Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supporting Information

Enantioselective Construction of Multifunctionalized Spirocyclohexaneoxindoles through Organocatalytic Michael-Aldol Cyclization of Isatin Derived Alkenes with Linear Dialdehydes

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A: General Information:

Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. All reactions were carried out in air and using undistilled solvent, without any precautions to exclude moisture unless otherwise noted. Organic solutions were concentrated under reduced pressure on an EYELA N-1001 rotary evaporator. Reactions were monitored by thin-layer chromatography (TLC) on silica gel precoated glass plates (0.2±0.03 mm thickness, GF-254, particle size 0.01–0.04 mm) from Yantai Chemical Industry Research Institute, P. R. China. Chromatograms were visualized by fluorescence quenching with UV light at 254 nm. Flash column chromatography was performed using silica gel (particle size 0.04–0.05 mm) from Yantai Chemical Industry Research Institute, P. R. China. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded in $CDCl_3$ on Varian Inova-400 NMR spectometer. Chemical shifts (δ ppm) were relative to the resonance of the deuterated solvent as the internal standard ($CDCl_3$, δ 7.26 ppm for proton NMR, δ 77.00 ppm for carbon NMR). Melting points were measured on an X-5 melting point apparatus and uncorrected. ^{1}H NMR data were reported as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, q = quartet, m = multiplet), coupling constants (J) and assignment. Data for ^{13}C NMR were reported in terms of chemical shift (δ, ppm). Mass spectra were carried out using Agilent 6120 Quadrupole LC/MS system with ESI resource. High-resolution mass spectra (HRMS) for all the compounds were determined on Micromass GCT-TOF mass spertrometer with ESI resource. High performance liquid chromatography (HPLC) was performed on an Agilent 1200 Series chromatographs using a Chiralcel AS-H column (0.46cm x 25 cm), Chiralpak AD-H (0.46cm x 25 cm). X-ray data were recorded on a Rigaku Mercury CCD/AFC diffractomrter. Optical rotations are reported as follows: $[\alpha]_D^{rt}$ (c in g per 100 mL, solvent). ECD spectra were recorded on a circular dirchroism spectromete model 410 at 25°C in ethanol solutions, using path lengths of 1.0 cm, in the range 220-300 nm; reported Δε values are expressed as L $mol^{-1}cm.^{-1}$ DFT Calculations were used Gaussian 03, Reversion B.04.

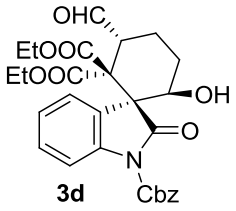
The Isatin Derived Alkenes were prepared according to reported methods.[1-2]

B: General Procedure for the Michael-Aldol Cyclization

To a stirred solution of 1a-r (0.2 mmol) and I or II (0.02 mmol) in dichloromethane (1.0 mL) was added tetrahydro-2H-pyran-2,6-diol (50% in solution, 91 μL, 0.5 mmol) at room temperature. After being stirred for the given time, the desired domino Michael-Aldol cyclization product was purified by flash chromatography over silica gel (petroleum ether/ethyl acetate = 2:1-4:1, v/v as eluent)

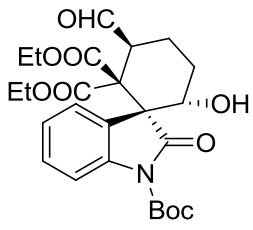
C: Characterization Data of Domino Michael-Aldol Cyclization Products

benzyl-2,2-diethyl-3-formyl-6-hydroxy-2'-oxospiro[cyclohexane-1,3'-indoline]-1', 2,2-tricarboxylate (3d): yellow oil ,72% yield, 95% ee. The enantiomeric excess was determined by HPLC on Daicel Chiralpak AD-H with hexane/i-PrOH (80:20) as the eluent. Flow: 1.0 mL/min; λ = 210 nm: t_{minor} = 15.462 min; t_{major} = 26.119 min. $[\alpha]_D^{20}$ -24.1 (c 0.50 in CH_3COCH_3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 7.2 Hz, 2H), 7.40 - 7.32 (m, 4H), 7.24 (d, *J* = 7.6 Hz, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 5.46 (d, *J* = 12.4 Hz, 1H), 5.37 (d, *J* = 12.4 Hz, 1H), 4.64 (dd, *J* = 11.5, 4.6Hz, 1H), 4.30 - 4.23 (m, 2H), 4.07 - 4.03 (m, 1H), 3.89 - 3.84 (m, 2H), 2.28 - 2.21 (m, 1H), 2.11 - 2.07 (m, 2H), 2.02 - 1.98 (m, 1H), 1.67 (s, 1H), 1.21 (t, *J* = 7.2 Hz, 3H), 0.82 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.86, 174.10, 168.56, 167.96, 150.40, 141.17, 134.86, 128.81, 128.76, 128.53, 128.35, 128.02, 124.58, 122.87, 114.67, 73.12, 68.53, 62.15, 62.07, 61.64, 56.66, 49.60, 26.48, 21.06, 13.64, 13.01. ESI-MS: $[M + Na]^+$ m/z = 546.2; HRMS: m/z $[M + H]^+$ calcd for $C_{28}H_{30}NO_9$: 524.1915; found: 524.1937.



3d

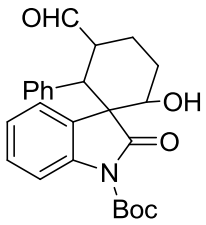
1'-tert-butyl2,2-diethyl-3-formyl-6-hydroxy-2'-oxospiro[cyclohexane-1,3'-indolin e]-1',2,2-tricarboxylate (3e): White solid; m.p. 131-132 ºC; 86% yield, >99% ee. The enantiomeric excess was determined by HPLC on Daicel Chiralpak AS-H with hexane/i-PrOH (92:8) as the eluent. Flow: 1.0 mL/min; λ = 210 nm: t_{minor} = 11.878 min; t_{major} = 13.377 min. $[\alpha]_D^{10}$ +19.8 (c 0.85 in CH_3COCH_3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.71 (s, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.26 (t, *J* = 7.6 Hz 1H), 7.17 (d, *J* = 7.6 Hz, 1H), 7.06 (t, *J* = 7.6 Hz, 1H), 4.53 (d, *J* = 10.4 Hz, 1H),



3e

4.20 (q, *J* = 3.2 Hz, 2H), 4.06 - 3.96 (m, 1H), 3.92 - 3.80 (m, 2H), 2.23 - 2.13 (m, 1H), 2.01 (s, 1H), 1.95 - 1.88 (m, 3H), 1.56 (s, 9H), 1.16 (t, *J* = 6.8 Hz, 3H), 0.87 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.93, 173.99, 168.46, 167.85, 148.71, 141.48, 128.62, 128.46, 124.03, 122.77, 114.31, 84.12, 72.83, 61.85, 61.51, 56.40, 49.41, 27.85, 26.36, 20.88, 13.52, 12.94. ESI-MS: $[M + Na]^+$ m/z = 512.2; HRMS: m/z $[M + Na]^+$ calcd for $C_{25}H_{31}NNaO_9$: 512.1891; found: 512.1877.

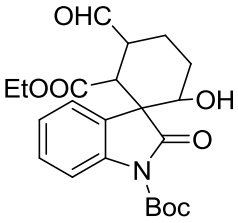
tert-butyl-3-formyl-6-hydroxy-2'-oxo-2-phenylspiro[cyclohexane-1,3'-indoline]-1'-carboxylate. The reaction was carried out following the general procedure using **II** as catalyst to furnish the crude product **3f:** White solid; m.p. 112-113 ºC; 52% yield, 94.5% ee. The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/i-PrOH (90:10) as the eluent. Flow: 1 mL/min; λ = 210 nm: t_{minor} = 10.458 min; t_{major} = 12.154 min. $[\alpha]_D^{10}$ +4.6 (c 0.50 in CH_3COCH_3).



3f

The reaction was carried out following the general procedure using **I** as catalyst to furnish the crude product *ent*-**3f:** 48% yield, -99% ee. The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/i-PrOH (90:10) as the eluent. Flow: 1 mL/min; λ = 210 nm: t_{minor} = 12.271 min; t_{major} = 10.708 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 7.66 (d, *J* = 6.4 Hz, 1H), 7.24 (s, 1H), 7.17 (d, *J* = 7.6 Hz, 1H), 7.10 (d, *J* = 6.8 Hz, 2H), 7.05(t, *J* = 7.2, 3H), 6.99 (t, *J* = 7.2 Hz, 1H), 4.15 (d, *J* = 5.6 Hz, 1H), 3.71 (s, 1H), 2.64 (s, 1H), 2.42 (d, *J* = 15.2 Hz, 1H), 2.34 (d, *J* = 14 Hz, 1H), 2.22 (s, 1H), 2.12 (d, *J* = 12.8 Hz, 1H), 1.73 (d, *J* = 12 Hz, 1H), 1.63 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.18, 176.75, 148.84, 138.79, 138.10, 129.14, 128.60, 128.43, 126.99, 124.47, 124.10, 114.74, 84.87, 69.65, 55.65, 50.38, 45.04, 28.05, 23.92, 18.40. ESI-MS: $[M + Na]^+$ m/z = 444.2; HRMS: m/z $[M + Na]^+$ calcd for $C_{25}H_{27}NaNO_5$: 444.1781; found: 444.1784.

1'-tert-butyl-2-ethyl-3-formyl-6-hydroxy-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2-dicarboxylate. The reaction was carried out following the general procedure using **II** as catalyst to furnish the crude product **3g:** White solid; m.p. 53-54 ºC; 54% yield, >99% ee. The enantiomeric excess was determined by HPLC on Daicel

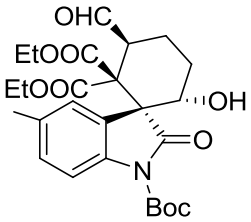


3g

Chiralpak OD-H with hexane/i-PrOH (90:10) as the eluent. Flow: 1 mL/min; λ = 210 nm: t_{minor} = 15.597 min; t_{major} = 12.186 min. $[\alpha]_D^{10}$ +4.1 (c 0.25 in CH_3COCH_3).

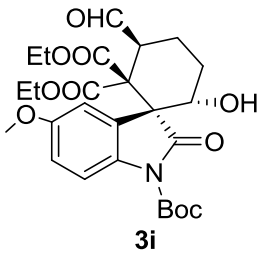
The reaction was carried out following the general procedure using **I** as catalyst to furnish the crude product *ent*-**3en:** 51% yield, -95.7% ee. The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/i-PrOH (90:10) as the eluent. Flow: 1 mL/min; λ = 210 nm: t_{minor} = 11.829 min; t_{major} = 14.982 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.61 (s, 1H), 7.81 (d, *J* =8.0 Hz, 1H), 7.33 - 7.27 (m, 2H), 7.12 (t, *J* = 7.2 Hz, 1H), 4.01 - 3.91 (m, 2H), 3.69 (s, 1H), 3.66 (d, *J* = 6.0 Hz, 1H), 2.93 - 2.92 (m, 1H), 2.41 (dd, *J* = 10.0, 3.6 Hz, 1H), 2.21 (t, *J* = 13.2 Hz, 1H), 2.09 - 2.05 (m, 1H), 2.00 (s, 1H), 1.69 (dd, *J* = 10.4, 3.6 Hz, 1H), 1.59 (s, 9H), 1.03 (t, *J* = 7.2, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.34, 175.56, 170.85, 148.90, 139.69, 129.71, 128.78, 123.98, 123.44, 115.14, 84.51, 68.57, 61.27, 52.73, 46.21, 44.66, 28.05, 17.41, 13.66. ESI-MS: $[M + Na]^+$ m/z = 440.2; HRMS: m/z $[M + NH_4]^+$ calcd for $C_{22}H_{31}N_2O_7$: 435.2131; found: 435.2135.

1'-tert-butyl-2,2-diethyl3-formyl-6-hydroxy-5'-methyl-2'-oxospiro[cyclohexane-1, 3'-indoline]-1',2,2-tricarboxylate (3h): White solid; m.p. 134-135 ºC; 84% yield, >99% ee. The enantiomeric excess was determined by HPLC on Daicel Chiralpak AD-H with hexane/i-PrOH (92:8) as the eluent. Flow: 1.0 mL/min; λ = 210 nm: t_{minor} = 40.648 min; t_{major} = 25.100 min. $[\alpha]_D^{10}$ -1.1 (c 1.00 in CH_3COCH_3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.75 (s, 1H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.10(d, *J* = 8.4 Hz, 1H), 7.01 (s, 1H), 4.56 (d, *J* = 3.6 Hz, 1H), 4.25(q, *J* = 6.8 Hz, 2H), 4.04 - 3.94 (m, 1H), 3.92 - 3.84 (m, 2H), 2.304 (s, 3H), 2.25 - 2.18 (m, 1H), 2.09 - 2.05 (m, 2H), 1.95 (d, *J* = 9.2 Hz, 1H), 1.68 (s, 1H), 1.58(s, 9H), 1.21 (t, *J* = 7.2 Hz, 3H), 0.92 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, CDCl3) δ 200.25, 174.54, 168.88, 168.36, 149.13, 139.49, 133.96, 129.37, 128.71, 123.74, 114.57, 84.38, 73.37, 62.28, 62.17, 61.76, 56.76, 49.91, 28.25, 26.66, 21.43, 21.33, 13.95, 13.36. ESI-MS: $[M + Na]^+$ m/z = 526.2; HRMS: m/z $[M + Na]^+$ calcd for $C_{26}H_{33}NNaO_9$: 526.2048; found: 526.2036.



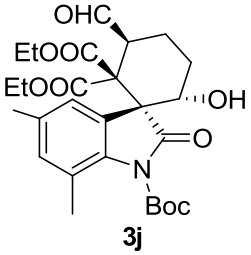
3h

1'-tert-butyl-2,2-diethyl-3-formyl-6-hydroxy-5'-methoxy-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2,2-tricarboxylate (3i): White solid; m.p. 61-62 ºC; 88% yield, 98.5% ee. The enantiomeric excess was determined by HPLC on Daicel Chiralpak AD-H with hexane/i-PrOH (80:20) as the eluent. Flow: 1.0 mL/min; λ = 210 nm: t_{minor} = 24.027 min; t_{major} = 11.497 min. $[\alpha]_D^{10}$ +6.3 (c 1.00 in CH_3COCH_3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.75 (s, 1H), 7.73 (d, *J* = 8.4 Hz, 1H), 6.79 (s, 2H), 4.61 - 4.58 (m, 1H), 4.24 (t, *J* = 6.8 Hz, 2H), 4.06 - 4.02 (m, 1H), 3.98 - 3.85 (m, 2H), 3.73 (s, 3H), 2.24 - 2.17 (m, 1H), 2.06 - 1.99 (m, 3H), 1.84 (s, 1H), 1.57(s, 9H), 1.21 (t, *J* = 7.2 Hz, 3H), 0.92 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.01, 174.09, 168.50, 167.94, 156.54, 148.85, 134.92, 129.90, 115.19, 112.61, 109.97, 84.04, 73.05, 62.02, 61.64, 56.70, 55.40, 49.48, 27.96, 26.49, 20.94, 13.60, 13.07. ESI-MS: $[M + Na]^+$ m/z = 542.2; HRMS: m/z $[M + Na]^+$ calcd for $C_{26}H_{33}NNaO_{10}$: 542.1997; found: 542.1980.



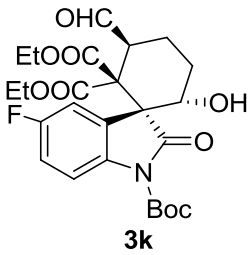
3i

1'-tert-butyl-2,2-diethyl-3-formyl-6-hydroxy-5',7'-dimethyl-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2,2-tricarboxylate (3j) : White solid; m.p. 42-43 ºC; 71% yield, 98.4% ee. The enantiomeric excess was determined by HPLC on Daicel Chiralpak AD-H with hexane/i-PrOH (80:20) as the eluent. Flow: 1.0 mL/min; λ = 210 nm: t_{minor} = 9.117 min; t_{major} = 6.690 min. $[\alpha]_D^{10}$ +28.1 (c 1.00 in CH_3COCH_3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 6.95 (s, 1H), 6.90 (s, 1H), 4.60 - 4.58 (m, 1H), 4.27 (t, *J* = 5.2 Hz, 2H), 4.09 - 4.00 (m, 2H), 3.93 - 3.89 (m, 1H), 2.30 (s, 3H), 2.22 (s, 1H), 2.19 (s, 3H), 2.07 - 2.05 (m, 2H), 1.99 (d, *J* = 9.6 1H), 1.59(s, 9H), 1.23 (t, *J* = 6.8 Hz, 3H), 0.94 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.16, 175.23, 168.63, 168.10, 148.95, 137.86, 133.74, 132.20, 129.67, 123.10, 121.28, 84.36, 72.90, 62.18, 61.88, 61.56, 57.29, 49.57, 27.75, 26.43, 21.13, 21.02, 19.49, 13.73, 13.15. ESI-MS: $[M + Na]^+$ m/z = 540.3; HRMS: m/z $[M + Na]^+$ calcd for $C_{27}H_{35}NNaO_9$: 540.2204; found: 540.2193.



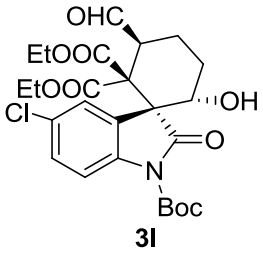
3j

1'-tert-butyl2,2-diethyl5'-fluoro-3-formyl-6-hydroxy-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2,2-tricarboxylate (3k) : White solid; m.p. 78-79 ºC; 82% yield, 97.6% ee. The enantiomeric excess was determined by HPLC on Daicel Chiralpak AD-H with hexane/i-PrOH (80:20) as the eluent. Flow: 1.0 mL/min; λ = 210 nm: t_{minor} = 14.475 min; t_{major} = 7.007 min. $[\alpha]_D^{10}$ +25.2 (c 1.00 in CH_3COCH_3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 7.81 (q, *J* = 4.4 Hz, 1H), 7.00 - 7.02 (m, 2H), 4.65 - 4.61 (m, 1H), 4.27 (q, *J* = 6.4 Hz, 2H), 4.10 - 4.03 (m, 1H), 3.99 - 3.88 (m, 2H), 2.26 - 2.22 (m, 1H), 2.07 - 2.06 (m, 1H), 2.03 - 2.00 (m, 2H), 1.93 (s, 1H), 1.59(s, 9H), 1.22 (t, *J* = 6.8 Hz, 3H), 0.93 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100MHz, $CDCl_3$) δ 200.15, 174.08, 168.62, 168.12, 161.13, 158.72, 149.02, 137.83, 131.05, 130.97, 115.84, 115.76, 115.21, 114.98, 111.34, 111.09, 84.77, 73.22, 62.49, 62.42, 61.93, 57.00, 49.64, 28.21, 27.00, 21.12, 13.89, 13.36. ESI-MS: $[M + Na]^+$ m/z = 530.2; HRMS: m/z $[M + Na]^+$ calcd for $C_{25}H_{30}FNaNO_9$: 530.1797; found: 530.1799.



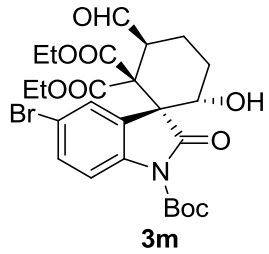
3k

1'-tert-butyl-2,2-diethyl-5'-chloro-3-formyl-6-hydroxy-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2,2-tricarboxylate (3l) : White solid; m.p. 131-135 ºC;79% yield, 97.4% ee. The enantiomeric excess was determined by HPLC on Daicel Chiralpak AD-H with hexane/i-PrOH (80:20) as the eluent. Flow: 1.0 mL/min; λ = 210 nm: t_{minor} = 14.732 min; t_{major} = 8.859 min. $[\alpha]_D^{10}$ -14.3 (c 0.80 in CH_3COCH_3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.28 (d, *J* = 4.4 Hz, 1H), 7.2 (s, 1H), 4.59 - 4.56 (m, 1H), 4.32 - 4.22 (m, 2H), 4.01 - 3.93 (m, 2H), 3.92 - 3.87 (m, 1H), 2.27 - 2.16 (m, 1H), 2.07 - 2.05 (m, 2H), 1.99 - 1.94 (m, 1H), 1.85 (s, 1H), 1.58 (s, 9H), 1.22 (t, *J* = 6.8 Hz, 3H), 0.93 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.71, 173.59, 168.38, 167.92, 148.64, 140.17, 130.69, 129.60, 128.47, 123.32, 115.62, 84.65, 73.02, 62.26, 62.19, 61.48, 56.53, 49.49, 27.94, 26.66, 20.96, 13.69, 13.12. ESI-MS: $[M + Na]^+$ m/z = 546.2; HRMS: m/z $[M + Na]^+$ calcd for $C_{25}H_{30}ClNaNO_9$: 546.1501; found: 546.1506.



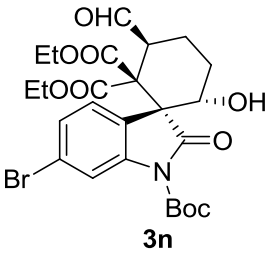
3l

1'-tert-butyl-2,2-diethyl-5'-bromo-3-formyl-6-hydroxy-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2,2-tricarboxylate (3m) : White solid; m.p. 122-126 ºC; 83% yield, 97.5% ee. The enantiomeric excess was determined by HPLC on Daicel Chiralpak AD-H with hexane/i-PrOH (80:20) as the eluent. Flow: 1.0 mL/min; λ = 210 nm: t_{minor} = 14.868 min; t_{major} = 10.030 min. $[\alpha]_D^{10}$ -22.4 (c 1.00 in CH_3COCH_3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1H), 7.73 (d, *J* = 8.8 Hz, 1H), 7.44 (d, *J* = 8.8 Hz, 1H), 7.33 (s, 1H), 4.59 - 4.55 (m, 1H), 4.32 - 4.22 (m, 2H), 3.99 - 3.93 (m, 2H), 3.92 - 3.87 (m, 1H), 2.27 - 2.16 (m, 1H), 2.08 - 1.94 (m, 3H), 1.87 (s, 1H), 1.58 (s, 9H), 1.23 (t, *J* = 7.2 Hz, 3H), 0.94 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.66, 173.49, 168.40, 167.95, 148.63, 140.69, 131.40, 131.04, 126.07, 117.14, 116.05, 84.66, 73.03, 62.26, 62.19, 61.45, 56.47, 49.53, 27.94, 26.66, 21.00, 13.72, 13.13. ESI-MS: $[M + Na]^+$ m/z = 590.1; HRMS: m/z $[M + Na]^+$ calcd for $C_{25}H_{30Br}{}^{79}NO_9$: 590.0996; found: 590.0993.



