

Enantioselective Conjugate Addition of 3-Fluoro-Oxindoles to Vinyl Sulfone: An Organocatalytic Access to Chiral 3-Fluoro-3-Substituted Oxindoles

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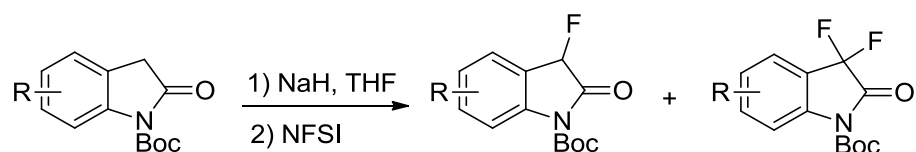
Supporting Information

A.	General Information	S2
B.	Preparation of the 3-F-Oxindole Substrates	S2
C.	Representative Procedure for the Conjugate Addition Reactions	S7
D.	Analytical Data and HPLC Chromatogram of the Products	S7
E.	X-Ray Crystallographic Analysis and Determination of the Absolute Configurations of the Products	S24
F.	NMR Spectra of the Substrates and the Products	S26

A. General Information

All the starting materials were obtained from commercial sources and used without further purification unless otherwise stated. ^1H and ^{13}C NMR spectra were recorded on a Bruker ACF300 or AMX500 (500 MHz) spectrometer. Chemical shifts were reported in parts per million (ppm), and the residual solvent peak was used as an internal reference: proton (chloroform δ 7.26), carbon (chloroform δ 77.0). Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), br s (broad singlet). Coupling constants were reported in Hertz (Hz). Low resolution mass spectra were obtained on a Finnigan/MAT LCQ spectrometer in ESI mode, and a Finnigan/MAT 95XL- T mass spectrometer in FAB mode. All high resolution mass spectra were obtained on a Finnigan/MAT 95XL- T spectrometer. For thin layer chromatography (TLC), Merck pre-coated TLC plates (Merck 60 F254) were used, and compounds were visualized with a UV light at 254 nm. Further visualization was achieved by staining with iodine, or ceric ammonium molybdate followed by heating on a hot plate. Flash chromatographic separations were performed on Merck 60 (0.040- 0.063 mm) mesh silica gel. The enantiomeric excesses of products were determined by chiral-phase HPLC analysis.

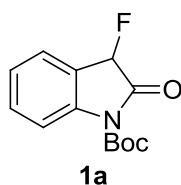
B. Preparation of the 3-F-Oxindole Substrates



Boc-protected oxindole (1 mmol) was dissolved in dry THF (5 mL) under N_2 protection and the solution was cooled to 0 °C. NaH (1 mmol) was added and the mixture was stirred at 0 °C for 30 min. NFSI (1 mmol) was added to the mixture in one portion and the resulting mixture was stirred at 0 °C to room temperature for 15 min. The reaction mixture was quenched by addition of water (10 mL) and the mixture was extracted with CH_2Cl_2 (15 mL $\times$ 3). The combined organic phase was dried over MgSO_4 , filtered and concentrated *in*

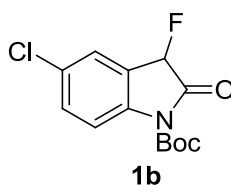
vacuo, which was purified by flash column chromatography (ethyl acetate/hexane = 1:7) to afford the desired monofluorinated product (38-46% yield), the bisfluorinated side product (8-13% yield) and the recovered Boc-protected oxindole (23-41% recovered).

tert-Butyl 3-fluoro-2-oxoindoline-1-carboxylate **1a**



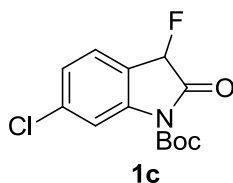
A white solid; ^1H NMR (500 MHz, CDCl_3) δ 1.63 (s, 9H), 5.70 (d, J = 51.1 Hz, 1H), 7.22 (t, J = 7.6 Hz, 1H), 7.43 (t, J = 7.9 Hz, 1H), 7.49 (d, J = 7.6 Hz, 1H), 7.87 (d, J = 8.2 Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 28.0, 85.0 (d, J = 187.7 Hz), 85.1, 115.6, 121.8 (d, J = 16.4 Hz), 125.0 (d, J = 2.7 Hz), 125.9, 131.7 (d, J = 2.7 Hz), 140.9 (d, J = 4.6 Hz), 148.7, 169.0 (d, J = 17.3 Hz); ^{19}F NMR (282.38 MHz, CDCl_3) δ -111.1 (d, J = 51.6 Hz); HRMS (ESI) m/z calcd for $\text{C}_{13}\text{H}_{14}\text{FNO}_3\text{Na}$ $[\text{M}+\text{Na}]^+ = 274.0850$, found = 274.0860.

tert-Butyl 5-chloro-3-fluoro-2-oxoindoline-1-carboxylate **1b**



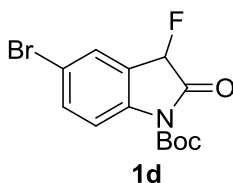
A white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.63 (s, 9H), 5.68 (d, J = 50.9 Hz, 1H), 7.40-7.44 (m, 1H), 7.48 (s, 1H), 7.85 (dd, J = 1.3 Hz, 8.7 Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 28.0, 84.6 (d, J = 190.4 Hz), 85.4, 117.0, 123.3 (d, J = 16.4 Hz), 126.1, 130.6 (d, J = 2.7 Hz), 131.7 (d, J = 2.7 Hz), 139.4 (d, J = 4.6 Hz), 148.5, 168.1 (d, J = 18.2 Hz); ^{19}F NMR (282.38 MHz, CDCl_3) δ -112.2 (d, J = 52.6 Hz); HRMS (ESI) m/z calcd for $\text{C}_{13}\text{H}_{13}\text{FCINO}_3\text{Na}$ $[\text{M}+\text{Na}]^+ = 308.0460$, found = 308.0452.

tert-Butyl 6-chloro-3-fluoro-2-oxoindoline-1-carboxylate **1c**



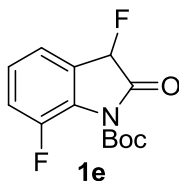
A white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.64 (s, 9H), 5.68 (d, J = 51.1 Hz, 1H), 7.21-7.24 (m, 1H), 7.43 (dd, J = 1.1 Hz, 7.9 Hz, 1H), 7.97 (s, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 28.0, 84.4 (d, J = 189.5 Hz), 85.6, 116.5, 120.0 (d, J = 16.4 Hz), 125.2 (d, J = 2.7 Hz), 126.8, 137.8 (d, J = 3.7 Hz), 141.9 (d, J = 4.6 Hz), 148.4, 168.4 (d, J = 18.2 Hz); ^{19}F NMR (282.38 MHz, CDCl_3) δ -110.8 (d, J = 51.6 Hz); HRMS (ESI) m/z calcd for $\text{C}_{13}\text{H}_{13}\text{FCINO}_3\text{Na}$ $[\text{M}+\text{Na}]^+ = 308.0460$, found = 308.0452.

tert-Butyl 5-bromo-3-fluoro-2-oxoindoline-1-carboxylate 1d



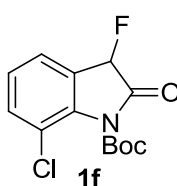
A white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.63 (s, 9H), 5.69 (d, J = 50.9 Hz, 1H), 7.55-7.59 (m, 1H), 7.63 (s, 1H), 7.76-7.82 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 28.0, 84.4 (d, J = 190.4 Hz), 85.5, 117.1, 117.3, 123.6 (d, J = 16.4 Hz), 128.9 (d, J = 34.6 Hz), 134.7 (d, J = 3.7 Hz), 139.9, 148.5, 168.1 (d, J = 21.0 Hz); ^{19}F NMR (282.38 MHz, CDCl_3) δ -112.1 (dd, J = 2.1 Hz, 27.3 Hz); HRMS (ESI) m/z calcd for $\text{C}_{13}\text{H}_{13}\text{F}^{79}\text{BrNO}_3\text{Na}$ $[\text{M}+\text{Na}]^+ = 351.9951$, found = 351.9926, $\text{C}_{13}\text{H}_{13}\text{F}^{81}\text{BrNO}_3\text{Na}$ $[\text{M}+\text{Na}]^+ = 353.9937$, found = 353.9918.

tert-Butyl 3,7-difluoro-2-oxoindoline-1-carboxylate 1e



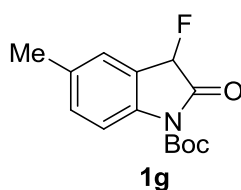
A white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.61 (s, 9H), 5.75 (d, J = 50.8 Hz, 1H), 7.17-7.24 (m, 2H), 7.31-7.34 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 27.6, 76.5, 84.6 (d, J = 160.4 Hz), 86.1 (d, J = 2.2 Hz), 119.8 (d, J = 3.3 Hz), 120.1 (d, J = 2.7 Hz), 121.8 (d, J = 3.3 Hz), 124.7 (d, J = 15.3 Hz), 126.2 (d, J = 2.7 Hz), 126.3, 146.7 (d, J = 14.2 Hz), 150.2, 168.4 (d, J = 18.5 Hz); ^{19}F NMR (282.38 MHz, CDCl_3) δ -111.0 (d, J = 50.5 Hz), (-42.2) (t, J = 7.2 Hz); HRMS (ESI) m/z calcd for $\text{C}_{13}\text{H}_{13}\text{F}_2\text{NO}_3\text{Na}$ $[\text{M}+\text{Na}]^+ = 292.0761$, found = 292.0753.

tert-Butyl 7-chloro-3-fluoro-2-oxoindoline-1-carboxylate **1f**



A white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.63 (s, 9H), 5.74 (d, J = 50.8 Hz, 1H), 7.15-7.21 (m, 1H), 7.41-7.44 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 27.7, 85.1 (d, J = 191.3 Hz), 86.3, 119.5, 124.5, 125.0 (d, J = 21.9 Hz), 125.8, 133.3, 138.2, 147.1, 169.2 (d, J = 20.0 Hz); ^{19}F NMR (282.38 MHz, CDCl_3) δ -112.5 (d, J = 50.5 Hz); HRMS (ESI) m/z calcd for $\text{C}_{13}\text{H}_{13}\text{FCINO}_3\text{Na}$ $[\text{M}+\text{Na}]^+ = 308.0460$, found = 308.0452.

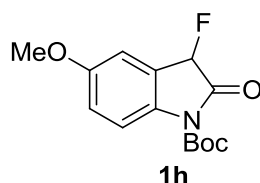
tert-Butyl 3-fluoro-5-methyl-2-oxoindoline-1-carboxylate **1g**



A colorless oil; ^1H NMR (300 MHz, CDCl_3) δ 1.63 (s, 9H), 2.37 (s, 3H), 5.68 (d, J = 51.3 Hz, 1H), 7.24 (d, J = 8.4 Hz, 1H), 7.31 (s, 1H), 7.74 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 20.8, 28.0, 84.8, 85.1 (d, J = 187.6 Hz), 115.3 (d, J = 1.6 Hz), 121.6 (d, J = 16.4 Hz), 126.3, 132.1 (d, J = 3.3 Hz), 134.8 (d, J = 2.7 Hz), 138.4 (d, J = 5.5 Hz), 148.6, 169.0 (d, J = 17.5 Hz); ^{19}F NMR

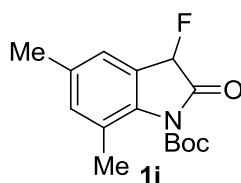
(282.38 MHz, CDCl₃) δ -110.8 (d, J = 51.6 Hz); HRMS (ESI) m/z calcd for C₁₄H₁₆FNO₃Na [M+Na]⁺ = 288.1006, found = 288.1020.

tert-Butyl 3-fluoro-5-methoxy-2-oxoindoline-1-carboxylate **1h**



A white solid; ¹H NMR (500 MHz, CDCl₃) δ 1.63 (s, 9H), 3.83 (s, 3H), 5.69 (d, J = 51.1 Hz, 1H), 6.95-6.98 (m, 1H), 7.06 (s, 1H), 7.79 (dd, J = 1.3 Hz, 8.8 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 28.1, 55.8, 84.9, 85.2 (d, J = 188.6 Hz), 111.4, 116.7, 117.0 (d, J = 3.6 Hz), 122.8 (d, J = 16.4 Hz), 134.1 (d, J = 3.6 Hz), 148.7, 157.2 (d, J = 3.7 Hz), 169.0 (d, J = 19.1 Hz); ¹⁹F NMR (282.38 MHz, CDCl₃) δ -111.4 (t, J = 25.8 Hz); HRMS (ESI) m/z calcd for C₁₄H₁₆FNO₄Na [M+Na]⁺ = 304.0956, found = 304.0965.

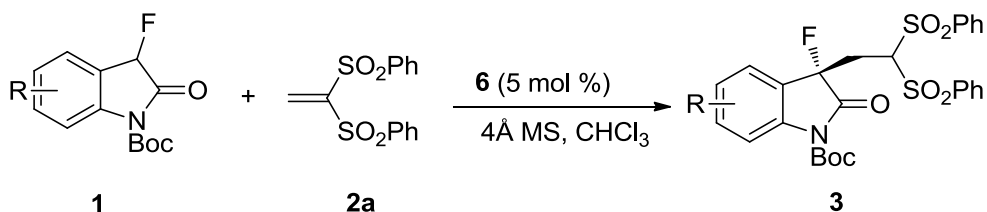
tert-Butyl 3-fluoro-5,7-dimethyl-2-oxoindoline-1-carboxylate **1i**



A white solid; ¹H NMR (300 MHz, CDCl₃) δ 1.62 (s, 9H), 2.19 (s, 3H), 2.32 (s, 3H), 5.67 (d, J = 51.3 Hz, 1H), 7.05 (s, 1H), 7.14 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 19.3, 20.7, 27.7, 85.1, 85.6 (d, J = 188.7 Hz), 123.0 (d, J = 16.4 Hz), 124.0, 124.2 (d, J = 1.6 Hz), 134.7 (d, J = 3.3 Hz), 135.0 (d, J = 3.3 Hz), 136.8 (d, J = 4.9 Hz), 148.5, 170.1 (d, J = 17.5 Hz); ¹⁹F NMR (282.38 MHz, CDCl₃) δ -110.6 (d, J = 51.6 Hz); HRMS (ESI) m/z calcd for C₁₅H₁₇FNO₃ [M-H]⁻ = 278.0810, found = 278.0818.

C. Representative procedure

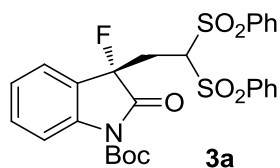
Asymmetric Conjugate Addition of 3-F-Oxindoles to Vinylsulfone



Oxindole **1** (0.05 mmol) was at room temperature added to a mixture of vinylsulfone **2** (0.05 mmol), catalyst **6** (1.5 mg, 0.0025 mmol) and 4 Å molecular sieves (10 mg) in CHCl₃ (1.0 mL) in a sample vial, and the resulting mixture was sealed and stirred at room temperature for the time specified in Table 2. At the end of the reaction, the reaction mixture was filtered and concentrated *in vacuo* to yield the crude product, which was purified by flash column chromatography (ethyl acetate/hexane = 1:3) to afford the desired adducts **3**. The enantiomeric excesses of **3** were determined by chiral HPLC analysis.

D. Analytical data and HPLC chromatogram of the conjugate addition adducts

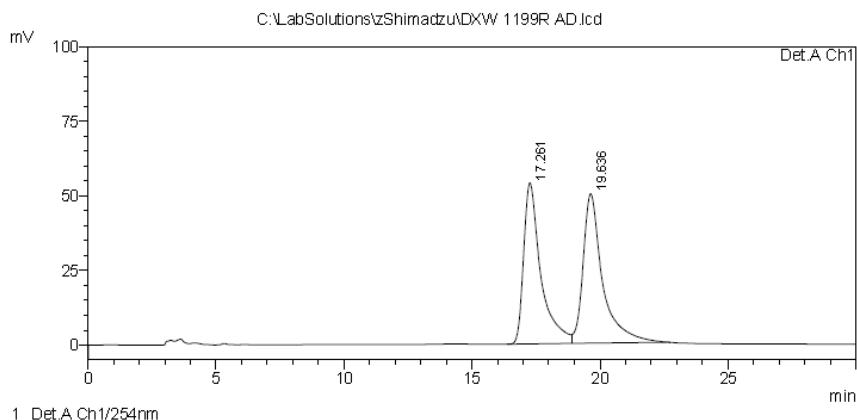
(S)-tert-Butyl 3-(2,2-bis(phenylsulfonyl)ethyl)-3-fluoro-2-oxindoline-1-carboxylate **3a**



A white solid; ¹H NMR (500 MHz, CDCl₃) δ 1.62 (s, 9H), 3.00-3.08 (m, 1H), 3.10-3.23 (m, 1H), 5.38 (t, *J* = 4.4 Hz, 1H), 7.24 (d, *J* = 7.6 Hz, 1H), 7.36 (d, *J* = 7.6 Hz, 1H), 7.48 (t, *J* = 7.9 Hz, 1H), 7.51-7.58 (m, 4H), 7.65-7.71 (m, 2H), 7.86 (d, *J* = 7.6 Hz, 2H), 7.93 (d, *J* = 8.2 Hz, 1H), 8.01-8.03 (m, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 28.0, 31.2 (d, *J* = 31.0 Hz), 76.8, 85.0, 89.2 (d, *J* = 189.5 Hz), 116.1, 123.7 (d, *J* = 18.2 Hz), 124.0, 125.2, 129.1 (d, *J* = 23.7 Hz), 129.7 (d, *J*

= 1.8 Hz), 132.2 (d, J = 2.7 Hz), 134.6 (d, J = 30.1 Hz), 137.0, 138.3, 140.0 (d, J = 4.6 Hz), 148.3, 170.1 (d, J = 22.8 Hz); ^{19}F NMR (282.38 MHz, CDCl_3) δ -75.6 (dd, J = 11.3 Hz, 32.0 Hz); The ee value was 93%, t_{R} (minor) = 17.52 min, t_{R} (major) = 20.04 min (Chiralcel AD-H, λ = 254 nm, 10% *i*PrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI) m/z calcd for $\text{C}_{27}\text{H}_{26}\text{FNO}_7\text{S}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ = 582.1027, found = 582.1025; $[\alpha]_{\text{D}}^{27}$ = +21.2 (c = 0.95, CHCl_3).

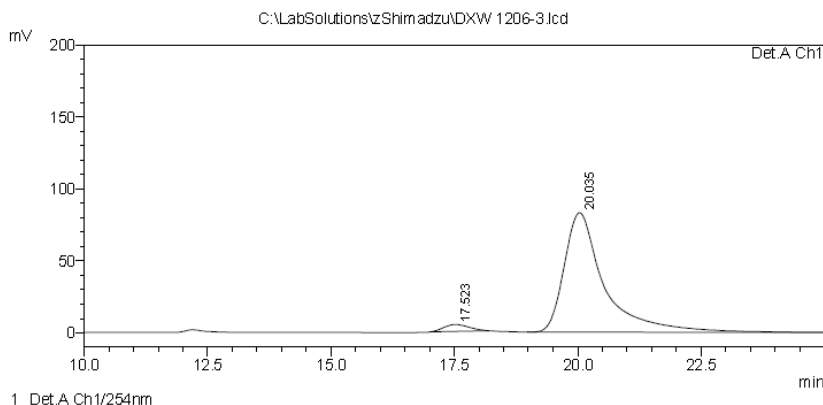
<Chromatogram>



PeakTable					
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1	17.261	2516209	53937	48.624	51.846
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Total		5174788	104033	100.000	100.000

(racemic **3a**)

<Chromatogram>

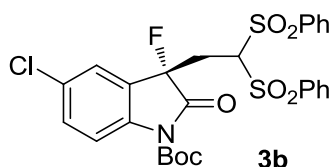


PeakTable					
Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.523	168224	4722	3.450	5.389
2	20.035	4708397	82903	96.550	94.611
Total		4876620	87625	100.000	100.000

(enantiomerically enriched **3a**)

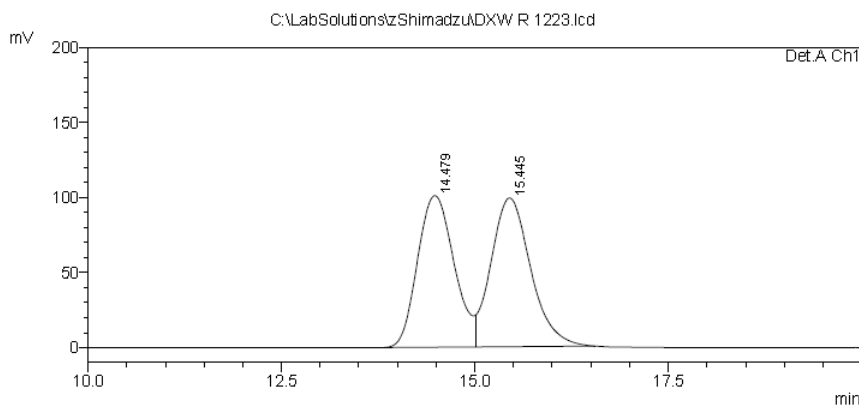
(S)-tert-Butyl-3-(2,2-bis(phenylsulfonyl)ethyl)-5-chloro-3-fluoro-2-oxoindoline-1-carboxylate

e 3b



A white solid; ^1H NMR (500 MHz, CDCl_3) δ 1.62 (s, 9H), 2.98-3.09 (m, 1H), 3.13-3.19 (m, 1H), 5.32 (t, J = 4.4 Hz, 1H), 7.30 (t, J = 1.9 Hz, 1H), 7.45 (d, J = 8.2 Hz, 1H), 7.54-7.59 (m, 4H), 7.68-7.72 (m, 2H), 7.88-7.92 (m, 3H), 8.02 (d, J = 8.2 Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 28.0, 31.3 (d, J = 31.0 Hz), 85.4, 88.9 (d, J = 192.3 Hz), 117.6, 124.2, 125.3 (d, J = 18.2 Hz), 129.2 (d, J = 23.7 Hz), 129.7 (d, J = 10.9 Hz), 130.8 (d, J = 2.7 Hz), 132.2 (d, J = 1.8 Hz), 134.7 (d, J = 31.9 Hz), 136.8, 138.3, 138.5 (d, J = 4.6 Hz), 148.2, 169.5 (d, J = 22.8 Hz); ^{19}F NMR (282.38 MHz, CDCl_3) δ -76.5 (dd, J = 11.9 Hz, 31.4 Hz); The ee value was 93%, t_R (minor) = 14.51 min, t_R (major) = 15.43 min (Chiralcel AD-H, λ = 254 nm, 10% *i*PrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI) m/z calcd for $\text{C}_{27}\text{H}_{25}\text{FCINO}_7\text{S}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ = 616.0637, found = 616.0613; $[\alpha]_D^{27}$ = +23.4 (c = 1.20, CHCl_3).

