Supporting Information

Ag-catalyzed difluorohydration of β-alkynyl ketones for diastereoselective synthesis of 1,5-diconboyl compounds

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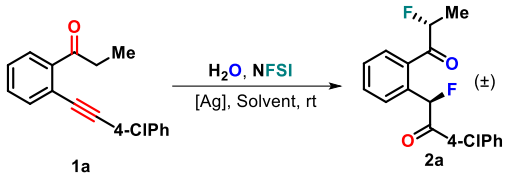
Context

General Information

^{1}H NMR (^{13}C NMR) spectra were measured on a Bruker DPX 400 MHz spectrometer in $CDCl_3$ (DMSO-d_6) with chemical shift (δ) given in ppm relative to TMS as internal standard [(s = singlet, d = doublet, t = triplet, brs = broad singlet, m = multiplet), coupling constant (Hz)]. HRMS (ESI) was determined by using microTOF-QII HRMS/MS instrument (BRUKER). X-Ray crystallographic analysis was performed with a Siemens SMART CCD and a Siemens P4 diffractometer.

Condition optimization

Table 1. Optimization of Reaction Conditions[a]



Entry	NFSI (equiv)	H_2O (equiv)	Cat. (mol %)	Solvent[b]	Yield (%)[c]
1	2.0	2.0	AgOAc (20)	1,4-dioxane	49%
2	2.0	2.0	AgF (20)	1,4-dioxane	31%
3	2.0	2.0	$AgSbF_6$ (20)	1,4-dioxane	39%
4	2.0	2.0	AgOTf (20)	1,4-dioxane	38%
5	2.0	2.0	AgTFA (20)	1,4-dioxane	trace
6	2.0	2.0	Ag_2CO_3 (20)	1,4-dioxane	trace
7	2.0	2.0	$AgNO_3$ (20)	1,4-dioxane	59%
8	2.5	2.0	$AgNO_3$ (20%)	1,4-dioxane	65%
9	3.0	2.0	$AgNO_3$ (20%)	1,4-dioxane	73%
10	3.0	2.0	$AgNO_3$ (20%)	CH_3CN	44%
11	3.0	2.0	$AgNO_3$ (20%)	DCM	52%
12	3.0	2.0	$AgNO_3$ (20%)	THF	trace
13	3.0	2.0	$AgNO_3$ (20%)	DCE	trace
14	3.0	2.0	$AgNO_3$ (10%)	1,4-dioxane	74%
15	3.0	2.0	$AgNO_3$ (5%)	1,4-dioxane	63%
16	3.0	3.0	$AgNO_3$ (10%)	1,4-dioxane	60%
17	3.0	1.5	$AgNO_3$ (10%)	1,4-dioxane	79%
18	3.0	1.2	$AgNO_3$ (10%)	1,4-dioxane	82%
19	3.0	1.0	$AgNO_3$ (10%)	1,4-dioxane	76%
20	3.0	-	$AgNO_3$ (10%)	1,4-dioxane	ND[d]
21	3.0	1.2	$AgNO_3$ (10%)	1,4-dioxane	50%[e]

[a] Reaction conditions: **1a** (0.5 mmol), NFSI (X equiv), H_2O (Y equiv), Ag-catalyst (Z mol%), solvent (2.0 mL), under Ar conditions, [b] Dry solvent. [c] Isolated yield. [d] Not detected (ND).[e] Under air conditions

Our initial investigation commenced with the reaction of the preformed β-alkynyl ketones **1a** with NFSI in a 1:2 mole ratio in the presence of water (2.0 equiv) using AgOAc (20 mol%) as a catalyst. The reaction was performed in 1,4-dioxane solvent at room temperature under Ar conditions, delivering the unexpected difluoride product **2a** in 49% yield (Table S1, entry S1). This satisfactory result promoted us to further search the optimal

conditions for accessing product **2a**. Several others silver catalysts often used in the catalytic transformation, including AgF, $AgSbF_6$, AgOTf, AgTFA, Ag_2CO_3, and $AgNO_3$, were screened for this difluorohydration by using 2.0 equivalents of NFSI as a difluorination reagent (entries S2-S7). The silver salts like AgF, $AgSbF_6$, or AgOTf behaved lower catalytic activities than AgOAc (entries S2-S4) whereas the use of AgTFA and Ag_2CO_3 completely suppressed the reaction process (entries S5-S6). In another case of $AgNO_3$, the reaction worked more efficiently, affording a higher yield of product **2a** (59%) as compared with AgOAc (entry S7). The increase of the dosage of NFSI is beneficial to the transformation (entries S8-S9). Adjusting the ratio of **1a** with NFSI to 1:3 improved the yield of **2a** to 73%. Afterward, taking the combination of NFSI (3.0 equiv) with $AgNO_3$ (20 mol%), we investigated the effect of the solvent. Screening followed by other aprotic solvents such ascetonitrile (CH_3CN), dichloromethane (DCM), tetrahydrofuran (THF), and 1,2-dichloroethane (DCE) revealed that all these solvents did not show any improvements with respect to the reaction yield (entries S10-S13). The simultaneous decrease of the amount of $AgNO_3$ and water is beneficial to this transformation (entries S14-S19). After careful optimizations, we found that the combination of 10 mol% of $AgNO_3$ with 1.2 equivalents of water was proven to be most effective for this reaction, affording 82% yield (entry S18). Without water, the reaction did not work and the starting materials were recovered (entry S20). A lower conversion was detected when the identical reaction was carried out under air conditions (entry S21).

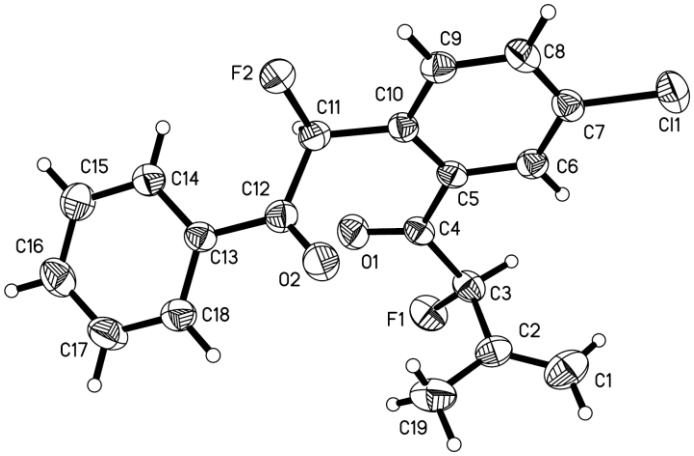


Figure 1 The ORTEP Drawing of **2w** (Thermal ellipsoids are set at 30% probability level)

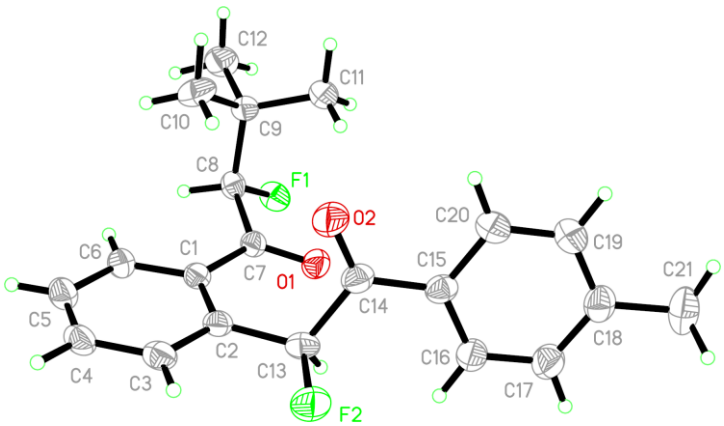
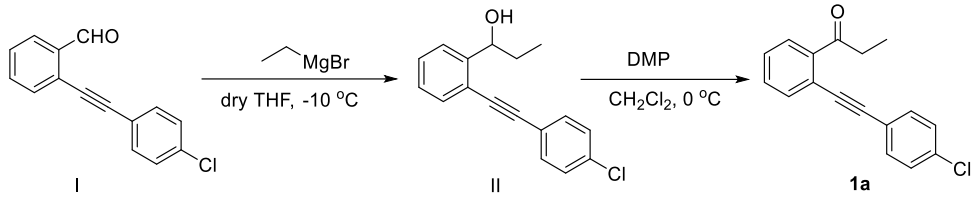


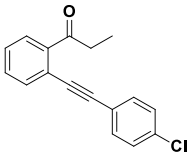
Figure 2 The ORTEP Drawing of **2z** (Thermal ellipsoids are set at 30% probability level)

1. General Procedure for the Preparation of *β*-Alkynyl Ketones.



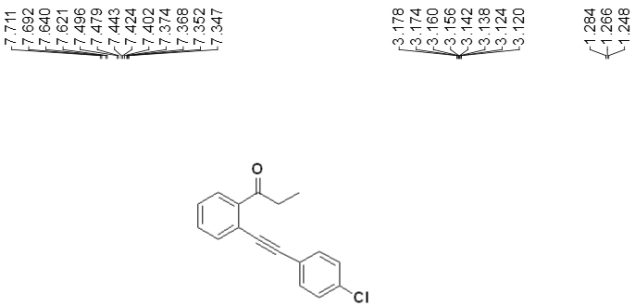
Representative Procedure：To a stirred solution of 2-((4-chlorophenyl)ethynyl)benzaldehyde (1.0 equiv, 5.0 mmol, I) in anhydrous THF (10 mL) was added by dropwise a 1.00 mol/L solution of ethylmagnesium bromide in THF (1.5 equiv, 7.5 mL, 7.5 mmol) at -10 ℃. The mixture was stirred for 1 hour at -10 ℃ and then stirred at room temperature. After the completion of the reaction monitored by TLC, the reaction system was quenched by saturated aqueous NH_4Cl and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. After purification by flash column chromatography on silica gel, compound II (1.26 g, 4.65 mmol) was obtained in 93% yield as an oil.

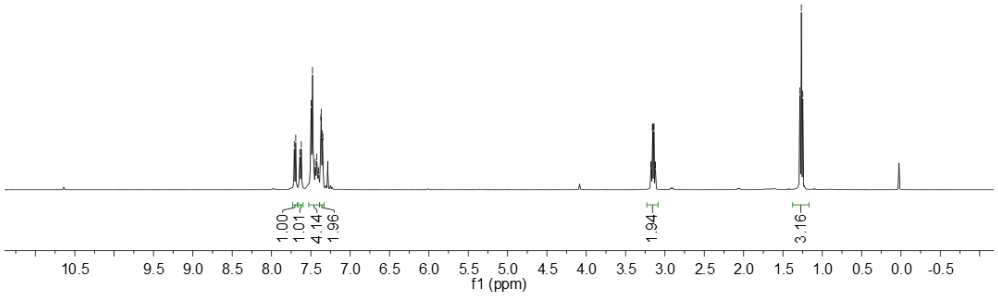
In an oven dried flask, compound II (1.0 equiv, 2 mmol) and dry CH_2Cl_2 (4.0 mL/mmol) were added. The resulting solution was cooled to 0 ℃, and then Dess-Martin periodinane (1.5 equiv., 3 mmol) was added into this reaction system. The resulting suspension was stirred at 0 ℃ for 3 h. The reaction mixture was diluted with CH_2Cl_2 (10.0 mL/mmol) and saturated aqueous $NaHCO_3$ (10.0 mL/mmol). Organic layers was separated and the aqueous layer was extracted with CH_2Cl_2 (1 × 10 mL). The combined organic phase was washed with brine (1 × 10.00 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by column chromatography over silica gel with petrolem ether/ethyl acetate as eluent afforded **1a** (0.48g, 1.8 mmol).



1-(2-((4-chlorophenyl)ethynyl)phenyl)propan-1-one (1a)

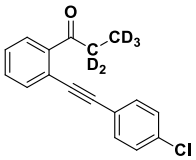
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.6 Hz, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.52-7.39 (m, 4H), 7.39-7.33 (m, 2H), 3.23-3.09 (m, 2H), 1.27 (t, *J* = 7.2 Hz, 3H).



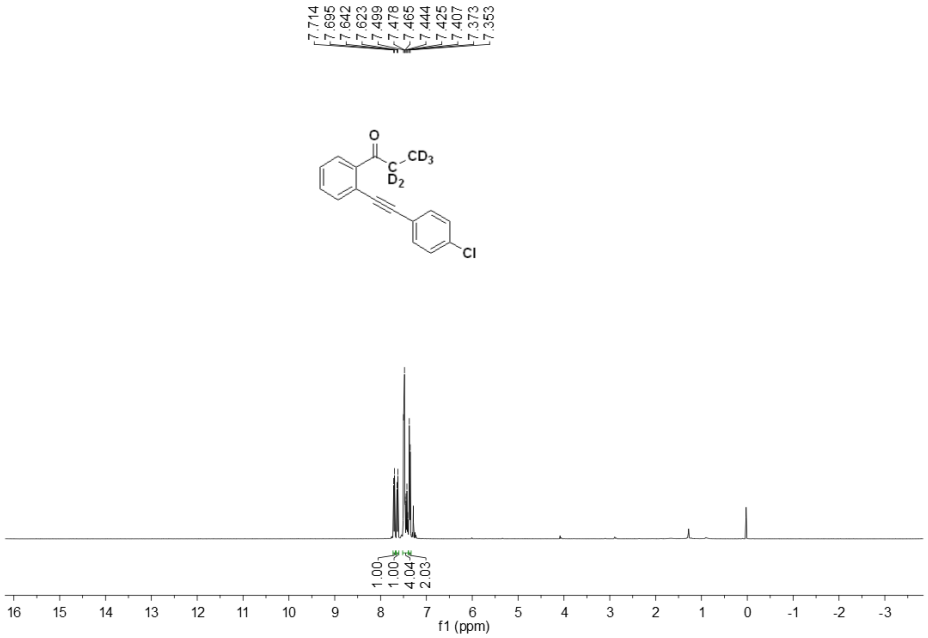


2. Isotopic labeling experiments

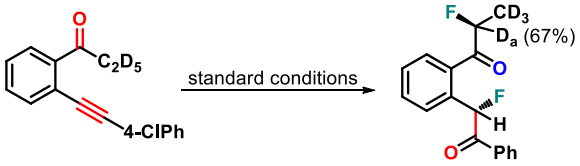
The isotopic labeled 1-(2-((4-chlorophenyl)ethynyl)phenyl)propan-1-one is produced as the method of 1.1.



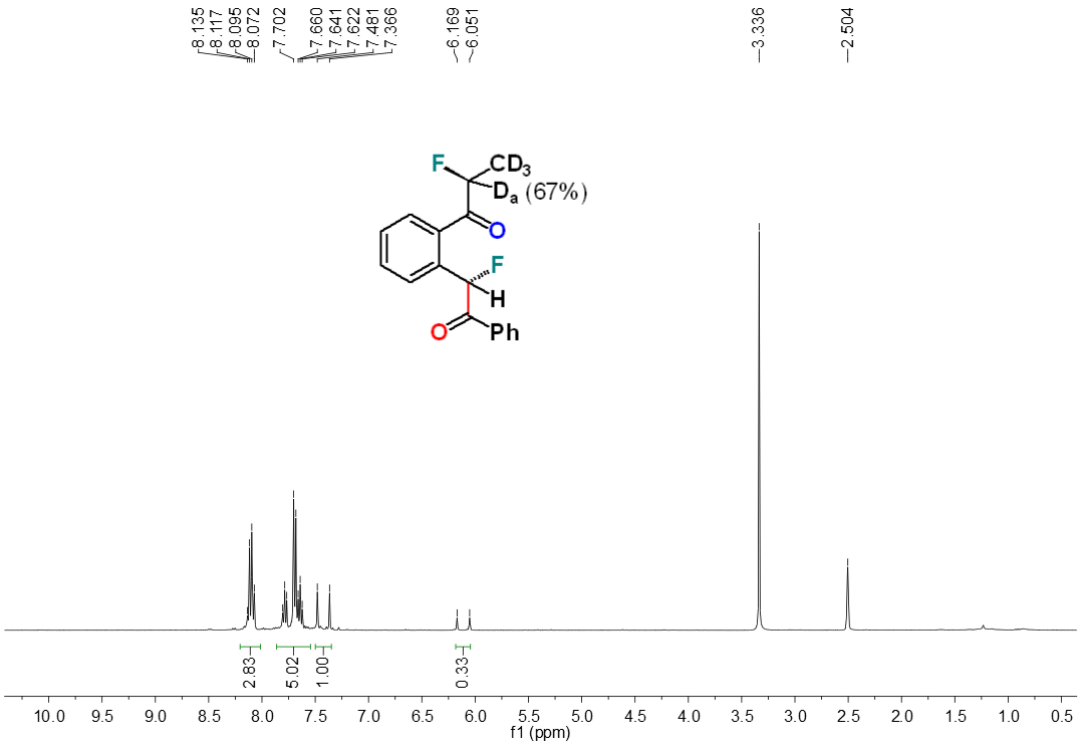
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.6 Hz, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.45 (dt, *J* = 14.8, 7.8 Hz, 4H), 7.36 (d, *J* = 8.2 Hz, 2H).



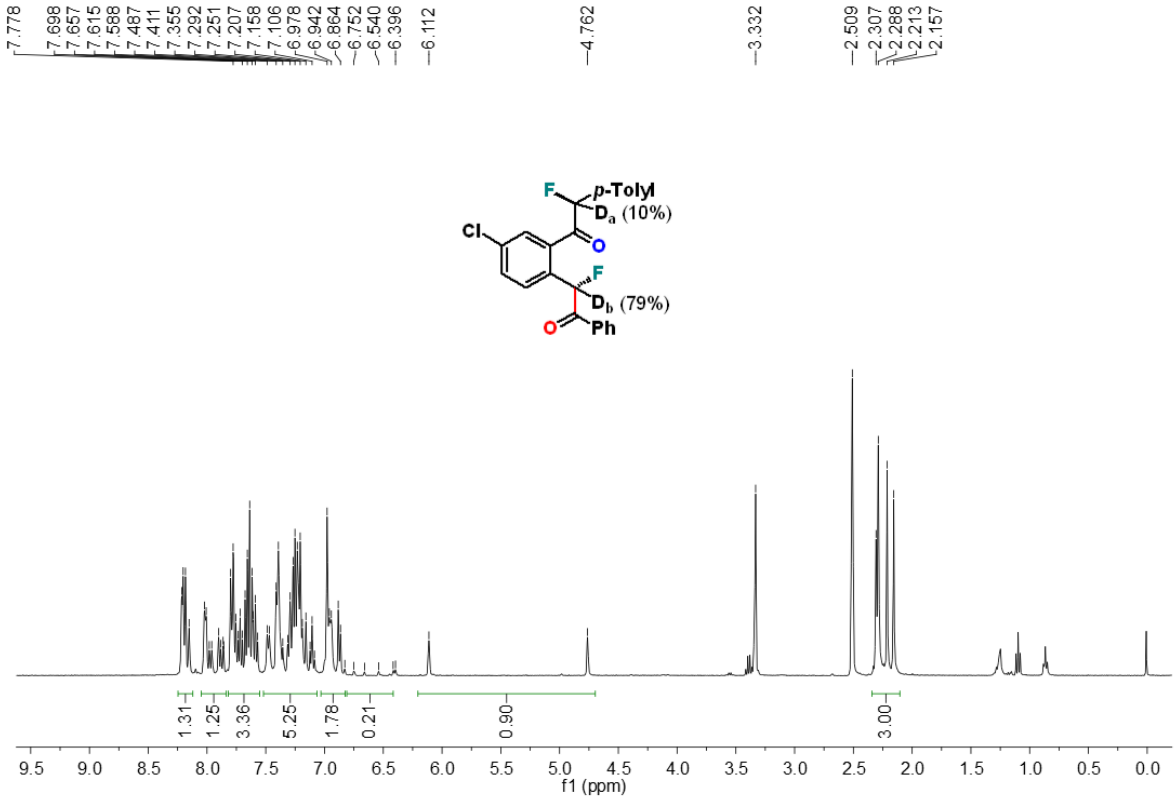
In an oven-dried Schlenk tube, to a solution of isotopic labeled 1-(2-((4-chlorophenyl)ethynyl)phenyl)propan-1-one (**1a**, 1.0 equiv., 0.2 mmol), N-fluorobenzenesulfonimide (2.5 equiv, 0.5 mmol), $AgNO_3$ (10 mol%, 0.1 mmol) and water (1.2 equiv, 0.24 mmol) in anhydrous 1,4-dioxane (1.0 mL) under Ar atmosphere. After the reaction was completed, the product was checked by checked by ^{1}H-NMR in DMSO-d_6.



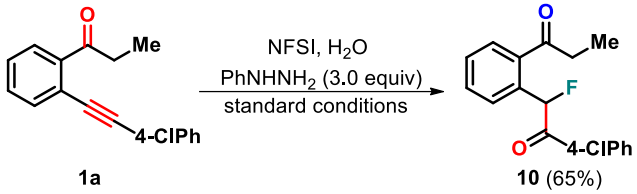
[D$_5$]-1a **[D]-4a** (72%)



In an oven-dried Schlenk tube, to a solution of 1-(5-chloro-2-(phenylethynyl)phenyl)-2-(*p*-tolyl)ethanone (1v, 1.0 equiv., 0.2 mmol), N-fluorobenzenesulfonimide (2.5 equiv, 0.5 mmol), $AgNO_3$ (10 mol%, 0.1 mmol) and D_2O (1.2 equiv. 0.24 mmol) in anhydrous 1,4-dioxane (1.0 mL) under Ar atmosphere. After the reaction was completed, the product was checked by ^{1}H-NMR in DMSO-d_6.



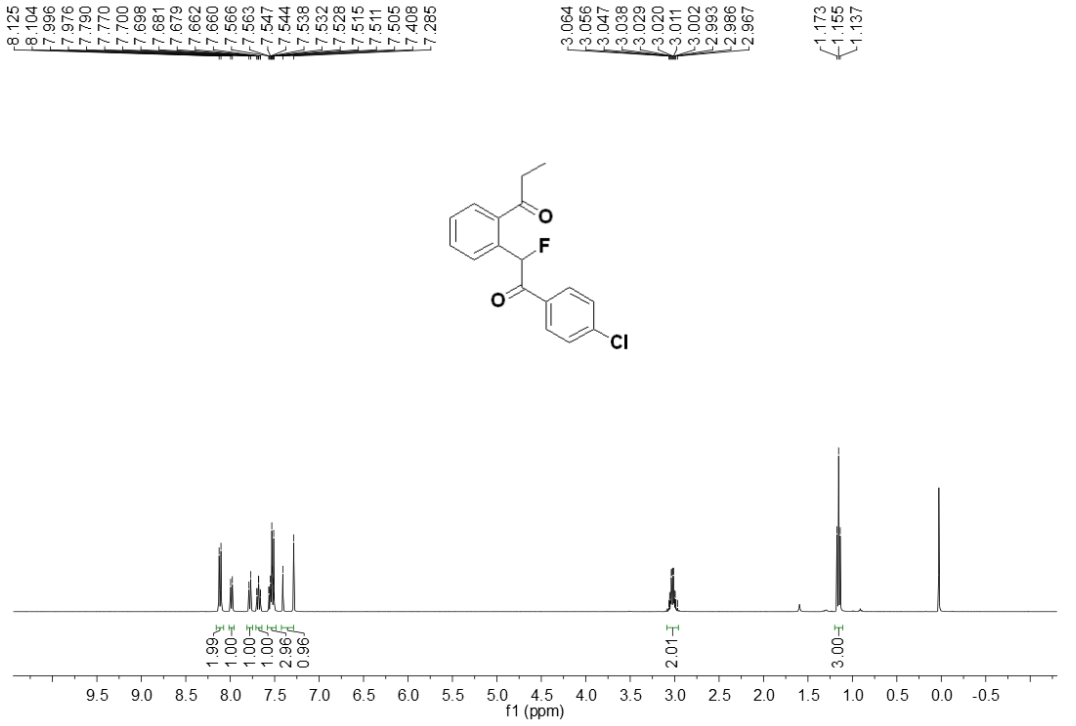
3. Control experiments

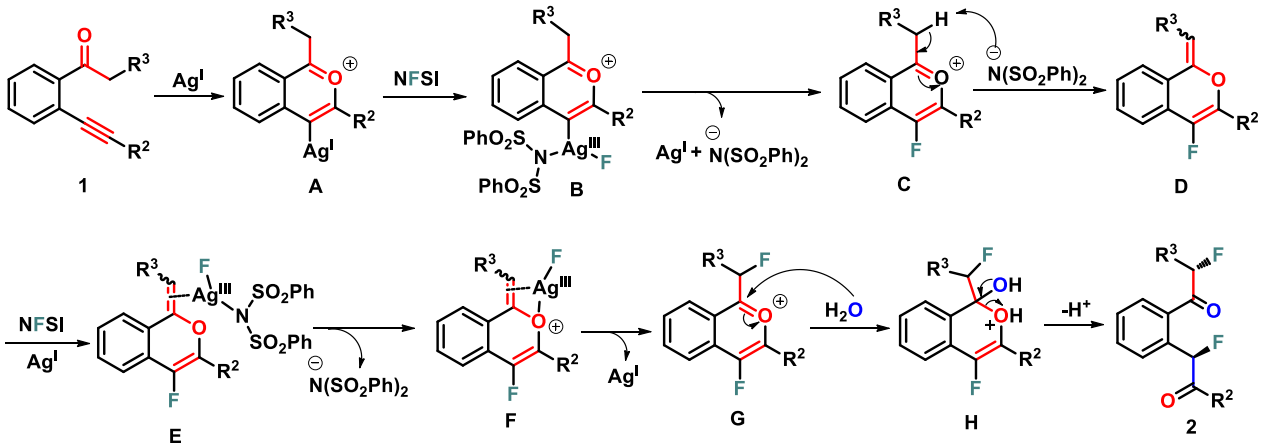


In an oven-dried Schlenk tube, to a solution of isotopic labeled 1-(2-((4-chlorophenyl)ethynyl)phenyl)propan-1-one (**1a**, 1.0 equiv., 0.2 mmol), N-fluorobenzenesulfonimide (2.5 equiv, 0.5 mmol), $AgNO_3$ (10 mol%, 0.1 mmol), water (1.2 equiv, 0.24 mmol), and Phenylhydrazine (3.0 equiv, 0.6 mmol) in anhydrous 1,4-dioxane (1.0 mL) under Ar atmosphere. After the reaction was completed, the product was checked by checked by ^{1}H-NMR in $CDCl_3$.

1-(2-(2-(4-chlorophenyl)-1-fluoro-2-oxoethyl)phenyl)propan-1-one (10)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.4 Hz, 2H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.71-7.64 (m, 1H), 7.58-7.49 (m, 3H), 7.42-7.28 (m, 1H), 3.12-2.90 (m, 2H), 1.15 (t, *J* = 7.2 Hz, 3H).





Scheme S1. Plausible mechanism for forming **2**

LC-MS experiments for reaction solution containing intermediate B, C and D.

Operator:MSQ Timebase:LCMS Sequence:SJ201606132

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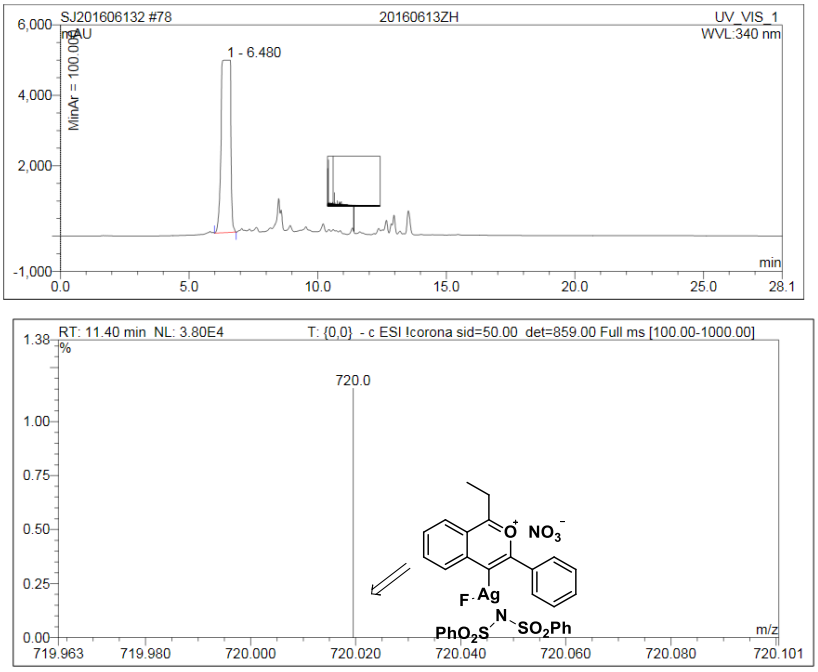
Overlay of Samples and Spectra from Integration View



LC-MS Spectra of Intermediate B

Operator:MSQ Timebase:LCMS Sequence:SJ201606132

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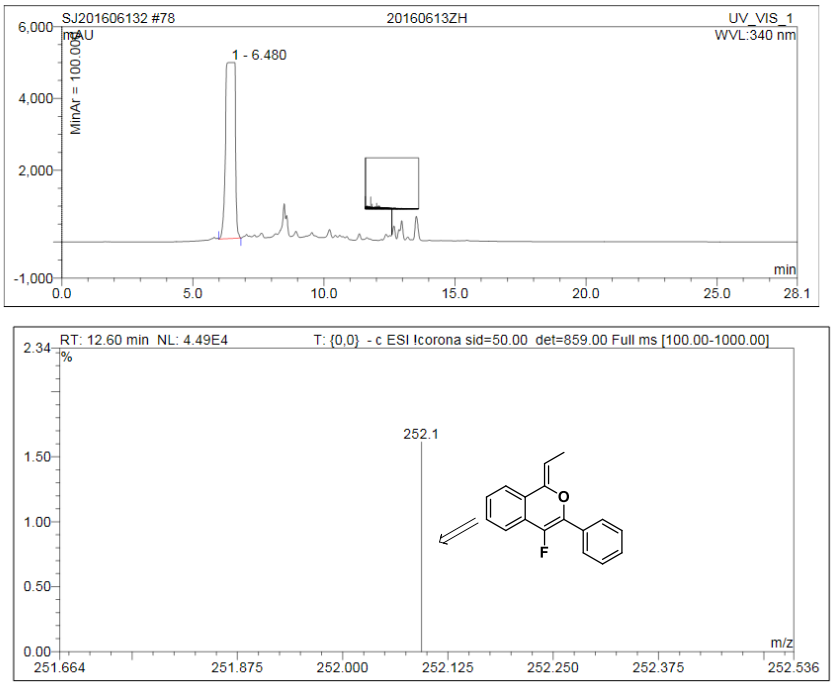
Overlay of Samples and Spectra from Integration View

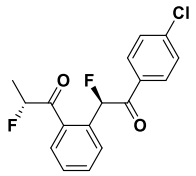


LC-MS Spectra of Intermediate D

Typical Procedure for the Synthesis of Products 2

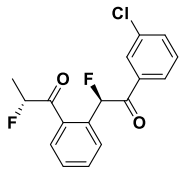
In an oven-dried Schlenk tube, to a solution of *β*-alkynyl ketones (**1**, 1.0 equiv, 0.5 mmol), *N*-fluorobenzenesulfonimide (3.0 equiv, 1.5 mmol), $AgNO_3$ (10 mol%, 0.05 mmol) and water (1.2 equiv, 0.60 mmol) in anhydrous 1,4-dioxane (2.0 mL) under Ar atmosphere. The reaction mixture was stirred at room temperature for 12.0 hours. After the reaction monitored by TLC was completed, the organic solvent was removed under vacuum, and the residue was purified by silica gel column with petroleum ether/ethyl acetate to afford pure products **2**.

1-(2-(2-(4-Chlorophenyl)-1-fluoro-2-oxoethyl)phenyl)-2-fluoropropan-1-one (2a)



white solid, mp 71-73 °C; ^{1}H NMR (400 MHz, $CDCl_3$; *δ*, ppm) 8.14 (d, *J* = 8.4 Hz 2H), 7.97-7.90 (m, 1H), 7.81 (m, 1H), 7.75-7.61 (m, 2H), 7.59-7.50 (m, 3H), 7.39 (d, *J* = 47.6 Hz, 1H), 5.85-5.62 (m, 1H), 1.63 (dd, *J* = 24.0, 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; *δ*, ppm) 198.9 (d, *J* = 19.5 Hz), 191.2 (d, *J* = 22.1 Hz), 140.2, 136.8 (d, *J* = 18.1 Hz), 133.6, 133.4 (d, *J* = 1.7 Hz), 131.9 (d, *J* = 1.9 Hz), 130.7 (d, *J* = 1.9 Hz), 130.0 (d, *J* = 5.5 Hz), 129.1, 128.5, 127.3 (d, *J* = 15.9 Hz), 90.3 (d, *J* = 181.3 Hz), 89.6 (d, *J* = 179.1 Hz), 17.8 (d, *J* = 22.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; *δ*, ppm) -179.3 (d, *J* = 47.4 Hz, 1F), -179.9--180.4 (m, 1F, major), -181.2--181.5 (m, 1F), -181.6 (d, *J* = 47.4 Hz, 1F, major). IR (film, *ν*, cm^{-1}) 3068, 3028, 1725, 1590, 1507, 1448, 1359, 1220, 1199, 1173, 1155, 1083, 844. HR-MS (ESI) m/z calcd for $C_{17}H_{13}ClF_2O_2$ $[M+Na]^+$ 345.0470, found 345.0468.

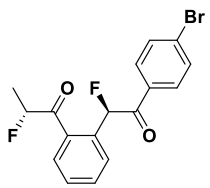
1-(2-(2-(3-Chlorophenyl)-1-fluoro-2-oxoethyl)phenyl)-2-fluoropropan-1-one (2b)



oil; ^{1}H NMR (400 MHz, $CDCl_3$; *δ*, ppm) 8.11 (s, 1H), 8.04 (d, *J* = 7.6 Hz, 1H), 7.98-7.92 (m, 1H), 7.85-7.77 (m, 1H), 7.73 (t, *J* = 7.6 Hz, 1H), 7.66-7.59 (m, 1H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.52-7.45 (m, 1H), 7.33 (d, *J* = 47.2 Hz, 1H), 5.85-5.62 (m, 1H), 1.62 (dd, *J* = 24.0, 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$; *δ*, ppm) 198.8 (d, *J* = 19.9Hz), 191.1 (d, *J* = 22.2 Hz), 136.7 (d, *J* = 18.9 Hz), 135.1 (d, *J* = 2.0 Hz), 133.6, 131.8 (d, *J* = 2.6 Hz), 130.1, 130.0 (d, *J* = 5.4 Hz), 129.2 (d, *J* = 2.1 Hz), 128.6, 127.7 (d, *J* = 14.8 Hz), 127.3 (d, *J* = 6.8 Hz), 127.2, 89.9 (d, *J* = 176.9 Hz), 89.6 (d, *J* = 179.1 Hz), 17.8 (d, *J* = 22.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; *δ*, ppm) -179.77 (d, *J* = 1.5 Hz, 1F), -180.34 (s, 1F, major), -181.44 (s, 1F), -181.81 (d, *J* = 1.9 Hz, 1F, major). HR-MS (ESI) m/z calcd for $C_{17}H_{13}ClF_2O_2$ $[M+Na]^+$ 345.0470, found 345.0471.

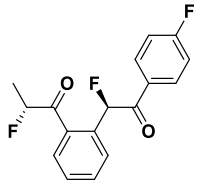
1-(2-(2-(4-Bromophenyl)-1-fluoro-2-oxoethyl)phenyl)-2-fluoropropan-1-one (2c)



white solid, mp 81-82 °C; ^{1}H NMR (400 MHz, $CDCl_3$; *δ*, ppm) 8.01 (d, *J* = 8.4 Hz, 2H), 7.97-7.91 (m, 1H), 7.79

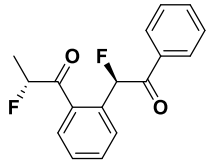
(t, *J* = 7.6 Hz, 1H), 7.74-7.65 (m, 3H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.29 (d, *J* = 47.6 Hz, 1H), 5.85-5.60 (m, 1H), 1.62 (dd, *J* = 24.4, 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; *δ*, ppm) 198.9 (d, *J* = 19.7 Hz), 191.4 (d, *J* = 22.0 Hz), 136.8 (d, *J* = 18.3 Hz), 133.6 (d, *J* = 7.1 Hz), 132.1, 130.7 (d, *J* = 2.1 Hz), 130.0 (d, *J* = 5.5 Hz), 129.8 (d, *J* = 5.4 Hz), 129.0, 128.6, 127.8 (d, *J* = 14.3 Hz), 127.3 (d, *J* = 16.0 Hz), 89.8 (d, *J* = 176.8 Hz), 89.7 (d, *J* = 179.0 Hz), 17.8 (d, *J* = 22.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; *δ*, ppm) -179.27 (s, 1F), -180.21 (s, 1F, major), -181.36 (s, 1H), -181.52 (s, 1F, major). IR (film, ν, cm^{-1}) 3068, 3028, 1725, 1590, 1507, 1448, 1359, 1220, 1199, 1173, 1155, 1083, 844. HR-MS (ESI) m/z calcd for $C_{17}H_{13}BrF_2O_2$ $[M+Na]^+$ 388.9965, found 388.9962.

2-Fluoro-1-(2-(1-fluoro-2-(4-fluorophenyl)-2-oxoethyl)phenyl)propan-1-one (2d)



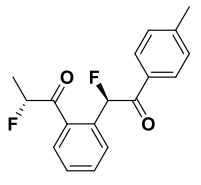
white solid, mp 66-68 °C; ^{1}H NMR (400 MHz, $CDCl_3$; *δ*, ppm) 8.19 (d, *J* = 8.4 Hz, 2H), 8.00-7.89 (m, 1H), 7.84-7.77 (m, 1H), 7.72 (t, *J* = 7.6 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.41-7.14 (m, 3H), 5.85-5.60 (m, 1H), 1.64 (dd, *J* = 24.0, 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; *δ*, ppm) 199.0(d, *J* = 19.7 Hz), 190.8 (d, *J* = 21.9 Hz), 166.1 (d, *J* = 254.3 Hz), 136.9 (d, *J* = 18.2 Hz), 133.5 (d, *J* = 1.7 Hz), 132.1 (d, *J* = 2.5 Hz), 132.0 (d, *J* = 2.5 Hz), 131.5 (d, *J* = 4.7 Hz), 129.9 (d, *J* = 5.5 Hz), 128.5, 127.3 (d, *J* = 15.9 Hz), 116.0 (d, *J* = 21.8 Hz), 89.8 (d, *J* = 176.9 Hz), 89.7 (d, *J* = 179.1 Hz), 17.8 (d, *J* = 22.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; *δ*, ppm) -103.8 (s, 1F, major), -103.9(s, 1F, major), -178.9 (s, 1F), -180.3 (s, 1F, major), -181.3 (d, *J* = 5.3 Hz, 1F, major), -181.4 (d, *J* = 5.3 Hz, 1F). IR (film, ν, cm^{-1}) 3000, 1702, 1683, 1595, 1506, 1240, 1212, 1160, 1086, 991, 839. HR-MS (ESI) m/z calcd for $C_{17}H_{13}F_3O_2$ $[M+Na]^+$ 329.0765, found 329.0764.

2-Fluoro-1-(2-(1-fluoro-2-oxo-2-phenylethyl)phenyl)propan-1-one (2e)



white solid, mp 67-69 °C; ^{1}H NMR (400 MHz, $CDCl_3$; *δ*, ppm) 8.14 (d, *J* = 7.6 Hz, 2H), 7.96-7.90 (m, 1H), 7.84-7.77 (m, 1H), 7.74-7.61 (m, 2H), 7.59-7.50 (m, 3H), 7.46-7.20 (m, 1H), 5.89-5.62 (m, 1H), 1.63 (dd, *J* = 24.4, 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; *δ*, ppm) 199.0 (d, *J* = 19.7 Hz), 192.5 (d, *J* = 21.9 Hz), 137.0 (d, *J* = 18.5 Hz), 135.0 (d, *J* = 1.7 Hz), 133.7, 133.4, 132.2 (d, *J* = 3.3 Hz), 129.8 (d, *J* = 5.5 Hz), 129.2 (d, *J* = 2.2 Hz), 128.8, 128.4, 127.3 (d, *J* = 15.8 Hz), 89.8 (d, *J* = 177.5 Hz), 89.4 (d, *J* = 176.6 Hz), 17.8 (d, *J* = 22.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; *δ*, ppm) -178.85 (s, 1F), -180.33 (s, 1F, major), -181.38 (s, 1F, major), -181.39 (s, 1F). IR (film, ν, cm^{-1}) 3069, 2987, 1689, 1596, 1573, 1450, 1318, 1239, 1218, 1114, 1081, 1012,977, 824. HR-MS (ESI) m/z calcd for $C_{17}H_{14}F_2O_2$ $[M+Na]^+$ 311.0860, found 311.0864.

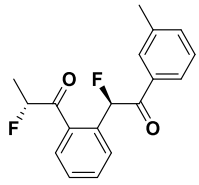
2-Fluoro-1-(2-(1-fluoro-2-oxo-2-(p-tolyl)ethyl)phenyl)propan-1-one (2f)



white solid, mp 88-90 °C; ^{1}H NMR (400 MHz, $CDCl_3$; *δ*, ppm) 8.03 (d, *J* = 8.0 Hz, 2H), 7.97-7.88 (m, 1H), 7.79

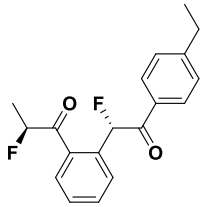
(m, 1H), 7.68 (m, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.44-7.17 (m, 3H), 5.84-5.59 (m, 1H), 2.46 (s, 3H), 1.64 (dd, *J* = 24.0, 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; *δ*, ppm) 199.1 (d, *J* = 19.7 Hz), 192.1 (d, *J* = 21.7 Hz), 144.7, 137.0 (d, *J* = 18.5 Hz), 133.4 (d, *J* = 1.2 Hz), 132.3 (d, *J* = 3.1 Hz), 129.8 (d, *J* = 5.4 Hz), 129.5, 129.4 (d, *J* = 2.1 Hz), 128.8 (d, *J* = 1.1 Hz), 127.4 (d, *J* = 15.5 Hz), 89.7 (d, *J* = 176.8 Hz), 89.3 (d, *J* = 176.5 Hz), 21.8, 17.9 (d, *J* = 22.4 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; *δ*, ppm) -178.30 (s, 1F), -180.26 (s, 1F), -180.95 (s, 1F), -181.31 (s, 1F). IR (film, ν, cm^{-1}) 3069, 2997, 2940, 1696, 1603, 1575, 1223, 1213, 1087, 978. HR-MS (ESI) m/z calcd for $C_{18}H_{16}F_2O_2$ $[M+Na]^+$ 325.1016, found 325.1021.

2-Fluoro-1-(2-(1-fluoro-2-oxo-2-(m-tolyl)ethyl)phenyl)propan-1-one (2g)



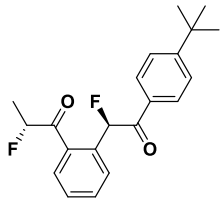
white solid, mp 67-69 °C; ^{1}H NMR (400 MHz, $CDCl_3$; *δ*, ppm) 7.98-7.89 (m, 3H), 7.84-7.76 (m, 1H), 7.74-7.66 (m, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.49-7.18 (m, 3H), 5.72 (m, 1H), 2.46 (s, 3H), 1.63 (dd, *J* = 24.0, 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; *δ*, ppm) 199.0 (d, *J* = 19.4 Hz), 192.6 (d, *J* = 21.7 Hz), 138.6, 137.0 (d, *J* = 18.4 Hz), 135.1 (d, *J* = 1.6 Hz), 134.6, 133.4 (d, *J* = 1.6 Hz), 132.2 (d, *J* = 2.4 Hz), 129.8 (d, *J* = 5.4 Hz), 129.7 (d, *J* = 1.9 Hz), 128.6, 128.4 (d, *J* = 1.1 Hz), 127.3 (d, *J* = 15.7 Hz), 126.5 (d, *J* = 2.3 Hz), 89.8 (d, *J* = 179.5 Hz), 89.7 (d, *J* = 176.7 Hz), 21.4, 17.9 (d, *J* = 22.6 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; *δ*, ppm) -178.32--178.77 (m, 1F), -180.33 (s, 1F, major), -181.08--181.19 (m, 1F, major), -181.23 (s, 1F). IR (film, ν, cm^{-1}) 3028, 2994, 1688, 1603, 1575, 1314, 1240, 1164, 1114, 1075, 1037, 986. HR-MS (ESI) m/z calcd for $C_{18}H_{16}F_2O_2$ $[M+Na]^+$ 325.1016, found 325.1017.

1-(2-(2-(4-Ethylphenyl)-1-fluoro-2-oxoethyl)phenyl)-2-fluoropropan-1-one (2h)



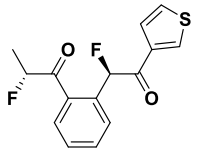
white solid, mp 88-82 °C; ^{1}H NMR (400 MHz, $CDCl_3$; *δ*, ppm) 8.07 (d, *J* = 8.0 Hz, 2H), 7.95-7.88 (m, 1H), 7.83-7.76 (m, 1H), 7.73-7.66 (m, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.44-7.19 (m, 3H), 5.84-5.59 (m, 1H), 2.81-2.68 (m, 2H), 1.62 (dd, *J* = 24.0, 6.8 Hz, 3H), 1.34-1.26 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; *δ*, ppm) 199.1 (d, *J* = 19.9 Hz), 192.1 (d, *J* = 21.5 Hz), 150.9, 137.1 (d, *J* = 18.4 Hz), 133.4, 132.7 (d, *J* = 1.6 Hz), 132.5 (d, *J* = 1.0 Hz), 132.3 (d, *J* = 2.4 Hz), 129.74 (d, *J* = 5.3 Hz), 129.5 (d, *J* = 1.9 Hz), 128.3, 127.4 (d, *J* = 15.6 Hz), 89.6 (d, *J* = 176.9 Hz), 89.3 (d, *J* = 176.4 Hz), 29.1, 17.85 (d, *J* = 22.6 Hz), 15.2. ^{19}F NMR (376 MHz, $CDCl_3$; *δ*, ppm) -178.3 (s, 1F), -180.3 (s, 1F, major), -180.9 (s, 1F, major), -181.3 (s, 1F). IR (film, ν, cm^{-1}) 3052, 2965, 2930, 2869, 1683, 1604, 1574, 1240, 1219, 1010, 980. HR-MS (ESI) m/z calcd for $C_{19}H_{18}F_2O_2$ $[M+Na]^+$ 339.1172, found 339.1174.

1-(2-(2-(4-(tert-Butyl)phenyl)-1-fluoro-2-oxoethyl)phenyl)-2-fluoropropan-1-one (2i)



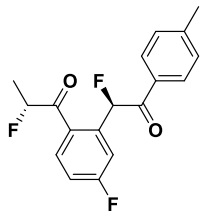
white solid, mp 85-87 °C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.09 (d, J = 8.4 Hz, 2H), 7.92 (d, J = 8.0 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.74-7.67 (m, 1H), 7.59-7.52 (m, 3H), 7.40 (d, J = 47.6 Hz, 1H), 5.84-5.63 (m, 1H), 1.64 (dd, J = 24.0, 6.8 Hz, 3H), 1.39 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 199.1 (d, J = 19.8 Hz), 192.1 (d, J = 21.6 Hz), 157.6, 137.0 (d, J = 18.4 Hz), 133.3 (d, J = 1.4 Hz), 132.4 (d, J = 1.6 Hz), 132.3 (d, J = 2.5 Hz), 129.7 (d, J = 5.3 Hz), 129.24 (d, J = 2.1 Hz), 128.4, 127.4 (d, J = 15.6 Hz), 125.8, 89.8 (d, J = 179.2 Hz), 89.8 (d, J = 176.9 Hz), 35.2, 31.1, 17.9 (d, J = 22.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; δ, ppm) -178.4 (s, 1F), -179.6 (s, 1F), -180.3 (s, 1F,major), -181.0 (s, 1F, major). IR (film, ν, cm^{-1}) 3037, 2971, 2873, 1697, 1682, 1600, 1572, 1317, 1222, 1190, 1085, 1014, 973. HR-MS (ESI) m/z calcd for $C_{21}H_{22}F_2O_2$ $[M+Na]^+$ 367.1486, found 367.1480.

2-Fluoro-1-(2-(1-fluoro-2-oxo-2-(thiophen-3-yl)ethyl)phenyl)propan-1-one (2j)



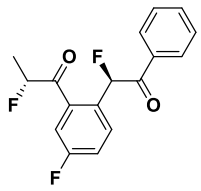
oil; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.44-8.38 (m, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.81-7.72 (m, 1H), 7.71-7.62 (m, 2H), 7.57-7.49 (m, 1H), 7.41-7.33 (m, 1H), 7.10 (d, J = 47.6 Hz, 1H), 5.83-5.62 (m, 1H), 1.64 (dd, J = 24.0, 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 199.7 (d, J = 20.1 Hz), 187.1 (d, J = 22.7 Hz), 139.2 (d, J = 2.1 Hz), 136.1 (d, J = 18.5 Hz), 134.6 (d, J = 5.9 Hz), 133.1 (d, J = 1.0 Hz), 132.8 (d, J = 2.7 Hz), 129.5 (d, J = 5.3 Hz), 128.6 (d, J = 1.4 Hz), 127.7 (d, J = 1.5 Hz), 127.4 (d, J = 14.3 Hz), 126.2, 91.1 (d, J = 178.8 Hz), 90.0 (d, J = 179.6 Hz), 17.91 (d, J = 22.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; δ, ppm) -177.55--177.65 (m, 1F), -180.20 (s, 1F, major), -180.76--180.83 (m, 1F, major), -181.00 (s, 1F). IR (film, ν, cm^{-1}) 3110, 2991, 1690, 1575, 1509, 1415, 1232, 1180, 1082, 879. HR-MS (ESI) m/z calcd for $C_{15}H_{12}F_2O_2S$ $[M+Na]^+$ 317.0424, found 317.0430.

2-Fluoro-1-(4-fluoro-2-(1-fluoro-2-oxo-2-(p-tolyl)ethyl)phenyl)propan-1-one (2l)



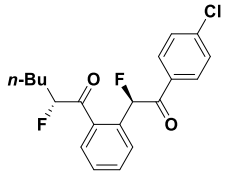
white solid, mp 115-117 °C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.10-7.98 (m, 3H), 7.55 (d, J = 10.0 Hz, 1H), 7.44-7.29 (m, 3H), 7.25-7.18 (m, 1H), 5.78-5.50 (m, 1H), 2.48 (s, 3H), 1.64 (dd, J = 24.4, 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 197.1 (d, J = 19.7 Hz), 191.0 (d, J = 21.5 Hz), 165.7 (d, J = 255.3 Hz), 144.9, 141.8 (dd, J = 18.6, 9.0 Hz), 132.8 (dd, J = 9.5, 6.9 Hz), 132.4 (d, J = 1.7 Hz), 129.6, 129.4 (d, J = 1.9 Hz), 115.3 (d, J = 16.2 Hz), 115.1 (dd, J = 24.6, 18.9 Hz), 89.8 (d, J = 178.9 Hz), 89.3 (d, J = 177.8 Hz), 21.8, 17.7 (d, J = 21.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; δ, ppm) -102.2 (s, 1F), -102.3 (s, 1F, major), -179.2 (s, 1F, major), -179.6 (s, 1F), -179.8 (s, 1F), -181.1 (s, 1F, major). IR (film, ν, cm^{-1}) 3059, 2995, 2944, 1689, 1608, 1586, 1244, 1226, 1188, 1106, 1092, 996. HR-MS (ESI) m/z calcd for $C_{18}H_{15}F_3O_2$ $[M+Na]^+$ 343.0922, found 343.0925.

2-Fluoro-1-(5-fluoro-2-(1-fluoro-2-oxo-2-phenylethyl)phenyl)propan-1-one (2m)



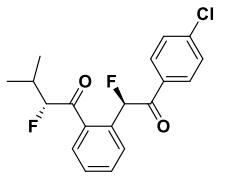
white solid, mp 78-80°C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.12 (d, J = 7.6 Hz, 2H), 7.80-7.73 (m, 1H), 7.69-7.62 (m, 2H), 7.55 (t, J = 7.6 Hz, 2H), 7.43-7.36 (m, 1H), 7.24 (d, J = 47.6 Hz, 1H), 5.74-5.50 (m, 1H), 1.63 (dd, J = 24.4, 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 198.3 (d, J = 18.8 Hz), 192.4 (d, J = 21.8 Hz), 162.0 (d, J = 248.4 Hz), 134.8 (d, J = 1.7 Hz), 133.9, 132.6 (dd, J = 18.8, 3.4 Hz), 129.4 (dd, J = 15.8, 8.1 Hz), 129.2 (d, J = 2.3 Hz), 128.8, 128.4 (d, J = 3.3 Hz), 120.2 (dd, J = 21.0, 1.4 Hz), 117.0 (dd, J = 23.2, 6.8 Hz), 90.1 (d, J = 179.9 Hz), 89.5 (d, J = 177.6 Hz), 17.6 (d, J = 22.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; δ, ppm) -111.4 (s, 1F), -111.9 (s, 1F, major), -111.3--111.4 (m, 1F), -178.3--178.5 (m, 1F, major), -180.3--180.4 (m, 1F), -180.4- -180.6(m, 1F, major). IR (film, ν, cm^{-1}) 3000, 2946, 2924, 1693, 1582, 1495, 1450, 1256, 1212, 1196, 1093, 1013, 1002, 913. HR-MS (ESI) m/z calcd for $C_{17}H_{13}F_3O_2$ $[M+Na]^+$ 329.0765, found 329.0767.

1-(2-(2-(4-Chlorophenyl)-1-fluoro-2-oxoethyl)phenyl)-2-fluorohexan-1-one (2n)



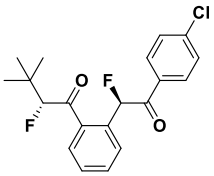
oil; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.12-8.05 (m, 2H), 7.96-7.89 (m, 1H), 7.82-7.76 (m, 1H), 7.72 (t, J = 7.6 Hz, 1H), 7.60-7.48 (m, 3H), 7.25 (d, J = 47.6 Hz, 1H), 5.66-5.48 (m, 1H), 2.07-1.81 (m, 2H), 1.59-1.28 (m, 4H), 0.93 (dd, J = 13.2, 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 199.1 (d, J = 19.7 Hz), 191.1 (d, J = 21.8 Hz), 140.2, 136.7 (d, J = 18.3 Hz), 133.5 (d, J = 3.9 Hz), 133.2 (d, J = 1.3 Hz), 132.3 (d, J = 2.9 Hz), 130.6 (d, J = 2.3 Hz), 129.8 (d, J = 5.6 Hz), 129.1, 128.5, 127.3 (d, J = 16.0 Hz), 93.3 (d, J = 182.0 Hz), 89.8 (d, J = 177.0 Hz), 32.0 (d, J = 21.1 Hz), 26.9 (d, J = 2.9 Hz), 22.2 (d, J = 5.3 Hz), 13.8 (s, 1H). ^{19}F NMR (376 MHz, $CDCl_3$; δ, ppm) -178.41 (d, J = 47.4 Hz, 1F), -181.35 (d, J = 47.4 Hz, 1F, major), -188.40--188.99 (m, 1F, major), -189.46--189.88 (m, 1F). IR (film, ν, cm^{-1}) 3068, 3028, 1725, 1590, 1507, 1448, 1359, 1220, 1199, 1173, 1155, 1083, 844. HR-MS (ESI) m/z calcd for $C_{20}H_{19}ClF_2O_2$ $[M+Na]^+$ 387.0939, found 387.0931.

