N-Heterocyclic Carbene-Catalyzed Enantioselective Synthesis of Spirocyclic Ketones Bearing *gem*-Difluoromethylenes

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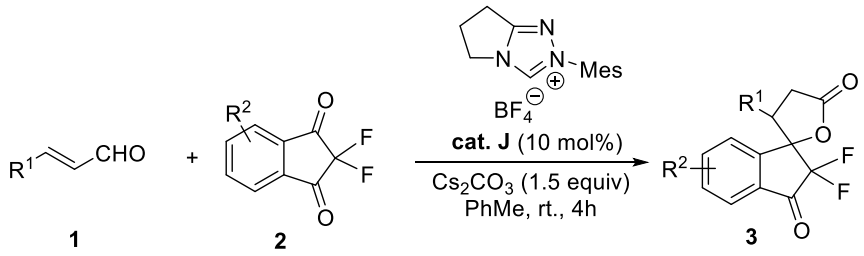
1. General methods and materials

All reactions were carried out under an atmosphere of nitrogen in dry glassware, and were monitored by analytical thin-layer chromatography (TLC), which was visualized by ultraviolet light (254 nm). All solvents were obtained from commercial sources and were purified according to standard procedures. Purification of the products was accomplished by flash chromatography using silica gel (200~300 mesh). Substrates **1**[1] and **2**[2] were known compounds and were prepared according to known procedures. All NMR spectra were recorded on spectrometers, running at 300 MHz or 400 MHz for ^{1}H and 75 MHz or 100 MHz for ^{13}C respectively. Chemical shifts (δ) and coupling constants (J) are reported in ppm and Hz respectively. The solvent signals were used as references (residual $CHCl_3$ in $CDCl_3$: δ_H = 7.26 ppm, δc = 77.0 ppm). The following abbreviations are used to indicate the multiplicity in NMR spectra: s (singlet); d (doublet); t (triplet); q (quartet); m (multiplet). High resolution mass spectrometry (HRMS) was recorded on TOF perimer for ES^+. The d.r. values were determined by ^{1}H NMR analysis of the crude products. The *e.r.* values were determined *via* chiral HPLC analysis.

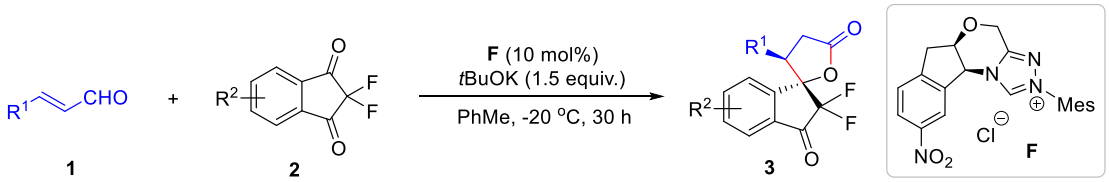
2. General experimental procedure for the synthesis of racemic products 3



To an oven-dried 10 mL flask was charged with substrate **1** (0.2 mmol, 1.0 equiv.), substrate **2** (0.24 mmol, 1.2 equiv.), Cs_2CO_3 (97.7 mg, 0.3 mmol, 1.5 equiv.), precatalyst **J** (6.3 mg, 0.02 mmol, 10 mol%). Then anhydrous PhMe (4 mL) was added to the flask. The resulting mixture was stirred under nitrogen atmosphere at rt typically for 4 h. After completion of the reaction as monitored by TLC, the reaction mixture was concentrated under reduced pressure. The residue was purified by chromatography on silica gel using

PE/EtOAc (8:1) as the eluent to afford racemic products **3**.

3. General experimental procedure for the synthesis of products 3



To an oven-dried 10 mL flask was charged with substrate **1** (0.2 mmol, 1.0 equiv.), substrate **2** (0.24 mmol, 1.2 equiv.), *t*BuOK (33.7 mg, 0.3 mmol, 1.5 equiv.), precatalyst **F** (8.2 mg, 0.02 mmol, 10 mol%). Then anhydrous PhMe (4 mL) was added to the flask. The resulting mixture was stirred under nitrogen atmosphere at -20℃ (typically for 30 h). After completion of the reaction as monitored by TLC, the reaction mixture was concentrated under reduced pressure. The residue was purified by chromatography on silica gel using PE/EtOAc (8:1) as the eluent to afford products **3**.

4. Procedure for the scale-up Synthesis of 3a

To an oven-dried 50 mL bottle was charged with substrate **1a** (1.0 mmol, 1.0 equiv.), substrate **2a** (1.2 mmol, 1.2 equiv.), *t*BuOK (1.5 mmol, 1.5 equiv.), precatalyst **F** (41.3 mg, 0.1 mmol, 10 mol%). Then anhydrous PhMe (20 mL) was added to the flask. The resulting mixture was stirred under nitrogen atmosphere at -20℃ for 5 days. After completion of the reaction as monitored by TLC, the reaction mixture was concentrated under reduced pressure. The residue was purified by chromatography on silica gel using PE/EtOAc (8:1) as the eluent to afford product **3a** (226.7mg, 65%, 98:2 er, >20:1 dr).

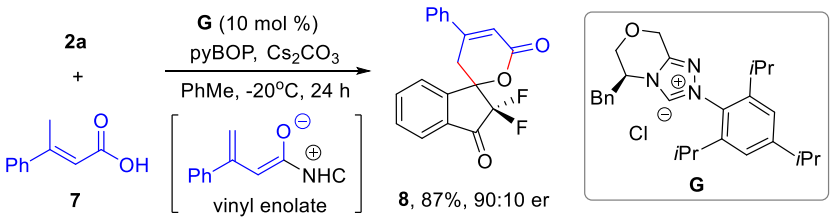
5. Procedure for the synthesis of product 6

Compound **3a** (0.1 mmol), NaOH (0.1 mmol), H_2O/MeOH (10%, 2 mL) were charged in a 10 mL round bottom flask. Then, the reaction mixture was stirred at room temperature for 3 h. After the reaction was completed as detected by TLC, the PH of the reaction mixture was adjusted to 5 with 1M HCl, and the mixture was extracted with EtOAc. The combined organic layer was washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The crude product was purified by

recrystallization to afford the product **6** as a white solid (33.0 mg, 90%, 97:3 er).

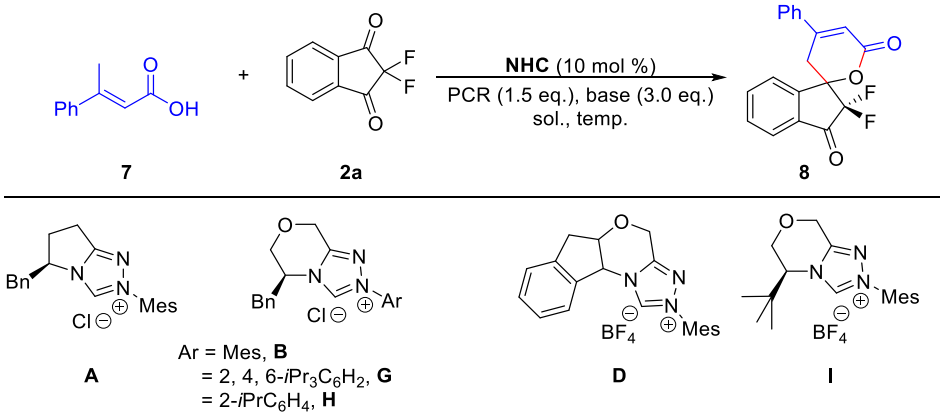
6. Study on the [4+2] annulation of vinyl enolate with ketone 2a

Procedure for the synthesis of product 8



To an oven-dried 10 mL flask was charged with substrate **7** (0.1 mmol, 1.0 equiv.), substrate **2a** (0.12 mmol, 1.2 equiv.), Cs_2CO_3 (97.7 mg, 0.3 mmol, 3.0 equiv.), pyBOP (78 mg, 0.15 mmol, 1.5 equiv.), precatalyst **G** (8.2 mg, 0.02 mmol, 10 mol%). Then anhydrous PhMe (4 mL) was added to the flask. The resulting mixture was stirred under nitrogen atmosphere at -20°C for 24h. After completion of the reaction as monitored by TLC, the reaction mixture was concentrated under reduced pressure. The residue was purified by chromatography on silica gel using PE/EtOAc (5:1) as the eluent to afford product **8** as a white solid (56.8 mg, 87% yield, 90:10 er).

Table S1 Reaction condition optimization for the synthesis of **8** using acid **7** as the precursor

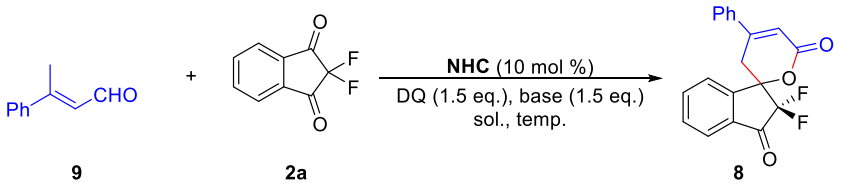


entry	NHC	PCR	base	sol.	temp.	yield (%)	er
1	**A**	pyBOP	Cs_2CO_3	PhMe	rt	85	50:50 er
2	**B**	pyBOP	Cs_2CO_3	PhMe	rt	89	72.5:27.5 er
3	**D**	pyBOP	Cs_2CO_3	PhMe	rt	90	50:50 er
4	**G**	pyBOP	Cs_2CO_3	PhMe	rt	91	84.5:15.5 er
5	**H**	pyBOP	Cs_2CO_3	PhMe	rt	92	67:33 er
6	**I**	pyBOP	Cs_2CO_3	PhMe	rt	75	62.5:37.5 er
7	**G**	pyBOP	DABCO	PhMe	rt	80	67.5:32.5 er

8	**G**	pyBOP	CsOAc	PhMe	rt	73	65:35 er
9	**G**	pyBOP	K_2CO_3	PhMe	rt	75	72:28 er
10	**G**	pyBOP	K_2HPO_4	PhMe	rt	65	70:30 er
11	**G**	pyBOP	Cs_2CO_3	DCM	rt	67	70:30 er
12	**G**	pyBOP	Cs_2CO_3	CH_3CN	rt	52	50:50 er
13	**G**	pyBOP	Cs_2CO_3	THF	rt	77	78:22 er
14	**G**	pyBOP	Cs_2CO_3	1,4-dioxane	rt	79	75:25 er
15	**G**	HBTU	Cs_2CO_3	PhMe	rt	85	83:17 er
16	**G**	pyBOP	Cs_2CO_3	PhMe	0°C	88	86:14 er
17	**G**	pyBOP	Cs_2CO_3	PhMe	-20°C	87	90:10 er

Reaction Conditions: all reactions were performed in a 10 mL flask on a 0.1 mmol scale with 1.0 equiv of **2a**, 1.2 equiv of **7**, 10 mol% of an NHC precursor, 1.5 equiv. of PCR, 3.0 equiv. of a base in an anhydrous solvent (4 mL) at temp. under N_2.

Table S2. Reaction condition optimization for the synthesis of **8** using enal **9** as the precursor

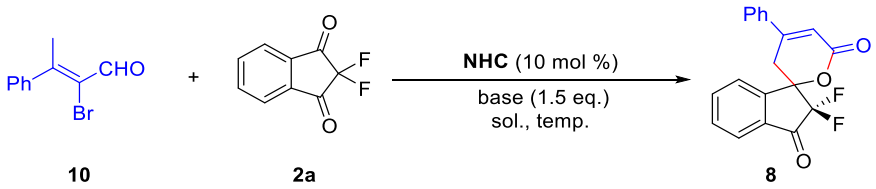


9 **2a** **8**

entry	NHC	base	sol.	temp.	yield (%)	er
1	**A**	Cs_2CO_3	PhMe	rt	77	50:50 er
2	**B**	Cs_2CO_3	PhMe	rt	85	79:21 er
3	**D**	Cs_2CO_3	PhMe	rt	80	50:50 er
4	**G**	Cs_2CO_3	PhMe	rt	87	85:15 er
5	**H**	Cs_2CO_3	PhMe	rt	89	76:24 er
6	**I**	Cs_2CO_3	PhMe	rt	82	85:15 er

Reaction Conditions: all reactions were performed in a 10 mL flask on a 0.1 mmol scale with 1.0 equiv of **2a**, 1.2 equiv of **9**, 10 mol% of an NHC precursor, 1.5 equiv. of DQ, 1.5 equiv. of Cs_2CO_3 in anhydrous PhMe (2 mL) at temp. under N_2.

Table S3. Reaction condition optimization for the synthesis of **8** using 2-bromoenal **10** as the precursor



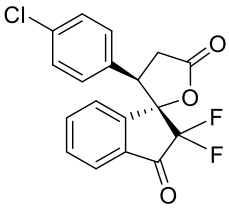
10 **2a** **8**

entry	NHC	base	sol.	temp.	yield (%)	er
1	**A**	Cs_2CO_3	PhMe	rt	81	50:50 er
2	**B**	Cs_2CO_3	PhMe	rt	76	77:23 er
3	**D**	Cs_2CO_3	PhMe	rt	84	50:50 er
4	**G**	Cs_2CO_3	PhMe	rt	85	83:27 er

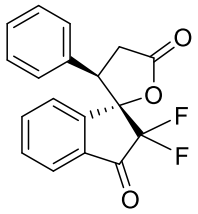
5	**I**	Cs_2CO_3	PhMe	rt	74	62:38 er

Reaction Conditions: all reactions were performed in a 10 mL flask on a 0.1 mmol scale with 1.0 equiv of **2a**, 1.2 equiv of **10**, 10 mol% of an NHC precursor, 1.5 equiv. of Cs_2CO_3 in anhydrous PhMe (2 mL) at temp. under N_2.

7. Characterization of the products

(2*S*,3*R*)-3-(4-chlorophenyl)-2',2'-difluoro-3,4-dihydro-5H-spiro[furan-2,1'-indene]-3',5(2'H)-dione (3a). 

White solid, MP: 160-162 °C; 58.6 mg, 84% yield, 96:4 er, >20:1 dr. $[\alpha]_D^{23}$ = +7.444 (C = 0.403 in $CHCl_3$). HPLC DAICEL CHIRALCEL IC, n-hexane/2- propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 12.41 min (major), 14.95 min (minor). ^{1}H NMR (300 MHz, Chloroform-d) δ 8.05-7.96 (m, 1H), 7.95-7.81 (m, 2H), 7.80-7.69 (m, 1H), 7.13 (d, *J* = 8.5 Hz, 2H), 6.56-6.52 (m, 2H), 4.05 (ddd, *J* = 12.8, 7.6, 4.2 Hz, 1H), 3.51 (ddd, *J* = 16.5, 13.9, 2.3 Hz, 1H), 2.99 (ddd, *J* = 17.0, 7.6, 1.7 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-d) δ 185.3 (dd, $^2J_{C\text{-}F}$ = 25.6, 23.3 Hz), 172.72, 146.4 (d, $^4J_{C\text{-}F}$ = 4.1 Hz), 138.31, 134.89, 133.4 (dd, $^4J_{C\text{-}F}$ = 4.5, 2.3 Hz), 132.07, 129.7 (d, $^4J_{C\text{-}F}$ = 3.3 Hz), 128.94, 128.7 (d, $^4J_{C\text{-}F}$ =1.8 Hz), 124.74, 124.7 (d, $^4J_{C\text{-}F}$ = 1.9 Hz), 115.6 (dd, $^1J_{C\text{-}F}$ = 273.5, 261.6 Hz), 86.5 (dd, $^2J_{C\text{-}F}$ = 21.4, 16.9 Hz), 52.02, 31.9 (d, $^4J_{C\text{-}F}$ = 2.8 Hz). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -109.0 (d, *J* = 270.7Hz), -128.9 (d, *J* = 270.7Hz). HRMS (ESI) calcd for $C_{18}H_{12}ClF_2O_3$ $(M+H)^+$: 349.0438, found 349.0422.

(2*S*,3*R*)-2',2'-difluoro-3-phenyl-3,4-dihydro-5H-spiro[furan-2,1'-indene]-3',5(2'H)-dione (3b). 

White solid, MP: 133-135 °C; 52.2 mg, 83% yield, 96:4 er, >20:1 dr. $[\alpha]_D^{23}$ = +31.884 (C = 0.276 in $CHCl_3$). HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 12.79 min (major), 15.48 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.00 (t, *J* = 7.5 Hz, 1H), 7.92 (d, *J* = 7.8 Hz, 1H), 7.82 (d, *J* = 7.7 Hz, 1H), 7.73 (t, *J* = 7.5 Hz, 1H), 7.23 (t, *J* = 7.4 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 2H), 6.60 (d, *J* = 7.7 Hz, 2H), 4.08 (ddd, *J* = 12.9, 7.6, 4.3 Hz, 1H), 3.57

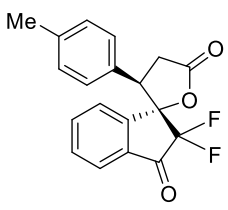
(ddd, *J* = 16.5, 13.9, 2.3 Hz, 1H), 2.99 (ddd, *J* = 17.1, 7.6, 1.7 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 185.4 (dd, $^{2}J_{C\text{-}F}$ = 25.5, 23.3 Hz), 173.2, 146.7 (d, $^{3}J_{C\text{-}F}$ = 8.0 Hz), 138.1, 133.5 (dd, $^{4}J_{C\text{-}F}$ = 4.7, 2.1 Hz), 131.9, 130.0 (d, $^{4}J_{C\text{-}F}$ = 1.6Hz), 128.8, 128.6, 128.5 (d, $^{4}J_{C\text{-}F}$ = 3.1 Hz), 124.7 (d, $^{4}J_{C\text{-}F}$ = 1.4 Hz), 124.5, 115.8 (dd, $^{1}J_{C\text{-}F}$ = 274.3, 260.3 Hz), 86.9 (dd, $^{2}J_{C\text{-}F}$ = 21.3, 16.8 Hz), 52.6, 31.8 (d, $^{4}J_{C\text{-}F}$ = 2.9 Hz). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -109.0(d, *J* = 264.24 Hz), -129.4 (d, *J* = 270.7.0 Hz). HRMS (ESI) calcd for $C_{18}H_{13}F_2O_3$ $(M+H)^+$: 315.0828, found 315.0837.

(2*S*,3*R*)-2',2'-difluoro-3-(4-fluorophenyl)-3,4-dihydro-5H-spiro[furan-2,1'-indene]-3',5(2'H)-dione (3c). White solid, MP: 158-159 °C; 43.2 mg, 65% yield, 98:2 er, >20:1 dr. $[\alpha]_D^{23}$ = -39.140 (C = 0.155 in $CHCl_3$). HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 11.93 min (major), 14.19 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.00 (t, *J* = 7.5 Hz, 1H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.82 (d, *J* = 7.7 Hz, 1H), 7.73 (t, *J* = 7.5 Hz, 1H), 6.84 (t, *J* = 8.4 Hz, 2H), 6.60-6.56 (m, 2H), 4.05 (ddd, *J* = 12.9, 7.6, 4.3 Hz, 1H), 3.51 (ddd, *J* = 16.6, 13.9, 2.3 Hz, 1H), 3.05-2.92 (m, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 185.3 (dd, $^{2}J_{C\text{-}F}$ = 25.3, 23.3 Hz), 172.9, 162.7 (d, $^{1}J_{C\text{-}F}$ = 250.1 Hz),146.4 (d, $^{3}J_{C\text{-}F}$ = 8.0 Hz), 138.3, 133.4 (dd, $^{4}J_{C\text{-}F}$ = 4.6, 2.2 Hz), 132.0, 130.2 (dd, $^{3}J_{C\text{-}F}$ = 8.3, 3.3 Hz), 125.8, 124.7 (d, $^{4}J_{C\text{-}F}$ = 1.4 Hz), 124.6, 115.74 (dd, $^{1}J_{C\text{-}F}$ = 273.9, 260.6 Hz), 115.73 (d, $^{2}J_{C\text{-}F}$ = 21.7 Hz), 86.7 (dd, $^{2}J_{C\text{-}F}$ = 21.2, 16.9 Hz), 52.0, 31.0 (d, $^{4}J_{C\text{-}F}$ = 2.9 Hz). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -109.1 (d, *J* = 270.7Hz), -112.23, -129.5 (d, *J* = 270.7Hz). HRMS (ESI) calcd for $C_{19}H_{15}F_2O_4$: 345.0933, found 345.0934. HRMS (ESI) calcd for $C_{18}H_{12}F_3O_3$ $(M+H)^+$: 333.0734, found 333.0737.

(2*S*,3*R*)-3-(4-bromophenyl)-2',2'-difluoro-3,4-dihydro-5H-spiro[furan-2,1'-indene]-3',5(2'H)-dione (3d). White solid, MP: 180-181 °C; 48.0 mg, 61% yield, 97:3 er, >20:1 dr. $[\alpha]_D^{23}$ = -39.140 (C = 0.155 in $CHCl_3$). HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 13.68 min (major), 16.06 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.01 (t, *J* = 7.5 Hz,

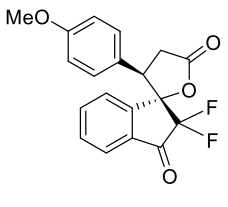
1H), 7.92 (d, *J* = 7.8 Hz, 1H), 7.85 (d, *J* = 7.7 Hz, 1H), 7.75 (t, *J* = 7.5 Hz, 1H), 7.28 (d, *J* = 8.4 Hz, 2H), 6.50-6.47 (m, 2H), 4.05 (ddd, *J* = 12.7, 7.5, 4.2 Hz, 1H), 3.51 (ddd, *J* = 16.4, 13.8, 2.2 Hz, 1H), 3.00 (ddd, *J* = 17.0, 7.6, 1.6 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-d) δ 185.4 (dd, $^{2}J_{C\text{-}F}$ = 25.4, 23.3 Hz), 172.7, 146.4 (d, $^{3}J_{C\text{-}F}$ = 7.9 Hz), 138.3, 133.4 (dd, $^{4}J_{C\text{-}F}$ = 4.6, 1.7 Hz), 132.1, 131.9, 130.0 (d, $^{4}J_{C\text{-}F}$ = 3.3 Hz), 129.3 (d, $^{4}J_{C\text{-}F}$ = 1.9 Hz), 124.74, 124.70, 123.0, 115.6 (dd, $^{1}J_{C\text{-}F}$ = 273.7, 261.6 Hz), 86.4 (dd, $^{2}J_{C\text{-}F}$ = 21.3, 16.8 Hz), 52.0, 31.9 (d, $^{4}J_{C\text{-}F}$ = 2.8 Hz). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -109.0 (d, *J* = 270.7Hz), -128.7 (d, *J* = 274.5Hz). HRMS (ESI) calcd for $C_{18}H_{12}BrF_2O_3$ $(M+H)^+$: 392.9933, 394.9912, found 392.39930, 394.9903.

(2*S*,3*R*)-2',2'-difluoro-3-(p-tolyl)-3,4-dihydro-5H-spiro[furan-2,1'-indene]-



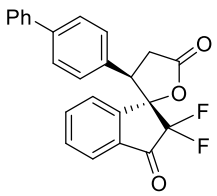
3',5(2'H)-dione (3e). White solid, MP: 170-172 °C; 48.0 mg, 75% yield, 98:2 er, >20:1 dr. $[\alpha]_D^{23}$ = -9.524 (C = 0.154 in $CHCl_3$). HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 85/15, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 16.57 min (major), 19.84 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.98 (t, *J* = 7.5 Hz, 1H), 7.91 (d, *J* = 7.7 Hz, 1H), 7.81 (d, *J* = 7.7 Hz, 1H), 7.72 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 7.8 Hz, 2H), 6.48 (d, *J* = 5.8 Hz, 2H), 4.03 (ddd, *J* = 13.0, 7.5, 4.3 Hz, 1H), 3.54 (ddd, *J* = 16.7, 14.0, 2.4 Hz, 1H), 2.96 (ddd, *J* = 17.0, 7.5, 1.7 Hz, 1H), 2.25 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 185.4 (dd, $^{2}J_{C\text{-}F}$ =25.2, 23.3 Hz), 173.4, 146.8 (d, $^{3}J_{C\text{-}F}$ = 8.0 Hz), 138.7, 138.1, 133.5 (dd, $^{4}J_{C\text{-}F}$ = 4.7, 2.1 Hz), 131.8, 129.4, 128.3 (d, $^{4}J_{C\text{-}F}$ = 3.1 Hz), 126.7 (d, $^{4}J_{C\text{-}F}$ = 1.8 Hz), 124.7 (d, $^{4}J_{C\text{-}F}$ = 1.2 Hz), 124.5, 115.8 (dd, $^{1}J_{C\text{-}F}$ = 274.7, 259.8 Hz), 86.8 (dd, $^{2}J_{C\text{-}F}$ = 21.2, 16.7 Hz), 52.5, 31.9 (d, $^{4}J_{C\text{-}F}$ = 2.9 Hz), 21.2. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -108.9(d, *J* = 270.7Hz), -129.8 (d, *J* = 270.7Hz). HRMS (ESI) calcd for $C_{19}H_{14}F_2NaO_3$ $(M+Na)^+$: 351.0804, found 351.0812.

(2*S*,3*R*)-2',2'-difluoro-3-(4-methoxyphenyl)-3,4-dihydro-5H-spiro[furan-2,1'-



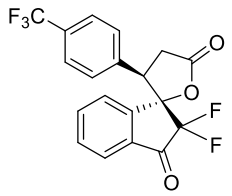
indene]-3',5(2'H)-dione (3f). White solid, MP: 191-192 °C; 58.5 mg, 85% yield, 95.5:4.5 er, >20:1 dr. $[\alpha]_D^{23}$ = -0.683 (C = 0.293 in $CHCl_3$). HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 85/15, flow rate = 1.0 mL/min, λ = 254 nm, retention

time: 23.63 min (major), 29.44 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.98 (t, *J* = 7.6 Hz, 1H), 7.89 (d, *J* = 7.8 Hz, 1H), 7.81 (d, *J* = 7.7 Hz, 1H), 7.71 (t, *J* = 7.5 Hz, 1H), 6.66 (d, *J* = 8.8 Hz, 2H), 6.55-6.45 (m, 2H), 3.99 (ddd, *J* = 12.9, 7.6, 4.4 Hz, 1H), 3.72 (s, 3H), 3.51 (ddd, *J* = 16.8, 14.1, 2.4 Hz, 1H), 2.96 (ddd, *J* = 17.1, 7.6, 1.9 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 185.3 (t, $^{2}J_{C\text{-}F}$ = 23.2 Hz), 173.4, 159.8, 146.7 (d, $^{3}J_{C\text{-}F}$ = 8.3 Hz), 138.1, 133.4 (d, $^{4}J_{C\text{-}F}$ = 3.3 Hz), 129.7, 129.7, 124.6 (d, $^{4}J_{C\text{-}F}$ = 1.7 Hz), 124.5, 121.4 (d, $^{4}J_{C\text{-}F}$ = 1.7 Hz), 115.9 (dd, $^{1}J_{C\text{-}F}$ = 274.7, 259.7 Hz), 114.0, 86.9 (dd, $^{2}J_{C\text{-}F}$ = 25.6, 23.1 Hz), 55.3, 52.3, 32.0 (d, $^{4}J_{C\text{-}F}$ = 3.1 Hz). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -109.0 (d, *J* = 267.0Hz), -130.3 (d, *J* = 267.0Hz). HRMS (ESI) calcd for $C_{19}H_{15}F_2O_4$ $(M+H)^+$: 345.0933, found 345.0934.

(2*S*,3*R*)-3-([1,1'-biphenyl]-4-yl)-2',2'-difluoro-3,4-dihydro-5H-spiro[furan-2,1'-indene]-3',5(2'H)-dione (3g). 

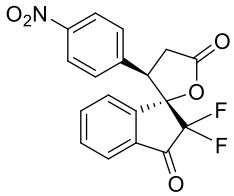
White solid, MP: 188-189 °C; 54.7 mg, 70% yield, 97:3 er, >20:1 dr. $[\alpha]_D^{23}$ = 62.319 (C = 0.391 in $CHCl_3$). HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 16.94 min (major), 22.31 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.00 (t, *J* = 7.5 Hz, 1H), 7.94 (d, *J* = 7.8 Hz, 1H), 7.84 (d, *J* = 7.7 Hz, 1H), 7.74 (t, *J* = 7.5 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 2H), 7.44-7.30 (m, 5H), 6.68 (dd, *J* = 8.3, 2.3 Hz, 2H), 4.13 (ddd, *J* = 12.9, 7.6, 4.2 Hz, 1H), 3.60 (ddd, *J* = 16.6, 13.7, 2.2 Hz, 1H), 3.02 (dd, *J* = 17.0, 7.5 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-d) δ 185.4 (dd, $^{2}J_{C\text{-}F}$ = 25.4, 23.1 Hz), 173.2, 146.7 (d, $^{3}J_{C\text{-}F}$ = 7.9 Hz), 141.5, 140.0, 138.2, 133.5 (dd, $^{4}J_{C\text{-}F}$ = 4.4, 1.8 Hz), 131.9, 128.9 (d, $^{4}J_{C\text{-}F}$ = 1.9 Hz), 128.9, 128.8 (d, $^{4}J_{C\text{-}F}$ = 3.1 Hz), 127.8, 127.2, 127.1, 124.7 (d, $^{4}J_{C\text{-}F}$ = 1.6 Hz), 124.6, 115.8 (dd, $^{1}J_{C\text{-}F}$ = 274.0, 260.6 Hz), 86.8 (dd, $^{2}J_{C\text{-}F}$ = 21.3, 16.8 Hz), 52.3, 31.9 (d, $^{4}J_{C\text{-}F}$ = 2.8 Hz). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -109.0 (d, *J* = 270.7Hz), -129.0 (d, *J* = 270.7Hz). HRMS (ESI) calcd for $C_{19}H_{14}F_2NaO_3$ $(M+Na)^+$: 391.1140, found 391.1134.

(2*S*,3*R*)-2',2'-difluoro-3-(4-(trifluoromethyl)phenyl)-3,4-dihydro-5H-spiro[furan-2,1'-indene]-3',5(2'H)-dione (3h). White solid, MP: 180-181 °C; 50.5 mg, 66% yield,



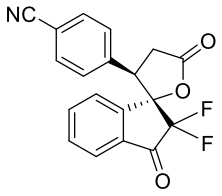
94:6 er, >20:1 dr. $[\alpha]_D^{23}$ = -4.444 (C = 0.240 in $CHCl_3$). HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 95/5, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 31.92 min (major), 37.19 min (minor). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.03 (t, *J* = 7.5 Hz, 1H), 7.95 (d, *J* = 7.8 Hz, 1H), 7.86 (d, *J* = 7.7 Hz, 1H), 7.77 (t, *J* = 7.4 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 2H), 6.76 (d, *J* = 8.0 Hz, 2H), 4.17 (ddd, *J* = 12.8, 7.5, 4.0 Hz, 1H), 3.57 (ddd, *J* = 16.2, 13.6, 2.1 Hz, 1H), 3.05 (dd, *J* = 17.0, 7.6 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-d) δ 185.4 (t, $^2J_{C\text{-}F}$ = 23.5 Hz), 172.4, 146.3 (d, $^3J_{C\text{-}F}$ = 7.9 Hz), 138.5, 134.7, 133.4 (dd, $^4J_{C\text{-}F}$ = 4.5, 2.7 Hz), 132.3, 131.0 (q, $^1J_{C\text{-}F}$ = 32.5 Hz), 128.8 (d, $^4J_{C\text{-}F}$ = 3.2 Hz), 125.6 (q, $^3J_{C\text{-}F}$ = 3.7 Hz), 123.7 (q, $^1J_{C\text{-}F}$ = 272.5 Hz), 124.9, 124.8, 115 .5 (dd, $^1J_{C\text{-}F}$ = 272.8, 262.7 Hz), 86.4 (dd, $^2J_{C\text{-}F}$ = 21.8, 17.2 Hz), 52.0, 31.9 (d, $^4J_{C\text{-}F}$ = 2.6 Hz). ^{19}F NMR (282 MHz, Chloroform-*d*) δ -62.84, -109.2 (d, *J* = 272.8 Hz), -127.7 (d, *J* = 272.8 Hz). HRMS (ESI) calcd for $C_{19}H_{11}F_5KO_3$ $(M+K)^+$: 421.0260, found 421.0630.

(2*S*,3*R*)-2',2'-difluoro-3-(4-nitrophenyl)-3,4-dihydro-5H-spiro[furan-2,1'-indene]-3',5(2'H)-dione (3i).



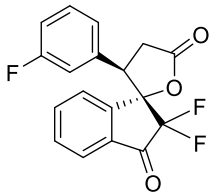
Yellow solid, MP: 175-177 ºC; 39.5 mg, 55% yield, 95:5 er, >20:1 dr. $[\alpha]_D^{23}$ = 15.385 (C = 0.013 in $CHCl_3$). HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 15.27 min (major), 19.06 min (minor). ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.33 (d, *J* = 7.8 Hz, 1H), 8.28-8.20 (m, 1H), 8.05 (d, *J* = 8.4 Hz, 2H), 7.93 (q, *J* = 8.2, 7.6 Hz, 2H), 7.01 (d, *J* = 6.9 Hz, 2H), 4.75 (ddd, *J* = 12.7, 7.7, 3.8 Hz, 1H), 3.88-3.70 (m, 1H), 3.16 (dd, *J* = 17.4, 7.8 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 186.3(dd, $^2J_{C\text{-}F}$ = 25.5, 23.7 Hz), 173.52, 147.46, 146.7(d, $^3J_{C\text{-}F}$ = 7.2 Hz), 140.11, 133.32, 132.40, 130.25, 130.22, 126.49, 125.09, 123.72, 115.8 (dd, $^1J_{C\text{-}F}$ = 272.0, 259.7 Hz), 86.0 (dd, $^2J_{C\text{-}F}$ = 20.9, 15.0 Hz), 49.96, 31.86. ^{19}F NMR (282 MHz, DMSO-d_6) δ -109.6 (d, *J* = 270.3 Hz), -125.9 (d, *J* = 270.2 Hz). HRMS (ESI) calcd for $C_{18}H_{11}F_2KNO_5$ $(M+K)^+$: 398.0237, found 398.0219.

4-**((2*S*,3*R*)-2',2'-difluoro-3',5-dioxo-2',3',4,5-tetrahydro-3H-spiro[furan-2,1'-inden]-3-yl)benzonitrile (3j).** White solid, MP: 150-152 ºC; 40.7 mg, 60% yield, 95:5



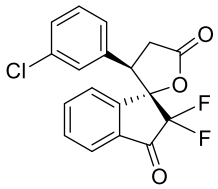
er, 5:1 dr. $[\alpha]_D^{23}$ = 49.083 (C = 0.218 in $CHCl_3$). HPLC DAICEL CHIRALCEL IC, n-hexane/Ethanol = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, retention time: for major diastereomer: 17.41 min (major), 20.78 min (minor); for minor diastereomer: 29.21 min (major), 33.92 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.03 (t, *J* = 7.6 Hz, 1H), 7.94 (d, *J* = 7.8 Hz, 1H), 7.86 (d, *J* = 7.7 Hz, 1H), 7.78 (t, *J* = 7.5 Hz, 1H), 7.45 (d, *J* = 8.2 Hz, 2H), 6.77-6.74 (m, 2H), 4.17 (ddd, *J* = 12.5, 7.6, 3.9 Hz, 1H), 3.54 (ddd, *J* = 16.0, 13.6, 2.1 Hz, 1H), 3.05 (ddd, *J* = 17.0, 7.6, 1.5 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 185.3 (dd, $^2J_{C\text{-}F}$ = 25.3, 23.8 Hz), 172.1, 146.1 (d, $^3J_{C\text{-}F}$ = 7.5 Hz), 138.6, 136.0, 133.3 (dd, $^4J_{C\text{-}F}$ = 4.5, 2.8 Hz), 132.42, 132.37, 129.1 (d, $^4J_{C\text{-}F}$ = 3.3 Hz), 124.9, 124.8, 118.0, 115.4 (dd, $^1J_{C\text{-}F}$ = 272.3, 263.5 Hz), 112.8, 86.30 (dd, $^2J_{C\text{-}F}$ = 21.6, 17.1 Hz), 52.0, 31.8 (d, $^4J_{C\text{-}F}$ = 2.6 Hz). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -109.5 (d, *J* = 274.5 Hz), -127.3 (d, *J* = 270.7 Hz). HRMS (ESI) calcd for $C_{19}H_{12}F_2NO_3$ $(M+H)^+$: 340.0780, found 340.0784.

(2*S*,3*R*)-2',2'-difluoro-3-(3-fluorophenyl)-3,4-dihydro-5H-spiro[furan-2,1'-indene]-

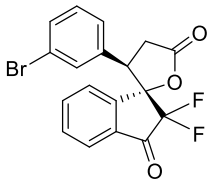


3',5(2'H)-dione (3k). White solid, MP: 117-119 ºC; 49.8 mg, 75% yield, 99:1 er, >20:1 dr. $[\alpha]_D^{23}$ = -15.569 (C = 0.167 in $CHCl_3$). HPLC DAICEL CHIRALCEL IG, n-hexane/Ethanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 20.16 min (major), 23.50 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.01 (t, *J* = 7.5 Hz, 1H), 7.92 (d, *J* = 7.8 Hz, 1H), 7.85 (d, *J* = 7.7 Hz, 1H), 7.75 (t, *J* = 7.5 Hz, 1H), 7.15-7.09 (m, 1H), 6.95-6.90 (m, 1H), 6.46 - 6.26 (m, 2H), 4.10 (ddd, *J* = 12.7, 7.6, 4.1 Hz, 1H), 3.51 (ddd, *J* = 16.4, 13.8, 2.2 Hz, 1H), 3.09 - 2.94 (m, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 185.4 (dd, $^2J_{C\text{-}F}$ =25.3, 23.4 Hz), 172.7, 162.51(d, $^1J_{C\text{-}F}$ =248.5 Hz), 146.4(d, $^3J_{C\text{-}F}$ = 7.9 Hz), 138.3, 133.5 (dd, $^4J_{C\text{-}F}$ = 4.5, 2.2 Hz), 132.8(dd, $^3J_{C\text{-}F}$ = 7.5, 1.9 Hz), 132.1, 130.3(d, $^3J_{C\text{-}F}$ = 8.4 Hz), 124.7, 124.040 (d, $^4J_{C\text{-}F}$ = 6.0 Hz), 124.039, 115.8(d, $^2J_{C\text{-}F}$ = 21.1 Hz), 115.5590(dd, $^1J_{C\text{-}F}$ = 279.2, 259.6 Hz), 115.5589 (d, $^2J_{C\text{-}F}$ = 25.8 Hz), 86.5 (dd, $^2J_{C\text{-}F}$ = 21.6, 16.9 Hz), 52.0, 31.9 (d, $^4J_{C\text{-}F}$ =2.8 Hz). ^{19}F NMR (376 MHz,

Chloroform-*d*) δ -109.1 (d, *J* = 270.7Hz), -111.57, -128.5 (d, *J* = 274.5Hz). HRMS (ESI) calcd for $C_{18}H_{12}F_3O_3$ $(M+H)^+$: 333.0734, found 333.0737.

(2*S*,3*R*)-3-(3-chlorophenyl)-2',2'-difluoro-3,4-dihydro-5H-spiro[furan-2,1'-indene]-3',5(2'H)-dione (3l). 

White solid, MP: 155-156 ºC; 53.0 mg, 76% yield, 97:3 er, >20:1 dr. $[\alpha]_D^{23}$ = -7.375 (C = 0.348 in $CHCl_3$). HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 93/7, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 30.16 min (major), 37.24 min (minor). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.04-7.99 (m, 1H), 7.95-7.79 (m, 2H), 7.80-7.70 (m, 1H), 7.20 (d, *J* = 8.3 Hz, 1H), 7.09 (t, *J* = 7.9 Hz, 1H), 6.65 - 6.40 (m, 2H), 4.06 (ddd, *J* = 12.6, 7.6, 4.1 Hz, 1H), 3.51 (ddd, *J* = 16.4, 13.8, 2.2 Hz, 1H), 3.00 (ddd, *J* = 17.0, 7.6, 1.6 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 185.4 (dd, $^2J_{C\text{-}F}$ = 25.6, 23.9 Hz), 172.6, 146.4 (d, $^3J_{C\text{-}F}$ = 7.8 Hz), 138.4, 134.6, 133.5 (dd, $^4J_{C\text{-}F}$ = 4.4, 2.4 Hz), 132.4 (d, $^4J_{C\text{-}F}$ = 1.9 Hz), 132.1, 129.9, 129.0, 128.7, 128.7, 126.4 (d, $^4J_{C\text{-}F}$ = 3.2 Hz), 124.7, 115.5 (dd, $^1J_{C\text{-}F}$ = 273.5, 261.9 Hz), 86.5 (dd, $^2J_{C\text{-}F}$ = 21.4, 16.8 Hz), 52.0, 31.8 (d, $^4J_{C\text{-}F}$ = 2.7Hz). ^{19}F NMR (282 MHz, Chloroform-*d*) δ -109.1 (d, *J* = 271.8 Hz), -128.6 (d, *J* = 271.8 Hz). HRMS (ESI) calcd for $C_{18}H_{12}ClF_2O_3$ $(M+H)^+$: 349.0438, found 349.0442.

(2S,3R)-3-(3-bromophenyl)-2',2'-difluoro-3,4-dihydro-5H-spiro[furan-2,1'-indene]-3',5(2'H)-dione (3m). 

White solid, MP: 172-174 ºC; 49.5 mg, 63% yield, 97:3 er, 3.5:1 dr. $[\alpha]_D^{23}$ = -7.375 (C = 0.348 in $CHCl_3$). HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: for minor diastereomer: 14.90 min (minor), 18.62 min (major); for major diastereomer: 22.99 min (major), 28.82 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.01 (t, *J* = 7.5 Hz, 1H), 7.97-7.82 (m, 2H), 7.76 (t, *J* = 7.5 Hz, 1H), 7.35 (d, *J* = 7.9 Hz, 1H), 7.03 (t, *J* = 7.9 Hz, 1H), 6.68 (s, 1H), 6.56 (d, *J* = 7.6 Hz, 1H), 4.06 (ddd, *J* = 12.6, 7.5, 4.1 Hz, 1H), 3.50 (ddd, *J* = 16.3, 13.7, 2.2 Hz, 1H), 3.00 (ddd, *J* = 17.0, 7.6, 1.7 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 185.3 (dd, $^2J_{C\text{-}F}$ = 28.3, 23.3 Hz), 172.6, 146.3 (d, $^3J_{C\text{-}F}$ = 7.9 Hz), 138.4, 133.5 (dd, $^4J_{C\text{-}F}$ = 4.7, 2.5 Hz), 132.6 (d, $^4J_{C\text{-}F}$ = 1.9 Hz), 132.1, 131.9, 131.6,

131.6, 130.1, 126.8 (d, $^{4}J_{C\text{-}F}$ = 3.3 Hz), 124.7, 122.6, 115.5 (dd, $^{1}J_{C\text{-}F}$ = 273.6, 261.9 Hz), 86.5 (dd, $^{2}J_{C\text{-}F}$ = 21.5, 17.0 Hz), 51.9, 31.7 (d, $^{4}J_{C\text{-}F}$ = 2.8 Hz). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -109.2 (d, *J* = 270.7Hz), -128.6 (d, *J* = 270.7Hz). HRMS (ESI) calcd for $C_{18}H_{12}BrF_2O_3$ $(M+H)^+$: 392.9933, 394.9912, found 392.39930, 394.9903.

(2S,3R)-2',2'-difluoro-3-(3-methoxyphenyl)-3,4-dihydro-5H-spiro[furan-2,1'-indene]-3',5(2'H)-dione (3n). White solid, MP: 130-132 °C; 53.0 mg, 77% yield, 98:2 er, >20:1 dr. $[\alpha]_D^{23}$ = -11.463 (C = 0.410 in $CHCl_3$). HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 15.11 min (major), 17.98 min (minor) ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.99 (t, *J* = 6.9 Hz, 1H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.83 (d, *J* = 7.7 Hz, 1H), 7.73 (t, *J* = 7.3 Hz, 1H), 7.06 (t, *J* = 8.0 Hz, 1H), 6.74 (dd, *J* = 8.2, 2.4 Hz, 1H), 6.20 (d, *J* = 7.6 Hz, 1H), 6.08 (s, 1H), 4.06 (ddd, *J* = 12.8, 7.5, 4.3 Hz, 1H), 3.58 (s, 3H), 3.52 (ddd, *J* = 16.5, 13.9, 2.2 Hz, 1H), 2.98 (ddd, *J* = 17.0, 7.6, 1.6 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 185.5 (dd, $^{2}J_{C\text{-}F}$ = 25.1, 23.3 Hz), 173.1, 159.5, 146.8 (d, $^{3}J_{C\text{-}F}$ = 8.6 Hz), 138.2, 133.6 (dd, $^{4}J_{C\text{-}F}$ = 4.6, 2.3 Hz), 131.9, 131.6 (d, $^{4}J_{C\text{-}F}$ = 1.8 Hz), 129.7, 124.7 (d, $^{4}J_{C\text{-}F}$ = 1.7 Hz), 124.5, 120.5 (d, $^{4}J_{C\text{-}F}$ = 3.2 Hz), 115.7 (dd, $^{1}J_{C\text{-}F}$ = 274.7, 260.3 Hz), 114.5 (d, $^{4}J_{C\text{-}F}$ = 2.9 Hz), 113.9, 86.7 (dd, $^{2}J_{C\text{-}F}$ = 21.3, 16.8 Hz), 55.1, 52.3, 31.9 (d, $^{4}J_{C\text{-}F}$ = 2.8 Hz). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -108.9 (d, *J* = 270.7Hz), -129.1 (d, *J* = 270.7Hz). HRMS (ESI) calcd for $C_{19}H_{15}F_2O_4$ $(M+H)^+$: 345.0933, found 345.0934.

(2S,3R)-2',2'-difluoro-3-(m-tolyl)-3,4-dihydro-5H-spiro[furan-2,1'-indene]-3',5(2'H)-dione (3o). White solid, MP: 128-130 °C; 38.7 mg, 59% yield, 96:4 er, >20:1 dr. $[\alpha]_D^{23}$ = -32.873 (C = 0.145 in $CHCl_3$). HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 85/15, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 14.46 min (major), 17.96 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.98 (t, *J* = 7.5 Hz, 1H), 7.91 (d, *J* = 7.7 Hz, 1H), 7.81 (d, *J* = 7.7 Hz, 1H), 7.72 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 7.8 Hz, 2H), 6.48 (d, *J* = 5.8 Hz, 2H), 4.03 (ddd, *J* = 13.0, 7.5, 4.3 Hz, 1H), 3.54 (ddd, *J* = 16.7, 14.0, 2.4 Hz, 1H), 2.96 (ddd, *J* = 17.0, 7.5, 1.7 Hz, 1H), 2.25 (s, 3H). ^{13}C NMR (101 MHz,

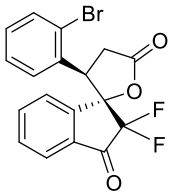
Chloroform-d) δ 185.4 (dd, $^{2}J_{C\text{-}F}$ = 25.2,23.3 Hz), 173.4, 146.8 (d, $^{3}J_{C\text{-}F}$ = 8.0Hz), 138.7, 138.1, 133.5 (dd, $^{4}J_{C\text{-}F}$ = 4.7, 2.1 Hz), 131.8, 129.4, 128.3 (d, $^{4}J_{C\text{-}F}$ = 3.1 Hz), 126.7 (d, $^{4}J_{C\text{-}F}$ = 1.8 Hz), 124.7 (d, $^{4}J_{C\text{-}F}$ = 1.2 Hz), 124.5, 115.8 (dd, $^{1}J_{C\text{-}F}$ = 274.7, 259.8 Hz), 86.8 (dd, $^{2}J_{C\text{-}F}$ = 21.2, 16.7 Hz), 52.5, 31.9 (d, $^{4}J_{C\text{-}F}$ = 2.9 Hz), 21.2. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -108.9 (d, *J* = 270.7Hz), -129.8 (d, *J* = 267.0Hz). HRMS (ESI) calcd for $C_{19}H_{14}F_2NaO_3$ $(M+Na)^+$: 351.0804, found 351.0812.

