Supporting Information

Palladium-Catalyzed Intramolecular Heck Dearomative *gem*-Difluorovinylation of Indoles

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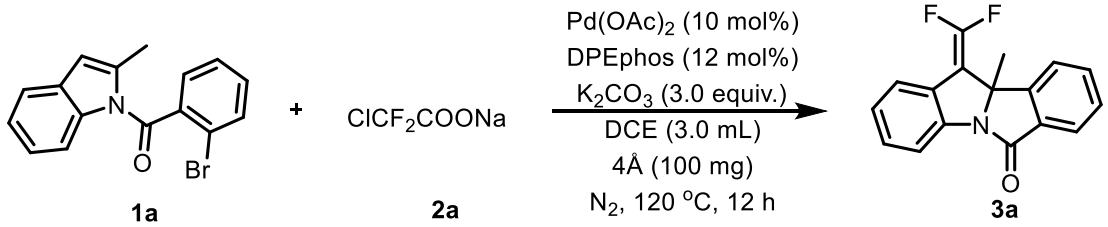
1.General information

General. ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on Varian 400 MHz or Bruker 400 MHz spectrometers. ^{1}H and ^{13}C NMR chemical shifts were determined relative to internal standard TMS at δ 0.0, $CDCl_3$ (δ(^{1}H), 7.26 ppm; δ(^{13}C), 77.16 ppm), DMSO-*d*6 (δ(^{1}H), 2.50 ppm; δ(^{13}C), 39.51 ppm). Chemical shifts (δ) are reported in ppm, and coupling constants (*J*) are in Hertz (Hz). The following abbreviations are used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. The HRMS analysis was obtained on an Agilent6540 UHD Q-TOF mass spectrometer. The melting point was recorded on BÜCHI (M-560) and uncorrected. The X-ray single crystal diffraction data were collected on a Bruker D8 VENTURE. Analytical thin layer chromatography (TLC) was performed on 0.25 mm silica gel 60 F254 plates and viewed by UV light (254 nm). Column chromatographic purification was performed using 200-300 mesh silica gel.

Materials. All the chemical reagents were purchased from commercial sources and used as received unless otherwise indicated. Substrates **1** were prepared according to the known method.[1]

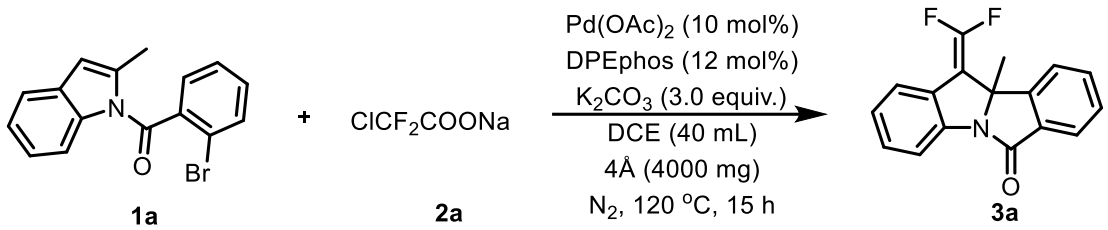
2. Experimental procedures

2.1 General procedure for synthesis of products (taking 3a as an example)



To a Schlenk tube was added $Pd(OAc)_2$ (10 mol%), DPEphos (12 mol%), **1a** (0.2 mmol), K_2CO_3 (0.6 mmol), 4Å MS (100 mg), and **2a** (0.4 mmol) under N_2, after which 3.0 mL DCE was added into the reaction mixture by a syringe and the tube was sealed with Teflon cap. The mixture was stirred at 120 °C for 12 hours. When the reaction was completed, the solvent was removed under vacuum and the residue was purified by column chromatography on silica gel to afford the product **3a** in 79% yield.

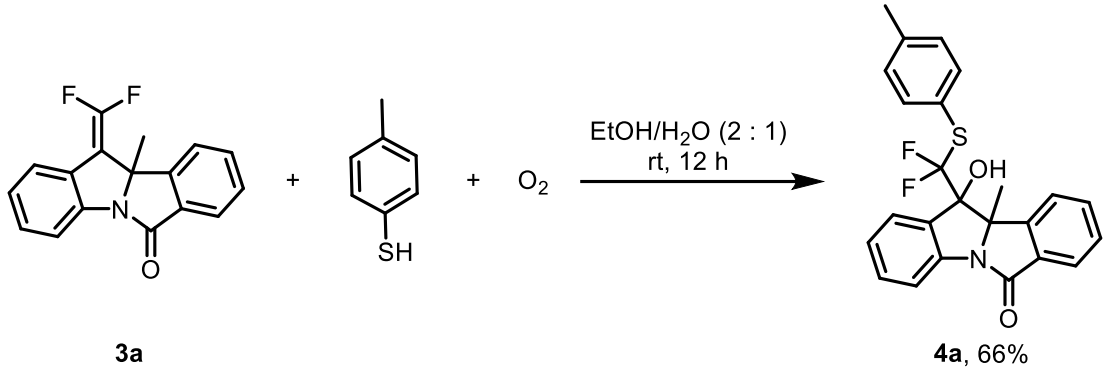
2.2 Gram-scale reaction



To a Schlenk tube was added $Pd(OAc)_2$ (10 mol%), DPEphos (12 mol%), **1a** (8 mmol), K_2CO_3 (24 mmol), 4Å MS (4000 mg), and **2a** (16 mmol) under N_2, after which 40 mL DCE was added into the reaction mixture by a syringe and the tube was sealed with Teflon cap. The mixture was stirred at 120 ℃ for 15 hours. When the reaction was completed, the solvent was removed under vacuum and the residue was purified by column chromatography on silica gel to afford the product **3a** in 45% yield.

2.3 Synthetic transformations of product 3a

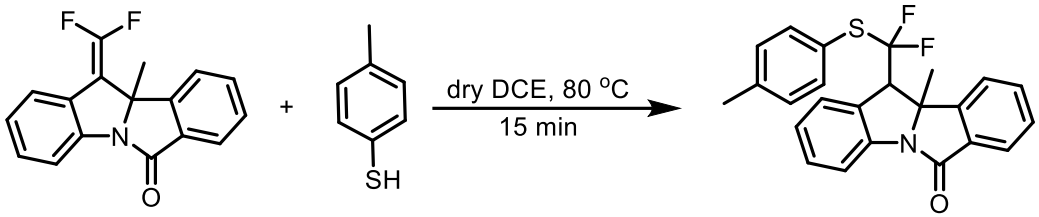
2.3.1 Procedure for synthesis of 4a



The synthesis of **4a** was conducted according to a reported procedure.[2] To a 25 mL Schlenk flask was charged with *gem*-difluoroalkene **3a** (0.2 mmol, 1.0 equiv.), 4-methylbenzenethiol (0.4 mmol, 2.0 equiv.), and $EtOH/H_2O$ (2.0 mL, *v*/*v* = 2:1). The flask was then evacuated and backfilled with O_2 three times and sealed with a Teflon cap. The resulting solution was stirred at room temperature for 12 h. Upon competition of the reaction, CH_2Cl_2 (10 mL) was added. The organic layer was washed with H_2O (10 mL × 2) and brine (10 mL × 1), and the combined aqueous layers was extracted with CH_2Cl_2 (10 mL × 2) twice. The combine organic layers were dried over anhydrous Na_2SO_4. Then the solvents were removed via rotary evaporator and the residue was purified by column chromatography on silica gel to afford alcohol product **4a** in 66%

yield.

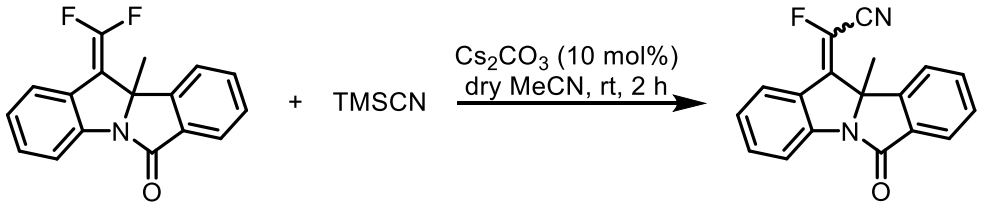
2.3.2 Procedure for synthesis of 4b



3a **4b**, 85%

The synthesis of **4b** was conducted according to a reported procedure.[3] To a 10 mL Schlenk tube was charged with *gem*-difluoroalkene **3a** (0.2 mmol, 1.0 equiv.), 4-methylbenzenethiol (0.24 mmol, 1.2 equiv.), and dry DCE (40 μL). The reaction mixture was placed in a preheated metal block and stirred at 80 °C for 15 min. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel to afford product **4b** in 85% yield.

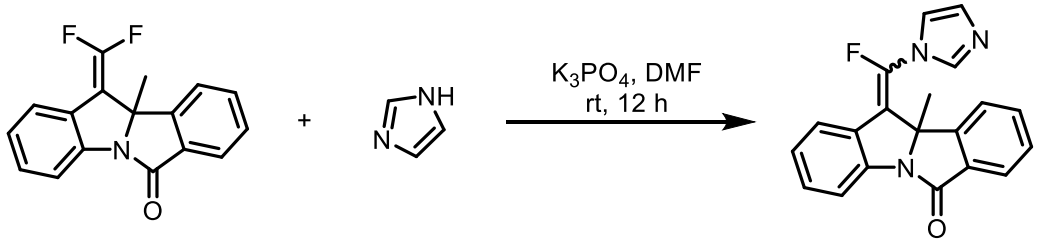
2.3.3 Procedure for synthesis of 4c



3a **4c**, 83 %

The synthesis of **4c** was conducted according to a reported procedure.[4] An oven-dried 10 mL Schlenk tube was charged with Cs_2CO_3 (0.03 mmol), TMSCN (0.9 mmol, 3 equiv.), **3a** (0.3 mmol, 1.0 equiv.), and dry MeCN (1.0 mL). The reaction mixture was stirred at room temperature for 2 h. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel to afford product **4c** in 83% yield.

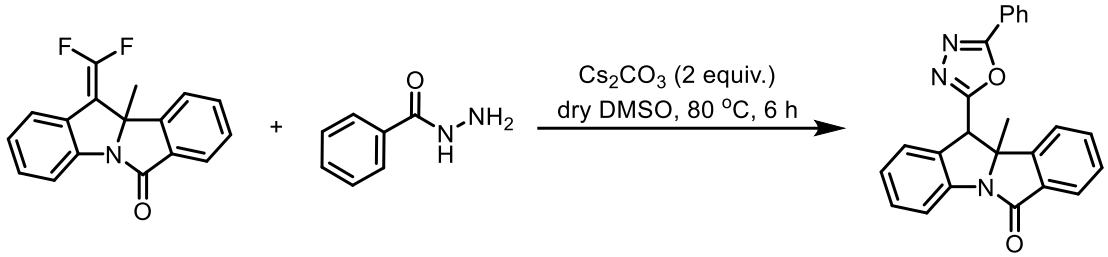
2.3.4 Procedure for synthesis of 4d



3a **4d**, 85%

The reduction was conducted according to a reported procedure.[5] A solution of imidazole (0.5 mmol, 1.0 equiv.) in DMF (0.5 mL) was added dropwise to a mixture of *gem*-difluoroalkene **3a** (0.6 mmol, 1.2 equiv.) and K_3PO_4 (1 mmol, 2 equiv.) in DMF (0.5 mL) via syring and then stirred at room temperature for 12 h (monitored by TLC). After completion of the reaction, the mixture was quenched with H_2O (20 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The organic layer was dried over $MgSO_4$ and filtered, and the filtrate was concentrated in vacuo. The crude product was purified by column chromatography on silica gel to afford product **4d** in 85% yield.

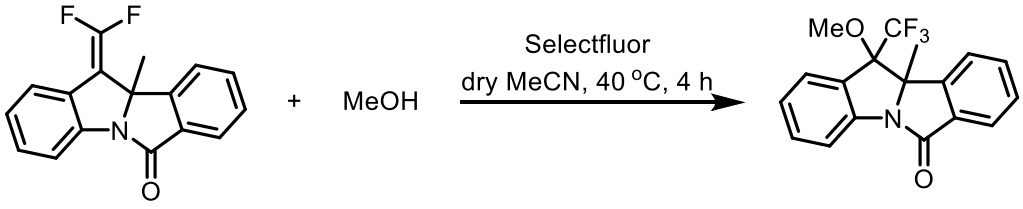
2.3.5 Procedure for synthesis of 4e



3a **4e**, 79%

The reduction was conducted according to a reported procedure.[6] A 25 mL of dried round-bottom flask was charged with *gem*-difluoroalkene **3a** (0.2 mmol, 1.0 equiv.), benzoyl hydrazide (0.24 mmol, 1.2 equiv.), Cs_2CO_3 (0.4 mmol, 2 equiv.), and dry DMSO (1 mL) under N_2 atmosphere. The mixture was stirred at 80 °C for 6 h (monitored by TLC). After the reaction completed, the reaction mixture was quenched with H_2O (20 mL) and extracted with EtOAc (3×10 mL). The combined organic layer was washed with brine (3×10 mL), dried 3 over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel to afford product **4e** in 79% yield.

2.3.6 Procedure for synthesis of 4f

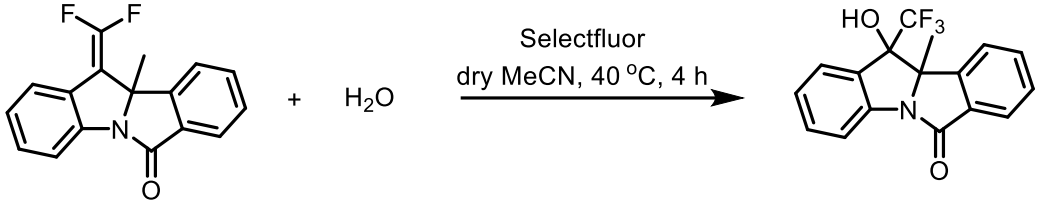


3a **4f**, 77%

The reduction was conducted according to a reported procedure.[7] Selectfluor (0.3

mmol, 1.5 equiv.), and *gem*-difluoroalkene **3a** (0.2 mmol, 1 equiv.) were added in turn to an oven-dried 10 mL Schlenk tube equipped with a stir bar under a nitrogen atmosphere. The reactants were dissolved in dry CH_3CN (0.8 mL), followed by the addition of dry MeOH (1 mmol, 5 equiv.). The reaction mixture was stirred at 40 °C for 4 h. The reaction mixture was diluted with ethyl acetate (20.0 mL) and transferred to a flask. The solvent was evaporated under vacuum. The residue was purified by column chromatography on silica gel to afford product **4f** in 77% yield.

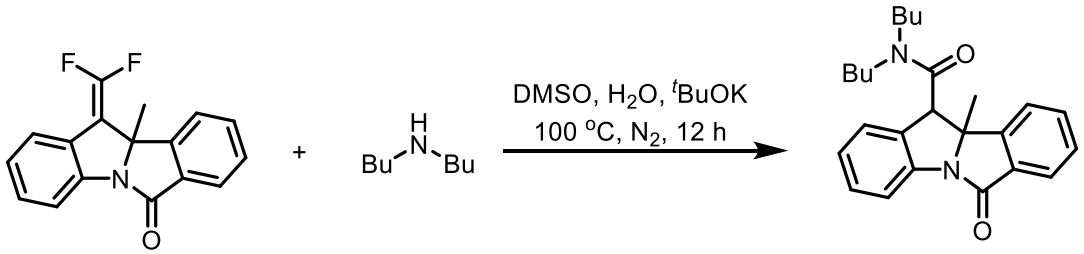
2.3.7 Procedure for synthesis of 4g



3a **4g**, 95%

The reduction was conducted according to a reported procedure.[7] Selectfluor (0.3 mmol, 1.5 equiv.), and *gem*-difluoroalkene **3a** (0.2 mmol, 1 equiv.) were added in turn to an oven-dried 10 mL Schlenk tube equipped with a stir bar under a nitrogen atmosphere. The reactants were dissolved in dry CH_3CN (0.8 mL), followed by the addition of H_2O (1.6 mmol, 8 equiv.). The reaction mixture was stirred at 40 °C for 4 h. The reaction mixture was diluted with ethyl acetate (20.0 mL) and transferred to a flask. The solvent was evaporated under vacuum. The residue was purified by column chromatography on silica gel to afford product **4g** in 95% yield.

2.3.8 Procedure for synthesis of 4h



3a **4h**, 43%

The reduction was conducted according to a reported procedure.[8] A solution of ^{t}BuOK (0.6 mmol, 3 equiv.) and dibuthylamine (0.4 mmol, 2 equiv.) in DMSO (1.2 mL) was stirred at 100 °C under a nitrogen atmosphere for about 10 minutes, and then H_2O (0.02 mL) was added via a syringe. Twenty minutes later, *gem*-difluoroalkene **3a** (0.2

mmol, 1 equiv.) was added to the mixture under N_2. Stirring was continued at 100 °C for 12 h. After the completion of reaction, the reaction mixture was quenched with H_2O (20 mL) and extracted with ethyl acetate (10 mL × 3). The organic layer was separated and dried over Na_2SO_4, filtered and evaporated under vacuum. The residue was purified by column chromatography on silica gel to afford product **4h** in 43% yield.

3. References

1. D. A. Petrone, A. Yen, N. Zeidan and M. Lautens, *Org. Lett.*, 2015, **17**, 4838-4841.
2. C. Liu, C. Zhu, Y. Cai and H. Jiang, *Angew. Chem., Int. Ed.*, 2021, **60**, 12038-12045.
3. X. Jiang, G. Wang, Z. Zheng, X. Yu, Y. Hong, H. Xia and C. Yu, *Org. Lett.*, 2020, **22**, 9762-9766.
4. L.-F. Jiang, B.-T. Ren, B. Li, G.-Y. Zhang, Y. Peng, Z.-Y. Guan and Q.-H. Deng, *J. Org. Chem.*, 2019, **84**, 6557-6564.
5. Y. Xiong, X. Zhang, T. Huang and S. Cao, *J. Org. Chem.*, 2014, **79**, 6395-6402.
6. X. Zhang, J. He and S. Cao, *Asian J. Org. Chem.*, 2019, **8**, 279-282.
7. J. Hu, Y. Yang, Z. Lou, C. Ni and J. Hu, *Chin. J. Chem.*, 2018, **36**, 1202-1208.
8. B. Wang, X. Zhao, Q. Liu and S. Cao, *Org. Biomol. Chem.*, 2018, **16**, 8546-8552.

4. Crystallographic data and molecular structure of compounds 3a, 3t, and 4h

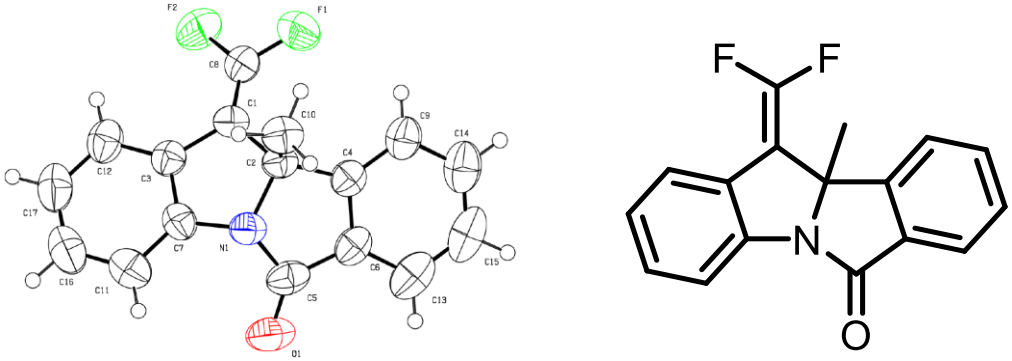
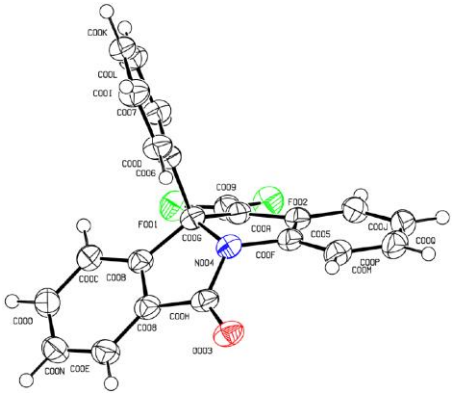


Figure S1. X-ray crystal structure of **3a**

Table S1. Crystal data and structure refinement details for **3a**.

Compound	**3a**
Empirical formula	$C_{17}H_{11}F_2NO$
Formula weight	283.27
Temperature/K	296.15
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	13.160(4)

b/Å	7.282(2)
c/Å	14.200(4)
α/°	90
β/°	99.631(6)
γ/°	90
Volume/Å^3	1341.6(7)
Z	4
ρ_{calc}g/cm^3	1.402
μ/mm^{-1}	0.107
F(000)	584.0
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.82 to 49.986
Index ranges	-15 ≤ h ≤ 15, -6 ≤ k ≤ 8, -16 ≤ l ≤ 16
Reflections collected	6537
Independent reflections	2358 [R_{int} = 0.0836, R_{sigma} = 0.0903]
Data/restraints/parameters	2358/0/191
Goodness-of-fit on F^2	0.974
Final R indexes [I>=2σ (I)]	R_1 = 0.0488, wR_2 = 0.0836
Final R indexes [all data]	R_1 = 0.1363, wR_2 = 0.1102
Largest diff. peak/hole / e Å^{-3}	0.14/-0.16



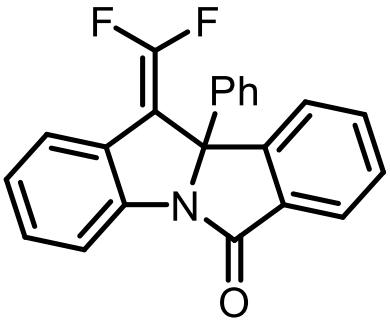


Figure S2. X-ray crystal structure of **3t**

Table S2. Crystal data and structure refinement details for **3t**.

Compound	**3t**
Empirical formula	$C_{22}H_{13}F_2NO$
Formula weight	345.33
Temperature/K	150.00
Crystal system	monoclinic
Space group	C2/*c*
a/Å	24.1916(17)
b/Å	9.9649(5)
c/Å	14.5436(11)
α/°	90.00
β/°	112.784(3)
γ/°	90.00
Volume/Å^3	3232.4(4)
Z	8
ρ_{calc}g/cm^3	1.419
μ/mm^{-1}	0.103
F(000)	1424.0
Crystal size/mm^3	0.2 × 0.15 × 0.12
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.476 to 52.93
Index ranges	-30 ≤ h ≤ 30, -12 ≤ k ≤ 12, -18 ≤ l ≤ 18
Reflections collected	28476
Independent reflections	3311 [R_{int} = 0.0705, R_{sigma} = 0.0334]
Data/restraints/parameters	3311/0/235
Goodness-of-fit on F^2	1.105
Final R indexes [I>=2σ (I)]	R_1 = 0.0425, wR_2 = 0.1029

Final R indexes [all data]	$R_1 = 0.0563$, $wR_2 = 0.1139$
Largest diff. peak/hole / e Å^{-3}	0.24/-0.18

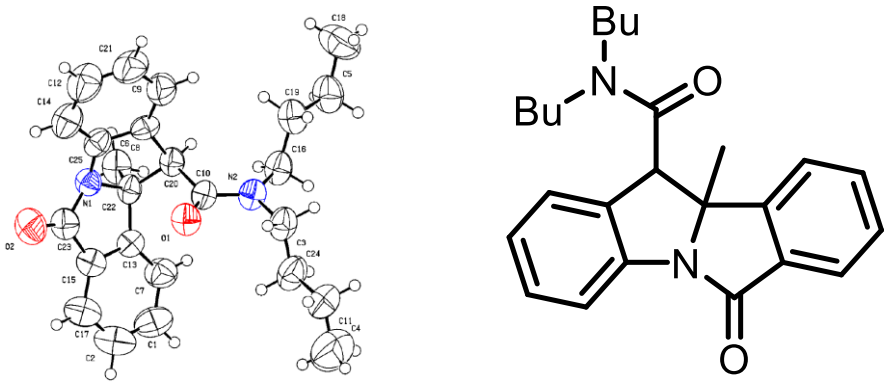


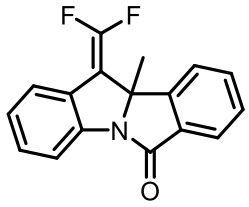
Figure S3. X-ray crystal structure of **4h**

Table S3. Crystal data and structure refinement details for **4h**.

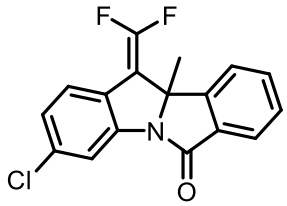
Compound	**4h**
Empirical formula	$C_{25}H_{30}N_2O_2$
Formula weight	390.51
Temperature/K	296.15
Crystal system	tetragonal
Space group	P-42$_1$/c
a/Å	20.1920(8)
b/Å	20.1920(8)
c/Å	11.0430(5)
α/°	90.00
β/°	90.00
γ/°	90.00
Volume/Å^3	4502.4(4)
Z	8
ρ_{calc}g/cm^3	1.152
μ/mm^{-1}	0.073
F(000)	1680.0

Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.468 to 49.998
Index ranges	-23 ≤ h ≤ 23, -17 ≤ k ≤ 24, -13 ≤ l ≤ 13
Reflections collected	21458
Independent reflections	3966 [R_{int} = 0.1637, R_{sigma} = 0.1123]
Data/restraints/parameters	3966/0/265
Goodness-of-fit on F^2	0.952
Final R indexes [I>=2σ (I)]	R_1 = 0.0709, wR_2 = 0.1481
Final R indexes [all data]	R_1 = 0.1518, wR_2 = 0.1737
Largest diff. peak/hole / e $Å^{-3}$	0.14/-0.14
Flack parameter	-1.4(10)

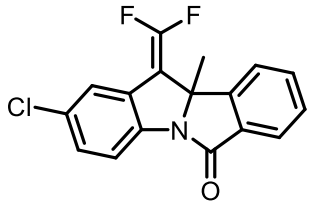
5. Analytical data



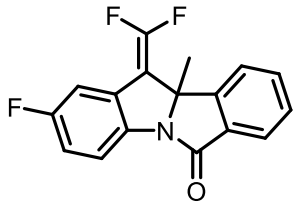
11-(difluoromethylene)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3a): New compound. 44.7 mg, 79% yield. White solid. m.p.: 98.5-99.1 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.7 Hz, 1H), 7.78-7.69 (m, 2H), 7.65 (td, *J* = 7.5, 1.2 Hz, 1H), 7.51 (td, *J* = 7.4, 1.1 Hz, 1H), 7.41 (d, *J* = 7.7 Hz, 1H), 7.35 (td, *J* = 7.7, 1.3 Hz, 1H), 7.16 (td, *J* = 7.6, 1.1 Hz, 1H), 1.79 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.8, 152.2 (dd, *J* = 295.1, 288.5 Hz), 148.7, 140.2 (d, *J* = 5.4 Hz), 133.7 (d, *J* = 1.7 Hz), 132.0, 129.4, 129.3, 127.6 (dd, *J* = 6.0, 3.9 Hz), 125.3, 125.2, 123.9 (dd, *J* = 9.5, 2.2 Hz), 123.7 (d, *J* = 9.5 Hz), 117.5, 96.7 (dd, *J* = 25.1, 18.5 Hz), 71.7 (dd, *J* = 5.0, 3.5 Hz), 28.0 (t, *J* = 2.9 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -84.30 (d, *J* = 45.2 Hz), -85.00 (d, *J* = 45.3 Hz). **HRMS** (ESI) m/z Calcd for $C_{17}H_{12}F_2NO$ $[M+H]^+$: 284.0882; Found: 284.0880.



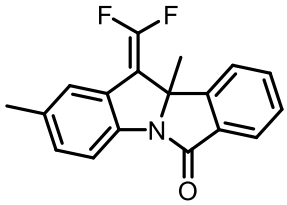
3-chloro-11-(difluoromethylene)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3b): New compound. 25.4 mg, 40% yield. Light yellow solid. m.p.: 149.7-150.7 ℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.6 Hz, 1H), 7.74 (d, *J* = 2.1 Hz, 1H), 7.73-7.63 (m, 2H), 7.53 (td, *J* = 7.5, 1.5 Hz, 1H), 7.31 (d, *J* = 8.3 Hz, 1H), 7.14 (dd, *J* = 8.3, 2.0 Hz, 1H), 1.79 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.7, 152.3 (dd, *J* = 293.5, 287.6 Hz), 148.6, 141.1 (d, *J* = 6.6 Hz), 135.0 (t, *J* = 2.9 Hz), 134.0 (d, *J* = 1.8 Hz), 131.5, 129.5, 126.2 (dd, *J* = 5.9, 3.7 Hz), 125.5, 125.4, 124.5 (dd, *J* = 9.5, 2.6 Hz), 123.7 (d, *J* = 9.2 Hz), 117.9, 96.2 (dd, *J* = 25.7, 18.7 Hz), 72.2 (dd, *J* = 4.8, 3.3 Hz), 28.1 (t, *J* = 2.8 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -83.86 (d, *J* = 44.3 Hz), -84.20 (d, *J* = 44.3 Hz). **HRMS** (ESI) m/z Calcd for $C_{17}H_{11}ClF_2NO$ $[M+H]^+$: 318.0492; Found: 318.0489.



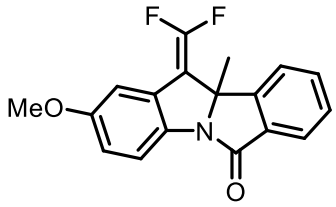
2-chloro-11-(difluoromethylene)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3c): New compound. 22.2 mg, 35% yield. Light yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.7 Hz, 1H), 7.73-7.62 (m, 3H), 7.54 (t, *J* = 8.1 Hz, 1H), 7.38 (d, *J* = 2.6 Hz, 1H), 7.32 (dd, *J* = 8.4, 2.3 Hz, 1H), 1.79 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.8, 152.4 (dd, *J* = 294.6, 288.4 Hz), 148.5, 138.8 (d, *J* = 5.5 Hz), 133.9 (d, *J* = 1.8 Hz), 131.6, 130.8, 129.6, 129.4 (t, *J* = 2.4 Hz), 125.4, 124.0 (dd, *J* = 9.9, 2.6 Hz), 123.7, 123.6, 118.3, 96.3 (dd, *J* = 26.0, 18.3 Hz), 72.1 (dd, *J* = 4.3, 3.3 Hz), 28.0 (t, *J* = 2.9 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -82.84 (d, *J* = 41.6 Hz), -83.21 (d, *J* = 41.6 Hz). **HRMS** (ESI) m/z Calcd for $C_{17}H_{11}ClF_2NO$ $[M+H]^+$: 318.0492; Found: 318.0490.



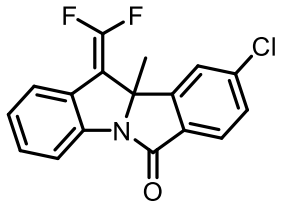
11-(difluoromethylene)-2-fluoro-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3d): New compound. 17.1 mg, 28% yield. Light yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.6 Hz, 1H), 7.73-7.63 (m, 3H), 7.53 (td, *J* = 7.3, 1.4 Hz, 1H), 7.12 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.05 (td, *J* = 8.8, 2.6 Hz, 1H), 1.80 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.0, 160.6 (d, *J* = 243.2 Hz), 152.4 (dd, *J* = 296.6, 289.8 Hz), 148.5, 136.4 (d, *J* = 5.8 Hz), 133.8, 131.8, 129.5, 129.2 (dd, *J* = 9.8, 5.3 Hz), 125.3, 123.6 (d, *J* = 9.2 Hz), 118.4 (d, *J* = 8.8 Hz), 116.1 (d, *J* = 23.8 Hz), 111.2 (dd, *J* = 25.9, 9.4 Hz), 96.8 (dd, *J* = 27.1, 16.6 Hz), 72.3 (t, *J* = 4.0 Hz), 27.9 (t, *J* = 2.9 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -83.09 (dd, *J* = 41.8, 1.4 Hz), -83.54 (d, *J* = 42.0 Hz), -116.95 (d, *J* = 1.6 Hz). **HRMS** (ESI) m/z Calcd for $C_{17}H_{11}F_3NO$ $[M+H]^+$: 302.0787; Found: 302.0784.



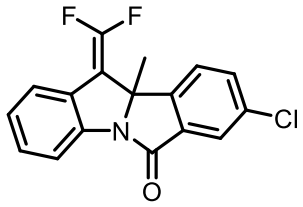
11-(difluoromethylene)-2,10b-dimethyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3e): New compound. 44.5 mg, 75% yield. Light yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.6 Hz, 1H), 7.70 (dd, *J* = 7.8, 4.2 Hz, 1H), 7.63 (t, *J* = 8.6 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.24 (d, *J* = 13.0 Hz, 1H), 7.16 (d, *J* = 8.3 Hz, 1H), 2.35 (s, 3H), 1.77 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.9, 152.1 (dd, *J* = 295.3, 288.3 Hz), 148.7, 137.9 (d, *J* = 5.5 Hz), 135.1, 133.5 (d, *J* = 2.2 Hz), 132.0, 130.0 (t, *J* = 2.4 Hz), 129.3, 127.7 (dd, *J* = 6.2, 4.0 Hz), 125.1, 124.4 (dd, *J* = 9.4, 2.4 Hz), 123.6 (d, *J* = 9.5 Hz), 117.2, 96.7 (dd, *J* = 24.9, 18.3 Hz), 71.9 (dd, *J* = 5.1, 3.3 Hz), 27.9 (t, *J* = 2.8 Hz), 21.4; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -84.41 (d, *J* = 45.6 Hz), -85.24 (d, *J* = 46.3 Hz). **HRMS** (ESI) m/z Calcd for $C_{18}H_{14}F_2NO$ $[M+H]^+$: 298.1038; Found: 298.1033.



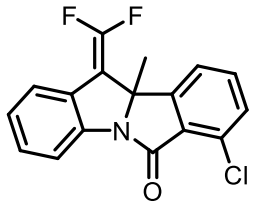
11-(difluoromethylene)-2-methoxy-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3f): New compound. 36.2 mg, 58% yield. Light yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.6 Hz, 1H), 7.70 (dd, *J* = 7.8, 4.3 Hz, 1H), 7.67-7.60 (m, 2H), 7.51 (t, *J* = 7.4 Hz, 1H), 6.96 (s, 1H), 6.90 (dd, *J* = 8.6, 2.6 Hz, 1H), 3.81 (s, 3H), 1.78 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.0, 157.7, 152.2 (dd, *J* = 293.8, 287.3 Hz), 148.6, 133.9 (d, *J* = 5.5 Hz), 133.5 (d, *J* = 1.8 Hz), 132.1, 129.3, 128.9 (dd, *J* = 5.9, 4.0 Hz), 125.1, 123.6 (d, *J* = 9.5 Hz), 118.1, 114.8 (t, *J* = 2.4 Hz), 109.7 (dd, *J* = 9.4, 2.0 Hz), 97.0 (dd, *J* = 25.1, 17.8 Hz), 72.1 (dd, *J* = 5.1, 3.3 Hz), 55.9, 27.8 (t, *J* = 2.8 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -83.91 (d, *J* = 45.0 Hz), -84.75 (d, *J* = 44.3 Hz). **HRMS** (ESI) m/z Calcd for $C_{18}H_{14}F_2NO_2$ $[M+H]^+$: 314.0987; Found: 314.0982.



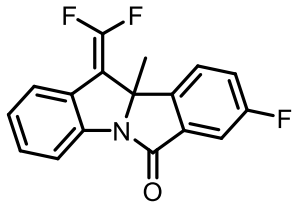
9-chloro-11-(difluoromethylene)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3g): New compound. 35.4 mg, 56% yield. White solid. m.p.: 170.5-171.5 ℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.2 Hz, 1H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.69 (dd, *J* = 3.8, 1.7 Hz, 1H), 7.50 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.42 (d, *J* = 7.7 Hz, 1H), 7.36 (td, *J* = 7.7, 1.3 Hz, 1H), 7.18 (td, *J* = 7.6, 1.2 Hz, 1H), 1.79 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.7, 152.2 (dd, *J* = 294.2, 286.6 Hz), 150.2, 140.1 (d, *J* = 1.8 Hz), 140.0 (d, *J* = 4.4 Hz), 130.5, 130.0, 129.5 (t, *J* = 2.6 Hz), 127.3 (dd, *J* = 6.1, 3.9 Hz), 126.4, 125.6, 124.2 (d, *J* = 9.9 Hz), 124.0 (dd, *J* = 9.2, 2.2 Hz), 117.5, 96.4 (dd, *J* = 24.9, 19.1 Hz), 71.4 (dd, *J* = 5.1, 3.7 Hz), 27.9 (t, *J* = 2.9 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -83.88 (d, *J* = 45.6 Hz), -84.60 (d, *J* = 45.6 Hz). **HRMS** (ESI) m/z Calcd for $C_{17}H_{11}ClF_2NO$ $[M+H]^+$: 318.0492; Found: 318.0490.



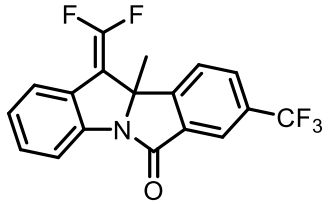
8-chloro-11-(difluoromethylene)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3h): New compound. 33.6 mg, 53% yield. Colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 1.7 Hz, 1H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.68-7.57 (m, 2H), 7.42 (d, *J* = 7.7 Hz, 1H), 7.37 (td, *J* = 7.7, 1.3 Hz, 1H), 7.19 (td, *J* = 7.6, 1.2 Hz, 1H), 1.79 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.3, 152.2 (dd, *J* = 295.6, 288.3 Hz), 146.8, 139.9 (d, *J* = 4.0 Hz), 135.7, 133.9, 133.7 (d, *J* = 1.8 Hz), 129.5 (t, *J* = 2.5 Hz), 127.5 (dd, *J* = 5.9, 3.7 Hz), 125.6, 125.1, 125.0 (d, *J* = 9.5 Hz), 124.0 (dd, *J* = 9.2, 2.2 Hz), 117.5, 96.5 (dd, *J* = 25.3, 18.7 Hz), 71.5 (dd, *J* = 5.1, 3.3 Hz), 27.9 (t, *J* = 2.8 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -84.27 (d, *J* = 45.6 Hz), -84.76 (d, *J* = 45.6 Hz). **HRMS** (ESI) m/z Calcd for $C_{17}H_{11}ClF_2NO$ $[M+H]^+$: 318.0492; Found: 318.0490.



7-chloro-11-(difluoromethylene)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3i): New compound. 30.6 mg, 48% yield. White solid. m.p.: 131.4-132.2 ℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.1 Hz, 1H), 7.63 (ddd, *J* = 7.7, 4.0, 1.1 Hz, 1H), 7.57 (t, *J* = 7.8 Hz, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.41 (d, *J* = 7.7 Hz, 1H), 7.36 (td, *J* = 7.8, 1.3 Hz, 1H), 7.18 (td, *J* = 7.6, 1.2 Hz, 1H), 1.79 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) 167.5, 152.2 (dd, *J* = 295.6, 288.7 Hz), 151.1, 140.2 (d, *J* = 4.8 Hz), 134.3 (d, *J* = 1.8 Hz), 132.8, 131.0, 129.5 (t, *J* = 2.6 Hz), 128.0, 127.4 (dd, *J* = 6.1, 3.9 Hz), 125.6, 123.9 (dd, *J* = 9.5, 2.2 Hz), 122.2 (d, *J* = 10.3 Hz), 117.7, 96.7 (dd, *J* = 24.8, 18.9 Hz), 70.4 (dd, *J* = 5.1, 3.3 Hz), 28.1 (t, *J* = 2.8 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -83.93 (d, *J* = 45.0 Hz), -84.51 (d, *J* = 45.6 Hz). **HRMS** (ESI) m/z Calcd for $C_{17}H_{11}ClF_2NO$ $[M+H]^+$: 318.0492; Found: 318.0489.

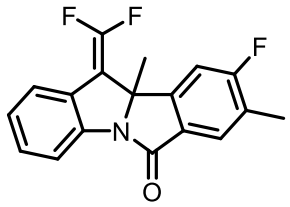


11-(difluoromethylene)-8-fluoro-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3j): New compound. 21.0 mg, 35% yield. Light yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.9 Hz, 1H), 7.68 (dt, *J* = 8.4, 4.2 Hz, 1H), 7.52 (dd, *J* = 7.4, 2.5 Hz, 1H), 7.42 (d, *J* = 7.7 Hz, 1H), 7.39-7.30 (m, 2H), 7.19 (td, *J* = 7.6, 1.2 Hz, 1H), 1.79 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.5 (d, *J* = 3.3 Hz), 163.4 (d, *J* = 249.7 Hz), 152.2 (dd, *J* = 295.4, 288.2 Hz), 144.2 (d, *J* = 2.4 Hz), 139.9 (d, *J* = 4.4 Hz), 134.4 (d, *J* = 8.5 Hz), 129.5 (t, *J* = 2.3 Hz), 127.6 (dd, *J* = 5.8, 3.7 Hz), 125.6, 125.4 (t, *J* = 8.9 Hz), 124.0 (dd, *J* = 9.2, 2.2 Hz), 121.1 (dd, *J* = 23.6, 1.6 Hz), 117.5, 111.7 (d, *J* = 23.3 Hz), 96.7 (dd, *J* = 25.0, 18.5 Hz), 71.5 (dd, *J* = 4.9, 3.3 Hz), 28.0 (t, *J* = 2.6 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -84.52 (dd, *J* = 45.7, 4.0 Hz), -84.94 (d, *J* = 45.6 Hz), -111.37 (td, *J* = 8.0, 4.2 Hz). **HRMS** (ESI) m/z Calcd for $C_{17}H_{11}F_3NO$ $[M+H]^+$: 302.0787; Found: 302.0783.

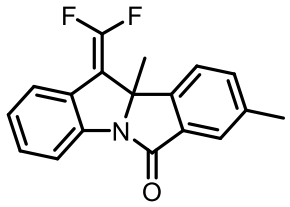


11-(difluoromethylene)-10b-methyl-8-(trifluoromethyl)-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3k): New compound. 29.6 mg, 42% yield. Light yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.92 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.86 (dd, *J* = 8.1, 3.9 Hz, 1H), 7.75 (d, *J* = 7.9 Hz, 1H), 7.43 (d, *J* = 7.7 Hz, 1H), 7.38 (td, *J* = 7.7, 1.2 Hz, 1H), 7.21 (td, *J* = 7.6, 1.1 Hz, 1H), 1.83 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.2, 152.2 (dd, *J* = 295.8, 288.2 Hz), 151.7, 139.8 (d, *J* = 5.5 Hz), 133.1, 132.2 (q, *J* = 33.3 Hz), 130.4 (dd, *J* = 3.5, 1.7 Hz), 129.6 (t, *J* = 2.3 Hz), 127.4 (dd, *J* = 5.9, 3.7 Hz), 125.8, 124.5 (d, *J* = 9.9 Hz), 124.1 (dd, *J* = 9.3, 2.1 Hz), 123.6 (q, *J* = 272.8 Hz), 122.5 (q, *J* = 3.9 Hz), 117.6, 96.4 (dd, *J* = 25.0, 19.1 Hz), 71.8 (dd, *J* = 4.8,

3.5 Hz), 27.9 (t, J = 2.6 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.58, -83.96 (dd, J = 45.6, 4.0 Hz), -84.49 (d, J = 45.3 Hz). **HRMS** (ESI) m/z Calcd for $C_{18}H_{11}F_5NO$ $[M+H]^+$: 352.0755; Found: 352.0750.

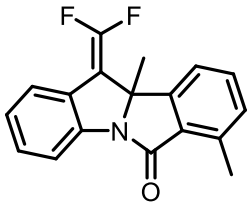


11-(difluoromethylene)-9-fluoro-8,10b-dimethyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3l): New compound. 44.7 mg, 71% yield. White solid. m.p.: 120.2-122.2 ℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70 (dd, J = 6.6, 5.0 Hz, 2H), 7.41 (d, J = 7.7 Hz, 1H), 7.38-7.29 (m, 2H), 7.17 (td, J = 7.6, 1.1 Hz, 1H), 2.35 (d, J = 2.2 Hz, 3H), 1.77 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.2, 164.9 (dd, J = 253.4, 1.2 Hz), 152.2 (dd, J = 295.5, 288.1 Hz), 148.6 (d, J = 9.8 Hz), 140.3 (d, J = 5.4 Hz), 129.5 (t, J = 2.3 Hz), 128.1 (d, J = 6.9 Hz), 127.6 (d, J = 2.5 Hz), 127.3 (dd, J = 5.8, 3.7 Hz), 127.3 (d, J = 19.2 Hz), 125.4, 124.0 (dd, J = 9.2, 2.2 Hz), 117.4, 110.7 (dd, J = 25.8, 9.4 Hz), 96.6 (dd, J = 25.0, 18.6 Hz), 71.1 (ddd, J = 5.1, 3.3, 2.9 Hz), 27.9 (t, J = 2.7 Hz), 14.9 (d, J = 4.0 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -84.52 (d, J = 46.3 Hz), -84.97 (d, J = 46.3 Hz). **HRMS** (ESI) m/z Calcd for $C_{18}H_{13}F_3NO$ $[M+H]^+$: 316.0944; Found: 316.0940.

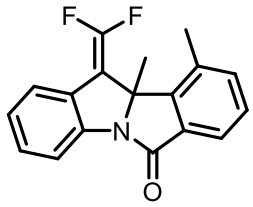


11-(difluoromethylene)-8,10b-dimethyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3m): New compound. 41.8 mg, 70% yield. Light yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (d, J = 7.9 Hz, 1H), 7.66 (s, 1H), 7.59 (dd, J = 7.9, 4.4 Hz, 1H), 7.47 (d, J = 7.8 Hz, 1H), 7.41 (d, J = 7.7 Hz, 1H), 7.35 (t, J = 7.8 Hz, 1H), 7.17 (t, J = 7.6 Hz, 1H), 2.45 (s, 3H), 1.77 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.1, 152.2 (dd, J = 293.4, 286.8 Hz), 146.1, 140.3 (d, J = 5.4 Hz), 139.6, 134.7 (d, J = 1.4 Hz),

132.1, 129.3 (t, J = 2.3 Hz), 127.7 (dd, J = 5.9, 3.9 Hz), 125.3, 125.3, 123.9 (dd, J = 9.3, 2.1 Hz), 123.4 (d, J = 9.1 Hz), 117.5, 96.8 (dd, J = 25.2, 18.2 Hz), 71.6 (dd, J = 5.0, 3.5 Hz), 28.0 (t, J = 2.9 Hz), 21.4; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -84.55 (d, J = 45.6 Hz), -85.23 (d, J = 45.6 Hz). **HRMS** (ESI) m/z Calcd for $C_{18}H_{14}F_2NO$ $[M+H]^+$: 298.1038; Found: 298.1035.

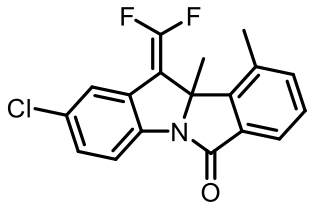


11-(difluoromethylene)-7,10b-dimethyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3n): New compound. 49.9 mg, 84% yield. Light yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (d, J = 7.9 Hz, 1H), 7.57-7.47 (m, 2H), 7.40 (d, J = 7.7 Hz, 1H), 7.34 (t, J = 7.8 Hz, 1H), 7.24 (d, J = 7.5 Hz, 1H), 7.15 (t, J = 7.6 Hz, 1H), 2.70 (s, 3H), 1.77 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.9, 152.3 (dd, J = 294.9, 288.7 Hz), 149.4, 140.6 (d, J = 5.4 Hz), 139.6, 133.2 (d, J = 1.6 Hz), 131.3, 129.3 (t, J = 2.5 Hz), 128.8, 127.6 (dd, J = 6.0, 3.9 Hz), 125.2, 123.9 (dd, J = 9.6, 2.3 Hz), 121.1 (d, J = 9.7 Hz), 117.5, 97.0 (dd, J = 24.8, 18.3 Hz), 70.8 (dd, J = 5.0, 3.7 Hz), 28.1 (t, J = 2.8 Hz), 17.8; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -84.26 (d, J = 45.9 Hz), -84.97 (d, J = 45.8 Hz). **HRMS** (ESI) m/z Calcd for $C_{18}H_{14}F_2NO$ $[M+H]^+$: 298.1038; Found: 298.1036.

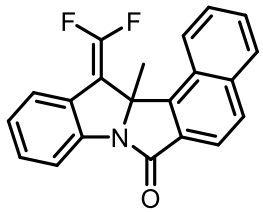


11-(difluoromethylene)-10,10b-dimethyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3o): New compound. 10.2 mg, 17% yield. White solid. m.p.: 92.0-94.5 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78-7.68 (m, 2H), 7.49-7.41 (m, 3H), 7.37 (td, J = 7.8, 1.3 Hz, 1H), 7.20 (td, J = 7.7, 1.1 Hz, 1H), 2.61 (d, J = 5.1 Hz, 3H), 1.90 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.2, 151.1 (dd, J = 291.3, 289.2 Hz), 144.0, 139.0 (d, J = 5.3 Hz), 136.5, 135.1, 133.2, 129.6, 129.4 (t, J = 4.8 Hz), 129.2 (t, J = 1.9

Hz), 125.5, 124.3 (dd, J = 10.3, 1.8 Hz), 122.9, 118.4, 97.1 (dd, J = 23.9, 19.1 Hz), 73.1 (dd, J = 4.9, 2.8 Hz), 26.2 (t, J = 2.7 Hz), 19.8 (d, J = 16.2 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -81.56 (d, J = 43.0 Hz), -85.46 (d, J = 42.9 Hz). **HRMS** (ESI) m/z Calcd for $C_{18}H_{14}F_2NO$ $[M+H]^+$: 298.1038; Found: 298.1035.

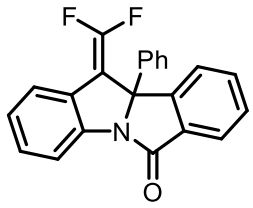


2-chloro-11-(difluoromethylene)-10,10b-dimethyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3p): New compound. 22.0 mg, 33% yield. Light yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 (dd, J = 7.0, 2.1 Hz, 1H), 7.64 (d, J = 8.3 Hz, 1H), 7.49-7.42 (m, 2H), 7.40 (t, J = 1.8 Hz, 1H), 7.34 (dd, J = 8.4, 2.1 Hz, 1H), 2.60 (d, J = 5.1 Hz, 3H), 1.89 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.2, 151.4 (dd, J = 294.3, 292.5 Hz), 143.8, 137.6 (d, J = 5.3 Hz), 136.8, 135.2, 132.9, 131.1 (t, J = 5.0 Hz), 131.0, 129.8, 129.2 (t, J = 1.9 Hz), 124.3 (dd, J = 11.0, 1.8 Hz), 123.0, 119.2, 96.7 (dd, J = 24.9, 18.8 Hz), 73.4 (dd, J = 4.6, 2.8 Hz), 26.2 (t, J = 2.6 Hz), 19.7 (d, J = 16.0 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -80.09 (d, J = 39.1 Hz), -83.68 (d, J = 39.3 Hz). **HRMS** (ESI) m/z Calcd for $C_{18}H_{13}ClF_2NO$ $[M+H]^+$: 332.0648; Found: 332.0645.