1-(2-(2-(4-Chlorophenyl)-1-fluoro-2-oxoethyl)phenyl)-2-fluoro-3-methylbutan-1-one (2o)



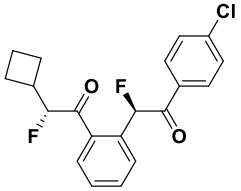
oil; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.09 (d, J = 8.4 Hz, 2H), 7.97 (d, J = 8.0 Hz, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.76-7.68 (m, 1H), 7.61-7.46 (m, 3H), 7.26 (d, J = 48.0 Hz, 1H), 5.53-5.28 (m, 1H), 2.57-2.14 (m, 1H), 1.10 (d, J = 6.8 Hz, 3H), 0.96 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 198.9 (d, J = 20.1 Hz), 191.2 (d, J = 21.7 Hz), 140.2, 136.8 (d, J = 18.1 Hz), 133.6 (d, J = 1.8 Hz), 132.4 (d, J = 2.4 Hz), 130.6 (d, J = 2.1 Hz), 130.1 (d, J = 6.2 Hz), 129.2, 129.1, 128.5, 127.3 (d, J = 16.3 Hz), 97.1 (d, J = 185.5 Hz), 89.8 (d, J = 176.8 Hz), 31.4 (d, J = 20.5 Hz), 19.0 (d, J = 4.0 Hz), 16.0 (d, J = 5.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; δ, ppm) -177.53 (s, 1F), -180.84 (s, 1F, major), -198.53 (s, 3F,major), -199.65 (s, 1F). IR (film, ν, cm^{-1}) 3072, 2969, 2935, 2878, 1698, 1590, 1574, 1489, 1402, 1231, 1214, 1093, 101, 928. HR-MS (ESI) m/z calcd for $C_{19}H_{17}ClF_2O_2$ $[M+Na]^+$ 373.0783, found 373.0786.

1-(2-(2-(4-Chlorophenyl)-1-fluoro-2-oxoethyl)phenyl)-2-fluoro-3,3-dimethylbutan-1-one (2p)



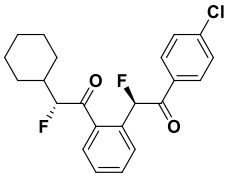
white solid, mp 95-97 °C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.09 (d, J = 8.4 Hz, 2H), 8.04 (d, J = 8.0 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.74-7.67 (m, 1H), 7.58-7.49 (m, 3H), 7.33 (d, J = 47.6 Hz, 1H), 5.32 (d, J = 48.4 Hz, 1H), 1.03 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 199.4 (d, J = 20.8 Hz), 191.5 (d, J = 21.7 Hz), 140.1, 136.4 (d, J = 17.9 Hz), 134.1 (d, J = 2.4 Hz), 133.6 (d, J = 1.7 Hz), 133.4 (d, J = 1.6 Hz), 130.6 (d, J = 2.1 Hz), 130.5, (d, J = 6.0 Hz), 129.1, 128.4, 127.3 (d, J = 16.2 Hz), 98.1 (d, J = 186.2 Hz), 89.97 (d, J = 176.9 Hz), 35.86 (d, J = 19.7 Hz), 25.9 (d, J = 4.6 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; δ, ppm) -180.17 (s, 1F), -190.40 (s, 1F). IR (film, ν, cm^{-1}) 3049, 2979, 2942, 2876, 1698, 1671, 1591, 1574, 1403, 1314, 1249, 1213, 1095, 1013, 985. HR-MS (ESI) m/z calcd for $C_{20}H_{19}ClF_2O_2$ $[M+Na]^+$ 387.0939, found 387.0944.

1-(4-Chlorophenyl)-2-(2-(2-cyclobutyl-2-fluoroacetyl)phenyl)-2-fluoroethanone (2q)



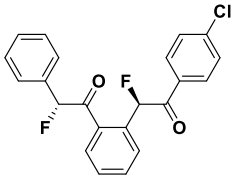
oil; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.06 (d, J = 8.4 Hz, 2H), 7.92 (d, J = 7.6 Hz, 1H), 7.80-7.66 (m, 2H), 7.58-7.46 (m, 3H), 7.21 (d, J = 48.0 Hz, 1H), 5.62-5.45 (m, 1H), 3.02-2.80 (m, 1H), 2.20-1.78 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 198.2 (d, J = 19.9 Hz), 191.23 (d, J = 21.7 Hz), 140.1, 136.64 (d, J = 18.2 Hz), 133.5 (d, J = 1.6 Hz), 133.4, 130.6 (d, J = 2.0 Hz), 129.9 (d, J = 5.3 Hz), 129.1, 128.9 (d, J = 1.8 Hz), 128.5, 127.3 (d, J = 16.0 Hz), 94.2 (d, J = 182.8 Hz), 89.8 (d, J = 176.8 Hz), 37.1 (d, J = 22.4 Hz), 22.5 (d, J = 4.6 Hz), 18.1 (d, J = 12.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; δ, ppm) -177.4 (d, J = 47.8 Hz, 1F), -181.1 (d, J = 47.4 Hz, 1F, major), -196.8 (dd, J = 49.6, 26.7 Hz, 1F, major), -197.5 (dd, J = 49.6, 26.7 Hz, 1F). IR (film, ν, cm^{-1}) 3071, 2983, 2945, 2866, 1697, 1590, 1574, 1489, 1402, 1245, 1214, 1093, 1012, 976. HR-MS (ESI) m/z calcd for $C_{20}H_{17}ClF_2O_2$ $[M+Na]^+$ 385.0783, found 385.0777.

1-(4-Chlorophenyl)-2-(2-(2-cyclohexyl-2-fluoroacetyl)phenyl)-2-fluoroethanone (2r)



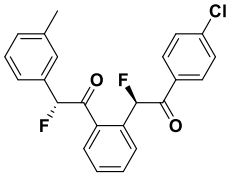
white solid, mp 88-90 °C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.08 (d, J = 8.8 Hz, 2H), 7.97 (d, J = 7.6 Hz, 1H), 7.80 (d, J = 7.6 Hz, 1H), 7.72 (t, J = 7.6 Hz, 1H), 7.56 (t, J = 7.6 Hz, 1H), 7.52 (d, J = 8.4 Hz, 2H), 7.25 (d, J = 47.6 Hz, 1H), 5.45-5.19 (m, 1H), 2.13-1.94 (m, 1H), 1.84-1.56 (m, 5H), 1.42-1.09 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 199.2 (d, J = 20.1 Hz), 191.3 (d, J = 21.8 Hz), 140.2, 136.6 (d, J = 18.1 Hz), 133.5, 132.6 (d, J = 2.0 Hz), 130.6 (d, J = 2.2 Hz), 130.1 (d, J = 6.6 Hz), 129.1, 128.5, 127.3 (d, J = 16.0 Hz), 97.0 (d, J = 184.8 Hz), 89.8 (d, J = 177.0 Hz), 40.7 (d, J = 19.9 Hz), 29.1 (d, J = 3.3 Hz), 26.0, 25.7 (d, J = 21.4 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; δ, ppm) -177.4 (s, 1F), -180.8 (s, 1F, major), -195.9 (s, 1F, major), -197.0 (s, 1F). IR (film, ν, cm^{-1}) 3092, 2935, 2853, 1701, 1682, 1588, 1572, 1450, 1403, 1229, 1216, 1093, 1014, 989.. HR-MS (ESI) m/z calcd for $C_{22}H_{21}ClF_2O_2$ $[M+Na]^+$ 413.1096, found 413.1107.

1-(4-Chlorophenyl)-2-fluoro-2-(2-(2-fluoro-2-phenylacetyl)phenyl)ethanone (2s)



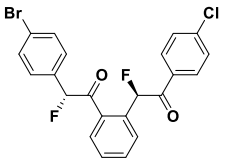
white solid, mp 145-147 °C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.11 (d, J = 8.4 Hz, 2H), 7.88 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.66 (t, J = 7.6 Hz, 1H), 7.53 (d, J = 8.4 Hz, 2H), 7.50-7.38 (m, 6H), 7.24 (d, J = 47.6 Hz, 1H), 6.51 (d, J = 48.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 196.2 (d, J = 22.0 Hz), 190.9 (d, J = 21.7 Hz), 140.2, 136.9 (d, J = 19.0 Hz), 133.8 (d, J = 20.1 Hz), 133.6, 133.2 (d, J = 1.3 Hz), 131.9 (d, J = 2.9 Hz), 130.6 (d, J = 1.8 Hz), 130.1 (d, J = 3.3 Hz), 129.8 (d, J = 2.4 Hz), 129.2, 128.6 (d, J = 1.5 Hz), 127.8, 127.7 (d, J = 4.5 Hz), 127.1 (d, J = 5.5 Hz), 93.7 (d, J = 186.1 Hz), 89.3 (d, J = 176.4 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; δ, ppm) -173.1 (s, 1F), -175.9 (s, 1F, major), -179.2 (s, 1F, major), -180.9 (s, 1F). IR (film, ν, cm^{-1}) 3066, 2962, 1686, 1589, 1574, 1489, 1402, 1229, 1214, 1092, 1053, 1012, 972. HR-MS (ESI) m/z calcd for $C_{22}H_{15}ClF_2O_2$ $[M+Na]^+$ 407.0626, found 407.0621.

1-(4-Chlorophenyl)-2-fluoro-2-(2-(2-fluoro-2-(m-tolyl)acetyl)phenyl)ethanone (2t)



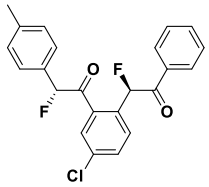
oil; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.09 (d, J = 8.0 Hz, 2H), 7.84 (d, J = 7.6 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.66 (t, J = 7.6 Hz, 1H), 7.56-7.49 (m, 2H), 7.48-7.39 (m, 1H), 7.36-7.29 (m, 1H), 7.27-7.14 (m, 4H), 6.48 (d, J = 48.8 Hz, 1H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 196.2 (d, J = 21.8 Hz), 190.9 (d, J = 21.8 Hz), 140.2, 139.1 (d, J = 1.1 Hz), 137.0 (d, J = 18.1 Hz), 133.8 (d, J = 9.4 Hz), 133.5 (d, J = 17.3 Hz), 131.7 (d, J = 2.7 Hz), 130.8 (d, J = 2.9 Hz), 130.7, 130.3 (d, J = 2.9 Hz), 129.1, 128.5 (d, J = 1.1 Hz), 128.4 (d, J = 4.9 Hz), 127.8 (dd, J = 10.2, 4.7 Hz), 127.3 (d, J = 15.9 Hz), 124.9 (d, J = 5.2 Hz), 93.7 (d, J = 184.4 Hz), 89.8 (d, J = 177.1 Hz), 21.4. ^{19}F NMR (376 MHz, $CDCl_3$; δ, ppm) -172.30 (s, 1F, major), -175.13 (s, 1F), -179.18 (s, 1F), -180.88 (s, 1F, major). IR (film, ν, cm^{-1}) 3067, 2961, 2922, 2863, 1686, 1589, 1574, 1489, 1401, 1247, 1213, 1093, 1012, 973. HR-MS (ESI) m/z calcd for $C_{23}H_{17}ClF_2O_2$ $[M+Na]^+$ 421.0783, found 421.0791.

2-(4-Bromophenyl)-1-(2-(2-(4-chlorophenyl)-1-fluoro-2-oxoethyl)phenyl)-2-fluoroethanone (2u)



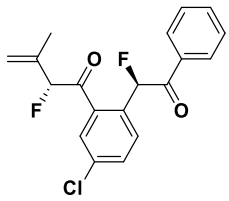
white solid, mp 124-126°C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.06 (d, J = 8.4 Hz, 2H), 7.89-7.74 (m, 2H), 7.72-7.66 (m, 1H), 7.61-7.43 (m, 5H), 7.39-7.29 (m, 2H), 7.27-7.02 (m, 1H), 6.46 (d, J = 48.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 195.8 (d, J = 21.8 Hz), 191.0 (d, J = 21.9 Hz), 140.3, 137.1 (d, J = 18.3 Hz), 133.9, 133.3 (d, J = 1.8 Hz), 132.9 (d, J = 20.1 Hz), 132.4, 131.5 (d, J = 2.8 Hz), 130.7 (d, J = 2.2 Hz), 130.2 (d, J = 3.6 Hz), 129.2 (d, J = 1.8 Hz), 129.2, 128.5, 127.4 (d, J = 16.1 Hz), 124.3 (d, J = 3.3 Hz), 92.9 (d, J = 185.7 Hz), 89.9 (d, J = 177.7 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; δ, ppm) -174.35 (s, 1F, major), -176.83 (s, 1F), -179.45 (s, 1F), -181.50 (s, 1F, major). IR (film, ν, cm^{-1}) 3089, 2966, 1690, 1588, 1573, 1489, 1403, 1315, 1227, 1212, 1095, 1012, 971. HR-MS (ESI) m/z calcd for $C_{22}H_{14}BrClF_2O_2$ $[M+Na]^+$ 484.9713, found 484.9729.

1-(5-Chloro-2-(1-fluoro-2-oxo-2-phenylethyl)phenyl)-2-fluoro-2-(p-tolyl)ethanone (2v)



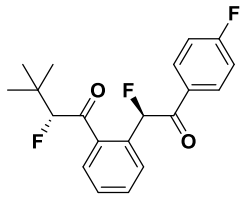
white solid, mp 92-94 °C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.13 (dd, J = 12.8, 7.6 Hz, 2H), 7.79 (s, 1H), 7.75-7.51 (m, 5H), 7.37-7.29 (m, 2H), 7.28-7.02 (m, 3H), 6.41 (d, J = 48.4 Hz, 1H), 2.39 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 195.5 (d, J = 22.6 Hz), 191.8 (d, J = 21.6 Hz), 140.3 (d, J = 3.0 Hz), 135.5 (d, J = 18.8 Hz), 134.6 (d, J = 1.7 Hz), 134.5 (d, J = 2.0 Hz), 133.9, 133.4 (d, J = 2.7 Hz), 133.3 (d, J = 1.7 Hz), 130.5 (d, J = 20.1 Hz), 130.0, 129.8 (d, J = 3.5 Hz), 129.3 (d, J = 14.6 Hz), 128.8 (d, J = 3.5 Hz), 127.6 (d, J = 5.0 Hz), 93.8 (d, J = 185.7 Hz), 89.5 (d, J = 178.0 Hz), 21.3. ^{19}F NMR (376 MHz, $CDCl_3$; δ, ppm) -172.16 (d, J = 4.1 Hz, 1F, major), -174.40 (d, J = 3.1 Hz, 1F), -179.09 (s, 1F), -180.75 (s, 1F, major). IR (film, ν, cm^{-1}) 3071, 2922, 1694, 1597, 1562, 1449, 1219, 1182, 1115, 1062, 1014, 977. HR-MS (ESI) m/z calcd for $C_{23}H_{17}ClF_2O_2$ $[M+Na]^+$ 421.0783, found 421.0788.

1-(5-Chloro-2-(1-fluoro-2-oxo-2-phenylethyl)phenyl)-2-fluoro-3-methylbut-3-en-1-one (2w)



white solid, mp 77-79 °C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.18-8.08 (m, 2H), 7.97 (s, 1H), 7.76-7.62 (m, 3H), 7.59-7.50 (m, 2H), 7.27 (d, J = 47.6 Hz, 1H), 5.80 (d, J = 48.4 Hz, 1H), 5.38-5.22 (m, 2H), 1.81-1.73 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 195.7 (d, J = 22.1 Hz), 191.7 (d, J = 21.6 Hz), 138.5 (d, J = 18.0 Hz), 135.4 (d, J = 4.8 Hz), 134.8 (d, J = 1.7 Hz), 134.6 (d, J = 2.1 Hz), 133.9, 133.4 (d, J = 1.6 Hz), 130.1 (d, J = 5.4 Hz), 129.3 (d, J = 2.5 Hz), 128.8, 128.7 (d, J = 16.2 Hz), 118.0 (d, J = 9.1 Hz), 96.0 (d, J = 186.8 Hz), 89.0 (d, J = 177.1 Hz), 17.8 (d, J = 2.7 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; δ, ppm) -178.54 (s, 1F), -181.42 (s, 1F), -181.81 (s, 1F), -182.33 (s, 1F). IR (film, ν, cm^{-1}) 3071, 2987, 1694, 1597, 1562, 1451, 1219, 1117, 1062, 1016, 992. HR-MS (ESI) m/z calcd for $C_{19}H_{15}ClF_2O_2$ $[M+Na]^+$ 371.0626, found 371.0631.

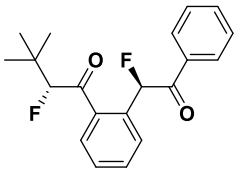
2-Fluoro-1-(2-(1-fluoro-2-(4-fluorophenyl)-2-oxoethyl)phenyl)-3,3-dimethylbutan-1-one (2x)



white solid, mp 62-64 °C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.19 (dd, J = 8.0, 5.6 Hz, 2H), 8.03 (d, J = 7.6 Hz, 1H), 7.79 (d, J = 7.6 Hz, 1H), 7.70 (t, J = 7.6 Hz, 1H), 7.55 (t, J = 7.6 Hz, 1H), 7.43-7.17 (m, 3H), 5.33 (d, J = 48.0 Hz, 1H), 1.03 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 199.5 (d, J = 20.7 Hz), 191.1 (d, J = 21.5 Hz), 166.1 (d, J = 254.2 Hz), 136.5 (d, J = 18.0 Hz), 134.1 (d, J = 2.4 Hz), 133.4 (d, J = 1.5 Hz), 131.9 (dd, J = 9.4, 2.2 Hz), 131.6 (dd, J = 2.7, 2.0 Hz), 130.5 (d, J = 7.3 Hz), 128.4, 127.3 (d, J = 16.2 Hz), 116.0 (d, J = 21.8 Hz), 98.0 (d, J = 186.1 Hz), 89.98 (d, J = 176.9 Hz), 35.9 (d, J = 19.7 Hz), 25.9 (d, J = 4.6 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; δ, ppm) -103.95 (s, 1F), -180.03 (s, 1F), -190.48 (s, 1F). IR (film, ν, cm^{-1}) 3080, 2964, 1703, 1680, 1599, 1575, 1508, 1309, 1221, 1160, 1019, 983. HR-MS (ESI) m/z calcd for $C_{20}H_{19}F_3O_2$ $[M+Na]^+$ 371.1235,

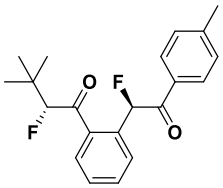
found 371.1236.

2-Fluoro-1-(2-(1-fluoro-2-oxo-2-phenylethyl)phenyl)-3,3-dimethylbutan-1-one (2y)



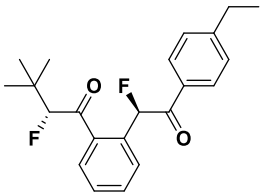
white solid, mp 84-86 °C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.12 (d, J = 7.6 Hz, 2H), 8.00 (d, J = 8.0 Hz, 1H), 7.77 (d, J = 7.6 Hz, 1H), 7.70-7.58 (m, 2H), 7.51 (t, J = 7.6 Hz, 3H), 7.38 (d, J = 48.0 Hz, 1H), 5.29 (d, J = 48.4 Hz, 1H), 1.02 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 199.5 (d, J = 21.0 Hz), 192.7 (d, J = 21.5 Hz), 136.6 (d, J = 18.0 Hz), 135.2 (d, J = 1.5 Hz), 134.3 (d, J = 2.3 Hz), 133.7, 133.3 (d, J = 1.1 Hz), 130.4 (d, J = 7.3 Hz), 129.2 (d, J = 2.0 Hz), 128.8, 128.3, 127.4 (d, J = 16.0 Hz), 98.2 (d, J = 186.2 Hz), 89.9 (d, J = 176.8 Hz), 35.9 (d, J = 19.7 Hz), 25.9 (d, J = 4.6 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; δ, ppm) -174.92 (s, 1F), -179.92 (s, 1F, major), -190.19 (s, 1F), -190.41 (s, 1F, major). IR (film, ν, cm^{-1}) 3076, 2985, 2967, 2944, 2913, 2875, 1702, 1671, 1598, 1571, 1452, 1314, 1239, 1215, 1183, 1068, 1016, 984. HR-MS (ESI) m/z calcd for $C_{20}H_{20}F_2O_2$ $[M+Na]^+$ 353.1329, found 353.1329.

2-fluoro-1-(2-(1-fluoro-2-oxo-2-(p-tolyl)ethyl)phenyl)-3,3-dimethylbutan-1-one (2z)



white solid, mp 100-102 °C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.04 (d, J = 8.0 Hz, 2H), 8.00 (d, J = 8.0 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.67 (t, J = 7.6 Hz, 1H), 7.53 (t, J = 7.6 Hz, 1H), 7.47-7.31 (m, 3H), 5.31 (d, J = 48.0 Hz, 1H), 2.46 (s, 3H), 1.04 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 199.6 (d, J = 20.8 Hz), 192.3 (d, J = 21.2 Hz), 144.7, 136.6 (d, J = 18.2 Hz), 134.4 (d, J = 2.5 Hz), 133.2 (d, J = 1.1 Hz), 132.7 (d, J = 1.4 Hz), 130.3 (d, J = 7.4 Hz), 129.5, 129.3 (d, J = 2.0 Hz), 128.3, 127.4 (d, J = 15.7 Hz), 98.3 (d, J = 186.2 Hz), 89.9 (d, J = 176.8 Hz), 35.9 (d, J = 19.6 Hz), 25.9 (d, J = 4.6 Hz), 21.8. ^{19}F NMR (376 MHz, $CDCl_3$; δ, ppm) -179.55 (s, 1F), -190.33 (s, 1F). IR (film, ν, cm^{-1}) 3011, 2988, 1686, 1671, 1607, 1571, 1370, 1319, 1241, 1225, 1209, 1067, 1017, 983. HR-MS (ESI) m/z calcd for $C_{21}H_{22}F_2O_2$ $[M+Na]^+$ 367.1486, found 367.1488.

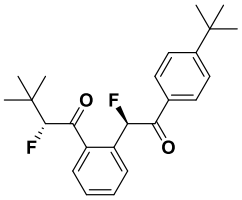
1-(2-(2-(4-ethylphenyl)-1-fluoro-2-oxoethyl)phenyl)-2-fluoro-3,3-dimethylbutan-1-one (2aa)



white solid, mp 85-87 °C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.07 (d, J = 8.0 Hz, 2H), 8.00 (d, J = 7.6 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.68 (t, J = 7.6 Hz, 1H), 7.53 (t, J = 7.6 Hz, 1H), 7.46-7.32 (m, 3H), 5.32 (d, J = 48.4 Hz, 1H), 2.75 (q, J = 7.6 Hz, 1H), 1.30 (t, J = 7.6 Hz, 3H), 1.04 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 199.6 (d, J = 21.1 Hz), 192.3 (d, J = 21.3 Hz), 150.7, 136.6 (d, J = 18.1 Hz), 134.4 (d, J = 2.6 Hz), 133.2, 132.8 (d, J = 1.5 Hz), 130.3 (d, J = 7.4 Hz), 129.4 (d, J = 2.0 Hz), 128.3, 127.4 (d, J = 15.6 Hz), 98.3 (d, J = 186.3 Hz), 89.9 (d, J = 176.8 Hz), 35.9 (d, J = 19.7 Hz), 29.1, 25.9 (d, J = 4.6 Hz), 15.1. ^{19}F NMR (376 MHz,

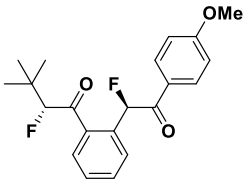
$CDCl_3$; *δ*, ppm) -179.58 (s, 1F), -190.42 (s, 1F). IR (film, ν, cm^{-1}) 3013, 2972, 2936, 1686, 1670, 1607, 1571, 1370, 1319, 1241, 1224, 1068, 1015, 985. HR-MS (ESI) m/z calcd for $C_{22}H_{24}F_2O_2$ $[M+Na]^+$ 381.1642, found 381.1647.

1-(2-(2-(4-(tert-butyl)phenyl)-1-fluoro-2-oxoethyl)phenyl)-2-fluoro-3,3-dimethylbutan-1-one (2bb)



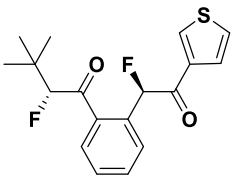
oil; ^{1}H NMR (400 MHz, $CDCl_3$; *δ*, ppm) 8.09 (d, *J* = 8.0 Hz, 2H), 8.01 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 7.6 Hz, 1H), 7.68 (t, *J* = 7.6 Hz, 1H), 7.58-7.50 (m, 3H), 7.40 (d, *J* = 48.0 Hz, 1H), 5.33 (d, *J* = 48.4 Hz, 1H), 1.38 (s, 9H), 1.04 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$; *δ*, ppm) 199.7 (d, *J* = 20.9 Hz), 192.3 (d, *J* = 21.3 Hz), 157.5, 136.6 (d, *J* = 18.0 Hz), 134.4 (d, *J* = 2.4 Hz), 133.2, 132.5, 130.3 (d, *J* = 7.2 Hz), 129.2 (d, *J* = 2.0 Hz), 128.3, 127.4 (d, *J* = 15.8 Hz), 125.8, 98.3 (d, *J* = 186.2 Hz), 93.18 (d, *J* = 176.7 Hz), 35.9 (d, *J* = 19.6 Hz), 35.2, 31.1, 25.9 (d, *J* = 4.6 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; *δ*, ppm) -179.59 (s, 1F), -190.48 (s, 1F). IR (film, ν, cm^{-1}). HR-MS (ESI) m/z calcd for $C_{24}H_{28}F_2O_2$ $[M+Na]^+$ 409.1955, found 409.1958.

2-fluoro-1-(2-(1-fluoro-2-(4-methoxyphenyl)-2-oxoethyl)phenyl)-3,3-dimethylbutan-1-one (2cc)



white solid, mp 91-93 °C; ^{1}H NMR (400 MHz, $CDCl_3$; *δ*, ppm) 8.13 (d, *J* = 8.8 Hz, 2H), 7.99 (d, *J* = 7.6 Hz, 1H), 7.77 (d, *J* = 7.6 Hz, 1H), 7.71-7.63 (m, 1H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.36 (d, *J* = 48.4 Hz, 1H), 7.00 (d, *J* = 8.8 Hz, 2H), 5.31 (d, *J* = 48.4 Hz, 1H), 3.91 (s, 3H), 1.04 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$; *δ*, ppm) 199.8 (d, *J* = 21.3 Hz), 191.2 (d, *J* = 21.3 Hz), 164.0, 136.6 (d, *J* = 17.9 Hz), 134.6 (d, *J* = 2.8 Hz), 133.1 (d, *J* = 0.9 Hz), 131.6 (d, *J* = 2.1 Hz), 130.2 (d, *J* = 7.5 Hz), 128.2, 128.1 (d, *J* = 1.5 Hz), 127.4 (d, *J* = 15.3 Hz), 114.0, 98.4 (d, *J* = 186.3 Hz), 89.8 (d, *J* = 176.9 Hz), 55.5, 35.9 (d, *J* = 19.7 Hz), 25.9 (d, *J* = 4.7 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; *δ*, ppm) -179.04 (s, 1F), -190.34 (s, 1F). IR (film, ν, cm^{-1}) 3072, 2976, 1686, 1673, 1602, 1575, 1423, 1263, 1248, 1033, 1016, 983. HR-MS (ESI) m/z calcd for $C_{21}H_{22}F_2O_3$ $[M+Na]^+$ 383.1435, found 383.1429.

2-Fluoro-1-(2-(1-fluoro-2-oxo-2-(thiophen-3-yl)ethyl)phenyl)-3,3-dimethylbutan-1-one (2dd)



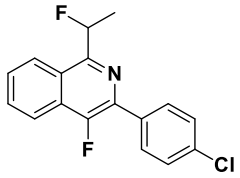
white solid, mp 82-84 °C; ^{1}H NMR (400 MHz, $CDCl_3$; *δ*, ppm) 8.44-8.40 (m, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.76-7.62 (m, 3H), 7.57-7.49 (m, 1H), 7.39-7.33 (m, 1H), 7.13 (d, *J* = 48.0 Hz, 1H), 5.29 (d, *J* = 48.0 Hz, 1H), 1.06 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$; *δ*, ppm) 200.2 (d, *J* = 21.7 Hz, 1H), 187.3 (d, *J* = 22.3 Hz), 139.4 (d, *J* = 2.0 Hz), 135.6 (d, *J* = 18.2 Hz), 135.0 (d, *J* = 2.7 Hz), 134.5 (d, *J* = 5.6 Hz), 132.9, 130.0 (d, *J* = 7.6 Hz), 128.5, 127.7 (d, *J* = 13.7 Hz), 127.6, 126.2, 98.7 (d, *J* = 186.9 Hz), 91.2 (d, *J* = 179.0 Hz), 35.9 (d, *J* = 19.6 Hz), 25.9 (d, *J* = 4.6 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; *δ*, ppm) -178.87 (s, 1F), -190.04 (s, 1F). IR (film, ν, cm^{-1})

3097, 2968, 1679, 1574, 1511, 1415, 1238, 1180, 1073, 984. HR-MS (ESI) m/z calcd for $C_{18}H_{18}F_2O_2S[M+Na]^+$ 359.0893, found 359.0898.

Typical Procedure for the Synthesis of Products 3.

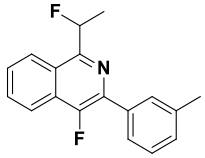
In an oven-dried Schlenk tube, to a methanol solution (1.0 mL) of products **2** (1.0 equiv, 0.2 mmol), NH_4OAc (3 equiv, 0.6 mmol) was added under air condition. The reaction mixture was stirred at room temperature for 8 hours. After the reaction monitored by TLC was completed, the organic solvent was removed under vacuum, and the residue was purified by silica gel column with petroleum ether/ethyl acetate to afford products.

3-(4-Chlorophenyl)-4-fluoro-1-(1-fluoroethyl)isoquinoline (3a)



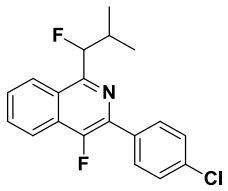
white solid, mp 106-107 °C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.44 (d, J = 8.8 Hz, 1H), 8.22 (d, J = 8.4 Hz, 1H), 8.16 (d, J = 8.4 Hz, 2H), 7.82 (t, J = 7.6 Hz, 1H), 7.75-7.67 (m, 1H), 7.51 (d, J = 8.8 Hz, 2H), 6.48-6.23 (m, 1H), 2.00 (dd, J = 24.0, 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 152.7 (dd, J = 19.7, 5.7 Hz), 152.5 (d, J = 266.6 Hz), 152.4 (d, J = 264.4 Hz), 134.7 (d, J = 1.4 Hz), 134.0 (d, J = 6.1 Hz), 133.0 (d, J = 10.2 Hz), 130.5 (d, J = 1.8 Hz), 130.2 (d, J = 7.2 Hz), 128.7, 128.2 (d, J = 16.3 Hz), 127.3 (d, J = 2.6 Hz), 125.2 (dd, J = 6.0, 1.2 Hz), 120.7 (d, J = 6.6 Hz), 90.8 (d, J = 166.6 Hz), 19.8 (d, J = 23.1 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; δ, ppm) -135.86 (d, J = 4.9 Hz, 1F), -167.18 (d, J = 4.5 Hz, 1F). IR (film, ν, cm^{-1}) 3052, 2985, 1623, 1591, 1502, 1450, 1319, 1264, 1182, 1070, 1054, 1011, 988. HR-MS (ESI) m/z calcd for $C_{17}H_{12}ClF_2N$ $[M+Na]^+$ 326.0524, found 326.0528.

4-Fluoro-1-(1-fluoroethyl)-3-(m-tolyl)isoquinoline (3b)



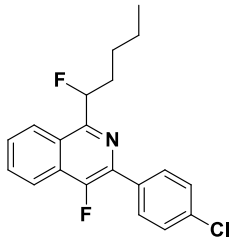
white solid, mp 73-75 °C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.46 (d, J = 8.4 Hz, 1H), 8.24 (d, J = 8.4 Hz, 1H), 7.98 (d, J = 10.0 Hz, 2H), 7.81 (t, J = 7.6 Hz, 1H), 7.75-7.66 (m, 1H), 7.45 (t, J = 7.6 Hz, 1H), 7.28 (d, J = 7.6 Hz, 1H), 6.49-6.27 (m, 1H), 2.51 (s, 3H), 2.01 (dd, J = 24.0, 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 152.6 (d, J = 20.8 Hz), 152.6 (d, J = 20.7 Hz), 152.34 (dd, J = 263.7, 1.7 Hz), 138.1, 135.5 (d, J = 5.8 Hz), 134.6 (d, J = 10.8 Hz), 130.3 (d, J = 1.8 Hz), 129.6 (d, J = 6.0 Hz), 129.5, 128.4, 127.9, 127.1 (d, J = 2.4 Hz), 126.1 (d, J = 6.7 Hz), 125.2 (dd, J = 6.3, 1.3 Hz), 120.7 (d, J = 6.6 Hz), 91.2 (d, J = 166.5 Hz), 21.7, 20.0 (d, J = 23.2 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; δ, ppm) -136.52 (d, J = 4.7 Hz, 1F), -167.21 (d, J = 4.7 Hz, 1F). IR (film, ν, cm^{-1}) 3051, 2921, 1622, 1588, 1501, 1373, 1263, 1162, 1059, 1040, 989. HR-MS (ESI) m/z calcd for $C_{18}H_{15}F_2N$ $[M+Na]^+$ 306.1070, found 306.1071.

3-(4-Chlorophenyl)-4-fluoro-1-(1-fluoro-2-methylpropyl)isoquinoline (3c)



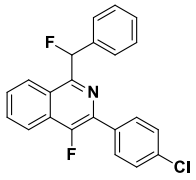
white solid, mp 86-88 °C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.45 (d, J = 8.4 Hz, 1H), 8.23 (d, J = 8.4 Hz, 1H), 8.15 (d, J = 8.4 Hz, 2H), 7.85-7.77 (m, 1H), 7.69 (t, J = 7.6 Hz, 1H), 7.51 (d, J = 8.4 Hz, 2H), 5.72 (dd, J = 47.6, 8.8 Hz, 1H), 2.89-2.68 (m, 1H), 1.30 (d, J = 6.8 Hz, 3H), 0.88 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 152.4 (d, J = 262.5 Hz), 152.3 (d, J = 21.6 Hz), 152.2 (d, J = 21.4 Hz, 2H), 134.7 (d, J = 1.1 Hz), 134.0 (d, J = 6.1 Hz), 133.1 (d, J = 10.2 Hz), 130.5 (d, J = 1.8 Hz), 130.2 (d, J = 7.0 Hz), 128.7, 128.3 (d, J = 1.0 Hz), 128.0 (d, J = 0.8 Hz), 125.3 (d, J = 1.2 Hz), 120.7 (d, J = 6.8 Hz), 99.8 (d, J = 174.6 Hz), 32.7 (d, J = 20.8 Hz), 18.7 (d, J = 6.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; δ, ppm) -136.36 (d, J = 4.1 Hz, 1F), -177.79 (d, J = 4.1Hz, 1F). IR (film, ν, cm^{-1}) 3073, 2976, 1624, 1590, 1503, 1377, 1251, 1187, 1091, 1011, 996. HR-MS (ESI) m/z calcd for $C_{19}H_{16}ClF_2N$ $[M+Na]^+$ 354.0837 found 354.0831.

3-(4-Chlorophenyl)-4-fluoro-1-(1-fluoropentyl)isoquinoline (3d)



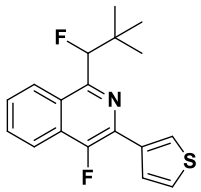
white solid, mp 68-69 °C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.44 (d, J = 8.8 Hz, 1H), 8.23 (d, J = 8.4 Hz, 1H), 8.15 (d, J = 8.8 Hz, 2H), 7.85-7.77 (m, 1H), 7.75-7.66 (m, 1H), 7.52 (d, J = 8.4 Hz, 2H), 6.24-5.97 (m, 1H), 2.50-2.15 (m, 2H), 1.76-1.60 (m, 1H), 1.58-1.41 (m, 3H), 1.02-0.92 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 152.69 (dd, J = 21.0, 5.7 Hz), 152.5 (dd, J = 264.1, 1.6 Hz) 134.7 (d, J = 1.3 Hz), 134.0 (d, J = 6.0 Hz), 133.1 (d, J = 10.2 Hz), 130.5 (d, J = 1.8 Hz), 130.2 (d, J = 7.1 Hz), 128.7, 128.3 (d, J = 16.2 Hz), 128.1, 127.4 (d, J = 2.5 Hz), 125.2 (dd, J = 6.5, 1.1 Hz), 120.7 (d, J = 6.7 Hz), 94.9 (d, J = 170.9 Hz), 34.1 (d, J = 21.6 Hz), 27.6 (d, J = 4.7 Hz), 22.5, 14.0. ^{19}F NMR (376 MHz, $CDCl_3$; δ, ppm) -136.20 (d, J = 4.1 Hz, 1F), -174.65 (d, J = 4.1 Hz, 1F). IR (film, ν, cm^{-1}) 3073, 2953, 1622, 1591, 1502, 1490, 1377, 1328, 1264, 1180, 1092, 1057, 1011, 947. HR-MS (ESI) m/z calcd for $C_{20}H_{18}ClF_2N$ $[M+Na]^+$ 368.0994, found 368.0986.

3-(4-Chlorophenyl)-4-fluoro-1-(fluoro(phenyl)methyl)isoquinoline (3e)



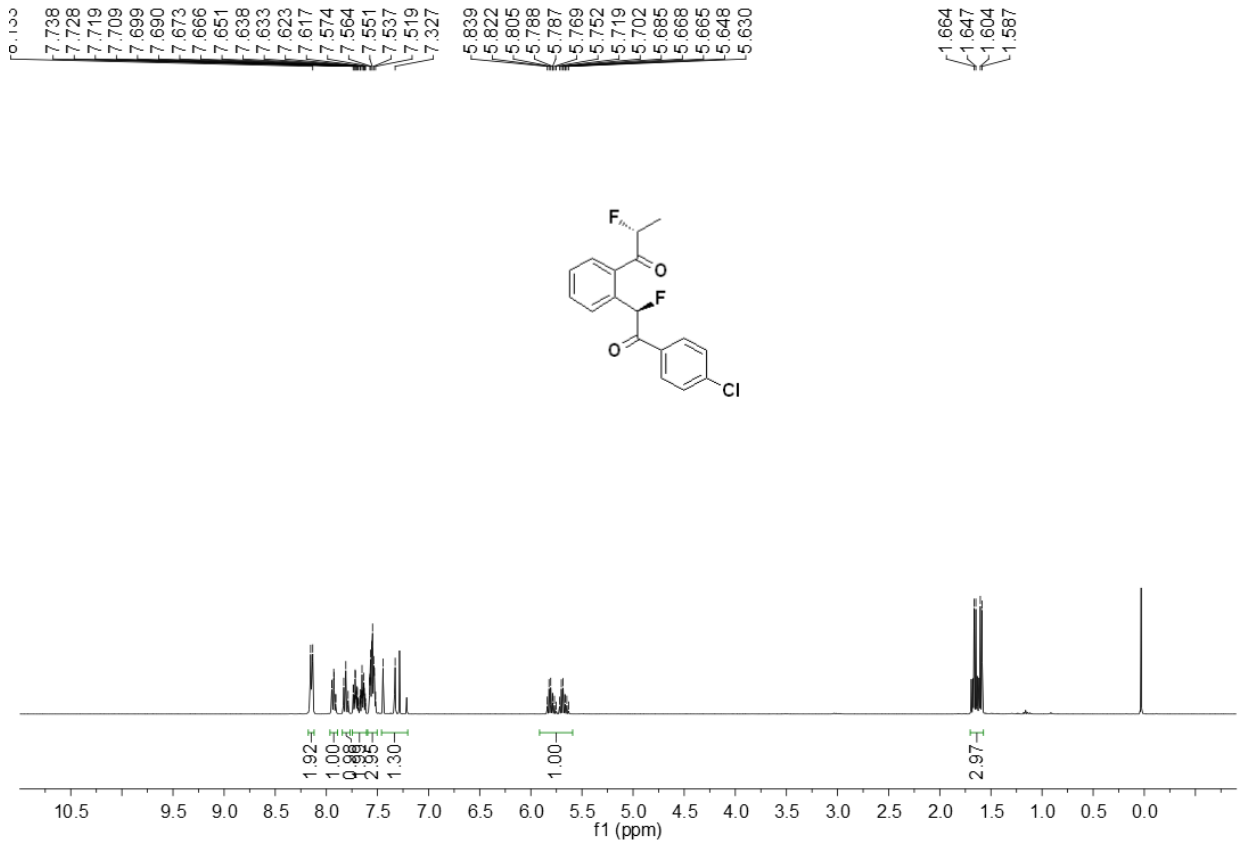
white solid, mp 114-116 °C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm)8.31 (d, J = 8.0 Hz, 1H), 8.22 (d, J = 8.4 Hz, 1H), 8.16 (d, J = 8.4 Hz, 2H), 7.80-7.75 (m, 1H), 7.63-7.57 (m, 1H), 7.55-7.46 (m, 3H), 7.4-7.31 (m, 3H), 7.15 (d, J = 47.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 152.6 (dd, J = 264.9, 1.6 Hz), 152.3 (d, J = 22.1 Hz), 152.2 (d, J = 22.1 Hz), 138.5 (d, J = 21.7 Hz), 134.8, 133.8 (d, J = 6.0 Hz), 133.3 (d, J = 10.2 Hz), 130.6 (d, J = 1.8 Hz), 130.2 (d, J = 7.1 Hz), 128.8 (d, J = 34.9 Hz), 128.7, 128.5, 128.3 (d, J = 1.4 Hz), 128.2, 127.1 (d, J = 2.7 Hz), 125.8 (d, J = 6.7 Hz), 120.7 (d, J = 6.7 Hz), 96.0 (d, J = 175.2 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; δ, ppm) -135.63 (d, J = 3.6 Hz, 1F), -174.68 (d, J = 3.6 Hz, 1F). IR (film, ν, cm^{-1}) 3061, 1622, 1592, 1502, 1448, 1372, 1175, 1162, 1093, 1057, 1012, 961. HR-MS (ESI) m/z calcd for $C_{22}H_{14}ClF_2N$ $[M+Na]^+$ 388.0681, found 388.0676.

4-Fluoro-1-(1-fluoro-2,2-dimethylpropyl)-3-(thiophen-3-yl)isoquinoline (3f)

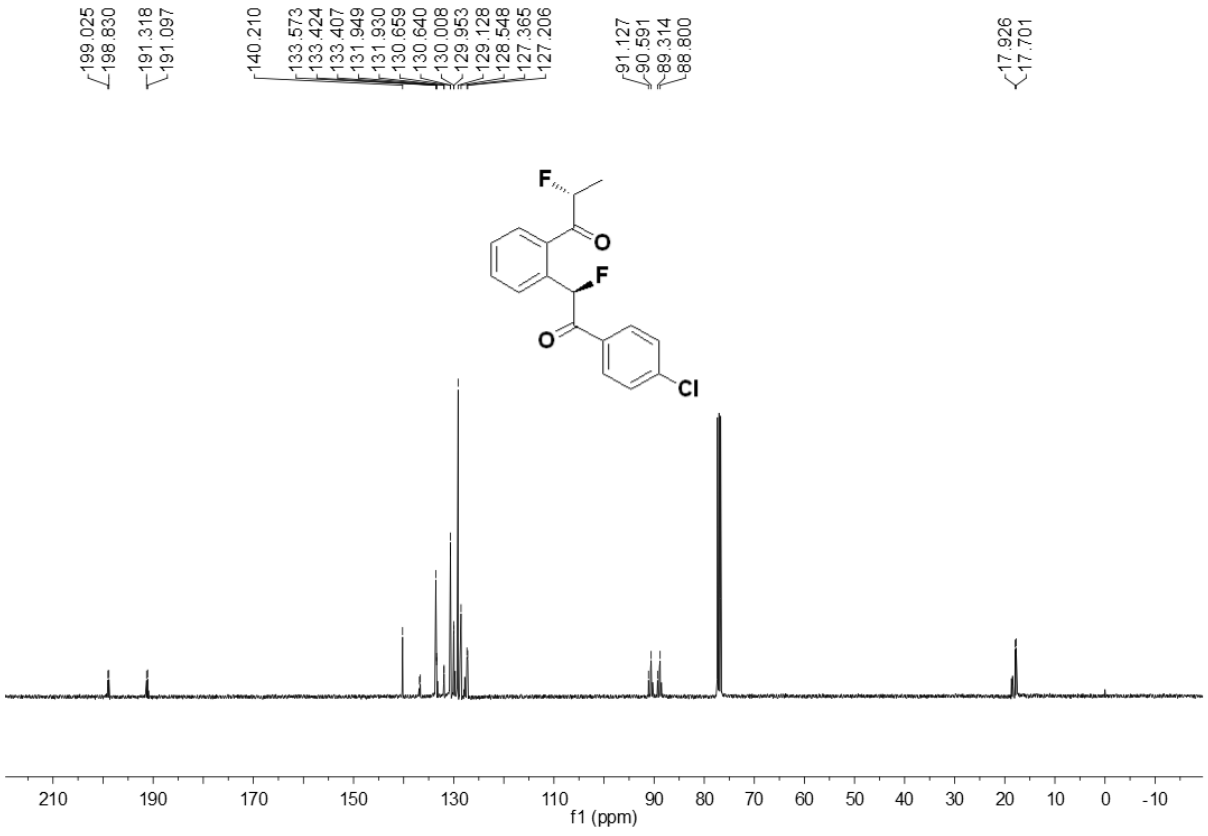


white solid, mp 89-91 °C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.45 (d, J = 8.4 Hz, 1H), 8.20 (d, J = 8.4 Hz, 2H), 7.99 (d, J = 4.8 Hz, 1H), 7.80-7.72 (m 1H), 7.67-7.58 (m, 1H), 7.46 (dd, J = 4.4, 3.2 Hz, 1H), 5.90 (d, J = 46.4 Hz, 1H), 1.16 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.3 (dd, J = 21.8, 6.0 Hz\), 150.84 (dd, J = 263.1, 1.2 Hz), 137.2 (d, J = 6.5 Hz), 130.7 (dd, J = 11.3, 1.1 Hz), 130.1 (d, J = 1.8 Hz), 128.0 (d, J = 15.6 Hz), 127.9 (d, J = 6.0 Hz), 127.8 (d, J = 1.2 Hz), 127.3 (d, J = 1.7 Hz), 126.3 (dd, J = 10.8, 1.2 Hz), 125.6 (d, J = 9.8 Hz), 125.4 (d, J = 1.0 Hz), 120.3 (d, J = 6.9 Hz), 101.2 (d, J = 179.6 Hz), 36.6 (d, J = 20.5 Hz), 26.4 (d, J = 4.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$; δ, ppm) -136.29 (s, 1F), -185.14 (d, J = 1.9 Hz, 1F). IR (film, ν, cm^{-1}) 3067, 2970, 1623, 1591, 1476, 1395, 1213, 1174, 1057, 995. HR-MS (ESI) m/z calcd for $C_{18}H_{17}F_2NS$ $[M+Na]^+$ 340.0947, found 340.0948.

