Ag(I)-Mediated Hydrogen Isotope Exchange of Mono-Fluorinated (Hetero)arenes

Guang-Qi Hu, En-Ci Li, Hong-Hai Zhang* and Wei Huang

Key Laborabory of Flexible Electronics (KLOFE) & Institute of Advanced Materials (IAM), Jiangsu National Synergistic Innovation Center for Advanced Materials (SICAM), Nanjing Tech University (Nanjing Tech), 30 Puzhu Road, Nanjing 211816, P.R. China

iamhhzhang@njtech.edu.cn

Supporting Information

General: General: NMR spectra were recorded at 23 ºC on a Varian VNMRS 300 MHz NMR spectrometer in $CDCl_3$ unless otherwise noted. Chemical shifts were determined relative to residual $CHCl_3$ (7.26 ppm) for proton, and to the $CDCl_3$ "triplet" at 77.23 ppm for carbon. GC-MS experiments were carried out using an Agilent GC/MS instrument consisting of a 6890N series GC and a 5973 Mass Selective Detector System. All yields reported refer to isolated yields unless otherwise indicated. All the reagents and solvents were purchased from commercial sources and used as received. The atom% deuterium incorporation was determined by both of GC-MS and ^{1}H NMR spectrum. Since the relative intensity was found to depend on the pulse delay, the pulse delay was adjusted to 120s to ensure complete relaxation occurred. The method to determine atom% deuterium incorporation using GC-MS is shown below.

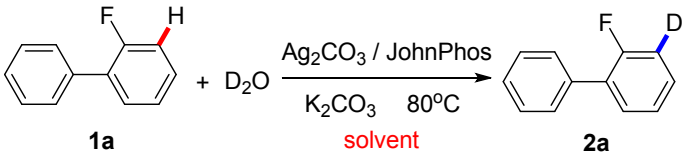
The incorporation of deuterium into each substrate was verified by GC-MS, observing a shift in the isotope distribution in the starting material (M) to show M+1 (d_1), M+2 (d_2), etc. Data processing was performed using the following formula:

Using compound **2h** as example: isotope distribution (GC-MS): 2% d_0, 20% d_1, 78% d_2.

Atom% deuterium incorporation = [(%d_1 x 1) + (%d_2 x 2)] / 2

Atom% deuterium incorporation = [(20% x 1) + (78% x 2)] / 2 = 88%

Table S1: Optimization of Solvent:

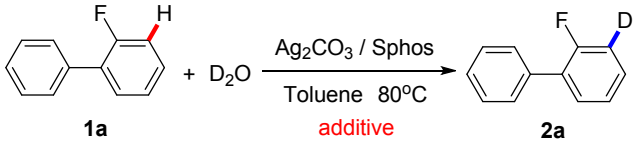


1a **2a**

Entry[a]	solvent	D incorpration[b]
1	DMSO (0.3 M)	5%
2	Toluene (0.3 M)	15%
3	DCM (0.3 M)	1%
4	DMF (0.3 M)	3%
5	Ethyl Acetate (0.3 M)	0%
6	DMA (0.3 M)	12%
7	1,4-dioxane (0.3 M)	2%
8	Toluene (1 M)	43%

[a]The reaction was conducted on 0.2 mmol of **1a**, 4 mmol of D_2O, 0.1 mmol of Ag_2CO_3, 0.1 mmol of JohnPhos, 0.2 mmol of K_2CO_3 in DMSO at 80°C. [b]Determined by GC-MS

Table S2: Optimization of the Additives:

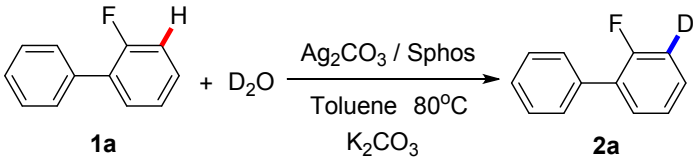


1a **2a**

Entry[a]	additive	D incorpration[b]
1	K_2CO_3	91%
2	Na_2CO_3	39%
3	Cs_2CO_3	40%
4	Li_2CO_3	80%
5	$CdCO_3$	73%
6	$MnCO_3$	60%
7	$SrCO_3$	83%
8	$KHCO_3$	55%
9	$BaCO_3$	85%
10	$Cu_2(OH)_2CO_3$	78%

[a]The reaction was conducted on 0.2 mmol of **1a**, 2 mmol of D_2O, 0.1 mmol of Ag_2CO_3, 0.1 mmol of Sphos, 0.2 mmol of additive in 0.2 mL toluene at 80°C. [b]Determined by GC-MS

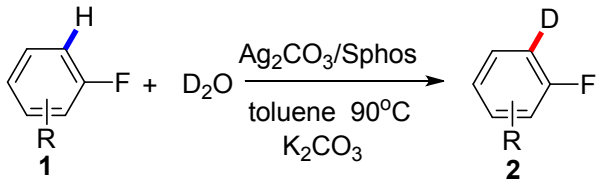
Table S3: Screening the ratio of Ag_2CO_3 and Sphos:



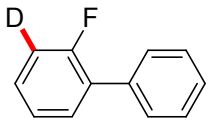
1a **2a**

Entry[a]	Ag_2CO_3 (%)	Sphos (%)	D incorpration[b]
1	50	50	91%
2	50	40	80%
3	50	30	76%
4	50	20	70%
5	50	10	53%
6	40	50	50%
7	30	50	48%
8	20	50	46%
9	10	50	36%

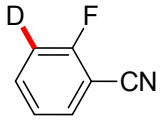
[a]The reaction was conducted on 0.2 mmol of **1a**, 2 mmol of D_2O, Ag_2CO_3, Sphos, 0.2 mmol of K_2CO_3 in 0.2 mL Toluene at 80°C.
[b]Determined by GC-MS



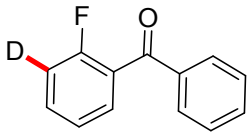
General Procedure for Ag_2CO_3 Catalyzed H/D Exchange with 2-fluorobiphenyl (1a) as example: 2-fluorobiphenyl (172 mg, 1 mmol) was added to a vigorously stirred solution of silver cabonate (138 mg, 0.5 mmol), sphos (205 mg, 0.5 mmol), potassium carbonate (138 mg, 1 mmol) and D_2O (200 mg, 10 mmol) in toluene (1 mL) in the air. The reaction mixture was stirred at 90°C for 12 h. Then the reaction was quenched with saturated NH_4Cl solution. The product was extracted with dichloromethane (3 x 20 mL). The combined organic layer was washed with brine and dried over Na_2SO_4. After removal of solvents under vacuum, the crude product was purified via column chromatography.



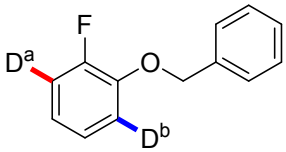
2a: Isolated yield: 85%, yellow oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64 (d, J = 7.8 Hz, 2 H), 7.53 (t, J = 7.2 Hz, 3 H), 7.47 ~ 7.37 (m, 2 H), 7.31 ~ 7.28 (m, 1 H), 7.22 (t, J = 9.0 Hz, **labeled**, **<u>0.10 H</u>**).
^{19}F NMR (300 MHz, $CDCl_3$): -117.8 (s, 0.14 F), -118.2 (s, 0.86 F).
^{13}C NMR (125 MHz, $CDCl_3$): 160.97, 159.00, 136.05, 130.98, 130.95, 129.26, 129.24, 129.08, 129.01, 128.63, 127.85, 124.53, 124.51, 116.38, 116.19.
HRMS (ESI) *m*/*z*: calcd for $C_{12}H_8DF^+$ ([M]$^+$) 173.051; Found 173.0760.
The level of deuterium incorporation was estimated: 90% from ^{1}H NMR; 96% from GC-MS



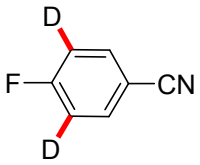
2b: Isolated yield: 40% (volatile liquid), yellow oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.63 ~ 7.56 (m, 2 H), 7.25 ~ 7.21 (m, 1 H), 7.18 (t, J = 9.0 Hz, **<u>0.11 H</u>**).
^{19}F NMR (300 MHz, $CDCl_3$): -106.0 (s, 0.13 F), -106.3 (s, 0.87 F).
^{13}C NMR (125 MHz, $CDCl_3$): 164.41, 162.35, 135.16, 133.79, 125.00, 124.89, 116.80, 116.65, 114.10, 77.42.
HRMS (ESI) *m*/*z*: calcd for $C_7H_3DNF^+$ ([M]$^+$) 122.0391; Found 122.0386.
The level of deuterium incorporation was estimated: 89% from ^{1}H NMR; 95% from GC-MS



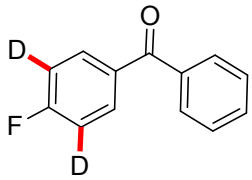
2c: Isolated yield: 95%, yellow oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.83 (d, J = 8.1 Hz, 2 H), 7.61 ~ 7.44 (m, 5 H), 7.25 (t, J = 7.8 Hz, 1 H), 7.15 (t, J = 9.0 Hz, **0.11 H**).
^{19}F NMR (300 MHz, $CDCl_3$): -110.9 (s, 0.13 F), -111.2 (s, 0.87 F).
^{13}C NMR (125 MHz, $CDCl_3$): 193.55, 161.23, 159.23, 137.59, 133.54, 133.22, 133.15, 133.12, 133.06, 130.87, 130.85, 129.94, 128.61, 127.30, 127.18, 124.44, 116.50, 116.32.
HRMS (ESI) *m*/*z*: calcd for $C_{13}H_8DOF^+$ ([M]$^+$) 201.0700; Found 201.0706.
The level of deuterium incorporation was estimated: 89% from ^{1}H NMR; 95% from GC-MS



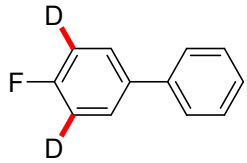
2d: Isolated yield: 90%, yellow oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.46 (d, J = 4.2 Hz, 2 H), 7.40 (t, J = 4.5 Hz, 2 H), 7.34 (t, J = 4.2 Hz, 1 H), 7.13 ~ 7.09 (m, **0.26 H**), 7.04 ~ 7.00 (m, **1.72 H**), 6.94 ~ 6.90 (m, 1 H).
^{19}F NMR (300 MHz, $CDCl_3$): -133.8 (s, 0.24 F), -133.9 (s, 0.05 F), -134.1 (s, 0.51 F), -134.2 (s, 0.20 F).
^{13}C NMR (125 MHz, $CDCl_3$): 154.71, 151.45, 146.88, 146.74, 136.68, 128.61, 128.09, 127.45, 124.28, 121.60, 121.50, 121.41, 116.46, 116.22, 115.98, 71.47.
HRMS (ESI) *m*/*z*: calcd for $C_{13}H_9D_2OF^+$ ([M]$^+$) 204.0919; Found 204.0924.
The level of deuterium incorporation was estimated: 74% (D[a]) and 28% (D[b]) from ^{1}H NMR; 57% (average) from GC-MS



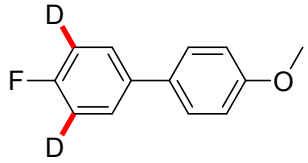
2e: Isolated yield: 40% (volatile liquid), yellow oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.68 (d, J = 4.8 Hz, 2 H), 7.17 (t, J = 8.7 Hz, **0.13 H**).
^{19}F NMR (300 MHz, $CDCl_3$): -102.5 (s, 0.09 F), -102.8 (s, 0.91 F).
^{13}C NMR (125 MHz, $CDCl_3$): 166.22, 164.18, 134.80, 134.73, 118.19, 117.11, 116.93, 116.73, 116.53, 108.80, 108.70, 77.43.
HRMS (ESI) *m*/*z*: calcd for $C_7H_2D_2NF^+$ ([M]$^+$) 123.0453; Found 123.0446.
The level of deuterium incorporation was estimated: 93% from ^{1}H NMR; 90% from GC-MS



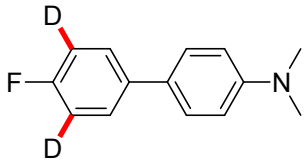
2f: Isolated yield: 92%, yellow oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.84 (d, *J* = 3.3 Hz, 2 H), 7.77 (d, *J* = 4.5 Hz, 2 H), 7.59 (t, *J* = 4.2 Hz, 1 H), 7.48 (t, *J* = 4.5 Hz, 2 H), 7.15 (t, *J* = 5.1 Hz, **0.09 H**).
^{19}F NMR (300 MHz, $CDCl_3$): -106.1 (s, 0.10 F), -106.3 (s, 0.90 F),
^{13}C NMR (125 MHz, $CDCl_3$): 195.34, 167.21, 163.84, 137.74, 132.76, 132.64, 132.80, 130.02, 128.52, 115.76, 115.47, 115.22.
HRMS (ESI) *m*/*z*: calcd for $C_{13}H_7D_2OF^+$ ($[M]^+$) 202.0763; Found 202.0771.
The level of deuterium incorporation was estimated: 95% from ^{1}H NMR; 97% from GC-MS



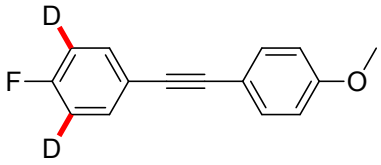
2g: Isolated yield: 92%, yellow oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.62 ~ 7.54 (m, 4 H), 7.45 (t, *J* = 7.2 Hz, 2 H), 7.38 ~ 7.33 (m, 1 H), 7.14 (t, *J* = 8.7 Hz, **0.29 H**).
^{19}F NMR (300 MHz, $CDCl_3$): -115.7 (s, 0.03 F), -116.0 (s, 0.27 F), -116.3 (s, 0.69 F).
^{13}C NMR (125 MHz, $CDCl_3$): 140.52, 129.04, 128.97, 128.85, 128.74, 127.48, 127.39, 127.25, 115.97, 115.69.
HRMS (ESI) *m*/*z*: calcd for $C_{12}H_7D_2F^+$ ($[M]^+$) 174.0814; Found 174.0807.
The level of deuterium incorporation was estimated: 85% from ^{1}H NMR; 83% from GC-MS



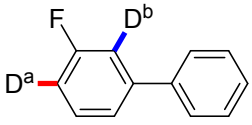
2h: Isolated yield: 87%, yellow oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51 ~ 7.46 (m, 4 H), 7.11 (t, *J* = 8.7 Hz, **0.41 H**), 6.98 (d, *J* = 8.7 Hz, 2 H).
^{19}F NMR (300 MHz, $CDCl_3$): -116.6 (s, 0.04 F), -116.9 (s, 0.32 F), -117.1 (s, 0.64 F).
^{13}C NMR (125 MHz, $CDCl_3$): 163.93, 159.40, 133.10, 128.47, 128.37, 128.25, 128.16, 115.88, 115.60, 114.51, 55.52.
HRMS (ESI) *m*/*z*: calcd for $C_{13}H_9D_2OF^+$ ($[M]^+$) 204.0919; Found 204.0930.
The level of deuterium incorporation was estimated: 80% from ^{1}H NMR; 88% from GC-MS.



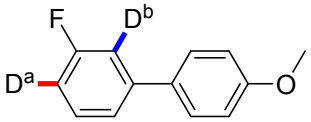
2i: Isolated yield: 93%, yellow oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51 (d, *J* = 4.9 Hz, 2 H), 7.46 (d, *J* = 6.6 Hz, 2 H), 7.10 (t, *J* = 6.6 Hz, **0.54 H**), 6.81 (d, *J* = 6.6 Hz, 2 H), 2.99 (s, 6 H).
^{19}F NMR (300 MHz, $CDCl_3$): -117.6 (s, 0.09 F), -117.9 (s, 0.37 F), -118.1 (s, 0.54 F).
^{13}C NMR (125 MHz, $CDCl_3$): 163.04, 160.63, 150.04, 137.47, 128.42, 127.84, 127.77, 127.73, 127.69, 127.65, 115.64, 115.43, 112.92, 40.34.
HRMS (ESI) *m*/*z*: calcd for $C_{14}H_{12}D_2NF^+$ ($[M]^+$) 217.1236; Found 217.1243.
Deuterium incorporation expected at δ 7.08.
The level of deuterium incorporation was estimated: 73% from ^{1}H NMR; 72% from GC-MS.



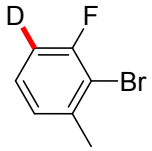
2j: Isolated yield: 95%, yellow oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50 ~ 7.45 (m, 4 H), 7.03 (t, *J* = 8.7 Hz, **0.23 H**), 6.88 (d, *J* = 8.7 Hz, 2 H), 3.83 (s, 3 H).
^{19}F NMR (300 MHz, $CDCl_3$): -111.3 (s, 0.01 F), -111.6 (s, 0.18 F), -111.9 (s, 0.80 F).
^{13}C NMR (125 MHz, $CDCl_3$): 163.94, 160.65, 159.72, 133.33, 133.23, 133.12, 133.01, 132.91, 115.72, 115.42, 115.24, 114.06, 89.05, 86.99, 55.29.
HRMS (ESI) *m*/*z*: calcd for $C_{15}H_9D_2OF^+$ ($[M]^+$) 228.0919; Found 228.0936.
The level of deuterium incorporation was estimated: 89% from ^{1}H NMR; 85% from GC-MS.



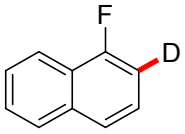
2k: Isolated yield: 90%, yellow oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64 ~ 7.60 (m, 2 H), 7.48 (t, *J* = 4.2 Hz, 2 H), 7.44 ~ 7.39 (m, 3 H), 7.33 (d, *J* = 6.0 Hz, **0.62 H**), 7.07 (t, *J* = 6.0 Hz, **0.14 H**).
^{19}F NMR (300 MHz, $CDCl_3$): -112.9 (s, 0.12 F), -113.2 (s, 0.62 F), -113.5 (s, 0.26 F).
^{13}C NMR (125 MHz, $CDCl_3$): 164.87, 161.62, 143.63, 140.00, 130.17, 130.06, 128.91, 127.87, 127.13, 122.76, 114.20, 113.91.
HRMS (ESI) *m*/*z*: calcd for $C_{12}H_{18}D_2F^+$ ($[M]^+$) 173.0751; Found 173.0740.
The level of deuterium incorporation was estimated: 86% (D^a) and 38% (D^b) from ^{1}H NMR; 65% (average) from GC-MS.



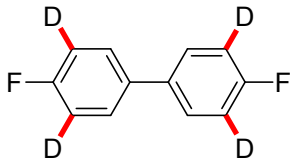
2l: Isolated yield: 80%, yellow oil.
^{1}H NMR (300 MHz, DMSO-d_6): δ 7.65 (d, J = 5.1 Hz, 2 H), 7.46 (s, 2 H), 7.44 (s, **0.75 H**), 7.11 (d, J = 4.2 Hz, **0.28 H**), 7.03 (d, J = 5.1 Hz, 2 H), 3.81 (s, 3 H).
^{19}F NMR (300 MHz, DMSO-d_6): -112.8 (s, 0.29 F), -113.1 (s, 0.57 F), -113.4 (s, 0.14 F).
^{13}C NMR (125 MHz, DMSO-d_6): 164.29, 159.31, 142.33, 142.23, 131.04, 130.68, 130.58, 130.47, 127.87, 122.05, 114.35, 113.38, 113.10, 112.84, 112.55, 55.13.
HRMS (ESI) *m*/*z*: calcd for $C_{13}H_{10}DOF^+$ ([M]$^+$) 203.0857; Found 203.0863.
The level of deuterium incorporation was estimated: 72% (D^a) and 25% (D^b) from ^{1}H NMR; 52% (average) from GC-MS.



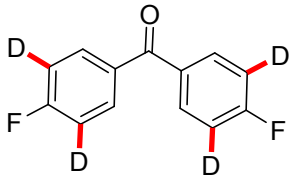
2m: Isolated yield: 86%, yellow oil.
^{1}H NMR (300 MHz, DMSO-d_6): δ 7.30 (t, J = 4.8 Hz, 1 H), 7.17 ~ 7.20 (m, 1 H), 7.14 ~ 7.16 (m, **0.10 H**).
^{19}F NMR (300 MHz, DMSO-d_6): -116.0 (s, 0.12 F), -116.3 (s, 0.88 F).
^{13}C NMR (125 MHz, DMSO-d_6): 159.97, 156.75, 140.00, 128.64, 128.53, 126.49, 113.89, 113.59, 110.61, 110.35, 22.00.
HRMS (ESI) *m*/*z*: calcd for $C_7H_5DFBr^+$ ([M]$^+$) 188.9700; Found 188.9703.
The level of deuterium incorporation was estimated: 90% from ^{1}H NMR; 85% from GC-MS.



2n: Isolated yield: 95%, yellow oil.
^{1}H NMR (300 MHz, DMSO-d_6): δ 7.91 ~ 7.99 (m, 2 H), 7.70 (d, J = 6.3 Hz, 1 H), 7.52 ~ 7.56 (m, 2 H), 7.40 ~ 7.45 (m, 1 H), 7.23 ~ 7.28 (m, **0.15 H**).
^{19}F NMR (300 MHz, DMSO-d_6): -123.5 (s, 0.18 F), -123.8 (s, 0.82 F).
^{13}C NMR (125 MHz, DMSO-d_6): 159.48, 159.17, 134.48, 127.65, 127.04, 126.60, 125.88, 125.76, 123.94, 122.85, 122.63, 119.74, 119.68, 109.72, 109.46.
HRMS (ESI) *m*/*z*: calcd for $C_{10}H_6DF^+$ ([M]$^+$) 147.0595; Found 147.0601.
The level of deuterium incorporation was estimated: 85% from ^{1}H NMR; 88% from GC-MS.

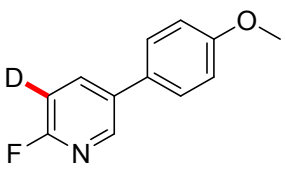


2o: Isolated yield: 90%, yellow oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.49 (d, *J* = 2.7 Hz, 4 H), 7.12 (t, *J* = 5.4 Hz, **1.40 H**).
^{19}F NMR (300 MHz, $CDCl_3$): -115.6 (s, 0.13 F), -115.9 (s, 0.46 F), -116.1 (s, 0.41 F).
^{13}C NMR (125 MHz, $CDCl_3$): 164.06, 160.80, 136.40, 128.62, 128.51, 128.41, 115.82, 115.54.
HRMS (ESI) *m*/*z*: calcd for $C_{12}H_4D_4F_2^+$ ([M]$^+$) 194.0845; Found 194.0848.
Deuterium incorporation expected at δ 7.12.
The level of deuterium incorporation was estimated: 65% from ^{1}H NMR; 60% from GC-MS.

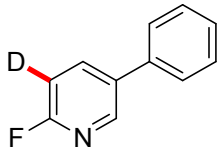


2p: Isolated yield: 88%, yellow oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.81 (d, *J* = 5.4 Hz, 4 H), 7.17 (t, *J* = 9.0 Hz, **0.37 H**).
^{19}F NMR (300 MHz, $CDCl_3$): -105.9 (s, 0.30 F), -106.2 (s, 1.70 F).
^{13}C NMR (125 MHz, $CDCl_3$): 193.74, 166.35, 164.32, 133.71, 132.38, 132.31, 115.62, 115.44, 115.20, 115.00.
HRMS (ESI) *m*/*z*: calcd for $C_{13}H_4D_4OF_2^+$ ([M]$^+$) 222.0794; Found 222.0802.
The level of deuterium incorporation was estimated: 91% from ^{1}H NMR; 94% from GC-MS.

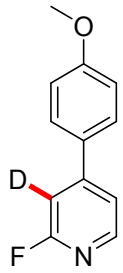
General Procedure for Ag_2CO_3 Catalyzed H/D Exchange of nitrogen-containing mono-fluorinated heteroarenes: heteroarene (1 mmol) was added to a vigorously stirred solution of silver cabonate (138 mg, 0.5 mmol), sphos (205 mg, 0.5 mmol), potassium carbonate (138 mg, 1 mmol) and D_2O (200 mg, 10 mmol) in toluene (1 mL) in the air. The reaction mixture was stirred at 90^{o}C for 12 h. Then the reaction was quenched with saturated NH_4Cl solution. The product was extracted with dichloromethane (3 x 20 mL). The combined organic layer was washed with brine and dried over Na_2SO_4. After removal of solvents under vacuum, the crude product was purified via column chromatography.



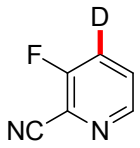
4a: Isolated yield: 90%, yellow oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.37 (s, 1 H), 7.91 (d, *J* = 6.3 Hz, 1 H), 7.45 (d, *J* = 8.7 Hz, 2 H), 7.00 (d, *J* = 8.7 Hz, 2 H), 6.95 (d, *J* = 3.0 Hz, **0.06 H**).
^{19}F NMR (300 MHz, $CDCl_3$): -71.4 (s, 0.10 F), -71.6 (s, 0.90 F).
^{13}C NMR (125 MHz, $CDCl_3$): 163.69, 161.79, 159.80, 145.35, 145.23, 139.25, 139.19, 19.15, 139.09, 134.49, 129.12, 128.11, 114.61, 109.42, 109.12, 55.35.
HRMS (ESI) *m*/*z*: calcd for $C_{12}H_9DNOF^+$ ([M]$^+$) 204.0809; Found 204.0820.
Deuterium incorporation expected at δ 6.95.
The level of deuterium incorporation was estimated: 94% from ^{1}H NMR; 92% from GC-MS.



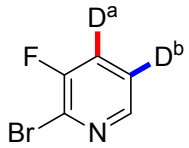
4b: Isolated yield: 80%, yellow oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.42 (s, 1 H), 7.96 (d, *J* = 6.6 Hz, 1 H), 7.55 ~ 7.38 (m, 5 H), 6.99 (d, *J* = 5.7 Hz, **0.12 H**).
^{19}F NMR (300 MHz, $CDCl_3$): -70.4 (s, 0.07 F), -70.7 (s, 0.92 F).
^{13}C NMR (125 MHz, $CDCl_3$): 164.06, 162.16, 145.87, 145.75, 139.61, 139.55, 136.70, 134.85, 129.13, 128.31, 127.03, 109.54, 109.21.
HRMS (ESI) *m*/*z*: calcd for $C_{11}H_7DNF^+$ ([M]$^+$) 174.0704; Found 174.0713.
Deuterium incorporation expected at δ 6.99.
The level of deuterium incorporation was estimated: 88% from ^{1}H NMR; 83% from GC-MS.



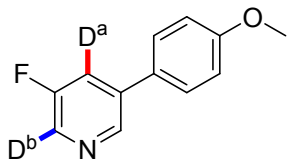
4c: Isolated yield: 96%, yellow oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.20 (d, *J* = 3.3 Hz, 1 H), 7.57 (d, *J* = 5.4 Hz, 2 H), 7.34 (d, *J* = 3.0 Hz, 1 H), 7.06 (s, **0.45 H**), 7.00 (d, *J* = 5.4 Hz, 2 H), 3.85 (s, 3 H).
^{19}F NMR (300 MHz, $CDCl_3$): -68.4 (s, 0.31 F), -68.6 (s, 0.69 F).
^{13}C NMR (125 MHz, $CDCl_3$): 165.56, 163.67, 161.01, 153.52, 153.44, 153.38, 147.87, 147.75, 129.22, 128.22, 118.83, 114.64, 106.30, 106.00, 55.14.
HRMS (ESI) *m*/*z*: calcd for $C_{12}H_9DNOF^+$ ([M]$^+$) 204.0809; Found 204.0819.
Deuterium incorporation expected at δ 7.06.
The level of deuterium incorporation was estimated: 55% from ^{1}H NMR; 45% from GC-MS.



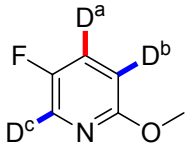
4d: Isolated yield: 53%, yellow oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.56 (d, J = 3.6 Hz, 1 H), 7.59 (s, 1 H), 7.34 (s, **0.03 H**).
^{19}F NMR (300 MHz, $CDCl_3$): -114.9 (s, 0.02 F), -115.1 (s, 0.98 F).
^{13}C NMR (125 MHz, $CDCl_3$): 162.30, 160.15, 146.99, 128.53, 123.11, 112.85, 77.13.
HRMS (ESI) *m*/*z*: calcd for $C_6H_2DN_2F^+$ ([M]$^+$) 123.0343; Found 123.0340.
Deuterium incorporation expected at δ 7.34.
The level of deuterium incorporation was estimated: 97% from ^{1}H NMR; 99% from GC-MS.



