Supporting Information

Stereoselective formal [3+3] Annulation of 3-Alkylidine-2-oxindole with β,γ–Unsaturated α–keto esters

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1. General information:

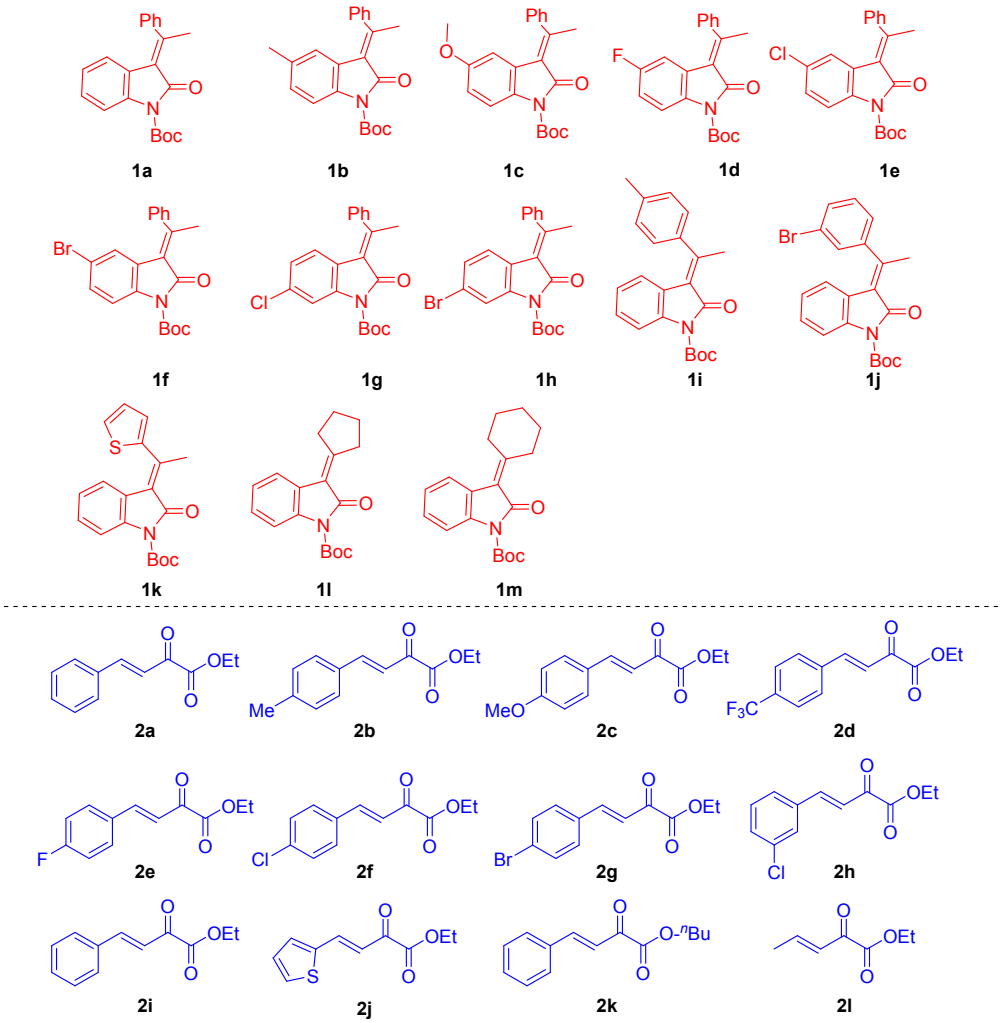
All the reagents and solvents were used as supplied commercially. Starting materials 3–alkylidene–2–oxindoles[1] **1** and β,γ–unsaturated α–keto esters **2a-2k**[2], **2l**[3] were known and prepared according to the literature procedures. Perkin Elmer FT-IR spectrometer used to record infrared spectra on KBr pellets and data are reported in terms of frequency of absorption. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV–300 instrument (300/400 MHz and 75/100 MHz, respectively) and internally referenced to Tetramethylsilane signal or residual protonated solvent signals. Data for ^{1}H NMR are reported as follows: chemical shift (δ, ppm), multiplicity (s– singlet; d– doublet; t– triplet; q– quartet; m– multiplet), integration, coupling constant (Hz). Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm). MS–TOF mass spectrometer and ESI mass spectrometer were used to record low resolution and high-resolution mass spectra. Column chromatographic separations were carried out on silica gel (230–400 mesh).

Dulbecco's Modified Eagle Medium (DMEM), Antibiotic-Antimycotic solution, heat-inactivated fetal bovine serum (FBS), Dulbecco's Phosphate-buffered Saline (DPBS) powder, N-2-hydroxyethylpiperazine-N-2-ethane sulfonic acid (HEPES), TrypLE™ Express Enzyme (1X) were obtained from Thermo Fisher Scientific. 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT), was obtained from Invitrogen. MG63 cell line were procured from National Centre for Cell Sciences (NCCS), Pune, India. MTT Assay is quantitative technique to study assess cell viability. The yellow water-soluble tetrazolium dye, 3-[4,5-dimethylthiazole-2-yl]-2,5-diphenyltetrazolium bromide (MTT), is reduced to water insoluble purple MTT-formazan crystal, by mitochondrial reductase, predominantly succinate dehydrogenase. These enzymes are only present in live and active cells, so the readout corresponds to the viable number of cells. Thus, MTT assay is a representation of mitochondrial respiration which indirectly relates to the cellular energy capacity of a cell. The purple formazan crystals are analyzed spectrophotometrically (575nm) after dissolution in DMSO.

High performance liquid chromatography (HPLC) analysis was performed on an Agilent 1220 Infinity LC instrument equipped with a quaternary pump, using a Chiralpak IC column (250 x 4.6 mm).

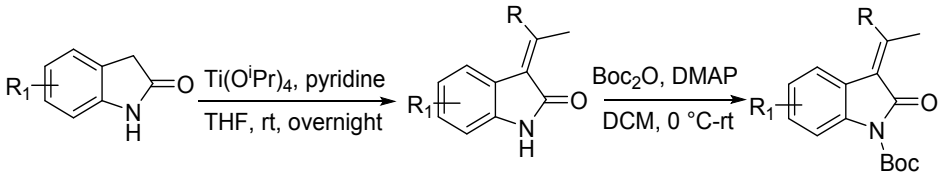
2. Typical experimental procedure and data

2.1 Preparation of the starting materials:



Scheme. 1 The Structure of 3-Alkylidene-2-oxindole 1 and β,γ–unsaturated α–keto ester 2.

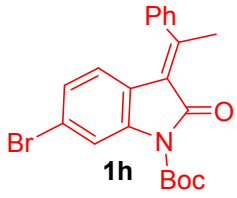
General procedure for the synthesis of 3-alkylidine oxindole (1) 3-alkylidine oxindole were prepared by following the reported literature procedure.[1]



Scheme. 1 Synthesis of 3-alkylidine oxindole.

A mixture of 2-oxindole (10 mmol), acetophenone (12 mmol), and pyridine (20 mmol) in dry THF (20 ml) was stirred for 10 min followed by addition of titanium isopropoxide (30 mmol).

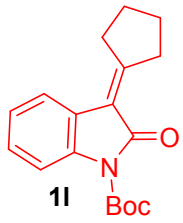
The resulting mixture was stirred at room temperature for 15h. The reaction mixture was diluted with ethyl acetate and wash with 1N HCL, $NaHCO_3$, and brine. The organic layer was dried over Na2SO4, concentrated, and purified by chromatography to provide intermediate I. Subsequently the intermediate I in 50 ml of DCM was treated with boc-anhydride (12 mmol), and DMAP (2 mmol) at 0 °C. The solution was then allowed to room temperature, and was stirred for 4h. After quenching with water, the reaction mixture was extracted with ethyl acetate. Organic phase was washed with water and brine, dried ($MgSO_4$), and solvent was evaporated in vacuum. The residue was purified by flash chromatography on silica gel.



tert-butyl (*E*)-6-bromo-2-oxo-3-(1-phenylethylidene)indoline-1-carboxylate (1h)

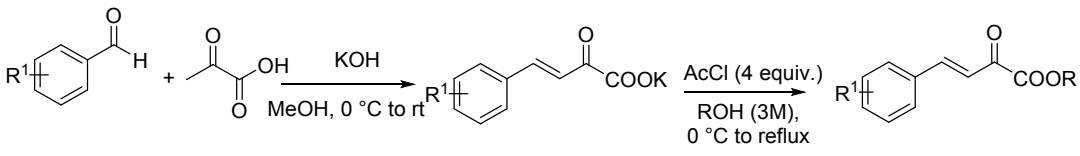
Yellow solid (65%): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.05 (d, *J* = 1.2 Hz, 1H), 7.54 – 7.37 (m, 3H), 7.23 (d, *J* = 6.8 Hz, 2H), 6.86 (dd, *J* = 8.4, 1.3 Hz, 1H), 6.01 (d, *J* = 8.4 Hz, 1H), 2.76 (s, 3H), 1.68 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.6, 157.7, 149.4, 142.7, 139.1, 129.5, 128.9, 126.46, 126.28, 123.82, 122.1, 122.0, 121.9, 117.9, 84.6, 28.28, 23.97.

tert-butyl 3-cyclopentylidene-2-oxoindoline-1-carboxylate (1l)



Yellow solid (72%): **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.1 Hz, 1H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.29 (d, *J* = 7.7 Hz, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 3.24 – 3.07 (m, 2H), 2.95 – 2.79 (m, 2H), 1.97 – 1.77 (m, 4H), 1.66 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.5, 165.6, 149.9, 138.2, 127.6, 124.2, 123.8, 122.3, 118.8, 114.7, 83.8, 35.5, 35.2, 28.3, 26.3, 26.0.

General procedure for the synthesis of *β,γ*–unsaturated α–keto ester (2)[2]

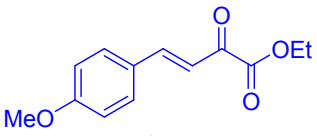


Scheme. 2 Synthesis of *β,γ*–unsaturated α–keto ester.

To a solution of benzaldehyde (0.1 mol) and pyruvic acid (0.1 mol) in MeOH (10 mL) was added a solution of KOH (0.15 mol) in MeOH (30 mL) at 0 °C dropwise. The reaction mixture was stirred at 40 °C for 1 h and then 0 °C overnight. The precipitate was collected by filtration,

washed twice with chilled MeOH, once with Et_2O and dried under vacuum to furnish the potassium salt (70%) as yellow solid. Acetyl chloride (0.04M, 4 equiv.) was added dropwise to the corresponding alcohol (3M) at 0 °C to produce hydrochloric acid. Potassium salt (0.01M, 1 equiv.) was then added, and reaction was warmed to room temperature and stirred at room temperature for 2 h, after that mixture was refluxed overnight. Then the solvent was removed, and the yellow residue was added water (50 mL) and then extracted with CH_2Cl_2 (3×25 mL). The combined organics were washed with saturated $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4 and concentrated in vacuum. The crude product was purified by flash chromatography (petroleum ether/ethyl acetate = 30:1 to 25:1) to give the yellow product.

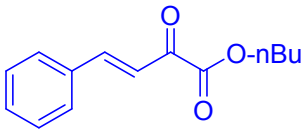
ethyl (*E*)-4-(4-methoxyphenyl)-2-oxobut-3-enoate (2c)



2c

Yellow solid (82%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 16.1 Hz, 1H), 7.53 (d, *J* = 7.9 Hz, 2H), 7.34 (s, 1H), 7.23 (d, *J* = 7.8 Hz, 2H), 4.39 (q, *J* = 7.1 Hz, 2H), 2.40 (s, 3H), 1.41 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.00, 162.45, 148.68, 142.57, 131.44, 129.9, 129.20, 119.66, 62.52, 21.72, 14.15.

butyl (*E*)-2-oxo-4-phenylbut-3-enoate (2k)

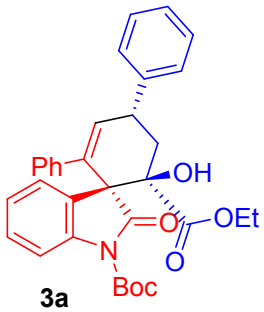


2k

Yellow oil (75%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.85 (d, *J* = 16.1 Hz, 1H), 7.63 (d, *J* = 6.9 Hz, 2H), 7.48 – 7.40 (m, 3H), 7.35 (d, *J* = 16.1 Hz, 1H), 4.34 (t, *J* = 6.7 Hz, 2H), 1.76 (dd, *J* = 14.7, 7.1 Hz, 2H), 1.45 (dd, *J* = 15.0, 7.5 Hz, 2H), 0.97 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.0, 162.4, 148.50, 134.1, 131.7, 129.2, 129.1 120.7, 66.39, 30.52, 19.14, 13.75.

2.2 General reaction procedure for the synthesis of spirocyclohexene-oxindole

To a solution of 3–alkylidene–2–oxindole **1** (0.20 mmol) and β,γ–unsaturated α–keto ester **2** (0.20 mmol) in 1 mL acetonitrile was added DABCO (0.04 mmol) and the reaction mixture was stirred at rt for 12 h. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup.

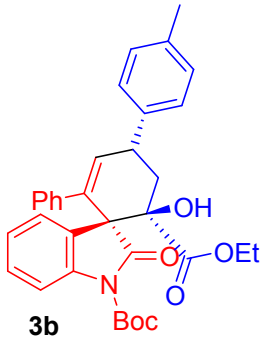


3a

1'-*tert*-butyl 6-ethyl -6-hydroxy-2'-oxo-2,4-diphenyl-1',2'-dihydrospiro[cyclohexane-1,3'-indol]-2-ene-1',6-dicarboxylate (3a):

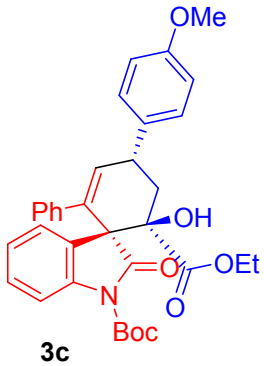
To a solution of 3–alkylidene–2–oxindole **1a** (67mg, 0.20 mmol) and β,γ–unsaturated α–keto ester **2a** (40.8mg, 0.20 mmol) in 1 mL acetonitrile was added DABCO (4.5mg, 0.04 mmol) and the reaction mixture was stirred at rt for 12 h. The *dr* (>19:1) was determined by ^{1}H NMR analysis of crude product. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup to give white solid **3a** (97.0 mg, 90% yield); mp: 120–121 °C;.R_f = 0.33 (ethyl acetate/petroleum ether = 1/9); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 – 7.55 (m, 3H), 7.41 – 7.31 (m, 2H), 7.29 – 7.23 (m, 2H), 7.21 – 7.12 (m, 1H), 7.07 – 6.99 (m, 3H), 6.98 – 6.90 (m, 3H), 6.26 (s, 1H), 4.29 – 3.81 (m, 4H), 3.14 (t, *J* = 12.17 Hz, 1H), 2.09 (ddd, *J* = 13.51, 6.14, 1.44 Hz, 1H), 1.69 (d, *J* = 2.30 Hz, 9H), 1.11 (td, *J* = 7.11, 2.30 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.1, 173.4, 149.1, 144.2, 140.2, 139.6, 135.7, 135.3, 128.9, 128.7, 128.7, 127.9, 127.3, 127.3, 127.0, 126.9, 126.8, 124.2, 114.4, 84.6, 78.1, 63.0, 58.8, 40.7, 35.4, 28.3, 22.4, 13.8. FTIR (KBr) cm^{-1}: 3469, 2982, 2927, 1757, 1728, 1604. **HRMS ESI**: $[M+Na]^+$, Calcd for $C_{33}H_{33}NNaO_6$ 562.2206; found 562.2200.

1'-*tert*-butyl 6-ethyl -6-hydroxy-4-(4-methylphenyl)-2'-oxo-2-phenyl-1',2'-dihydrospiro[cyclohexane-1,3'-indol]-2-ene-1',6-dicarboxylate (3b): To a solution of 3–alkylidene–2–oxindole **1a** (67mg, 0.20 mmol) and β,γ–unsaturated α–keto ester **2b** (43.6mg, 0.20 mmol) in 1 mL acetonitrile was added DABCO (4.5mg, 0.04 mmol) and the reaction mixture was stirred at rt for 12 h. The *dr* (>19:1) was determined by ^{1}H NMR analysis of crude product. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup to give white solid **3b** (97.3 mg, 88% yield) ; mp: 132–133 °C;. R_f = 0.33 (ethyl acetate/petroleum ether = 1/9); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.17 Hz, 1H), 7.47 (d, *J* = 7.97 Hz, 2H), 7.26 (s, 1H), 7.21 – 7.11 (m, 3H), 7.07 – 6.98 (m, 3H), 6.97 – 6.88 (m, 3H), 6.24 (d, *J* = 2.39 Hz, 1H), 4.14 – 3.87 (m, 4H), 3.11 (dd, J = 13.30, 11.05 Hz, 1H), 2.34 (s, 3H), 2.06 (dd, J = 13.47, 6.20 Hz, 1H), 1.68 (s, 9H), 1.10 (t, J = 7.31 Hz, 3H). **^{13}C NMR** (101 MHz, CDCl3) δ 174.1, 173.4, 149.1, 141.1, 140.2, 139.6, 136.4, 135.6, 135.5, 129.4, 128.9, 128.5, 127.9, 127.3, 127.3, 127.0, 126.9, 124.2, 114.4, 84.6, 78.2, 63.0, 58.8, 40.3, 35.5, 28.3, 21.2, 13.8. FTIR (KBr) cm^{-1}: 3484, 2984, 2928, 1762, 1726, 1602. **HRMS ESI**: $[M+Na]^+$, Calcd for $C_{34}H_{35}NNaO_6$ 576.2362; found 576.2364



3b

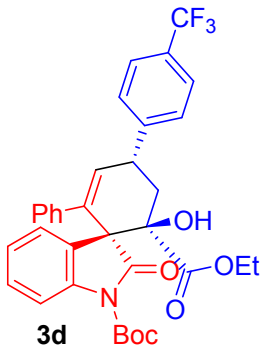
1'-*tert*-butyl 6-ethyl-6-hydroxy-4-(4-methoxyphenyl)-2'-oxo-2-phenyl-1',2'-dihydrospiro[cyclohexane-1,3'-indol]-2-ene-1',6-dicarboxylate (3c):



3c

To a solution of 3–alkylidene–2–oxindole **1a** (67mg, 0.20 mmol) and β,γ–unsaturated α–keto ester **2c** (46.8mg, 0.20 mmol) in 1 mL acetonitrile was added DABCO (4.5mg, 0.04 mmol) and the reaction mixture was stirred at rt for 12 h. The *dr* (>19:1) was determined by ^{1}H NMR analysis of crude product. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup to give white solid **3c** (96.7 mg, 85% yield); mp: 139–140 °C; R_f = 0.33 (ethyl acetate/petroleum ether = 1/9); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 – 7.46 (m, 3H), 7.41 – 7.30 (m, 2H), 7.23 (d, *J* = 7.28 Hz, 1H), 7.09 – 6.98 (m, 3H), 6.94 (dd, *J* = 6.64, 2.91 Hz, 2H), 6.82 (d, *J* = 2.69 Hz, 1H), 6.69 (dd, *J* = 8.92, 2.75 Hz, 1H), 6.25 (d, *J* = 2.29 Hz, 1H), 4.17 – 3.89 (m, 4H), 3.65 (s, 3H), 3.13 (dd, *J* = 13.30, 10.98 Hz, 1H), 2.20 – 1.94 (m, 1H), 1.68 (s, 9H), 1.12 (t, *J* = 7.12 Hz, 3H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.1, 173.4, 156.3, 149.1, 144.1, 140.2, 135.7, 135.4, 133.0, 128.7, 128.7, 128.3, 127.9, 127.3, 127.0, 126.8, 115.3, 114.2, 113.1, 84.4, 78.1, 63.1, 59.0, 55.6, 40.7, 35.4, 28.3, 13.8. FTIR (KBr) cm^{-1}: 3480, 2983, 2930, 1766, 1726, 1607. **HRMS ESI**: $[M+Na]^+$, Calcd for $C_{34}H_{35}NNaO_7$ 592.2311; found 592.2305.

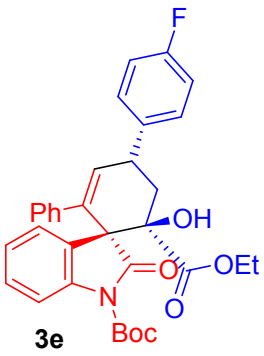
1'-*tert*-butyl 6-ethyl-6-hydroxy-4-[(4-trifluoromethyl)phenyl]-2'-oxo-2- phenyl-1',2'-dihydrospiro[cyclohexane-1,3'-indol]-2-ene-1',6-dicarboxylate (3d):



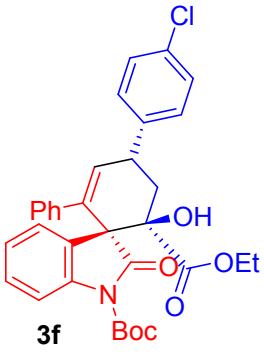
3d

To a solution of 3–alkylidene–2–oxindole **1a** (67mg, 0.20 mmol) and β,γ–unsaturated α–keto ester **2d** (54.4mg, 0.20 mmol) in 1 mL acetonitrile was added DABCO (4.5mg, 0.04 mmol) and the reaction mixture was stirred at rt for 12 h. The *dr* (>19:1) was determined by ^{1}H NMR analysis of crude product. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup to give white solid **3d** (114.1 mg, 94% yield); mp: 135–136 °C; R_f = 0.33 (ethyl acetate/petroleum ether = 1/9); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.17 Hz, 1H), 7.38 – 7.30 (m, 2H), 7.29 (s, 1H), 7.25 (d, *J* = 8.93 Hz, 1H), 7.17 (t, *J* = 7.86 Hz, 1H), 7.06 – 6.99 (m, 3H), 6.94 (t, *J* = 7.31 Hz, 4H), 6.20 (d, *J* = 1.84 Hz, 1H), 4.17 – 3.83 (m, 4H), 3.15 – 3.01 (m, 1H), 2.07 (dd, *J* = 13.46, 6.24 Hz, 1H), 1.69 (s, 9H), 1.11 (t, *J* = 7.13 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.0, 173.3, 164.4, 161.9, 149.1, 146.8 (d, *J* = 7.04 Hz), 139.8 (d, *J* = 43.60 Hz), 136.2, 134.4, 130.2 (d, *J* = 8.16

Hz), 129.0, 127.9, 126.8, 126.3, 124.3, 124.2, 115.6, 115.4, 114.4, 113.7 (d, J = 21.12 Hz), 84.7, 78.0, 63.1, 58.8, 40.5, 35.2, 28.3, 13.8. FTIR (KBr) cm^{-1}: 3481, 2984, 2929, 1762, 1724, 1602. **HRMS ESI**: $[M+Na]^+$, Calcd for $C_{34}H_{32}F_3NNaO_6$ 630.2079; found 630.2072.

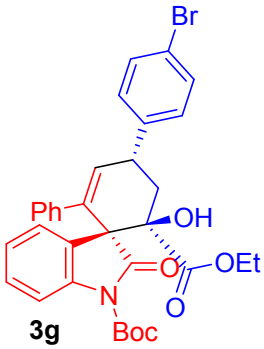


1'-*tert*-butyl 6-ethyl-6-hydroxy-4-(4-flourophenyl)-2'-oxo-2-phenyl-1',2'-dihydrospiro[cyclohexane-1,3'-indol]-2-ene-1',6-dicarboxylate (3e): To a solution of 3–alkylidene–2–oxindole **1a** (67mg, 0.20 mmol) and β,γ–unsaturated α–keto ester **2e** (44.4mg, 0.20 mmol) in 1 mL acetonitrile was added DABCO (4.5mg, 0.04 mmol) and the reaction mixture was stirred at rt for 12 h. The *dr* (>19:1) was determined by ^{1}H NMR analysis of crude product. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup to give white solid **3e** (100.2 mg, 90% yield); mp: 120–121 °C;. R_f = 0.33 (ethyl acetate/petroleum ether = 1/9); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.14 Hz, 1H), 7.59 – 7.51 (m, 2H), 7.31 – 7.12 (m, 3H), 7.11 - 6.98 (m, 5H), 6.97 – 6.88 (m, 2H), 6.20 (d, J = 2.49 Hz, 1H), 4.19 – 3.87 (m, 4H), 3.08 (dd, J = 13.36, 10.87 Hz, 1H), 2.06 (dd, J = 13.19, 6.45 Hz, 1H), 1.69 (s, 9H), 1.11 (t, J = 7.14 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.24, 173.3, 149.0, 140.1, 139.9, 139.6, 135.9, 135.1, 130.2, 130.1, 129.0, 127.9, 127.3, 127.0, 126.9, 124.2, 115.6, 115.3, 114.4, 84.8, 78.1, 63.1, 58.7, 40.0, 35.5, 28.3, 13.8. FTIR (KBr) cm^{-1}: 3484, 2980, 2932, 1760, 1720, 1600. **HRMS ESI**: $[M+Na]^+$, Calcd for $C_{33}H_{32}FNNaO_6$ 580.2111; found 580.2105



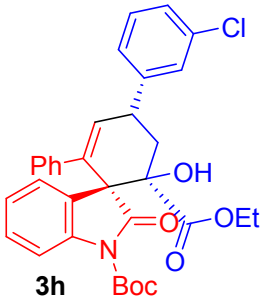
1'-*tert*-butyl 6-ethyl-6-hydroxy-4-(4-chlorophenyl)-2'-oxo-2-phenyl-1',2'-dihydrospiro[cyclohexane-1,3'-indol]-2-ene-1',6-dicarboxylate (3f). To a solution of 3–alkylidene–2–oxindole **1a** (67mg, 0.20 mmol) and β,γ–unsaturated α–keto ester **2f** (47.6mg, 0.20 mmol) in 1 mL acetonitrile was added DABCO (4.5mg, 0.04 mmol) and the reaction mixture was stirred at rt for 12 h. The *dr* (>19:1) was determined by ^{1}H NMR analysis of crude product. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup to give white solid **3f** (105.6 mg, 92% yield); mp: 136–137 °C;. R_f = 0.33 (ethyl acetate/petroleum ether = 1/9); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.17 Hz, 1H), 7.57 – 7.47 (m, 2H), 7.35 – 7.27 (m, 2H), 7.27 – 7.21 (m, 1H), 7.17 (t, J = 7.74 Hz, 1H), 7.07 – 6.98 (m, 3H), 6.93 (dd, J = 9.45, 5.72 Hz, 3H), 6.18 (d, J = 1.98 Hz, 1H), 4.11 – 3.84 (m, 4H), 3.18 – 2.97 (m, 1H), 2.05 (dd, J

= 13.49, 6.22 Hz, 1H), 1.69 (s, 9H), 1.11 (t, *J* = 7.12 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.1, 173.2, 149.0, 142.7, 140.0, 139.5, 136.1, 134.6, 132.5, 130.1, 129.0, 128.8, 127.9, 127.2, 127.0, 126.8, 124.2, 114.4, 84.8, 78.0, 63.1, 58.7, 40.1, 35.3, 28.2, 13.8. FTIR (KBr) cm^{-1}: 3475, 2982, 2927, 1763, 1728, 1604. **HRMS ESI**: $[M+Na]^+$, Calcd for $C_{33}H_{32}ClNNaO_6$ 596.1816; found 596.1810



3g

1'-*tert*-butyl 6-ethyl-6-hydroxy-4-(4-bromophenyl)-2'-oxo-2-phenyl-1',2'-dihydrospiro[cyclohexane-1,3'-indol]-2-ene-1',6-dicarboxylate (3g): To a solution of 3–alkylidene–2–oxindole **1a** (67mg, 0.20 mmol) and β,γ–unsaturated α–keto ester **2g** (53.6mg, 0.20 mmol) in 1 mL acetonitrile was added DABCO (4.5mg, 0.04 mmol) and the reaction mixture was stirred at rt for 12 h. The *dr* (>19:1) was determined by ^{1}H NMR analysis of crude product. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup to give white solid **3g** (113.7 mg, 92% yield); mp: 149–150 °C; R_f = 0.33 (ethyl acetate/petroleum ether = 1/9); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.15 Hz, 1H), 7.46 (s, 4H), 7.25 (d, *J* = 2.43 Hz, 1H), 7.19 – 7.12 (m, 1H), 7.02 (dd, *J* = 4.90, 1.62 Hz, 3H), 6.96 – 6.88 (m, 3H), 6.17 (d, *J* = 2.33 Hz, 1H), 4.06 (dd, *J* = 10.68, 7.15 Hz, 1H), 3.95 (ddd, *J* = 11.00, 8.90, 5.61 Hz, 2H), 3.90 (s, 1H), 3.07 (dd, *J* = 13.27, 11.04 Hz, 1H), 2.05 (dd, *J* = 13.45, 6.23 Hz, 1H), 1.69 (s, 9H), 1.10 (t, *J* = 7.13 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.1, 173.2, 149.0, 143.2, 140.0, 139.6, 136.2, 134.5, 131.8, 130.5, 129.0, 127.9, 127.0, 127.1, 126.8, 124.2, 120.6, 114.4, 84.8, 78.1, 63.1, 58.8, 40.2, 35.3, 28.3, 13.8. FTIR (KBr) cm^{-1}: 3474, 2983, 2928, 1760, 1725, 1601. **HRMS ESI**: $[M+Na]^+$, Calcd for $C_{33}H_{32}BrNNaO_6$ 640.1311; found 640.1305

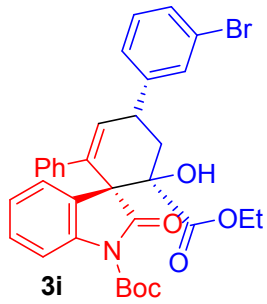


3h

1'-*tert*-butyl 6-ethyl-6-hydroxy-4-(3-chlorophenyl)-2'-oxo-2-phenyl-1',2'-dihydrospiro[cyclohexane-1,3'-indol]-2-ene-1',6-dicarboxylate (3h): To a solution of 3–alkylidene–2–oxindole **1a** (67mg, 0.20 mmol) and β,γ–unsaturated α–keto ester **2h** (47.6mg, 0.20 mmol) in 1 mL acetonitrile was added DABCO (4.5mg, 0.04 mmol) and the reaction mixture was stirred at rt for 12 h. The *dr* (>19:1) was determined by ^{1}H NMR analysis of crude product. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup to give white solid **3h** (101.0 mg, 88% yield); mp: 113–114 °C; R_f = 0.33 (ethyl acetate/petroleum ether = 1/9); **^{1}H NMR**

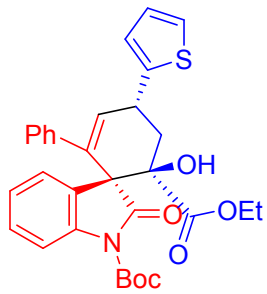
(400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.19 Hz, 1H), 7.55 – 7.47 (m, 2H), 7.29 – 7.13 (m, 4H), 7.09 – 6.99 (m, 3H), 6.98 – 6.87 (m, 3H), 6.20 (d, *J* = 2.33 Hz, 1H), 4.17 – 3.84 (m, 4H), 3.09 (dd, *J* = 13.25, 11.03 Hz, 1H), 2.06 (dd, *J* = 13.44, 6.17 Hz, 1H), 1.69 (s, 9H), 1.11 (t, *J* = 7.14 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.0, 173.2, 149.0, 146.2, 140.0, 139.6, 136.3, 134.3, 130.1, 129.0, 128.7, 127.9, 127.2, 127.1, 127.1, 126.9, 126.8, 124.2, 114.4, 84.8, 78.0, 63.2, 58.7, 40.5, 35.2, 28.3, 13.8. FTIR (KBr) cm^{-1}: 3465, 2927, 2855, 1759, 1733, 1599. **HRMS ESI**: $[M+Na]^+$, Calcd for $C_{33}H_{32}ClNNaO_6$ 596.1816; found 596.1812.