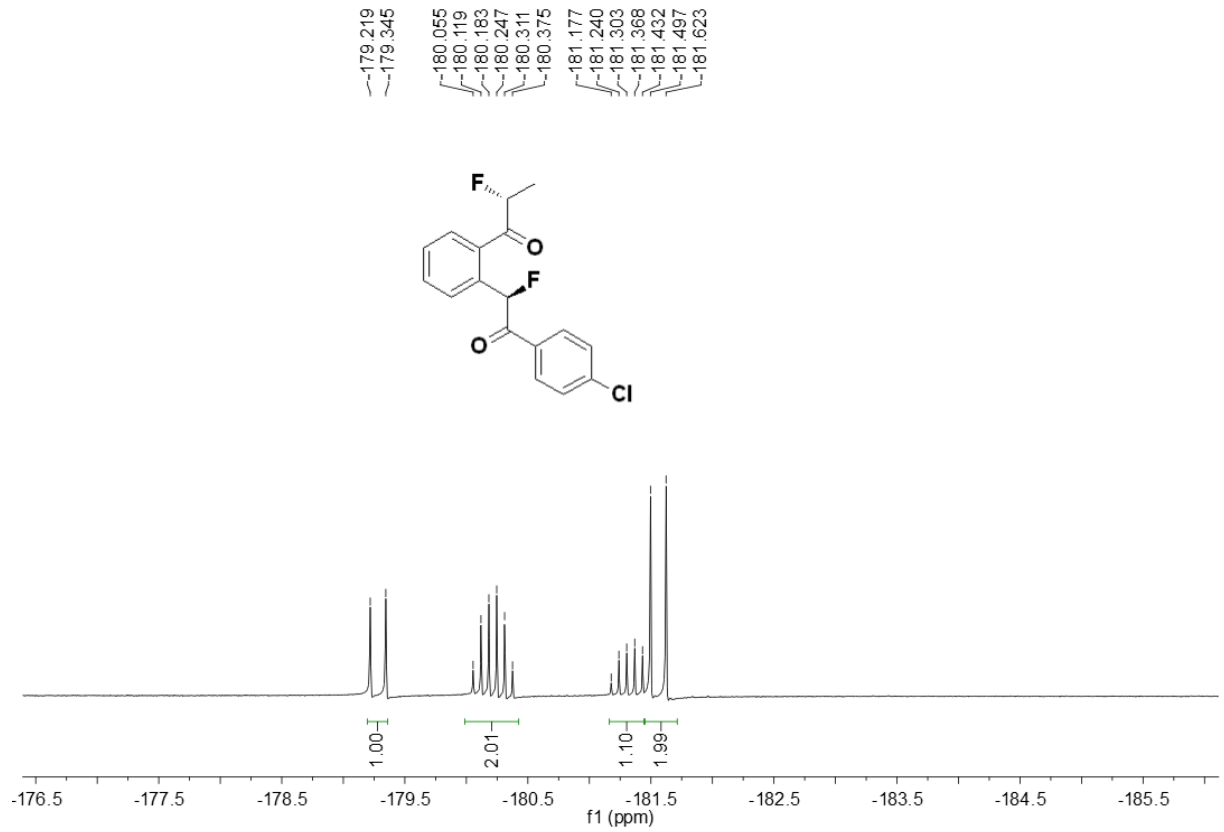
Copies of ^{1}H, ^{13}C and ^{19}F NMR Spectra for Compounds