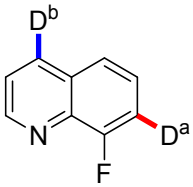
4e[1]: Isolated yield: 86%, yellow oil.
^{1}H NMR (300 MHz, DMSO-d_6): δ 8.24 ~ 8.25 (m, 1 H), 7.82 ~ 7.86 (m, **0.14 H**), 7.50 (t, J = 3.6 Hz, **0.35 H**).
^{19}F NMR (300 MHz, DMSO-d_6): -111.3 (s, 0.13 F), -111.6 (s, 0.87 F).
HRMS (ESI) *m*/*z*: calcd for $C_5HD_2NFBr^+$ ([M]$^+$) 176.9558; Found 176.9566.
The level of deuterium incorporation was estimated as: 86% (D^a) and 65% (D^b) from ^{1}H NMR; 73% (average) from GC-MS.



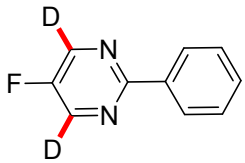
4f: Isolated yield: 80%, yellow oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.63 (s, 1 H), 8.39 (s, **0.93 H**), 7.53 (s, **0.05 H**), 7.50 (d, J = 5.4 Hz, 2 H), 7.50 (d, J = 5.4 Hz, 2 H).
^{19}F NMR (300 MHz, $CDCl_3$): -127.2 (s, 0.09 F), -127.4 (s, 0.66 F), -127.7 (s, 0.24 F).
^{13}C NMR (125 MHz, $CDCl_3$): 160.73, 160.21, 158.69, 143.69, 137.80, 136.01, 135.83, 128.70, 128.30, 120.41, 120.27, 114.68, 55.35.
HRMS (ESI) *m*/*z*: calcd for $C_{12}H_8D_2NOF^+$ ([M]$^+$) 205.0872; Found 205.0873.
Deuterium incorporation expected at δ 8.39 and 7.53.
The level of deuterium incorporation was estimated: 95% (D^a) and 7% (D^b) from ^{1}H NMR; 92% (total), 46% (average) from GC-MS.



4g: Isolated yield: 50%, yellow oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.98 (s, **0.96 H**), 7.31 (s, **0.04 H**), 6.69 (s, **0.65 H**), 3.90 (s, 3 H).
^{19}F NMR (300 MHz, $CDCl_3$): -139.5 (s, 0.01 F), -139.7 (s, 0.99 F).
^{13}C NMR (125 MHz, $CDCl_3$): 160.33, 156.33, 154.38, 133.19, 132.98, 126.14, 125.91, 111.32, 77.12, 53.67.
HRMS (ESI) *m*/*z*: calcd for $C_6H_3D_3NOF^+$ ([M]$^+$) 130.0622; Found 130.0617.
Deuterium incorporation expected at δ 7.98, 7.31 and 6.69.
The level of deuterium incorporation was estimated: 96% (D^a), 35% (D^b) and 4% (D^c) from ^{1}H NMR; 125% (total), 42% (average) from GC-MS.

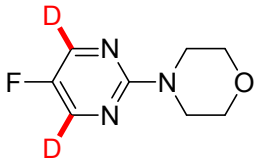


4h: Isolated yield: 89%, yellow oil.
^{1}H NMR (300 MHz, DMSO-*d*6): δ 8.87 (d, *J* = 2.1 Hz, 1 H), 8.34 (d, *J* = 6.3 Hz, **0.72 H**), 7.72 (d, *J* = 6.3 Hz, 1 H), 7.48 ~ 7.56 (m, **2.16 H**).
^{19}F NMR (300 MHz, DMSO-*d*6): -125.8 (s, 0.21 F), -126.2 (s, 0.78 F).
^{13}C NMR (125 MHz, DMSO-*d*6): 158.84, 155.46, 150.68, 135.88, 135.84, 129.51, 126.51, 126.42, 126.31, 123.94, 123.88, 122.39, 122.28, 113.62, 113.38.
HRMS (ESI) *m*/*z*: calcd for $C_9H_4D_2NF^+$ ([M]$^+$) 149.0610; Found 149.0619.
The level of deuterium incorporation was estimated as: 84% (D^a) and 28% (D^b) from ^{1}H NMR; 68% (average) from GC-MS.

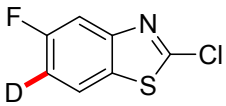


4i: Isolated yield: 86%, yellow oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.65 (s, **0.33 H**), 8.40 ~ 8.39 (m, 2 H), 7.49 ~ 7.48 (m, 3 H).
^{19}F NMR (300 MHz, $CDCl_3$): -140.5 (s, 0.03 F), -140.8 (s, 0.23 F), -141.0 (s, 0.74 F).
^{13}C NMR (125 MHz, $CDCl_3$): 161.08, 157.72, 155.57, 144.99, 144.83, 144.63, 144.43, 136.66, 130.60, 128.63, 128.11.
HRMS (ESI) *m*/*z*: calcd for $C_{10}H_5D_2N_2F^+$ ([M]$^+$) 176.0719; Found 176.0719.
Deuterium incorporation expected at δ 8.65.

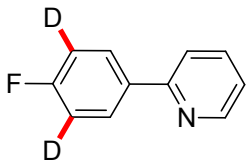
The level of deuterium incorporation was estimated as: 84% from ^{1}H NMR; 76% from GC-MS.



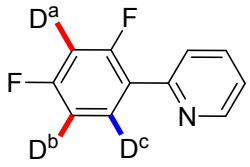
4j: Isolated yield: 93%, yellow oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.20 (s, **0.16 H**), 3.76 ~ 3.71 (m, 4 H).
^{19}F NMR (300 MHz, $CDCl_3$): -156.1 (s, 0.03 F), -156.3 (s, 0.27 F), -156.5 (s, 0.70 F).
^{13}C NMR (125 MHz, $CDCl_3$): 158.98, 153.39, 150.09, 145.27, 144.99, 66.70, 44.79.
HRMS (ESI) *m*/*z*: calcd for $C_8H_8D_2N_3OF^+$ ([M]$^+$) 185.0933; Found 185.0946.
Deuterium incorporation expected at δ 8.20.
The level of deuterium incorporation was estimated as: 92% from ^{1}H NMR; 88% from GC-MS.



4k: Isolated yield: 80%, yellow oil.
^{1}H NMR (300 MHz, DMSO-*d*6): δ 7.97 (d, *J* = 1.8 Hz, **0.08 H**), 7.95 (q, *J* = 3.6 Hz, 1 H), 7.38 (t, *J* = 6.6 Hz, 1 H).
^{19}F NMR (300 MHz, DMSO-*d*6): -114.2 (s, 0.11 F), -114.5 (s, 0.89 F).
^{13}C NMR (125 MHz, DMSO-*d*6): 161.50, 158.17, 152.37, 147.22, 136.86, 136.70, 123.82, 123.69, 115.49, 115.27, 109.03, 108.68.
HRMS (ESI) *m*/*z*: calcd for $C_7H_2DNFSCl^+$ ([M]$^+$) 187.9722; Found 187.926.
The level of deuterium incorporation was estimated as: 92% from ^{1}H NMR; 80% from GC-MS.

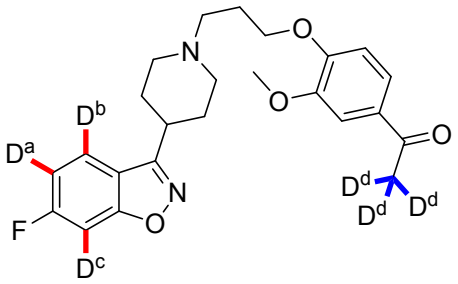


4l: Isolated yield: 90%, yellow oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.65 ~ 8.67 (m, 1 H), 7.96 (d, *J* = 4.2 Hz, 2 H), 7.70 ~ 7.74 (m, 1 H), 7.64 ~ 7.66 (m, 1 H), 7.19 ~ 7.22 (m, 1 H), 7.14 (t, *J* = 6.6 Hz, **0.41 H**).
^{19}F NMR (300 MHz, $CDCl_3$): -113.0 (s, 0.02 F), -113.3 (s, 0.23 F), -113.6 (s, 0.75 F).
^{13}C NMR (125 MHz, $CDCl_3$): 164.78, 162.34, 156.53, 149.69, 136.86, 136.80, 128.81, 128.70, 128.63, 122.13, 120.31, 115.84, 115.63, 115.60, 115.38, 115.35, 115.13.
HRMS (ESI) *m*/*z*: calcd for $C_{14}H_6D_2NF^+$ ([M]$^+$) 175.0766; Found 175.0767.
The level of deuterium incorporation was estimated as: 80% from ^{1}H NMR; 86% from GC-MS.



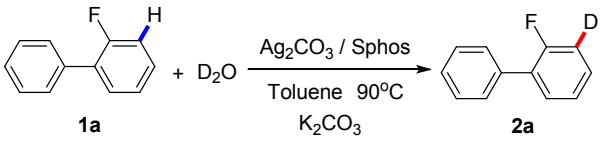
4m: Isolated yield: 96%, yellow oil.
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.62 (d, J = 4.5 Hz, 1 H), 7.92 (t, J = 7.5 Hz, **0.64 H**), 7.66 (d, J = 3.9 Hz, 2 H), 7.16 (dd, J_1 = 4.5 Hz, J_2 = 8.7 Hz, 1 H), 6.92 (t, J = 8.4 Hz, **0.07 H**), 6.82 (dd, J_1 = 9.0 Hz, J_2 = 11.4 Hz, **0.07 H**).
^{19}F NMR (300 MHz, $CDCl_3$): -109.4 (s, 0.10 F), -109.7 (s, 0.87 F), -112.9 (s, 0.04 F), -113.2 (s, 1.00 F).
^{13}C NMR (125 MHz, $CDCl_3$): 164.18, 164.09, 162.19, 162.09, 161.60, 161.51, 159.59, 159.50, 152.52, 149.74, 136.44, 132.05, 132.01, 131.97, 131.94, 124.20, 124.13, 123.80, 123.72, 122.38, 104.51, 104.31, 104.11, 103.90.
HRMS (ESI) *m*/*z*: calcd for $C_{11}H_4D_3NF_2^+$ ($[M]^+$) 194.0735; Found 194.0742.
The level of deuterium incorporation was estimated as: 93% (D^a), 93% (D^b) and 36% (D^c) from ^{1}H NMR; 86% (average) from GC-MS.

Procedure for synthesis of D-iloperidone: iloperidone (426 mg, 1 mmol) was added to a vigorously stirred solution of silver cabonate (138 mg, 0.5 mmol), sphos (205 mg, 0.5 mmol), potassium carbonate (138 mg, 1 mmol) and D_2O (200 mg, 10 mmol) in toluene (1 mL) in the air. The reaction mixture was stirred at 90°C for 12 h. Then the reaction was quenched with saturated NH_4Cl solution. The product was extracted with dichloromethane (3 x 20 mL). The combined organic layer was washed with brine and dried over Na_2SO_4. After removal of solvents under vacuum, the crude product was purified via column chromatography.



6a: Isolated yield: 80%
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.66 (d, J = 3.9 Hz, **0.44 H**), 7.53 (dd, J_1 = 1.5 Hz, J_2 = 6.0 Hz, 1 H), 7.50 (d, J = 1.5 Hz, 1 H), 7.22 (d, J = 6.3 Hz, **0.08 H**), 7.01 ~ 7.05 (m, **0.09 H**), 6.91 (d, J = 6.3 Hz, 1 H), 4.17 (t, J = 5.1 Hz, 2 H), 3.90 (s, 3 H), 3.04 ~ 3.07 (m, 3 H), 2.57 (t, J = 5.1 Hz, 2 H), 2.51 (s, **0.33 H**), 2.02 ~ 2.19 (m, 8 H).
^{19}F NMR (300 MHz, $CDCl_3$): -109.7 (s, 0.19 F), -110.0 (s, 0.81 F).
^{13}C NMR (125 MHz, $CDCl_3$): 196.33, 165.20, 161.79, 160.57, 152.43, 148.82, 129.96, 122.70, 121.96, 121.81, 110.84, 110.08, 66.92, 55.55, 54.59, 53.08, 34.09, 30.10, 26.14.
HRMS (ESI) *m*/*z*: calcd for $C_{24}H_{21}D_6N_2O_4F^+$ ($[M]^+$) 432.2331; Found 432.2354.
The level of deuterium incorporation was estimated as: 92% (D^a), 56% (D^b), 92% (D^c) and 90% (D^d) from ^{1}H NMR; 90% (average) from GC-MS.

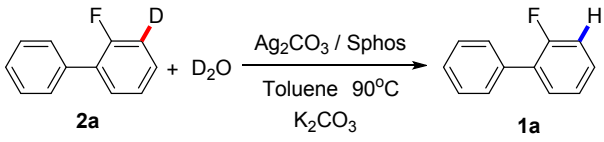
Scheme S1: Kinetic Isotope Effect Study



1a **2a**

Entry[a]	time (hours)	D incorpration[b]
1	1	26%
2	6	78%
3	12	100%

[a]The reaction was conducted on 0.3 mmol of **1a**, D_2O, 50 mol % of Ag_2CO_3, 50 mol % of Sphos, 1 equiv of K_2CO_3 in 1 mL of Toluene at 90°C. [b]Determined by GC-MS



2a **1a**

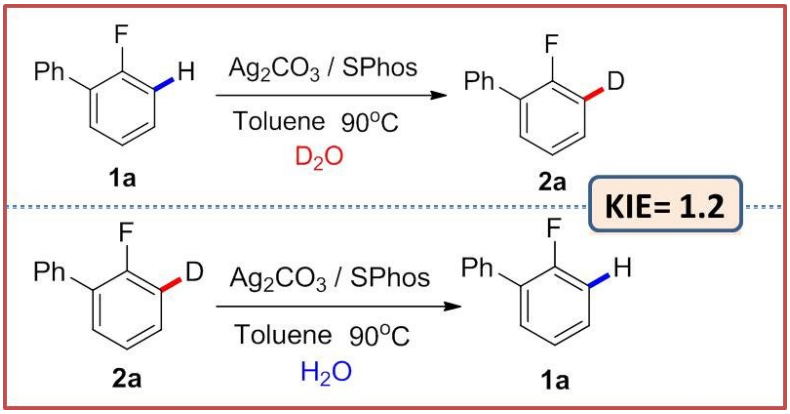
Entry[a]	time (hours)	H incorpration[b]
1	1	23%
2	6	63%
3	12	84%

[a]The reaction was conducted on 0.3 mmol of **2a**, H_2O, 50 mol % of Ag_2CO_3, 50 mol % of Sphos, 1 equiv of K_2CO_3 in 1 mL of Toluene at 90°C. [b]Determined by GC-MS

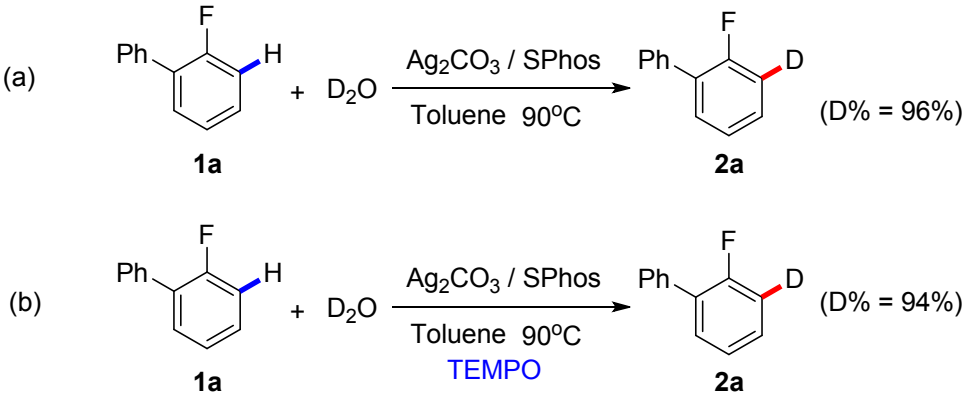
Reactions to incorporate deuterium were carried out following "General Procedure for Ag_2CO_3 Catalyzed H/D Exchange with 2-fluorobiphenyl (1a) as example", using 2-fluorobiphenyl (172 mg, 1 mmol) as model substrate.

Reactions to incorporate hydrogen were carried out following the same procedure as above, using H_2O instead of D_2O as reagent.

The deuterium/hydrogen incorporation was assigned by GC-Ms result of small aliquots of organic phase of the reaction mixture sampled at different time.



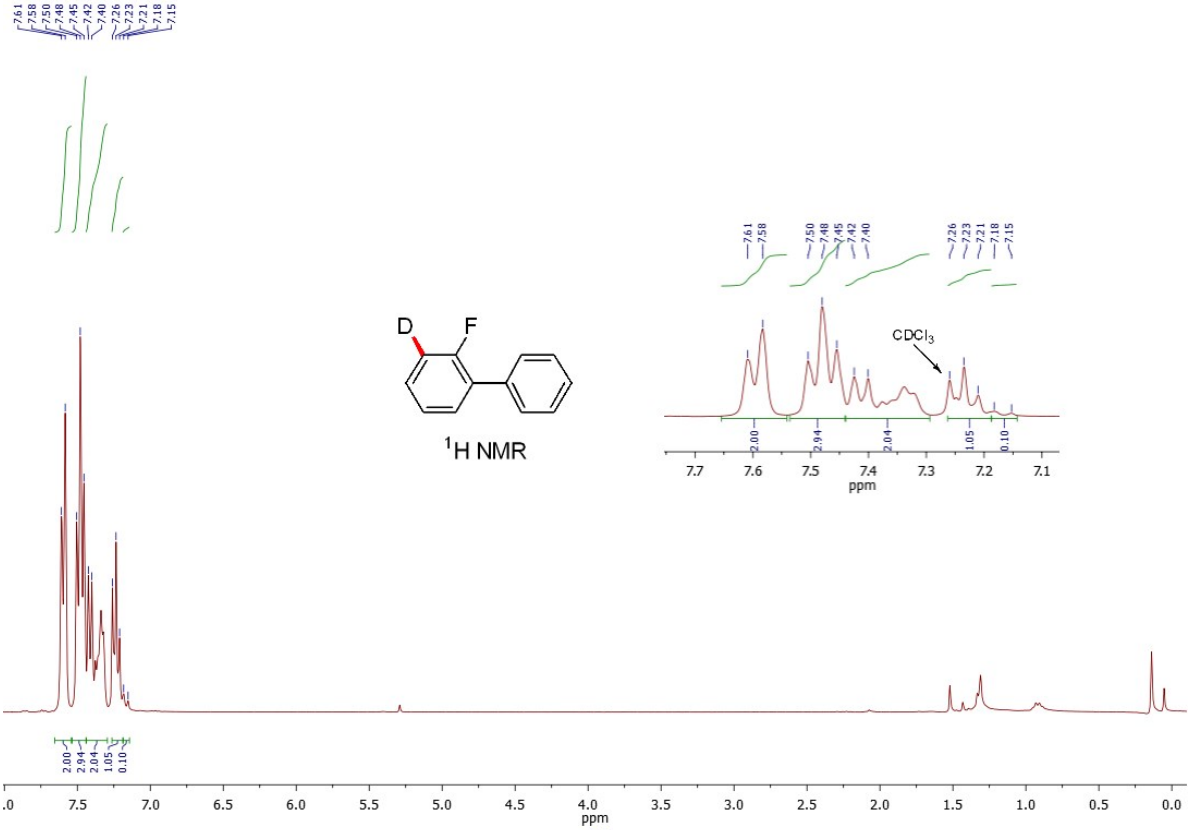
Procedure for Ag_2CO_3 Catalyzed H/D Exchange with TEMPO as additive: 2-fluorobiphenyl (1 mmol) was added to a vigorously stirred solution of silver cabonate (138 mg, 0.5 mmol), Sphos (205 mg, 0.5 mmol) and potassium carbonate (138 mg, 1 mmol) in toluene (1 mL) in the air. Then TEMPO (2 mmol) was added to the solution. The reaction mixture was stirred at 90°C for 12 h. Then the reaction was quenched with saturated NH_4Cl solution. The product was extracted with dichloromethane (3 x 20 mL). The combined organic layer was washed with brine and dried over Na_2SO_4. After removal of solvents under vacuum, the crude product was purified via column chromatography. The level of deuterium incorporation of the product was determined by ^1H NMR as 94%, which suggested that a mechanism involving free radicals should be ruled out.

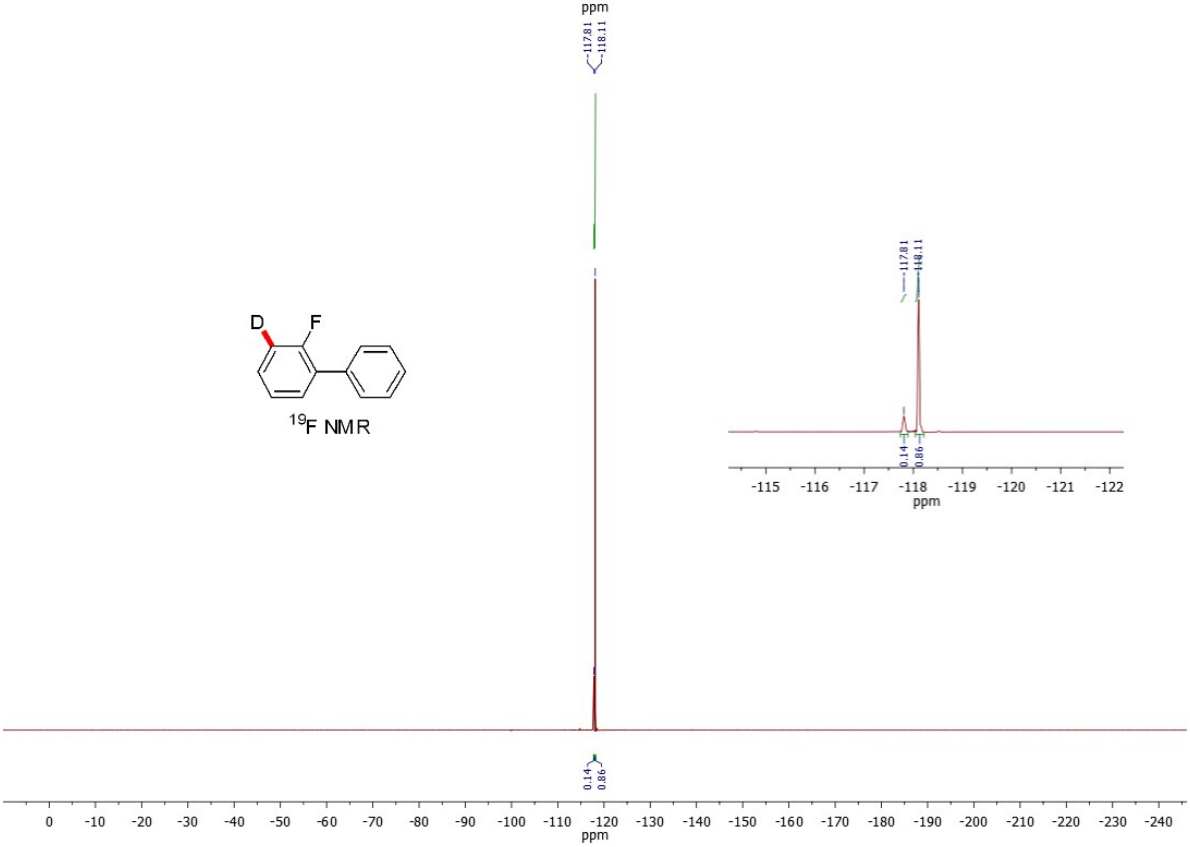


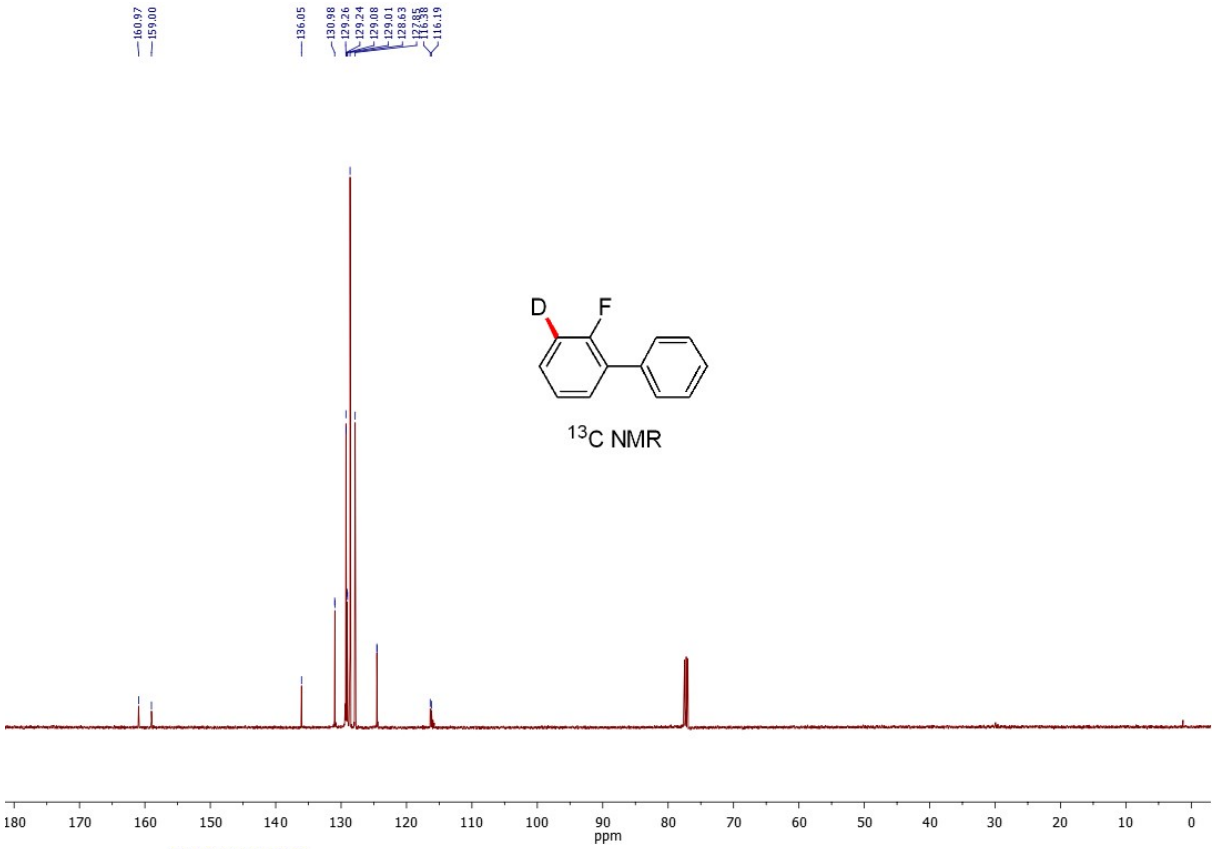
Reference:

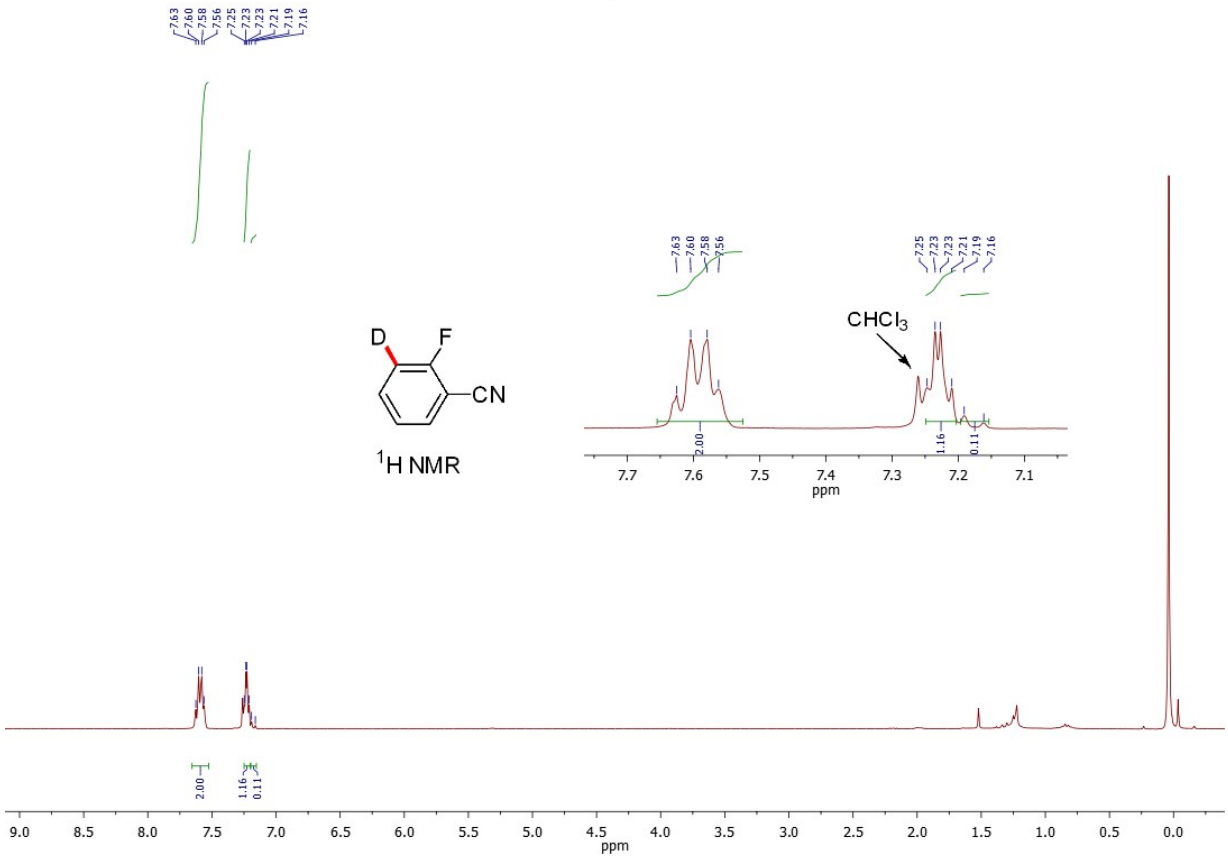
1. Queguiner, M. M. G. *Tetrahedron* **1986**, *42*, 2253-2262.