1'-*tert*-butyl 6-ethyl-6-hydroxy-4-(3-bromophenyl)-2'-oxo-2-phenyl-1',2'-dihydrospiro[cyclohexane-1,3'-indol]-2-ene-1',6-dicarboxylate (3i): To a solution of 3–alkylidene–2–oxindole **1** (67mg, 0.20 mmol) and β,γ–unsaturated α–keto ester **2i** (53.6mg, 0.20 mmol) in 1 mL acetonitrile was added DABCO (4.5mg, 0.04 mmol) and the reaction mixture was stirred at rt for 12 h. The *dr* (>19:1) was determined by ^{1}H NMR analysis of crude product. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup to give white solid **3i** (106.2 mg, 86% yield); mp: 118–119 °C; R_f = 0.33 (ethyl acetate/petroleum ether = 1/9); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.71 – 7.60 (m, 2H), 7.56 (d, *J* = 7.58 Hz, 1H), 7.38 (d, *J* = 7.92 Hz, 1H), 7.29 – 7.12 (m, 3H), 7.10 – 6.98 (m, 3H), 6.97 – 6.98 (m, 3H), 6.20 (s, 1H), 4.13 – 3.87 (m, 4H), 3.09 (t, *J* = 12.14 Hz, 1H), 2.06 (dd, *J* = 13.44, 6.07 Hz, 1H), 1.69 (d, 9H), 1.11 (td, *J* = 7.10, 1.99 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.0, 173.2, 149.0, 146.5, 140.0, 139.6, 136.4, 134.3, 131.5, 130.4, 130.0, 129.0, 127.9, 127.4, 127.3, 127.1, 126.8, 124.2, 122.6, 114.4, 84.8, 78.0, 63.1, 58.7, 40.5, 35.2, 28.3, 13.8. FTIR (KBr) cm^{-1}: 3463, 2978, 2931, 1759, 1732, 1598. **HRMS ESI**: $[M+Na]^+$, Calcd for $C_{33}H_{32}BrNNaO_6$ 640.1311; found 640.1308.



3i

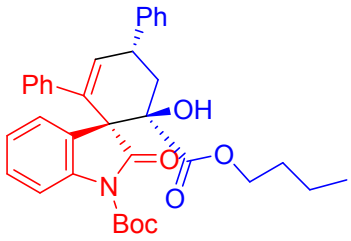
1'-*tert*-butyl 6-ethyl-6-hydroxy--2'-oxo-2-phenyl-4-(thiophen-2-yl)-1',2'-dihydrospiro[cyclohexane-1,3'-indol]-2-ene-1',6-dicarboxylate (3j). To a solution of 3–alkylidene–2–oxindole **1a** (67mg, 0.20 mmol) and β,γ–unsaturated α–keto ester **2j** (42.0mg, 0.20 mmol) in 1 mL acetonitrile was added DABCO (4.5mg, 0.04 mmol) and the reaction mixture was stirred at rt for 12 h. The *dr* (>19:1) was determined by ^{1}H NMR analysis of crude product. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup to give white solid **3j** (72.0



3j

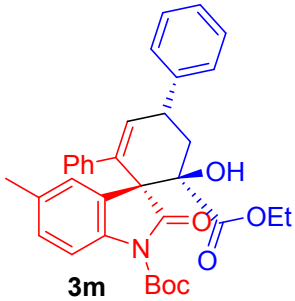
mg, 66% yield); mp: 110–111 °C;. R_f = 0.33 (ethyl acetate/petroleum ether = 1/9); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 (d, J = 8.12 Hz, 1H), 7.24 (d, J = 0.85 Hz, 1H), 7.21 – 7.10 (m, 3H), 7.01 (dd, J = 6.52, 3.78 Hz, 3H), 6.98 (dd, J = 5.06, 3.52 Hz, 1H), 6.96 -6.86 (m, 3H), 6.29 (d, J = 2.49 Hz, 1H), 4.35 – 4.26 (m, 1H), 4.11 – 3.93 (m, 2H), 3.88 (s, 1H), 3.33 – 3.10 (m, 1H), 2.19 (d, J = 5.92 Hz, 1H), 1.67 (s, 9H), 1.11 (t, J = 7.14 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.5, 173.2, 149.2, 147.1, 140.0, 134.6, 129.0, 127.9, 127.4, 127.3, 127.1, 127.1, 124.7, 124.1, 123.7, 114.4, 84.6, 77.9, 63.1, 35.6, 35.4, 28.3, 13.8. FTIR (KBr) cm^{-1}: 3460, 2970, 2930, 1750, 1732, 1590. **HRMS ESI**: $[M+Na]^+$, Calcd for $C_{31}H_{31}NNaO_6S$ 568.1770; found 568.1772.

6-butyl 1'-*tert*-butyl-6-hydroxy-2'-oxo-2,4-diphenyl-1',2'- dihydrospiro[cyclohexane-1,3'-indol]-2-ene-1',6-dicarboxylate (3k): To a solution of 3–alkylidene–2–oxindole **1a** (67mg, 0.20 mmol) and β,γ–unsaturated α–keto ester **2k** (46.4mg, 0.20 mmol) in 1 mL acetonitrile was added DABCO (4.5mg, 0.04 mmol) and the reaction mixture was stirred at rt for 12 h. The *dr* (>2:1) was determined by ^{1}H NMR analysis of crude product. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup to give white solid **3k** (74.0 mg, 66% yield, major:minor = 2:1, non-separable diastereomers]; mp: 108–109 °C; R_f = 0.33 (ethyl acetate/petroleum ether = 1/9); For major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.15 Hz, 1H), 7.60 – 7.55 (m, 2H), 7.43 – 7.38 (m, 2H), 7.36 – 7.34 (m, 1H), 7.27 – 7.22 (m, 2H), 7.17 – 7.12 (m, 1H), 7.08 (d, J = 7.60 Hz, 1H), 7.01 – 6.98 (m, 2H), 6.94 – 6.92 (m, 1H), 6.73 (d, J = 7.10 Hz, 1H), 6.23 (d, J = 2.4 Hz, 1H), 4.08 – 4.02 (m, 1H), 4.00 – 3.91 (m, 1H), 3.89 (s, 1H), 3.77 – 3.61 (m, 1H), 3.22 – 3.07 (m, 1H), 2.13 – 2.03 (m, 1H), 1.68 (s, 9H), 1.51 – 1.38 (m, 2H), 1.22 – 1.14 (m, 2H), 0.83 (t, J = 7.36 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.0, 173.4, 149.1, 144.2, 140.2, 139.7, 135.8, 129.0, 128.8, 128.7, 128.0, 127.8, 127.4, 127.3, 126.9, 126.8, 124.1, 114.4, 84.5, 78.3, 66.9, 58.8, 40.7, 35.5, 30.2, 28.3, 18.8, 13.6. FTIR (KBr) cm^{-1}: 3460, 2970, 2930, 1750, 1732, 1590. **HRMS ESI**: $[M+Na]^+$, Calcd for $C_{35}H_{37}NNaO_6$ 590.2519; found 590.2513.



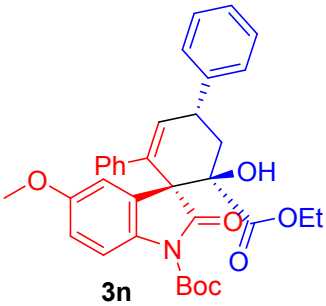
3k

1'-*tert*-butyl 6-ethyl-6-hydroxy-5'-methyl-2'-oxo-2,4-diphenyl-1',2'-dihydrospiro[cyclohexane-1,3'-indol]-2-ene-1',6-dicarboxylate (3m): To a solution of 3–alkylidene–2–oxindole **1b** (69.8mg, 0.20 mmol) and *β, γ*–unsaturated *α*–keto ester **2a** (40.8mg,



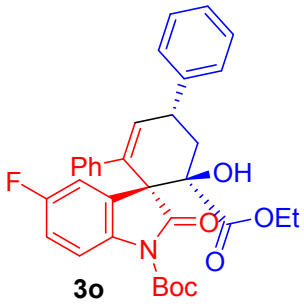
3m

0.20 mmol) in 1 mL acetonitrile was added DABCO (4.5mg, 0.04 mmol) and the reaction mixture was stirred at rt for 12 h. The *dr* (>19:1) was determined by ^{1}H NMR analysis of crude product. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup to give white solid **3m** (99.5 mg, 90% yield); mp: 130–131 °C; R_f = 0.33 (ethyl acetate/petroleum ether = 1/9); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.18 Hz, 1H), 7.49 (d, *J* = 7.94 Hz, 2H), 7.28 (s, 1H), 7.24 – 7.12 (m, 3H), 7.02 (dd, *J* = 10.62, 8.55 Hz, 3H), 6.99 – 6.89 (m, 3H), 6.26 (d, *J* = 2.36 Hz, 1H), 4.27 – 3.82 (m, 4H), 3.13 (dd, *J* = 13.32, 11.05 Hz, 1H), 2.36 (s, 3H), 2.08 (dd, *J* = 13.46, 6.22 Hz, 1H), 1.71 (s, 9H), 1.13 (t, *J* = 7.14 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.1, 173.4, 149.1, 141.1, 140.2, 139.6, 136.4, 135.6, 135.5, 129.4, 128.9, 128.5, 127.9, 127.3, 127.0, 126.9, 124.2, 114.4, 84.6, 78.2, 63.0, 58.8, 40.3, 35.5, 28.3, 21.2, 13.8. FTIR (KBr) cm^{-1}: 3483, 2923, 2854, 1762, 1727, 1601. **HRMS ESI**: $[M+Na]^+$, Calcd for $C_{34}H_{35}NNaO_6$ 576.2362; found 576.2360.



3n

1'-*tert*-butyl 6-ethyl-6-hydroxy-5'-methoxy-2'-oxo-2,4-diphenyl-1',2'-dihydrospiro[cyclohexane-1,3'-indol]-2-ene-1',6-dicarboxylate (3n): To a solution of 3–alkylidene–2–oxindole **1c** (72.6mg, 0.20 mmol) and β,γ–unsaturated α–keto ester **2a** (40.8mg, 0.20 mmol) in 1 mL acetonitrile was added DABCO (4.5mg, 0.04 mmol) and the reaction mixture was stirred at rt for 12 h. The *dr* (>19:1) was determined by ^{1}H NMR analysis of crude product. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup to give white solid **3n** (104.6 mg, 92% yield); mp: 141–142 °C; R_f = 0.33 (ethyl acetate/petroleum ether = 1/9); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 – 7.40 (m, 3H), 7.28 (m, 2H), 7.16 (d, *J* = 7.56 Hz, 1H), 7.00 – 6.91 (m, 3H), 6.88 – 6.79 (m, 2H), 6.75 (d, *J* = 2.75 Hz, 1H), 6.62 (dd, *J* = 8.93, 2.79 Hz, 1H), 6.18 (d, *J* = 2.36 Hz, 1H), 4.08 – 3.81 (m, 4H), 3.57 (s, 3H), 3.06 (dd, *J* = 13.33, 11.11 Hz, 1H), 2.00 (dd, *J* = 13.48, 6.18 Hz, 1H), 1.61 (s, 9H), 1.04 (d, *J* = 7.11 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.2, 173.4, 156.3, 149.1, 144.1, 140.2, 135.6, 135.4, 133.0, 128.8, 128.7, 128.3, 127.9, 127.3, 127.0, 126.8, 115.3, 114.2, 113.1, 84.4, 78.1, 63.1, 59.0, 55.6, 40.7, 35.4, 28.3, 22.4, 14.2, 13.8. FTIR (KBr) cm^{-1}: 3484, 2925, 2855, 1762, 1725, 1604. **HRMS ESI**: $[M+Na]^+$, Calcd for $C_{34}H_{35}NNaO_6$ 592.2311; found 592.2310

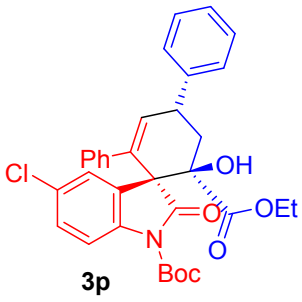


3o

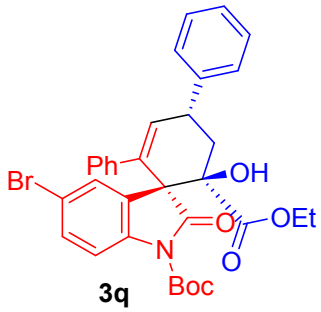
1'-*tert*-butyl 6-ethyl-6-hydroxy-5'-flouro-2'-oxo-2,4-diphenyl-1',2'-dihydrospiro[cyclohexane-1,3'-indol]-2-ene-1',6-

dicarboxylate (3o). To a solution of 3–alkylidene–2–oxindole **1d** (70mg, 0.20 mmol) and β,γ–unsaturated α–keto ester **2a** (40.8mg, 0.20 mmol) in 1 mL acetonitrile was added DABCO (4.5mg, 0.04 mmol) and the reaction mixture was stirred at rt for 12 h. The *dr* (>19:1) was determined by ^{1}H NMR analysis of crude product. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup to give white solid **3o** (100.2 mg, 90% yield); mp: 145–146 °C; R_f = 0.33 (ethyl acetate/petroleum ether = 1/9); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 8.97, 4.60 Hz, 1H), 7.58 (s, 1H), 7.55 (s, 1H), 7.39 – 7.31 (m, 2H), 7.28 – 7.24 (m, 1H), 7.08 – 6.98 (m, 4H), 6.96 – 6.80 (m, 3H), 6.24 (d, *J* = 2.31 Hz, 1H), 4.14 – 3.88 (m, 4H), 3.10 (dd, *J* = 13.37, 110.99 Hz, 1H), 2.07 (dd, *J* = 13.52, 6.19 Hz, 1H), 1.68 (s, 9H), 1.11 (t, *J* = 7.14 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.7, 173.3, 149.0, 144.0, 139.9, 135.5, 135.3, 128.8, 128.6, 128.0, 127.3, 127.2, 126.9, 115.7, 115.6, 115.5, 115.4, 115.0, 114.7, 84.9, 78.1, 63.2, 58.8, 40.6, 35.6, 28.3, 13.8. FTIR (KBr) cm^{-1}: 3468, 2985, 2928, 1767, 1726, 1606. **HRMS ESI**: $[M+Na]^+$, Calcd for $C_{33}H_{32}FNNaO_6$ 580.2111; found 580.2106

1'-*tert*-butyl 6-ethyl-6-hydroxy-5'-chloro-2'-oxo-2,4-diphenyl-1',2'-dihydrospiro[cyclohexane-1,3'-indol]-2-ene-1',6-dicarboxylate (3p). To a solution of 3–alkylidene–2–oxindole **1e** (73.8mg, 0.20 mmol) and β,γ–unsaturated α–keto ester **2a** (40.8mg, 0.20 mmol) in 1 mL acetonitrile was added DABCO (4.5mg, 0.04 mmol) and the reaction mixture was stirred at rt for 12 h. The *dr* (>19:1) was determined by ^{1}H NMR analysis of crude product. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup to give white solid **3p** (103.3 mg, 90% yield); mp: 157–158 °C; R_f = 0.33 (ethyl acetate/petroleum ether = 1/9); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 – 7.49 (m, 3H), 7.42 – 7.23 (m, 4H), 7.13 (dd, *J* = 8.71, 2.23 Hz, 1H), 7.07 – 7.00 (m, 3H), 6.97 – 6.88 (m, 2H), 6.23 (d, *J* = 2.26 Hz, 1H), 4.20 – 3.84 (m, 4H), 3.09 (dd, *J* = 13.33, 11.02 Hz, 1H), 2.08 (dd, *J* = 14.01, 6.68 Hz, 1H), 1.68 (s, 9H), 1.11 (t, *J* = 7.13 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.2, 173.1, 148.8, 143.8, 139.7, 138.1, 135.4, 135.1, 129.4, 128.8, 128.7, 128.5, 127.9, 127.3, 127.2, 127.1, 126.8, 115.4, 84.9, 77.9, 63.1, 58.6, 40.4, 35.5, 28.1, 13.7. FTIR (KBr) cm^{-1}: 3473, 2926, 1768, 1726, 1600. **HRMS ESI**: $[M+Na]^+$, Calcd for $C_{33}H_{32}ClNNaO_6$ 596.1816; found 596.1812

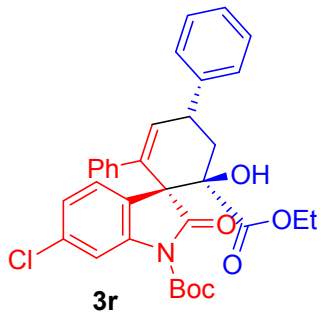


3p



3q

1'-*tert*-butyl 6-ethyl-6-hydroxy-5'-bromo-2'-oxo-2,4-diphenyl-1',2'-dihydrospiro[cyclohexane-1,3'-indol]-2-ene-1',6-dicarboxylate (3q). To a solution of 3–alkylidene–2–oxindole **1f** (82.4mg, 0.20 mmol) and β,γ–unsaturated α–keto ester **2a** (40.8mg, 0.20 mmol) in 1 mL acetonitrile was added DABCO (4.5mg, 0.04 mmol) and the reaction mixture was stirred at rt for 12 h. The *dr* (>19:1) was determined by ^{1}H NMR analysis of crude product. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup to give white solid **3q** (113.7 mg, 92% yield); mp: 159–160 °C; R_f = 0.33 (ethyl acetate/petroleum ether = 1/9); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61 – 7.47 (m, 3H), 7.44 (d, *J* = 1.13 Hz, 1H), 7.38 – 7.32 (m, 2H), 7.30 – 7.21 (m, 2H), 7.05 (s, 3H), 6.95 – 6.85 (m, 2H), 6.23 (s, 1H), 4.14 – 4.05 (m, 1H), 4.04 – 3.95 (m, 2H), 3.93 (s, 1H), 3.21 – 2.92 (m, 1H), 2.07 (dt, *J* = 13.78, 8.04 Hz, 1H), 1.67 (s, 9H), 1.11 (t, *J* = 7.10 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.3, 173.2, 148.9, 143.9, 139.8, 138.7, 135.5, 135.3, 131.8, 130.3, 129.1, 128.8, 128.6, 128.0, 127.3, 127.2, 126.9, 117.2, 115.9, 85.0, 78.0, 63.2, 58.6, 40.5, 35.6, 28.2, 13.8. FTIR (KBr) cm^{-1}: 3477, 2985, 2925, 1768, 1726, 1600. **HRMS ESI**: $[M+Na]^+$, Calcd for $C_{33}H_{32}BrNNaO_6$ 640.1311; found 640.1306

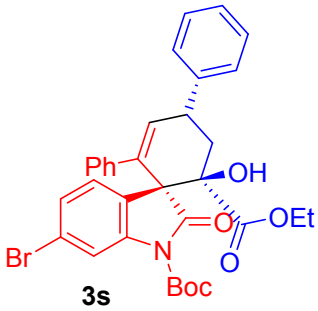


3r

1'-*tert*-butyl 6-ethyl-6-hydroxy-6'-chloro-2'-oxo-2,4-diphenyl-1',2'-dihydrospiro[cyclohexane-1,3'-indol]-2-ene-1',6-dicarboxylate (3r): To a solution of 3–alkylidene–2–oxindole **1g** (73.8mg, 0.20 mmol) and β,γ–unsaturated α–keto ester **2a** (40.8mg, 0.20 mmol) in 1 mL acetonitrile was added DABCO (4.5mg, 0.04 mmol) and the reaction mixture was stirred at rt for 12 h. The *dr* (>19:1) was determined by ^{1}H NMR analysis of crude product. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup to give white solid **3r** (103.3 mg, 90% yield); mp: 148–149 °C; R_f = 0.33 (ethyl acetate/petroleum ether = 1/9); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 1.73 Hz, 1H), 7.61 – 7.51 (m, 2H), 7.41 – 7.30 (m, 2H), 7.29 – 7.23 (m, 1H), 7.20 (d, *J* = 8.15 Hz, 1H), 7.10 – 7.00 (m, 3H), 6.98 – 6.84 (m, 3H), 6.24 (d, *J* = 2.09 Hz, 1H), 4.19 – 3.85 (m, 4H), 3.08 (dd, *J* = 13.20, 11.16 Hz, 1H), 2.07 (dd, *J* = 13.43, 6.08 Hz, 1H), 1.69 (s, 9H), 1.13 (t, *J* = 7.13 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.6, 173.3, 148.8, 143.9, 140.4, 140.0, 135.5, 135.4, 134.6, 128.8, 128.6,

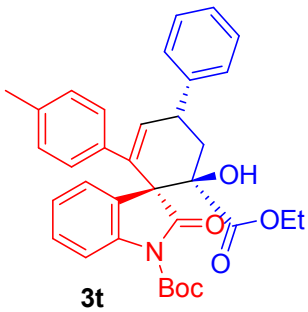
128.2, 128.0, 127.2, 127.1, 126.9, 125.5, 124.3, 115.1, 85.2, 78.1, 63.2, 58.4, 40.6, 35.6, 28.2, 13.8. FTIR (KBr) cm^{-1}: 3465, 2984, 2931, 1765, 1735, 1602. **HRMS ESI**: $[M+Na]^+$, Calcd for $C_{33}H_{32}ClNNaO_6$ 596.1816; found 596.1813

1'-*tert*-butyl 6-ethyl-6-hydroxy-6'-bromo-2'-oxo-2,4-diphenyl-1',2'-dihydrospiro[cyclohexane-1,3'-indol]-2-ene-1',6-dicarboxylate (3s). To a solution of 3–alkylidene–2–oxindole **1h** (82.4mg, 0.20 mmol) and β,γ–unsaturated α–keto ester **2a** (40.8mg, 0.20 mmol) in 1 mL acetonitrile was added DABCO (4.5mg, 0.04 mmol) and the reaction mixture was stirred at rt for 12 h. The *dr* (>19:1) was determined by ^{1}H NMR analysis of crude product. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup to give white solid **3s** (116.2 mg, 94% yield); mp: 145–146 °C; R_f = 0.33 (ethyl acetate/petroleum ether = 1/9); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.62 – 7.47 (m, 2H), 7.40 - 7.30 (m, 2H), 7.26 (d, *J* = 6.33 Hz, 1H), 7.14 (d, *J* = 8.09 Hz, 1H), 7.10 – 7.00 (m, 4H), 6.95 – 6.86 (m, 2H), 6.24 (d, *J* = 2.11 Hz, 1H), 4.19 – 3.83 (m, 4H), 3.08 (dd, *J* = 13.19, 11.19 Hz, 1H), 2.07 (dd, *J* = 13.50, 6.17 Hz, 1H), 1.69 (s, 9H), 1.13 (t, *J* = 7.01 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.4, 173.3, 148.8, 143.9, 140.5, 139.9, 135.5, 135.3, 128.8, 128.6, 128.5, 128.0, 127.2, 127.1, 126.9, 126.0, 122.7, 117.8, 85.2, 78.0, 63.2, 58.5, 40.6, 35.6, 28.2, 13.8. FTIR (KBr) cm^{-1}: 3467, 3025, 2985, 1766, 1734, 1598. **HRMS ESI**: $[M+Na]^+$, Calcd for $C_{33}H_{32}BrNNaO_6$ 640.1311; found 640.1307



3s

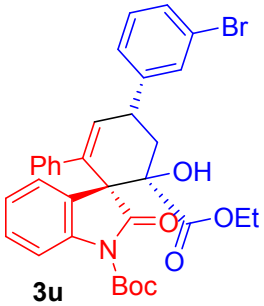
1'-*tert*-butyl 6-ethyl-6-hydroxy-2-(4-methylphenyl)-2'-oxo-4-phenyl-1',2'-dihydrospiro[cyclohexane-1,3'-indol]-2-ene-1',6-dicarboxylate (3t): To a solution of 3–alkylidene–2–oxindole **1i** (69.8mg, 0.20 mmol) and β,γ–unsaturated α–keto ester **2a** (40.8mg, 0.20 mmol) in 1 mL acetonitrile was added DABCO (4.5mg, 0.04 mmol) and the reaction mixture was stirred at rt for 12 h. The *dr* (>19:1) was determined by ^{1}H NMR analysis of crude product. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup to give white solid **3t** (97.3 mg, 88% yield); mp: 130–131 °C; R_f = 0.33 (ethyl acetate/petroleum ether = 1/9); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.18 Hz, 1H), 7.52 – 7.41 (m, 2H), 7.26 (s, 1H), 7.21 – 7.10 (m, 3H), 7.05 – 6.98 (m, 3H), 6.97 – 6.86 (m, 3H), 6.23 (d, *J* = 2.36 Hz, 1H), 4.15 – 3.85 (m, 4H), 3.11 (dd, *J* = 13.29, 11.04 Hz, 1H), 2.34 (s, 3H), 2.06 (dd, *J* = 13.44, 6.22 Hz, 1H), 1.68



3t

(s, 9H), 1.10 (t, J = 7.13 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.1, 173.4, 149.1, 141.1, 140.2, 139.6, 136.4, 135.6, 135.5, 129.4, 128.9, 128.5, 127.9, 127.3, 127.3, 127.0, 126.9, 124.2, 114.4, 84.6, 78.2, 63.0, 58.8, 40.3, 35.5, 28.3, 21.2, 13.8. FTIR (KBr) cm^{-1}: 3476, 3026, 2856, 1766, 1727, 1604. **HRMS ESI**: $[M+Na]^+$, Calcd for $C_{34}H_{35}NNaO_6$ 576.2362; found 576.2358

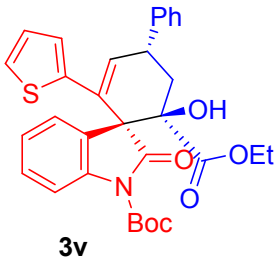
1'-*tert*-butyl 6-ethyl-6-hydroxy-2-(3-bromophenyl)-2'-oxo-4-phenyl-1',2'-dihydrospiro[cyclohexane-1,3'-indol]-2-ene-1',6-dicarboxylate (3u).



