

Supporting Information

Switchable Synthesis of 1,4-Bridged Dihydroisoquinoline-3-ones and Isoquinoline-1,3,4-triones Through Radical Oxidation of Isoquinolinium Salts with Phenyliodine (III) Diacetate

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1 General Methods

Unless otherwise noted, commercially available reagents were used as received. All solvents for chromatographic separations were distilled before use. Solvents for the water-free reactions were dried with standard procedures and stored with Schlenk flasks over molecular sieves. Column chromatography was carried out with 200–300 mesh silica gel. Thin-layer chromatography (TLC) was performed on glassbacked silica plates. UV light, I_2 , and solutions of 2,4-dinitrophenylhydrazine were used to visualize products. Concentrating a solution under reduced pressure refers to distillation using a rotary evaporator attached to a vacuum pump (3–10 mmHg). Products obtained as solids or high boiling oils were dried under vacuum (1–3 mmHg). ^1H and ^{13}C NMR spectra were recorded on a 600 MHz NMR spectrometer at 293 K, and the chemical shifts (δ) were internally referenced by the residual solvent signals relative to tetramethylsilane (CDCl_3 at 7.26 ppm for ^1H , and at 77.00 ppm for ^{13}C). Data are reported as s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad; coupling constant(s) in Hz; integration. The yields in the text refer to isolated yields of compounds.

2 In situ NMR spectra for the mechanistic experiments

2.1 The in situ NMR spectra of the reaction mixture

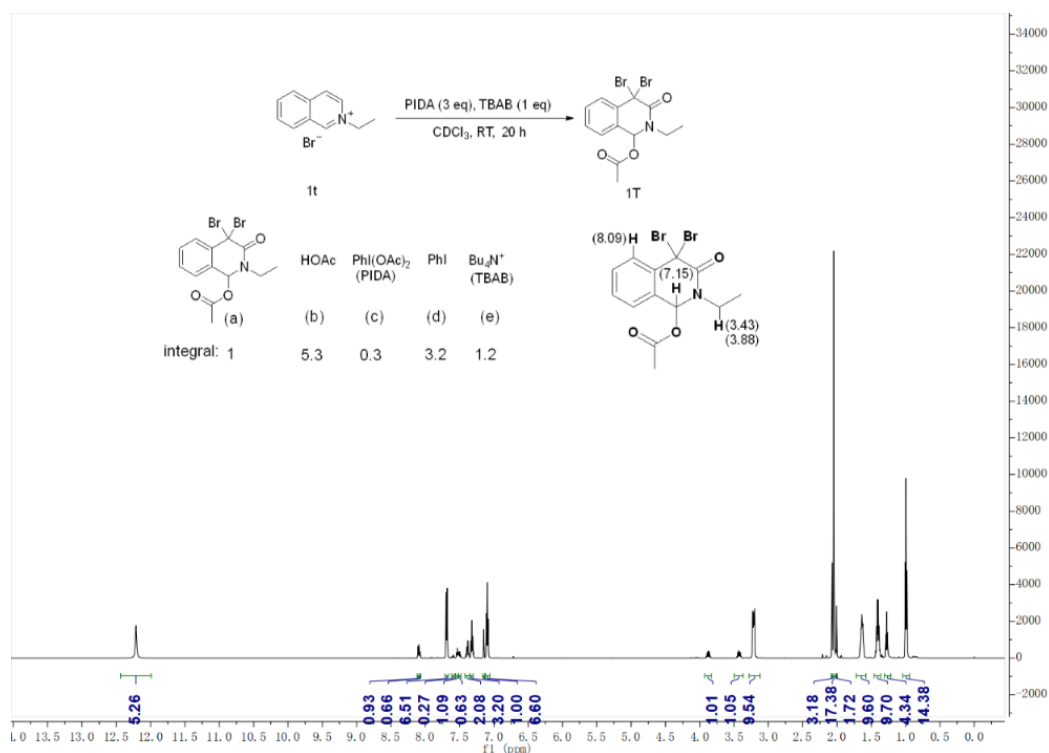


Figure S1. *In situ* ¹H NMR of 1T

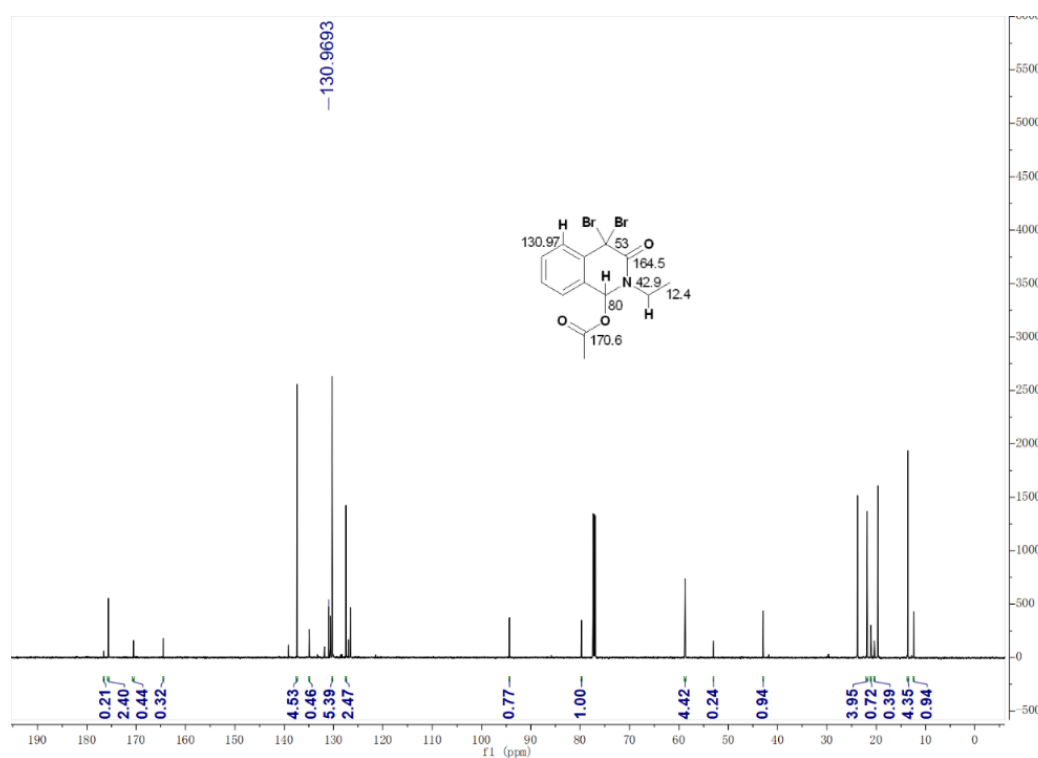


Figure S2. *In situ* ¹³C NMR of 1T

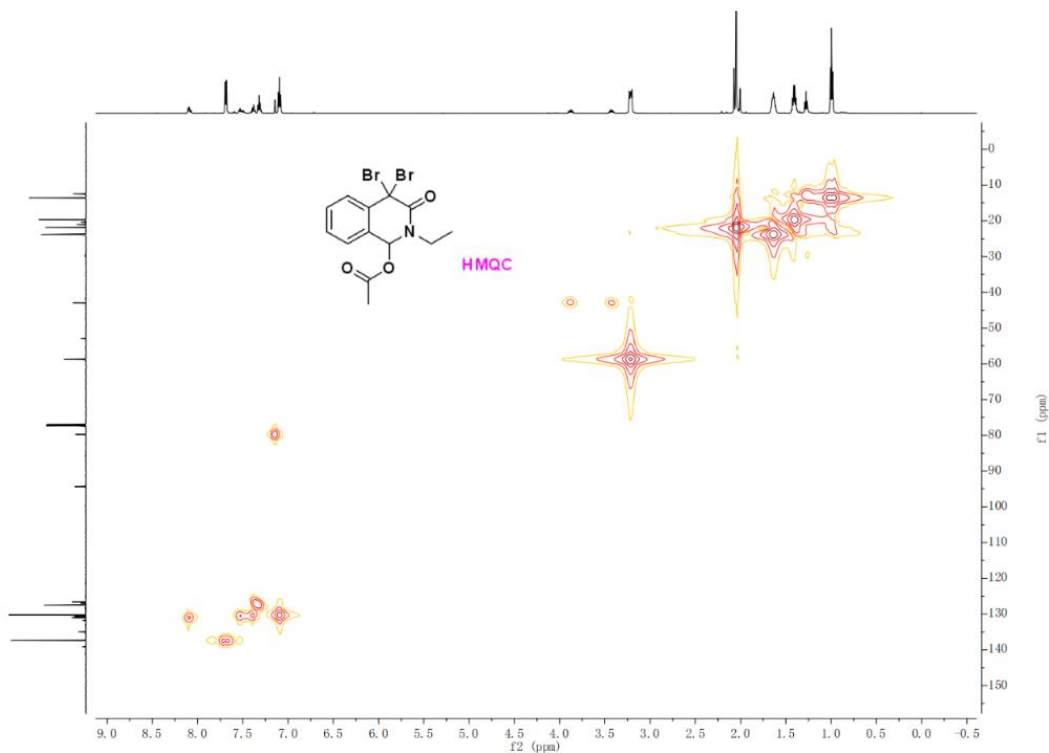


Figure S3. *In situ* HMQC of **1T**

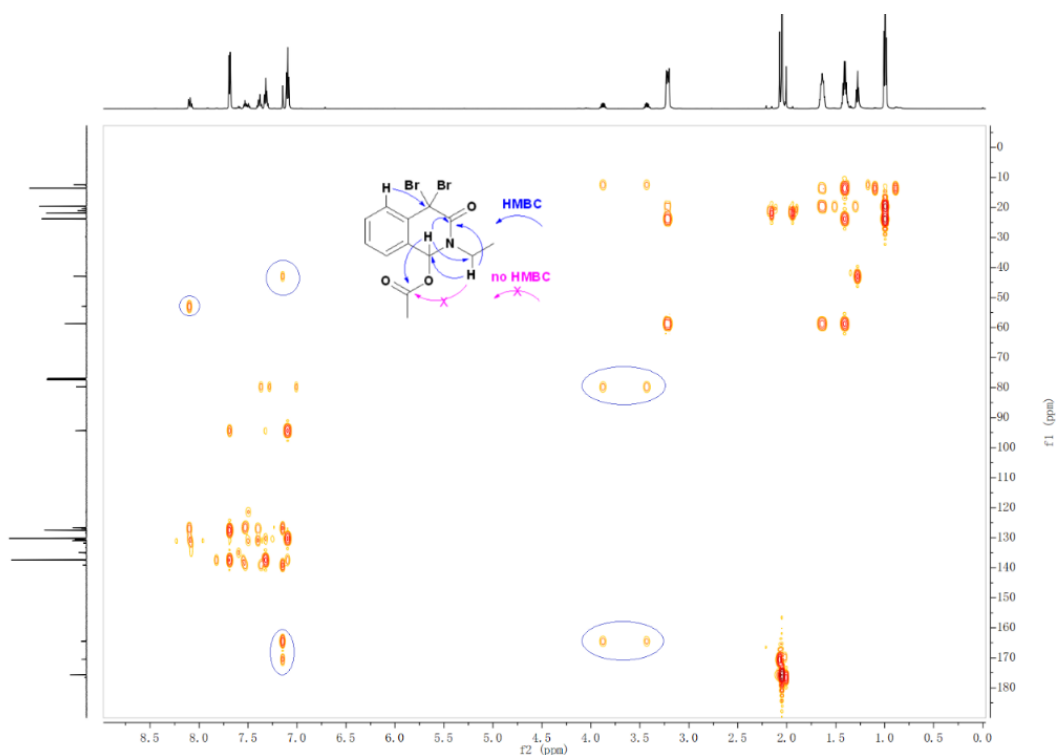


Figure S4. *In situ* HMBC of **1T**

4,4-dibromo-2-ethyl-3-oxo-1,2,3,4-tetrahydroisoquinolin-1-yl acetate (1T): ^1H NMR (600 MHz, Chloroform-*d*) δ 8.10 (d, $J = 8.3$ Hz, 1H), 7.53 (td, $J = 8.3, 7.6, 1.8$ Hz, 1H), 7.41 – 7.38 (m, 1H), 7.37 (d, $J = 5.9$ Hz, 1H), 7.15 (s, 1H), 3.88 (dq, $J = 14.3, 7.2$ Hz, 1H), 3.43 (dq, $J = 14.3, 7.2$ Hz, 1H), 2.07 (s, 3H),

1.28 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (151 MHz, Chloroform- d) δ 170.56, 164.48, 139.12, 134.94, 130.97, 130.64, 126.96, 126.59, 79.75, 52.99, 42.92, 21.09, 12.44. HRMS (ESI-TOF) calcd for $\text{C}_{13}\text{H}_{13}\text{Br}_2\text{NNaO}_3$ $[\text{M} + \text{Na}]^+$: 411.9154; found: 411.9152.

2.2 The ^1H NMR spectra of PIDA and its mixture with TBAB

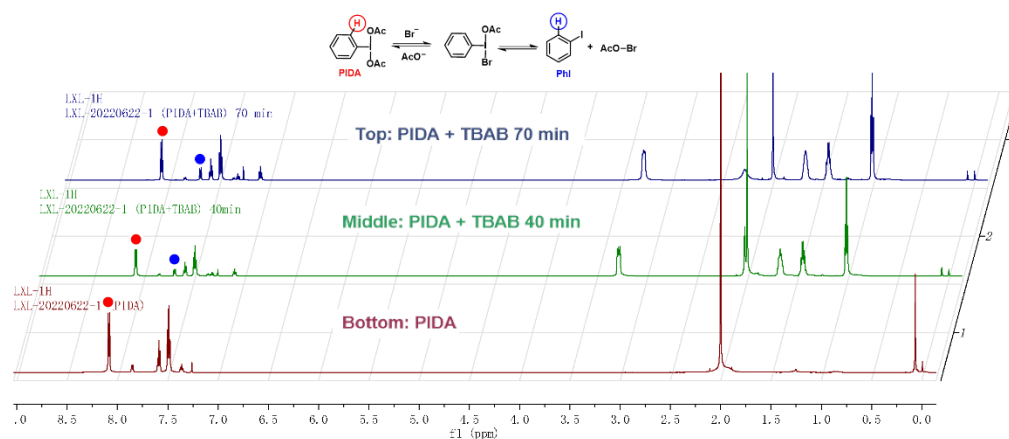


Figure S5. ^1H NMR of PIDA and its mixture with TBAB

Note: The ratios of integration (area) of proton signals are: (1) at 40 min, PIDA:PhI = 3.7:1; (2) at 70 min, PIDA:PhI = 3.4:1. At 40 min, 21.3% of PIDA converted to PhI, while at 70 min, 22.7% of PIDA converted to PhI, implying that this conversion slows down rapidly over time.

3 Investigations on the mechanism of the PIDA-mediated oxidation

3.1 The HRMS spectrum of the reaction mixture

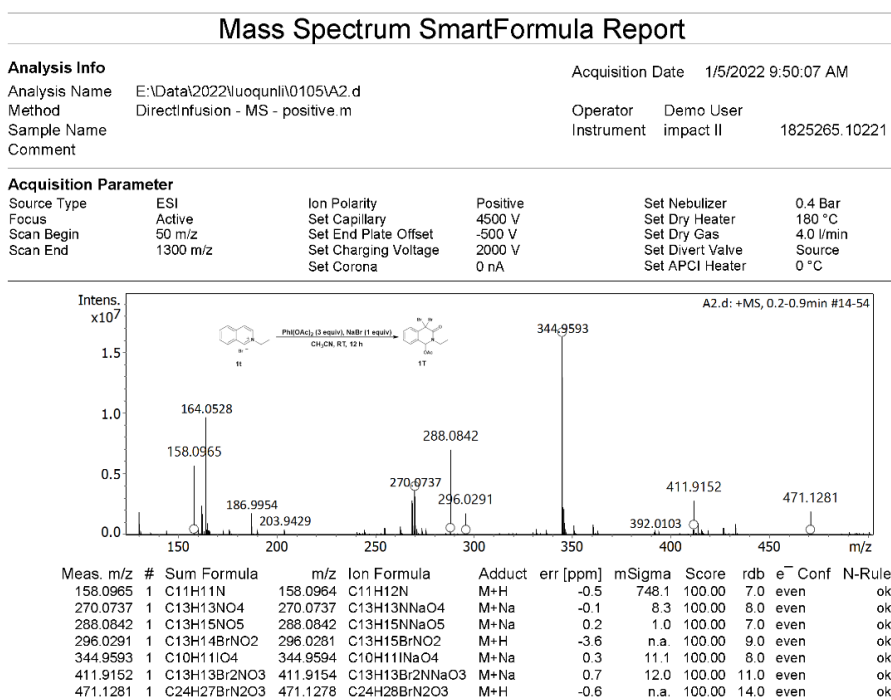


Figure S6. The HRMS spectrum of the reaction mixture.

3.2 The ESI-MS spectrum of the TEMPO-added reaction mixture

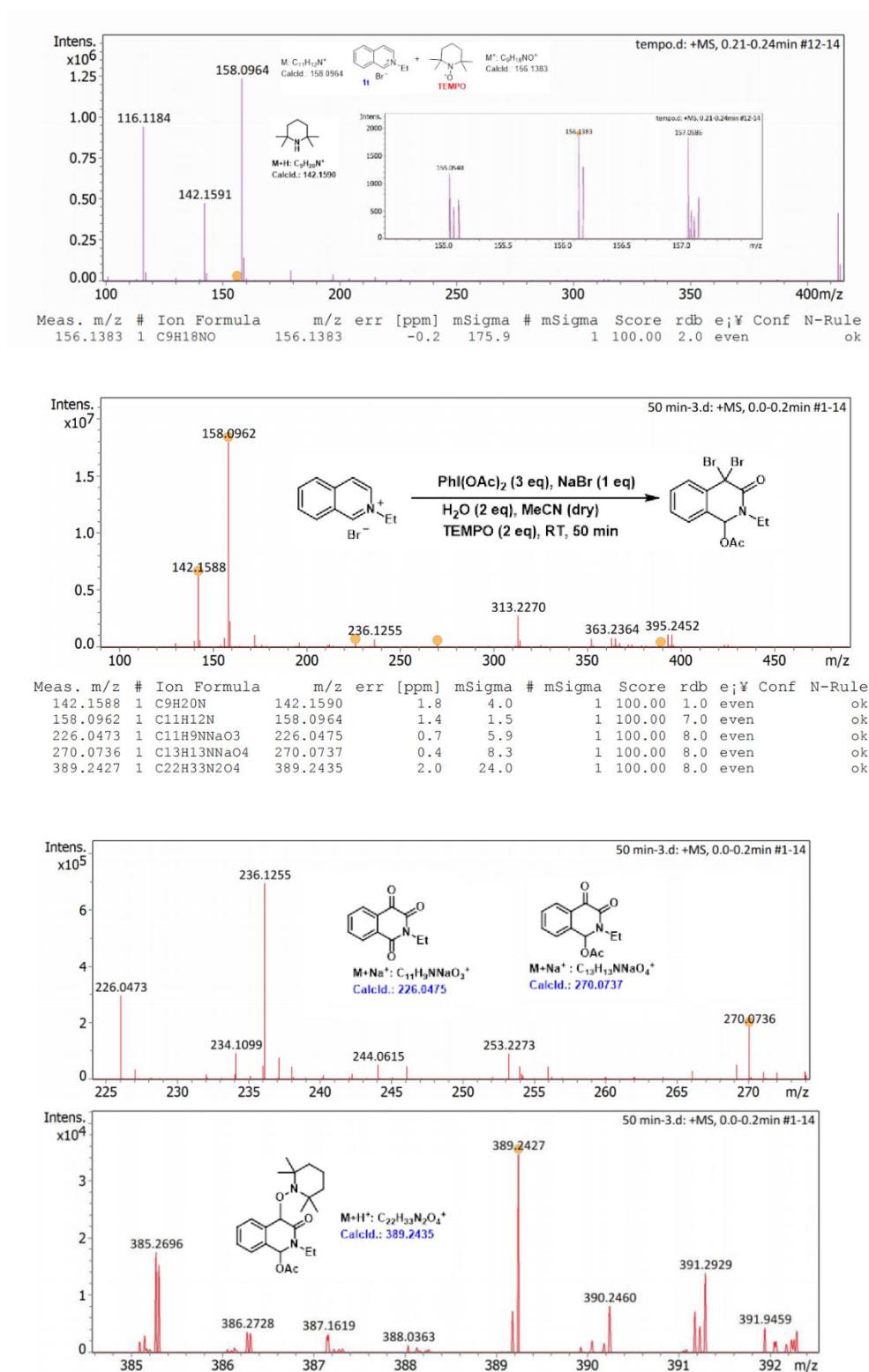


Figure S7. The HRMS spectra of the TEMPO-added reaction mixture.

3.3 The NMR spectra and characterization data of (1,2-dibromoethyl)benzene

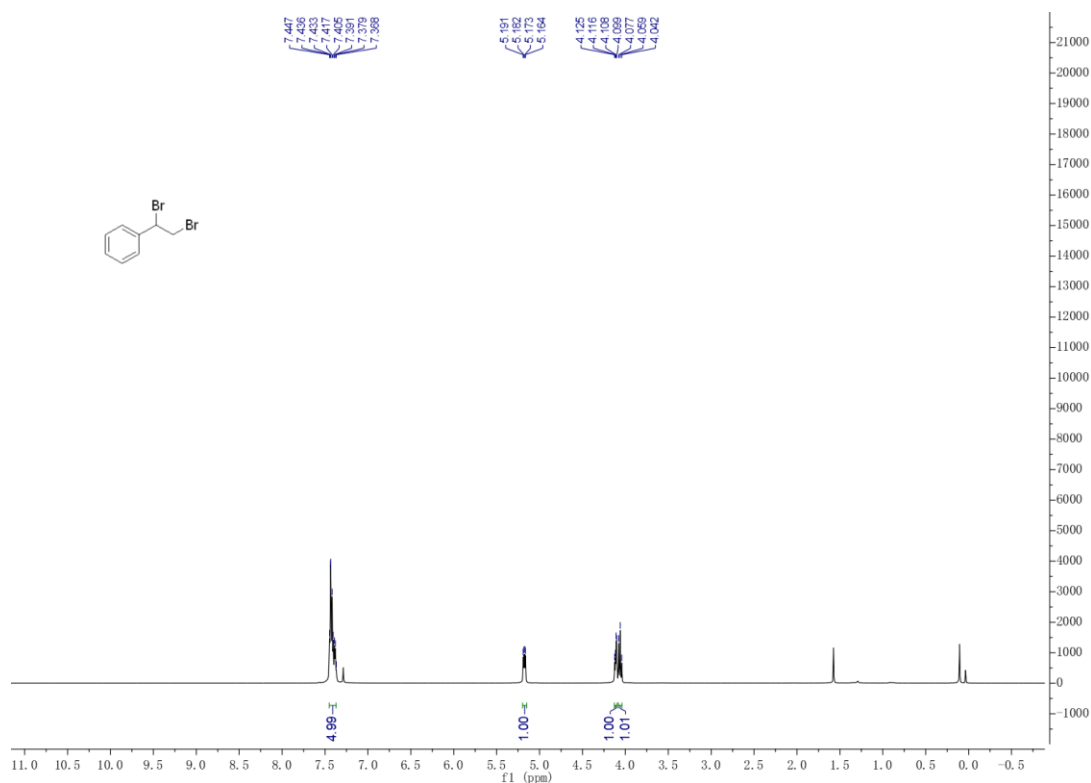


Figure S8. ^1H NMR of (1,2-dibromoethyl)benzene

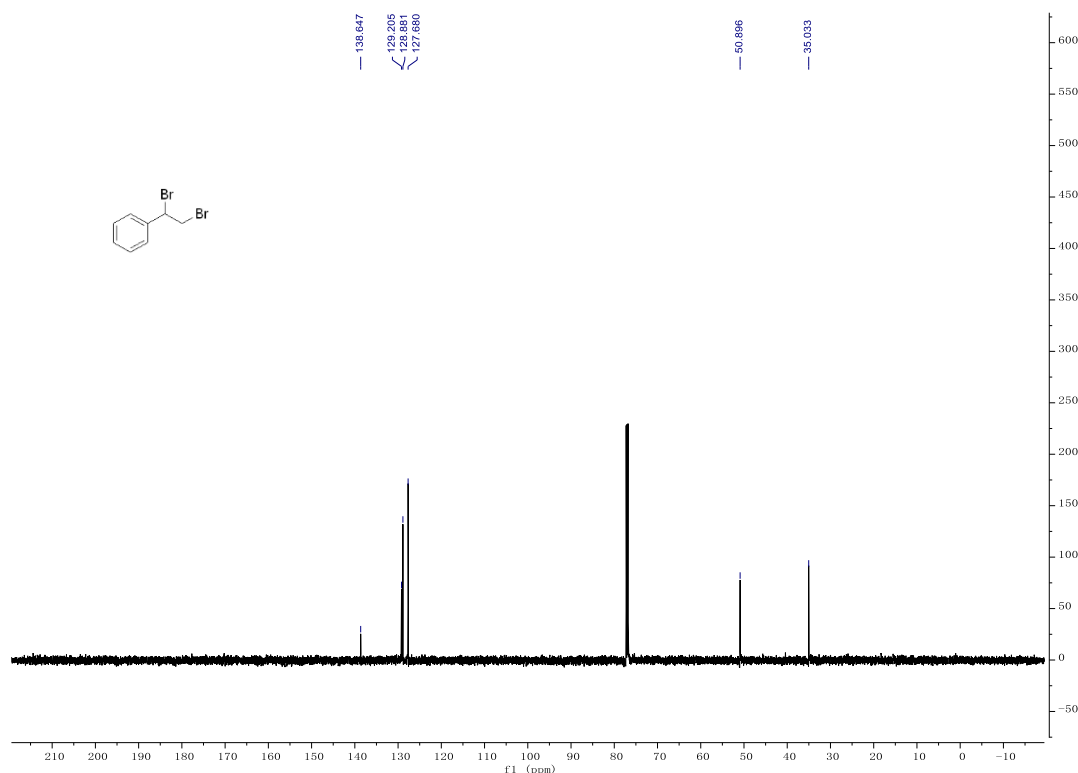
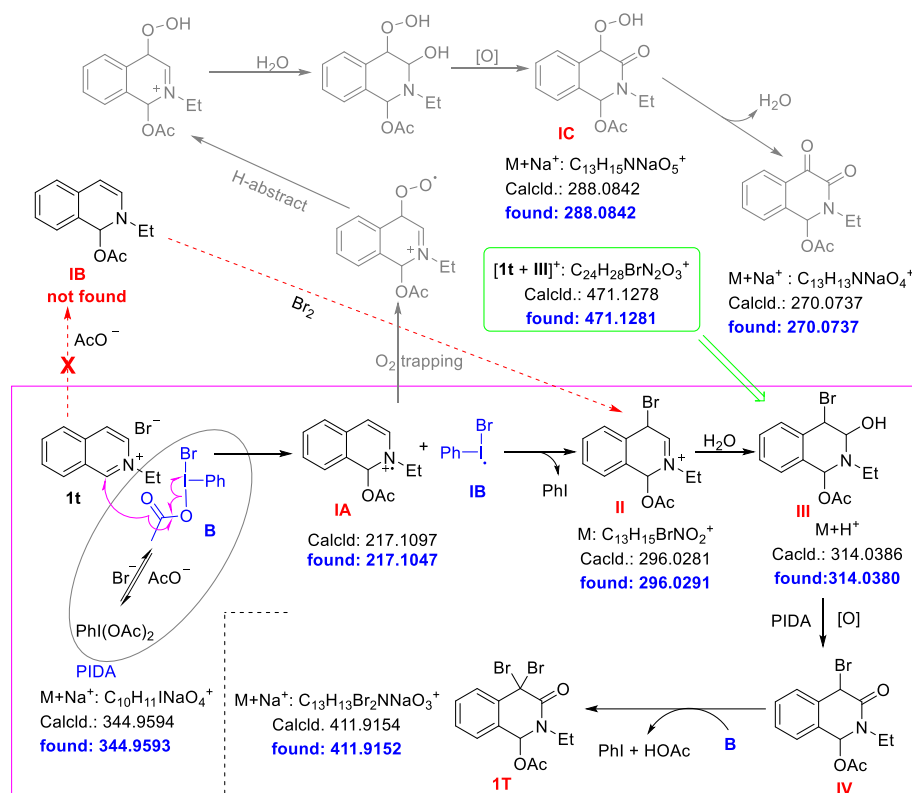


Figure S9. ^{13}C NMR of (1,2-dibromoethyl)benzene

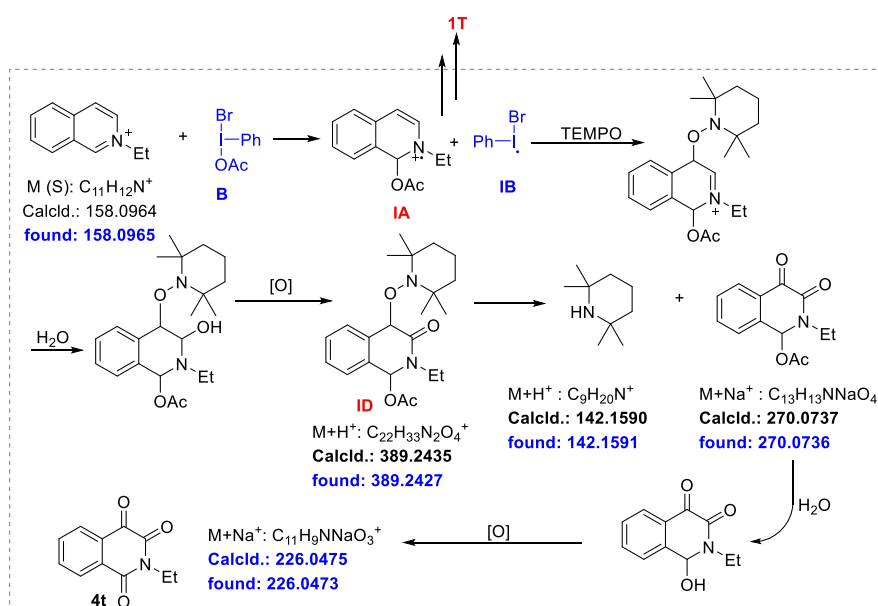
Characterization data of (1,2-dibromoethyl)benzene:^[1] Purification by flash column chromatography eluting with petroleum ether gave as white solid (16mg, 30%). ^1H NMR (600 MHz, Chloroform-*d*) δ 7.46 – 7.36 (m, 5H), 5.18 (dd, $J = 10.7, 5.3$ Hz, 1H), 4.11 (dd, $J = 10.3, 5.3$ Hz, 1H),

4.06 (t, $J = 10.5$ Hz, 1H). ^{13}C NMR (151 MHz, Chloroform- d) δ 138.65, 129.21, 128.88, 127.68, 50.90, 35.03.

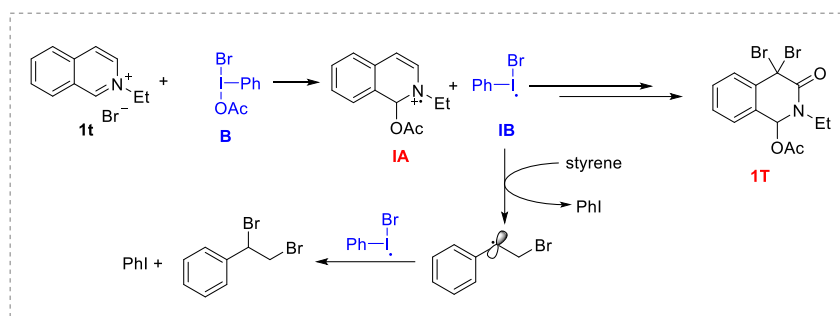
3.4 Possible reaction pathway for the PIDA-mediated oxidation



Scheme S1. Possible reaction pathway for the PIDA-mediated oxidation



Scheme S2. Possible reaction pathway for the TEMPO-added oxidation



Scheme S3. Possible reaction pathway for the styrene-added oxidation

4 Crystallographic data of 3a

Table S1 Crystal data and structure refinement for **3a**.

Empirical formula	C ₂₅ H ₁₆ BrNO ₄
Formula weight	474.30
Temperature/K	292.00(10)
Crystal system	monoclinic
Space group	P2 ₁ /c
a/Å	9.50407(12)
b/Å	13.07175(19)
c/Å	16.7222(2)
α/°	90
β/°	100.3725(13)
γ/°	90
Volume/Å ³	2043.53(5)
Z	4
ρ _{calc} /cm ³	1.542
μ/mm ⁻¹	3.024
F(000)	960.0
Crystal size/mm ³	0.31 × 0.28 × 0.24
Radiation	CuKα (λ = 1.54184)
2θ range for data collection/°	8.64 to 143.728
Index ranges	-11 ≤ h ≤ 11, -15 ≤ k ≤ 11, -20 ≤ l ≤ 20
Reflections collected	19329
Independent reflections	3926 [R _{int} = 0.0377, R _{sigma} = 0.0202]
Data/restraints/parameters	3926/0/280
Goodness-of-fit on F ²	1.129
Final R indexes [I >= 2σ (I)]	R ₁ = 0.0993, wR ₂ = 0.2526
Final R indexes [all data]	R ₁ = 0.1065, wR ₂ = 0.2595
Largest diff. peak/hole / e Å ⁻³	2.40/-2.09

Table S2. Bond lengths [Å] for **3a**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Br1	C17	1.938(6)	C8	C9	1.437(7)
O1	C9	1.207(7)	C8	C10	1.510(7)
O2	C1	1.366(7)	C10	C11	1.510(7)
O2	C9	1.370(7)	C11	C12	1.378(9)
O3	C7	1.353(6)	C11	C16	1.407(9)
O3	C17	1.464(7)	C12	C13	1.421(15)
O4	C18	1.219(7)	C13	C14	1.333(18)
N1	C10	1.469(7)	C14	C15	1.367(17)
N1	C18	1.341(8)	C15	C16	1.387(8)
N1	C19	1.467(6)	C16	C17	1.480(9)
C1	C2	1.397(7)	C17	C18	1.537(8)
C1	C6	1.380(7)	C19	C20	1.502(8)
C2	C3	1.368(9)	C20	C21	1.383(8)
C3	C4	1.368(10)	C20	C25	1.391(9)
C4	C5	1.375(9)	C21	C22	1.372(9)
C5	C6	1.404(8)	C22	C23	1.359(10)
C6	C7	1.443(7)	C23	C24	1.356(10)
C7	C8	1.344(7)	C24	C25	1.380(10)

Table S3. Bond Angles for **3a**

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C1	O2	C9	121.0(4)	C12	C11	C16	120.7(6)
C7	O3	C17	121.8(4)	C16	C11	C10	115.1(5)
C18	N1	C10	119.2(4)	C11	C12	C13	118.4(9)
C18	N1	C19	120.5(5)	C14	C13	C12	119.3(9)
C19	N1	C10	119.3(5)	C13	C14	C15	123.7(10)
O2	C1	C2	116.4(5)	C14	C15	C16	118.6(10)
O2	C1	C6	121.8(4)	C11	C16	C17	114.0(5)
C6	C1	C2	121.8(5)	C15	C16	C11	119.2(7)
C3	C2	C1	118.3(6)	C15	C16	C17	126.7(7)
C4	C3	C2	121.1(5)	O3	C17	Br1	100.7(4)
C3	C4	C5	120.7(6)	O3	C17	C16	111.1(5)
C4	C5	C6	120.0(6)	O3	C17	C18	108.6(5)
C1	C6	C5	118.0(5)	C16	C17	Br1	113.5(4)
C1	C6	C7	117.4(4)	C16	C17	C18	112.4(5)
C5	C6	C7	124.6(5)	C18	C17	Br1	109.9(4)
O3	C7	C6	113.0(4)	O4	C18	N1	125.0(6)
C8	C7	O3	126.0(4)	O4	C18	C17	122.5(6)
C8	C7	C6	121.1(4)	N1	C18	C17	112.5(5)
C7	C8	C9	119.6(4)	N1	C19	C20	112.4(4)
C7	C8	C10	121.7(4)	C21	C20	C19	121.4(6)

C9	C8	C10	118.6(4)	C21	C20	C25	117.4(5)
O1	C9	O2	116.0(5)	C25	C20	C19	121.2(5)
O1	C9	C8	125.0(5)	C22	C21	C20	120.8(6)
O2	C9	C8	119.0(5)	C23	C22	C21	120.8(6)
N1	C10	C8	110.4(4)	C24	C23	C22	119.8(6)
N1	C10	C11	109.6(4)	C23	C24	C25	120.3(6)
C8	C10	C11	108.5(4)	C24	C25	C20	120.8(6)
C12	C11	C10	124.1(7)				

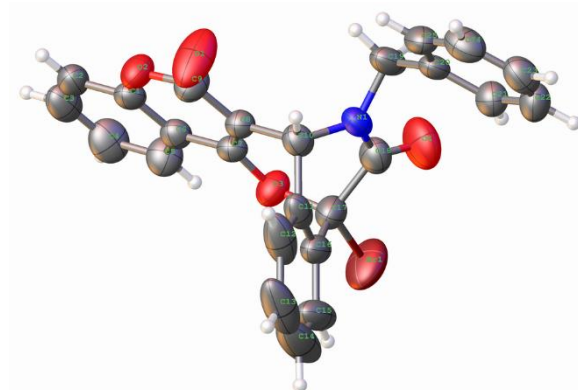
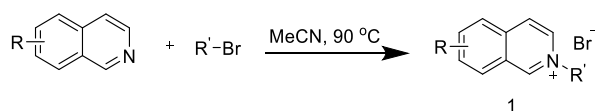


Figure S10. ORTEP drawing of **3a** with thermal ellipsoids at 50 % probability.

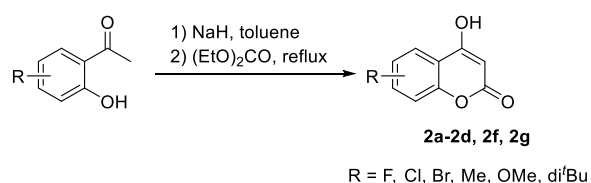
5 Syntheses of compounds 1-6

5.1 General procedure for the syntheses of **1**

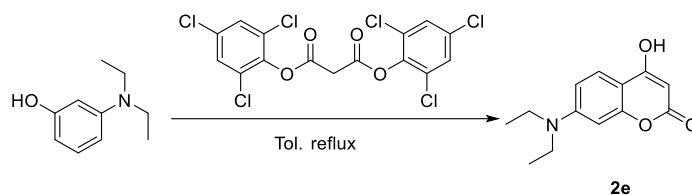


N-alkyl iminium salt **1** was prepared according to the literature procedure.^[2] An oven-dried flask was charged with CH₃CN (10 mL), Isoquinoline (3 mmol) and alkyl halide (3.3 mmol). The reaction mixture was refluxed until the Isoquinoline was consumed as indicated by TLC. Then it was cooled to room temperature, and concentrated under reduced pressure. The residue was diluted with diethyl ether, and the iminium salt was precipitated quickly. The solid was washed with diethyl ether to give purified **1**. If the iminium salt could not be precipitated, the residue was thoroughly washed with diethyl ether by ultrasonic vibration. Normally, washing three times will lead to the purified salt.

5.2 General procedure for the syntheses of **2**

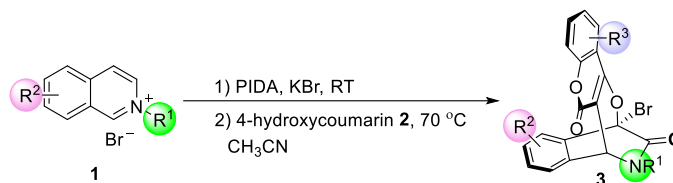


4-Hydroxy-2H-chromen-2-one (**2**) was prepared according to the literature procedure.^[3] NaH (50 mmol, 5 equiv) in 40 mL toluene was cooled in an ice bath. To the suspension was added 2'-hydroxyacetophenone (10 mmol, 1 equiv) in one portion and the result mixture was allowed to warm to room temperature and stirred for 30 min. Then diethyl carbonate (15 mmol, 1.5 equiv) was added to the reaction mixture at room temperature by drop-wise. The reaction was heated to reflux and stirred for 4 h. On completing of the reaction monitored by TLC, the reaction was allowed to cool to room temperature and the precipitate was collected and washed with 1N HCl solution and water to give the crude product. It was further purified by column chromatography to give the desired 4-hydroxycoumarin **2** as a white solid.

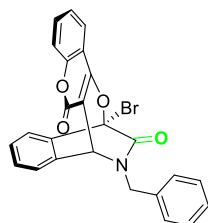


Prepared according to a reported literature.^[4] A solution of bis(2,4,6-trichlorophenyl) malonate (0.92 g, 2 mmol) and 3-(diethylamino)phenol (0.34 g, 2 mmol) in 5 mL toluene was heated to reflux for 5 h. After cooling down, the precipitation was collected and washed with cold toluene and hexane to afford the desired compound **2e** (317 mg, 68%) as a gray solid.

5.3 General procedure for the syntheses of **3**

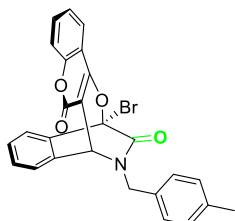


Under an argon atmosphere, a 5 mL Schlenk flask was charged with iminium salt **1** (0.2 mmol), PIDA (0.6 mmol), KBr (0.2 mmol), H₂O (7 μ L), and dry MeCN (2 mL). The mixture was continually stirred at room temperature until **1** was consumed as indicated by thin-layer chromatography (TLC, typically, for 8 h). 4-Hydroxycoumarin **2** (0.4 mmol) was added. The reaction mixture was heated at 70 °C in the oil bath until the intermediate was consumed as indicated by TLC (typically, for 8 h), then cooled to room temperature, diluted with water (5 mL), and extracted with ethyl acetate (3 \times 5 mL). The combined organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate as the eluent) to give the desired product **3**.



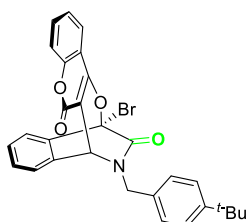
15-benzyl-12-bromo-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3a). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3a** as a white solid (68mg, 72%). mp 172 - 174 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.05 (d, *J* = 7.8 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.49 (t, *J* = 8.0 Hz, 1H), 7.45

(t, $J = 7.7$ Hz, 1H), 7.36 (t, $J = 7.5$ Hz, 1H), 7.25 (s, 5H), 7.22 (d, $J = 7.7$ Hz, 1H), 7.19 (d, $J = 8.3$ Hz, 1H), 7.17 (d, $J = 7.5$ Hz, 1H), 5.49 (s, 1H), 5.03 (d, $J = 14.7$ Hz, 1H), 4.62 (d, $J = 14.7$ Hz, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 162.27, 160.63, 159.24, 152.68, 138.97, 135.08, 132.90, 131.75, 131.46, 130.19, 129.34, 128.81, 128.54, 128.18, 124.37, 123.04, 122.31, 116.65, 114.96, 106.29, 97.88, 52.94, 50.73. HRMS (ESI-TOF) calcd for $\text{C}_{25}\text{H}_{16}\text{BrNO}_4$ [$\text{M} + \text{Na}$] $^+$: 496.0155; found: 496.0151.



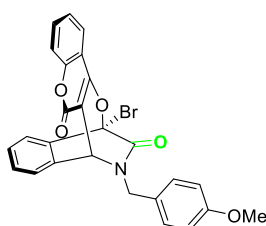
12-bromo-15-(4-methylbenzyl)-7,12-dihydro-6H-7,12-

(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3b). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3b** as a white solid (48mg, 49%). mp 197 – 199 °C ^1H NMR (600 MHz, Chloroform-*d*) δ 8.05 (d, $J = 7.8$ Hz, 1H), 7.75 – 7.72 (m, 1H), 7.53 – 7.49 (m, 1H), 7.45 (t, $J = 7.6$ Hz, 1H), 7.37 (t, $J = 7.5$ Hz, 1H), 7.26 – 7.17 (m, 2H), 7.17 – 7.13 (m, 2H), 7.06 (d, $J = 7.6$ Hz, 2H), 5.48 (s, 1H), 5.01 (d, $J = 14.5$ Hz, 1H), 4.55 (d, $J = 14.6$ Hz, 1H), 2.28 (s, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 162.22, 160.69, 159.24, 152.71, 139.02, 137.92, 132.86, 131.78, 130.16, 129.46, 129.28, 128.52, 124.36, 123.06, 122.31, 116.61, 115.02, 106.31, 97.91, 52.79, 50.45, 21.11. HRMS (ESI-TOF) calcd for $\text{C}_{26}\text{H}_{18}\text{BrNO}_4$ [$\text{M} + \text{H}$] $^+$: 488.0492; found: 488.0487.



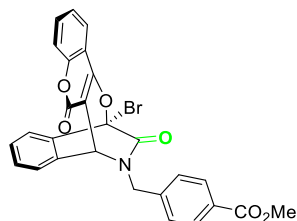
12-bromo-15-(4-(tert-butyl)benzyl)-7,12-dihydro-6H-7,12-

(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3c). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3c** as a white solid (73mg, 69%). mp 196 – 198 °C. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.05 (d, $J = 7.8$ Hz, 1H), 7.73 (dd, $J = 8.0, 1.6$ Hz, 1H), 7.50 (td, $J = 7.8$ Hz, 1.4 Hz, 1H), 7.45 (td, $J = 7.8$ Hz, 1.2 Hz, 1H), 7.38 (td, $J = 7.8$ Hz, 1.2 Hz, 1H), 7.26 – 7.21 (m, 3H), 7.21–7.17 (m, 4H), 5.50 (s, 1H), 4.91 (d, $J = 15.0$ Hz, 1H), 4.69 (d, $J = 14.4$ Hz, 1H), 1.24 (s, 9H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 162.30, 160.54, 159.07, 152.63, 151.16, 139.02, 132.77, 132.16, 131.72, 131.42, 130.19, 129.28, 128.24, 125.64, 124.31, 123.03, 122.33, 116.58, 114.99, 106.50, 97.89, 53.07, 50.54, 34.51, 31.22. HRMS (ESI-TOF) calcd for $\text{C}_{29}\text{H}_{24}\text{BrNO}_4$ [$\text{M} + \text{Na}$] $^+$: 552.0781; found: 552.0778.

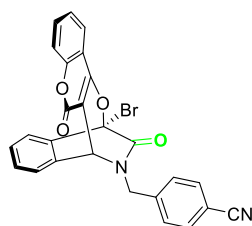


12-bromo-15-(4-methoxybenzyl)-7,12-dihydro-6H-7,12-

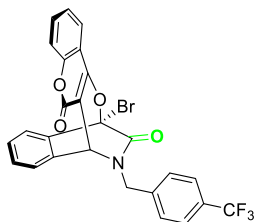
(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3d). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3d** as a white solid (66mg, 65%). mp 229 - 231 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.05 (d, *J* = 7.8 Hz, 1H), 7.73 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.53 – 7.49 (m, 1H), 7.44 (td, *J* = 7.7, 1.2 Hz, 1H), 7.38 – 7.35 (m, 1H), 7.21 (d, *J* = 8.3 Hz, 3H), 7.17 (d, *J* = 7.5 Hz, 2H), 6.78 (d, *J* = 8.5 Hz, 2H), 5.49 (s, 1H), 4.97 (d, *J* = 14.6 Hz, 1H), 4.54 (d, *J* = 14.6 Hz, 1H), 3.76 (s, 3H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 162.15, 160.70, 159.53, 159.23, 152.70, 139.02, 132.85, 131.79, 131.41, 130.15, 130.01, 129.27, 127.12, 124.36, 123.05, 122.30, 116.64, 115.02, 114.21, 106.32, 97.93, 55.25, 52.66, 50.17. HRMS (ESI-TOF) calcd for C₂₆H₁₈BrNO₅ [M + Na]⁺: 526.0261; found: 526.0258.



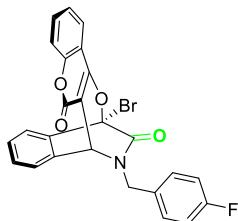
Methyl 4-((-12-bromo-6,14-dioxo-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromen-15-yl)methyl)benzoate (3e). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3e** as a white solid (68mg, 64%). mp 210 - 212 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.07 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.94 (d, *J* = 8.3 Hz, 2H), 7.74 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.52 (td, *J* = 8.0, 7.3, 1.6 Hz, 1H), 7.47 (td, *J* = 7.7, 1.3 Hz, 1H), 7.39 (td, *J* = 7.6, 1.2 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.27 (dd, *J* = 5.8, 2.3 Hz, 1H), 7.22 (d, *J* = 8.4 Hz, 1H), 7.18 (dd, *J* = 7.5, 1.3 Hz, 1H), 5.47 (s, 1H), 5.13 (d, *J* = 15.1 Hz, 1H), 4.62 (d, *J* = 15.1 Hz, 1H), 3.89 (s, 3H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 166.60, 162.40, 160.73, 159.40, 152.71, 140.19, 138.75, 133.06, 131.66, 131.59, 130.26, 130.13, 130.04, 129.48, 128.33, 124.48, 123.07, 122.32, 116.74, 114.90, 106.02, 97.64, 53.26, 52.13, 50.41. HRMS (ESI-TOF) calcd for C₂₇H₁₈BrNO₆ [M + Na]⁺: 554.0210; Found: 554.0207



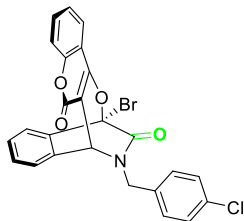
4-((-12-bromo-6,14-dioxo-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromen-15-yl)methyl)benzonitrile (3f). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3f** as a white solid (49mg, 49%). mp 230 - 232 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.07 (d, *J* = 7.8 Hz, 1H), 7.74 (d, *J* = 7.9 Hz, 1H), 7.57 (td, *J* = 8.1, 2.1 Hz, 2H), 7.49 (td, *J* = 7.8, 1.4 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.29 – 7.21 (m, 4H), 5.46 (s, 1H), 5.05 (d, *J* = 15.0 Hz, 1H), 4.69 (d, *J* = 15.0 Hz, 1H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 162.54, 160.72, 159.45, 152.71, 140.60, 138.54, 133.23, 132.64, 131.71, 131.56, 130.35, 129.63, 129.05, 124.57, 123.07, 122.32, 118.35, 116.79, 114.80, 112.24, 105.91, 97.40, 53.64, 50.53. HRMS (ESI-TOF) calcd for C₂₆H₁₅BrN₂O₄ [M + Na]⁺: 521.0107; found: 521.0105.



12-bromo-15-(4-(trifluoromethyl)benzyl)-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3g). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3g** as a white solid (46mg, 42%). mp 181 - 183 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 7.8 Hz, 1H), 7.76 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.54 (d, *J* = 7.8 Hz, 3H), 7.50 (t, *J* = 7.8 Hz, 1H), 7.42 (t, *J* = 7.2 Hz, 3H), 7.30 – 7.27 (m, 1H), 7.24 (d, *J* = 7.8 Hz, 2H), 5.50 (s, 1H), 5.11 (d, *J* = 15.0 Hz, 1H), 4.69 (d, *J* = 15.0 Hz, 1H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 162.49, 160.72, 159.38, 152.71, 139.28, 138.66, 133.09, 131.63, 130.47 (q, *J* = 33.2 Hz), 130.29, 129.53, 128.71, 125.80 (d, *J* = 3.8 Hz), 124.48, 123.9 (q, *J* = 272.2 Hz), 123.03, 122.34, 116.73, 114.85, 106.01, 97.54, 53.45, 50.36. ¹⁹F NMR (565 MHz, Chloroform-*d*) δ -62.72. HRMS (ESI-TOF) calcd for C₂₆H₁₅BrF₃NO₄ [M + Na]⁺: 564.0029; found: 564.0025.

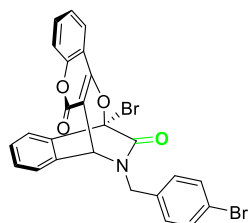


12-bromo-15-(4-fluorobenzyl)-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3h). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3h** as a white solid (48mg, 49%). mp 182 - 184 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.06 (d, *J* = 7.8 Hz, 1H), 7.73 (d, *J* = 7.8 Hz, 1H), 7.52 (t, *J* = 7.8 Hz, 1H), 7.46 (t, *J* = 7.8 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.29 – 7.23 (m, 3H), 7.20 (dd, *J* = 15.6, 7.8 Hz, 2H), 6.95 (t, *J* = 8.4 Hz, 2H), 5.48 (s, 1H), 4.98 (d, *J* = 15.0 Hz, 1H), 4.60 (d, *J* = 14.4 Hz, 1H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 162.60 (d, *J* = 3.3 Hz), 162.26, 160.71, 159.31, 152.69, 138.83, 133.00, 131.69, 131.52, 130.98 (d, *J* = 3.3 Hz), 130.40 (d, *J* = 8.2 Hz), 130.22, 129.41, 124.44, 123.04, 122.28, 116.71, 115.84, 115.70, 114.91, 106.15, 97.74, 52.96, 50.06. ¹⁹F NMR (565 MHz, Chloroform-*d*) δ -113.59. HRMS (ESI-TOF) calcd for C₂₅H₁₅BrFNO₄ [M + H]⁺: 492.0241; found: 492.0236.

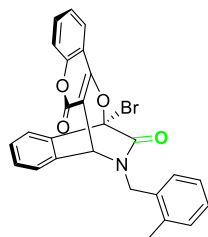


12-bromo-15-(4-chlorobenzyl)-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3i). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3i** as a white solid (53mg, 52%). mp 228 - 230 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.06 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.73 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.52 (td, *J* = 7.2, 1.8 Hz, 1H), 7.46 (td, *J* = 7.8, 1.2 Hz, 1H), 7.39 (td, *J* = 7.5, 1.2 Hz, 1H), 7.27 – 7.18 (m, 7H), 5.47 (s,

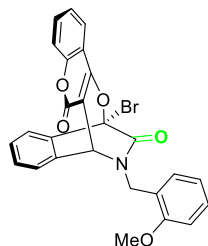
1H), 5.01 (d, $J = 15.0$ Hz, 1H), 4.55 (d, $J = 14.4$ Hz, 1H). ^{13}C NMR (151 MHz, Chloroform- d) δ 162.32, 160.75, 159.36, 152.71, 138.77, 134.17, 133.67, 133.03, 131.67, 131.56, 130.23, 129.91, 129.44, 129.02, 124.46, 123.05, 122.32, 116.73, 114.91, 106.08, 97.67, 53.08, 50.10. HRMS (ESI-TOF) calcd for $\text{C}_{25}\text{H}_{15}\text{BrClNO}_4$ $[\text{M} + \text{H}]^+$: 507.9946; found: 507.9941.



12-bromo-15-(4-bromobenzyl)-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3j). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3j** as a white solid (65mg, 59%). mp 231 - 233 °C. ^1H NMR (600 MHz, Chloroform- d) δ 8.06 (d, $J = 7.8$ Hz, 1H), 7.74 (dd, $J = 7.8, 1.8$ Hz, 1H), 7.53 (td, $J = 7.8, 1.8$ Hz, 1H), 7.47 (td, $J = 7.8, 1.2$ Hz, 1H), 7.39 (t, $J = 6.6$ Hz, 2H), 7.28 - 7.22 (m, 3H), 7.20 (d, $J = 7.2$ Hz, 1H), 7.15 (d, $J = 8.4$ Hz, 2H), 5.46 (s, 1H), 5.00 (d, $J = 15.0$ Hz, 1H), 4.53 (d, $J = 15.0$ Hz, 1H). ^{13}C NMR (151 MHz, Chloroform- d) δ 162.34, 160.75, 159.36, 152.73, 138.76, 134.20, 133.03, 131.99, 131.67, 131.57, 130.23, 130.21, 129.44, 124.46, 123.05, 122.32, 122.30, 116.74, 114.92, 106.07, 97.66, 53.12, 50.16. HRMS (ESI-TOF) calcd for $\text{C}_{25}\text{H}_{15}\text{Br}_2\text{NO}_4$ $[\text{M} + \text{H}]^+$: 551.9441; found: 551.9435.

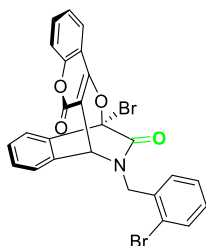


12-bromo-15-(2-methylbenzyl)-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3k). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3k** as a white solid (66mg, 67%). mp 170 - 172 °C. ^1H NMR (600 MHz, Chloroform- d) δ 8.06 (d, $J = 8.4$ Hz, 1H), 7.75 (dd, $J = 8.1, 1.5$ Hz, 1H), 7.51 (td, $J = 8.1, 1.5$ Hz, 1H), 7.45 (td, $J = 7.8, 1.6$ Hz, 1H), 7.36 (td, $J = 7.5, 1.2$ Hz, 1H), 7.26 - 7.19 (m, 3H), 7.19 - 7.13 (m, 2H), 7.12 (d, $J = 7.8$ Hz, 2H), 5.42 (s, 1H), 5.16 (d, $J = 15.0$ Hz, 1H), 4.51 (d, $J = 14.4$ Hz, 1H), 2.19 (s, 3H). ^{13}C NMR (151 MHz, Chloroform- d) δ 162.00, 160.66, 159.44, 152.73, 138.89, 137.08, 132.95, 132.58, 131.83, 131.46, 130.75, 130.15, 129.64, 129.34, 128.45, 126.36, 124.41, 123.06, 122.41, 116.70, 115.00, 106.00, 97.88, 52.01, 48.16, 19.10. HRMS (ESI-TOF) calcd for $\text{C}_{26}\text{H}_{18}\text{BrNO}_4$ $[\text{M} + \text{Na}]^+$: 510.0311; found: 510.0310.

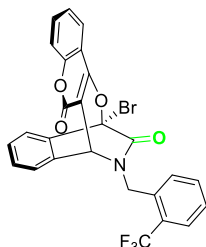


12-bromo-15-(2-methoxybenzyl)-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3l). Purification by flash

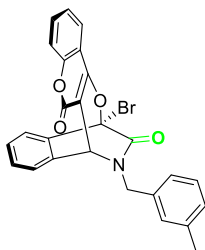
column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3l** as a white solid (70mg, 69%). mp 182 - 184 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.03 (d, *J* = 8.4 Hz, 1H), 7.74 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.49 (td, *J* = 7.8, 1.2 Hz, 1H), 7.43 (td, *J* = 7.8, 1.4 Hz, 1H), 7.37 (td, *J* = 7.8, 1.4 Hz, 1H), 7.25 – 7.21 (m, 4H), 7.19 (d, *J* = 8.4 Hz, 1H), 6.85 (t, *J* = 7.5 Hz, 1H), 6.74 (d, *J* = 8.4 Hz, 1H), 5.59 (s, 1H), 4.86 (d, *J* = 14.4 Hz, 1H), 4.82 (d, *J* = 15.0 Hz, 1H), 3.69 (s, 3H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 162.11, 160.32, 158.95, 157.70, 152.62, 139.50, 132.70, 131.80, 131.28, 130.89, 130.18, 129.65, 129.15, 124.29, 123.33, 122.97, 122.21, 120.58, 116.59, 115.12, 110.21, 106.56, 98.21, 55.11, 53.41, 46.70. HRMS (ESI-TOF) calcd for C₂₆H₁₈BrNO₅ [M + Na]⁺: 526.0261; found: 526.0261.



12-bromo-15-(2-bromobenzyl)-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3m). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3m** as a white solid (62mg, 56%). mp 206 - 208 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.07 (d, *J* = 7.8 Hz, 1H), 7.75 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.52 (dd, *J* = 11.7, 7.5 Hz, 2H), 7.47 (td, *J* = 7.8, 1.4 Hz, 1H), 7.40 (t, *J* = 7.5 Hz, 1H), 7.28 – 7.20 (m, 5H), 7.17 – 7.14 (m, 1H), 5.51 (s, 1H), 5.08 (d, *J* = 15.2 Hz, 1H), 4.80 (d, *J* = 15.2 Hz, 1H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 162.28, 160.47, 159.38, 152.71, 138.97, 134.24, 133.25, 132.96, 131.70, 131.53, 130.59, 130.28, 129.82, 129.43, 127.75, 124.42, 124.10, 123.07, 122.42, 116.69, 115.03, 106.09, 97.79, 53.22, 50.88. HRMS (ESI-TOF) calcd for C₂₅H₁₅Br₂NO₄ [M + Na]⁺: 573.9260; found: 573.9255.

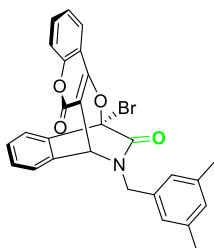


12-bromo-15-(2-(trifluoromethyl)benzyl)-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3n). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3n** as a white solid (50mg, 46%). mp 189 - 191 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 7.8 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.51 (dt, *J* = 16.0, 7.8 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.38 (t, *J* = 7.7 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.28 – 7.24 (m, 1H), 7.22 (dd, *J* = 8.0, 4.1 Hz, 2H), 7.14 (d, *J* = 7.6 Hz, 1H), 5.44 (s, 1H), 5.30 (d, *J* = 16.1 Hz, 1H), 4.84 (d, *J* = 16.2 Hz, 1H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 162.78, 160.41, 159.32, 152.75, 138.86, 133.56, 133.04, 132.06, 131.68, 131.63, 130.35, 129.54, 128.94, 128.84 (q, *J* = 30.7 Hz), 128.07, 126.50 (q, *J* = 5.7 Hz), 124.44, 124.12 (q, *J* = 205.4 Hz), 123.07, 122.40, 116.73, 114.93, 106.04, 97.59, 53.31, 46.93 (d, *J* = 3.1 Hz). ¹⁹F NMR (565 MHz, Chloroform-*d*) δ -59.55. HRMS (ESI-TOF) calcd for C₂₆H₁₅BrF₃NO₄ [M + Na]⁺: 564.0029; found: 564.0026.



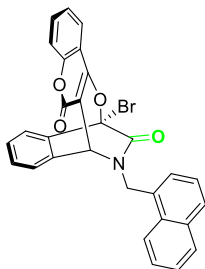
12-bromo-15-(3-methylbenzyl)-7,12-dihydro-6H-7,12-

(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3o). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3o** as a white solid (50mg, 51%). mp 175 - 177 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.06 (d, *J* = 7.8 Hz, 1H), 7.74 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.51 (td, *J* = 7.8, 2.2 Hz, 1H), 7.45 (td, *J* = 7.8, 1.2 Hz, 1H), 7.38 (td, *J* = 7.5, 1.2 Hz, 1H), 7.24 (d, *J* = 7.8 Hz, 1H), 7.22 – 7.18 (m, 2H), 7.14 (t, *J* = 7.8 Hz, 1H), 7.07 – 7.03 (m, 3H), 5.48 (s, 1H), 4.94 (d, *J* = 15.0 Hz, 1H), 4.65 (d, *J* = 15.0 Hz, 1H), 2.20 (s, 3H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 162.30, 160.57, 159.16, 152.69, 139.02, 138.51, 134.95, 132.86, 131.75, 131.41, 130.20, 129.30, 129.24, 128.90, 128.68, 125.56, 124.36, 123.04, 122.32, 116.61, 114.99, 106.42, 97.90, 52.98, 50.76, 21.14. HRMS (ESI-TOF) calcd for C₂₆H₁₈BrNO₄ [M + Na]⁺: 510.0311; found: 510.0308.



12-bromo-15-(3,5-dimethylbenzyl)-7,12-dihydro-6H-7,12-

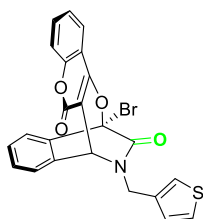
(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3p). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3p** as a white solid (54mg, 54%). mp 174 - 176 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.06 (d, *J* = 7.8 Hz, 1H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.50 (t, *J* = 8.1 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.27 – 7.18 (m, 3H), 6.85 (d, *J* = 5.4 Hz, 3H), 5.47 (s, 1H), 4.85 (d, *J* = 15.0 Hz, 1H), 4.67 (d, *J* = 14.4 Hz, 1H), 2.16 (s, 6H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 162.32, 160.48, 159.04, 152.70, 139.10, 138.37, 134.87, 132.80, 131.76, 131.37, 130.20, 129.73, 129.27, 126.29, 124.32, 123.02, 122.32, 116.57, 115.02, 106.57, 97.94, 53.03, 50.80, 21.02. HRMS (ESI-TOF) calcd for C₂₇H₂₀BrNO₄ [M + Na]⁺: 524.0468; found: 524.0466.



12-bromo-15-(naphthalen-1-ylmethyl)-7,12-dihydro-6H-7,12-

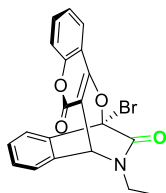
(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3q). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3q** as a white

solid (58mg, 55%). mp 191 - 193 °C. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.02 (d, $J = 7.8$ Hz, 1H), 7.88 (d, $J = 7.8$ Hz, 1H), 7.85 (d, $J = 7.8$ Hz, 1H), 7.73 (dd, $J = 7.5, 1.5$ Hz, 1H), 7.65 (dd, $J = 8.1, 1.5$ Hz, 1H), 7.56 (d, $J = 6.6$ Hz, 1H), 7.49 (t, $J = 7.5$ Hz, 1H), 7.43 (t, $J = 7.8$ Hz, 1H), 7.39 (t, $J = 7.8$ Hz, 1H), 7.28 (t, $J = 7.5$ Hz, 1H), 7.24 – 7.17 (m, 3H), 7.06 (dd, $J = 8.1, 5.7$ Hz, 2H), 5.44 (s, 1H), 5.31 (d, $J = 15.0$ Hz, 1H), 5.25 (d, $J = 14.4$ Hz, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 162.15, 159.91, 158.97, 152.51, 138.82, 133.76, 132.59, 131.55, 131.52, 131.36, 130.42, 130.18, 129.66, 129.27, 129.19, 128.56, 126.63, 125.72, 125.40, 124.16, 123.41, 122.83, 122.39, 116.47, 114.88, 106.28, 97.89, 51.88, 48.80. HRMS (ESI-TOF) calcd for $\text{C}_{29}\text{H}_{18}\text{BrNO}_4$ [$\text{M} + \text{Na}$] $^+$: 546.0311; found: 546.0307.



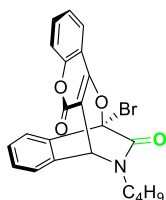
12-bromo-15-(thiophen-3-ylmethyl)-7,12-dihydro-6H-7,12-

(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3r). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3r** as a white solid (44mg, 46%). mp 213 - 215 °C. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.05 (dd, $J = 7.8, 1.2$ Hz, 1H), 7.72 (dt, $J = 8.4, 1.2$ Hz, 1H), 7.50 (t, $J = 8.4$ Hz, 1H), 7.45 (td, $J = 7.8, 1.2$ Hz, 1H), 7.39 (td, $J = 7.5, 1.2$ Hz, 1H), 7.27 (d, $J = 3.0$ Hz, 1H), 7.27 (d, $J = 3.0$ Hz, 1H), 7.23 (d, $J = 7.8$ Hz, 1H), 7.20 (d, $J = 8.4$ Hz, 1H), 7.17 (dd, $J = 4.8, 3.0$ Hz, 1H), 6.94 (dd, $J = 5.1, 1.5$ Hz, 1H), 5.53 (s, 1H), 4.91 (d, $J = 14.4$ Hz, 1H), 4.75 (d, $J = 15.0$ Hz, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 162.04, 160.66, 159.14, 152.67, 138.94, 135.62, 132.90, 131.71, 131.48, 130.21, 129.35, 127.44, 126.78, 124.53, 124.38, 123.03, 122.33, 116.66, 114.94, 106.30, 97.77, 53.01, 45.84. HRMS (ESI-TOF) calcd for $\text{C}_{23}\text{H}_{14}\text{BrNO}_4\text{S}$ [$\text{M} + \text{Na}$] $^+$: 501.9709; found: 501.9718.

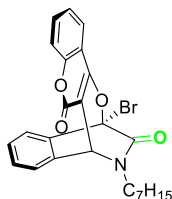


12-bromo-15-ethyl-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-

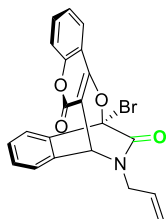
c]chromene-6,14-dione (3s). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3s** as a white solid (46mg, 43%). mp 224 - 226 °C. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.05 (d, $J = 7.2$ Hz, 1H), 7.75 (dd, $J = 7.8, 1.8$ Hz, 1H), 7.53 (td, $J = 7.8, 2.0$ Hz, 1H), 7.47 (t, $J = 7.8$ Hz, 1H), 7.44 (td, $J = 7.5, 1.4$ Hz, 1H), 7.38 (dd, $J = 7.2, 1.2$ Hz, 1H), 7.28 – 7.24 (m, 3H), 5.54 (s, 1H), 3.80 – 3.65 (m, 2H), 1.24 (td, $J = 7.2, 1.4$ Hz, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 161.44, 160.91, 159.36, 152.76, 139.18, 132.94, 131.97, 131.40, 130.18, 129.32, 124.45, 123.12, 122.25, 116.72, 115.11, 106.64, 98.07, 53.49, 42.92, 13.17. HRMS (ESI-TOF) calcd for $\text{C}_{20}\text{H}_{14}\text{BrNO}_4$ [$\text{M} + \text{H}$] $^+$: 412.0179; found: 412.0177.



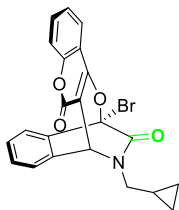
12-bromo-15-butyl-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3t). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3t** as a white solid (50mg, 57%). mp 164 - 166 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.05 (d, *J* = 7.8 Hz, 1H), 7.76 (d, *J* = 9.0 Hz, 1H), 7.53 (td, *J* = 7.8, 1.6 Hz, 1H), 7.47 (td, *J* = 7.8, 1.4 Hz, 1H), 7.44 (td, *J* = 7.5, 1.2 Hz, 1H), 7.37 (dd, *J* = 7.2, 1.8 Hz, 1H), 7.26 (d, *J* = 8.4 Hz, 2H), 5.52 (s, 1H), 3.71 – 3.60 (m, 2H), 1.65 – 1.58 (m, 2H), 1.31 – 1.23 (m, 2H), 0.88 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 161.75, 160.95, 159.36, 152.75, 139.17, 132.95, 131.95, 131.41, 130.20, 129.32, 124.46, 123.13, 122.27, 116.73, 115.09, 106.49, 98.12, 53.83, 47.78, 29.95, 19.93, 13.64. HRMS (ESI-TOF) calcd for C₂₂H₁₈BrNO₄ [M + H]⁺: 440.0492; found: 440.0490.



