SUPPORTING INFORMATION

Rhodium-Catalyzed Formal Four-Component Reaction with Hypervalent Iodine Diazoesters, Alcohols, and Isatins for the Synthesis of Multi-functionalized Oxindoles

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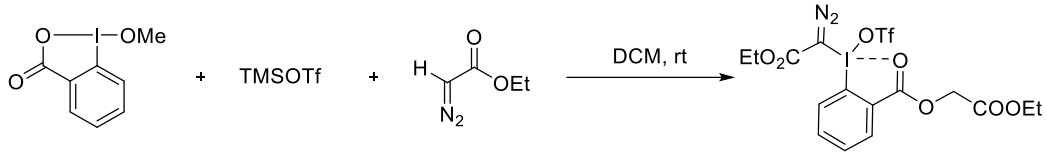
1. General Information

General: All reactions were carried out in oven-dried glassware. Flash column chromatography was performed using silica gel (300-400 mesh). Analytical thin-layer chromatography was performed using glass plates pre-coated with 200-300 mesh silica gel impregnated with a fluorescent indicator (254 nm). ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 on a 400 MHz spectrometer; chemical shifts were reported in ppm with the solvent signal as reference, and coupling constants (*J*) were given in Hertz. The peak information was described as: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, comp = composite. High-resolution mass spectra (HRMS) were recorded on a commercial apparatus (ESI Source) and (CI Source).

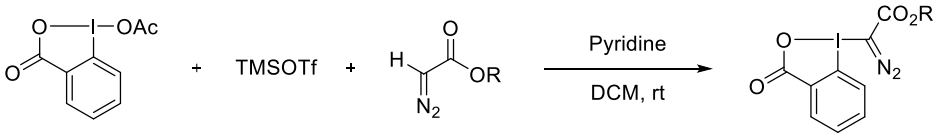
Materials: All reagents were used as purchased and used with no further purification. Solvent CH_2Cl_2 was distilled over calcium hydride. Isatin were prepared according to the literature method. 4 Å molecular sieve was dried in a Muffle furnace at 250 ℃ over 8 h.

2. General Procedure for the Preparation of Hypervalent Iodine Diazoesters[1-3]



1a

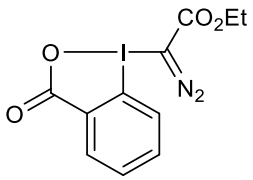
Method A: A solution of 1-methoxy-1,2-benziodoxol-3(*1H*)-one (4.0 g, 14.38 mmol, 1.0 equiv) in dichloromethane (0.5 M) was freated with trimethylsilyl trifluoromethanesulfonate (2.60 mL, 14.38 mmol, 1.0 equiv) atroom temperature. After 30 minutes, a cloudy suspension was observed and then the ethyl diazoacetate (3.3 mL, 31.64 mmol) was added dropwise during 15 minutes. Nitrogen evolution was observed and the resulting reaction mixture was stirred at room temperature until a clear yellow solutionwas observed (3 hours). Solvent was removed under vacmm and the crude was recrystallized from a mixture of diethyl ether/dichloromethane (5/1) during 12 hours at -30 °C (Note: the recrystallizationprocess may be repeated if impurities are observed). The desired product was collected by filtration,washed with cold diethyl ether (500 mL), dried under high vacum and stored a -30 °C. Product **1a** had physical and spectral properties identical to those earlier reported.[1]



1b-1bd

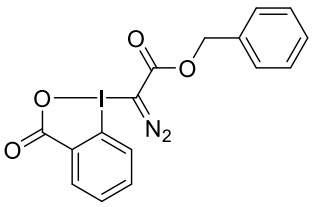
Method B: A solution of 1-acetoxy-1,2-benziodoxol-3(*1H*)-one (3.06 g, 10.0 mmol, 1.0 equiv.) in dichloromethane (0.5 M) was treated with trimethylsilyl trifluoromethanesulfonate (1.8 mL, 10.0 mmol, 1.0 equiv) at room temperature. After 10 minutes, a solution of pyridine (0.88 mL, 11.0 mmol, 1.1 eq) in dichloromethane (2.0 mL) was added dropwise over 10 minutes and the resulted suspension was stirred for 1 hour at room temperature. A solution of the corresponding diazo compound (12 mmol, 1.2 eq) in dichloromethane (2.0 mL) was added dropwise over 10 minutes and the resulting reaction mixture was stirred until a clear yellow solution was obtained (1-

6 hours). After this, the solution was washed with distilled water (200 mL x 2, no vigorously shaking) and dried with anhydrous sodium sulfate. Solvent was removed under vacuum and the residue was recrystallized from a mixture of diethyl ether/dichloromethane (5/1) during 12 hours at -30 ℃ (Note: the recrystallization process may be repeated if impurities are observed). The desired product was collected by filtration, washed with cold diethyl ether (200 mL), dried under high vacuum and stored at -30 ℃.



1-(1-Diazo-2-ethoxy-2-oxoethyl)-1,2-benziodoxol-3(1*H*)-one (1b).

Prepared according to the general procedure A using ethyl diazoacetate (1.26 mL, 12.0 mmol). After the addition of the diazo compound, the reaction mixture was stirred for 2 hours. The title compound was isolated by recrystallization from diethyl ether/dichl-oromethane as a yellow solid (1.44 g, 40 %). The NMR data are consistent with the standard spectrogram. Products **1b** had physical and spectral properties identical to those earlier reported.[1]



Benzyl-2-diazo-2-(3-oxo-1l3-benzo[d][1,2]iodaoxol-1(3*H*)-yl)acetate (1bb)

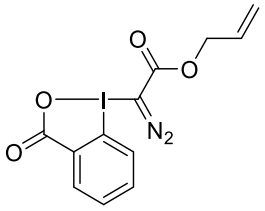
Prepared according to the general procedure A using 2-bromoethyl 2-diazoacetate (2.10 mL, 12 mmol). After the addition of the diazo compound, the reaction mixture was stirred for 4 hours. The title compound was isolated by recrystallization from diethyl ether/dichloromethane.

Result: yellow solid, 1.32g, 30% yield;

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.65 – 7.65 (m, 2H), 7.35 (d, J = 1.8 Hz, 1H), 5.27 (s, 1H);

^{13}C NMR (100 MHz, DMSO-d_6) δ 166.5, 163.8, 135.7, 134.6, 132.4, 131.5, 131.0, 128.5, 128.3, 127.9, 127.3, 116.8, 67.6;

HRMS (TOF MS ESI$^+$) calculated for $C_{16}H_{12}IN_2O_4$ $[M + H]^+$: 422.9836, found: 422.9826.



Allyl-2-diazo-2-(3-oxo-1l3-benzo[d][1,2]iodaoxol-1(3*H*)-yl)acetate (1bc)

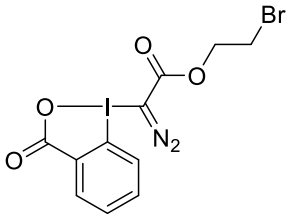
Prepared according to the general procedure A using 2-bromoethyl 2-diazoacetate (1.50 mL, 12 mmol). After the addition of the diazo compound, the reaction mixture was stirred for 2 hours. The title compound was isolated by recrystallization from diethyl ether/dichloromethane.

Result: yellow solid, 1.30 g, 38% yield;

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.10 (d, J = 7.4 Hz, 1H), 7.92 (d, J = 8.2 Hz, 1H), 7.86 – 7.80 (m, 1H), 7.76 (t, J = 7.2 Hz, 1H), 6.06 – 5.81 (m, 1H), 5.26 (dd, J = 32.8, 13.9 Hz, 2H), 4.72 (d, J = 5.3 Hz, 2H);

^{13}C NMR (125 MHz, DMSO-d_6) δ 166.5, 163.6, 134.7, 132.4, 132.2, 131.6, 131.0, 127.4, 118.2, 116.8, 66.5;

HRMS (TOF MS ESI$^+$) calculated for $C_{12}H_9IN_2O_4Na$ $[M + Na]^+$: 394.9499, found: 394.9498.



2-Bromoethyl 2-diazo-2-(3-oxo-1l3-benzo[d][1,2]iodaoxol-1(3*H*)-yl)acetate (1bd).

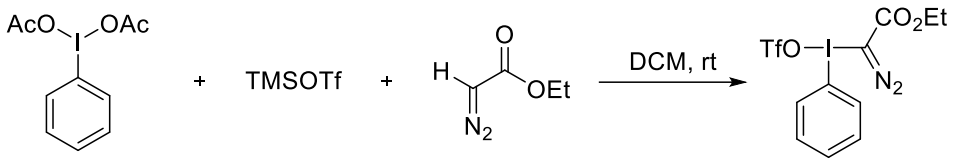
Prepared according to the general procedure A using 2-bromoethyl 2-diazoacetate (2.29 g, 12.0 mmol). After the addition of the diazo compound, the reaction mixture was stirred for 4 hours. The title compound was isolated by recrystallization from diethyl ether/dichloromethane.

Result: yellow solid, 1.98 g, 45% yield;

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.09 (dd, J = 7.4, 1.7 Hz, 1H), 7.90 (d, J = 8.2 Hz, 1H), 7.82 (td, J = 8.2, 7.7, 1.7 Hz, 1H), 7.75 (t, J = 7.3 Hz, 1H), 4.51 (t, J = 5.4 Hz, 2H), 3.69 (t, J = 5.4 Hz, 2H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 166.6, 163.6, 134.7, 132.4, 131.5, 130.9, 127.5, 65.7, 30.8;

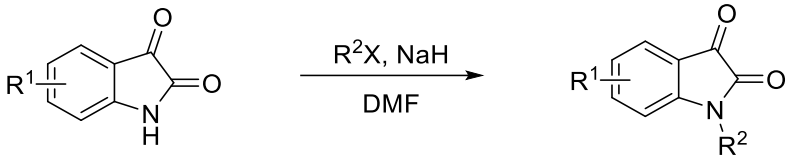
HRMS (TOF MS ESI$^+$) calculated for $C_{11}H_8BrIN_2O_4Na$ $[M + Na]^+$:460.8604, found: 460.8601.



1h

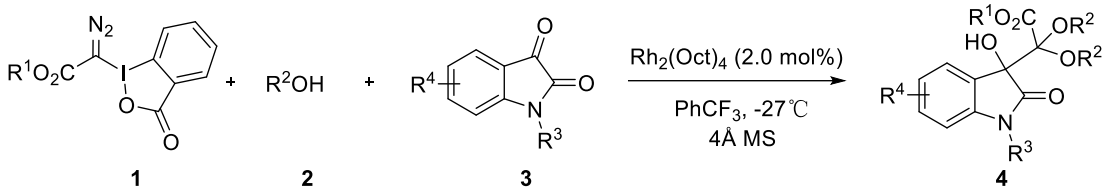
Method C: A solution of the corresponding aryliodos diacetate (5.0 mmol, 1.0 equiv.) in dichloromethane (0.25 M) was treated with trimethylsilyl trifluoromethanesulfonate (0.90 mL, 5.0 mmol, 1.0 equiv.) at room temperature. After this, ethyl diazoacetate (1.26 mL, 12.0 mmol, 2.4 equiv.) was added dropwise during 10 minutes. Nitrogen evolution was observed and the resulting yellow reaction mixture was stirred for 1 hour at room temperature. Solvent was removed under vacuum and the crude was recrystallized from a mixture of diethyl ether/dichloromethane (5/1) during 12 hours at -30 °C. The product was collected by filtration, washed with cold diethyl ether (200 mL), dried under high vacuum and stored at -30 °C. Products **1h** had physical and spectral properties identical to those earlier reported.[1]

3. General Procedure for the Preparation of Isatin reagents



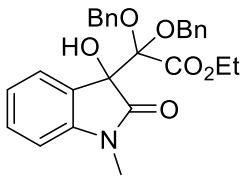
To a solution of corresponding isatin (10 mmol, 1.0 equiv.) in DMF (20 mL), was added NaH (12 mmol, 480 mg, 60% dispersion in mineral oil) in portions at 0 ℃. Then the reaction mixture was stirred at 0 ℃ for 10 minutes. Subsequently, the corresponding halide was added, and the reaction mixture was stirred at room temperature overnight. The reaction mixture was quenched with saturated aqueous NH_4Cl (100 mL), then washed with saturated aqueous $NaHCO_3$ (100 mL), and saturated aqueous NaCl (100 mL) in sequence. The separated organic phase was dried with anhydrous Na2SO4. After filtration, the solvent was evaporated under vacuum, and the residue was purified by column chromatography on silica gel (eluent: EtOAc/light petroleum ether = 1/10~1/4) to provide isatin compounds **3** as solid (> 90% yield). The NMR data are consistent with the standard spectrogram.[4]

4. General Procedure for Multi-Component Reaction



To a 10-mL oven-dried vial equipped with a magnetic stirring bar, $Rh_2(Oct)_4$ (1.50 mg, 2.0 mol%), alcohol **2** (0.30 mmol, 3.0 equiv.), isatin **3** (0.10 mmol, 1.0 equiv.), and 4 Å MS (100 mg) were added in $PhCF_3$ (1.5 mL). Subsequently, diazo compound **1** (0.15 mmol, 1.5 equiv.) was added at -27 ℃. The reaction mixture was stirred for an additional 24-48 hours under these conditions until the material was completely consumed (monitored by TLC). The crude reaction mixture was then concentrated under vacuum, and the resulting product was purified by column chromatography on silica gel (Hexanes: EtOAc = 20:1) to afford the pure products **4** in good to high yields.

5. NMR, HRMS(ESI) Data for compounds 4



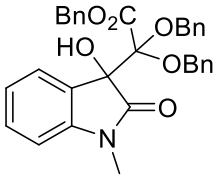
Ethyl-2,2-bis(benzyloxy)-2-(3-hydroxy-1-methyl-2-oxoindolin-3-yl)acetate(4a).

Result: White solid. mp = 70 – 73 ºC. 42.8 mg, 93% yield;

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.57 (d, *J* = 7.4 Hz, 1H), 7.45 – 7.20 (m, 9H), 7.16 (d, *J* = 7.0 Hz, 2H), 7.04 (t, *J* = 7.6 Hz, 1H), 6.69 (d, *J* = 7.8 Hz, 1H), 4.90 (d, *J* = 11.3 Hz, 1H), 4.83 (d, *J* = 1.3 Hz, 1H), 4.81 – 4.72 (m, 2H), 4.50 (d, *J* = 12.5 Hz, 1H), 4.31 – 4.13 (m, 2H), 3.10 (s, 3H), 1.22 (t, *J* = 7.2 Hz, 3H);

^{13}C NMR (100 MHz, Chloroform-*d*) δ 174.5, 168.1, 144.9, 138.2, 137.0, 130.5, 128.5, 128.3, 128.0, 127.5, 127.4, 126.8, 126.75, 126.72, 126.66, 122.9, 108.2, 101.0, 79.6, 68.4, 66.0, 62.5, 26.3, 14.0;

HRMS (TOF MS ESI$^+$) calculated for $C_{27}H_{27}NO_6Na$ $[M + Na]^+$: 484.1731, found: 484.1736.



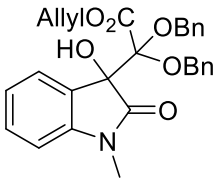
Benzyl-2,2-bis(benzyloxy)-2-(3-hydroxy-1-methyl-2-oxoindolin-3-yl)acetate (4b).

Result: White solid. mp = 112.6 – 115.7 ºC. 49.7 mg, 91% yield;

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.54 (d, *J* = 7.4 Hz, 1H), 7.43 – 7.22 (m, 14H), 7.18 (d, *J* = 7.7 Hz, 2H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.59 (d, *J* = 7.8 Hz, 1H), 5.20 (d, *J* = 12.1 Hz, 1H), 5.03 (d, *J* = 12.1 Hz, 1H), 4.90 (d, *J* = 11.4 Hz, 1H), 4.83 (d, *J* = 12.4 Hz, 1H), 4.70 (d, *J* = 11.3 Hz, 1H), 4.63 (s, 1H), 4.56 (d, *J* = 12.4 Hz, 1H), 2.91 (s, 3H);

^{13}C NMR (125 MHz, Chloroform-*d*) δ 174.2, 167.7, 144.7, 138.1, 137.0, 134.7, 130.5, 128.82, 128.76, 128.73, 128.69, 128.6, 128.5, 128.4, 128.0, 127.6, 127.5, 126.92, 126.87, 126.7, 126.5, 122.9, 108.4, 101.1, 79.5, 68.3, 68.0, 66.1, 26.1;

HRMS (TOF MS ESI$^+$) calculated for $C_{32}H_{29}NO_6Na$ $[M + Na]^+$: 546.1887, found: 546.1887.



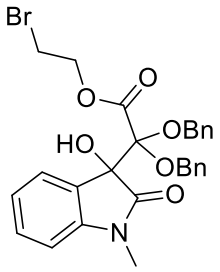
Allyl-2,2-bis(benzyloxy)-2-(3-hydroxy-1-methyl-2-oxoindolin-3-yl)acetate (4c).

Result: White solid. mp = 79.1 – 80.1 °C. 44.6 mg, 90% yield;

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.56 (d, *J* = 7.5 Hz, 1H), 7.44 – 7.15 (m, 11H), 7.04 (t, *J* = 7.5 Hz, 1H), 6.69 (d, *J* = 7.8 Hz, 1H), 5.85 – 5.74 (m, 1H), 5.32 (dd, *J* = 17.1, 1.5 Hz, 1H), 5.23 (d, *J* = 10.4 Hz, 1H), 4.94 (d, *J* = 11.3 Hz, 1H), 4.82 (d, *J* = 12.4 Hz, 1H), 4.77 (d, *J* = 11.3 Hz, 1H), 4.71 (s, 1H), 4.64 (dd, *J* = 12.9, 6.0 Hz, 1H), 4.58 (dd, *J* = 12.9, 5.9 Hz, 1H), 4.54 (d, *J* = 12.4 Hz, 1H), 3.09 (s, 3H);

^{13}C NMR (125 MHz, Chloroform-*d*) δ 174.3, 167.7, 144.8, 138.1, 137.0, 131.1, 130.6, 128.6, 128.4, 128.0, 127.6, 127.5, 126.9, 126.8, 126.6, 123.0, 119.8, 108.3, 101.2, 79.6, 77.2, 68.4, 67.0, 66.1, 26.3;

HRMS (TOF MS ESI$^+$) calculated for $C_{28}H_{27}NO_6Na$ $[M + Na]^+$: 496.1731, found: 496.1737.



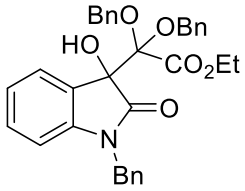
Allyl-2,2-bis(benzyloxy)-2-(3-hydroxy-1-methyl-2-oxoindolin-3-yl)acetate (4d).

Result: White solid. mp = 107.4 – 108.7 °C. 49.4 mg, 88% yield;

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.61 – 7.55 (m, 1H), 7.40 – 7.28 (m, 6H), 7.27 – 7.19 (m, 3H), 7.15 – 6.97 (m, 3H), 6.76 – 6.58 (m, 1H), 4.87 – 4.70 (m, 3H), 4.58 – 4.50 (m, 1H), 4.49 – 4.35 (m, 2H), 3.55 – 3.40 (m, 2H), 3.08 (d, *J* = 12.1 Hz, 3H);

^{13}C NMR (126 MHz, Chloroform-*d*) δ 174.6, 168.0, 144.9, 138.0, 136.78, 136.76, 130.7, 128.59, 128.57, 128.31, 128.30, 128.09, 128.07, 127.54, 127.52, 127.39, 127.37, 126.91, 126.89, 126.6, 126.54, 126.50, 123.05, 123.03, 108.41, 108.39, 101.27, 101.25, 79.7, 79.6, 68.72, 68.70, 66.0, 65.6, 65.5, 28.02, 28.00, 26.37, 26.36;

HRMS (TOF MS ESI$^+$) calculated for $C_{27}H_{26}BrNO_6Na$ $[M + Na]^+$: 562.0836, found: 562.0836.



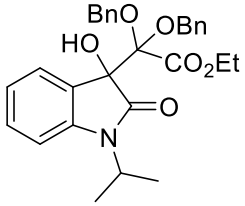
Ethyl-2-(1-benzyl-3-hydroxy-2-oxoindolin-3-yl)-2,2-bis(benzyloxy)acetate(4e).

Result: White solid. mp = 104.4 – 107.9 ºC. 51.0 mg, 95% yield;

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.60 (d, *J* = 7.5 Hz, 1H), 7.42 – 7.05 (m, 16H), 7.04 – 6.93 (m, 1H), 6.56 (d, *J* = 7.8 Hz, 1H), 5.07 (d, *J* = 1.1 Hz, 1H), 4.95 (d, *J* = 15.9 Hz, 1H), 4.84 (s, 2H), 4.74 (d, *J* = 12.5 Hz, 1H), 4.68 (d, *J* = 15.9 Hz, 1H), 4.36 (d, *J* = 12.5 Hz, 1H), 4.34 – 4.23 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (100 MHz, Chloroform-*d*) δ 174.9, 168.4, 144.0, 138.1, 136.9, 135.3, 130.3, 128.7, 128.5, 128.3, 128.0, 127.4, 127.3, 127.1, 126.9, 126.74, 126.71, 122.9, 109.3, 101.0, 79.8, 68.6, 65.9, 62.6, 43.8, 14.0;

HRMS (TOF MS ESI$^+$) calculated for $C_{33}H_{31}NO_6Na$ $[M + Na]^+$: 560.2044, found: 560.2047.



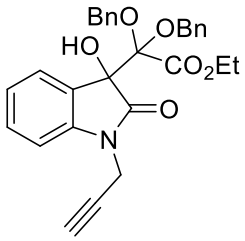
Ethyl-2,2-bis(benzyloxy)-2-(3-hydroxy-1-isopropyl-2-oxoindolin-3-yl)acetate (4f).

Result: White solid. mp = 81.3 – 82.1 ºC. 45.9 mg, 94% yield;

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 7.4 Hz, 1H), 7.47 – 7.17 (m, 9H), 7.12 (d, *J* = 7.6 Hz, 2H), 7.01 (t, *J* = 7.5 Hz, 1H), 6.89 (d, *J* = 7.9 Hz, 1H), 4.86 (s, 1H), 4.84 (d, *J* = 11.4 Hz, 1H), 4.79 (d, *J* = 11.4 Hz, 1H), 4.71 (d, *J* = 12.2 Hz, 1H), 4.56 – 4.45 (m, 1H), 4.42 (d, *J* = 12.1 Hz, 1H), 4.35 – 4.19 (m, 2H), 1.39 (d, *J* = 7.0 Hz, 3H), 1.33 (d, *J* = 7.0 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (100 MHz, Chloroform-*d*) δ 174.3, 168.3, 143.7, 138.1, 137.1, 130.2, 128.5, 128.3, 127.9, 127.4, 127.2, 126.9, 122.3, 109.9, 101.1, 79.4, 68.5, 66.1, 62.5, 44.0, 19.2, 19.1, 14.0;

HRMS (TOF MS ESI$^+$) calculated for $C_{29}H_{31}NO_6Na$ [M + Na]$^+$: 512.2044, found: 512.2044.



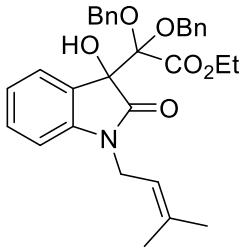
Ethyl-2,2-bis(benzyloxy)-2-(3-hydroxy-2-oxo-1-(prop-2-yn-1-yl)indolin-3-yl)aceta -te (4g).

Result: White solid. mp = 88.3 – 89.6 ºC. 45.6 mg, 94% yield;

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.58 (d, *J* = 7.6 Hz, 1H), 7.41 – 7.22 (m, 9H), 7.21 – 7.16 (m, 2H), 7.07 (t, *J* = 7.6 Hz, 1H), 6.96 (d, *J* = 7.8 Hz, 1H), 4.89 (d, *J* = 11.4 Hz, 1H), 4.82 (s, 1H), 4.78 (dd, *J* = 11.8, 3.3 Hz, 2H), 4.53 (d, *J* = 12.3 Hz, 1H), 4.45 (dd, *J* = 17.7, 2.5 Hz, 1H), 4.35 (dd, *J* = 17.7, 2.5 Hz, 1H), 4.27 – 4.17 (m, 2H), 2.14 (t, *J* = 2.5 Hz, 1H), 1.21 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.4, 167.8, 142.9, 138.0, 136.9, 130.4, 128.5, 128.3, 127.9, 127.45, 127.39, 126.9, 126.8, 126.5, 123.2, 109.3, 100.9, 79.5, 72.5, 68.3, 66.0, 62.6, 29.4, 13.9;

HRMS (TOF MS ESI$^+$) calculated for $C_{29}H_{27}NO_6Na$ [M + Na]$^+$: 508.1731, found: 508.1738.



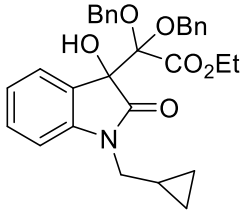
Ethyl-2,2-bis(benzyloxy)-2-(3-hydroxy-1-(3-methylbut-2-en-1-yl)-2-oxoindolin-3-yl) acetate (4h).

Result: White solid. mp = 83.9 – 85.3 ºC. 46.3 mg, 90% yield;

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.56 (d, *J* = 7.5 Hz, 1H), 7.41 – 7.21 (m, 9H), 7.14 (d, *J* = 5.8 Hz, 2H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.68 (d, *J* = 7.8 Hz, 1H), 5.04 (t, *J* = 6.6 Hz, 1H), 4.87 (d, *J* = 9.8 Hz, 2H), 4.79 (d, *J* = 11.4 Hz, 1H), 4.74 (d, *J* = 12.3 Hz, 1H), 4.45 (d, *J* = 12.3 Hz, 1H), 4.34 – 4.15 (comp, 4H), 1.76 (s, 3H), 1.62 (s, 3H), 1.23 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (100 MHz, Chloroform-*d*) δ 174.1, 168.2, 144.3, 138.2, 137.1, 136.8, 130.4, 128.6, 128.3, 128.0, 127.5, 127.4, 126.9, 126.8, 122.7, 118.2, 109.0, 101.1, 79.7, 68.4, 66.0, 62.6, 38.2, 25.6, 18.2, 14.0;

HRMS (TOF MS ESI$^+$) calculated for $C_{31}H_{33}NO_6Na$ $[M + Na]^+$: 538.2200, found: 538.2205.



Ethyl-2,2-bis(benzyloxy)-2-(1-(cyclopropylmethyl)-3-hydroxy-2-oxoindolin-3-yl)a-cetate (4i).

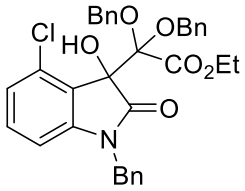
Result: White solid. mp = 110.1 – 111.6 ºC. 45.6 mg, 91% yield;

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 7.4 Hz, 1H), 7.43 – 7.17 (m, 9H), 7.17 – 7.08 (m, 2H), 7.04 (t, *J* = 7.6 Hz, 1H), 6.81 (d, *J* = 7.8 Hz, 1H), 4.90 (d, *J* = 0.8 Hz, 1H), 4.84 (d, *J* = 11.4 Hz, 1H), 4.78 (d, *J* = 11.4 Hz, 1H), 4.72 (d, *J* = 12.3 Hz, 1H),

4.44 (d, *J* = 12.3 Hz, 1H), 4.27 (qd, *J* = 7.1, 1.3 Hz, 2H), 3.50 (qd, *J* = 14.5, 6.8 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.09 – 1.00 (m, 1H), 0.46 – 0.25 (m, 4H);

^{13}C NMR (100 MHz, Chloroform-*d*) δ 174.7, 168.3, 144.6, 138.2, 137.1, 130.4, 128.6, 128.3, 128.0, 127.5, 127.4, 127.1, 126.8, 122.7, 108.7, 101.1, 79.7, 68.5, 66.0, 62.6, 44.4, 14.0, 9.5, 4.1, 3.7;

HRMS (TOF MS ESI$^+$) calculated for $C_{30}H_{31}NO_6Na$ $[M + Na]^+$: 524.2044, found: 524.2052.



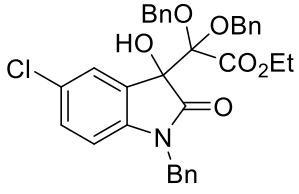
Ethyl-2-(1-benzyl-4-chloro-3-hydroxy-2-oxoindolin-3-yl)-2,2-bis(benzyloxy)acetat -e (4j).

Result: White solid. mp = 141.7 – 142.6 ºC. 54.2 mg, 95% yield;

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.19 (m, 10H), 7.19 – 7.04 (m, 6H), 6.97 (d, *J* = 8.3 Hz, 1H), 6.43 (d, *J* = 7.8 Hz, 1H), 5.04 (s, 1H), 4.96 (d, *J* = 15.9 Hz, 1H), 4.89 (d, *J* = 11.4 Hz, 1H), 4.80 (d, *J* = 11.4 Hz, 1H), 4.76 (d, *J* = 12.4 Hz, 1H), 4.62 (d, *J* = 15.9 Hz, 1H), 4.38 – 4.17 (m, 3H), 1.27 (t, *J* = 7.2 Hz, 3H);

^{13}C NMR (100 MHz, Chloroform-*d*) δ 174.5, 167.9, 146.0, 137.9, 136.9, 134.9, 133.3, 131.2, 128.8, 128.4, 128.4, 128.3, 127.9, 127.8, 127.7, 127.5, 127.2, 126.9, 125.0, 124.1, 107.8, 102.4, 82.4, 69.0, 65.9, 62.7, 44.2, 14.1;

HRMS (TOF MS ESI$^+$) calculated for $C_{33}H_{30}ClNO_6Na$ $[M + Na]^+$: 594.1654, found: 594.1655.

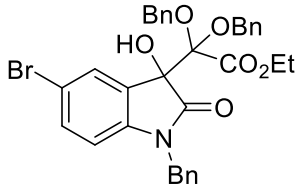


Ethyl-2-(1-benzyl-5-chloro-3-hydroxy-2-oxoindolin-3-yl)-2,2-bis(benzyloxy)aceta -te (4k).

Result: White solid. mp = 89.4 – 91.0 ºC. 53.2 mg, 93% yield;

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.57 (d, *J* = 2.2 Hz, 1H), 7.50 – 7.30 (m, 5H), 7.29 – 7.23 (m, 3H), 7.22 – 6.89 (m, 8H), 6.46 (d, *J* = 8.4 Hz, 1H), 5.10 (d, *J* = 0.9 Hz, 1H), 4.93 (d, *J* = 15.9 Hz, 1H), 4.88 (s, 2H), 4.78 (d, *J* = 12.2 Hz, 1H), 4.66 (d, *J* = 15.9 Hz, 1H), 4.47 (d, *J* = 12.2 Hz, 1H), 4.40 – 4.23 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 174.6, 168.3, 142.7, 137.9, 136.8, 134.9, 130.1, 128.8, 128.7, 128.5, 128.4, 128.3, 128.2, 127.7, 127.6, 127.4, 127.1, 126.9, 110.3, 100.9, 79.9, 69.2, 66.4, 62.9, 44.0, 14.1;

HRMS (TOF MS ESI$^+$) calculated for $C_{33}H_{30}ClNO_6Na$ $[M + Na]^+$: 594.1654, found: 594.1661.



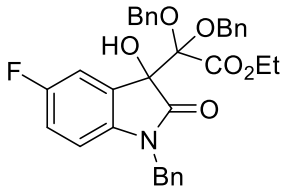
Ethyl-2-(1-benzyl-5-bromo-3-hydroxy-2-oxoindolin-3-yl)-2,2-bis(benzyloxy)aceta -te (4l).

Result: White solid. mp = 122.1 – 122.9 ºC. 54.7 mg, 89% yield;

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.71 (d, *J* = 2.1 Hz, 1H), 7.45 – 7.03 (m, 16H), 6.41 (d, *J* = 8.3 Hz, 1H), 5.09 (s, 1H), 4.92 (d, *J* = 15.9 Hz, 1H), 4.88 (s, 2H), 4.78 (d, *J* = 12.2 Hz, 1H), 4.65 (d, *J* = 15.9 Hz, 1H), 4.48 (d, *J* = 12.2 Hz, 1H), 4.37 – 4.16 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (100 MHz, Chloroform-*d*) δ 174.4, 168.2, 143.1, 137.8, 136.7, 134.8, 132.9, 130.1, 128.8, 128.7, 128.6, 128.3, 128.0, 127.6, 127.5, 127.3, 127.0, 126.9, 115.5, 110.7, 100.8, 79.8, 69.1, 66.4, 62.8, 43.9, 14.9;

HRMS (TOF MS ESI$^+$) calculated for $C_{33}H_{30}BrNO_6Na$ $[M + Na]^+$: 638.1149, found: 638.1157.



Ethyl-2-(1-benzyl-5-fluoro-3-hydroxy-2-oxoindolin-3-yl)-2,2-bis(benzyloxy)acetat -e (4m).

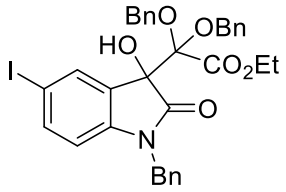
Result: White solid. mp = 88.9 – 89.6 ºC. 49.9 mg, 90% yield;

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.39 – 7.06 (m, 16H), 6.89 (td, *J* = 8.9, 2.7 Hz, 1H), 6.46 (dd, *J* = 8.6, 4.1 Hz, 1H), 5.16 (s, 1H), 4.95 (d, *J* = 15.9 Hz, 1H), 4.88 – 4.81 (m, 2H), 4.77 (d, *J* = 12.3 Hz, 1H), 4.65 (d, *J* = 15.9 Hz, 1H), 4.41 (d, *J* = 12.3 Hz, 1H), 4.39 – 4.27 (m, 2H), 1.30 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (125 MHz, Chloroform-*d*) δ 174.9, 168.4, δ 159.2 (d, *J* = 241.4 Hz), 140.1, 137.9, 136.7, 135.0, 128.8, 128.7, 128.5, 128.4, 128.2, 127.6, 127.6, 127.5, 127.1, 126.9, 116.6 (d, *J* = 23.6 Hz), 115.1 (d, *J* = 25.4 Hz), 109.9 (d, *J* = 8.1 Hz), 100.9, 80.0, 69.2, 66.2, 62.9, 44.0, 14.1;

^{19}F NMR (376 MHz, Chloroform-*d*) δ -120.1;

HRMS (TOF MS ESI$^+$) calculated for $C_{33}H_{30}FNO_6Na$ $[M + Na]^+$: 578.1949, found: 578.1953.



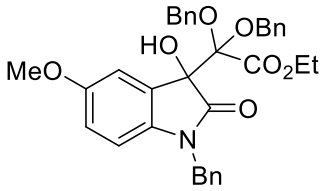
Ethyl-2-(1-benzyl-3-hydroxy-5-iodo-2-oxoindolin-3-yl)-2,2-bis(benzyloxy)acetate (4n).