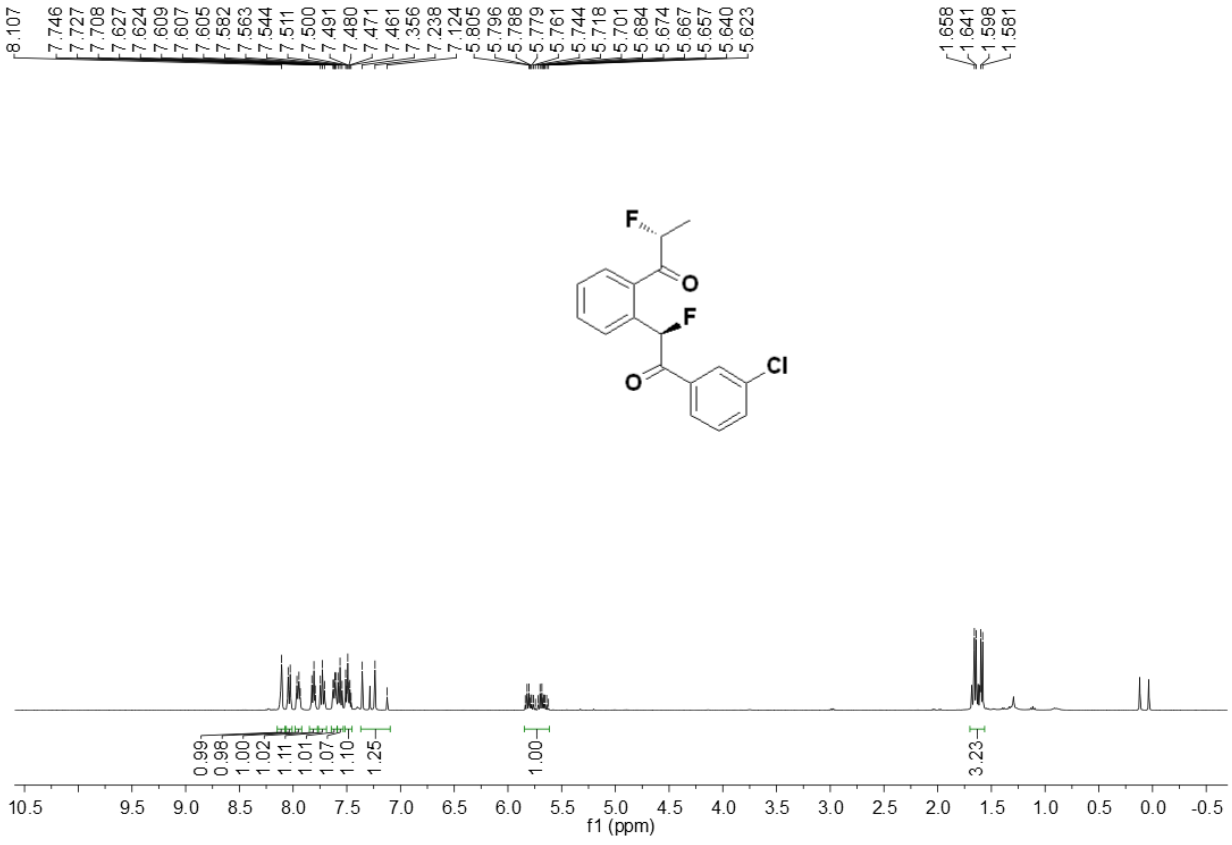
^{1}H NMR Spectrum of Compound 2a



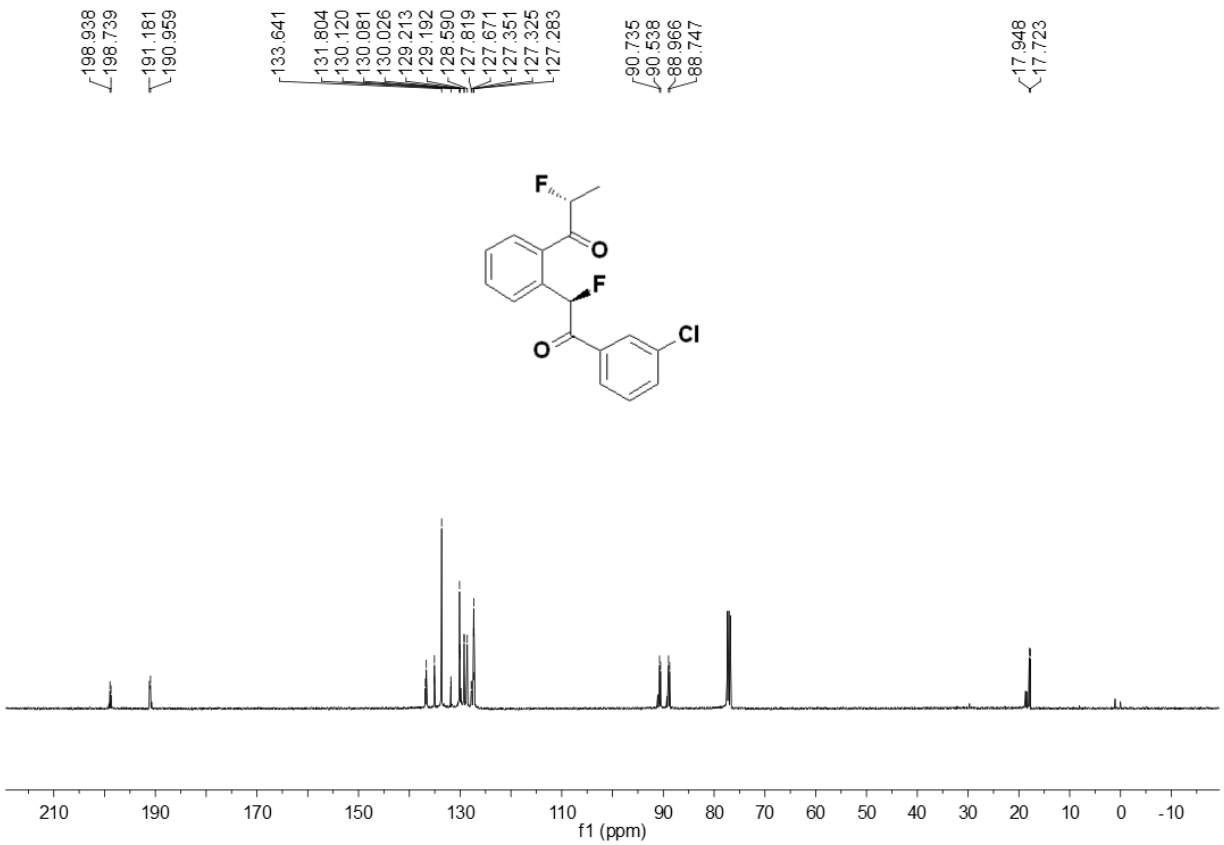
^{13}C NMR Spectrum of Compound 2a



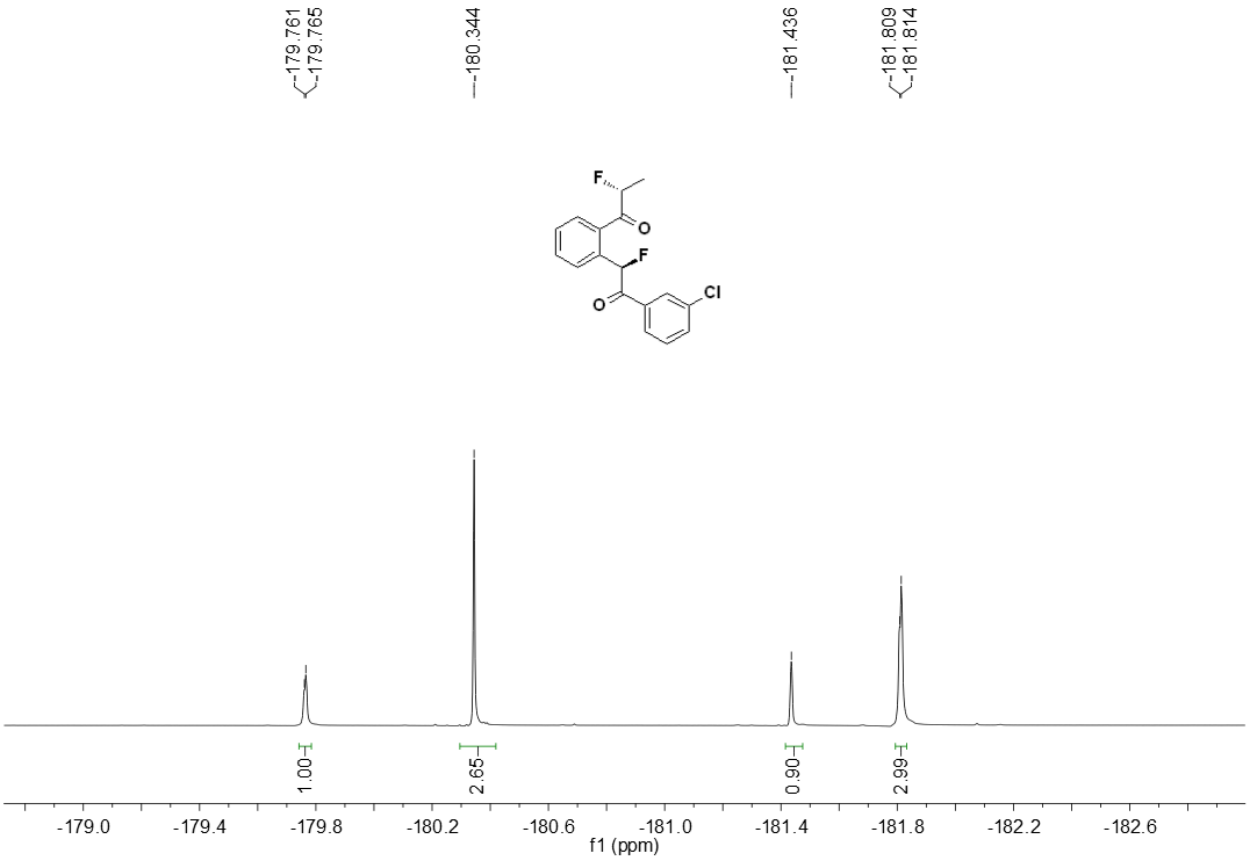
^{19}F NMR Spectrum of Compound 2a



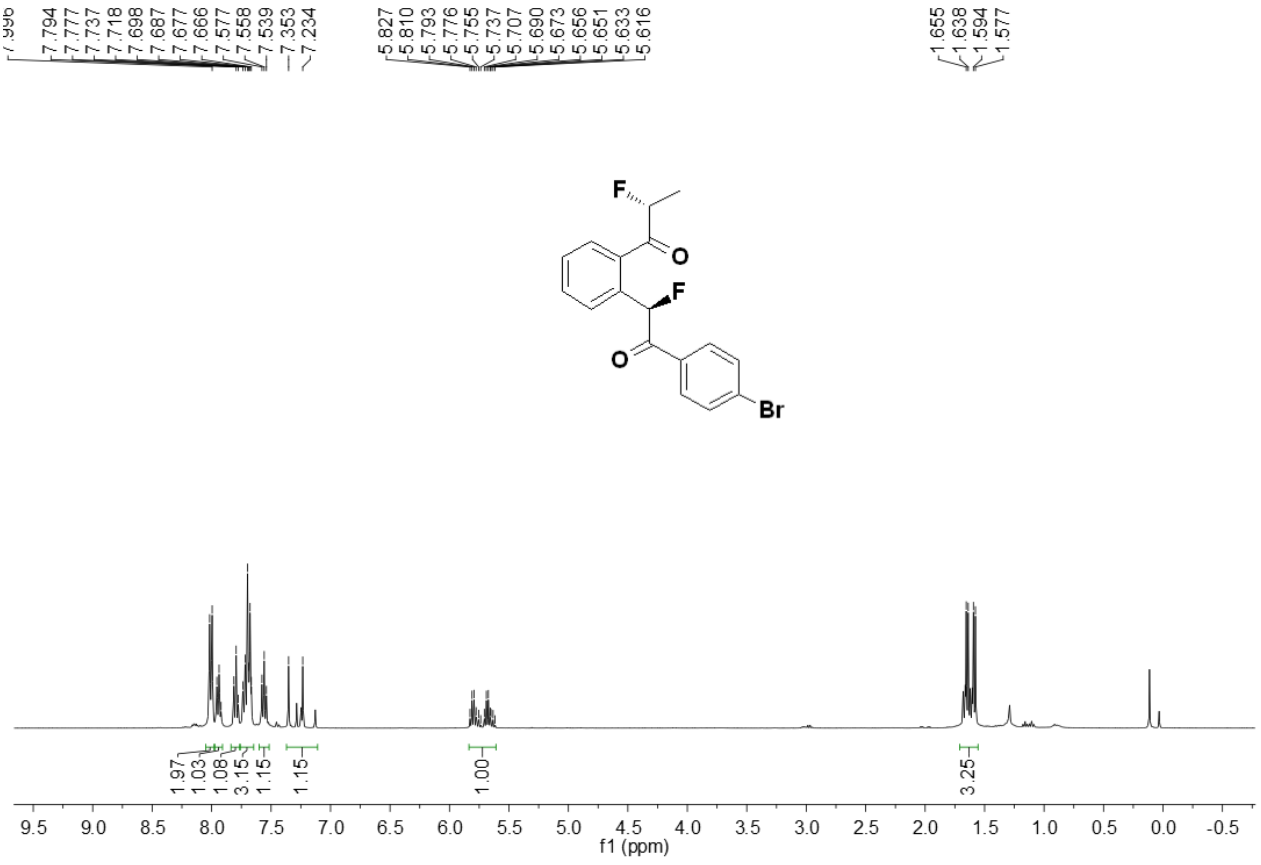
^{1}H NMR Spectrum of Compound 2b



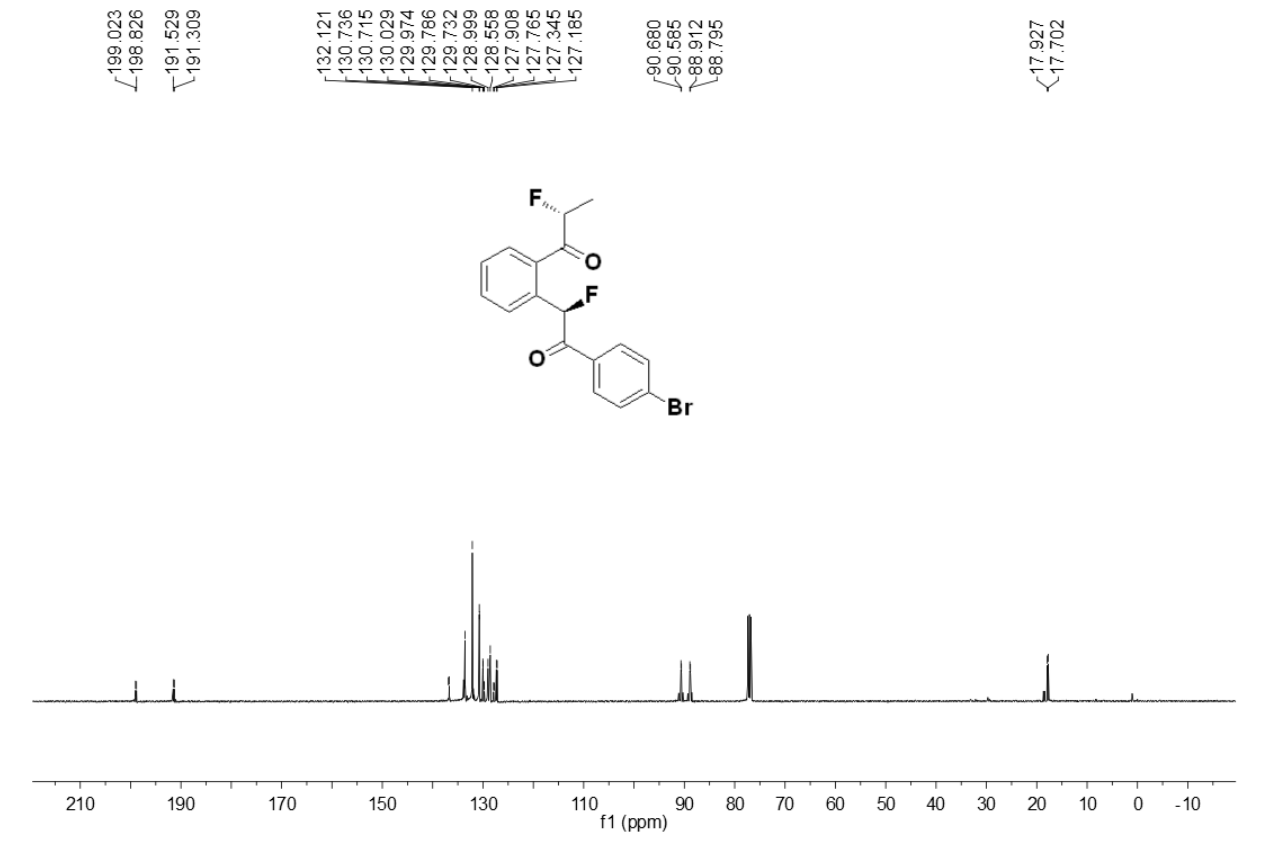
^{13}C NMR Spectrum of Compound 2b



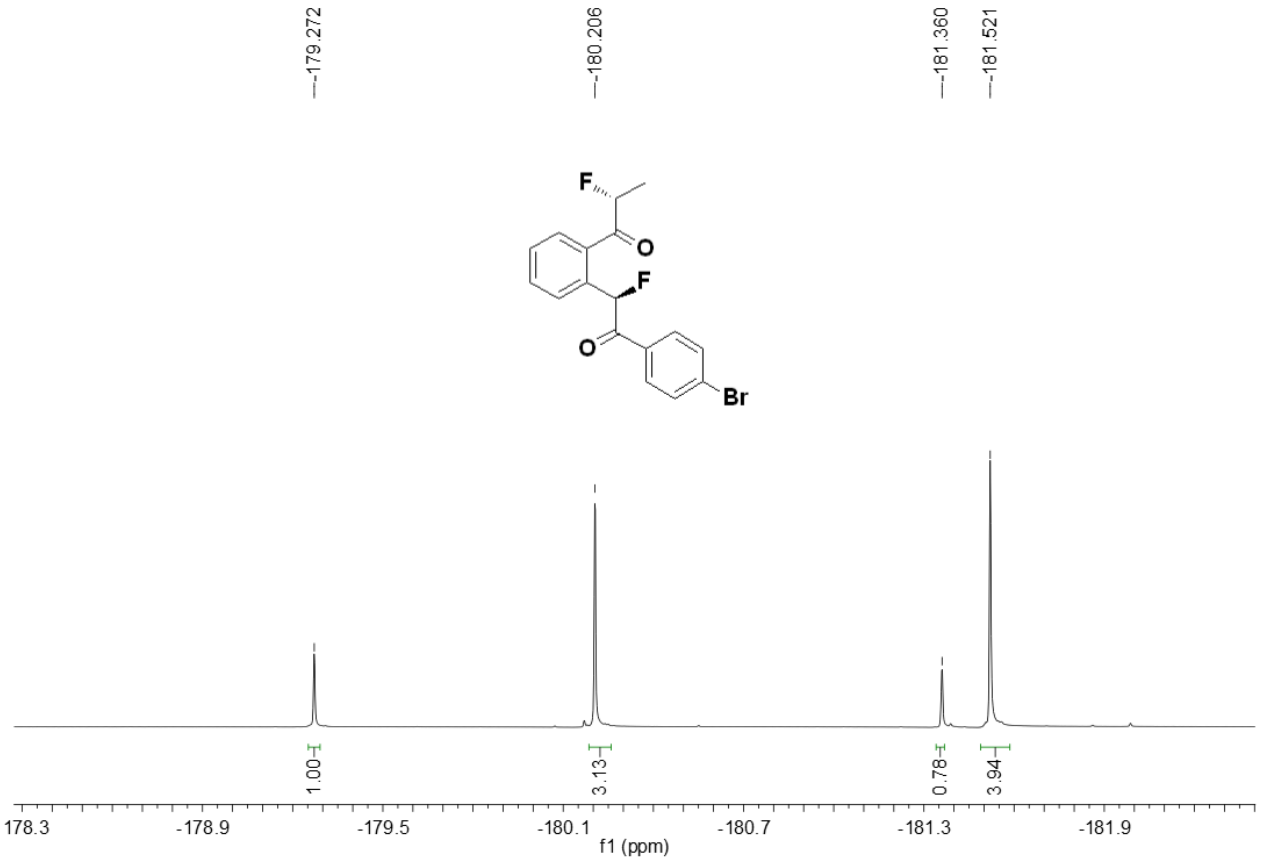
^{19}F NMR Spectrum of Compound 2b



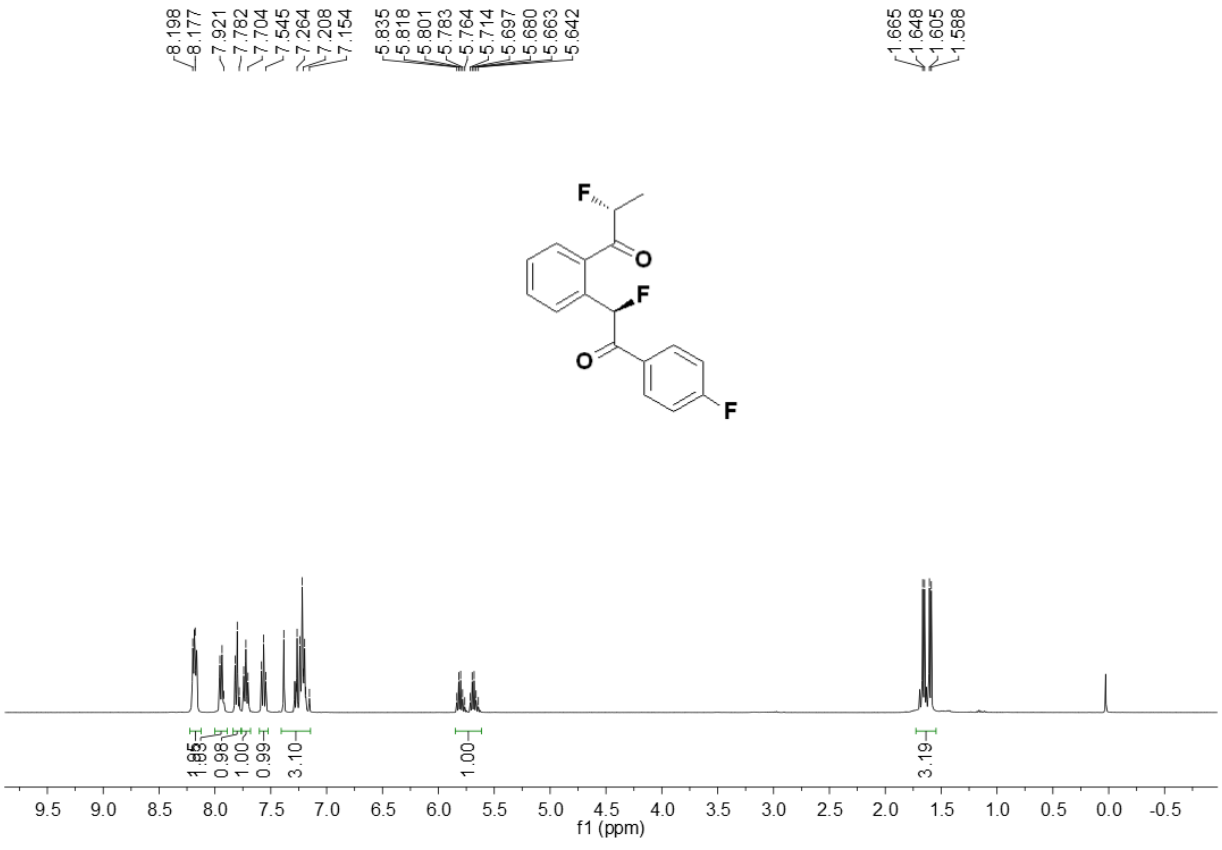
^{1}H NMR Spectrum of Compound 2c



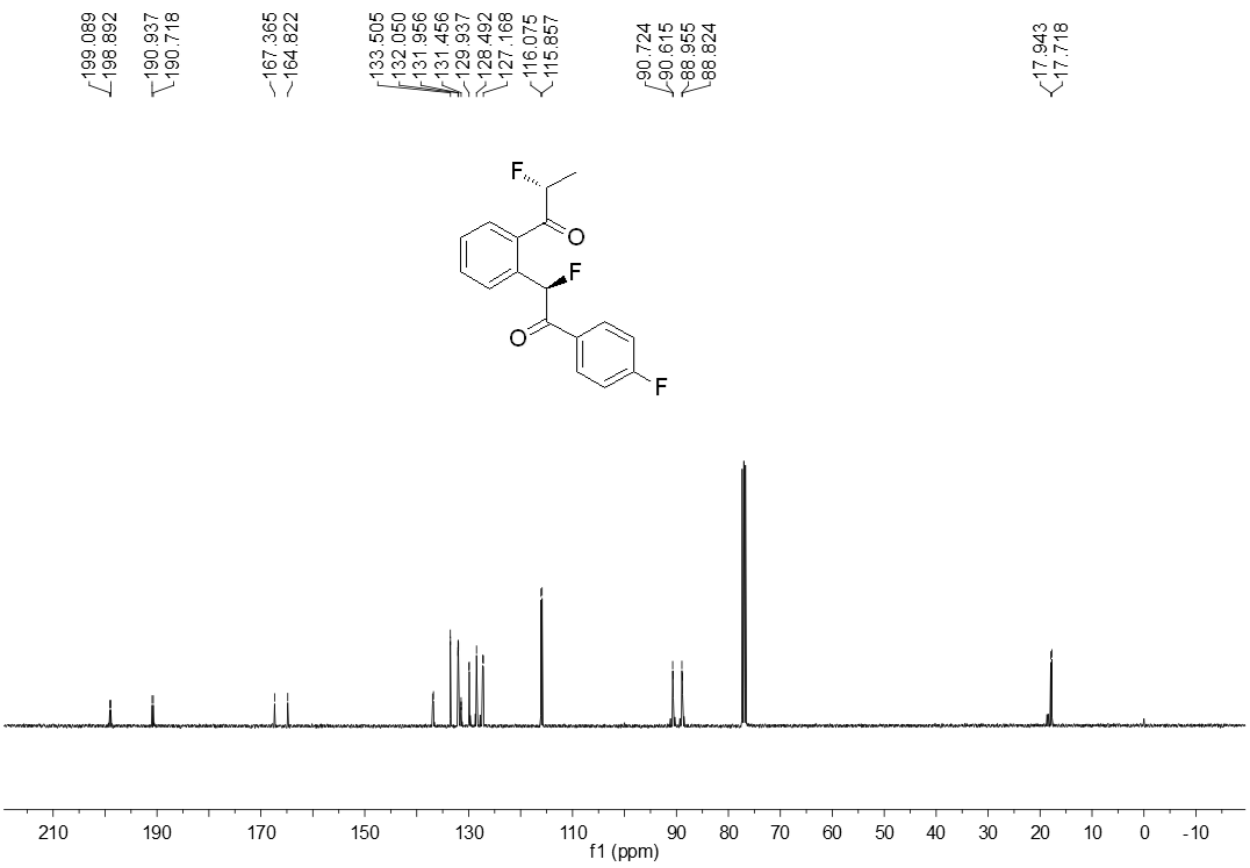
^{13}C NMR Spectrum of Compound 2c



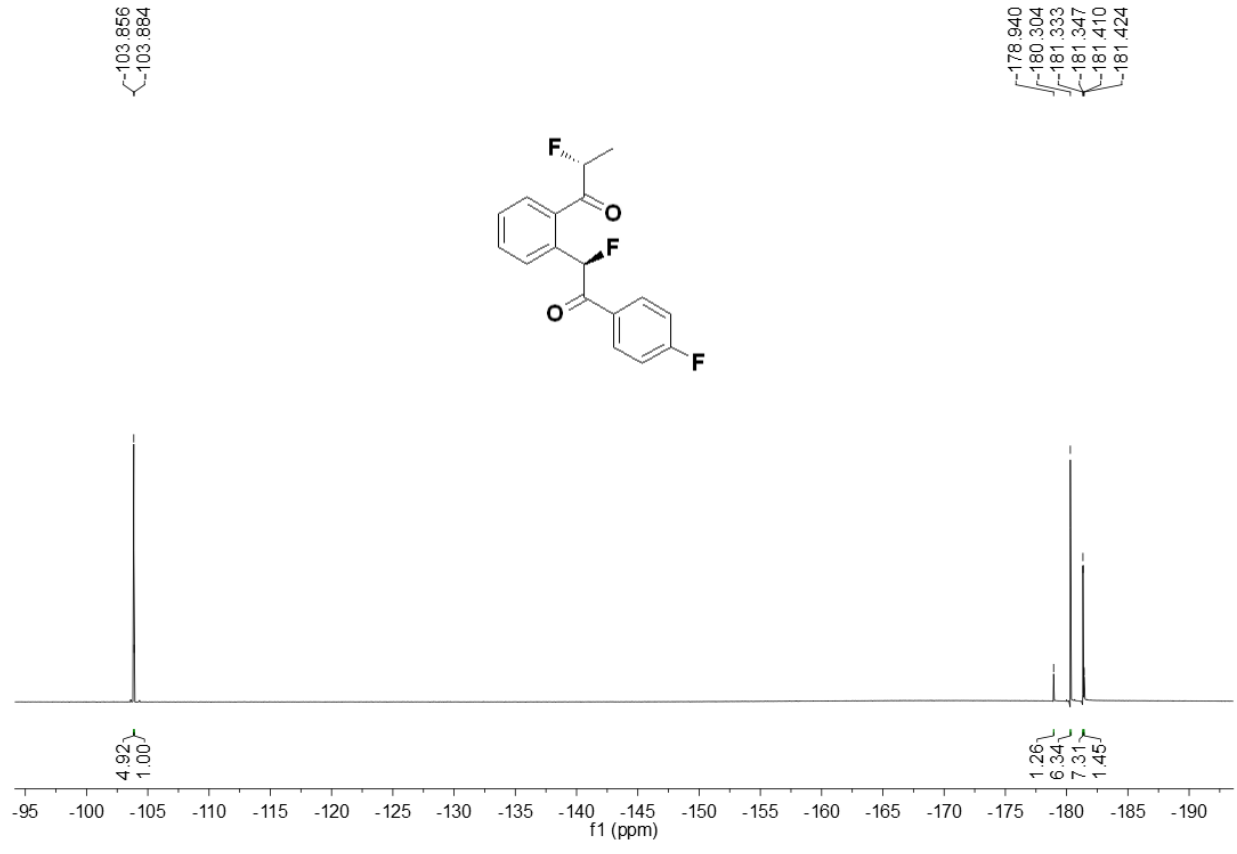
^{19}F NMR Spectrum of Compound 2c



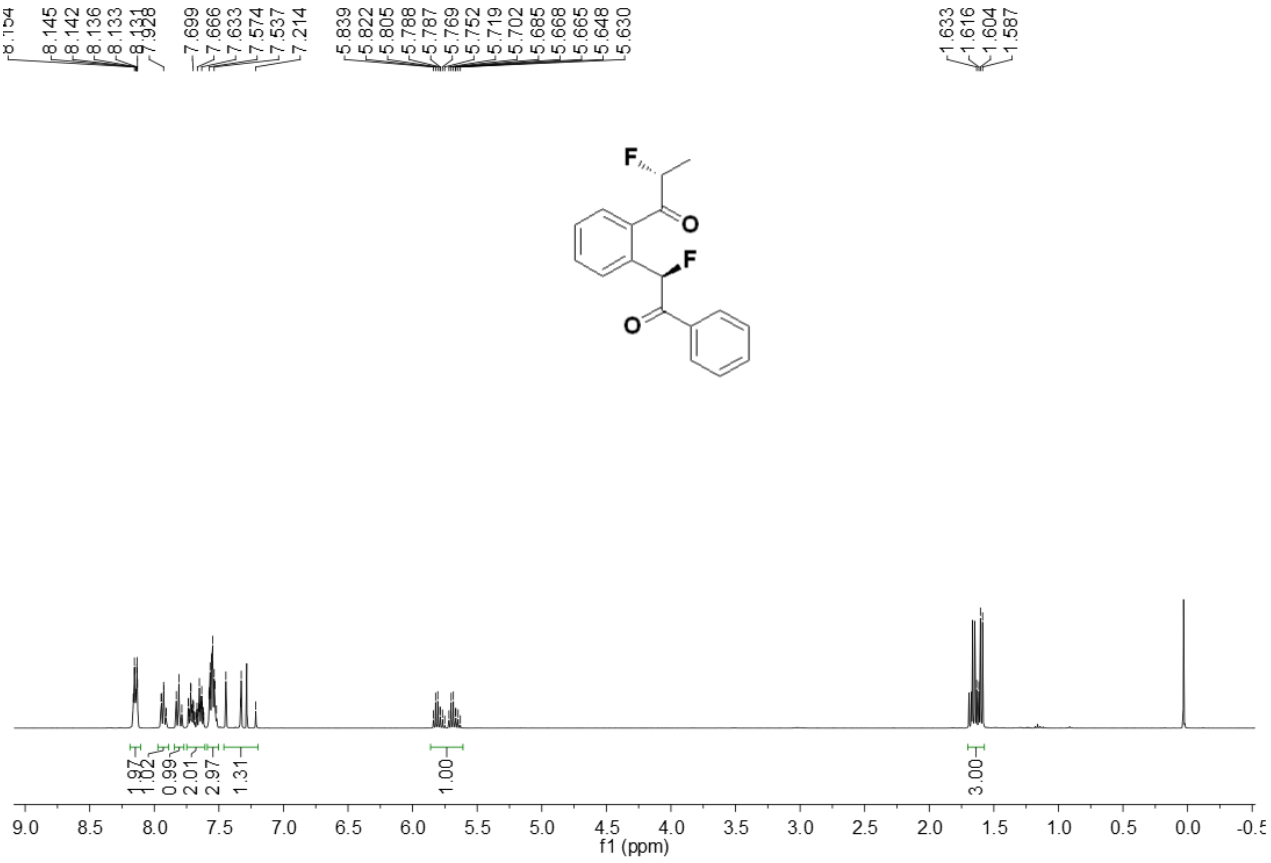
^{1}H NMR Spectrum of Compound 2d



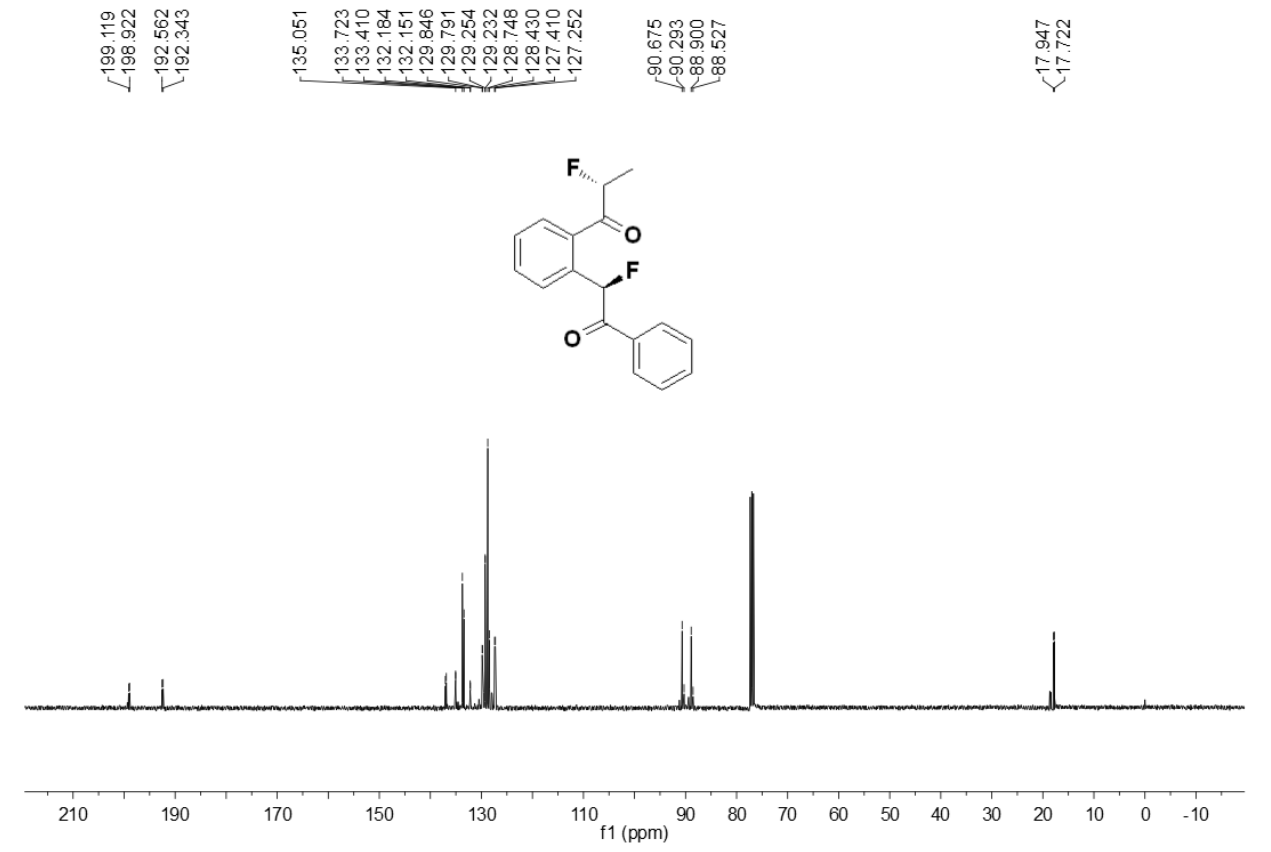
^{13}C NMR Spectrum of Compound 2d



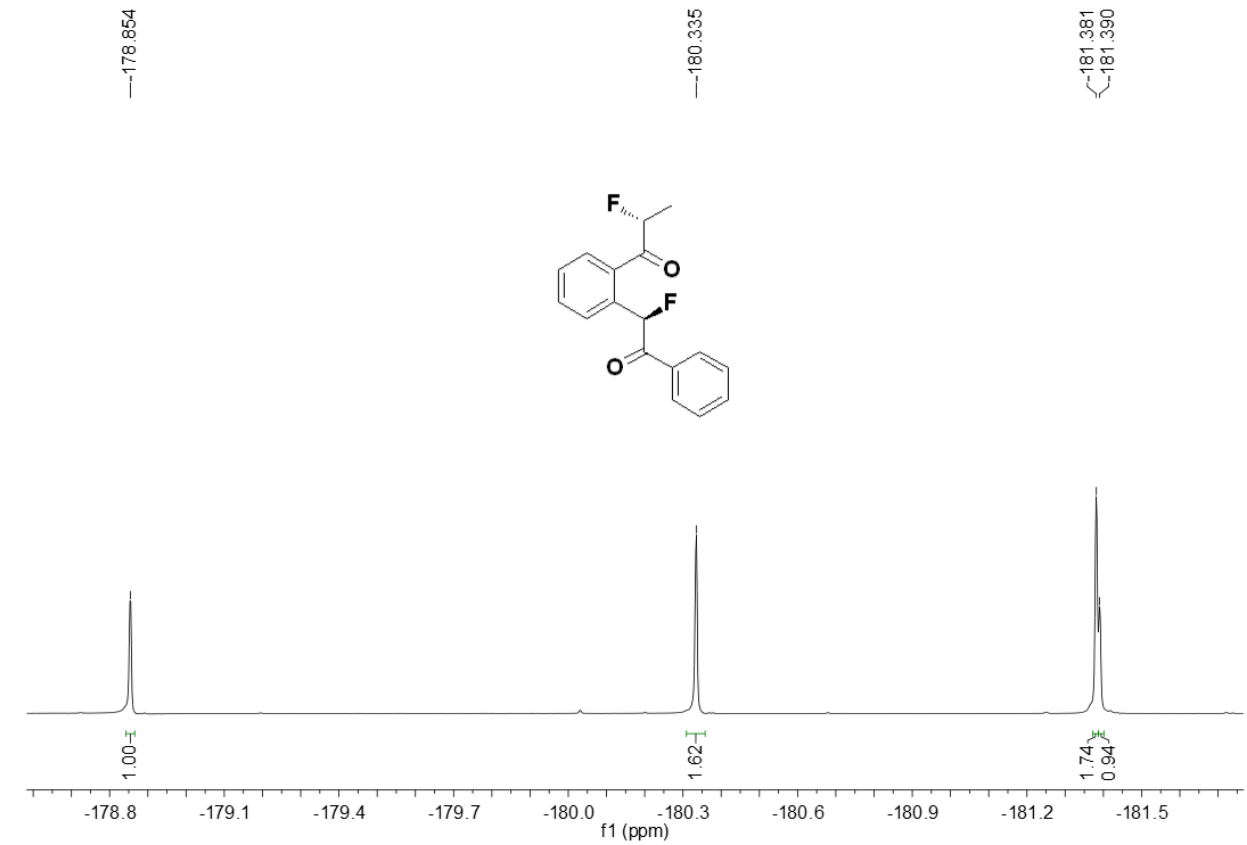
^{19}F NMR Spectrum of Compound 2d



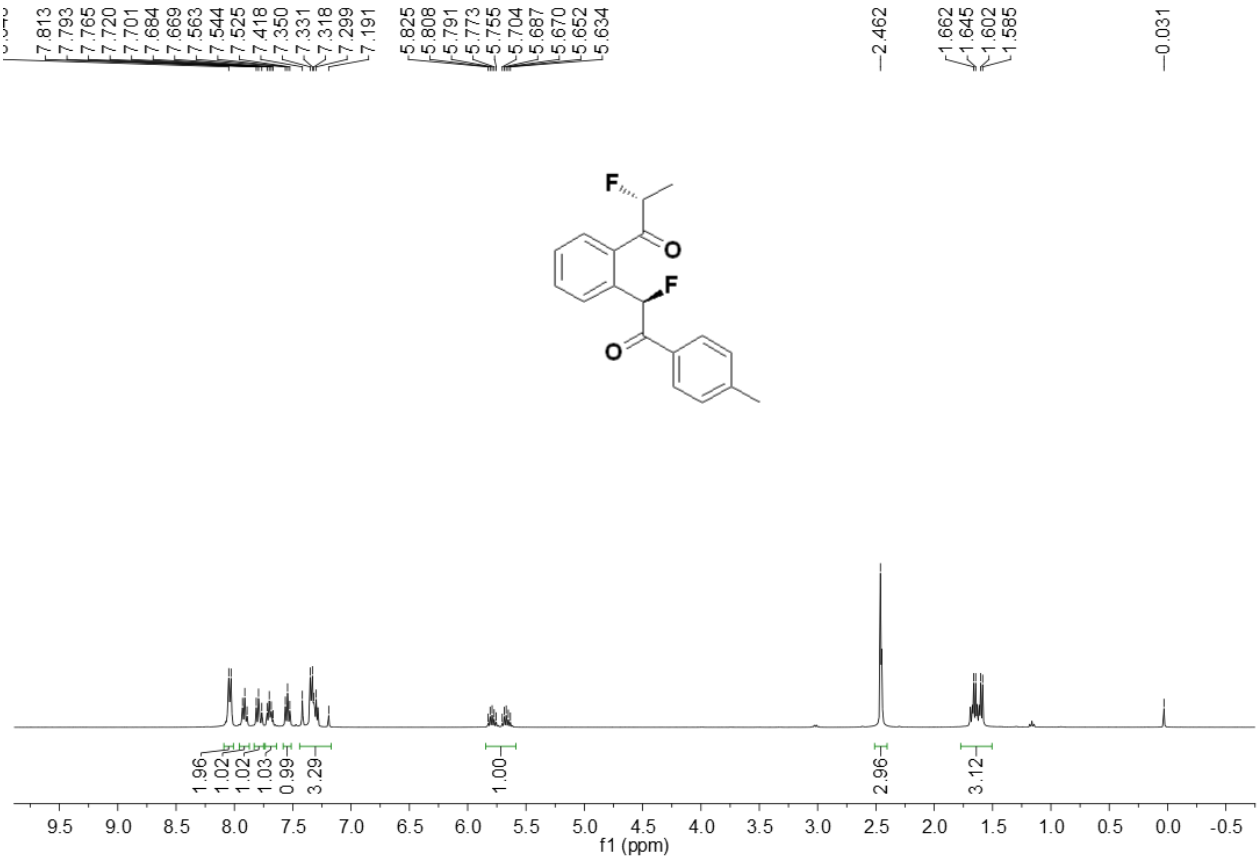
^{1}H NMR Spectrum of Compound 2e



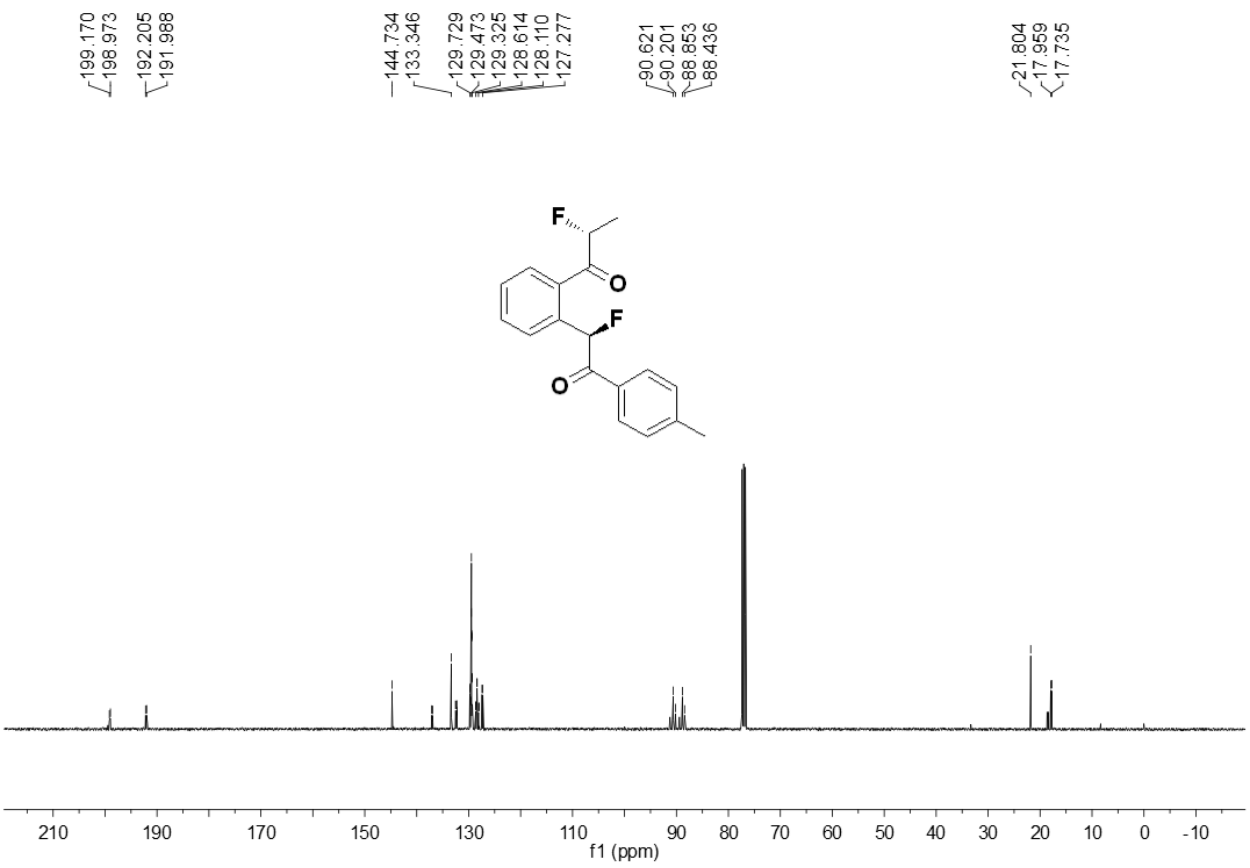
^{13}C NMR Spectrum of Compound 2e



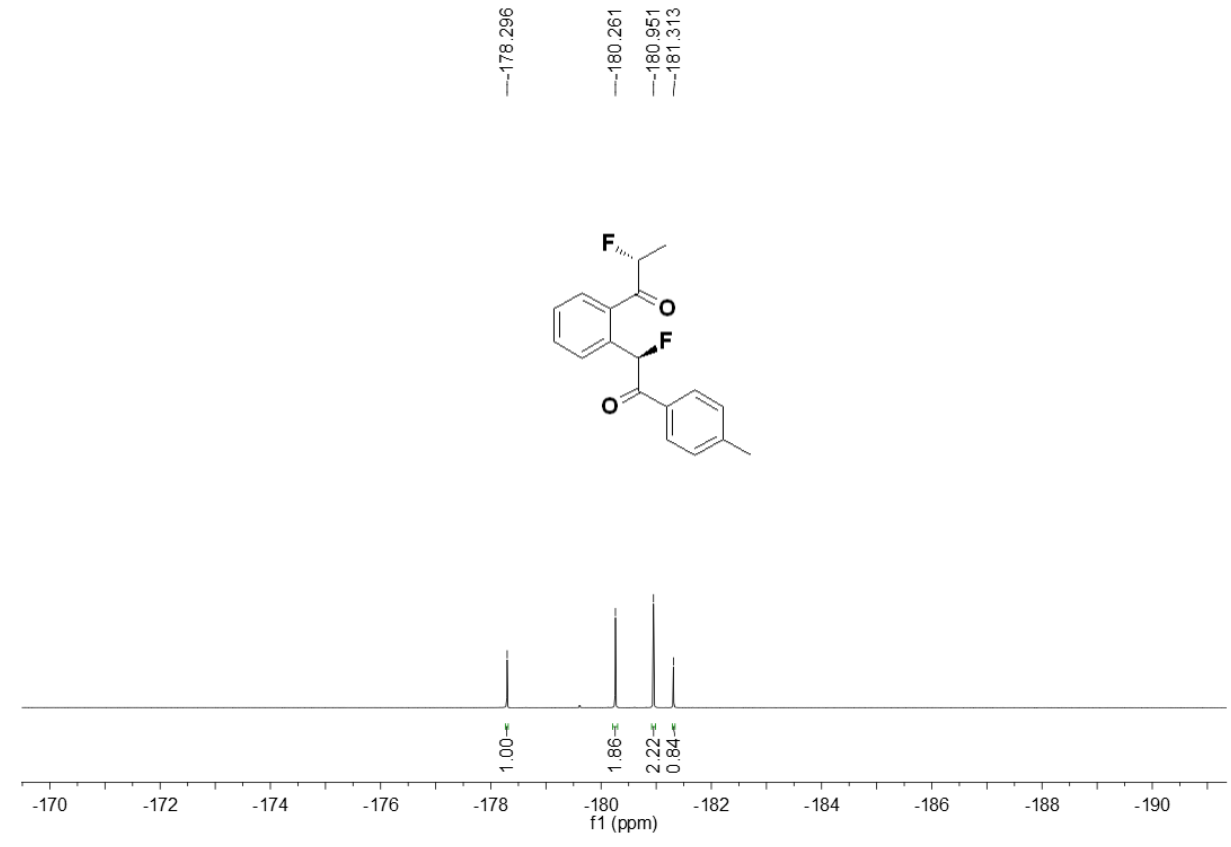
^{19}F NMR Spectrum of Compound 2e



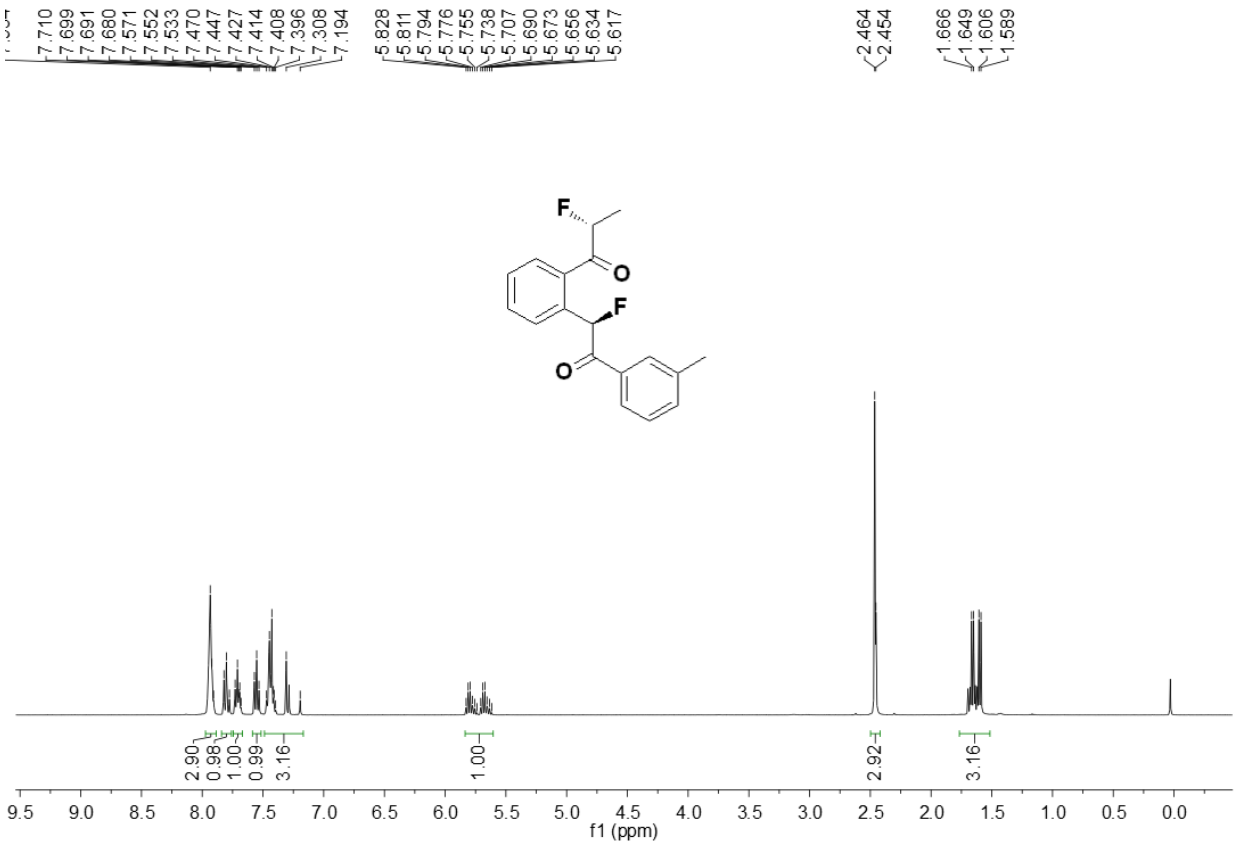
^{1}H NMR Spectrum of Compound 2f



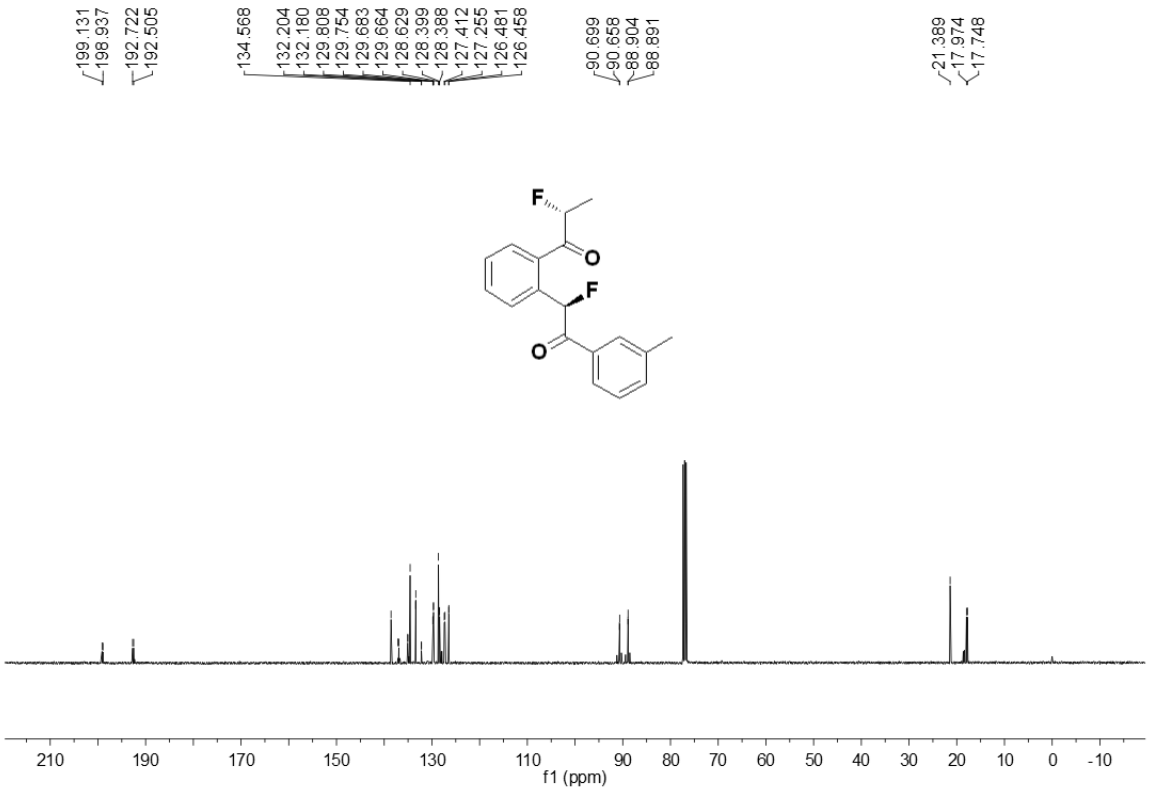
^{13}C NMR Spectrum of Compound 2f



^{19}F NMR Spectrum of Compound 2f

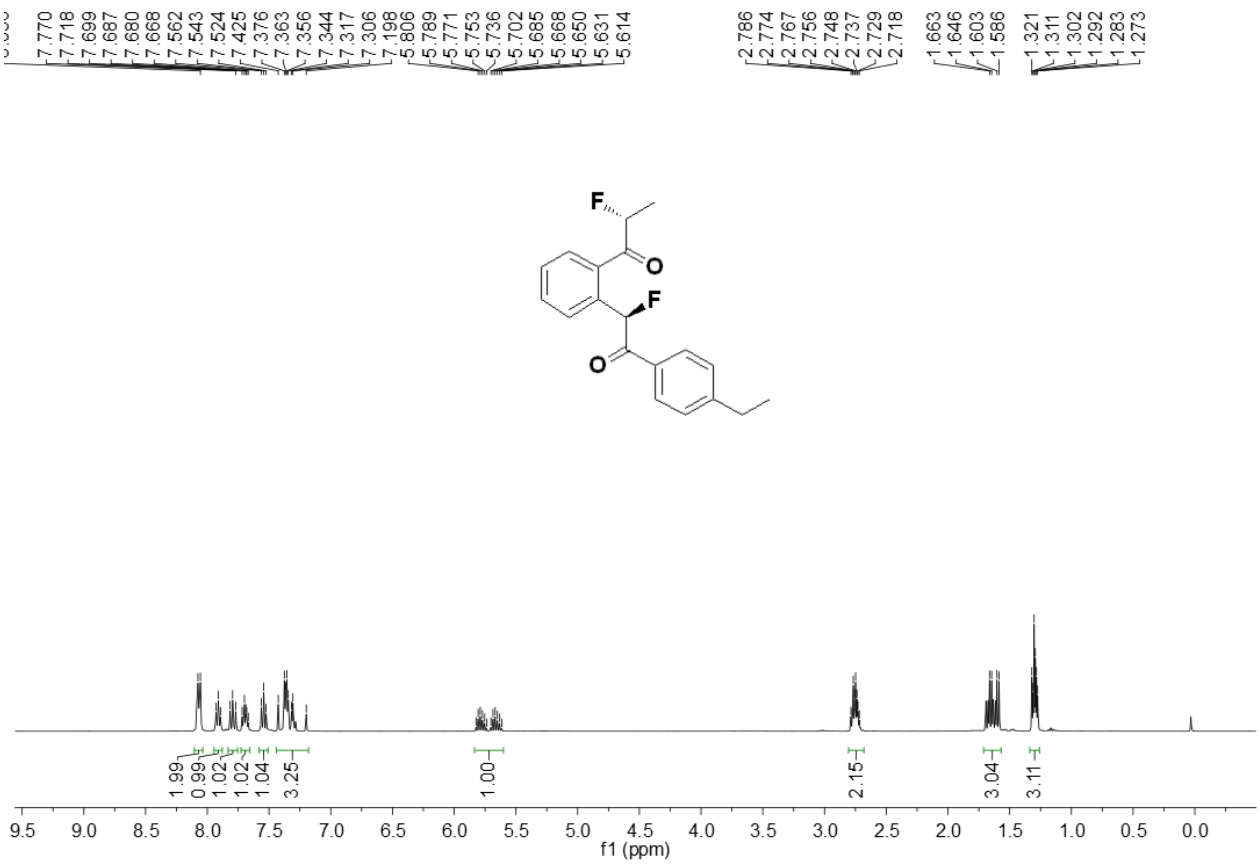


[1]H NMR Spectrum of Compound 2g

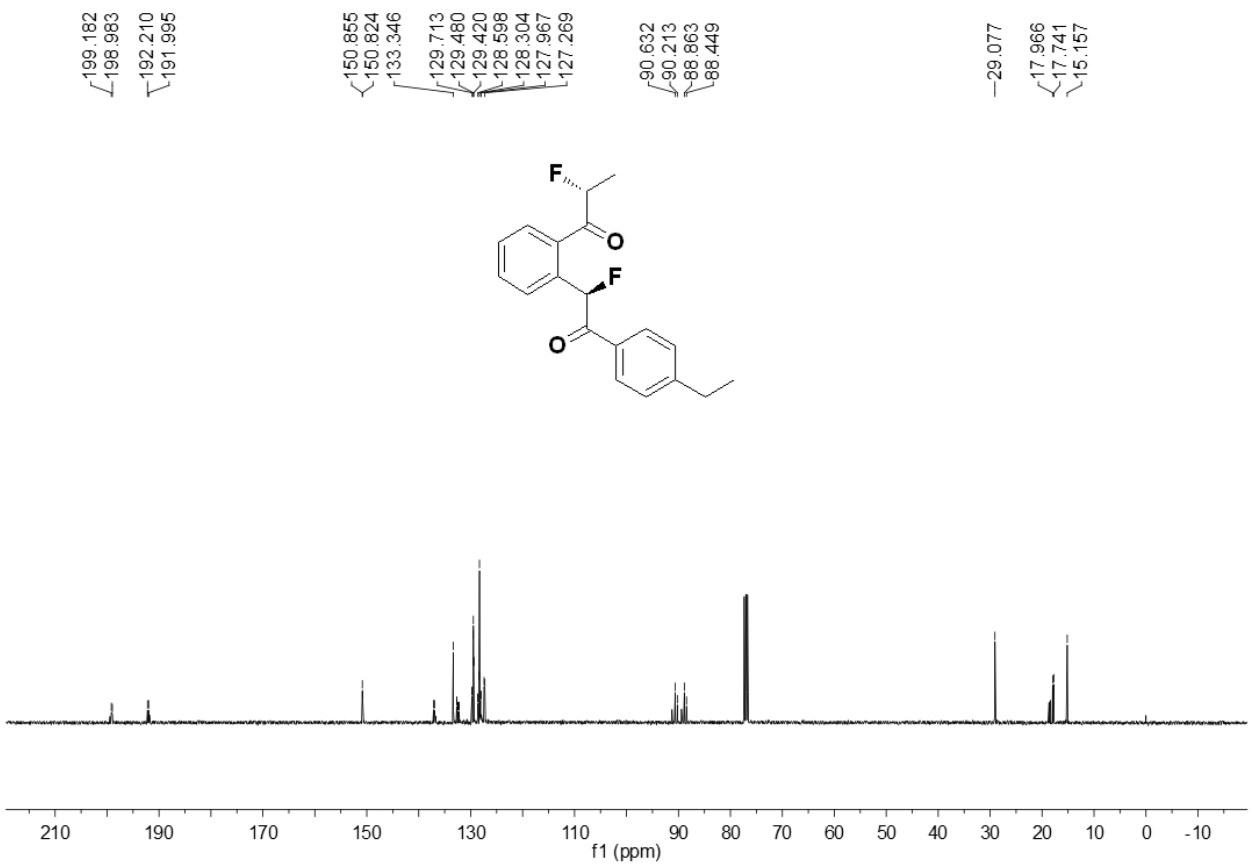


[13]C NMR Spectrum of Compound 2g

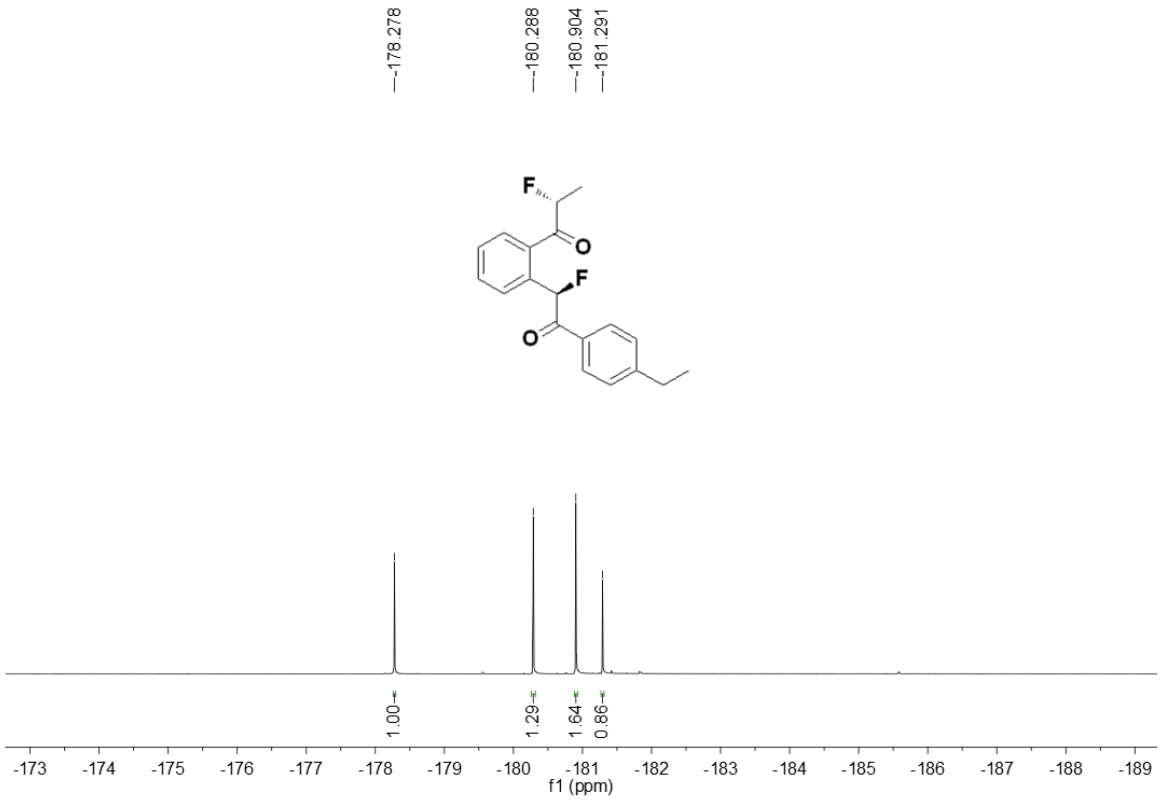
^{19}F NMR Spectrum of Compound 2g



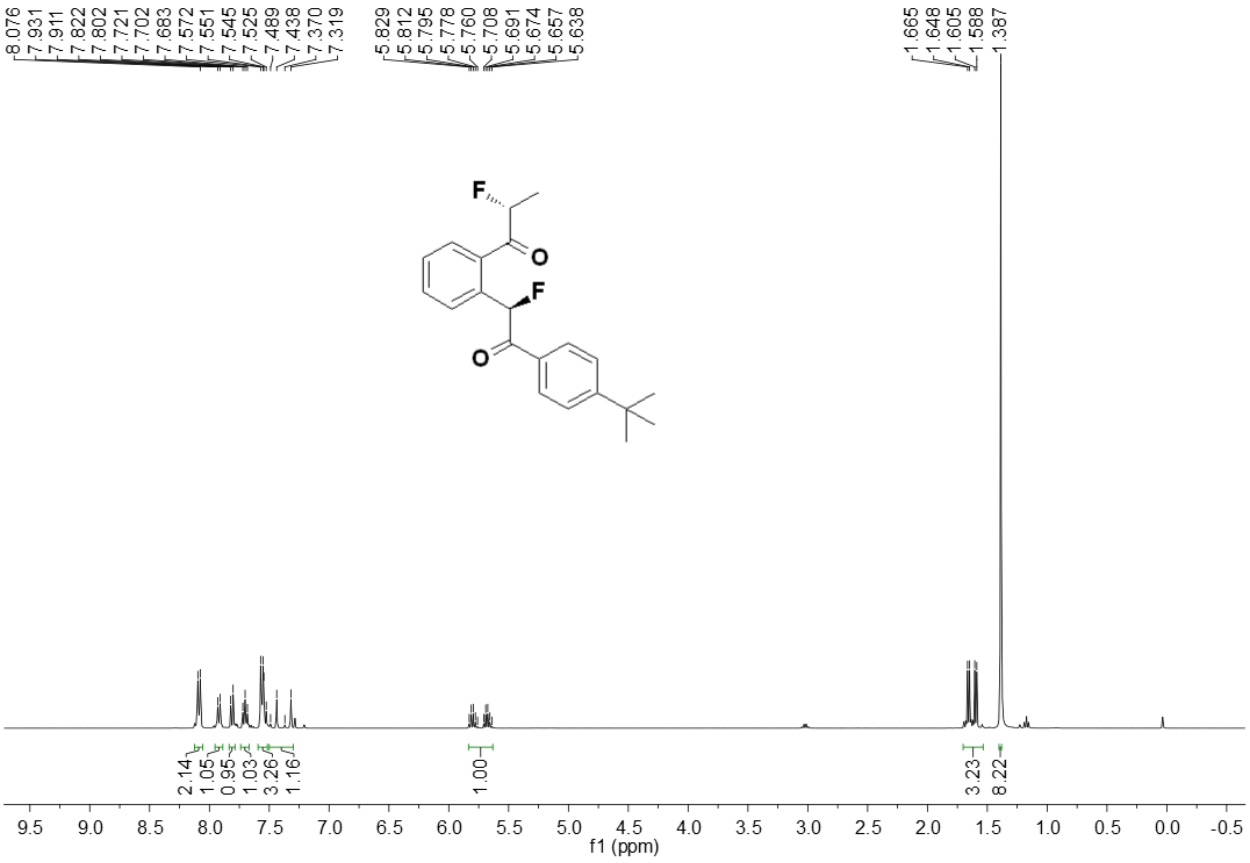
