.6, 128.2, 127.6, 120.2, 51.5, 44.0, 21.8, 17.2. HRMS (ESI): Calcd for $C_{18}H_{17}ClNO_2$ [M +Na]$^+$: 314.0767, found: 314.0775.

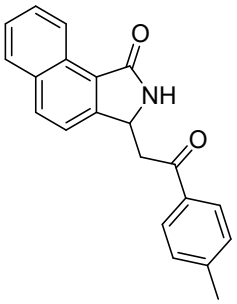
4-Chloro-7-methyl-3-(2-oxo-2-(*p*-tolyl)ethyl)isoindolin-1-one (**3n**)



3n

24.9 mg (40%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.1 Hz, 2H), 7.39 (d, *J* = 8.1 Hz, 1H), 7.27 (d, *J* = 7.3 Hz, 2H), 7.19 (d, *J* = 8.1 Hz, 1H), 6.94 (s, 1H), 5.07 (d, *J* = 10.6 Hz, 1H), 4.28 (dd, *J* = 18.1, 2.0 Hz, 1H), 2.85 (dd, *J* = 18.1, 10.8 Hz, 1H), 2.69 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.9, 169.4, 144.9, 143.7, 137.2, 133.6, 132.1, 131.8, 131.3, 129.5, 128.2, 126.2, 51.5, 41.5, 21.7, 16.9. HRMS (ESI): Calcd for $C_{18}H_{17}ClNO_2$ $[M+H]^+$: 314.0942, found: 314.0958.

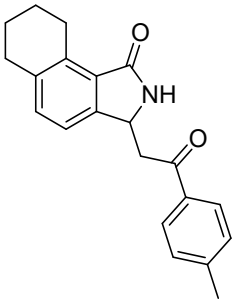
3-(2-Oxo-2-(*p*-tolyl)ethyl)-2,3-dihydro-1H-benzo[e]isoindol-1-one (**3o**)



3o

40.4 mg (64%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.22 (d, *J* = 8.3 Hz, 1H), 8.04 (d, *J* = 8.4 Hz, 1H), 7.92 (d, *J* = 8.2 Hz, 1H), 7.85 (d, *J* = 8.2 Hz, 2H), 7.67 – 7.63 (m, 1H), 7.59 – 7.55 (m, 1H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.26 – 7.24 (m, 2H), 7.07 (s, 1H), 5.16 (dd, *J* = 10.2, 1.9 Hz, 1H), 3.74 (dd, *J* = 17.9, 3.1 Hz, 1H), 3.06 (dd, *J* = 17.9, 10.3 Hz, 1H), 2.40 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.5, 171.1, 147.1, 144.8, 133.6, 133.2, 133.0, 129.6, 129.5, 128.2, 128.1, 128.1, 126.7, 126.0, 123.9, 119.4, 52.2, 43.5, 21.7. HRMS (ESI): Calcd for $C_{21}H_{18}NO_2$ $[M+H]^+$: 316.1332, found: 316.1331.

3-(2-Oxo-2-(*p*-tolyl)ethyl)-2,3,6,7,8,9-hexahydro-1H-benzo[e]isoindol-1-one (**3p**)

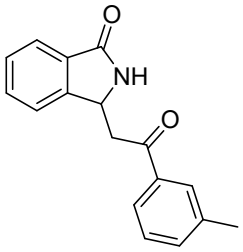


3p

40.2 mg (63%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 40:60), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* =

8.1 Hz, 2H), 7.28 – 7.26 (m, 3H), 7.17 (d, *J* = 7.7 Hz, 1H), 6.75 (s, 1H), 5.01 (d, *J* = 9.3 Hz, 1H), 3.64 (dd, *J* = 18.0, 2.9 Hz, 1H), 3.31 (s, 2H), 3.02 (dd, *J* = 18.0, 10.3 Hz, 1H), 2.84 (s, 2H), 2.42 (s, 3H), 1.86 – 1.78 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.8, 171.2, 145.0, 144.8, 137.8, 137.6, 133.7, 132.9, 129.5, 128.5, 128.2, 119.0, 51.4, 44.3, 29.6, 25.0, 22.8, 22.4, 21.7. HRMS (ESI): Calcd for $C_{21}H_{22}NO_2$ $[M+H]^+$: 320.1645 , found: 320.1642.

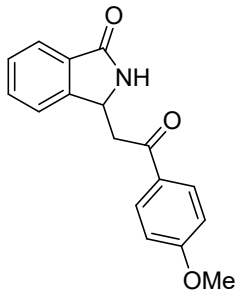
3-(2-Oxo-2-(*m*-tolyl)ethyl)isoindolin-1-one (**4a**)



4a

35.6 mg (67%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.4 Hz, 1H), 7.76 – 7.73 (m, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 2H), 7.42 – 7.33 (m, 2H), 7.04 (s, 1H), 5.13 (dd, *J* = 10.0, 2.6 Hz, 1H), 3.70 (dd, *J* = 18.1, 3.3 Hz, 1H), 3.10 (dd, *J* = 18.1, 10.1 Hz, 1H), 2.40 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.5, 170.0, 146.6, 144.9, 133.6, 132.0, 131.9, 129.5, 128.5, 128.2, 124.1, 122.4, 52.5, 43.9, 21.7. HRMS (ESI): Calcd for $C_{17}H_{16}NO_2$ $[M+H]^+$: 266.1176 , found: 266.1179.

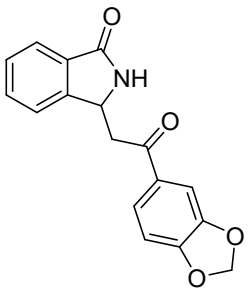
3-(2-(4-Methoxyphenyl)-2-oxoethyl)isoindolin-1-one (**4b**) [1]



4b

38.3 mg (68%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.8 Hz, 2H), 7.87 (d, *J* = 7.5 Hz, 1H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.51 – 7.46 (m, 2H), 7.01 (s, 1H), 6.93 (d, *J* = 8.8 Hz, 2H), 5.12 (dd, *J* = 9.8, 1.8 Hz, 1H), 3.86 (s, 3H), 3.66 (dd, *J* = 17.9, 3.1 Hz, 1H), 3.04 (dd, *J* = 17.9, 10.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.3, 169.9, 164.1, 146.7, 132.0, 131.9, 130.4, 129.1, 128.5, 124.1, 122.4, 114.0, 55.6, 52.6, 43.7.

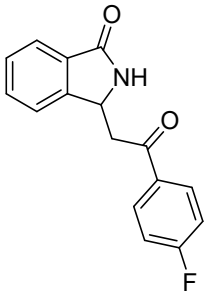
3-(2-(Benzo[d][1,3]dioxol-5-yl)-2-oxoethyl)isoindolin-1-one (**4c**)



4c

36.6 mg (62%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.5 Hz, 1H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.52 – 7.46 (m, 3H), 7.42 (s, 1H), 7.12 (s, 1H), 6.82 (d, *J* = 8.2 Hz, 1H), 6.04 (s, 2H), 5.10 (dd, *J* = 9.8, 2.4 Hz, 1H), 3.61 (dd, *J* = 17.9, 3.3 Hz, 1H), 3.02 (dd, *J* = 17.9, 10.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.8, 170.1, 152.4, 148.4, 146.6, 131.9, 130.9, 128.5, 127.4, 124.6, 124.1, 122.4, 108.0, 107.7, 102.0, 52.6, 43.7. HRMS (ESI): Calcd for $C_{17}H_{14}NO_4$ $[M+H]^+$: 296.0917, found: 296.0920.

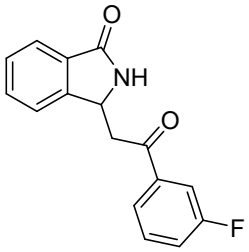
3-(2-(4-Fluorophenyl)-2-oxoethyl)isoindolin-1-one (**4d**) [1]



4d

42.6 mg (79%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 – 7.96 (m, 2H), 7.85 (d, *J* = 7.4 Hz, 1H), 7.60 – 7.56 (m, 1H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.25 (d, *J* = 6.6 Hz, 1H), 7.13 (t, *J* = 8.6 Hz, 2H), 5.13 (dd, *J* = 9.7, 3.0 Hz, 1H), 3.66 (dd, *J* = 18.0, 3.5 Hz, 1H), 3.10 (dd, *J* = 18.0, 9.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.3, 170.1, 166.1 (d, *J* = 254.6 Hz), 146.5, 132.5 (d, *J* = 3.0 Hz), 132.0, 130.8 (d, *J* = 9.5 Hz), 128.6, 127.4, 124.1, 122.4, 116.0 (d, *J* = 21.9 Hz), 52.4, 44.0.

3-(2-(3-Fluorophenyl)-2-oxoethyl)isoindolin-1-one (**4e**) [3]

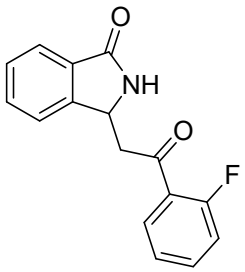


4e

38.8 mg (72%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^{1}H NMR (400 MHz, DMSO-d6) δ 8.58 (s, 1H), 7.85 (d, *J* = 7.6 Hz, 1H), 7.77 (d, *J* = 9.7 Hz, 1H), 7.66 (d, *J* = 7.4 Hz, 1H), 7.62 – 7.56 (m, 3H),

7.53 – 7.46 (m , 2H), 5.10 (dd, *J* = 7.5, 4.5 Hz, 1H), 3.72 (dd, *J* = 18.0, 4.4 Hz, 1H), 3.42 – 3.32 (m, 1H, H_2O). ^{13}C NMR (101 MHz, DMSO-d6) δ 196.8 (d, *J* = 2.1 Hz), 169.3, 162.3 (d, *J* = 246.3 Hz), 147.4, 138.6 (d, *J* = 6.2 Hz), 132.4, 131.6, 131.0 (d, *J* = 7.8 Hz), 128.2, 124.5 (d, *J* = 2.7 Hz), 123.4, 122.9, 120.5 (d, *J* = 21.4 Hz), 114.7 (d, *J* = 22.4 Hz), 52.2, 43.8.

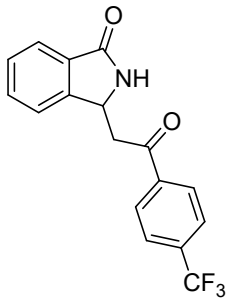
3-(2-(2-fluorophenyl)-2-oxoethyl)isoindolin-1-one (**4f**) [3]



4f

33.4 mg (62%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (td, *J* = 7.7, 1.8 Hz, 1H), 7.87 (d, *J* = 7.5 Hz, 1H), 7.61 – 7.54 (m, 2H), 7.51 – 7.47 (m, 2H), 7.29 – 7.25 (m, 1H), 7.14 (ddd, *J* = 11.4, 8.3, 0.8 Hz, 1H), 7.04 (s, 1H), 5.13 (dd, *J* = 10.0, 2.2 Hz, 1H), 3.74 (dt, *J* = 18.8, 3.3 Hz, 1H), 3.10 (ddd, *J* = 18.8, 10.2, 3.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.1 (d, *J* = 4.1 Hz), 170.1, 162.4 (d, *J* = 256.2 Hz), 146.4, 135.6 (d, *J* = 9.3 Hz), 132.0 (d, *J* = 5.5 Hz), 130.6 (d, *J* = 2.2 Hz), 128.5, 124.8 (d, *J* = 3.3 Hz), 124.5 (d, *J* = 12.6 Hz), 124.1, 122.4, 116.9 (d, *J* = 23.8 Hz), 52.5 (d, *J* = 2.8 Hz), 48.9 (d, *J* = 8.1 Hz).

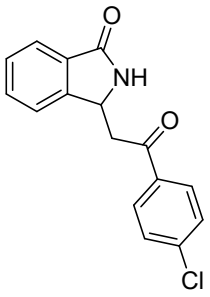
3-(2-Oxo-2-(4-(trifluoromethyl)phenyl)ethyl)isoindolin-1-one (**4g**) [3]



4g

29.4 mg (46%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.1 Hz, 2H), 7.88 (d, *J* = 7.5 Hz, 1H), 7.75 (d, *J* = 8.2 Hz, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.53 – 7.48 (m, 2H), 7.11 (s, 1H), 5.16 (dd, *J* = 9.6, 2.1 Hz, 1H), 3.73 (dd, *J* = 18.2, 3.2 Hz, 1H), 3.16 (dd, *J* = 18.2, 9.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.1, 170.1, 146.3, 138.6, 135.3 (CF_3), 135.0 (CF_3), 132.1, 132.0, 128.7, 128.5, 126.0(d, *J* = 11.0 Hz), 124.8 (CF_3), 124.3, 122.4, 122.1 (CF_3), 52.3, 44.5.

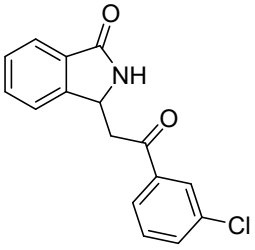
3-(2-(4-Chlorophenyl)-2-oxoethyl)isoindolin-1-one (**4h**) [1]



4h

41.7 mg (73%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.84 (m, 3H), 7.59 – 7.55 (m, 1H), 7.51 – 7.40 (m, 4H), 7.32 (s, 1H), 5.13 (dd, *J* = 9.6, 3.0 Hz, 1H), 3.65 (dd, *J* = 18.1, 3.5 Hz, 1H), 3.10 (dd, *J* = 18.1, 9.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.7, 170.2, 146.4, 140.4, 134.3, 132.0, 129.5, 129.2, 128.6, 127.4, 124.1, 122.40, 52.4, 44.0.

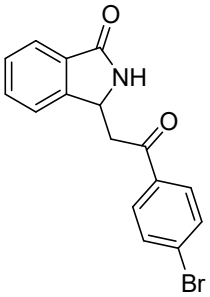
3-(2-(3-Chlorophenyl)-2-oxoethyl)isoindolin-1-one (**4i**) [3]



4i

40.6 mg (70%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.87 (d, *J* = 7.5 Hz, 1H), 7.82 (d, *J* = 7.7 Hz, 1H), 7.58 (dd, *J* = 15.4, 7.8 Hz, 2H), 7.49 (dd, *J* = 12.0, 7.5 Hz, 2H), 7.42 (t, *J* = 7.9 Hz, 1H), 7.14 (s, 1H), 5.14 (dd, *J* = 9.7, 2.6 Hz, 1H), 3.68 (dd, *J* = 18.2, 3.3 Hz, 1H), 3.11 (dd, *J* = 18.2, 9.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.7, 170.1, 146.3, 137.5, 135.2, 133.8, 132.1, 130.2, 128.7, 128.2, 127.4, 126.2, 124.2, 122.4, 52.3, 44.2.

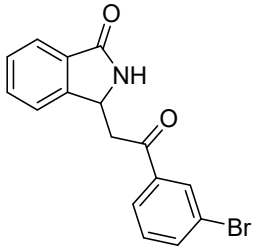
3-(2-(4-Bromophenyl)-2-oxoethyl)isoindolin-1-one (**4j**) [1]



4j

52.8 mg (80%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.5 Hz, 1H), 7.80 (d, *J* = 8.5 Hz, 2H), 7.61 –7.56 (m, 3H), 7.50 – 7.46 (m, 2H), 7.22 (s, 1H), 5.13 (dd, *J* = 9.7, 2.9 Hz, 1H), 3.65 (dd, *J* = 18.1, 3.4 Hz, 1H), 3.09 (dd, *J* = 18.1, 9.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.9, 170.1, 146.4, 134.7, 132.1, 132.0, 131.9, 129.6, 129.2, 128.6, 124.1, 122.4, 52.3, 44.0.

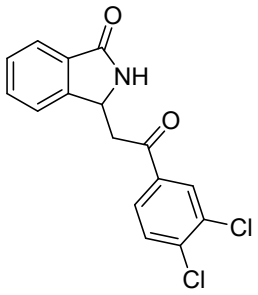
3-(2-(3-Bromophenyl)-2-oxoethyl)isoindolin-1-one (**4k**)



4k

46.2 mg (70%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.86 (d, *J* = 7.6 Hz, 2H), 7.70 (dd, *J* = 8.0, 0.6 Hz, 1H), 7.59 (t, *J* = 7.2 Hz, 1H), 7.49 (t, *J* = 8.1 Hz, 2H), 7.35 (t, *J* = 7.9 Hz, 1H), 7.21 (s, 1H), 5.13 (dd, *J* = 9.7, 2.9 Hz, 1H), 3.66 (dd, *J* = 18.2, 3.4 Hz, 1H), 3.11 (dd, *J* = 18.2, 9.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.6, 170.1, 146.3, 137.7, 136.7, 132.0, 131.9, 131.1, 130.4, 128.6, 126.6, 124.2, 123.2, 122.4, 52.3, 44.2. HRMS (ESI): Calcd for $C_{16}H_{13}BrNO_2$ $[M+H]^+$: 351.9958, found: 351.9949.

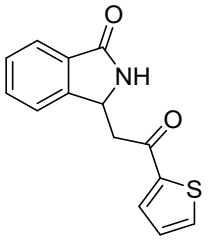
3-(2-(3,4-Dichlorophenyl)-2-oxoethyl)isoindolin-1-one (**4l**)



4l

42.9 mg (67%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 1.9 Hz, 1H), 7.88 (d, *J* = 7.5 Hz, 1H), 7.78 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.63 – 7.56 (m 2H), 7.53 – 7.47 (m, 2H), 6.97 (s, 1H), 5.14 (dd, *J* = 9.9, 2.3 Hz, 1H), 3.67 (dd, *J* = 18.2, 3.2 Hz, 1H), 3.08 (dd, *J* = 18.2, 10.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.8, 170.0, 146.2, 138.7, 135.5, 133.7, 132.1, 131.9, 131.0, 130.1, 128.8, 127.1, 124.3, 122.4, 52.2, 44.2. HRMS (ESI): Calcd for $C_{16}H_{12}Cl_2NO_2$ $[M+H]^+$: 320.0240, found: 320.0244.

3-(2-Oxo-2-(thiophen-2-yl)ethyl)isoindolin-1-one (**4m**) [1]

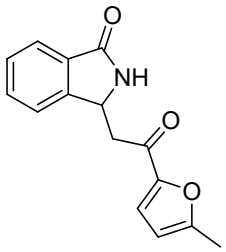


4m

34.5 mg (67%), whitle solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.4 Hz, 1H), 7.69 (t, *J* = 4.0 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 8.0 Hz, 2H), 7.14 – 7.10 (m, 2H), 5.13 (dd, *J* = 9.7, 2.7 Hz, 1H), 3.63 (dd, *J* = 17.6, 3.5 Hz, 1H), 3.07 (dd, *J* = 17.6, 10.0 Hz, 1H). ^{13}C

NMR (101 MHz, CDCl3) δ 190.5, 170.0, 146.3, 143.1, 134.7, 132.7, 132.0, 128.6, 128.4, 127.4, 124.2, 122.4, 52.5, 44.5.

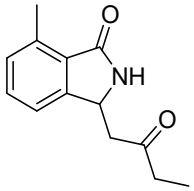
3-(2-(5-Methylfuran-2-yl)-2-oxoethyl)isoindolin-1-one (**4n**)



4n

29.1 mg (57%), white solid (R_f = 0.4, V_{THF}/V_{PE} = 30:70), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 7.5 Hz, 1H), 7.56 (t, *J* = 7.1 Hz, 1H), 7.46 (t, *J* = 6.8 Hz, 2H), 7.15 (d, *J* = 3.0 Hz, 2H), 6.16 (d, *J* = 2.9 Hz, 1H), 5.08 (dd, *J* = 9.8, 3.0 Hz, 1H), 3.49 (dd, *J* = 17.6, 3.5 Hz, 1H), 2.92 (dd, *J* = 17.6, 10.0 Hz, 1H), 2.36 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.7, 170.1, 158.5, 150.8, 146.5, 131.9, 131.8, 128.4, 124.0, 122.4, 120.0, 109.4, 52.3, 43.1, 14.0. HRMS (ESI): Calcd for $C_{15}H_{14}NO_3$ $[M+H]^+$: 256.0968, found: 256.0967.

3-(2-Oxobutyl)isoindolin-1-one (**4o**)



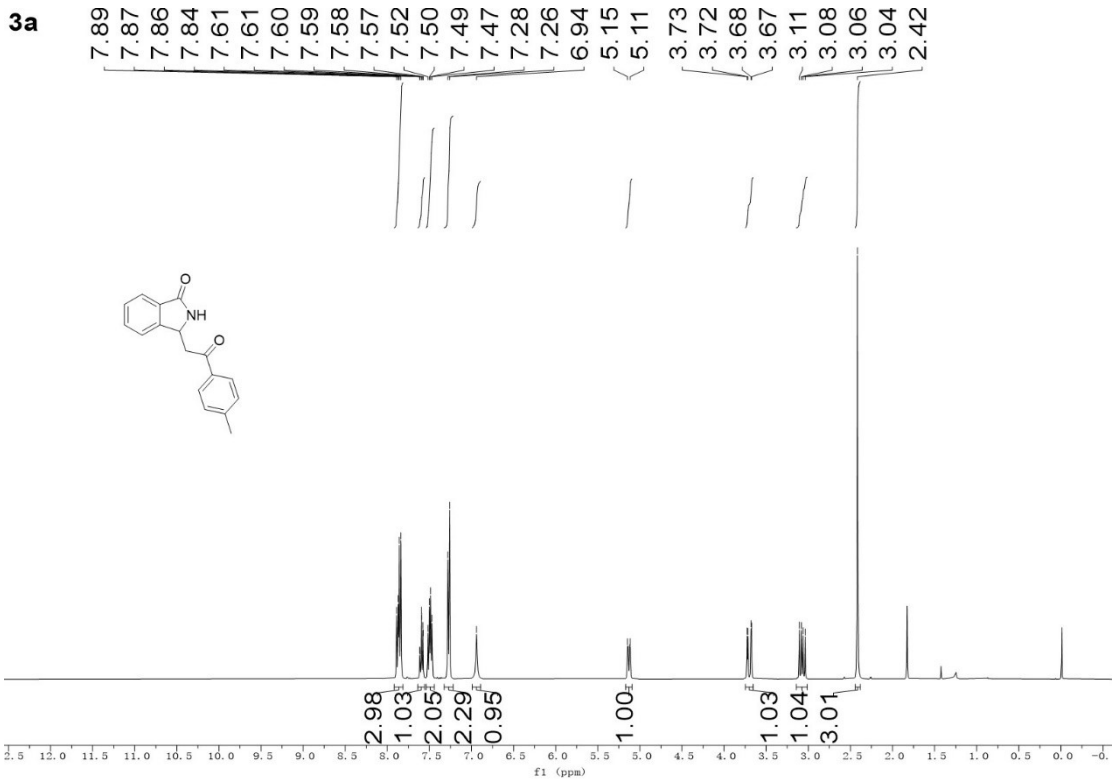
4o

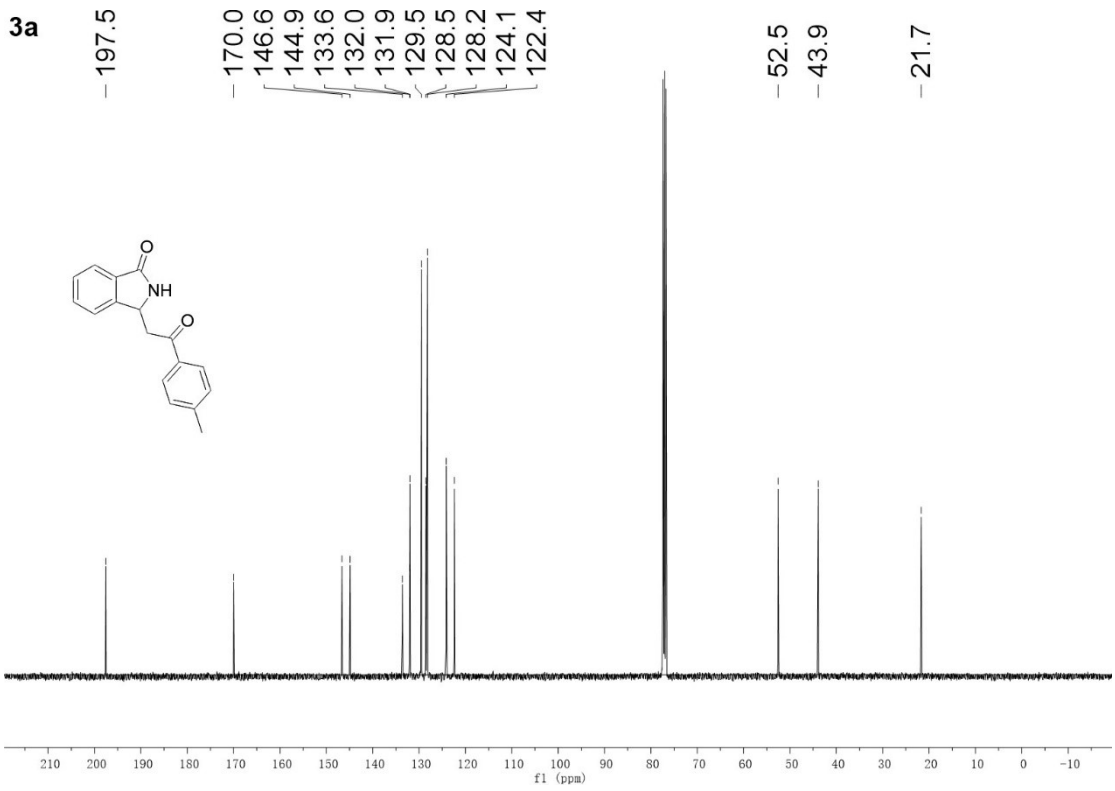
14.3 mg (33%), white solid (Rf = 0.4, V_{THF}/V_{PE} = 40:60), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (t, *J* = 7.6 Hz, 1H), 7.17 (t, *J* = 7.2 Hz, 2H), 6.78 (s, 1H), 4.87 (dd, *J* = 10.2, 3.0 Hz, 1H), 3.11 (dd, *J* = 18.1, 3.3 Hz, 1H), 2.69 (s, 3H), 2.56 – 2.44 (m, 3H), 1.09 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 209.6, 171.0, 147.1, 138.4, 131.5, 130.4, 128.9, 119.5, 51.4, 47.5, 36.2, 17.3, 7.7. HRMS (ESI): Calcd for $C_{13}H_{16}NO_2$ $[M+H]^+$: 218.1176 found: 218.1174.