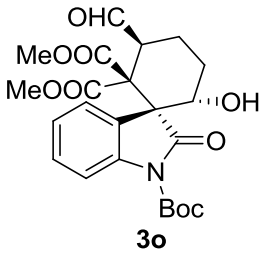
3m

1'-tert-butyl-2,2-diethyl-6'-bromo-3-formyl-6-hydroxy-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2,2-tricarboxylate (3n) : White solid; m.p. 130-131 ºC; 74% yield, 97.2% ee. The enantiomeric excess was determined by HPLC on Daicel Chiralpak AD-H with hexane/i-PrOH (80:20) as the eluent. Flow: 1.0 mL/min; λ = 210 nm: t_{minor} = 9.430 min; t_{major} = 5.566 min. $[\alpha]_D^{10}$ +10.5 (c 1.00 in CH_3COCH_3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 8.06 (s, 1H), 7.28 (d, *J* = 8.8 Hz, 1H), 7.10 (d, *J* =4.0 Hz,1H), 4.61 - 4.57 (m, 1H), 4.27 - 4.23 (m, 2H), 4.02 - 3.98 (m, 2H), 3.96 - 3.88 (m, 1H), 2.26 - 2.17 (m, 1H), 2.14 (s, 1H), 2.08 - 1.96 (m, 3H), 1.60 (s, 9H), 1.22 (t, *J* = 6.8 Hz, 3H), 0.98 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100MHz, $CDCl_3$) δ199.77, 173.68, 168.39, 167.87, 148.51, 142.60, 127.95, 127.07, 124.21, 122.25, 117.86, 84.81, 72.82, 62.18, 62.14, 61.53, 56.43, 49.42, 27.88, 26.65, 20.91, 13.62, 13.12. ppm; ESI-MS: $[M + Na]^+$ m/z = 590.1; HRMS: m/z $[M + Na]^+$ calcd for $C_{25}H_{30Br}{}^{79}NaNO_9$: 590.0996; found: 590.0991.



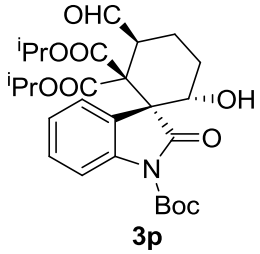
3n

1'-tert-butyl-2,2-dimethyl-3-formyl-6-hydroxy-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2,2-tricarboxylate (3o) : White solid; m.p. 57-58 ºC; 67% yield, 98.3% ee. The enantiomeric excess was determined by HPLC on Daicel Chiralpak AD-H with hexane/i-PrOH (80:20) as the eluent. Flow: 1.0 mL/min; λ = 210 nm: t_{minor} = 15.542 min; t_{major} = 8.964 min. $[\alpha]_D^{10}$ +68.8 (c 0.80 in CH_3COCH_3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 7.84 (d, *J* = 8.4 Hz, 1H), 7.35 (t, *J* = 6.8 Hz, 1H), 7.17 - 7.13 (m, 2H), 4.63 - 4.58 (m, 1H), 4.09 - 4.05 (m, 1H), 3.78 (m, 3H), 3.48 (s, 3H), 2.30 - 2.22 (m, 1H), 2.12 - 2.07 (m, 2H), 2.04 (s, 1H), 2.02 - 1.98 (m, 1H), 1.62 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ200.09, 174.57, 169.37, 168.77, 149.05, 141.86, 129.11, 128.74, 124.70, 122.83, 114.93, 84.66, 73.34, 61.89, 56.86, 53.09, 53.05, 50.05, 28.27, 26.72, 21.27. ESI-MS: $[M + Na]^+$ m/z = 484.2; HRMS: m/z $[M + H]^+$ calcd for $C_{23}H_{28}NO_9$: 462.1759; found: 462.1769.



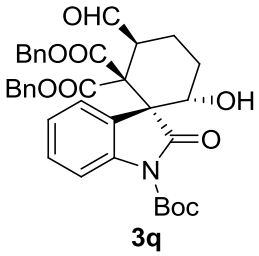
3o

1'-tert-butyl-2,2-diisopropyl-3-formyl-6-hydroxy-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2,2-tricarboxylate (3p): White solid; m.p. 101-102 ºC; 87% yield, >99% ee. The enantiomeric excess was determined by HPLC on Daicel Chiralpak AD-H with hexane/i-PrOH (75:25) as the eluent. Flow: 0.6 mL/min; λ = 210 nm: t_{minor} = 16.091 min; t_{major} = 8.159 min. $[\alpha]_D^{10}$ +10.5 (c 1.00 in CH_3COCH_3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.32 (m, 2H), 7.13 (t, *J* =6.8 Hz,1H), 5.23 - 5.17 (m, 1H), 4.85 - 4.80 (m, 1H), 4.68 (dd, *J* = 4.4, 6.8 Hz, 1H), 4.065 (t, *J* = 8.0 Hz, 1H), 2.27 - 2.20 (m, 1H), 2.11 - 2.04 (m, 2H), 2.00 - 1.96 (m, 1H), 1.93 (s, 1H), 1.61 (s, 9H), 1.27 (d, *J* = 6.4 Hz, 3H), 1.16 (d, *J* = 6.4 Hz, 3H), 0.95 (d, *J* = 6.4 Hz, 3H), 0.86 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.12, 173.94, 168.09, 167.56, 148.90, 141.61, 128.74, 128.64, 124.08, 123.11, 114.45, 84.29, 73.13, 70.27, 69.99, 61.49, 56.54, 49.57, 28.01, 26.43, 21.58, 21.26, 21.01, 20.84, 20.56. ESI-MS: $[M + Na]^+$ m/z = 540.3; HRMS: m/z $[M + Na]^+$ calcd for $C_{27}H_{35}NaNO_9$: 540.2204; found: 540.2194.



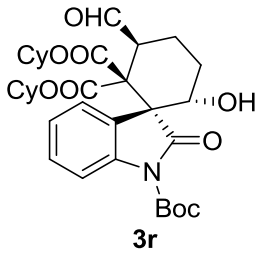
3p

2,2-dibenzyl-1'-tert-butyl-3-formyl-6-hydroxy-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2,2-tricarboxylate (3q) : White solid; m.p. 41-43 ºC; 83% yield, >99% ee. The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/i-PrOH (90:10) as the eluent. Flow: 1 mL/min; λ = 210 nm: t_{minor} = 27.711 min; t_{major} = 17.986 min. $[\alpha]_D^{10}$ -2.52 (c 0.75 in CH_3COCH_3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 7.51 (d, *J* = 7.2 Hz, 1H), 7.27 (d, *J* = 8.0 Hz, 4H), 7.14 (d, *J* = 6.4 Hz, 5H), 7.03 (d, *J* = 6.4 Hz, 1H), 6.87 (s, 1H), 6.73 (d, *J* =5.2 Hz, 2H), 5.30 (d, *J* = 12 Hz, 1H), 5.08 (d, *J* = 11.6 Hz, 1H), 4.89 (d, *J* = 11.6 Hz, 1H), 4.71 (d, *J* = 12 Hz, 1H), 4.60 (d, *J* = 4.4 Hz, 1H), 4.15 (s, 1H), 2.25 - 2.23 (m, 1H), 2.11 (s, 2H), 1.98 (d, *J* = 8.8 Hz, 1H), 1.58 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ199.94, 174.10, 168.44, 167.92, 148.57, 141.31, 134.34, 133.68, 128.54, 128.45, 128.22, 128.08, 124.16, 122.58, 114.67, 84.26, 73.20, 68.16, 67.90, 61.44, 56.50, 49.85, 28.00, 26.35, 21.01. ESI-MS: $[M + Na]^+$ m/z = 636.3; HRMS: m/z $[M + Na]^+$ calcd for $C_{35}H_{35}NaNO_9$: 636.2204; found: 636.2197.



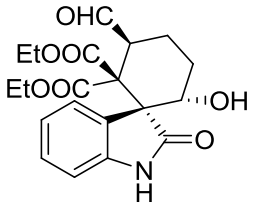
3q

1'-tert-butyl-2,2-dicyclohexyl-3-formyl-6-hydroxy-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2,2-tricarboxylate (3r) : White solid; m.p. 68-69 ºC; 88% yield, >99% ee. The enantiomeric excess was determined by HPLC on Daicel Chiralpak AD-H with hexane/i-PrOH (90:10) as the eluent. Flow: 1 mL/min; λ = 210 nm: t_{minor} = 30.646 min; t_{major} = 8.641 min. $[\alpha]_D^{10}$ +4.9 (c 0.80 in CH_3COCH_3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.35 - 7.27 (m, 2H), 7.13 (t, *J* = 6.8 Hz, 1H), 4.97 (s, 1H), 4.65 (d, *J* = 8.8 Hz, 1H), 4.57 (s, 1H), 4.06 (d, *J* = 6.4 Hz, 1H), 2.24 - 2.19 (m, 1H), 2.08 (s, 2H), 2.00 - 1.91 (m, 2H), 1.77 (s, 1H), 1.61 (s, 9H), 1.51 - 1.32 (m, 11H), 1.19 (d, *J* = 7.2 Hz, 4H), 1.07 - 0.89 (m, 4H). ^{13}C NMR (100MHz, $CDCl_3$) δ 200.11, 174.02, 168.23, 167.61, 148.86, 141.58, 128.65, 124.13, 123.02, 114.55, 84.22, 75.33, 75.22, 73.28, 61.63, 56.53, 49.68, 31.22, 30.94, 30.66, 30.53, 28.00, 26.38, 25.06, 24.95, 23.61, 23.39, 21.14. ESI-MS: $[M + Na]^+$ m/z = 620.3; HRMS: m/z $[M + Na]^+$ calcd for $C_{33}H_{43}NaNO_9$: 620.2836; found: 620.2831.



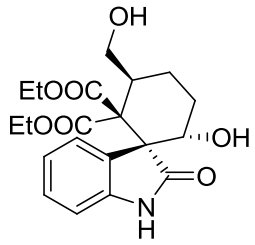
3r

diethyl-3-formyl-6-hydroxy-2'-oxospiro[cyclohexane-1,3'-indoline]-2,2-dicarboxylate (4): White solid; m.p. 135-136 ºC; 93% yield, >99% ee. The enantiomeric excess was determined by HPLC on Daicel Chiralpak AD-H with hexane/i-PrOH (80:20) as the eluent. Flow: 1 mL/min; λ = 210 nm: t_{minor} = 56.182 min; t_{major} = 15.200 min. $[\alpha]_D^{10}$ +11.2 (c 0.20 in CH_3COCH_3). ^1H NMR (300 MHz, $CDCl_3$) δ 9.78 (s, 1H), 8.67 (s, 1H) 7.27 (d, *J* = 7.8 Hz, 1H), 7.19(t, *J* = 7.8 Hz, 1H), 6.97 (t, *J* = 8.1 Hz, 1H), 6.75 (d, *J* = 7.8 Hz, 1H), 4.64 - 4.59 (m, 1H), 4.23 - 4.21(m, 2H), 4.15 - 4.11 (d, *J* = *12*, 1H), 3.92 - 3.84 (m, 2H), 2.63(s, 1H), 2.26 (s, 1H), 2.09 - 2.05 (m, 1H), 1.91 - 1.77 (m, 2H), 1.19 (t, *J* = 7.8 Hz, 3H), 0.83 (t, *J* =7.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.73, 177.42, 168.45, 167.89, 142.56, 130.16, 128.39, 124.24, 122.35, 109.51, 72.06, 61.96, 61.92, 61.41, 57.20, 48.76, 26.38, 20.68, 13.72, 13.07. ESI-MS: $[M + Na]^+$ m/z = 412.1; HRMS: m/z $[M + Na]^+$ calcd for $C_{20}H_{23}NNaO_7$: 412.1367; found: 412.1376.



4

diethyl-6-hydroxy-3-(hydroxymethyl)-2'-oxospiro[cyclohexane-1,3'-indoline]-2,2-dicarboxylate (5): White solid; m.p. 151-152 ºC; 97% yield, 98% ee. The enantiomeric excess was determined by HPLC on Daicel Chiralpak AD-H with hexane/i-PrOH (70:30) as the eluent. Flow: 1 mL/min; λ = 210 nm: t_{minor} = 16.209 min; t_{major} = 10.345 min. $[\alpha]_D^{10}$ +74.1 (c 0.65 in CH_3COCH_3). ^1H NMR (400 MHz, CD_3OD) 7.37 (d, *J* = 7.6 Hz, 1H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.00 (t, *J* = 7.6 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 4.34 - 4.27 (m, 1H), 4.16 - 4.12 (m, 1H), 3.96 - 3.85 (m, 2H), 3.81 - 3.74 (m, 1H), 3.34 (s, 1H), 3.31 - 3.25 (m, 1H), 3.14 (t, *J* = 8.8 Hz, 1H), 2.46 - 2.35 (m, 1H), 2.22 - 2.18 (m, 1H), 1.89 - 1.85 (m, 1H), 1.75 - 1.64 (m, 1H), 1.26 (t, *J* =7.2 Hz, 3H), 0.83 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, CD_3OD) δ 178.71, 169.74, 169.38, 144.81, 133.74, 128.81, 125.69, 123.04, 109.98, 72.81, 65.22, 63.60, 62.41, 62.06, 59.39, 40.10, 28.64, 24.53, 14.43, 13.47. ESI-MS: $[M + Na]^+$ m/z = 414.1; HRMS: m/z $[M + H]^+$ calcd for $C_{20}H_{26}NO_7$: 392.1704; found: 392.1708.



5

D: X-ray crystal structure of *ent*-3e

Crystal structure determination of compound *ent*-**3e**: $C_{25}H_{31}NO_9$, M = 489.51; a block crystal (0.75 x 0. 5 x 0.4 mm), T = 293(2), λ (Mo-Ka) = 0.71070 Å, Monoclinic, space group: P 65, a = 18.8854(16) Å, b = 18.8854 (16) Å, c = 12.9167(11) Å, V = 3989.6(6) Å3, 19575 total reflections, 4808 unique, Rint = 0.0426, R1 = 0.0819 (I > 2 σ), wR2 = 0.2389, Absolute structure parameter: -0.6(19). An ORTEP drawing of *ent*-**3e** is shown in Figure S1.

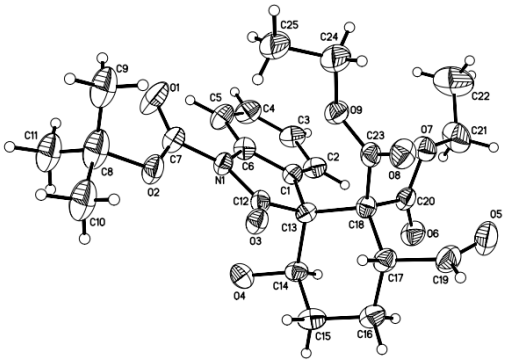


Figure S1. ORTEP drawing of *ent*-***3e*** (40% thermal ellipsoids).

The crystal was prepared from the solution of *ent*-**3e** in dichloromethane. CCDC 875824 contains the supplementary crystallographic data for this paper. Thes e data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data request/cif.

E: References

1. X-C. hang, S-H. Cao, Y. Wei, M. Shi, *Org. Lett.* 2011, **13**, 1142.

2. S.J. Garden, C.R.W. Guimarães, M.B. Corréa, C.A.F.D. Oliveira, A.d.C. Pinto, R.B.d. Alencastro, *J. Org. Chem.* 2003, **68**, 8815.

3. M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R.Cheeseman,; J. A. Jr. Montgomery, T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O.Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J.

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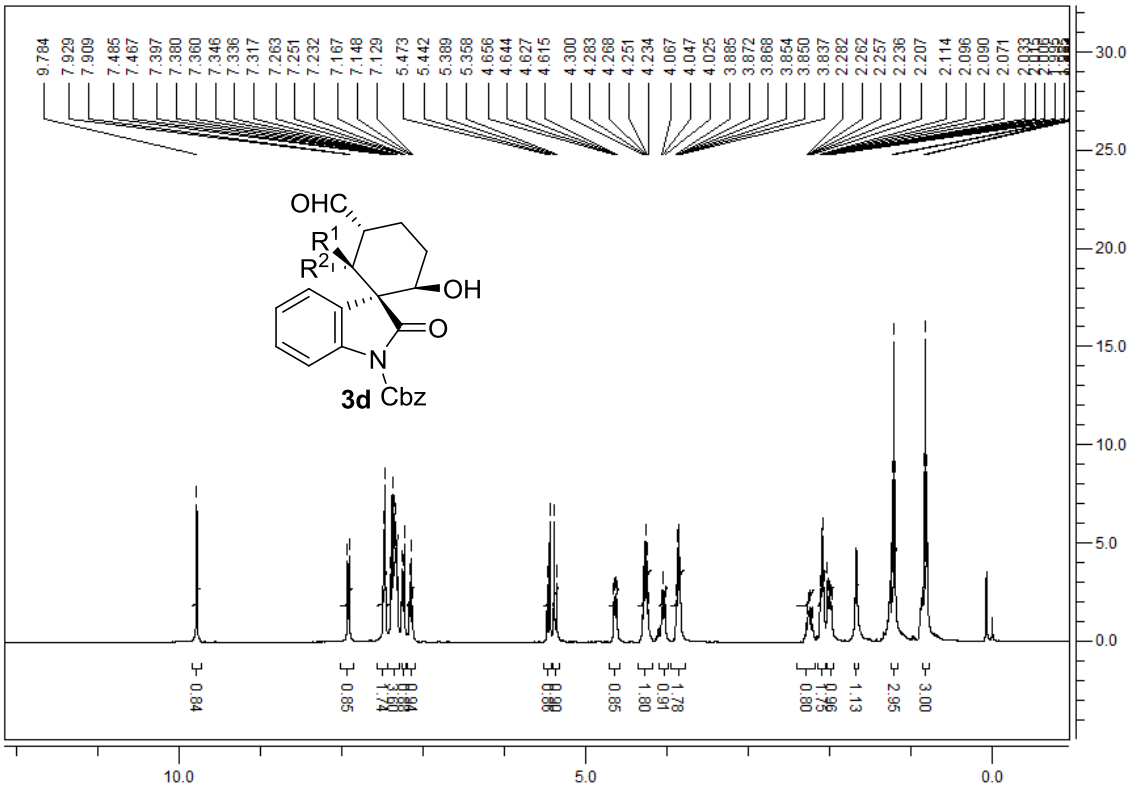
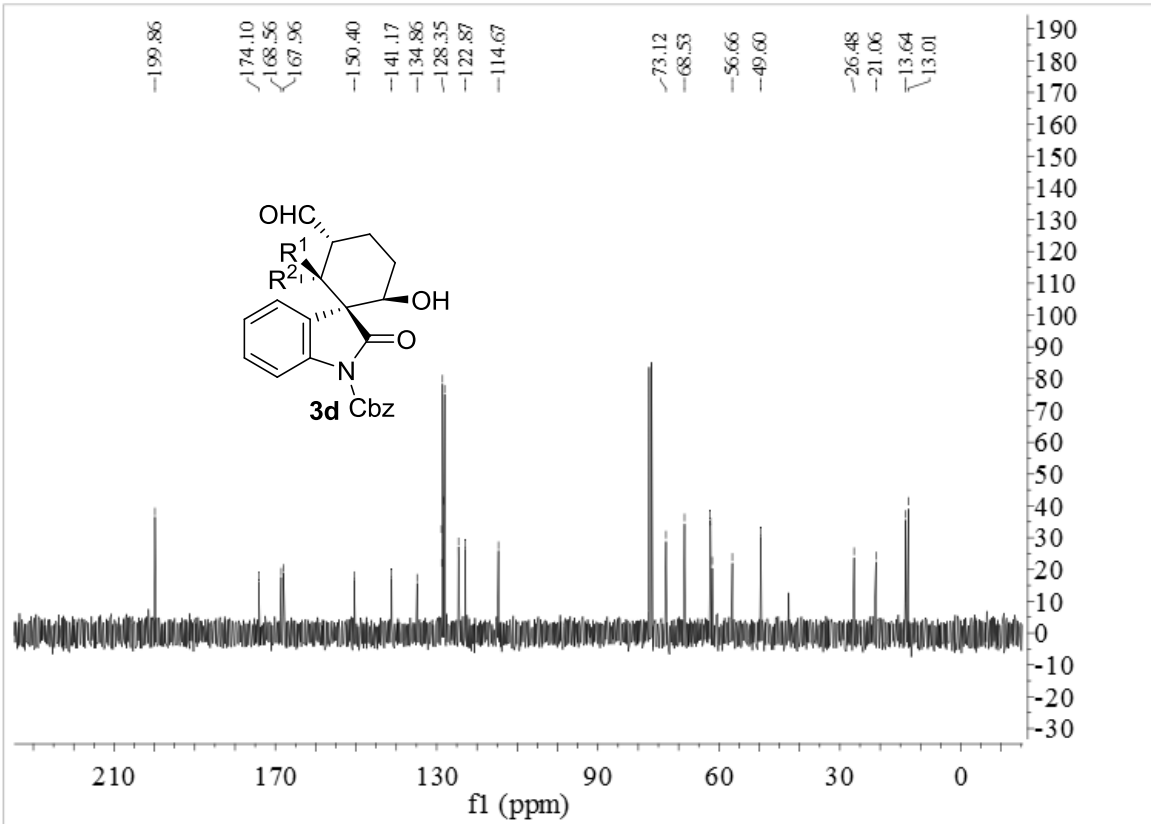
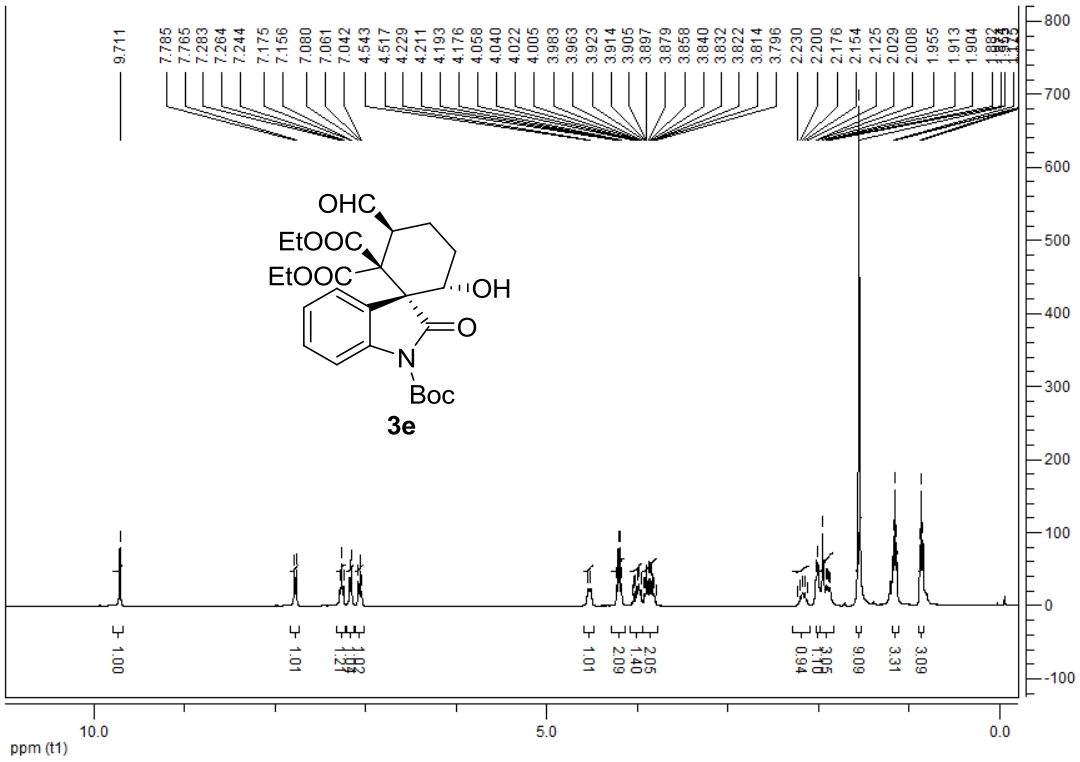
F: ^{1}H NMR and ^{13}C NMR Spectra