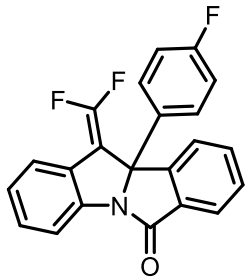


13-(difluoromethylene)-13a-methyl-13,13a-dihydro-7*H*-benzo[6,7]isoindolo[2,1-*a*]indol-7-one (3q): New compound. 45.5 mg, 68% yield. White solid. m.p.: 148.4-149.0 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.32 (t, J = 9.0 Hz, 1H), 8.05-7.99 (m, 2H), 7.90 (d, J = 8.3 Hz, 1H), 7.77 (d, J = 7.0 Hz, 1H), 7.71-7.63 (m, 2H), 7.47 (d, J = 7.7 Hz, 1H), 7.40 (td, J = 7.7, 1.3 Hz, 1H), 7.21 (td, J = 7.6, 1.1 Hz, 1H), 2.10 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.3, 152.1 (t, J = 293.2 Hz), 145.0, 138.9 (d, J = 5.4 Hz), 136.9, 131.5, 131.0, 129.7, 129.4 (dd, J = 5.3, 4.4 Hz), 129.3 (t, J = 1.8 Hz), 128.5,

128.1, 126.9 (d, J = 1.3 Hz), 125.9 (d, J = 14.5 Hz), 125.5, 124.4 (dd, J = 10.6, 1.7 Hz), 120.5, 118.2, 97.1 (dd, J = 23.6, 19.7 Hz), 73.5 (dd, J = 4.9, 2.5 Hz), 27.7 (t, J = 2.6 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -77.47 (d, J = 41.3 Hz), -84.18 (d, J = 41.1 Hz). **HRMS** (ESI) m/z Calcd for $C_{21}H_{14}F_2NO$ $[M+H]^+$: 334.1038; Found: 334.1033.

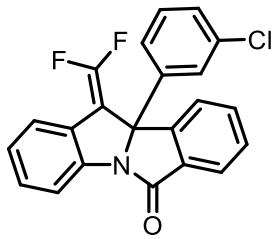


11-(difluoromethylene)-10b-phenyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3t): New compound. 23.4 mg, 34% yield. White solid. m.p.: 141.4-142.5 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 (d, J = 7.6 Hz, 1H), 7.73 (d, J = 7.9 Hz, 1H), 7.60 (d, J = 4.6 Hz, 2H), 7.55-7.49 (m, 1H), 7.44 (dd, J = 14.4, 7.0 Hz, 3H), 7.36-7.26 (m, 4H), 7.17 (t, J = 7.6 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.9, 152.8 (dd, J = 295.4, 289.7 Hz), 147.8, 140.7 (t, J = 2.8 Hz), 140.1 (d, J = 5.3 Hz), 133.7 (d, J = 1.3 Hz), 132.2, 129.5, 129.0, 128.7, 128.6, 125.6, 125.6, 125.6, 125.3 (d, J = 9.2 Hz), 125.1, 123.9 (dd, J = 9.3, 1.8 Hz), 117.8, 95.9 (dd, J = 23.9, 20.0 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -80.96 (d, J = 41.4 Hz), -84.67 (d, J = 41.2 Hz). **HRMS** (ESI) m/z Calcd for $C_{22}H_{14}F_2NO$ $[M+H]^+$: 346.1038; Found: 346.1034.

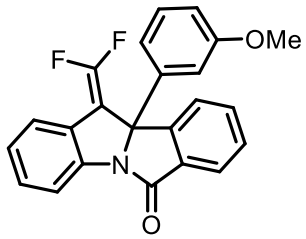


11-(difluoromethylene)-10b-(4-fluorophenyl)-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3u): New compound. 37.0 mg, 51% yield. Light yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 (d, J = 7.6 Hz, 1H), 7.73 (d, J = 7.8 Hz, 1H), 7.65-7.51 (m, 3H), 7.46 (d, J = 7.7 Hz, 1H), 7.41-7.32 (m, 3H), 7.18 (td, J = 7.6, 1.1 Hz, 1H), 7.03-6.92 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.8, 162.8 (d, J = 248.3 Hz), 152.7 (dd, J = 295.8, 289.8 Hz), 147.6, 140.0 (d, J = 5.3 Hz), 136.4 (q, J = 3.0 Hz), 133.9 (d, J = 1.4 Hz), 132.1, 129.7, 129.6 (t, J = 2.1 Hz), 128.4 (dd, J = 5.7, 3.8 Hz), 127.6 (d, J =

8.4 Hz), 125.7, 125.2 (t, J = 4.7 Hz), 123.9 (dd, J = 9.3, 1.9 Hz), 117.8, 115.9 (d, J = 21.7 Hz), 96.0 (dd, J = 23.8, 19.9 Hz), 76.4 (dd, J = 5.3, 3.9 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -80.79 (d, J = 40.8 Hz), -84.41 (d, J = 40.8 Hz), -113.36. **HRMS** (ESI) m/z Calcd for $C_{22}H_{13}F_3NO$ $[M+H]^+$: 364.0944; Found: 364.0939.

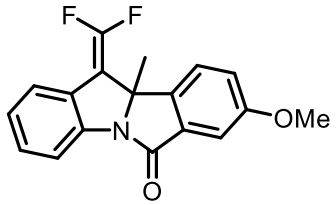


10b-(3-chlorophenyl)-11-(difluoromethylene)-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3v): New compound. 21.3 mg, 28% yield. Light yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 (d, J = 7.6 Hz, 1H), 7.74 (d, J = 7.9 Hz, 1H), 7.63 (td, J = 7.4, 1.3 Hz, 1H), 7.60-7.56 (m, 1H), 7.54 (td, J = 7.2, 1.5 Hz, 1H), 7.45 (d, J = 7.7 Hz, 1H), 7.39-7.30 (m, 3H), 7.26-7.23 (m, 2H), 7.18 (td, J = 7.7, 1.2 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.8, 152.8 (dd, J = 296.1, 290.0 Hz), 147.1, 142.8 (t, J = 2.9 Hz), 140.0 (d, J = 5.2 Hz), 135.0, 133.9 (d, J = 1.3 Hz), 132.1, 130.3, 129.8, 129.7 (t, J = 2.0 Hz), 128.9, 128.3 (dd, J = 5.7, 3.8 Hz), 125.8 (d, J = 12.9 Hz), 125.3, 125.3, 125.2, 124.0 (d, J = 1.7 Hz), 123.9, 117.9, 95.8 (dd, J = 23.7, 20.2 Hz), 76.4 (dd, J = 5.5, 3.8 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -80.57 (dd, J = 40.3, 4.8 Hz), -84.06 (d, J = 40.1 Hz). **HRMS** (ESI) m/z Calcd for $C_{22}H_{13}ClF_2NO$ $[M+H]^+$: 380.0648; Found: 380.0643.

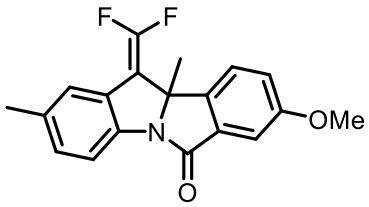


11-(difluoromethylene)-10b-(3-methoxyphenyl)-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3w): New compound. 22.2 mg, 30% yield. White solid. m.p.: 161.1-162.7 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (d, J = 7.6 Hz, 1H), 7.73 (d, J = 7.9 Hz, 1H), 7.64-7.57 (m, 2H), 7.53-7.48 (m, 1H), 7.44 (d, J = 7.7 Hz, 1H), 7.33 (t, J = 7.8 Hz, 1H), 7.22 (t, J = 8.1 Hz, 1H), 7.16 (t, J = 7.6 Hz, 1H), 7.02 (d, J = 7.8 Hz, 1H), 6.96 (t, J = 2.3 Hz, 1H), 6.79 (dd, J = 8.3, 2.5 Hz, 1H), 3.72 (s, 3H); **^{13}C NMR** (100 MHz,

$CDCl_3$) δ 169.9, 160.0, 152.7 (dd, *J* = 295.4, 289.7 Hz), 147.6, 142.4 (t, *J* = 2.9 Hz), 140.1 (d, *J* = 5.1 Hz), 133.7 (d, *J* = 1.4 Hz), 132.2, 130.1, 129.5, 129.5 (t, *J* = 2.1 Hz), 128.6 (dd, *J* = 5.7, 3.9 Hz), 125.6, 125.3 (d, *J* = 9.2 Hz), 125.1, 123.9 (dd, *J* = 9.3, 1.8 Hz), 118.0 (d, *J* = 1.1 Hz), 117.8, 113.2, 112.3, 96.0 (dd, *J* = 23.8, 20.0 Hz), 55.4; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -81.00 (dd, *J* = 41.3, 4.1 Hz), -84.66 (d, *J* = 41.1 Hz). **HRMS** (ESI) m/z Calcd for $C_{23}H_{16}F_2NO_2$ $[M+H]^+$: 376.1144; Found: 376.1139.

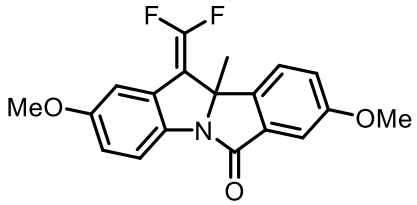


11-(difluoromethylene)-8-methoxy-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3x): New compound. 51.0 mg, 81% yield. Light yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.9 Hz, 1H), 7.59 (dd, *J* = 8.4, 4.3 Hz, 1H), 7.41 (d, *J* = 7.7 Hz, 1H), 7.35 (td, *J* = 7.7, 1.3 Hz, 1H), 7.32 (d, *J* = 2.6 Hz, 1H), 7.22-7.14 (m, 2H), 3.87 (s, 3H), 1.77 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.8, 160.8, 152.2 (dd, *J* = 295.0, 288.2 Hz), 141.1, 140.1 (d, *J* = 5.4 Hz), 133.4, 129.3 (t, *J* = 2.4 Hz), 127.7 (dd, *J* = 5.9, 3.8 Hz), 125.3, 124.5 (d, *J* = 9.2 Hz), 124.0 (dd, *J* = 9.4, 2.2 Hz), 121.9 (d, *J* = 1.8 Hz), 117.5, 107.5, 96.8 (dd, *J* = 25.3, 18.0 Hz), 71.4 (dd, *J* = 5.1, 3.4 Hz), 55.8, 27.9 (t, *J* = 2.8 Hz); **^{19}F NMR (376 MHz, $CDCl_3$)** δ -84.79 (d, *J* = 45.8 Hz), -85.37 (d, *J* = 45.8 Hz). **HRMS** (ESI) m/z Calcd for $C_{18}H_{14}F_2NO_2$ $[M+H]^+$: 314.0987; Found: 314.0984.

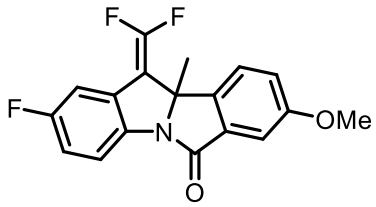


11-(difluoromethylene)-8-methoxy-2,10b-dimethyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3y): New compound. 55.6 mg, 85% yield. Light yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63-7.54 (m, 2H), 7.32 (d, *J* = 2.6 Hz, 1H), 7.22 (s, 1H), 7.19 (dd, *J* = 8.5, 2.5 Hz, 1H), 7.16 (d, *J* = 8.1 Hz, 1H), 3.86 (s, 3H), 2.36 (s, 3H),

1.75 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.9, 160.8, 152.1 (dd, *J* = 295.0, 288.1 Hz), 141.1, 137.9 (d, *J* = 5.5 Hz), 135.1, 133.5, 129.9 (t, *J* = 2.4 Hz), 127.8 (dd, *J* = 6.0, 3.9 Hz), 124.5 (d, *J* = 9.2 Hz), 124.5 (dd, *J* = 9.2, 2.2 Hz), 121.8 (d, *J* = 1.8 Hz), 117.2, 107.5, 96.8 (dd, *J* = 25.1, 17.9 Hz), 71.6 (dd, *J* = 5.2, 3.5 Hz), 55.9, 27.9 (t, *J* = 2.8 Hz), 21.4; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -84.93 (d, *J* = 46.3 Hz), -85.61 (d, *J* = 46.3 Hz). **HRMS** (ESI) m/z Calcd for $C_{19}H_{16}F_2NO_2$ $[M+H]^+$: 328.1144; Found: 328.1139.

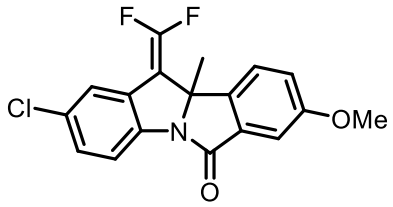


11-(difluoromethylene)-2,8-dimethoxy-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3z): New compound. 47.3 mg, 69% yield. Light yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.6 Hz, 1H), 7.57 (dd, *J* = 8.5, 4.4 Hz, 1H), 7.31 (d, *J* = 2.5 Hz, 1H), 7.18 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.95 (d, *J* = 2.6 Hz, 1H), 6.89 (dd, *J* = 8.6, 2.6 Hz, 1H), 3.85 (s, 3H), 3.80 (s, 3H), 1.75 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.9, 160.8, 157.7, 152.1 (dd, *J* = 295.4, 288.7 Hz), 140.9, 133.9 (d, *J* = 5.4 Hz), 133.5, 129.0 (dd, *J* = 5.2, 4.4 Hz), 124.5 (d, *J* = 9.2 Hz), 121.7, 118.1, 114.7, 109.7 (d, *J* = 9.2 Hz), 107.5, 97.1 (dd, *J* = 25.3, 17.3 Hz), 71.8 (dd, *J* = 4.6, 3.6 Hz), 55.8, 55.8, 27.7 (t, *J* = 2.7 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -84.42 (d, *J* = 45.6 Hz), -85.11 (d, *J* = 45.0 Hz). **HRMS** (ESI) m/z Calcd for $C_{19}H_{16}F_2NO_3$ $[M+H]^+$: 344.1093; Found: 344.1090.

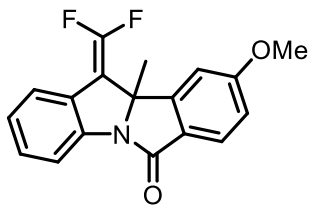


11-(difluoromethylene)-2-fluoro-8-methoxy-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3aa): New compound. 27.2 mg, 41% yield. Light yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 (dd, *J* = 8.6, 4.7 Hz, 1H), 7.58 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.32 (d, *J* = 2.5 Hz, 1H), 7.21 (dd, *J* = 8.5, 2.5 Hz, 1H), 7.11 (dd, *J* = 8.6, 2.6

Hz, 1H), 7.05 (td, *J* = 8.9, 2.7 Hz, 1H), 3.87 (s, 3H), 1.77 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.0, 160.9, 160.6 (d, *J* = 242.9 Hz), 152.3 (dd, *J* = 295.4, 290.4 Hz), 140.9, 136.3 (d, *J* = 6.9 Hz), 133.2, 129.4 (ddd, *J* = 9.6, 5.5, 4.0 Hz), 124.5 (d, *J* = 8.7 Hz), 122.1 (d, *J* = 1.5 Hz), 118.4 (d, *J* = 8.9 Hz), 116.0 (dt, *J* = 23.8, 2.3 Hz), 111.2 (ddd, *J* = 26.0, 9.1, 2.2 Hz), 107.6, 96.9 (ddd, *J* = 25.9, 17.6, 2.8 Hz), 71.9 (dd, *J* = 4.4, 3.3 Hz), 55.9, 27.8 (t, *J* = 2.7 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -83.61 (dd, *J* = 42.3, 2.5 Hz), -83.93 (dd, *J* = 42.2, 1.8 Hz), -116.96 (t, *J* = 2.0 Hz). **HRMS** (ESI) m/z Calcd for $C_{18}H_{13}F_3NO_2$ $[M+H]^+$: 332.0893; Found: 332.0889.

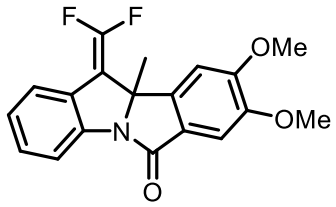


2-chloro-11-(difluoromethylene)-8-methoxy-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3ab): New compound. 38.4 mg, 55% yield. White solid. m.p.: 138.4-138.9 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.4 Hz, 1H), 7.58 (dd, *J* = 8.5, 4.1 Hz, 1H), 7.37 (s, 1H), 7.32 (d, *J* = 6.4 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 1H), 3.87 (s, 3H), 1.76 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.8, 160.9, 152.4 (dd, *J* = 296.0, 290.2 Hz), 140.9, 138.8 (d, *J* = 4.9 Hz), 133.1, 130.7, 129.4 (dd, *J* = 5.1, 4.0 Hz), 129.3 (t, *J* = 2.4 Hz), 124.5 (d, *J* = 8.5 Hz), 124.0 (dd, *J* = 9.2, 2.4 Hz), 122.2, 118.3, 107.6, 96.5 (dd, *J* = 25.6, 18.1 Hz), 71.7 (t, *J* = 3.7 Hz), 55.9, 28.0 (t, *J* = 2.8 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -83.39 (d, *J* = 41.9 Hz), -83.62 (d, *J* = 42.0 Hz). **HRMS** (ESI) m/z Calcd for $C_{18}H_{13}ClF_2NO_2$ $[M+H]^+$: 348.0597; Found: 348.0593.

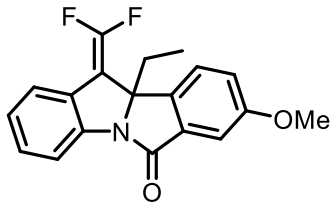


11-(difluoromethylene)-9-methoxy-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3ad): New compound. 45.2 mg, 72% yield. White solid. m.p.: 126.0-127.4 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.4 Hz, 1H), 7.72 (d, *J* = 7.9 Hz,

1H), 7.40 (d, *J* = 7.7 Hz, 1H), 7.34 (td, *J* = 7.7, 1.2 Hz, 1H), 7.19-7.12 (m, 2H), 7.01 (dd, *J* = 8.5, 2.2 Hz, 1H), 3.91 (s, 3H), 1.78 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.9, 164.4 (d, *J* = 1.5 Hz), 152.2 (dd, *J* = 295.1, 288.0 Hz), 151.2, 140.7 (d, *J* = 5.3 Hz), 129.3 (t, *J* = 2.4 Hz), 127.2 (dd, *J* = 5.9, 3.8 Hz), 126.7, 125.1, 124.1, 123.8 (dd, *J* = 9.5, 2.2 Hz), 117.3, 115.7, 108.7 (d, *J* = 9.9 Hz), 96.8 (dd, *J* = 24.9, 18.4 Hz), 71.2 (dd, *J* = 5.1, 3.4 Hz), 55.9, 27.9 (t, *J* = 2.9 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -84.40 (d, *J* = 46.5 Hz), -84.97 (d, *J* = 46.9 Hz). **HRMS** (ESI) m/z Calcd for $C_{18}H_{14}F_2NO_2$ $[M+H]^+$: 314.0987; Found: 314.0983.

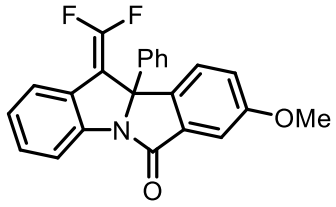


11-(difluoromethylene)-8,9-dimethoxy-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3ae): New compound. 43.9 mg, 64% yield. Light yellow solid. m.p.: 183.5-184.5 ℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.9 Hz, 1H), 7.40 (d, *J* = 7.7 Hz, 1H), 7.35 (t, *J* = 7.8 Hz, 1H), 7.28 (s, 1H), 7.18-7.11 (m, 2H), 4.02 (s, 3H), 3.94 (s, 3H), 1.79 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.4, 154.3 (d, *J* = 1.4 Hz), 152.3 (dd, *J* = 294.7, 287.4 Hz), 150.6, 143.1, 140.7 (dd, *J* = 5.1, 1.2 Hz), 129.4 (t, *J* = 2.4 Hz), 127.4 (dd, *J* = 5.3, 3.3 Hz), 125.1, 123.9 (dd, *J* = 9.0, 2.8 Hz), 123.9, 117.4, 106.0, 105.4 (d, *J* = 9.3 Hz), 96.9 (dd, *J* = 24.7, 18.5 Hz), 71.3 (dd, *J* = 4.3, 2.9 Hz), 56.4, 56.4, 27.8 (t, *J* = 2.9 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -85.15 (d, *J* = 47.9 Hz), -85.39 (d, *J* = 48.2 Hz). **HRMS** (ESI) m/z Calcd for $C_{19}H_{16}F_2NO_3$ $[M+H]^+$: 344.1093; Found: 344.1088.

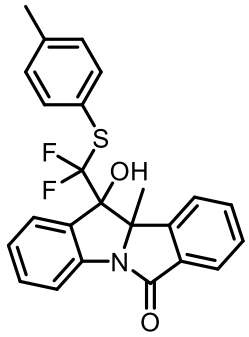


11-(difluoromethylene)-10b-ethyl-8-methoxy-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3af): New compound. 48.6 mg, 74% yield. Light yellow oil. **^{1}H NMR**

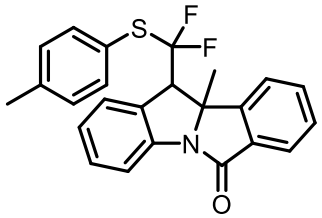
(400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.8 Hz, 1H), 7.54 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.40 (d, *J* = 7.8 Hz, 1H), 7.36-7.30 (m, 2H), 7.20 (dd, *J* = 8.5, 2.5 Hz, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 3.86 (s, 3H), 2.17 (dq, *J* = 14.5, 7.3 Hz, 1H), 2.05 (dq, *J* = 14.3, 7.3 Hz, 1H), 0.69 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.4, 160.8, 152.3 (dd, *J* = 294.9, 288.3 Hz), 140.8 (d, *J* = 4.6 Hz), 139.7, 134.3, 129.2 (t, *J* = 2.3 Hz), 128.3 (dd, *J* = 5.8, 4.0 Hz), 125.2, 124.6 (d, *J* = 9.3 Hz), 123.8 (dd, *J* = 9.4, 2.2 Hz), 121.8 (d, *J* = 1.6 Hz), 117.2, 107.4, 96.1 (dd, *J* = 25.0, 18.0 Hz), 74.7 (dd, *J* = 4.7, 3.7 Hz), 55.8, 33.3 (t, *J* = 2.6 Hz), 8.1; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -84.59 (dd, *J* = 46.3, 4.2 Hz), -85.12 (d, *J* = 46.1 Hz). **HRMS** (ESI) m/z Calcd for $C_{19}H_{16}F_2NO_2$ $[M+H]^+$: 328.1144; Found: 328.1140.



11-(difluoromethylene)-8-methoxy-10b-phenyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (3ag): New compound. 43.6 mg, 58% yield. Colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) 7.72 (d, *J* = 7.8 Hz, 1H), 7.49-7.42 (m, 2H), 7.42-7.37 (m, 2H), 7.36 (d, *J* = 2.6 Hz, 1H), 7.34-7.22 (m, 4H), 7.19-7.12 (m, 2H), 3.87 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.9, 160.9, 152.8 (dd, *J* = 295.5, 289.4 Hz), 140.8 (t, *J* = 2.8 Hz), 140.2, 140.1 (d, *J* = 5.2 Hz), 133.7, 129.4 (t, *J* = 2.2 Hz), 128.9, 128.7 (dd, *J* = 5.8, 3.8 Hz), 128.6, 126.1 (d, *J* = 9.1 Hz), 125.6, 125.6, 123.9 (dd, *J* = 9.2, 2.0 Hz), 122.0 (d, *J* = 1.7 Hz), 117.7, 107.3, 96.0 (dd, *J* = 24.1, 19.5 Hz), 76.5 (dd, *J* = 5.5, 3.5 Hz), 55.9; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -81.44 (d, *J* = 41.5 Hz), -85.02 (d, *J* = 41.5 Hz). **HRMS** (ESI) m/z Calcd for $C_{23}H_{16}F_2NO_2$ $[M+H]^+$: 376.1144; Found: 376.1138.

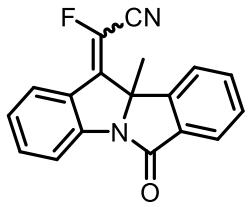


11-(difluoro(*p*-tolylthio)methyl)-11-hydroxy-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (4a): New compound. 55.6 mg, 66% yield. White solid. m.p.: 234.0-234.5 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.03 (d, J = 7.6 Hz, 1H), 7.80-7.72 (m, 3H), 7.64 (t, J = 8.5 Hz, 3H), 7.61-7.56 (m, 1H), 7.54 (td, J = 7.6, 1.3 Hz, 1H), 7.36-7.28 (m, 3H), 6.79 (s, 1H), 2.38 (s, 3H), 1.55 (s, 3H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 166.8, 146.9, 140.3, 139.1, 136.7, 135.1 (d, J = 3.9 Hz), 132.9, 131.0 (t, J = 287.2 Hz), 130.5, 130.1, 129.0, 126.2, 124.6, 124.4 (d, J = 5.1 Hz), 123.8, 122.2, 117.4, 83.9 (t, J = 26.3 Hz), 78.8, 22.7, 20.8; **^{19}F NMR** (376 MHz, DMSO-d_6) δ -71.59 (d, J = 209.8 Hz), -74.25 (d, J = 210.1 Hz). **HRMS** (ESI) m/z Calcd for $C_{24}H_{20}F_2NO_2S$ $[M+H]^+$: 424.1177; Found: 424.1174.

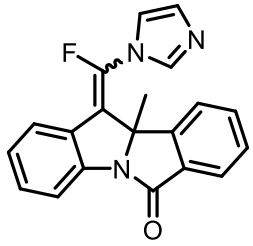


11-(difluoro(*p*-tolylthio)methyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (4b): New compound. 69.4 mg, 85% yield. White solid. m.p.: 190.0-190.9 ℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 (dd, J = 7.7, 3.8 Hz, 2H), 7.68 (d, J = 7.9 Hz, 2H), 7.60 (t, J = 7.5 Hz, 1H), 7.56 (d, J = 8.1 Hz, 2H), 7.48 (t, J = 7.5 Hz, 1H), 7.39 (t, J = 7.7 Hz, 1H), 7.24-7.15 (m, 3H), 4.02 (dd, J = 21.6, 4.4 Hz, 1H), 2.36 (s, 3H), 1.74 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.7, 149.7, 141.0, 139.4, 136.6, 133.1, 132.7, 132.2 (d, J = 3.5 Hz), 130.2, 129.2, 129.1, 129.1 (t, J = 281.7 Hz), 126.3, 125.0, 124.9, 123.7 (d, J = 6.1 Hz), 122.3 (d, J = 3.2 Hz), 117.8, 75.1 (d, J = 1.9 Hz), 57.0 (dd, J = 25.9, 23.2 Hz), 23.1 (d, J = 3.0 Hz), 21.4; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.42 (d,

J = 213.5 Hz), -78.20 (d, *J* = 213.5 Hz). **HRMS** (ESI) m/z Calcd for $C_{24}H_{20}F_2NOS$ $[M+H]^+$: 408.1228; Found: 408.1227.

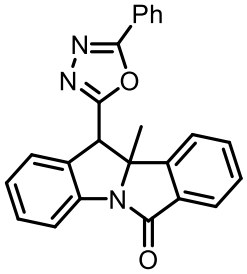


2-fluoro-2-(10b-methyl-6-oxo-6,10b-dihydro-11*H*-isoindolo[2,1-*a*]indol-11-ylidene)acetonitrile (4c): New compound. 72.0 mg, 83% yield. White solid. m.p.: 140.0-141.8 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.9 Hz, 1H), 7.89-7.80 (m, 3H), 7.70 (td, *J* = 7.5, 1.2 Hz, 1H), 7.55 (td, *J* = 7.2, 3.9 Hz, 2H), 7.26 (t, *J* = 7.2 Hz, 1H), 1.86 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.9, 147.1, 143.7 (d, *J* = 4.7 Hz), 138.2 (d, *J* = 19.6 Hz), 134.2 (d, *J* = 2.3 Hz), 133.4 (d, *J* = 2.9 Hz), 131.8, 129.8, 128.2 (d, *J* = 15.1 Hz), 126.1 (d, *J* = 237.0 Hz), 125.6, 125.3, 124.8 (d, *J* = 13.5 Hz), 123.9 (d, *J* = 2.5 Hz), 117.9, 112.5 (d, *J* = 46.2 Hz), 75.2 (d, *J* = 3.7 Hz), 27.7 (d, *J* = 2.7 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -129.15. **HRMS** (ESI) m/z Calcd for $C_{18}H_{12}FN_2O$ $[M+H]^+$: 291.0928; Found: 291.0926.

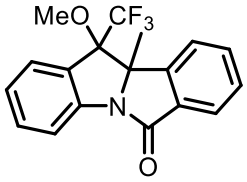


11-(fluoro(1*H*-imidazol-1-yl)methylene)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (4d): New compound. 141.1 mg, 85% yield. Yellow solid. m.p.: 68.7-71.2 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.1 Hz, 2H), 7.77 (d, *J* = 7.9 Hz, 1H), 7.70 (s, 2H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.38-7.29 (m, 2H), 7.14 (s, 1H), 6.95 (t, *J* = 7.8 Hz, 1H), 6.02 (d, *J* = 7.9 Hz, 1H), 1.93 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.2, 148.1, 141.6 (d, *J* = 5.1 Hz), 139.1 (d, *J* = 265.6 Hz), 137.1, 133.8 (d, *J* = 2.0 Hz), 132.0, 131.2, 130.9 (d, *J* = 2.7 Hz), 129.4, 126.7 (d, *J* = 2.5 Hz), 125.4, 125.0, 124.5 (d, *J* = 12.6 Hz), 122.8 (d, *J* = 2.6 Hz), 119.8 (d, *J* = 30.9 Hz), 118.6, 117.7, 73.5 (d, *J* = 4.6 Hz), 27.8 (d, *J* = 2.8 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -81.25. **HRMS**

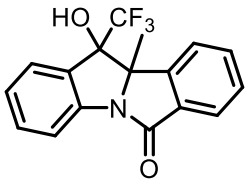
(ESI) m/z Calcd for $C_{20}H_{15}FN_3O$ $[M+H]^+$: 332.1194; Found: 332.1199.



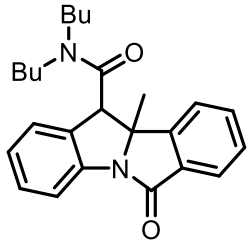
10b-methyl-11-(5-phenyl-1,3,4-oxadiazol-2-yl)-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (4e): New compound. 59.8 mg, 79% yield. White solid. m.p.: 180.8-183.7 ℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.84 (t, *J* = 7.8 Hz, 2H), 7.47 (t, *J* = 6.8 Hz, 3H), 7.41 (d, *J* = 7.5 Hz, 1H), 7.38-7.26 (m, 6H), 7.16 (t, *J* = 7.5 Hz, 1H), 4.92 (s, 1H), 1.85 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.6, 165.2, 163.9, 147.0, 139.8, 133.2, 132.9, 131.8, 130.3, 129.5, 128.9, 126.6, 126.5, 125.4, 124.7, 123.0, 122.5, 118.3, 74.5, 47.8, 27.4. **HRMS** (ESI) m/z Calcd for $C_{24}H_{18}N_3O_2$ $[M+H]^+$: 380.1394; Found: 380.1392.



11-methoxy-10b-methyl-11-(trifluoromethyl)-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (4f): New compound. 51.6 mg, 77% yield. White solid. m.p.: 115.4-117.0 ℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.6 Hz, 1H), 7.80 (d, *J* = 7.9 Hz, 1H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.62-7.51 (m, 4H), 7.27 (t, *J* = 7.6 Hz, 1H), 2.70 (s, 3H), 1.63 (d, *J* = 2.6 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.6, 146.8, 140.5, 133.1, 133.0, 132.1, 129.2, 128.1, 127.6, 125.5 (q, *J* = 285.9 Hz), 124.8, 124.6, 123.5 (q, *J* = 1.9 Hz), 118.6, 86.0 (q, *J* = 29.1 Hz), 78.7, 54.2 (d, *J* = 1.7 Hz), 23.1 (q, *J* = 3.4 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -69.17. **HRMS** (ESI) m/z Calcd for $C_{18}H_{15}F_3NO_2$ $[M+H]^+$: 334.1049; Found: 334.1054.



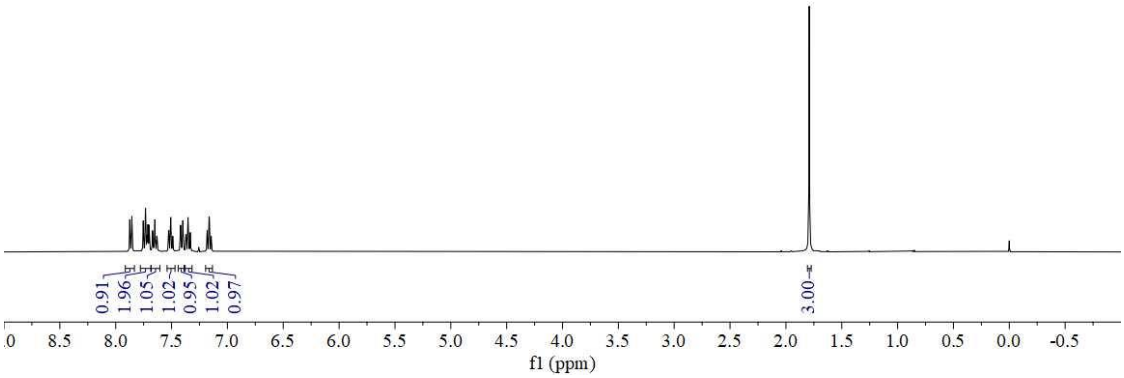
11-hydroxy-10b-methyl-11-(trifluoromethyl)-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one (4g): New compound. 60.8 mg, 95% yield. White solid. m.p.: 259.2-259.8 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.82-7.73 (m, 2H), 7.66-7.50 (m, 5H), 7.30 (t, J = 7.6 Hz, 1H), 6.94 (s, 1H), 1.55 (d, J = 2.6 Hz, 3H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 167.3, 146.5, 139.1, 133.3, 133.2, 132.4, 131.1, 129.2, 125.3 (q, J = 284.3 Hz), 125.3, 125.0, 124.0, 123.6, 117.6, 80.6 (q, J = 29.5 Hz), 77.2, 22.2 (d, J = 3.2 Hz); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -70.16. **HRMS** (ESI) m/z Calcd for $C_{17}H_{13}F_3NO_2$ $[M+H]^+$: 320.0893; Found: 320.0897.



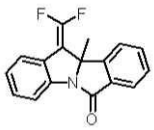
***N*,*N*-dibutyl-10b-methyl-6-oxo-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indole-11-carboxamide (4h)**: New compound. 33.8 mg, 43% yield. Light yellow solid. m.p.: 138.4-139.2 ℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 (d, J = 7.5 Hz, 1H), 7.75 (d, J = 7.1 Hz, 1H), 7.53 (td, J = 7.5, 1.2 Hz, 1H), 7.45 (t, J = 7.5 Hz, 1H), 7.35 (q, J = 7.4 Hz, 2H), 7.18 (d, J = 6.5 Hz, 1H), 7.10 (td, J = 7.5, 1.1 Hz, 1H), 4.27 (s, 1H), 3.75-3.00 (m, 3H), 2.85-2.62 (m, 1H), 1.67 (s, 5H), 1.43 (s, 2H), 1.07-1.02 (m, 3H), 1.01-0.77 (m, 4H), 0.70 (t, J = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.5, 148.0, 140.7, 135.8, 133.8, 132.3, 129.0, 128.8, 125.1, 124.6, 121.6, 117.8, 74.4, 52.2, 48.3, 46.3, 32.5, 29.5, 28.1, 20.2, 20.1, 14.0, 13.8. **HRMS** (ESI) m/z Calcd for $C_{25}H_{31}N_2O_2$ $[M+H]^+$: 391.2380; Found: 391.2385.

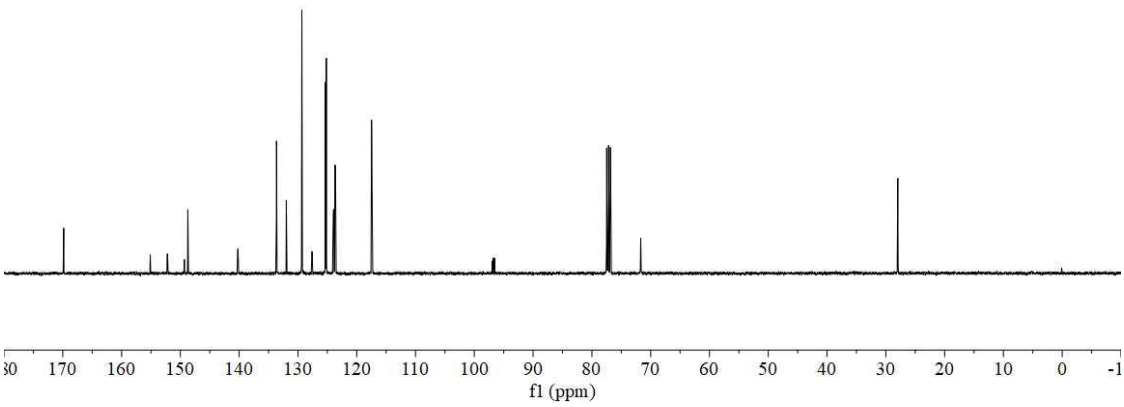
6. Copies of NMR spectra

^{1}H NMR of product 3a in $CDCl_3$ (400 MHz)

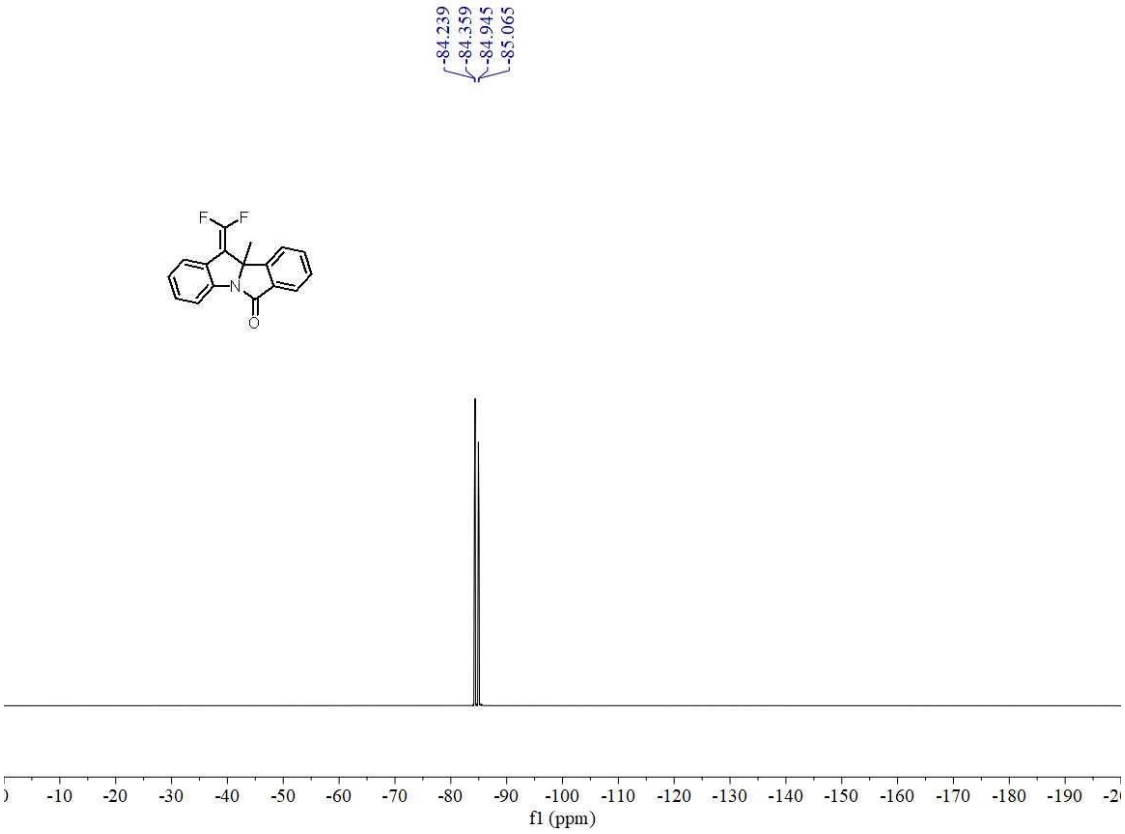


^{13}C NMR of product 3a in $CDCl_3$ (100 MHz)

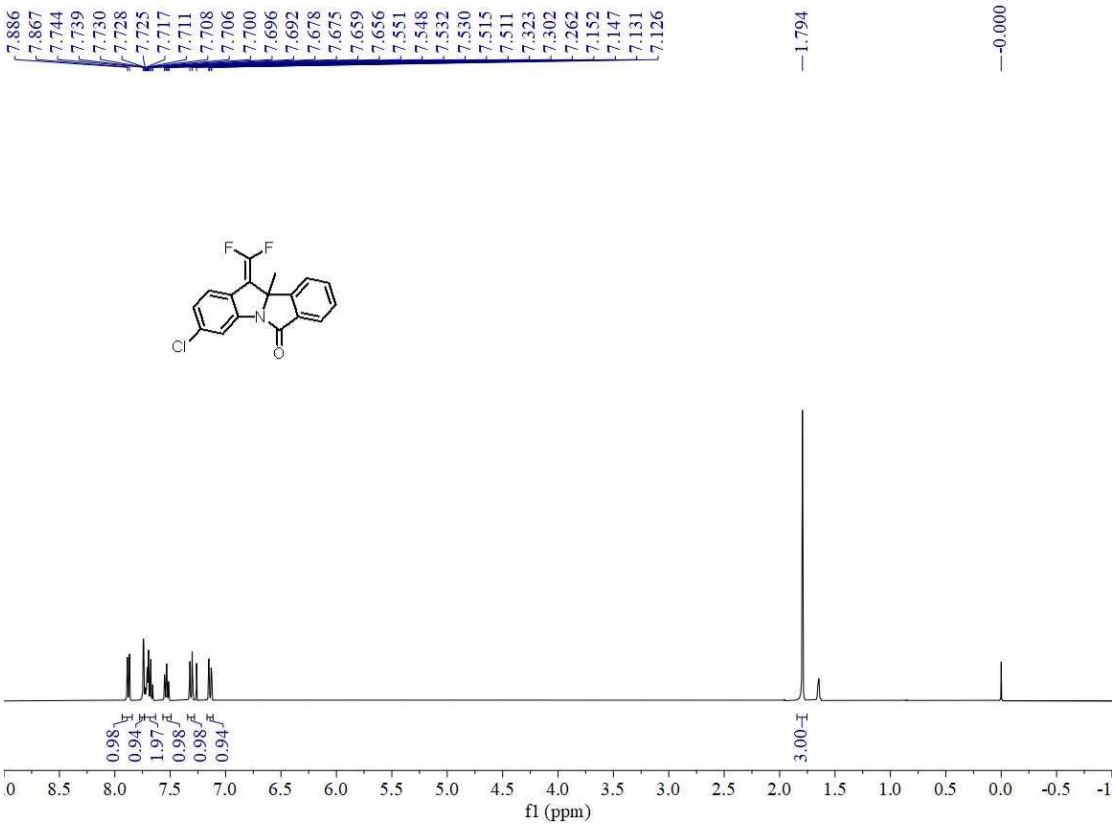




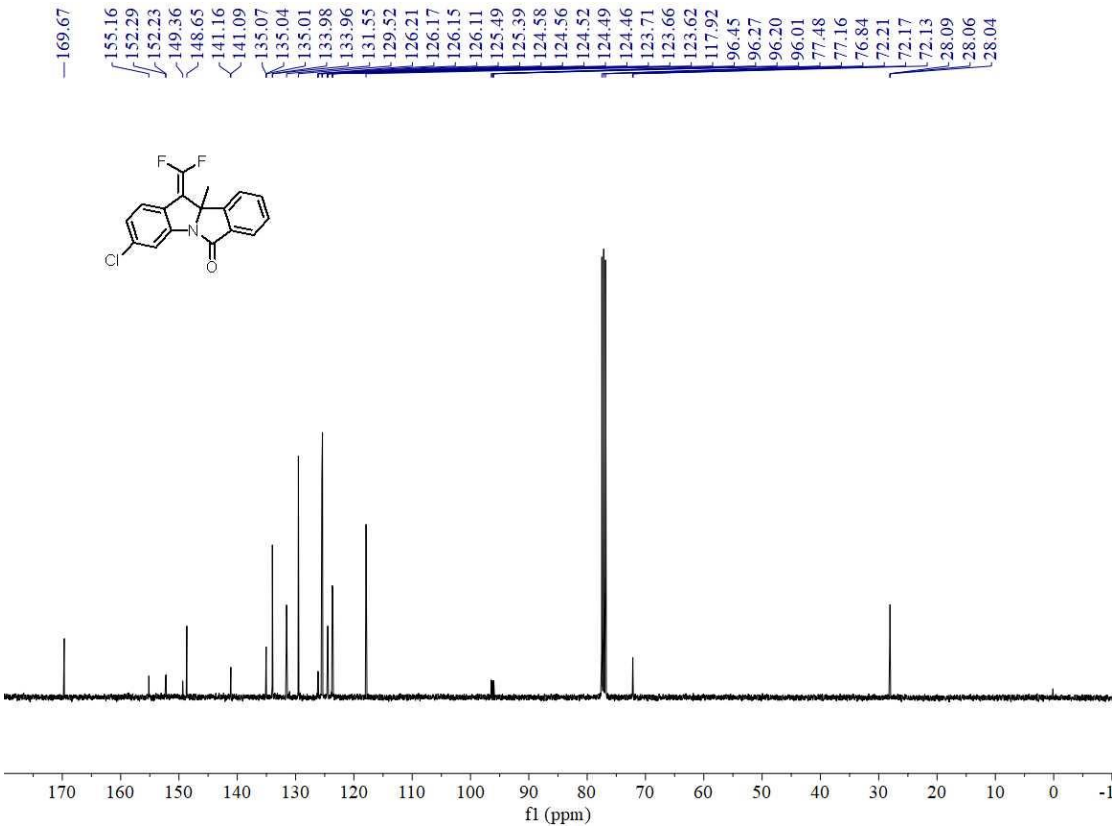
^{19}F NMR of product 3a in $CDCl_3$ (376 MHz)



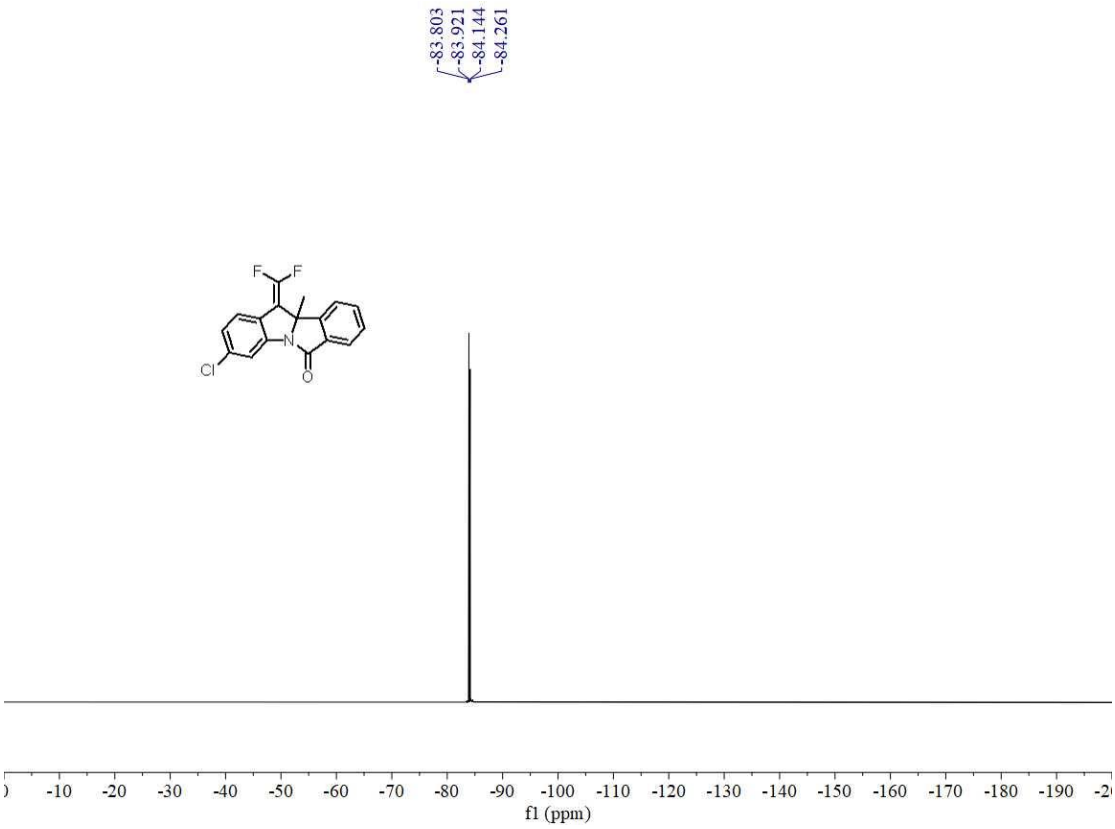
^{1}H NMR of product 3b in $CDCl_3$ (400 MHz)



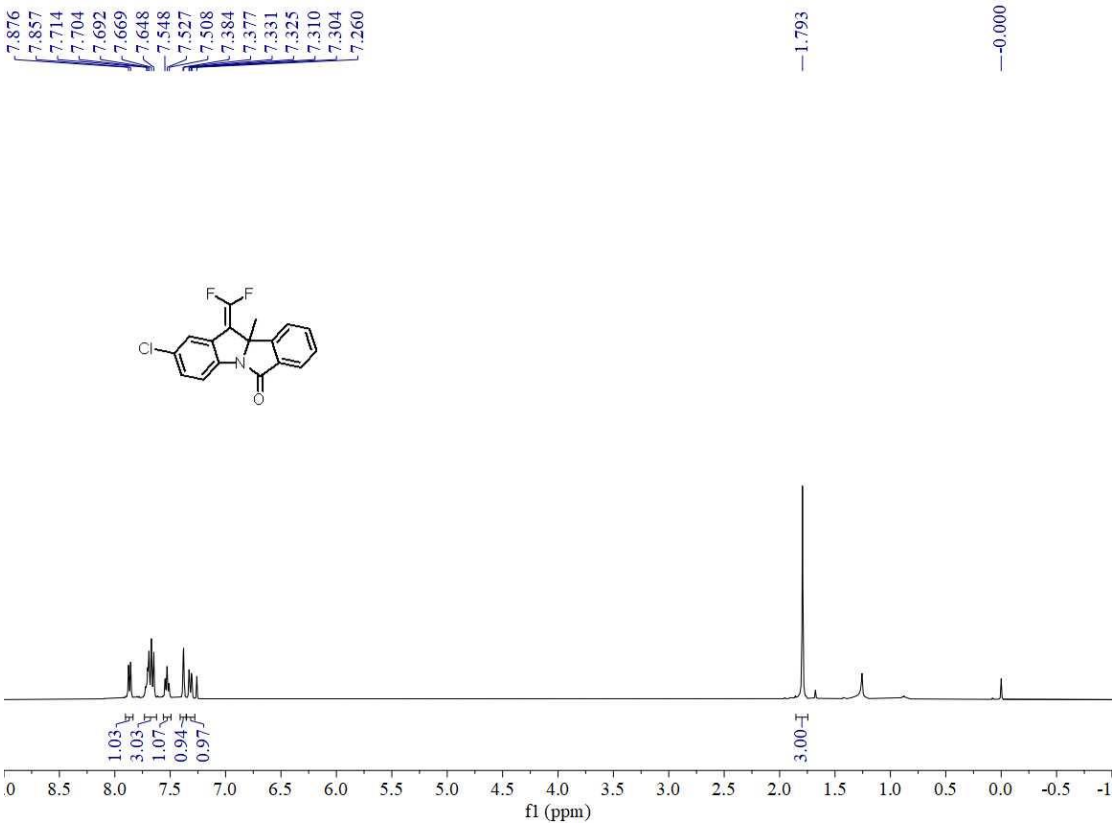
^{13}C NMR of product 3b in $CDCl_3$ (100 MHz)