(2*S*,3*R*)-2',2'-difluoro-3-(2-fluorophenyl)-3,4-dihydro-5H-spiro[furan-2,1'-indene]-3',5(2'H)-dione (3p). White solid, MP: 130-131 °C; 46.5 mg, 70% yield, 98:2 er, >20:1 dr. $[\alpha]_D^{23}$ = -8.491 (C = 0.212 in $CHCl_3$). HPLC DAICEL CHIRALCEL IG, n-hexane/Ethanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 17.61 min (major), 21.05 min (minor). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.89-7.82 (m, 2H), 7.71 (d, J = 7.7 Hz, 1H), 7.61 (t, J = 7.4 Hz, 1H), 7.21-7.12 (m, 2H), 7.04 (t, J = 7.6 Hz, 1H), 6.69 (t, J = 9.5 Hz, 1H), 4.29 (ddd, J = 12.5, 7.8, 3.7 Hz, 1H), 3.57-3.44 (m, 1H), 2.93 (dd, J = 17.2, 7.9 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 185.4 (dd, $^{2}J_{C\text{-}F}$ = 25.1, 23.3 Hz), 172.9, 161.0 (d, $^{1}J_{C\text{-}F}$ = 249.7 Hz), 146.7 (d, $^{3}J_{C\text{-}F}$ = 7.5 Hz), 138.0, 132.6, 131.7, 130.9 (d, $^{3}J_{C\text{-}F}$ = 8.3 Hz), 130.0 (dd, $^{3}J_{C\text{-}F}$ = 7.2, 3.1 Hz), 124.7 (d, $^{2}J_{C\text{-}F}$ = 34.1 Hz), 124.5, 117.6, 117.5, 115.9 (dd, $^{1}J_{C\text{-}F}$ = 272.6, 261.9 Hz), 115.7 (d, $^{2}J_{C\text{-}F}$ = 22.7 Hz), 86.4 (dd, $^{2}J_{C\text{-}F}$ = 21.7, 17.1 Hz), 45.5, 34.2 (t, $^{4}J_{C\text{-}F}$ = 1.6 Hz). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -110.5 (d, *J* = 270.7 Hz), -114.7 (d, *J* = 3.8 Hz), -128.5 (dd, *J*= 270.7, 3.8 Hz). HRMS (ESI) calcd for $C_{18}H_{12}F_3O_3$ $(M+H)^+$: 333.0734, found 333.0737.

(2*S*,3*R*)-3-(2-chlorophenyl)-2',2'-difluoro-3,4-dihydro-5H-spiro[furan-2,1'-indene]-3',5(2'H)-dione (3q). White solid, MP: 152-153 °C; 47.4 mg, 68% yield, 98:2 er, 3.6:1 dr. $[\alpha]_D^{23}$ = -11.779 (C = 0.416 in $CHCl_3$). HPLC DAICEL CHIRALCEL IG, n-hexane/Ethanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: for minor diastereomer: 12.70 min (minor), 15.08 min (major); for major diastereomer: 17.77 min (major), 19.76 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.97-7.85 (m, 2H), 7.76 (d, *J* = 7.7 Hz, 1H), 7.70-7.63 (m, 1H), 7.52 (t, *J* = 7.3 Hz, 1H), 7.30 (t, *J* = 7.4 Hz, 1H), 7.24-7.17

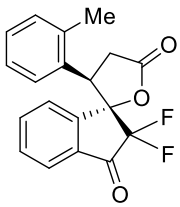
(m, 1H), 7.15-7.12 (m, 1H), 4.63 (ddd, *J* = 12.2, 8.1, 3.6 Hz, 1H), 3.49 (ddd, *J* = 17.3, 12.6, 2.1 Hz, 1H), 3.06 (dd, *J* = 17.3, 8.1 Hz, 1H).^{13}C NMR (101 MHz, Chloroform-*d*) δ 185.2 (dd, $^{2}J_{C\text{-}F}$ = 24.8, 23.1 Hz), 172.8, 146.7 (d, $^{3}J_{C\text{-}F}$ = 7.0 Hz), 137.8, 135.8, 132.5 (dd, $^{4}J_{C\text{-}F}$ = 4.4, 2.3 Hz), 131.8, 130.5 (d, $^{3}J_{C\text{-}F}$ = 7.0 Hz), 130.2, 130.1, 128.1, 127.2, 125.3 (d, $^{4}J_{C\text{-}F}$ = 1.6 Hz), 124.9, 116.2 (dd, $^{1}J_{C\text{-}F}$ = 273.1, 261.6 Hz), 86.7 (dd, $^{2}J_{C\text{-}F}$ = 22.0, 17.1 Hz), 47.2, 33.7 (d, $^{1}J_{C\text{-}F}$ = 2.3 Hz). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -110.2 (d, *J* = 267.0 Hz), -128.1 (d, *J* = 267.0 Hz). HRMS (ESI) calcd for $C_{18}H_{12}ClF_2O_3$ $(M+H)^+$: 349.0438, found 349.0442.

(2*S*,3*R*)-3-(2-bromophenyl)-2',2'-difluoro-3,4-dihydro-5H-spiro[furan-2,1'-indene]-



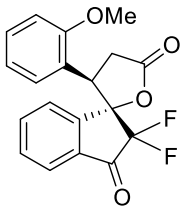
3',5(2'H)-dione (3r). White solid, MP: 162-164 ºC; 47.2 mg, 60% yield, 98:2 er, 5:1 dr. $[\alpha]_D^{23}$ = -11.276 (C = 0.269 in $CHCl_3$). HPLC DAICEL CHIRALCEL IG, n-hexane/Ethanol = 95/5, flow rate = 1.0 mL/min, λ = 254 nm, retention time: for minor diastereomer: 19.44 min (minor), 23.66 min (major); for major diastereomer: 32.43 min (major), 35.38 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.98-7.83 (m, 2H), 7.79 (d, *J* = 7.7 Hz, 1H), 7.73-7.63 (m, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.36 (m, 2H), 7.14 (m, 1H), 4.66 (ddd, *J* = 11.8, 8.3, 3.4 Hz, 1H), 3.44 (ddd, *J* = 17.5, 11.9, 2.1 Hz, 1H), 3.12 (ddd, *J* = 17.4, 8.3, 1.4 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 185.3 (dd, $^{2}J_{C\text{-}F}$ = 24.6, 23.7 Hz), 172.8, 146.7 (d, $^{3}J_{C\text{-}F}$ = 7.3 Hz), 137.8, 133.6, 132.6, 131.9, 130.5, 130.3, 127.9, 126.8, 125.6, 125.0, 116.2 (dd, $^{1}J_{C\text{-}F}$ = 272.4, 262.5 Hz), 86.8 (dd, $^{2}J_{C\text{-}F}$ = 22.4, 17.2 Hz), 49.1, 34.4 (d, $^{4}J_{C\text{-}F}$ = 1.9 Hz). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -111.1 (d, *J* = 267.0 Hz), -127.1 (d, *J* = 267.0 Hz). HRMS (ESI) calcd for $C_{18}H_{12}BrF_2O_3$ $(M+H)^+$: 392.9933, 394.9912, found 392.39930, 394.9903.

(2*S*,3*R*)-2',2'-difluoro-3-(o-tolyl)-3,4-dihydro-5H-spiro[furan-2,1'-indene]-

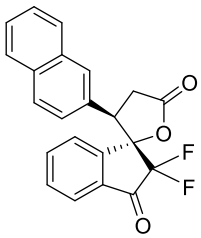


3',5(2'H)-dione (3s). White solid, MP: 192-193 ºC; 42.7 mg, 65% yield, 97.5:2.5 er, 3.6:1 dr. $[\alpha]_D^{23}$ = -17.087 (C = 0.119 in $CHCl_3$). HPLC DAICEL CHIRALCEL IG, n-hexane/Ethanol = 94/6, flow rate = 1.0 mL/min, λ = 254 nm, retention time: for minor diastereomer: 18.09 min (major), 23.32 min (minor); for major diastereomer: 29.70 min (major),

32.20 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.98-7.83 (m, 2H), 7.79 (d, *J* = 7.7 Hz, 1H), 7.73-7.63 (m, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.36 (m, 2H), 7.14 (m, 1H), 4.66 (ddd, *J* = 11.8, 8.3, 3.4 Hz, 1H), 3.44 (ddd, *J* = 17.5, 11.9, 2.1 Hz, 1H), 3.12 (ddd, *J* = 17.4, 8.3, 1.4 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 185.3 (dd, $^{2}J_{C\text{-}F}$ = 24.6, 23.7 Hz), 172.8, 146.7 (d, $^{3}J_{C\text{-}F}$ = 7.3 Hz), 137.8, 133.6, 132.6, 131.9, 130.5, 130.3, 127.9, 126.8, 125.6, 125.0, 116.2 (dd, $^{1}J_{C\text{-}F}$ = 272.4, 262.5 Hz), 86.8 (dd, $^{2}J_{C\text{-}F}$ = 22.4, 17.2 Hz), 49.1, 34.4 (d, $^{4}J_{C\text{-}F}$ = 1.9 Hz). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -111.1 (d, *J* = 267.0 Hz), -127.1 (d, *J* = 267.0 Hz). HRMS (ESI) calcd for $C_{19}H_{14}F_2NaO_3$ $(M+Na)^+$: 351.0804, found 351.0812.

(2*S*,3*R*)-2',2'-difluoro-3-(2-methoxyphenyl)-3,4-dihydro-5H-spiro[furan-2,1'-indene]-3',5(2'H)-dione (3t). 

White solid, MP: 164-165 °C; 47.5 mg, 69% yield, 96:4 er, >20:1 dr. $[\alpha]_D^{23}$ = -75.877 (C = 0.228 in $CHCl_3$). HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 15.21 min (major), 19.94 min (minor). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.92 (d, *J* = 6.4 Hz, 2H), 7.73 (d, *J* = 7.7 Hz, 1H), 7.66-7.60 (m, 1H), 7.39-7.28 (m, 1H), 7.26-7.20 (m, 1H), 6.95 (t, *J* = 7.6 Hz, 1H), 6.55 (d, *J* = 8.2 Hz, 1H), 4.50 (ddd, *J* = 12.7, 8.0, 3.9 Hz, 1H), 3.53 (ddd, *J* = 16.4, 13.7, 2.3 Hz, 1H), 3.01 (s, 3H), 2.90 (ddd, *J* = 17.1, 8.0, 1.7 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-d) δ 185.5 (dd, $^{2}J_{C\text{-}F}$ = 24.2, 23.2 Hz), 173.7, 157.0, 148.3 (d, $^{3}J_{C\text{-}F}$ = 7.5 Hz), 137.1, 132.6 (dd，$^{4}J_{C\text{-}F}$ = 4.0, 2.0Hz), 131.0, 130.3, 129.7 (d, $^{3}J_{C\text{-}F}$ = 8.0 Hz), 125.0 (d, $^{4}J_{C\text{-}F}$ = 1.5 Hz), 124.0, 120.7, 118.2, 116.3 (dd, $^{1}J_{C\text{-}F}$ = 274.1, 260.1 Hz), 110.0, 86.5 (dd, $^{2}J_{C\text{-}F}$ = 21.4, 16.9 Hz), 54.5, 45.4, 32.5 (d, $^{4}J_{C\text{-}F}$ = 2.7 Hz). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -109.9 (d, *J* = 267.0 Hz), -129.1 (d, *J* = 263.2 Hz). HRMS (ESI) calcd for $C_{19}H_{15}F_2O_4$ $(M+H)^+$: 345.0933, found 345.0934.

(2*S*,3*R*)-2',2'-difluoro-3-(naphthalen-2-yl)-3,4-dihydro-5H-spiro[furan-2,1'-indene]-3',5(2'H)-dione (3u). 

White solid, MP: 213-215 °C; 42.3 mg, 58% yield, 97:3 er, >20:1 dr. $[\alpha]_D^{23}$ = 33.452 (C = 0.278 in $CHCl_3$). HPLC DAICEL CHIRALCEL IG, n-hexane/Ethanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 13.22 min (major),

16.01 min (minor). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.09-7.94 (m, 2H), 7.84-7.70 (m, 3H), 7.59 (d, *J* = 8.3 Hz, 2H), 7.48-7.41 (m, 2H), 7.15 (s, 1H), 6.57 (dd, *J* = 8.6, 2.1 Hz, 1H), 4.26 (ddd, *J* = 12.8, 7.5, 4.2 Hz, 1H), 3.70 (ddd, *J* = 16.4, 13.9, 2.3 Hz, 1H), 3.08 (ddd, *J* = 16.9, 7.5, 1.6 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 185.4 (dd, $^{2}J_{C\text{-}F}$ = 25.4, 24.0 Hz), 173.2, 146.8 (d, $^{3}J_{C\text{-}F}$ = 8.0 Hz), 138.2, 133.5 (dd, $^{4}J_{C\text{-}F}$ = 4.6, 2.8 Hz), 132.94, 132.86, 131.9, 128.4, 128.1 (d, $^{4}J_{C\text{-}F}$ = 3.1 Hz), 127.9, 127.7, 127.5 (d, $^{4}J_{C\text{-}F}$ = 1.9 Hz), 126.9, 126.8, 125.3 (d, $^{4}J_{C\text{-}F}$ = 2.8 Hz), 124.8, 124.6, 115.7 (dd, $^{1}J_{C\text{-}F}$ = 274.1, 260.9 Hz), 86.8 (dd, $^{2}J_{C\text{-}F}$ = 21.3, 16.8 Hz), 52.6, 32.0 (d, $^{4}J_{C\text{-}F}$ = 2.9 Hz). ^{19}F NMR (282 MHz, Chloroform-*d*) δ -109.1 (d, *J* = 270.7 Hz), -128.8 (d, *J* = 270.7 Hz). HRMS (ESI) calcd for $C_{22}H_{15}F_2O_3$ $(M+H)^+$: 365.0984, found 365.0991.

(2*S*,3*R*)-2',2'-difluoro-3-(naphthalen-1-yl)-3,4-dihydro-5H-spiro[furan-2,1'-indene]-3',5(2'H)-dione (3v). White solid, MP: 249-251 °C; 39.3 mg, 54% yield, 97:3 er, >20:1 dr. $[\alpha]_D^{23}$ = -25.510 (C = 0.098 in $CHCl_3$). HPLC DAICEL CHIRALCEL IG, n-hexane/Ethanol = 85/15, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 12.35 min (major), 15.09 min (minor). ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.34 (d, *J* = 7.8 Hz, 1H), 8.14 (t, *J* = 7.8 Hz, 1H), 7.84-7.73 (m, 3H), 7.65 (t, *J* = 7.6 Hz, 1H), 7.47 (t, *J* = 7.8 Hz, 1H), 7.33 (d, *J* = 7.8 Hz, 1H), 7.23 (t, *J* = 7.4 Hz, 1H), 6.84 -6.65 (m, 2H), 5.28 (ddd, *J* = 12.6, 7.8, 4.1 Hz, 1H), 3.91 (ddd, *J* = 17.5, 12.9, 2.4 Hz, 1H), 3.15-3.03 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 184.94 (t, $^{2}J_{C\text{-}F}$ = 23.5 Hz), 174.43, 147.0 (d, $^{3}J_{C\text{-}F}$ = 7.6 Hz), 139.14, 133.41, 132.38, 132.06,132.0 (d, $^{4}J_{C\text{-}F}$ = 3.2 Hz), 129.58, 129.02, 128.4 (d, $^{3}J_{C\text{-}F}$ = 8.9 Hz), 126.61, 126.16, 126.00, 125.53, 125.47, 124.61, 121.83, 116.8 (dd, $^{1}J_{C\text{-}F}$ = 277.5, 254.4 Hz), 86.8 (dd, $^{2}J_{C\text{-}F}$ = 20.7, 16.3 Hz), 45.78, 33.08. ^{19}F NMR (282 MHz, DMSO-d_6) δ -108.0 (d, *J* = 345.9 Hz), -130.0 (d, *J* = 349.7 Hz). HRMS (ESI) calcd for $C_{22}H_{15}F_2O_3$ $(M+H)^+$: 365.0984, found 365.0991.

(2*S*,3*S*)-2',2'-difluoro-3-(thiophen-2-yl)-3,4-dihydro-5H-spiro[furan-2,1'-indene]-3',5(2'H)-dione (3w). Yellow solid, MP: 145-146 °C; 42.9 mg, 67% yield, 98:2 er, >20:1 dr. $[\alpha]_D^{23}$ = 33.452 (C = 0.278 in $CHCl_3$). HPLC DAICEL CHIRALCEL IG, n-hexane/Ethanol = 80/20, flow rate = 1.0

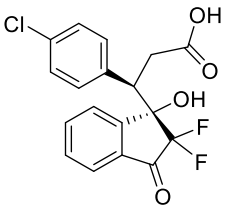
mL/min, λ = 254 nm, retention time: 10.67 min (major), 13.72 min (minor). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.03-7.93 (m, 1H), 7.88 (d, *J* = 8.1 Hz, 2H), 7.74 (t, *J* = 7.3 Hz, 1H), 7.14 (dd, *J* = 5.2, 1.1 Hz, 1H), 6.86 (dd, *J* = 5.2, 3.6 Hz, 1H), 6.54 (s, 1H), 4.33-4.14 (m, 1H), 3.48 (ddd, *J* = 16.5, 13.8, 2.5 Hz, 1H), 3.12 (ddd, *J* = 17.1, 7.7, 1.8 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 185.4 (dd, $^{2}J_{C\text{-}F}$ = 275.2, 258.9 Hz), 172.5, 146.0 (d, $^{3}J_{C\text{-}F}$ = 8.0 Hz), 138.2, 133.8 (dd, $^{4}J_{C\text{-}F}$ = 4.6, 2.1 Hz), 132.7 (d, $^{4}J_{C\text{-}F}$ = 1.8 Hz), 132.0, 127.5 (d, $^{4}J_{C\text{-}F}$ = 3.4 Hz), 127.3, 126.3, 124.7 (d, $^{4}J_{C\text{-}F}$ = 1.7 Hz), 124.6, 115.7 (dd, $^{1}J_{C\text{-}F}$ = 25.2, 23.2 Hz), 86.3 (dd, $^{2}J_{C\text{-}F}$ = 20.9, 17.0 Hz), 48.5, 33.7 (d, $^{4}J_{C\text{-}F}$ = 3.2 Hz). ^{19}F NMR (282 MHz, Chloroform-*d*) δ -108.8 (d, *J* = 270.7 Hz), -130.0 (d, *J* = 270.7 Hz). HRMS (ESI) calcd for $C_{16}H_{11}F_2O_3S$ $(M+H)^+$: 321.0392, found 321.0393.

(2*S*,3*S*)-3-(benzo[b]thiophen-2-yl)-2',2'-difluoro-3,4-dihydro-5H-spiro[furan-2,1'-indene]-3',5(2'H)-dione (3x). Yellow solid, MP: 213-215 ºC; 39.3 mg, 53% yield, 97:3 er, >20:1 dr. $[\alpha]_D^{23}$ = 4.977 (C = 0.221 in $CHCl_3$). HPLC DAICEL CHIRALCEL IG, n-hexane/Ethanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 18.06 min (major), 21.66 min (minor).^{1}H NMR (400 MHz, DMSO-d_6) δ 8.29 (d, *J* = 7.8 Hz, 1H), 8.26-8.15 (m, 1H), 8.03 (d, *J* = 7.7 Hz, 1H), 7.93 (t, *J* = 7.5 Hz, 1H), 7.82-7.71 (m, 2H), 7.39-7.22 (m, 3H), 4.85 (ddd, *J* = 12.4, 7.6, 4.3 Hz, 1H), 3.67 (ddd, *J* = 17.2, 13.1, 2.1 Hz, 1H), 3.29 (dd, *J* = 17.3, 7.7 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 186.01 (t, $^{2}J_{C\text{-}F}$ = 24.6 Hz), 172.76, 146.08 (d, $^{3}J_{C\text{-}F}$ = 7.8 Hz), 139.34, 138.72, 138.64, 135.08, 135.06, 132.89, 132.81, 126.08, 124.72, 124.58, 124.0 (d, $^{4}J_{C\text{-}F}$ = 3.3 Hz), 123.55, 122.27, 115.39 (dd, $^{1}J_{C\text{-}F}$ = 275.2, 258.9 Hz), 84.91 (dd, $^{2}J_{C\text{-}F}$ = 21.0, 16.3 Hz), 47.05, 32.89. ^{19}F NMR (376 MHz, DMSO-d_6) δ -107.8 (d, *J* = 270.7 Hz), -128.0 (d, *J* = 270.7 Hz). HRMS (ESI) calcd for $C_{20}H_{13}F_2O_3S$ $(M+H)^+$: 371.0548, found 371.0551.

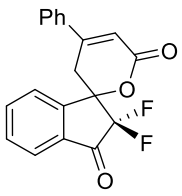
(2S,3R)-4',5',6',7'-tetrachloro-3-(4-chlorophenyl)-2',2'-difluoro-3,4-dihydro-5H-spiro[furan-2,1'-indene]-3',5(2'H)-dione (3y). White solid, MP: 208-209 ºC; 52.5 mg, 54% yield, 92:8 er, >20:1 dr. $[\alpha]_D^{23}$ = +33.452 (C = 0.278 in $CHCl_3$). HPLC DAICEL CHIRALCEL IG, n-hexane/Ethanol = 80/20, flow rate = 1.0 mL/min, λ = 254

nm, retention time: 7.28 min (major), 8.83 min (minor)。^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.23 (d, *J* = 8.2 Hz, 2H), 6.66 (d, *J* = 6.0 Hz, 2H), 4.45 (ddd, *J* = 13.2, 8.0, 4.2 Hz, 1H), 3.51 (ddd, *J* = 16.7, 13.9, 2.5 Hz, 1H), 3.03 (dd, *J* = 17.1, 8.0 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.07 (t, $^{2}J_{C\text{-}F}$ = 26.9 Hz),, 162.96, 134.58, 131.8 (d, $^{3}J_{C\text{-}F}$ = 9.0 Hz), 129.20, 126.12, 121.83, 121.53, 120.93, 120.90, 119.89, 118.52, 105.33 (dd, $^{1}J_{C\text{-}F}$ = 274.5, 255.4 Hz), 76.6(dd, $^{2}J_{C\text{-}F}$ = 22.1, 16.7 Hz), 38.16, 21.4(d, $^{4}J_{C\text{-}F}$ = 2.9 Hz). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -106.9 (d, *J* = 267.0 Hz), -131.2 (d, *J* = 270.7 Hz). HRMS (ESI) calcd for $C_{18}H_8Cl_5F_2O$ $(M+H)^+$: 484.8879, found 484.8911.

(*R*)-3-(4-chlorophenyl)-3-((*S*)-2,2-difluoro-1-hydroxy-3-oxo-2,3-dihydro-1H-inden-1-yl)propanoic acid (6). White solid, MP: 163-165 °C; 66.0 mg, 90% yield, 97:3 er, >20:1 dr. $[\alpha]_D^{23}$ = 537.143 (C = 0.070 in $CHCl_3$). HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 6.69 min (minor), 8.54 min (major). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.23 (s, 1H), 7.95 (m, *J* = 7.4, 1.5 Hz, 1H), 7.66 (m, *J* = 22.0, 14.7, 7.7 Hz, 3H), 7.13 (d, *J* = 8.3 Hz, 2H), 6.81 (d, *J* = 8.0 Hz, 2H), 3.79-3.68 (m, 1H), 3.41 (s, 1H), 3.02 (d, *J* = 16.5 Hz, 1H), 2.78-2.66 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 188.3 (dd, $^{2}J_{C\text{-}F}$ = 25.9, 24.1 Hz), 172.54, 151.8 (d, $^{3}J_{C\text{-}F}$ = 9.8 Hz), 137.76, 135.71, 131.82, 131.49, 131.28, 130.75, 127.61, 126.24, 123.50, 117.4 (dd, $^{1}J_{C\text{-}F}$ = 274.3, 254.2 Hz), 77.9 (dd, $^{2}J_{C\text{-}F}$ = 20.8, 17.7 Hz), 49.75, 33.5 (d, $^{4}J_{C\text{-}F}$ = 5.1 Hz). ^{19}F NMR (376 MHz, DMSO-d_6) δ -108.6 (d, *J* = 270.7 Hz), -129.5 (d, *J* = 267.0Hz). HRMS (ESI) calcd for $C_{18}H_{14}ClF_2O_4$ $(M+H)^+$: 367.0543, found 367.0543.



2,2-difluoro-4'-phenylspiro[indene-1,2'-pyran]-3,6'(2H,3'H)-dione (8). White solid, MP: 185-187 °C; 56.8 mg, 87% yield, 90:10 er. $[\alpha]_D^{23}$ = 83.162 (C = 0.679 in $CHCl_3$). HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 60/40, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 13.23 min (major), 19.35 min (minor)。^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.92 (m, 3H), 7.72 (t, *J* = 7.0 Hz, 1H), 7.56 (m, 2H), 7.52-7.40 (m,



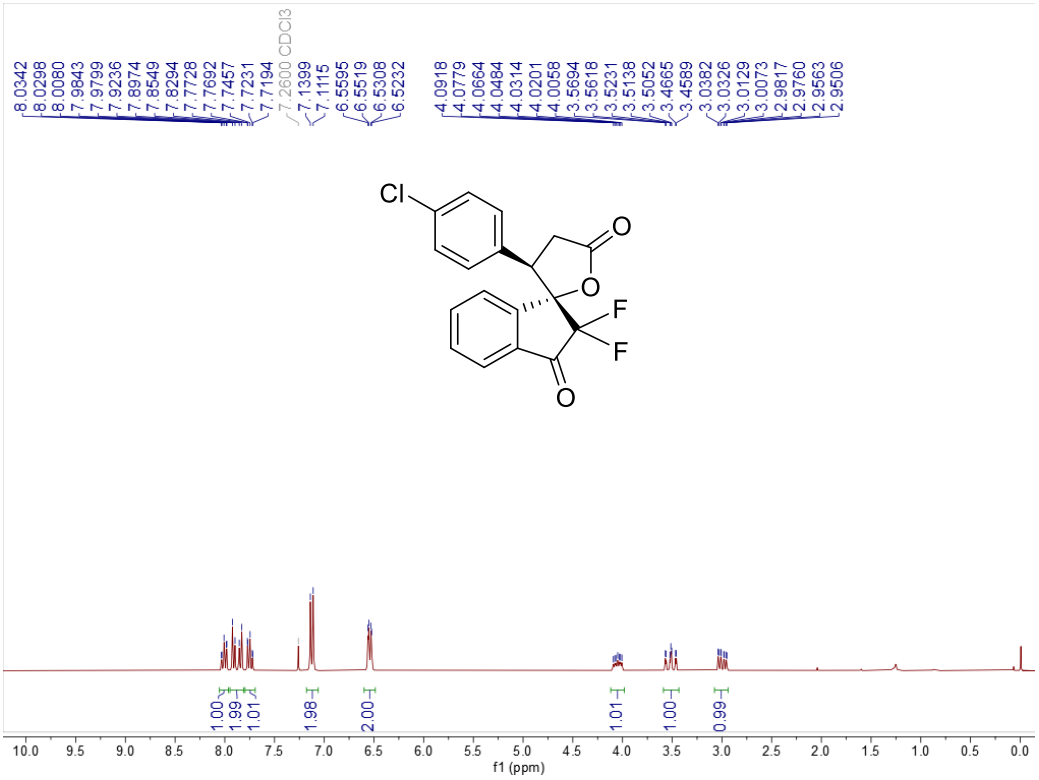
3H), 6.49 (d, *J* = 2.4 Hz, 1H), 3.50 (dq, *J* = 17.9, 3.2 Hz, 1H), 3.27 (dd, *J* = 17.9, 2.7 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 187.9 (t, $^{2}J_{C\text{-}F}$ = 26.4 Hz), 162.53, 152.80, 148.4 (t, $^{4}J_{C\text{-}F}$ = 4.0 Hz), 138.20, 135.32, 132.17, 132.0 (t, $^{4}J_{C\text{-}F}$ = 3.8 Hz), 131.24, 129.20, 126.30, 125.77, 125.21, 114.3 (dd, $^{1}J_{C\text{-}F}$ = 273.2, 265.2 Hz), 111.61, 81.1 (dd, $^{2}J_{C\text{-}F}$ = 23.5, 18.2 Hz), 31.2 (d, $^{3}J_{C\text{-}F}$ = 6.4 Hz). ^{19}F NMR (282 MHz, Chloroform-*d*) δ -115.8 (d, *J* = 279.7 Hz), -117.7 (d, *J* = 280.0 Hz). HRMS (ESI) calcd for $C_{19}H_{13}F_2O_3$ $(M+H)^+$: 327.0827, found 327.0827.

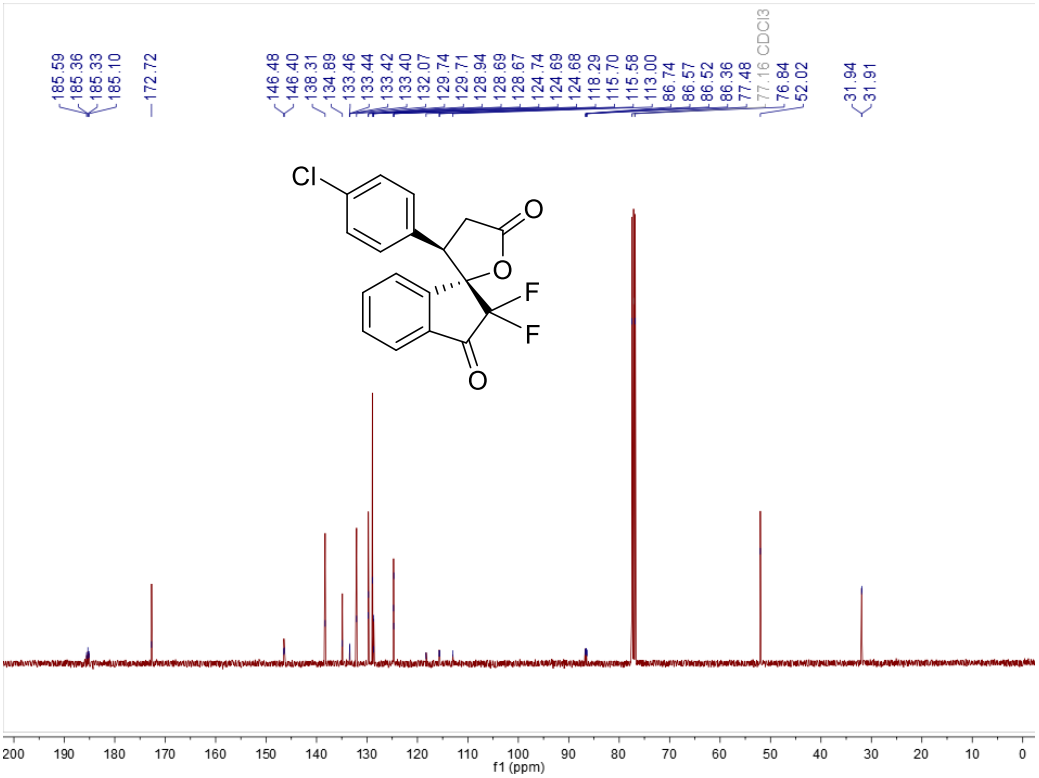
References:

1. Zhang, J.; Liang, Z.; Zhang, S.; Du, D. *Org. Chem. Front.* **2022**, *9*, 3763-3768.
2. Matarlo, J.; Evans, C.; Sharma I; Tonge, P. *Biochem.* **2015**, *54*, 6514-6524.

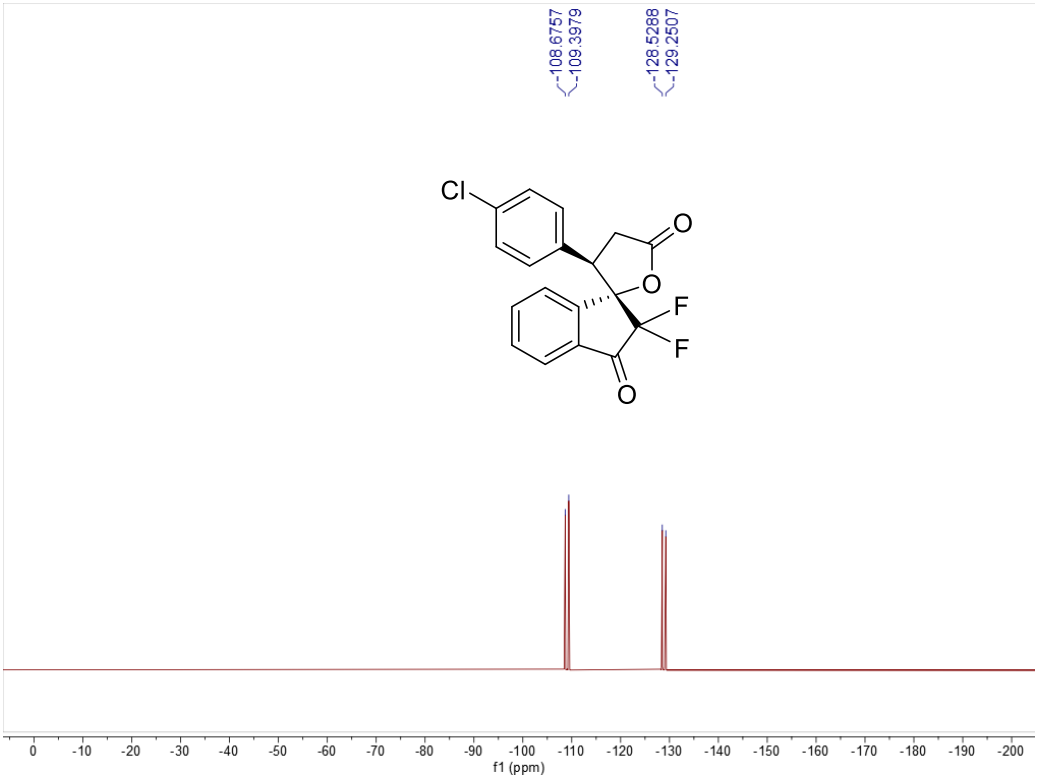
8. Copies of the NMR Spectra

3a ^{1}H NMR (300 MHz, Chloroform-d)/ ^{13}C{1H} NMR (101 MHz, Chloroform-d)

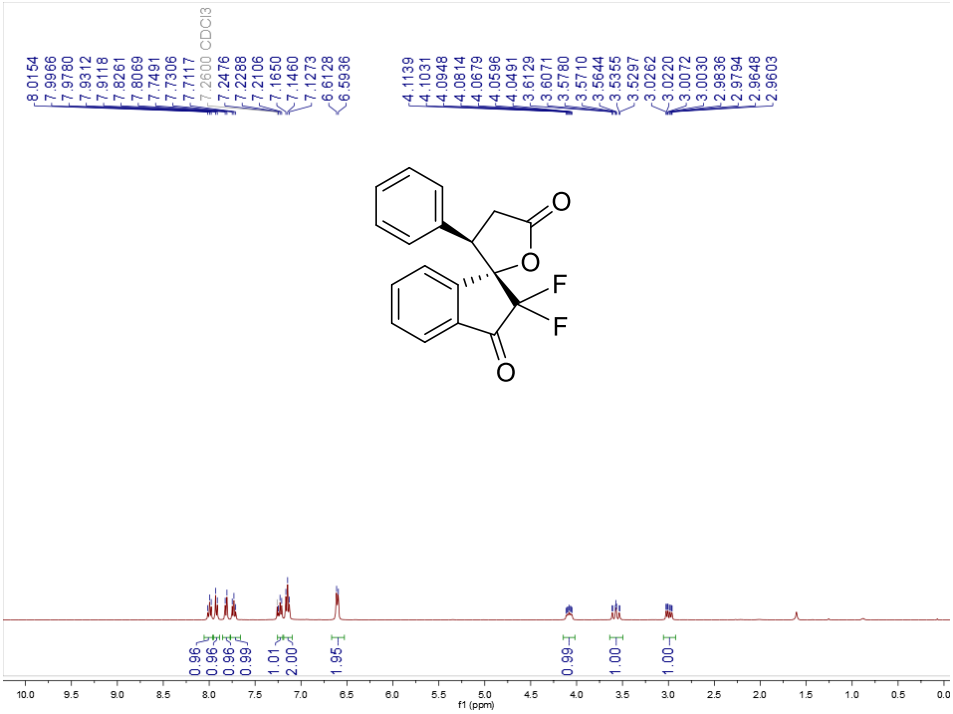


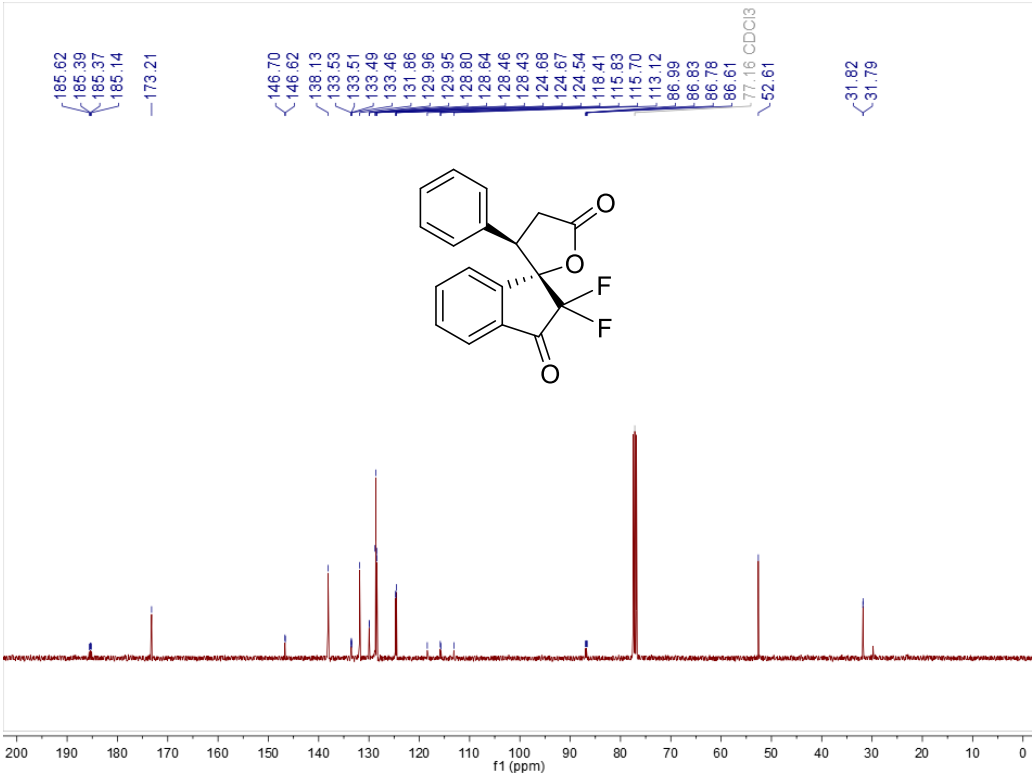


3a ^{19}F NMR (376 MHz, Chloroform-*d*)

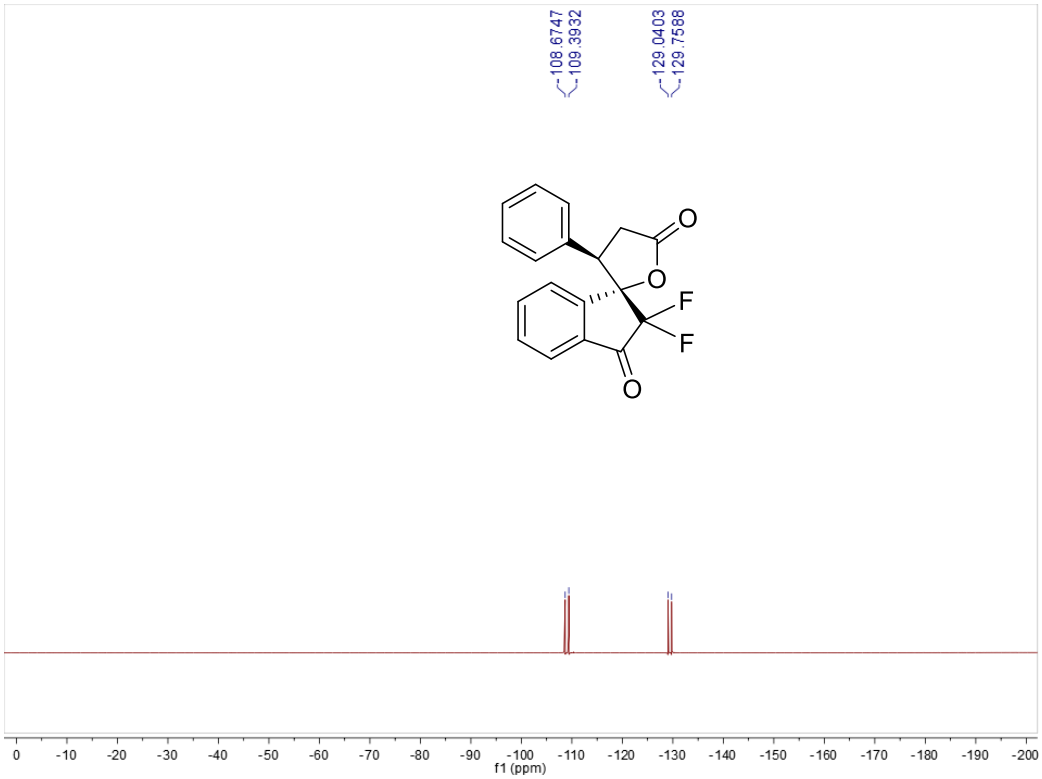


3b ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C{1H} NMR (101 MHz, Chloroform-*d*)

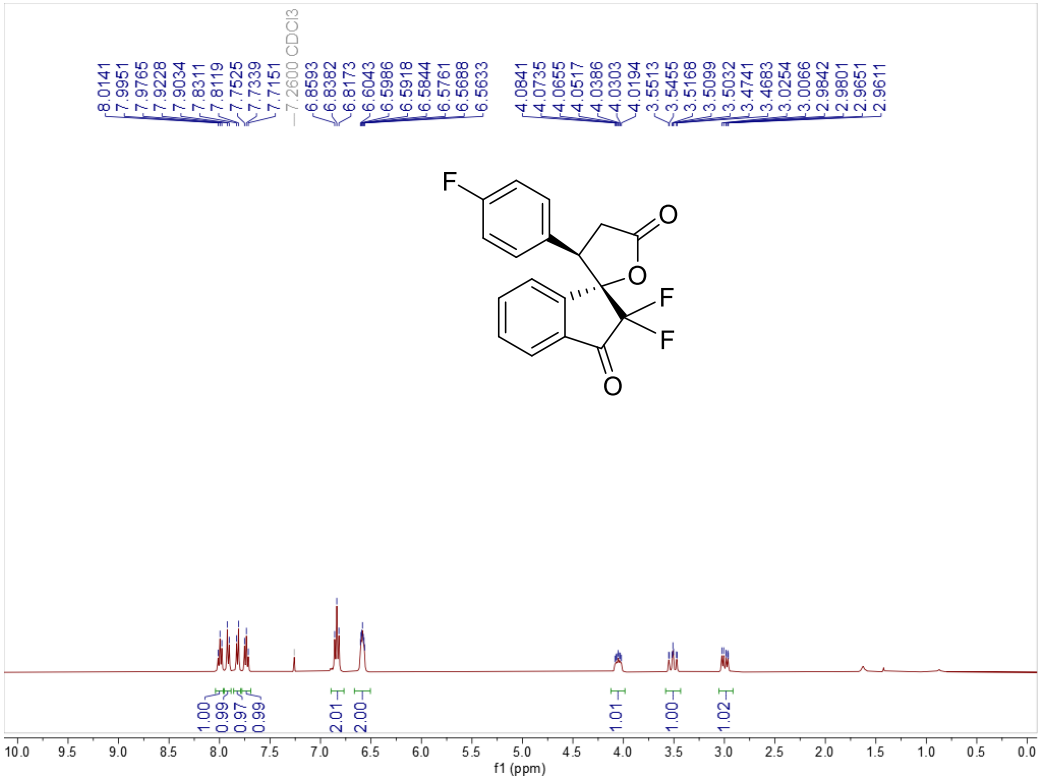


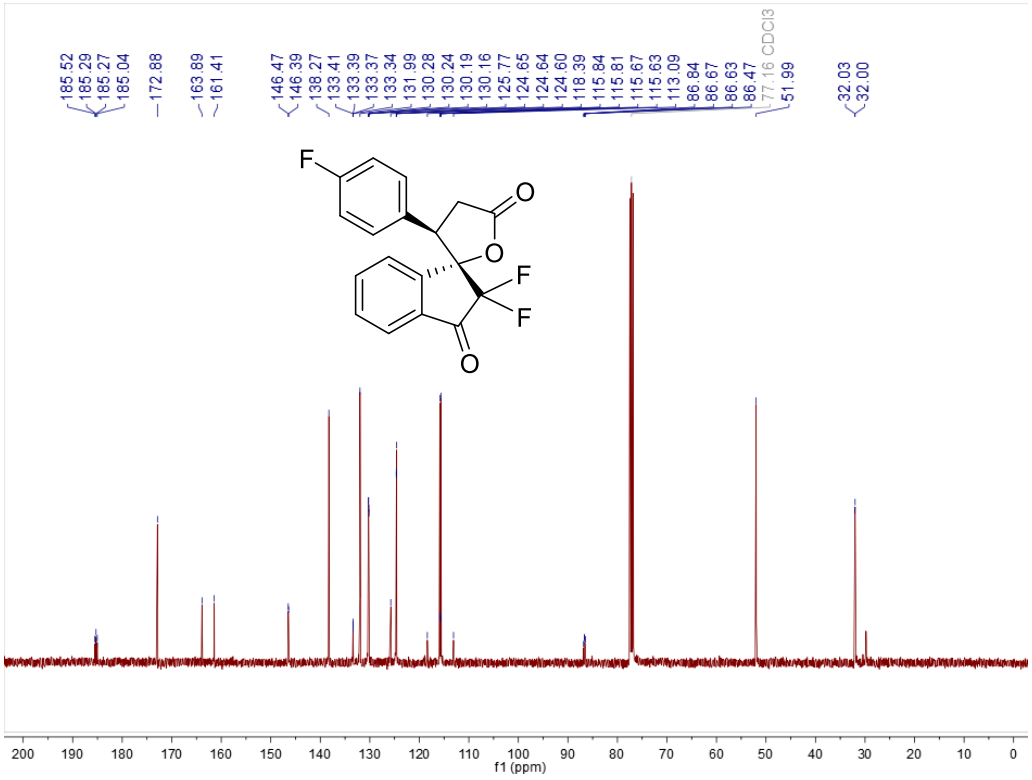


3b ^{19}F NMR (376 MHz, Chloroform-*d*)

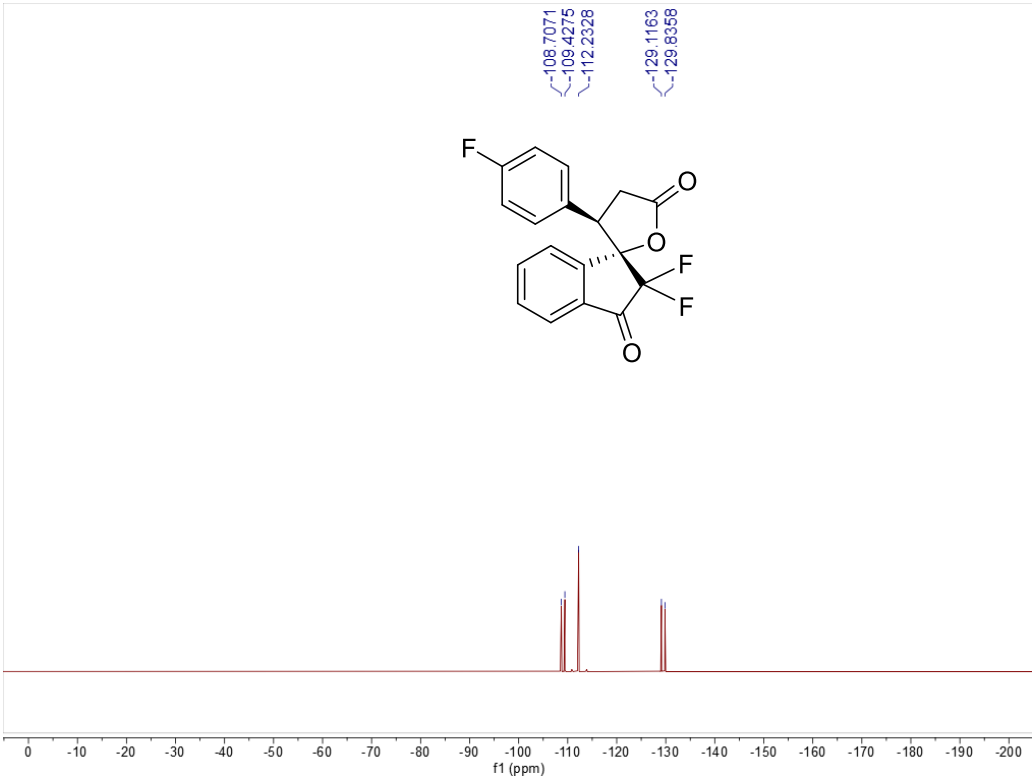


3c ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C{H} NMR (101 MHz, Chloroform-*d*)