Result: White solid. mp = 129.4 – 131.1 ºC. 59.7 mg, 90% yield;

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.89 (s, 1H), 7.67 – 6.88 (m, 16H), 6.31 (d, *J* = 8.2 Hz, 1H), 5.08 (s, 1H), 4.90 (comp, *J* = 16.8 Hz, 3H), 4.77 (d, *J* = 12.2 Hz, 1H), 4.65 (d, *J* = 15.9 Hz, 1H), 4.48 (d, *J* = 12.2 Hz, 1H), 4.38 – 4.27 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (125 MHz, Chloroform-*d*) δ 174.3, 168.3, 143.8, 139.0, 137.9, 136.8, 135.7, 134.9, 129.1, 128.8, 128.7, 128.4, 128.1, 127.7, 127.6, 127.4, 127.1, 127.0, 111.4, 100.9, 85.3, 79.8, 77.2, 69.1, 66.5, 62.9, 43.9, 14.1;

HRMS (TOF MS ESI$^+$) calculated for $C_{33}H_{30}INO_6Na$ $[M + Na]^+$: 686.1010, found: 686.1012.



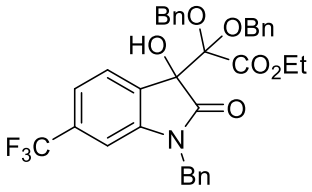
Ethyl-2-(1-benzyl-3-hydroxy-5-methoxy-2-oxoindolin-3-yl)-2,2-bis(benzyloxy)ace -tate (4o).

Result: White solid. mp = 107.4 – 108.9 °C. 51.6 mg, 91% yield;

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.50 – 7.29 (m, 6H), 7.29 – 7.19 (m, 5H), 7.19 – 7.02 (m, 5H), 6.99 (d, *J* = 8.1 Hz, 1H), 6.46 (d, *J* = 7.9 Hz, 1H), 5.02 (s, 1H), 4.91 (d, *J* = 15.9 Hz, 1H), 4.89 – 4.79 (m, 2H), 4.74 (d, *J* = 12.4 Hz, 1H), 4.69 (d, *J* = 15.9 Hz, 1H), 4.41 (d, *J* = 12.4 Hz, 1H), 4.36 – 4.19 (m, 2H), 2.26 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (125 MHz, Chloroform-*d*) δ 174.9, 168.5, 141.6, 138.2, 137.1, 135.5, 132.4, 130.6, 128.7, 128.6, 128.3, 128.0, 127.8, 127.5, 127.4, 127.4, 127.2, 126.9, 126.8, 109.2, 101.1, 80.0, 68.6, 66.1, 62.7, 43.9, 21.2, 14.0;

HRMS (TOF MS ESI$^+$) calculated for $C_{34}H_{33}NO_7Na$ $[M + Na]^+$: 590.2149, found: 590.2150.



Ethyl-2-(1-benzyl-3-hydroxy-2-oxo-6-(trifluoromethyl)indolin-3-yl)-2,2-bis(benzy -loxy)acetate (4p).

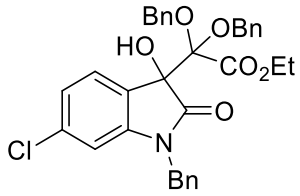
Result: White solid. mp = 120.4 – 122.3 ºC. 53.2 mg, 88% yield;

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.84 (d, *J* = 7.5 Hz, 1H), 7.59 (d, *J* = 8.1 Hz, 1H), 7.49 – 7.29 (m, 5H), 7.29 – 7.21 (m, 3H), 7.21 – 6.93 (m, 8H), 5.11 (d, *J* = 10.4 Hz, 3H), 4.89 (d, *J* = 11.2 Hz, 1H), 4.83 (d, *J* = 11.2 Hz, 1H), 4.76 (d, *J* = 12.0 Hz, 1H), 4.48 (d, *J* = 12.0 Hz, 1H), 4.31 (q, *J* = 7.1 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (126 MHz, Chloroform-*d*) δ 176.5, 168.2, 142.5, 137.7, 136.7, 135.9, 130.7, 129.7, 128.7, 128.42, 128.36, 128.2, 127.7, 127.5, 126.9, 126.7, 125.7, 123.28 (q, *J* = 272.1 Hz), 122.5, 113.05 (q, *J* = 32.4 Hz), 101.0, 77.9, 69.5, 66.3, 63.0, 45.82 (q, *J* = 5.2 Hz), 14.0;

^{19}F NMR (376 MHz, Chloroform-*d*) δ -54.87;

HRMS (TOF MS ESI$^+$) calculated for $C_{34}H_{30}F_3NO_6Na$ $[M + Na]^+$: 628.1917, found: 628.1928.



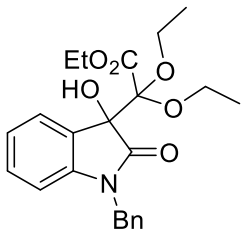
Ethyl-2-(1-benzyl-6-chloro-3-hydroxy-2-oxoindolin-3-yl)-2,2-bis(benzyloxy)acetat -e (4q).

Result: White solid. mp = 95.6 – 97.4 ºC. 52.8 mg, 92% yield;

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.48 (d, *J* = 7.9 Hz, 1H), 7.41 – 7.06 (m, 16H), 6.98 (d, *J* = 8.1 Hz, 1H), 6.54 (d, *J* = 1.8 Hz, 1H), 5.11 (d, *J* = 1.2 Hz, 1H), 4.90 (d, *J* = 15.9 Hz, 1H), 4.85 (d, *J* = 11.3 Hz, 1H), 4.81 (d, *J* = 11.3 Hz, 1H), 4.75 (d, *J* = 12.3 Hz, 1H), 4.65 (d, *J* = 15.9 Hz, 1H), 4.44 (d, *J* = 12.3 Hz, 1H), 4.37 – 4.26 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (100 MHz, Chloroform-*d*) δ 174.9, 168.3, 145.3, 137.8, 136.6, 136.1, 134.7, 128.8, 128.6, 128.3, 128.1, 127.8, 127.6, 127.4, 127.0, 126.7, 125.1, 122.8, 109.8, 100.8, 79.5, 69.0, 66.1, 62.8, 43.9, 14.0;

HRMS (TOF MS ESI$^+$) calculated for $C_{33}H_{30}ClNO_6Na$ $[M + Na]^+$: 594.1654, found: 594.1680.



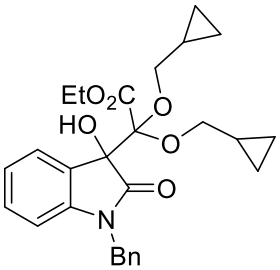
Ethyl-2-(1-benzyl-3-hydroxy-2-oxoindolin-3-yl)-2,2-diethoxyacetate (4r).

Result: Colourle -ss oil. 33.1 mg, 80% yield;

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.57 (d, *J* = 7.4 Hz, 1H), 7.36 – 7.22 (m, 5H), 7.18 (t, *J* = 7.7 Hz, 1H), 7.00 (t, *J* = 7.5 Hz, 1H), 6.61 (d, *J* = 7.8 Hz, 1H), 5.08 – 4.91 (m, 2H), 4.72 (d, *J* = 15.7 Hz, 1H), 4.37 – 4.18 (m, 2H), 3.87 – 3.77 (m, 1H), 3.76 – 3.68 (m, 1H), 3.64 – 3.50 (m, 1H), 3.31 – 3.17 (m, 1H), 1.33 (t, *J* = 7.0 Hz, 3H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.00 (t, *J* = 7.0 Hz, 3H);

^{13}C NMR (125 MHz, Chloroform-*d*) δ 175.2, 168.7, 144.1, 135.7, 130.2, 128.8, 127.7, 127.5, 127.1, 126.9, 122.8, 109.2, 100.9, 79.4, 77.2, 62.5, 62.2, 60.0, 43.9, 15.6, 15.2, 14.1;

HRMS (TOF MS ESI$^+$) calculated for $C_{23}H_{27}NO_6Na$ $[M + Na]^+$: 436.1731, found: 436.1740.



Ethyl-2-(1-benzyl-3-hydroxy-2-oxoindolin-3-yl)-2,2-bis(cyclopropylmethoxy)acetate (4s).

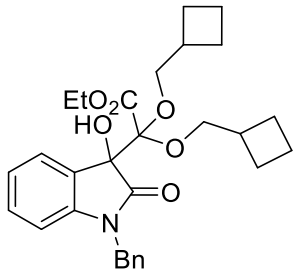
Result: Colourless oil. 42.7 mg, 92% yield;

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.81 – 7.66 (m, 1H), 7.53 – 7.33 (m, 5H), 7.33 – 7.23 (m, 1H), 7.23 – 7.04 (m, 1H), 6.88 – 6.54 (m, 1H), 5.10 (d, *J* = 16.0 Hz, 1H), 4.85 (d, *J* = 16.0 Hz, 1H), 4.56 – 4.22 (m, 2H), 3.90 – 3.77 (m, 1H), 3.76 – 3.52 (m, 2H),

3.40 – 3.18 (m, 1H), 1.45 – 1.25 (m, 5H), 1.02 – 0.96 (m, 1H), 0.72 (d, *J* = 7.0 Hz, 2H), 0.65 – 0.37 (m, 4H), 0.25 – 0.15 (m, 1H), 0.10 (td, *J* = 9.5, 4.9 Hz, 1H);

^{13}C NMR (125 MHz, Chloroform-*d*) δ 175.0, 168.6, 144.1, 135.7, 130.1, 128.8, 127.6, 127.4, 127.3, 126.8, 122.8, 109.1, 100.5, 79.6, 71.4, 68.6, 62.3, 43.9, 14.0, 10.8, 10.7, 3.2, 3.0, 2.9, 2.7;

HRMS (TOF MS ESI$^+$) calculated for $C_{27}H_{31}NO_6Na$ $[M + Na]^+$: 488.2050, found: 488.2044.



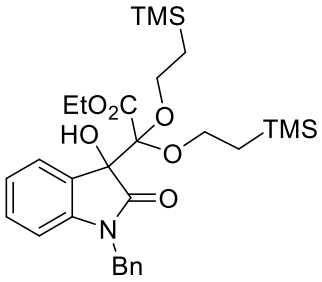
Ethyl-2-(1-benzyl-3-hydroxy-2-oxoindolin-3-yl)-2,2-bis(cyclobutylmethoxy)acetat-e (4t).

Result: Colourless oil. 45.3 mg, 92% yield;

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.55 (d, *J* = 7.8 Hz, 1H), 7.43 – 7.21 (m, 5H), 7.21 – 7.08 (m, 1H), 7.05 – 6.86 (m, 1H), 6.59 (d, *J* = 7.8 Hz, 1H), 5.06 (s, 1H), 4.95 (d, *J* = 15.8 Hz, 1H), 4.72 (d, *J* = 15.8 Hz, 1H), 4.45 – 4.15 (m, 2H), 3.85 – 3.63 (m, 2H), 3.59 – 3.43 (m, 1H), 3.31 – 3.11 (m, 1H), 2.84 – 2.62 (m, 1H), 2.39 – 2.26 (m, 1H), 2.20 – 2.05 (m, 2H), 2.02 – 1.63 (m, 8H), 1.57 – 1.50 (m, 1H), 1.46 – 1.39 (m, 1H), 1.29 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (125 MHz, Chloroform-*d*) δ 175.4, 169.0, 144.1, 135.7, 130.0, 128.8, 127.6, 127.40, 127.38, 126.8, 122.7, 109.0, 100.4, 79.9, 77.2, 71.3, 68.0, 62.3, 43.9, 35.4, 35.3, 25.1, 25.0, 24.6, 24.5, 18.8, 18.5, 14.1;

HRMS (TOF MS ESI$^+$) calculated for $C_{29}H_{35}NO_6Na$ $[M + Na]^+$: 516.2357, found: 516.2347.



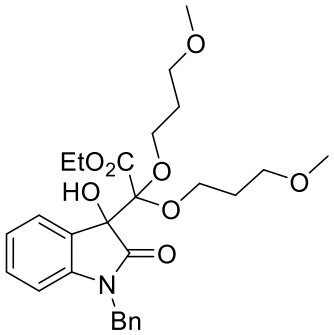
Ethyl-2-(1-benzyl-3-hydroxy-2-oxoindolin-3-yl)-2,2-bis(2-(trimethylsilyl)ethoxy)a -cetate (4u).

Result: White solid. mp = 72.3 – 74.1 ºC. 52.9 mg, 95% yield;

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.88 (d, *J* = 7.4 Hz, 1H), 7.63 – 7.50 (m, 5H), 7.46 (td, *J* = 7.7, 1.3 Hz, 1H), 7.29 (td, *J* = 7.6, 1.0 Hz, 1H), 6.90 (dd, *J* = 8.1, 3.1 Hz, 1H), 5.36 (s, 1H), 5.22 (d, *J* = 15.7 Hz, 1H), 5.02 (d, *J* = 15.7 Hz, 1H), 4.66 – 4.52 (m, 2H), 4.08 – 3.99 (m, 1H), 3.98 – 3.89 (m, 1H), 3.81 – 3.70 (m, 1H), 3.42 – 3.29 (m, 1H), 1.56 (t, *J* = 7.1 Hz, 3H), 1.47 – 1.41 (m, 1H), 1.33 – 1.25 (m, 1H), 1.06 – 0.95 (m, 1H), 0.94 – 0.83 (m, 1H), 0.33 (s, 9H), 0.12 (s, 9H);

^{13}C NMR (100 MHz, Chloroform-*d*) δ 175.3, 169.1, 144.1, 135.6, 130.3, 128.8, 127.7, 127.6, 127.2, 127.1, 122.8, 109.2, 100.7, 79.3, 63.6, 62.5, 61.9, 43.9, 18.7, 18.4, 14.1, -1.3, -1.5;

HRMS (TOF MS ESI$^+$) calculated for $C_{29}H_{43}NO_6Si_2Na$ $[M + Na]^+$: 580.2521, found: 580.2519.



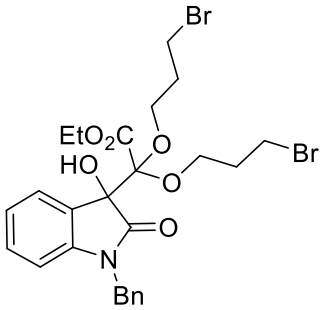
Ethyl-2-(1-benzyl-3-hydroxy-2-oxoindolin-3-yl)-2,2-bis(3-methoxypropoxy)aceta -te (4v).

Result: Colourless oil. 46.6 mg, 93% yield;

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.61 – 7.51 (m, 1H), 7.48 – 7.22 (m, 5H), 7.21 – 7.10 (m, 1H), 7.06 – 6.87 (m, 1H), 6.74 – 6.53 (m, 1H), 5.00 (d, *J* = 15.7, 2.3 Hz, 1H), 4.69 (d, *J* = 15.7, 2.3 Hz, 1H), 4.38 – 4.15 (m, 2H), 4.00 – 3.86 (m, 1H), 3.85 – 3.75 (m, 1H), 3.75 – 3.65 (m, 1H), 3.63 – 3.49 (m, 2H), 3.46 – 3.37 (m, 1H), 3.34 (s, 3H), 3.23 – 3.00 (comp, 5H), 2.03 – 1.93 (m, 2H), 1.69 – 1.58 (m, 2H), 1.25 (t, *J* = 6.1 Hz, 3H);

^{13}C NMR (125 MHz, Chloroform-*d*) δ 175.2, 168.6, 144.0, 135.7, 130.1, 128.8, 127.7, 127.4, 127.3, 126.7, 122.8, 109.1, 100.9, 79.7, 69.4, 69.3, 64.3, 62.4, 61.4, 58.7, 58.6, 43.9, 30.2, 30.2, 14.0;

HRMS (TOF MS ESI$^+$) calculated for $C_{27}H_{35}NO_8Na$ $[M + Na]^+$: 524.2255, found: 524.2242.



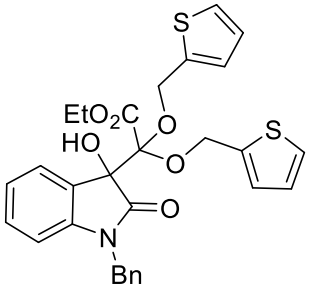
Ethyl-2-(1-benzyl-3-hydroxy-2-oxoindolin-3-yl)-2,2-bis(3-bromopropoxy)acetate (4w).

Result: White solid. mp = 91.6 – 92.6 ºC. 54.9 mg, 92% yield;

^{1}H NMR (500 MHz, Chloroform-*d*)) δ 7.56 – 7.48 (m, 1H), 7.36 – 7.17 (m, 6H), 7.08 – 6.93 (m, 1H), 6.70 – 6.57 (m, 1H), 5.06 – 4.95 (m, 1H), 4.95 – 4.82 (m, 1H), 4.76 – 4.62 (m, 1H), 4.42 – 4.24 (m, 2H), 4.04 – 3.93 (m, 1H), 3.93 – 3.84 (m, 1H), 3.82 – 3.71 (m, 1H), 3.69 – 3.55 (m, 2H), 3.53 – 3.42 (m, 1H), 3.23 – 3.12 (m, 1H), 3.07 – 2.96 (m, 1H), 2.36 – 2.18 (m, 2H), 1.94 – 1.80 (m, 2H), 1.36 – 1.27 (m, 3H).

^{13}C NMR (125 MHz, Chloroform-*d*) δ 174.9, 168.3, 143.9, 135.6, 130.3, 128.9, 128.8, 127.8, 127.49, 127.48, 126.8, 126.6, 123.00, 122.98, 109.2, 100.7, 79.7, 65.0, 62.8, 61.9, 43.9, 33.1, 33.0, 30.2, 30.1, 14.1;

HRMS (TOF MS ESI$^+$) calculated for $C_{25}H_{29}Br_2NO_6Na$ [M + Na]$^+$: 620.0254, found: 620.0252.



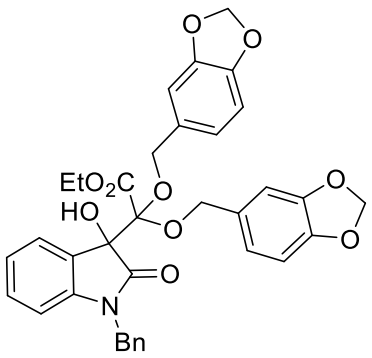
Ethyl-2-(1-benzyl-3-hydroxy-2-oxoindolin-3-yl)-2,2-bis(thiophen-2-ylmethoxy)ac -etate (4x).

Result: White solid. mp = 109.1 – 111.6 ºC. 35.7 mg, 65% yield;

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 7.4 Hz, 1H), 7.33 (d, *J* = 5.1 Hz, 1H), 7.29 – 7.23 (m, 3H), 7.23 – 7.12 (m, 4H), 7.08 (d, *J* = 3.4 Hz, 1H), 7.05 – 6.96 (m, 2H), 6.95 – 6.89 (m, 1H), 6.84 (d, *J* = 3.4 Hz, 1H), 6.60 (d, *J* = 7.8 Hz, 1H), 5.23 (d, *J* = 11.6 Hz, 1H), 5.06 (d, *J* = 11.6 Hz, 1H), 4.98 (s, 1H), 4.95 (d, *J* = 3.5 Hz, 1H), 4.75 (d, *J* = 16.4 Hz, 2H), 4.62 (d, *J* = 12.3 Hz, 1H), 4.29 – 4.14 (m, 2H), 1.17 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (125 MHz, Chloroform-*d*) δ 174.3, 167.7, 143.9, 140.6, 139.4, 135.5, 130.5, 128.8, 127.6, 127.3, 126.9, 126.8, 126.8, 126.7, 126.6, 126.3, 125.92, 125.87, 123.0, 109.4, 100.9, 79.4, 63.9, 62.7, 61.8, 44.0, 13.9;

HRMS (TOF MS ESI$^+$) calculated for $C_{29}H_{27}NO_6S_2Na$ [M + Na]$^+$: 572.1172, found: 572.1198.



Ethyl-2,2-bis(benzo[d][1,3]dioxol-5-ylmethoxy)-2-(1-benzyl-3-hydroxy-2-oxoindo

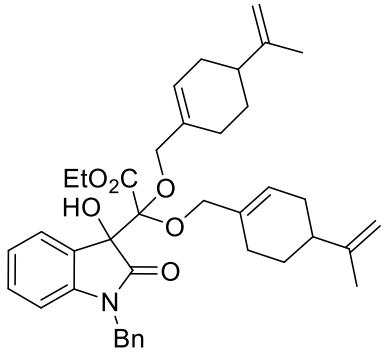
-lin-3-yl)acetate (4y).

Result: Colourless oil. 52.9 mg, 85% yield;

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.55 (d, *J* = 7.4 Hz, 1H), 7.23 – 7.11 (m, 6H), 7.01 (t, *J* = 7.6 Hz, 1H), 6.93 (s, 1H), 6.82 (d, *J* = 7.9 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.68 (d, *J* = 7.9 Hz, 1H), 6.62 – 6.53 (m, 3H), 5.97 (s, 2H), 5.91 (d, *J* = 4.3 Hz, 2H), 5.00 – 4.94 (m, 2H), 4.77 – 4.67 (m, 3H), 4.62 (d, *J* = 11.9 Hz, 1H), 4.34 – 4.23 (m, 3H), 1.25 (t, *J* = 7.1 Hz, 4H);

^{13}C NMR (126 MHz, Chloroform-*d*) δ 174.9, 168.4, 147.9, 147.7, 147.5, 147.0, 144.1, 135.4, 132.0, 130.7, 130.4, 128.7, 127.6, 127.3, 126.9, 126.8, 123.0, 121.3, 120.3, 109.4, 108.5, 108.3, 108.0, 107.8, 101.2, 101.21, 101.04, 79.8, 68.8, 65.9, 62.7, 43.9, 14.0;

HRMS (TOF MS ESI$^+$) calculated for $C_{35}H_{31}NO_{10}Na$ $[M + Na]^+$: 648.1840, found: 648.1827.



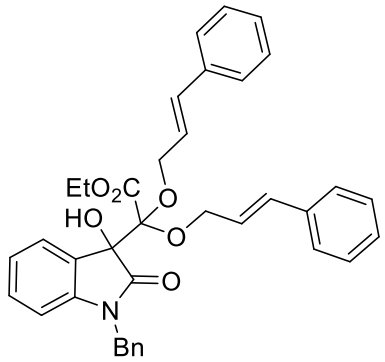
Ethyl-2-(1-benzyl-3-hydroxy-2-oxoindolin-3-yl)-2,2-bis(((E)-3,7-dimethylocta2,6-dien-1-yl)oxy)acetate (4z).

Result: Colourless oil. 55.0 mg, 88% yield;

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.57 (d, *J* = 7.7 Hz, 1H), 7.34 – 7.22 (m, 5H), 7.18 (t, *J* = 7.7 Hz, 1H), 7.02 (t, *J* = 7.5 Hz, 1H), 6.60 (d, *J* = 7.8 Hz, 1H), 5.79 (s, 1H), 5.53 (s, 1H), 5.09 (s, 1H), 4.97 (dd, *J* = 15.9, 5.1 Hz, 1H), 4.78 – 4.63 (m, 5H), 4.37 – 4.25 (m, 2H), 4.15 – 4.02 (m, 2H), 3.94 (dd, *J* = 12.1, 7.4 Hz, 1H), 3.52 (d, *J* = 12.1 Hz, 1H), 2.24 – 2.12 (m, 4H), 2.10 – 1.79 (m, 7H), 1.76 (s, 3H), 1.71 (s, 3H), 1.32 – 1.23 (m, 6H);

^{13}C NMR (125 MHz, Chloroform-*d*) δ 175.3, 168.9, 150.0, 149.9, 144.1, 135.6, 134.5, 134.4, 133.62, 133.59, 130.2, 128.8, 127.6, 127.37, 127.36, 127.0, 124.54, 124.51, 122.9, 122.80, 122.78, 109.3, 109.2, 108.9, 108.7, 100.48, 100.46, 79.9, 79.8, 77.2, 70.6, 67.9, 67.8, 62.51, 62.49, 43.9, 41.2, 41.2, 41.1, 30.64, 30.56, 27.53, 27.51, 27.47, 26.6, 26.5, 26.0, 20.98, 20.96, 20.9, 14.1;

HRMS (TOF MS ESI$^+$) calculated for $C_{39}H_{47}NO_6Na$ $[M + Na]^+$: 648.3296, found: 648.3297.



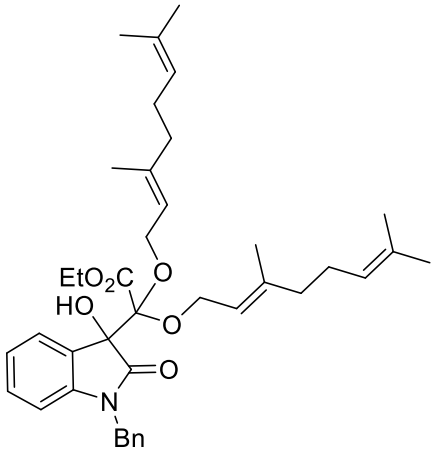
Ethyl-2-(1-benzyl-3-hydroxy-2-oxoindolin-3-yl)-2,2-bis(cinnamyloxy)acetate(4aa).

Result: Colourless oil. 39.6 mg, 67% yield;

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.65 (d, *J* = 7.4 Hz, 1H), 7.44 – 7.12 (m, 17H), 7.08 – 7.00 (m, 1H), 6.68 (d, *J* = 15.9 Hz, 1H), 6.63 (d, *J* = 7.8 Hz, 1H), 6.45 (d, *J* = 15.9 Hz, 1H), 6.40 – 6.30 (m, 1H), 6.10 – 5.98 (m, 1H), 5.04 (s, 1H), 4.99 (d, *J* = 15.8 Hz, 1H), 4.72 (d, *J* = 15.8 Hz, 1H), 4.50 – 4.39 (m, 2H), 4.37 – 4.21 (m, 3H), 3.86 (dd, *J* = 13.6, 5.5 Hz, 1H), 1.29 (t, *J* = 7.1 Hz, 3H)；

^{13}C NMR (125 MHz, Chloroform-*d*) δ 175.0, 168.6, 144.1, 136.8, 136.5, 135.5, 133.1, 131.2, 130.5, 128.9, 128.8, 128.7, 128.1, 127.7, 127.73, 127.68, 127.1, 126.8, 126.6, 125.7, 124.3, 123.0, 109.4, 100.8, 79.6, 67.2, 64.9, 62.8, 44.0, 14.1;

HRMS (TOF MS ESI$^+$) calculated for $C_{37}H_{35}NO_6Na$ $[M + Na]^+$: 612.2357, found: 612.2357.



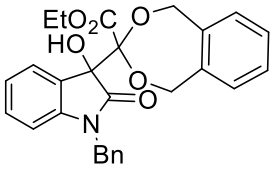
Ethyl-2-(1-benzyl-3-hydroxy-2-oxoindolin-3-yl)-2,2-bis(((E)-3,7-dimethylocta-2,6-dien-1-yl)oxy)acetate (4ab).

Result: Colourless oil. 56.6 mg, 90% yield;

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.58 (d, *J* = 7.5 Hz, 1H), 7.34 – 7.21 (m, 5H), 7.17 (t, *J* = 7.8 Hz, 1H), 7.00 (t, *J* = 7.5 Hz, 1H), 6.60 (d, *J* = 7.8 Hz, 1H), 5.43 (t, *J* = 6.7 Hz, 1H), 5.16 (t, *J* = 6.5 Hz, 1H), 5.11 (t, *J* = 6.8 Hz, 1H), 5.08 – 5.02 (m, 1H), 4.98 – 4.86 (m, 2H), 4.78 (d, *J* = 15.7 Hz, 1H), 4.40 – 4.33 (m, 1H), 4.30 – 4.18 (m, 3H), 4.14 – 4.03 (m, 1H), 3.85 – 3.71 (m, 1H), 2.14 – 1.99 (m, 6H), 1.96 – 1.90 (m, 2H), 1.72 – 1.66 (m, 9H), 1.62 (s, 3H), 1.58 (s, 3H), 1.42 (s, 3H), 1.20 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (125 MHz, Chloroform-*d*) δ 175.0, 168.6, 144.0, 140.5, 139.0, 135.6, 131.9, 131.7, 130.3, 128.8, 127.6, 127.4, 127.2, 126.9, 124.1, 124.0, 122.9, 120.9, 119.9, 109.2, 100.7, 79.4, 63.2, 62.4, 61.4, 44.0, 39.7, 39.6, 39.6, 26.5, 25.8, 25.8, 17.8, 17.8, 16.8, 16.5, 14.0;

HRMS (TOF MS ESI^{+}) calculated for $C_{39}H_{51}NO_6Na$ $[M + Na]^{+}$: 652.3609, found: 652.3609.



Ethyl 3-(1-benzyl-3-hydroxy-2-oxoindolin-3-yl)-1,5-dihydrobenzo[e][1,3] dioxepine-3-carboxylate (4ac).

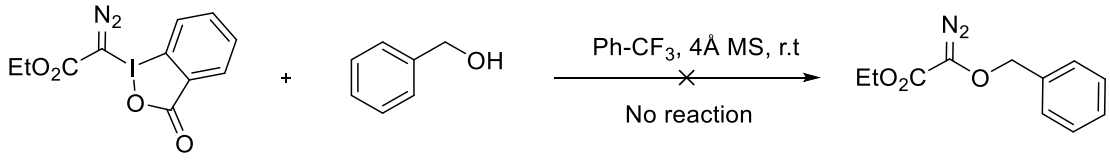
Result: Colourless oil. 20.2 mg, 22% yield;

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.56 (d, *J* = 7.8 Hz, 1H), 7.36 – 7.17 (m, 5H), 7.11 – 7.09 (m, 2H), 7.02 – 6.97 (m, 2H), 6.67 (d, *J* = 7.8 Hz, 1H), 5.42 (d, *J* = 16.0 Hz, 1H), 5.16 (t, *J* = 6.5 Hz, 1H), 5.11 (t, *J* = 6.8 Hz, 1H), 5.04 – 4.97 (m, 3H), 4.81 – 4.73 (m, 2H), 4.61 (br, 1H), 4.19 (q, *J* = 8.0 Hz, 2H), 1.11 (t, *J* = 8.0 Hz, 3H)；

^{13}C NMR (100 MHz, Chloroform-*d*) δ 174.4, 167.8, 143.9, 136.7, 135.5, 128.8, 127.7, 127.6, 127.5, 127.2, 126.5, 126.0, 122.9, 109.3, 102.8, 79.2, 70.5, 68.4, 62.6, 44.0, 13.8;

HRMS (TOF MS ESI$^+$) calculated for $C_{27}H_{25}NNaO_6$ $[M + Na]^+$: 482.1580, found: 482.1580.

6. Control Experiments



1b **2a** **5**

To a 10-mL oven-dried vial containing a magnetic stirring bar, **2a** (0.20 mmol, 2.0 equiv.), 4 Å MS (100 mg) in $PhCF_3$ (1.5 mL), was added diazo compound **1b** (0.10 mmol, 1.0 equiv.) and the reaction mixture was stirred at room temperature, Then the reaction crude mixture was subjected to proton NMR analysis in $CDCl_3$ after the solvent was evaporated (see Figure S1). No reaction was occurred under these conditions.

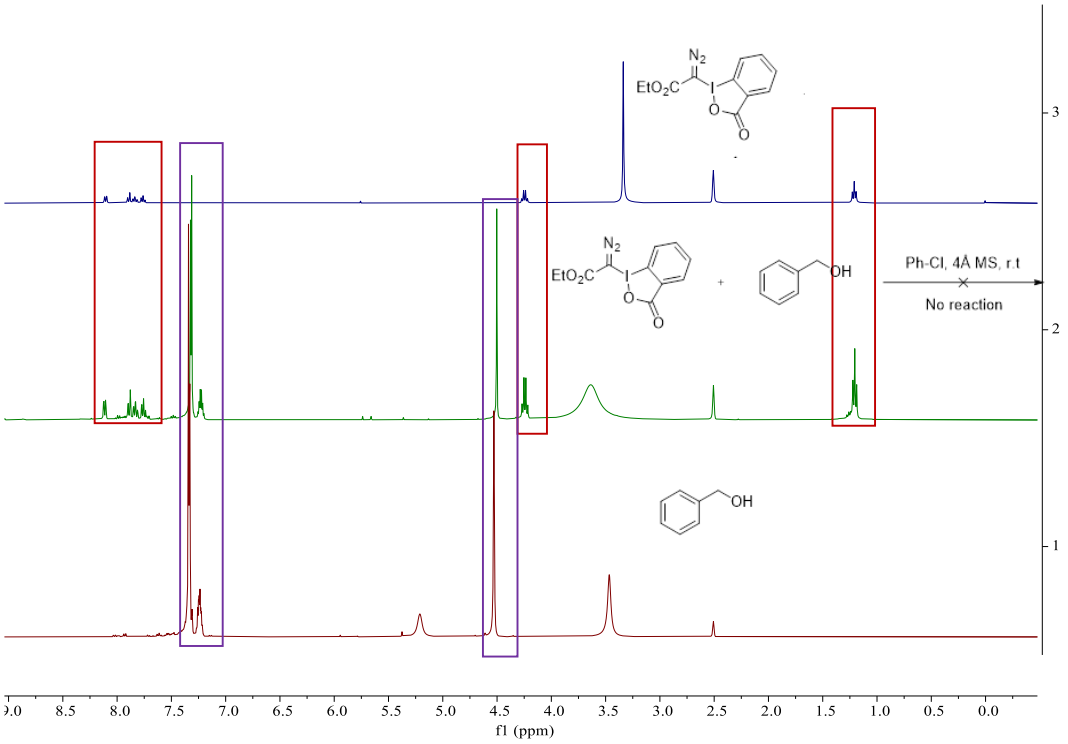
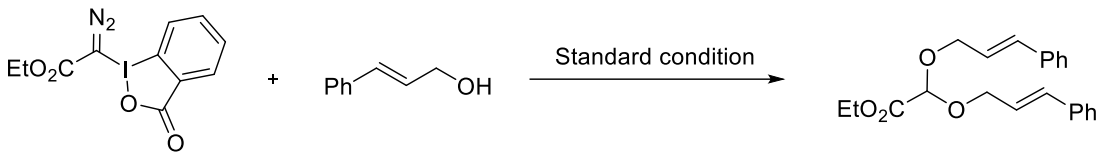


Figure S1: Proton NMR spectrum of crude reaction mixture of **1b** with **2a**.



1b **2y** **6**, 65% yield

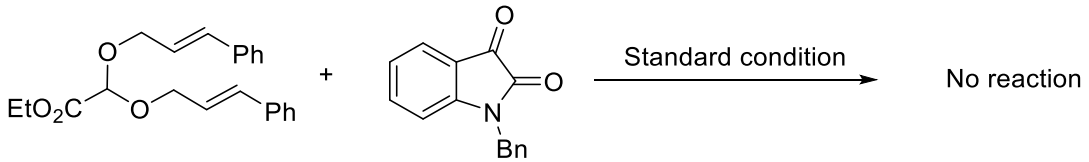
To a 10-mL oven-dried vial containing a magnetic stirring bar, $Rh_2(Oct)_4$ (1.50 mg, 2.0 mol%), **2y** (0.20 mmol, 2.0 equiv.), and 4 Å MS (100 mg) in PhCl (1.5 mL), was added diazo compound **1b** (0.10 mmol, 1.0 equiv.) at -27 ℃. After addition, the reaction mixture was stirred for additional 24 h under these conditions. The crued reaction mixture concentrated in vacuo and the product was purified by column chromatography on silica gel without any additional treatment (Hexanes : EtOAc = 10:1) to give the pure products **6**.