^{1}H NMR Spectrum of Compound 2h



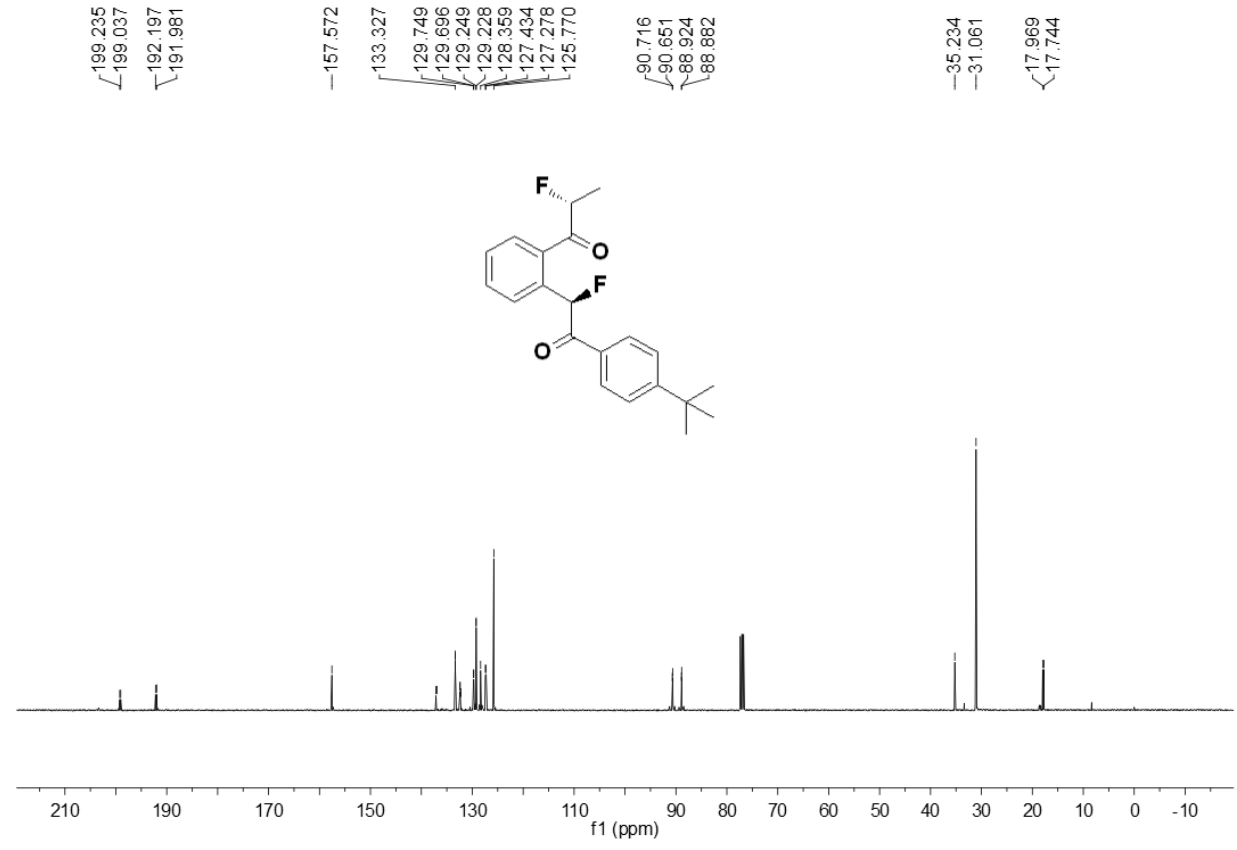
^{13}C NMR Spectrum of Compound 2h



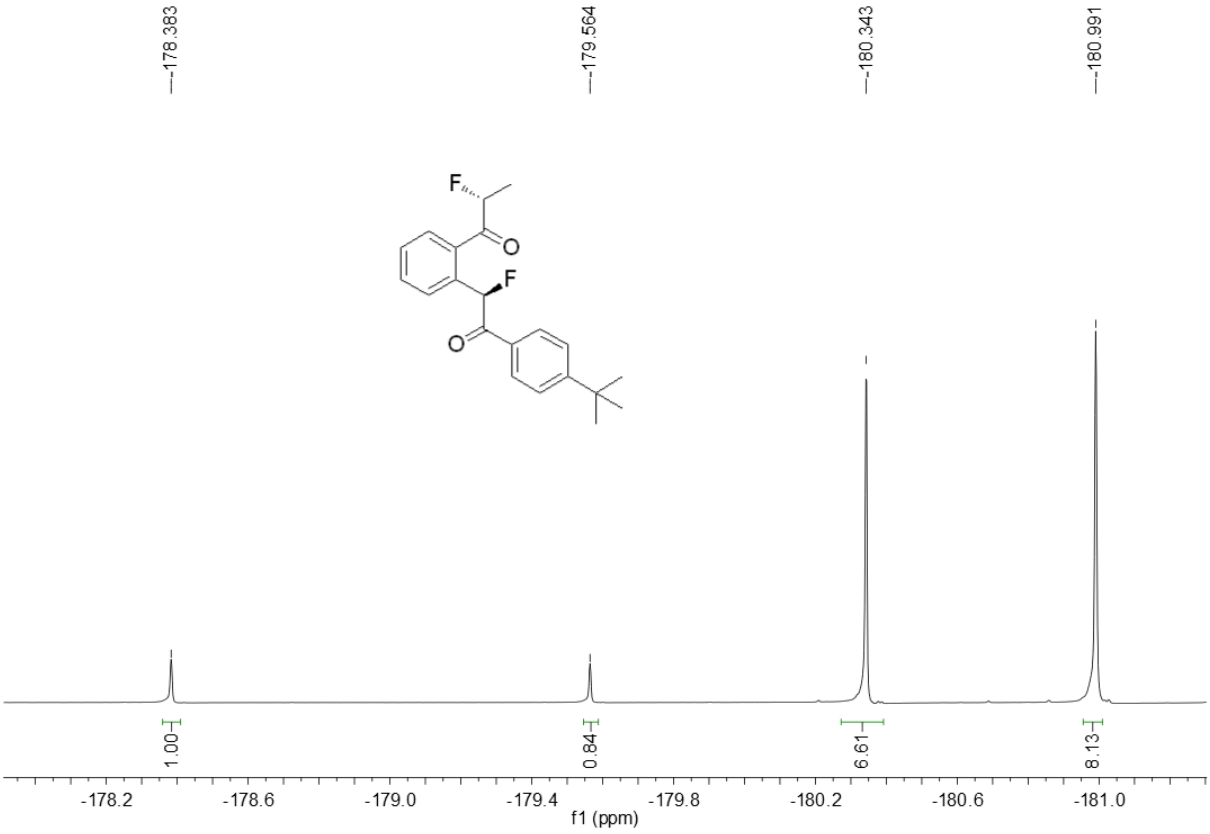
^{19}F NMR Spectrum of Compound 2h



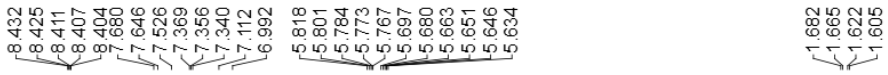
^{1}H NMR Spectrum of Compound 2i

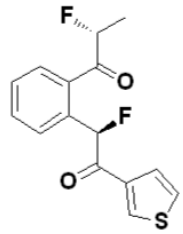


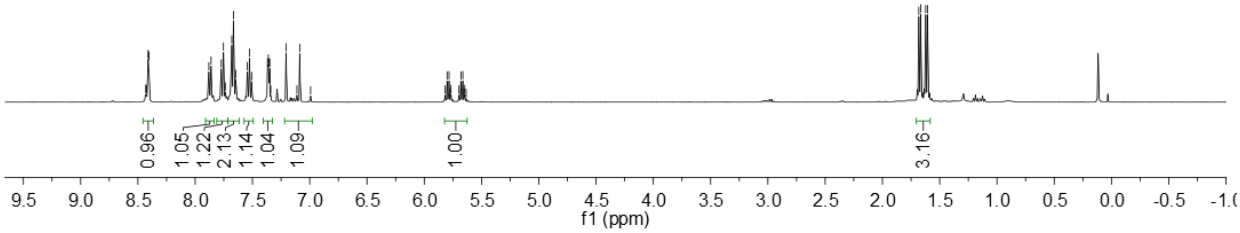
^{13}C NMR Spectrum of Compound 2i



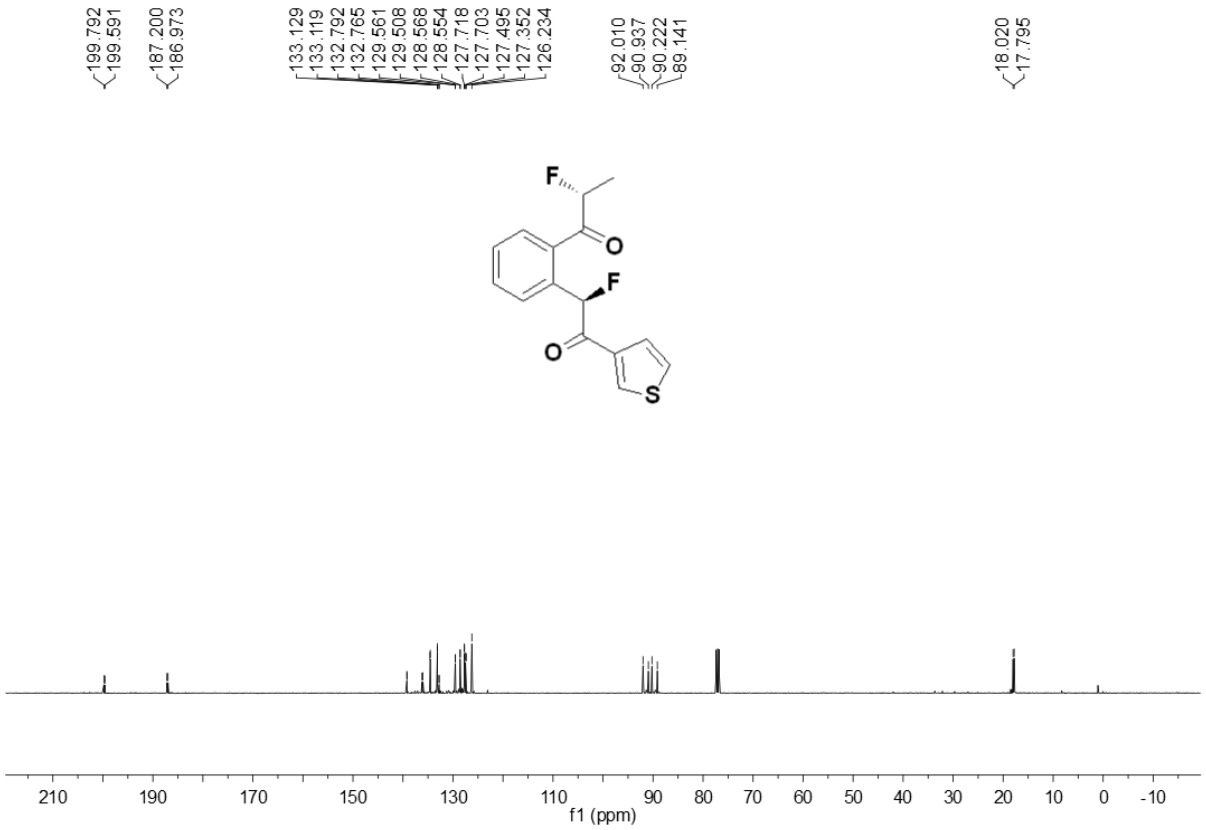
^{19}F NMR Spectrum of Compound 2i



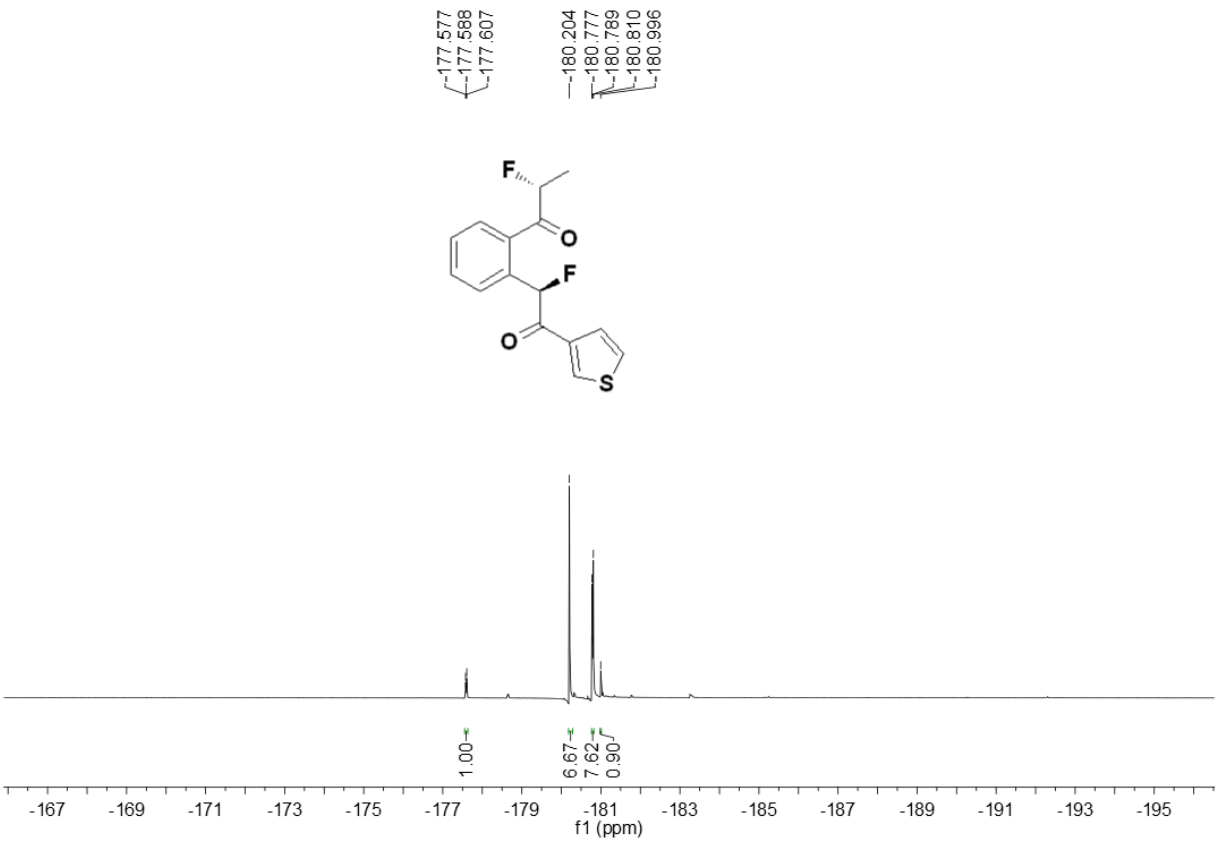




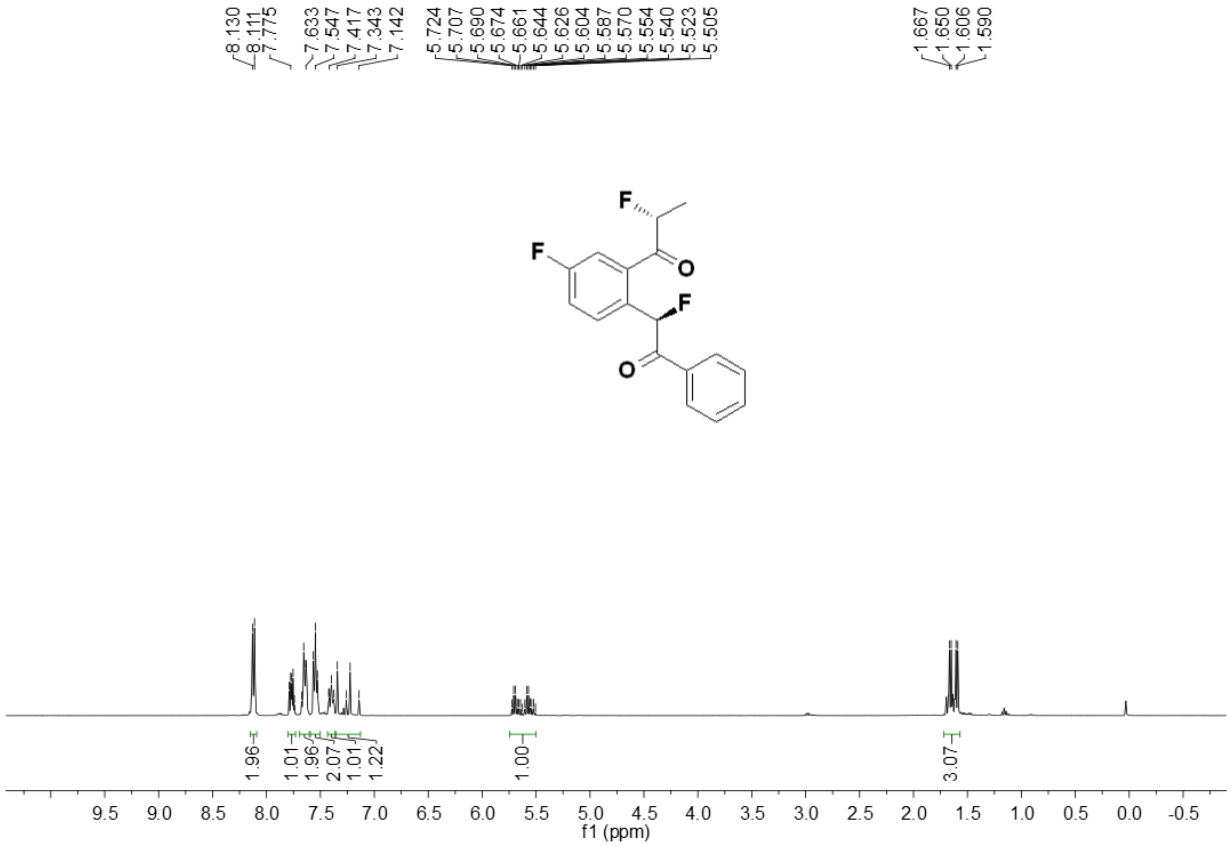
^{1}H NMR Spectrum of Compound 2j



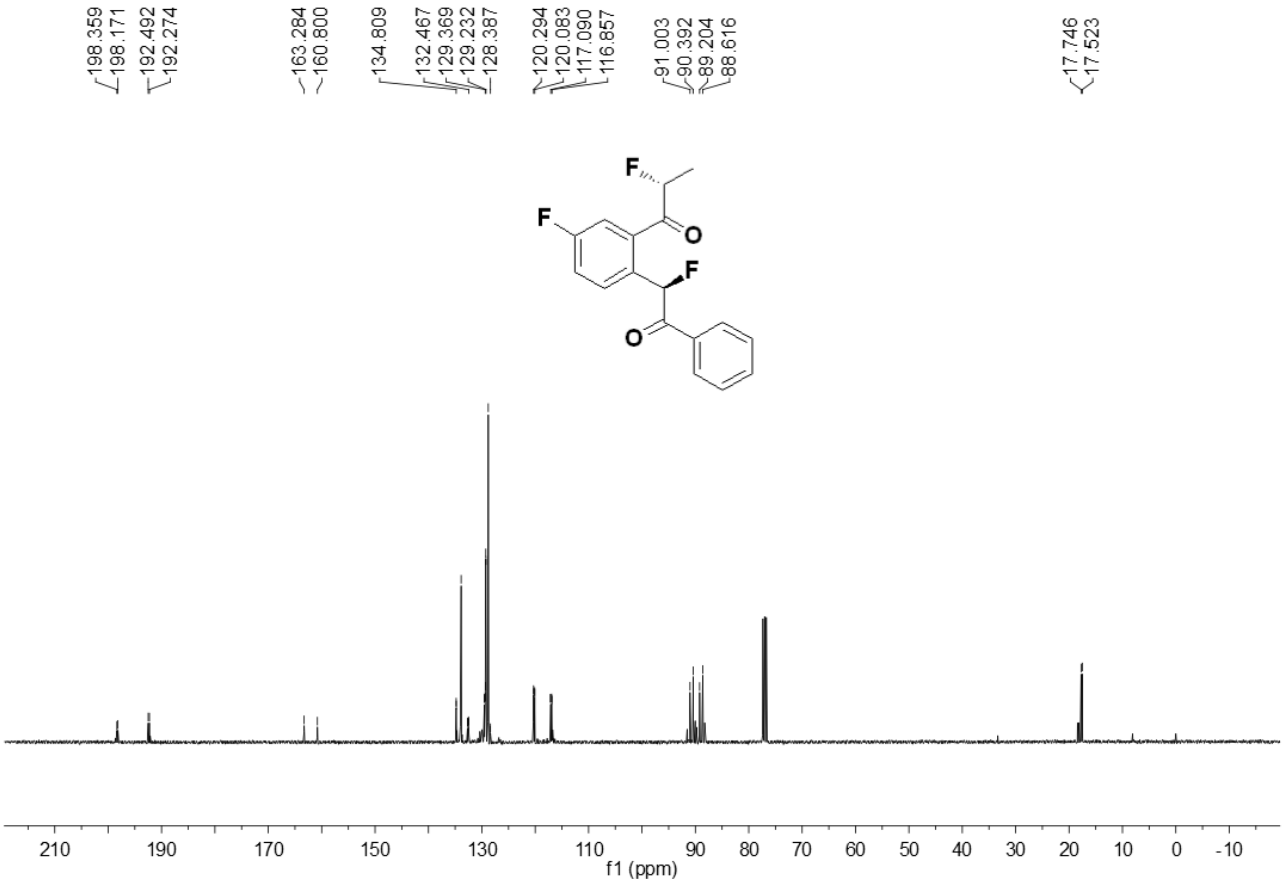
^{13}C NMR Spectrum of Compound 2j



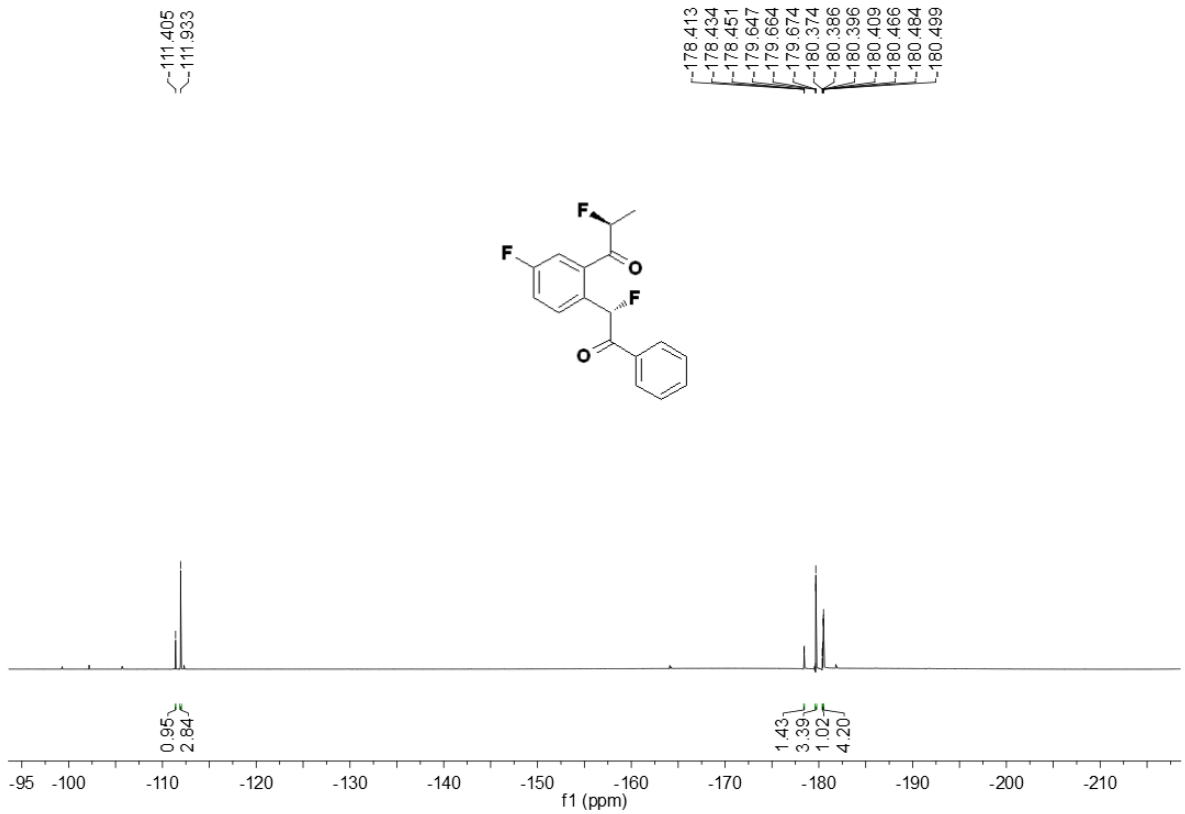
^{19}F NMR Spectrum of Compound 2j



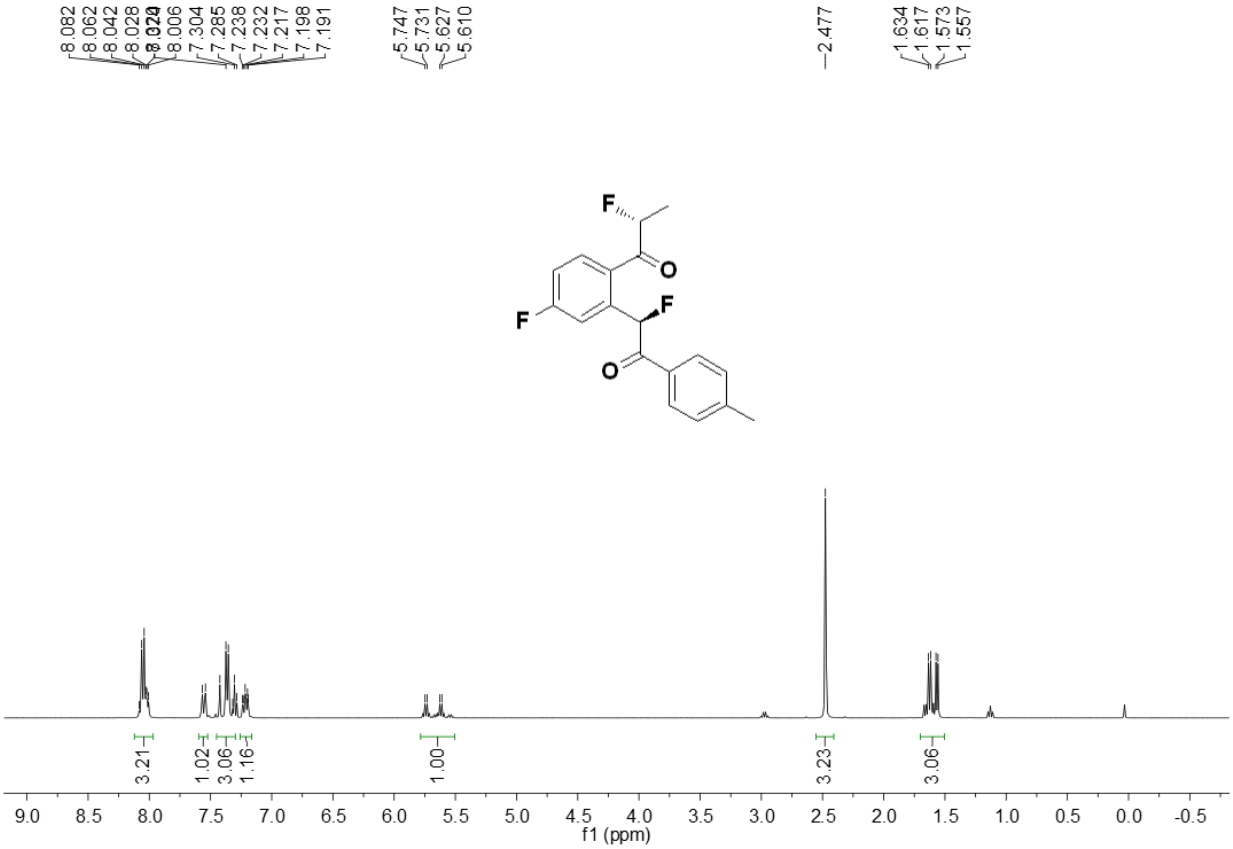
^{1}H NMR Spectrum of Compound 2m



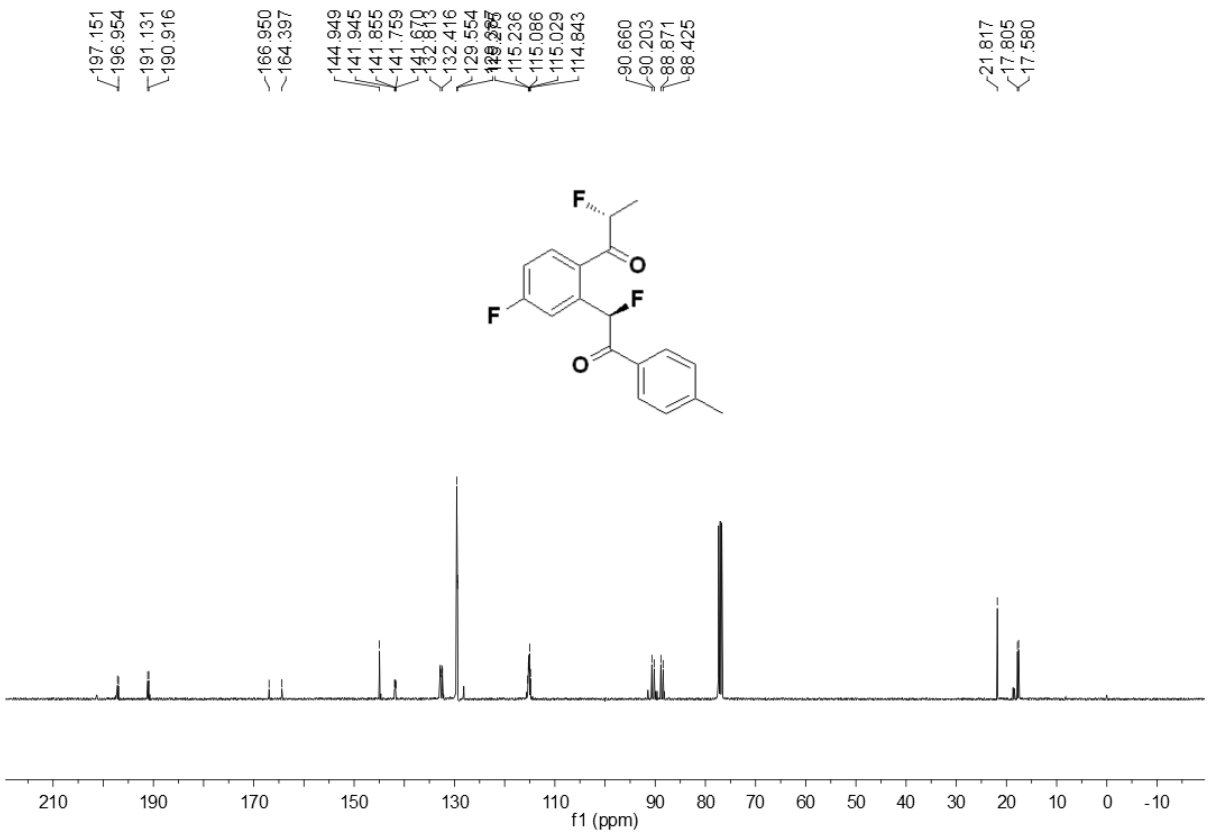
^{13}C NMR Spectrum of Compound 2m



^{19}F NMR Spectrum of Compound 2m

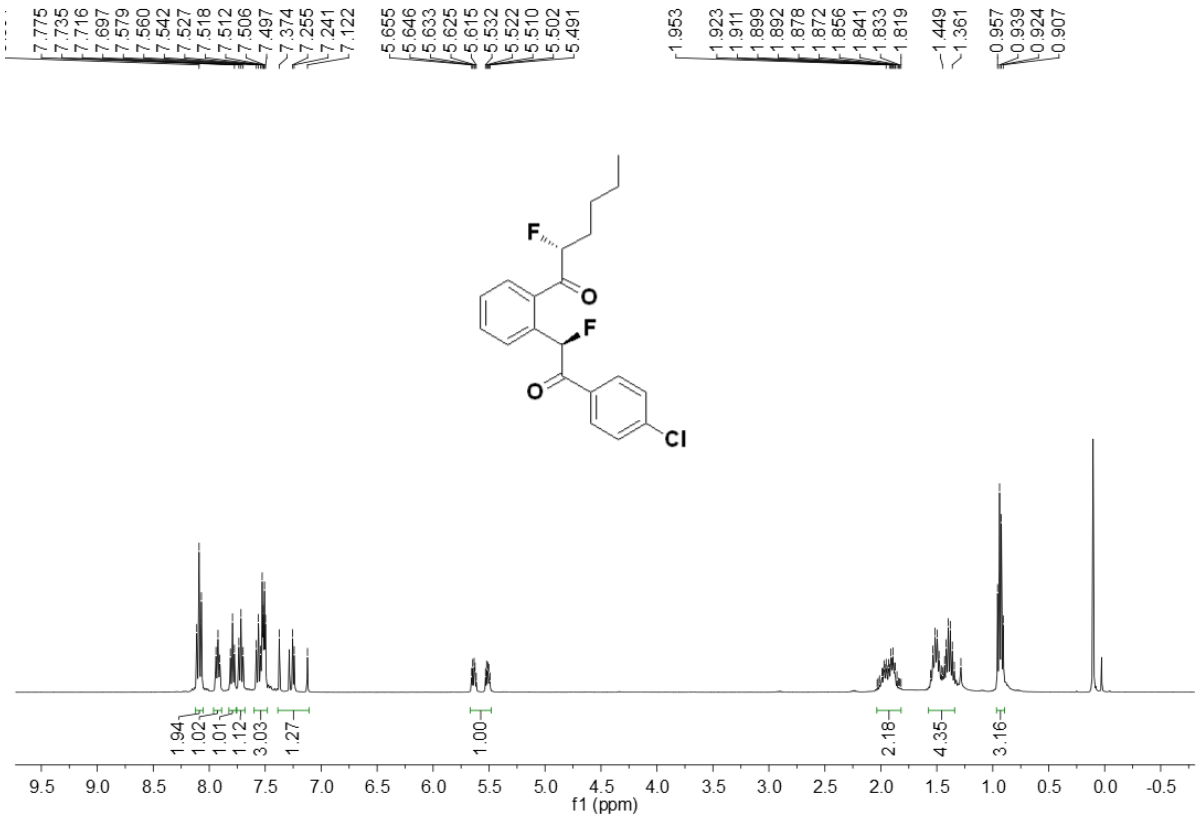


^{1}H NMR Spectrum of Compound 2l

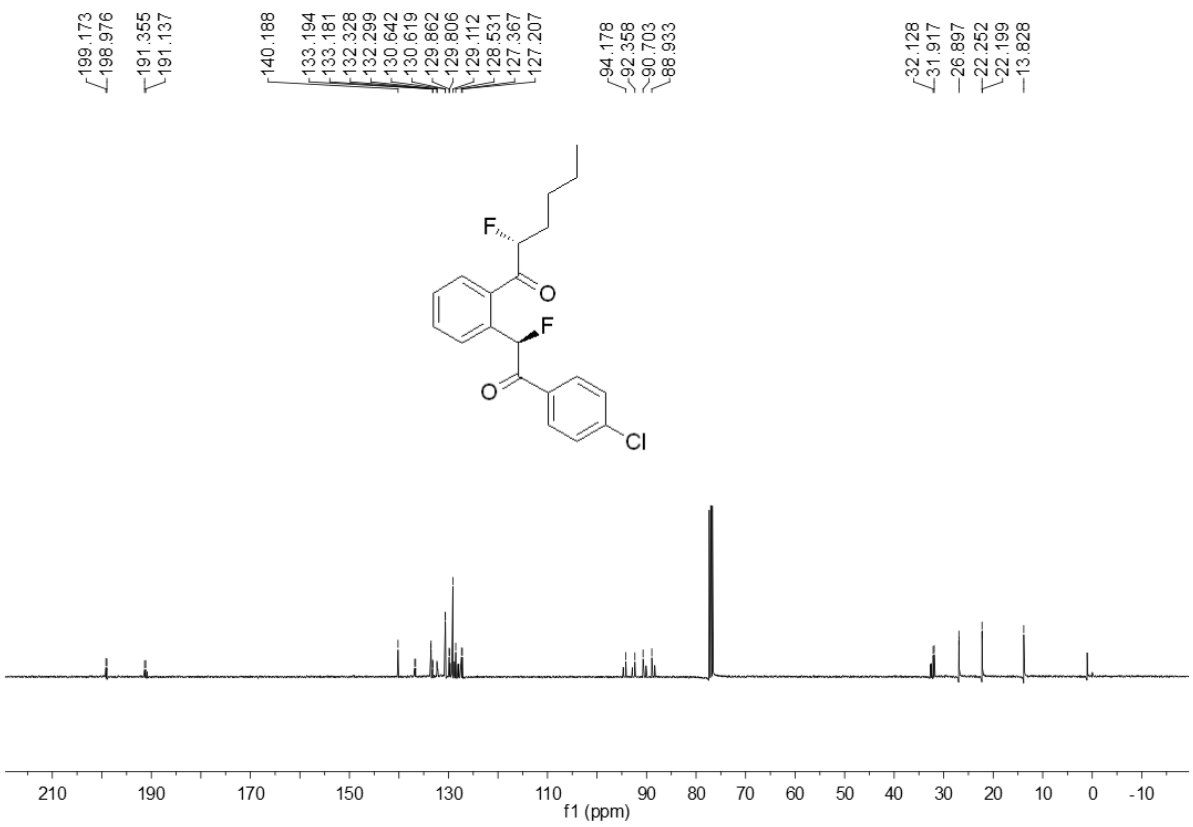


^{13}C NMR Spectrum of Compound 2l

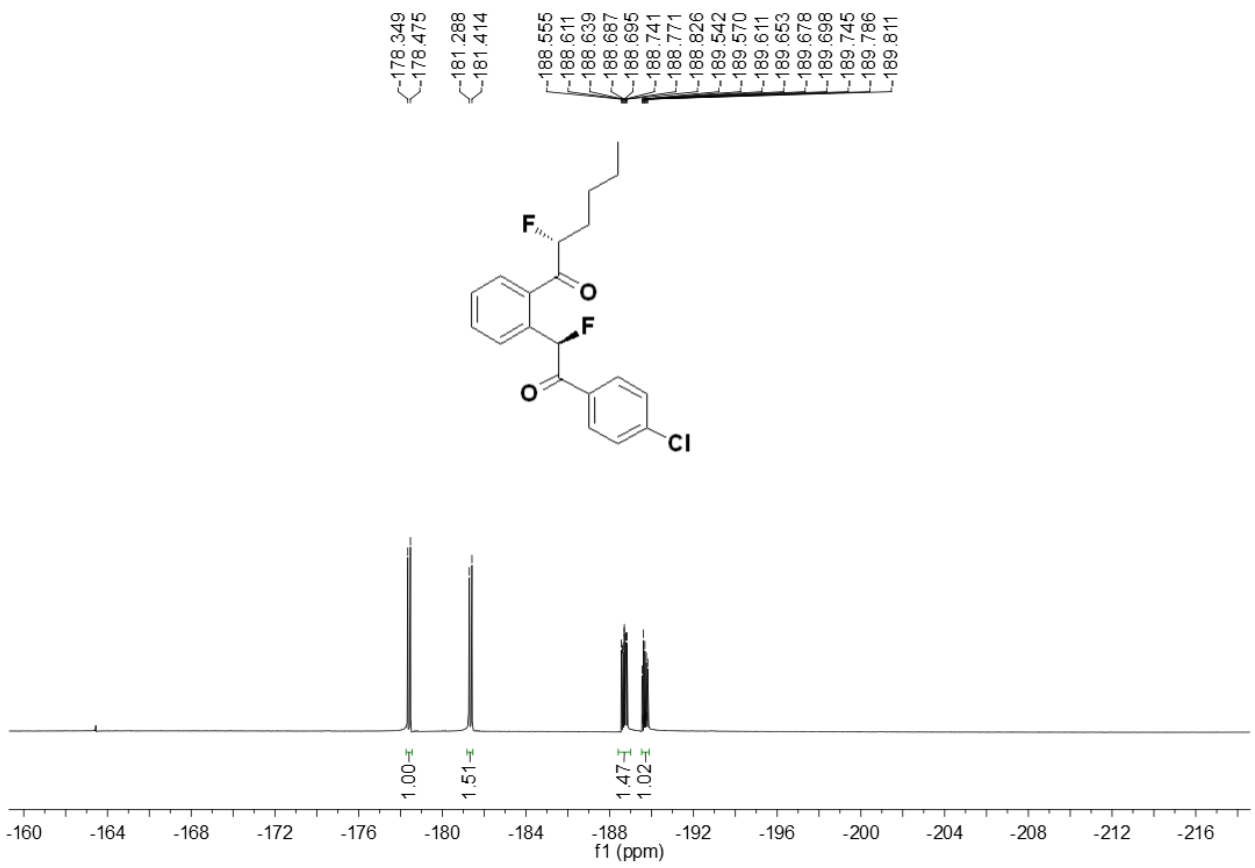
^{19}F NMR Spectrum of Compound 2l



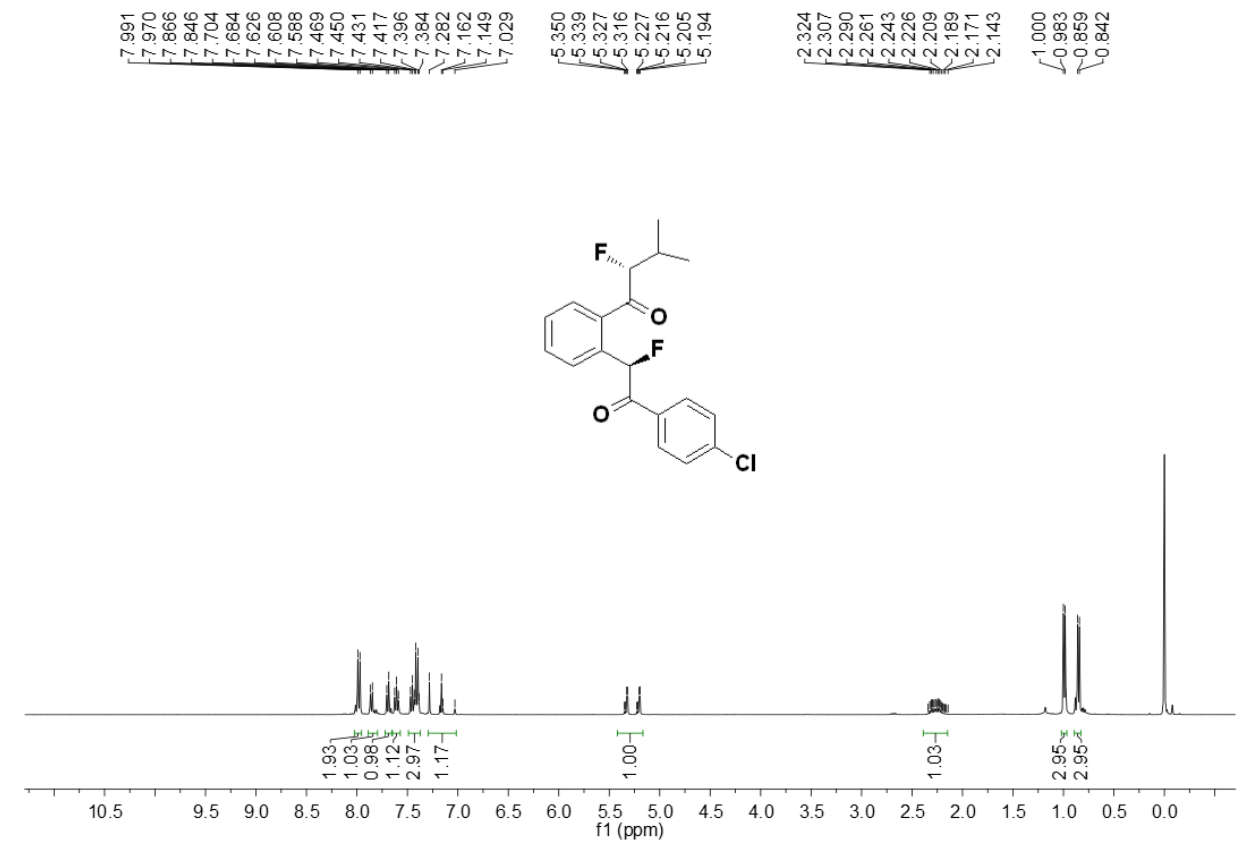
^{1}H NMR Spectrum of Compound 2n



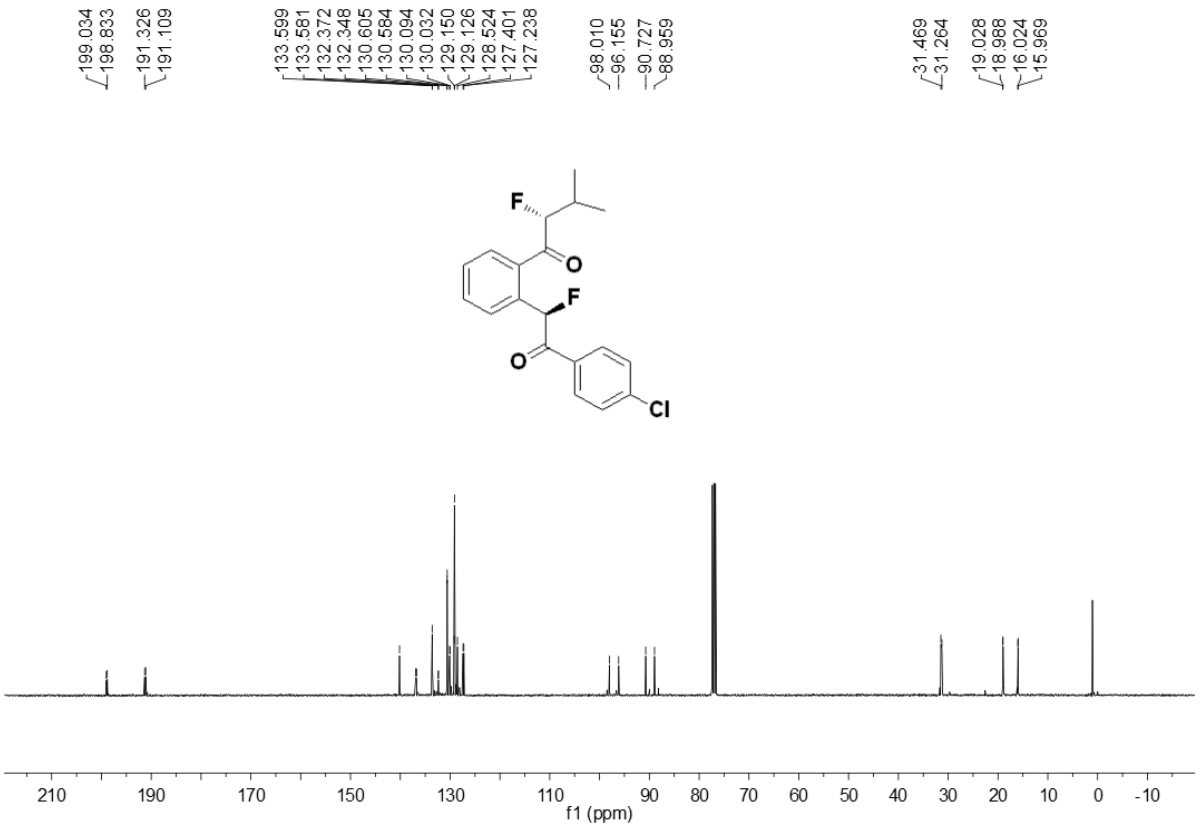
^{13}C NMR Spectrum of Compound 2n



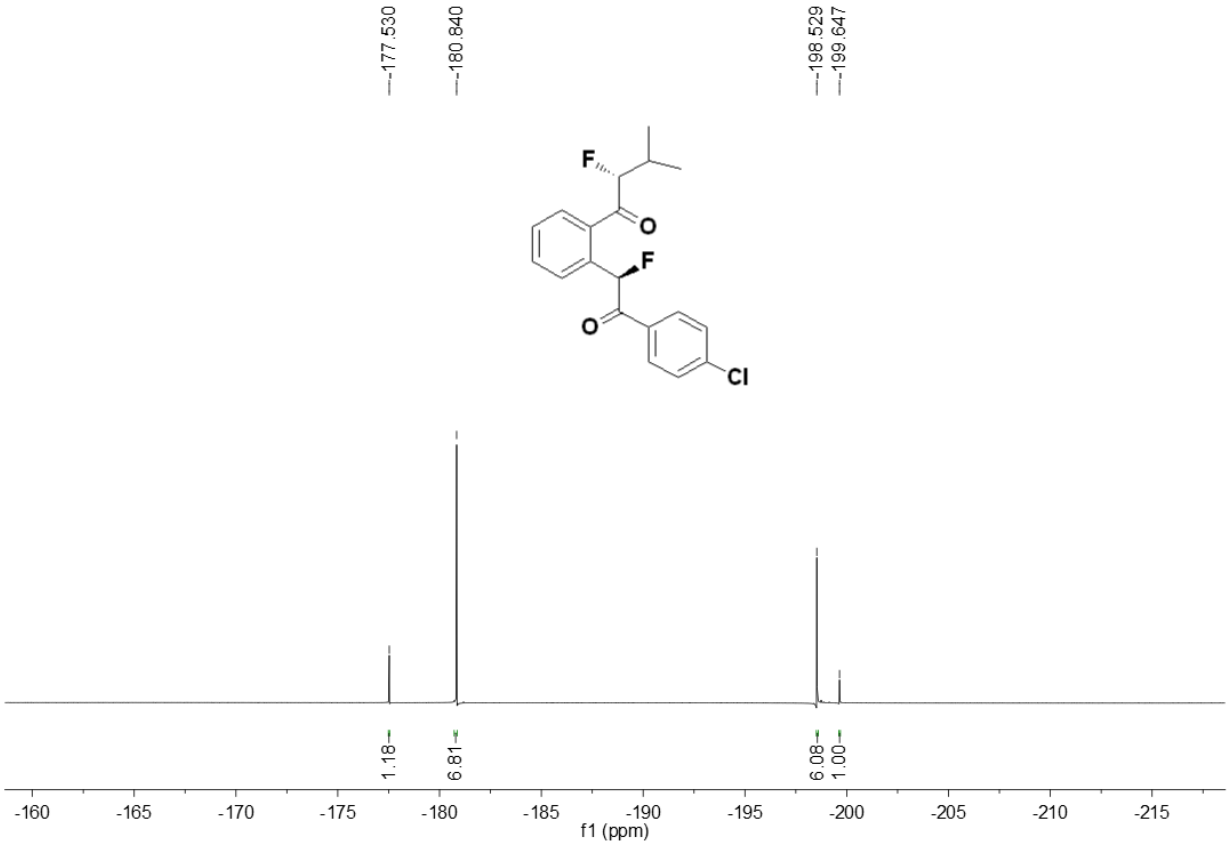
^{19}F NMR Spectrum of Compound 2n



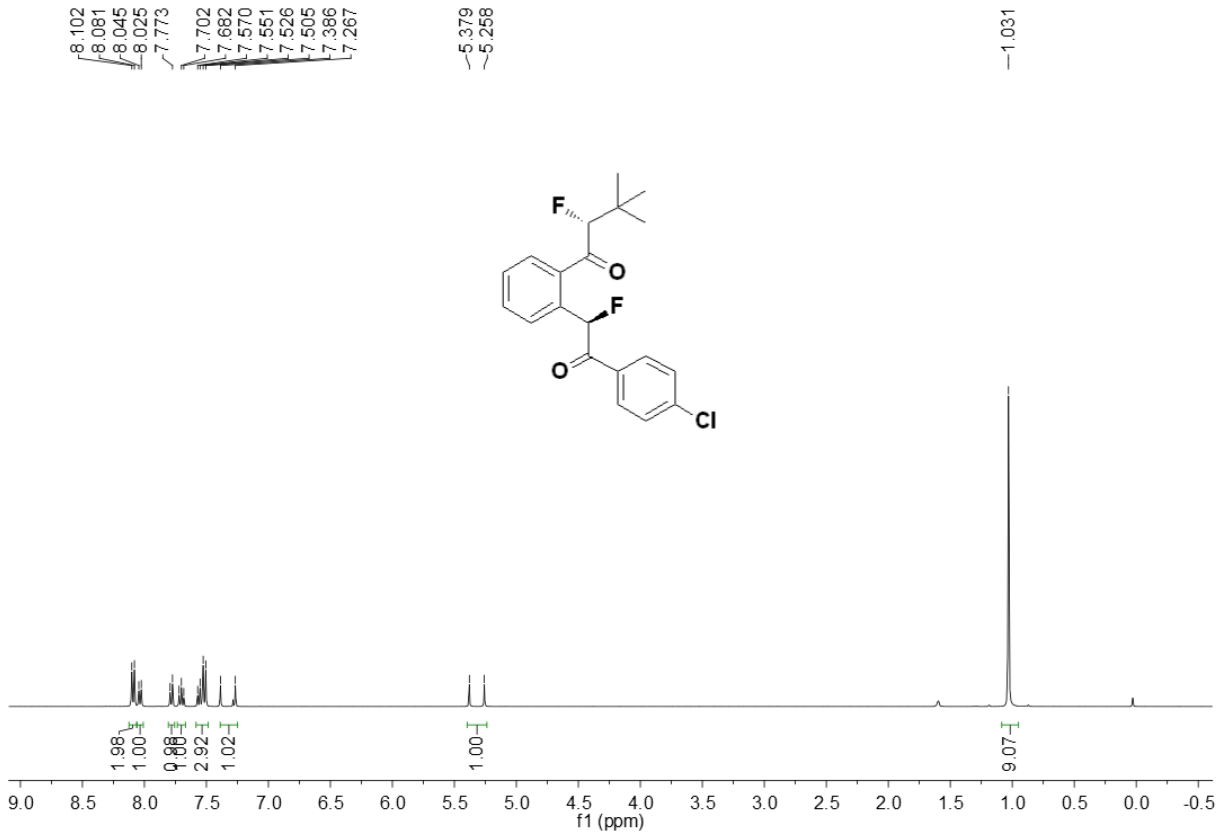
^{1}H NMR Spectrum of Compound 2o



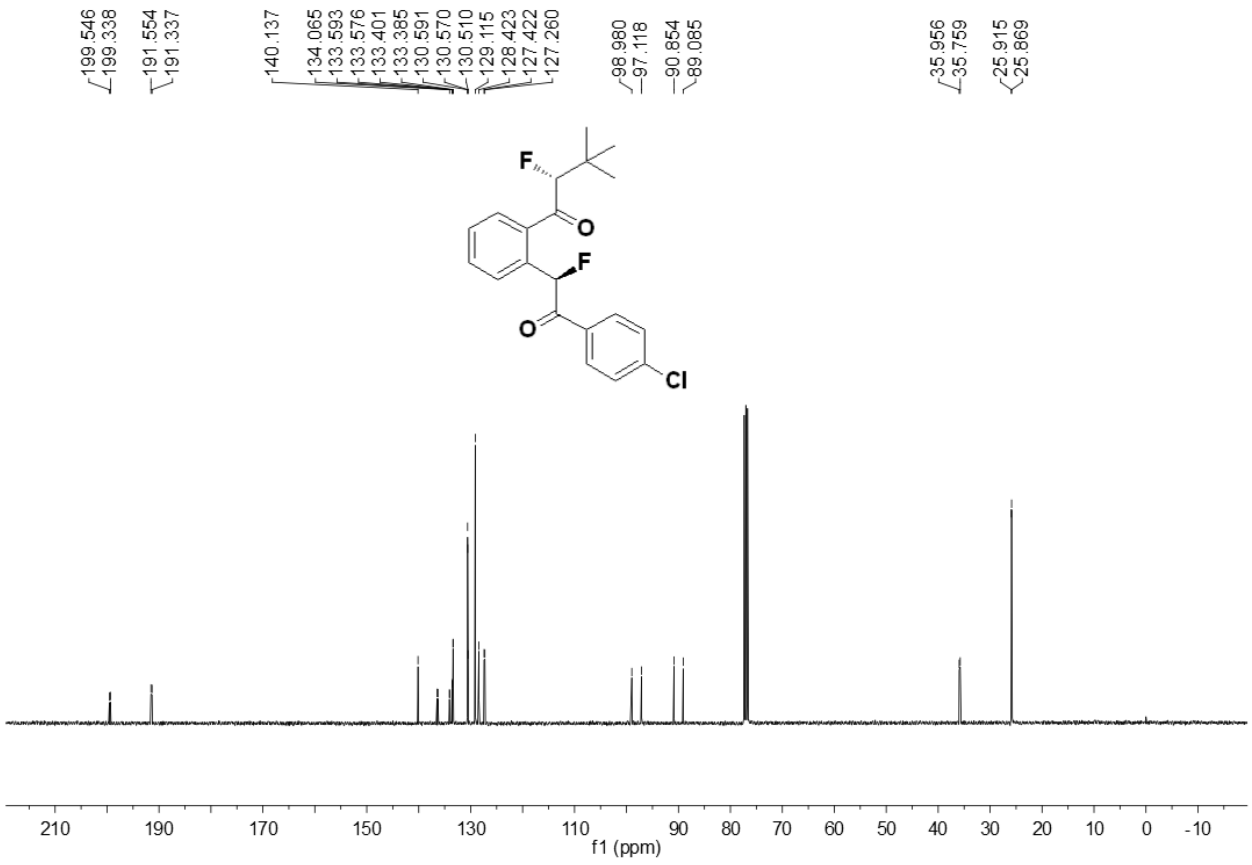
^{13}C NMR Spectrum of Compound 2o



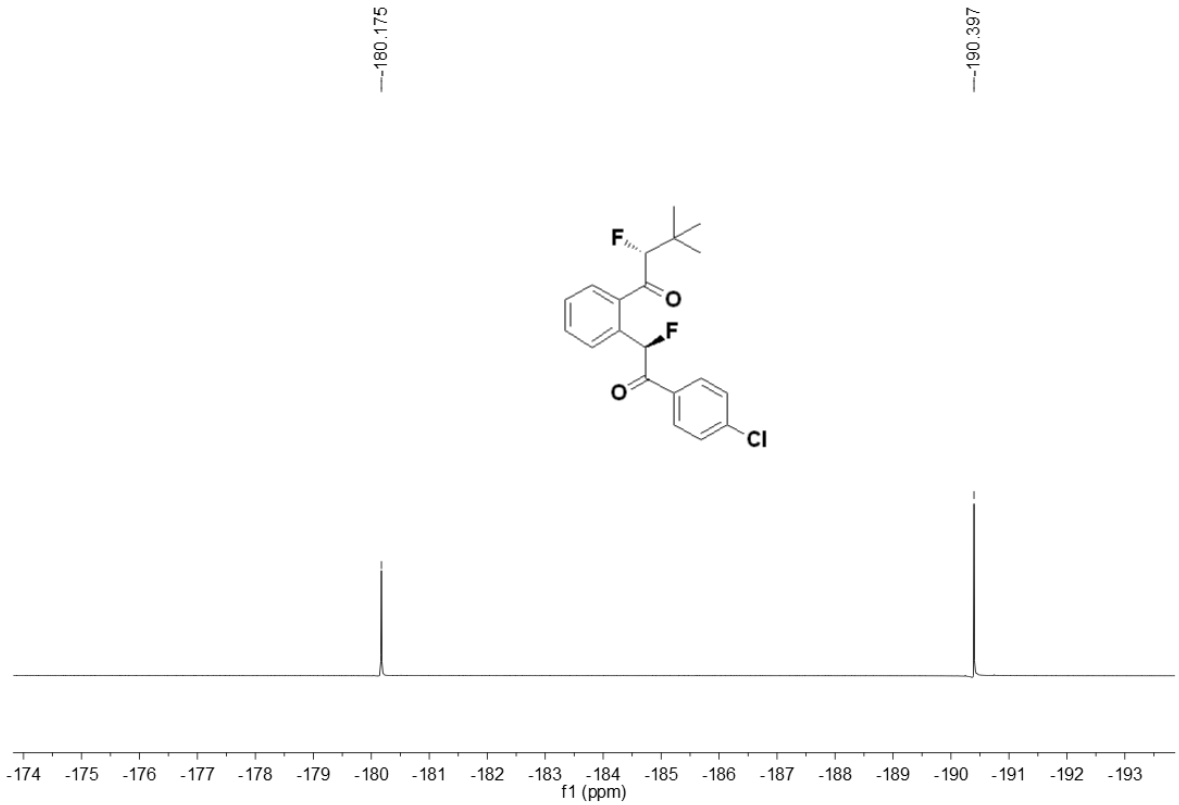