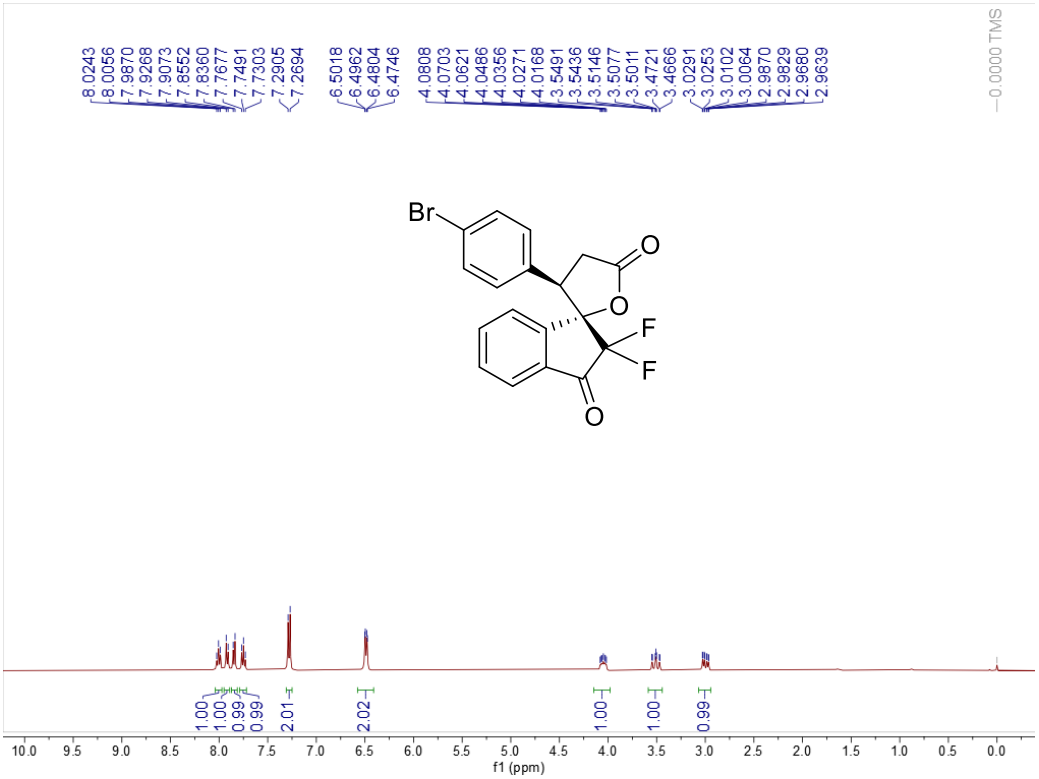


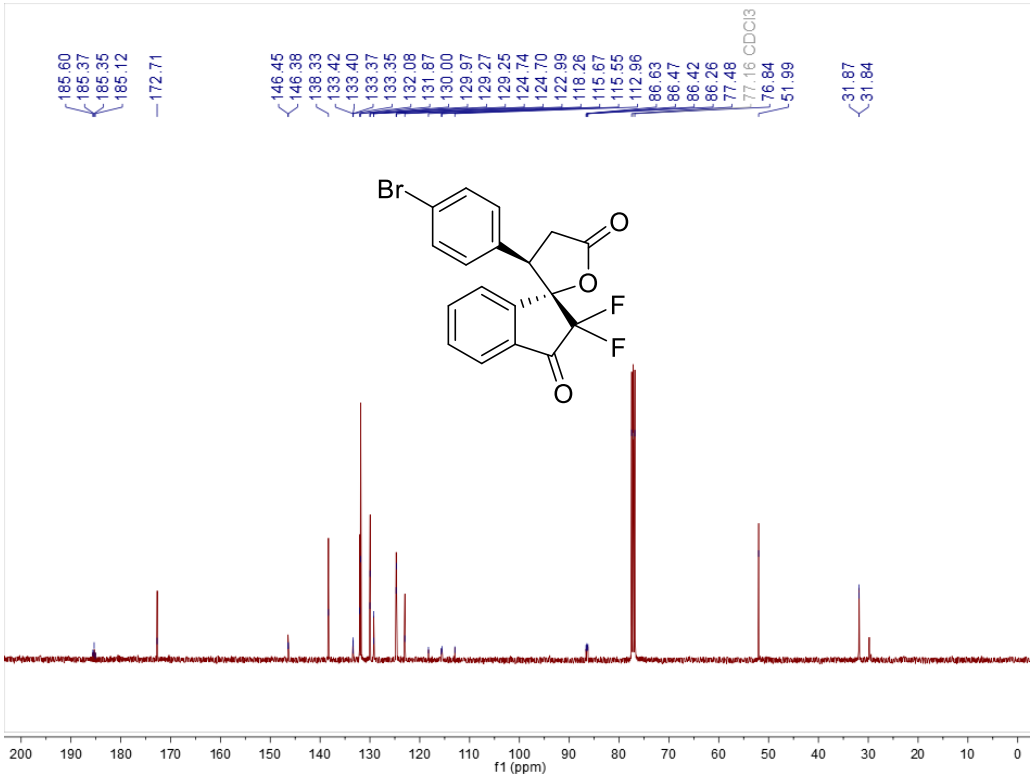


3c ^{19}F NMR (376 MHz, Chloroform-*d*)

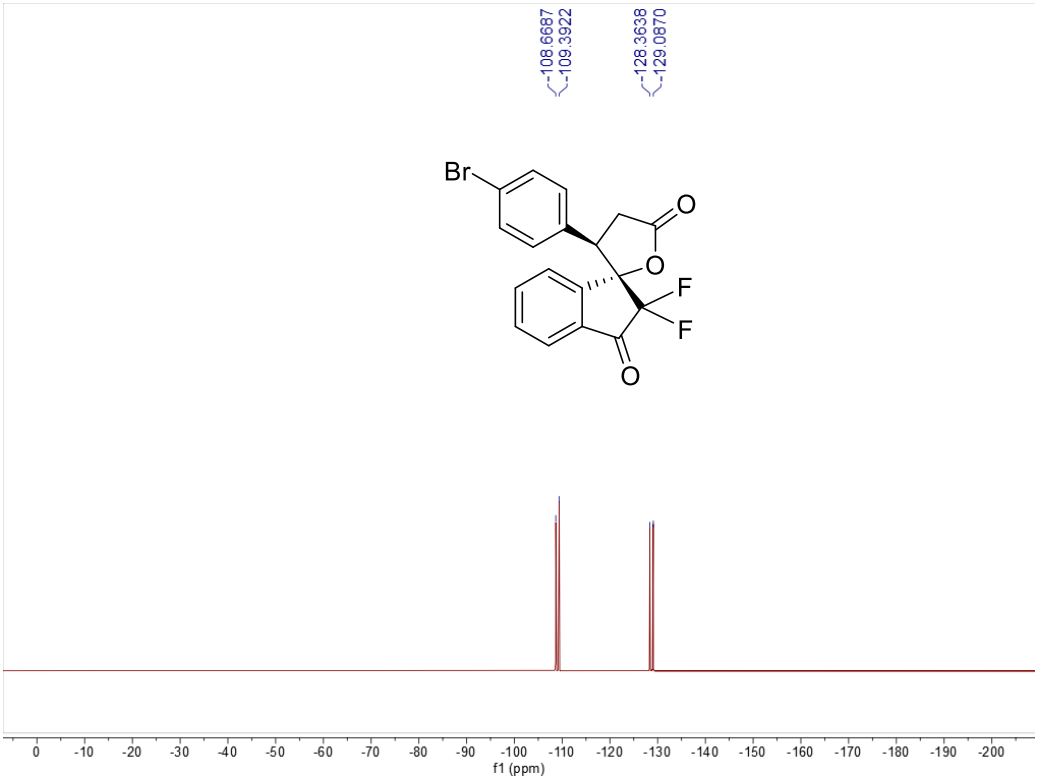


3d ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C{H} NMR (101 MHz, Chloroform-d)

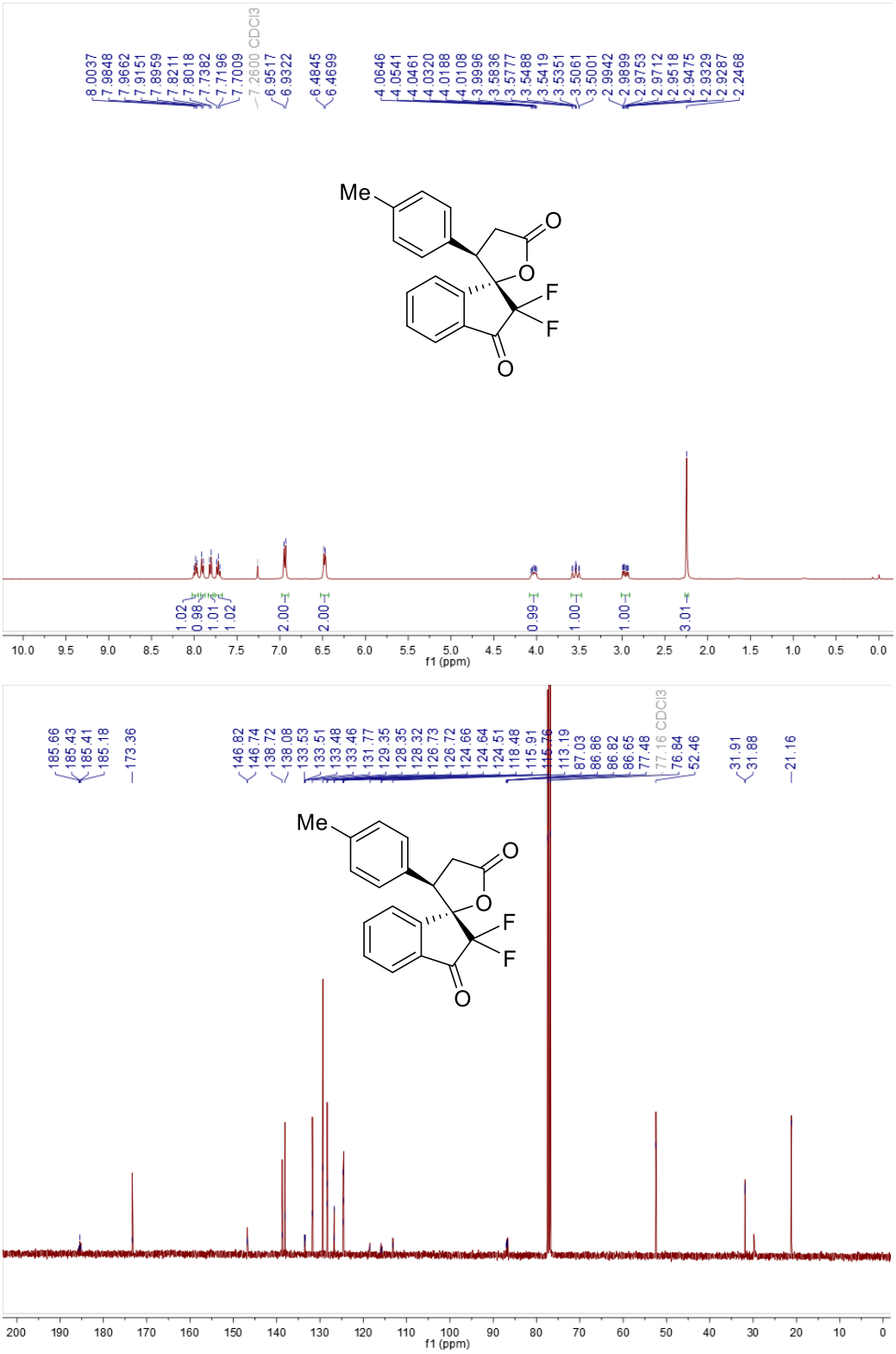




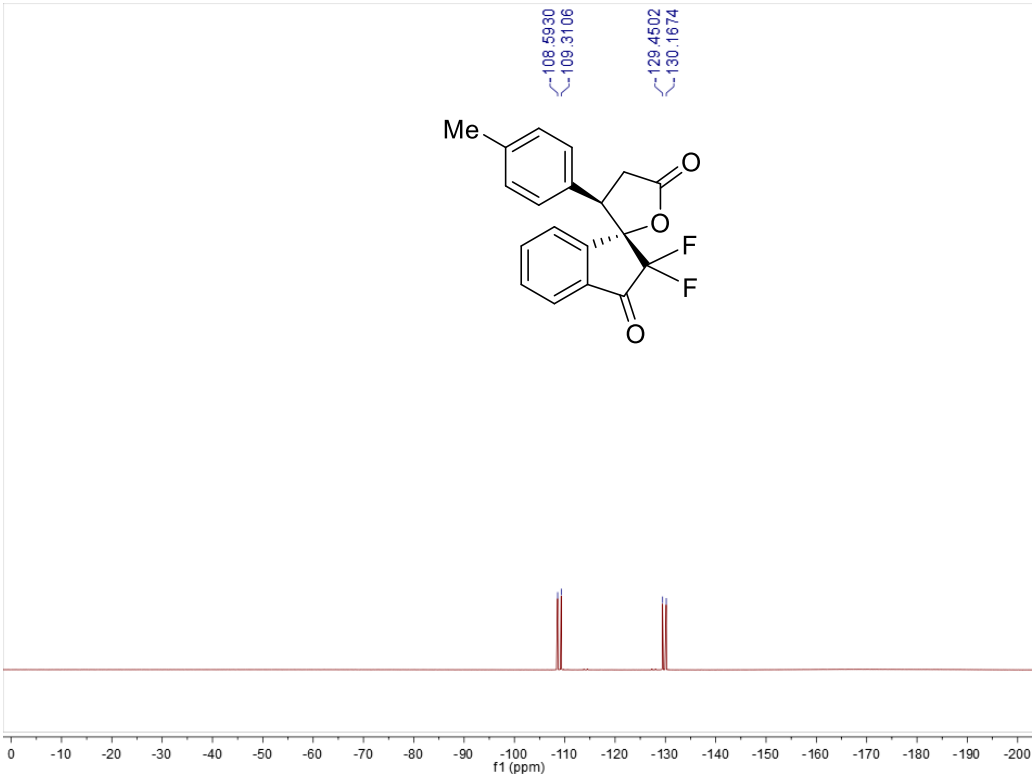
3d ^{19}F NMR (376 MHz, Chloroform-*d*)



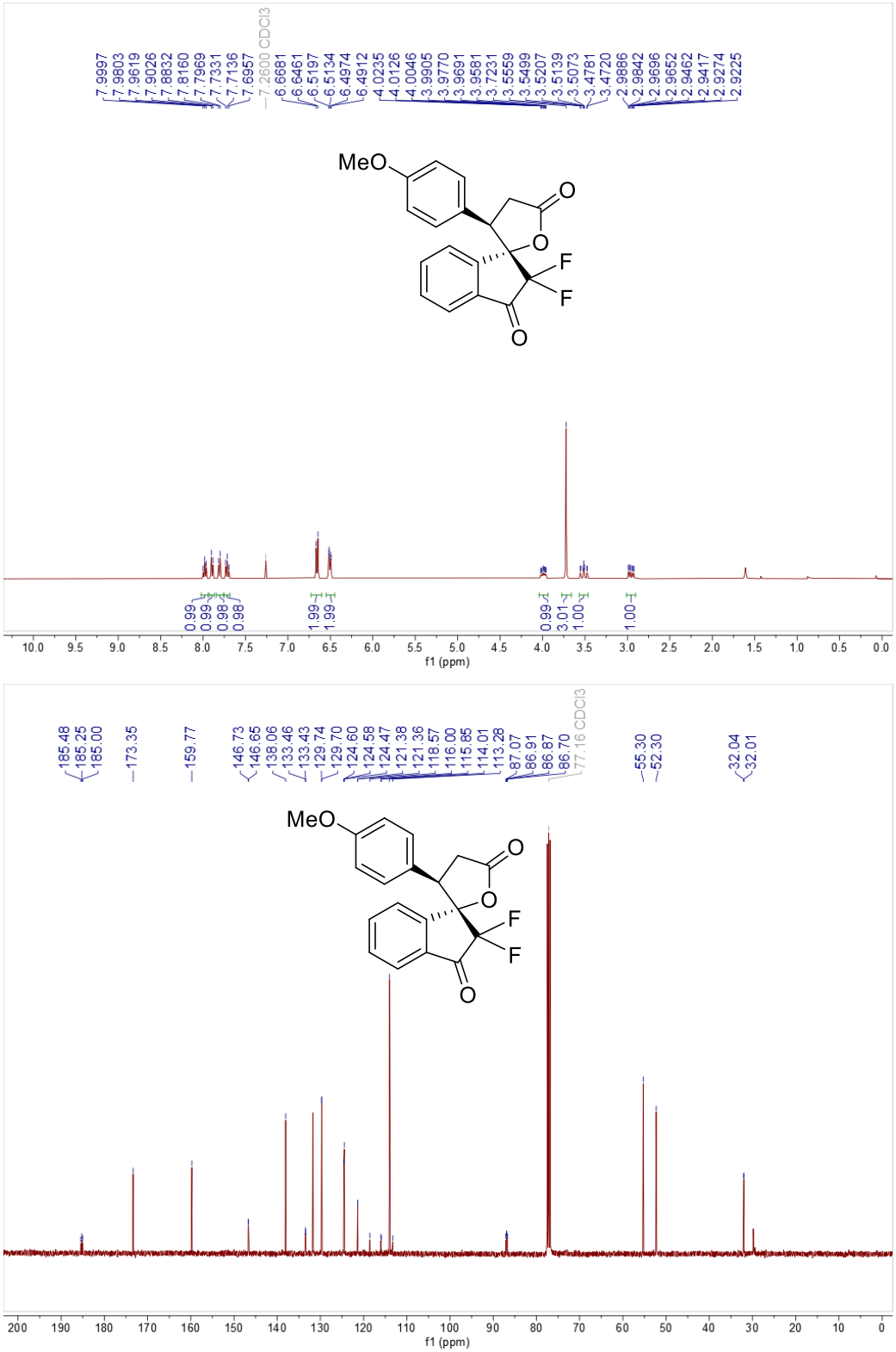
3e ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C{1H} NMR (101 MHz, Chloroform-*d*)



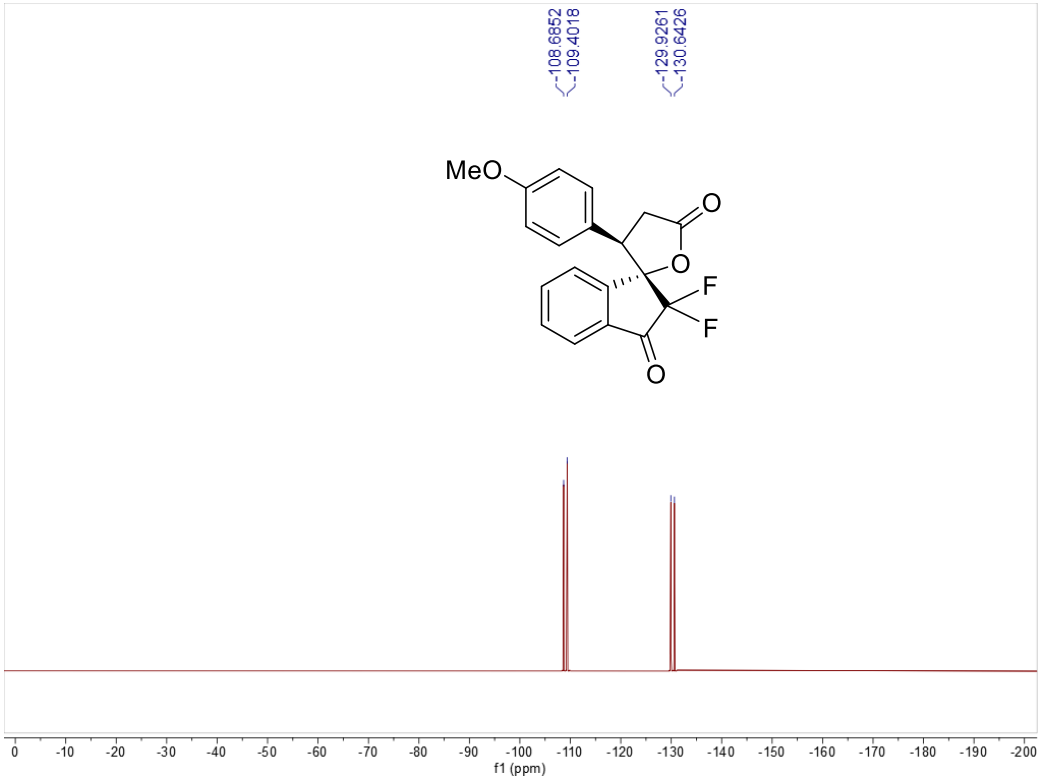
3e ^{19}F NMR (376 MHz, Chloroform-*d*)



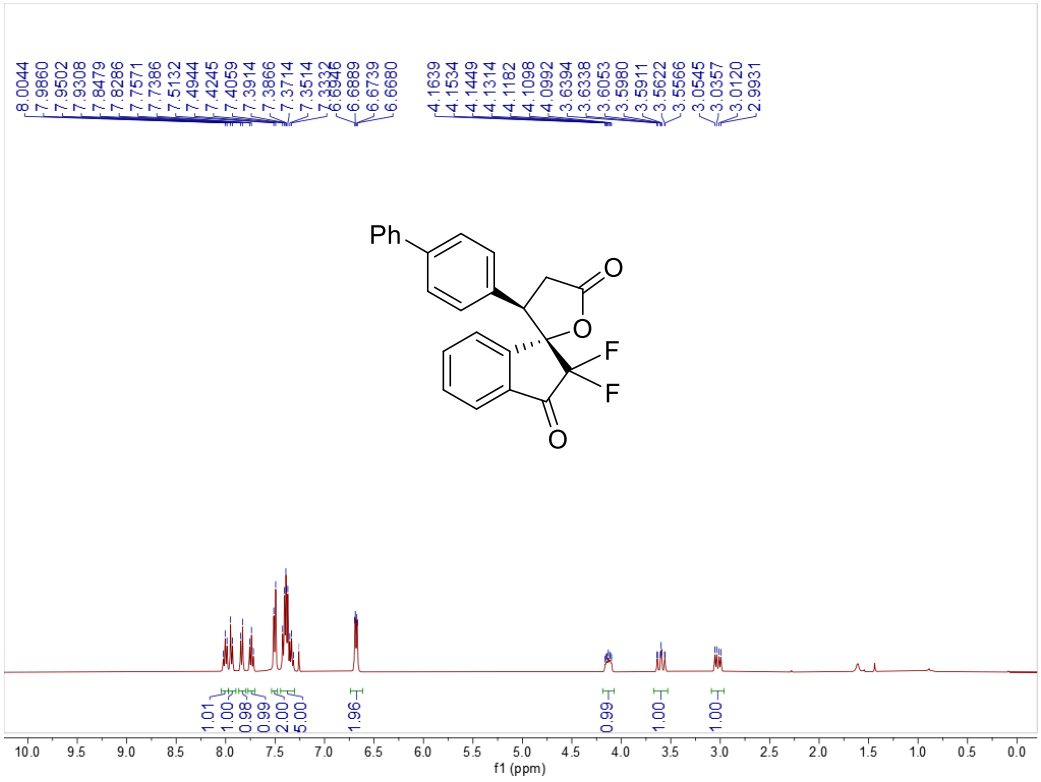
3f ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C{H} NMR (101 MHz, Chloroform-*d*)

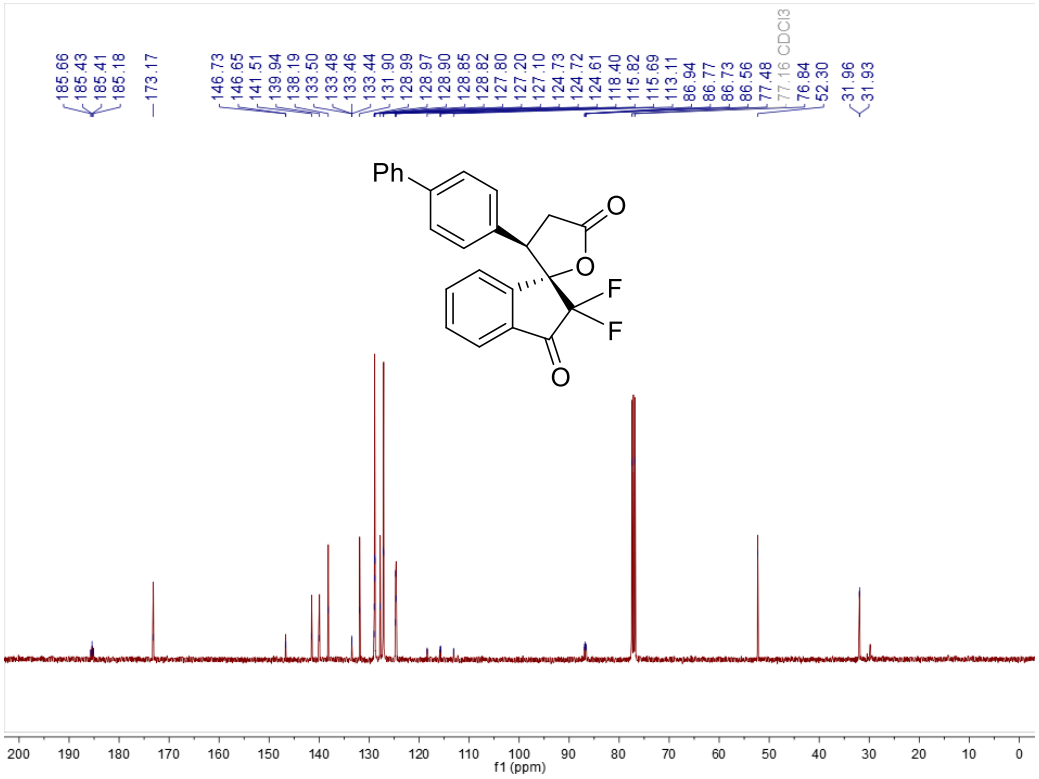


3f ^{19}F NMR (376 MHz, Chloroform-*d*)

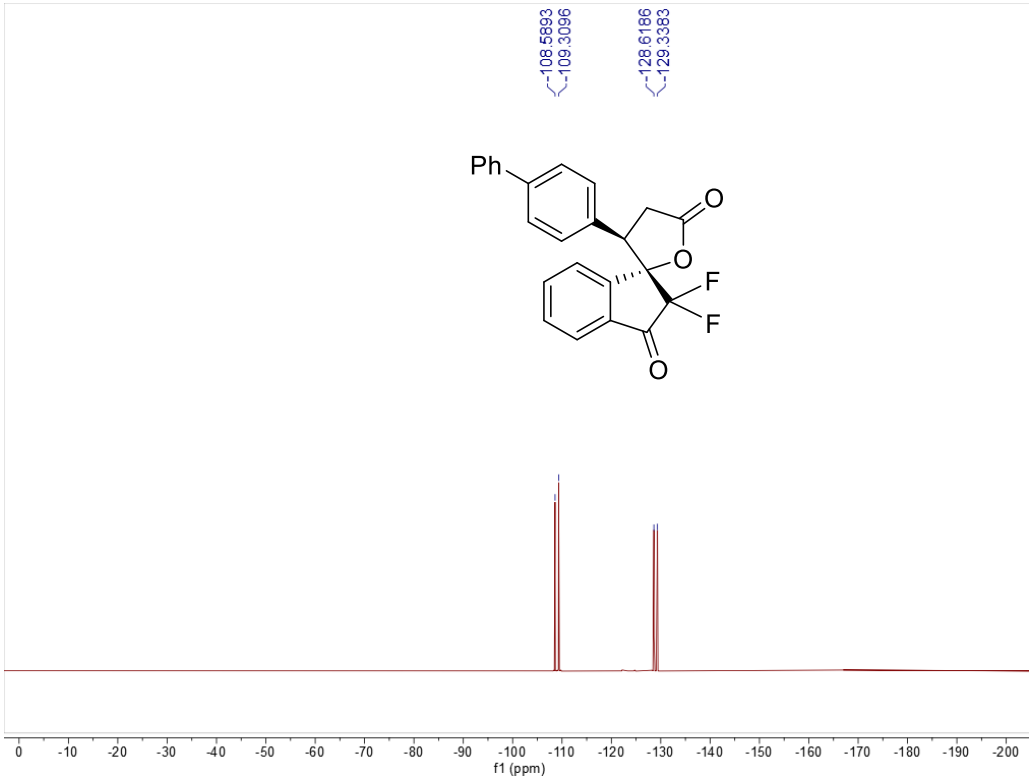


3g ^{1}H NMR (400 MHz, Chloroform-*d*)/ ^{13}C{H} NMR (101 MHz, Chloroform-d)

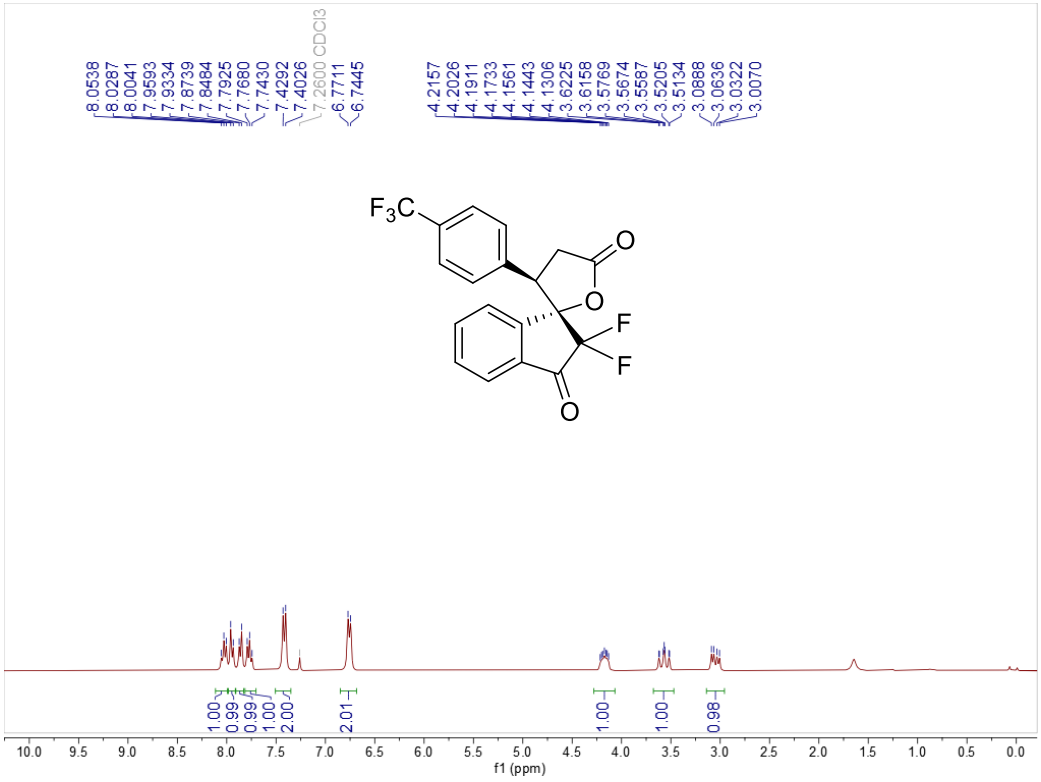


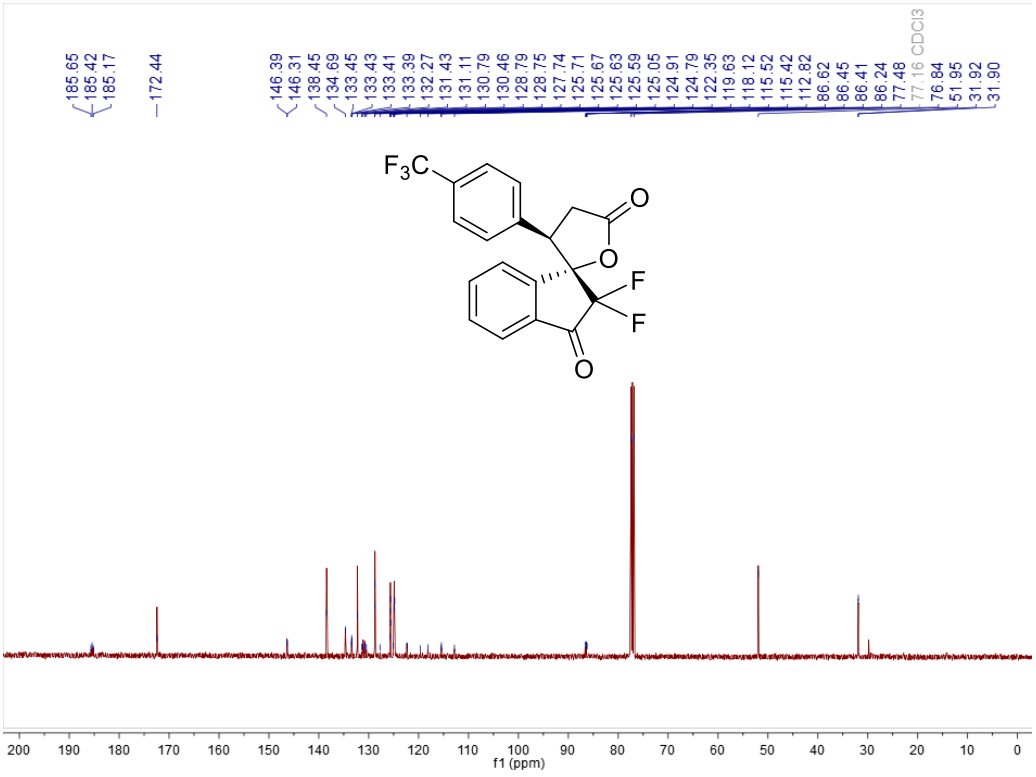


3g ^{19}F NMR (376 MHz, Chloroform-*d*)

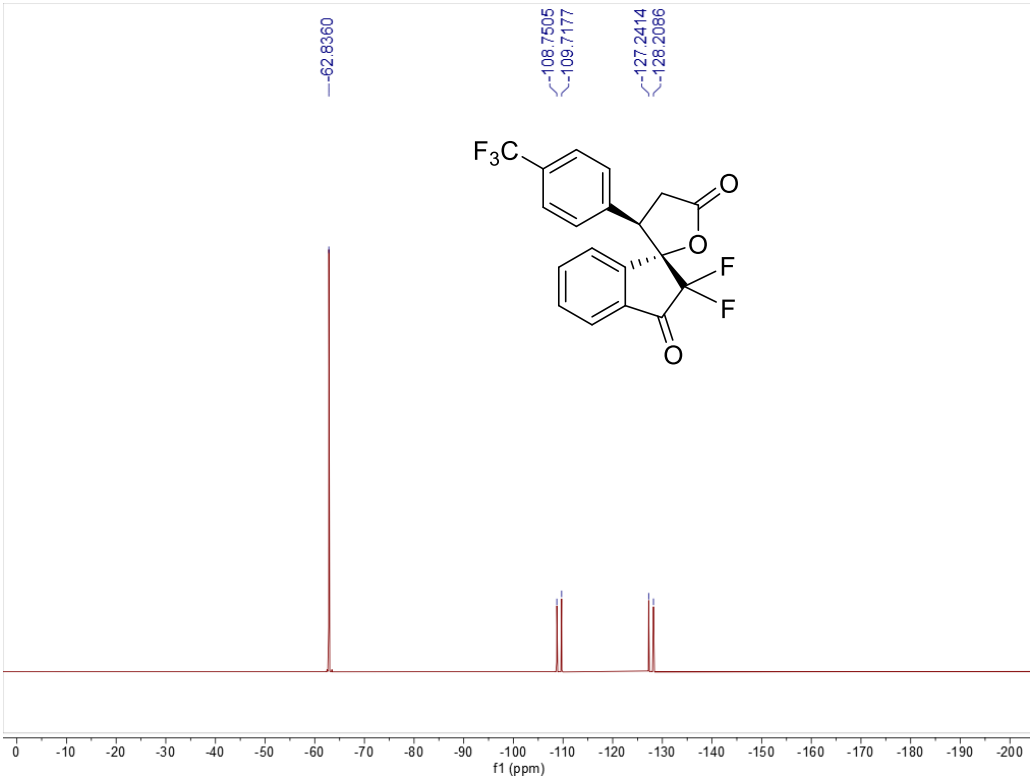


3h ^{1}H NMR (300 MHz, Chloroform-*d*)/ ^{13}C{H} NMR (101 MHz, Chloroform-d)

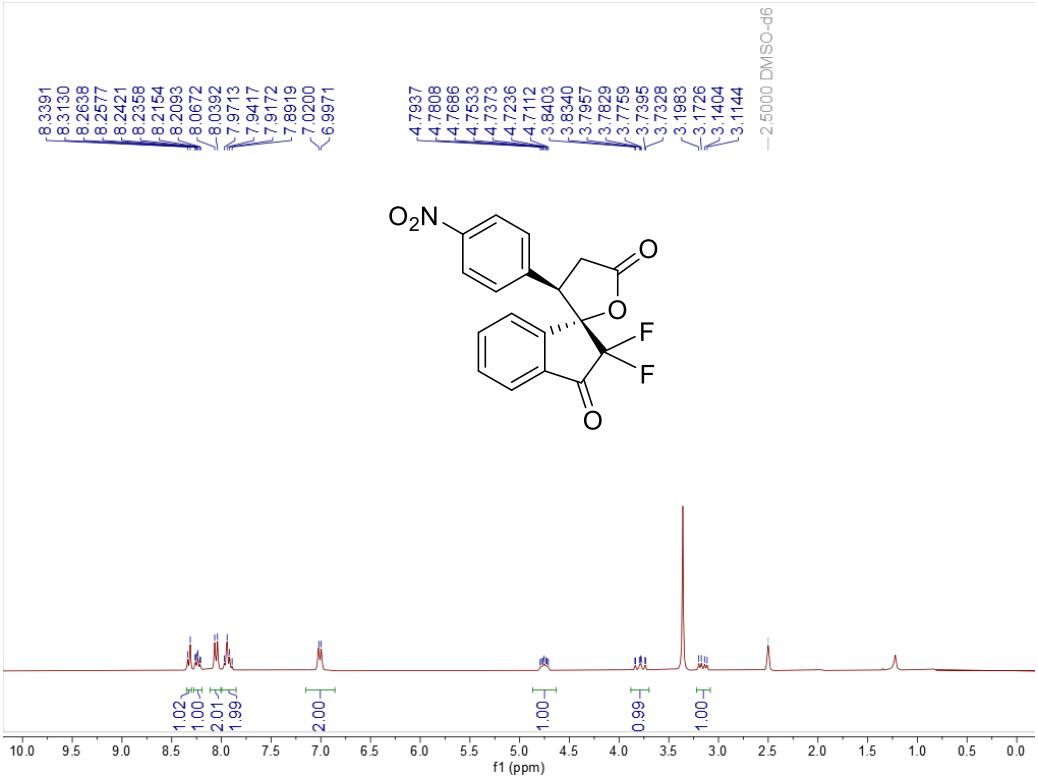


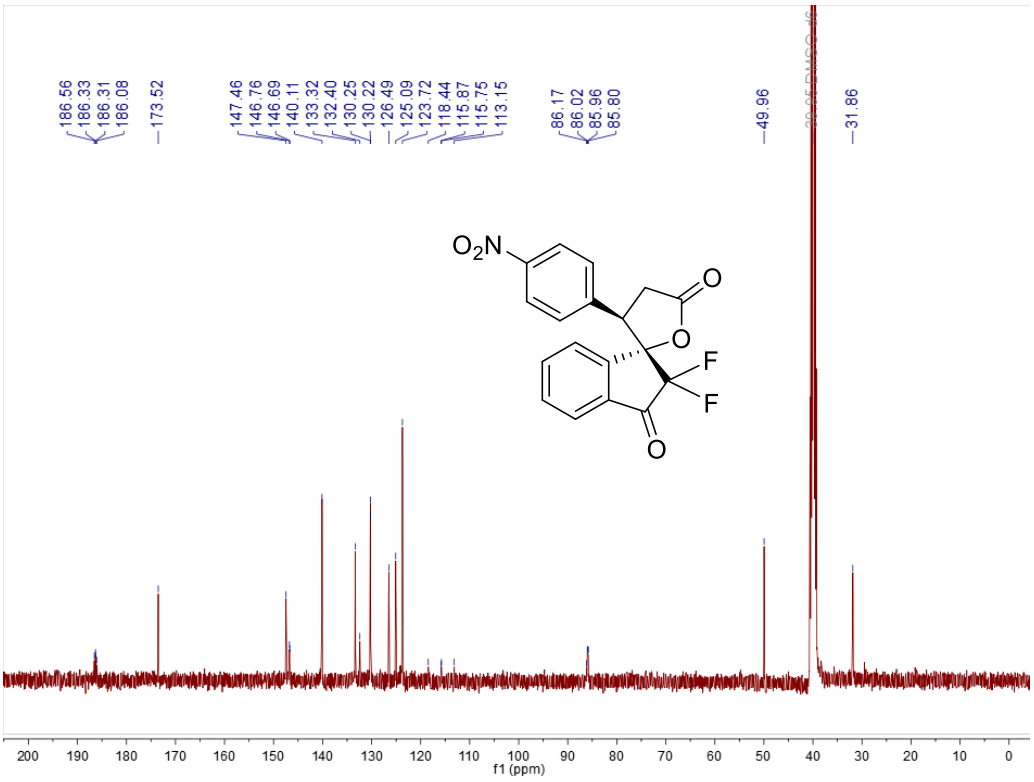


3h ^{19}F NMR (282 MHz, Chloroform-*d*)

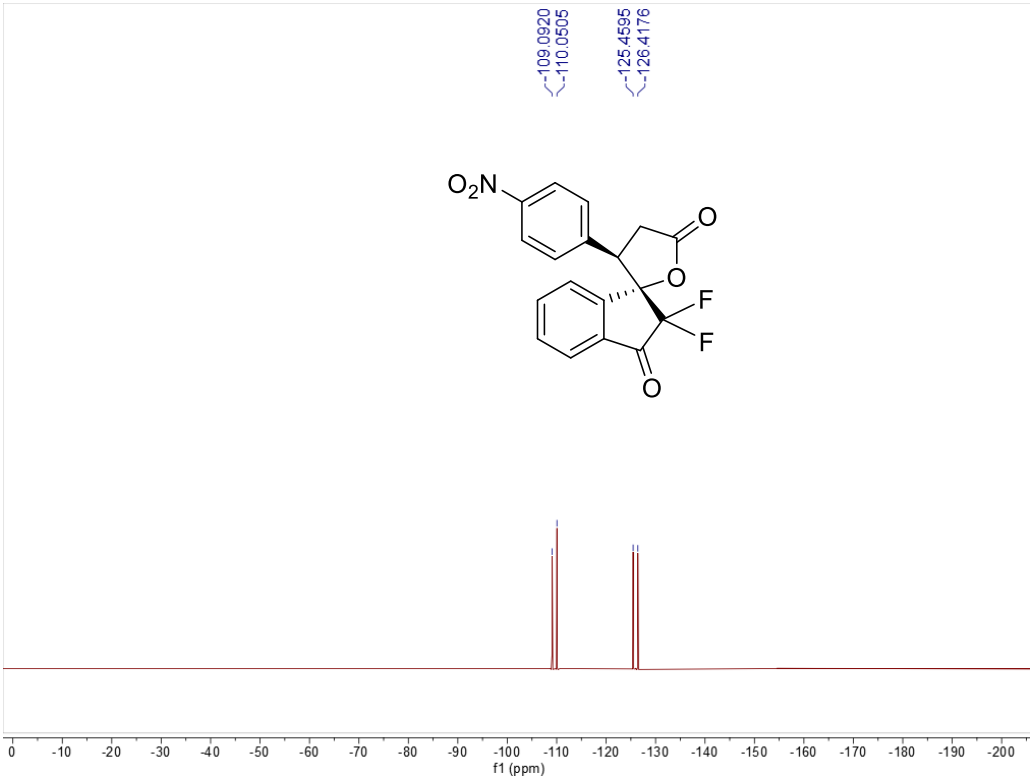


3i ^{1}H NMR (300 MHz, DMSO-d_6)/^{13}C{H} NMR (101 MHz, DMSO-d_6)

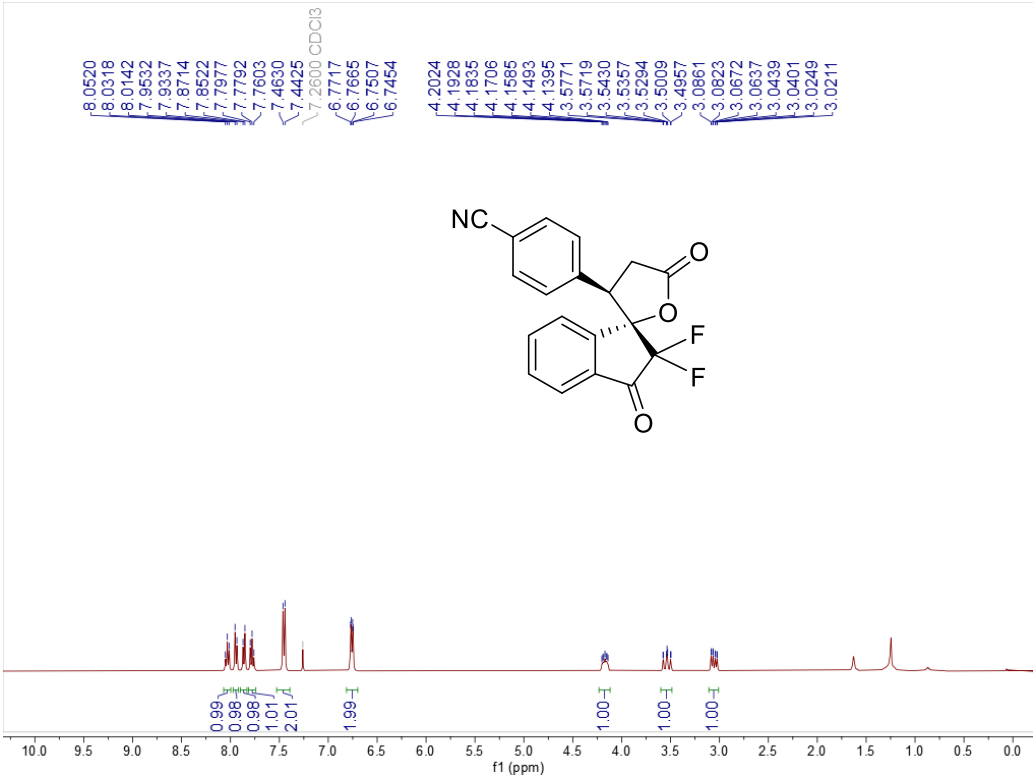


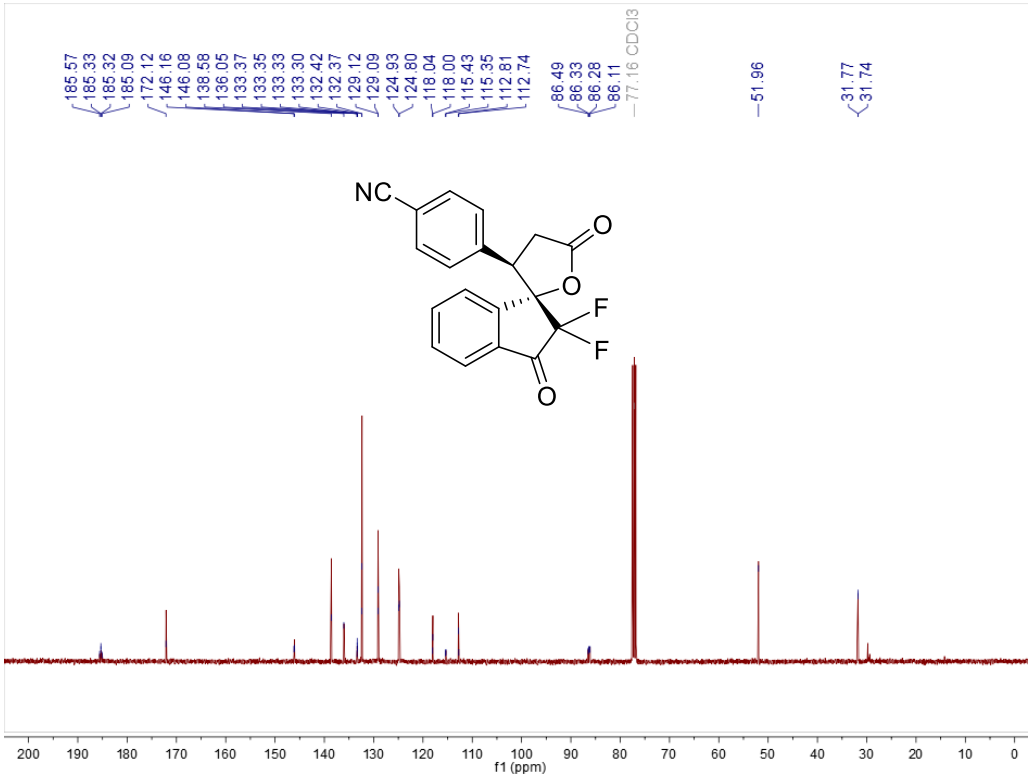


3i ^{19}F NMR (282 MHz, DMSO-d_6)