Result: Colorless oil, 22.8 mg, 65% yield;

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.33 – 7.28 (m, 4H), 7.26 – 7.22 (m, 4H), 7.20 – 7.17 (m, 2H), 6.57 (d, *J* = 15.9 Hz, 2H), 6.24 (dt, *J* = 15.8, 6.4 Hz, 2H), 5.03 (s, 1H), 4.34 – 4.26 (m, 4H), 4.19 (q, *J* = 7.4 Hz, 3H), 1.25 (t, *J* = 7.3 Hz, 3H);

^{13}C NMR (125 MHz, DMSO) δ 167.6, 136.5, 133.7, 128.7, 128.0, 126.7, 126.7, 124.8, 96.2, 67.4, 61.8, 14.3.

HRMS (TOF MS ESI$^+$) calculated for $C_{22}H_{24}O_4Na$ $[M + Na]^+$: 375.1567, found: 375.1567.



6 **3**

To a 10-mL oven-dried vial containing a magnetic stirring bar, **6** (0.05 mmol, 1.0 equiv.), $Rh_2(OCt)_4$(1.50 mg, 2.0 mol%), 4 Å MS (100 mg), **3** (0.05 mmol, 1.0 equiv.) in $PhCF_3$ (1.5 mL) and the reaction mixture was stirred at -27 ℃, Then the reaction crude mixture was subjected to proton NMR analysis in $CDCl_3$ after the solvent was evaporated (see Figure S2). No reaction was occurred under these conditions.

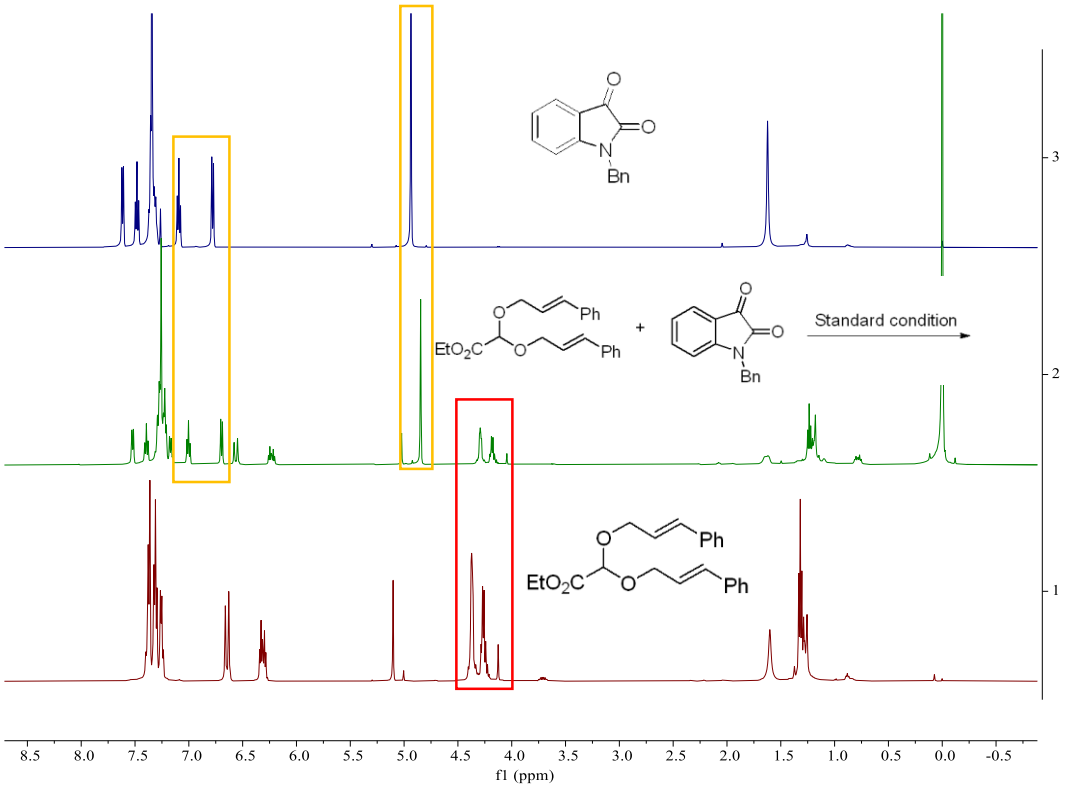
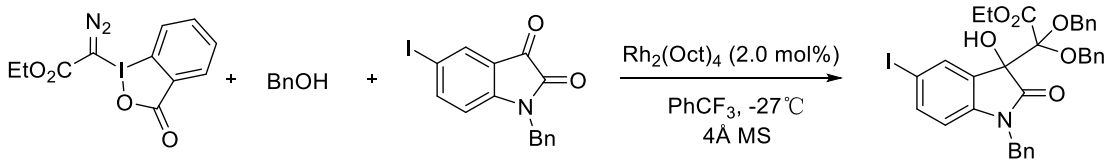


Figure S2. Proton NMR spectrum of crude reaction mixture of **6** with **3** under standard conditions.

7. Procedures for Scale up and Derivations

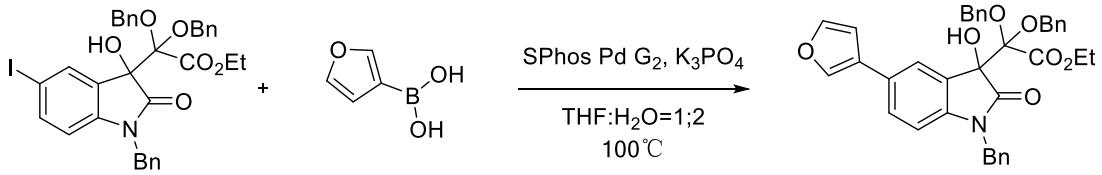
General Procedure for the Scale Up



1a	2a	3n	4n
2.2 mmol	3.3 mmol	1.1mmol	650 mg, 89% yield

To a 25-mL oven-dried vial containing a magnetic stirring bar, $Rh_2(Oct)_4$ (1.50 mg, 2.0 mol%), **2a** (3.30 mmol, 3.0 equiv.), **3n** (1.10 mmol, 1.0 equiv.), and 4 Å MS (100 mg) in PhCl (16.5 mL), was added diazo compound **1a** (2.20 mmol, 2.0 equiv.) at -27 °C. After addition, the reaction mixture was stirred for additional 24 h-48 h under these conditions. Until consumption of the material (monitored by TLC), the crude reaction mixture concentrated in vacuo and the product was purified by column chromatography on silica gel without any additional treatment (Hexanes : EtOAc = 5:1) to give the pure products **4n** in 89% yield.

General Procedure for the Synthesis of 7



4n **7**, 85% yield

In a 10-mL oven-dried vial equipped with a magnetic stirring bar, **4n** (66.3 mg, 0.1 mmol, 1.0 equiv.), furan-3-boronic acid (22.4 mg, 0.12 mmol, 2 equiv.), SPhos Pd G2 (7.0 mg, 10 mol%), and K_3PO_4 (59.0 mg, 0.3 mmol, 3.0 equiv.) were dissolved in 1.0 mL of ultra-dry tetrahydrofuran mixed with a 1:2 (v/v) solution of deionized water. The tube was sealed and placed in a microwave at 100℃ for 20 minutes. After the reaction goes complete (confirmed by TLC), ethyl acetate extraction (2×10 mL) was performed. The combined organic phases were washed with saturated salt water, dried over anhydrous sodium sulfate, and concentrated under reduced pressure to obtain the crude

product. The crude product was further purified by column chromatography (petroleum ether: ethyl acetate = 5:1) to yield the purified product **7**.

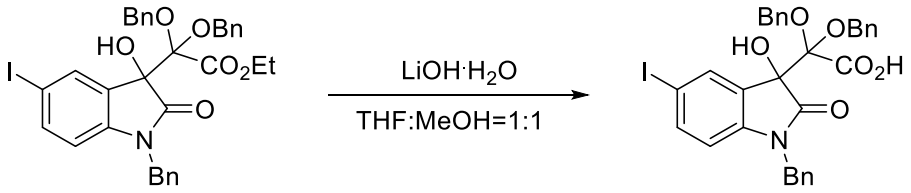
Result: White solid, mp = 89 – 91 ºC. 51.2 mg, 85% yield;

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.72 (s, 1H), 7.49 (s, 1H), 7.43 – 7.29 (m, 7H), 7.23 – 7.06 (m, 10H), 6.55 (d, *J* = 8.2 Hz, 1H), 6.50 (s, 1H), 5.17 (s, 1H), 4.98 – 4.84 (m, 3H), 4.78 – 4.65 (m, 2H), 4.43 (d, *J* = 12.3 Hz, 1H), 4.39 – 4.26 (m, 2H), 1.29 (t, *J* = 7.2 Hz, 3H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 174.9, 168.5, 143.7, 142.9, 138.1, 138.0, 136.9, 135.3, 129.2, 128.8, 128.6, 128.3, 128.2, 127.6, 127.53, 127.47, 127.46, 127.42, 127.37, 127.2, 126.9, 126.1, 125.4, 124.7, 109.6, 108.7, 100.8, 79.9, 68.8, 66.2, 62.8, 43.9, 14.1;

HRMS (TOF MS ESI$^+$) calculated for $C_{31}H_{26}NO_6Na$ $[M + Na]^+$: 658.0697, found: 658.0695.

General Procedure for the Synthesis of 8



4n **8,** 90% yield

In a 10-mL oven-dried vial equipped with a magnetic stirring bar, **4n** (66.3 mg, 0.1 mmol, 1.0 equiv.) and $LiOH{\cdot}H_2O$ (59.0 mg, 1.0 mmol, 10.0 equiv.) were dissolved in 1.0 mL of ultra-dry tetrahydrofuran mixed with a 1:1 (v/v) solution of MeOH. The reaction mixture was then stirred at room temperature overnight. After the reaction goes complete (confirmed by TLC), the pH of the mixture was adjusted to 4-5 using a citric acid solution. Ethyl acetate extraction (3×10 mL) was performed, and the combined organic phases were washed with saturated salt water, dried over anhydrous sodium sulfate, and concentrated under reduced pressure to obtain the crude product. The crude product was further purified by column chromatography (dichloromethane: methanol = 20:1) to yield the purified product **8**.

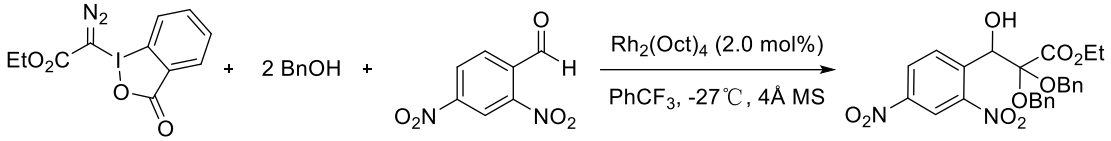
Result: White solid, mp = 110.2 – 110.8 ºC. 57.2 mg, 90% yield;

^{1}H NMR (500 MHz, DMSO-d_6) δ 9.96 (s, 1H), 7.76 (s, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.34 – 7.27 (m, 4H), 7.25 – 7.21 (m, 1H), 7.14 – 7.13 (m, 6H), 7.00-6.93 (m, 4H), 6.48 (d, *J* = 8.0 Hz, 1H), 5.01 (dd, *J* = 16.7, 12.5 Hz, 2H), 4.88 (dd, *J* = 16.0, 12.0 Hz, 2H), 4.65 (dd, *J* = 16.0, 12.0 Hz, 2H), 3.57 (s, 1H);

^{13}C NMR (125 MHz, DMSO) δ 175.8, 169.4, 143.7, 140.2, 138.9, 136.9, 135.9, 135.2, 132.4, 128.3, 128.2, 127.7, 127.1, 127.0, 126.8, 126.7, 126.49, 126.46, 110.8, 100.1, 84.5, 79.9, 68.6, 66.4, 65.3, 45.6, 42.2, 39.7, 39.5, 39.3.

HRMS (TOF MS ESI$^+$) calculated for $C_{33}H_{37}NO_7Na$ $[M + Na]^+$: 626.2149, found: 626.2149.

General Procedure for the Synthesis of 10



1b **2a** **9** **10:** 38% yield

To a 10-mL oven-dried vial equipped with a magnetic stirring bar, $Rh_2(Oct)_4$ (1.50 mg, 2.0 mol%), alcohol **2** (0.30 mmol, 3.0 equiv.), aldehyde **10** (0.10 mmol, 1.0 equiv.), and 4 Å MS (100 mg) were added in $PhCF_3$ (1.5 mL). Subsequently, diazo compound **1** (0.15 mmol, 1.5 equiv.) was added at -27 ℃. The reaction mixture was stirred for an additional 24 hours under these conditions until the material was completely consumed (monitored by TLC). The crude reaction mixture was then concentrated under vacuum, and the resulting product was purified by column chromatography on silica gel (Hexanes: EtOAc = 10:1) to afford the pure products **11** in 38% yields.

Ethyl 2,2-bis(benzyloxy)-3-(2,4-dinitrophenyl)-3-hydroxypropanoate (10).

Result: white solid. mp = 141.7-143.0 ºC.18.8 mg, 38% yield;

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.63 (d, *J* = 4.0 Hz, 1H), 8.36 (d, *J* = 7.8 Hz, 1H), 7.97 (d, *J* = 7.8 Hz, 1H), 7.46 – 7.44 (m, 2H), 7.41 (t, *J* = 4.0 Hz, 2H), 7.32 – 7.26 (m, 4H), 7.15 – 7.14 (m, 2H), 6.33 (d, *J* = 4.0 Hz, 1H), 4.87 (d, *J* = 12.0 Hz, 1H), 4.75 (d, *J* = 12.0 Hz, 1H), 4.50 (dd, *J* = 20.0, 12.0 Hz,2H), 4.15 – 4.03 (m, 2H), 3.08 (d, *J* = 4.0 Hz, 1H), 1.16 (t, *J* = 6.0 Hz, 3H);

^{13}C NMR (100 MHz, Chloroform-*d*) δ 166.3, 149.3, 147.1, 139.6, 137.2, 135.9, 128.9, 128.4, 128.3, 128.2, 128.0, 127.4, 119.6, 104.0, 68.2, 67.9, 64.9, 62.2, 14.1;

HRMS (TOF MS ESI$^+$) calculated for $C_{25}H_{24}N_2NaO_9$ $[M + Na]^+$: 519.1380, found: 519.1382.

8. References

[1] Wang, Z. F.; Herraiz, A. G.; Del Hoyo, A. M.; Marcos G. Suero. Generating Carbyne Equivalents with Photoredox Catalysis. *Nature* **2018**, 554, 86-91.

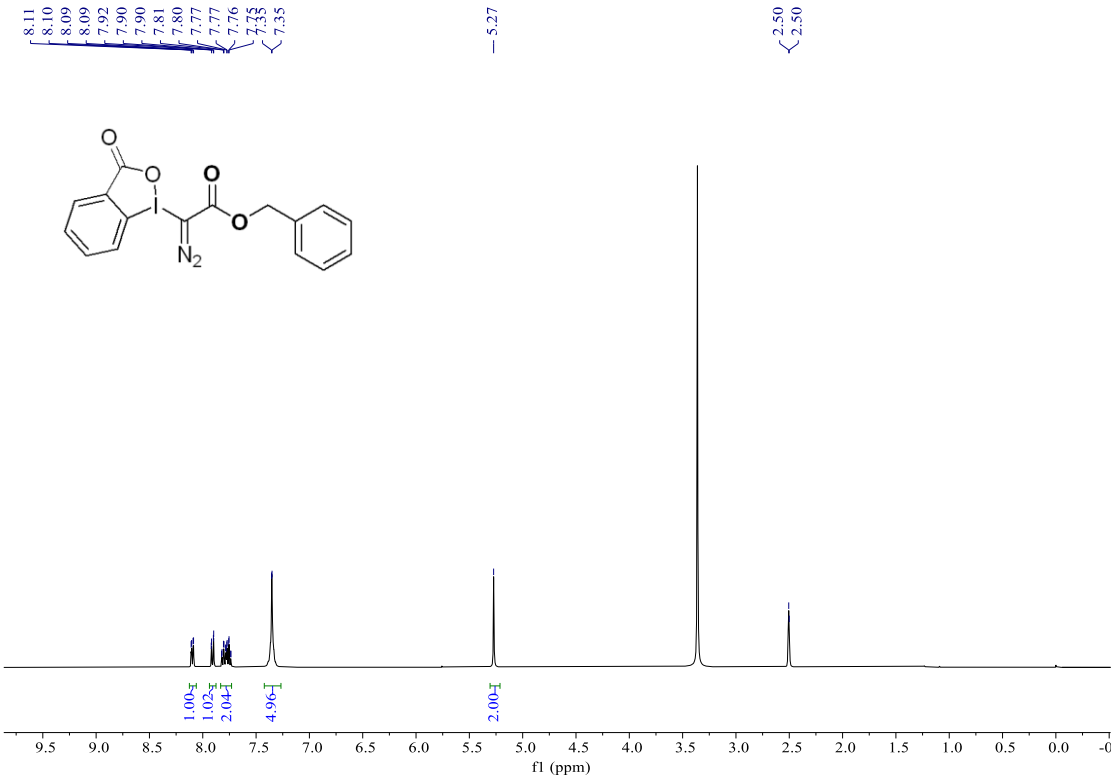
[2] Weiss, R.; Seubert, J.; Hampel, F. α-Aryliodonio diazo compounds: SN reactions at the a-C atom as a novel reaction type for diazo compounds. *Angew. Chem. Int. Ed.* **1994**, 33, 1952–1953.

[3] Schnaars C.; Hennum M.; Bongehansen T. Nucleophilic Halogenations of Diazo Compounds, a Complementary Principle for the Synthesis of Halodiazo Compounds: Experimental and Theoretical Studies. *J. Org. Chem.* **2013**, 78, 7488−7497.

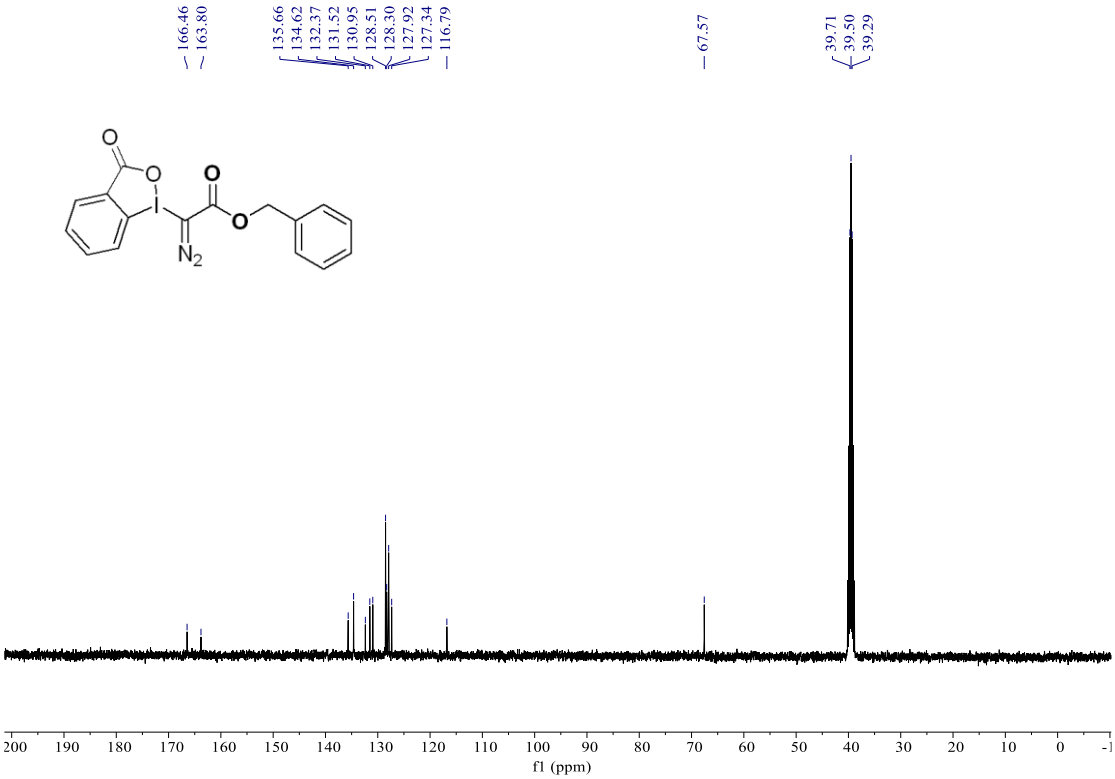
[4] Kamal, A.; Mahesh, R.; Nayak, V. L.; Babu, K. S.; Kumar, G. B.; Shaik, A. B.; Kapure, J. S.; Alarifi, A. Discovery of pyrrolospirooxindole derivatives as novel cyclin dependent kinase 4 (CDK4) inhibitors by catalyst-free, green approach. *European Journal of Medicinal Chemistry* **2016**, 108, 476-485.

9. NMR Spectra Analysis Figures

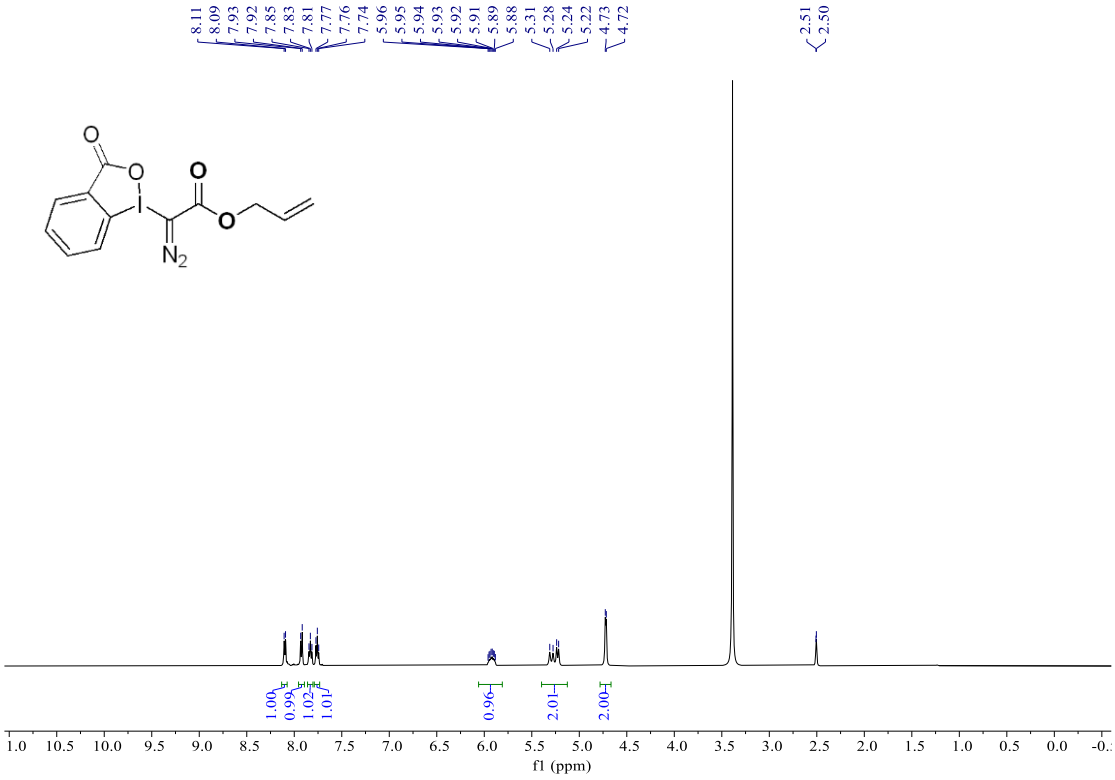
^{1}H NMR (500 MHz, DMSO) spectra for 1bb



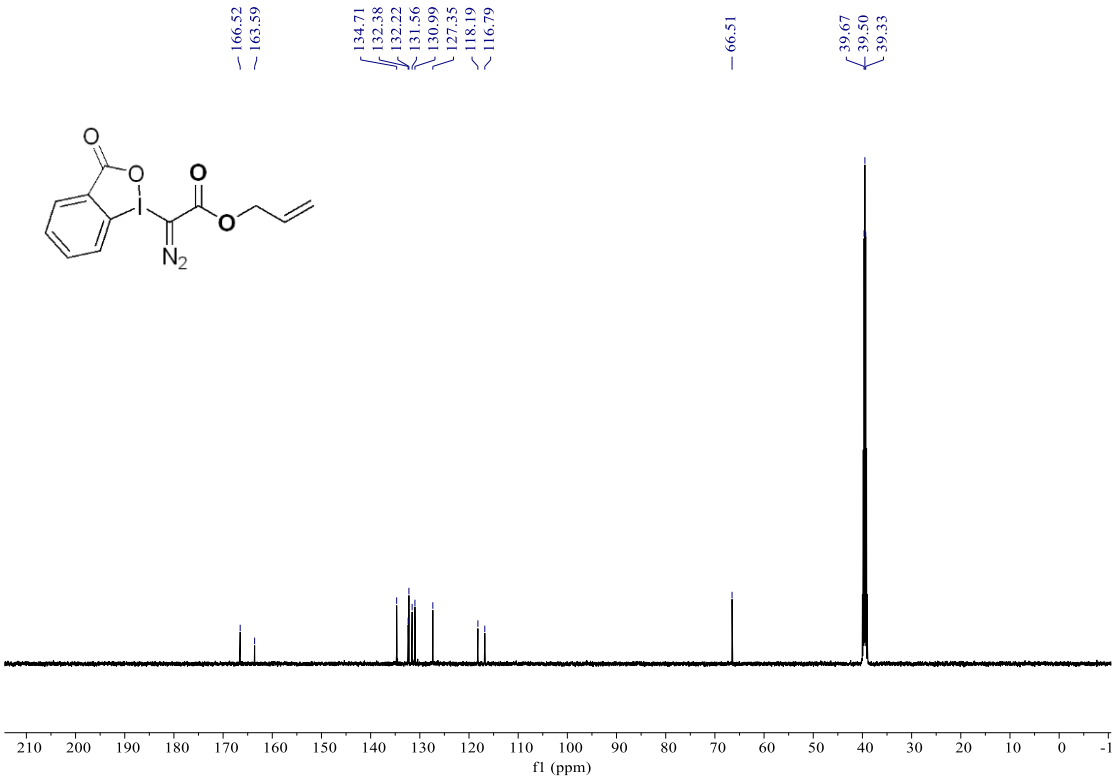
^{13}C NMR (125 MHz, DMSO) spectra for 1c



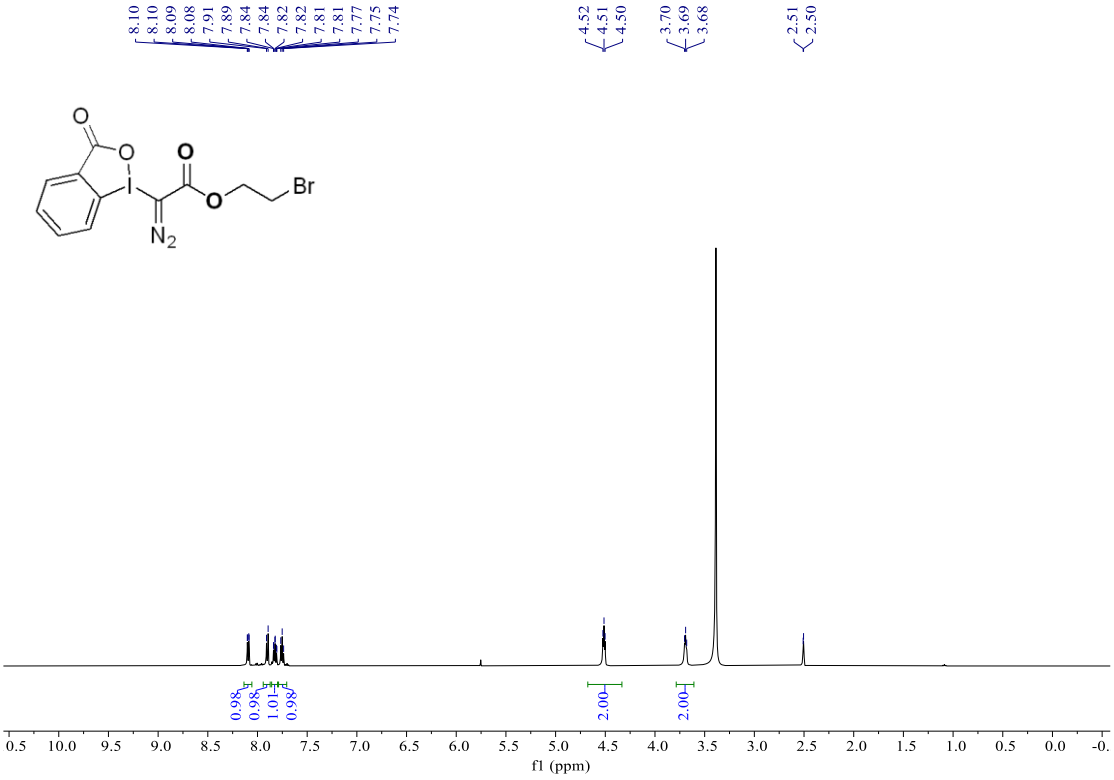
^{1}H NMR (500 MHz, DMSO) spectra for 1bc



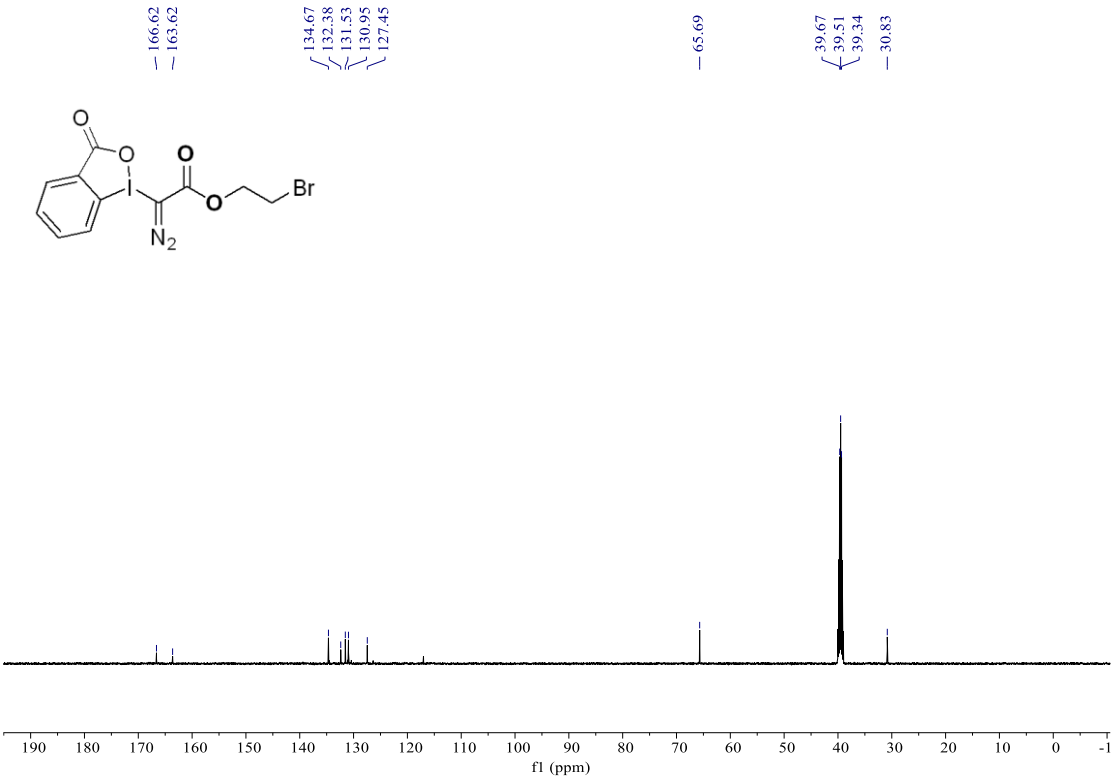
^{13}C NMR (125 MHz, DMSO) spectra for 1d



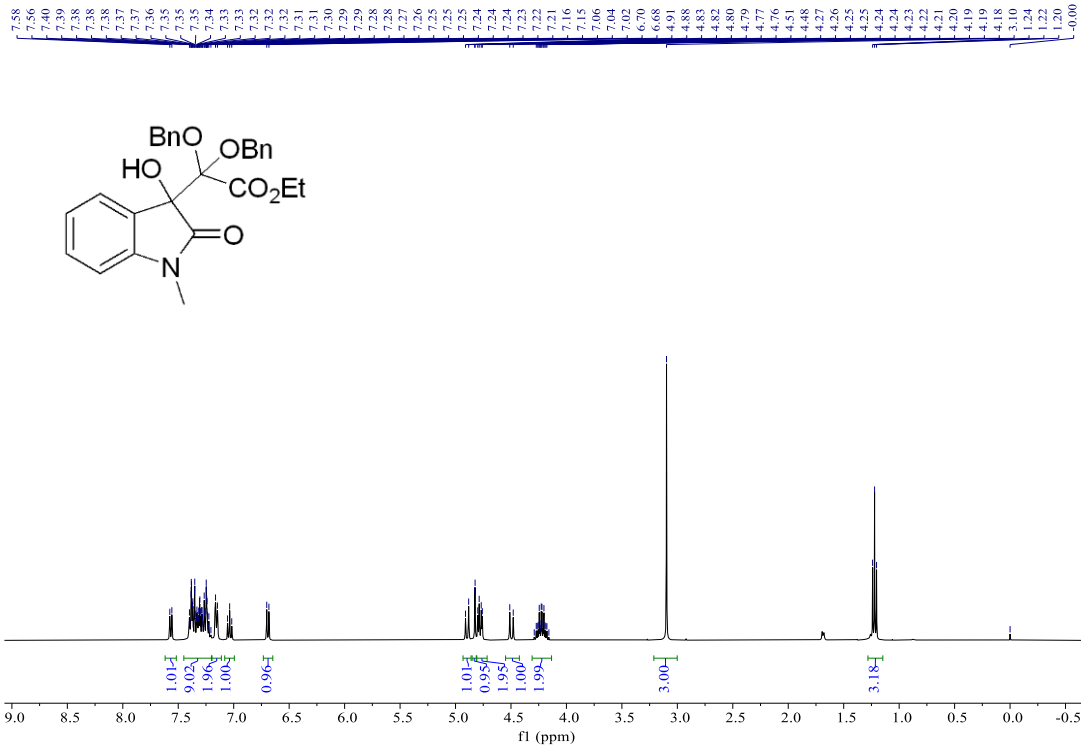
^{1}H NMR (500 MHz, DMSO) spectra for 1bd