^{19}F NMR Spectrum of Compound 2o



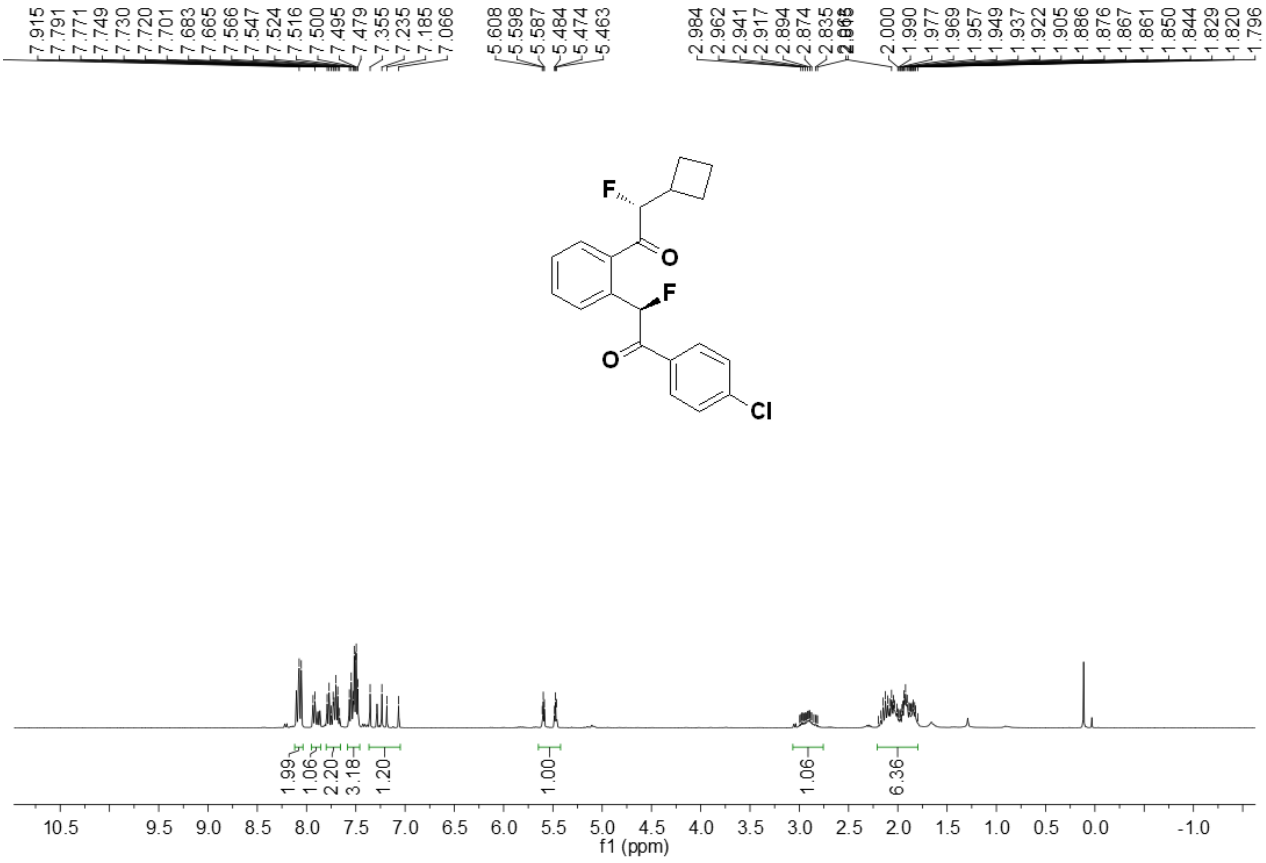
[1]H NMR Spectrum of Compound 2p



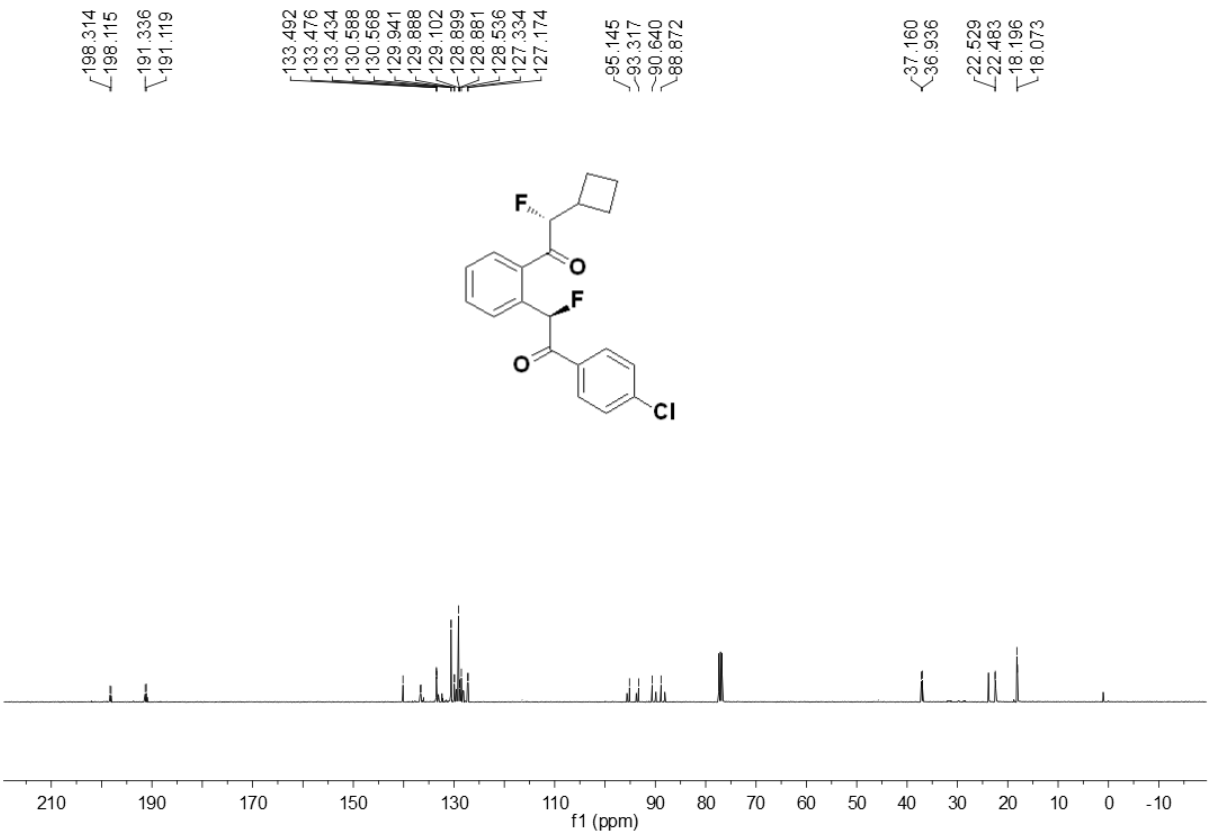
[13]C NMR Spectrum of Compound 2p



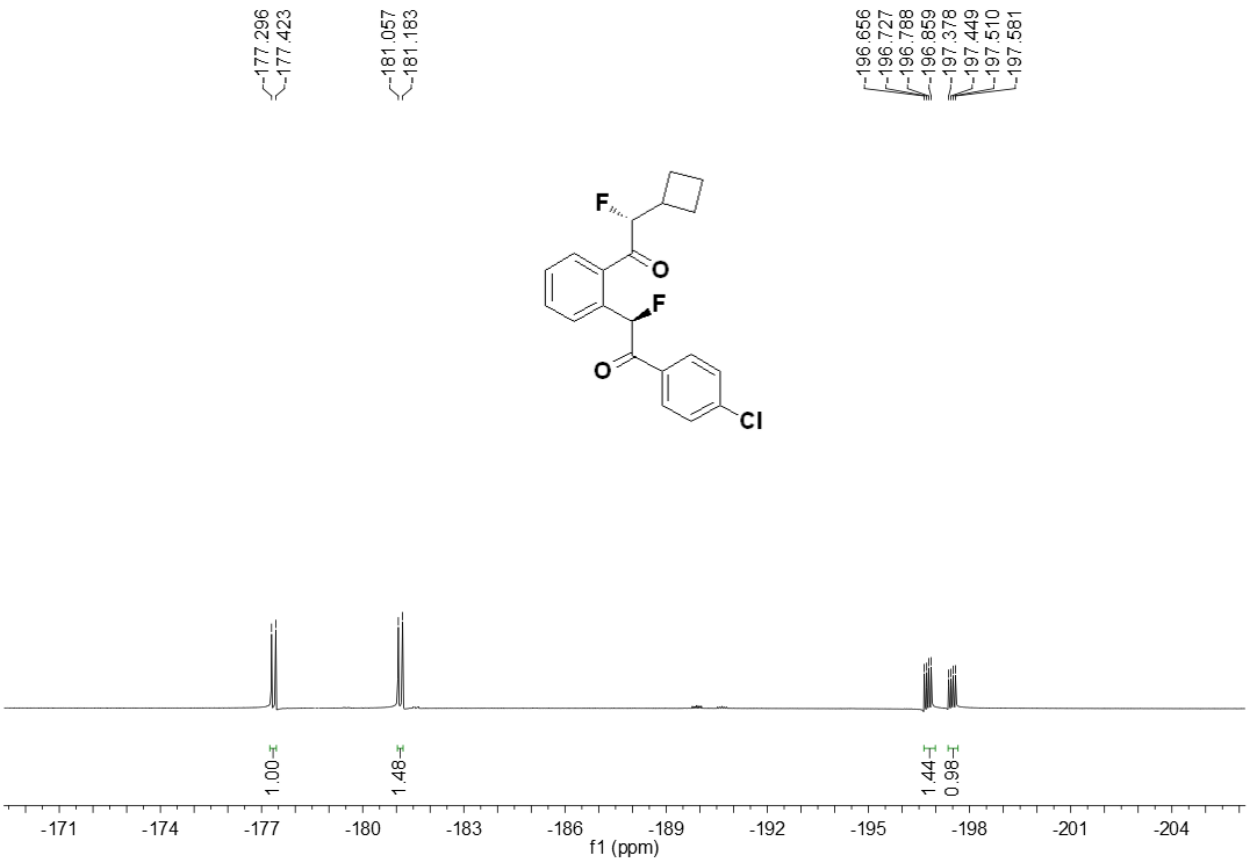
^{19}F NMR Spectrum of Compound 2p



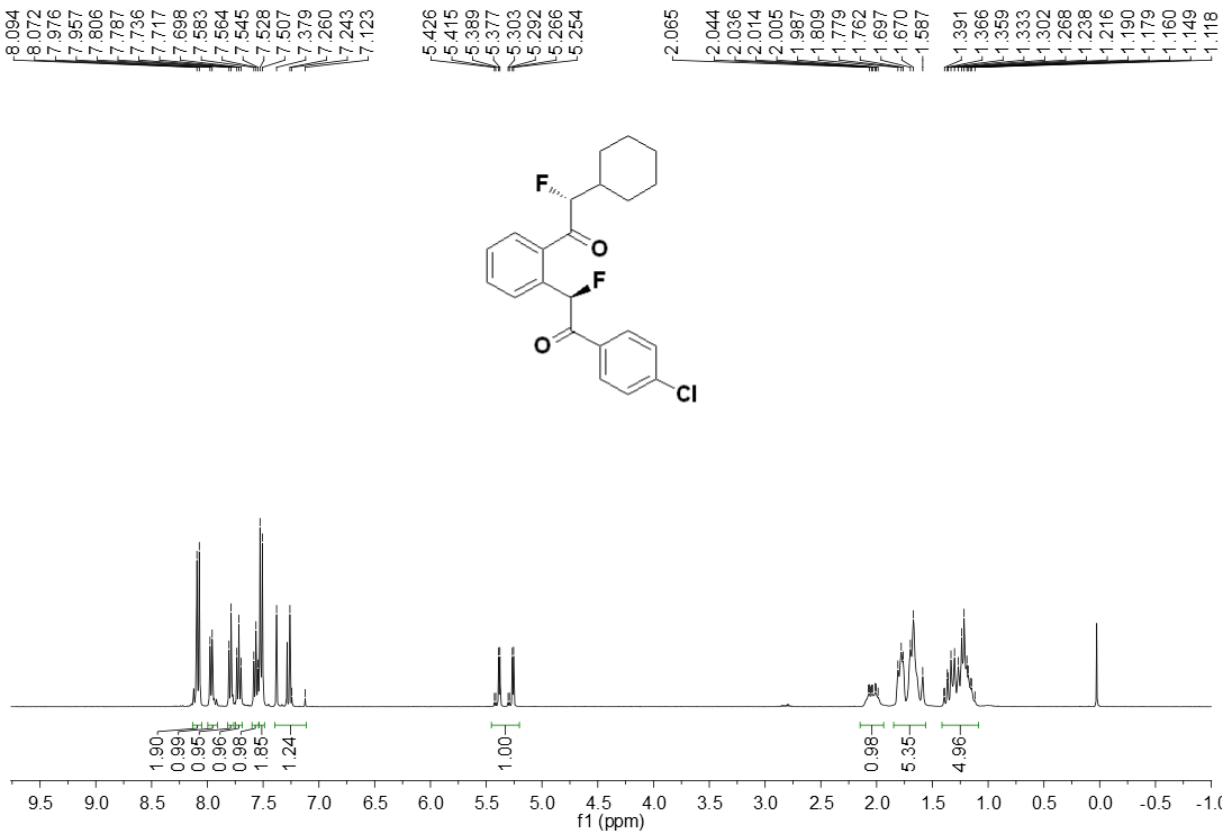
^{1}H NMR Spectrum of Compound 2q



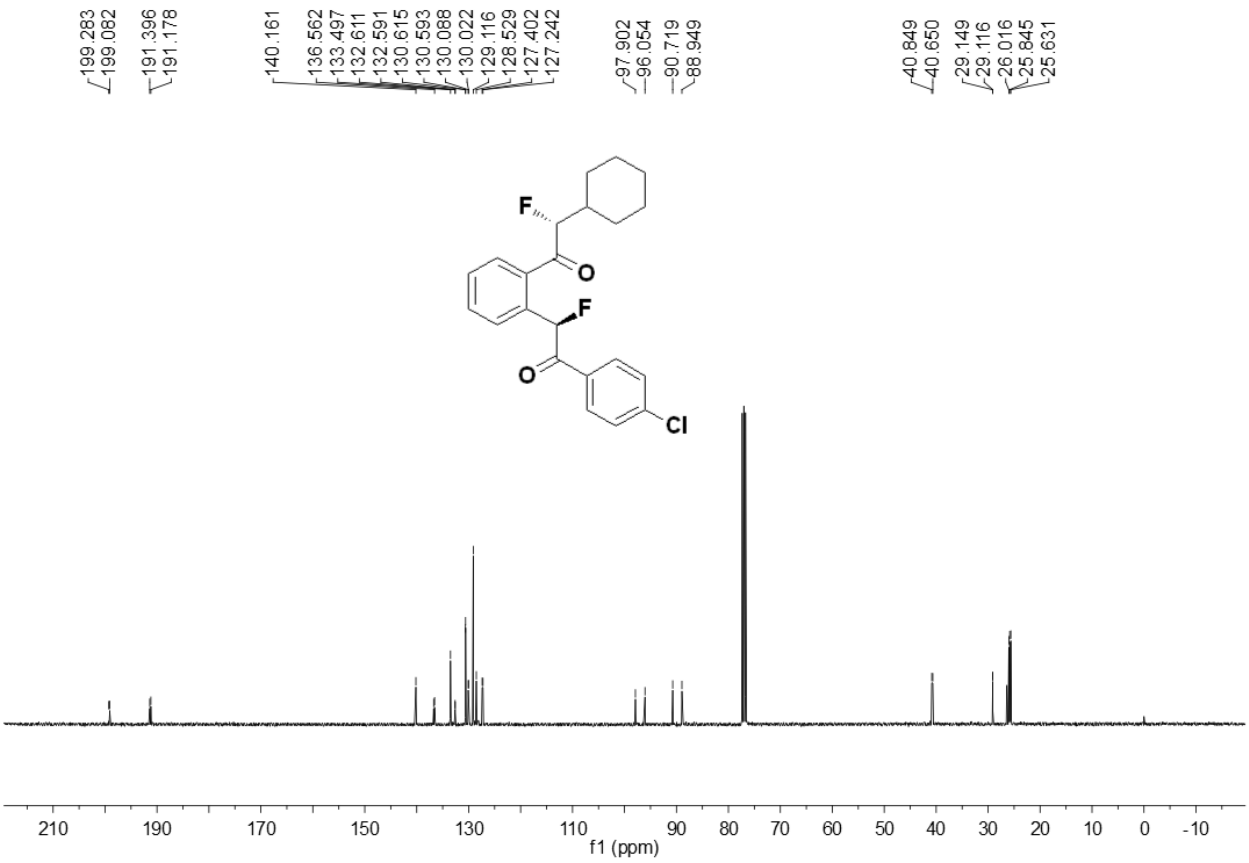
^{13}C NMR Spectrum of Compound 2q



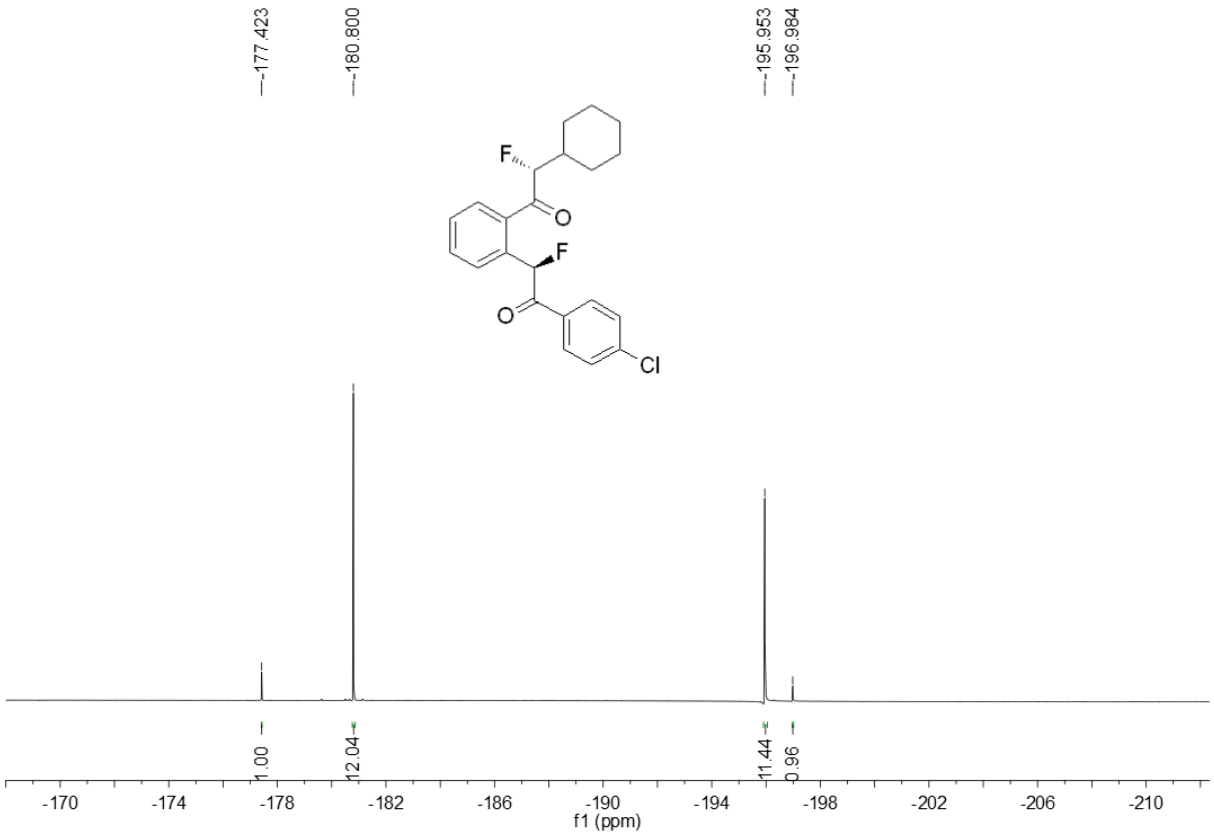
^{19}F NMR Spectrum of Compound 2q



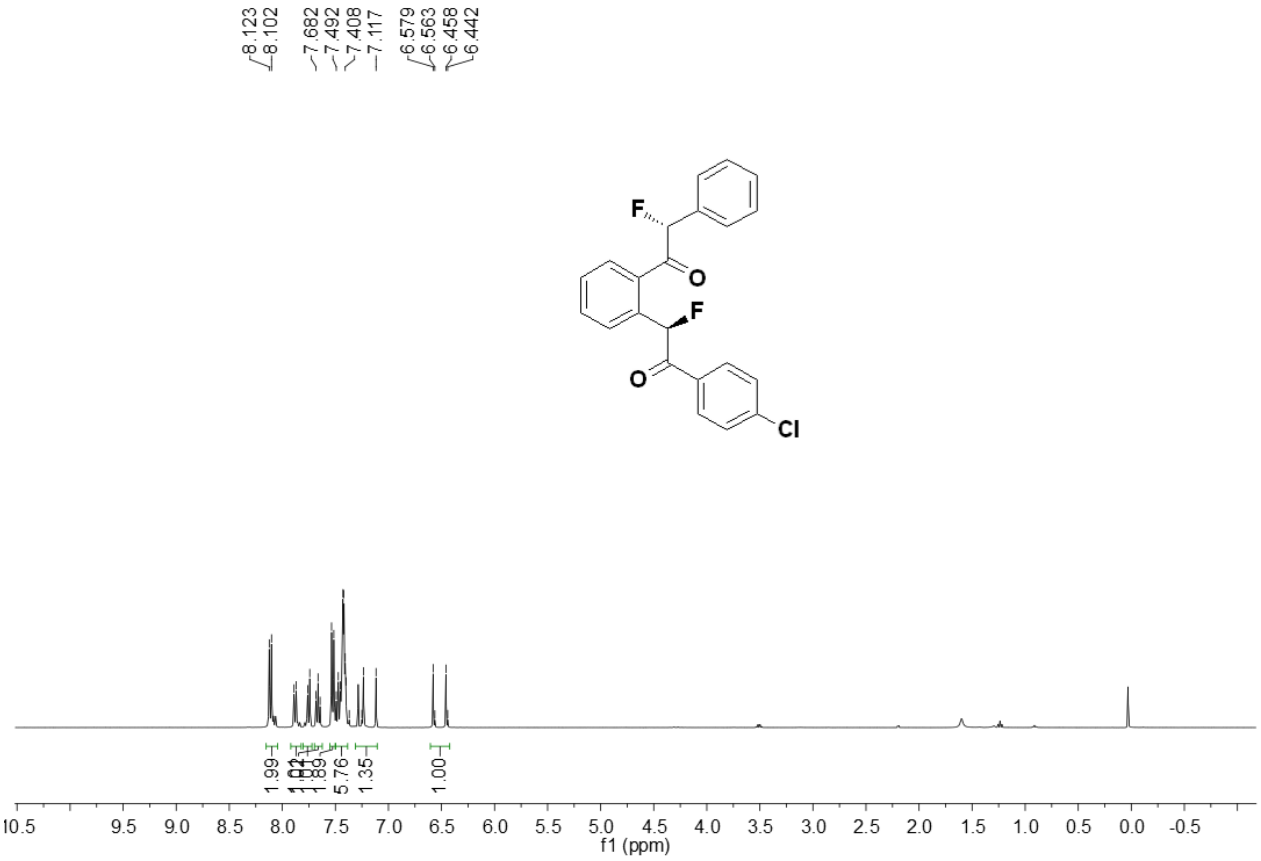
^{1}H NMR Spectrum of Compound 2r



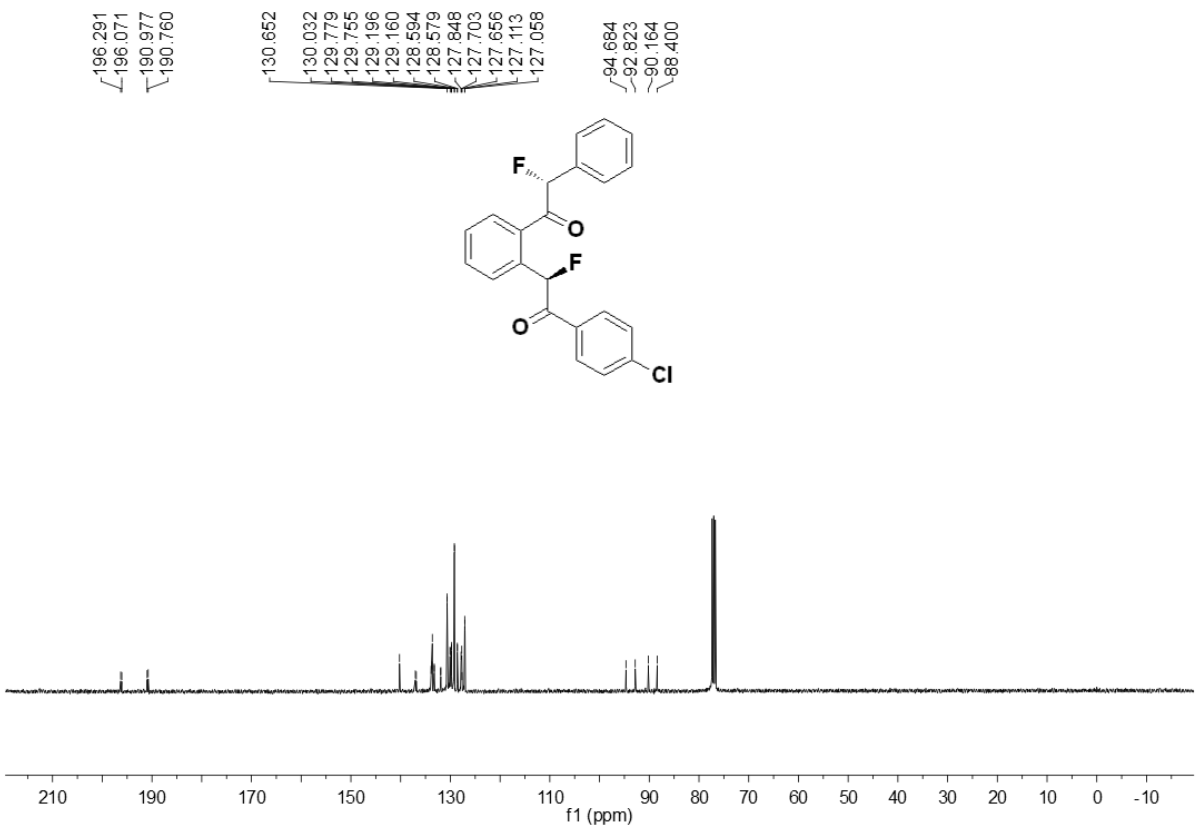
^{13}C NMR Spectrum of Compound 2r



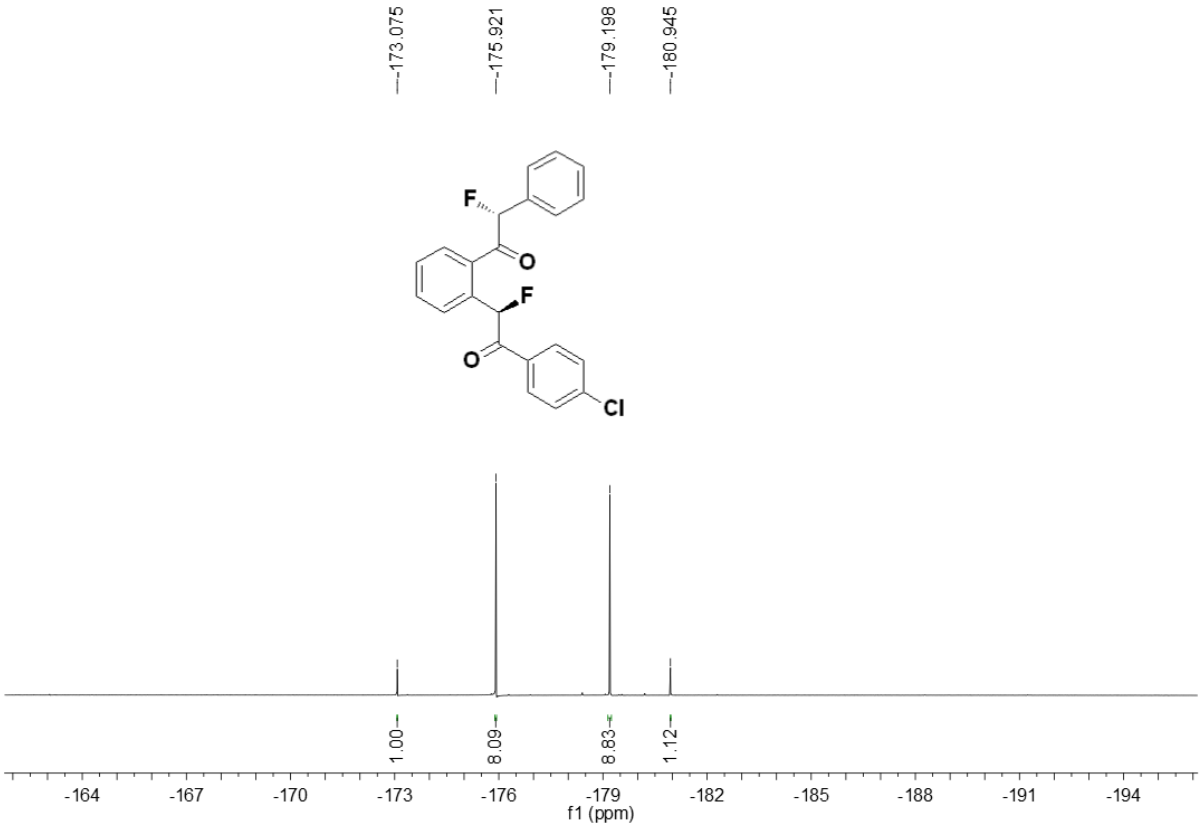
^{19}F NMR Spectrum of Compound 2r



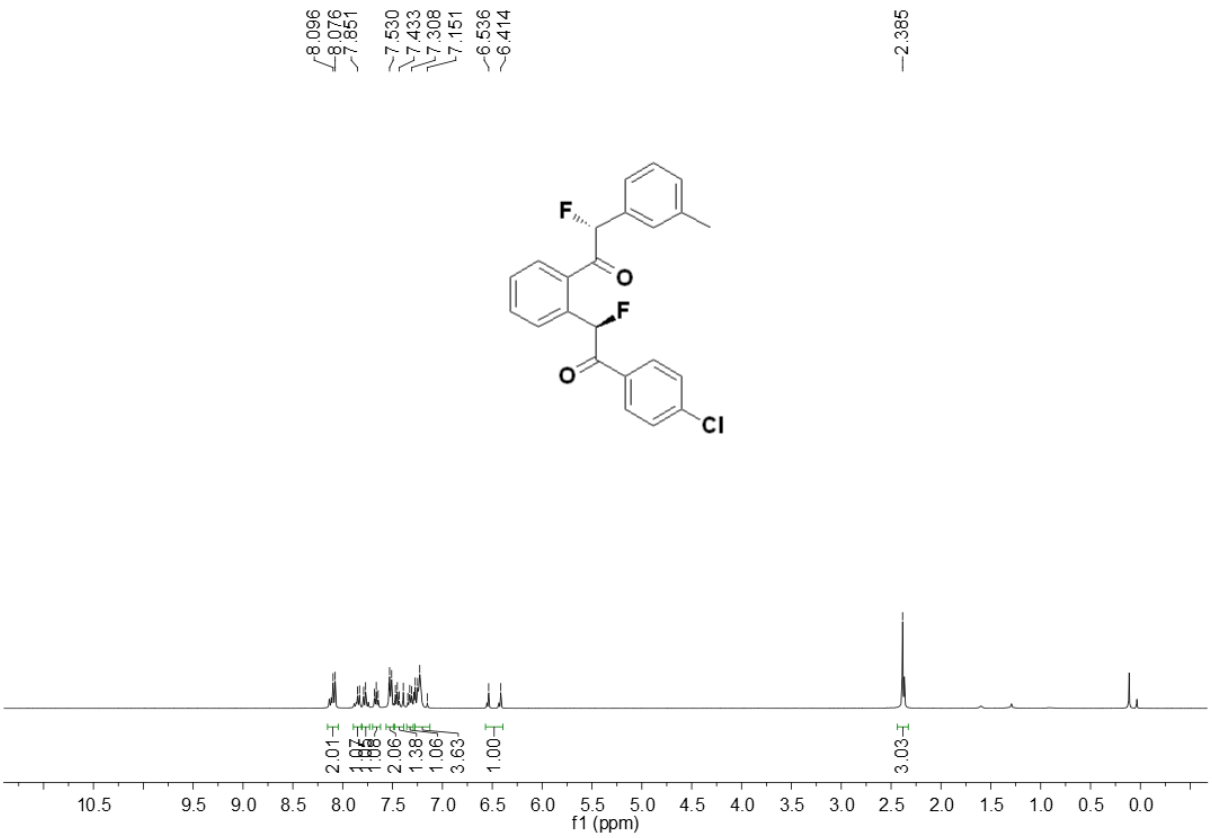
^{1}H NMR Spectrum of Compound 2s



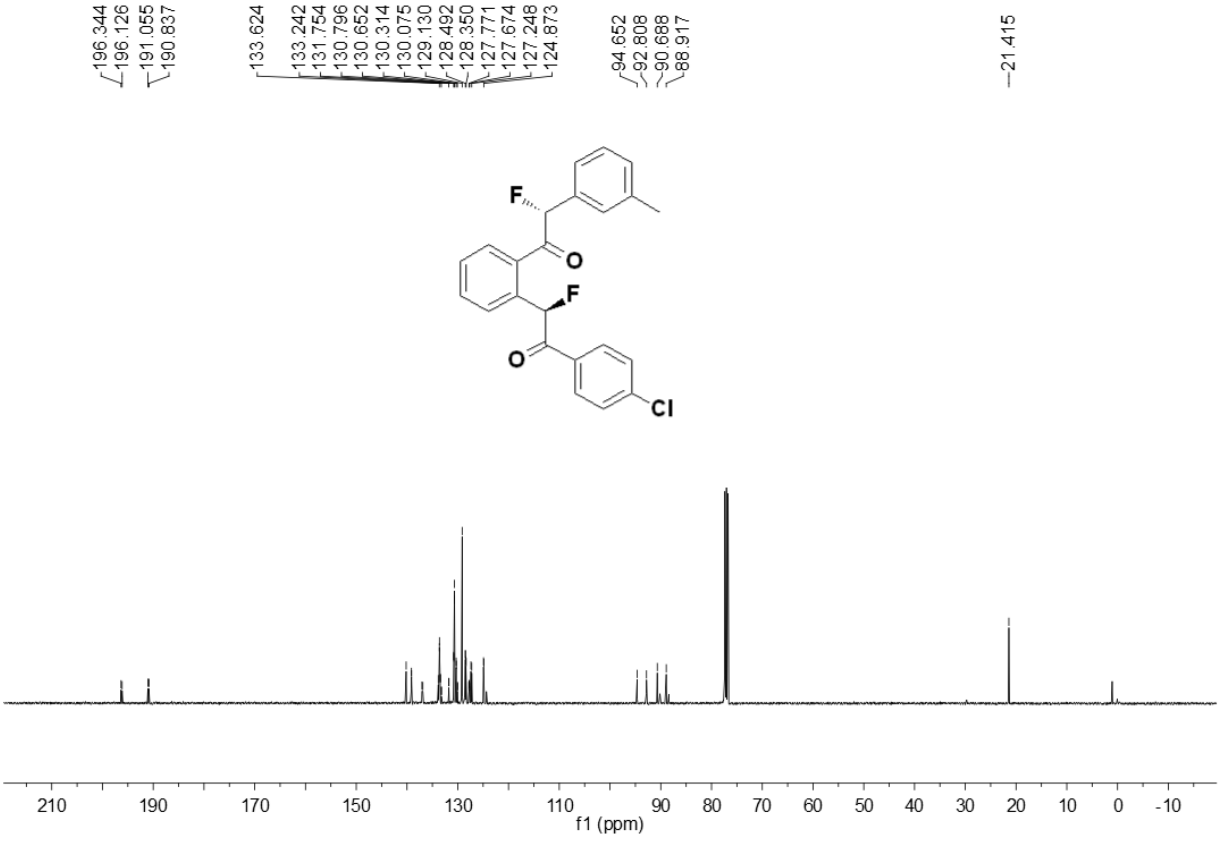
^{13}C NMR Spectrum of Compound 2s



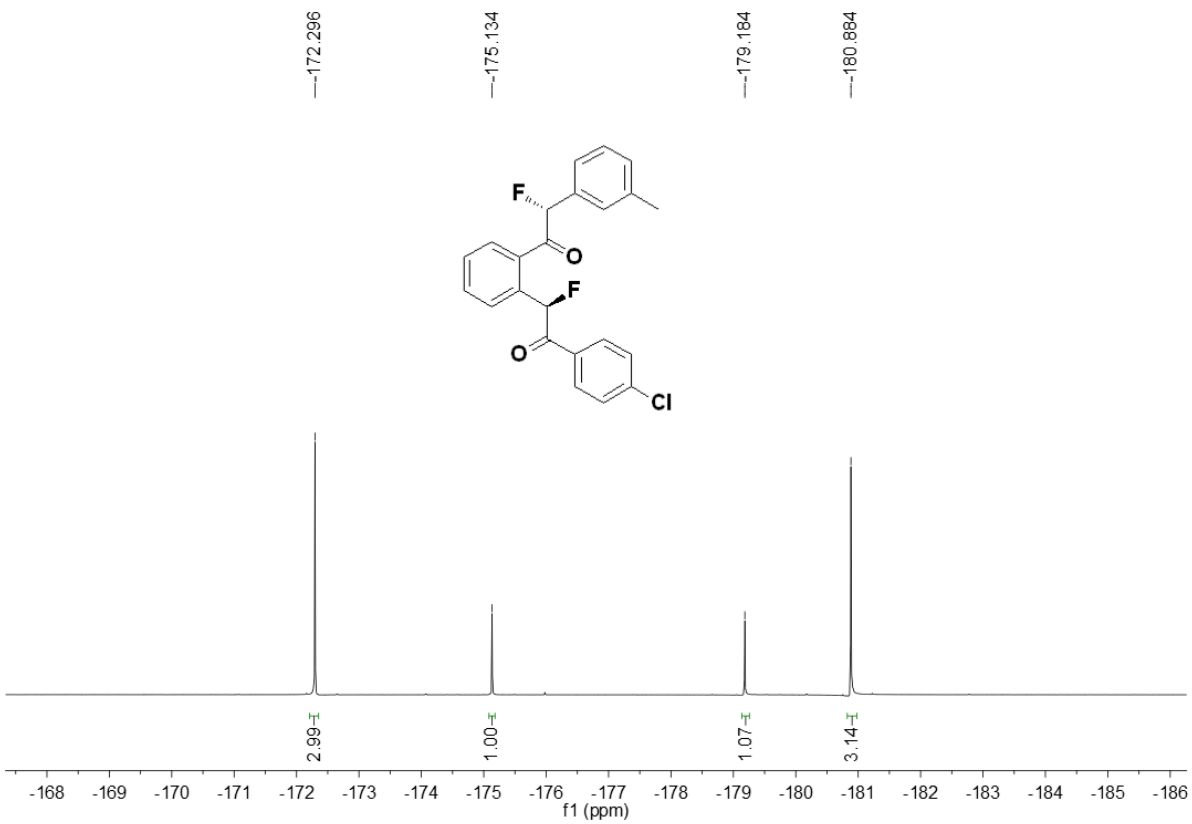
^{19}F NMR Spectrum of Compound 2s



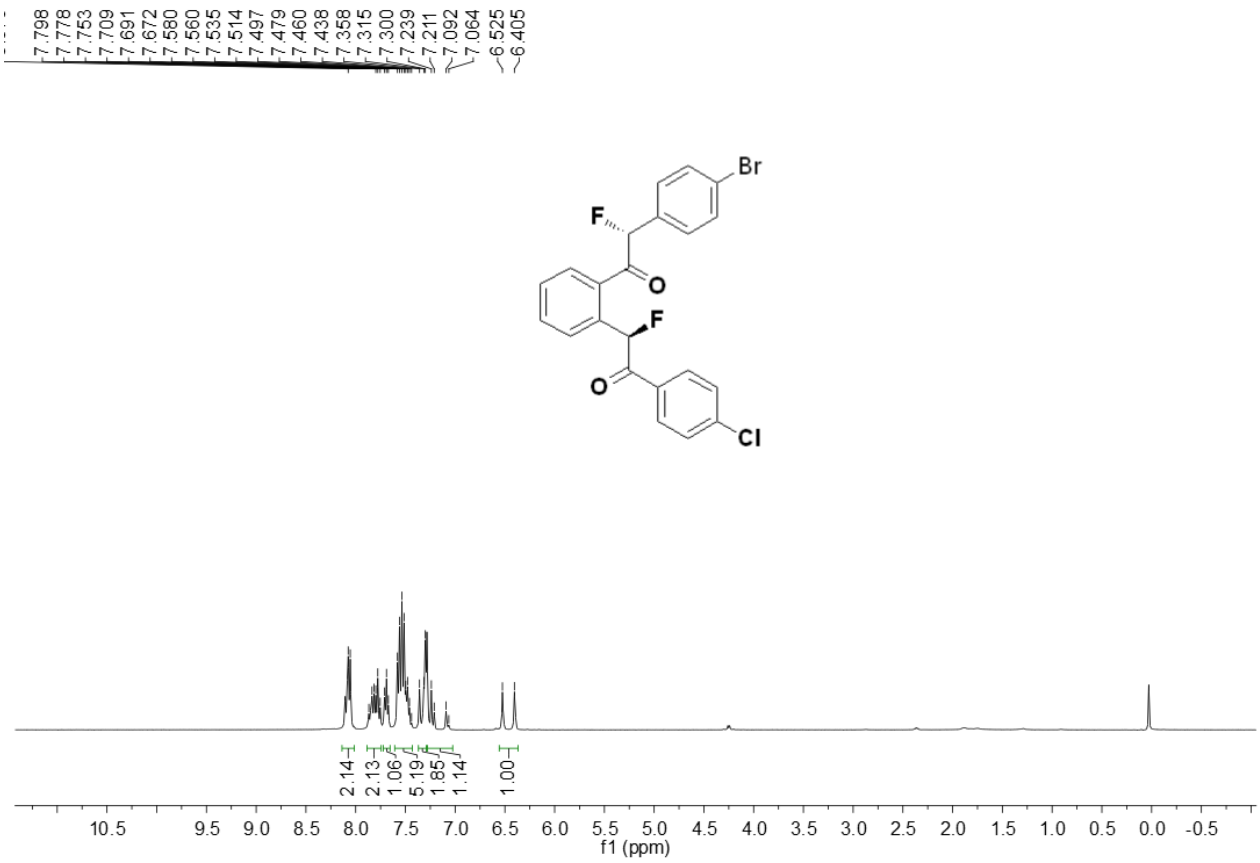
[1]H NMR Spectrum of Compound 2t



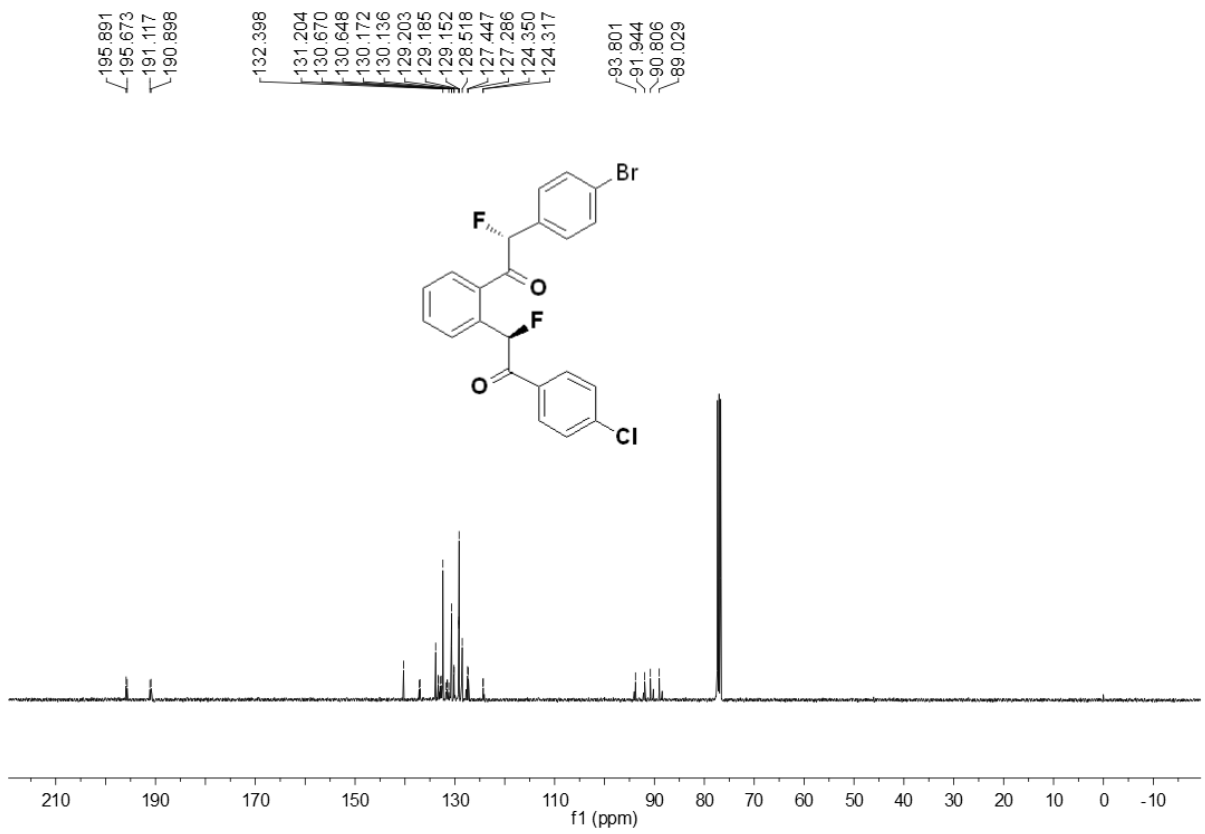
[13]C NMR Spectrum of Compound 2t



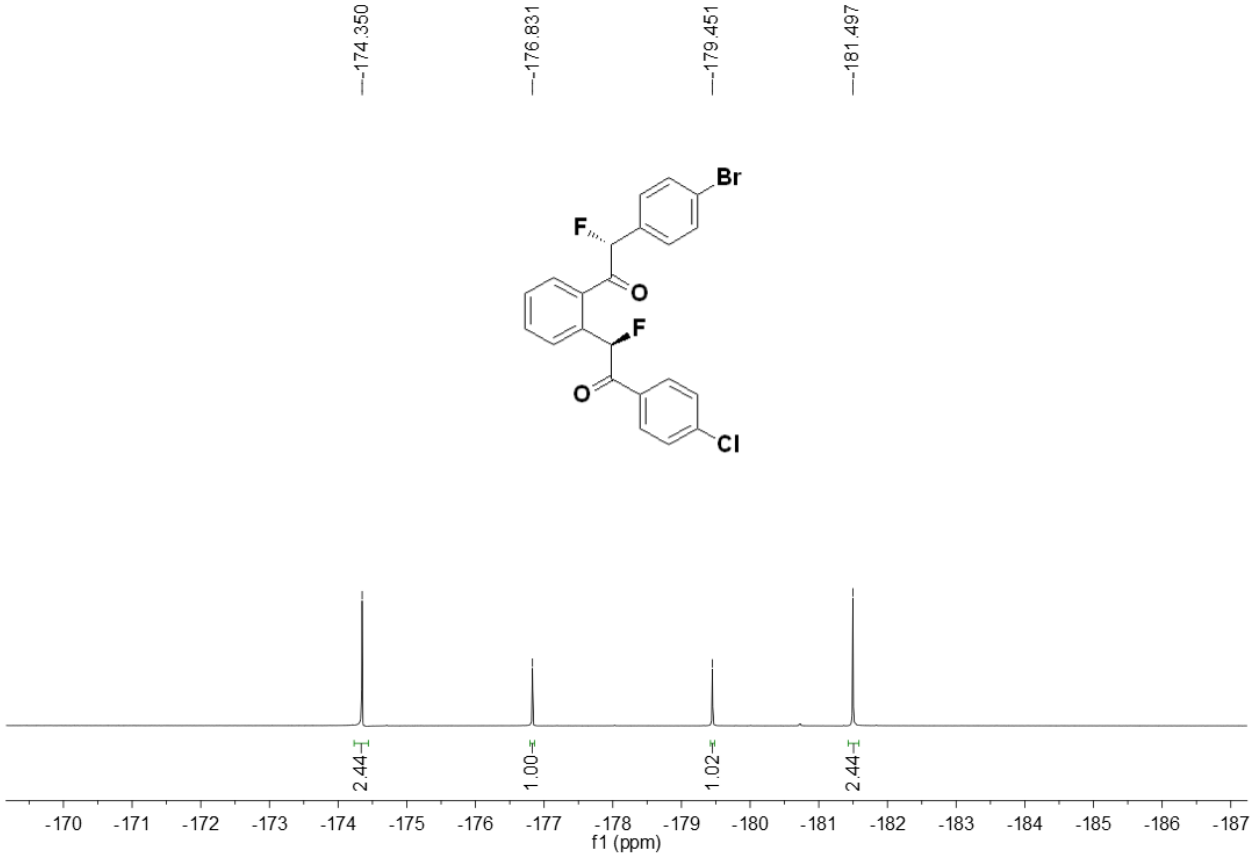
^{19}F NMR Spectrum of Compound 2t



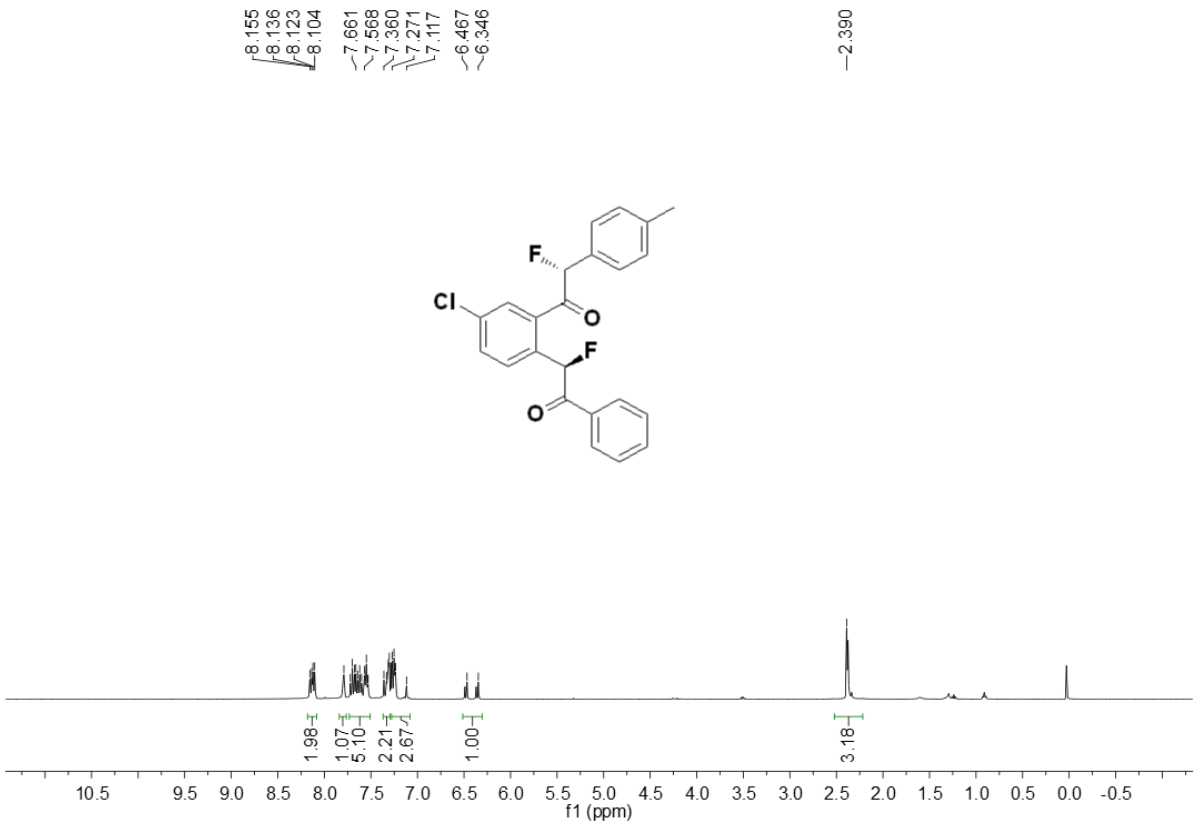
^{1}H NMR Spectrum of Compound 2u



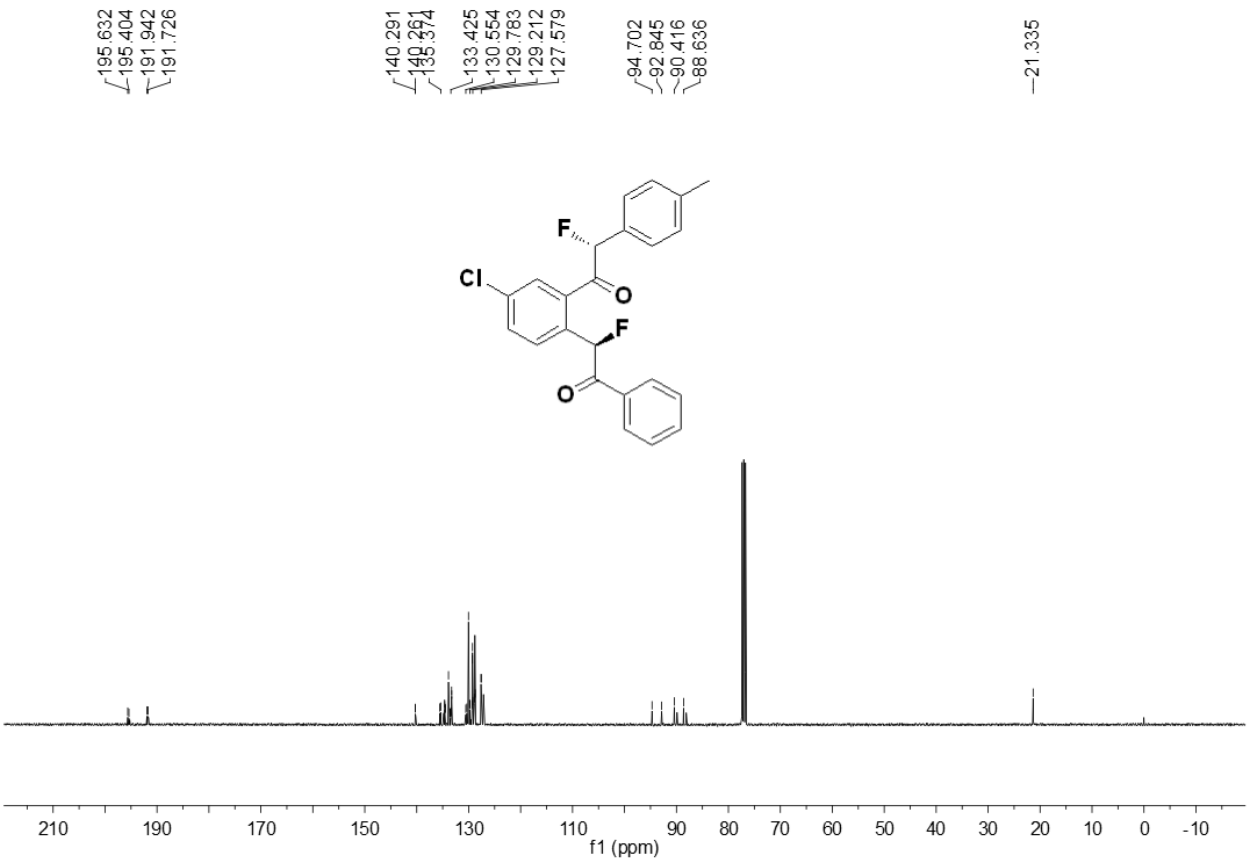
^{13}C NMR Spectrum of Compound 2u



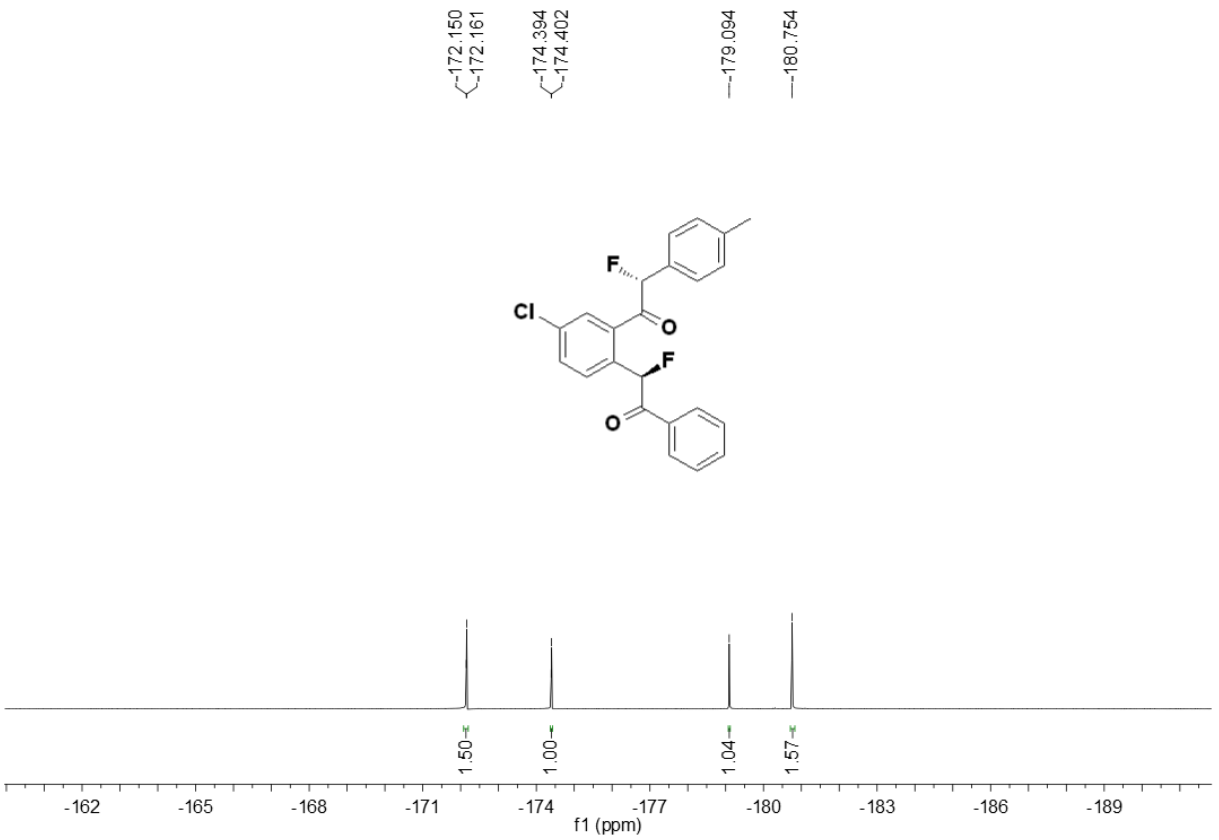
^{19}F NMR Spectrum of Compound 2u



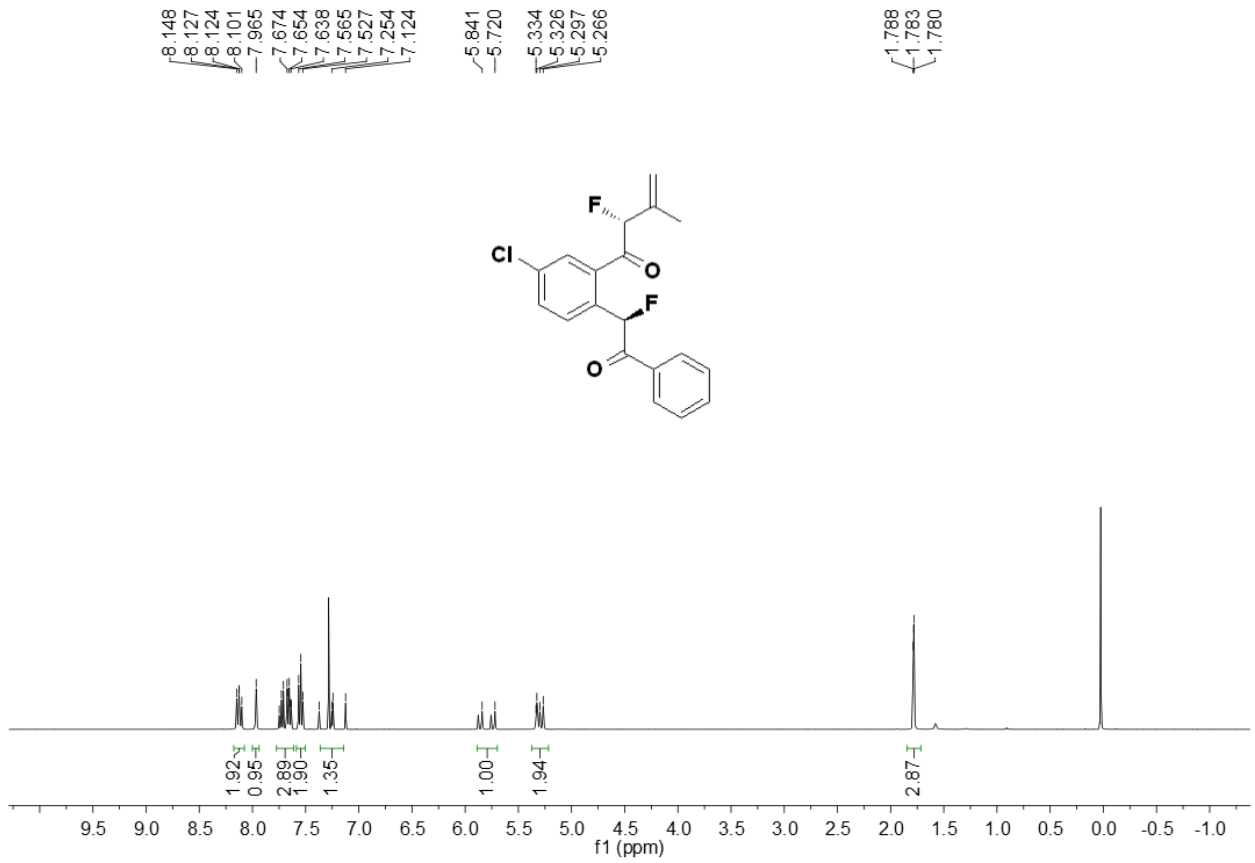
^{1}H NMR Spectrum of Compound 2v



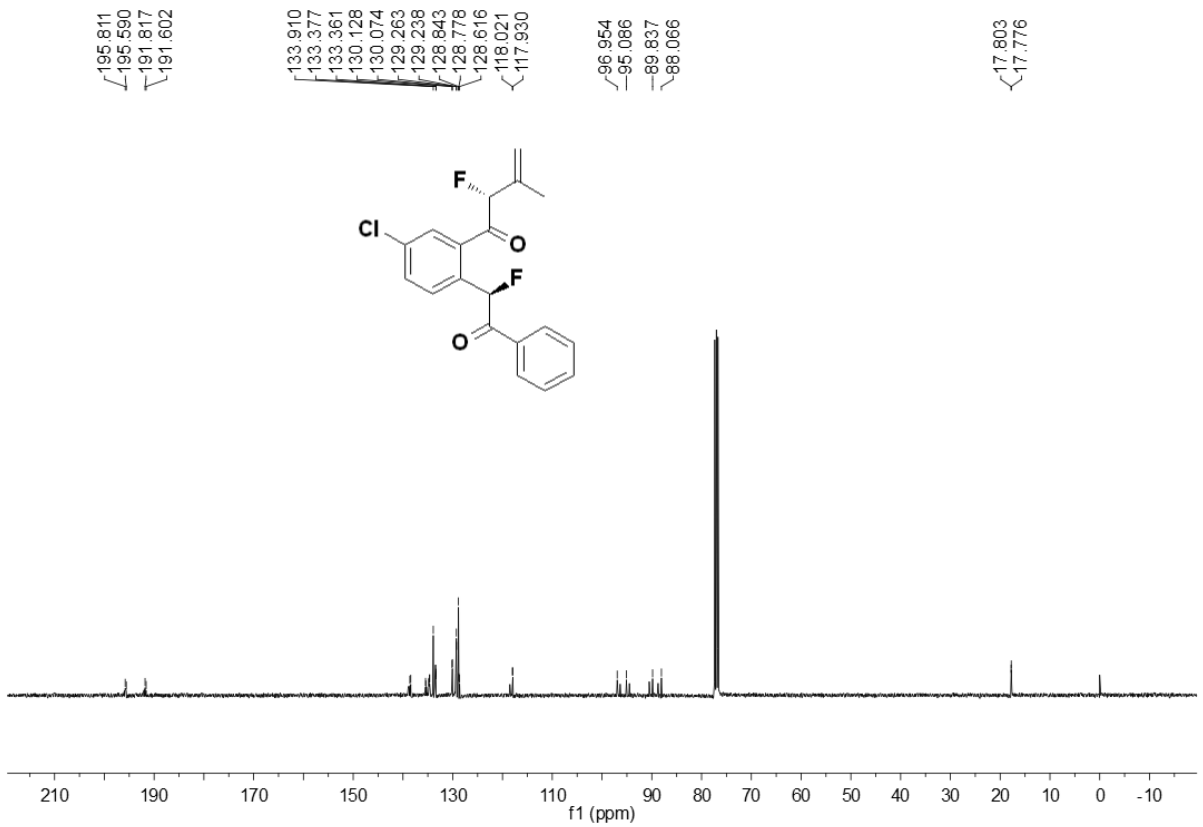
^{13}C NMR Spectrum of Compound 2v