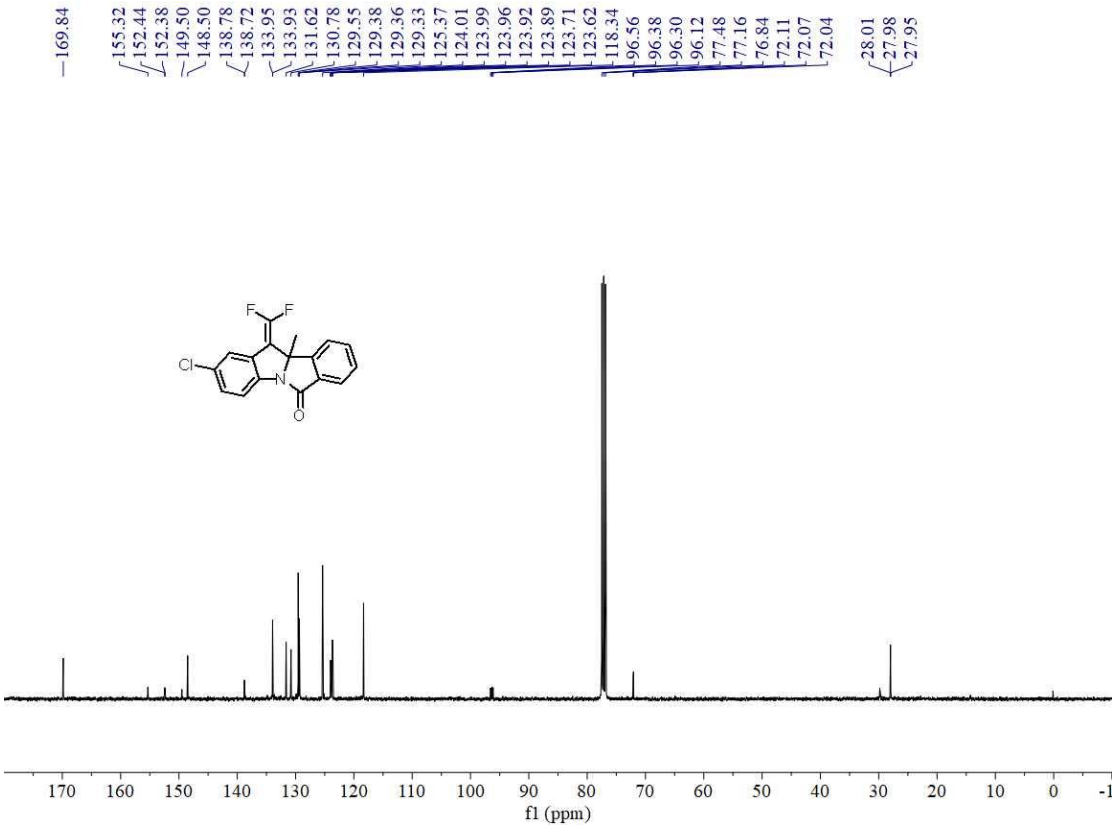
^{19}F NMR of product 3b in $CDCl_3$ (376 MHz)



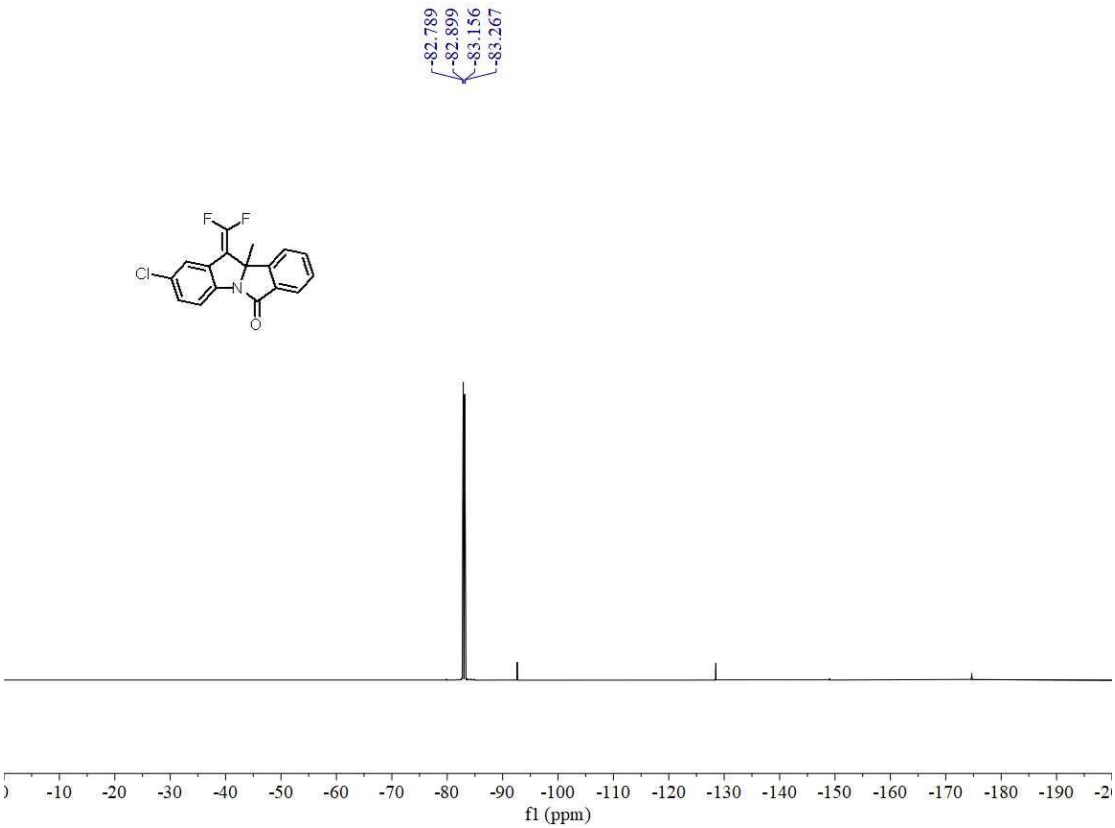
^{1}H NMR of product 3c in $CDCl_3$ (400 MHz)



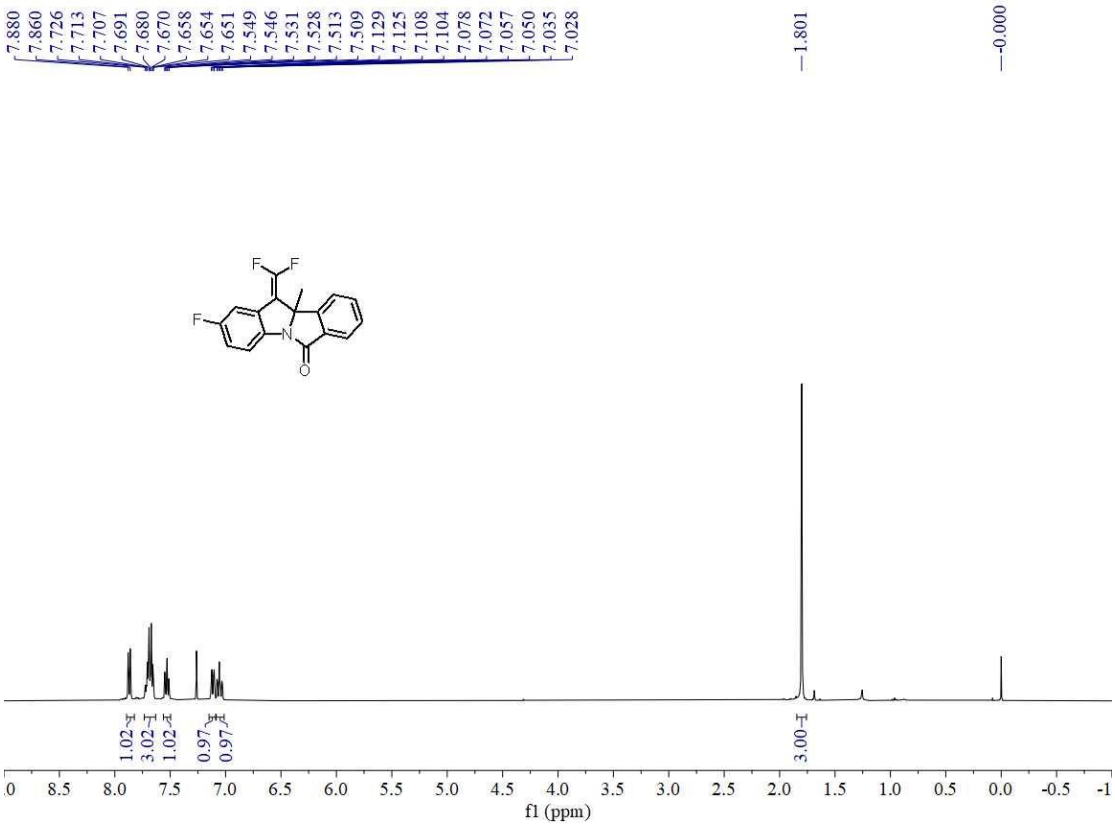
^{13}C NMR of product 3c in $CDCl_3$ (100 MHz)



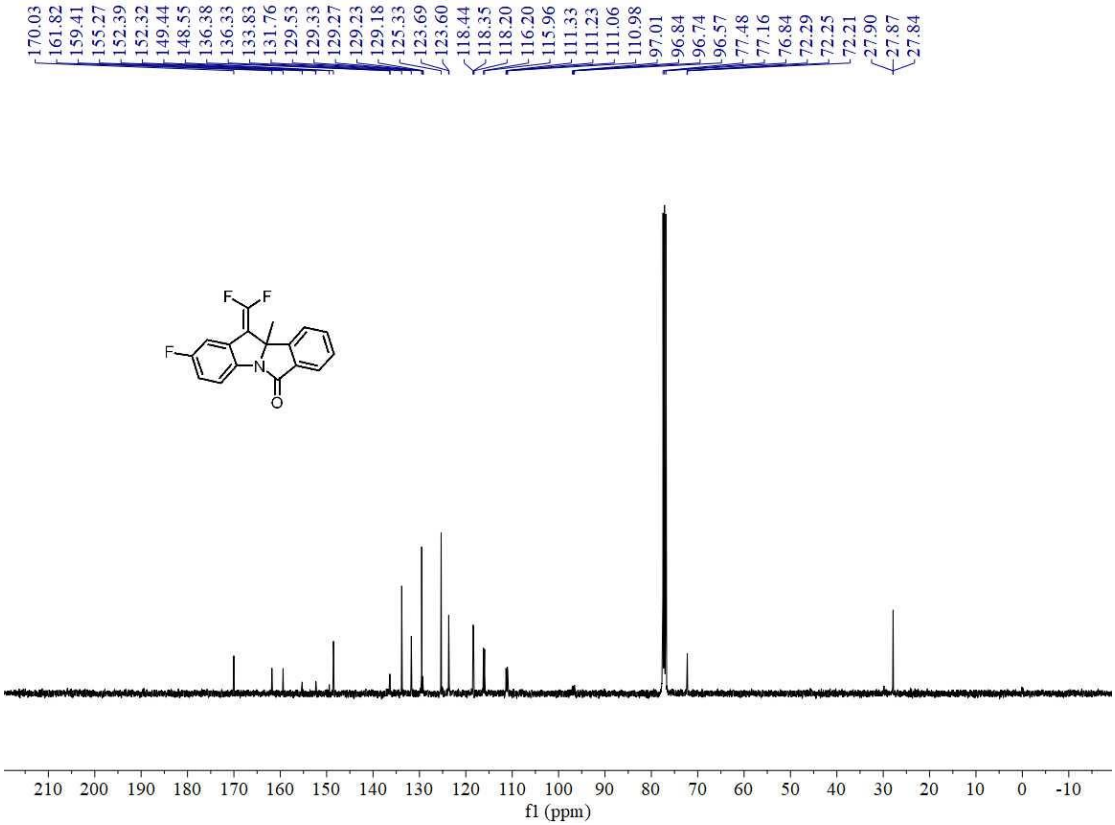
^{19}F NMR of product 3c in $CDCl_3$ (376 MHz)



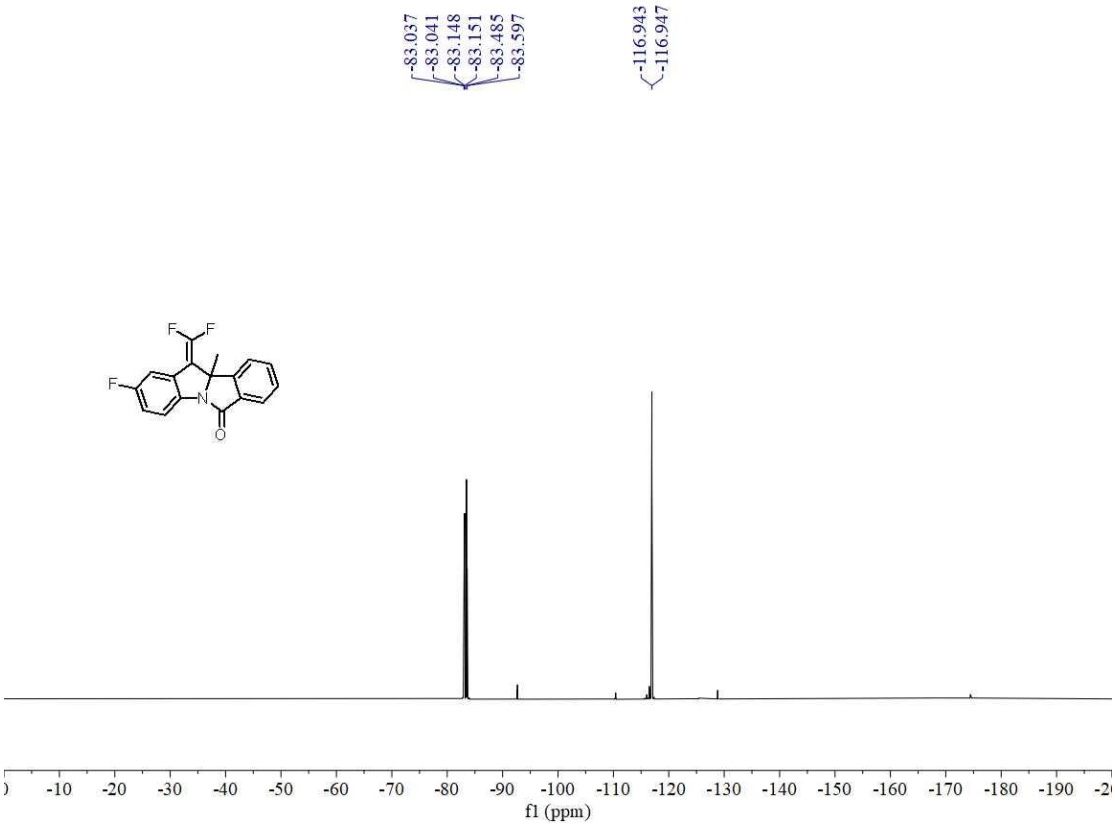
^{1}H NMR of product 3d in $CDCl_3$ (400 MHz)



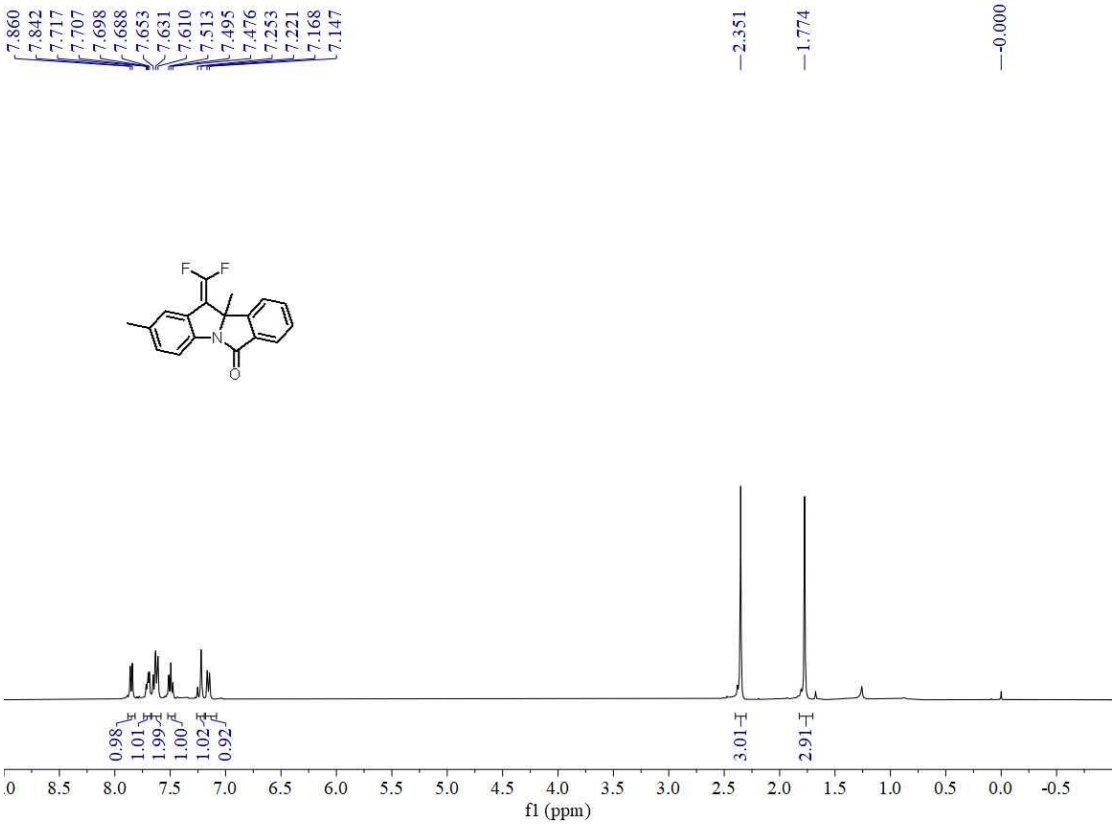
^{13}C NMR of product 3d in $CDCl_3$ (100 MHz)



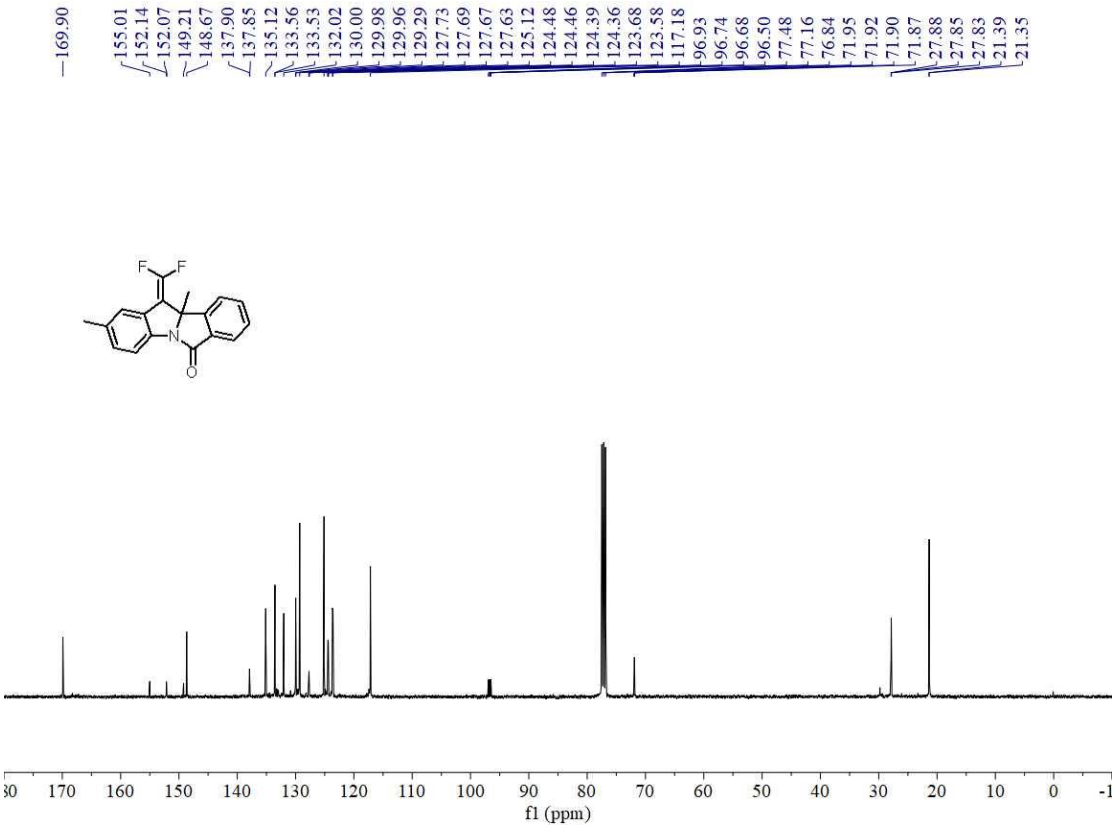
^{19}F NMR of product 3d in $CDCl_3$ (376 MHz)



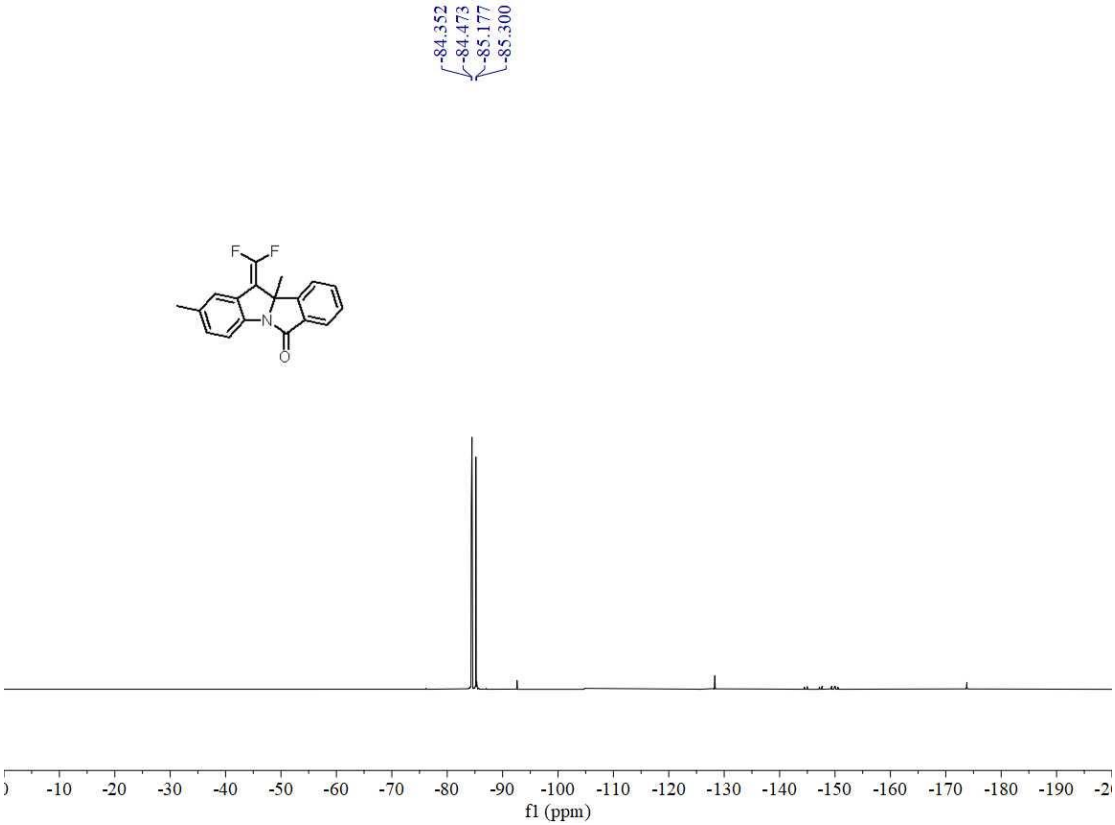
^{1}H NMR of product 3e in $CDCl_3$ (400 MHz)



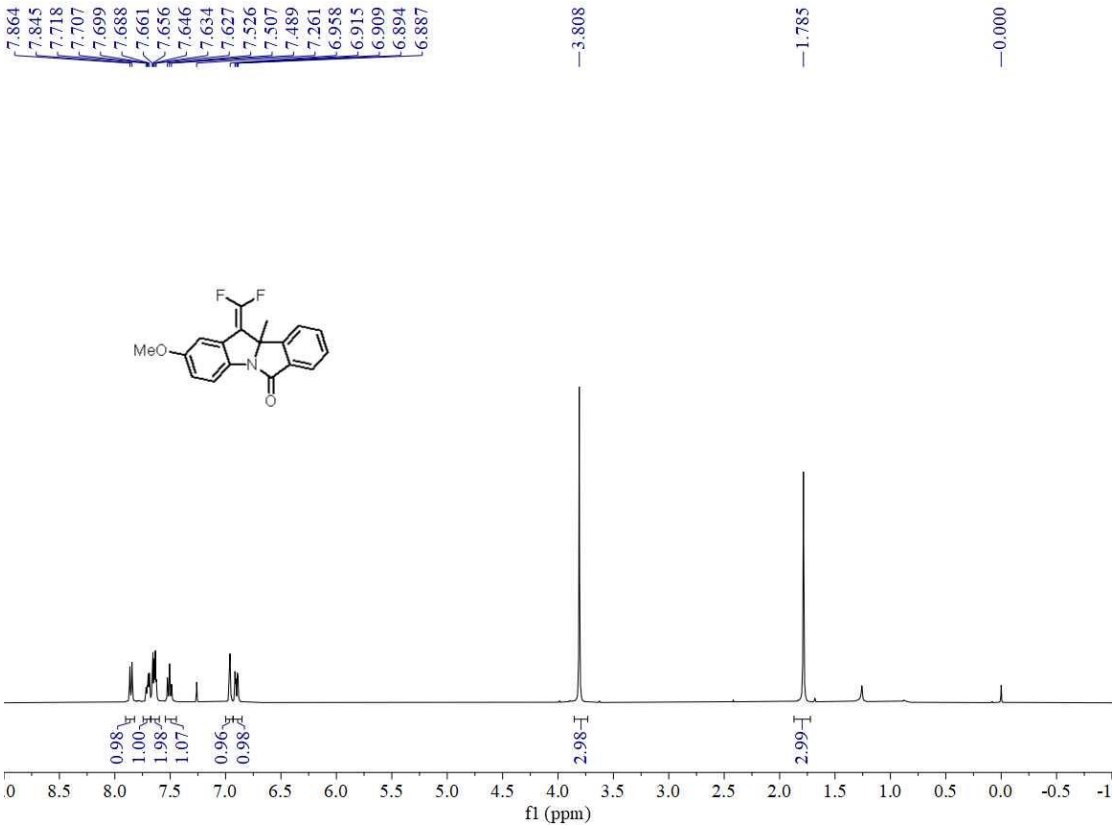
^{13}C NMR of product 3e in $CDCl_3$ (100 MHz)



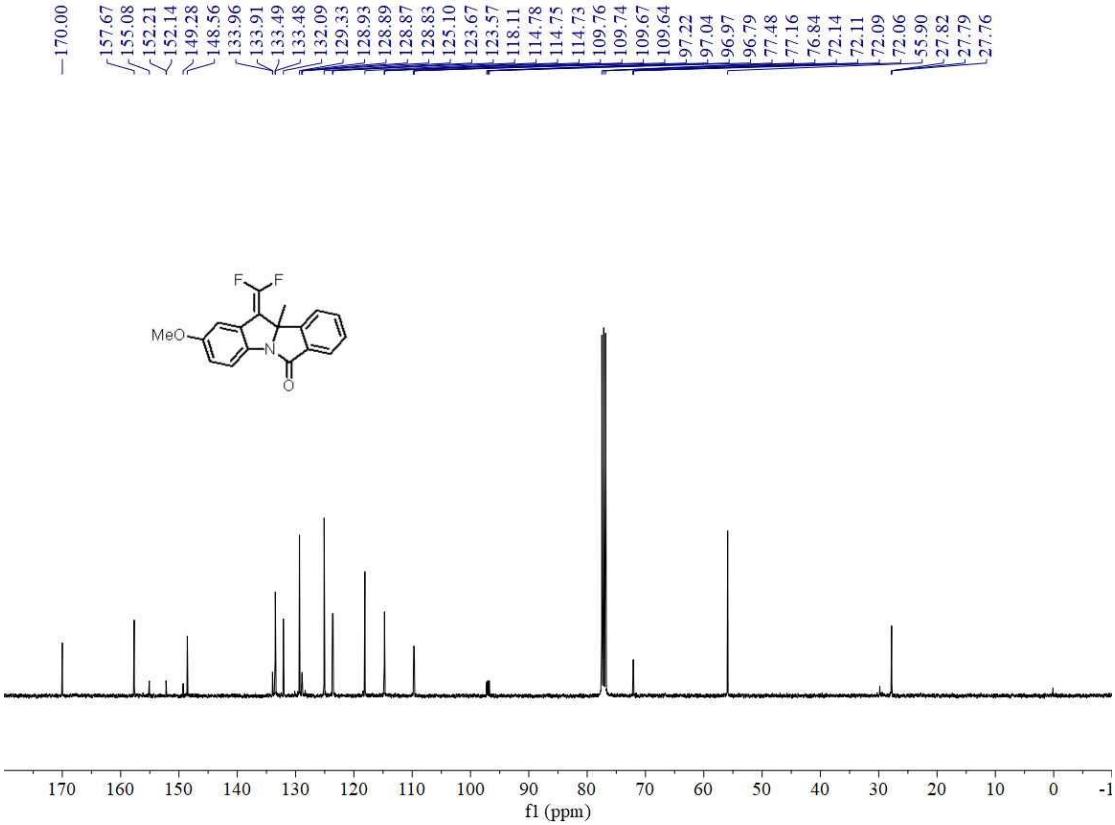
^{19}F NMR of product 3e in $CDCl_3$ (376 MHz)



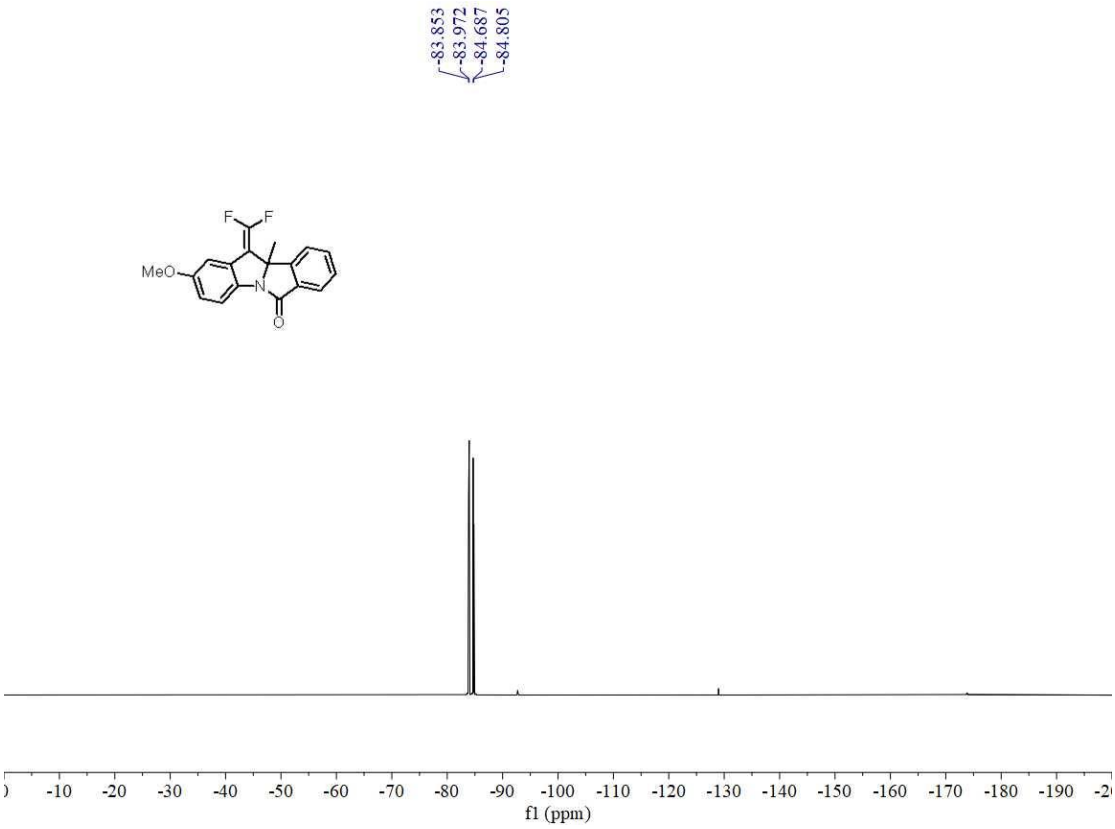
^{1}H NMR of product 3f in $CDCl_3$ (400 MHz)



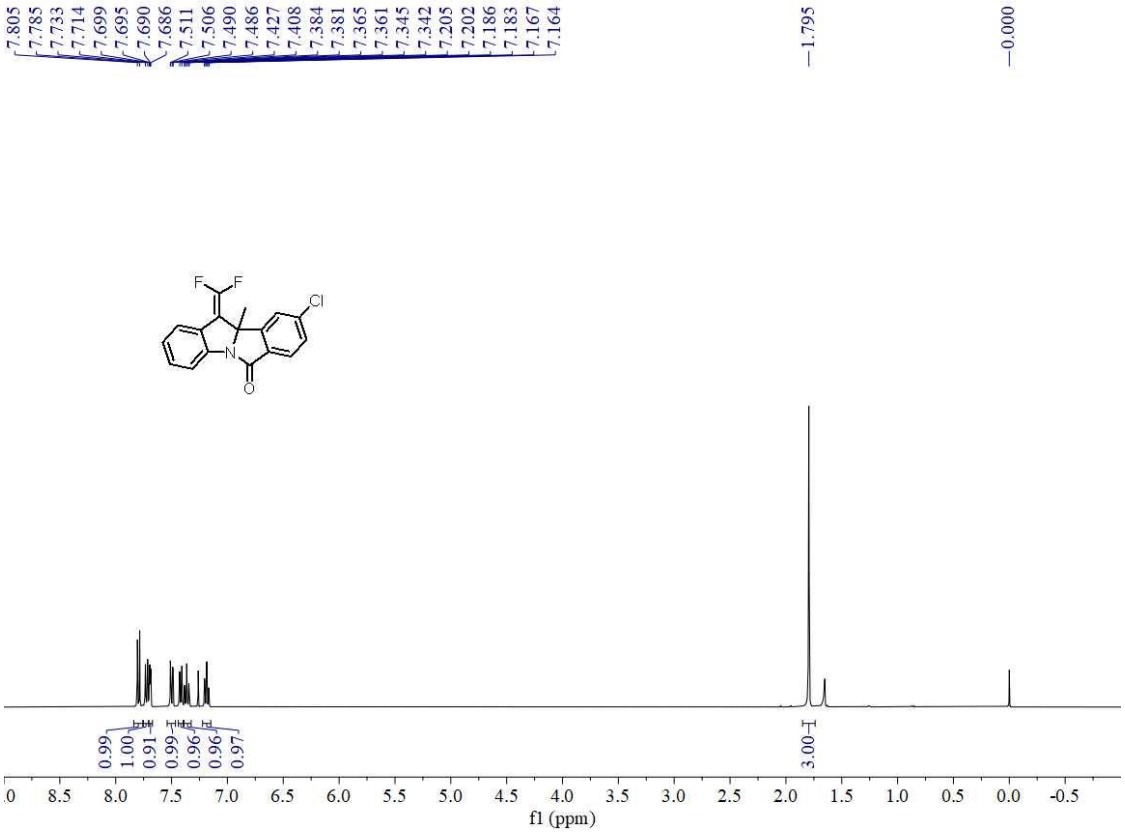
^{13}C NMR of product 3f in $CDCl_3$ (100 MHz)



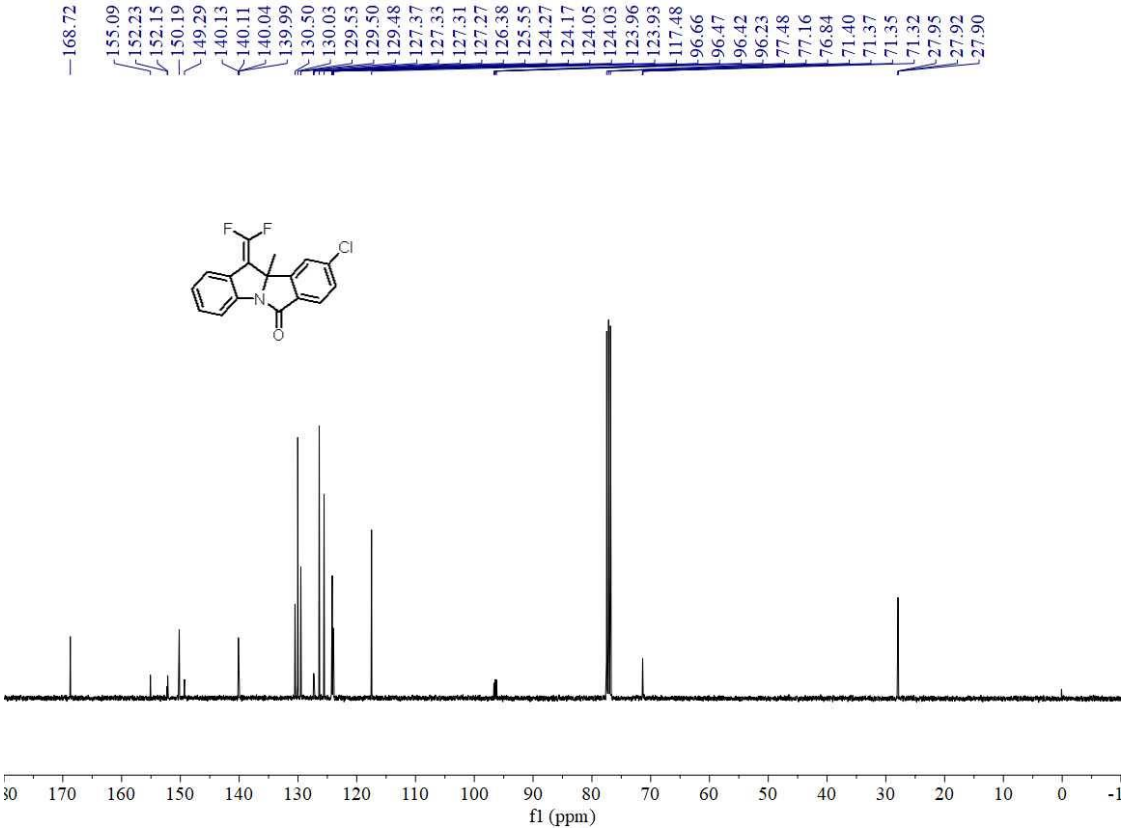
^{19}F NMR of product 3f in $CDCl_3$ (376 MHz)



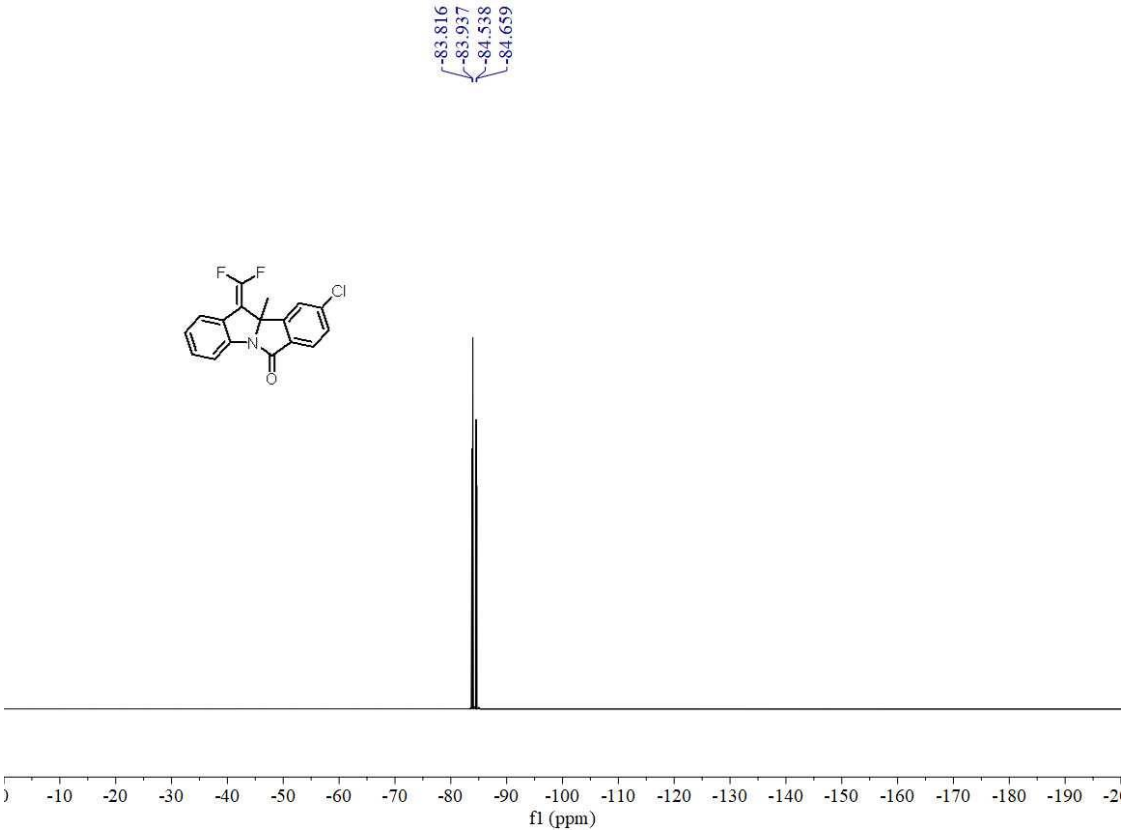
^{1}H NMR of product 3g in $CDCl_3$ (400 MHz)



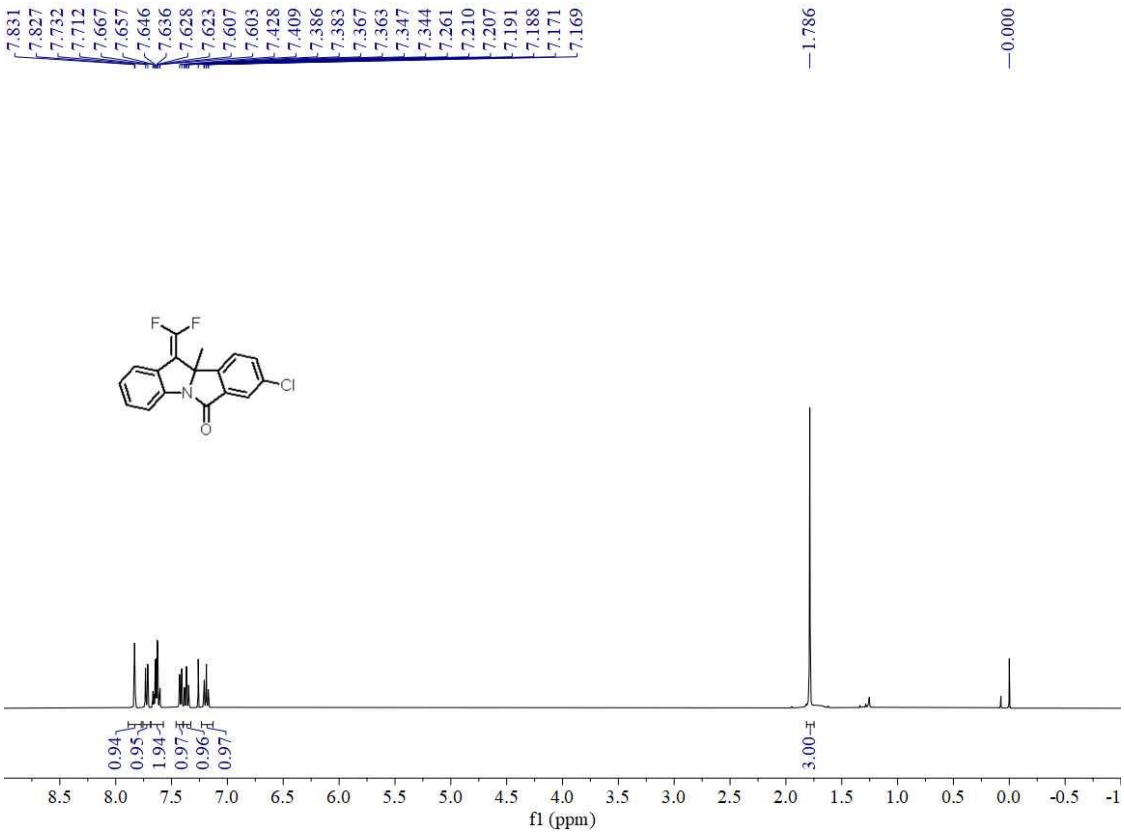
^{13}C NMR of product 3g in $CDCl_3$ (100 MHz)



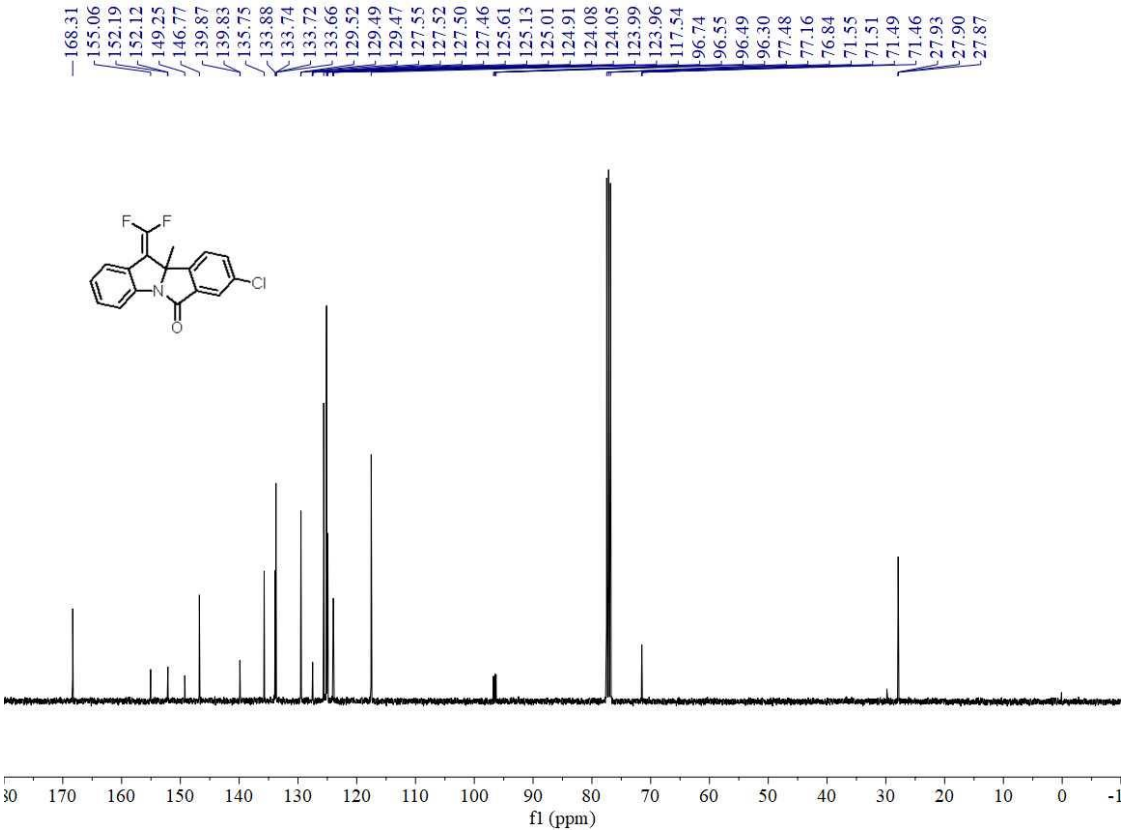
^{19}F NMR of product 3g in $CDCl_3$ (376 MHz)



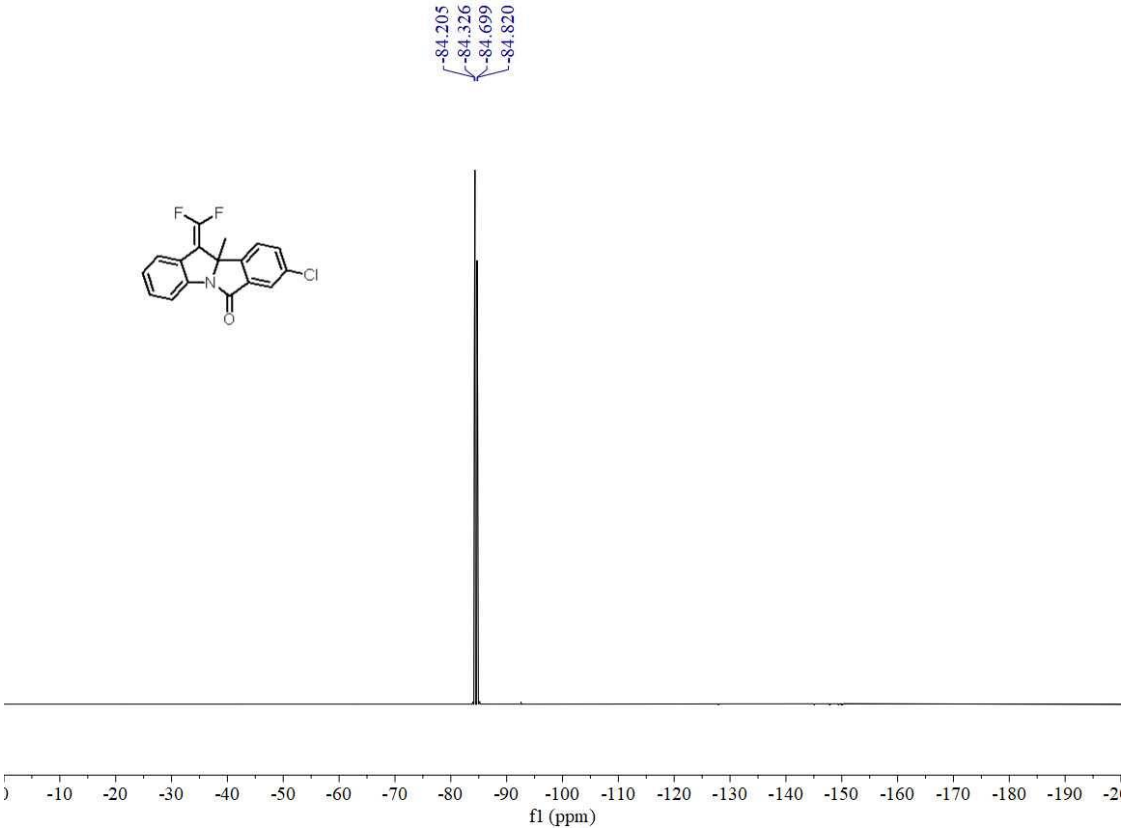
^{1}H NMR of product 3h in $CDCl_3$ (400 MHz)