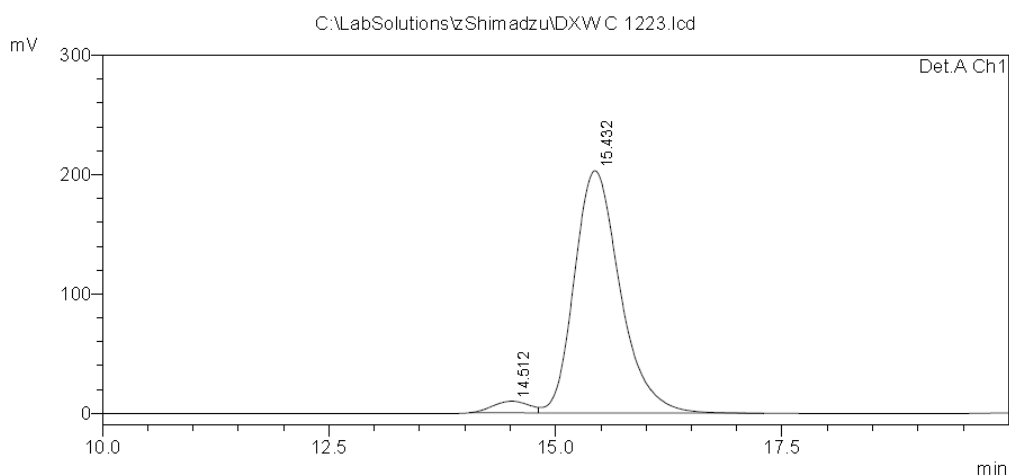
<Chromatogram>



PeakTable						
Detector A Ch1 254nm						
Peak#	Ret. Time	Area	Height	Area %	Height %	
1	14.479	3333637	101018	48.543	50.500	
2	15.445	3533768	99018	51.457	49.500	
Total		6867405	200036	100.000	100.000	

(racemic **3b**)

<Chromatogram>



1 Det.A Ch1/254nm

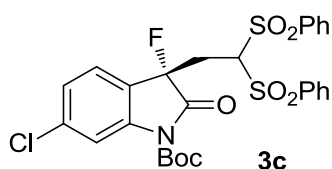
PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.512	266631	9571	3.607	4.509
2	15.432	7124400	202699	96.393	95.491
Total		7391031	212270	100.000	100.000

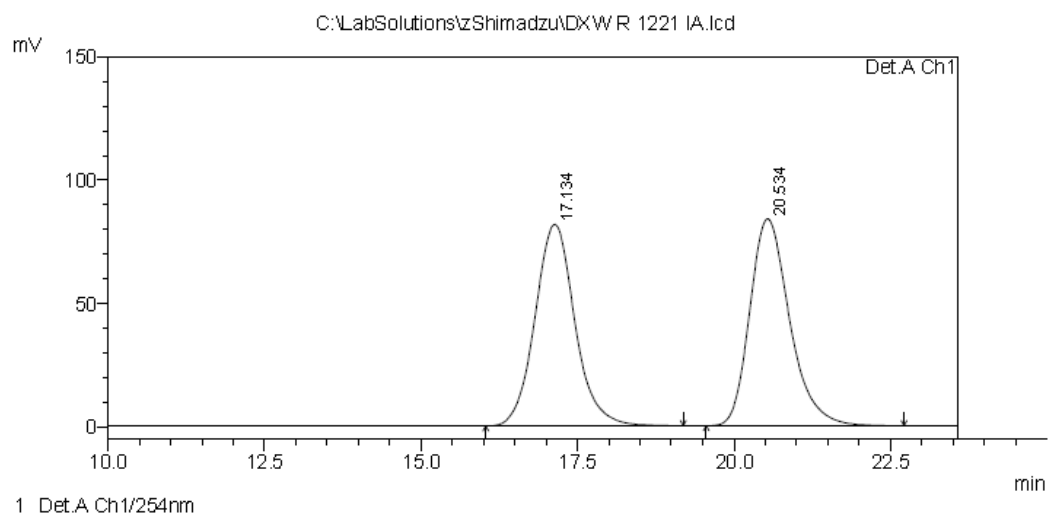
(enantiomerically enriched **3b**)

(S)-tert-Butyl-3-(2,2-bis(phenylsulfonyl)ethyl)-6-chloro-3-fluoro-2-oxindoline-1-carboxylate **3c**



A white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.62 (s, 9H), 2.94-3.23 (m, 2H), 5.33 (t, J = 4.5 Hz, 1H), 7.22-7.32 (m, 2H), 7.51-7.59 (m, 4H), 7.65-7.73 (m, 2H), 7.84-7.87 (m, 2H), 7.99-8.03 (m, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 28.0, 31.3 (d, J = 31.9 Hz), 76.8, 85.6, 89.0 (d, J = 190.4 Hz), 117.0, 122.1 (d, J = 19.1 Hz), 125.0, 125.4 (d, J = 2.7 Hz), 129.2 (d, J = 23.7 Hz), 129.7 (d, J = 2.7 Hz), 134.7 (d, J = 28.2 Hz), 137.1, 138.3, 138.4 (d, J = 3.7 Hz), 141.0 (d, J = 4.6 Hz), 148.2, 169.7 (d, J = 22.8 Hz); ^{19}F NMR (282.38 MHz, CDCl_3) δ -75.2 (dd, J = 11.4 Hz, 32.0 Hz); The ee value was 91%, t_R (minor) = 17.20 min, t_R (major) = 20.55 min (Chiralcel IA, λ = 254 nm, 10% *i*PrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI) m/z calcd for $\text{C}_{27}\text{H}_{25}\text{FCINO}_7\text{S}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ = 616.0637, found = 616.0613; $[\alpha]_D^{27}$ = +16.0 (c = 0.80, CHCl_3).

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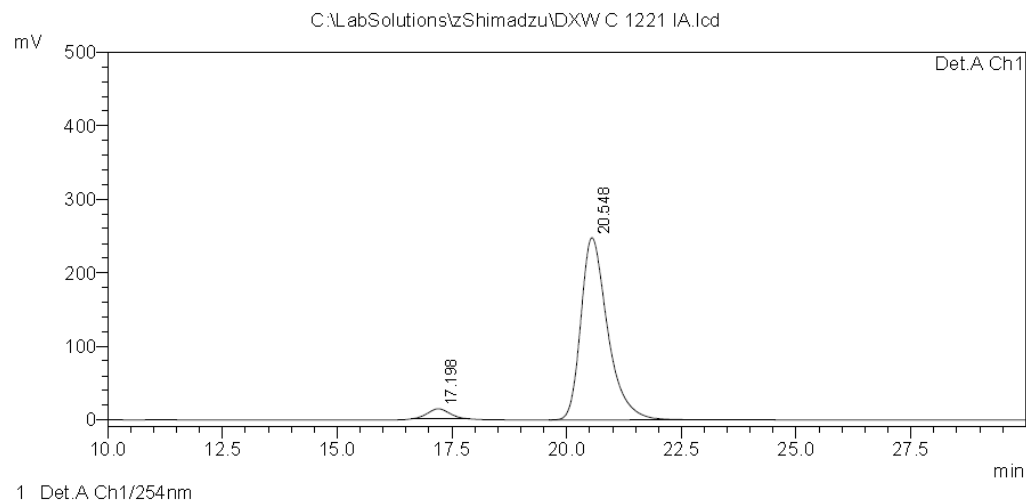


PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.134	3608447	81480	49.343	49.327
2	20.534	3704574	83705	50.657	50.673
Total		7313021	165185	100.000	100.000

(racemic **3c**)

<Chromatogram>



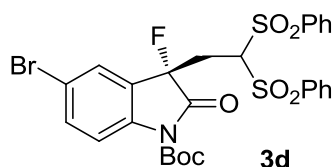
PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.198	462446	13692	4.394	5.237
2	20.548	10062921	247739	95.606	94.763
Total		10525367	261431	100.000	100.000

(enantiomerically enriched **3c**)

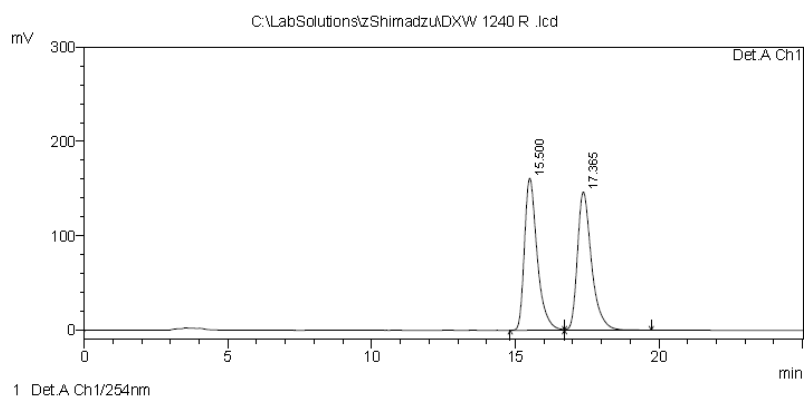
(S)-tert-Butyl-3-(2,2-bis(phenylsulfonyl)ethyl)-5-bromo-3-fluoro-2-oxoindoline-1-carboxylate

e 3d



A white solid; ^1H NMR (500 MHz, CDCl_3) δ 1.62 (s, 9H), 2.99-3.19 (m, 2H), 5.30 (t, J = 4.7 Hz, 1H), 7.44 (t, J = 1.9 Hz, 1H), 7.55-7.62 (m, 5H), 7.68-7.73 (m, 2H), 7.85-7.90 (m, 3H), 8.01-8.03 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 28.0, 31.3 (d, J = 31.0 Hz), 85.5, 88.9 (d, J = 191.3 Hz), 117.9, 118.1 (d, J = 2.7 Hz), 125.7 (d, J = 17.3 Hz), 127.0, 129.2 (d, J = 22.8 Hz), 129.7 (d, J = 14.6 Hz), 134.8 (d, J = 32.8 Hz), 135.2, 136.8, 138.3, 139.1 (d, J = 5.5 Hz), 148.2, 169.4 (d, J = 21.9 Hz); ^{19}F NMR (282.38 MHz, CDCl_3) δ -76.2 (dd, J = 12.4 Hz, 32.0 Hz); The ee value was 93%, t_R (minor) = 15.53 min, t_R (major) = 17.34 min (Chiralcel IA, λ = 254 nm, 10% *i*PrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI) m/z calcd for $\text{C}_{27}\text{H}_{25}\text{F}^{79}\text{BrNO}_7\text{S}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ = 660.0132, found = 660.0109, $\text{C}_{27}\text{H}_{25}\text{F}^{81}\text{BrNO}_7\text{S}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ = 662.0112, found = 662.0091; $[\alpha]_D^{27}$ = +15.5 (c = 0.75, CHCl_3).

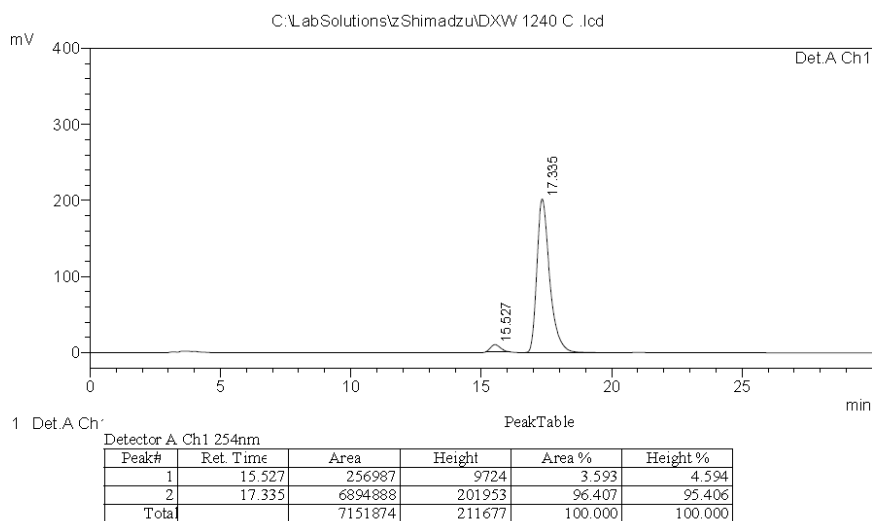
<Chromatogram>



PeakTable					
Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.500	4960014	160967	49.795	52.363
2	17.365	5000937	146440	50.205	47.637
Total		9960952	307408	100.000	100.000

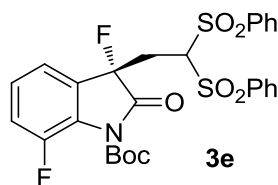
(racemic **3d**)

<Chromatogram>



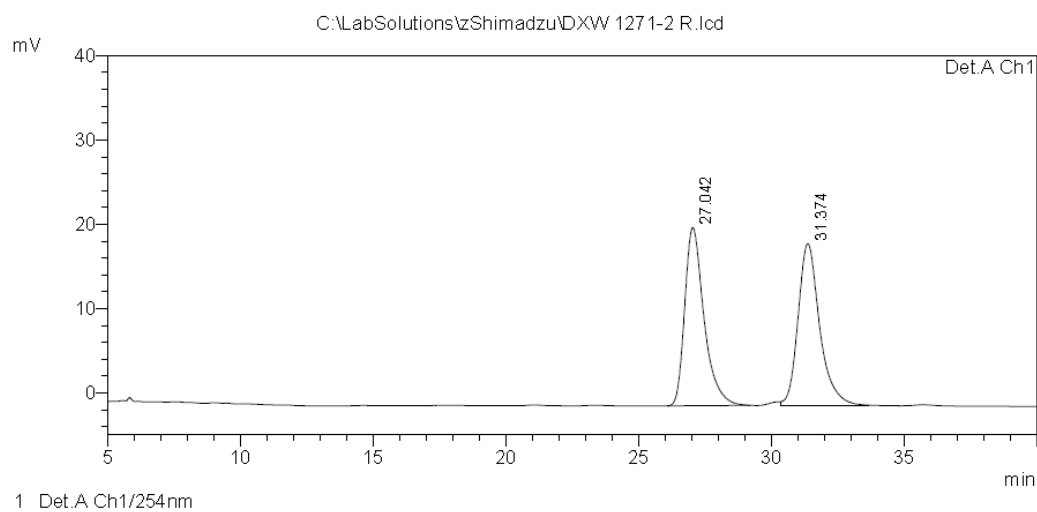
(enantiomerically enriched **3d**)

(S)-tert-Butyl 3-(2,2-bis(phenylsulfonyl)ethyl)-3,7-difluoro-2-oxoindoline-1-carboxylate **3e**



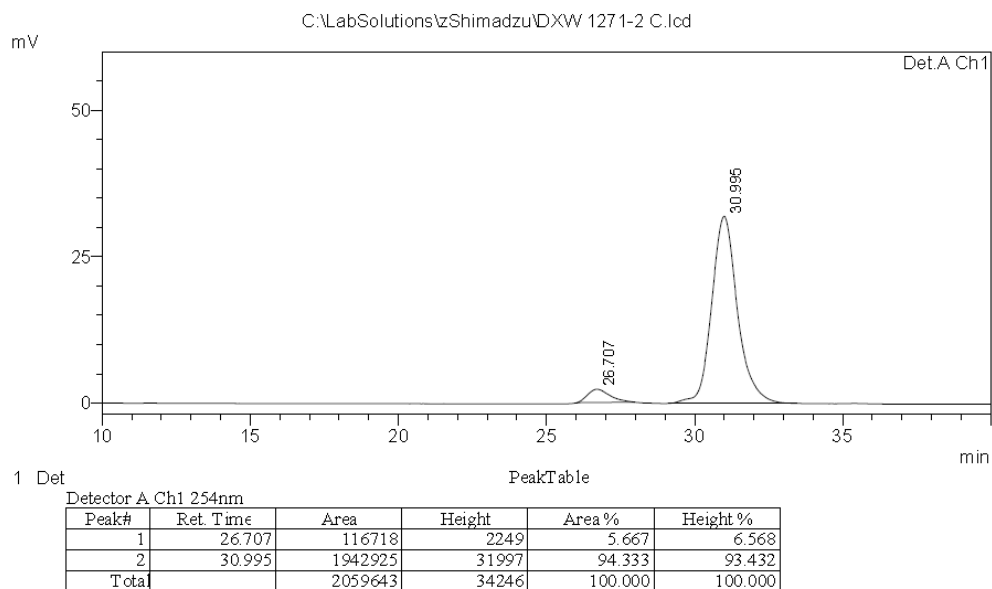
A white solid; ^1H NMR (500 MHz, CDCl_3) δ 1.59 (s, 9H), 3.02-3.13 (m, 1H), 3.19-3.25 (m, 1H), 5.36 (t, J = 4.4 Hz, 1H), 7.18 (t, J = 3.2 Hz, 1H), 7.25 (d, J = 6.9 Hz, 2H), 7.52-7.59 (m, 4H), 7.65-7.72 (m, 2H), 7.86 (d, J = 7.6 Hz, 2H), 8.00 (d, J = 8.2 Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 27.6, 31.3 (d, J = 31.9 Hz), 77.2, 85.7, 89.6 (d, J = 194.0 Hz), 119.9 (d, J = 3.7 Hz), 120.5, 120.7 (d, J = 2.7 Hz), 126.7 (d, J = 4.6 Hz), 126.9 (d, J = 10.0 Hz), 127.0, 129.1 (d, J = 18.2 Hz), 129.7 (d, J = 9.1 Hz), 134.7 (d, J = 23.7 Hz), 137.1, 138.1, 146.3, 148.0, 150.6, 169.7 (d, J = 22.8 Hz); ^{19}F NMR (282.38 MHz, CDCl_3) δ -75.1 (dd, J = 12.1 Hz, 32.0 Hz), -40.1 (t, J = 7.7 Hz); The ee value was 89%, t_R (minor) = 26.71 min, t_R (major) = 31.00 min (Chiralcel IA, λ = 254 nm, 10% *i*PrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI) m/z calcd for $\text{C}_{27}\text{H}_{25}\text{F}_2\text{NO}_7\text{S}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ = 600.0933, found = 600.0943; $[\alpha]_D^{27}$ = +15.8 (c = 0.84, CHCl_3).

<Chromatogram>



(racemic **3e**)

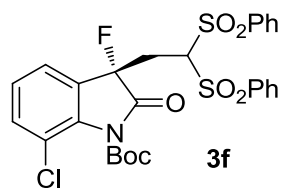
<Chromatogram>



(enantiomerically enriched **3e**)

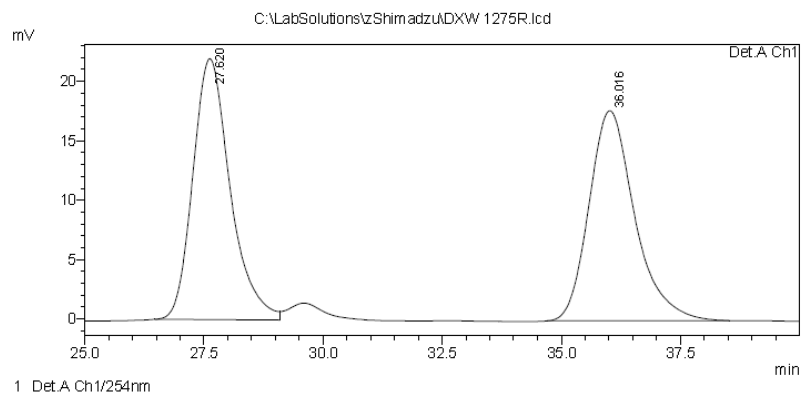
(S)-tert-Butyl-3-(2,2-bis(phenylsulfonyl)ethyl)-7-chloro-3-fluoro-2-oxoindoline-1-carboxylate

e 3f



A white solid; ^1H NMR (500 MHz, CDCl_3) δ 1.60 (s, 9H), 3.01-3.12 (m, 1H), 3.19-3.25 (m, 1H), 5.40 (t, J = 4.4 Hz, 1H), 7.21 (t, J = 7.6 Hz, 1H), 7.29 (d, J = 7.6 Hz, 1H), 7.48 (d, J = 8.2 Hz, 1H), 7.51-7.58 (m, 4H), 7.65-7.72 (m, 2H), 7.86 (dd, J = 1.3 Hz, 8.2 Hz, 2H), 8.00 (t, J = 4.1 Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 27.6, 31.4 (d, J = 31.0 Hz), 76.7, 86.1, 89.7 (d, J = 193.1 Hz), 120.6, 122.6, 126.2, 127.2 (d, J = 19.1 Hz), 129.2 (d, J = 22.8 Hz), 129.7 (d, J = 17.3 Hz), 133.9 (d, J = 2.7 Hz), 134.7 (d, J = 23.7 Hz), 137.3, 138.2, 146.5, 170.3 (d, J = 22.8 Hz); ^{19}F NMR (282.38 MHz, CDCl_3) δ -76.7 (dd, J = 11.3 Hz, 33.0 Hz); The ee value was 87%, t_{R} (minor) = 27.51 min, t_{R} (major) = 36.01 min (Chiralcel IA, λ = 254 nm, 10% *i*PrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI) m/z calcd for $\text{C}_{27}\text{H}_{25}\text{FCINO}_7\text{S}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ = 616.0637, found = 616.0613; $[\alpha]_{\text{D}}^{27}$ = +12.4 (c = 1.10, CHCl_3).

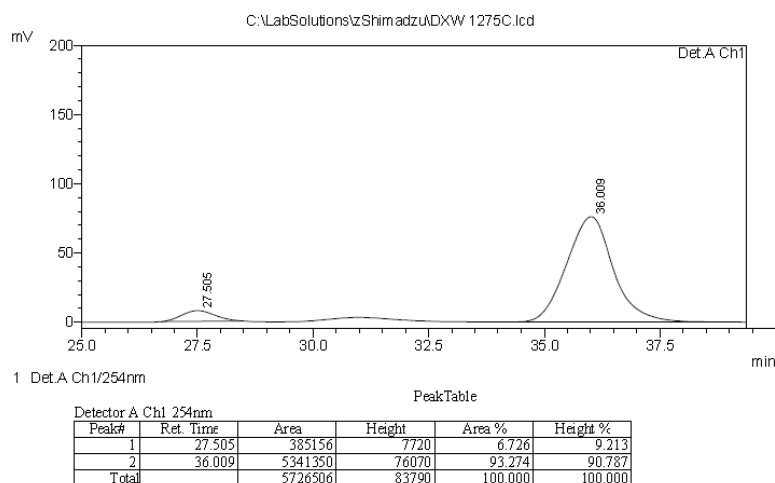
<Chromatogram>



PeakTable					
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1	27.620	1197808	21961	50.423	55.397
2	36.016	1177699	17682	49.577	44.603
Total		2375508	39643	100.000	100.000

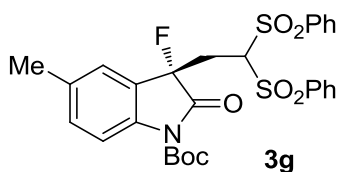
(racemic **3f**)

<Chromatogram>



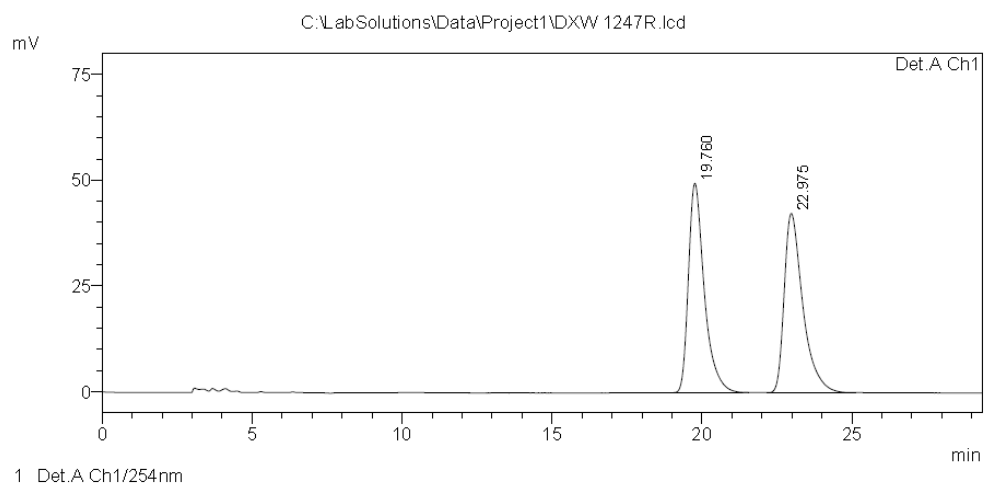
(enantiomerically enriched **3f**)

(S)-tert-Butyl-3-(2,2-bis(phenylsulfonyl)ethyl)-3-fluoro-5-methyl-2-oxindoline-1-carboxylate
e 3g



A white solid; ^1H NMR (500 MHz, CDCl_3) δ 1.62 (s, 9H), 2.38 (s, 3H), 2.98-3.23 (m, 2H), 5.39 (t, $J = 4.4$ Hz, 1H), 7.14 (s, 1H), 7.28 (s, 1H), 7.52-7.58 (m, 4H), 7.65-7.71 (m, 2H), 7.79 (d, $J = 8.2$ Hz, 1H), 7.86-7.88 (m, 2H), 8.01-8.03 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 21.0, 28.0, 31.3 (d, $J = 31.0$ Hz), 76.9, 84.9, 89.4 (d, $J = 190.4$ Hz), 116.0, 123.7 (d, $J = 18.2$ Hz), 124.4, 129.1 (d, $J = 22.8$ Hz), 129.7 (d, $J = 2.7$ Hz), 132.7 (d, $J = 1.8$ Hz), 134.6 (d, $J = 29.2$ Hz), 135.2 (d, $J = 2.7$ Hz), 137.3, 137.7 (d, $J = 4.6$ Hz), 138.5, 148.5, 170.3 (d, $J = 22.8$ Hz); ^{19}F NMR (282.38 MHz, CDCl_3) δ -75.3 (dd, $J = 10.3$ Hz, 32.0 Hz); The ee value was 89%, t_R (minor) = 19.79 min, t_R (major) = 22.86 min (Chiralcel IA, $\lambda = 254$ nm, 10% *i*PrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI) m/z calcd for $\text{C}_{28}\text{H}_{28}\text{FNO}_7\text{S}_2\text{Na}$ $[\text{M}+\text{Na}]^+ = 596.1183$, found = 596.1175; $[\alpha]_D^{27} = +17.3$ ($c = 0.98$, CHCl_3).