3d





3e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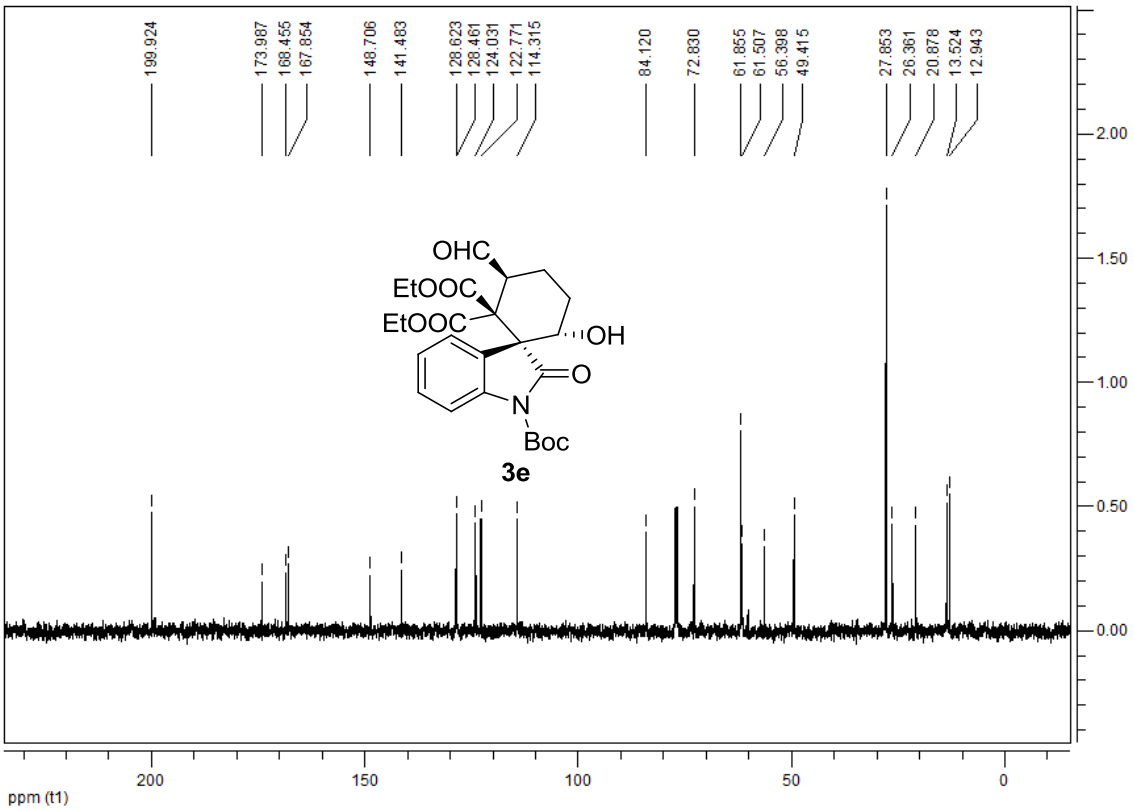
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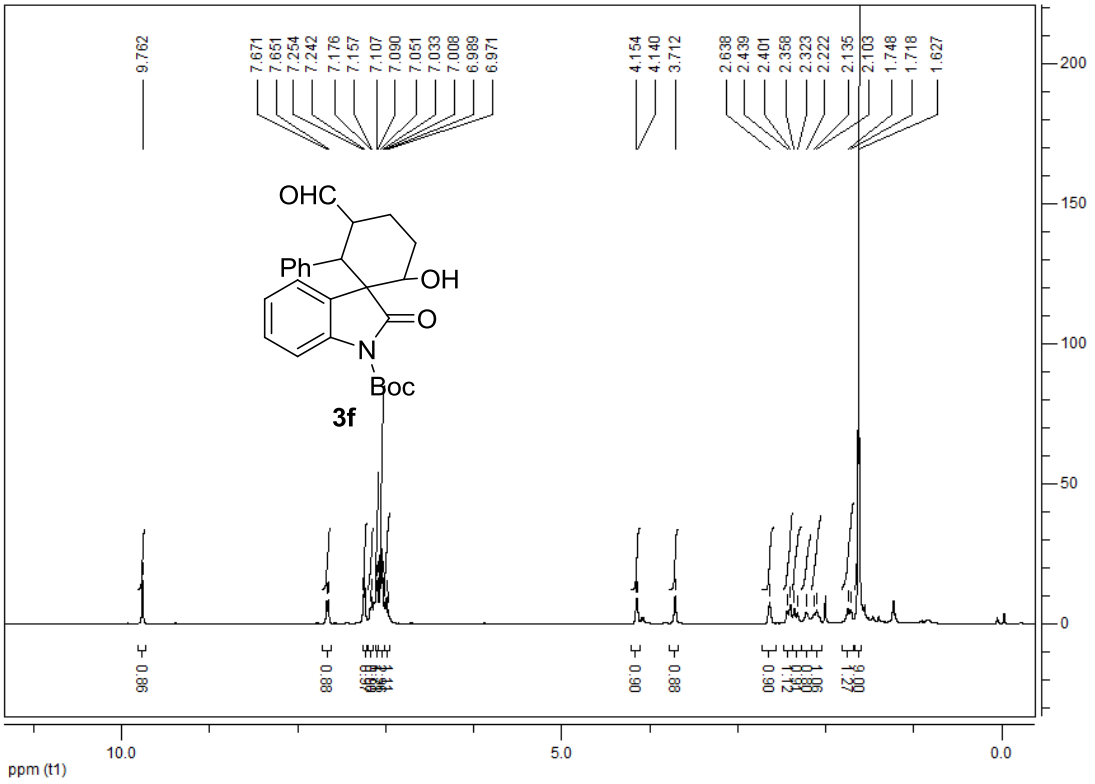
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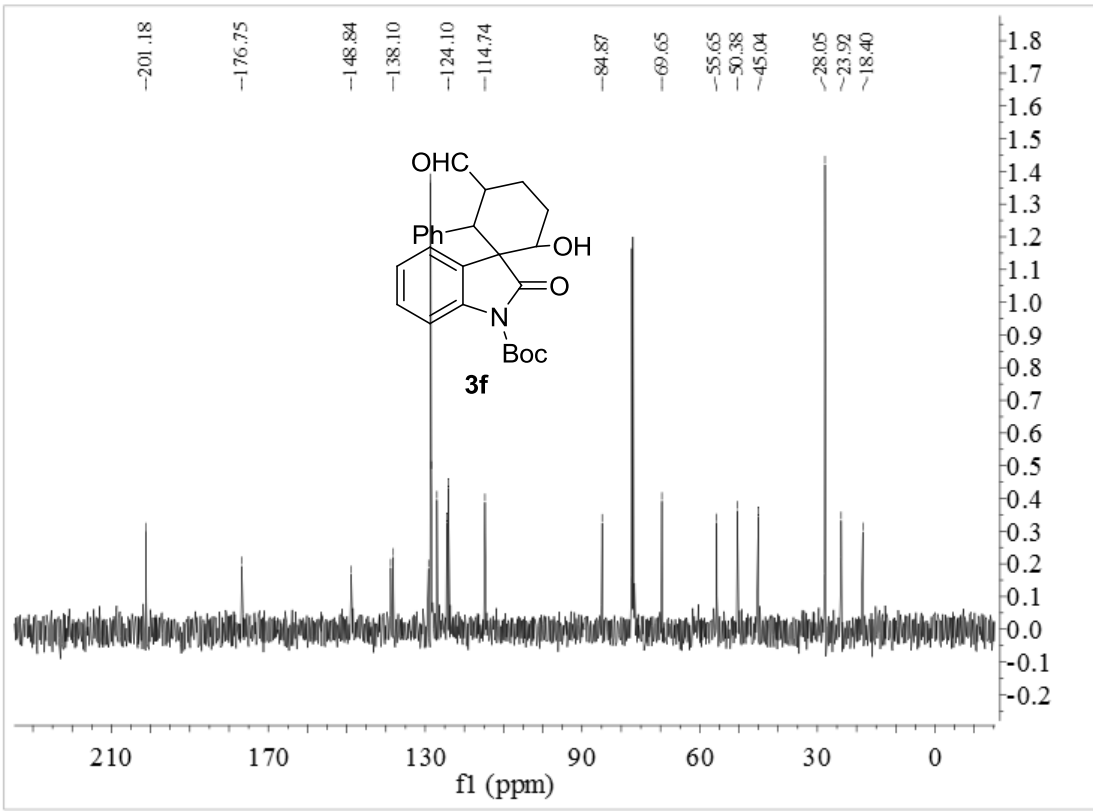
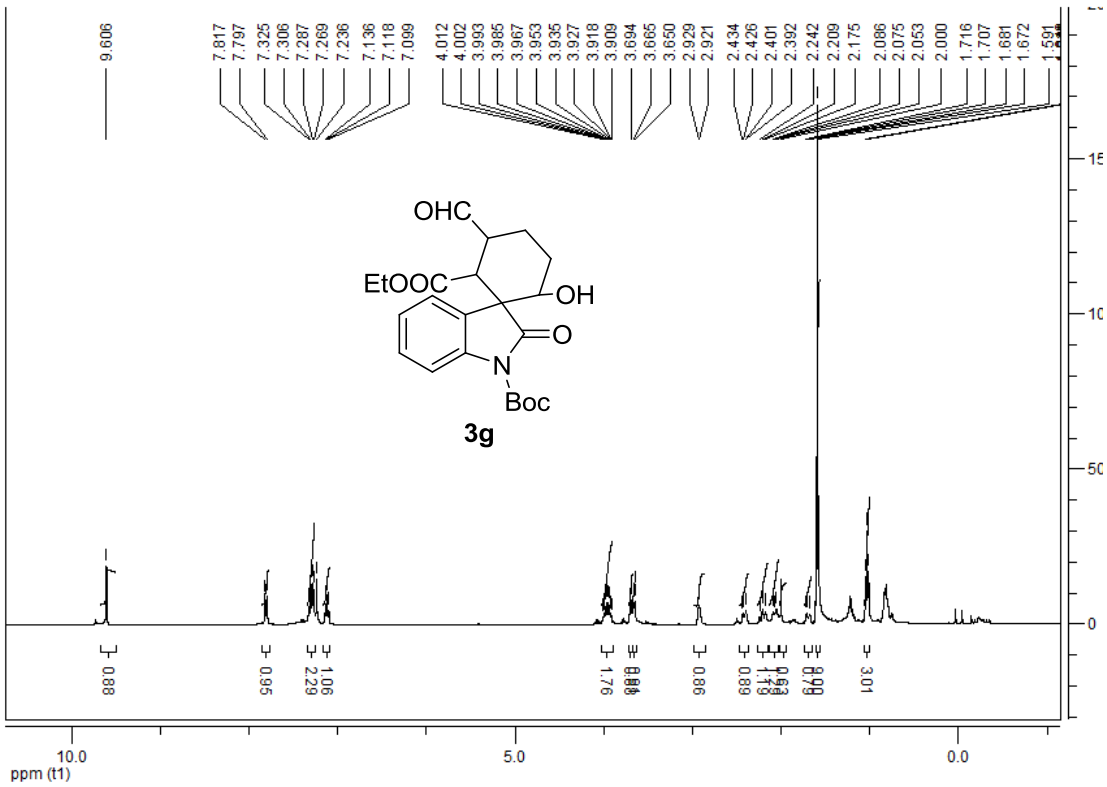
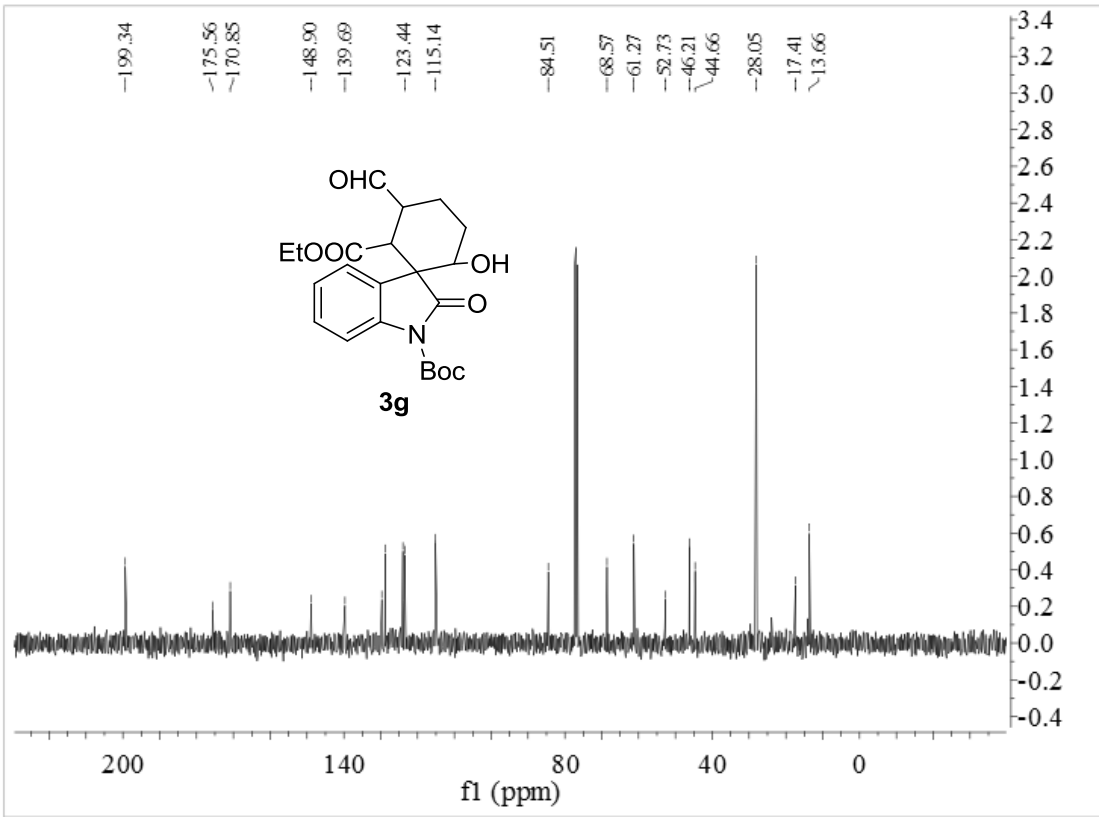
3f
ppm (t1)

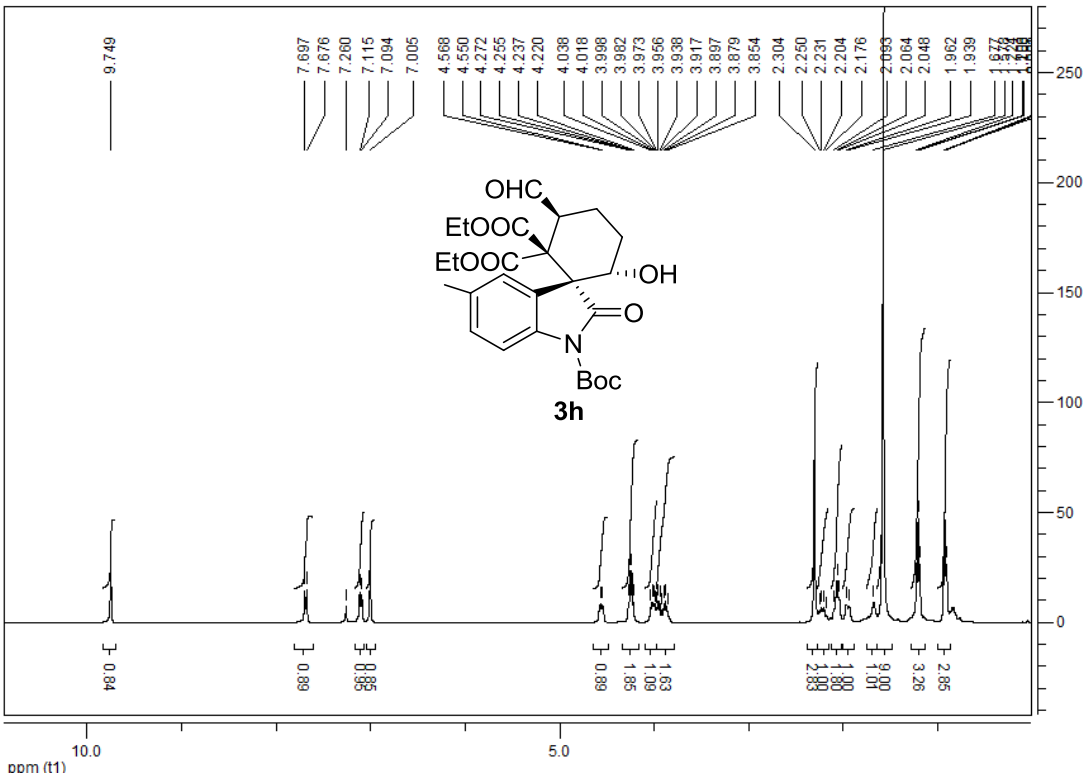

201.18
176.75
148.84
138.10
124.10
114.74
84.87
69.65
55.65
50.38
45.04
28.05
23.92
18.40
OHC
Ph
OH
O
N
Boc
3f
f1 (ppm)

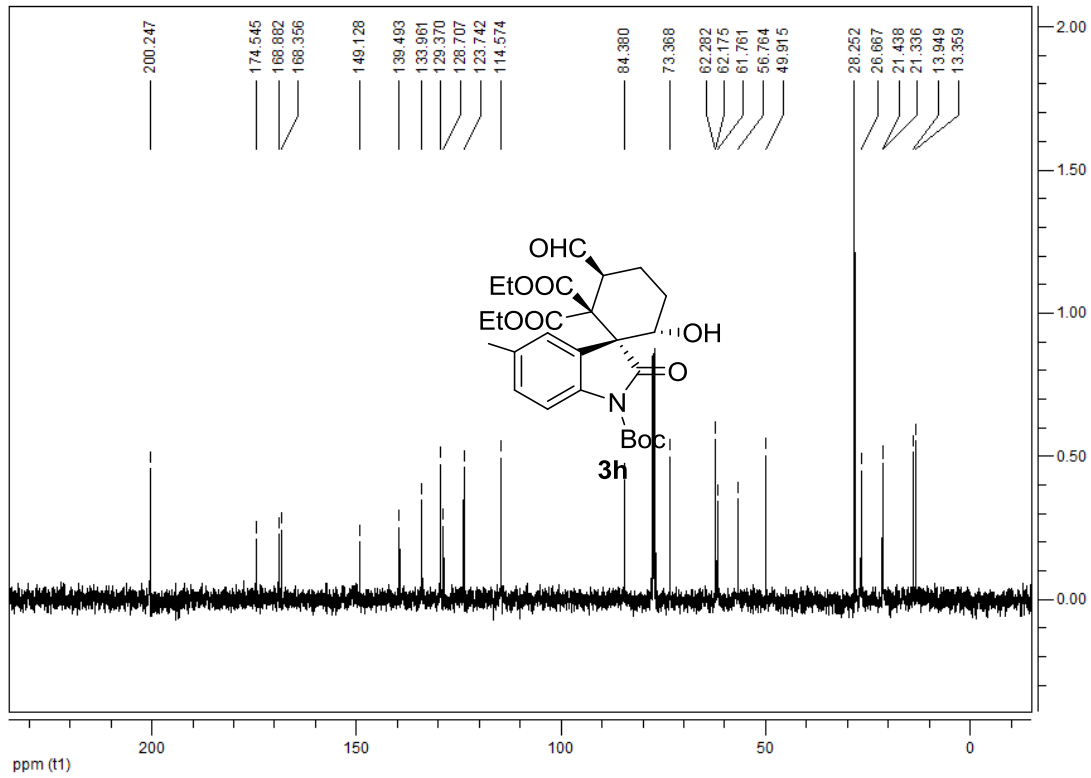
3g


9.606
7.817
7.797
7.325
7.306
7.287
7.269
7.236
7.136
7.118
7.099
4.012
4.002
3.993
3.985
3.967
3.953
3.935
3.927
3.918
3.909
3.694
3.665
3.650
2.929
2.921
2.434
2.426
2.401
2.392
2.242
2.209
2.175
2.086
2.075
2.053
2.000
1.716
1.707
1.681
1.672
1.591
OHC
EtOOC
OH
O
N
Boc
3g
0.88
0.95
2.29
1.06
1.76
0.86
0.89
3.01
10.0
5.0
0.0
ppm (t1)

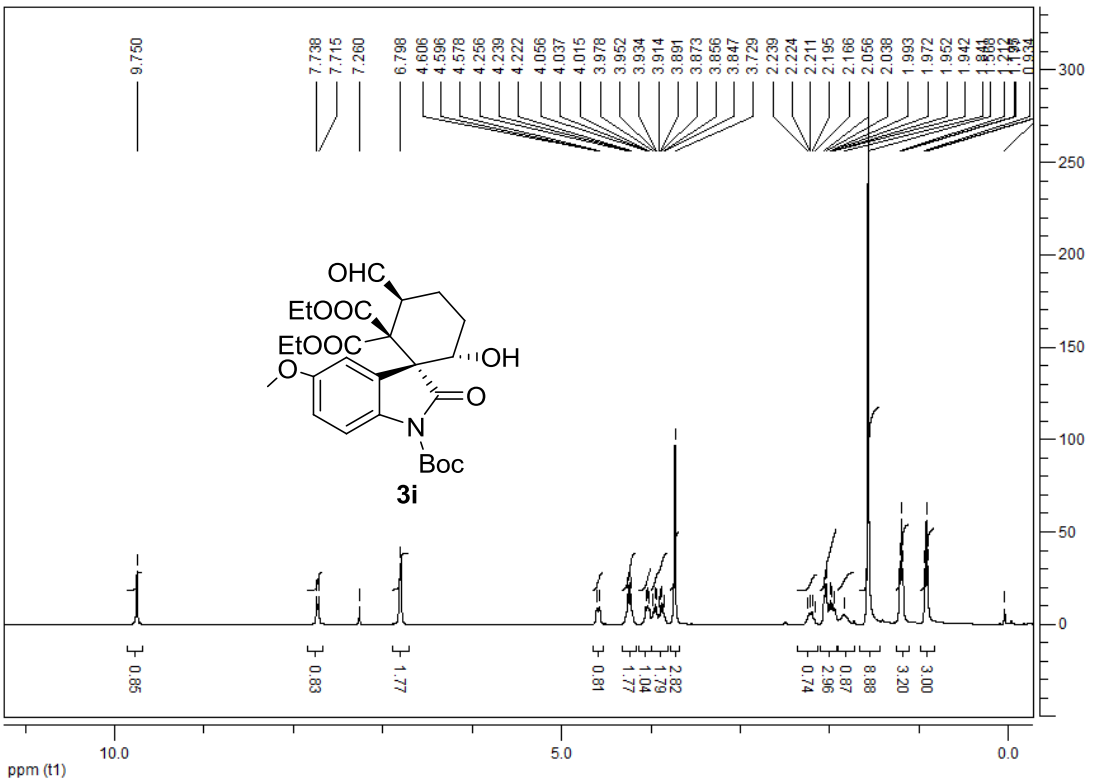

199.34
175.56
170.85
148.90
139.69
123.44
115.14
84.51
68.57
61.27
52.73
46.21
44.66
28.05
17.41
13.66
OHC
EtOOC
OH
O
N
Boc
3g
200
140
80
40
0
f1 (ppm)