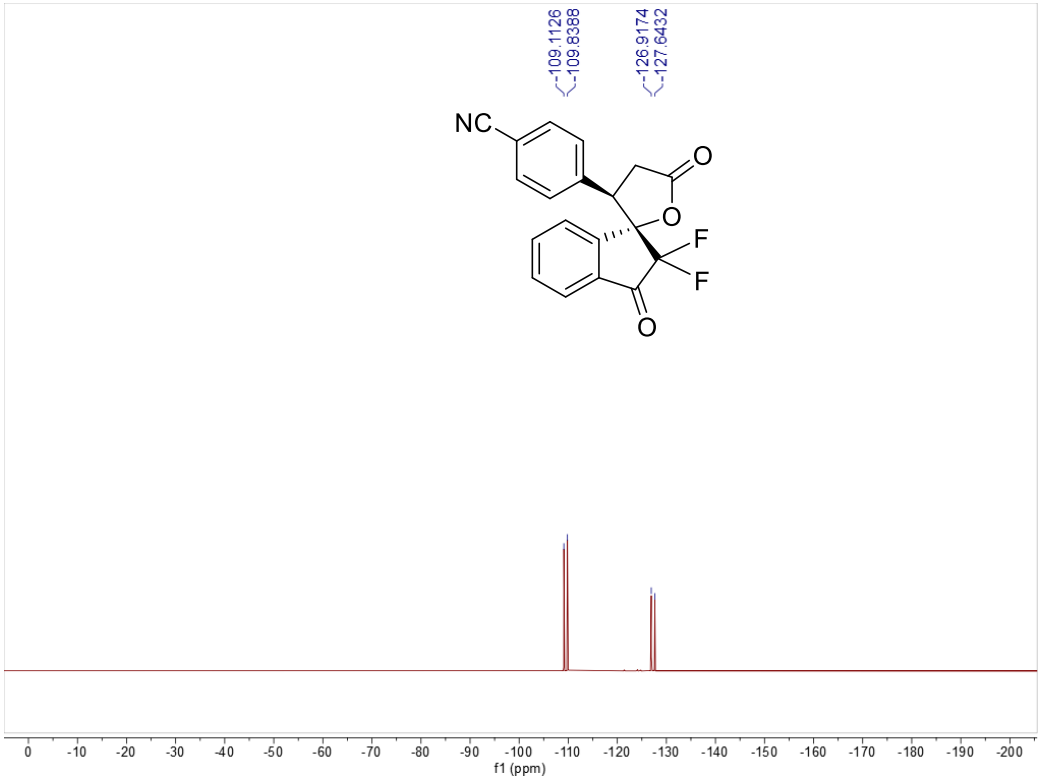


3j ^{1}H NMR (400 MHz, Chloroform-*d*)/^{13}C{H} NMR (101 MHz, Chloroform-*d*)

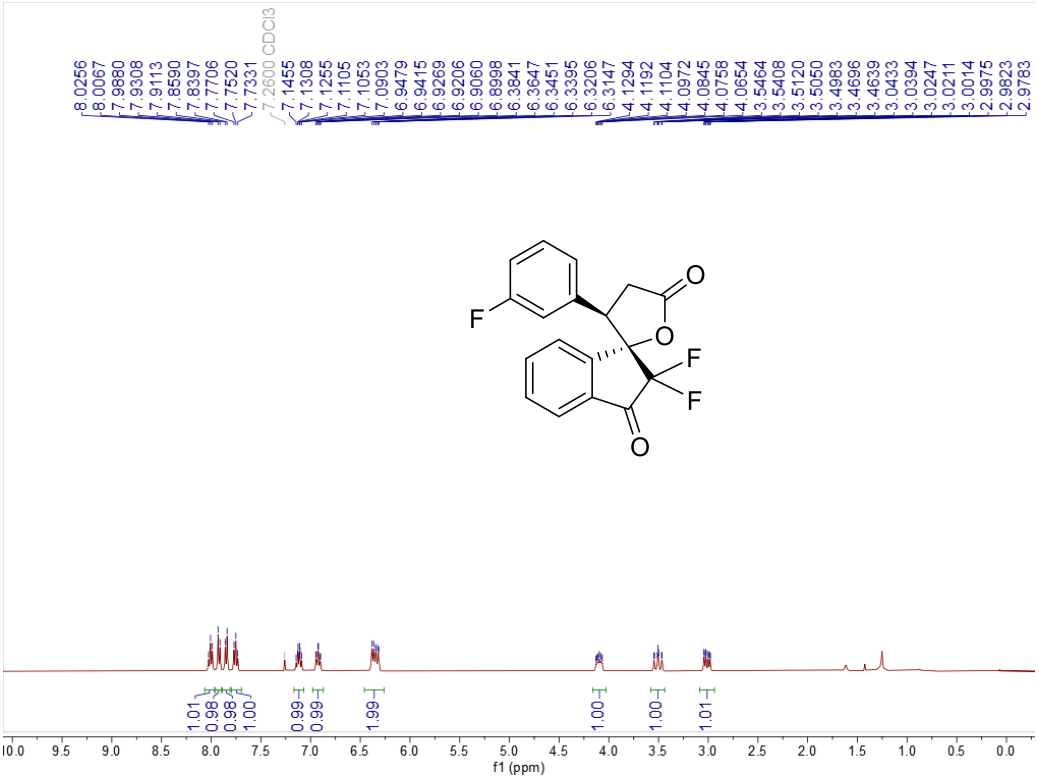


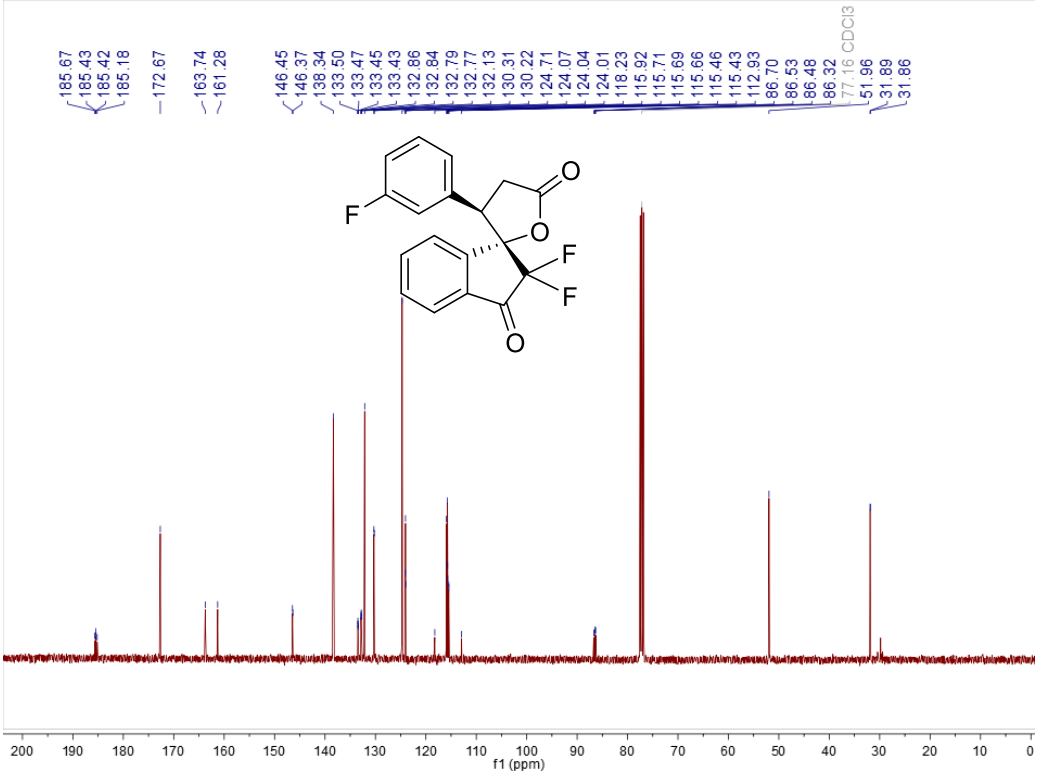


3j ^{19}F NMR (376 MHz, Chloroform-*d*)

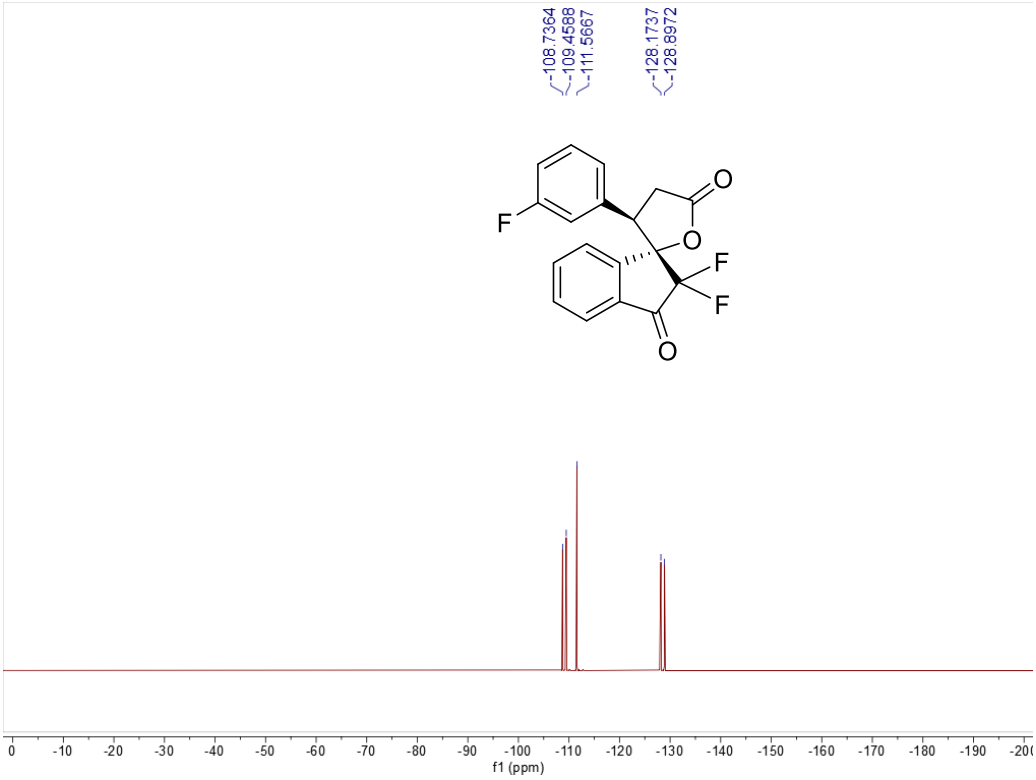


3k ^{1}H NMR (400 MHz, Chloroform-*d*)/^{13}C{H} NMR (101 MHz, Chloroform-*d*)

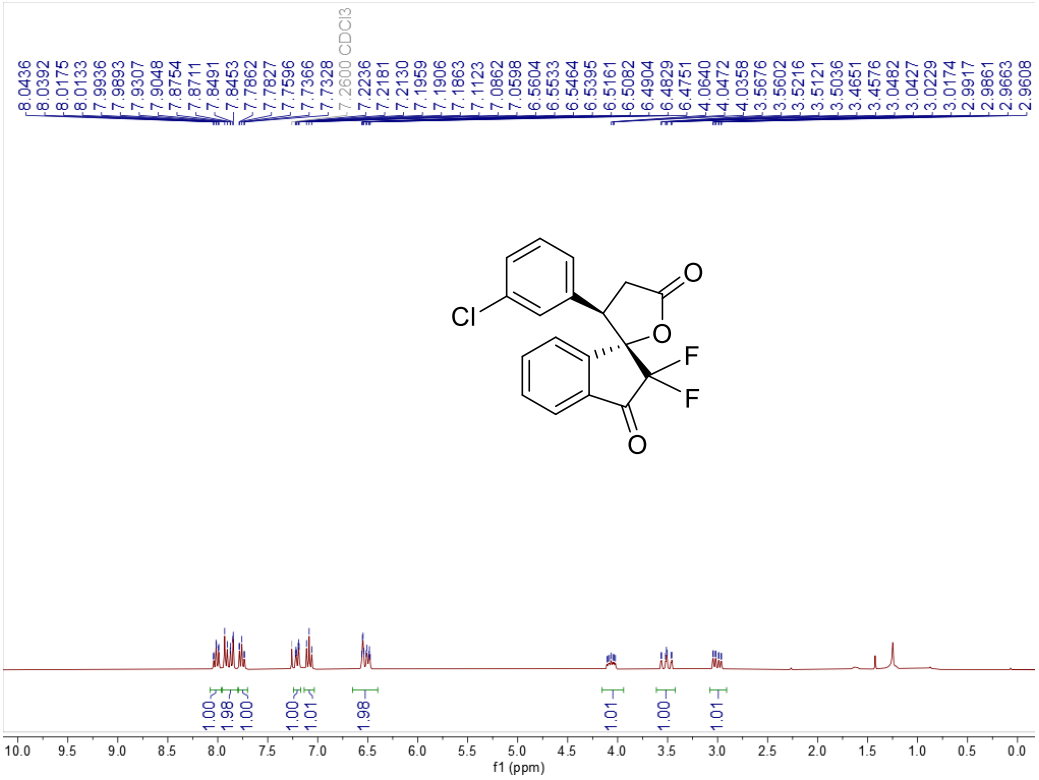


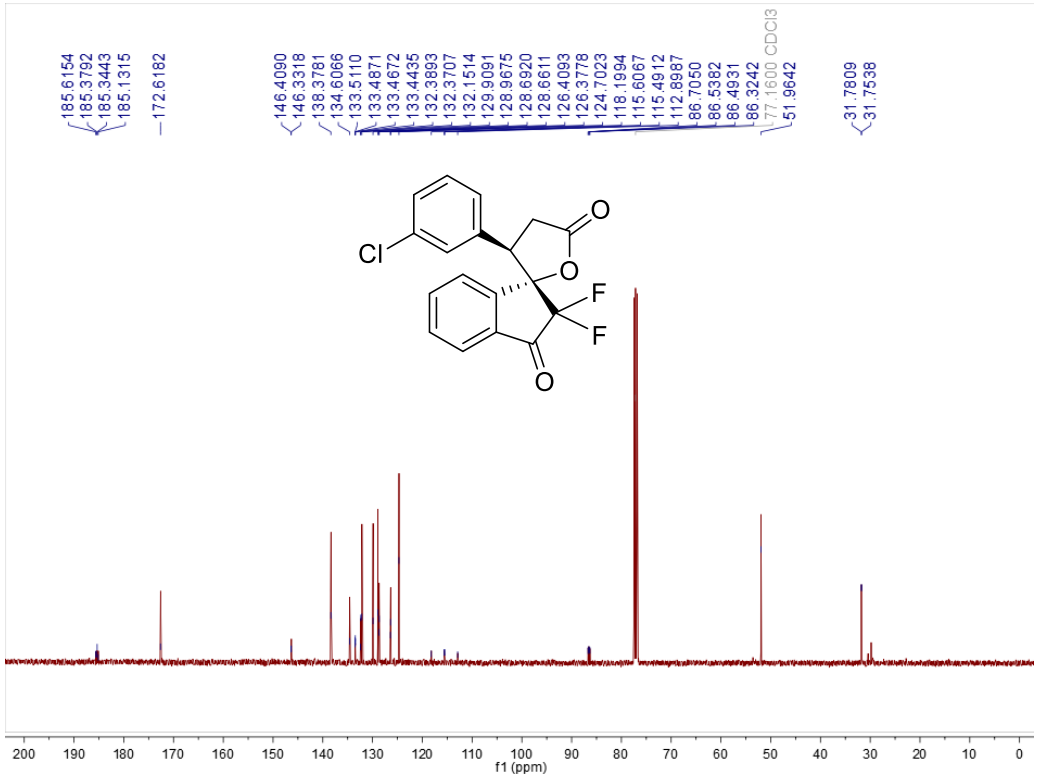


3k ^{19}F NMR (376 MHz, Chloroform-*d*)

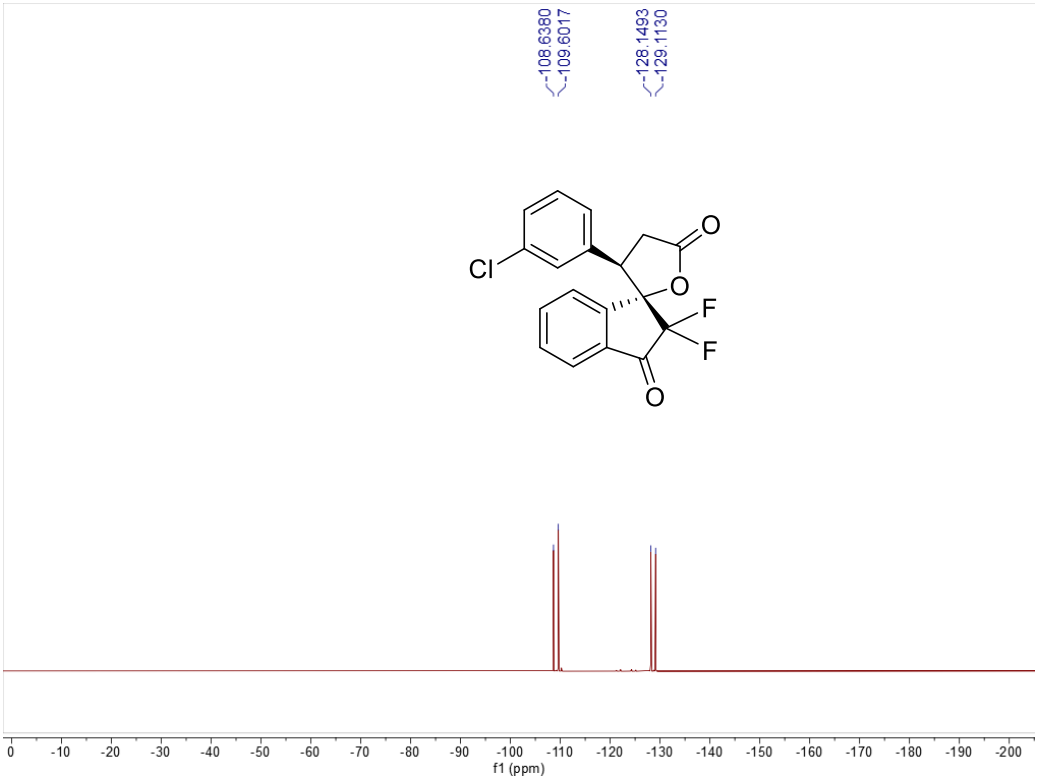


3l ^{1}H NMR (300 MHz, Chloroform-*d*)/^{13}C{1H} NMR (101 MHz, Chloroform-*d*)

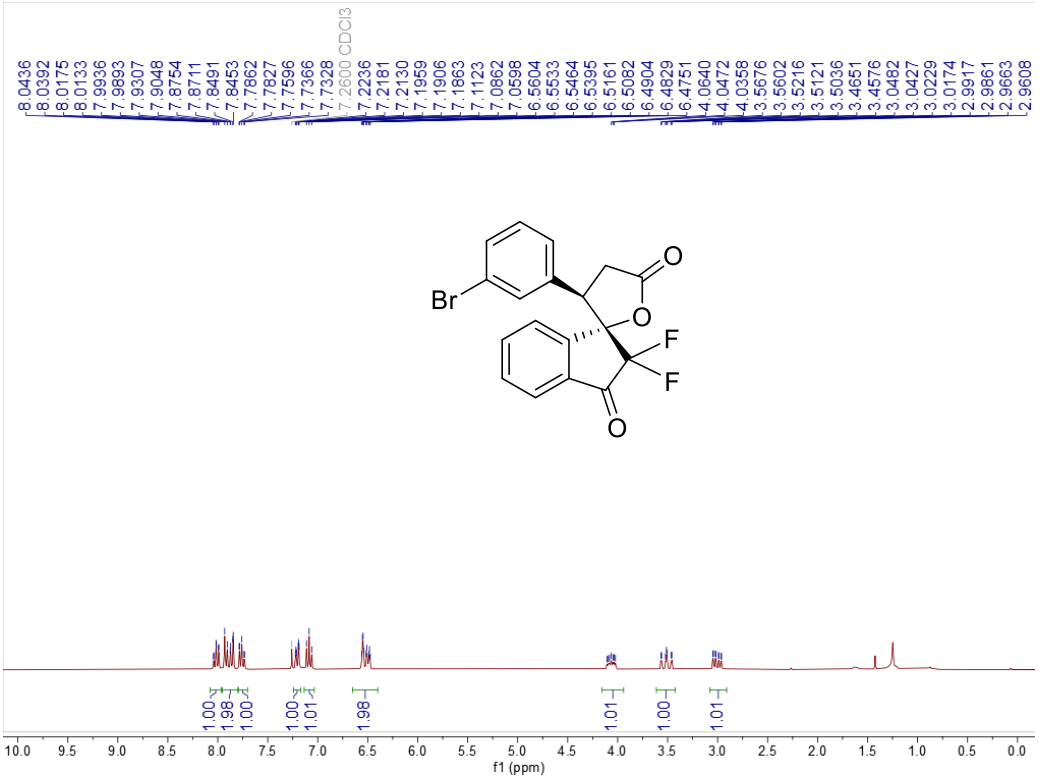


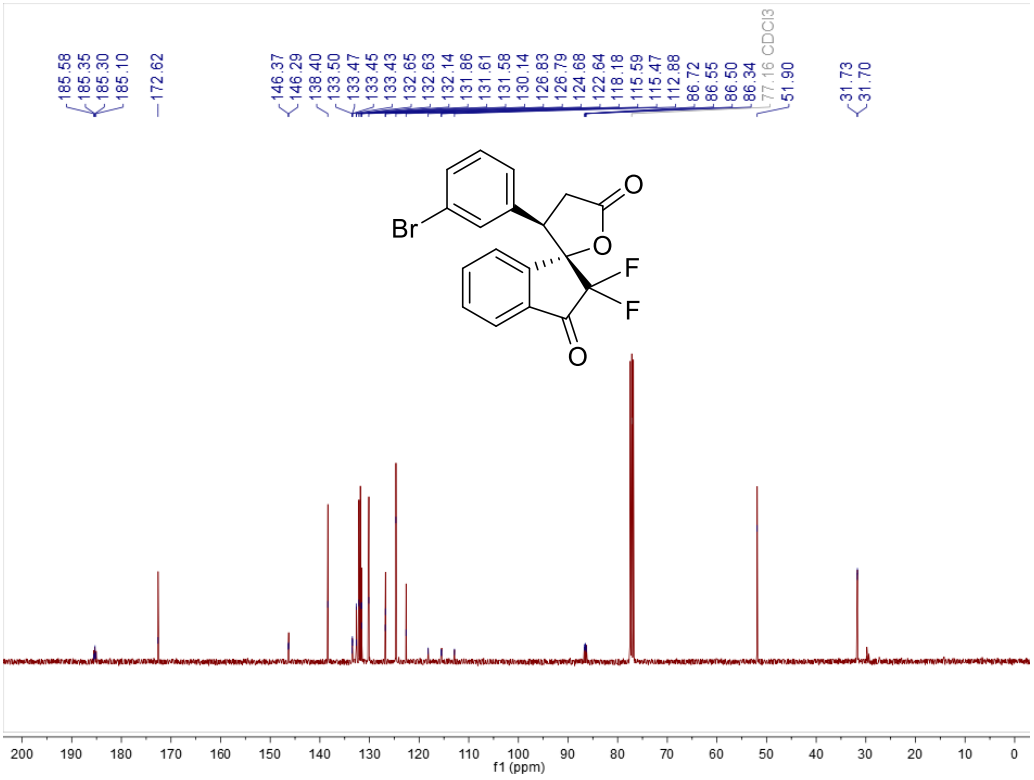


3l ^{19}F NMR (282 MHz, Chloroform-*d*)

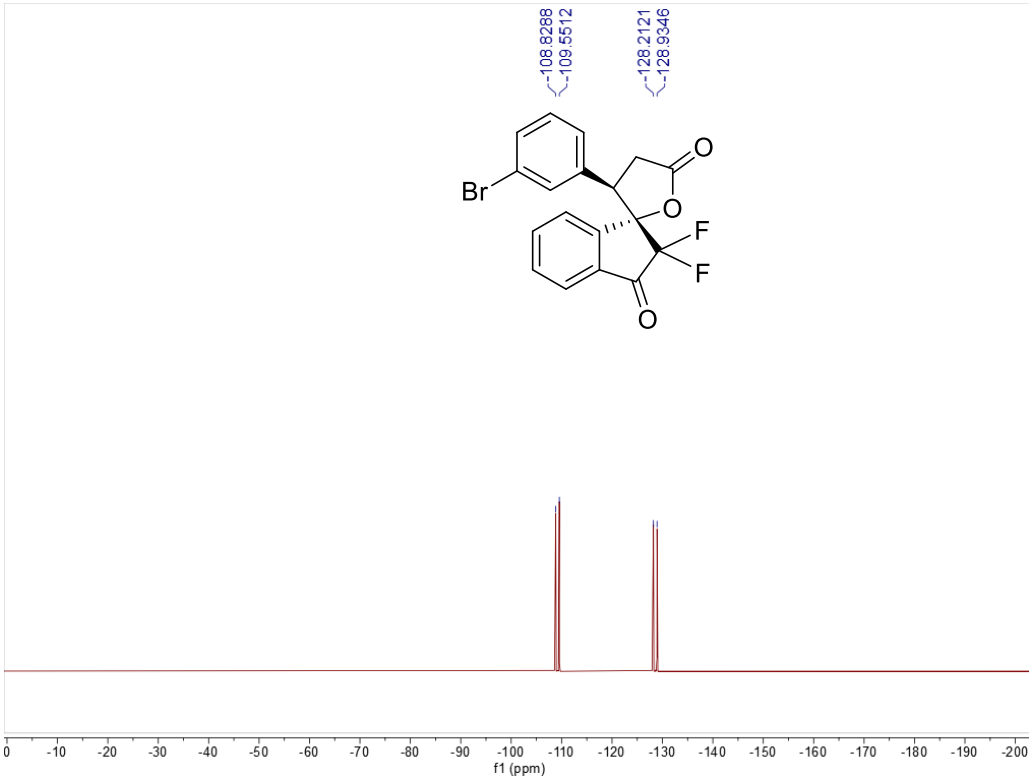


3m ^{1}H NMR (400 MHz, Chloroform-*d*)/^{13}C{H} NMR (101 MHz, Chloroform-*d*)

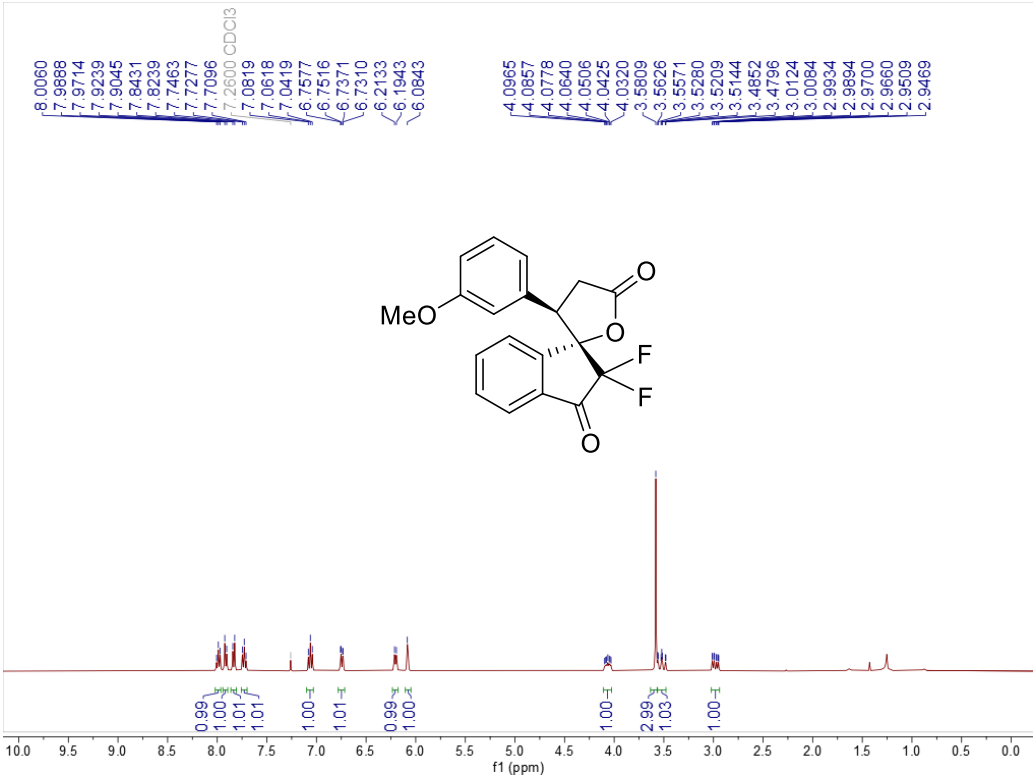


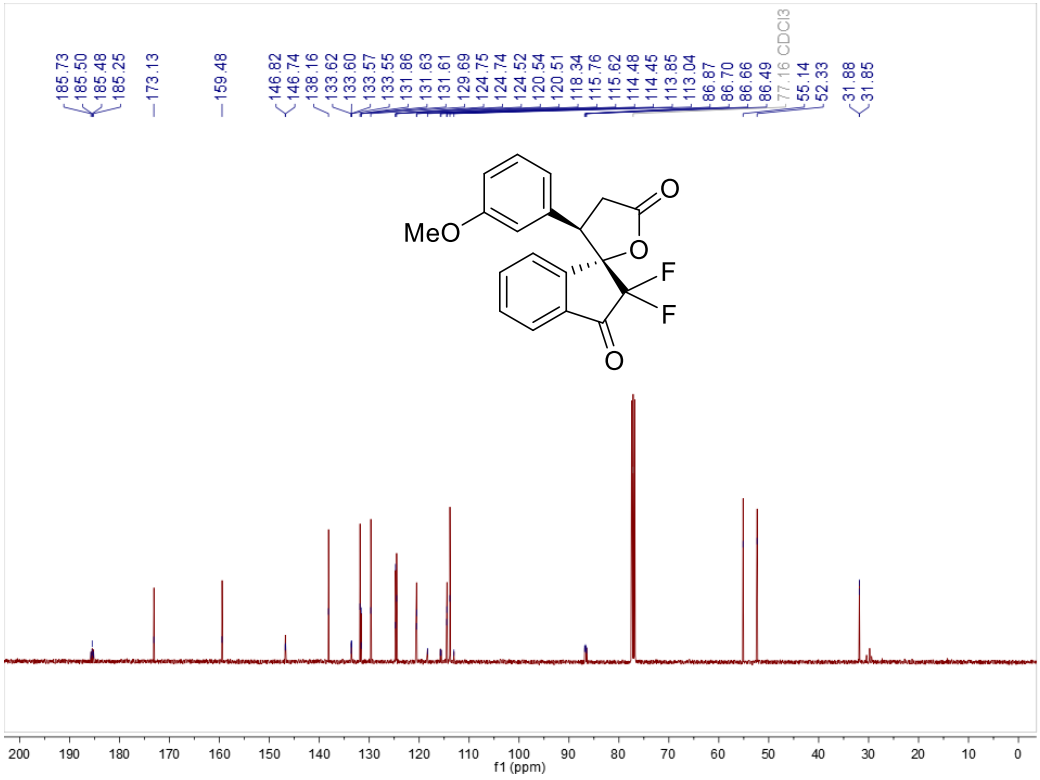


3m ^{19}F NMR (376 MHz, Chloroform-*d*)

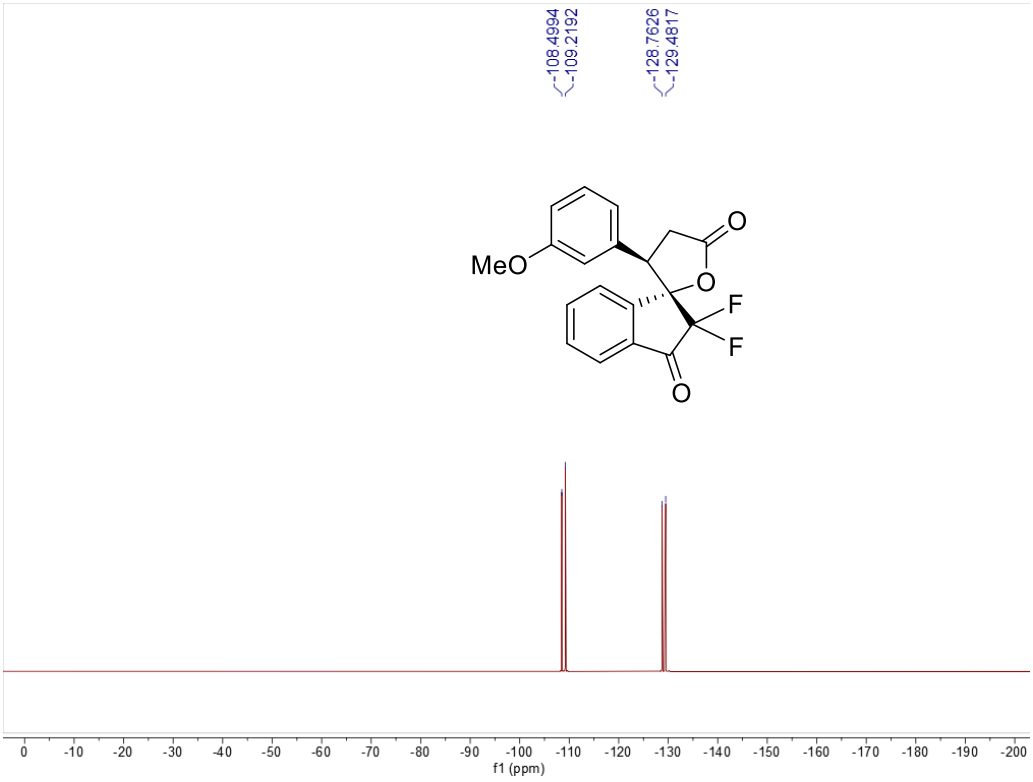


3n ^{1}H NMR (400 MHz, Chloroform-*d*)/^{13}C{H} NMR (101 MHz, Chloroform-*d*)

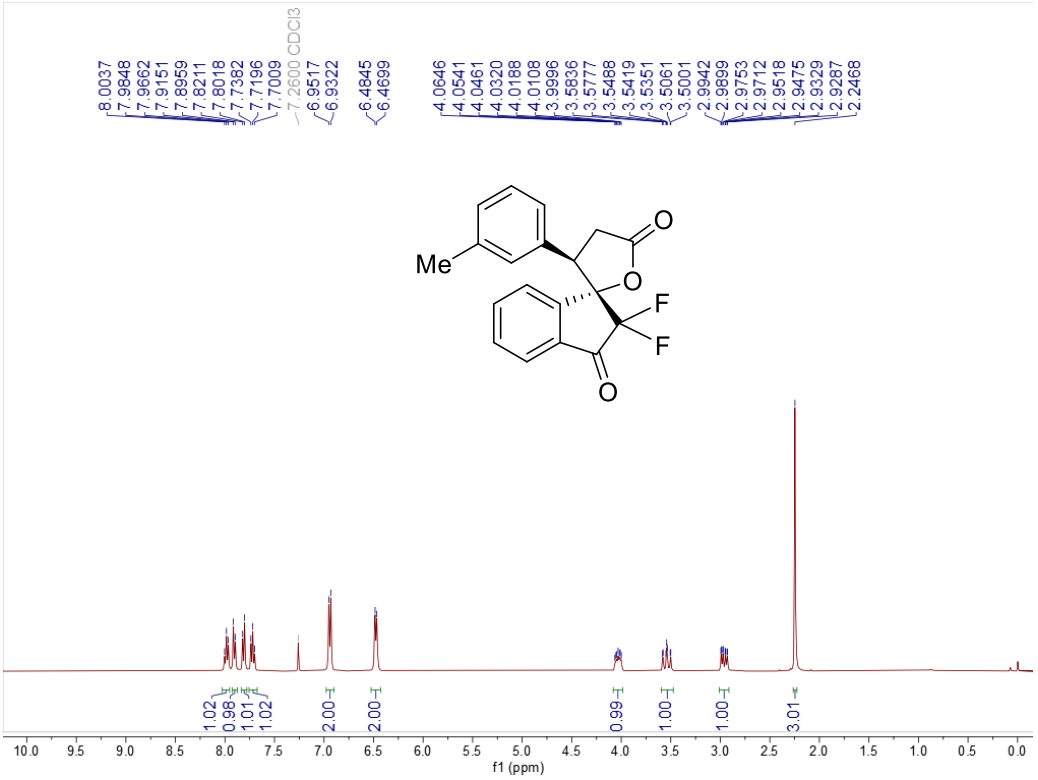


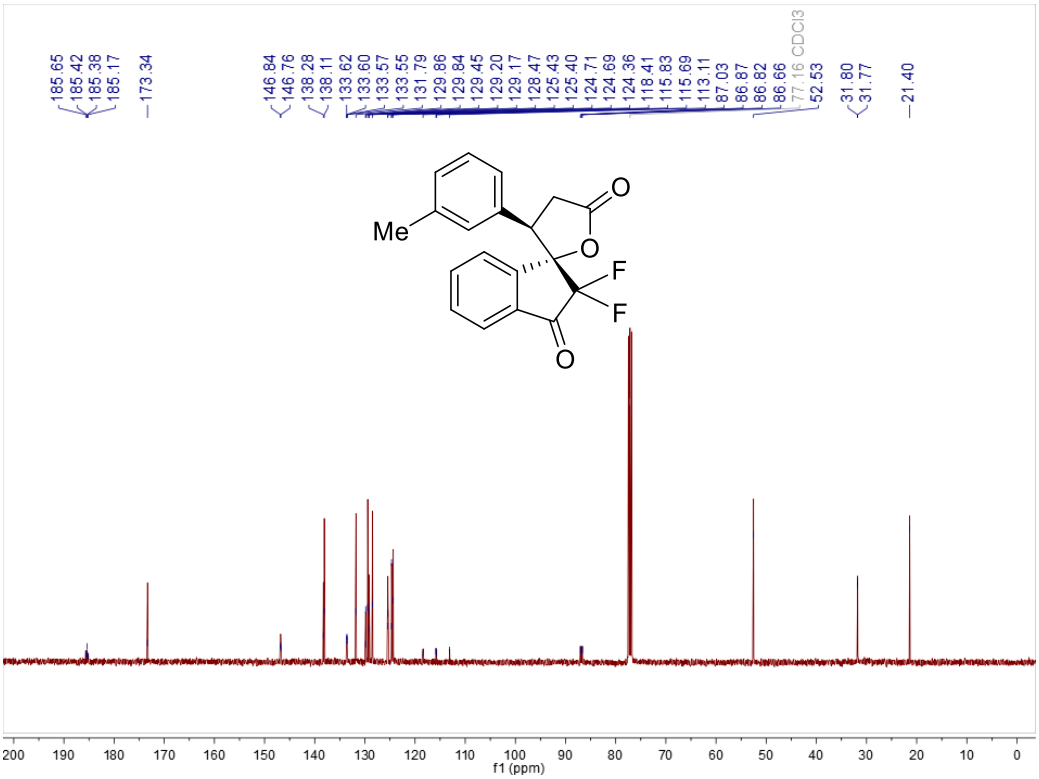


3n ^{19}F NMR (376 MHz, Chloroform-*d*)

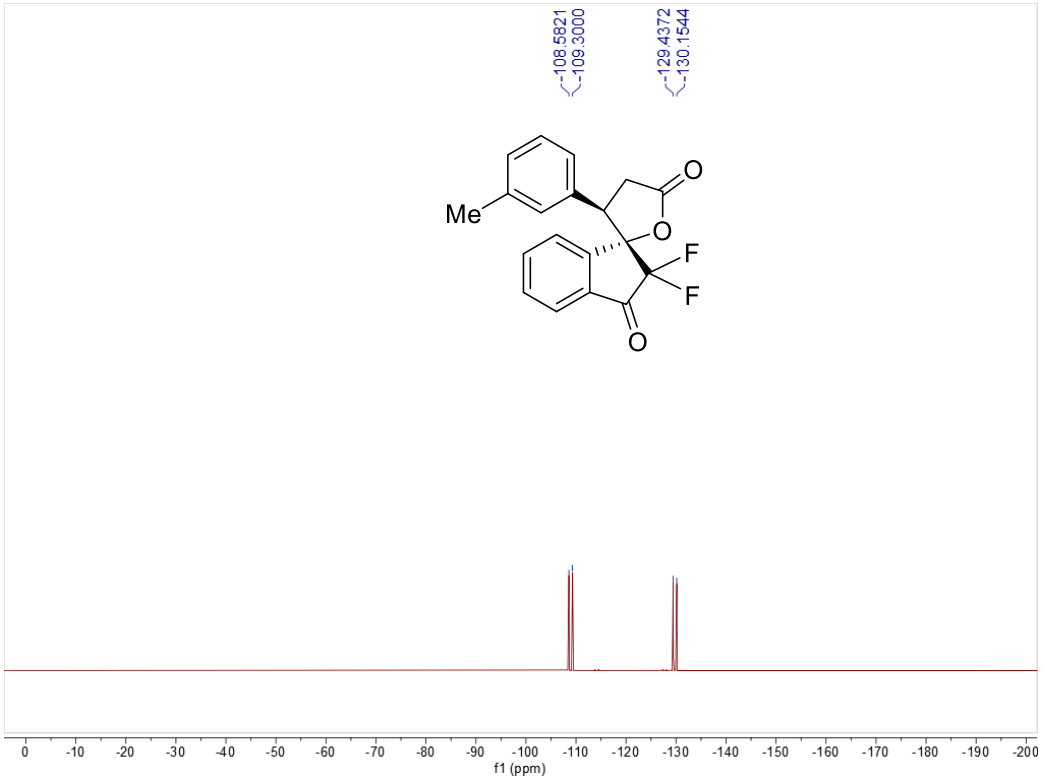


3o ^{1}H NMR (400 MHz, Chloroform-*d*)/^{13}C{H} NMR (101 MHz, Chloroform-d)

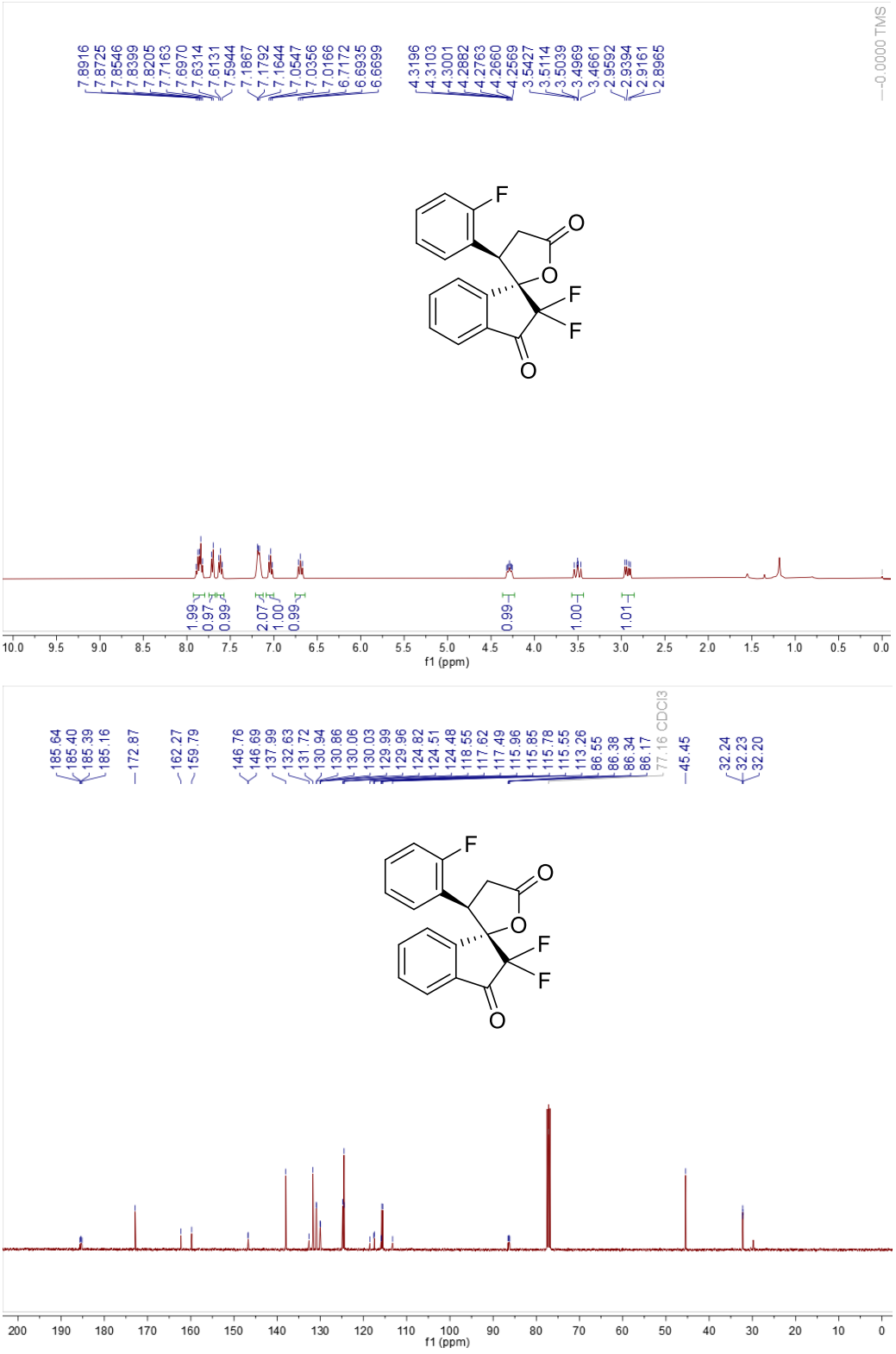




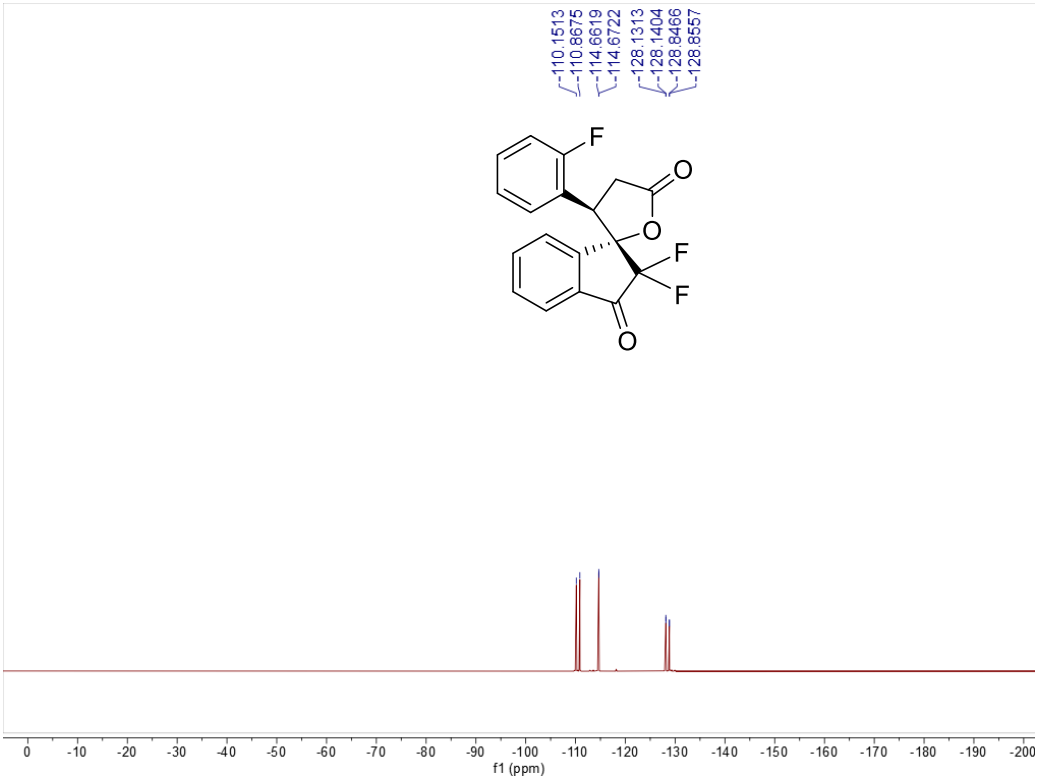
3o ^{19}F NMR (376 MHz, Chloroform-*d*)