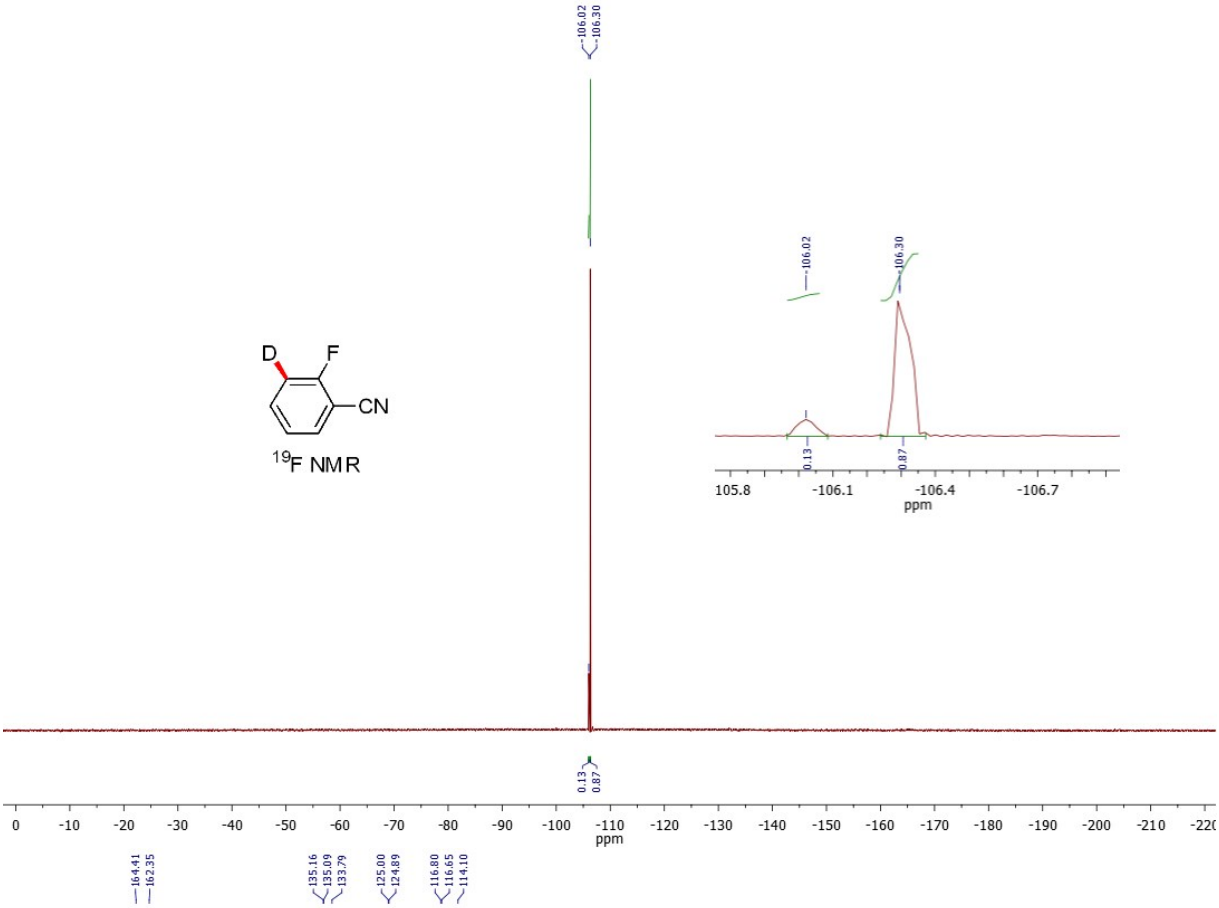
Proton, Fluorine and Carbon NMR Spectra:

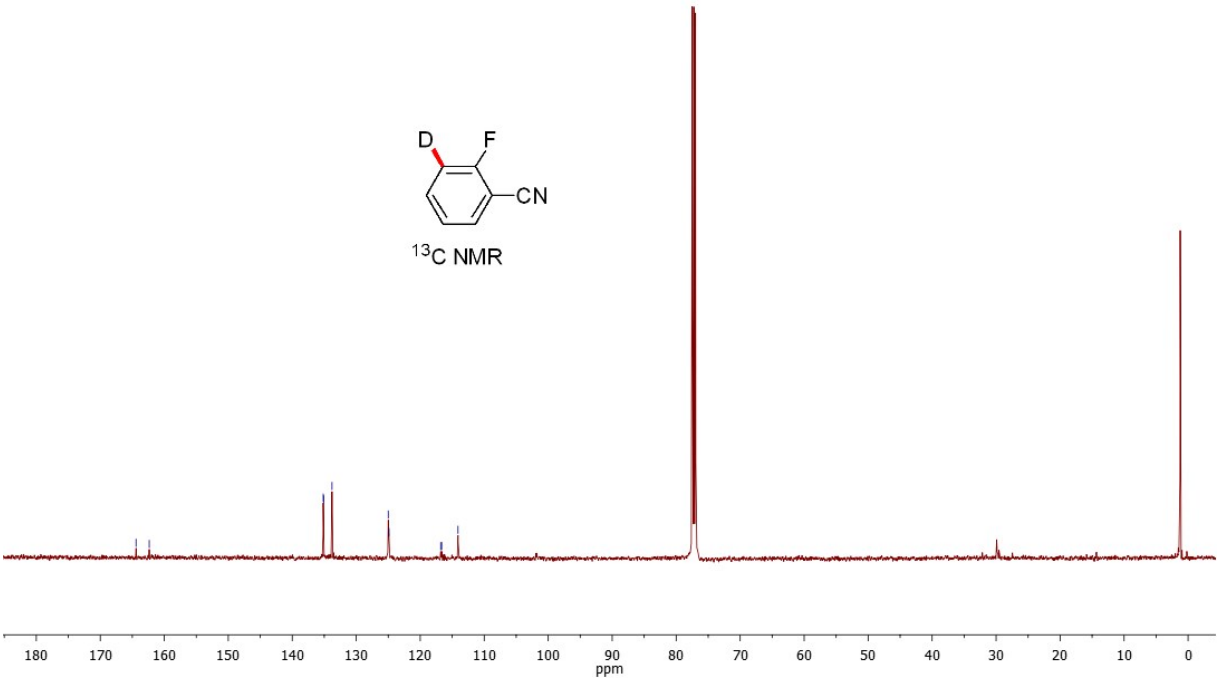


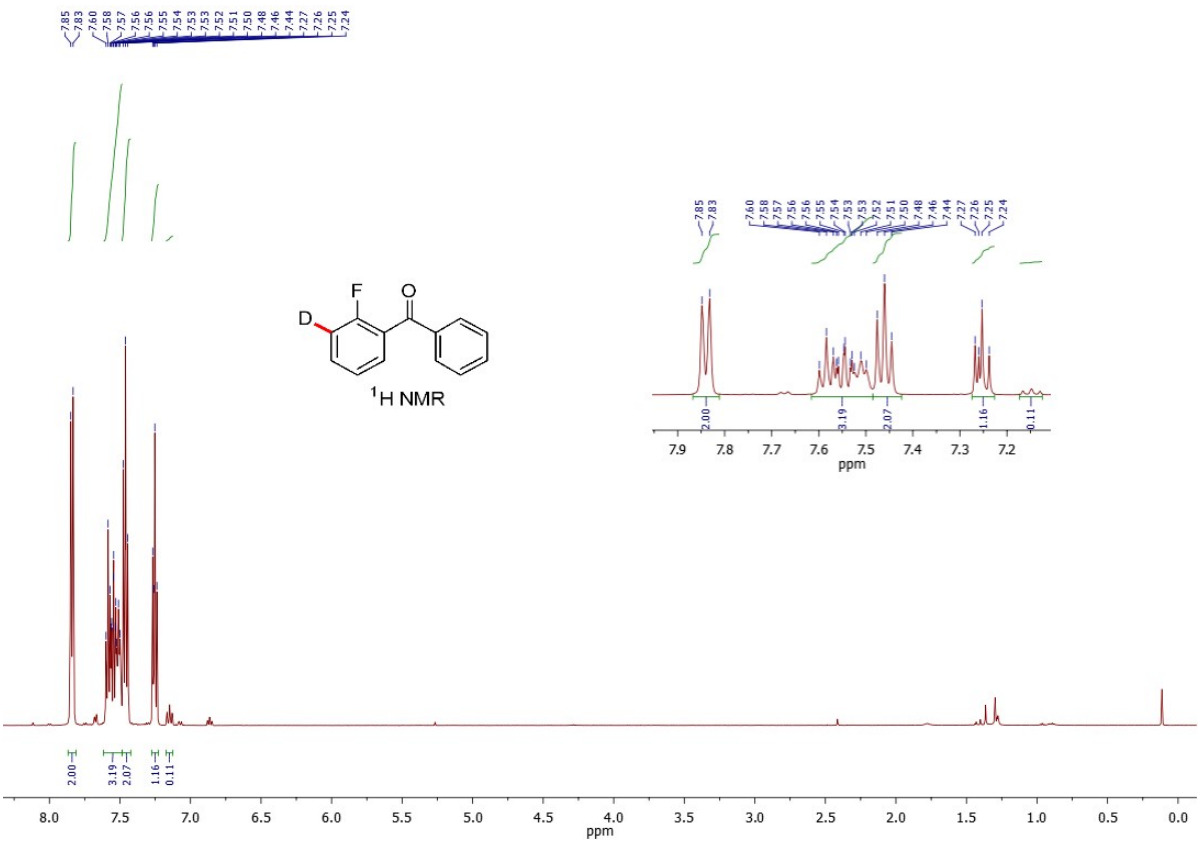


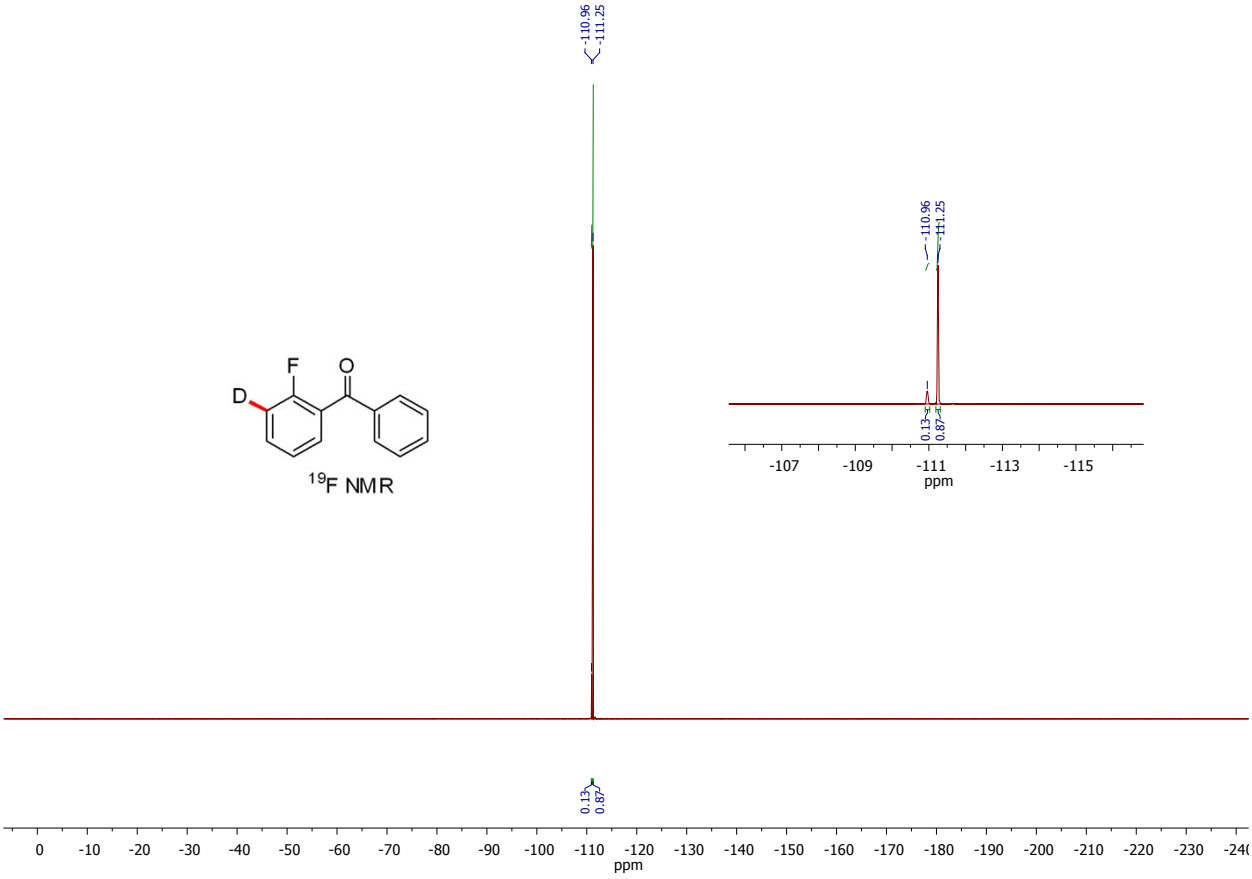

160.97
159.00
136.05
130.98
129.26
129.24
129.08
129.01
128.83
117.55
117.38
116.19
D
F
^{13}C NMR
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm

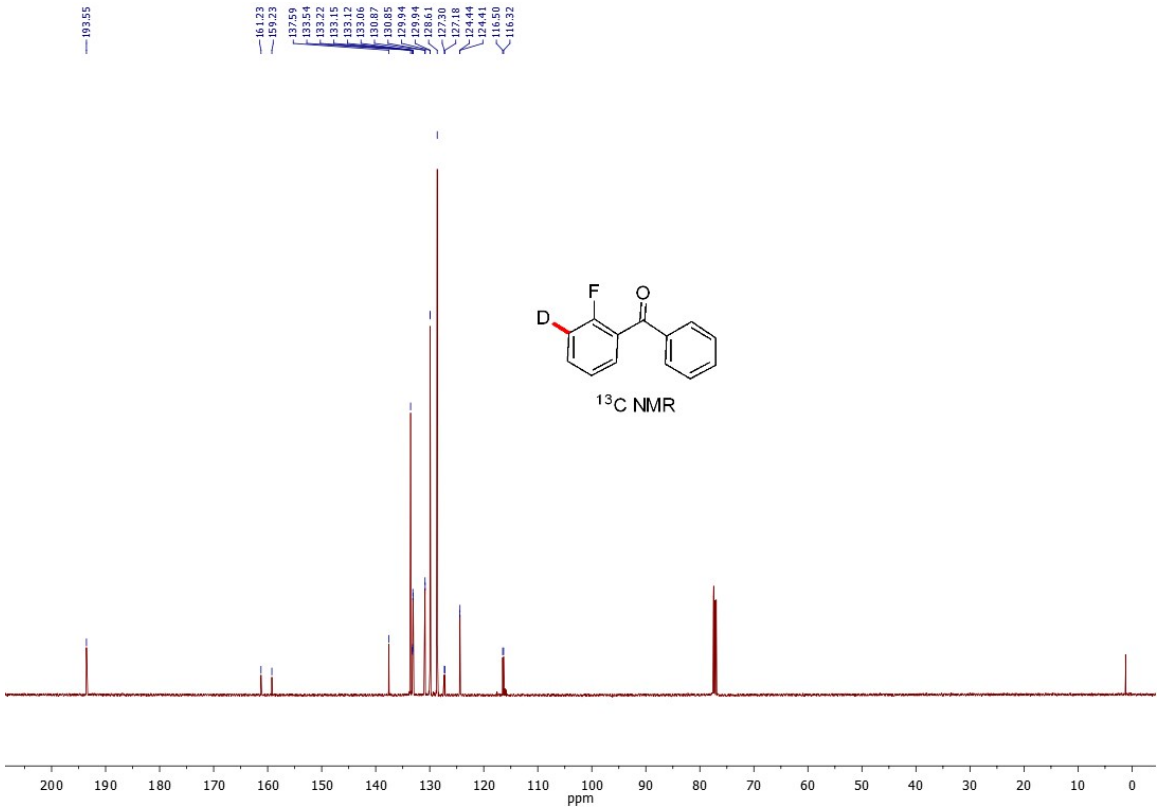

7.63
7.60
7.58
7.56
7.25
7.23
7.23
7.21
7.19
7.16
D
F
CN
^{1}H NMR
CHCl$_3$
2.00
1.16
0.11
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm
7.7 7.6 7.5 7.4 7.3 7.2 7.1
ppm

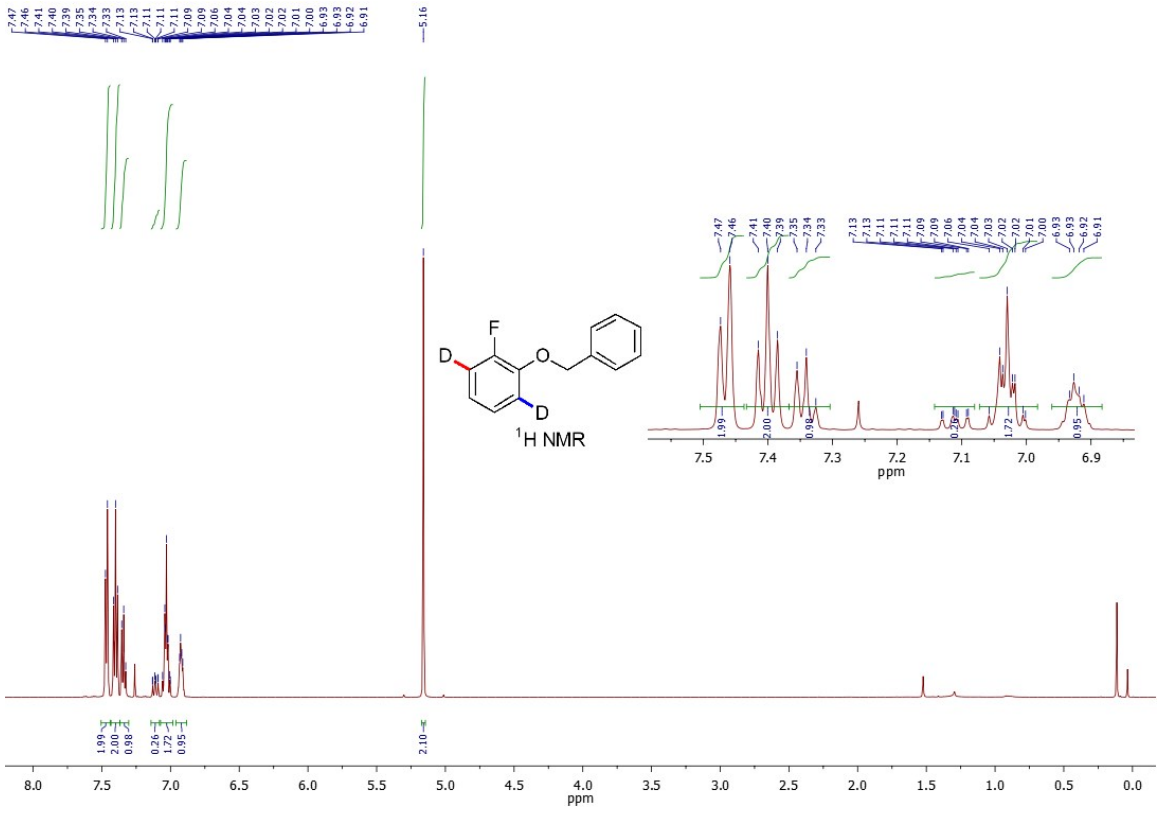

D
F
CN
19F NMR
-106.02
-106.30
0.13
0.87
105.8
-106.1
-106.4
-106.7
ppm
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220