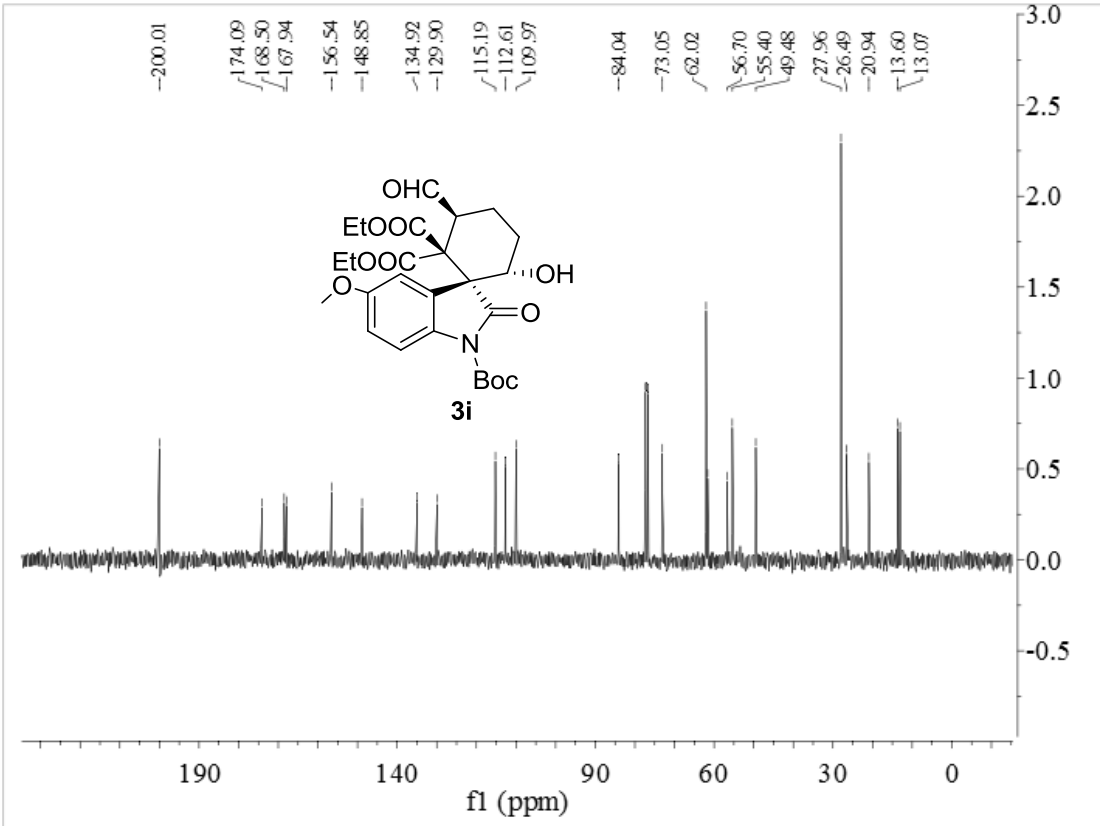
3h


9.749
7.697
7.676
7.260
7.115
7.094
7.005
4.568
4.550
4.272
4.255
4.237
4.220
4.038
4.018
3.998
3.982
3.973
3.956
3.938
3.917
3.897
3.879
3.854
2.304
2.250
2.231
2.204
2.176
2.093
2.064
2.048
1.962
1.939
OHC
EtOOC
EtOOC
OH
O
N
Boc
3h
0.84
0.89
0.96
0.85
0.89
1.85
1.09
1.63
2.83
2.80
2.00
1.80
1.01
9.00
3.26
2.85
10.0
5.0
ppm (t1)

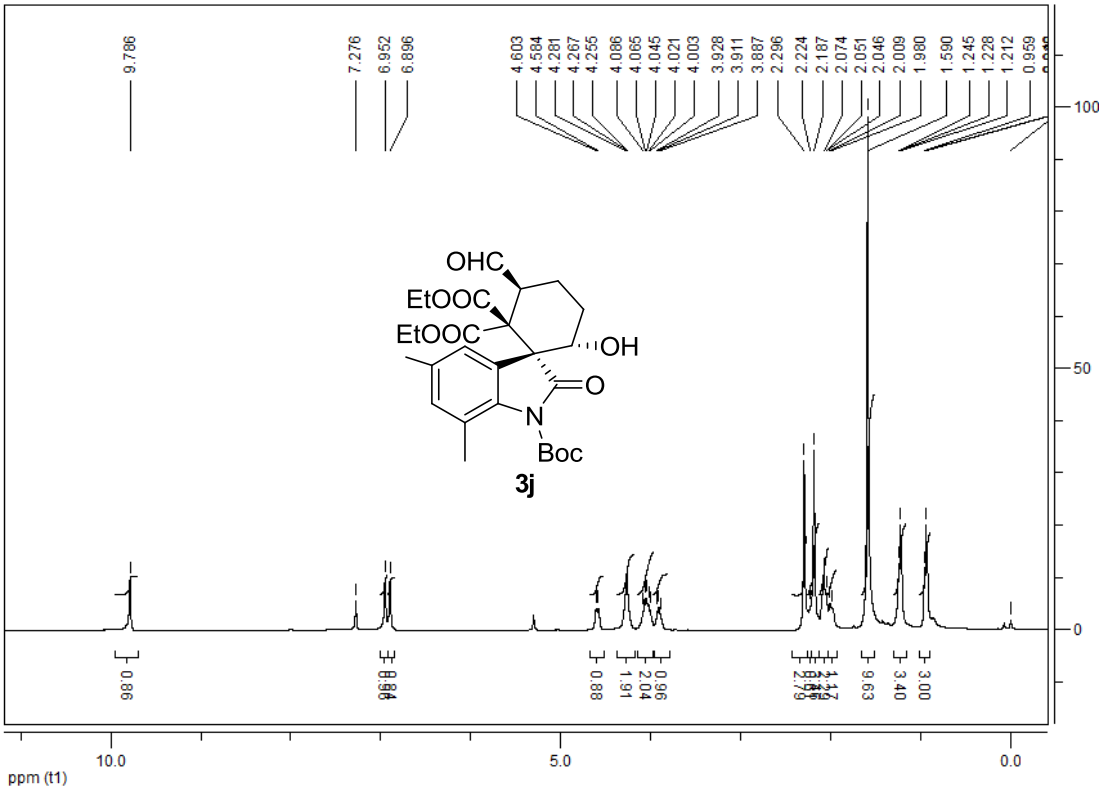

200.247
174.545
168.882
168.356
149.128
139.493
133.961
129.370
128.707
123.742
114.574
84.380
73.368
62.282
62.175
61.761
56.764
49.915
28.252
26.667
21.438
21.336
13.949
13.359
OHC
EtOOC
EtOOC
OH
O
N
Boc
3h
200
150
100
50
0
ppm (t1)

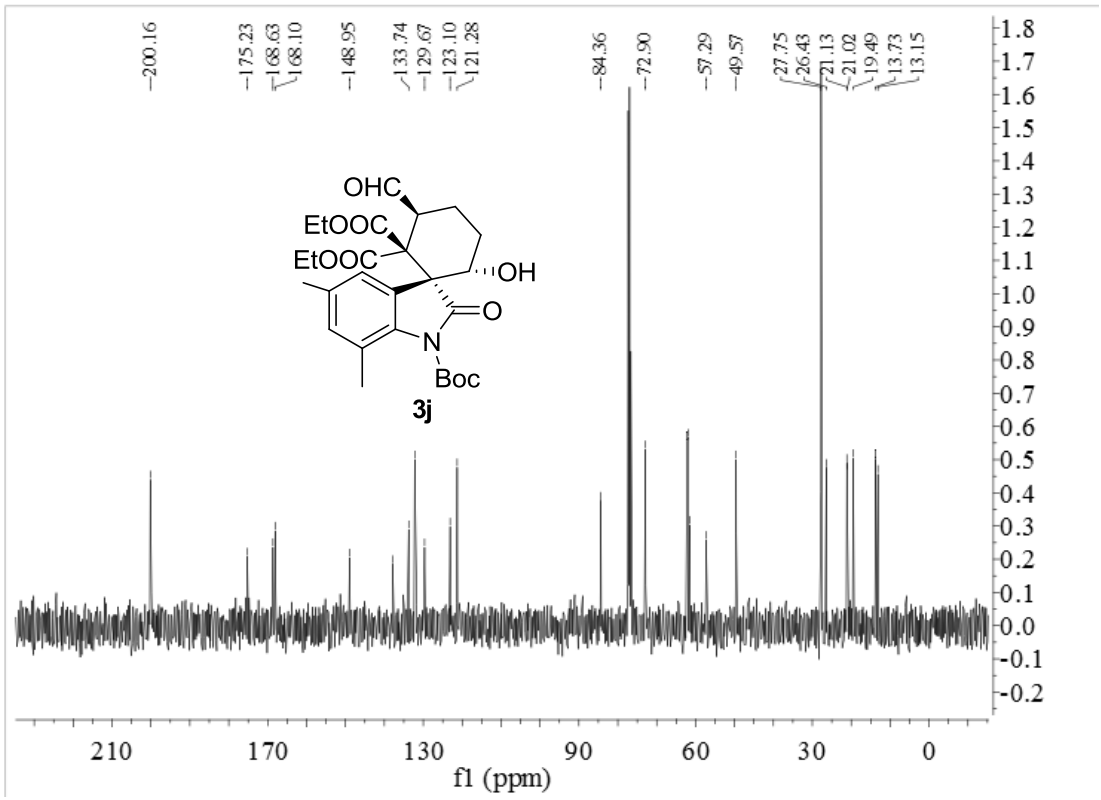
3i


9.750
7.738
7.715
7.260
6.798
4.606
4.596
4.578
4.256
4.239
4.222
4.056
4.037
4.015
3.978
3.952
3.934
3.914
3.891
3.873
3.856
3.847
3.729
2.239
2.224
2.211
2.195
2.166
2.056
2.038
1.993
1.972
1.952
1.942
0.85
0.83
1.77
0.81
1.77
1.04
1.79
2.82
0.74
2.96
0.87
8.88
3.20
3.00
OHC
EtOOC
EtOOC
OH
O
O
N
Boc
3i
ppm (t1)

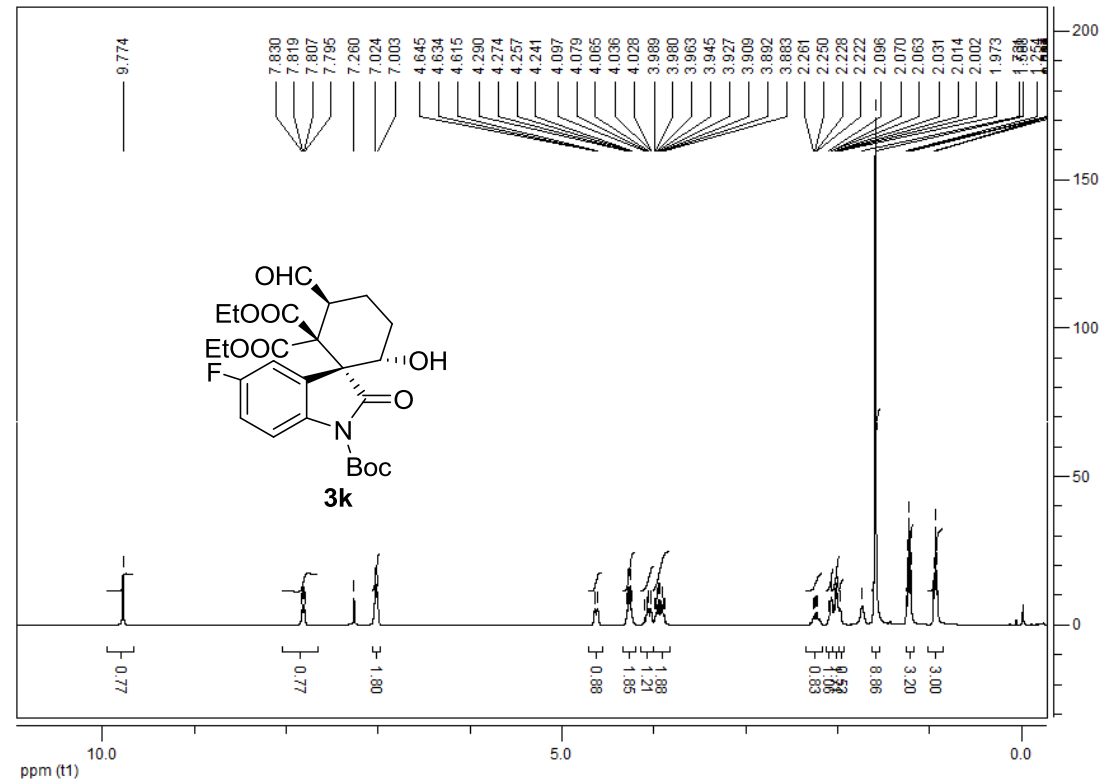

200.01
174.09
168.50
167.94
156.54
148.85
134.92
129.90
115.19
112.61
109.97
84.04
73.05
62.02
56.70
55.40
49.48
27.96
26.49
20.94
13.60
13.07
OHC
EtOOC
EtOOC
OH
O
O
N
Boc
3i
f1 (ppm)

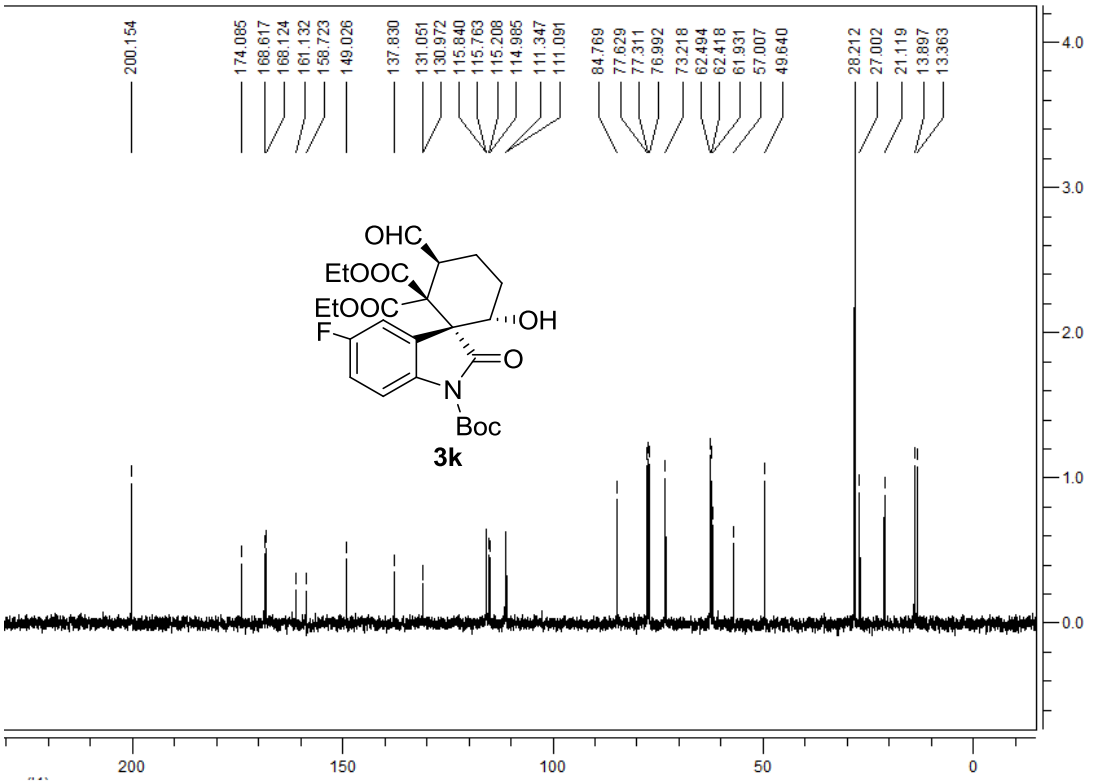
3j


9.786
7.276
6.952
6.896
4.603
4.584
4.281
4.267
4.255
4.086
4.065
4.045
4.021
4.003
3.928
3.911
3.887
2.296
2.224
2.187
2.074
2.051
2.046
2.009
1.980
1.590
1.245
1.228
1.212
0.959
OHC
EtOOC
EtOOC
OH
O
N
Boc
3j
100
50
0
0.86
0.88
1.91
2.04
0.96
9.63
3.40
3.00
10.0
5.0
0.0
ppm (t1)

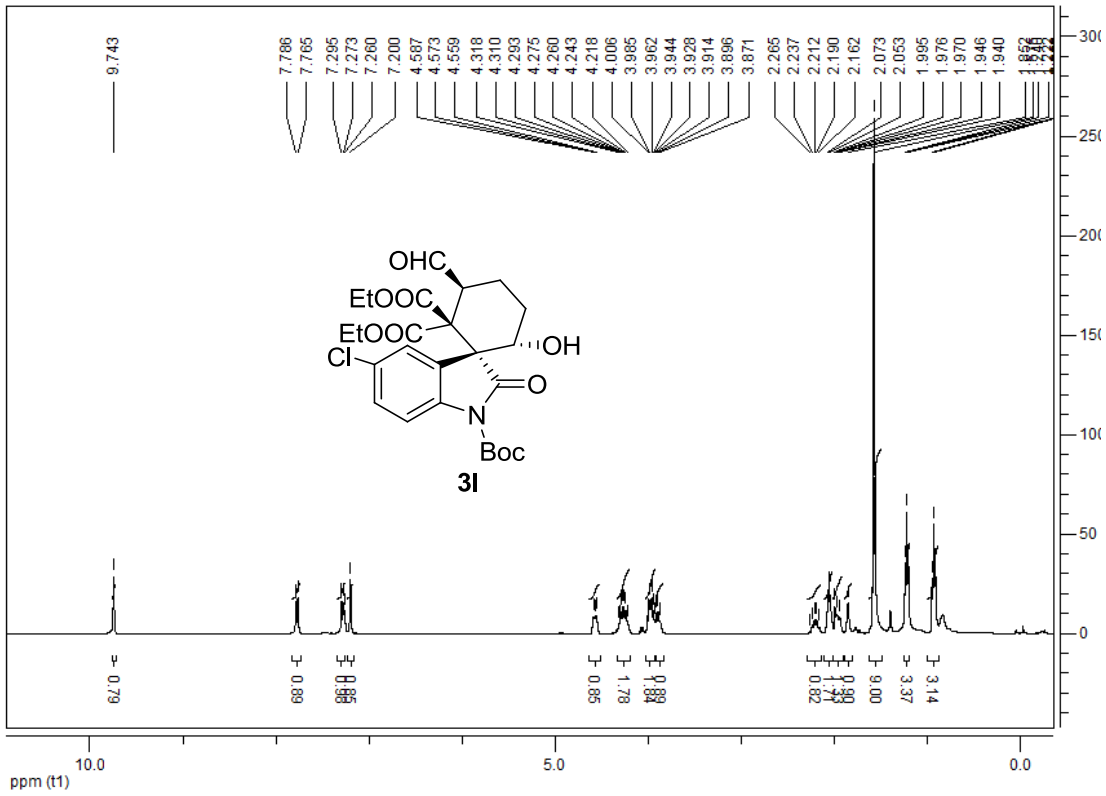

200.16
175.23
168.63
168.10
148.95
133.74
129.67
123.10
121.28
84.36
72.90
57.29
49.57
27.75
26.43
21.13
21.02
19.49
13.73
13.15
OHC
EtOOC
EtOOC
OH
O
N
Boc
3j
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
-0.1
-0.2
210
170
130
90
60
30
0
f1 (ppm)

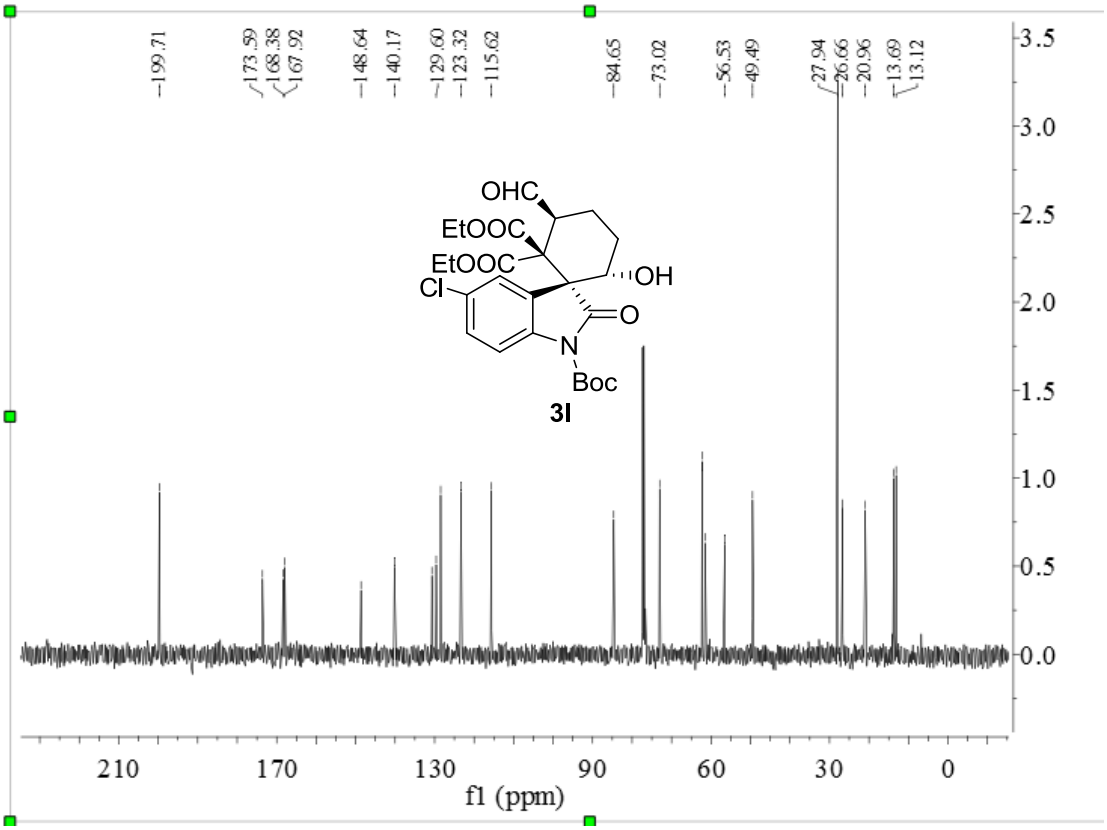
3k


9.774
7.830
7.819
7.807
7.795
7.260
7.024
7.003
4.645
4.634
4.615
4.290
4.274
4.257
4.241
4.097
4.079
4.065
4.036
4.028
3.989
3.980
3.963
3.945
3.927
3.909
3.892
3.883
2.261
2.250
2.228
2.222
2.096
2.070
2.063
2.031
2.014
2.002
1.973
OHC
EtOOC
EtOOC
F
OH
O
N
Boc
3k
0.77
0.77
1.80
0.88
1.85
1.27
1.88
0.83
8.86
3.20
3.00
10.0
5.0
0.0
ppm (t1)

