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Supporting Information

L-Isoleucine Derived Bifunctional Phosphine Catalyses Asymmetric [3+2]-Annulation of Allenyl-Esters and -Ketones with Ketimines

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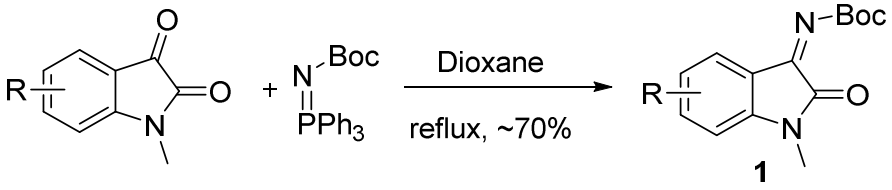
Content

I. General Information

All the chemicals were purchased from Aldrich, Acros, or Alfa and were used without further purification. Reactions were carried out in standard glassware or a Radleys Carousel 12 parallel reactor. Thin layer chromatography (TLC) was performed on *Merck silica gel* $^{60}F_{254}$ *aluminum* sheet. Column chromatography (CC) purifications were carried out using silica gel (Acros Organics, particle size 35-70 μm) was used. Solvents used for CC are commercially available. ^{1}H and ^{13}C-NMR spectroscopic data were recorded on a *Varian Mercury VX 400* or *Varian 500-inova500* spectrometer at RT. ^{1}H and ^{13}C-NMR spectra were calibrated to the solvent signals of $CDCl_3$ (= 7.26 and 77.00 ppm); multiplicities are indicated brs (broadened singlet), s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublets of a doublet); coupling constants (*J*) are given in Hertz (Hz). LC/MS analysis were done using an Agilent 6150 single quadrupole (SQ) mass spectrometer coupled to an Agilent 1290 Infinity LC System. High resolution mass spectra were recorded on a *LTQ Orbitrap* mass spectrometer coupled to an *Acceka HPLC*-System (HPLC column: *Hypersyl GOLD*, 50 mm x 1 mm, particle size 1.9 μm, ionization method: electron spray ionization). Optical rotations were measured in a *Schmidt + Haensch Polartronic HH8* polarimeter. The enantiomeric excesses were determined by Agilent-1100 series HPLC system using a chiral stationary phase column (column: CHIRALPAK IC, CHIRALPAK IA, eluent: (DCM/EtOH = 100/2), iso-hexane). Chemical yields refer to pure isolated substances.

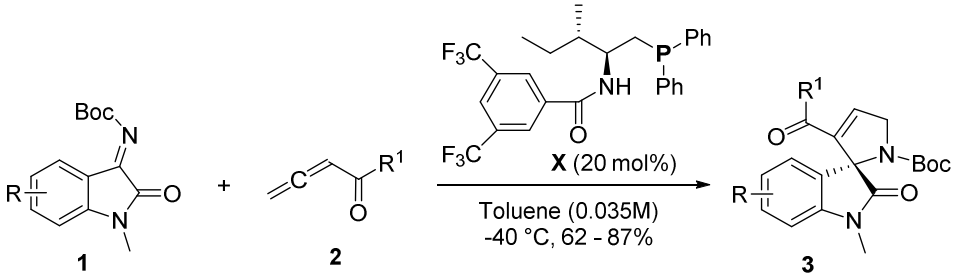
All reactions were carried out under argon atmosphere except noted. The allene-esters and benzoylallene were prepared according to the literature procedure and stored at 4 °C prior to use.[1] The acetylallene was prepared from acetyl acetone by treating with dibromotriphenylphosphorane followed by triethylamine.[2] All the bifunctional *N*-acyl aminophosphine catalysts (**V**-**XV**) were prepared according to the literature procedures.[3]

II. Preparation of Isatinimines 1

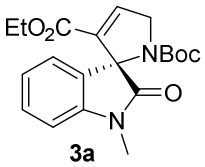


The required isatin-imine was prepared according to the reported in the literature.[4] In an oven–dried Schlenk flask under argon atmosphere, isatin (10 mmol) and *N*-Boc iminophosphorane (11 mmol) were placed. To this reaction mixture anhydrous 1,4-dioxane (10 mL) was added and was heated under reflux until complete disappearance of the starting materials. Then the reaction was cooled to room temperature. After an evaporation of the volatile organic solvents, the crude residue was purified by flash chromatography (silica gel, hexane/ethyl acetate) and afforded the required isatin-imine **1** in good yields (60-75%).

III. Dipolar [3+2]-annulation reaction of allenoate zwitterions with isatin-imines



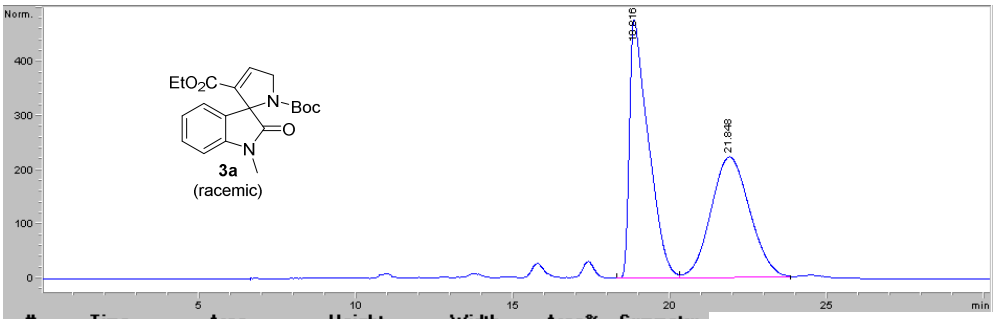
General procedure for the [3+2]-dipolar annulation reaction: To a stirred solution of iastinimine **1** (1.0 equiv.) and allene **2x** (1.2 equiv.) in degassed toluene (0.035 M) was added the bifunctional aminophosphine catalyst **XIV** (20 mol%) at -40 °C and continued to stir at -40 °C overnight (12 h). The reaction was monitored by TLC using Pet.ether/ethyl acetate (1:1) as eluent. After completion, the reaction mixture was concentrated to give the crude compound. The crude product thus obtained was purified by flash column chromatography on silicagel using 35-60% Ethyl acetate in Petroleum ether as gradient eluent and afforded the spirooxindole **3**.



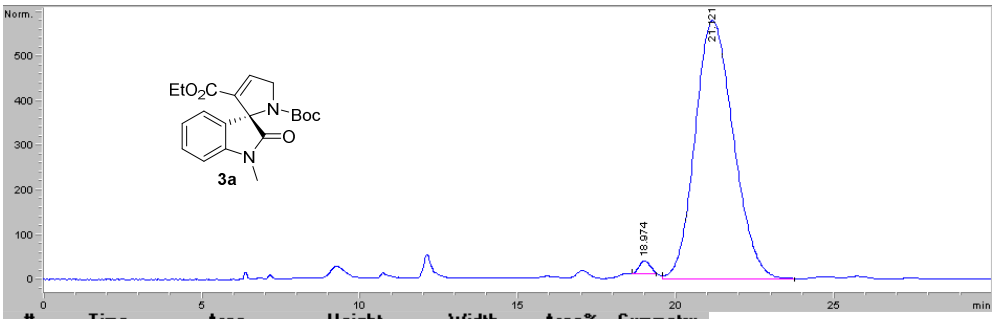
3a

Chemical Formula: $C_{20}H_{24}N_2O_5$
Exact Mass: 372.16852
Molecular Weight: 372.42100

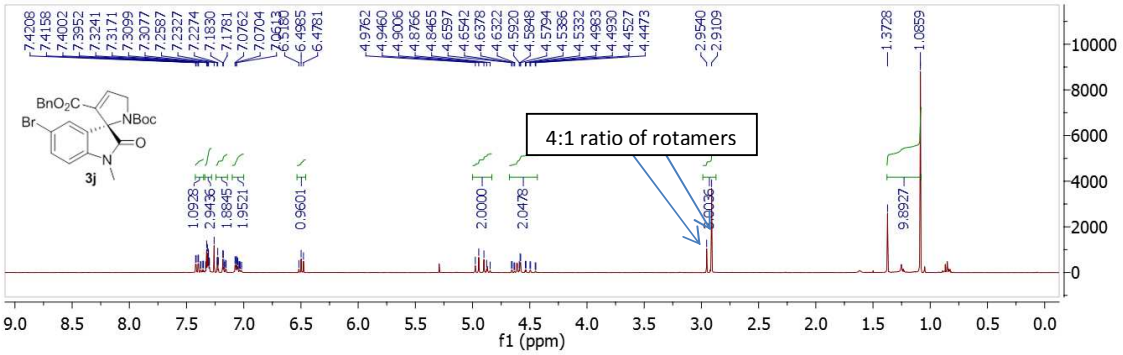
Yield: 84%; *e.e* = 97.1%; $[\alpha]^{20}_{D}$ = -19.8° (*c* 1.17, CH_2Cl_2); IR ν_{max}/cm^{-1} 3058, 2978, 2934, 1788, 1721, 1703; ^1H NMR (5:1 rotamer ratio, asterisks denote minor rotamer peaks, 400 MHz, $CDCl_3$) δ 7.30 (td, *J* = 7.6, 1.5 Hz, 1H), 7.13 (t, *J* = 2.2 Hz, 1H), 7.08* (t, *J* = 2.2 Hz, 0.2H), 7.06 – 7.03 (m, 1H), 7.00 (td, *J* = 7.4, 0.9 Hz, 1H), 6.97* (td, *J* = 7.4, 0.9 Hz, 0.2H), 6.83* (d, *J* = 7.7 Hz, 0.3H), 6.79 (d, *J* = 7.7 Hz, 1H), 4.62 (dd, *J* = 18.3, 2.2 Hz, 1H), 4.56 (dd, *J* = 18.3, 2.2 Hz, 1H), 4.48* (dd, *J* = 18.1, 2.1 Hz, 0.2H), 4.05 – 3.86 (m, 2H), 3.28* (s, 0.5H), 3.23 (s, 3H), 1.36 (s, 1.5 H), 1.07 (s, 9H), 1.09 – 0.99 (m, 3H); ^{13}C NMR (asterisks denote minor rotamer peaks, 101 MHz, $CDCl_3$) δ 174.24, 161.02, 152.56, 144.88*, 144.81, 140.20*, 140.06, 134.87*, 134.78, 134.68*, 130.28*, 129.67, 129.44, 129.09*, 128.67*, 122.87, 122.76, 122.74*, 122.59*, 108.29*, 108.02*, 107.86, 98.42, 83.41*, 80.95, 80.88*, 72.61, 60.99, 60.93*, 54.31*, 54.02, 53.62*, 28.54, 28.29*, 28.01, 27.89, 26.87*, 26.61, 14.01, 13.96*; HRMS [ESI]: Calculated for $C_{20}H_{25}N_2O_5$ $[M+H^+]$: 373.17580, found: 373.17624; RT = 21.1 min. (Chiral HPLC, column : chiralpak IC, eluent: 50% of mixture of EtOH-DCM (1 : 50) in isohexane, Flow rate: 0.5 mL/min).

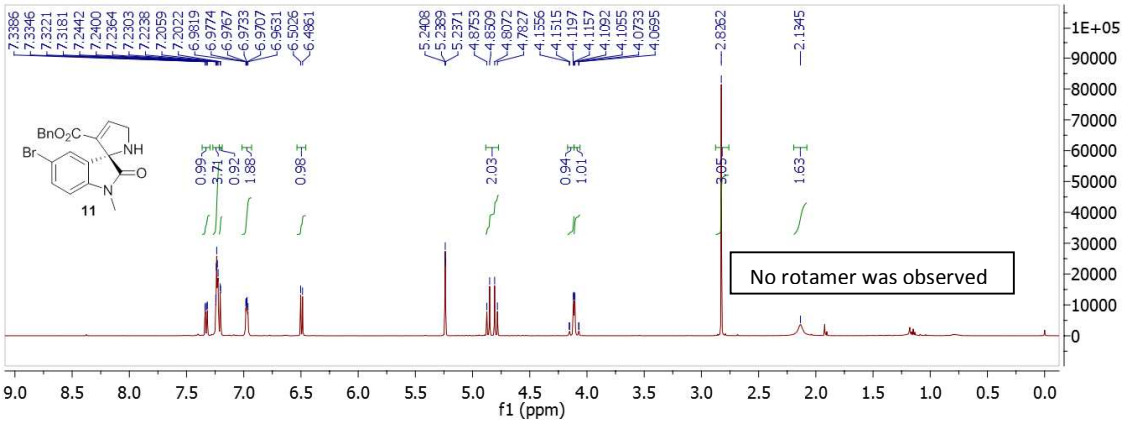


#	Time	Area	Height	Width	Area%	Symmetry
1	18.82	20047	476.1	0.5553	50.740	0.309
2	21.849	19462	224.4	1.0896	49.260	0.877

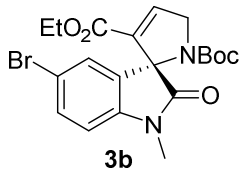


#	Time	Area	Height	Width	Area%	Symmetry
1	18.974	717.5	29.2	0.4091	1.434	0.86
2	21.121	49314.1	580.8	1.415	98.566	0.782





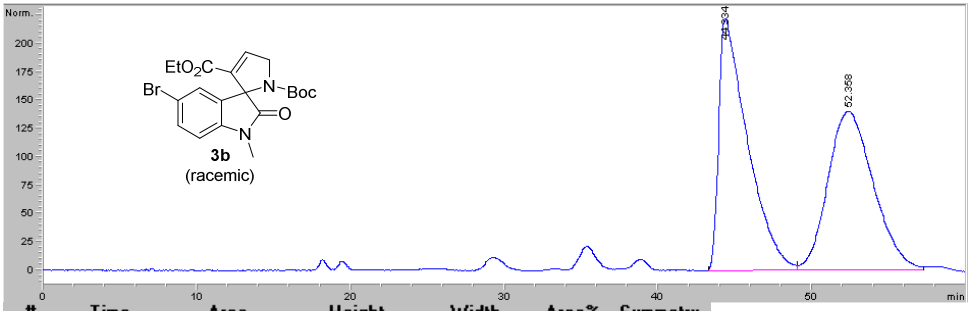
N-Boc moeity in spirooxindole adducts **3** causes a barrier to rotation and thus lead to form rotamers that can be detected in the NMR spectra and display low intensity signal. Boc-removal led to dissolving of rotamers into one enantiopure compound as shown in the above 1H NMR snapshots.



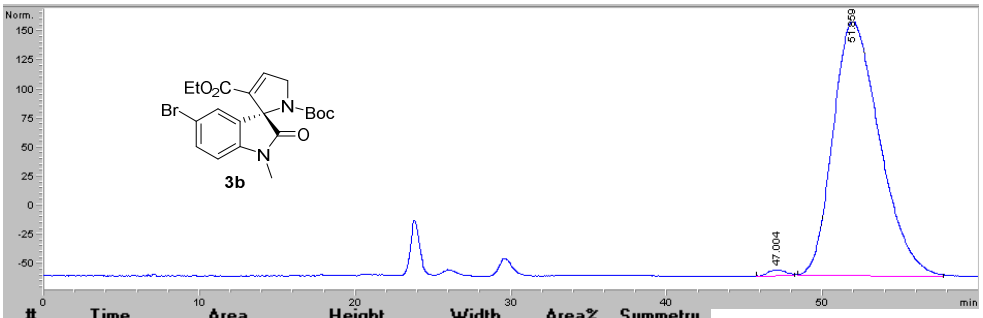
3b

Chemical Formula: $C_{20}H_{23}BrN_2O_5$
Exact Mass: 450.07903
Molecular Weight: 451.31700

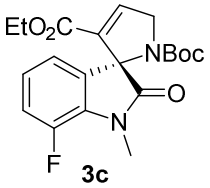
Yield: 86%; *e.e* = 98.1%; $[\alpha]^{20}_D$ = -66.4° (*c* 0.95, CH_2Cl_2); IR ν_{max}/cm^{-1} 3060, 2977, 2929, 2869, 1789, 1725, 1704; ^1H NMR (4:1 rotamer ratio, asterisks denote minor rotamer peaks, 400 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.40* (dd, *J* = 8.2, 2.0 Hz, 0.3H), 7.18 (d, *J* = 2.0 Hz, 1H), 7.15* (d, *J* = 1.9 Hz, 0.3H), 7.15 (t, *J* = 2.1 Hz, 1H), 7.10* (t, *J* = 2.1 Hz, 0.3H), 6.71* (d, *J* = 8.3 Hz, 0.3H), 6.68 (d, *J* = 8.2 Hz, 1H), 4.63 (dd, *J* = 18.4, 2.2 Hz, 1H), 4.61* (dd, *J* = 18.2, 2.1 Hz, 0.3H), 4.56 (dd, *J* = 18.4, 2.1 Hz, 1H), 4.47* (dd, *J* = 18.2, 2.1 Hz, 0.3H), 4.06 – 3.93 (m, 2H), 3.26* (s, 0.8H), 3.22 (s, 3H), 1.38 (s, 2H), 1.11 (s, 9H), 1.12 – 1.06 (m, 3H); ^{13}C NMR (asterisks denote minor rotamer peaks, 101 MHz, $CDCl_3$) δ 173.72, 173.68*, 160.88*, 160.83, 152.31, 151.91*, 144.06*, 143.92, 140.66*, 140.50, 134.41*, 134.36, 132.46*, 132.42, 131.48, 126.20, 126.05*, 115.21, 115.12*, 109.77*, 109.30, 81.35, 81.28*, 72.40, 61.20, 61.13*, 54.35*, 54.12, 28.54, 28.07, 26.96*, 26.72, 14.07, 14.02*; HRMS [ESI]: Calculated for $C_{20}H_{24}BrN_2O_5$ $[M+H^+]$: 451.08631, found: 451.08619; Calculated for $C_{20}H_{24}{}^{81}BrN_2O_5$ $[M+H^+]$: 453.08426, found: 453.08414; RT = 51.9 min. (Chiral HPLC, chiralpak IC-column and using 30% of mixture of EtOH-DCM (1 : 50) in isohexane as eluent, Flow rate: 0.5 mL/min). (Chiral HPLC, column : chiralpak IC, eluent: 30% of mixture of EtOH-DCM (1 : 50) in isohexane, Flow rate: 0.5 mL/min).



#	Time	Area	Height	Width	Area%	Symmetry
1	44.311	15575.6	124.5	1.4738	50.540	0.283
2	52.314	15242.6	76.6	2.3241	49.460	0.771

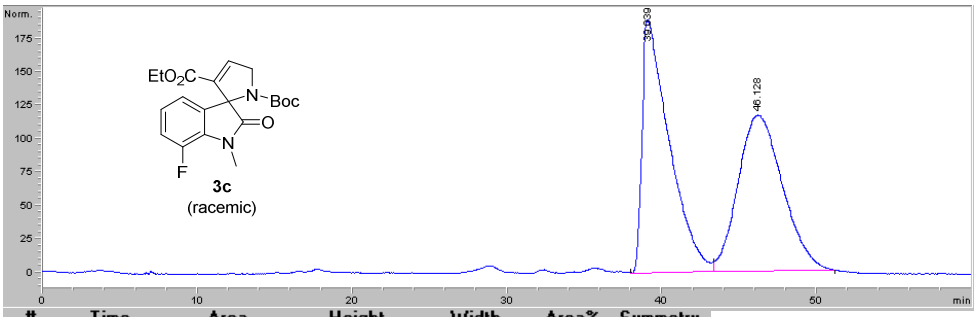


#	Time	Area	Height	Width	Area%	Symmetry
1	47.004	435.3	5.4	1.3468	0.946	1.026
2	51.859	45557.6	218.8	3.4703	99.054	0.689



Chemical Formula: $C_{20}H_{23}FN_2O_5$
Exact Mass: 390.15910
Molecular Weight: 390.41140

Yield: 85%; *e.e* = 98.0%; $[\alpha]^{20}_{D}$ = -26.8° (*c* 1.25, CH_2Cl_2); IR ν_{max}/cm^{-1} 2980, 2937, 2871, 1793, 1725, 1704; ^{1}H NMR (4:1 rotamer ratio, asterisks denote minor rotamer peaks, 400 MHz, $CDCl_3$) δ 7.14 (t, *J* = 2.2 Hz, 1H), 7.09* (t, *J* = 2.2 Hz, 0.25H), 7.03 (ddd, *J* = 11.5, 8.4, 1.1 Hz, 1H), 6.99* (ddd, *J* = 11.4, 8.4, 1.2 Hz, 0.25H), 6.96 – 6.91 (m, 1H), 6.90 – 6.87* (m, 0.25H), 6.84 (dd, *J* = 7.3, 1.1 Hz, 1H), 6.83* (dd, *J* = 7.2, 1.1 Hz, 0.2H), 4.62 (dd, *J* = 18.3, 2.2 Hz, 1H), 4.61* (dd, *J* = 18.2, 2.3 Hz, 0.25H), 4.55 (dd, *J* = 18.3, 2.1 Hz, 1H), 4.47* (dd, *J* = 18.2, 2.1 Hz, 0.25H), 4.07 – 3.92 (m, 2H), 3.48* (d, *J* = 2.6 Hz, 0.7H), 3.45 (d, *J* = 2.7 Hz, 3H), 1.37* (s, 2H), 1.13 (s, 9H), 1.10 (t, *J* = 7.2 Hz, 3H), 1.06* (t, *J* = 7.2 Hz, 0.7H); ^{13}C NMR (asterisks denote minor rotamer peaks, 101 MHz, $CDCl_3$) δ 173.98, 160.95*, 160.91, 152.37, 151.93*, 149.10*, 148.97, 146.68*, 146.56, 140.45*, 140.30, 134.68*, 134.57, 132.43, 132.40*, 131.35, 131.26*, 123.32, 123.26, 123.10*, 123.04*, 118.79, 118.75, 118.64*, 118.61*, 117.89*, 117.70, 117.50, 81.28, 81.15*, 72.57, 72.54*, 61.14, 61.06*, 54.29*, 54.04, 29.49*, 29.43*, 29.25, 29.19, 28.53, 28.04, 27.93*, 14.03, 13.97*; HRMS [ESI]: Calculated for $C_{20}H_{24}FN_2O_5$ [M+H$^+$]: 391.16638, found: 391.16687; RT = 45.8 min. (Chiral HPLC, column : chiralpak IC, eluent: 30% of mixture of EtOH-DCM (1 : 50) in isohexane, Flow rate: 0.5 mL/min).



#	Time	Area	Height	Width	Area%	Symmetry
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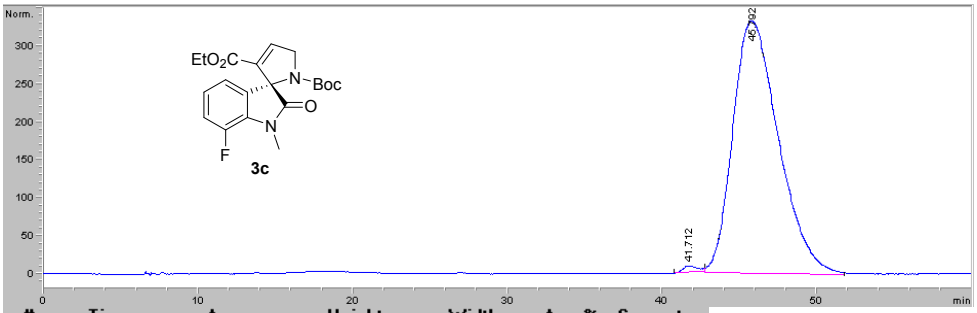
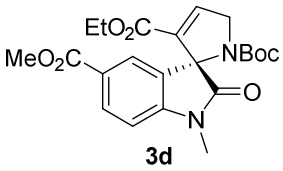
2	46.128	23481.2	117.1	3.3432	50.362	0.755



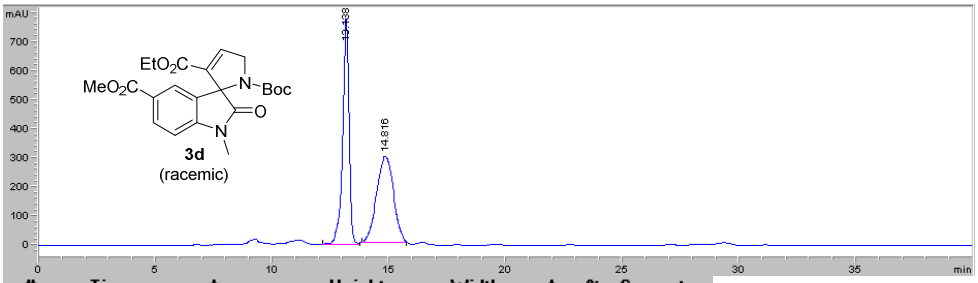
#	Time	Area	Height	Width	Area%	Symmetry
1	41.712	682.4	9.1	1.2454	0.985	3.65E-3
2	45.792	68603.9	333.4	3.4291	99.015	0.603



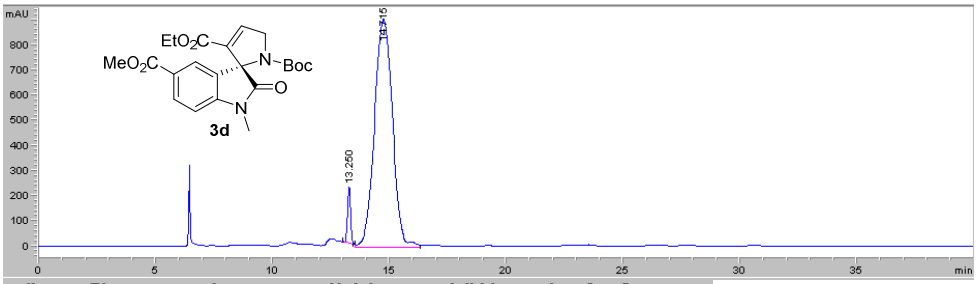
Chemical Formula: $C_{22}H_{26}N_2O_7$
Exact Mass: 430.17400
Molecular Weight: 430.45700

Yield: 88%; *e.e* = 93.0%; $[\alpha]^{20}_D$ = -73.3° (*c* 1.4, CH_2Cl_2); IR ν_{max}/cm^{-1} 2978, 1981, 1791, 1715; ^1H NMR (3:1 rotamer ratio, asterisks denote minor rotamer peaks, 400 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 8.2, 1.7 Hz, 1H), 8.04* (dd, *J* = 8.2, 1.7 Hz, 0.34H), 7.74 (d, *J* = 1.6 Hz, 1H), 7.16 (t, *J* = 2.1 Hz, 1H), 7.11* (t, *J* = 2.1 Hz, 0.3H), 6.87* (d, *J* = 8.3 Hz, 0.35H), 6.84 (d, *J* = 8.2 Hz, 1H), 4.66 (dd, *J* = 18.5, 2.3 Hz, 1H), 4.63* (dd, *J* = 18.1, 2.2 Hz, 0.3H), 4.60 (dd, *J* = 18.4, 2.2 Hz, 1H), 4.52* (dd, *J* = 18.2, 2.2 Hz, 0.3H), 4.04 – 3.91 (m, 2H), 3.88 (s, 3H), 3.87* (s, 1H), 3.31* (s, 1H), 3.27 (s, 3H), 1.36* (s, 3H), 1.08 (t, *J* = 7.1 Hz, 3H), 1.08 (s, 9H), 1.04* (t, *J* = 7.1 Hz, 1H); ^{13}C NMR (asterisks denote minor rotamer peaks, 101 MHz, $CDCl_3$) δ 174.62, 166.85, 160.88, 152.27, 151.92*, 149.11*, 148.90, 140.74*, 140.56, 134.34*, 134.30, 132.47, 130.68, 130.59*, 129.60, 129.11, 124.77, 124.54*, 124.17, 107.85*, 107.44, 81.29, 81.23*, 72.17, 61.17, 61.10*, 54.35*, 54.14, 52.26, 52.18*, 28.53, 28.07, 27.08*, 26.85, 26.18*, 14.06, 14.01*; HRMS [ESI]: Calculated for $C_{22}H_{27}N_2O_7$ $[M+H^+]$: 431.18128, found:

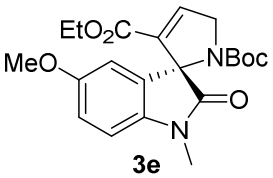
431.18165; RT = 14.7 min. (Chiral HPLC, column : chiralpak IA, eluent: 30% of mixture of EtOH-DCM (1 : 50) in isohexane, Flow rate: 0.5 mL/min).



#	Time	Area	Height	Width	Area%	Symmetry
1	13.138	15479.3	777.1	0.332	50.351	1.293
2	14.816	15263.3	299	0.8507	49.649	1.068



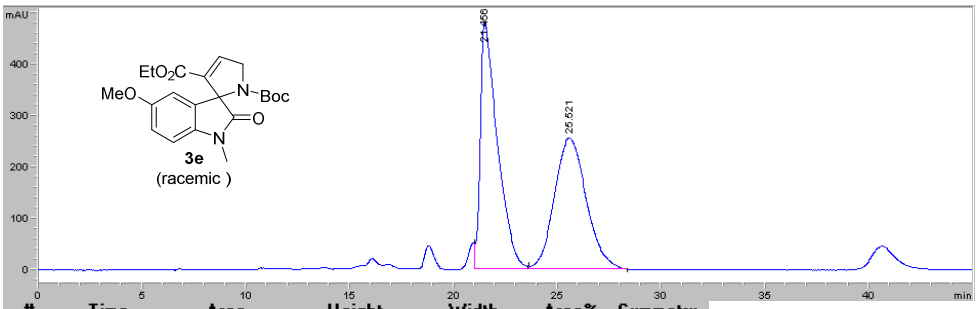
#	Time	Area	Height	Width	Area%	Symmetry
1	13.25	1836.6	223.6	0.1369	3.641	1.114
2	14.715	48607.6	908.5	0.8917	96.359	0.97



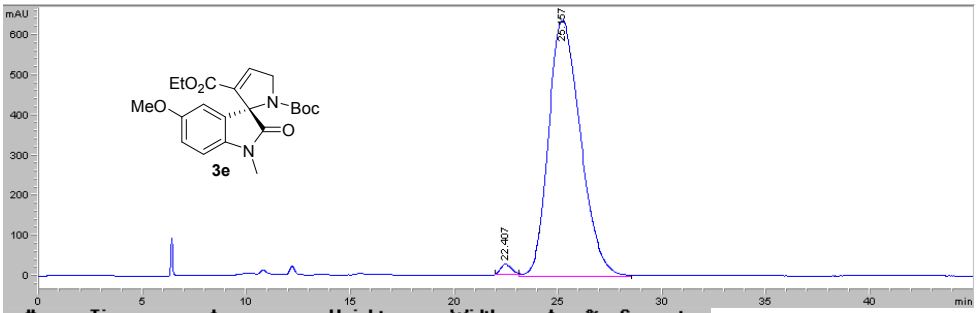
Chemical Formula: $C_{21}H_{26}N_2O_6$
Exact Mass: 402.17909
Molecular Weight: 402.44700

Yield: 79%; *e.e* = 97.1%; $[\alpha]^{20}_D$ = -49.2° (*c* 0.93, CH_2Cl_2); IR ν_{max}/cm^{-1} 2978, 2935, 1788, 1719, 1701; ^1H NMR (5:1 rotamer ratio, asterisks denote minor rotamer peaks, 400 MHz, $CDCl_3$) δ 7.13 (t, *J* = 2.1 Hz, 1H), 7.08* (t, *J* = 2.2 Hz, 0.2H), 6.82 (dd, *J* = 8.4, 2.6 Hz, 1H), 6.79* (dd, *J* = 8.4, 2.6 Hz, 0.2H), 6.73* (d, *J* = 8.4 Hz, 0.2H), 6.69 (d, *J* = 8.4 Hz, 1H), 6.67 (d, *J* = 2.6 Hz, 1H), 6.66* (d, *J* = 2.6 Hz, 0.2H), 4.62 (dd, *J* = 18.3, 2.2 Hz, 1H), 4.61* (dd, *J* = 18.3, 2.2 Hz, 0.2H), 4.56 (dd, *J* = 18.3, 2.1 Hz, 1H), 4.47* (dd, *J* = 18.2, 2.1 Hz, 0.2H), 4.04 – 3.89 (m, 2H), 3.74 (s, 3H), 3.74* (s, 0.7H), 3.25* (s, 0.7H), 3.20 (s, 3H), 1.37* (s, 2H), 1.09 (s, 9H), 1.06 (t, *J* = 7.1 Hz, 3H), 1.03* (t, *J* = 7.1 Hz, 0.5H); ^{13}C NMR (asterisks denote minor rotamer peaks, 101 MHz, $CDCl_3$) δ 173.92, 173.84*, 161.06*, 161.00, 156.30, 156.10*, 152.58, 151.86*, 140.23*, 140.10, 138.54*, 138.40, 134.88*, 134.80, 130.66, 129.99*, 113.94, 113.40*, 110.75*, 110.31, 108.50*, 108.18, 81.01, 80.91*, 72.92, 61.01,

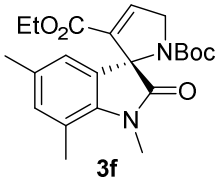
60.95*, 56.06, 55.95*, 54.33*, 54.03, 28.55, 28.07, 27.94*, 26.95*, 26.69, 14.02, 13.98*; HRMS [ESI]: Calculated for $C_{21}H_{27}N_2O_6$ [M+H$^+$]: 403.18636, found: 403.18667; RT = 25.2 min. (Chiral HPLC, column : chiralpak IC, eluent: 50% of mixture of EtOH-DCM (1 : 50) in isohexane, Flow rate: 0.5 mL/min).