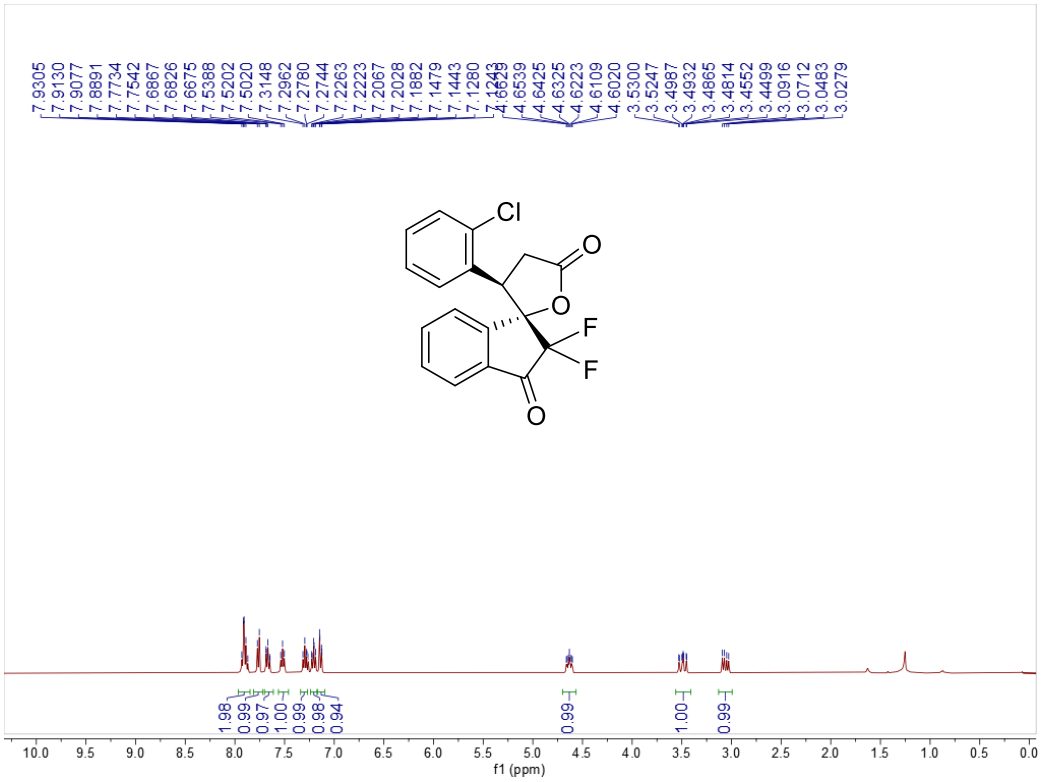
3p ^{1}H NMR (400 MHz, Chloroform-d)/^{13}C{H} NMR (101 MHz, Chloroform-*d*)

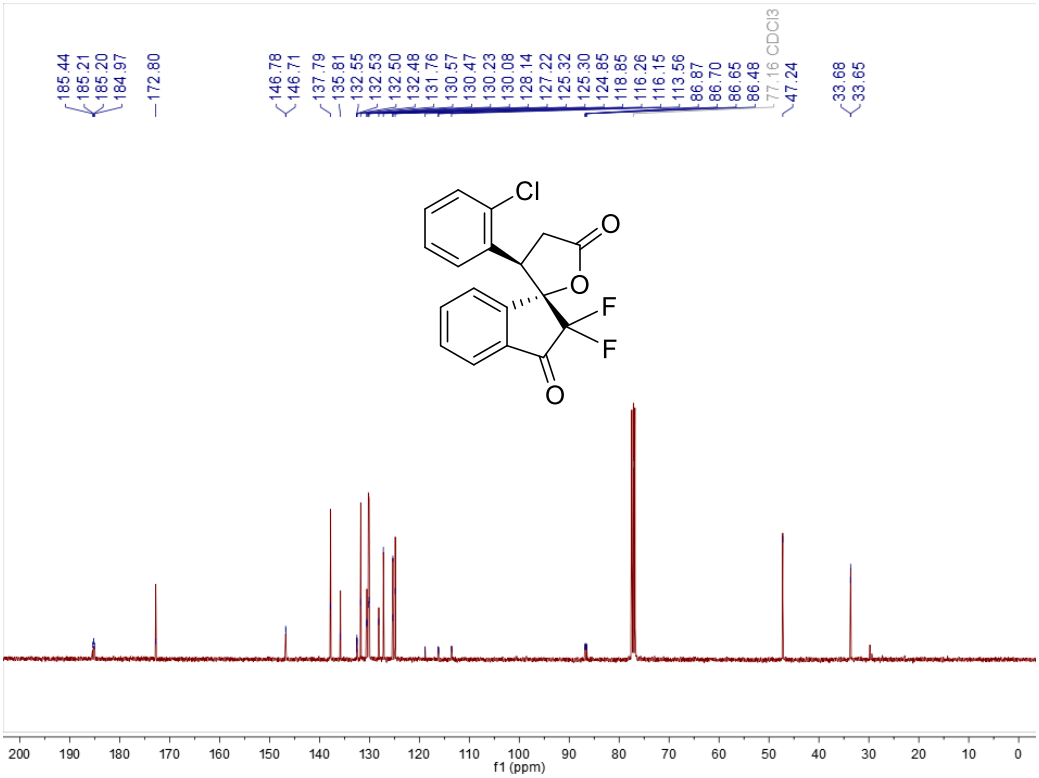


3p ^{19}F NMR (376 MHz, Chloroform-*d*)

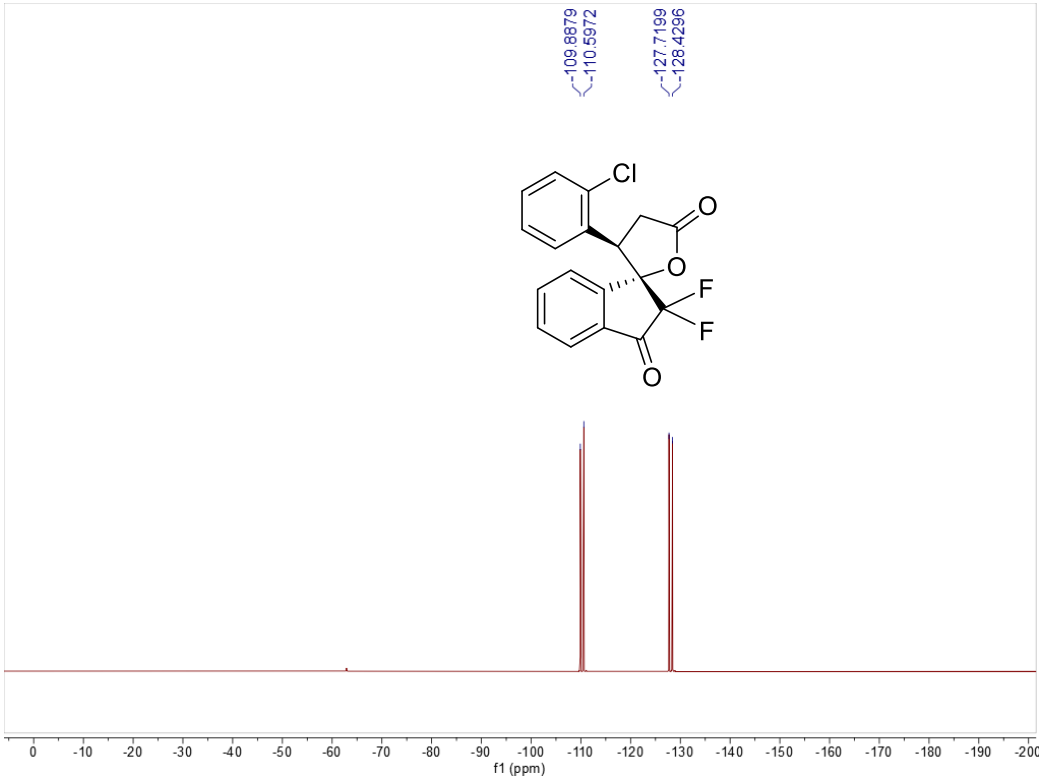


3q ^{1}H NMR (400 MHz, Chloroform-*d*)/^{13}C{H} NMR (101 MHz, Chloroform-*d*)

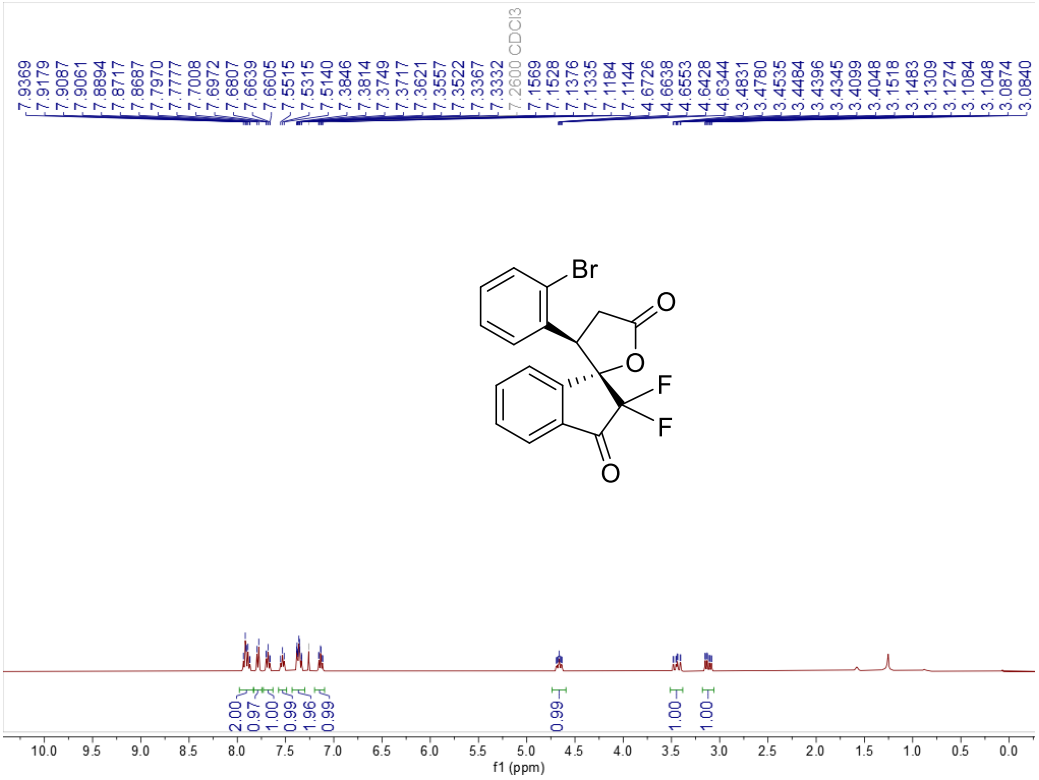


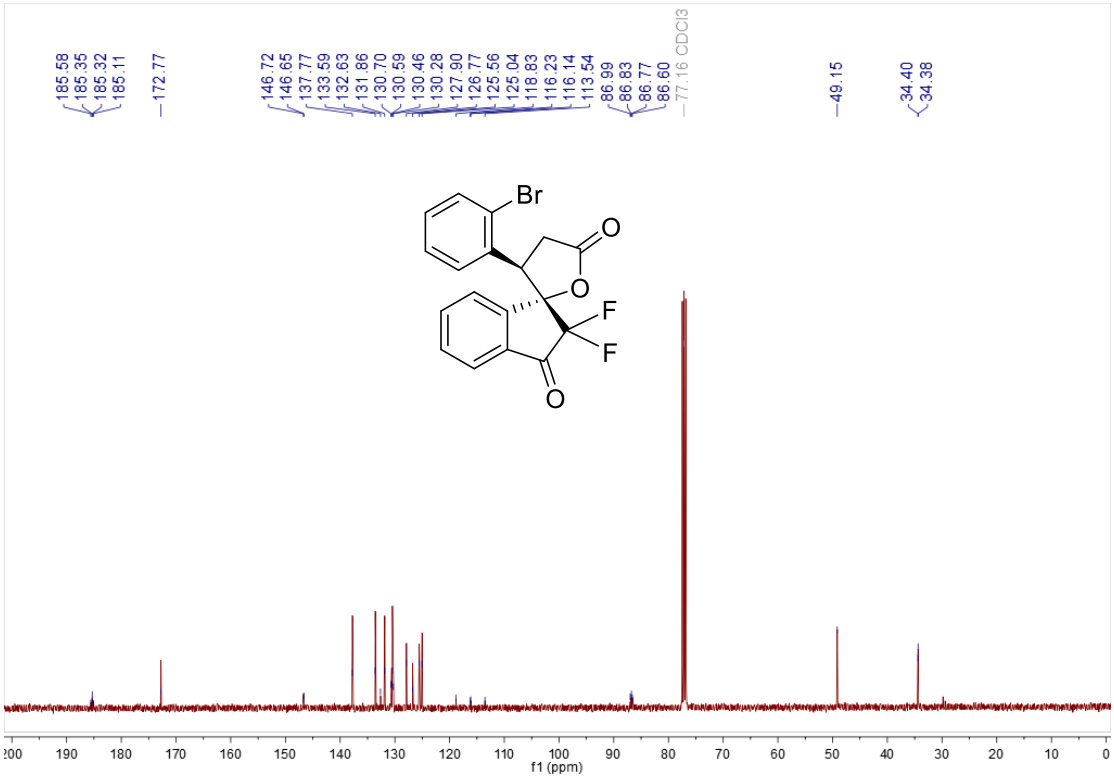


3q ^{19}F NMR (376 MHz, Chloroform-*d*)

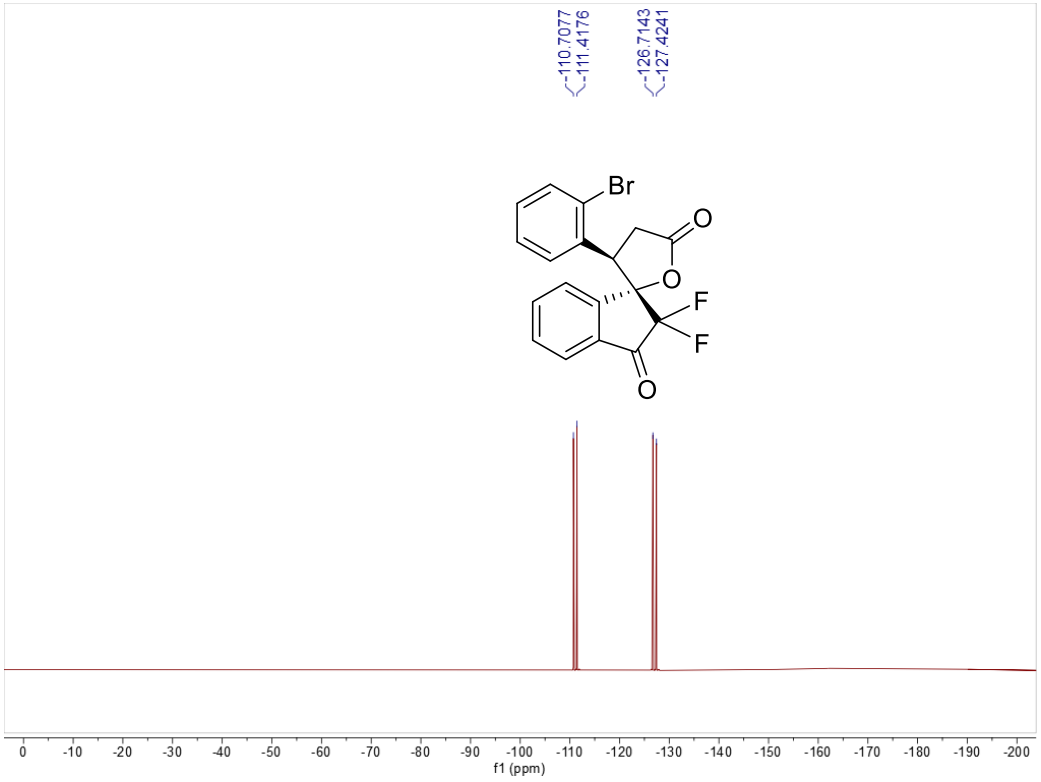


3r ^{1}H NMR (400 MHz, Chloroform-*d*)/^{13}C{H} NMR (101 MHz, Chloroform-*d*)

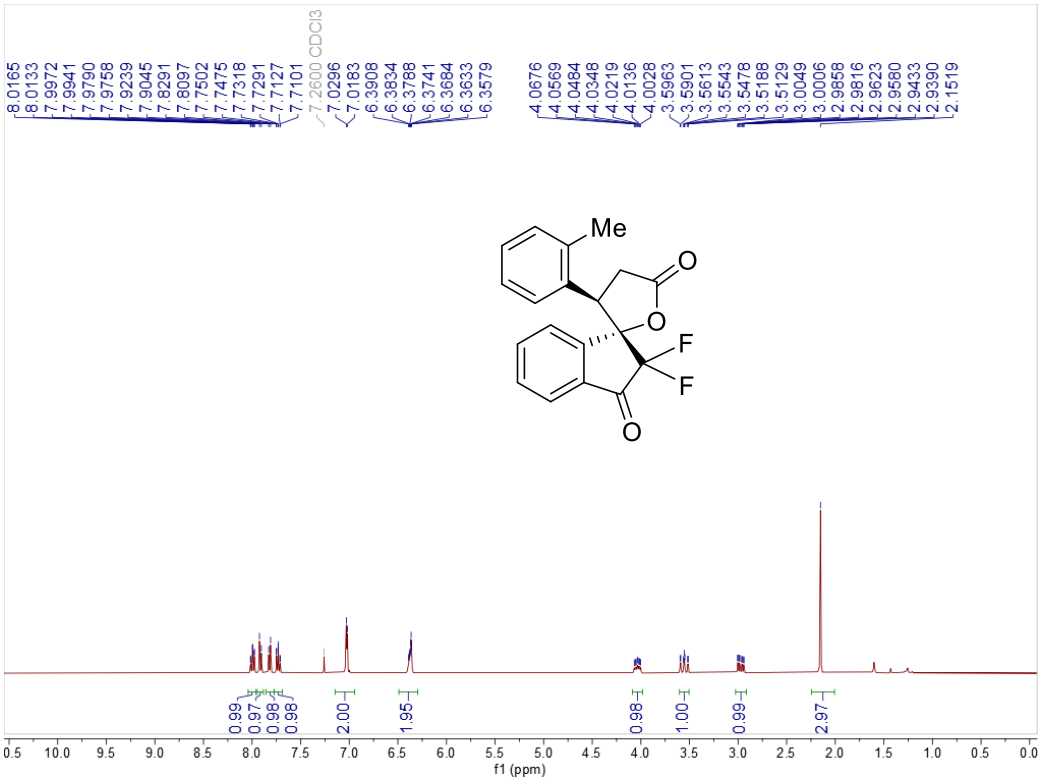


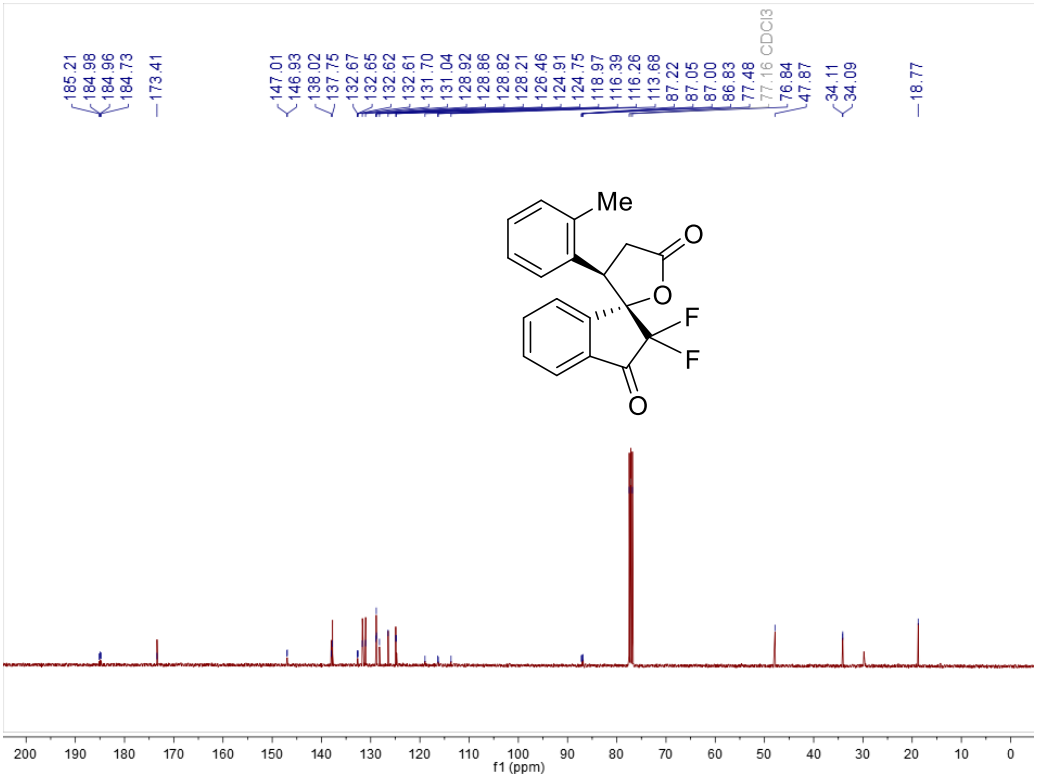


3r ^{19}F NMR (376 MHz, Chloroform-*d*)

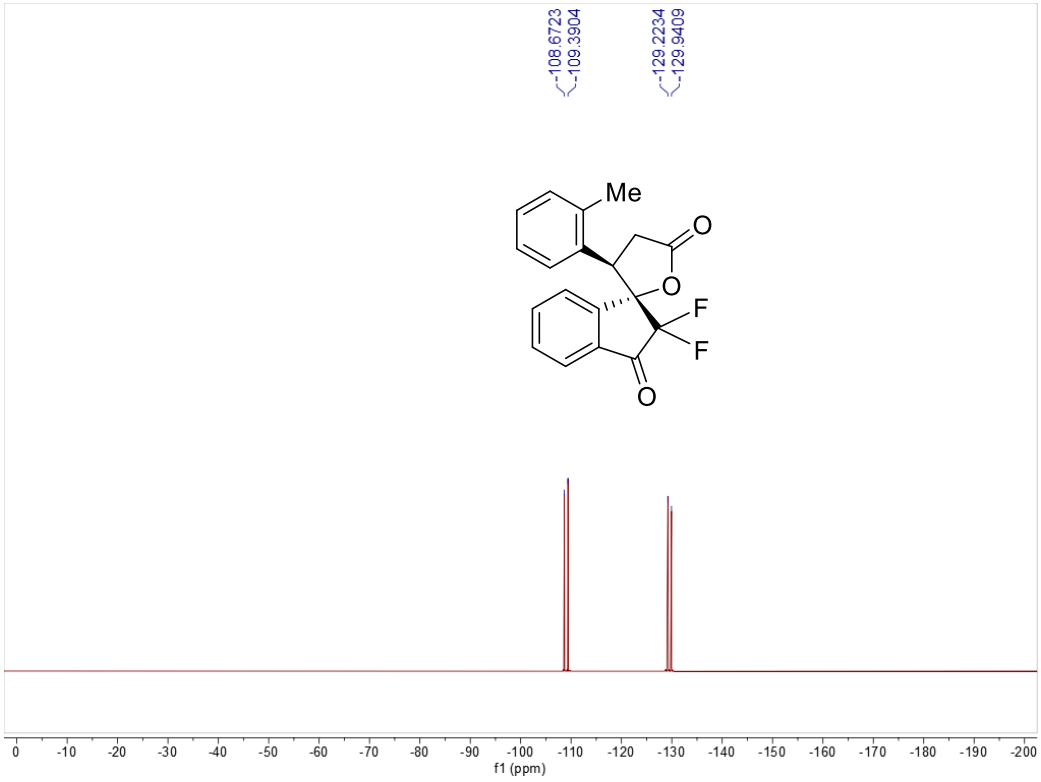


3s ^{1}H NMR (400 MHz, Chloroform-*d*)/^{13}C{H} NMR (101 MHz, Chloroform-*d*)

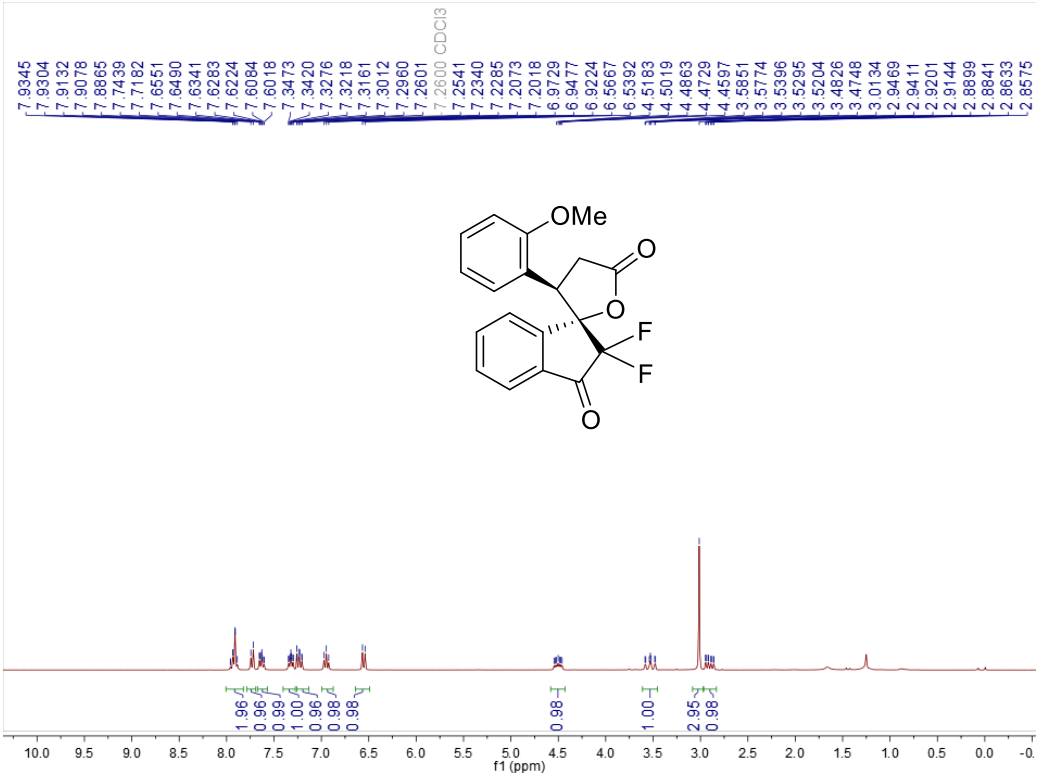


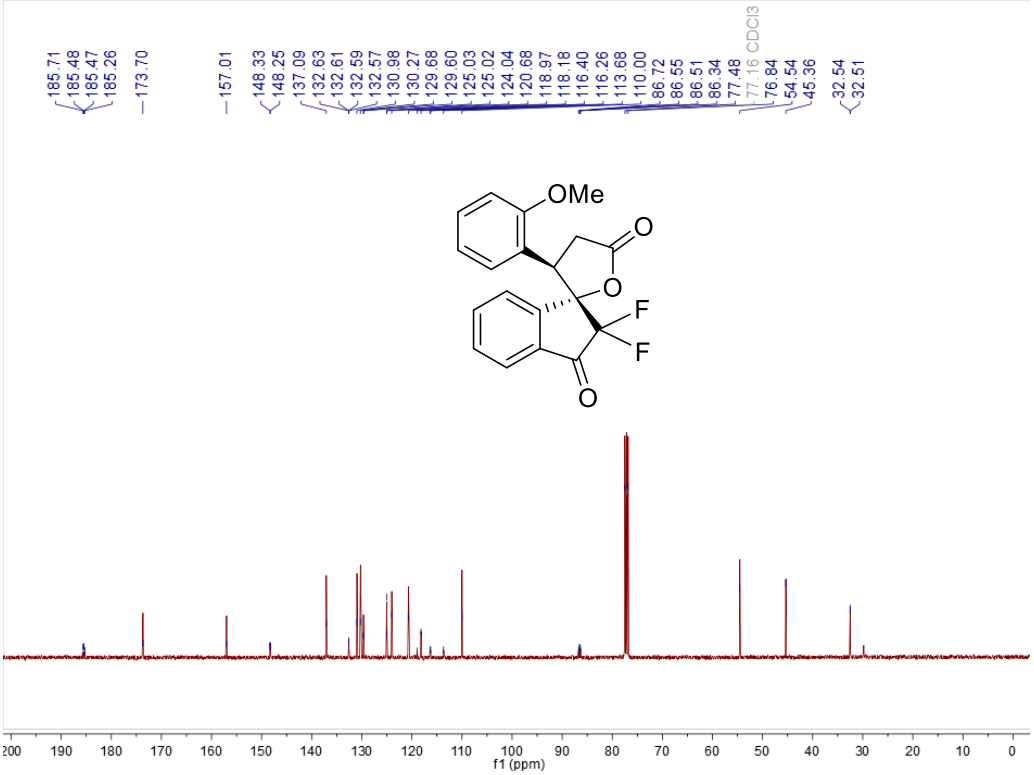


3s ^{19}F NMR (376 MHz, Chloroform-*d*)

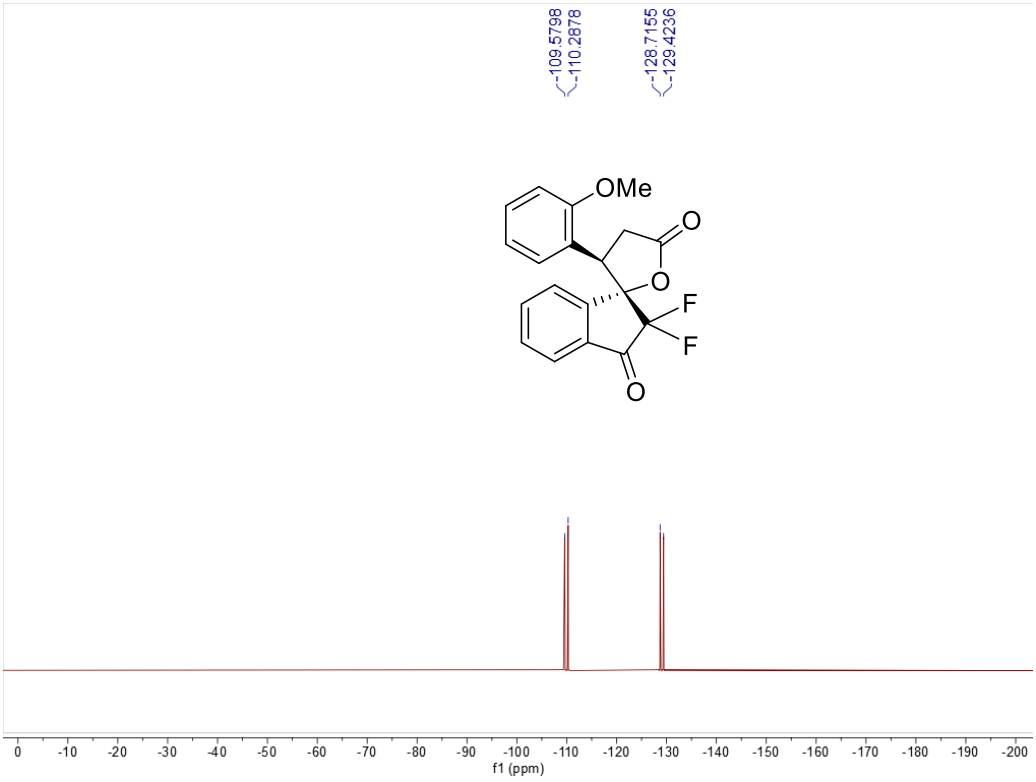


3t ^{1}H NMR (300 MHz, Chloroform-*d*)/^{13}C{H} NMR (101 MHz, Chloroform-d)

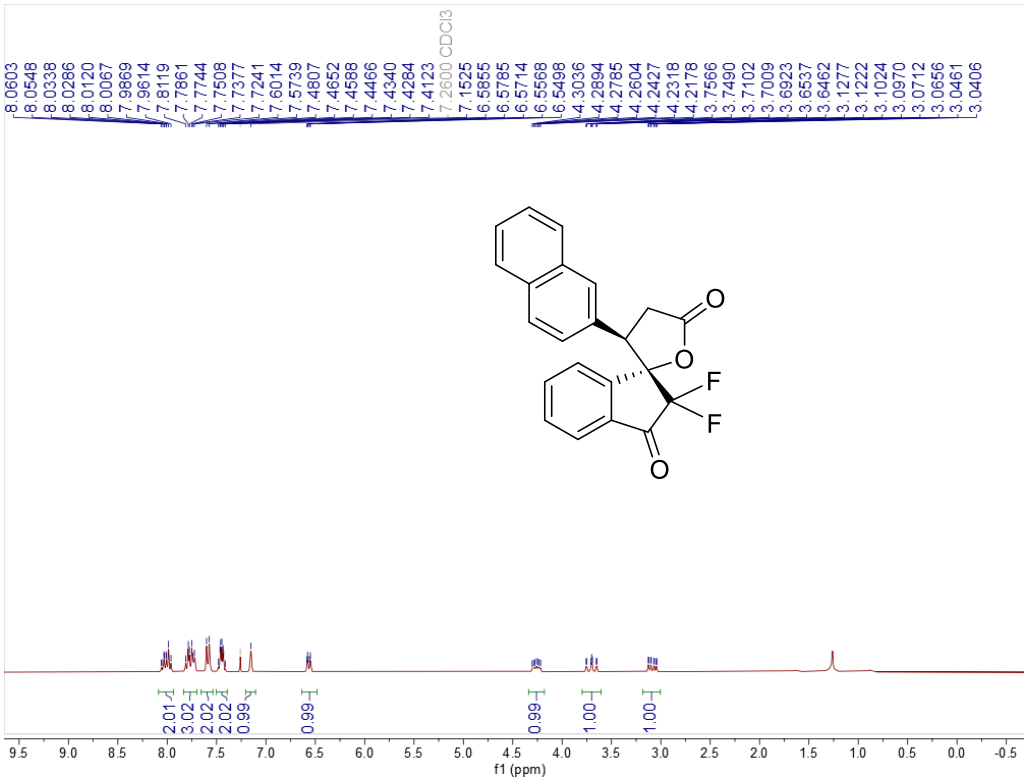


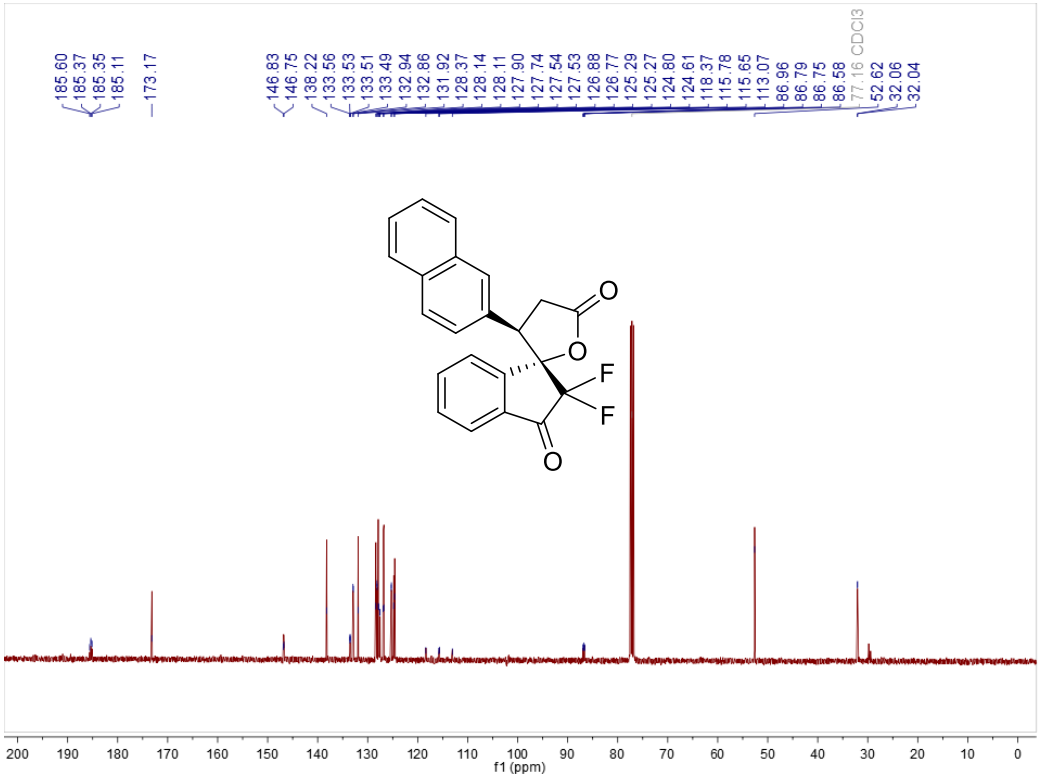


3t ^{19}F NMR (376 MHz, Chloroform-*d*)

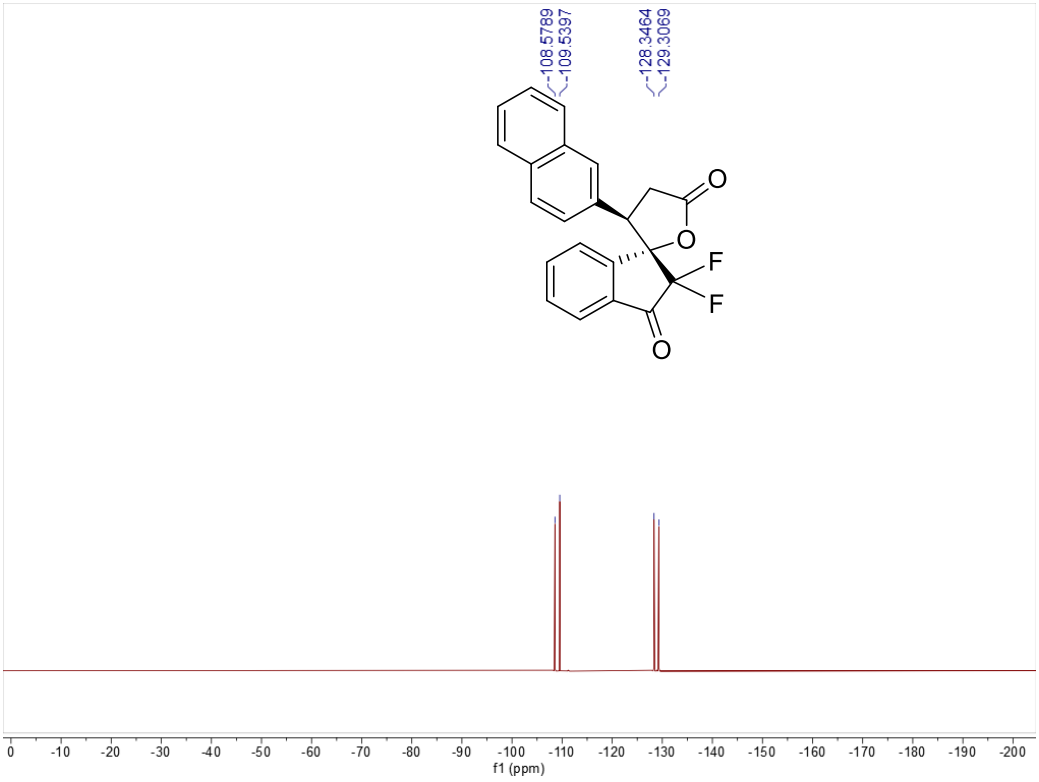


3u ^{1}H NMR (300 MHz, Chloroform-*d*)/^{13}C{H} NMR (101 MHz, Chloroform-*d*)

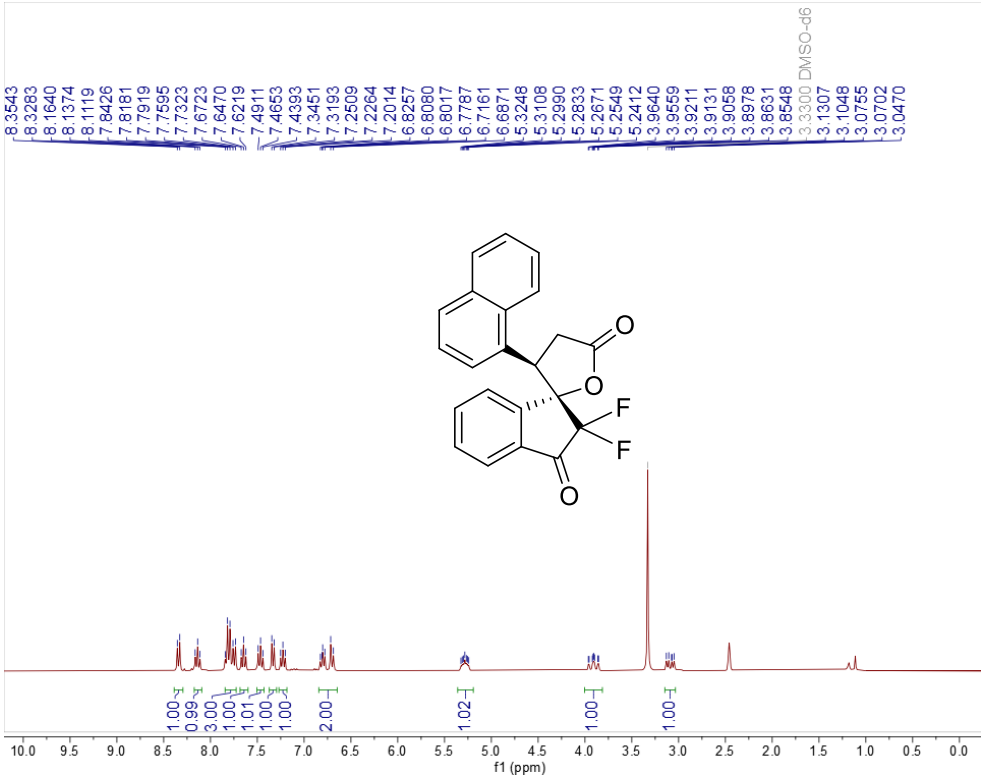


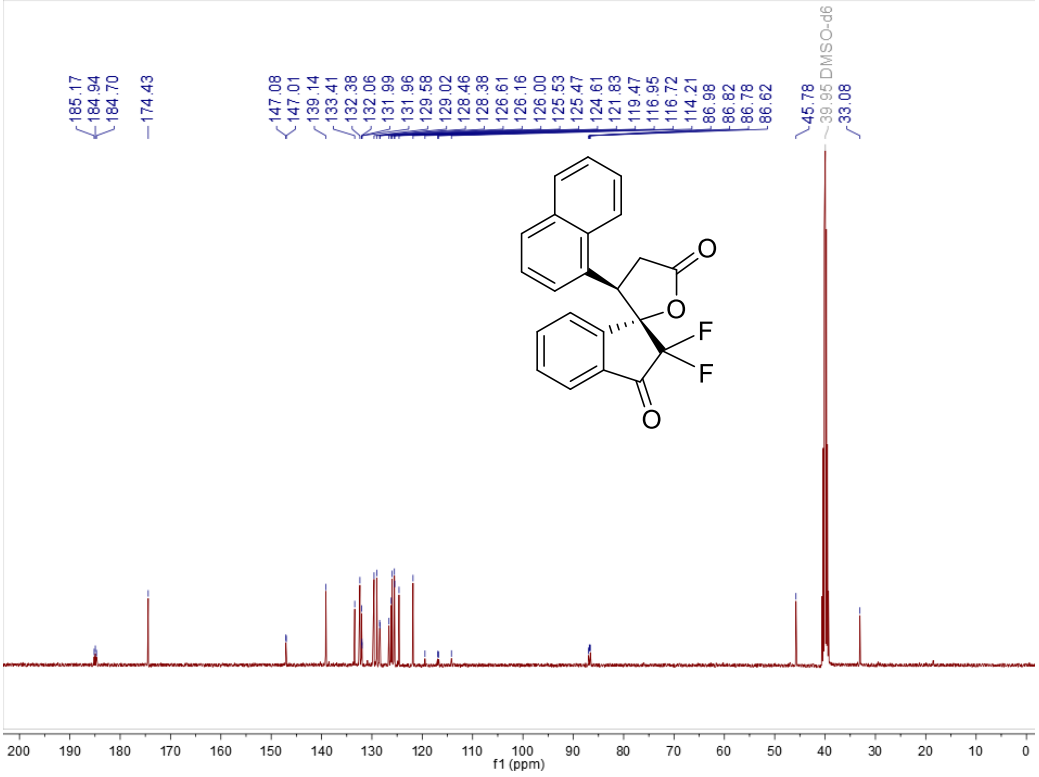


3u ^{19}F NMR (282 MHz, Chloroform-*d*)

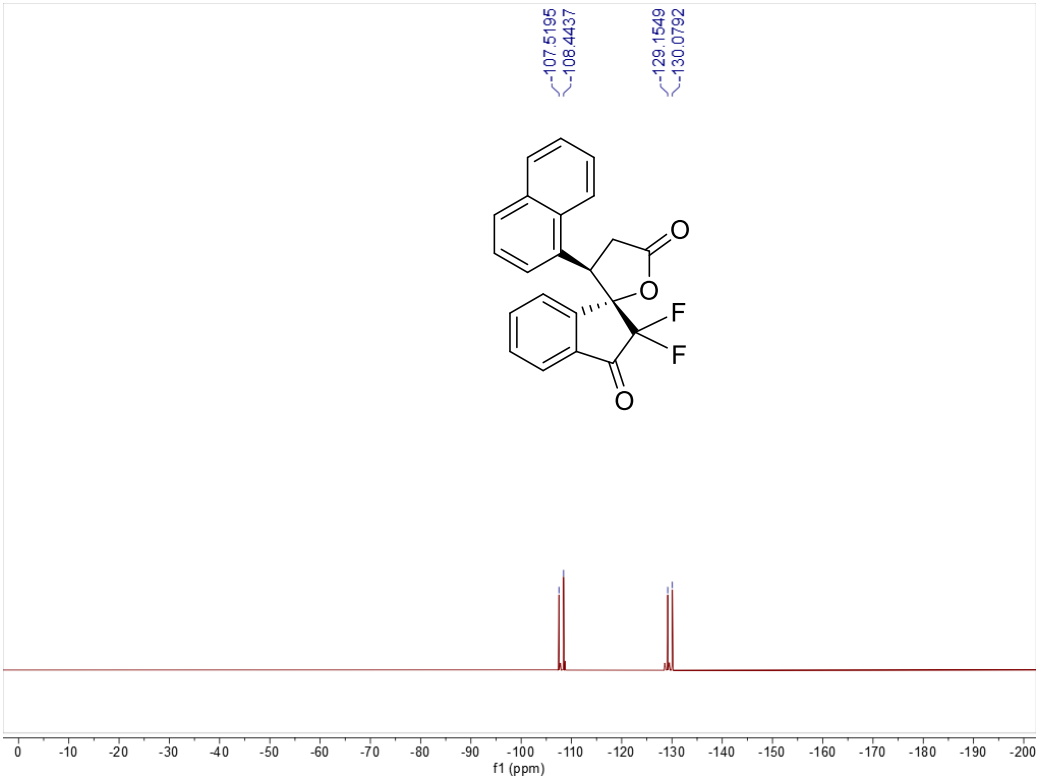


3v ^{1}H NMR (300 MHz, DMSO-d_6)/^{13}C{H} NMR (101 MHz, DMSO-d_6)