3u

To a solution of 3–alkylidene–2–oxindole **1j** (82.4mg, 0.20 mmol) and *β, γ*–unsaturated *α*–keto ester **2a** (40.8mg, 0.20 mmol) in 1 mL acetonitrile was added DABCO (4.5mg, 0.04 mmol) and the reaction mixture was stirred at rt for 12 h. The *dr* (>19:1) was determined by ^{1}H NMR analysis of crude product. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup to give white solid **3u** (103.8 mg, 84% yield); mp: 135–136 °C; R_f = 0.33 (ethyl acetate/petroleum ether = 1/9); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 (d, J = 8.20 Hz, 1H), 7.57 (d, J = 7.16 Hz, 2H), 7.36 (t, J = 7.32 Hz, 2H), 7.28 (s, 1H), 7.25 – 7.22 (m, 1H), 7.22 – 7.11 (m, 3H), 6.97 (t, J = 7.55 Hz, 1H), 6.88 (t, J = 7.74 Hz, 1H), 6.79 (d, J = 7.71 Hz, 1H), 6.26 (d, J = 2.34 Hz, 1H), 4.12 – 3.86 (m, 4H), 3.13 (dd, J = 13.27, 11.09 Hz, 1H), 2.08 (dd, J = 13.42, 6.20 Hz, 1H), 1.69 (s, 9H), 1.10 (t, J = 7.13 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.9, 173.3, 149.0, 143.8, 142.2, 139.6, 136.3, 134.6, 130.5, 129.4, 129.2, 128.8, 128.6, 127.7, 126.6, 125.8, 124.4, 122.0, 114.4, 84.8, 78.1, 63.1, 58.6, 40.7, 35.4, 28.3, 13.8. FTIR (KBr) cm^{-1}: 3457, 2926, 2854, 1762, 1732, 1603. **HRMS ESI**: $[M+Na]^+$, Calcd for $C_{33}H_{32}BrNNaO_6$ 640.1311; found 640.1306.

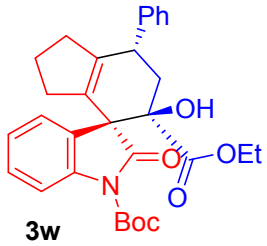
1'-*tert*-butyl 6-ethyl-6-hydroxy-2'-oxo-4-phenyl-2-(thiophen-2-yl)-1',2'-dihydrospiro[cyclohexane-1,3'-indol]-2-ene-1',6-dicarboxylate (3v). To a solution of 3–alkylidene–2–oxindole **1k** (68.2mg, 0.20 mmol) and β,γ–unsaturated α–keto ester **2a** (40.8mg, 0.20 mmol) in 1 mL acetonitrile was added DABCO (4.5mg, 0.04 mmol) and the reaction mixture was stirred at rt for 12 h. The *dr* (>19:1) was determined by ^{1}H NMR analysis of crude product. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup to give white solid **3v** (92.68 mg, 85% yield); mp: 108–109 °C; R_f = 0.32 (ethyl acetate/petroleum ether = 1/9); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.20 Hz, 1H), 7.66 – 7.51 (m, 2H), 7.50 – 7.31 (m, 4H), 7.31



3v

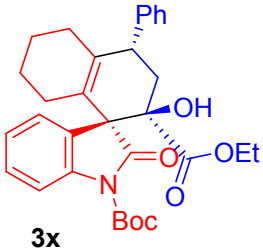
– 7.27 (m, 1H), 7.15 – 7.00 (m, 1H), 6.90 (d, *J* = 4.99 Hz, 1H), 6.63 (dd, *J* = 5.09, 3.64 Hz, 1H), 6.49 (s, 1H), 6.32 (s, 1H), 4.29 – 3.83 (m, 4H), 3.22 – 2.94 (m, 1H), 2.16 – 1.97 (m, 1H), 1.65 (s, 9H), 1.10 (t, *J* = 7.13 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.4, 173.2, 149.1, 144.0, 142.1, 140.1, 135.7, 129.5, 129.1, 128.8, 128.7, 127.3, 127.0, 126.9, 126.8, 124.4, 124.3, 114.7, 84.7, 78.0, 63.1, 40.60 35.4, 28.3, 13.8. FTIR (KBr) cm^{-1}: 3471, 2982, 2931, 1765, 1728, 1603. **HRMS ESI**: $[M+Na]^+$, Calcd for $C_{31}H_{31}NNaO_6S$ 568.1770; found 568.1765.

1'-*tert*-butyl 5-ethyl -5-hydroxy-2'-oxo-7-phenyl-1,1',2,2',3,5,6,7-octahydrospiro[indene-4,3'-indol]-1',5-dicarboxylate (3w). To a solution of 3–alkylidene–2–oxindole **1l** (60mg, 0.20 mmol) and *β, γ*–unsaturated *α*–keto ester **2a** (40.8mg, 0.20 mmol) in 1 mL acetonitrile was added DABCO (4.5mg, 0.04 mmol) and the reaction mixture was stirred at rt for 12 h. The *dr* (>19:1) was determined by ^{1}H NMR analysis of crude product. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup to give white solid **3w** (82.5 mg, 82% yield); mp: 126–127 °C; R_f = 0.33 (ethyl acetate/petroleum ether = 1/9); **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.78 (d, *J* = 8.16 Hz, 1H), 7.66 (dd, *J* = 7.56, 0.81 Hz, 1H), 7.50-7.43 (m, 2H), 7.39 – 7.30 (m, 3H), 7.28 – 7.21 (m, 1H), 7.19 – 7.13 (m, 1H), 5.20 (d, *J* = 2.13 Hz, 1H), 4.10 – 3.90 (m, 2H), 3.74 (s, 1H), 3.69 – 3.58 (m, 1H), 3.34 -3.16 (m, 1H), 3.10 – 2.94 (m, 1H), 2.41 – 2.24 (m, 1H), 2.20 – 2.04 (m, 1H), 2.01 – 1.90 (m, 1H), 1.81 (dd, *J* = 13.42, 3.92 Hz, 1H), 1.68 (s, 9H), 1.55 (dd, *J* = 9.23, 3.47 Hz, 1H), 1.06 (t, *J* = 7.14 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.0, 172.3, 149.2, 144.6, 141.0, 139.7, 129.0 128.8, 128.5, 128.0, 127.1, 126.8, 126.5, 126.5, 124.2, 114.5, 84.5, 78.1, 62.8, 57.4, 46.5, 46.5, 38.8, 31.2, 29.9, 28.2, 13.7. FTIR (KBr) cm^{-1}: 3448, 2975, 2930, 1729, 1602. **HRMS ESI**: $[M+Na]^+$, Calcd for $C_{30}H_{33}NNaO_6$ 526.2206; found 526.2200.



3w

1'-*tert*-butyl 6-ethyl-6-hydroxy-2-(4-methylphenyl)-2'-oxo-4-phenyl-1',2'-dihydrospiro[cyclohexane-1,3'-indol]-2-ene-1',6-dicarboxylate (3x). To a solution of 3–alkylidene–2–oxindole **1m** (62.6mg, 0.20 mmol) and *β, γ*–unsaturated *α*–keto ester **2a** (40.8mg, 0.20 mmol) in 1 mL acetonitrile was added DABCO (4.5mg, 0.04 mmol) and the reaction mixture was stirred at rt for 12 h. The *dr* (>19:1) was determined by ^{1}H NMR analysis of crude product. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup to give white solid **3x** (47.5 mg, 46% yield); mp: 145–146 °C;.



3x

R_f = 0.33 (ethyl acetate/petroleum ether = 1/9); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 (d, J = 8.05 Hz, 1H), 7.65 (d, J = 7.60 Hz, 1H), 7.53 – 7.44 (m, 2H), 7.38 – 7.29 (m, 3H), 7.24 (d, J = 7.31 Hz, 1H), 7.17 (t, J = 7.50 Hz, 1H), 5.36 – 5.18 (m, 1H), 4.07 – 3.95 (m, 1H), 3.94 – 3.83 (m, 1H), 3.73 (s, 1H), 3.30 (s, 1H), 3.26 – 3.18 (m, 1H), 3.02 – 2.88 (m, 1H), 2.11 – 1.97 (m, 1H), 1.89 – 1.78 (m, 1H), 1.75 (dd, J = 13.3, 4.3 Hz, 1H), 1.69 (s, 9H), 1.55 – 1.47 (m, 1H), 1.41 – 1.11 (m, 3H), 1.01 (t, J = 7.14 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.1, 172.9, 149.2, 144.9, 139.8, 135.2, 129.0, 128.5, 128.3, 127.8, 126.6, 126.5, 124.0, 114.5, 84.5, 77.9, 62.7, 59.7, 45.5, 38.1, 37.2, 29.2, 28.3, 26.2, 21.2, 13.6. FTIR (KBr) cm^{-1}: 3502, 3446, 2977, 2930, 1729, 1602. **HRMS ESI**: $[M+Na]^+$, Calcd for $C_{31}H_{35}NaO_6$ 540.2362; found 540.2360.

3. Asymmetric Vinylogous Michael Addition of 3–Alkylidene–2–oxindole to β,γ–Unsaturated α–Keto Ester:

Racemic Michael Adduct:

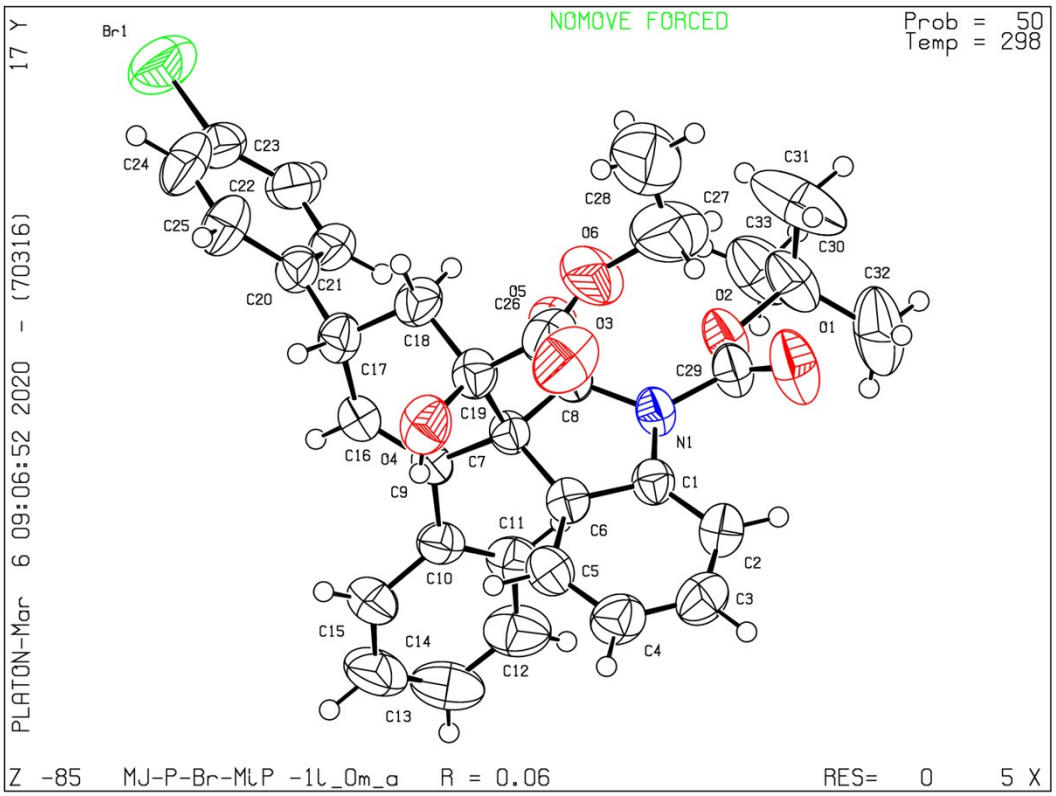
tert-butyl (*E*)-3-(6-ethoxy-5,6-dioxo-1,3-diphenylhexylidene)-2-oxoindoline-1 carb oxyl-ate (3a'): To a solution of 3–alkylidene–2–oxindole 1a (67 mg, 0.20 mmol) and β,γ–unsaturated α–keto ester 2a (40.8mg, 0.20 mmol) in 1 mL acetonitrile, NEt_3 as a base (15 mg, 20 µL, 0.24 mmol) and the reaction mixture was stirred at rt for 12 h. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup to give light yellow semi solid 3a'.

Chiral Michael Adduct:

tert-butyl (*E*)-3-(6-ethoxy-5,6-dioxo-1,3-diphenylhexylidene)-2-oxoindoline-1 carb oxyl-ate (3a'):[4] To a solution of 3–alkylidene–2–oxindole **1a** (67 mg, 0.20 mmol) and β,γ–unsaturated α–keto ester **2a** (40.8mg, 0.20 mmol) in 1 mL acetonitrile was added cinchona alkaloid derived thiourea as a catalyst (Quinine-9-amine thiourea, 11.5 mg, 20 mol%) and the reaction mixture was stirred at rt for 12 h. The *dr* (57:43) was determined by ^{1}H NMR analysis of crude product. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/petroleum ether = 1/10, v/v) without any workup to give light yellow semi solid **3a'** (39.0 mg, 36% yield). Rf = 0.3 (ethyl acetate/petroleum ether = 1/9); The ee of the **3a'** was determined to be 91% [determined by HPLC, Chiralpak IC, hexane: isopropanol = 90:10, flow rate 0.5 mL/min, λ = 254 nm, t_R (major) = 22.93 min, t_R (minor) = 18.20 min].

4. Crystallographic data

Single crystal X-ray structure of compound **3g** (**CCDC Number: 198866**)



Bond precision: C-C = 0.0064 Wavelength=0.71073

Cell: a=10.1020(17) b=10.4727(16) c=15.726(3)

alpha=104.702(5) beta=94.205(5) gamma=109.963(5)

Temperature: 298 K

	Calculated	Reported
Volume	1489.0(4)	1489.0(4)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C_{33} H_{32} Br N O_6	C_{33} H_{32} Br N O_6
Sum formula	C_{33} H_{32} Br N O_6	C_{33} H_{32} Br N O_6
Mr	618.50	618.50
Dx,g cm-3	1.380	1.380
Z	2	2
Mu (mm-1)	1.426	1.426
F000	640.0	640.0
F000'	639.71	
h,k,lmax	13,14,21	13,14,21
Nref	7459	7459
Tmin,Tmax	0.774,0.867	0.774,0.867
Tmin'	0.700	

Correction method= # Reported T Limits: Tmin=0.774 Tmax=0.867
AbsCorr = MULTI-SCAN

Data completeness= 1.000 Theta(max)= 28.385

R(reflections)= 0.0632(3719) wR2(reflections)= 0.2137(7459)

S = 0.935 Npar= 375

(Supplementary crystallographic data for the compound **3g** (**CCDC Number: 1988666**) can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK.; fax: (+44)-1223-336-033).

5. Cell viability of MG-63 cells in presence of a clinically approved anthracycline chemotherapeutic, Doxorubicin

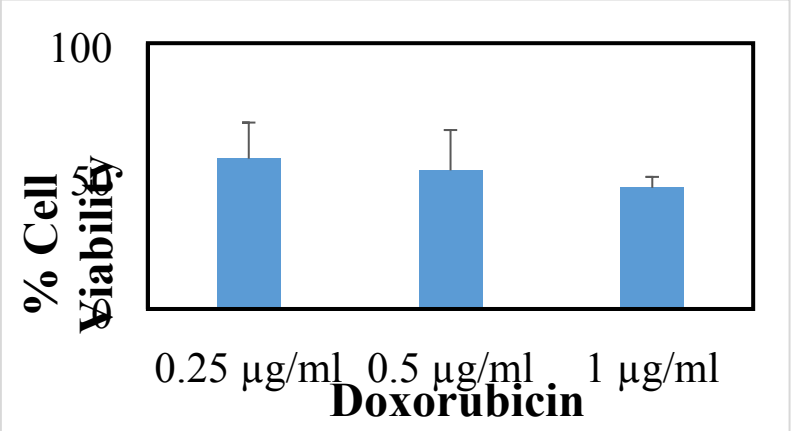


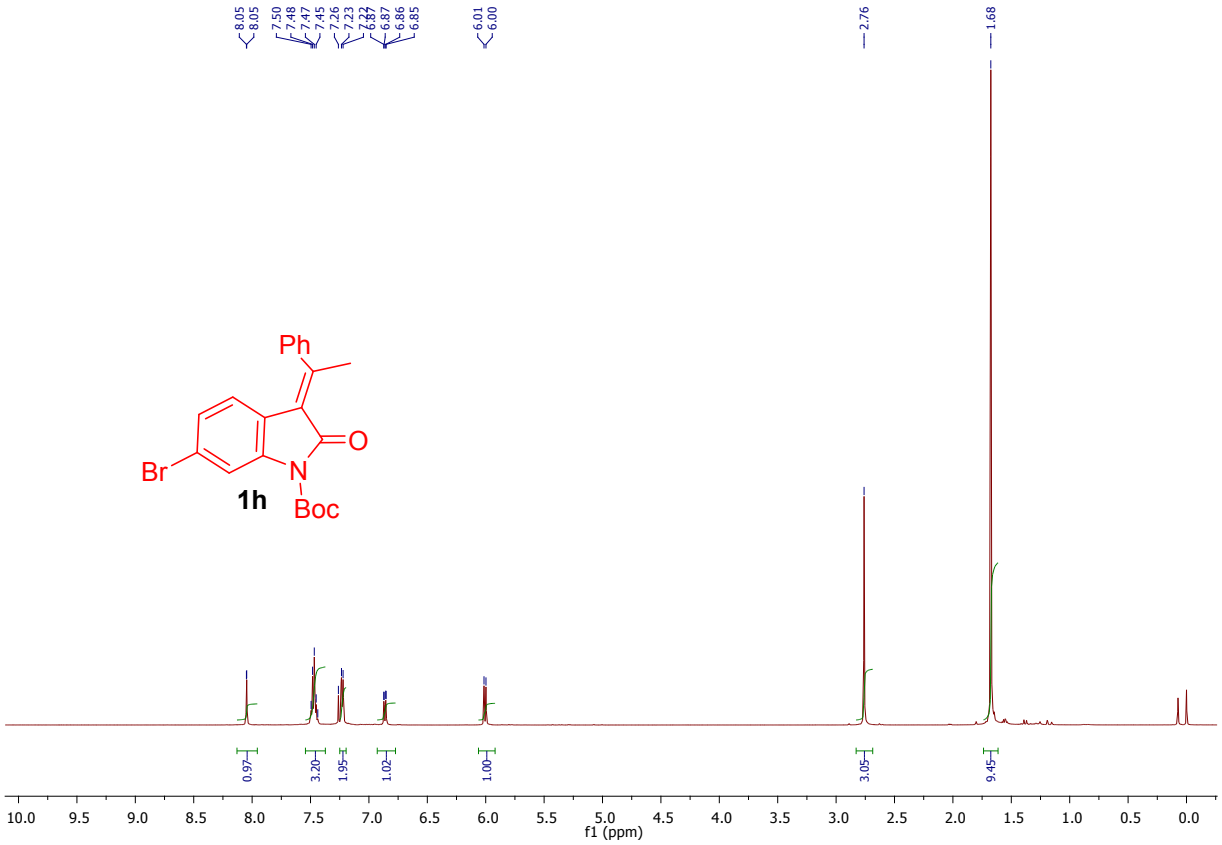
Figure S1: Cell viability as observed by MTT assay for positive control using chemotherapeutic drug Doxorubicin on MG-63 cells**.**

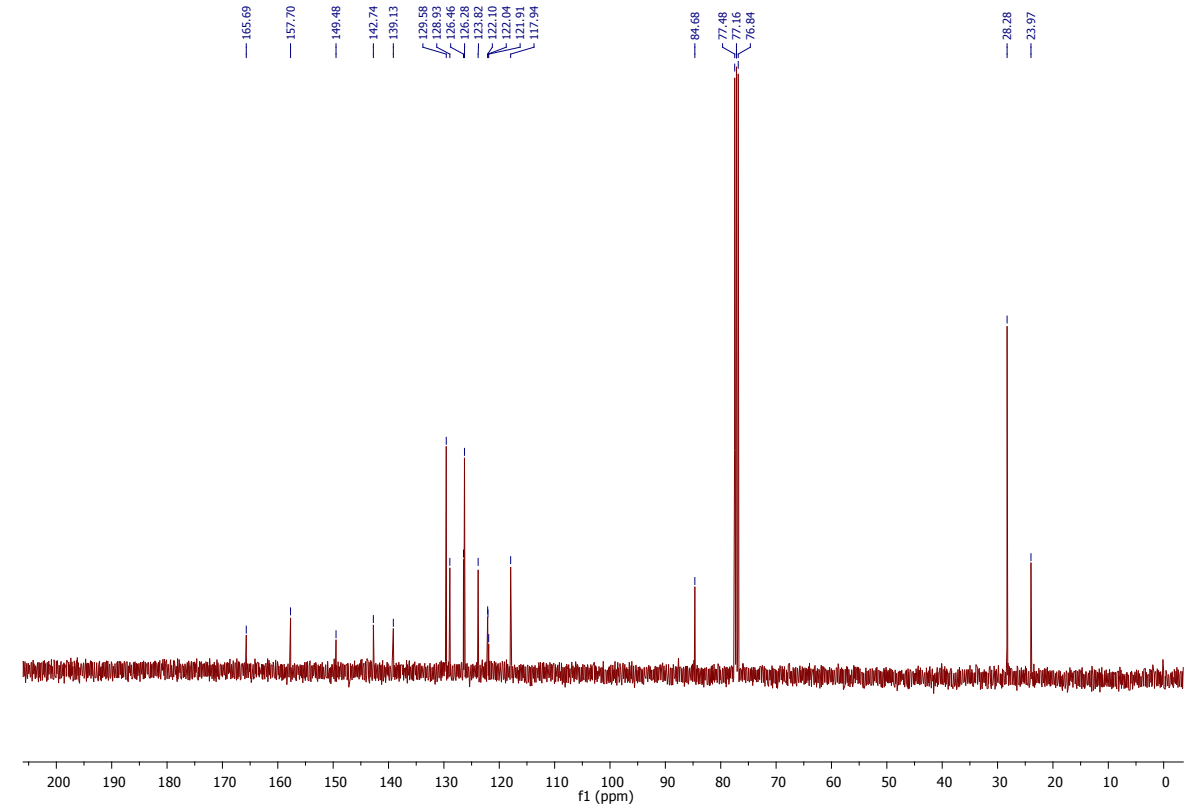
For comparing the bioactivity observed in Figure 4 and as a positive control for the MTT assay, cell viability studies with Doxorubicin was carried out. Briefly, Doxorubicin dilutions were

made in PBS an added to the MG63 cells at the concentration range for 0.25 µg/ml- 1 µg/ml. After 24 hours of treatment, the medium was removed and washed twice with PBS. 200 µL of MTT (500 µg/ml) diluted in medium was added to each well. When violet crystals were formed, MTT was removed and crystals were dissolved in dimethyl sulfoxide (DMSO) and absorbance was recorded at 570 nm. Cell viability was calculated, and a bar graph between percent cell viability versus concentration of different chemical compounds was plotted. Untreated cells were taken as the control. All the experiments were performed in triplicate.

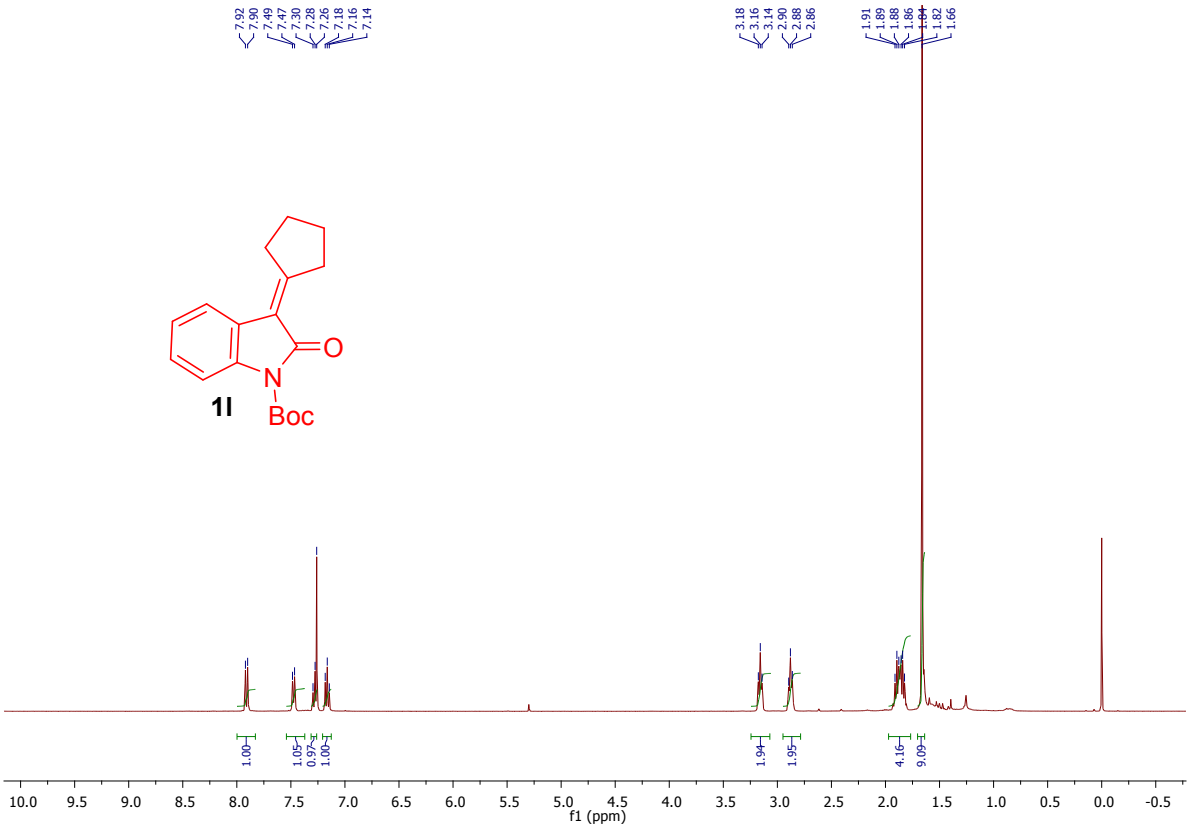
6. References

1. (a) S. M. Yang, P. Karanam, M. Wang, Y. J. Jang, Y. S. Yeh, P. Y. Tseng, M. R. Ganapuram, Y. C. Liou and W. W. Lin, *Chem. Commun.,* 2019, **55**, 1398; (b) J.-L. Han, Y.-D. Tsai and C.-H. Chang, *Adv. Synth. Catal*., 2017, **359**, 4043; (c) H. J. Lee, J. W. Lim, J. Yu and J. N. Kim, *Tetrahedron Lett.* 2014, **55**, 1183. (d) Y. Liu, Y. Yang, Y. Huang, X.-H. Xu, and F.-L. Qing, *Synlett.,* 2015*,* **26**, 67.
2. (a) X.-Z. Tang, L. Tong, H.-J. Liang, J. Liang, Y. Zou, X. J. Zhang, M. Yan and A. S. C. Chan, *Org. Biomol. Chem*., 2018, **16**, 3560; (b) P. Xing, W. Zang, Z.-G. Huang, Y.-X. Zhan, C.-J. Zhu and B. A. Jiang, *Synlett* 2012, **23**, 2269; (c) Q. Meng, L. Zhu and Z. Zhang, *J. Org. Chem.*, 2008, **73**, 7209.
3. C. Allais, F. Lieby-Muller, J. Rodriguez and T. Constantieux, *Eur. J. Org. Chem*., 2013, 4131.
4. M. K. Jaiswal, R. Kumar, S. Singh, S. Jain, K. Vanka and R. P. Singh*, Eur. J. Org. Chem.,* 2020, 5690.