#	Time	Area	Height	Width	Area%	Symmetry
1	21.456	27290.7	484.6	0.743	49.805	0.304
2	25.521	27504.8	256.6	1.2944	50.195	0.818



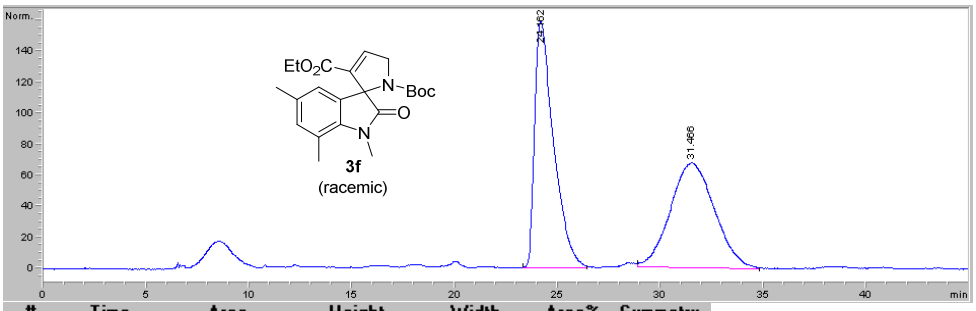
#	Time	Area	Height	Width	Area%	Symmetry
1	22.407	1003.1	27.1	0.6173	1.446	0.77
2	25.157	68362.5	637.4	1.7875	98.554	0.726



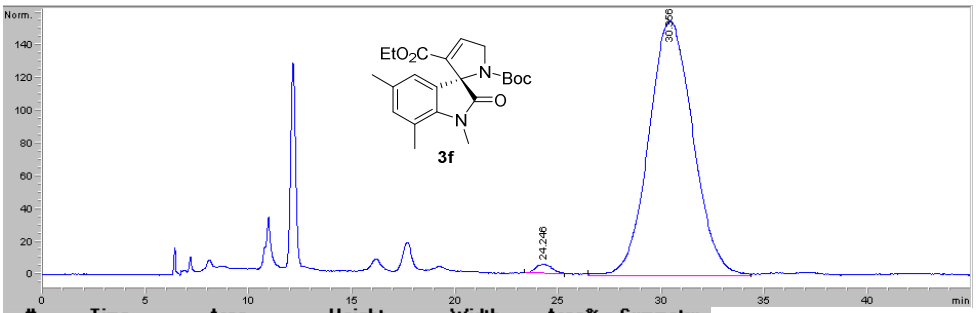
Chemical Formula: $C_{22}H_{28}N_2O_5$
Exact Mass: 400.19982
Molecular Weight: 400.47500

Yield: 82%; *e.e* = 97.5%; $[\alpha]^{20}_D$ = -28.4^o (*c* 0.74, CH_2Cl_2); IR ν_{max}/cm^{-1} 3337, 2980, 2934, 2864, 1789, 1724; ^{1}H NMR (5:1 rotamer ratio, asterisks denote minor rotamer peaks, 400 MHz, $CDCl_3$) δ 7.10 (t, *J* = 2.2 Hz, 1H), 7.05* (t, *J* = 2.2 Hz, 0.2H), 6.81 (s, 1H), 6.78* (s, 0.2H), 6.68 (s, 1H), 6.67 (s, 0.2H), 4.60 (dd, *J* = 18.3, 2.3 Hz, 1H), 4.55 (dd, *J* = 18.3, 2.2 Hz, 1H), 4.46* (dd, *J* = 18.2, 2.1 Hz, 0.2H), 4.08 – 3.90 (m, 2H), 3.52* (s, 0.6H), 3.49 (s, 3H), 2.51* (s, 0.7H), 2.50 (s, 3H), 2.21* (s, 0.6H), 2.20 (s, 1H), 1.38* (s, 1.8H), 1.11 (s, 9H), 1.10 (t, *J* = 7.1 Hz, 12H), 1.06* (t, *J* = 7.2 Hz, 0.7H; ^{13}C NMR (asterisks denote minor rotamer peaks, 101 MHz, $CDCl_3$) δ 174.95, 164.07, 161.13, 152.66, 139.97, 139.81*, 139.66, 135.13,

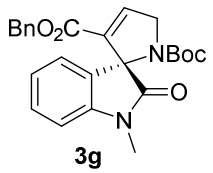
134.00*, 133.68, 132.23*, 132.13, 130.16, 121.67, 121.61*, 119.25*, 118.98, 80.85, 80.72*, 72.31, 60.95, 60.86*, 53.93, 53.62*, 30.34*, 30.08, 28.01, 27.88*, 20.95*, 20.86, 19.16*, 18.96, 14.04, 13.96*; HRMS [ESI]: Calculated for $C_{22}H_{29}N_2O_5$ [M+H$^+$]: 401.20710, found: 401.20732; RT = 30.4 min. (Chiral HPLC, column : chiralpak IC, eluent: 50% of mixture of EtOH-DCM (1 : 50) in isohexane, Flow rate: 0.5 mL/min).



#	Time	Area	Height	Width	Area%	Symmetry
1	24.162	10114.6	158.6	0.8478	49.844	0.438
2	31.466	10178.1	67.9	1.7584	50.156	0.874



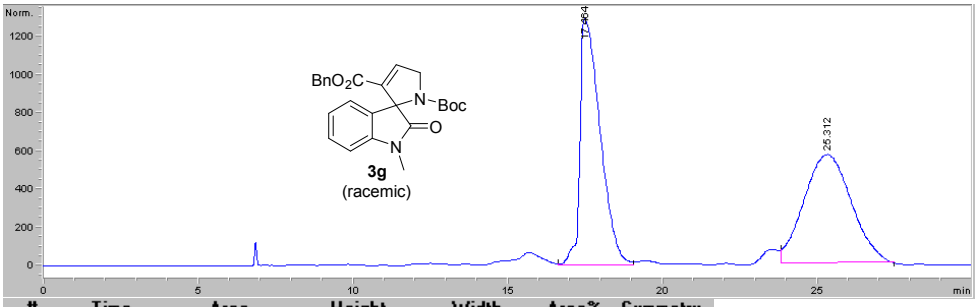
#	Time	Area	Height	Width	Area%	Symmetry
1	24.246	290.9	5.5	0.88	1.222	0.882
2	30.356	23502.5	156.1	2.5095	98.778	0.869



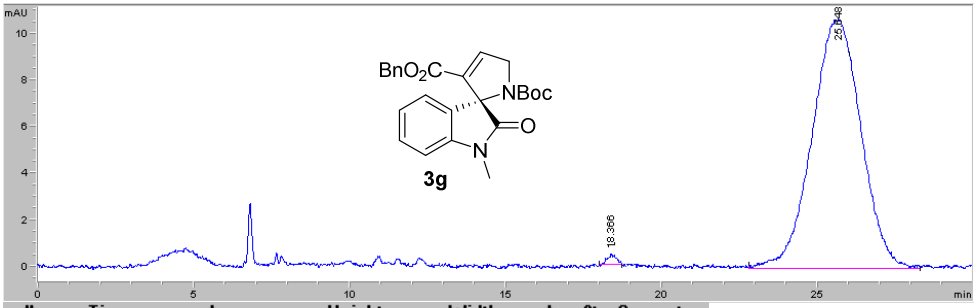
Chemical Formula: $C_{25}H_{26}N_2O_5$
Exact Mass: 434.18417
Molecular Weight: 434.49200

Yield: 76%; *e.e* = 98.3%; $[\alpha]^{20}_D$ = -25.7° (*c* 1.1, CH_2Cl_2); IR ν_{max}/cm^{-1} 2977, 2932, 1787, 17269, 1703; ^{1}H NMR (4:1 rotamer ratio, asterisks denote minor rotamer peaks, 400 MHz, $CDCl_3$) δ 7.25 – 7.19 (m, 4H), 7.14 (t, *J* = 2.2 Hz, 1H), 7.09* (t, *J* = 2.1 Hz, 0.21H), 7.01 – 6.90 (m, 4H), 6.58* (d, *J* = 7.8 Hz, 0.21H), 6.55 (d, *J* = 7.7 Hz, 1H), 4.86 (d, *J* = 12.1 Hz, 1H), 4.85* (d, *J* = 12.0 Hz, 0.21H), 4.80 (d, *J* = 12.1 Hz, 1H), 4.78* (d, *J* = 12.2 Hz, 0.21H), 4.56 (dd, *J* = 18.4, 2.2 Hz, 1H), 4.55* (dd, *J* = 18.4, 2.2 Hz, 0.21H), 4.50 (dd, *J* = 18.4, 2.2 Hz, 1H), 4.42* (dd, *J* = 18.2, 2.1 Hz, 0.21H), 2.90* (s, 0.55H), 2.85 (s, 1H), 1.29* (s, 1.8H), 0.98 (s, 9H); ^{13}C NMR (asterisks denote minor rotamer peaks, 101 MHz, $CDCl_3$) δ 174.08,

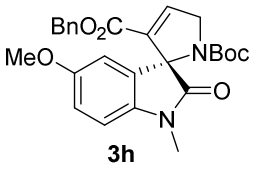
160.94, 152.52, 144.69, 141.14*, 141.01, 134.95, 134.43, 129.60, 129.30*, 128.98*, 128.72, 128.60, 128.56*, 122.90, 122.74, 122.56*, 108.63*, 108.15, 80.96, 80.90*, 77.56, 77.25, 76.93, 72.52, 67.10, 54.29*, 54.01, 29.50*, 28.53, 27.99, 26.52*, 26.25; HRMS [ESI]: Calculated for $C_{25}H_{27}N_2O_5$ [M+H$^+$]: 435.19145, found: 435.19162; RT = 25.6 min. (Chiral HPLC, column : chiralpak IC, eluent: 50% of mixture of EtOH-DCM (1 : 50) in isohexane, Flow rate: 0.5 mL/min).



#	Time	Area	Height	Width	Area%	Symmetry
1	17.464	59314.4	1292.2	0.5835	49.642	0.314
2	25.312	60170.1	567.5	1.767	50.358	0.978



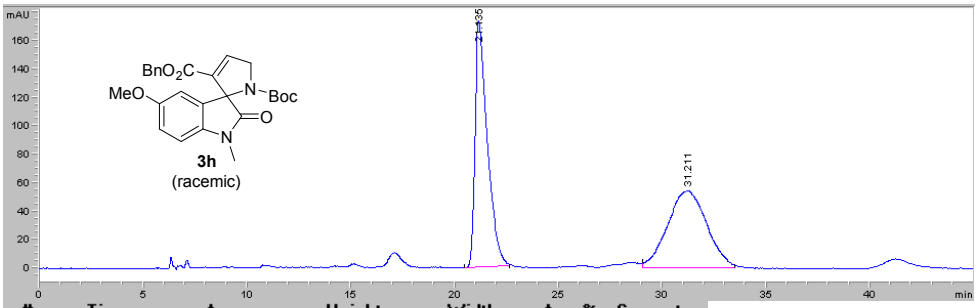
#	Time	Area	Height	Width	Area%	Symmetry
1	18.366	10.3	4.7E-1	0.3624	0.865	0.791
2	25.648	1182.7	10.8	1.8332	99.135	1.108



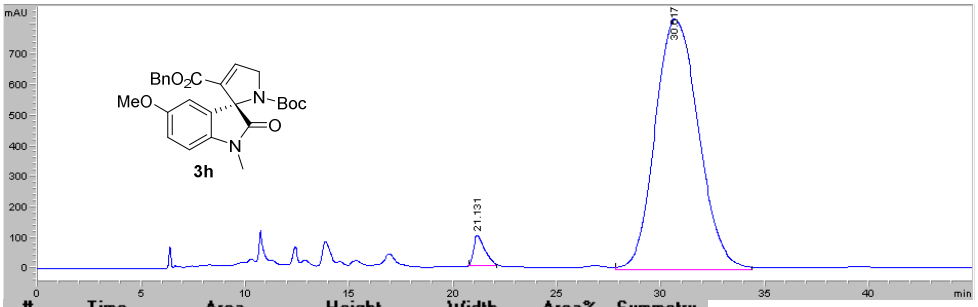
Chemical Formula: $C_{26}H_{28}N_2O_6$
Exact Mass: 464.19474
Molecular Weight: 464.51800

Yield: 71%; *e.e* = 93.9%; $[\alpha]^{20}_D$ = -37.3° (*c* 1.13, CH_2Cl_2); IR ν_{max}/cm^{-1} 2977, 2937, 1723, 1705, 1645; ^{1}H NMR (4:1 rotamer ratio, asterisks denote minor rotamer peaks, 400 MHz, $CDCl_3$) δ 7.26 – 7.20 (m, 3H), 7.14 (t, *J* = 2.2 Hz, 1H), 7.09* (t, *J* = 2.1 Hz, 0.25H), 6.98 (dd, *J* = 6.5, 3.1 Hz, 2H), 6.96* (dd, *J* = 7.1, 3.3 Hz, 0.45H), 6.75 (dd, *J* = 8.4, 2.6 Hz, 1H), 6.71* (dd, *J* = 8.5, 2.6 Hz, 0.26H), 6.61 (d, *J* = 2.6 Hz, 1H), 6.60* (d, *J* = 2.7 Hz, 0.25H), 6.49* (d, *J* = 8.4 Hz, 0.26H), 6.46 (d, *J* = 8.4 Hz, 1H), 4.88 (d, *J* = 12.1 Hz, 1H), 4.81 (d, *J* = 12.1 Hz,

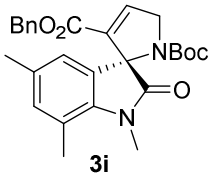
1H), 4.79* (d, *J* = 12.2 Hz, 0.42H), 4.56 (dd, *J* = 18.4, 2.2 Hz, 1H), 4.55* (dd, *J* = 18.4, 2.2 Hz, 0.25H), 4.49 (dd, *J* = 18.4, 2.2 Hz, 1H), 4.41* (dd, *J* = 18.2, 2.1 Hz, 0.25H), 3.69 (s, 1H), 2.89* (s, 0.6H), 2.84 (s, 3H), 1.30* (s, 1.9H), 1.01 (s, 9H); ^{13}C NMR (asterisks denote minor rotamer peaks, 101 MHz, $CDCl_3$) δ 172.53, 172.44*, 159.78*, 159.68, 155.08, 154.88*, 151.31, 150.58*, 139.94*, 139.82, 137.17*, 137.05, 133.74, 133.31*, 133.23, 129.26, 128.57*, 127.51, 127.47, 127.43*, 127.38, 127.33*, 112.79, 112.26*, 109.39*, 108.96, 107.61*, 107.26, 79.80, 79.71*, 71.62, 65.89, 54.86, 54.76*, 53.09*, 52.80, 27.32, 26.82, 25.39*, 25.11; HRMS [ESI]: Calculated for $C_{26}H_{29}N_2O_6$ [M+H$^+$]: 465.20201, found: 465.20188; RT = 30.6 min. (Chiral HPLC, column : chiralpak IC, eluent: 50% of mixture of EtOH-DCM (1 : 50) in isohexane, Flow rate: 0.5 mL/min).



#	Time	Area	Height	Width	Area%	Symmetry
1	21.135	7216.7	173.3	0.5779	50.028	0.459
2	31.211	7208.5	54.7	1.5646	49.972	1.06



#	Time	Area	Height	Width	Area%	Symmetry
1	21.131	3734.4	98.2	0.634	3.033	0.513
2	30.617	119377.7	821.4	2.4223	96.967	0.791

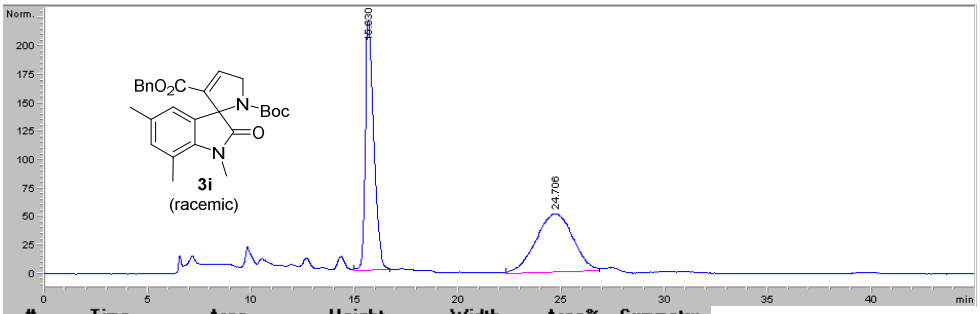


3i

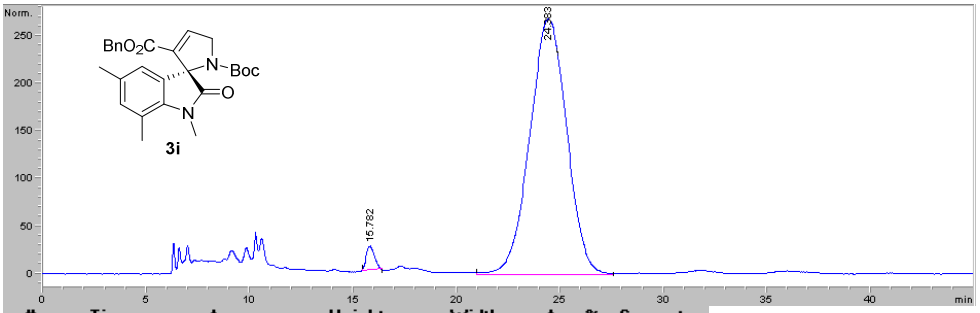
Chemical Formula: $C_{27}H_{30}N_2O_5$
Exact Mass: 462.21547
Molecular Weight: 462.54600

Yield: 62%; *e.e* = 96.0%; $[\alpha]^{20}_D$ = -27.6^o (*c* 1.02, CH_2Cl_2); IR ν_{max}/cm^{-1} 2977, 2931, 2868, 1788, 1721, 1704; ^{1}H NMR (5:1 rotamer ratio, asterisks denote minor rotamer peaks, 400

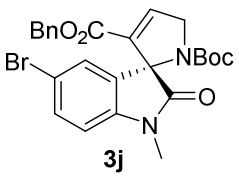
MHz, $CDCl_3$) δ 7.36 – 7.27 (m, 4H), 7.20 (t, *J* = 2.1 Hz, 1H), 7.13* (t, *J* = 2.0 Hz, 0.2H), 7.07 – 7.01 (m, 2H), 6.80 (s, 1H), 6.76* (s, 0.2H), 6.69 (s, 1H), 4.98 (d, *J* = 12.1 Hz, 1H), 4.87 (d, *J* = 12.2 Hz, 1H), 4.86* (d, *J* = 12.1 Hz, 0.2H), 4.60 (dd, *J* = 18.3, 2.0 Hz, 1H), 4.55 (dd, *J* = 18.4, 2.1 Hz, 1H), 4.46* (dd, *J* = 18.1, 2.1 Hz, 0.2H), 3.22* (s, 0.5H), 3.16 (s, 3H), 2.32 (s, 3H), 2.23 (s, 3H), 2.22* (s, 0.5H), 1.37* (s, 1.7H), 1.08 (s, 9H); ^{13}C NMR (asterisks denote minor rotamer peaks, 101 MHz, $CDCl_3$) δ 174.77, 161.11, 152.61, 152.56*, 140.74, 139.92, 135.06, 134.79, 134.02*, 133.65, 132.40*, 132.14, 129.99, 128.74, 128.70*, 128.65, 128.56, 128.51*, 128.32*, 121.70, 121.61*, 119.17, 98.07, 80.86, 80.74*, 72.17, 67.07, 67.00*, 54.29*, 53.91, 53.62*, 30.03*, 29.71, 28.61, 28.51*, 28.08*, 27.98, 20.96*, 20.87, 18.89; HRMS [ESI]: Calculated for $C_{27}H_{31}N_2O_5$ $[M+H^+]$: 463.22275, found: 463.22298; RT = 24.4 min. (Chiral HPLC, column : chiralpak IC, eluent: 60% of mixture of EtOH-DCM (1 : 50) in isohexane, Flow rate: 0.5 mL/min).



#	Time	Area	Height	Width	Area%	Symmetry
1	15.63	6469.3	220.2	0.4347	49.755	0.599
2	24.706	6533	51.6	2.1087	50.245	1.168

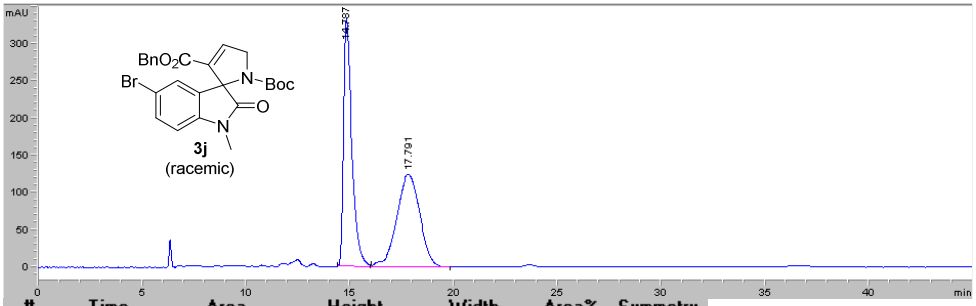


#	Time	Area	Height	Width	Area%	Symmetry
1	15.782	689.2	25.2	0.4551	1.988	0.814
2	24.383	33975.8	269.6	2.1006	98.012	0.957

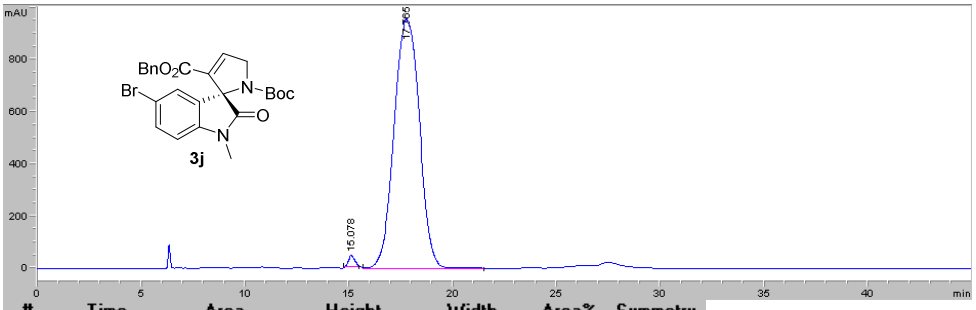


Chemical Formula: $C_{25}H_{25}BrN_2O_5$
Exact Mass: 512.09468
Molecular Weight: 513.38800

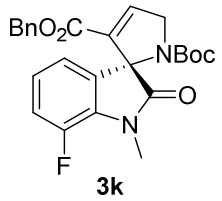
Yield: 80%; *e.e* = 97.6%; $[\alpha]^{20}_{D}$ = -62.8^{o} (*c* 1.1, CH_2Cl_2); IR ν_{max}/cm^{-1} 3064, 2976, 2934, 1727, 1703; ^{1}H NMR (3.5:1 rotamer ratio, asterisks denote minor rotamer peaks, 400 MHz, $CDCl_3$) δ 7.41 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.37* (dd, *J* = 8.2, 2.0 Hz, 0.28H), 7.34 – 7.29 (m, 3H), 7.23 (t, *J* = 2.2 Hz, 1H), 7.18 (d, *J* = 2.0 Hz, 1H), 7.17* (t, *J* = 2.2 Hz, 0.28H), 7.16* (d, *J* = 2.0 Hz, 0.28H), 7.08 – 7.05 (m, 2H), 7.03* (dd, *J* = 6.3, 3.2 Hz, 0.56H), 6.51* (d, *J* = 7.8 Hz, 0.28H), 6.49 (d, *J* = 8.2 Hz, 1H), 4.96 (d, *J* = 12.1 Hz, 1H), 4.89 (d, *J* = 12.1 Hz, 1H), 4.86* (d, *J* = 12.1 Hz, 0.28H), 4.63 (dd, *J* = 18.5, 2.2 Hz, 1H), 4.61* (dd, *J* = 18.5, 2.2 Hz, 0.28H), 4.56 (dd, *J* = 18.5, 2.2 Hz, 1H), 4.47* (dd, *J* = 18.3, 2.1 Hz, 0.3H), 2.95* (s, 0.8H), 2.91 (s, 3H), 1.37* (s, 2.6H), 1.09 (s, 9H); ^{13}C NMR (asterisks denote minor rotamer peaks, 101 MHz, $CDCl_3$) δ 173.56, 173.51*, 160.78*, 160.69, 152.26, 151.86*, 143.90*, 143.78, 141.65*, 141.49, 134.83, 134.06*, 134.00, 132.34, 131.33, 129.00, 128.79, 128.76*, 128.73*, 126.20, 126.03*, 115.17, 115.07*, 110.02*, 109.51, 81.36, 81.31*, 72.30, 67.26, 54.33*, 54.10, 28.53, 28.04, 26.61*, 26.36; HRMS [ESI]: Calculated for $C_{25}H_{26}BrN_2O_5$ [M+H^{+}]: 513.10196, found: 513.10250; Calculated for $C_{25}H_{26}{}^{81}BrN_2O_5$ [M+H^{+}]: 515.09991, found: 515.10048; RT = 17.7 min. (Chiral HPLC, column : chiralpak IC, eluent: 50% of mixture of EtOH-DCM (1 : 50) in isohexane, Flow rate: 0.5 mL/min).



#	Time	Area	Height	Width	Area%	Symmetry
1	14.787	9332.6	332.9	0.4051	49.349	0.448
2	17.791	9578.8	124.7	0.9702	50.651	1.02



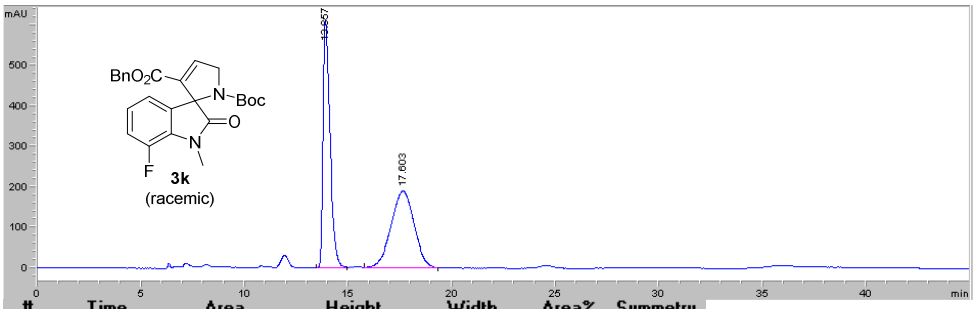
#	Time	Area	Height	Width	Area%	Symmetry
1	15.078	981.1	43.5	0.3755	1.178	0.78
2	17.765	82332.9	960	1.4294	98.822	0.997



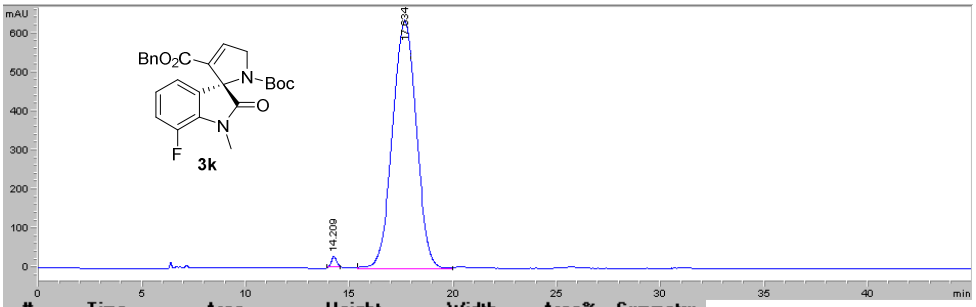
3k

Chemical Formula: $C_{25}H_{25}FN_2O_5$
Exact Mass: 452.17475
Molecular Weight: 452.48240

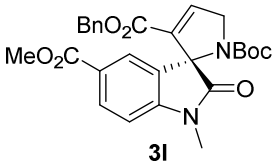
Yield: 86%; *e.e* = 98.1%; $[\alpha]^{20}_{D}$ = -26.4° (*c* 0.9, CH_2Cl_2); IR ν_{max}/cm^{-1} 3037, 2979, 2868, 1792, 1729; ^{1}H NMR (4:1 rotamer ratio, asterisks denote minor rotamer peaks, 400 MHz, $CDCl_3$) δ 7.33 – 7.28 (m, 3H), 7.22 (t, *J* = 1.8 Hz, 1H), 7.16* (t, *J* = 2.0 Hz, 0.23H), 7.08 – 6.88 (m, 4H), 6.85 (dd, *J* = 7.3, 1.1 Hz, 1H), 6.82* (s, 0.1H), 4.96 (d, *J* = 12.0 Hz, 1H), 4.95* (d, *J* = 12.0 Hz, 0.25H), 4.88 (d, *J* = 12.1 Hz, 1H), 4.86* (d, *J* = 12.1 Hz, 0.25H), 4.62 (dd, *J* = 18.4, 2.0 Hz, 1H), 4.60* (dd, *J* = 18.3, 2.3 Hz, 0.25H), 4.54 (dd, *J* = 18.5, 2.1 Hz, 1H), 4.46* (dd, *J* = 18.3, 2.0 Hz, 0.25H), 3.15* (d, *J* = 2.5 Hz, 0.7H), 3.11 (d, *J* = 2.6 Hz, 3H), 1.36* (s, 2.2H), 1.10 (s, 9H); ^{13}C NMR (asterisks denote minor rotamer peaks, 101 MHz, $CDCl_3$) δ 173.81, 173.77*, 160.89*, 160.79, 152.32, 151.85*, 149.00*, 148.90, 146.57*, 146.48, 141.41*, 141.31, 134.73, 134.32*, 134.19, 132.26, 132.22, 131.53*, 131.44*, 131.32, 131.24, 128.85, 128.83*, 128.76, 128.72*, 128.65, 123.30, 123.23, 123.06*, 123.00*, 118.82, 118.79, 118.65*, 118.62*, 117.91*, 117.69, 117.50, 81.28, 81.15*, 72.44, 72.41, 67.31, 54.27*, 54.02, 29.11*, 29.05*, 28.84, 28.79, 28.52, 28.02; HRMS [ESI]: Calculated for $C_{25}H_{26}FN_2O_5$ $[M+H^+]$: 453.18203, found: 453.18149; RT = 17.6 min. (Chiral HPLC, column : chiralpak IC, eluent: 50% of mixture of EtOH-DCM (1 : 50) in isohexane, Flow rate: 0.5 mL/min).



#	Time	Area	Height	Width	Area%	Symmetry
1	13.857	14203.9	613.3	0.3402	48.894	0.443
2	17.603	14846.5	192	0.9201	51.106	1.021

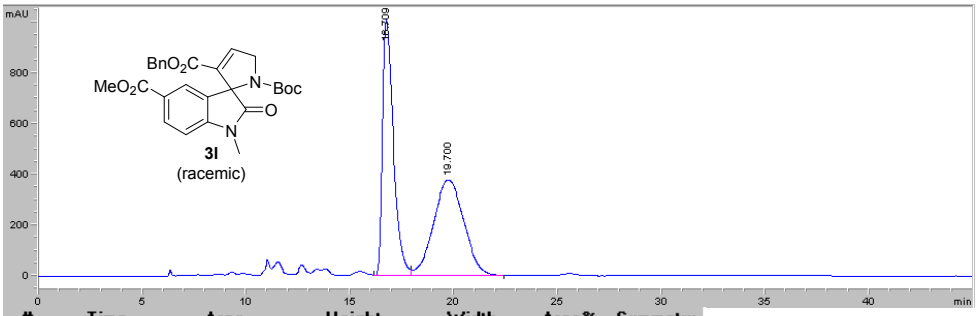


#	Time	Area	Height	Width	Area%	Symmetry
1	14.209	477.4	27.1	0.294	0.923	0.857
2	17.634	51223.3	637.5	1.3392	99.077	1.04

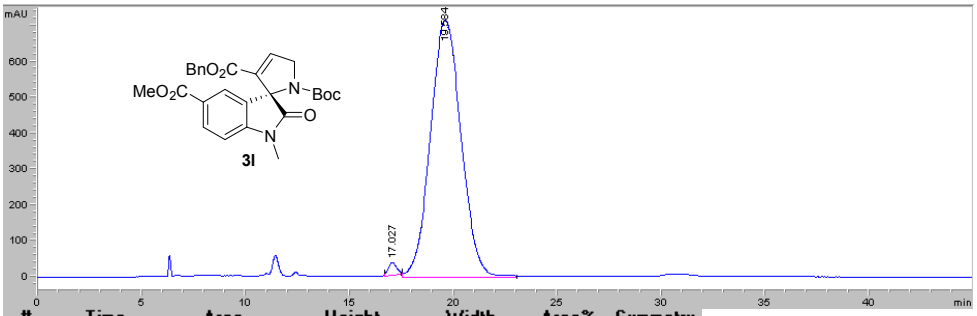


Chemical Formula: $C_{27}H_{28}N_2O_7$
Exact Mass: 492.18965
Molecular Weight: 492.52800

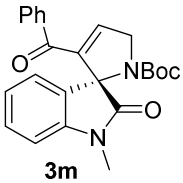
Yield: 77%; *e.e* = 97.5%; $[\alpha]^{20}_D$ = -60.4° (*c* 0.92, CH_2Cl_2); IR ν_{max}/cm^{-1} 3065, 2977, 2864, 1790, 1712; ^1H NMR (3:1 rotamer ratio, asterisks denote minor rotamer peaks, 400 MHz, $CDCl_3$) δ 8.05 (dd, *J* = 8.2, 1.7 Hz, 1H), 8.00* (dd, *J* = 8.2, 1.7 Hz, 0.33H), 7.84* (d, *J* = 1.6 Hz, 0.2H), 7.73 (d, *J* = 1.7 Hz, 1H), 7.33 – 7.26 (m, 4H), 7.24 (t, *J* = 2.1 Hz, 1H), 7.19* (t, *J* = 2.1 Hz, 0.3H), 7.07 – 6.96 (m, 2H), 6.65* (d, *J* = 8.2 Hz, 0.3H), 6.64 (d, *J* = 8.2 Hz, 1H), 4.91 (d, *J* = 12.0 Hz, 1H), 4.90* (d, *J* = 12.2 Hz, 0.3H), 4.86 (d, *J* = 12.0 Hz, 1H), 4.83* (d, *J* = 12.1 Hz, 0.3H), 4.65 (dd, *J* = 18.5, 2.2 Hz, 1H), 4.62* (dd, *J* = 18.2, 2.2 Hz, 0.3H), 4.59 (dd, *J* = 18.5, 2.2 Hz, 1H), 4.52* (dd, *J* = 18.3, 2.1 Hz, 0.3H), 3.89 (s, 3H), 3.88* (s, 1H), 2.98* (s, 1H), 2.94 (s, 3H), 1.35* (s, 2.6H), 1.05 (s, 8H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.46, 167.12*, 166.82, 160.80*, 160.71, 152.22, 151.86*, 148.94*, 148.74, 141.73*, 141.57, 134.76, 134.38*, 133.97*, 133.93, 132.99*, 132.37, 129.43, 128.85, 128.78, 128.75, 124.72, 124.49*, 124.17, 124.13*, 108.11*, 107.68, 81.29, 81.25*, 72.07, 67.27, 67.24*, 54.32*, 54.12, 52.28, 52.19*, 28.51, 28.03, 27.93*, 26.70*, 26.45; HRMS [ESI]: Calculated for $C_{27}H_{29}N_2O_7$ $[M+H^+]$: 493.19693, found: 493.19690; RT = 19.6 min. (Chiral HPLC, column : chiralpak IC, eluent: 50% of mixture of EtOH-DCM (1 : 50) in isohexane, Flow rate: 0.5 mL/min).