7. References

1. F. Z. Han, B. Su, L. N. Jia, P. W. Wang, X. P. Hu, *Adv. Synth. Catal*., 2017, **359**,146.
2. X. Zhou, H. Xu, Q. Yang, H. Chen, S. Wang, H. Zhao, *Chem. Commun*. 2019, **55**, 8603.
3. J. Li, Y. Li, Z. Wang, Y. Bian, S. Bai, L. Liu, J. Sun, *J. Org. Chem*., 2018, **83**, 4257.

8. ^{1}H and ^{13}C NMR spectra





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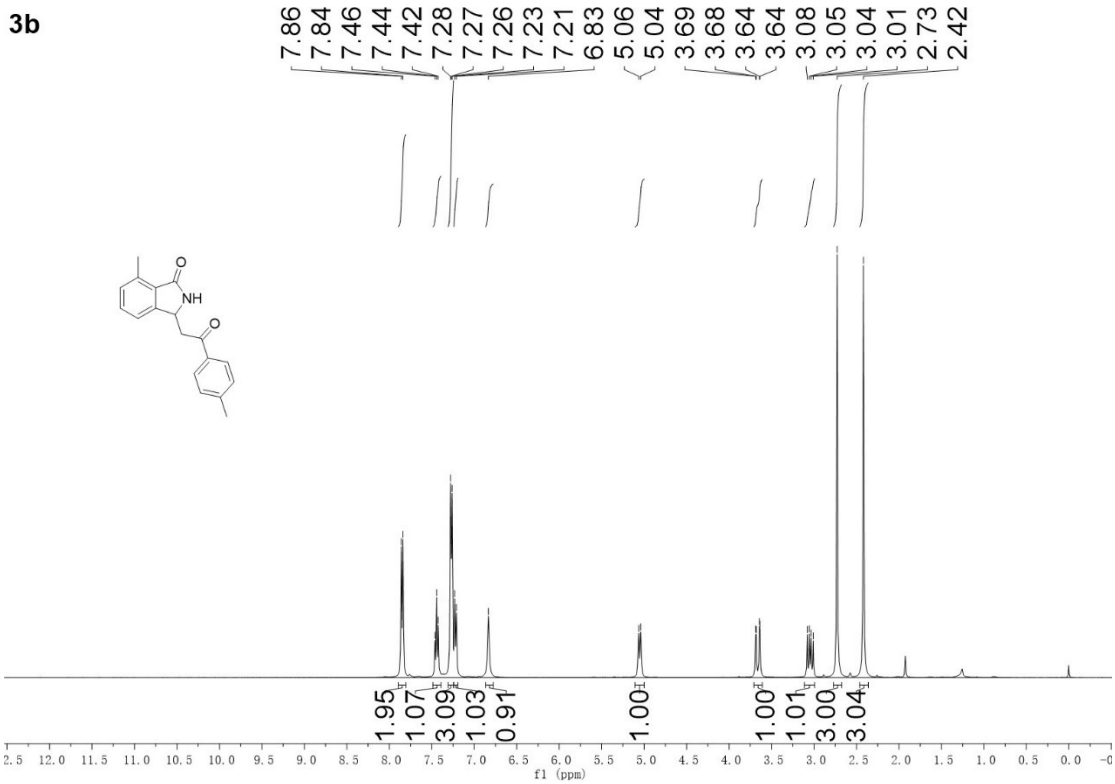
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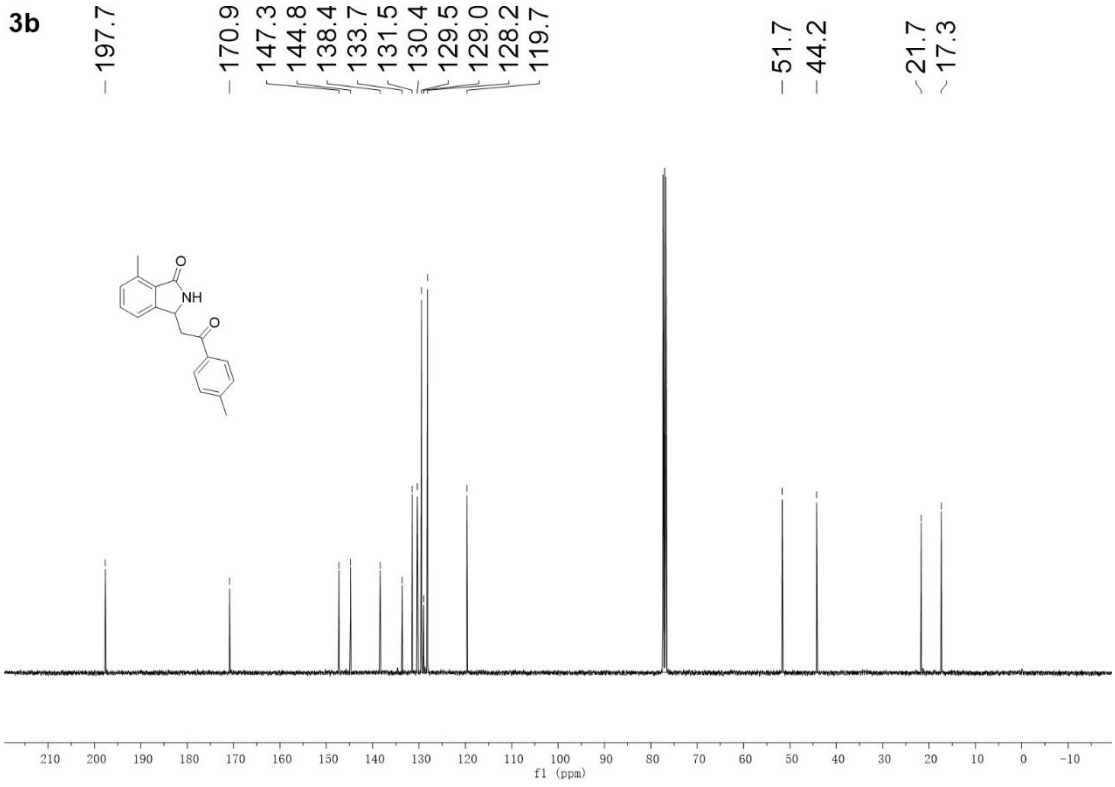
7.42
7.28
7.27
7.26
7.23
7.21
6.83
5.06
5.04
3.69
3.68
3.64
3.64
3.08
3.05
3.04
3.01
2.73
2.42
NH
O
O
1.95
1.07
3.09
1.03
0.91
1.00
1.00
1.01
3.00
3.04
f1 (ppm)

3b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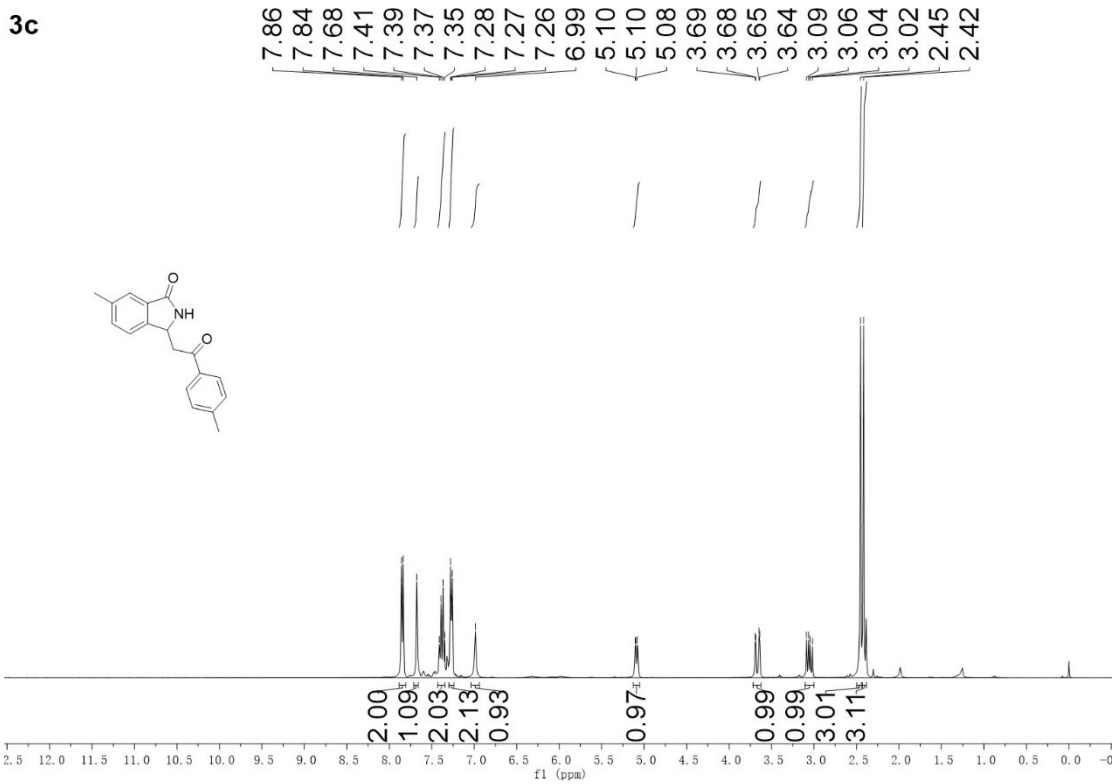
138.4
133.7
131.5
130.4
129.5
129.0
128.2
119.7
51.7
44.2
21.7
17.3
NH
O
O
f1 (ppm)

3c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3.69
3.68
3.65
3.64
3.09
3.06
3.04
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2.42
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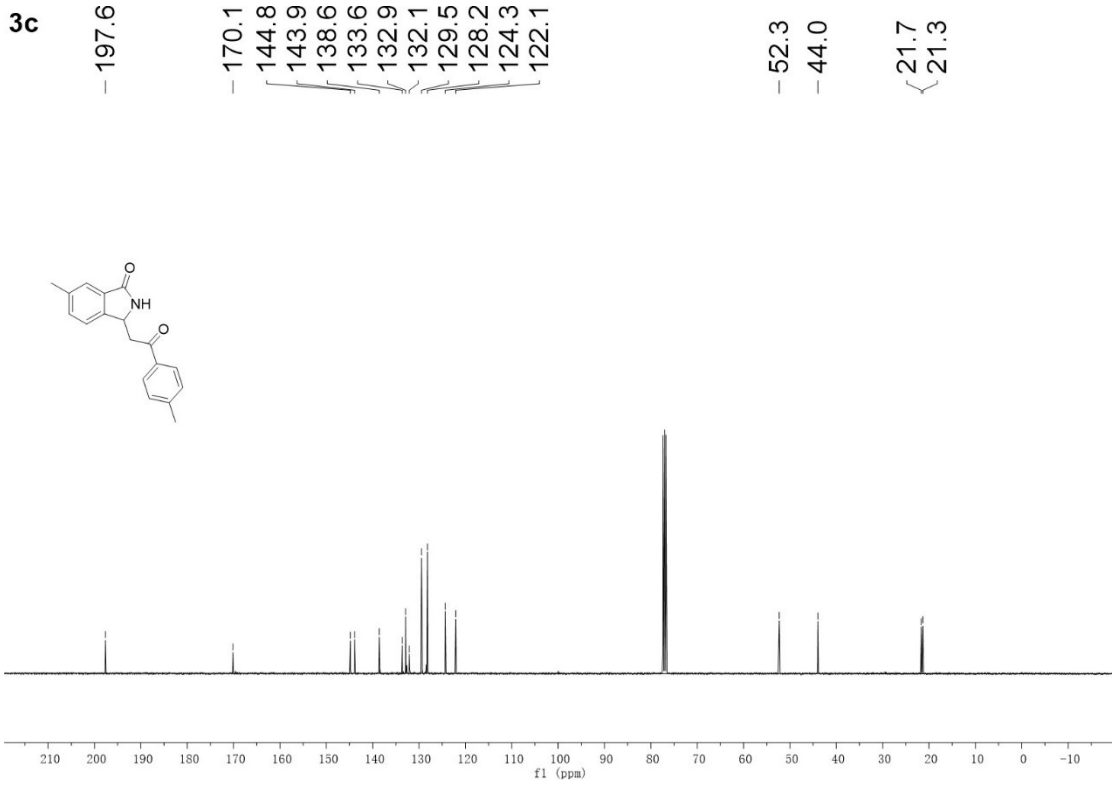
3.11
f1 (ppm)

3c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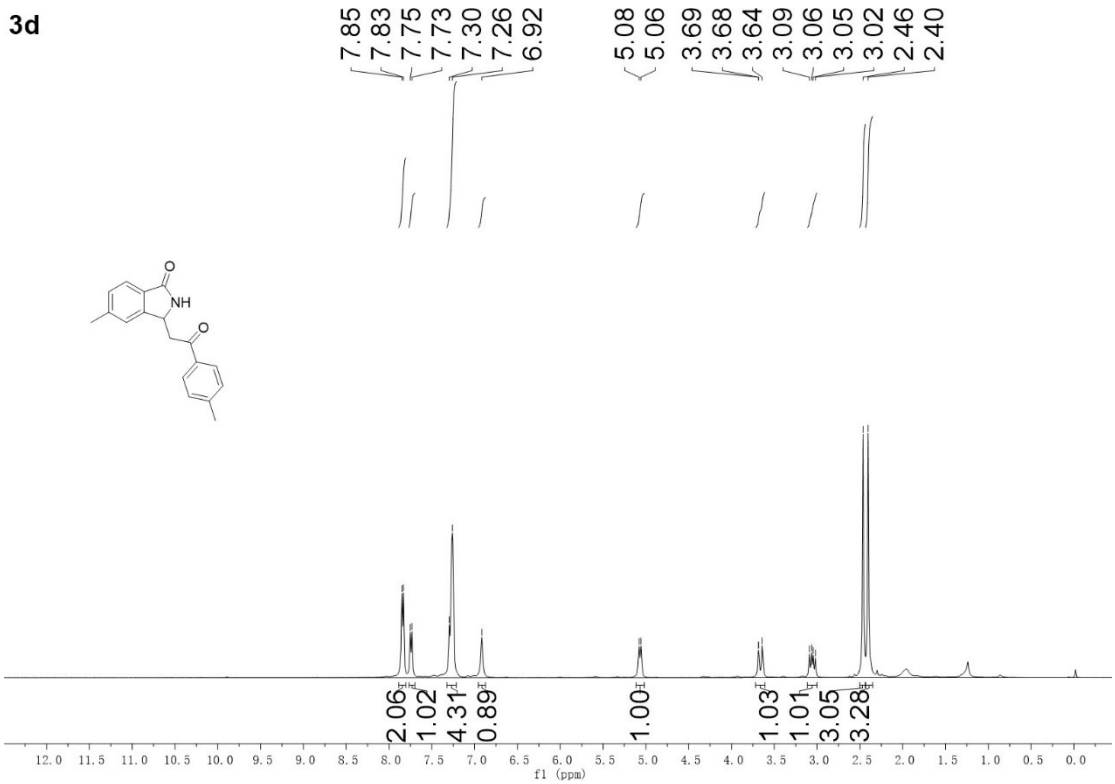
144.8
143.9
138.6
133.6
132.9
132.1
129.5
128.2
124.3
122.1
52.3
44.0
21.7
21.3
NH
O
O
f1 (ppm)

3d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3.09
3.06
3.05
3.02
2.46
2.40
NH
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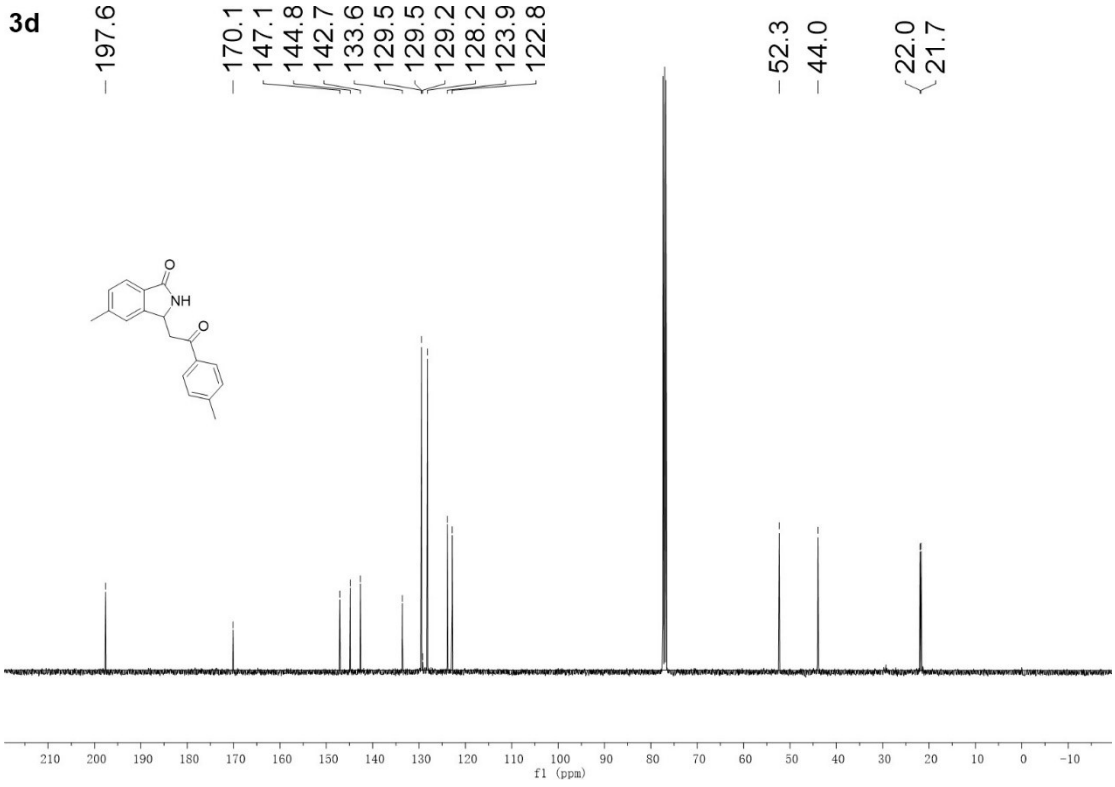
3.05
3.28
f1 (ppm)

3d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142.7
133.6
129.5
129.5
129.2
128.2
123.9
122.8
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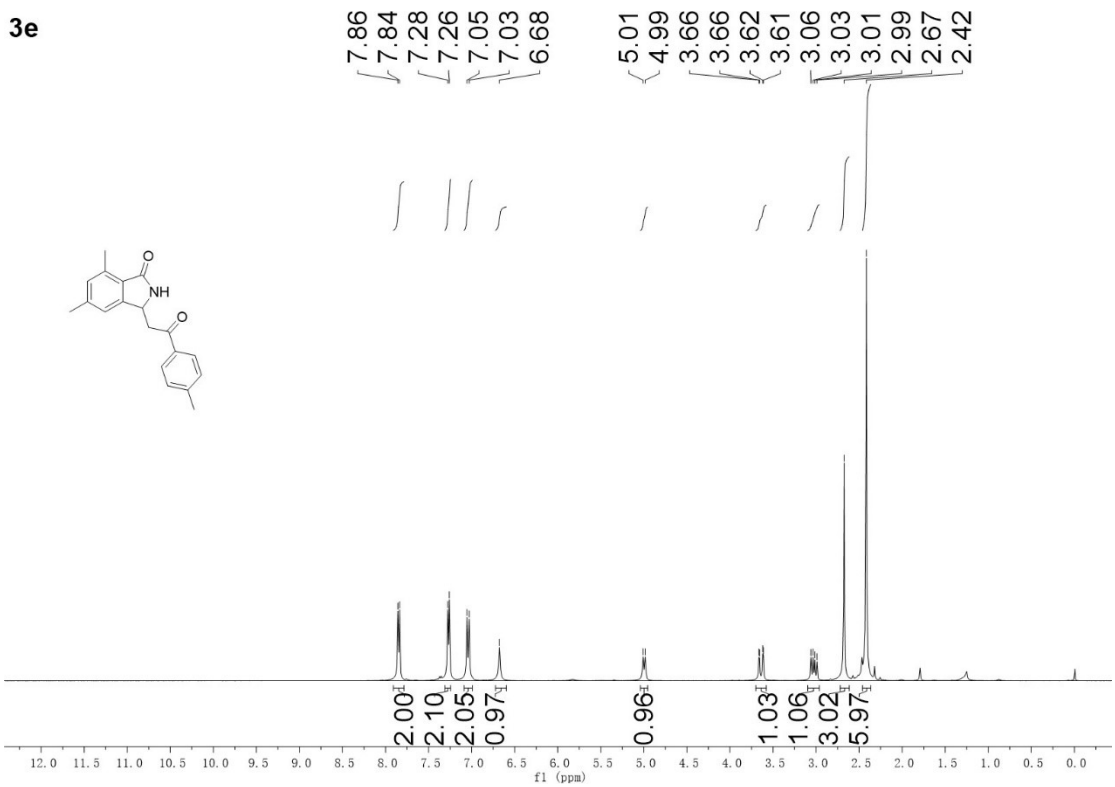
44.0
22.0
21.7
NH
O
O
f1 (ppm)

3e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3.06
3.03
3.01
2.99
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2.05
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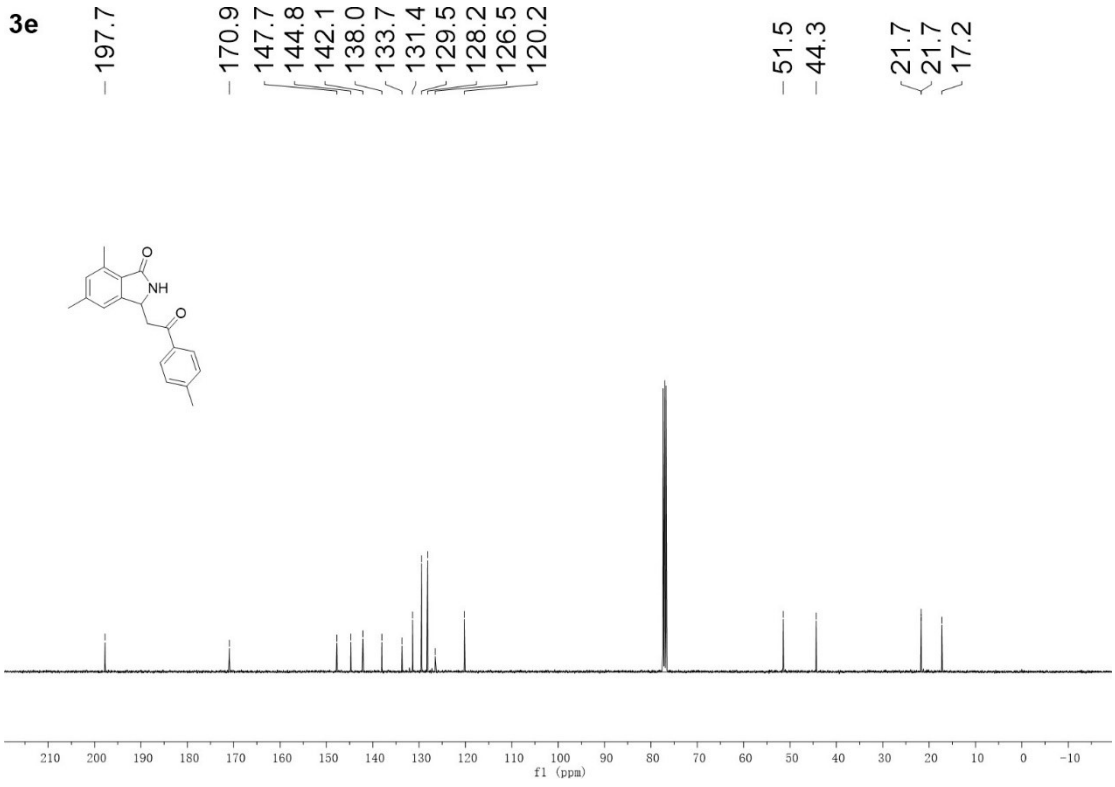
1.06
3.02
5.97
f1 (ppm)

3e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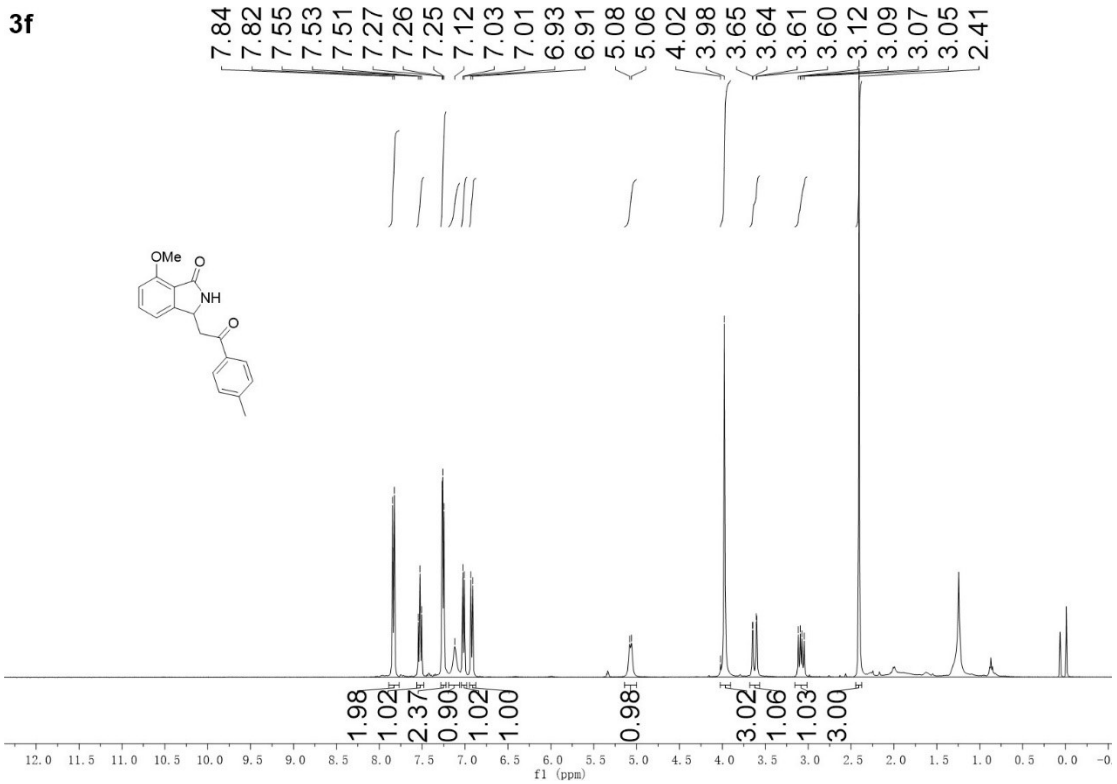
51.5
44.3
21.7
21.7
17.2
NH
O
O
f1 (ppm)