7. ^{1}H and ^{13}C spectra of compounds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3.18
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2.90
2.88
2.86
1.91
1.89
1.88
1.86
1.84
1.82
1.66
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N
Boc
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0.97
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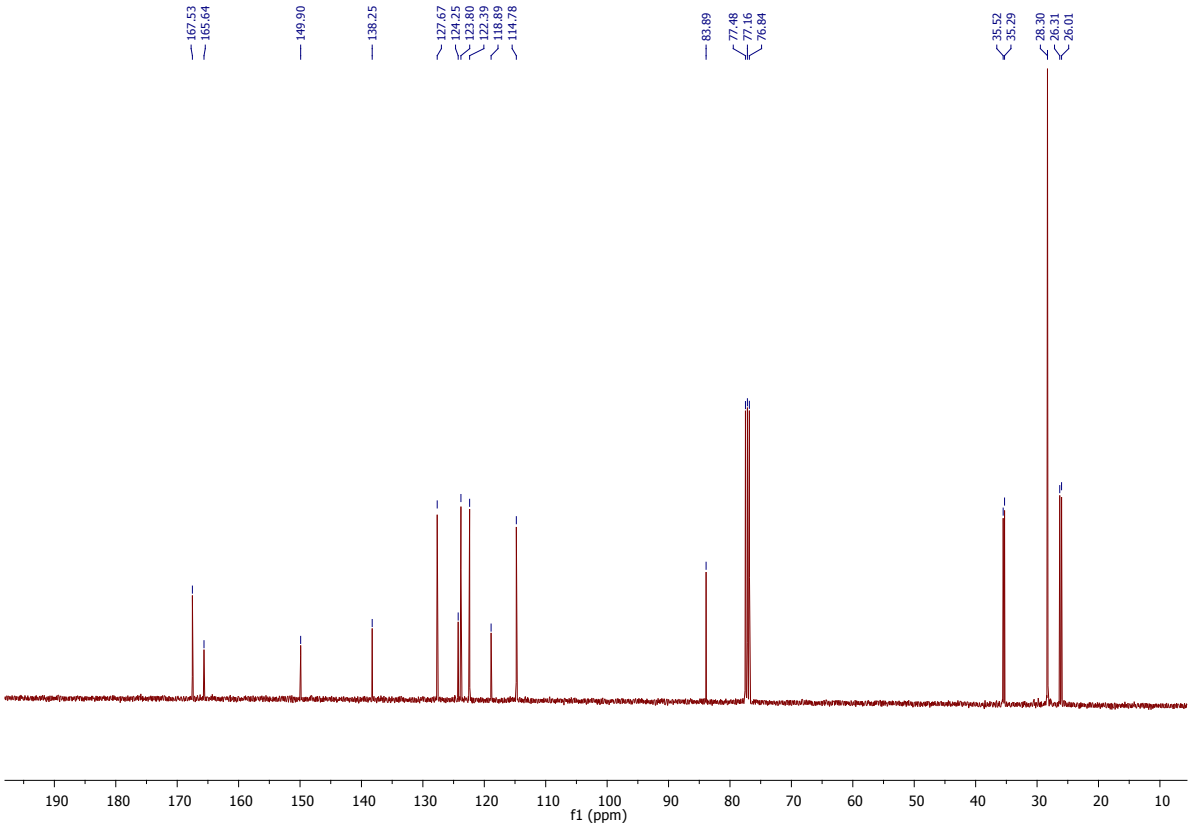
1.95
4.16
9.09
f1 (ppm)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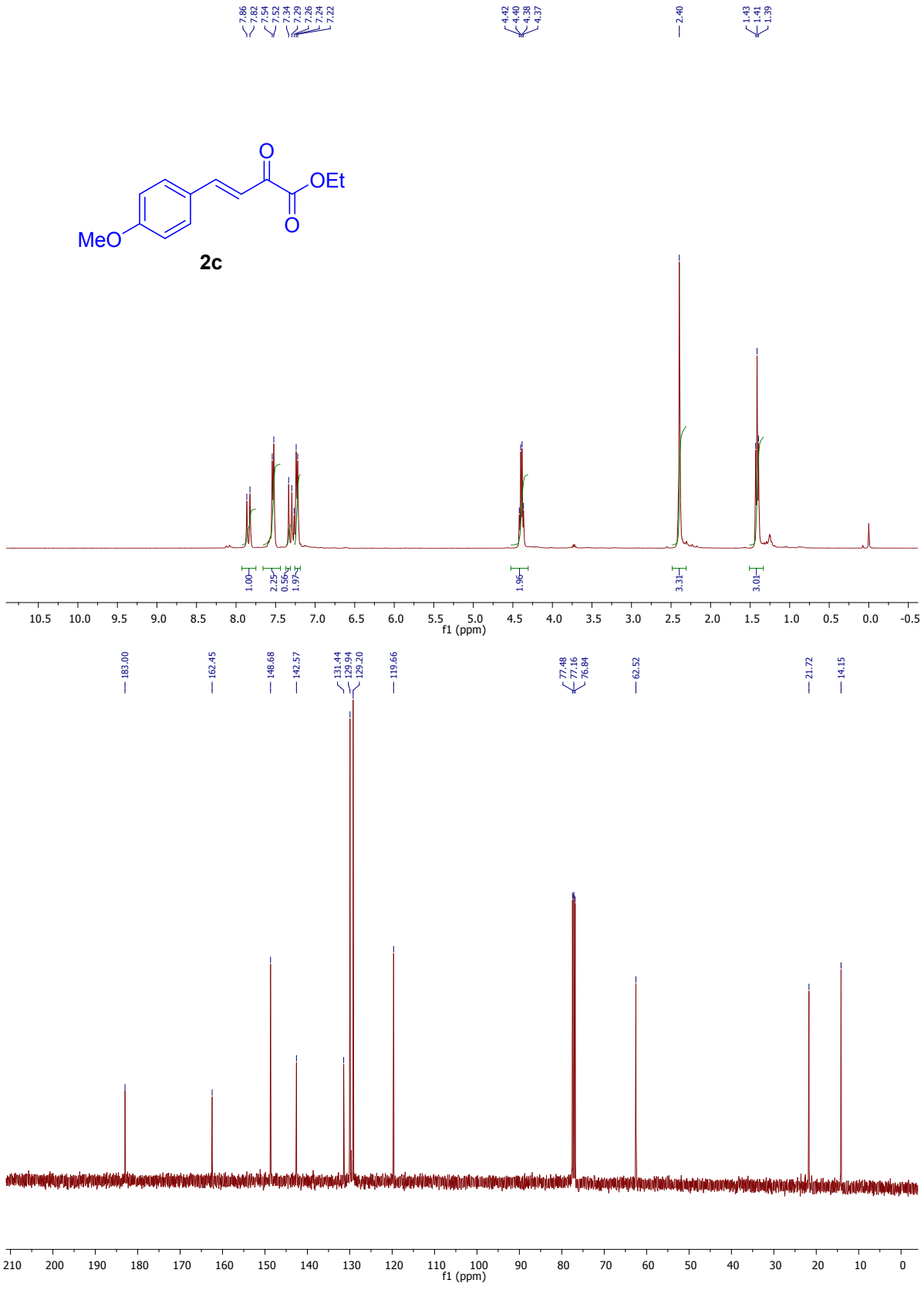
28.30
26.31
26.01
f1 (ppm)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2.40
1.43
1.41
1.39
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OEt
O
MeO
2c
1.00
2.25
0.56
1.97
1.96
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3.01
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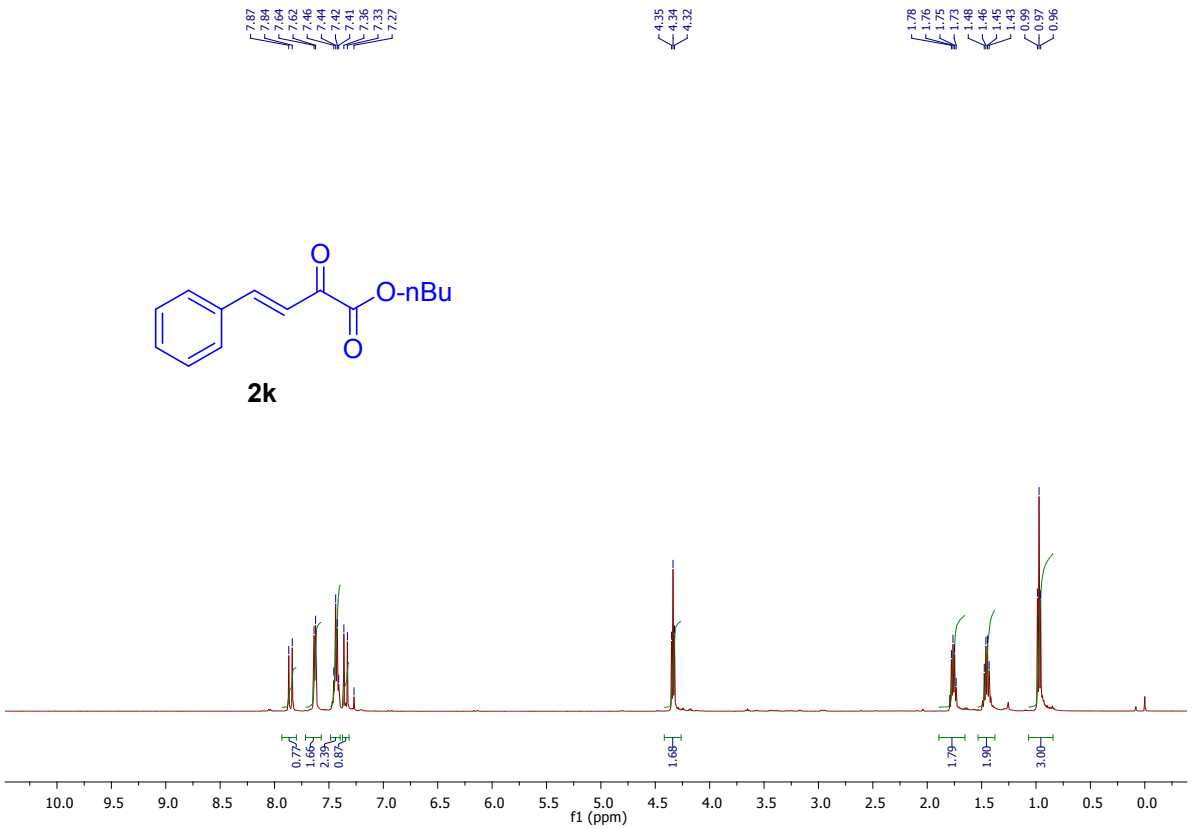
f1 (ppm)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4.32
1.78
1.76
1.75
1.73
1.48
1.46
1.45
1.43
0.99
0.97
0.96
O
O-nBu
O
0.77
1.66
2.39
0.87
1.68
1.79
1.90
3.00
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f1 (ppm)

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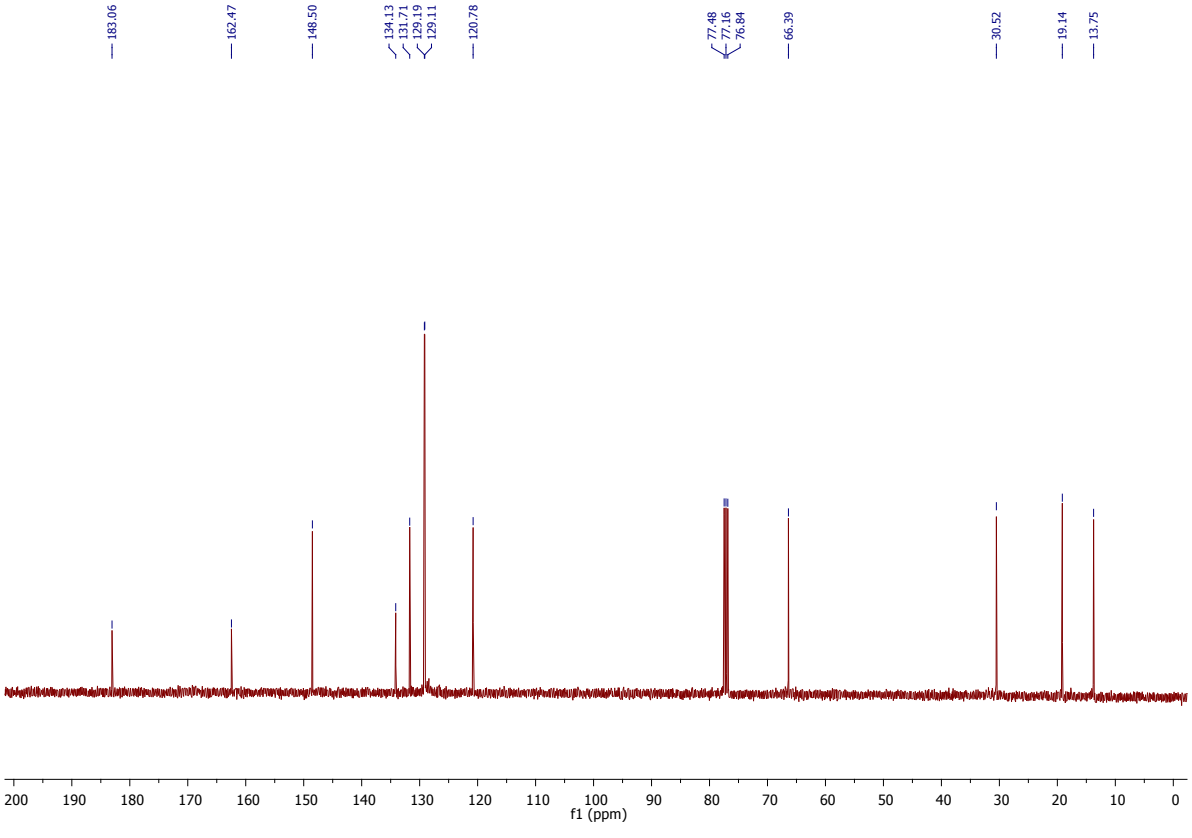
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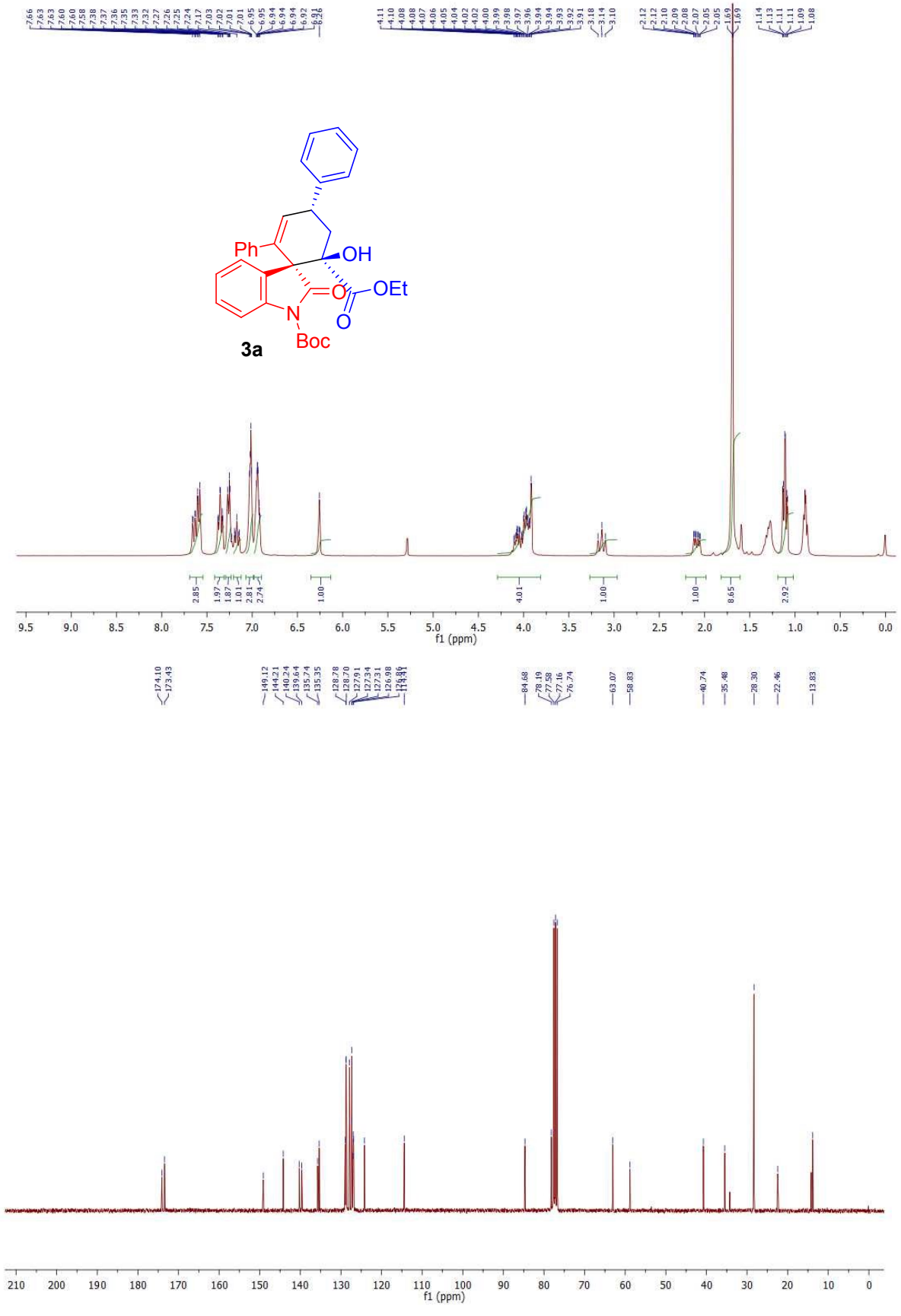
f1 (ppm)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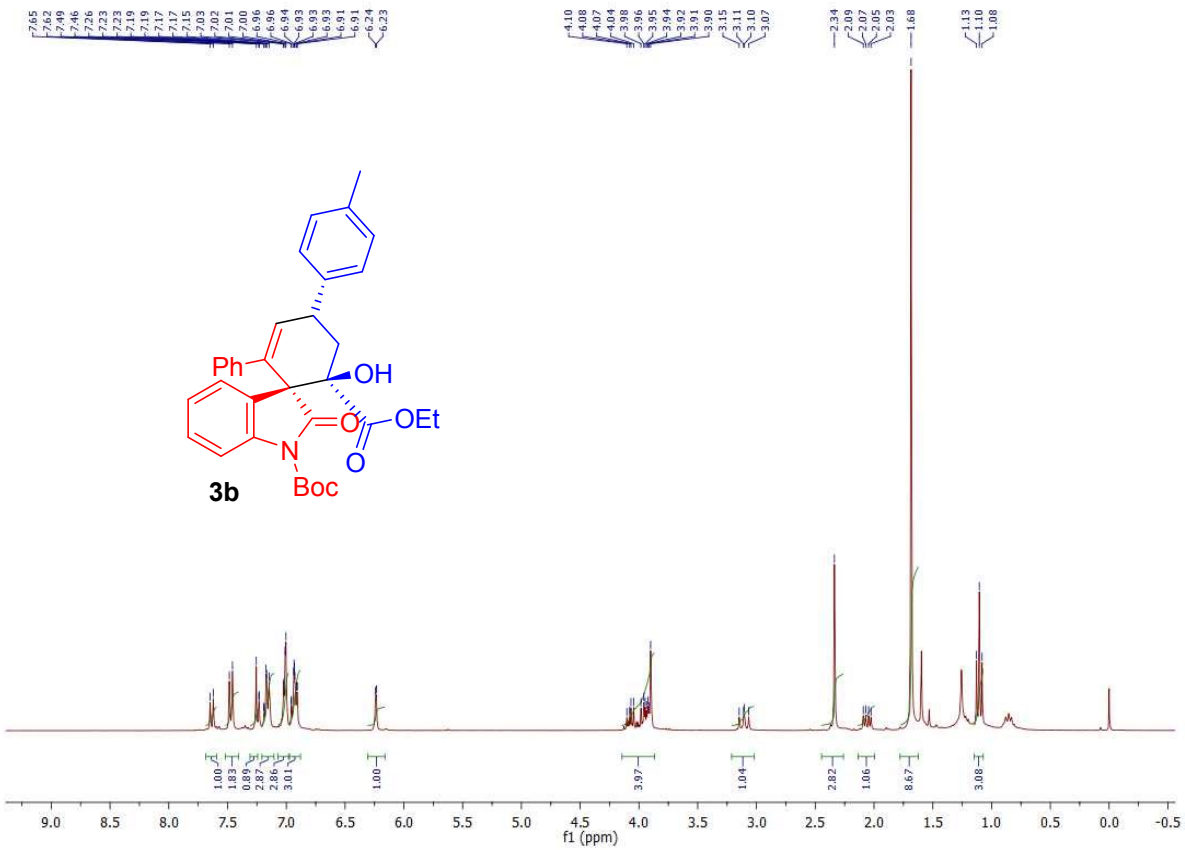
f1 (ppm)
f1 (ppm)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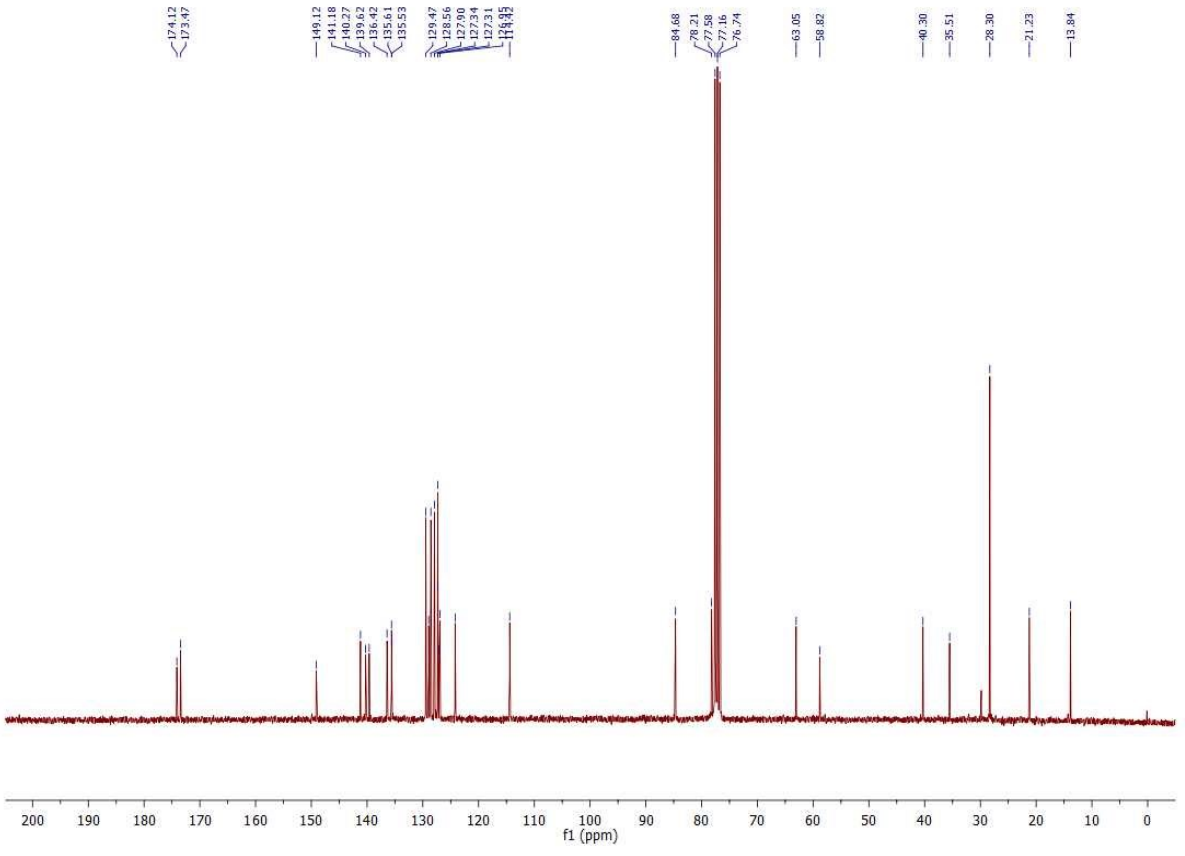
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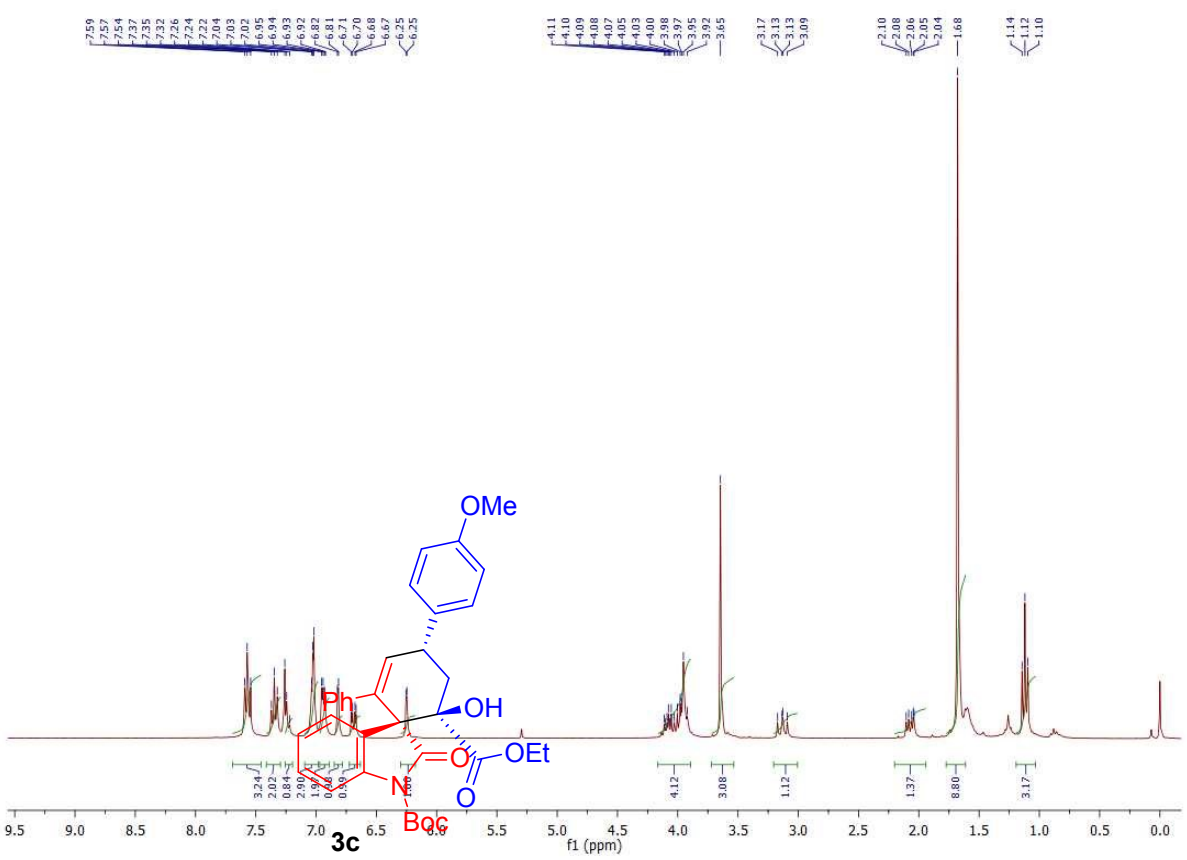