#	Time	Area	Height	Width	Area%	Symmetry
1	16.709	36184.4	1006.1	0.5356	48.553	0.469
2	19.7	38341.1	377.4	1.4152	51.447	0.927



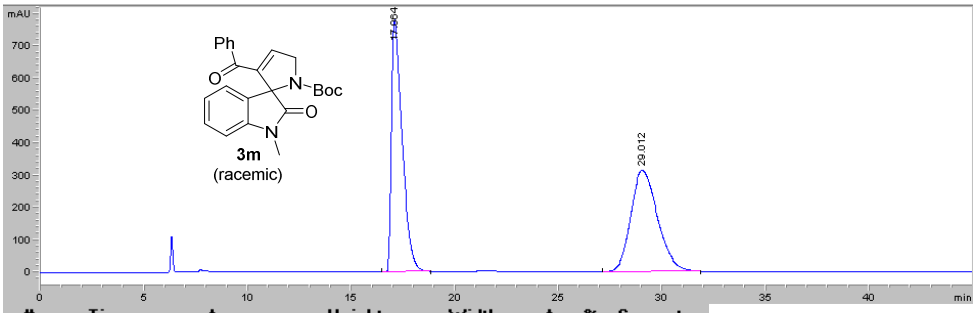
#	Time	Area	Height	Width	Area%	Symmetry
1	17.027	930.5	34	0.4559	1.251	0.961
2	19.584	73454.8	714.9	1.7124	98.749	0.927



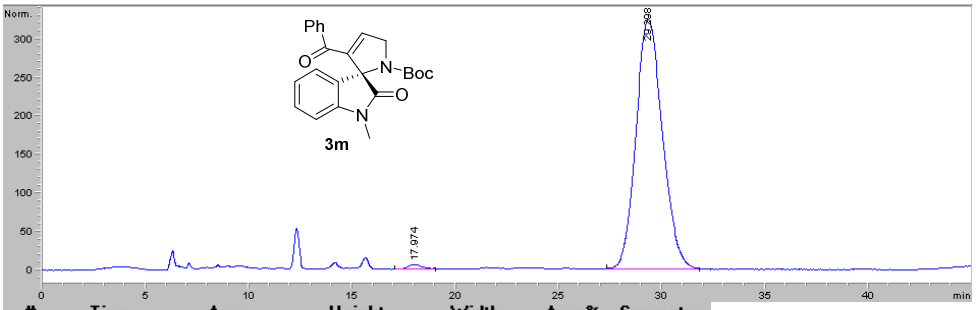
Chemical Formula: $C_{24}H_{24}N_2O_4$
Exact Mass: 404.17361
Molecular Weight: 404.46600

Yield: 71%; *e.e* = 97.7%; $[\alpha]^{20}_D$ = -3.1^o (*c* 0.7, CH_2Cl_2); IR ν_{max}/cm^{-1} 3058, 2981, 2930, 1786, 1724, 1705; ^{1}H NMR (7:1 rotamer ratio, asterisks denote minor rotamer peaks, 400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 7.1 Hz, 1H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.30 – 7.26 (m, 1H), 7.12 (d, *J* = 7.2 Hz, 1H), 6.98 (t, *J* = 7.4 Hz, 1H), 6.95* (t, *J* = 7.4 Hz, 0.15H), 6.85* (d, *J* = 7.9 Hz, 0.16H), 6.83 (t, *J* = 2.2 Hz, 1H), 6.81 (d, *J* = 7.8 Hz, 1H), 6.75* (t, *J* = 2.0 Hz, 1H), 4.74 (d, *J* = 2.1 Hz, 1H), 4.68* (dd, *J* = 20.5, 2.1 Hz, 1H), 3.35* (s, 0.4H), 3.30 (s, 1H), 1.39* (s, 1.4H), 1.09 (s, 9H); ^{13}C NMR (asterisks denote minor rotamer peaks, 101 MHz, $CDCl_3$) δ 189.69, 174.38, 152.70, 145.05, 145.01*, 141.60, 140.97, 140.81*, 137.66*, 137.58, 132.97, 132.90*, 129.77*, 129.73, 129.15, 128.66*, 128.63, 122.70, 122.55*, 122.46, 122.33*, 108.68*, 108.20, 81.05, 80.96*, 73.50, 54.95*, 54.71, 28.58, 28.04, 27.05*, 26.76; HRMS [ESI]: Calculated for $C_{24}H_{25}N_2O_4$ [M+H$^+$]: 405.18088, found:

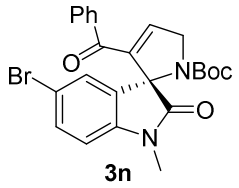
405.18136; RT = 29.3 min. (Chiral HPLC, column : chiralpak IC, eluent: 50% of mixture of EtOH-DCM (1 : 50) in isohexane, Flow rate: 0.5 mL/min).



#	Time	Area	Height	Width	Area%	Symmetry
1	17.064	27239.5	779.4	0.4997	48.994	0.367
2	29.012	28358.3	314.4	1.3062	51.006	0.723



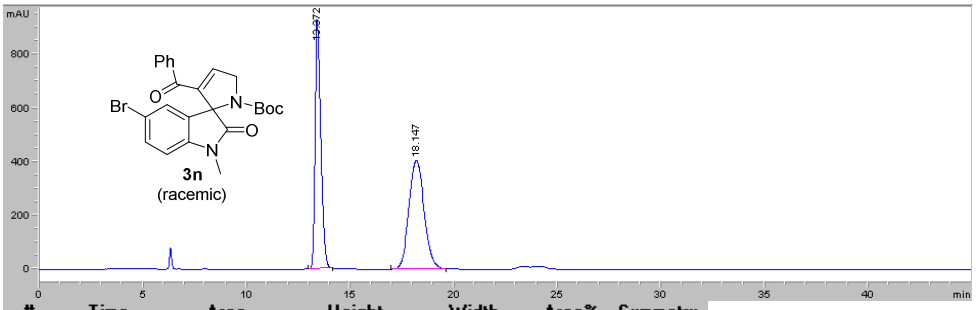
#	Time	Area	Height	Width	Area%	Symmetry
1	17.974	329	6.4	0.6103	1.122	0.827
2	29.298	28980.9	323.1	1.0545	98.878	0.828



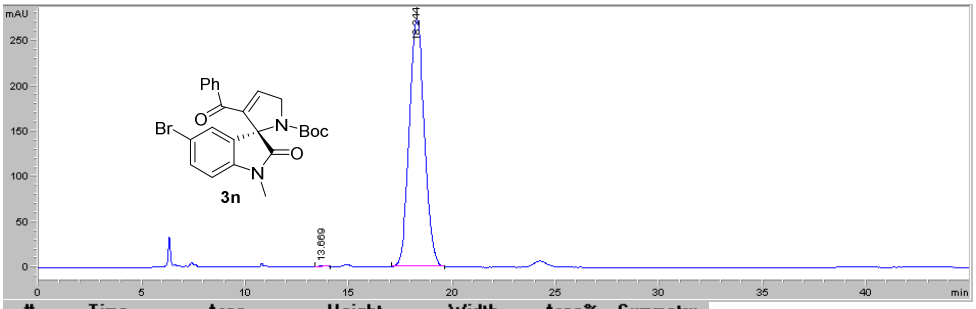
Chemical Formula: $C_{24}H_{23}BrN_2O_4$
Exact Mass: 482.08412
Molecular Weight: 483.36200

Yield: 78%; *e.e* = 99.6%; $[\alpha]^{20}_{D}$ = -35.4° (*c* 0.78, CH_2Cl_2); IR ν_{max}/cm^{-1} 2978, 2928, 1788, 1733, 1705; ^1H NMR (4:1 rotamer ratio, asterisks denote minor rotamer peaks, 400 MHz, $CDCl_3$) δ 7.67 – 7.62 (m, 2H), 7.56 – 7.50 (m, 1H), 7.44 – 7.39 (m, 3H), 7.37* (dd, *J* = 8.3, 2.0 Hz, 0.25H), 7.23 (d, *J* = 2.0 Hz, 1H), 7.22* (d, *J* = 2.0 Hz, 0.25H), 6.87 (t, *J* = 2.2 Hz, 1H), 6.79* (t, *J* = 2.2 Hz, 0.25H), 6.74* (d, *J* = 8.3 Hz, 0.25H), 6.70 (d, *J* = 8.3 Hz, 1H), 4.75 (dd, *J* = 18.6, 2.0 Hz, 1H), 4.72* (dd, *J* = 18.4, 2.2 Hz, 0.25H), 4.70 (dd, *J* = 18.7, 2.1 Hz, 1H), 4.62* (dd, *J* = 18.5, 2.1 Hz, 0.25H), 3.32* (s, 0.7H), 3.28 (s, 3H), 1.40* (s, 2H), 1.13 (s, 9H); ^{13}C NMR (asterisks denote minor rotamer peaks, 101 MHz, $CDCl_3$) δ 189.54, 173.87, 152.44, 151.95*, 144.26*, 144.15, 141.75, 141.62*, 141.25, 141.22*, 137.45*, 137.37, 133.10, 133.03*, 132.52*, 132.45, 131.28, 130.48*, 129.12, 128.75, 128.73*, 125.74,

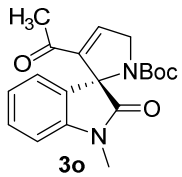
125.60*, 115.11, 115.04*, 110.10*, 109.61, 81.42, 81.33*, 73.65*, 73.25, 54.99*, 54.80, 29.90*, 28.57, 28.09, 27.11*, 26.84; HRMS [ESI]: Calculated for $C_{24}H_{24}BrN_2O_4$ [M+H$^+$]: 483.09140, found: 483.09130; Calculated for $C_{24}H_{24}{}^{81}BrN_2O_4$ [M+H$^+$]: 485.08935, found: 485.08951; RT = 18.2 min. (Chiral HPLC, column : chiralpak IC, eluent: 50% of mixture of EtOH-DCM (1 : 50) in isohexane, Flow rate: 0.5 mL/min).



#	Time	Area	Height	Width	Area%	Symmetry
1	13.372	19079.9	927	0.3221	47.934	0.631
2	18.147	20724.9	404	0.7745	52.066	0.875



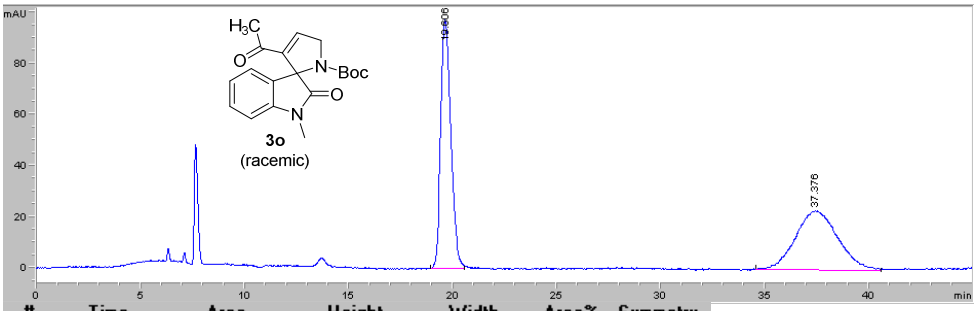
#	Time	Area	Height	Width	Area%	Symmetry
1	13.669	27.3	1.2	0.2758	0.196	1.087
2	18.244	13854.1	271.7	0.7808	99.804	0.908



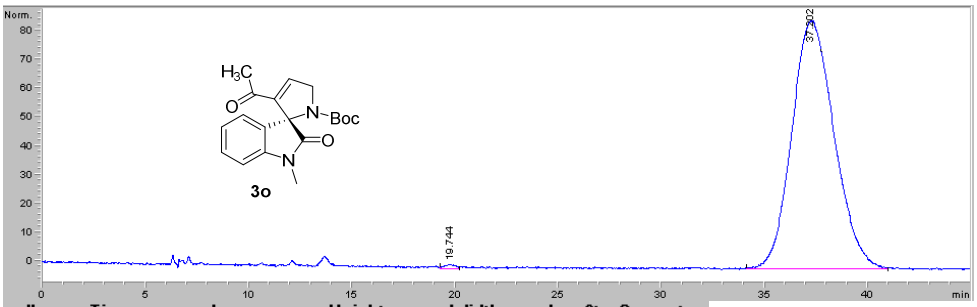
Chemical Formula: $C_{19}H_{22}N_2O_4$
Exact Mass: 342.15796
Molecular Weight: 342.39500

Yield: 87%; *e.e* = 99.1%; $[\alpha]^{20}_D$ = -48.99^o (*c* 1.14, CH_2Cl_2); IR ν_{max}/cm^{-1} 3058, 2977, 2931, 2865, 1784, 1723, 1700; ^{1}H NMR (7:1 rotamer ratio, asterisks denote minor rotamer peaks, 400 MHz, $CDCl_3$) δ 7.31 – 7.26 (m, 1H), 7.14* (d, *J* = 7.2 Hz, 0.1H), 7.02 (t, *J* = 2.1 Hz, 1H), 7.00 – 6.95 (m, 2H), 6.95 – 6.93* (m, 0.15H), 6.85* (d, *J* = 7.9 Hz, 0.16H), 6.80 (d, *J* = 7.7 Hz, 1H), 4.69 (dd, *J* = 18.8, 2.4 Hz, 1H), 4.67* (dd, *J* = 18.5, 2.3 Hz, 0.14H), 4.64 (dd, *J* = 19.1, 2.4 Hz, 1H), 4.55* (dd, *J* = 18.6, 2.1 Hz, 0.14H), 3.29* (s, 0.46H), 3.24 (s, 3H), 2.21 (s, 3H), 2.19* (s, 0.43H), 1.36* (s, 1.4H), 1.06 (s, 9H); ^{13}C NMR (asterisks denote minor

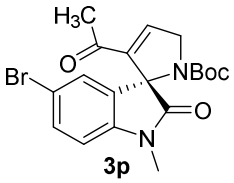
rotamer peaks, 101 MHz, $CDCl_3$) δ 192.30, 174.23, 152.64, 144.92, 143.32, 139.71, 139.67*, 129.62*, 129.58, 129.47*, 122.57, 122.42*, 122.33, 122.19*, 108.54*, 108.06, 81.01, 80.91*, 72.67, 54.52*, 54.29, 28.54, 28.00, 27.87*, 26.95*, 26.73, 26.65; HRMS [ESI]: Calculated for $C_{19}H_{23}N_2O_4$ [$M+H^+$]: 343.16523, found: 343.16574; RT = 37.2 min. (Chiral HPLC, column : chiralpak IC, eluent: 50% of mixture of EtOH-DCM (1 : 50) in isohexane, Flow rate: 0.5 mL/min).



#	Time	Area	Height	Width	Area%	Symmetry
1	19.606	3271.1	97.4	0.4899	50.042	0.733
2	37.376	3265.6	23.1	2.3584	49.958	0.828



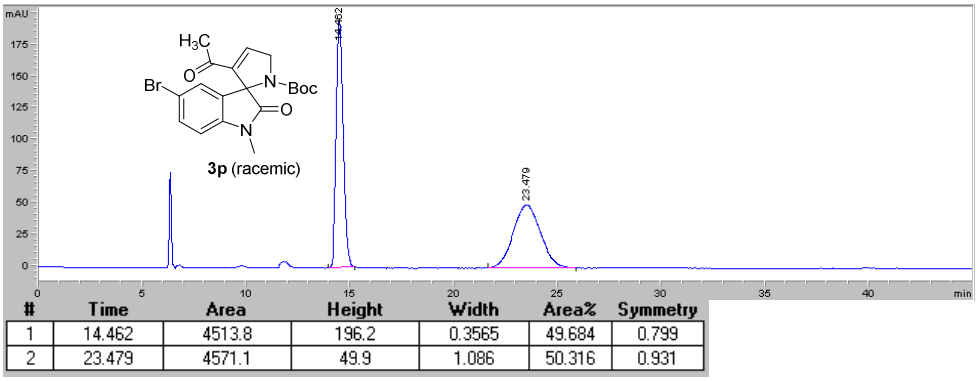
#	Time	Area	Height	Width	Area%	Symmetry
1	19.744	56.9	1.5	0.6272	0.455	1.061
2	37.202	12436.4	86.5	2.3963	99.545	0.779



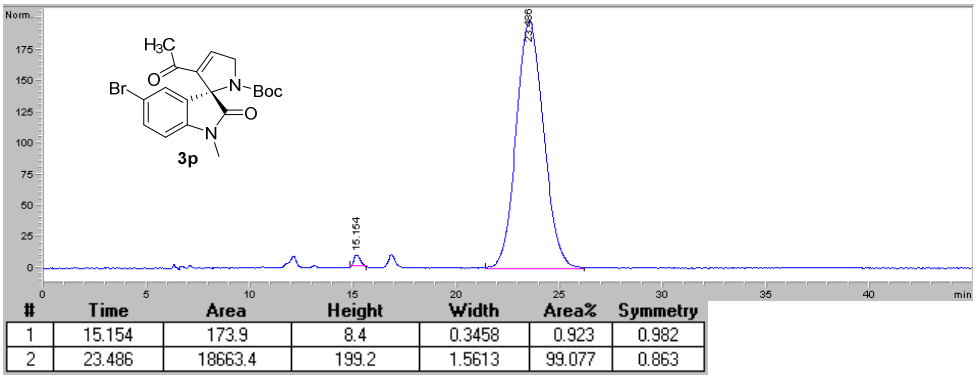
Chemical Formula: $C_{19}H_{21}BrN_2O_4$
Exact Mass: 420.06847
Molecular Weight: 421.29100

Yield: 82%; *e.e* = 98.1%; $[\alpha]^{20}_D$ = -121.5° (*c* 0.93, CH_2Cl_2); IR ν_{max}/cm^{-1} 3076, 2977, 2932, 2866, 1786, 1729, 1702; ^1H NMR (4.5:1 rotamer ratio, asterisks denote minor rotamer peaks, 400 MHz, $CDCl_3$) δ 7.39 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.36* (dd, *J* = 8.3, 2.0 Hz, 0.22H), 7.09 (d, *J* = 2.0 Hz, 1H), 7.07* (d, *J* = 2.0 Hz, 0.22H), 7.04 (t, *J* = 2.2 Hz, 1H), 6.97* (t, *J* = 2.2 Hz, 0.22H), 6.71* (d, *J* = 8.3 Hz, 0.22H), 6.67 (d, *J* = 8.2 Hz, 1H), 4.68 (dd, *J* = 18.9, 2.3 Hz, 1H), 4.65* (dd, *J* = 18.9, 2.3 Hz, 0.2H), 4.61 (dd, *J* = 18.8, 2.2 Hz, 1H), 4.53* (dd, *J* = 18.6,

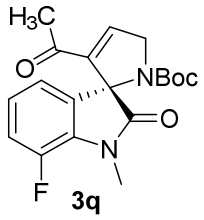
2.1 Hz, 0.22H), 3.25* (s, 0.7H), 3.20 (s, 3H), 2.22 (s, 3H), 2.21* (s, 0.7H), 1.36* (s, 2H), 1.09 (s, 9H); ^{13}C NMR (asterisks denote minor rotamer peaks, 101 MHz, $CDCl_3$) δ 192.31, 192.14*, 173.71, 152.36, 151.76*, 144.15*, 144.02, 142.93, 142.88*, 140.25, 132.33*, 132.27, 131.50, 130.74*, 125.66, 125.50*, 114.99, 114.92*, 109.98*, 109.48, 81.38, 81.28*, 72.76*, 72.42, 54.57*, 54.39, 28.53, 28.04, 27.01*, 26.73, 26.70; HRMS [ESI]: Calculated for $C_{19}H_{22}BrN_2O_4$ $[M+H^+]$: 421.07575, found: 421.07599; Calculated for $C_{19}H_{22}{}^{81}BrN_2O_4$ $[M+H^+]$: 423.07370, found: 423.07393; RT = 23.5 min. (Chiral HPLC, column : chiralpak IC, eluent: 50% of mixture of EtOH-DCM (1 : 50) in isohexane, Flow rate: 0.5 mL/min).



#	Time	Area	Height	Width	Area%	Symmetry
1	14.462	4513.8	196.2	0.3565	49.684	0.799
2	23.479	4571.1	49.9	1.086	50.316	0.931



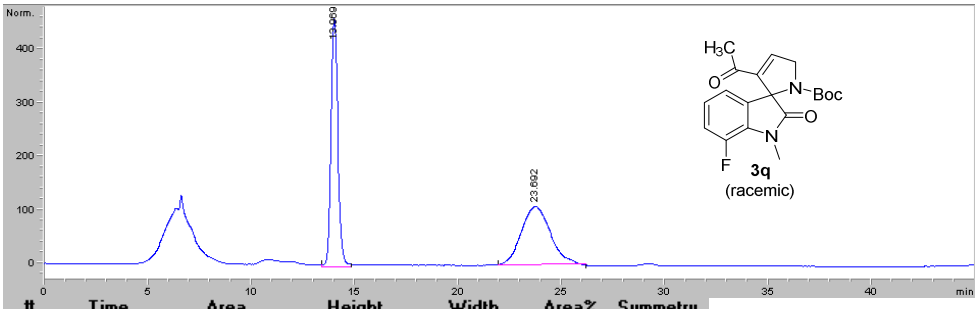
#	Time	Area	Height	Width	Area%	Symmetry
1	15.154	173.9	8.4	0.3458	0.923	0.982
2	23.486	18663.4	199.2	1.5613	99.077	0.863



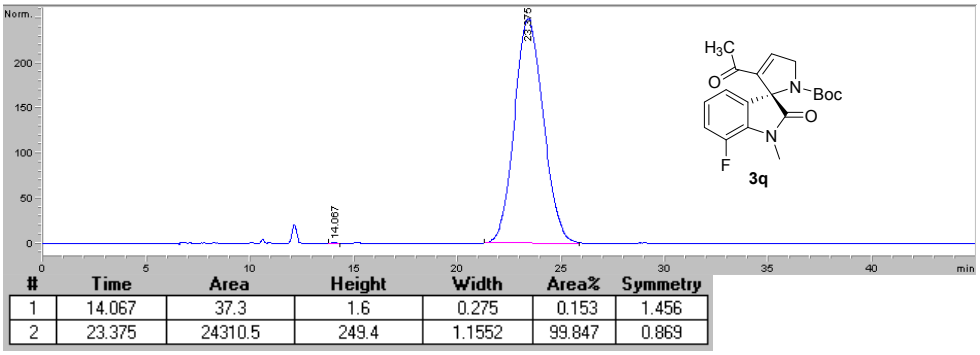
Chemical Formula: $C_{19}H_{21}FN_2O_4$
Exact Mass: 360.14854
Molecular Weight: 360.38540

Yield: 85%; *e.e* = 99.7%; $[\alpha]^{20}_D$ = -54.7° (*c* 1.0, CH_2Cl_2); IR ν_{max}/cm^{-1} 3076, 2978, 2931, 2866, 1786, 1729, 1702; ^{1}H NMR (6:1 rotamer ratio, asterisks denote minor rotamer peaks, 400 MHz, $CDCl_3$) δ 7.03 (t, *J* = 2.2 Hz, 1H), 7.02 – 6.97 (m, 1H), 6.96* (t, *J* = 2.2 Hz, 0.17H), 6.95 – 6.92 (m, 1H), 6.92 – 6.86* (m, 0.16H), 6.83 (dd, *J* = 8.2, 4.0 Hz, 1H), 6.77*

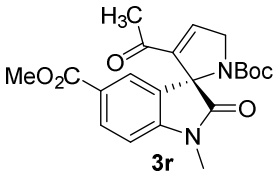
(dd, *J* = 7.3, 1.0 Hz, 0.15H), 6.76 (dd, *J* = 7.3, 1.1 Hz, 1H), 4.68 (dd, *J* = 18.8, 2.3 Hz, 1H), 4.67* (dd, *J* = 18.8, 2.2 Hz, 0.16H), 4.62 (dd, *J* = 18.9, 2.2 Hz, 1H), 4.53* (dd, *J* = 18.6, 2.1 Hz, 0.17H), 3.49* (d, *J* = 2.6 Hz, 0.5H), 3.45 (d, *J* = 2.7 Hz, 3H), 2.23 (s, 3H), 2.20* (s, 0.5H), 1.37* (s, 1.5H), 1.12 (s, 9H); ^{13}C NMR (asterisks denote minor rotamer peaks, 101 MHz, $CDCl_3$) δ 192.31, 192.11*, 173.99, 152.44, 151.77*, 149.07, 146.65, 143.19, 143.16*, 139.93, 139.87*, 132.41, 123.12, 123.06, 122.91*, 122.84*, 118.24, 118.21, 118.08*, 118.05*, 117.8*8, 117.68*, 117.64, 117.44, 81.33, 81.16*, 72.61, 72.58, 54.52*, 54.33, 29.54*, 29.49*, 29.27, 29.21, 28.53, 28.02, 27.91*, 26.71*, 26.68; HRMS [ESI]: Calculated for $C_{19}H_{22}FN_2O_4$ [M+H$^+$]: 361.15581, found: 361.15632; RT = 23.4 min. (Chiral HPLC, column : chiralpak IC, eluent: 50% of mixture of EtOH-DCM (1 : 50) in isohexane, Flow rate: 0.5 mL/min).



#	Time	Area	Height	Width	Area%	Symmetry
1	13.969	10972.2	463.3	0.3948	50.183	0.747
2	23.692	10892.1	110.3	1.6464	49.817	0.869



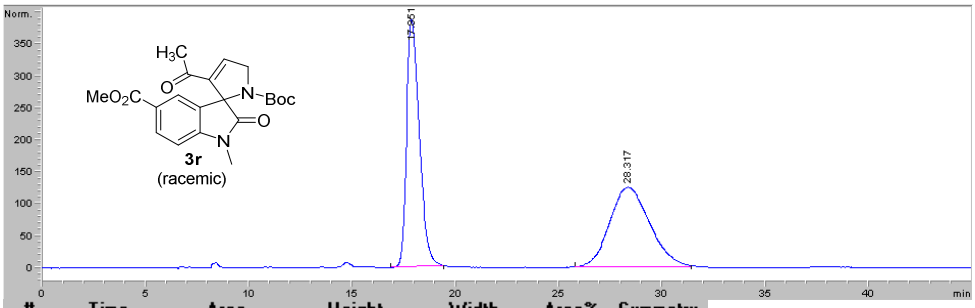
#	Time	Area	Height	Width	Area%	Symmetry
1	14.067	37.3	1.6	0.275	0.153	1.456
2	23.375	24310.5	249.4	1.1552	99.847	0.869



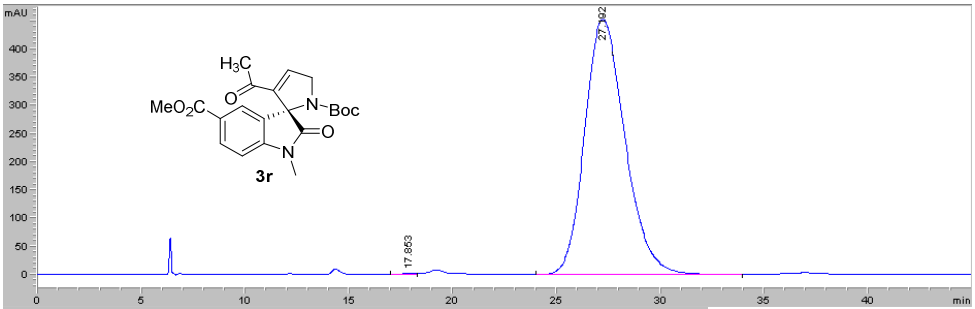
Chemical Formula: $C_{21}H_{24}N_2O_6$
Exact Mass: 400.16344
Molecular Weight: 400.43100

Yield: 87%; *e.e* = 99.6%; $[\alpha]^{20}_D$ = -129.3^o (*c* 1.15, CH_2Cl_2); IR ν_{max}/cm^{-1} 2977, 1787, 1736, 1711; ^{1}H NMR (4:1 rotamer ratio, asterisks denote minor rotamer peaks, 400 MHz, $CDCl_3$) δ

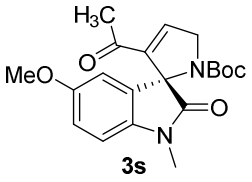
8.05 (dd, *J* = 8.2, 1.7 Hz, 1H), 8.01* (dd, *J* = 8.2, 1.7 Hz, 0.23H), 7.67 (dd, *J* = 1.7, 0.4 Hz, 1H), 7.06 (t, *J* = 2.2 Hz, 1H), 6.99* (t, *J* = 2.2 Hz, 0.25H), 6.88* (d, *J* = 8.2 Hz, 0.25H), 6.84 (d, *J* = 8.2 Hz, 1H), 4.72 (dd, *J* = 18.8, 2.2 Hz, 1H), 4.69* (dd, *J* = 18.8, 2.2 Hz, 0.24H), 4.67 (dd, *J* = 18.7, 2.1 Hz, 2H), 4.59* (dd, *J* = 18.6, 2.1 Hz, 0.25H), 3.87 (s, 3H), 3.86* (s, 0.74H), 3.32* (s, 0.74H), 3.27 (s, 3H), 2.23 (s, 3H), 2.21* (s, 0.74H), 1.36* (s, 2H), 1.07 (s, 9H); ^{13}C NMR (asterisks denote minor rotamer peaks, 101 MHz, $CDCl_3$) δ 192.40, 192.23*, 174.61, 167.24*, 166.90, 152.33, 151.77*, 149.23*, 149.03, 142.97*, 142.91, 140.31, 132.34, 129.63, 128.88*, 124.53, 124.31*, 123.69, 108.00*, 107.57, 81.33, 81.25*, 72.18, 54.5*8, 54.42, 53.62*, 52.22, 52.15*, 28.53, 28.05, 27.13*, 26.86, 26.66; HRMS [ESI]: Calculated for $C_{21}H_{24}N_2O_6$ [M+H$^+$]: 401.17071, found: 401.17101; RT = 27.2 min. (Chiral HPLC, column : chiralpak IC, eluent: 50% of mixture of EtOH-DCM (1 : 50) in isohexane, Flow rate: 0.5 mL/min).