3f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6.91
5.08
5.06
4.02
3.98
3.65
3.64
3.61
3.60
3.12
3.09
3.07
3.05
2.41
OMe
O
NH
O
1.98
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1.02
1.00
0.98
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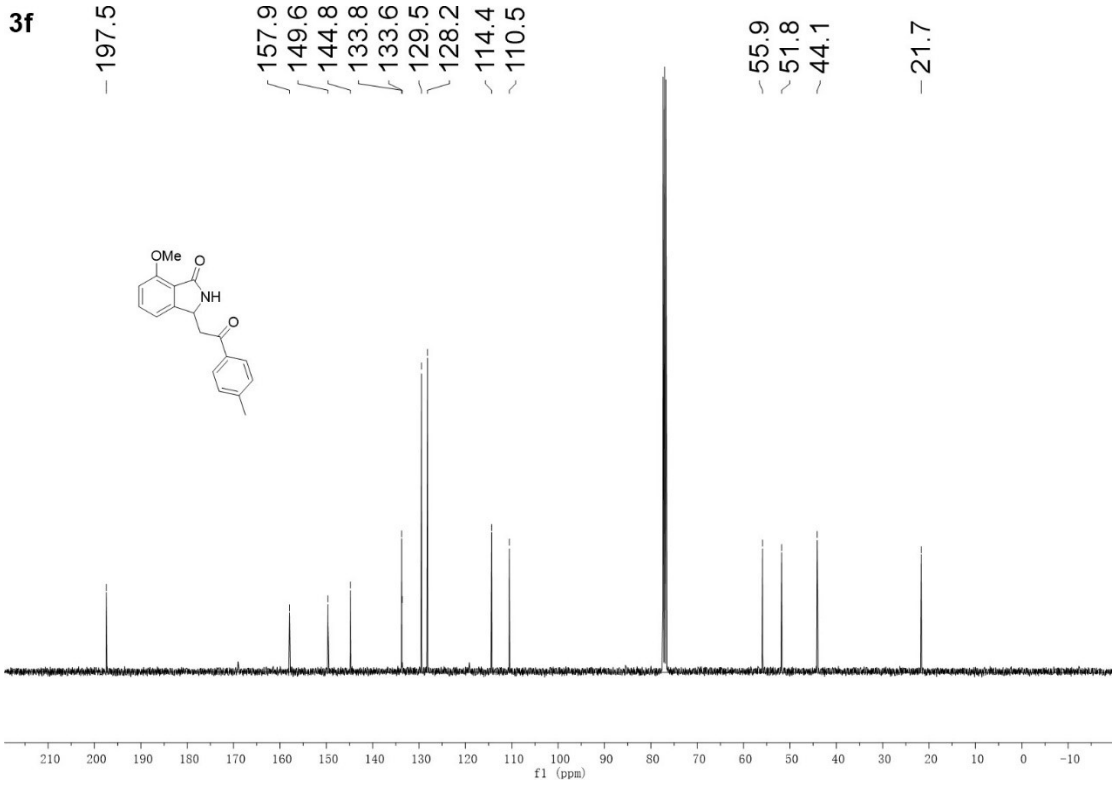
1.06
1.03
3.00
f1 (ppm)

3f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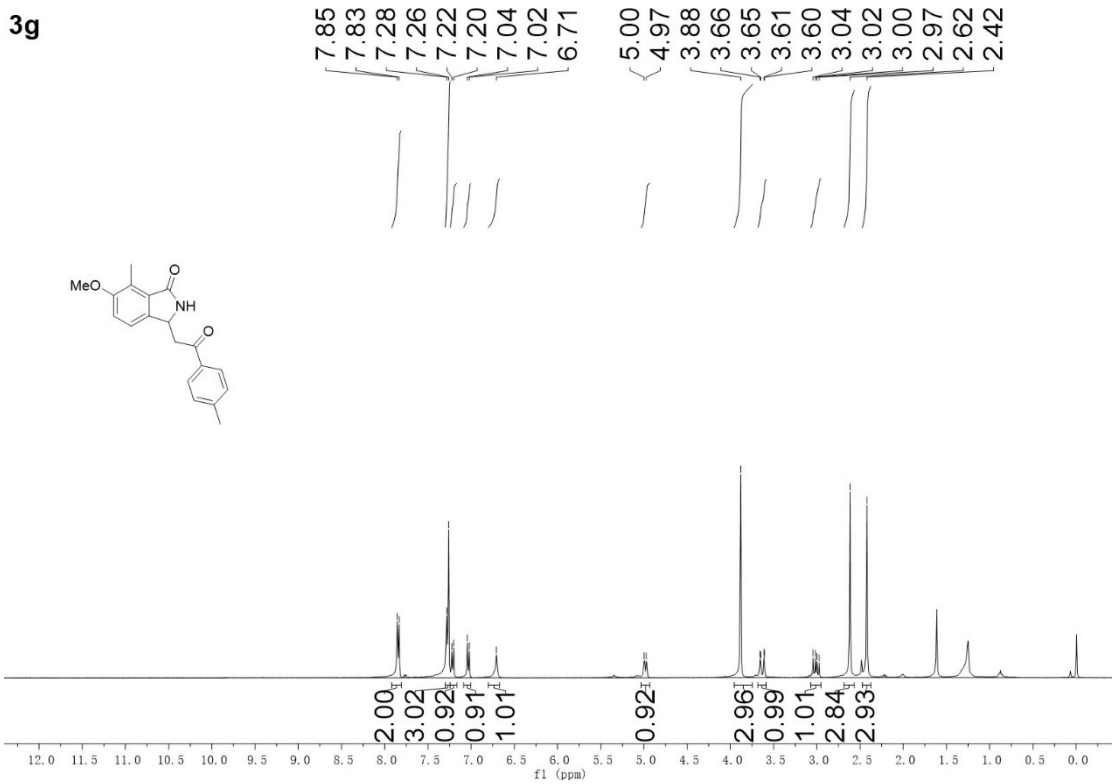
144.8
133.8
133.6
129.5
128.2
114.4
110.5
55.9
51.8
44.1
21.7
OMe
O
NH
O
f1 (ppm)

3g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3.66
3.65
3.61
3.60
3.04
3.02
3.00
2.97
2.62
2.42
MeO
NH
O
2.00
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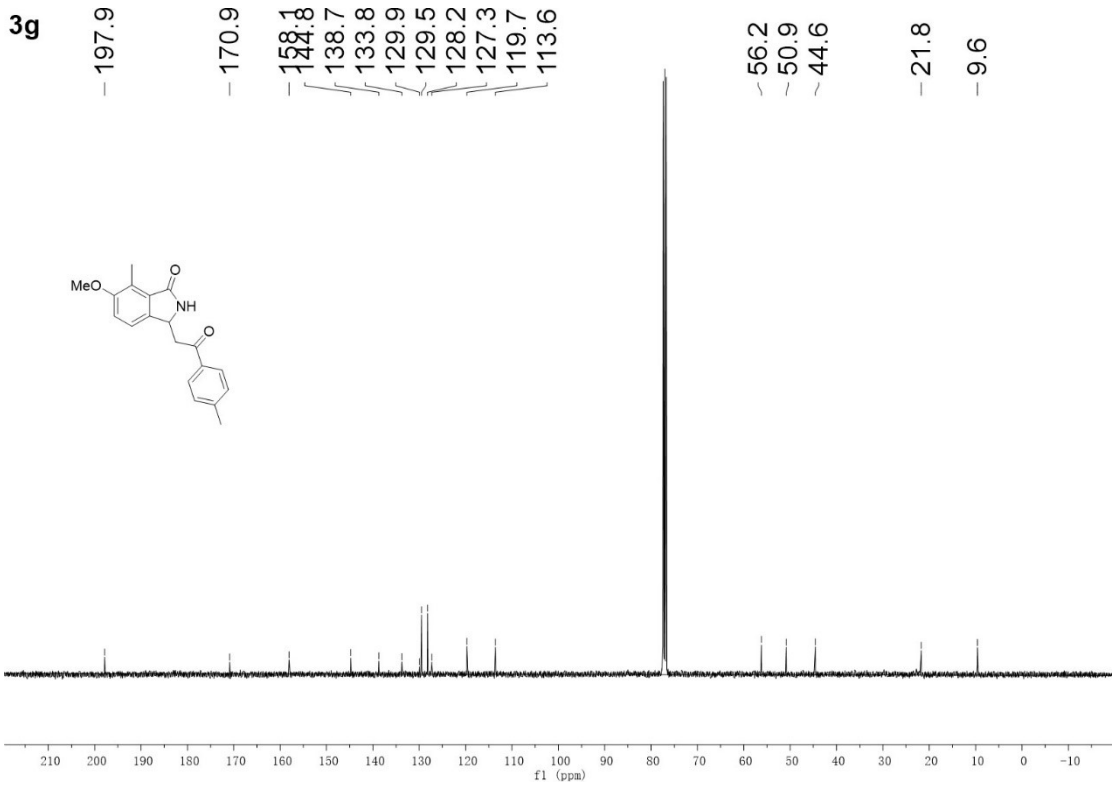
f1 (ppm)

3g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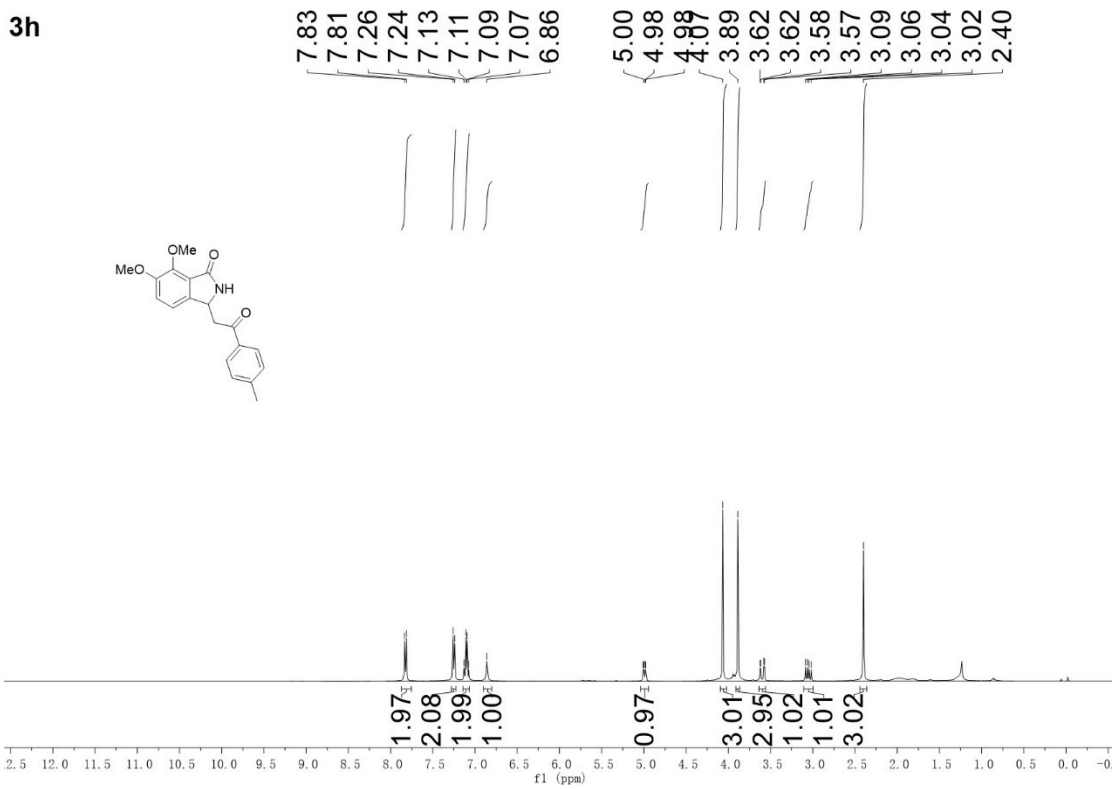
MeO
NH
O
f1 (ppm)

3h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3.09
3.06
3.04
3.02
2.40
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O
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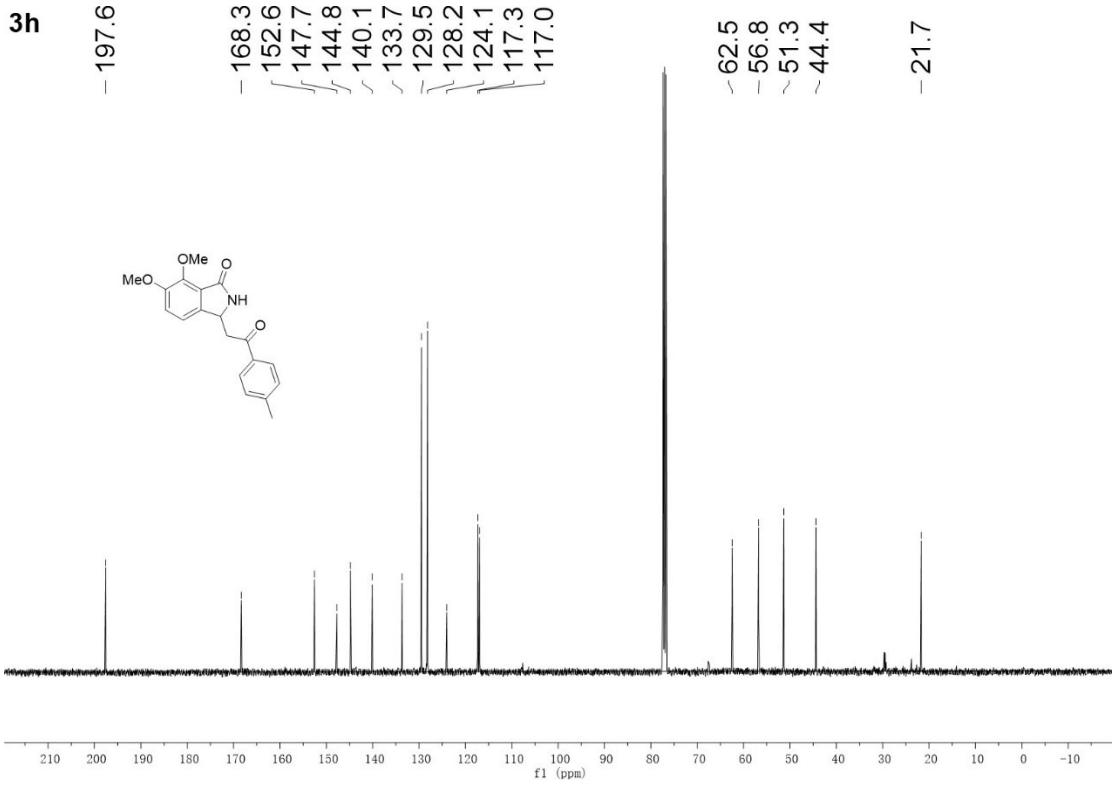
1.01
3.02
f1 (ppm)

3h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21.7
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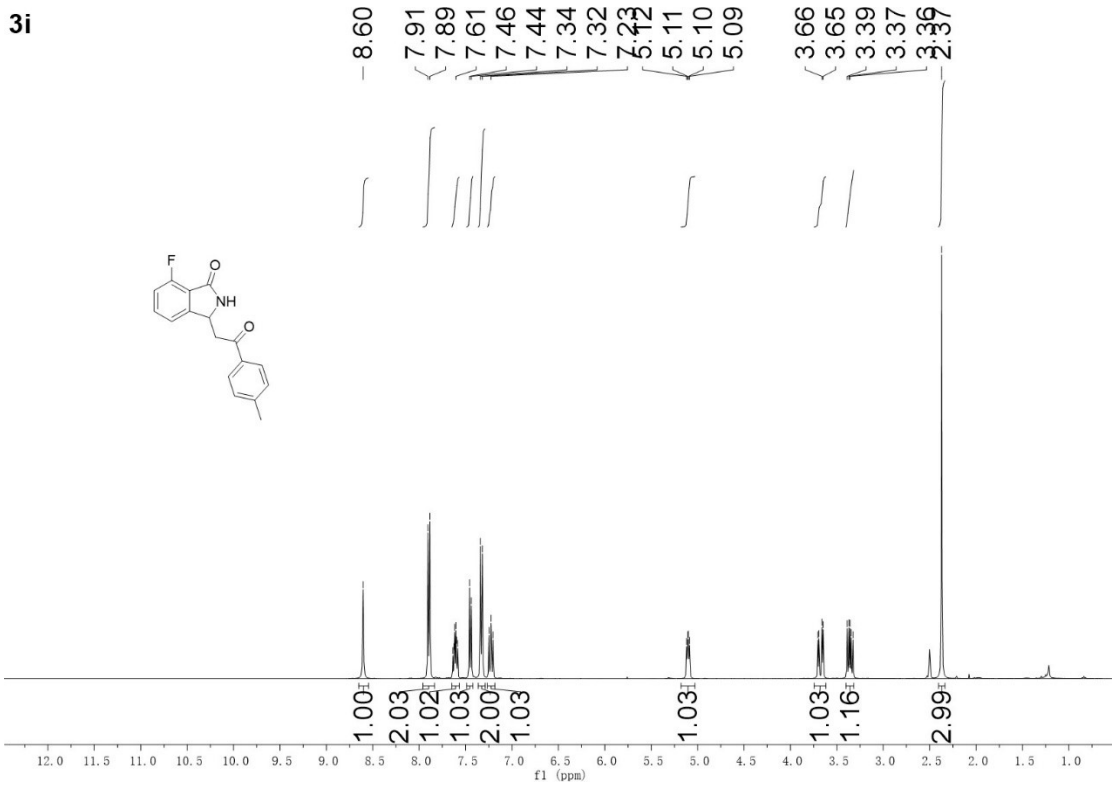
MeO
O
NH
O
f1 (ppm)

3i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O
NH
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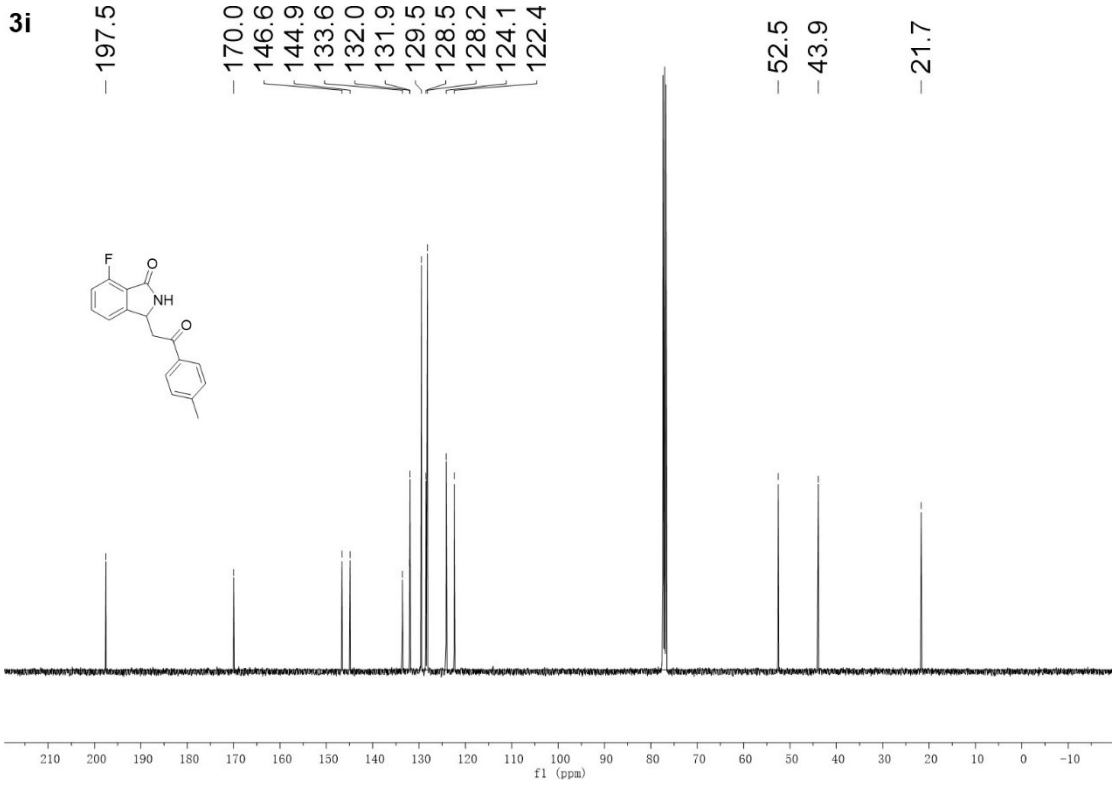
1.16
2.99
f1 (ppm)

3i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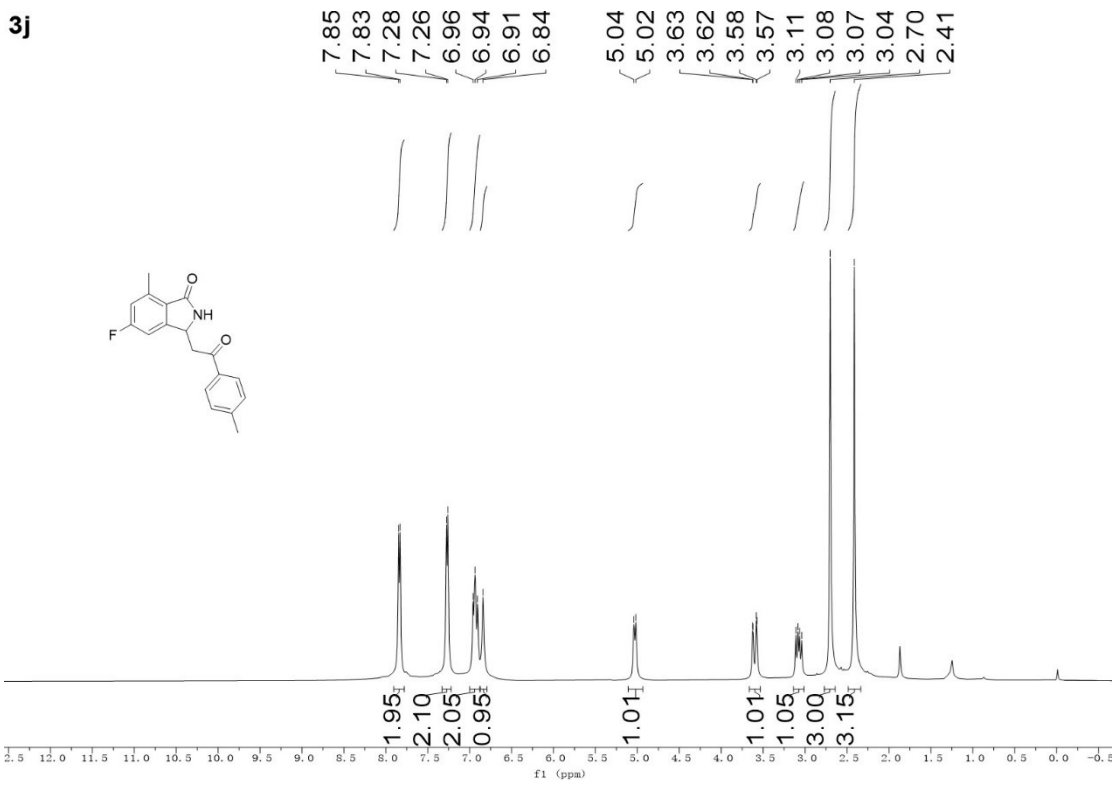
21.7
F
O
NH
O
f1 (ppm)

3j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3.62
3.58
3.57
3.11
3.08
3.07
3.04
2.70
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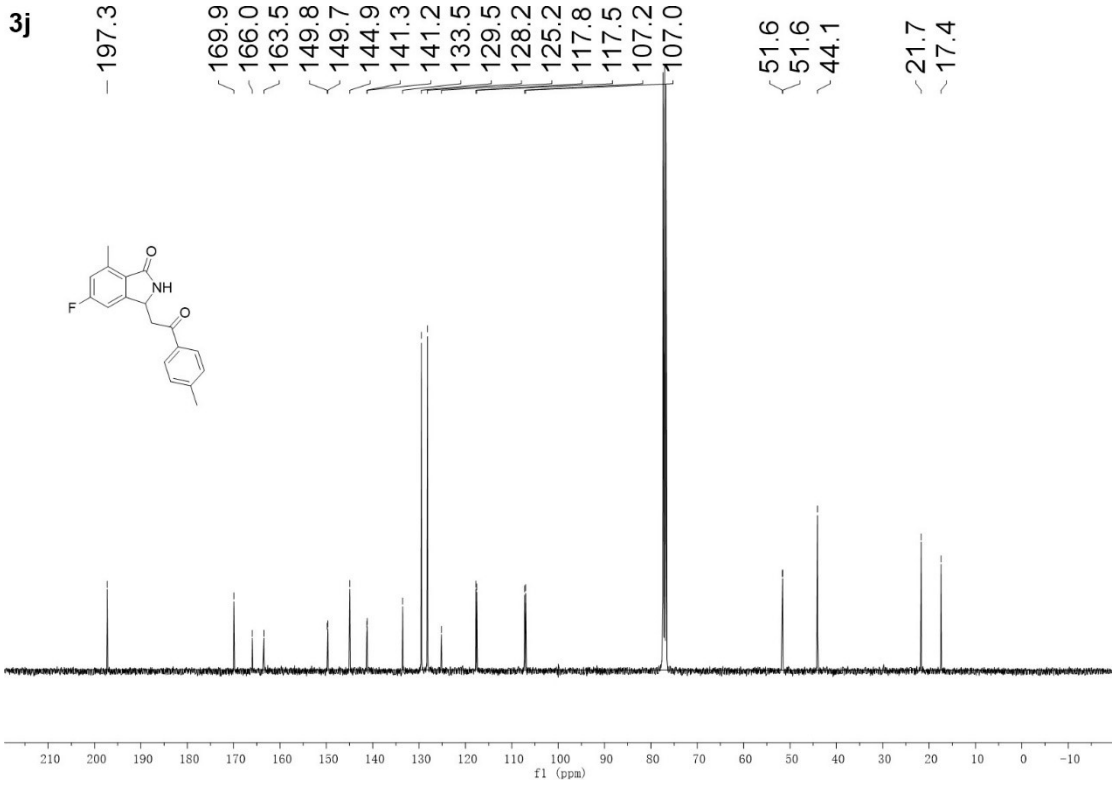
1.05
3.00
3.15
f1 (ppm)