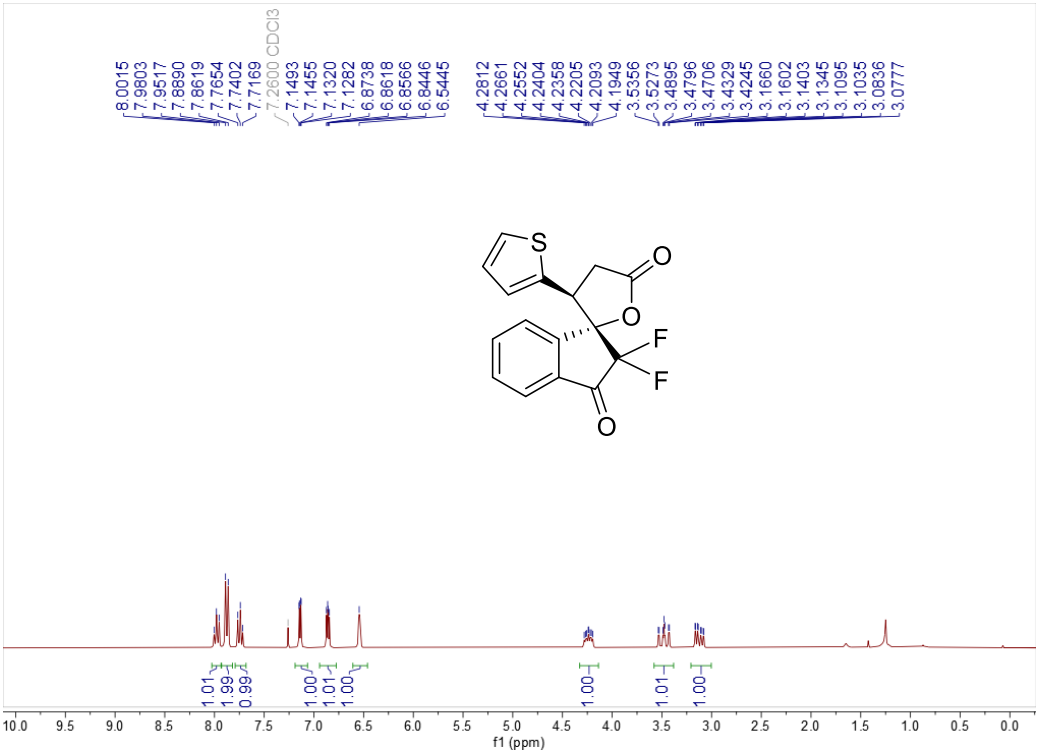


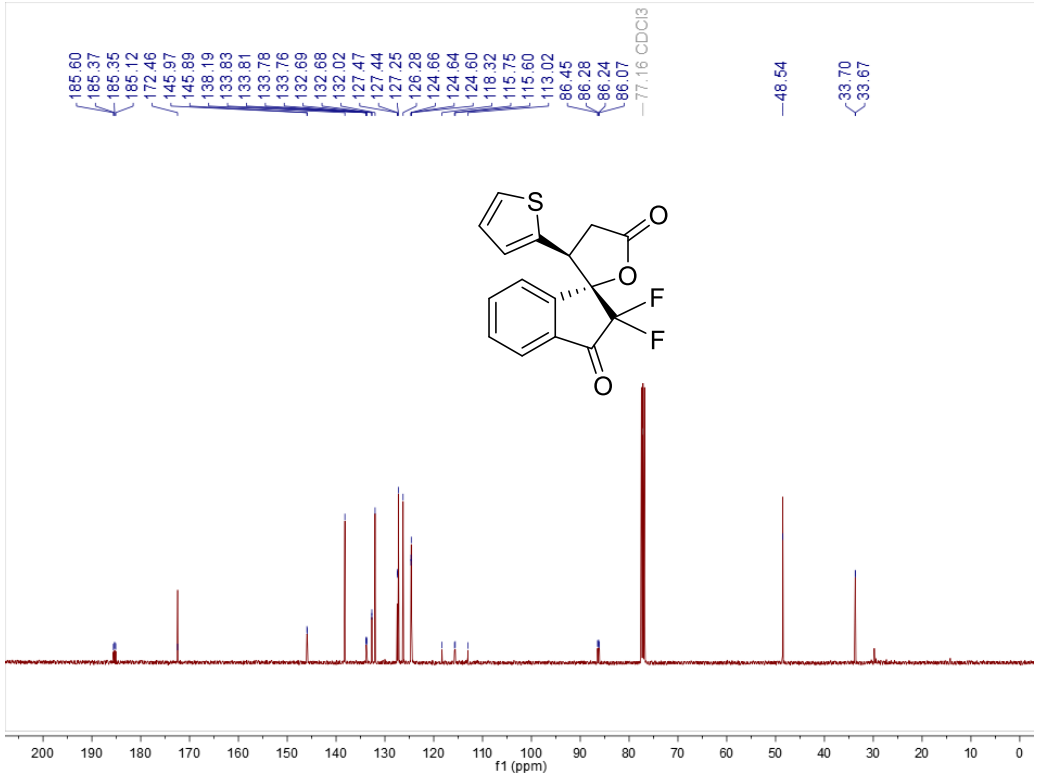


3v ^{19}F NMR (282 MHz, DMSO-d_6)

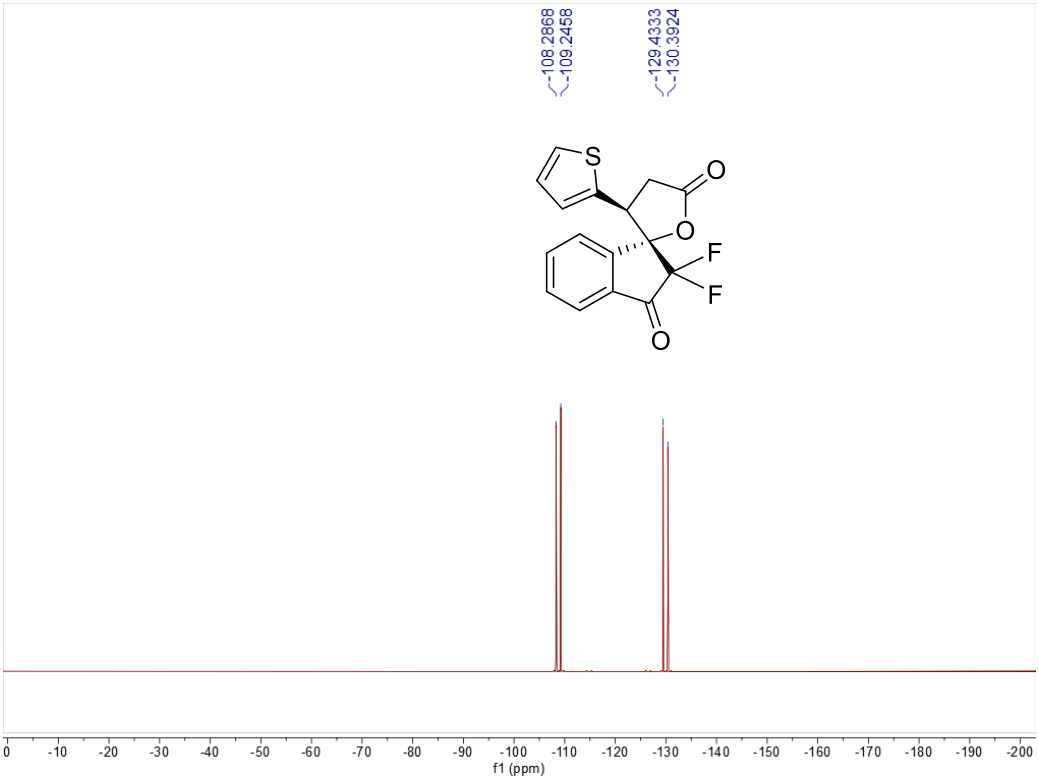


3w ^{1}H NMR (300 MHz, Chloroform-*d*)/ ^{13}C{1H} NMR (101 MHz, Chloroform-*d*)

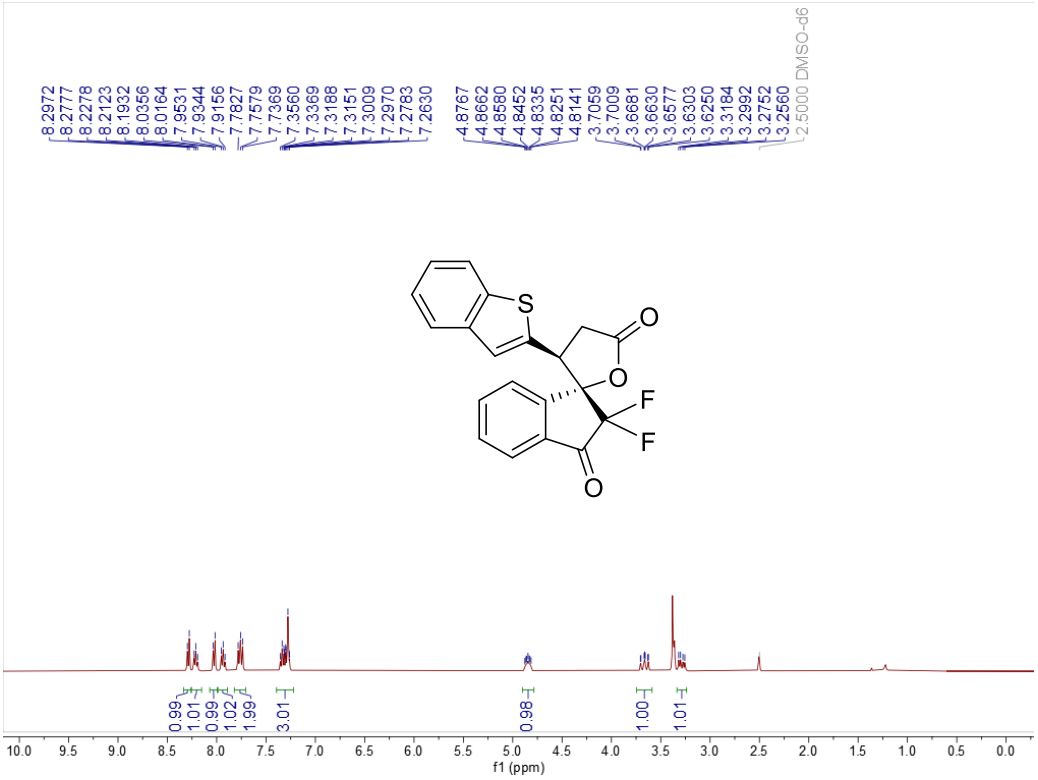


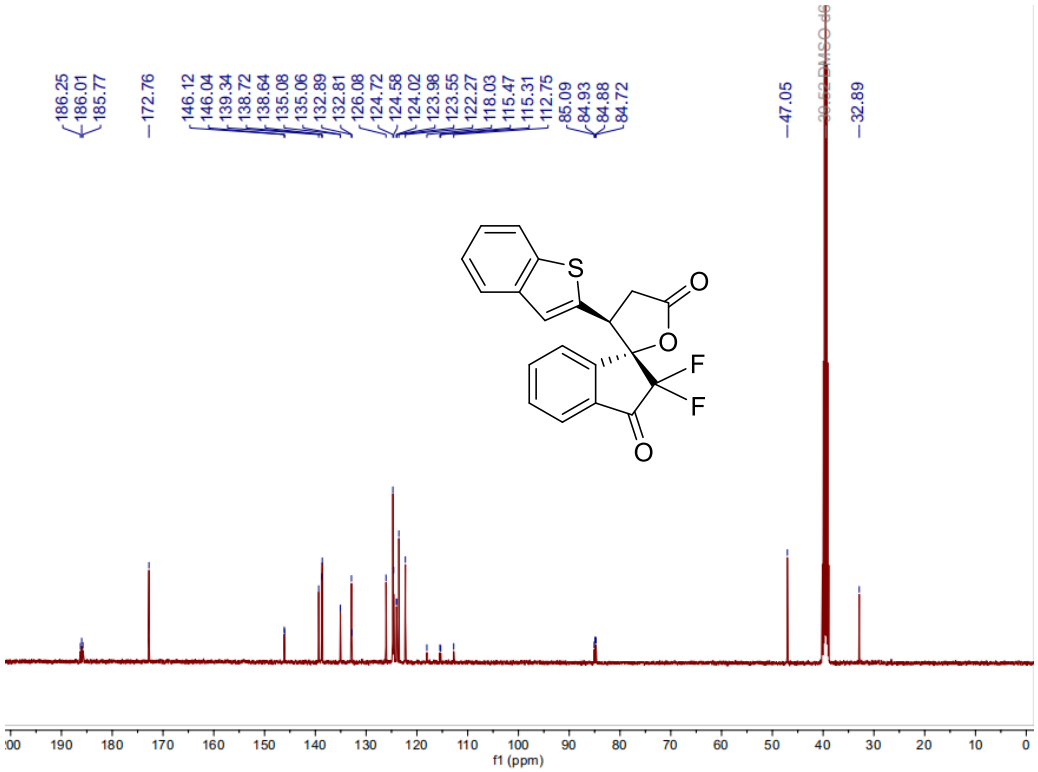


3w ^{19}F NMR (282 MHz, Chloroform-*d*)

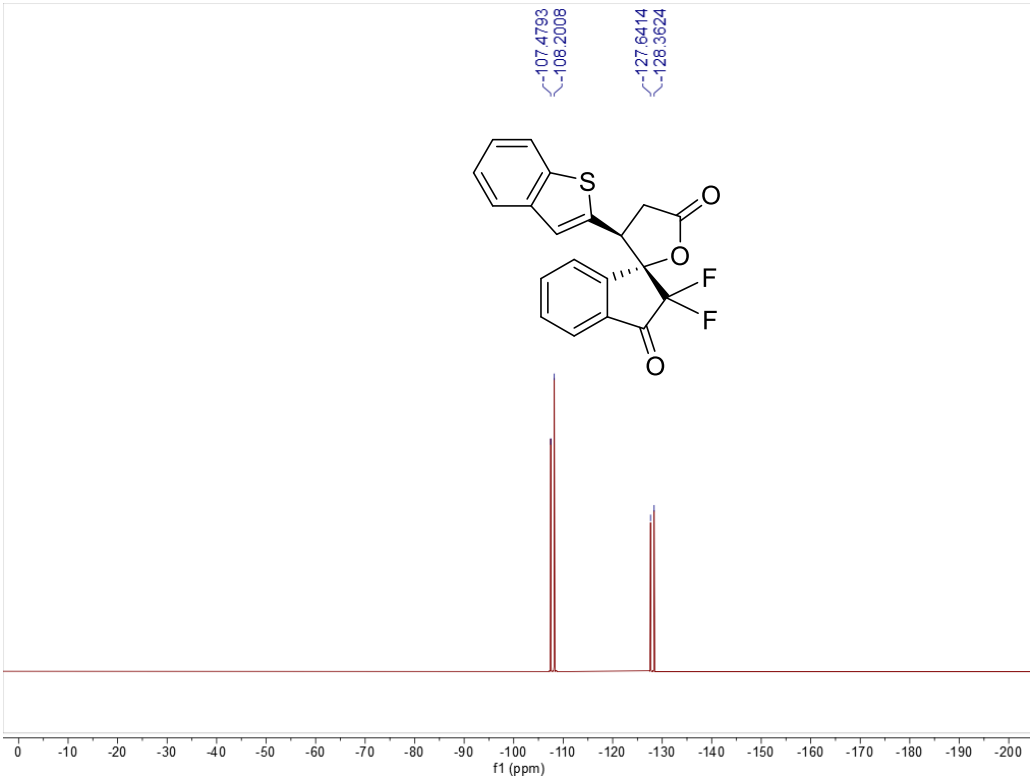


3x ^{1}H NMR (400 MHz, DMSO-d_6)/^{13}C{H} NMR (101 MHz, DMSO-d_6)

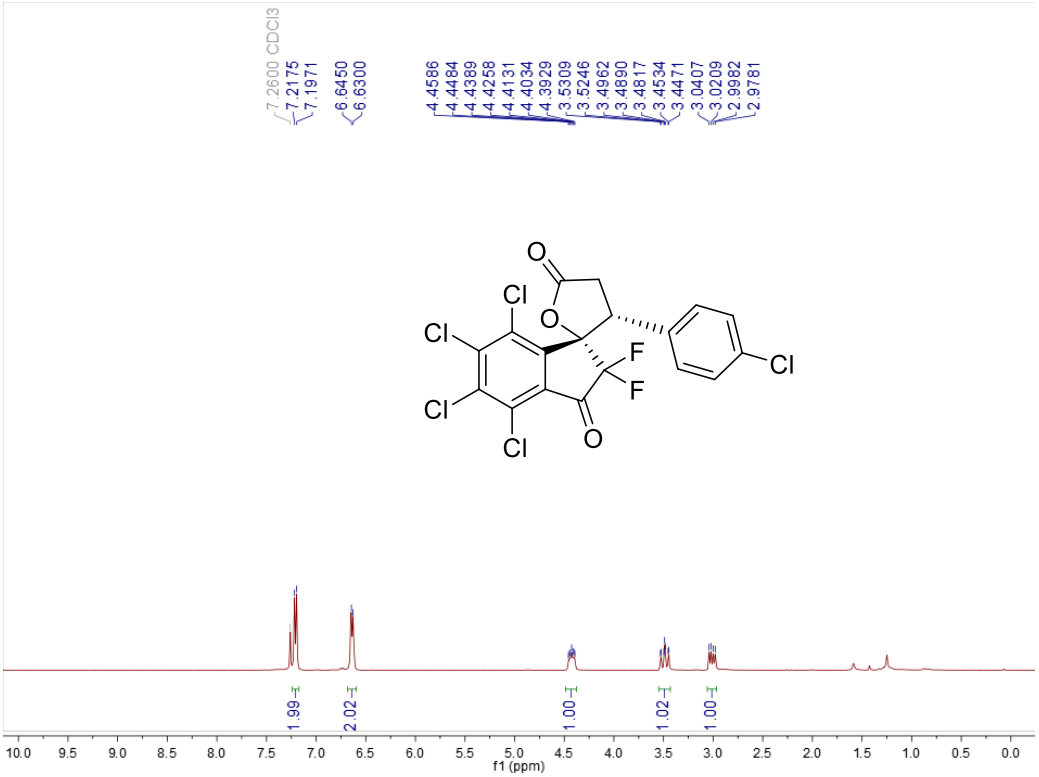


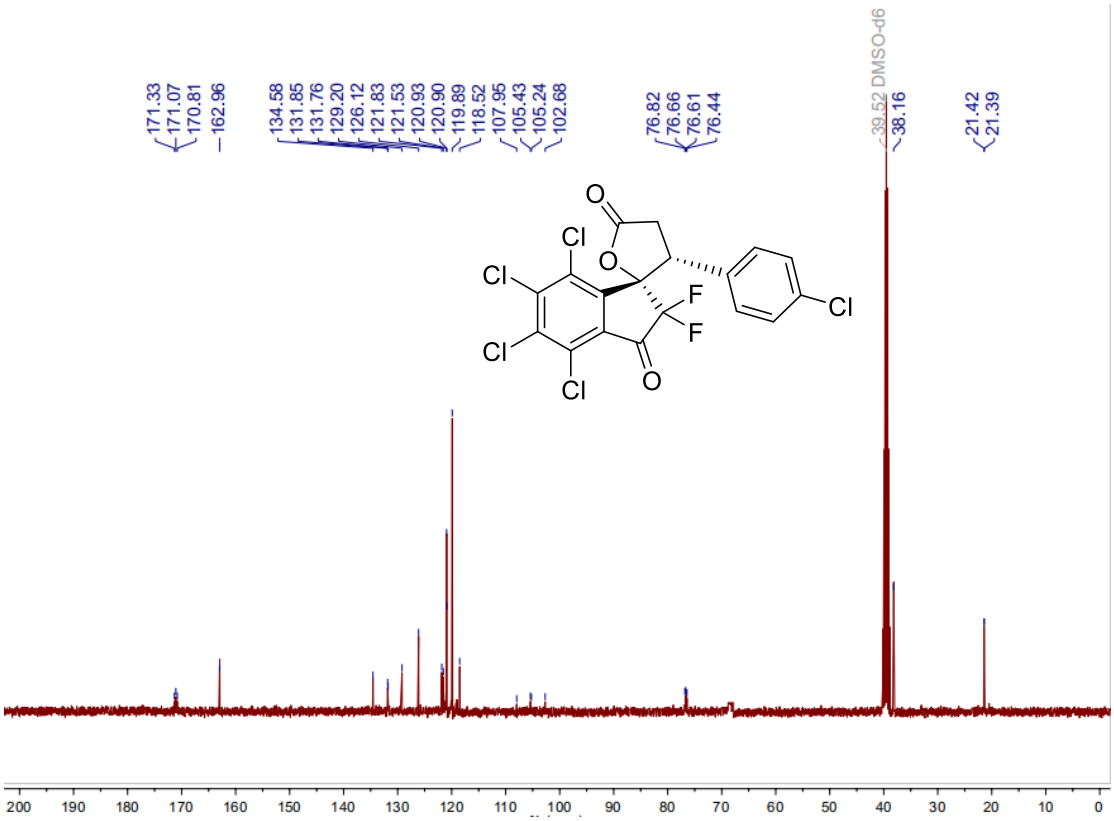


3x ^{19}F NMR (376 MHz, DMSO-d_6)

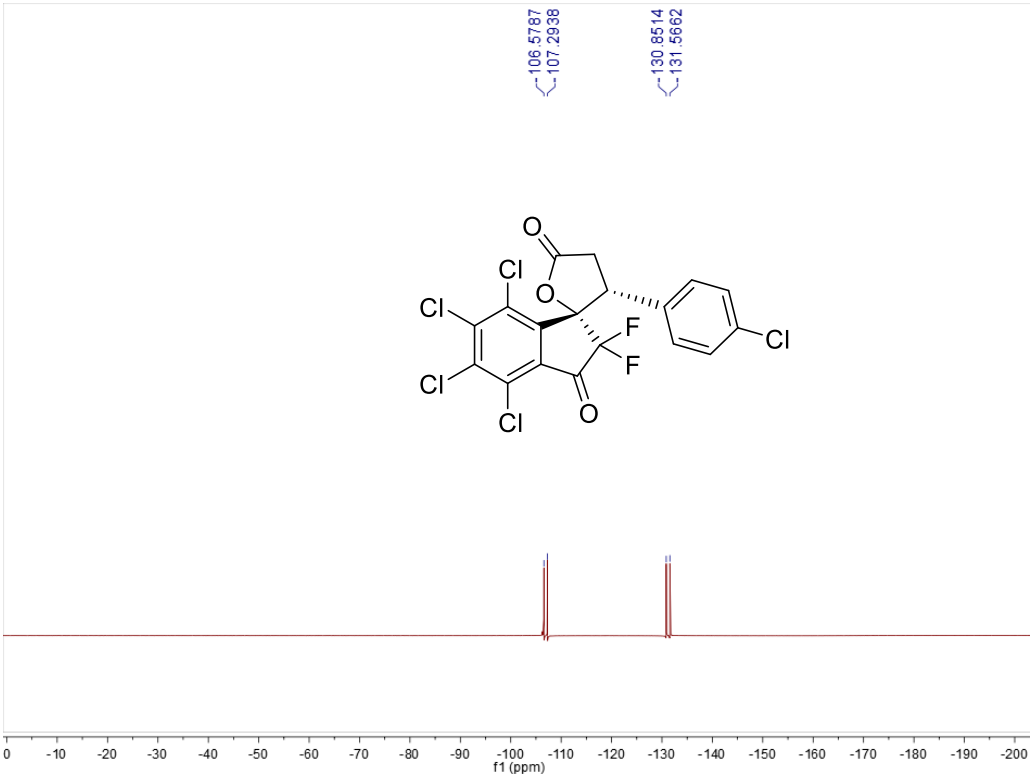


3y ^{1}H NMR (400 MHz, Chloroform-*d*)/^{13}C{H} NMR (101 MHz, Chloroform-*d*)

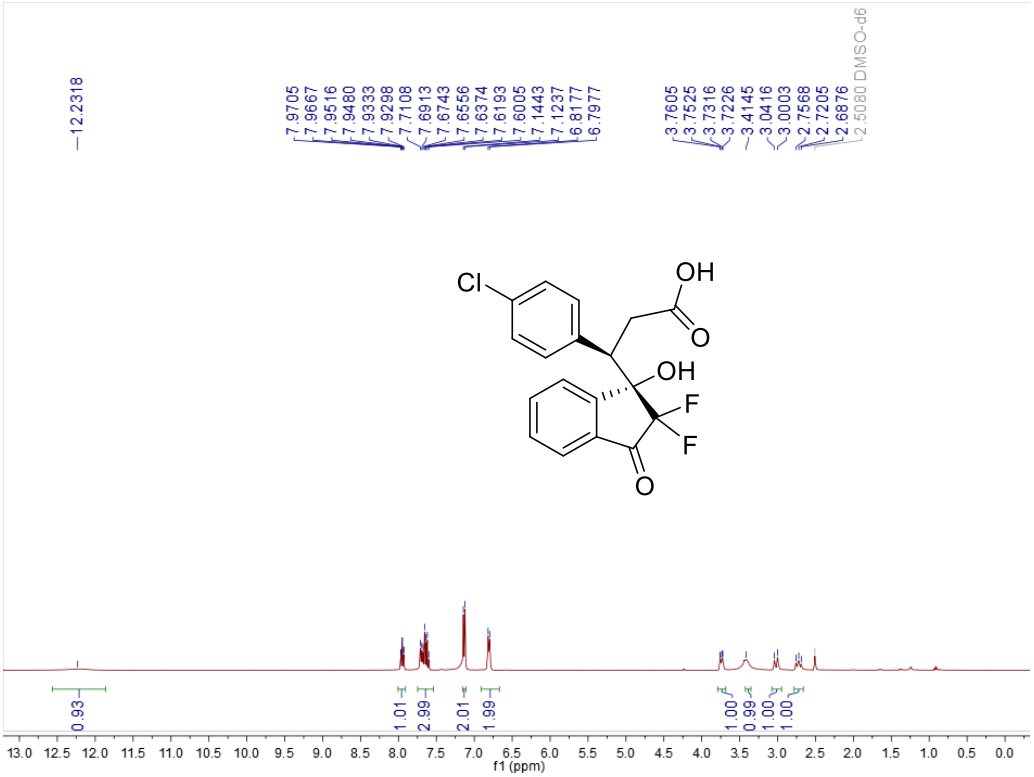


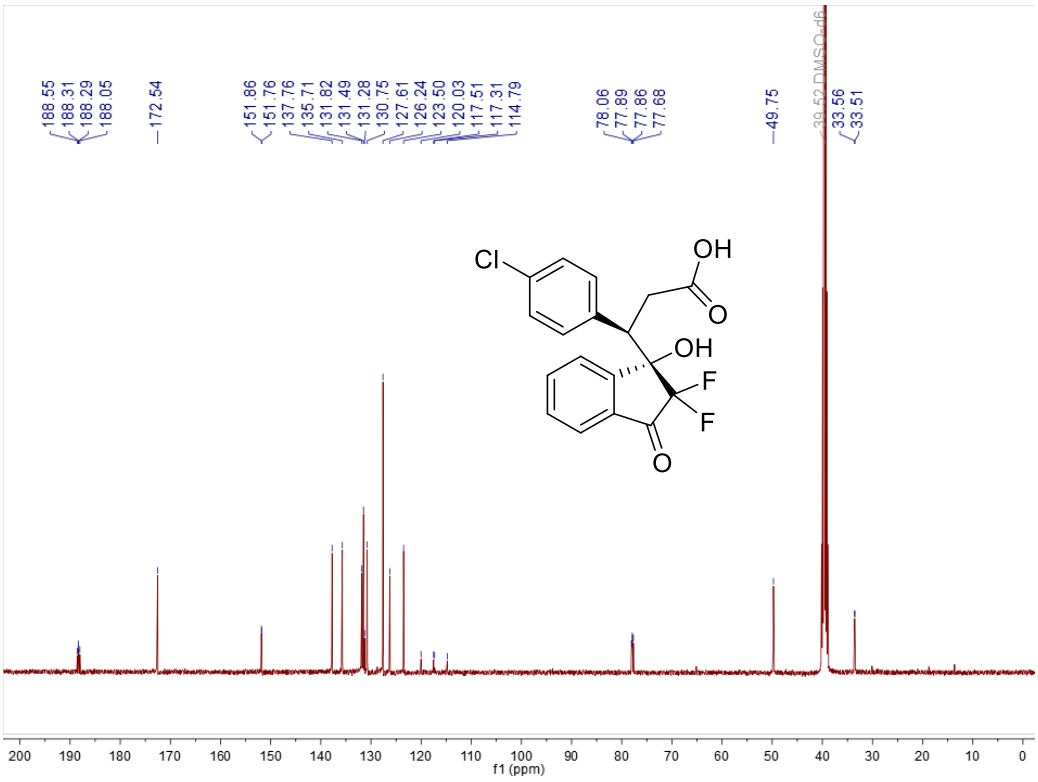


3y ^{19}F NMR (376 MHz, Chloroform-*d*)

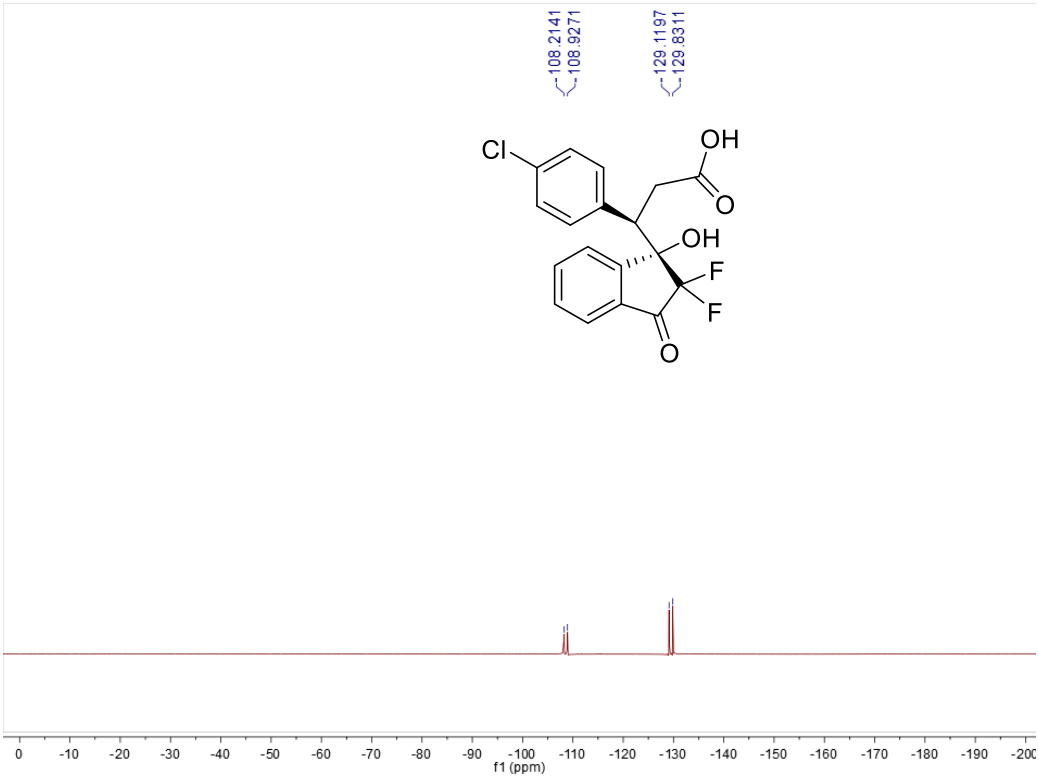


6 ^{1}H NMR (400 MHz, DMSO-d_6)/^{13}C{H} NMR (101 MHz, DMSO-d_6)

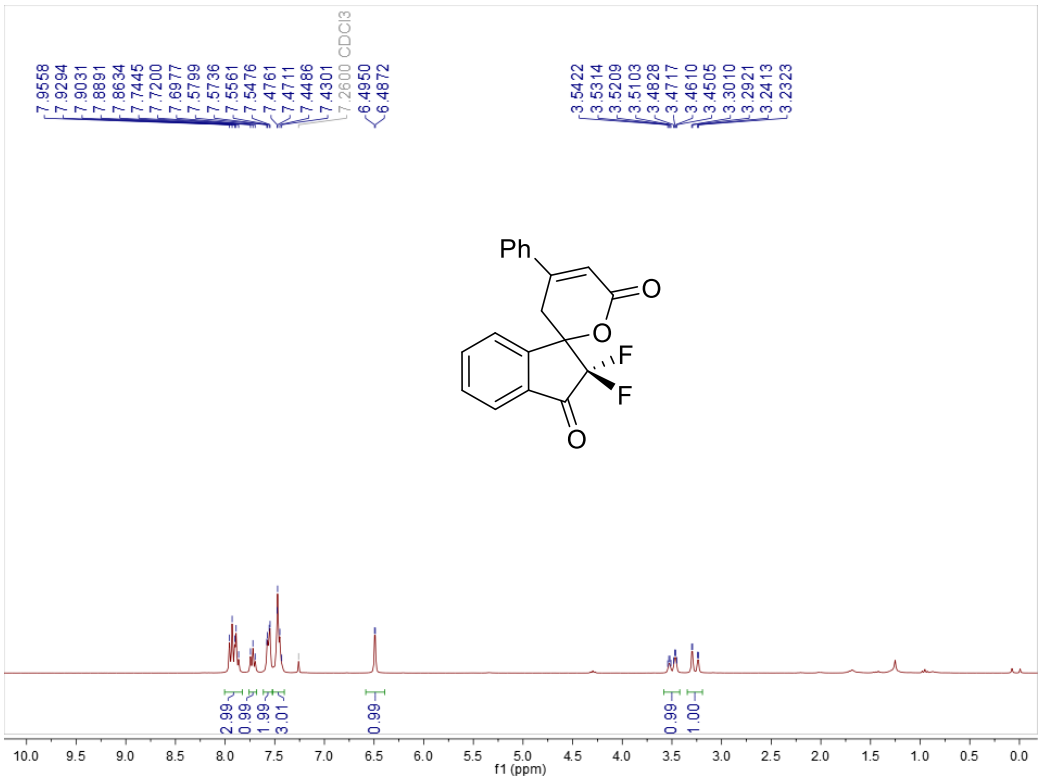


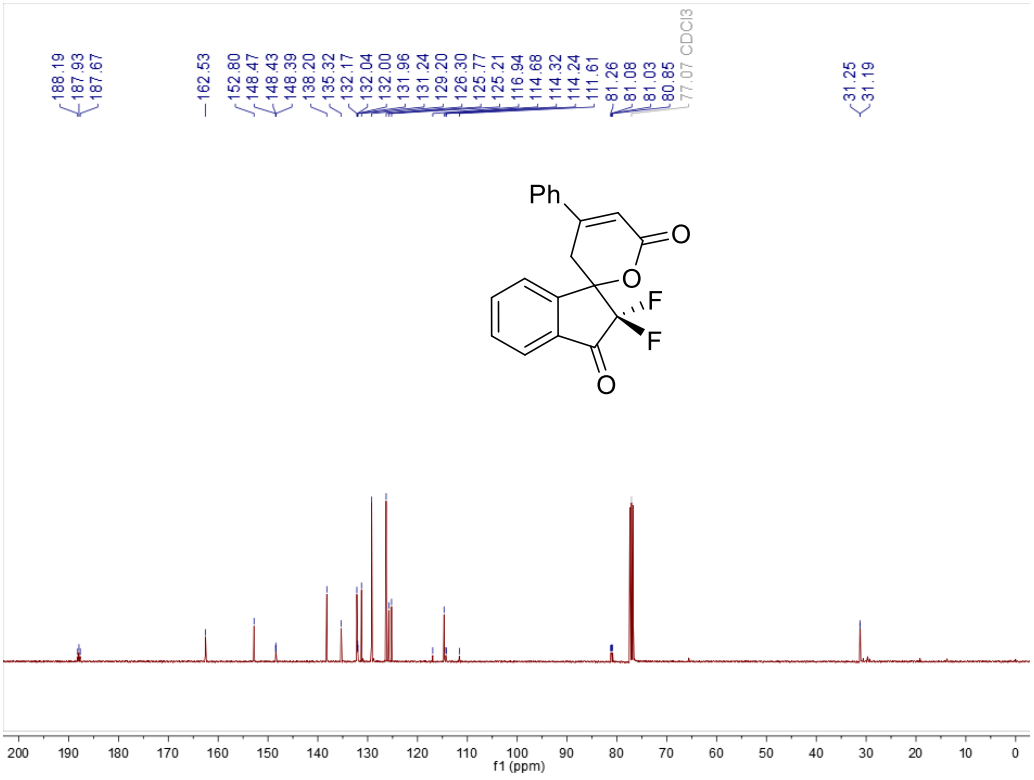


6 ^{19}F NMR (376 MHz, DMSO-d_6)

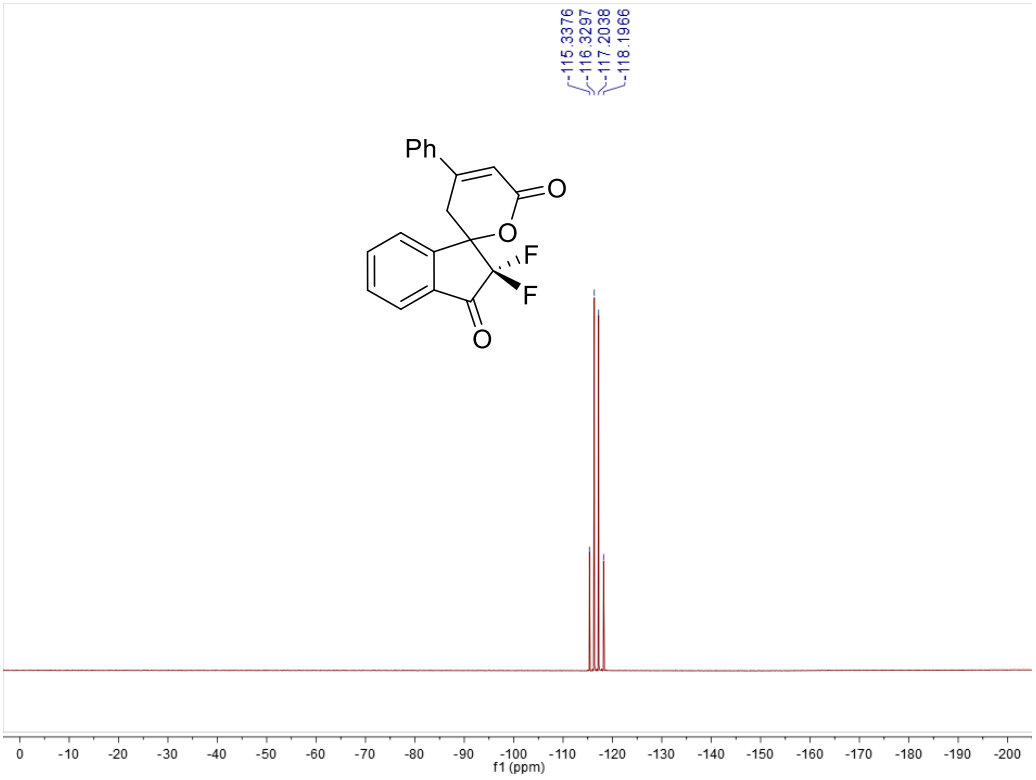


8 ^{1}H NMR (300 MHz, Chloroform-*d*)/^{13}C{H} NMR (101 MHz, Chloroform-*d*)



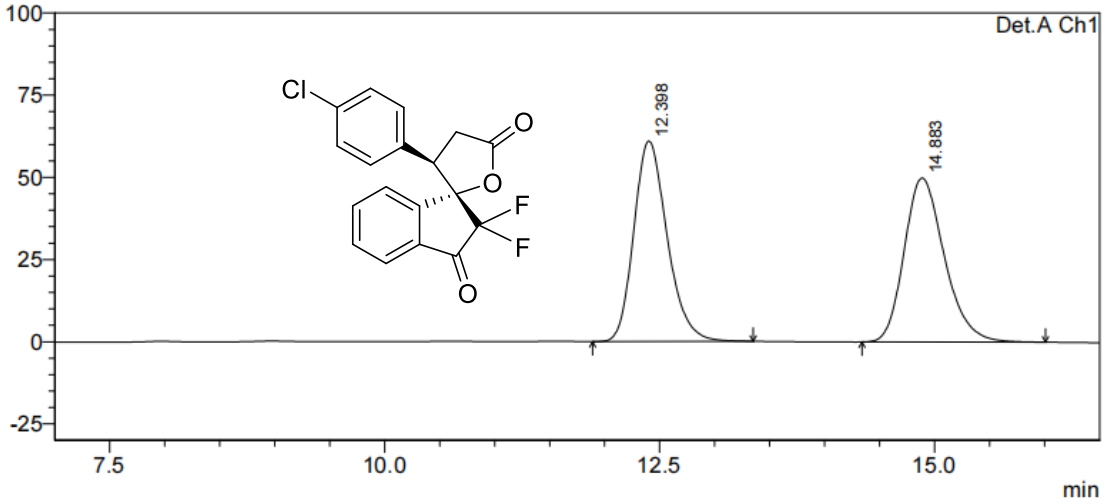


8 ^{19}F NMR (282 MHz, Chloroform-*d*)

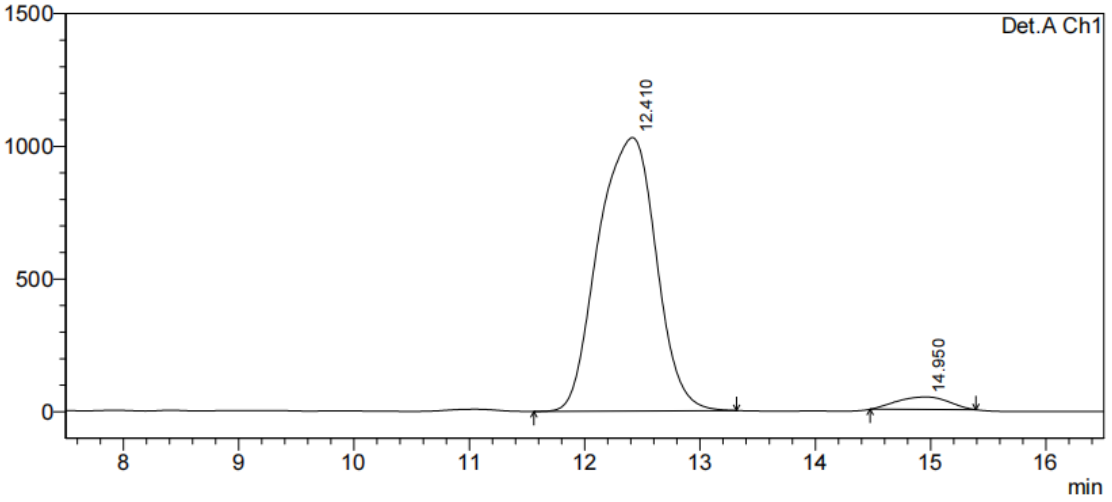


9. Copies of the HPLC spectra

3a

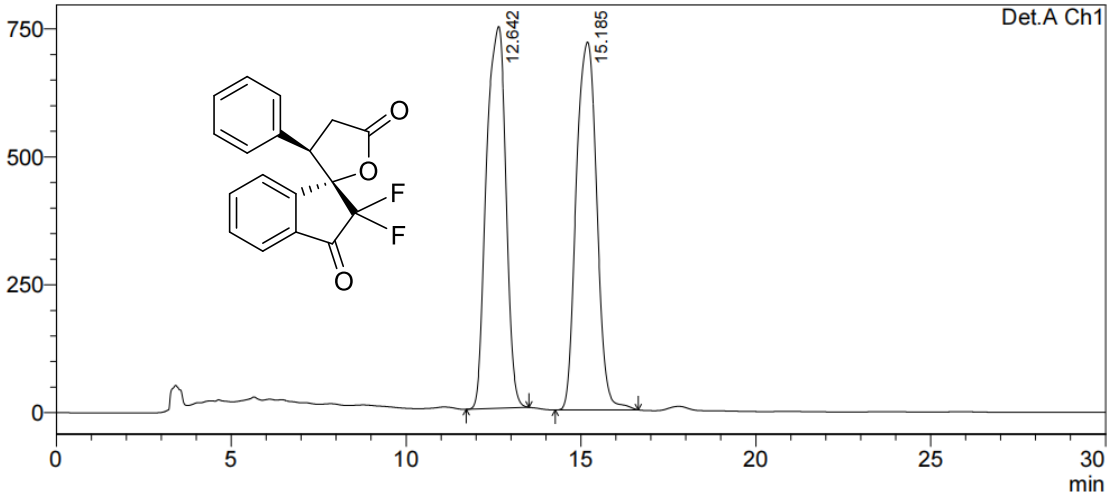


Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.398	1288268	60977	50.348	54.996
2	14.883	1270441	49899	49.652	45.004
Total		2558710	110876	100.000	100.000

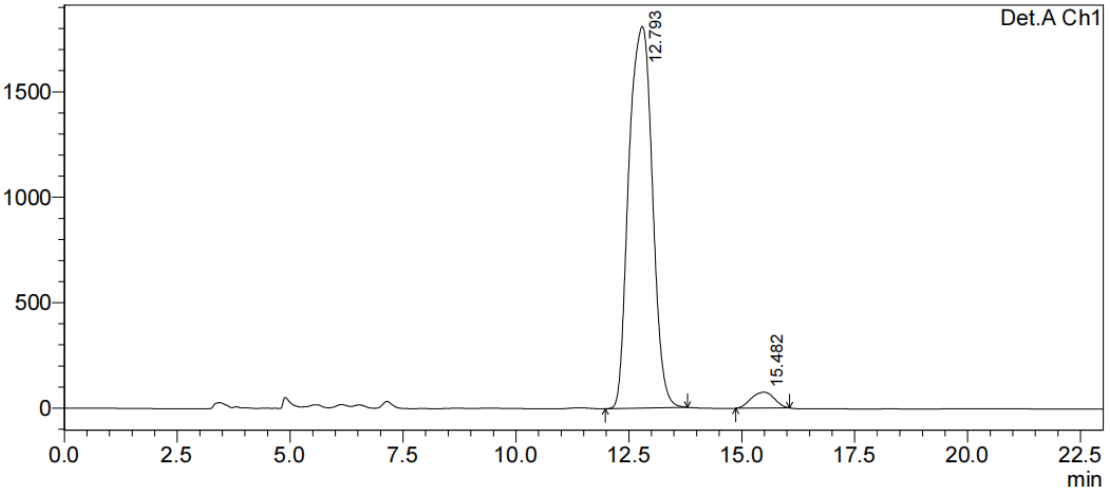


Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.410	36019641	1030178	96.038	95.607
2	14.950	1486114	47335	3.962	4.393
Total		37505755	1077513	100.000	100.000