#	Time	Area	Height	Width	Area%	Symmetry
1	17.851	16673.8	386.5	0.6313	49.324	0.645
2	28.317	17130.5	125.6	1.6009	50.676	0.806

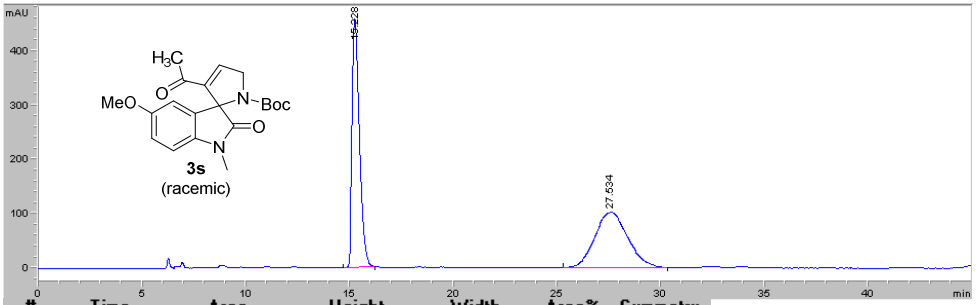


#	Time	Area	Height	Width	Area%	Symmetry
1	17.853	115.5	2.5	0.7742	0.188	0
2	27.192	61453.7	453.2	2.2601	99.812	0.785

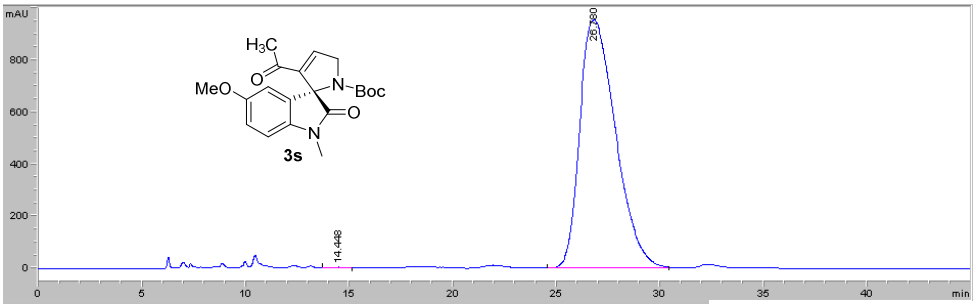


Chemical Formula: $C_{20}H_{24}N_2O_5$
Exact Mass: 372.16852
Molecular Weight: 372.42100

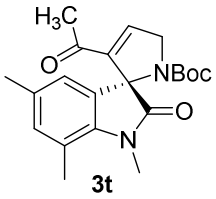
Yield: 83%; *e.e* = 99.7%; $[\alpha]^{20}_{D}$ = -91.6° (*c* 0.98, CH_2Cl_2); IR ν_{max}/cm^{-1} 3070, 2975, 2933, 2837, 1784, 1699, 1677; ^1H NMR (6:1 rotamer ratio, asterisks denote minor rotamer peaks, 400 MHz, $CDCl_3$) δ 7.02 (t, *J* = 2.2 Hz, 1H), 6.95* (t, *J* = 2.1 Hz, 0.16H), 6.79 (dd, *J* = 8.4, 2.5 Hz, 1H), 6.76* (d, *J* = 2.3 Hz, 0.15H), 6.74* (d, *J* = 8.5 Hz, 0.2H), 6.69 (d, *J* = 8.4 Hz, 1H), 6.60 (d, *J* = 2.4 Hz, 1H), 4.68 (dd, *J* = 18.8, 2.3 Hz, 1H), 4.66* (dd, *J* = 18.8, 2.3 Hz, 0.13H), 4.62 (dd, *J* = 18.8, 2.2 Hz, 1H), 4.53* (dd, *J* = 18.6, 2.0 Hz, 0.17H), 3.72 (s, 4H), 3.26* (s, 0.5H), 3.21 (s, 3H), 2.21 (s, 3H), 2.19* (s, 0.5H), 1.36* (s, 1.5H), 1.08 (s, 9H); ^{13}C NMR (asterisks denote minor rotamer peaks, 101 MHz, $CDCl_3$) δ 192.26, 192.10*, 173.88, 156.16, 155.96*, 152.64, 151.72*, 143.31, 143.26*, 139.77, 139.72*, 138.65*, 138.53, 130.73, 130.05*, 113.45, 112.93*, 110.60*, 110.18, 108.63*, 108.28, 81.05, 80.92*, 72.95, 56.01, 55.90*, 54.53*, 54.29, 28.55, 28.05, 27.03*, 26.75, 26.72; HRMS [ESI]: Calculated for $C_{20}H_{25}N_2O_5$ $[M+H^+]$: 373.17580, found: 373.17631; RT = 26.8 min. (Chiral HPLC, chiralpak IC-column and using 60% of mixture of EtOH-DCM (1 : 50) in isohexane as eluent, Flow rate: 0.5 mL/min).



#	Time	Area	Height	Width	Area%	Symmetry
1	15.228	11039.4	457.4	0.3636	49.097	0.576
2	27.534	11445.7	102.9	1.31	50.903	0.852



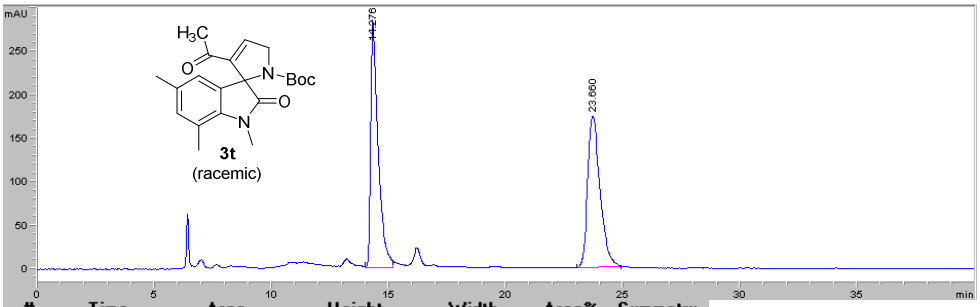
#	Time	Area	Height	Width	Area%	Symmetry
1	14.448	158.6	3.2	0.8141	0.138	1.486
2	26.78	115061.4	954.5	1.4164	99.862	0.63



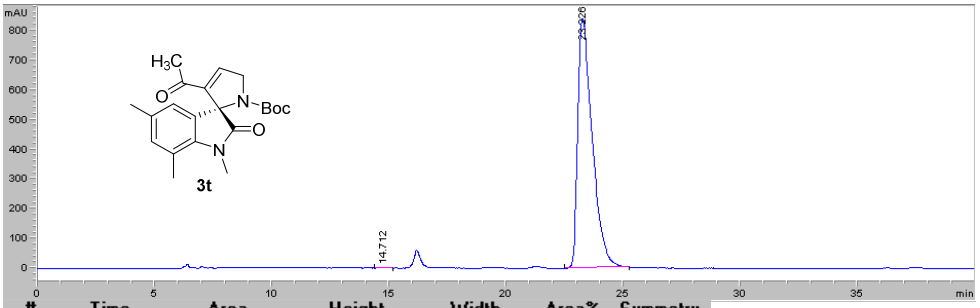
3t

Chemical Formula: $C_{21}H_{26}N_2O_4$
Exact Mass: 370.18926
Molecular Weight: 370.44900

Yield: 66%; *e.e* = 99.7%; $[\alpha]^{20}_{D}$ = -38.9° (*c* 0.62, CH_2Cl_2); IR ν_{max}/cm^{-1} 2975, 2924, 2862, 1703, 1680; ^1H NMR (7:1 rotamer ratio, asterisks denote minor rotamer peaks, 400 MHz, $CDCl_3$) δ 6.93 (t, *J* = 2.2 Hz, 1H), 6.86* (t, *J* = 2.2 Hz, 0.14H), 6.74 (s, 1H), 6.71* (s, 0.13H), 6.54 (s, 1H), 4.61 (dd, *J* = 18.4, 1.9 Hz, 1H), 4.60* (dd, *J* = 18.6, 2.1 Hz, 0.14H), 4.56 (dd, *J* = 18.4, 2.0 Hz, 1H), 4.47* (dd, *J* = 18.6, 2.1 Hz, 0.15H), 3.46* (s, 0.4H), 3.43 (s, 3H), 2.46* (s, 0.4H), 2.44 (s, 3H), 2.16 (s, 3H), 2.13 (s, 3H), 2.12* (s, 0.4H), 1.32* (s, 1.4H), 1.04 (s, 9H); ^{13}C NMR (asterisks denote minor rotamer peaks, 101 MHz, $CDCl_3$) δ 192.37, 174.98, 152.73, 143.69, 140.14, 139.36, 133.65, 131.92, 130.21, 121.15, 119.22, 80.92, 72.39, 54.20, 30.14, 28.62, 27.99, 26.77, 20.86, 19.00; HRMS [ESI]: Calculated for $C_{21}H_{27}N_2O_4$ $[M+H^+]$: 371.19653, found: 371.19723; RT = 23.2 min. (Chiral HPLC, column : chiralpak IA, eluent: 30% of mixture of EtOH-DCM (1 : 50) in isohexane, Flow rate: 0.5 mL/min).

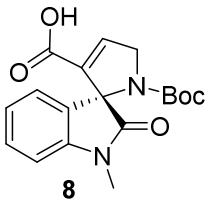


#	Time	Area	Height	Width	Area%	Symmetry
1	14.276	6528.9	285.1	0.3312	50.425	0.407
2	23.66	6418.8	174.2	0.5379	49.575	0.637



#	Time	Area	Height	Width	Area%	Symmetry
1	14.712	46.6	1.4	0.5742	0.130	0.603
2	23.226	35790.6	837.7	0.5924	99.870	0.434

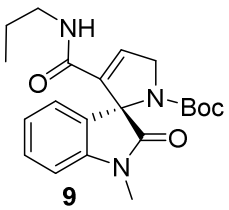
IV. Elaboration of the [3+2]-adducts:



8

Chemical Formula: $C_{18}H_{20}N_2O_5$
Exact Mass: 344.13722
Molecular Weight: 344.36700

To a solution of the [3+2-adduct] **3g** (170 mg, 0.39 mmol) in methanol (3 mL) 10 wt% palladium on carbon (34 mg, 20 wt%) was added under argon atmosphere and then it was purged with hydrogen gas. Then the reaction was stirred under 1 atm H_2 pressure at room temperature for 12 h. After completion of the reaction based on TLC and LCMS analysis, it was concentrated under reduced pressure to give crude compound. The crude was purified by column chromatography over silica gel using 5-15% MeOH in DCM as eluent to give **8**. Yield: 111 mg (83%); $[\alpha]^{20}_D$ = -37.4^o (*c* 0.9, CH_3OH); IR ν_{max}/cm^{-1} 3393, 2979, 2936, 2509, 1704; H NMR (4:1 rotamer ratio, asterisks denote minor rotamer peaks, 500 MHz, CD_3OD): δ 7.24 (td, *J* = 7.7, 1.0 Hz, 1H), 7.20* (td, *J* = 7.8, 1.2 Hz, 0.29H), 7.04 (d, *J* = 7.2 Hz, 1H), 7.02* (d, *J* = 7.4 Hz, 0.26H), 6.99 – 6.90 (m, 2H), 6.96 – 6.90* (m, 0.4H), 6.86 (d, *J* = 7.6 Hz, 1H), 6.85* (d, *J* = 6.7 Hz, 0.2H), 4.45 (dd, *J* = 17.8, 1.9 Hz, 1H), 4.40 (dd, *J* = 17.7, 2.1 Hz, 1H), 3.15* (s, 0.68H), 3.13 (s, 3H), 1.27* (s, 2H), 0.97 (s, 9H); 13C NMR (asterisks denote minor rotamer peaks, 126 MHz, CD_3OD): δ 175.68, 175.57*, 152.76, 152.14*, 144.62*, 144.55, 137.81, 129.71, 129.15, 129.08*, 128.92*, 122.61, 122.49*, 122.21, 122.20*,108.28*, 108.22, 80.74, 80.67*, 73.09*, 72.96, 53.85*, 53.53, 27.16, 26.79*, 26.75, 25.51*, 25.49; HRMS [ESI]: Calculated for $C_{18}H_{21}N_2O_5$ [M+H$^+$]: 345.14450, found: 345.14474.

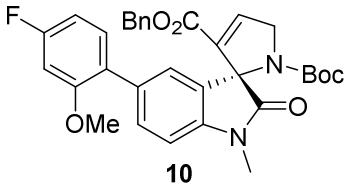


9

Chemical Formula: $C_{21}H_{27}N_3O_4$
Exact Mass: 385.20016
Molecular Weight: 385.46400

The solution of the acid **8** (50 mg, 0.145 mmol) and HBTU (110 mg, 0.290 mmol) in dry DMF (2 mL) was stirred for 10 min at rt. Then propylamine (13.0 mg, 0.22 mmol) was added followed by DIPEA (38 mg, 0.291 mmol) and was allowed to stir at rt overnight. LCMS was

used to monitor the reaction. Then the solvent was removed in vacuo to give crude. The crude was purified by column chromatography using 50-70% EtOAc in petroleum ether as eluent to afford pure compound **9**. Yield: 28 mg (50%); $[\alpha]^{20}_{D}$ = -5.4^{o} (*c* 1.0, CH_2Cl_2); IR ν_{max}/cm^{-1} 3348, 3058, 2964, 2929, 2873, 1783, 1715; ^{1}H NMR (4:1 rotamer ratio, asterisks denote minor rotamer peaks, 500 MHz, $CDCl_3$) δ 7.24 (t, *J* = 7.6 Hz, 1H), 7.03* (d, *J* = 8.0 Hz, 0.31H), 7.00 (d, *J* = 6.8 Hz, 1H), 6.95 (d, *J* = 7.4 Hz, 1H), 6.94* (d, *J* = 7.4 Hz, 0.35H), 6.81* (d, *J* = 7.8 Hz, 0.29H), 6.64* (t, *J* = 2.0 Hz, 0.26H), 6.75 (d, *J* = 7.8 Hz, 1H), 6.60 (t, *J* = 2.1 Hz, 1H), 5.63 (t, *J* = 5.4 Hz, 1H), 5.43* (t, *J* = 5.6 Hz, 0.23H), 4.54 (dd, *J* = 17.4, 2.2 Hz, 1H), 4.53* (dd, *J* = 17.2, 2.2 Hz, 0.26H), 4.48 (dd, *J* = 17.4, 2.1 Hz, 1H), 4.39* (dd, *J* = 17.2, 2.0 Hz, 0.25H), 3.24* (s, 0.6H), 3.19 (s, 2H), 3.03 – 2.94 (m, 2H), 1.38 – 1.33* (m, 0.7H), 1.34 – 1.26 (m, 2H), 1.18* (s, 3H), 0.67* (t, *J* = 7.4 Hz, 1H), 1.00 (s, 9H), 0.71 (t, *J* = 7.4 Hz, 3H; ^{13}C NMR (asterisks denote minor rotamer peaks, 126 MHz, $CDCl_3$) δ 173.23, 173.20*, 160.00, 151.40, 143.37, 143.16*, 137.10, 136.69*, 132.08*, 130.72, 128.80*, 128.58, 128.06, 121.78*, 121.76*, 121.63, 121.59, 107.60*, 107.05, 79.73, 79.69*, 72.22*, 72.06, 52.92*, 52.74, 40.01, 39.97*, 30.90*, 28.68, 28.64*, 27.28, 26.77, 26.72*, 26.66*, 25.80*, 25.52, 21.51, 21.42*, 10.14, 10.09*; HRMS [ESI]: Calculated for $C_{21}H_{28}N_3O_4$ [M+H^{+}]: 386.20743, found: 386.20767.

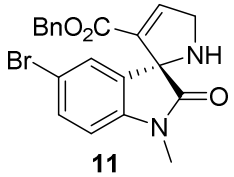


10

Chemical Formula: $C_{32}H_{31}FN_2O_6$
Exact Mass: 558.21661
Molecular Weight: 558.60640

To a solution of the [3+2-adduct] **3j** (14 mg, 0.027 mmol), 4-Fluoro-2-methoxyphenylboronic acid (5.6 mg, 0.033 mmol), K_2CO_3 (11.3 mg, 0.082 mmol) in DMF/H_2O (4:1, 0.5 mL) was added $Pd(PPh_3)_4$ (3.1 mg, 0.003 mmol) and argon was bubbled through the mixture for 2 min. The mixture was stirred at 80 °C (LC-MS control) for 4h and then it was cooled to room temperature. Diluted with water (5 mL), extracted with ether (3 x 15 mL). The combined ether layer was washed with water, dried over anhydrous sodium sulfate and concentrated under reduced pressure to give the crude. Purification of the crude material over silica gel column chromatography using 5-15% EtOAc in pet.ether afforded pure compound **10**. Yield: 8.4 mg (55%); $[\alpha]^{20}_{D}$ = -74.2^{o} (*c* 0.42, CH_2Cl_2); IR ν_{max}/cm^{-1} 3067, 2977, 2934, 1789, 1727, 1704; ^{1}H NMR (5:1 rotamer ratio, asterisks denote minor rotamer

peaks, 600 MHz, $CDCl_3$) δ 7.37* (dd, *J* = 8.1, 1.7 Hz, 0.2H), 7.35 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.28 – 7.24* (m, 0.6H), 7.24 – 7.20 (m, 3H), 7.16 (d, *J* = 1.6 Hz, 1H), 7.15 (t, *J* = 2.1 Hz, 1H), 7.10* (t, *J* = 2.0 Hz, 0.2H), 7.05 – 7.00* (m, 0.4H), 6.99 (dd, *J* = 7.1, 2.1 Hz, 2H), 6.96 – 6.93* (m, 0.4H), 6.92 – 6.86 (m, 2H), 6.84 – 6.78 (m, 1H), 6.62* (d, *J* = 8.1 Hz, 0.2H), 6.59 (d, *J* = 8.0 Hz, 1H), 4.912 (d, *J* = 12.2 Hz, 1H), 4.91* (d, *J* = 11.9 Hz, 0.2H), 4.82 (d, *J* = 12.2 Hz, 1H), 4.79* (d, *J* = 12.4 Hz, 0.2H), 4.57 (dd, *J* = 18.7, 2.0 Hz, 1H), 4.56* (dd, *J* = 17.0, 2.0 Hz, 0.2H), 4.53 (dd, *J* = 18.7, 2.2 Hz, 1H), 4.44* (dd, *J* = 18.3, 2.1 Hz, 0.2H), 3.63 (s, 3H), 3.61* (s, 0.6H), 2.96* (s, 0.6H), 2.92 (s, 3H), 1.30* (s, 1.8H), 1.01* (s, 9H); ^{13}C NMR (asterisks denote minor rotamer peaks, 151 MHz, $CDCl_3$) δ 174.04, 173.95*, 160.83*, 160.73, 158.07*, 157.94, 156.49*, 156.36, 152.70*, 152.64, 152.63, 152.33, 151.64*, 143.81*, 143.72, 141.03*, 140.89, 134.80, 134.32*, 134.19, 134.11*, 132.14 (d, *J* = 1.1 Hz), 132.07* (d, *J* = 7.6 Hz), 131.69*, 131.60 (d, *J* = 7.5 Hz), 131.36*, 130.62*, 130.38, 128.86, 128.71* (d, *J* = 1.9 Hz), 128.51 (d, *J* = 8.8 Hz), 128.51, 128.40, 128.37*, 128.35*, 128.13*, 127.90*, 123.95, 123.67*, 117.05* (d, *J* = 23.2 Hz), 117.01 (d, *J* = 23.3 Hz), 114.19 (d, *J* = 22.6 Hz), 113.96* (d, *J* = 22.6 Hz), 113.15* (d, *J* = 8.5 Hz), 112.58 (d, *J* = 8.4 Hz), 108.07*, 107.61, 80.83, 80.75*, 72.64*, 72.42, 66.89, 66.87*, 56.49*, 56.20, 54.12*, 53.83, 28.34, 27.76, 27.48*, 26.47*, 26.19; ^{19}F NMR (565 MHz, $CDCl_3$) δ -123.84; HRMS [ESI]: Calculated for $C_{32}H_{31}FN_2O_6$ [M+H$^+$]: 559.22389, found: 559.22392.

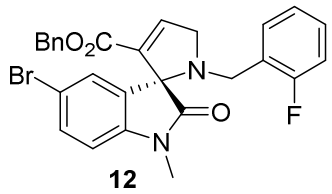


11

Chemical Formula: $C_{20}H_{17}BrN_2O_3$
Exact Mass: 412.04226
Molecular Weight: 413.27100

To a solution of the [3+2-adduct] **3j** (30 mg, 0.058 mmol) in DCM (2 mL), TFA (2mL) was added at 0 °C and then it was allowed to stir at rt. After 6 h, TLC analysis showed complete conversion. It was quenched with 1 M NaOH solution (5 mL) and extracted with DCM (2 x 10 mL), washed with water (5 mL), dried over anhydrous sodium sulfate and concentrated to give crude which was purifed by filter column using 2-5% MeOH in DCM to give the compound **11**. Yield: 24 mg (99%); $[\alpha]^{20}_D$ = - 4.5^o (*c* 0.95, CH_2Cl_2); IR ν_{max}/cm^{-1} 3289, 3072, 3064, 3056, 2931, 1723; ^1H NMR (500 MHz, CD_2Cl_2) δ 7.33 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.25 – 7.21 (m, 4H), 7.20 (d, *J* = 1.9 Hz, 1H), 6.99 – 6.95 (m, 2H), 6.49 (d, *J* = 8.3 Hz, 1H), 4.83 (dd, *J* = 34.1, 12.2 Hz, 2H), 4.14 (dd, *J* = 18.0, 2.0 Hz, 1H), 4.09 (dd, *J* = 18.0, 1.9 Hz, 1H), 2.83 (s, 3H), 2.13 (bs, 1H); ^{13}C NMR (126 MHz, CD_2Cl_2) δ 176.28, 161.43, 146.22, 143.02,

135.19, 135.03, 133.74, 131.99, 128.48, 128.29, 128.28, 126.64, 115.03, 109.80, 73.67, 66.61, 54.28, 26.06; HRMS [ESI]: Calculated for $C_{20}H_{18}BrN_2O_3$ [M+H$^+$]: 413.04953, found: 413.04980; Calculated for $C_{20}H_{18}{}^{81}BrN_2O_3$ [M+H$^+$]: 415.04748, found: 415.04758.



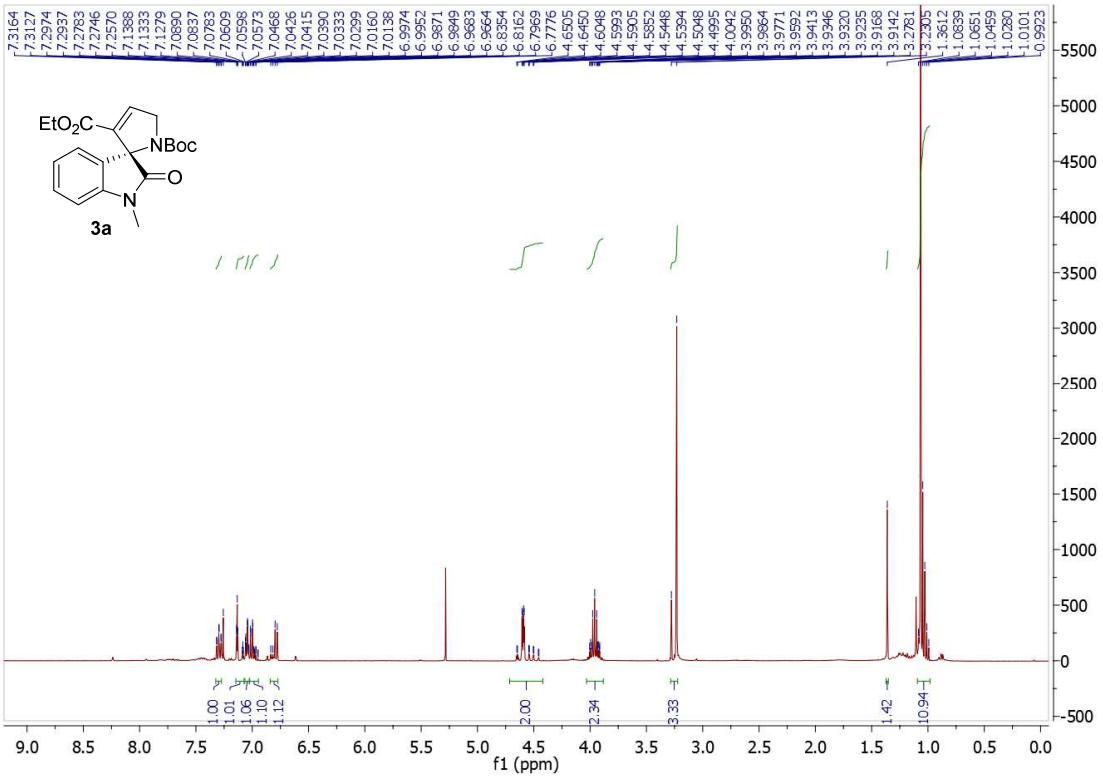
12

Chemical Formula: $C_{27}H_{22}BrFN_2O_3$
Exact Mass: 520.07978
Molecular Weight: 521.38640

To a solution of compound **11** (12 mg, 0.029 mmol) in dry 1,2-DCE (1 mL) 2-fluorobenzaldehyde (4.3 mg, 0.035 mmol) was added at rt and stirred for 10 min. To this sodium triacetoxyborohydride (14 mg, 0.064 mmol) was added portionwise and continued to stir at rt for 6 h. Saturated sodium bicarbonate solution (10 mL) was added and extracted with DCM (3 x 10 mL). The combined organic layer was washed with water, dried over anhydrous sodium sulfate and concentrated to give the crude. Purification of the crude over silica gel column chromatography using 5-15% EtOAc in petroleum ether afforded pure compound **12**. Yield: 13 mg (86%); $[\alpha]^{20}_D$ = -40.1^o (*c* 1.26, CH_2Cl_2); IR ν_{max}/cm^{-1} 3065, 3057, 2928, 1717; ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.30 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.26 (d, *J* = 2.0 Hz, 1H), 7.23 (dd, *J* = 6.7, 3.5 Hz, 3H), 7.18 (t, *J* = 2.0 Hz, 1H), 7.13 – 7.04 (m, 2H), 6.99 – 6.95 (m, 2H), 6.93 (t, *J* = 7.5 Hz, 1H), 6.81 (t, *J* = 7.4 Hz, 1H), 6.40 (d, *J* = 8.2 Hz, 1H), 4.86 (d, *J* = 12.2 Hz, 1H), 4.78 (d, *J* = 12.2 Hz, 1H), 3.92 (dd, *J* = 16.7, 2.0 Hz, 1H), 3.83 (dd, *J* = 16.7, 2.2 Hz, 1H), 3.63 (d, *J* = 13.5 Hz, 1H), 3.46 (d, *J* = 13.5 Hz, 1H), 2.76 (s, 3H); ^{13}C NMR (126 MHz, CD_2Cl_2) δ 174.37, 162.04, 161.41, 160.07, 144.55, 143.65, 135.40, 135.20, 132.05, 130.98, 130.94, 130.84, 129.06, 128.99, 128.46, 128.25, 127.63, 124.81, 124.70, 123.75, 123.72, 115.00, 114.94, 114.83, 109.60, 76.29, 66.52, 58.45, 46.30, 46.28, 25.77; HRMS [ESI]: Calculated for $C_{27}H_{23}BrFN_2O_3$ [M+H$^+$]: 521.08706, found: 521.08750; Calculated for $C_{27}H_{23}{}^{81}BrFN_2O_3$ [M+H$^+$]: 523.08501, found: 523.08544.