<Chromatogram>



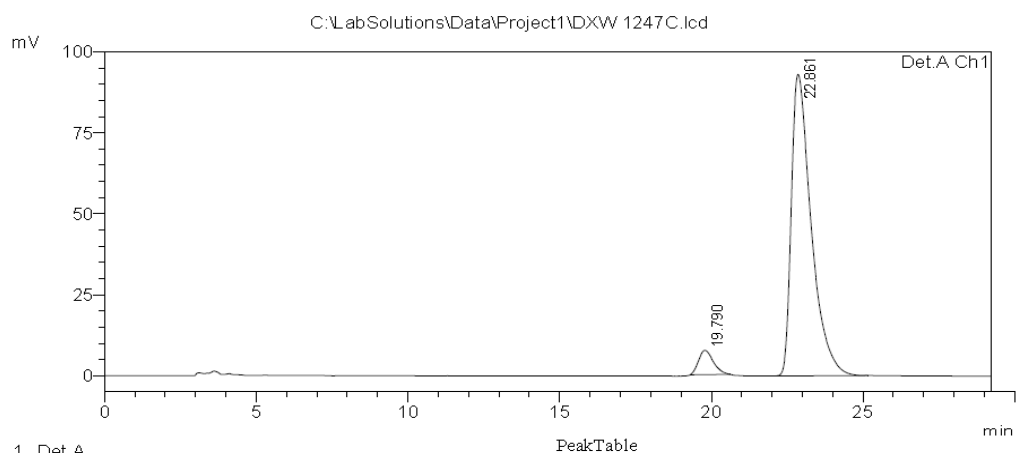
PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.760	1817478	49484	49.927	53.901
2	22.975	1822808	42322	50.073	46.099
Total		3640286	91806	100.000	100.000

(racemic **3g**)

<Chromatogram>



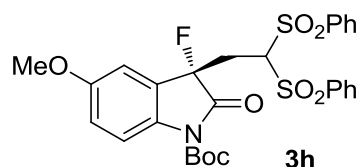
PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.790	255602	7500	5.679	7.458
2	22.861	4244864	93066	94.321	92.542
Total		4500466	100566	100.000	100.000

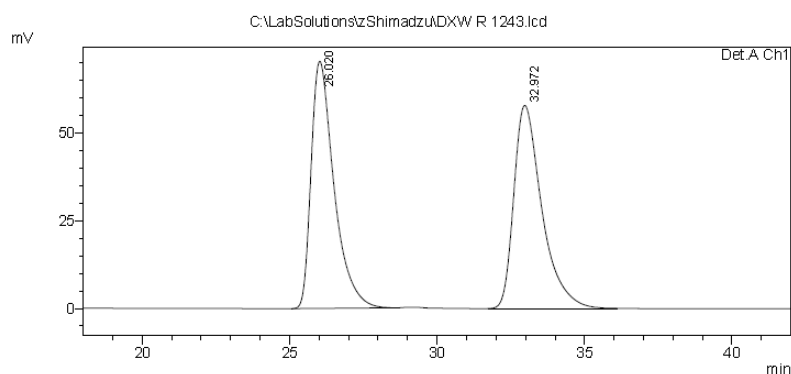
(enantiomerically enriched **3g**)

(S)-tert-Butyl-3-(2,2-bis(phenylsulfonyl)ethyl)-3-fluoro-5-methoxy-2-oxoindoline-1-carboxylate **3h**



A white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.62 (s, 9H), 2.96-3.25 (m, 2H), 3.85 (s, 3H), 5.41 (t, $J = 4.4$ Hz, 1H), 6.92-7.01 (m, 2H), 7.50-7.58 (m, 4H), 7.61-7.73 (m, 2H), 7.83-7.92 (m, 3H), 7.95-8.02 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 28.0, 31.3 (d, $J = 31.0$ Hz), 55.9, 76.9, 84.9, 89.4 (d, $J = 191.3$ Hz), 109.8, 117.3 (d, $J = 3.6$ Hz), 124.9 (d, $J = 17.3$ Hz), 129.1 (d, $J = 23.7$ Hz), 129.7 (d, $J = 1.8$ Hz), 133.1 (d, $J = 4.6$ Hz), 134.6 (d, $J = 31.9$ Hz), 137.2, 138.4, 148.5, 157.4 (d, $J = 2.7$ Hz), 170.2 (d, $J = 22.8$ Hz); ^{19}F NMR (282.38 MHz, CDCl_3) δ -76.2 (dd, $J = 11.3$ Hz, 31.9 Hz); The ee value was 90%, t_R (minor) = 26.12 min, t_R (major) = 32.68 min (Chiralcel IA, $\lambda = 254$ nm, 10% *i*PrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI) m/z calcd for $\text{C}_{28}\text{H}_{28}\text{FNO}_8\text{S}_2\text{Na}$ $[\text{M}+\text{Na}]^+ = 612.1133$, found = 611.1127; $[\alpha]_D^{27} = +24.8$ ($c = 0.85$, CHCl_3).

<Chromatogram>



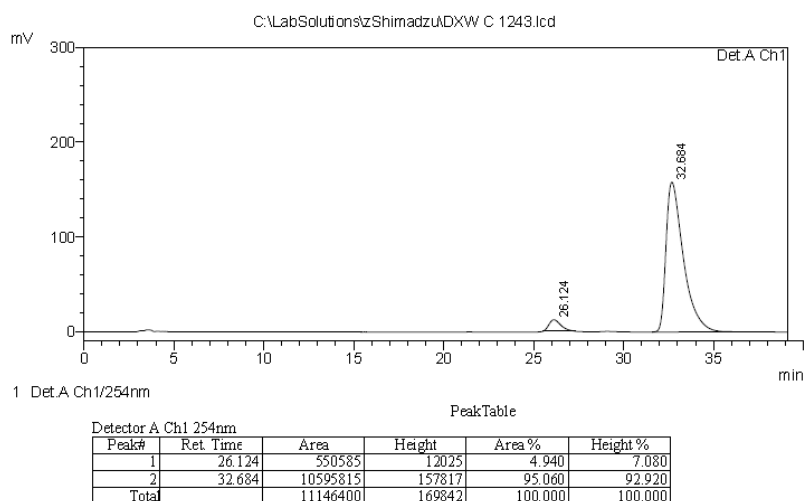
1 Det.A Ch1/254nm

PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.020	3801400	70442	49.870	54.898
2	32.972	3821150	57873	50.130	45.102
Total		7622550	128316	100.000	100.000

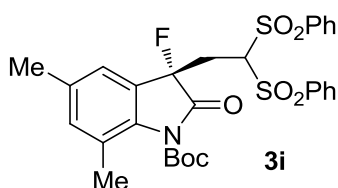
(racemic **3h**)

<Chromatogram>



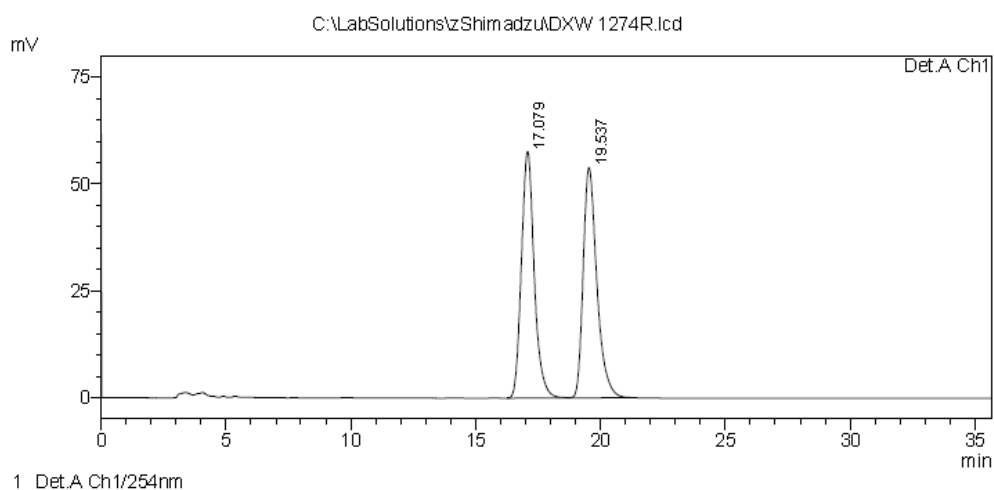
(enantiomerically enriched **3h**)

(S)-tert-Butyl-3-(2,2-bis(phenylsulfonyl)ethyl)-3-fluoro-5,7-dimethyl-2-oxoindoline-1-carboxylate **3i**



A white solid; ^1H NMR (500 MHz, CDCl_3) δ 1.60 (s, 9H), 2.22 (s, 3H), 2.33 (s, 3H), 2.98-3.22 (m, 2H), 5.39 (t, $J = 4.4$ Hz, 1H), 6.96 (s, 1H), 7.08 (s, 1H), 7.51-7.58 (m, 4H), 7.64-7.71 (m, 2H), 7.87 (d, $J = 7.6$ Hz, 2H), 8.02 (d, $J = 7.6$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 19.8, 20.8, 27.8, 31.5 (d, $J = 31.9$ Hz), 85.1, 90.1 (d, $J = 189.5$ Hz), 121.9, 125.1 (d, $J = 17.3$ Hz), 125.5, 129.1 (d, $J = 23.7$ Hz), 129.7 (d, $J = 9.1$ Hz), 134.6 (d, $J = 26.4$ Hz), 135.3 (d, $J = 2.7$ Hz), 135.7 (d, $J = 2.7$ Hz), 136.1 (d, $J = 5.5$ Hz), 137.4, 138.5, 148.1, 171.3 (d, $J = 22.8$ Hz); ^{19}F NMR (282.38 MHz, CDCl_3) δ -75.2 (dd, $J = 11.4$ Hz, 21.7 Hz); The ee value was 89%, t_R (minor) = 17.12 min, t_R (major) = 19.55 min (Chiralcel IA, $\lambda = 254$ nm, 10% *i*PrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI) m/z calcd for $\text{C}_{29}\text{H}_{30}\text{FNO}_7\text{S}_2\text{Na}$ $[\text{M}+\text{Na}]^+ = 610.1340$, found = 610.1346; $[\alpha]_D^{27} = +16.8$ ($c = 0.78$, CHCl_3).

<Chromatogram>

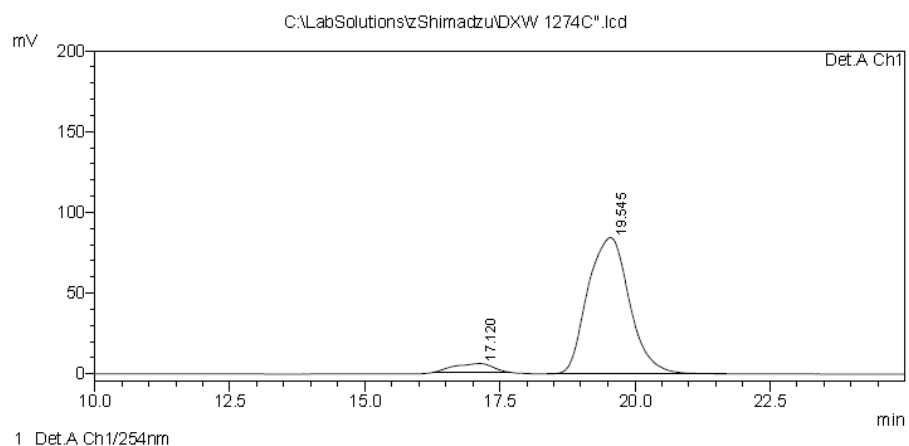


PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.079	2058100	57663	50.022	51.715
2	19.537	2056263	53839	49.978	48.285
Total		4114363	111502	100.000	100.000

(racemic **3i**)

<Chromatogram>



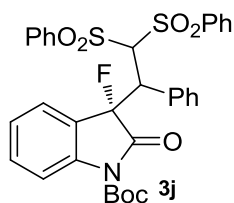
PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.120	272607	5512	5.667	6.132
2	19.545	4537999	84373	94.333	93.868
Total		4810606	89885	100.000	100.000

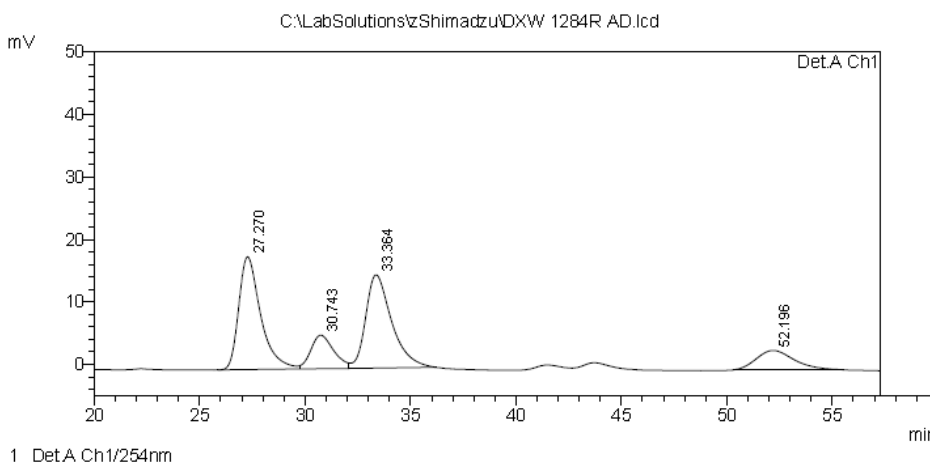
(enantiomerically enriched **3i**)

(3*S*)-*tert*-Butyl-fluoro-2-oxo-3-(1-phenyl-2,2-bis(phenylsulfonyl)ethyl)indoline-1-carboxylat

e **3j**



A white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.62 (s, 9H), 4.66 (dd, $J = 2.5$ Hz, 31.5 Hz, 1H), 6.39 (d, $J = 1.9$ Hz, 1H), 6.77 (d, $J = 7.6$ Hz, 1H), 6.95 (t, $J = 7.6$ Hz, 1H), 7.28 (d, $J = 6.9$ Hz, 3H), 7.35-7.41 (m, 4H), 7.43-7.49 (m, 3H), 7.55-7.61 (m, 3H), 7.85 (d, $J = 7.6$ Hz, 2H), 7.93 (d, $J = 8.2$ Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 28.0, 48.0 (d, $J = 26.4$ Hz), 77.2, 80.6, 85.1, 92.4 (d, $J = 199.5$ Hz), 115.6, 123.5 (d, $J = 19.1$ Hz), 124.5 (d, $J = 1.8$ Hz), 126.3, 128.0, 128.5, 128.9 (d, $J = 30.1$ Hz), 129.3 (d, $J = 31.0$ Hz), 129.9, 131.8 (d, $J = 7.3$ Hz), 133.3 (d, $J = 2.7$ Hz), 133.8, 134.1, 138.3, 139.7, 140.0 (d, $J = 18.3$ Hz), 148.4, 170.7 (d, $J = 22.8$ Hz); ^{19}F NMR (282.38 MHz, CDCl_3) δ -40.4 (d, $J = 20.6$ Hz); The ee value was 98%, t_{R} (minor) = 30.69 min, 52.43 min t_{R} (major) = 27.33 min, 33.48 min (Chiralcel AD-H, $\lambda = 254$ nm, 10% *i*PrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI) m/z calcd for $\text{C}_{33}\text{H}_{30}\text{FNO}_7\text{S}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ = 658.1340, found = 658.1348.



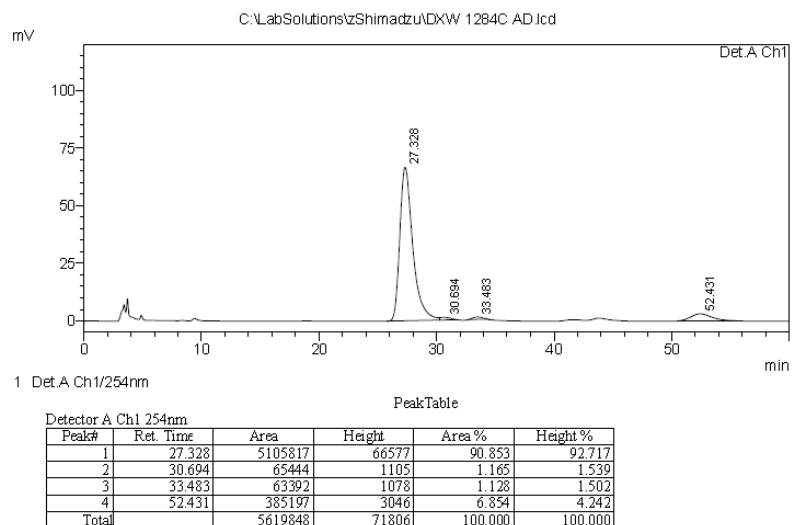
1 DetA Ch1/254nm

PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	27.270	1305561	18035	38.651	43.558
2	30.743	401903	5358	11.898	12.941
3	33.364	1280457	14907	37.908	36.002
4	52.196	389857	3105	11.542	7.499
Total		3377778	41405	100.000	100.000

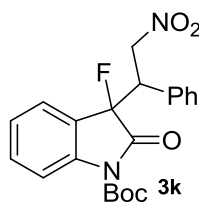
(racemic **3j**)

<Chromatogram>



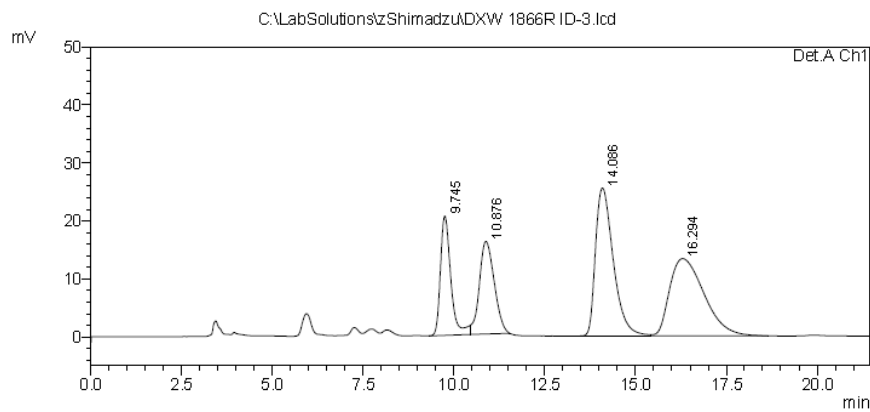
(enantiomerically enriched **3j**)

tert-Butyl- 3-fluoro-3-(2-nitro-1-phenylethyl)-2-oxindoline-1-carboxylate **3k**



A colorless oil; ^1H NMR (500 MHz, CDCl_3) The major isomer: δ 1.59 (s, 9H), 4.12-4.19 (m, 1H), 5.06 (dd, J = 10.4 Hz, 13.6 Hz, 1H), 5.55 (dd, J = 4.7 Hz, 13.6 Hz, 1H), 6.69 (d, J = 7.6 Hz, 1H), 7.00-7.14 (m, 3H), 7.22-7.31 (m, 3H), 7.40 (t, J = 15.8 Hz, 1H), 7.77 (d, J = 8.2 Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) The major isomer: δ 28.0, 49.4 (d, J = 24.6 Hz), 73.9 (d, J = 3.6 Hz), 85.2, 92.9 (d, J = 198.6 Hz), 115.4 (d, J = 16.4 Hz), 124.6, 125.1 (d, J = 2.7 Hz), 125.6, 128.7 (d, J = 9.1 Hz), 129.2 (d, J = 39.2 Hz), 131.7 (d, J = 3.7 Hz), 132.0 (d, J = 2.7 Hz), 140.1, 148.0, 170.0 (d, J = 22.8 Hz); ^{19}F NMR (282.38 MHz, CDCl_3) The major isomer: δ -85.5 (d, J = 19.6 Hz); The ee value was 46%, 28%, t_{R} (minor) = 10.26 min, 11.78 min t_{R} (major) = 15.26 min, 17.90 min (Chiralcel ID, λ = 254 nm, 3% *i*PrOH/hexanes, flow rate = 1.0 mL/min); MS (ESI) m/z calcd for $\text{C}_{21}\text{H}_{21}\text{FN}_2\text{O}_5\text{Na}$ $[\text{M}+\text{Na}]^+$ = 423, found = 423.1.

<Chromatogram>

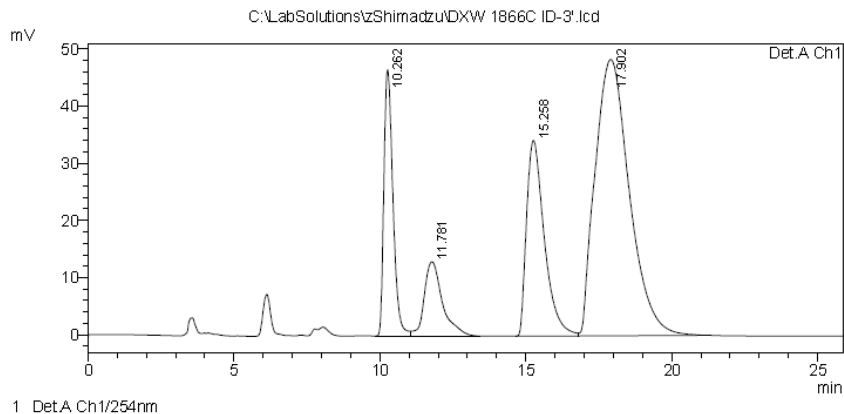


PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.745	412615	20591	15.751	27.297
2	10.876	454200	15980	17.339	21.185
3	14.086	871861	25529	33.283	33.844
4	16.294	880879	13332	33.627	17.675
Total		2619556	75433	100.000	100.000

(racemic **3k**)

<Chromatogram>



PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.262	1004931	46599	14.438	32.773
2	11.781	561404	12990	8.066	9.136
3	15.258	1454302	34242	20.894	24.083
4	17.902	3939818	48354	56.603	34.008
Total		6960456	142184	100.000	100.000

(enantiomerically enriched **3k**)

E. X-Ray Crystallographic Analysis and Determination of the Absolute Configurations of the Products

X-Ray Crystallographic Analysis of **3e**

The absolute configuration of the product **3e** was assigned based on the X-ray crystallographic analysis of a single crystal of **3e** (Figure S1). The configurations of other products **3** were assigned by analogy.