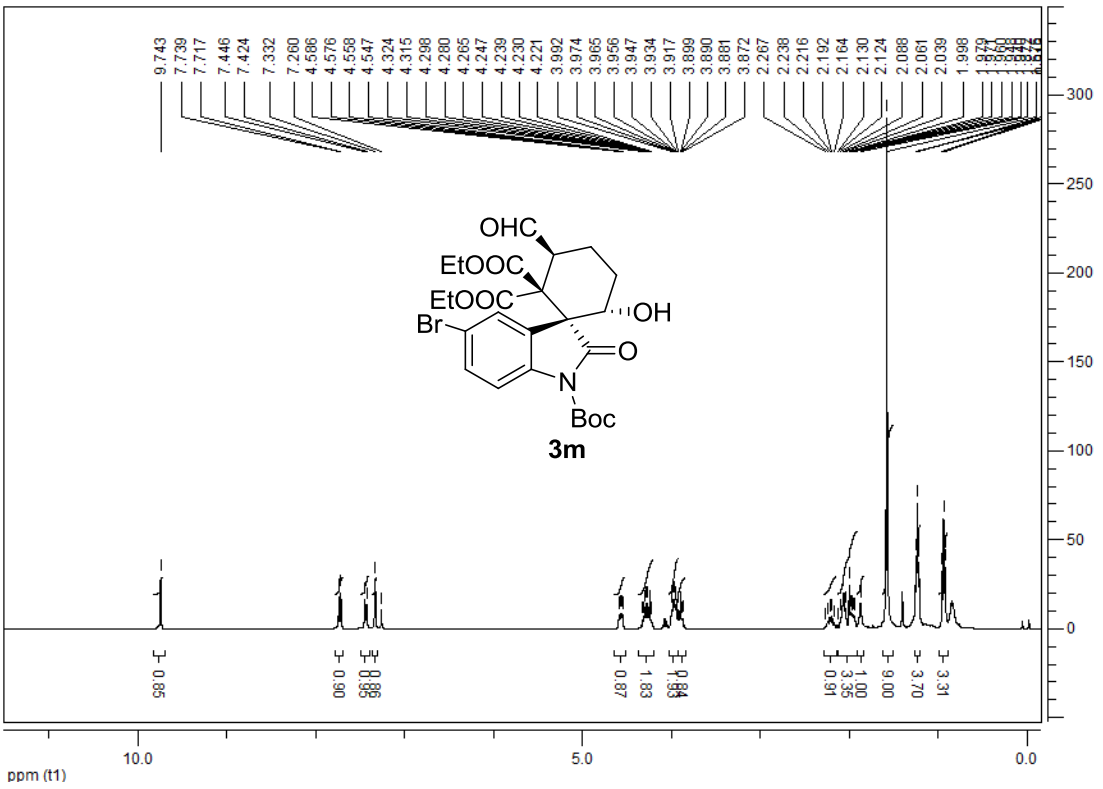

200.154
174.085
168.617
168.124
161.132
158.723
149.026
137.830
131.051
130.972
115.840
115.763
115.208
114.985
111.347
111.091
84.769
77.629
77.311
76.992
73.218
62.494
62.418
61.931
57.007
49.640
28.212
27.002
21.119
13.897
13.363
OHC
EtOOC
EtOOC
F
OH
O
N
Boc
3k
200
150
100
50
0

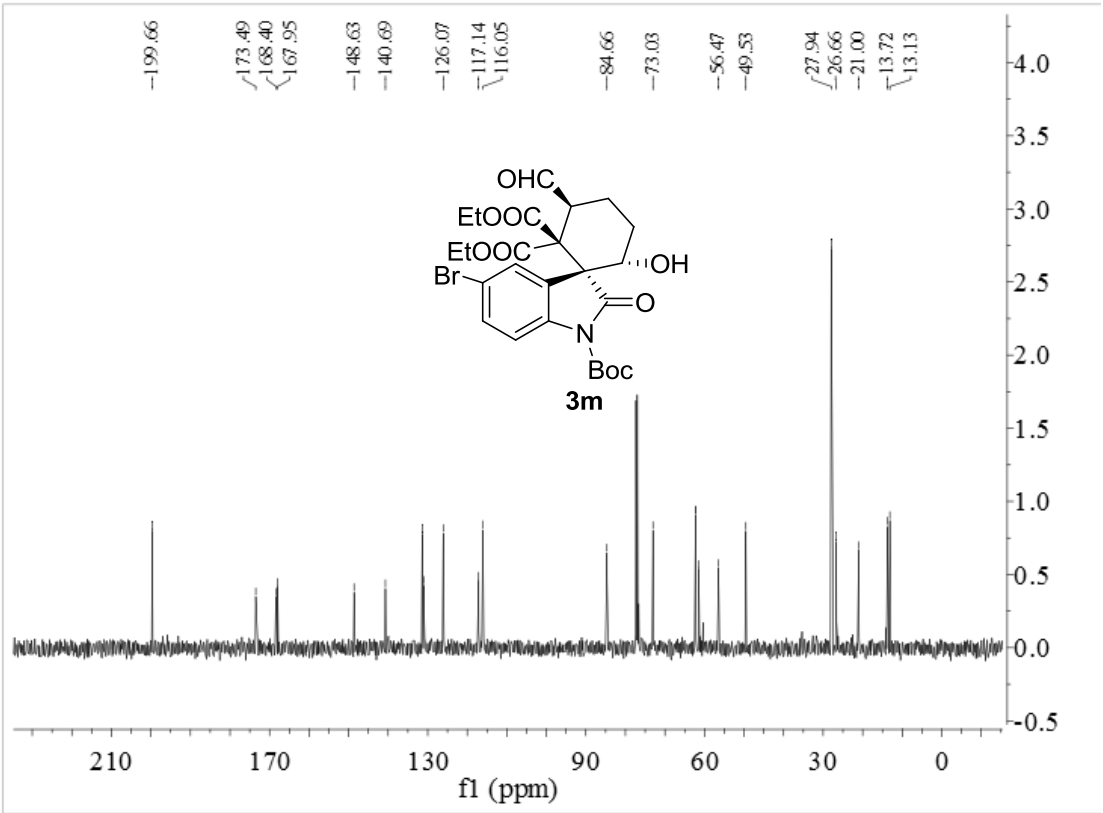
3l


9.743
7.786
7.765
7.295
7.273
7.260
7.200
4.587
4.573
4.559
4.318
4.310
4.293
4.275
4.260
4.243
4.218
4.006
3.985
3.962
3.944
3.928
3.914
3.896
3.871
2.265
2.237
2.212
2.190
2.162
2.073
2.053
1.995
1.976
1.970
1.946
1.940
OHC
EtOOC
EtOOC
Cl
OH
O
N
Boc
3l
0.79
0.89
0.86
1.78
9.00
3.37
3.14
10.0
5.0
0.0
ppm (t1)

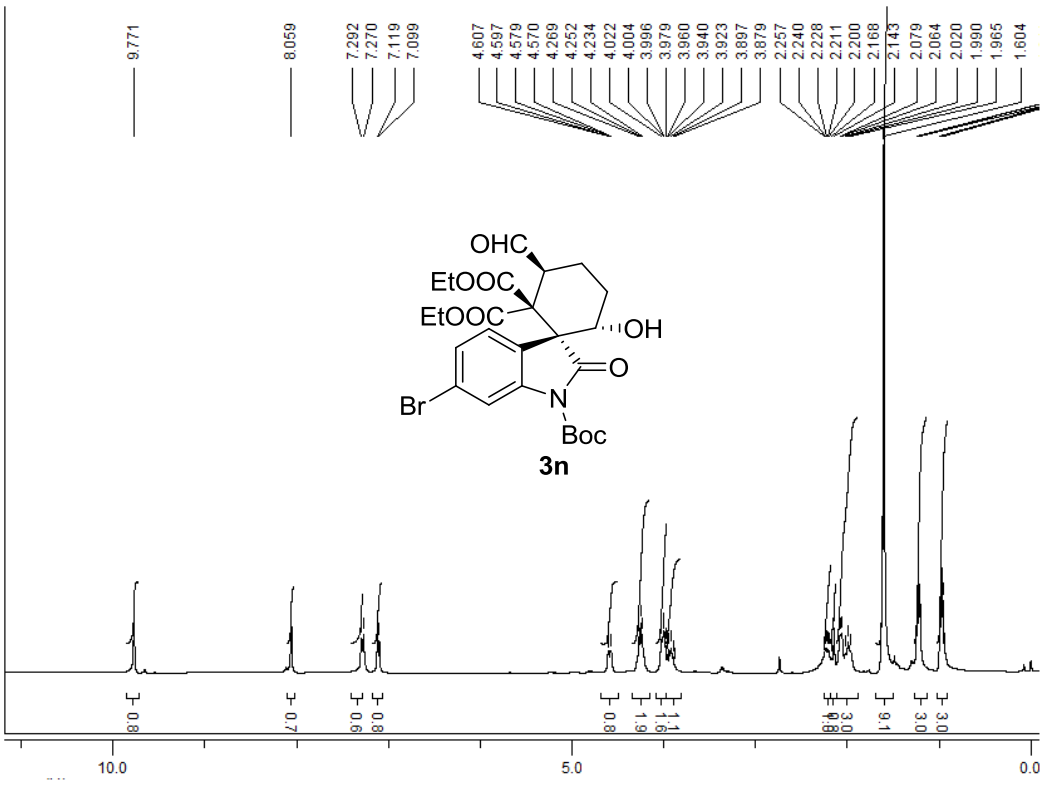

199.71
173.59
168.38
167.92
148.64
140.17
129.60
123.32
115.62
84.65
73.02
56.53
49.49
27.94
26.66
20.96
13.69
13.12
OHC
EtOOC
EtOOC
Cl
OH
O
N
Boc
3l
210
170
130
90
60
30
0
f1 (ppm)

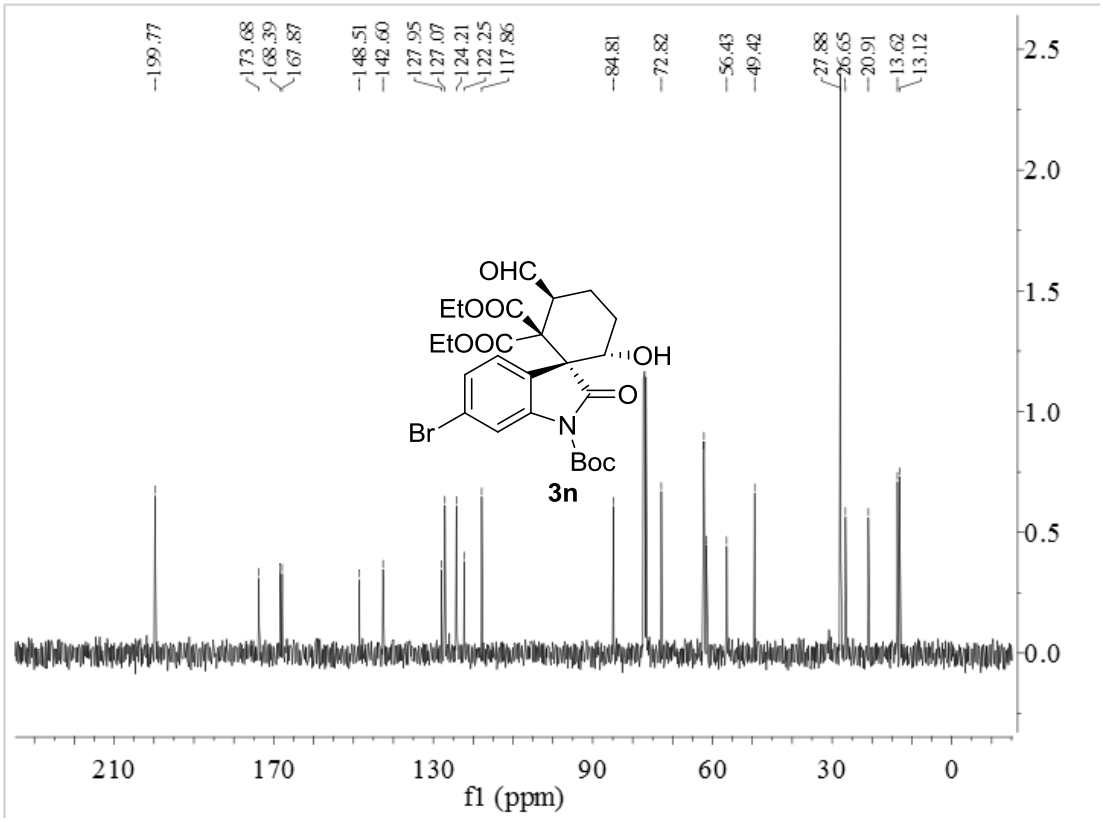
3m


OHC
EtOOC
EtOOC
OH
Br
O
N
Boc
3m
ppm (t1)

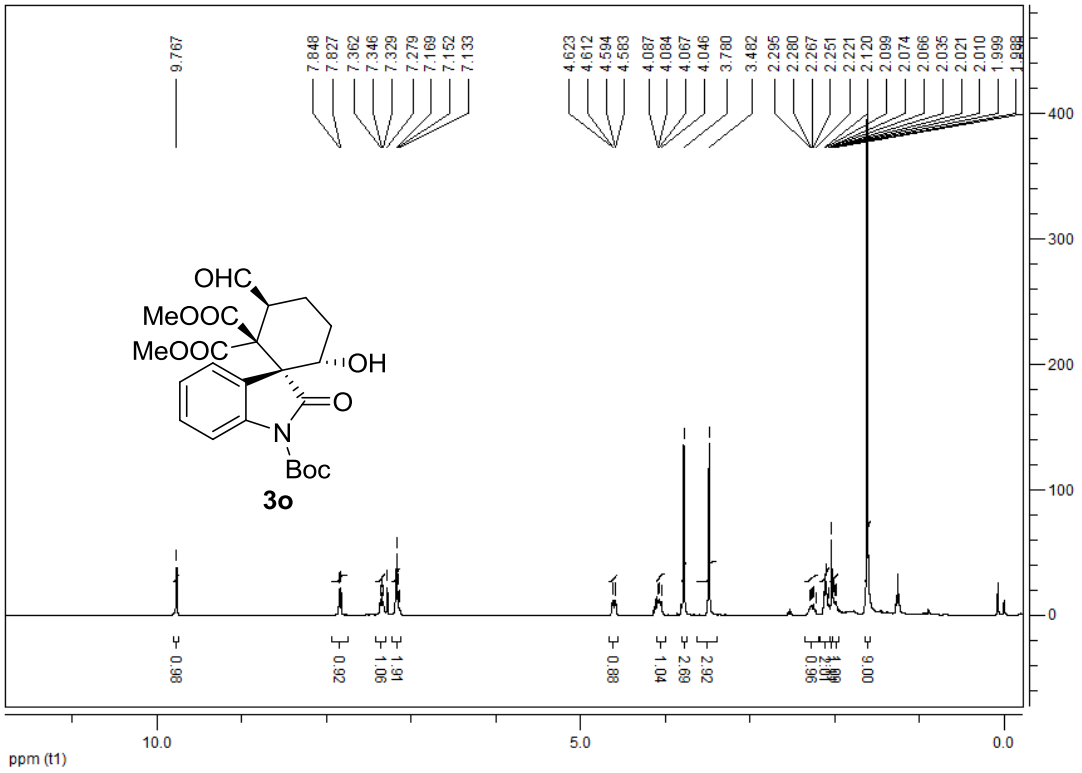

OHC
EtOOC
EtOOC
OH
Br
O
N
Boc
3m
f1 (ppm)

3n





3o


9.767
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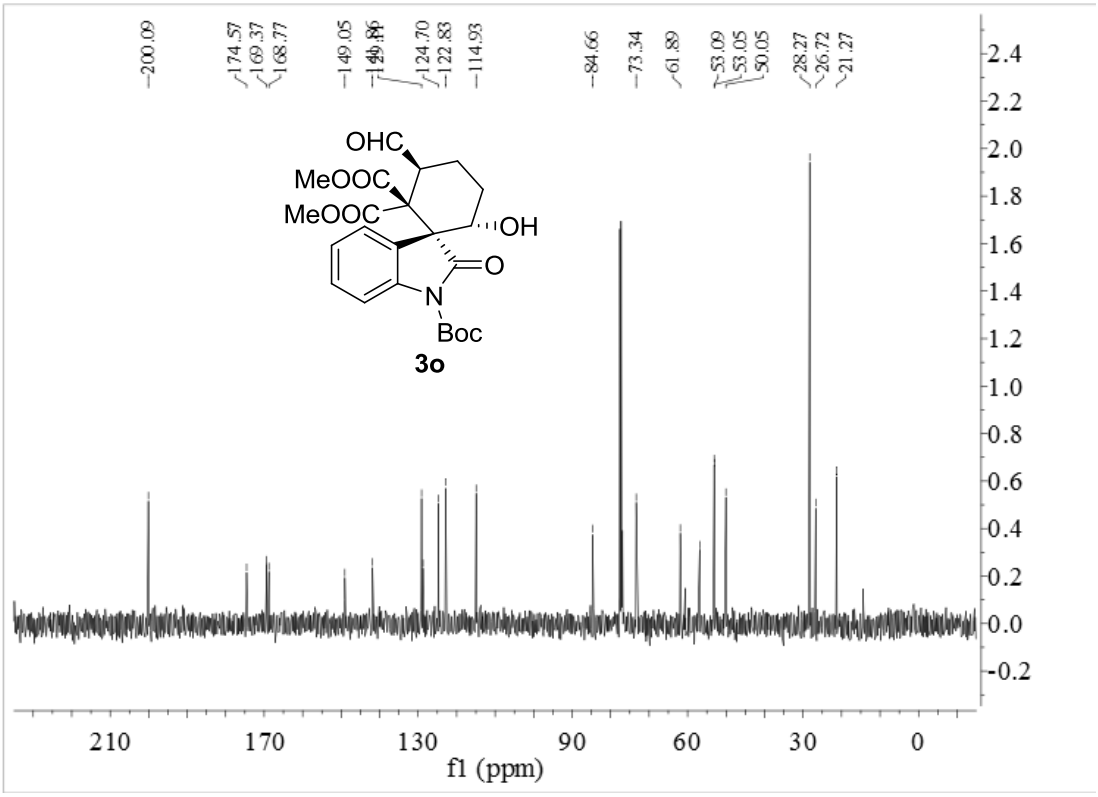
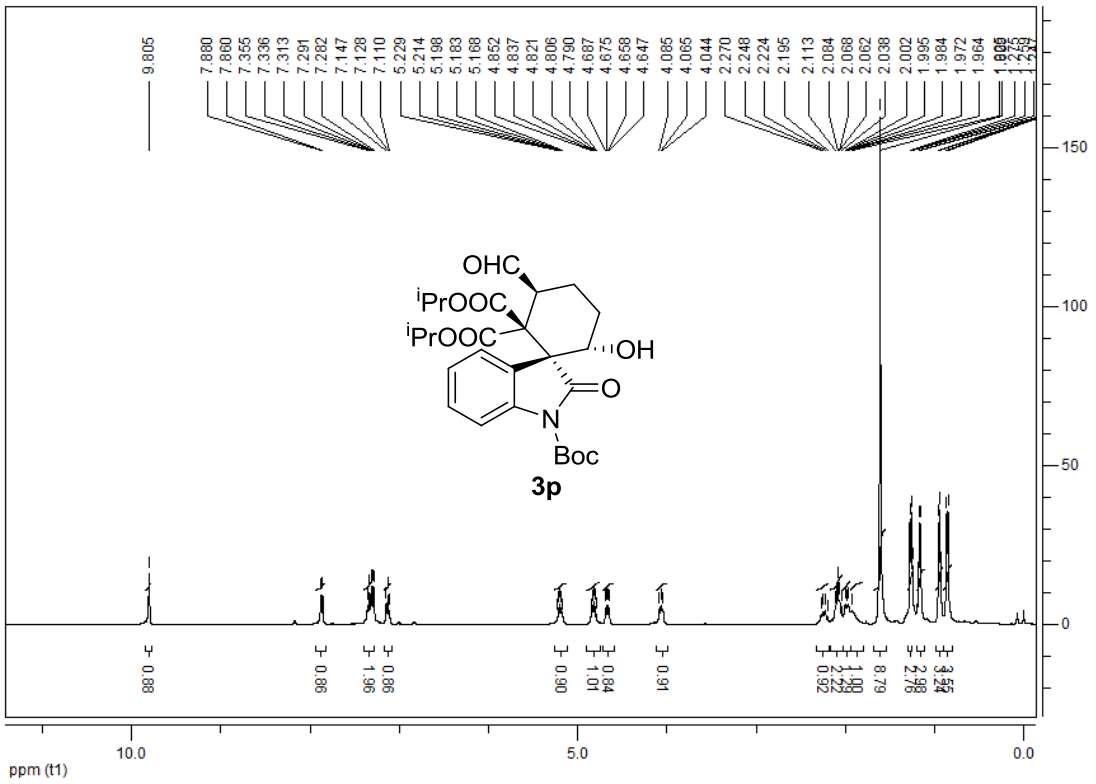
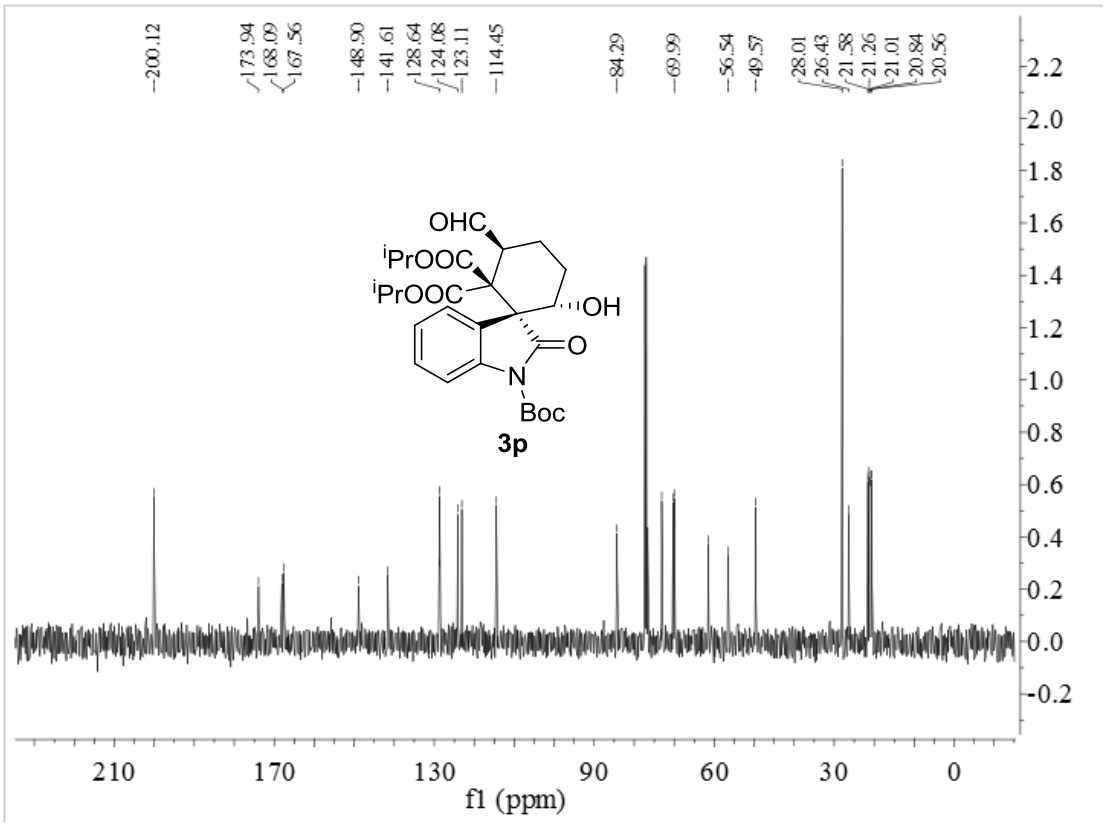
7.827
7.362
7.346
7.329
7.279
7.169
7.152
7.133
4.623
4.612
4.594
4.583
4.087
4.084
4.067
4.046
3.780
3.482
2.295
2.280
2.267
2.251
2.221
2.120
2.099
2.074
2.066
2.035
2.021
2.010
1.999
OHC
MeOOC
MeOOC
OH
O
N
Boc
3o
0.98
0.92
1.06
1.91
0.88
1.04
2.69
2.92
0.96
9.00
10.0
5.0
0.0
ppm (t1)