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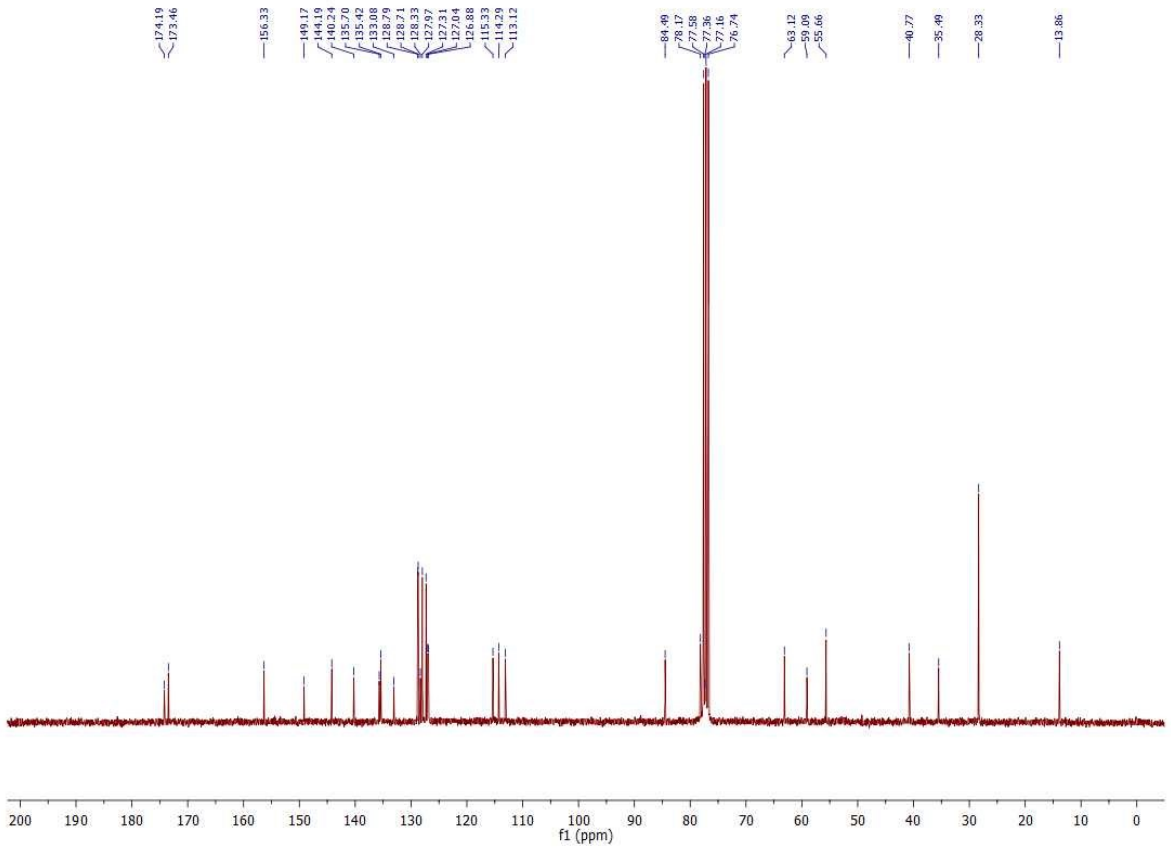

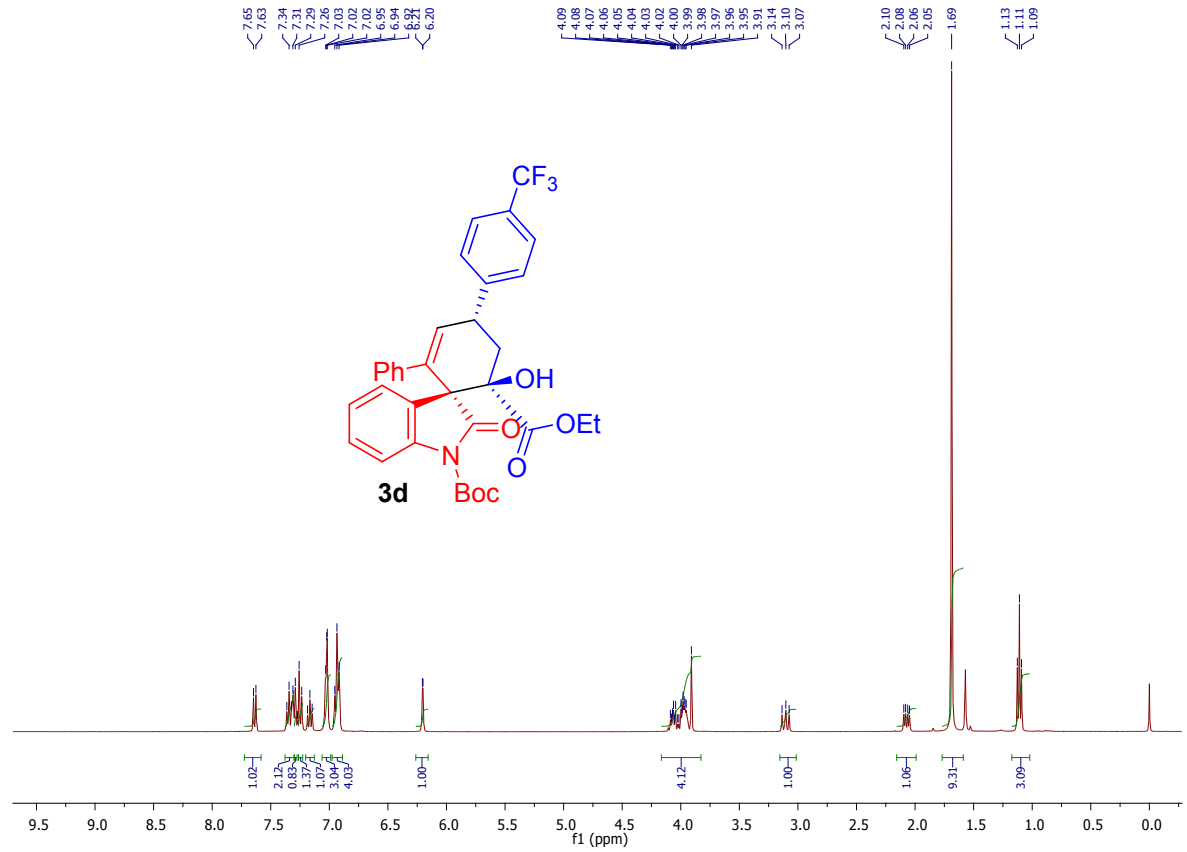
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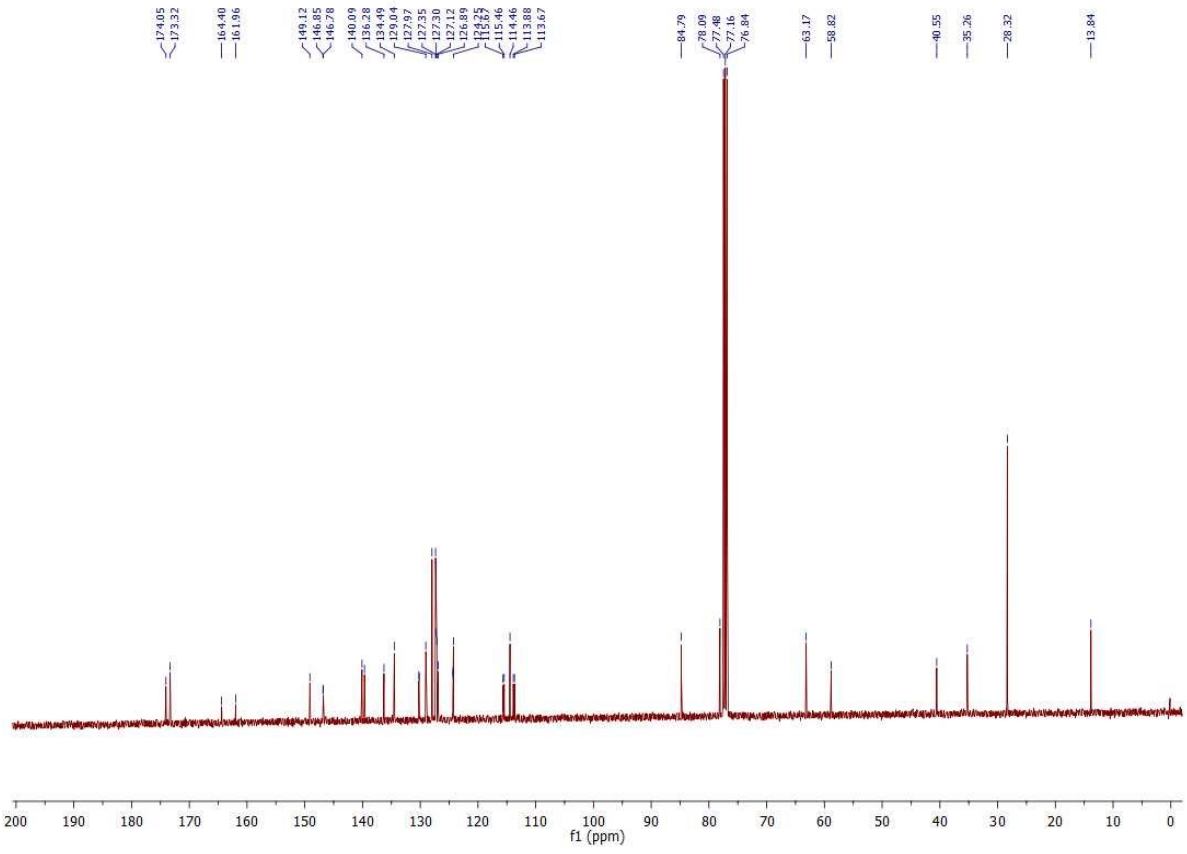
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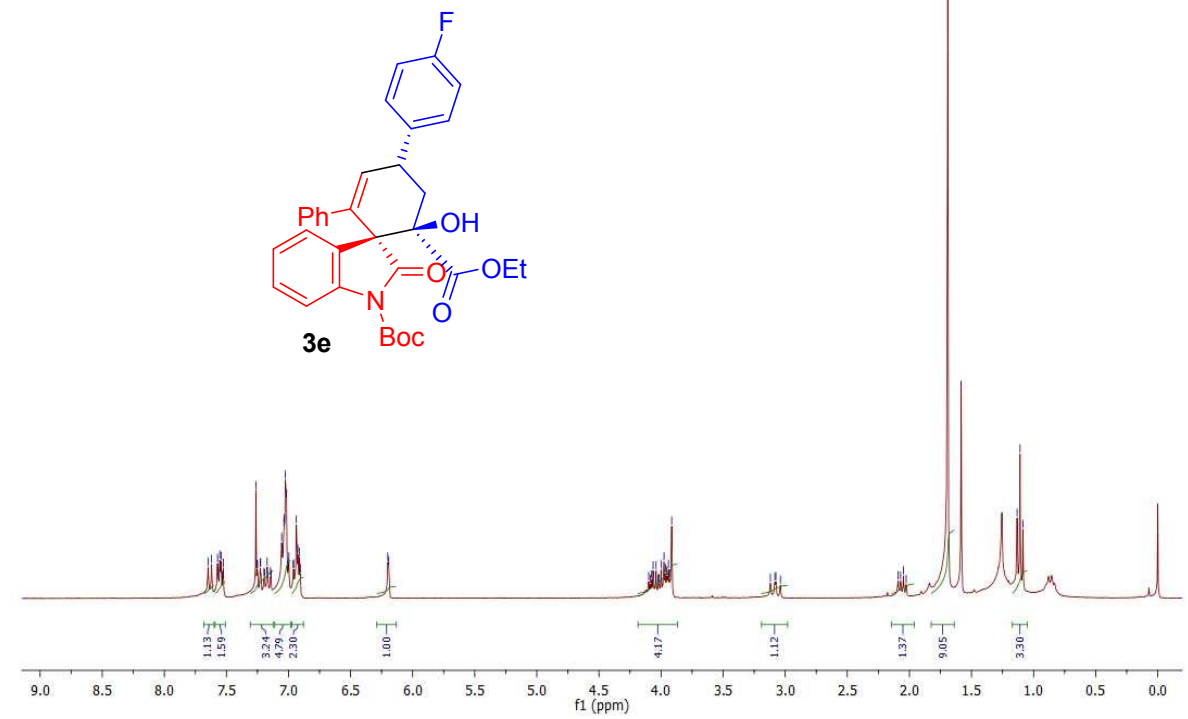

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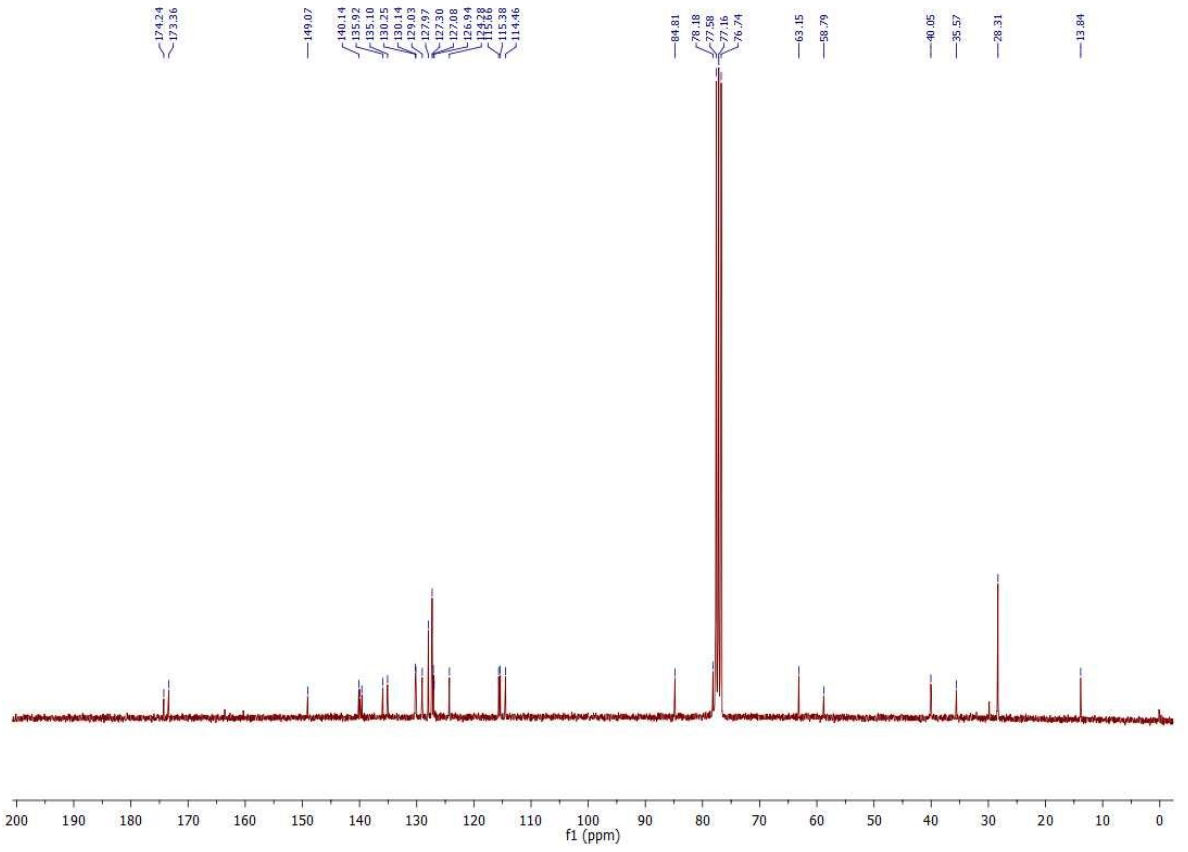

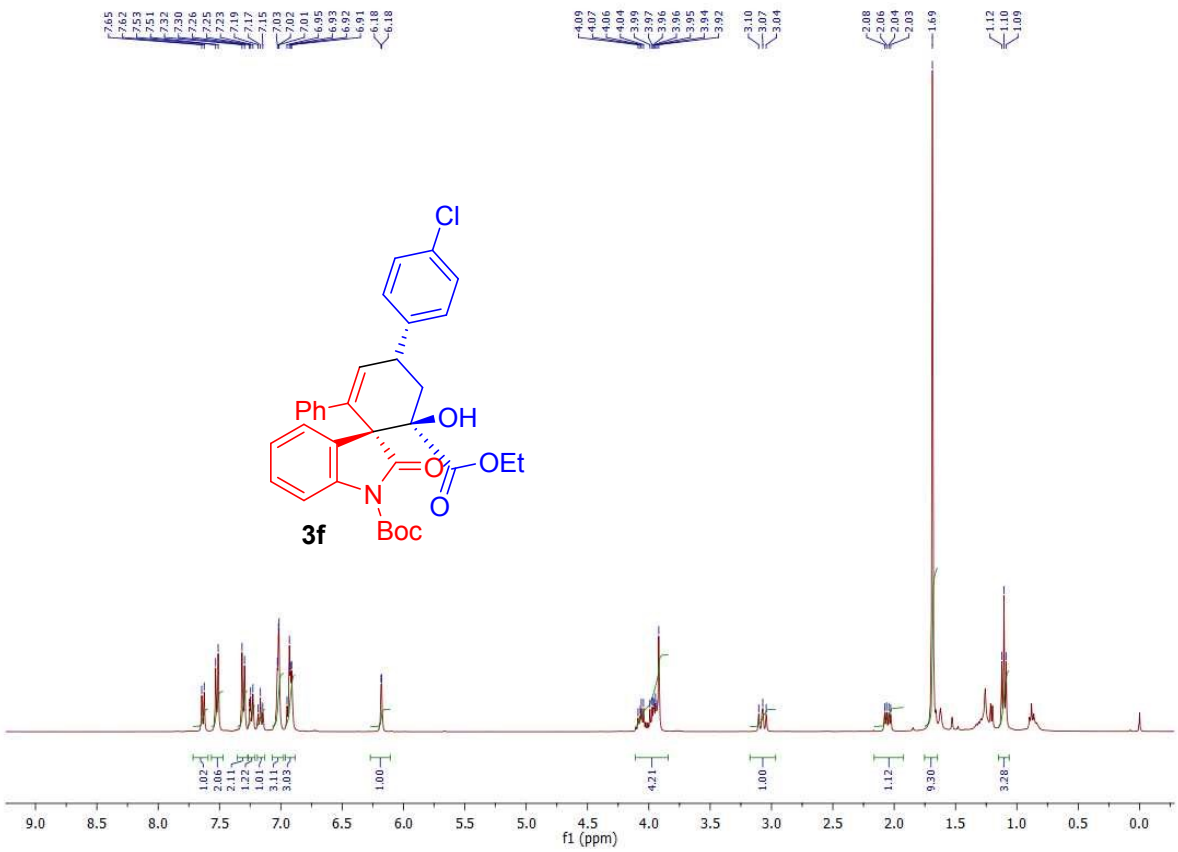
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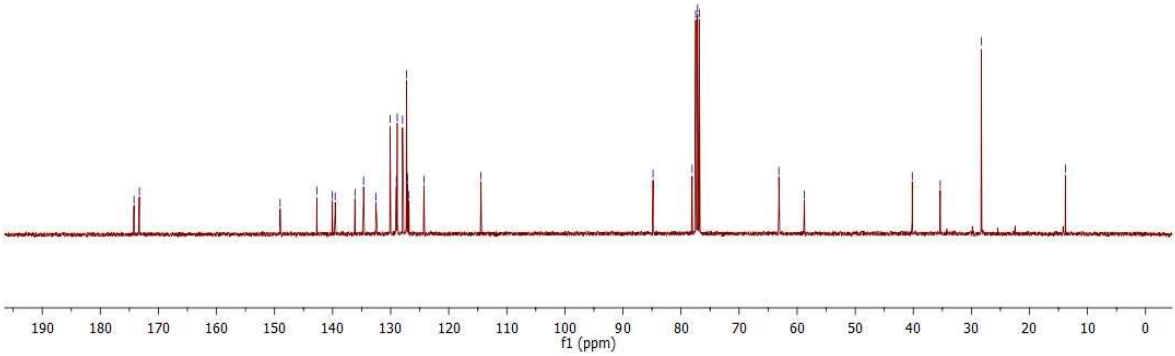
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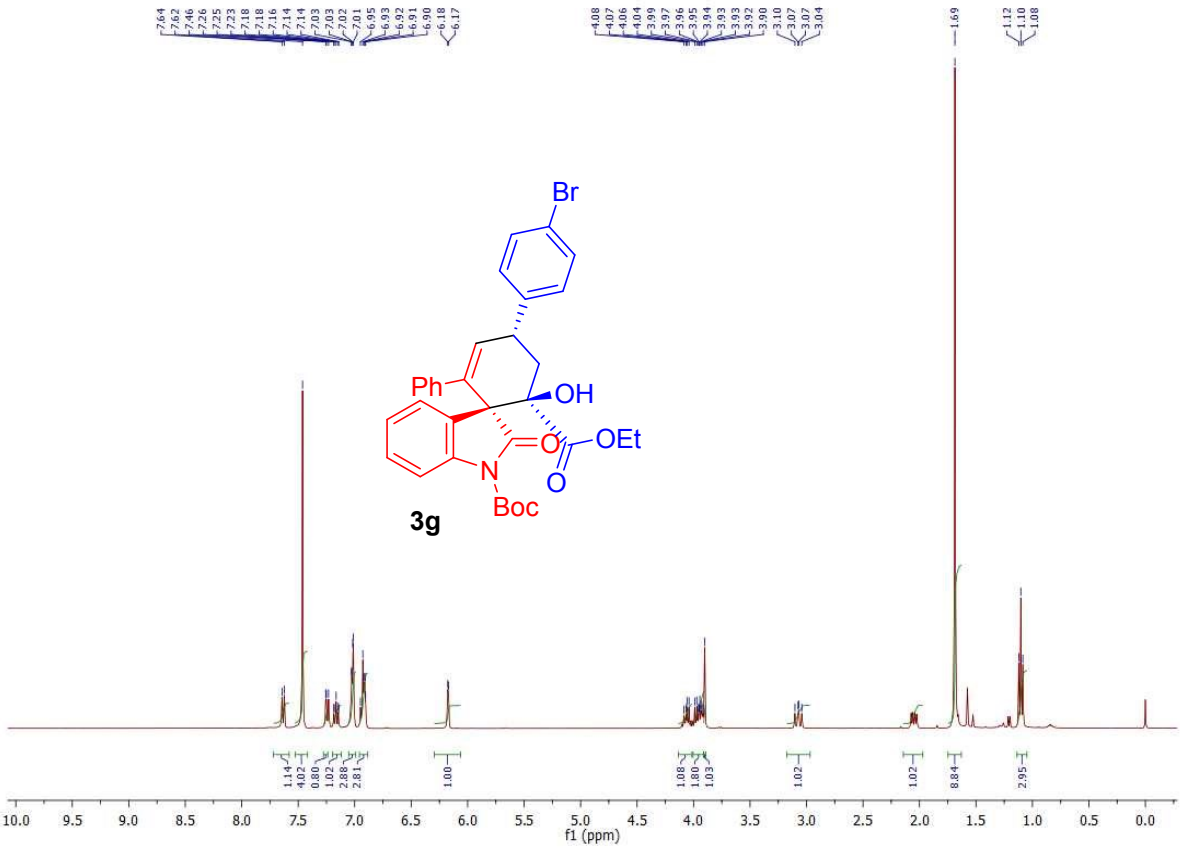
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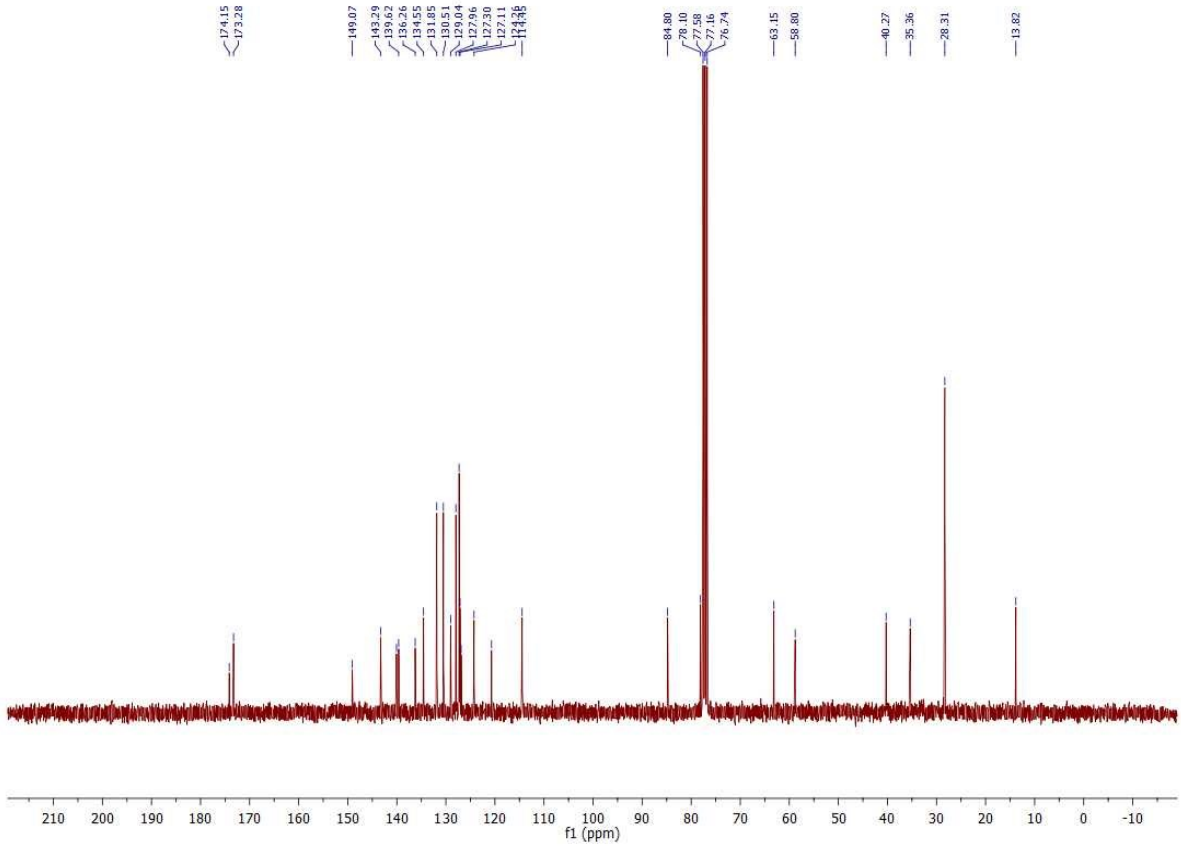
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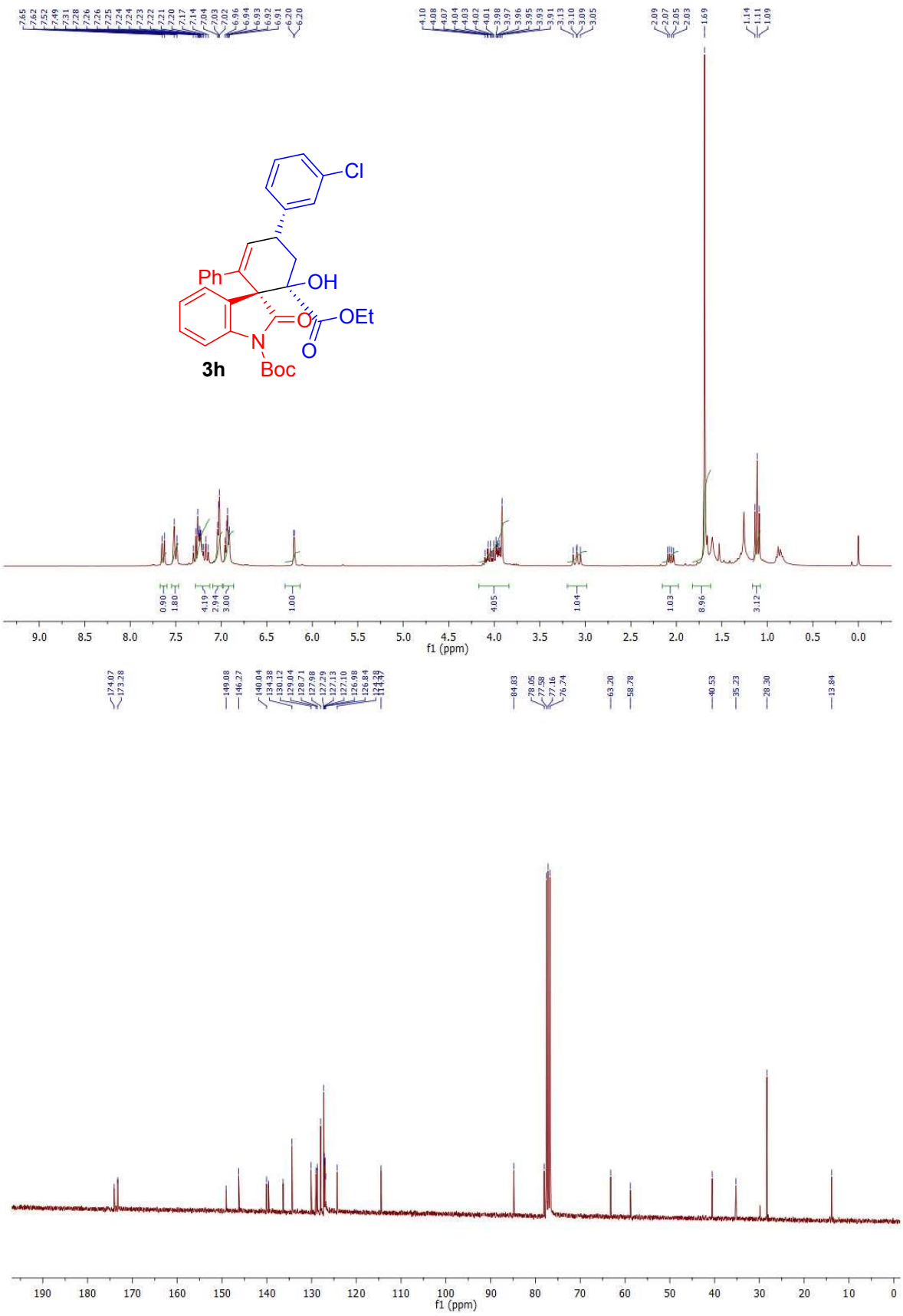
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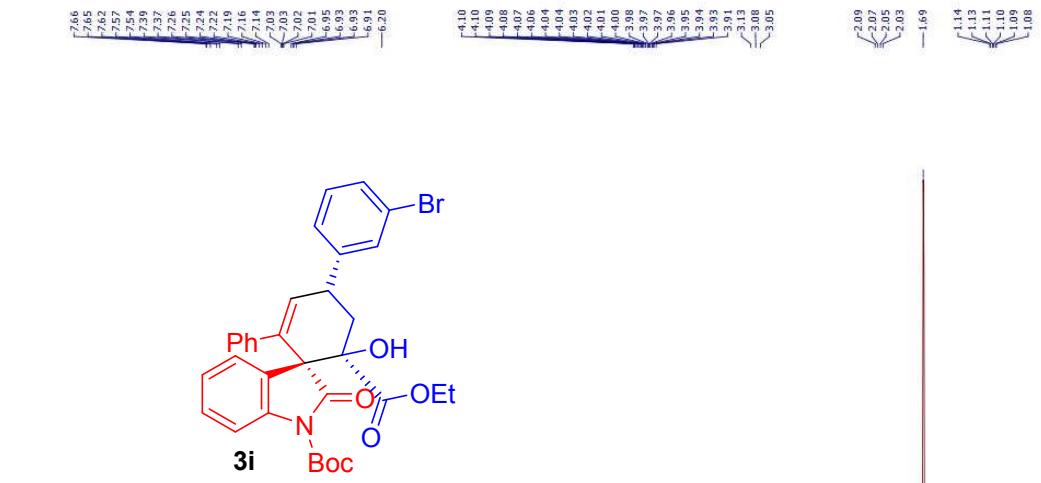