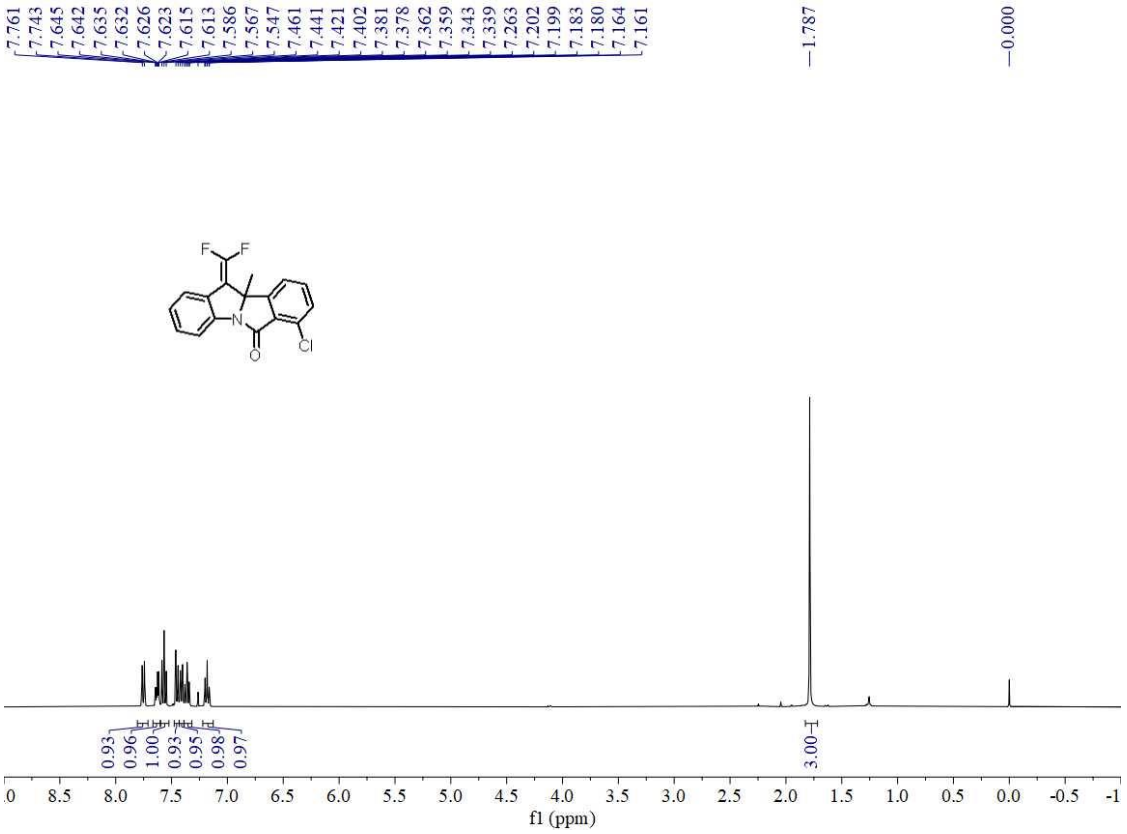
^{13}C NMR of product 3h in $CDCl_3$ (100 MHz)



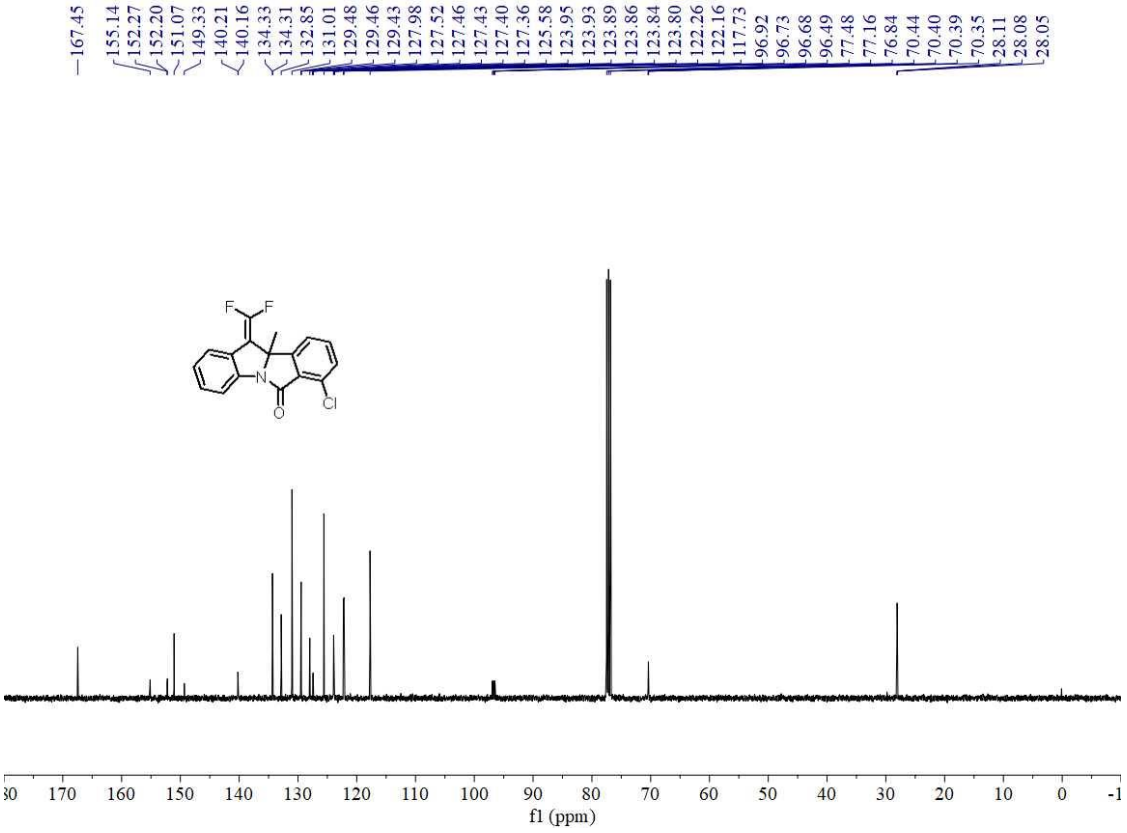
^{19}F NMR of product 3h in $CDCl_3$ (376 MHz)



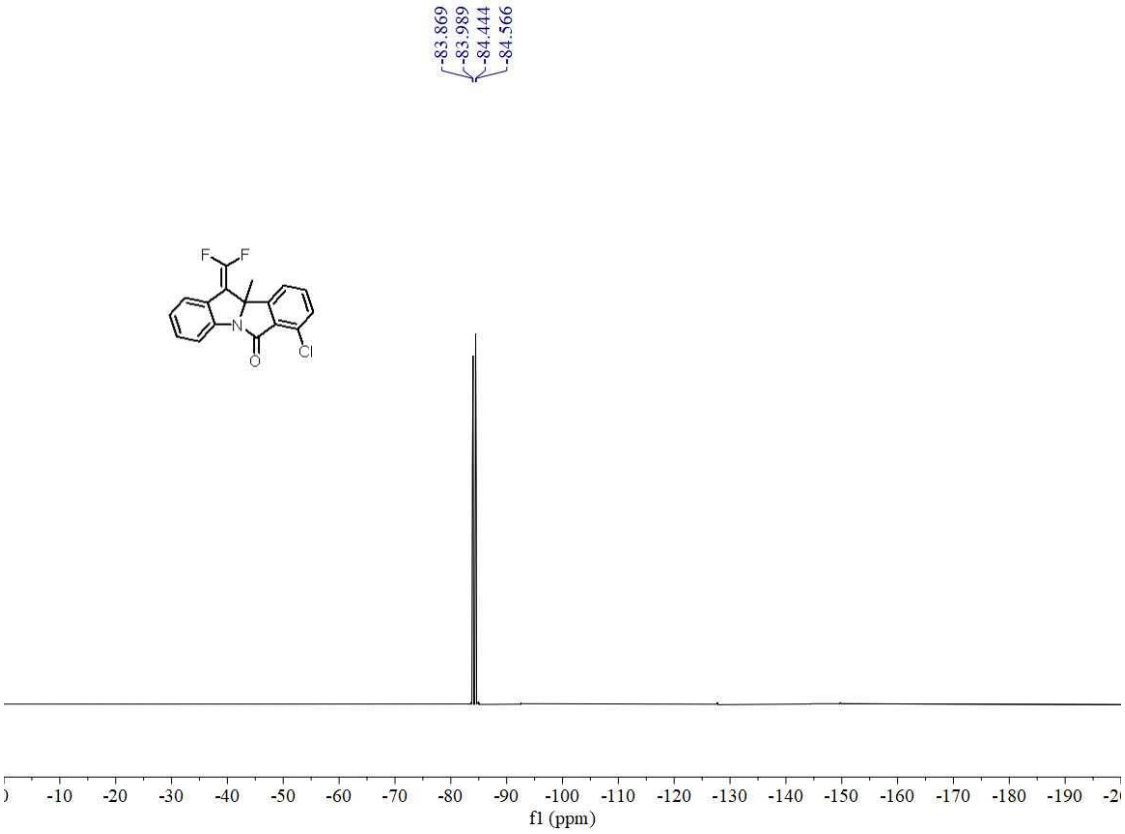
^{1}H NMR of product 3i in $CDCl_3$ (400 MHz)



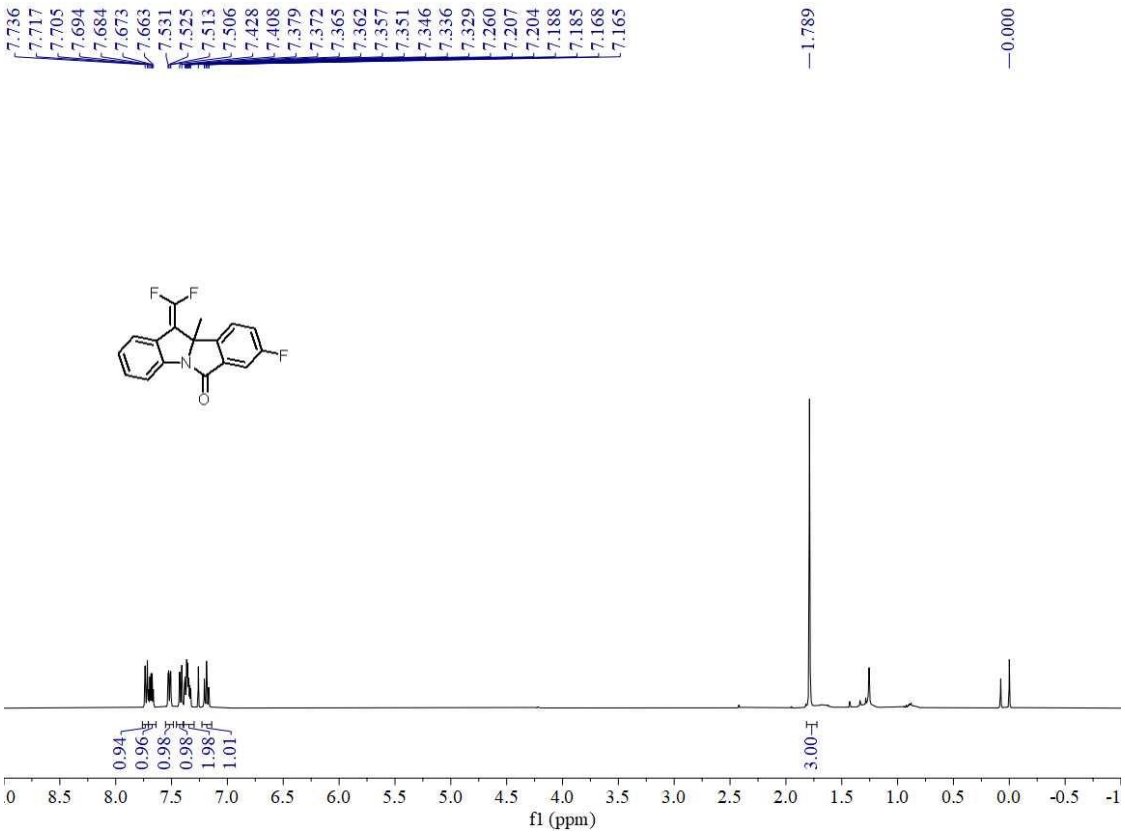
^{13}C NMR of product 3i in $CDCl_3$ (100 MHz)



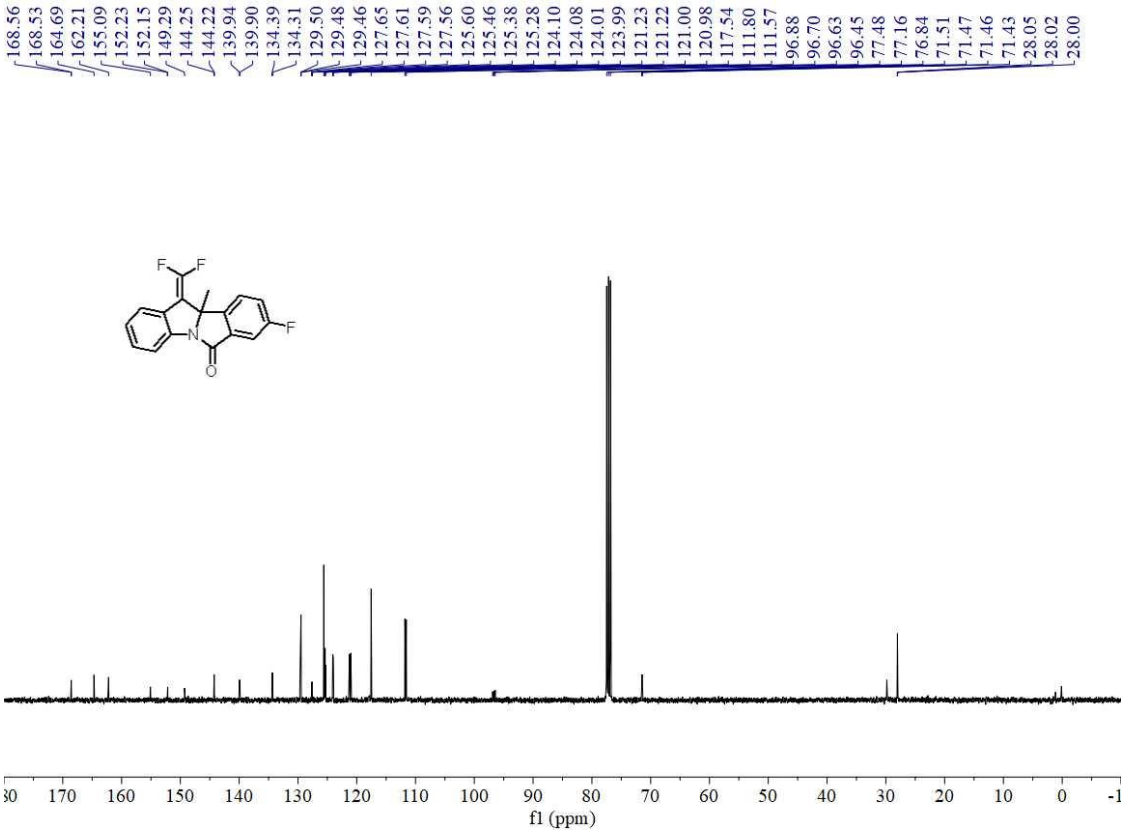
^{19}F NMR of product 3i in $CDCl_3$ (376 MHz)



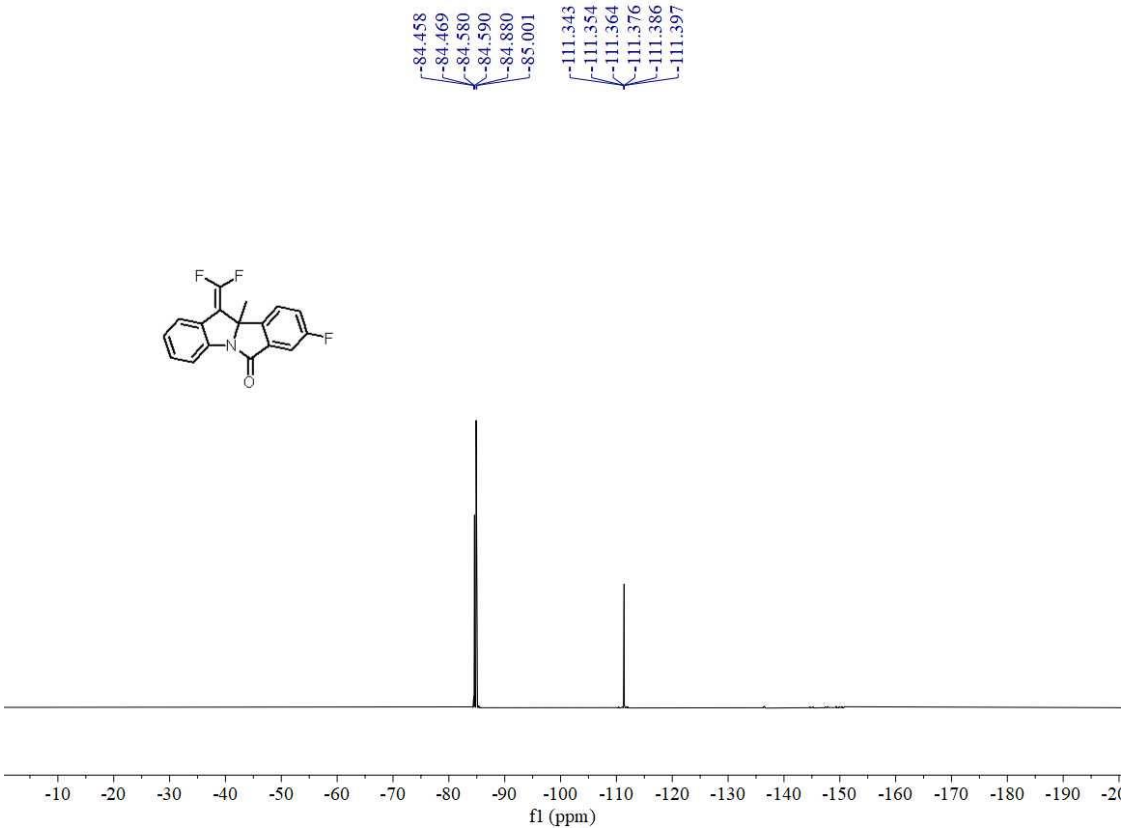
^{1}H NMR of product 3j in $CDCl_3$ (400 MHz)



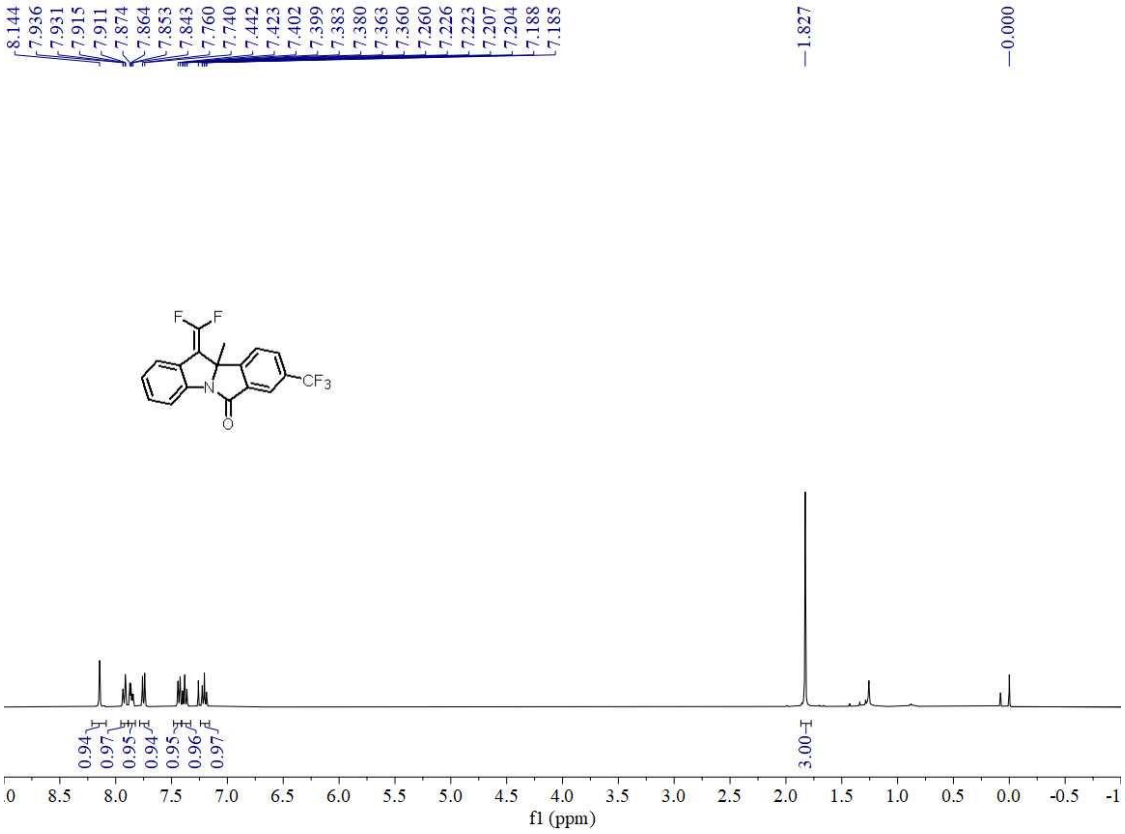
^{13}C NMR of product 3j in $CDCl_3$ (100 MHz)



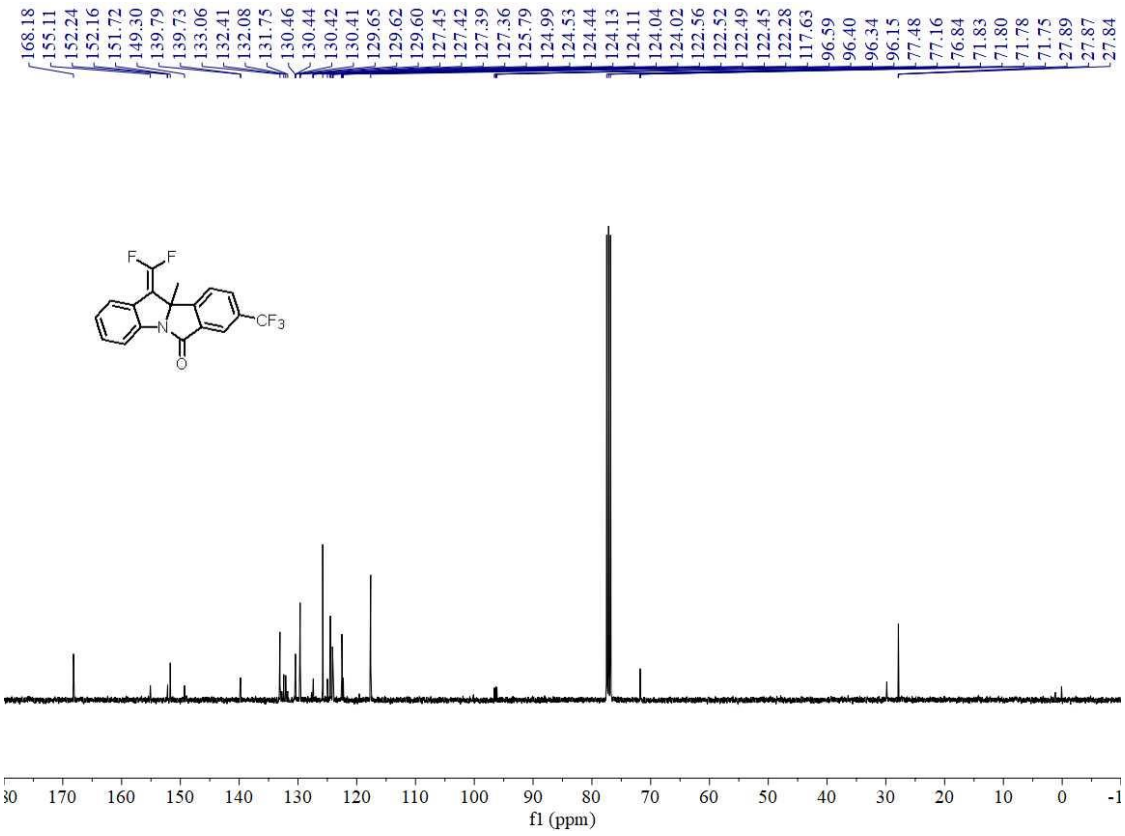
^{19}F NMR of product 3j in $CDCl_3$ (376 MHz)



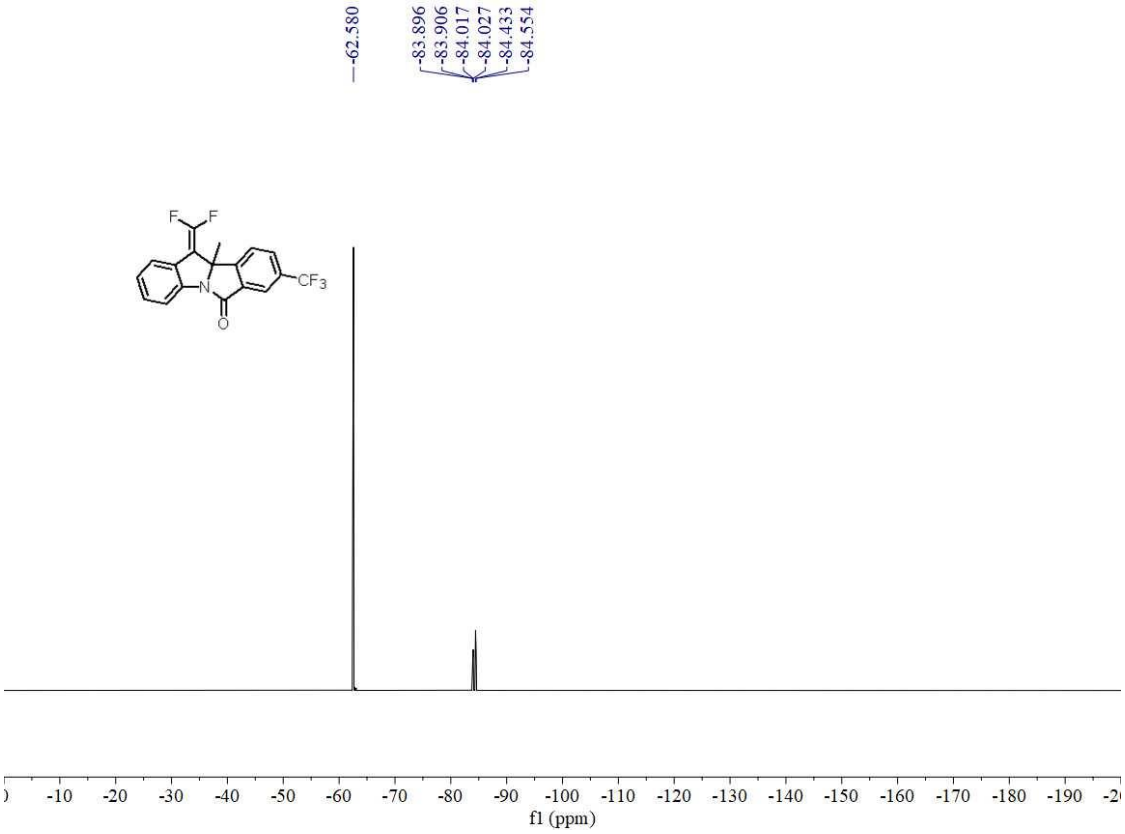
^{1}H NMR of product 3k in $CDCl_3$ (400 MHz)



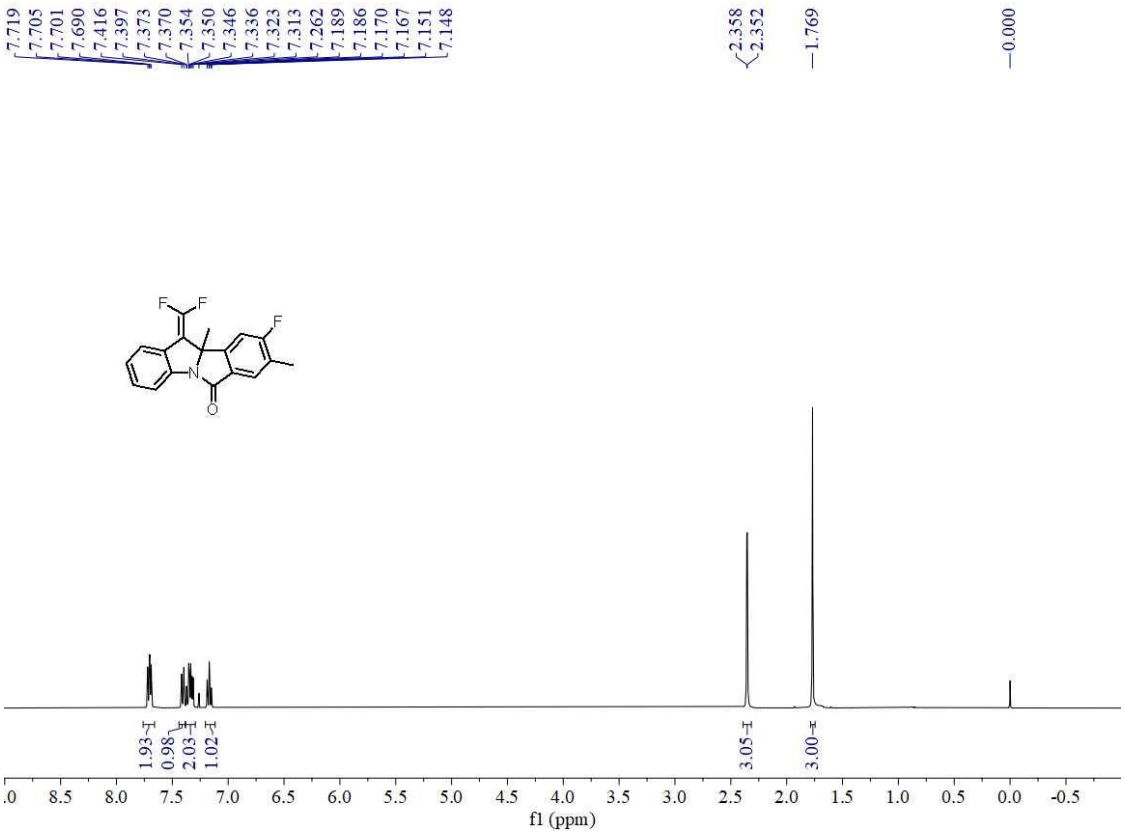
^{13}C NMR of product 3k in $CDCl_3$ (100 MHz)



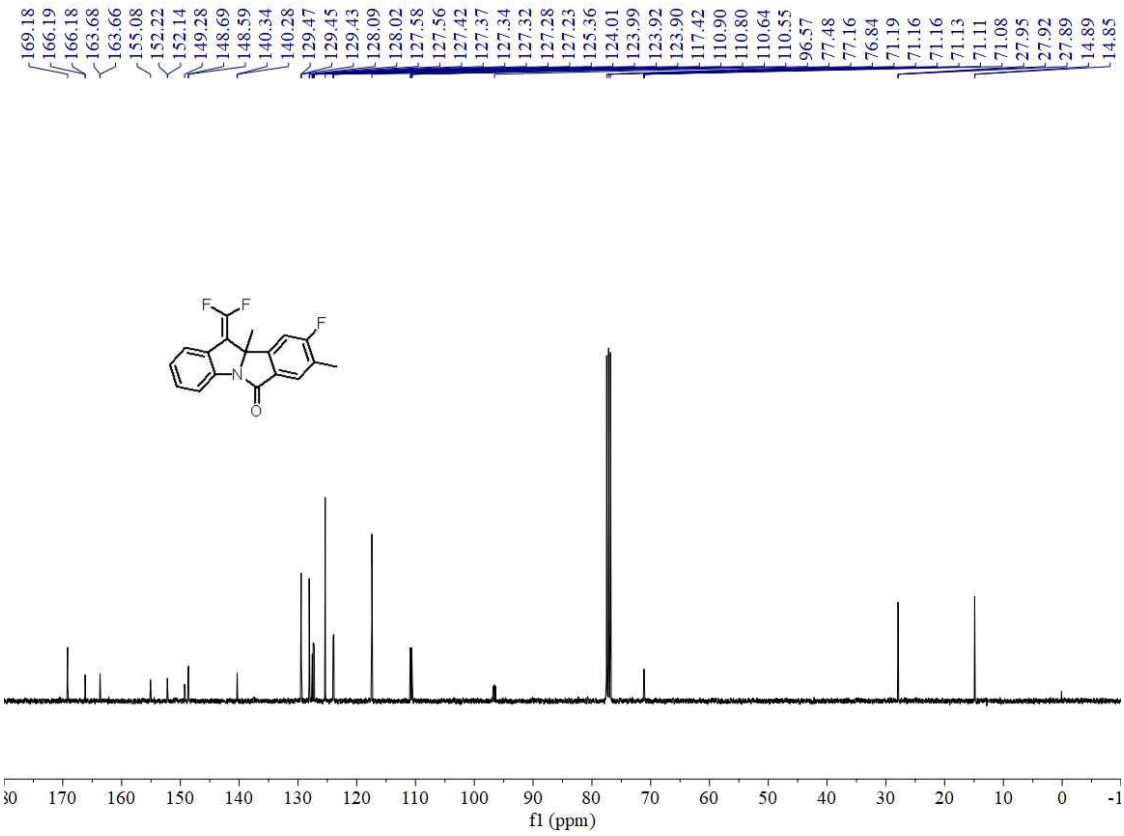
^{19}F NMR of product 3k in $CDCl_3$ (376 MHz)



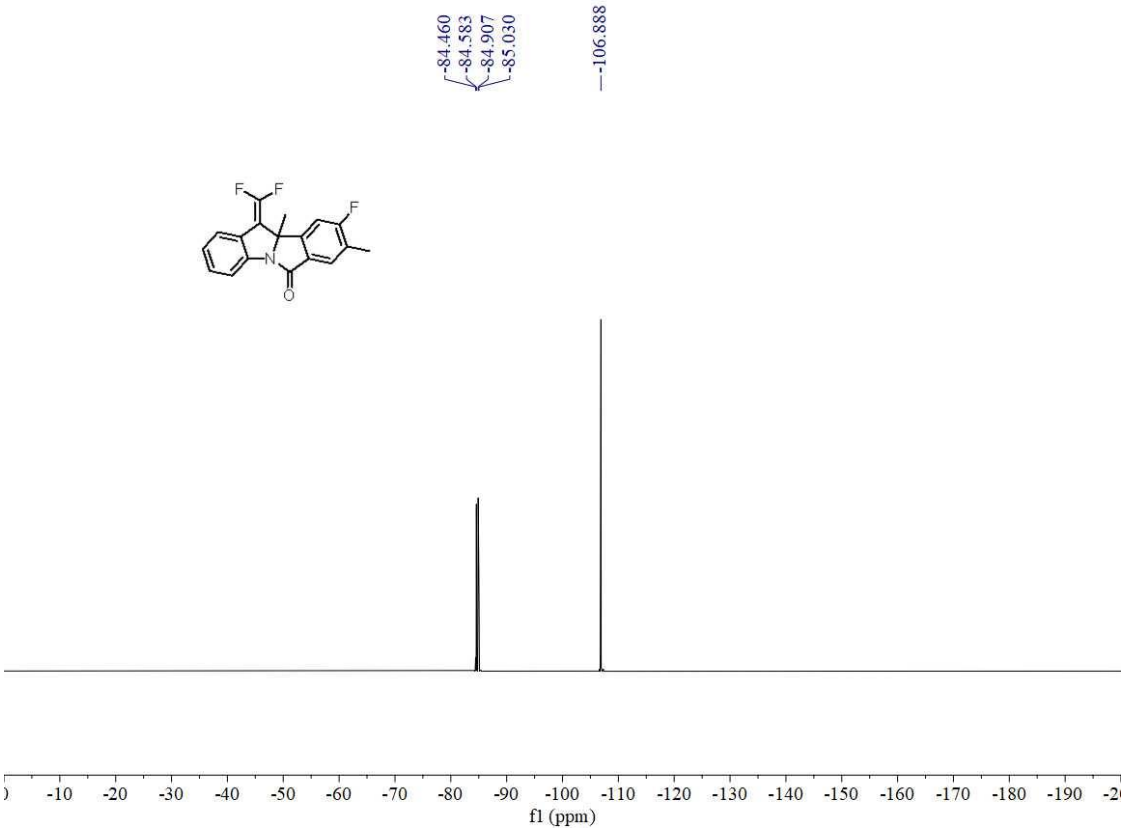
^{1}H NMR of product 3l in $CDCl_3$ (400 MHz)



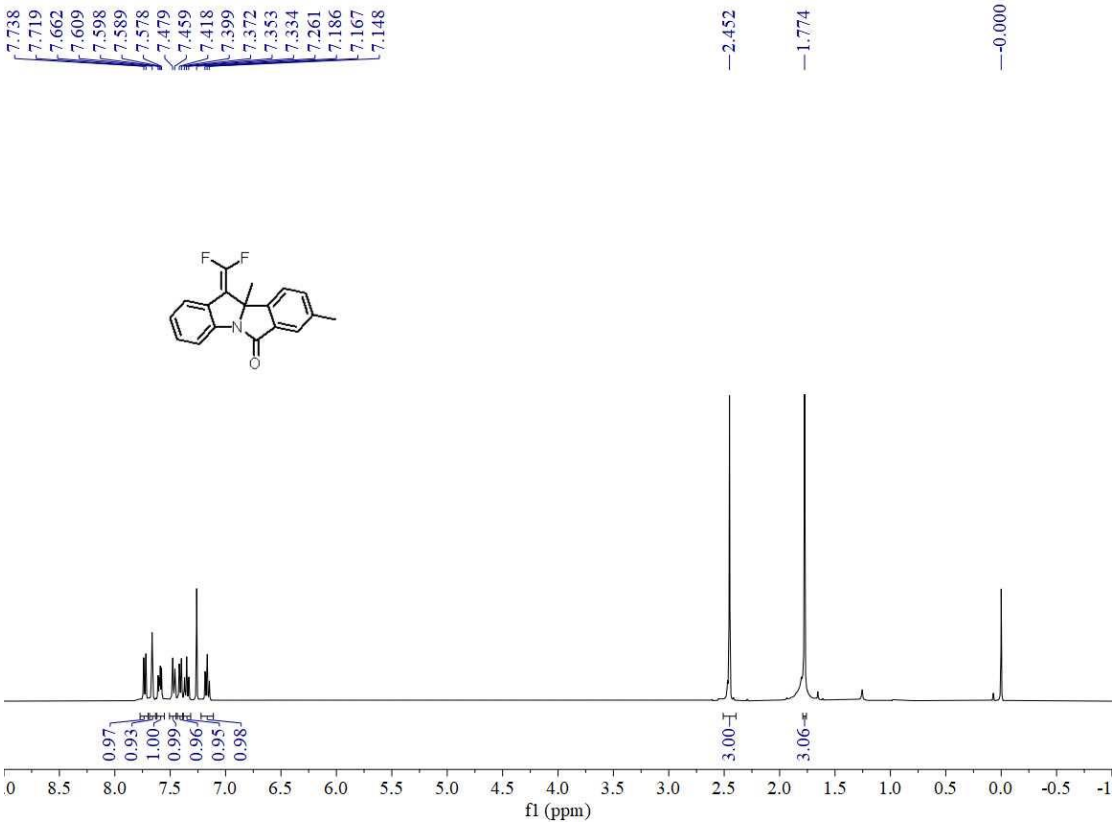
^{13}C NMR of product 3l in $CDCl_3$ (100 MHz)



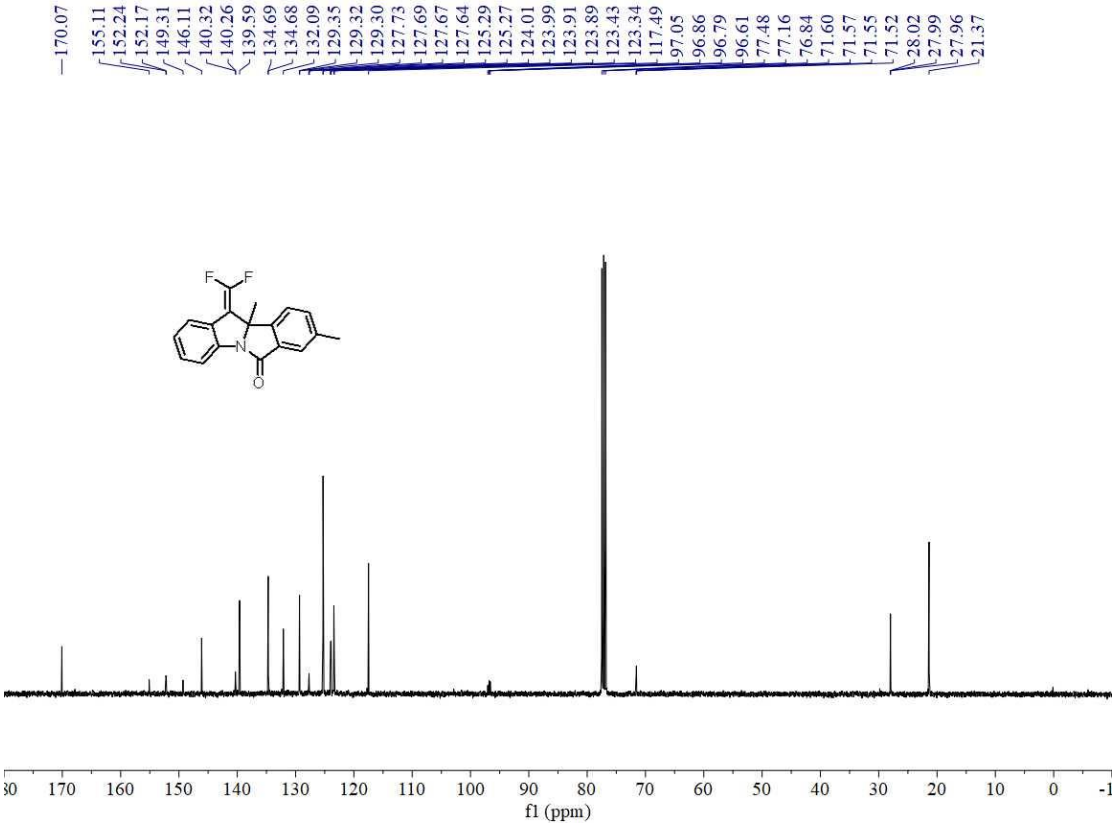
^{19}F NMR of product 3l in $CDCl_3$ (376 MHz)



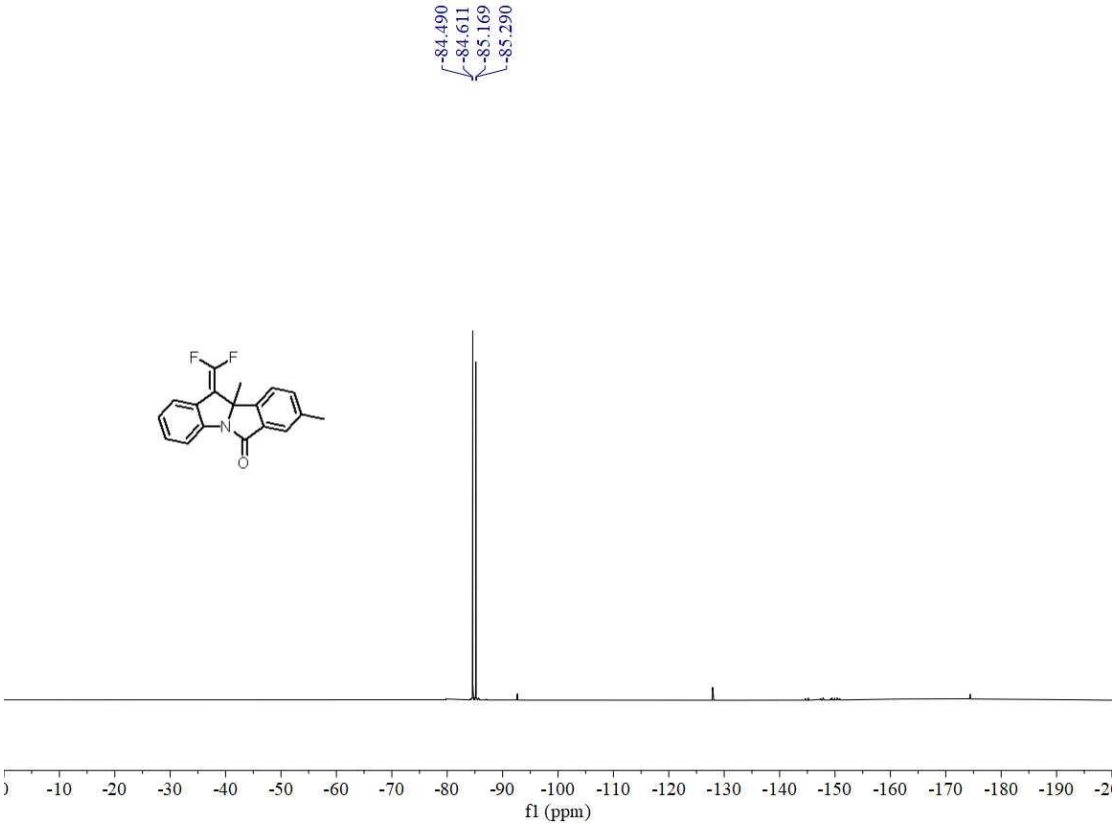
^{1}H NMR of product 3m in $CDCl_3$ (400 MHz)



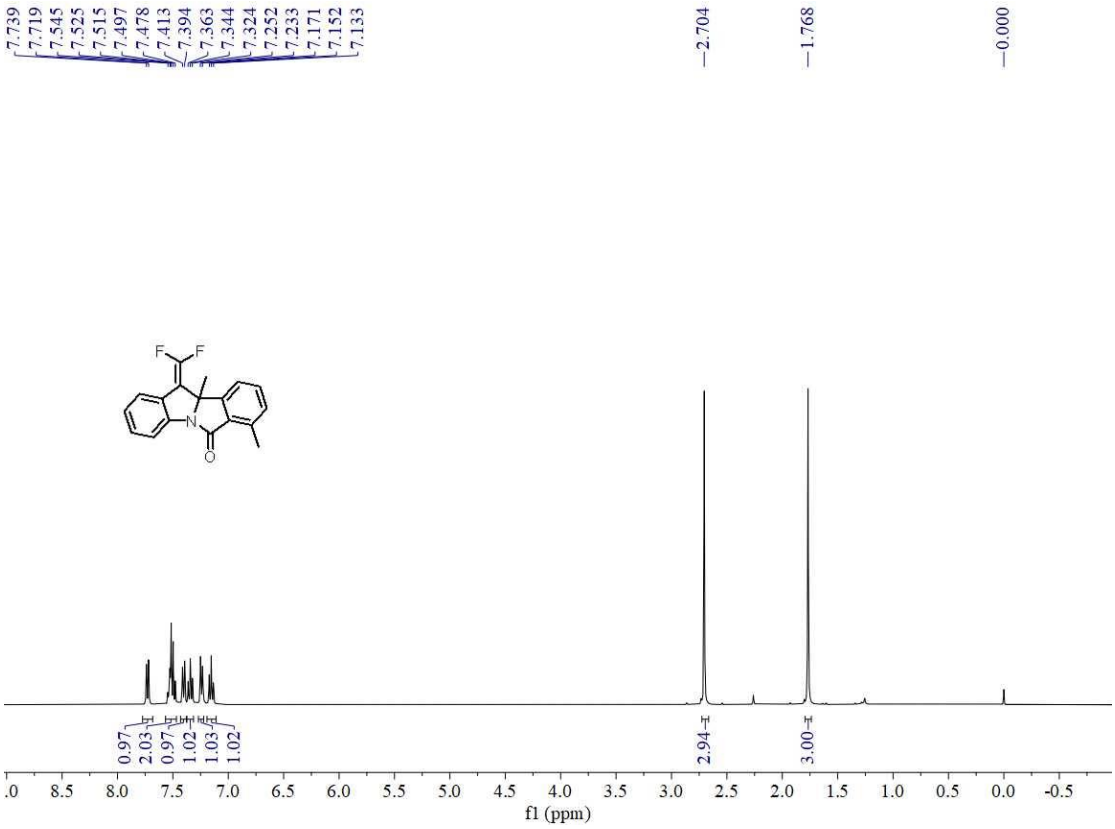
^{13}C NMR of product 3m in $CDCl_3$ (100 MHz)



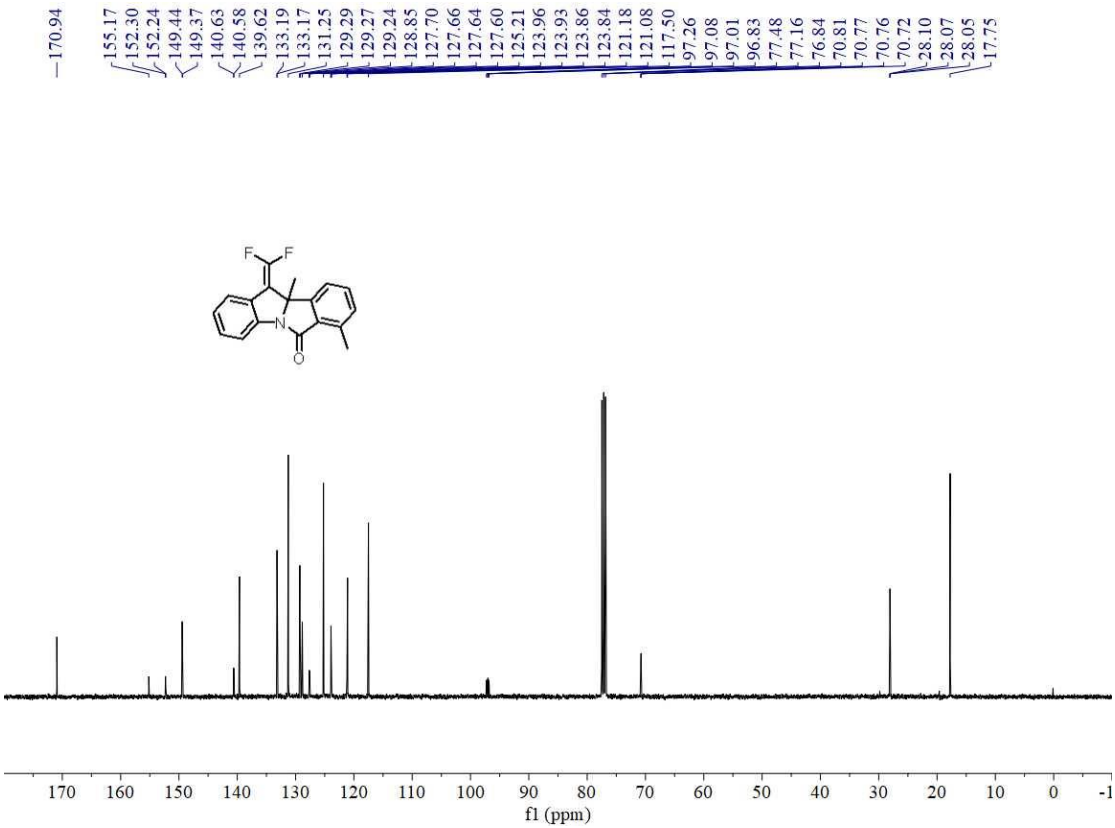
^{19}F NMR of product 3m in $CDCl_3$ (376 MHz)



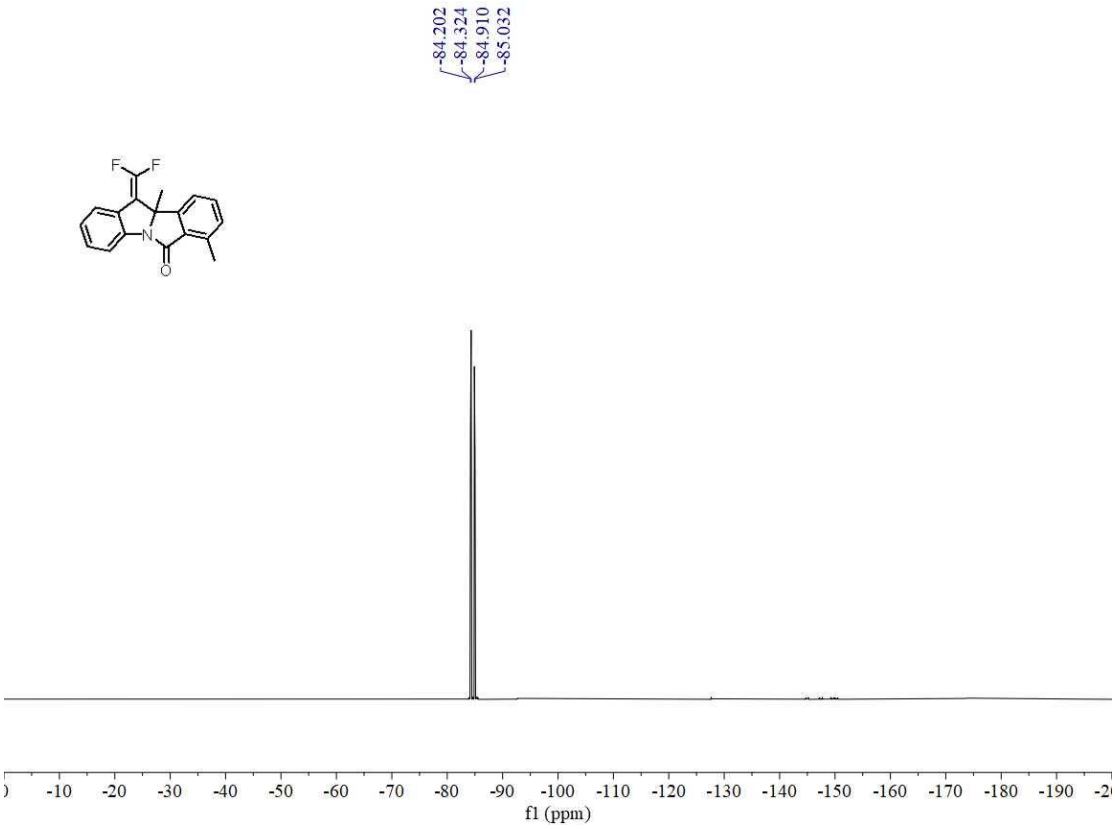
^{1}H NMR of product 3n in $CDCl_3$ (400 MHz)