D
F
CN
13C NMR
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


F
O
D
^{1}H NMR
ppm


F
O
D
^{19}F NMR
-110.96
-111.25
ppm


193.55
161.23
159.23
137.59
133.54
133.22
133.15
133.12
133.06
130.87
130.85
129.94
129.84
129.61
127.30
127.18
124.44
124.41
116.50
116.32
F
O
D
13C NMR
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm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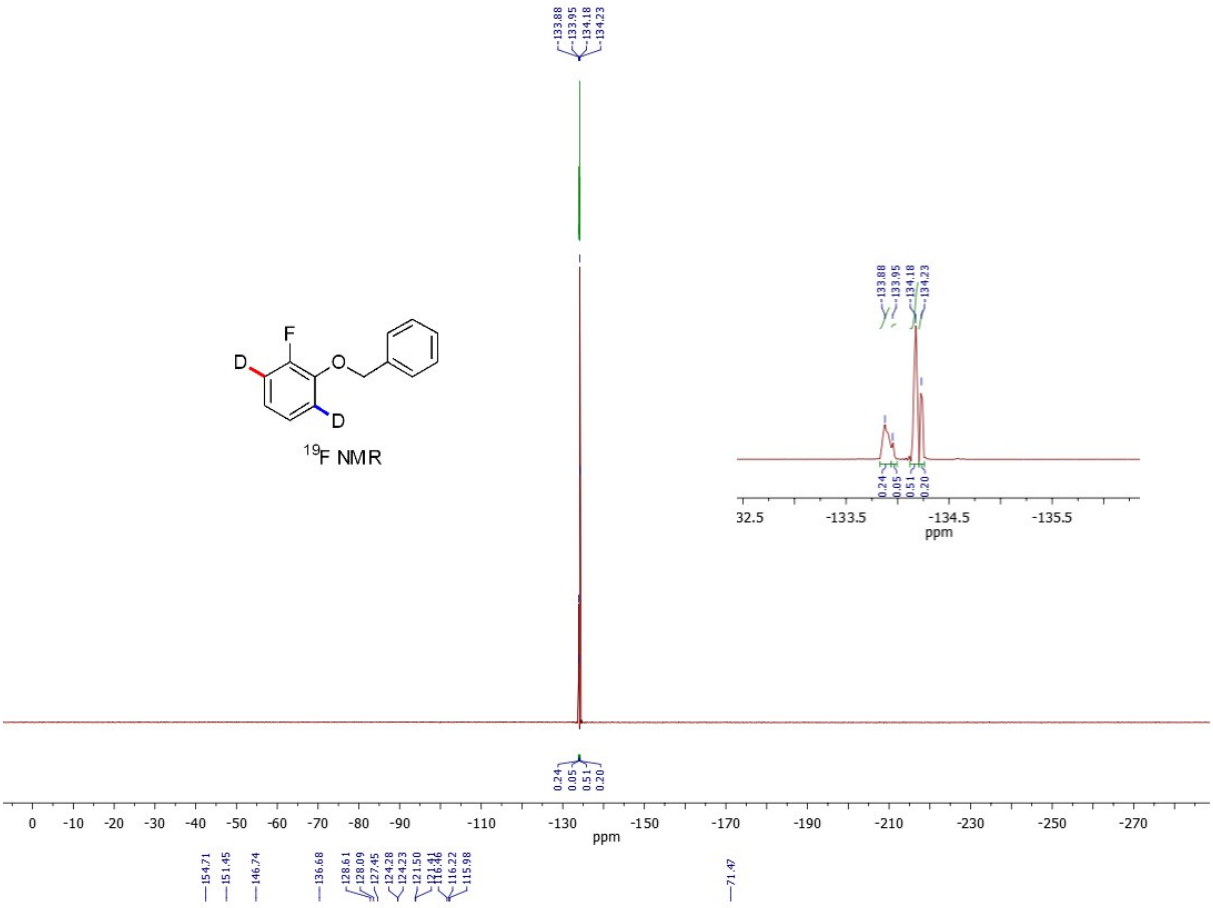
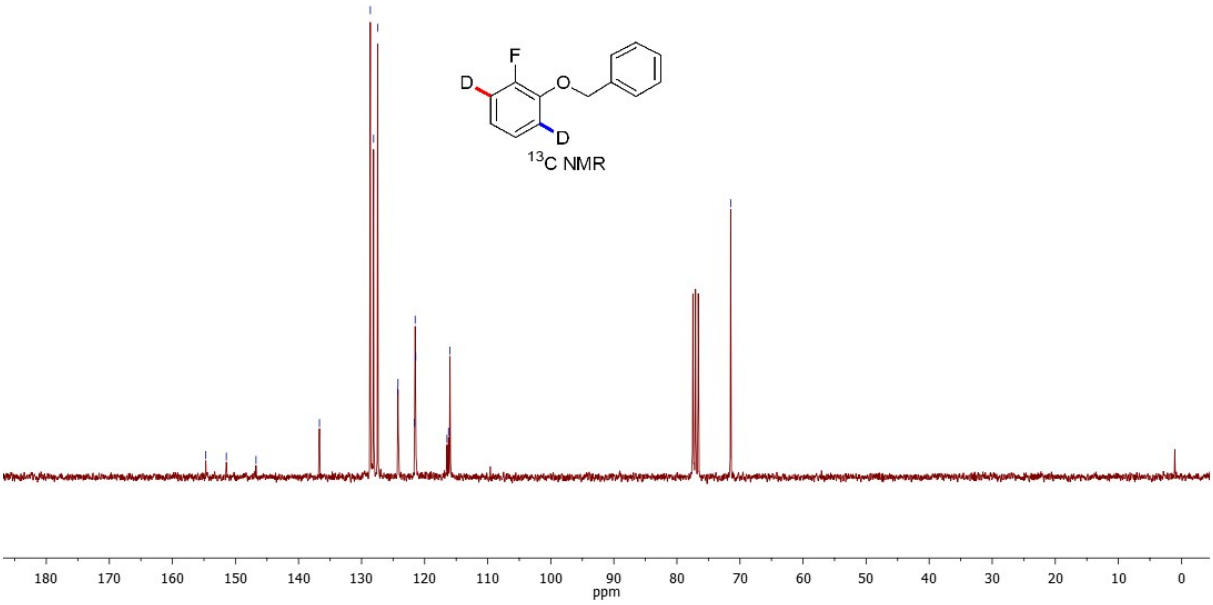
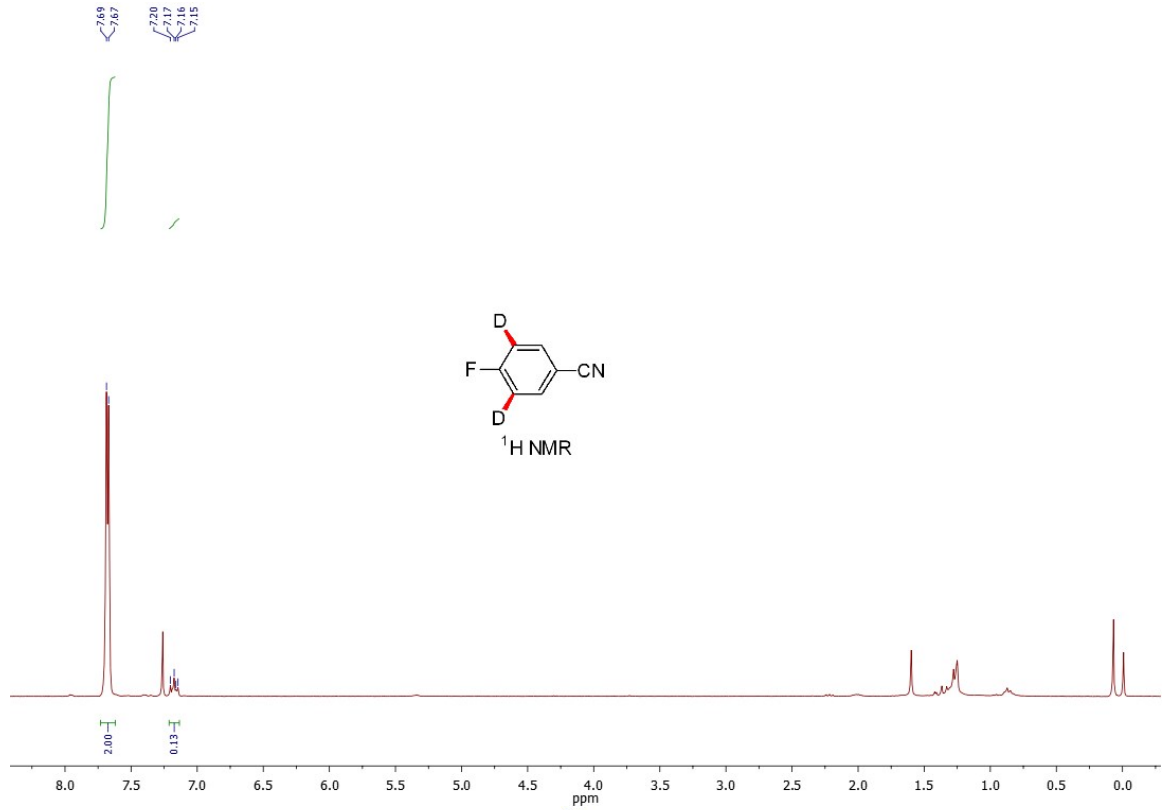
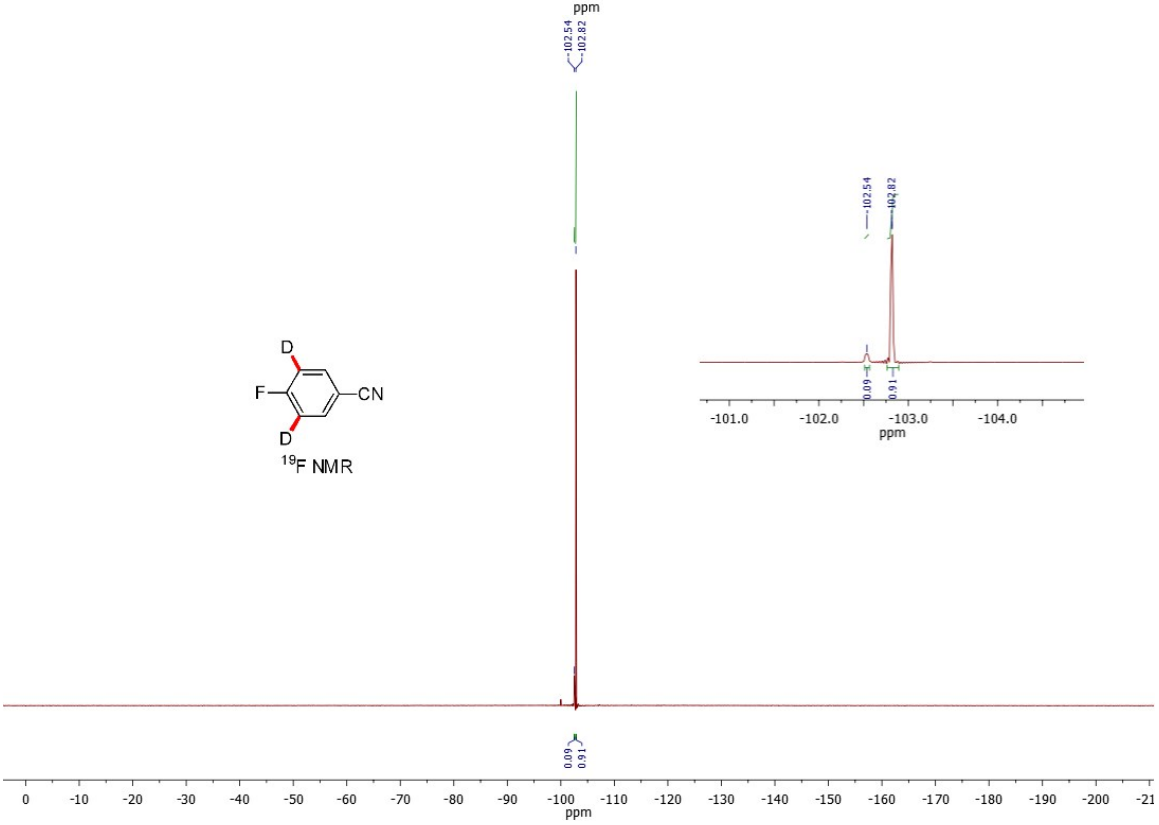
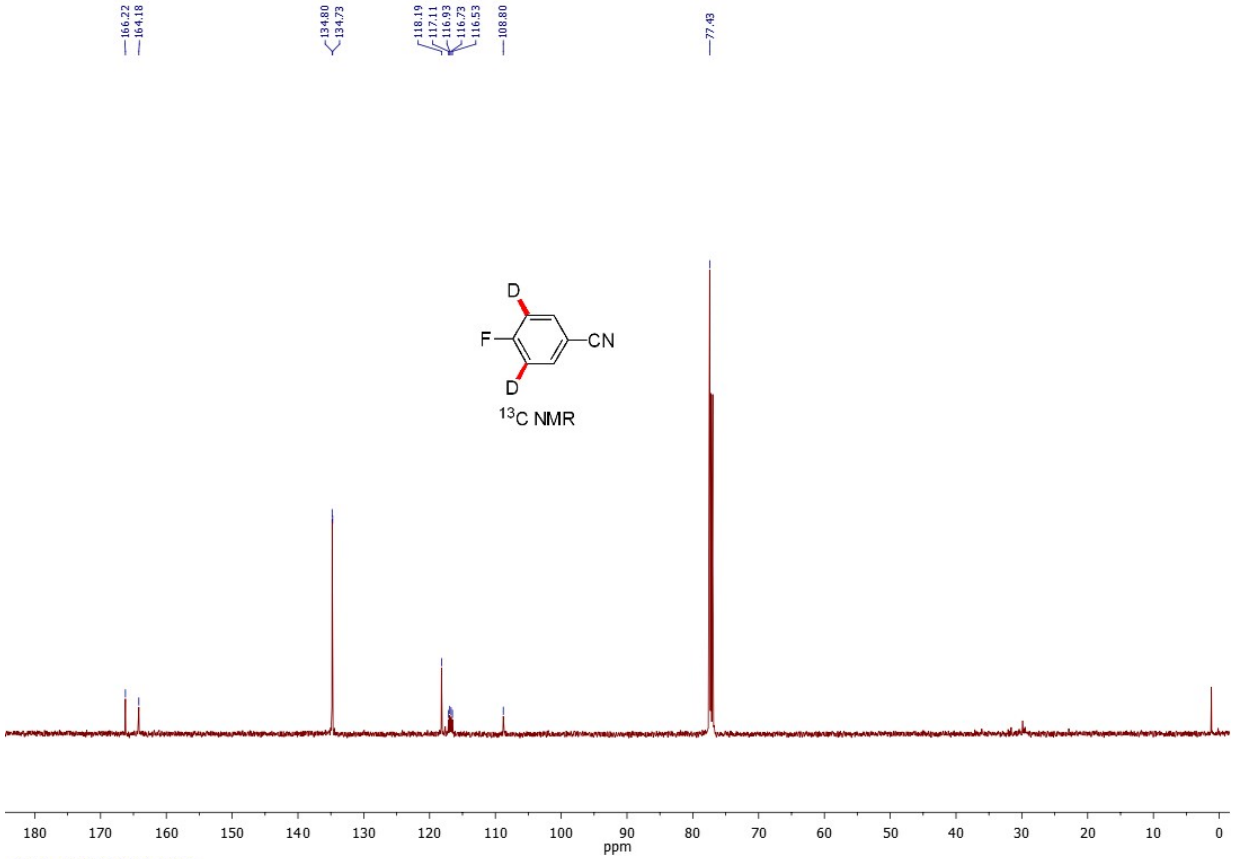
7.46
7.41
7.40
7.39
7.35
7.34
7.33
7.13
7.11
7.09
7.06
7.04
7.03
7.02
7.01
7.00
6.93
6.92
6.91
5.16
F
O
D
D
1H NMR
1.99
2.00
0.98
0.26
1.72
0.95
2.10
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm
7.5 7.4 7.3 7.2 7.1 7.0 6.9
ppm

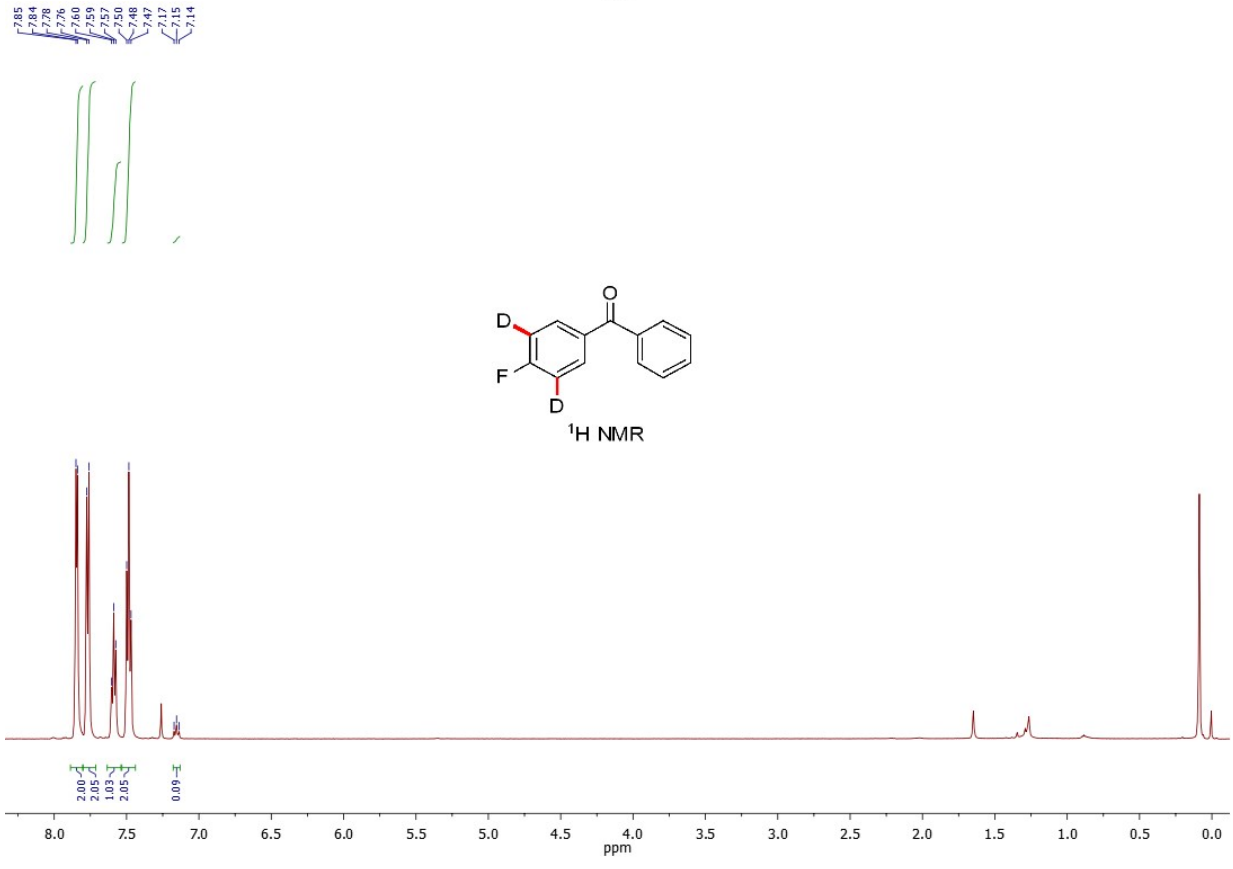

133.88
133.95
134.18
134.23
F
D
O
D
^{19}F NMR
0.24
0.05
0.51
0.20
32.5
-133.5
-134.5
-135.5
ppm
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 -130 -150 -170 -190 -210 -230 -250 -270
ppm

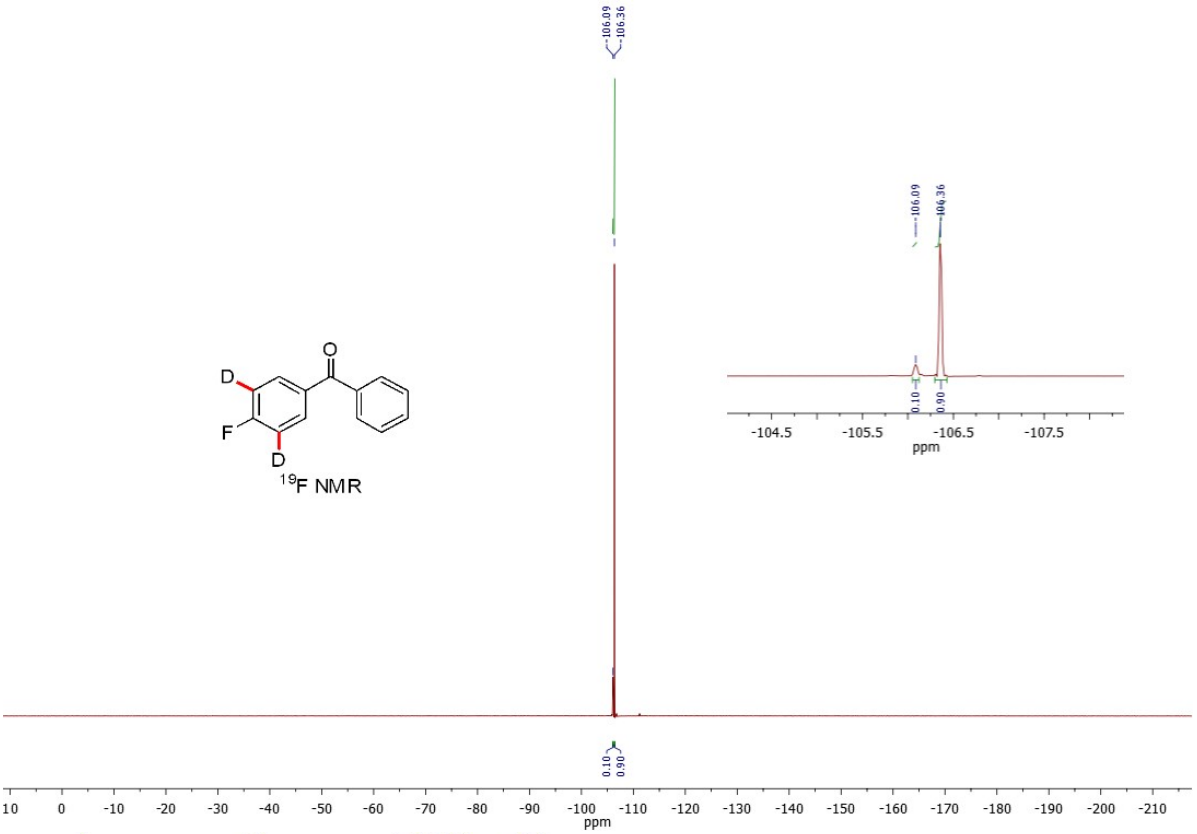

154.71
151.45
146.74
136.68
128.61
128.09
127.45
124.28
124.23
121.50
116.22
115.98
71.47
F
D
O
D
^{13}C NMR
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm

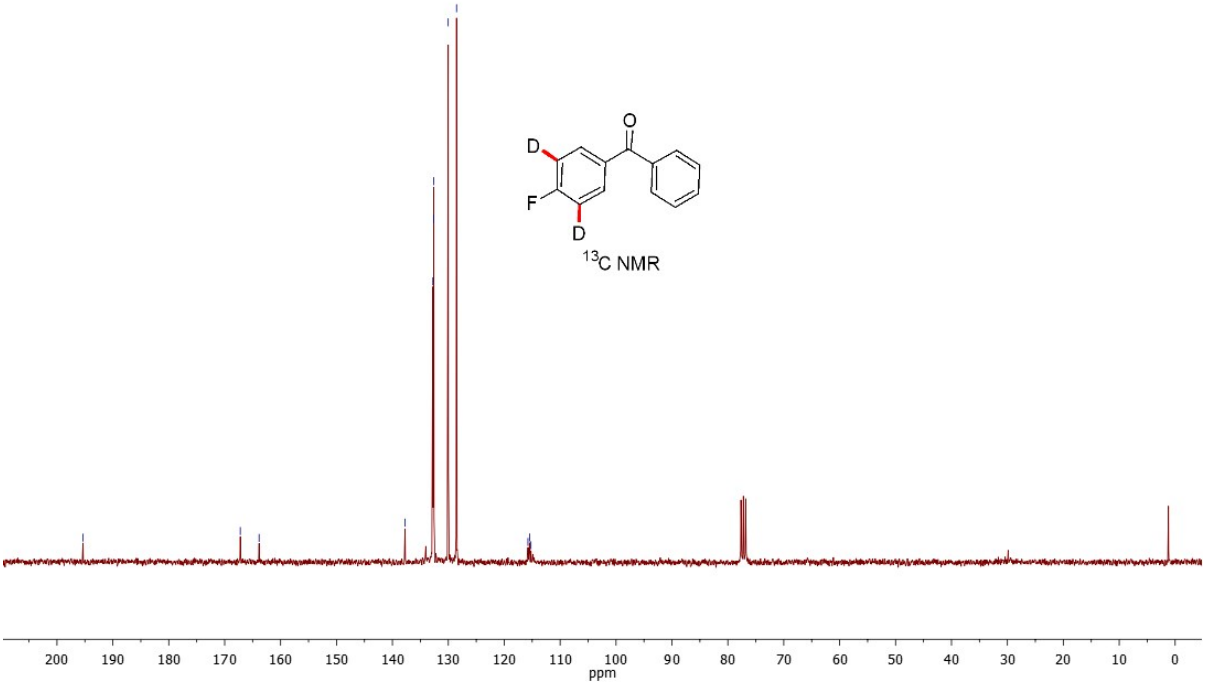

7.69
7.67
7.20
7.17
7.16
7.15
D
F
CN
D
^{1}H NMR
2.00
0.13
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


-102.54
-102.82
D
F
CN
D
^{19}F NMR
-102.54
-102.82
0.09
0.91
-101.0
-102.0
-103.0
-104.0
ppm
0.09
0.91
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-21
ppm


166.22
164.18
134.80
134.73
118.19
117.11
116.93
116.73
116.53
108.80
77.43
D
F
CN
D
13C NMR
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


7.85
7.84
7.78
7.76
7.60
7.59
7.57
7.50
7.48
7.47
7.17
7.15
7.14
O
D
F
D
1H NMR
2.00
2.05
1.03
2.05
0.09
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


-106.09
-106.36
D
F
D
O
^{19}F NMR
-104.5
-105.5
-106.5
-107.5
ppm
0.10
0.90
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
ppm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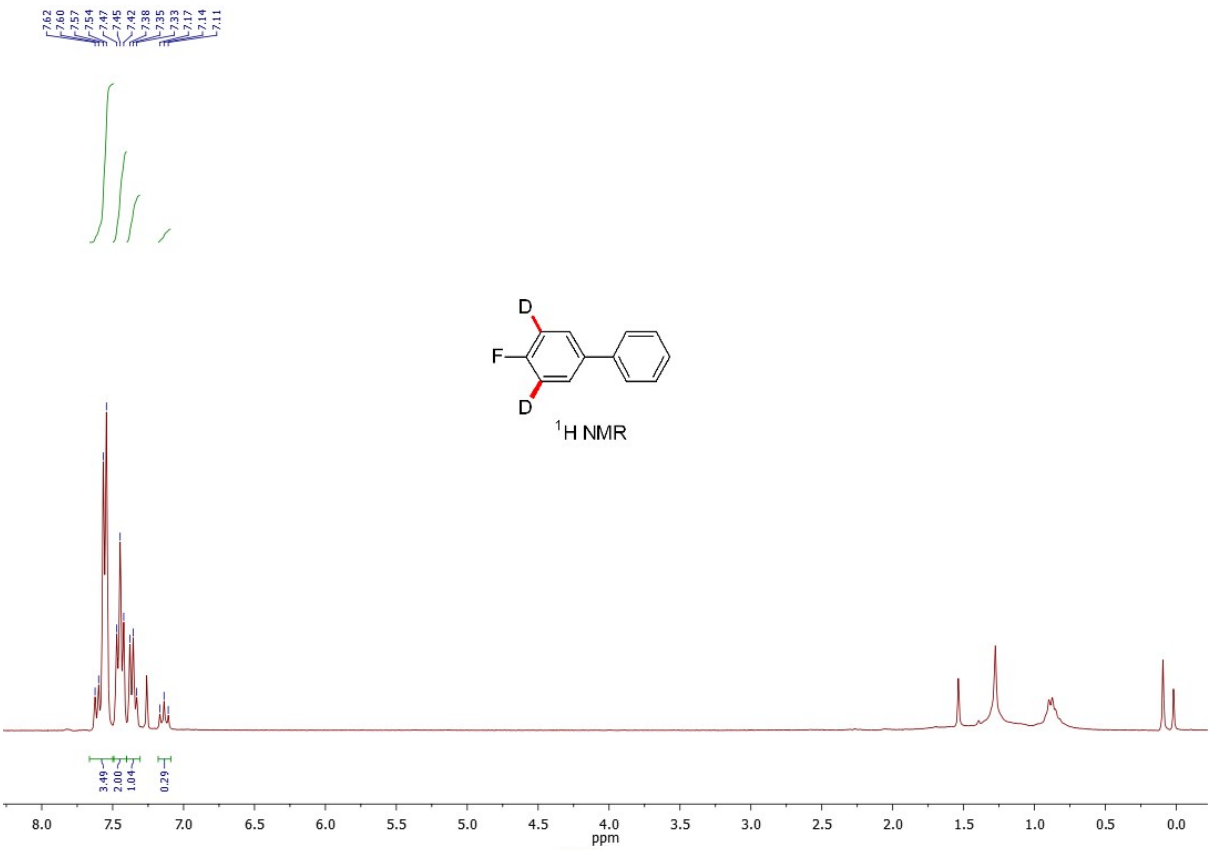
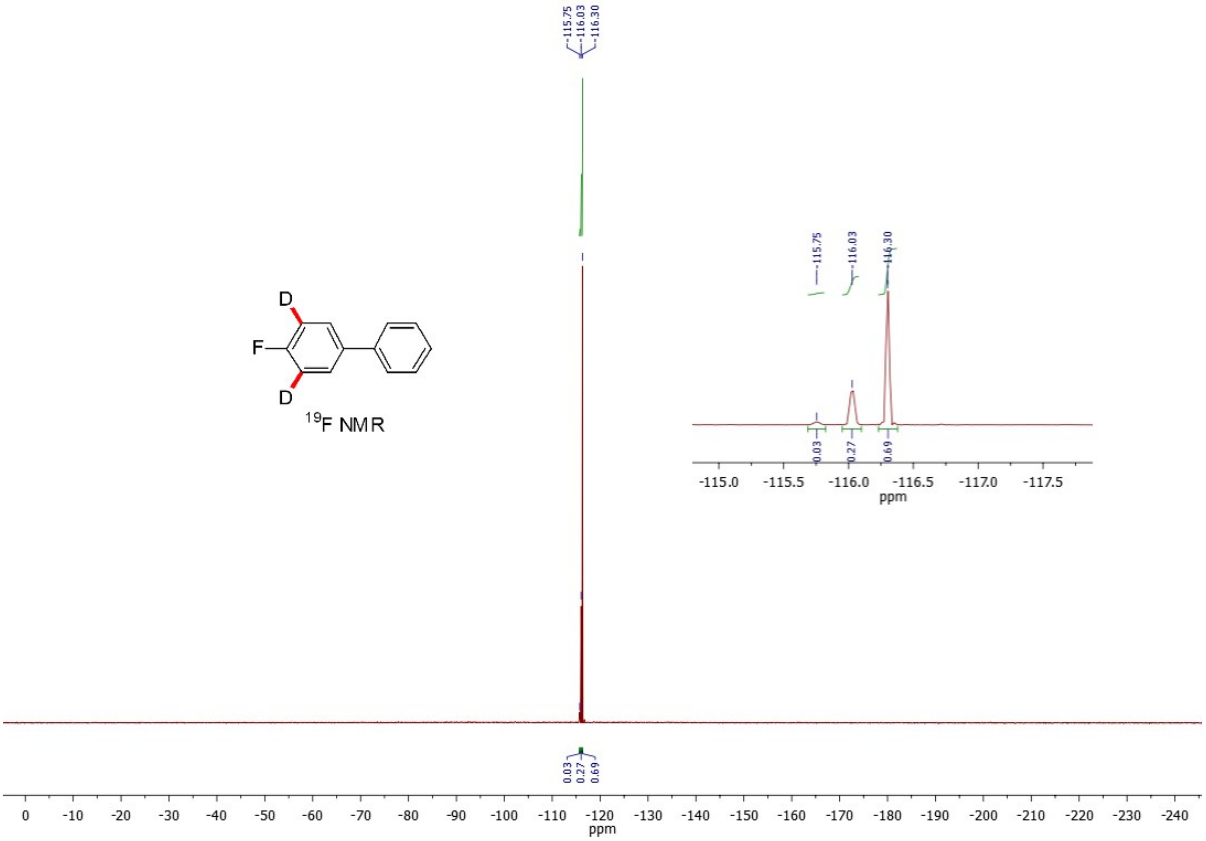
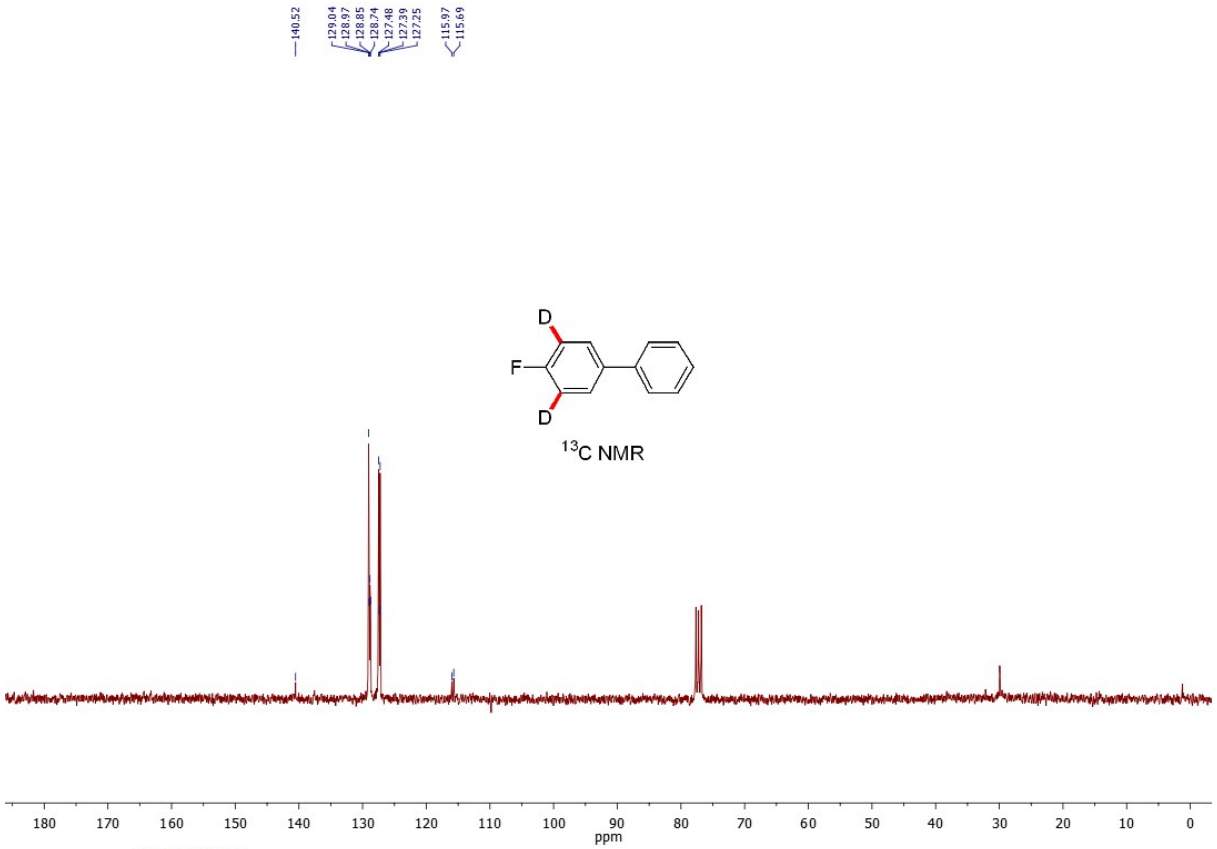
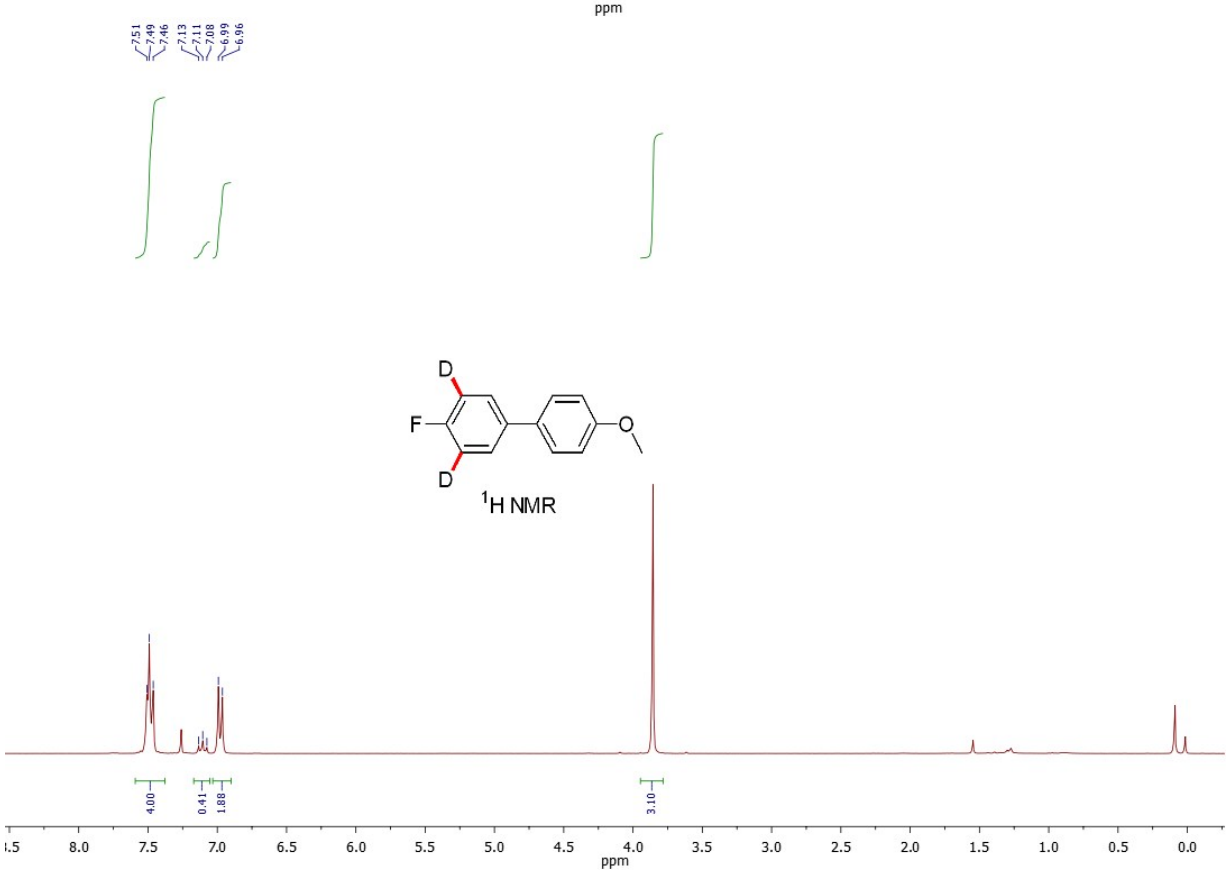
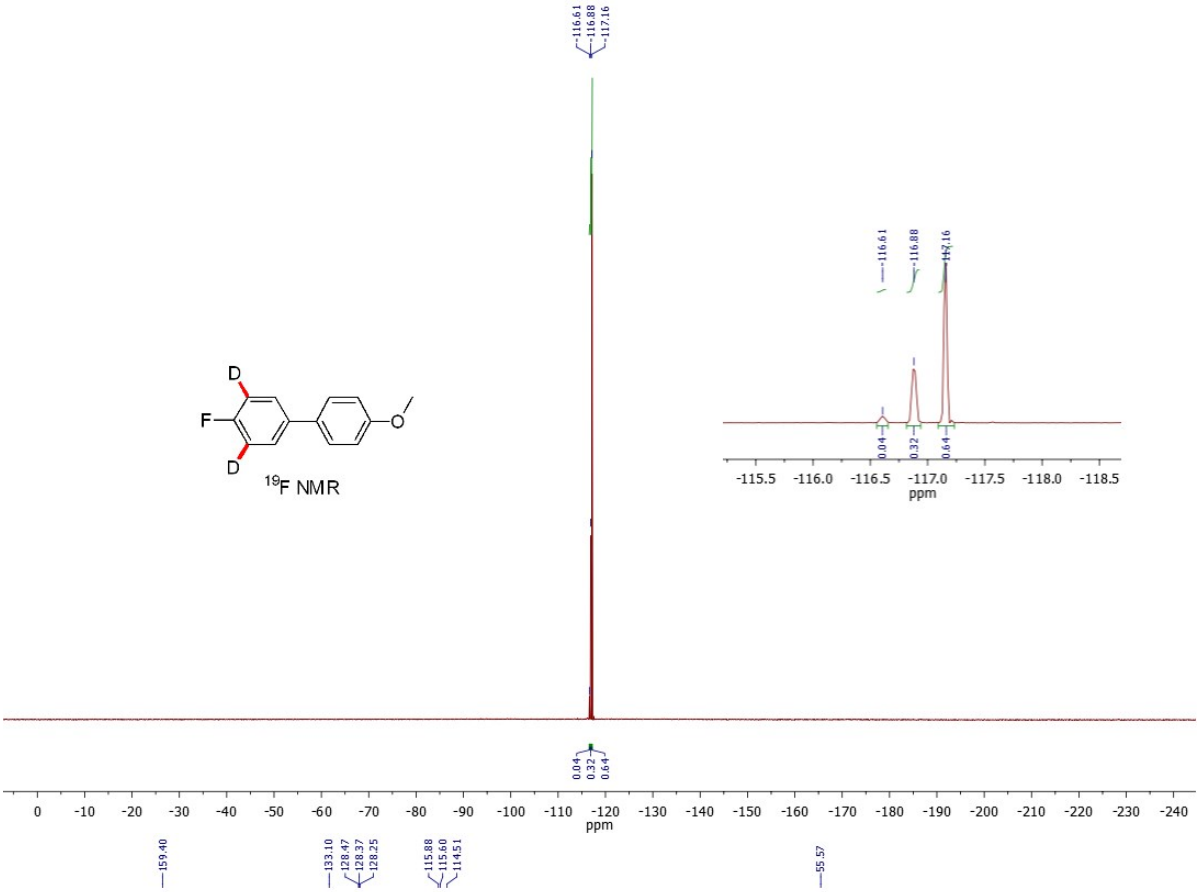
167.21
163.84
137.74
132.76
132.64
132.60
130.02
128.52
115.76
115.47
115.22
D
F
D
O
^{13}C NMR
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm