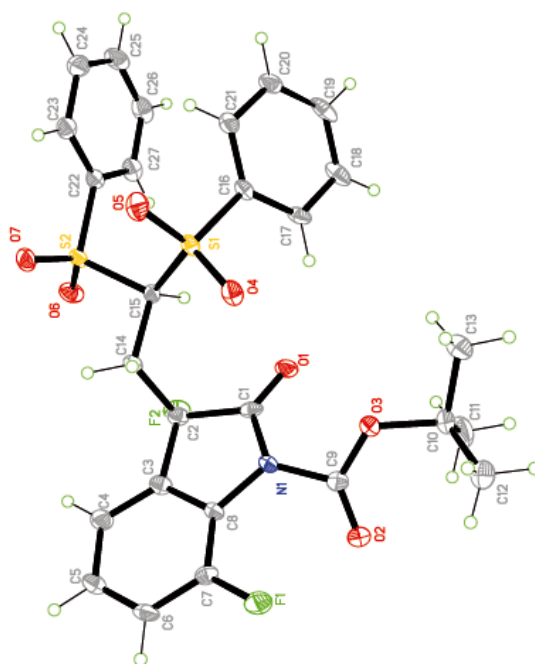


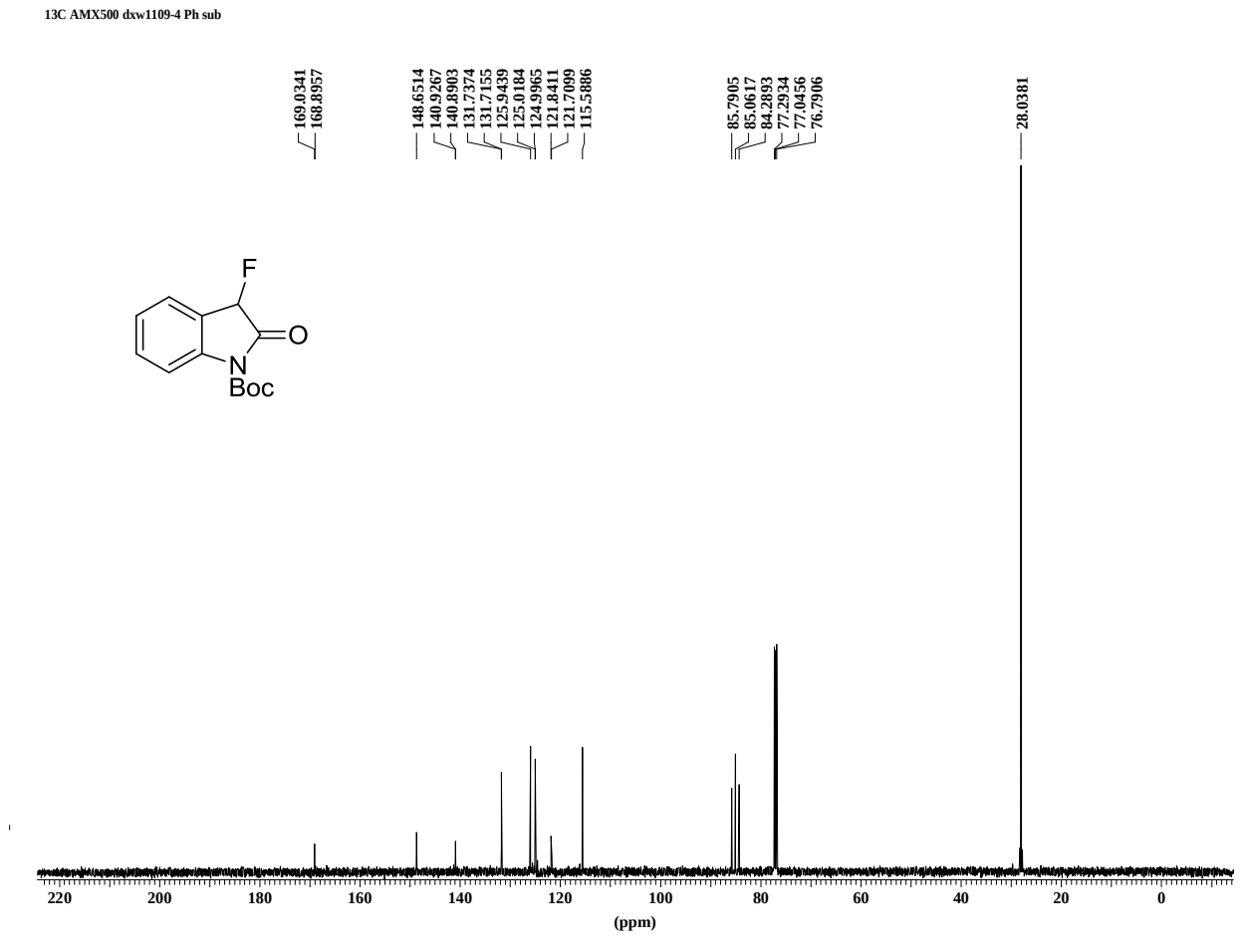
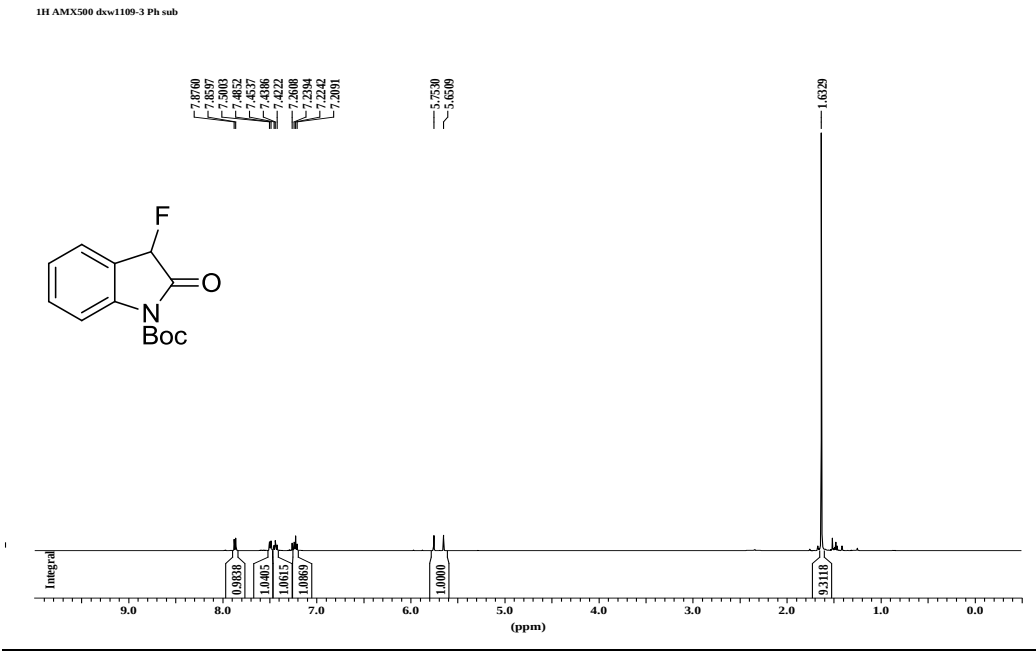
Figure S1. X-ray structure of **3e**

Table 1. Crystal data and structure refinement for C009.

Identification code	c009	
Empirical formula	C27 H25 F2 N O7 S2	
Formula weight	577.60	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 8.2718(7) Å	$\alpha = 90^\circ$.

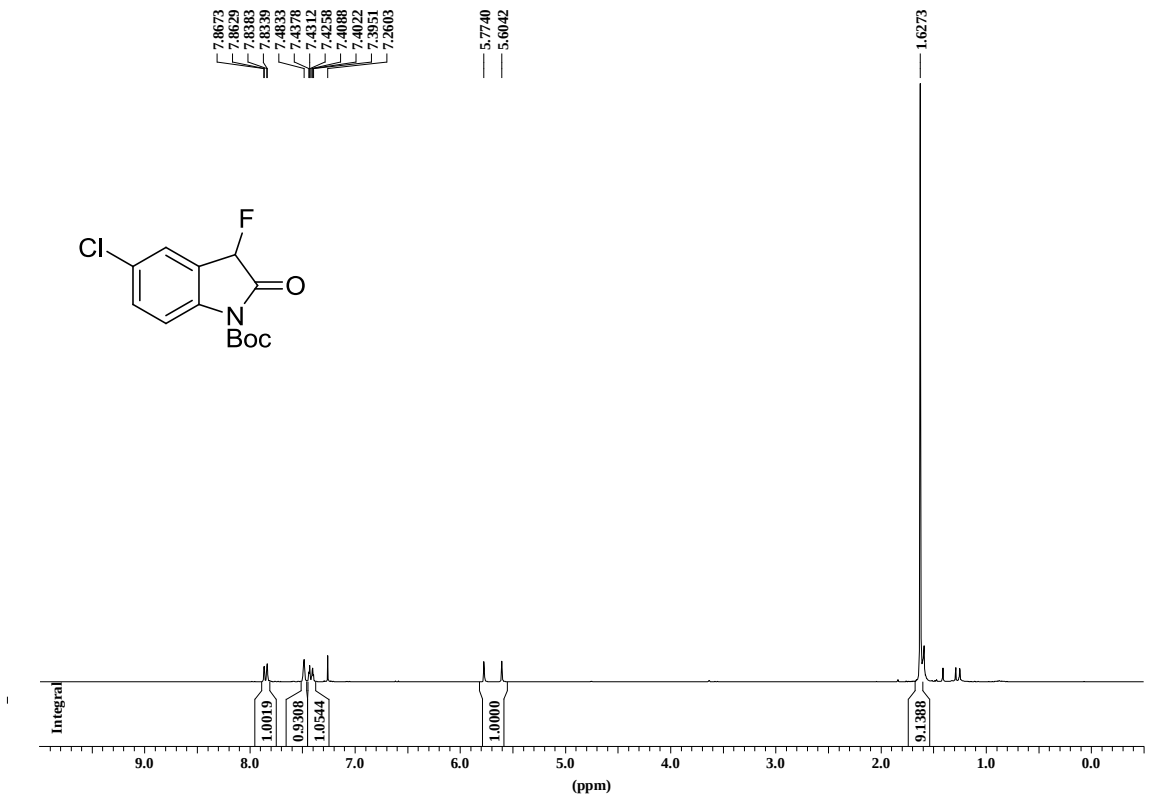
	b = 13.6799(13) Å	β = 90°.
	c = 23.831(2) Å	γ = 90°.
Volume	2696.7(4) Å ³	
Z	4	
Density (calculated)	1.423 Mg/m ³	
Absorption coefficient	0.258 mm ⁻¹	
F(000)	1200	
Crystal size	0.60 x 0.20 x 0.08 mm ³	
Theta range for data collection	1.71 to 27.50°.	
Index ranges	-10 ≤ h ≤ 10, -17 ≤ k ≤ 14, -28 ≤ l ≤ 30	
Reflections collected	19152	
Independent reflections	6196 [R(int) = 0.0465]	
Completeness to theta = 27.50°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7457 and 0.6628	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	6196 / 0 / 355	
Goodness-of-fit on F ²	1.028	
Final R indices [I > 2σ(I)]	R1 = 0.0402, wR2 = 0.0883	
R indices (all data)	R1 = 0.0458, wR2 = 0.0910	
Absolute structure parameter	0.12(6)	
Largest diff. peak and hole	0.472 and -0.260 e.Å ⁻³	

F. NMR Spectra of the Substrates and Products

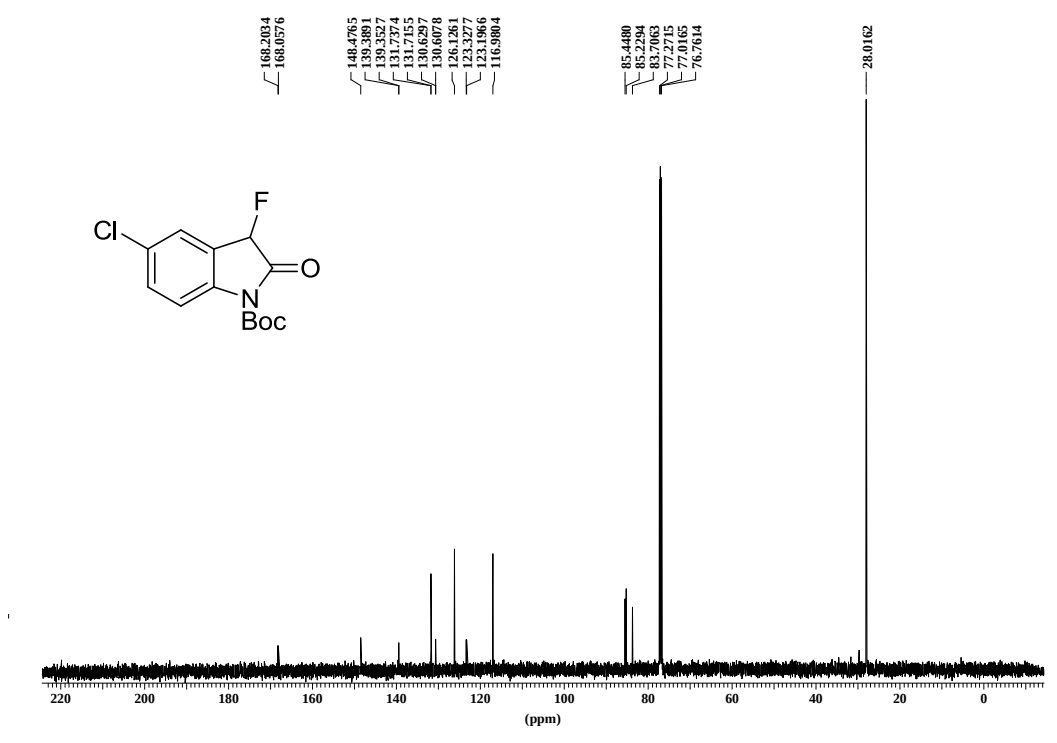


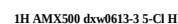


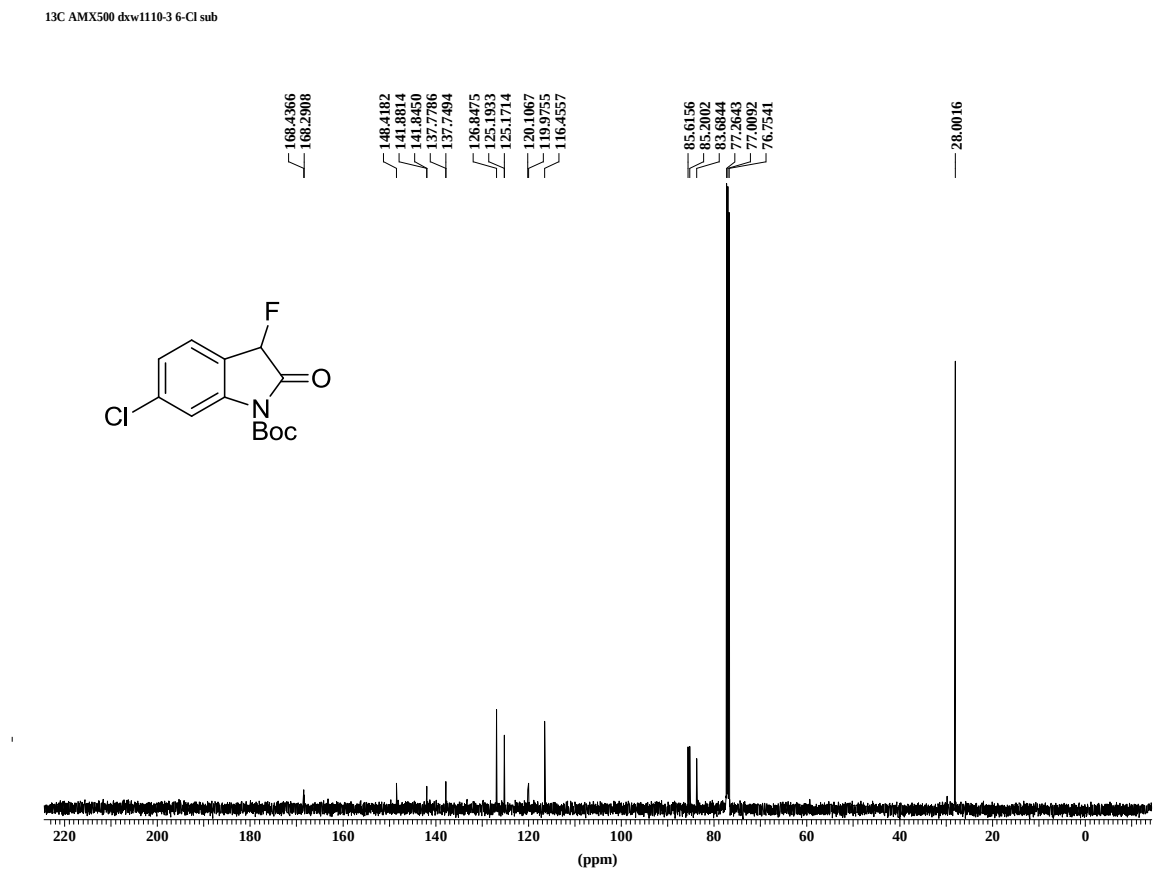
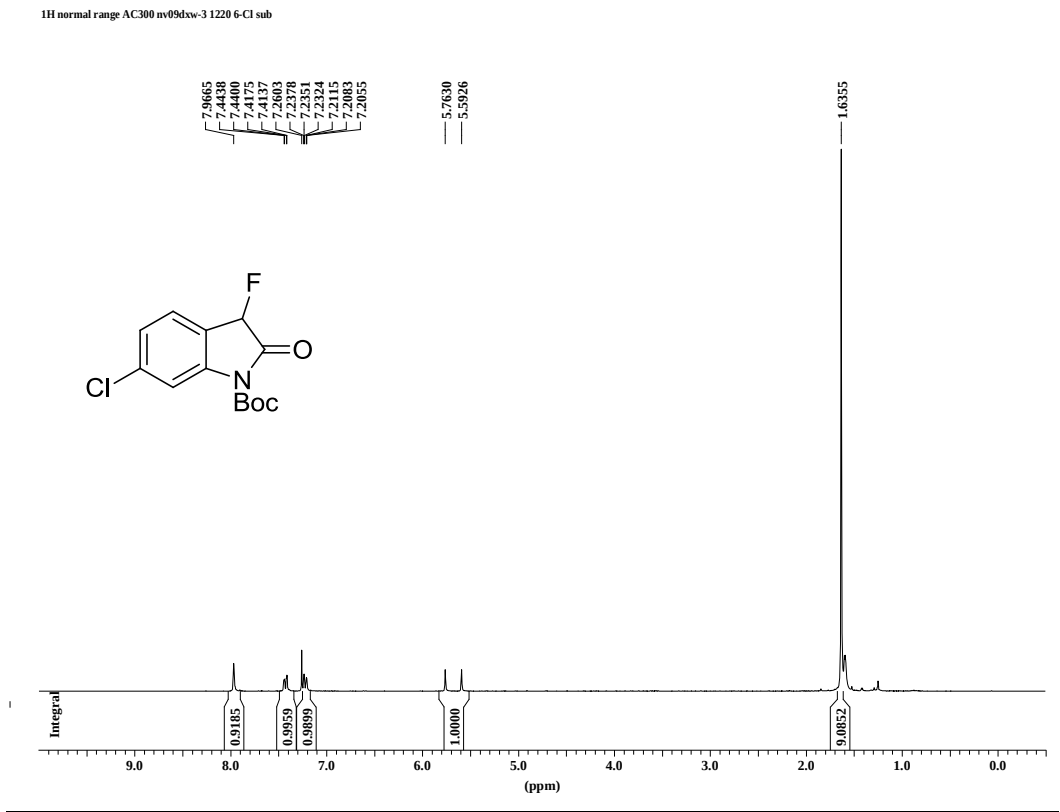
¹H normal range AC300 mv09dxw-2 1222 5-Cl sub



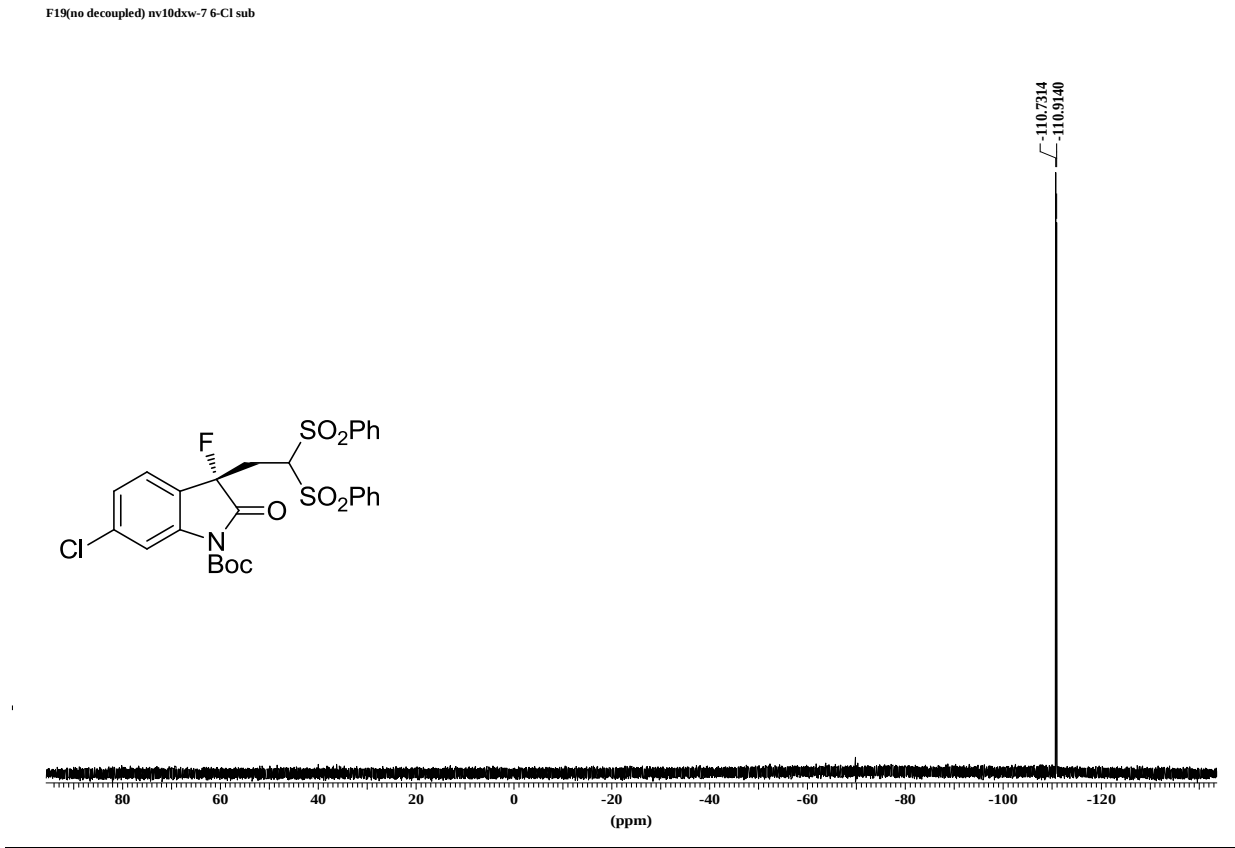
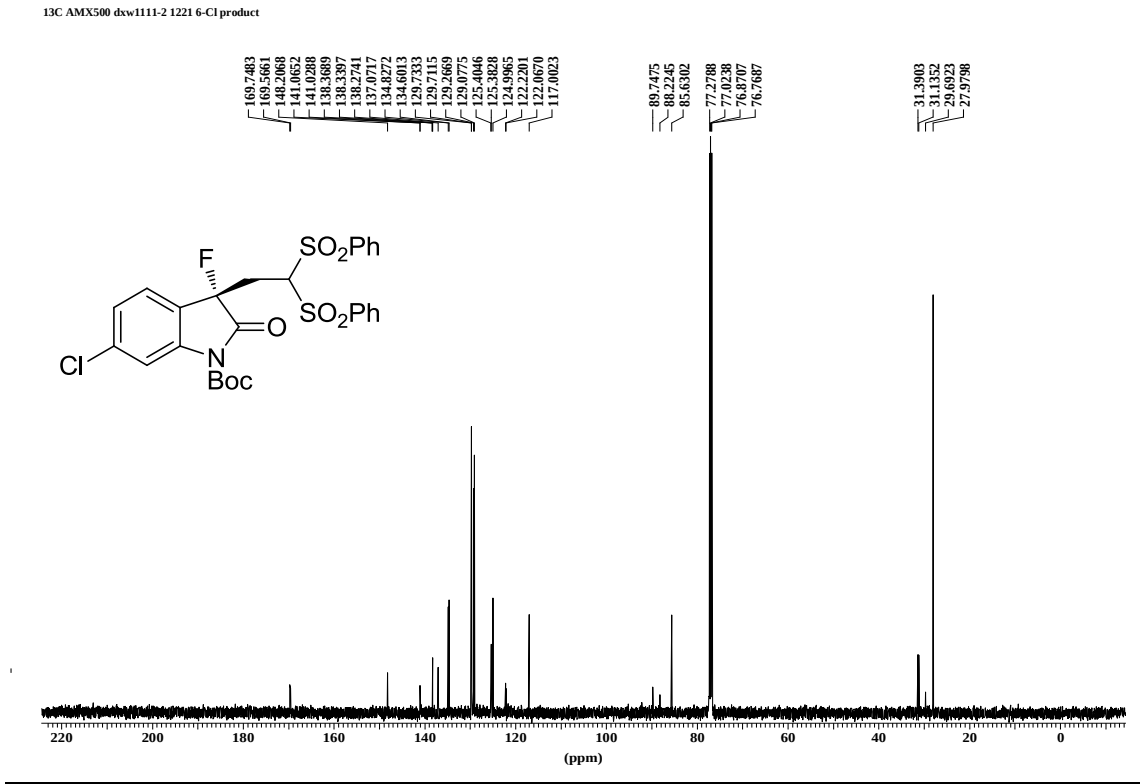
¹³C AMX500 dsw1109-5 5-Cl sub