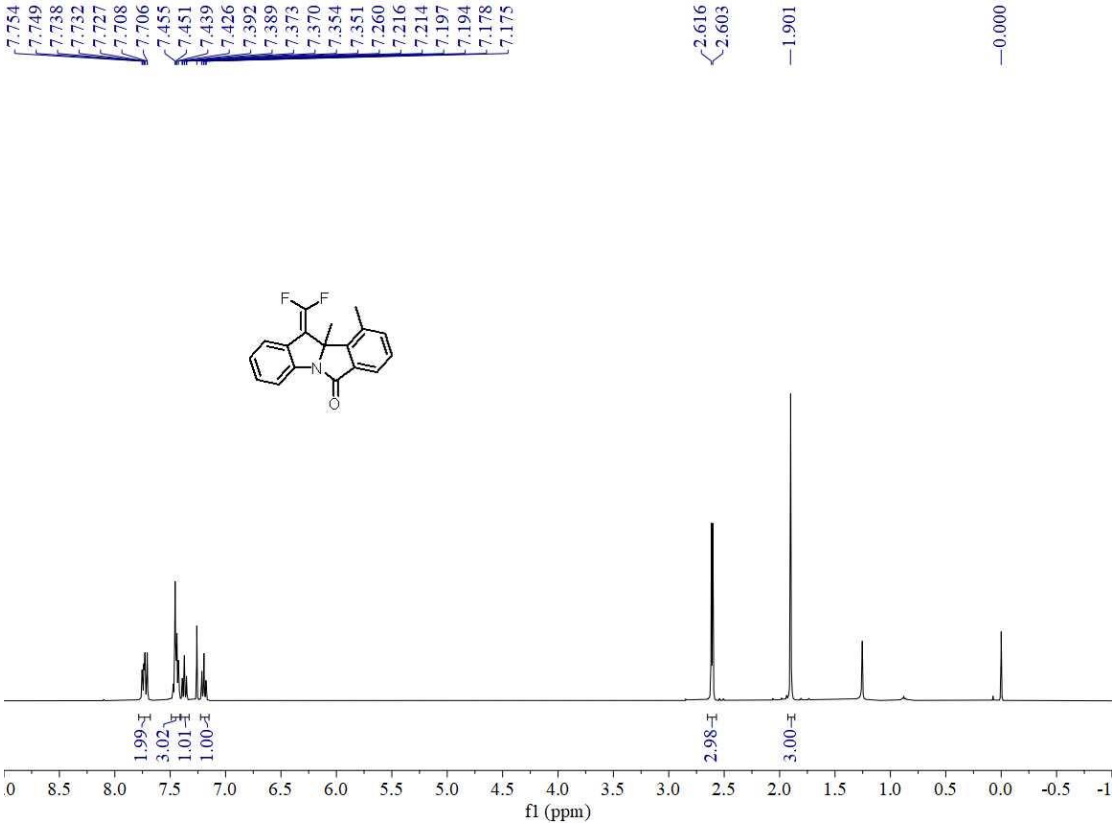
^{13}C NMR of product 3n in $CDCl_3$ (100 MHz)



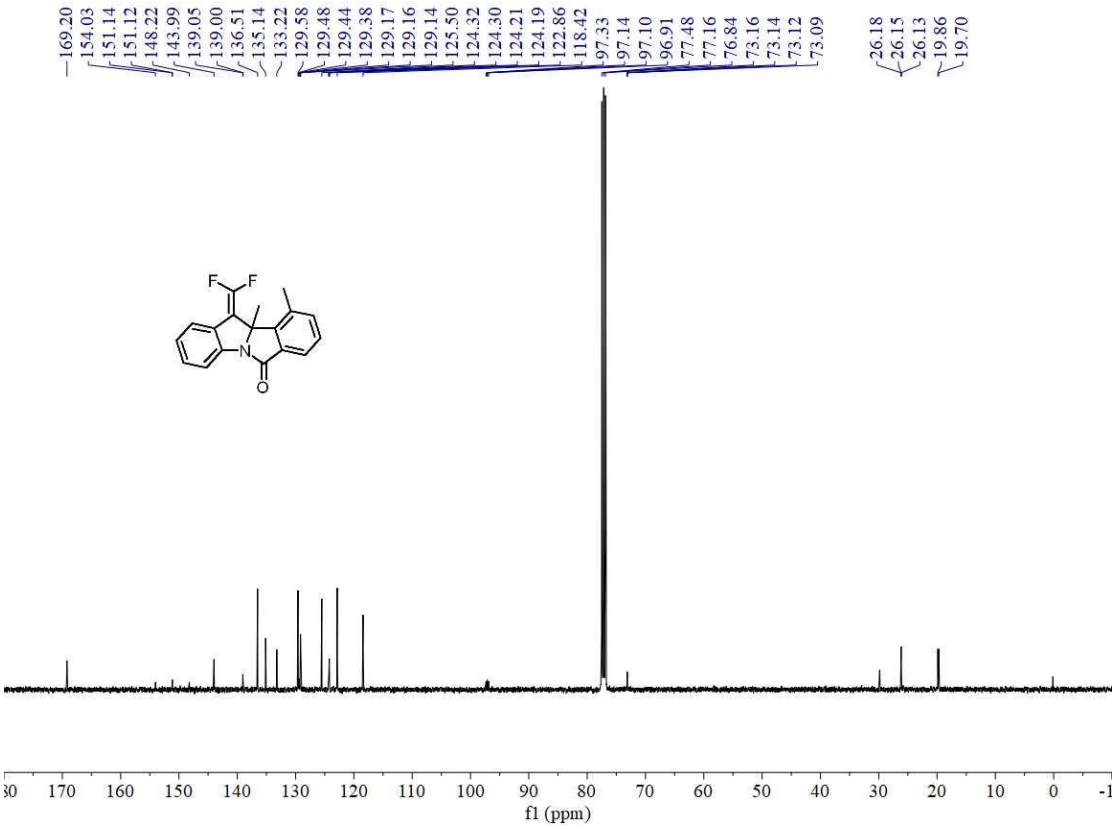
^{19}F NMR of product 3n in $CDCl_3$ (376 MHz)



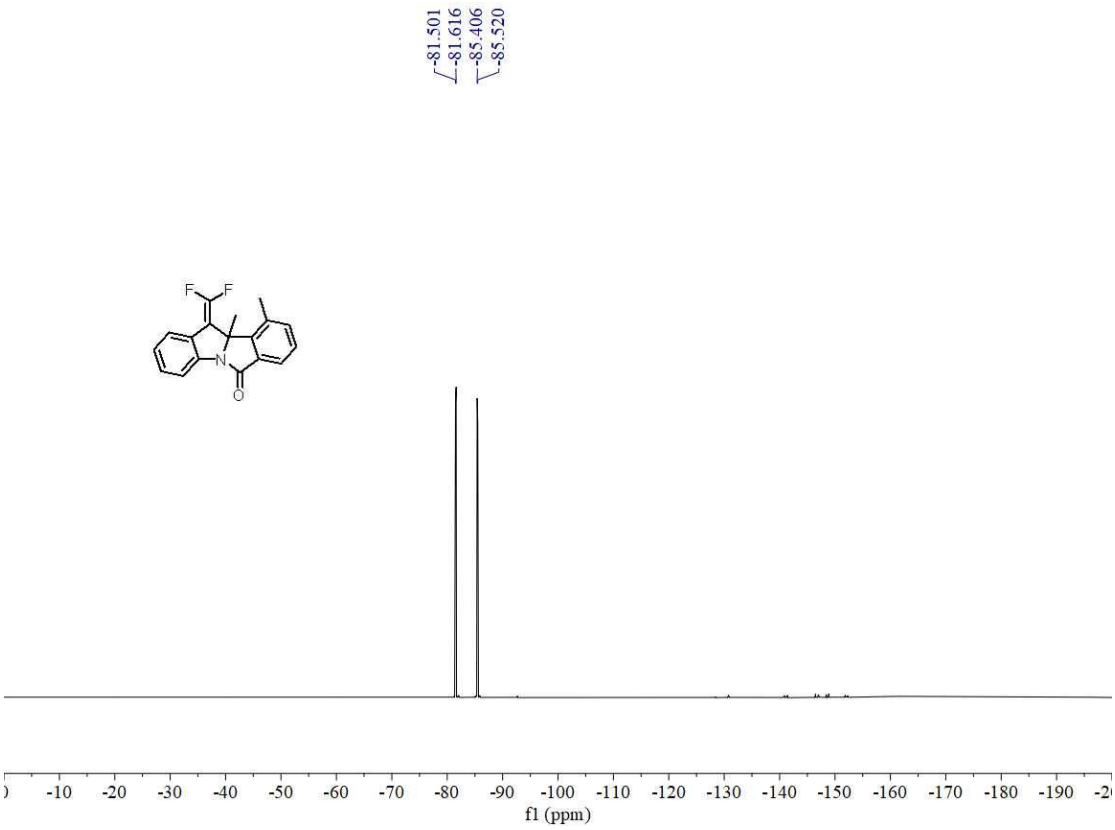
^{1}H NMR of product 3o in $CDCl_3$ (400 MHz)



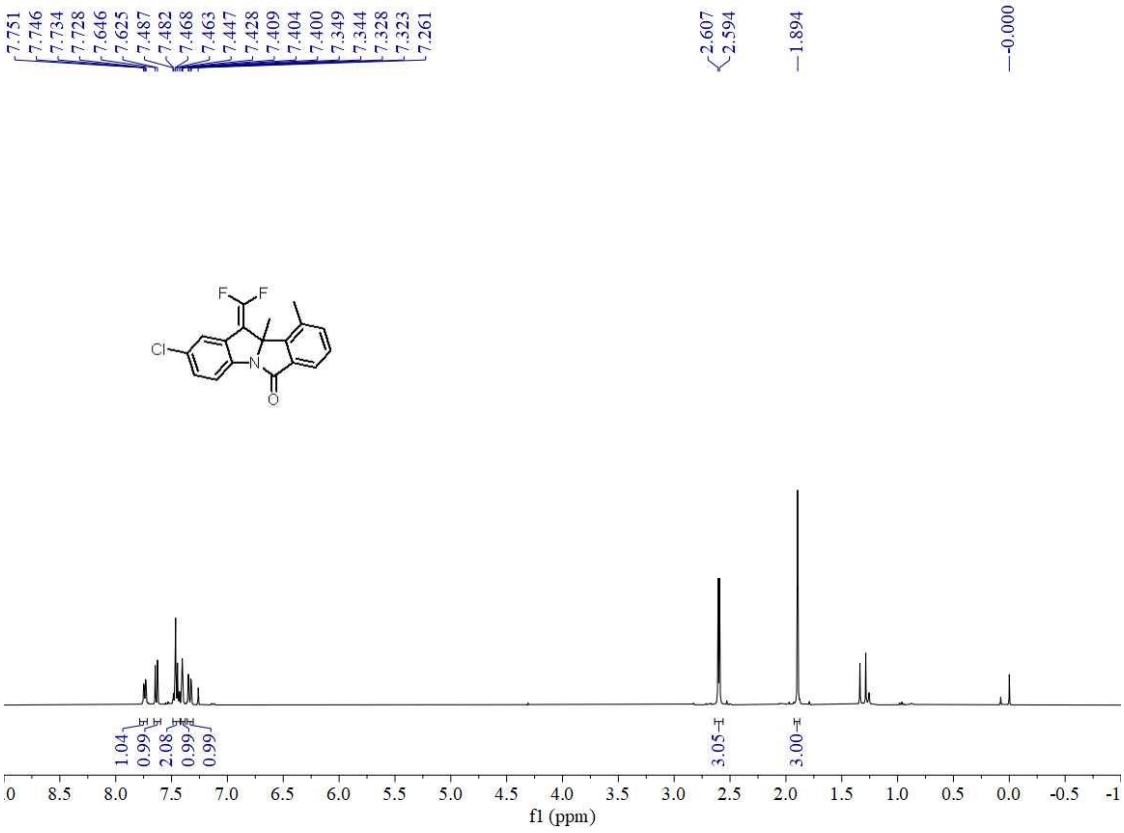
^{13}C NMR of product 3o in $CDCl_3$ (100 MHz)



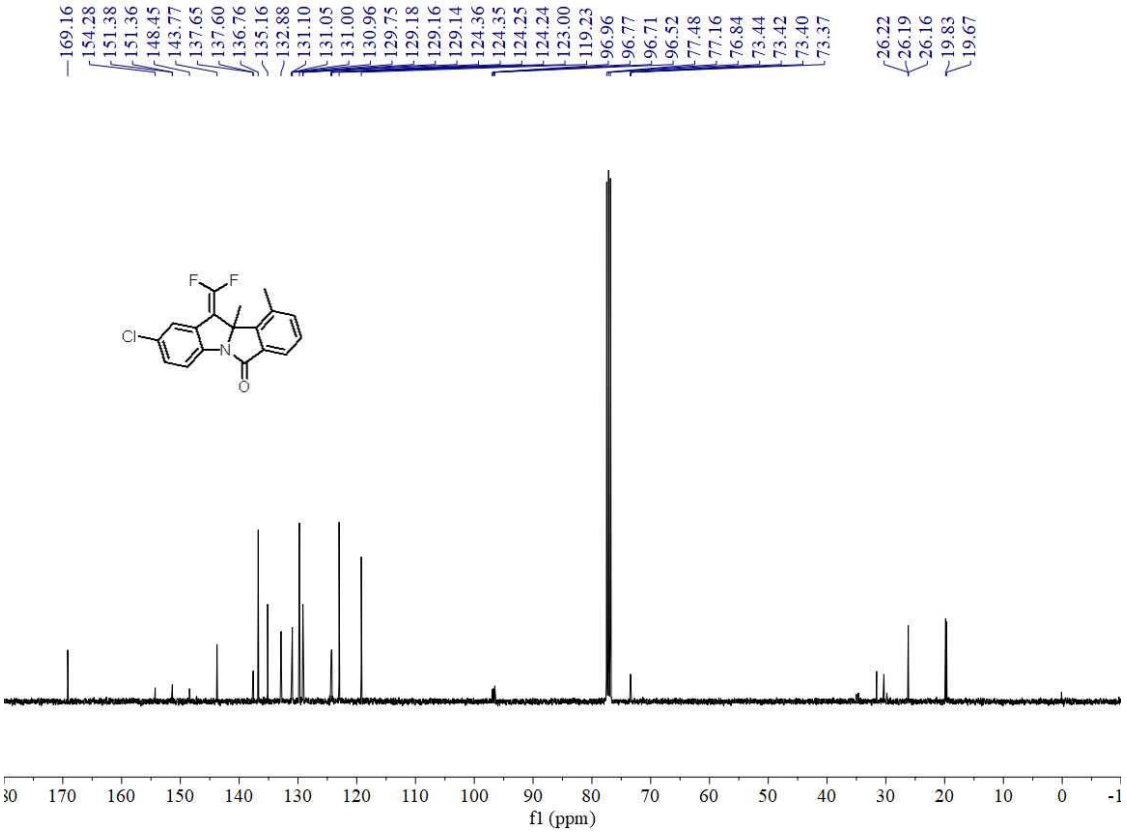
^{19}F NMR of product 3o in $CDCl_3$ (376 MHz)



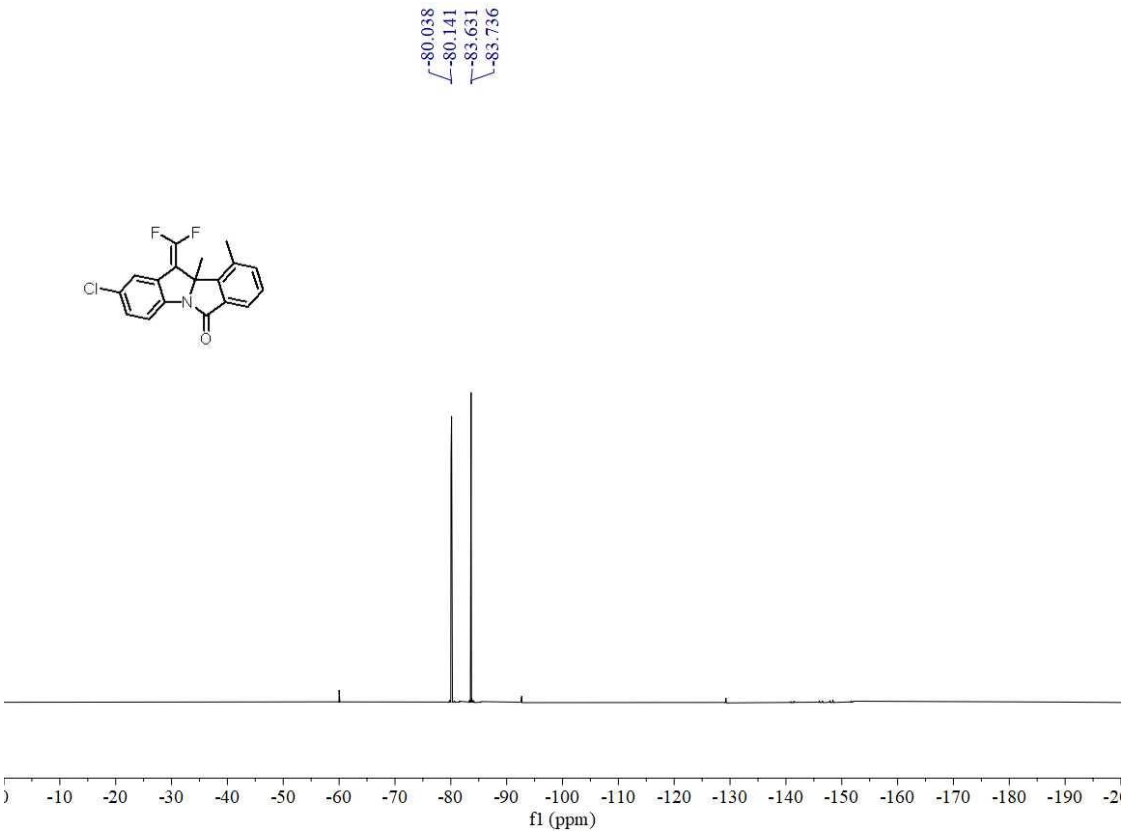
^{1}H NMR of product 3p in $CDCl_3$ (400 MHz)



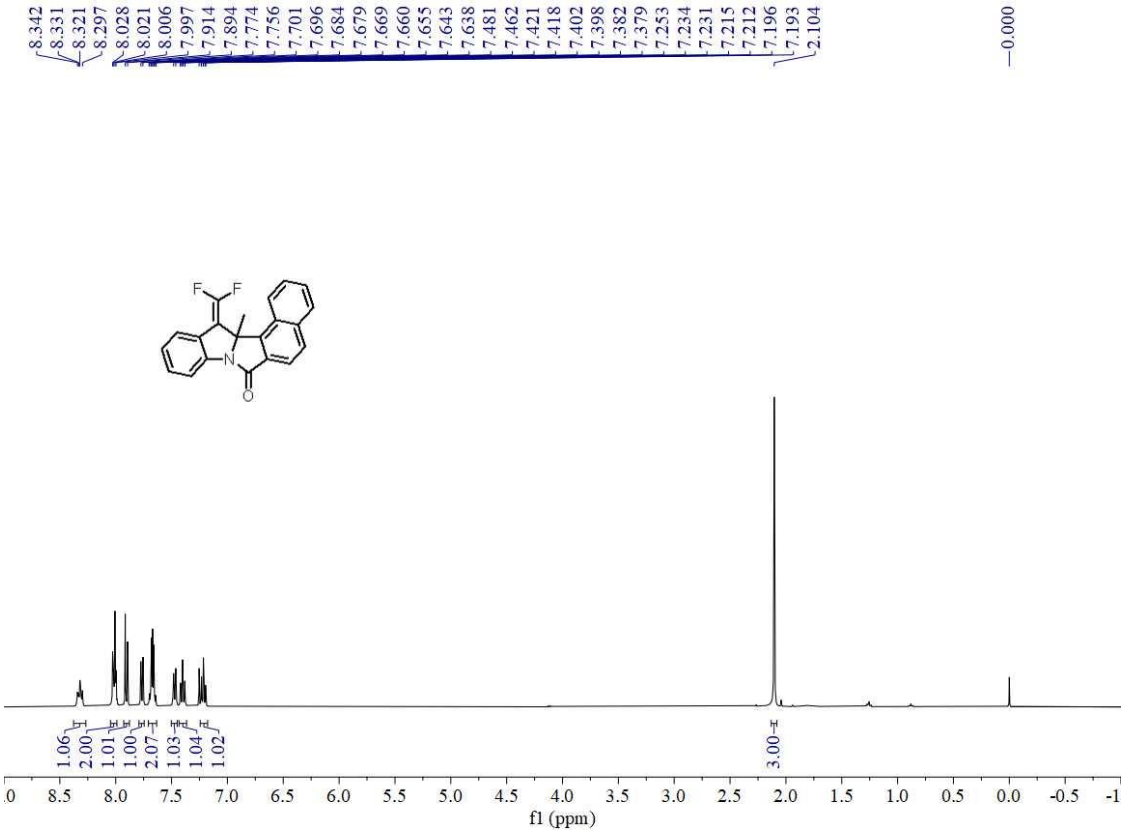
^{13}C NMR of product 3p in $CDCl_3$ (100 MHz)



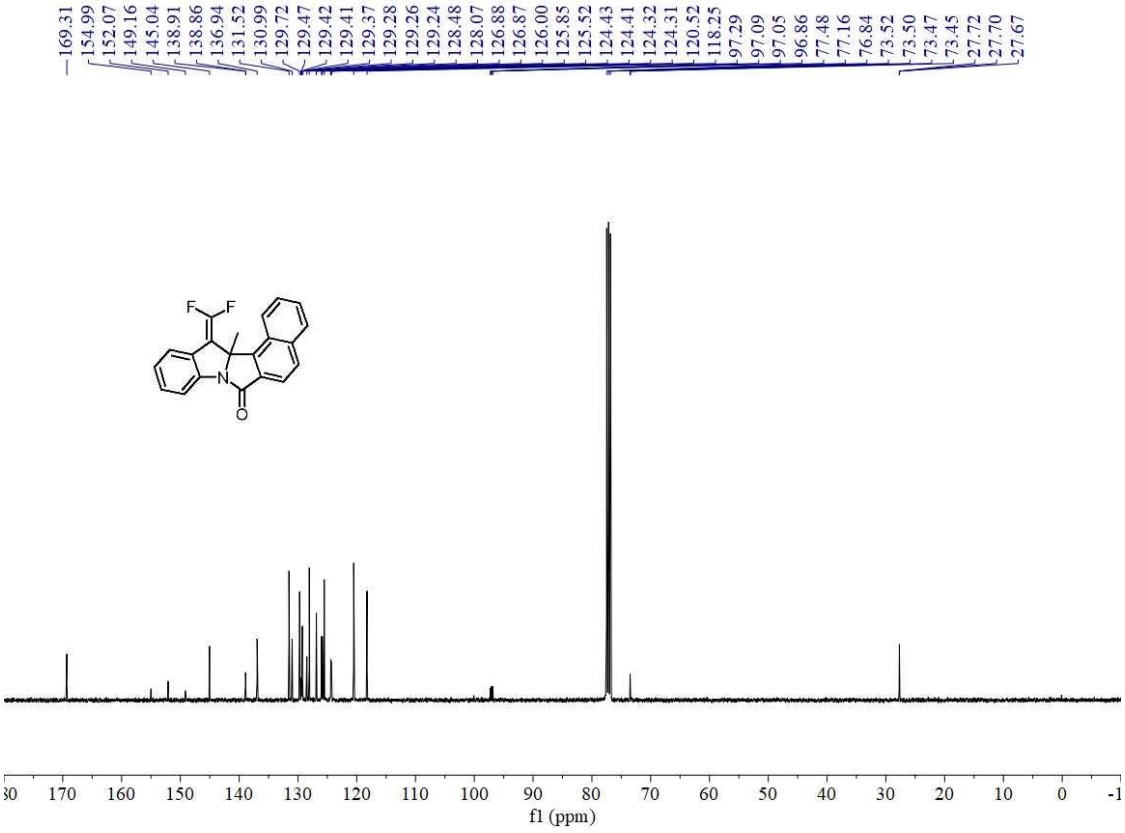
^{19}F NMR of product 3p in $CDCl_3$ (376 MHz)



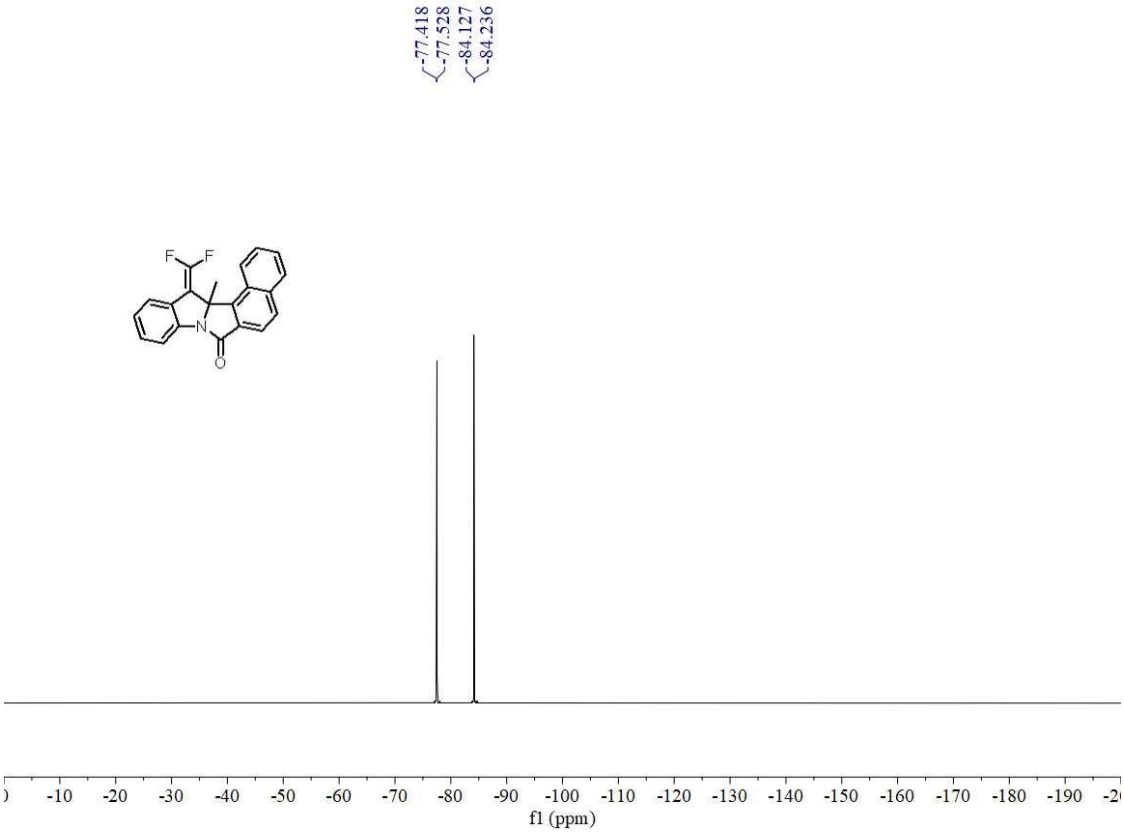
^{1}H NMR of product 3q in $CDCl_3$ (400 MHz)



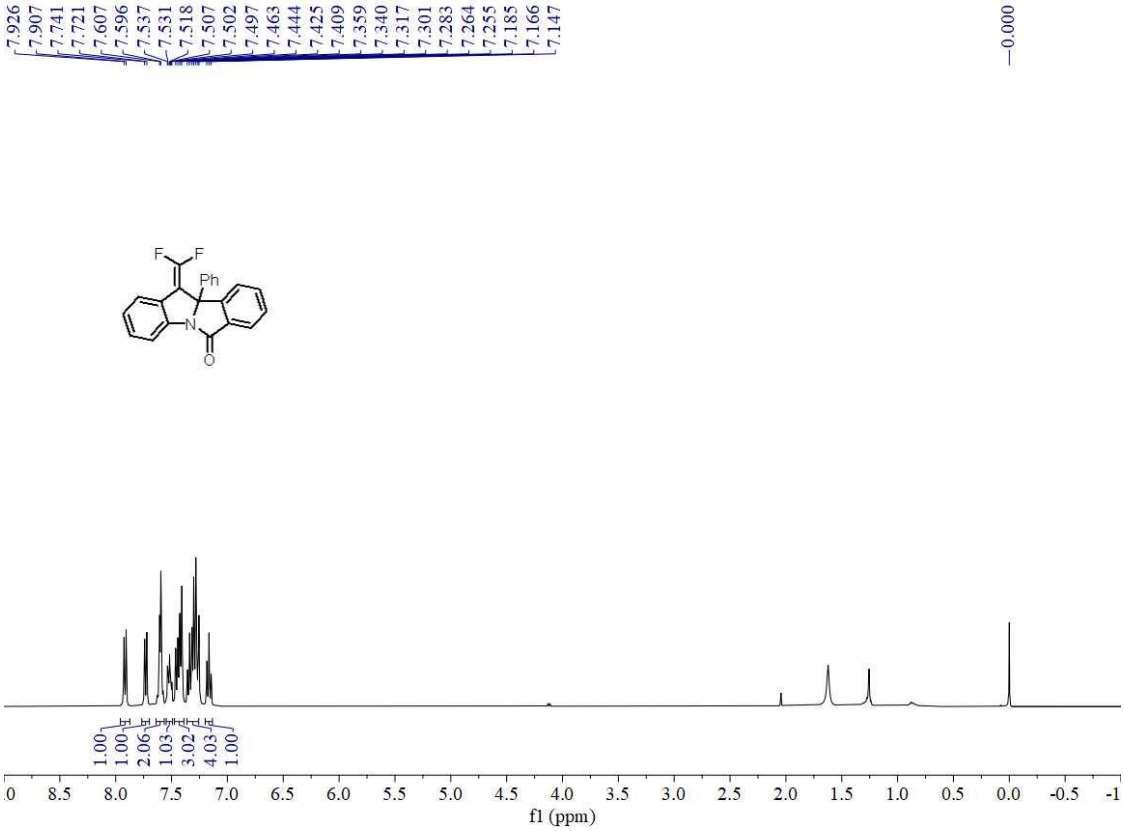
^{13}C NMR of product 3q in $CDCl_3$ (100 MHz)



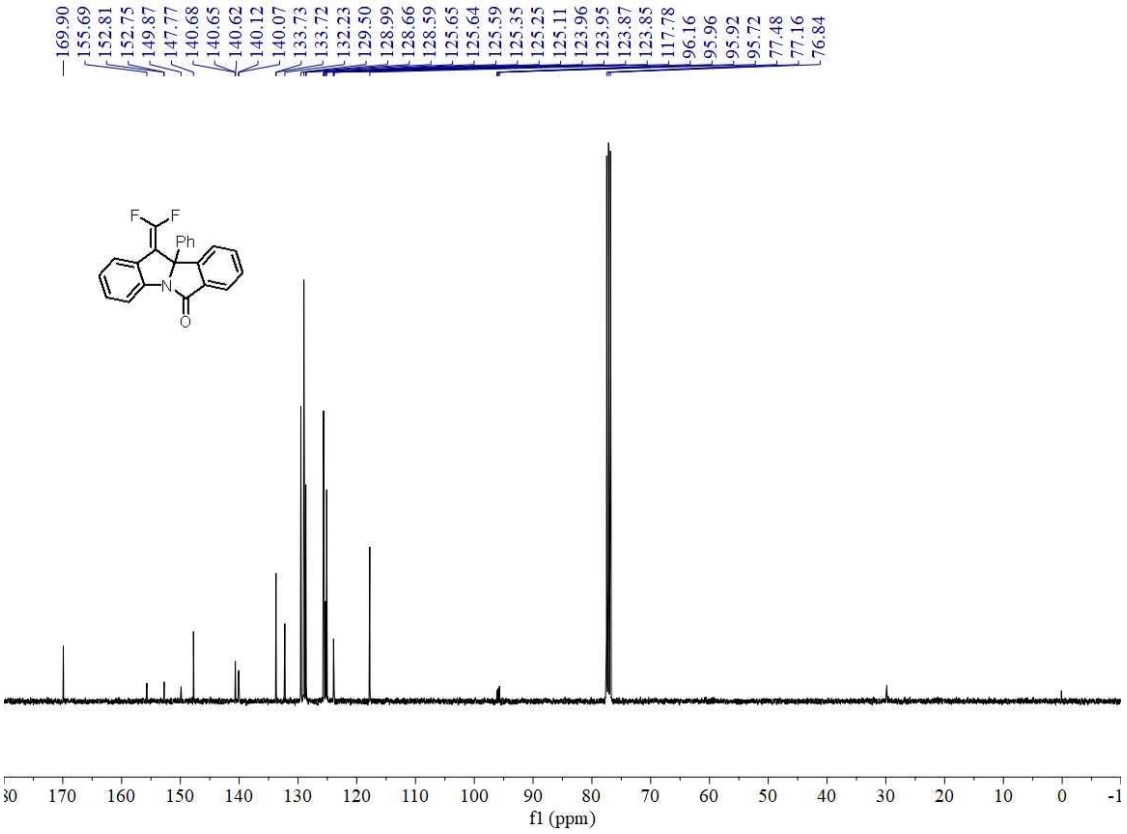
^{19}F NMR of product 3q in $CDCl_3$ (376 MHz)



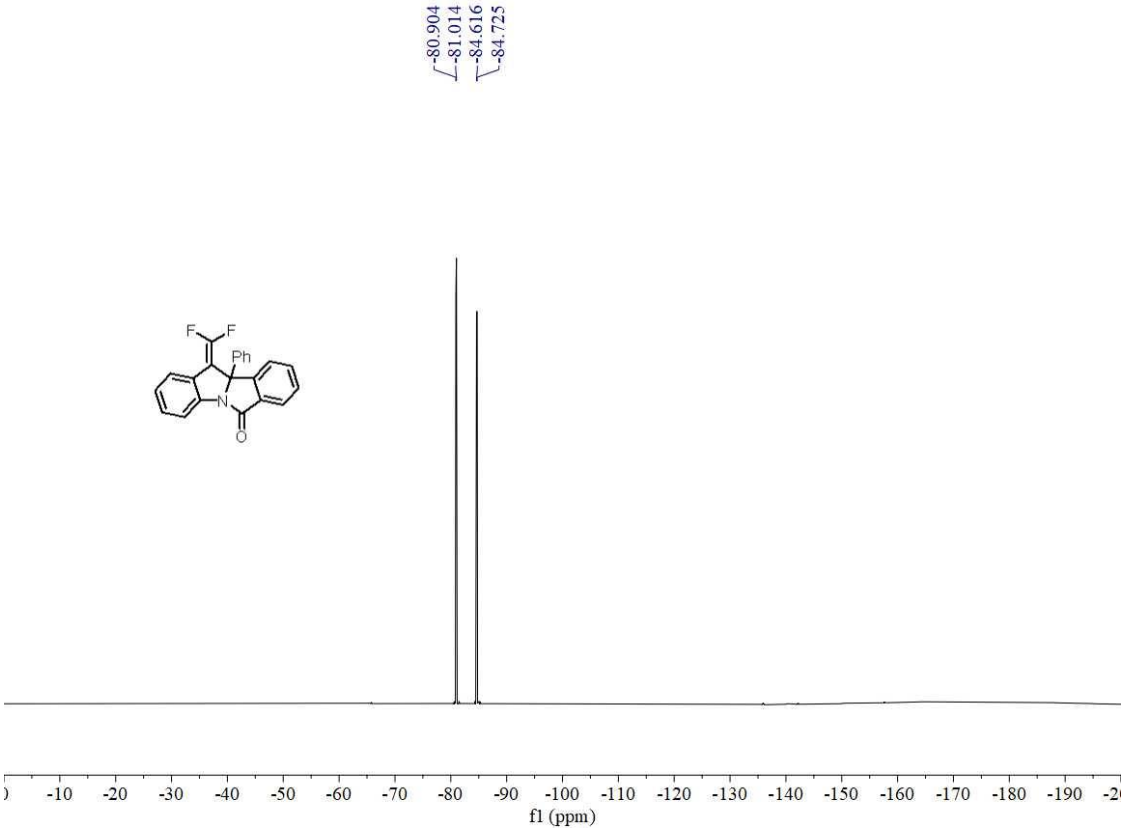
^{1}H NMR of product 3t in $CDCl_3$ (400 MHz)



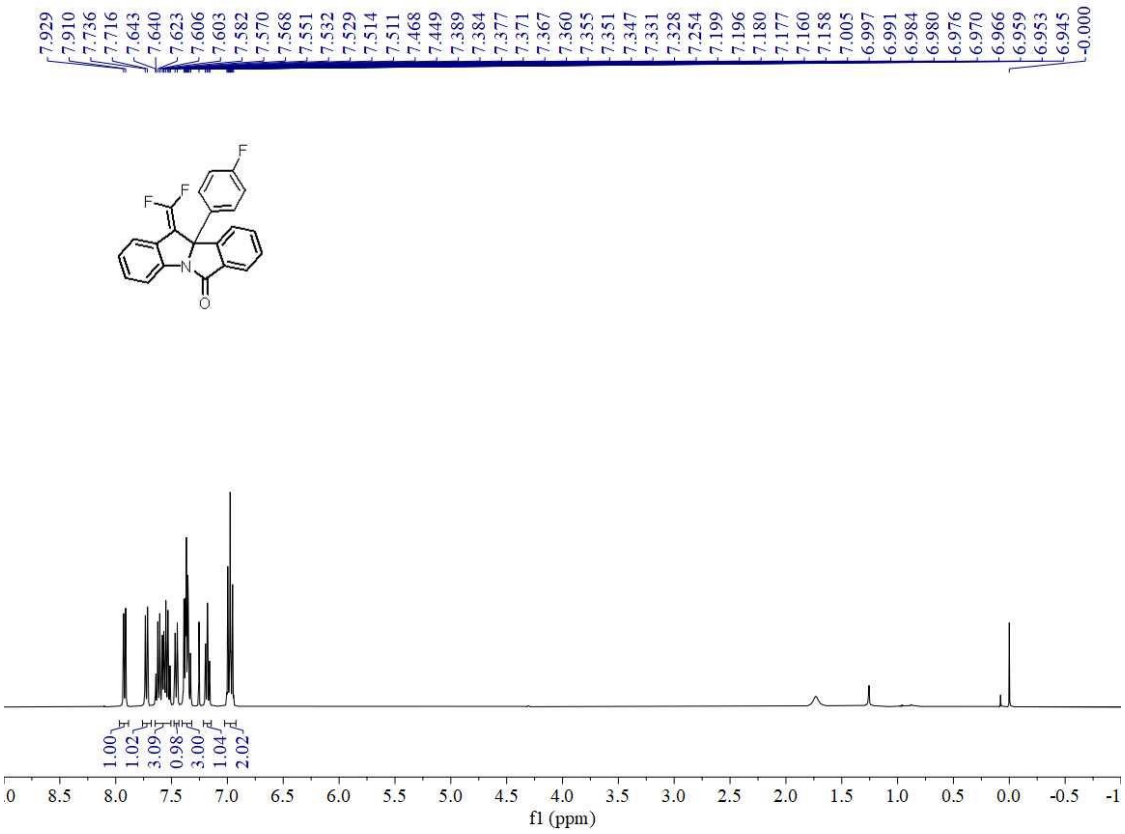
^{13}C NMR of product 3t in $CDCl_3$ (100 MHz)



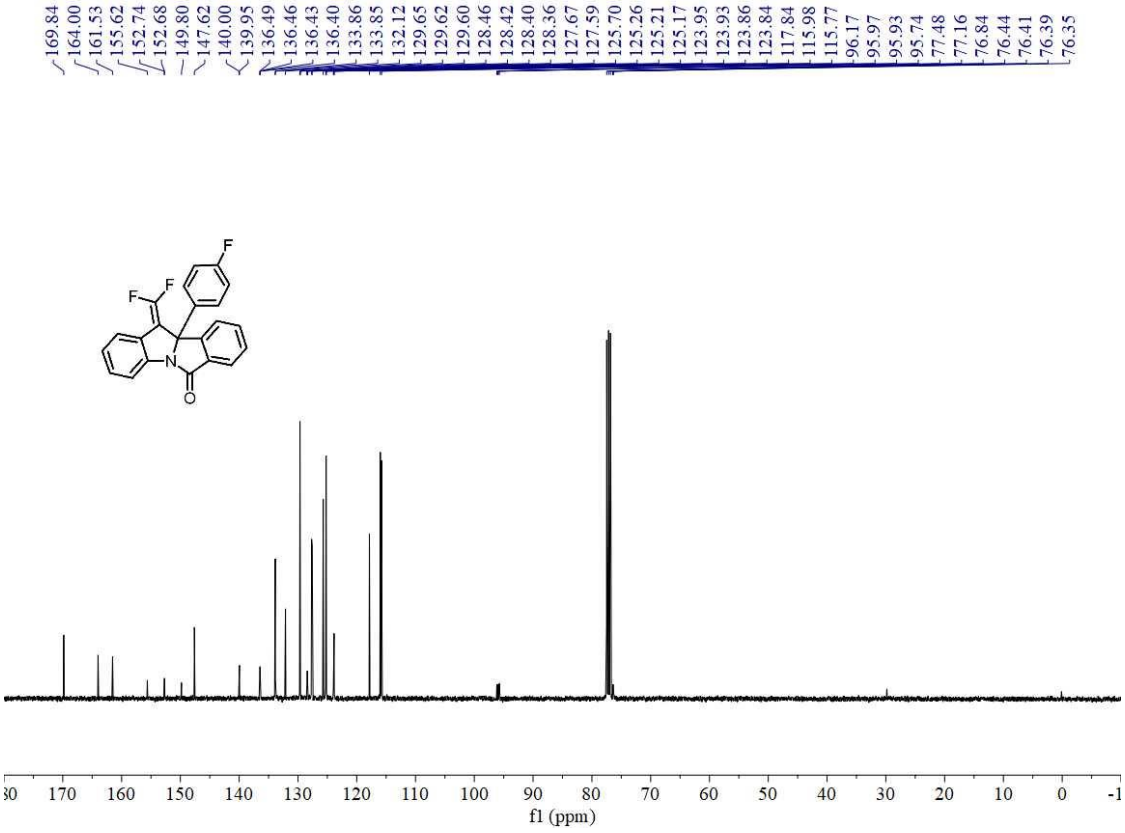
^{19}F NMR of product 3t in $CDCl_3$ (376 MHz)



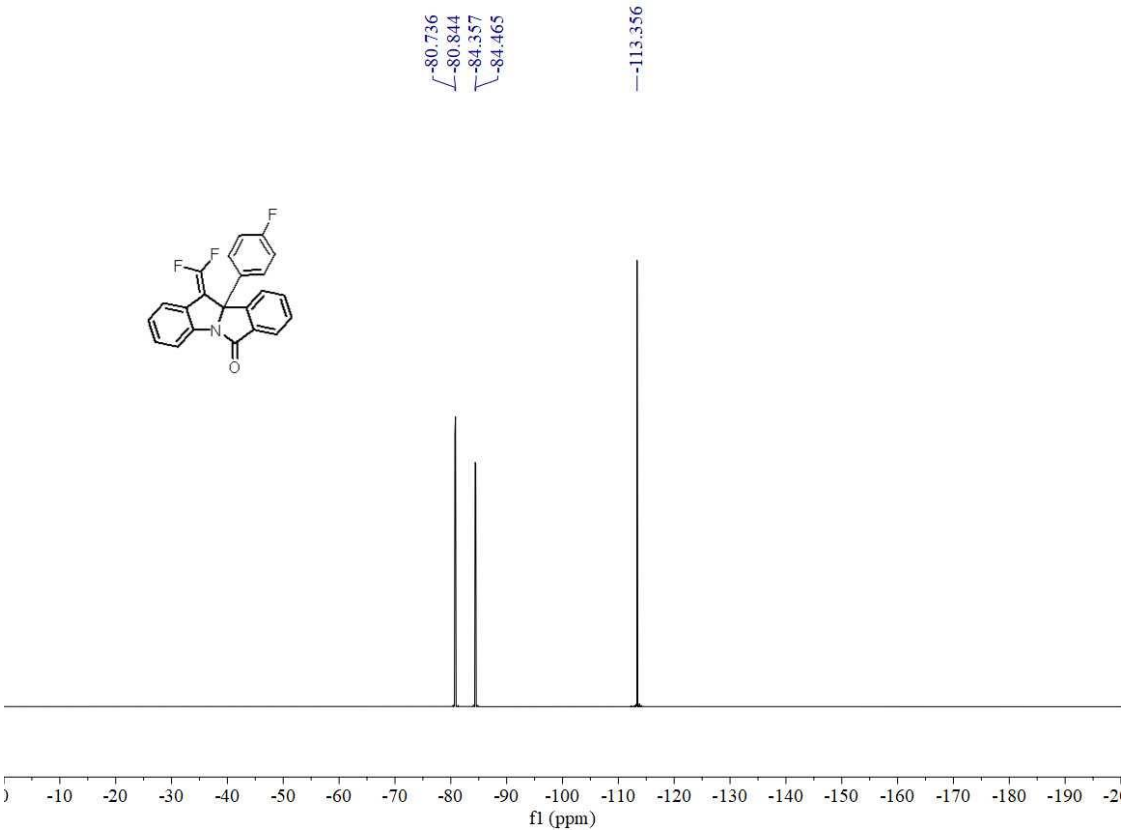
^{1}H NMR of product 3u in $CDCl_3$ (400 MHz)



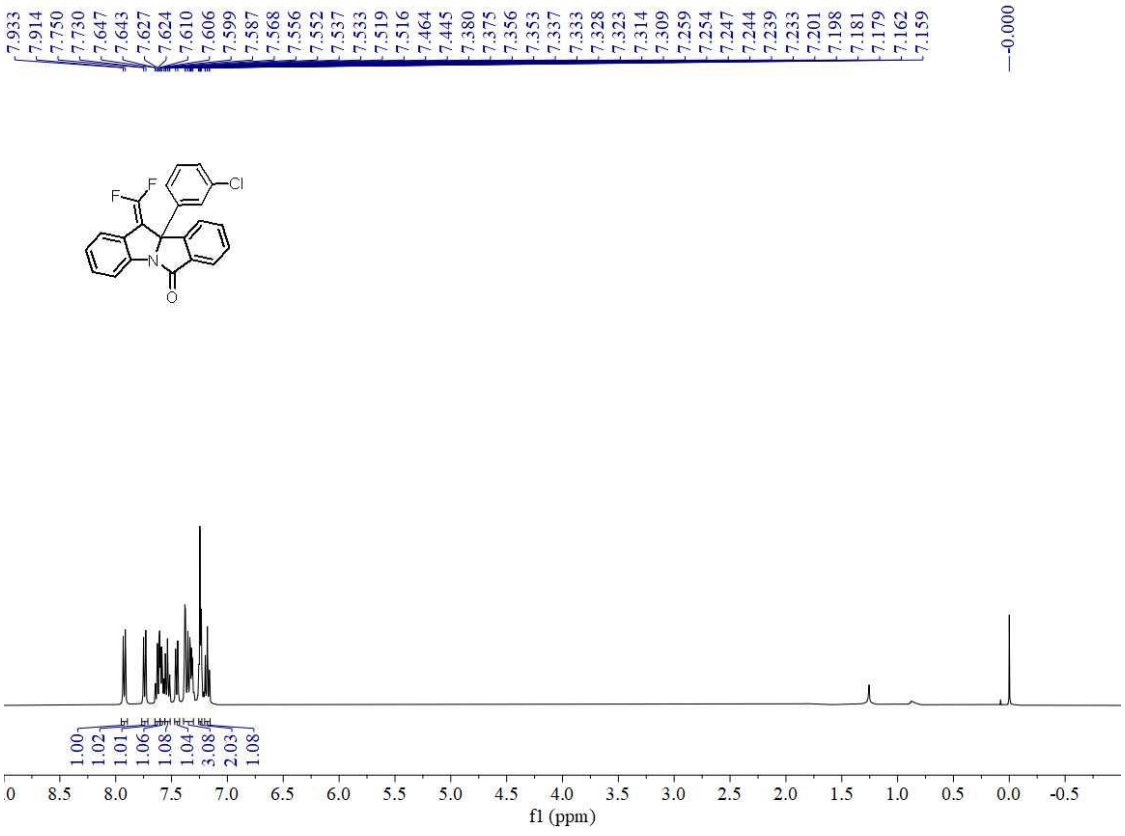
^{13}C NMR of product 3u in $CDCl_3$ (100 MHz)



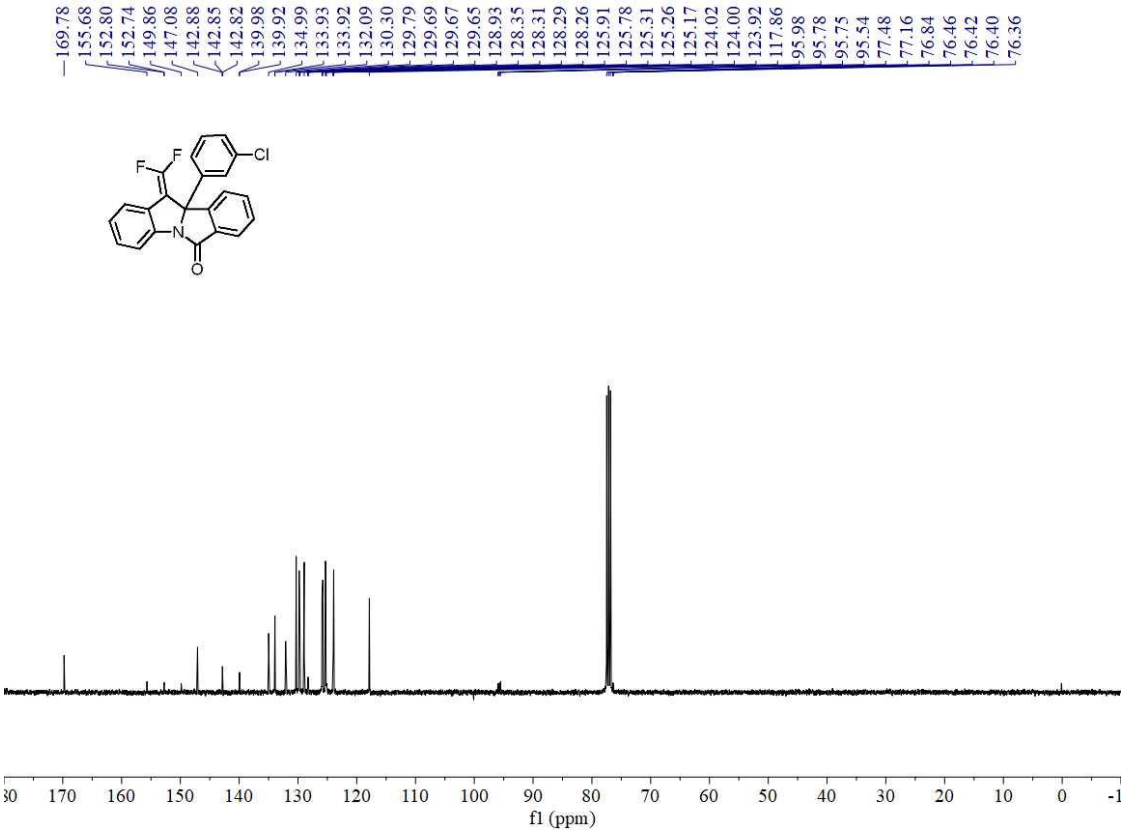
^{19}F NMR of product 3u in $CDCl_3$ (376 MHz)