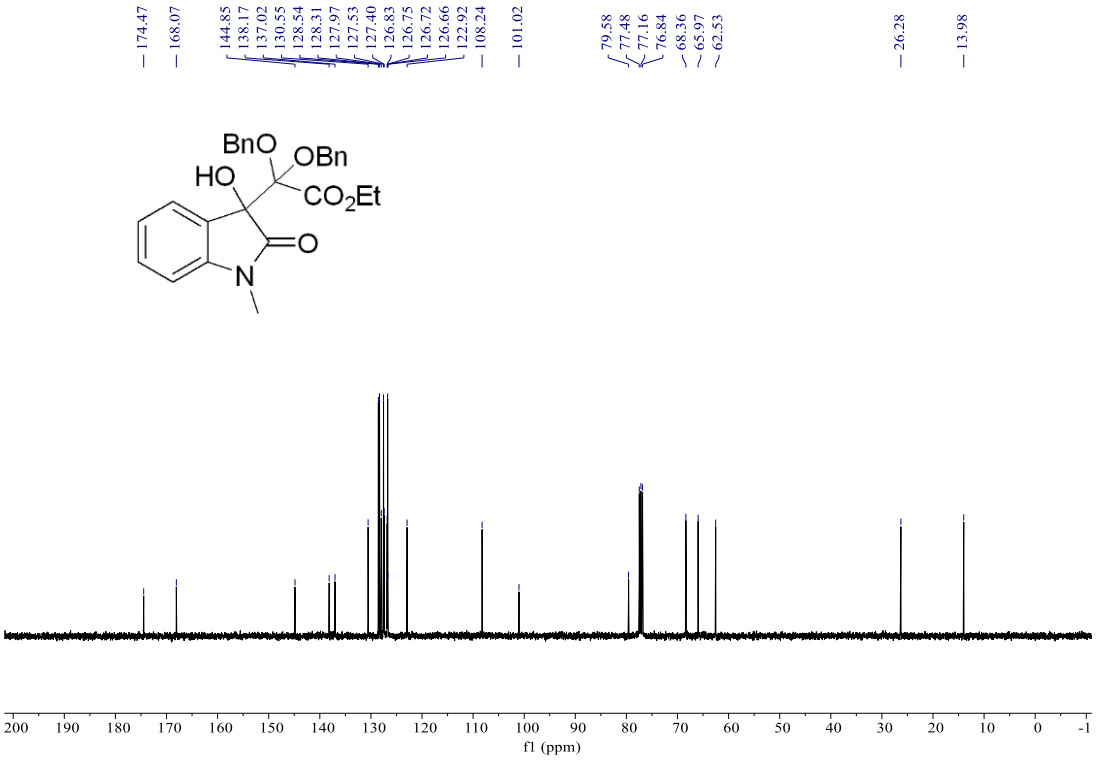
^{13}C NMR (125 MHz, DMSO) spectra for 1e



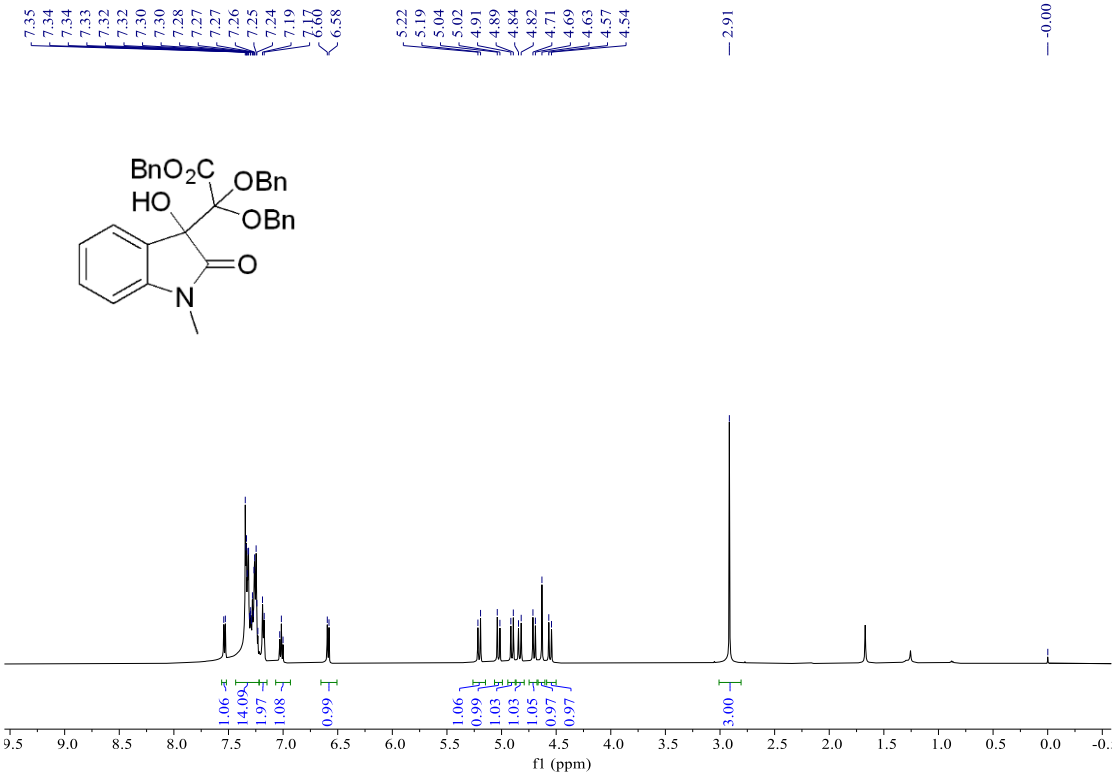
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4a



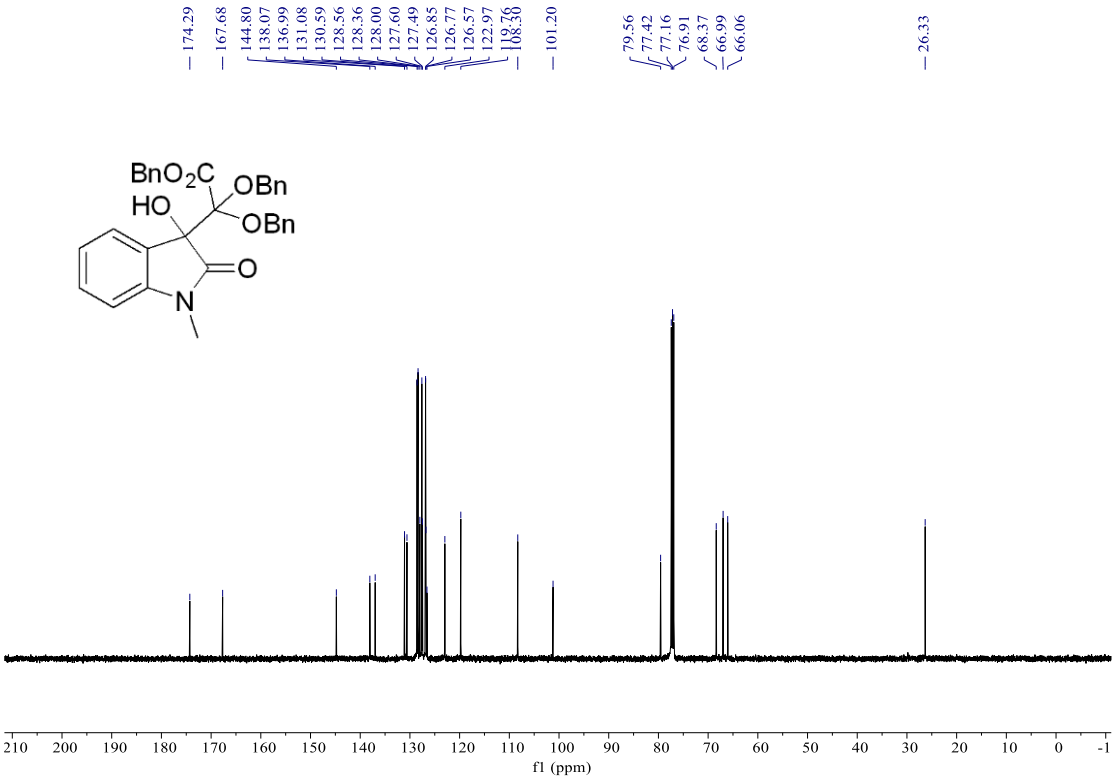
^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4a



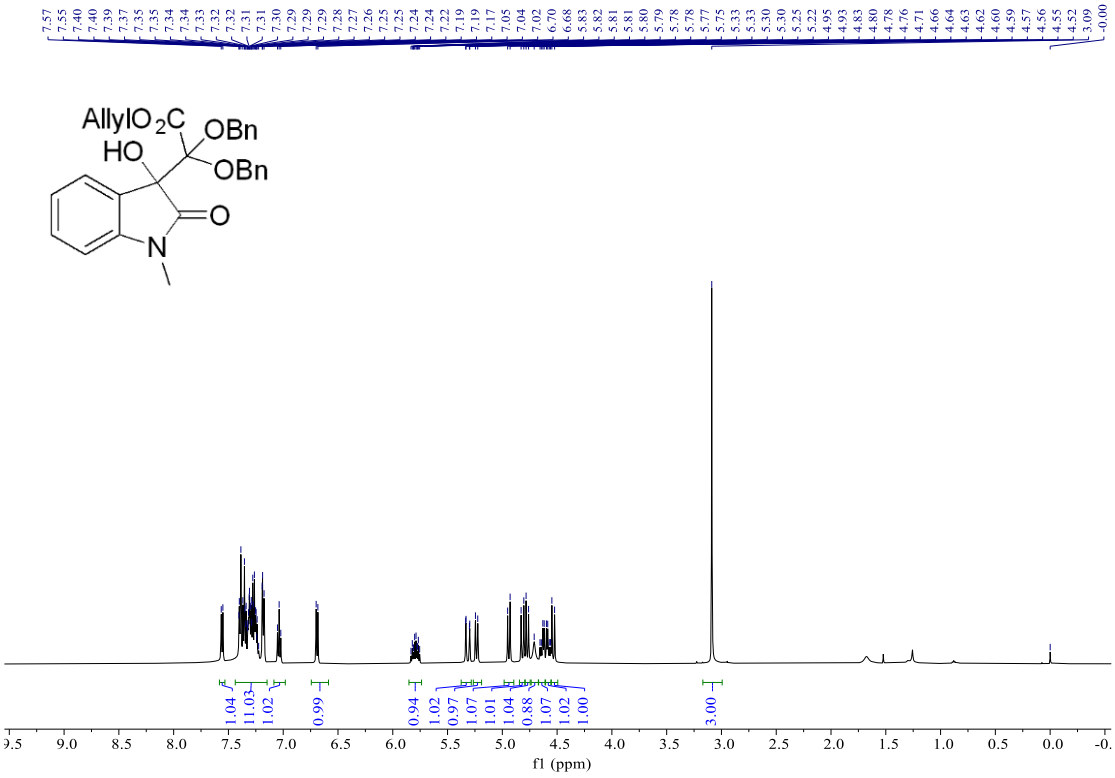
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4b



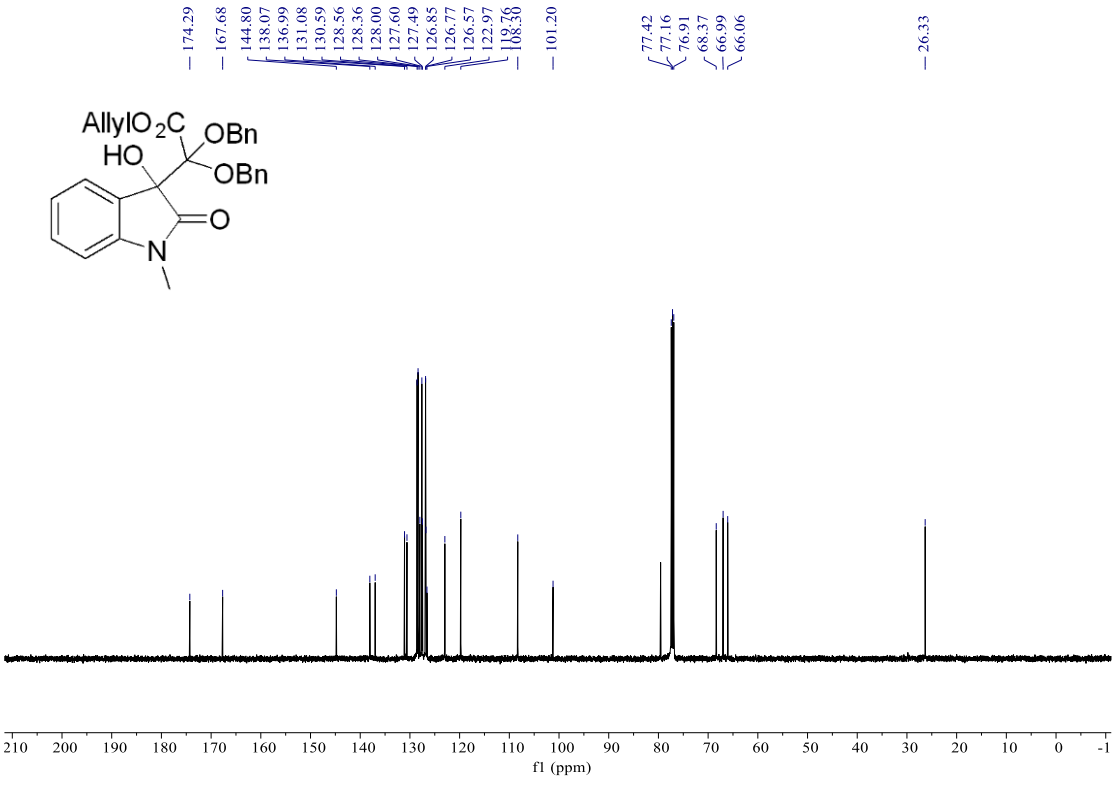
^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4b



^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4c



^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4c



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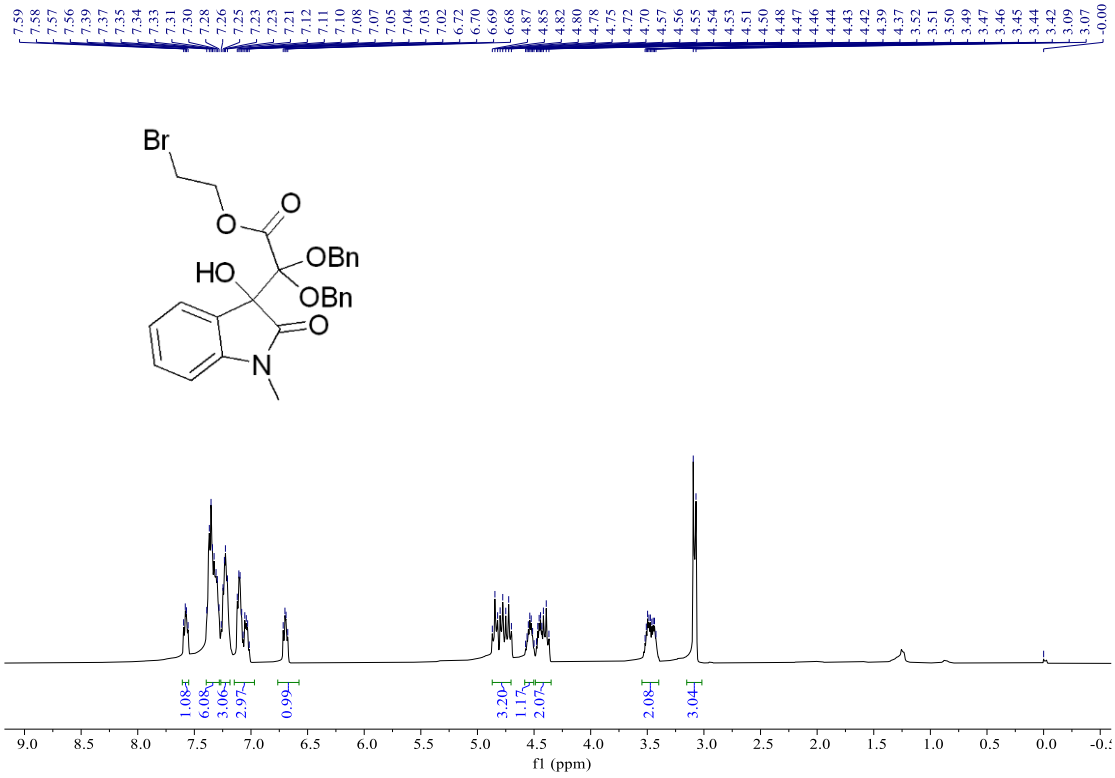

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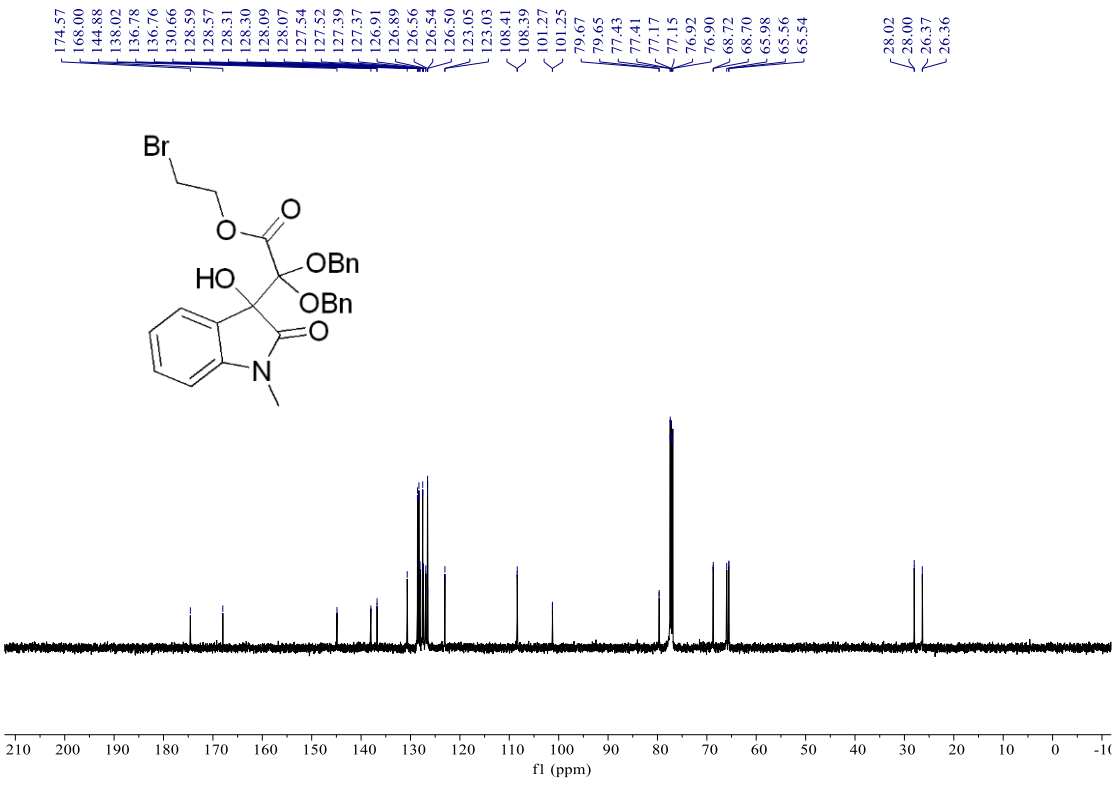
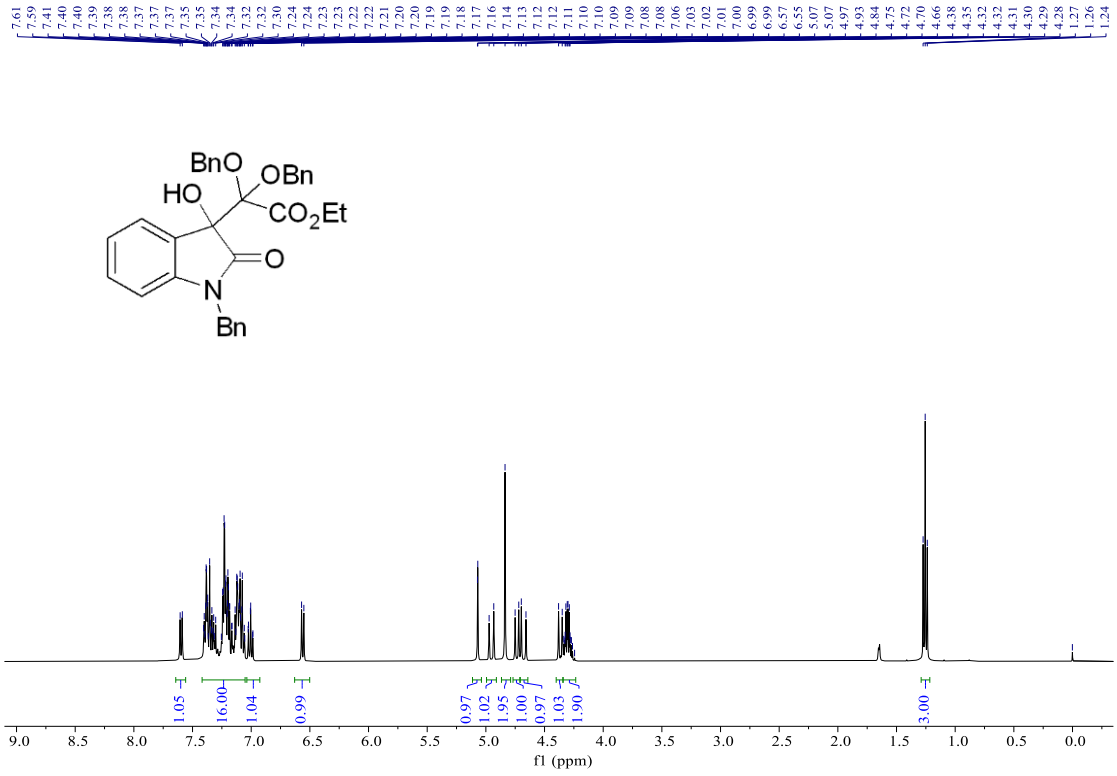
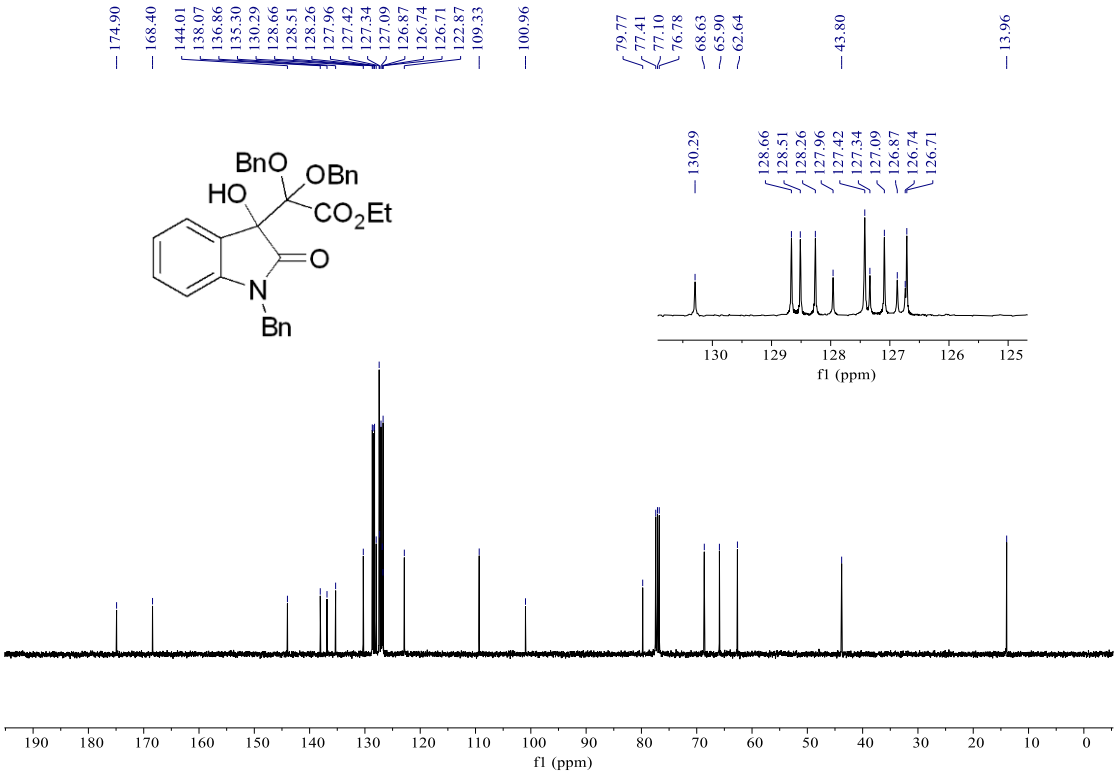


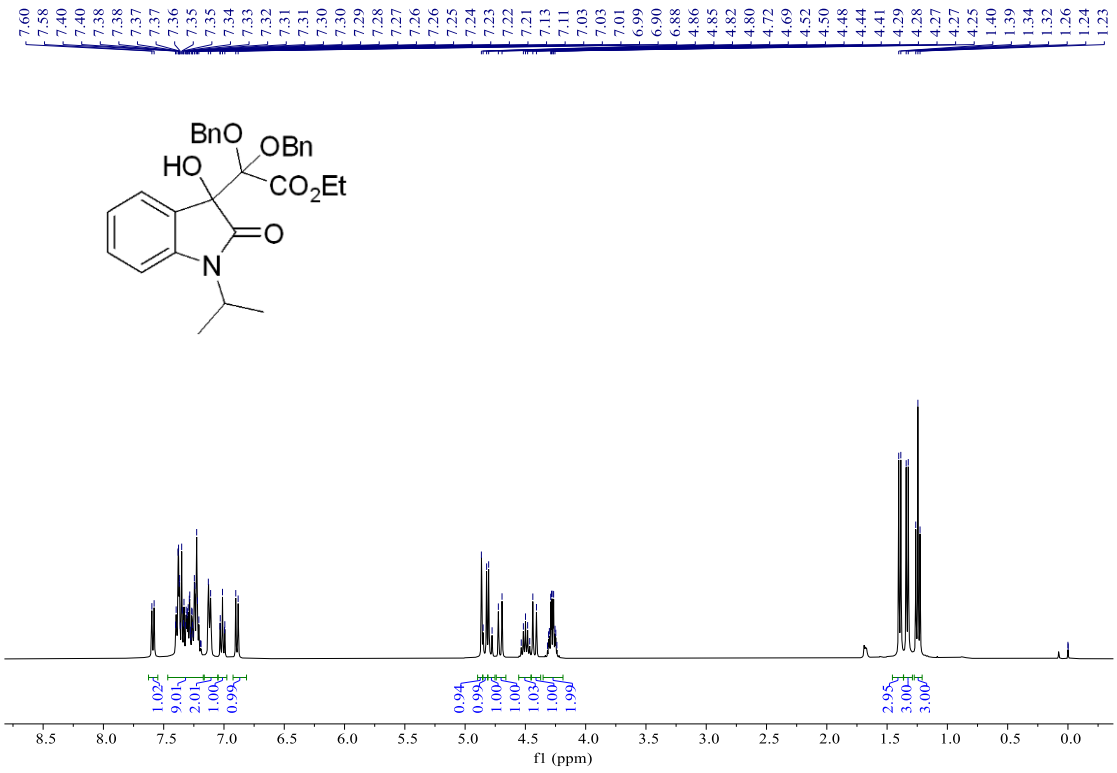
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4e



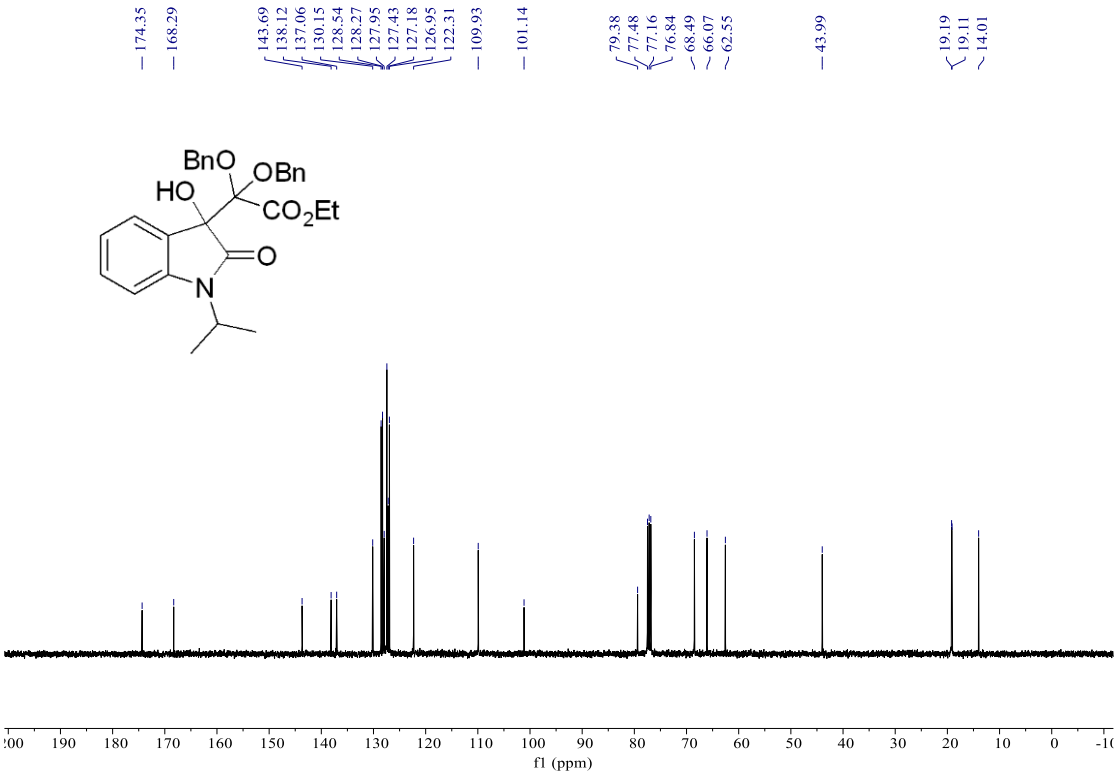
^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4e



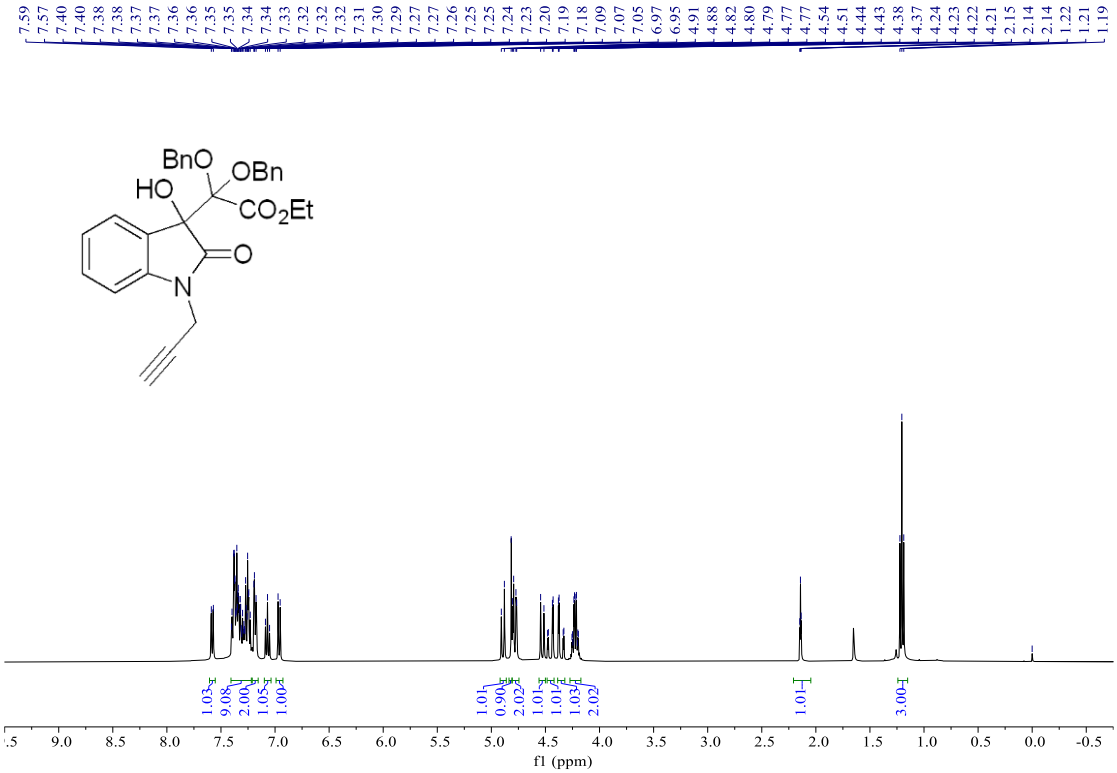
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4f



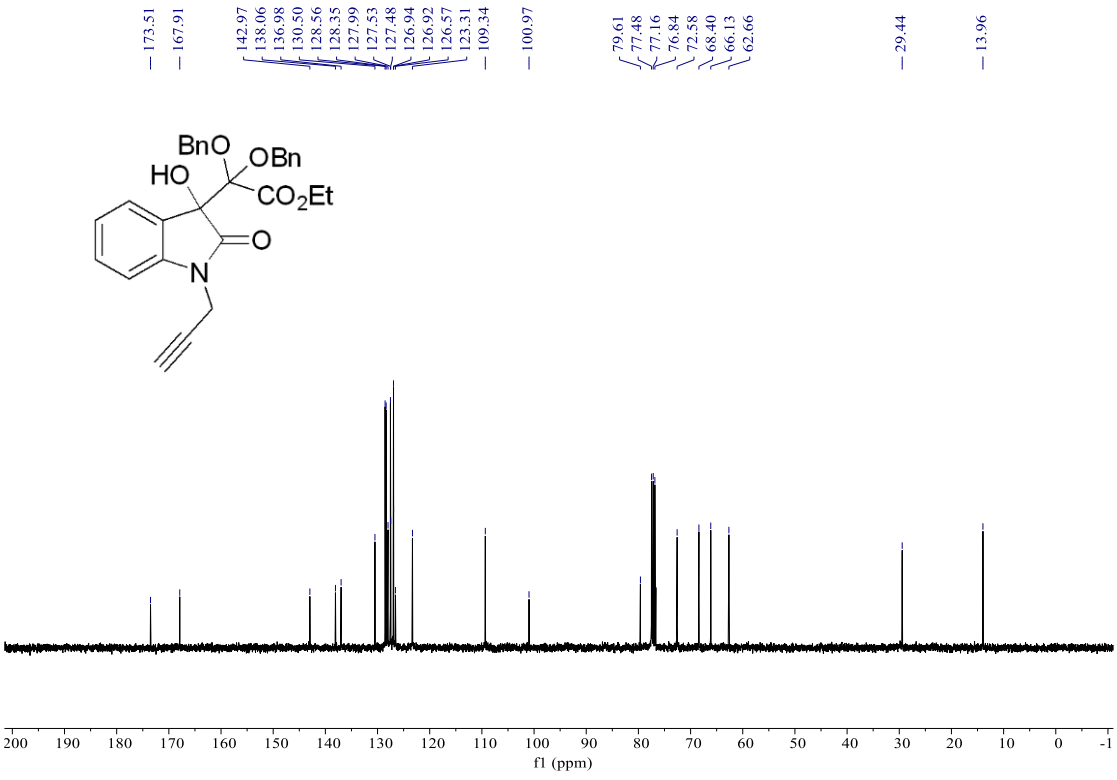
^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4f