V. References:

1. (a) L. Rout and A. M. Harned, *Chem. Eur. J.* **2009**, *15*, 12926 – 12928; (b) Y. H. Paik and P. Dowd, J. *Org. Chem.*, **1986**, *51*, 2910-2913; (c) Z. Hamlet and W. D. Barker, *Synthesis*, **1970**, 543-544.
2. T. Constantieux and G. Buono, *Org. Synth.*, **2002**, *78*, 135.
3. H. Xiao, Z. Chai, C.-W. Zheng, Y.-Q. Yang, W. Liu, J.-K. Zhang, G. Zhao, *Angew. Chem., Int. Ed.*, **2010**, *49*, 4467-4470.
4. (a) W. Yan, D. Wang, J. Feng, P. Li, D. Zhao and R. Wang, *Org. Lett.*, **2012**, *14*, 2512–2515; (b) M. G. Sankar, M. G. Castro, Y. Wang and K. Kumar, *Asian J. Org. Chem.* **2013**, *2*, 646 – 649; (c) M. Holmquist, G. Blay and J. R. Pedro, *Chem. Commun.* **2014**, *50*, 9309 – 9312.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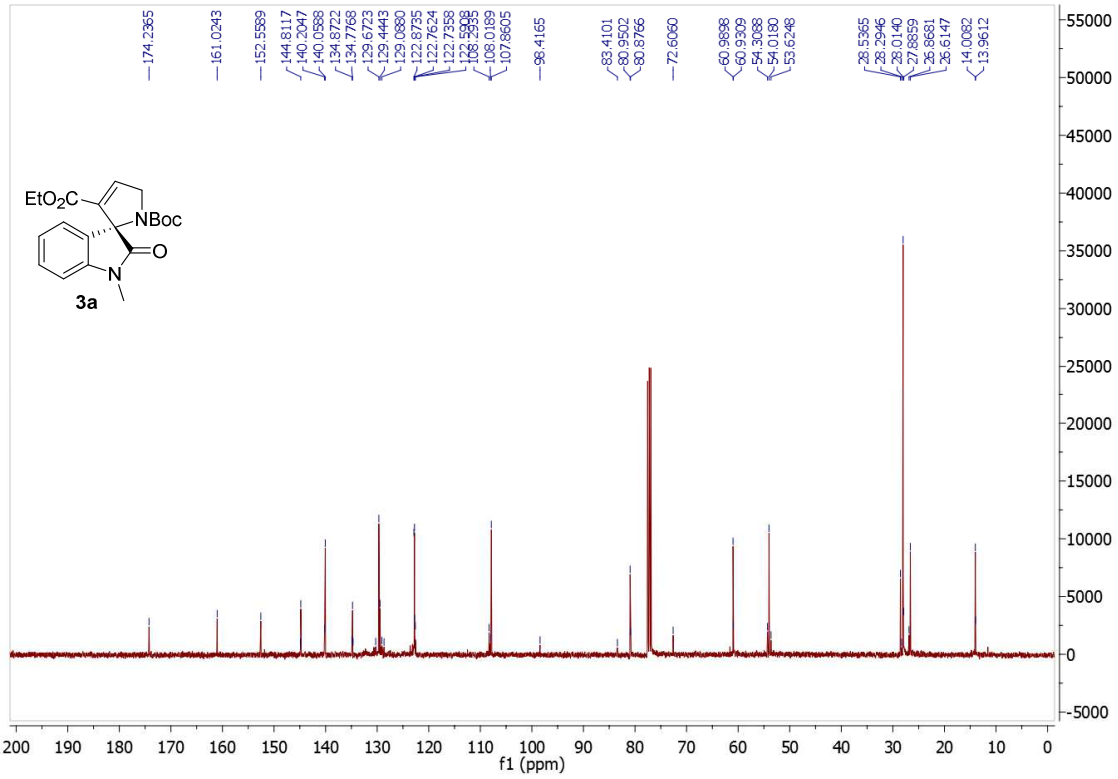
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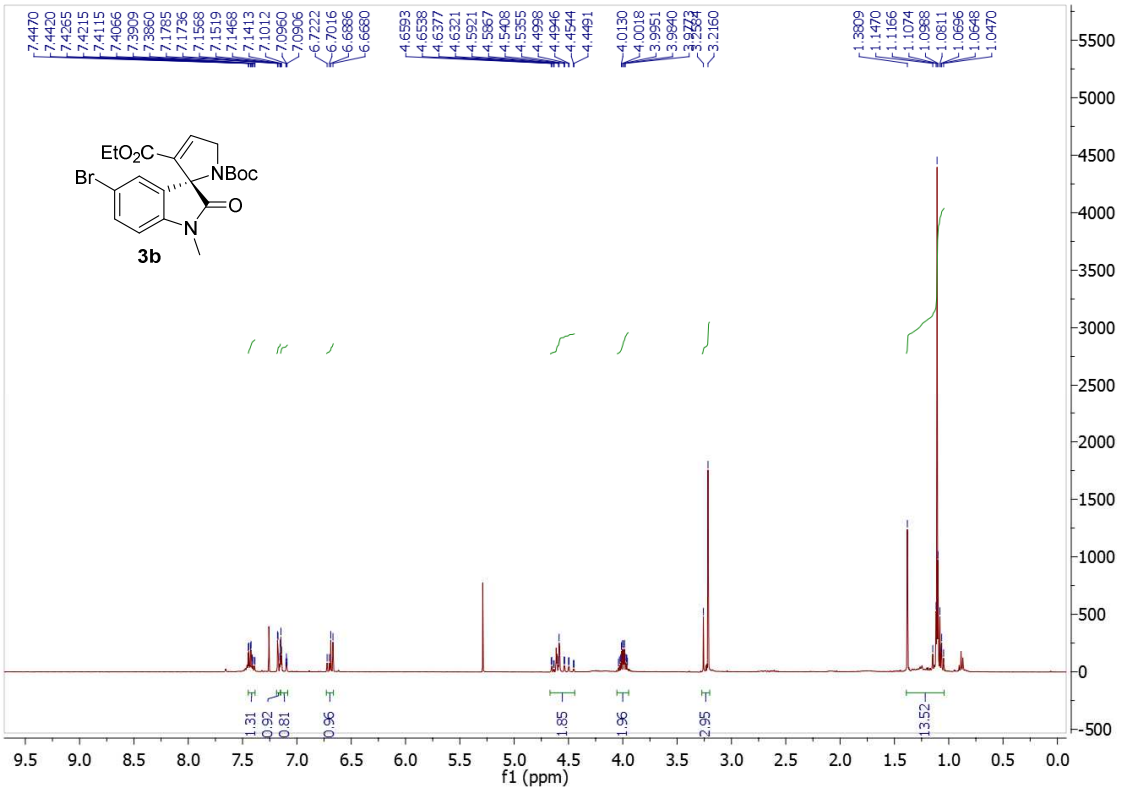
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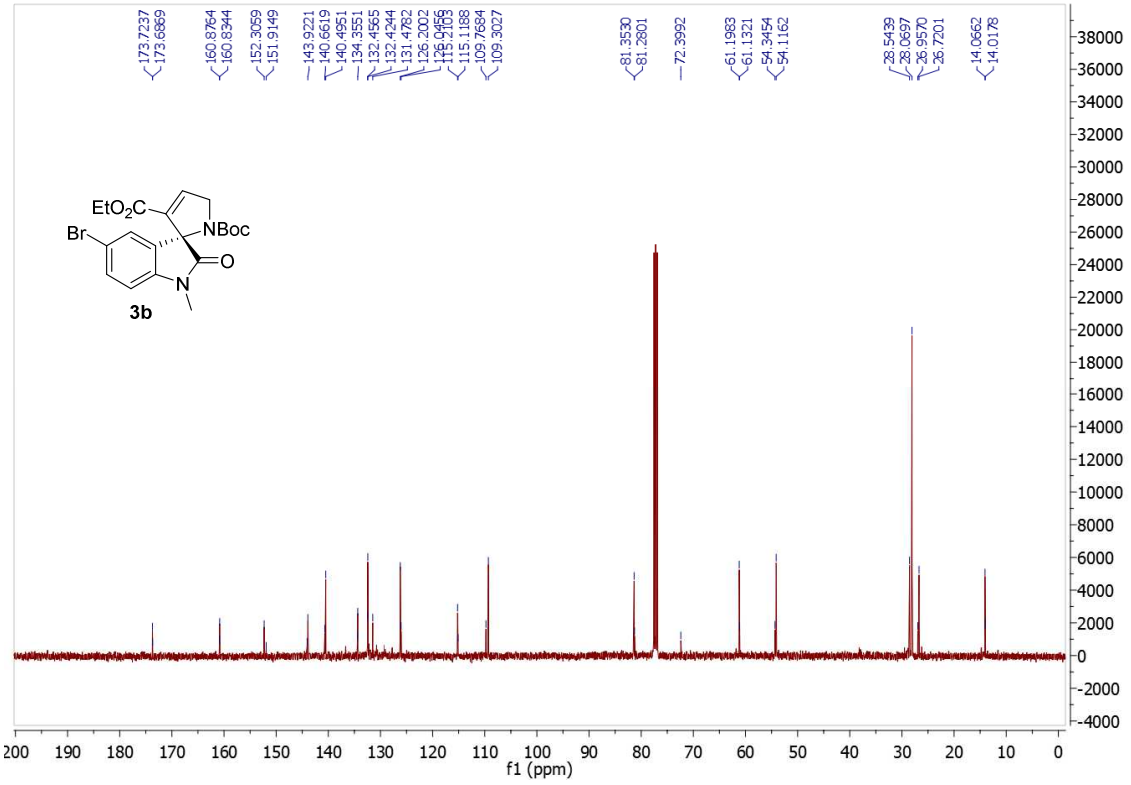
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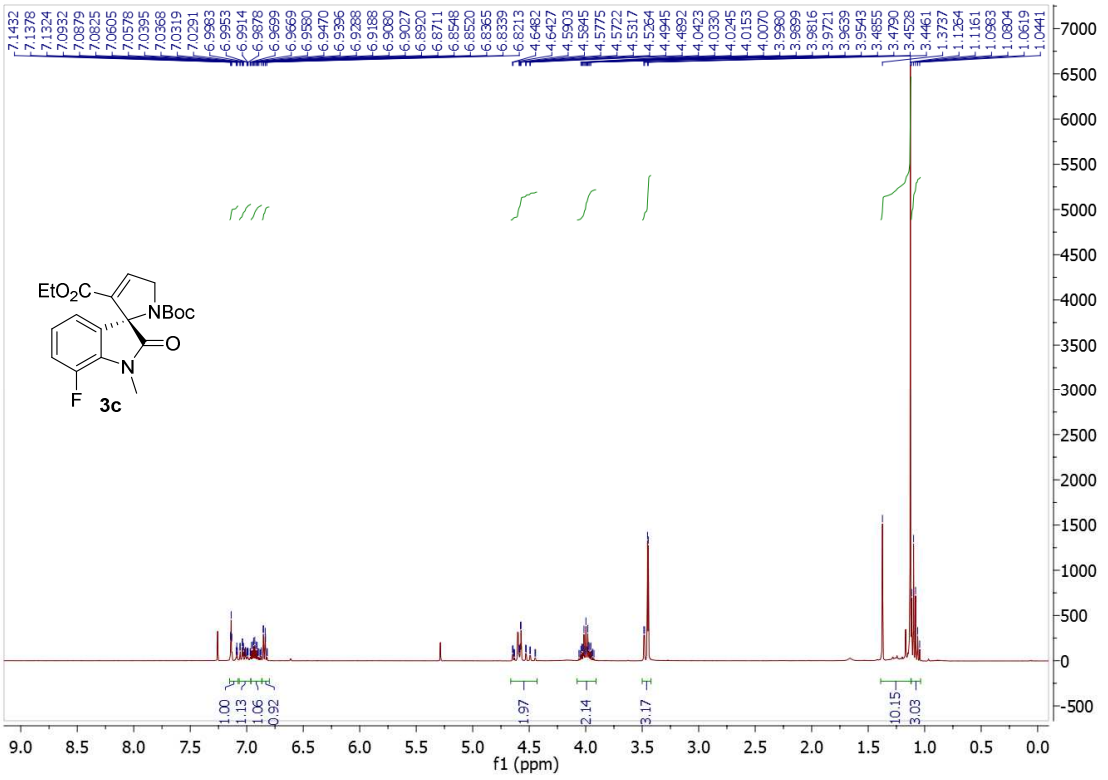
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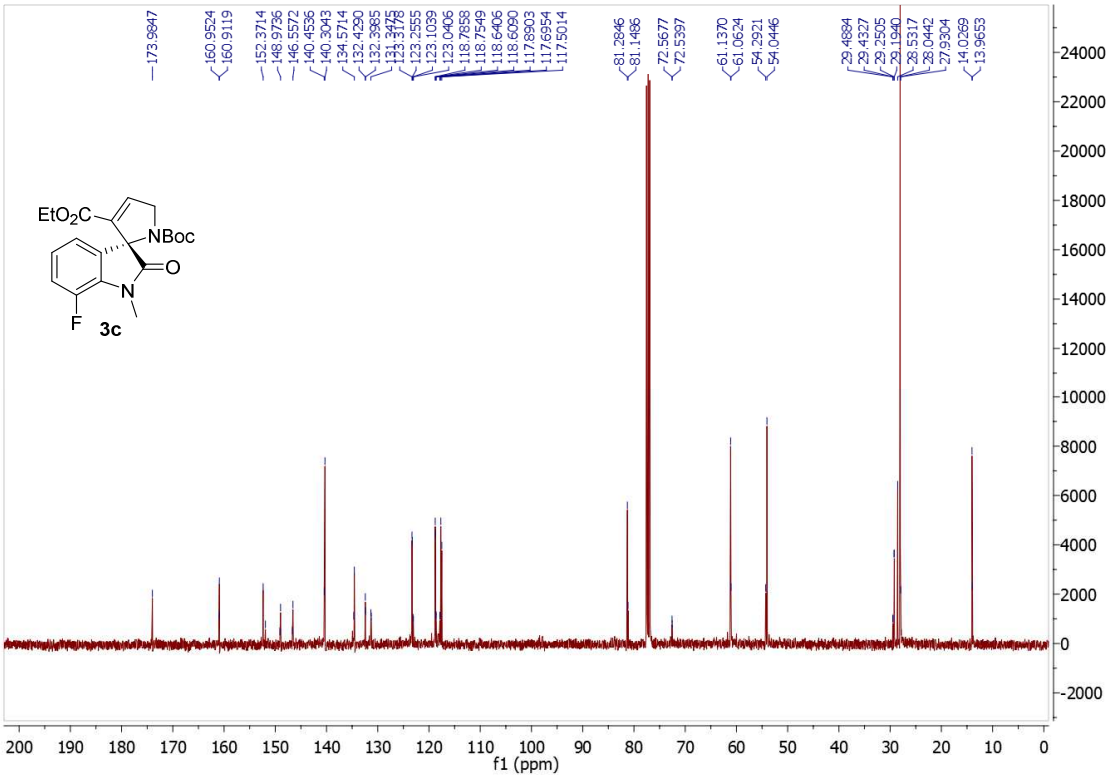
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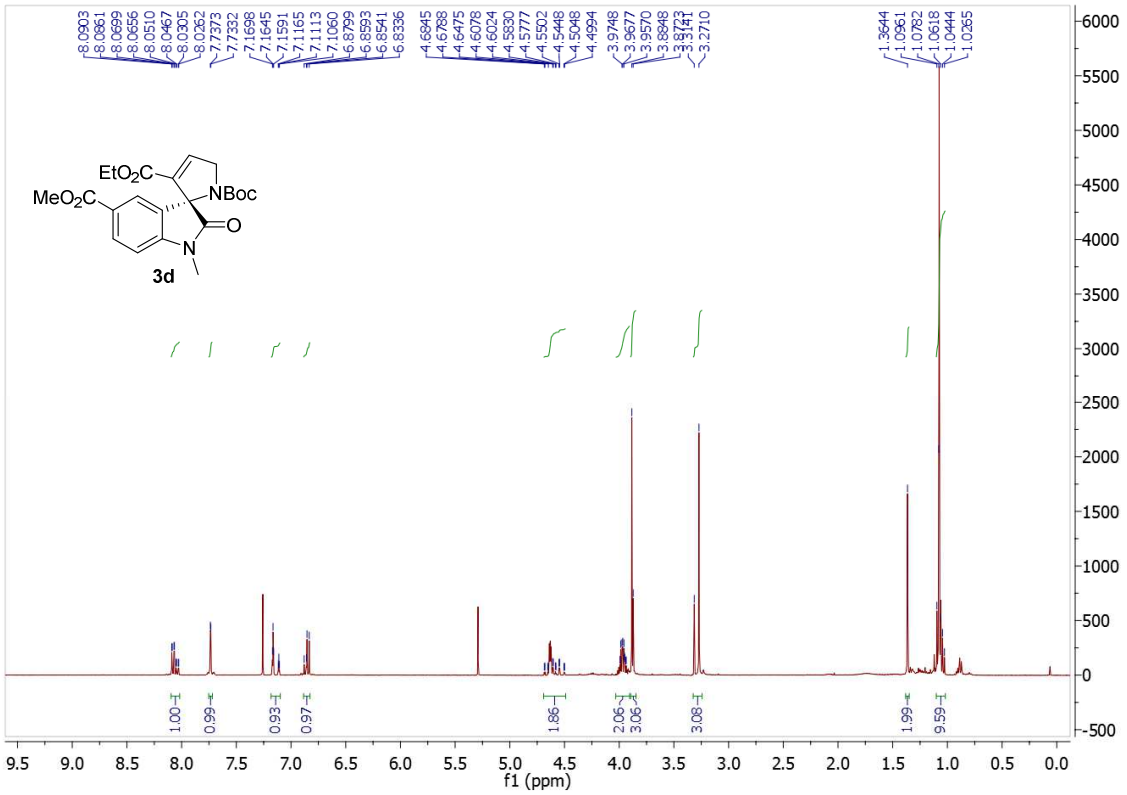
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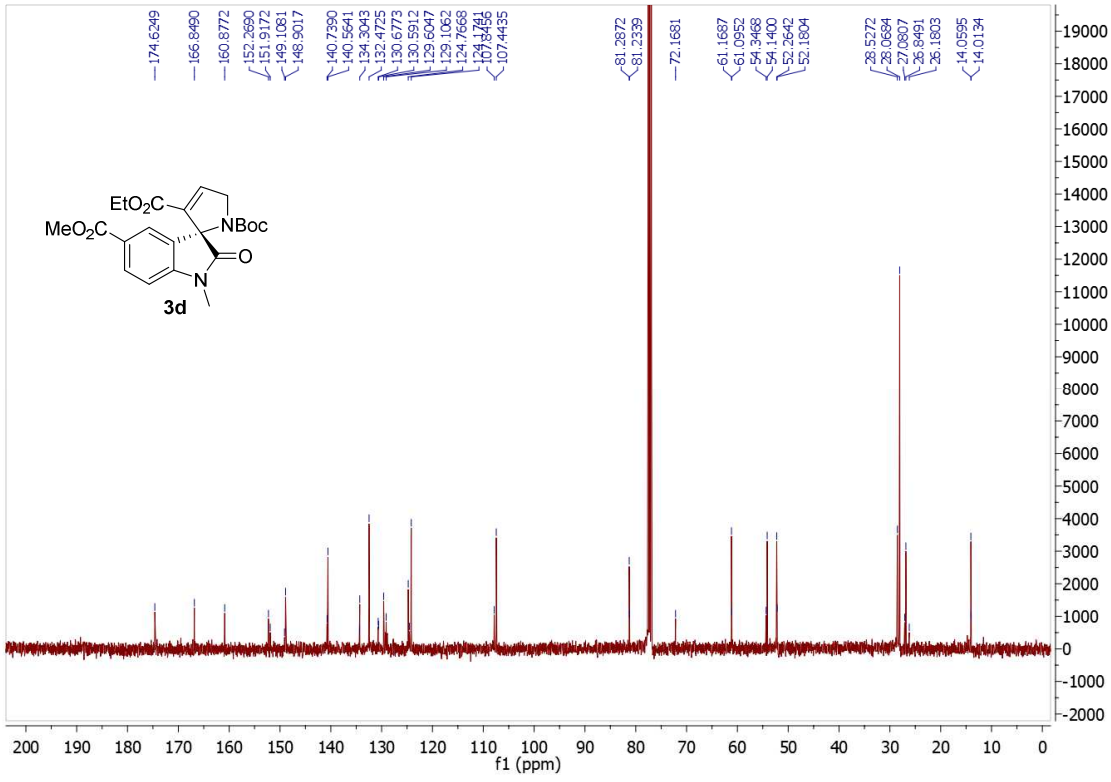
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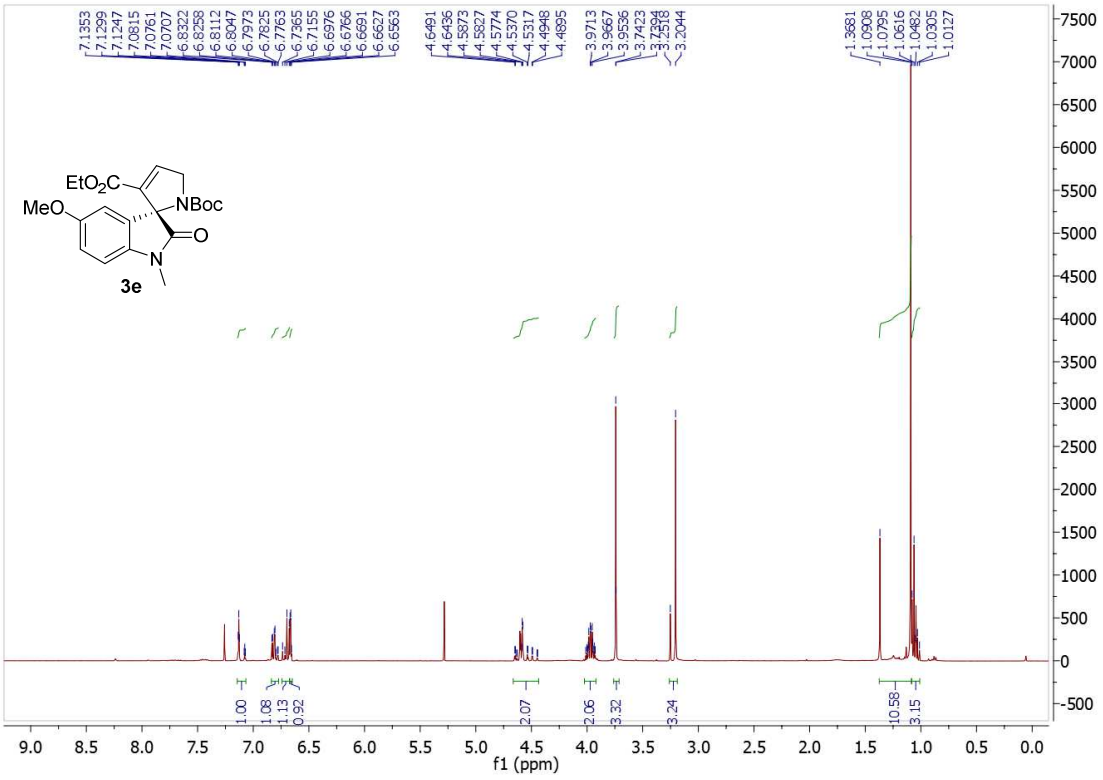
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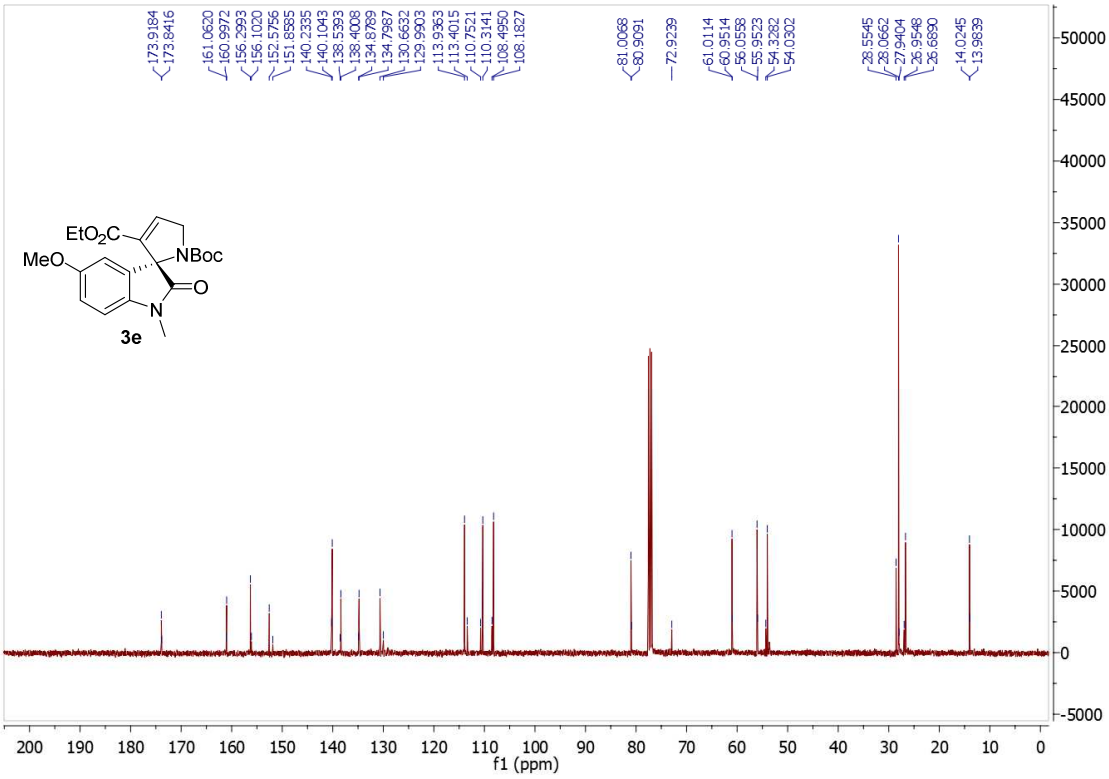
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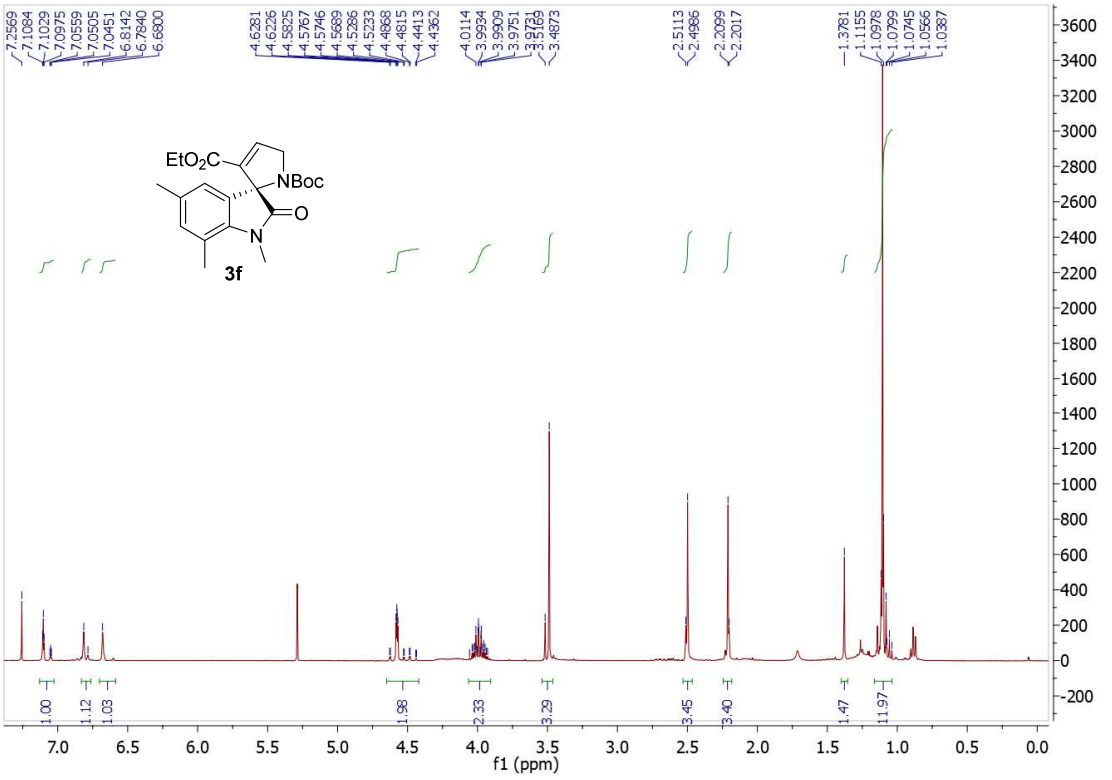
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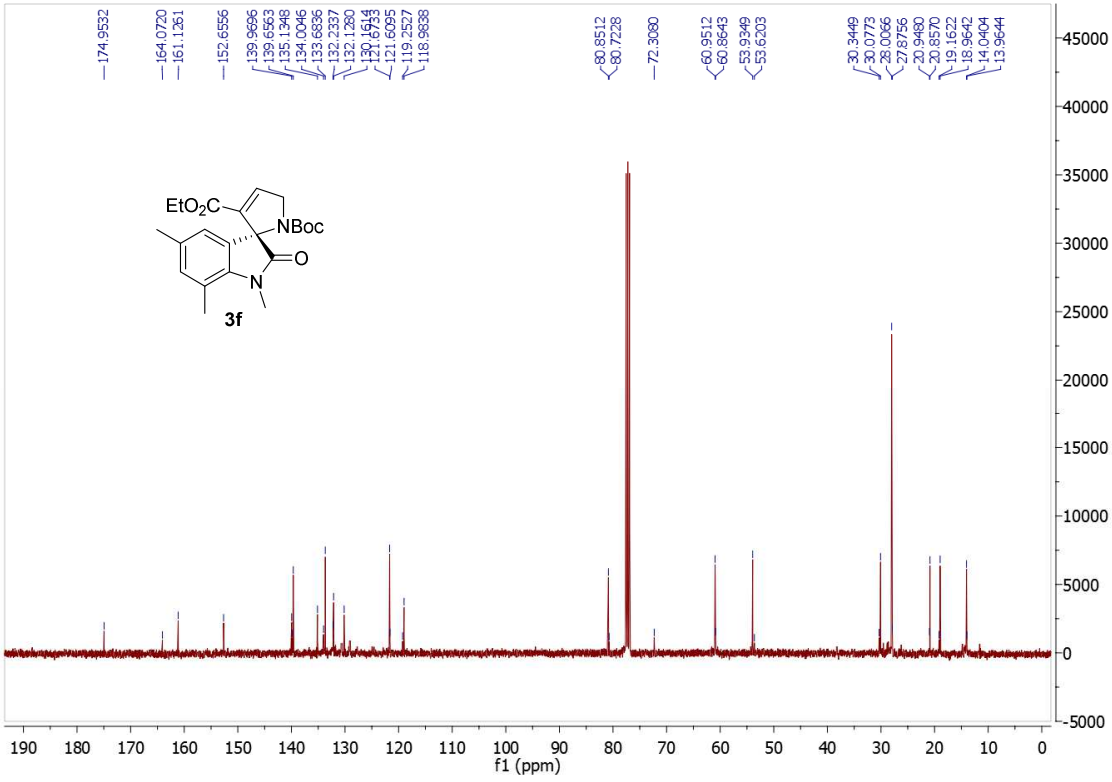