12-bromo-15-heptyl-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3u). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3u** as a white solid (46mg, 48%). mp 140 - 142 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.05 (d, *J* = 7.2 Hz, 1H), 7.75 (d, *J* = 7.8 Hz, 1H), 7.53 (t, *J* = 7.8 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.37 (d, *J* = 7.2 Hz, 1H), 7.29 – 7.21 (m, 2H), 5.51 (s, 1H), 3.68 – 3.62 (m, 2H), 1.64 – 1.58 (m, 2H), 1.30 – 1.07 (m, 8H), 0.79 (t, *J* = 6.9 Hz, 3H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 161.73, 160.89, 159.32, 152.74, 139.21, 132.92, 131.96, 131.38, 130.20, 129.30, 124.43, 123.11, 123.10, 122.26, 116.70, 115.09 (d, *J* = 2.7 Hz), 106.56, 98.15, 53.86, 48.13, 31.52, 28.79, 27.92, 26.65, 22.40, 13.93. HRMS (ESI-TOF) calcd for C₂₅H₂₄BrNO₄ [M + H]⁺: 482.0961; found: 482.0959.

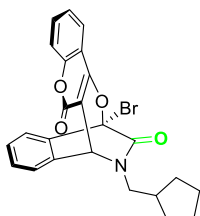


15-allyl-12-bromo-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3v). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3v** as a white solid (55mg, 65%). mp 180 - 182 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.06 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.74 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.55 – 7.49 (m, 1H), 7.47 (td, *J* = 8.1, 1.4 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.35 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.26 – 7.22 (m, 2H), 5.81 – 5.73 (m, 1H), 5.53 (s, 1H), 5.31 (d, *J* = 18.6 Hz, 1H), 5.26 (d, *J* = 10.2 Hz, 1H), 4.42 (dd, *J* = 5.7, 1.5 Hz, 1H), 4.09 (dd, *J* = 15.3, 6.9 Hz, 1H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 161.80, 160.80, 159.44, 152.79, 139.02, 132.94, 131.93, 131.47, 130.94, 130.20, 129.34, 124.42, 123.10, 122.39, 119.97, 116.72, 115.08, 106.36, 97.81, 52.92, 49.71. HRMS (ESI-TOF) calcd for C₂₁H₁₄BrNO₄ [M + H]⁺: 424.0179; found: 424.0176.



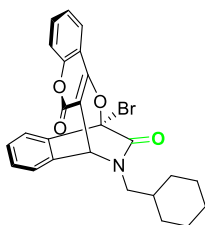
12-bromo-15-(cyclopropylmethyl)-7,12-dihydro-6H-7,12-

(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3w). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3w** as a white solid (54mg, 62%). mp 204 - 206 °C. ¹H NMR (600 MHz, Chloroform-d) δ 8.06 (d, J = 7.8 Hz, 1H), 7.76 (dd, J = 7.8, 2.4 Hz, 1H), 7.53 (t, J = 7.8 Hz, 1H), 7.48 (t, J = 7.8 Hz, H), 7.44 (td, J = 7.5, 1.2 Hz 1H), 7.39 (d, J = 7.2 Hz, 1H), 7.28 – 7.23 (m, 2H), 5.69 (s, 1H), 3.60 – 3.46 (m, 2H), 1.12 – 1.05 (m, 1H), 0.52 – 0.48 (m, 2H), 0.37 – 0.32 (m, 2H). ¹³C NMR (151 MHz, Chloroform-d) δ 161.84, 160.95, 159.23, 152.73, 139.27, 132.87, 131.91, 131.40, 130.23, 129.30, 124.42, 123.12, 123.10, 122.33, 116.70, 115.11, 106.70, 98.08, 53.54, 52.14, 9.53, 3.78. HRMS (ESI-TOF) calcd for C₂₂H₁₆BrNO₄ [M + H]⁺: 438.0355; found: 438.0332.



12-bromo-15-(cyclopentylmethyl)-7,12-dihydro-6H-7,12-

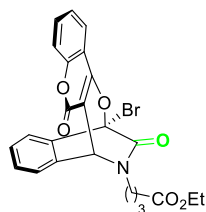
(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3x). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3x** as a white solid (44mg, 47%). mp 206 - 208 °C. ¹H NMR (600 MHz, Chloroform-d) δ 8.06 (d, J = 7.8 Hz, 1H), 7.75 (d, J = 7.2 Hz, 1H), 7.52 (t, J = 7.8 Hz, 1H), 7.47 (t, J = 7.8 Hz, 1H), 7.44 (t, J = 7.5 Hz, 1H), 7.37 (d, J = 7.8 Hz, 1H), 7.27 – 7.24 (m, 2H), 5.54 (s, 1H), 3.63 (dd, J = 13.2, 7.2 Hz, 1H), 3.54 (dd, J = 13.5, 8.7 Hz, 1H), 2.33 - 2.28 (m, 1H), 1.72 – 1.58 (m, 3H), 1.57 – 1.43 (m, 3H), 1.30 – 1.23 (m, 1H), 1.20 – 1.13 (m, 1H). ¹³C NMR (151 MHz, Chloroform-d) δ 162.03, 160.95, 159.33, 152.75, 139.24, 132.93, 131.95, 131.40, 130.24, 129.31, 124.45, 123.13, 122.28, 116.72, 115.06, 106.46, 98.24, 53.97, 52.49, 30.30, 30.19, 25.15, 24.97. HRMS (ESI-TOF) calcd for C₂₄H₂₀BrNO₄ [M + H]⁺: 466.0648; found: 466.0646.



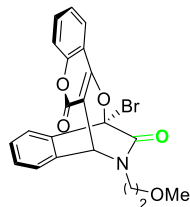
12-bromo-15-(cyclohexylmethyl)-7,12-dihydro-6H-7,12-

(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3y). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3y** as a white solid (53mg, 55%). mp 200 - 202 °C. ¹H NMR (600 MHz, Chloroform-d) δ 8.06 (d, J = 7.8 Hz, 1H), 7.75 (d, J = 7.2 Hz, 1H), 7.53 (t, J = 7.8 Hz, 1H), 7.47 (t, J = 7.8 Hz, 1H), 7.44 (t, J = 7.5 Hz, 1H), 7.36

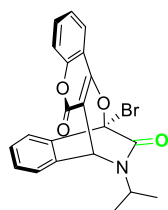
(d, $J = 7.2$ Hz, 1H), 7.28 – 7.23 (m, 2H), 5.49 (s, 1H), 3.63 (dd, $J = 13.8, 6.6$ Hz, 1H), 3.34 (dd, $J = 13.8, 8.4$ Hz, 1H), 1.76 – 1.71 (m, 1H), 1.68 – 1.52 (m, 5H), 1.20 – 1.06 (m, 3H), 1.04 – 0.91 (m, 2H). ^{13}C NMR (151 MHz, Chloroform- d) δ 162.12, 160.99, 159.34, 152.75, 139.16, 132.94, 132.01, 131.42, 130.22, 129.32, 124.44, 123.13, 122.32, 116.70, 115.06, 106.36, 98.21, 54.57, 54.31, 36.74, 30.75, 30.50, 26.20, 25.58. HRMS (ESI-TOF) calcd for $\text{C}_{25}\text{H}_{22}\text{BrNO}_4$ [$\text{M} + \text{H}$] $^+$: 480.0805; found: 480.0801.



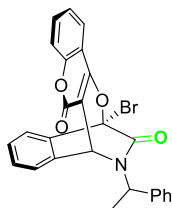
4-(12-bromo-6,14-dioxo-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-15-yl)butanoate (3z). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3z** as a white solid (43mg, 43%). mp 138 - 140 °C. ^1H NMR (600 MHz, Chloroform- d) δ 8.05 (dd, $J = 7.5, 1.5$ Hz, 1H), 7.75 (dd, $J = 8.1, 1.5$ Hz, 1H), 7.53 (td, $J = 7.8, 1.6$ Hz, 1H), 7.48 (td, $J = 7.8, 1.4$ Hz, 1H), 7.45 (td, $J = 7.5, 1.4$ Hz, 1H), 7.39 (dd, $J = 7.2, 1.8$ Hz, 1H), 7.27 – 7.24 (m, 2H), 5.55 (s, 1H), 4.08 – 4.03 (m, 2H), 3.81 – 3.76 (m, 1H), 3.65 – 3.61 (m, 1H), 2.27 (t, $J = 7.5$ Hz, 2H), 1.98 (p, $J = 7.2$ Hz, 2H), 1.21 (t, $J = 6.9$ Hz, 3H). ^{13}C NMR (151 MHz, Chloroform- d) δ 172.41, 162.04, 160.89, 159.37, 152.77, 139.00, 133.01, 131.80, 131.50, 130.21, 129.41, 124.46, 123.12, 122.43, 116.73, 115.04, 106.35, 97.89, 60.56, 54.03, 47.28, 31.35, 23.32, 14.15. HRMS (ESI-TOF) calcd for $\text{C}_{24}\text{H}_{20}\text{BrNO}_6$ [$\text{M} + \text{H}$] $^+$: 498.0547; found: 498.0549.



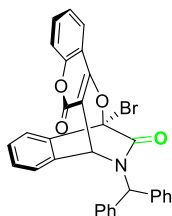
12-bromo-15-(2-methoxyethyl)-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3aa). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3aa** as a white solid (44mg, 50%). mp 140 - 142 °C. ^1H NMR (600 MHz, Chloroform- d) δ 8.07 (dd, $J = 7.5, 1.5$ Hz, 1H), 7.77 (dd, $J = 8.1, 1.5$ Hz, 1H), 7.54 (dd, $J = 7.8, 1.6$ Hz, 1H), 7.48 (td, $J = 7.8, 1.4$ Hz, 1H), 7.45 (td, $J = 7.5, 1.4$ Hz, 1H), 7.39 (dd, $J = 7.5, 1.8$ Hz, 1H), 7.30 – 7.24 (m, 2H), 5.68 (s, 1H), 3.94 (m, 1H), 3.79 (m, 1H), 3.61 – 3.52 (m, 2H), 3.23 (s, 3H). ^{13}C NMR (151 MHz, Chloroform- d) δ 162.07, 160.86, 158.76, 152.72, 139.54, 132.74, 131.72, 131.36, 130.19, 129.19, 124.34, 123.06, 122.44, 116.64, 115.18, 106.89, 97.95, 70.29, 58.68, 55.18, 47.96. HRMS (ESI-TOF) calcd for $\text{C}_{21}\text{H}_{16}\text{BrNO}_5$ [$\text{M} + \text{H}$] $^+$: 442.0285; found: 442.0282.



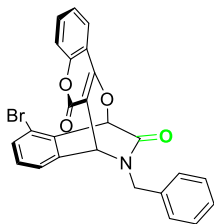
12-bromo-15-isopropyl-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3ab). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3ab** as a white solid (35mg, 41%). mp 232 - 234 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.05 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.76 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.52 (td, *J* = 7.8, 2.0 Hz, 1H), 7.46 (td, *J* = 7.5, 1.4 Hz, 1H), 7.43 (td, *J* = 7.5, 1.6 Hz, 1H), 7.38 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.26 – 7.23 (m, 2H), 5.62 (s, 1H), 4.87 – 4.81 (m, 1H), 1.28 (d, *J* = 7.2 Hz, 3H), 1.24 (d, *J* = 6.6 Hz, 3H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 161.27, 160.51, 159.33, 152.80, 139.67, 132.88, 131.97, 131.46, 130.27, 129.30, 124.44, 123.15, 121.98, 116.72, 115.13, 107.20, 98.50, 48.07, 47.14, 20.54, 19.36. HRMS (ESI-TOF) calcd for C₂₁H₁₆BrNO₄ [M + H]⁺: 426.0355; found: 426.0331.



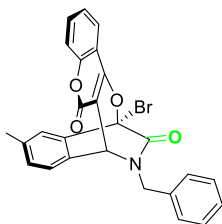
12-bromo-15-(1-phenylethyl)-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3ac). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3ac** as a white solid (34mg, 35%). mp 245 - 247 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.03 (d, *J* = 7.8 Hz, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.53 (td, *J* = 7.8, 1.6 Hz, 1H), 7.41 (t, *J* = 7.8 Hz, 1H), 7.31 – 7.28 (m, 3H), 7.28 – 7.24 (m, 5H), 6.88 (d, *J* = 7.2 Hz, 1H), 5.97 – 5.92 (m, 1H), 5.34 (s, 1H), 1.65 (d, *J* = 7.2 Hz, 3H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 161.60, 160.40, 159.35, 152.79, 139.51, 138.21, 132.90, 131.58, 131.29, 130.07, 129.15, 128.73, 128.07, 127.44, 124.43, 123.15, 121.89, 116.71, 115.06, 107.08, 98.34, 53.47, 48.84, 16.94. HRMS (ESI-TOF) calcd for C₂₆H₁₈BrNO₄ [M + H]⁺: 488.0492; found: 488.0487.



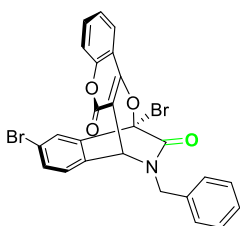
15-benzhydryl-12-bromo-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3ad). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3ad** as a white solid (35mg, 32%). mp 255 - 257 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.09 (d, *J* = 7.8 Hz, 1H), 7.70 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.52 – 7.41 (m, 3H), 7.33 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.30 (dd, *J* = 5.4, 1.8 Hz, 3H), 7.24 – 7.20 (m, 5H), 7.15 (s, 1H), 7.13 (d, *J* = 7.8 Hz, 1H), 7.10 – 7.05 (m, 2H), 5.61 (s, 1H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 162.94, 159.56, 158.39, 152.49, 139.84, 137.99, 137.02, 132.64, 131.66, 131.23, 130.69, 129.54, 129.45, 128.74, 128.69, 128.44, 127.82, 124.22, 122.98, 122.02, 116.47, 114.79, 107.15, 97.97, 62.84, 50.92. HRMS (ESI-TOF) calcd for C₃₁H₂₀BrNO₄ [M + H]⁺: 550.0648; found: 550.0463.



15-benzyl-11-bromo-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3ae). Until iminium salt **1ae** was consumed as indicated by TLC (for 8 h). 4-Hydroxycoumarin **2a** (0.4 mmol) and anhydrous DMF (0.5 mL) was added. The reaction mixture was heated at 70 °C in the oil bath until the intermediate was consumed as indicated by TLC (for 8 h), then cooled to room temperature. Diluted with water (5 mL), and extracted with ethyl acetate (3 × 5 mL). The combined organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) **3ae** as a white solid (36 mg, 38%). mp 255 - 257 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 7.81 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.56 (d, *J* = 8.4 Hz, 1H), 7.53 – 7.49 (m, 1H), 7.27 – 7.24 (m, 3H), 7.23 (t, *J* = 8.7 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 1H), 7.19 (d, *J* = 7.8 Hz, 1H), 7.14 (d, *J* = 7.2 Hz, 1H), 6.23 (s, 1H), 5.45 (s, 1H), 5.02 (d, *J* = 15.0 Hz, 1H), 4.51 (d, *J* = 15.0 Hz, 1H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 165.63, 160.98, 159.29, 152.78, 143.67, 135.23, 132.85, 132.76, 132.04, 129.61, 128.79, 128.38, 128.07, 124.26, 123.79, 123.12, 121.74, 116.63, 115.70, 106.13, 79.30, 53.20, 48.76. HRMS (ESI-TOF) calcd for C₂₅H₁₆BrNO₄ [M + H]⁺: 474.0335; found: 474.0335.

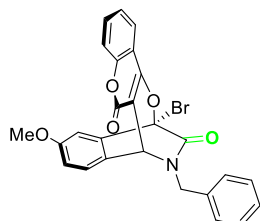


15-benzyl-12-bromo-10-methyl-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3af). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3af** as a white solid (43mg, 44%). mp 226 - 228 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 7.86 (s, 1H), 7.73 (d, *J* = 7.8 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 1H), 7.26 – 7.22 (m, 6H), 7.20 (d, *J* = 8.4 Hz, 1H), 7.16 (d, *J* = 7.2 Hz, 1H), 7.06 (d, *J* = 7.2 Hz, 1H), 5.45 (s, 1H), 5.04 (d, *J* = 14.4 Hz, 1H), 4.59 (d, *J* = 14.4 Hz, 1H), 2.40 (s, 3H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 162.35, 160.68, 159.17, 152.67, 139.51, 136.22, 135.14, 132.80, 131.90, 131.59, 130.70, 128.78, 128.50, 128.12, 124.33, 123.02, 122.27, 116.62, 115.05, 106.53, 98.13, 52.68, 50.68, 21.37. HRMS (ESI-TOF) calcd for C₂₆H₁₈BrNO₄ [M + Na]⁺: 510.0311; found: 510.0310.



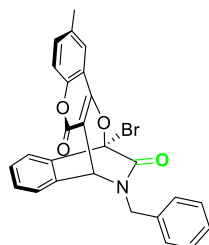
15-benzyl-10,12-dibromo-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-

c]chromene-6,14-dione (3ag). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3ag** as a white solid (62mg, 56%). mp 223 - 226 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.21 (d, *J* = 1.8 Hz, 1H), 7.73 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.50 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.26 (dp, *J* = 7.9, 4.1 Hz, 6H), 7.22 (d, *J* = 8.4 Hz, 1H), 7.05 (d, *J* = 7.8 Hz, 1H), 5.46 (s, 1H), 5.05 (d, *J* = 15.0 Hz, 1H), 4.57 (d, *J* = 15.0 Hz, 1H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 161.65, 160.50, 159.33, 152.72, 137.76, 134.82, 134.43, 133.58, 133.32, 133.11, 128.87 (d, *J* = 3.3 Hz), 128.53 (d, *J* = 3.3 Hz), 128.30, 124.50, 123.93, 123.36, 123.02, 116.71 (d, *J* = 3.3 Hz), 114.78, 105.90, 96.58, 52.33, 50.72. HRMS (ESI-TOF) calcd for C₂₅H₁₅Br₂NO₄ [M + Na]⁺: 573.9260; found: 573.9257.

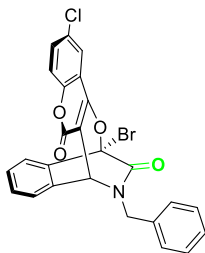


15-benzyl-12-bromo-9-methoxy-7,12-dihydro-6H-7,12-

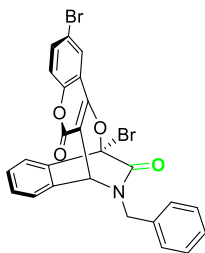
(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3ah). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3ah** as a white solid (44mg, 44%). mp 178 - 180 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 7.73 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.61 (d, *J* = 2.4 Hz, 1H), 7.50 (td, *J* = 7.8, 1.8 Hz, 1H), 7.26 – 7.23 (m, 6H), 7.21 (d, *J* = 8.4 Hz, 1H), 7.09 (d, *J* = 8.4 Hz, 1H), 6.85 (dd, *J* = 8.4, 2.4 Hz, 1H), 5.43 (s, 1H), 5.04 (d, *J* = 15.0 Hz, 1H), 4.58 (d, *J* = 15.0 Hz, 1H), 3.84 (s, 3H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 162.20, 160.69, 160.52, 159.04, 152.65, 135.11, 133.11, 132.79, 131.43, 128.78, 128.50, 128.12, 124.35, 123.70, 122.99, 116.63, 116.37, 116.25, 115.04, 106.88, 98.04, 55.68, 52.37, 50.68. HRMS (ESI-TOF) calcd for C₂₆H₁₈BrNO₅ [M + Na]⁺: 526.0261; found: 526.0259.



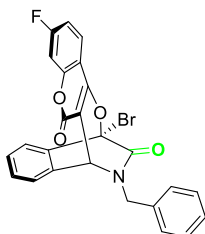
15-benzyl-12-bromo-2-methyl-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3aj). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3aj** as a white solid (70mg, 72%). mp 224 - 226 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.05 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.49 (d, *J* = 1.8 Hz, 1H), 7.44 (td, *J* = 7.8, 1.2 Hz, 1H), 7.36 (td, *J* = 7.5, 1.2 Hz, 1H), 7.30 (d, *J* = 9.0 Hz, 1H), 7.27 – 7.23 (m, 5H), 7.17 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.09 (dd, *J* = 9.0, 1.8 Hz, 1H), 5.49 (s, 1H), 5.02 (d, *J* = 14.4 Hz, 1H), 4.62 (d, *J* = 15.0 Hz, 1H), 2.37 (s, 3H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 162.29, 160.81, 159.26, 150.88, 139.02, 135.11, 134.26, 133.94, 131.79, 131.41, 130.13, 129.27, 128.78, 128.53, 128.15, 122.59, 122.29, 116.40, 114.61, 106.16, 97.90, 52.99, 50.72, 20.87. HRMS (ESI-TOF) calcd for C₂₆H₁₈BrNO₄ [M + Na]⁺: 510.0311; found: 510.0309.



15-benzyl-12-bromo-2-chloro-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3ak). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3ak** as a white solid (61mg, 60%). mp 228 - 230 °C. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.06 (d, J = 7.8 Hz, 1H), 7.69 (d, J = 2.3 Hz, 1H), 7.47 (d, J = 7.8 Hz, 1H), 7.45 (d, J = 8.4 Hz, 1H), 7.38 (t, J = 7.8 Hz, 1H), 7.26 (s, 5H), 7.18 (d, J = 7.5 Hz, 1H), 7.15 (dd, J = 8.8, 1.8 Hz, 1H), 5.46 (s, 1H), 4.98 (dd, J = 14.8, 1.9 Hz, 1H), 4.66 (dd, J = 14.7, 1.9 Hz, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 162.04, 160.06, 158.06, 151.01, 138.74, 135.02, 132.88, 131.57, 130.28, 130.09, 129.50, 128.82, 128.56, 128.24, 122.57, 122.35, 118.12, 116.10, 107.21, 97.80, 52.91, 50.82. HRMS (ESI-TOF) calcd for $\text{C}_{25}\text{H}_{15}\text{BrClNO}_4$ [$\text{M} + \text{Na}$] $^+$: 529.9765; found: 529.9763.

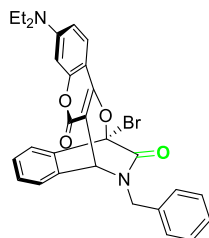


15-benzyl-2,12-dibromo-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3al). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3al** as a white solid (53mg, 48%). mp 224 - 226 °C. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.06 (d, J = 7.8 Hz, 1H), 7.82 (d, J = 2.4 Hz, 1H), 7.58 (dd, J = 8.7, 2.1 Hz, 1H), 7.46 (t, J = 7.8 Hz, 1H), 7.38 (t, J = 7.5 Hz, 1H), 7.25 (s, 6H), 7.17 (d, J = 7.8 Hz, 1H), 7.08 (d, J = 8.4 Hz, 1H), 5.46 (s, 1H), 4.97 (d, J = 14.4 Hz, 1H), 4.66 (d, J = 15.0 Hz, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 162.03, 159.99, 157.96, 151.49, 138.73, 135.71, 135.02, 131.57, 130.29, 129.51, 128.83, 128.57, 128.24, 125.58, 122.35, 118.38, 117.31, 116.51, 107.20, 97.81, 52.91, 50.83. HRMS (ESI-TOF) calcd for $\text{C}_{25}\text{H}_{18}\text{Br}_2\text{NO}_4$ [$\text{M} + \text{Na}$] $^+$: 573.9260; found: 573.9256.



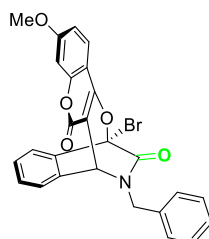
15-benzyl-12-bromo-3-fluoro-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3am). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3am** as a white solid (54 mg, 55%). mp 185 - 187 °C. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.05 (d, J = 7.8 Hz, 1H), 7.73 (dd, J = 9.0, 6.0 Hz, 1H), 7.46 (td, J = 7.5, 1.4 Hz, 1H), 7.38 (td, J = 7.5, 1.2 Hz, 1H), 7.26 (s, 5H), 7.17 (dd, J = 7.8, 1.2 Hz, 1H), 6.98 (td,

$J = 7.8, 2.0$ Hz, 1H), 6.92 (dd, $J = 8.7, 1.5$, Hz, 1H), 5.45 (s, 1H), 5.00 (d, $J = 15.0$ Hz, 1H), 4.64 (d, $J = 15.0$ Hz, 1H). ^{13}C NMR (151 MHz, Chloroform- d) δ 165.16 (d, $J = 255.3$ Hz), 162.17, 160.43, 158.90, 153.86 (d, $J = 13.1$ Hz), 138.90, 135.02, 131.65, 131.54, 130.23, 129.39, 128.82, 128.55, 128.23, 125.09 (d, $J = 10.4$ Hz), 122.32, 112.65 (d, $J = 22.7$ Hz), 111.58 (d, $J = 2.7$ Hz), 105.40 (d, $J = 2.4$ Hz), 104.20 (d, $J = 25.9$ Hz), 97.87, 52.92, 50.77. ^{19}F NMR (565 MHz, Chloroform- d) δ -103.11. HRMS (ESI-TOF) calcd for $\text{C}_{25}\text{H}_{15}\text{BrFNO}_4$ $[\text{M} + \text{H}]^+$: 492.0241; found: 492.0240.



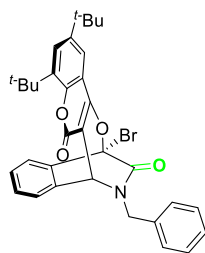
15-benzyl-12-bromo-3-(diethylamino)-7,12-dihydro-6H-7,12-

(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3an). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3an** as a white solid (80 mg, 73%). mp 156 - 158 °C. ^1H NMR (600 MHz, Chloroform- d) δ 7.51 (d, $J = 9.0$ Hz, 2H), 7.34 (td, $J = 7.2, 1.6$ Hz, 1H), 7.31 (td, $J = 7.5, 1.4$ Hz, 1H), 7.26 – 7.22 (m, 3H), 7.21 (dd, $J = 7.8, 1.8$ Hz, 1H), 7.18 (dd, $J = 7.2, 1.5$ Hz, 1H), 6.52 (dd, $J = 9.0, 2.4$ Hz, 1H), 6.35 (d, $J = 1.8$ Hz, 1H), 5.69 (s, 1H), 5.43 (s, 1H), 5.06 (d, $J = 14.4$ Hz, 1H), 4.46 (d, $J = 15.0$ Hz, 1H), 3.36 (q, $J = 7.0$ Hz, 4H), 1.16 (t, $J = 7.2$ Hz, 6H). ^{13}C NMR (151 MHz, Chloroform- d) δ 166.86, 162.16, 160.59, 155.33, 151.03, 142.71, 135.68, 130.44, 130.28, 128.66, 128.57, 128.33, 128.24, 127.75, 123.93, 122.32, 108.74, 104.07, 101.06, 97.15, 80.35, 53.68, 48.66, 44.88, 12.35. HRMS (ESI-TOF) calcd for $\text{C}_{29}\text{H}_{25}\text{BrN}_2\text{O}_4$ $[\text{M} + \text{H}]^+$: 545.1070; found: 545.1073.



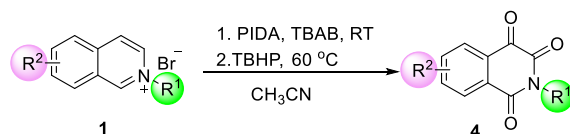
15-benzyl-12-bromo-3-methoxy-7,12-dihydro-6H-7,12-

(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3ao). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3ao** as a white solid (65 mg, 64%). mp 175 - 177 °C. ^1H NMR (600 MHz, Chloroform- d) δ 8.05 (d, $J = 7.8$ Hz, 1H), 7.62 (d, $J = 8.9$ Hz, 1H), 7.44 (t, $J = 7.8$ Hz, 1H), 7.36 (t, $J = 7.6$ Hz, 1H), 7.26 (s, 5H), 7.16 (d, $J = 7.5$ Hz, 1H), 6.80 (dd, $J = 9.0, 2.3$ Hz, 1H), 6.67 (d, $J = 2.5$ Hz, 1H), 5.45 (s, 1H), 5.04 (d, $J = 14.7$ Hz, 1H), 4.59 (d, $J = 14.7$ Hz, 1H), 3.83 (s, 3H). ^{13}C NMR (151 MHz, Chloroform- d) δ 163.69, 162.39, 161.10, 159.79, 154.59, 139.19, 135.13, 131.87, 131.37, 130.13, 129.15, 128.78, 128.53, 128.11, 124.21, 122.23, 112.68, 108.09, 103.49, 100.44, 97.89, 55.81, 53.01, 50.64. HRMS (ESI-TOF) calcd for $\text{C}_{26}\text{H}_{18}\text{BrNO}_5$ $[\text{M} + \text{H}]^+$: 504.0441; found: 504.0441.

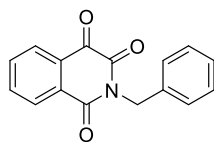


15-benzyl-12-bromo-2,4-di-tert-butyl-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (3ap). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (8/1, v/v) gave **3ap** as a white solid (81mg, 69%). mp 193 - 195 °C. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.10 (d, $J = 7.8$ Hz, 1H), 7.60 (d, $J = 2.2$ Hz, 1H), 7.58 (d, $J = 2.4$ Hz, 1H), 7.47 (t, $J = 7.7$ Hz, 1H), 7.39 (t, $J = 7.7$ Hz, 1H), 7.32 – 7.26 (m, 5H), 7.22 (d, $J = 7.6$ Hz, 1H), 5.53 (s, 1H), 5.05 (d, $J = 14.8$ Hz, 1H), 4.68 (d, $J = 14.7$ Hz, 1H), 1.46 (s, 9H), 1.35 (s, 9H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 162.47, 160.28, 159.92, 149.55, 146.60, 139.06, 137.19, 135.22, 131.90, 131.32, 130.15, 129.18, 128.74, 128.59, 128.09, 128.08, 122.29, 116.96, 114.55, 105.36, 97.88, 52.92, 50.67, 35.11, 34.81, 31.29, 29.89. HRMS (ESI-TOF) calcd for $\text{C}_{33}\text{H}_{32}\text{BrNO}_4$ $[\text{M} + \text{H}]^+$: 586.1587; found: 586.1592.

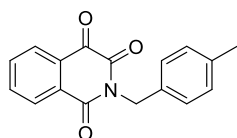
5.4 General procedure for the syntheses of **4**



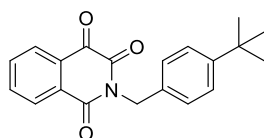
To the mixture of *N*-alkyl iminium salt **1** (0.3 mmol), PIDA (0.9 mmol), TBAB (0.3 mmol) was added dry MeCN (2 mL) and H_2O (5.5 μL) in a 5 mL reaction flask. The mixture was continually stirred at room temperature until **1** was consumed as indicated by TLC (typically, for 8 h). TBHP (0.6 mmol, in decane) was added. The reaction mixture was heated at 60 °C in the oil bath until the intermediate was consumed as indicated by TLC (typically, for 48 h), then cooled to room temperature, diluted with water (5 mL), and extracted with ethyl acetate (3 \times 5 mL). The combined organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate as the eluent) to give the desired product **4**.



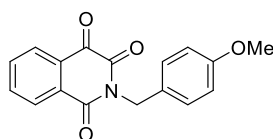
2-benzylisoquinoline-1,3,4(2H)-trione (4a) ^[5]. Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4a** (76mg, 96%) as a light yellow solid. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.35 (dd, $J = 7.8, 1.2$ Hz, 1H), 8.20 (dd, $J = 7.7, 1.3$ Hz, 1H), 7.89 (td, $J = 7.6, 1.4$ Hz, 1H), 7.82 (td, $J = 7.6, 1.3$ Hz, 1H), 7.52 – 7.48 (m, 2H), 7.33 – 7.29 (m, 2H), 7.29 – 7.27 (m, 1H), 5.24 (s, 2H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.60, 162.15, 156.98, 136.03, 135.90, 134.47, 130.86, 129.94, 129.89, 129.41, 128.61, 128.04, 127.80, 44.34.



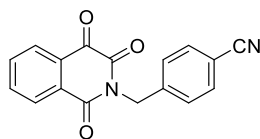
2-(4-methylbenzyl)isoquinoline-1,3,4(2H)-trione (4b) ^[5]. Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4b** (70mg, 84%) as a light yellow solid. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.35 (d, *J* = 7.8 Hz, 1H), 8.20 (d, *J* = 7.7 Hz, 1H), 7.91 – 7.87 (m, 1H), 7.83 – 7.79 (m, 1H), 7.40 (d, *J* = 7.7 Hz, 2H), 7.12 (d, *J* = 7.7 Hz, 2H), 5.21 (s, 2H), 2.30 (s, 3H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 174.66, 162.14, 157.01, 137.86, 136.02, 134.43, 132.95, 130.83, 129.93, 129.44, 129.27, 127.77, 44.10, 21.11.



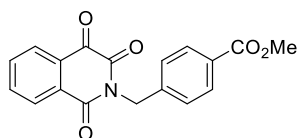
2-(4-(tert-butyl)benzyl)isoquinoline-1,3,4(2H)-trione (4c) ^[5]. Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4c** (78mg, 81%) as a light light yellow solid. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.35 (dd, *J* = 7.8, 1.2 Hz, 1H), 8.19 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.88 (td, *J* = 7.5, 1.3 Hz, 1H), 7.81 (td, *J* = 7.8, 1.2 Hz, 1H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 5.21 (s, 3H), 1.28 (s, 9H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 174.68, 162.16, 157.02, 151.07, 136.03, 134.44, 132.90, 130.82, 129.93, 129.28, 129.26, 127.76, 125.52, 43.99, 34.53, 31.28.



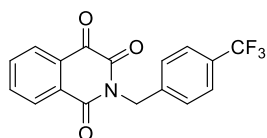
2-(4-methoxybenzyl)isoquinoline-1,3,4(2H)-trione (4d) ^[5]. Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4d** (69mg, 78%) as a light yellow solid. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.35 (d, *J* = 7.8 Hz, 1H), 8.19 (d, *J* = 7.7 Hz, 1H), 7.89 (t, *J* = 7.6 Hz, 1H), 7.81 (t, *J* = 7.6 Hz, 1H), 7.47 (d, *J* = 8.3 Hz, 2H), 6.83 (d, *J* = 8.6 Hz, 2H), 5.18 (s, 2H), 3.77 (s, 3H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 174.68, 162.15, 159.40, 156.96, 136.00, 134.41, 131.07, 130.84, 129.94, 129.90, 128.17, 127.76, 113.94, 55.25, 43.79.



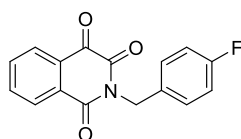
4-((1,3,4-trioxo-3,4-dihydroisoquinolin-2(1H)-yl)methyl)benzonitrile (4e) ^[5]. Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4e** (63mg, 72%) as a light yellow solid. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.36 (dd, *J* = 7.8, 1.2 Hz, 1H), 8.23 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.93 (td, *J* = 7.5, 1.2 Hz, 1H), 7.86 (td, *J* = 7.5, 1.2 Hz, 1H), 7.61 (s, 4H), 5.28 (s, 2H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 174.22, 162.12, 156.89, 140.85, 136.24, 134.82, 132.46, 130.86, 130.05, 129.51, 128.02, 118.43, 112.11, 43.92.



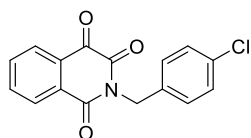
methyl 4-((1,3,4-trioxo-3,4-dihydroisoquinolin-2(1H)-yl)methyl)benzoate (4f) ^[5]. Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4f** (81mg, 72%) as a light yellow solid. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.36 (dd, $J = 7.8, 1.2$ Hz, 1H), 8.22 (dd, $J = 7.8, 1.2$ Hz, 1H), 7.98 (d, $J = 8.4$ Hz, 2H), 7.91 (td, $J = 7.5, 1.2$ Hz, 1H), 7.84 (td, $J = 7.5, 1.2$ Hz, 1H), 7.55 (d, $J = 8.4$ Hz, 2H), 5.28 (s, 2H), 3.89 (s, 3H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 174.40, 166.65, 162.12, 156.93, 130.87, 130.01, 129.93, 129.87, 129.69, 129.18, 127.92, 52.10, 44.04.



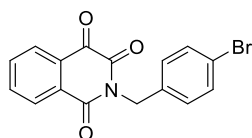
2-(4-(trifluoromethyl)benzyl)isoquinoline-1,3,4(2H)-trione (4g) ^[6]. Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4g** (64mg, 64%) as a light yellow solid. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.36 (dd, $J = 7.8, 1.8$ Hz, 1H), 8.22 (dd, $J = 7.8, 1.2$ Hz, 1H), 7.92 (td, $J = 7.5, 1.4$ Hz, 1H), 7.84 (td, $J = 7.5, 1.4$ Hz, 1H), 7.62 (d, $J = 8.4$ Hz, 2H), 7.57 (d, $J = 8.4$ Hz, 2H), 5.29 (s, 2H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 174.34, 162.13, 156.92, 139.67, 136.17, 134.70, 130.85, 130.32 (q, $J = 32.5$ Hz), 130.01, 129.70, 129.63, 127.94, 125.59 (q, $J = 3.8$ Hz), 123.95 (q, $J = 271.8$ Hz), 43.85. ¹⁹F NMR (565 MHz, Chloroform-*d*) δ -62.73.



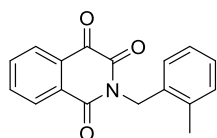
2-(4-fluorobenzyl)isoquinoline-1,3,4(2H)-trione (4h) ^[5]. Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4h** (64mg, 67%) as a light yellow solid. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.35 (d, $J = 7.8$ Hz, 1H), 8.21 (d, $J = 7.8$ Hz, 1H), 7.91 (t, $J = 7.5$ Hz, 1H), 7.83 (t, $J = 7.5$ Hz, 1H), 7.51 (td, $J = 7.8$ Hz, 1.8 Hz 2H), 6.99 (td, $J = 8.6, 1.7$ Hz, 2H), 5.20 (s, 2H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 174.52, 162.48 (d, $J = 247.03$ Hz), 162.13, 156.94, 136.10, 134.57, 131.72 (d, $J = 3.2$ Hz), 131.50 (d, $J = 7.8$ Hz), 130.83, 129.96, 129.78, 127.86, 115.54 (d, $J = 21.1$ Hz), 115.40, 43.60. ¹⁹F NMR (565 MHz, Chloroform-*d*) δ -113.75.



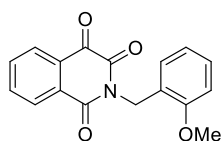
2-(4-chlorobenzyl)isoquinoline-1,3,4(2H)-trione (4i) ^[5]. Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4i** (73mg, 81%) as a light yellow solid. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.35 (d, $J = 7.8$ Hz, 1H), 8.21 (d, $J = 7.8$ Hz, 1H), 7.90 (t, $J = 7.5$ Hz, 1H), 7.83 (t, $J = 7.8$ Hz, 1H), 7.45 (d, $J = 7.8$ Hz, 2H), 7.28 (d, $J = 8.4$ Hz, 2H), 5.20 (s, 2H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 174.46, 162.11, 156.93, 136.12, 134.61, 134.31, 134.06, 130.97, 130.83, 129.97, 129.73, 128.79, 127.89, 43.67.



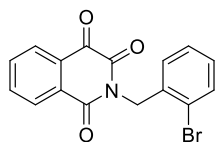
2-(4-bromobenzyl)isoquinoline-1,3,4(2H)-trione (4j) ^[5]. Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4j** (86mg, 83%) as a light yellow solid. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.35 (d, *J* = 7.8 Hz, 1H), 8.21 (d, *J* = 7.8 Hz, 1H), 7.91 (t, *J* = 7.8 Hz, 1H), 7.83 (t, *J* = 7.5 Hz, 1H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 8.4 Hz, 2H), 5.19 (s, 2H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 174.45, 162.11, 156.94, 136.14, 134.80, 134.63, 131.77, 131.28, 130.82, 129.98, 129.72, 127.90, 122.22, 43.74.



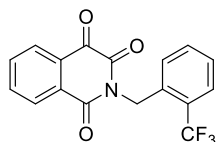
2-(2-methylbenzyl)isoquinoline-1,3,4(2H)-trione (4k) ^[5]. Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4k** (77mg, 92%) as a light yellow solid. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.36 (d, *J* = 7.8 Hz, 1H), 8.24 (dd, *J* = 7.8 Hz, 1.2 Hz, 1H), 7.92 (td, *J* = 7.8 Hz, 1.2 Hz, 1H), 7.85 (td, *J* = 7.8 Hz, 1.2 Hz, 1H), 7.19 – 7.08 (m, 4H), 5.27 (s, 2H), 2.51 (s, 3H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 174.60, 162.27, 157.17, 136.17, 136.12, 134.55, 133.71, 130.91, 130.54, 130.05, 129.90, 127.87, 127.60, 126.93, 126.17, 41.83, 19.44.



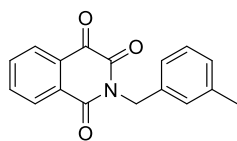
2-(2-methoxybenzyl)isoquinoline-1,3,4(2H)-trione (4l). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4l** (71mg, 80%) as a light yellow solid. mp 168 - 170 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.34 (d, *J* = 7.8 Hz, 1H), 8.23 (d, *J* = 7.8 Hz, 1H), 7.89 (t, *J* = 7.5 Hz, 1H), 7.83 (t, *J* = 7.5 Hz, 1H), 7.23 (t, *J* = 7.8 Hz, 1H), 7.14 (d, *J* = 7.8 Hz, 1H), 6.87 (dd, *J* = 7.8, 4.8 Hz, 2H), 5.29 (s, 2H), 3.84 (s, 3H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 174.84, 162.08, 157.28, 156.99, 136.02, 134.37, 130.94, 130.05, 129.94, 128.79, 128.43, 127.77, 123.70, 120.43, 110.62, 55.52, 40.12. HRMS (ESI-TOF) calcd for C₁₇H₁₃NO₄ [M + H]⁺: 296.0917; found: 296.0915.



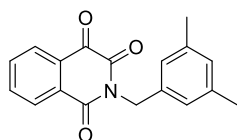
2-(2-bromobenzyl)isoquinoline-1,3,4(2H)-trione (4m) ^[5]. Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4m** (85mg, 82%) as a light yellow solid. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.36 (d, *J* = 7.2 Hz, 1H), 8.26 (d, *J* = 7.8 Hz, 1H), 7.93 (t, *J* = 7.5 Hz, 1H), 7.87 (t, *J* = 7.5 Hz, 1H), 7.58 (d, *J* = 7.8 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.12 (t, *J* = 7.8 Hz, 1H), 7.06 (d, *J* = 7.8 Hz, 1H), 5.35 (s, 2H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 174.43, 162.05, 156.99, 136.22, 134.72, 134.50, 133.11, 130.96, 130.11, 129.69, 129.02, 127.98, 127.60, 127.56, 123.02, 44.77.



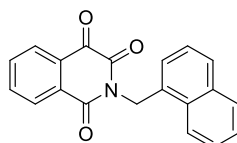
2-(2-(trifluoromethyl)benzyl)isoquinoline-1,3,4(2H)-trione (4n). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4n** (73mg, 73%) as a light yellow solid. mp 210 - 212 °C. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.37 (d, J = 7.8 Hz, 1H), 8.28 (d, J = 7.2 Hz, 1H), 7.94 (t, J = 7.5 Hz, 1H), 7.89 (t, J = 7.5 Hz, 1H), 7.71 (d, J = 7.8 Hz, 1H), 7.43 (t, J = 7.8 Hz, 1H), 7.36 (t, J = 7.8 Hz, 1H), 7.07 (d, J = 7.8 Hz, 1H), 5.48 (s, 2H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.31, 162.09, 157.02, 136.28, 134.82, 133.97, 132.11, 131.00, 130.13, 129.58, 128.04, 127.74 (q, J = 30.9 Hz), 127.40, 127.03, 126.42 (q, J = 5.7 Hz), 124.30 (q, J = 274.2 Hz), 41.36 (q, J = 3.6 Hz). ^{19}F NMR (565 MHz, Chloroform-*d*) δ -60.42. HRMS (ESI-TOF) calcd for $\text{C}_{17}\text{H}_{10}\text{F}_3\text{NO}_3$ [M + H] $^+$: 334.0686; found: 334.0681.



2-(3-methylbenzyl)isoquinoline-1,3,4(2H)-trione (4o) ^[5]. Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4o** (66mg, 79%) as a light yellow solid. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.36 (dd, J = 7.8 Hz, 1.2 Hz, 1H), 8.21 (dd, J = 7.8 Hz, 1.2 Hz, 1H), 7.89 (td, J = 7.8 Hz, 1.2 Hz, 1H), 7.82 (td, J = 7.5 Hz, 1.2 Hz, 1H), 7.30 (d, J = 9.0 Hz, 2H), 7.20 (t, J = 7.5 Hz, 1H), 7.08 (d, J = 7.5 Hz, 1H), 5.21 (s, 2H), 2.32 (s, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.65, 162.14, 157.02, 138.34, 136.04, 135.78, 134.46, 130.85, 130.02, 129.97, 129.93, 128.80, 128.50, 127.80, 126.43, 44.33, 21.33.

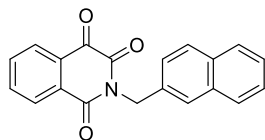


2-(3,5-dimethylbenzyl)isoquinoline-1,3,4(2H)-trione (4p) ^[5]. Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4p** (60mg, 68%) as a light yellow solid. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.34 (d, J = 7.8 Hz, 1H), 8.19 (d, J = 7.2 Hz, 1H), 7.89 (t, J = 7.8 Hz, 1H), 7.81 (t, J = 7.5 Hz, 1H), 7.10 (s, 2H), 6.89 (s, 1H), 5.16 (s, 2H), 2.27 (s, 6H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.66, 162.13, 156.99, 138.19, 135.99, 135.74, 134.40, 130.86, 129.96, 129.95, 129.66, 127.74, 127.07, 44.26, 21.20.

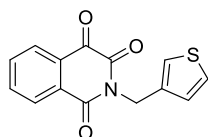


2-(naphthalen-1-ylmethyl)isoquinoline-1,3,4(2H)-trione (4q). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4q** (68mg, 72%) as a light yellow solid. mp 188 - 190 °C. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.33 (d, J = 7.8 Hz, 1H), 8.26 (d, J = 8.4 Hz, 1H), 8.21 (d, J = 7.2 Hz, 1H), 7.91 - 7.83 (m, 2H), 7.81 (t, J = 7.5 Hz, 1H), 7.77 (d, J = 7.8 Hz, 1H), 7.57 (t, J = 7.8 Hz, 1H), 7.49 (t, J = 7.5 Hz, 1H), 7.44 (d, J = 7.2 Hz, 1H), 7.37 (t, J = 7.5 Hz,

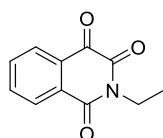
1H), 5.73 (s, 2H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 174.52, 162.33, 157.24, 136.10, 134.55, 133.79, 131.23, 130.88, 130.07, 129.88, 128.83, 128.54, 127.83, 126.53, 126.02, 125.85, 125.22, 123.34, 41.95. HRMS (ESI-TOF) calcd for C₂₀H₁₃NO₃ [M + H]⁺: 316.0968; found: 316.0967



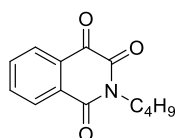
2-(naphthalen-2-ylmethyl)isoquinoline-1,3,4(2H)-trione (4r). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4r** (78mg, 80%) as a light yellow solid. mp 186 - 188 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.35 (dd, *J* = 7.8, 1.8 Hz, 1H), 8.20 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.97 (s, 1H), 7.88 (td, *J* = 7.5, 1.4 Hz, 1H), 7.83 – 7.79 (m, 2H), 7.78 (d, *J* = 8.4 Hz, 2H), 7.61 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.44 (qd, *J* = 6.6, 2.1 Hz, 2H), 5.40 (s, 2H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 174.60, 162.19, 157.08, 136.05, 134.49, 133.26, 132.96, 130.85, 129.97, 129.87, 128.70, 128.37, 128.00, 127.82, 127.60, 127.04, 126.23, 126.22, 44.52. HRMS (ESI-TOF) calcd for C₂₀H₁₃NO₃ [M + H]⁺: 316.0968; found: 316.0967



2-(thiophen-3-ylmethyl)isoquinoline-1,3,4(2H)-trione (4s). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4s** (63mg, 77%) as a light yellow solid. mp 154 - 156 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.34 (dd, *J* = 7.8, 1.2 Hz, 1H), 8.19 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.89 (td, *J* = 7.8, 1.2 Hz, 1H), 7.81 (td, *J* = 7.8, 1.4 Hz, 1H), 7.43 (dd, *J* = 2.7, 1.5 Hz, 1H), 7.22 (dd, *J* = 4.8, 3.0 Hz, 1H), 7.20 (dd, *J* = 4.8, 1.2 Hz, 1H), 5.21 (s, 2H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 174.61, 161.94, 156.72, 136.03, 135.90, 134.47, 130.86, 129.87, 129.84, 128.76, 127.79, 125.76, 125.73, 38.94. HRMS (ESI-TOF) calcd for C₁₄H₉NO₃S [M + H]⁺: 272.0376; found: 232.0374.

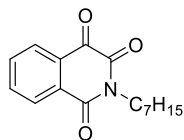


2-ethylisoquinoline-1,3,4(2H)-trione (4t) ^[7]. Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4t** (49mg, 80%) as a light yellow solid. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.35 (t, *J* = 7.5 Hz, 1H), 8.21 (t, *J* = 7.2 Hz, 1H), 7.91 (td, *J* = 7.8, 1.4 Hz, 1H), 7.83 (td, *J* = 7.5, 1.6 Hz, 1H), 4.13 (t, *J* = 7.5 Hz, 2H), 1.30 (q, *J* = 7.4 Hz, 3H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 174.74, 161.96, 156.82, 136.00, 134.36, 130.83, 130.03, 129.76 (d, *J* = 2.1 Hz), 127.75 (d, *J* = 2.6 Hz), 36.40 (d, *J* = 1.9 Hz), 13.18.

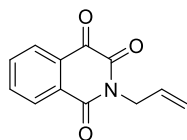


2-butylisoquinoline-1,3,4(2H)-trione (4u) ^[8]. Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4u** (51mg, 73%) as a light yellow solid. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.35 (d, *J* = 7.8 Hz, 1H), 8.21 (d, *J* = 7.8 Hz, 1H), 7.91 (t, *J* = 7.5 Hz, 1H),

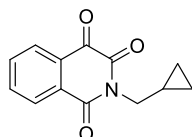
7.83 (t, $J = 7.5$ Hz, 1H), 4.06 (t, $J = 7.5$ Hz, 2H), 1.70 – 1.64 (m, 2H), 1.44 – 1.38 (m, 2H), 0.97 (t, $J = 7.3$ Hz, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.69, 162.15, 157.00, 135.95, 134.30, 130.88, 130.03, 129.76, 127.68, 41.00, 29.97, 20.18, 13.65.



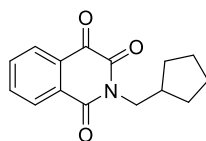
2-heptylisoquinoline-1,3,4(2H)-trione (4v). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4v** (62mg, 76%) as a yellow solid. mp 68 – 70 °C. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.35 (d, $J = 7.8$ Hz, 1H), 8.21 (d, $J = 7.8$ Hz, 1H), 7.91 (t, $J = 7.5$ Hz, 1H), 7.83 (t, $J = 7.5$ Hz, 1H), 4.05 (t, $J = 7.8$ Hz, 2H), 1.70 – 1.65 (m, 2H), 1.41 – 1.23 (m, 8H), 0.88 (t, $J = 6.8$ Hz, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.71, 162.15, 157.00, 135.96, 134.30, 130.88, 130.04, 129.78, 127.70, 41.27, 31.65, 28.86, 27.91, 26.90, 22.53, 13.99. HRMS (ESI-TOF) calcd for $\text{C}_{16}\text{H}_{19}\text{NO}_3$ [$\text{M} + \text{H}$] $^+$: 274.1438; found: 274.1435.



2-allylisoquinoline-1,3,4(2H)-trione (4w) [8]. Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4w** (48mg, 74%) as a brown solid. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.36 (dd, $J = 7.8, 1.5$ Hz, 1H), 8.23 (dd, $J = 7.5, 1.5$ Hz, 1H), 7.92 (td, $J = 7.5, 1.2$ Hz, 1H), 7.85 (td, $J = 7.8, 1.2$ Hz, 1H), 5.95 – 5.89 (m, 1H), 5.36 (dd, $J = 17.1, 1.5$ Hz, 1H), 5.25 (dd, $J = 10.2, 1.2$ Hz, 1H), 4.68 (d, $J = 6.6$ Hz, 2H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.62, 161.87, 156.71, 136.08, 134.49, 130.88, 130.84, 129.88, 129.88, 127.85, 119.25, 43.16.

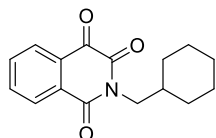


2-(cyclopropylmethyl)isoquinoline-1,3,4(2H)-trione (4x). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4x** (57mg, 83%) as a light yellow solid. mp 76 – 78 °C. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.35 (d, $J = 7.2$ Hz, 1H), 8.21 (d, $J = 7.8$ Hz, 1H), 7.90 (t, $J = 7.8$ Hz, 1H), 7.82 (t, $J = 7.5$ Hz, 1H), 3.95 (dd, $J = 7.2, 2.4$ Hz, 2H), 1.29–1.23 (m, 1H), 0.51–0.48 (m, 2H), 0.45 – 0.42 (m, 2H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.82, 162.39, 157.25, 135.97, 134.33, 130.92, 130.06, 129.82, 127.72, 45.64, 10.00, 3.95. HRMS (ESI-TOF) calcd for $\text{C}_{13}\text{H}_{11}\text{NO}_3$ [$\text{M} + \text{H}$] $^+$: 230.0812; found: 230.0811.

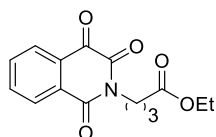


2-(cyclopentylmethyl)isoquinoline-1,3,4(2H)-trione (4y). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4y** (54mg, 70%) as a

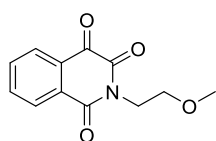
light yellow solid. mp 95 - 97 °C. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.35 (d, J = 7.6 Hz, 1H), 8.21 (d, J = 7.8 Hz, 1H), 7.91 (t, J = 7.5 Hz, 1H), 7.84 (t, J = 7.5 Hz, 1H), 4.05 (d, J = 7.6 Hz, 2H), 2.41 - 2.34 (m, 1H), 1.74 - 1.66 (m, 4H), 1.58 - 1.51 (m, 2H), 1.36 - 1.58 (m, 2H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.71, 162.47, 157.32, 135.96, 134.30, 130.92, 130.03, 129.85, 127.66, 45.41, 38.80, 30.37, 24.77. HRMS (ESI-TOF) calcd for $\text{C}_{15}\text{H}_{15}\text{NO}_3$ [$\text{M} + \text{H}$] $^+$: 258.1125; found: 258.1125.



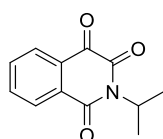
2-(cyclohexylmethyl)isoquinoline-1,3,4(2H)-trione (4z). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4z** (52mg, 64%) as a yellow solid. mp 122 - 124 °C. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.35 (d, J = 7.8 Hz, 1H), 8.22 (d, J = 7.6 Hz, 1H), 7.91 (t, J = 7.8 Hz, 1H), 7.83 (t, J = 7.5 Hz, 1H), 3.95 (dd, J = 7.2, 3.0 Hz, 2H), 1.85 - 1.78 (m, 1H), 1.74 - 1.70 (m, 2H), 1.69 - 1.62 (m, 3H), 1.23 - 1.15 (m, 3H), 1.10 - 1.04 (m, J = 12.0 Hz, 2H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.67, 162.50, 157.34, 135.98, 134.32, 130.92, 129.98, 129.89, 127.69, 46.88, 36.52, 30.82, 26.20, 25.73. HRMS (ESI-TOF) calcd for $\text{C}_{16}\text{H}_{17}\text{NO}_3$ [$\text{M} + \text{H}$] $^+$: 272.1281; found: 272.1281.



ethyl 4-(1,3,4-trioxo-3,4-dihydroisoquinolin-2(1H)-yl)butanoate (4aa). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4aa** (58mg, 67%) as yellow oil. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.34 (dd, J = 8.7, 4.5 Hz, 1H), 8.21 (dd, J = 8.4, 4.2 Hz, 1H), 7.91 (t, J = 7.8 Hz, 1H), 7.84 (t, J = 7.8 Hz, 1H), 4.17 - 4.06 (m, 4H), 2.42-2.37 (m, 2H), 2.06 - 2.00 (m, 2H), 1.26 - 1.20 (m, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.52, 172.57, 162.20, 157.08, 135.99, 134.41, 130.87, 129.89, 129.79, 127.73, 60.49, 40.41, 31.75, 23.15, 14.15. HRMS (ESI-TOF) calcd for $\text{C}_{15}\text{H}_{15}\text{NO}_5$ [$\text{M} + \text{H}$] $^+$: 290.1023; found: 290.1022.

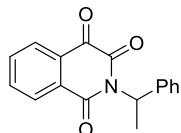


2-(2-methoxyethyl)isoquinoline-1,3,4(2H)-trione (4ab). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4ab** (47mg, 67%) as yellow oil. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.37 (d, J = 7.8 Hz, 1H), 8.23 (d, J = 7.8 Hz, 1H), 7.91 (t, J = 7.8 Hz, 1H), 7.83 (t, J = 7.5 Hz, 1H), 4.33 (t, J = 5.7 Hz, 2H), 3.69 (t, J = 5.7 Hz, 2H), 3.35 (s, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.53, 162.25, 157.10, 135.99, 134.41, 130.92, 129.91, 127.76, 69.03, 58.69, 39.96. HRMS (ESI-TOF) calcd for $\text{C}_{12}\text{H}_{11}\text{NO}_4$ [$\text{M} + \text{H}$] $^+$: 234.0761; found: 234.0758.

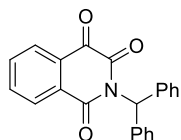


2-isopropylisoquinoline-1,3,4(2H)-trione (4ac) ^[9]. Purification by flash column chromatography

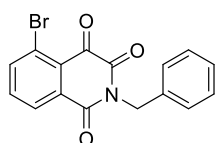
eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4ac** (45mg, 69%) as a light yellow solid. mp 134 - 136 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.34 (d, *J* = 7.8 Hz, 1H), 8.19 (d, *J* = 7.8 Hz, 1H), 7.90 (t, *J* = 7.5 Hz, 1H), 7.81 (t, *J* = 7.5 Hz, 1H), 5.23 - 5.18 (m, 1H), 1.54 (dd, *J* = 7.2, 2.4 Hz, 6H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 174.96, 162.37, 157.27, 135.93, 134.14, 130.86, 130.59, 129.82, 127.47, 46.68, 19.58.



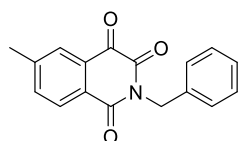
2-(1-phenylethyl)isoquinoline-1,3,4(2H)-trione (4ad). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4ad** (46mg, 55%) as a light yellow solid. mp 146 - 148 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.31 (d, *J* = 7.2 Hz, 1H), 8.18 (d, *J* = 7.8 Hz, 1H), 7.87 (t, *J* = 7.2 Hz, 1H), 7.80 (t, *J* = 7.2 Hz, 1H), 7.48 (d, *J* = 7.2 Hz, 2H), 7.32 (t, *J* = 7.5 Hz, 2H), 7.24 (d, *J* = 6.9 Hz, 1H), 6.30 (d, *J* = 7.8 Hz, 1H), 1.94 (d, *J* = 6.6 Hz, 3H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 174.74, 162.15, 157.03, 139.27, 136.00, 134.31, 130.89 (d, *J* = 2.7 Hz), 130.33 (d, *J* = 3.3 Hz), 129.99 (d, *J* = 3.0 Hz), 128.27 (d, *J* = 2.1 Hz), 127.62, 127.55 (d, *J* = 3.5 Hz), 51.80 (d, *J* = 4.0 Hz), 16.35. HRMS (ESI-TOF) calcd for C₁₇H₁₃NO₃ [M + H]⁺: 280.0968; found: 280.0967.



2-benzhydrylisoquinoline-1,3,4(2H)-trione (4ae). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4ae** (31mg, 30%) as a light yellow solid. mp 214 - 216 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.32 (d, *J* = 7.8 Hz, 1H), 8.20 (d, *J* = 7.8 Hz, 1H), 7.87 (t, *J* = 7.5 Hz, 1H), 7.81 (t, *J* = 7.5 Hz, 1H), 7.40 (d, *J* = 7.5 Hz, 5H), 7.33 (t, *J* = 7.5 Hz, 4H), 7.27 - 7.30 (m, 2H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 174.60, 162.17, 157.06, 137.46, 136.09, 134.48, 130.97, 130.26, 130.23, 128.87, 128.39, 127.71, 127.68, 60.34. HRMS (ESI-TOF) calcd for C₂₂H₁₅NO₃ [M + H]⁺: 342.1125; found: 342.1124.

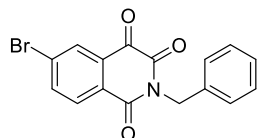


2-benzyl-5-bromoisoquinoline-1,3,4(2H)-trione (4af). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4af** (56mg, 54%) as a light yellow solid. mp 172 - 174 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.38 (dd, *J* = 7.8, 1.5 Hz, 1H), 8.03 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.65 (t, *J* = 8.1 Hz, 1H), 7.48 (dd, *J* = 7.2, 1.8 Hz, 2H), 7.30 (t, *J* = 7.2 Hz, 2H), 7.27 (d, *J* = 7.2 Hz, 1H), 5.21 (s, 2H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 173.02, 161.15, 156.51, 141.13, 135.56, 135.30, 132.63, 129.82, 129.42, 128.78, 128.65, 128.15, 123.78, 44.59. HRMS (ESI-TOF) calcd for C₁₆H₁₀NO₃ [M + H]⁺: 343.9917; found: 343.9914.

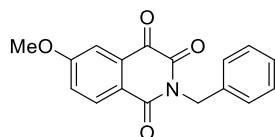


2-benzyl-6-methylisoquinoline-1,3,4(2H)-trione (4ah) ^[5]. Purification by flash column

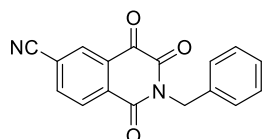
chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4ah** (62mg, 74%) as a light yellow solid. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.20 (d, J = 7.8 Hz, 1H), 7.97 (d, J = 1.8 Hz, 1H), 7.66 (dd, J = 8.4, 1.8 Hz, 1H), 7.48 (d, J = 7.2 Hz, 2H), 7.29 (t, J = 6.9 Hz, 2H), 7.25 (d, J = 7.2 Hz, 1H), 5.20 (s, 2H), 2.51 (s, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.82, 162.19, 157.14, 145.90, 136.02, 130.70, 129.99, 129.39, 128.57, 127.96, 127.95, 127.42, 44.20, 21.65.



2-benzyl-6-bromoisoquinoline-1,3,4(2H)-trione (4ai) ^[5]. Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4ai** (85mg, 82%) as a light yellow solid. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.31 (s, 1H), 8.20 (d, J = 8.4 Hz, 1H), 8.00 (d, J = 9.0 Hz, 1H), 7.48 (d, J = 7.2 Hz, 2H), 7.33 – 7.27 (m, 3H), 5.22 (s, 2H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 173.68, 161.55, 156.41, 139.09, 135.65, 131.75, 131.45, 130.55, 130.02, 129.43, 128.65, 128.48, 128.14, 44.46.

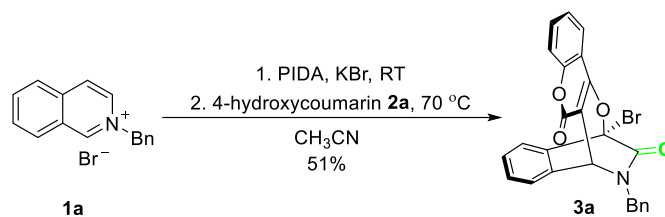


2-benzyl-6-methoxyisoquinoline-1,3,4(2H)-trione (4aj). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4aj** (77mg, 87%) as a light yellow solid. mp 167 - 169 °C. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.23 (d, J = 9.0 Hz, 1H), 7.56 (d, J = 3.0 Hz, 1H), 7.47 (d, J = 7.8 Hz, 2H), 7.34 (dd, J = 9.0, 2.4 Hz, 1H), 7.29 (t, J = 7.5 Hz, 2H), 7.24 (t, J = 7.2 Hz, 1H), 5.19 (s, 2H), 3.95 (s, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.78, 164.39, 161.87, 157.16, 136.08, 132.58, 131.99, 129.38, 128.56, 127.94, 123.41, 122.74, 110.12, 56.19, 44.10. HRMS (ESI-TOF) calcd for $\text{C}_{17}\text{H}_{13}\text{NO}_4$ [$\text{M} + \text{H}$] $^+$: 296.0917; found: 296.0916.



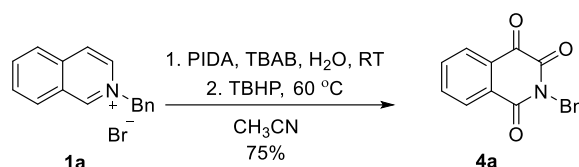
2-benzyl-1,3,4-trioxo-1,2,3,4-tetrahydroisoquinoline-6-carbonitrile (4ak). Purification by flash column chromatography eluting with petroleum ether/ethyl acetate (5/1, v/v) gave **4ak** (53mg, 61%) as a light yellow solid. mp 212 - 214 °C. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.49 (d, J = 8.4 Hz, 1H), 8.46 (d, J = 1.8 Hz, 1H), 8.13 (dd, J = 8.1, 1.5 Hz, 1H), 7.50 (d, J = 6.6 Hz, 1H), 7.34 – 7.27 (m, 3H), 5.25 (s, 2H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 173.04, 160.73, 155.93, 138.33, 135.27, 132.47, 131.38, 131.25, 130.85, 129.55, 128.74, 128.35, 118.59, 116.18, 44.78. HRMS (ESI-TOF) calcd for $\text{C}_{17}\text{H}_{10}\text{N}_2\text{O}_3$ [$\text{M} + \text{Na}$] $^+$: 313.0584; found: 313.0584.

5.5 Scale-up synthesis of 3a



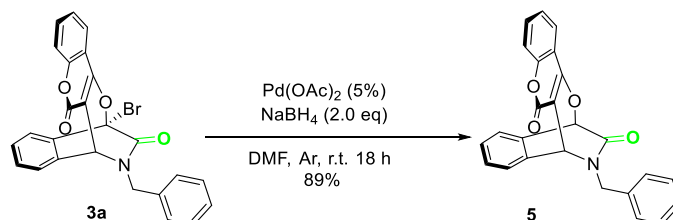
Under an argon atmosphere, a 50 mL Schlenk flask was charged with iminium salt **1a** (5 mmol), PIDA (15 mmol), KBr (5 mmol), H₂O (180 μ L), and dry MeCN (20 mL). The mixture was continually stirred at room temperature until **1a** was consumed as indicated by TLC (ca. 12 h). 4-Hydroxycoumarin **2a** (10 mmol) was added. The reaction mixture was heated at 70 $^\circ$ C in the oil bath until the intermediate was consumed as indicated by TLC (ca. 8 h), then cooled to room temperature, diluted with water (20 mL), and extracted with ethyl acetate (3 \times 20 mL). The combined organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate as the eluent) to give the desired product **3a** (1210 mg, 51%).

5.6 Scale-up synthesis of 4a



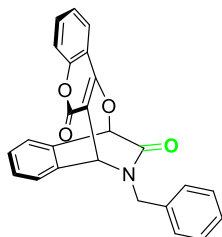
To the mixture of *N*-alkyl iminium salt **1a** (5 mmol), PIDA (15 mmol), TBAB (5 mmol) was added dry MeCN (15 mL) and H₂O (90 μ L) in a 50 mL reaction flask. The mixture was continually stirred at room temperature until **1a** was consumed as indicated by TLC (ca. 10 h). TBHP (10 mmol, in decane) was added. The reaction mixture was heated at 60 $^\circ$ C in the oil bath until the intermediate was consumed as indicated by TLC (ca. 60 h), then cooled to room temperature, diluted with water (20 mL), and extracted with ethyl acetate (3 \times 20 mL). The combined organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate as the eluent) to give the desired product **4a** (995 mg, 75%).

5.7 Synthesis of 5 via debrominative reduction of 3a



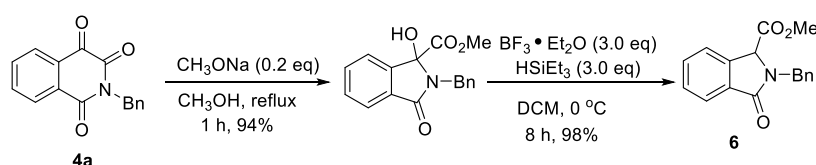
Under an argon atmosphere, a 10 mL Schlenk flask was charged with 1,4-bridged dihydroisoquinoline-3-ones **3a** (0.2 mmol), NaBH₄ (0.4 mmol), Pd(OAc)₂ (0.01 mmol) and anhydrous DMF (2 mL). The mixture was continually stirred at room temperature until **3a** was consumed as indicated by TLC (ca. 18 h). The reaction mixture was quenched by water, and extracted with ethyl acetate (3 \times 5 mL). The combined organic layer was washed with brine, dried

over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate=6:1) to give the desired product **5** (70 mg, 89%) as a white solid, m. p. 150–152 °C.