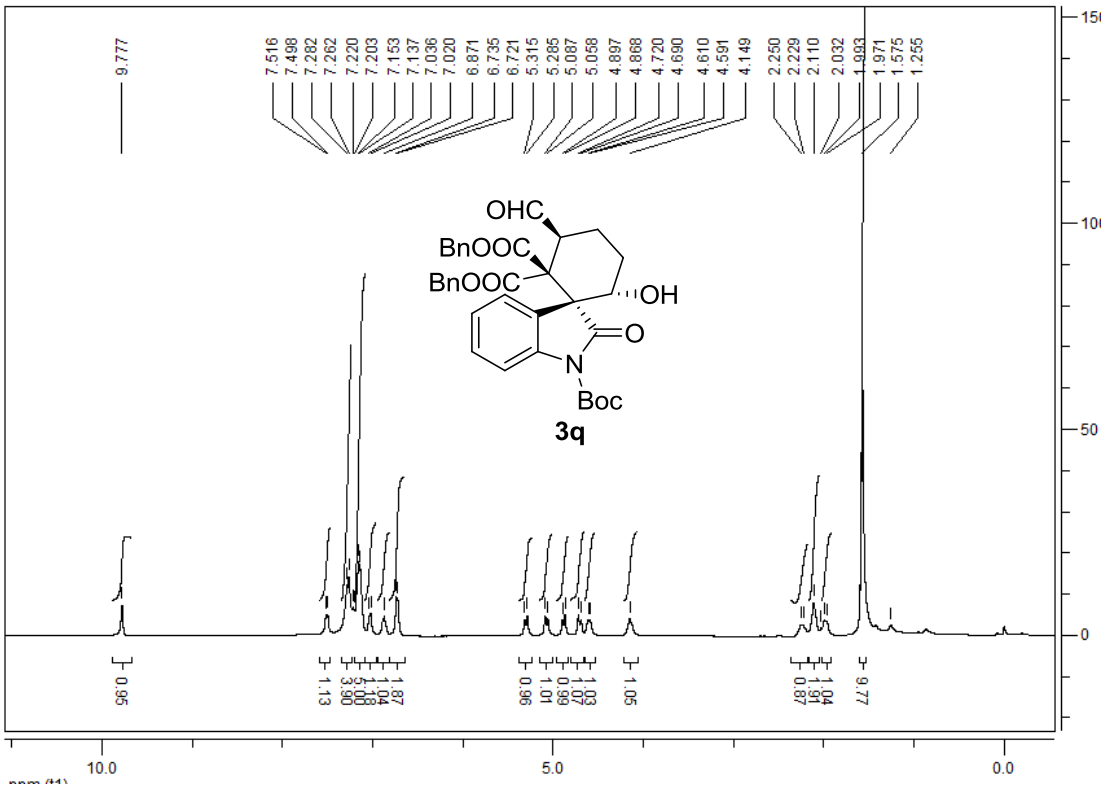

200.09
174.57
169.37
168.77
149.05
124.70
122.83
114.93
84.66
73.34
61.89
53.09
53.05
50.05
28.27
26.72
21.27
OHC
MeOOC
MeOOC
OH
O
N
Boc
3o
210
170
130
90
60
30
0
f1 (ppm)

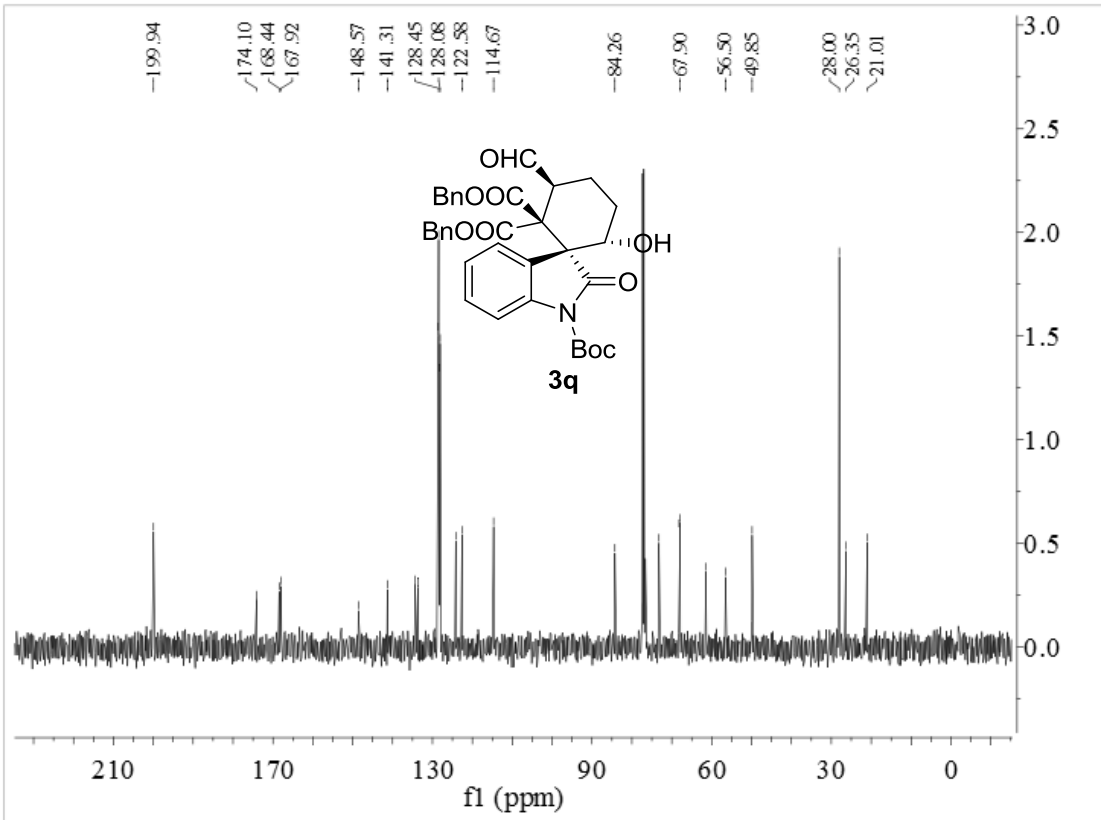
3p


9.805
7.880
7.860
7.355
7.336
7.313
7.291
7.282
7.147
7.128
7.110
5.229
5.214
5.198
5.183
5.168
4.852
4.837
4.821
4.806
4.790
4.687
4.675
4.658
4.647
4.085
4.065
4.044
2.270
2.248
2.224
2.195
2.113
2.084
2.068
2.062
2.038
2.002
1.995
1.984
1.972
1.964
OHC
iPrOOC
iPrOOC
OH
O
N
Boc
3p
ppm (t1)
10.0
5.0
0.0

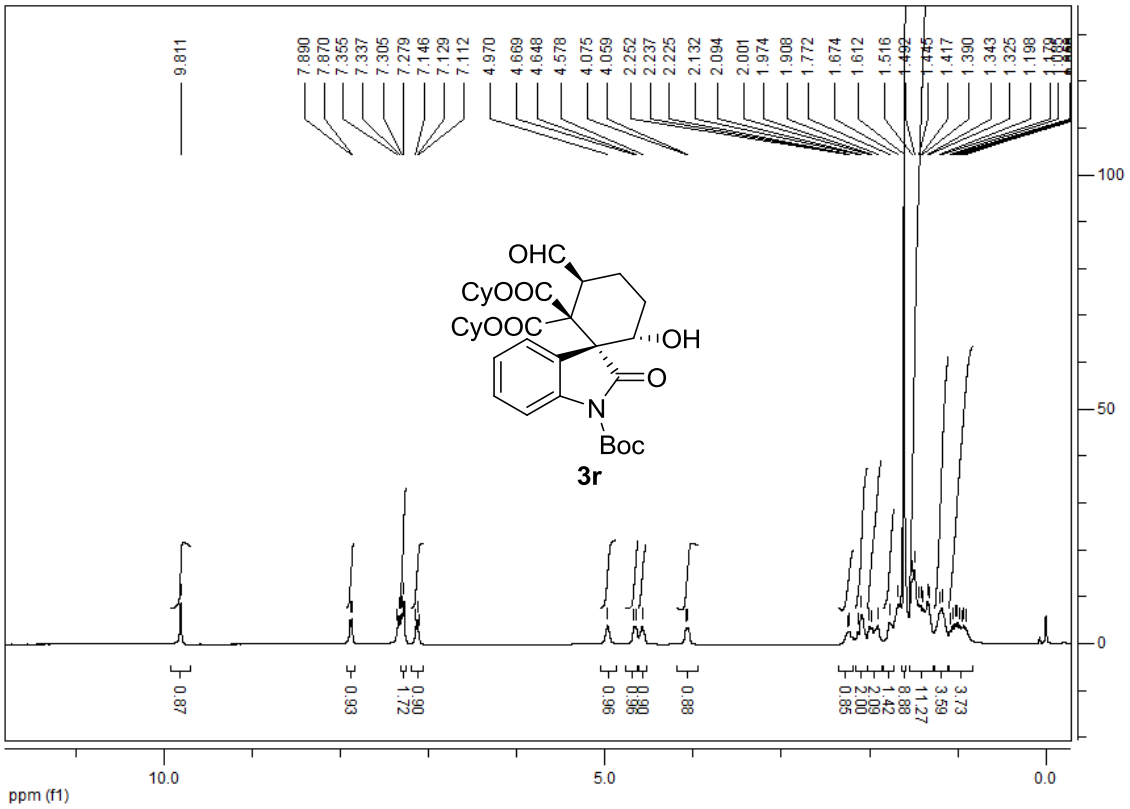

200.12
173.94
168.09
167.56
148.90
141.61
128.64
124.08
123.11
114.45
84.29
69.99
56.54
49.57
28.01
26.43
21.58
21.26
21.01
20.84
20.56
OHC
iPrOOC
iPrOOC
OH
O
N
Boc
3p
f1 (ppm)
210
170
130
90
60
30
0

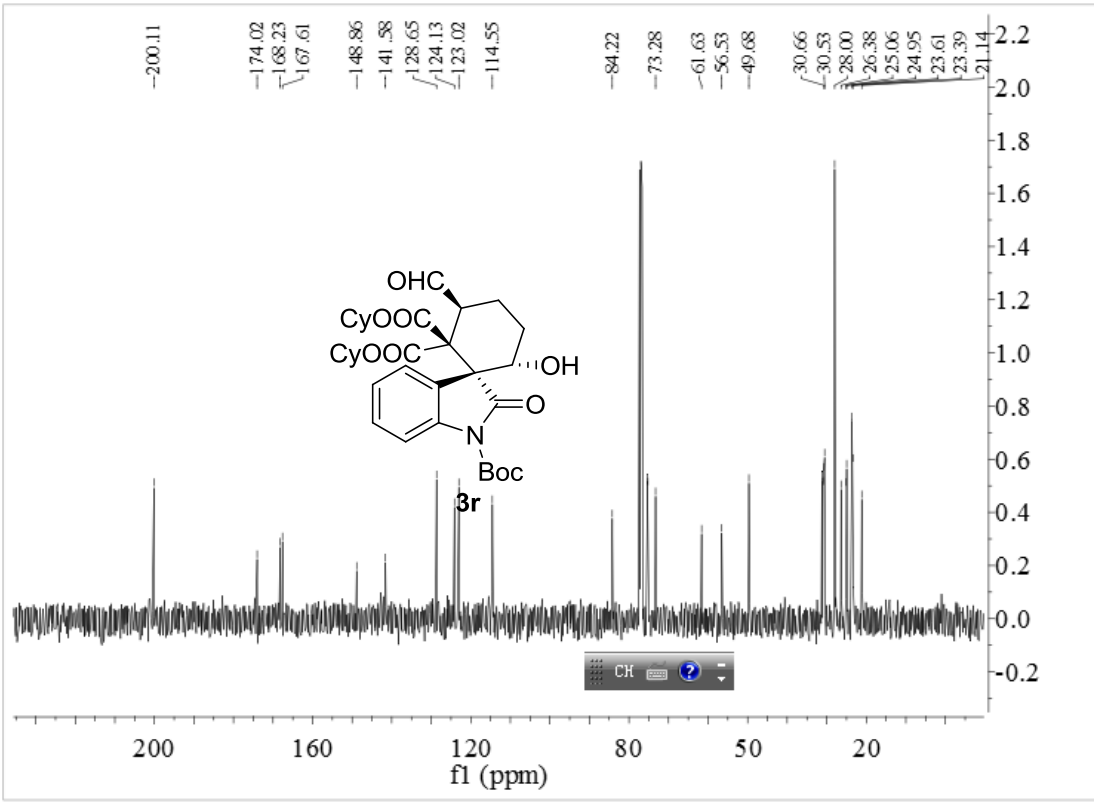
3q



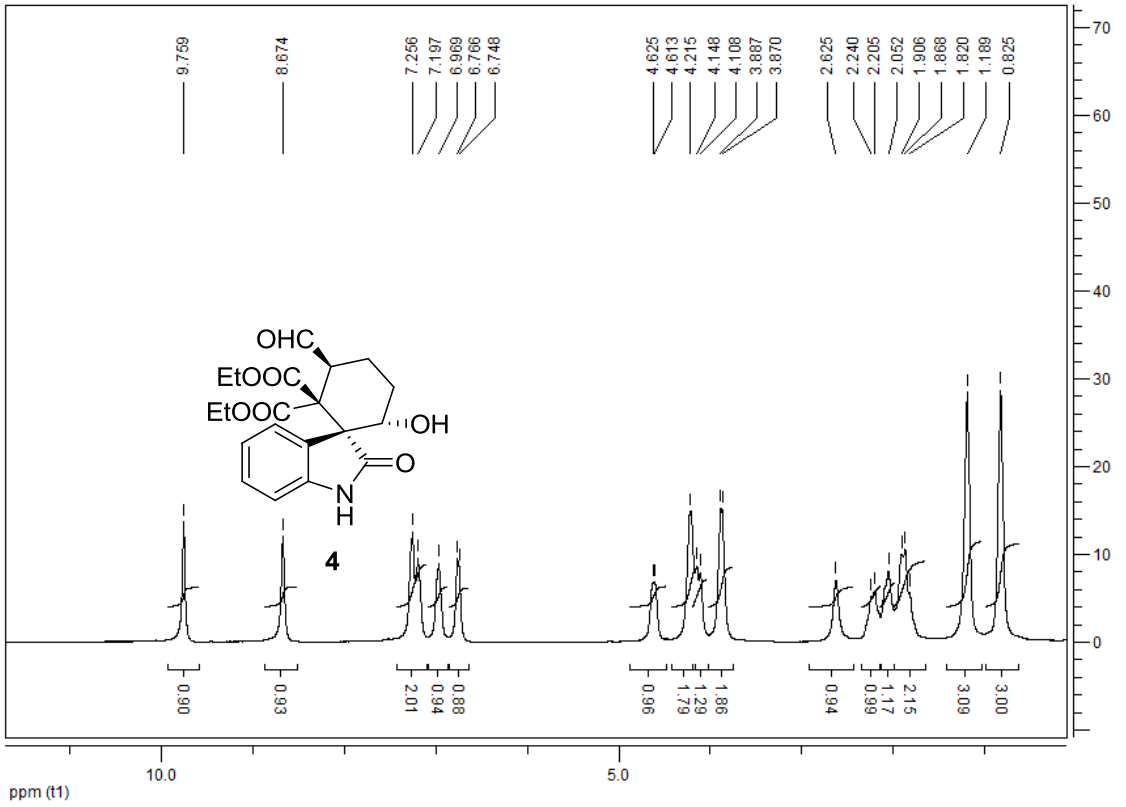


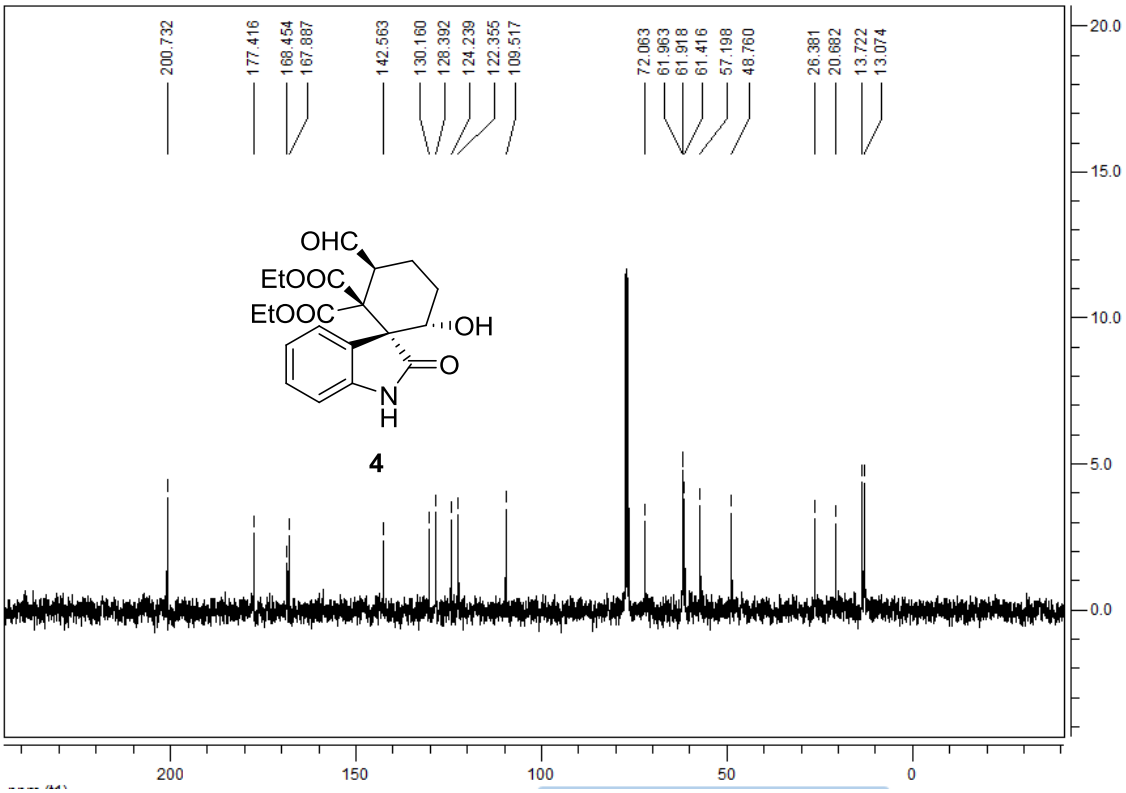
3r



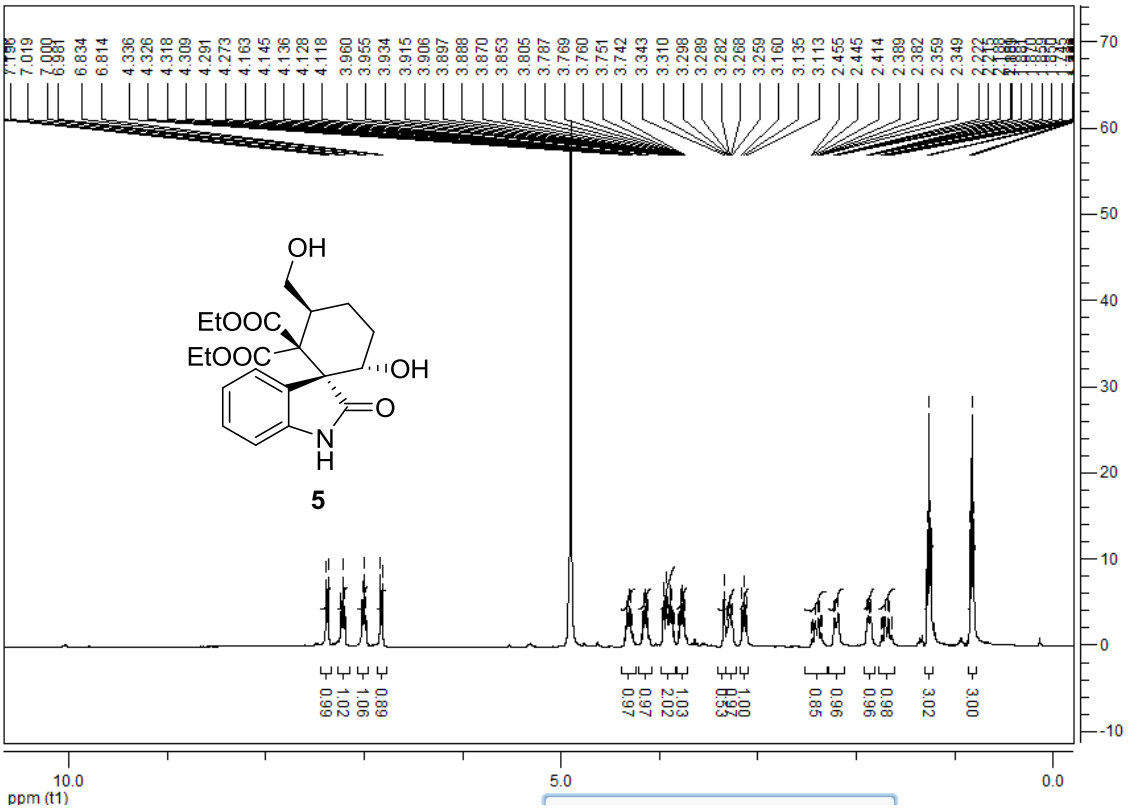


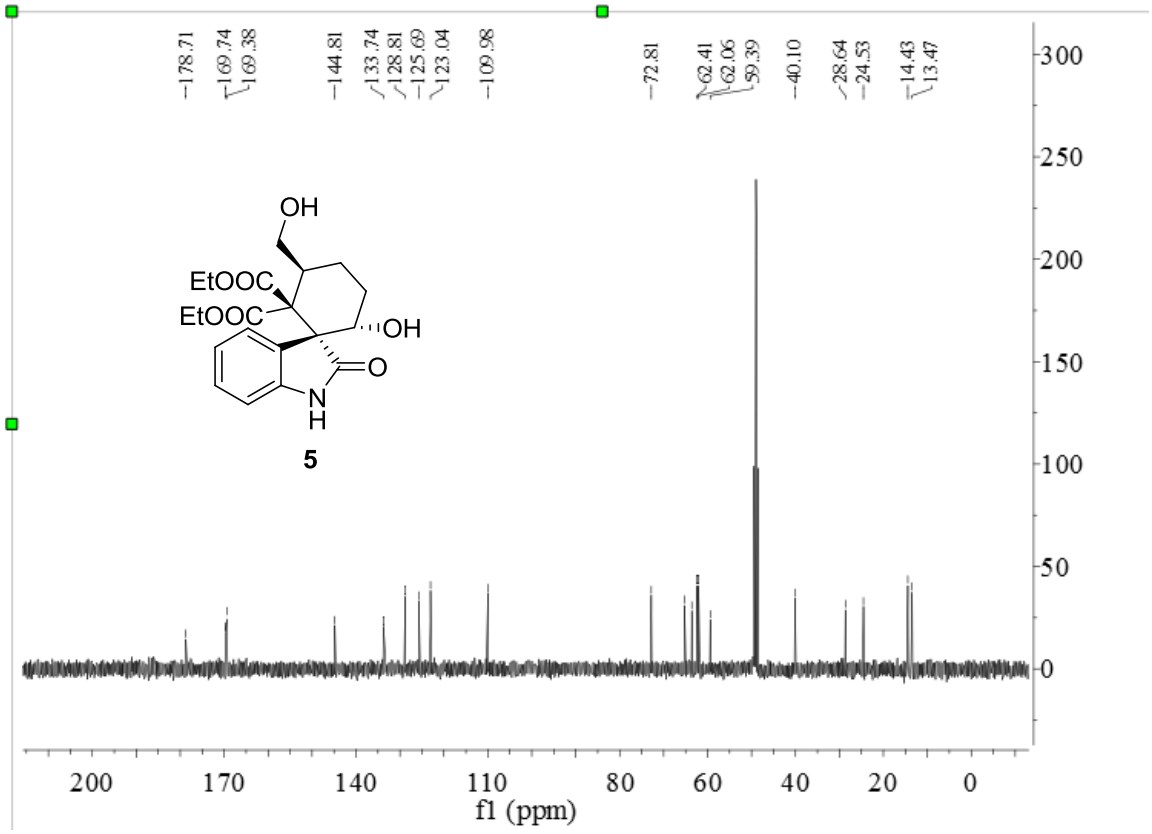
4


9.759
8.674
7.256
7.197
6.969
6.766
6.748
4.625
4.613
4.215
4.148
4.108
3.887
3.870
2.625
2.240
2.205
2.052
1.906
1.868
1.820
1.189
0.825
OHC
EtOOC
EtOOC
OH
O
N
H
4
0.90
0.93
2.01
0.94
0.88
0.96
1.79
1.29
1.86
0.94
0.99
1.17
2.15
3.09
3.00
10.0
5.0
ppm (t1)