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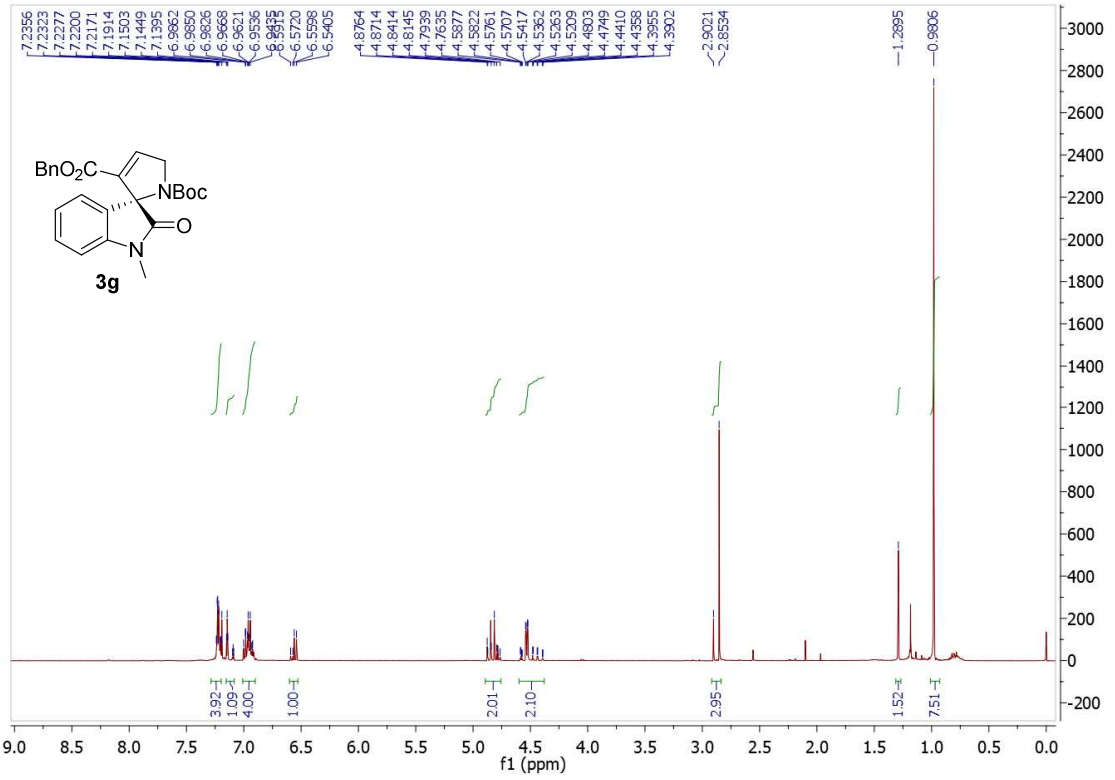
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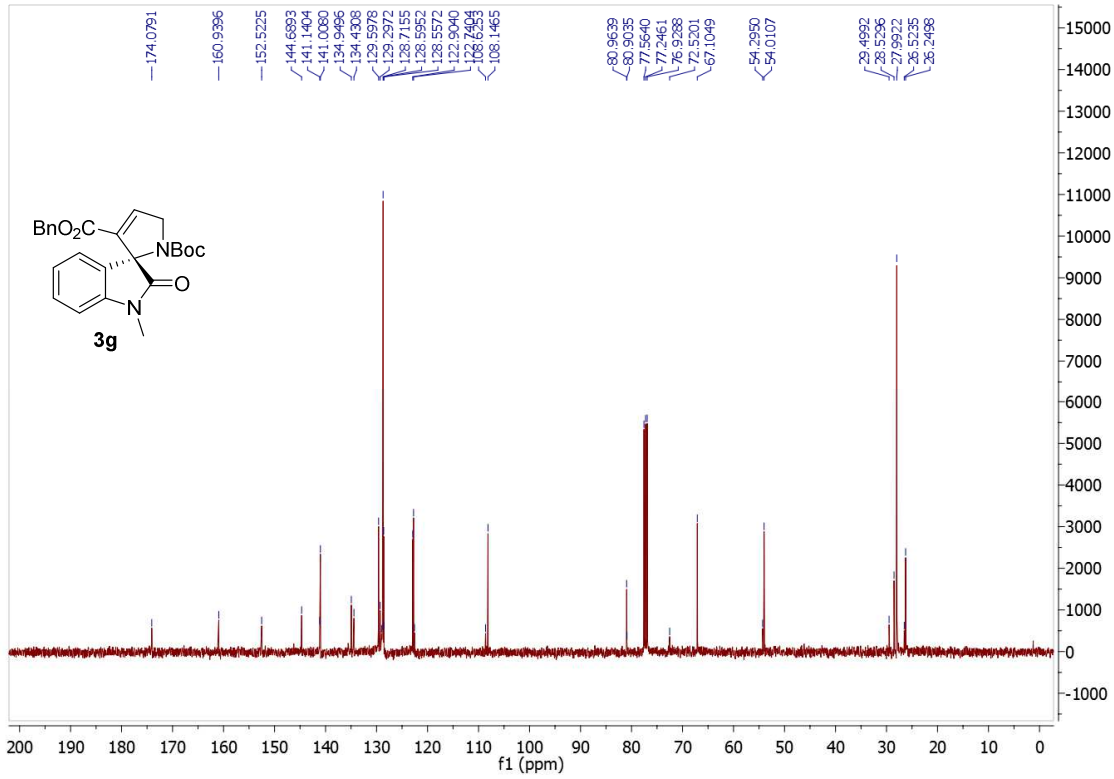
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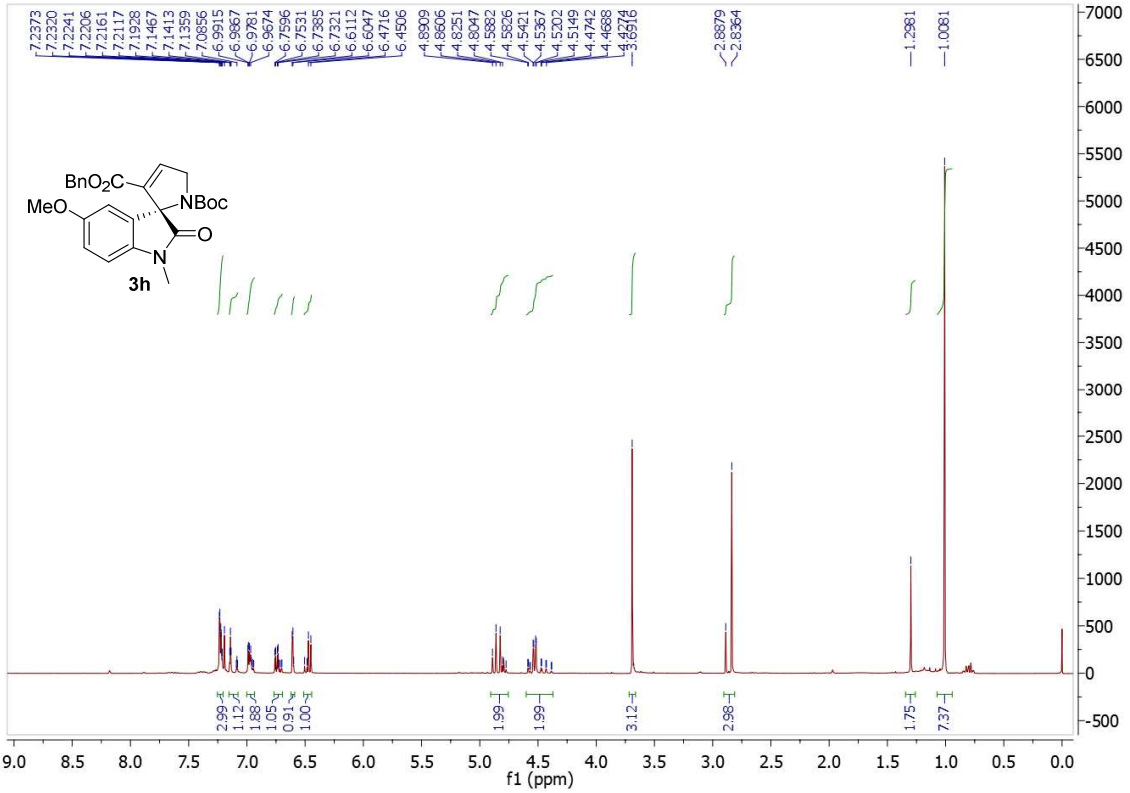
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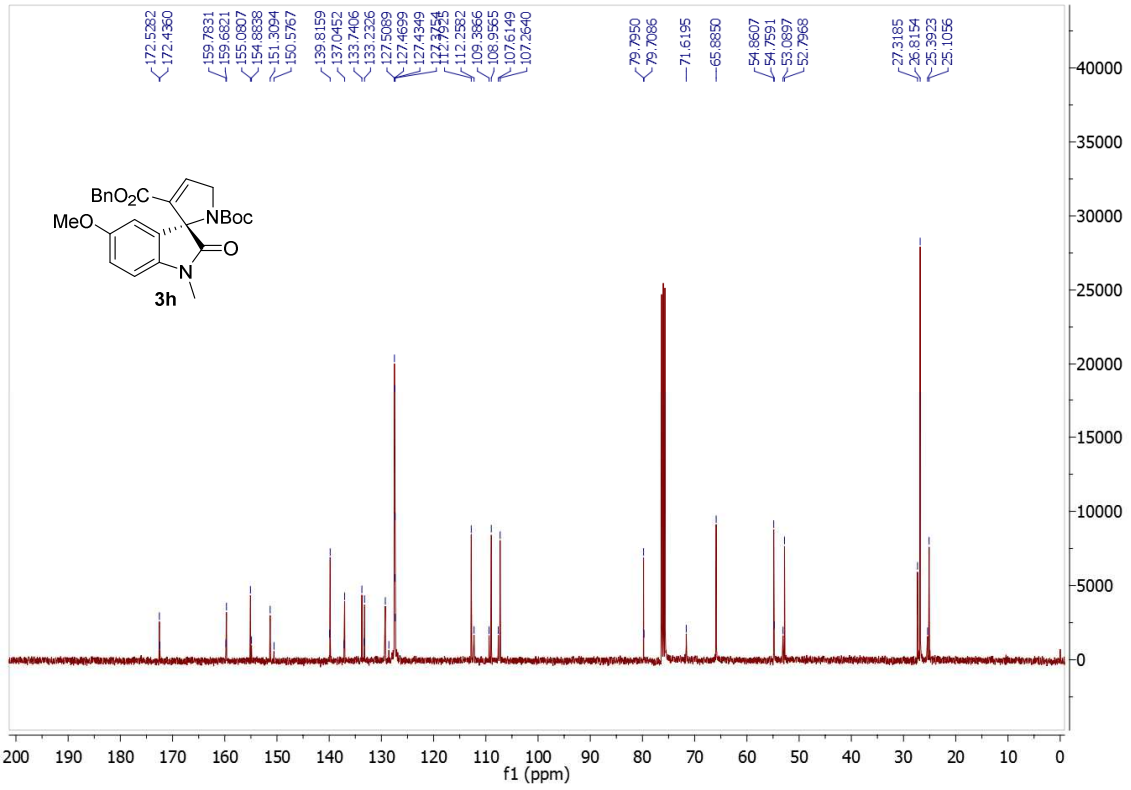
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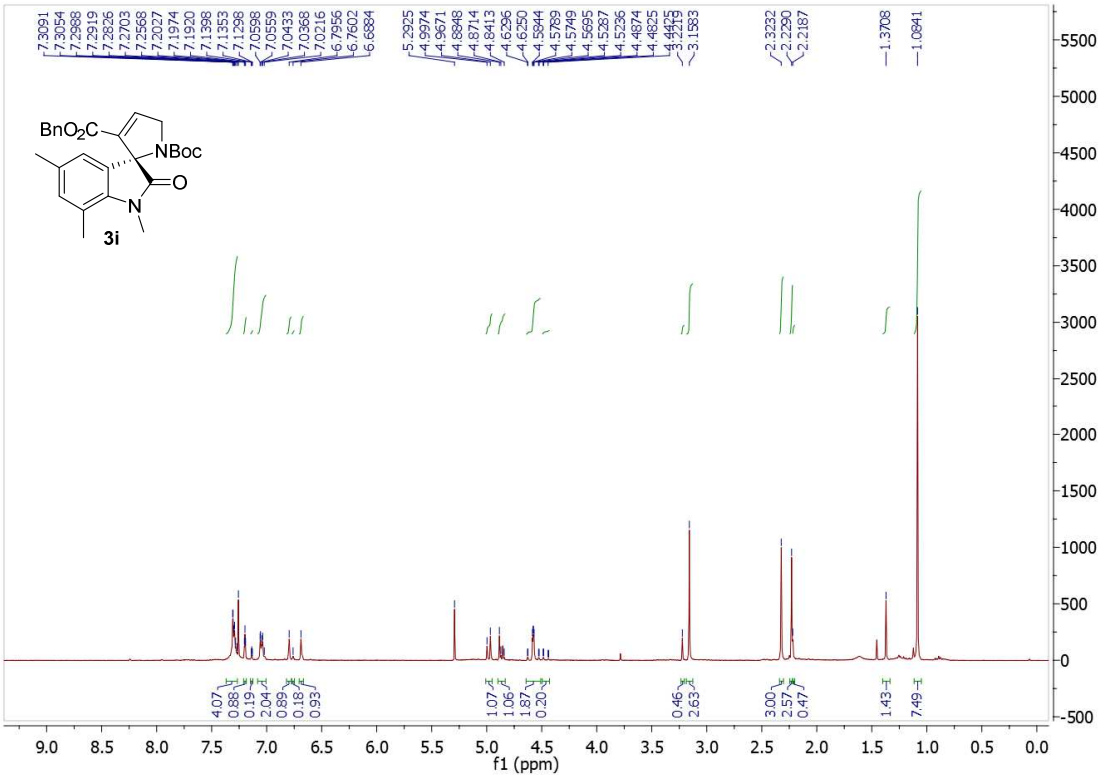
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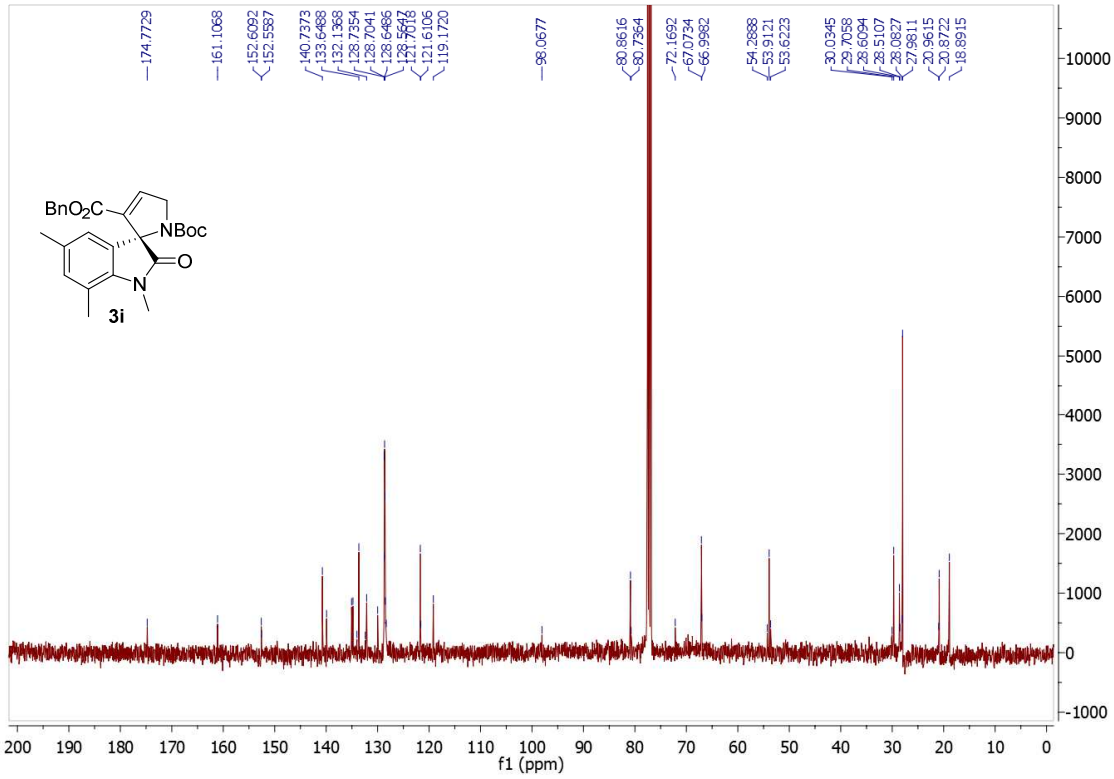
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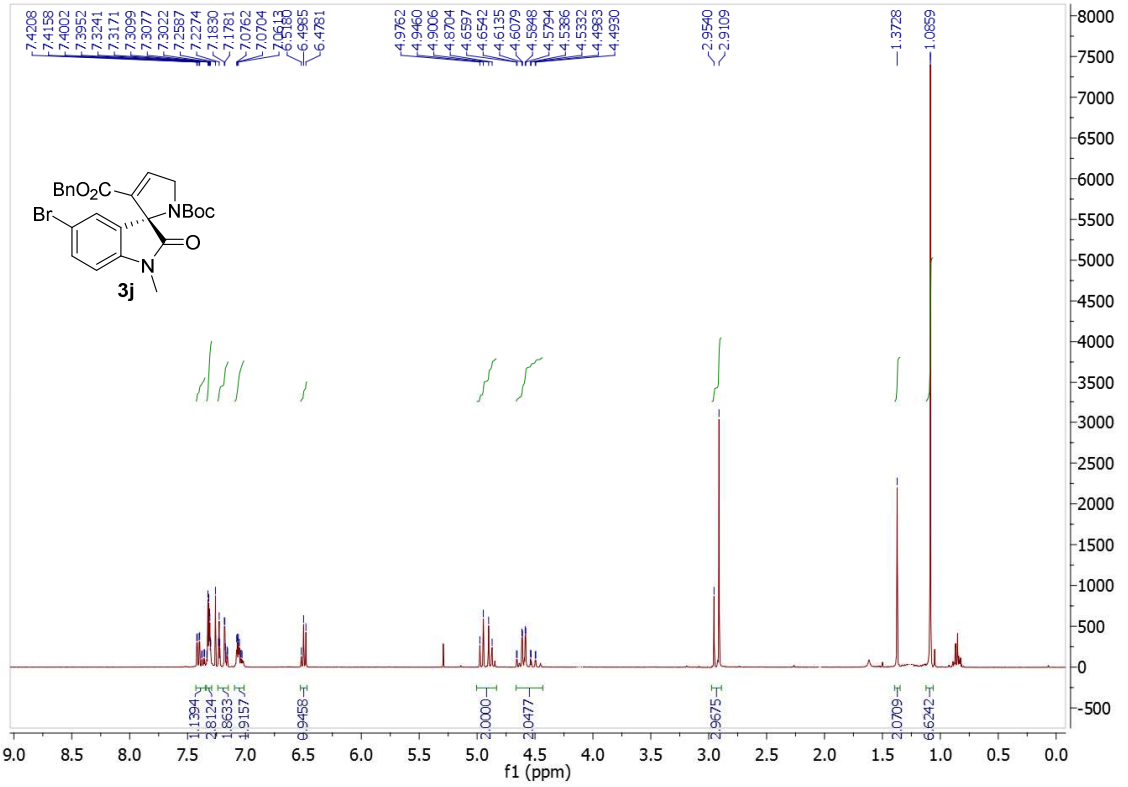
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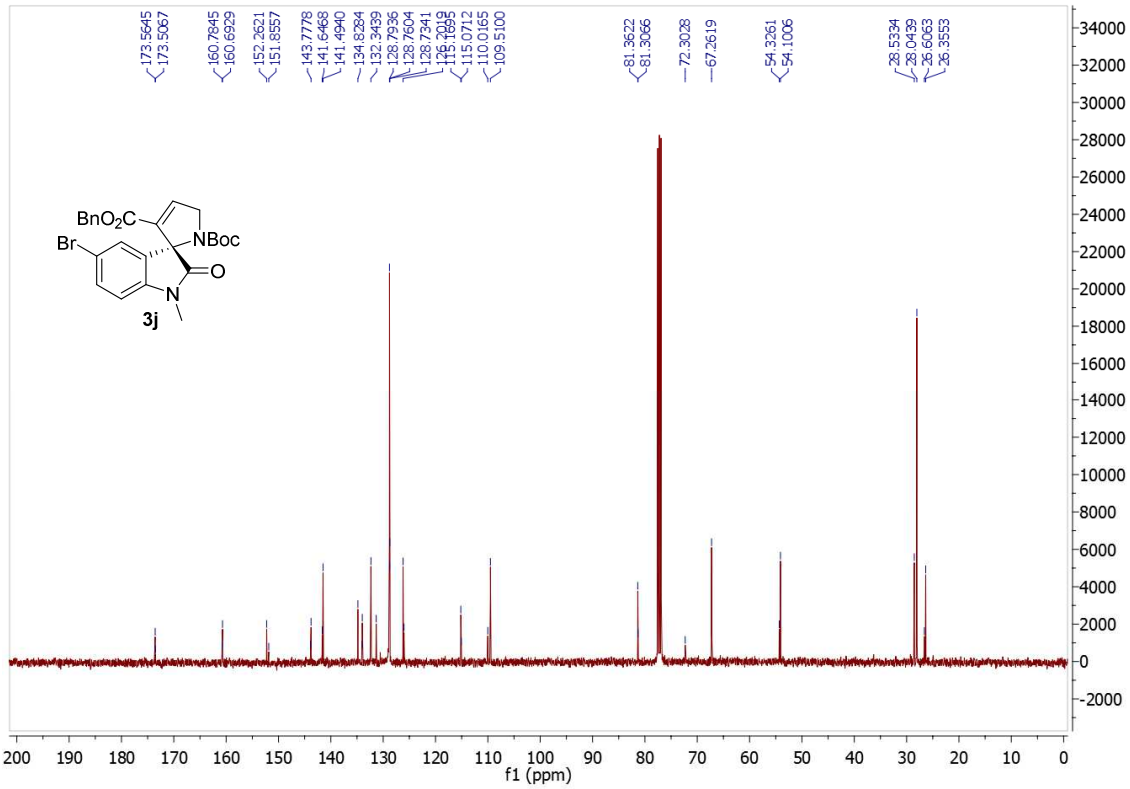
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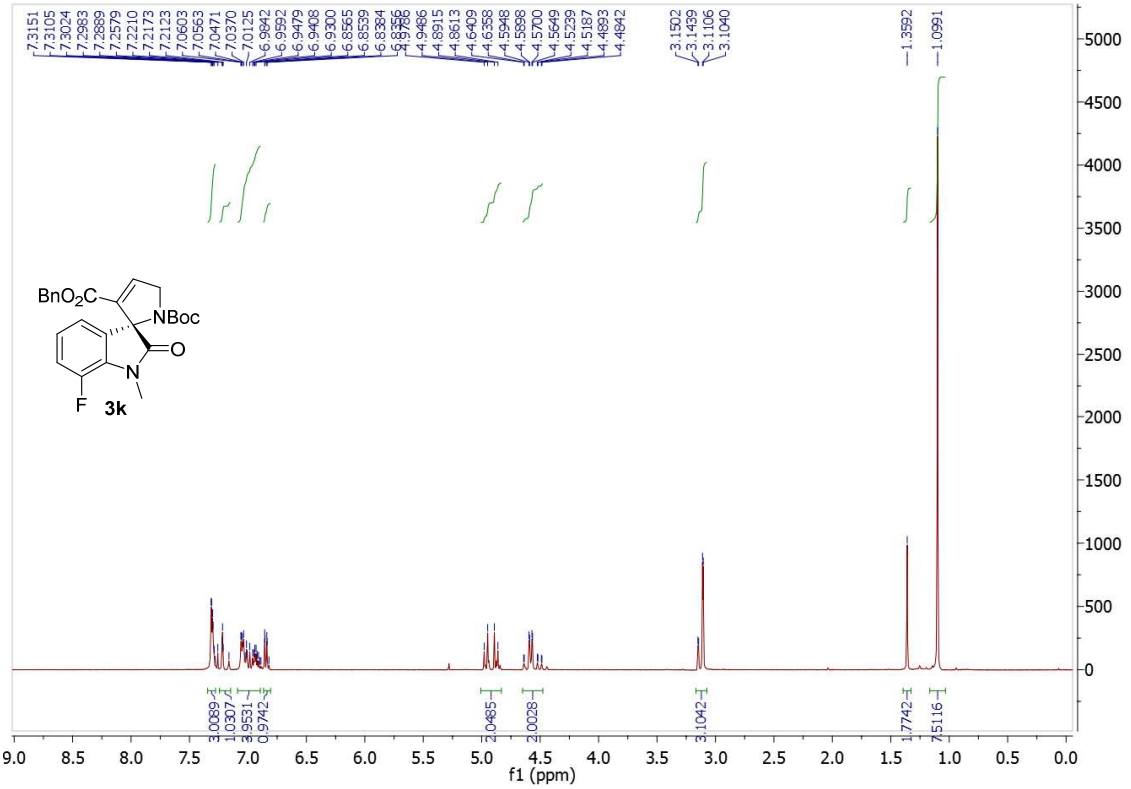
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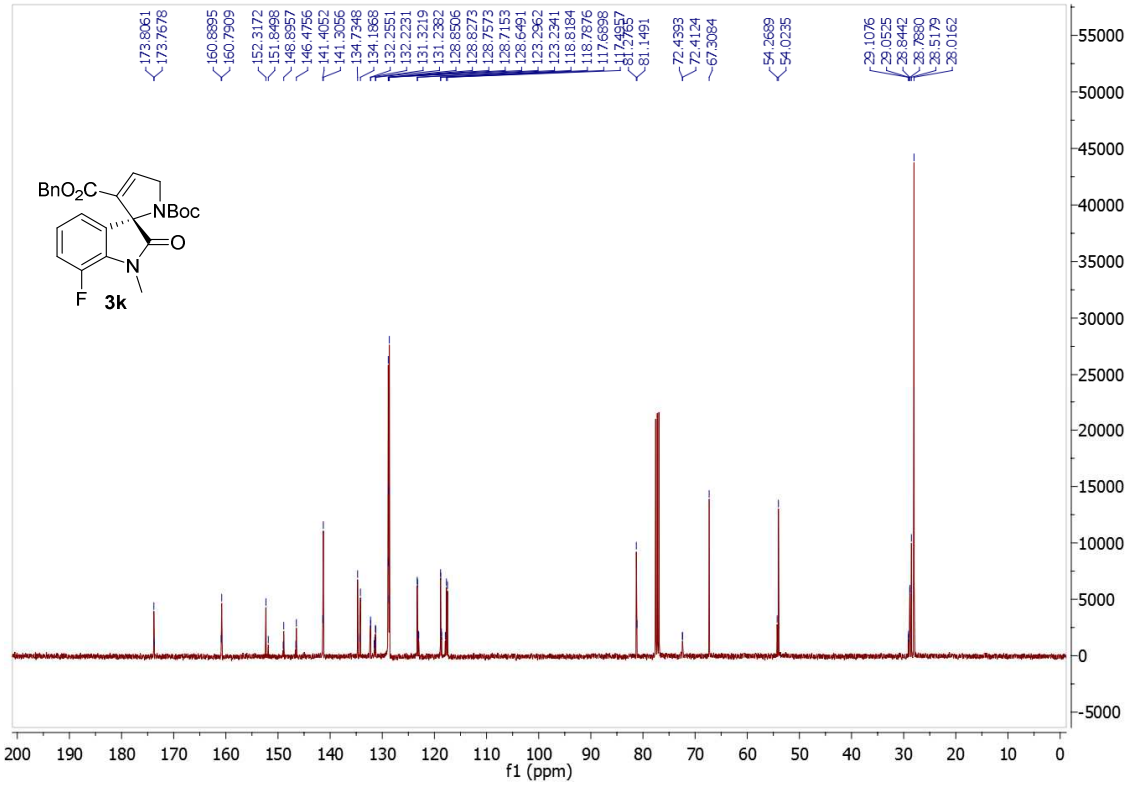
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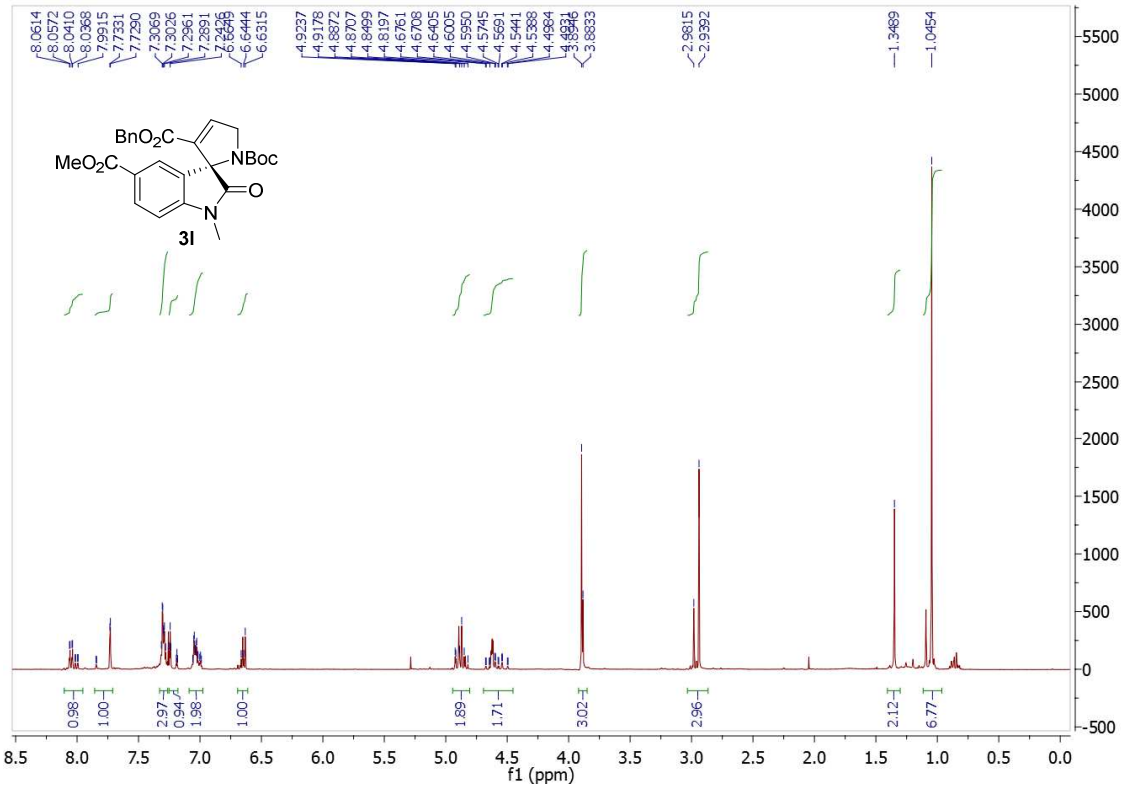
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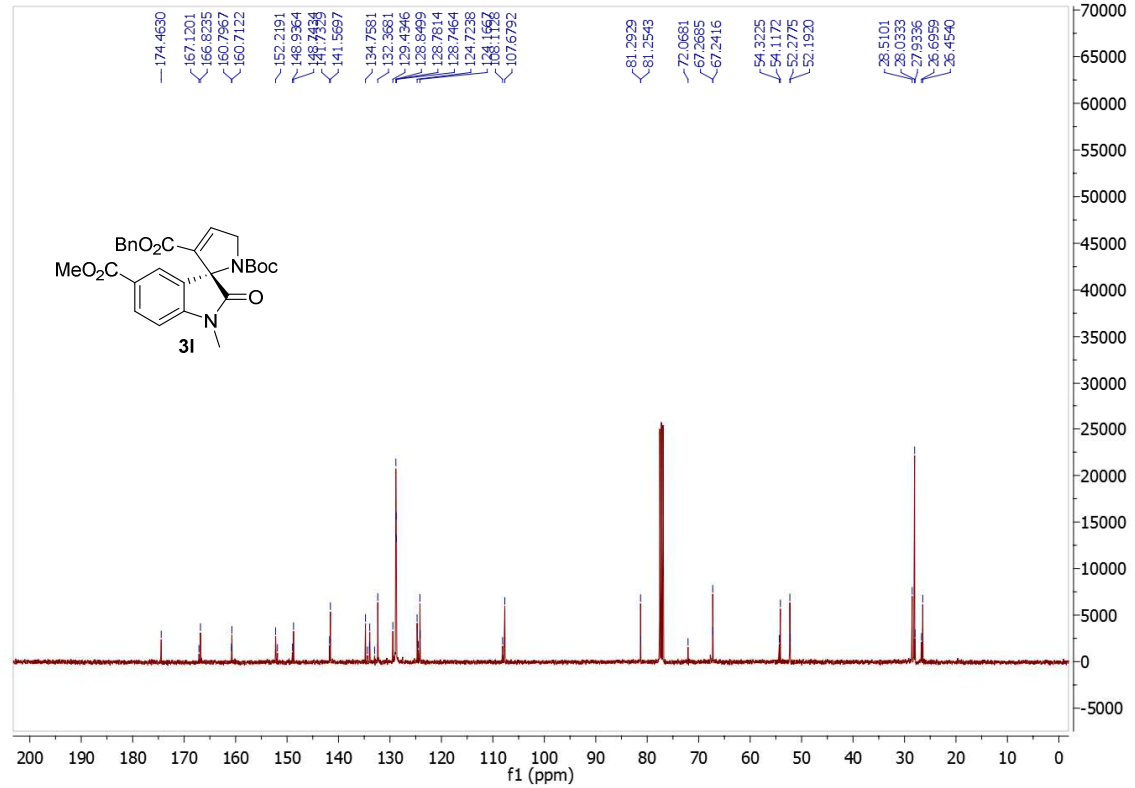
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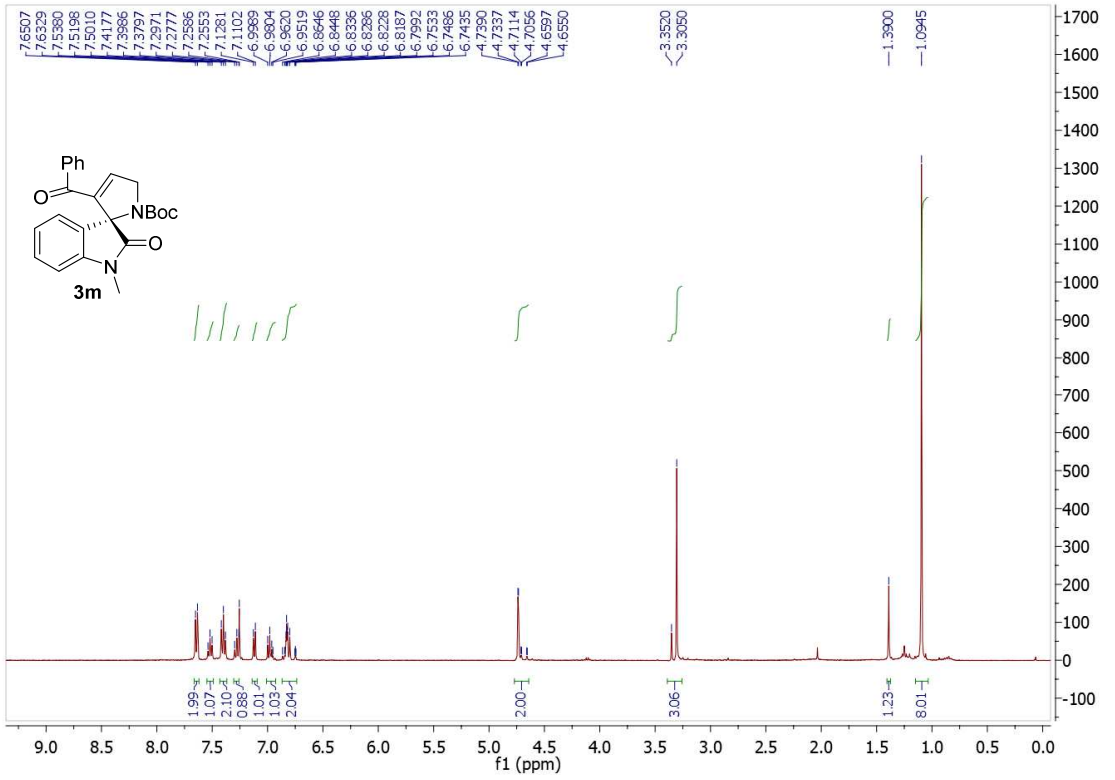
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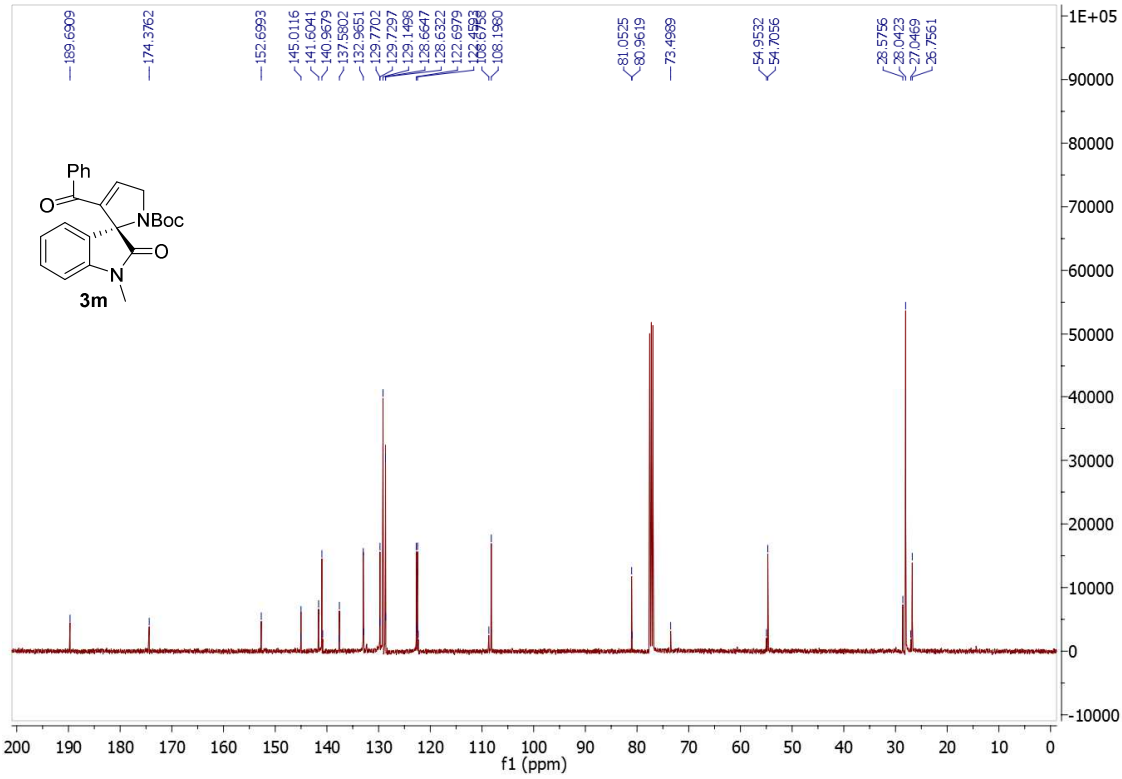
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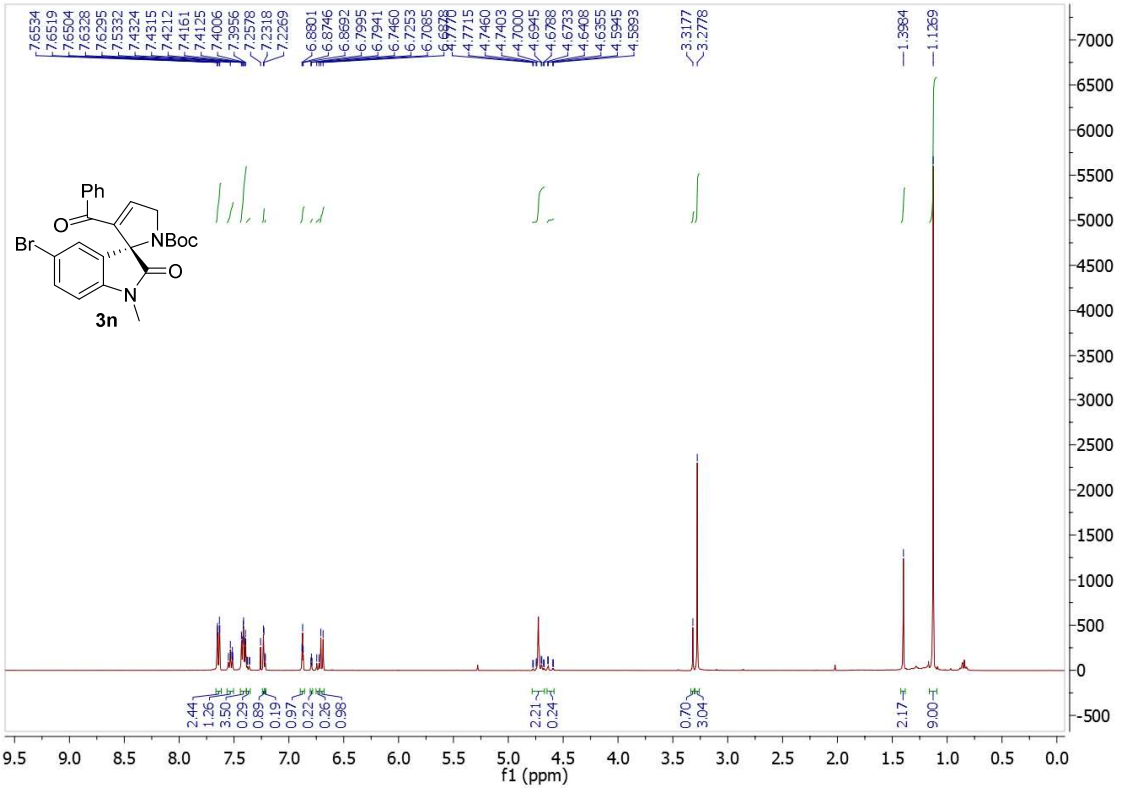
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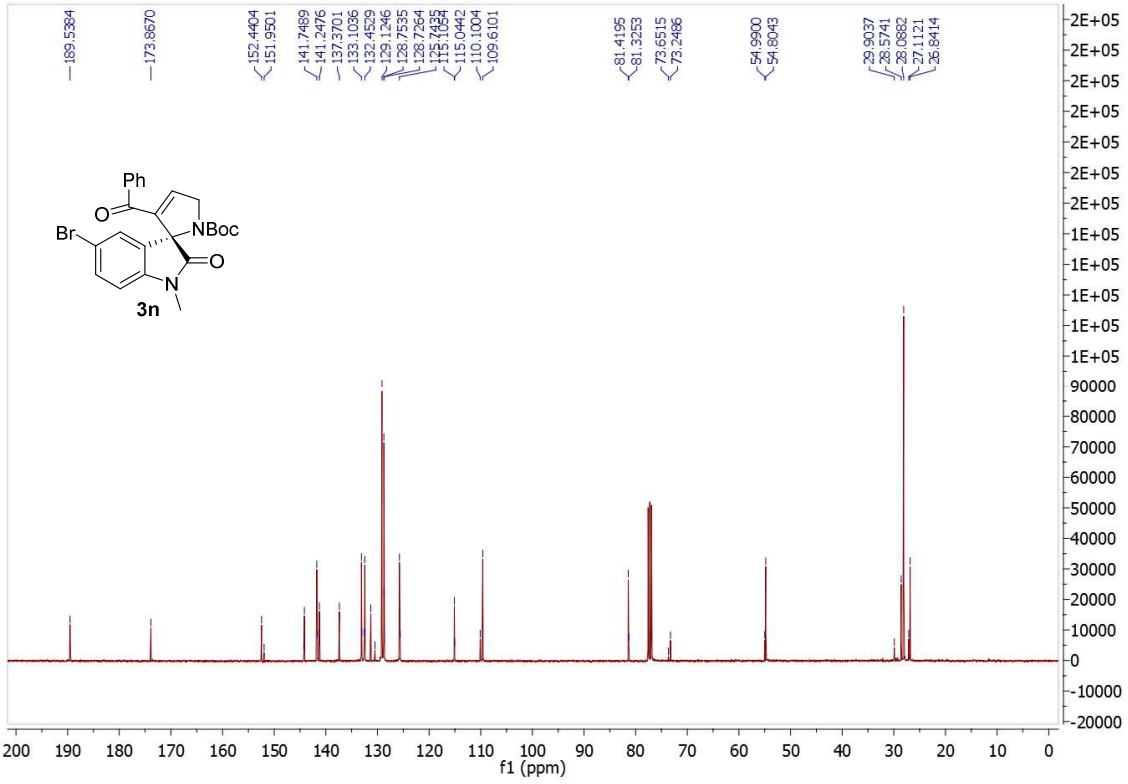
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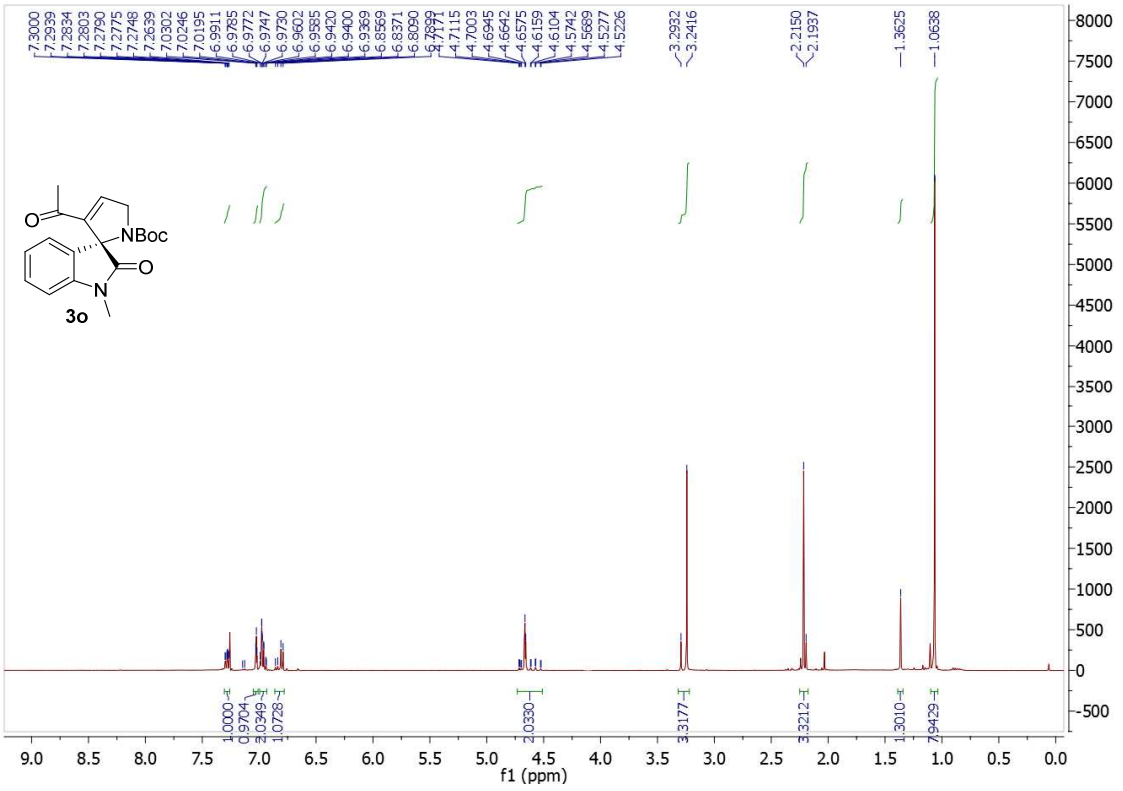
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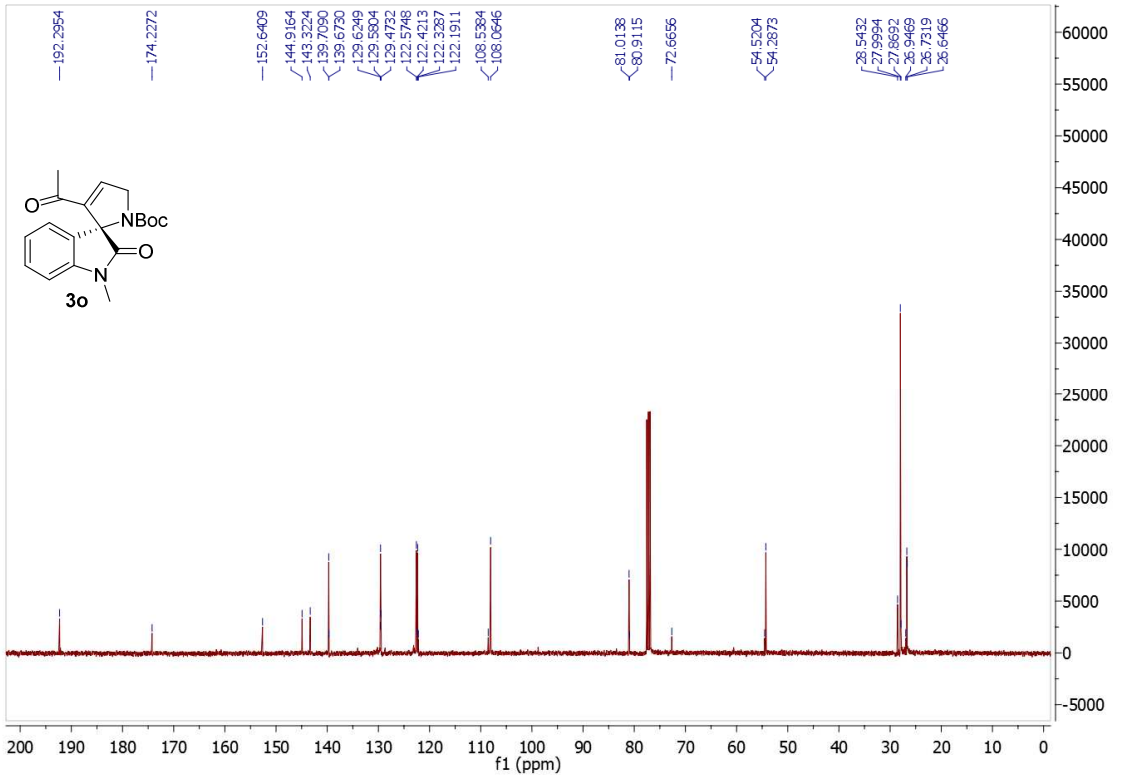