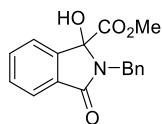


15-benzyl-7,12-dihydro-6H-7,12-(epiminomethano)benzo[5,6]oxepino[3,2-c]chromene-6,14-dione (5). ¹H NMR (600 MHz, Chloroform-*d*) δ 7.76 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.54 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.49 (td, *J* = 7.8, 2.0 Hz, 1H), 7.39 (td, *J* = 7.8, 1.4 Hz, 1H), 7.35 (td, *J* = 7.5, 1.6 Hz, 1H), 7.25 – 7.20 (m, 8H), 5.77 (s, 1H), 5.47 (s, 1H), 5.00 (d, *J* = 15.0 Hz, 1H), 4.54 (d, *J* = 15.0 Hz, 1H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 166.38, 161.11, 159.28, 152.75, 142.10, 135.47, 132.53, 130.72, 129.86, 128.83, 128.78, 128.73, 128.30, 127.94, 124.14, 122.93, 122.54, 116.63, 115.90, 106.55, 80.61, 53.40, 48.88. HRMS (ESI-TOF) calcd for C₂₅H₁₇NO₄ [M + Na]⁺: 418.1050; found: 418.1051.

5.8 Synthesis of **6** via rearrangement/reduction of **4a**



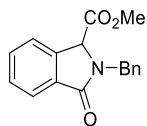
Base-promoted rearrangement of 4a. A 5 mL reaction flask was charged with sodium methoxide (0.04 mmol), CH₃OH (2 mL), and isoquinoline-1,3,4-triones **4a** (0.2 mmol). The mixture was refluxed at 70 °C in the oil bath until **4a** was consumed as indicated by TLC (ca. 1 h), then cooled to room temperature. Most of the solvent was removed under reduced pressure. The residue was diluted with ethyl acetate (5 mL) and water (5 mL), and extracted with EtOAc (3 × 15 mL). The combined organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate=3:1) to provide methyl 2-benzyl-1-hydroxy-3-oxoisindoline-1-carboxylate as a white solid (56 mg, 94% yield).



methyl 2-benzyl-1-hydroxy-3-oxoisindoline-1-carboxylate ^[10]. ¹H NMR (600 MHz, Chloroform-*d*) δ 7.89 (dt, *J* = 5.2, 2.9 Hz, 1H), 7.58 (td, *J* = 4.2, 1.8 Hz, 2H), 7.43 – 7.37 (m, 3H), 7.31 (t, *J* = 6.6 Hz, 2H), 7.26 (t, *J* = 7.5 Hz, 1H), 5.07 (d, *J* = 15.4 Hz, 1H), 4.94 – 4.86 (m, 1H), 4.35 (d, *J* = 15.2 Hz, 1H), 3.14 (d, *J* = 1.9 Hz, 3H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 171.55, 167.83, 143.57, 136.33, 132.56, 131.53, 130.35, 129.14, 128.35, 127.60, 123.86, 121.60, 86.89, 53.50, 42.32.

Reduction of methyl 2-benzyl-1-hydroxy-3-oxoisindoline-1-carboxylate. To the solution of 2-benzyl-1-hydroxy-3-oxoisindoline-1-carboxylate (0.2 mmol) and HSiEt₃ (0.6 mmol) in DCM was added BF₃·Et₂O (0.6 mmol) dropwise at 0 °C. The mixture was continually stirred at 0 °C until the carboxylate was consumed as indicated by TLC (ca. 8 h). It was quenched with saturated NH₄Cl

solution (5 mL), and extracted with CH₂Cl₂ (3 × 5 mL). The combined organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate as the eluent) to give the desired product **6** (55 mg, 98%) as colorless oil.



methyl 2-benzyl-3-oxoisindoline-1-carboxylate (6) ^[11]. ¹H NMR (600 MHz, Chloroform-*d*) δ 7.82 (dd, *J* = 7.0, 1.3 Hz, 1H), 7.47 – 7.43 (m, 3H), 7.26 – 7.22 (m, 2H), 7.20 (d, *J* = 6.5 Hz, 1H), 7.17 (d, *J* = 8.8 Hz, 2H), 5.38 (d, *J* = 15.0 Hz, 1H), 4.86 (s, 1H), 4.22 (d, *J* = 15.0 Hz, 1H), 3.67 (s, 3H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 168.61, 168.52, 139.34, 136.23, 132.06, 131.61, 129.36, 128.88, 128.53, 127.91, 124.21, 122.86, 61.40, 52.89, 45.32.

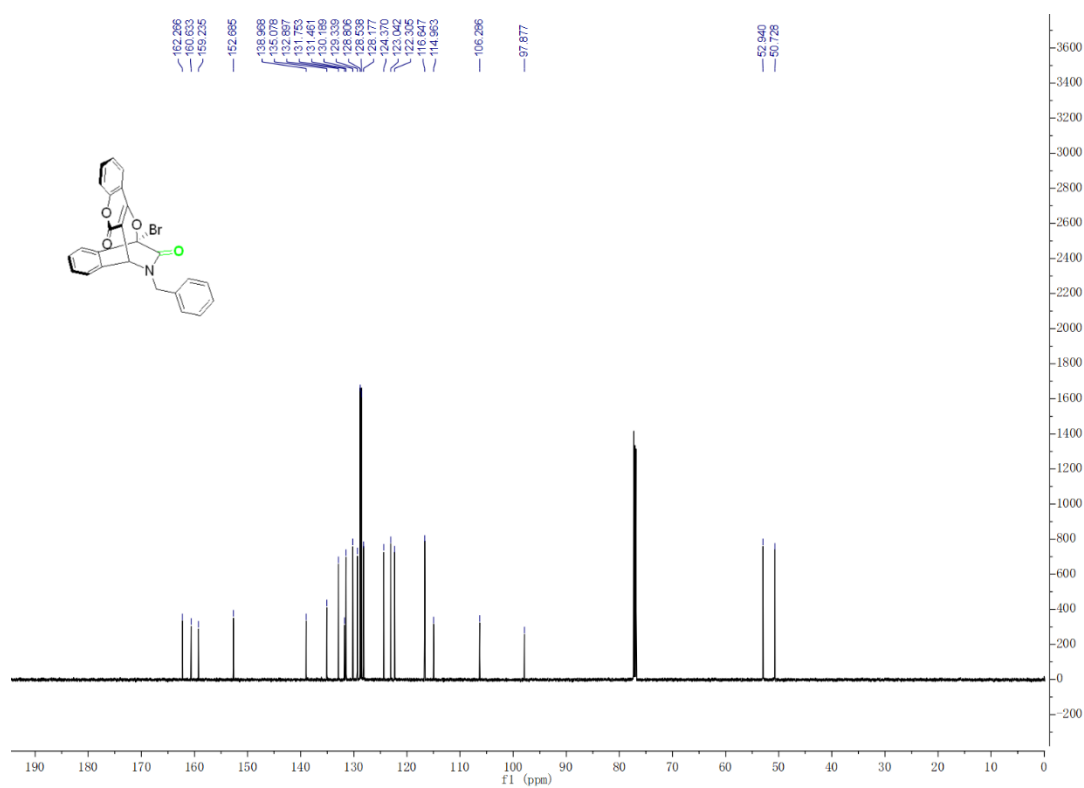
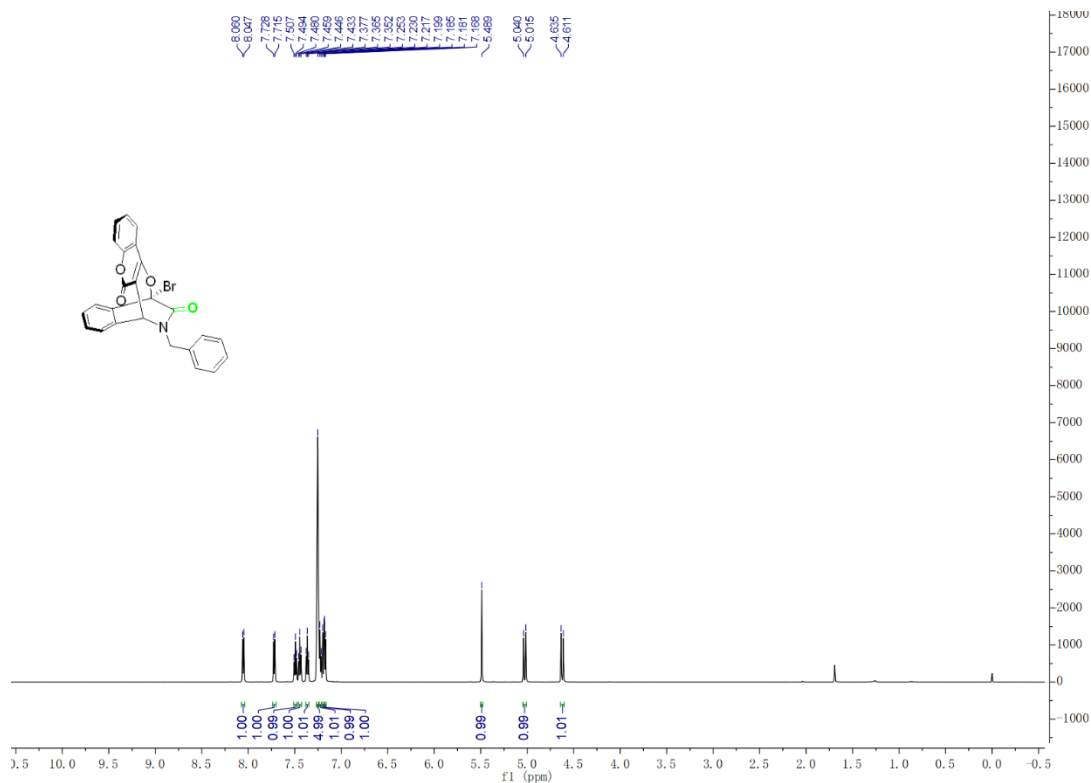
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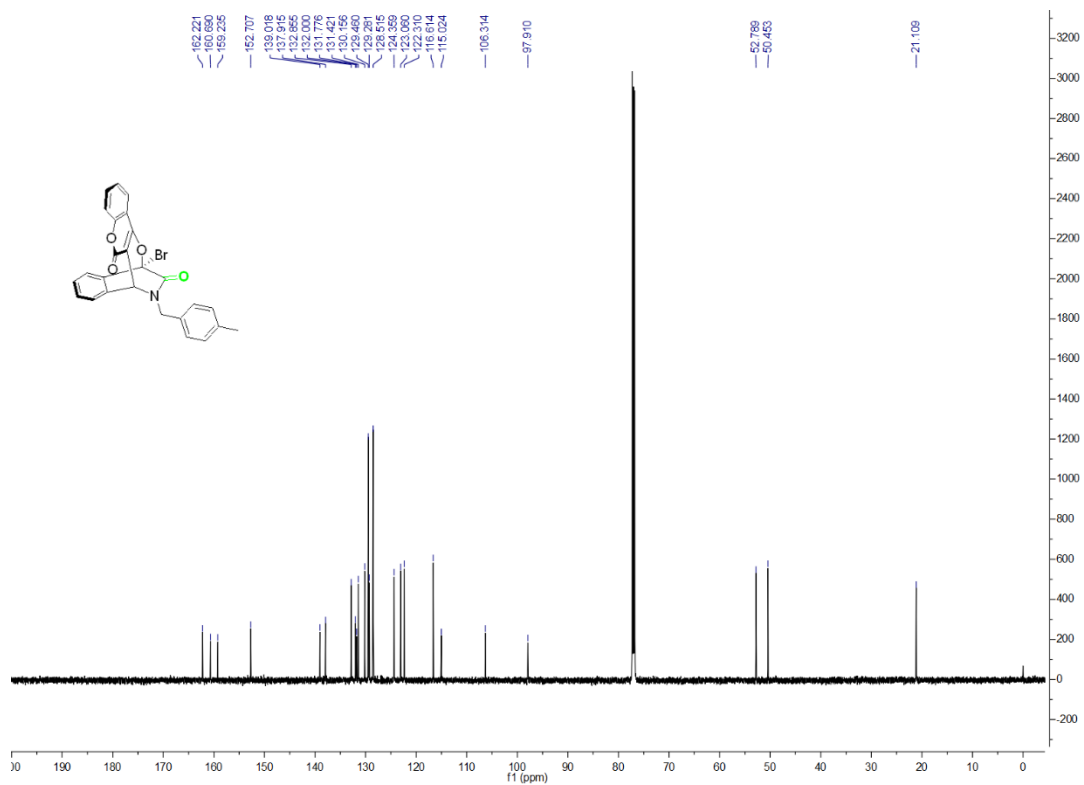
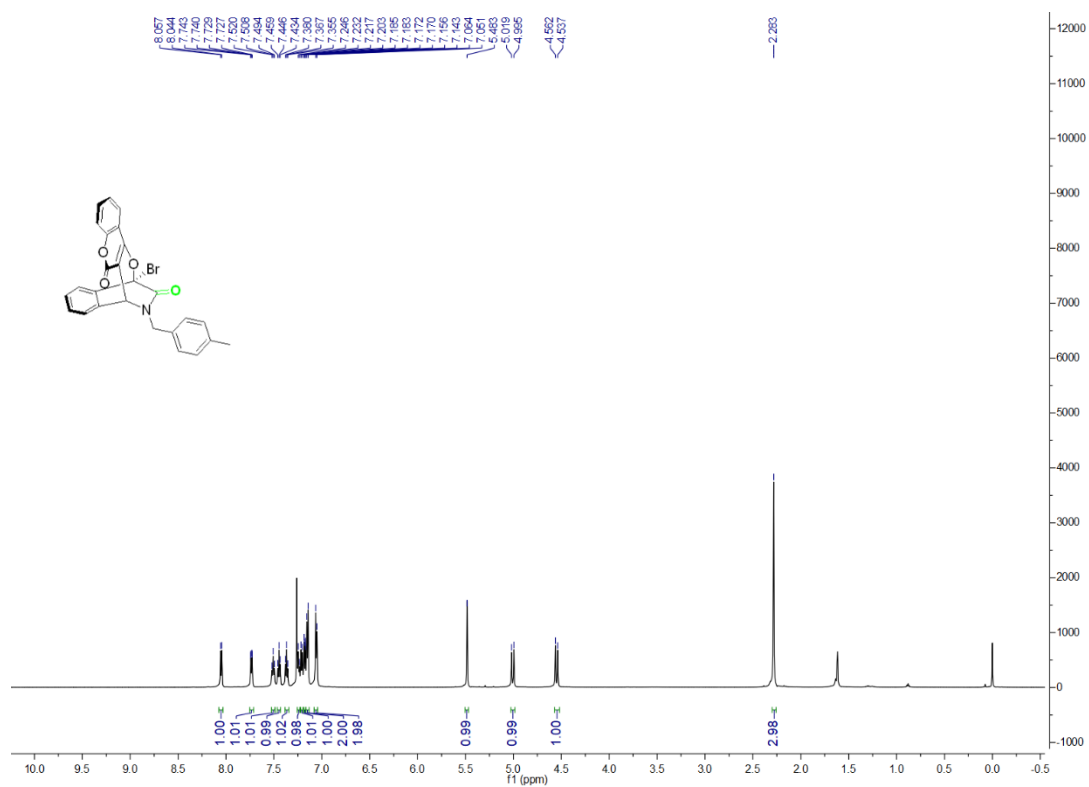
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7. NMR spectra of compounds 2 – 6

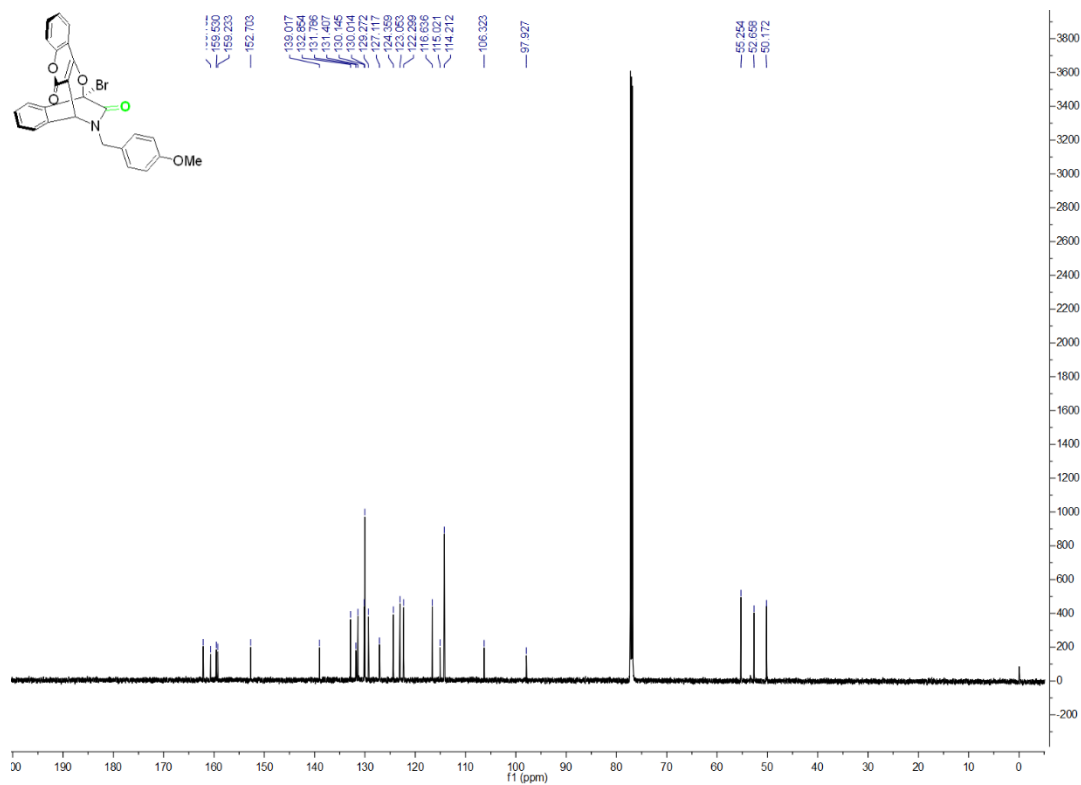
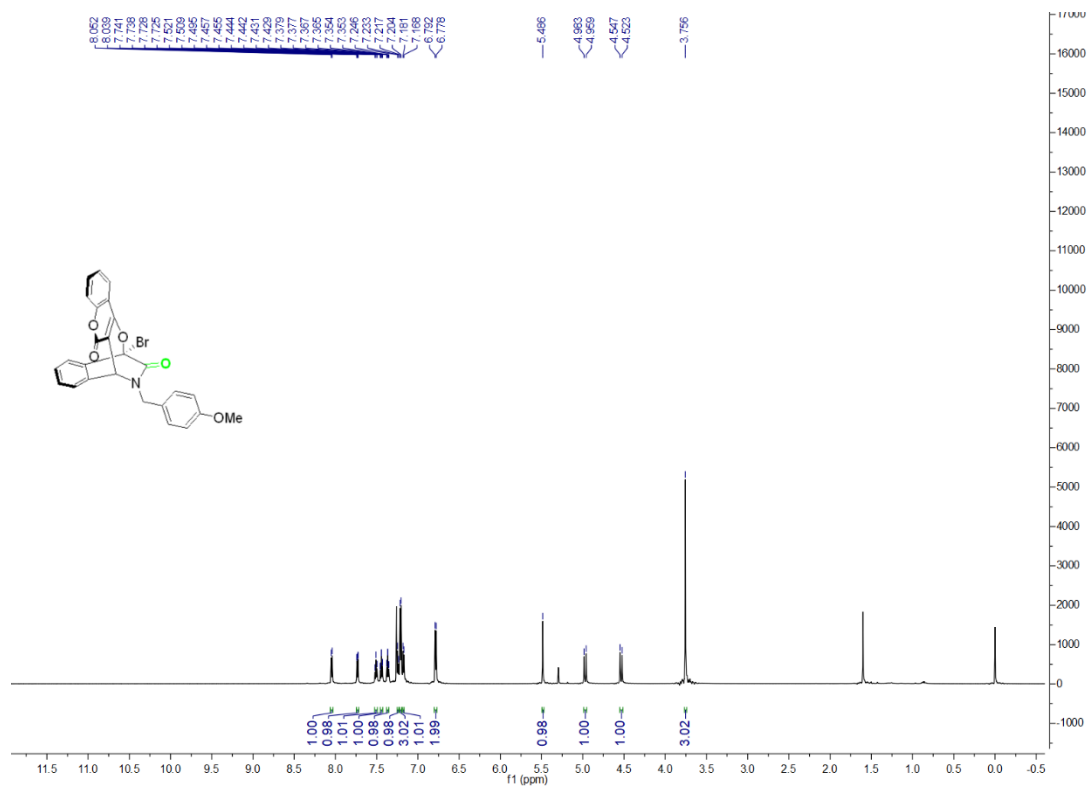
^1H NMR and ^{13}C NMR spectra of compound 3a