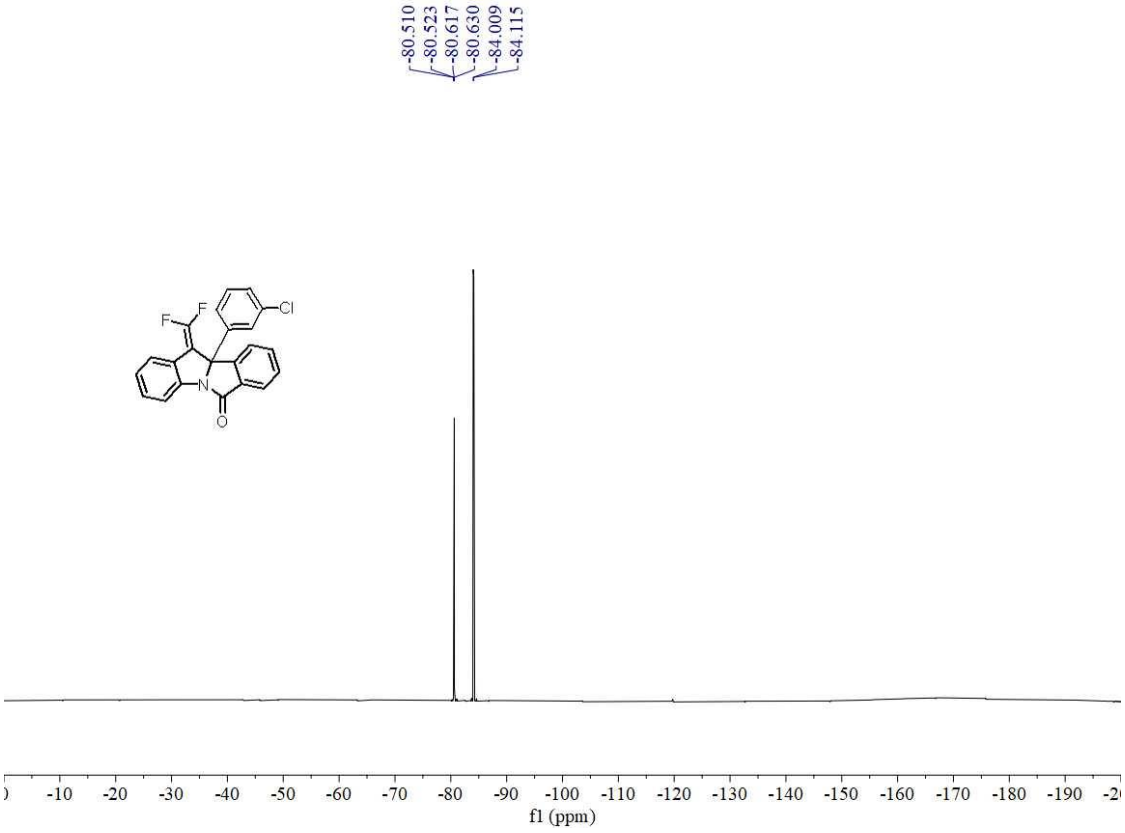
^{1}H NMR of product 3v in $CDCl_3$ (400 MHz)



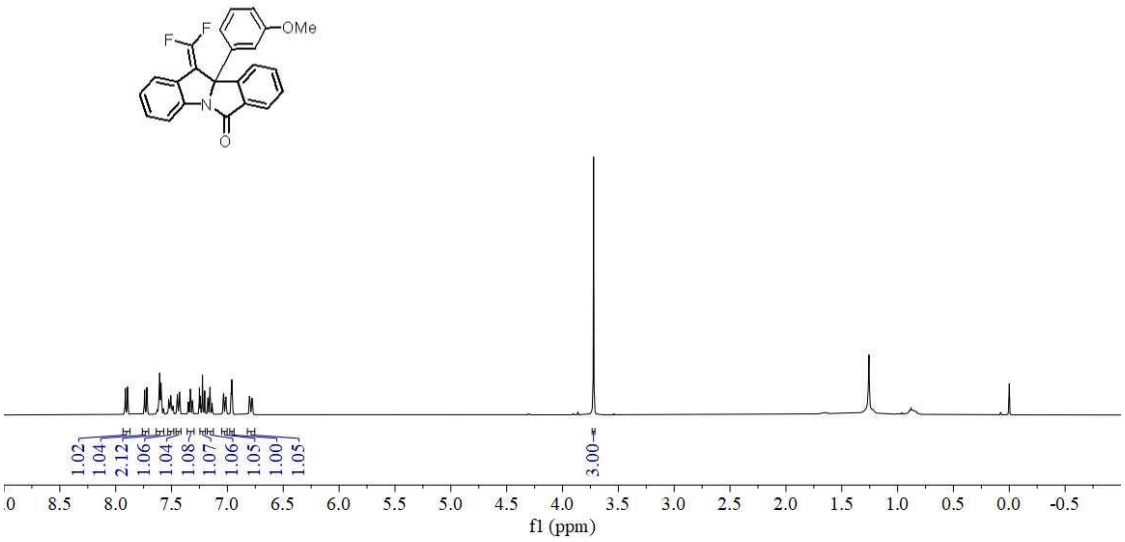
^{13}C NMR of product 3v in $CDCl_3$ (100 MHz)



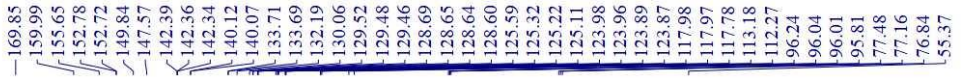
^{19}F NMR of product 3v in $CDCl_3$ (376 MHz)

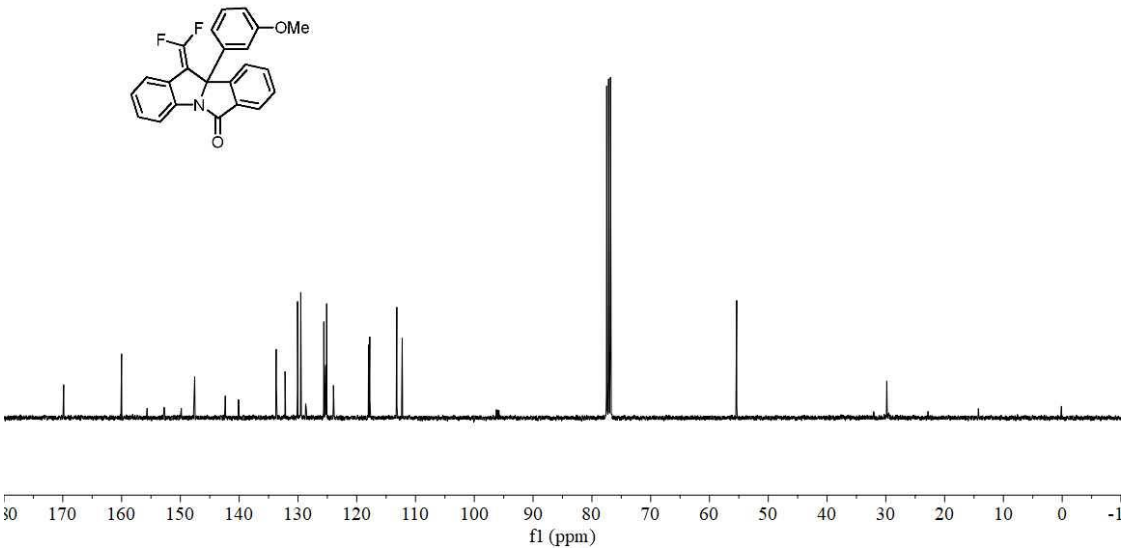


^{1}H NMR of product 3w in $CDCl_3$ (400 MHz)

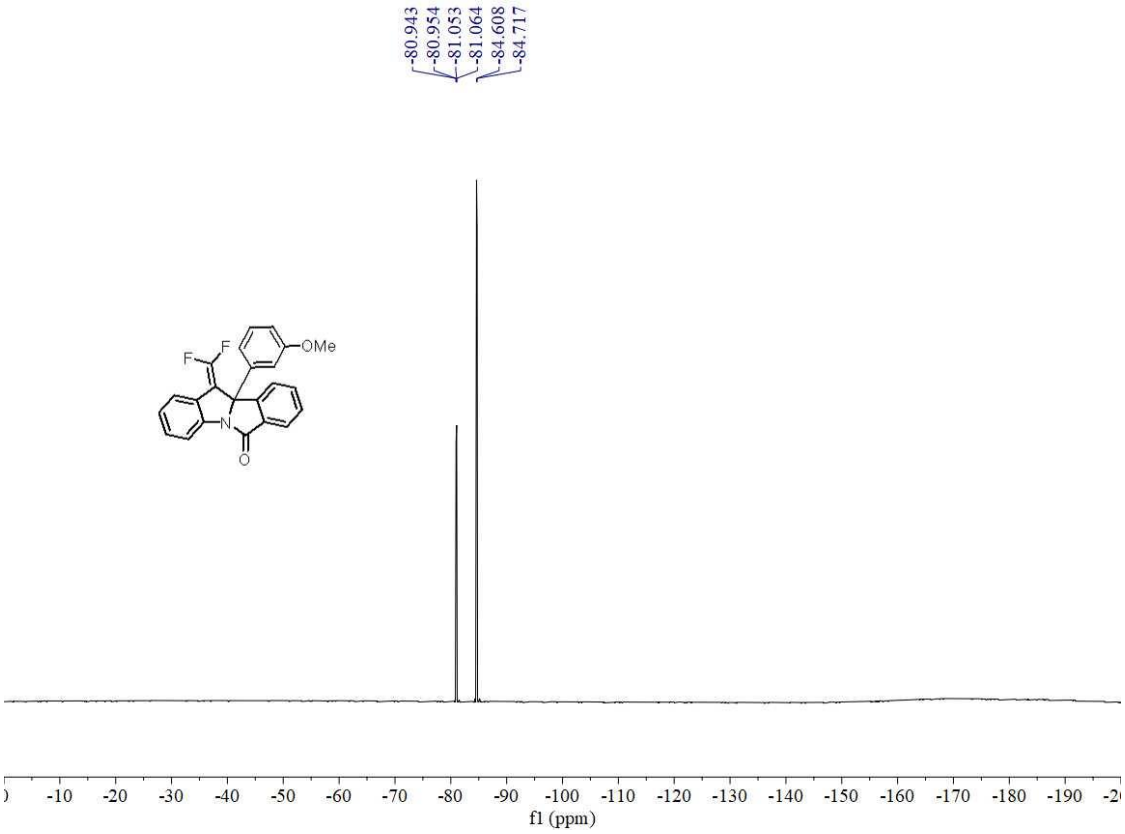


^{13}C NMR of product 3w in $CDCl_3$ (100 MHz)

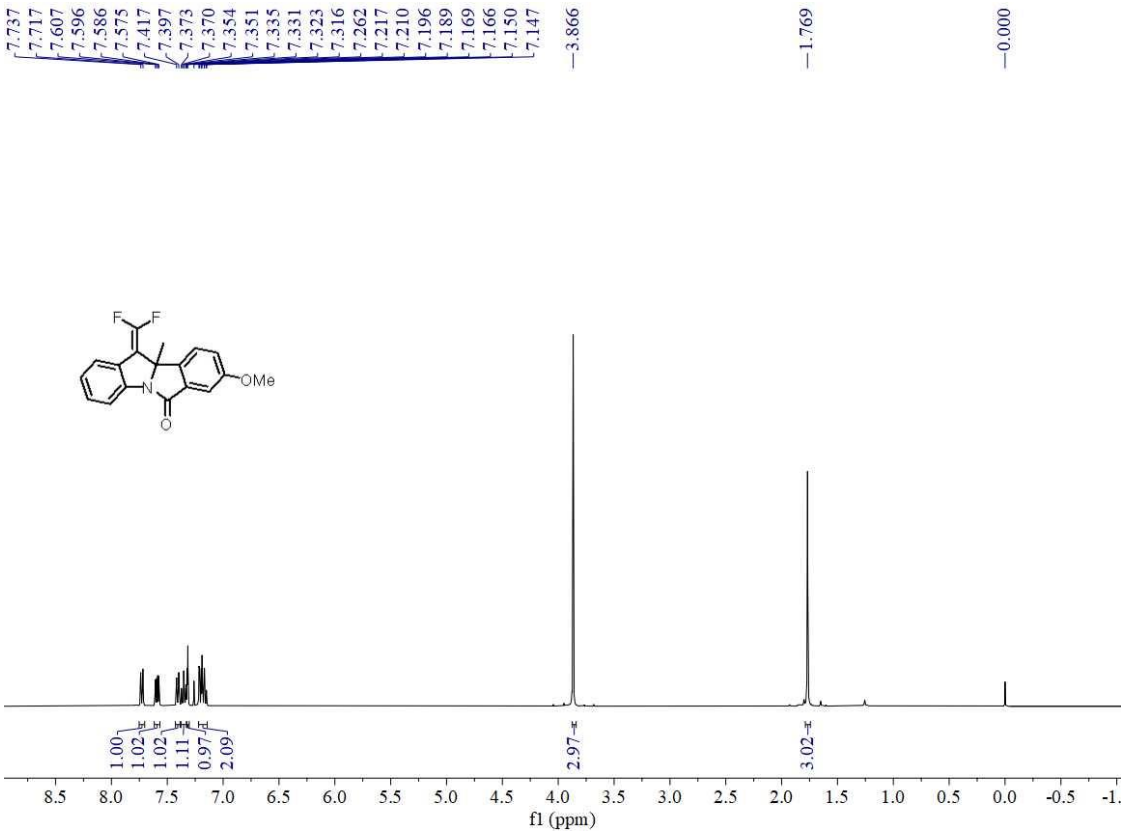




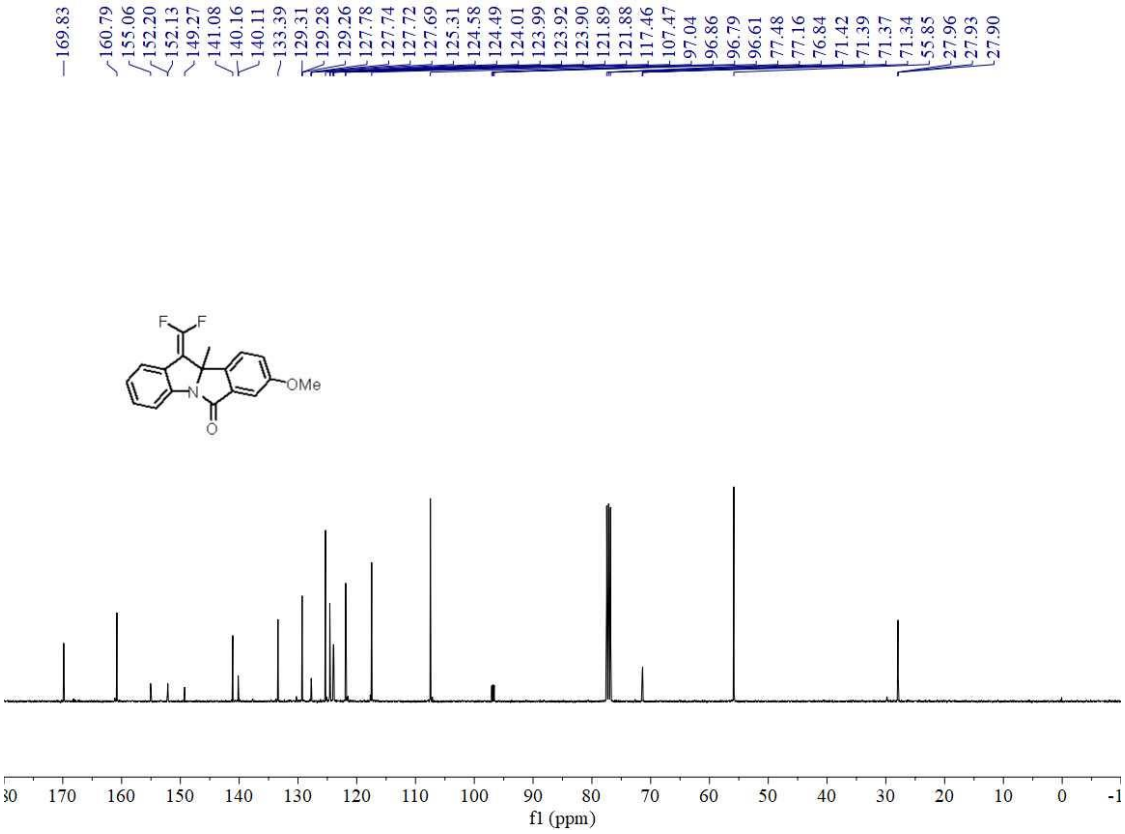
^{19}F NMR of product 3w in $CDCl_3$ (376 MHz)



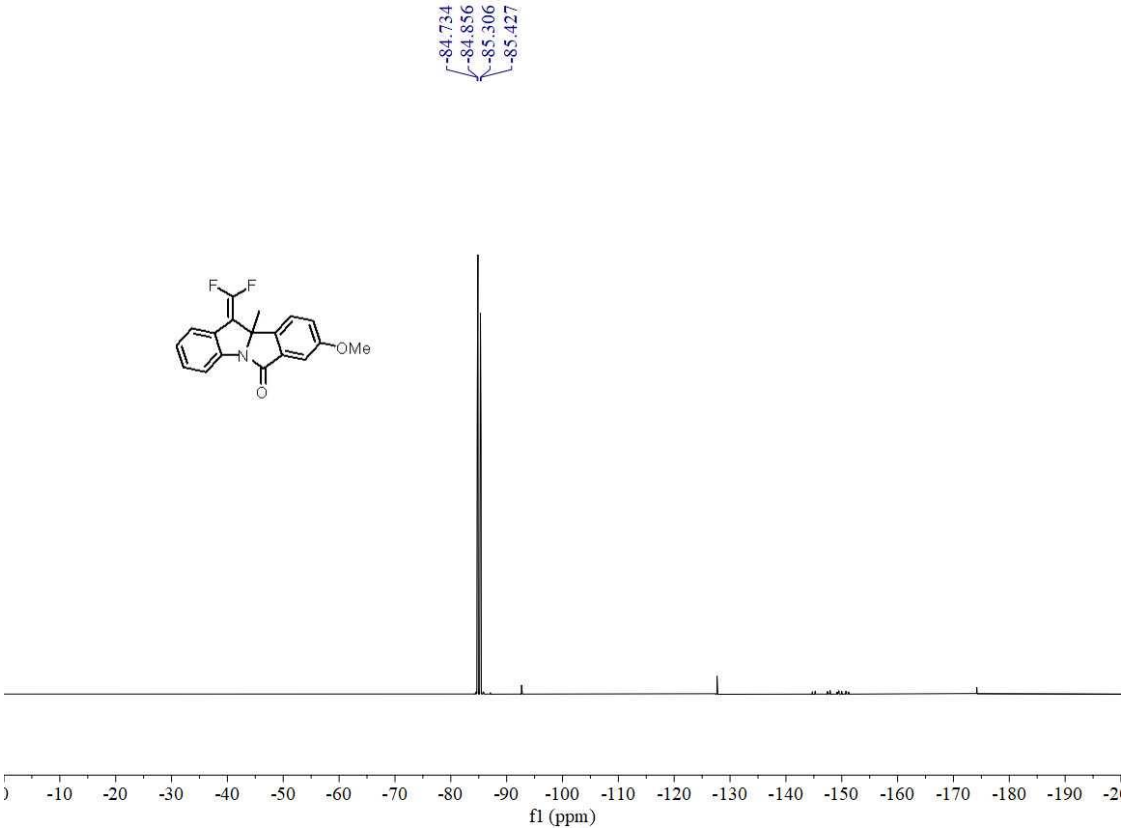
^{1}H NMR of product 3x in $CDCl_3$ (400 MHz)



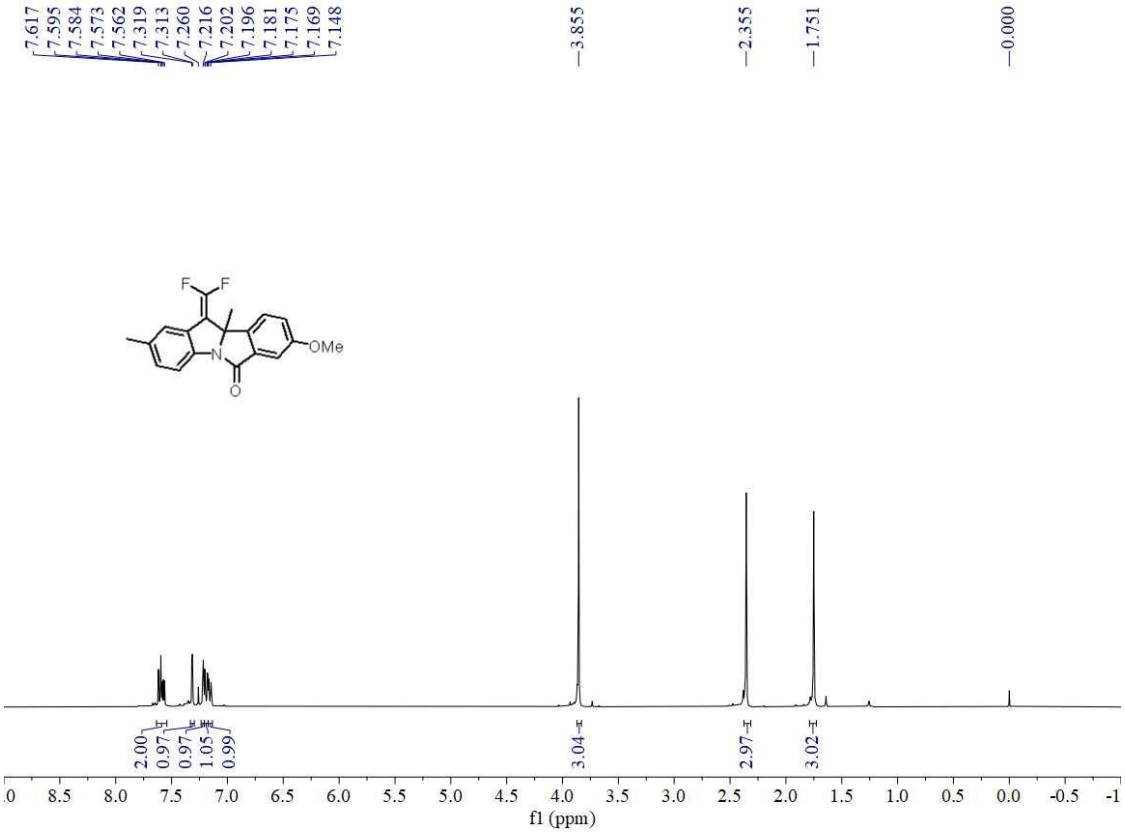
^{13}C NMR of product 3x in $CDCl_3$ (100 MHz)



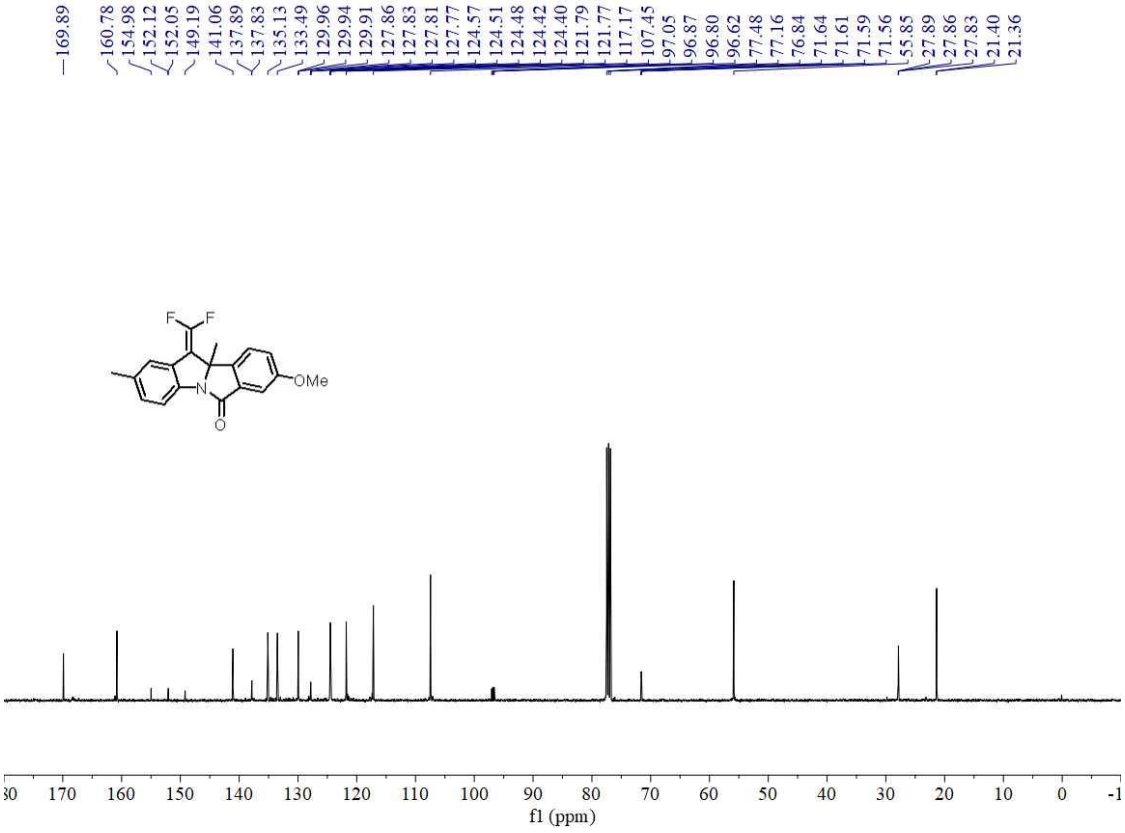
^{19}F NMR of product 3x in $CDCl_3$ (376 MHz)



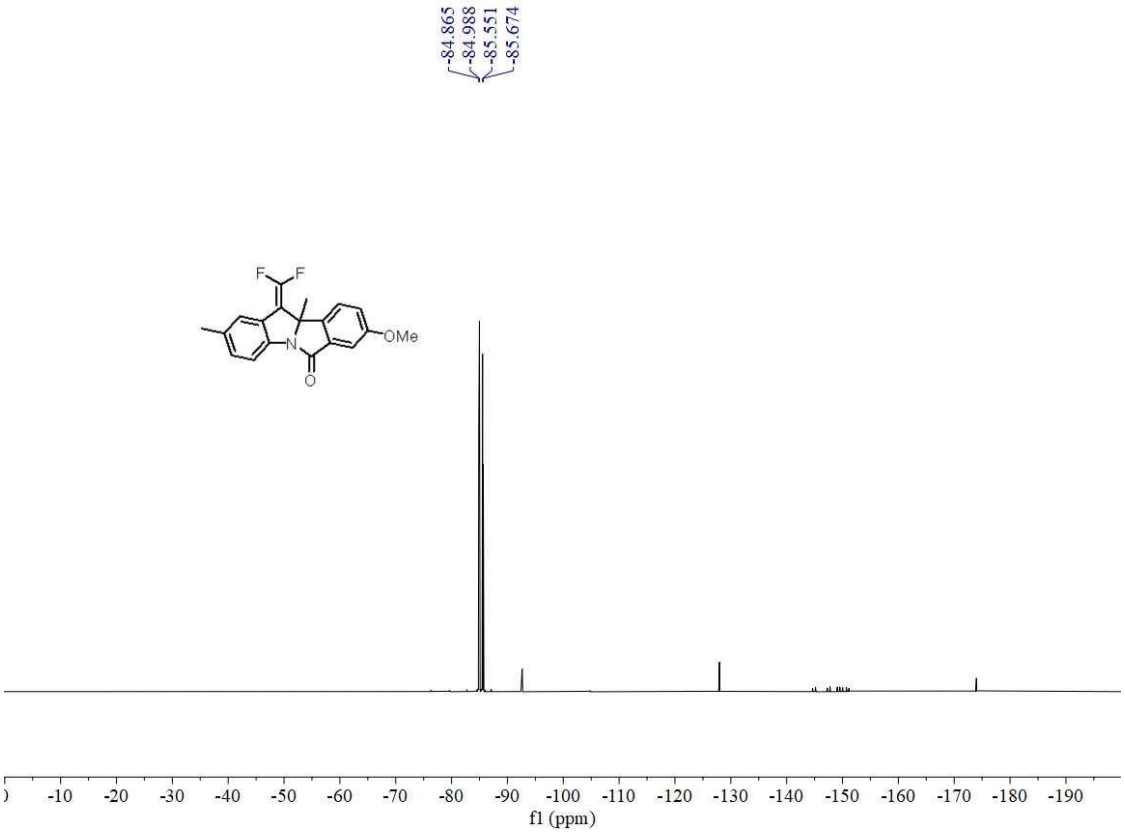
^{1}H NMR of product 3y in $CDCl_3$ (400 MHz)



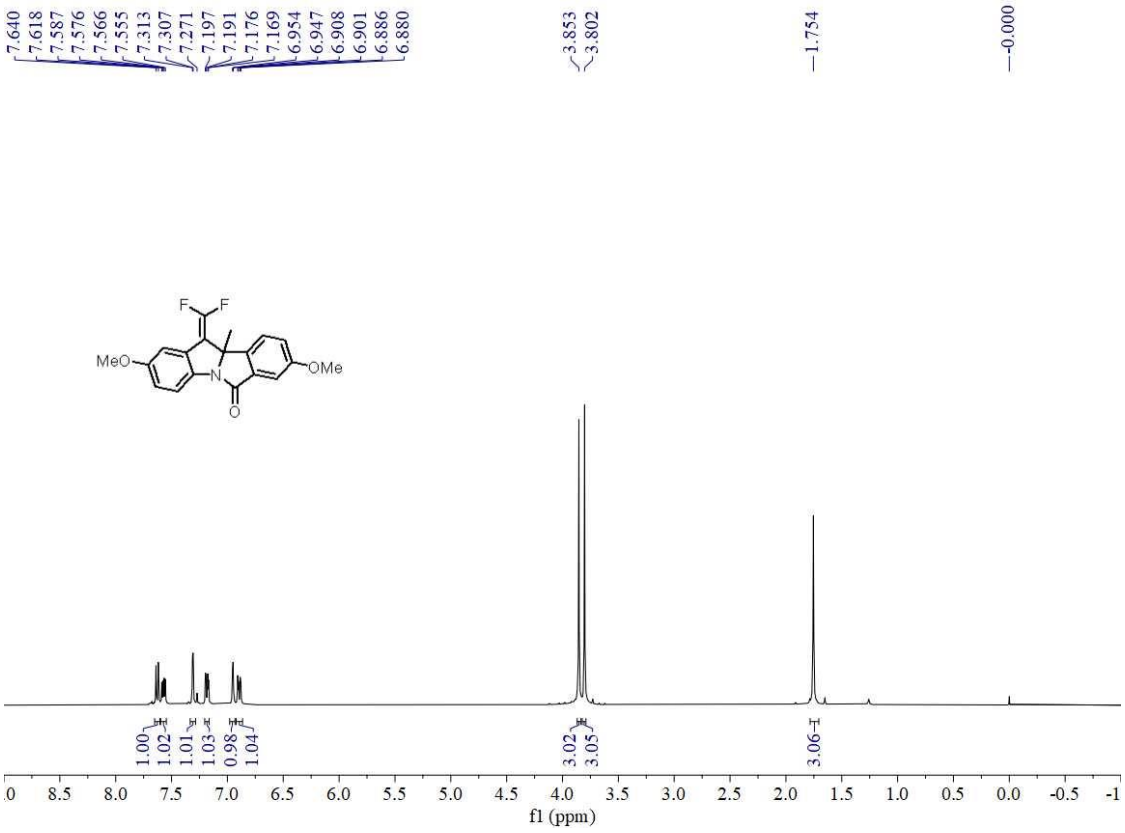
^{13}C NMR of product 3y in $CDCl_3$ (100 MHz)



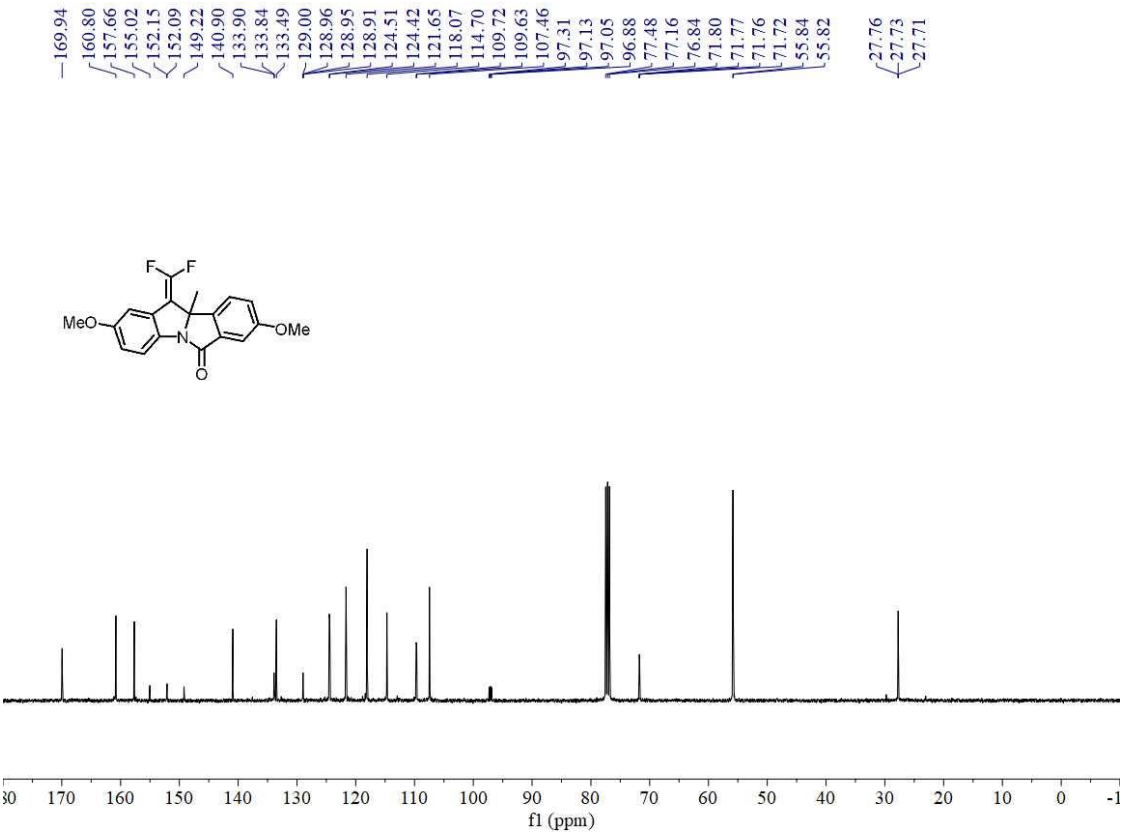
^{19}F NMR of product 3y in $CDCl_3$ (376 MHz)



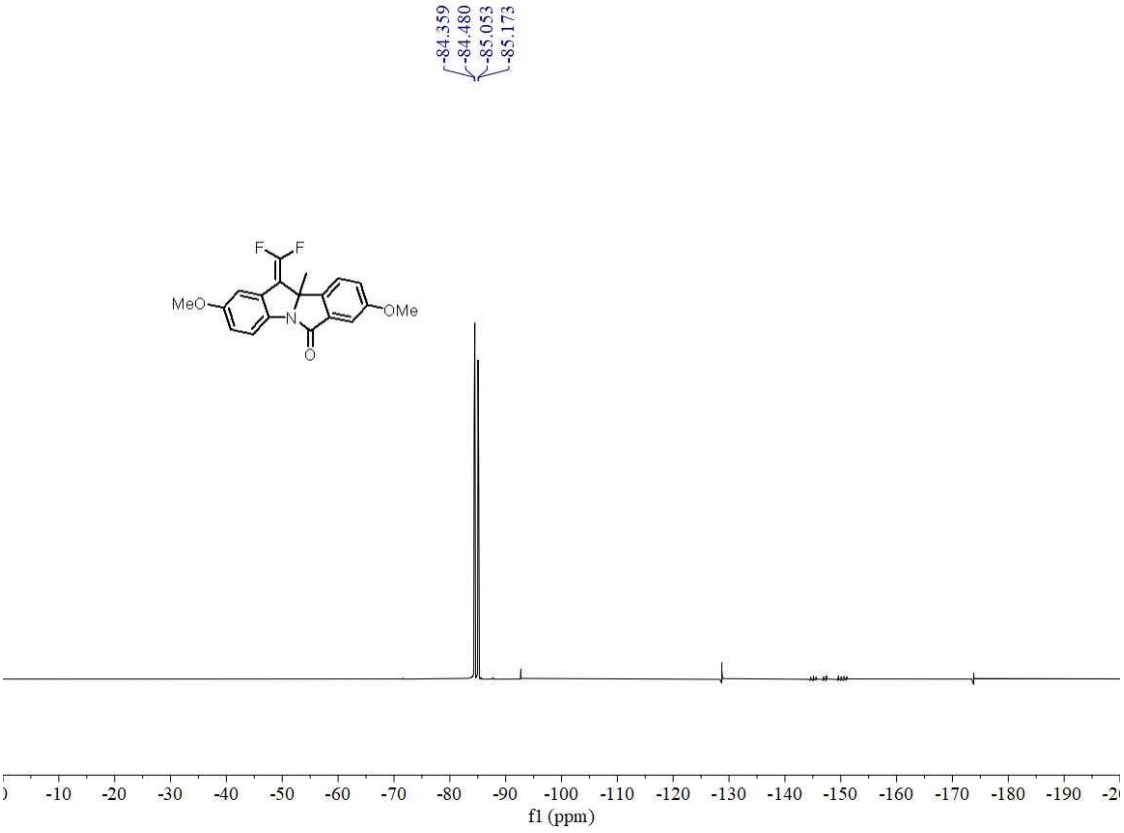
^{1}H NMR of product 3z in $CDCl_3$ (400 MHz)



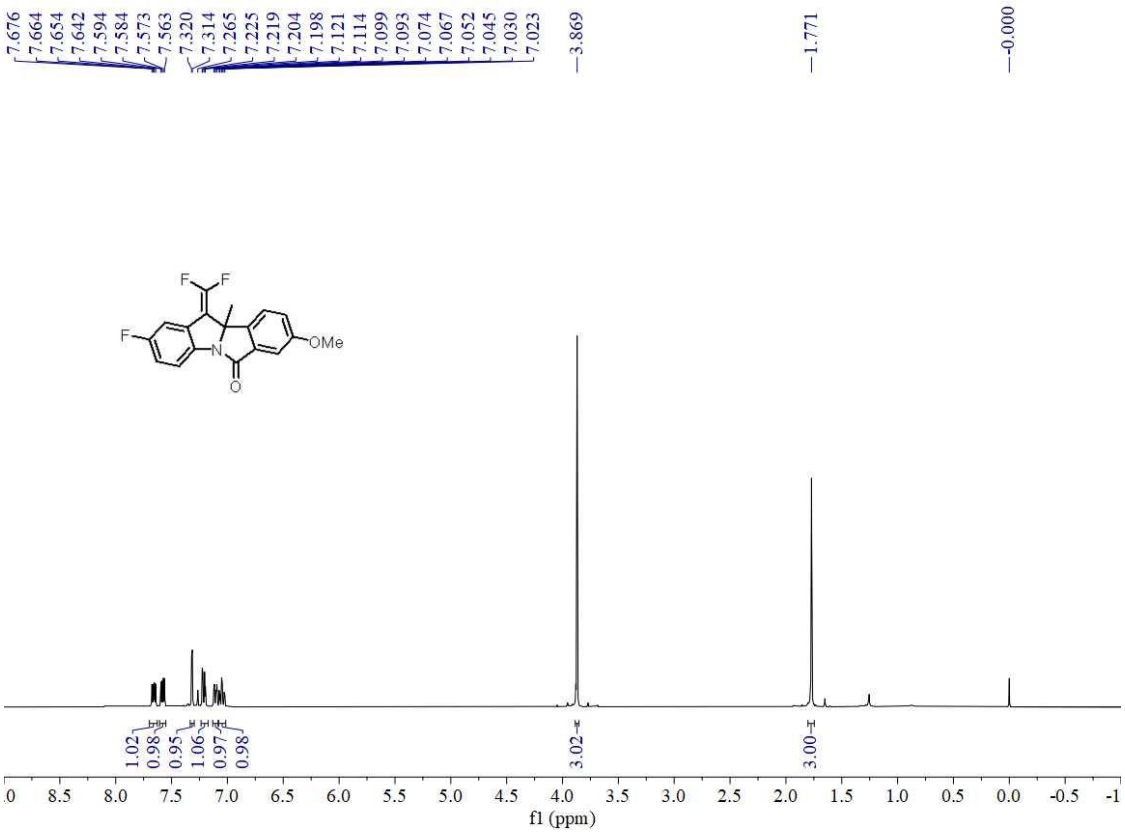
^{13}C NMR of product 3z in $CDCl_3$ (100 MHz)



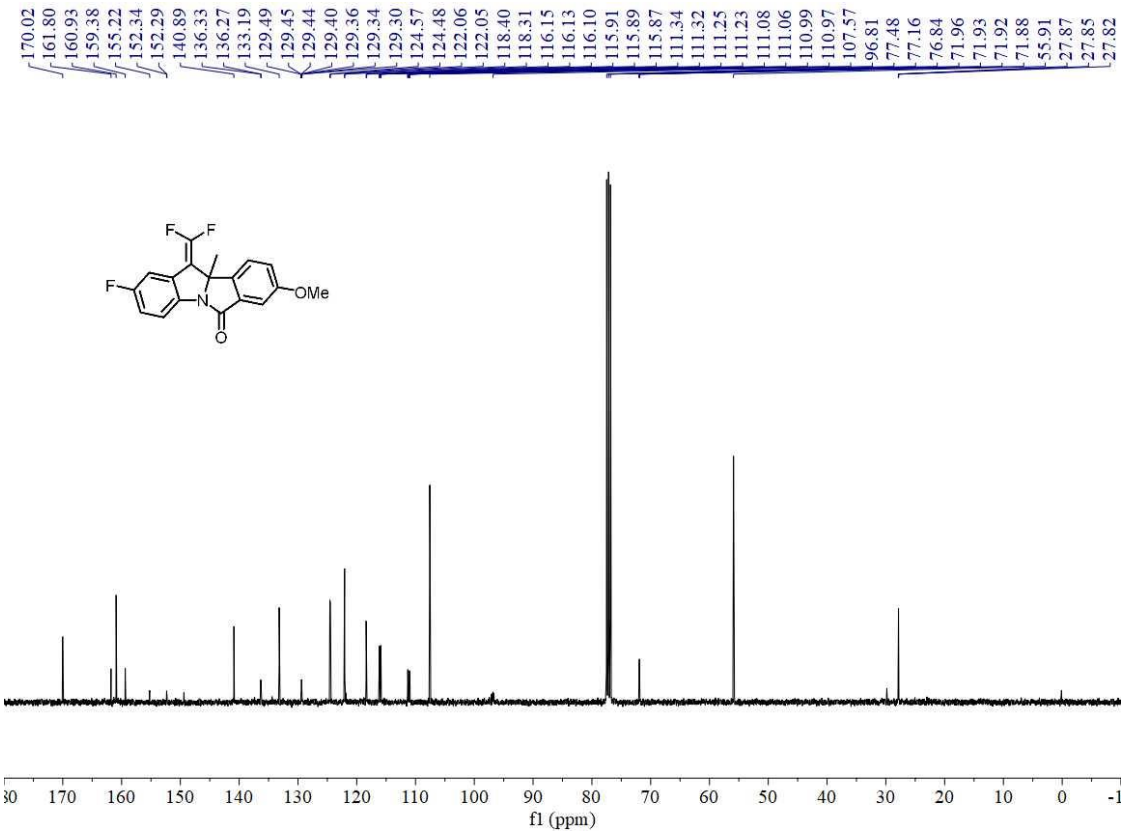
^{19}F NMR of product 3z in $CDCl_3$ (376 MHz)



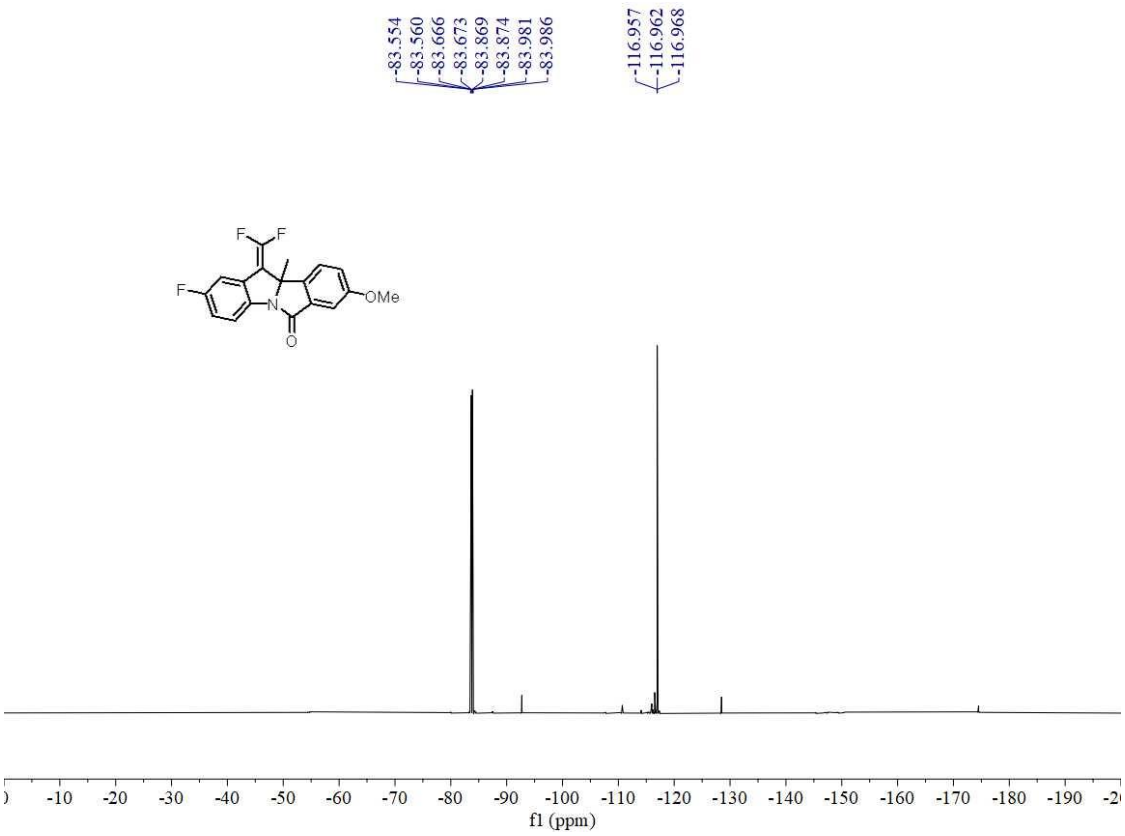
^{1}H NMR of product 3aa in $CDCl_3$ (400 MHz)



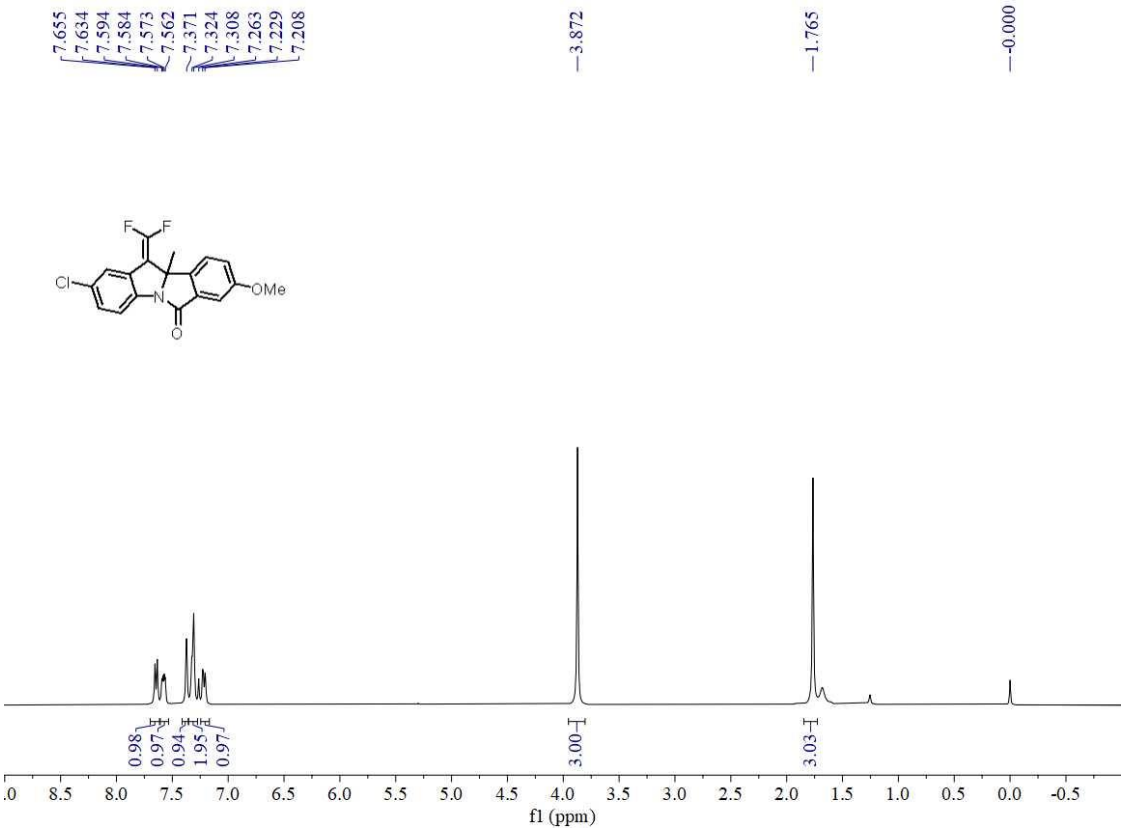
^{13}C NMR of product 3aa in $CDCl_3$ (100 MHz)



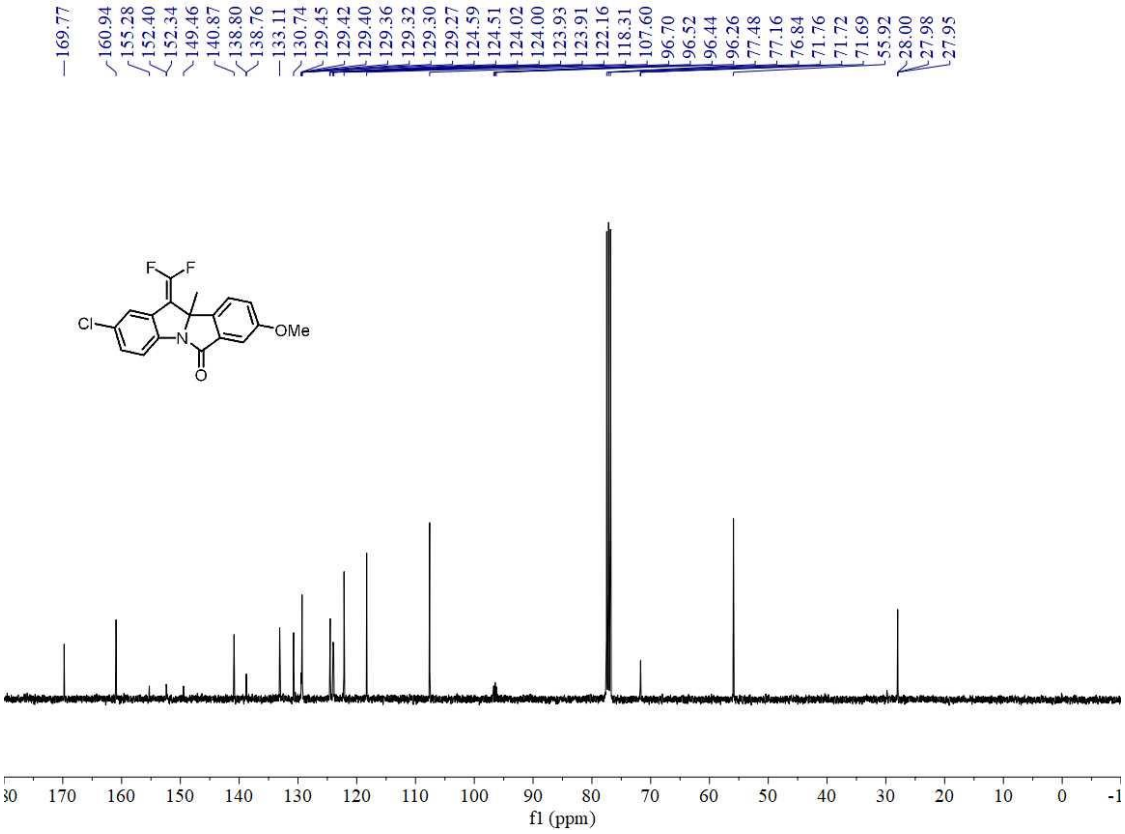
^{19}F NMR of product 3aa in $CDCl_3$ (376 MHz)