200.732
177.416
168.454
167.887
142.563
130.160
128.392
124.239
122.355
109.517
72.063
61.963
61.918
61.416
57.198
48.760
26.381
20.682
13.722
13.074
OHC
EtOOC
EtOOC
OH
O
N
H
4
200
150
100
50
0

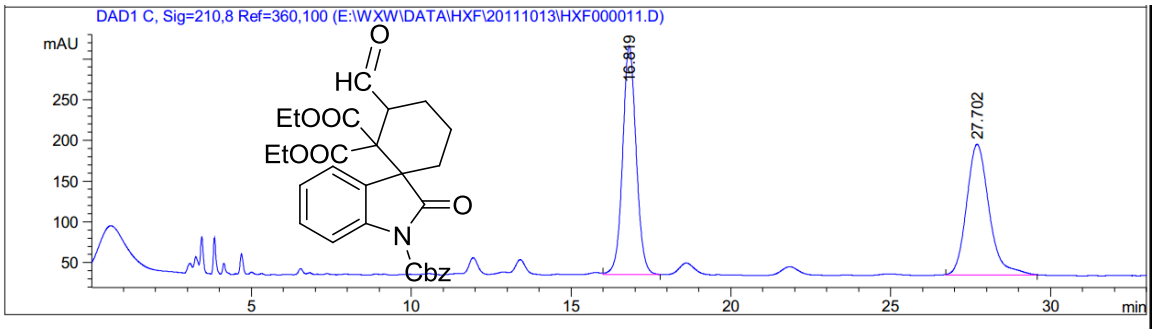
5



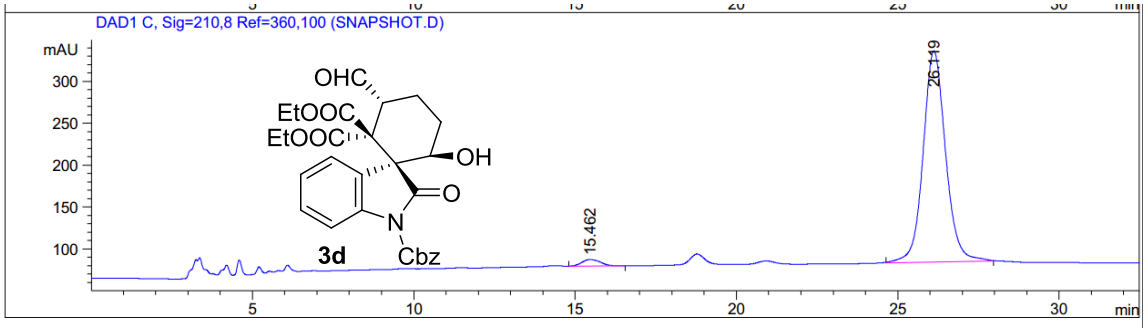


G: HPLC Analysis

3d

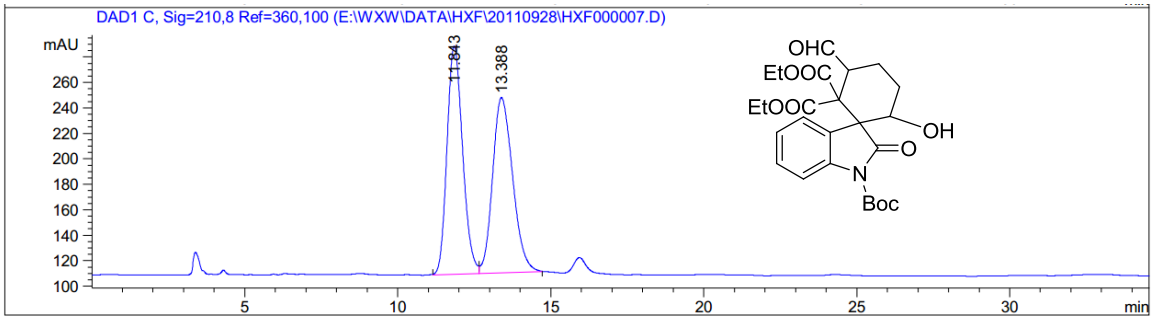


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.819	VB	0.4512	8263.34082	280.94308	51.1886
2	27.702	BB	0.7563	7879.58643	160.63753	48.8114

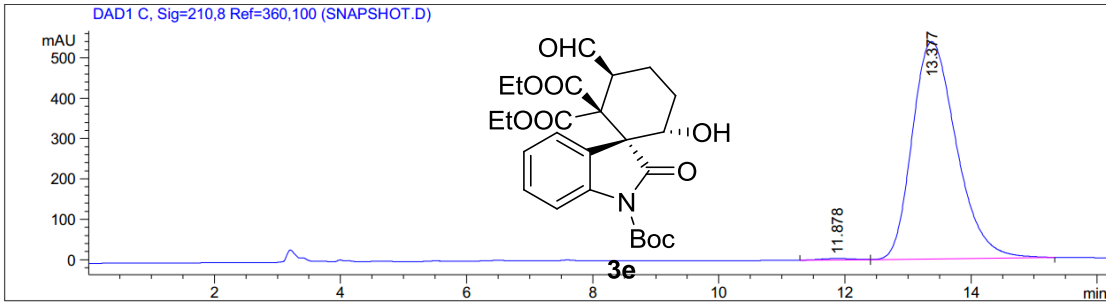


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.462	BB	0.5713	307.69272	7.81595	2.4614
2	26.119	BB	0.7388	1.21929e4	251.87439	97.5386

3e



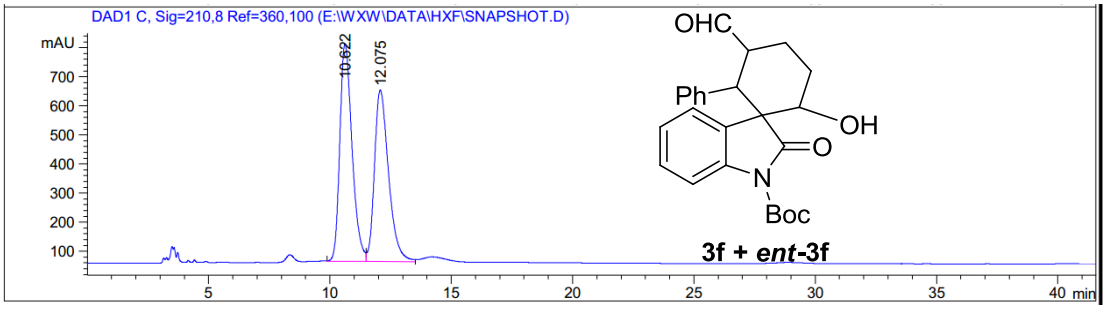
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.843	BV	0.5518	6347.70068	178.98714	50.2112
2	13.388	VB	0.7211	6294.29102	137.74464	49.7888



3e

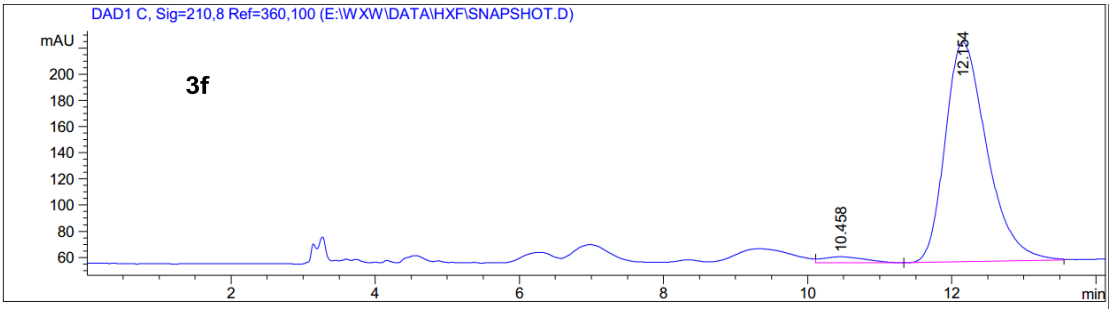
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.878	BV	0.5092	120.35364	3.57120	0.4574
2	13.377	VB	0.7559	2.61926e4	538.12329	99.5426

3f

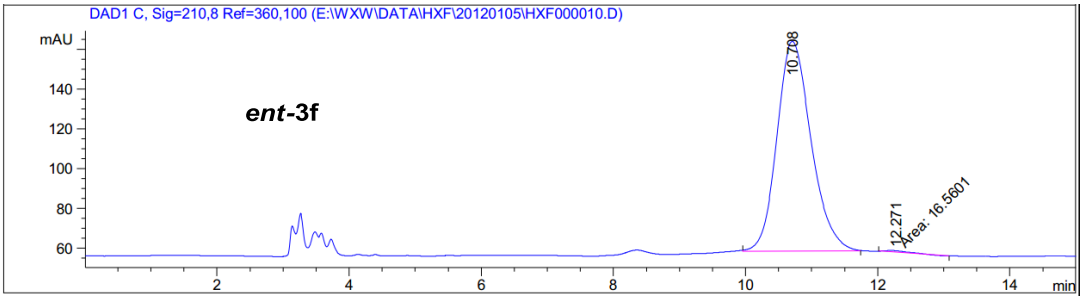


3f + *ent*-3f

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.622	BV	0.5387	2.61622e4	746.88885	52.2609
2	12.075	VB	0.6191	2.38986e4	589.39148	47.7391

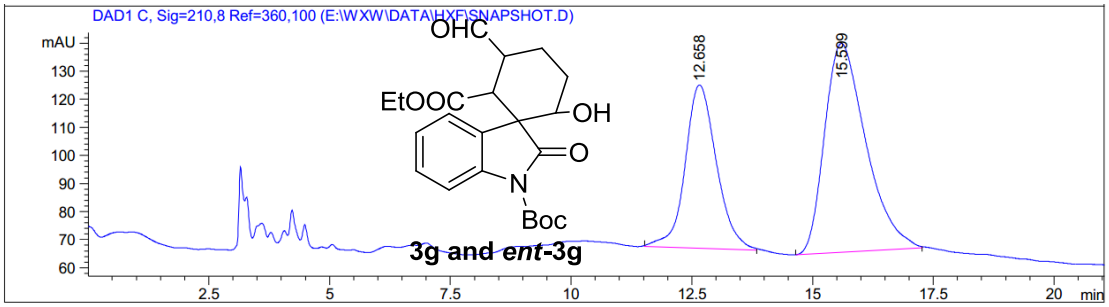


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.458	VV	0.5472	192.17303	4.65919	2.7744
2	12.154	VB	0.6114	6734.51367	168.11377	97.2256

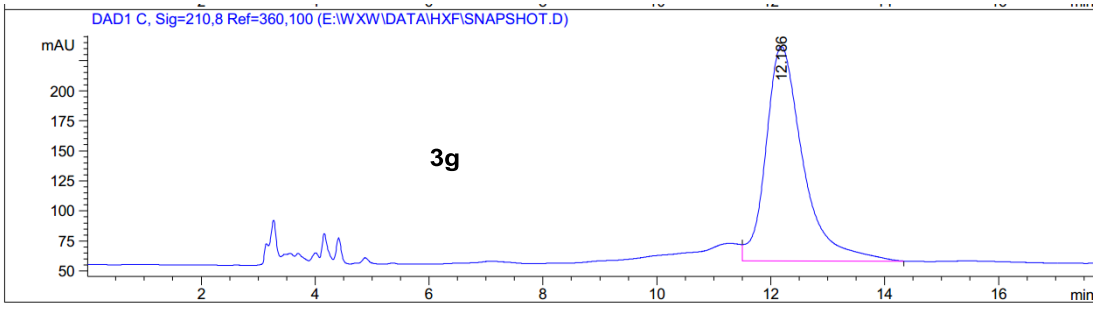


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.708	BB	0.5528	3790.00781	105.59081	99.5650
2	12.271	MM	0.3978	16.56010	6.93757e-1	0.4350

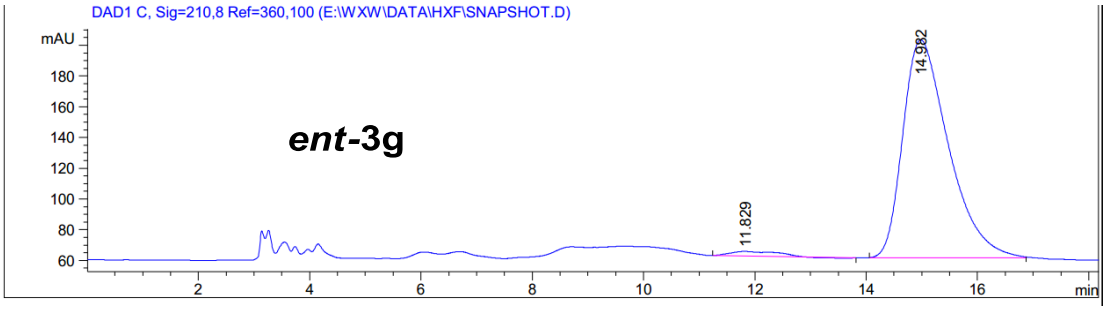
3g



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.658	BB	0.6927	2627.01001	58.18851	37.2520
2	15.599	BB	0.9199	4424.98584	74.39378	62.7480

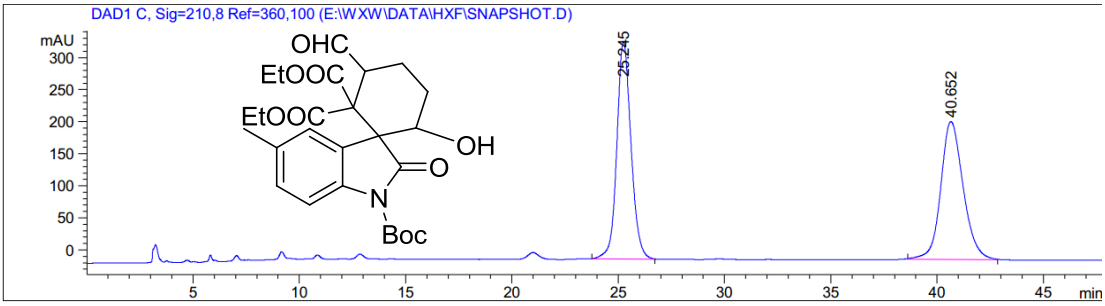


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.186	VB	0.6757	8066.46826	178.33591	100.0000

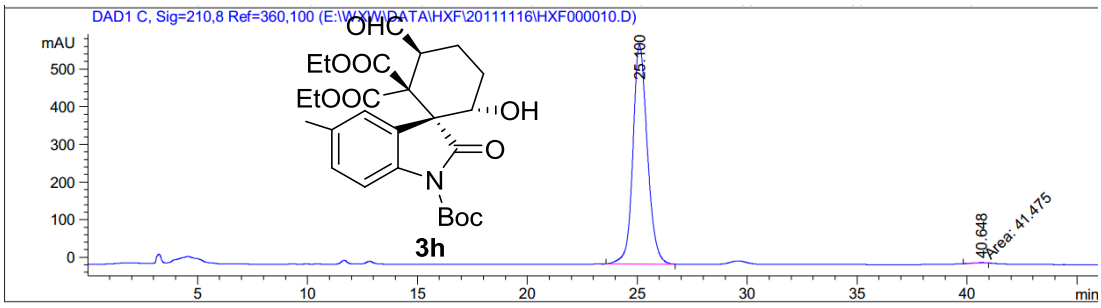


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.829	BB	0.6971	177.92854	3.05675	2.1553
2	14.982	BB	0.8607	8077.53955	141.78291	97.8447

3h

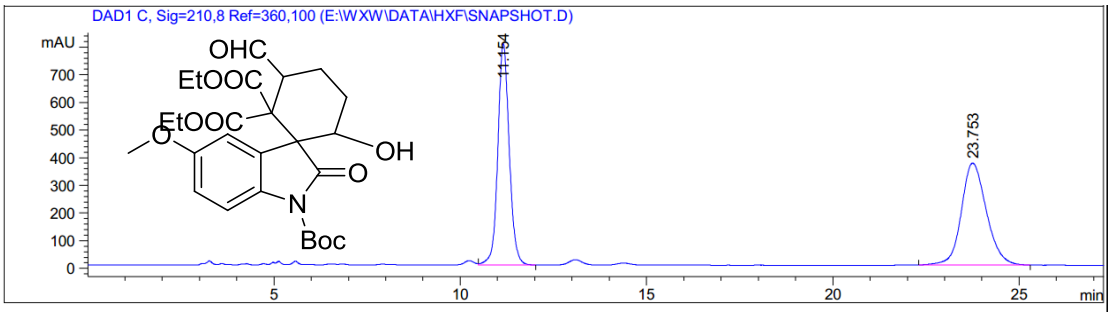


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.245	BB	0.7076	1.57442e4	339.14178	50.0612
2	40.652	BB	1.1193	1.57056e4	214.72945	49.9388

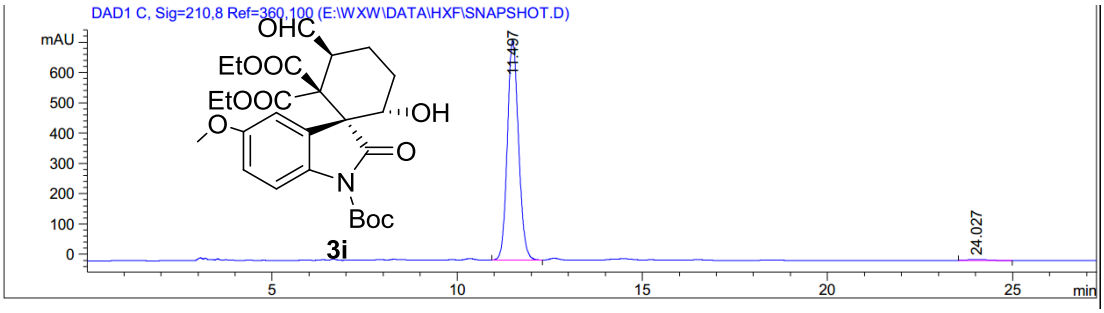


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.100	BB	0.6989	2.66019e4	582.35895	99.8443
2	40.648	MM	0.5252	41.47498	1.31624	0.1557

3i

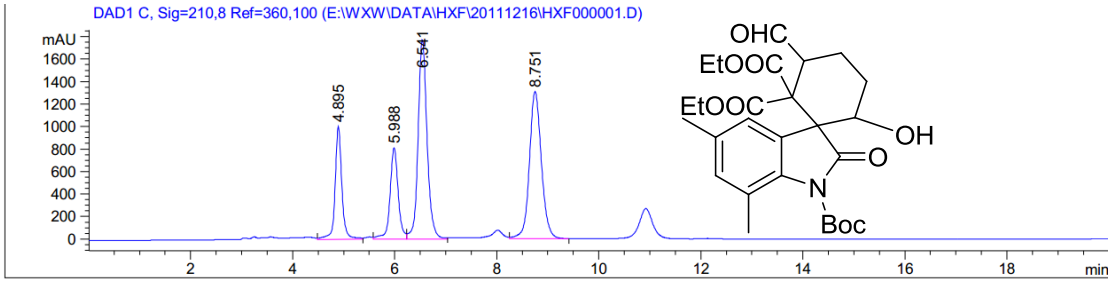


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.154	VB	0.3265	1.70449e4	800.29761	49.6351
2	23.753	BB	0.7164	1.72955e4	369.27396	50.3649

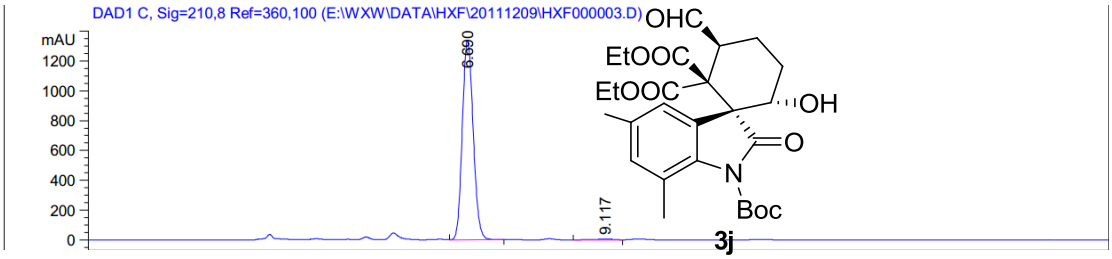


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.497	BB	0.3281	1.52769e4	724.29523	99.2223
2	24.027	BB	0.5109	119.74255	2.96685	0.7777

3j



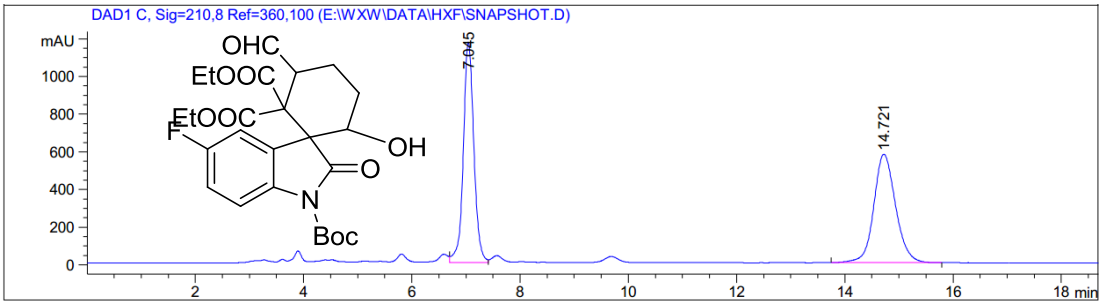
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.895	VV	0.1378	9283.92969	1005.08075	15.0949
2	5.988	VV	0.1681	9079.99707	814.29578	14.7633
3	6.541	VV	0.1872	2.17490e4	1772.05310	35.3620
4	8.751	VB	0.2490	2.13909e4	1306.84595	34.7798



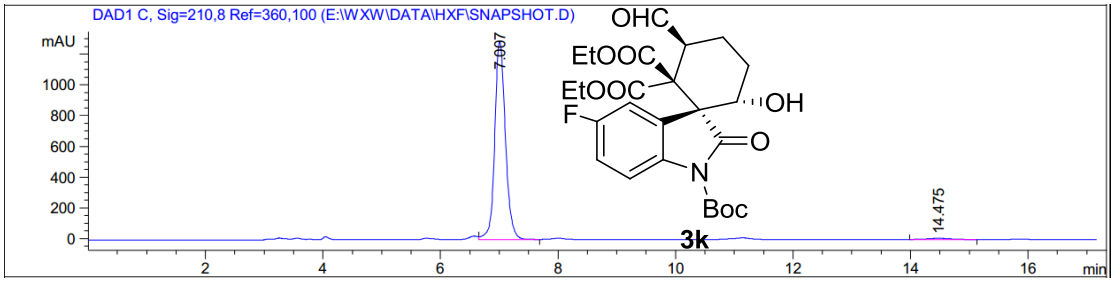
3j

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.690	VB	0.2094	1.78274e4	1338.71057	99.1635
2	9.117	BV	0.3224	150.38289	6.84290	0.8365