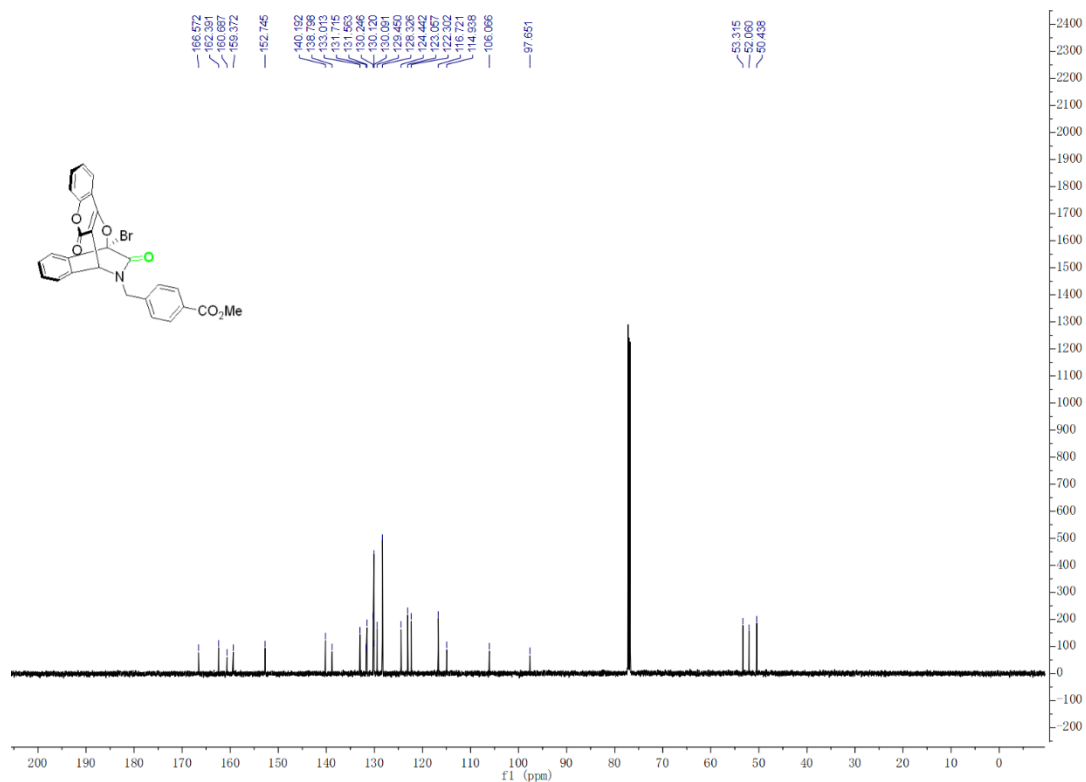
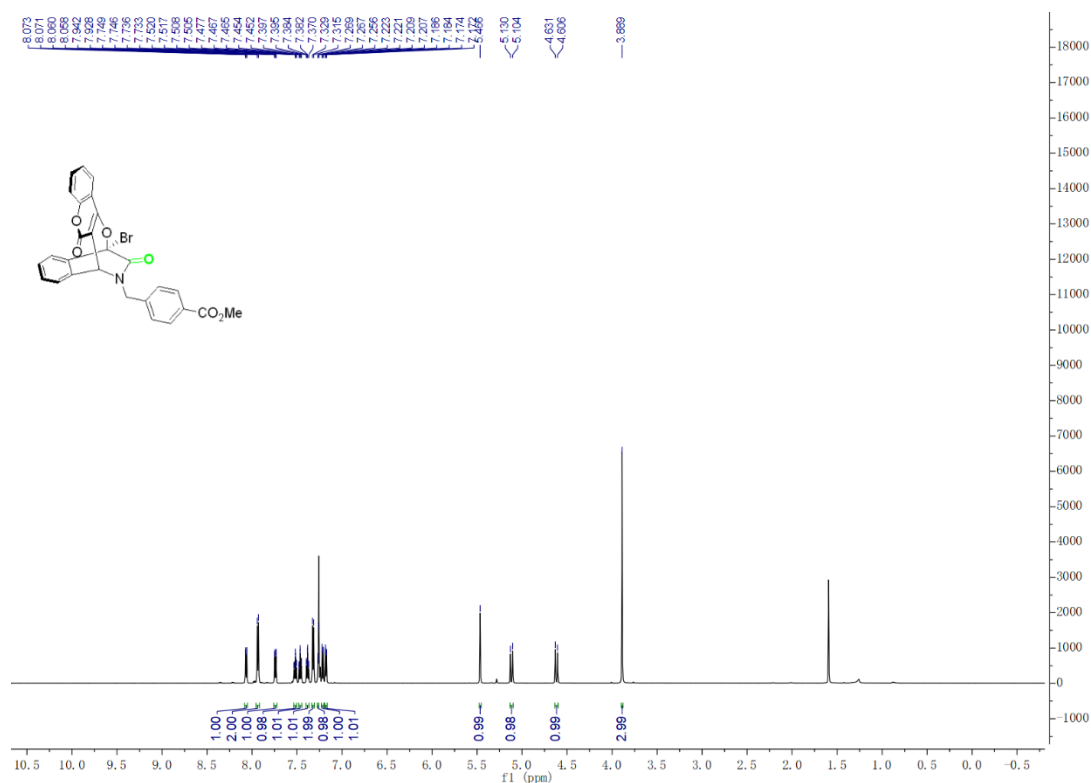
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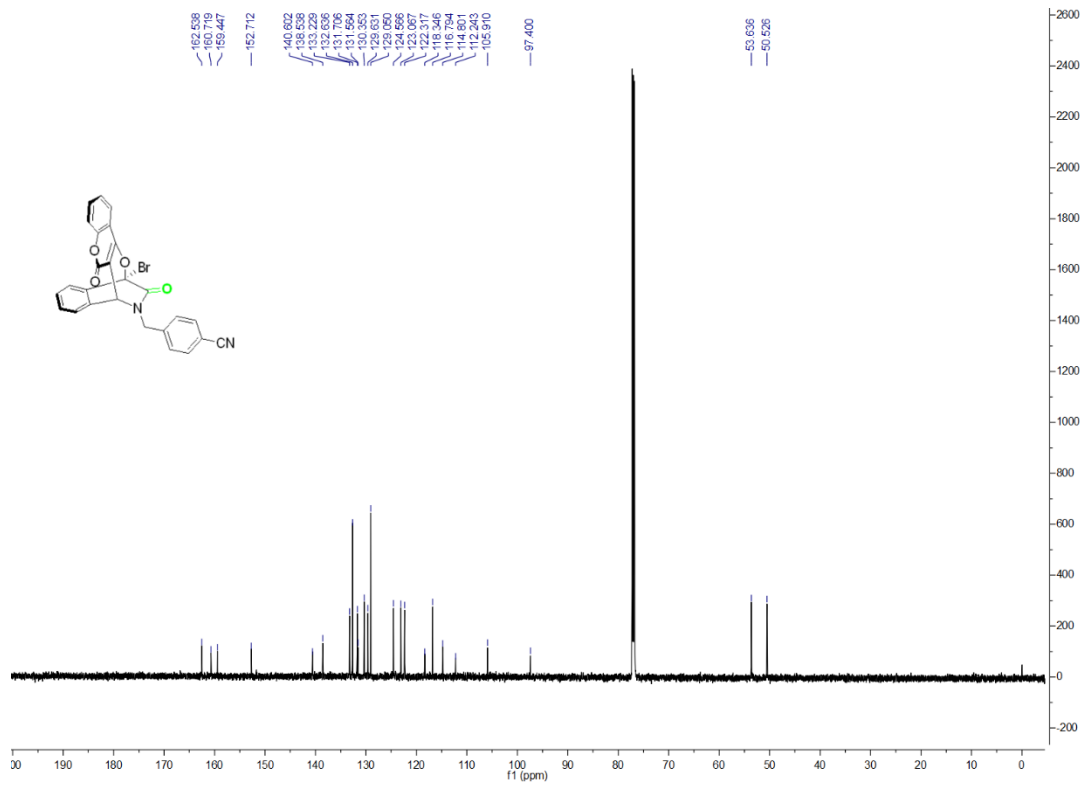
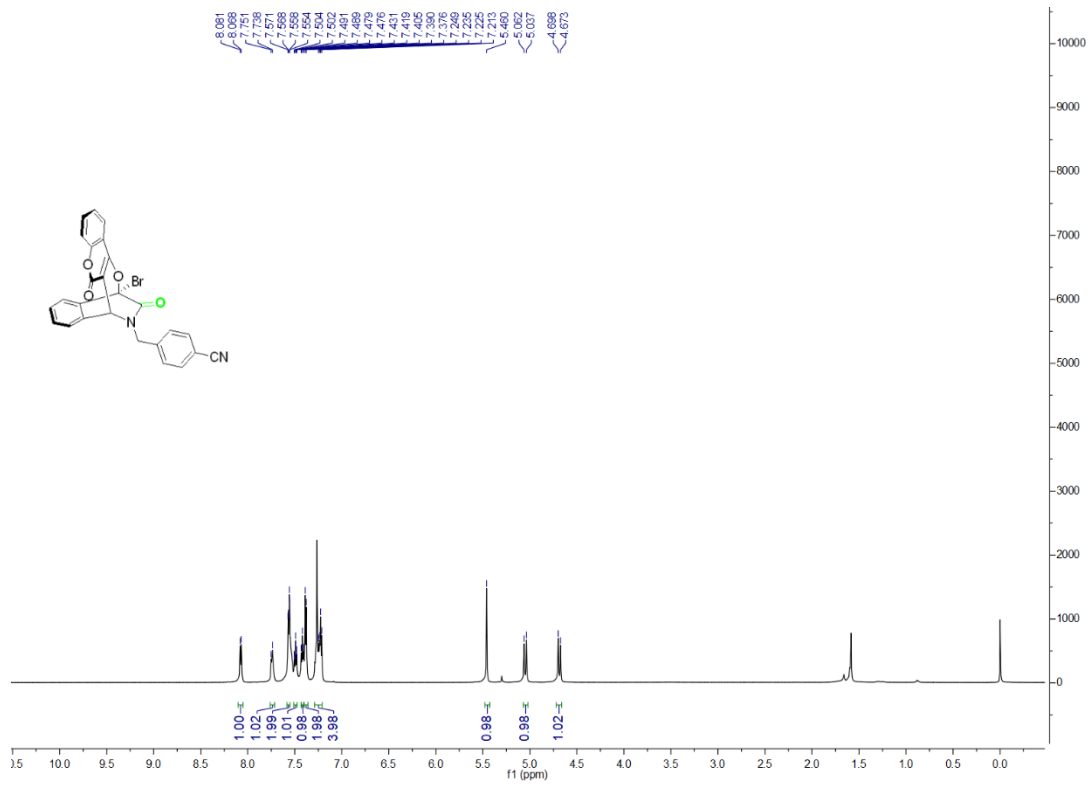
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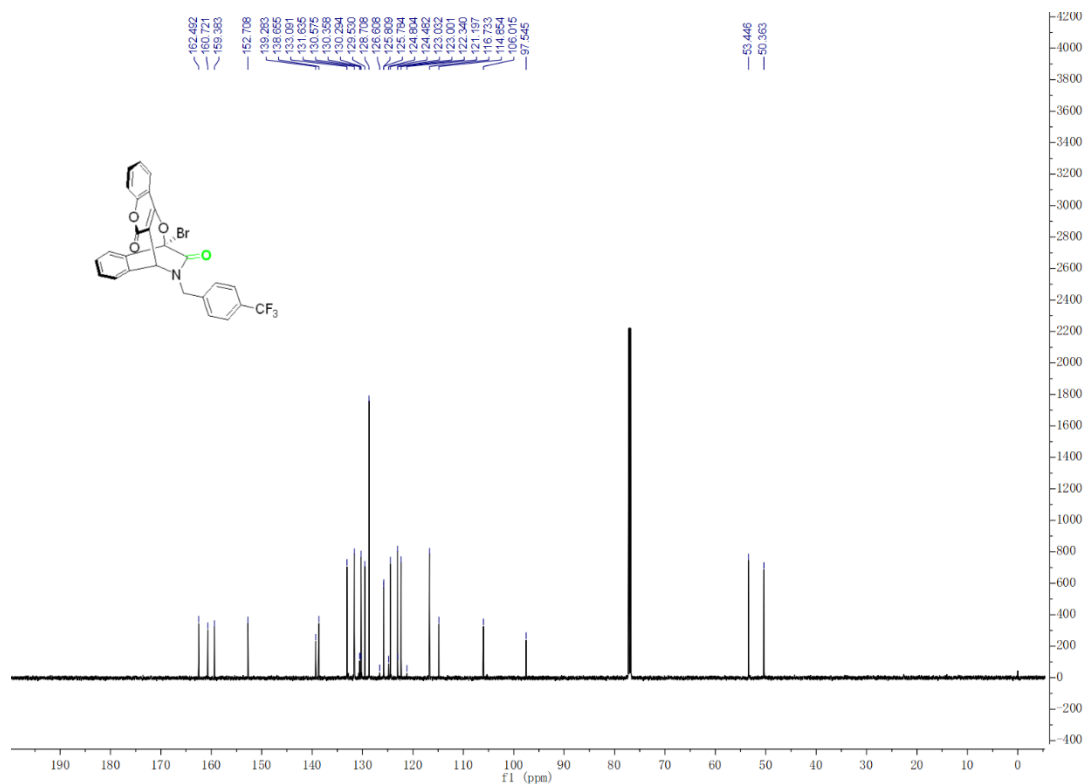
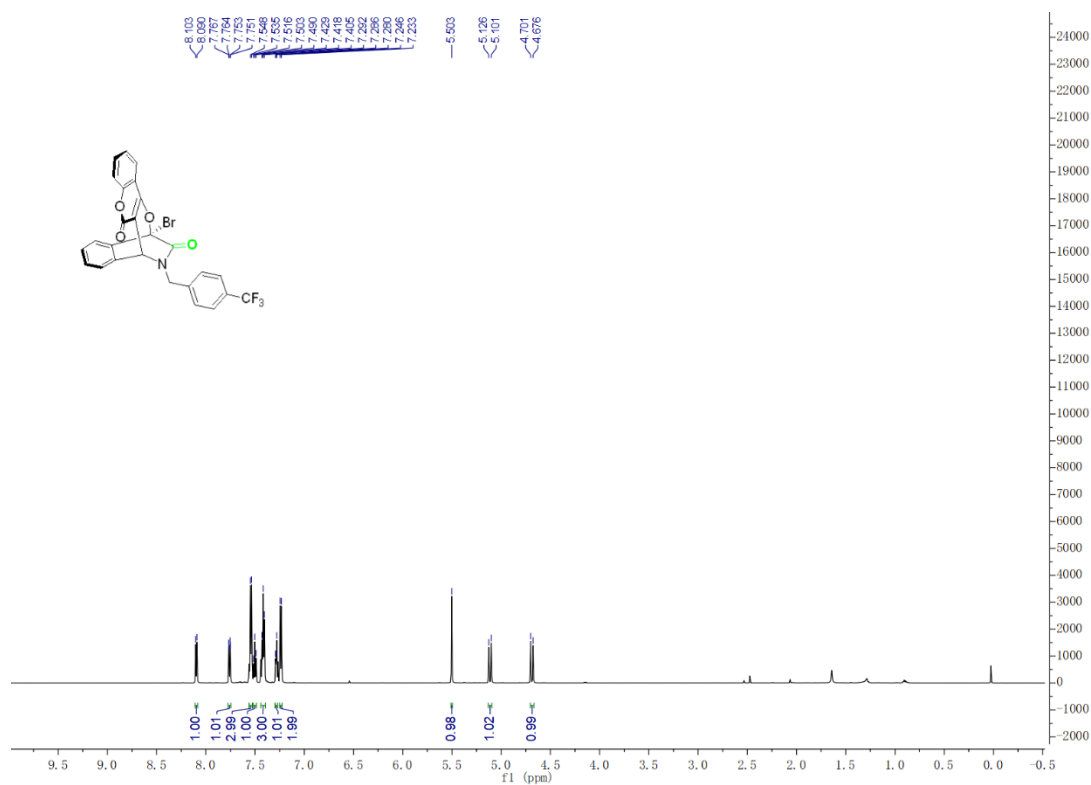
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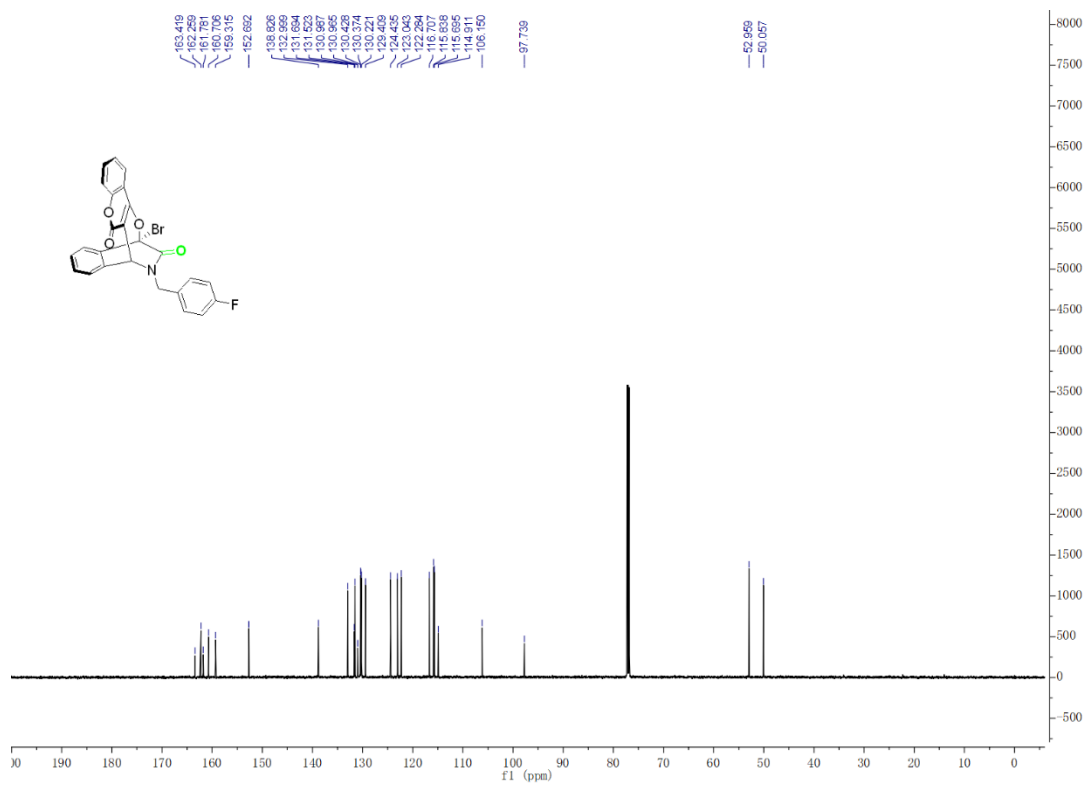
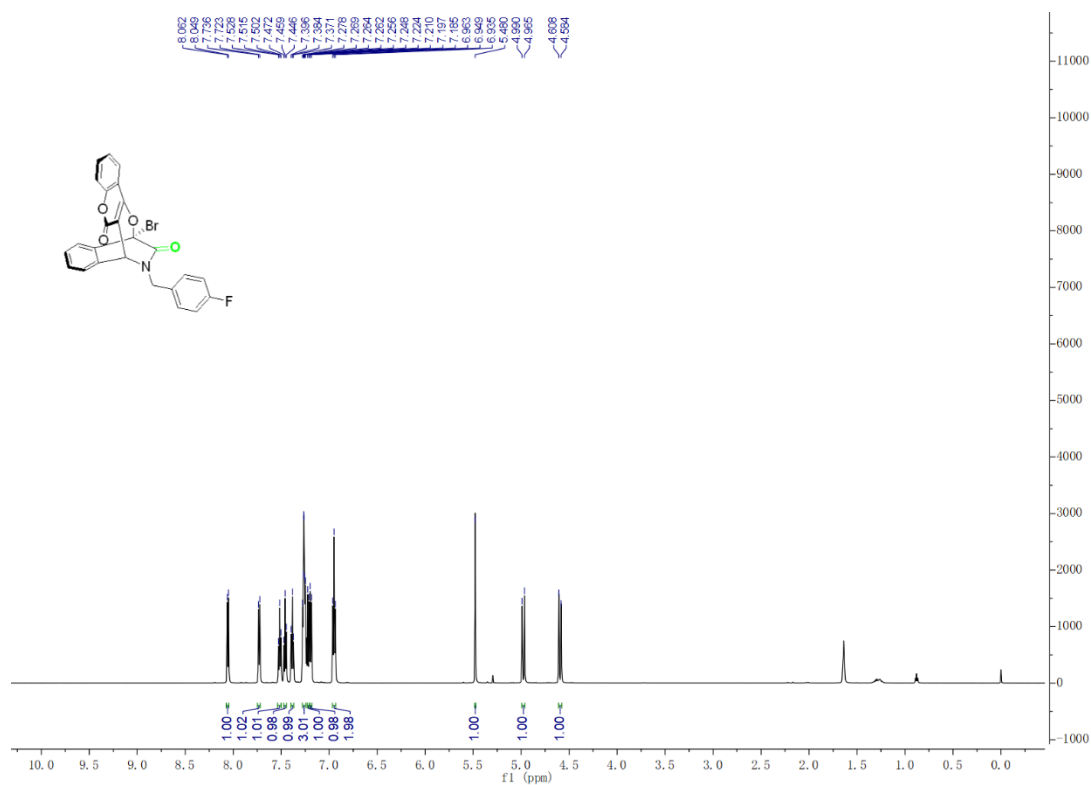
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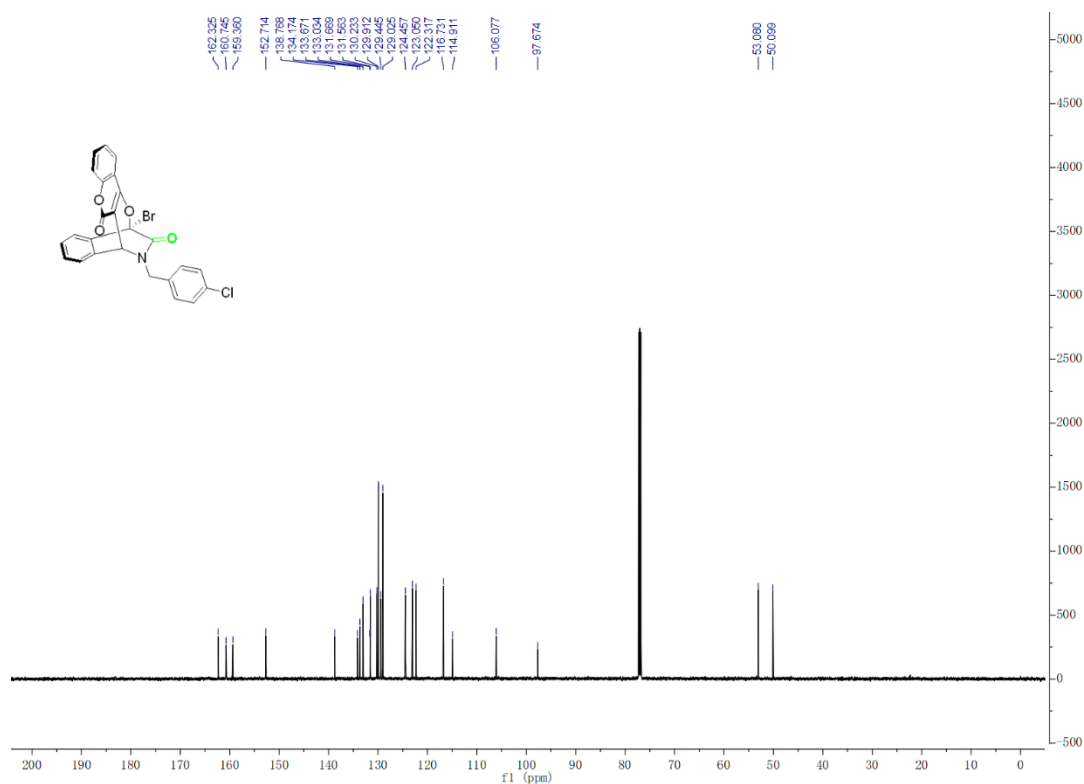
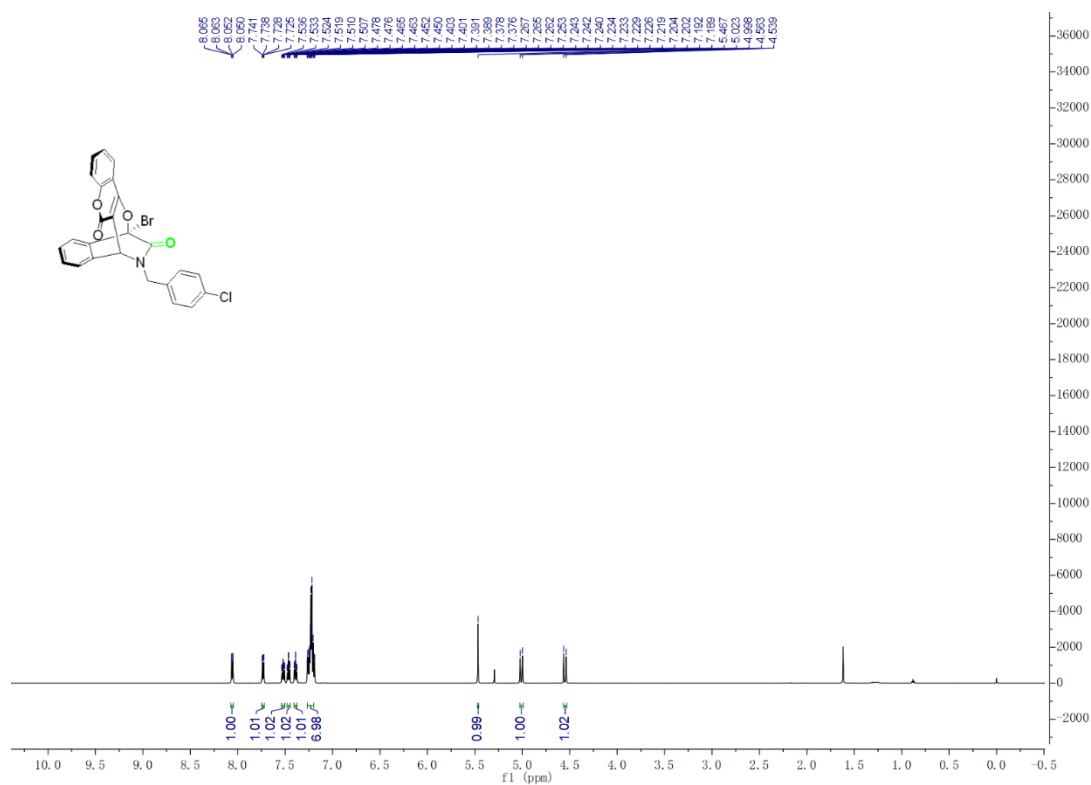
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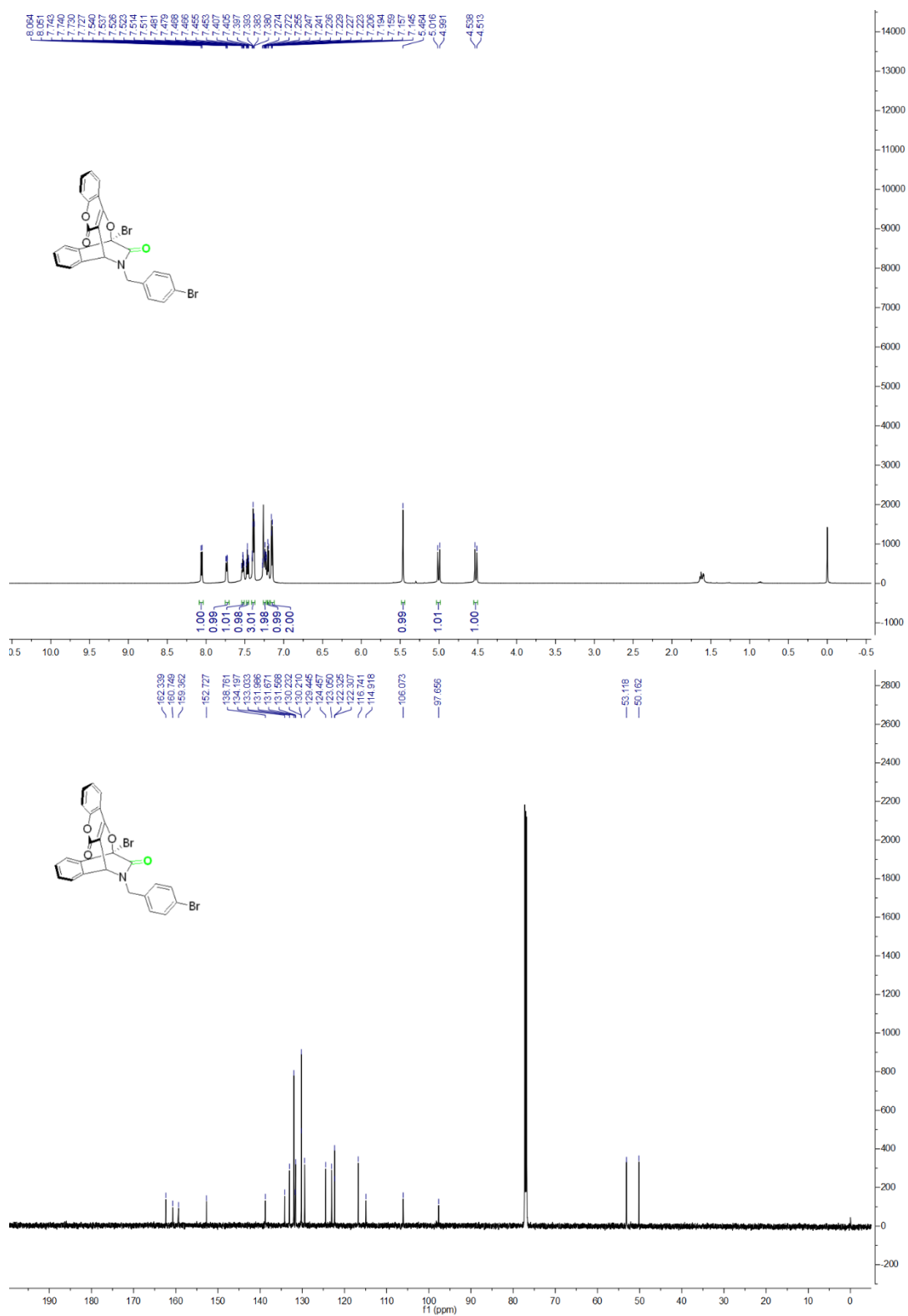
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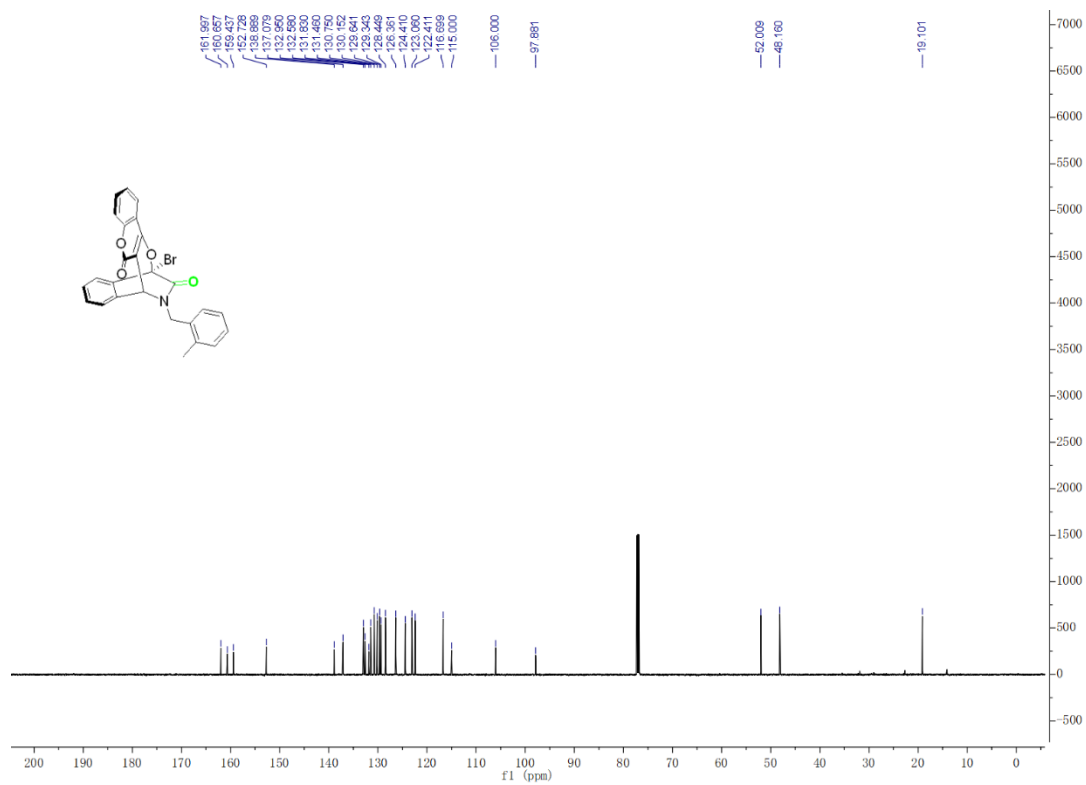
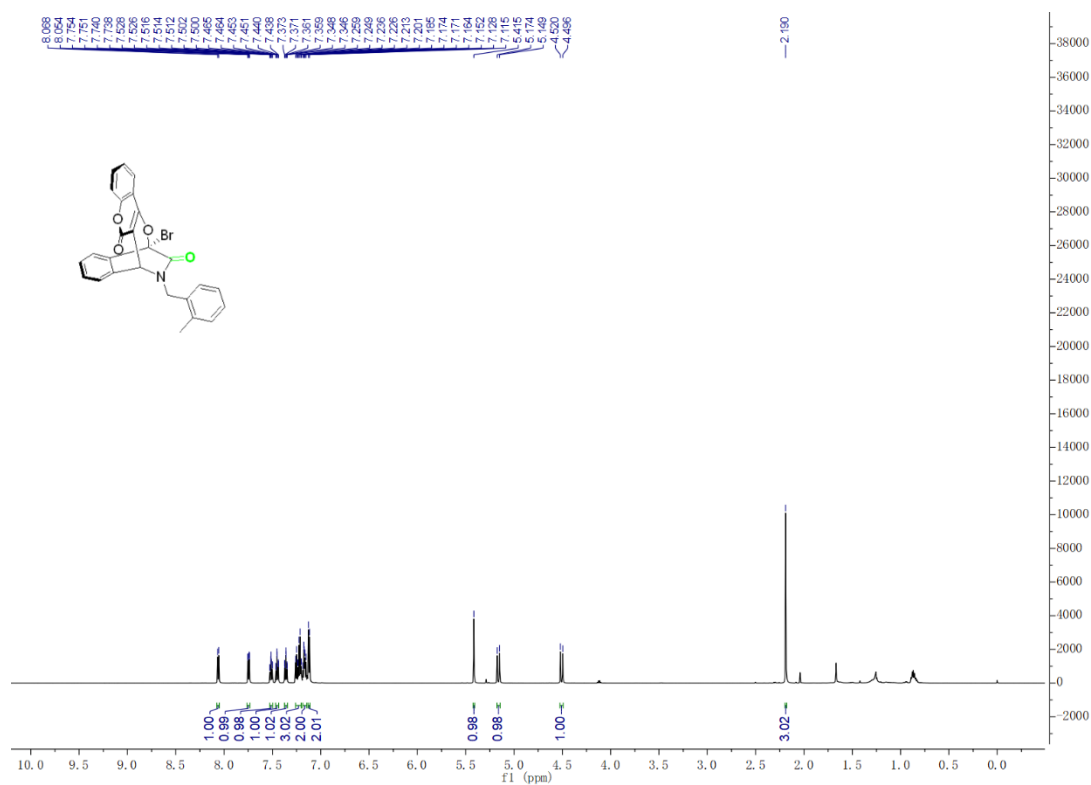
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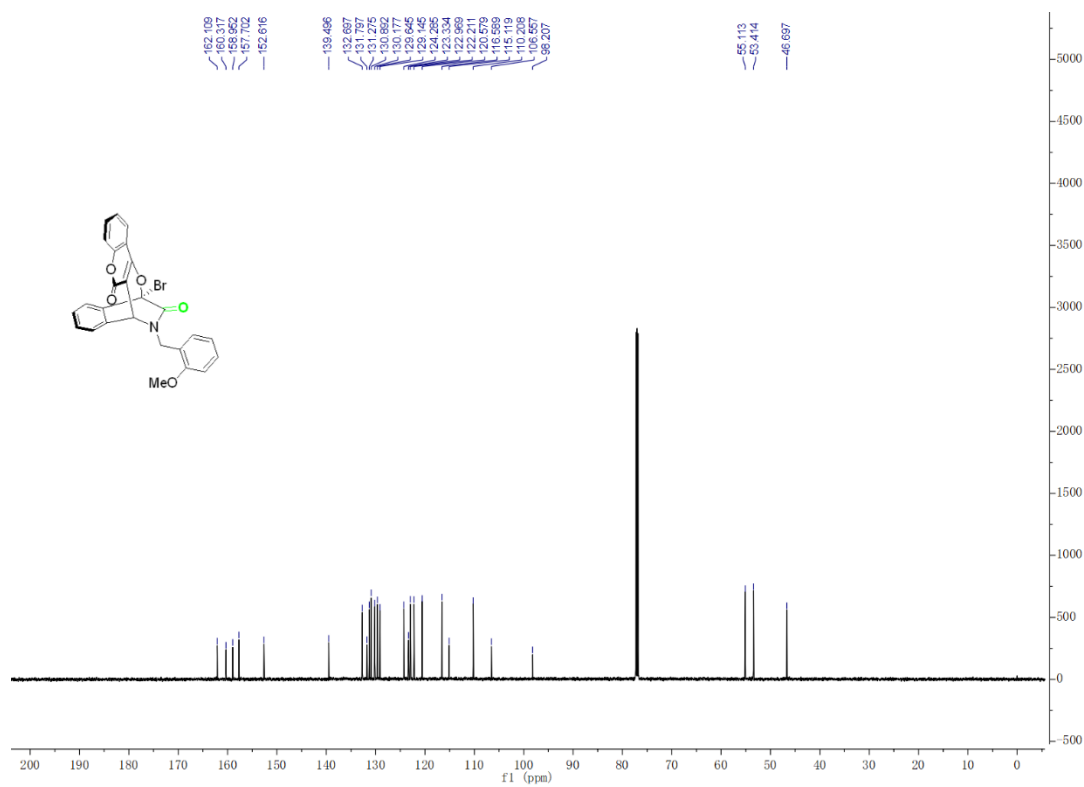
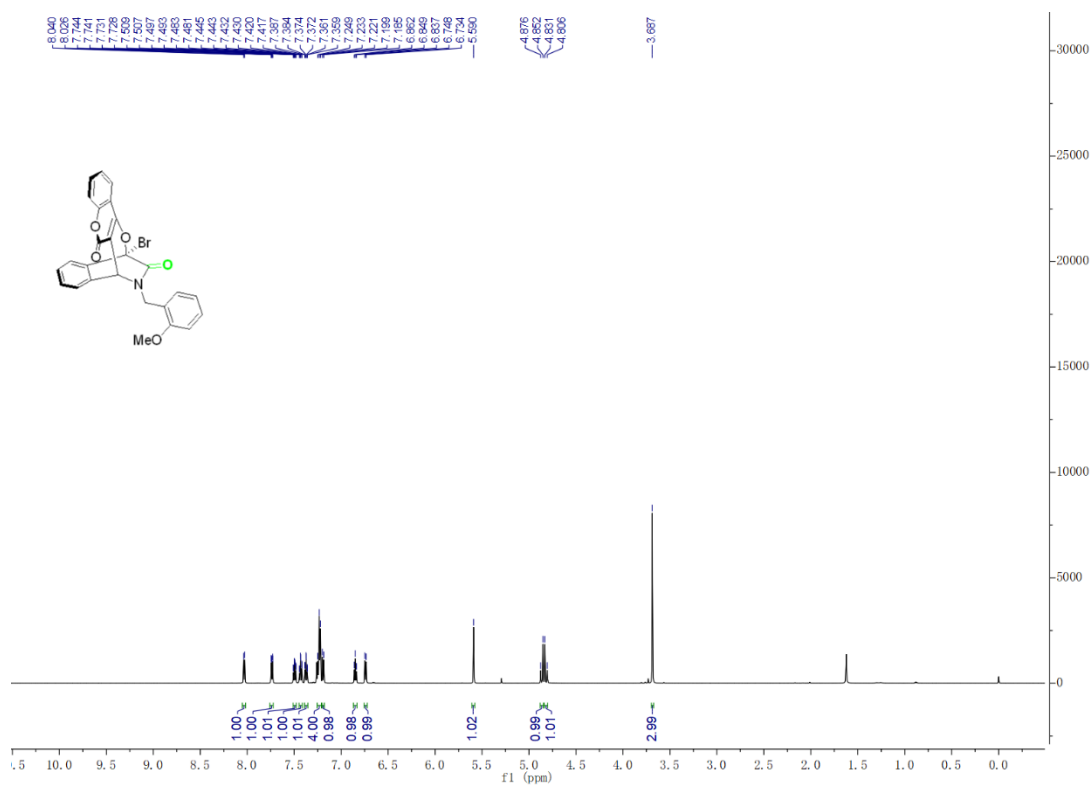
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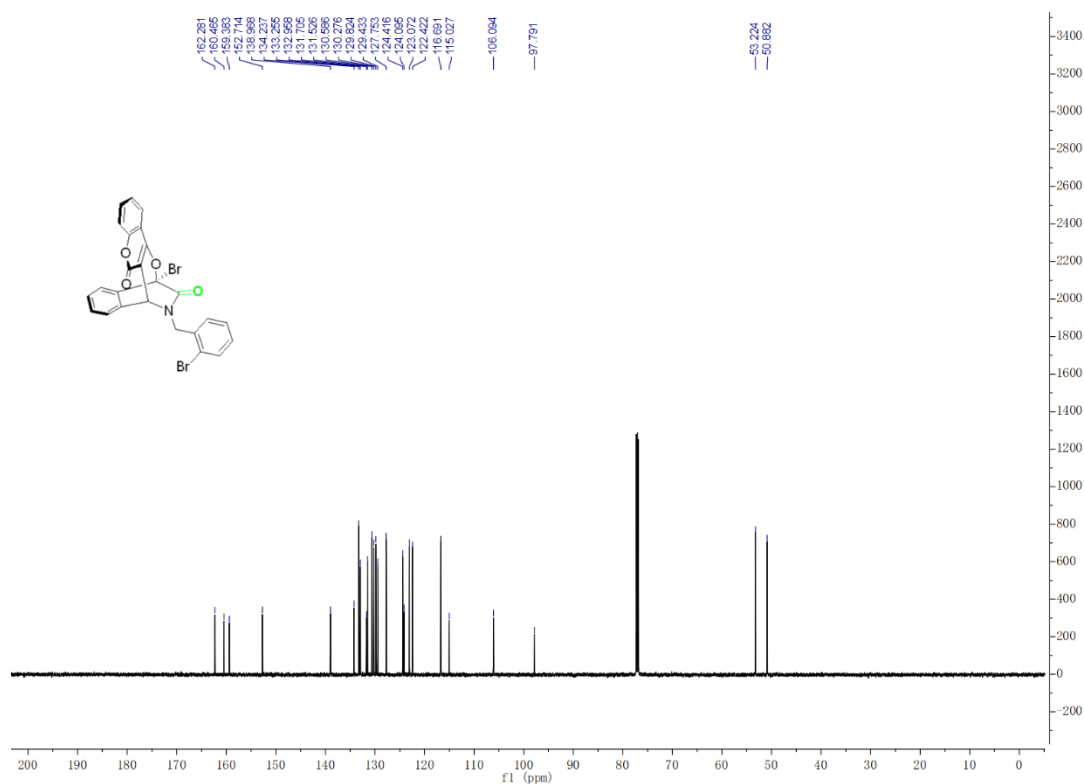
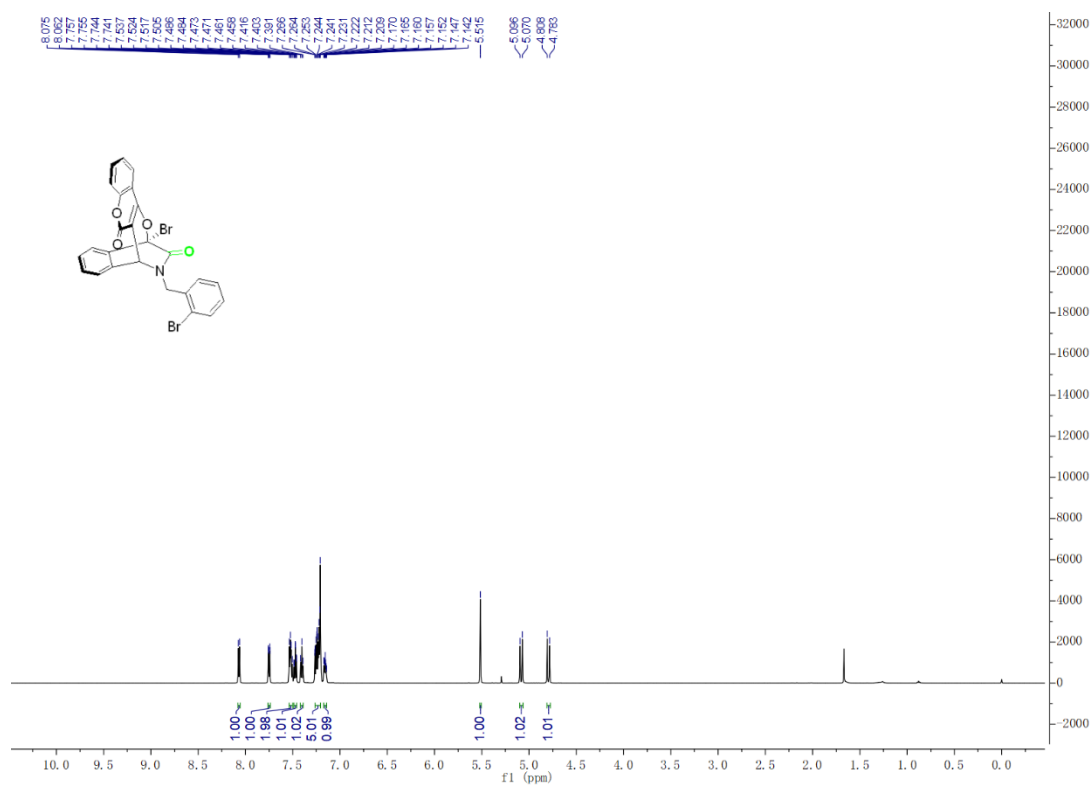
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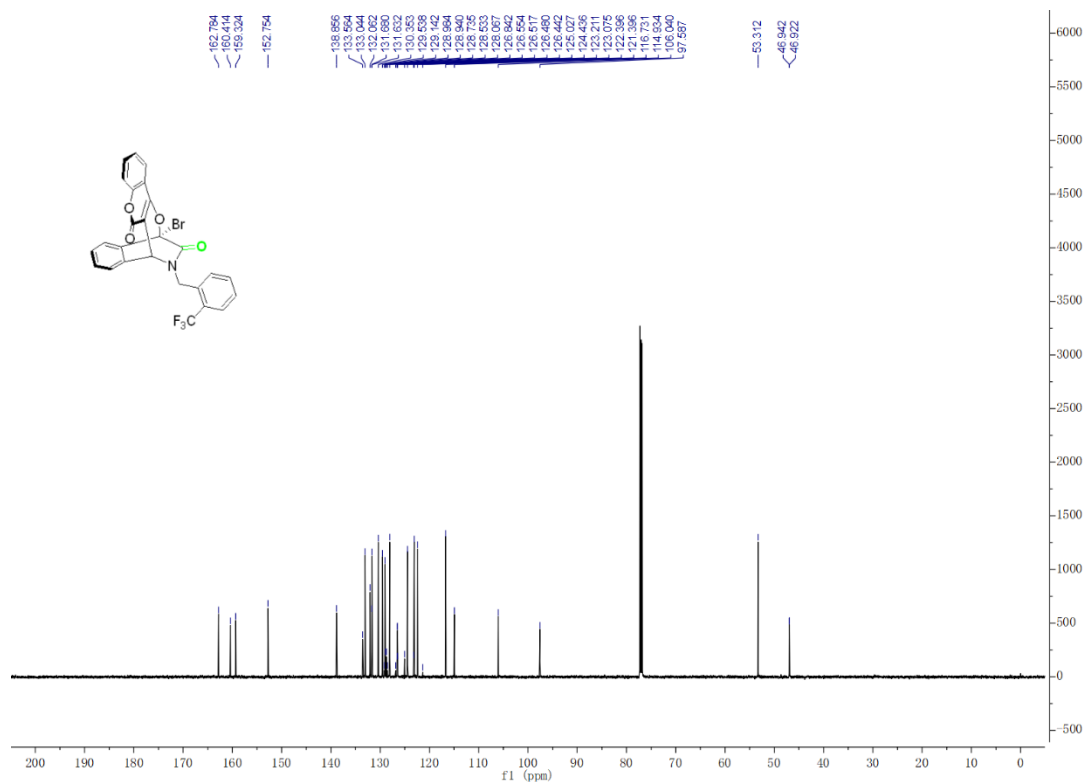
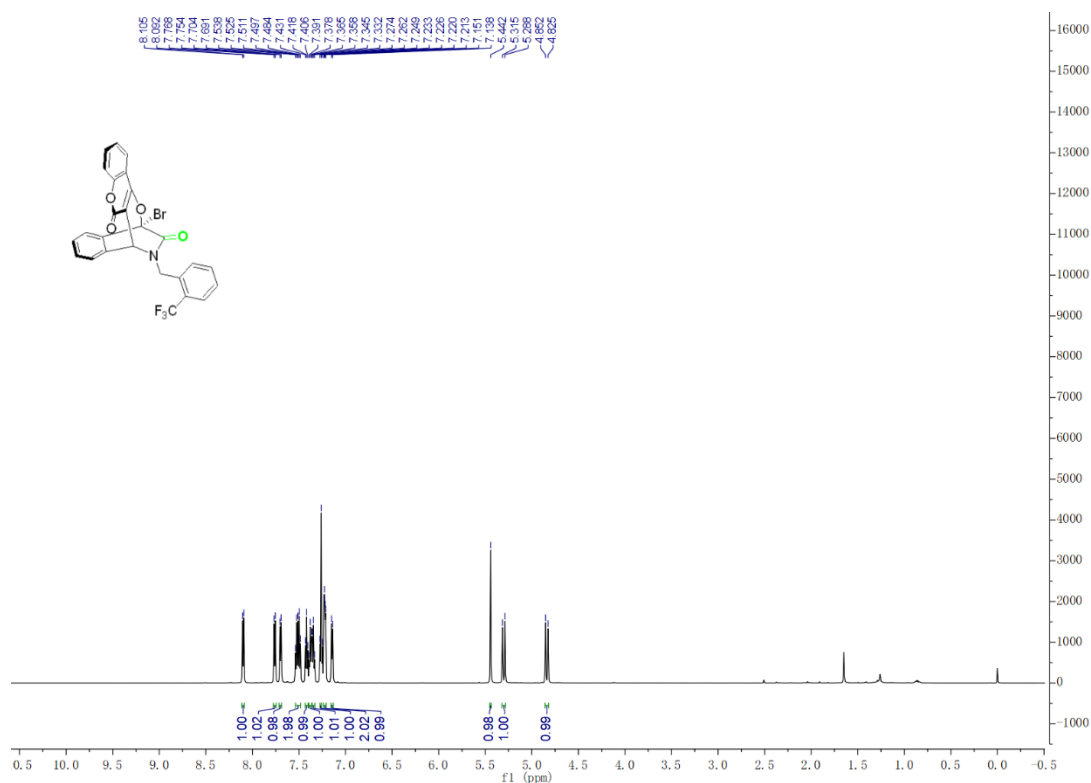
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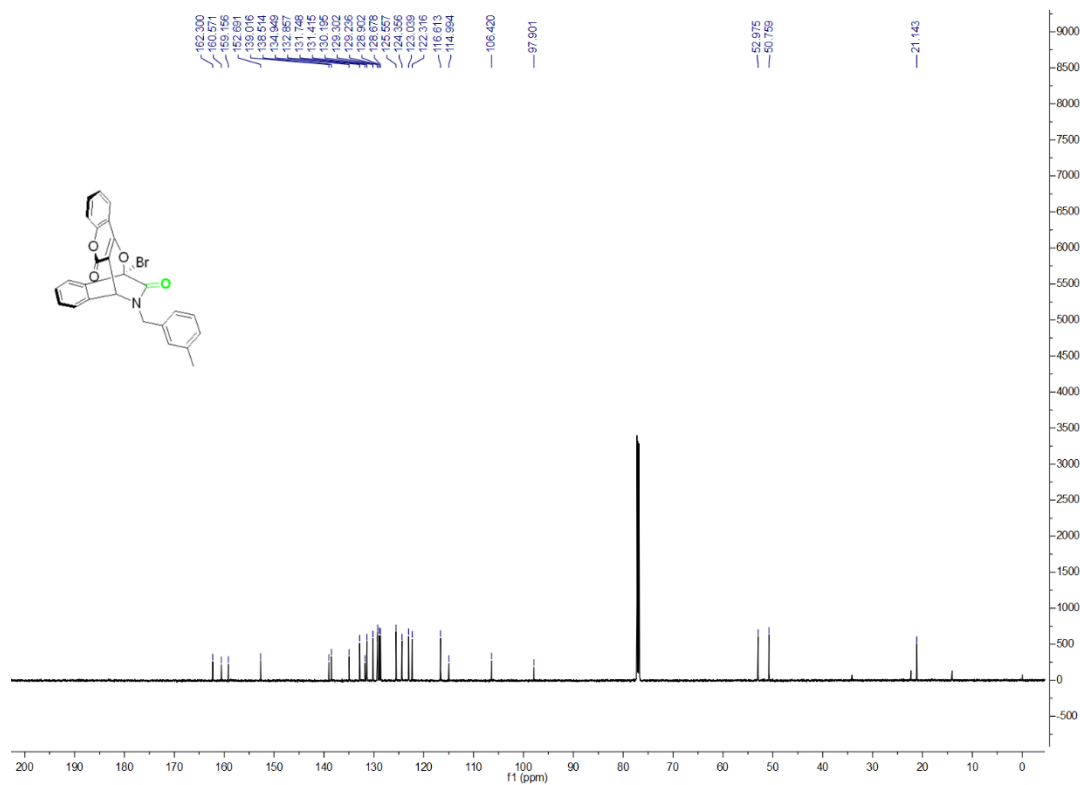
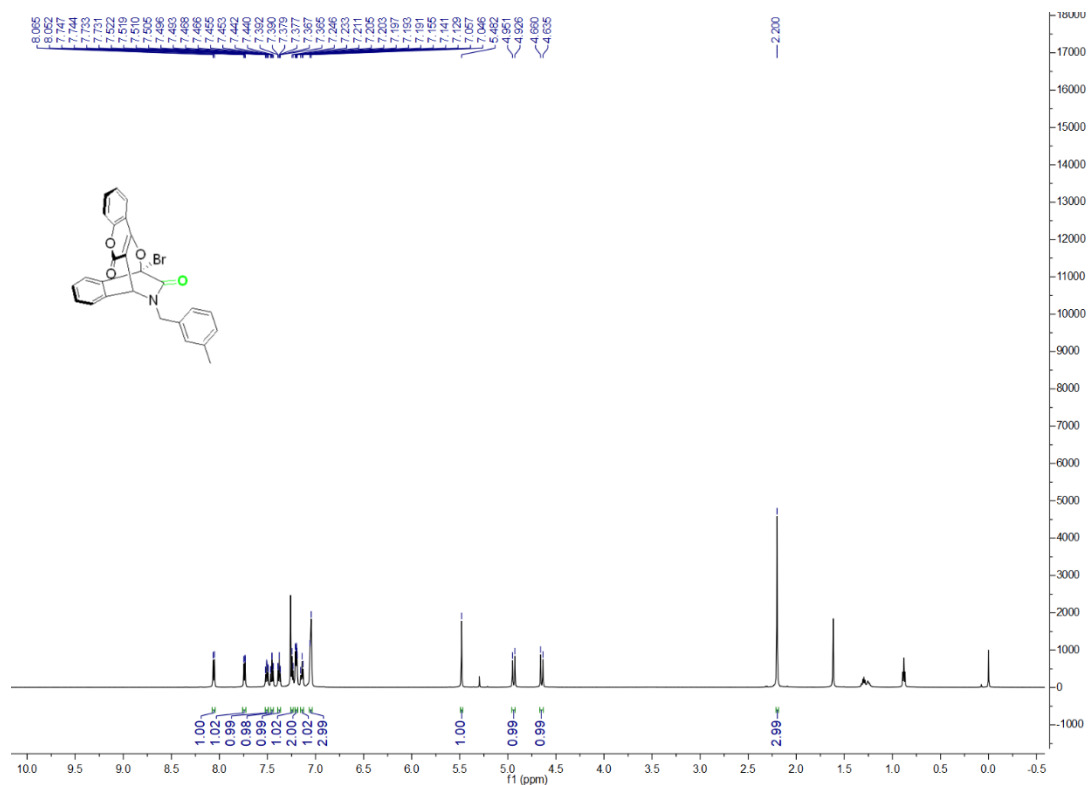
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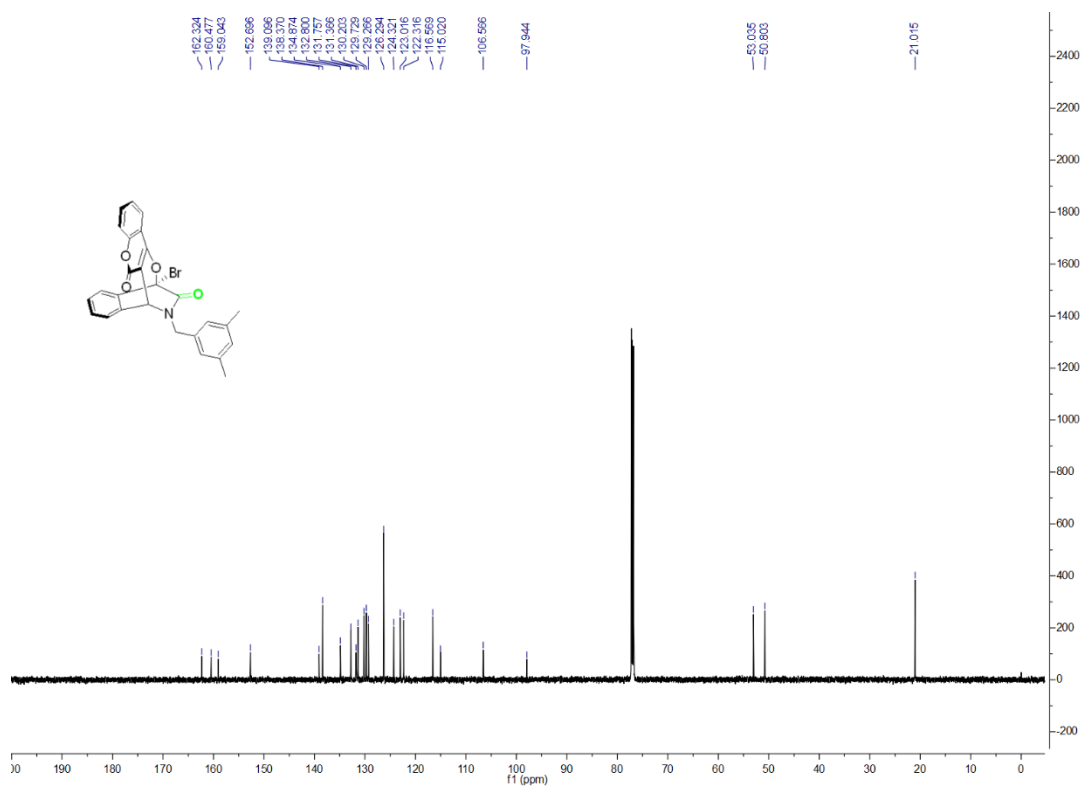
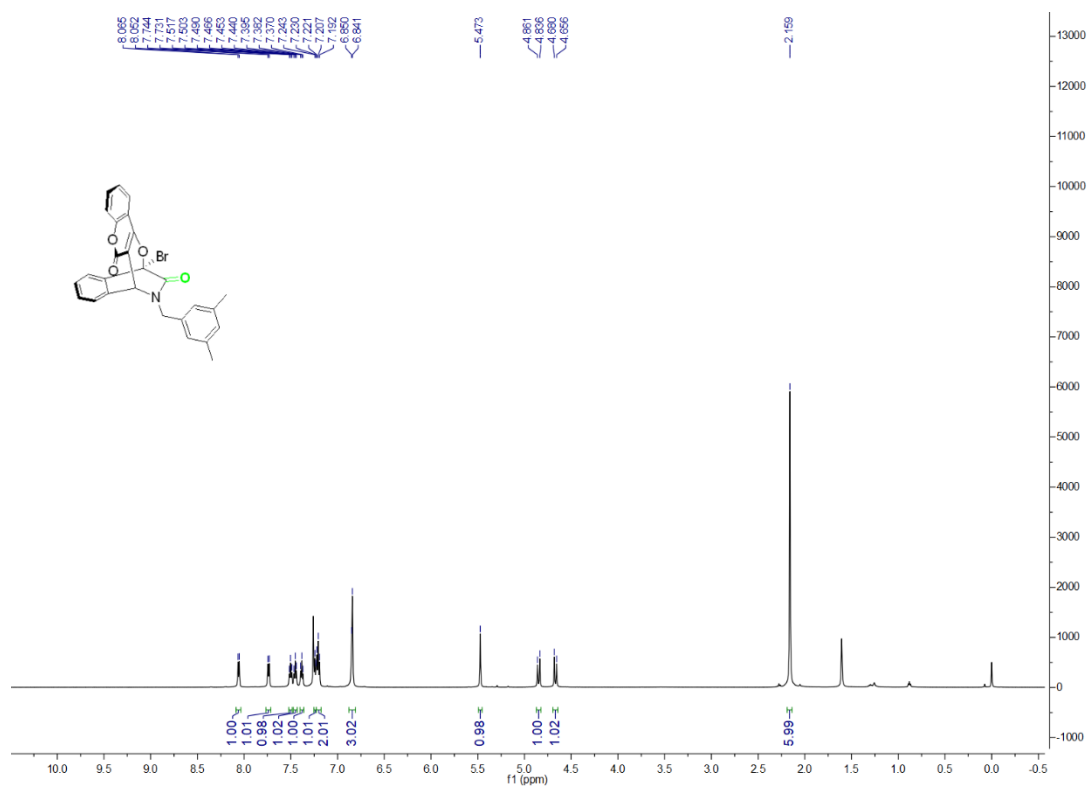
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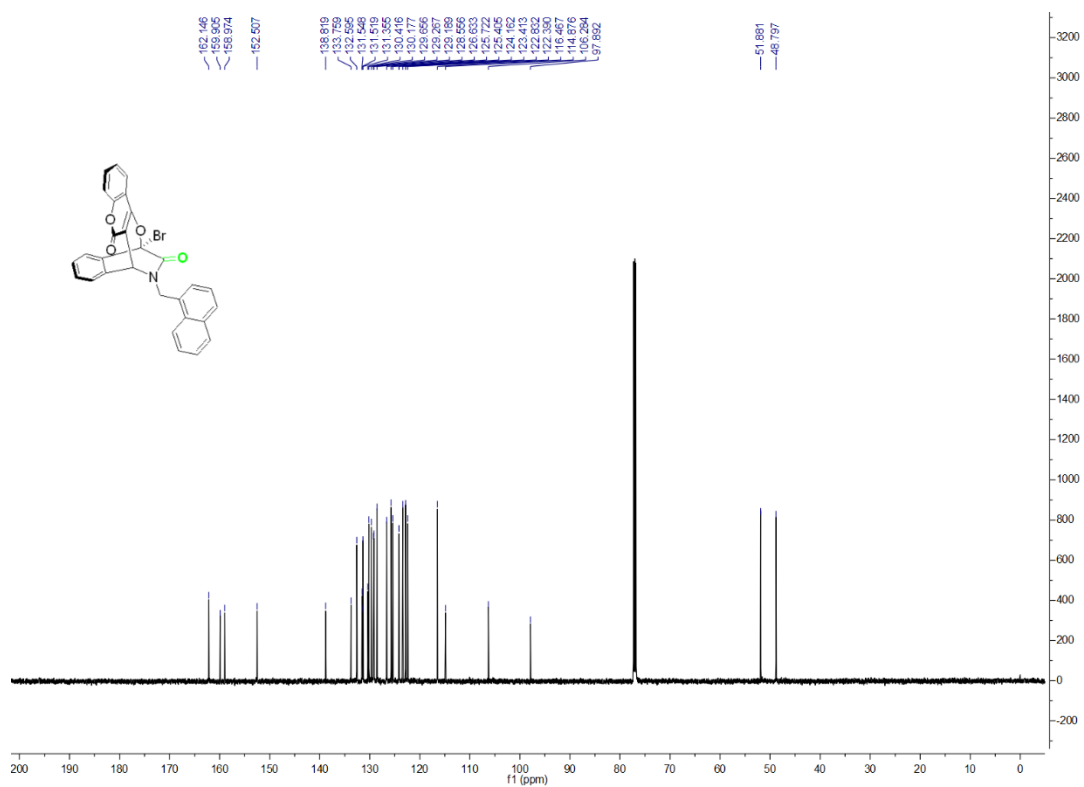
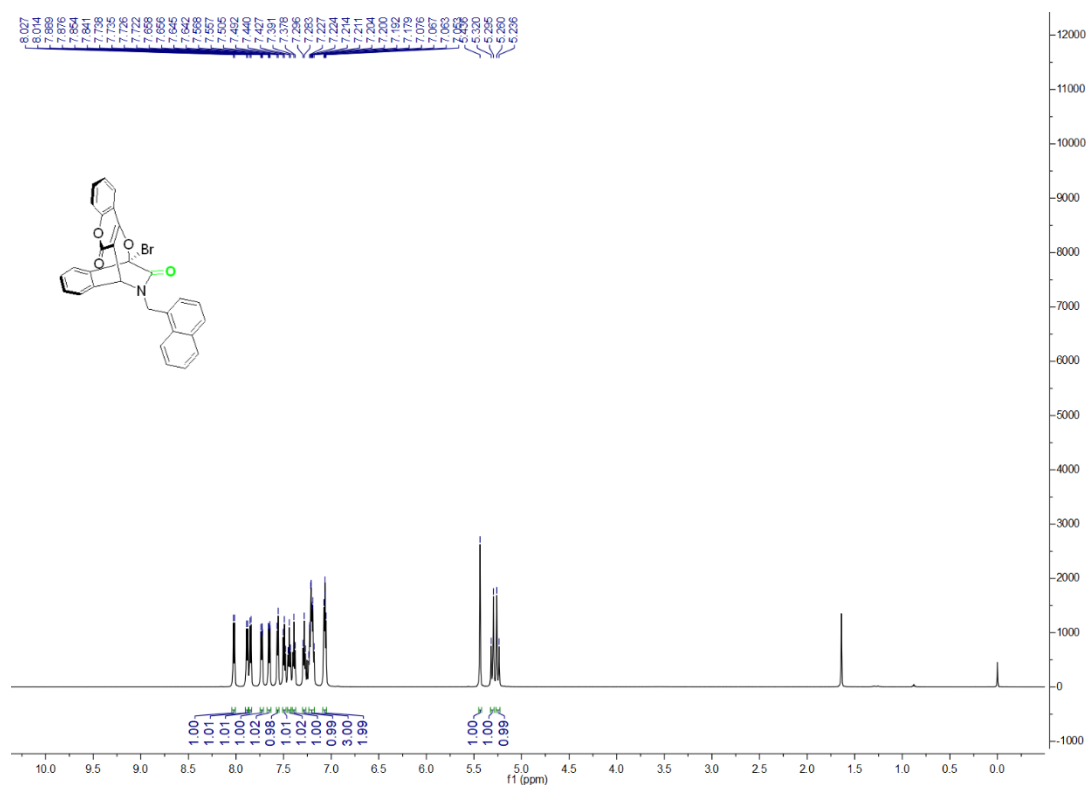
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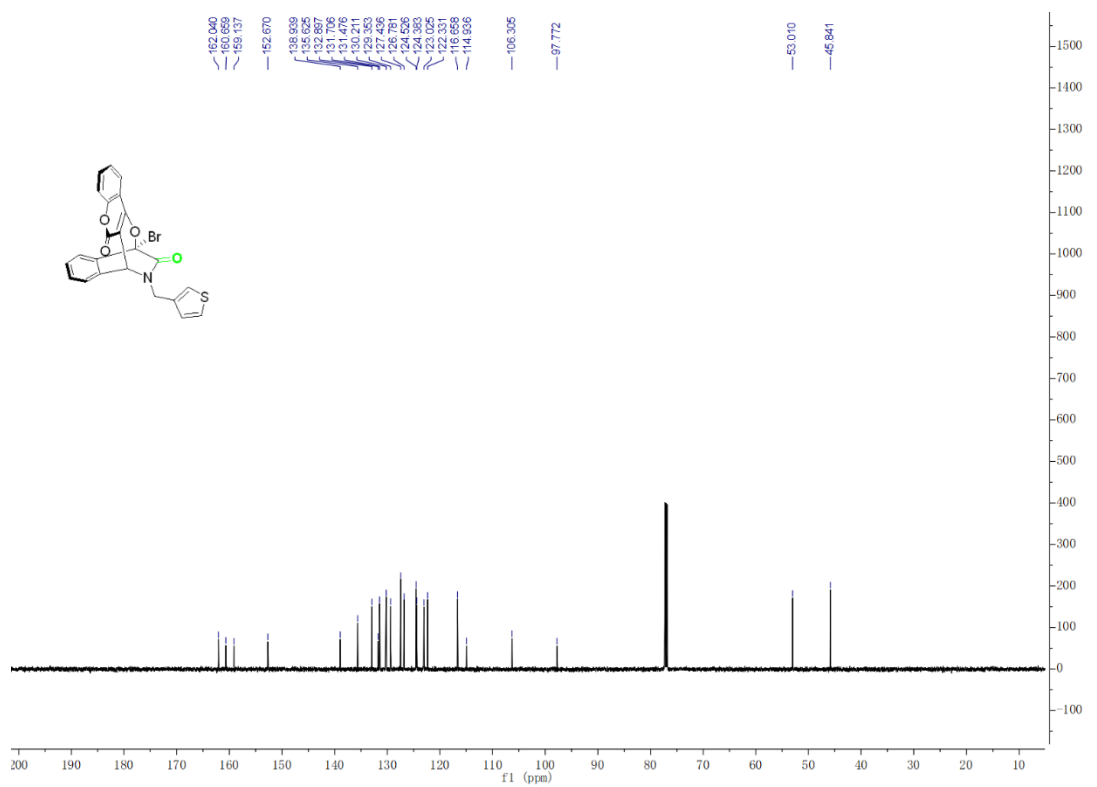
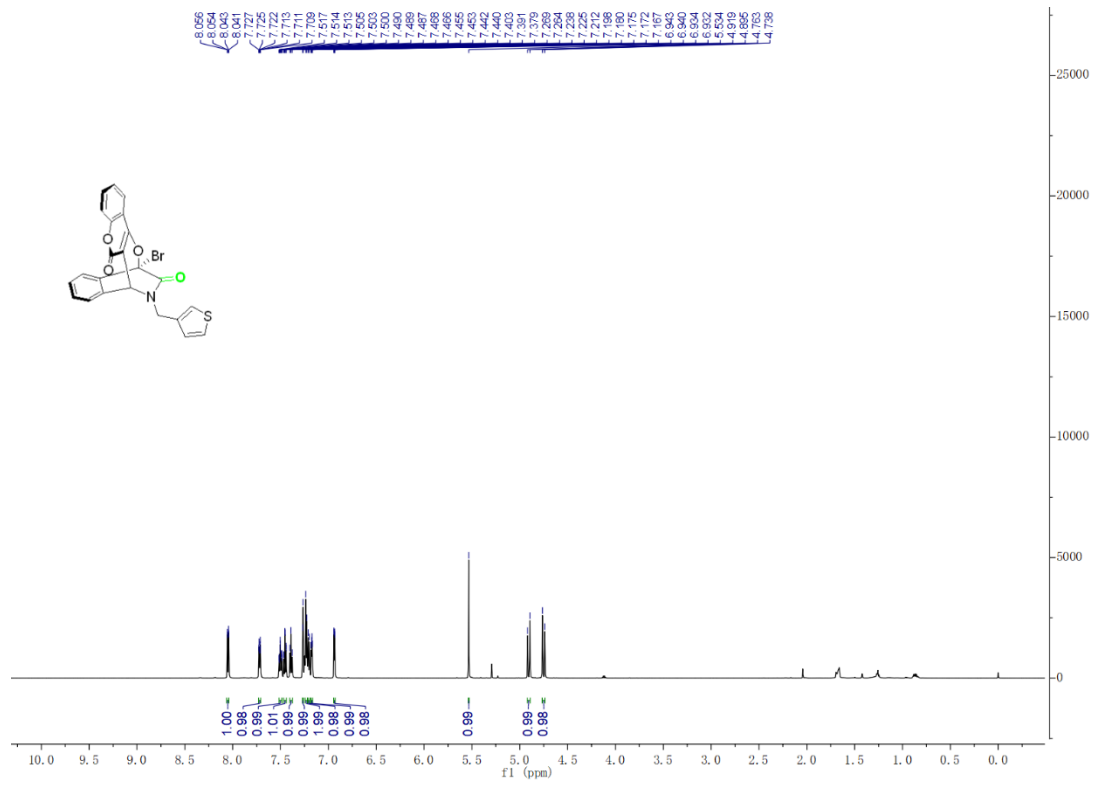
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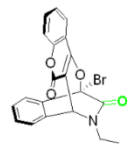
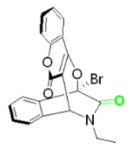
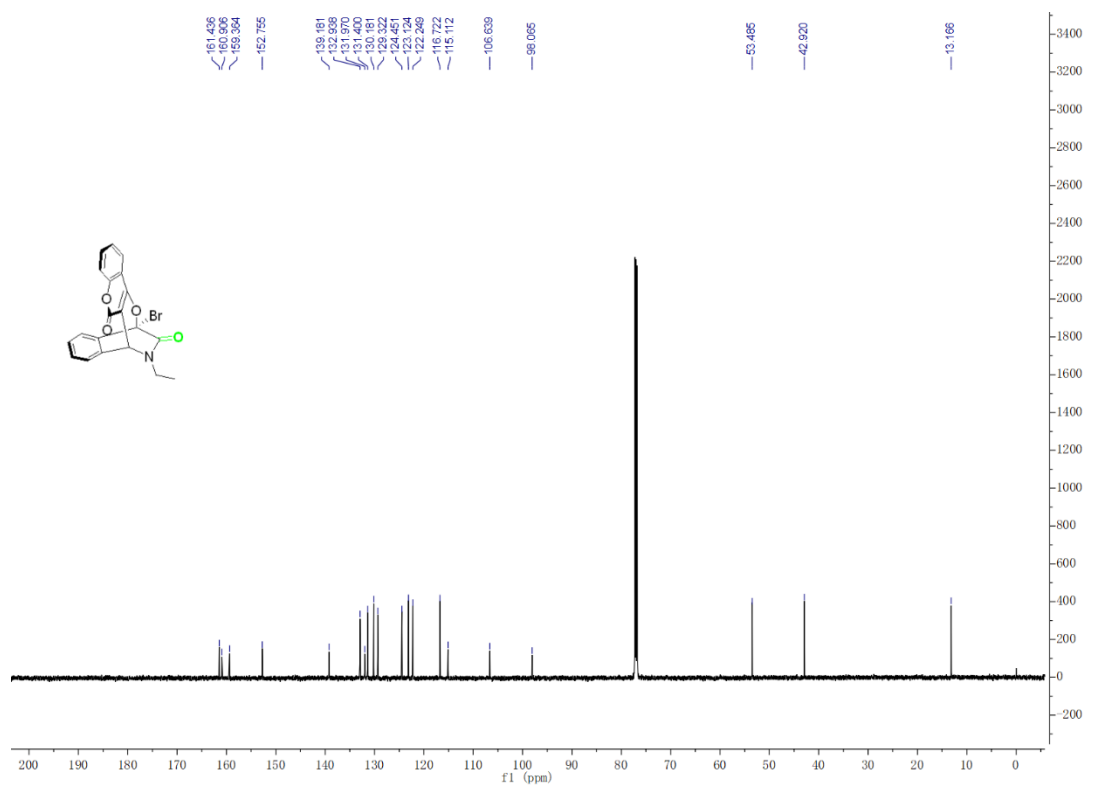
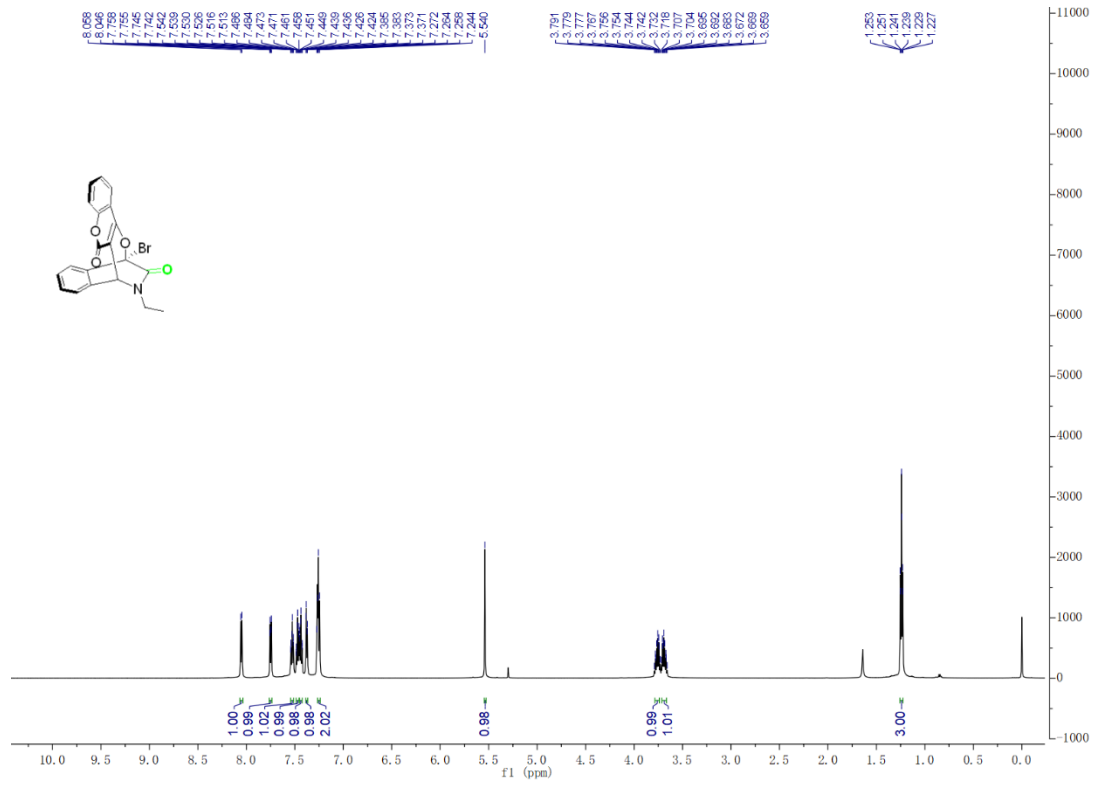
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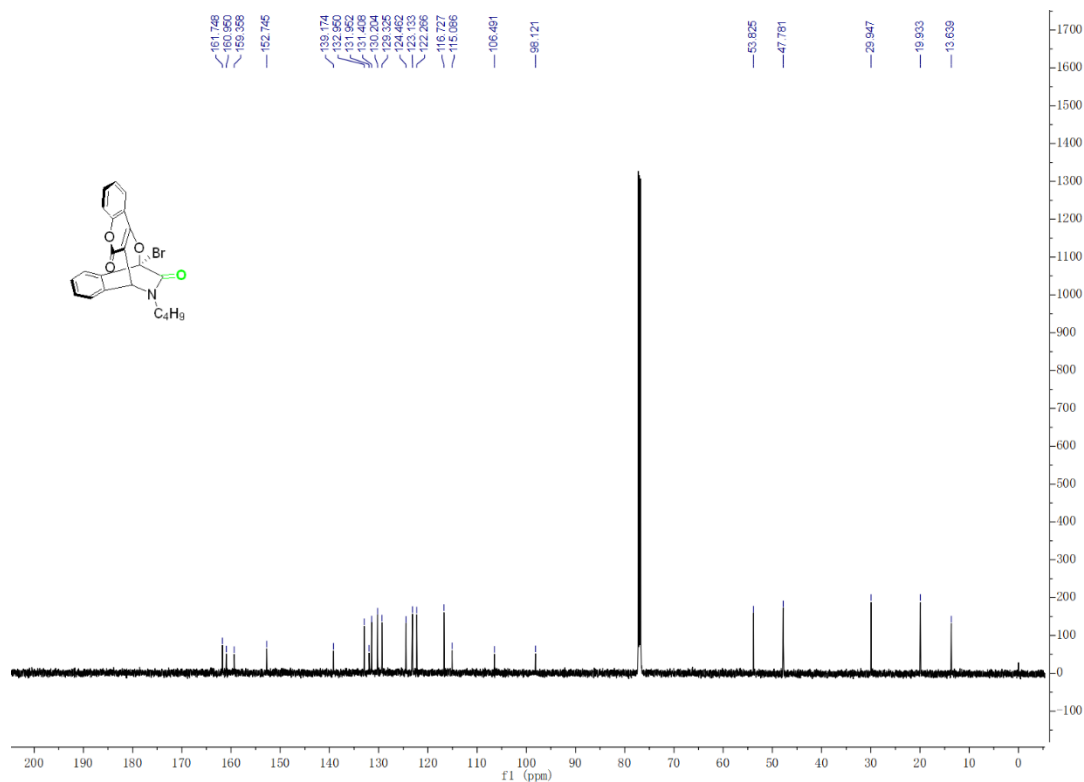
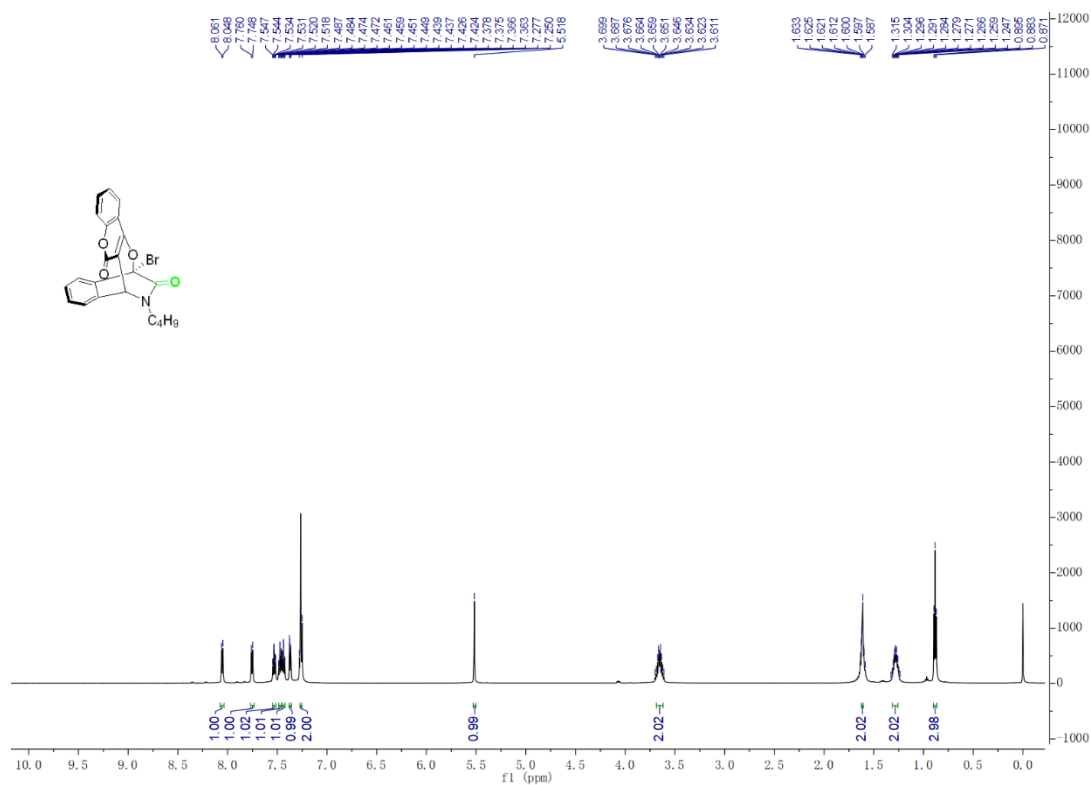
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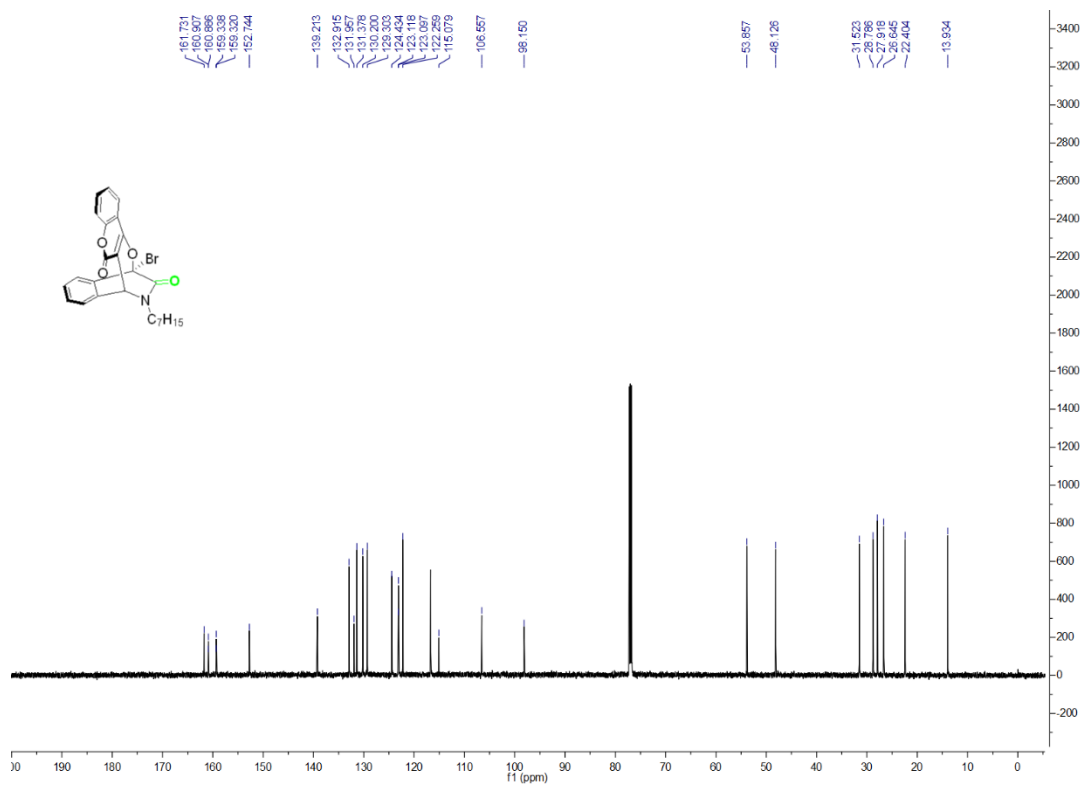
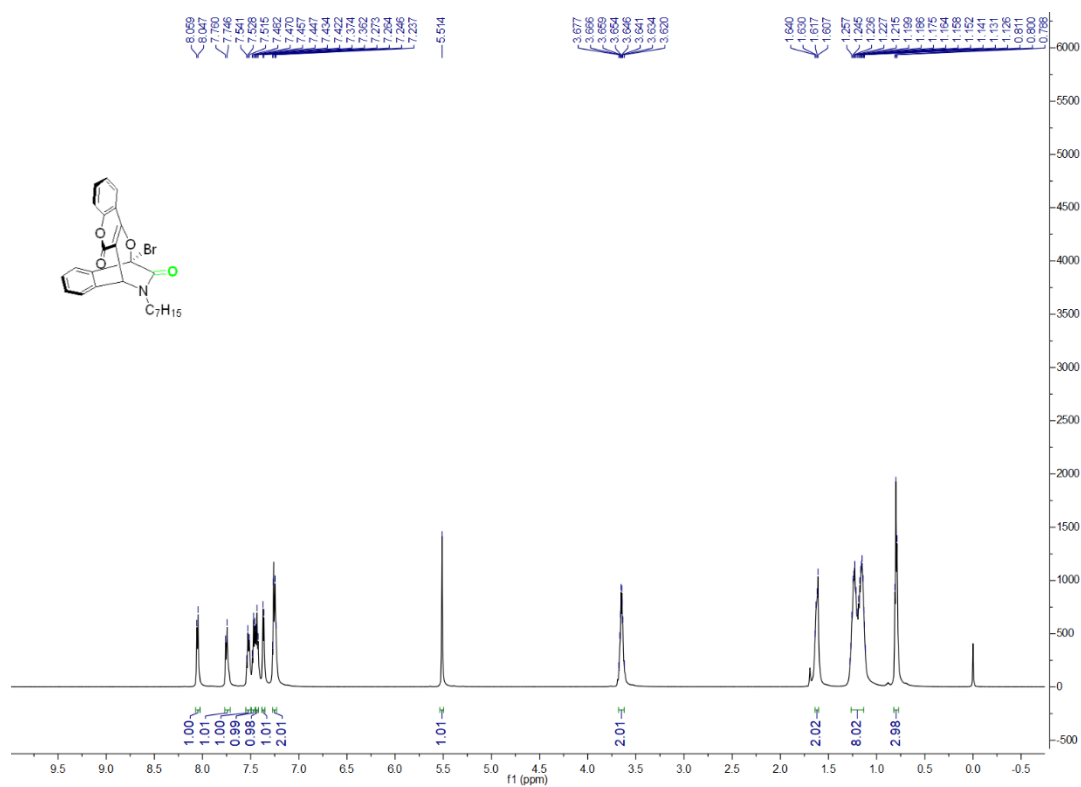
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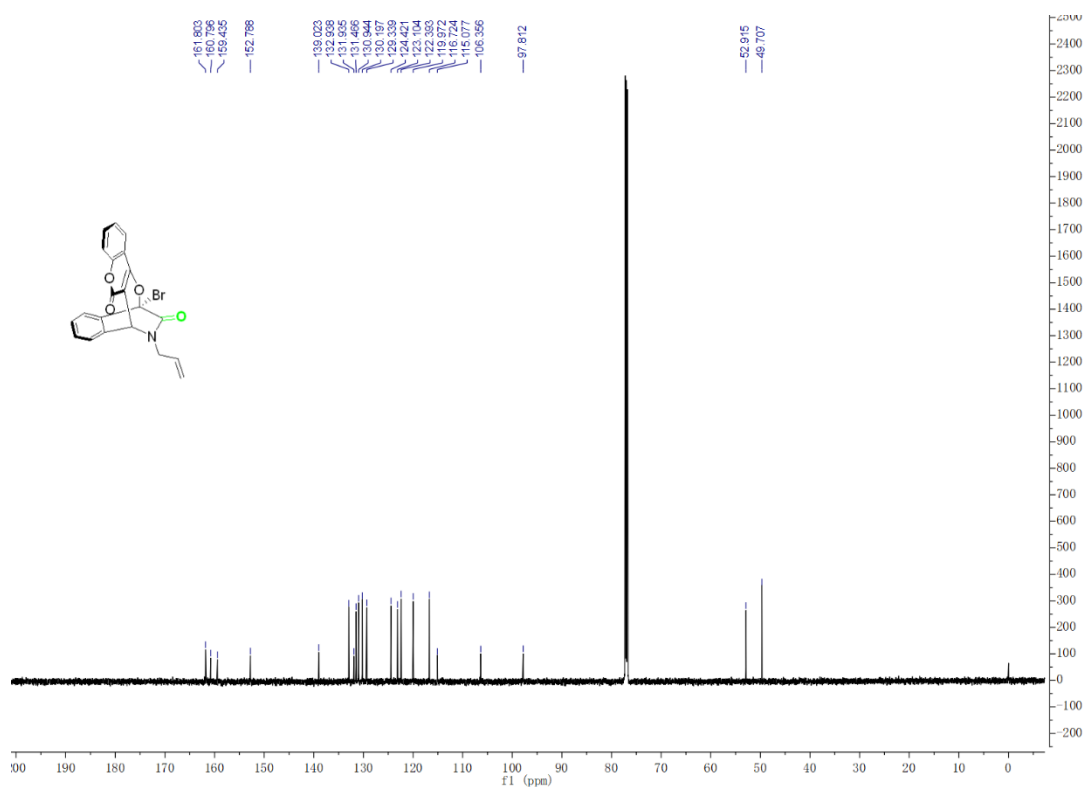
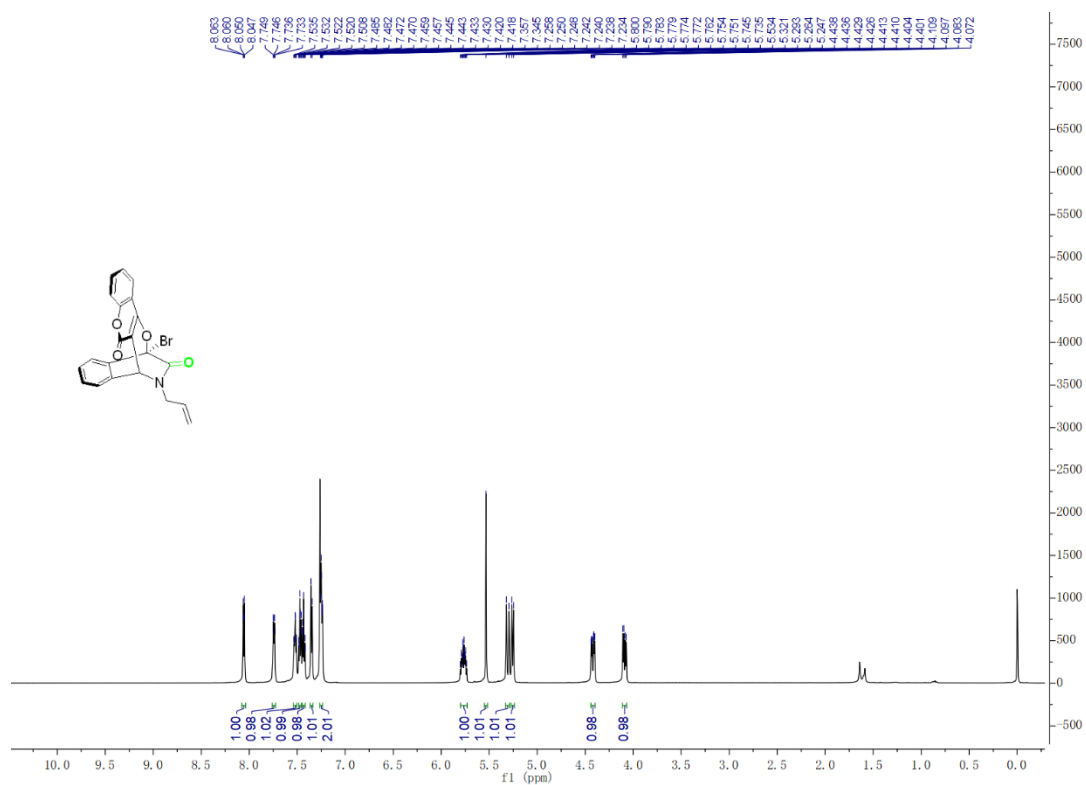
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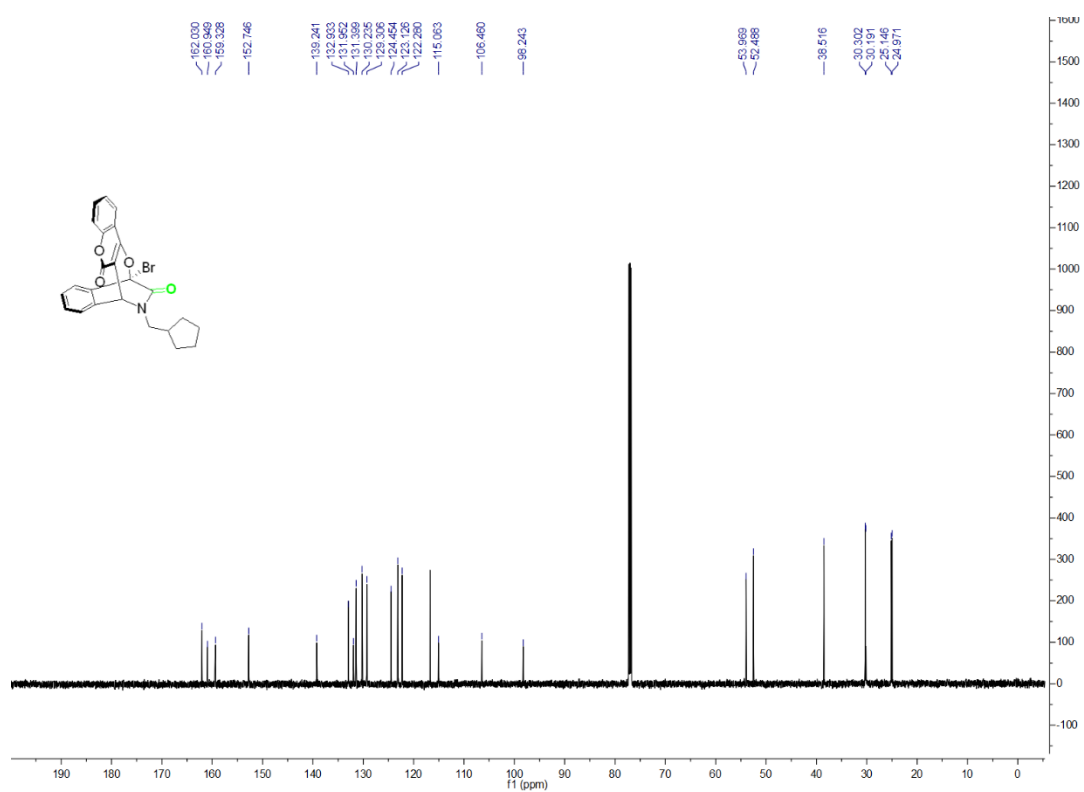
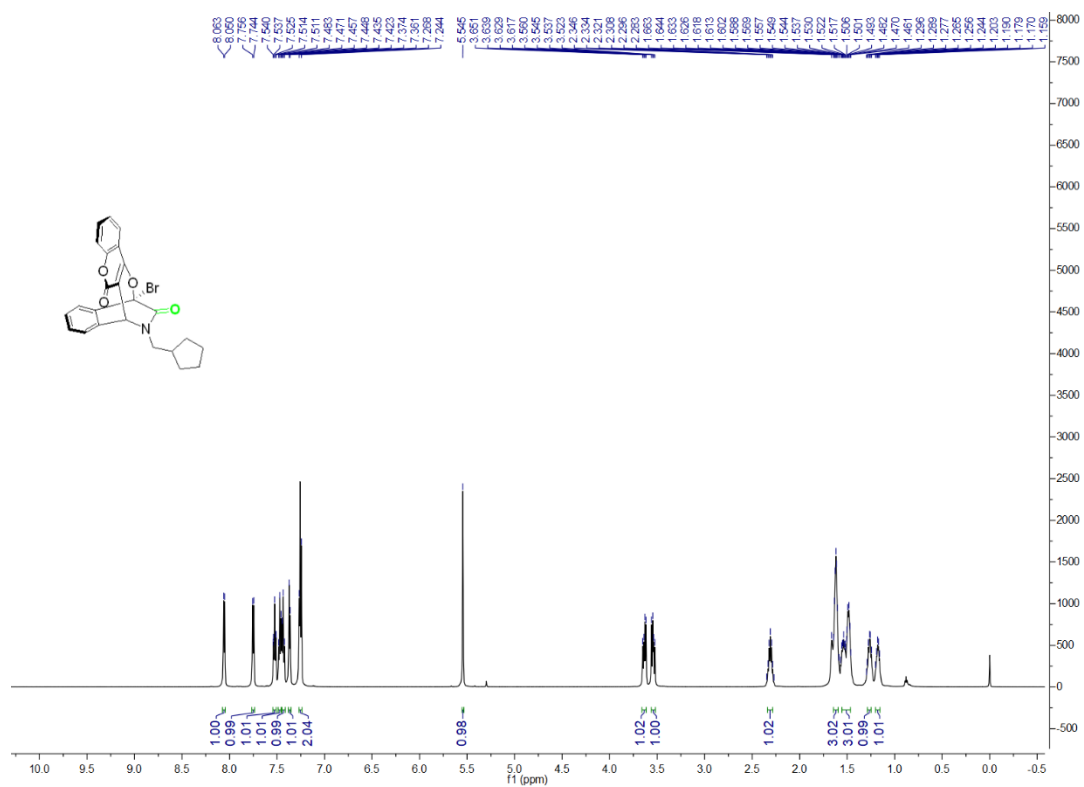
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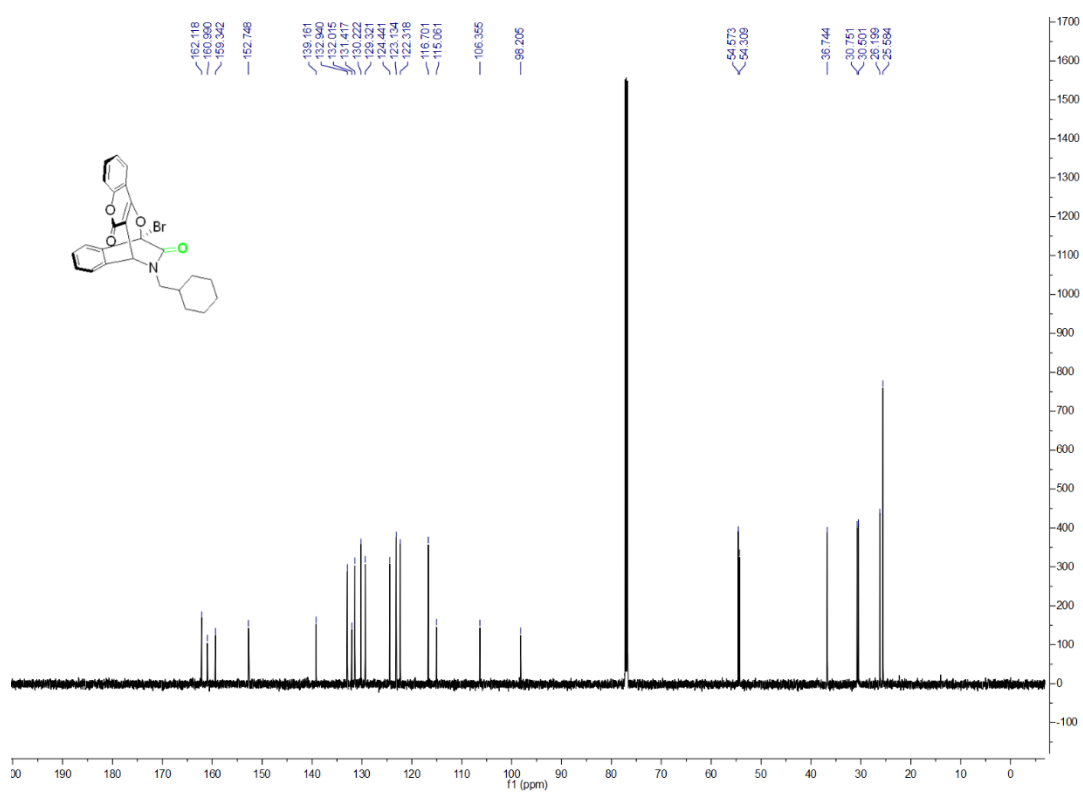
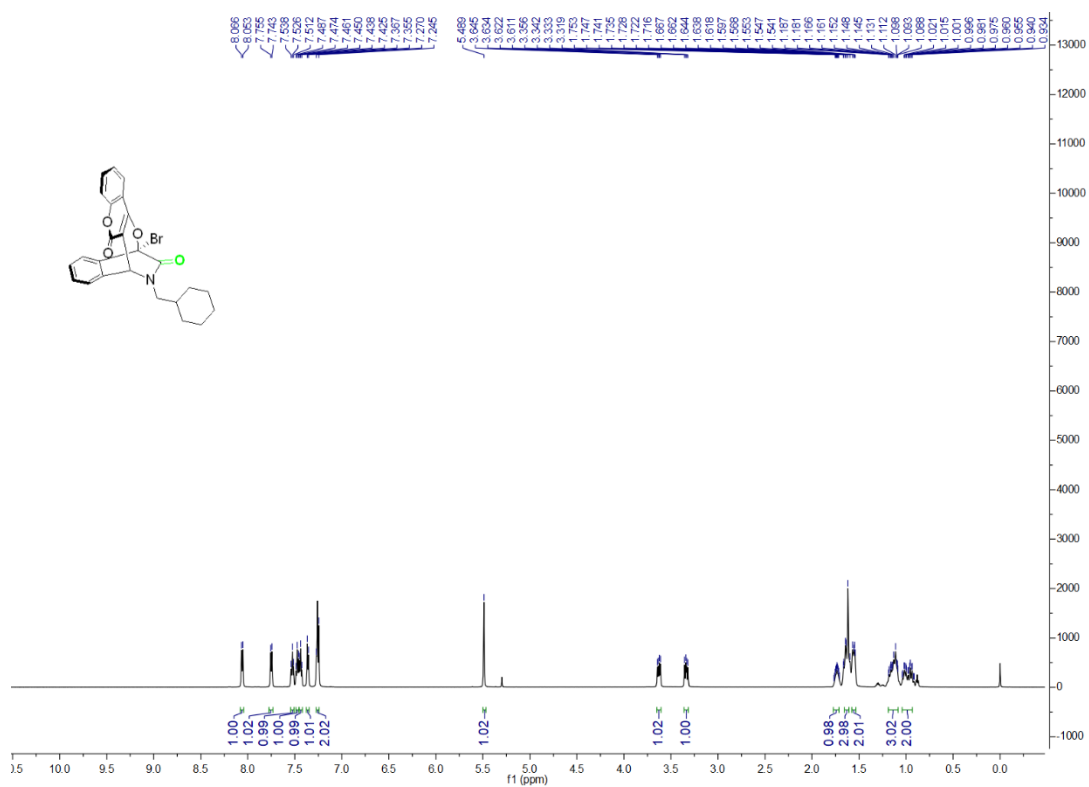
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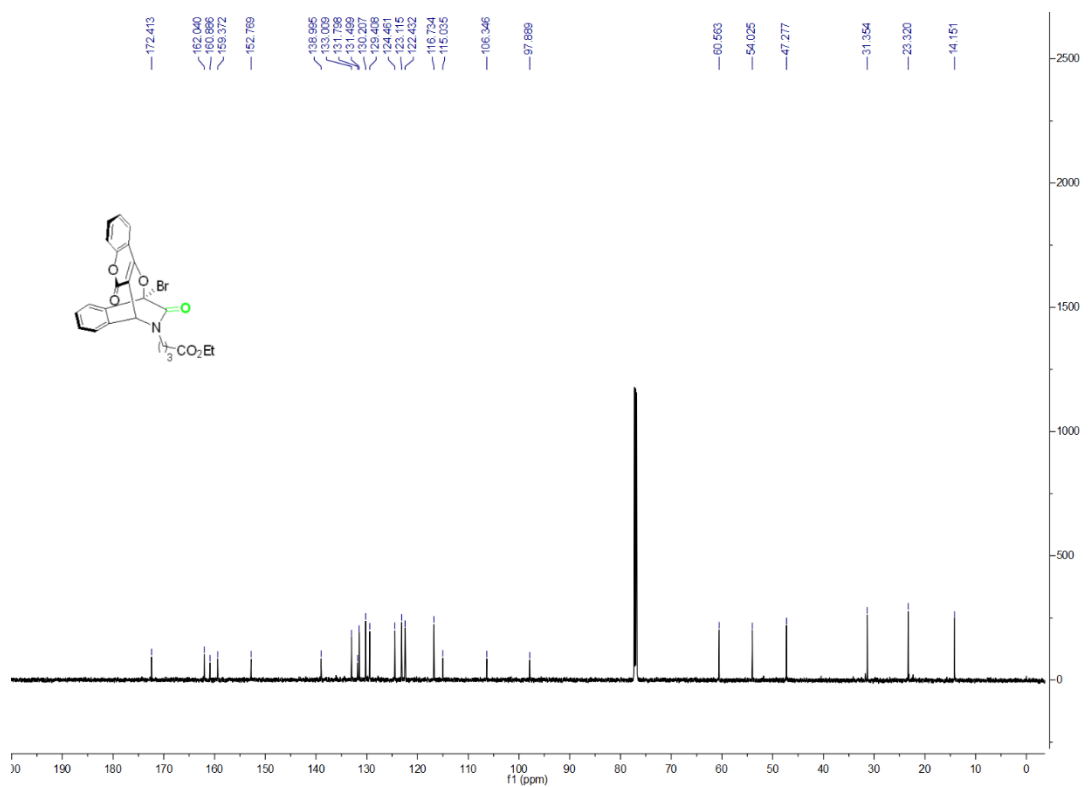
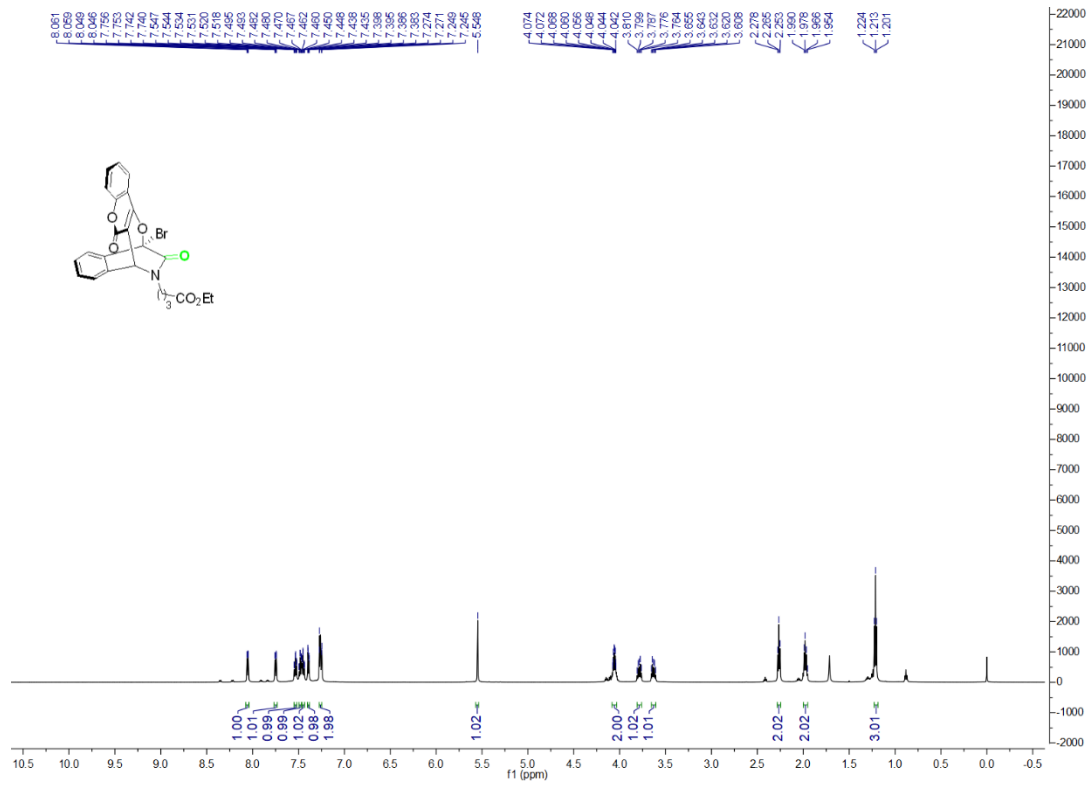
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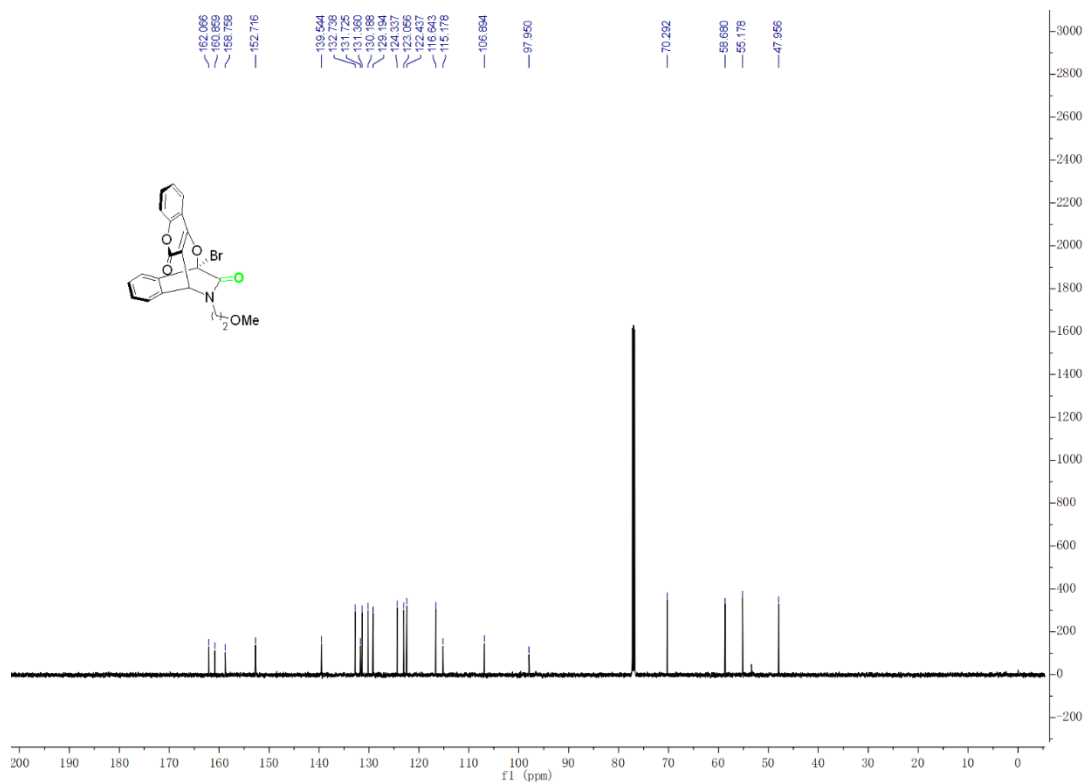
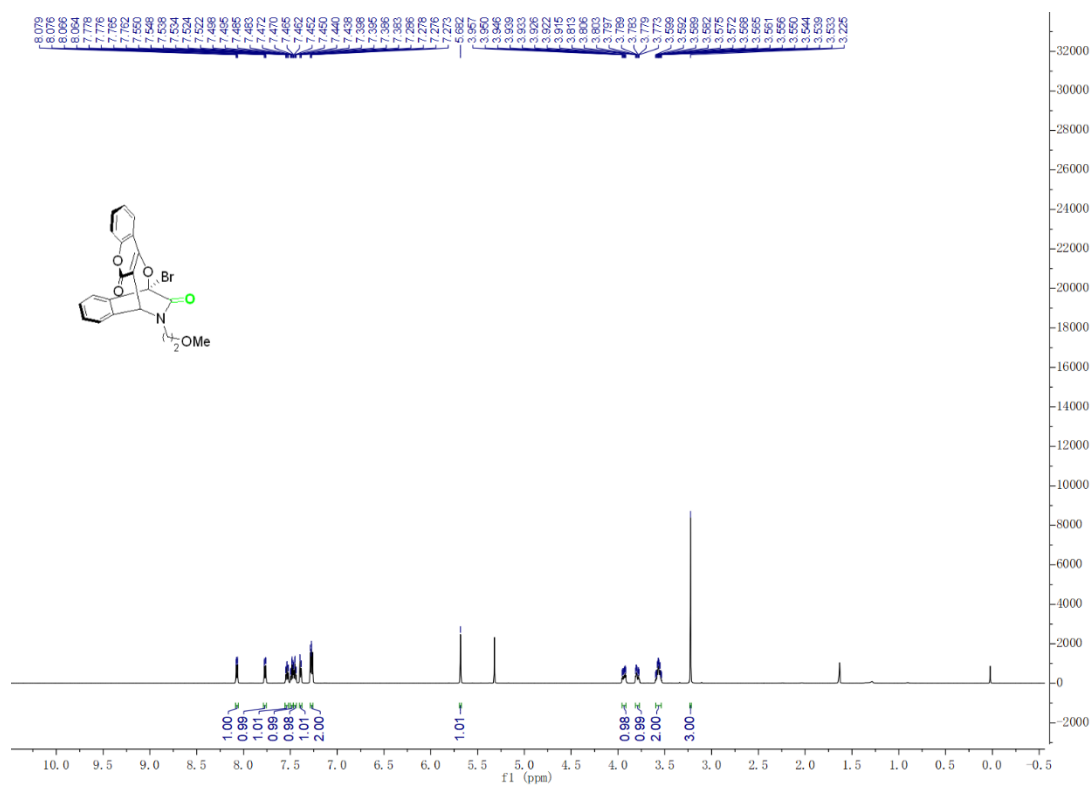
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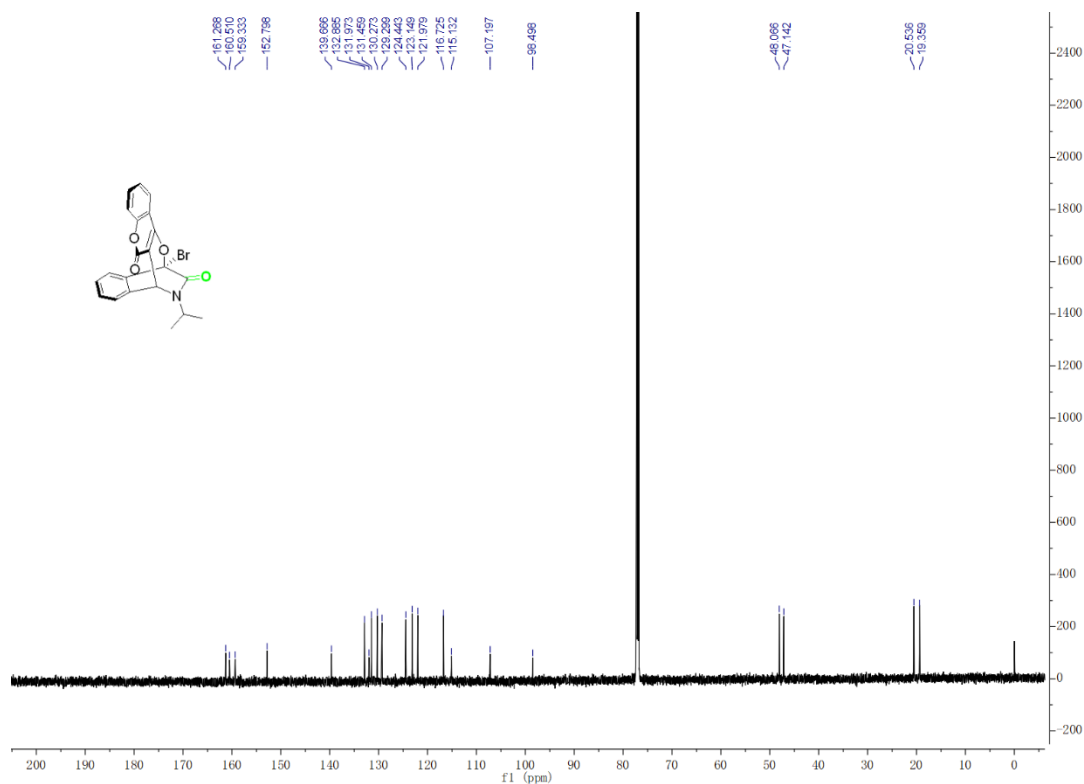
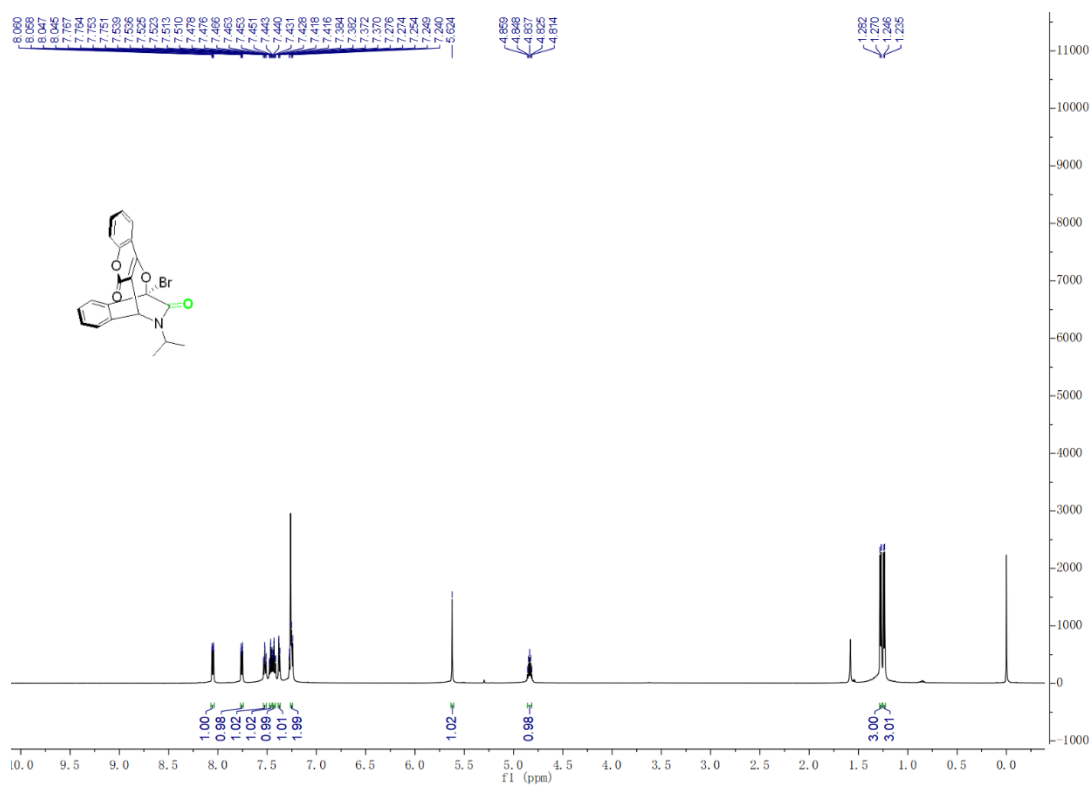
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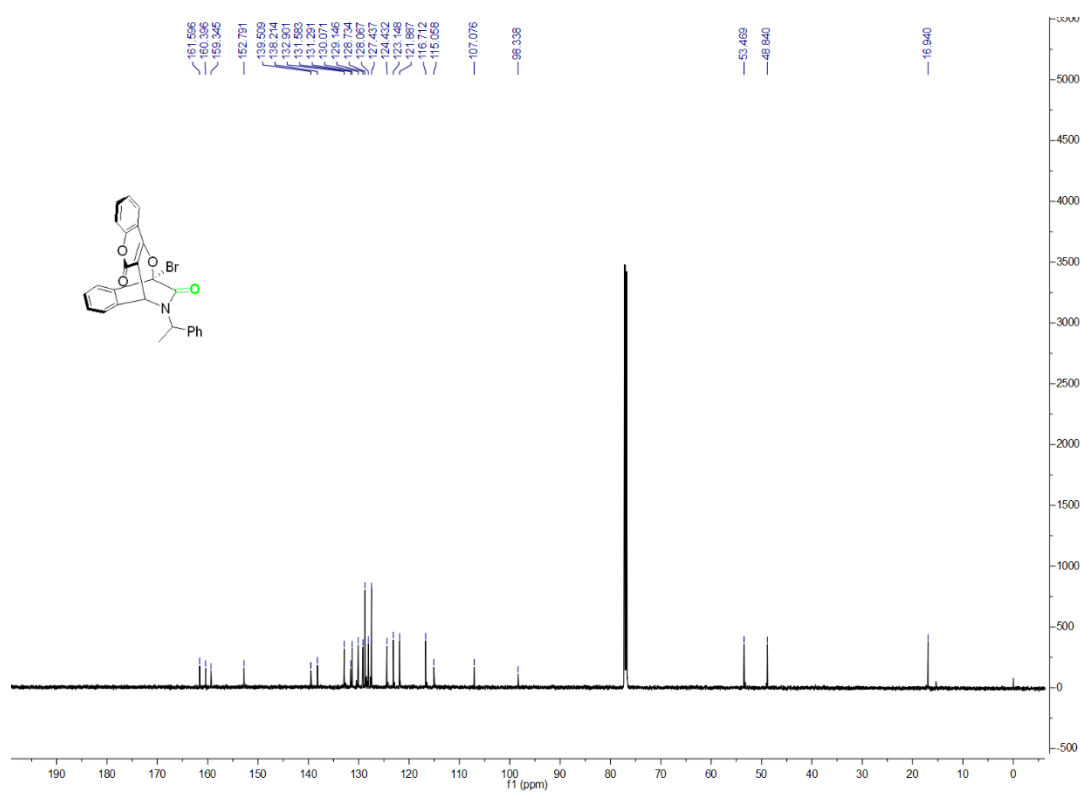
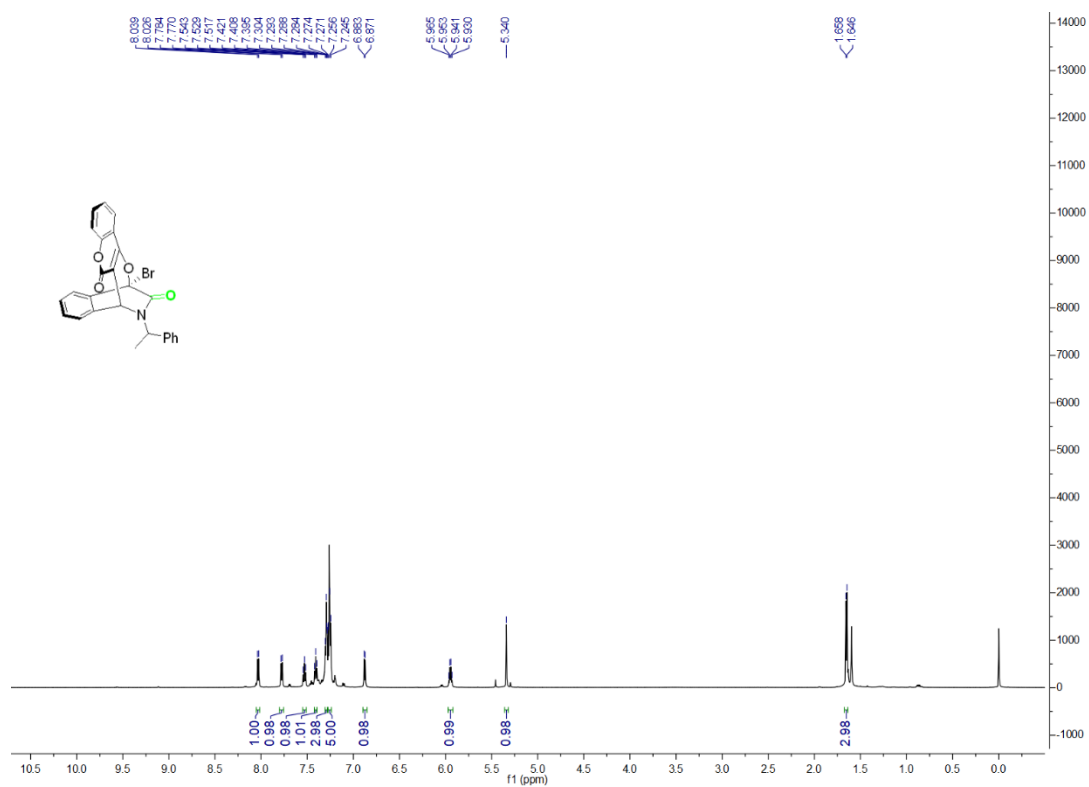
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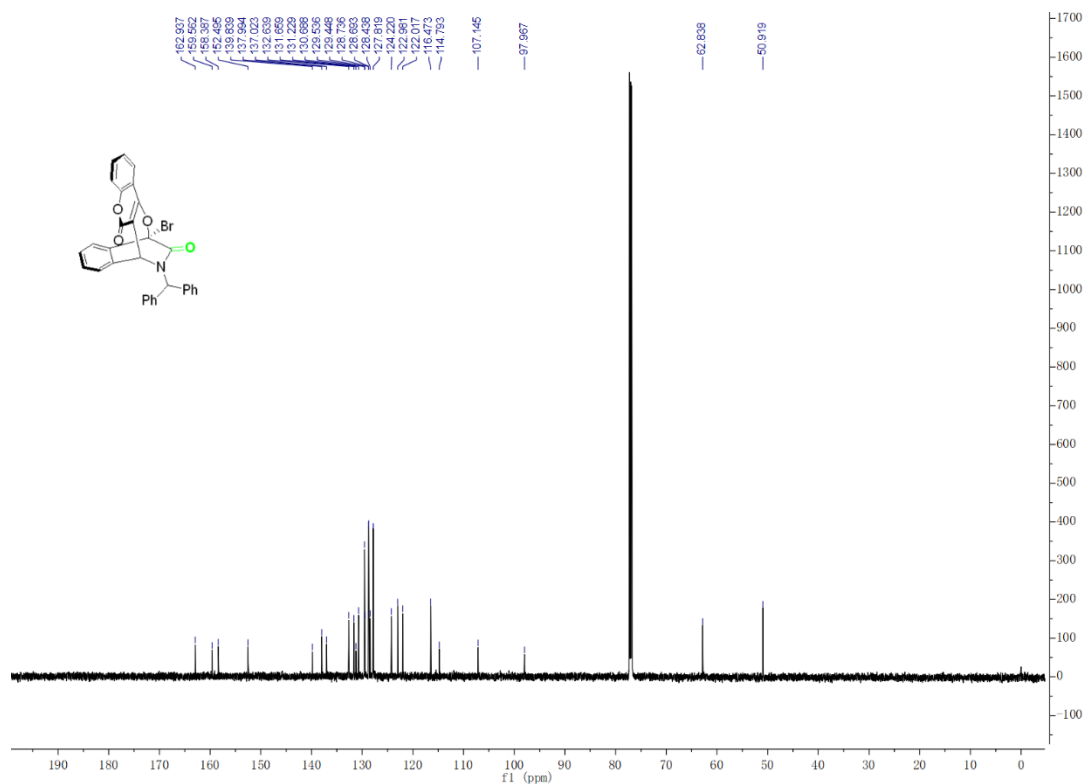
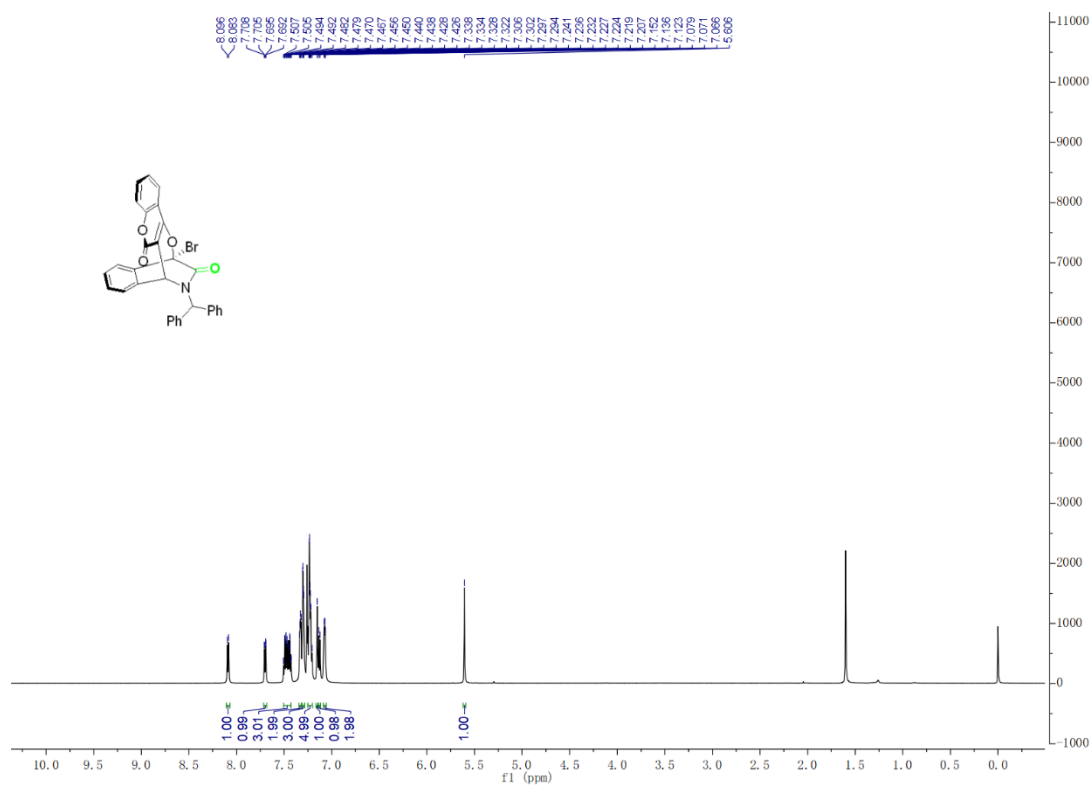
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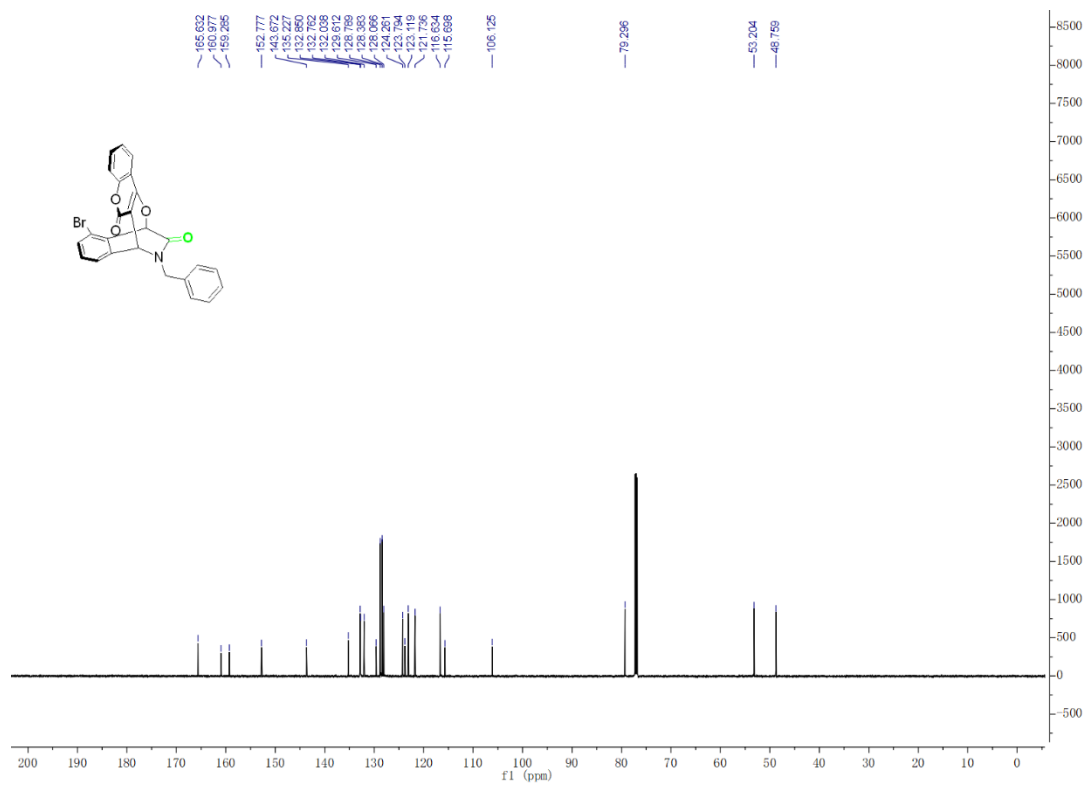
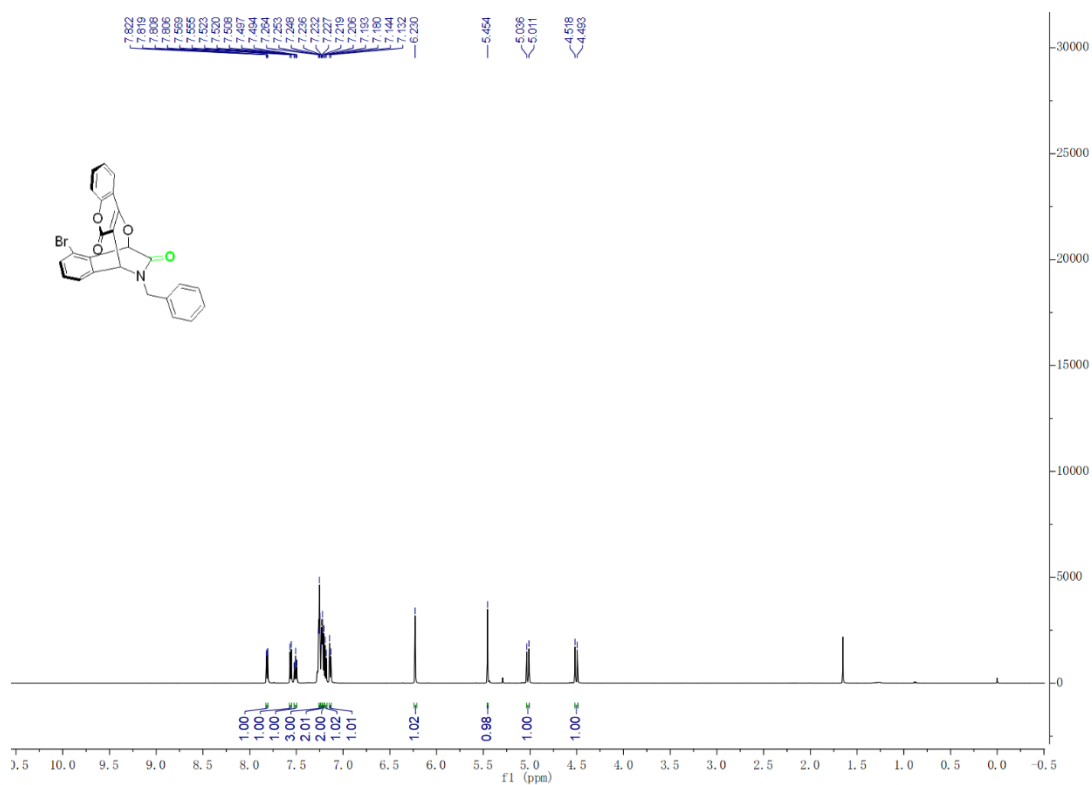
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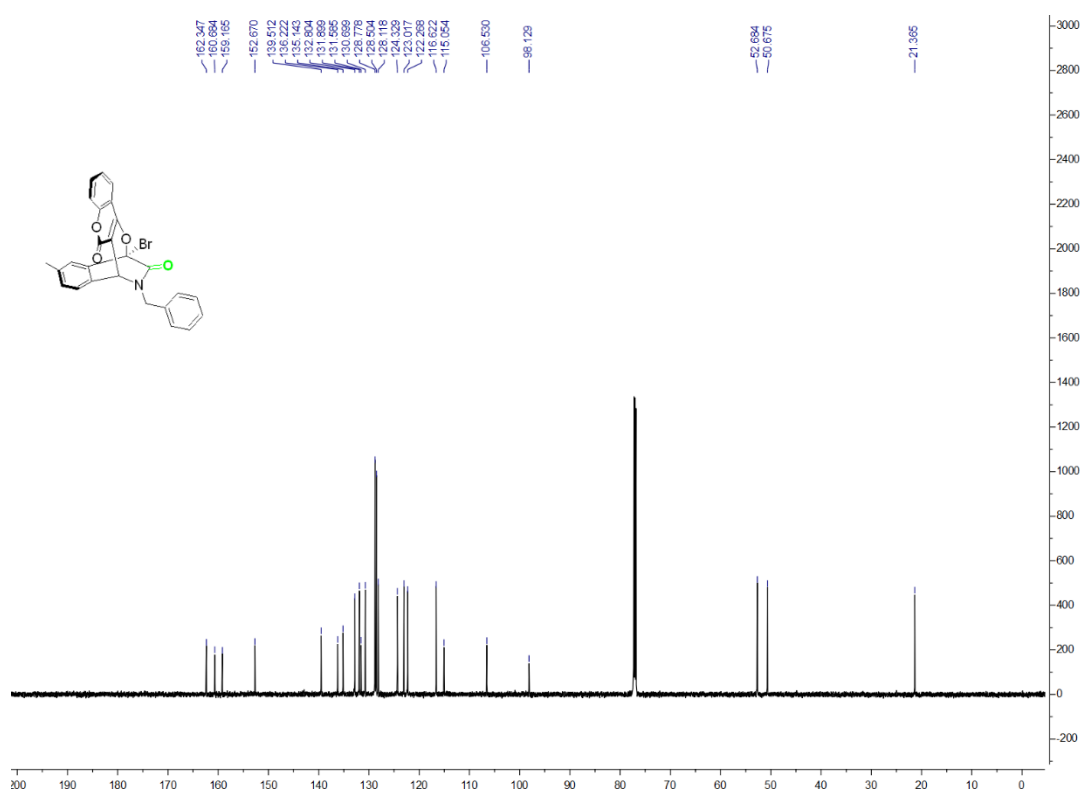
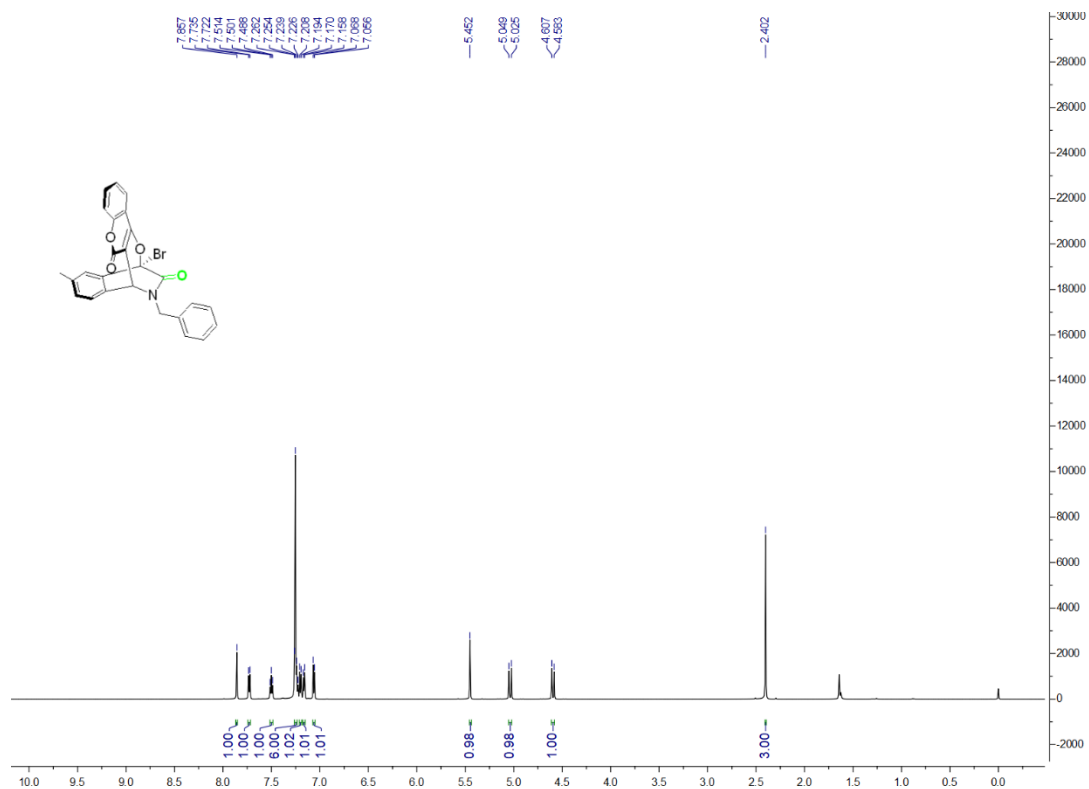
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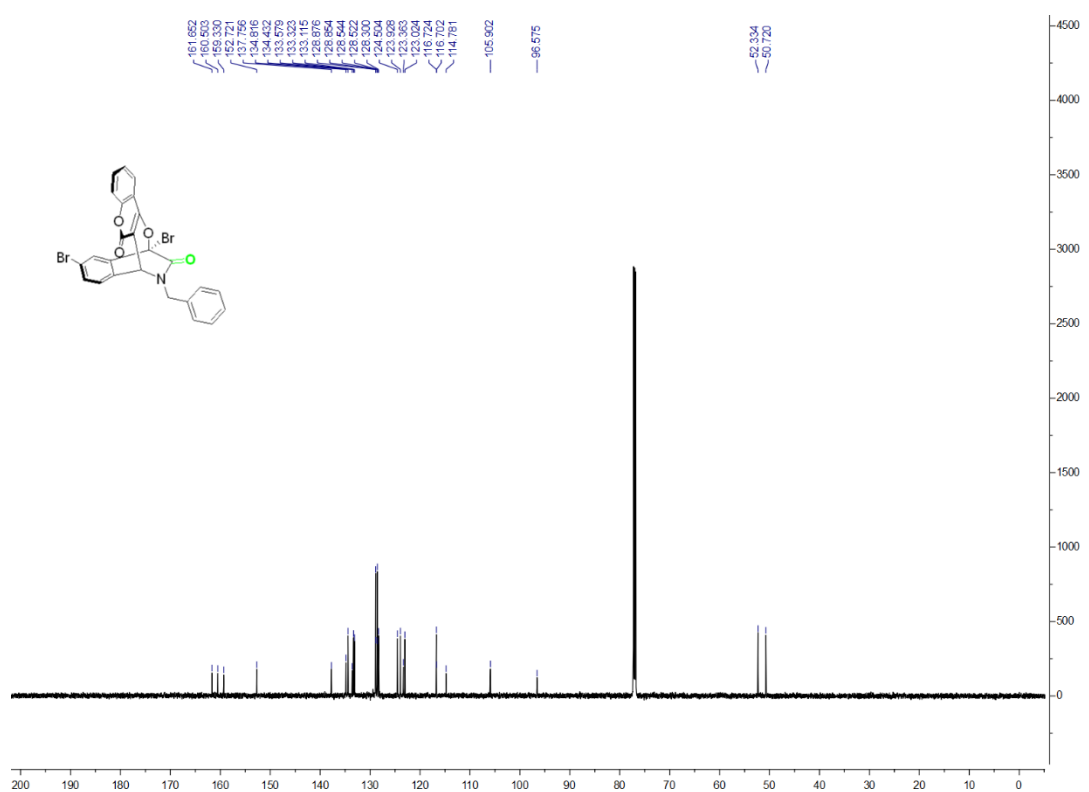
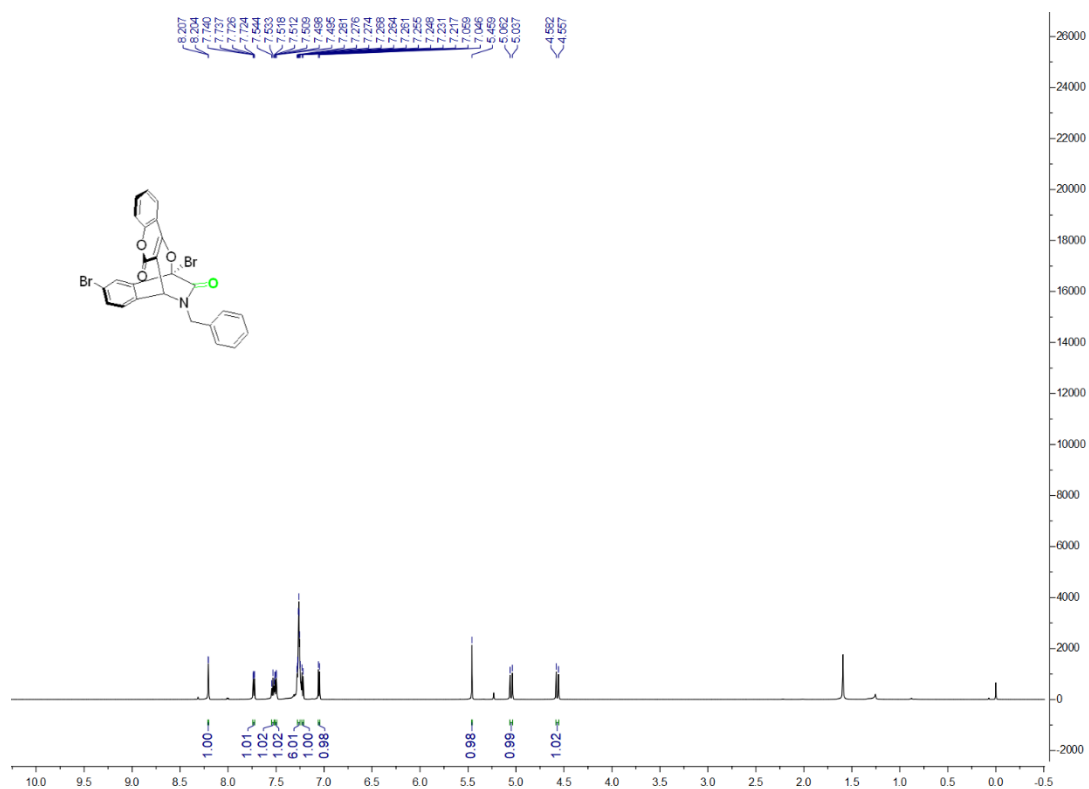
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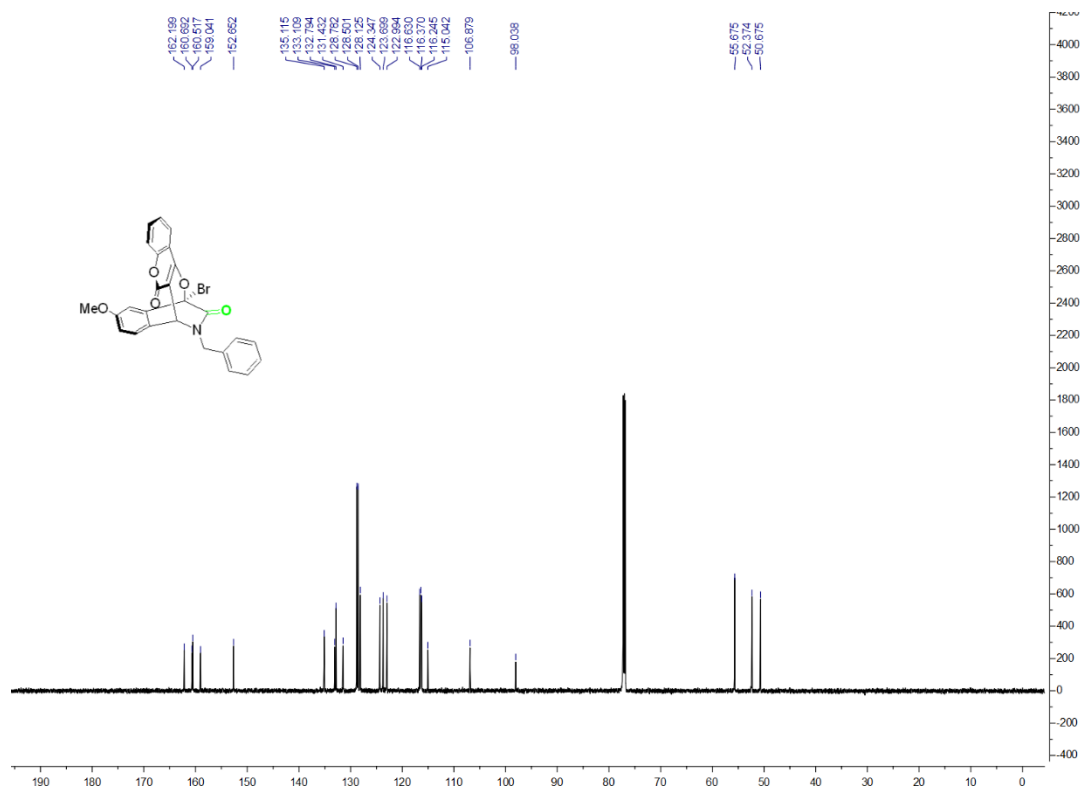
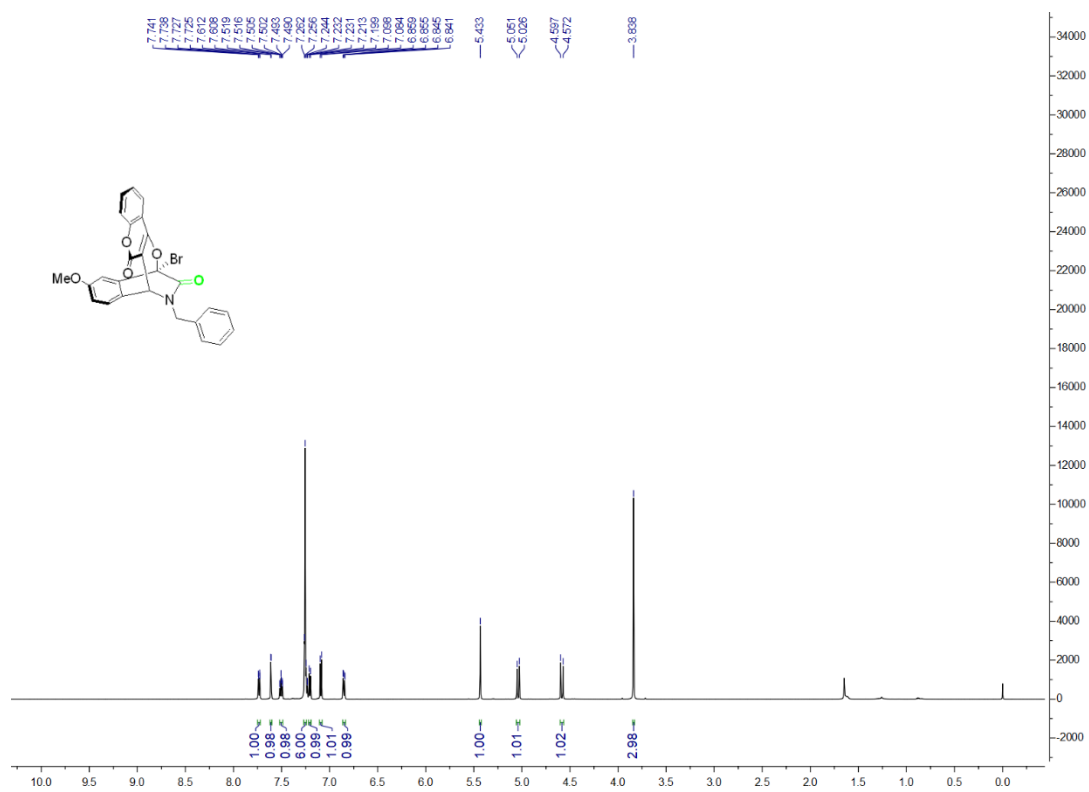
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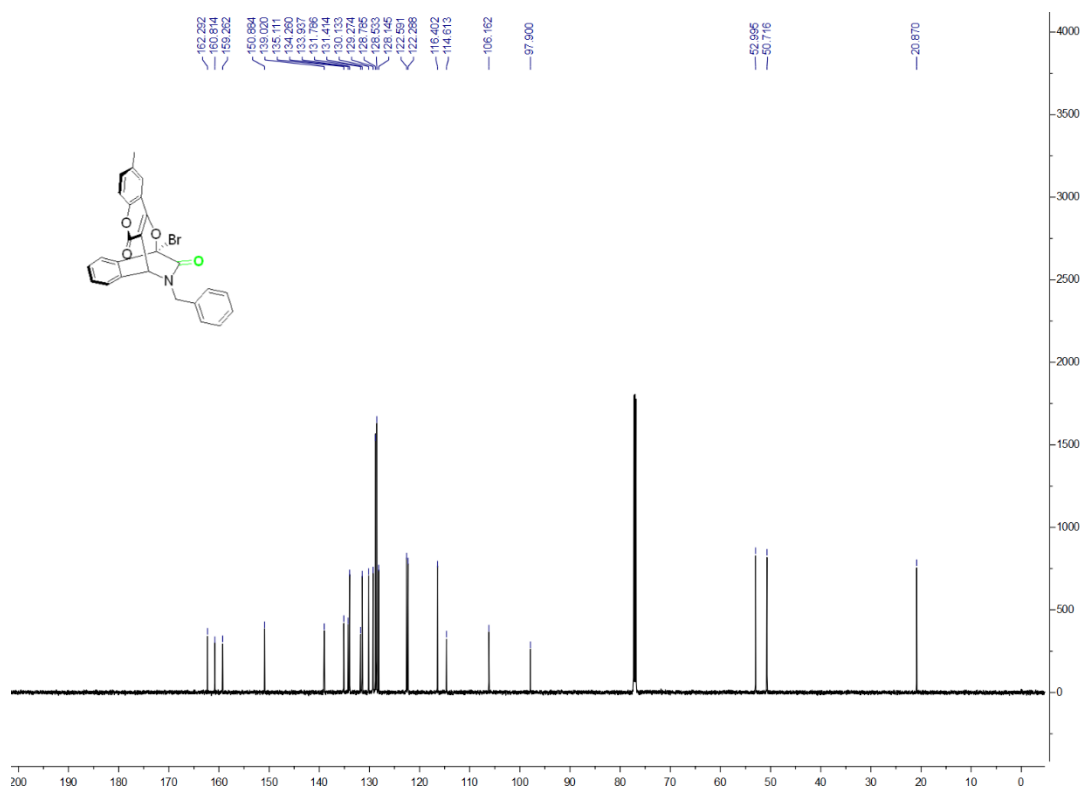
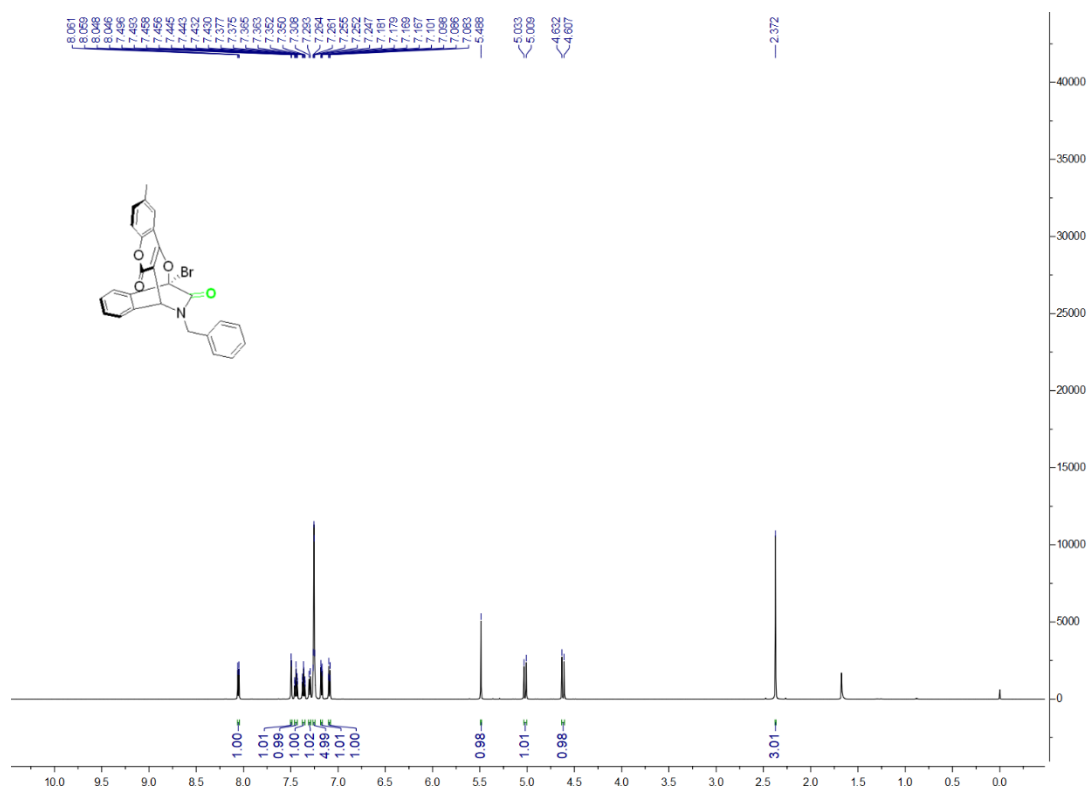
¹H NMR and ¹³C NMR spectra of compound **3ag**