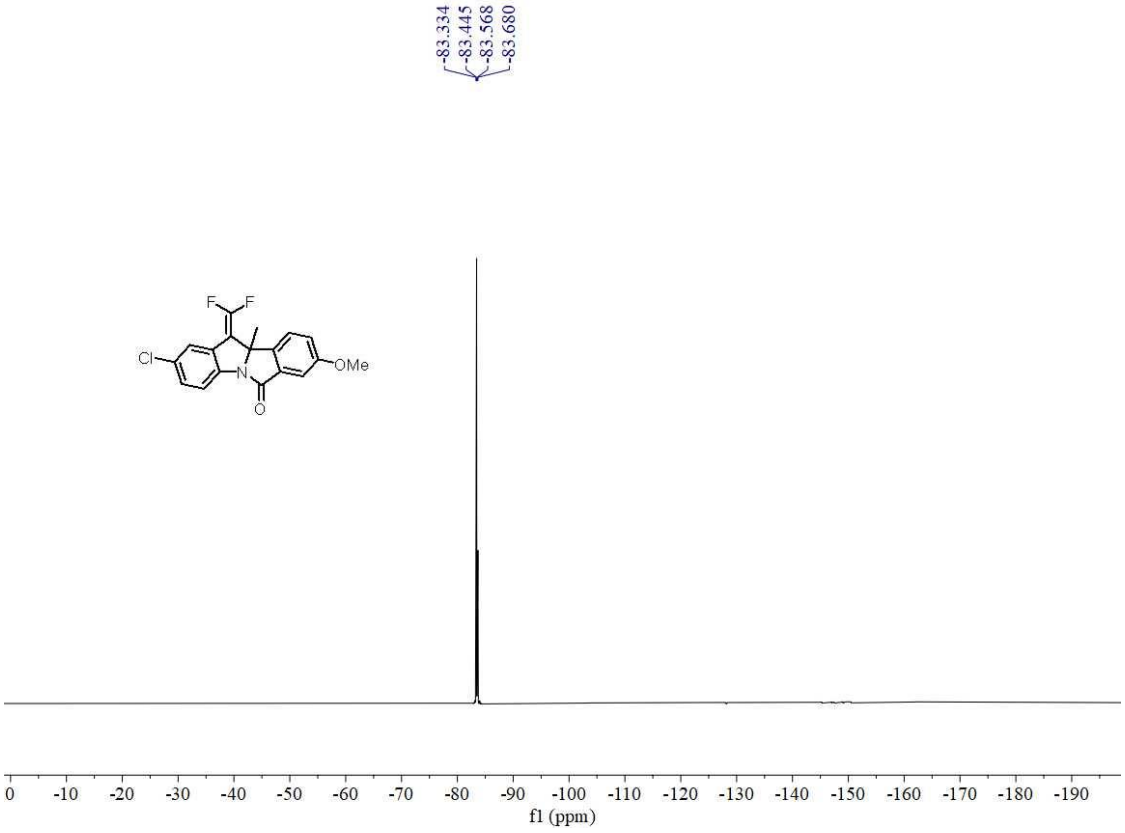
^{1}H NMR of product 3ab in $CDCl_3$ (400 MHz)



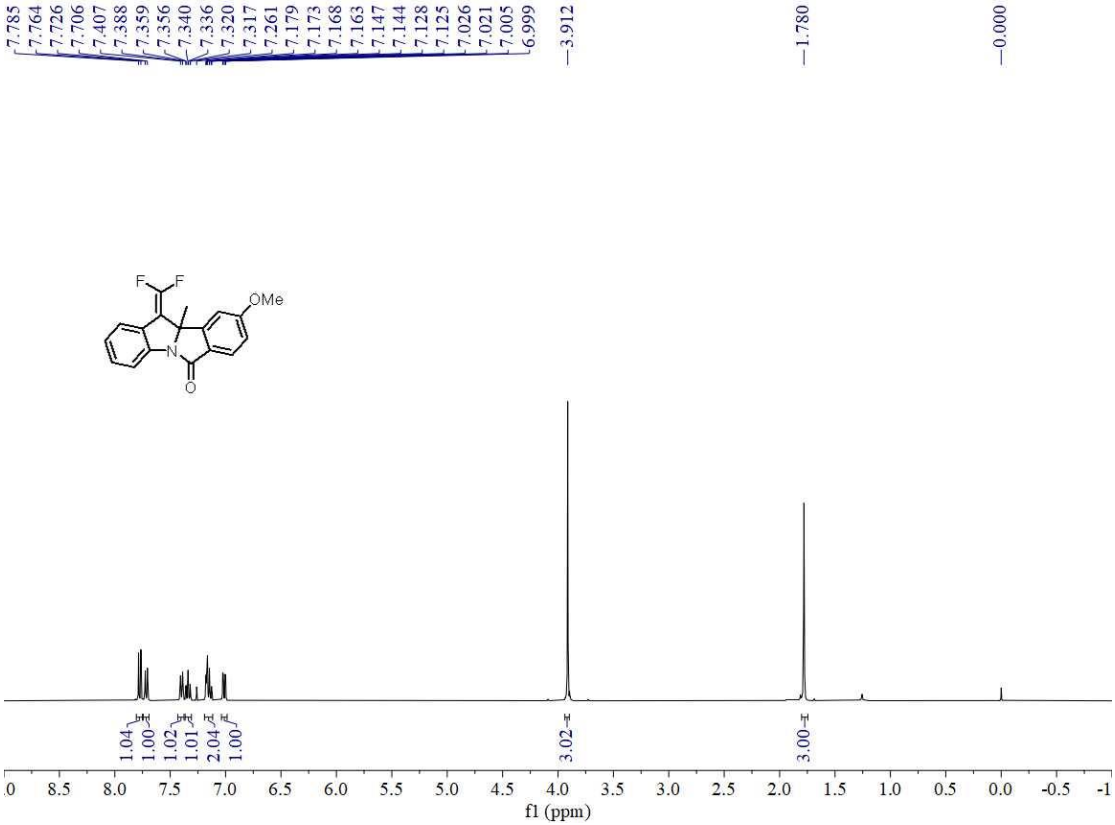
^{13}C NMR of product 3ab in $CDCl_3$ (100 MHz)



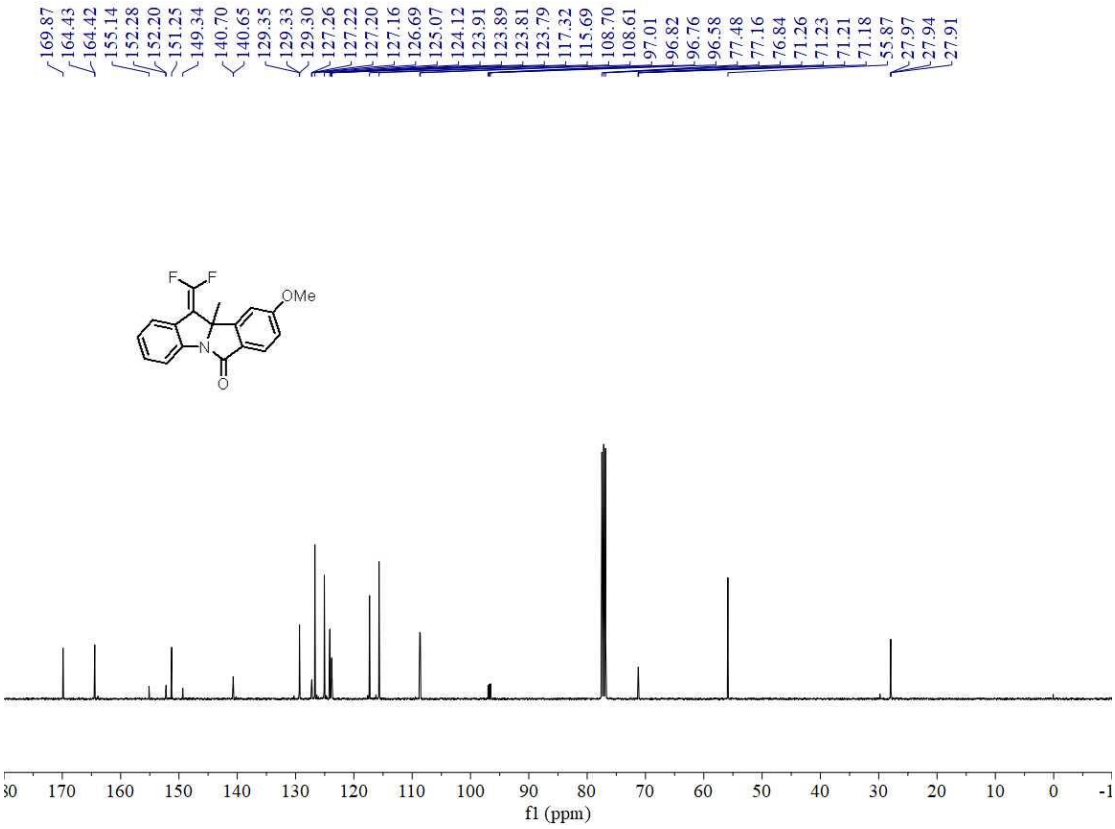
^{19}F NMR of product 3ab in $CDCl_3$ (376 MHz)



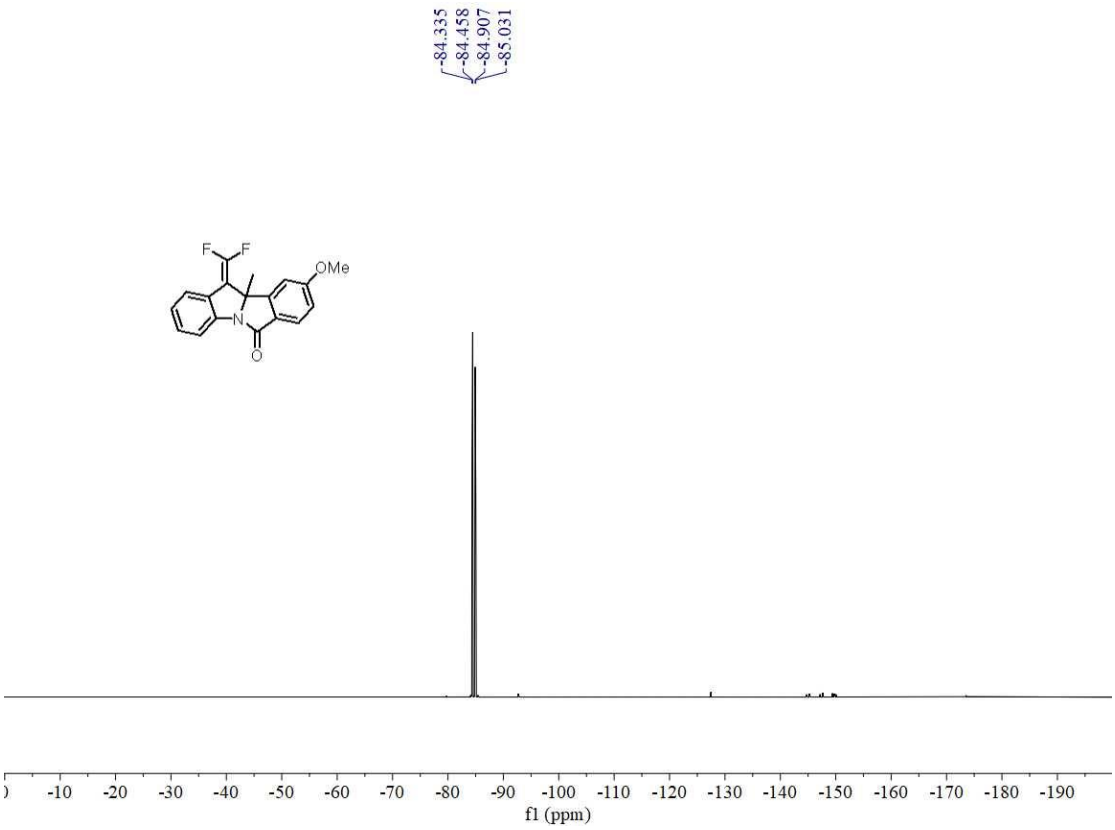
^{1}H NMR of product 3ad in $CDCl_3$ (400 MHz)



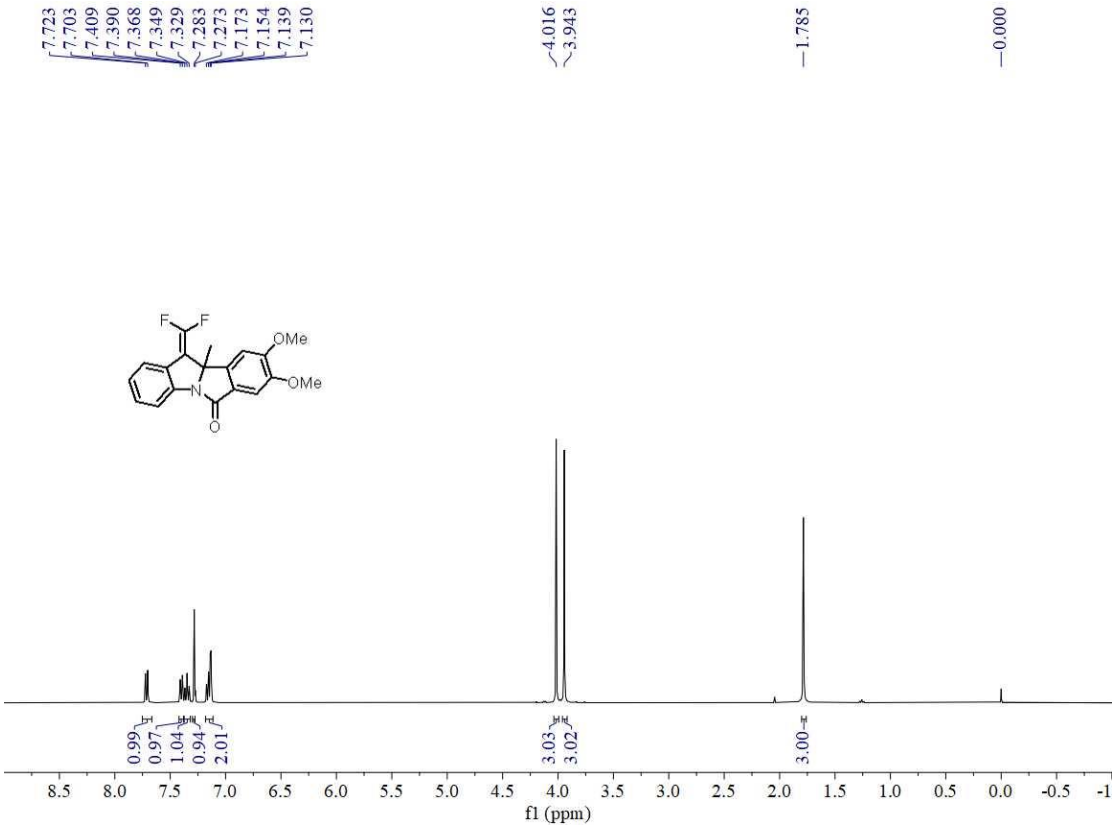
^{13}C NMR of product 3ad in $CDCl_3$ (100 MHz)



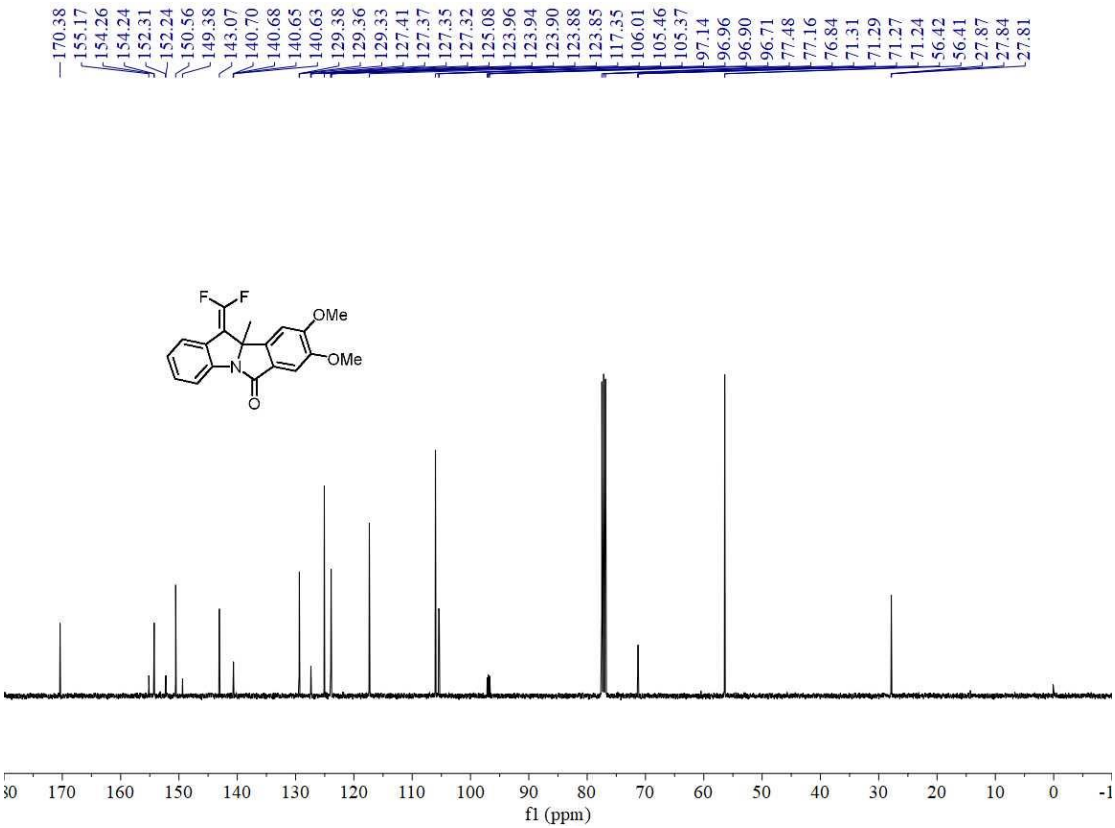
^{19}F NMR of product 3ad in $CDCl_3$ (376 MHz)



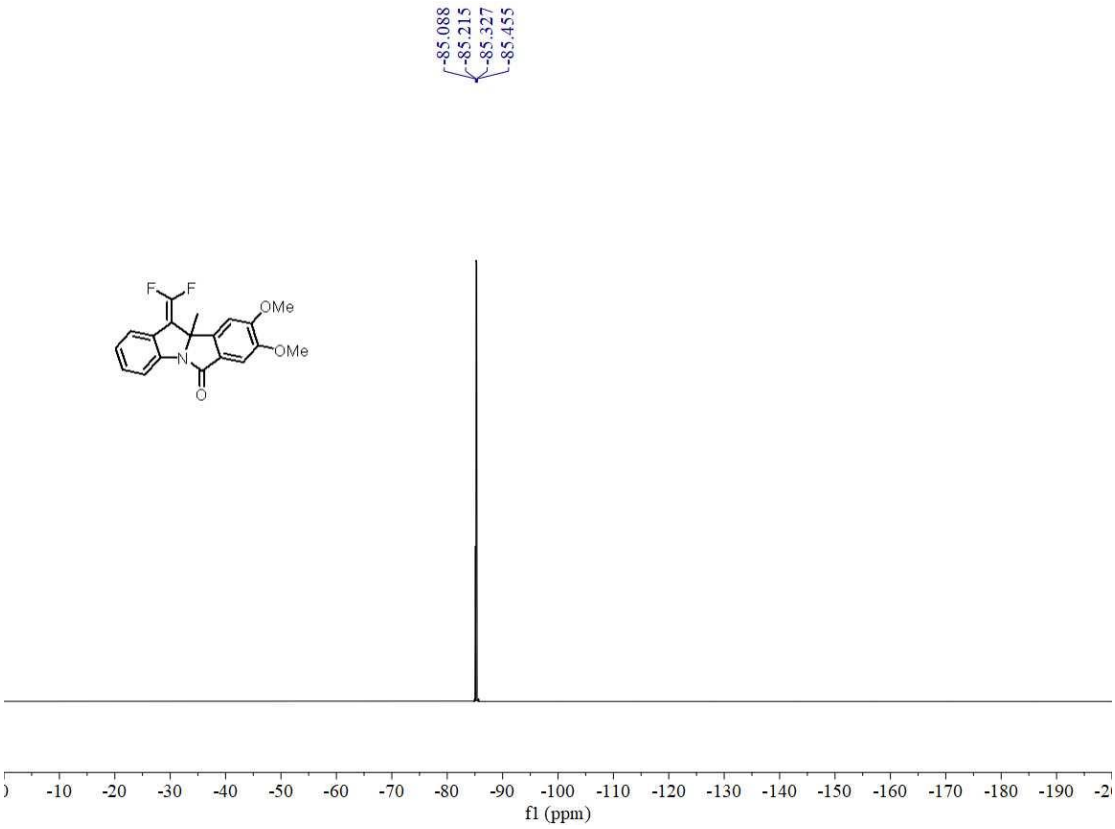
^{1}H NMR of product 3ae in $CDCl_3$ (400 MHz)



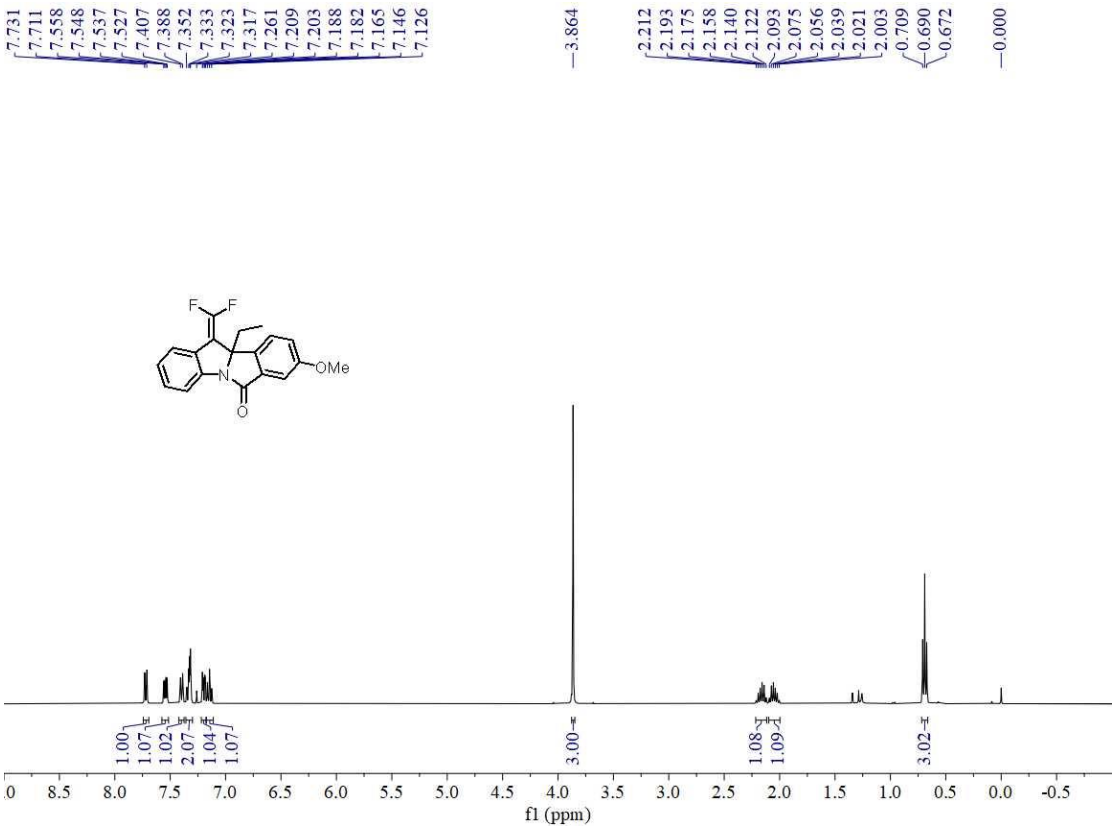
^{13}C NMR of product 3ae in $CDCl_3$ (100 MHz)



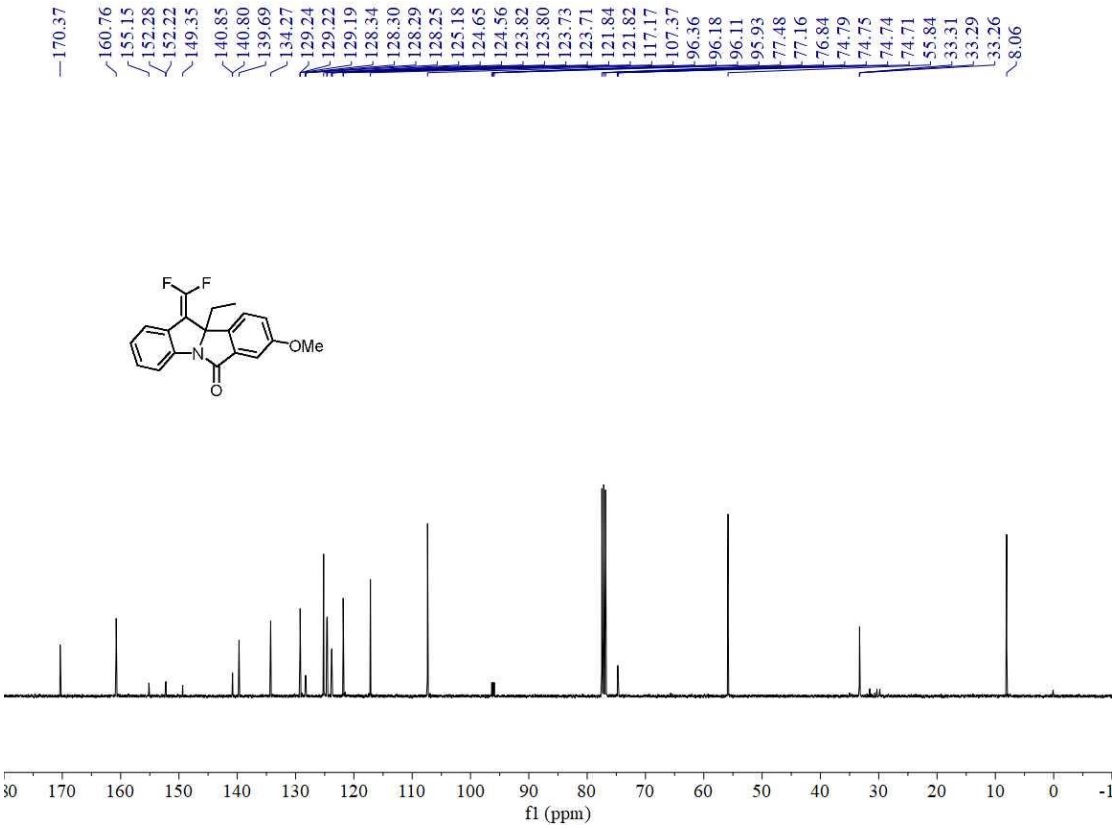
^{19}F NMR of product 3ae in $CDCl_3$ (376 MHz)



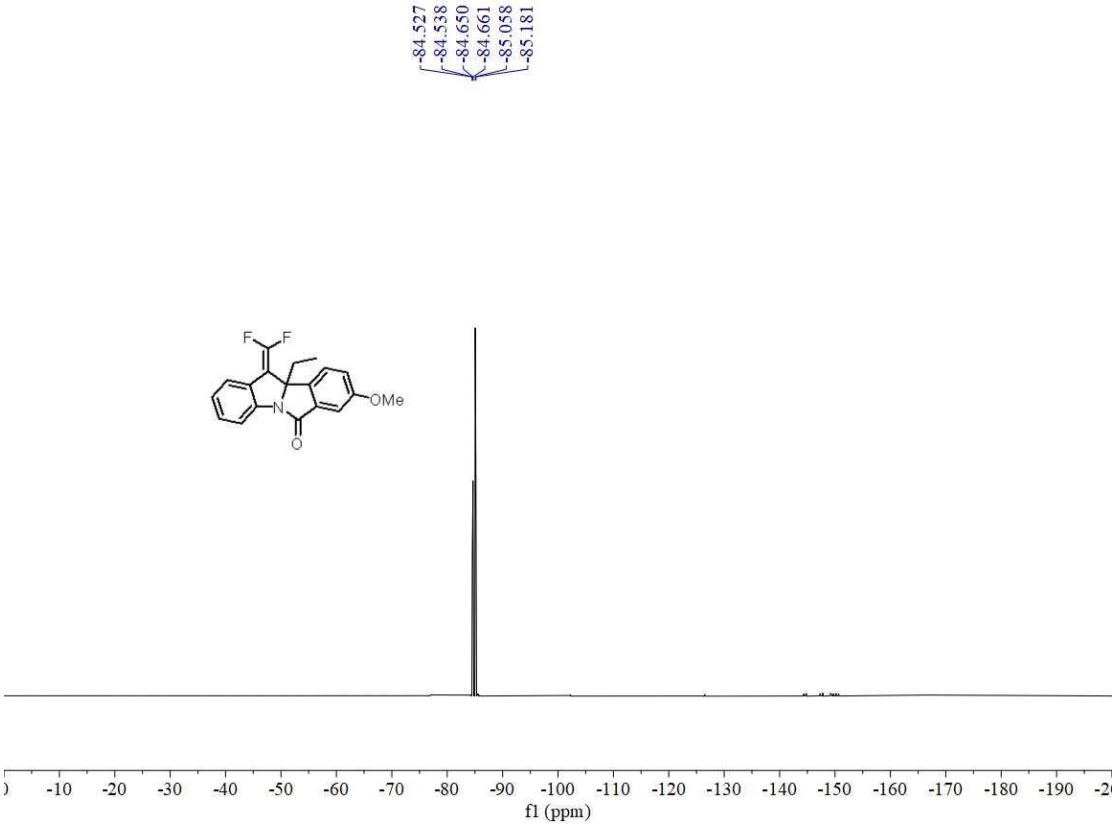
^{1}H NMR of product 3af in $CDCl_3$ (400 MHz)



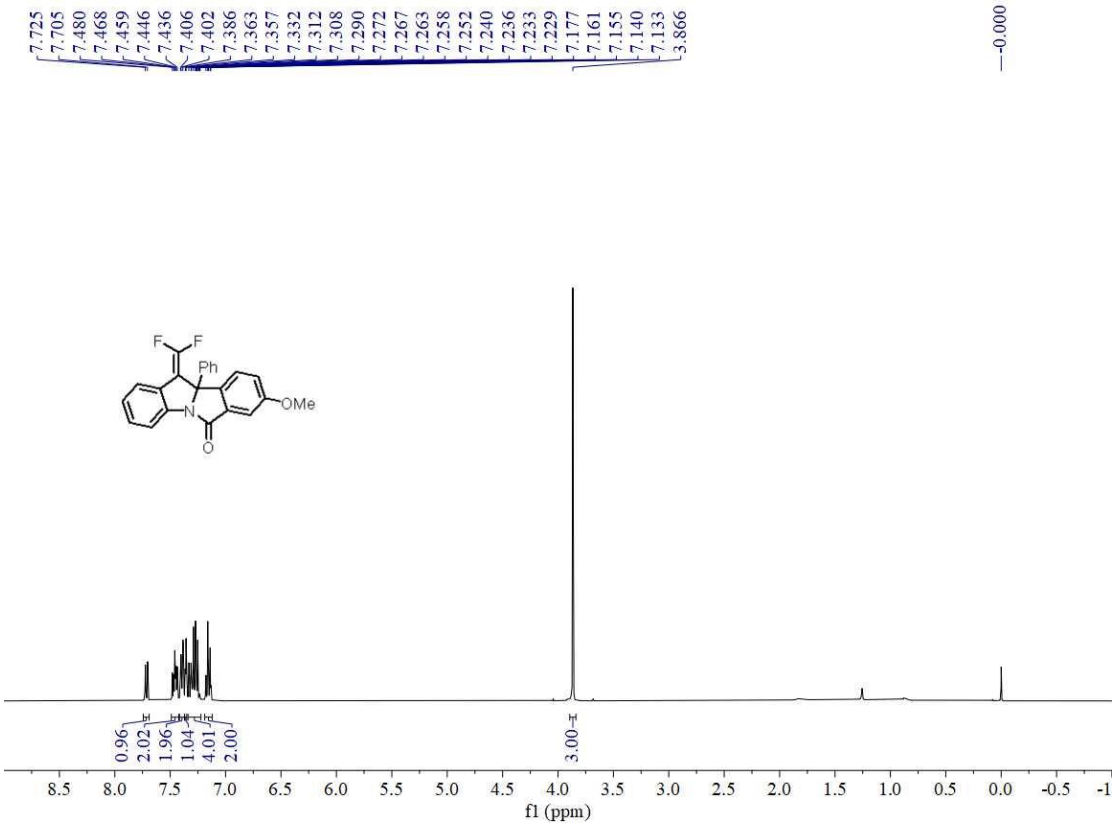
^{13}C NMR of product 3af in $CDCl_3$ (100 MHz)



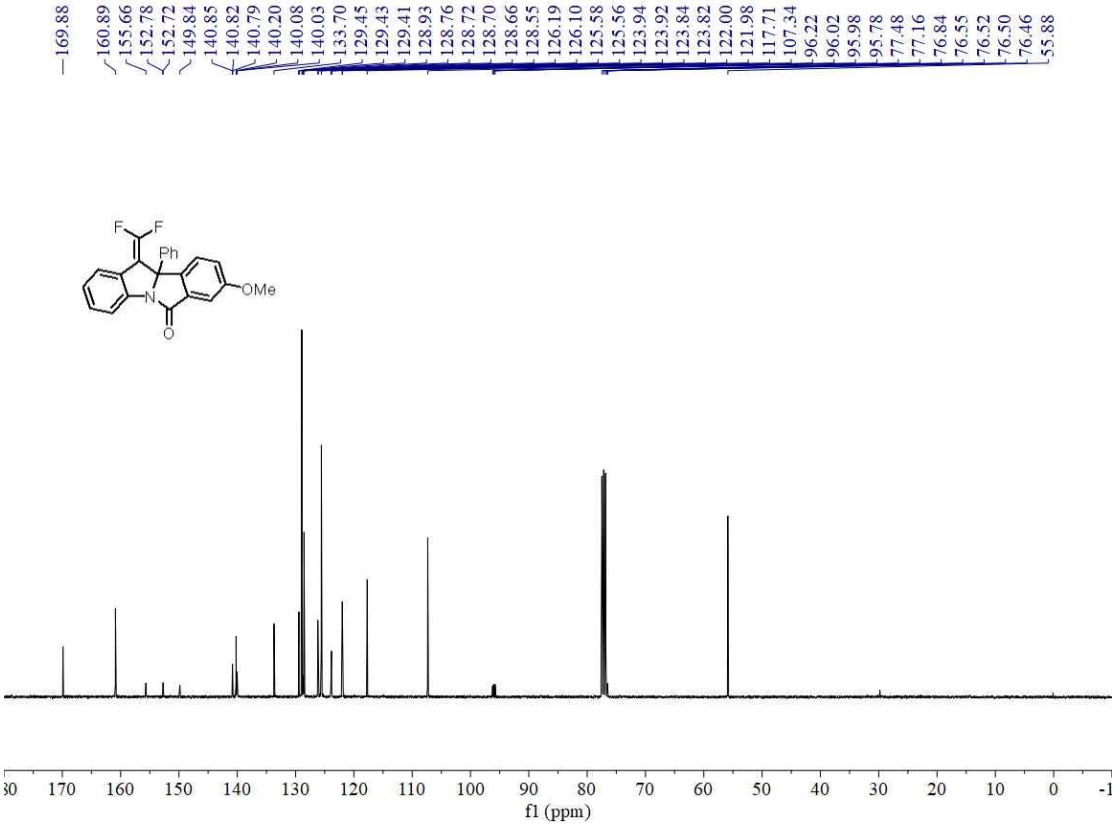
^{19}F NMR of product 3af in $CDCl_3$ (376 MHz)



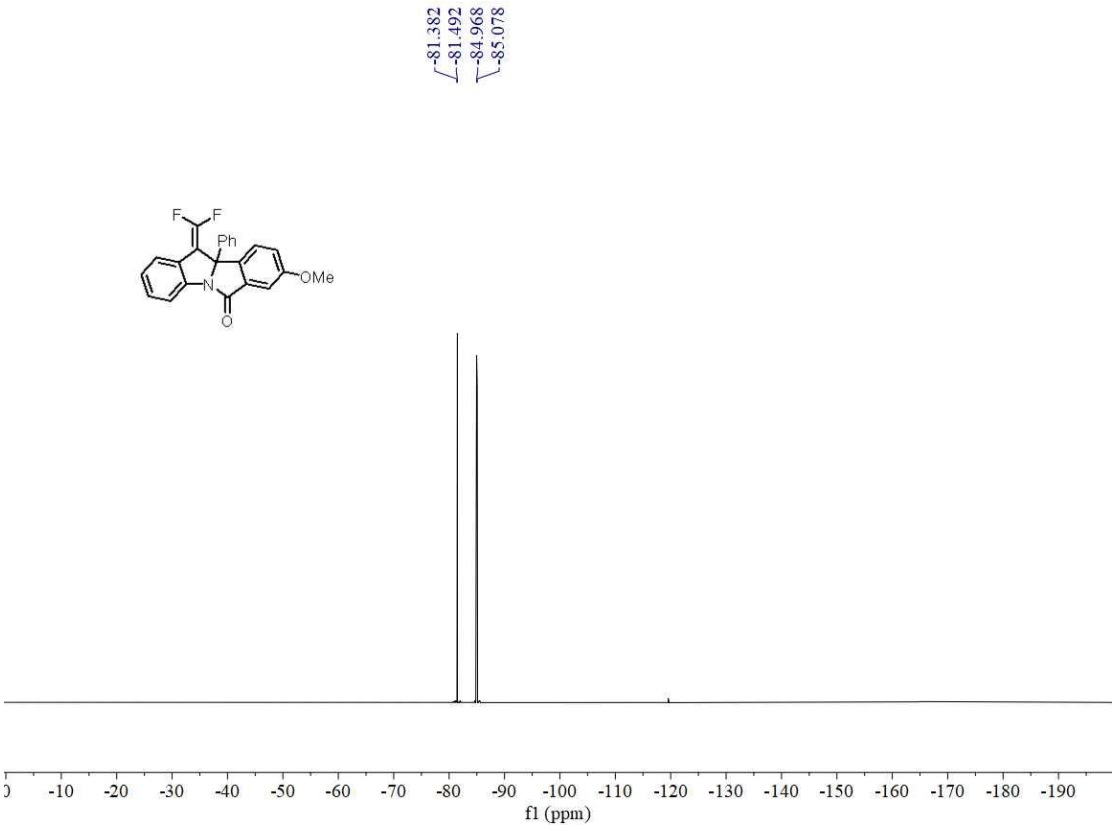
^{1}H NMR of product 3ag in $CDCl_3$ (400 MHz)



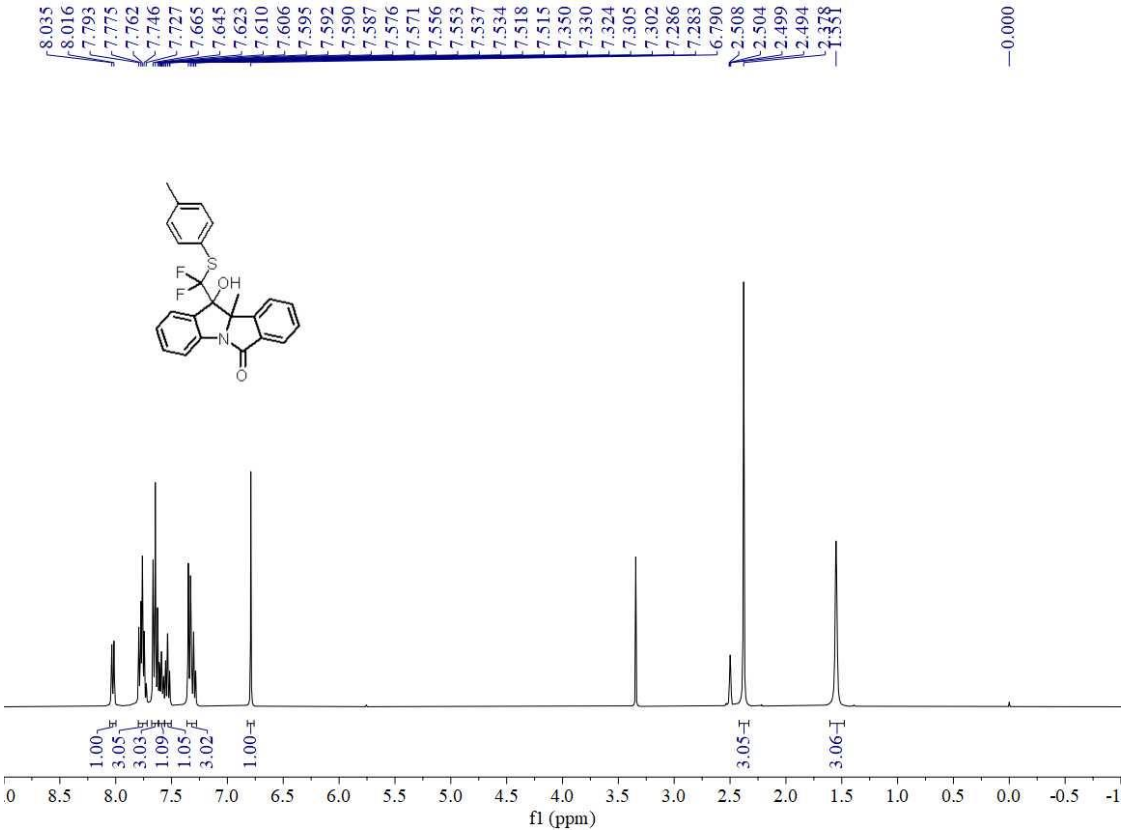
^{13}C NMR of product 3ag in $CDCl_3$ (100 MHz)



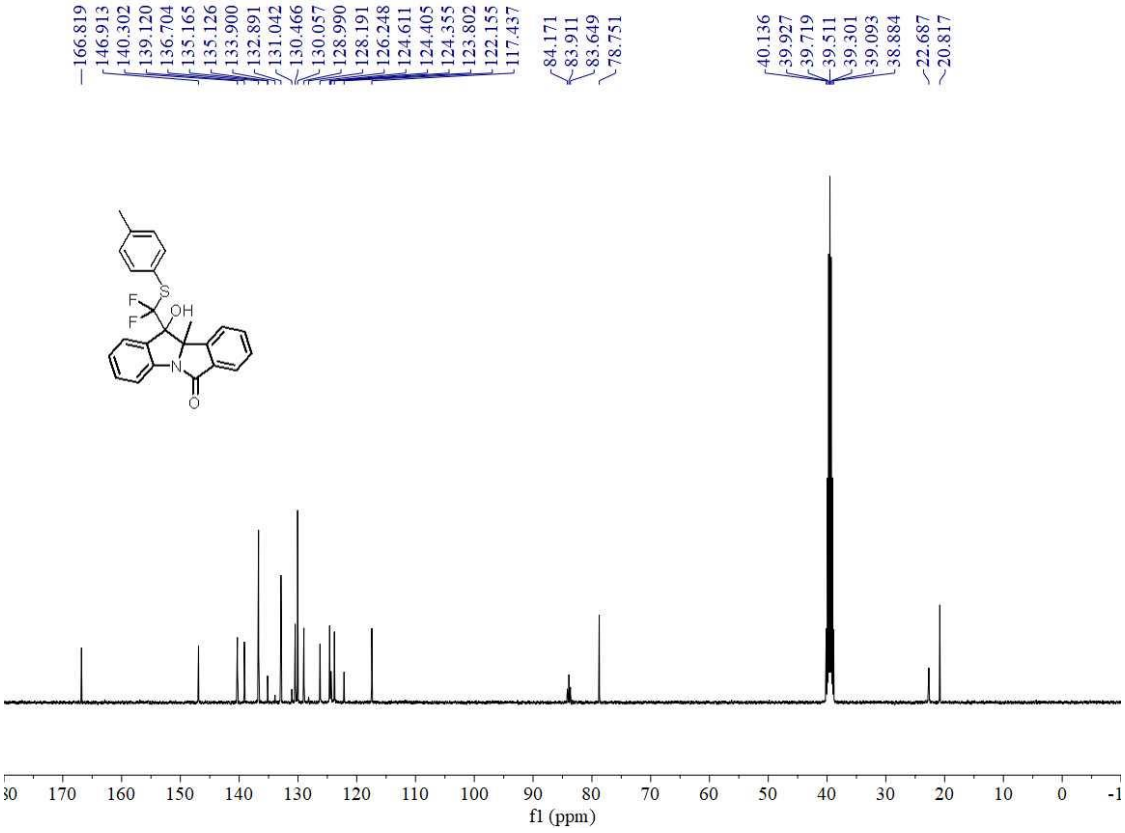
^{19}F NMR of product 3ag in $CDCl_3$ (376 MHz)



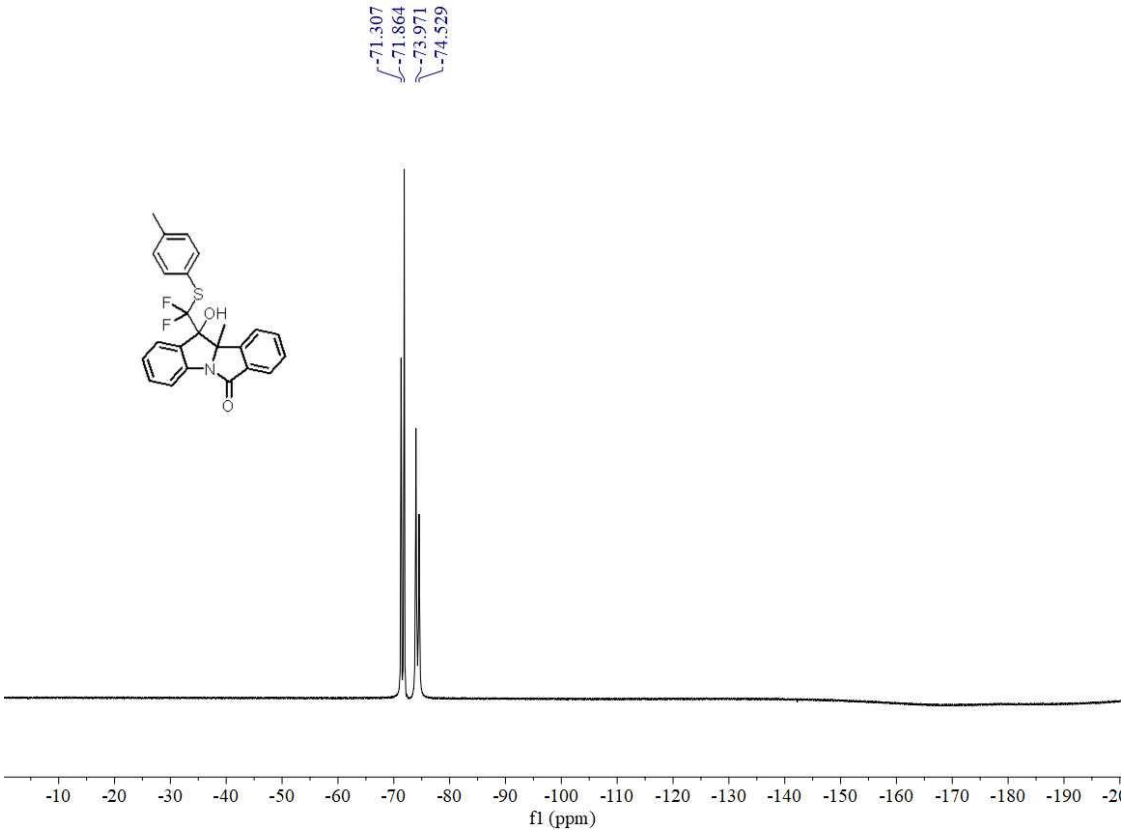
^{1}H NMR of product 4a in DMSO-d_6 (400 MHz)



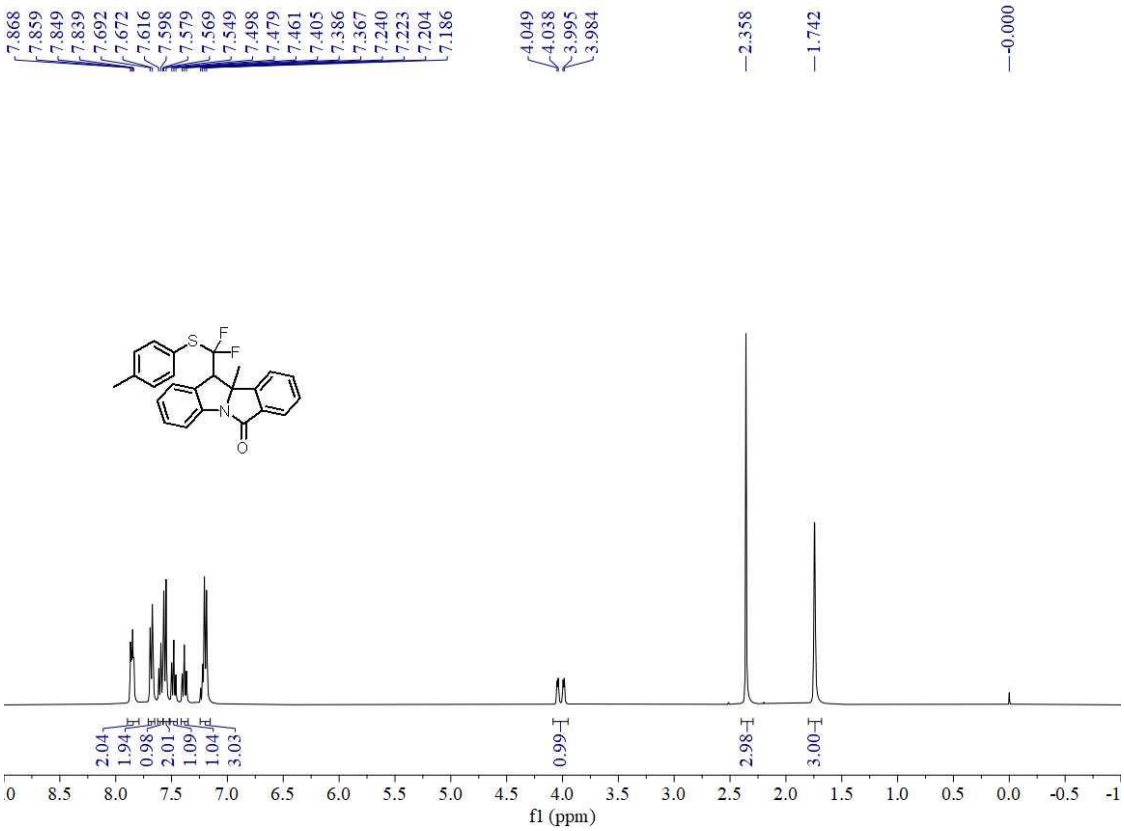
^{13}C NMR of product 4a in DMSO-d_6 (100 MHz)