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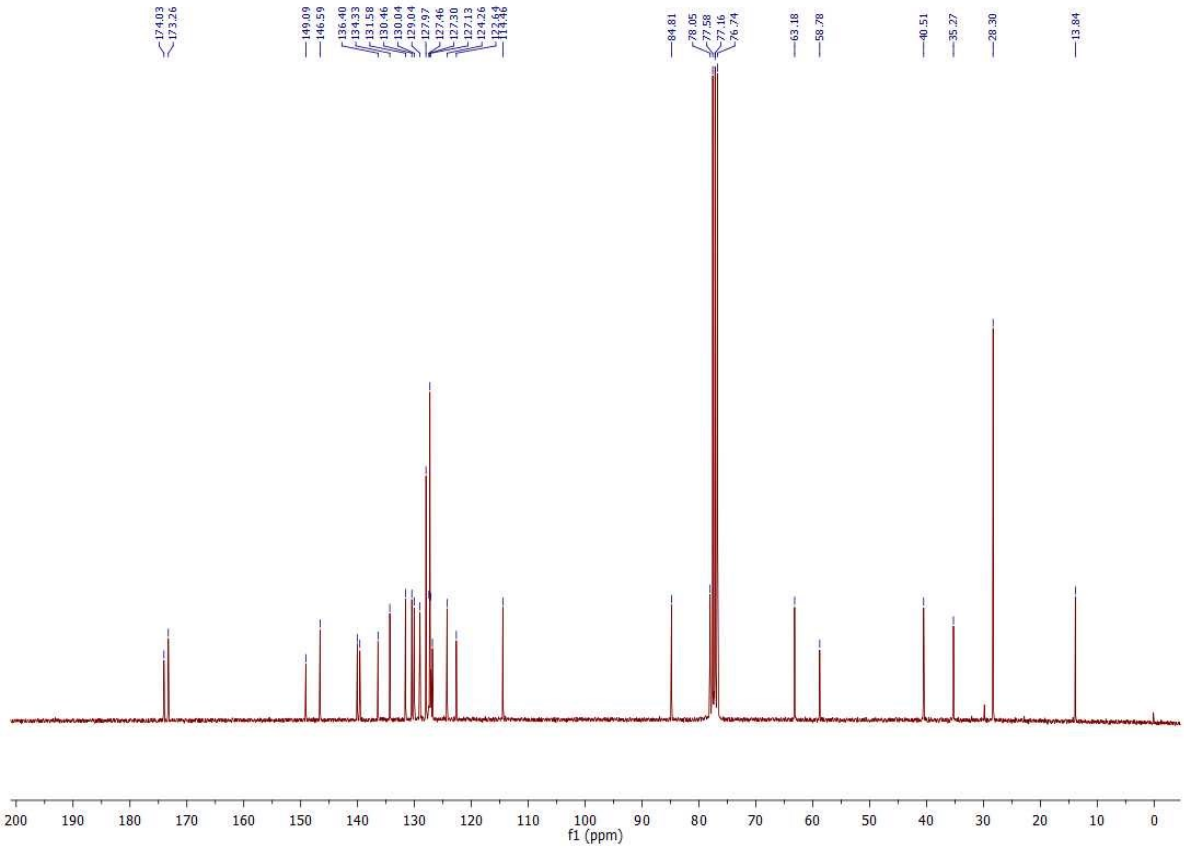
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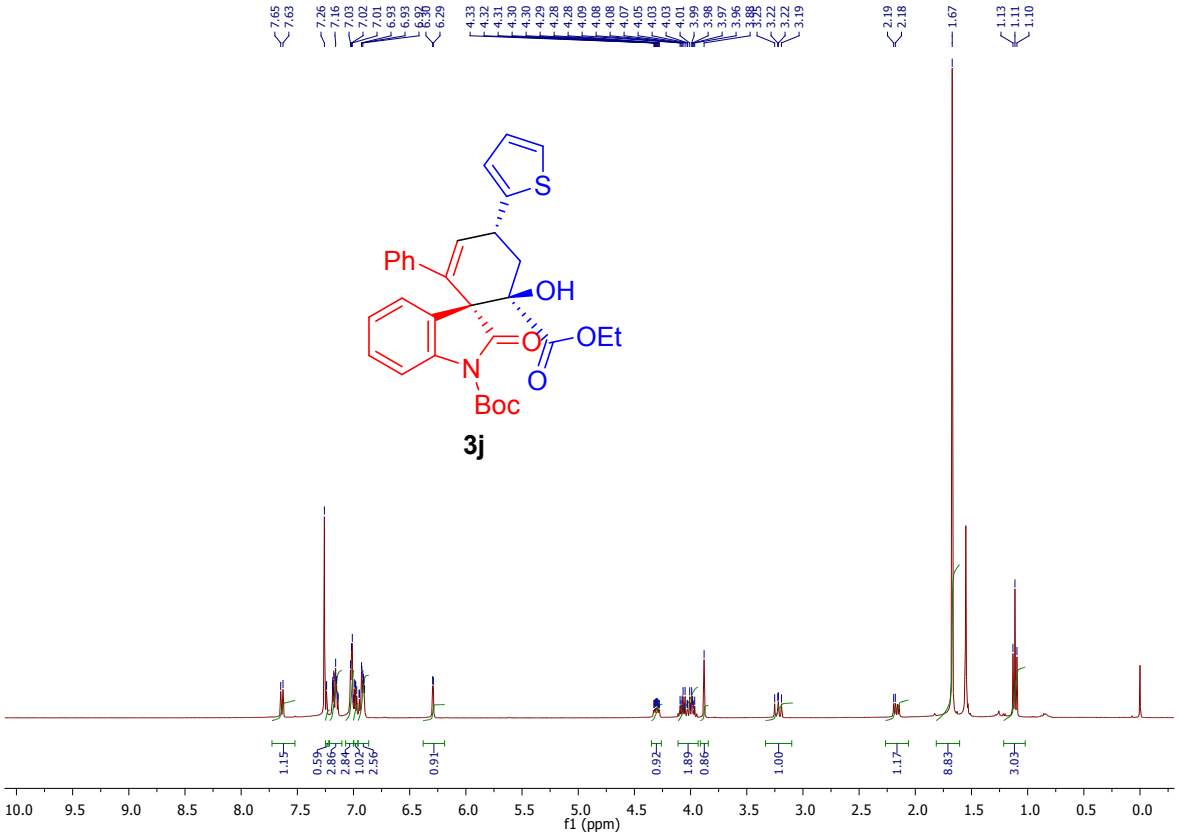

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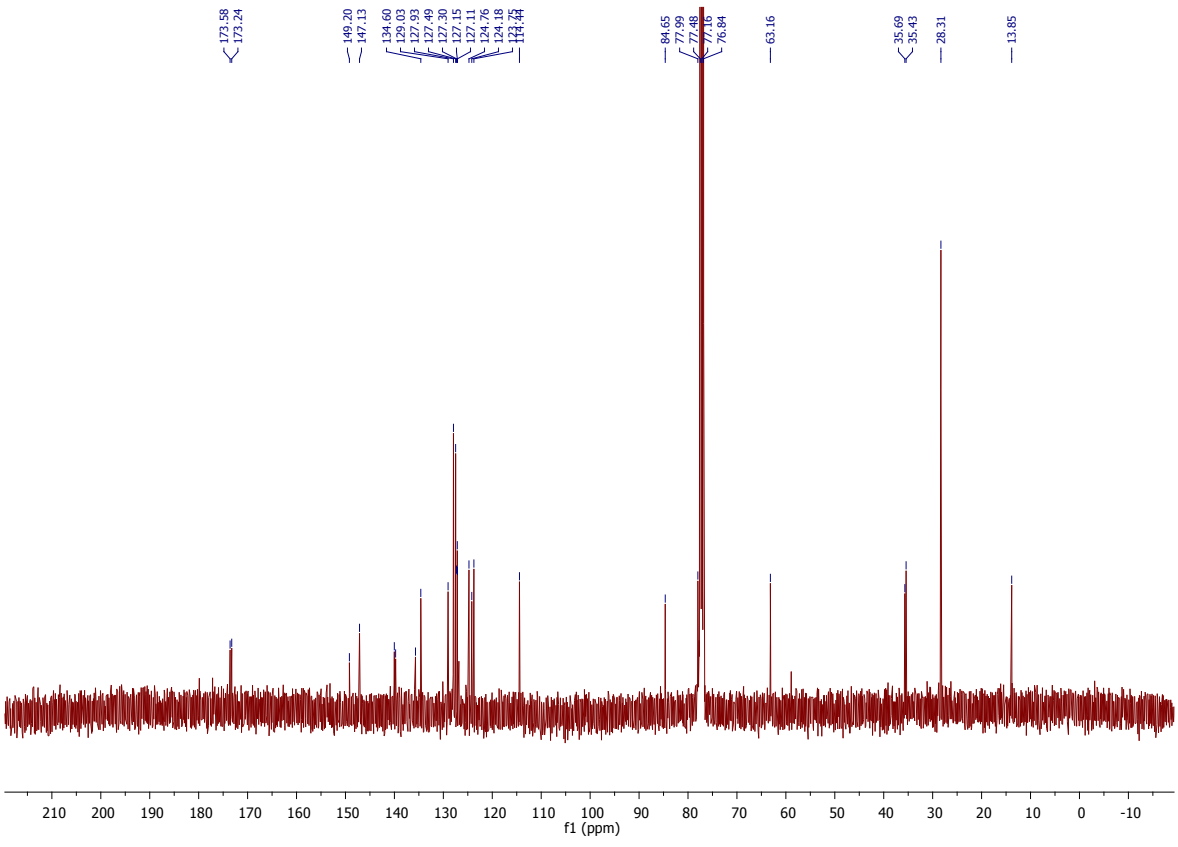

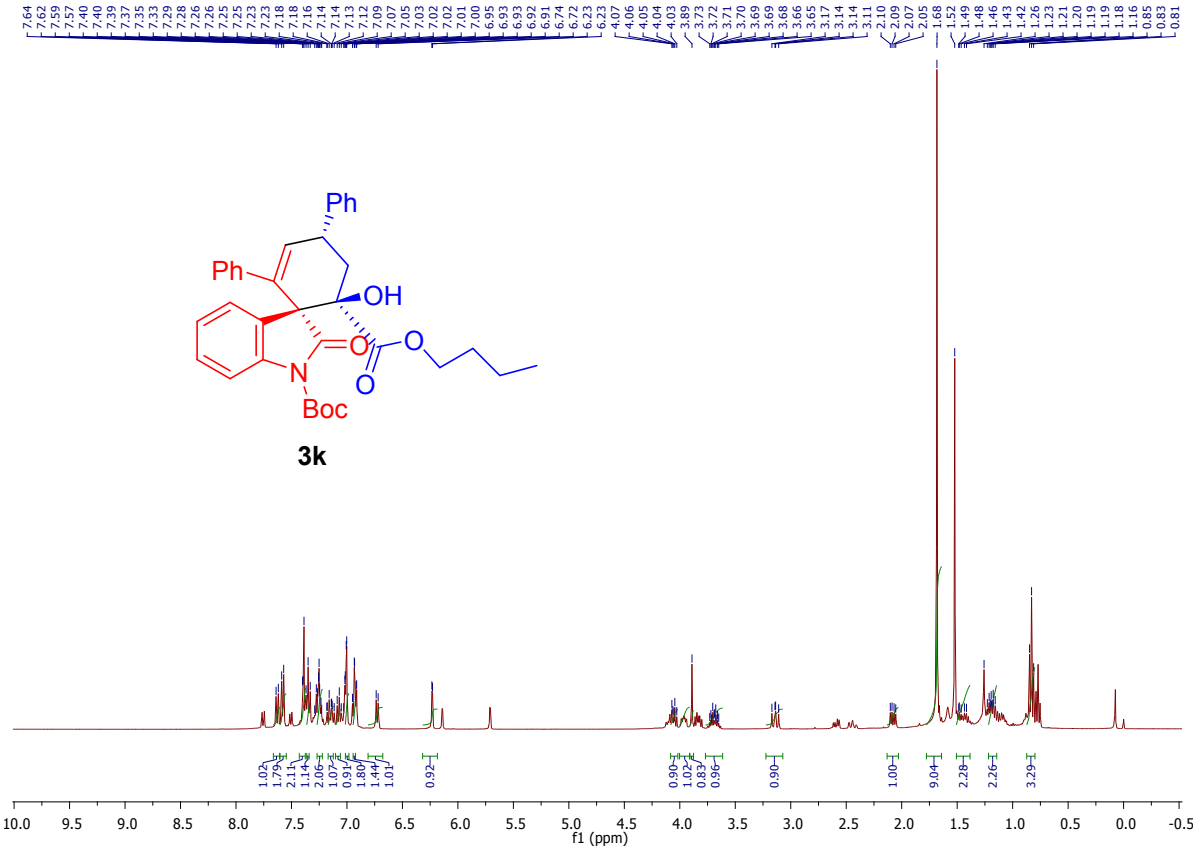

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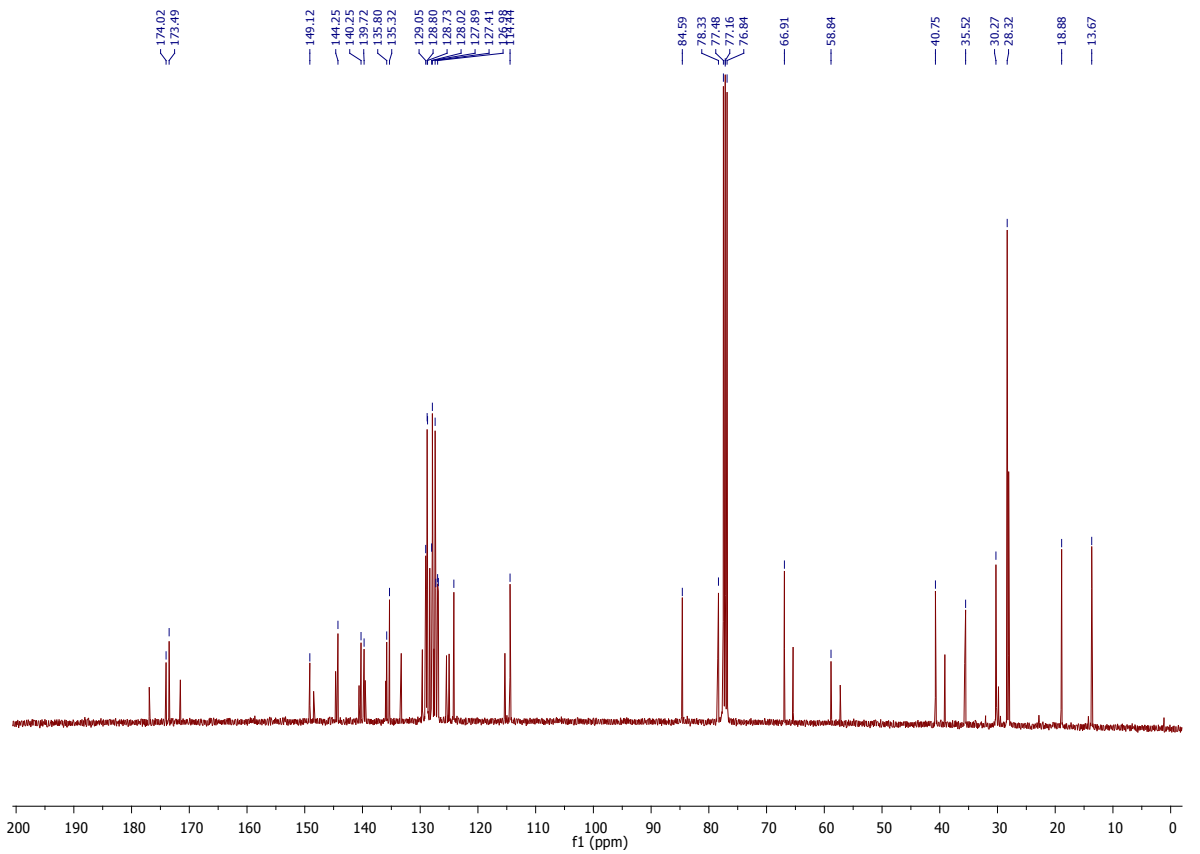