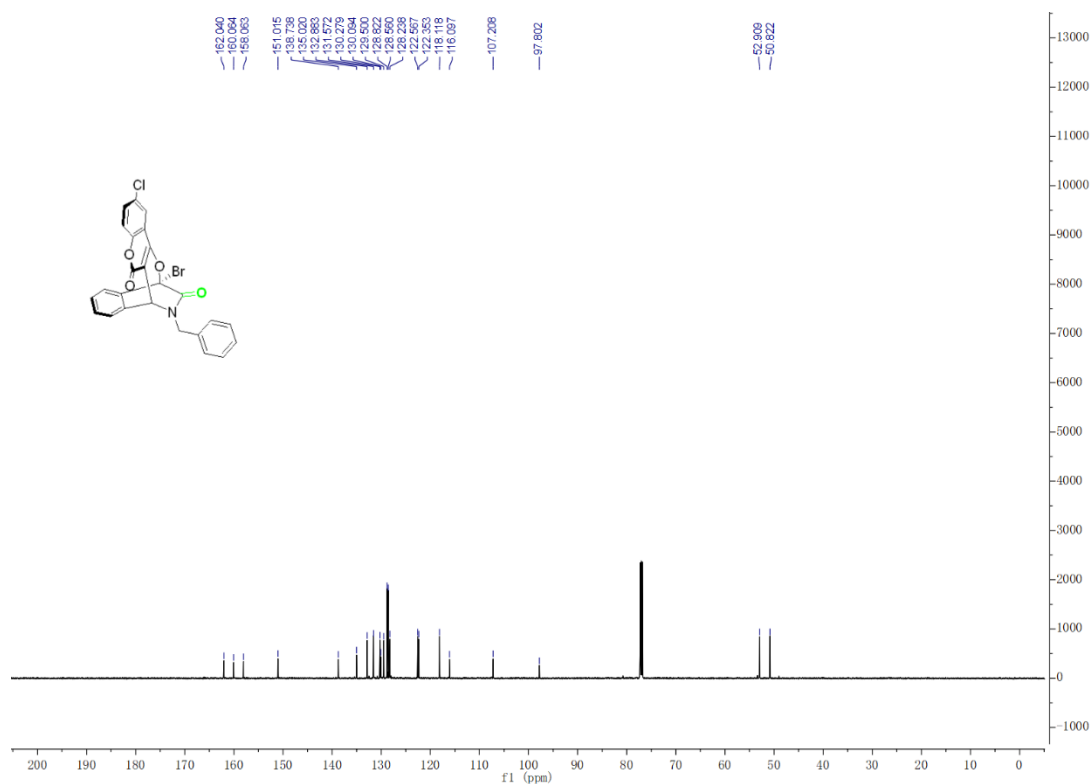
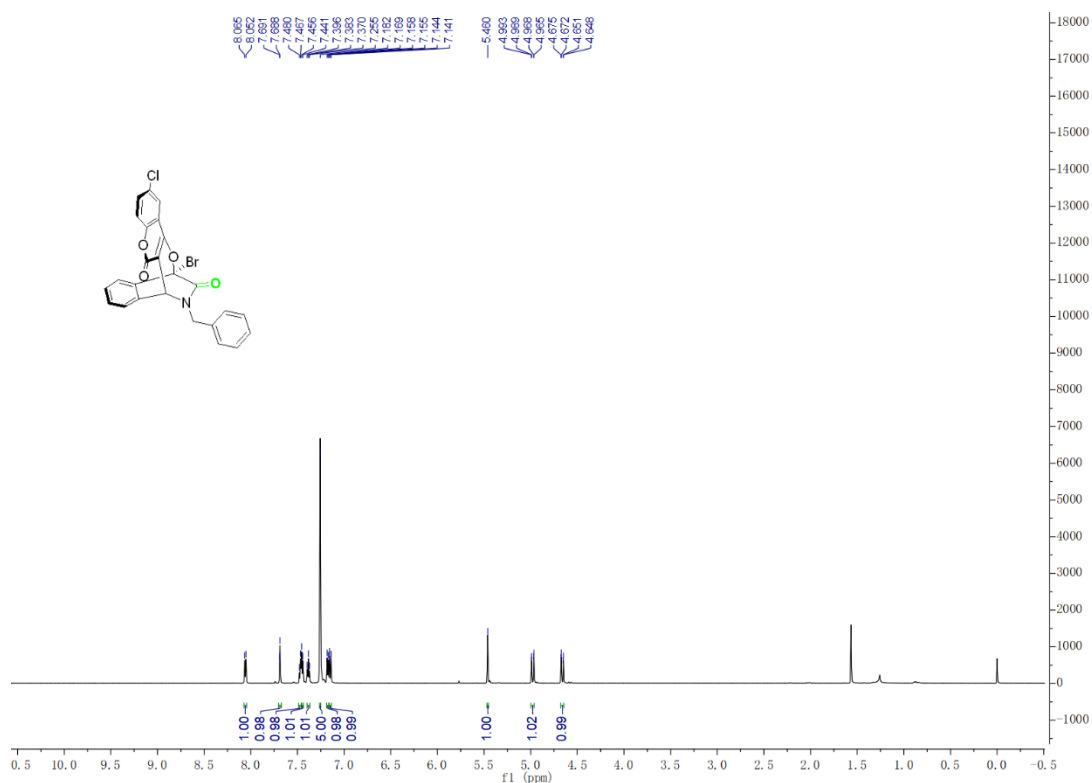
¹H NMR and ¹³C NMR spectra of compound **3ah**



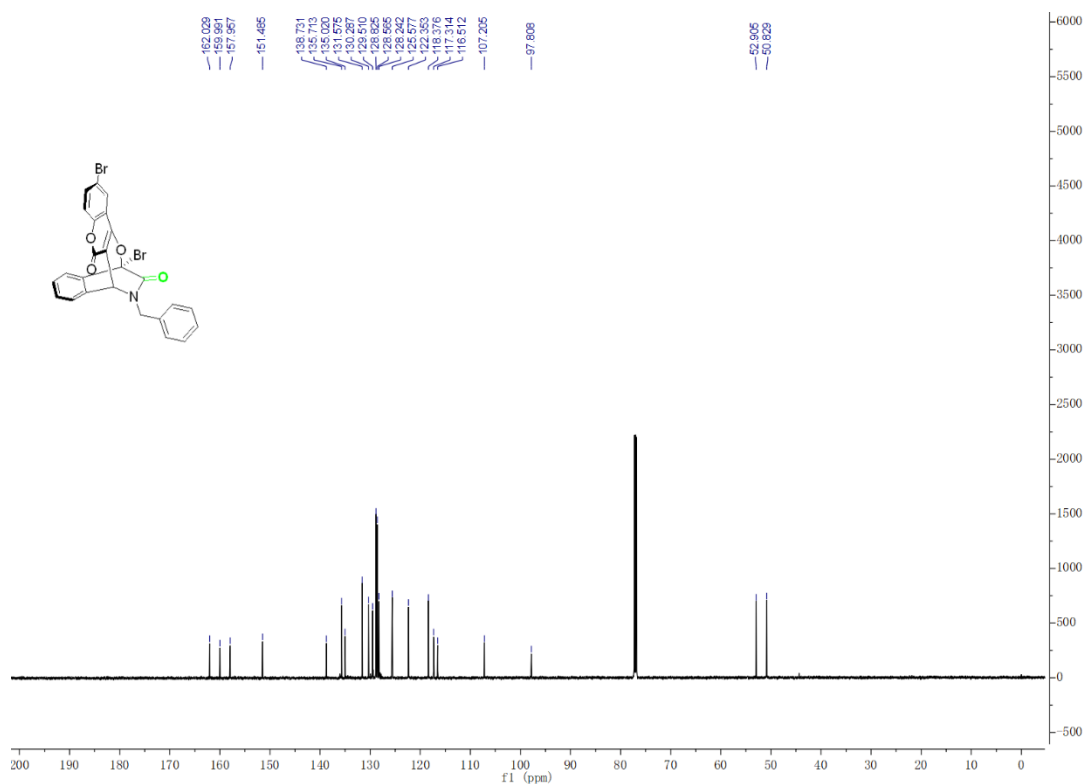
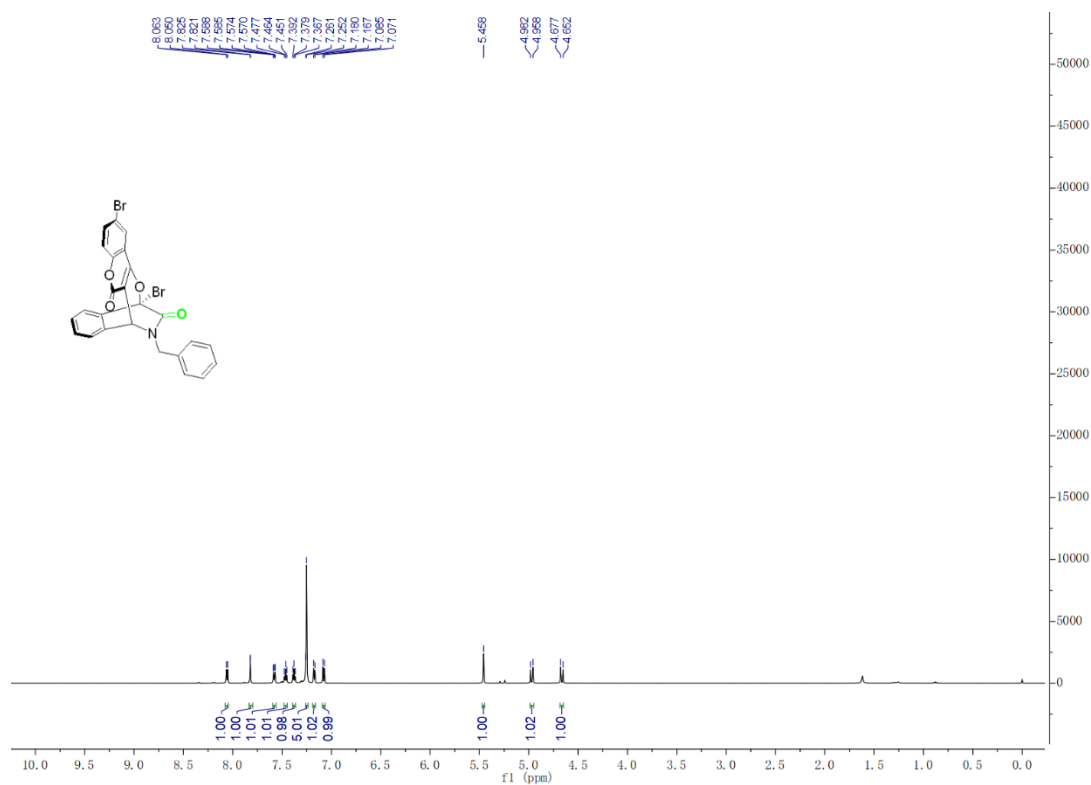
¹H NMR and ¹³C NMR spectra of compound **3aj**



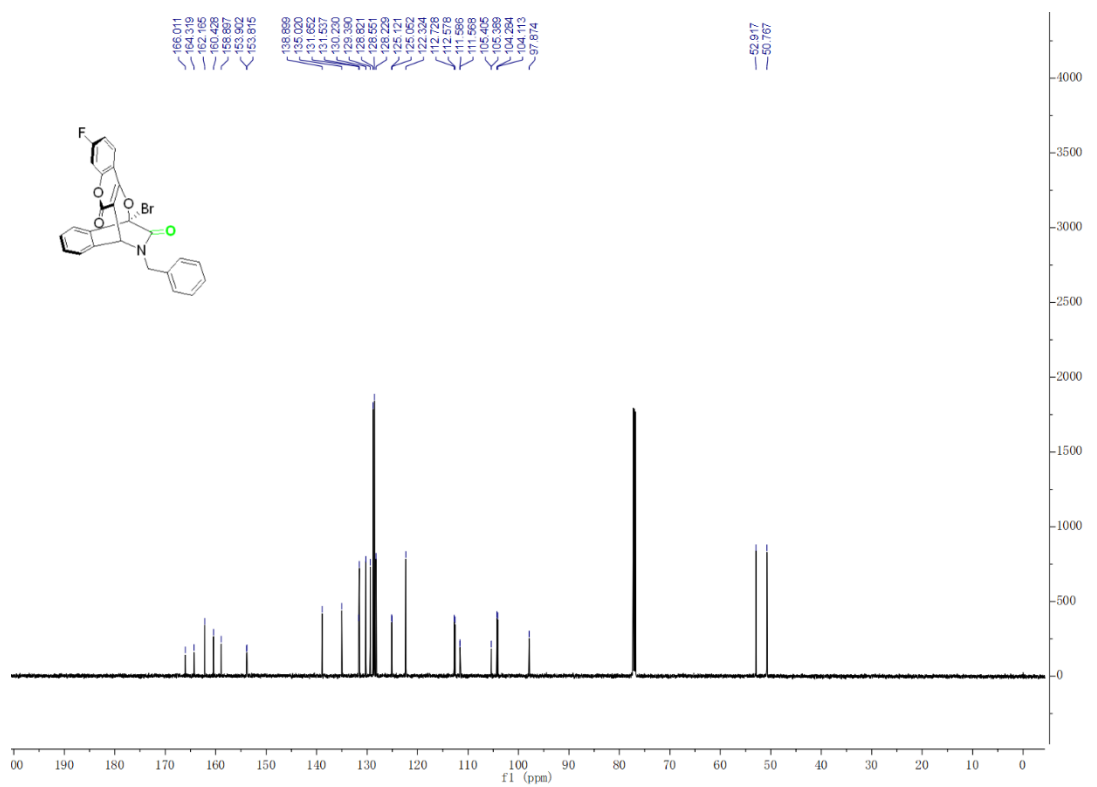
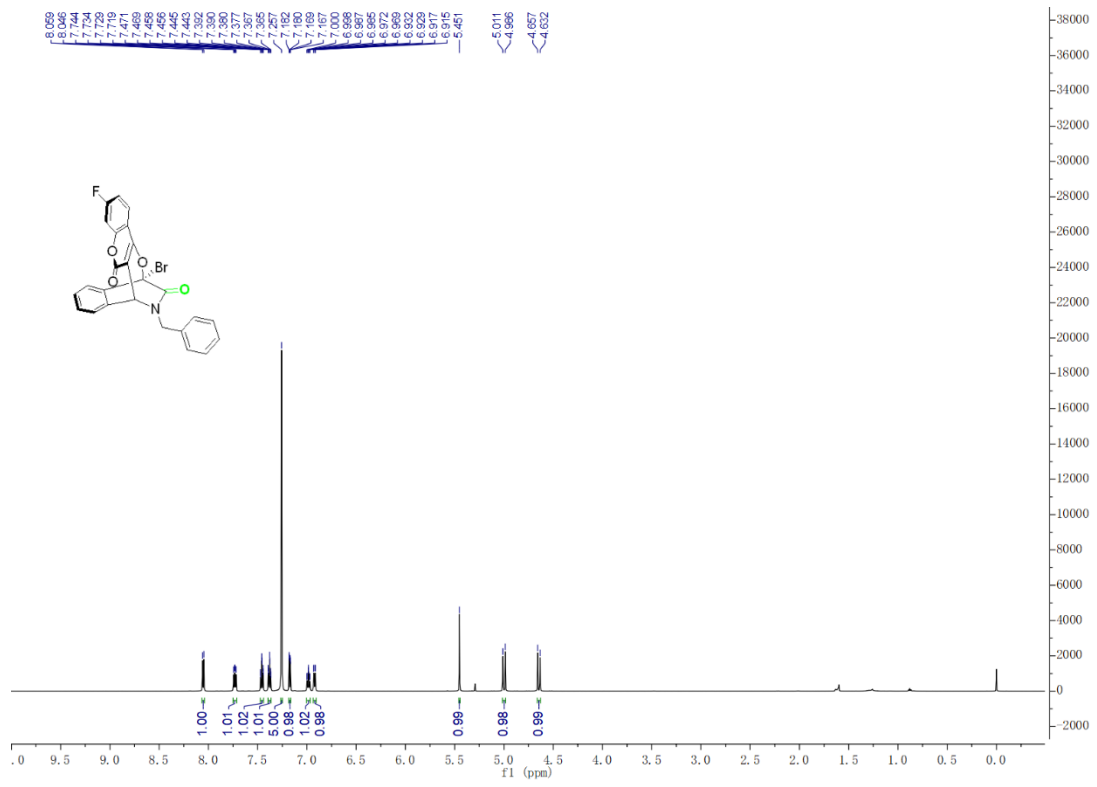
¹H NMR and ¹³C NMR spectra of compound **3ak**



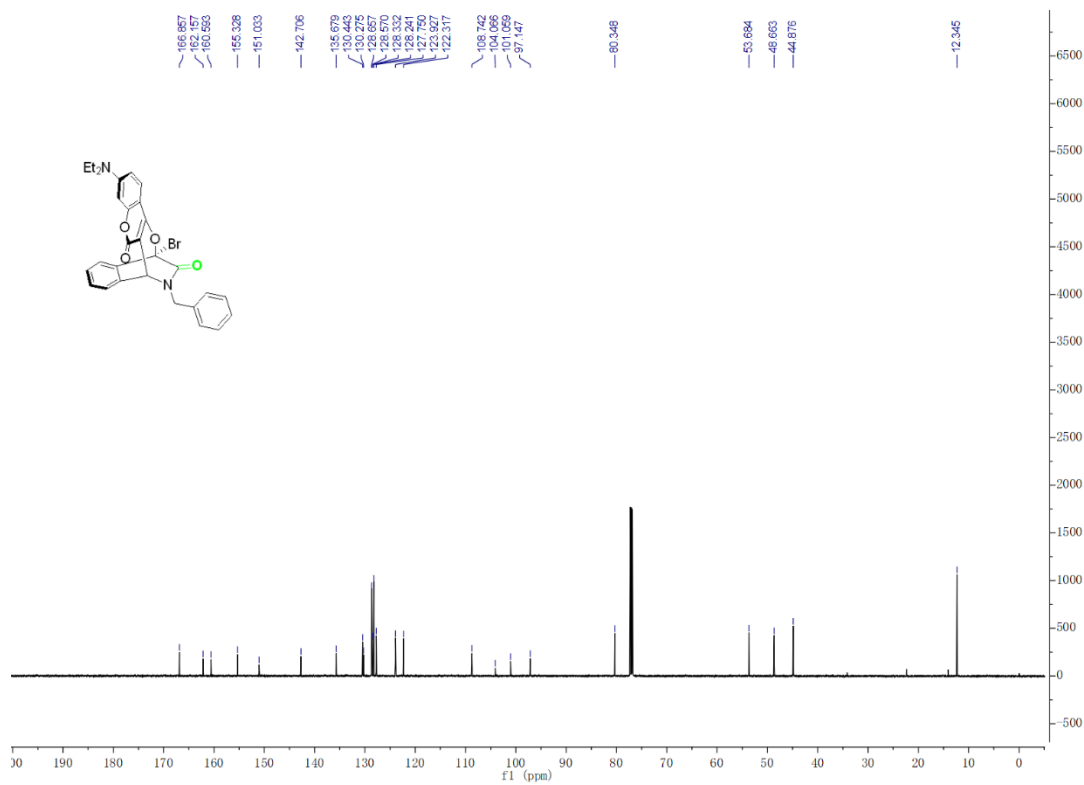
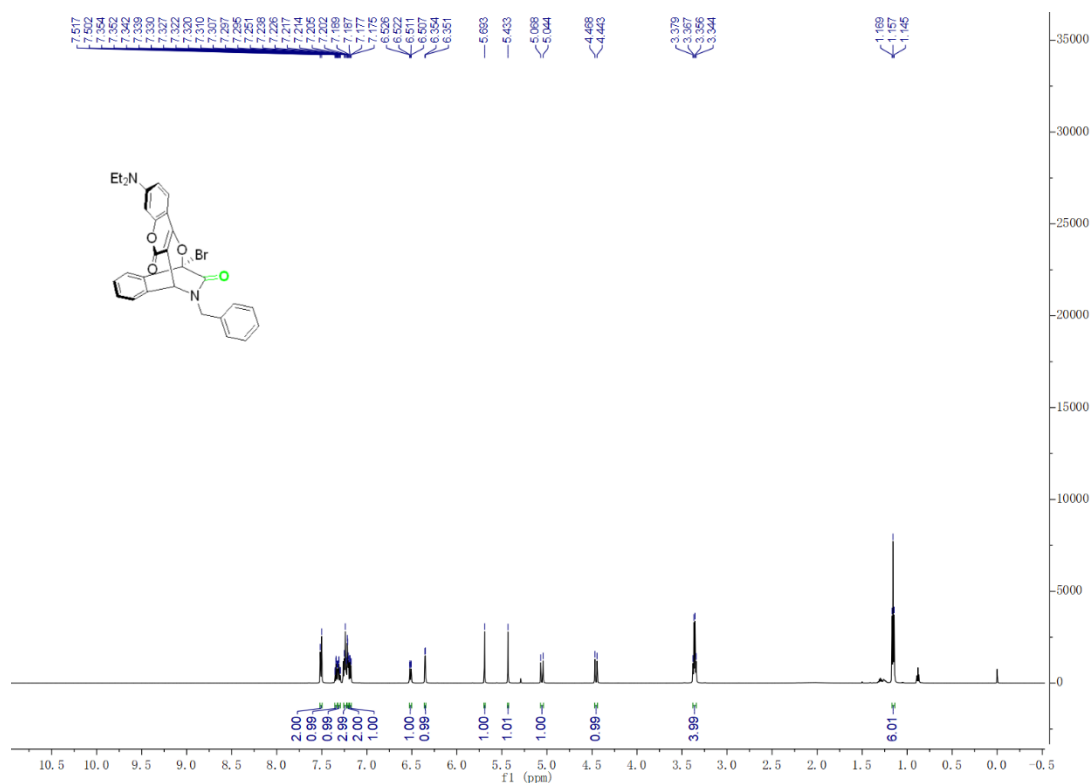
¹H NMR and ¹³C NMR spectra of compound **3al**



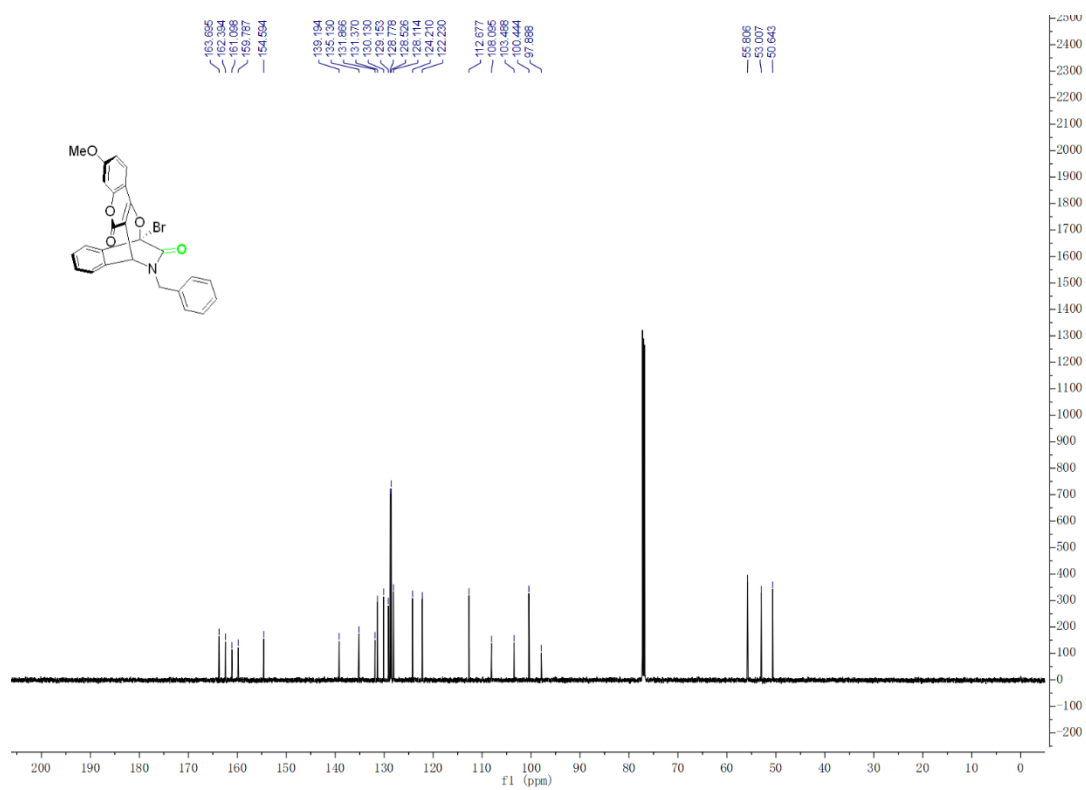
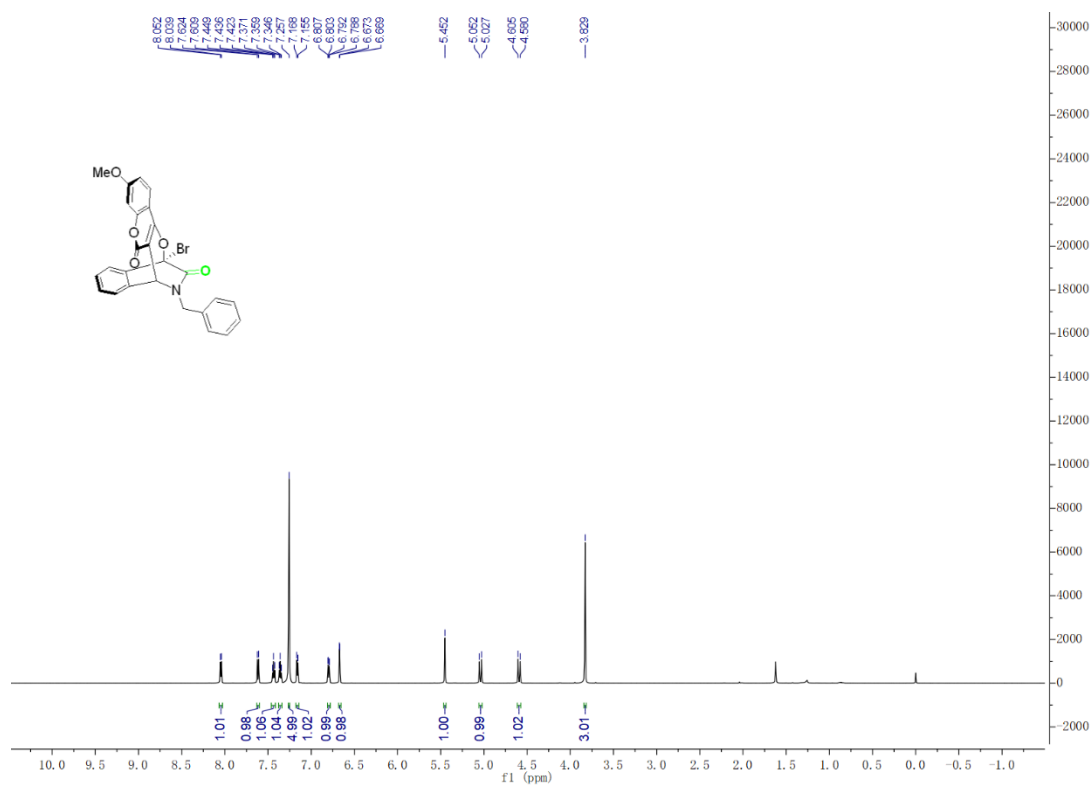
¹H NMR and ¹³C NMR spectra of compound **3am**