3j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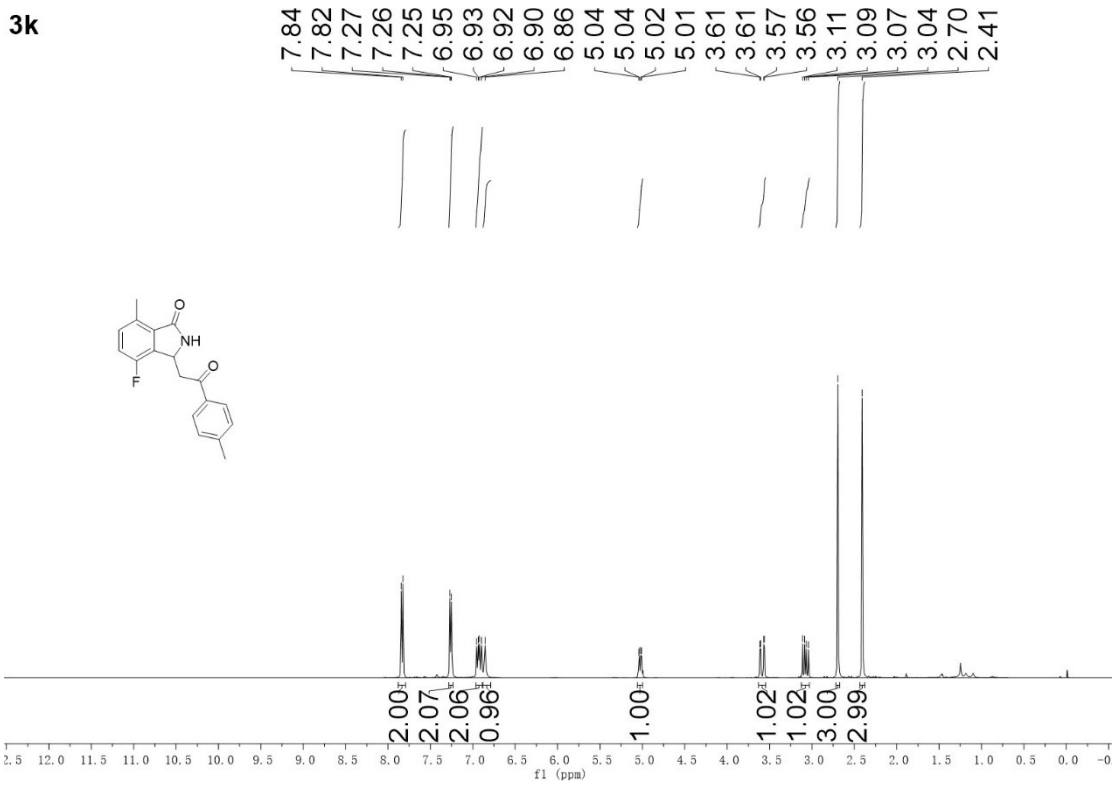
107.0
51.6
51.6
44.1
21.7
17.4
f1 (ppm)

3k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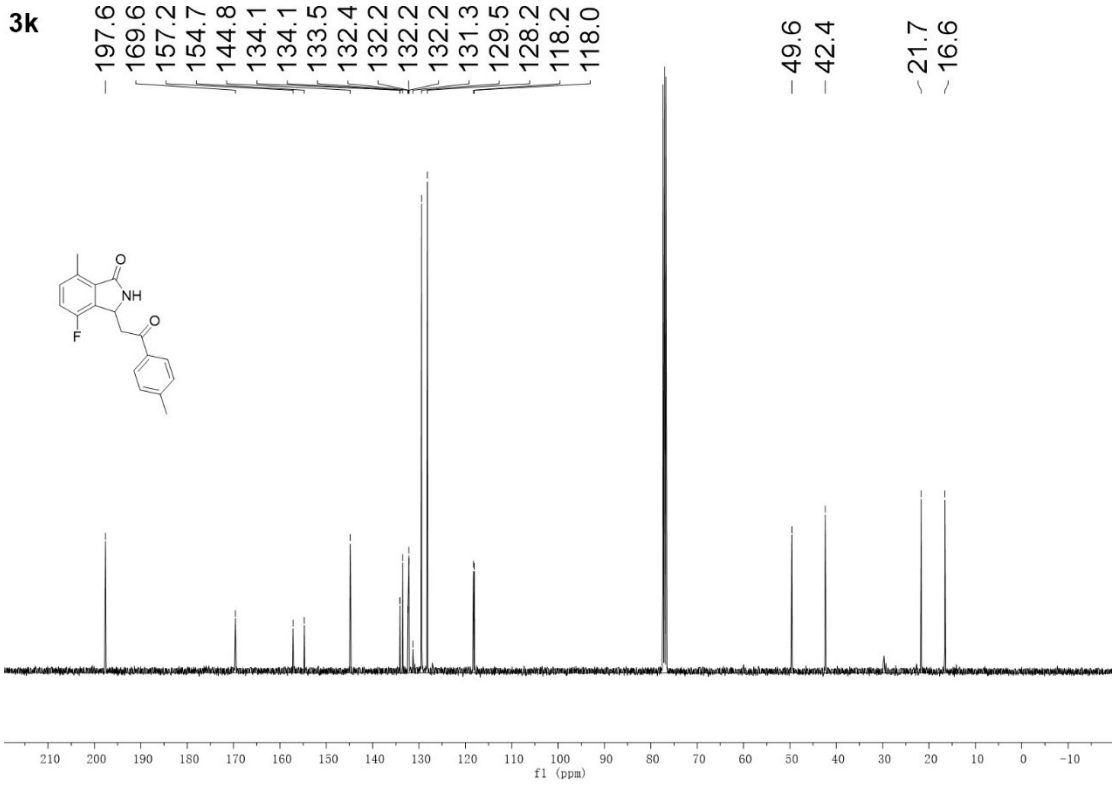
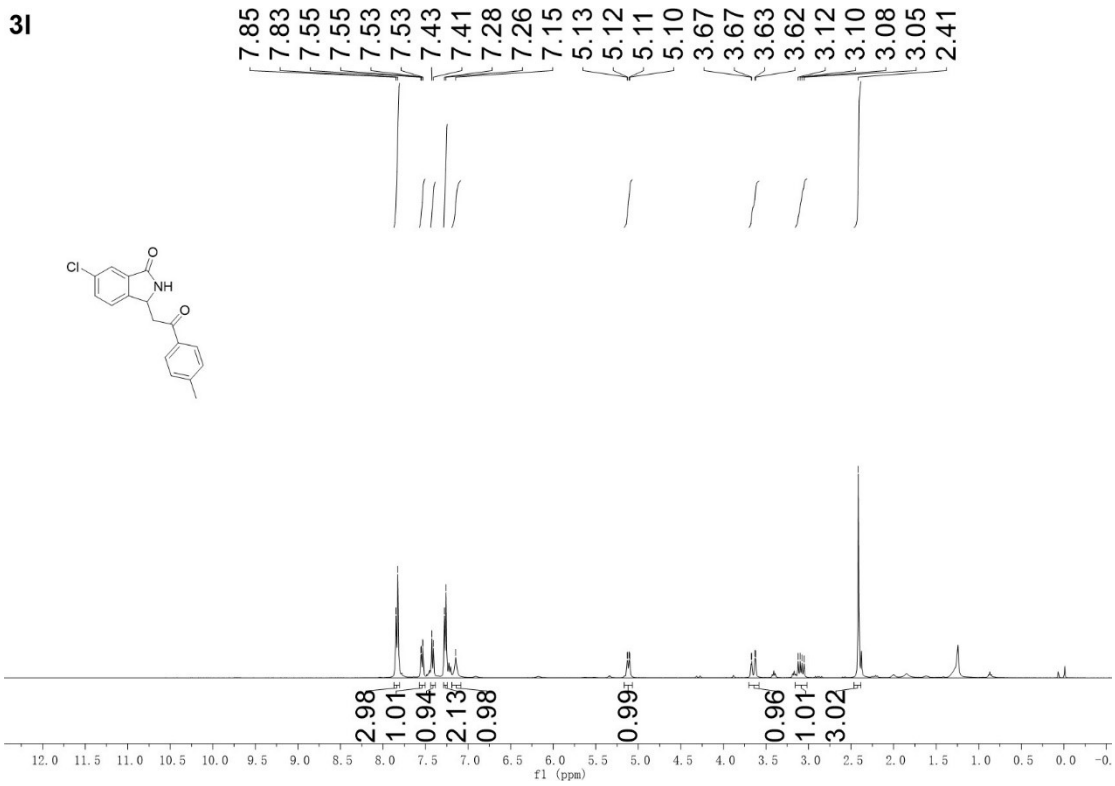
7.82
7.27
7.26
7.25
6.95
6.93
6.92
6.90
6.86
5.04
5.04
5.02
5.01
3.61
3.61
3.57
3.56
3.11
3.09
3.07
3.04
2.70
2.41
NH
O
F
2.00
2.07
2.06
0.96
1.00
1.02
1.02
3.00
2.99
f1 (ppm)

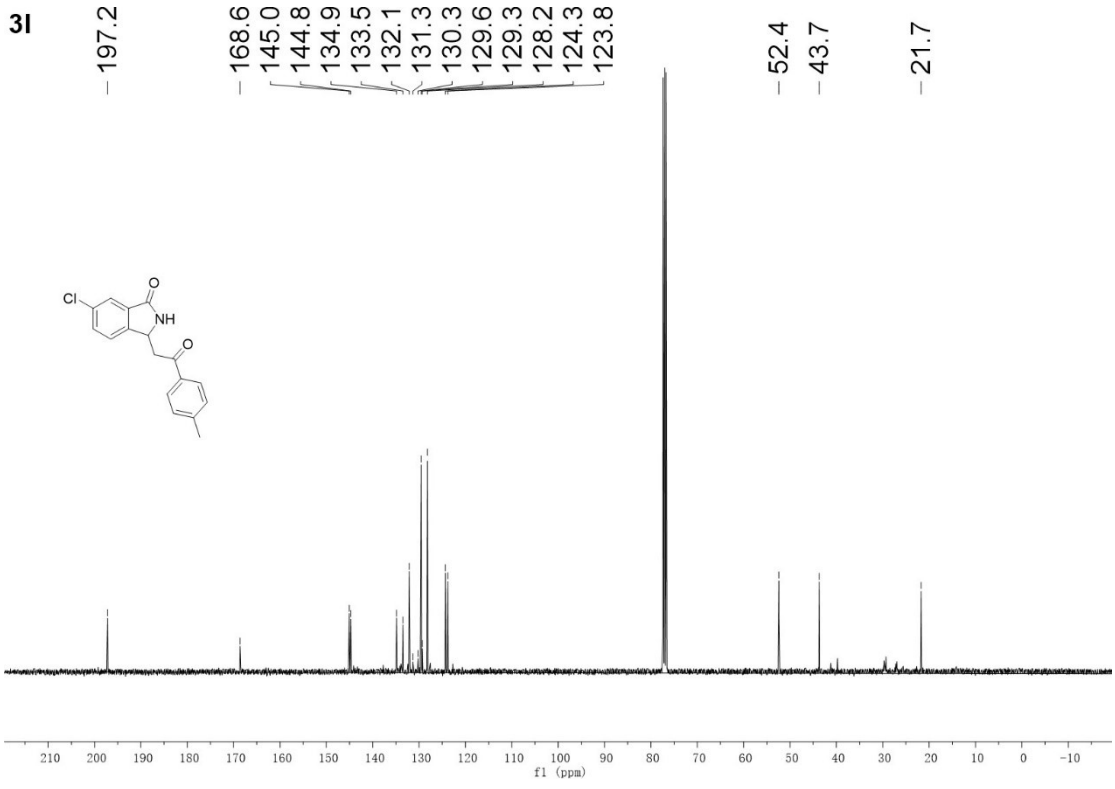
3k


197.6
169.6
157.2
154.7
144.8
134.1
134.1
133.5
132.4
132.2
132.2
132.2
131.3
129.5
128.2
118.2
118.0
49.6
42.4
21.7
16.6
NH
O
F
f1 (ppm)

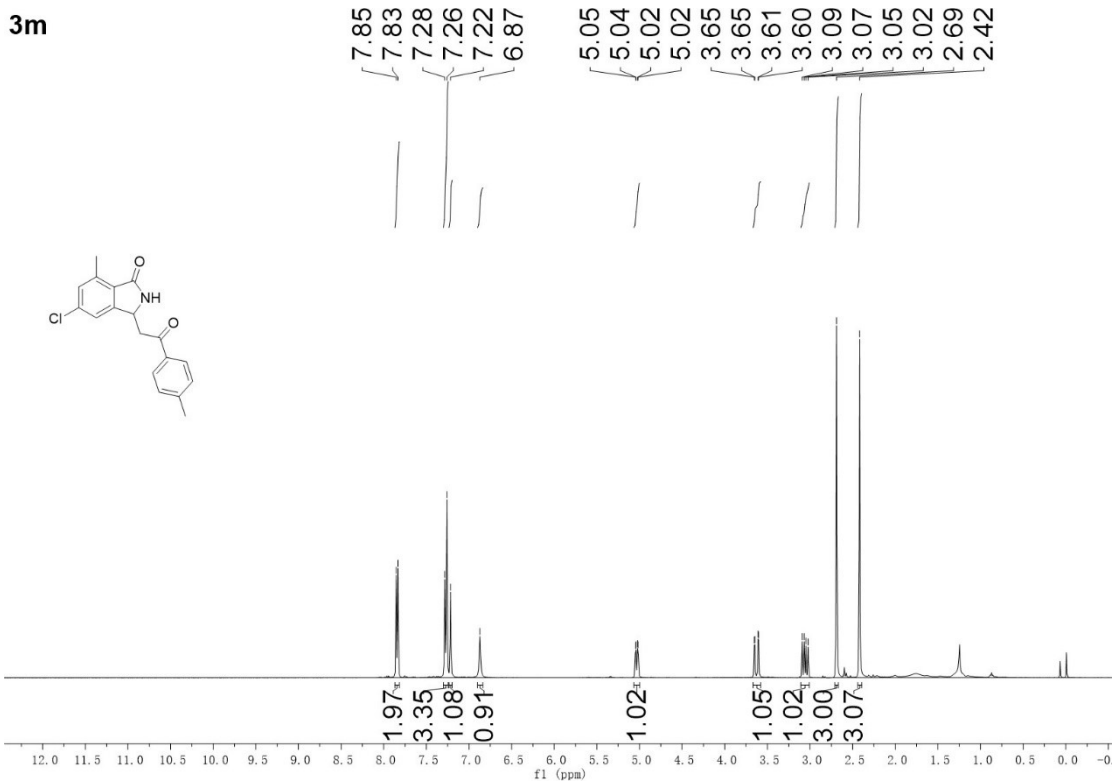
3l


7.85
7.83
7.55
7.55
7.53
7.53
7.43
7.41
7.28
7.26
7.15
5.13
5.12
5.11
5.10
3.67
3.67
3.63
3.62
3.12
3.10
3.08
3.05
2.41
Cl
NH
O
O
2.98
1.01
0.94
2.13
0.98
0.99
0.96
1.01
3.02
f1 (ppm)

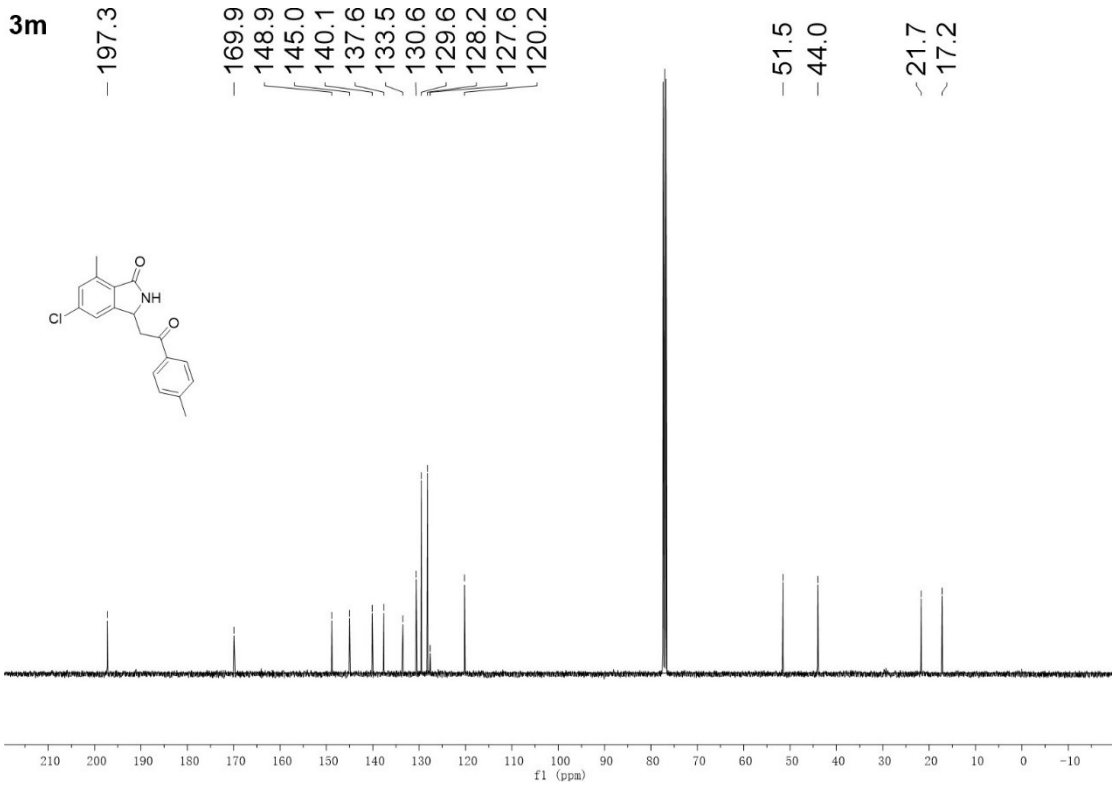
3l


197.2
168.6
145.0
144.8
134.9
133.5
132.1
131.3
130.3
129.6
129.3
128.2
124.3
123.8
52.4
43.7
21.7
Cl
NH
O
O
f1 (ppm)

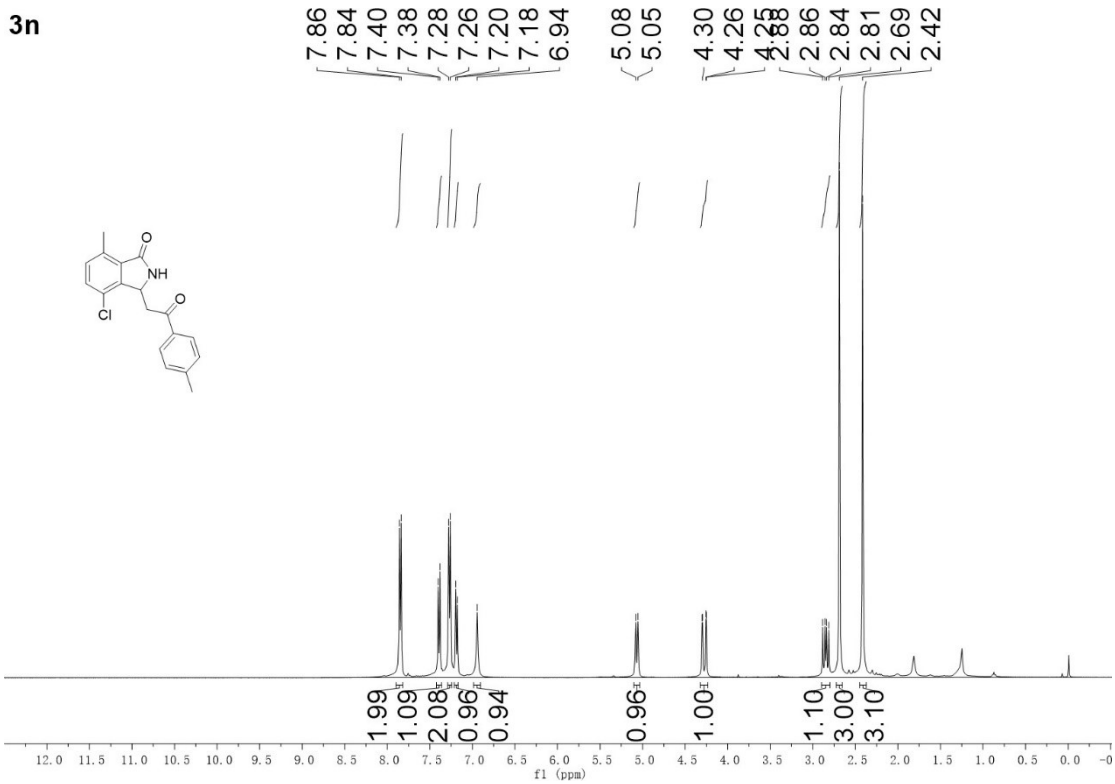
3m


7.85
7.83
7.28
7.26
7.22
6.87
5.05
5.04
5.02
5.02
3.65
3.65
3.61
3.60
3.09
3.07
3.05
3.02
2.69
2.42
O
NH
Cl
O
1.97
3.35
1.08
0.91
1.02
1.05
1.02
3.00
3.07
f1 (ppm)

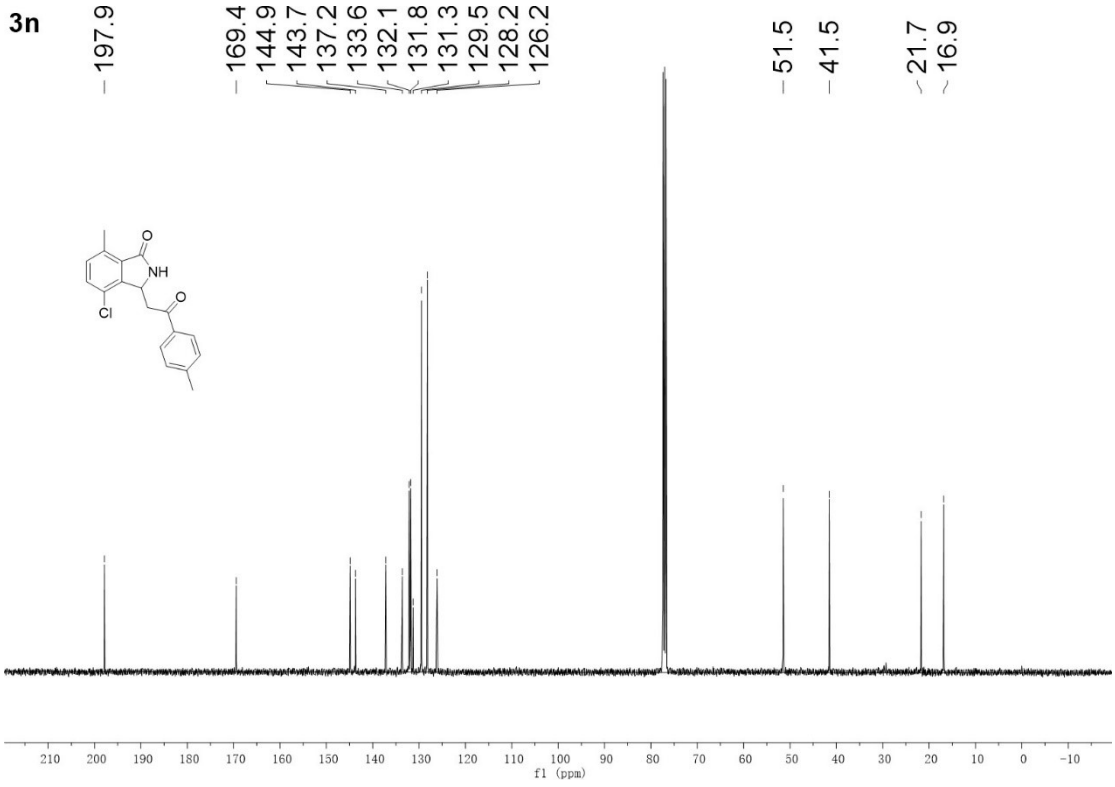
3m


197.3
169.9
148.9
145.0
140.1
137.6
133.5
130.6
129.6
128.2
127.6
120.2
51.5
44.0
21.7
17.2
O
NH
Cl
O
f1 (ppm)