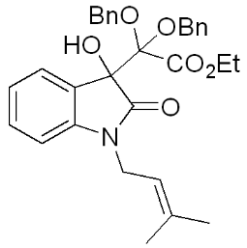
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4g

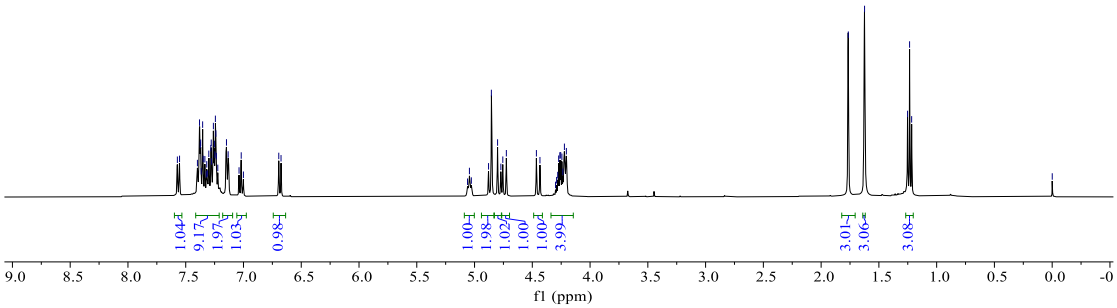


^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4g

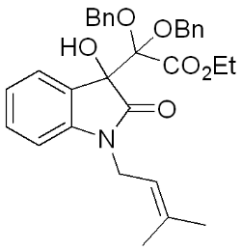


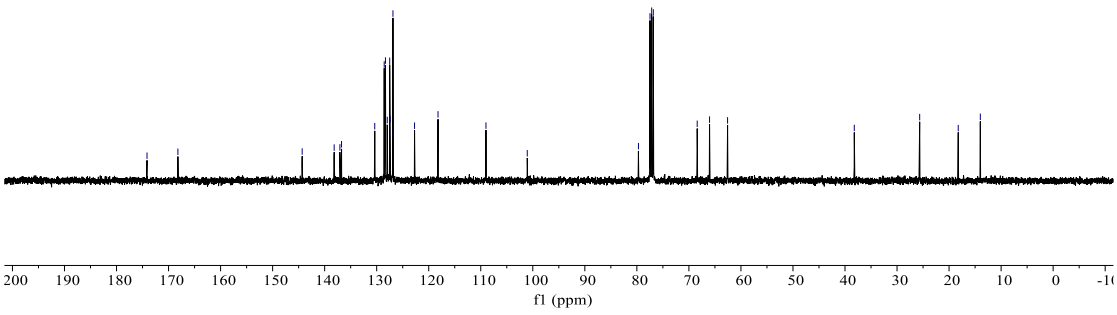
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4h



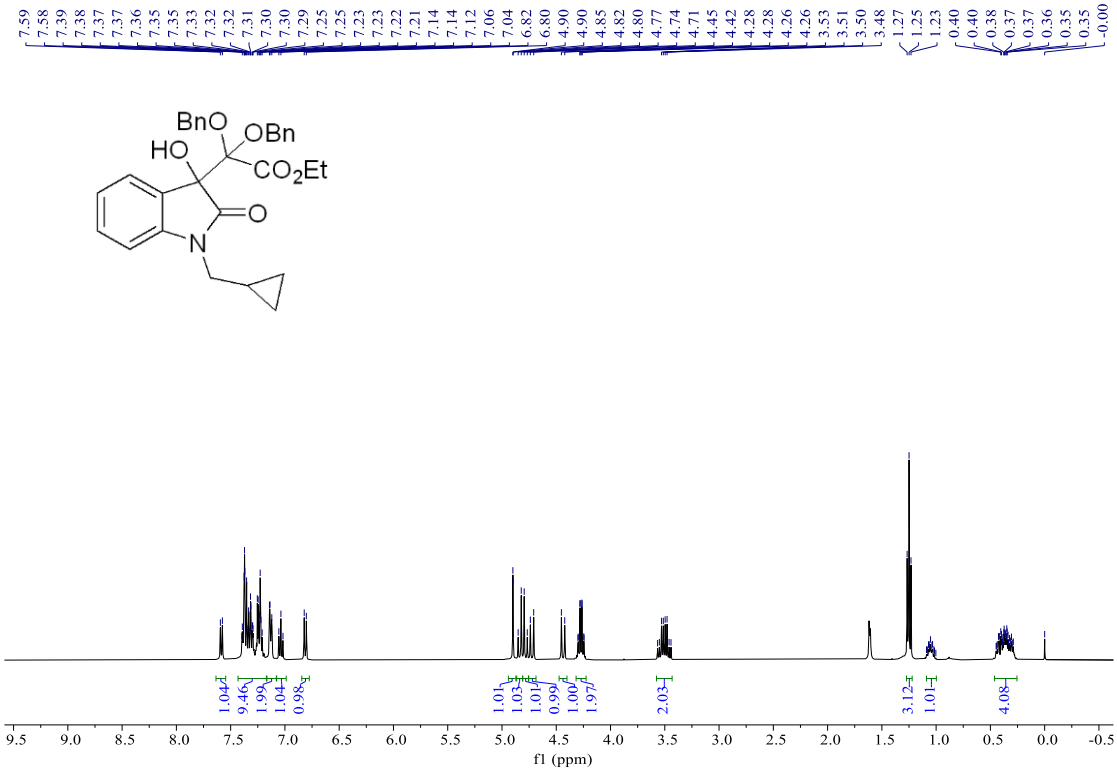


^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4h

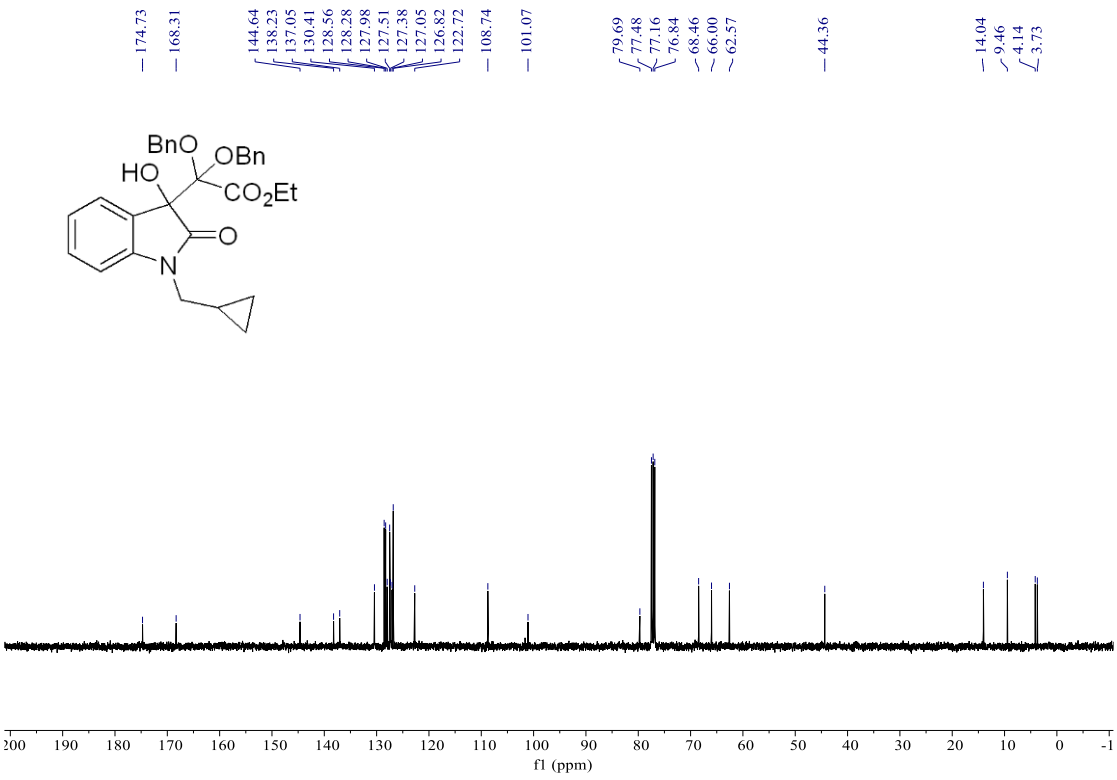




^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4i



^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4i



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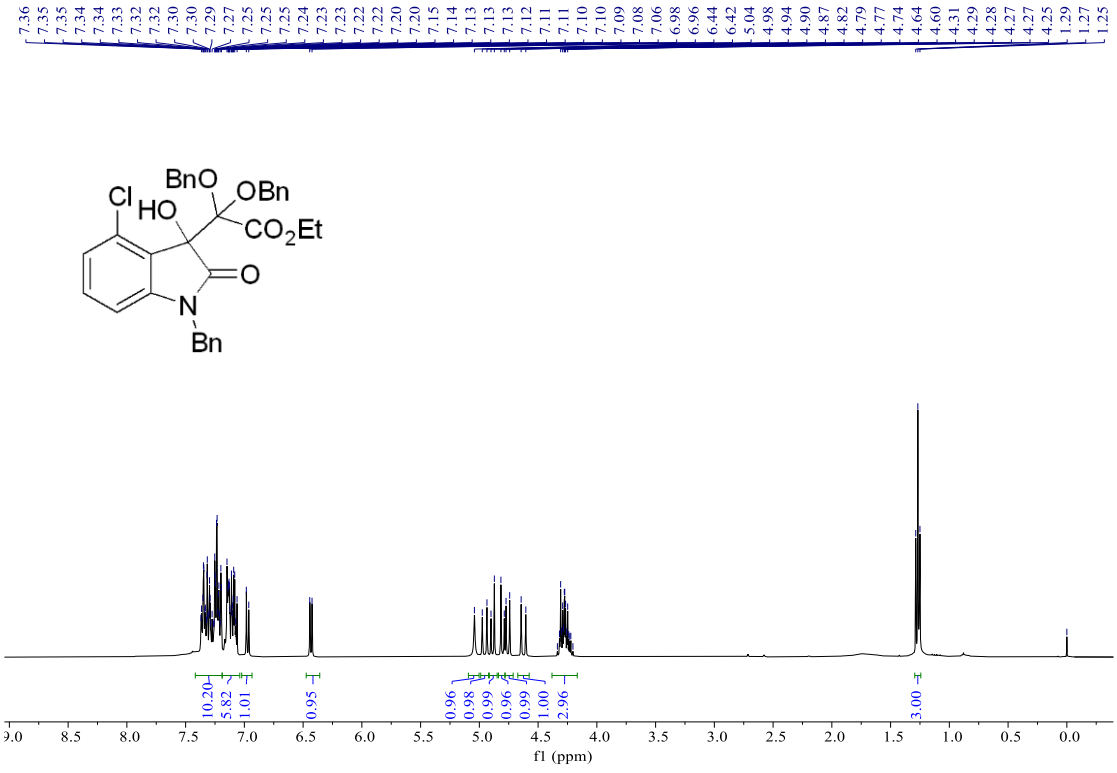
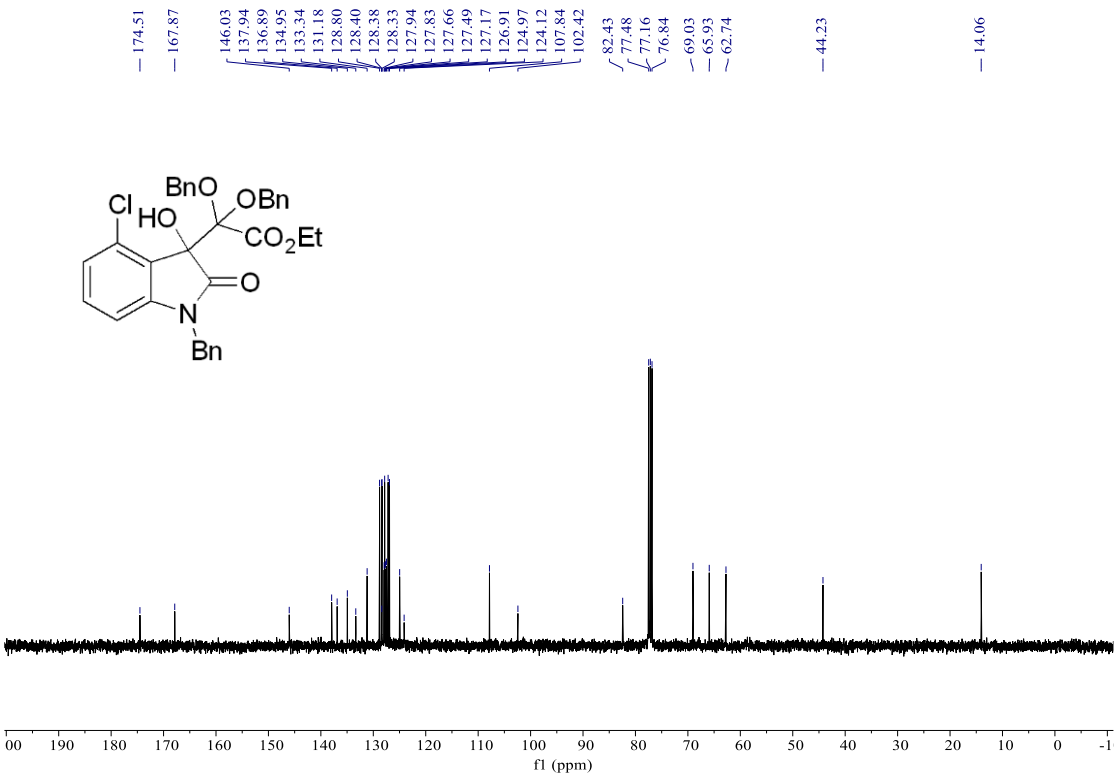
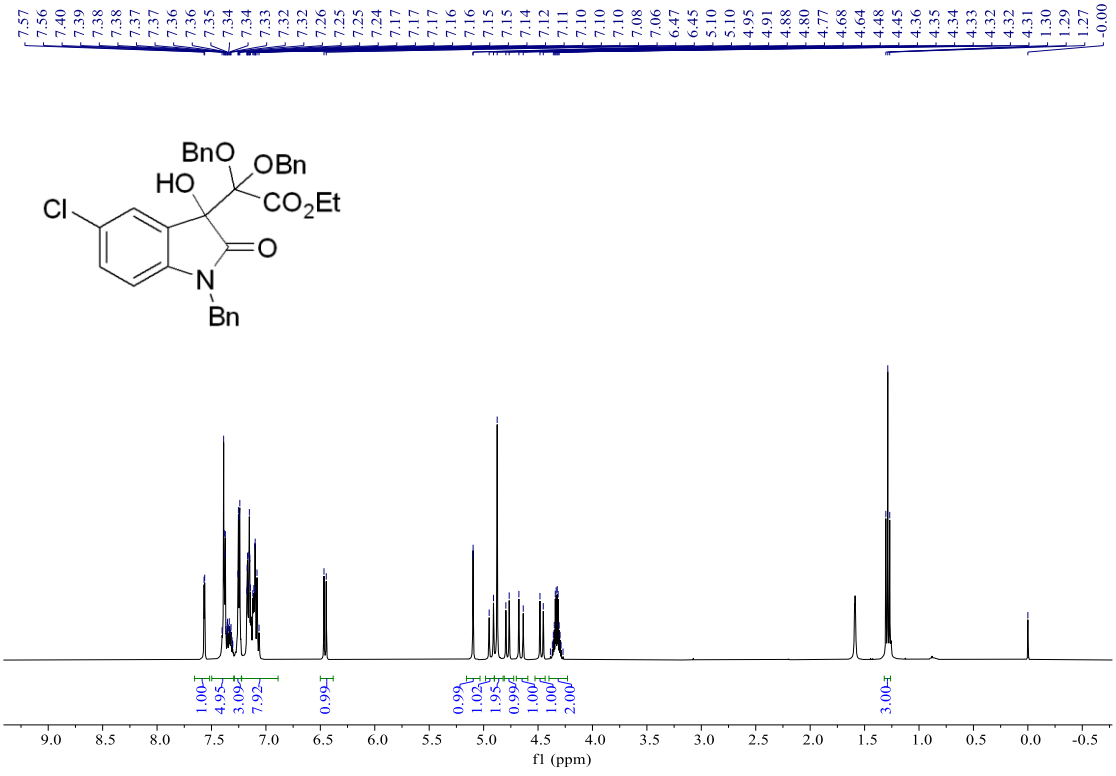


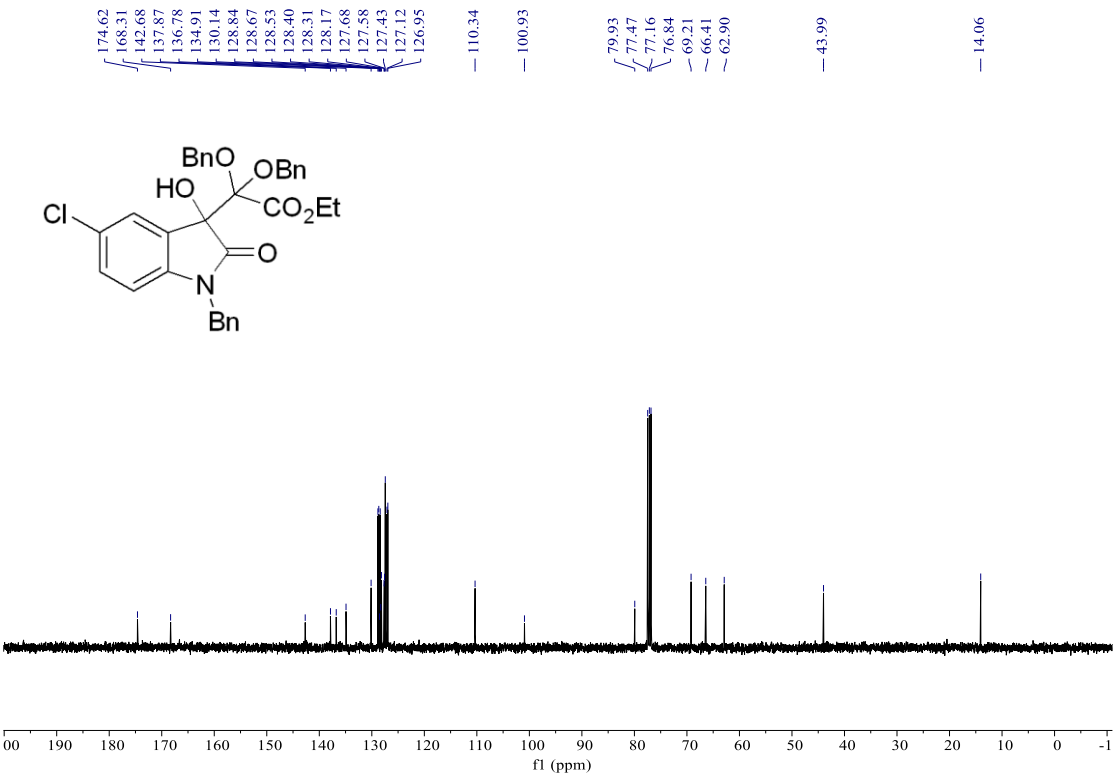
^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4j



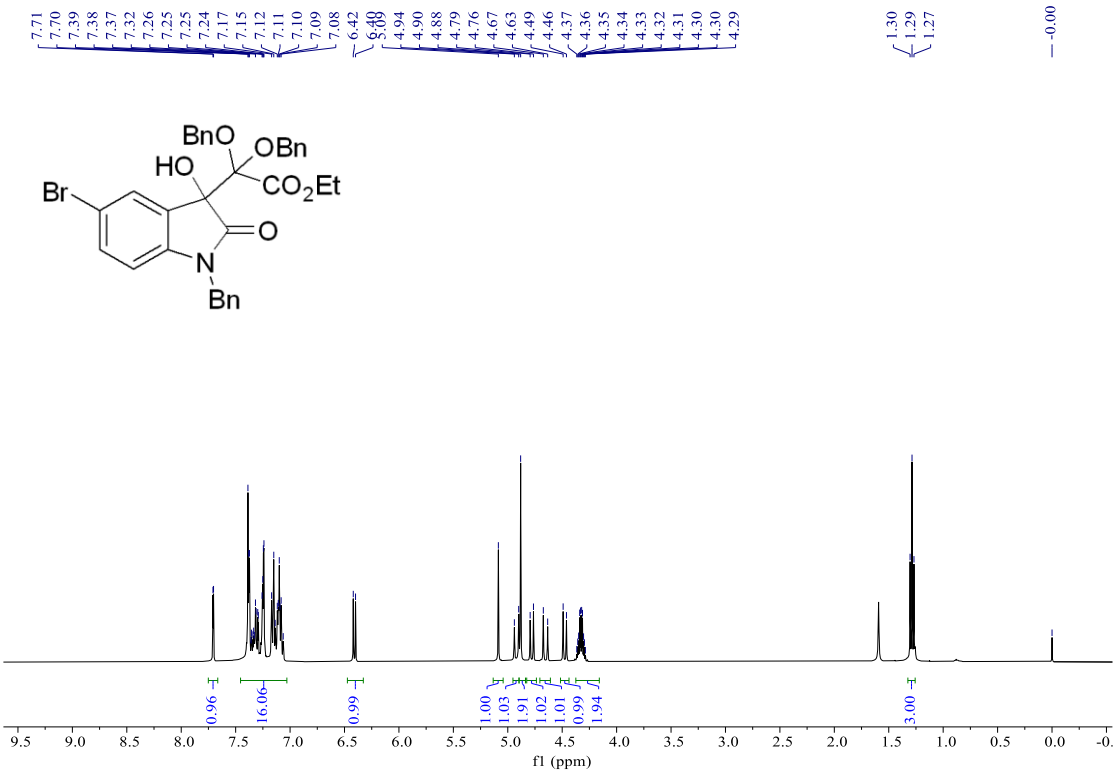
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4k



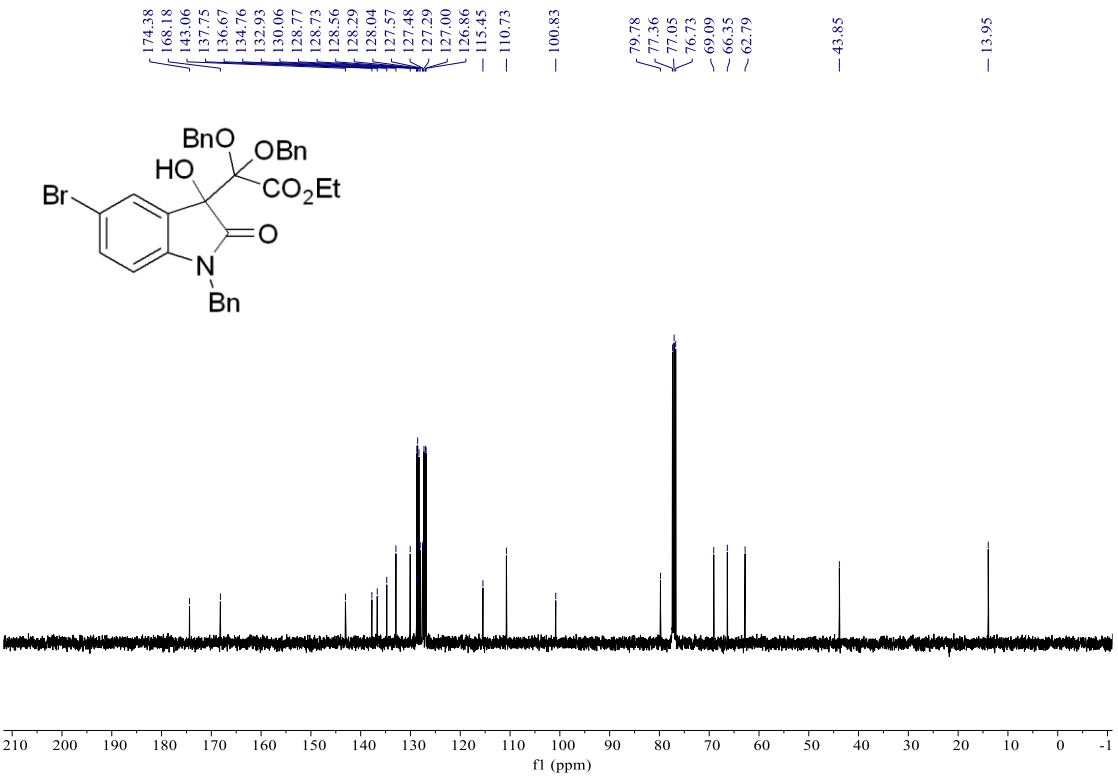
^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4k



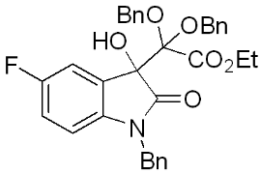
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4l

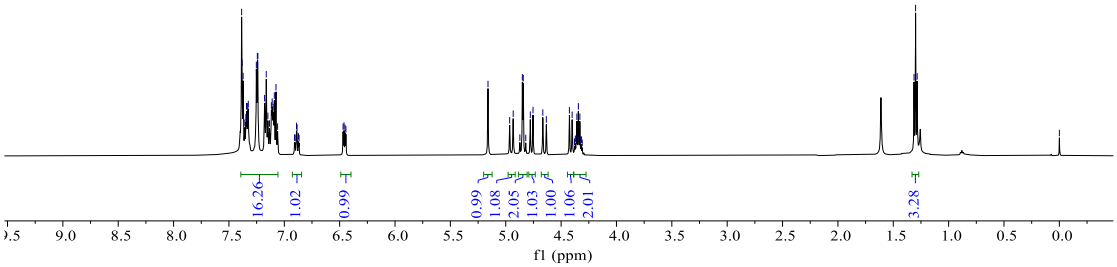


^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4l

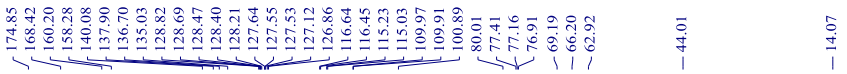


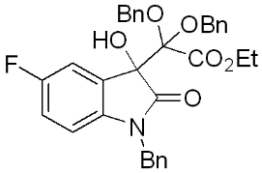
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4m

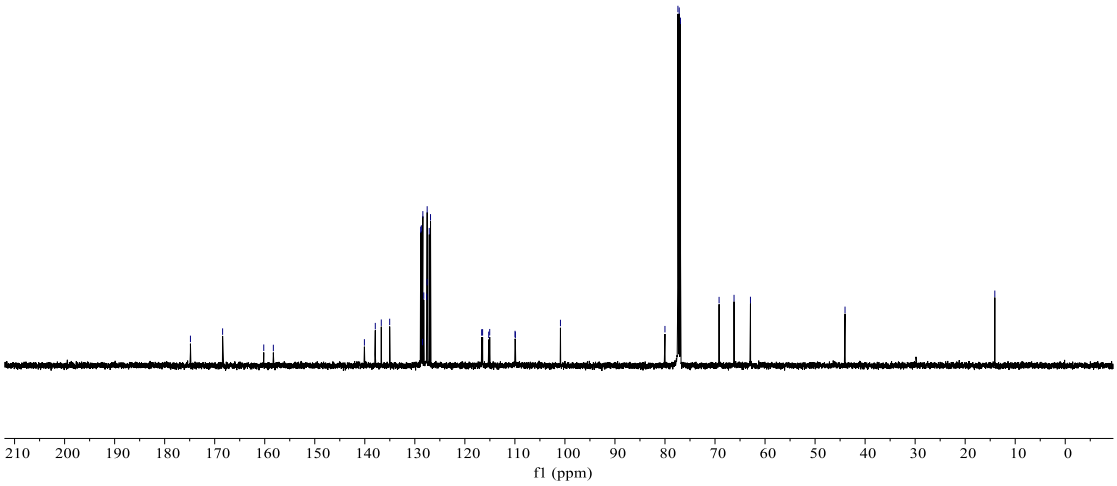




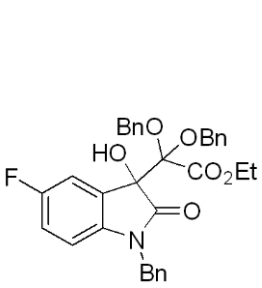
^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4m



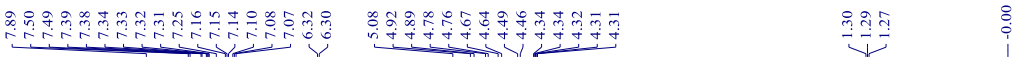


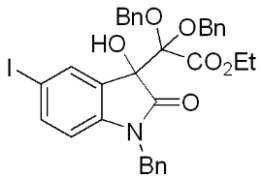


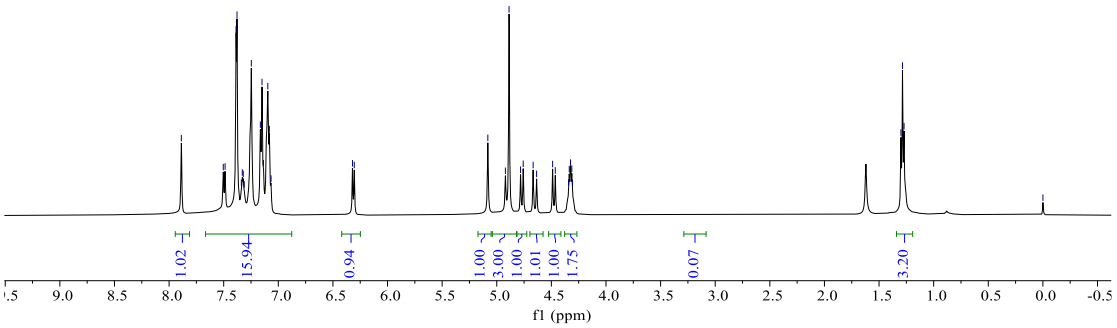
^{19}F NMR (375 MHz, Chloroform-*d*) spectra for 4m



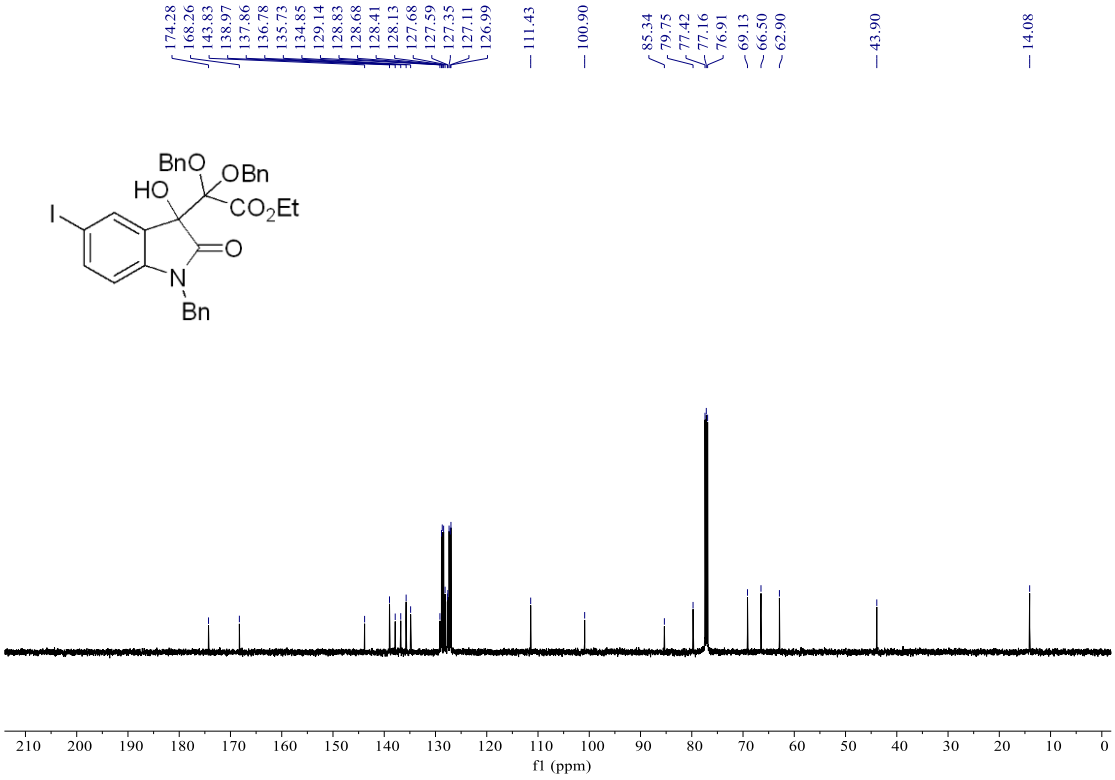
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4n