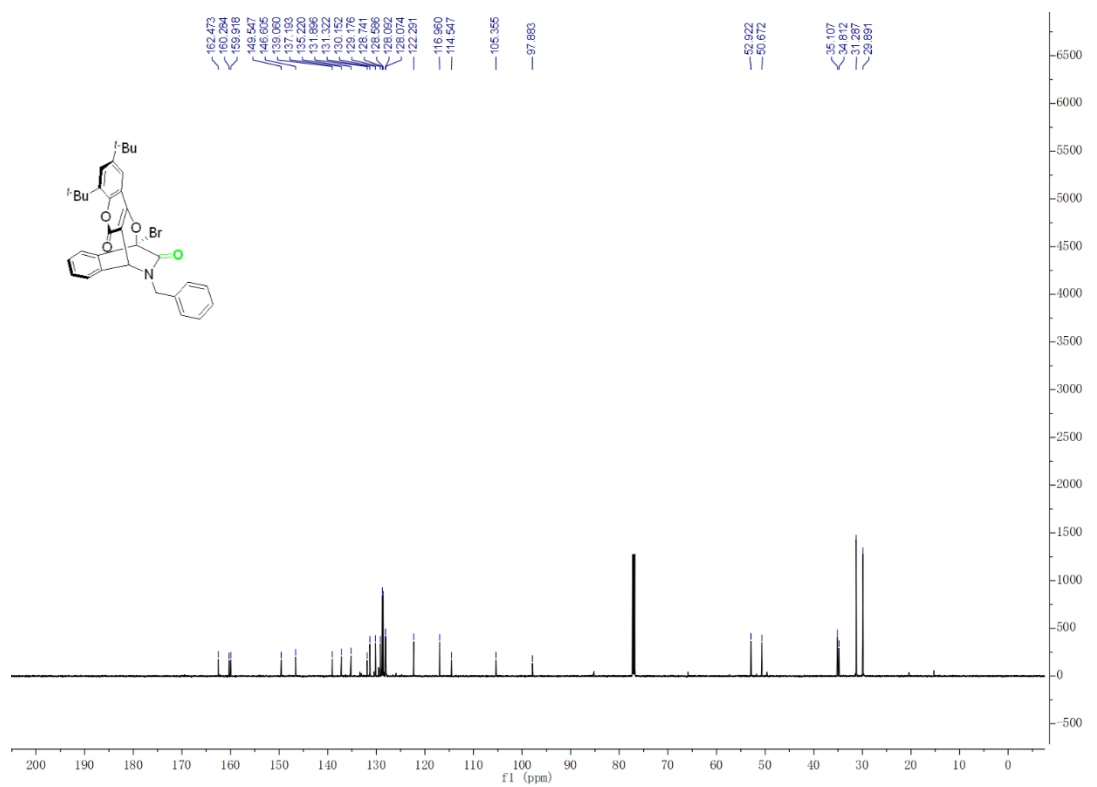
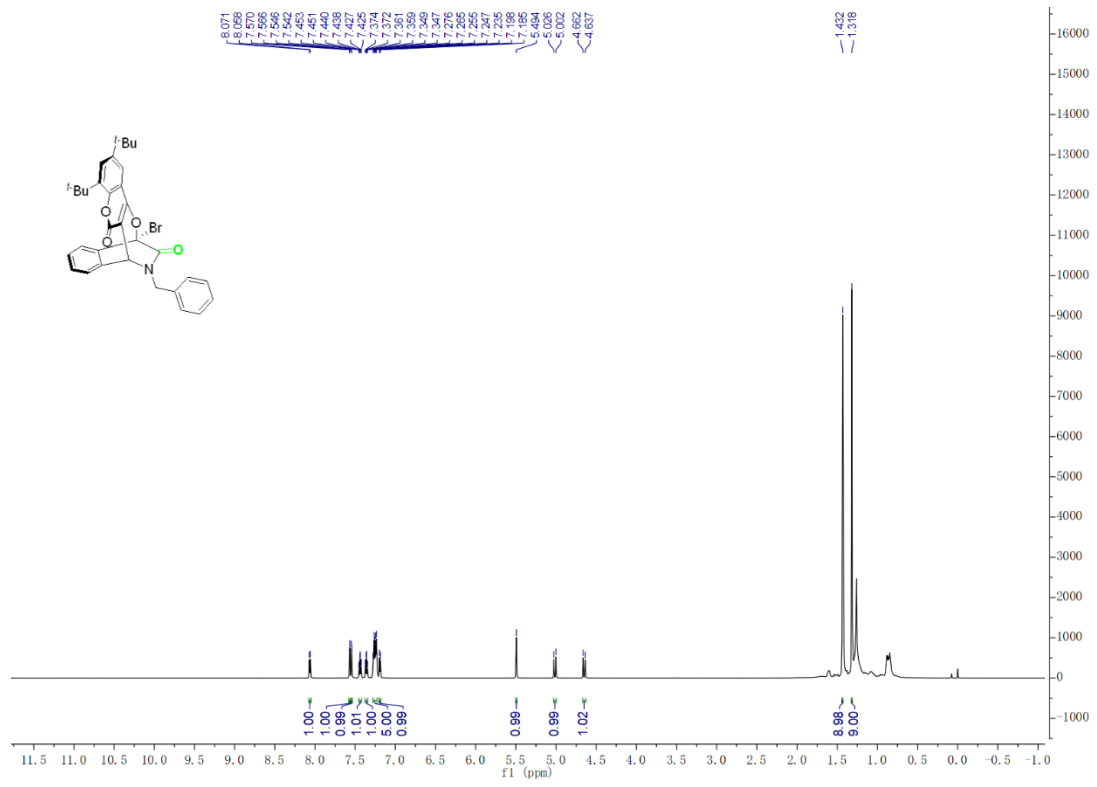
¹H NMR and ¹³C NMR spectra of compound **3an**



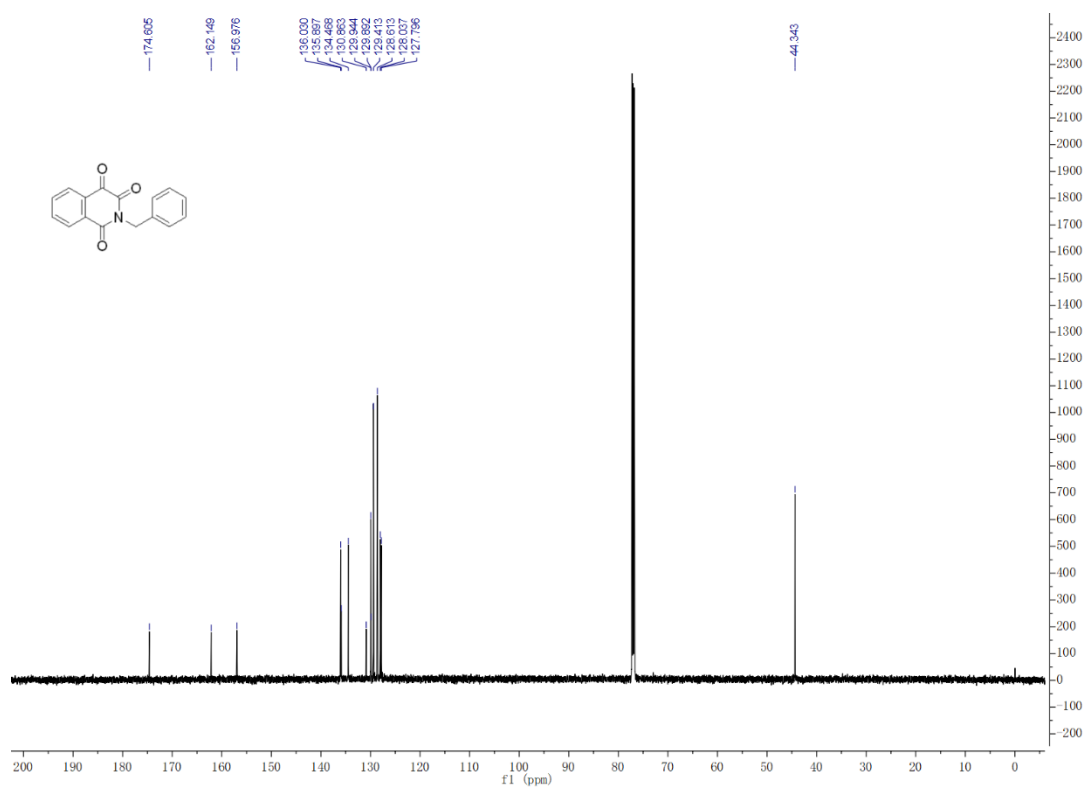
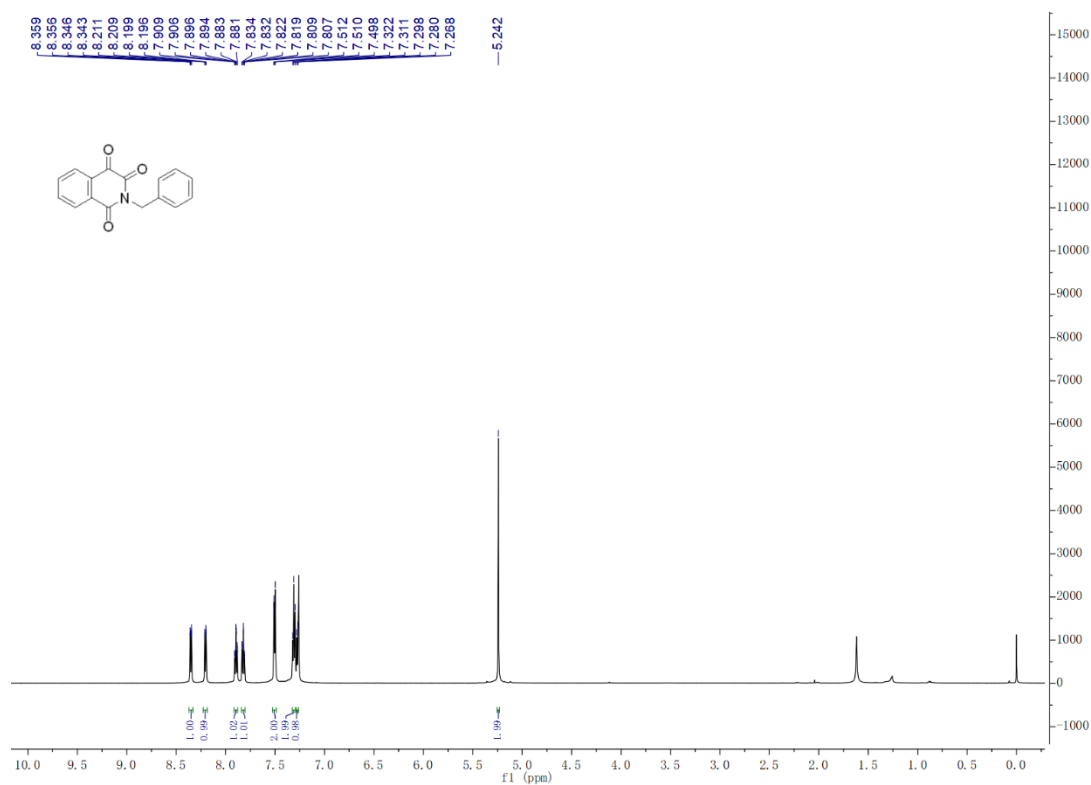
¹H NMR and ¹³C NMR spectra of compound **3ao**



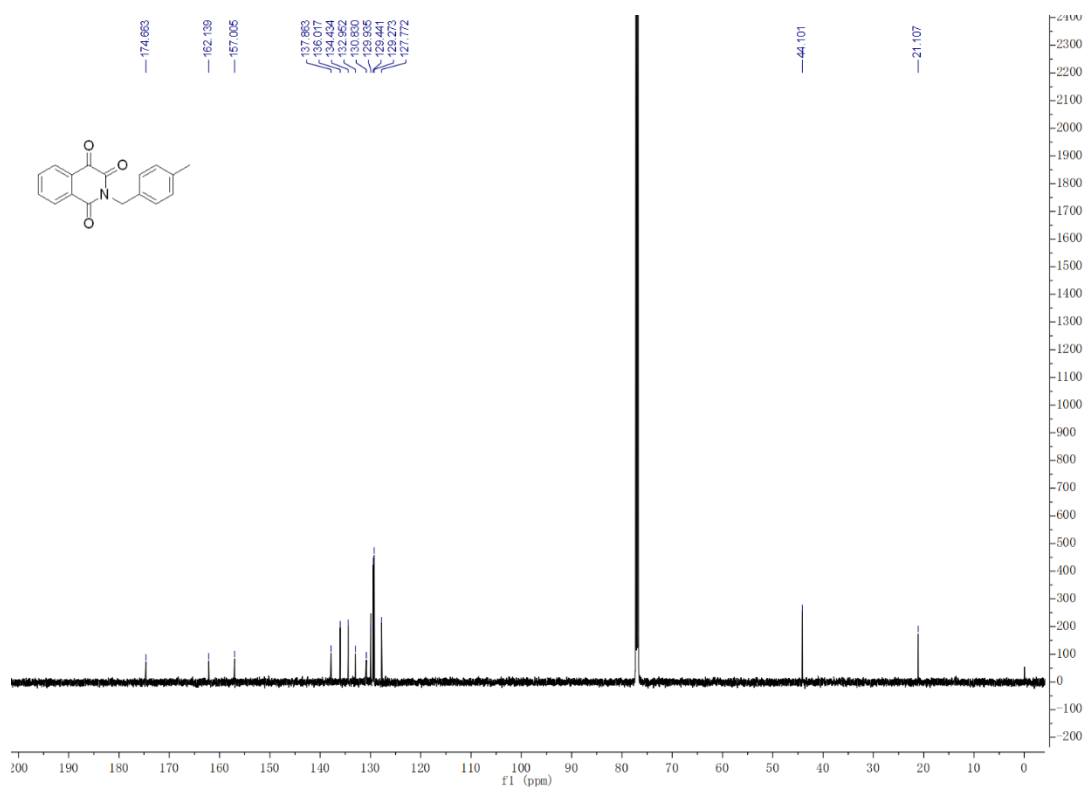
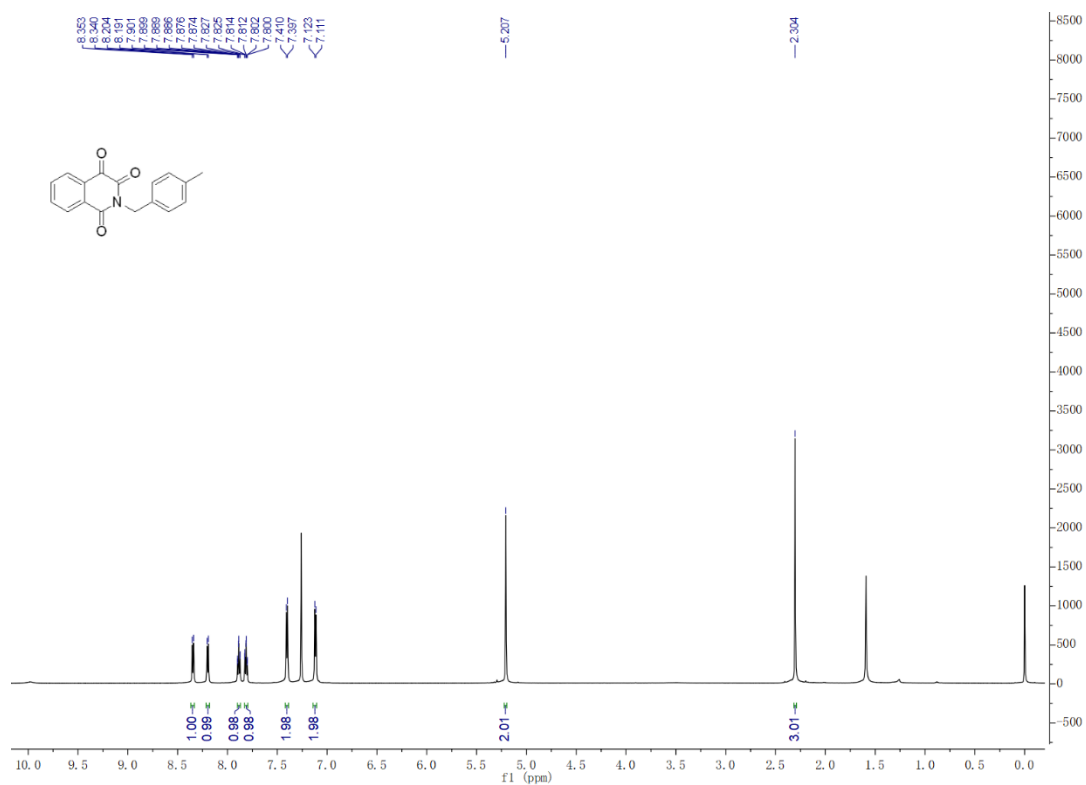
¹H NMR and ¹³C NMR spectra of compound **3ap**



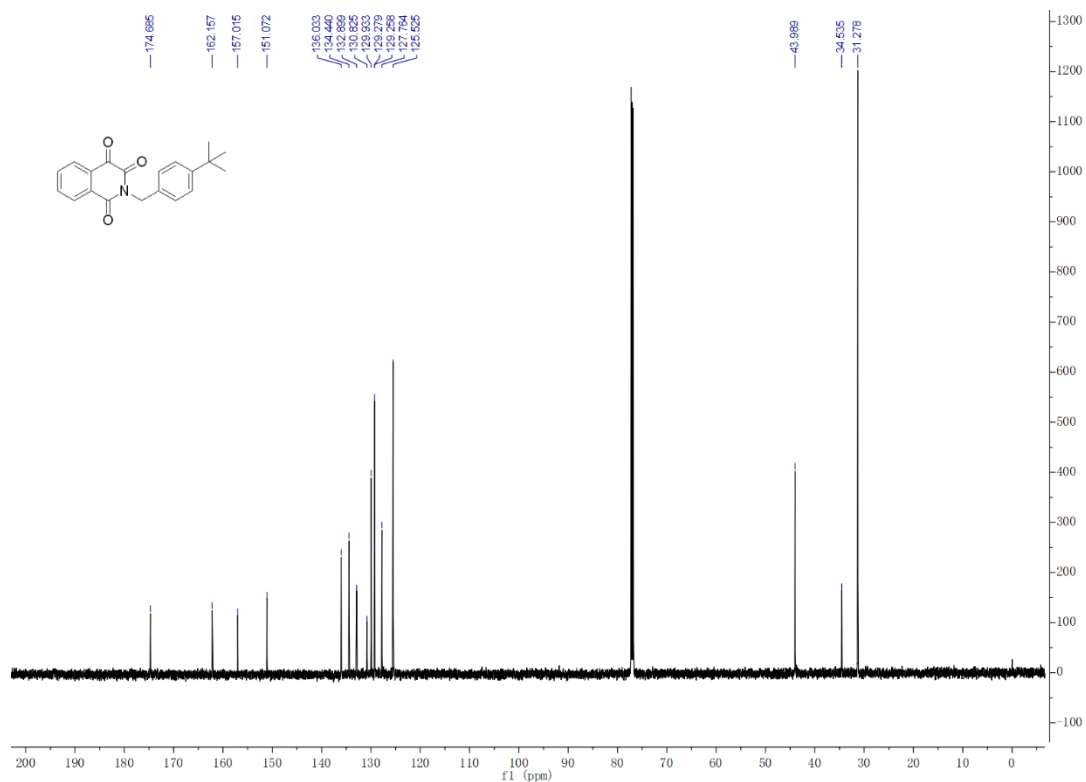
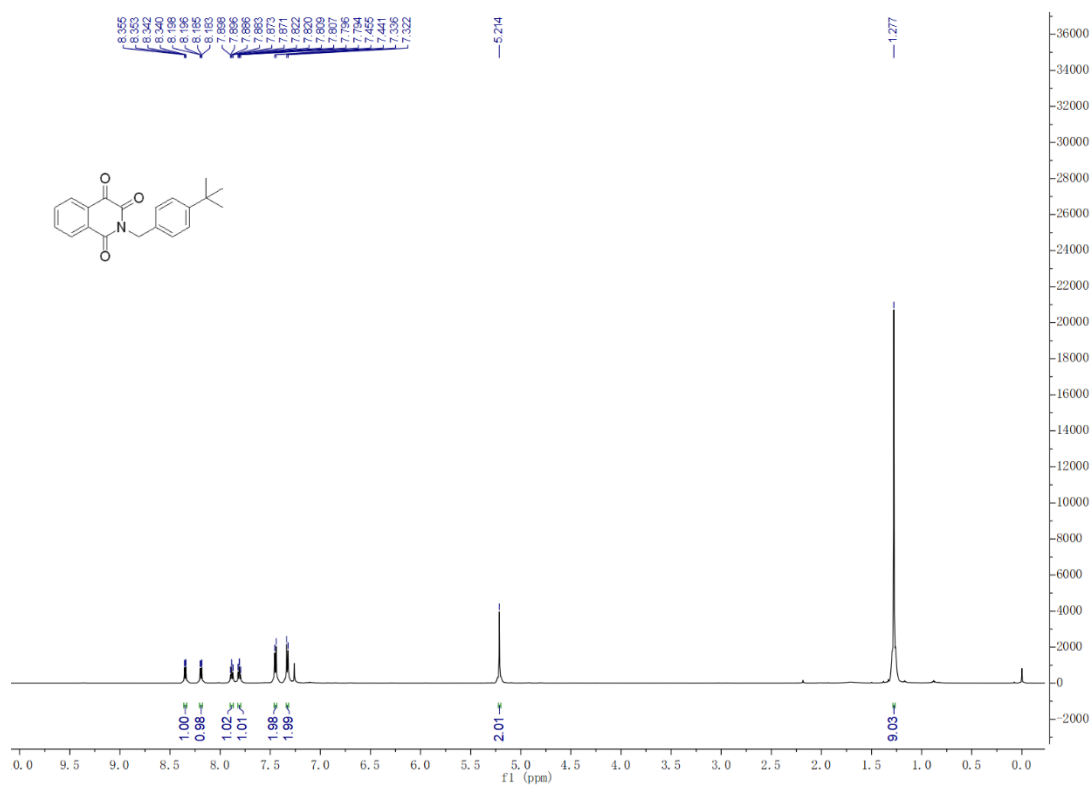
¹H NMR and ¹³C NMR spectra of compound 4a



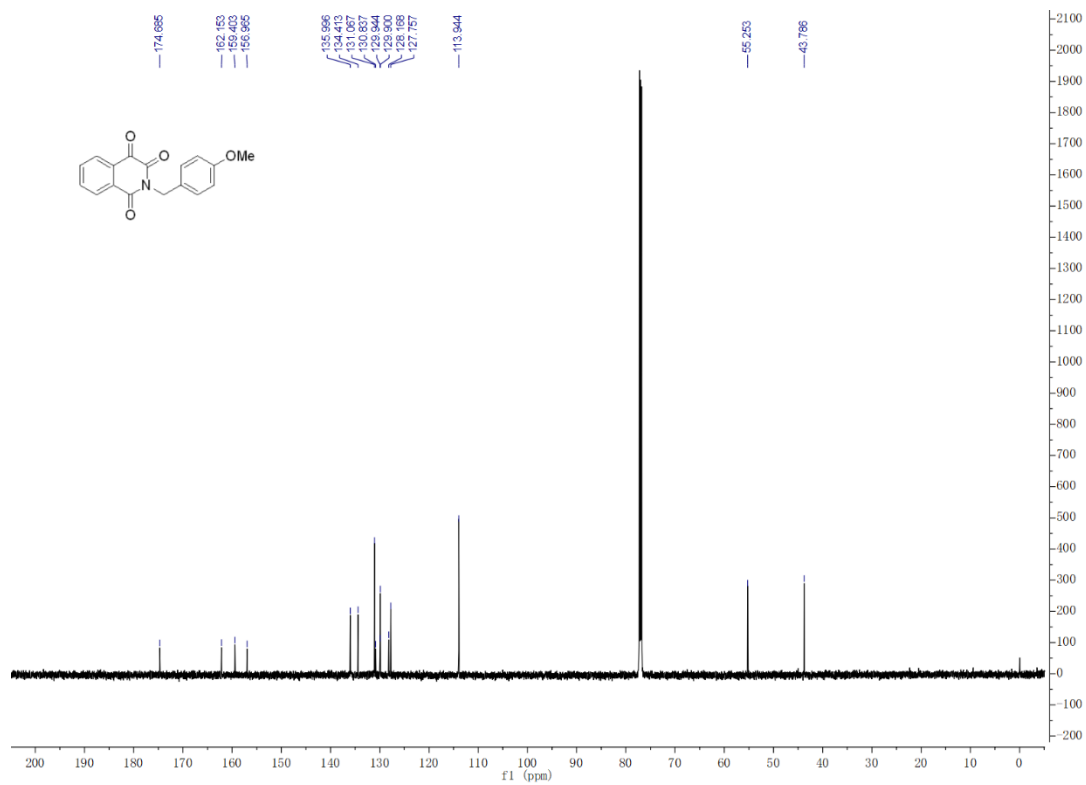
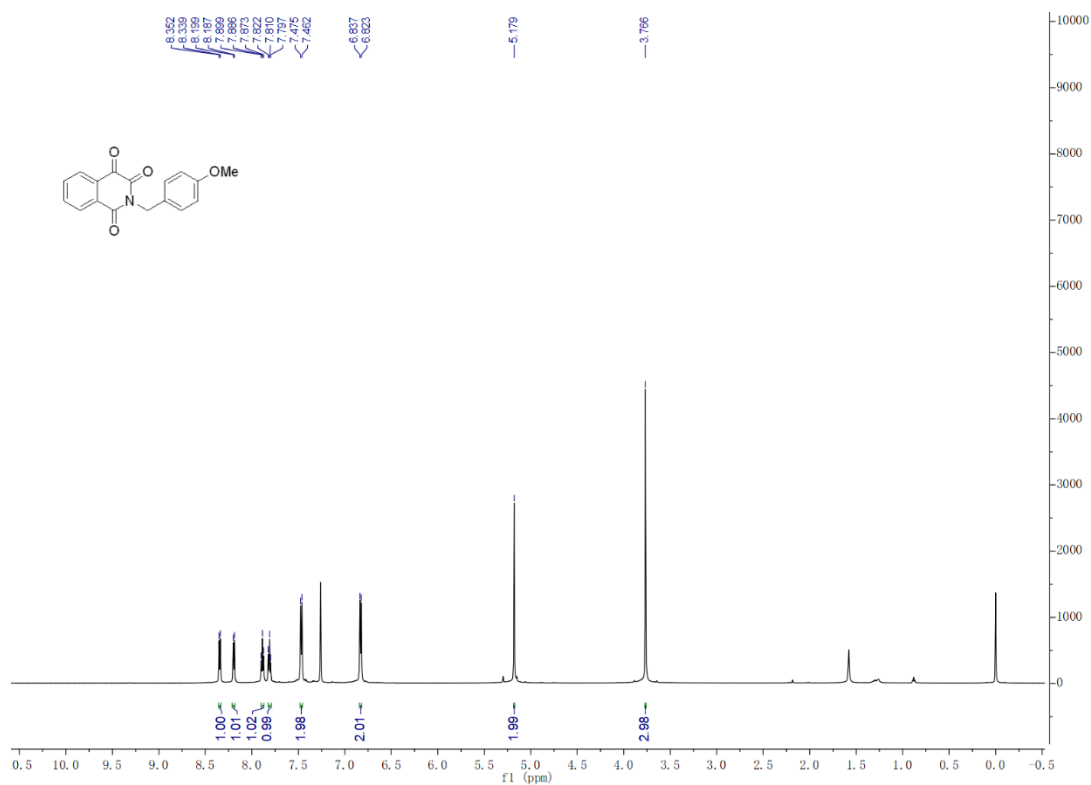
¹H NMR and ¹³C NMR spectra of compound 4b



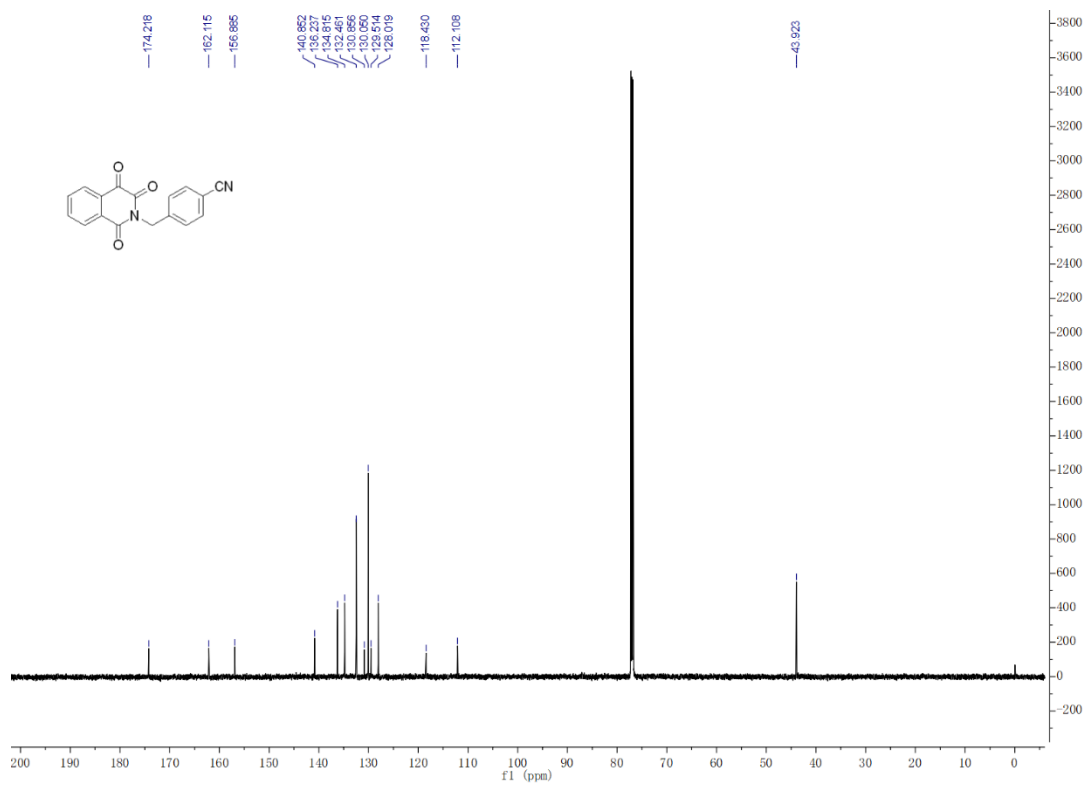
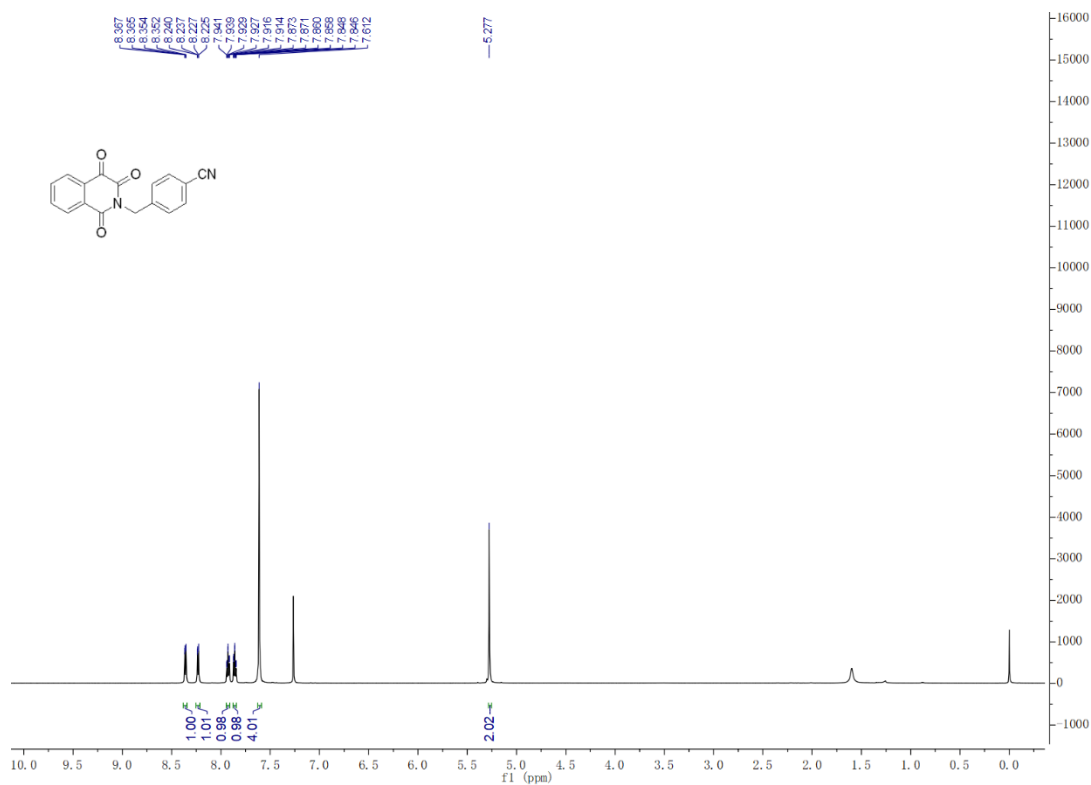
¹H NMR and ¹³C NMR spectra of compound 4c



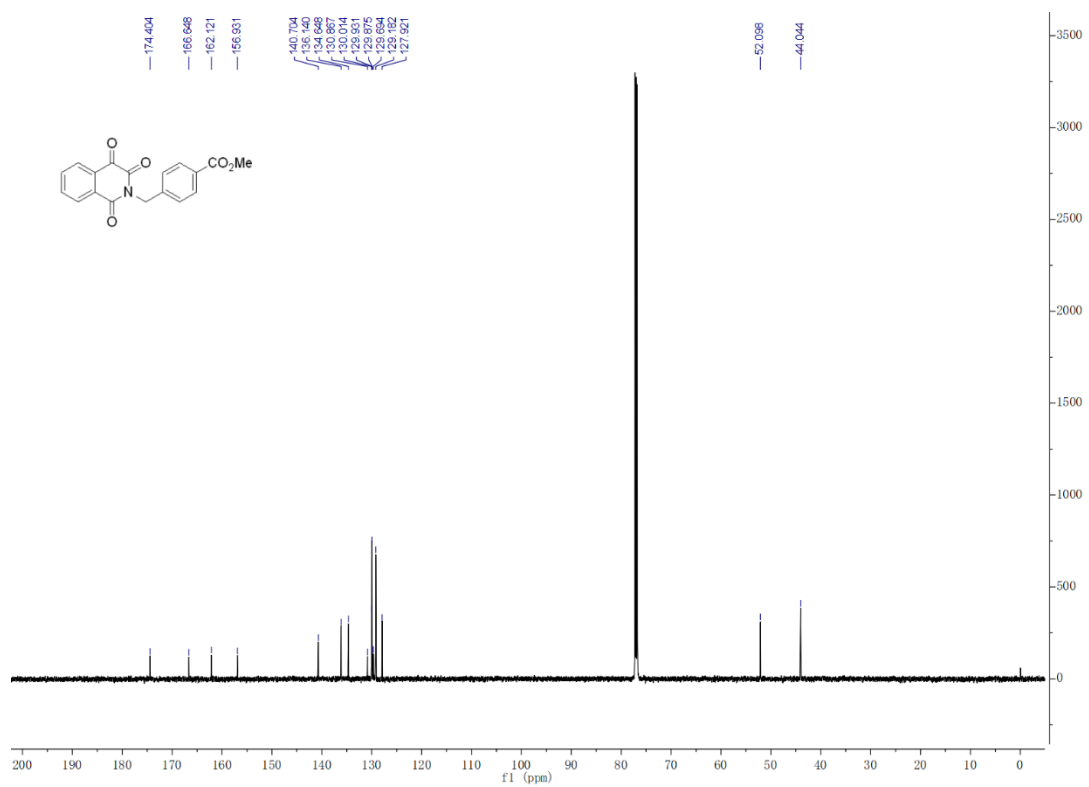
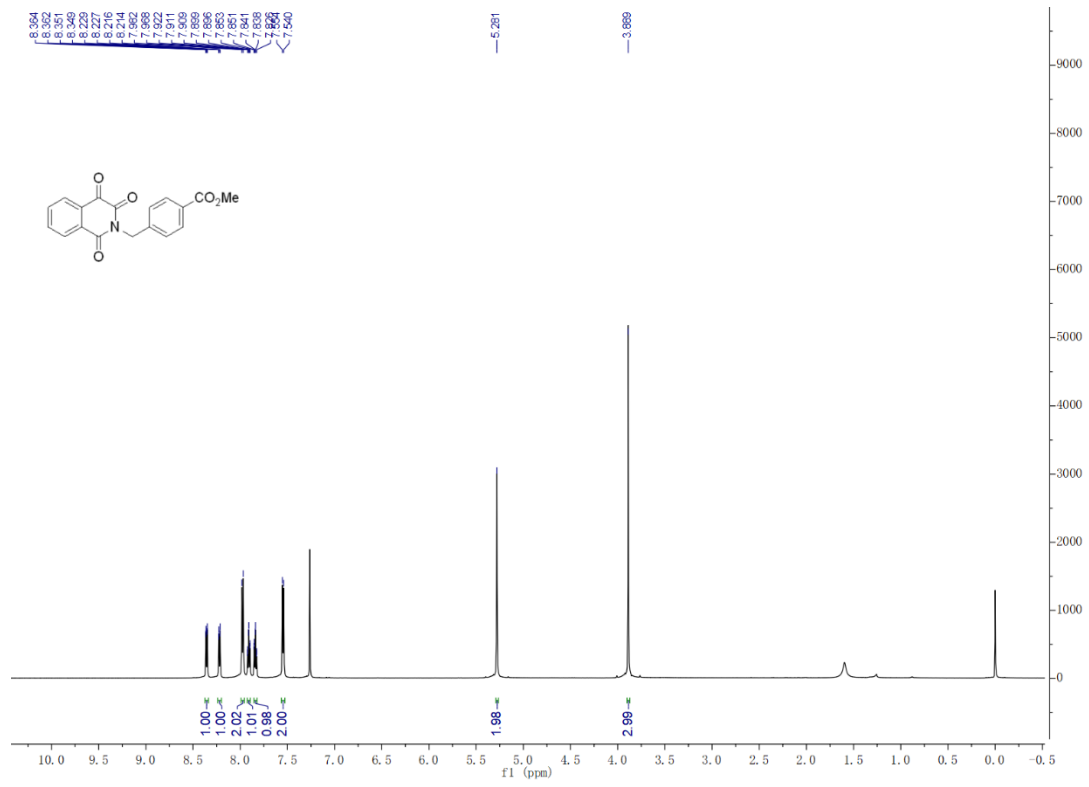
¹H NMR and ¹³C NMR spectra of compound 4d



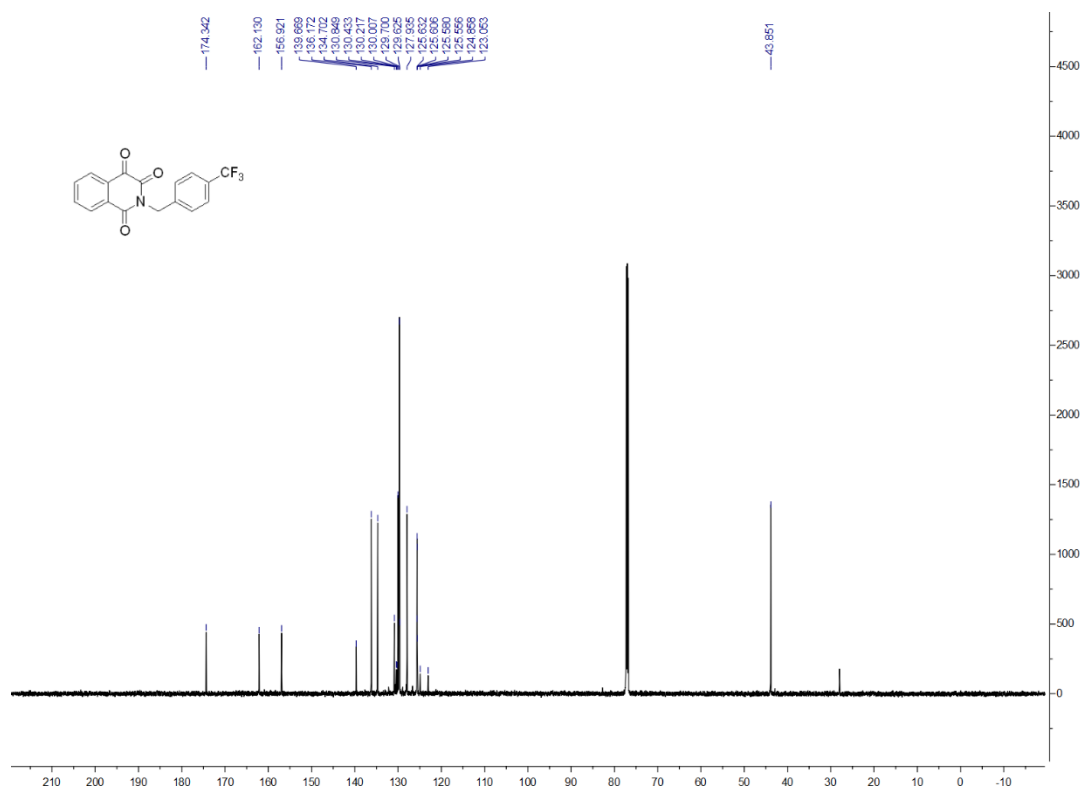
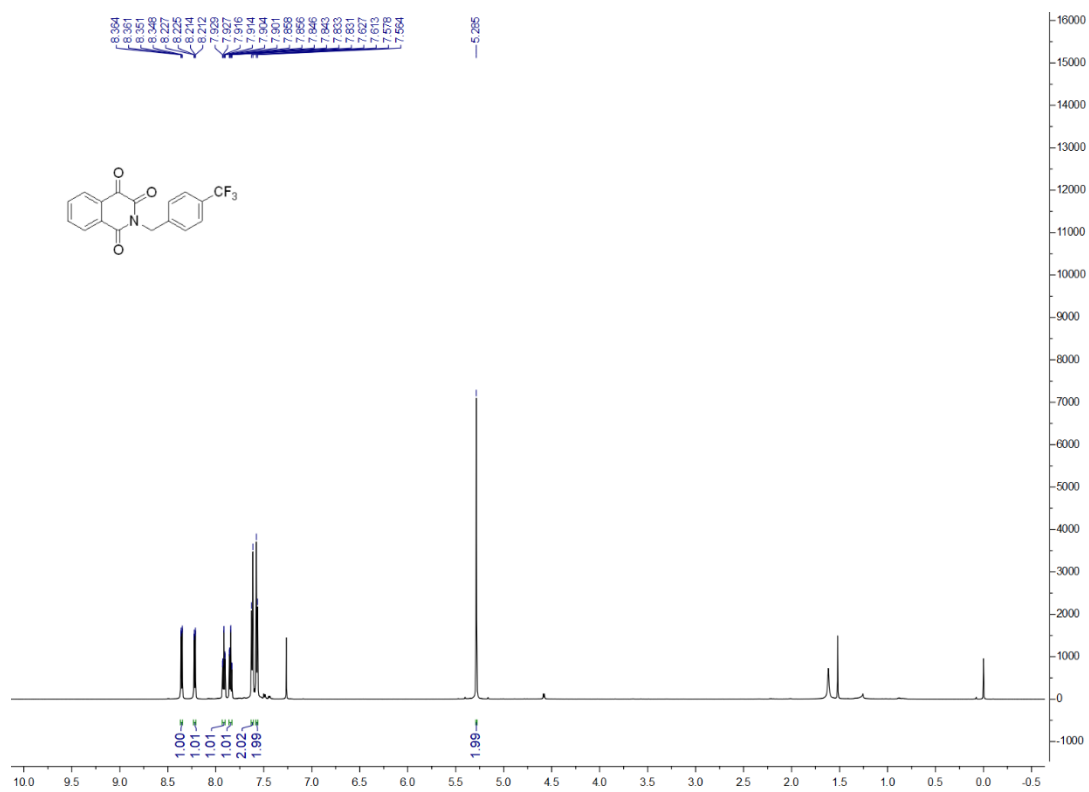
¹H NMR and ¹³C NMR spectra of compound 4e



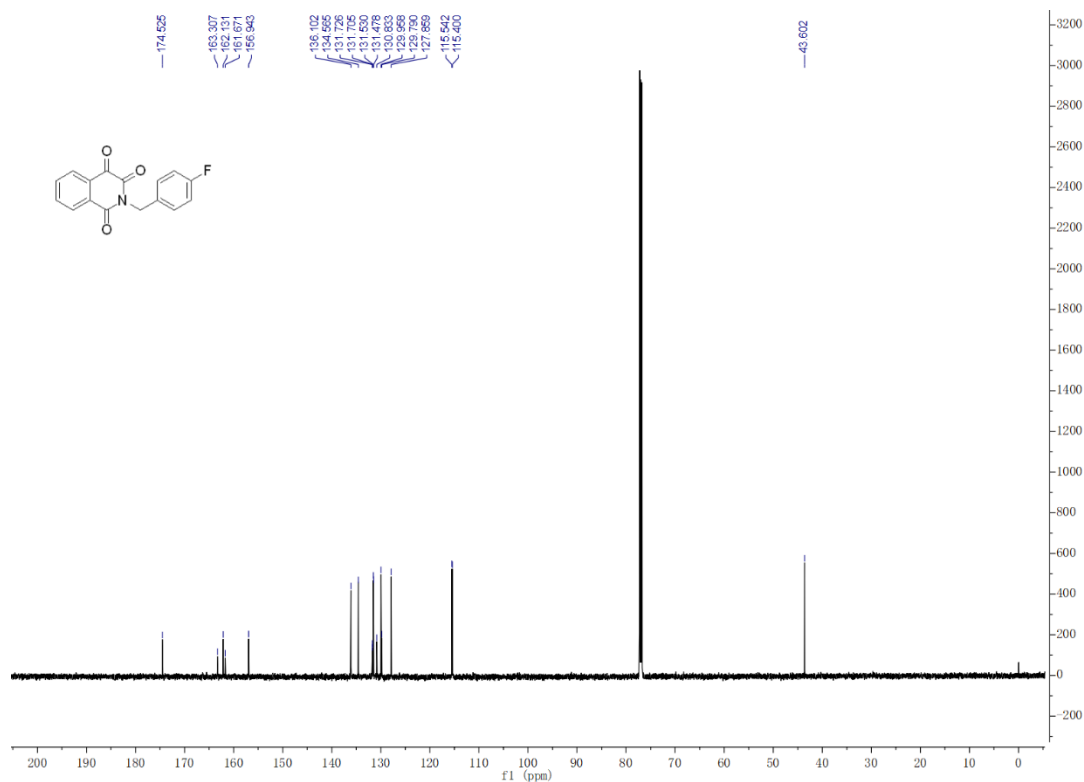
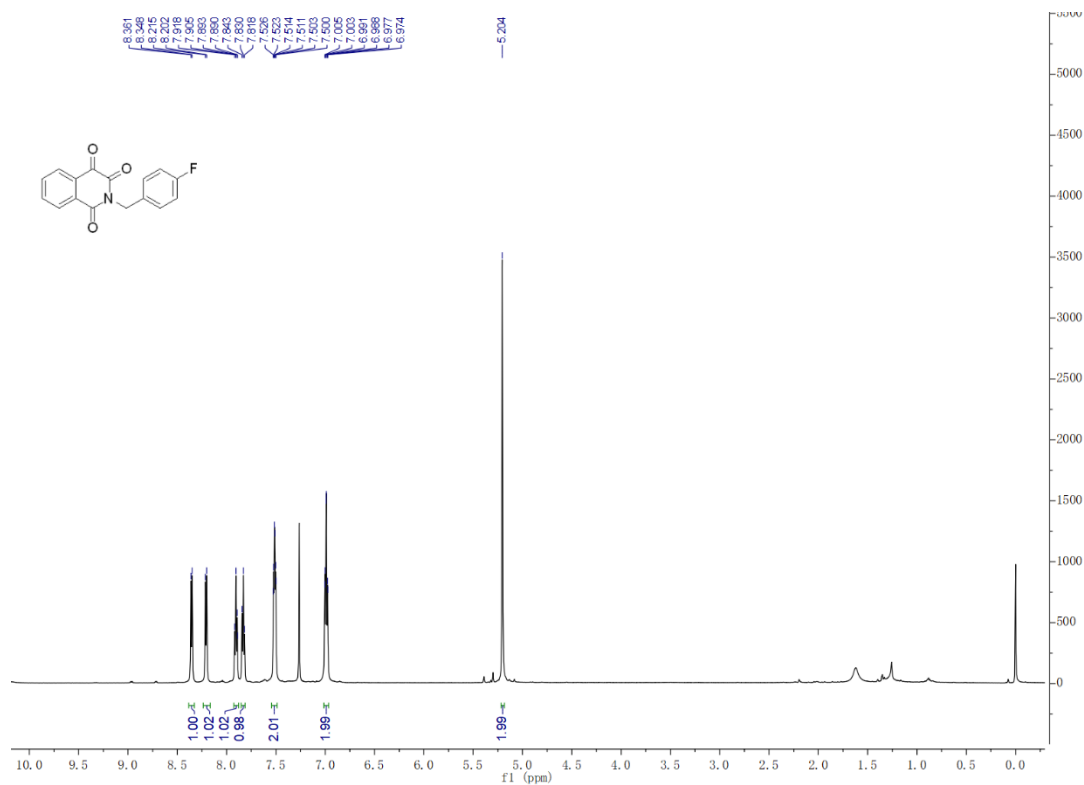
¹H NMR and ¹³C NMR spectra of compound 4f



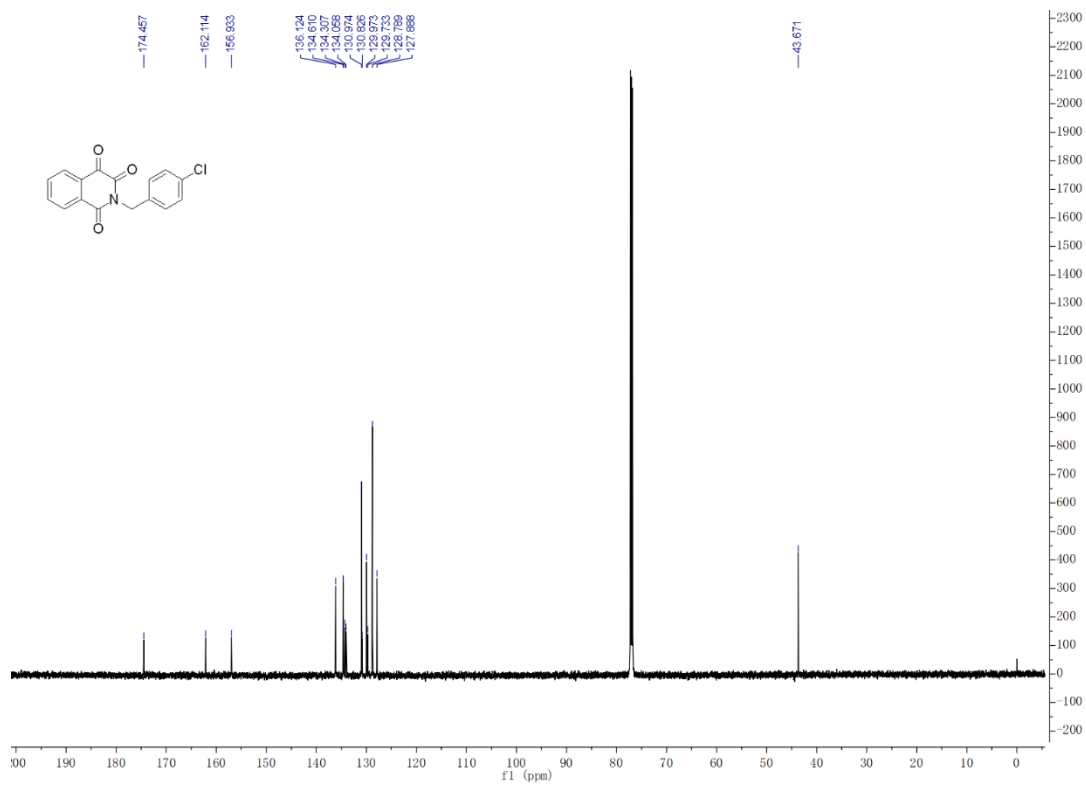
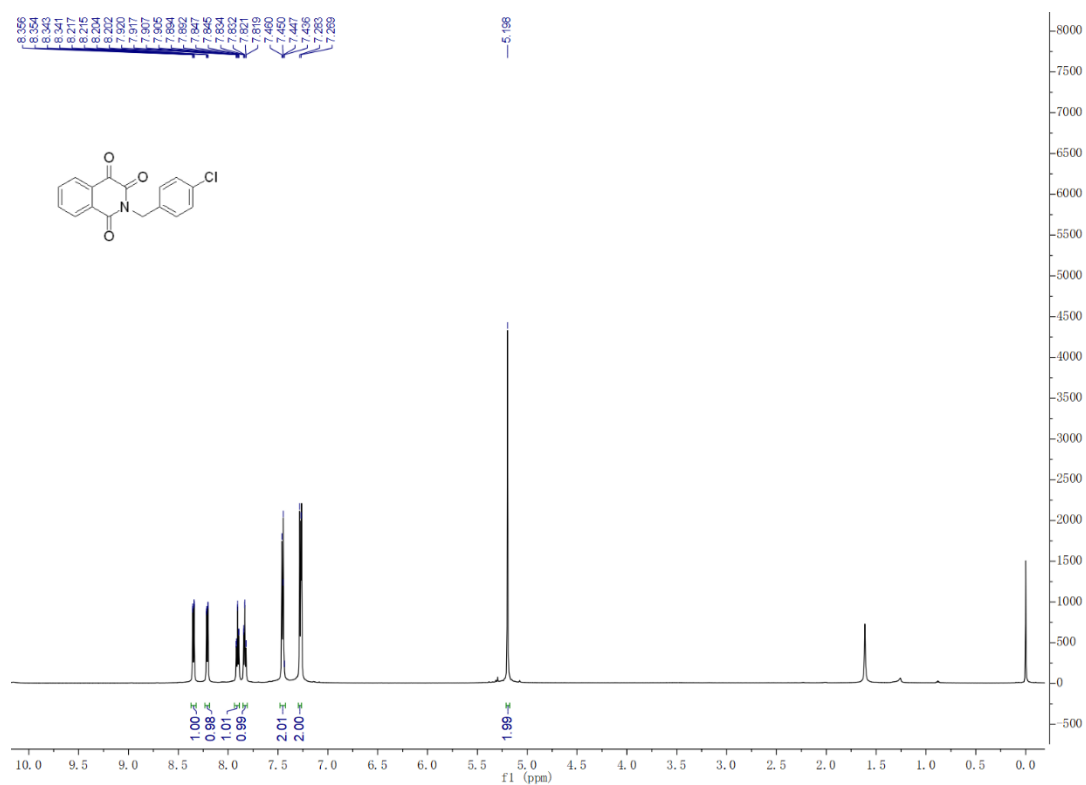
¹H NMR and ¹³C NMR spectra of compound 4g



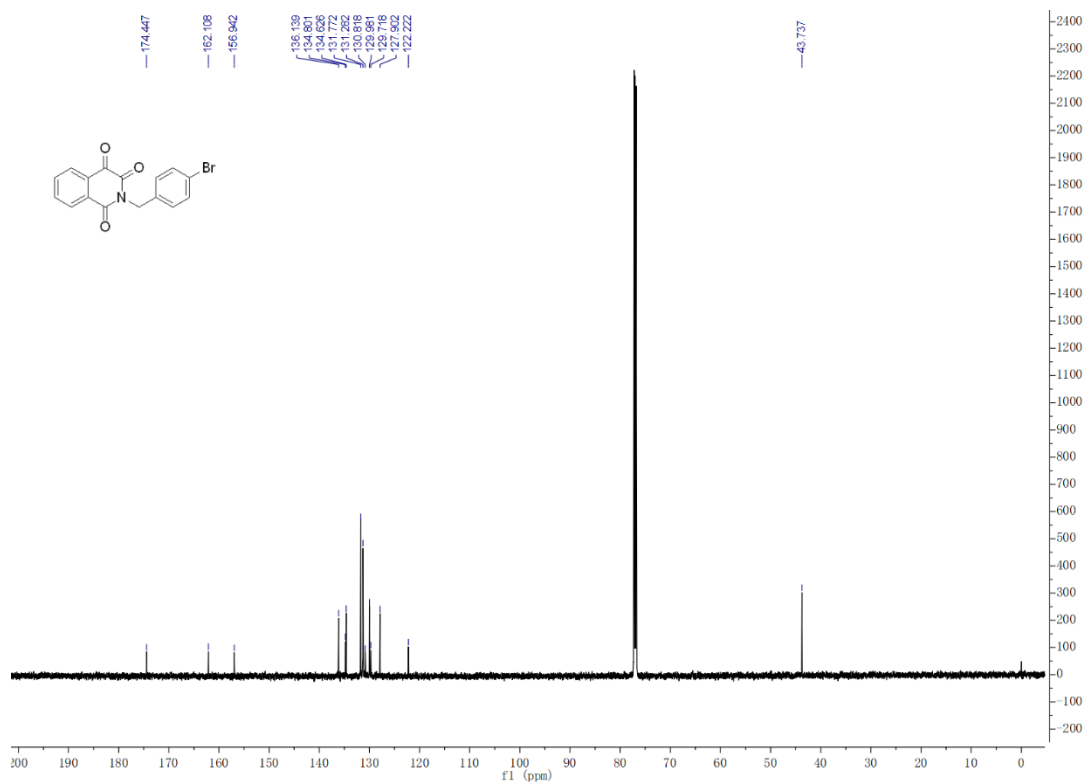
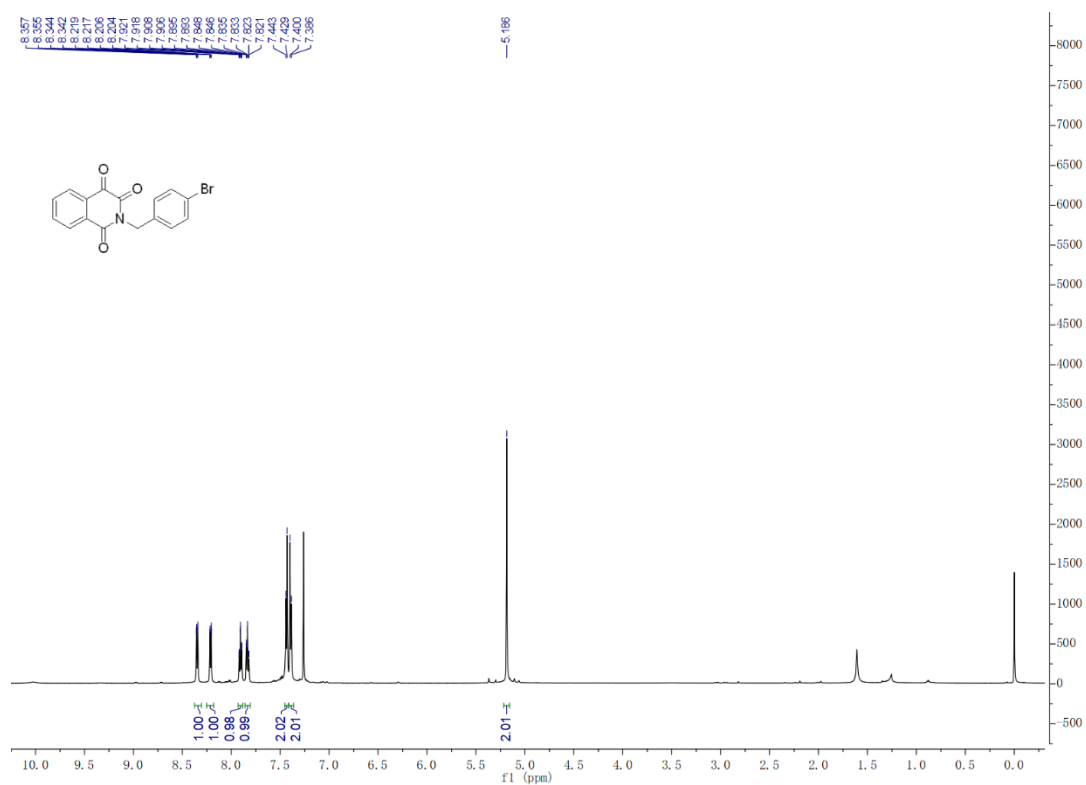
¹H NMR and ¹³C NMR spectra of compound 4h



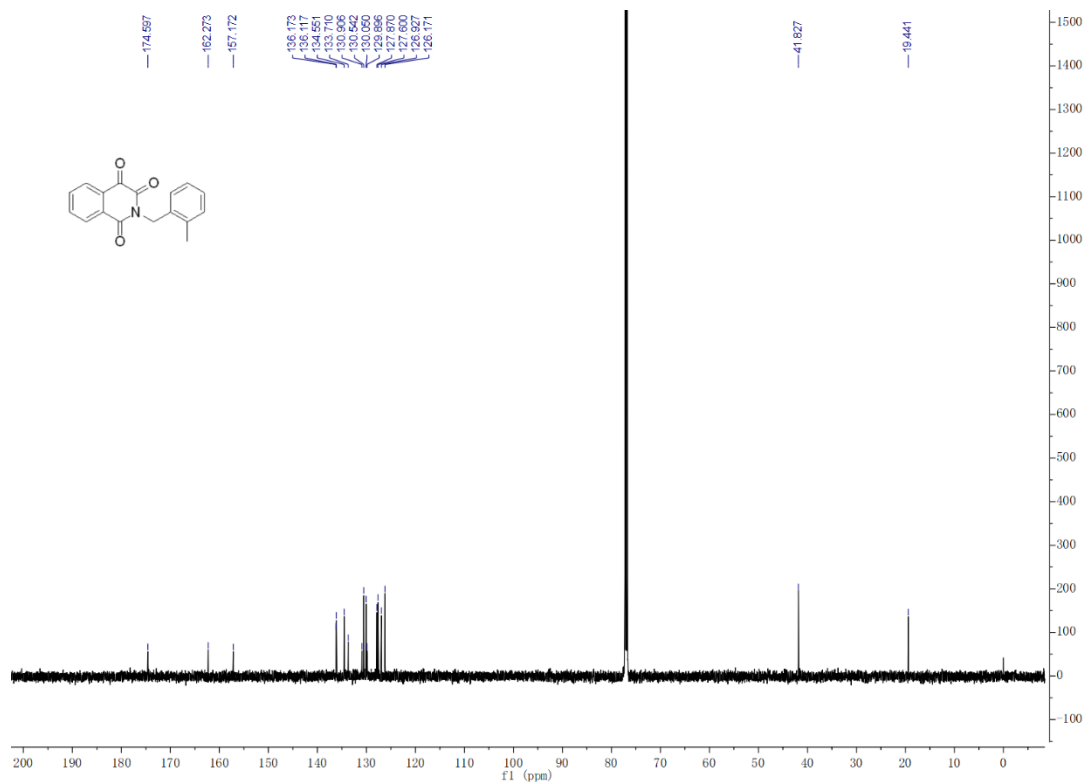
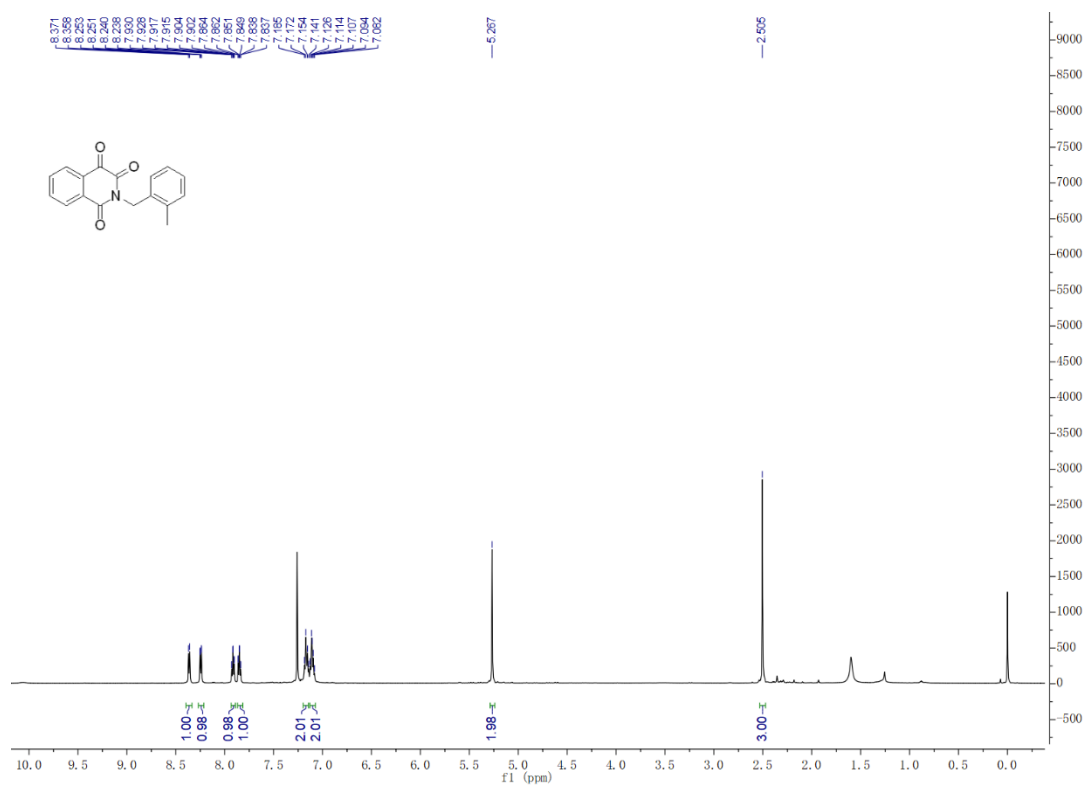
¹H NMR and ¹³C NMR spectra of compound 4i



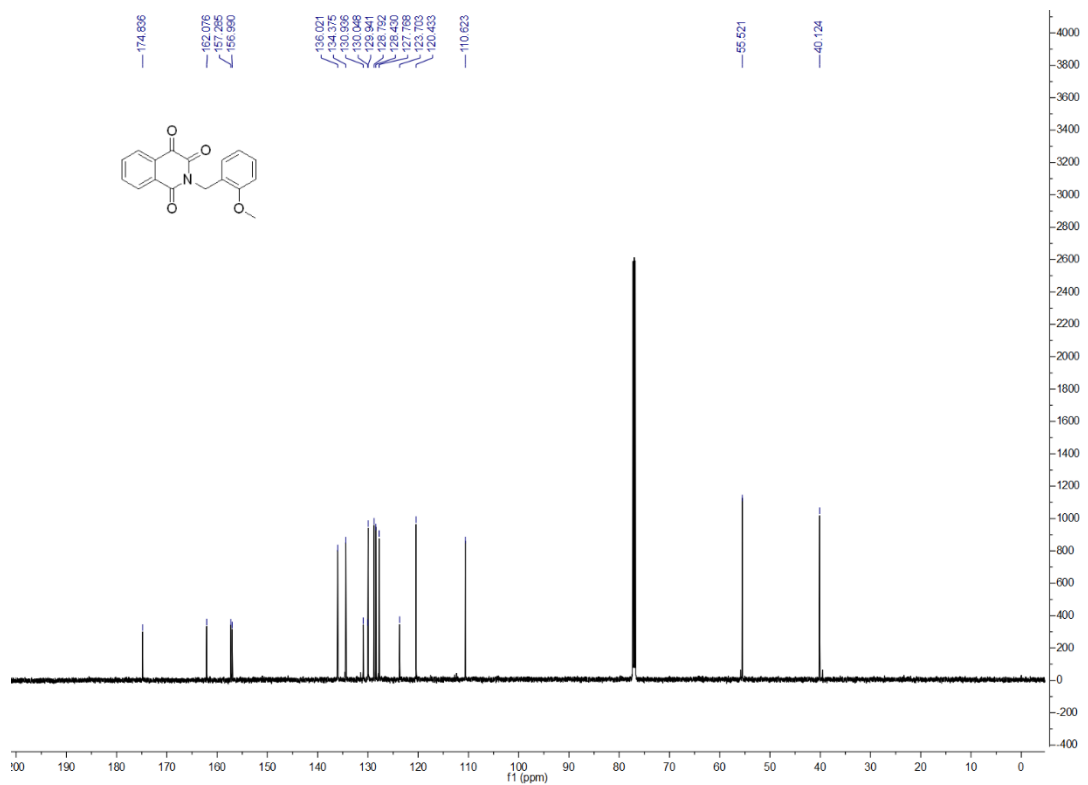
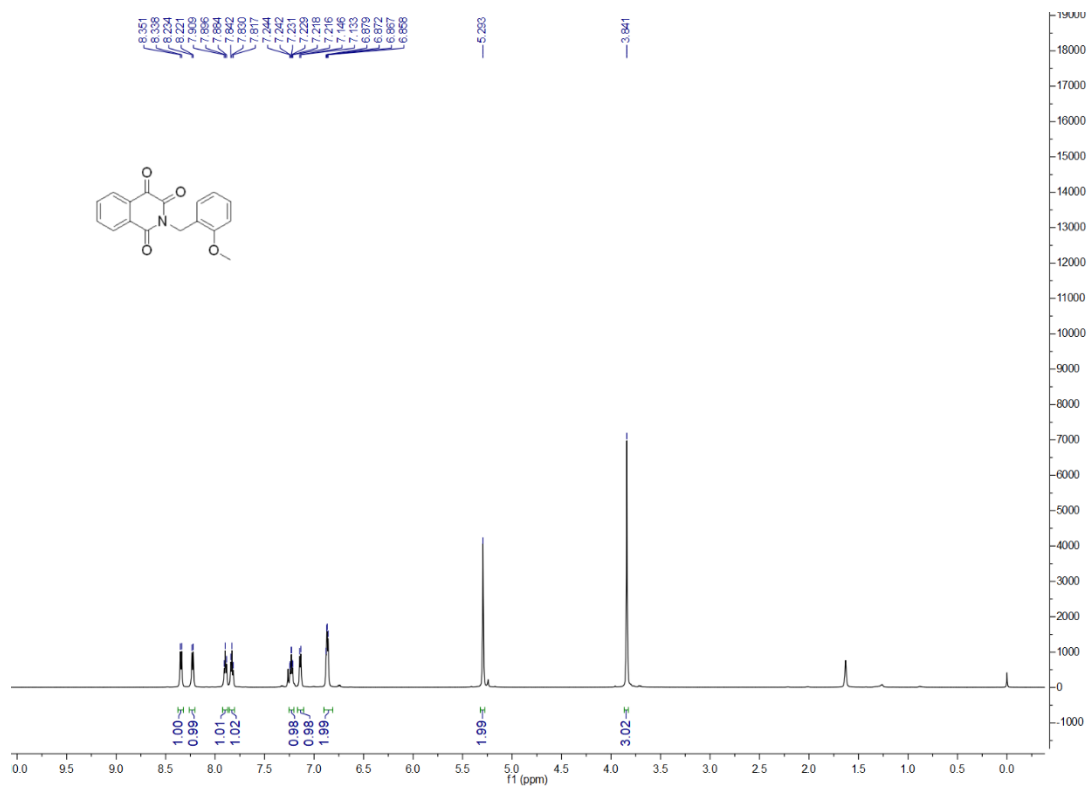
¹H NMR and ¹³C NMR spectra of compound **4j**