3k

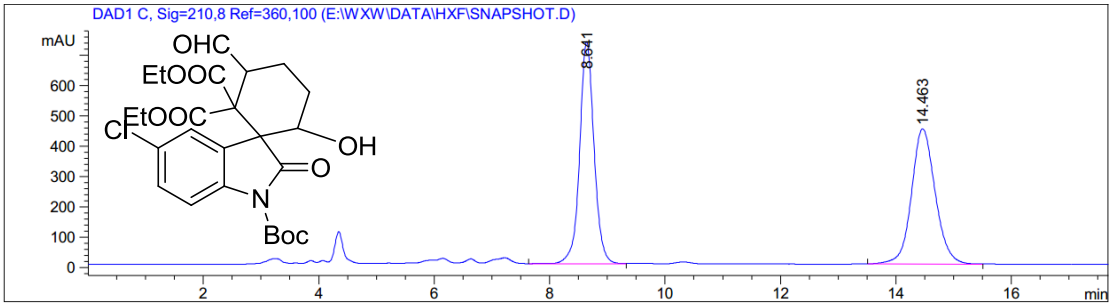


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.045	VV	0.2078	1.58133e4	1169.11597	49.4810
2	14.721	BB	0.4289	1.61450e4	576.13135	50.5190

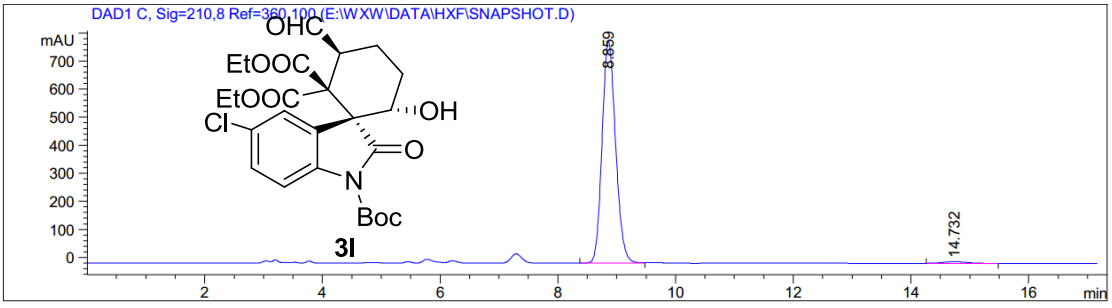


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.007	VB	0.1933	1.62991e4	1291.17505	98.7995
2	14.475	BB	0.4028	198.04033	7.58100	1.2005

3l

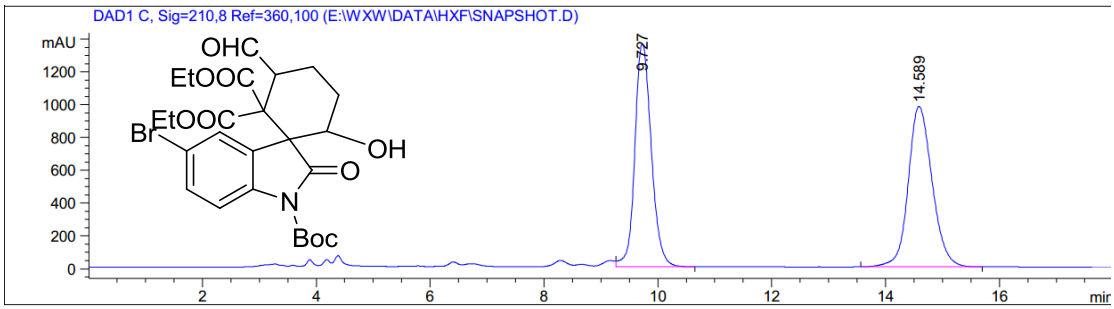


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.641	VB	0.2646	1.27211e4	732.40637	49.9377
2	14.463	BB	0.4374	1.27528e4	446.23685	50.0623

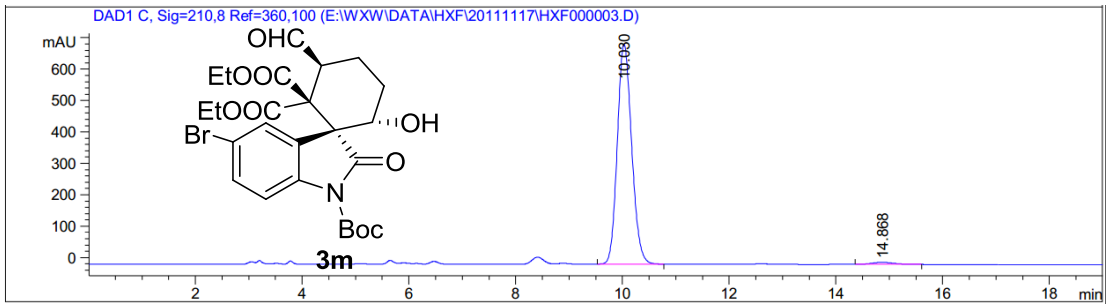


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.859	BB	0.2511	1.26676e4	789.79559	98.7227
2	14.732	BB	0.4292	163.89111	6.02865	1.2773

3m

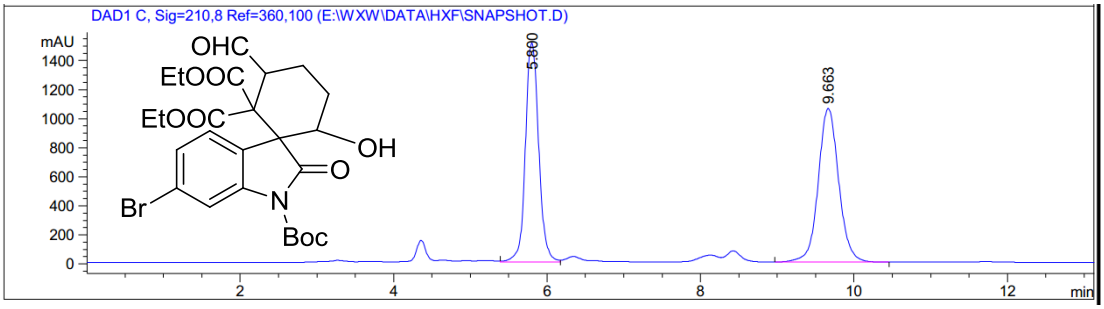


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.727	VB	0.3108	2.73570e4	1359.05933	48.9174
2	14.589	BB	0.4485	2.85679e4	978.80011	51.0826

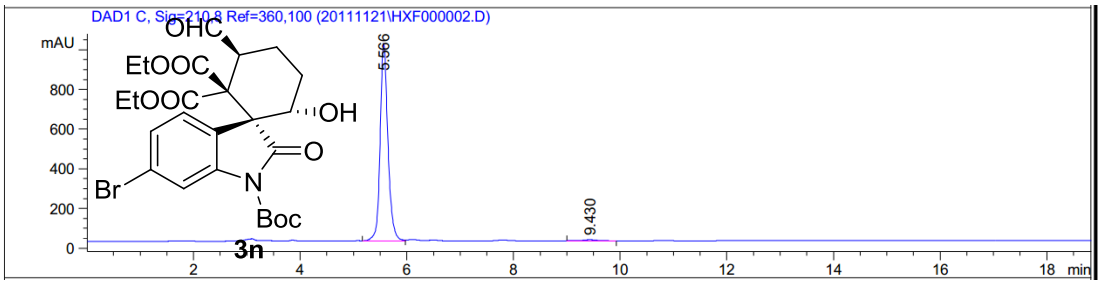


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.030	BB	0.2900	1.30994e4	700.88501	98.5678
2	14.868	BB	0.4467	190.32898	6.59554	1.4322

3n

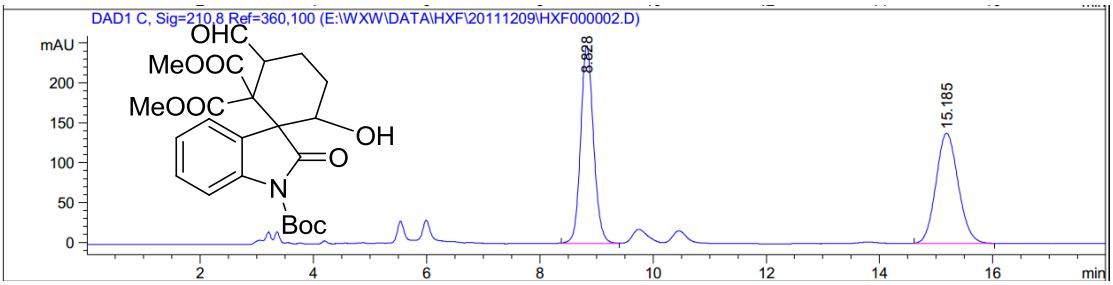


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.800	VV	0.1863	1.81166e4	1506.96082	47.9834
2	9.663	BB	0.2865	1.96394e4	1058.25818	52.0166

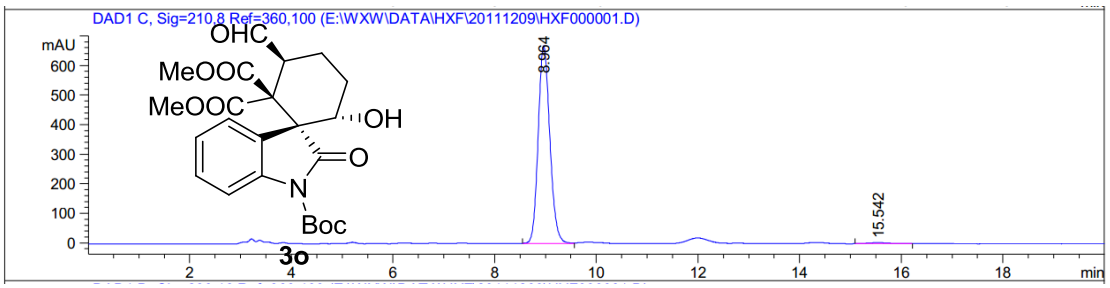


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.566	VV	0.1522	1.00847e4	995.55975	98.9632
2	9.430	BB	0.2936	105.65321	5.27757	1.0368

3o

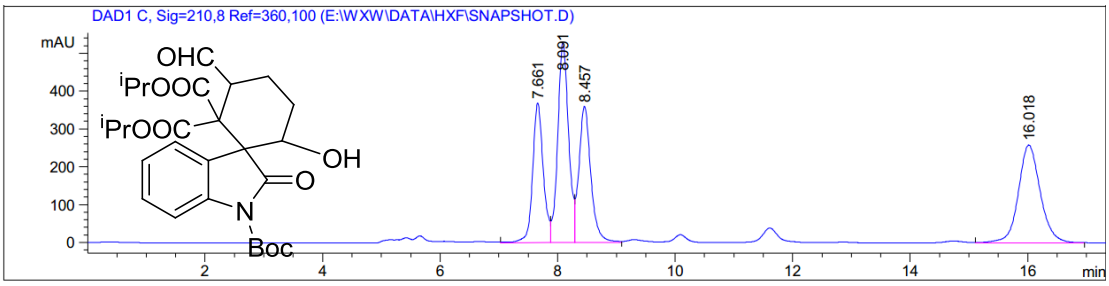


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.828	BB	0.2420	3912.85864	248.11314	50.7837
2	15.185	BB	0.4252	3792.09033	138.59007	49.2163

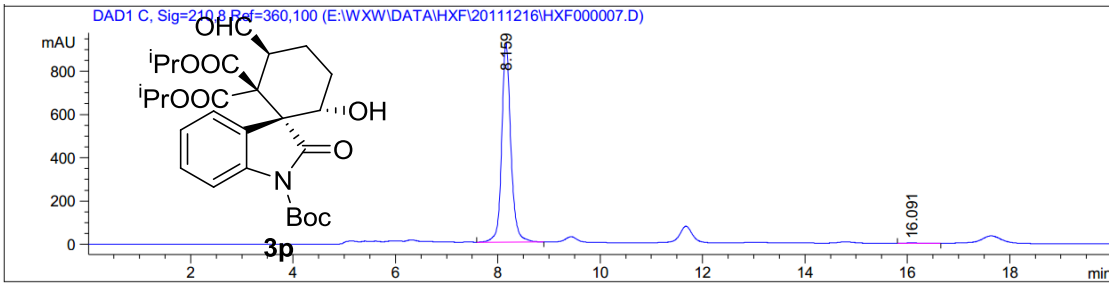


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.964	BB	0.2475	1.06418e4	669.15753	99.1276
2	15.542	BB	0.3956	93.65540	3.52902	0.8724

3p

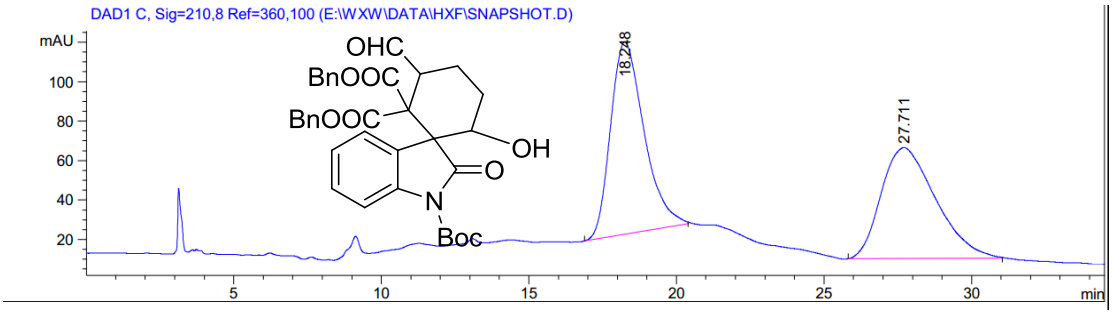


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.661	VV	0.1894	4663.69531	369.09717	20.0643
2	8.091	VV	0.1952	6767.93213	529.05225	29.1172
3	8.457	VV	0.2112	5110.42822	360.82385	21.9863
4	16.018	VB	0.3945	6701.67236	258.45273	28.8322

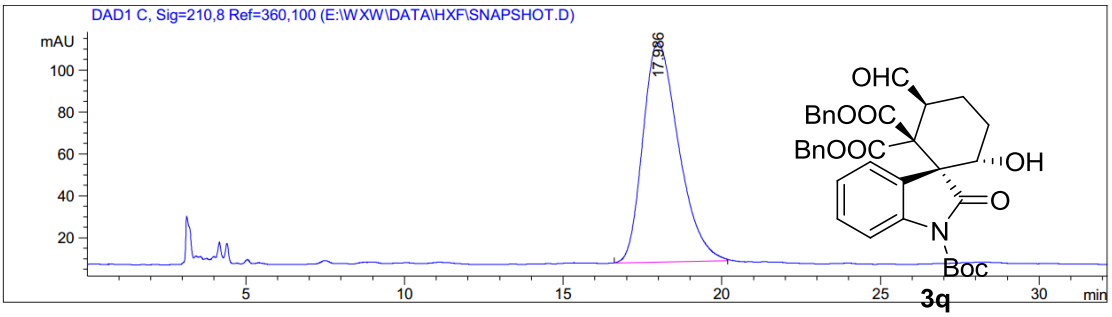


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.159	VB	0.1882	1.13891e4	921.46844	99.7211
2	16.091	BB	0.3393	31.85223	1.45576	0.2789

3q



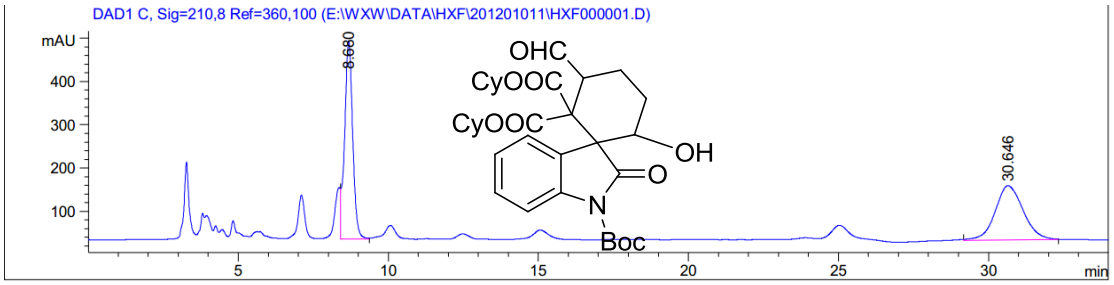
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.248	BB	1.1839	7689.36182	97.52584	51.5879
2	27.711	BB	1.6611	7216.00342	56.23308	48.4121



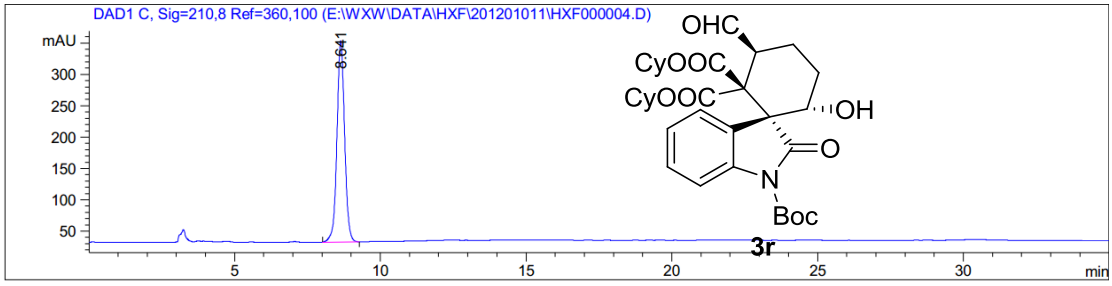
3q

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.986	BB	1.1824	8200.32422	104.62435	100.0000

3r

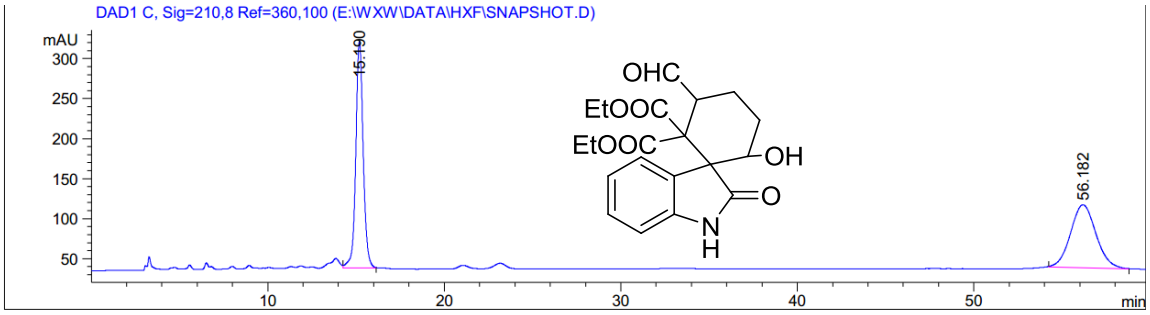


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.680	VB	0.2841	8543.01660	457.03152	51.2849
2	30.646	BB	0.9998	8114.93750	125.26167	48.7151

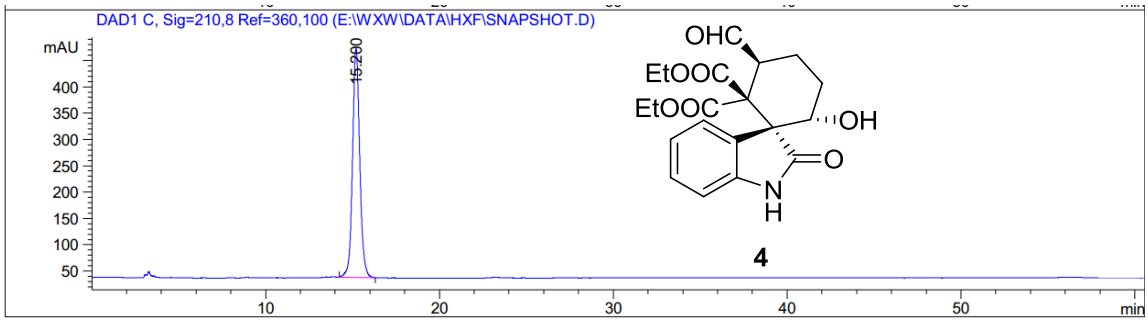


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.641	BB	0.2796	5876.50635	320.97714	100.0000

4

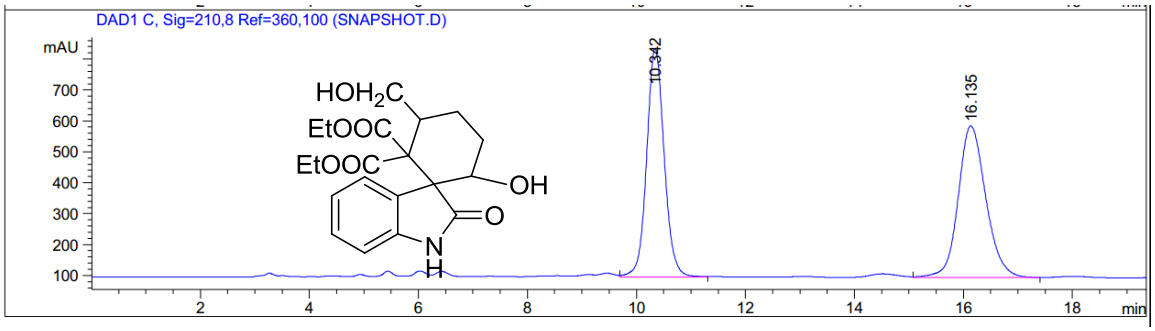


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.190	VB	0.4443	8262.58887	283.28412	51.1813
2	56.182	BB	1.5134	7881.17725	78.76503	48.8187

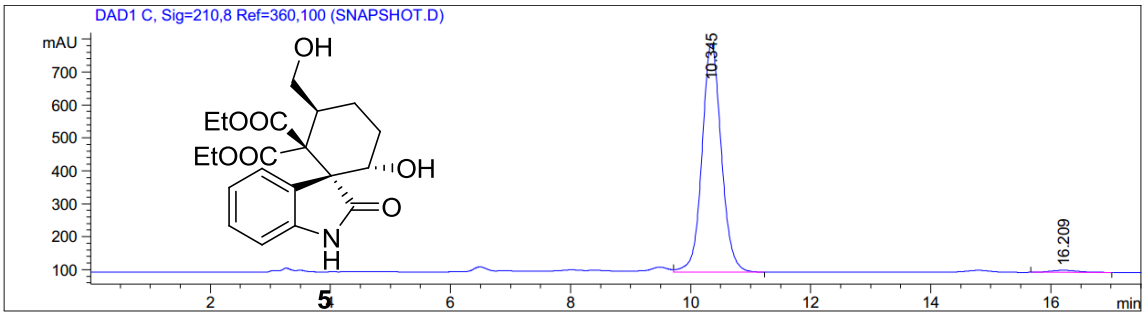


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.200	BB	0.4414	1.25689e4	434.59906	100.0000

5



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.342	VB	0.3447	1.65049e4	738.57568	48.8030
2	16.135	VB	0.5418	1.73146e4	490.53610	51.1970



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.345	VB	0.3433	1.55191e4	693.02985	98.7066
2	16.209	BB	0.4912	203.35672	6.28997	1.2934