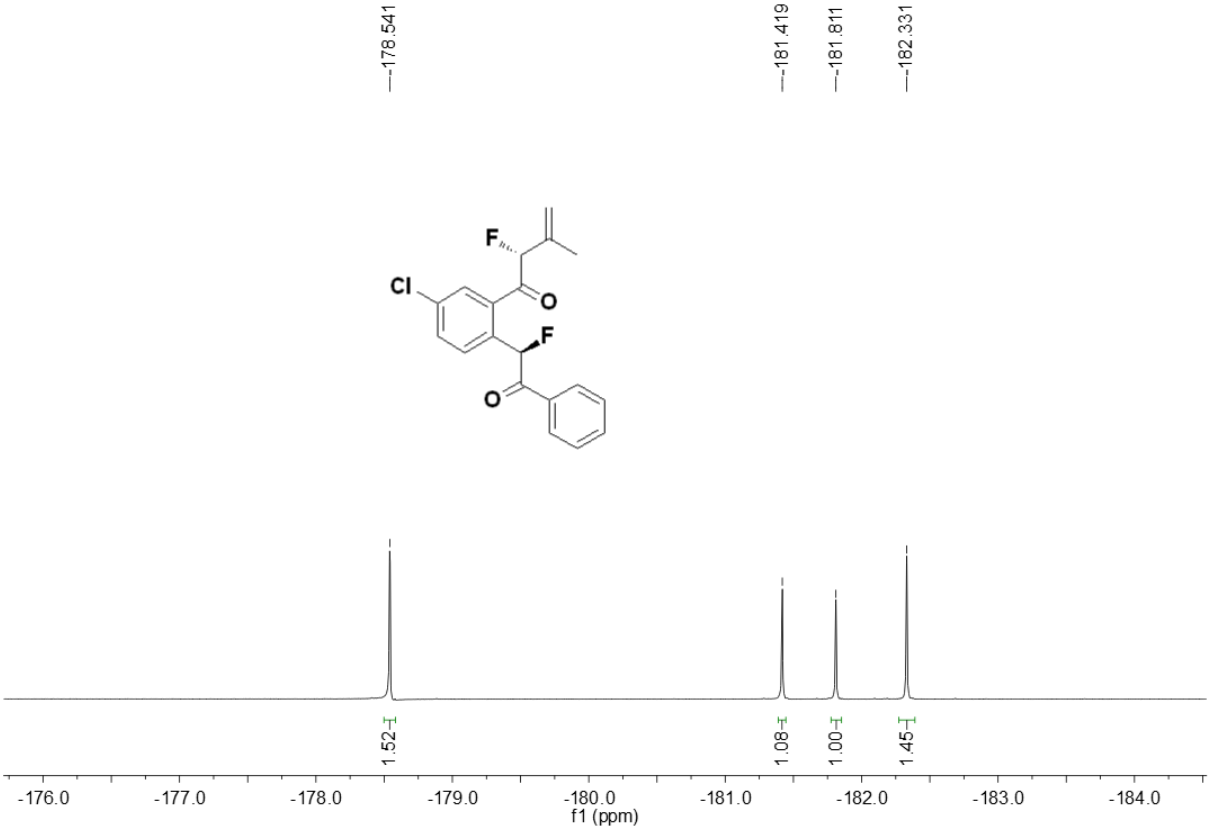
^{19}F NMR Spectrum of Compound 2v



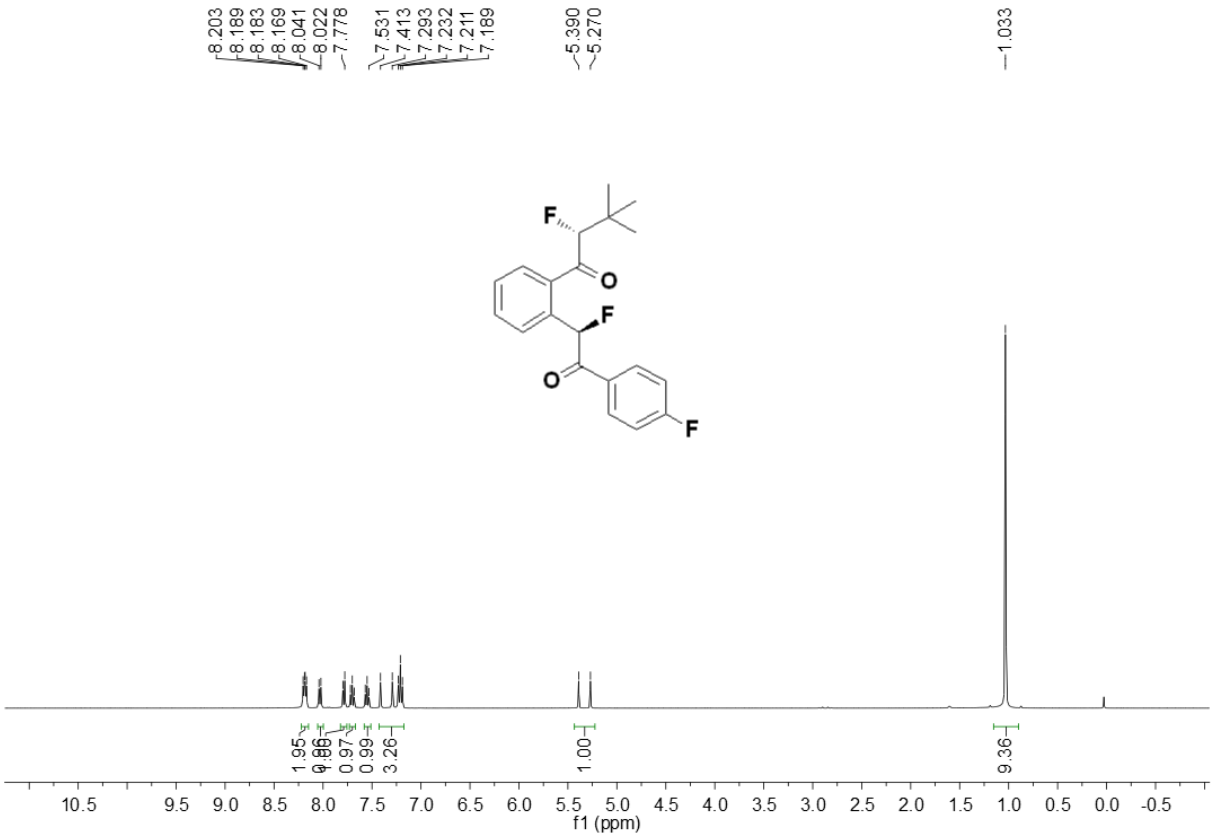
^{1}H NMR Spectrum of Compound 2w



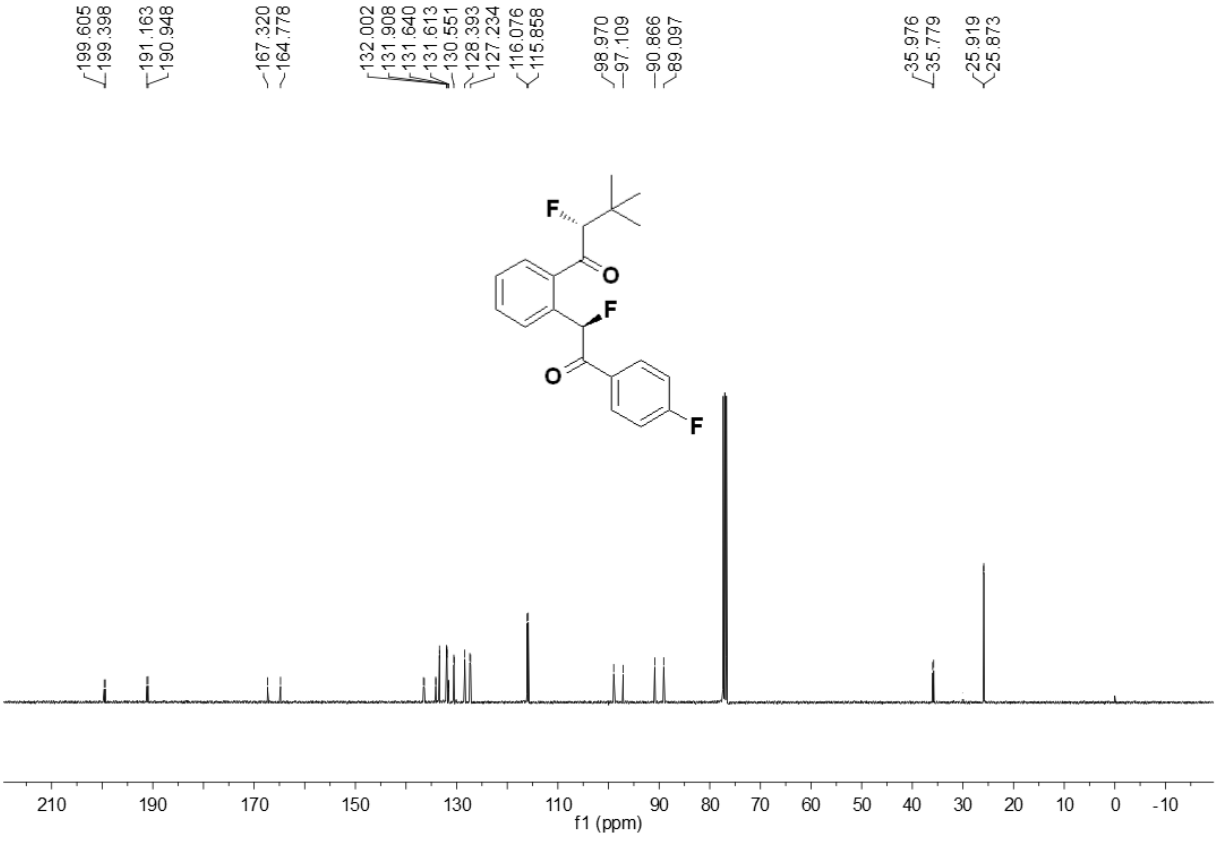
^{13}C NMR Spectrum of Compound 2w



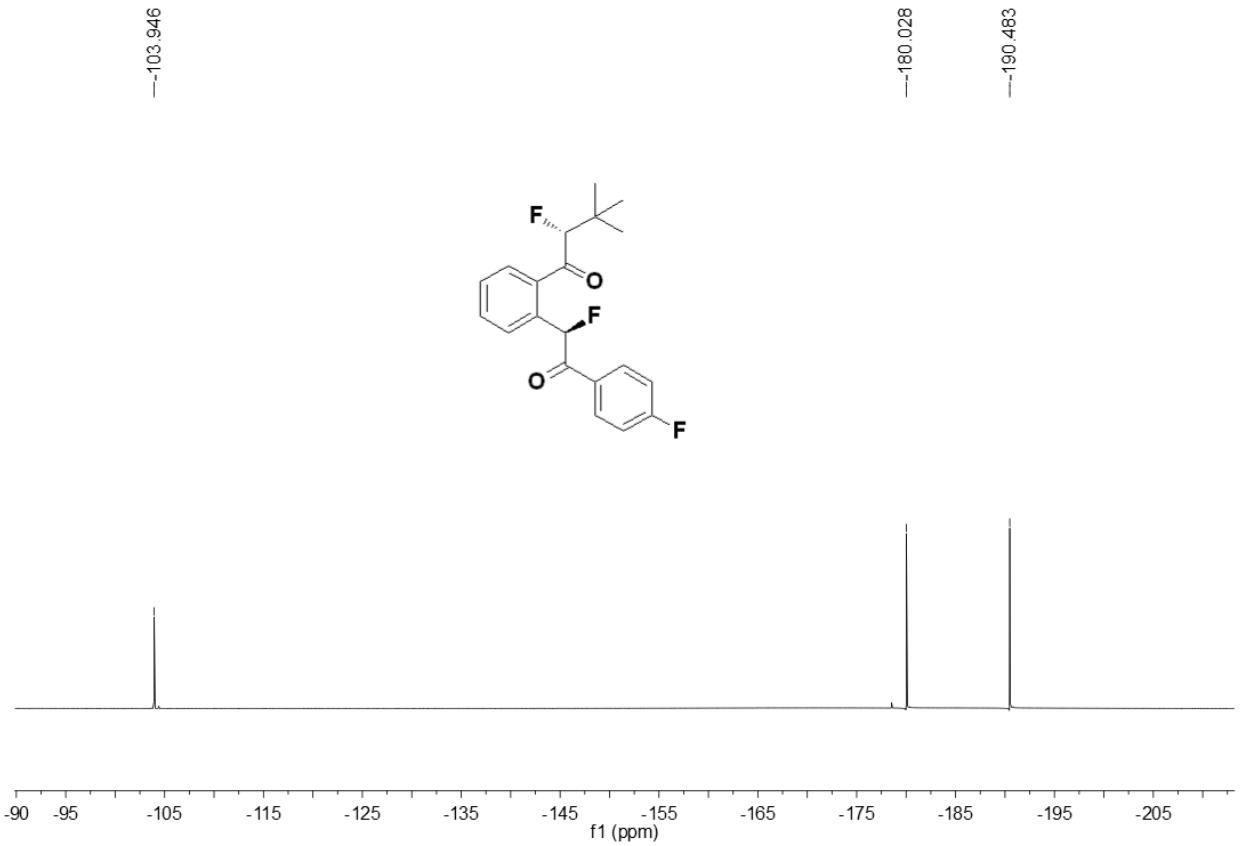
^{19}F NMR Spectrum of Compound 2w



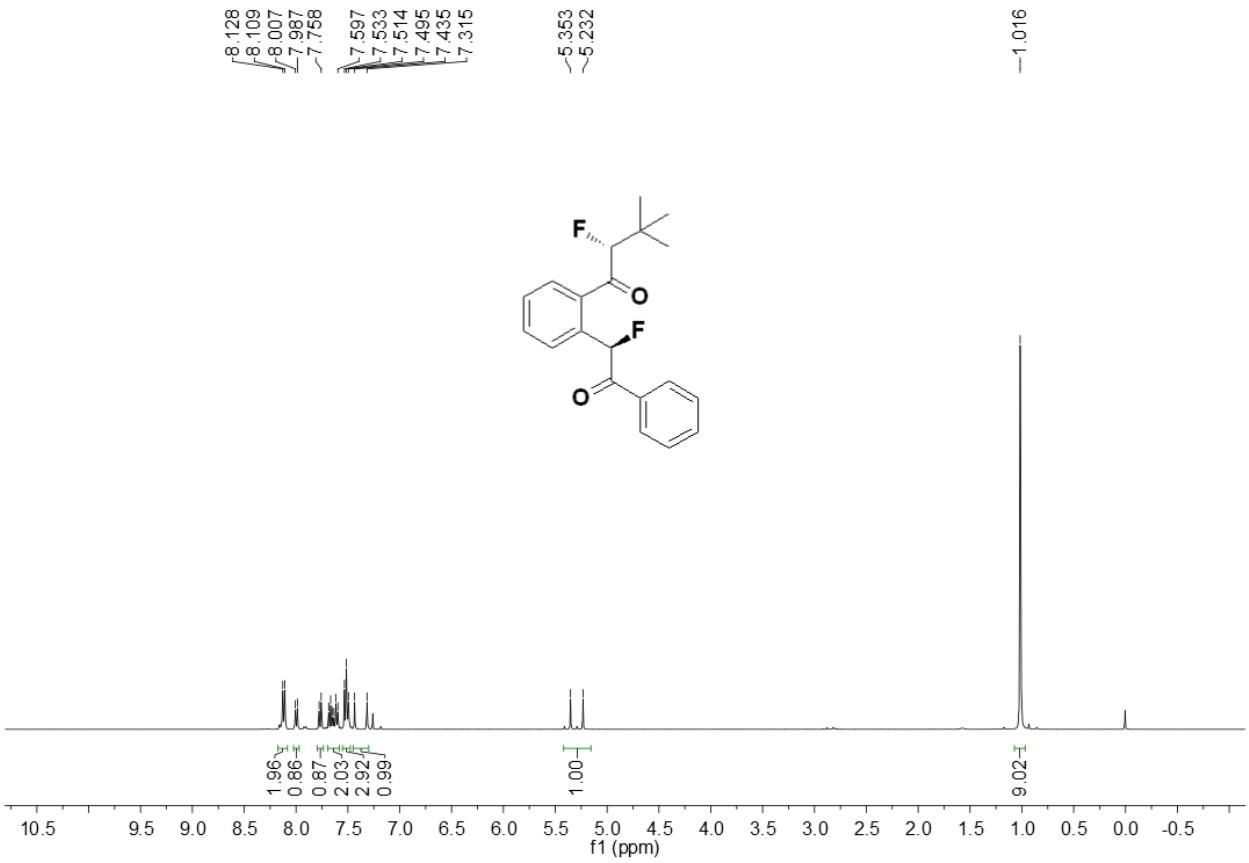
^{1}H NMR Spectrum of Compound 2x



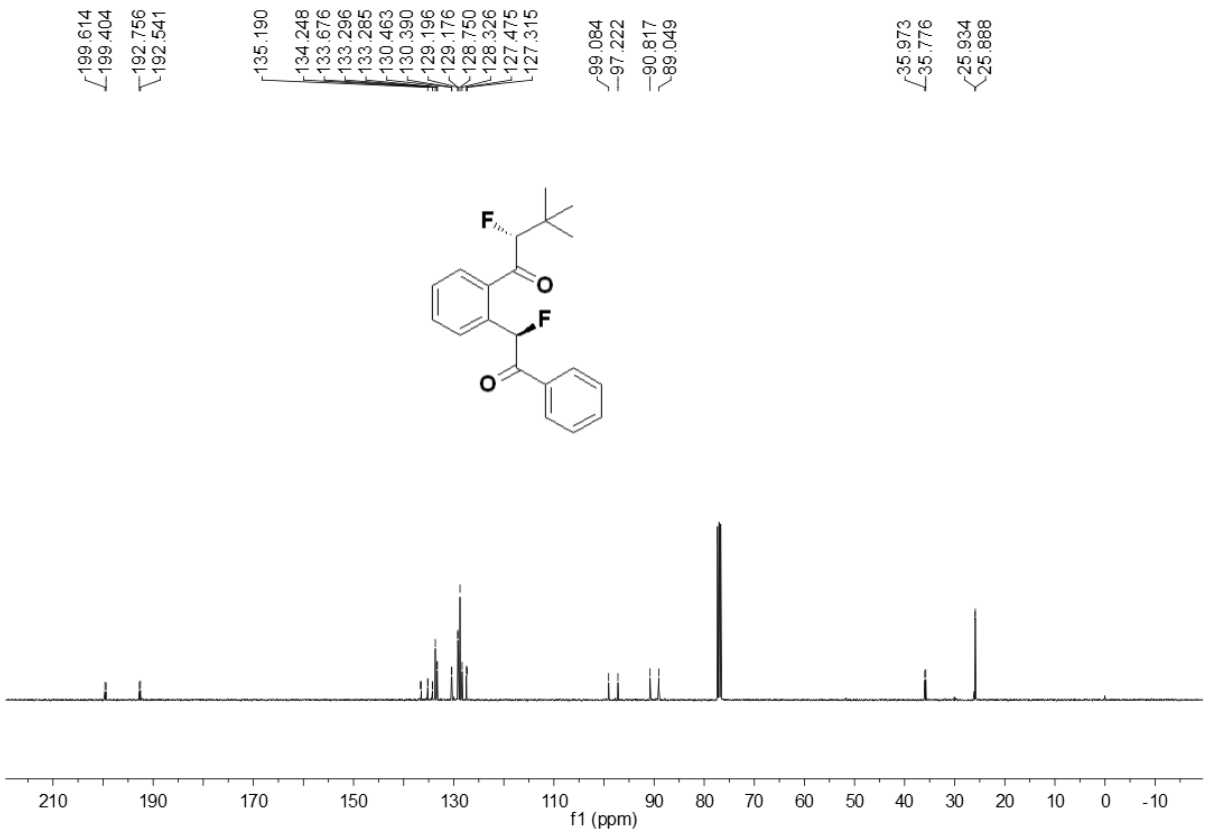
^{13}C NMR Spectrum of Compound 2x



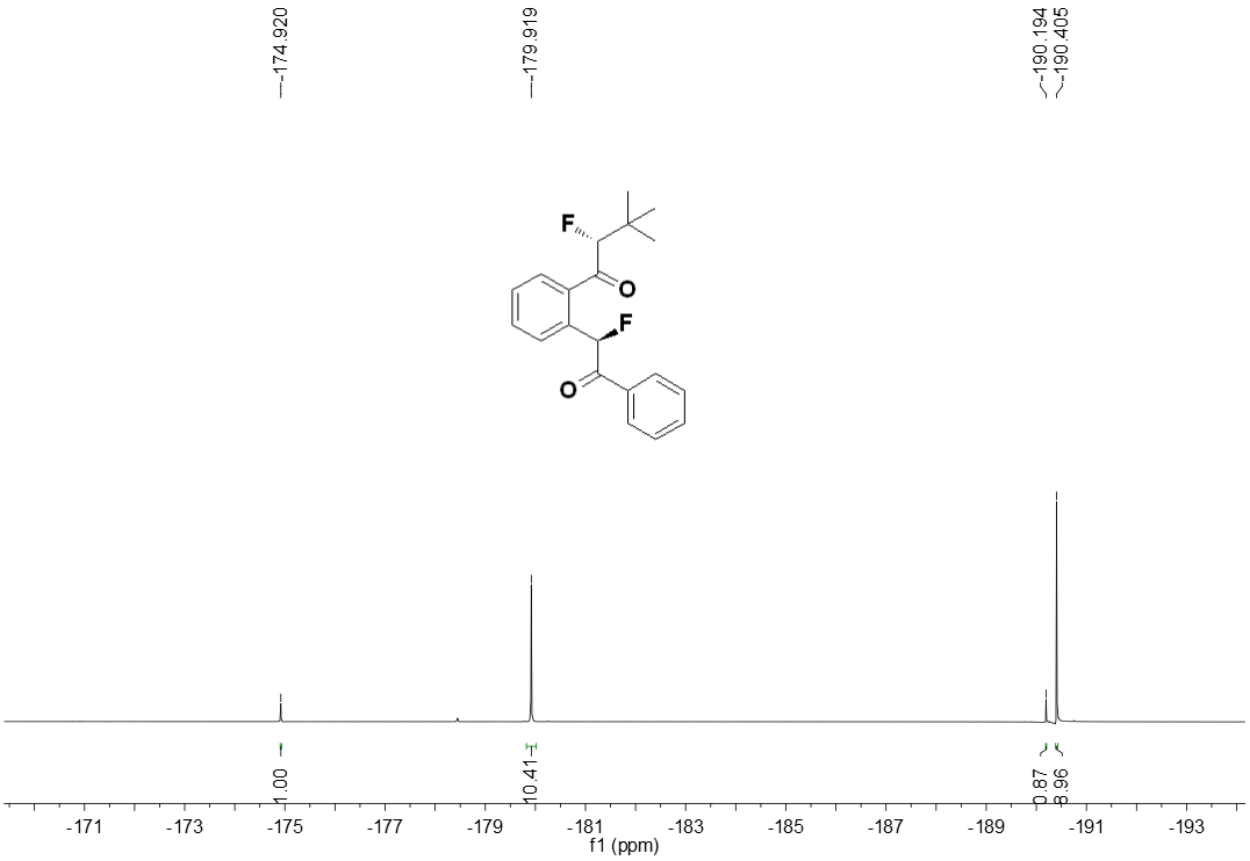
^{19}F NMR Spectrum of Compound 2x



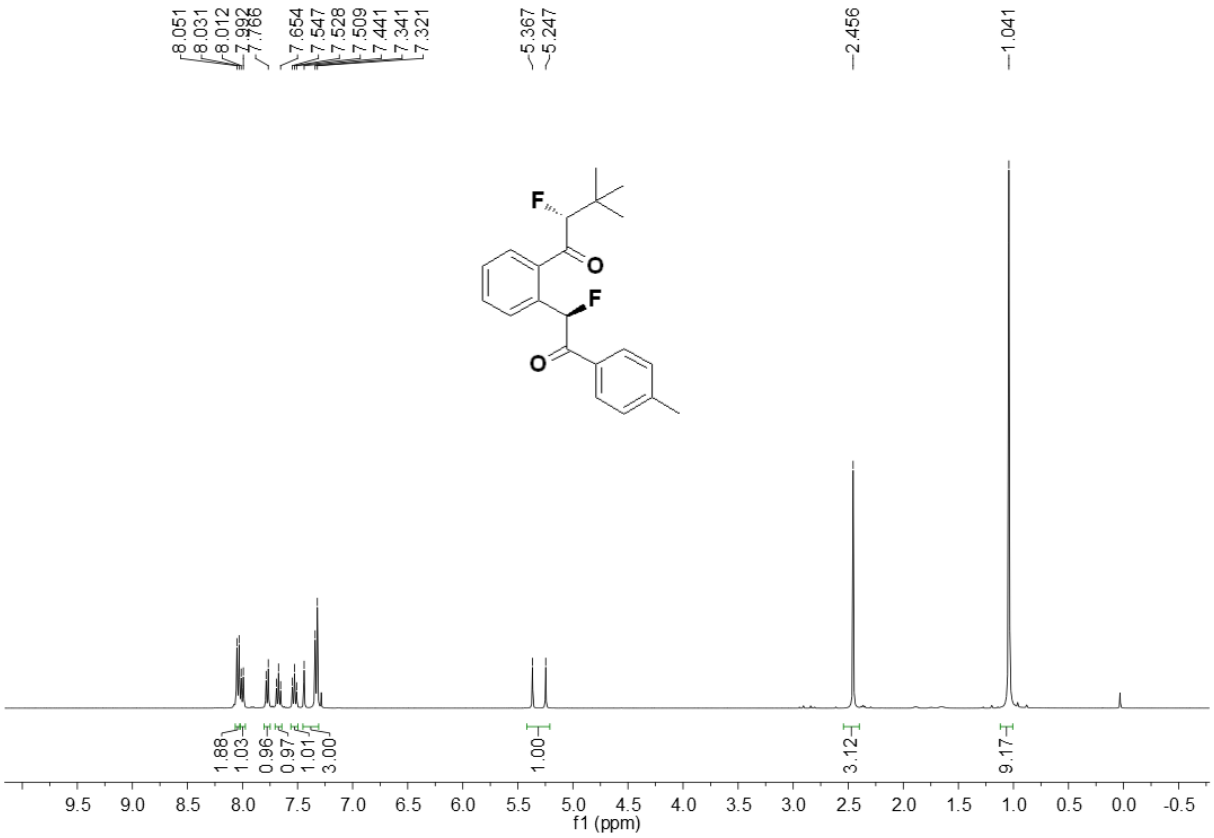
^{1}H NMR Spectrum of Compound 2y



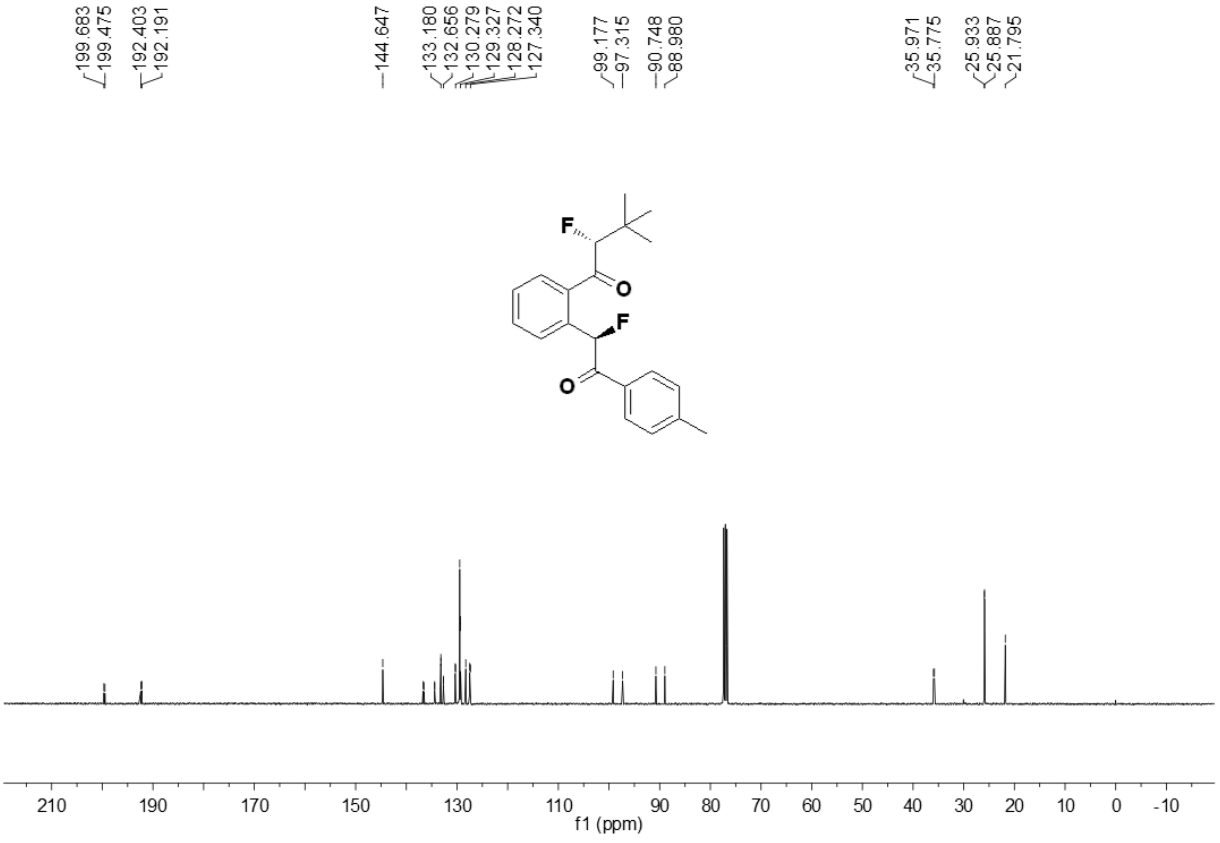
^{13}C NMR Spectrum of Compound 2y



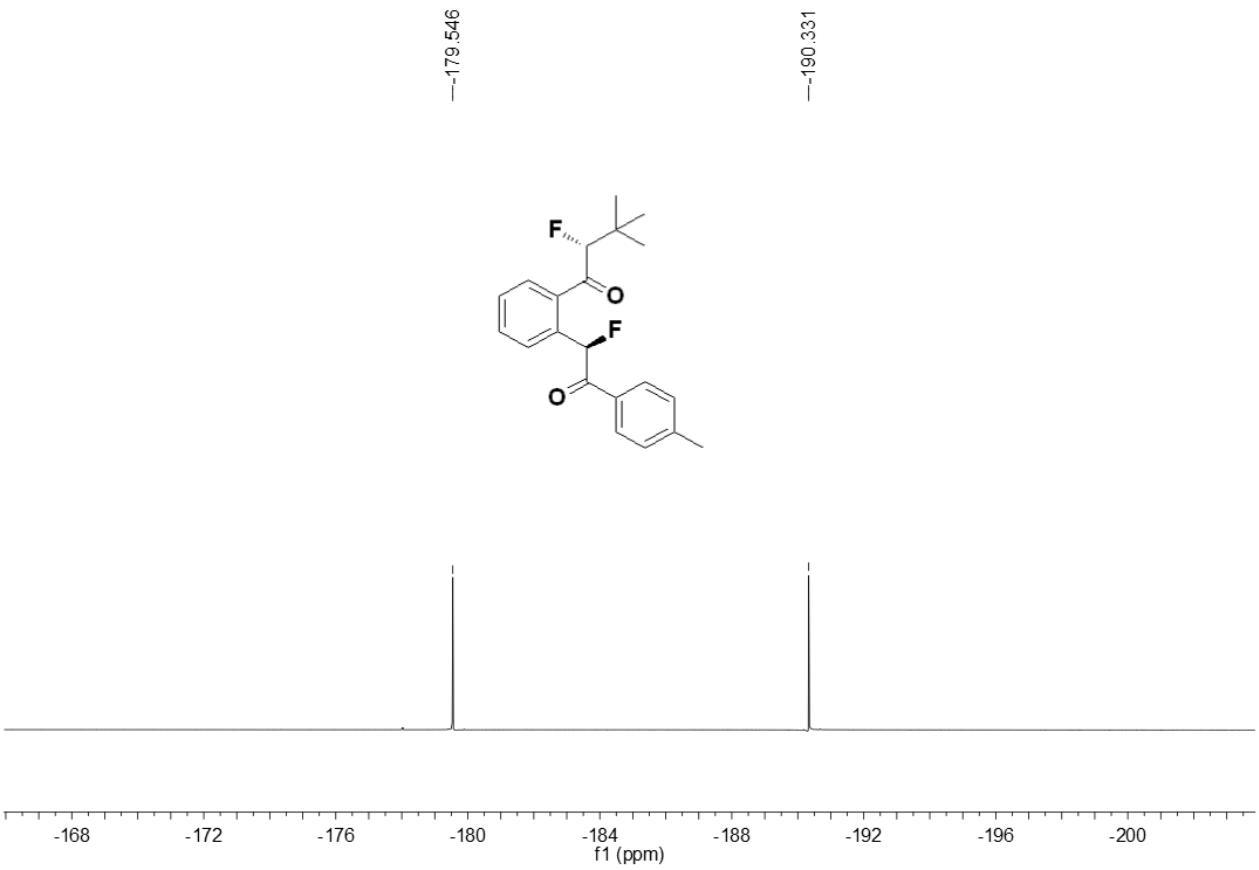
^{19}F NMR Spectrum of Compound 2y



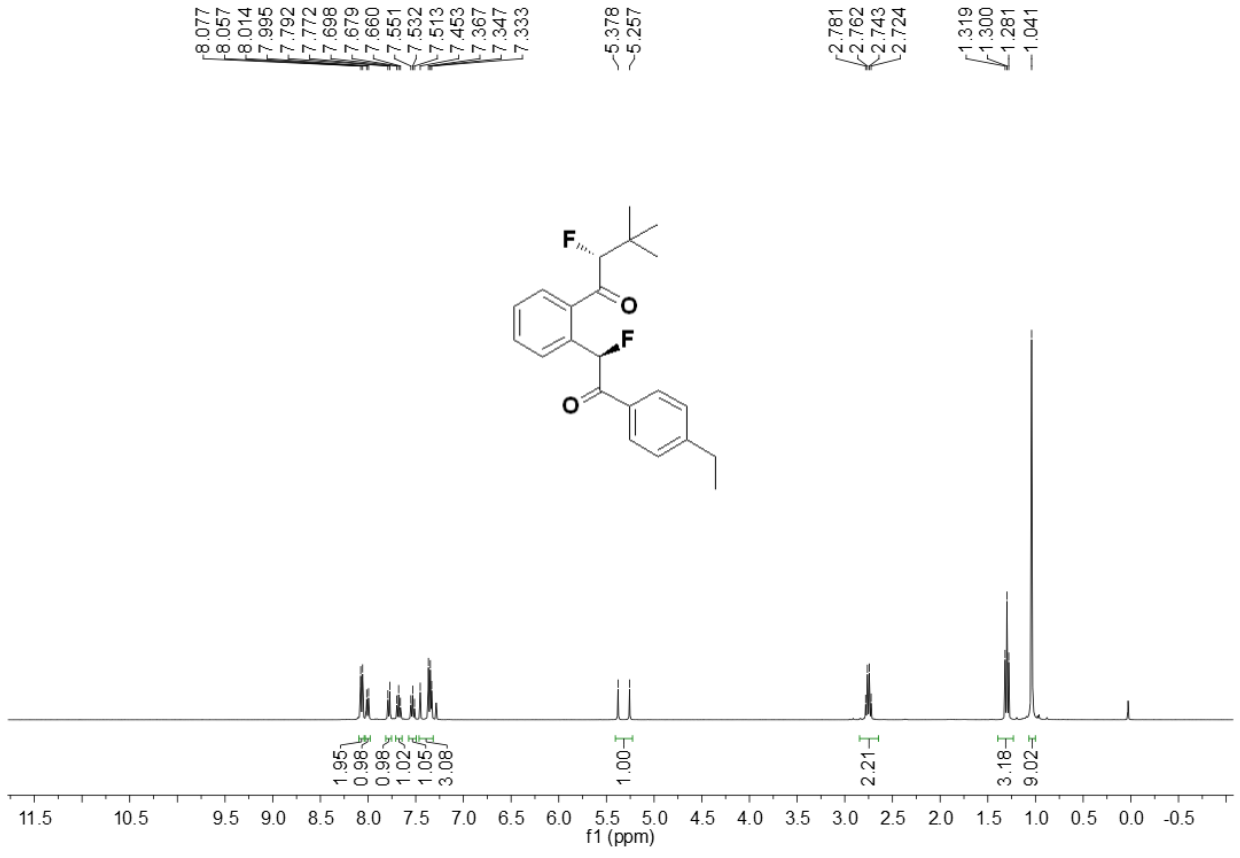
^{1}H NMR Spectrum of Compound 2z



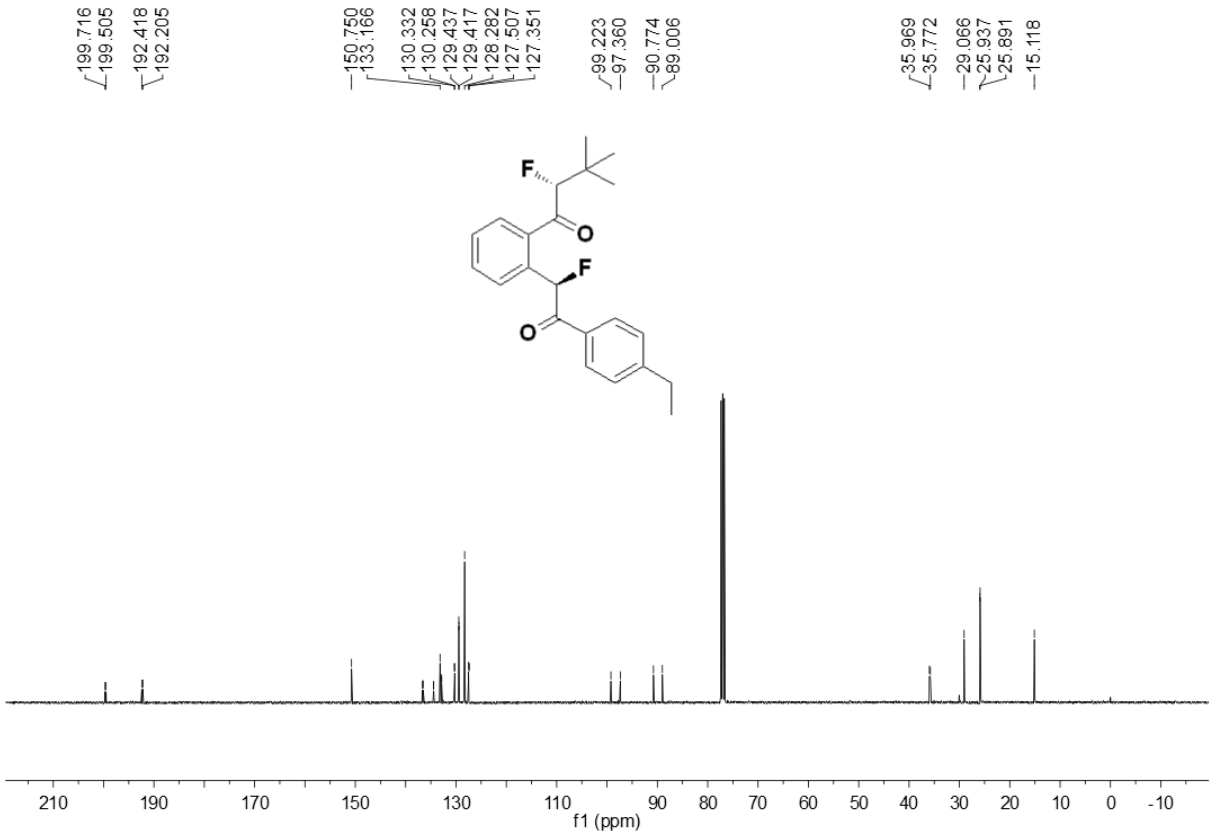
^{13}C NMR Spectrum of Compound 2z



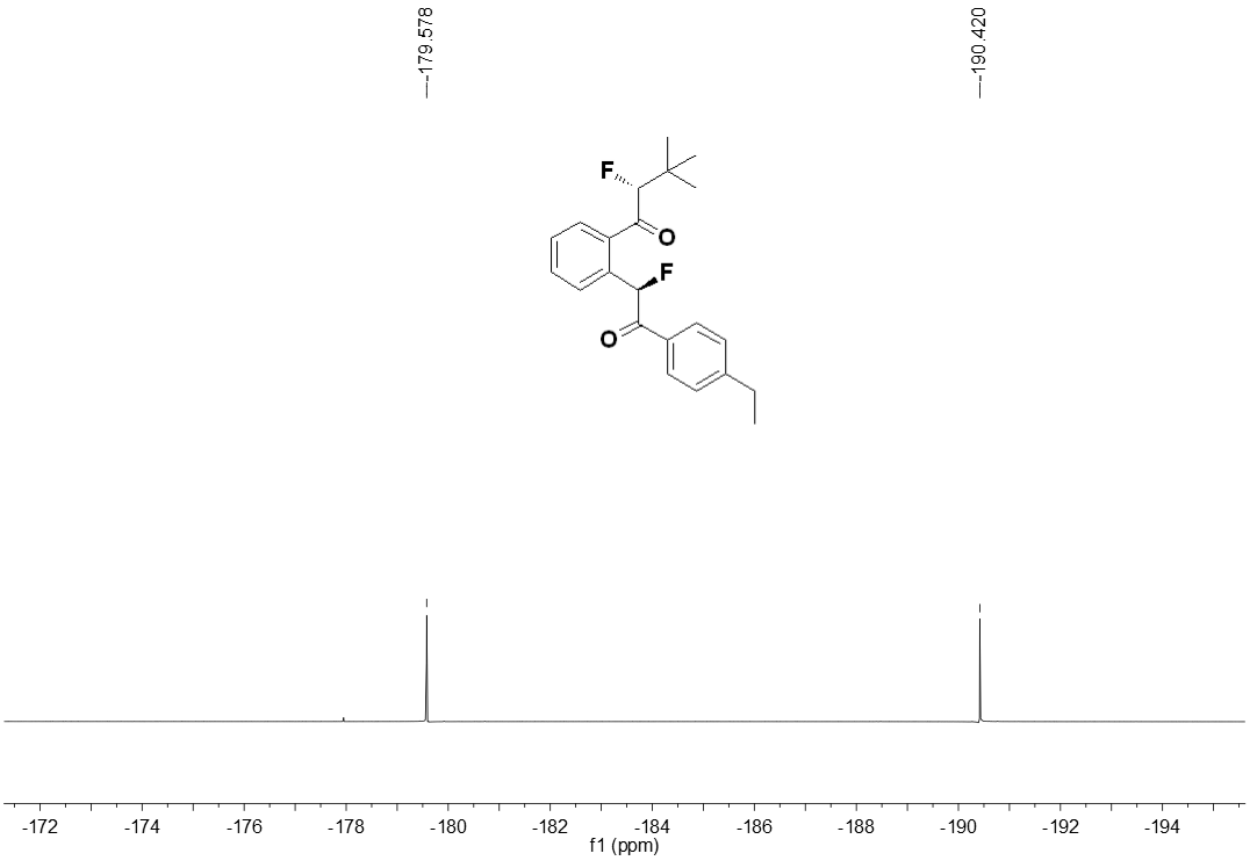
^{19}F NMR Spectrum of Compound 2z



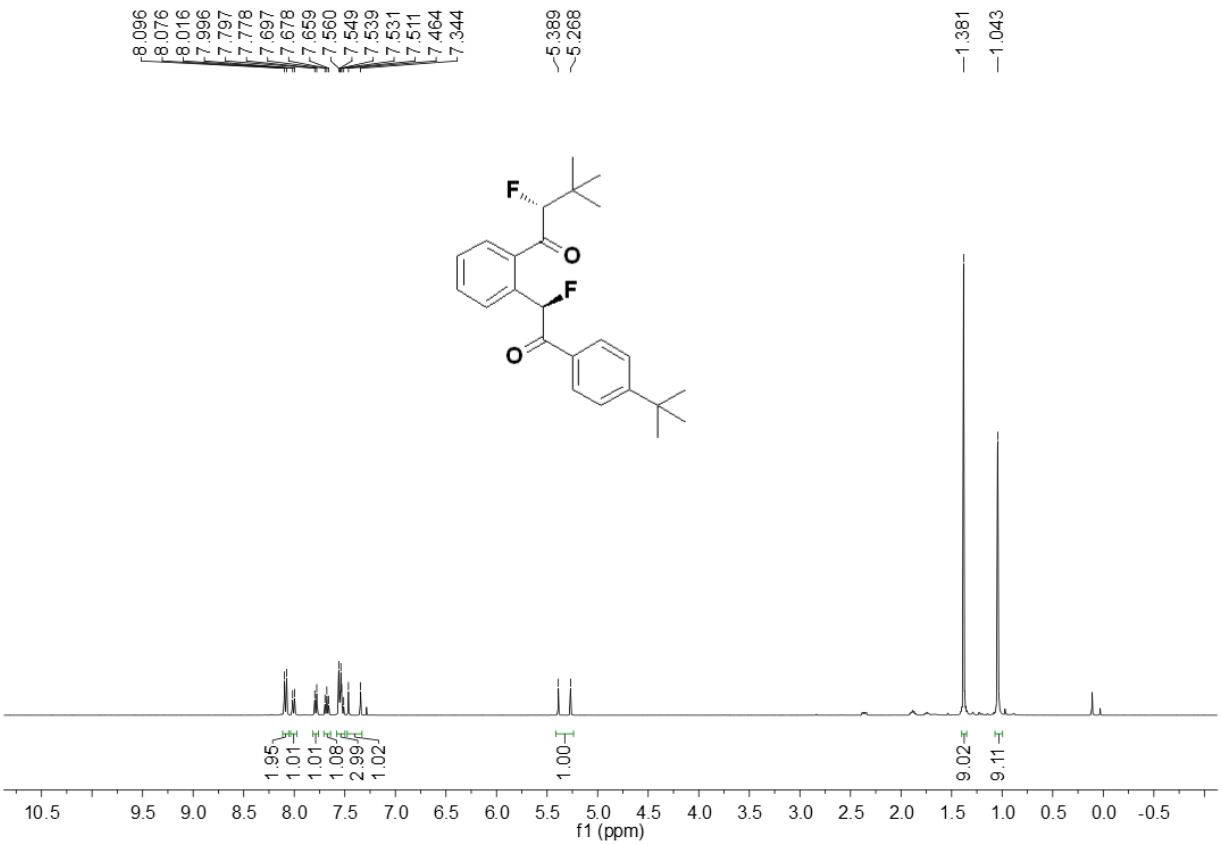
^{1}H NMR Spectrum of Compound 2aa



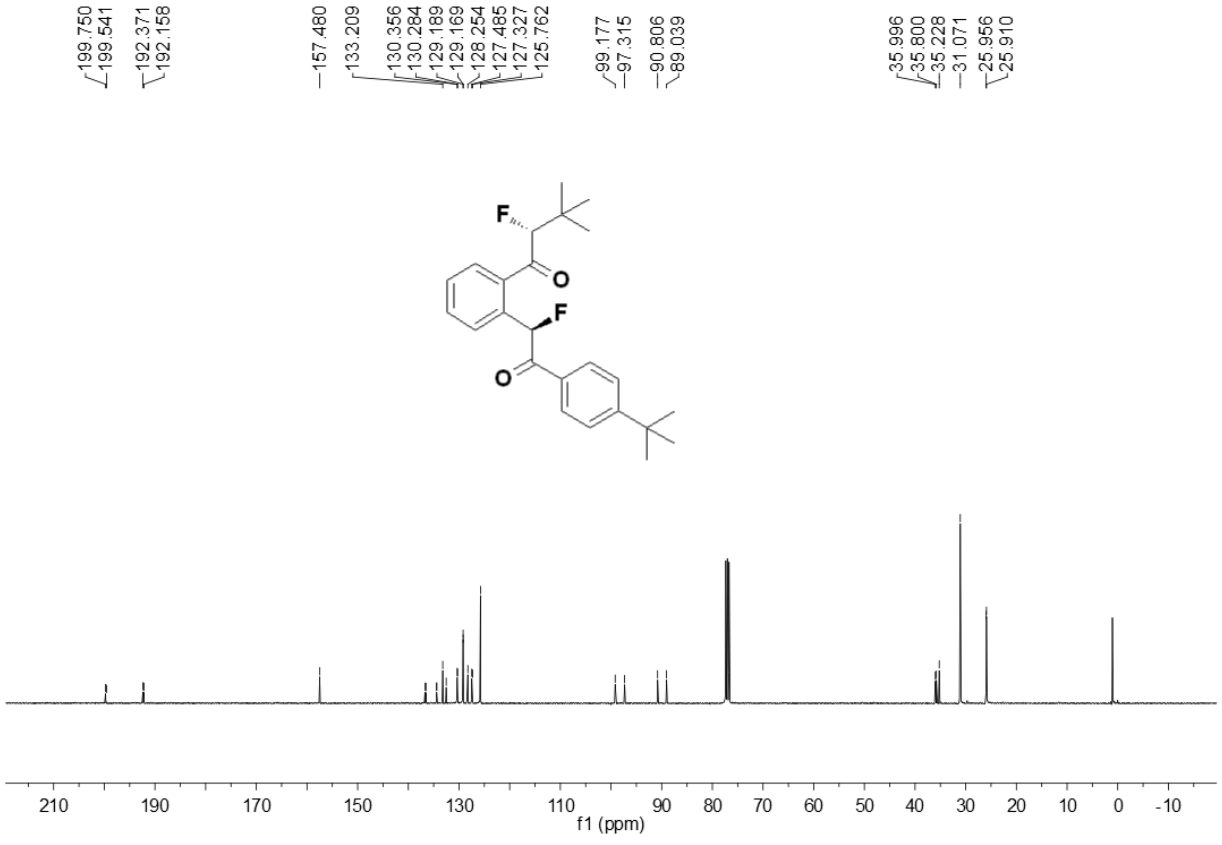
^{13}C NMR Spectrum of Compound 2aa



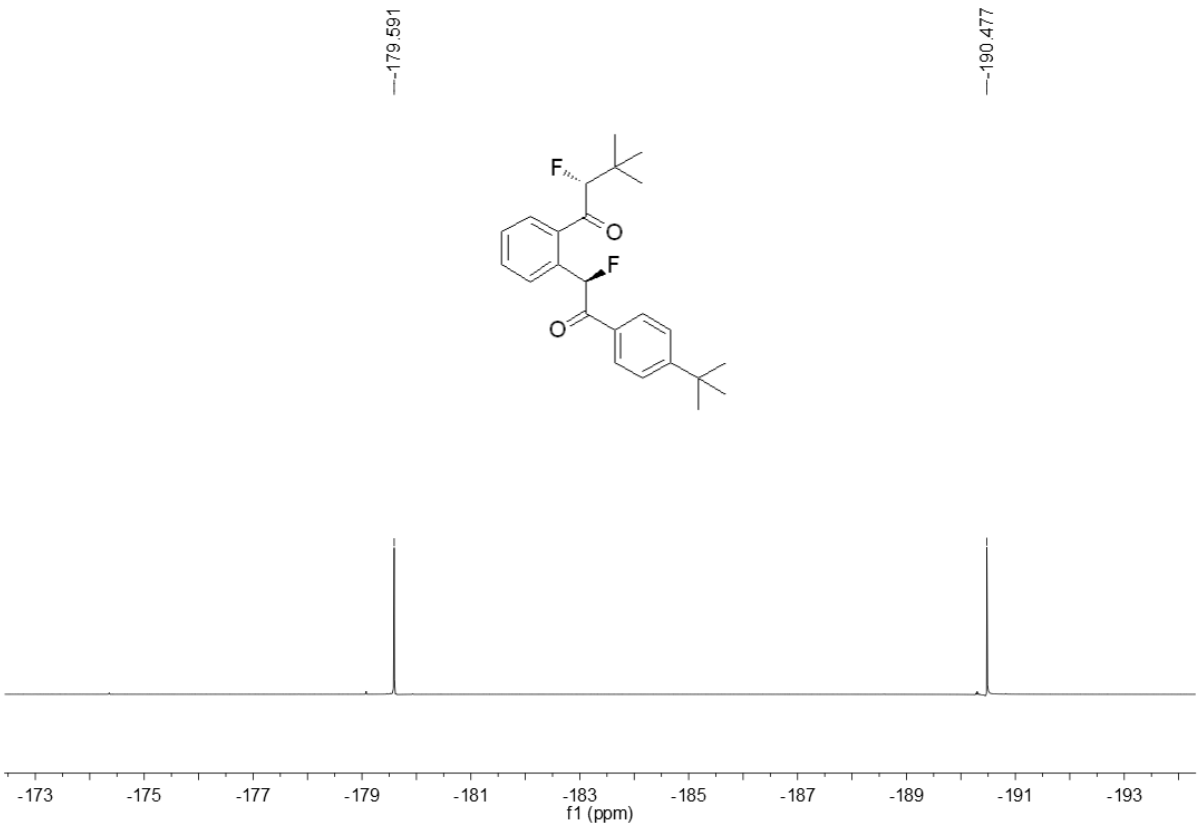
^{19}F NMR Spectrum of Compound 2aa



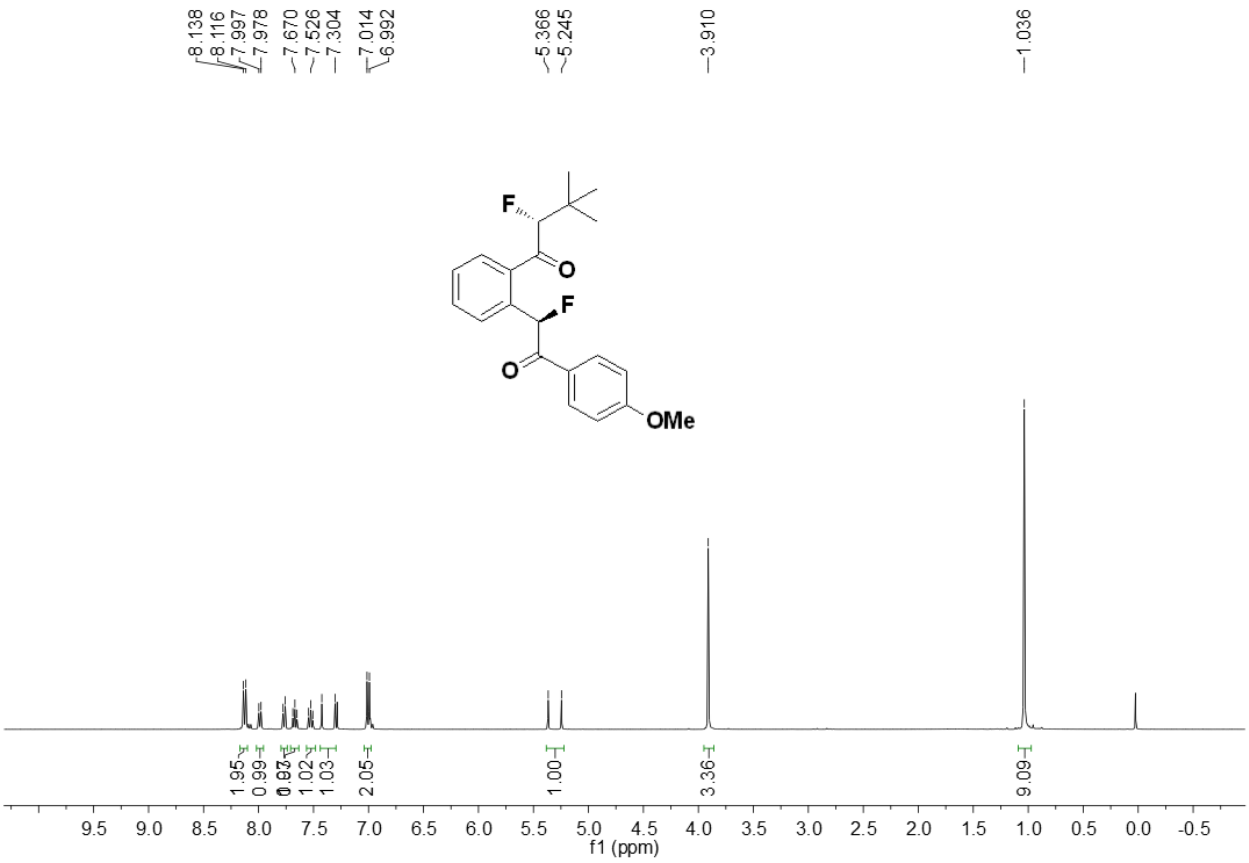
^{1}H NMR Spectrum of Compound 2bb



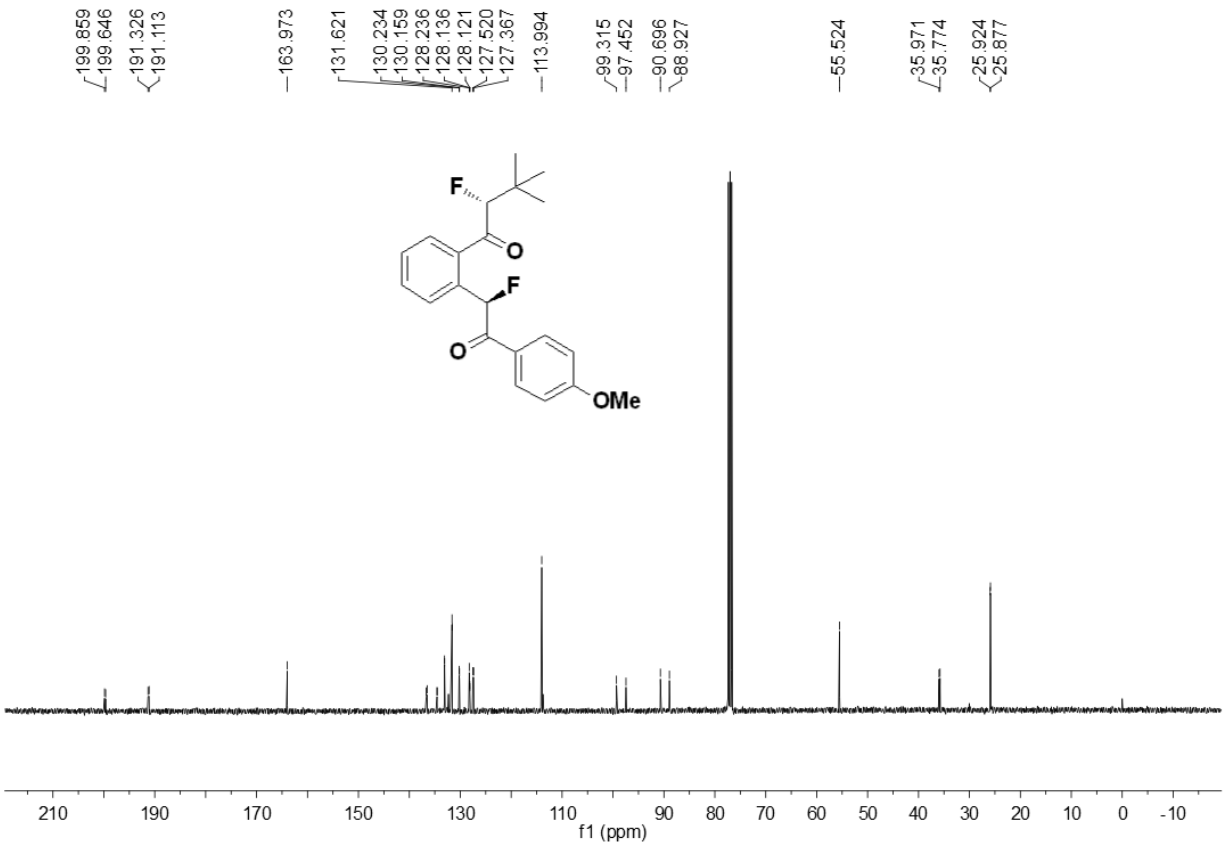
^{13}C NMR Spectrum of Compound 2bb



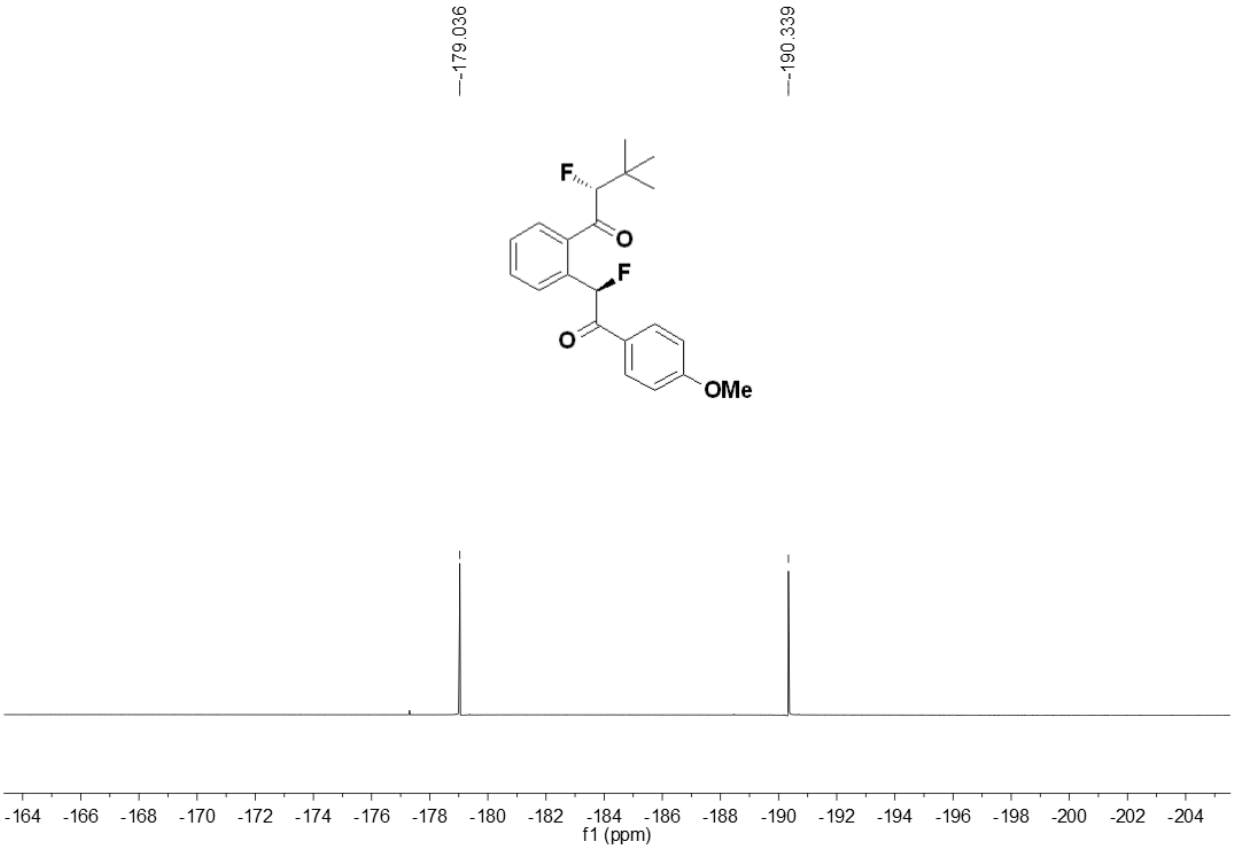
^{19}F NMR Spectrum of Compound 2bb



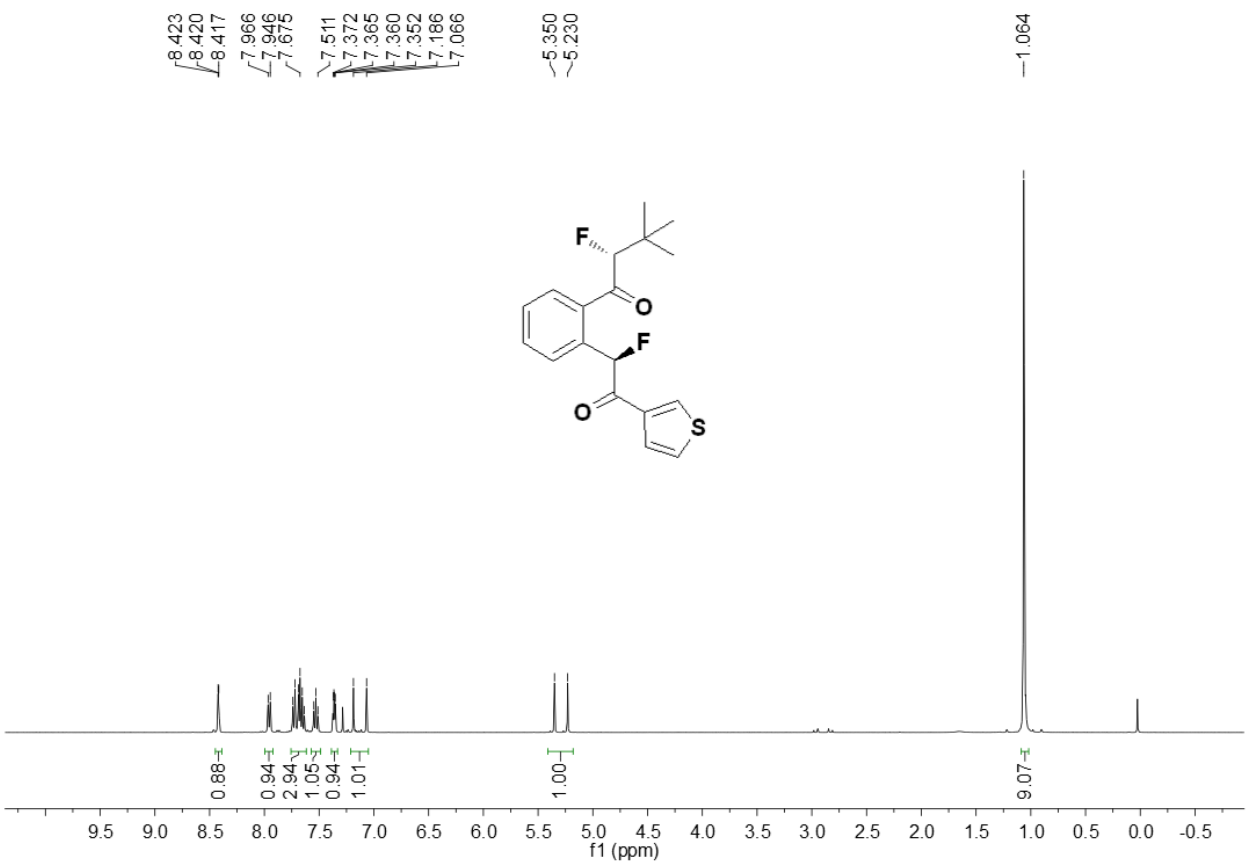
^{1}H NMR Spectrum of Compound 2cc



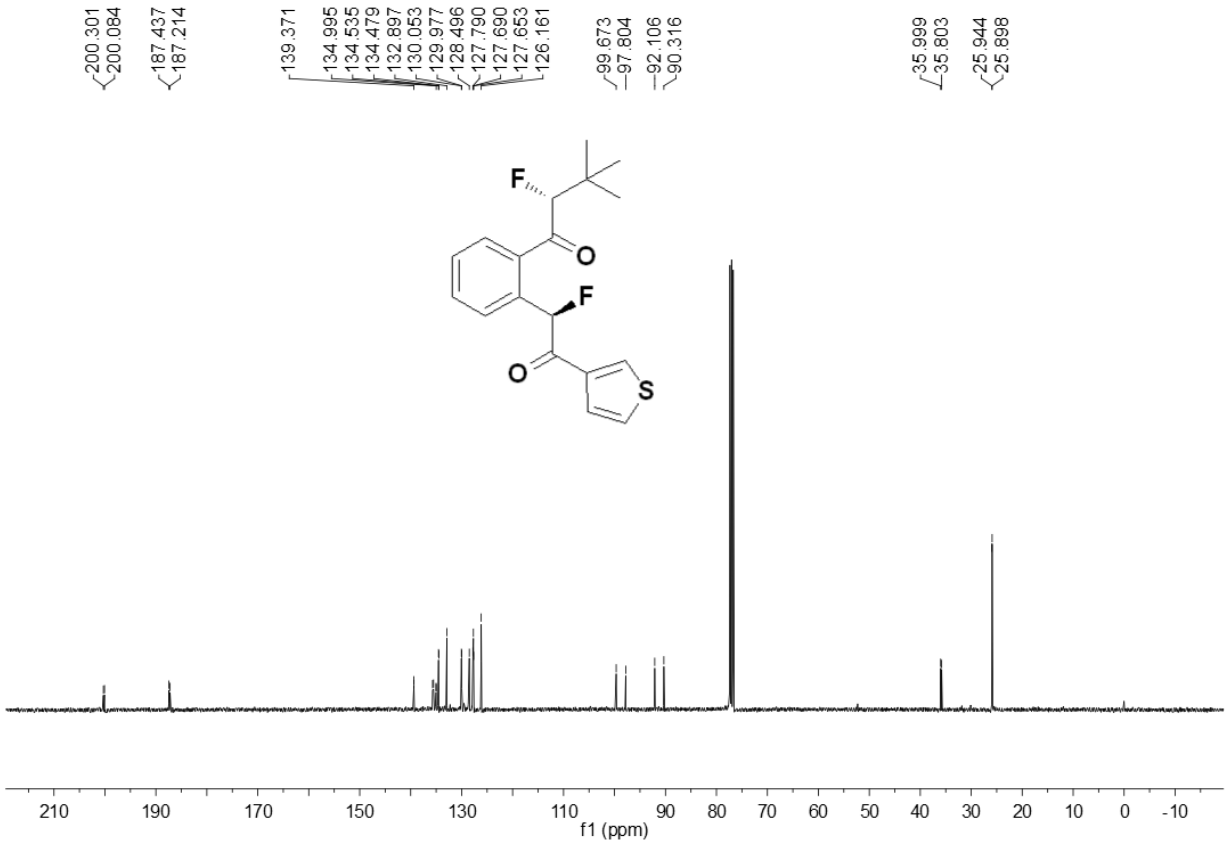