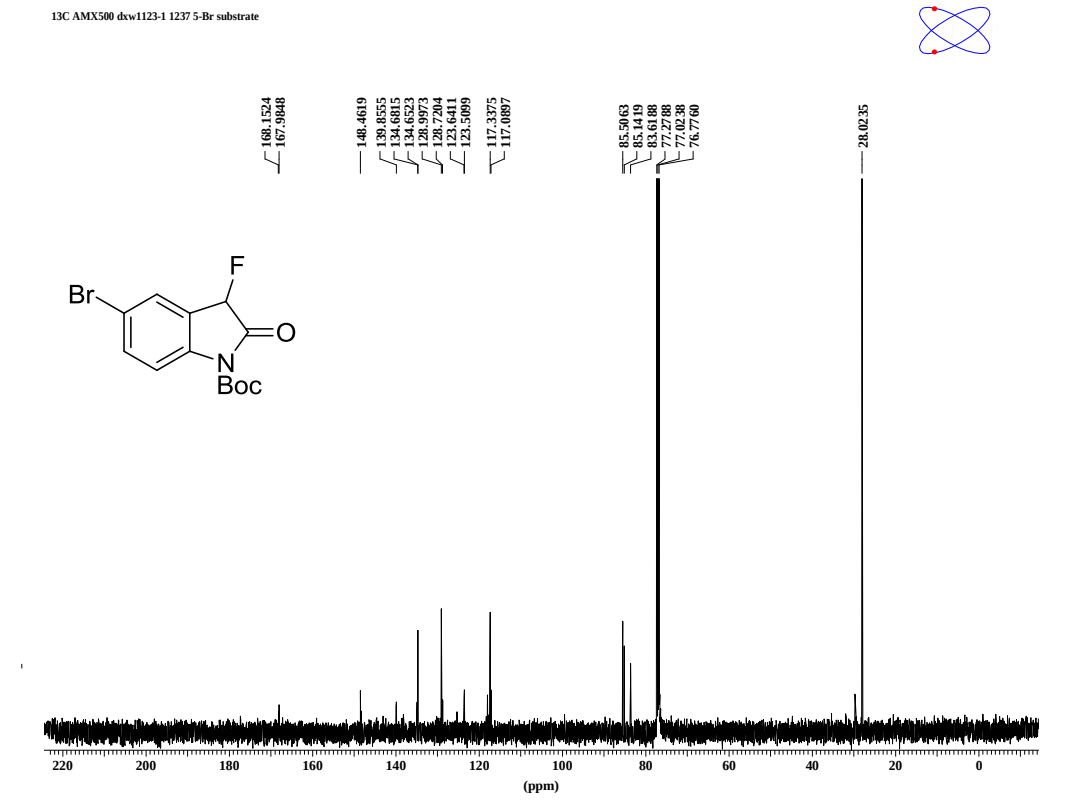
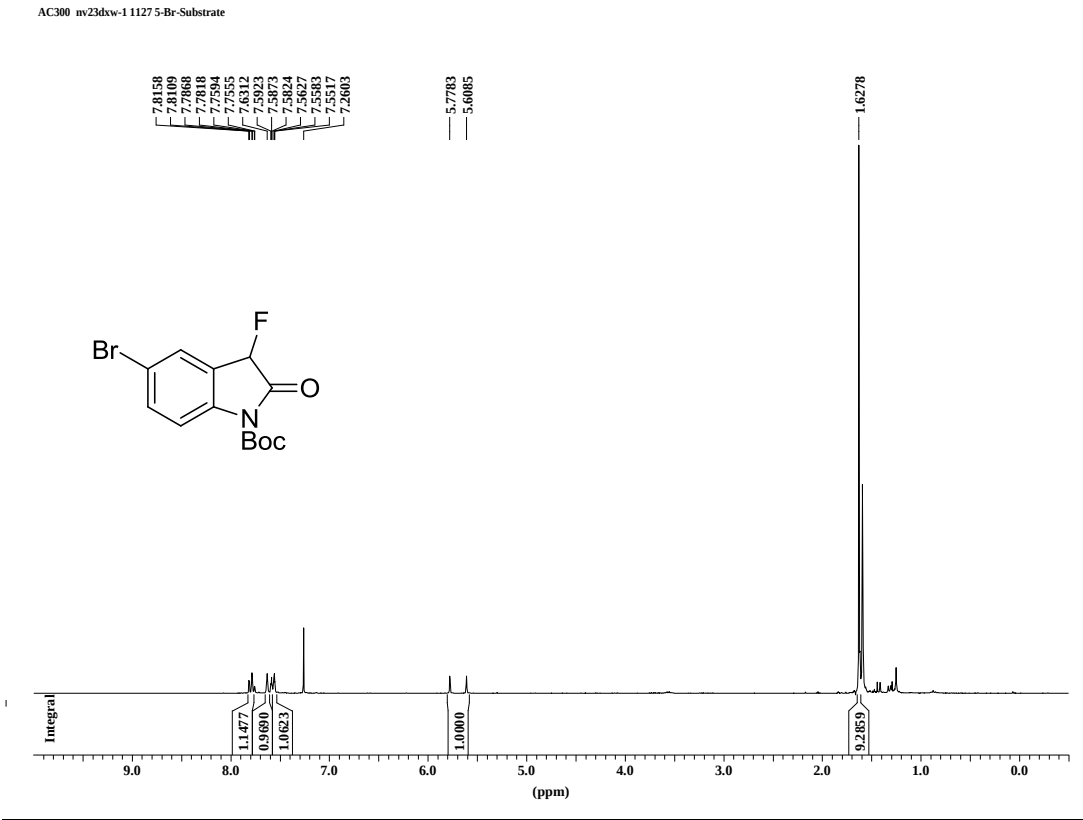


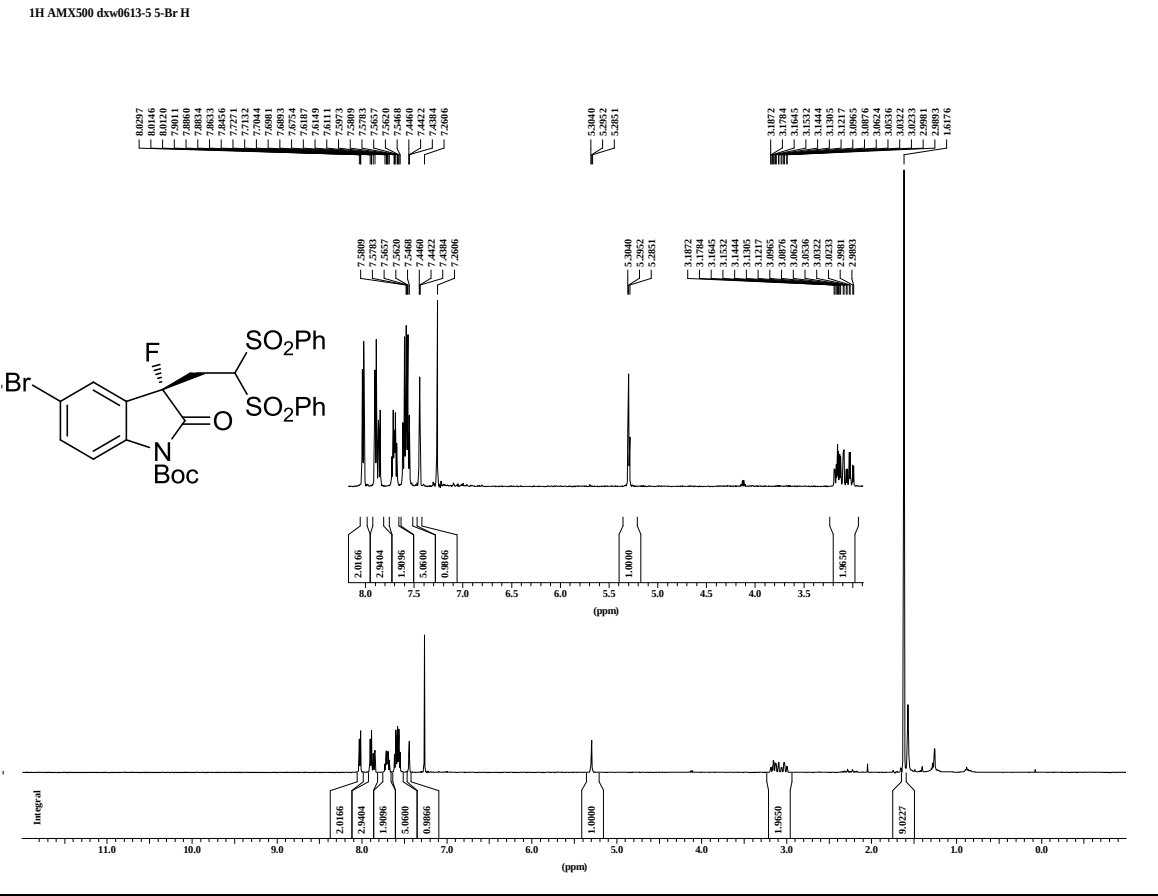
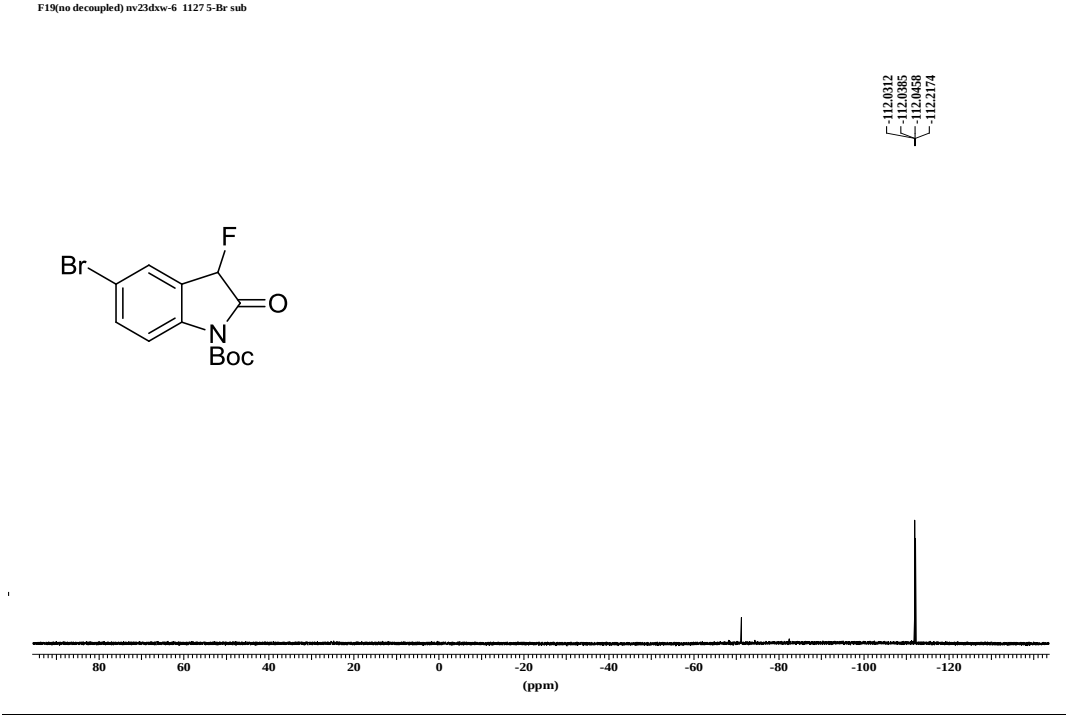




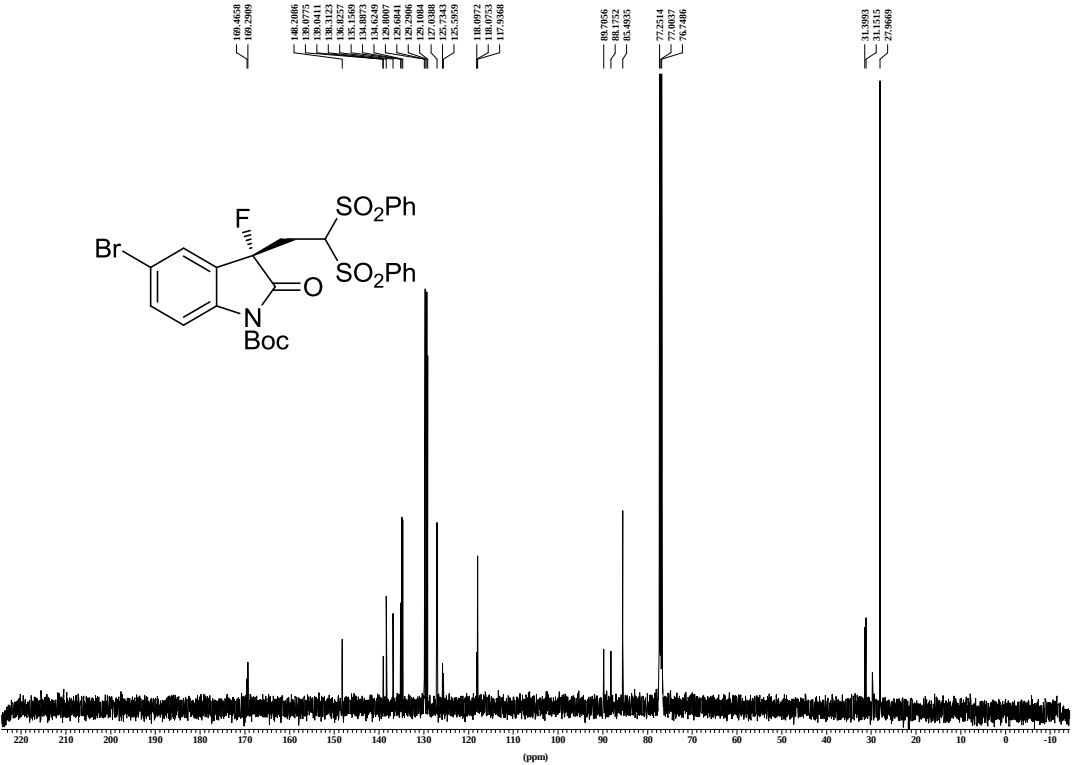




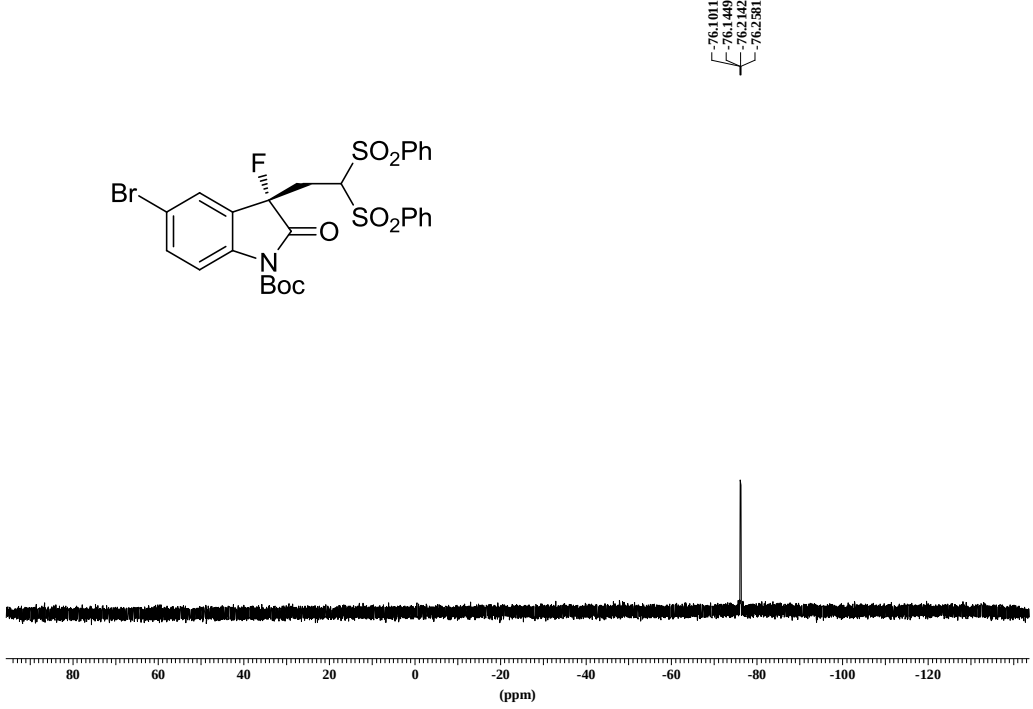


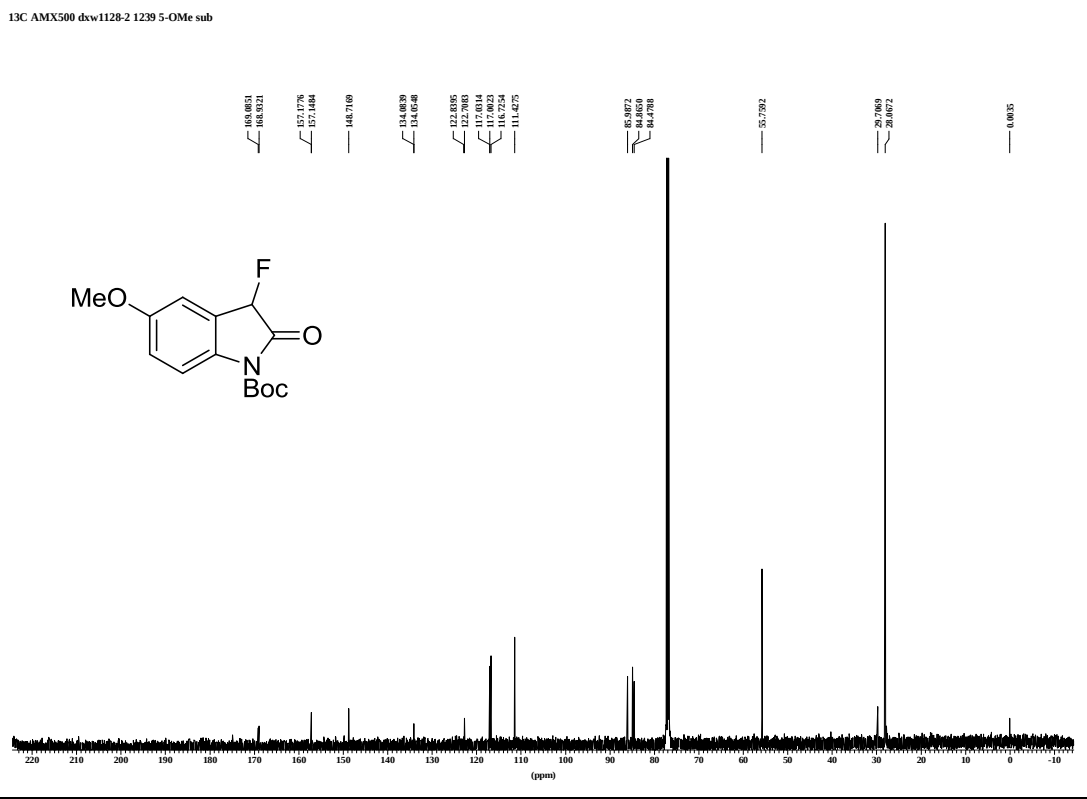
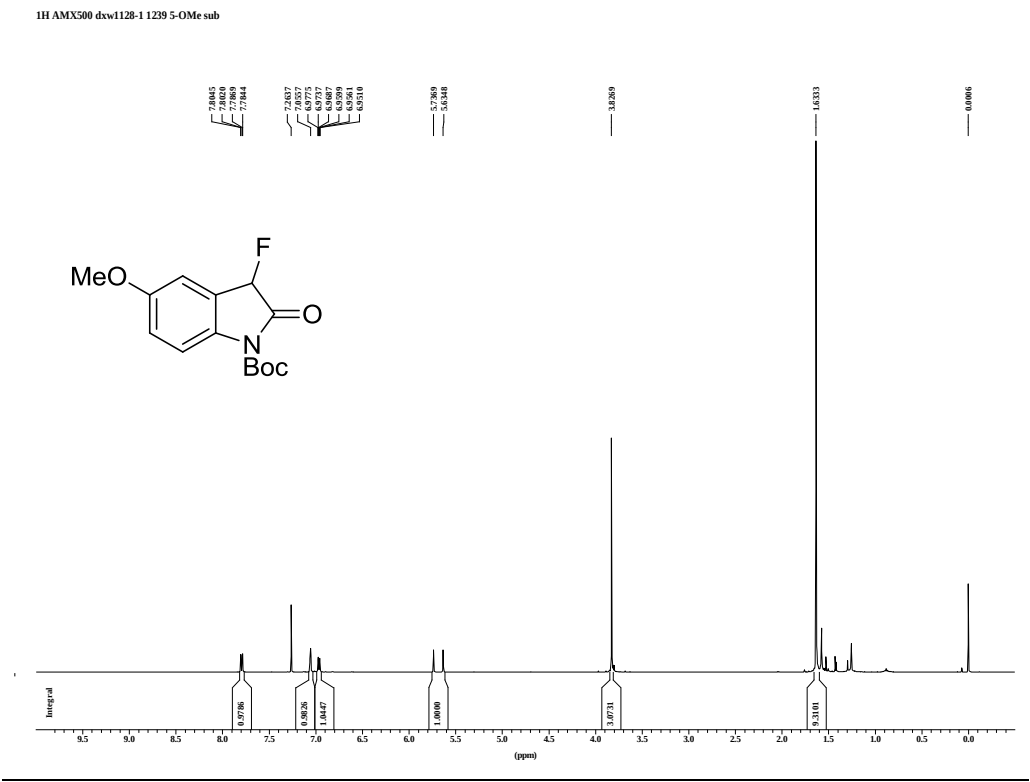