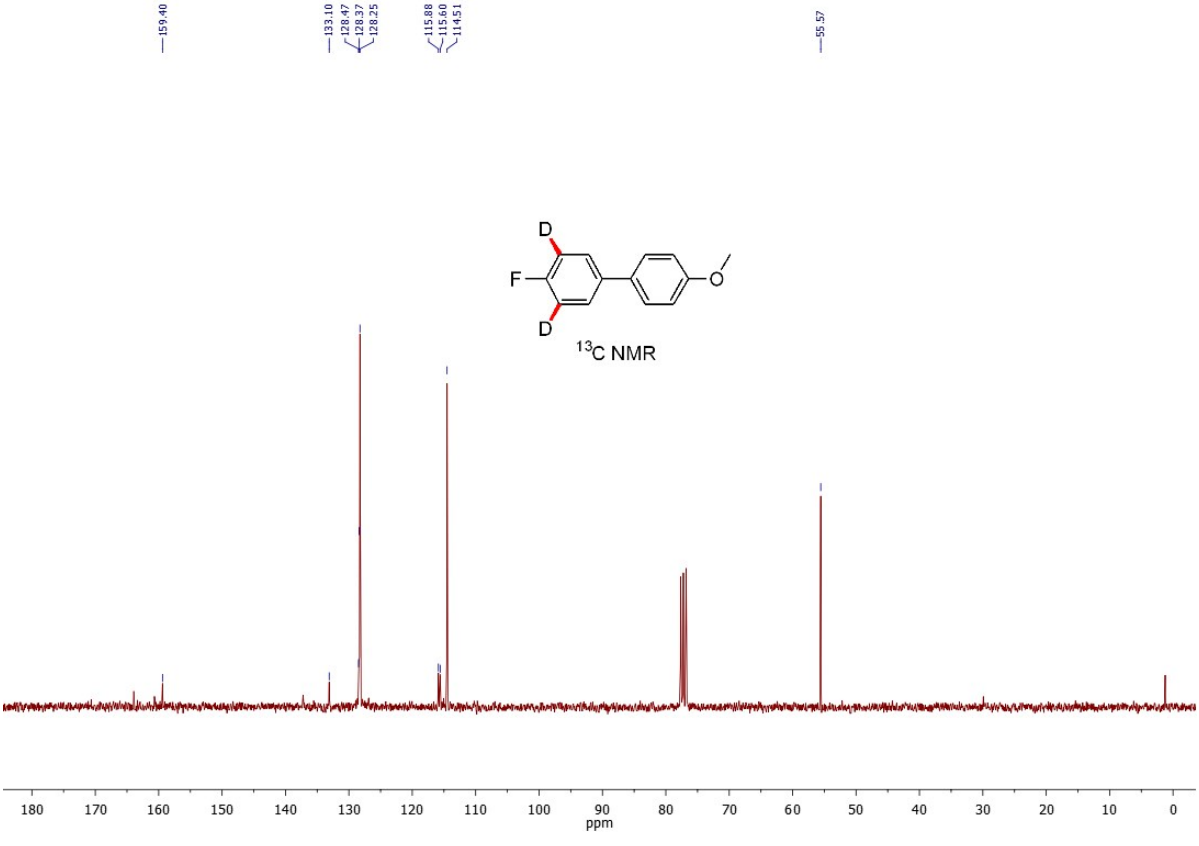

7.62
7.60
7.57
7.54
7.47
7.45
7.42
7.38
7.35
7.33
7.17
7.14
7.11
D
F
D
^{1}H NMR
3.49
2.00
1.04
0.29
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

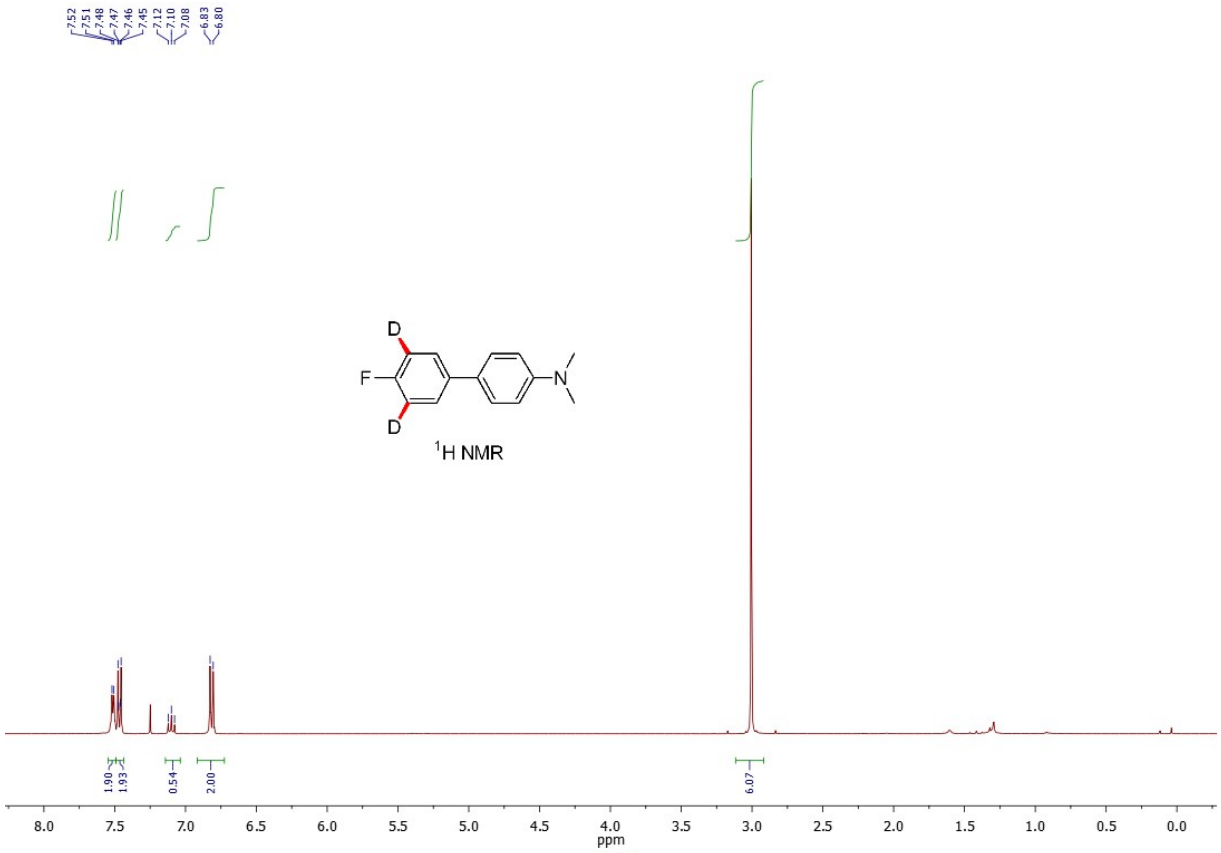

-115.75
-116.03
-116.30
D
F
D
^{19}F NMR
-115.75
-116.03
-116.30
0.03
0.27
0.69
-115.0
-115.5
-116.0
-116.5
-117.0
-117.5
ppm
0.03
0.27
0.69
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
-240
ppm

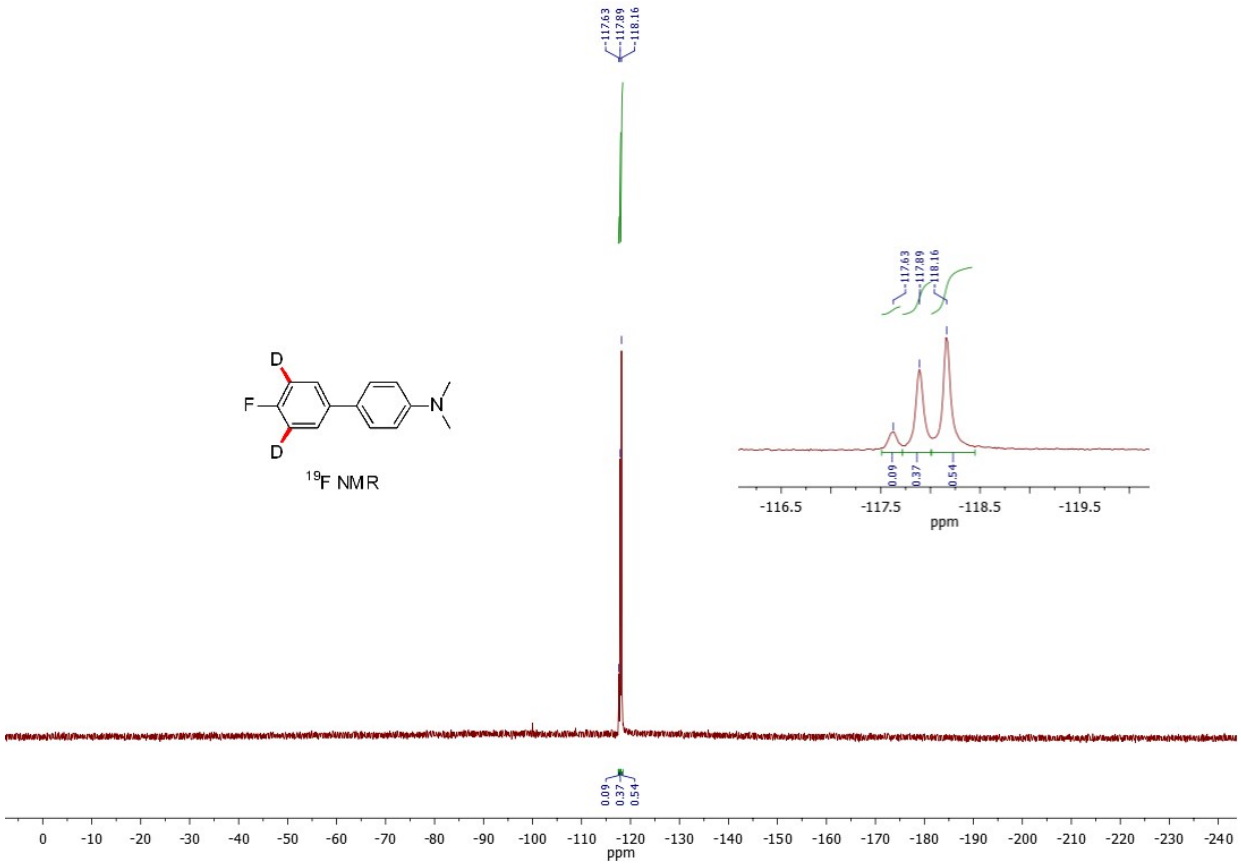

140.52
129.04
128.97
128.85
128.74
127.48
127.39
127.25
115.97
115.69
D
F
D
^{13}C NMR
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm


7.51
7.49
7.46
7.13
7.11
7.08
6.99
6.96
D
F
O
D
^{1}H NMR
4.00
0.41
1.88
3.10
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm


D
F
D
O
^{19}F NMR
-116.61
-116.88
-117.16
0.04
0.32
0.64
-115.5 -116.0 -116.5 -117.0 -117.5 -118.0 -118.5
ppm
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
ppm


159.40
133.10
128.47
128.37
128.25
115.88
115.60
114.51
55.57
D
F
D
O
^{13}C NMR
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm


7.52
7.51
7.48
7.47
7.46
7.45
7.12
7.10
7.08
6.83
6.80
D
F
D
N
^{1}H NMR
1.90
1.93
0.54
2.00
6.07
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


-117.63
-117.89
-118.16
D
F
D
N
^{19}F NMR
0.09
0.37
0.54
-116.5
-117.5
-118.5
-119.5
ppm
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
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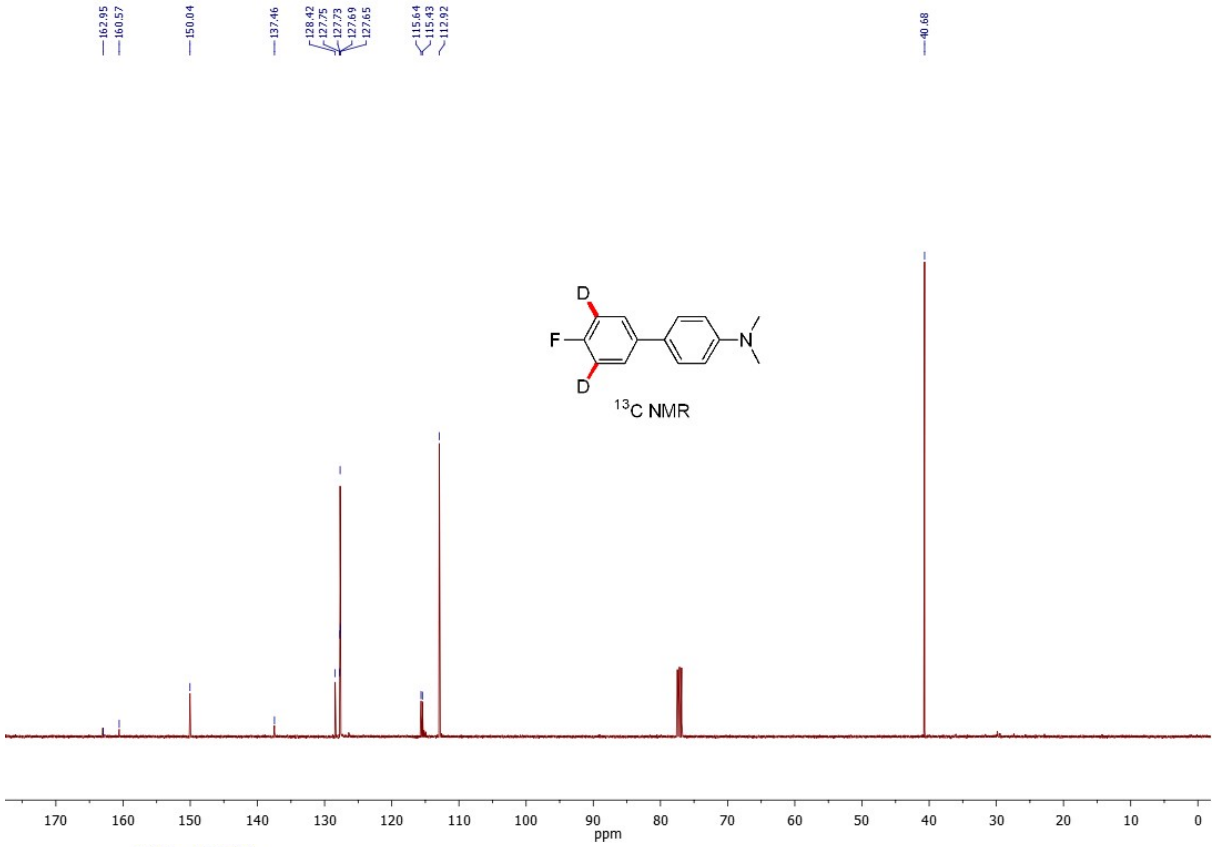
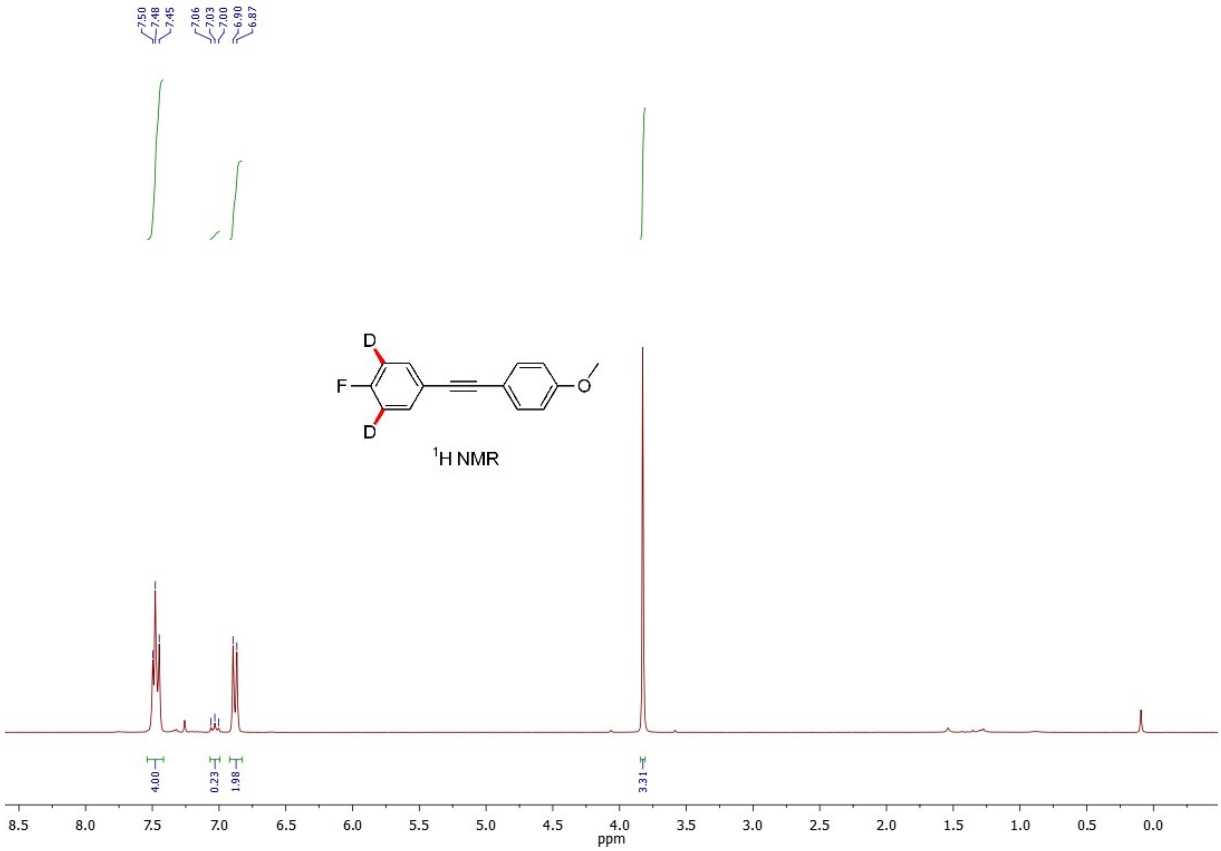
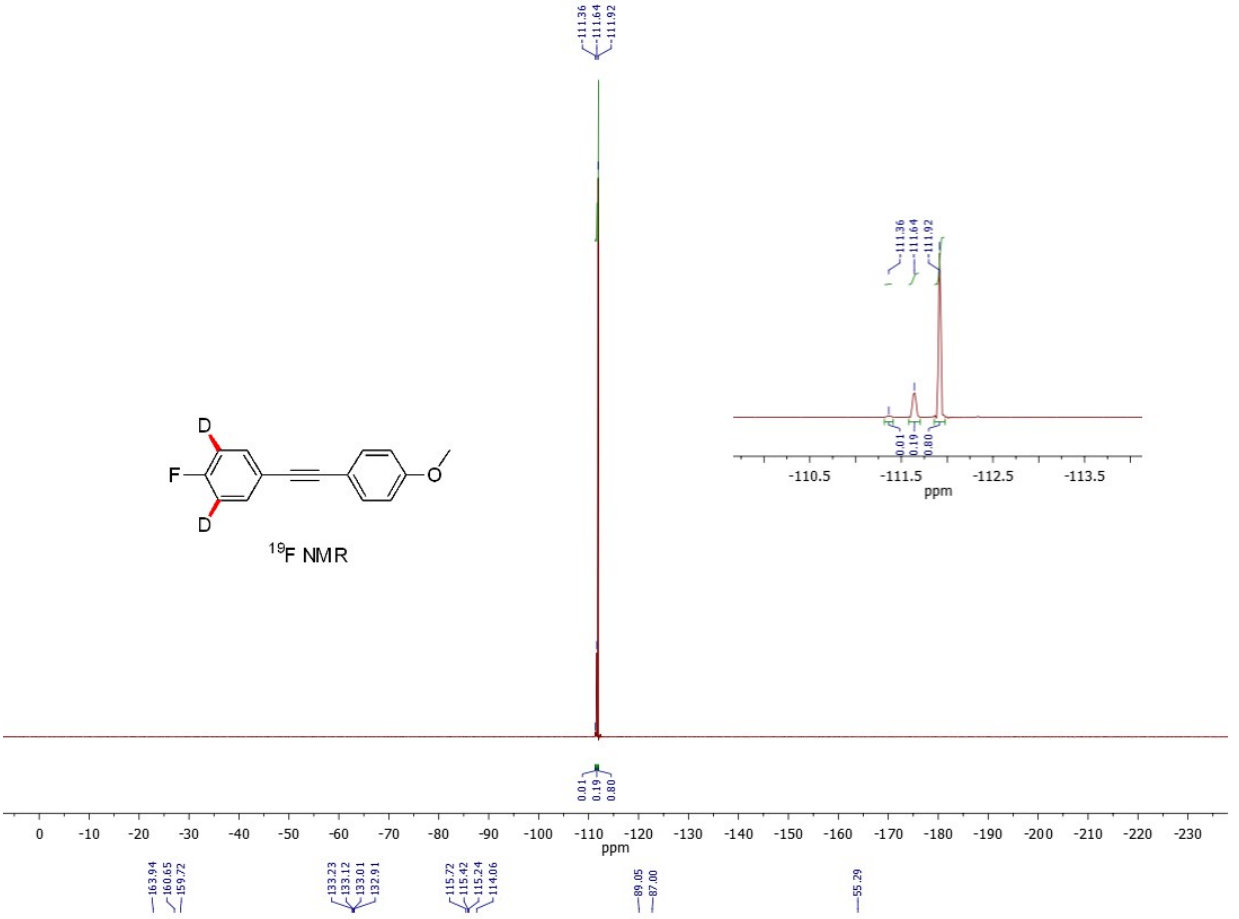
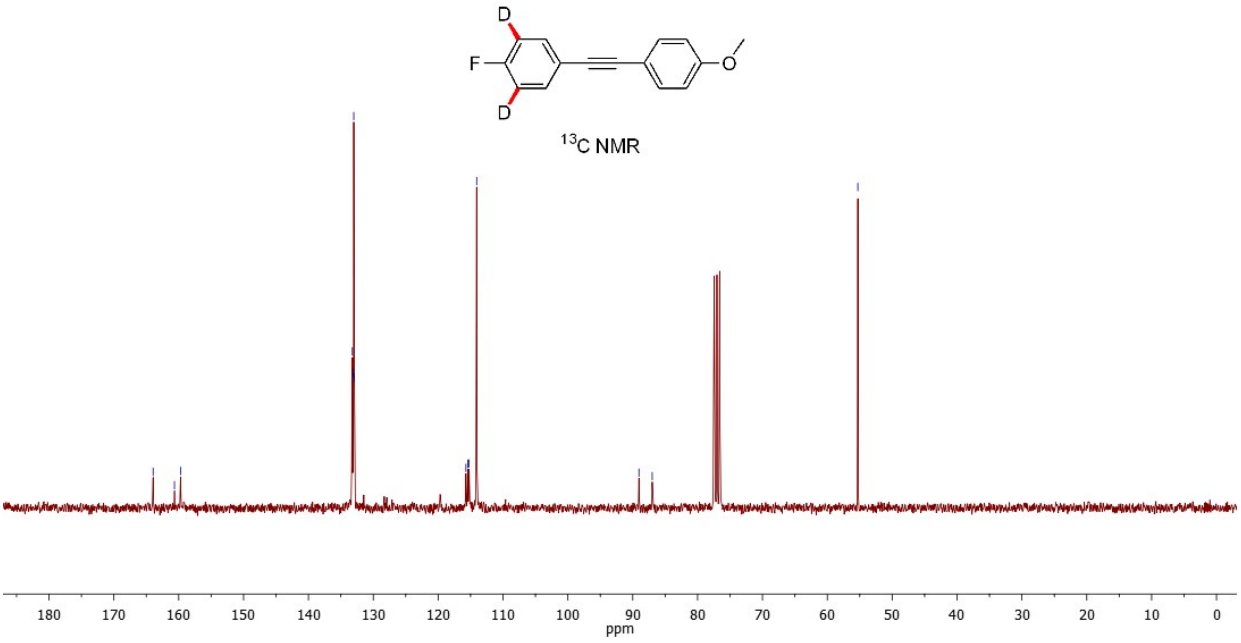
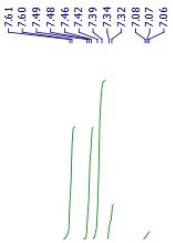
-190
-200
-210
-220
-230
-240
ppm