^{13}C NMR Spectrum of Compound 2cc



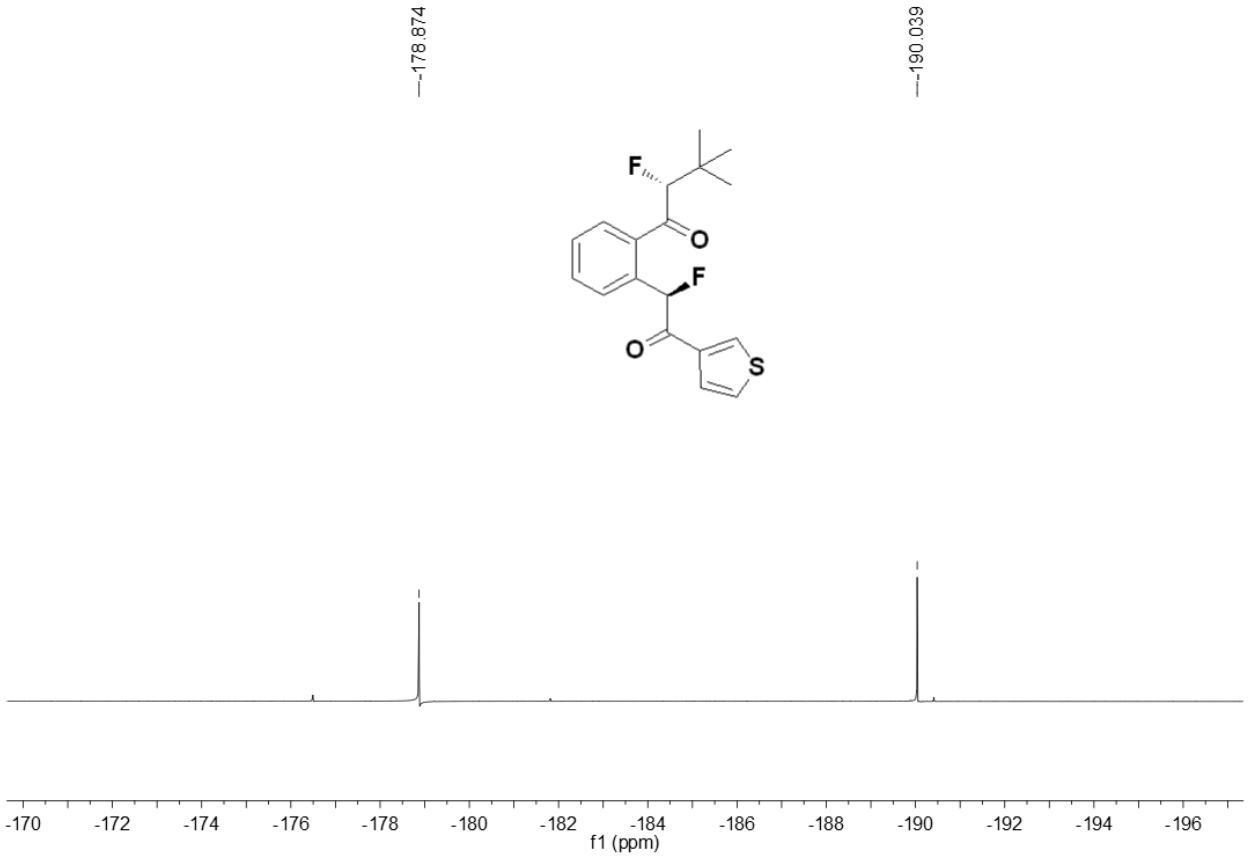
^{19}F NMR Spectrum of Compound 2cc



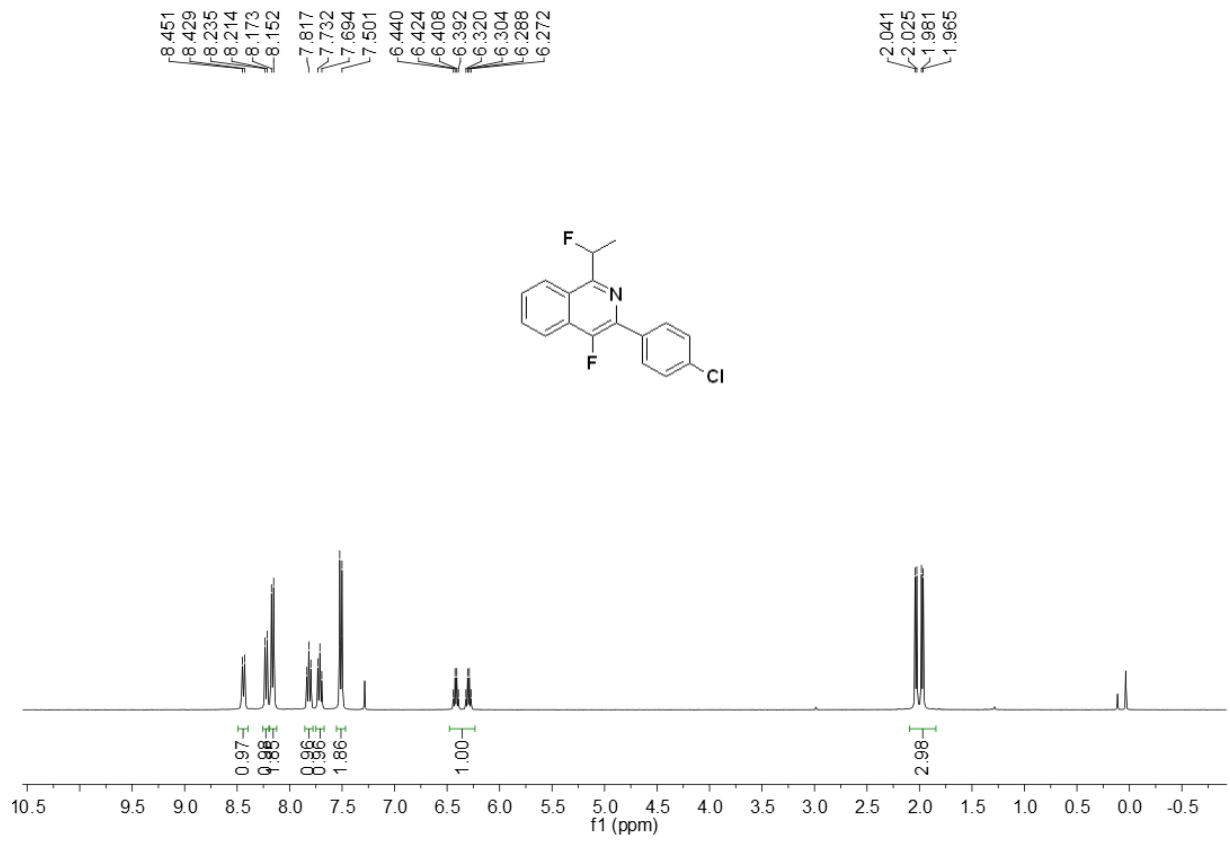
^{1}H NMR Spectrum of Compound 2dd



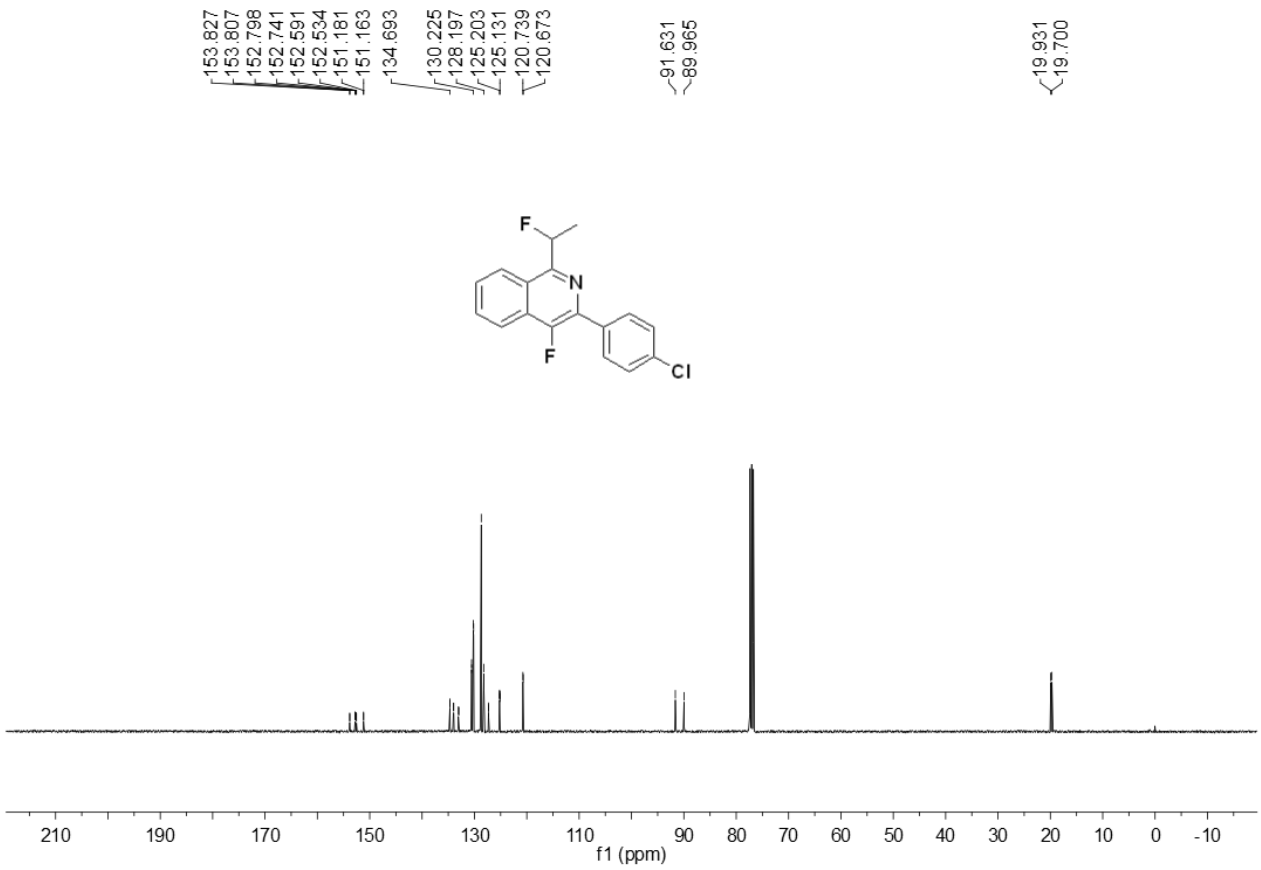
^{13}C NMR Spectrum of Compound 2dd



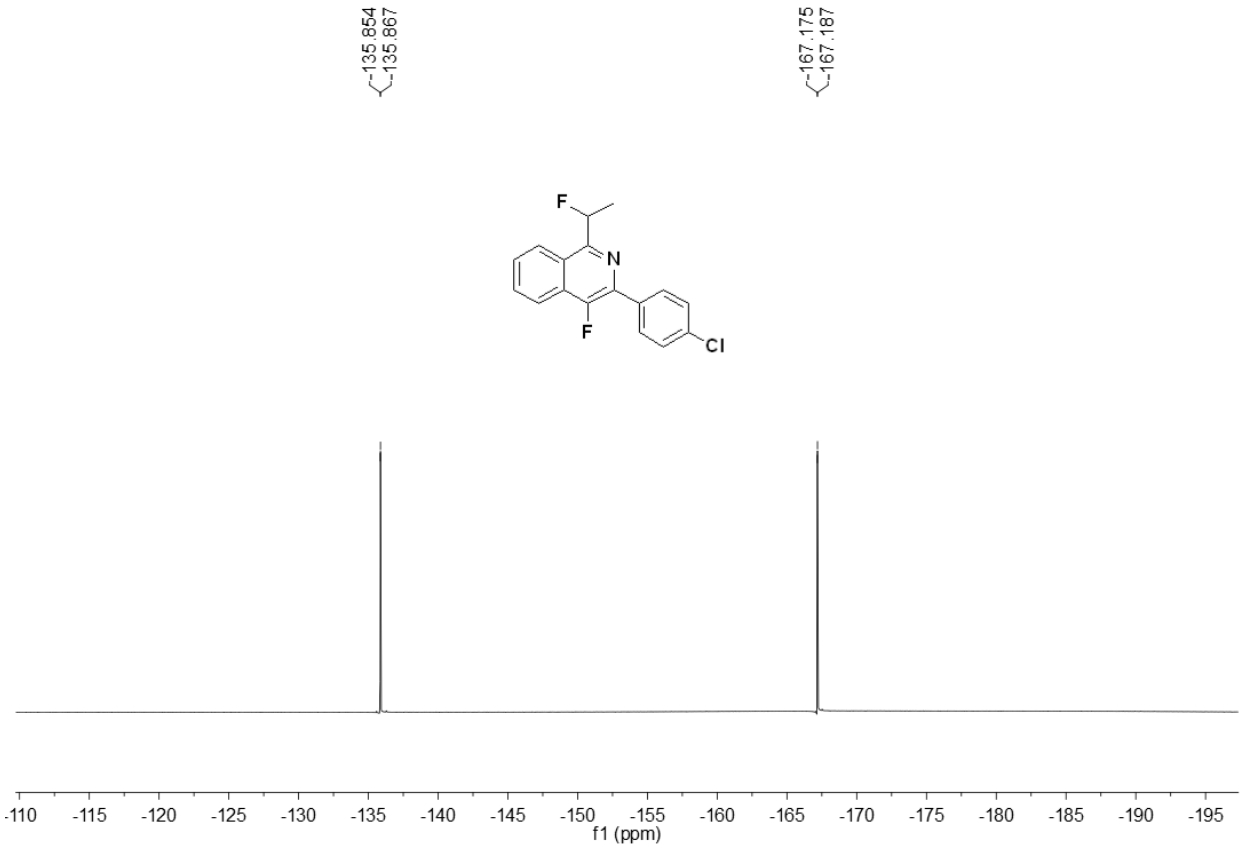
^{19}F NMR Spectrum of Compound 2dd



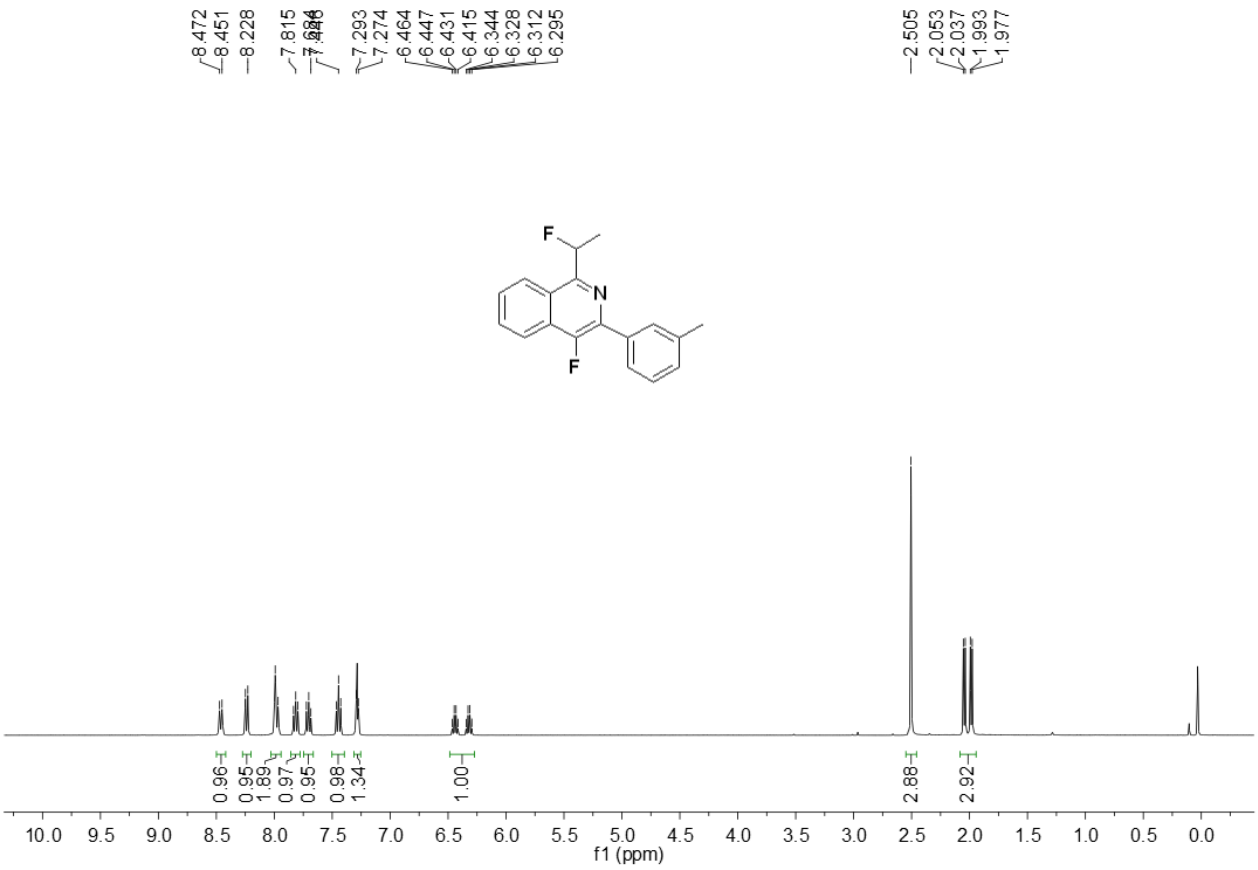
^{1}H NMR Spectrum of Compound 3a



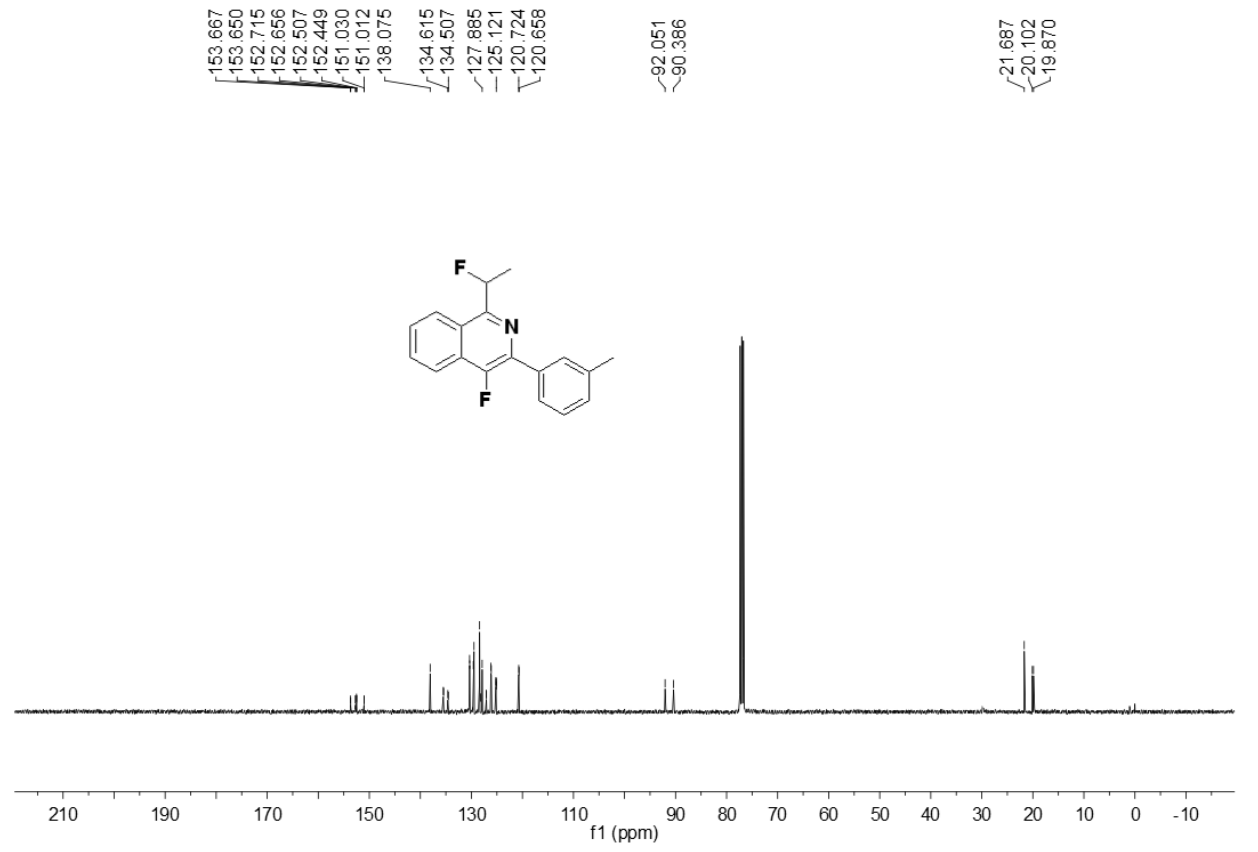
^{13}C NMR Spectrum of Compound 3a



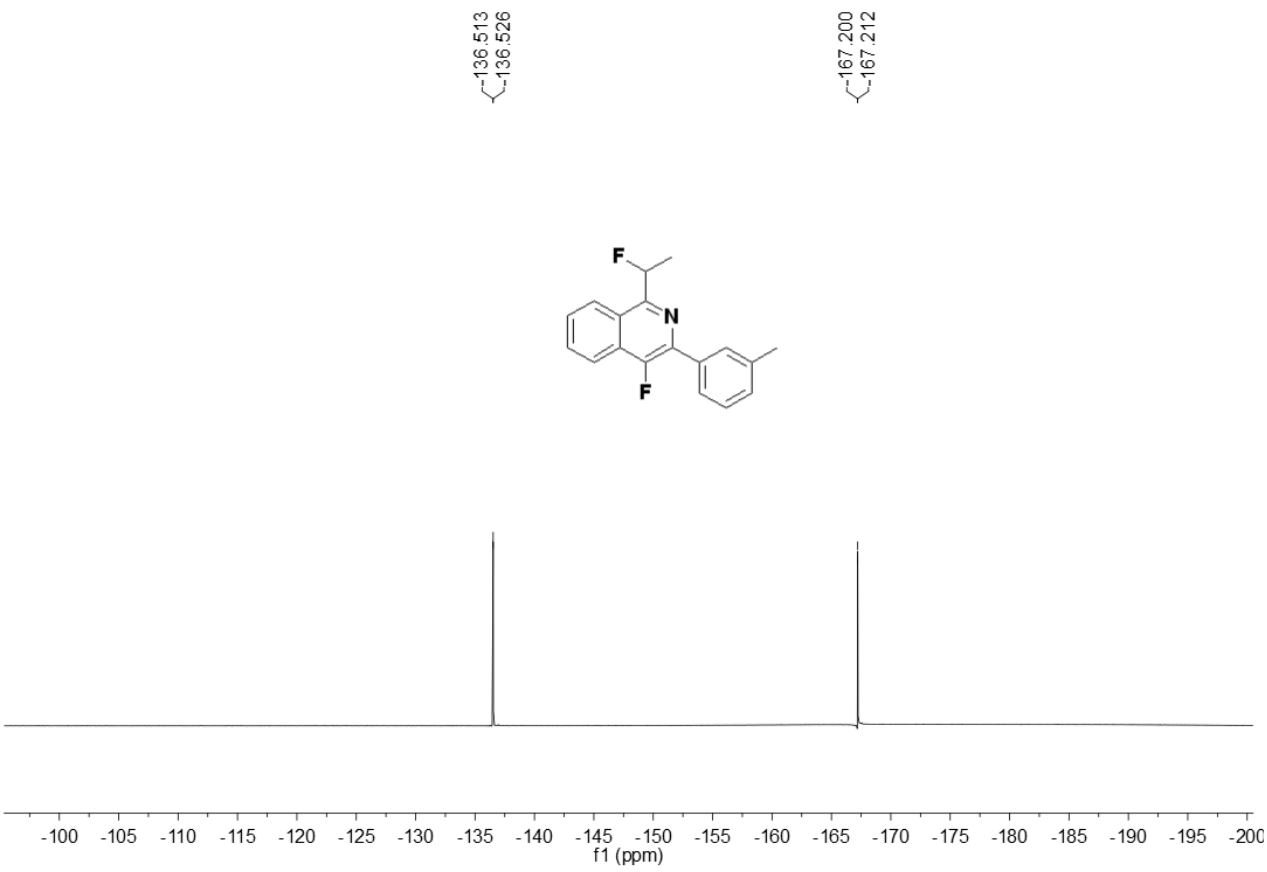
^{19}F NMR Spectrum of Compound 3a



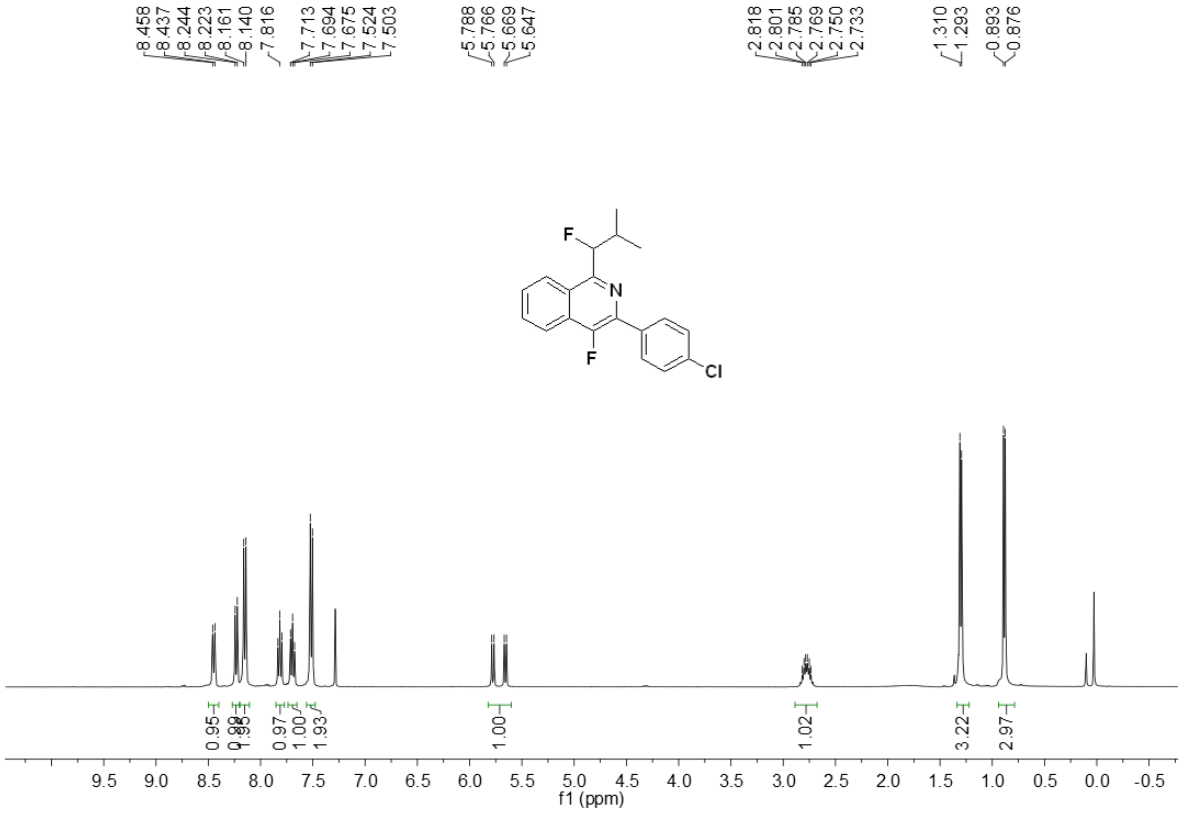
^{1}H NMR Spectrum of Compound 3b



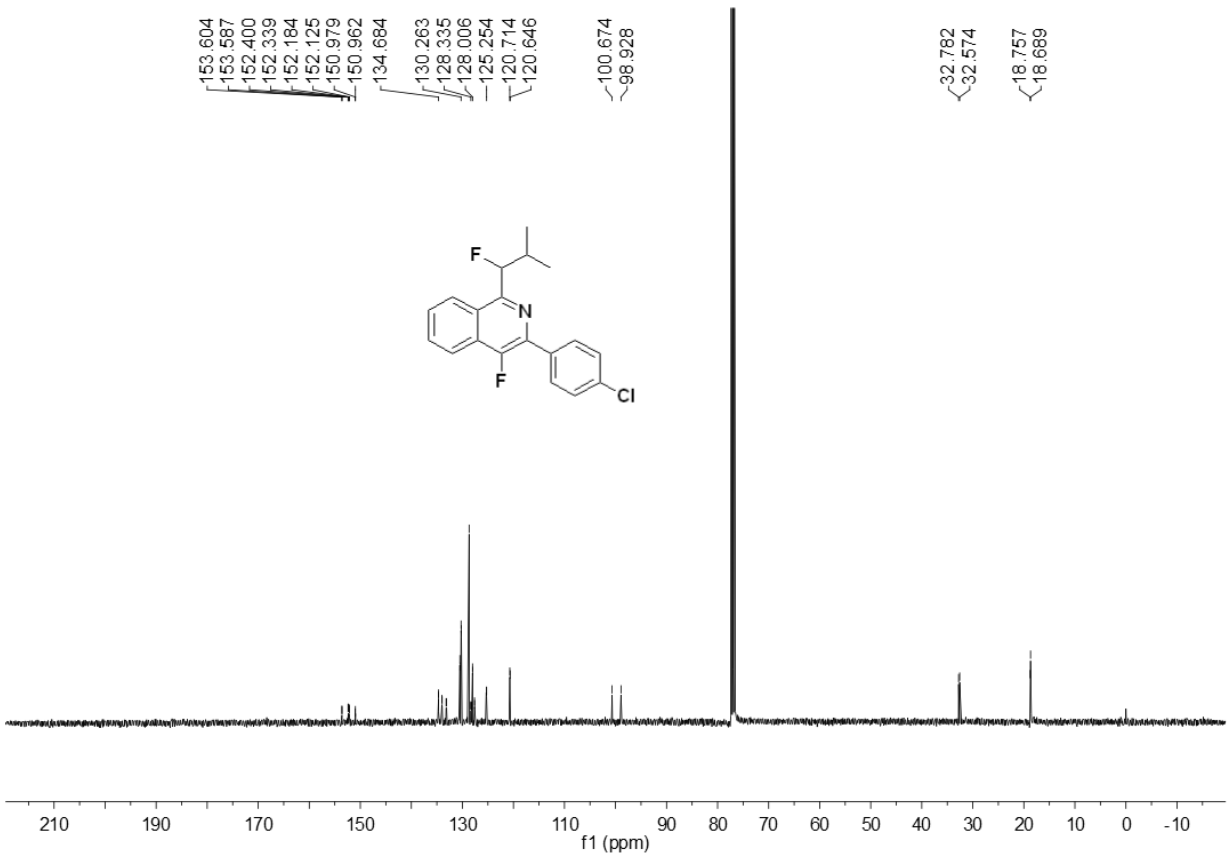
^{13}C NMR Spectrum of Compound 3b



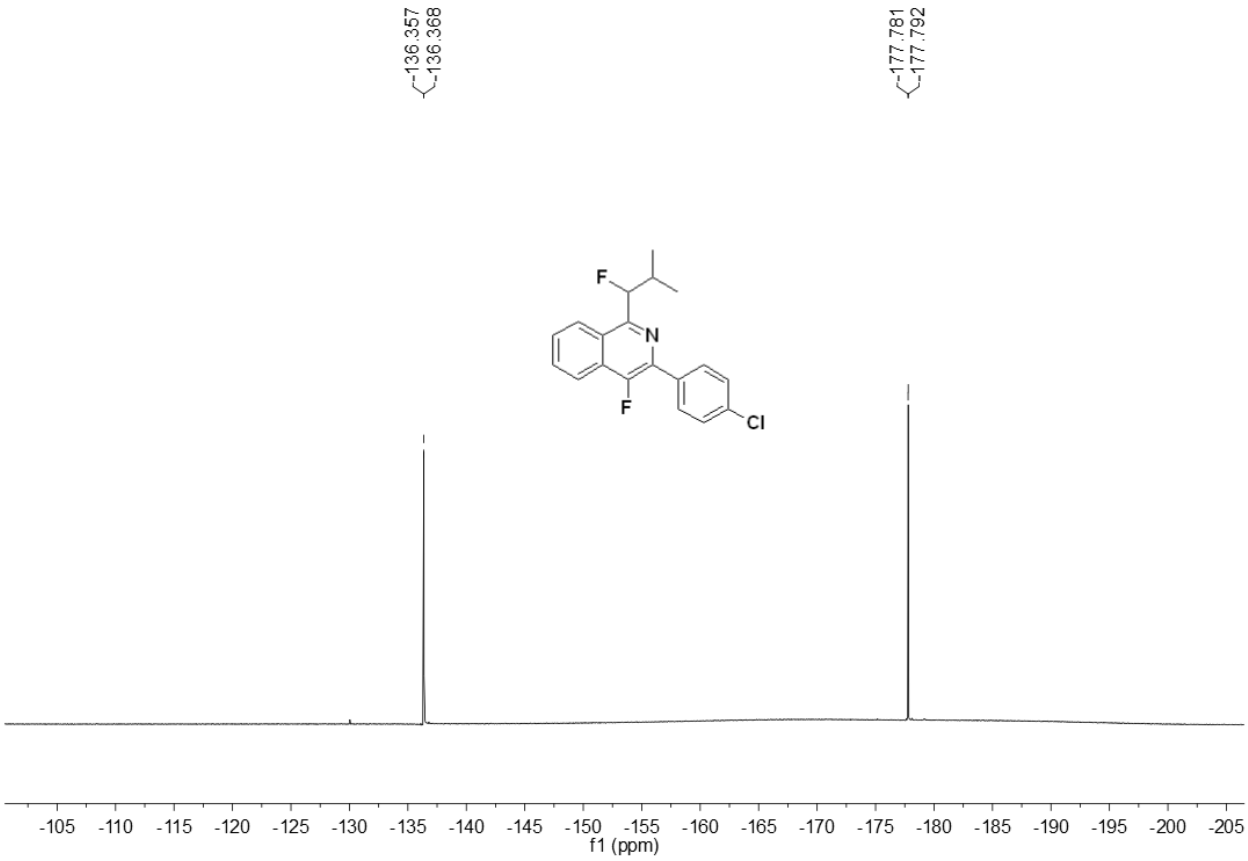
^{19}F NMR Spectrum of Compound 3b



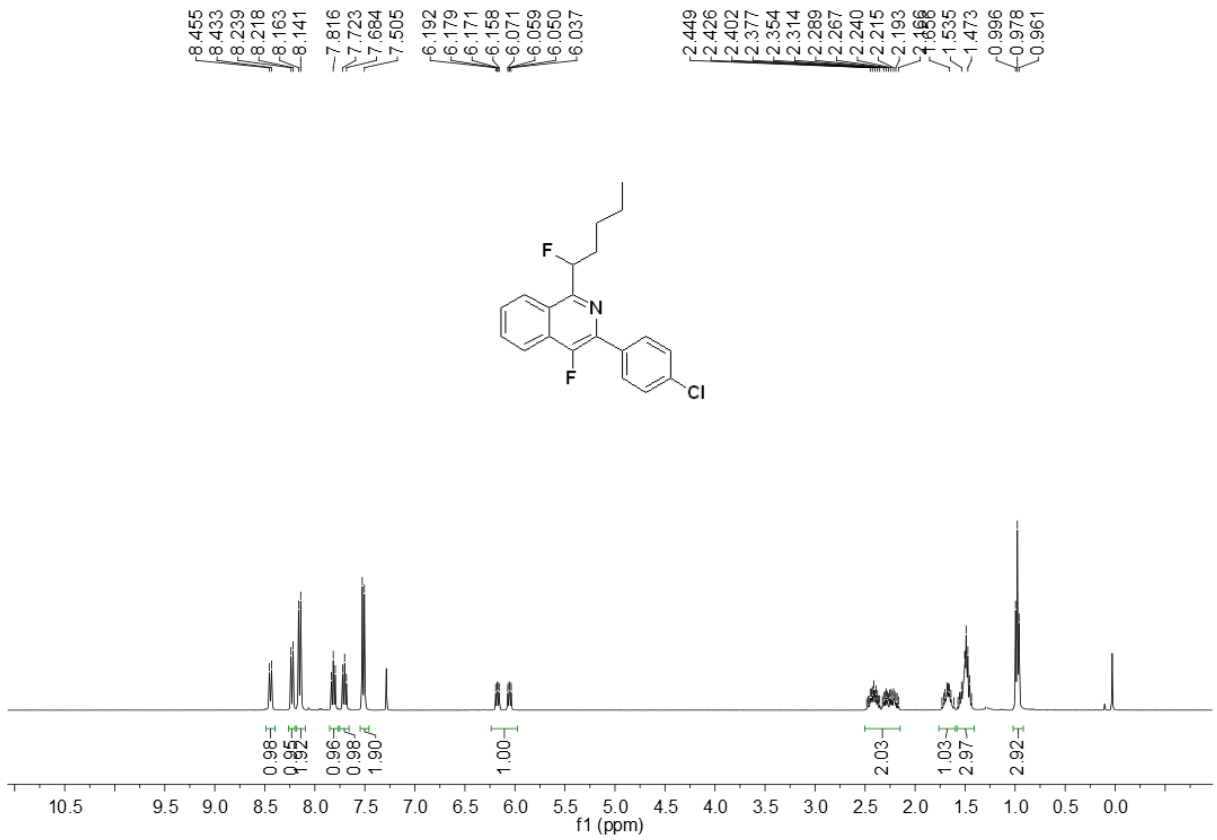
^{1}H NMR Spectrum of Compound 3c



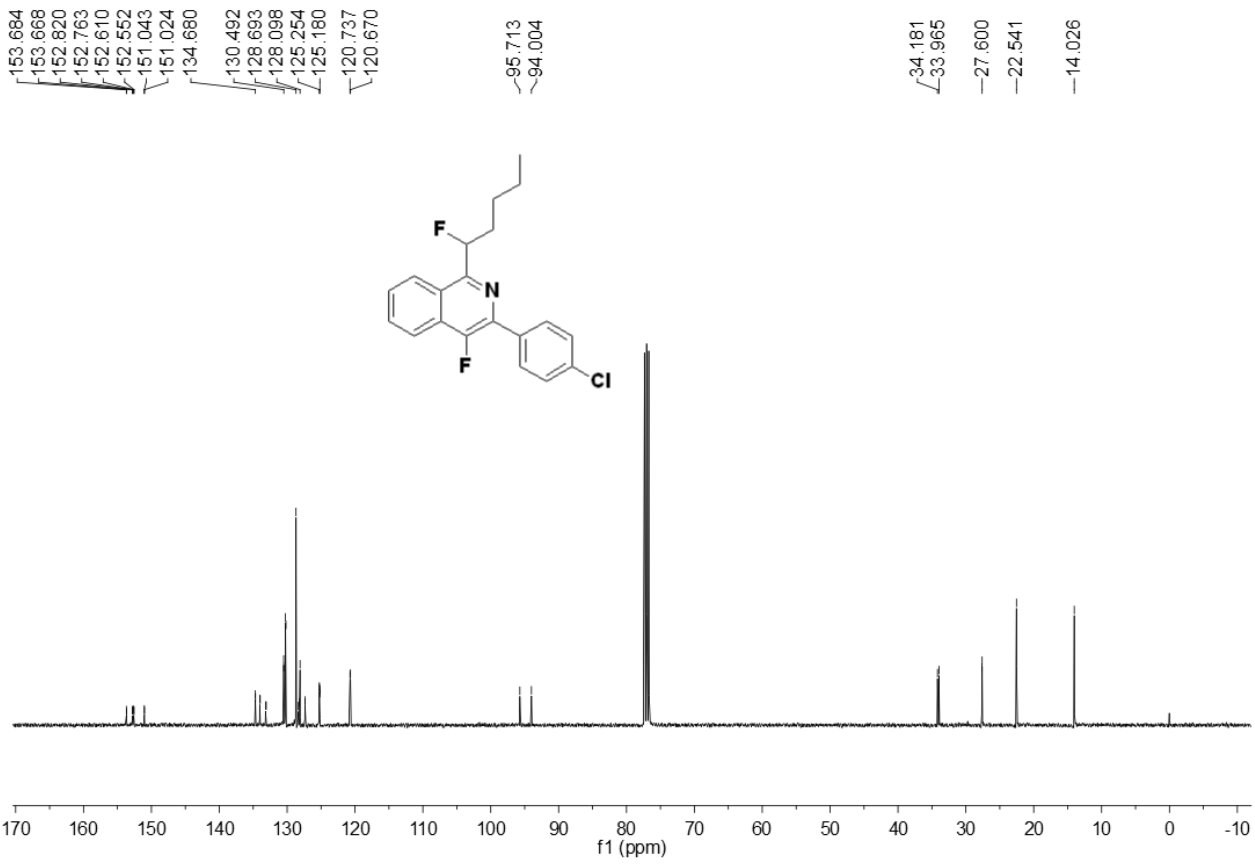
^{13}C NMR Spectrum of Compound 3c



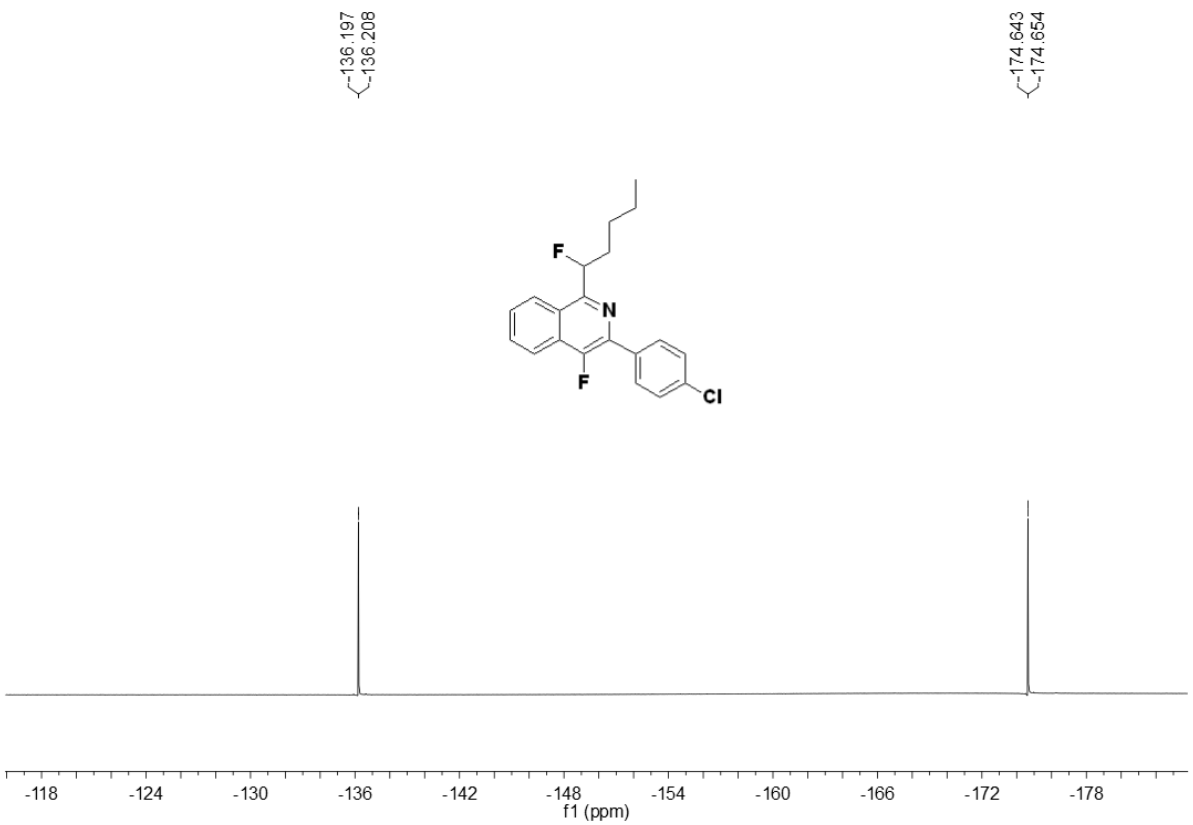
^{19}F NMR Spectrum of Compound 3c



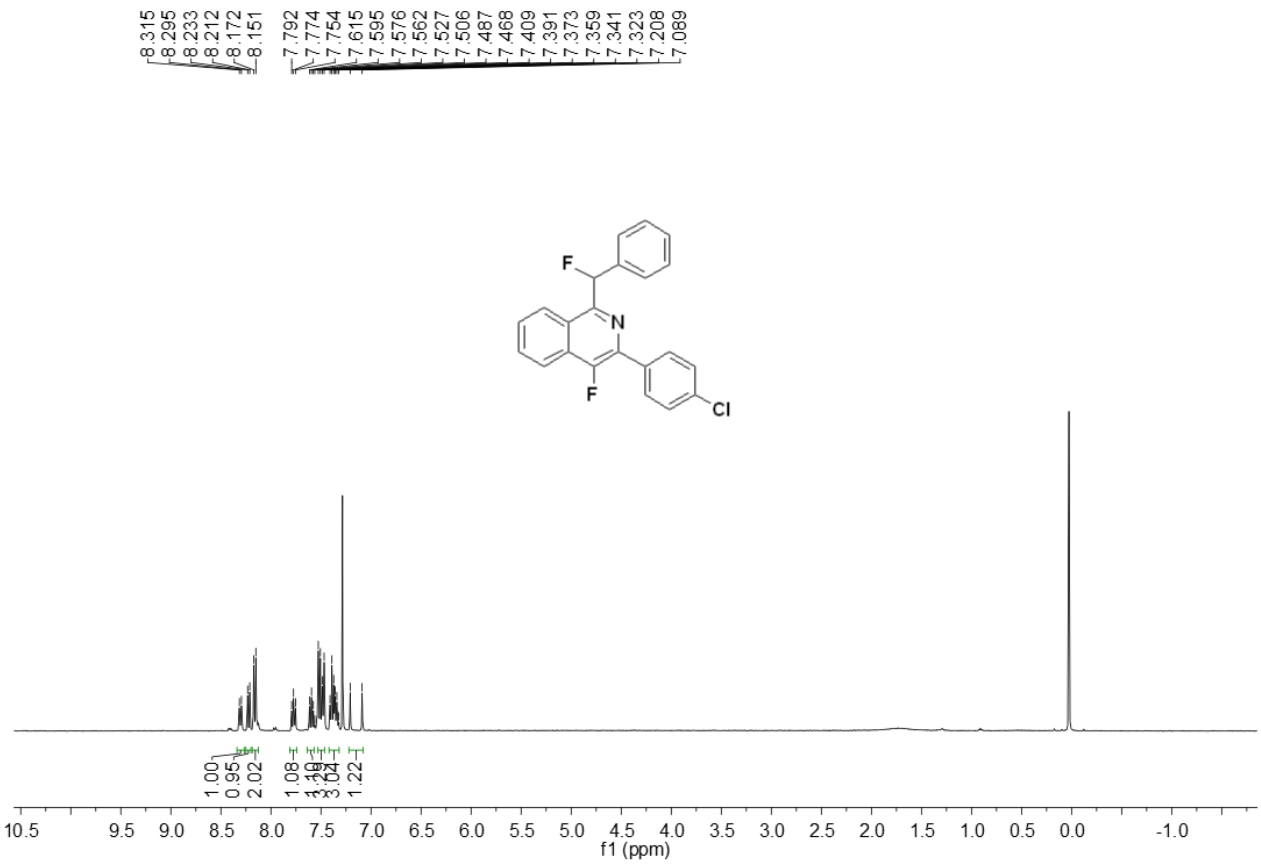
^{1}H NMR Spectrum of Compound 3d



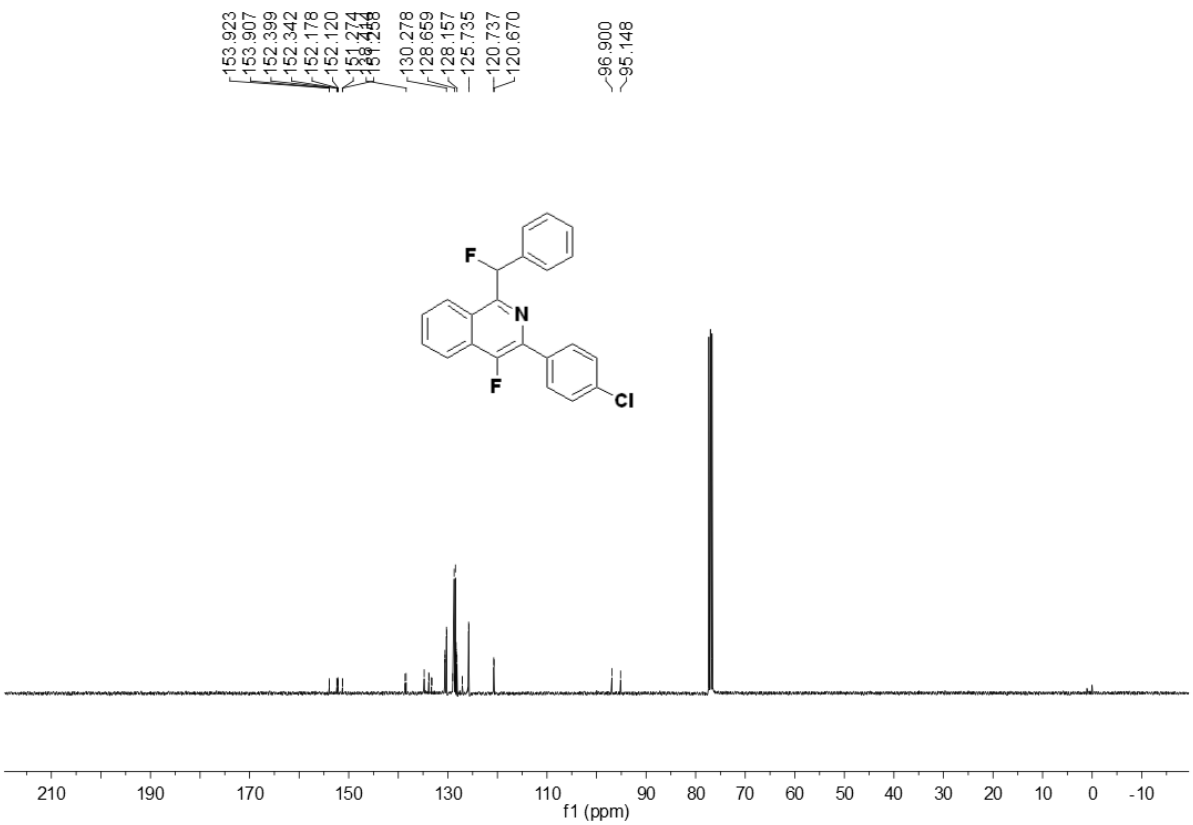
^{13}C NMR Spectrum of Compound 3d



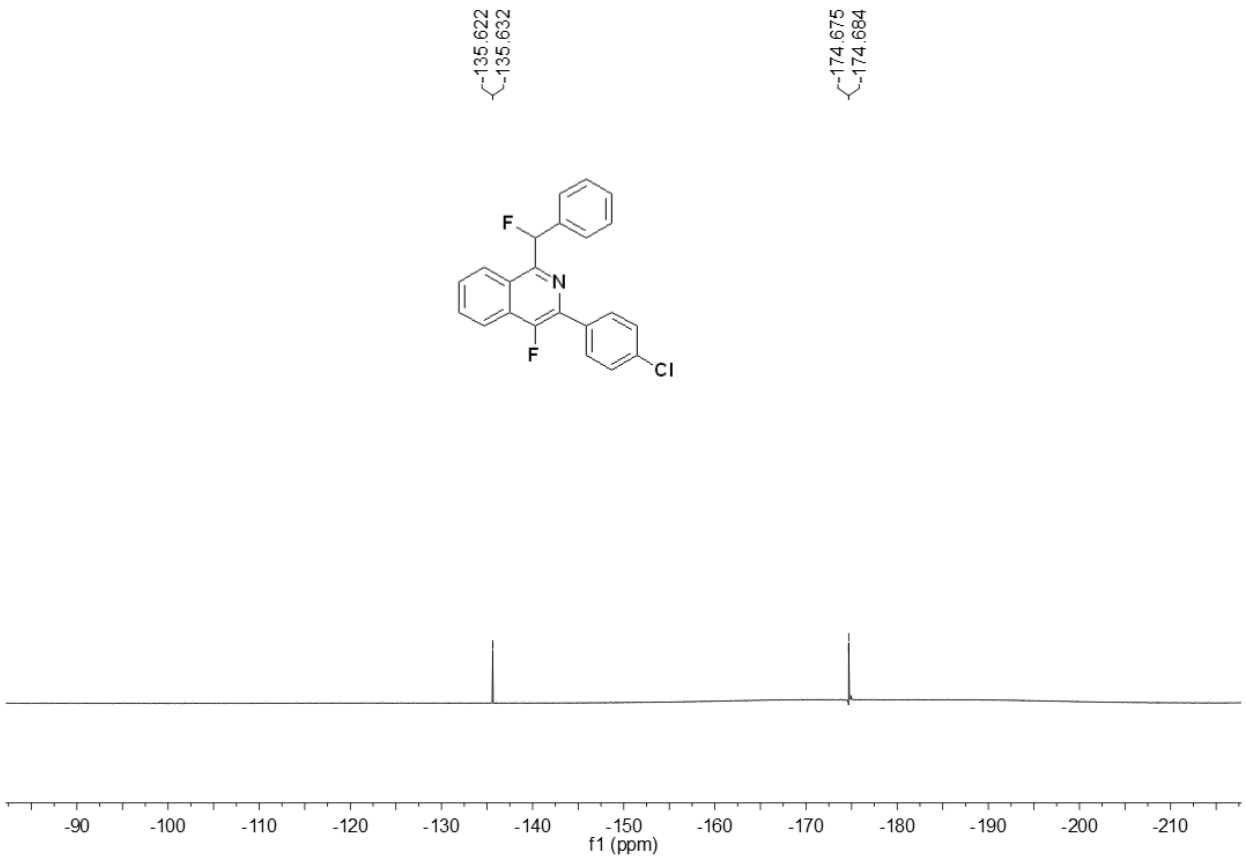
^{19}F NMR Spectrum of Compound 3d



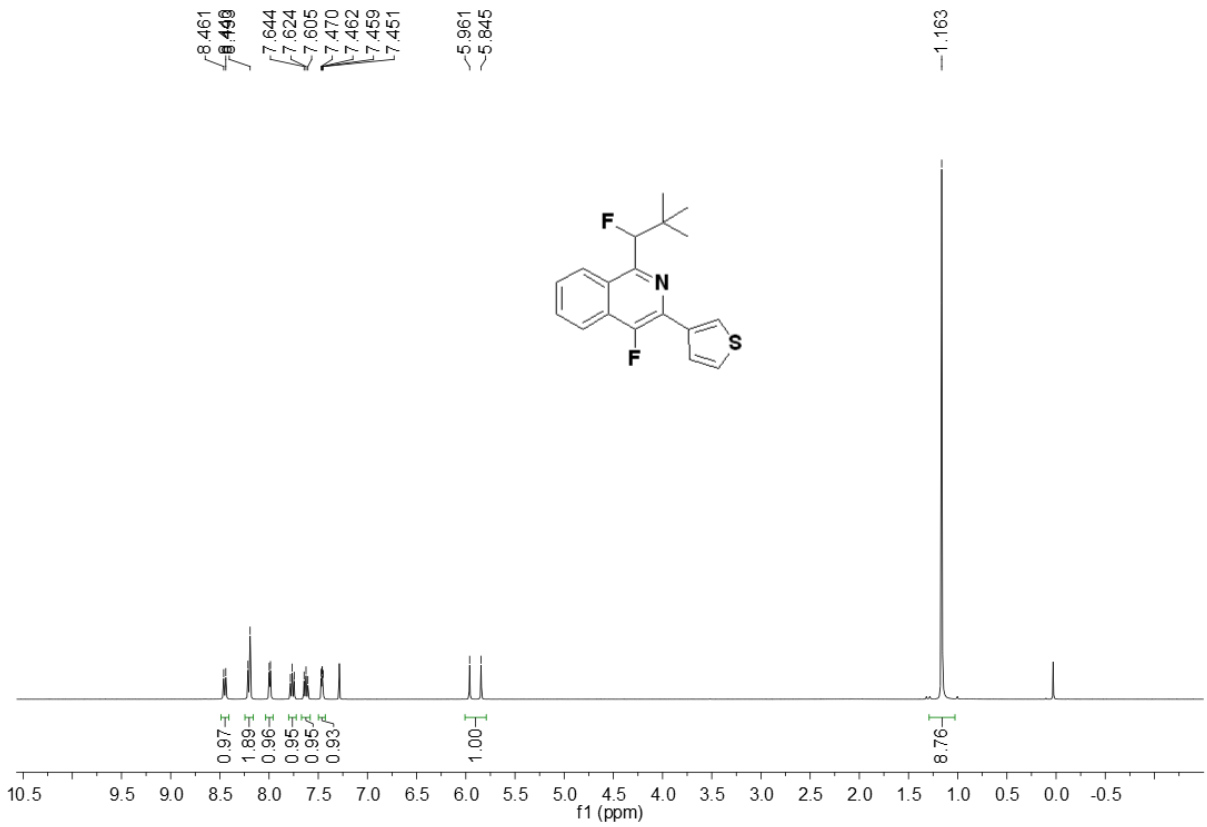
^{1}H NMR Spectrum of Compound 3e



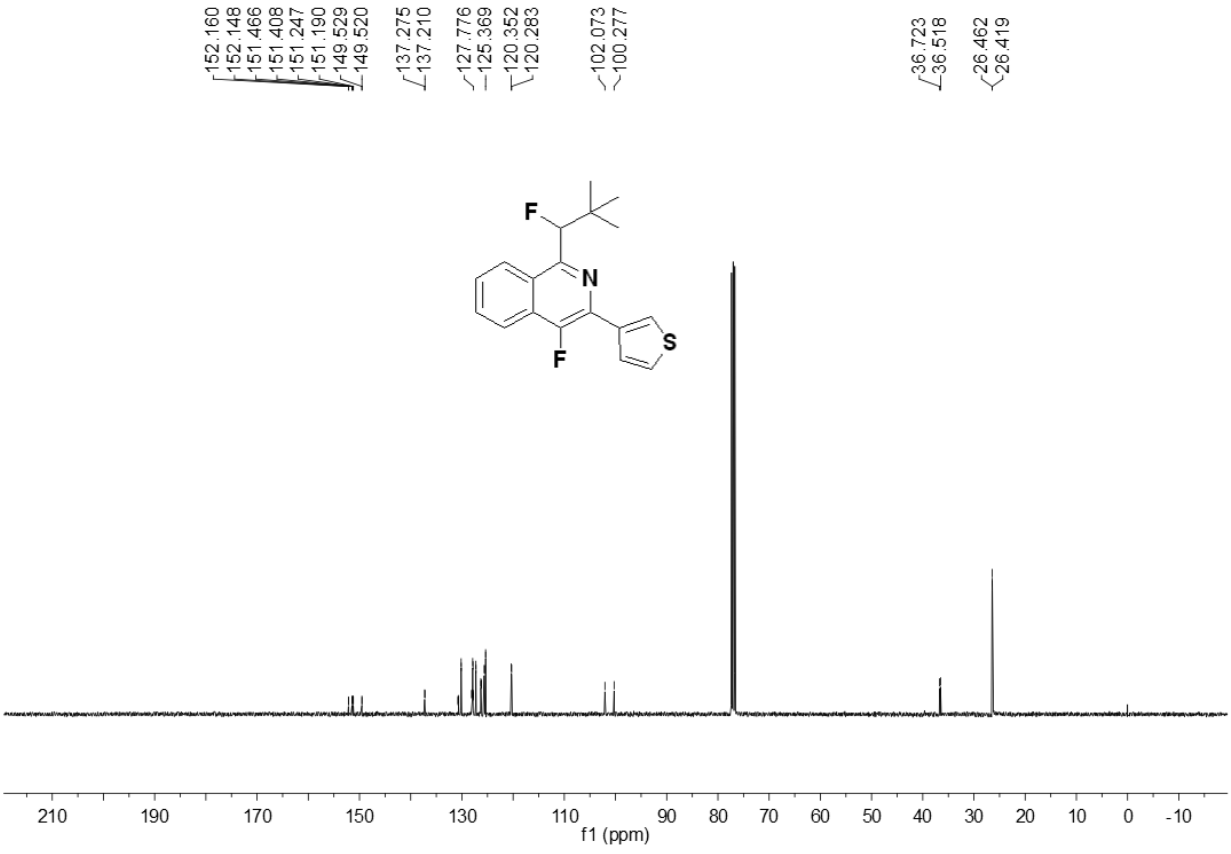
^{13}C NMR Spectrum of Compound 3e



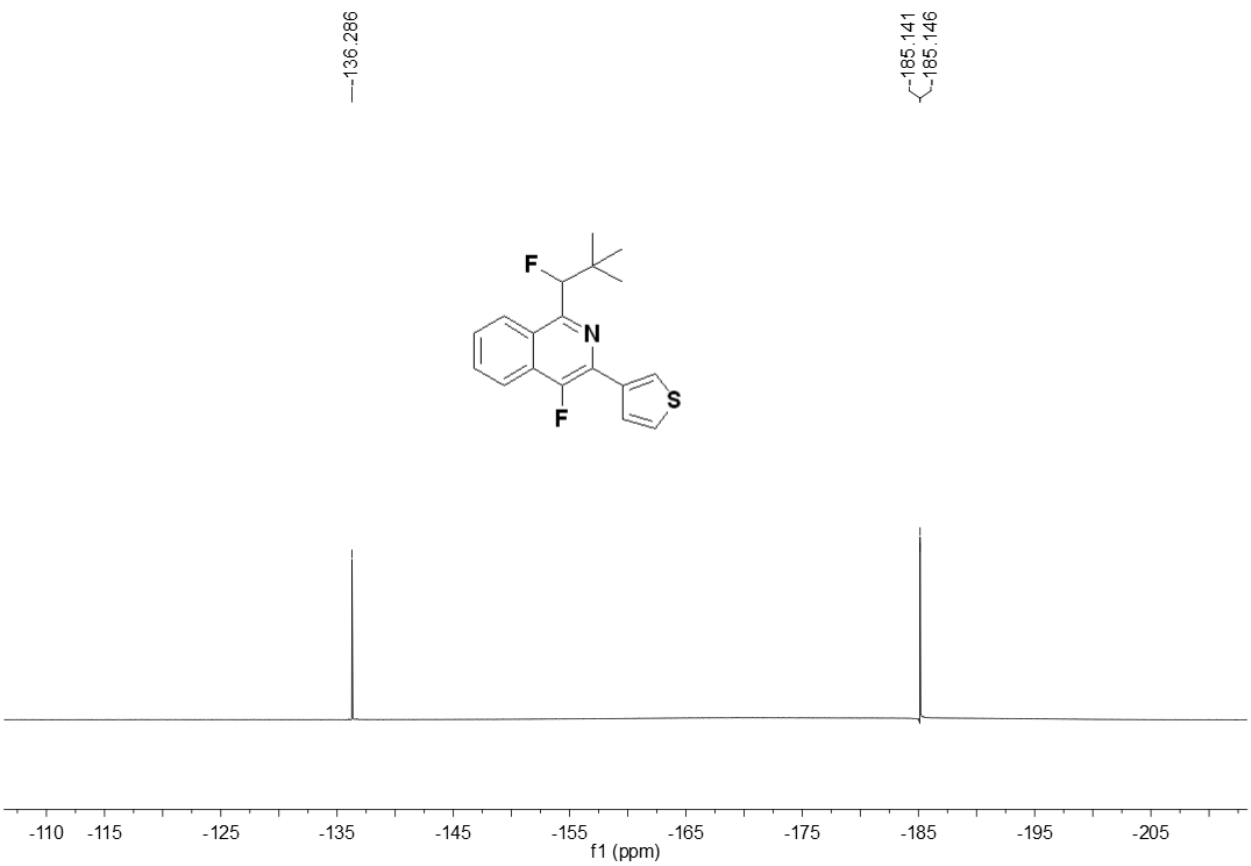
^{19}F NMR Spectrum of Compound 3e



^{1}H NMR Spectrum of Compound 3f



^{13}C NMR Spectrum of Compound 3f



^{19}F NMR Spectrum of Compound 3f