3b

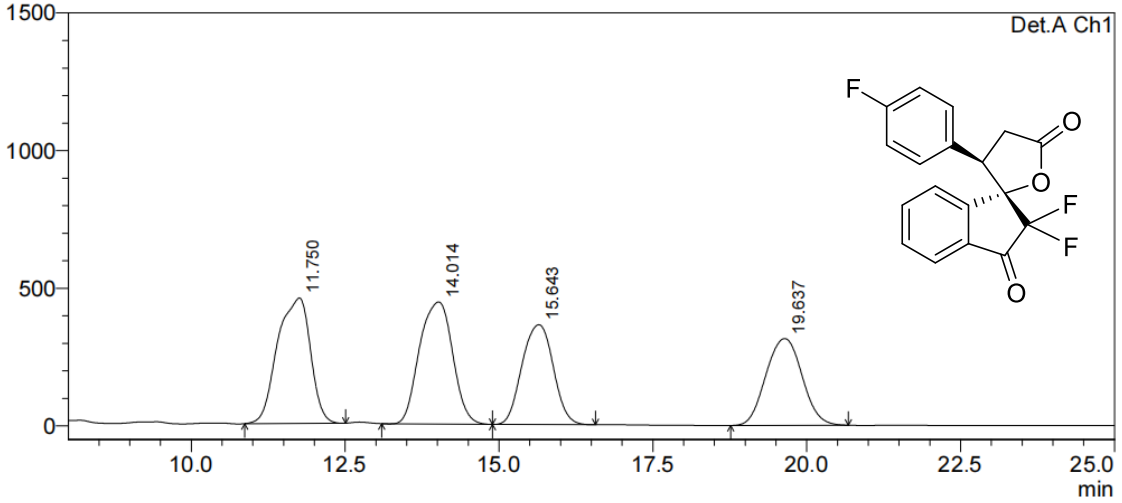


Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.642	28898023	745952	49.618	50.914
2	15.185	29343007	719165	50.382	49.086
Total		58241030	1465117	100.000	100.000

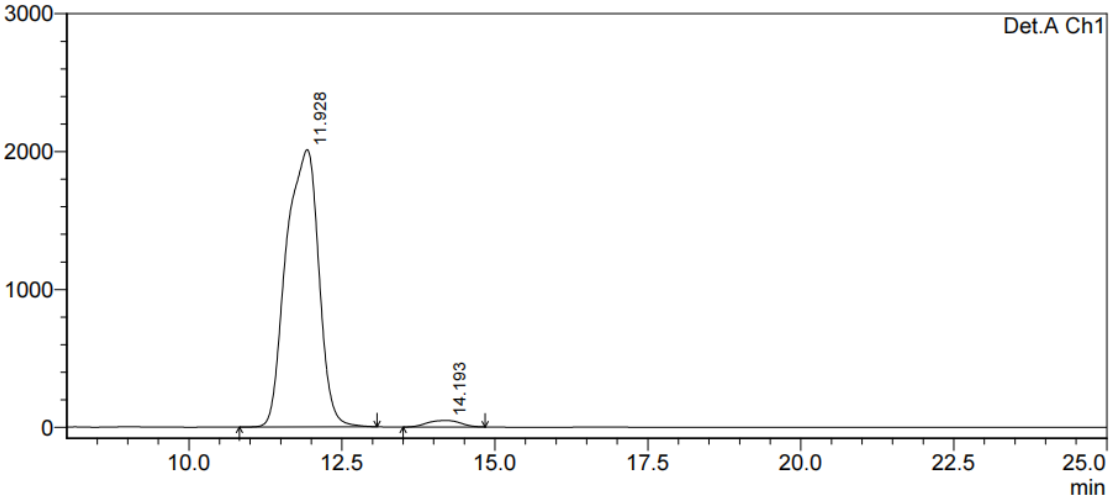


Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.793	65756566	1809342	96.078	95.997
2	15.482	2684255	75453	3.922	4.003
Total		68440821	1884795	100.000	100.000

3c

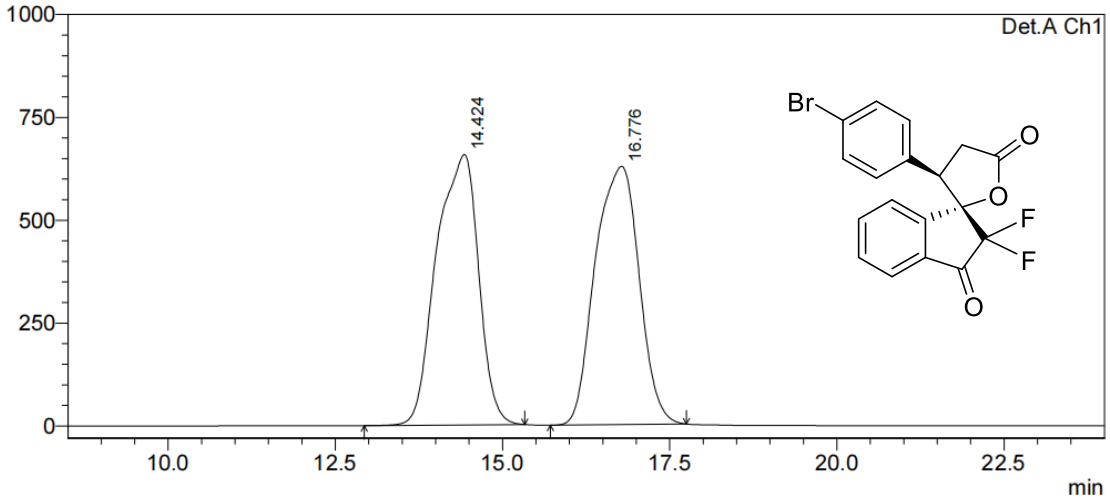


Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.750	16951030	455470	28.546	28.876
2	14.014	16664573	443712	28.064	28.131
3	15.643	12851173	362650	21.642	22.992
4	19.637	12914070	315485	21.748	20.001
Total		59380847	1577317	100.000	100.000

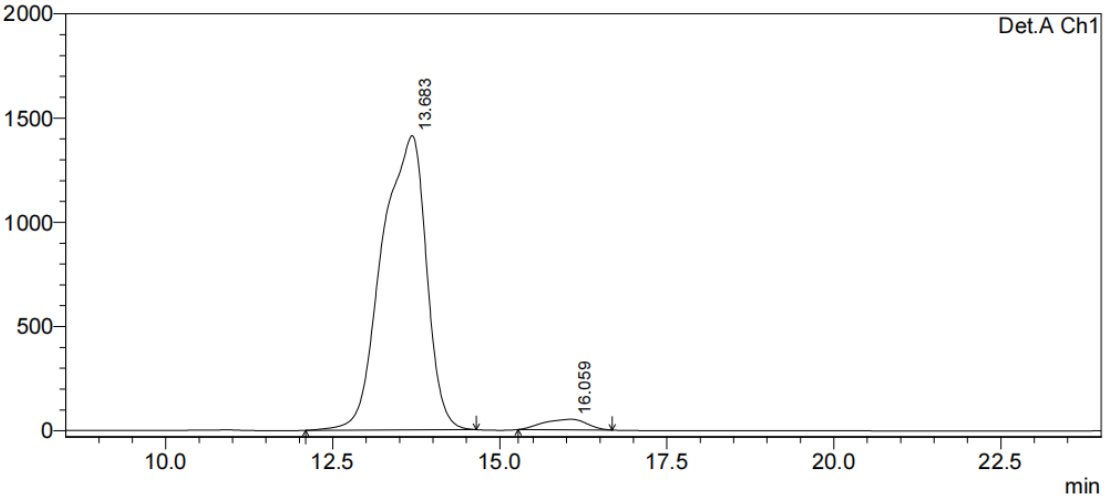


Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.928	74362663	2011650	97.666	97.728
2	14.193	1777079	46774	2.334	2.272
Total		76139741	2058424	100.000	100.000

3d

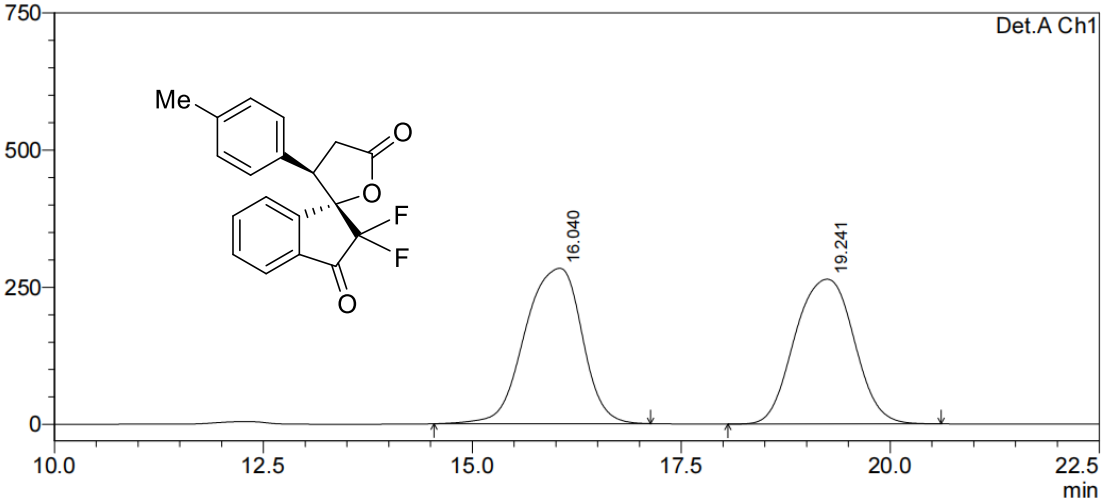


Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.424	28737197	657369	50.039	51.158
2	16.776	28692447	627610	49.961	48.842
Total		57429644	1284978	100.000	100.000

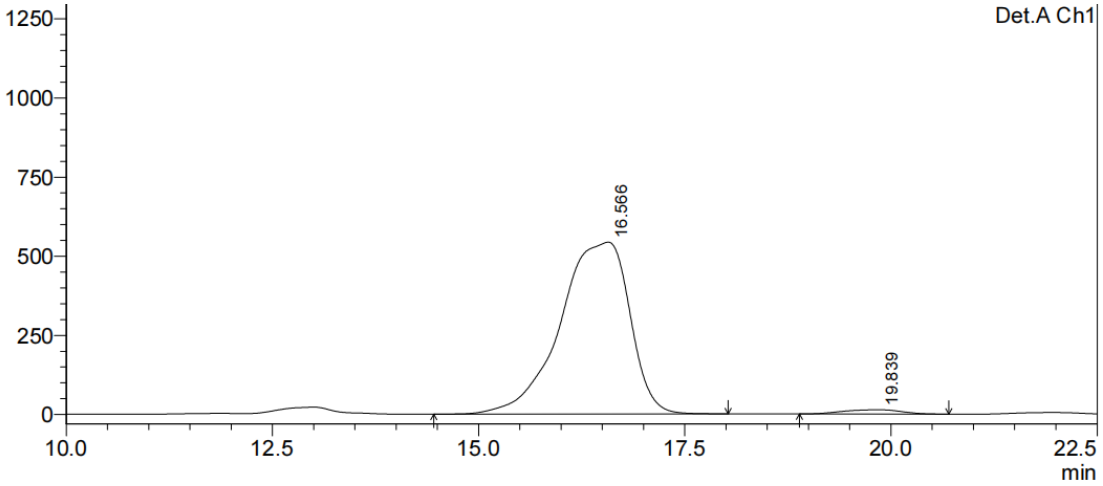


Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.683	65018598	1411645	96.613	96.539
2	16.059	2279231	50613	3.387	3.461
Total		67297829	1462258	100.000	100.000

3e

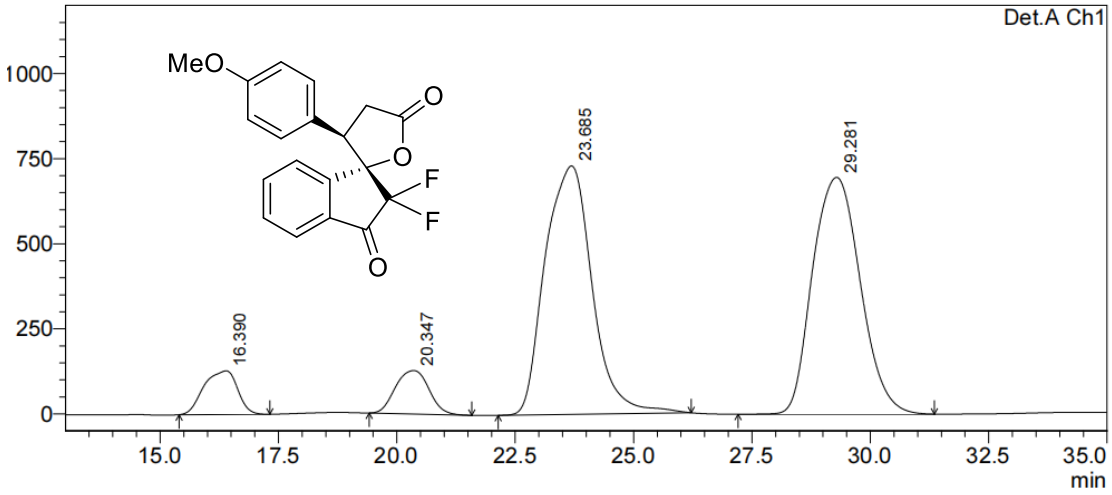


Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.040	13453603	283288	50.811	51.765
2	19.241	13024107	263975	49.189	48.235
Total		26477710	547263	100.000	100.000

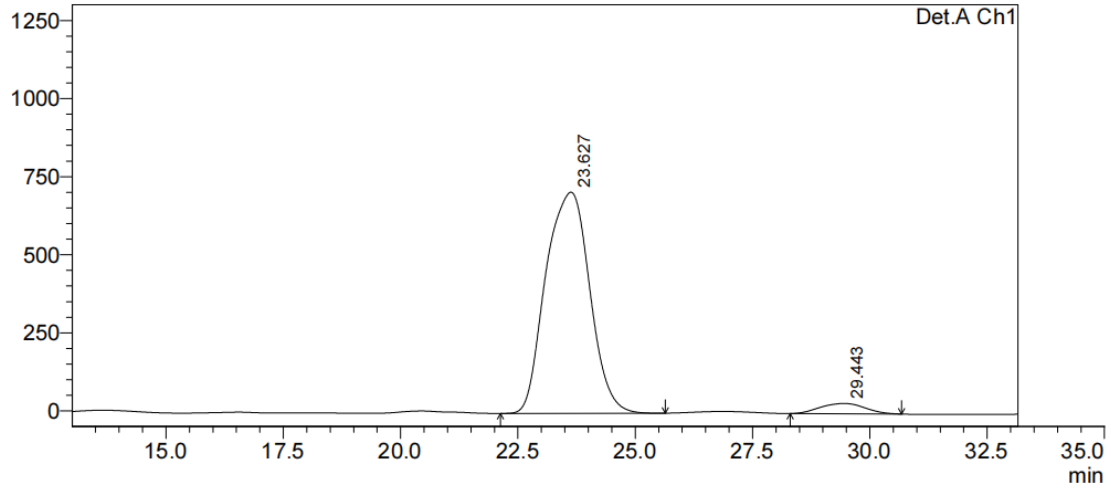


Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.566	31863574	542978	97.922	97.536
2	19.839	676141	13715	2.078	2.464
Total		32539715	556694	100.000	100.000

3f

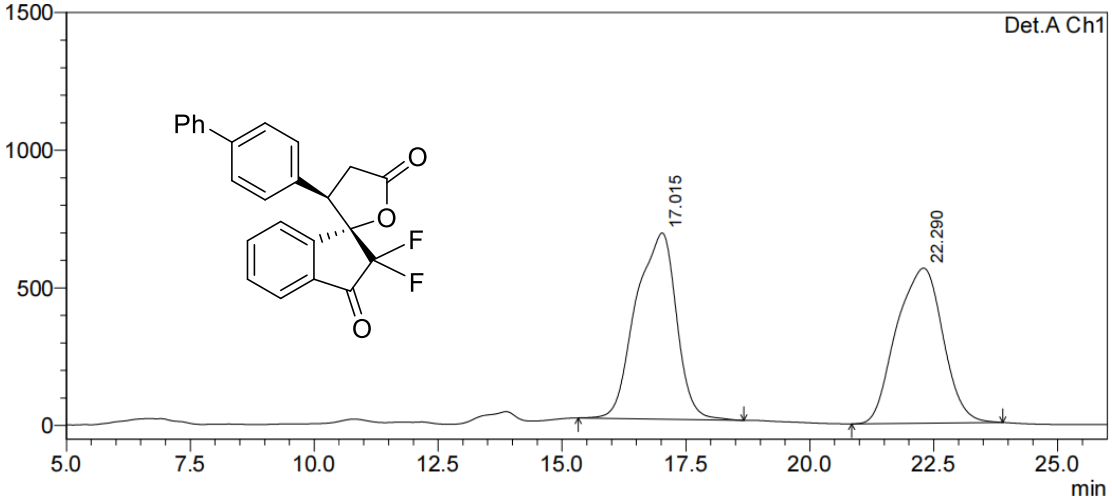


Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.390	6315382	128275	5.645	7.629
2	20.347	6293814	127618	5.626	7.590
3	23.685	50425190	729854	45.074	43.406
4	29.281	48836598	695719	43.654	41.376
Total		111870983	1681465	100.000	100.000

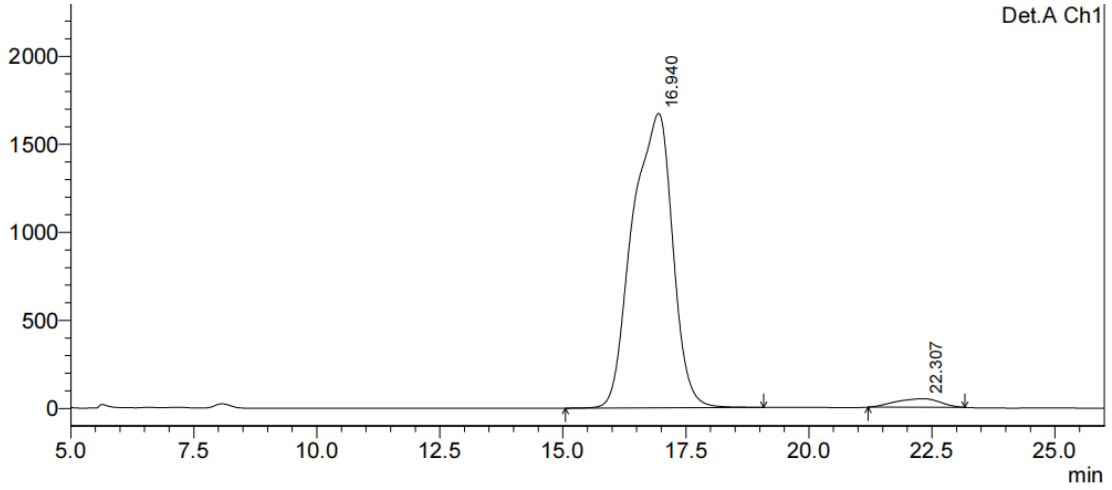


Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.627	46215890	708003	95.455	95.538
2	29.443	2200484	33066	4.545	4.462
Total		48416374	741069	100.000	100.000

3g

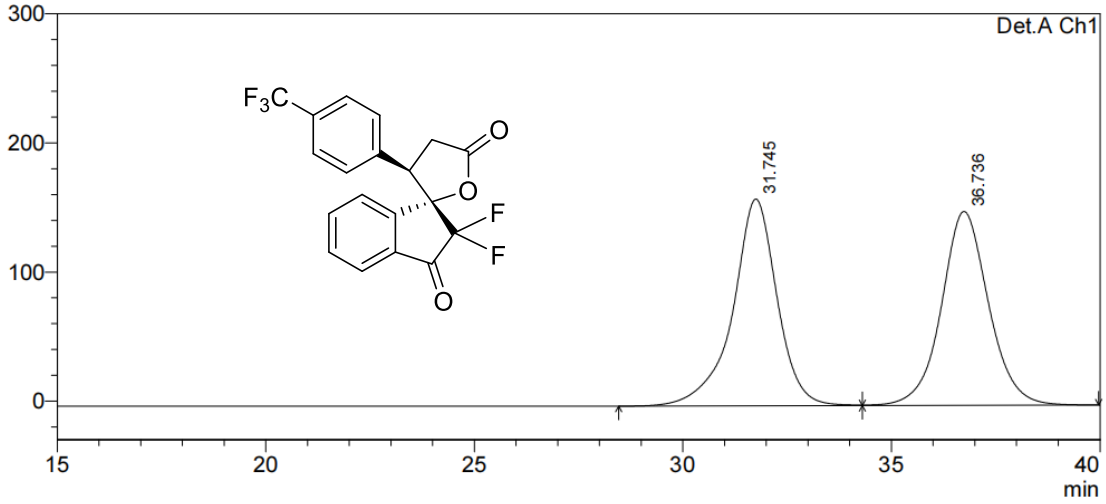


Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.015	38491535	676507	51.131	54.552
2	22.290	36788947	563618	48.869	45.448
Total		75280483	1240126	100.000	100.000

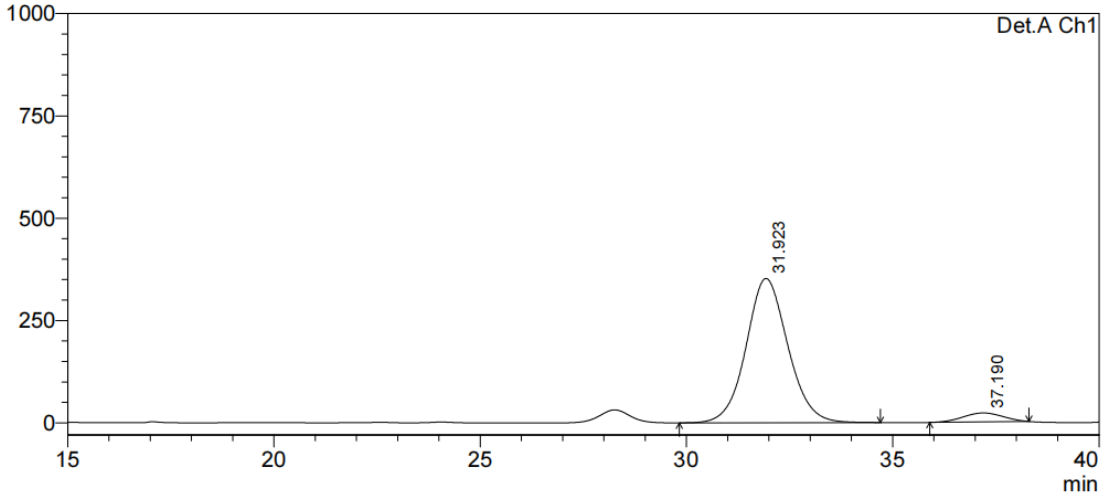


Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.940	94868031	1672795	96.883	97.159
2	22.307	3052412	48921	3.117	2.841
Total		97920444	1721715	100.000	100.000

3h

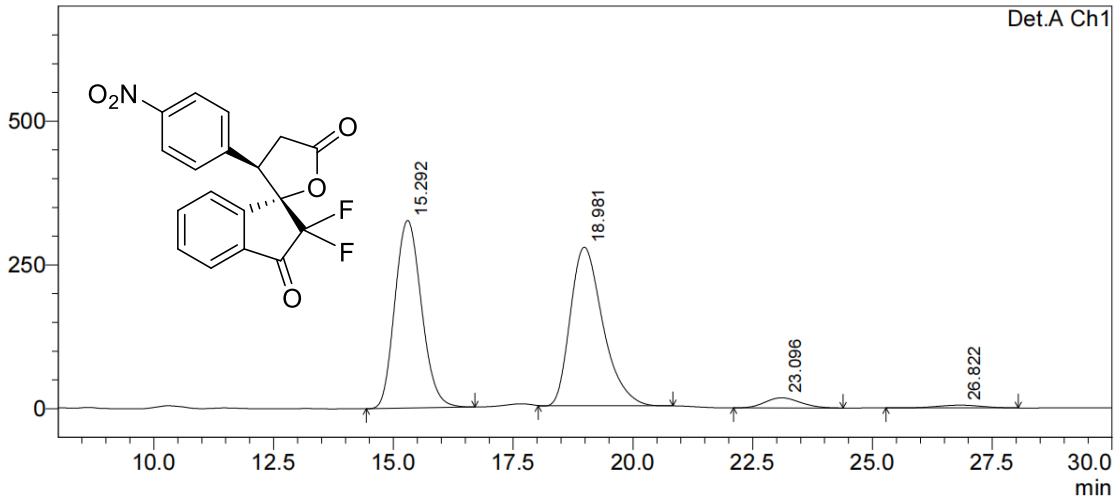


Peak#	Ret. Time	Area	Height	Area %	Height %
1	31.745	11883464	160211	50.108	51.604
2	36.736	11832381	150250	49.892	48.396
Total		23715845	310460	100.000	100.000

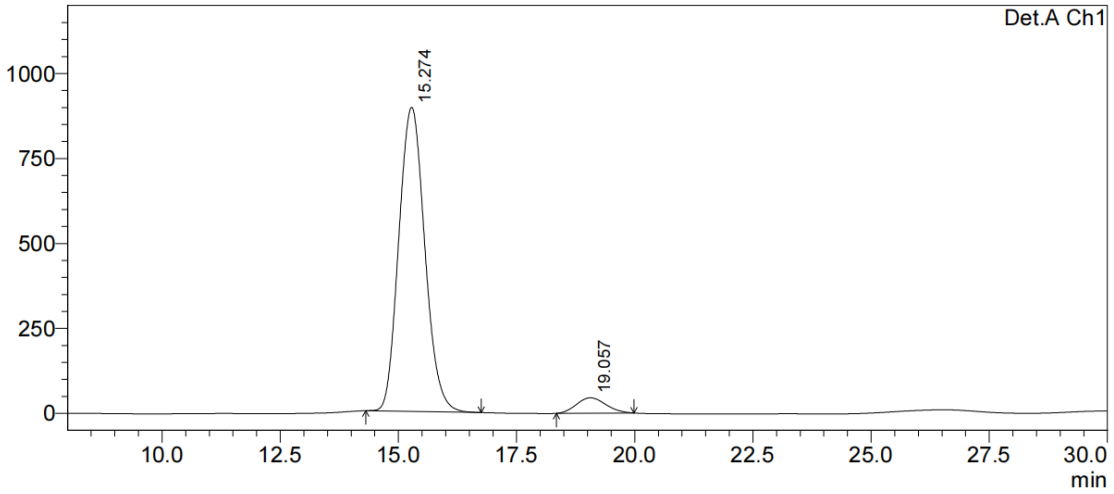


Peak#	Ret. Time	Area	Height	Area %	Height %
1	31.923	24869296	352533	94.421	94.150
2	37.190	1469472	21906	5.579	5.850
Total		26338768	374438	100.000	100.000

3i

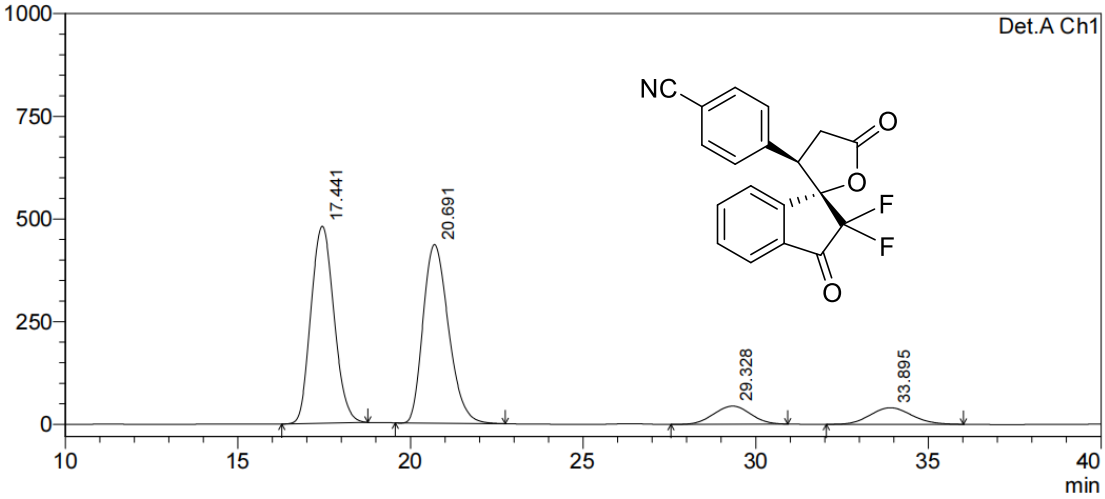


Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.292	12625336	326402	47.003	52.268
2	18.981	13032256	275718	48.518	44.152
3	23.096	905884	17624	3.373	2.822
4	26.822	297374	4729	1.107	0.757
Total		26860851	624473	100.000	100.000

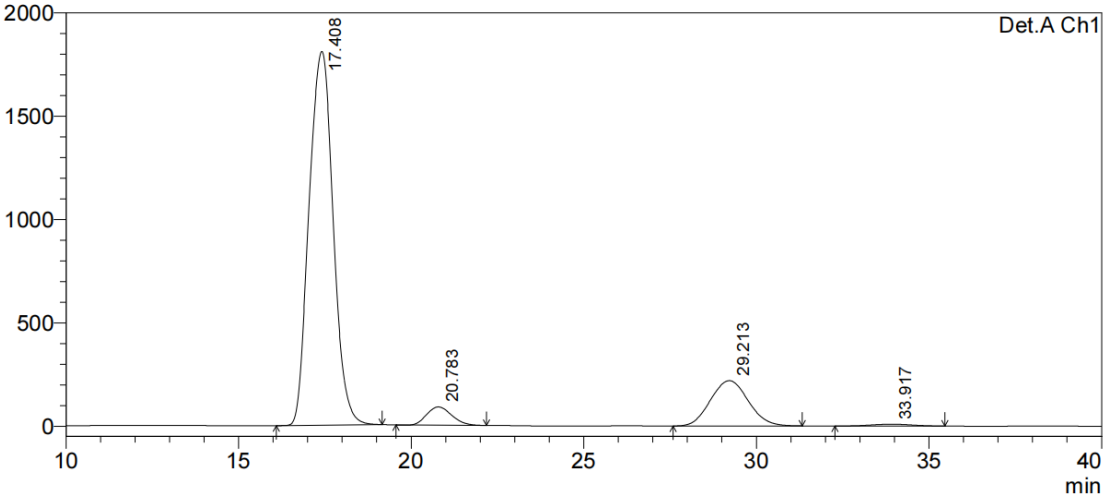


Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.274	34298763	894662	94.618	95.188
2	19.057	1950886	45229	5.382	4.812
Total		36249649	939892	100.000	100.000

3j

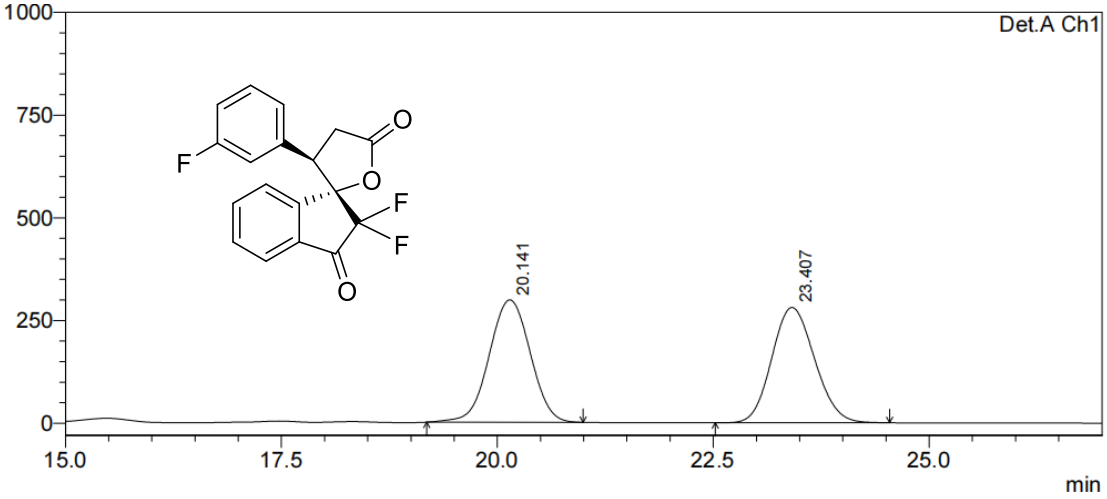


Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.441	22318893	479939	43.475	48.002
2	20.691	22353397	435442	43.542	43.552
3	29.328	3286130	44141	6.401	4.415
4	33.895	3379397	40304	6.583	4.031
Total		51337817	999826	100.000	100.000

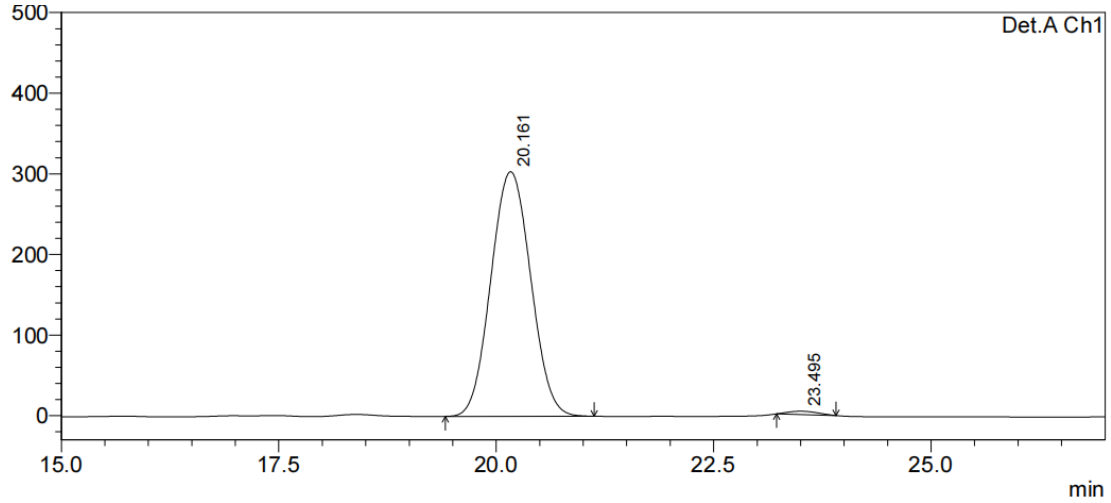


Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.408	87855464	1809210	80.055	85.101
2	20.783	4439636	88445	4.045	4.160
3	29.213	16708746	219248	15.225	10.313
4	33.917	740519	9056	0.675	0.426
Total		109744365	2125958	100.000	100.000

3k

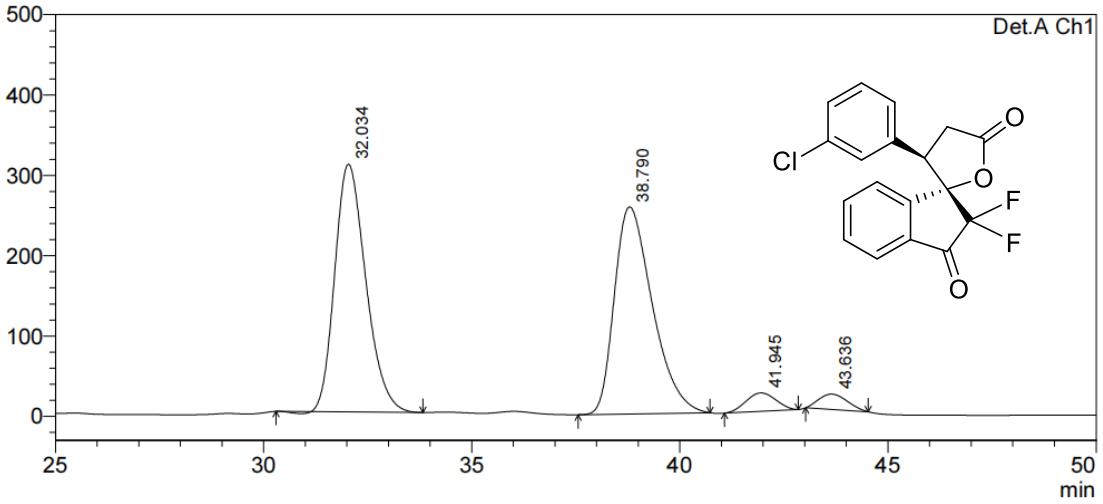


Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.141	9874816	298066	50.467	51.494
2	23.407	9692206	280774	49.533	48.506
Total		19567022	578839	100.000	100.000

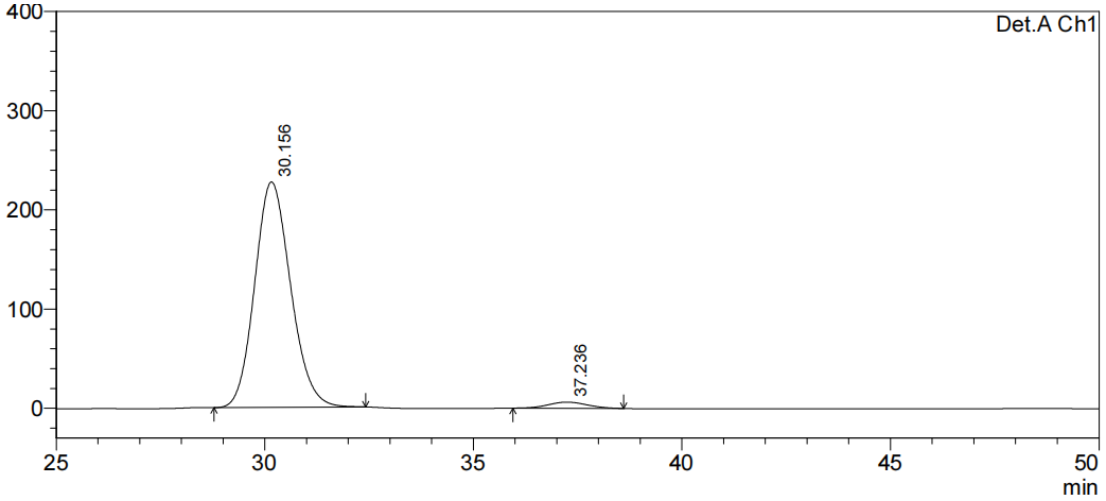


Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.161	9681038	303495	98.999	98.671
2	23.495	97884	4086	1.001	1.329
Total		9778922	307581	100.000	100.000

3l

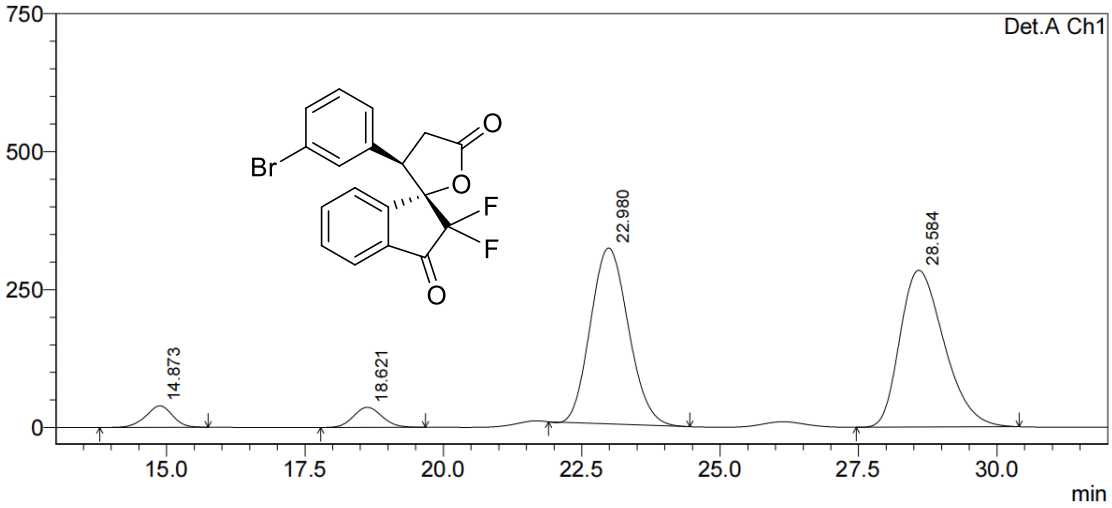


Peak#	Ret. Time	Area	Height	Area %	Height %
1	32.034	15967380	308380	46.472	50.722
2	38.790	16339999	257701	47.556	42.387
3	41.945	1140760	22874	3.320	3.762
4	43.636	911293	19021	2.652	3.129
Total		34359433	607975	100.000	100.000

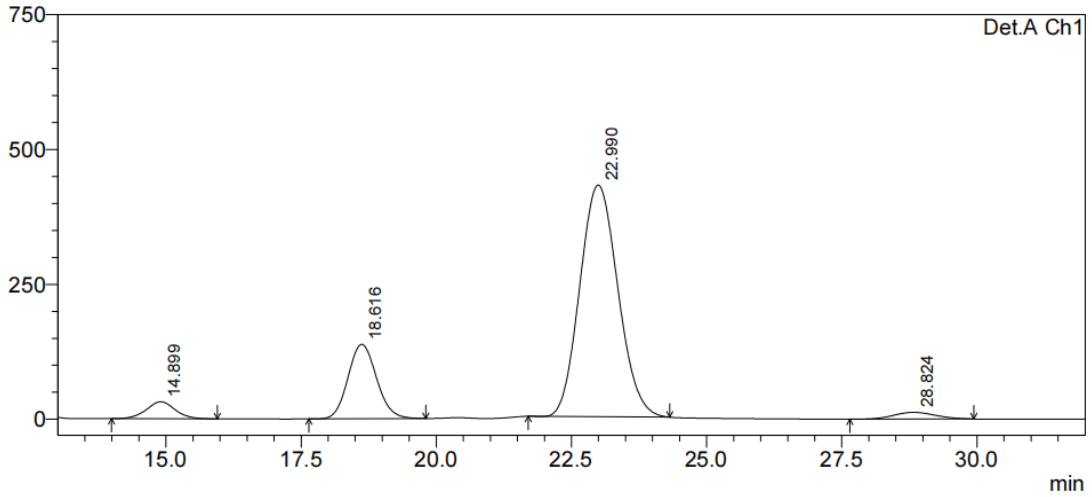


Peak#	Ret. Time	Area	Height	Area %	Height %
1	30.156	13607735	227261	97.091	97.331
2	37.236	407719	6231	2.909	2.669
Total		14015454	233492	100.000	100.000

3m

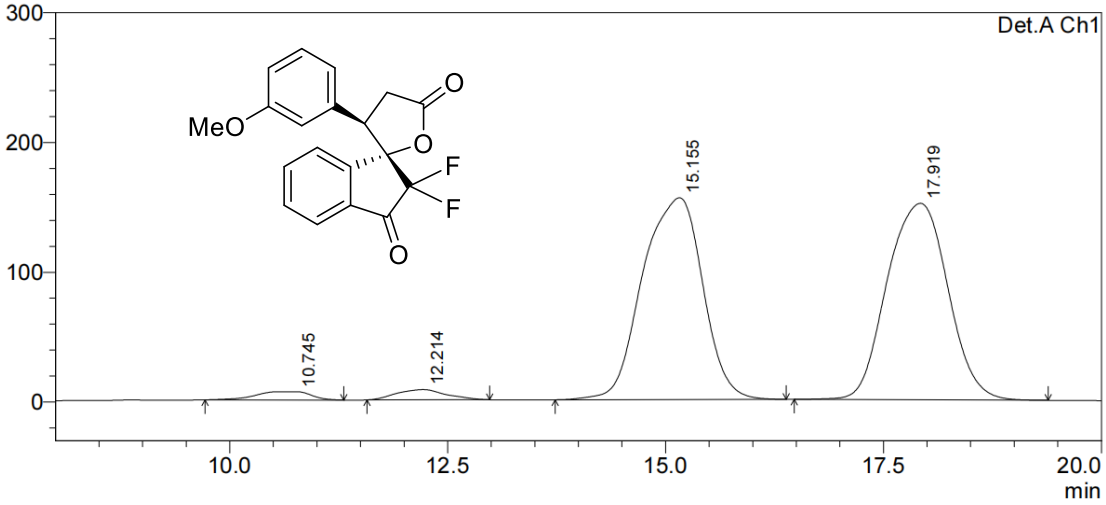


Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.873	1315800	38826	3.909	5.724
2	18.621	1306884	36416	3.883	5.368
3	22.980	15235459	318853	45.266	47.004
4	28.584	15799724	284251	46.942	41.904
Total		33657867	678345	100.000	100.000

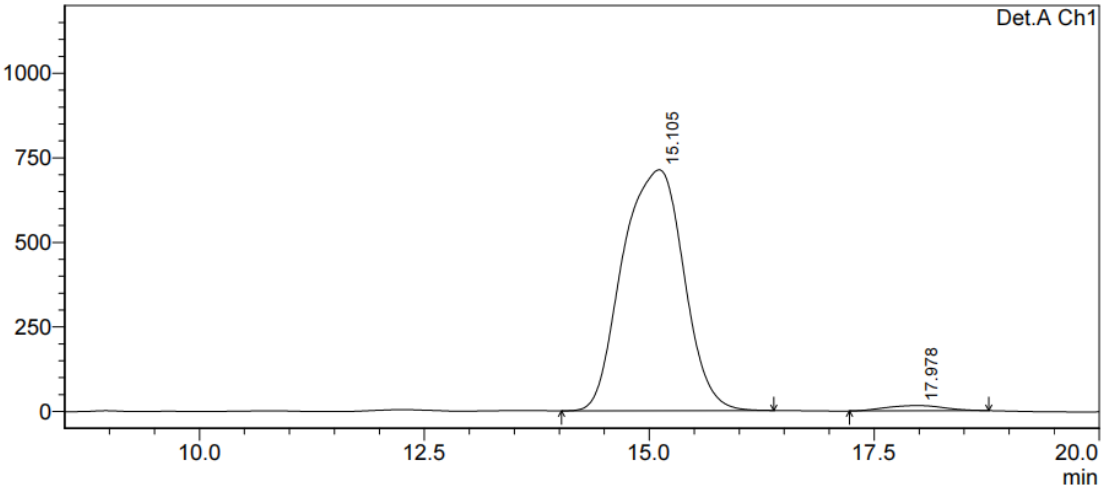


Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.899	1171635	31575	4.185	5.163
2	18.616	5069859	137966	18.110	22.561
3	22.990	21084618	429541	75.315	70.240
4	28.824	669147	12451	2.390	2.036
Total		27995260	611533	100.000	100.000

3n

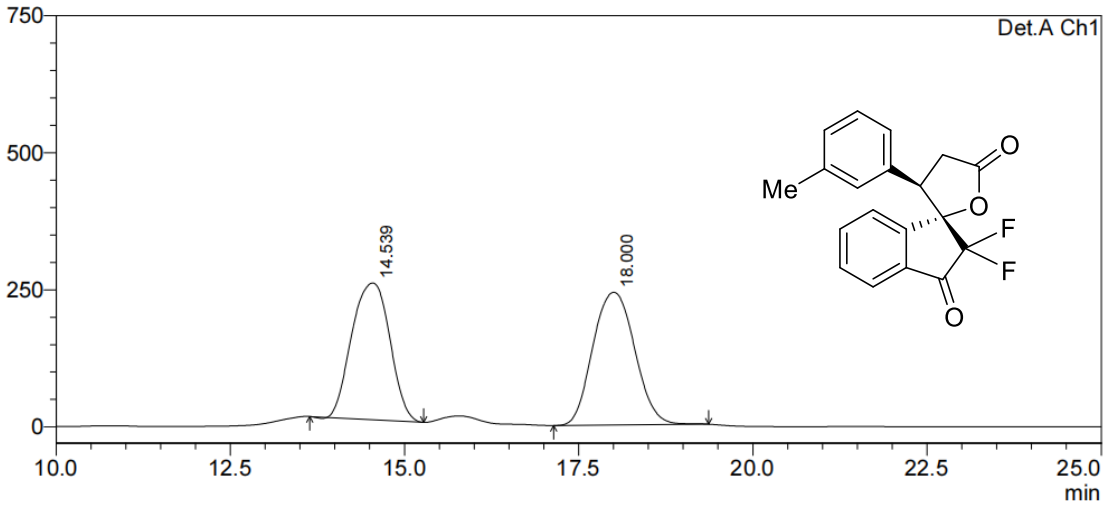


Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.745	279105	6372	1.808	1.983
2	12.214	312360	7902	2.024	2.459
3	15.155	7478779	155583	48.449	48.411
4	17.919	7366307	151520	47.720	47.147
Total		15436550	321377	100.000	100.000