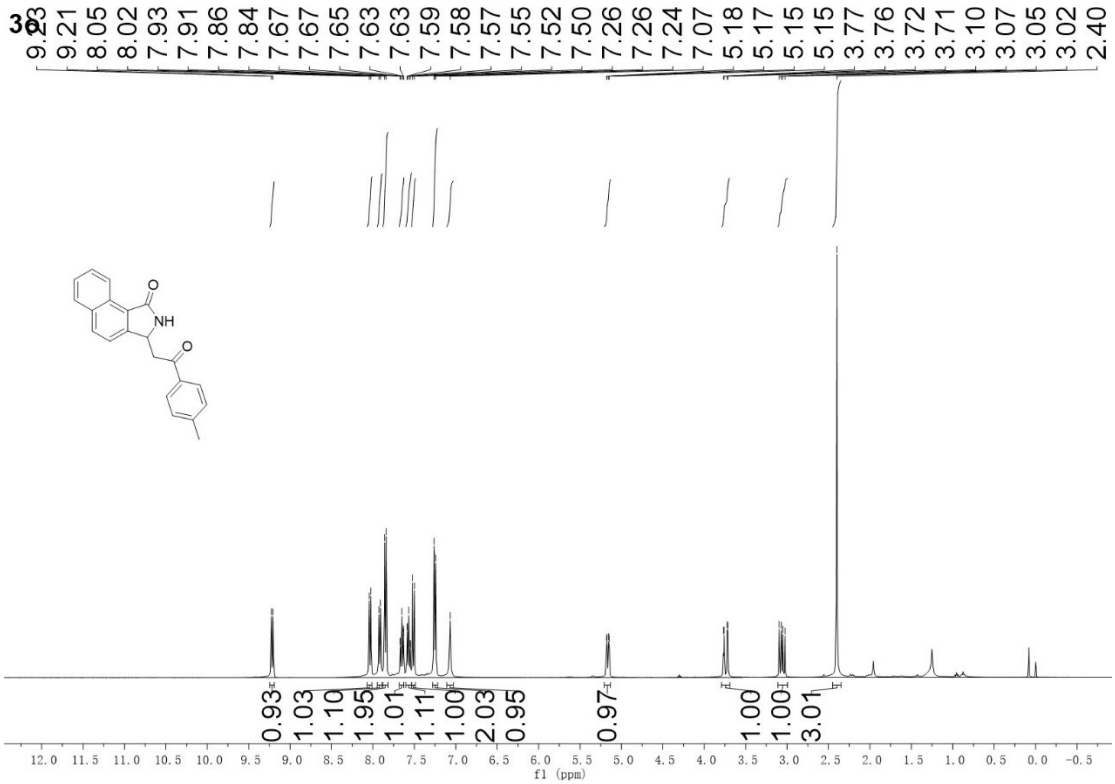
3n


7.86
7.84
7.40
7.38
7.28
7.26
7.20
7.18
6.94
5.08
5.05
4.30
4.26
2.86
2.84
2.81
2.69
2.42
1.99
1.09
2.08
0.96
0.94
0.96
1.00
1.10
3.00
3.10
f1 (ppm)

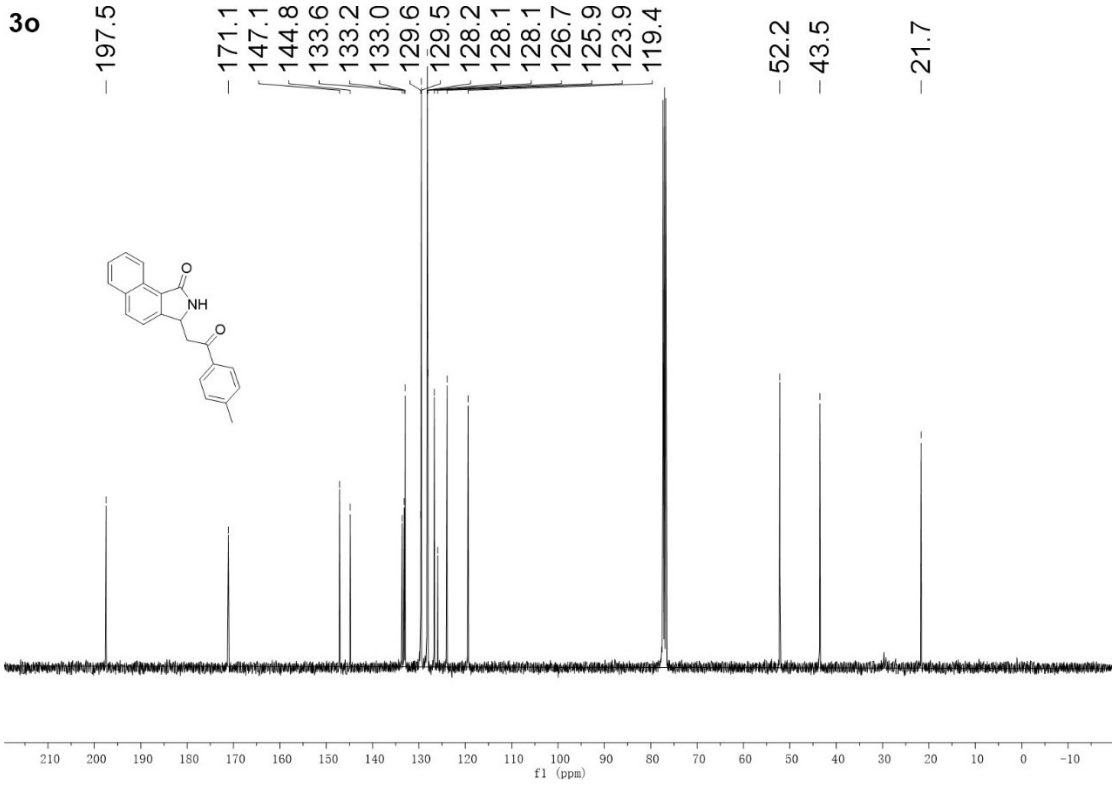
3n


197.9
169.4
144.9
143.7
137.2
133.6
132.1
131.8
131.3
129.5
128.2
126.2
51.5
41.5
21.7
16.9
f1 (ppm)

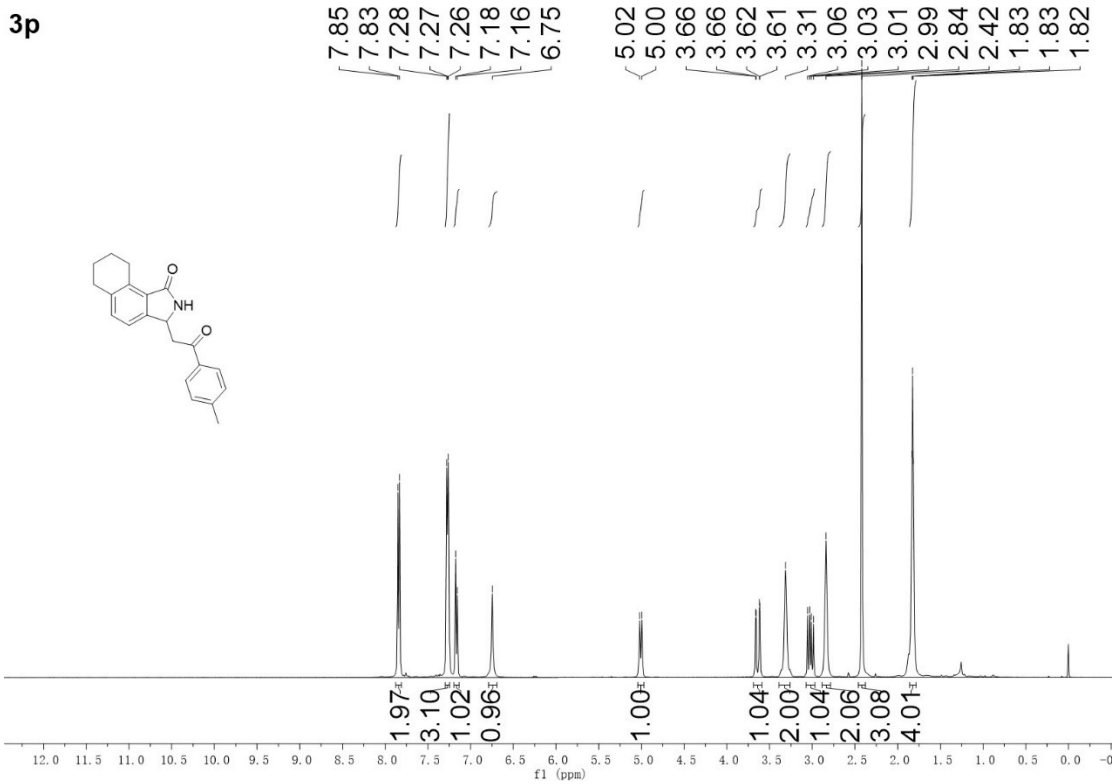
3o


9.23
9.21
8.05
8.02
7.93
7.91
7.86
7.84
7.67
7.67
7.65
7.63
7.63
7.59
7.58
7.57
7.55
7.52
7.50
7.26
7.26
7.24
7.07
5.18
5.17
5.15
5.15
3.77
3.76
3.72
3.71
3.10
3.07
3.05
3.02
2.40
O
NH
O
0.93
1.03
1.10
1.95
1.01
1.11
1.00
2.03
0.95
0.97
1.00
1.00
3.01
f1 (ppm)

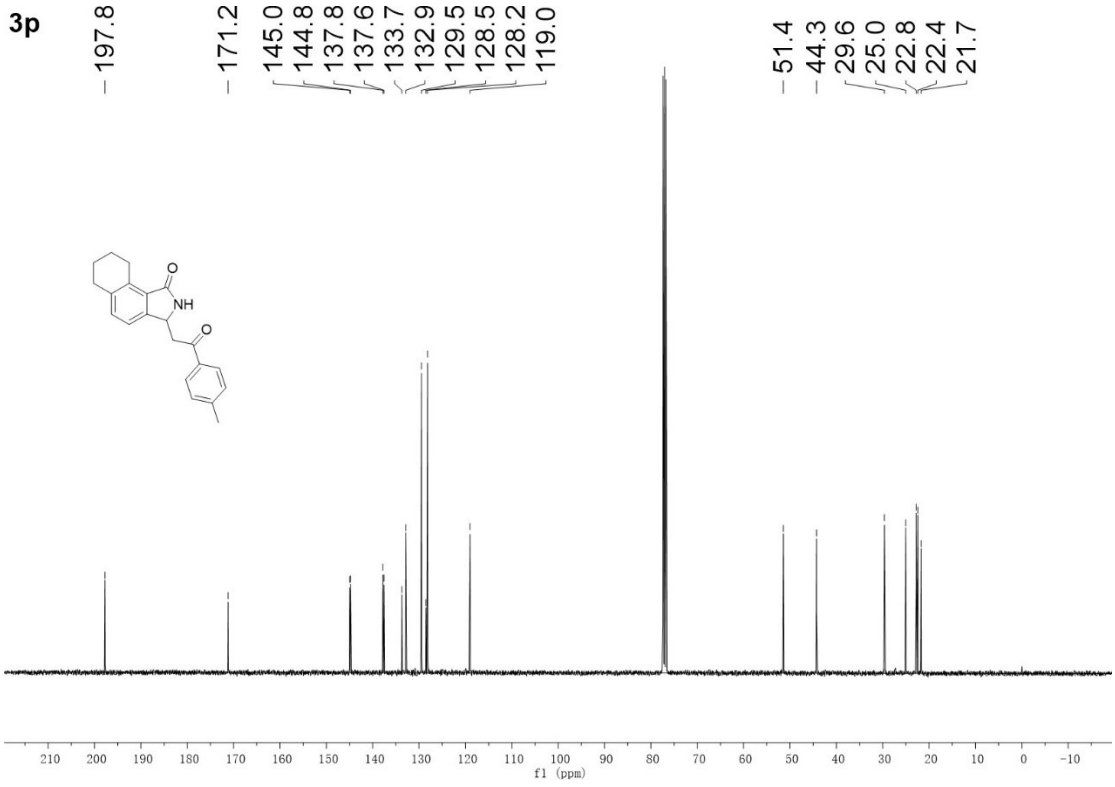
3o


197.5
171.1
147.1
144.8
133.6
133.2
133.0
129.6
129.5
128.2
128.1
128.1
126.7
125.9
123.9
119.4
52.2
43.5
21.7
O
NH
O
f1 (ppm)

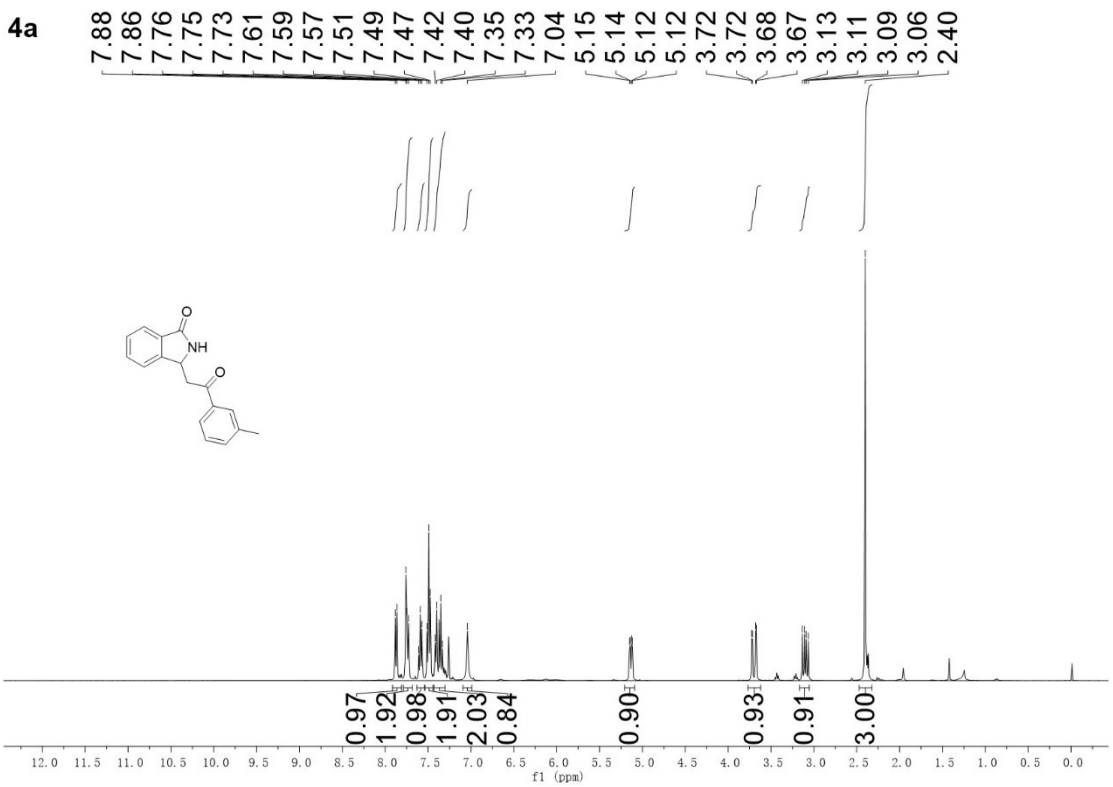
3p


7.85
7.83
7.28
7.27
7.26
7.18
7.16
6.75
5.02
5.00
3.66
3.66
3.62
3.61
3.31
3.06
3.03
3.01
2.99
2.84
2.42
1.83
1.83
1.82
NH
O
O
1.97
3.10
1.02
0.96
1.00
1.04
2.00
1.04
2.06
3.08
4.01
f1 (ppm)

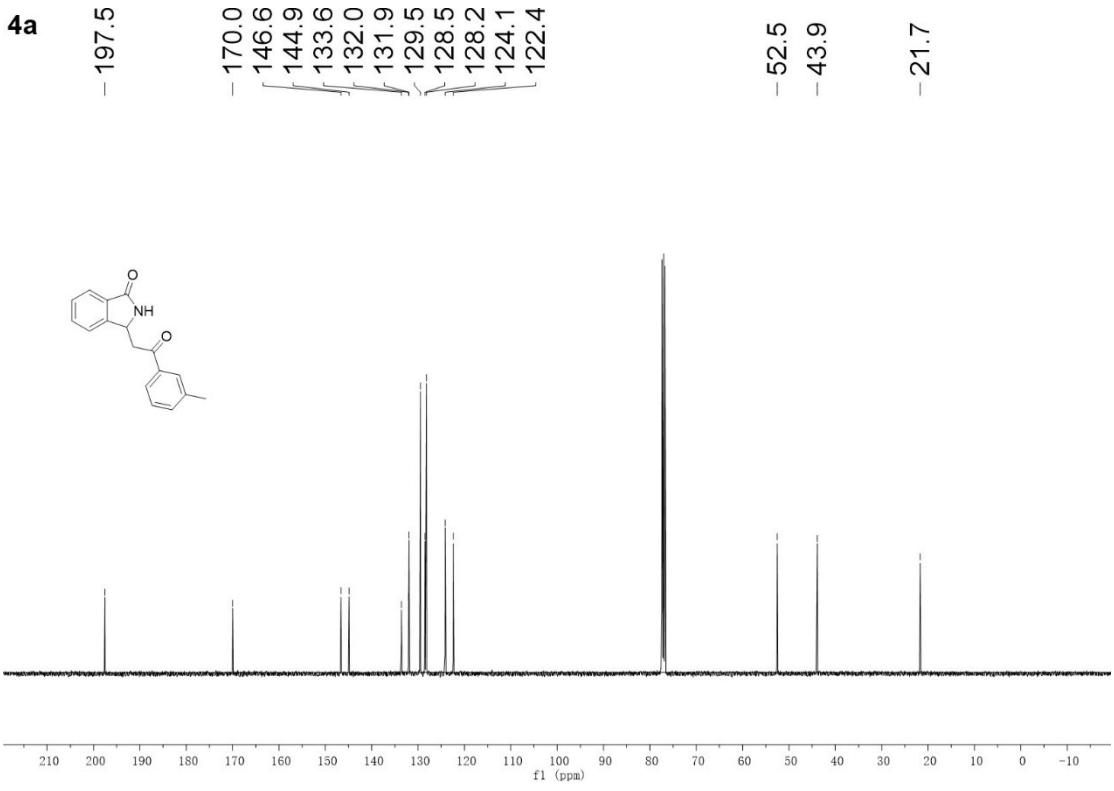
3p


197.8
171.2
145.0
144.8
137.8
137.6
133.7
132.9
129.5
128.5
128.2
119.0
51.4
44.3
29.6
25.0
22.8
22.4
21.7
NH
O
O
f1 (ppm)

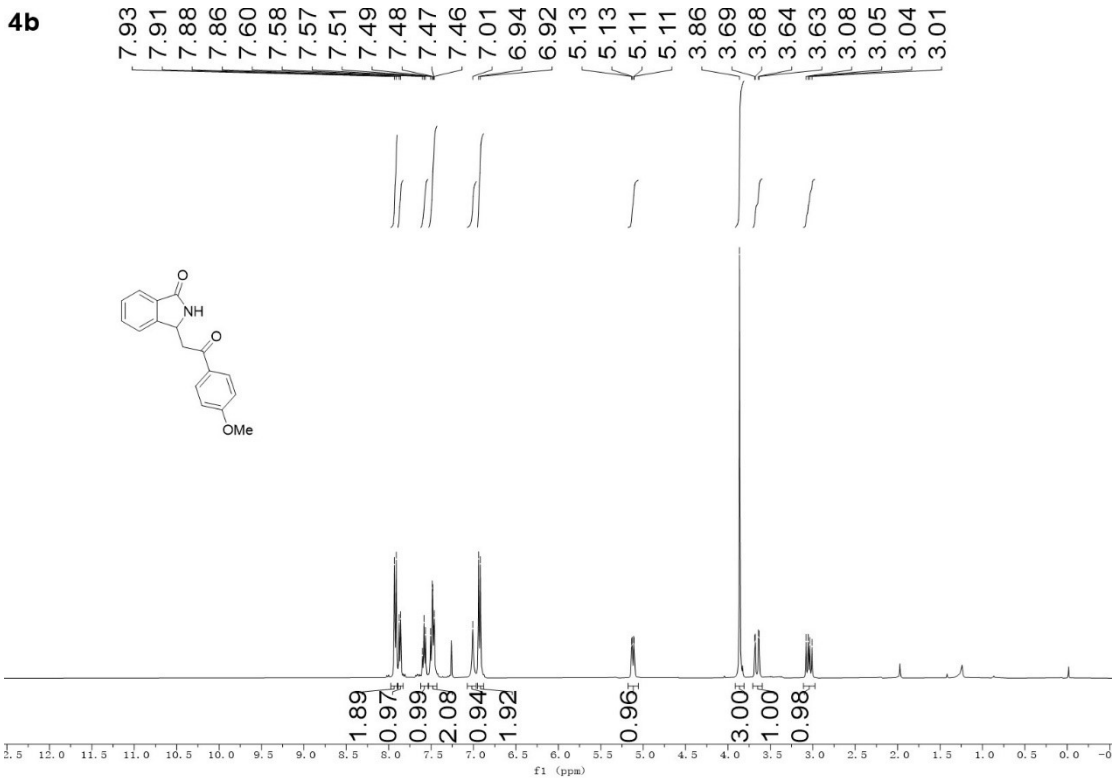
4a


7.88
7.86
7.76
7.75
7.73
7.61
7.59
7.57
7.51
7.49
7.47
7.42
7.40
7.35
7.33
7.04
5.15
5.14
5.12
5.12
3.72
3.72
3.68
3.67
3.13
3.11
3.09
3.06
2.40
0.97
1.92
0.98
1.91
2.03
0.84
0.90
0.93
0.91
3.00
f1 (ppm)

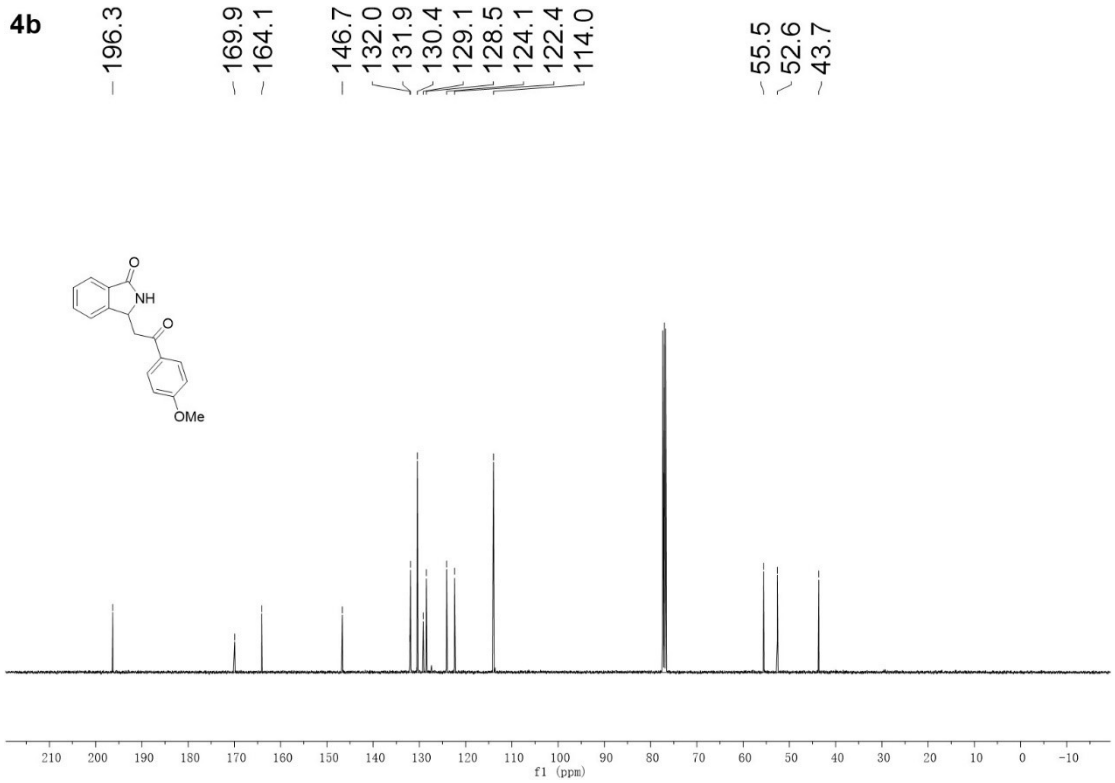
4a

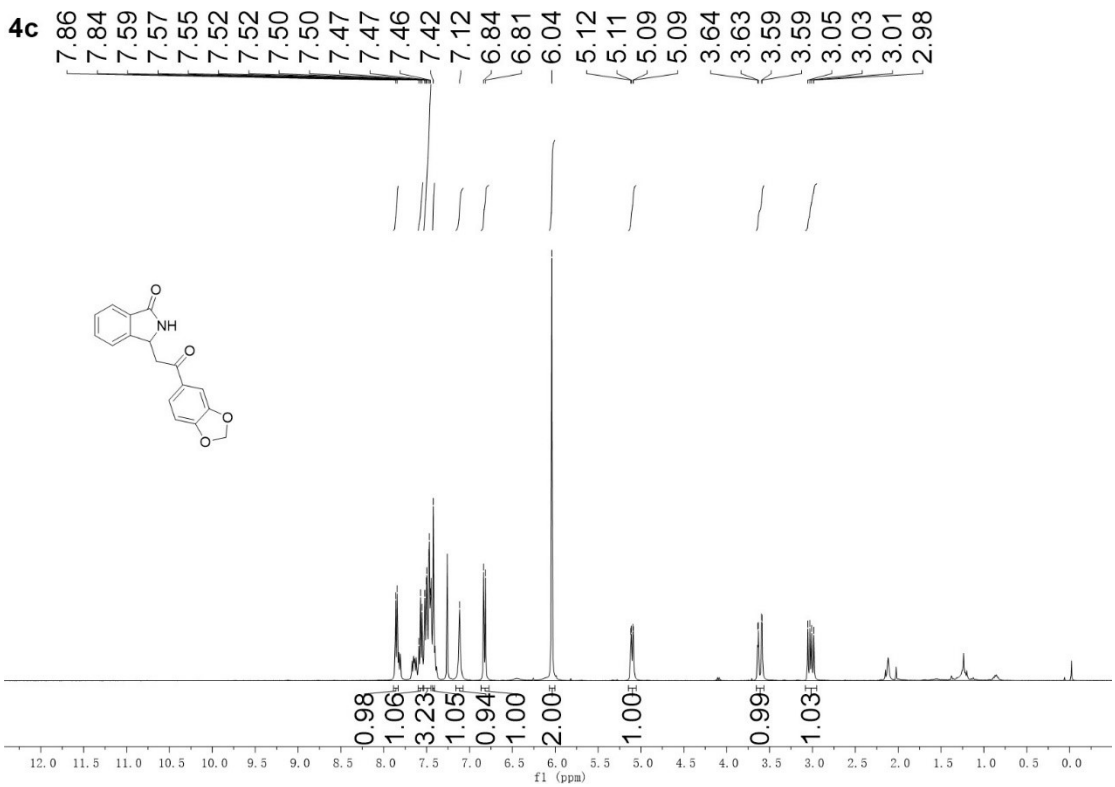

197.5
170.0
146.6
144.9
133.6
132.0
131.9
129.5
128.5
128.2
124.1
122.4
52.5
43.9
21.7
f1 (ppm)