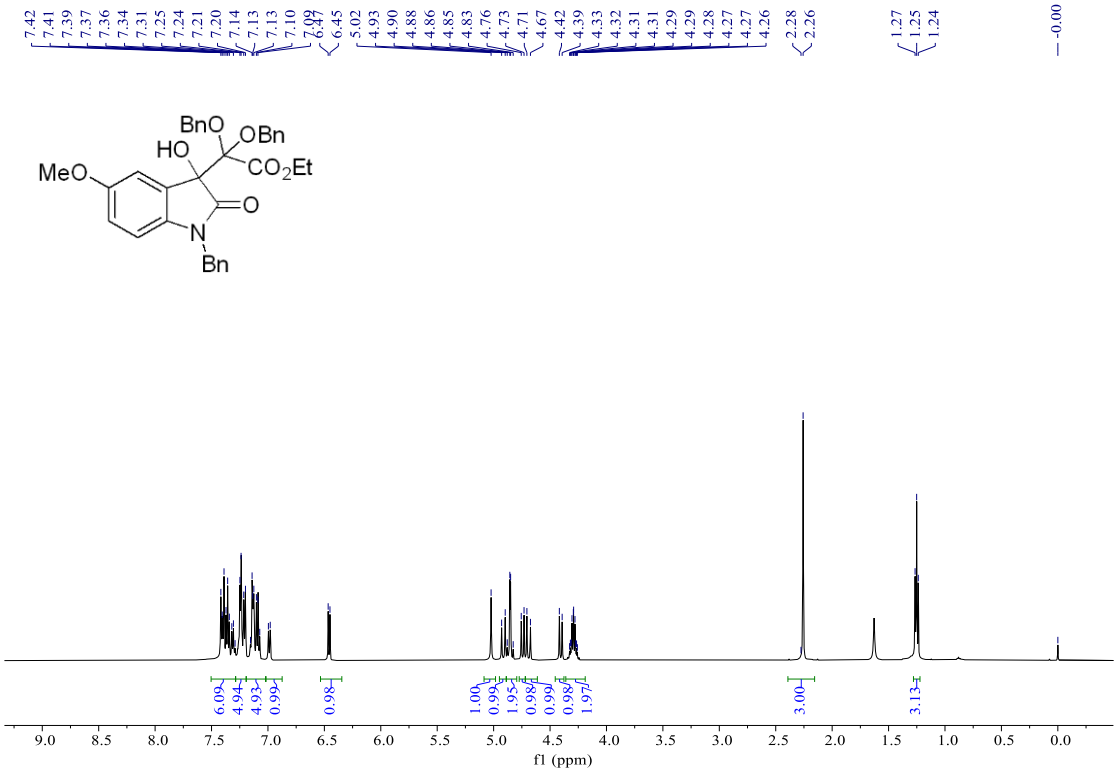




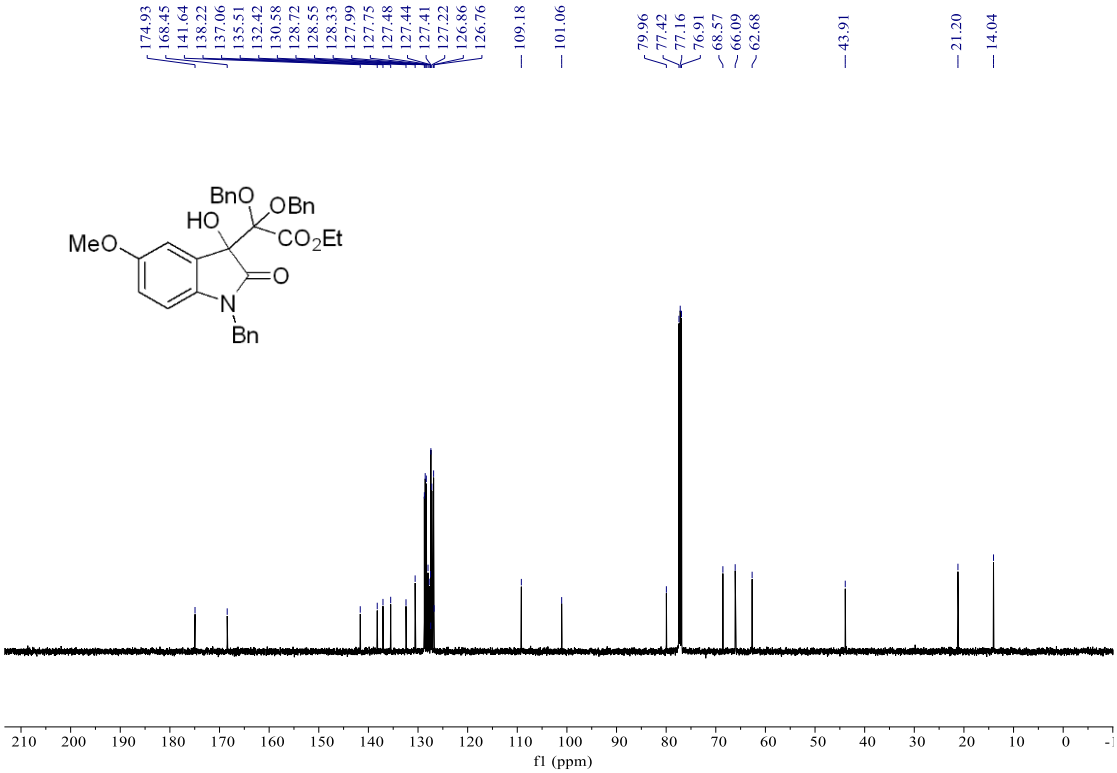
^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4n



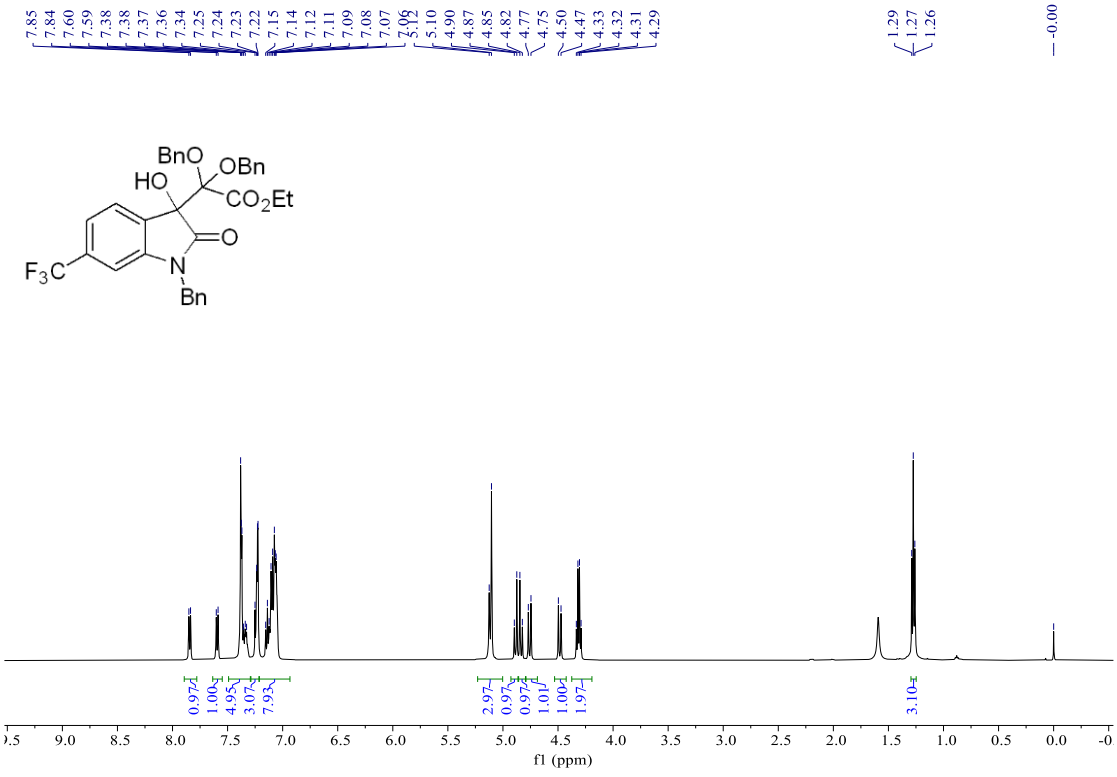
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4o



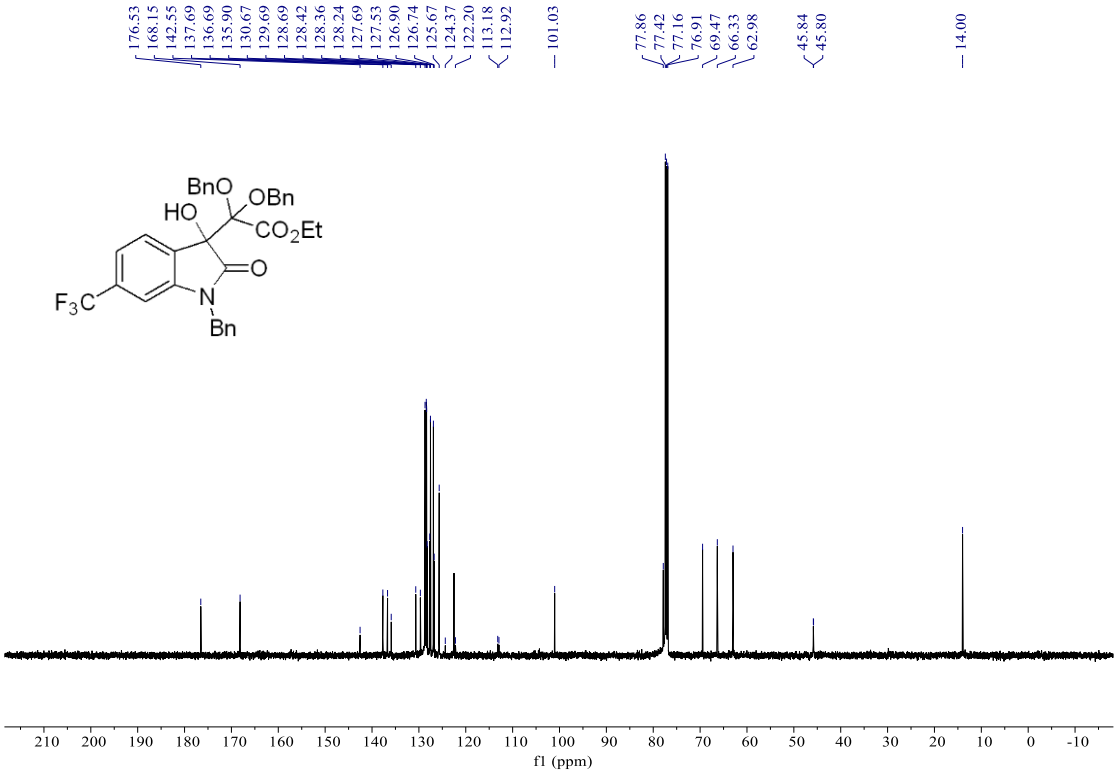
^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4o



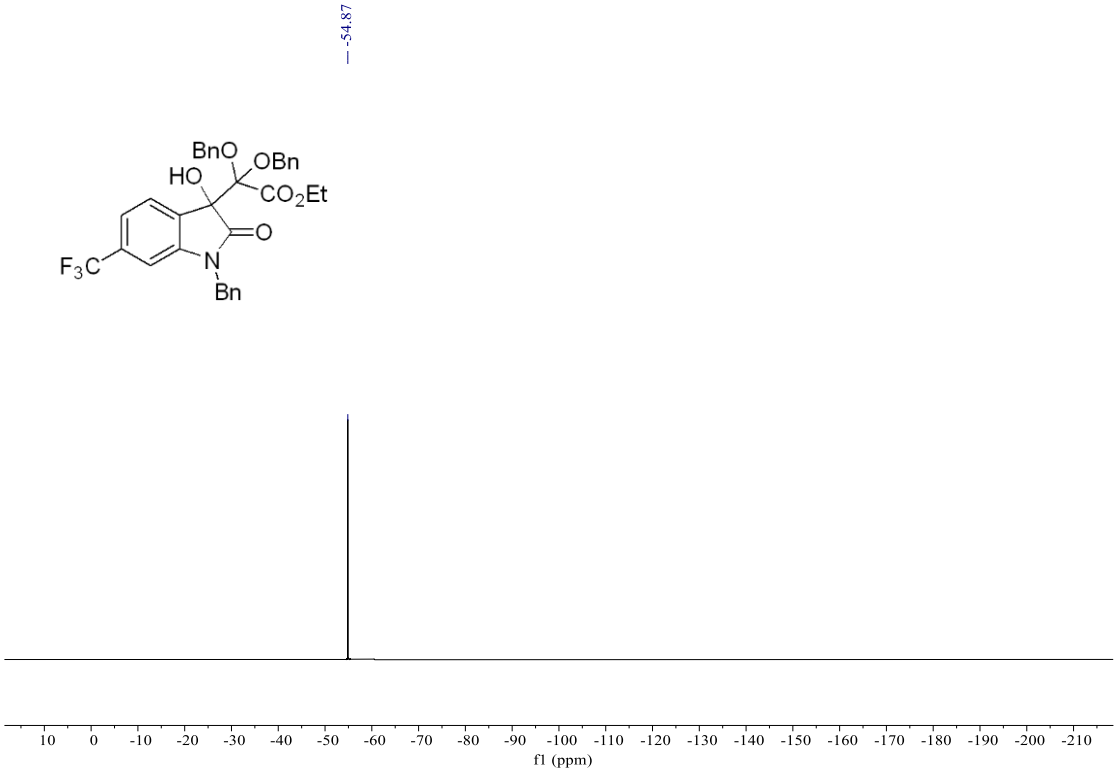
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4p



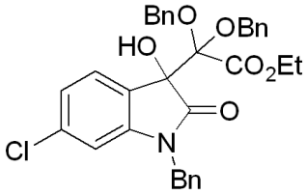
^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4p

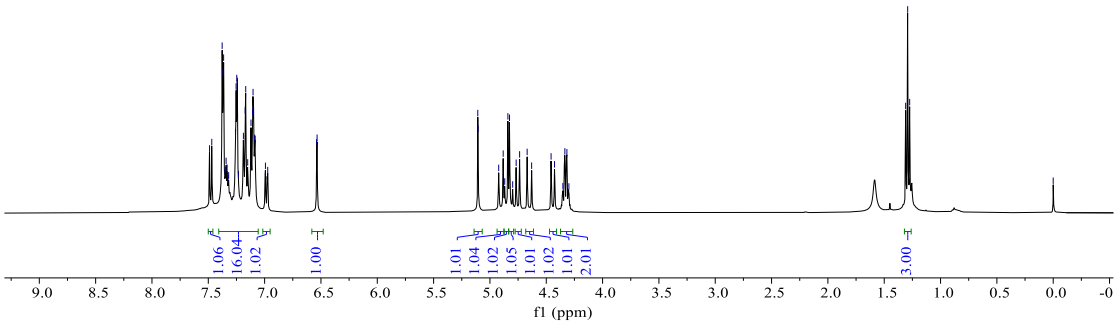


^{19}F NMR (375 MHz, Chloroform-*d*) spectra for 4p

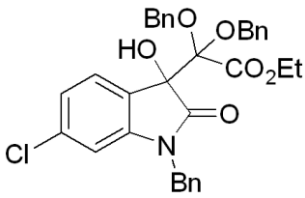


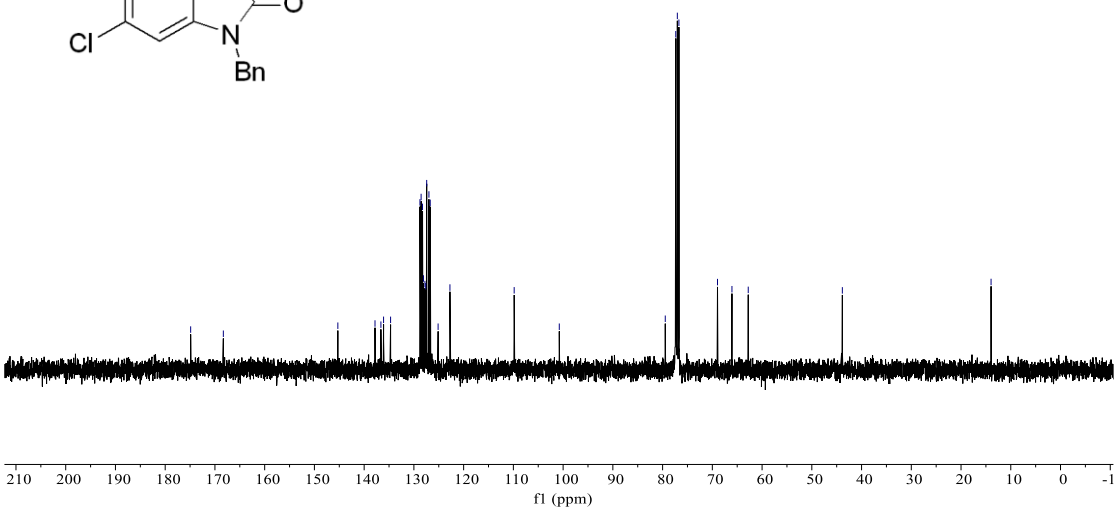
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4q



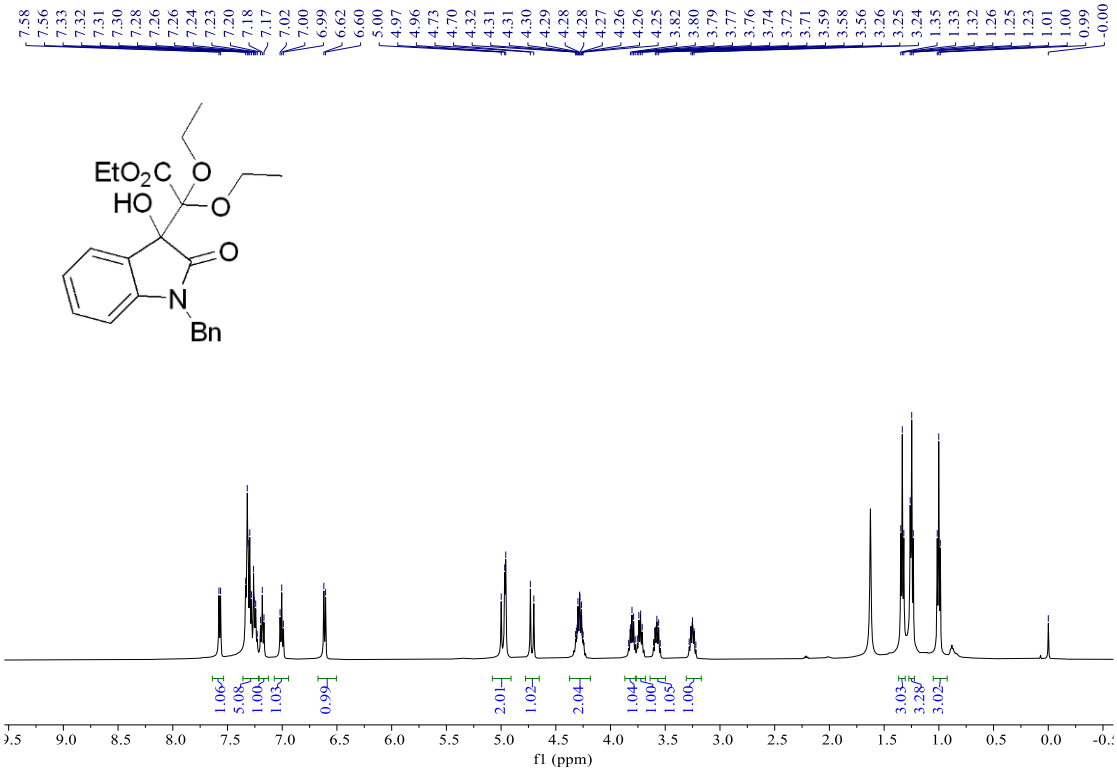


^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4q

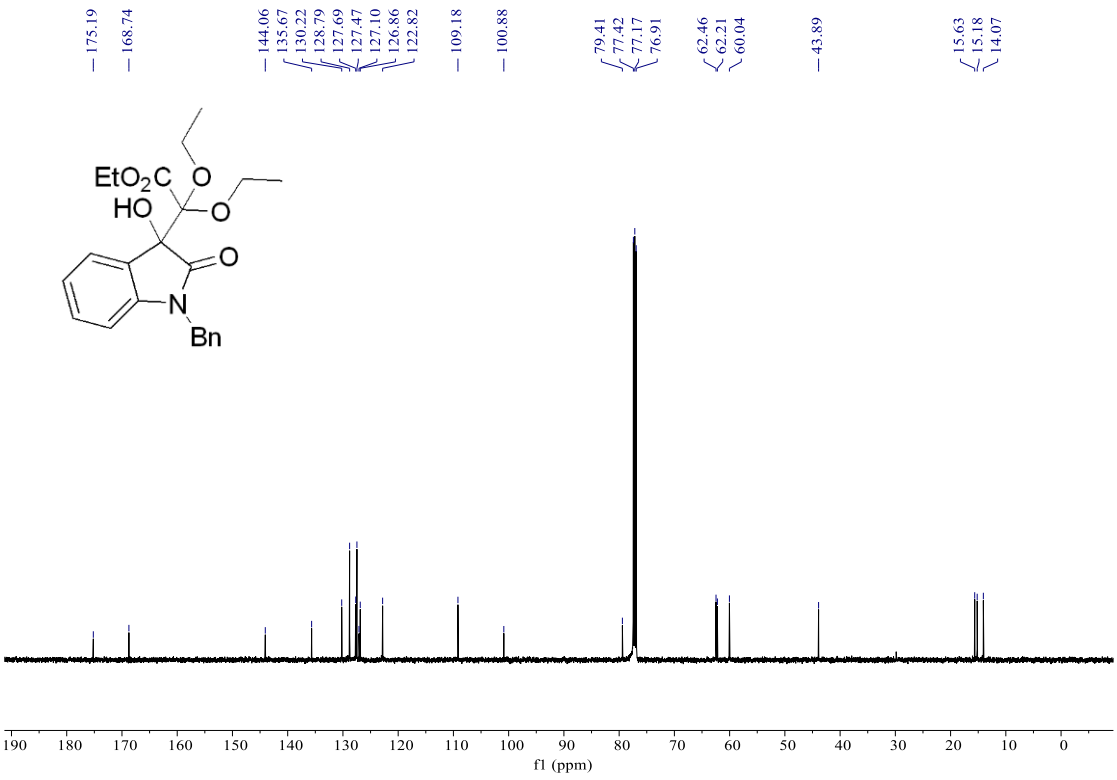




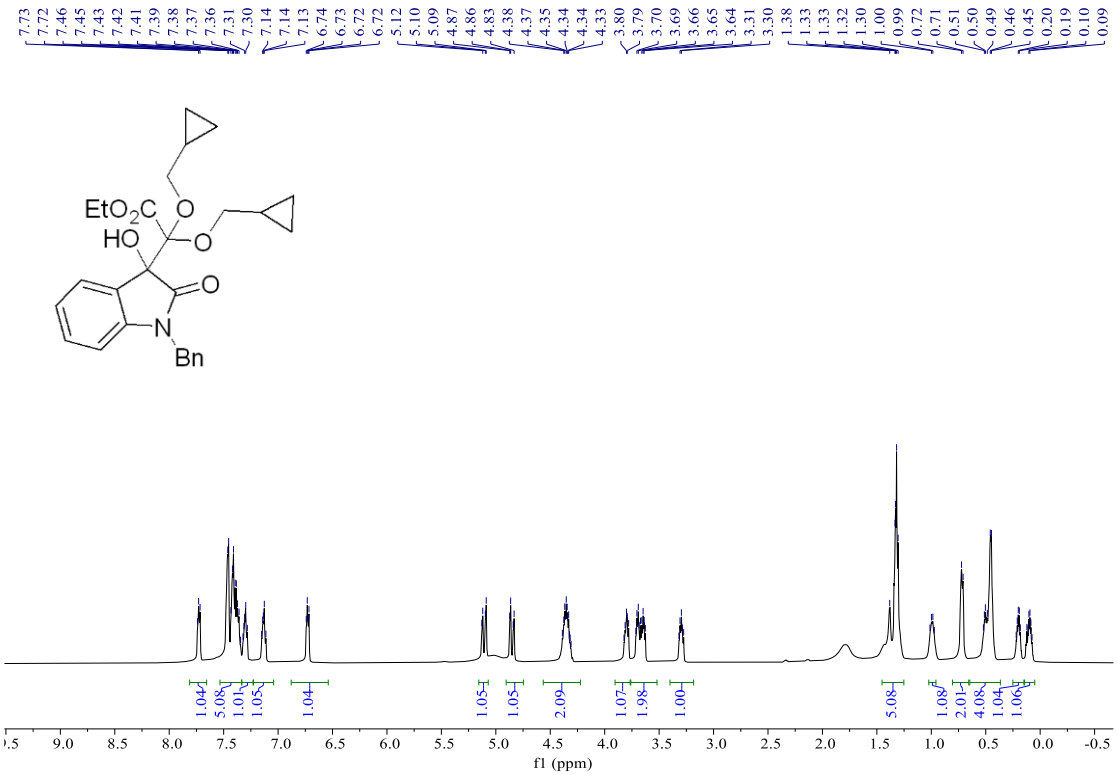
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4r



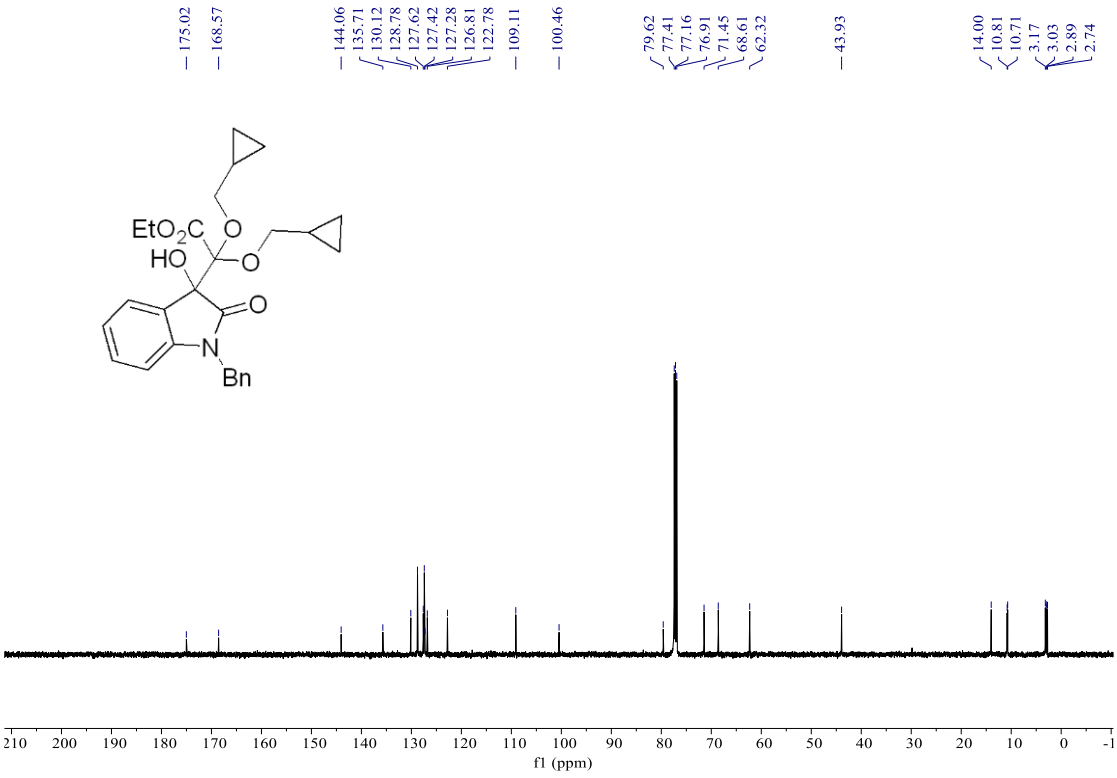
^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4r



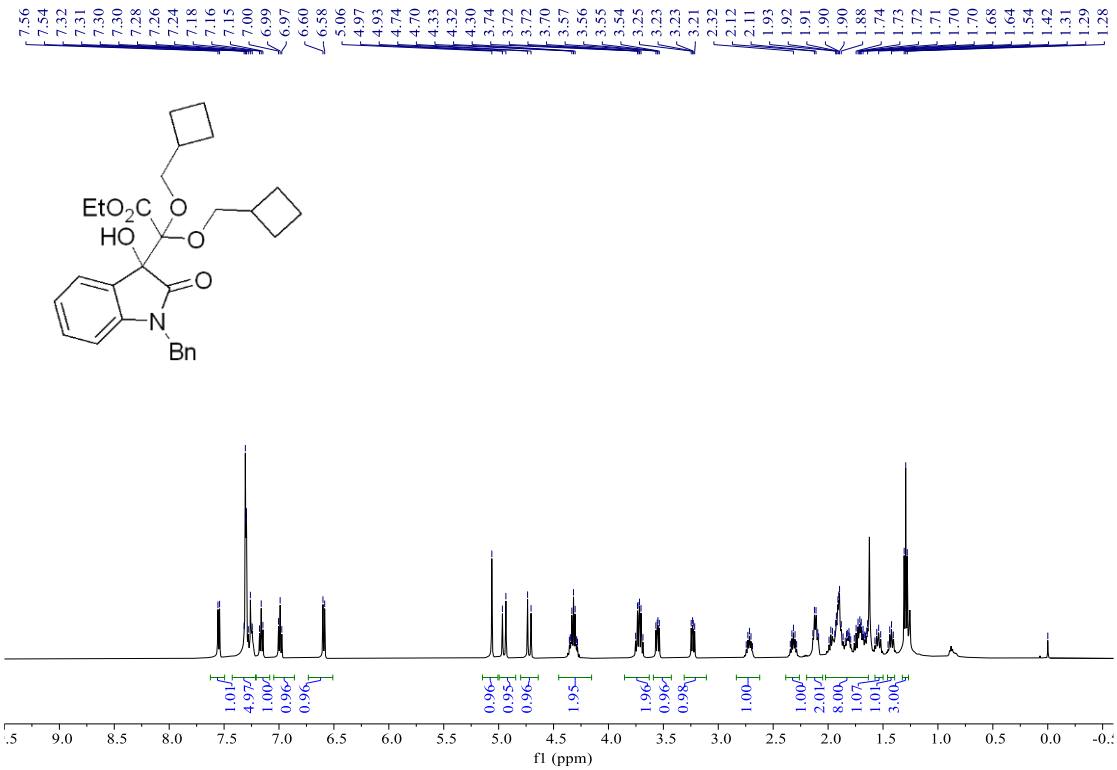
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4s



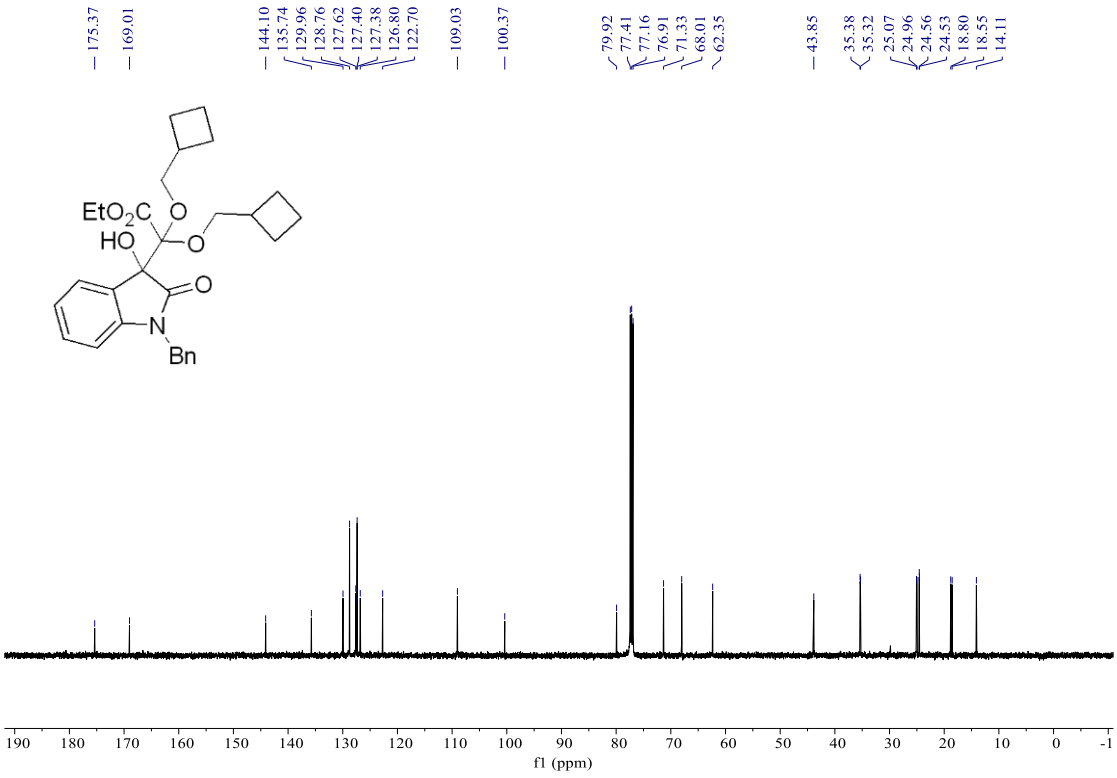
^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4s



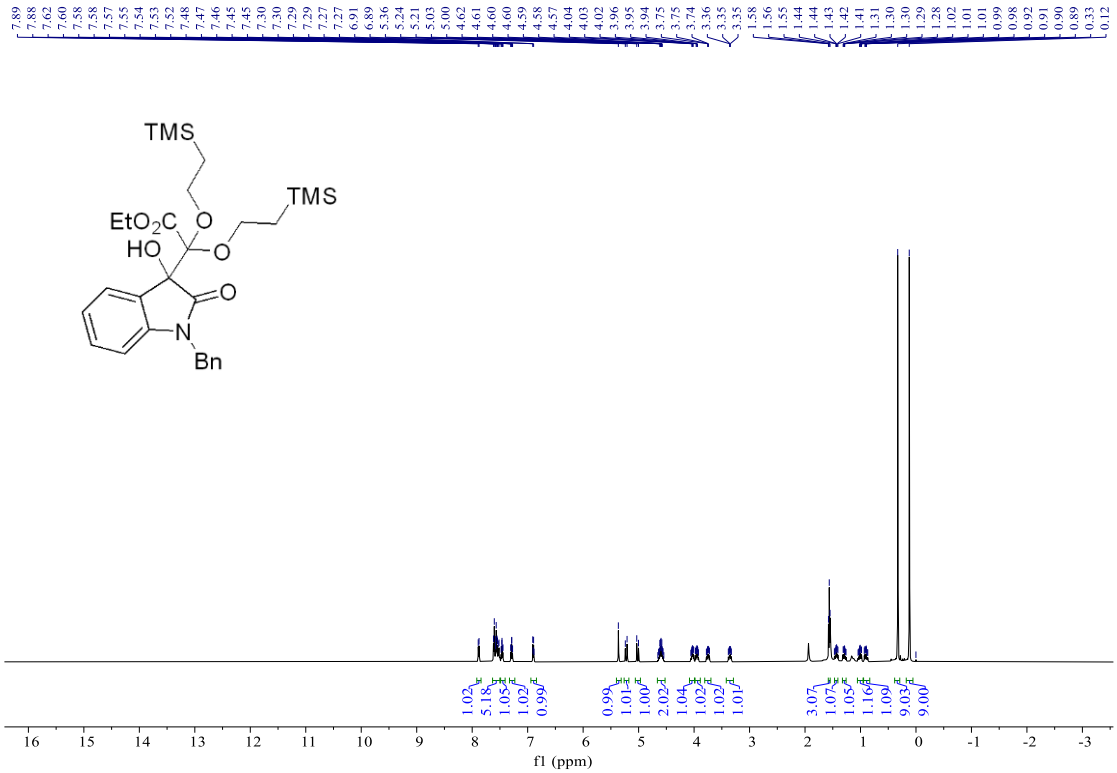
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4t