¹³C AMX500 dxw0613-6 5-Br C

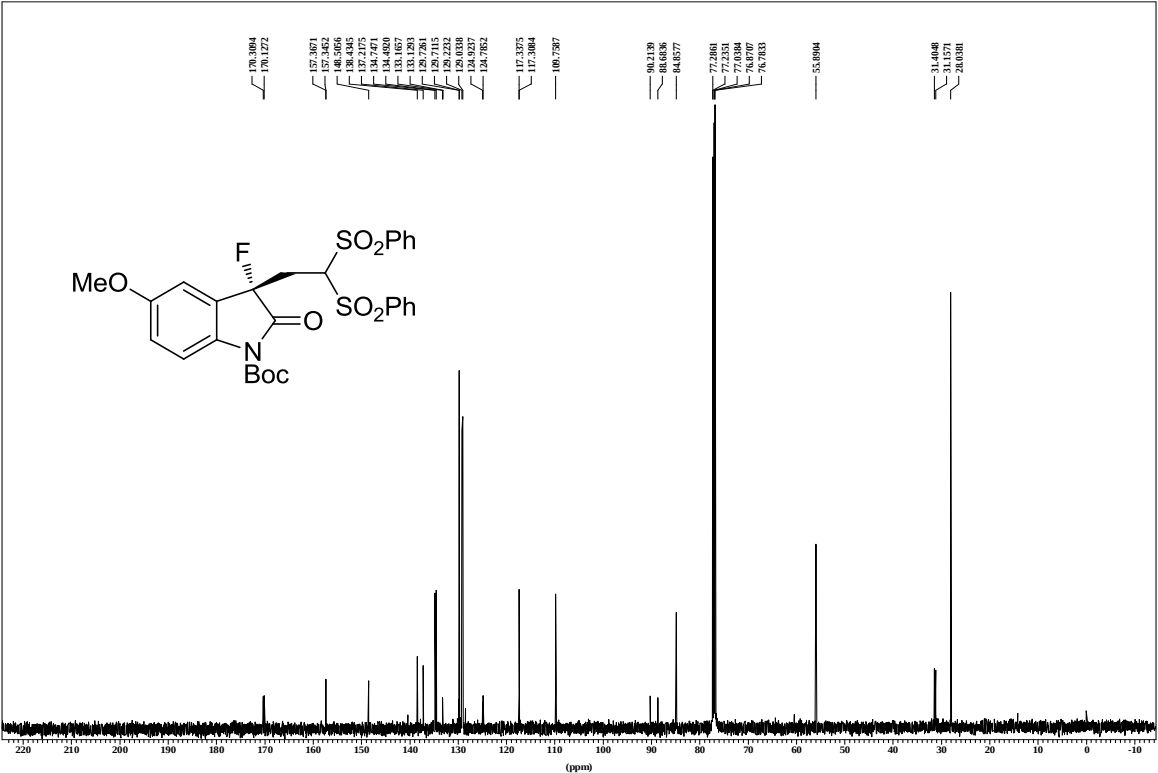


F19(no decoupled) nv25dxw-4 1140C 5-Br product

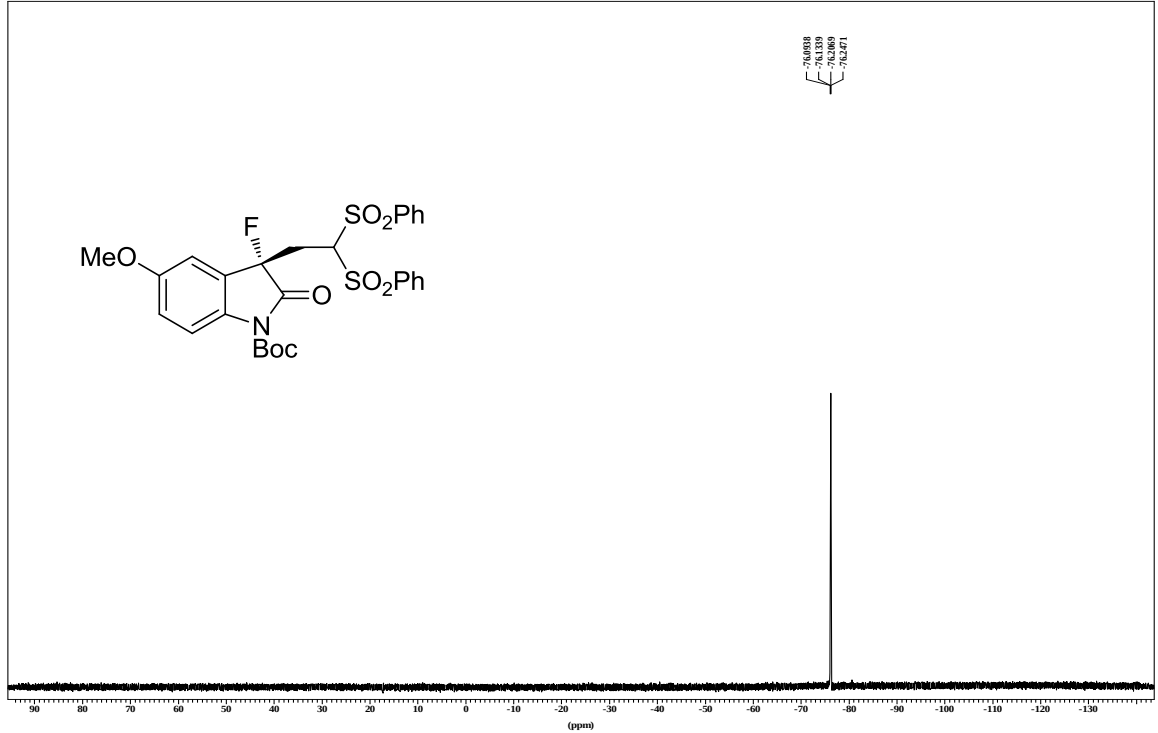


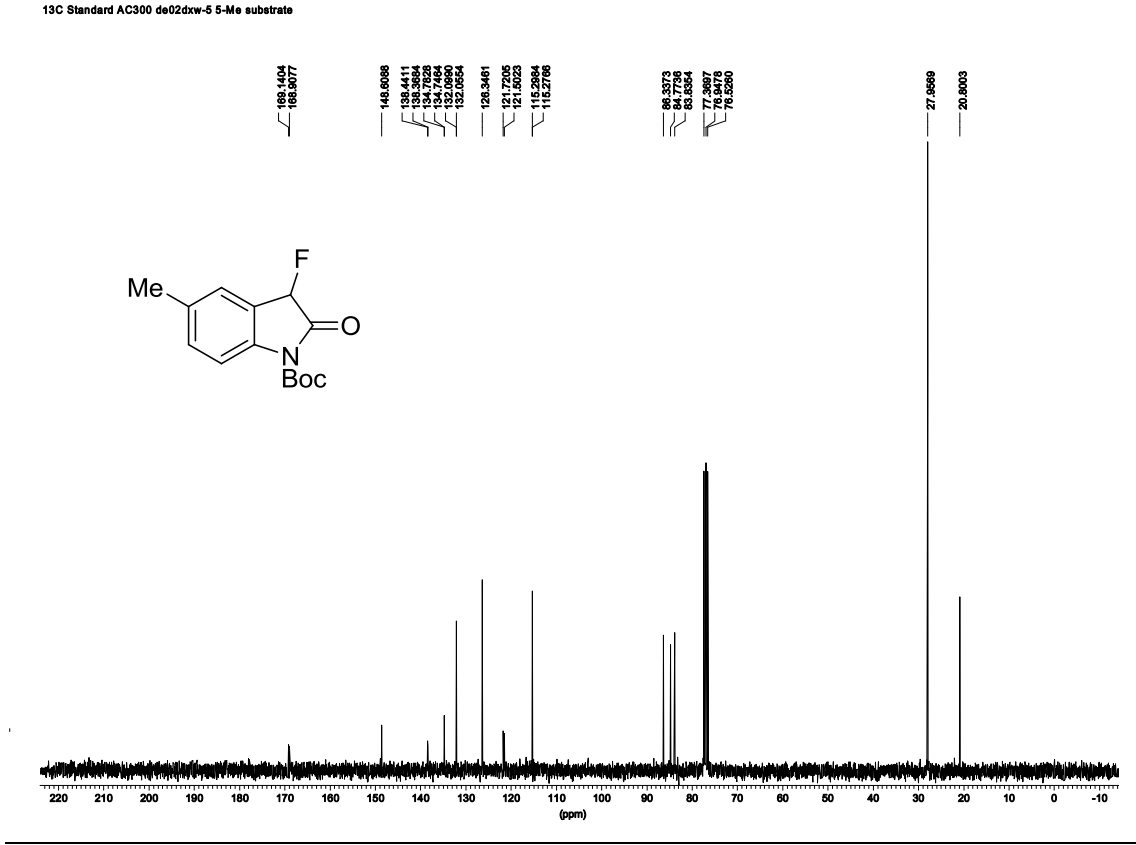
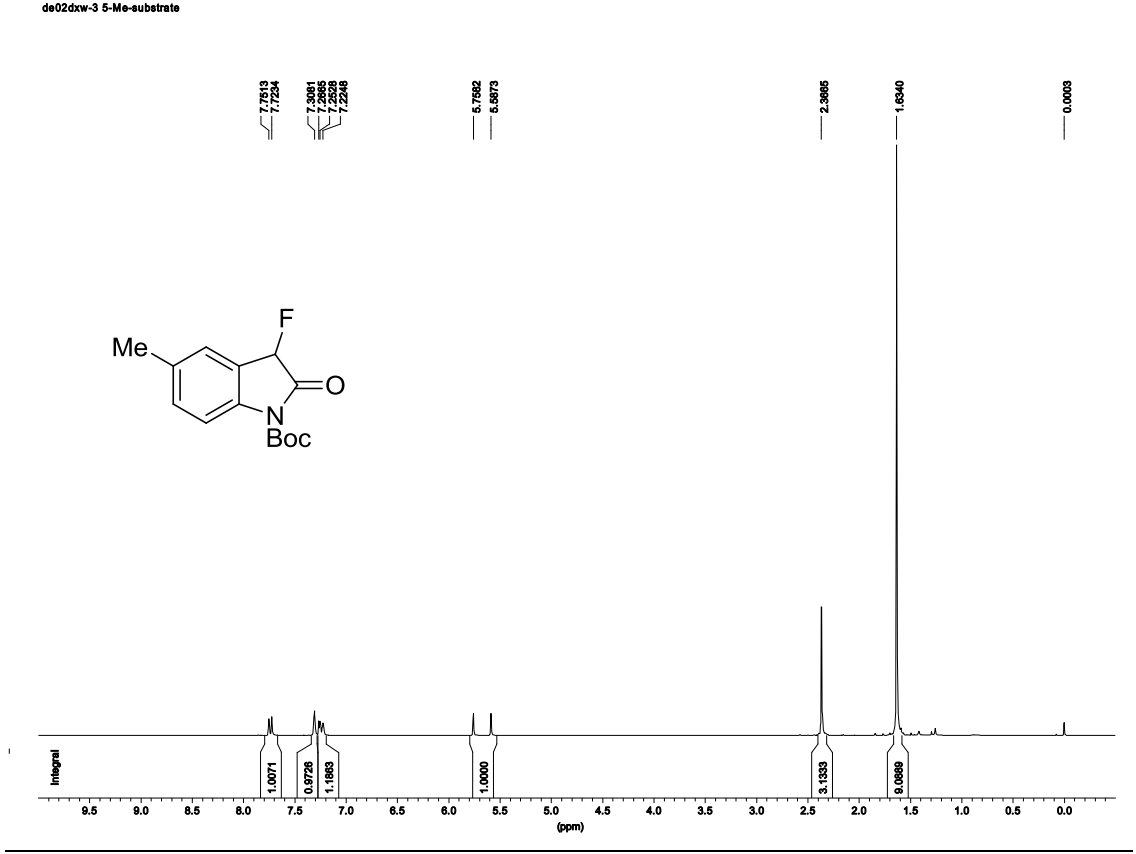


¹³C AMX500 dsw1130-1 1243 5-OMe product

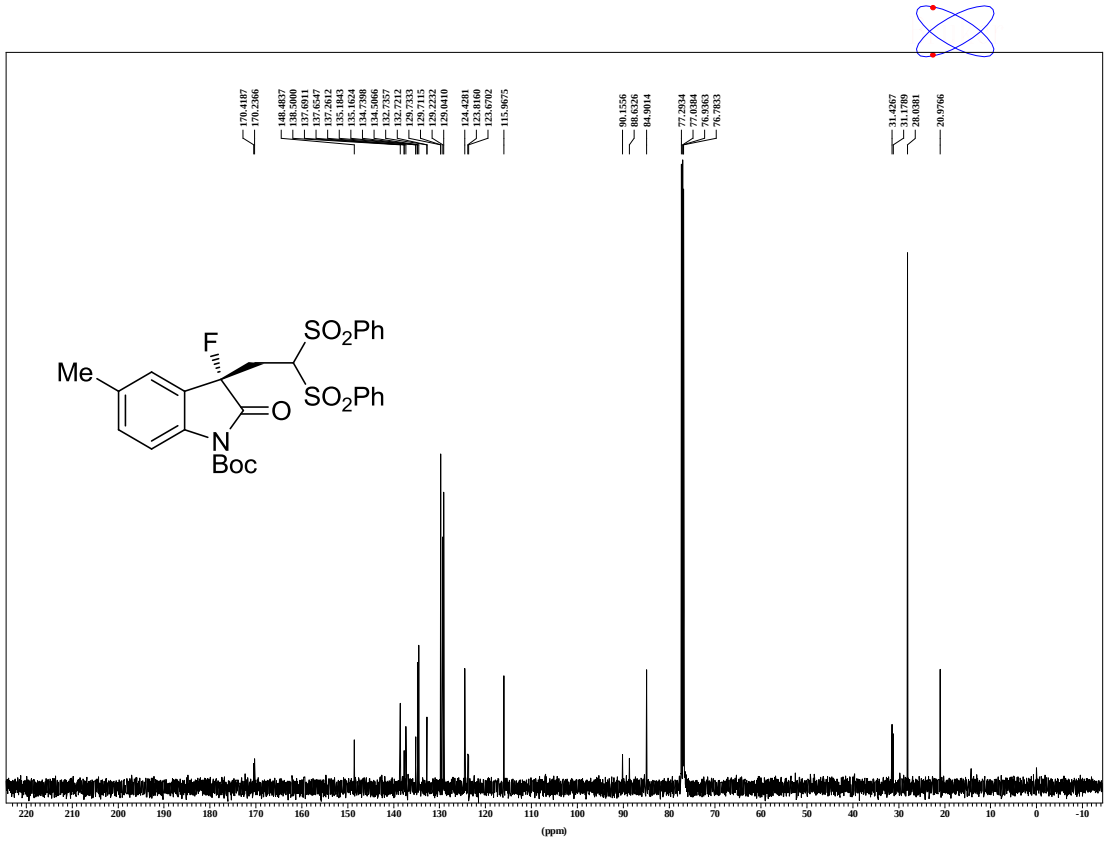


F19(no decoupled) nv30dsw-1 5-OMe product F

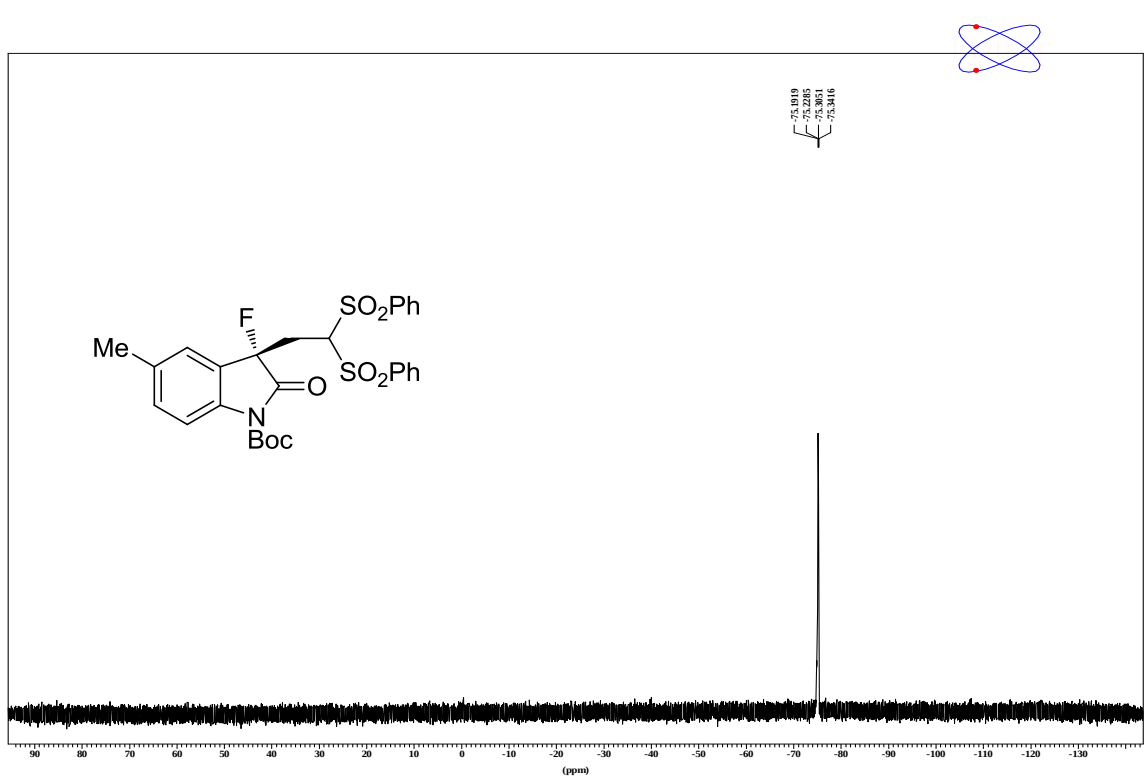


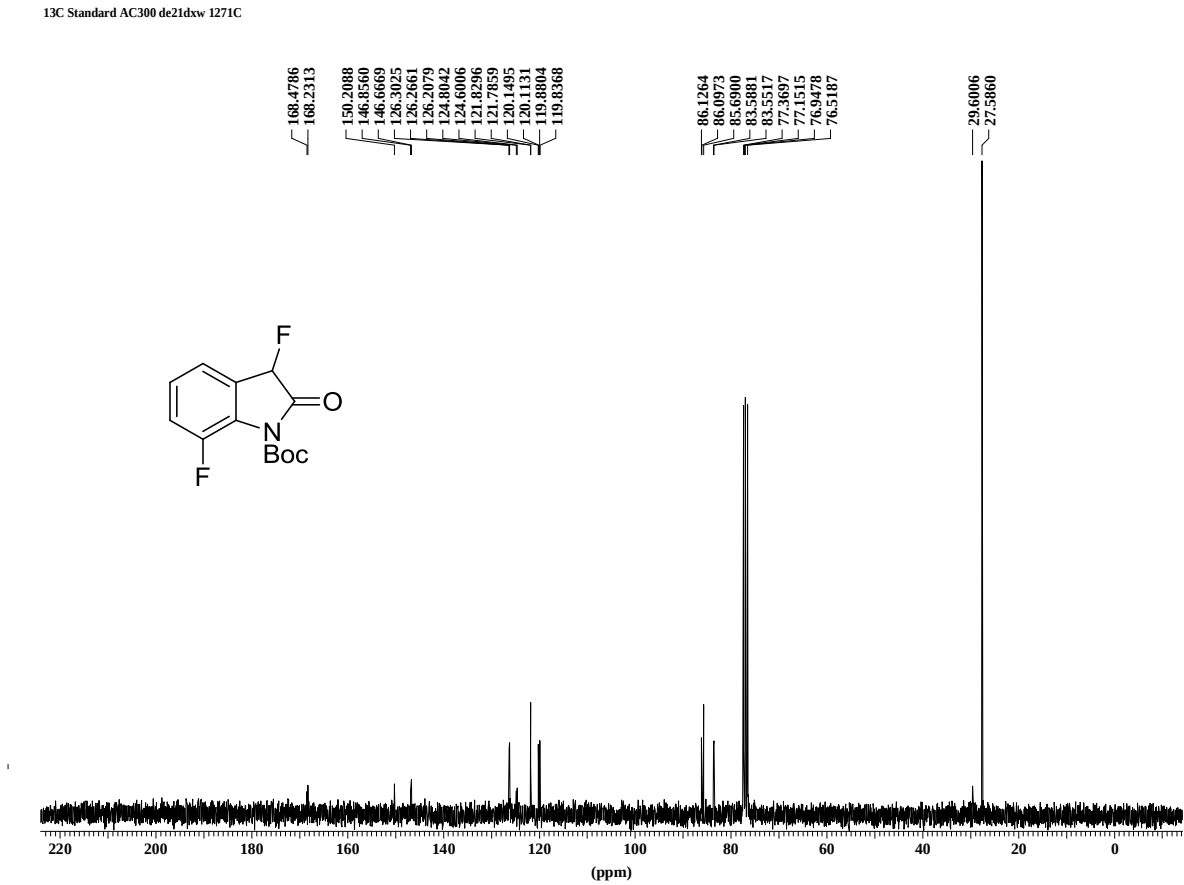
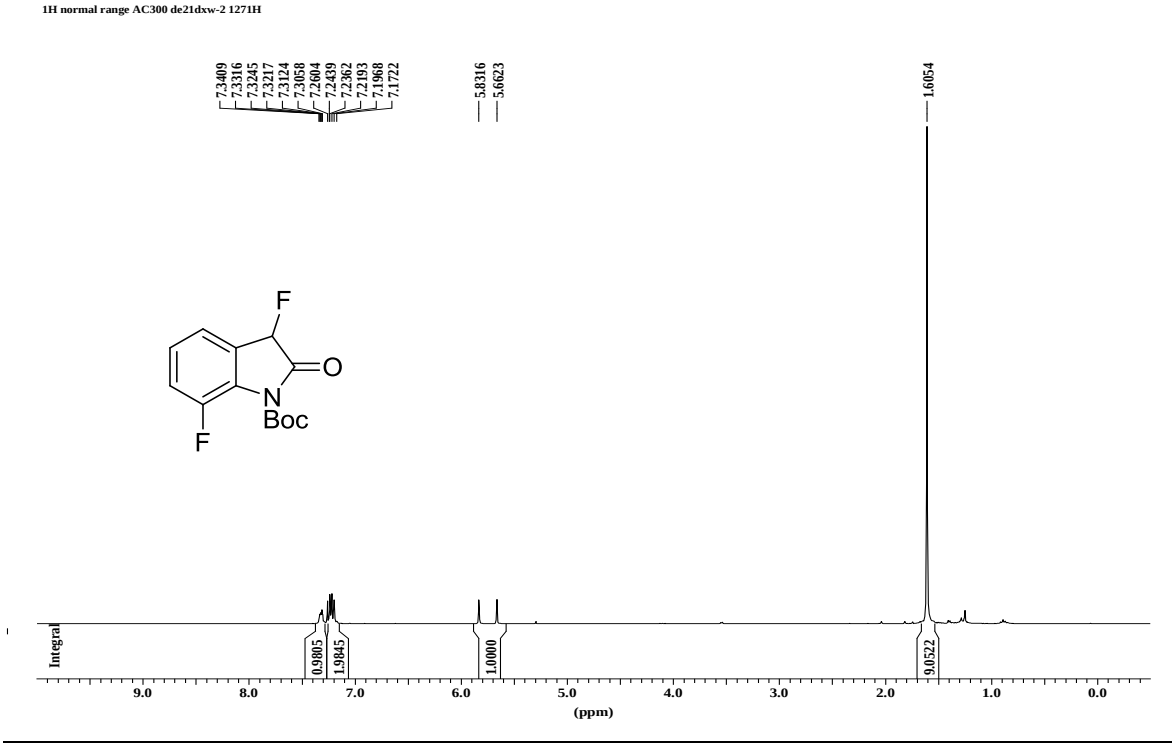