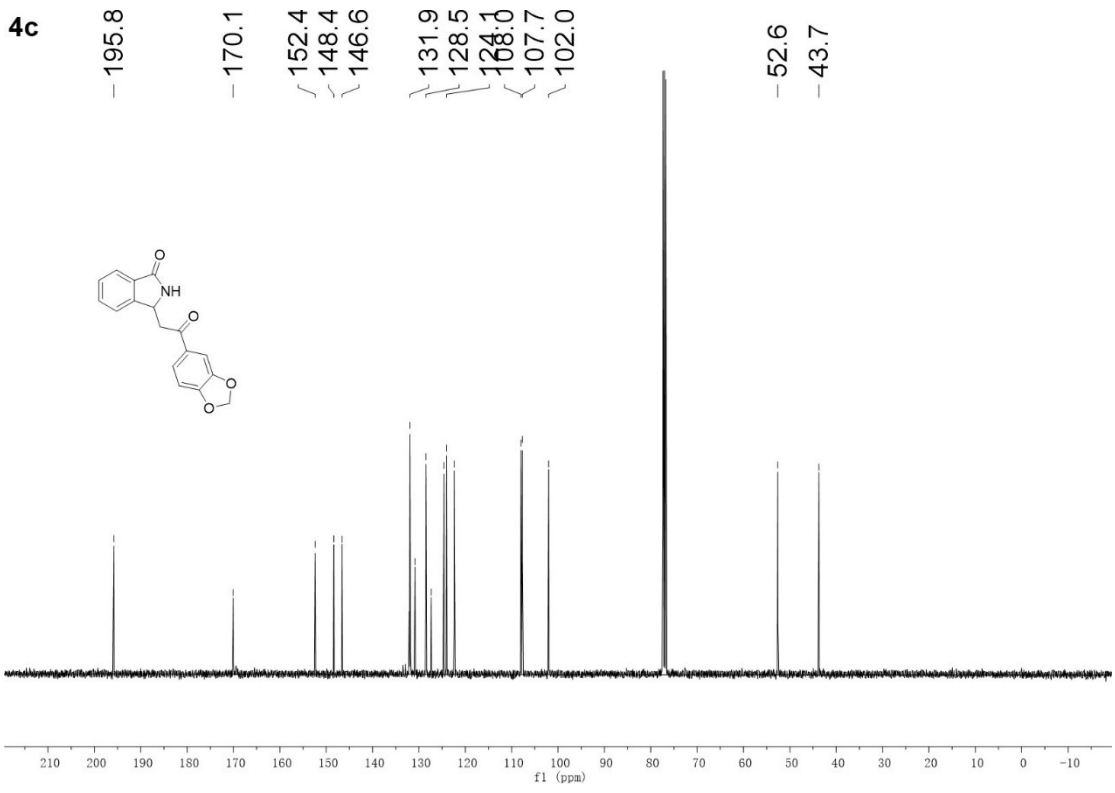
4b

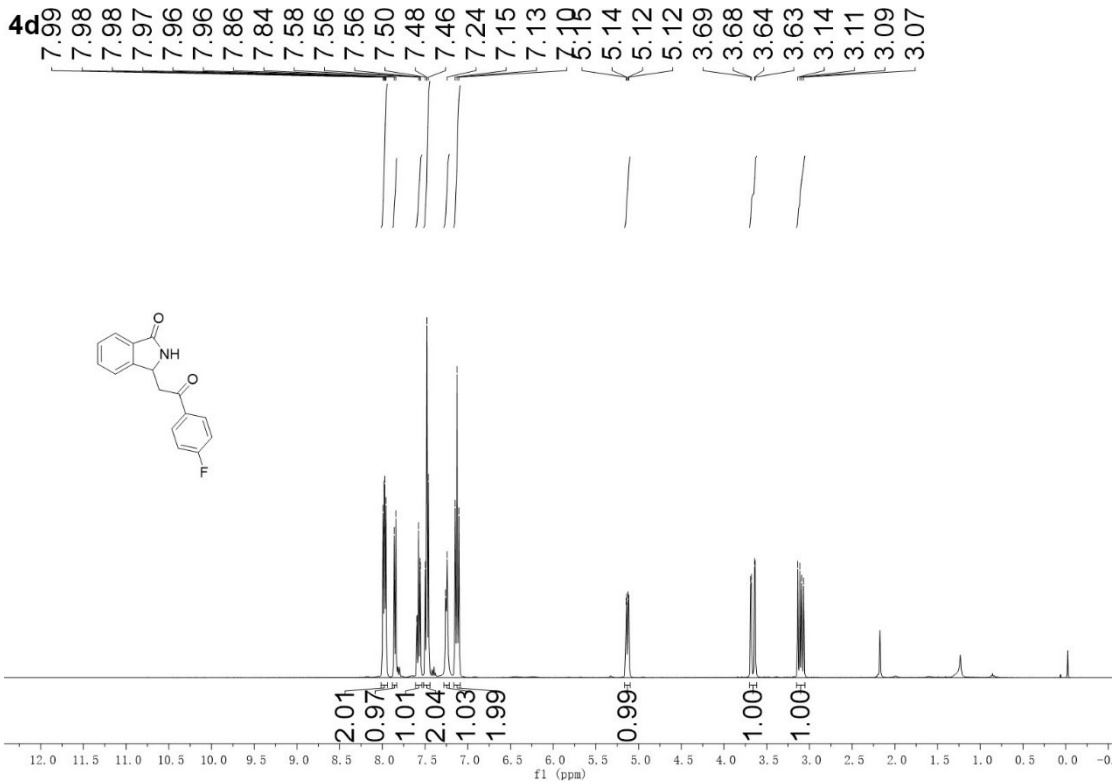

7.93
7.91
7.88
7.86
7.60
7.58
7.57
7.51
7.49
7.48
7.47
7.46
7.01
6.94
6.92
5.13
5.13
5.11
5.11
3.86
3.69
3.68
3.64
3.63
3.08
3.05
3.04
3.01
NH
O
O
OMe
1.89
0.97
0.99
2.08
0.94
1.92
0.96
3.00
1.00
0.98
f1 (ppm)

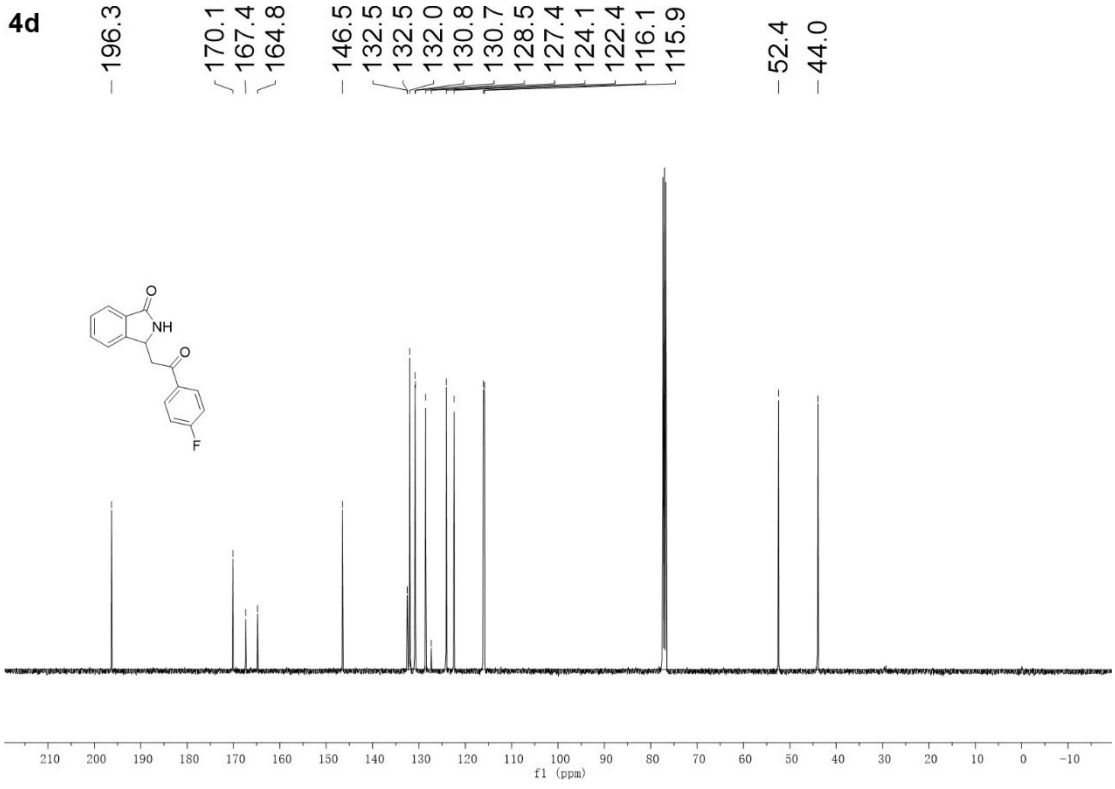
4b


196.3
169.9
164.1
146.7
132.0
131.9
130.4
129.1
128.5
124.1
122.4
114.0
55.5
52.6
43.7
NH
O
O
OMe
f1 (ppm)

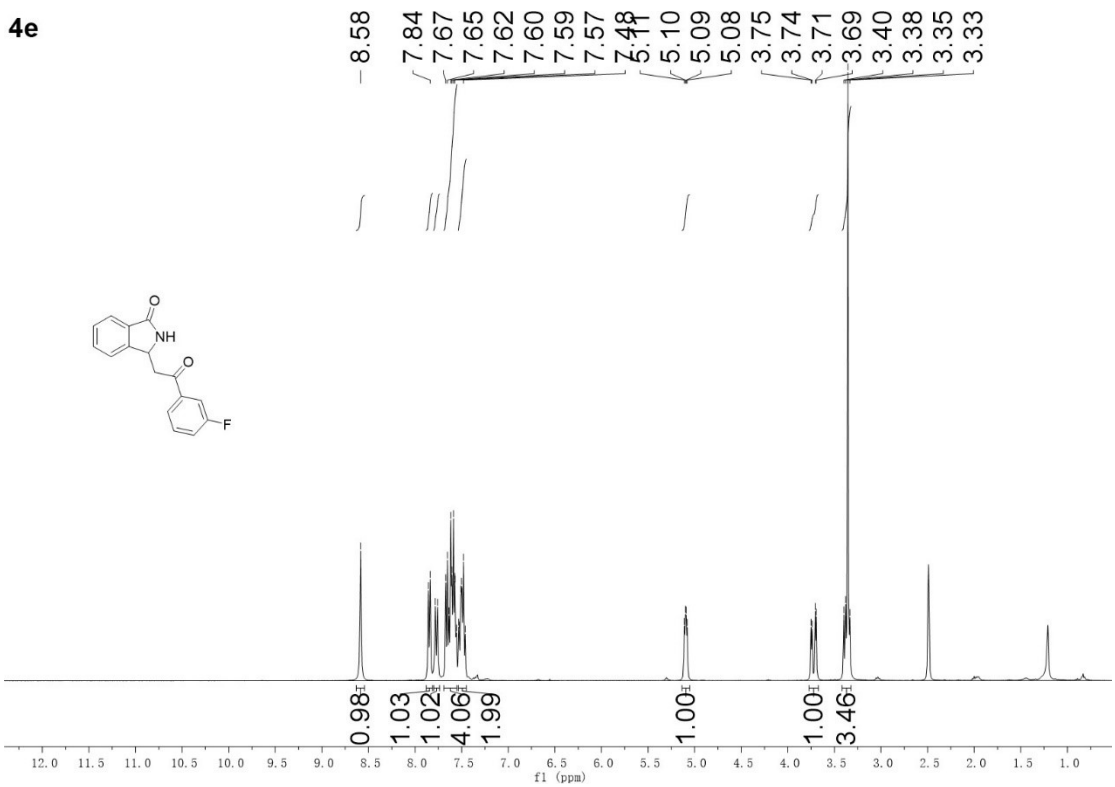

4c
7.86
7.84
7.59
7.57
7.55
7.52
7.52
7.50
7.50
7.47
7.47
7.46
7.42
7.12
6.84
6.81
6.04
5.12
5.11
5.09
5.09
3.64
3.63
3.59
3.59
3.05
3.03
3.01
2.98
NH
0.98
1.06
3.23
1.05
0.94
1.00
2.00
1.00
0.99
1.03
f1 (ppm)


4c
195.8
170.1
152.4
148.4
146.6
131.9
128.5
124.1
108.0
107.7
102.0
52.6
43.7
NH
f1 (ppm)

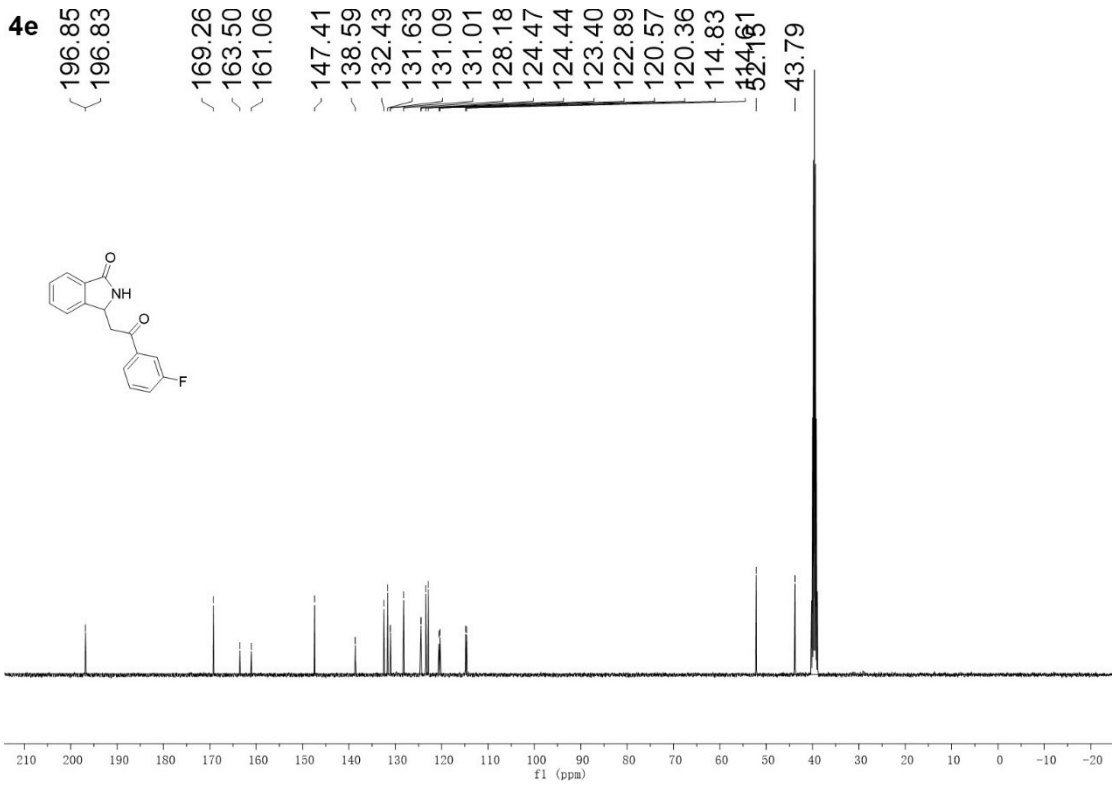

4d
7.99
7.98
7.98
7.97
7.96
7.96
7.86
7.84
7.58
7.56
7.56
7.50
7.48
7.46
7.24
7.15
7.13
7.10
5.15
5.14
5.12
5.12
3.69
3.68
3.64
3.63
3.14
3.11
3.09
3.07
NH
O
O
F
2.01
0.97
1.01
2.04
1.03
1.99
0.99
1.00
1.00
f1 (ppm)


4d
196.3
170.1
167.4
164.8
146.5
132.5
132.5
132.0
130.8
130.7
128.5
127.4
124.1
122.4
116.1
115.9
52.4
44.0
NH
O
O
F
f1 (ppm)

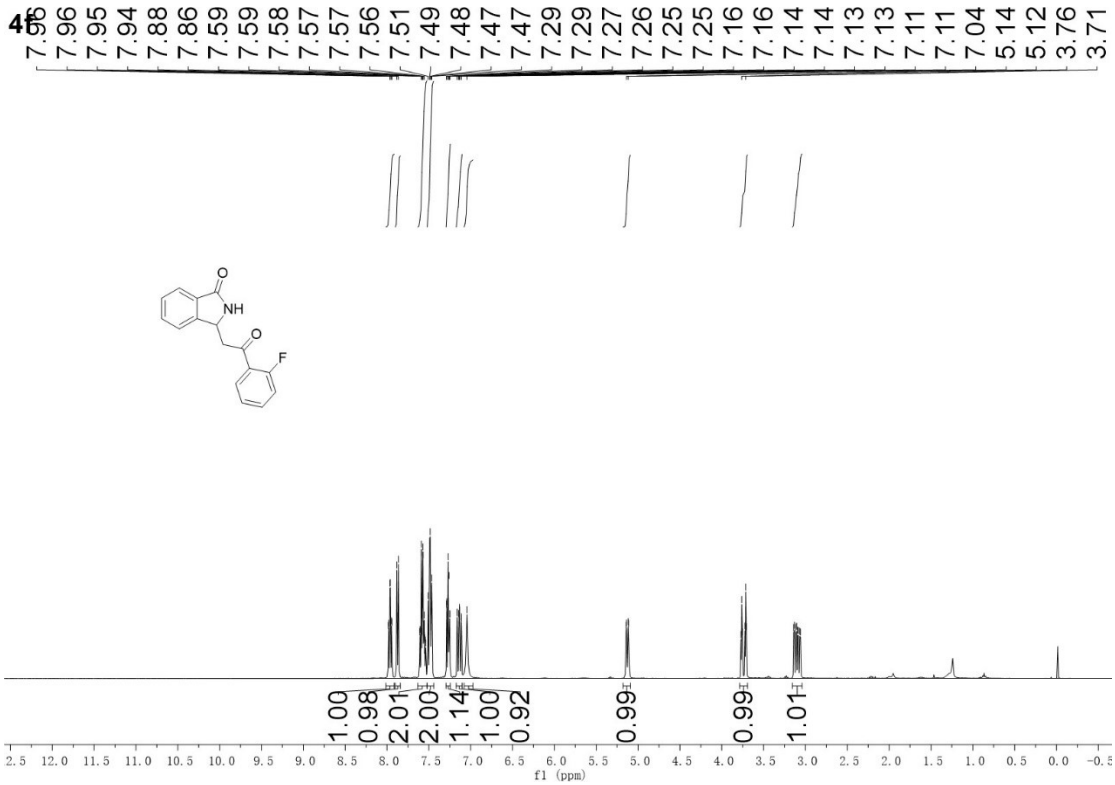
4e


8.58
7.84
7.67
7.65
7.62
7.60
7.59
7.57
7.48
5.11
5.10
5.09
5.08
3.75
3.74
3.71
3.69
3.40
3.38
3.35
3.33
NH
O
F
0.98
1.03
1.02
4.06
1.99
1.00
1.00
3.46
f1 (ppm)

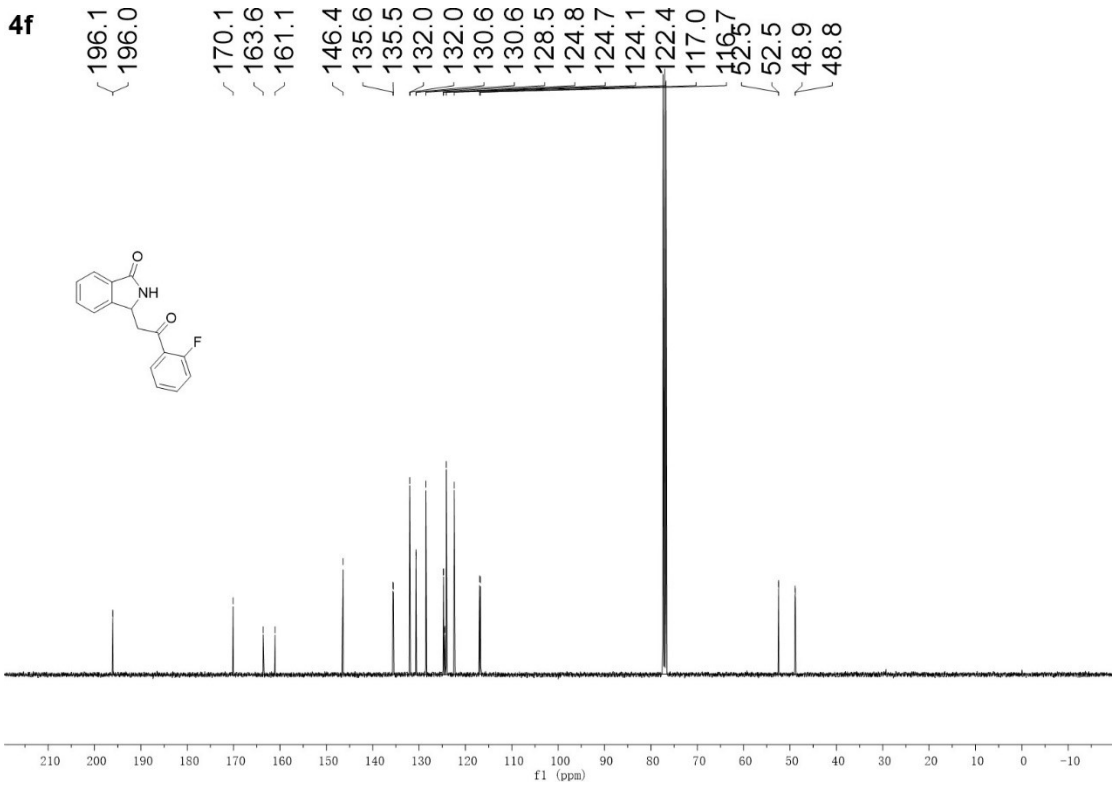
4e


196.85
196.83
169.26
163.50
161.06
147.41
138.59
132.43
131.63
131.09
131.01
128.18
124.47
124.44
123.40
122.89
120.57
120.36
114.83
114.61
52.15
43.79
NH
O
F
f1 (ppm)

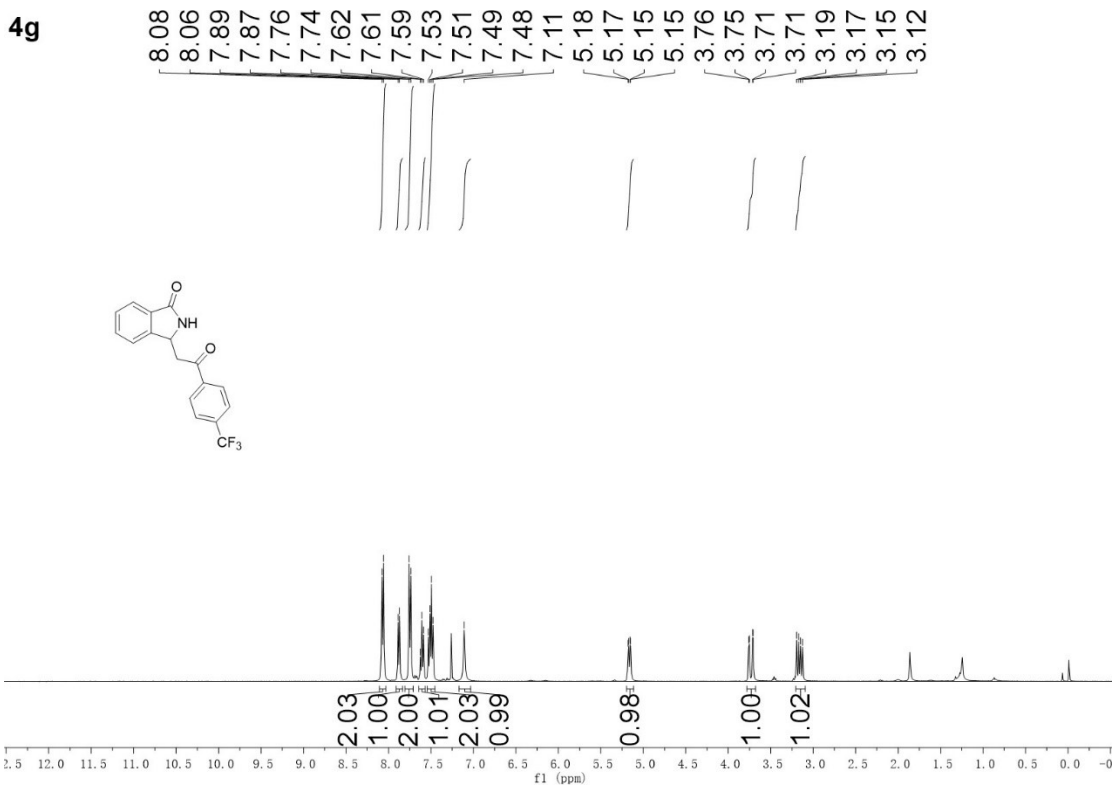
4f


7.96
7.96
7.95
7.94
7.88
7.86
7.59
7.59
7.58
7.57
7.57
7.56
7.51
7.49
7.48
7.47
7.47
7.29
7.29
7.27
7.26
7.25
7.25
7.16
7.16
7.14
7.14
7.13
7.13
7.11
7.11
7.04
5.14
5.12
3.76
3.71
O
NH
O
F
1.00
0.98
2.01
2.00
1.14
1.00
0.92
0.99
0.99
1.01
f1 (ppm)