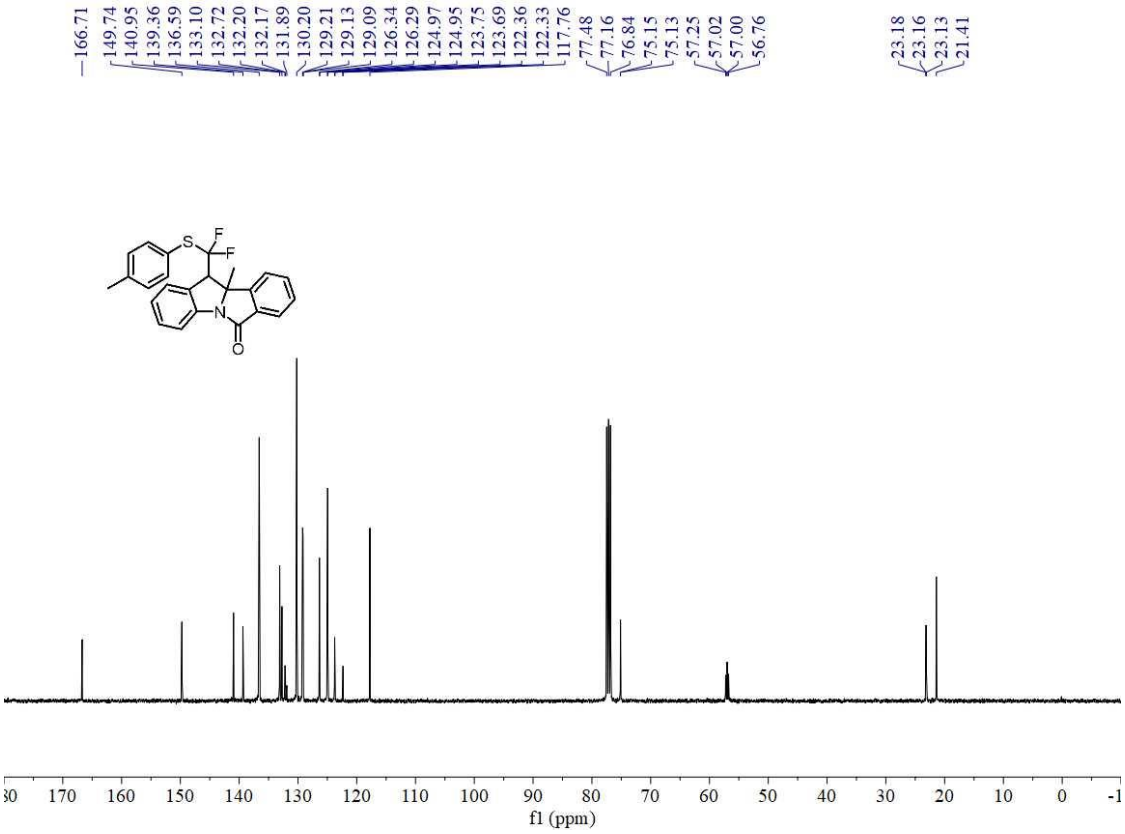
^{19}F NMR of product 4a in DMSO-d_6 (376 MHz)



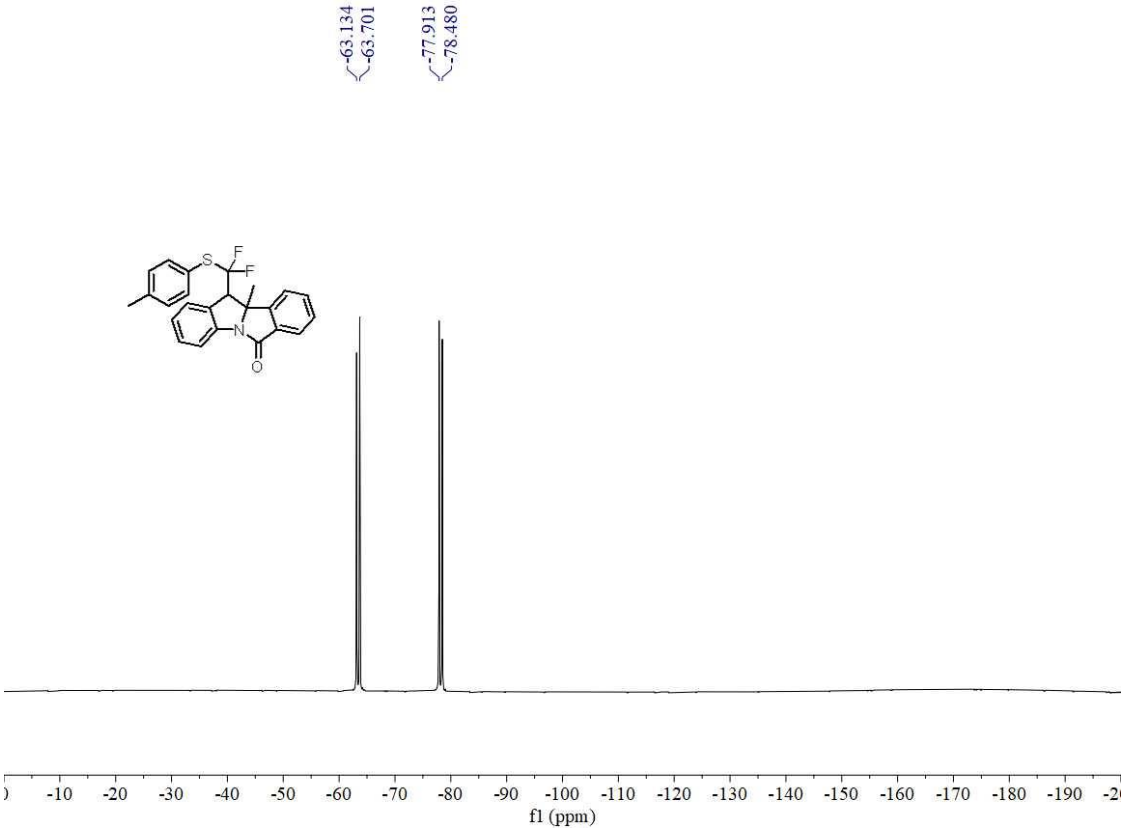
^{1}H NMR of product 4b in $CDCl_3$ (400 MHz)



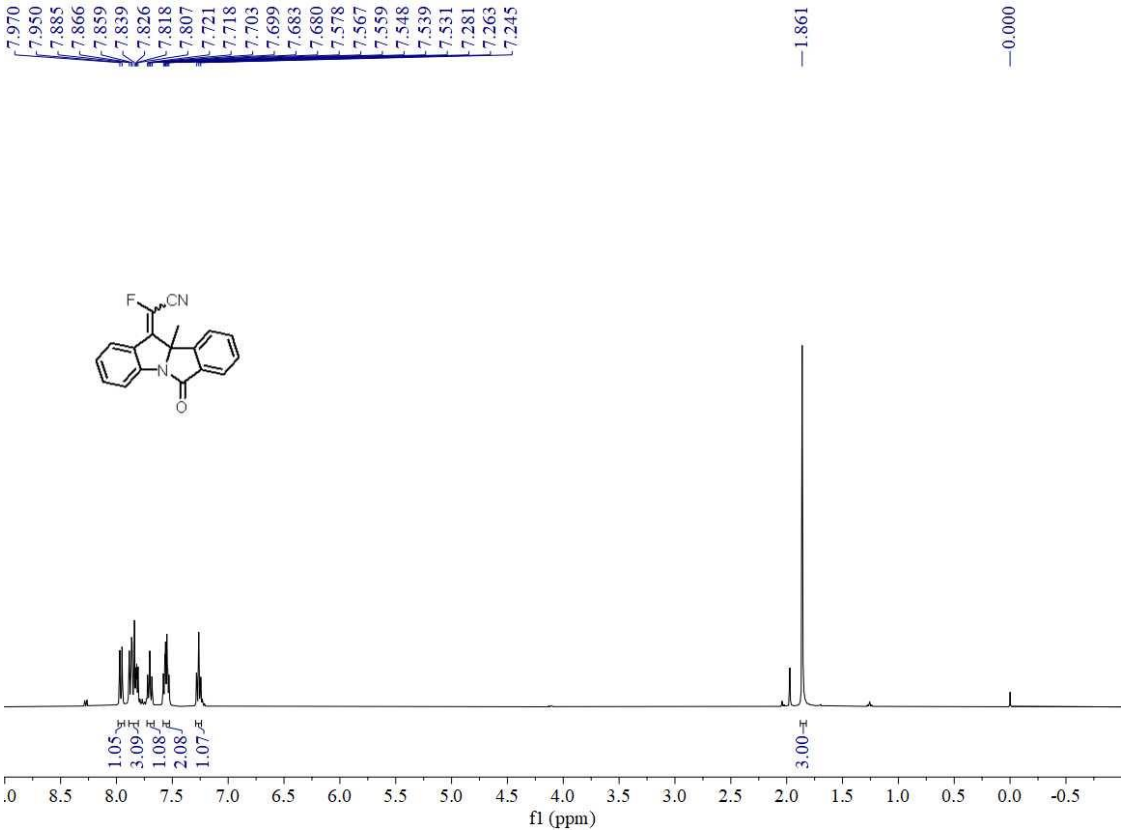
^{13}C NMR of product 4b in $CDCl_3$ (100 MHz)



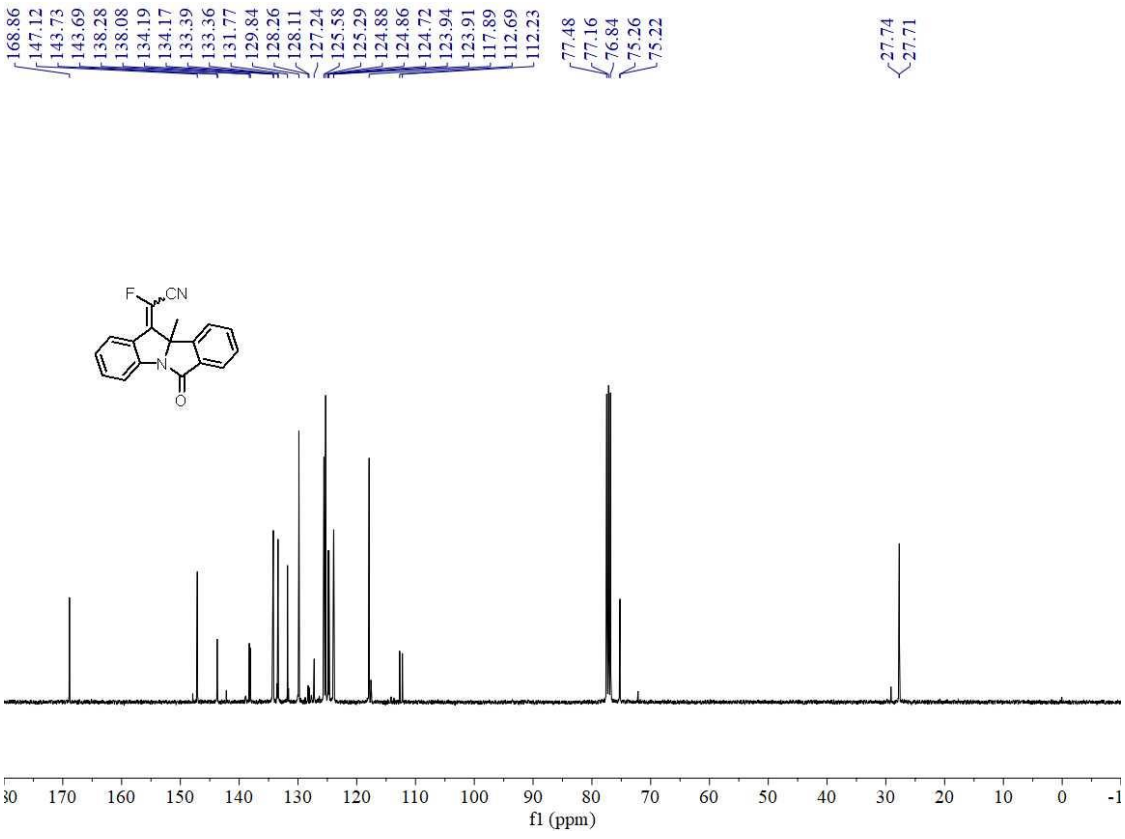
^{19}F NMR of product 4b in $CDCl_3$ (376 MHz)



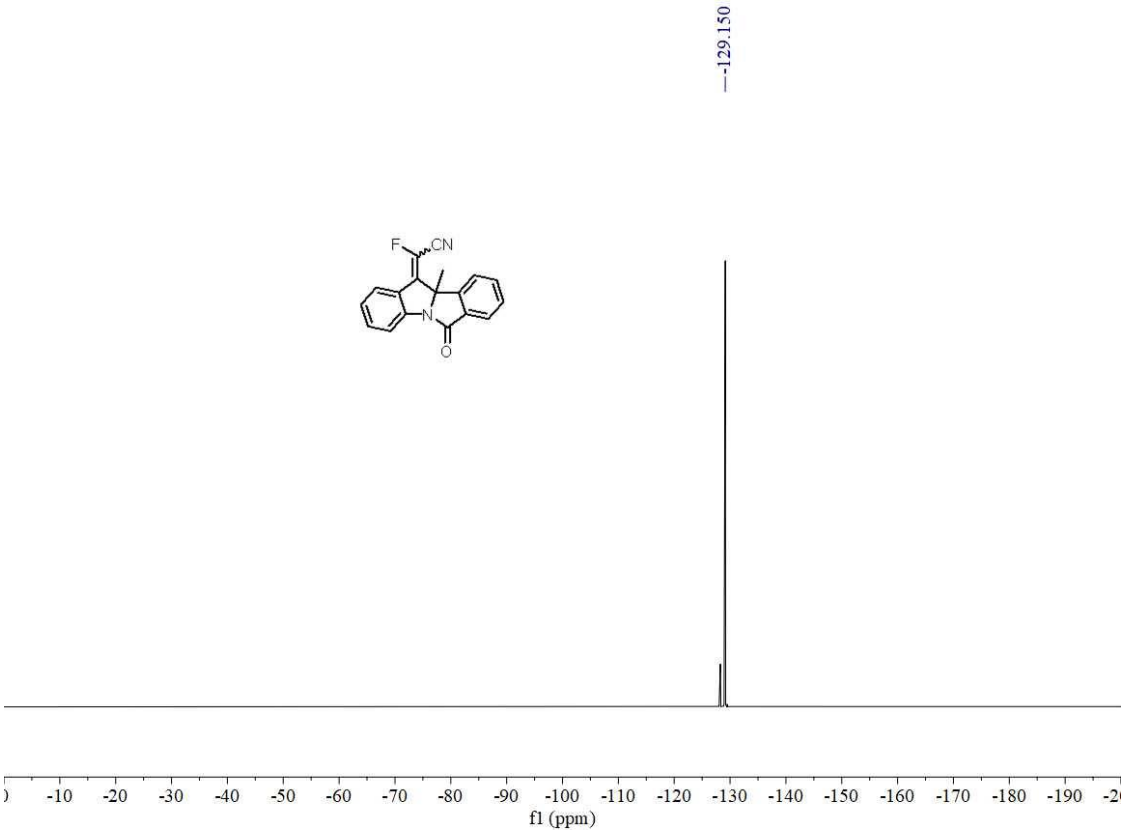
^{1}H NMR of product 4c in $CDCl_3$ (400 MHz)



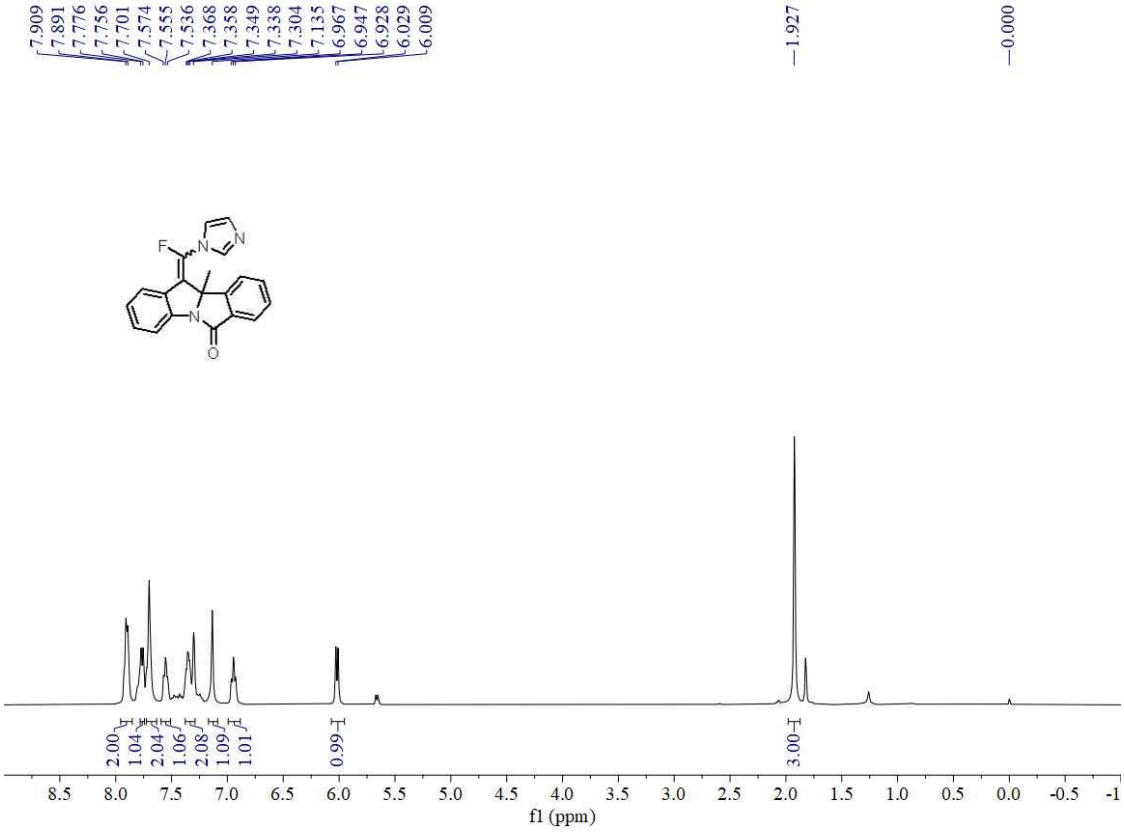
^{13}C NMR of product 4c in $CDCl_3$ (100 MHz)



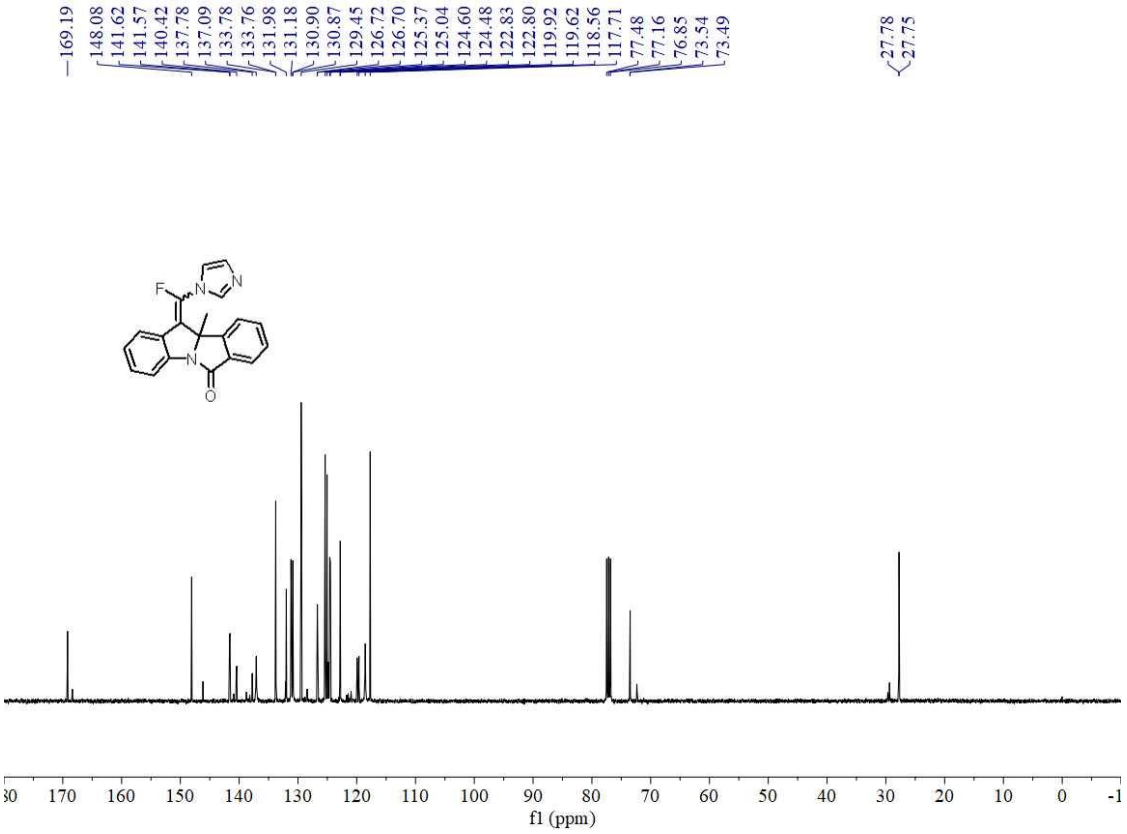
^{19}F NMR of product 4c in $CDCl_3$ (376 MHz)



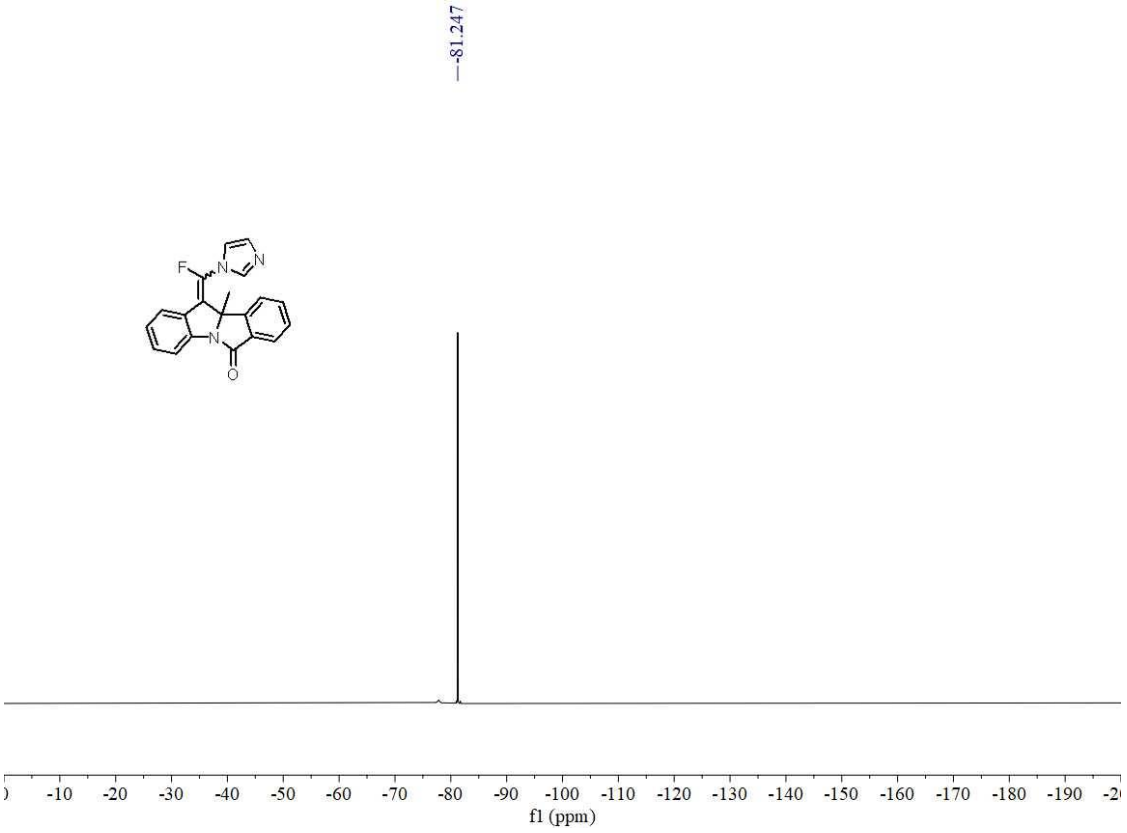
^{1}H NMR of product 4d in $CDCl_3$ (400 MHz)



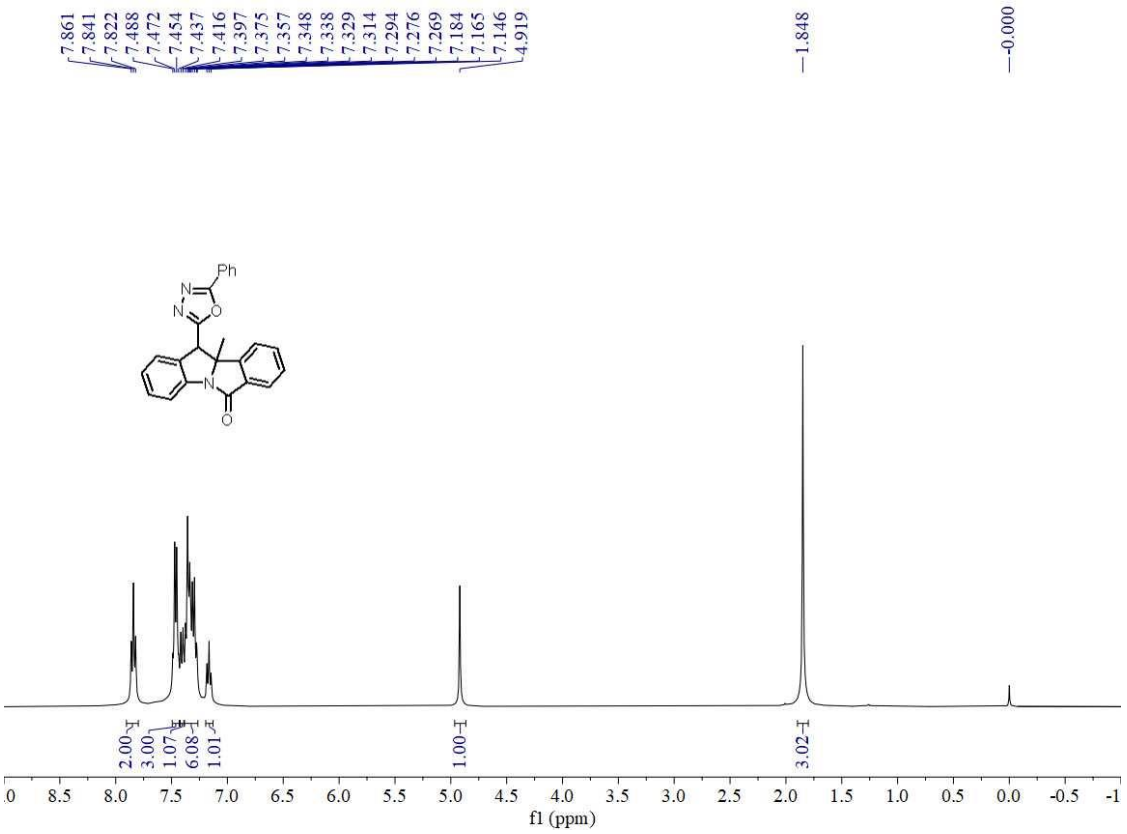
^{13}C NMR of product 4d in $CDCl_3$ (100 MHz)



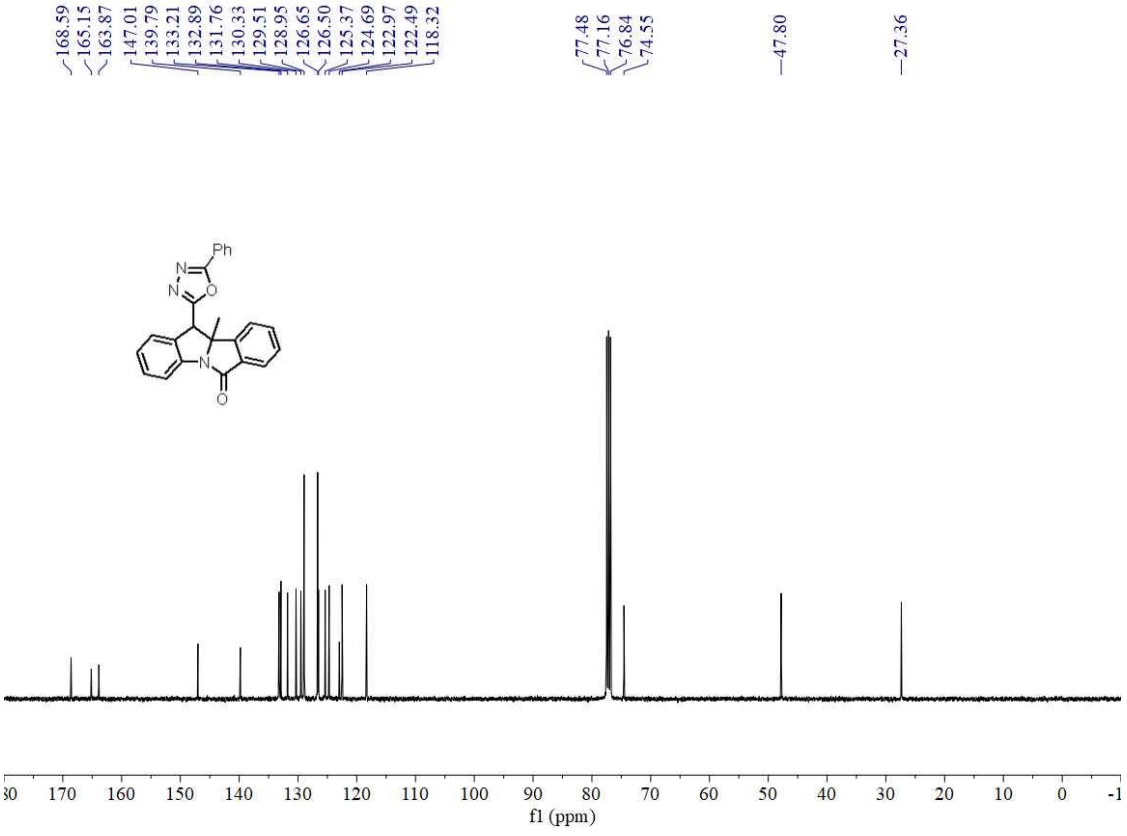
^{19}F NMR of product 4d in $CDCl_3$ (376 MHz)



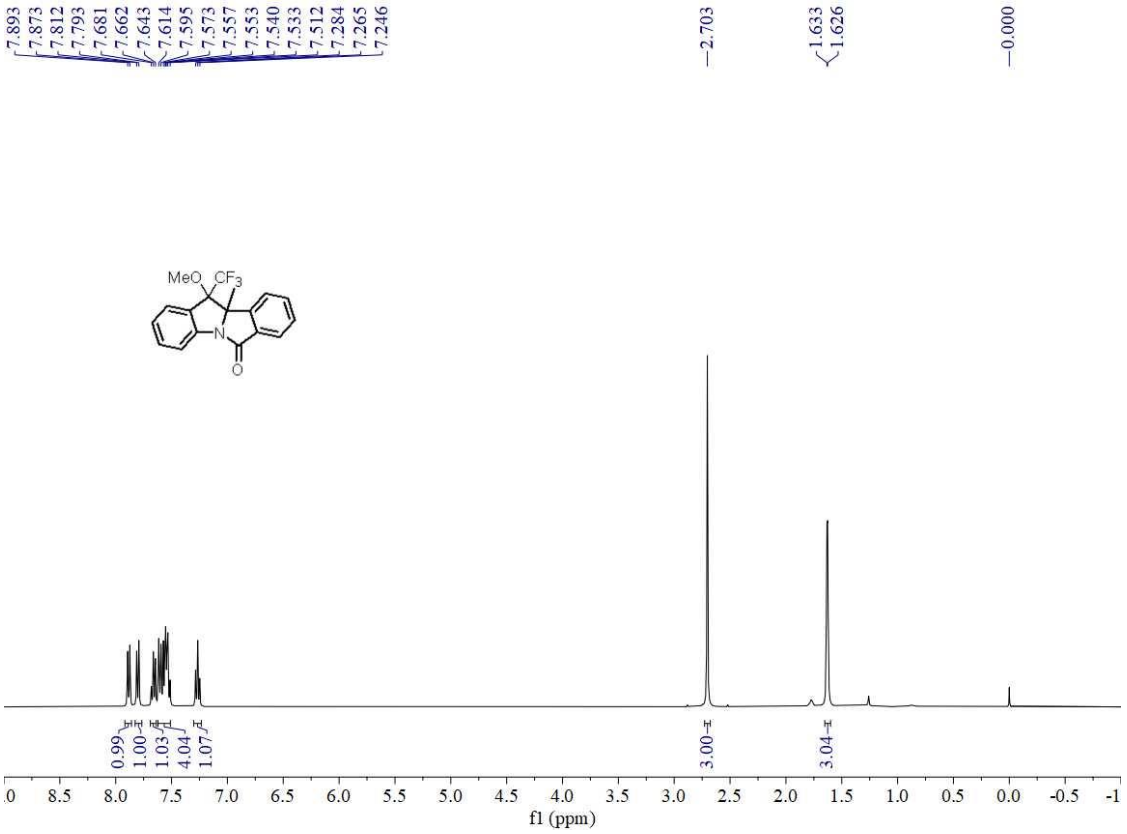
^{1}H NMR of product 4e in $CDCl_3$ (400 MHz)



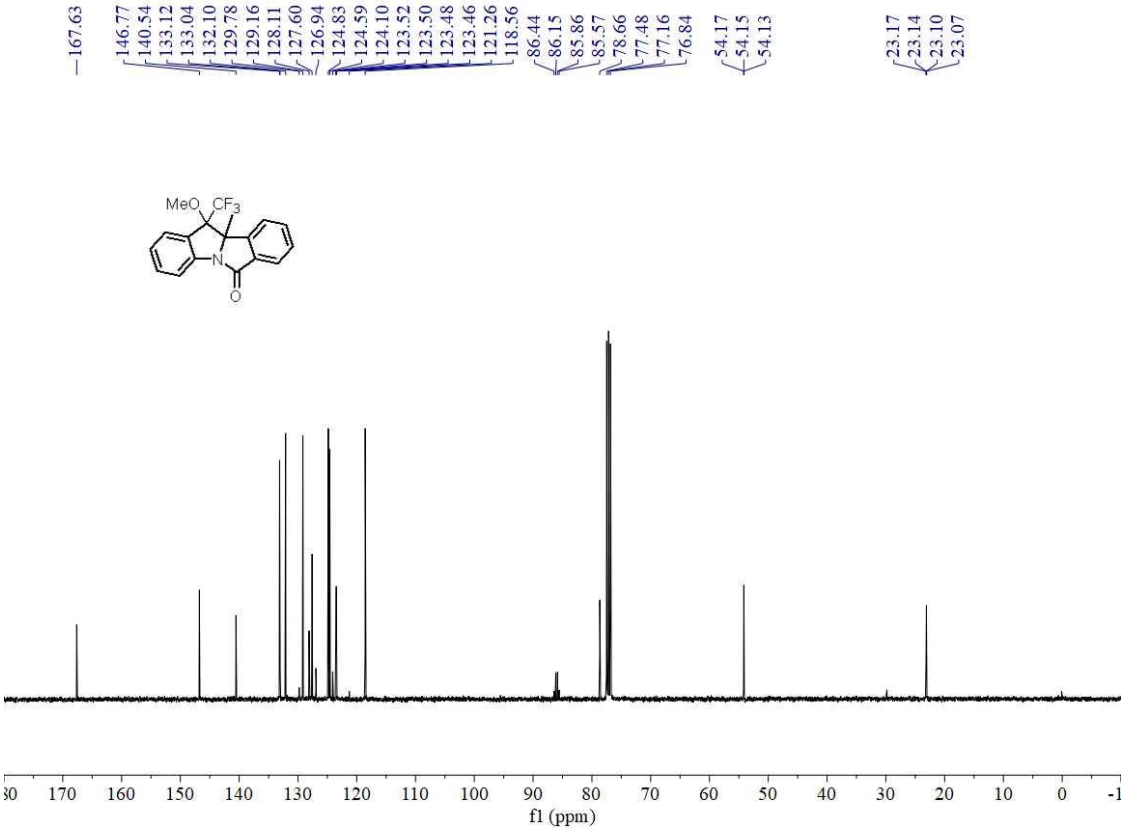
^{13}C NMR of product 4e in $CDCl_3$ (100 MHz)



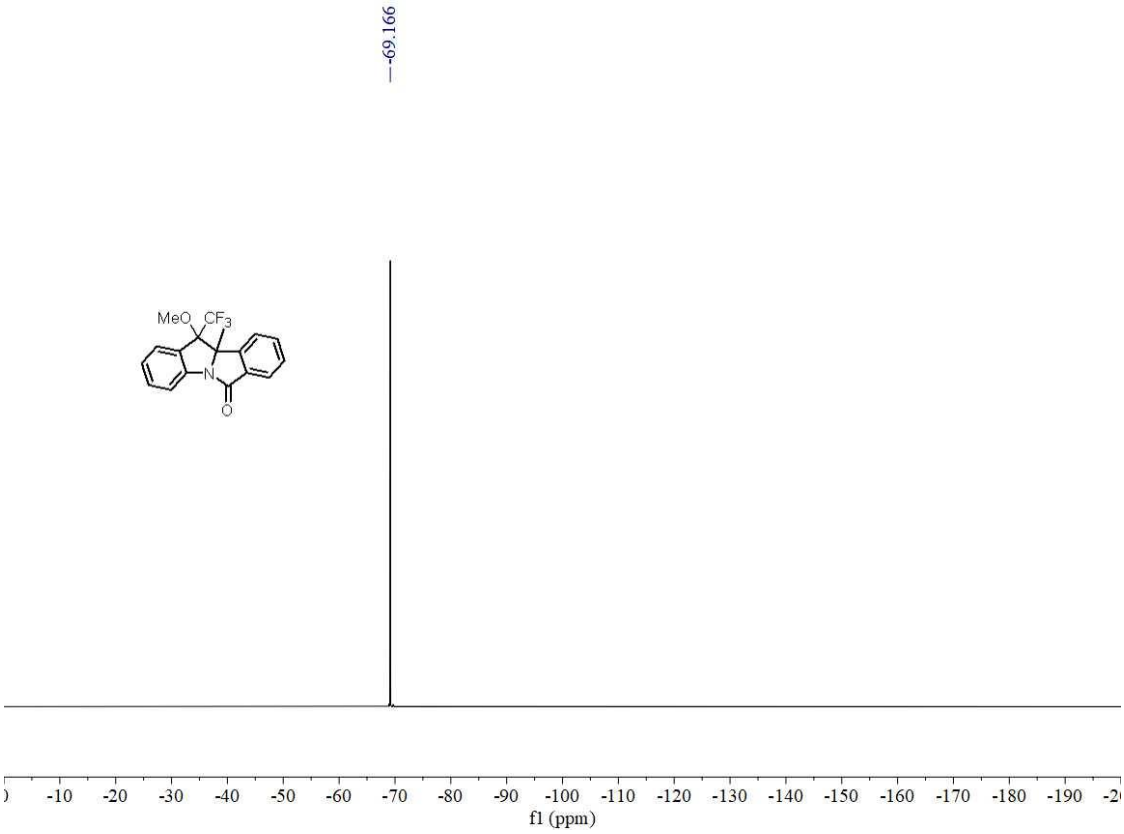
^{1}H NMR of product 4f in $CDCl_3$ (400 MHz)



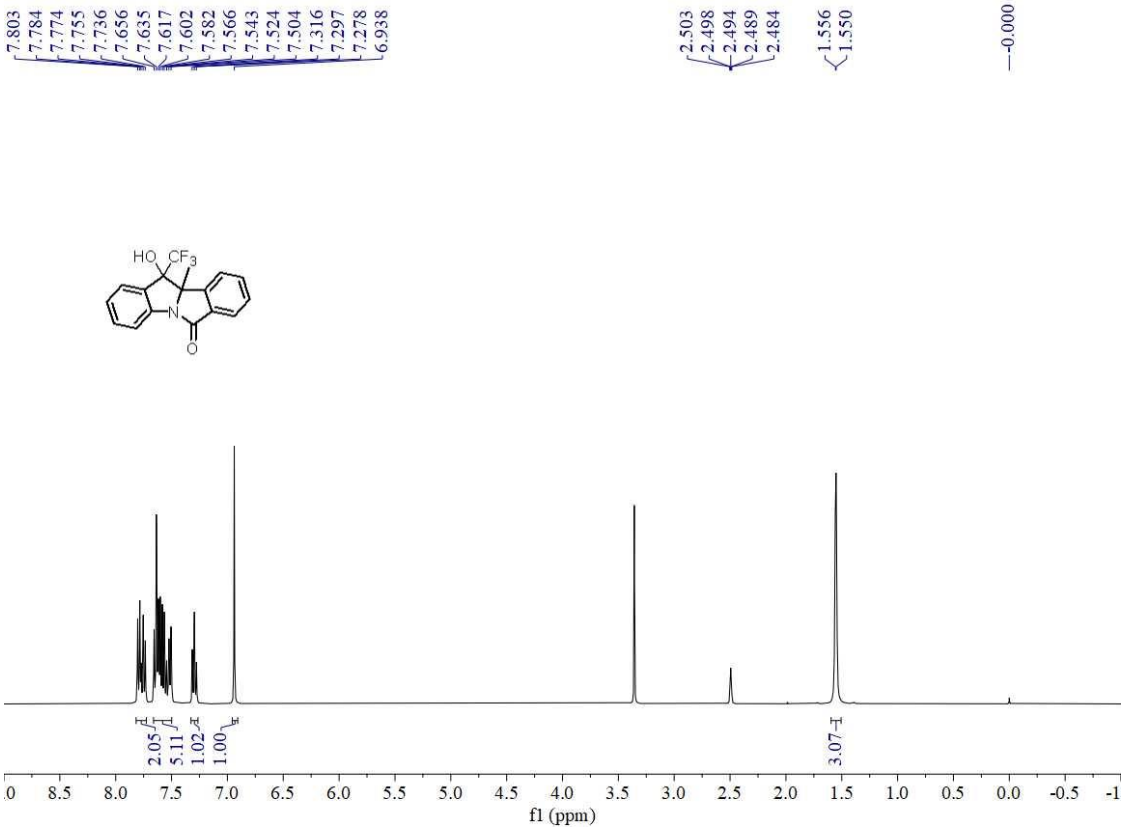
^{13}C NMR of product 4f in $CDCl_3$ (100 MHz)



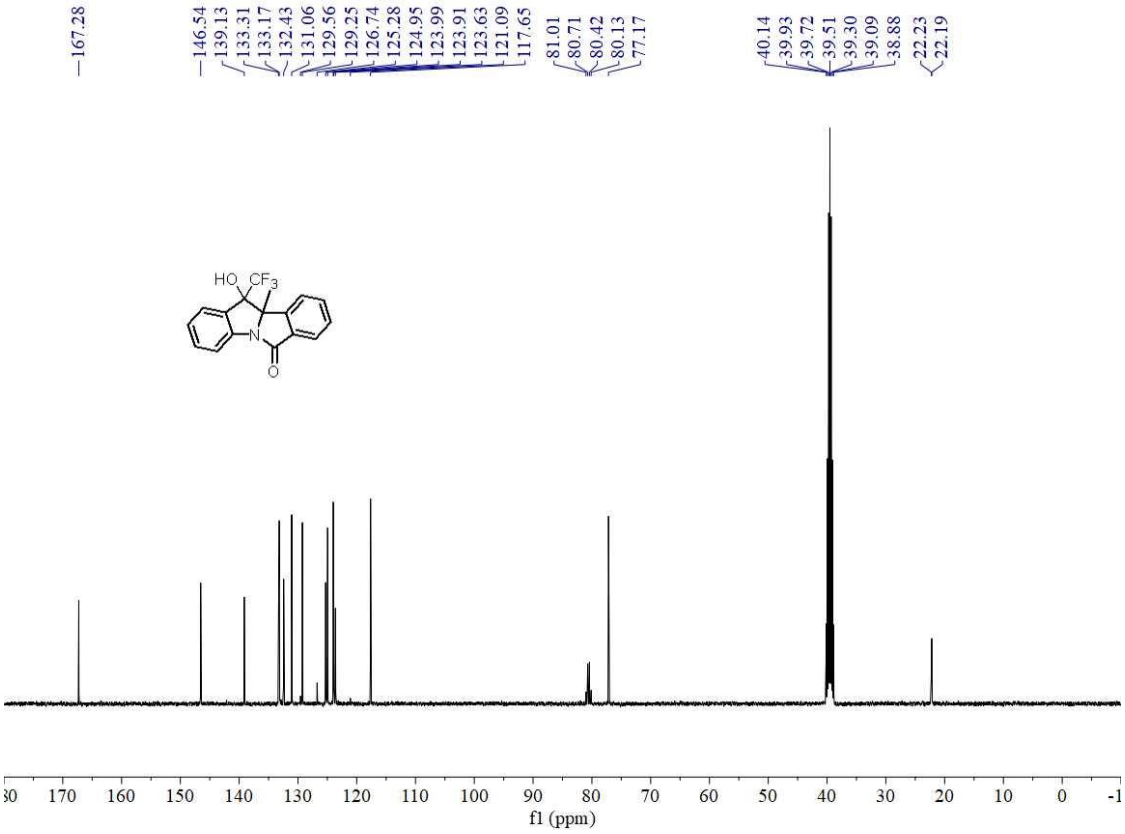
^{19}F NMR of product 4f in $CDCl_3$ (376 MHz)



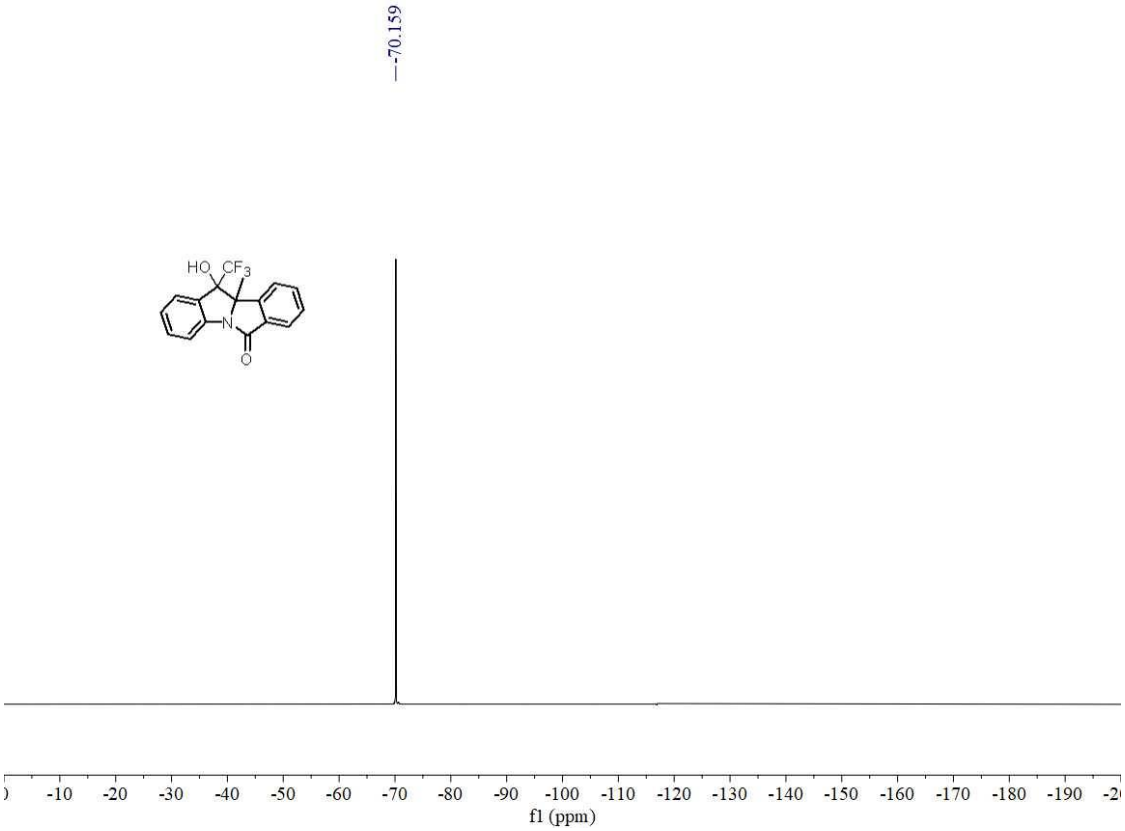
^{1}H NMR of product 4g in DMSO-d_6 (400 MHz)



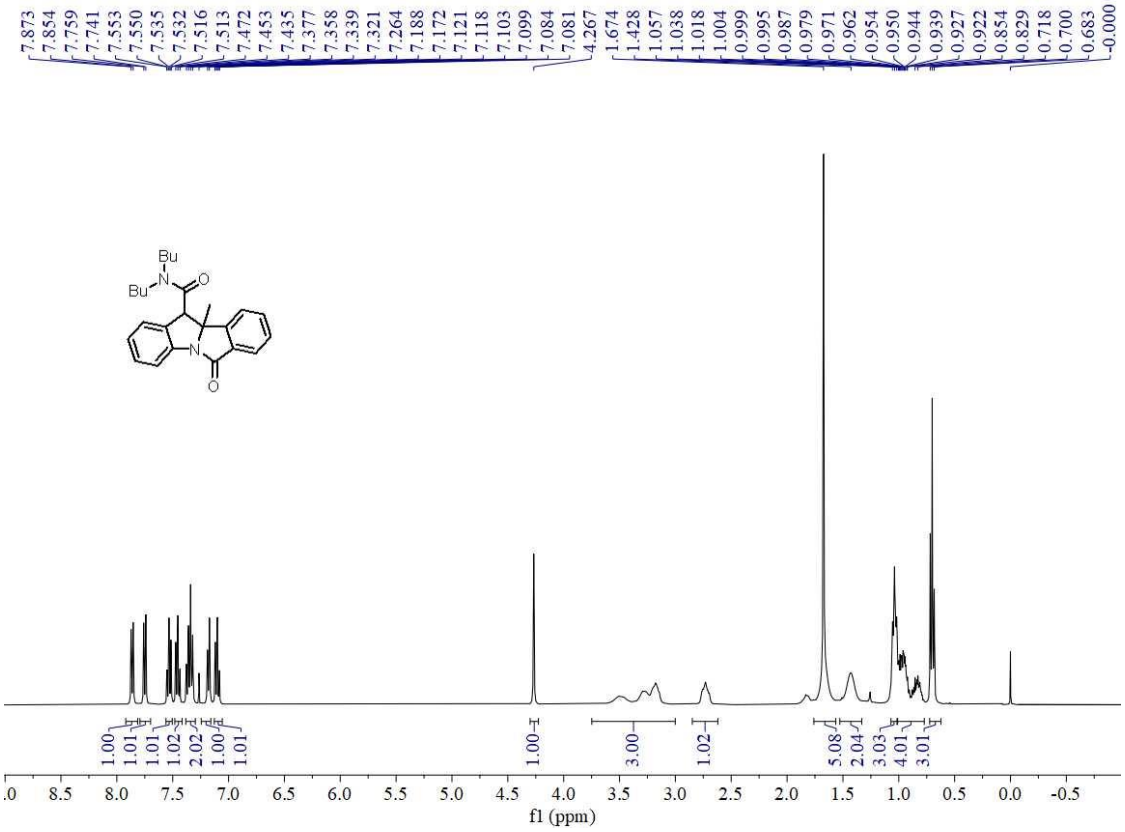
^{13}C NMR of product 4g in DMSO-d_6 (100 MHz)



^{19}F NMR of product 4g in DMSO-d_6 (376 MHz)



^{1}H NMR of product 4h in $CDCl_3$ (400 MHz)



^{13}C NMR of product 4h in $CDCl_3$ (100 MHz)