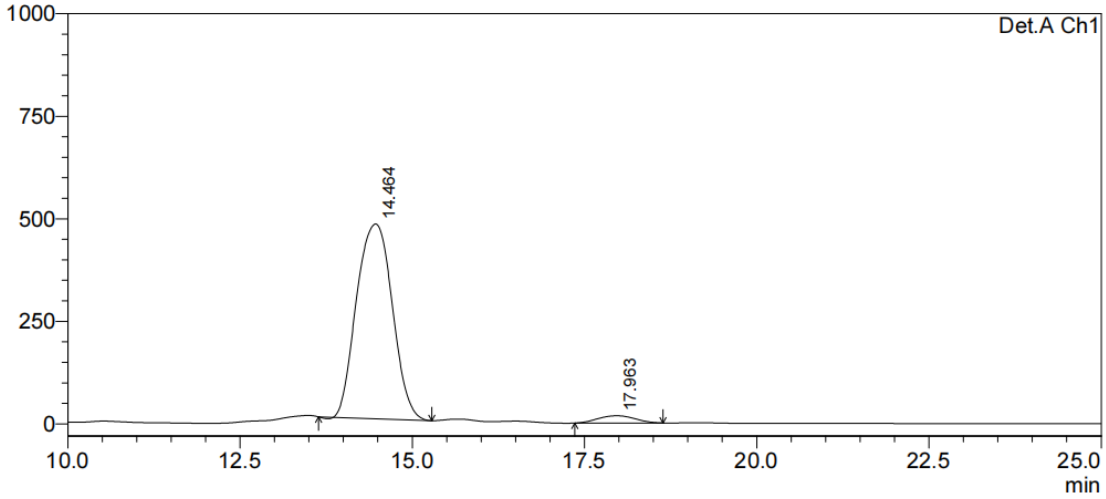


Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.105	33763376	712216	97.960	97.861
2	17.978	703088	15570	2.040	2.139
Total		34466464	727787	100.000	100.000

3o

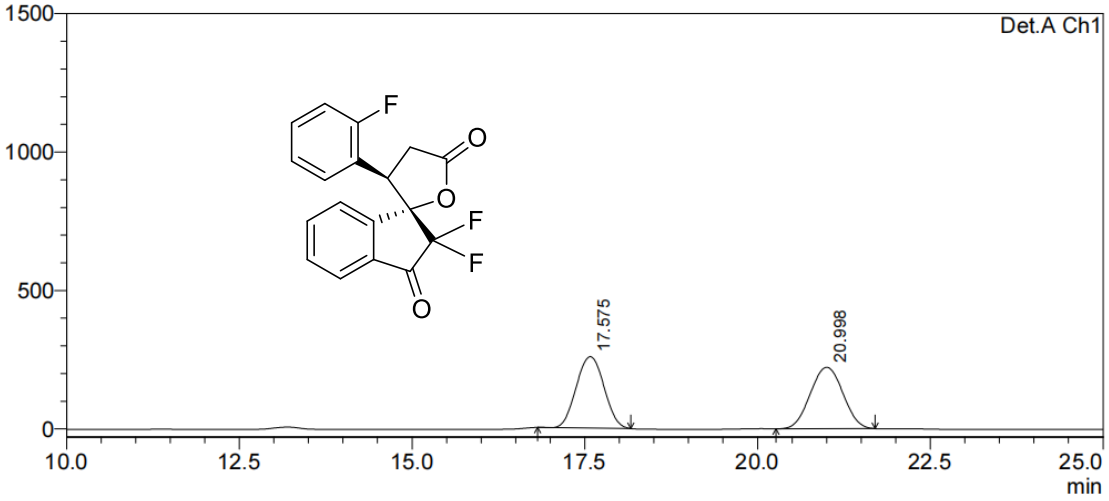


Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.539	9500554	249430	48.342	50.746
2	18.000	10152158	242096	51.658	49.254
Total		19652712	491526	100.000	100.000

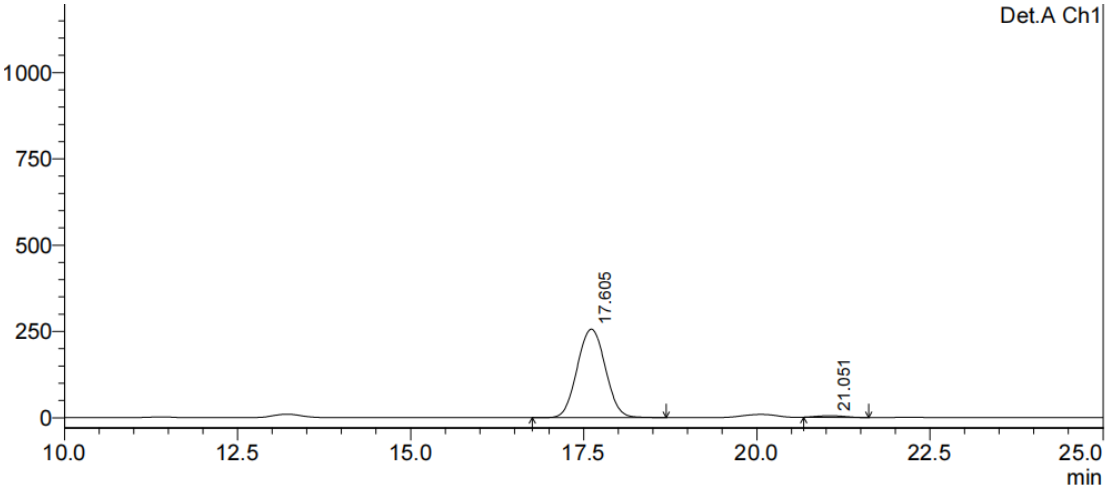


Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.464	17194368	475114	96.307	96.418
2	17.963	659328	17653	3.693	3.582
Total		17853695	492767	100.000	100.000

3p

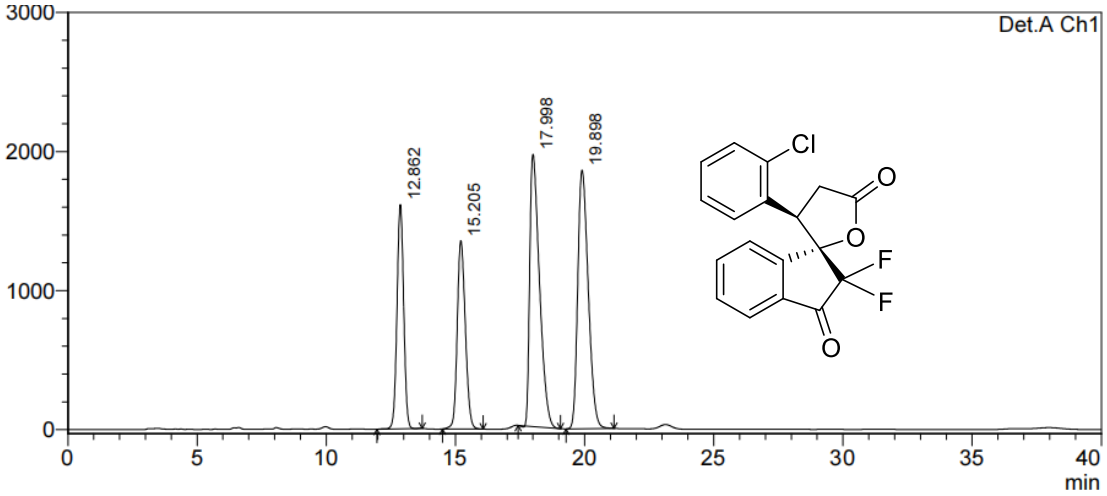


Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.575	7208230	258151	49.667	53.755
2	20.998	7305029	222086	50.333	46.245
Total		14513260	480237	100.000	100.000

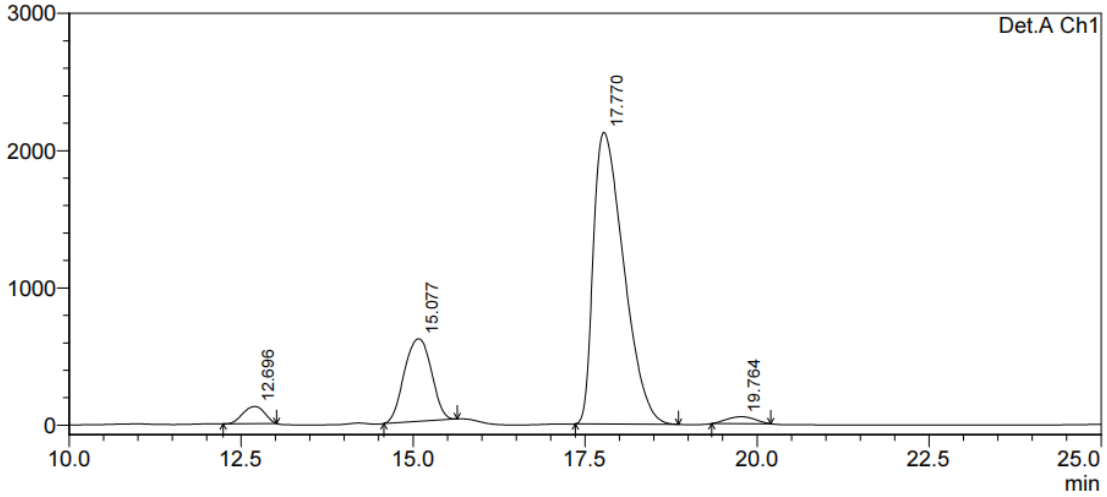


Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.605	7241720	256313	98.232	98.211
2	21.051	130318	4670	1.768	1.789
Total		7372037	260983	100.000	100.000

3q

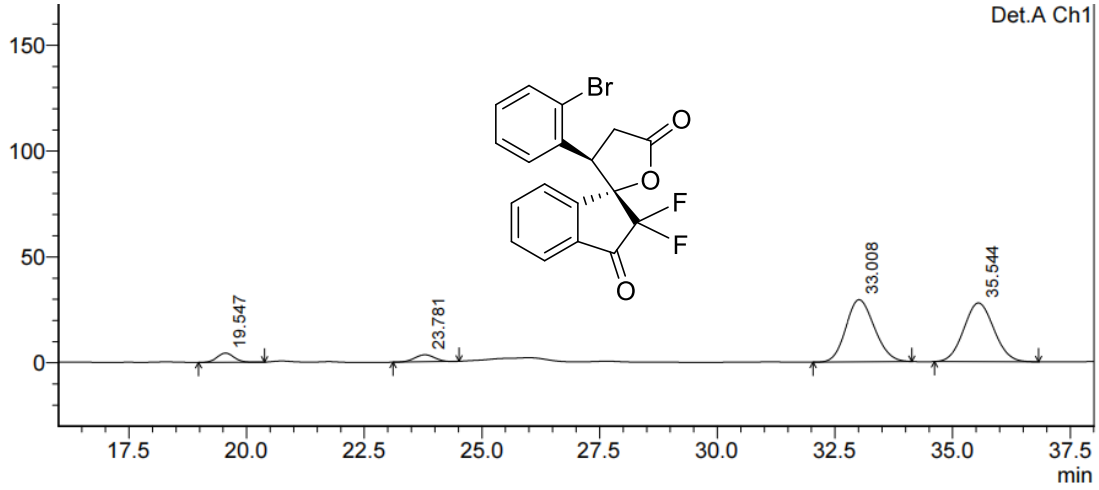


Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.862	28961247	1613444	17.862	23.773
2	15.205	29483837	1355190	18.184	19.968
3	17.998	51236523	1958613	31.600	28.859
4	19.898	52457477	1859704	32.353	27.401
Total		162139084	6786951	100.000	100.000

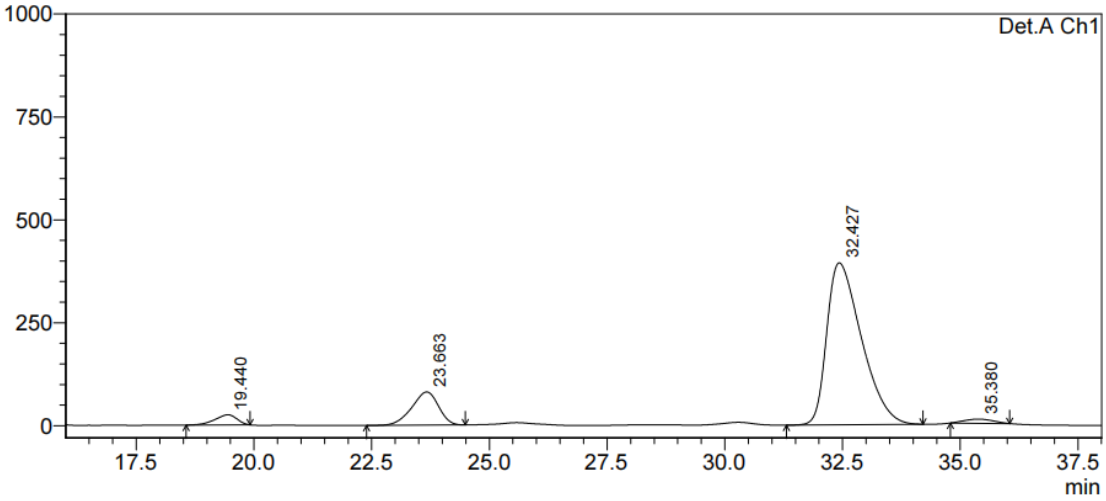


Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.696	2749489	124771	3.198	4.299
2	15.077	16523369	601147	19.221	20.713
3	17.770	65248536	2125697	75.900	73.244
4	19.764	1445422	50601	1.681	1.744
Total		85966816	2902217	100.000	100.000

3r

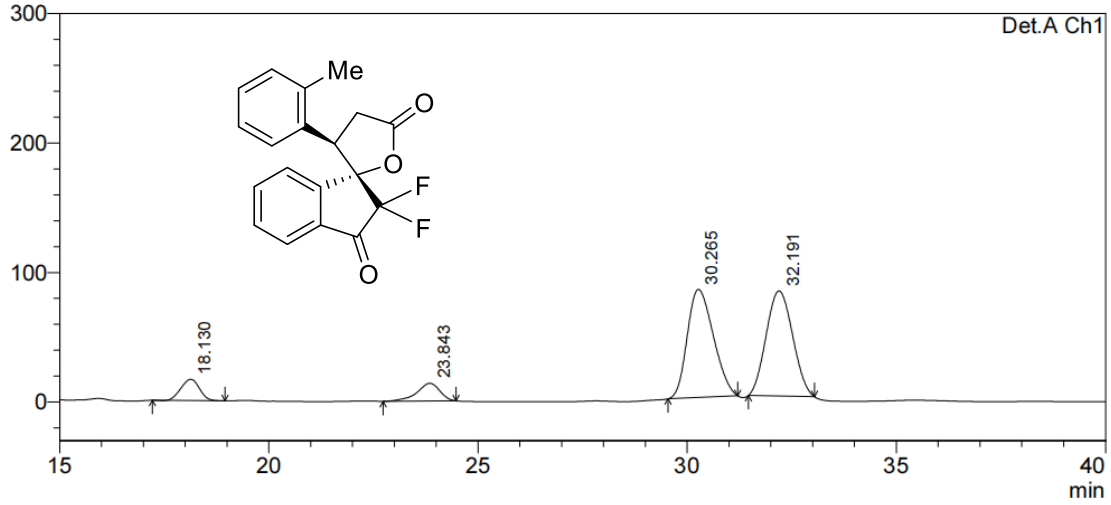


Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.547	106893	4344	3.991	6.702
2	23.781	95801	3313	3.577	5.112
3	33.008	1241228	29402	46.344	45.360
4	35.544	1234366	27759	46.088	42.826
Total		2678288	64819	100.000	100.000

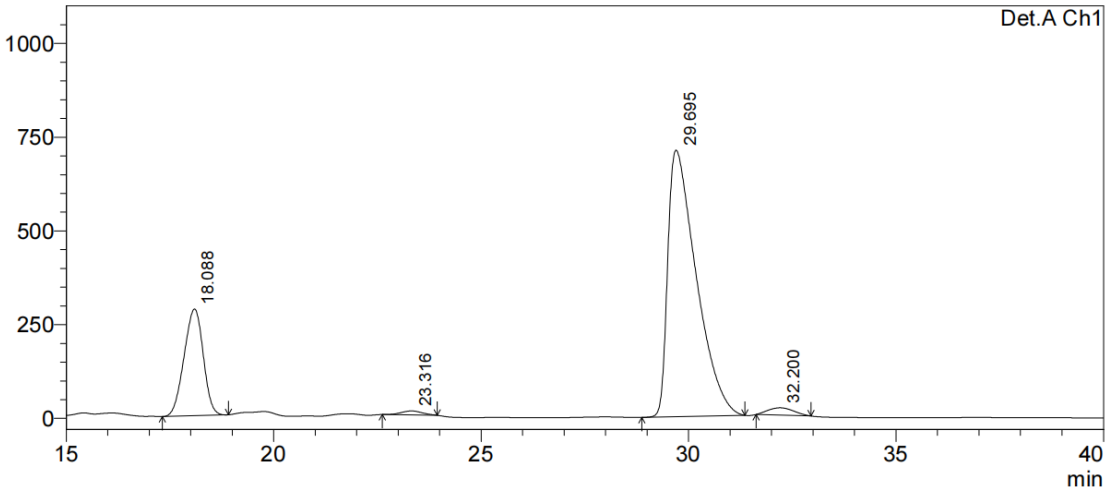


Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.440	803693	24735	3.269	4.860
2	23.663	3193420	80762	12.991	15.867
3	32.427	20164744	393555	82.030	77.321
4	35.380	420233	9936	1.710	1.952
Total		24582089	508989	100.000	100.000

3s

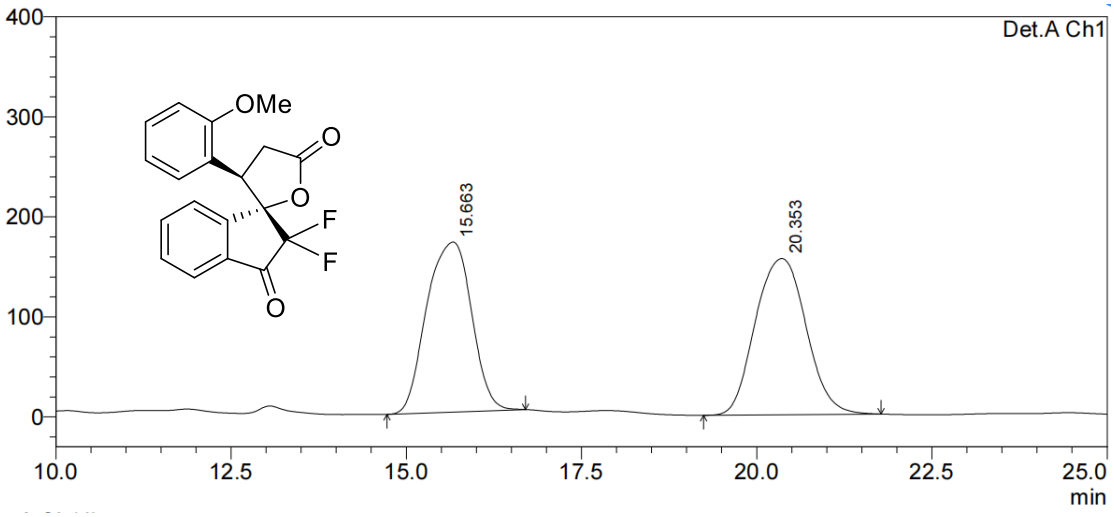


Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.130	509927	16468	6.200	8.453
2	23.843	518296	13664	6.302	7.014
3	30.265	3621636	83525	44.037	42.874
4	32.191	3574127	81158	43.460	41.659
Total		8223986	194814	100.000	100.000

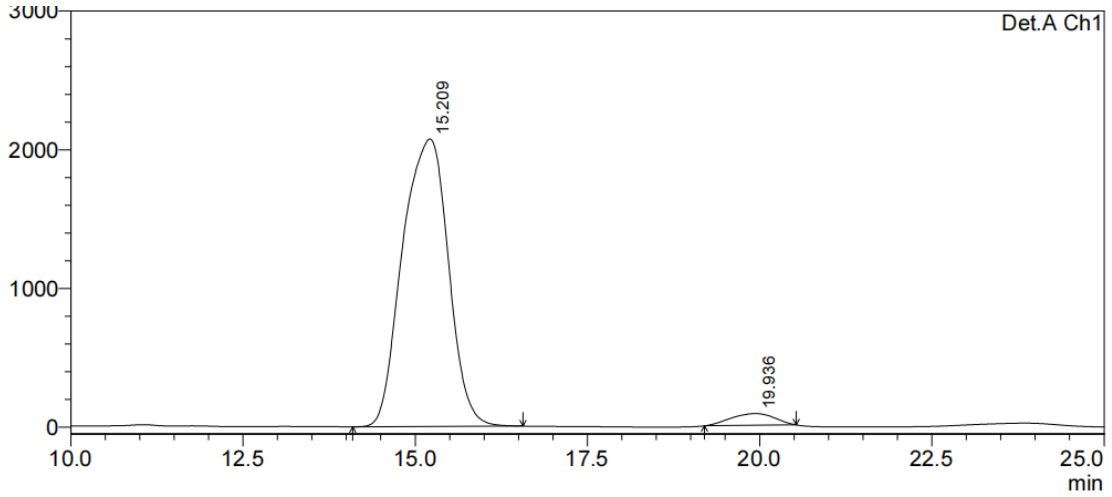


Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.088	9166165	284697	20.670	27.738
2	23.316	375850	10625	0.848	1.035
3	29.695	33947759	711372	76.553	69.309
4	32.200	855864	19677	1.930	1.917
Total		44345638	1026371	100.000	100.000

3t

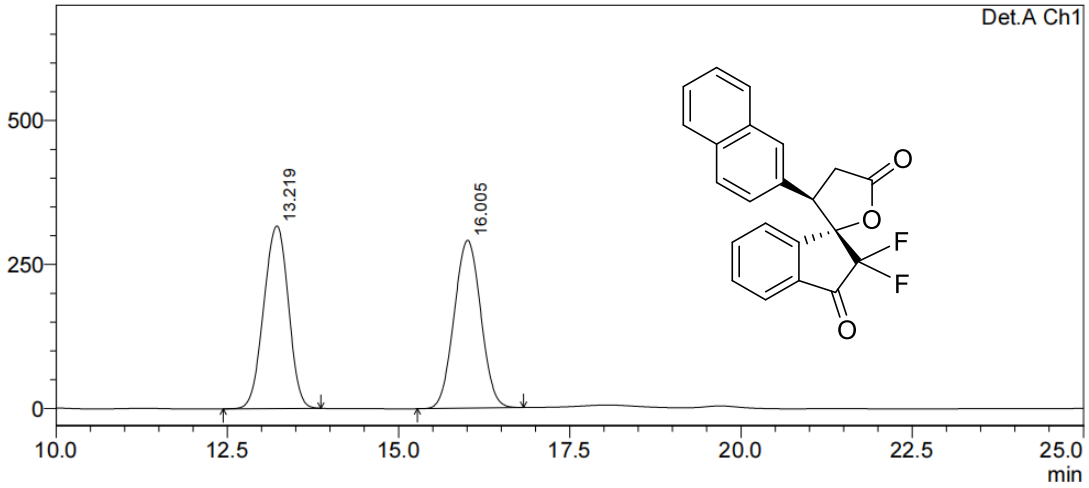


Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.663	7580426	170032	49.044	52.120
2	20.353	7875831	156197	50.956	47.880
Total		15456257	326230	100.000	100.000

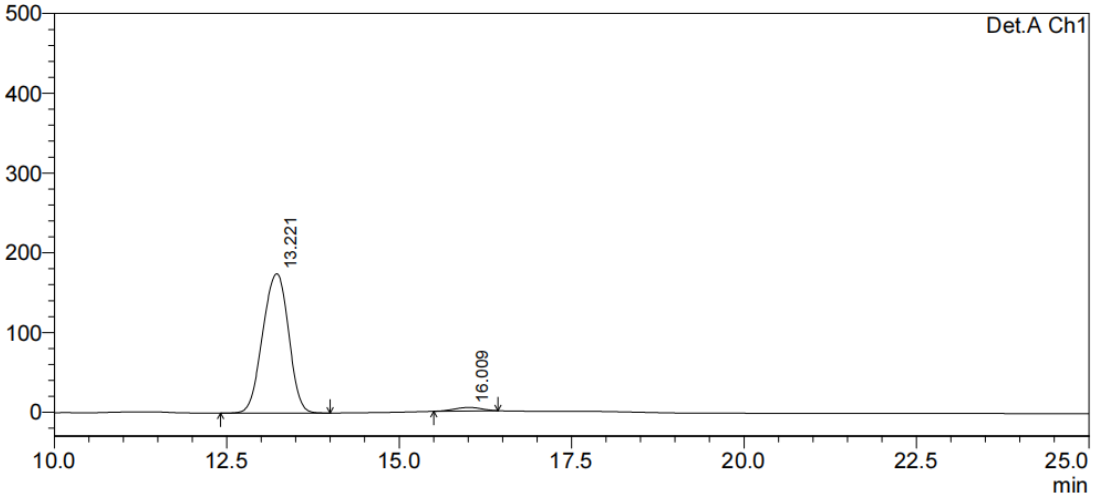


Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.209	96148794	2072720	96.243	96.077
2	19.936	3753800	84638	3.757	3.923
Total		99902594	2157358	100.000	100.000

3u

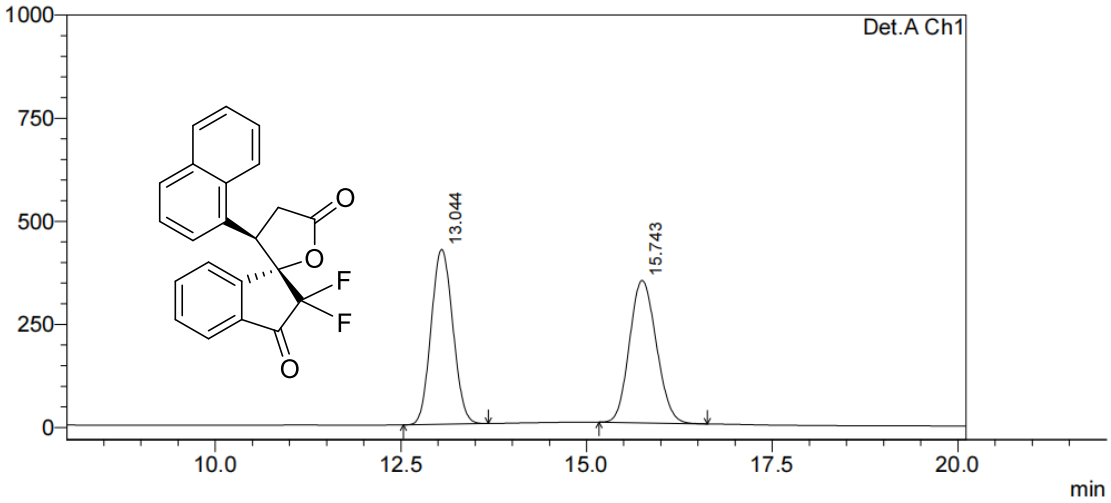


Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.219	7946448	317049	50.138	52.102
2	16.005	7902856	291464	49.862	47.898
Total		15849304	608513	100.000	100.000

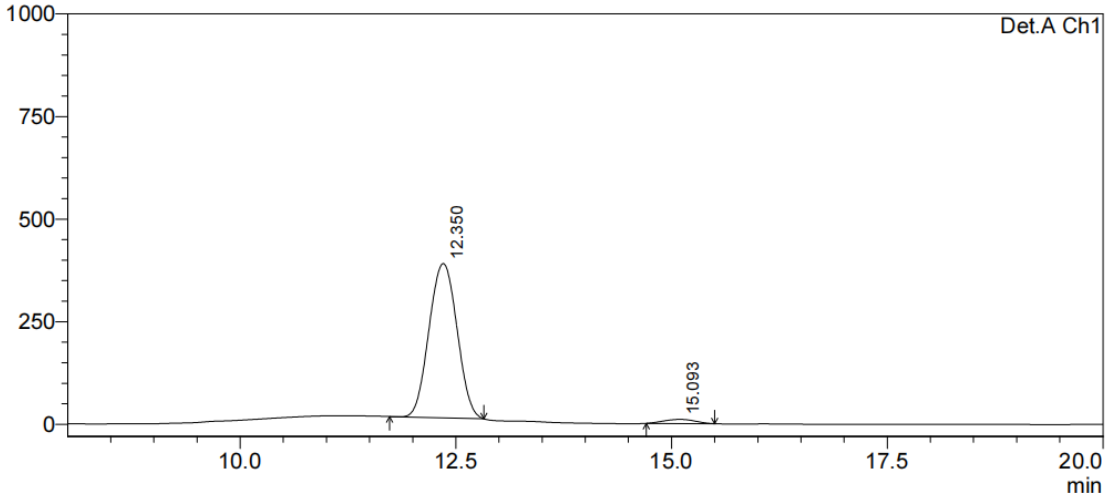


Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.221	4577208	174699	97.422	97.516
2	16.009	121114	4449	2.578	2.484
Total		4698322	179148	100.000	100.000

3v

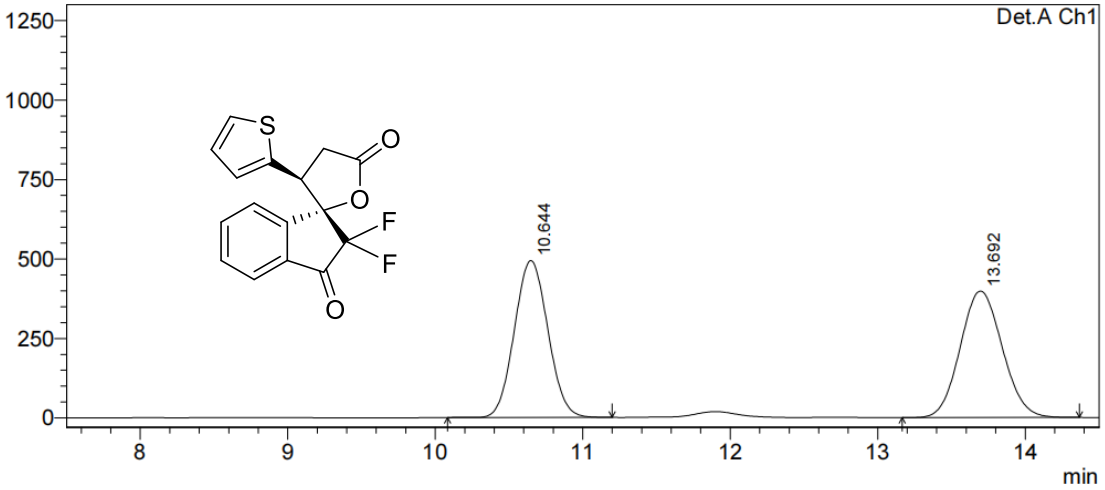


Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.044	8656502	424415	49.886	55.131
2	15.743	8696175	345412	50.114	44.869
Total		17352677	769827	100.000	100.000

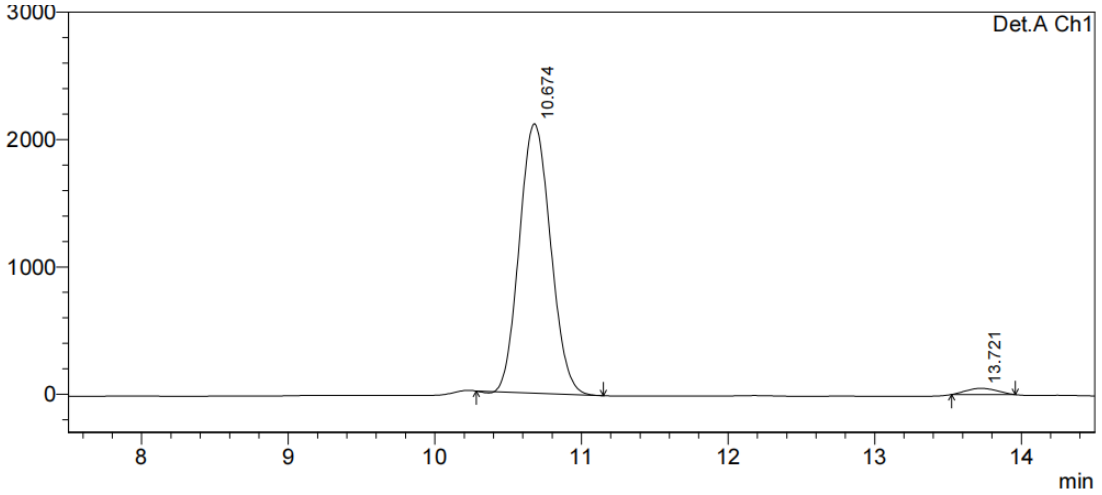


Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.350	8507509	376233	97.118	97.389
2	15.093	252505	10086	2.882	2.611
Total		8760014	386319	100.000	100.000

3w

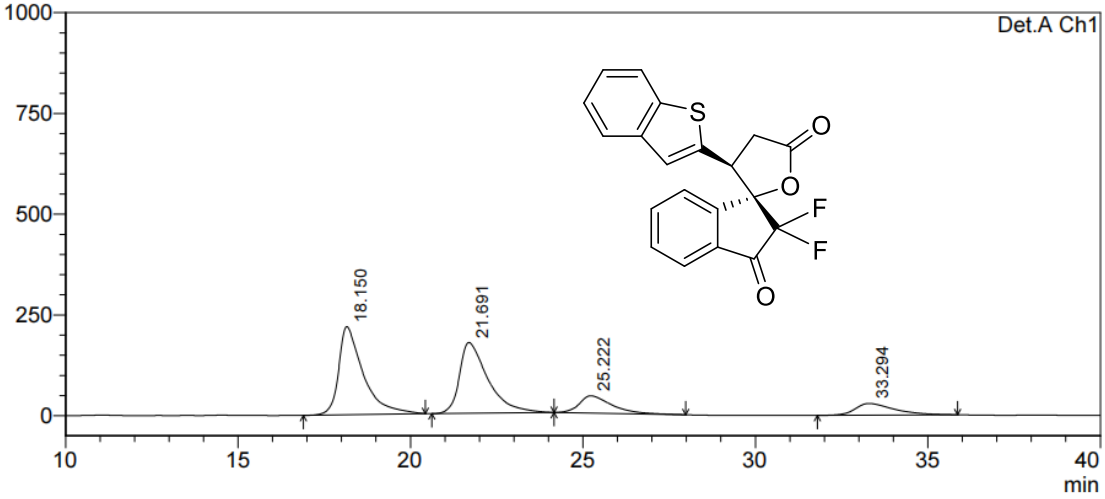


Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.644	7811573	493441	49.720	55.350
2	13.692	7899470	398051	50.280	44.650
Total		15711043	891492	100.000	100.000

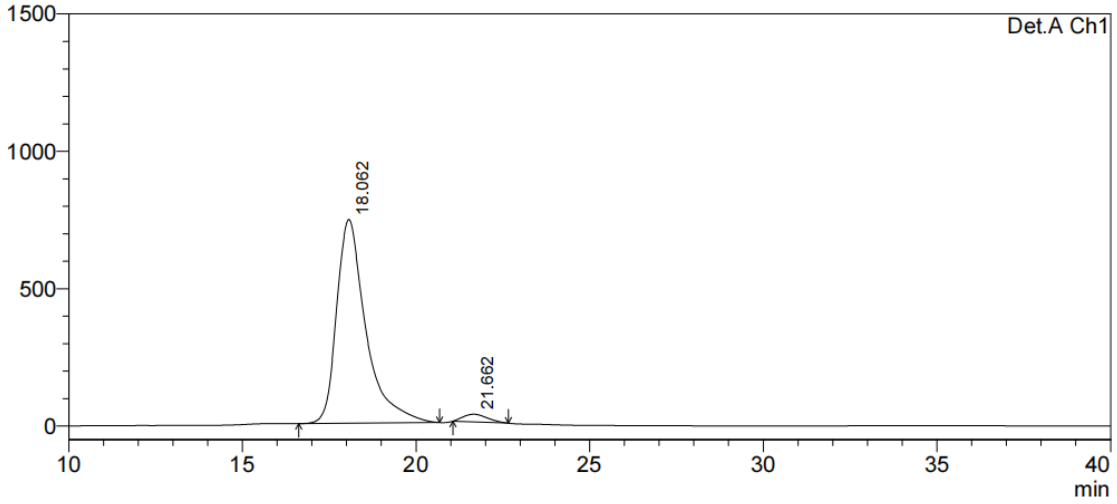


Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.674	31338409	2115900	97.823	97.766
2	13.721	697554	48357	2.177	2.234
Total		32035962	2164257	100.000	100.000

3x

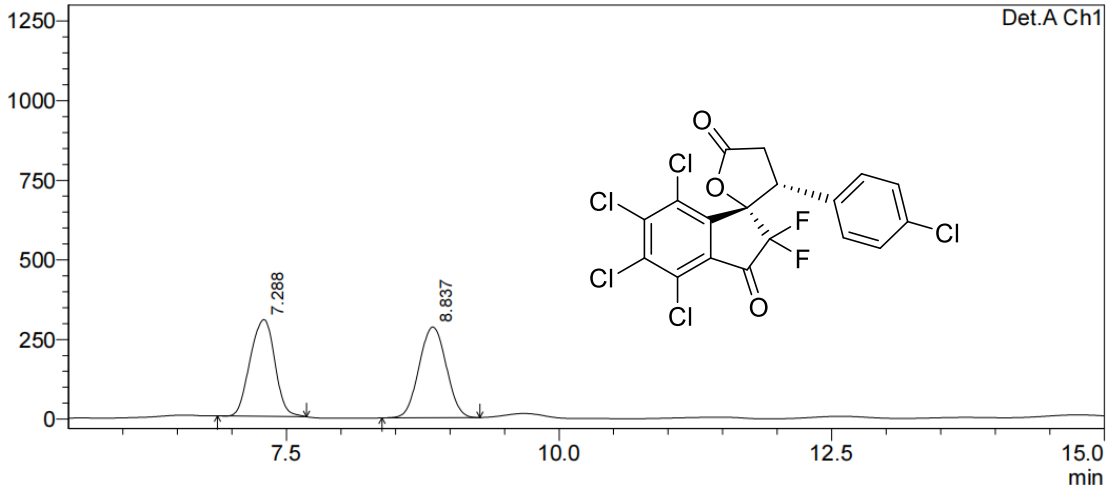


Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.150	10827639	218737	41.561	46.853
2	21.691	10100054	176105	38.769	37.722
3	25.222	2826814	42966	10.851	9.203
4	33.294	2297590	29045	8.819	6.221
Total		26052097	466854	100.000	100.000

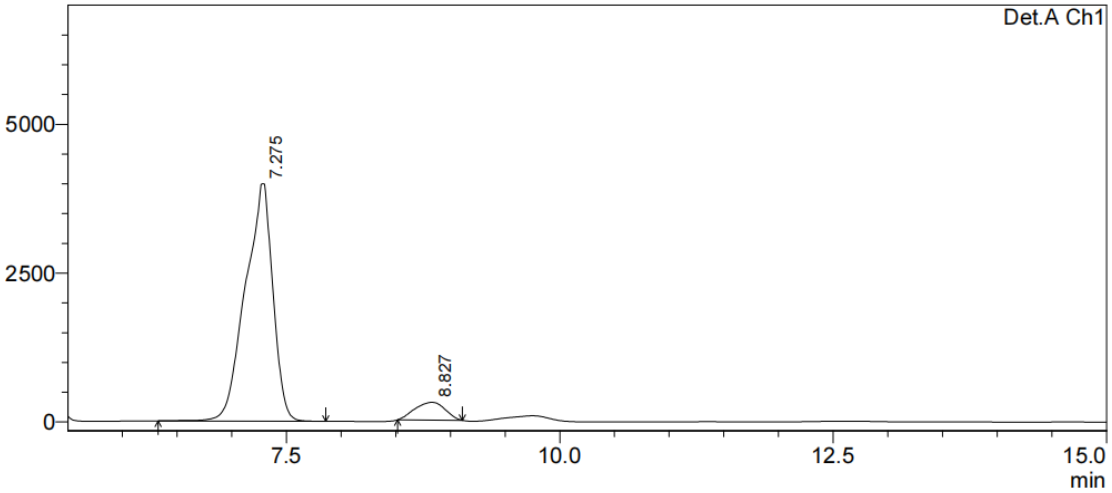


Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.062	43510809	741951	96.971	96.362
2	21.662	1359133	28009	3.029	3.638
Total		44869942	769960	100.000	100.000

3y

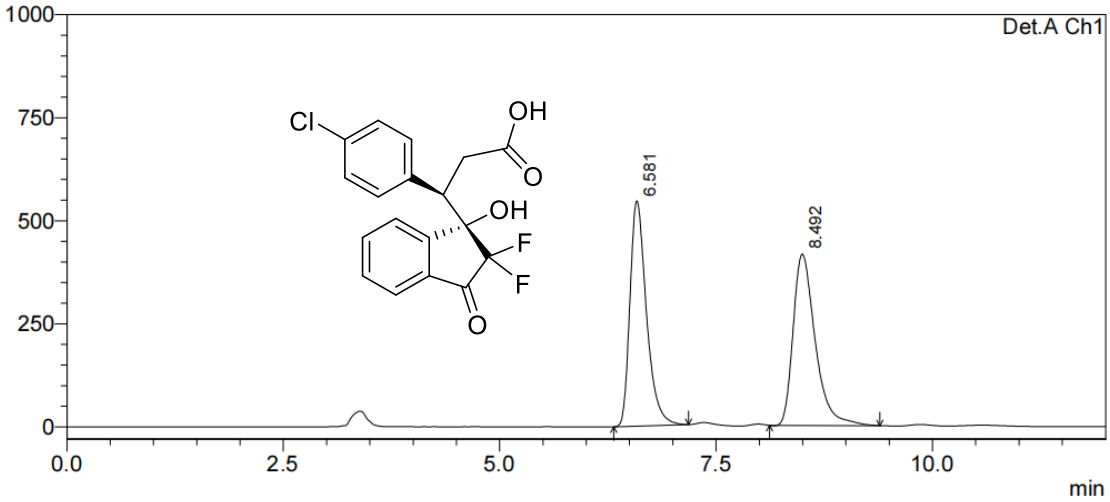


Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.288	4780647	303990	49.165	51.628
2	8.837	4943092	284822	50.835	48.372
Total		9723739	588813	100.000	100.000

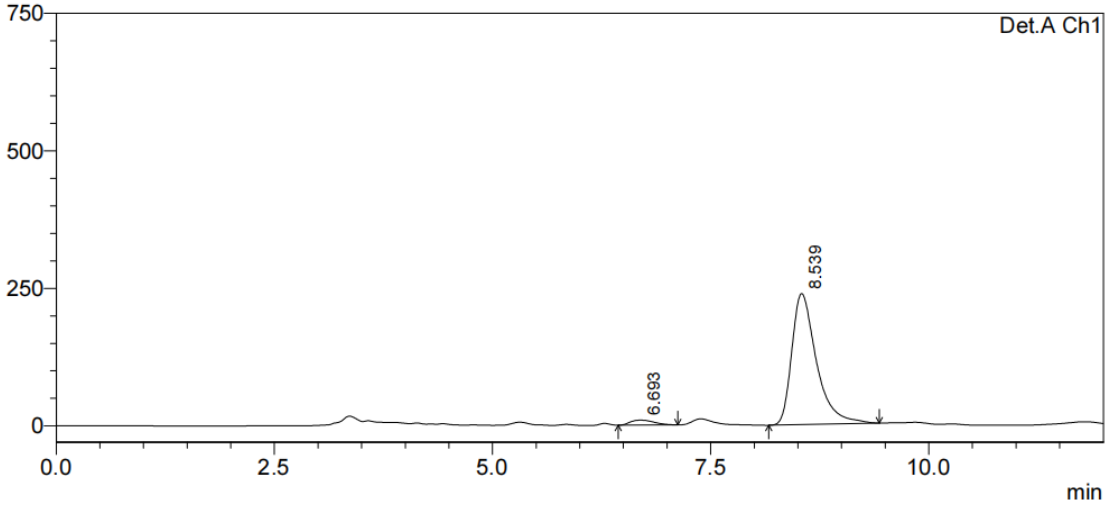


Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.275	69976967	3985585	92.430	93.040
2	8.827	5731275	298164	7.570	6.960
Total		75708242	4283749	100.000	100.000

6

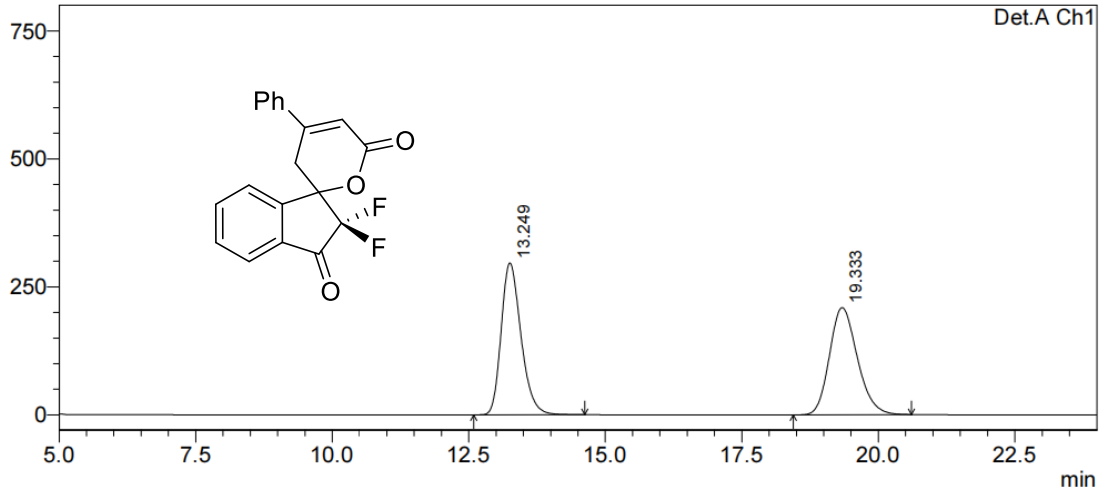


Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.581	7254233	546695	49.521	56.806
2	8.492	7394562	415700	50.479	43.194
Total		14648794	962395	100.000	100.000

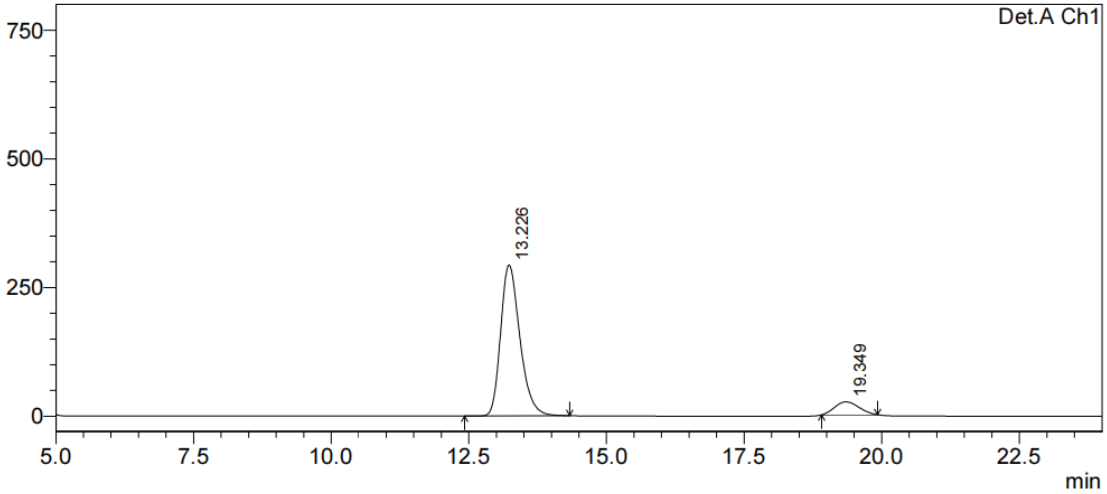


Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.693	172406	9027	3.542	3.646
2	8.539	4695735	238525	96.458	96.354
Total		4868141	247552	100.000	100.000

8



Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.249	7494206	296578	50.180	58.623
2	19.333	7440563	209333	49.820	41.377
Total		14934770	505910	100.000	100.000



Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.226	7142170	293484	90.352	92.121
2	19.349	762622	25102	9.648	7.879
Total		7904792	318587	100.000	100.000