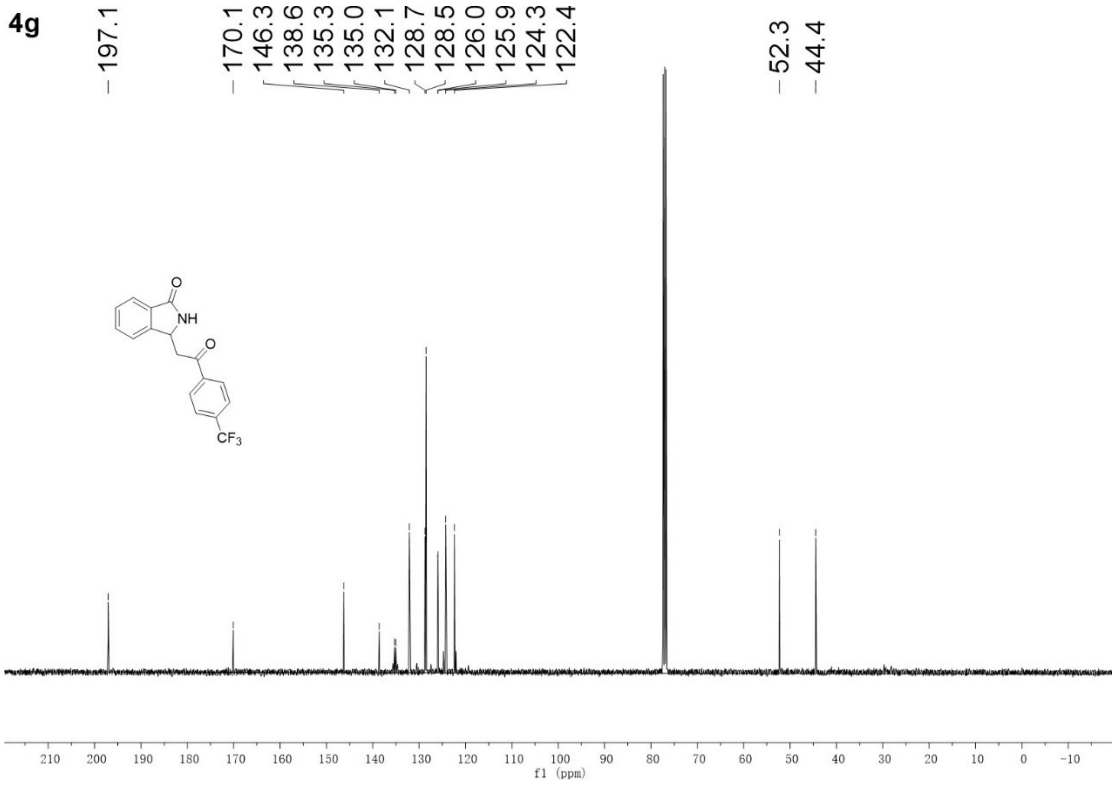
4f


196.1
196.0
170.1
163.6
161.1
146.4
135.6
135.5
132.0
132.0
130.6
130.6
128.5
124.8
124.7
124.1
122.4
117.0
116.7
52.5
52.5
48.9
48.8
O
NH
O
F
f1 (ppm)

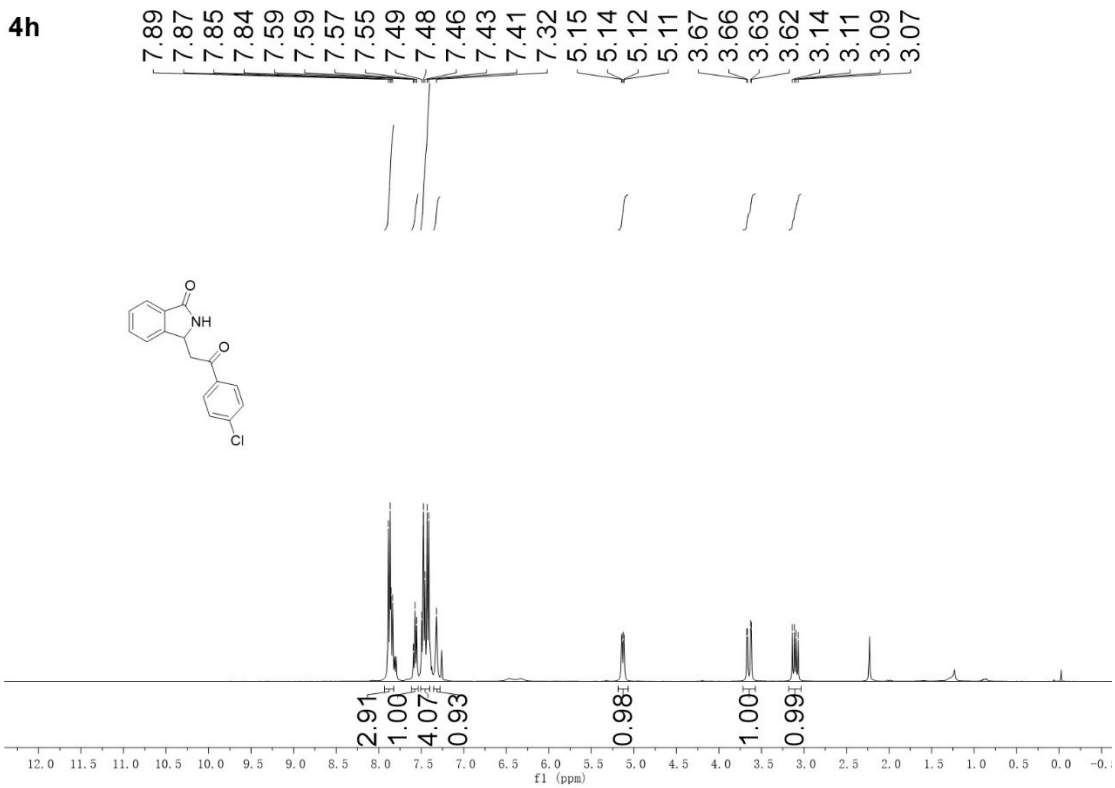
4g


8.08
8.06
7.89
7.87
7.76
7.74
7.62
7.61
7.59
7.53
7.51
7.49
7.48
7.11
5.18
5.17
5.15
5.15
3.76
3.75
3.71
3.71
3.19
3.17
3.15
3.12
NH
O
O
CF3
2.03
1.00
2.00
1.01
2.03
0.99
0.98
1.00
1.02
f1 (ppm)

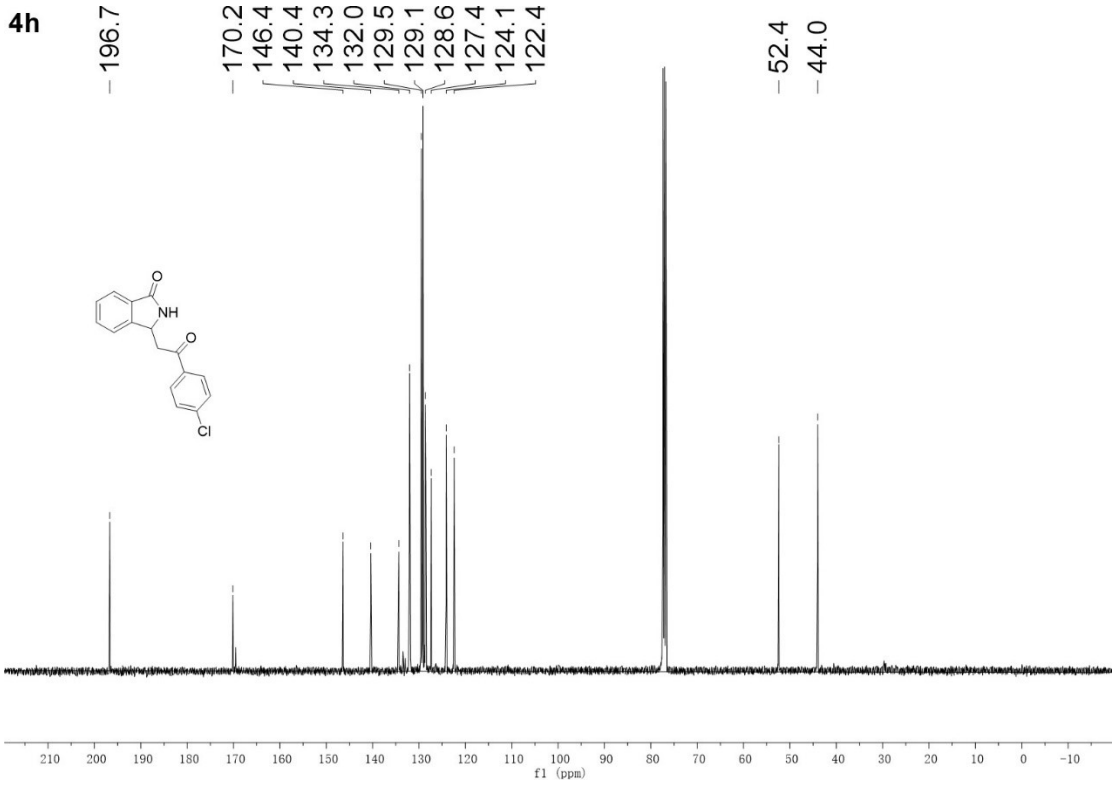
4g

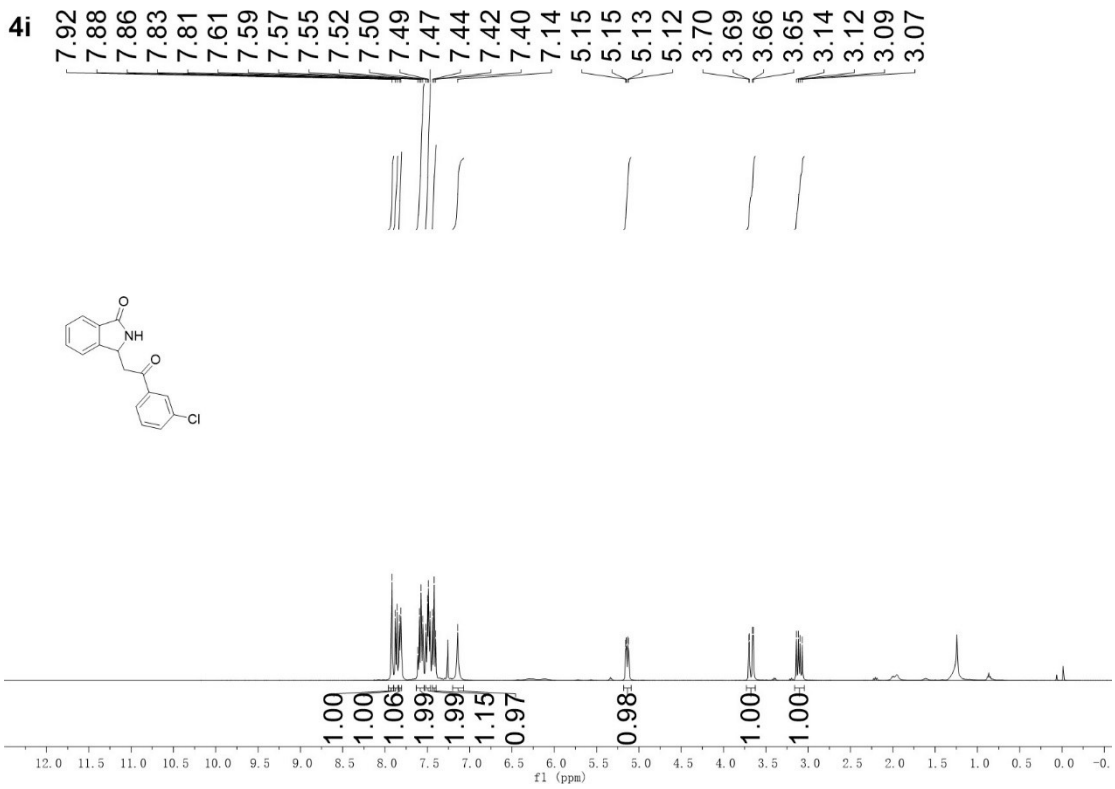

197.1
170.1
146.3
138.6
135.3
135.0
132.1
128.7
128.5
126.0
125.9
124.3
122.4
52.3
44.4
NH
O
O
CF3
f1 (ppm)

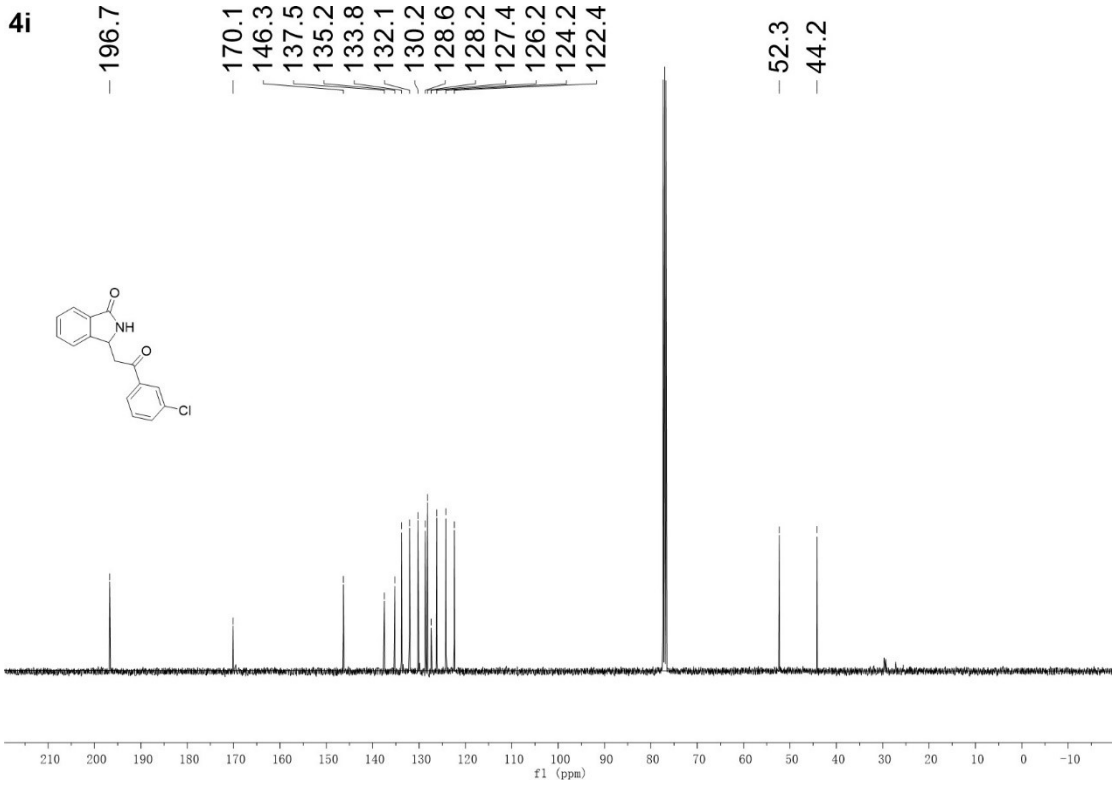
4h


7.89
7.87
7.85
7.84
7.59
7.59
7.57
7.55
7.49
7.48
7.46
7.43
7.41
7.32
5.15
5.14
5.12
5.11
3.67
3.66
3.63
3.62
3.14
3.11
3.09
3.07
NH
O
O
Cl
2.91
1.00
4.07
0.93
0.98
1.00
0.99
f1 (ppm)

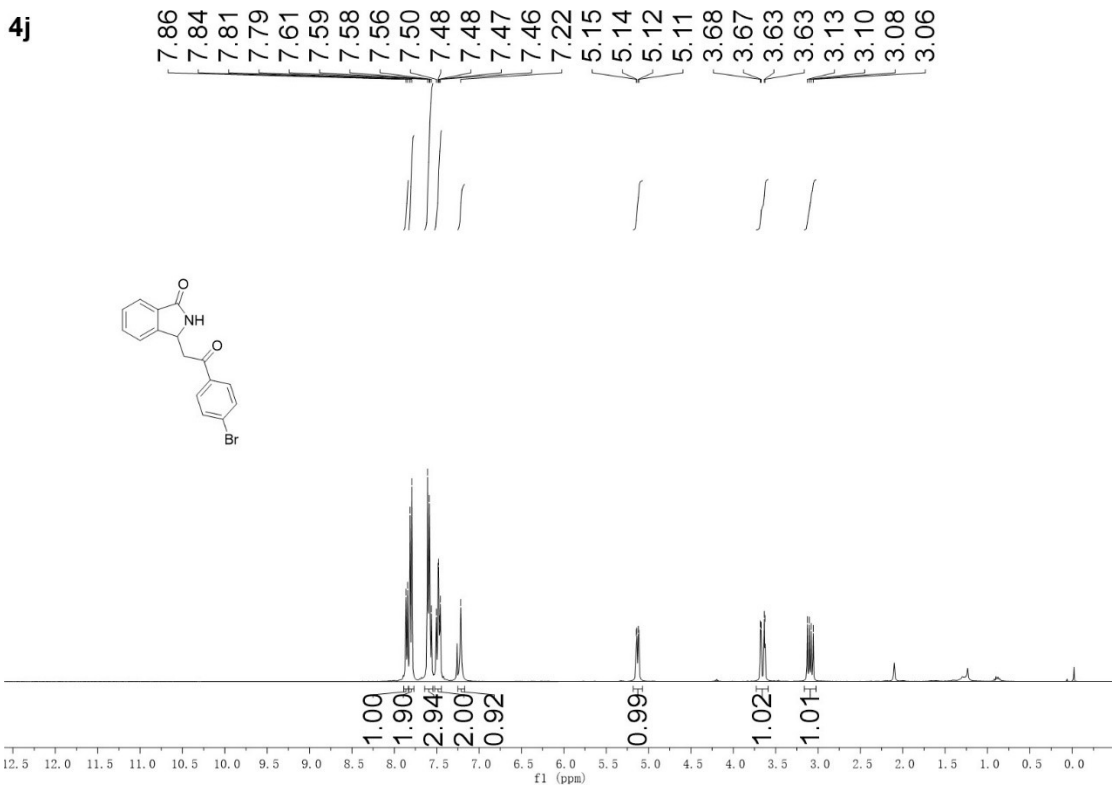
4h


196.7
170.2
146.4
140.4
134.3
132.0
129.5
129.1
128.6
127.4
124.1
122.4
52.4
44.0
NH
O
O
Cl
f1 (ppm)

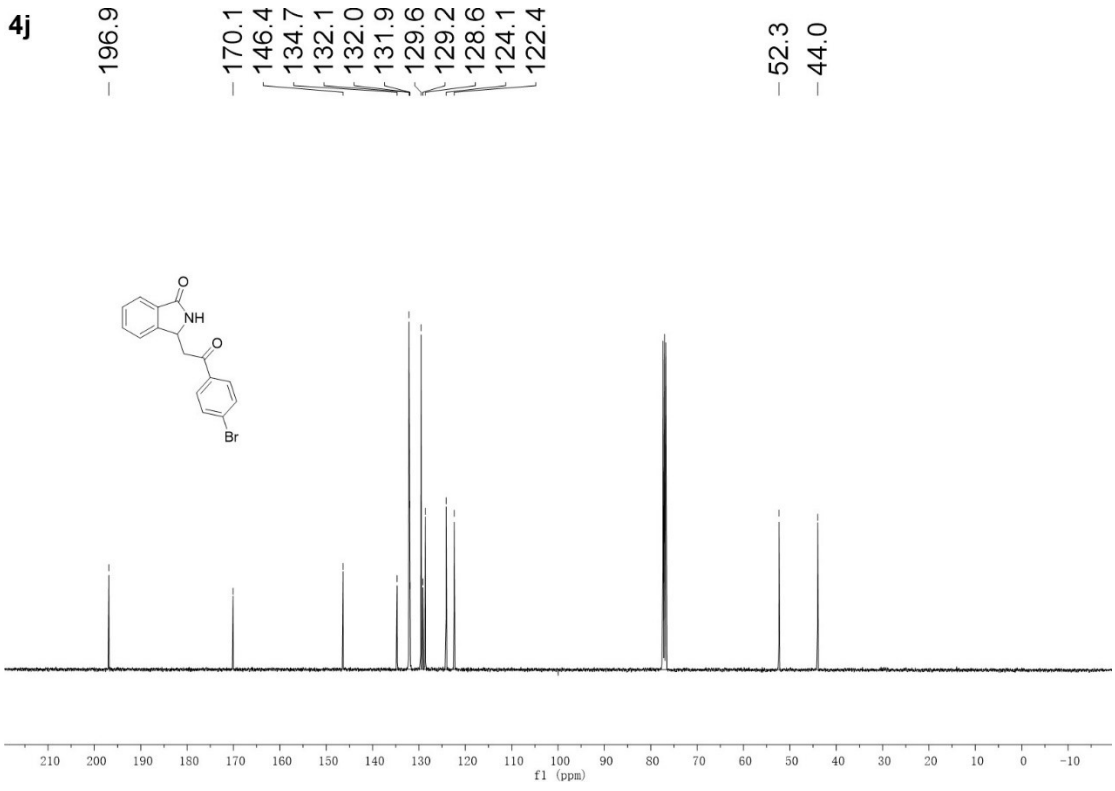

4i
7.92
7.88
7.86
7.83
7.81
7.61
7.59
7.57
7.55
7.52
7.50
7.49
7.47
7.44
7.42
7.40
7.14
5.15
5.15
5.13
5.12
3.70
3.69
3.66
3.65
3.14
3.12
3.09
3.07
NH
O
O
Cl
1.00
1.00
1.06
1.99
1.99
1.15
0.97
0.98
1.00
1.00
f1 (ppm)

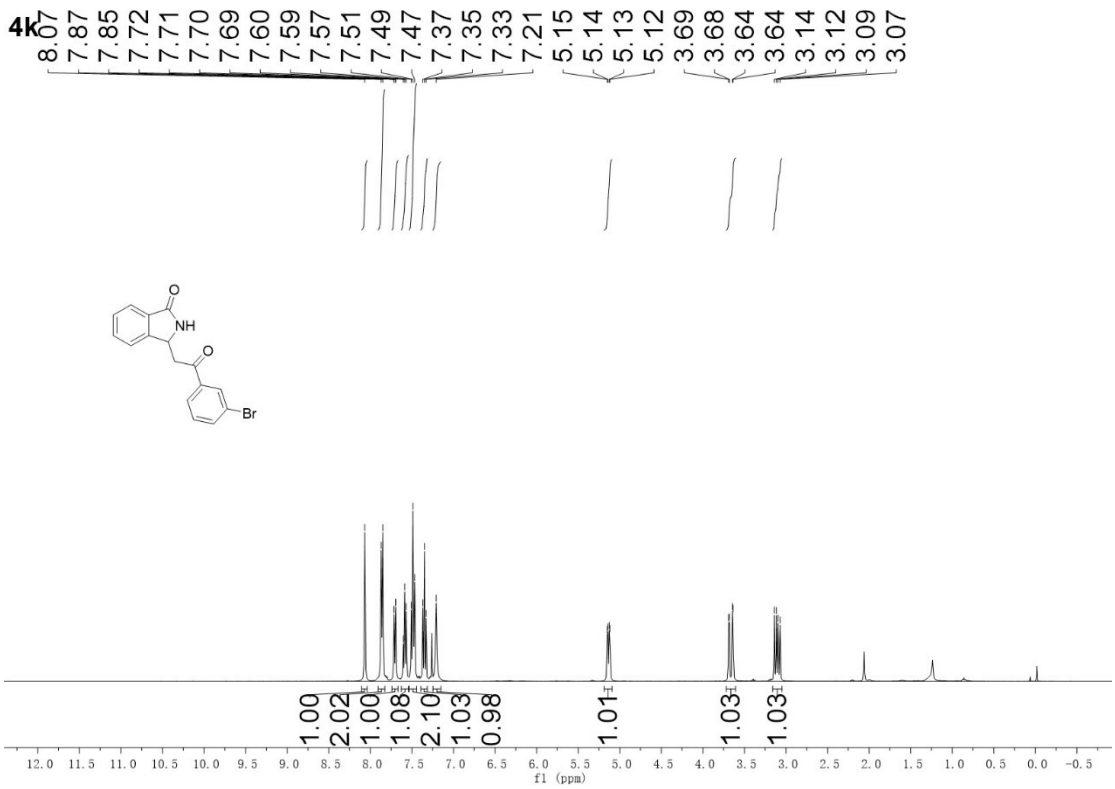

4i
196.7
170.1
146.3
137.5
135.2
133.8
132.1
130.2
128.6
128.2
127.4
126.2
124.2
122.4
52.3
44.2
NH
O
O
Cl
f1 (ppm)