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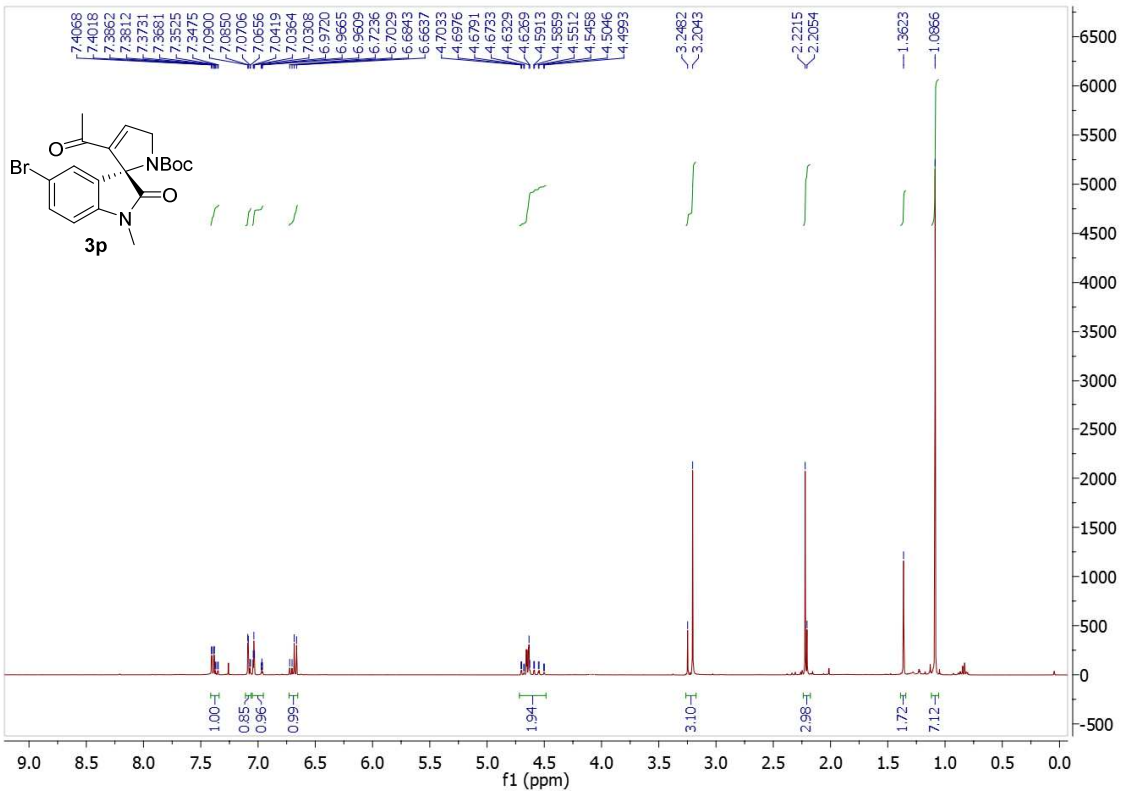
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4.4993
3.2482
3.2043
2.2215
2.2054
1.3623
1.0866
Br
O
NBoc
O
N
3p
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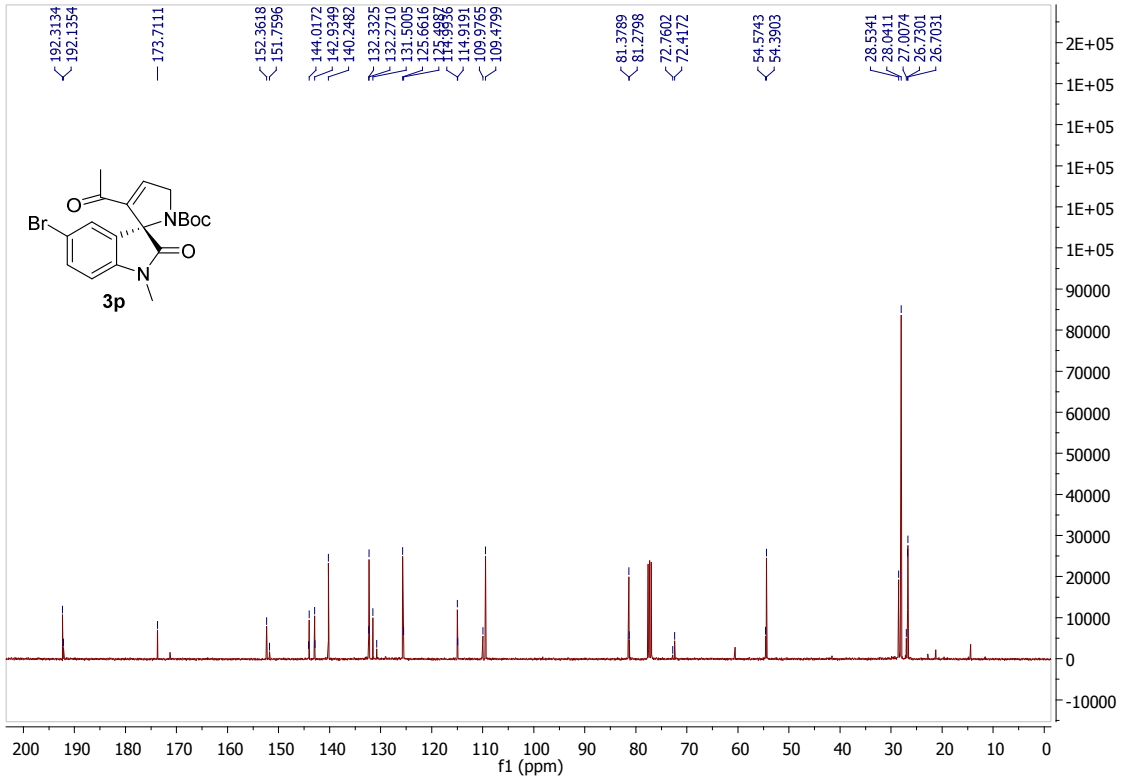
0.99
1.94
3.10
2.98
1.72
7.12
f1 (ppm)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125.6616
125.4987
114.9936
114.9191
109.9765
109.4799
81.3789
81.2798
72.7602
72.4172
54.5743
54.3903
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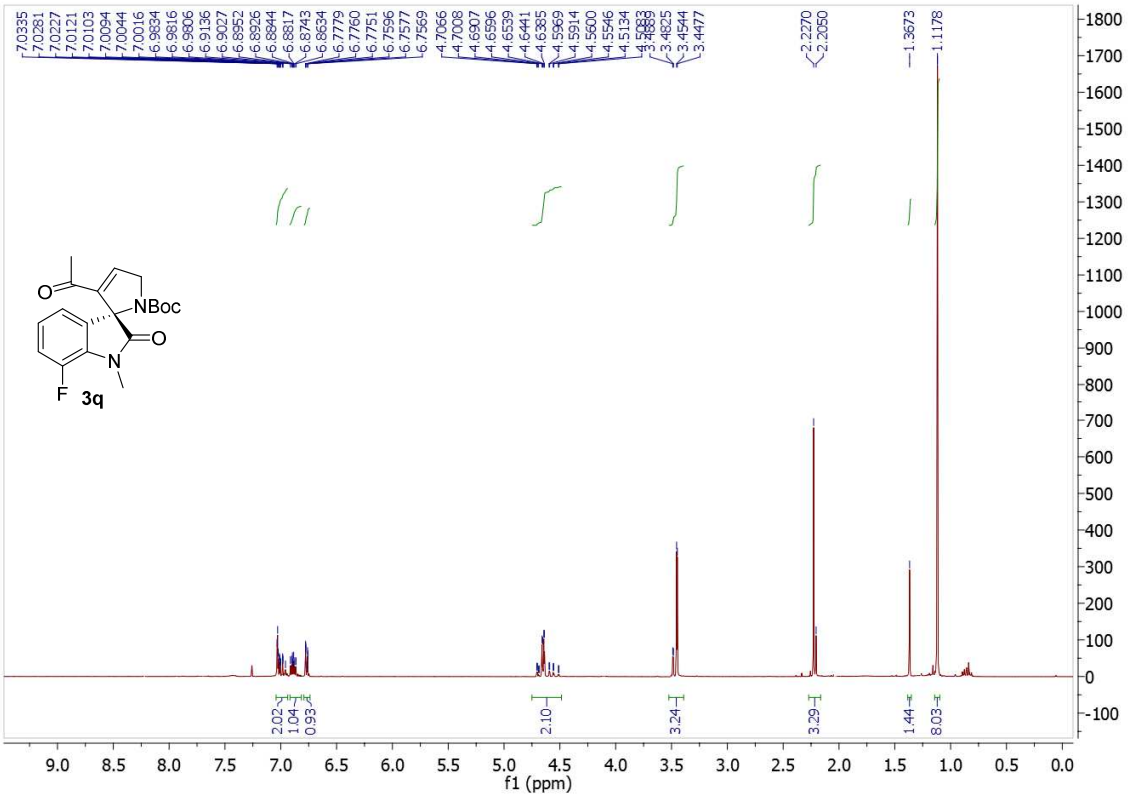
27.0074
26.7301
26.7031
Br
O
NBoc
O
N
3p
f1 (ppm)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7.0227
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7.0103
7.0094
7.0044
7.0016
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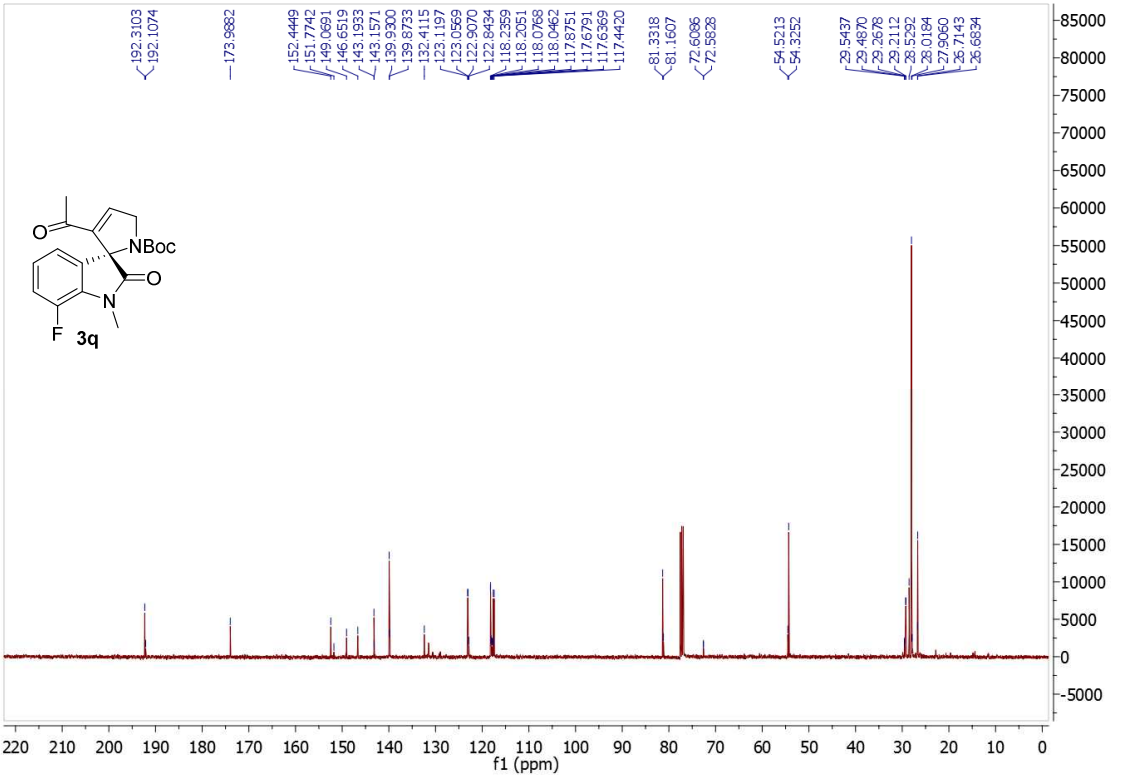
6.9816
6.9806
6.9136
6.9027
6.8952
6.8926
6.8844
6.8817
6.8743
6.8634
6.7779
6.7760
6.7751
6.7596
6.7577
6.7569
4.7066
4.7008
4.6907
4.6596
4.6539
4.6441
4.6385
4.5969
4.5914
4.5600
4.5546
4.5134
4.5083
4.4889
3.4825
3.4544
3.4477
2.2270
2.2050
1.3673
1.1178
2.02
1.04
0.93
2.10
3.24
3.29
1.44
8.03
f1 (ppm)
NBoc
O
N
F
3q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143.1571
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139.8733
132.4115
123.1197
123.0569
122.9070
122.8434
118.2359
118.2051
118.0768
118.0462
117.8751
117.6791
117.6369
117.4420
81.3318
81.1607
72.6086
72.5828
54.5213
54.3252
29.5437
29.4870
29.2678
29.2112
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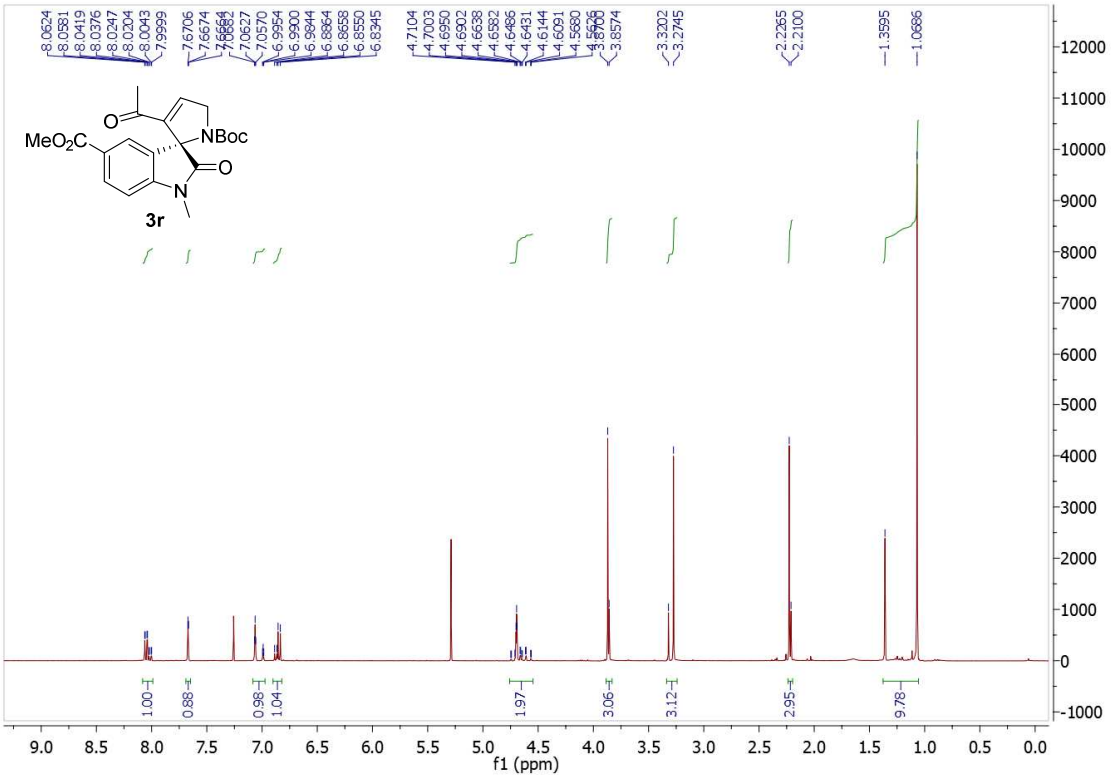
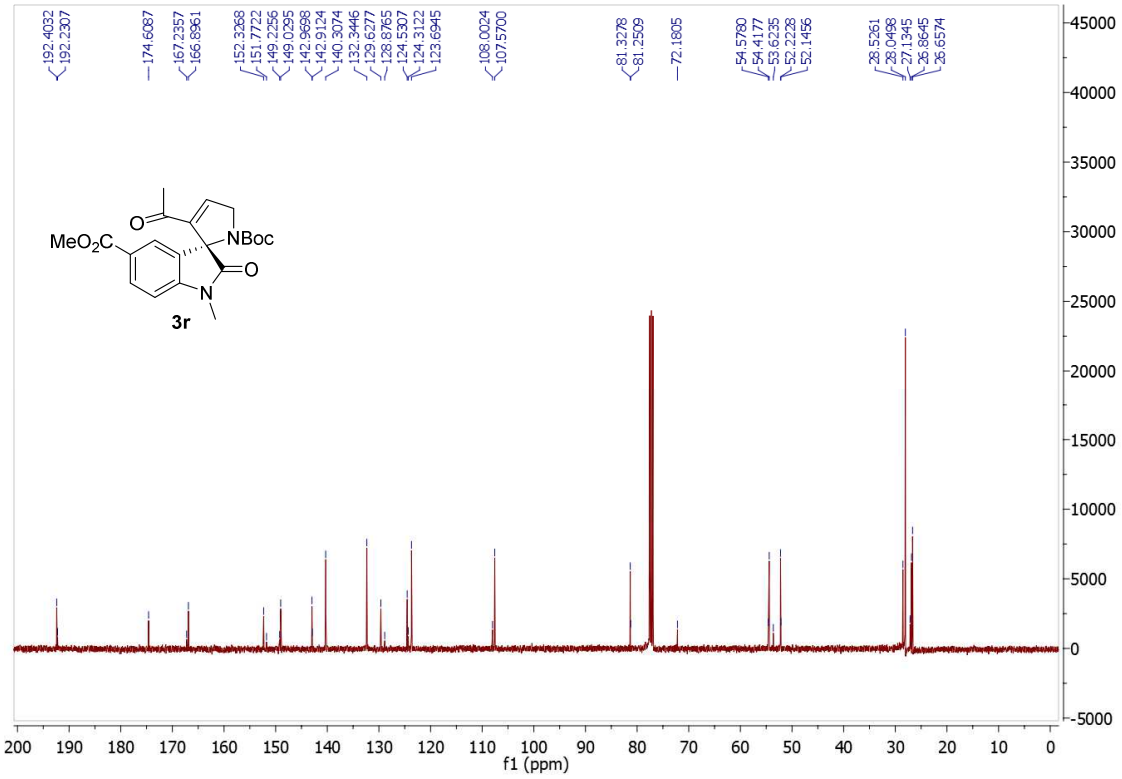
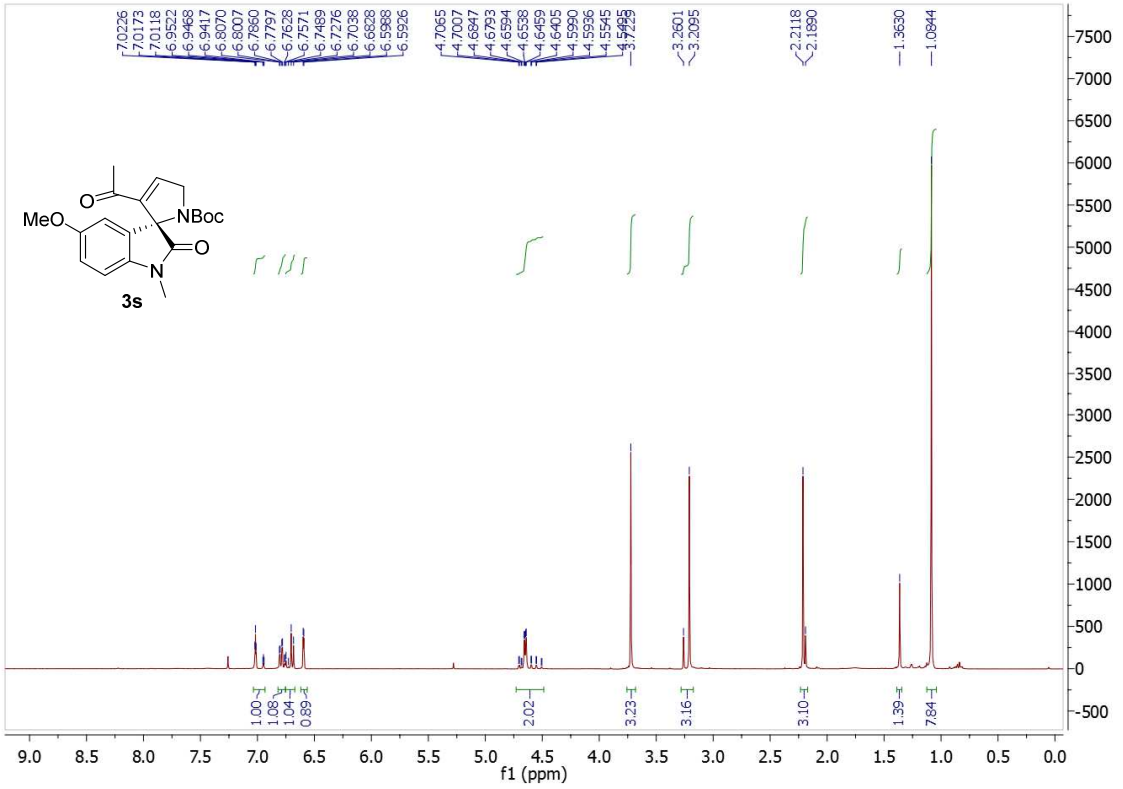
28.0184
27.9060
26.7143
26.6834
f1 (ppm)
NBoc
O
N
F
3q