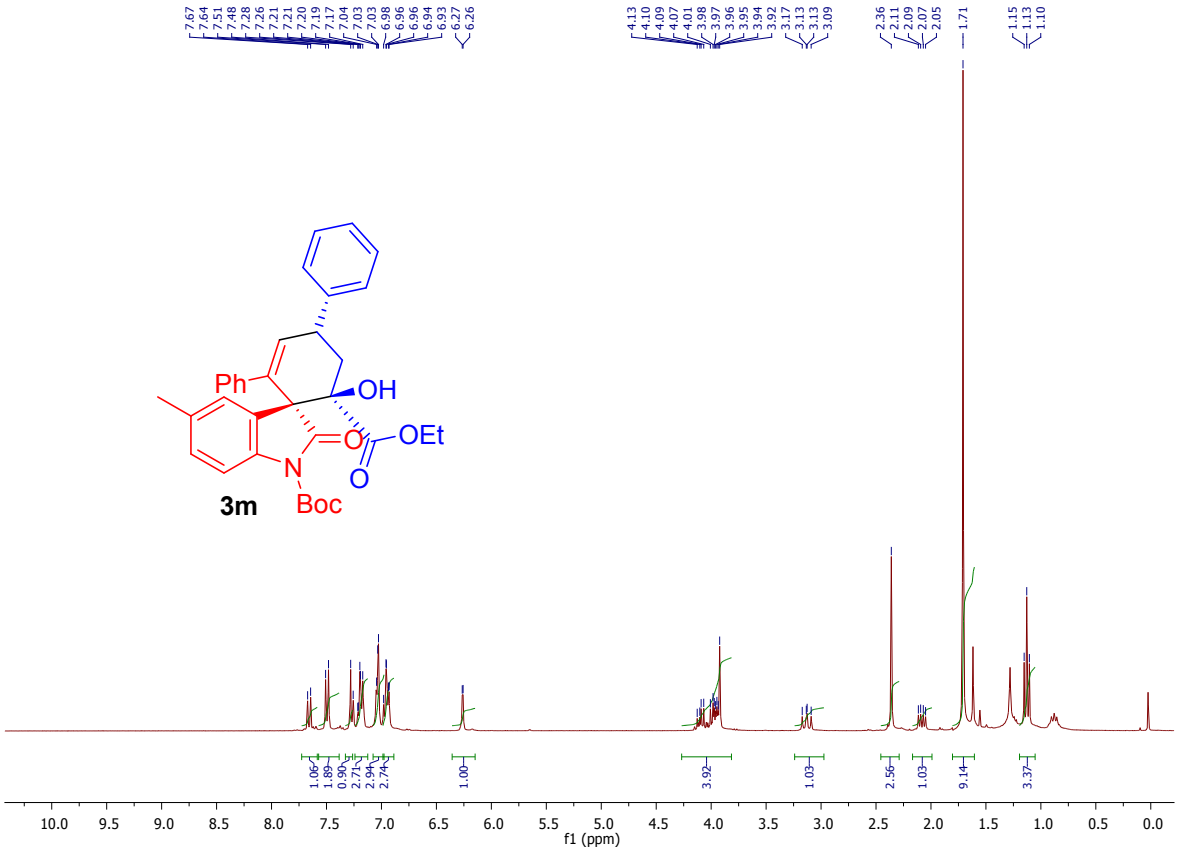
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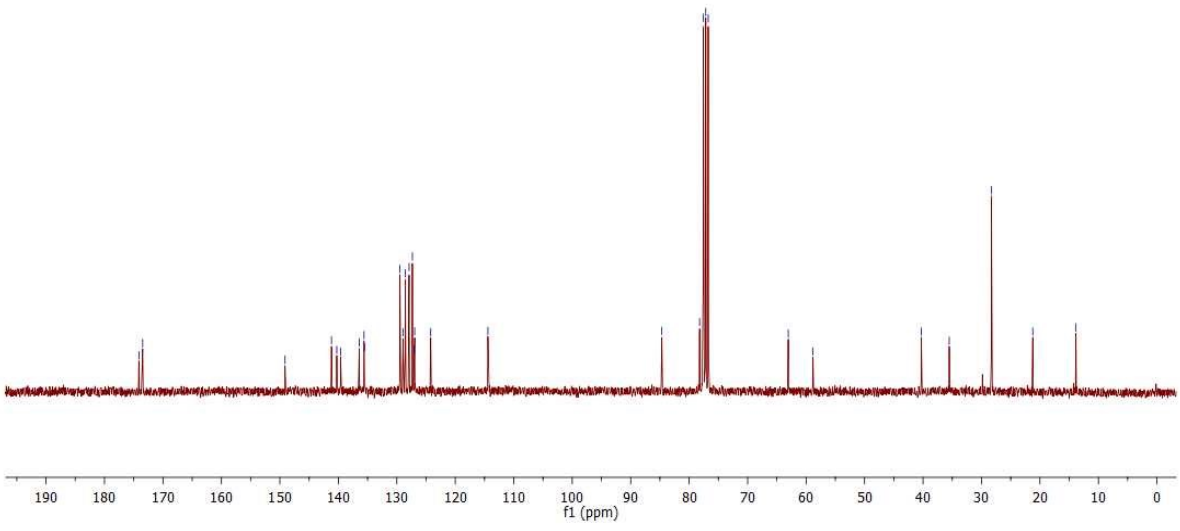
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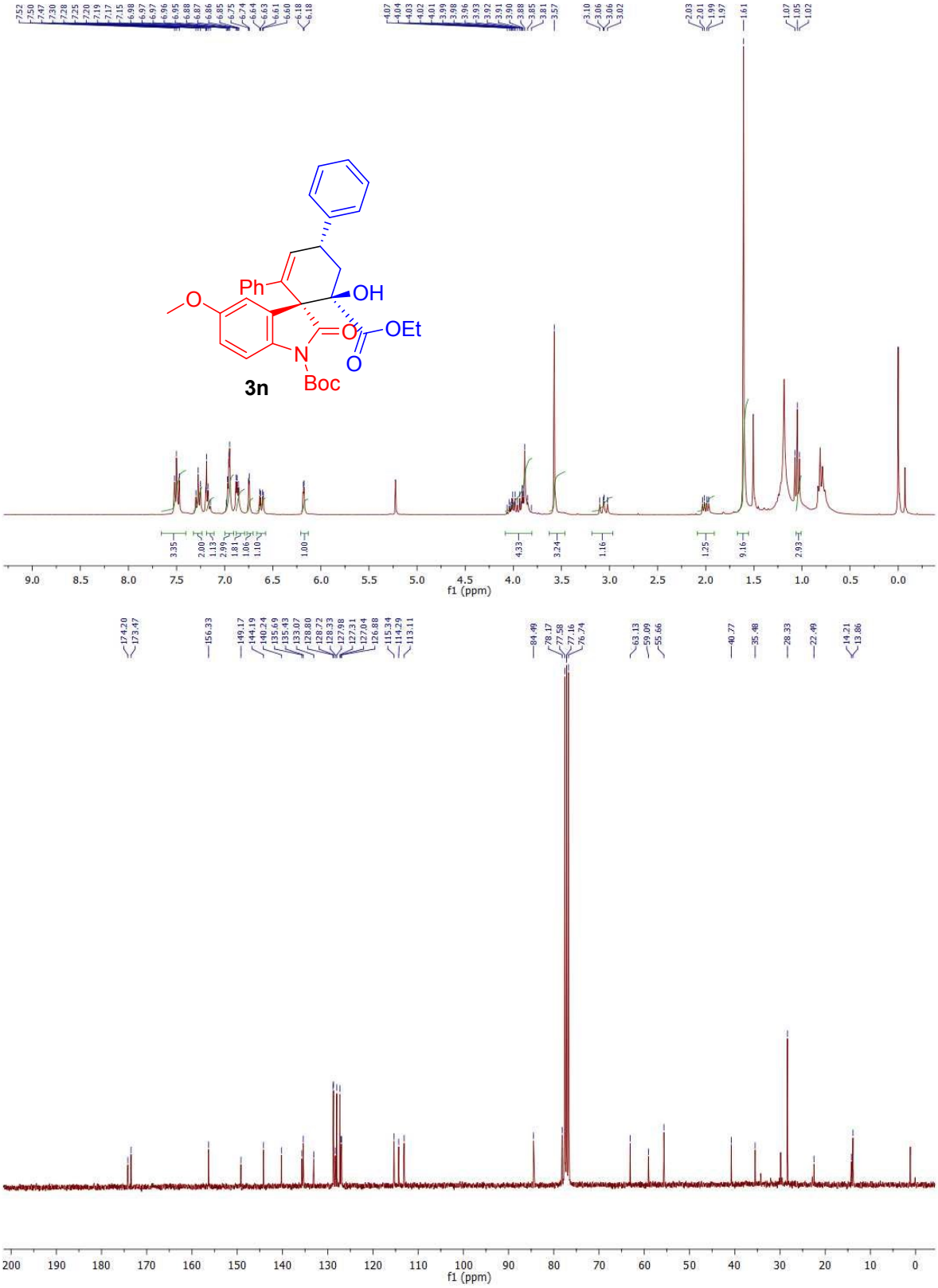
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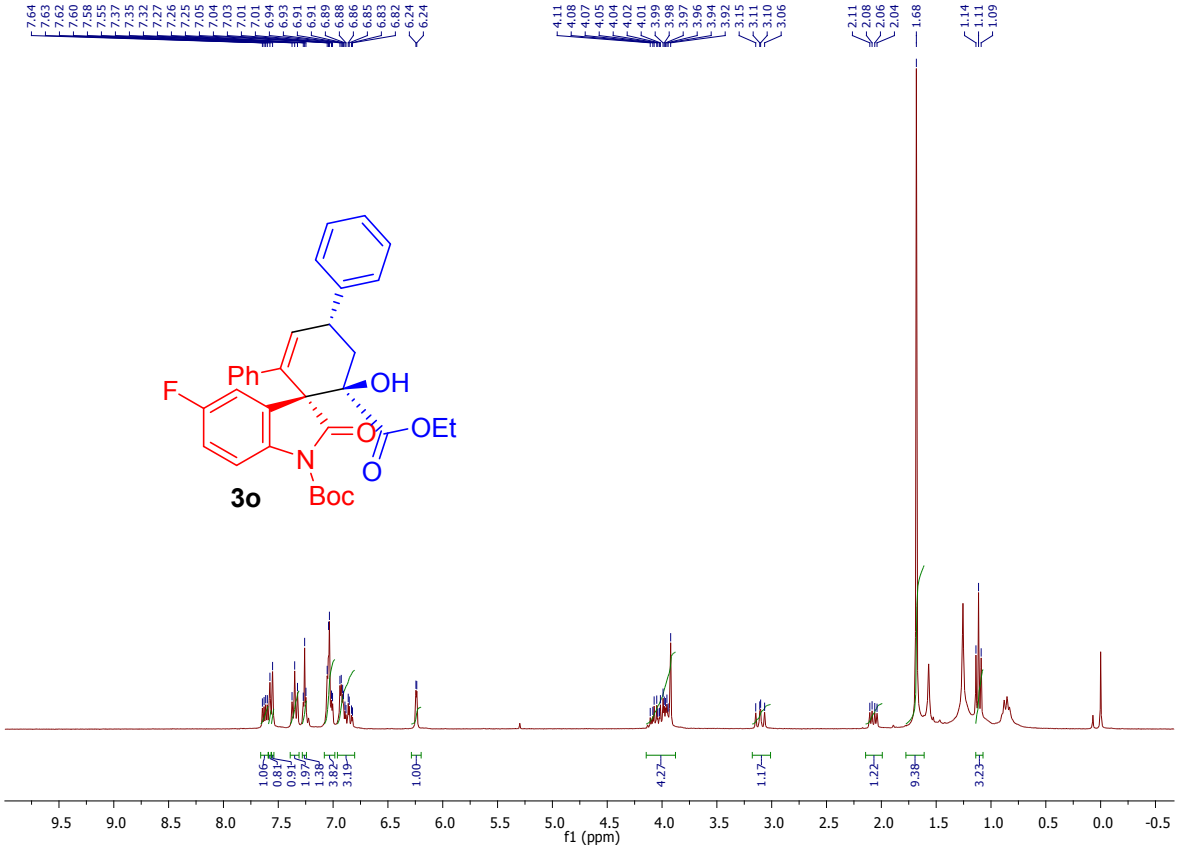
f1 (ppm)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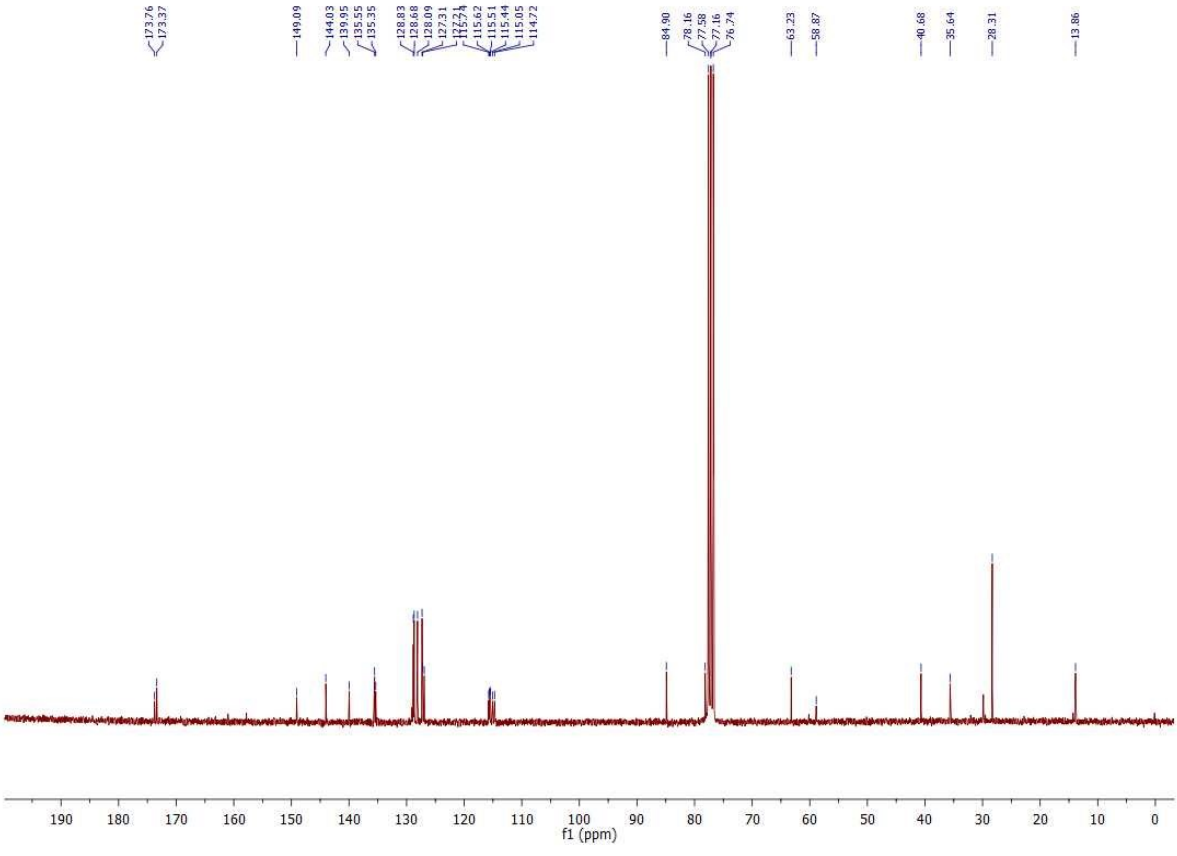
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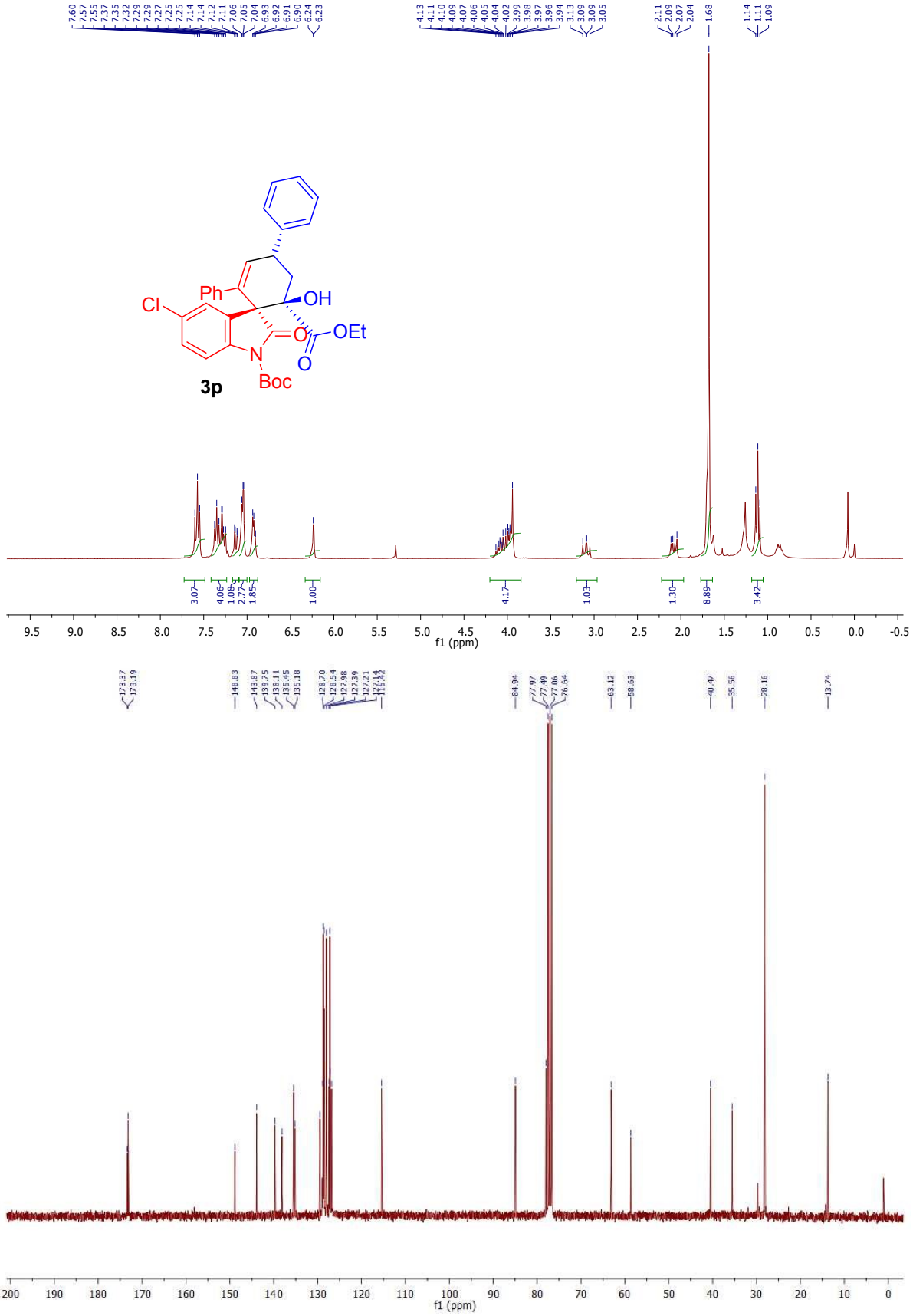
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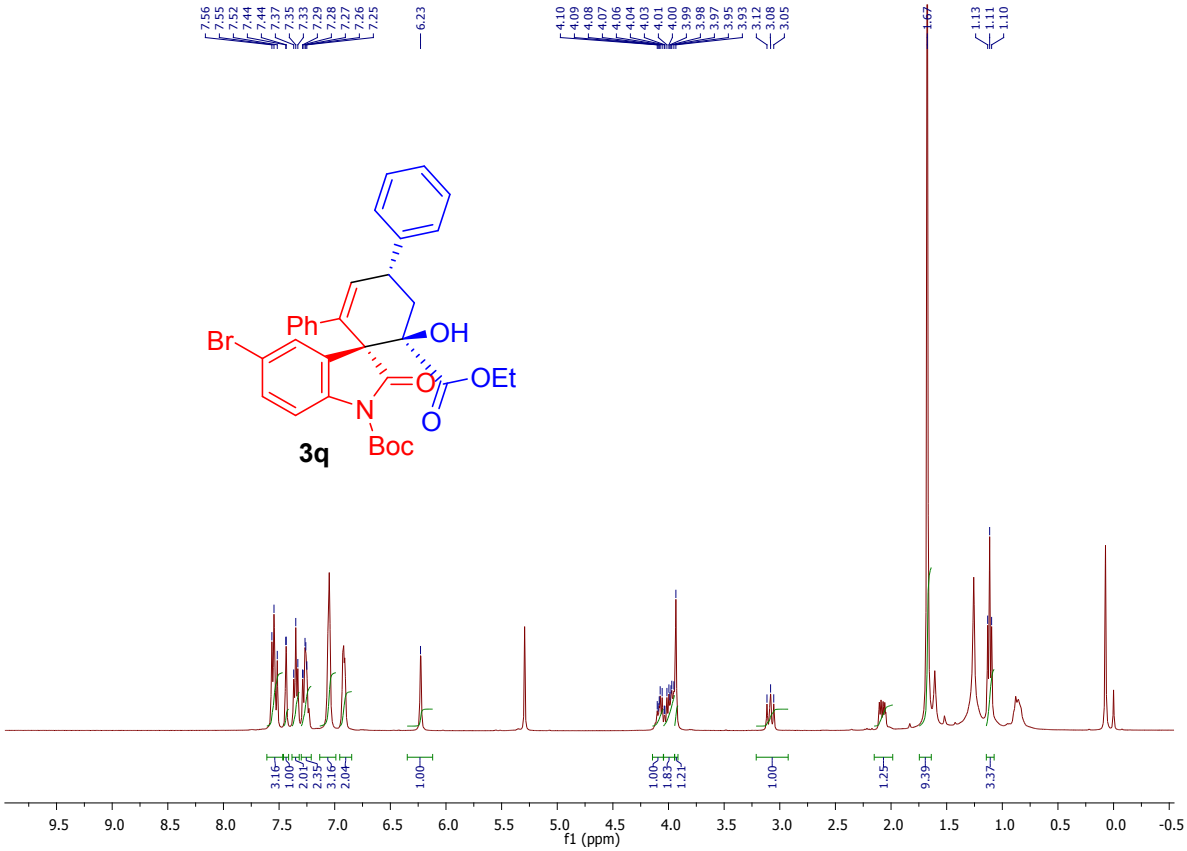
f1 (ppm)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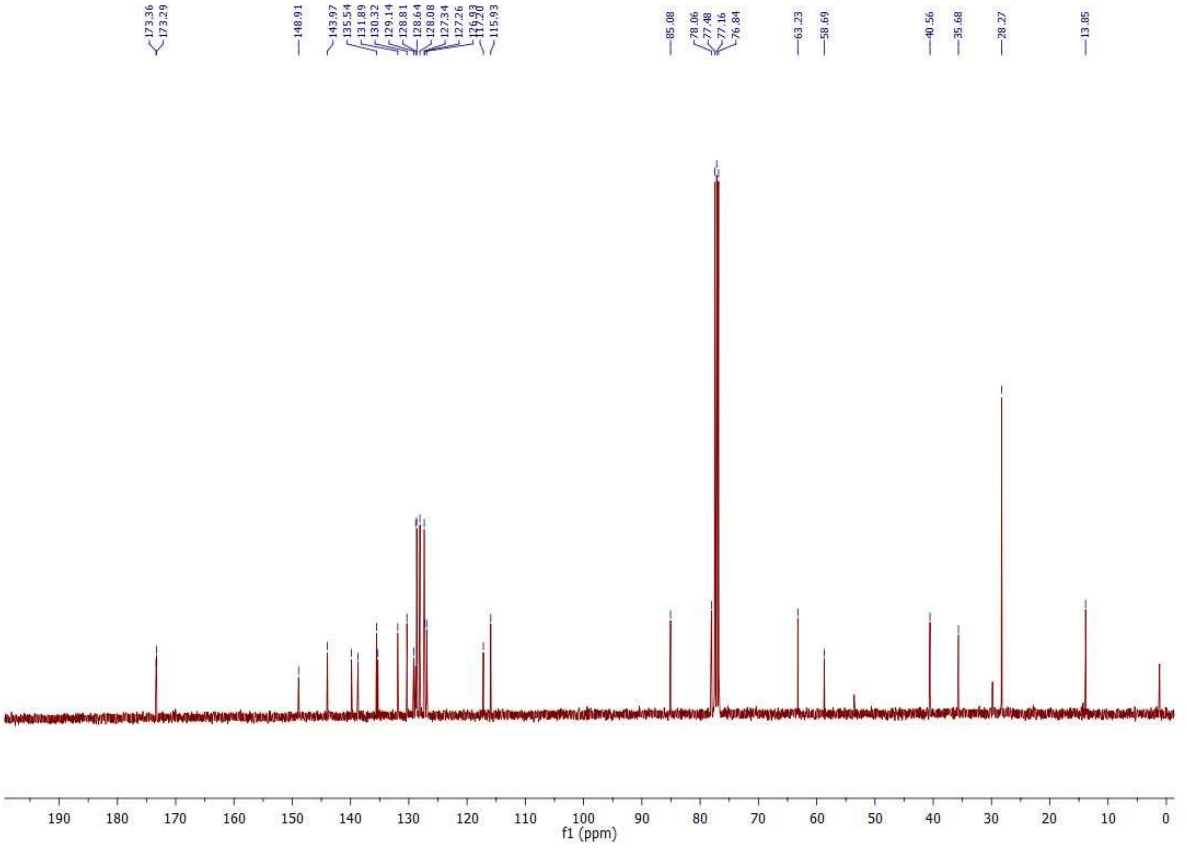
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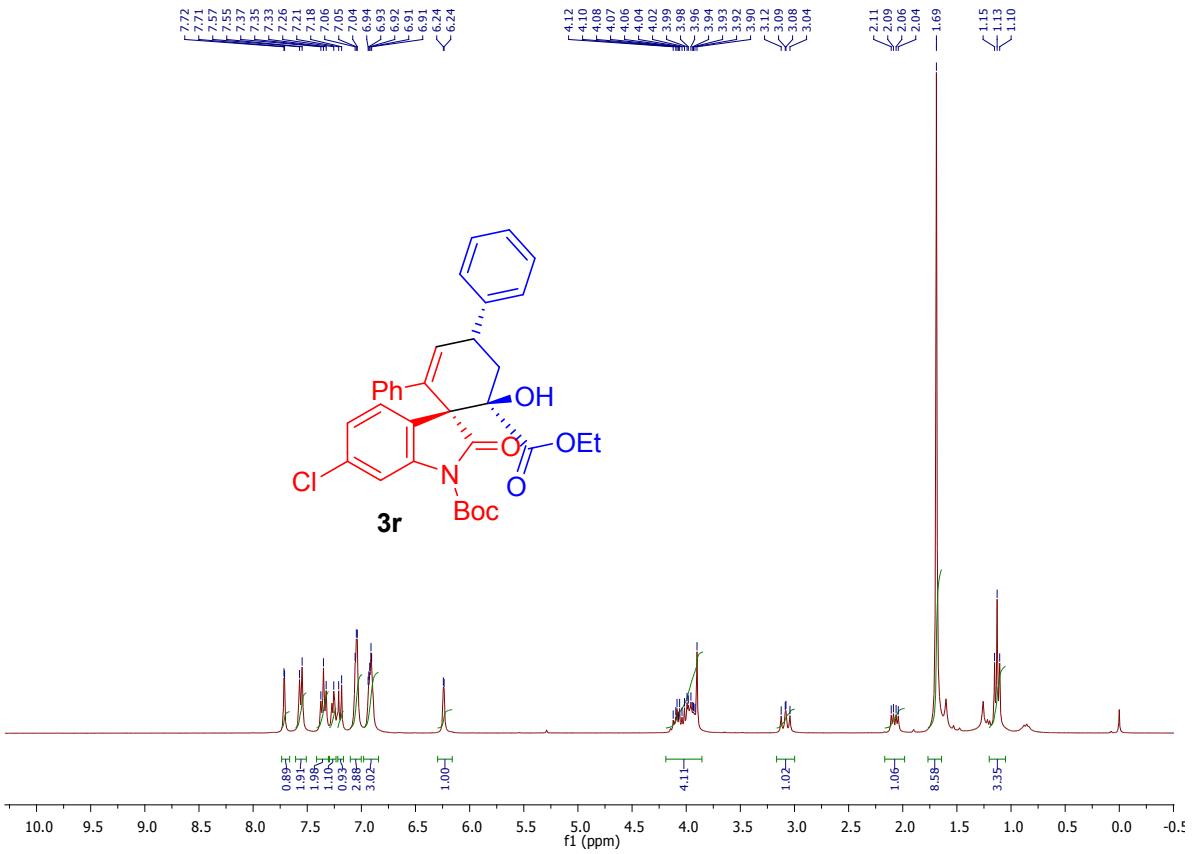
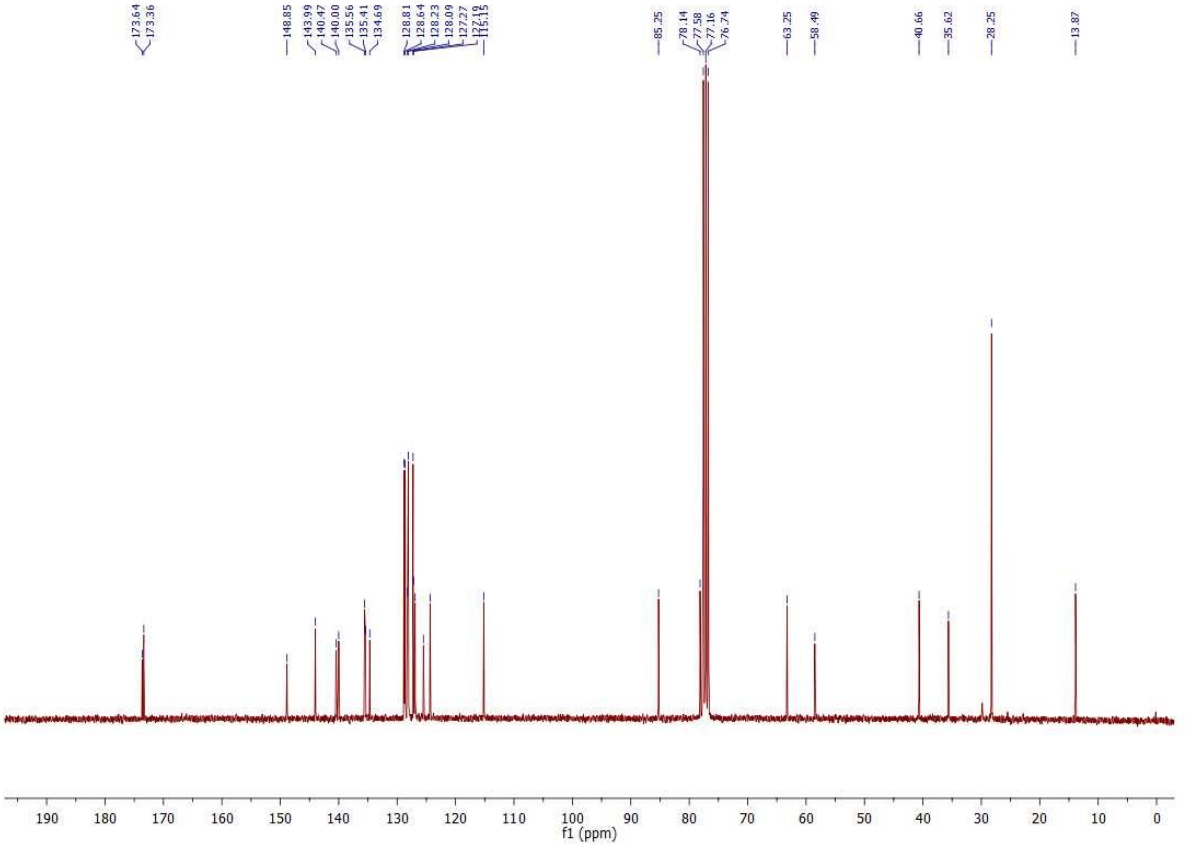
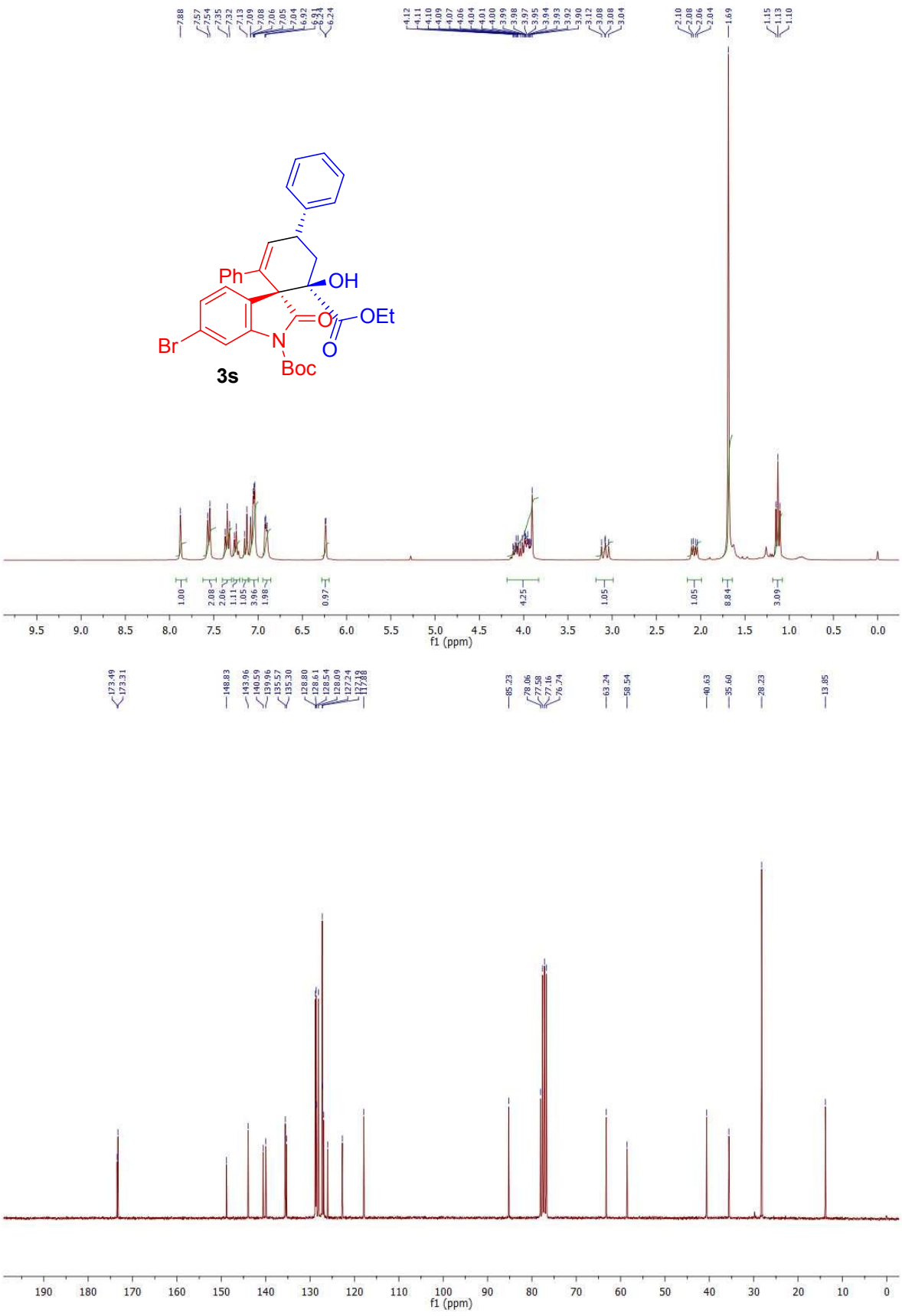
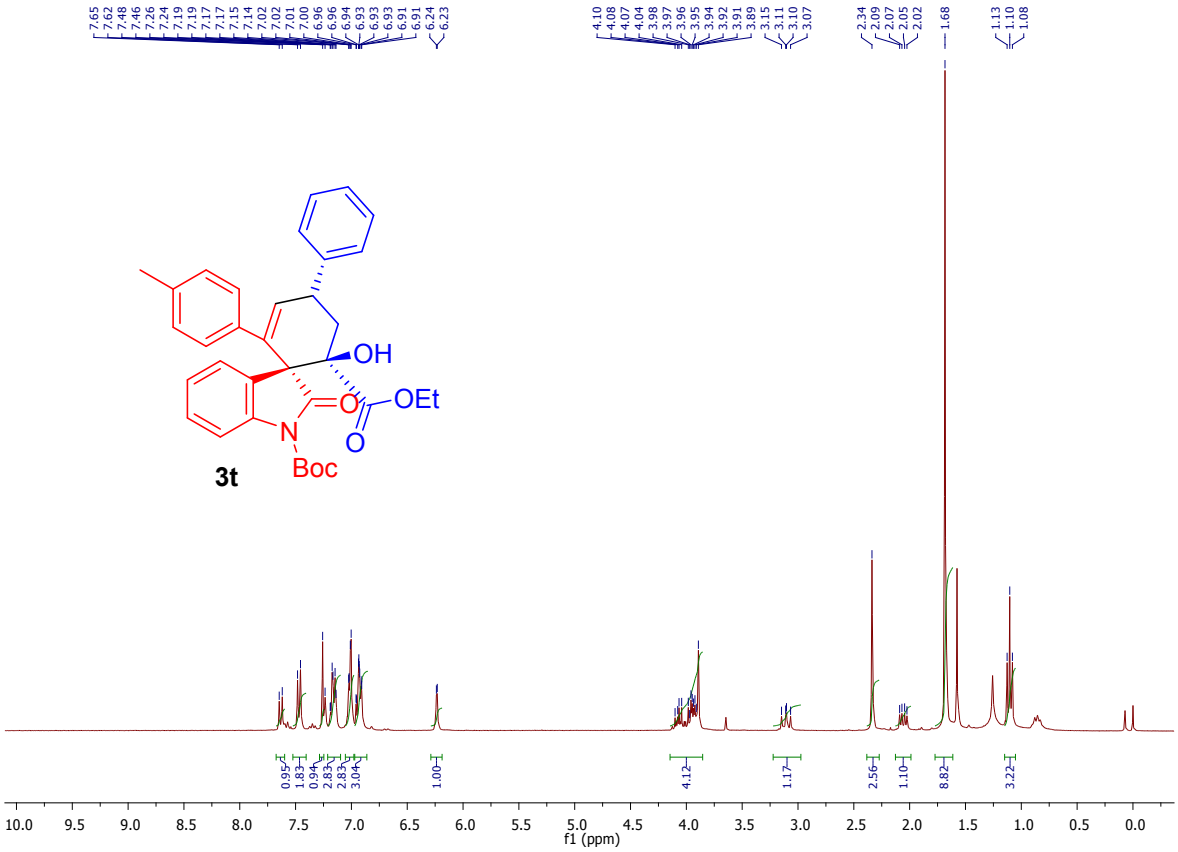
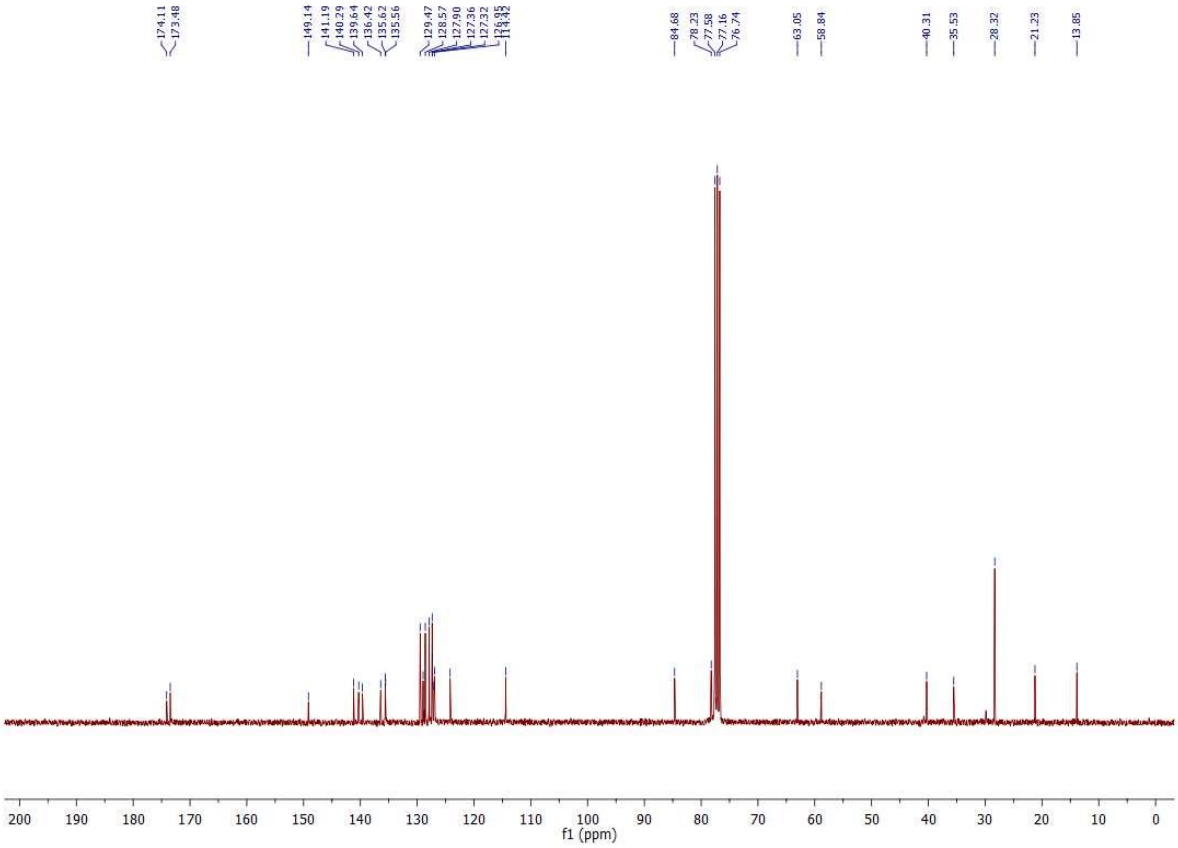
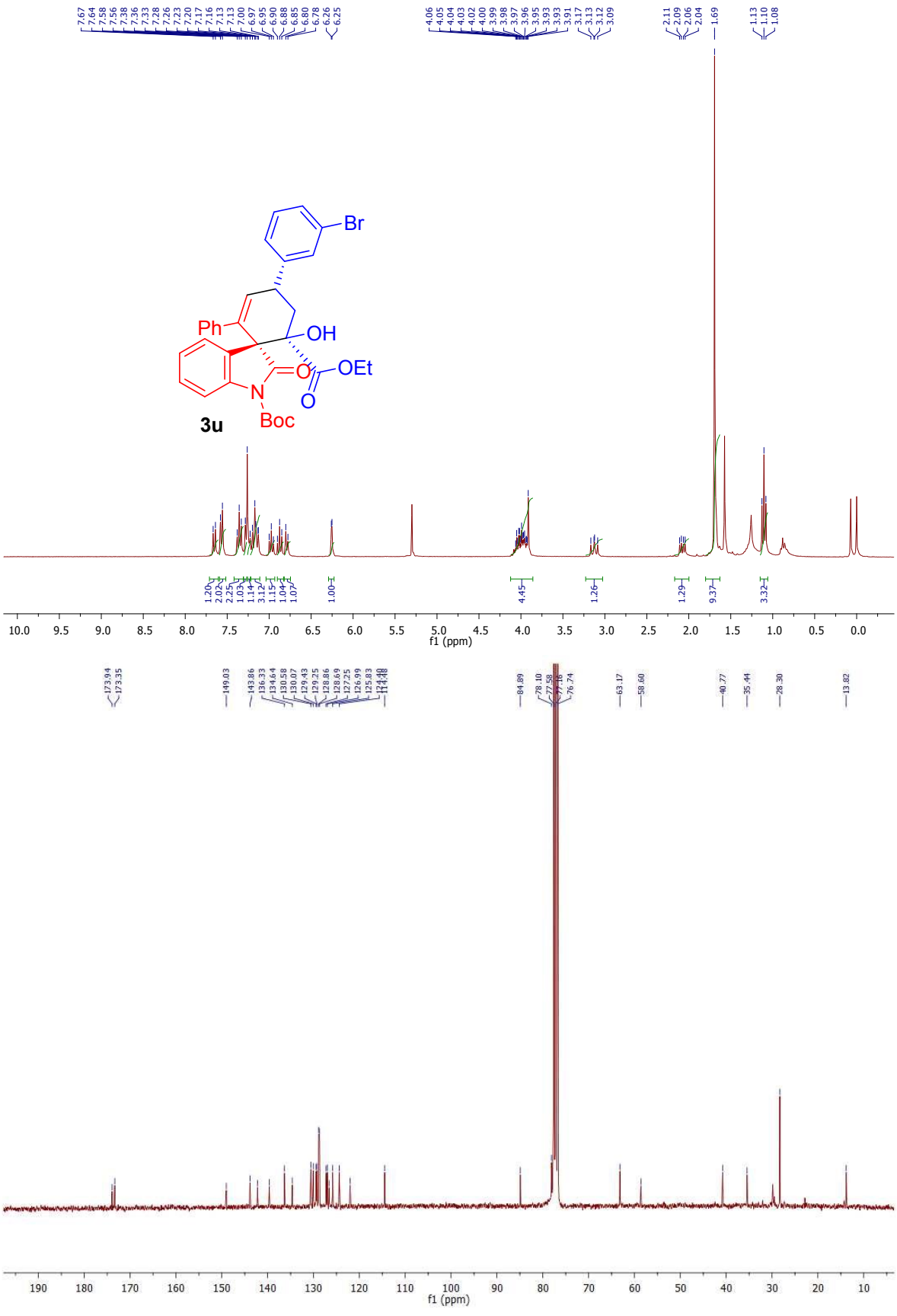