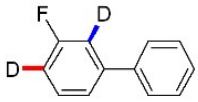

162.95
160.57
150.04
137.46
128.42
127.75
127.73
127.69
127.65
115.64
115.43
112.92
40.68
D
F
D
N
^{13}C NMR
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


7.50
7.48
7.45
7.06
7.03
7.00
6.90
6.87
D
F
D
O
^{1}H NMR
4.00
0.23
1.98
3.31
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

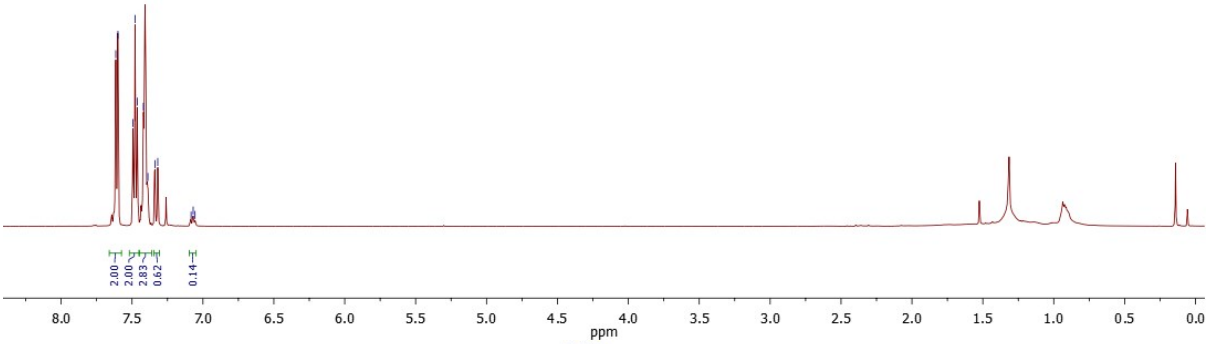

-111.36
-111.64
-111.92
D
F
D
O
^{19}F NMR
0.01
0.19
0.80
ppm
163.94
160.65
159.72
133.23
133.12
133.01
132.91
115.72
115.42
115.24
114.06
89.05
87.00
55.29

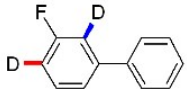

D
F
D
O
^{13}C NMR
ppm



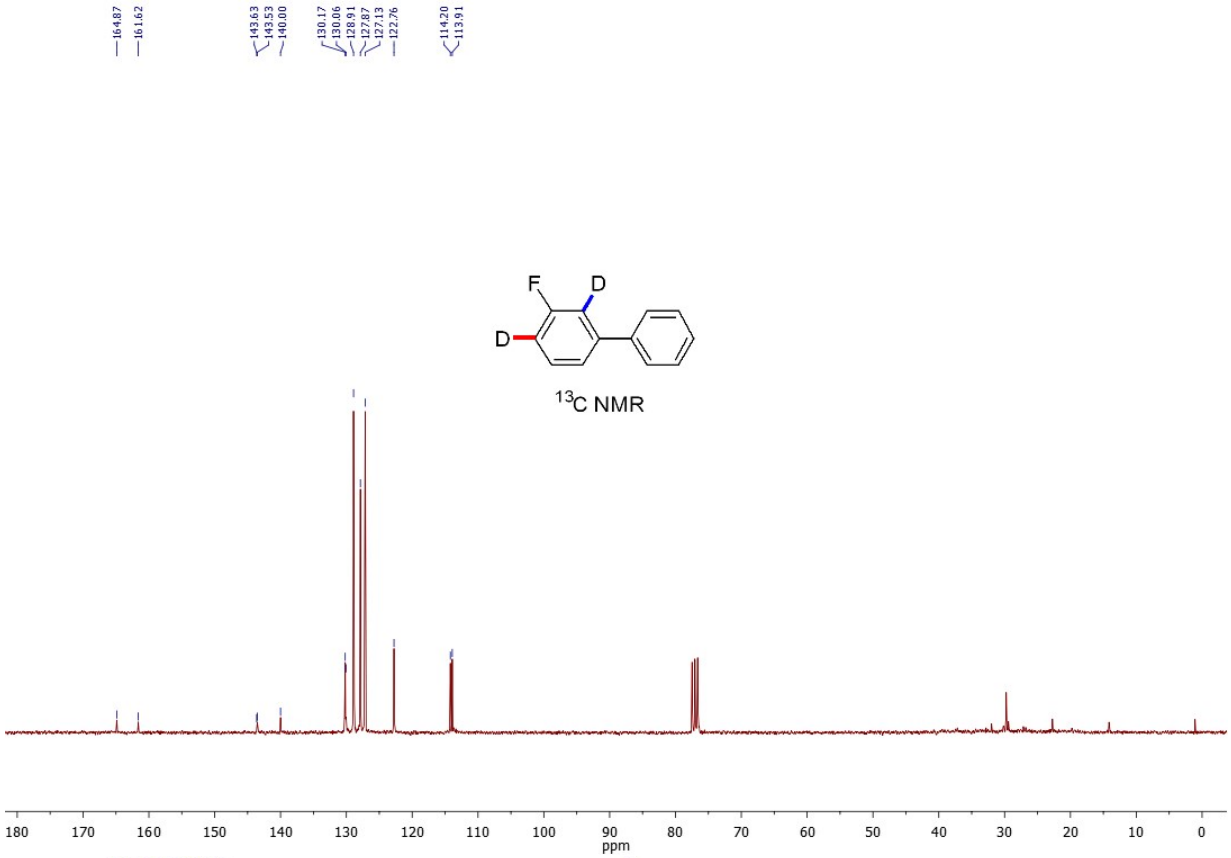


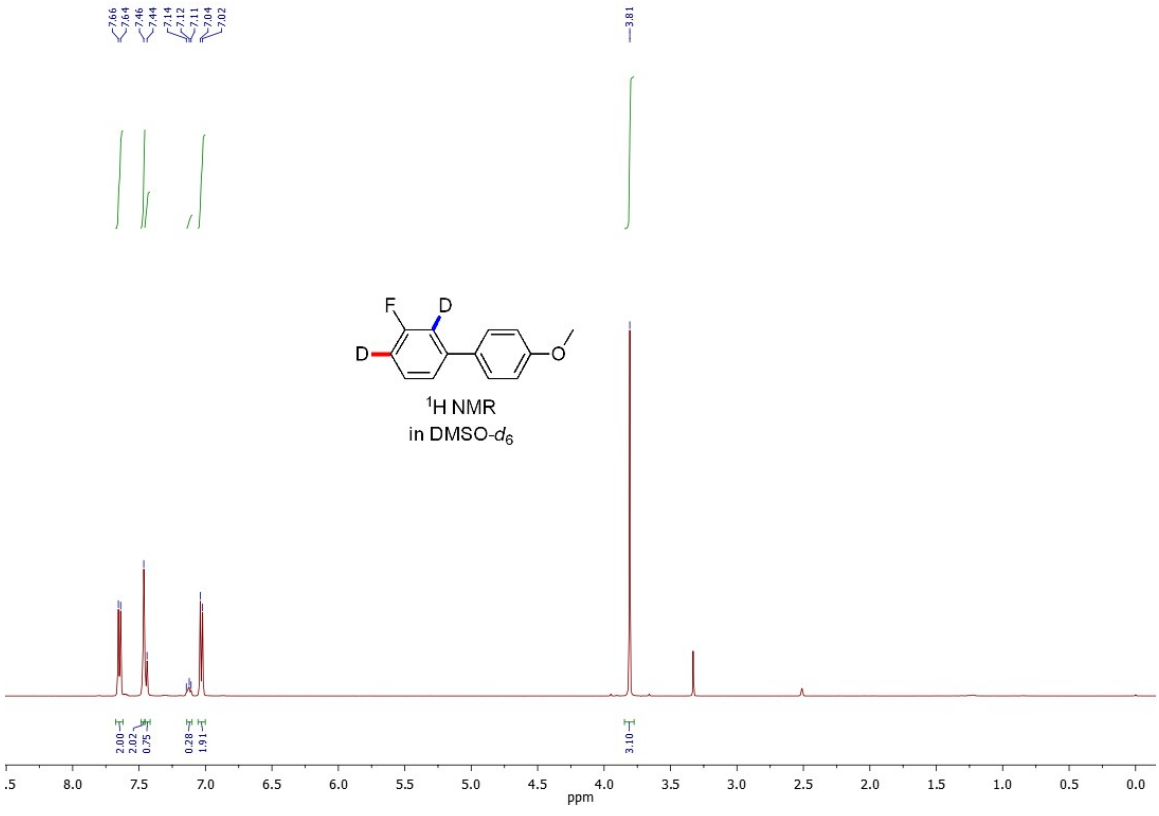
^{1}H NMR

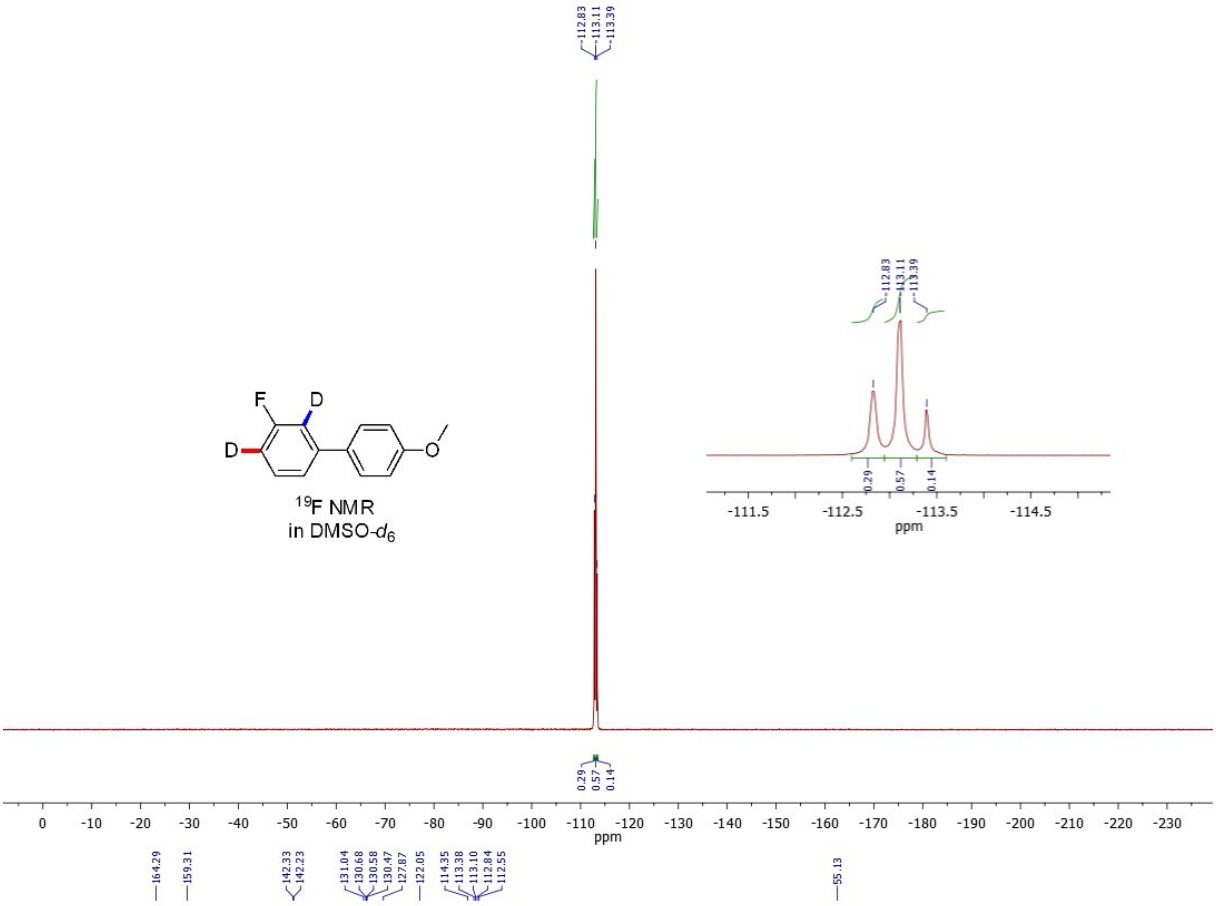


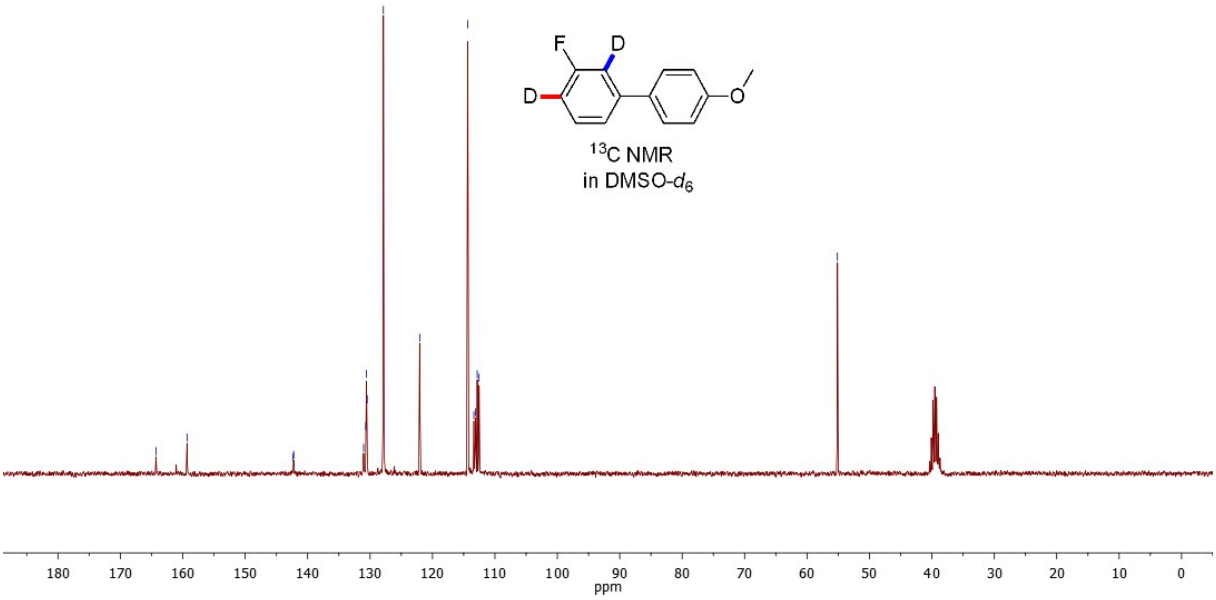


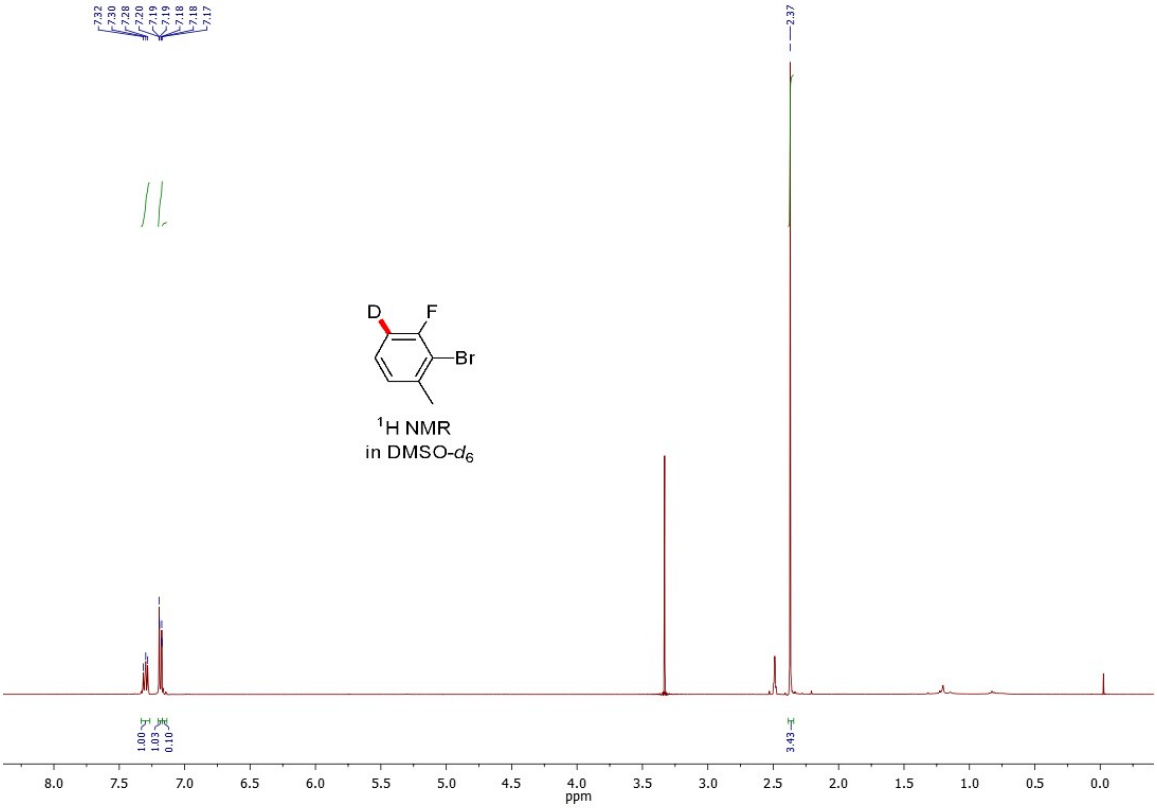
^{19}F NMR

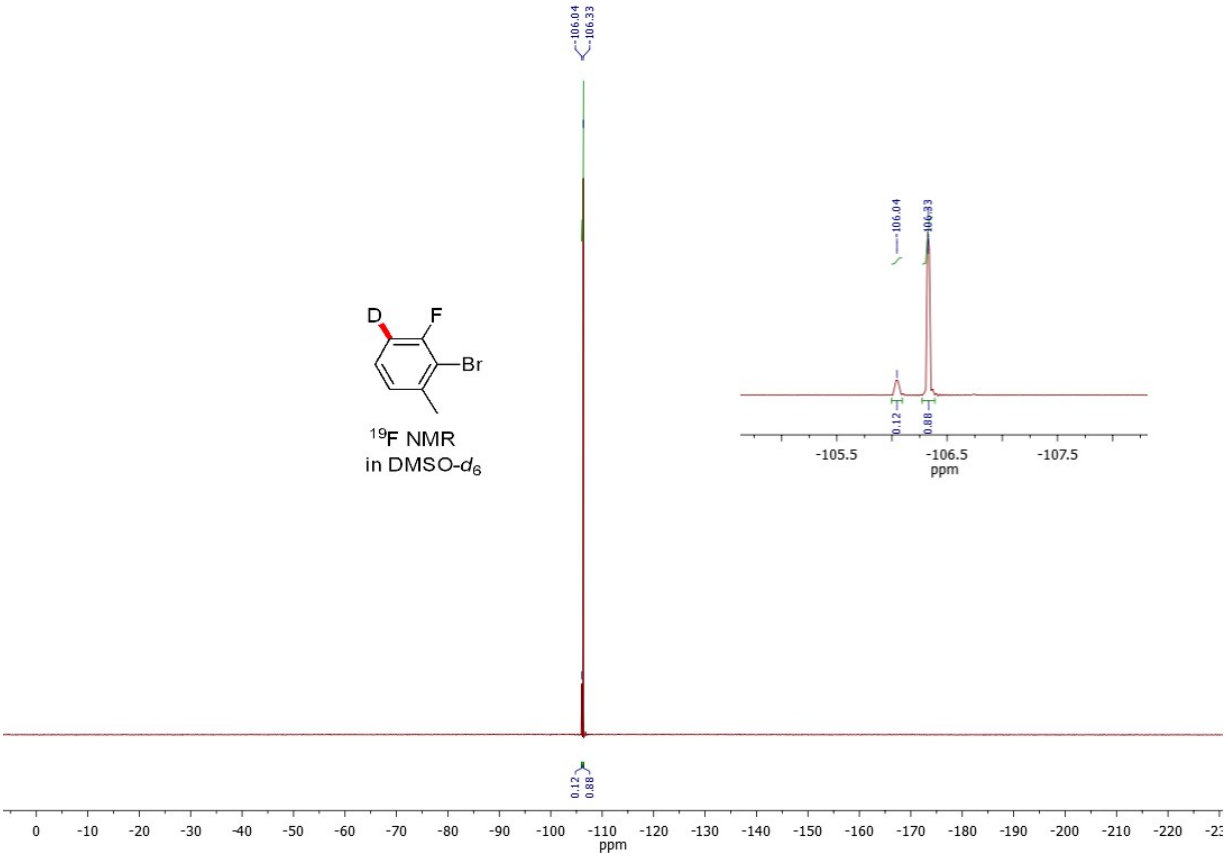

164.87
161.62
143.63
143.53
140.00
130.17
130.06
128.91
127.87
127.13
122.76
114.20
113.91
F
D
D
13C NMR
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

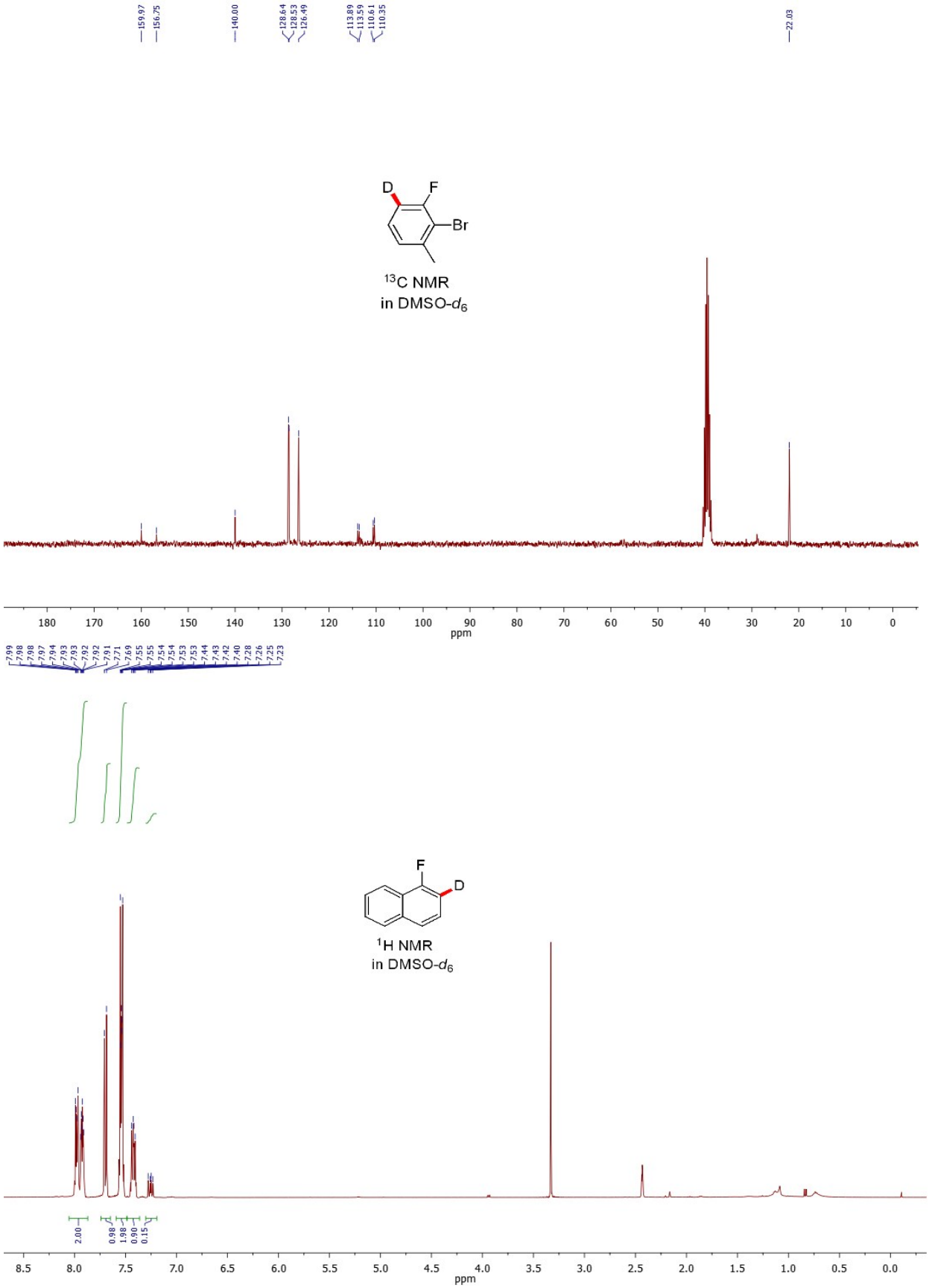

7.66
7.64
7.46
7.44
7.14
7.12
7.11
7.04
7.02
3.81
F
D
D
O
1H NMR
in DMSO-d6
2.00
2.02
0.75
0.28
1.91
3.10
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