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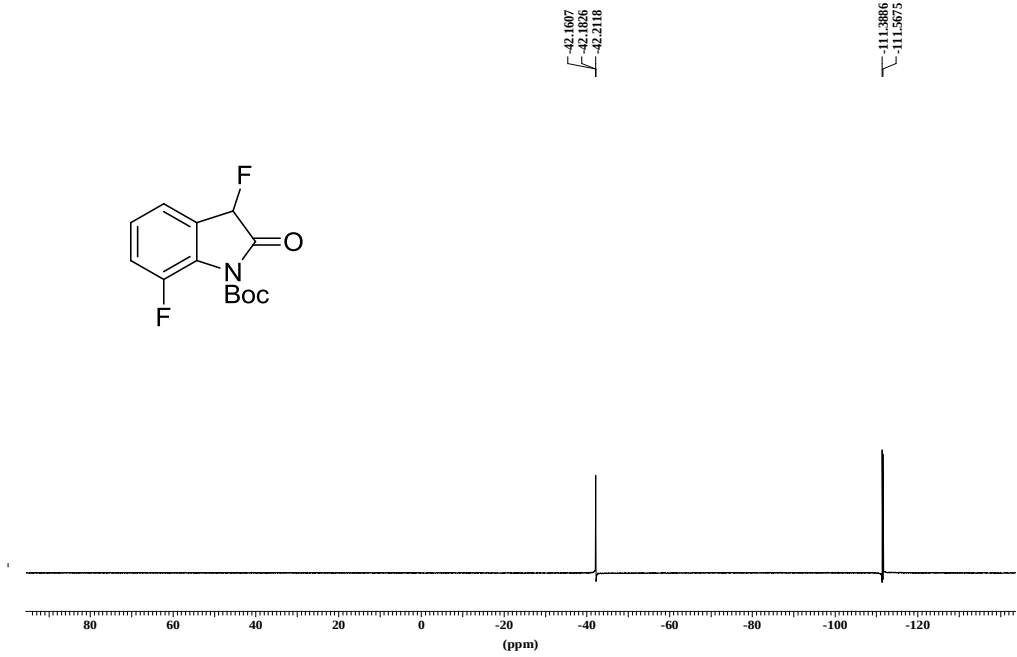


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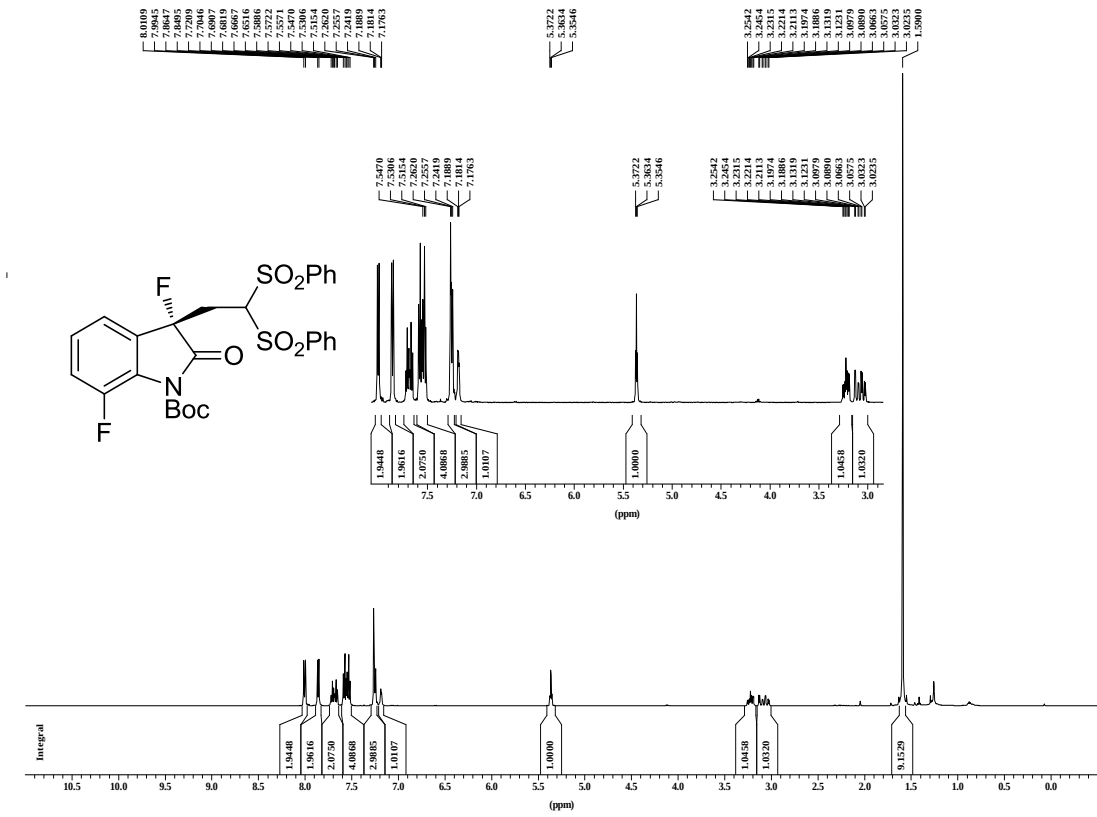




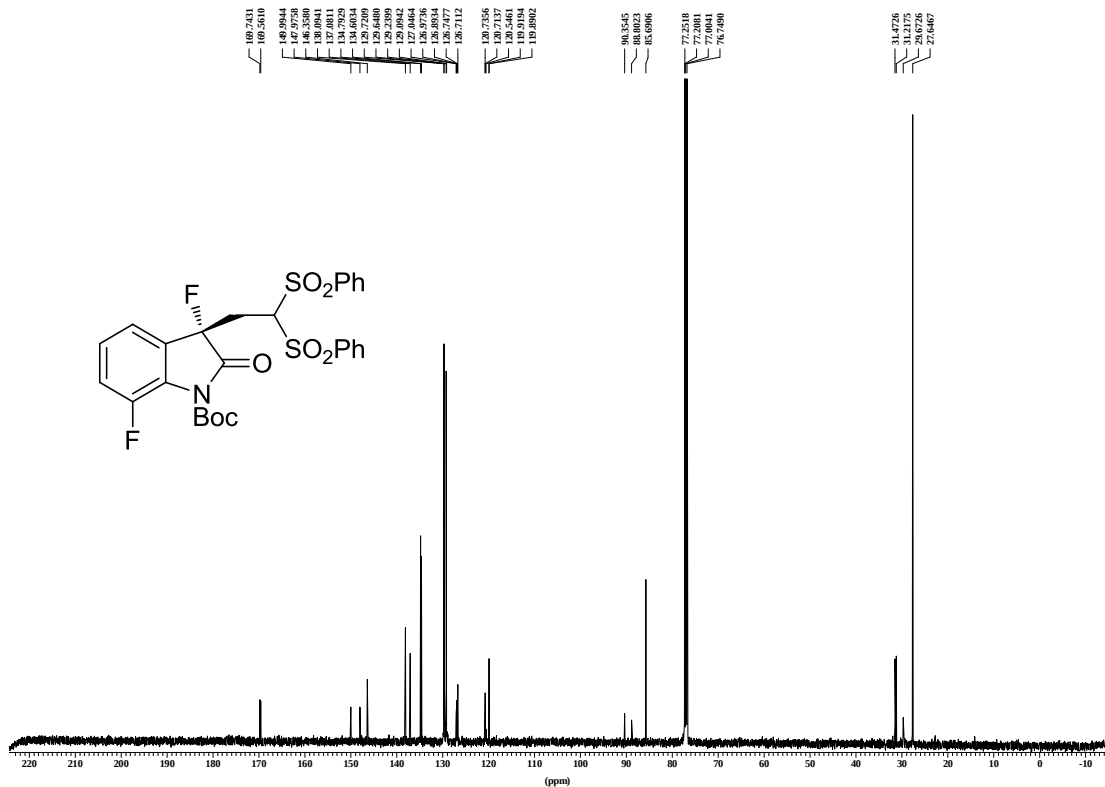
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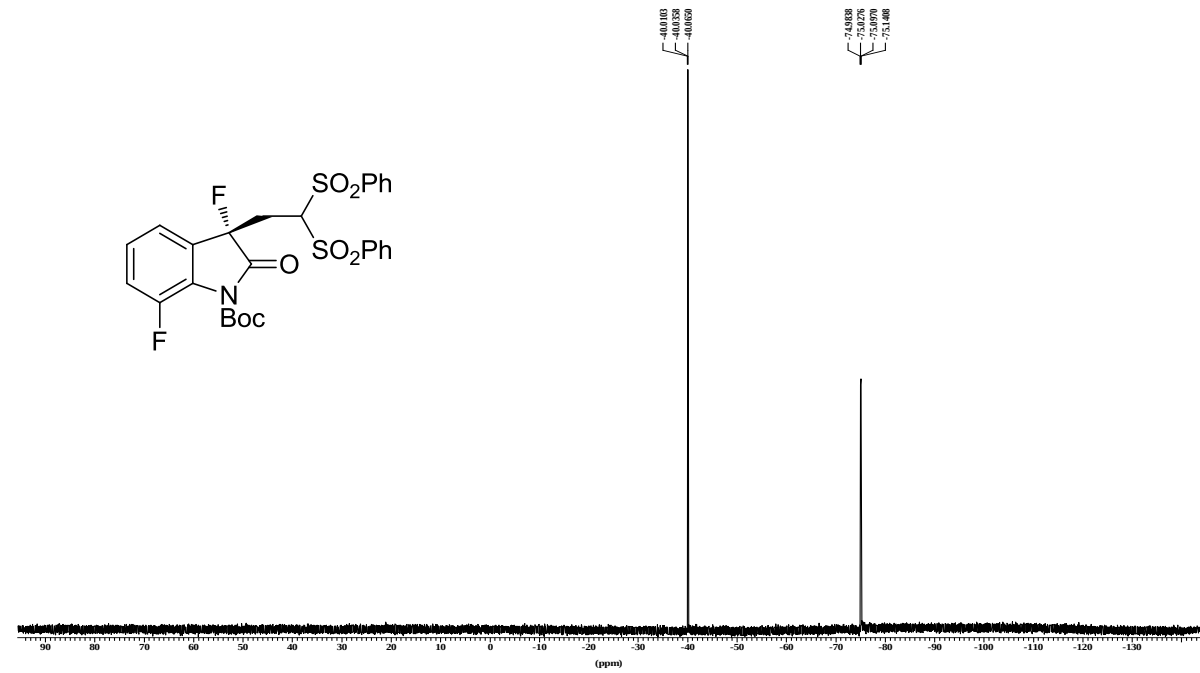
1H AMX500 dcw0617-5 1271H



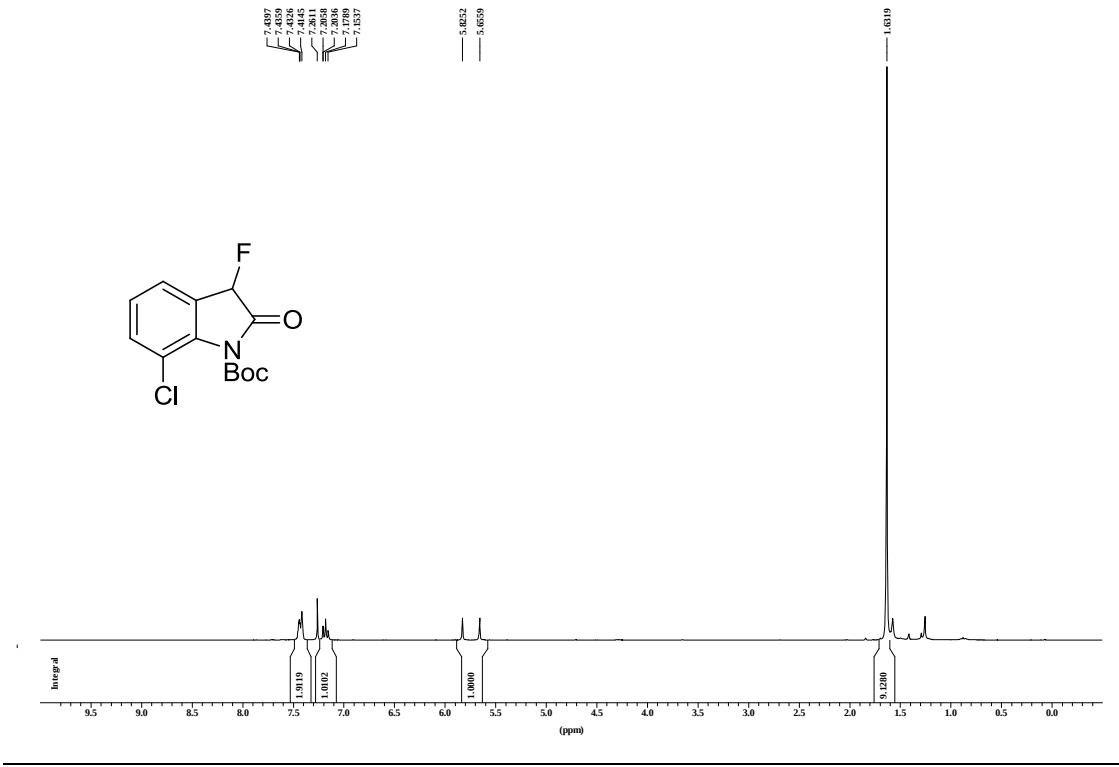
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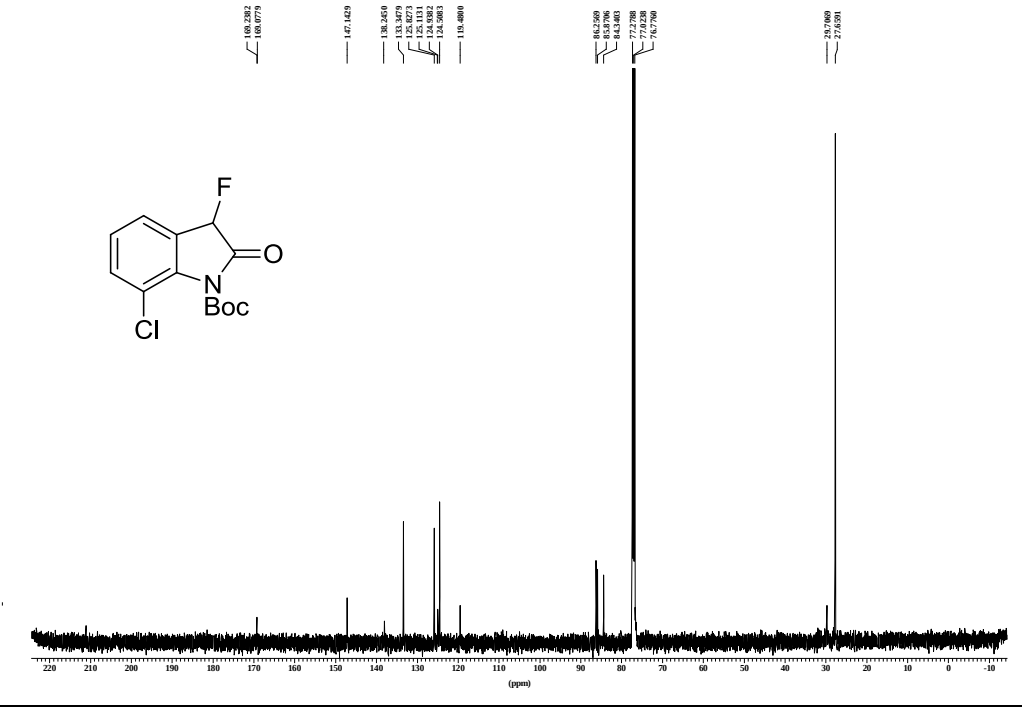
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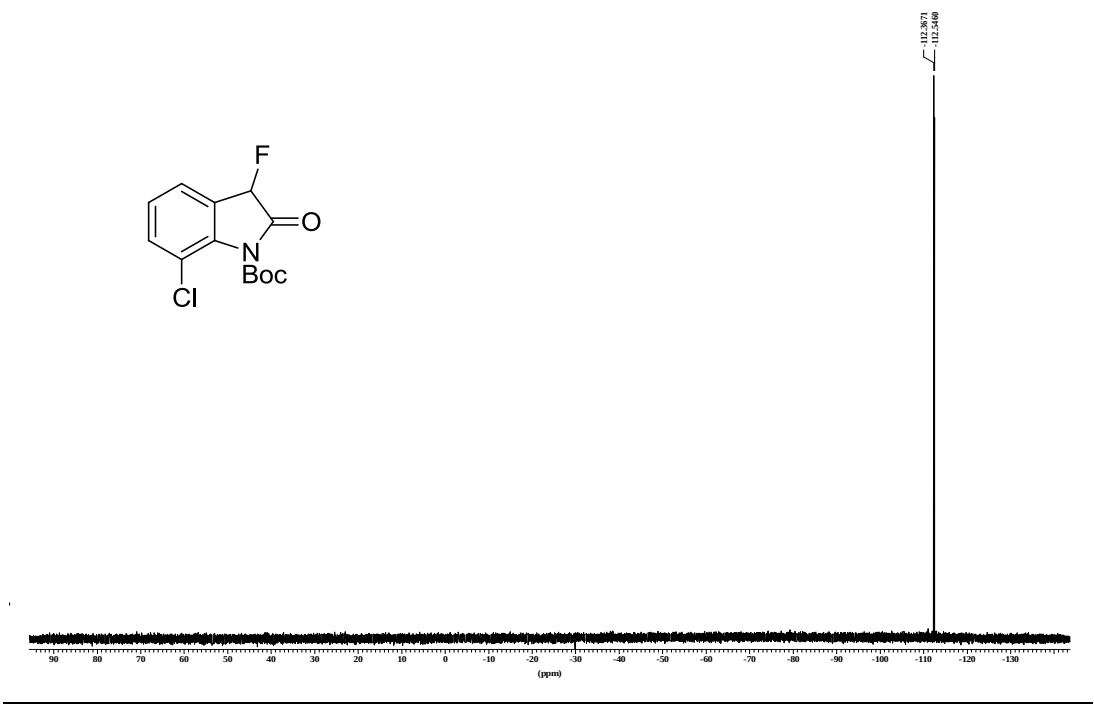
de27dxw-8 1272-2 7-Cl sub



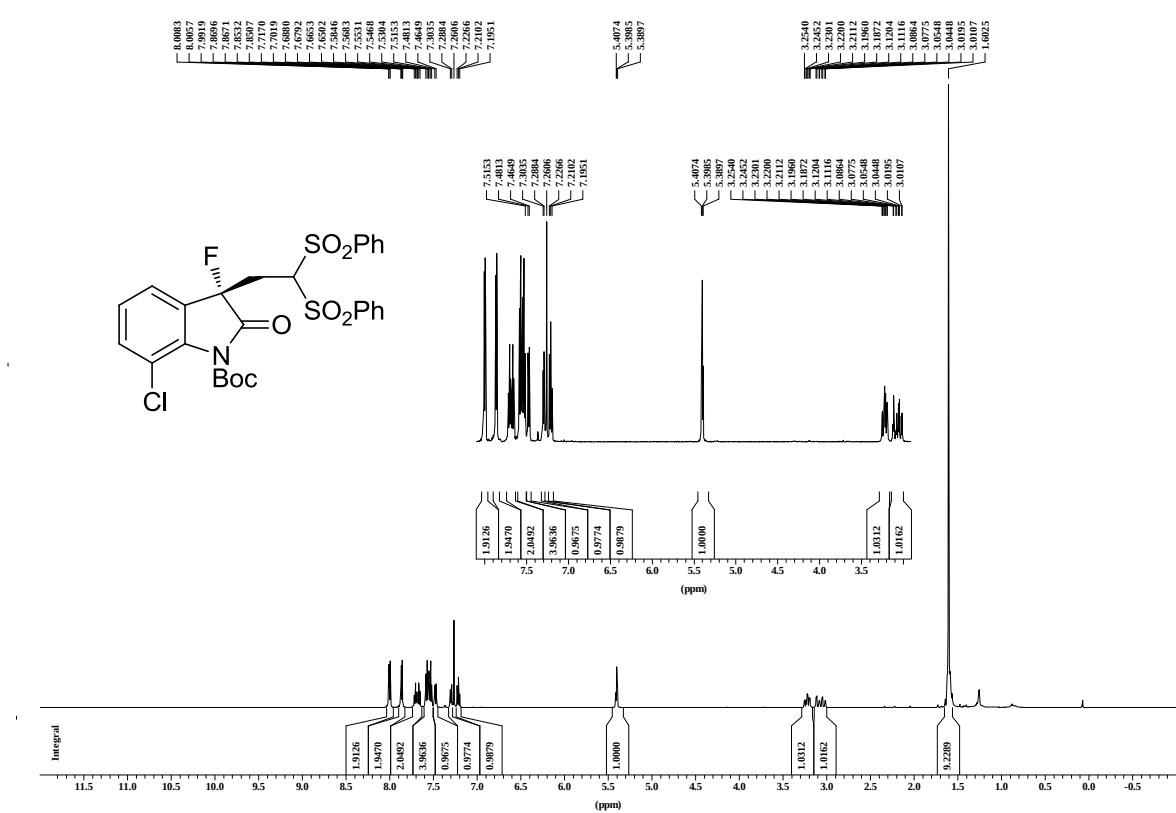
¹³C AMX500 dxw1229-2 1272-2 7-Cl substrate