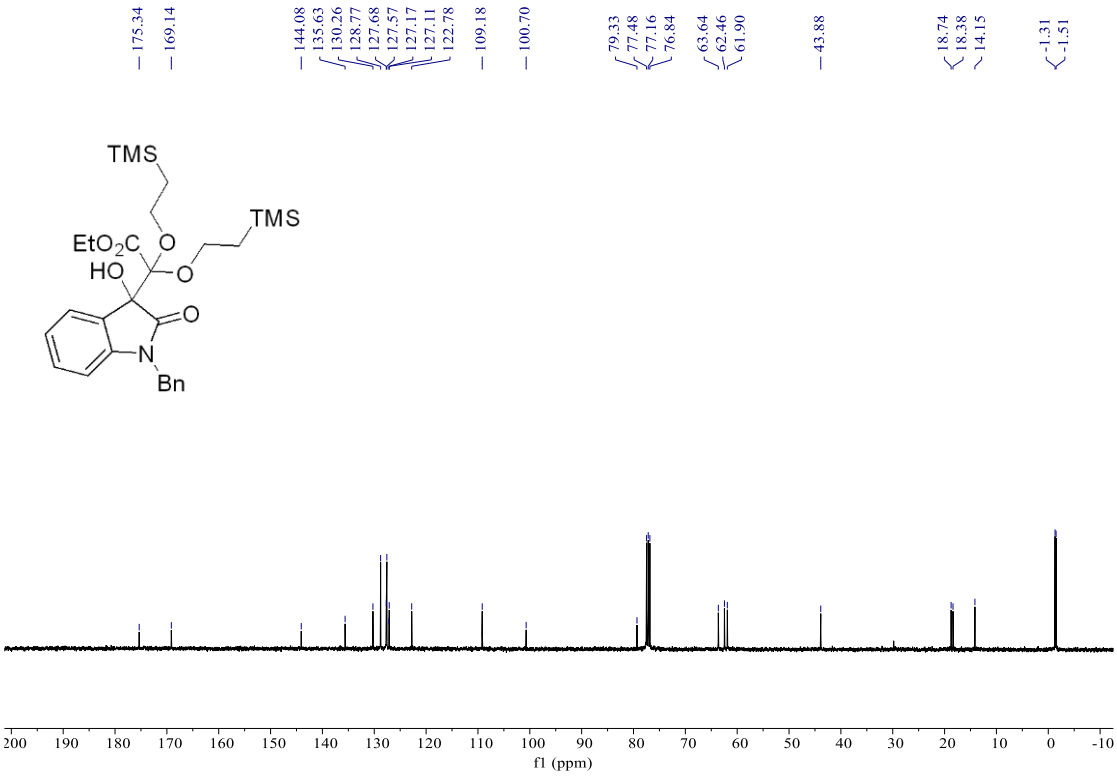
^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4t



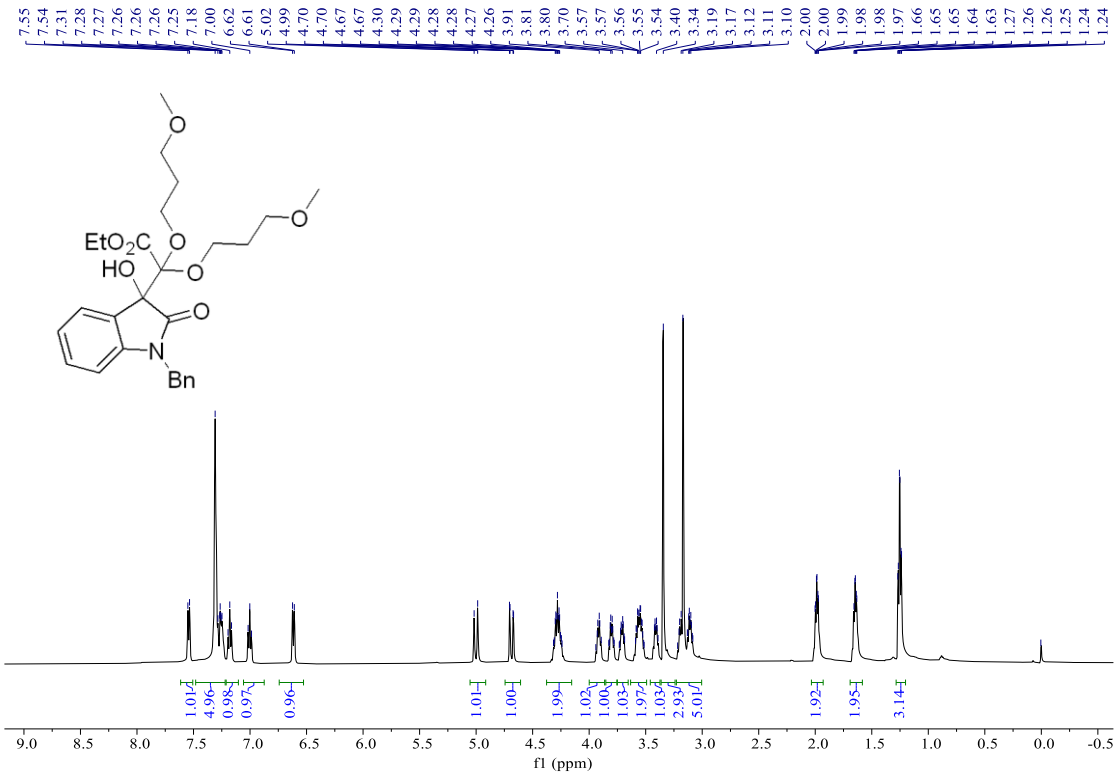
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4u



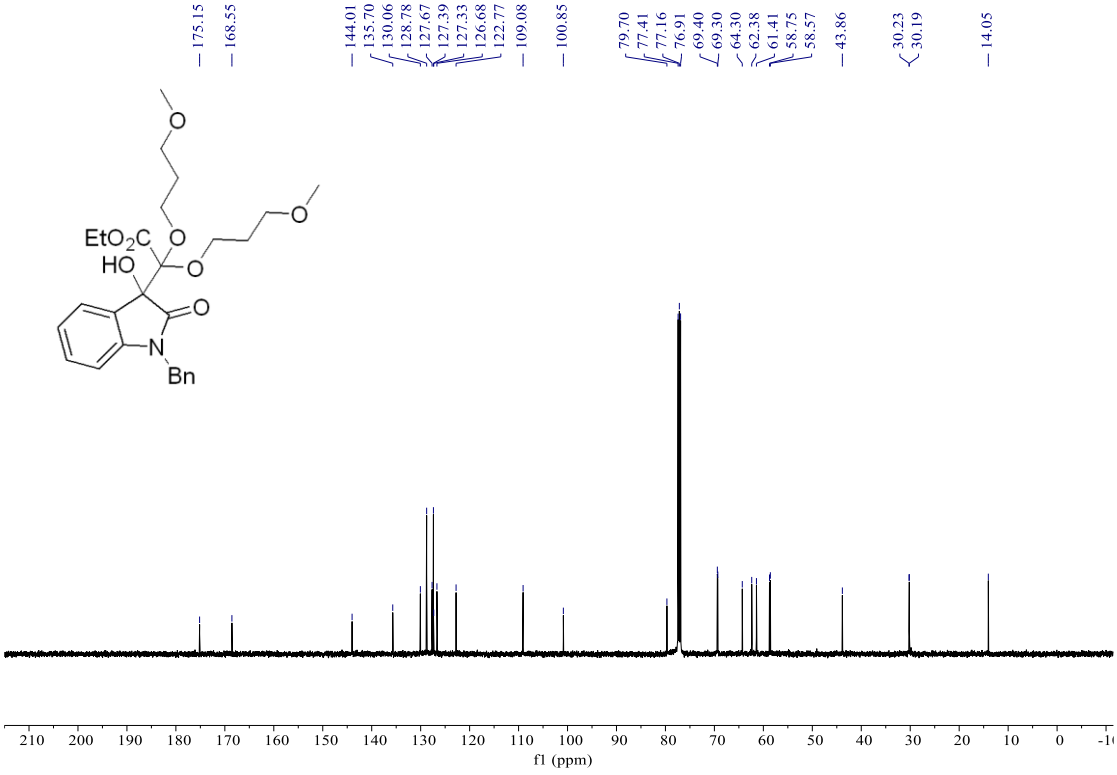
^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4u



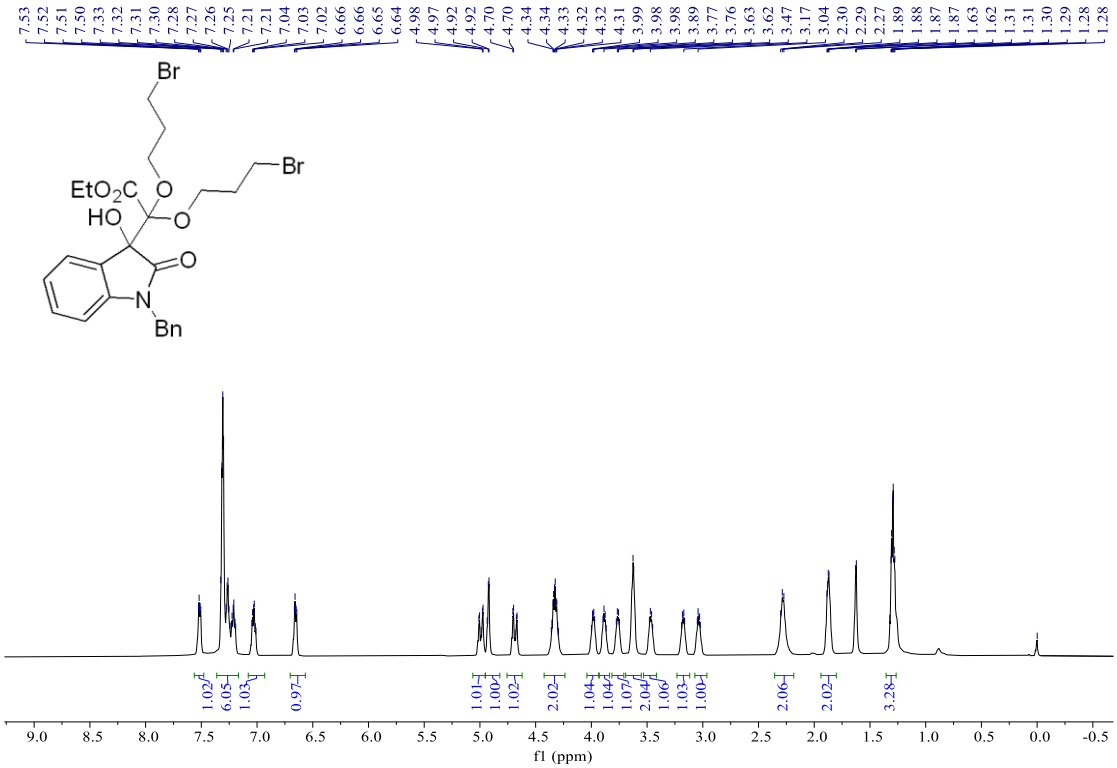
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4v



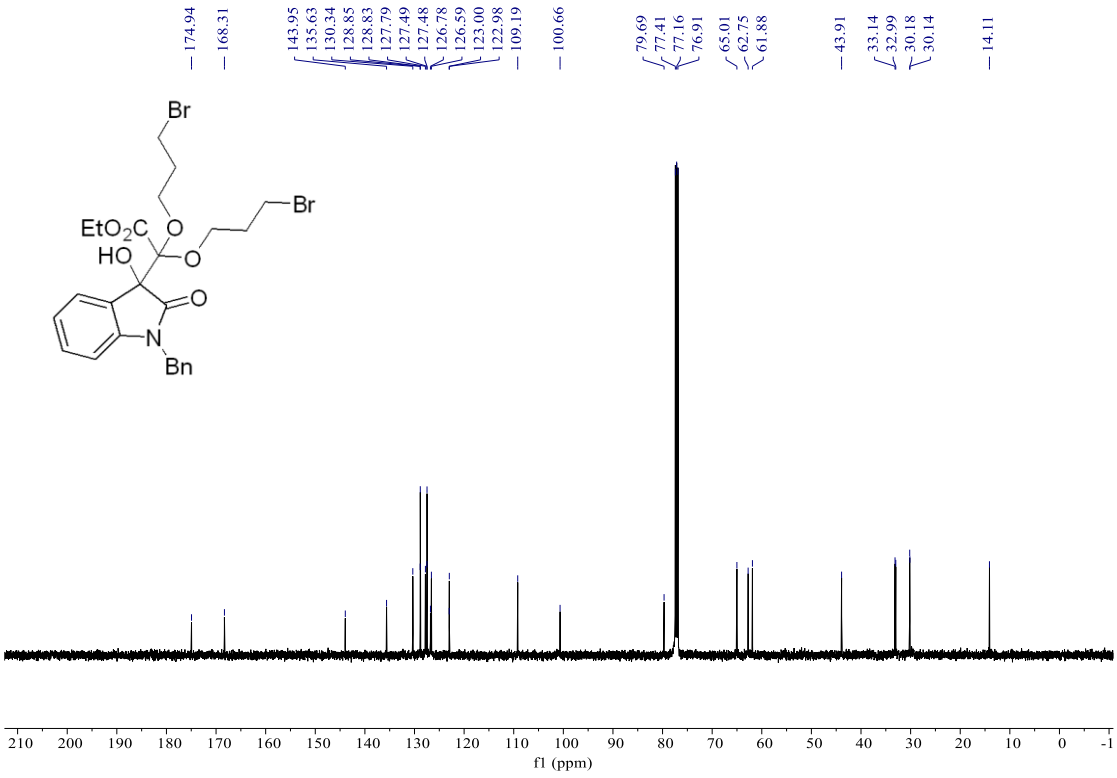
^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4v



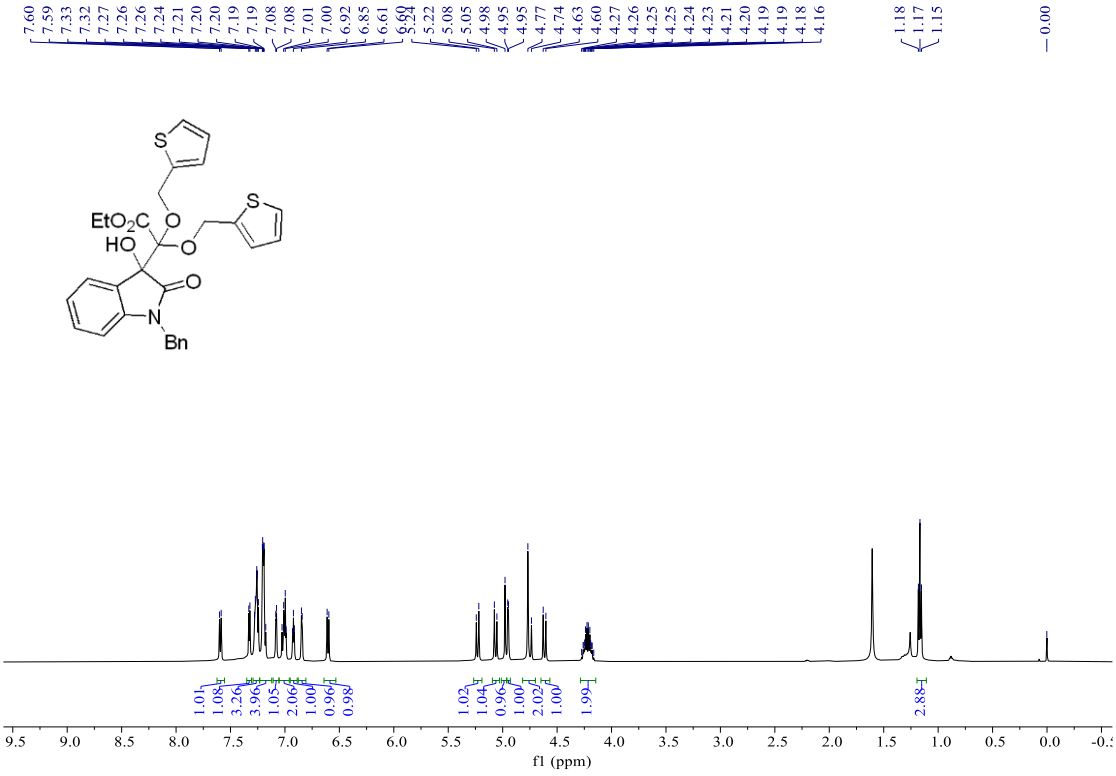
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4w



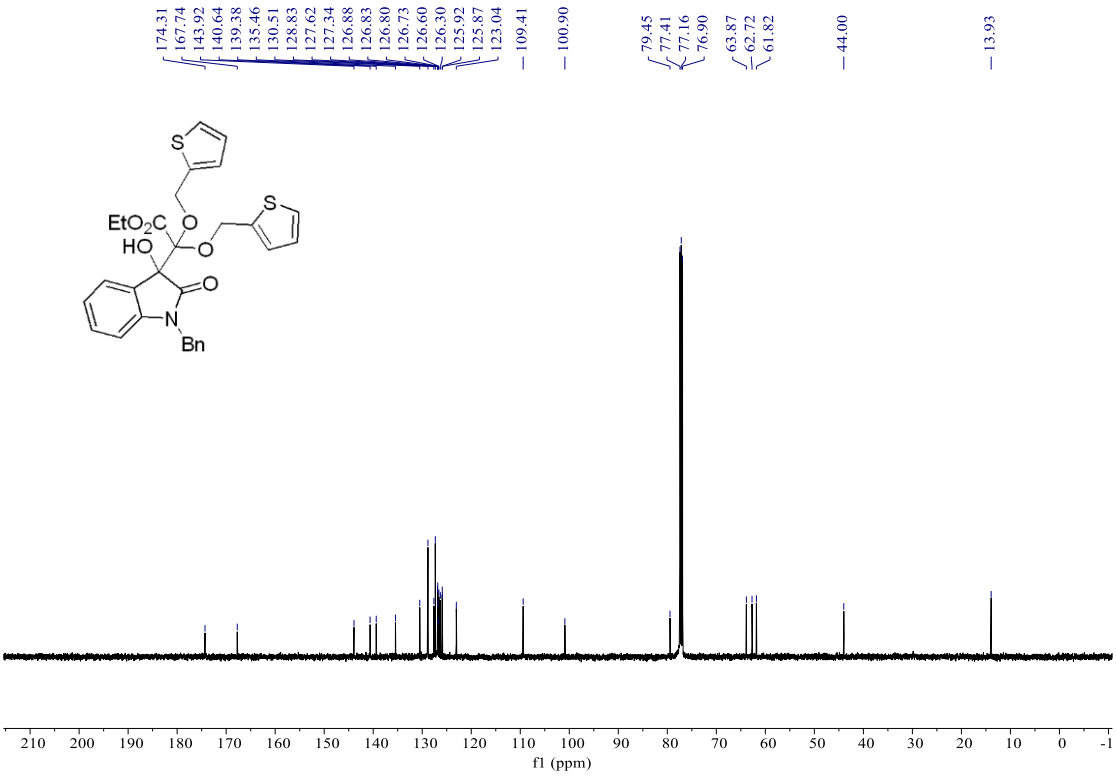
^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4w



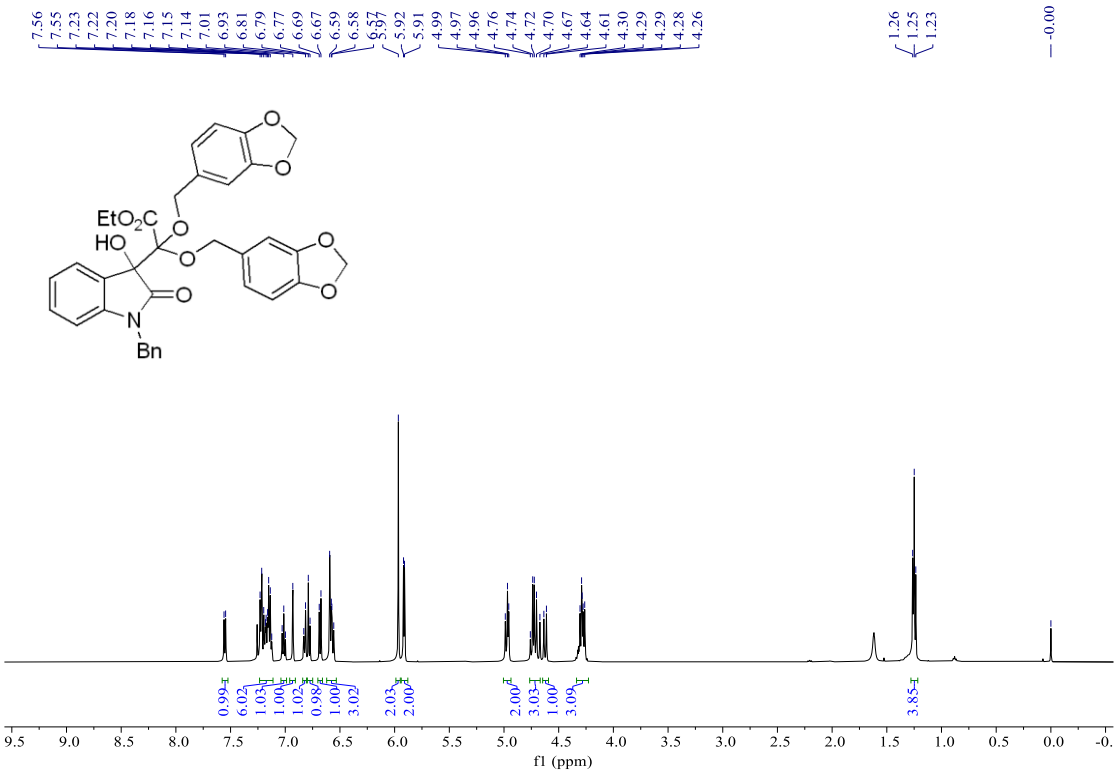
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4x



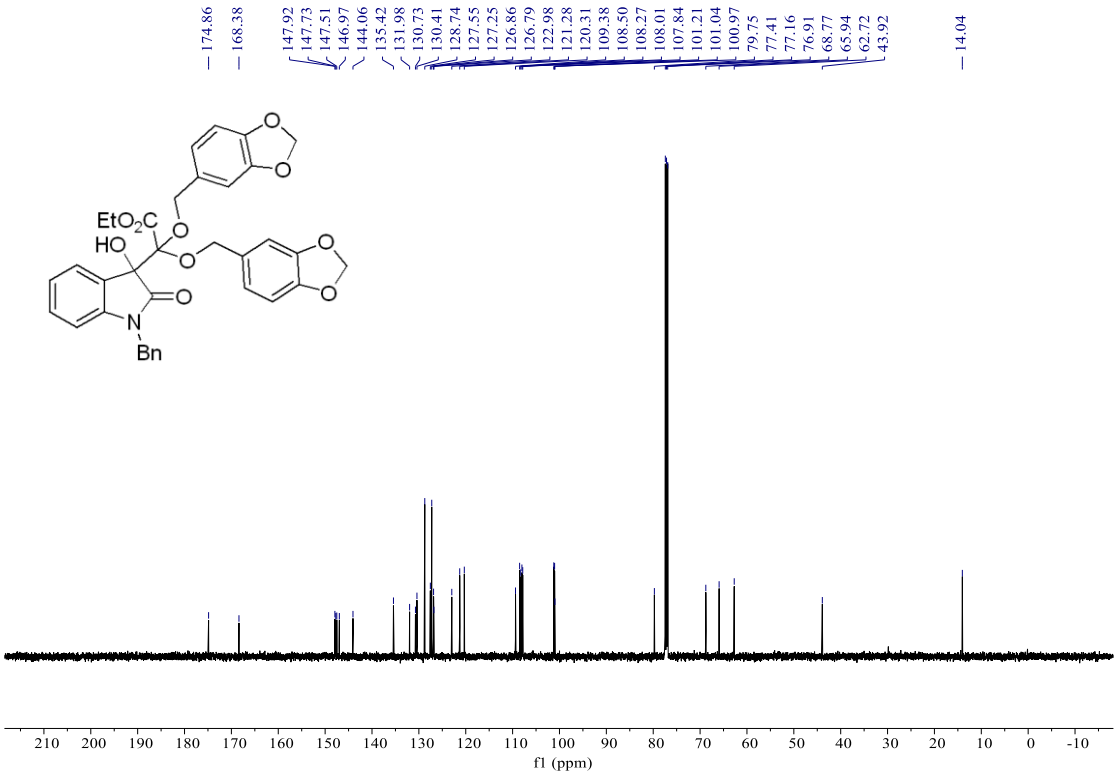
^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4x



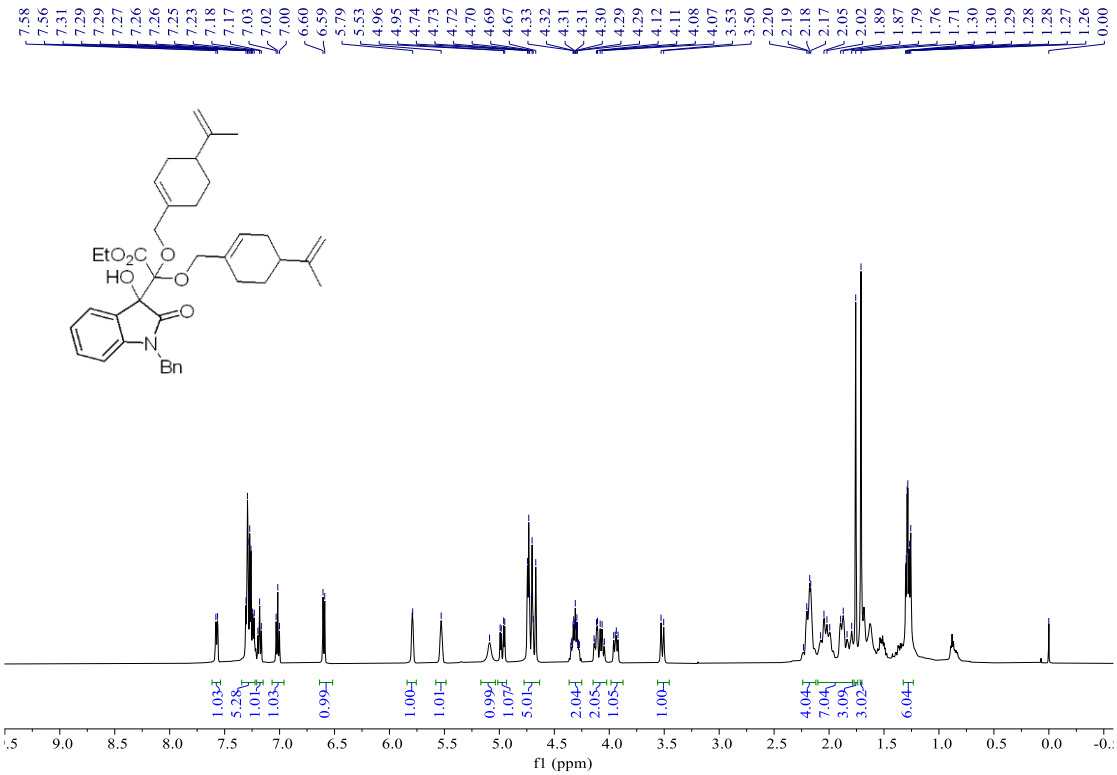
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4y



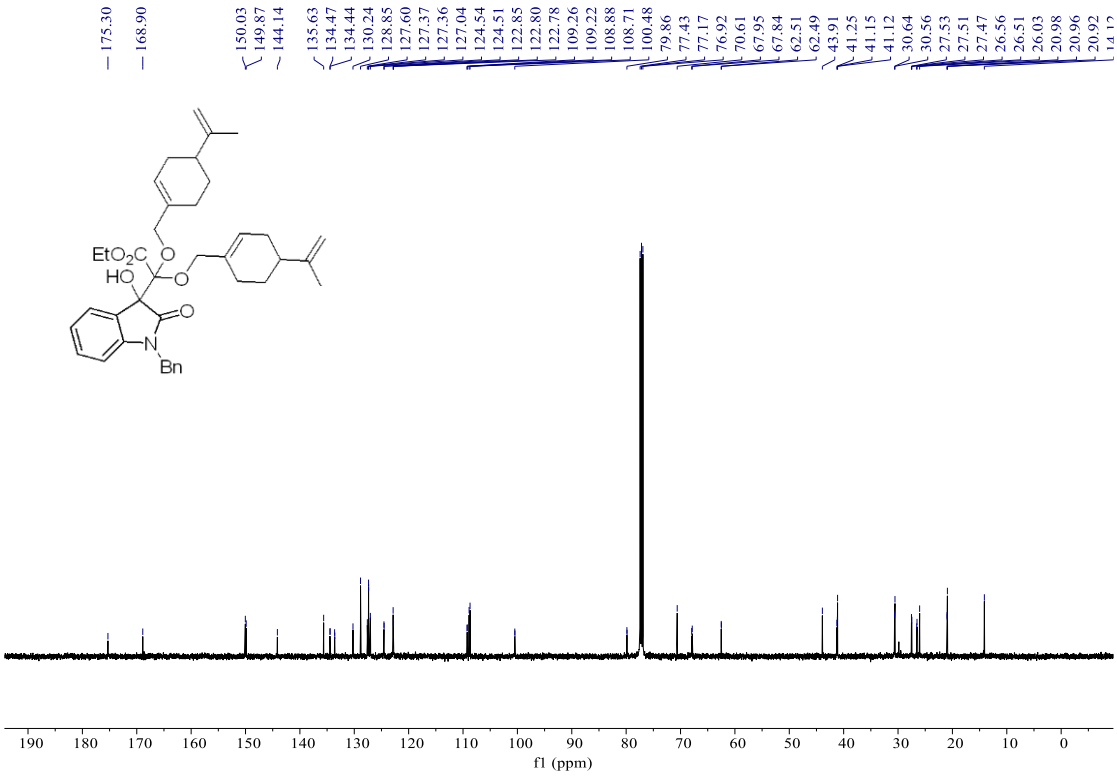
^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4y



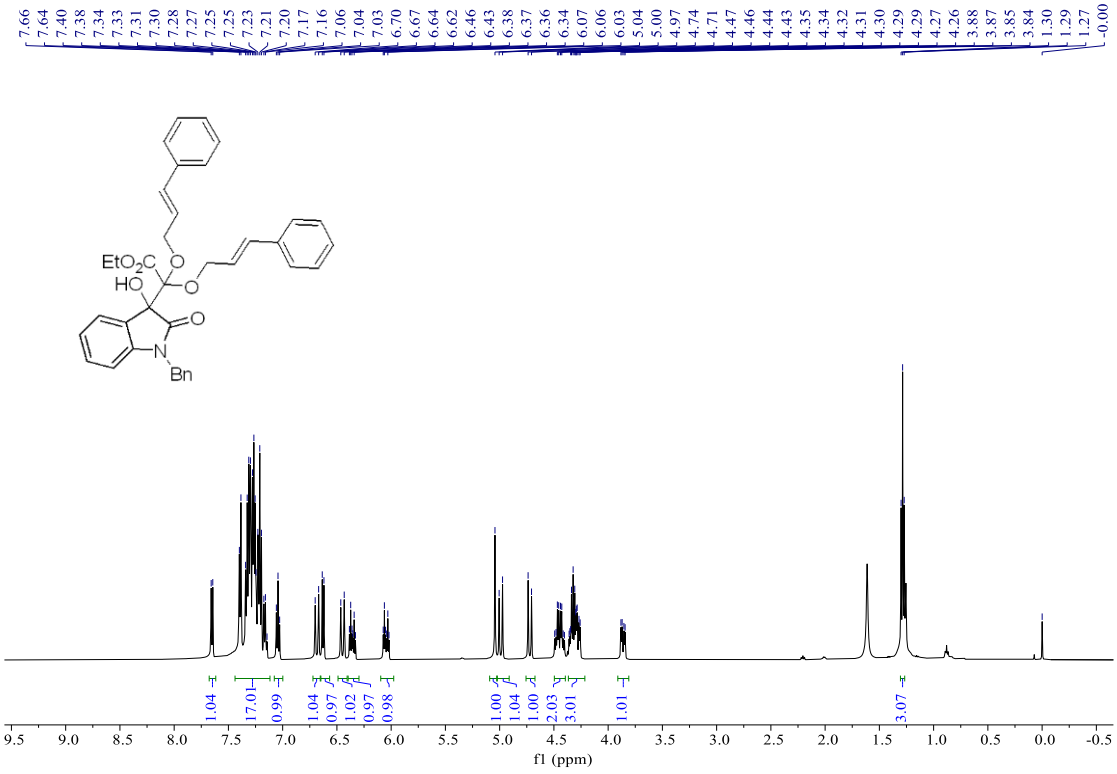
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4z



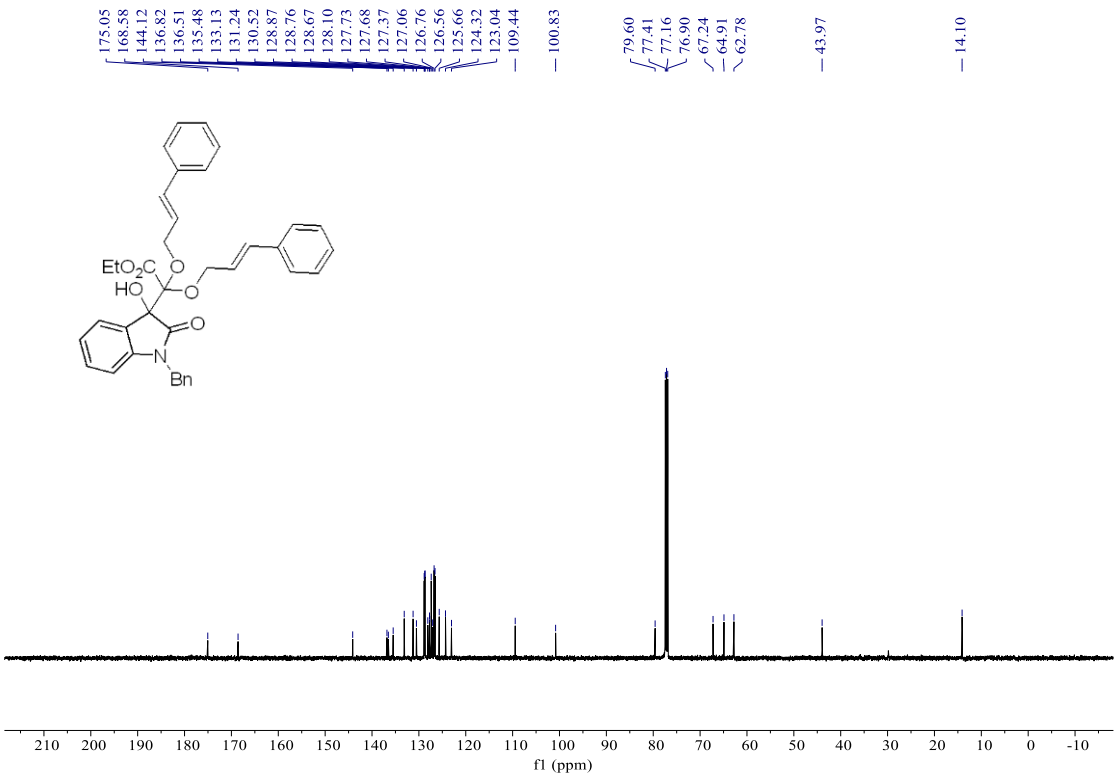
^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4z