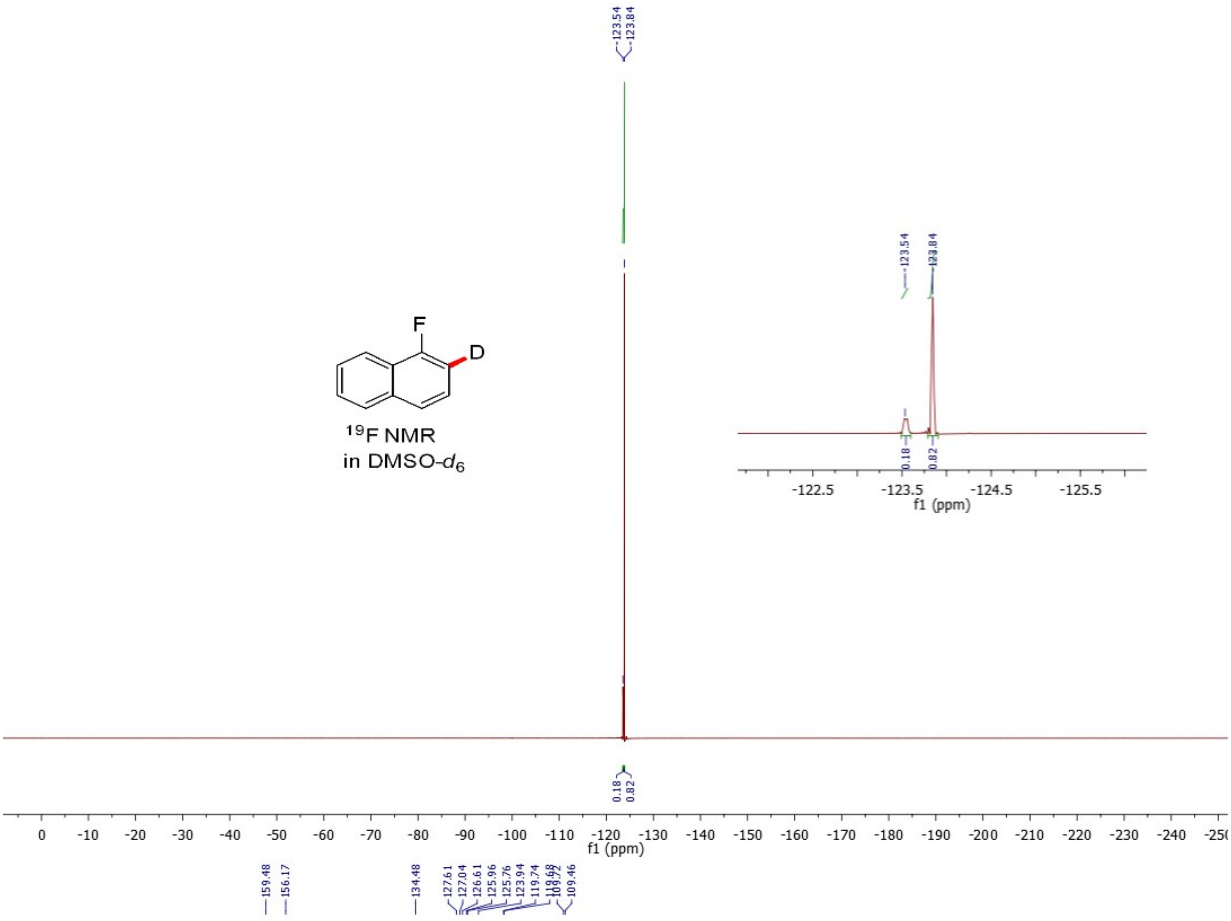

F
D
D
O
^{19}F NMR
in DMSO-d_6
-112.83
-113.11
-113.39
0.29
0.57
0.14
-111.5
-112.5
-113.5
-114.5
ppm
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
ppm

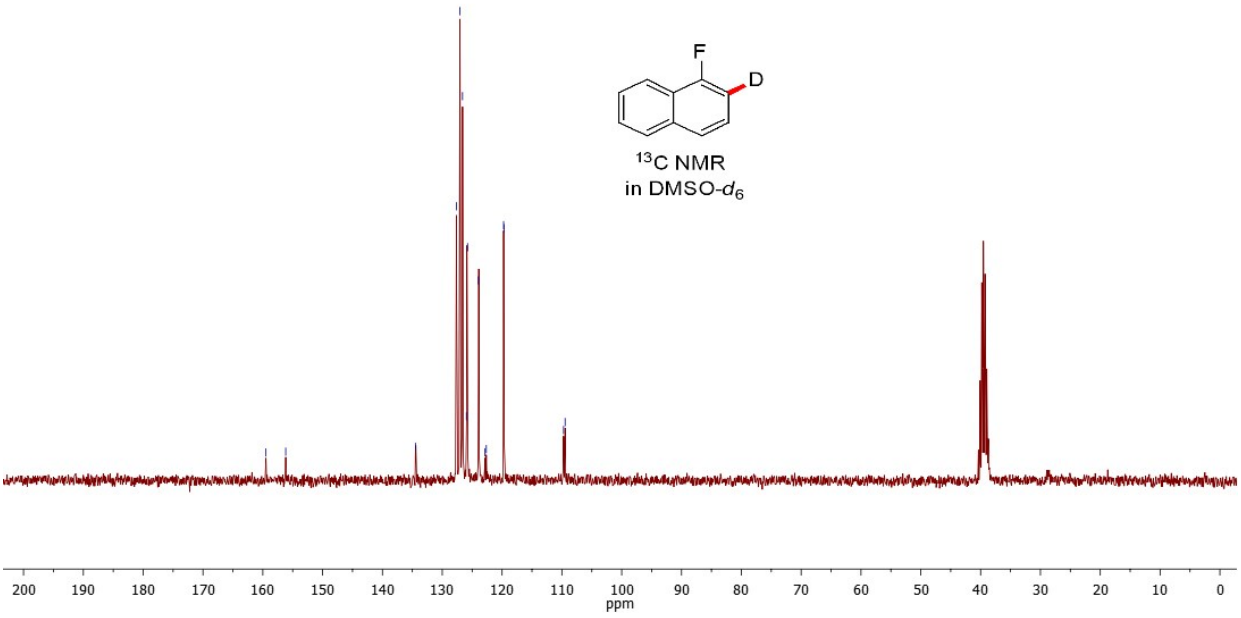

F
D
D
O
^{13}C NMR
in DMSO-d_6
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

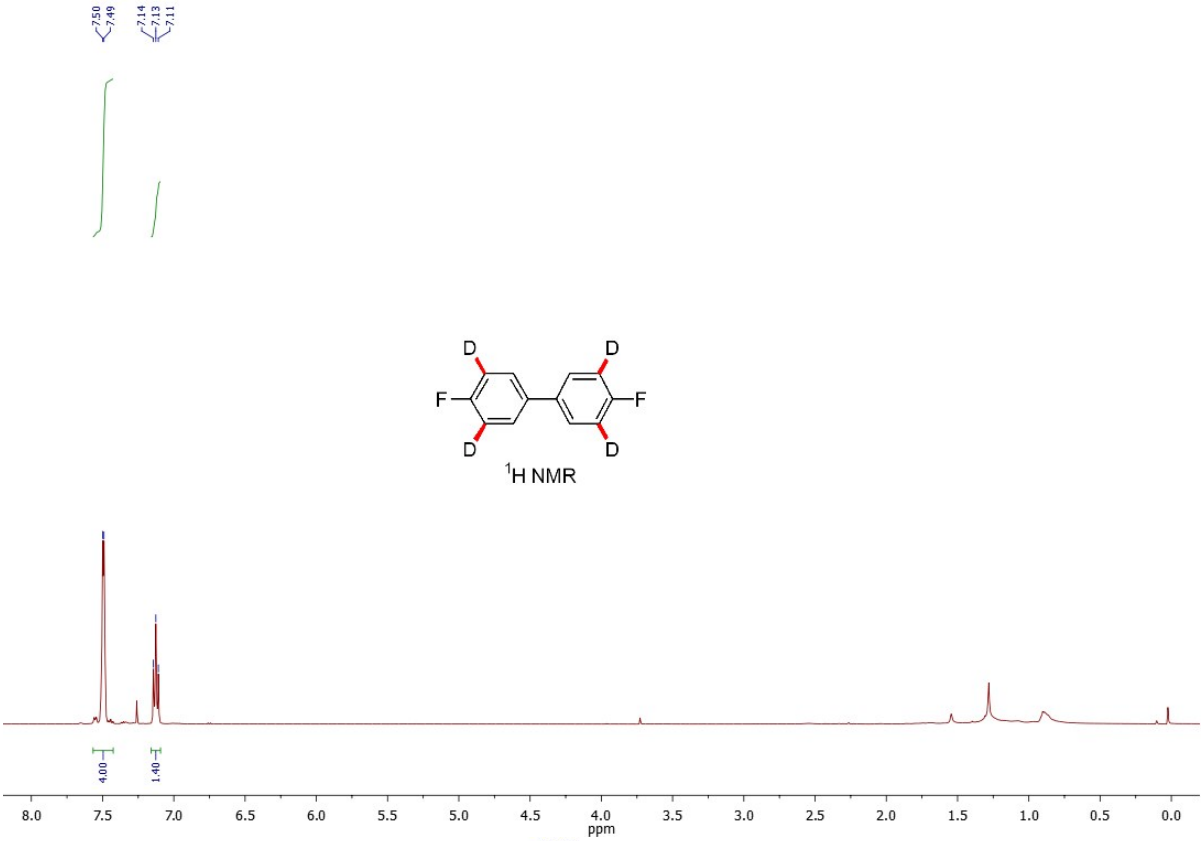

D
F
Br
^{1}H NMR
in DMSO-d_6
7.32
7.30
7.28
7.20
7.19
7.19
7.18
7.18
7.17
2.37
1.00
1.03
0.10
3.43
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

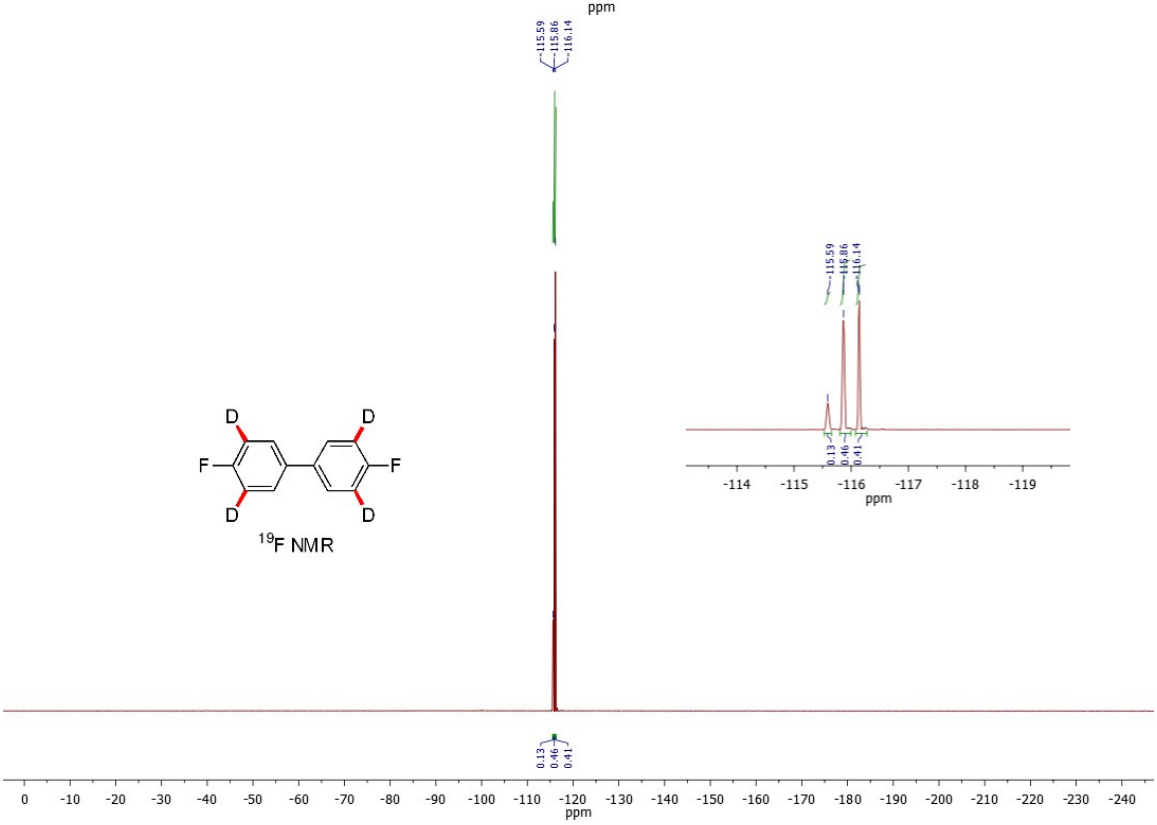

D
F
Br
^{19}F NMR
in DMSO-d_6
-106.04
-106.33
0.12
0.88
-105.5
-106.5
-107.5
ppm
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
ppm

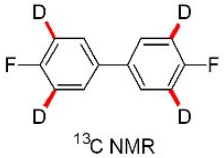

159.97
156.75
140.00
128.64
128.53
126.49
113.89
113.59
110.61
110.35
22.03
D
F
Br
^{13}C NMR
in DMSO-d_6
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm
7.99 7.98 7.98 7.97 7.94 7.93 7.93 7.92 7.92 7.91 7.71 7.69 7.55 7.55 7.54 7.54 7.53 7.53 7.44 7.43 7.42 7.40 7.28 7.26 7.25 7.23
F
D
^{1}H NMR
in DMSO-d_6
2.00 0.98 1.98 0.90 0.15
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm


F
D
^{19}F NMR
in DMSO-d_6
-123.54
-123.84
0.18
0.82
-122.5
-123.5
-124.5
-125.5
f1 (ppm)
f1 (ppm)

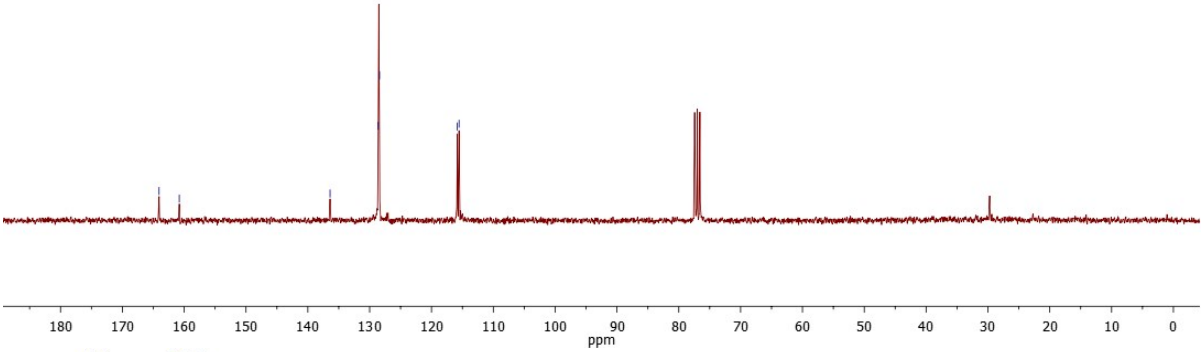

F
D
^{13}C NMR
in DMSO-d_6
ppm

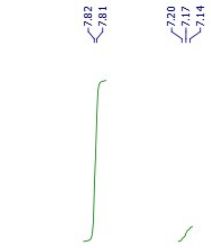

7.50
7.49
7.14
7.13
7.11
D
D
F
F
D
D
^{1}H NMR
4.00
1.40
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

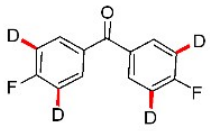

-115.59
-115.86
-116.14
D
D
F
F
D
D
^{19}F NMR
0.13
0.46
0.41
-114
-115
-116
-117
-118
-119
ppm
0.13
0.46
0.41
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
-240
ppm