MeO2C
NBoc
O
O
N
3r
f1 (ppm)


MeO2C
NBoc
O
O
N
3r
f1 (ppm)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7.0118
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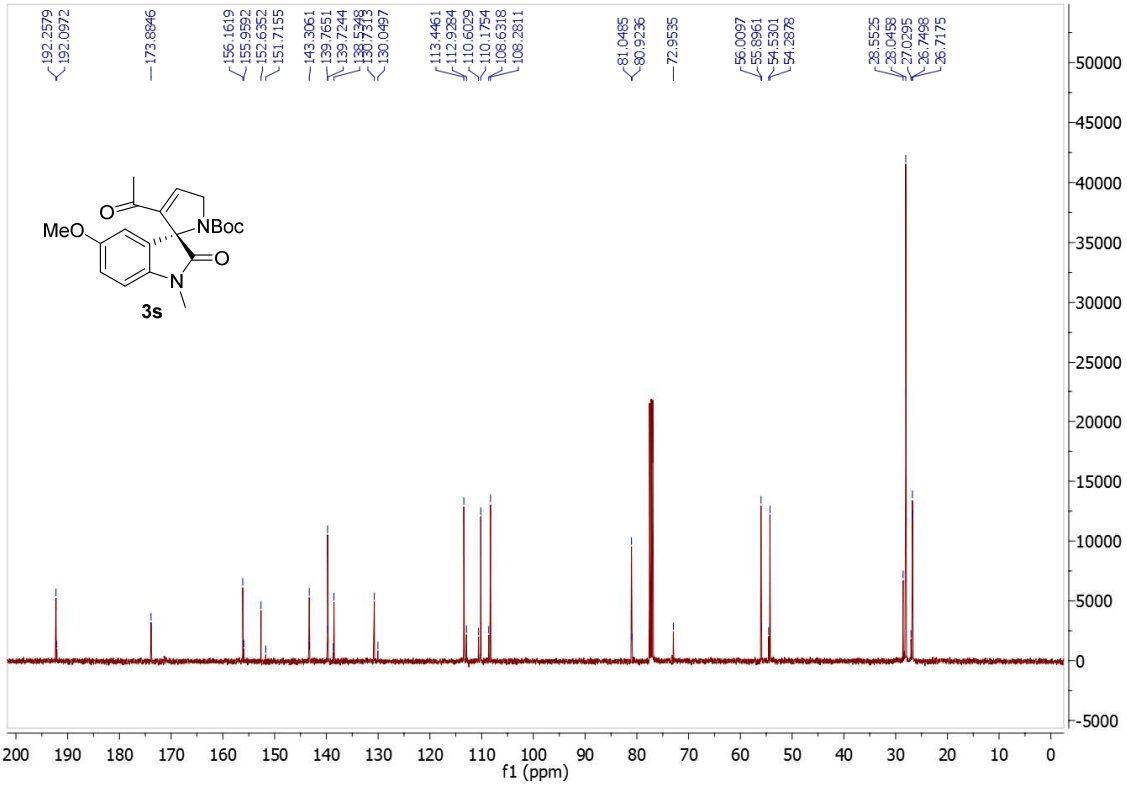
6.9468
6.9417
6.8070
6.8007
6.7860
6.7797
6.7628
6.7571
6.7489
6.7276
6.7038
6.6828
6.5988
6.5926
4.7065
4.7007
4.6947
4.6793
4.6694
4.6538
4.6459
4.6405
4.5990
4.5936
4.5545
3.7229
3.2601
3.2095
2.2118
2.1890
1.3630
1.0844
MeO
NBoc
O
O
N
3s
1.00
1.08
1.04
0.89
2.02
3.23
3.16
3.10
1.39
7.84
f1 (ppm)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173.8846
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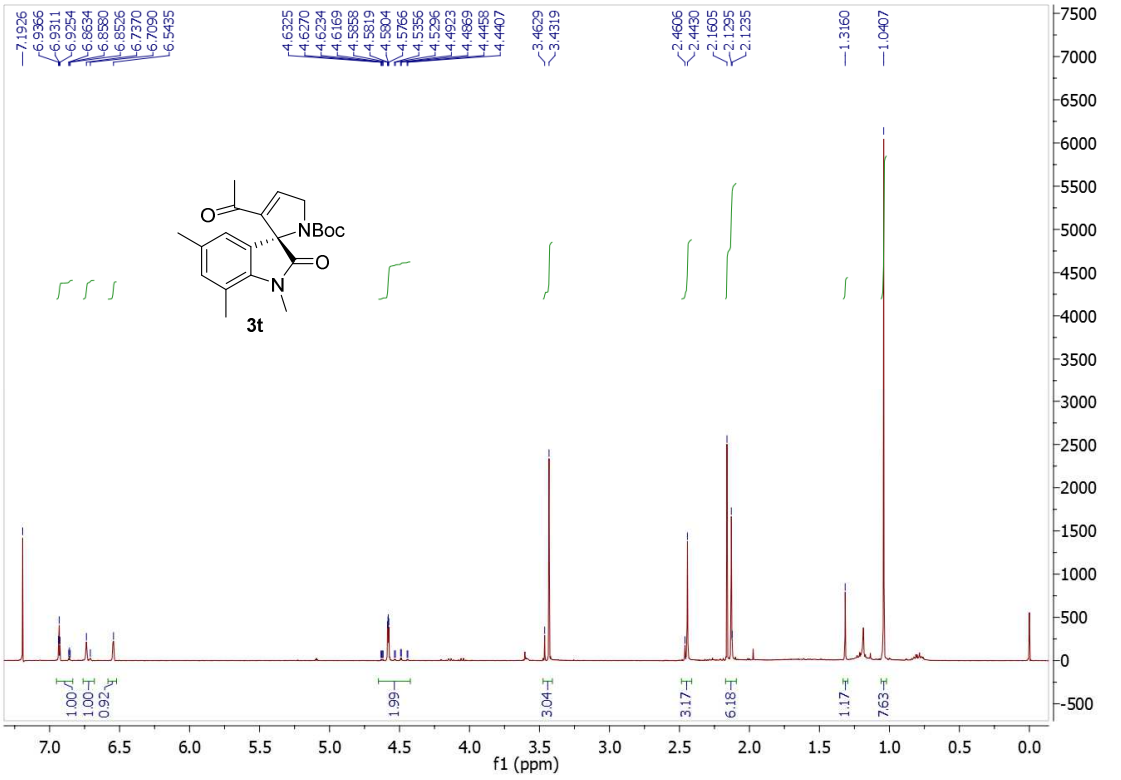
151.7155
143.3061
139.7651
139.7244
130.7313
130.0497
113.4461
112.9284
110.6029
110.1754
108.6318
108.2811
81.0485
80.9236
72.9535
56.0097
55.8961
54.5301
54.2878
28.5525
28.0458
27.0295
26.7498
26.7175
MeO
NBoc
O
O
N
3s
f1 (ppm)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6.8634
6.8580
6.8526
6.7370
6.7090
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4.6325
4.6270
4.6234
4.6169
4.5858
4.5819
4.5804
4.5766
4.5536
4.5296
4.4923
4.4869
4.4458
4.4407
3.4629
3.4319
2.4606
2.4430
2.1605
2.1295
2.1235
1.3160
1.0407
NBoc
O
N
3t
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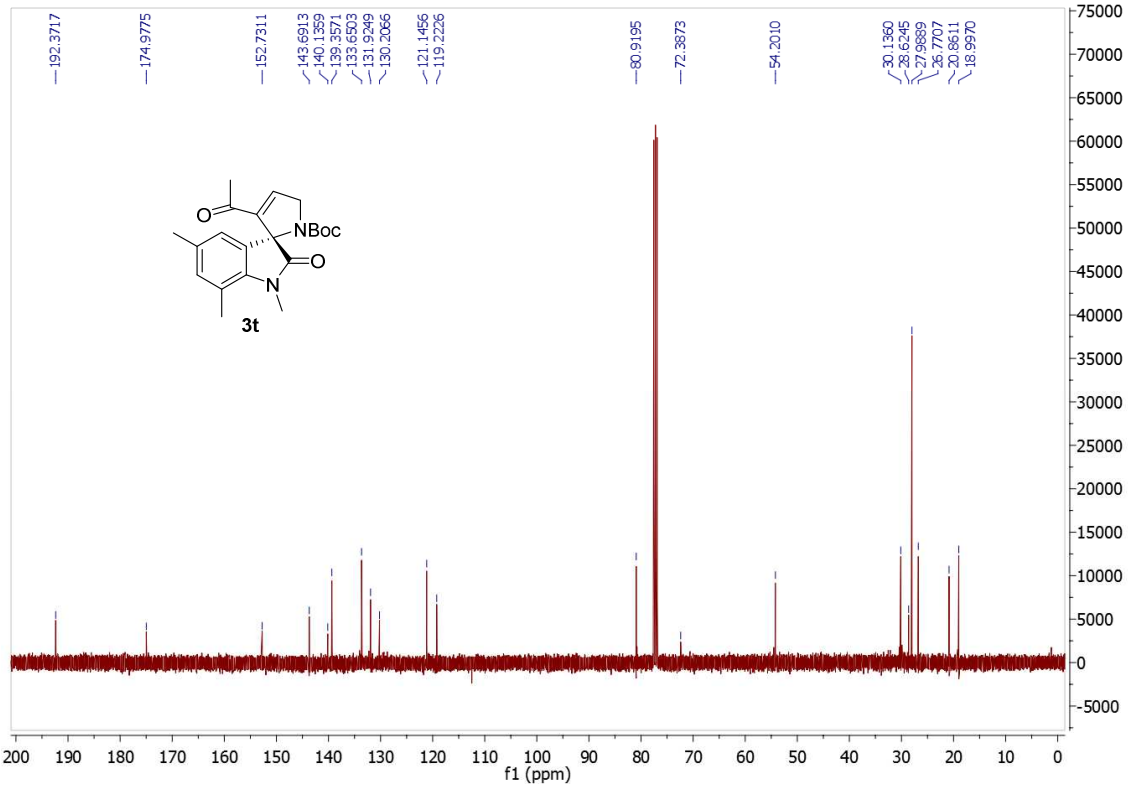
1.00
0.92
1.99
3.04
3.17
6.18
1.17
7.63
f1 (ppm)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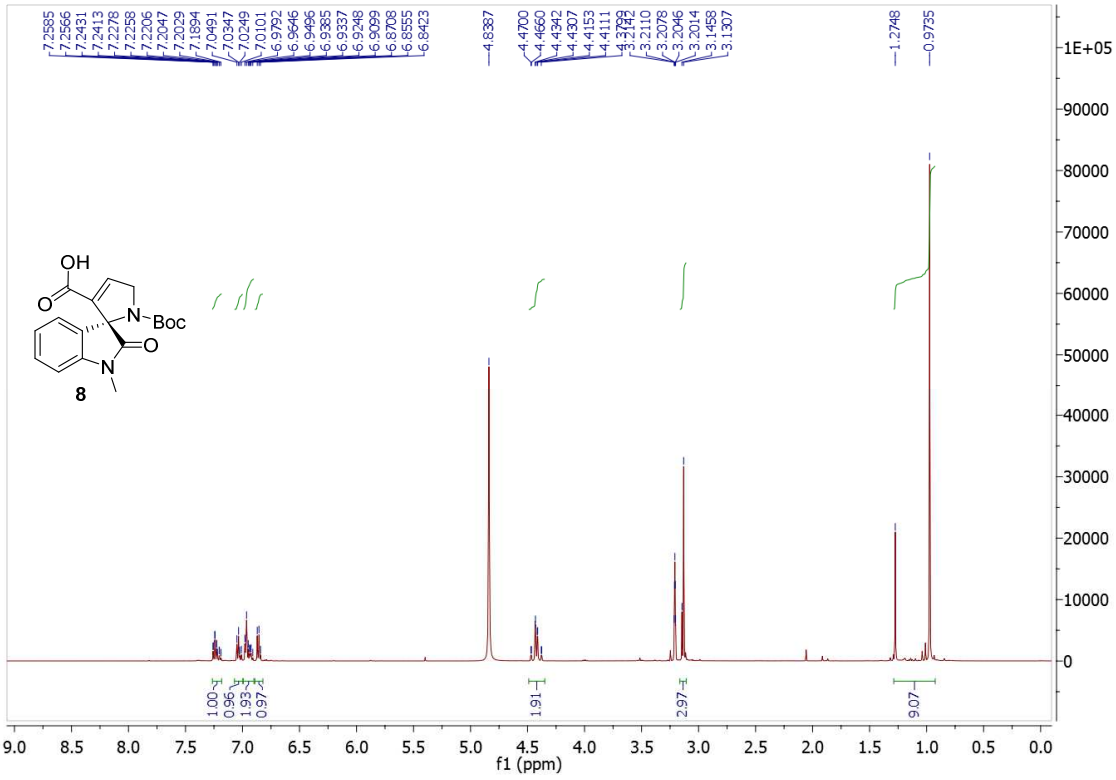
139.3571
133.6503
131.9249
130.2066
121.1456
119.2226
80.9195
72.3873
54.2010
30.1360
28.6245
27.9889
26.7707
20.8611
18.9970
NBoc
O
N
3t
f1 (ppm)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7.2413
7.2278
7.2258
7.2206
7.2047
7.2029
7.1894
7.0491
7.0347
7.0249
7.0101
6.9792
6.9646
6.9496
6.9385
6.9337
6.9248
6.9099
6.8708
6.8555
6.8423
4.8387
4.4700
4.4660
4.4342
4.4307
4.4153
4.4111
3.2142
3.2110
3.2078
3.2046
3.2014
3.1458
3.1307
1.2748
0.9735
OH
O
N
Boc
O
N
8
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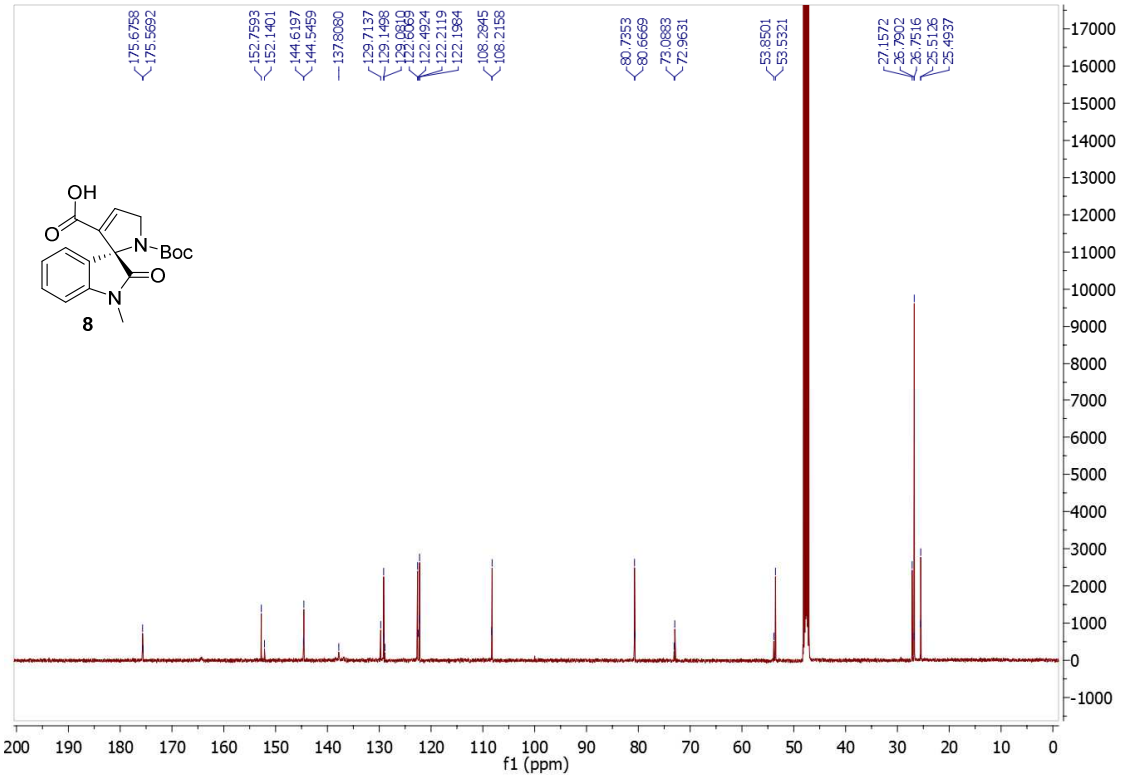
0.96
1.93
0.97
1.91
2.97
9.07
f1 (ppm)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137.8080
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122.2119
122.1984
108.2945
108.2158
80.7353
80.6669
73.0883
72.9631
53.8501
53.5321
27.1572
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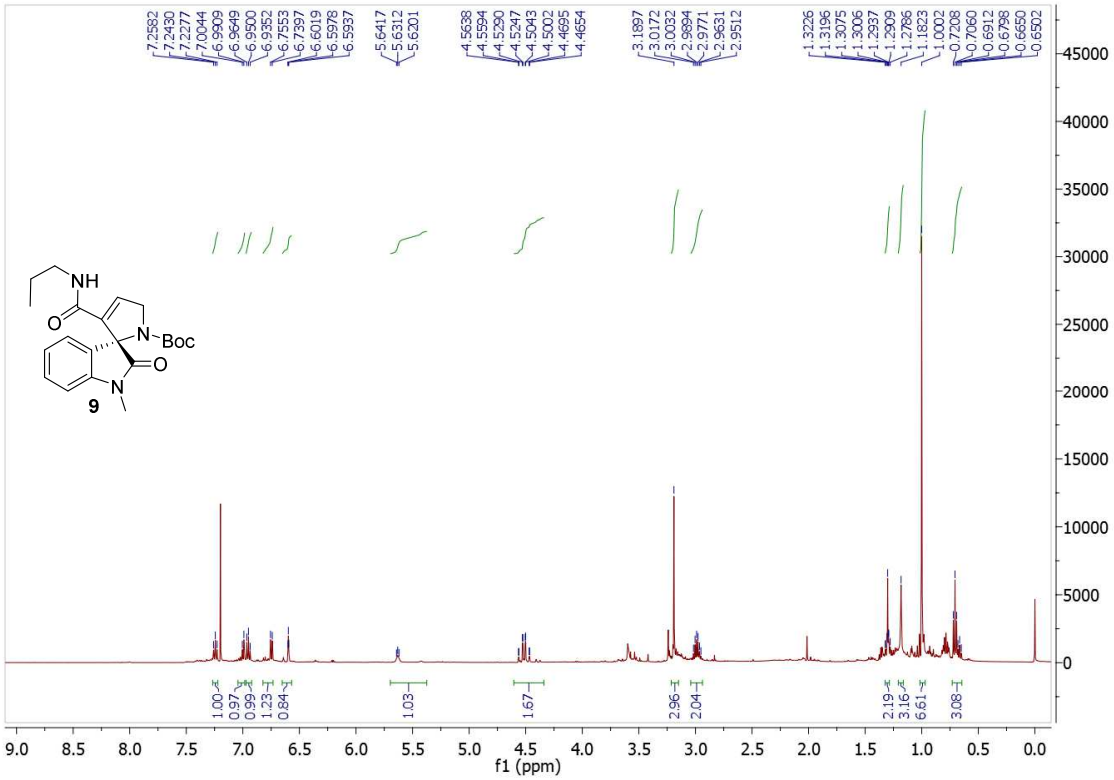
26.7516
25.5126
25.4937
OH
O
N
Boc
O
N
8
f1 (ppm)


NH
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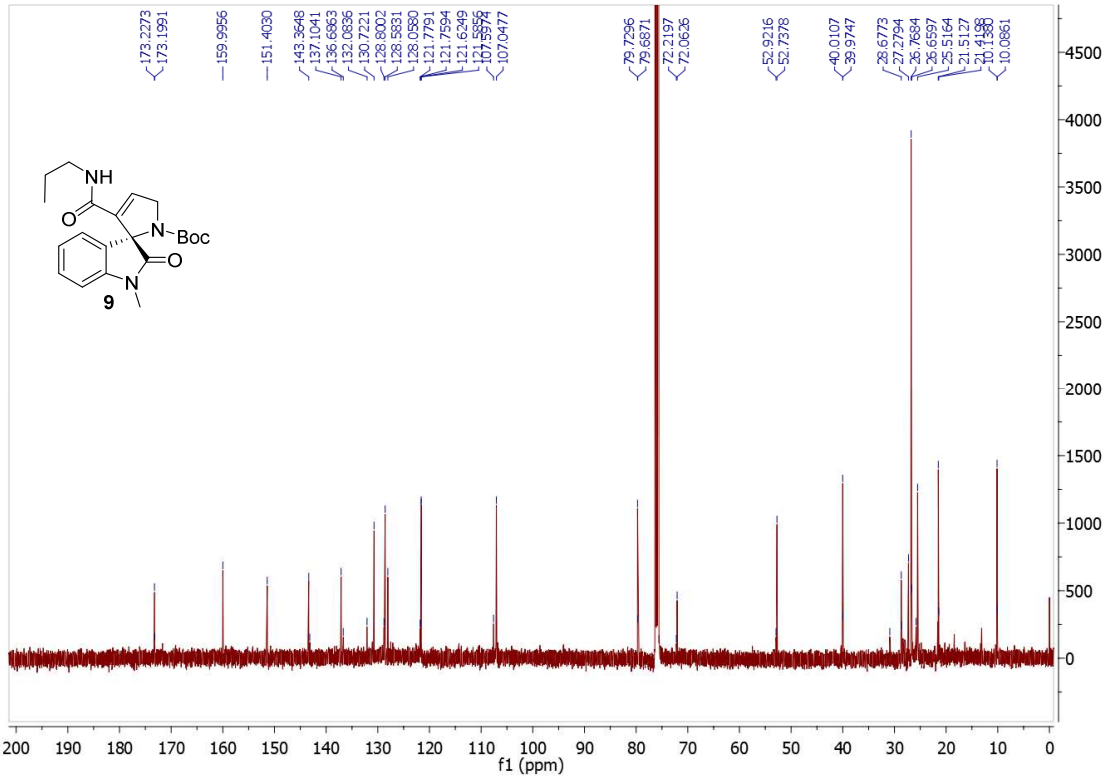
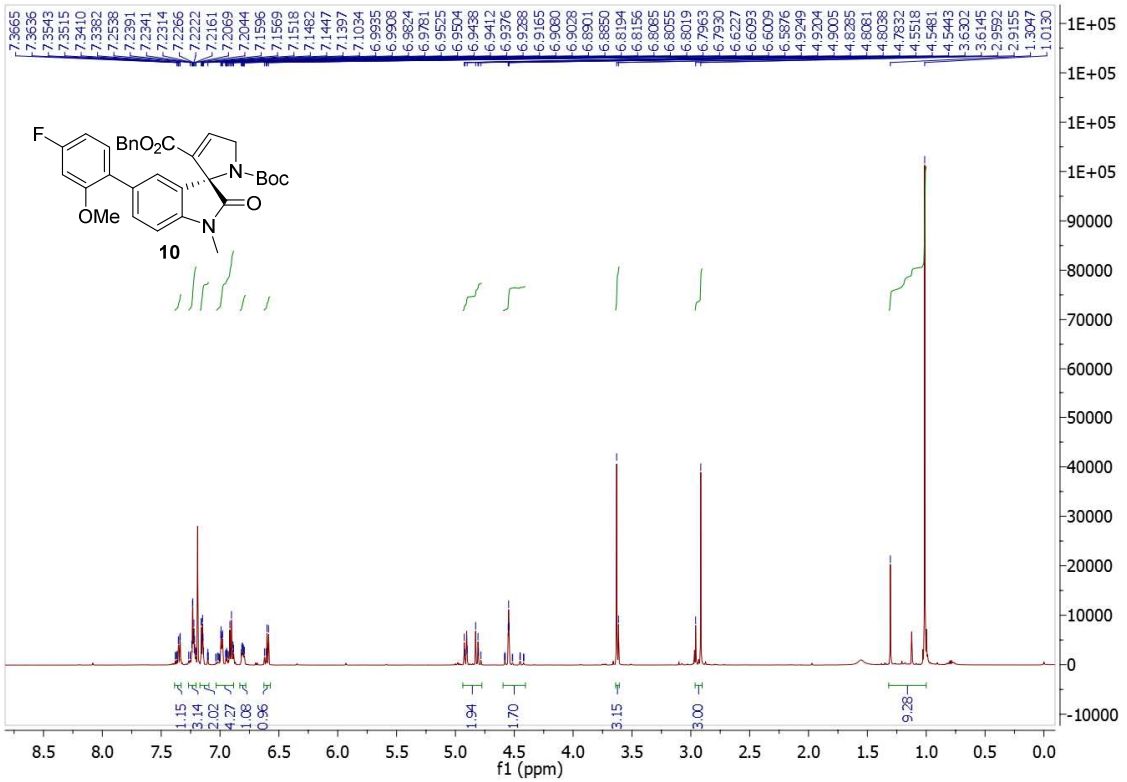
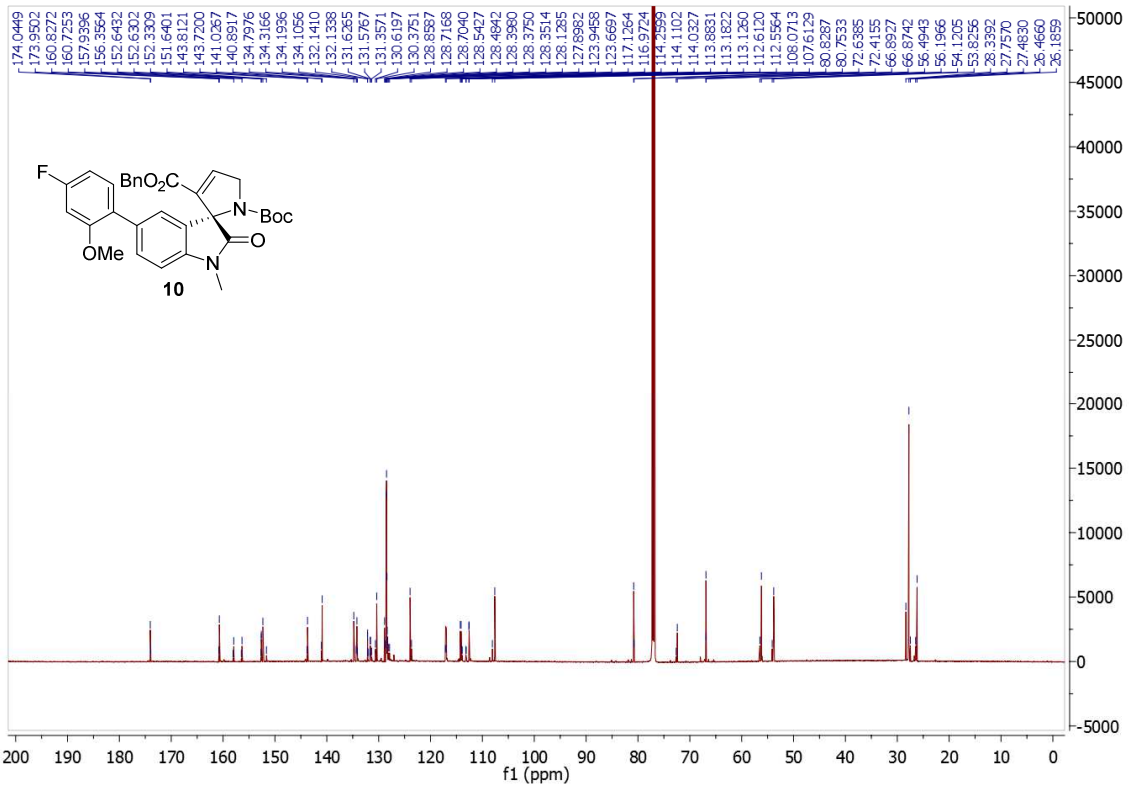
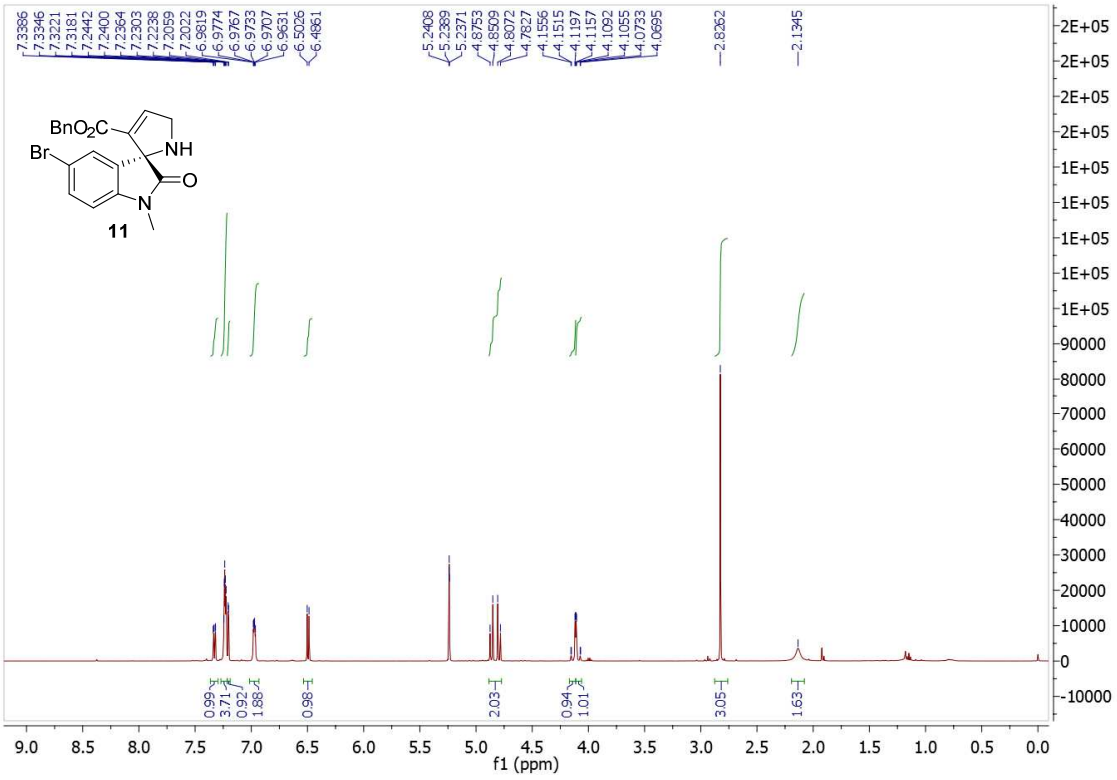
N
Boc
O
N
9
f1 (ppm)


NH
O
N
Boc
O
N
9
f1 (ppm)


F
BnO2C
N
Boc
O
OMe
N
10
f1 (ppm)


F
BnO2C
N
Boc
O
OMe
N
10
f1 (ppm)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7.2400
7.2364
7.2303
7.2238
7.2059
7.2022
6.9819
6.9774
6.9767
6.9733
6.9707
6.9631
6.5026
6.4861
5.2408
5.2389
5.2371
4.8753
4.8509
4.8072
4.7827
4.1556
4.1515
4.1197
4.1157
4.1092
4.1055
4.0733
4.0695
2.8262
2.1345
BnO2C
Br
NH
O
N
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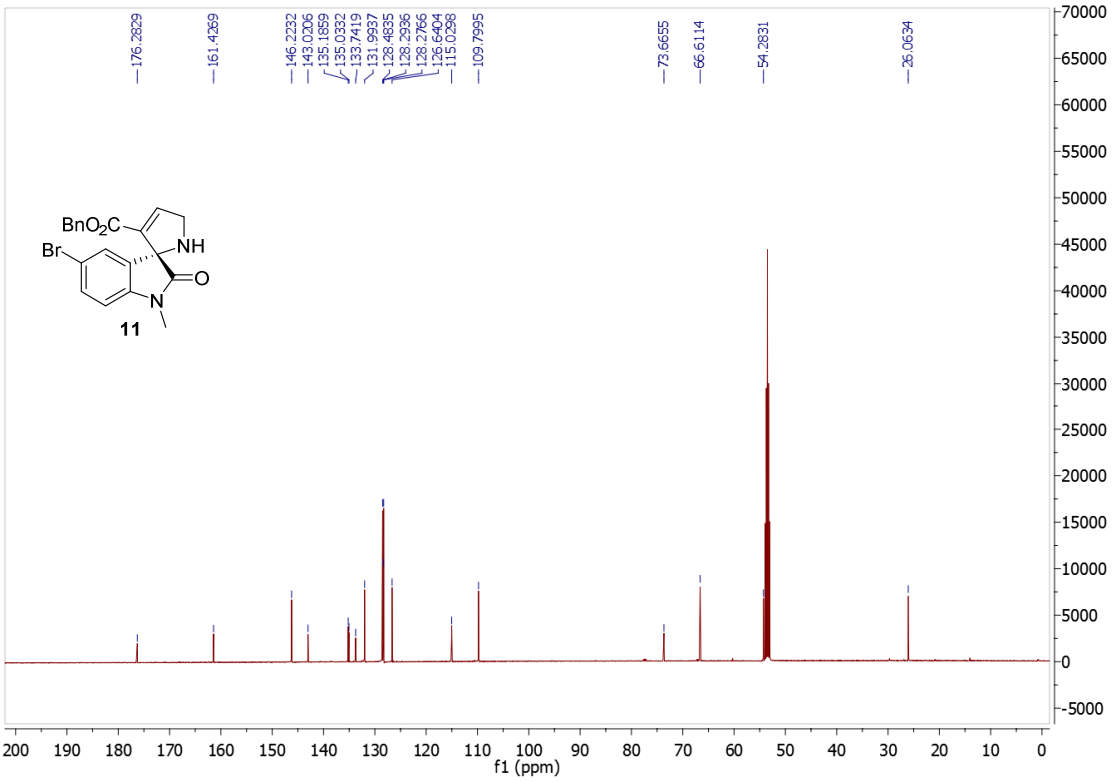
0.92
1.88
0.98
2.03
0.94
1.01
3.05
1.63
f1 (ppm)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135.1859
135.0332
133.7419
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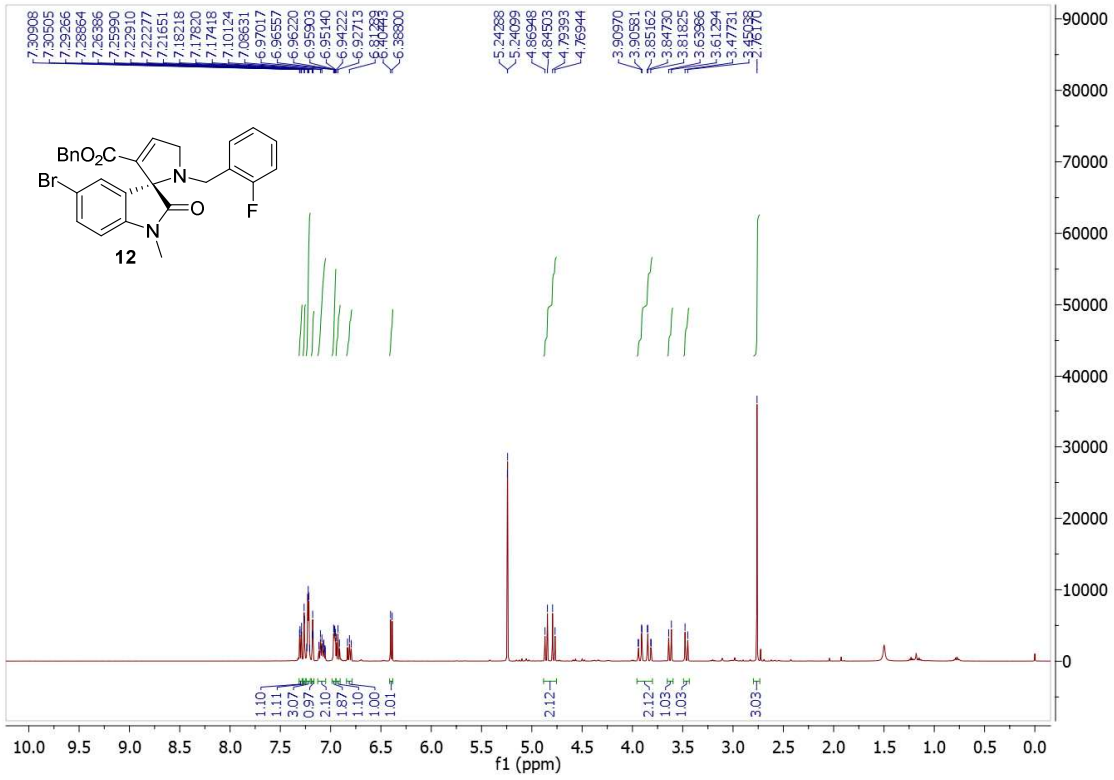
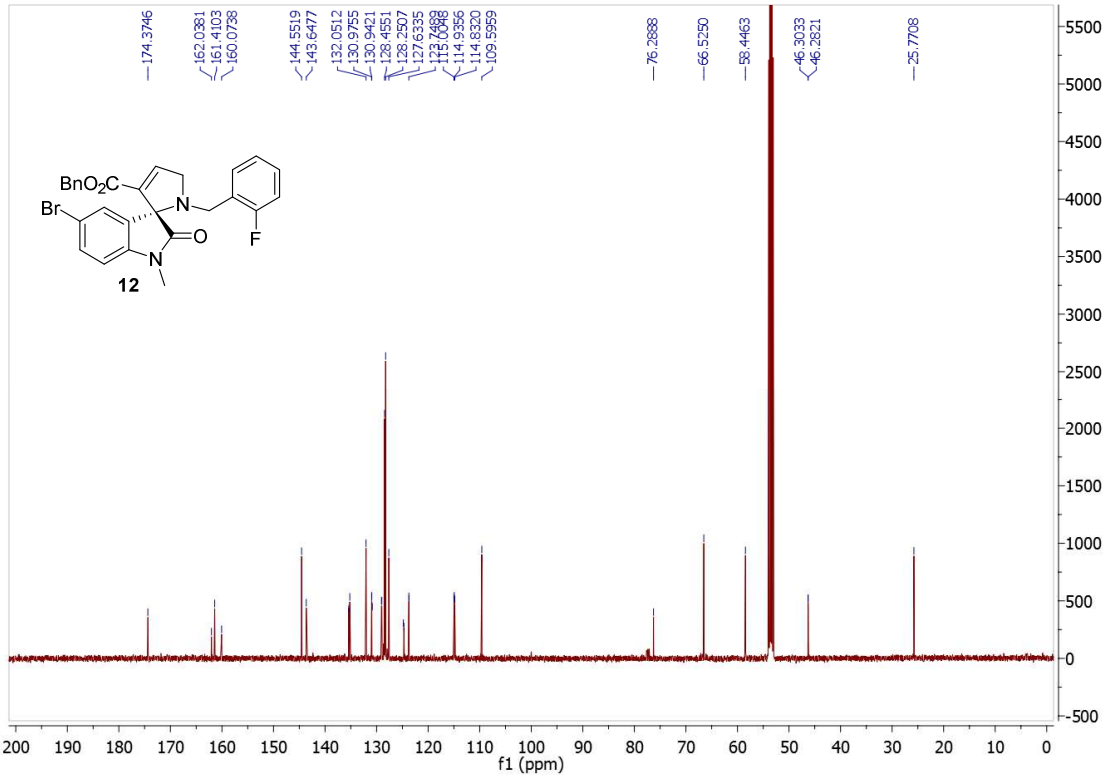
128.4835
128.2936
128.2766
126.6404
115.0298
109.7995
73.6655
66.6114
54.2831
26.0634
BnO2C
Br
NH
O
N
11
f1 (ppm)


BnO2C
Br
N
O
F
N
12
f1 (ppm)


BnO2C
Br
N
O
F
N
12
f1 (ppm)