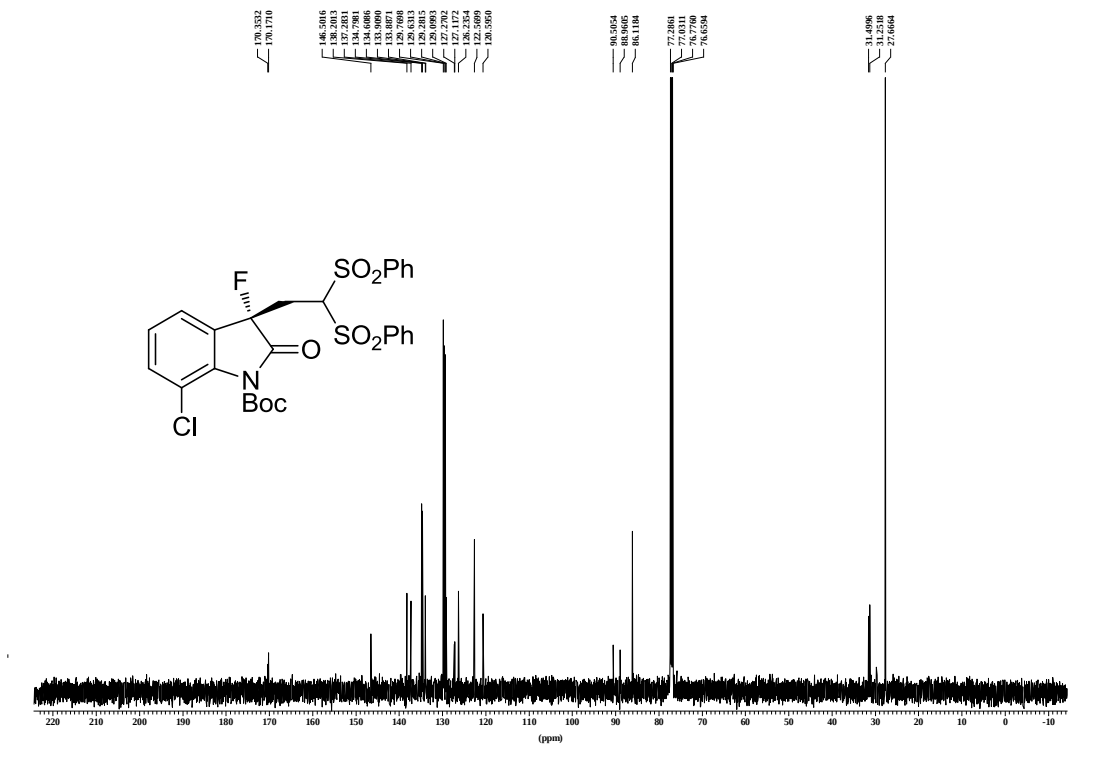
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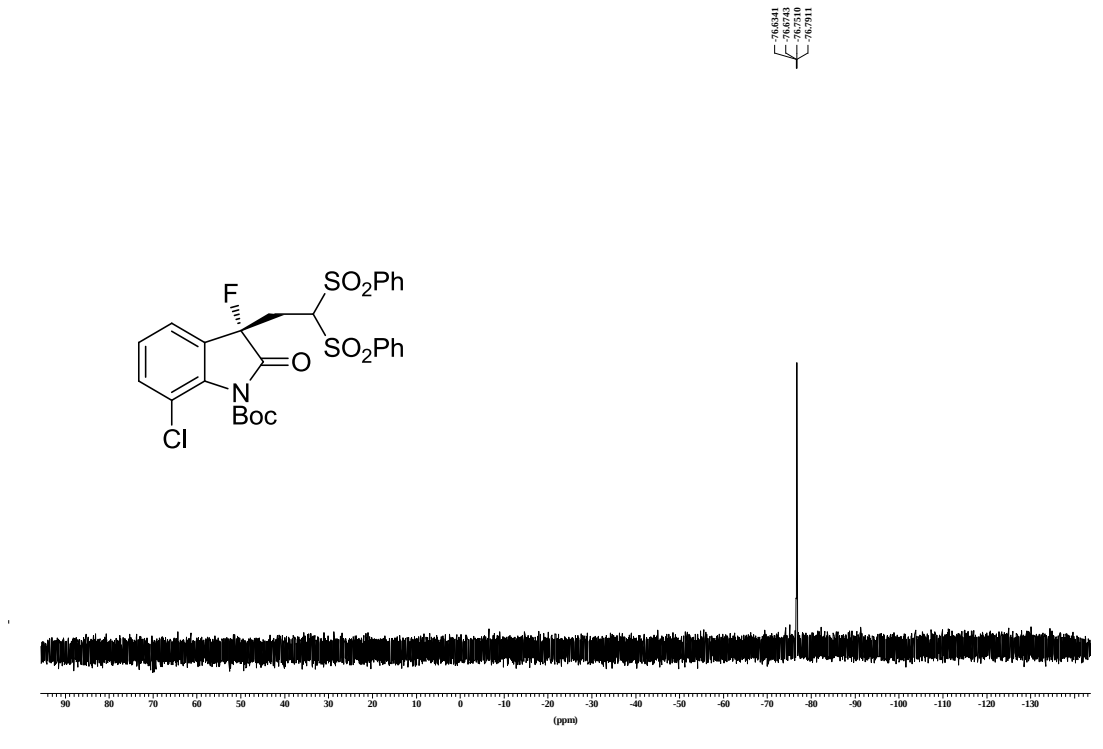
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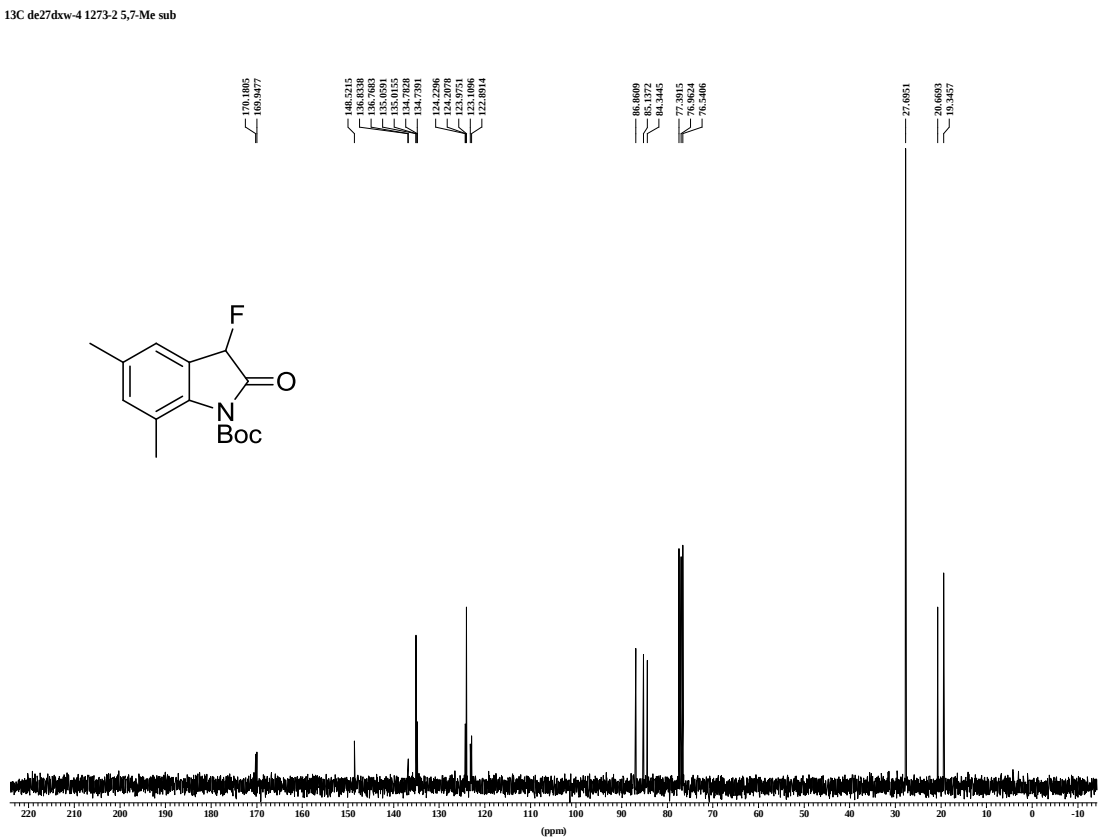
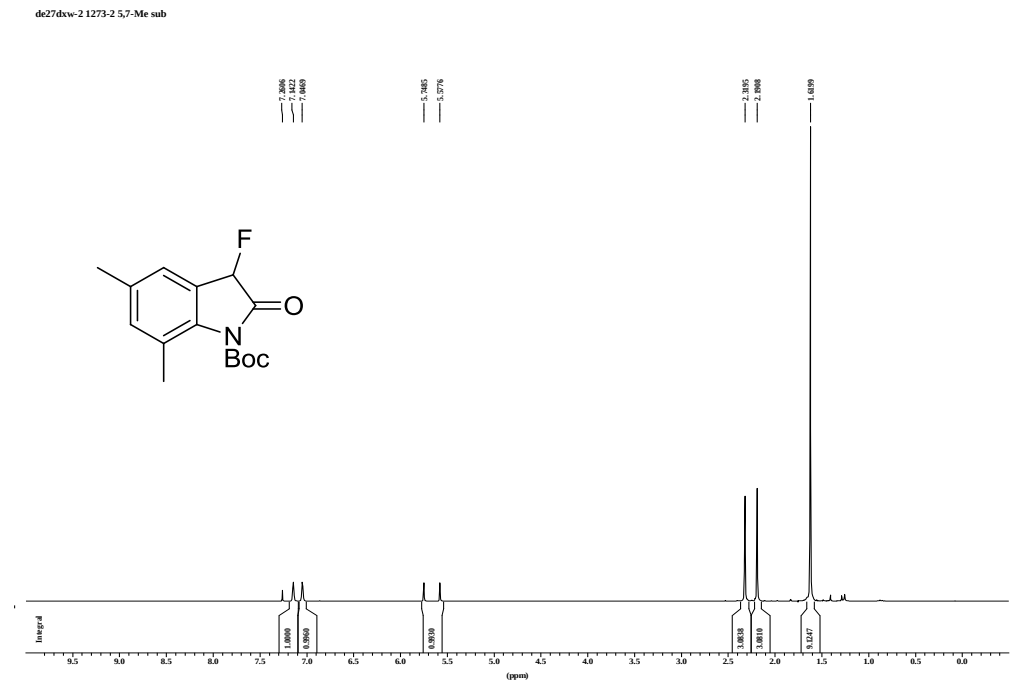


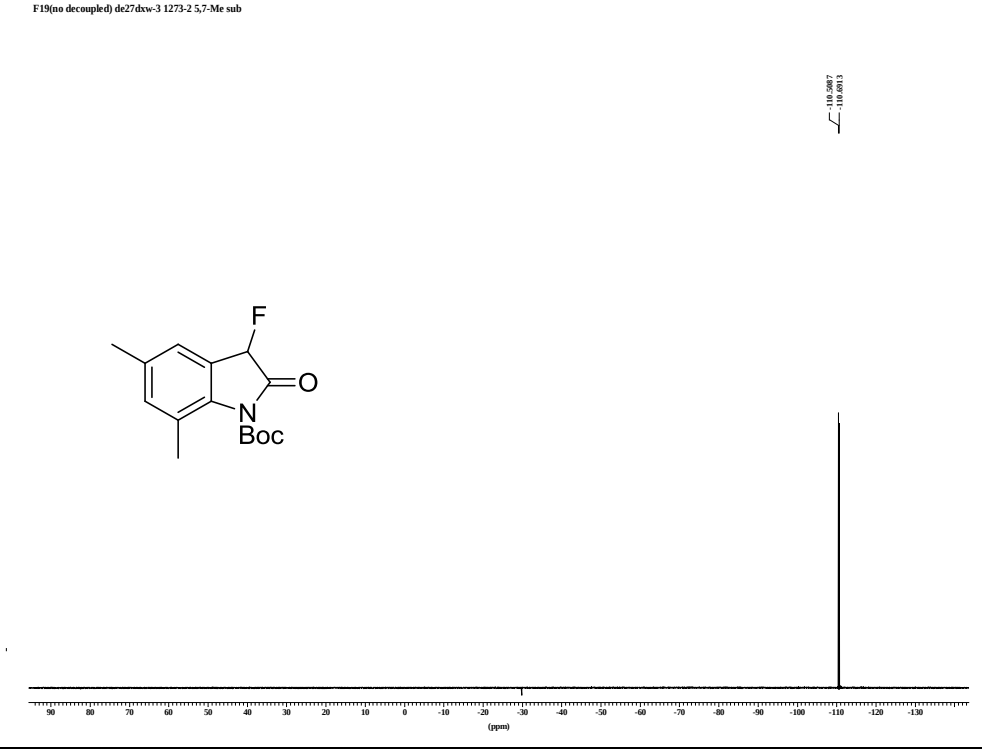
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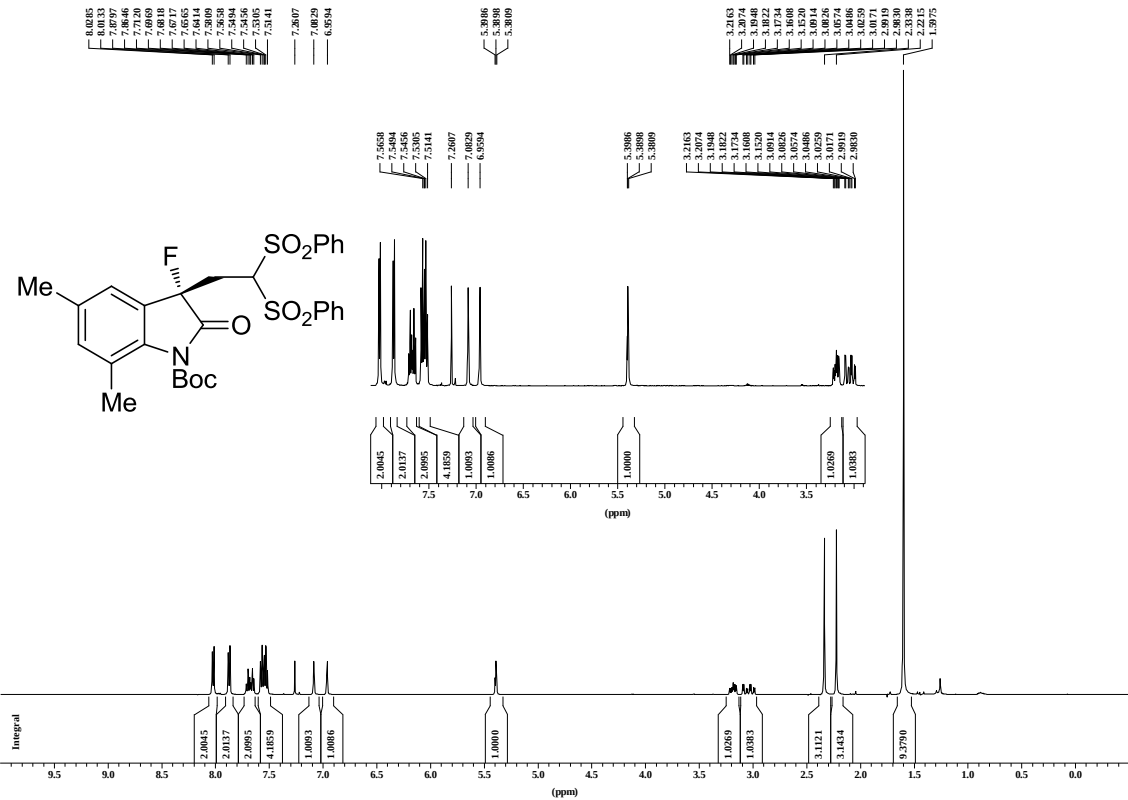
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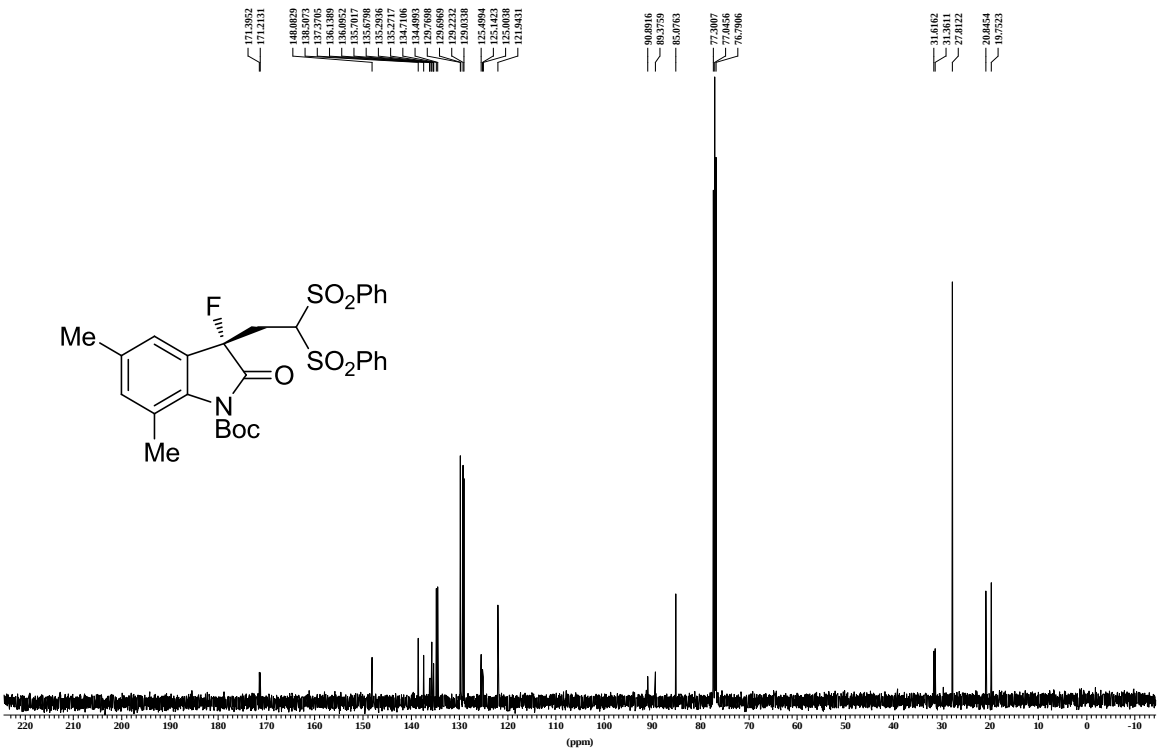




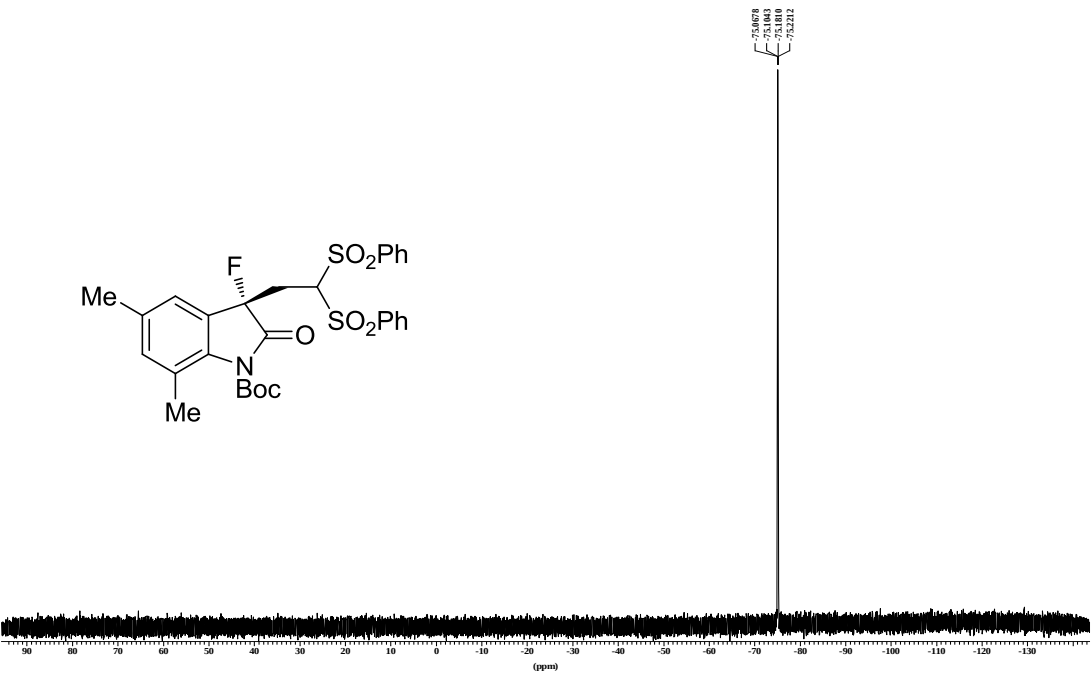
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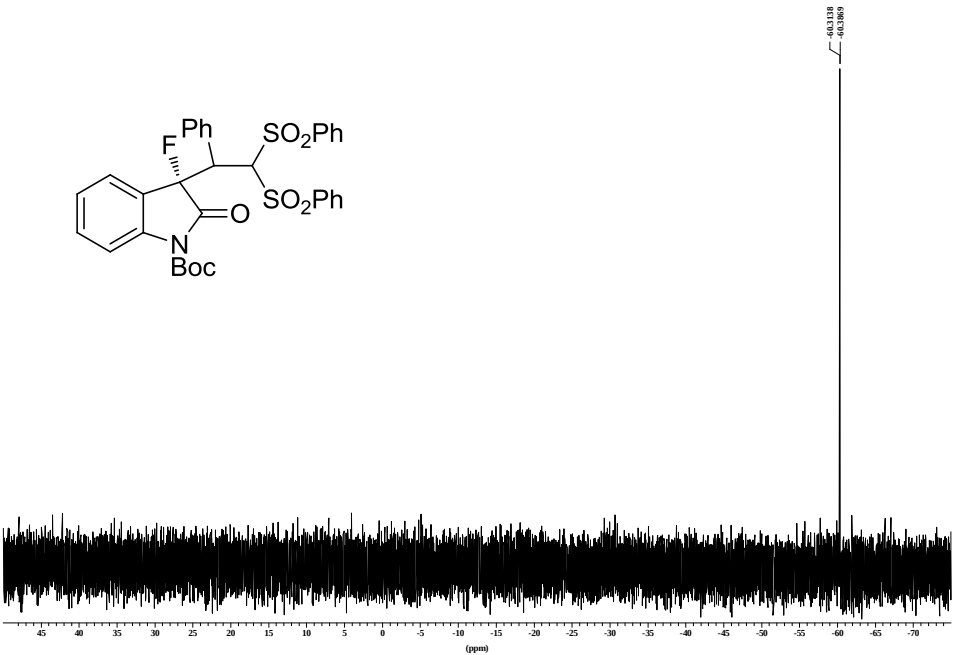
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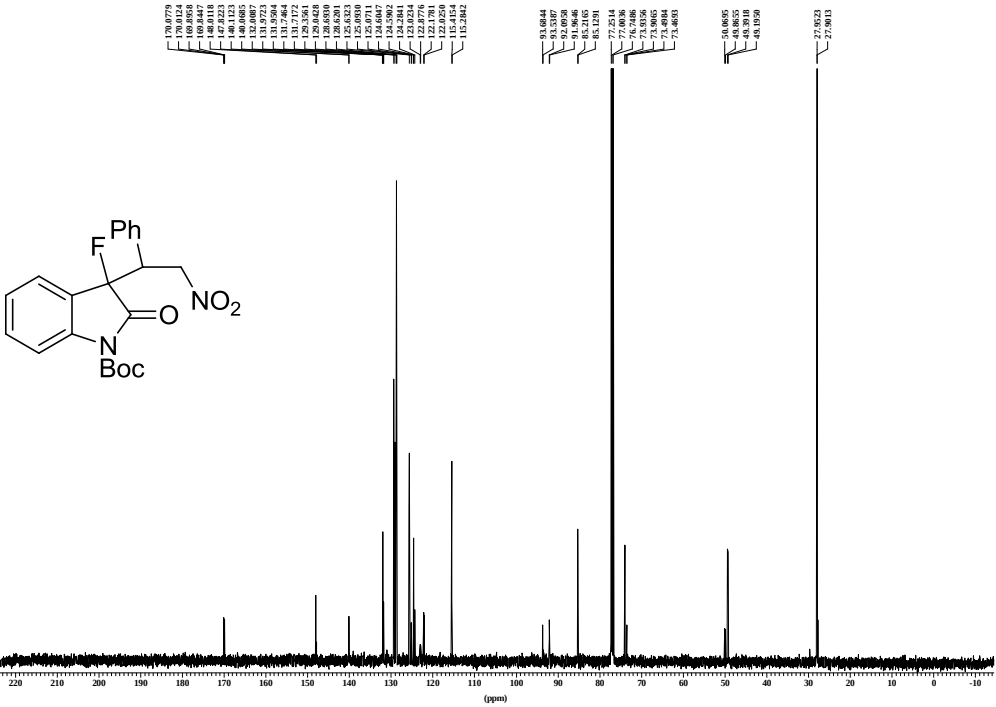
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F19(no decoupled) ja06dxcw-2 1284F



13C AMX500 dxw0617-2 1866C



F19(no decoupled) ju17dxw-1 1866F