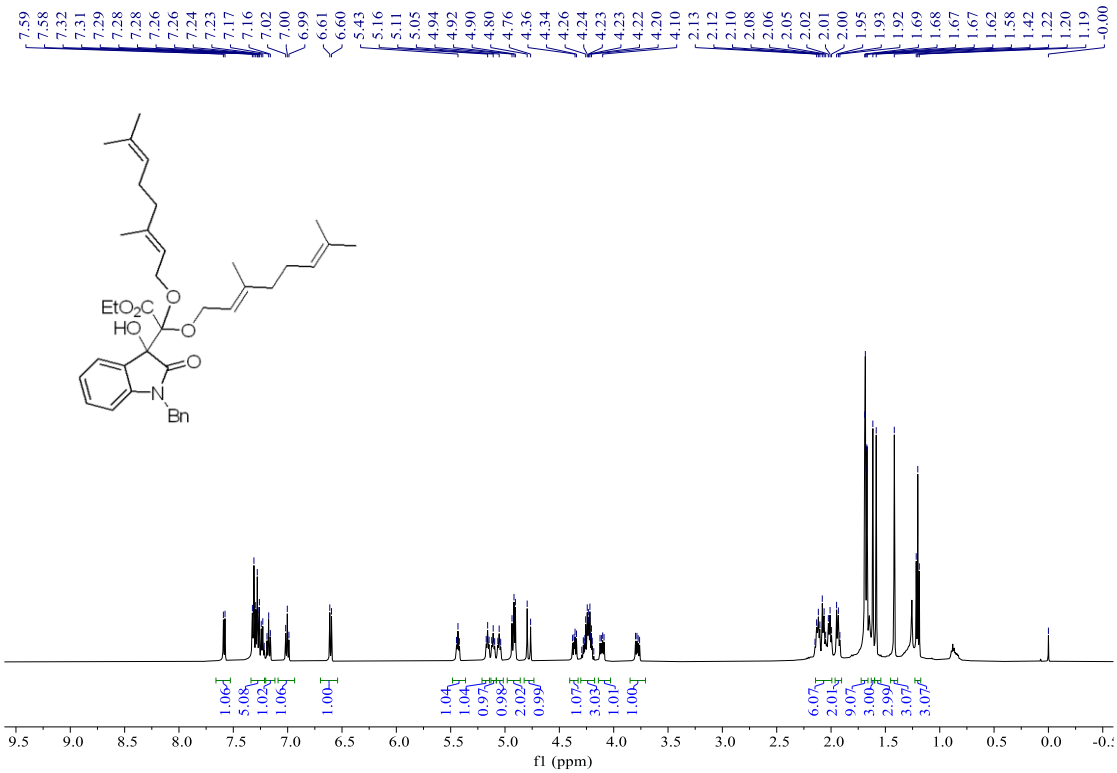
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4aa



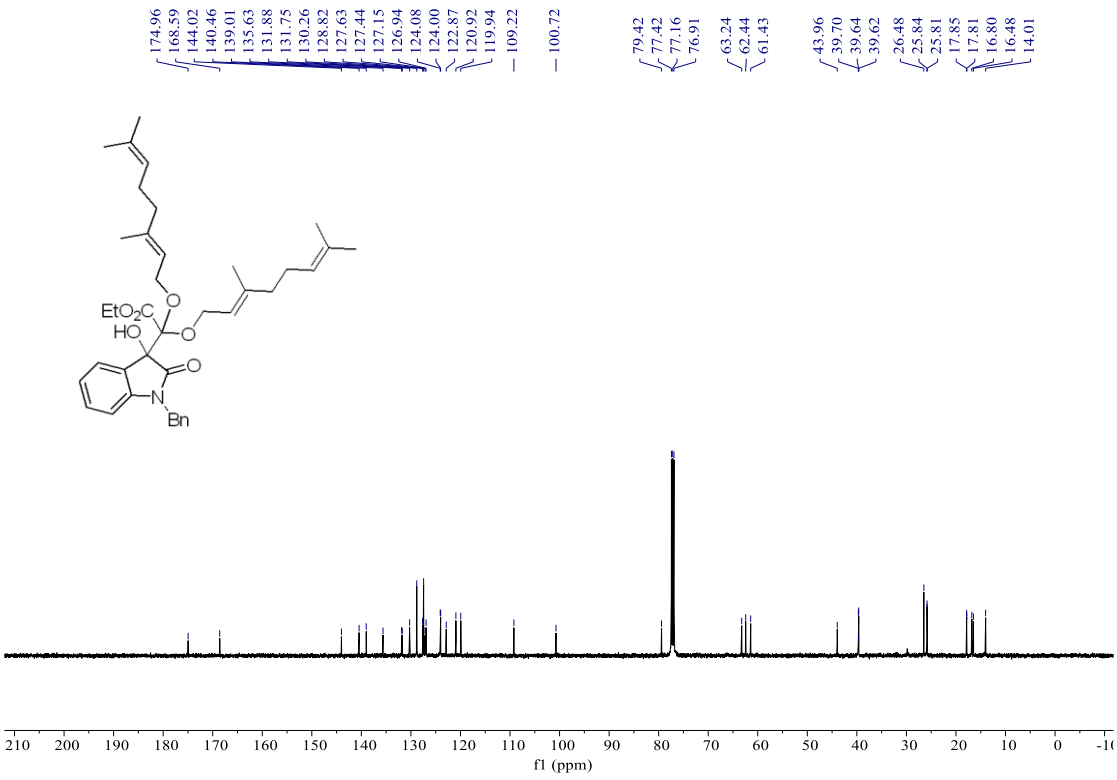
^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4aa



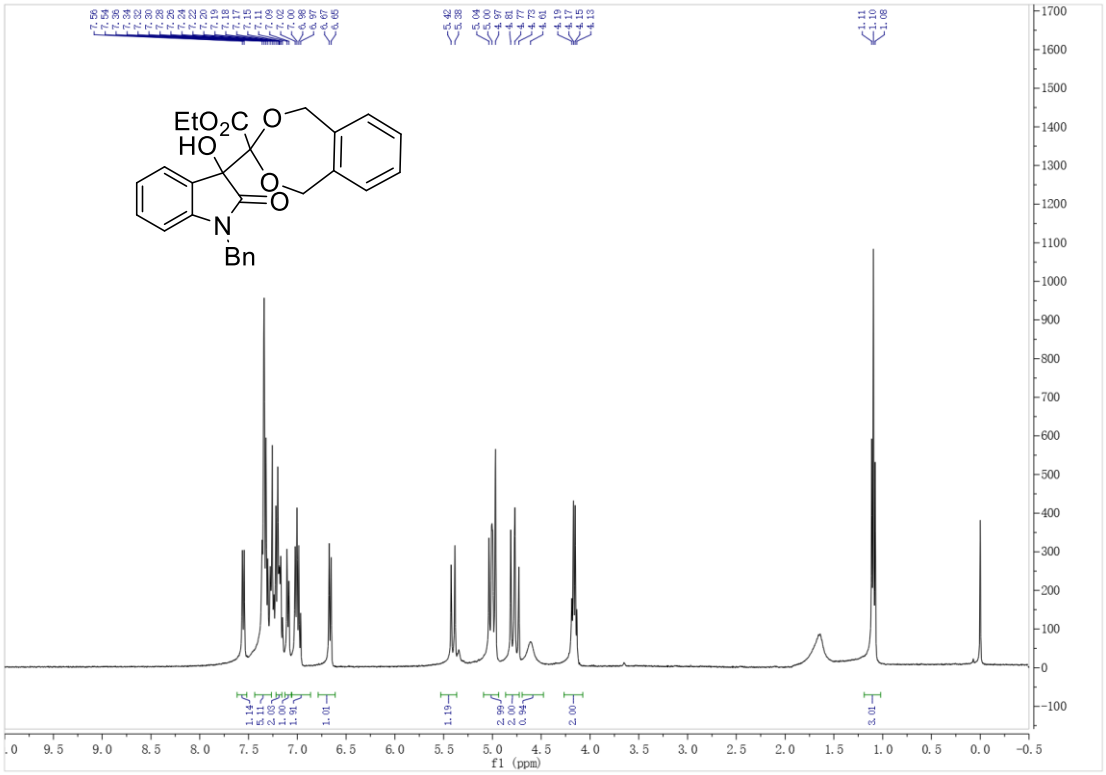
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 4ab



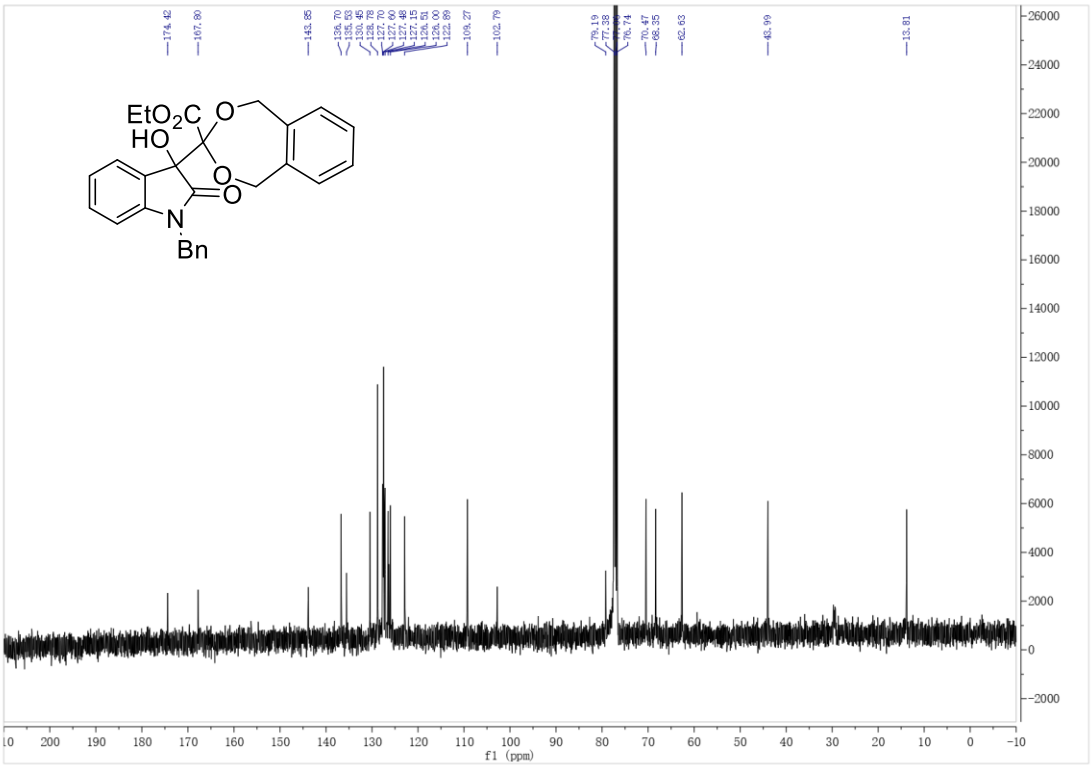
^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 4ab



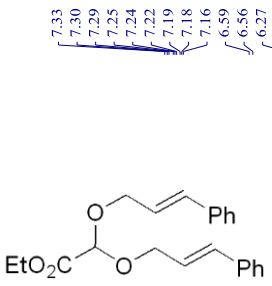
^{1}H NMR (400 MHz, Chloroform-*d*) spectra for 4ac

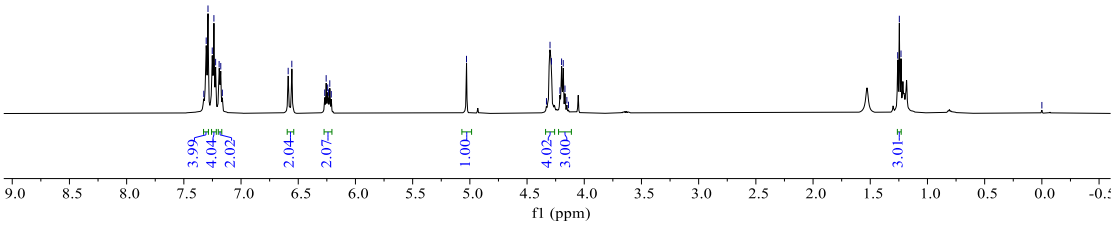


^{13}C NMR (100 MHz, Chloroform-*d*) spectra for 4ac

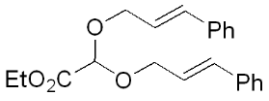


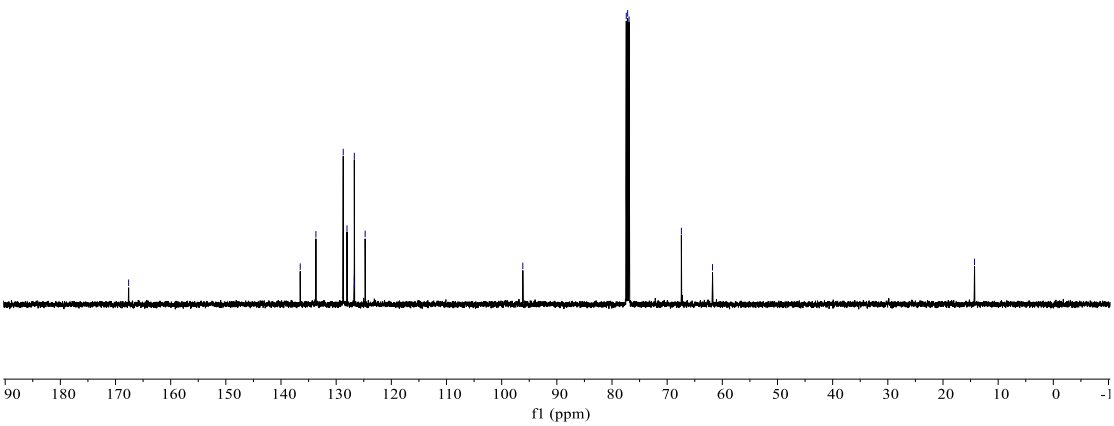
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 6



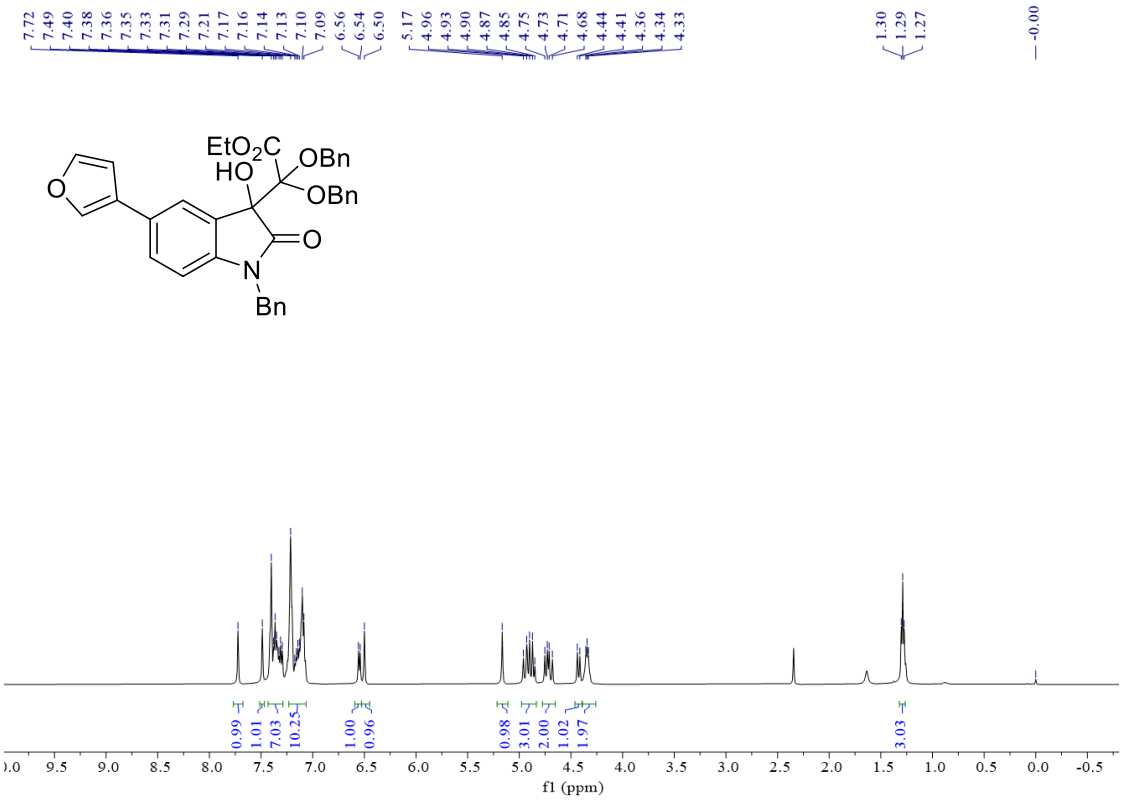


^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 6

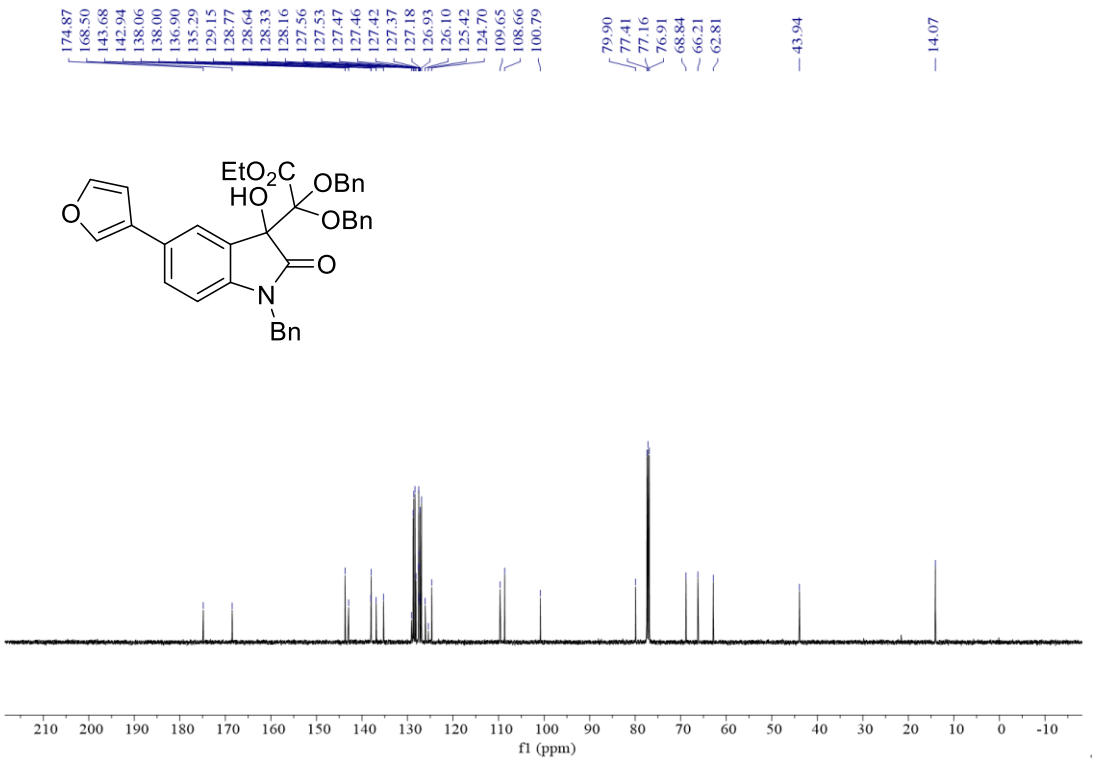




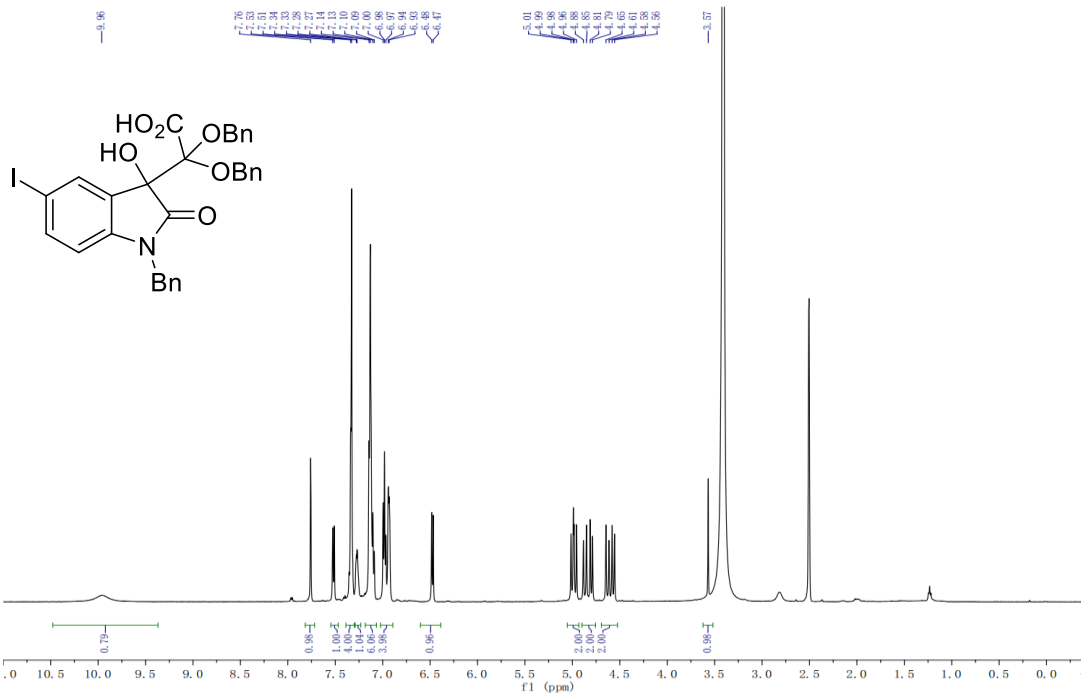
^{1}H NMR (500 MHz, Chloroform-*d*) spectra for 7



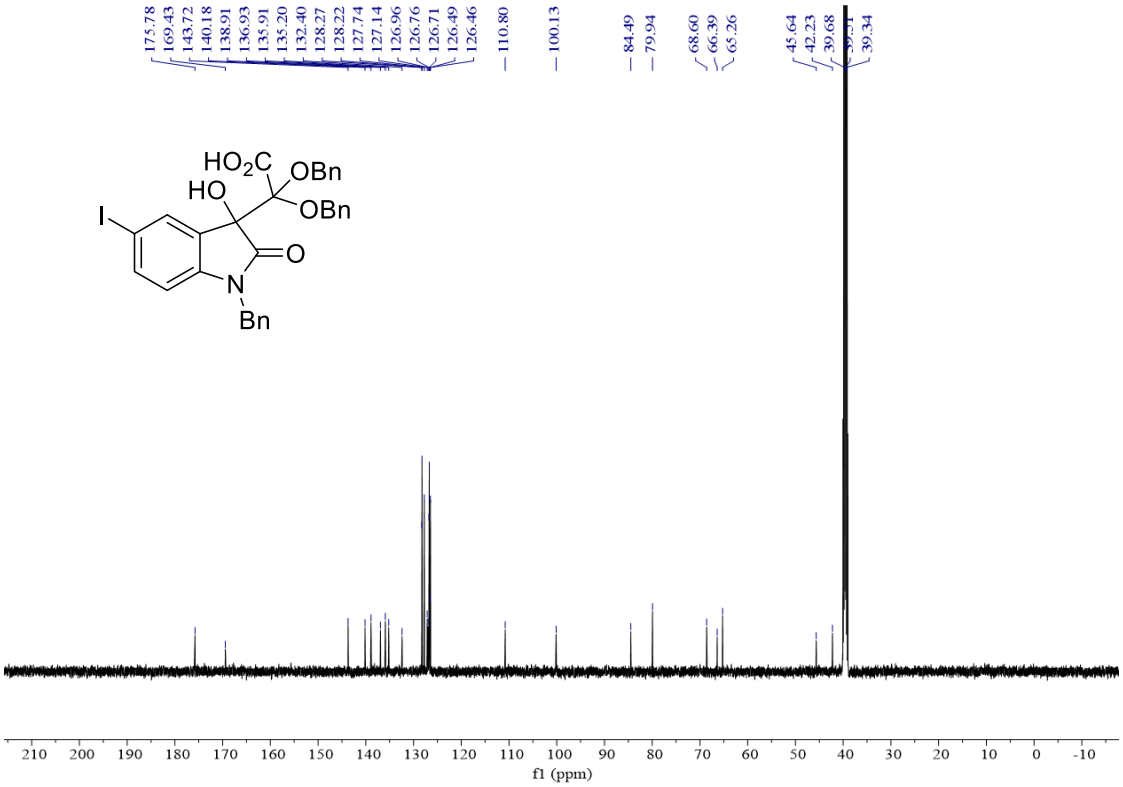
^{13}C NMR (125 MHz, Chloroform-*d*) spectra for 7



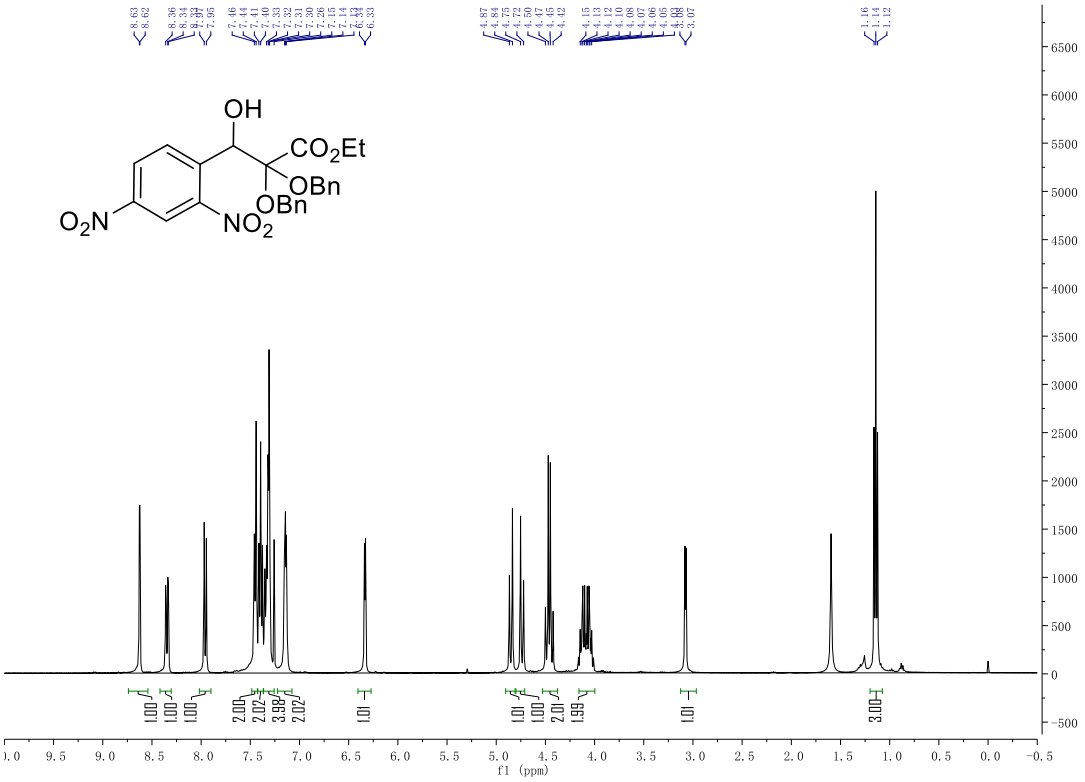
^{1}H NMR (500 MHz, DMSO-d_6) spectra for 8



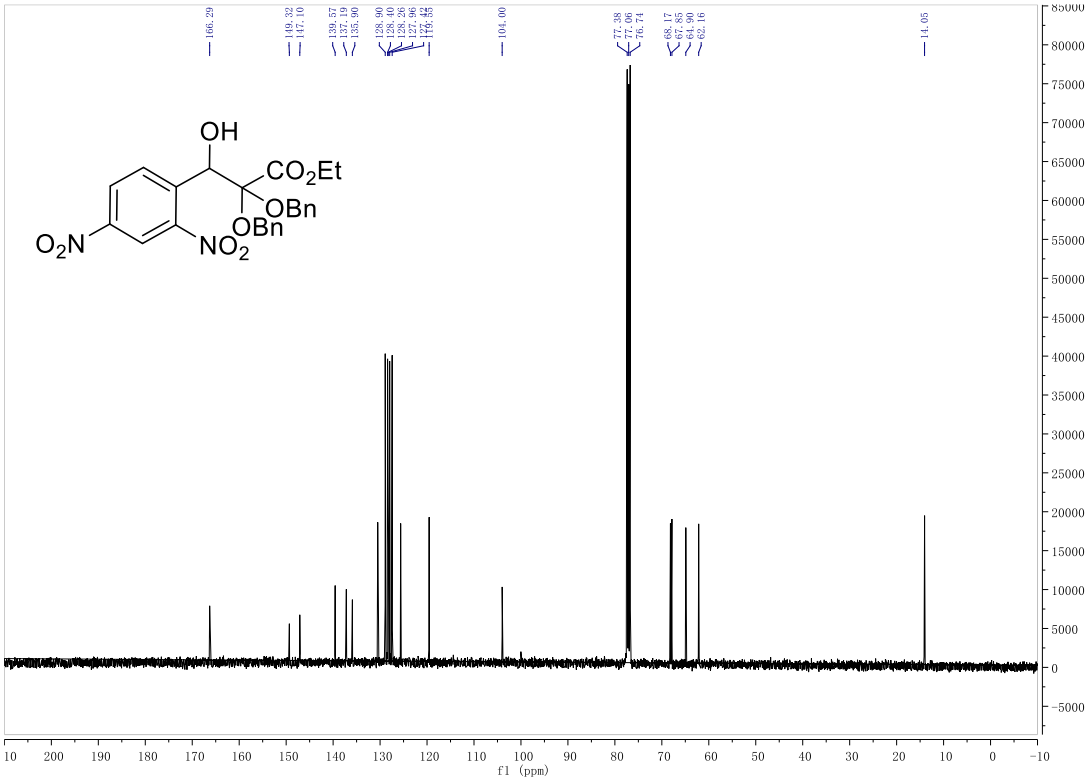
^{13}C NMR (125 MHz, DMSO-*d*$_6$) spectra for 8



^{1}H NMR (400 MHz, DMSO-*d*$_6$) spectra for 10

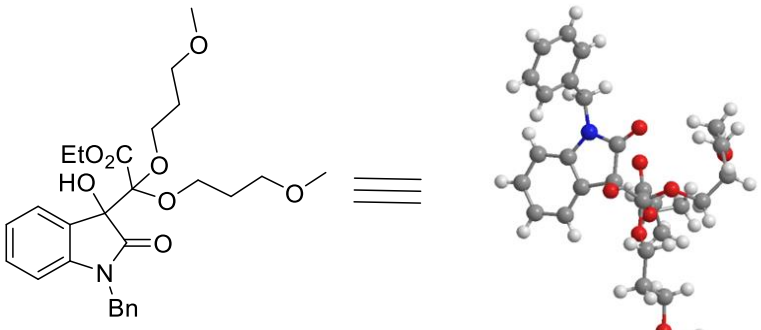


^{13}C NMR (100 MHz, DMSO-*d*$_6$) spectra for 10



10. Single-Crystal X-ray Diffraction Analysis of 4v

Single-crystal X-Ray difraction analysis of **4v**: The crystal of **4v** used for the single-crystal X-ray diffraction experiment was grown by slow evaporation of a solution of **4v** in dichloromethane and hexane at 0 ℃. An ORTEP diagram of the crystal structure of **4v** is shown below (CCDC No: 2247727)



4v

CCDC 2247727

```
Bond precision:   C-C = 0.0025 A          Wavelength=1.54184

Cell:           a=8.9155(5)       b=11.3804(5)      c=13.6631(8)
                alpha=85.750(4)   beta=80.095(5)    gamma=73.444(5)
Temperature:    100 K

                 Calculated                Reported
Volume           1308.54(13)               1308.54(13)
Space group      P -1                      P -1
Hall group       -P 1                      -P 1
Moiety formula   C27 H35 N O8              C27 H35 N O8
Sum formula      C27 H35 N O8              C27 H35 N O8
Mr               501.56                    501.56
Dx,g cm-3        1.273                     1.273
Z                2                         2
Mu (mm-1)        0.773                     0.773
F000             536.0                     536.0
F000'            537.76
h,k,lmax         10,13,16                  10,13,16
Nref             4678                      4650
Tmin,Tmax        0.725,0.793               0.687,1.000
Tmin'            0.647

Correction method= # Reported T Limits: Tmin=0.687 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.994          Theta(max)= 67.072

R(reflections)= 0.0482( 4125)                wR2(reflections)=
                                             0.1263( 4650)
S = 1.043                 Npar= 349
```

11. General Procedure for Anti-tumor Activity Studies in Vitro

Cell viability was measured by CCK-8 assay

Human cancer cell lines HCT116, MCF-7 and SJSA-1 were obtained from Cell Cook. Cells were cultured in RPMI1640 medium containing 10% fetal bovine serum and 1% penicillin/streptomycin (Gibco) in a humidified incubator containing 5% CO_2 at 37 ℃. For cell viability, cells were seeded in 96-well plates at 5000 cells per well. After 24 hours, serially diluted compounds were added and cells were cultured for another 48 hours. Cell viability was measured using a Cell Counting Kit-8 (CCK-8) assay according to the manufacturer's instructions (Yeasen Biotechnology, China).

These representative products **4d**, **4e**, **4h**, **4j**, **4k**, **4l**, **4m**, **4o**, **4p**, **4r**, **4s**, **6a**, **6c, 6e**, **6f**, **6i**, **6j**, and **6l** on cell viability was evaluated via CCK8 assay in HCT116 (colon cancer), MCF-7 (michigan cancer foundation-7) and SJSA-1 (osteosarcoma cancer) human cancer cell lines, and the in vitro anti-tumor activity results have been listed in **Table S1** and **Table S2**.

Table S1. Anti-tumor Activity Studies of Compounds **4a, 4c, 4e, 4g, 4h, 4i, 4m, 4o, 4q, 4r, 4s, 4t, 4u** and **4ab** (Inhibitory rate at 20 μM)

Compound	HCT116	MCF-7	SJSA-1
4a	21.37±10.97	17.26±2.25	61.24±1.81
4c	<10	53.07±3.45	<10
4e	21.08±8.21	60.25±3.14	44.13±2.26
4g	24.87±1.20	42.28±7.41	38.31±5.97
4h	56.21±5.29	55.42±6.44	46.04±0.80
4i	79.28±1.91	54.44±5.43	39.88±2.40
4m	21.47±1.32	65.82±4.54	39.14±2.34
4o	15.27±6.36	61.77±5.23	32.64±3.57

4q	21.45±6.89	60.34±7.56	41.14±4.19
4r	8.25±3.05	10.75±2.2	64.58±1.11
4s	45.52±8.07	34.8±7.97	28.31±0.81
4t	50.46±6.57	70.89±5.12	63.15±4.34
4u	27.40±5.12	60.52±7.12	45.20±4.13
4ab	40.30±5.28	60.05±11.12	53.85±8.12

Table S2. IC_{50} values of Compounds **4i**, **4o** and **4t** to HCT116, MCF-7 and SJSA-1 cells (IC_{50} / μM)

Compound	HCT116	MCF-7	SJSA-1
4i	19.95 ±1.48	16.12 ±2.15	25.80 ±0.94
4o	--	19.31 ±3.01	37.51 ±3.41
4t	19.51 ±1.45	19.11 ±1.48	19.82 ±0.61