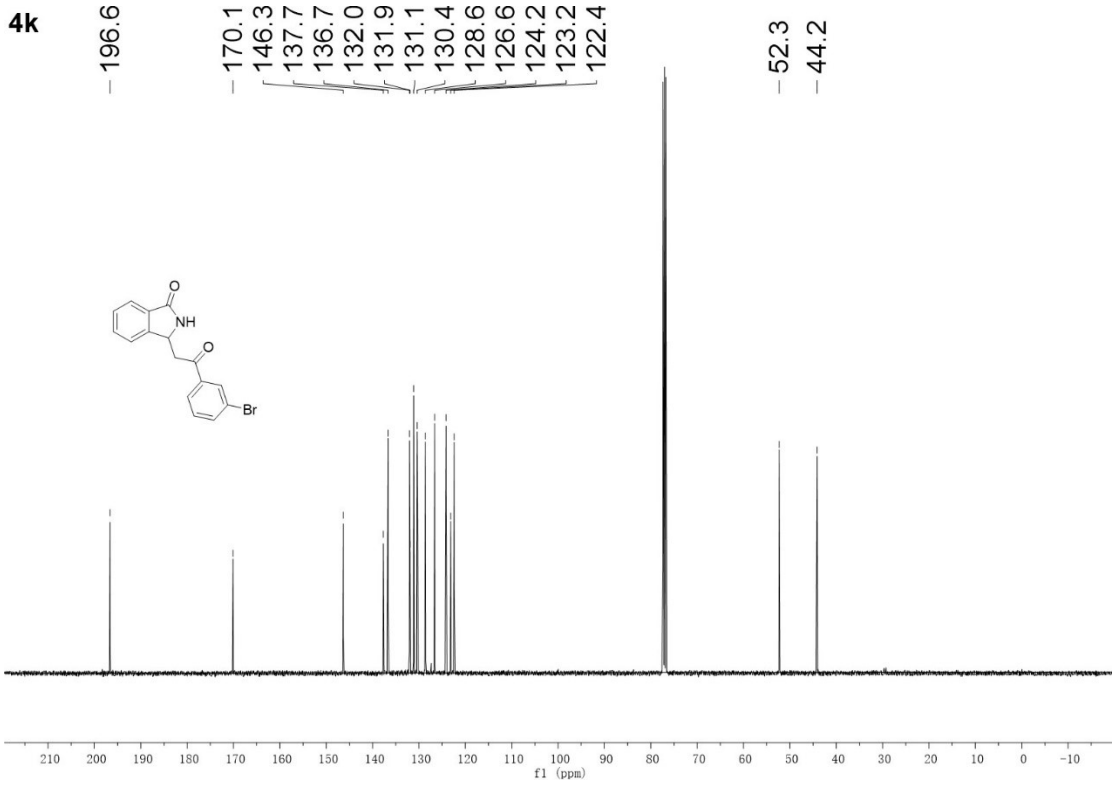
4j

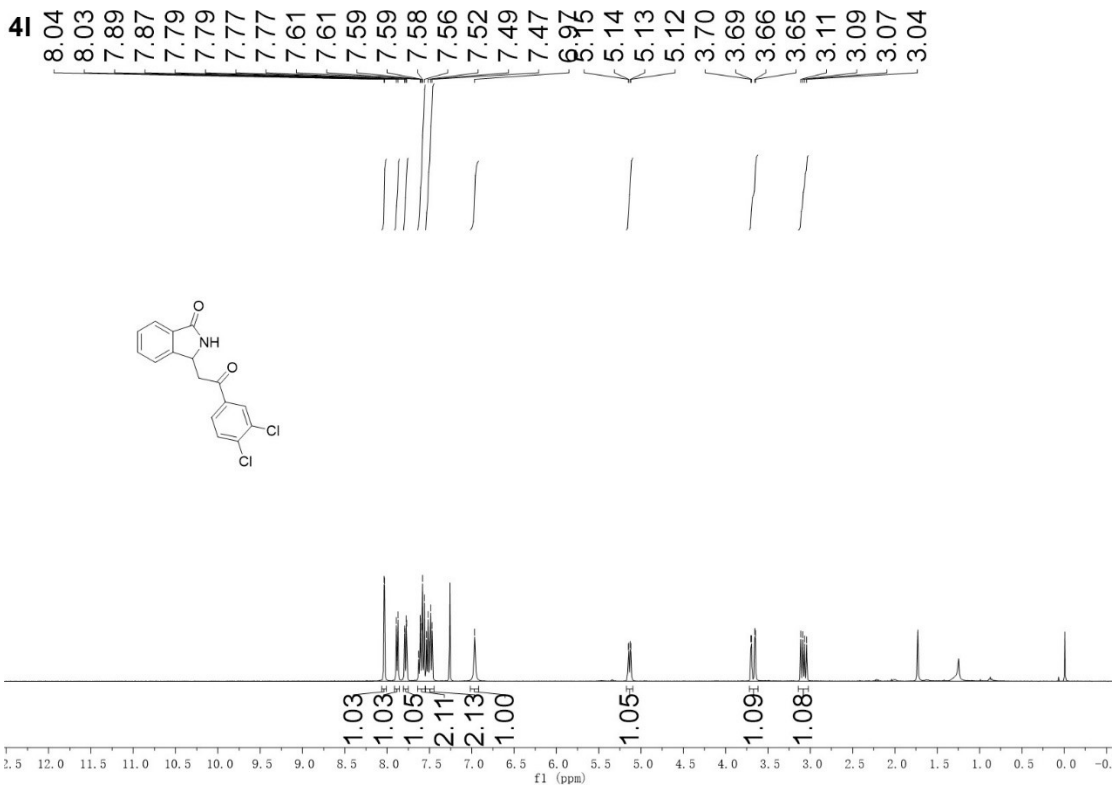

7.86
7.84
7.81
7.79
7.61
7.59
7.58
7.56
7.50
7.48
7.48
7.47
7.46
7.22
5.15
5.14
5.12
5.11
3.68
3.67
3.63
3.63
3.13
3.10
3.08
3.06
NH
O
O
Br
1.00
1.90
2.94
2.00
0.92
0.99
1.02
1.01
f1 (ppm)

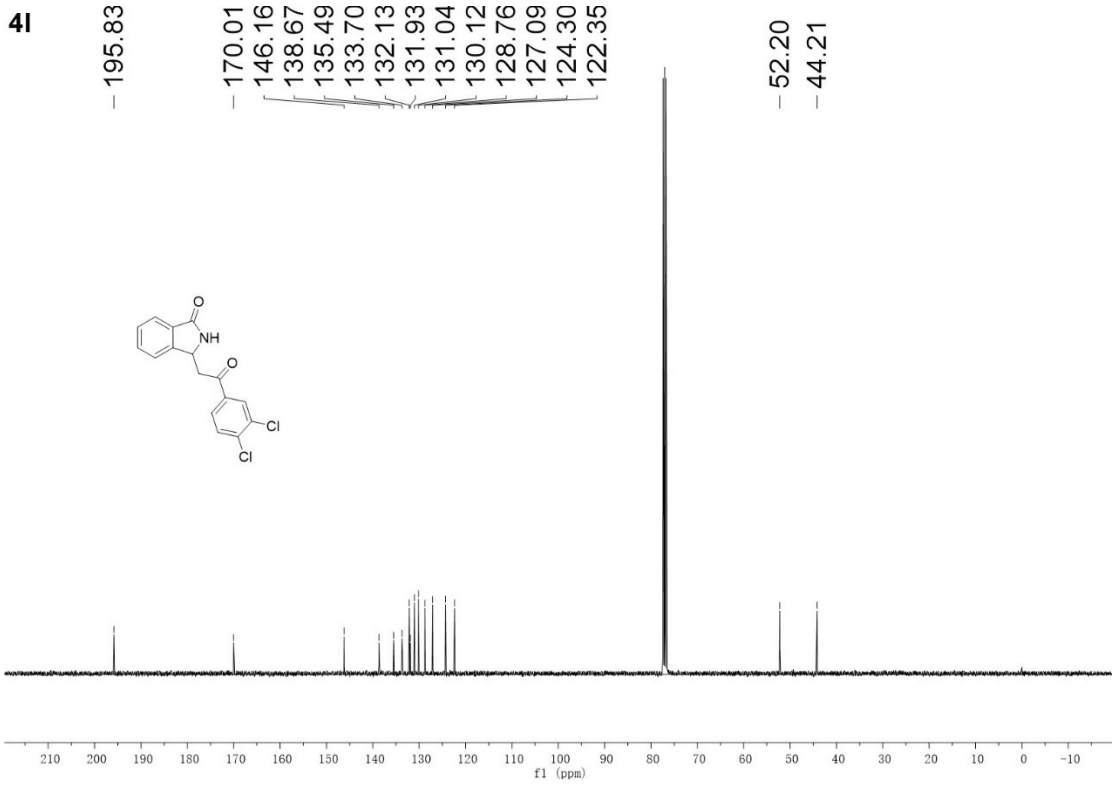
4j


196.9
170.1
146.4
134.7
132.1
132.0
131.9
129.6
129.2
128.6
124.1
122.4
52.3
44.0
NH
O
O
Br
f1 (ppm)

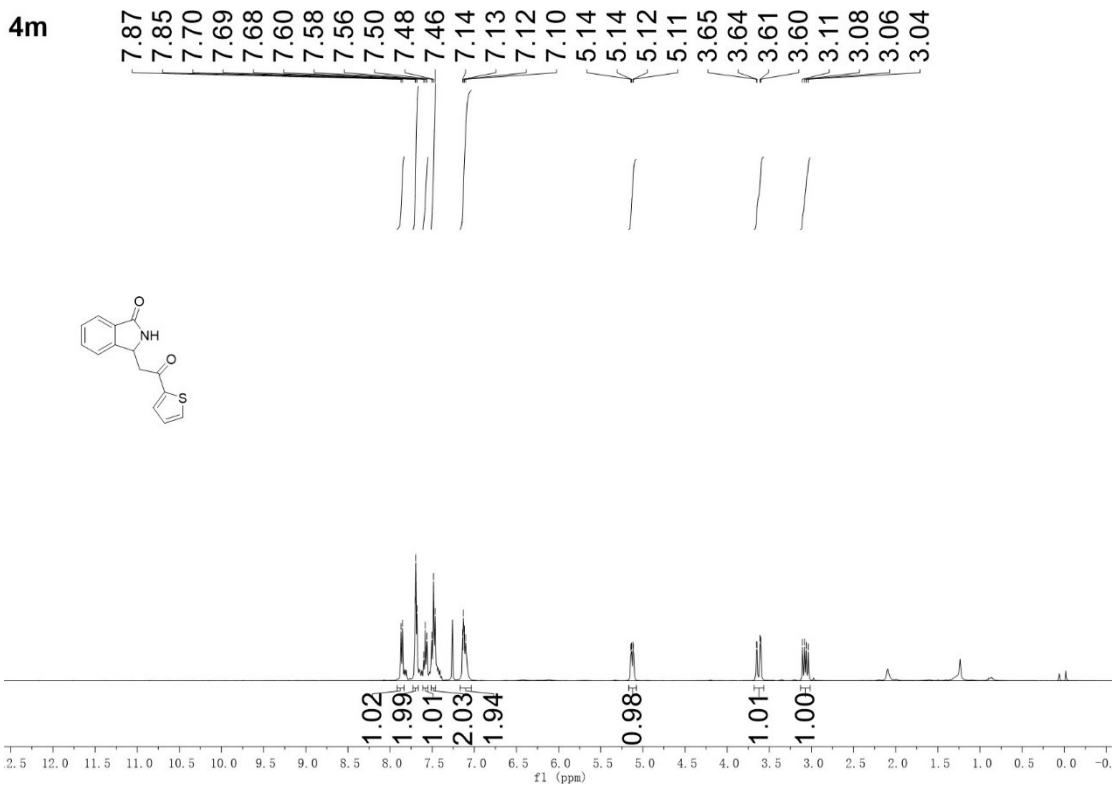

4k
8.07
7.87
7.85
7.72
7.71
7.70
7.69
7.60
7.59
7.57
7.51
7.49
7.47
7.37
7.35
7.33
7.21
5.15
5.14
5.13
5.12
3.69
3.68
3.64
3.64
3.14
3.12
3.09
3.07
O
NH
O
Br
1.00
2.02
1.00
1.08
2.10
1.03
0.98
1.01
1.03
1.03
f1 (ppm)


4k
196.6
170.1
146.3
137.7
136.7
132.0
131.9
131.1
130.4
128.6
126.6
124.2
123.2
122.4
52.3
44.2
O
NH
O
Br
f1 (ppm)

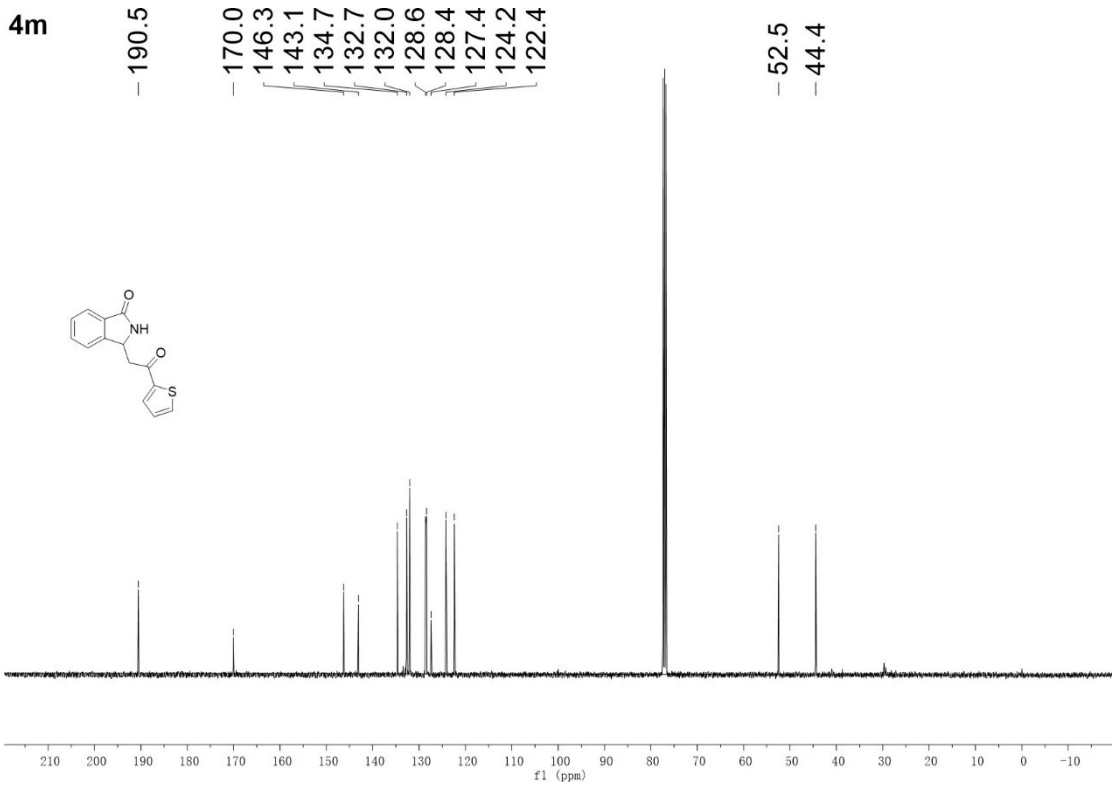

4l
8.04
8.03
7.89
7.87
7.79
7.79
7.77
7.77
7.61
7.61
7.59
7.59
7.58
7.56
7.52
7.49
7.47
6.97
5.15
5.14
5.13
5.12
3.70
3.69
3.66
3.65
3.11
3.09
3.07
3.04
O
NH
O
Cl
Cl
1.03
1.03
1.05
2.11
2.13
1.00
1.05
1.09
1.08
f1 (ppm)


4l
195.83
170.01
146.16
138.67
135.49
133.70
132.13
131.93
131.04
130.12
128.76
127.09
124.30
122.35
52.20
44.21
O
NH
O
Cl
Cl
f1 (ppm)

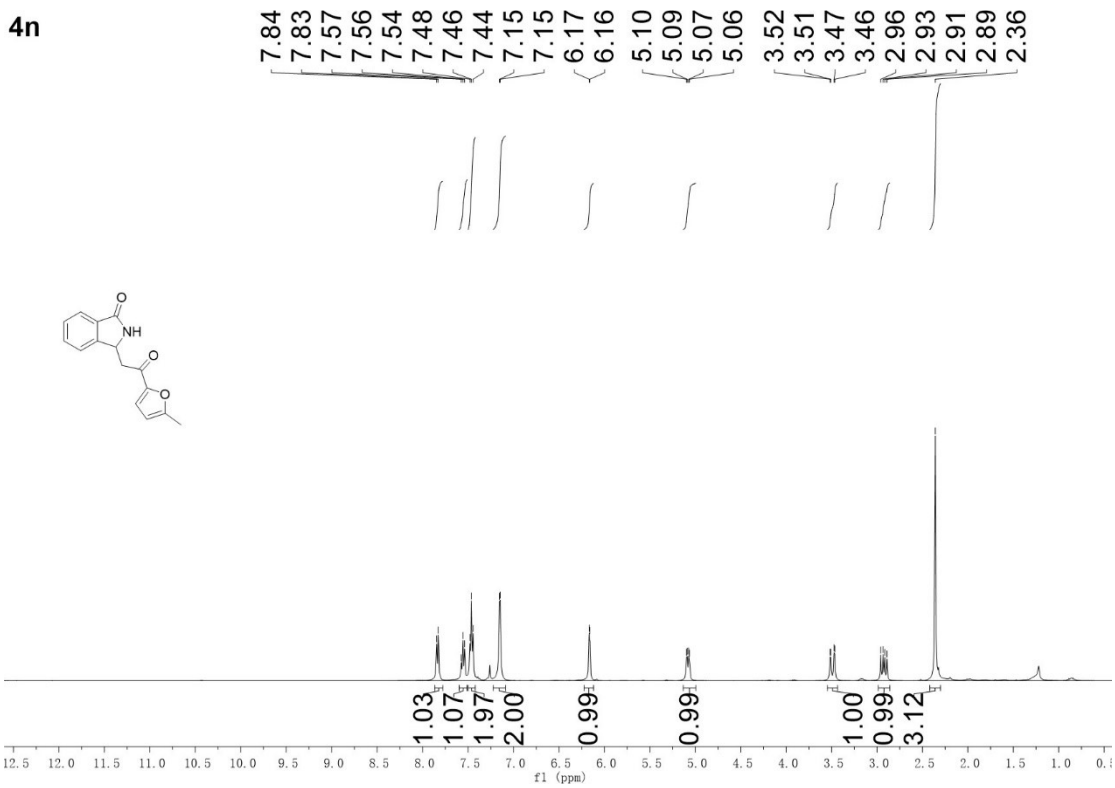
4m


7.87
7.85
7.70
7.69
7.68
7.60
7.58
7.56
7.50
7.48
7.46
7.14
7.13
7.12
7.10
5.14
5.14
5.12
5.11
3.65
3.64
3.61
3.60
3.11
3.08
3.06
3.04
O
NH
O
S
1.02
1.99
1.01
2.03
1.94
0.98
1.01
1.00
f1 (ppm)

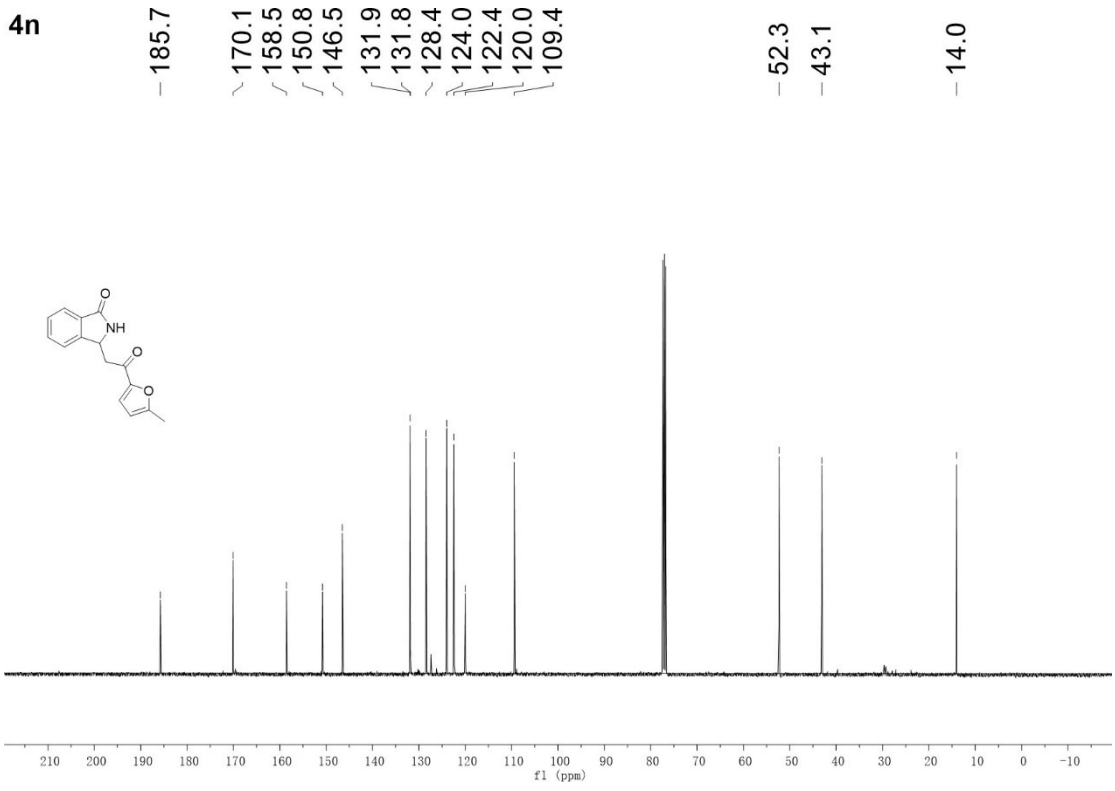
4m


190.5
170.0
146.3
143.1
134.7
132.7
132.0
128.6
128.4
127.4
124.2
122.4
52.5
44.4
O
NH
O
S
f1 (ppm)

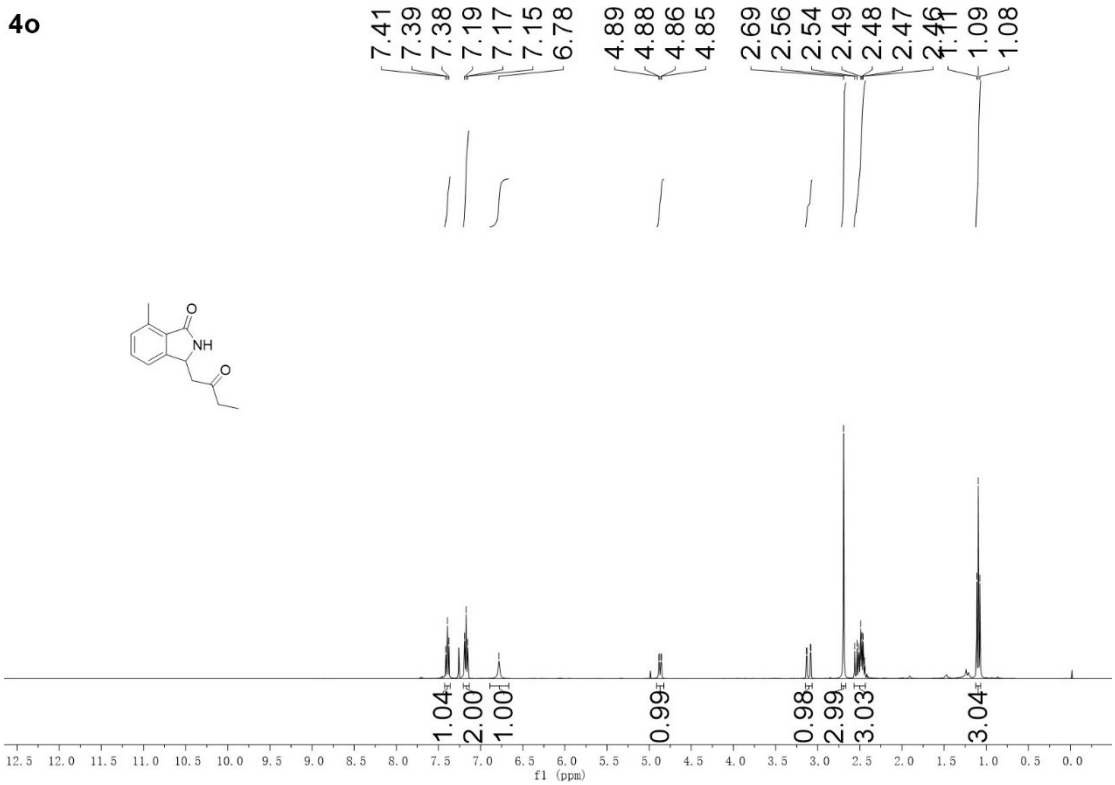
4n


7.84
7.83
7.57
7.56
7.54
7.48
7.46
7.44
7.15
7.15
6.17
6.16
5.10
5.09
5.07
5.06
3.52
3.51
3.47
3.46
2.96
2.93
2.91
2.89
2.36
NH
O
O
O
1.03
1.07
1.97
2.00
0.99
0.99
1.00
0.99
3.12
f1 (ppm)

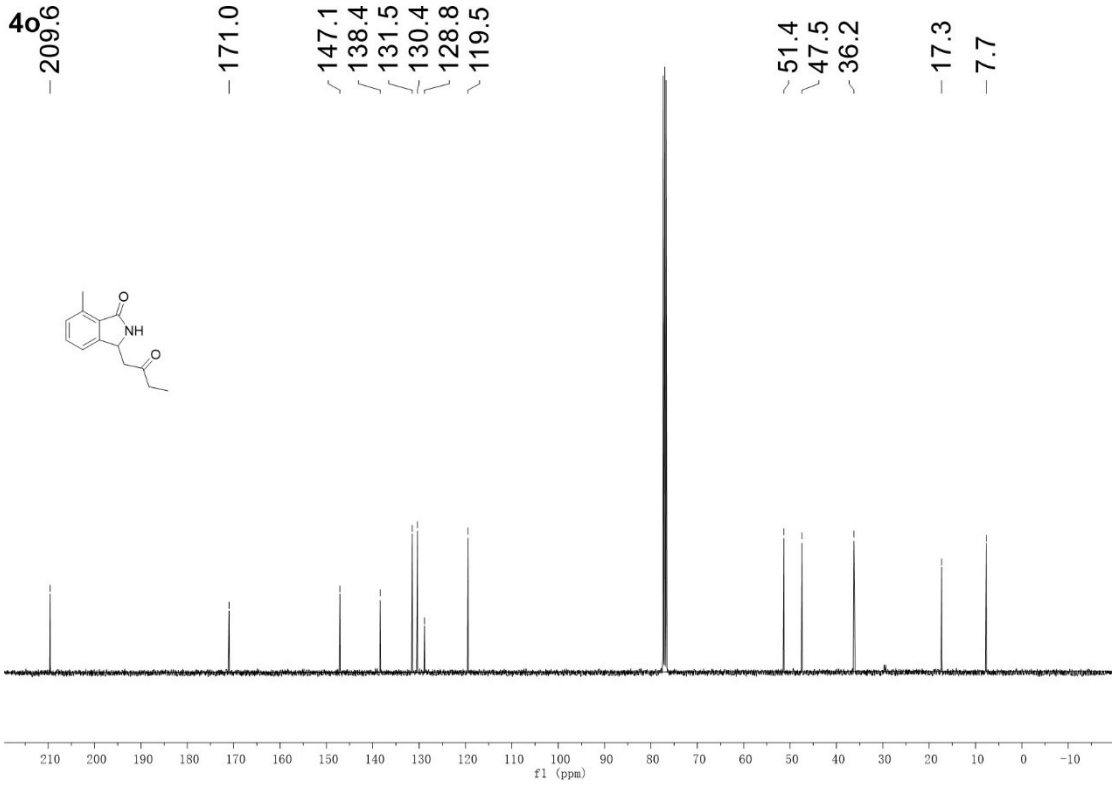
4n


185.7
170.1
158.5
150.8
146.5
131.9
131.8
128.4
124.0
122.4
120.0
109.4
52.3
43.1
14.0
NH
O
O
O
f1 (ppm)

4o


7.41
7.39
7.38
7.19
7.17
7.15
6.78
4.89
4.88
4.86
4.85
2.69
2.56
2.54
2.49
2.48
2.47
2.46
1.11
1.09
1.08
NH
O
O
1.04
2.00
1.00
0.99
0.98
2.99
3.03
3.04
f1 (ppm)

4o


209.6
171.0
147.1
138.4
131.5
130.4
128.8
119.5
51.4
47.5
36.2
17.3
7.7
NH
O
O
f1 (ppm)