Ph
OH
O
OEt
O
Cl
N
Boc
3r
f1 (ppm)

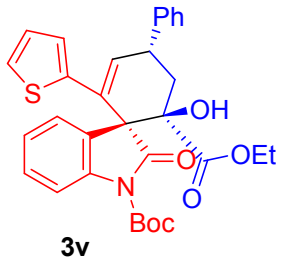

f1 (ppm)


Ph
OH
O
OEt
O
N
Br
Boc
3s
f1 (ppm)
f1 (ppm)

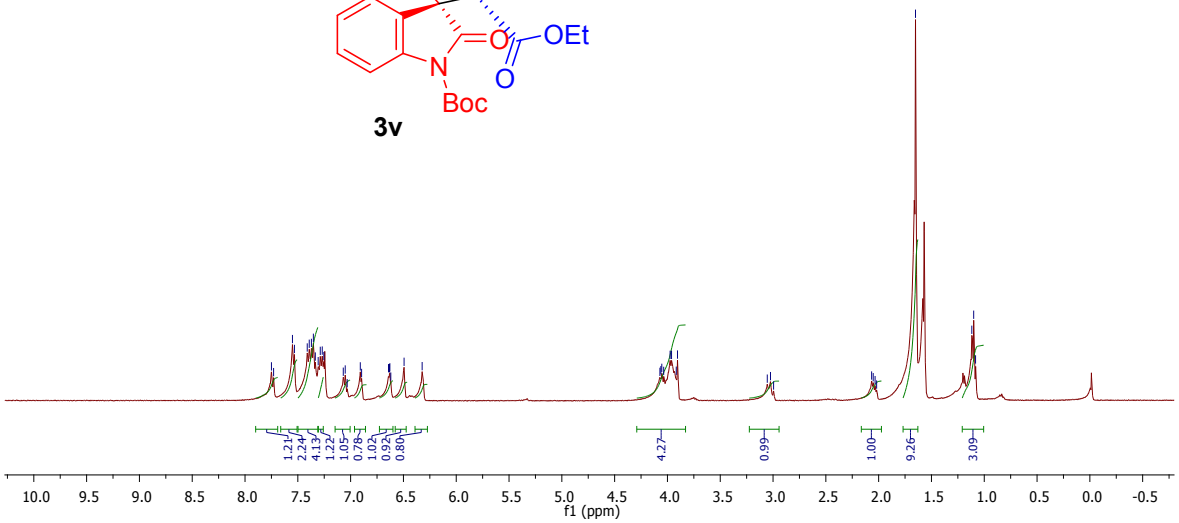

OH
O
OEt
O
N
Boc
3t
f1 (ppm)

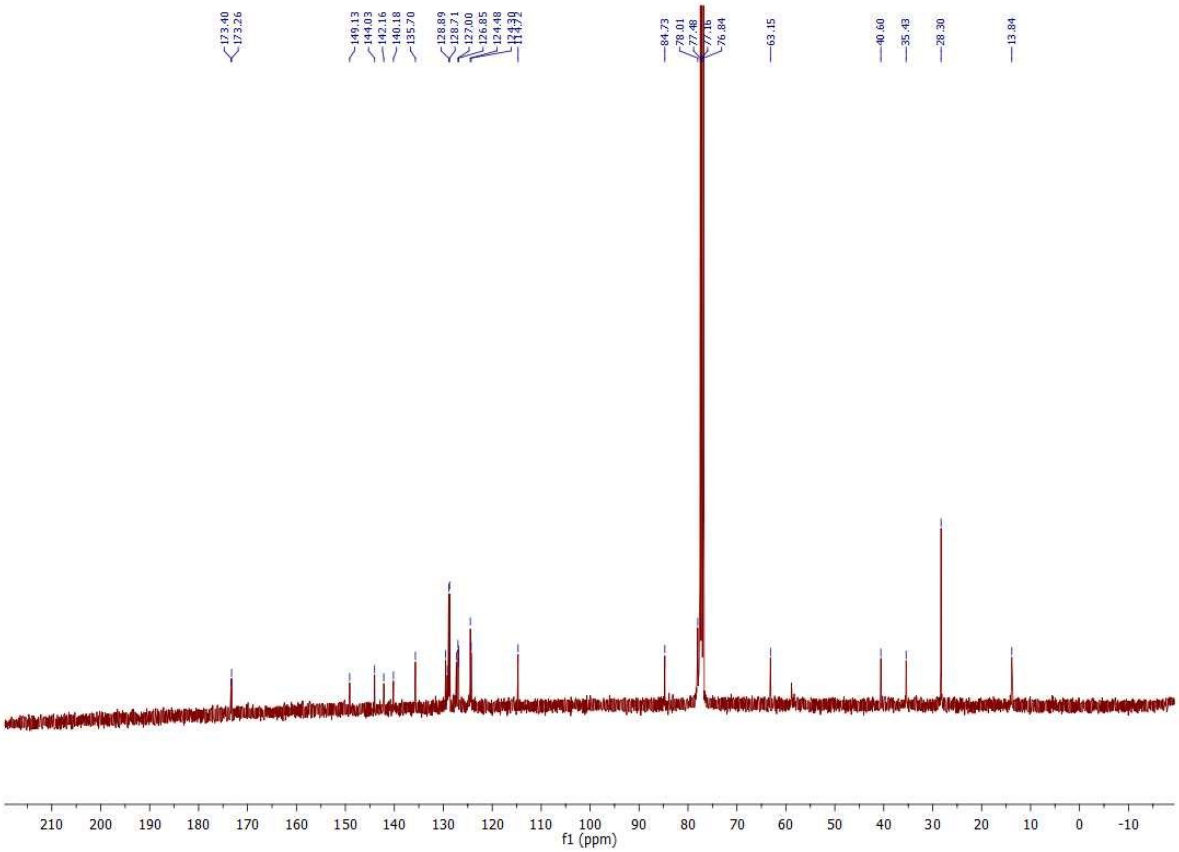

f1 (ppm)

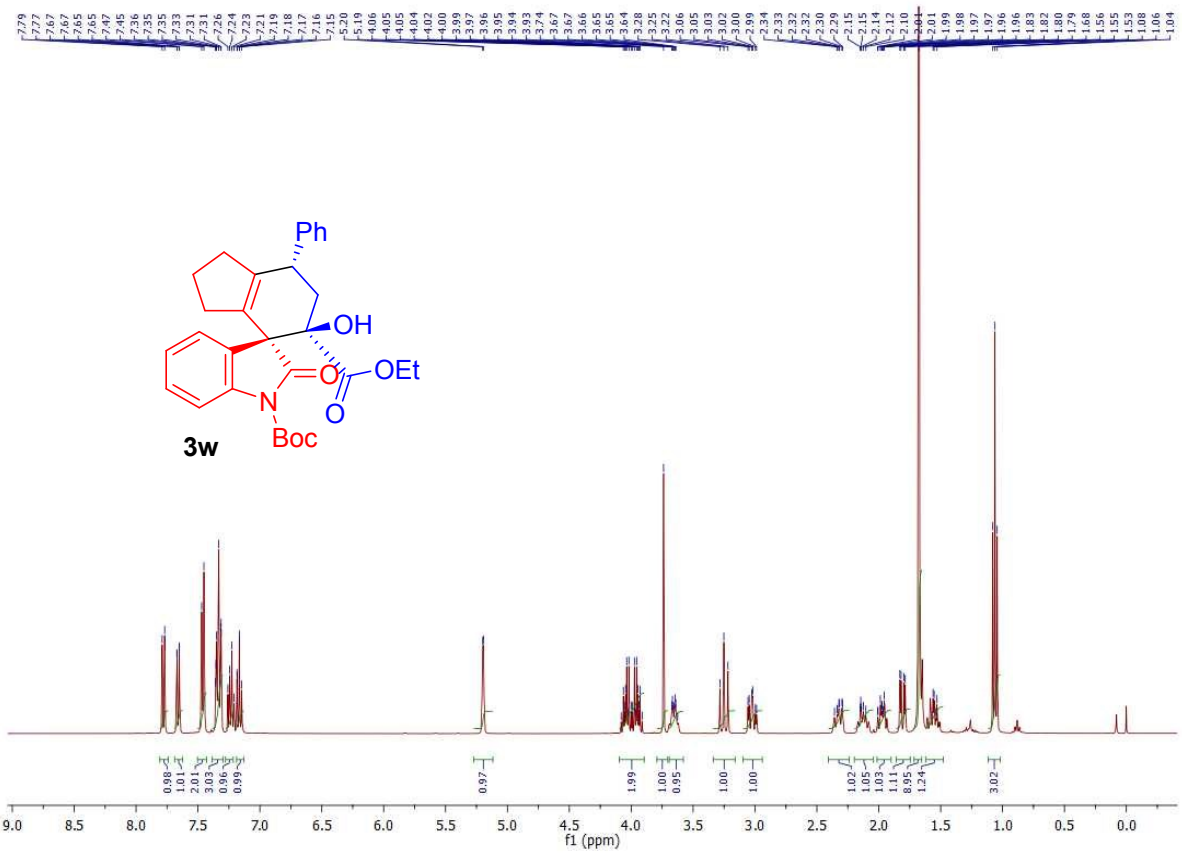

Br
Ph
OH
O
OEt
N
O
Boc
3u
f1 (ppm)
f1 (ppm)

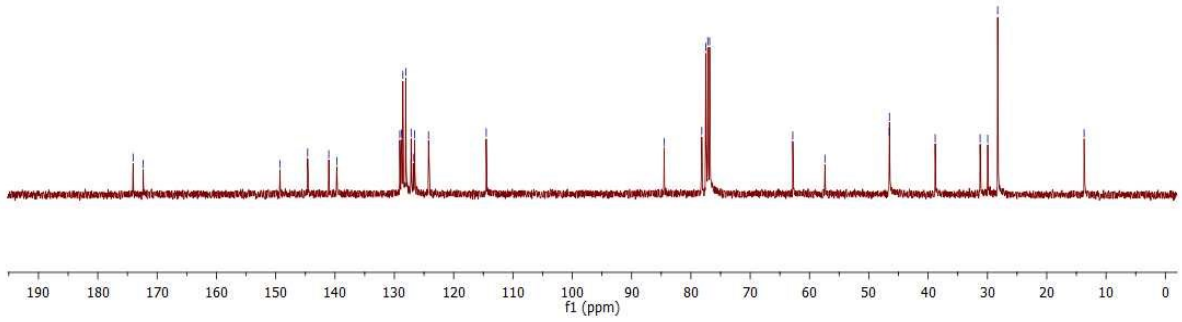


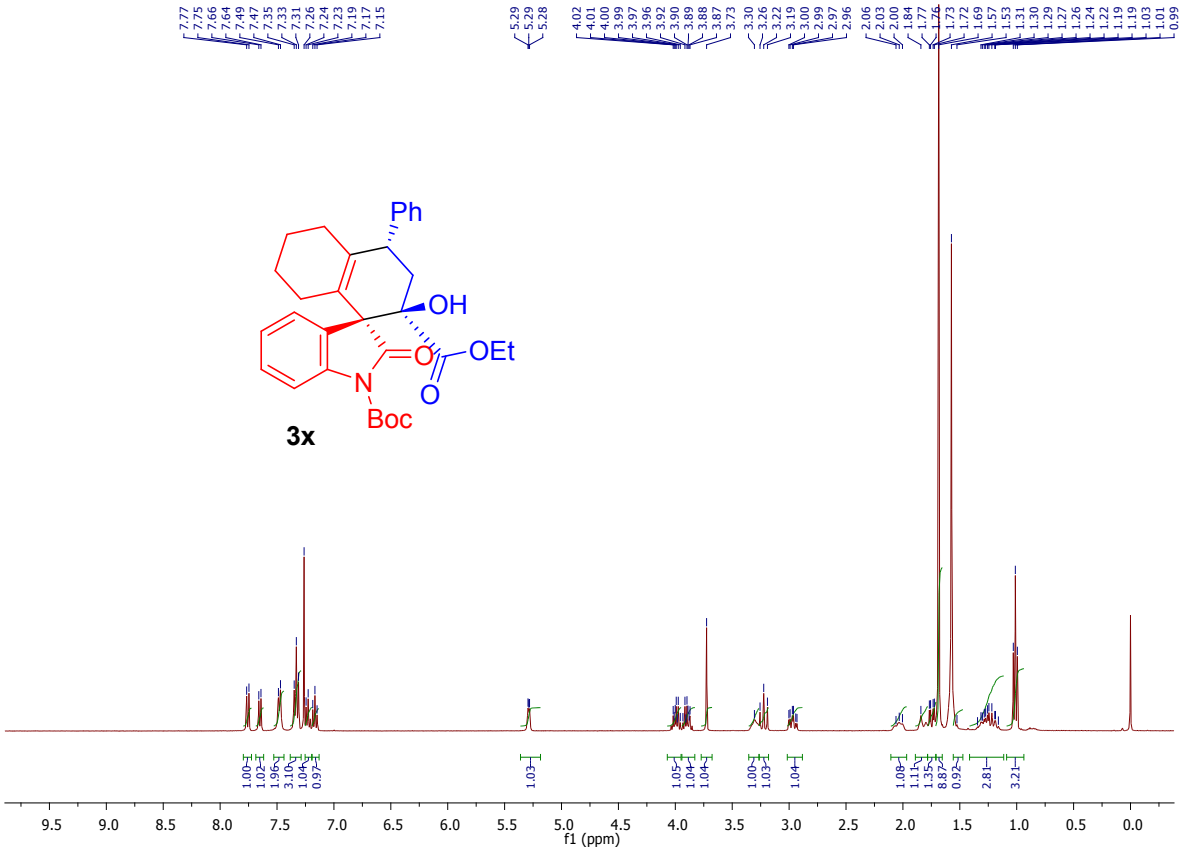
3v

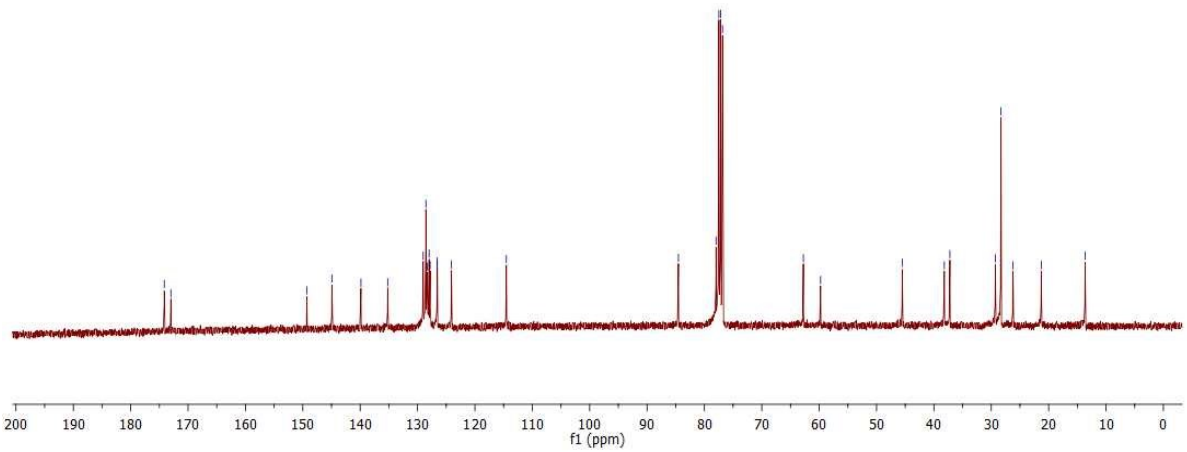





Ph
OH
O
OEt
N
O
Boc
3w
f1 (ppm)

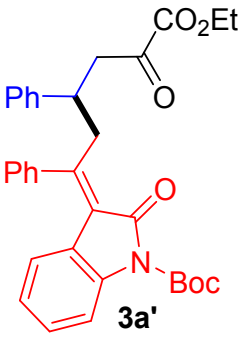

f1 (ppm)


Ph
OH
O
OEt
O
N
Boc
3x
f1 (ppm)

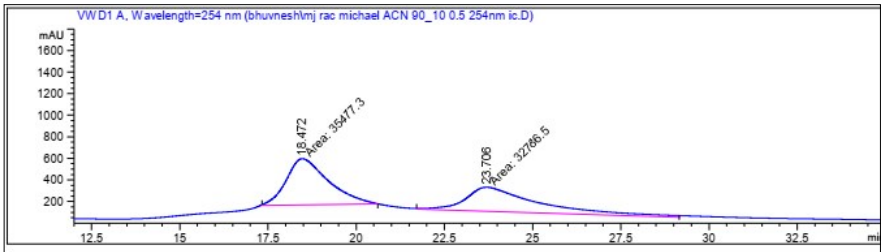

f1 (ppm)

8. HPLC data of synthesized compound 3a'

HPLC, Chiralpak IC, hexane : isopropanol= 90:10, 0.5mL/min, λ = 254 nm



3a'

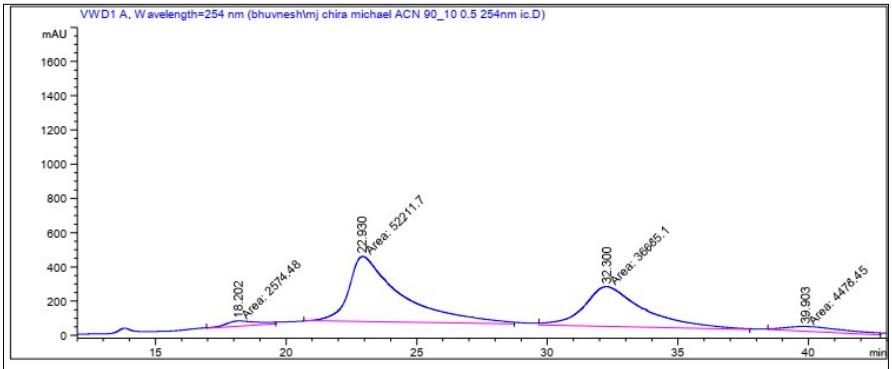



```
================================================================
                    Area Percent Report
================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  18.472 MM    1.3796 3.54773e4   428.59198  51.9709
   2  23.706 MM    2.4377 3.27865e4   224.16635  48.0291
```

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================================================================
                    Area Percent Report
================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  18.202 MM    1.4055 2574.48242   30.52891   2.6832
   2  22.930 MM    2.2963 5.22117e4   378.94815  54.4157
   3  32.300 MM    2.6443 3.66851e4   231.21779  38.2337
   4  39.903 MM    2.6643 4478.45215   28.01497   4.6675
```