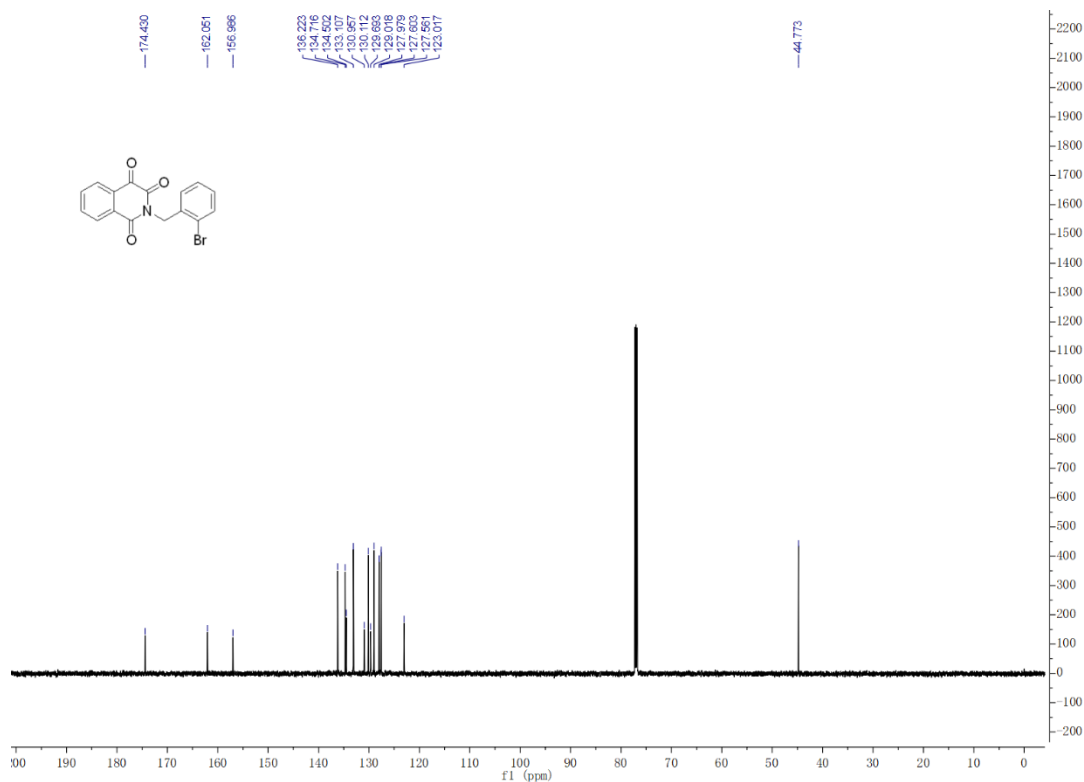
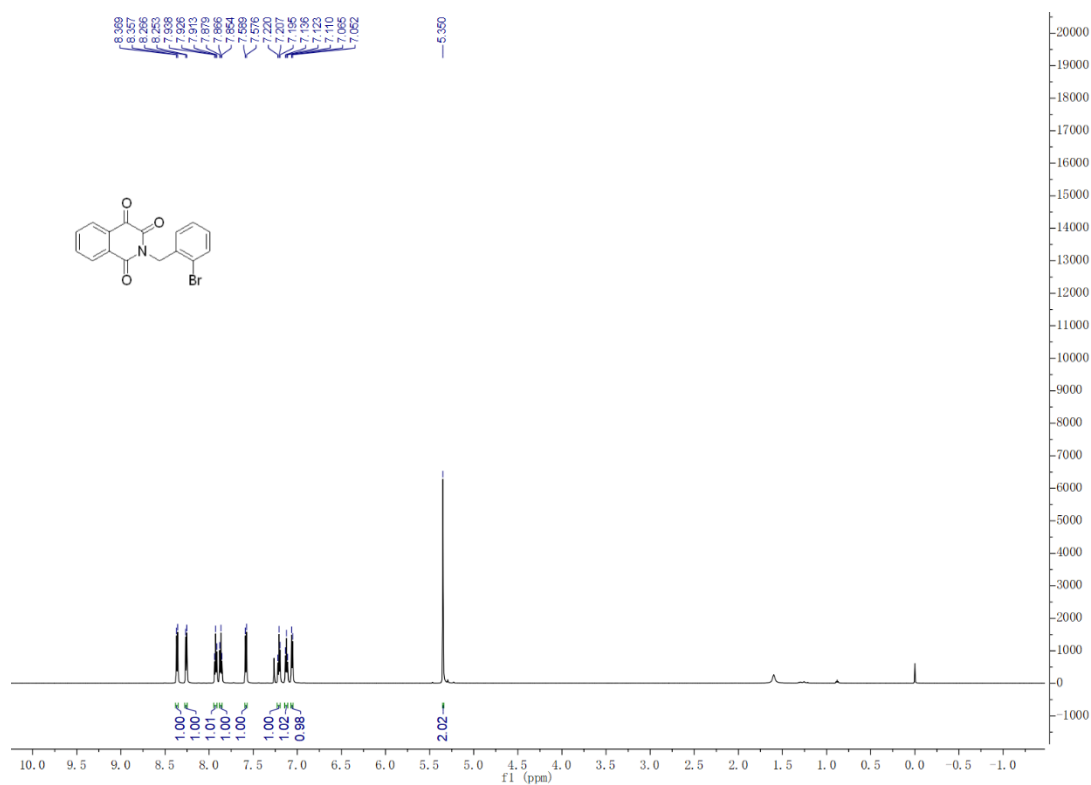
¹H NMR and ¹³C NMR spectra of compound 4k



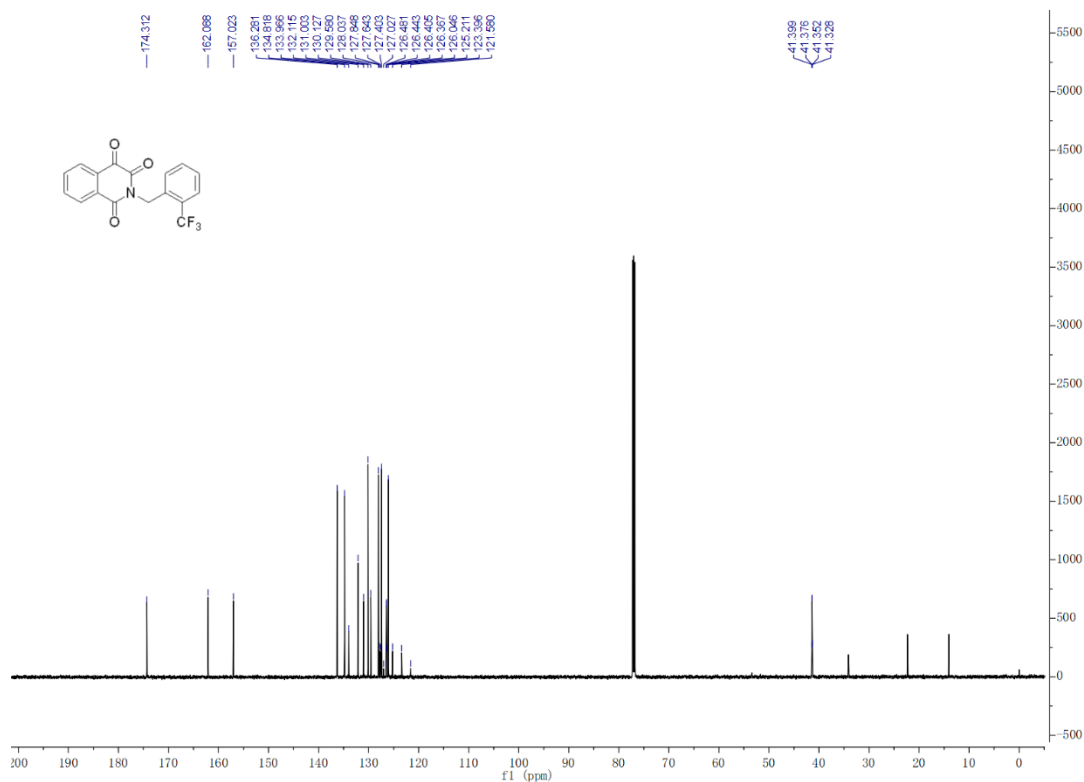
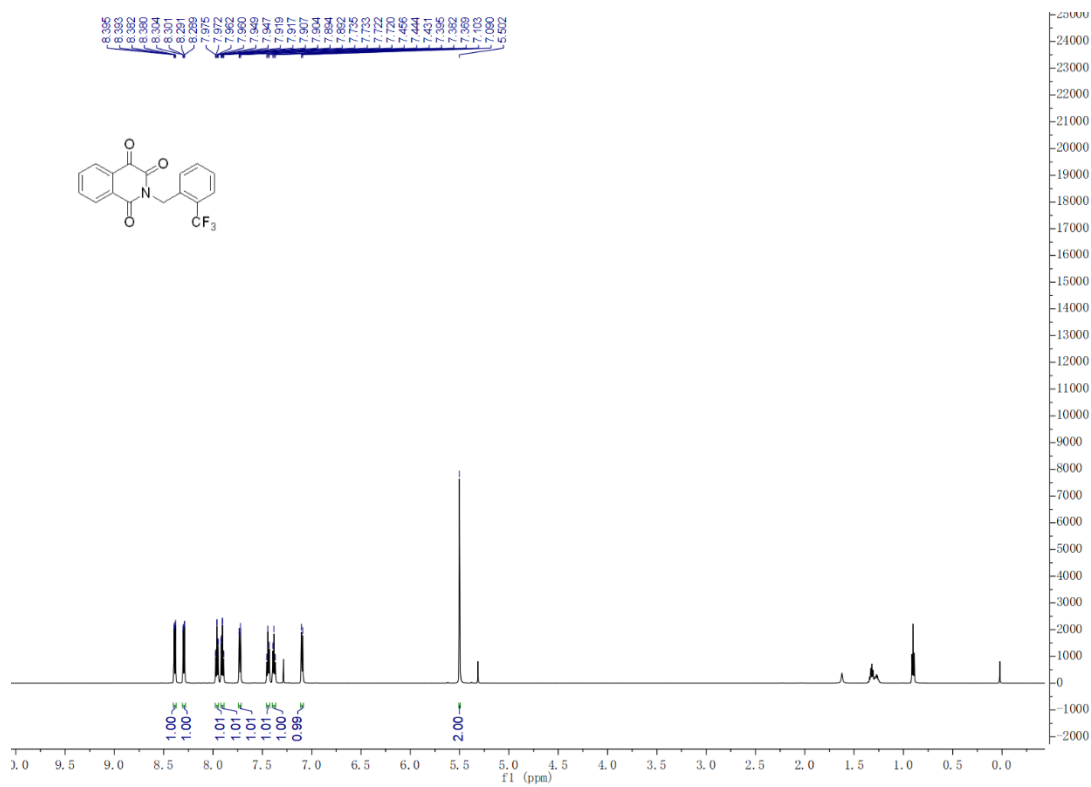
¹H NMR and ¹³C NMR spectra of compound **4I**



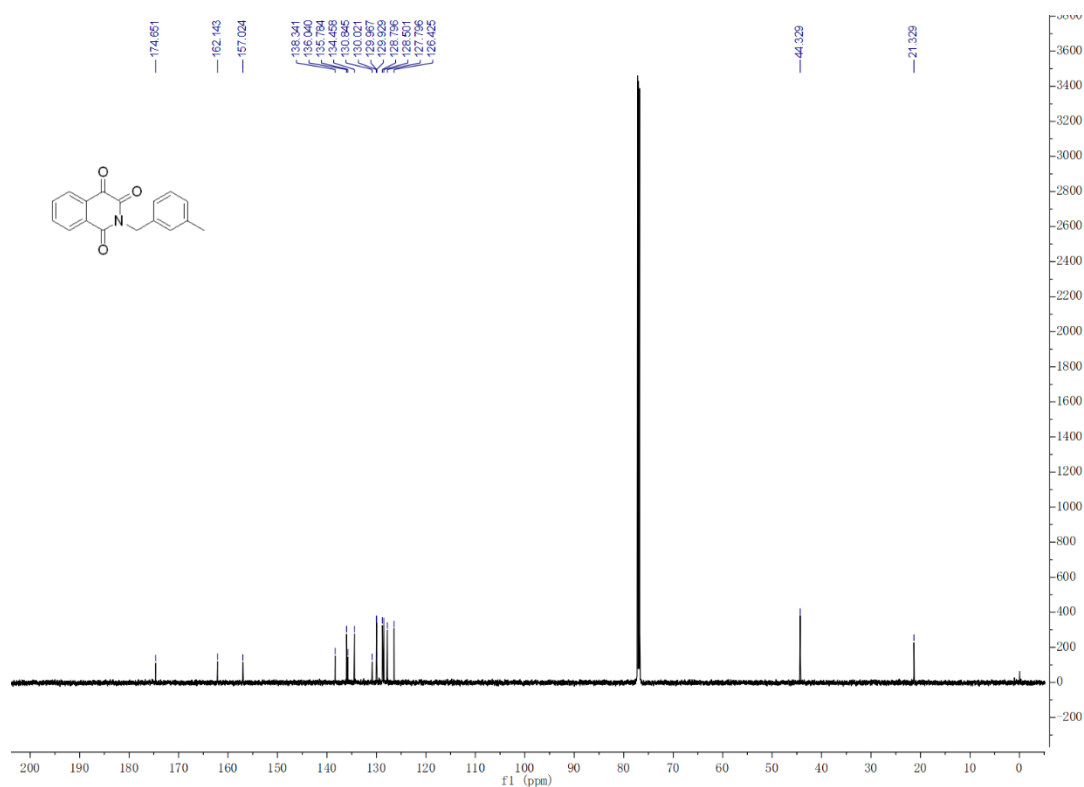
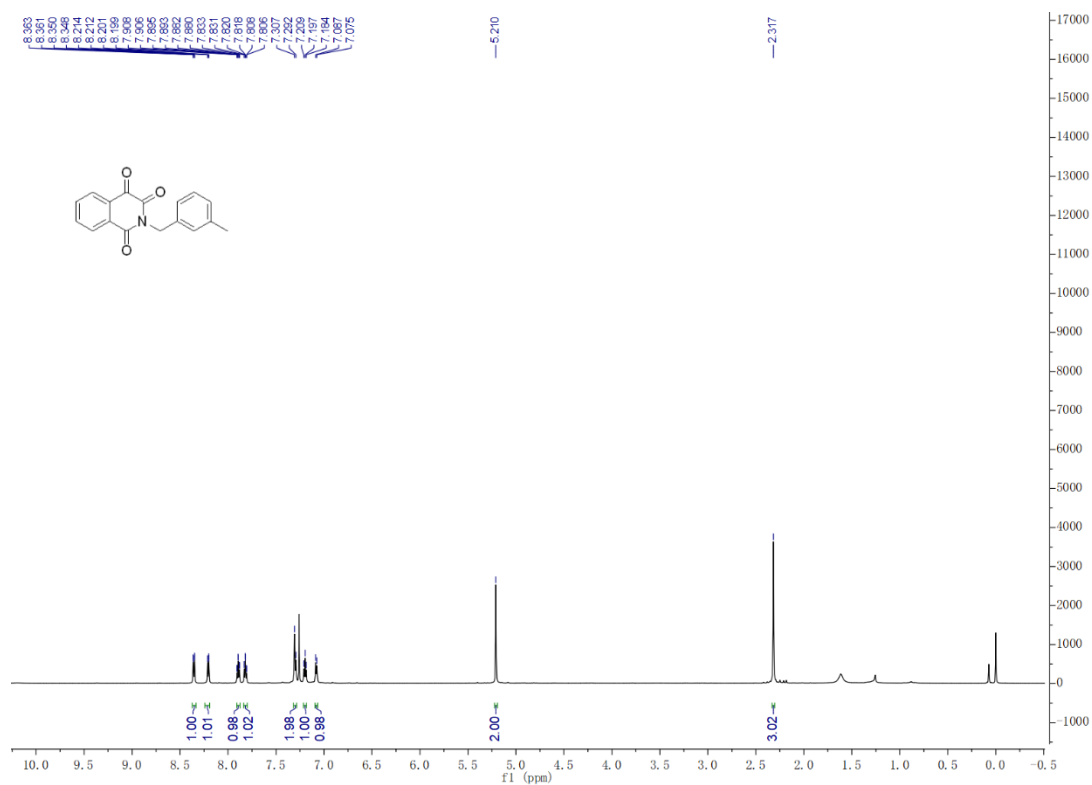
¹H NMR and ¹³C NMR spectra of compound 4m



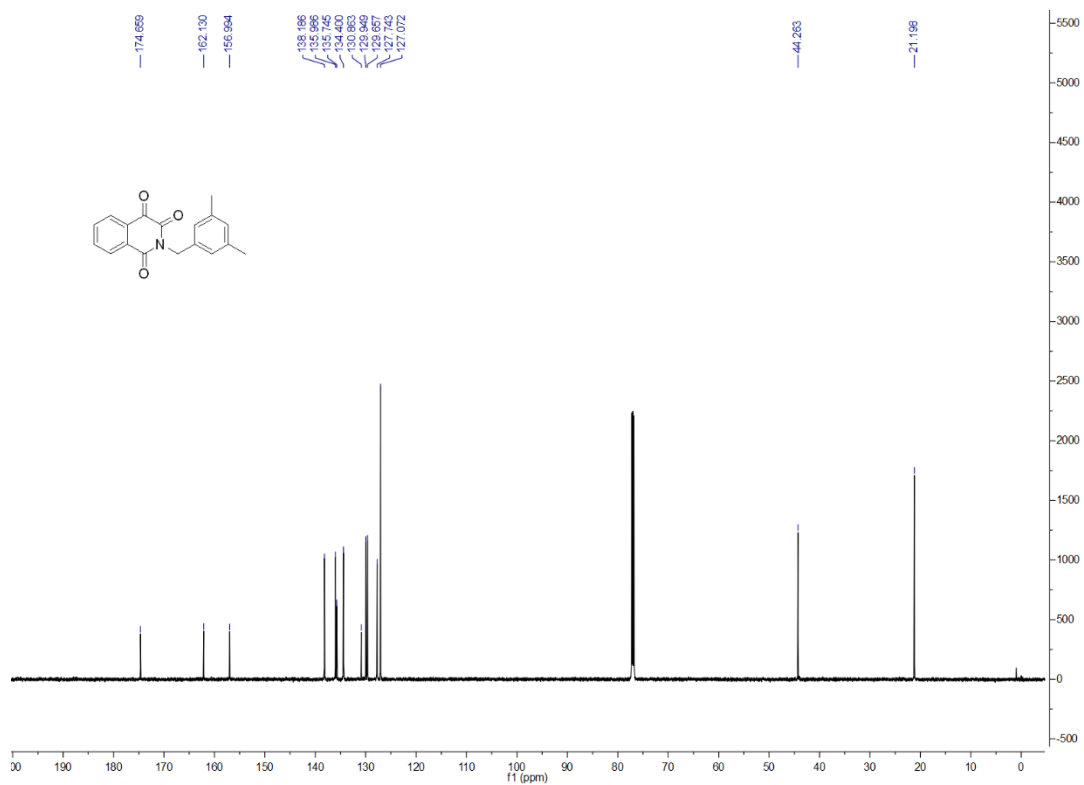
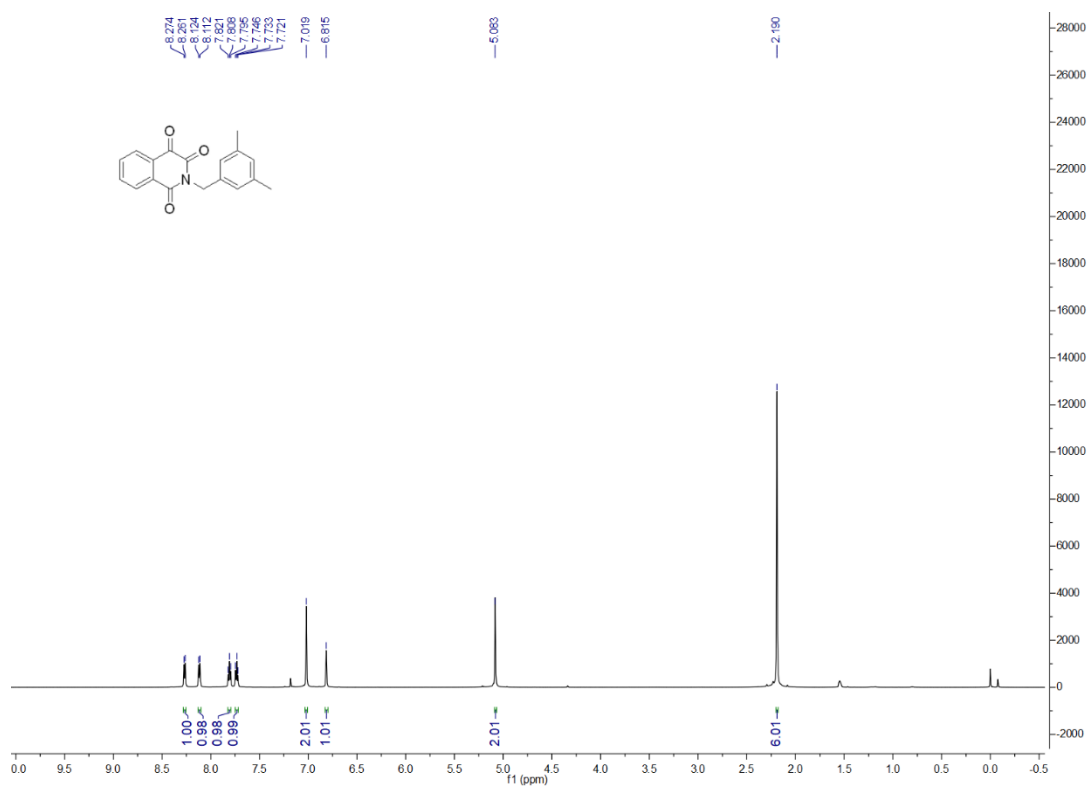
¹H NMR and ¹³C NMR spectra of compound 4n



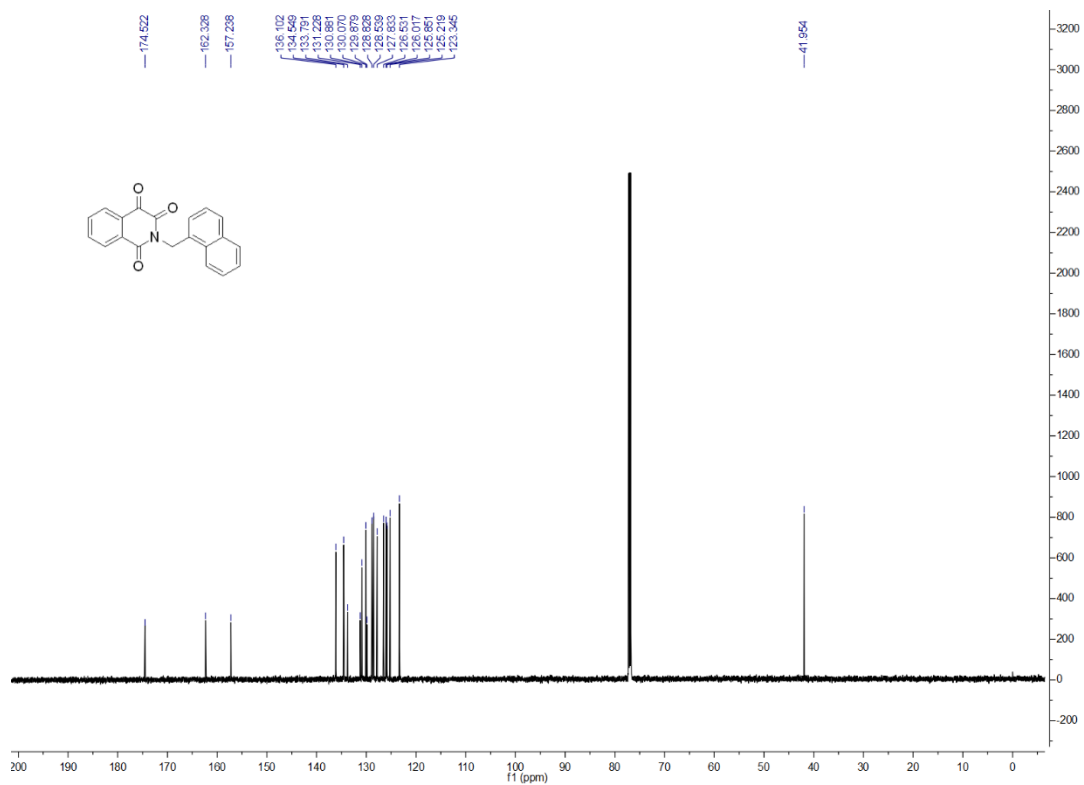
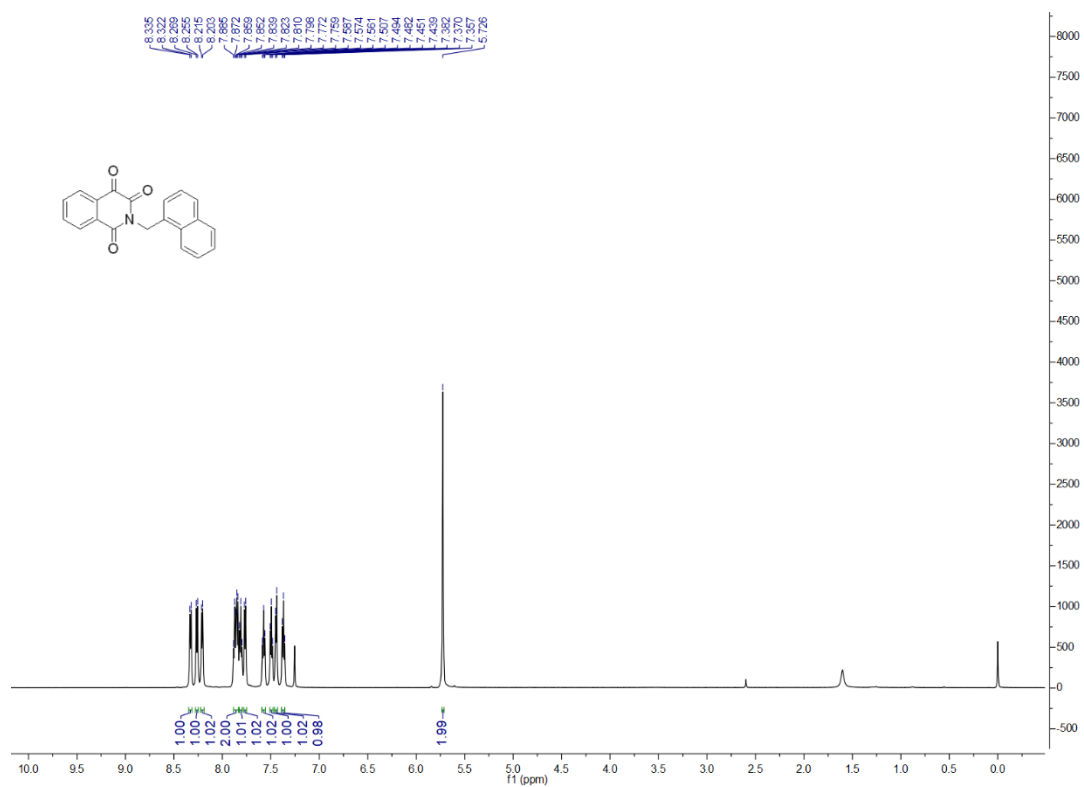
¹H NMR and ¹³C NMR spectra of compound **4o**



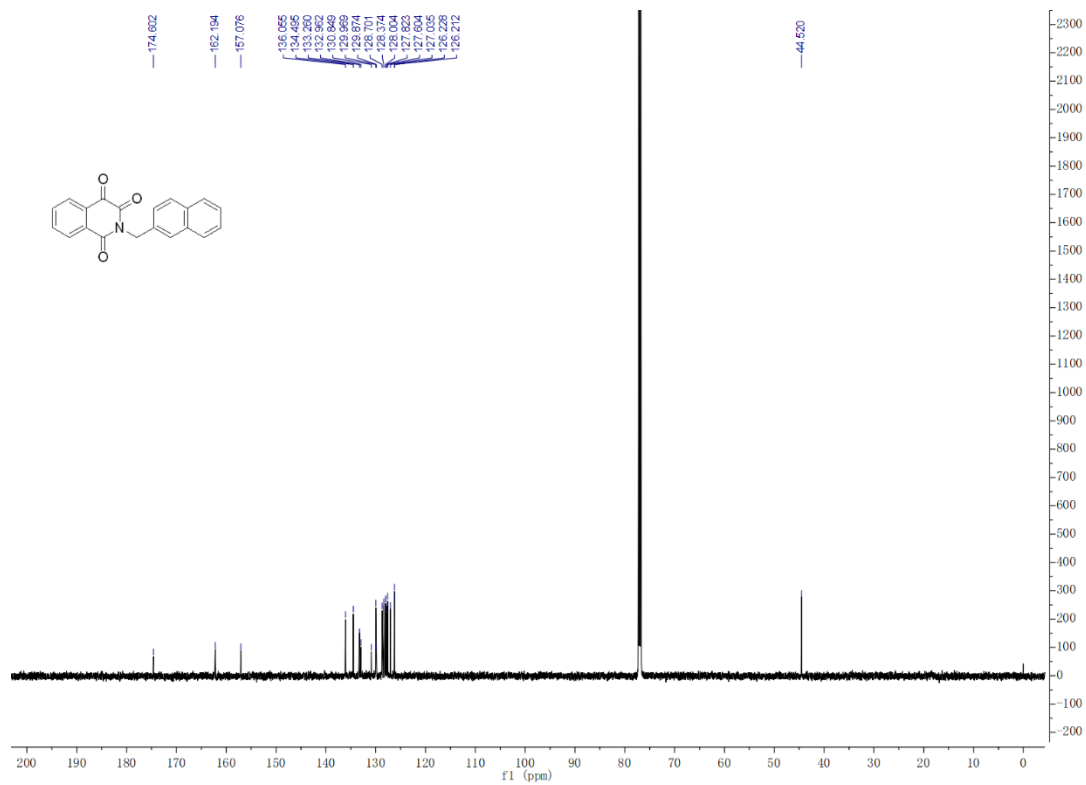
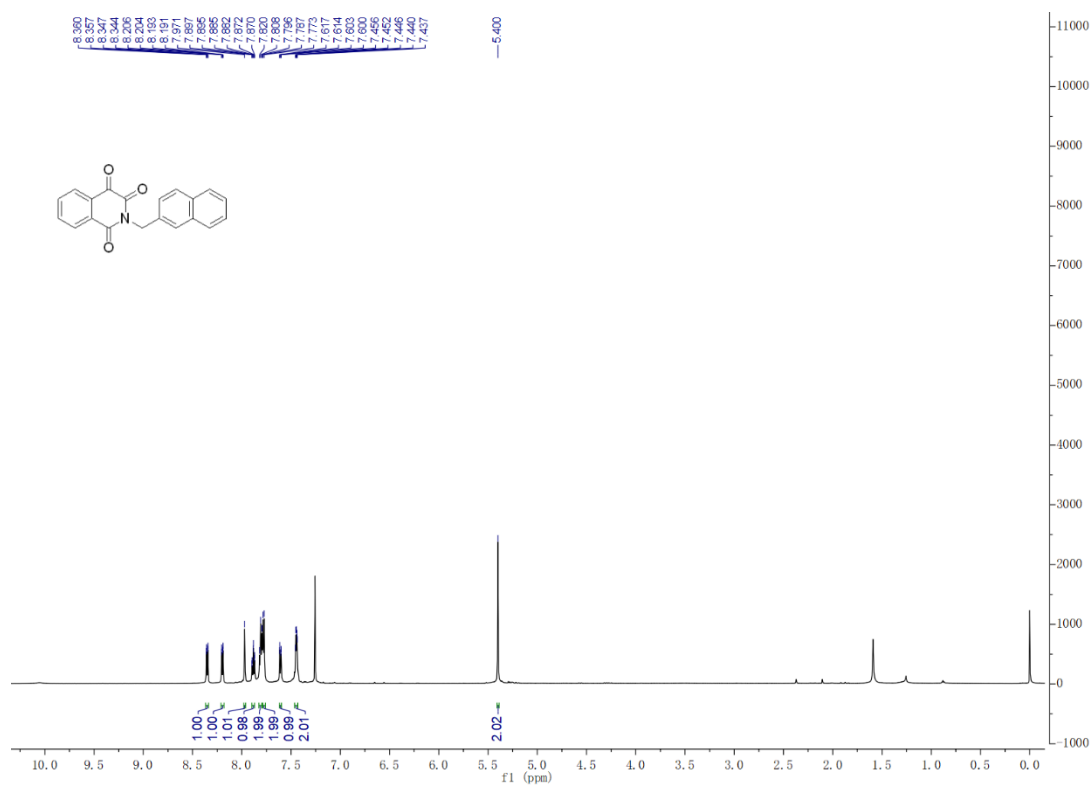
¹H NMR and ¹³C NMR spectra of compound 4p



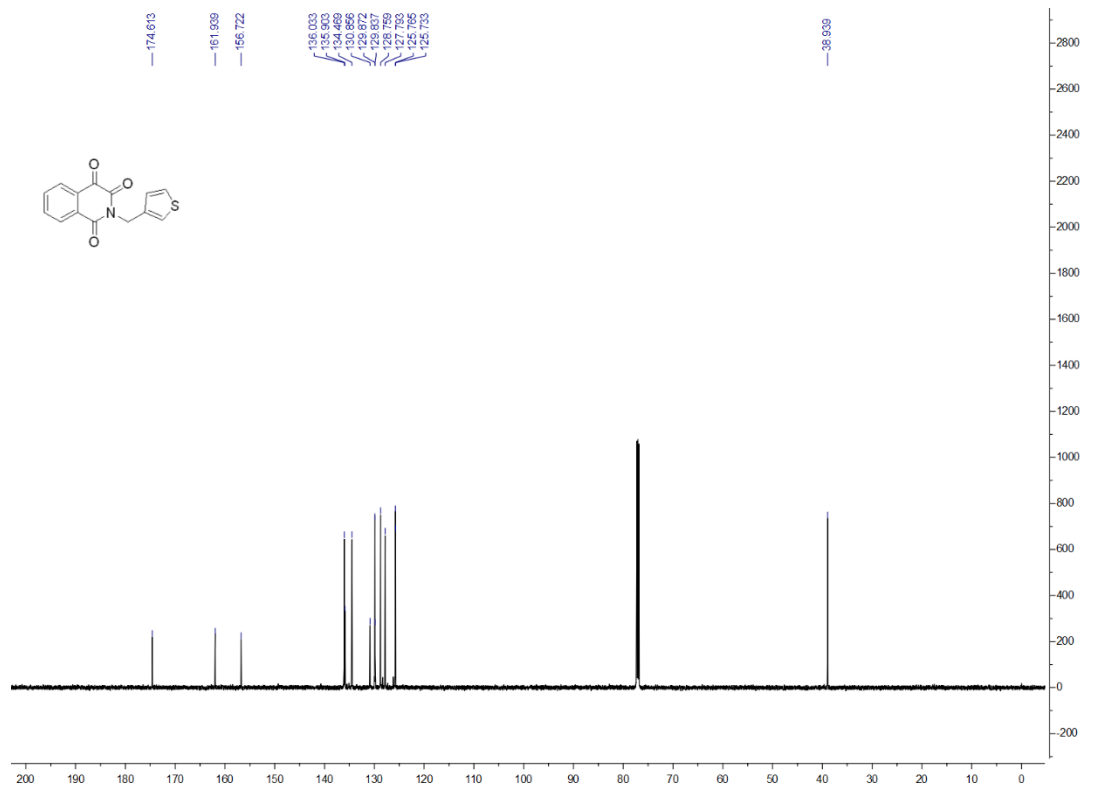
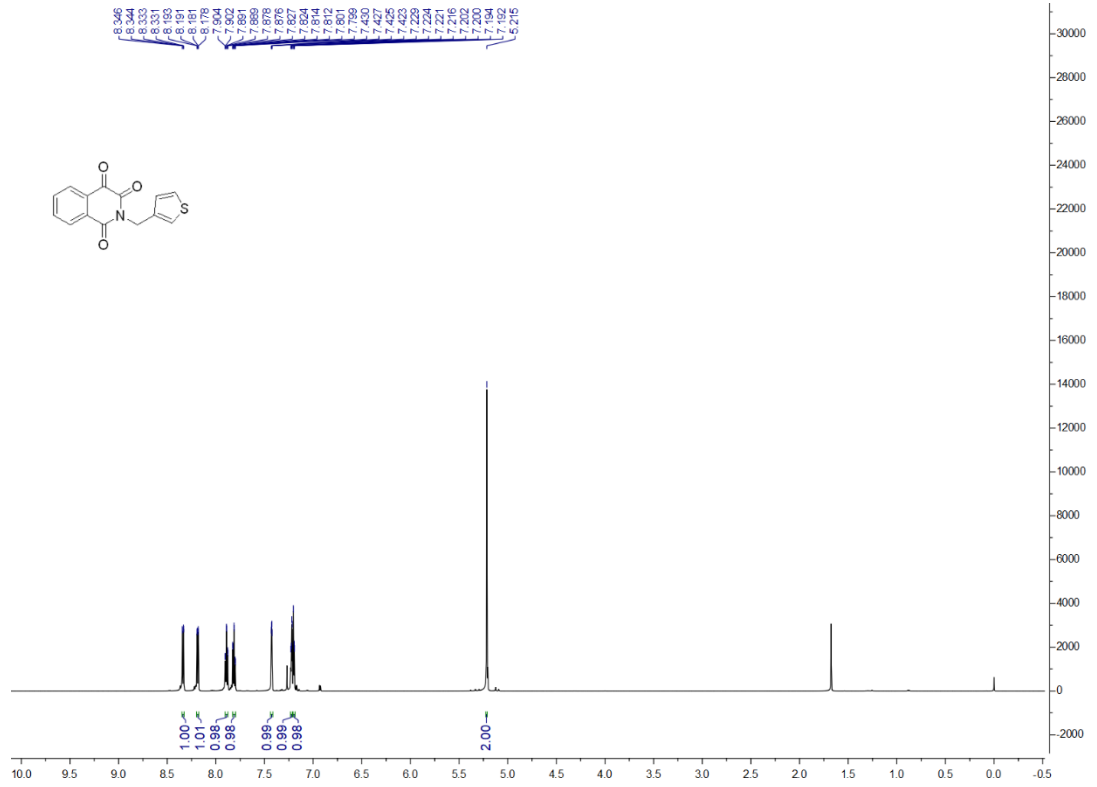
¹H NMR and ¹³C NMR spectra of compound **4q**



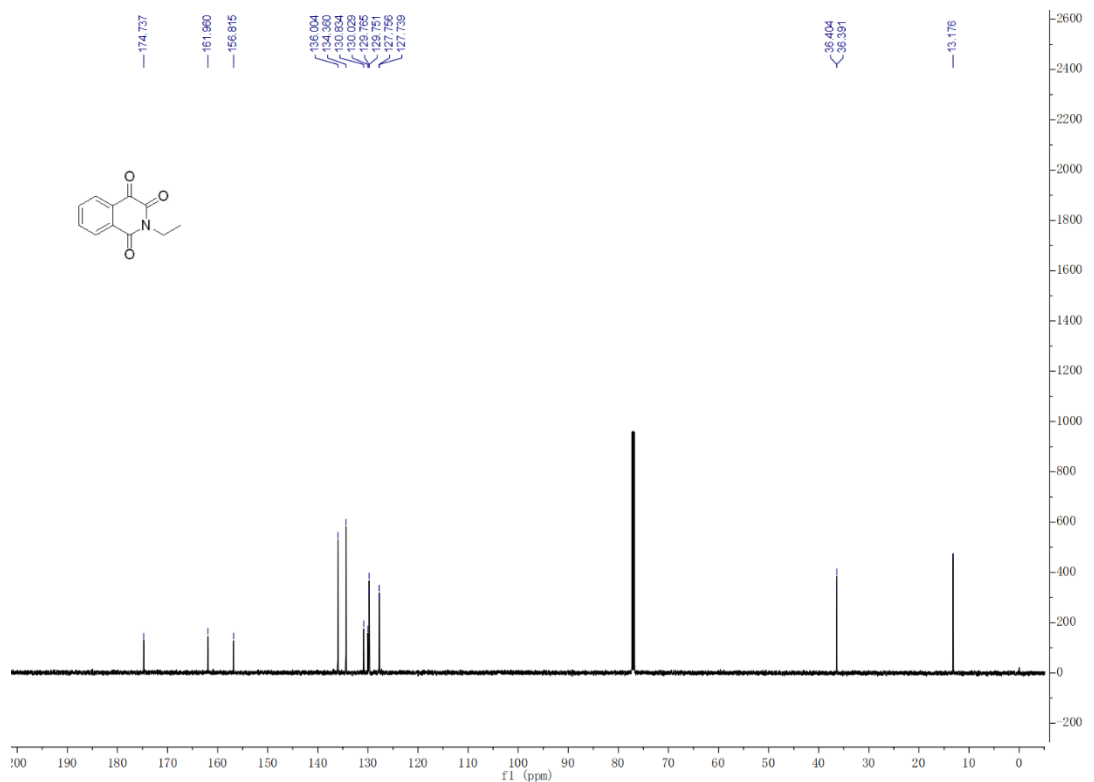
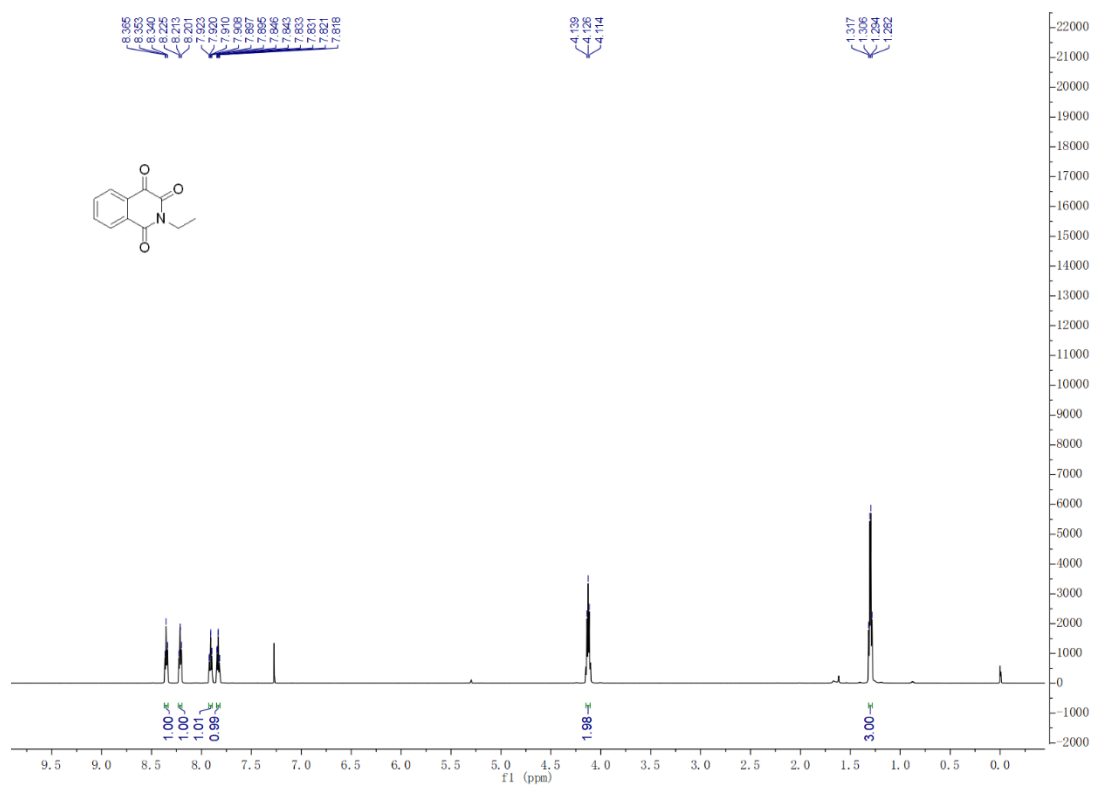
^1H NMR and ^{13}C NMR spectra of compound **4r**



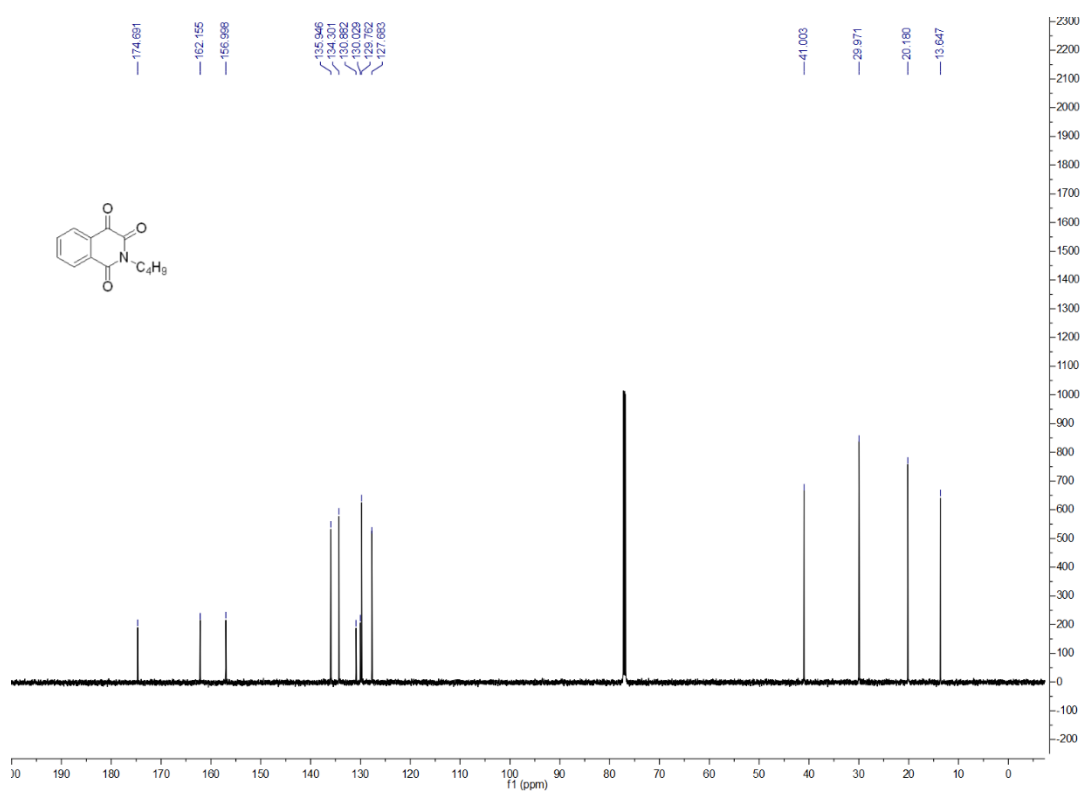
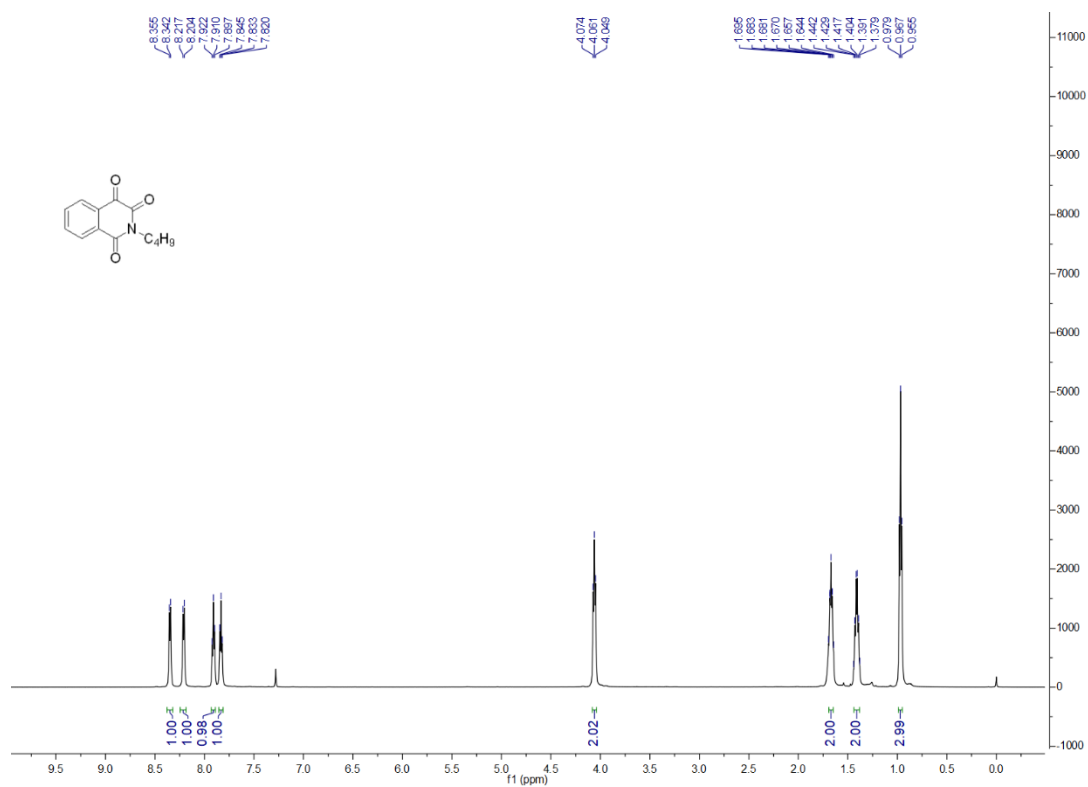
¹H NMR and ¹³C NMR spectra of compound 4s



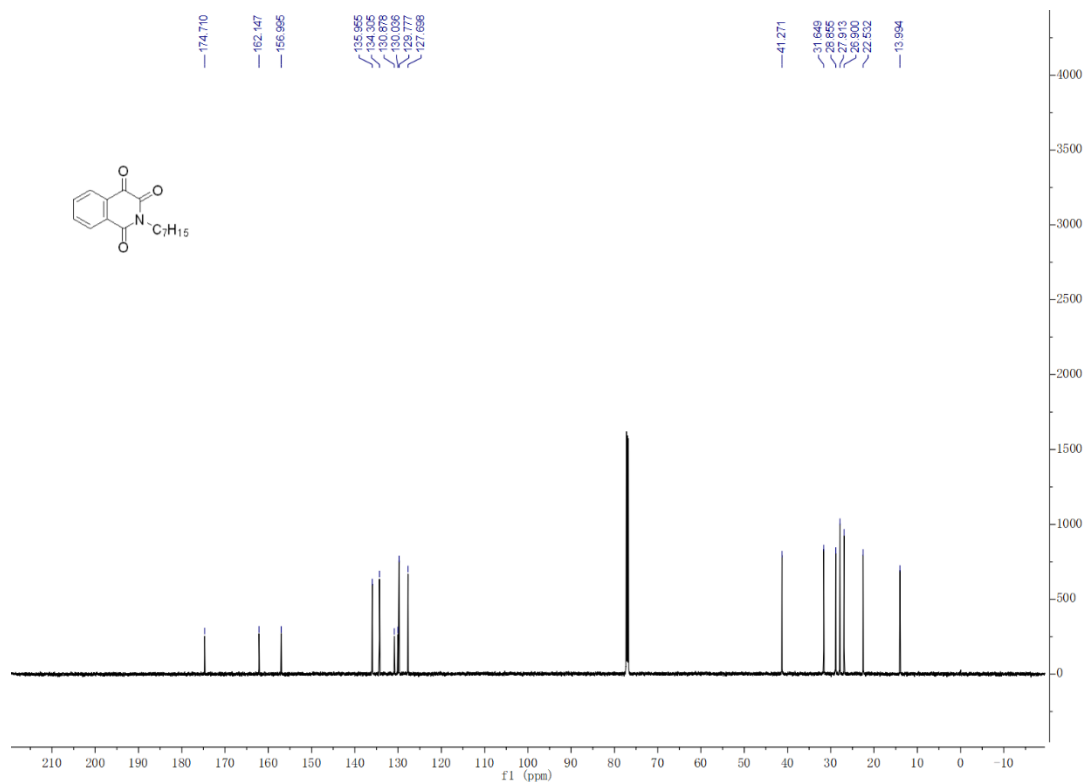
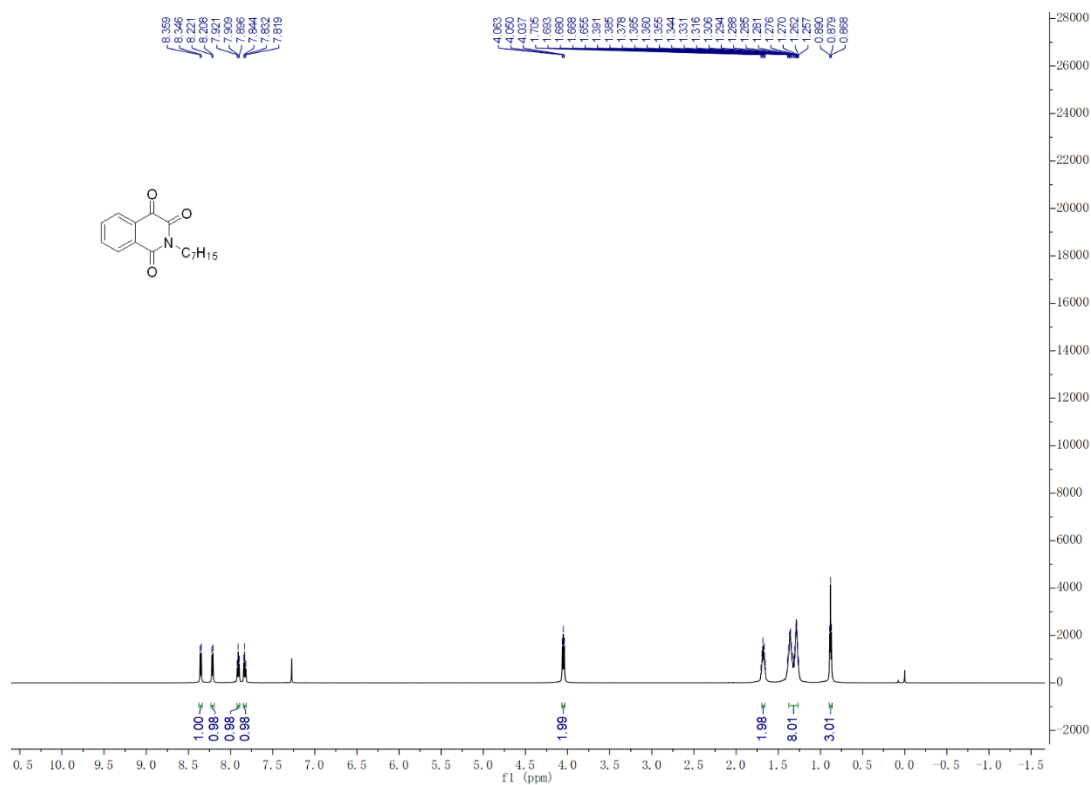
^1H NMR and ^{13}C NMR spectra of compound **4t**



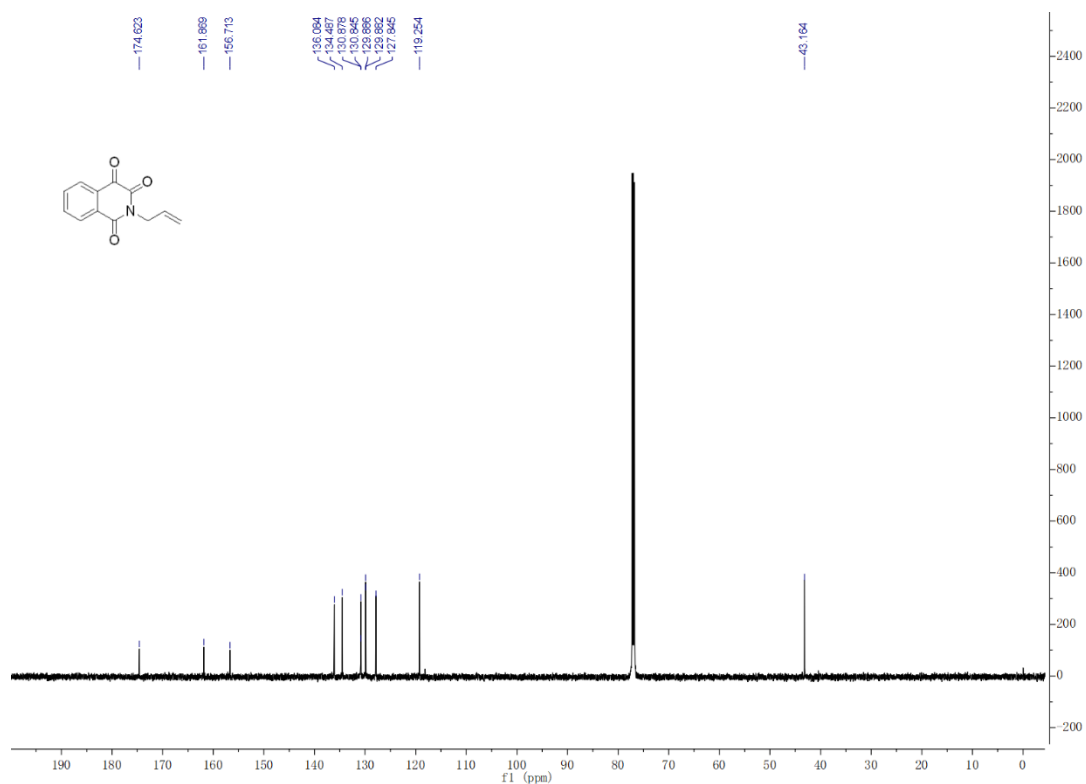
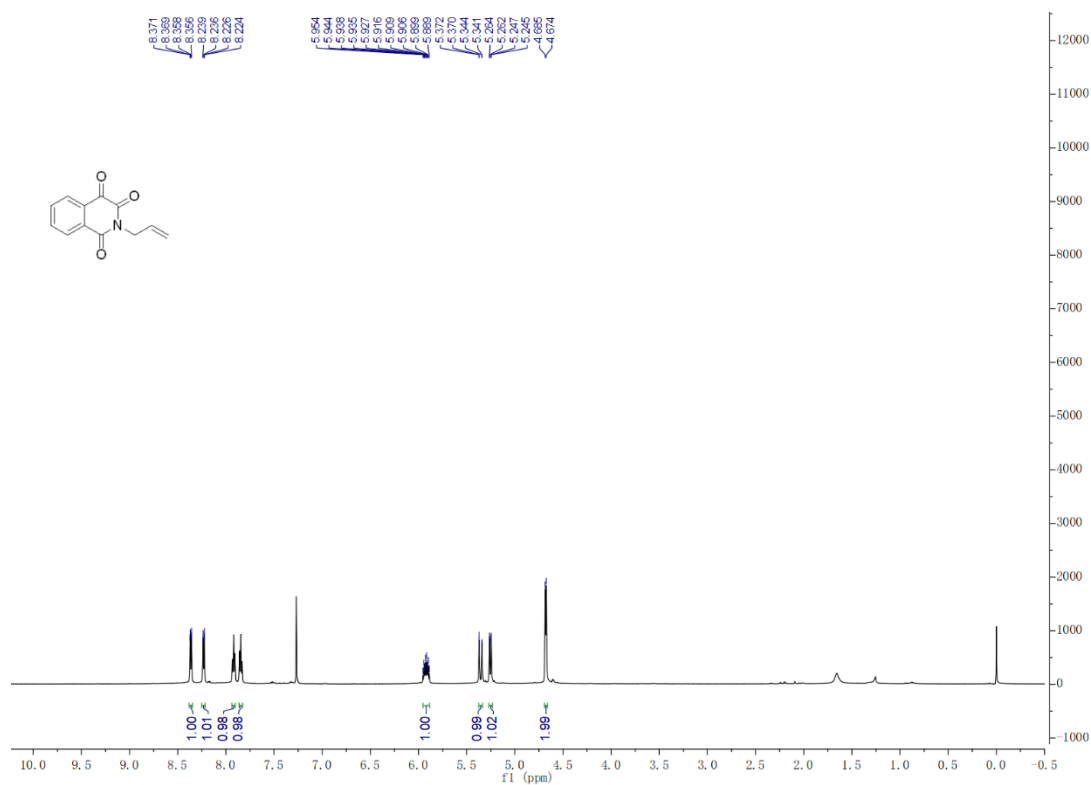
¹H NMR and ¹³C NMR spectra of compound 4u



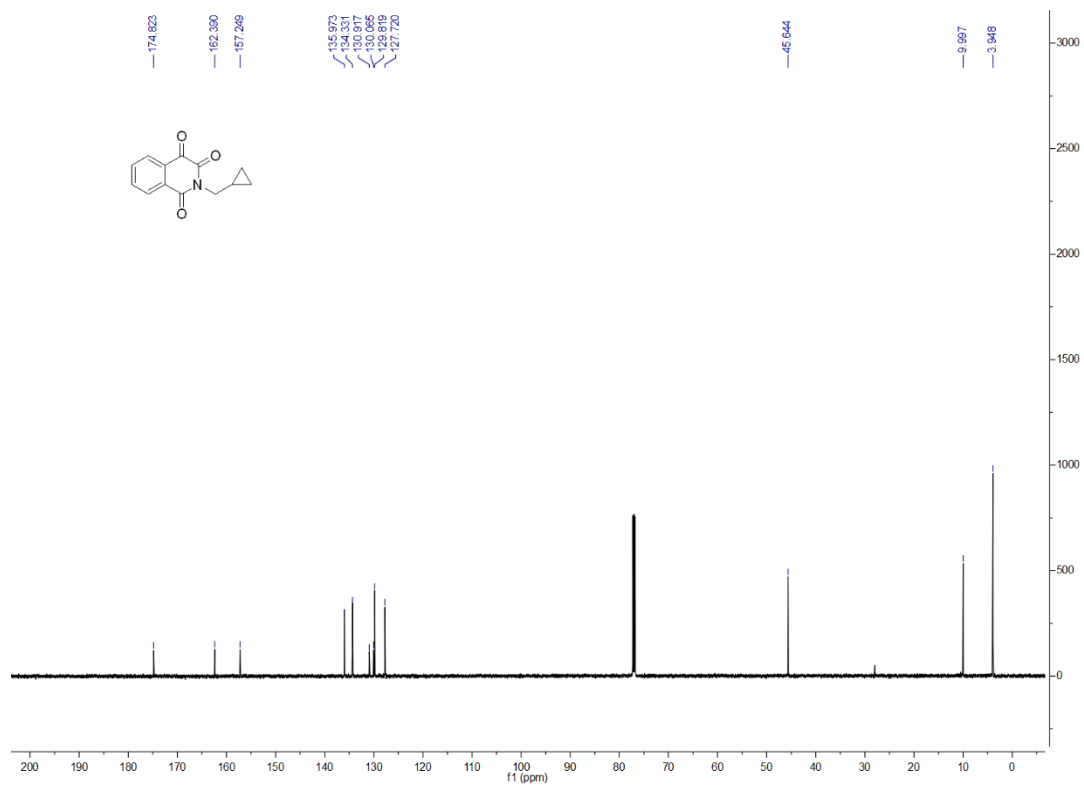
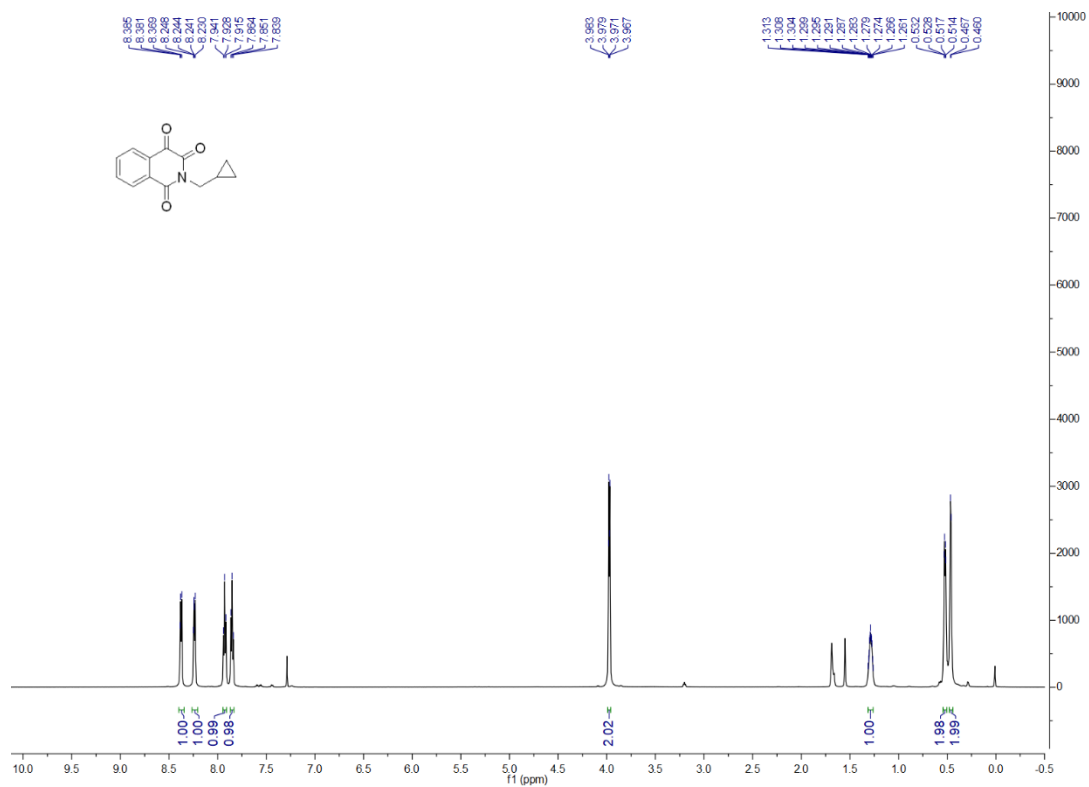
¹H NMR and ¹³C NMR spectra of compound 4v



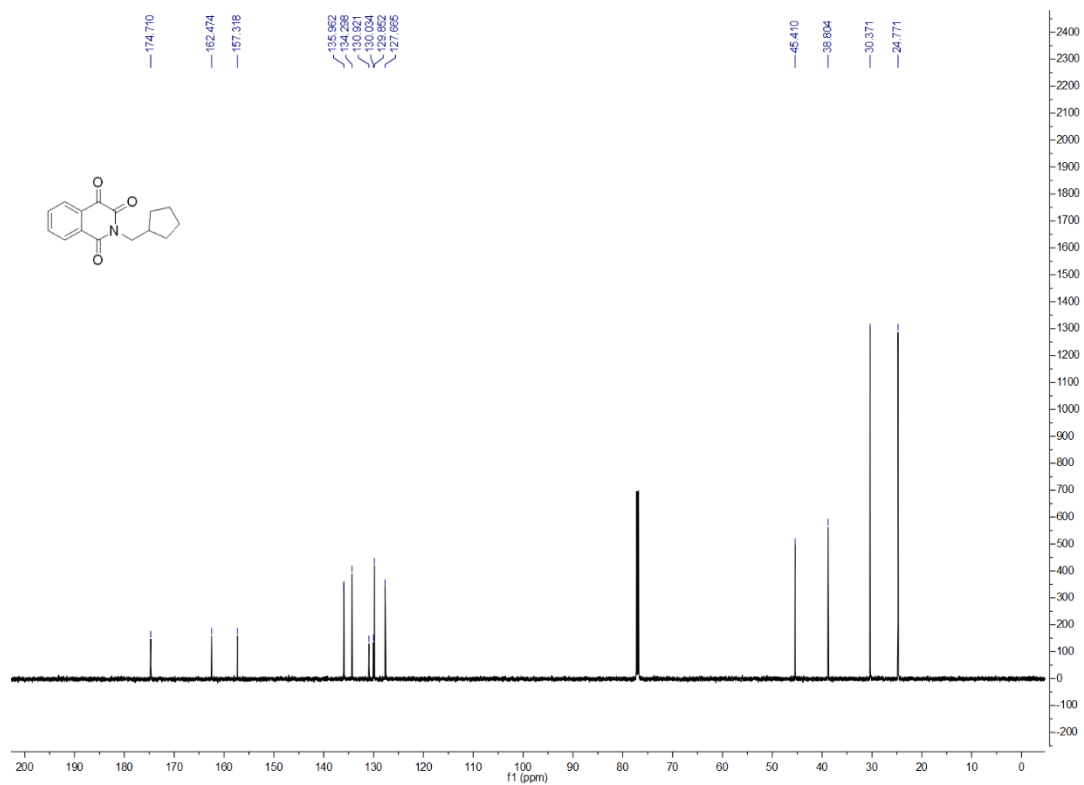
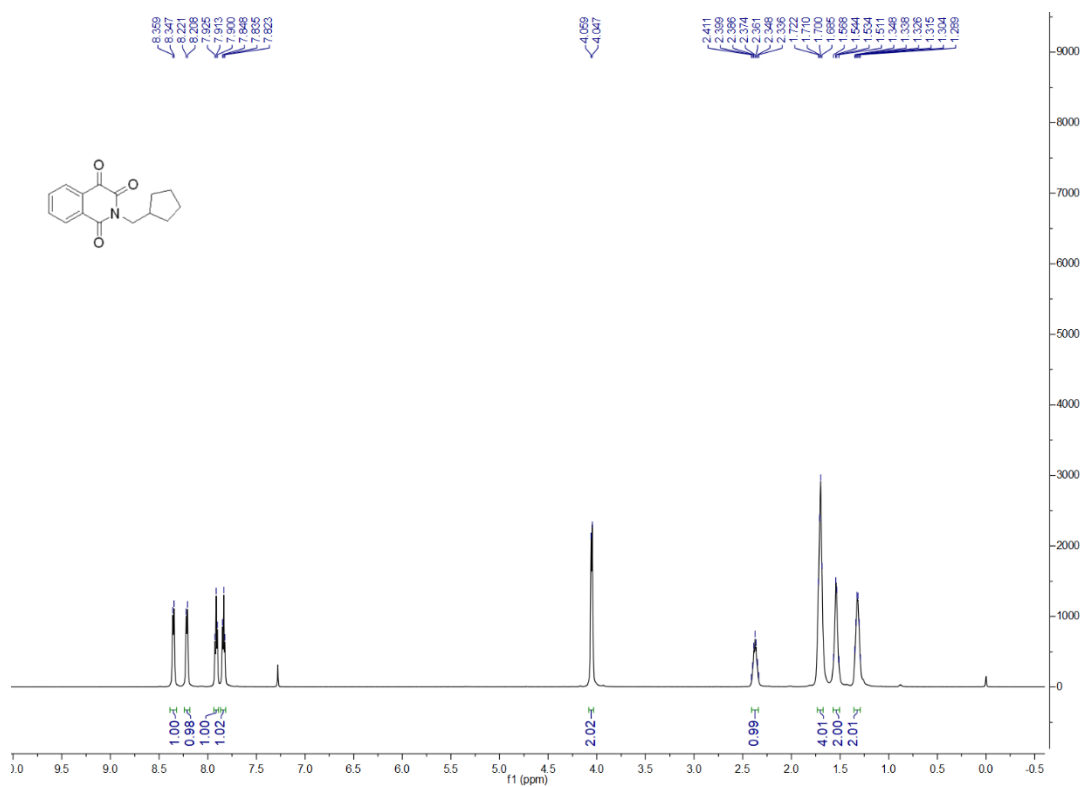
¹H NMR and ¹³C NMR spectra of compound **4w**



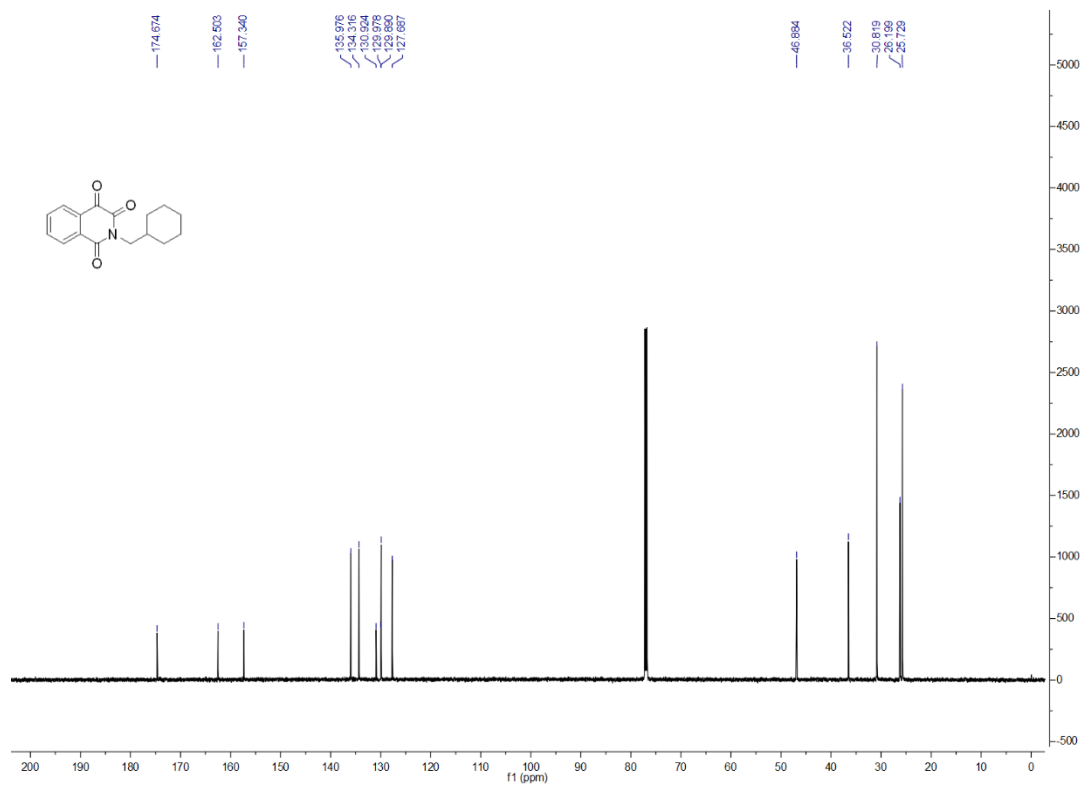
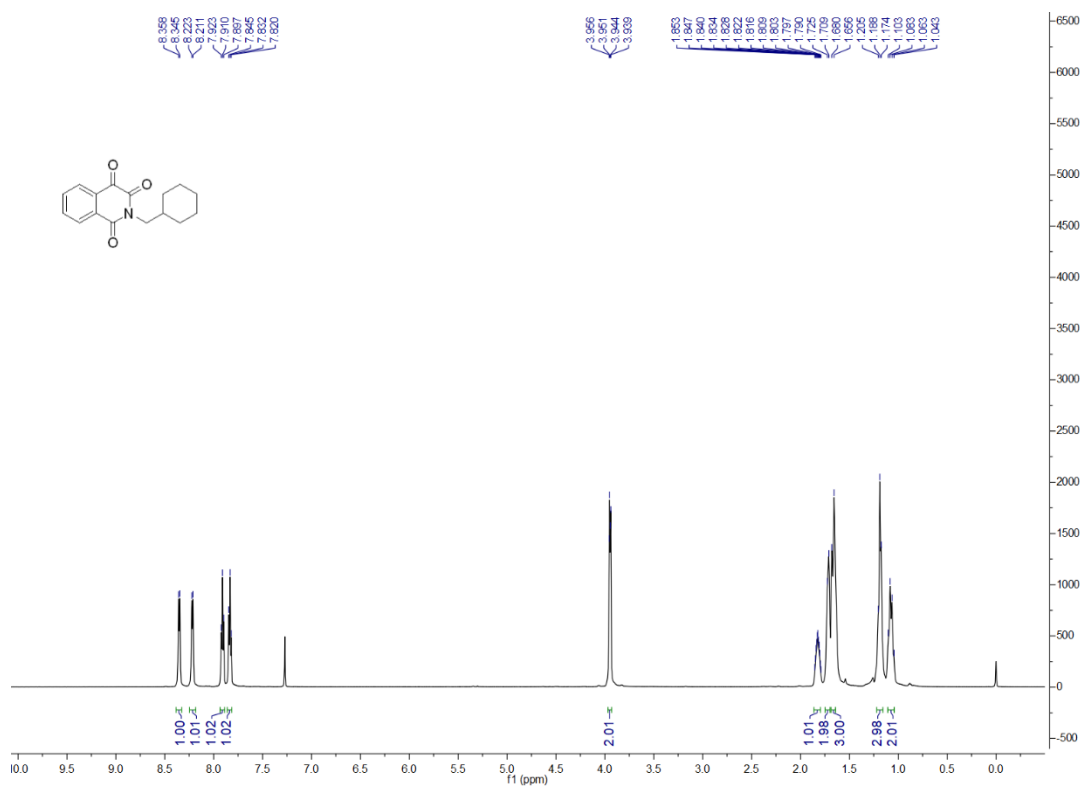
¹H NMR and ¹³C NMR spectra of compound 4x



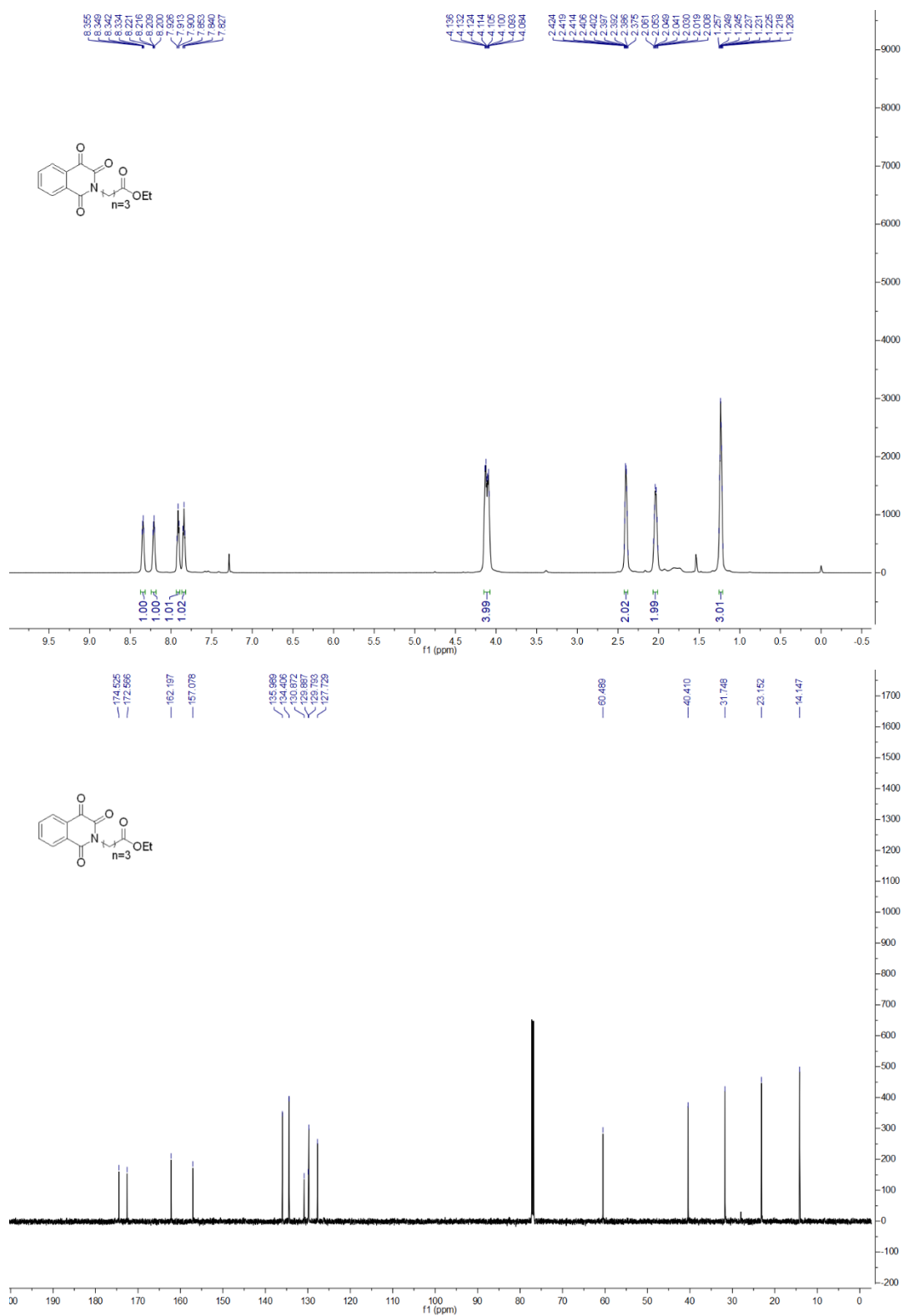
¹H NMR and ¹³C NMR spectra of compound **4y**



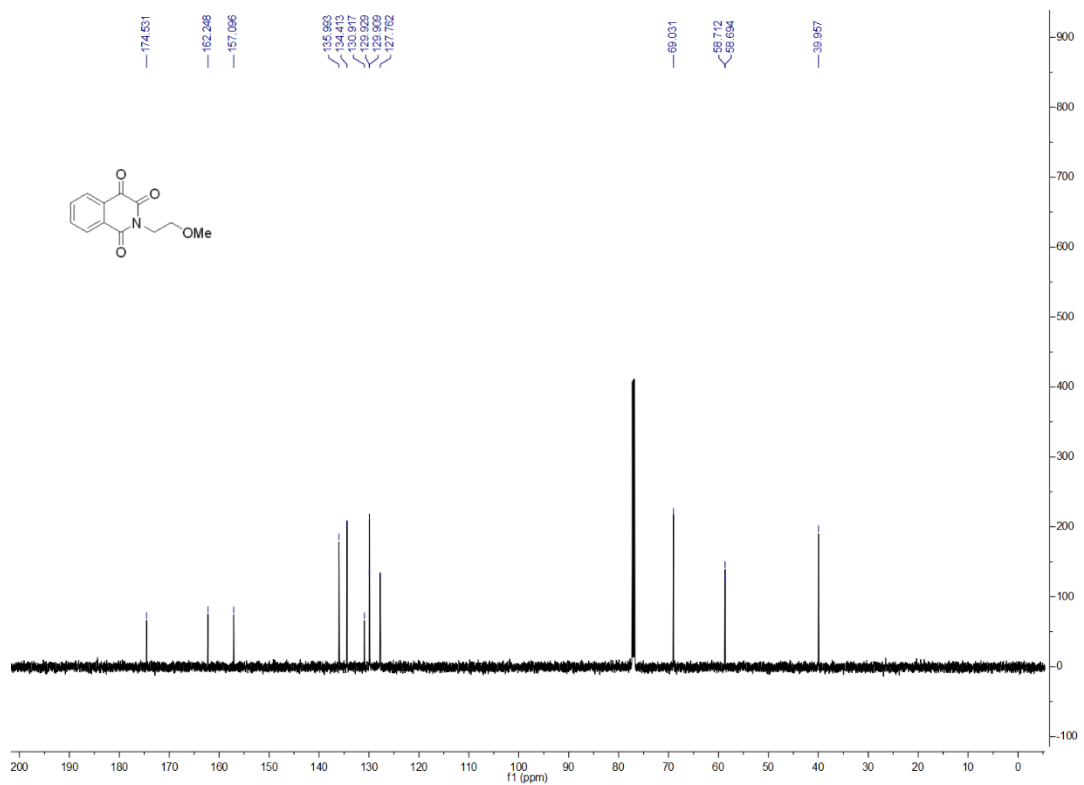
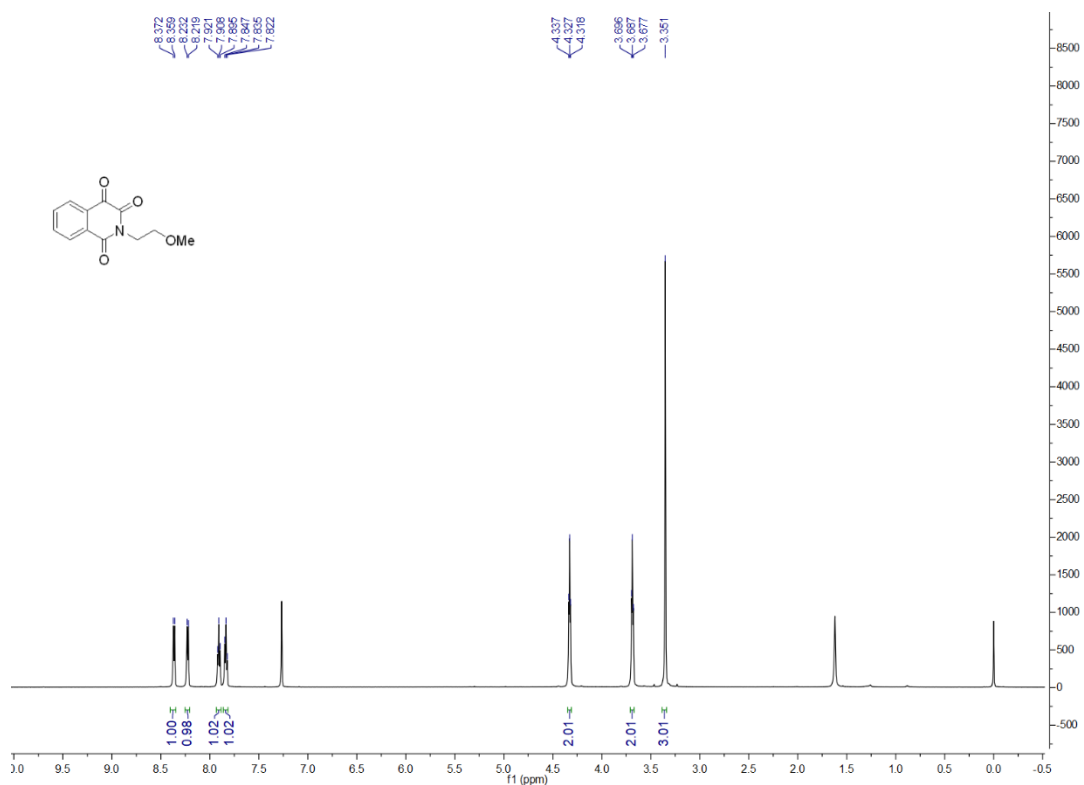
¹H NMR and ¹³C NMR spectra of compound 4z



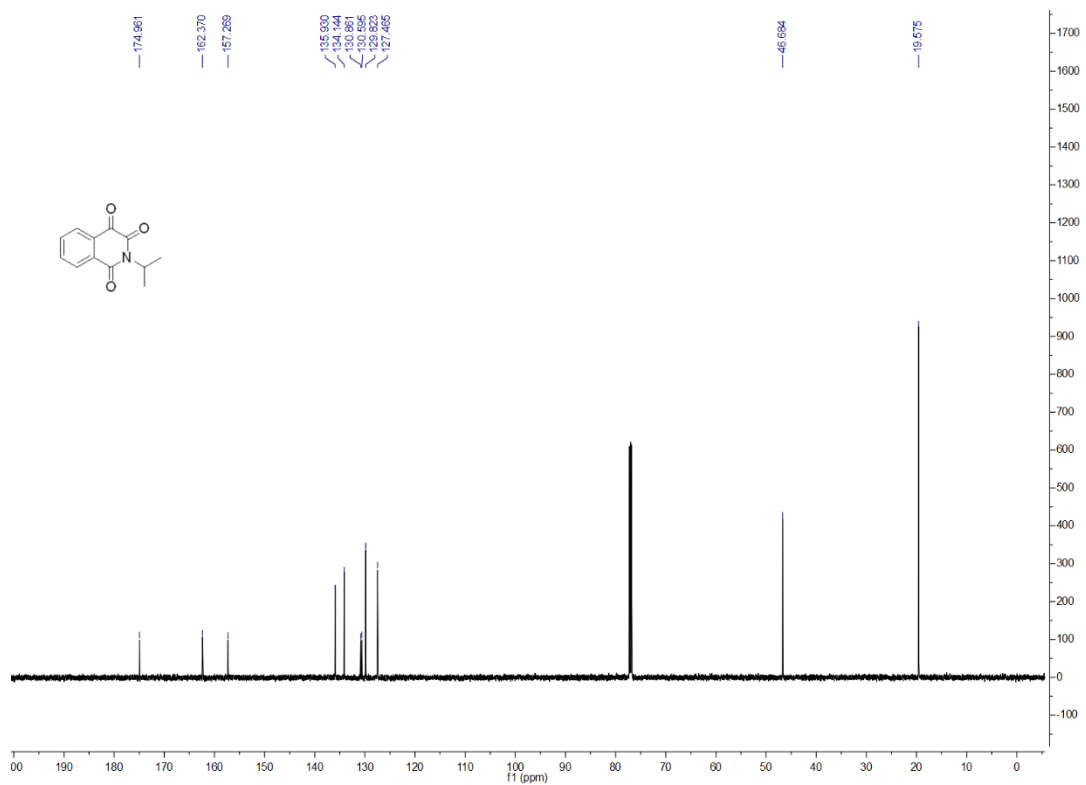
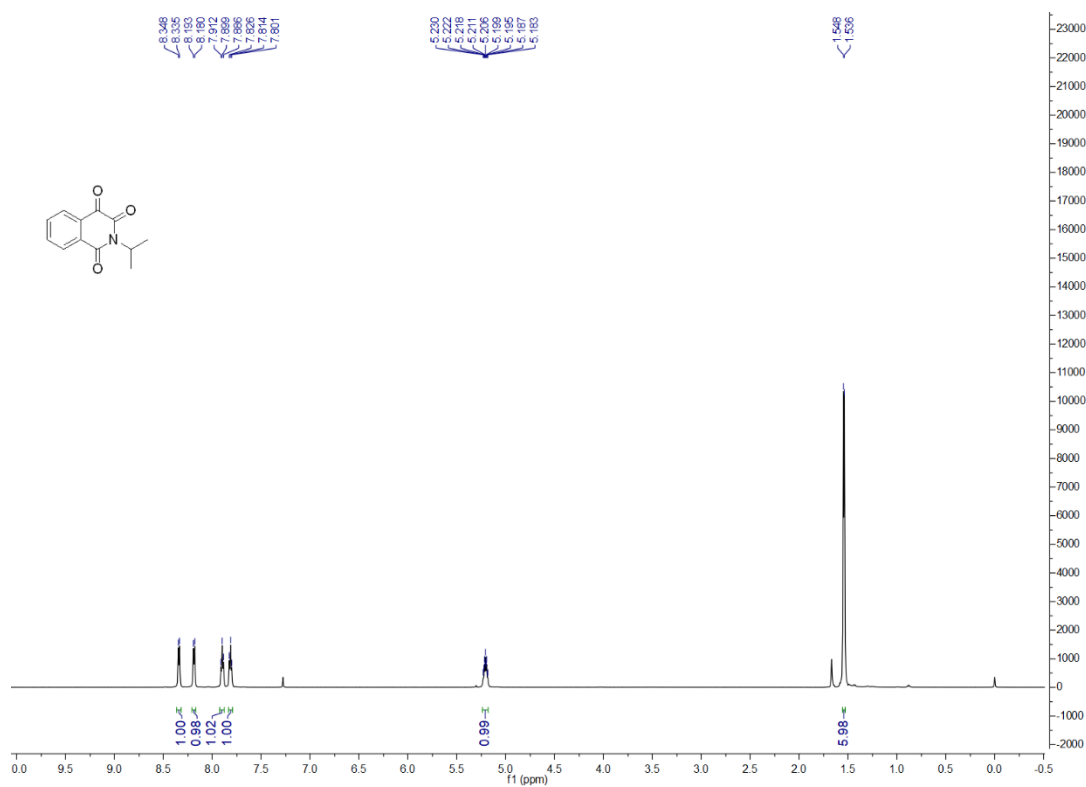
¹H NMR and ¹³C NMR spectra of compound 4aa



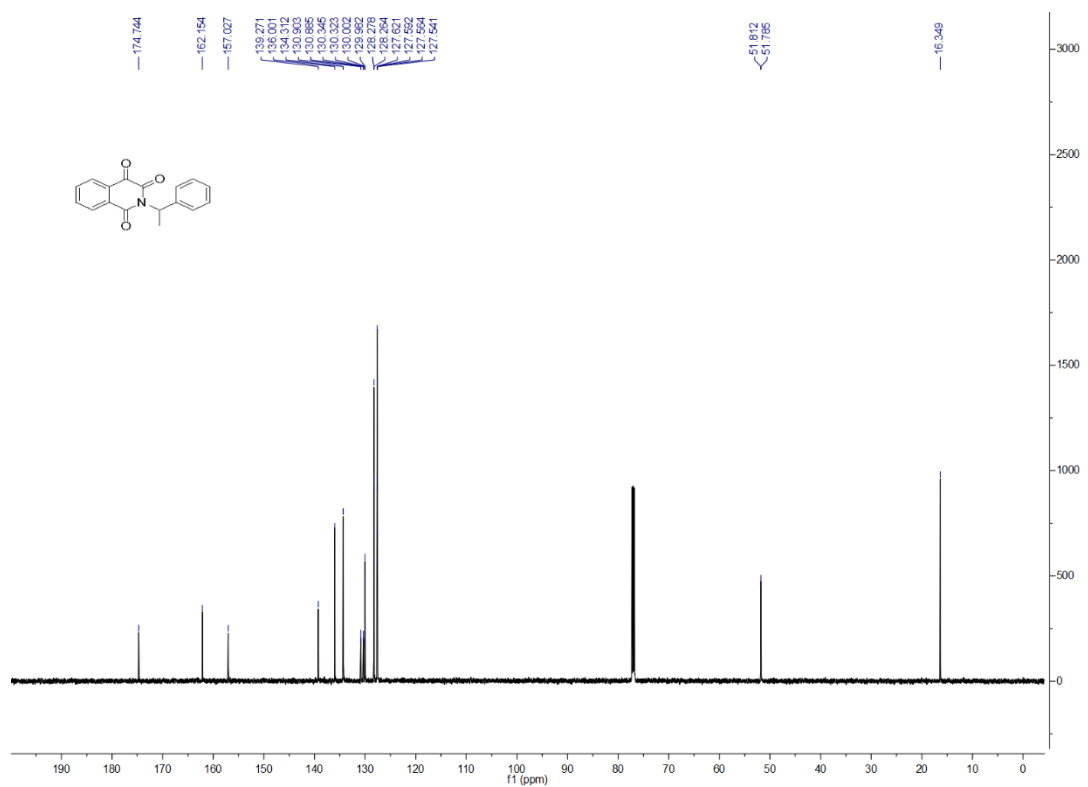
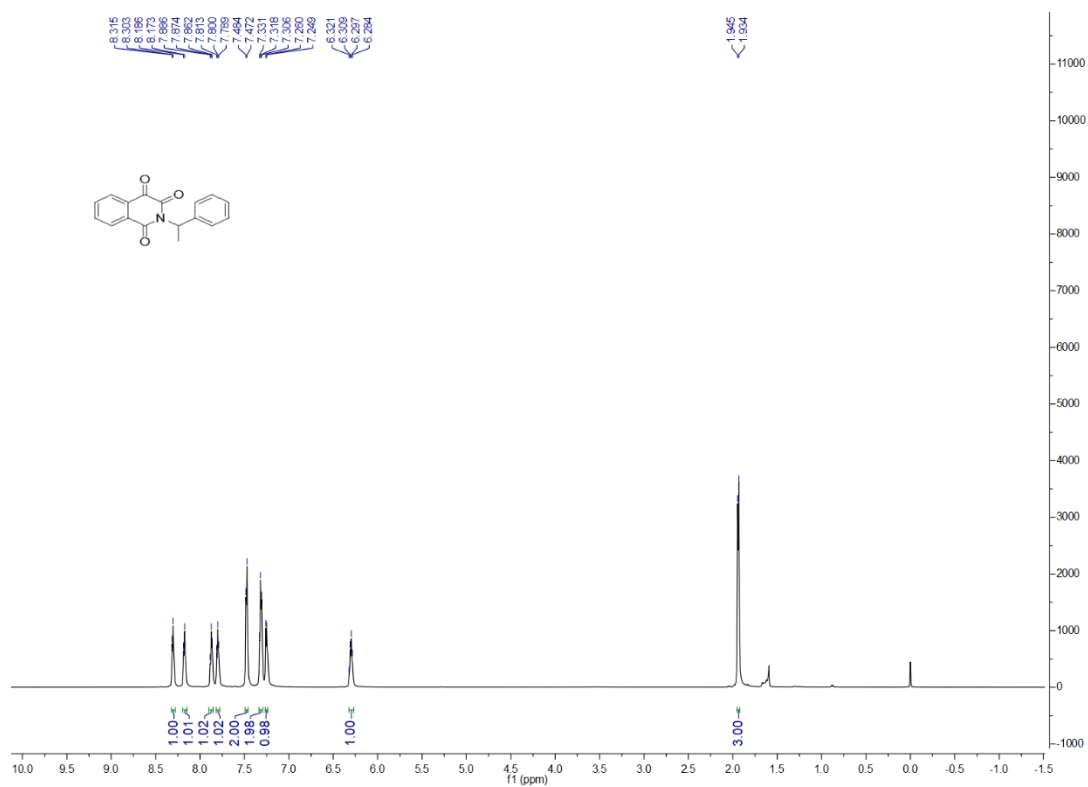
¹H NMR and ¹³C NMR spectra of compound 4ab



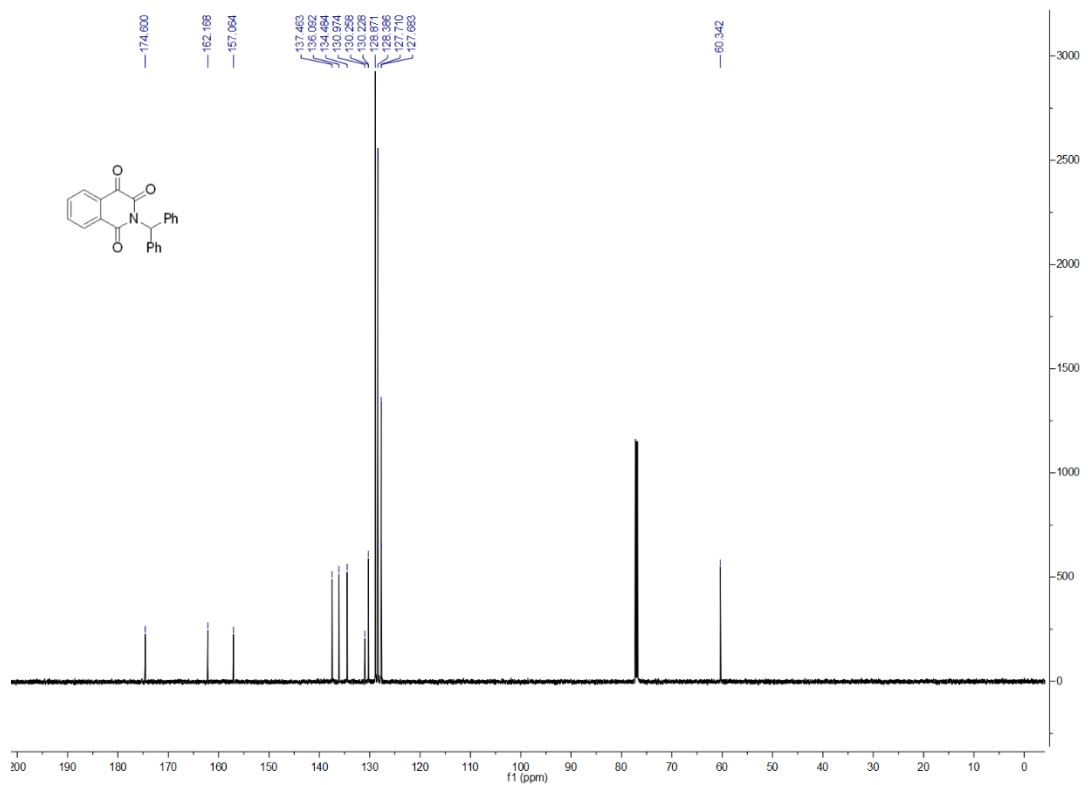
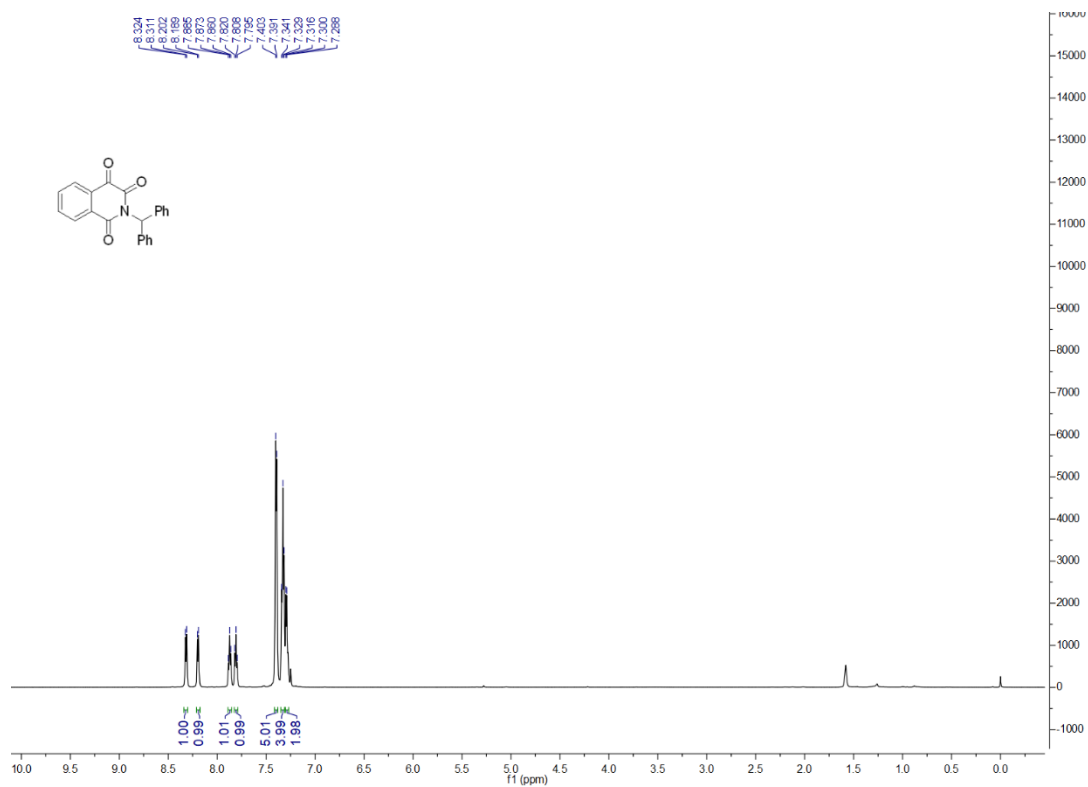
¹H NMR and ¹³C NMR spectra of compound **4ac**



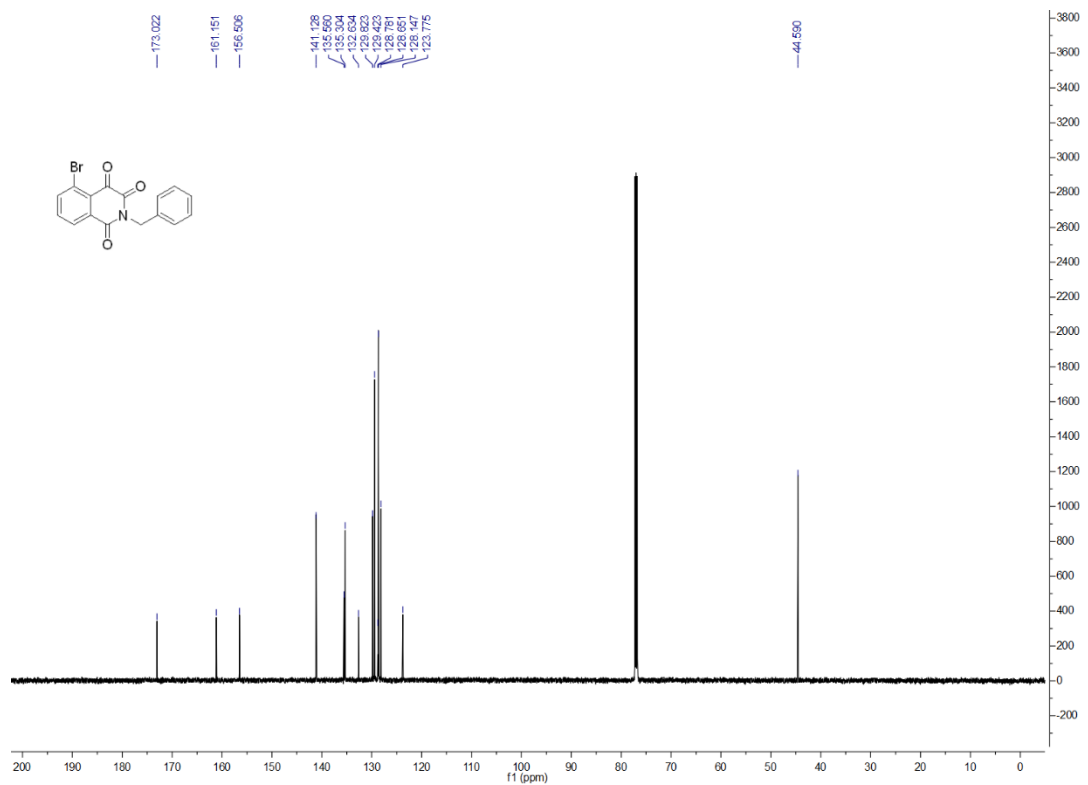
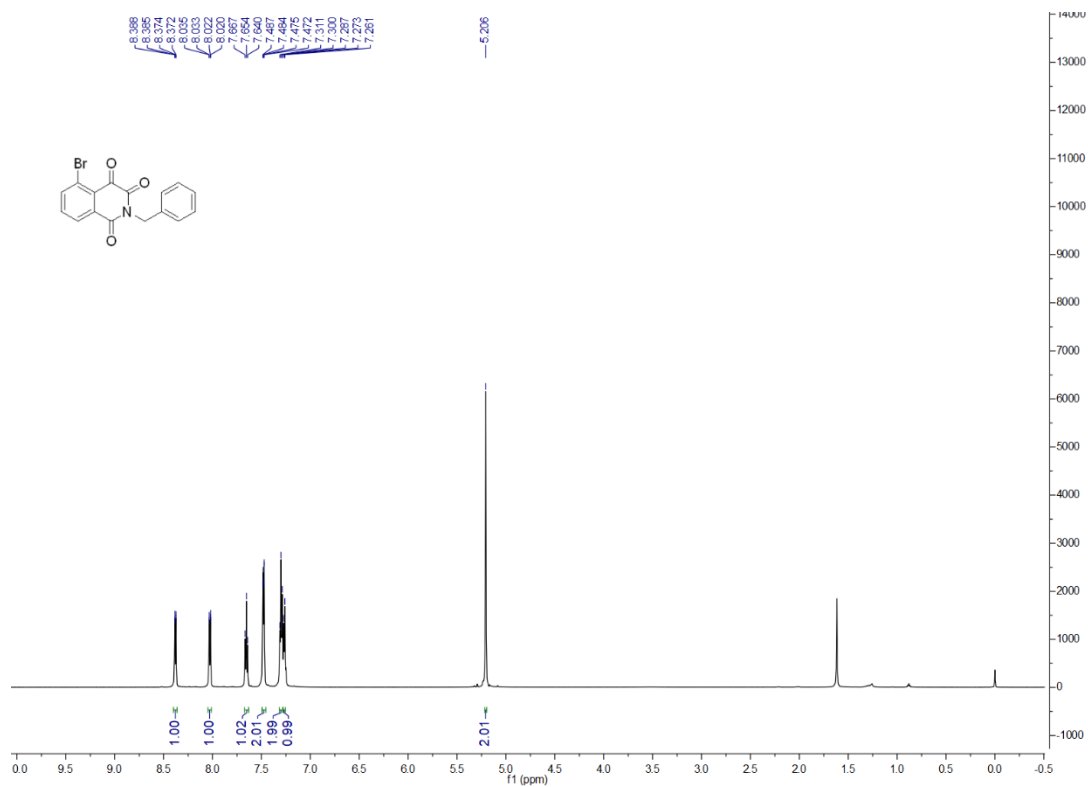
¹H NMR and ¹³C NMR spectra of compound 4ad



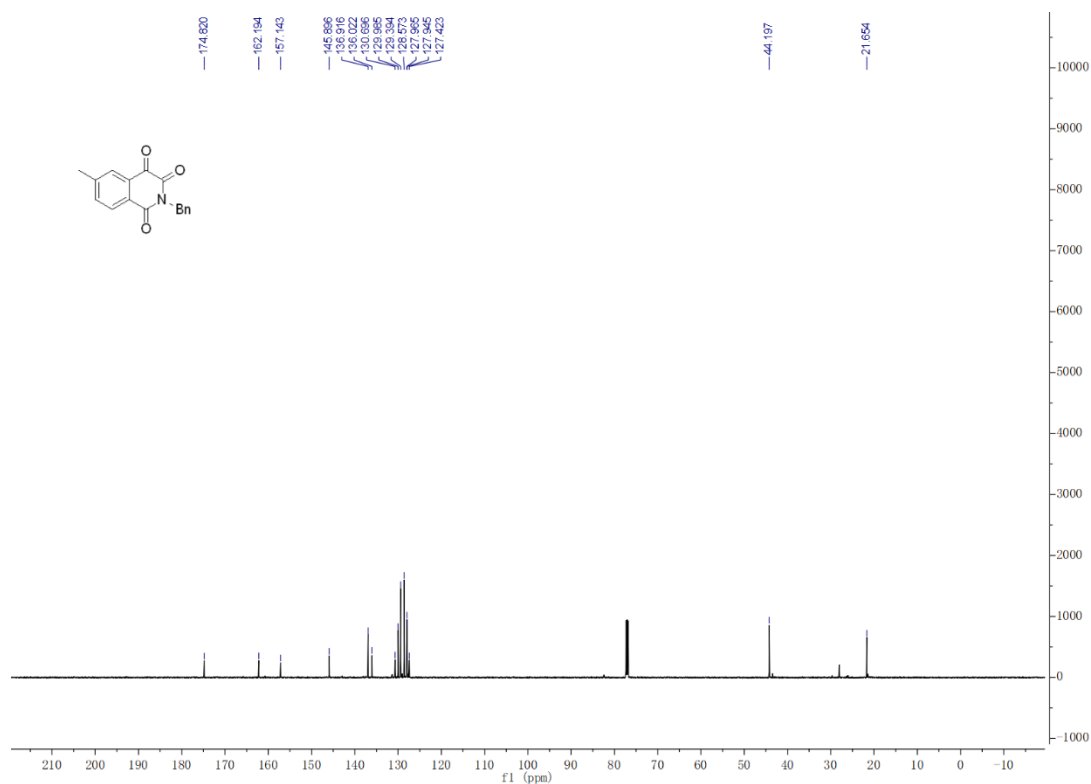
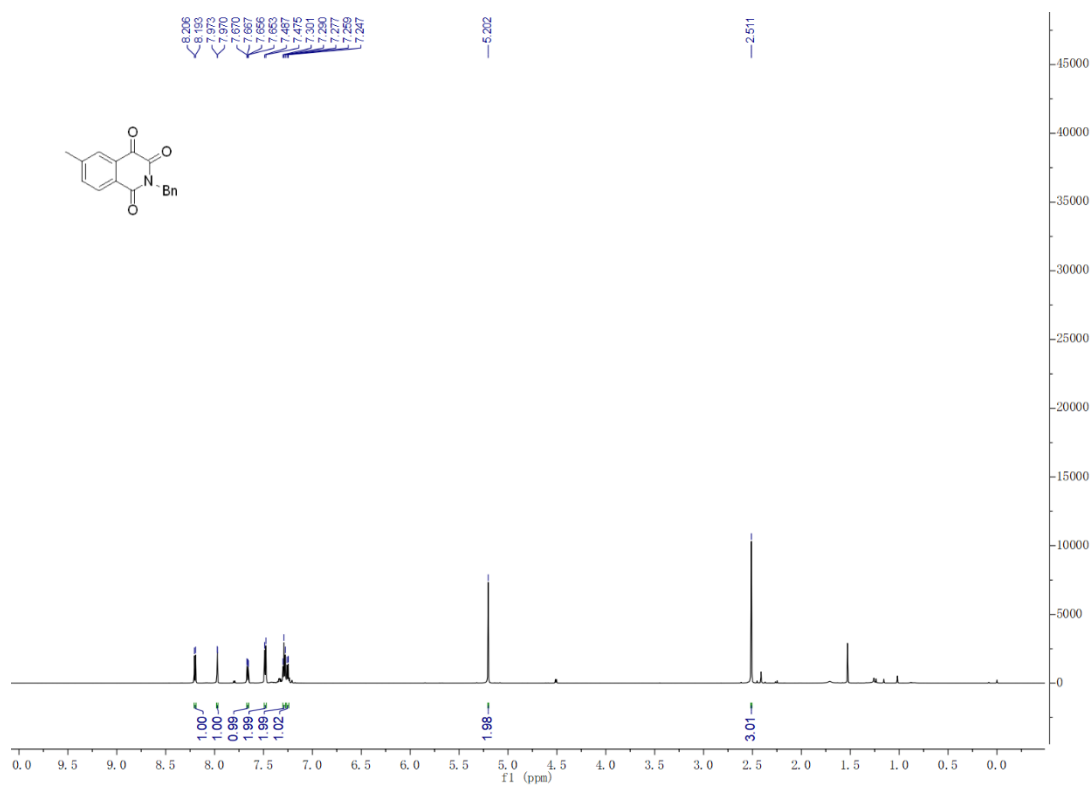
¹H NMR and ¹³C NMR spectra of compound 4ae



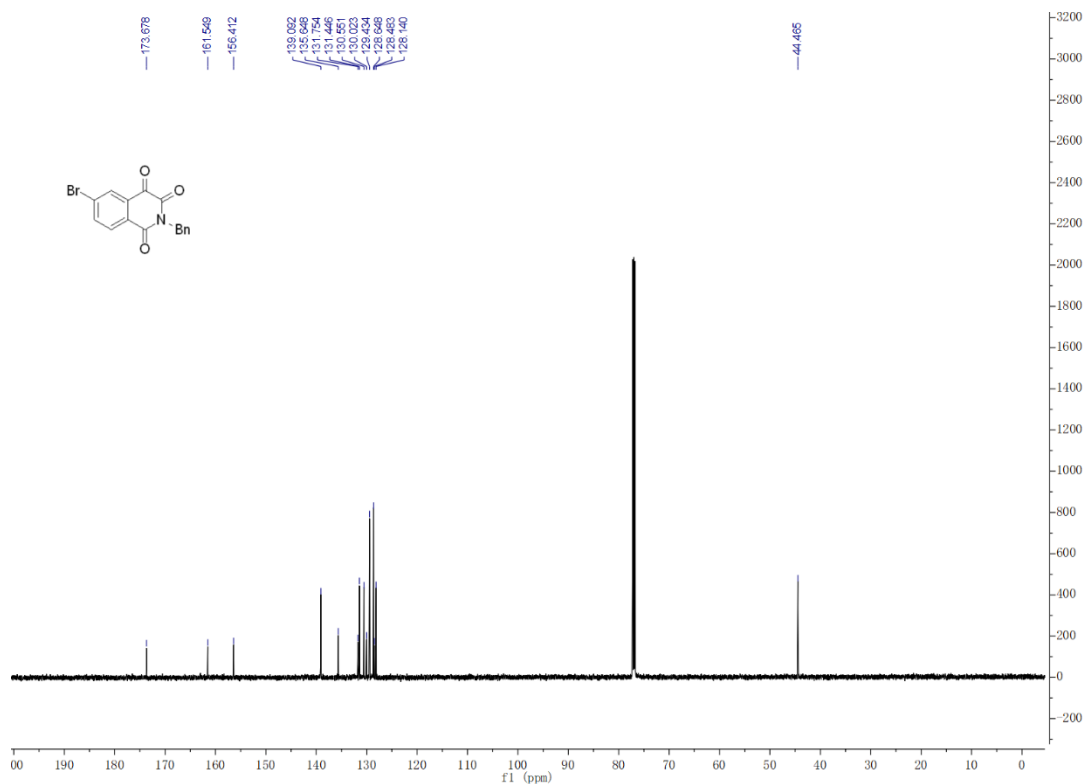
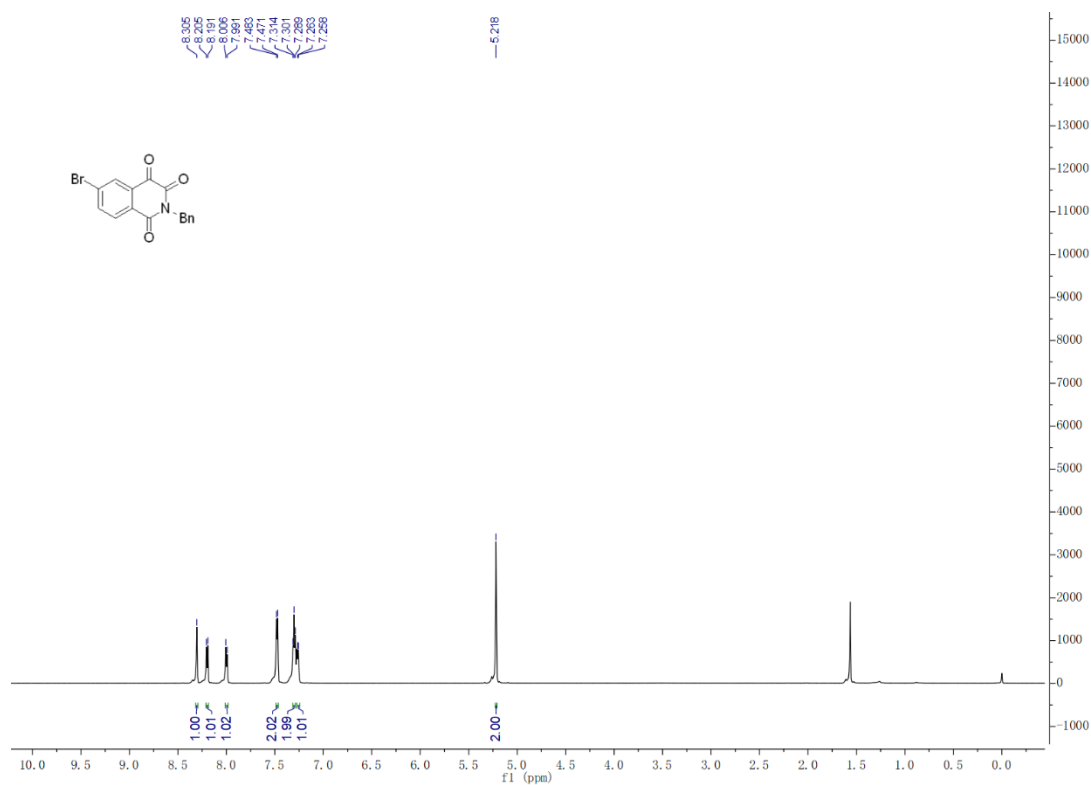
¹H NMR and ¹³C NMR spectra of compound 4af



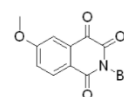
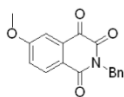
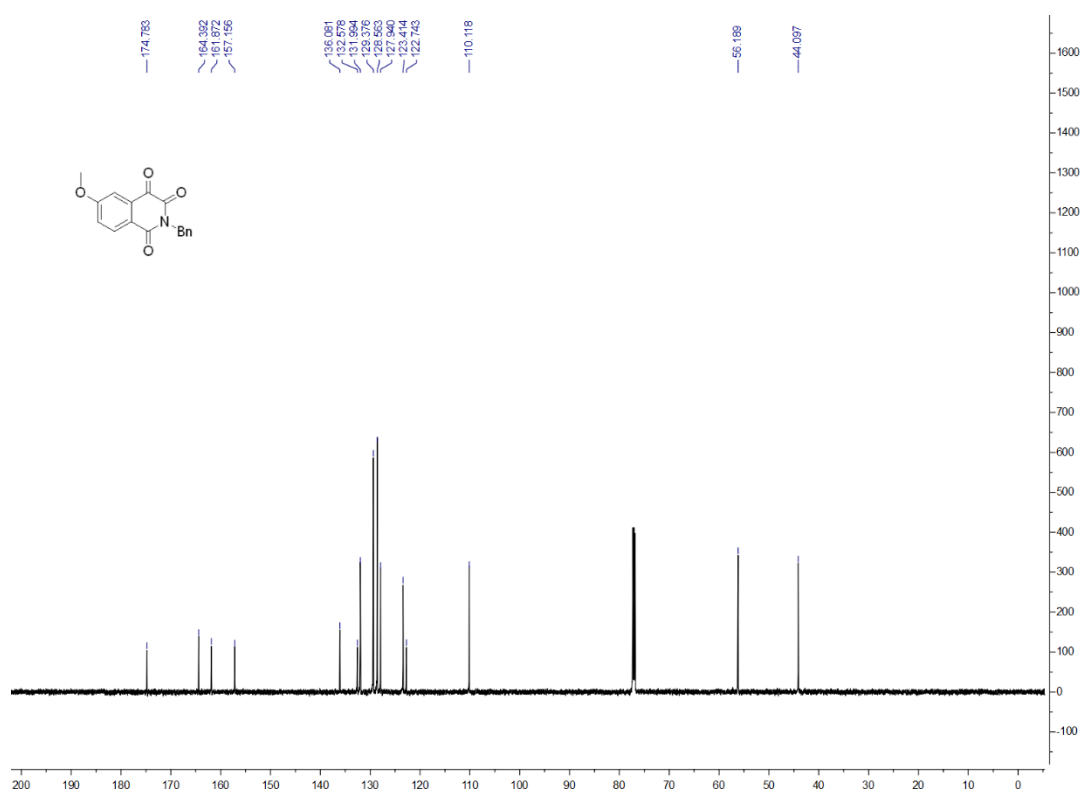
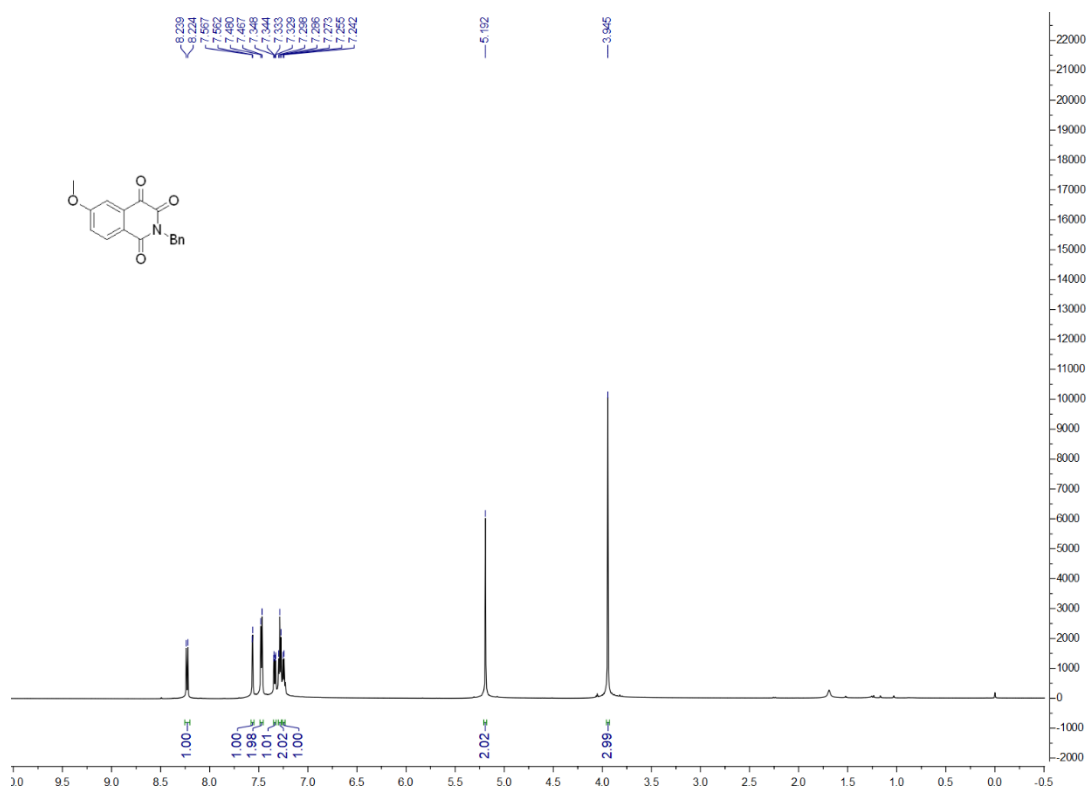
¹H NMR and ¹³C NMR spectra of compound 4ah



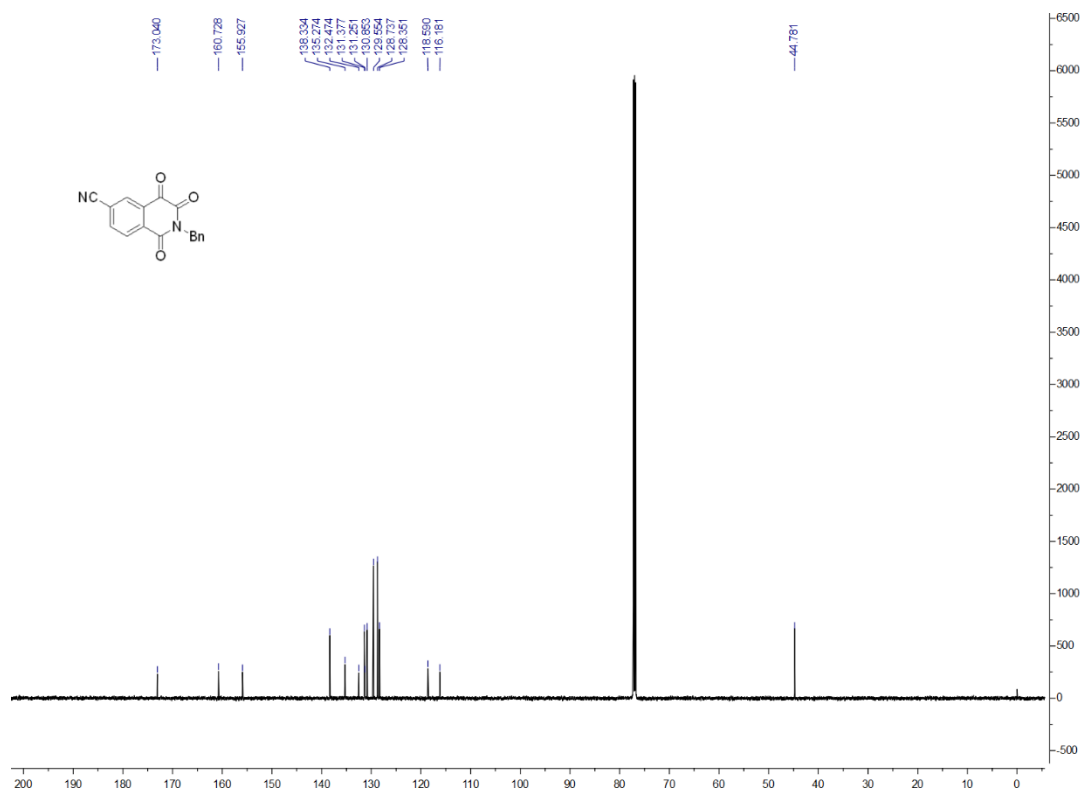
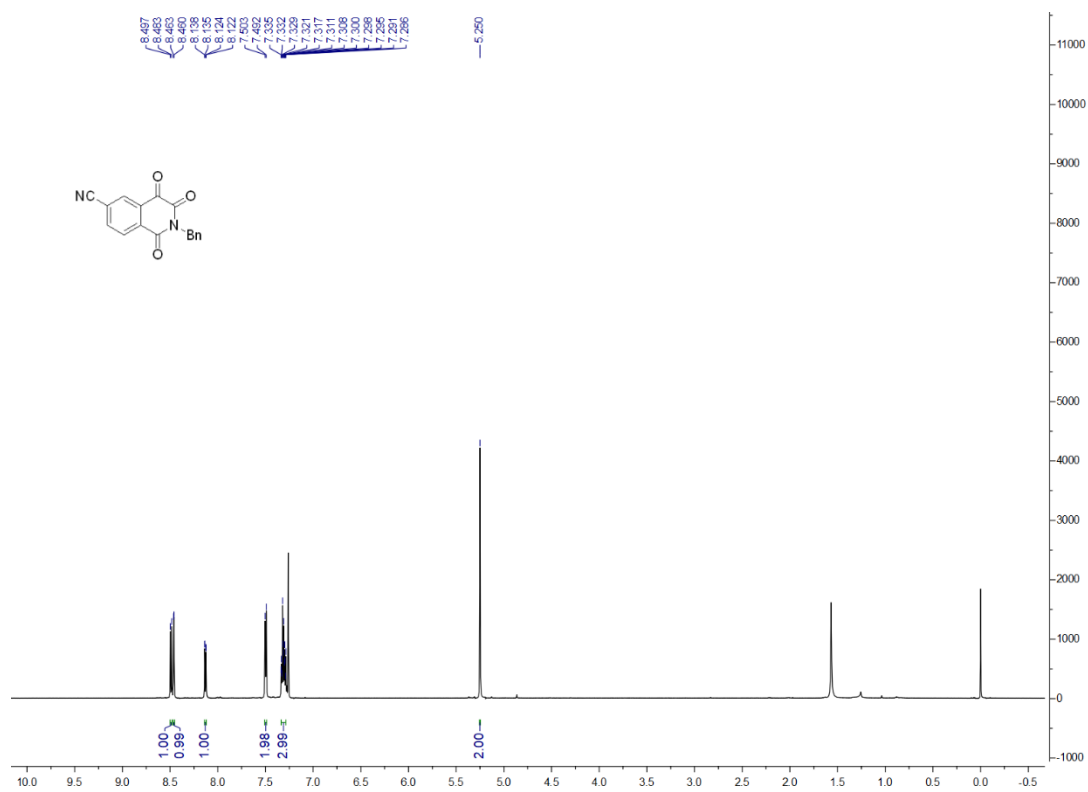
¹H NMR and ¹³C NMR spectra of compound 4ai



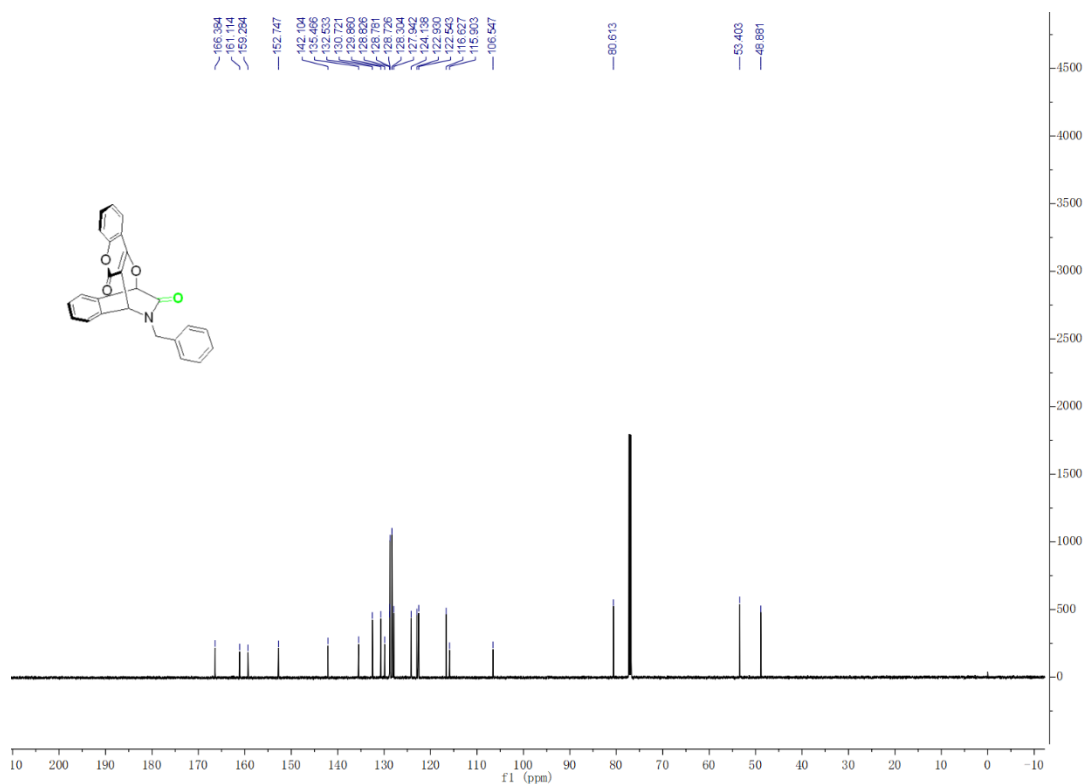
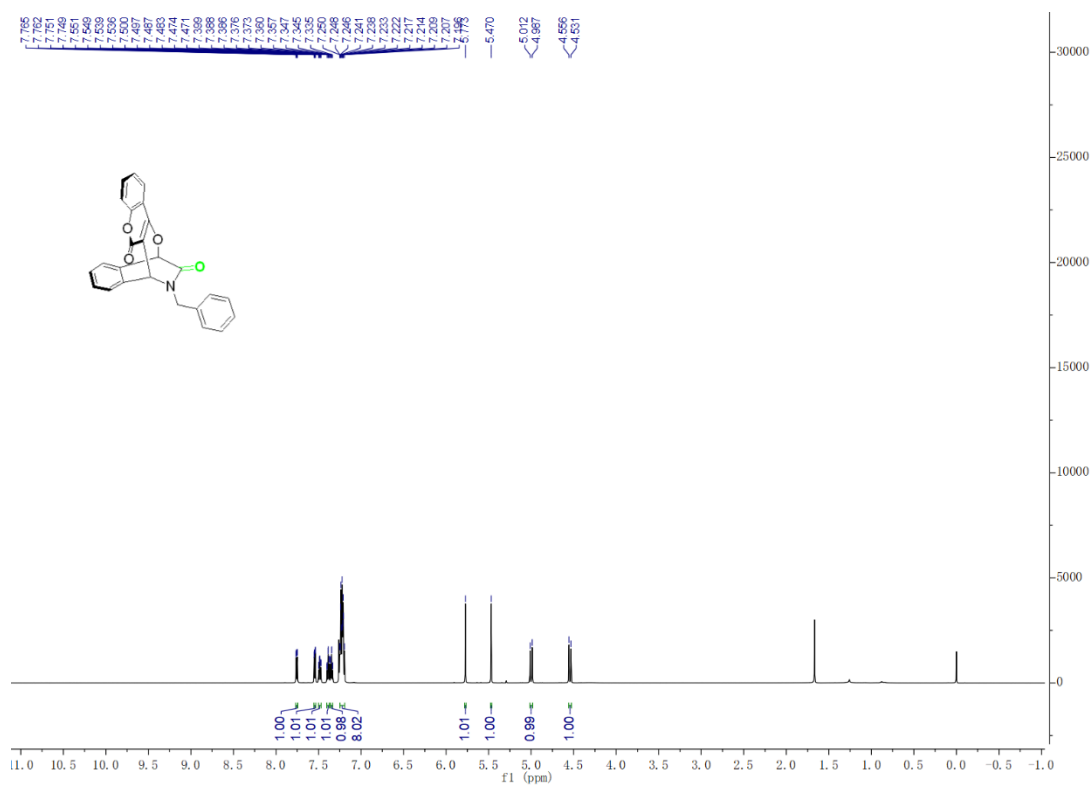
¹H NMR and ¹³C NMR spectra of compound 4aj



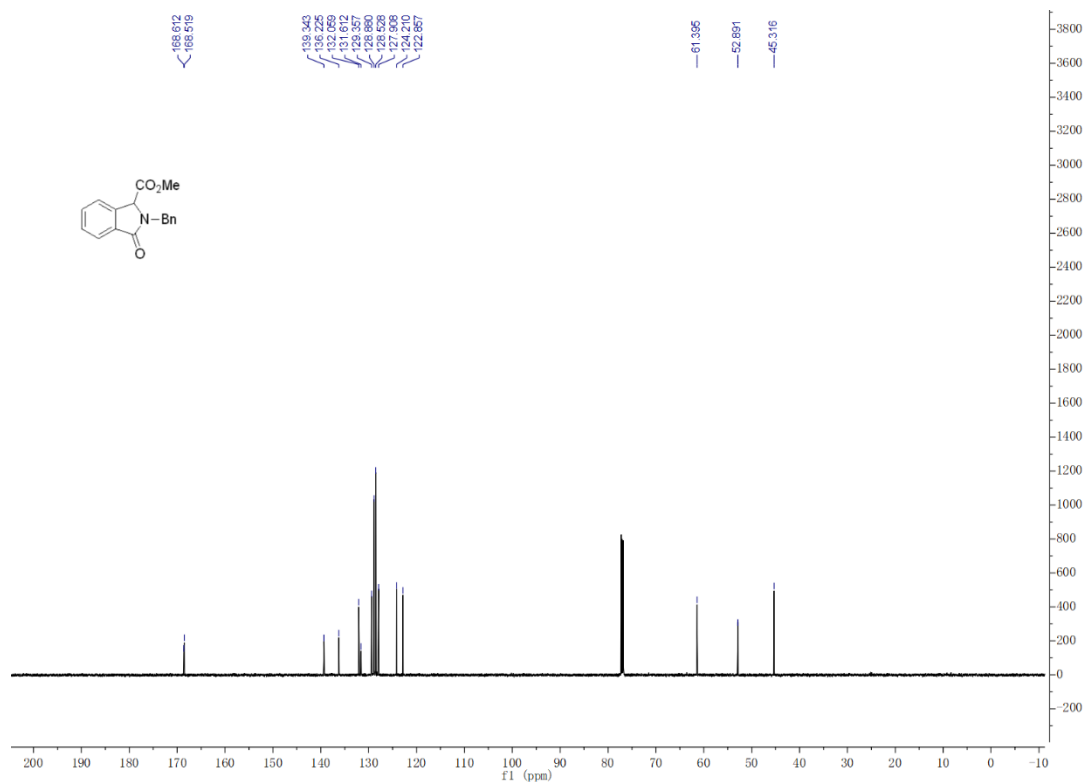
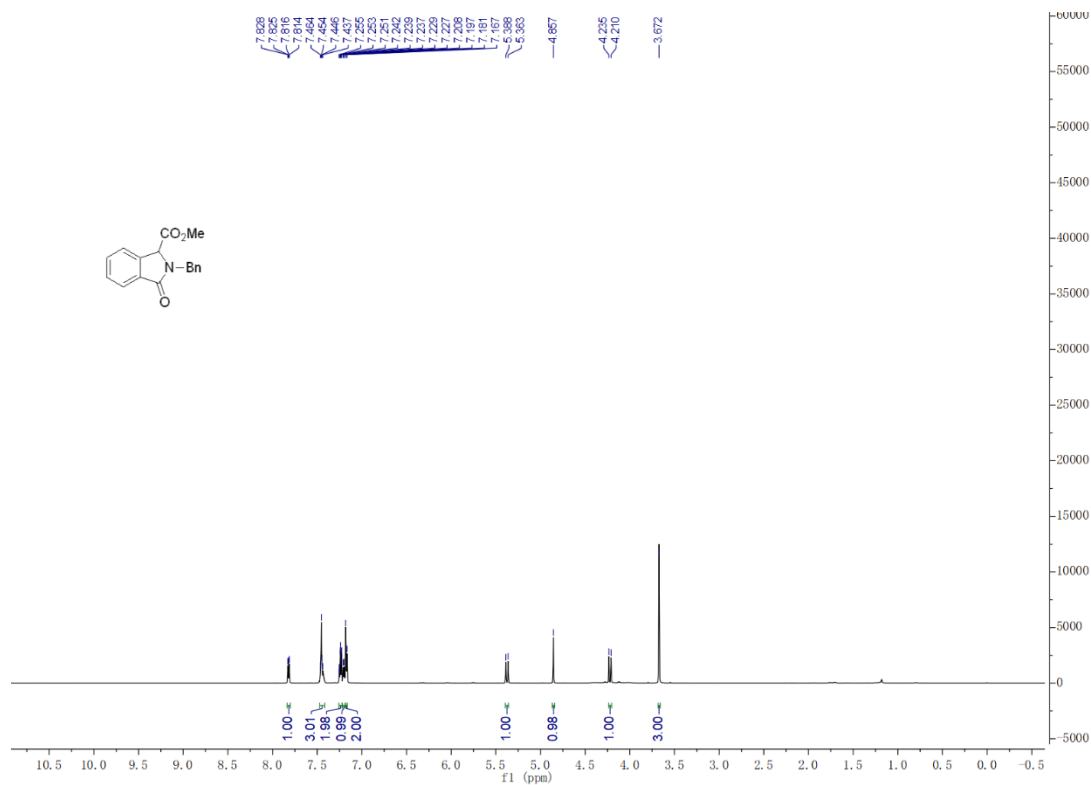
¹H NMR and ¹³C NMR spectra of compound **4ak**



¹H NMR and ¹³C NMR spectra of compound 5



1H NMR and 13C NMR spectra of compound 6



^{19}F NMR spectra of compounds **3g**, **3h**, **3n**, **3am**, **4g**, **4h**, **4n**.