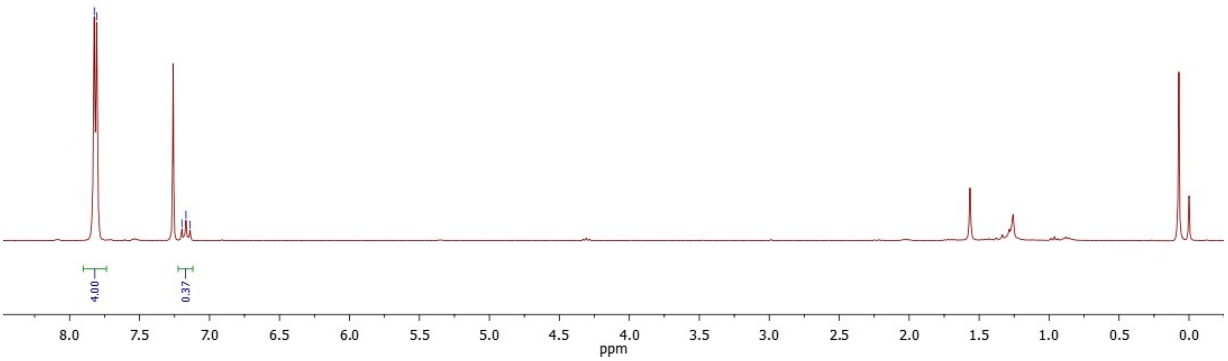
^{13}C NMR

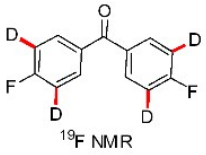




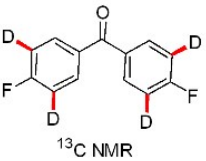


^{1}H NMR

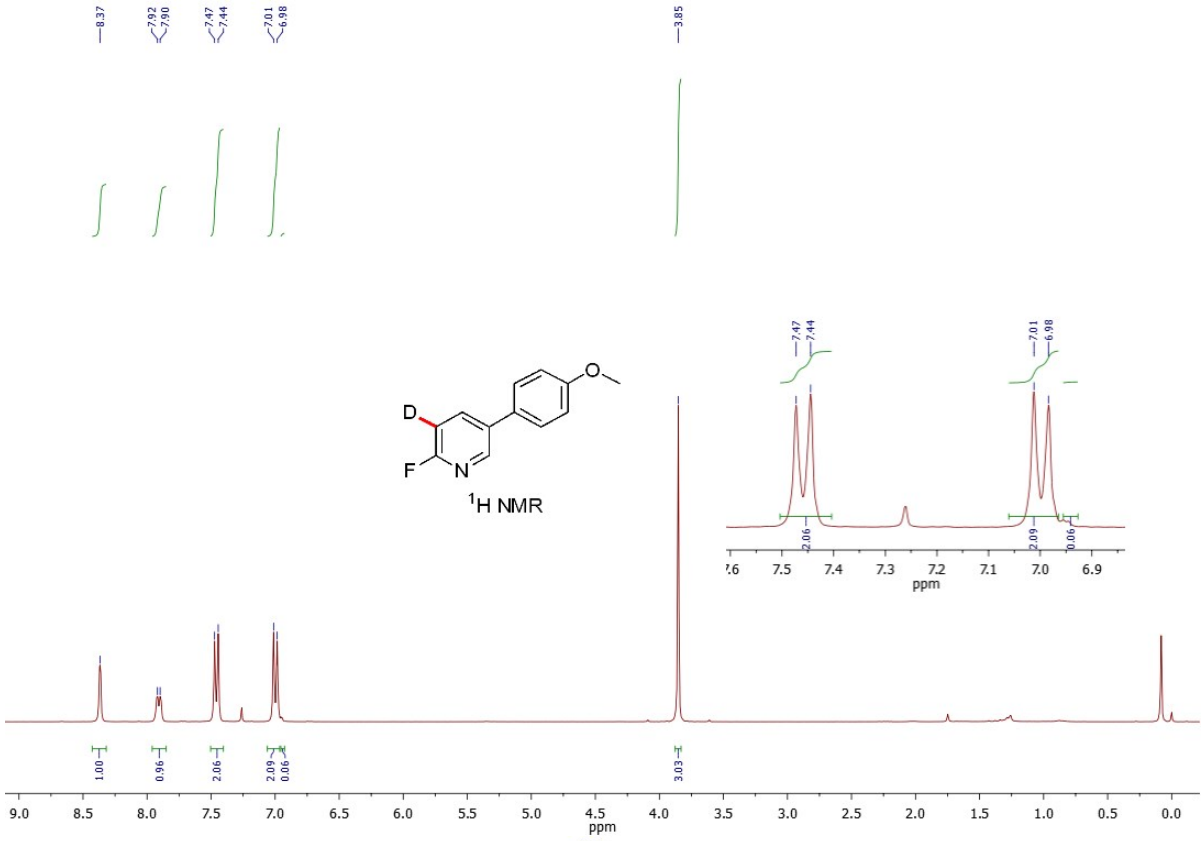


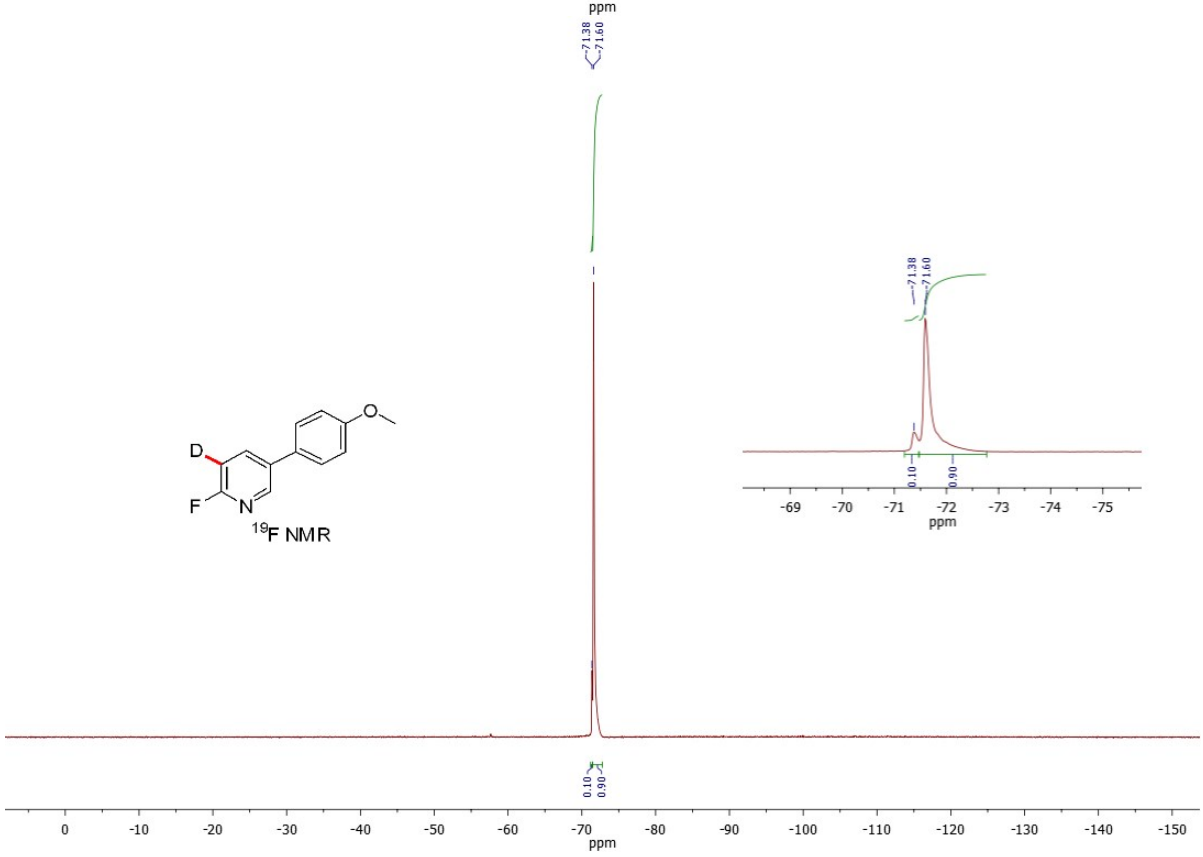


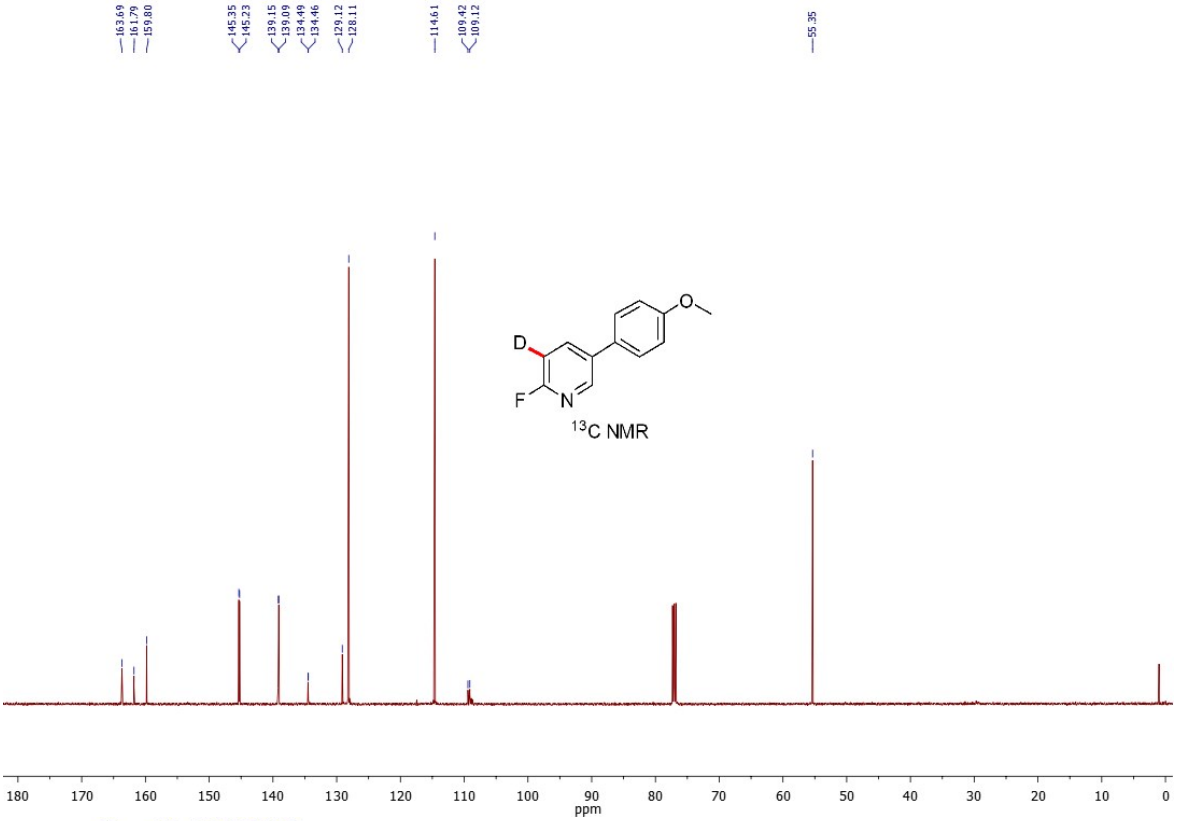
^{19}F NMR

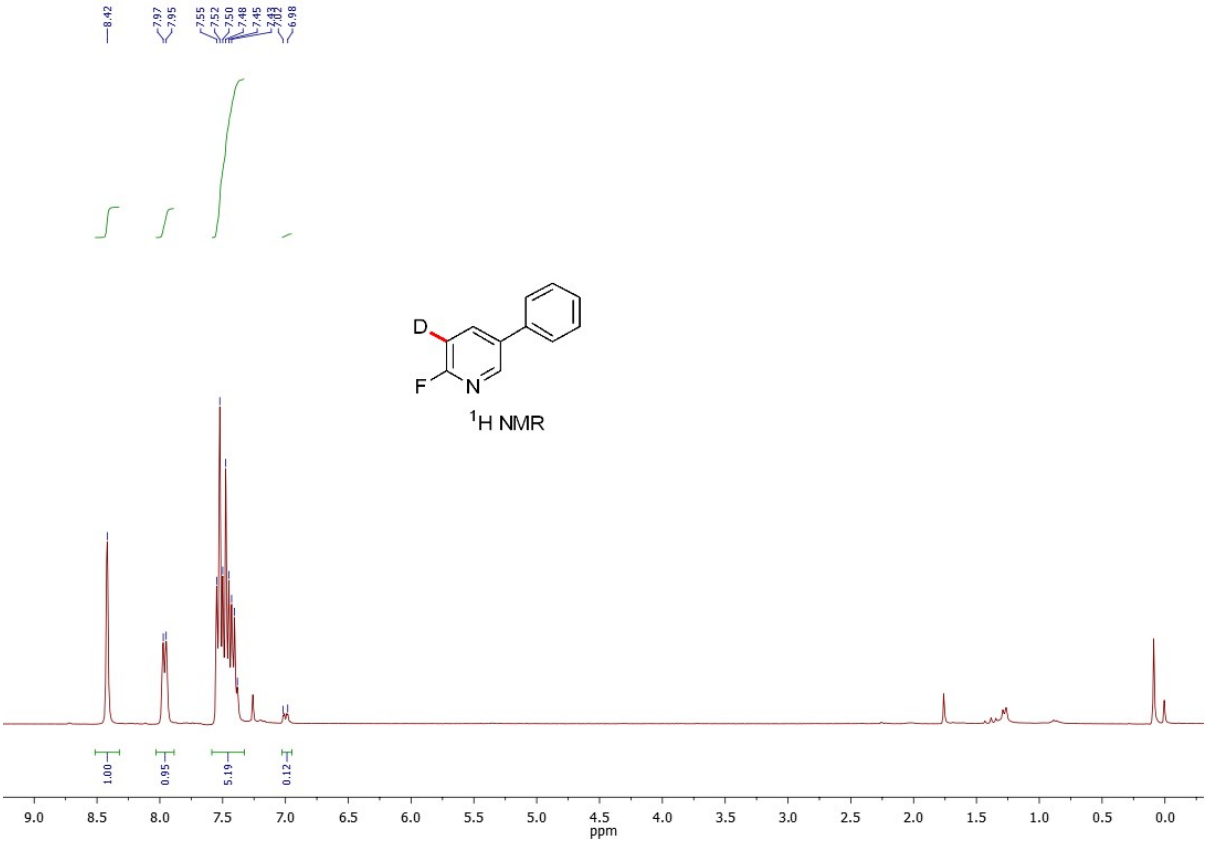


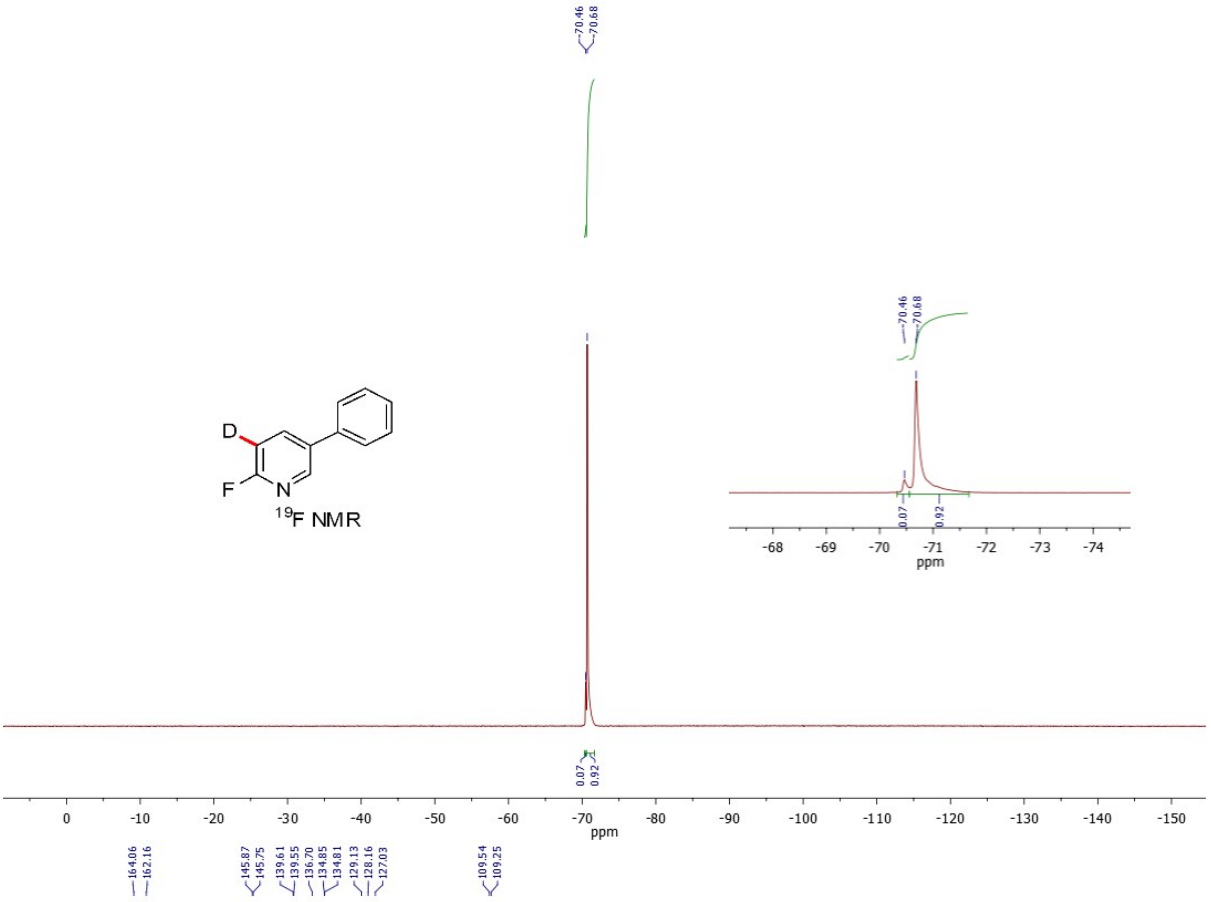
^{13}C NMR

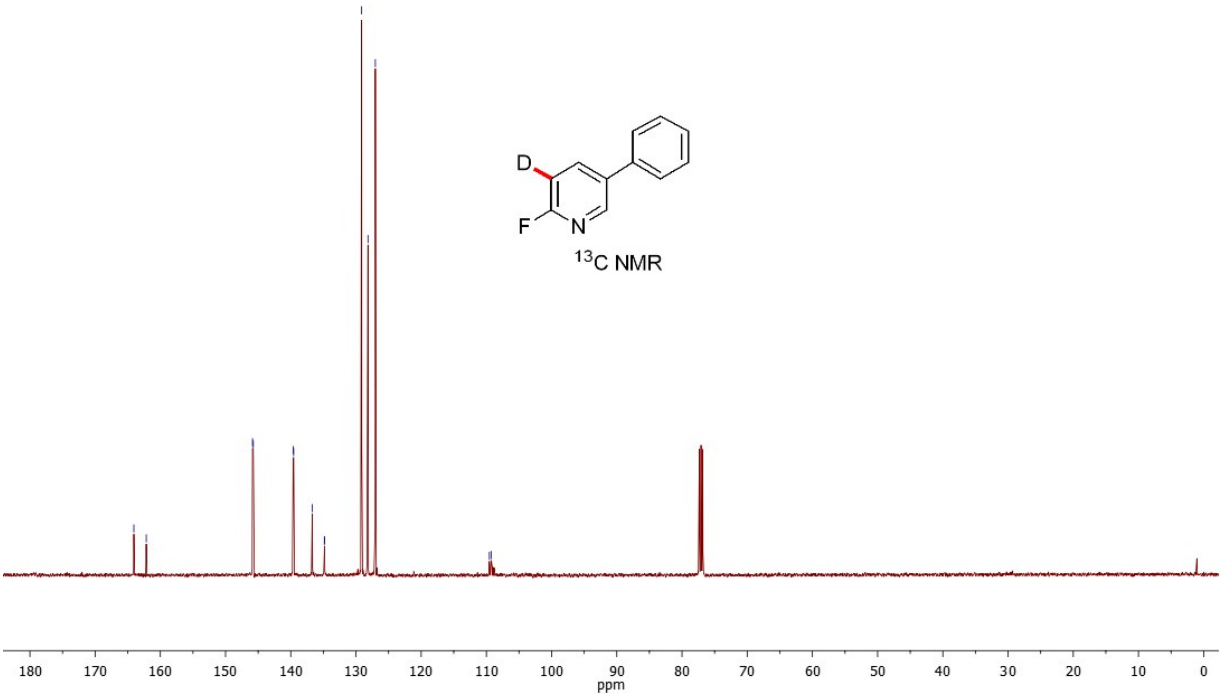

8.37
7.92
7.90
7.47
7.44
7.01
6.98
3.85
D
F
N
O
^{1}H NMR
1.00
0.96
2.06
2.09
0.06
3.03
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm
7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9
ppm

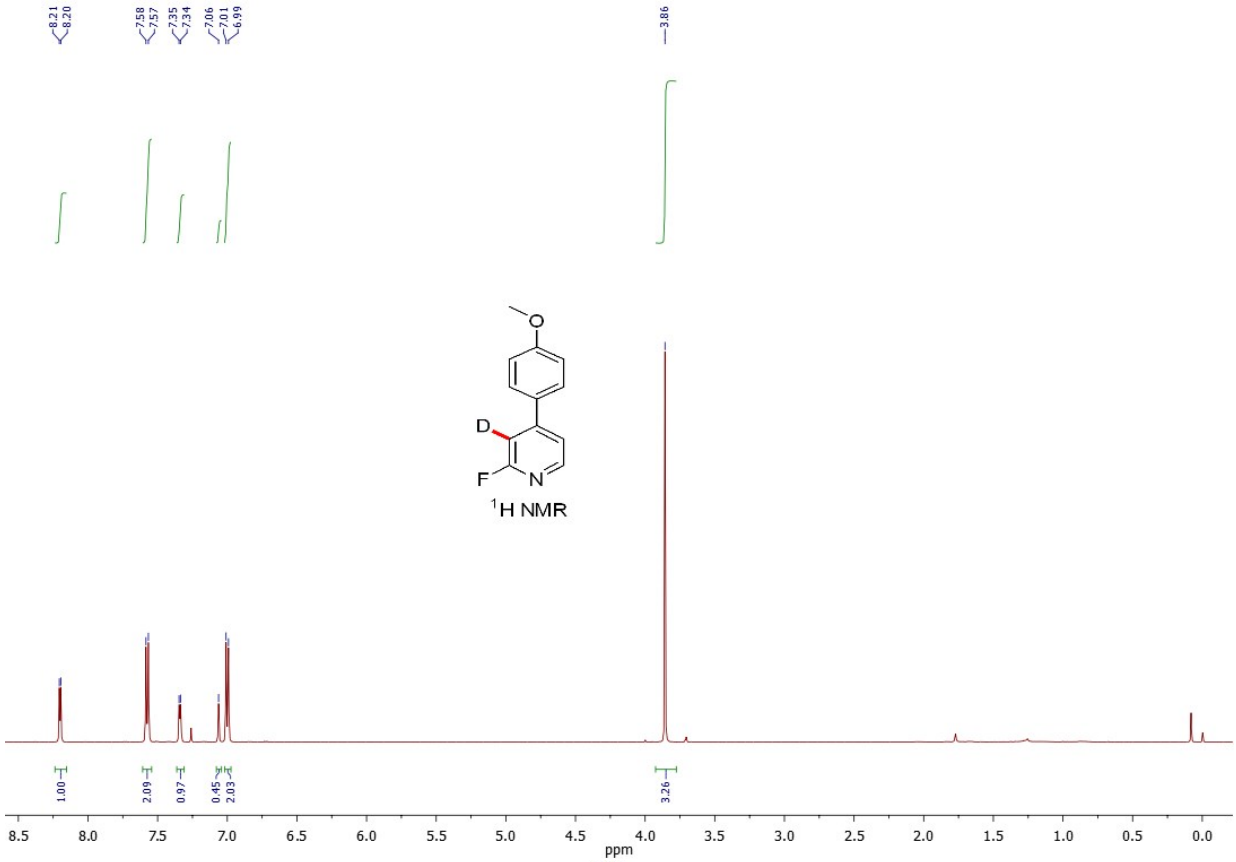

71.38
71.60
D
F
N
O
^{19}F NMR
0.10
0.90
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150
ppm
-69 -70 -71 -72 -73 -74 -75
ppm

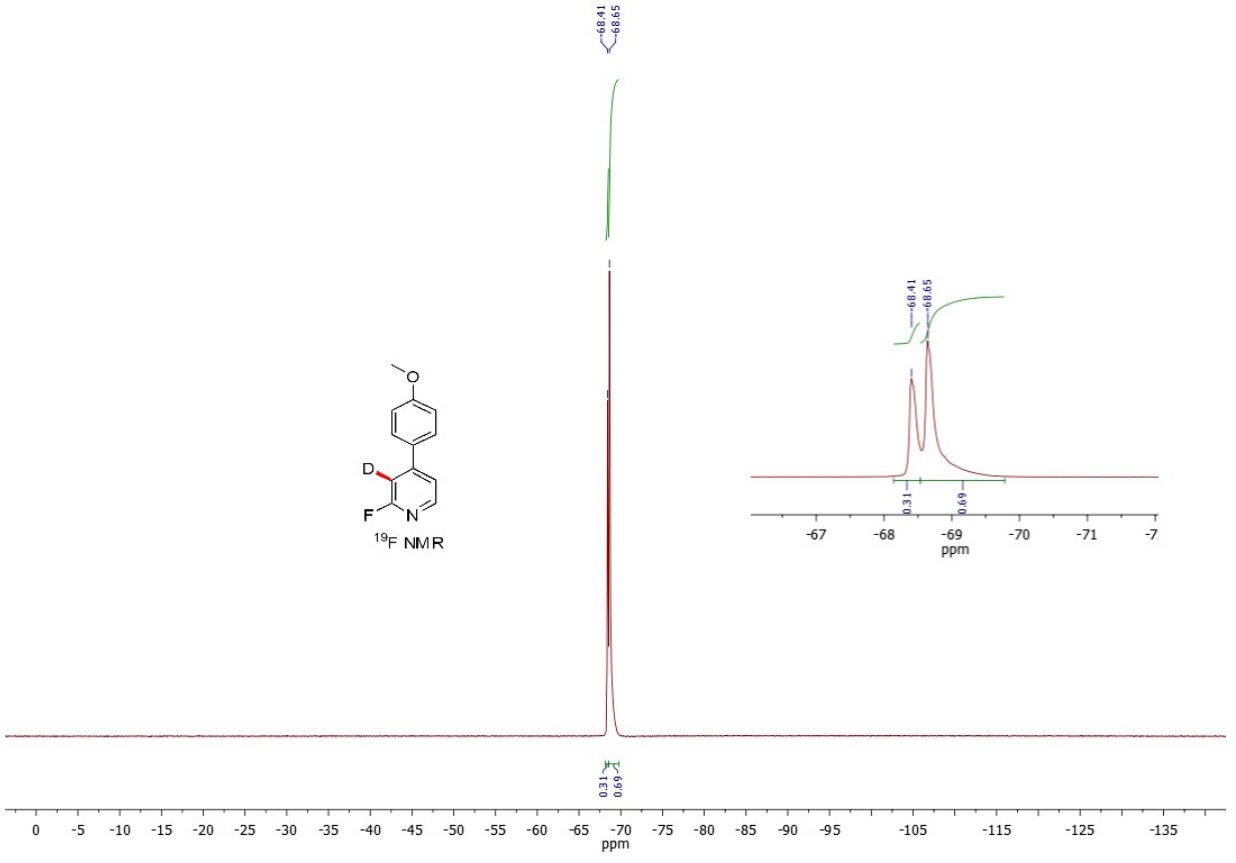

163.69
161.79
159.80
145.35
145.23
139.15
139.09
134.49
134.46
129.12
128.11
114.61
109.42
109.12
55.35
D
F
N
O
^{13}C NMR
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm

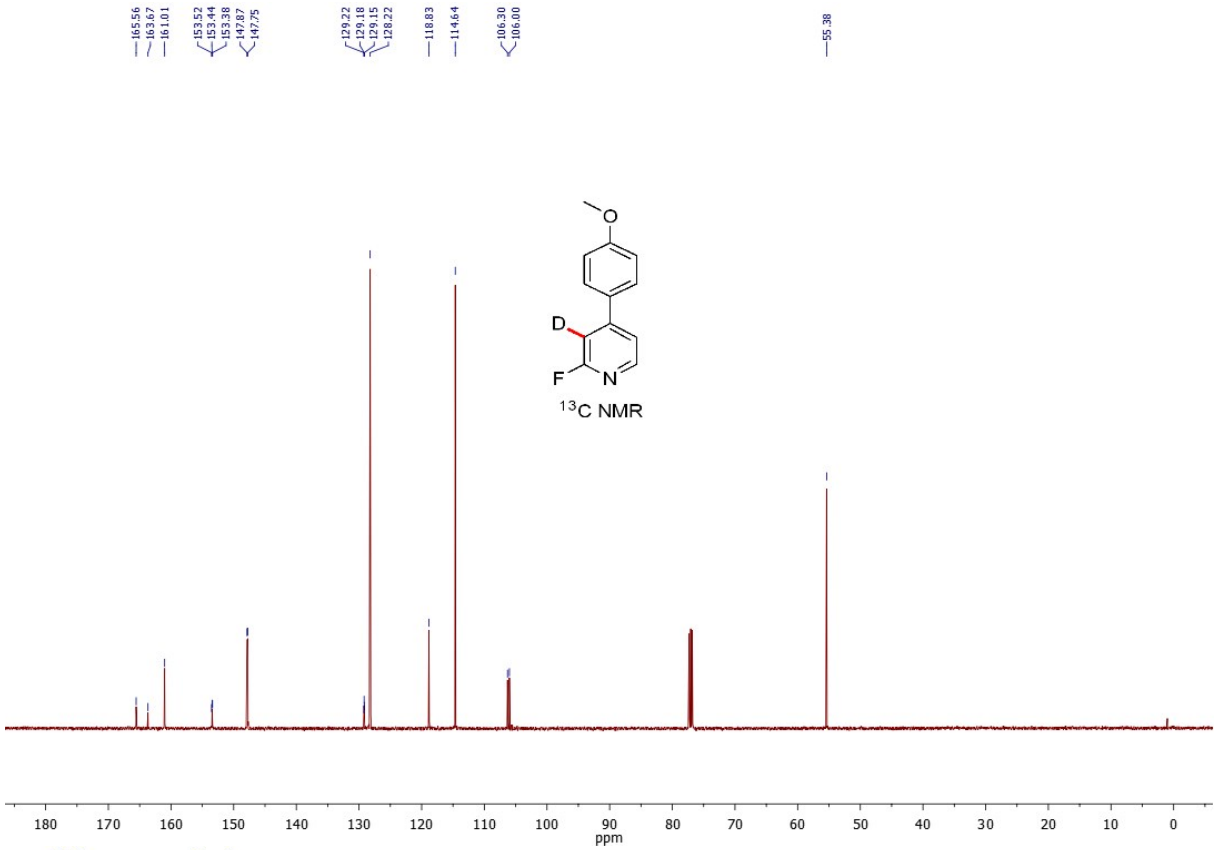

8.42
7.97
7.95
7.55
7.52
7.50
7.48
7.45
7.43
7.02
6.98
D
F
N
^{1}H NMR
1.00
0.95
5.19
0.12
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

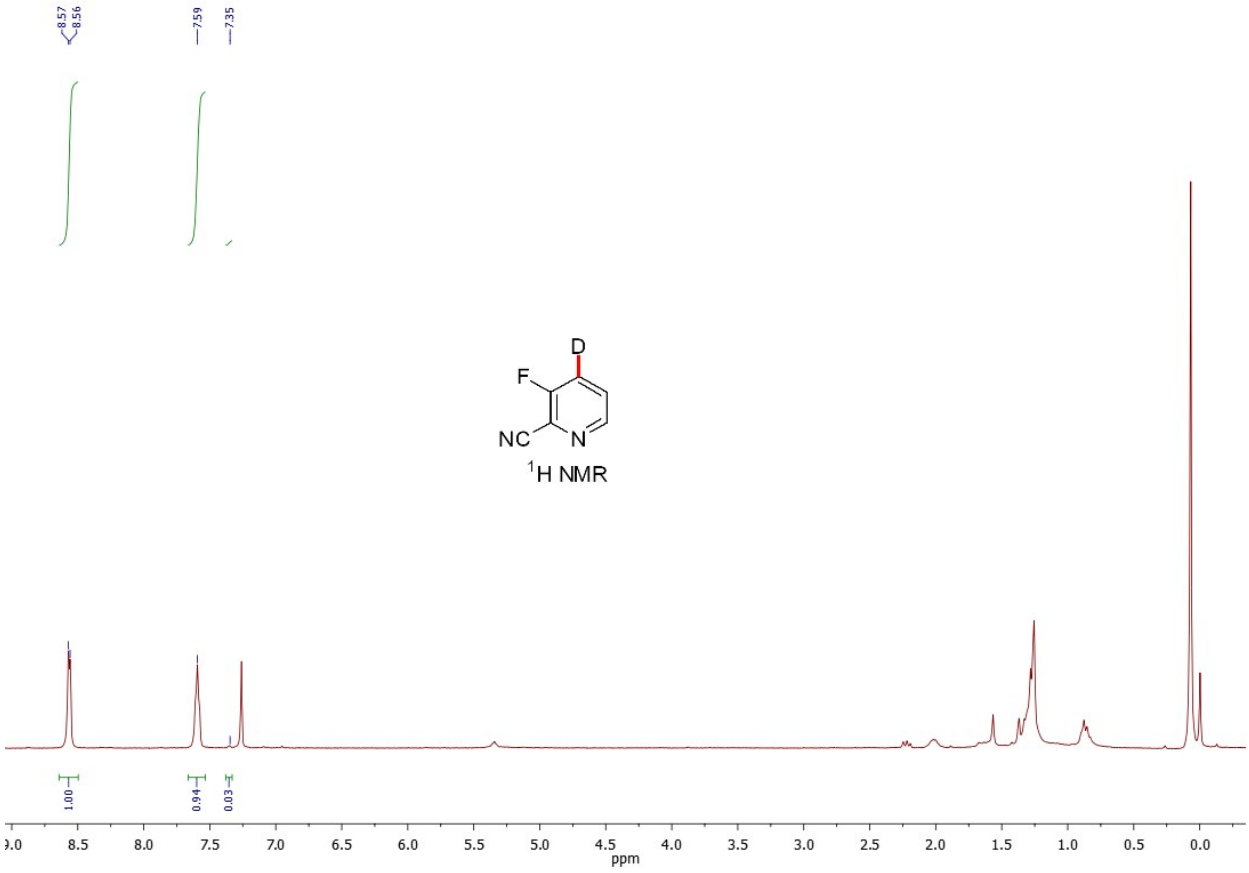

D
F
N
19F NMR
-70.46
-70.68
0.07
0.92
-68
-69
-70
-71
-72
-73
-74
ppm
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
ppm

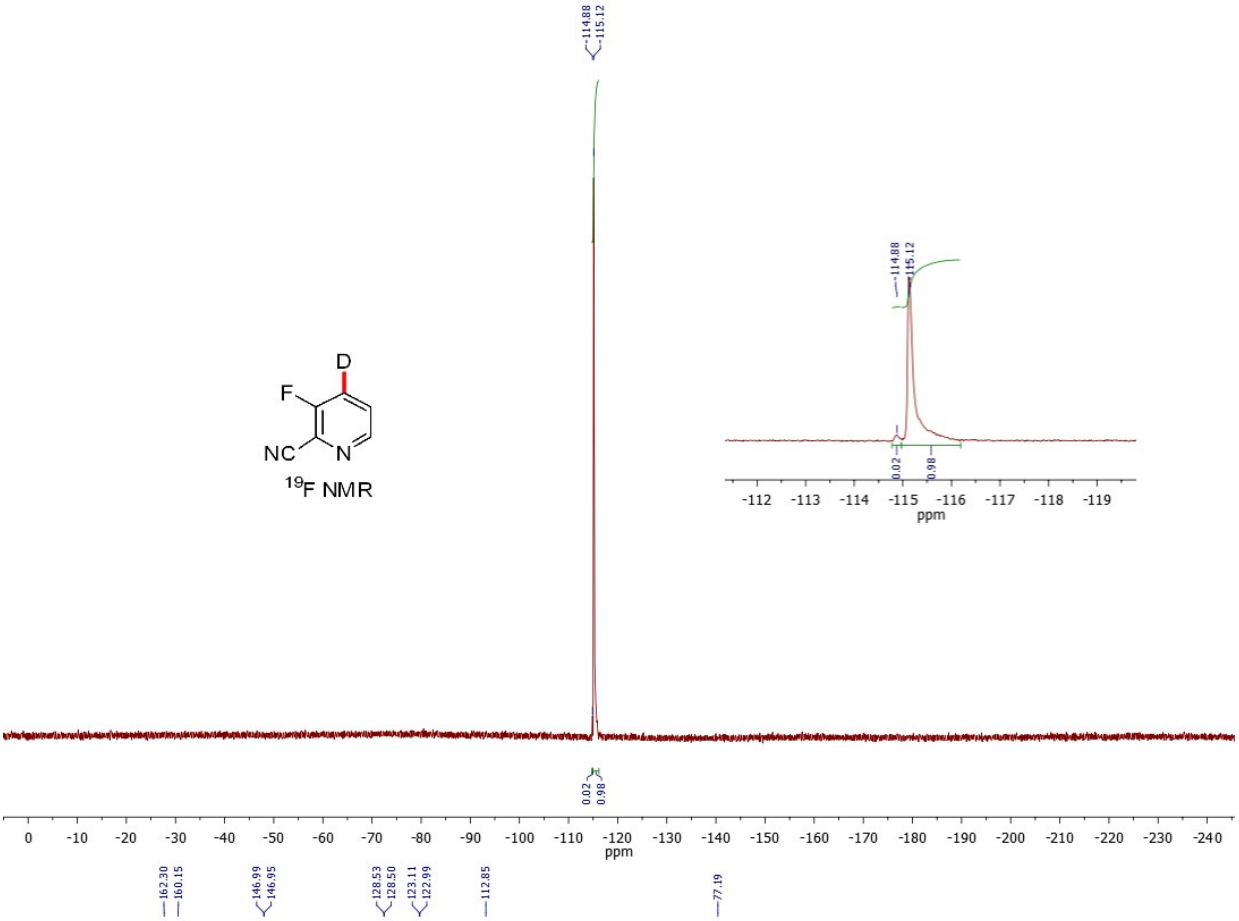

D
F
N
13C NMR
164.06
162.16
145.87
145.75
139.61
139.55
136.70
134.85
134.81
129.13
128.16
127.03
109.54
109.25
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

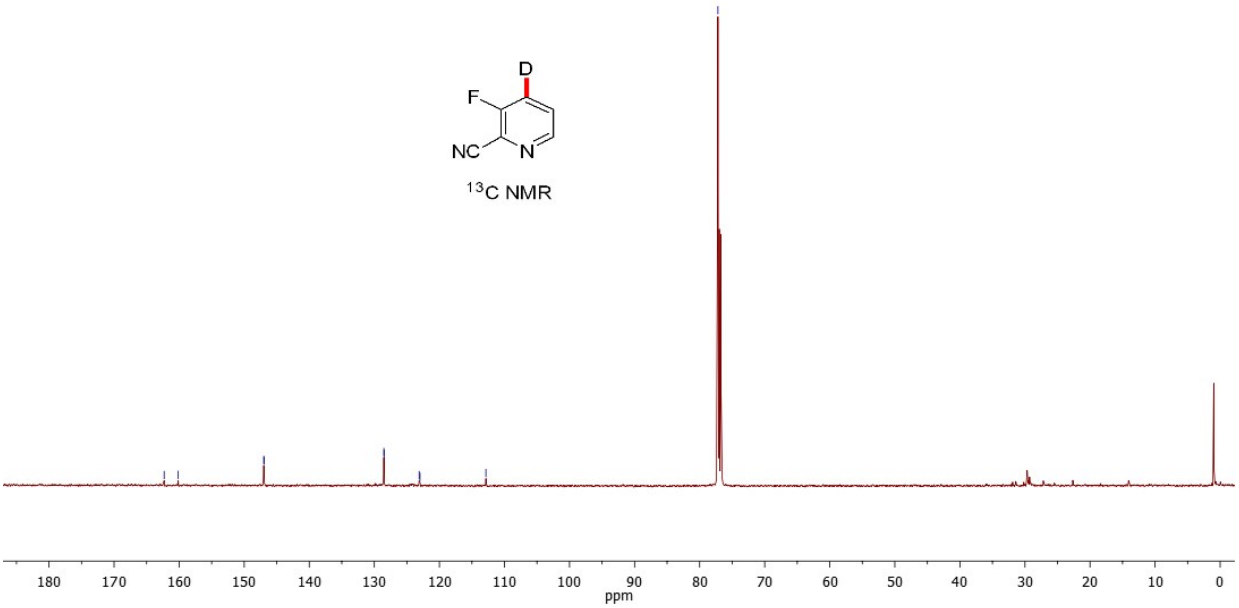

8.21
8.20
7.58
7.57
7.35
7.34
7.06
7.01
6.99
3.86
O
D
F
N
^{1}H NMR
1.00
2.09
0.97
0.45
2.03
3.26
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

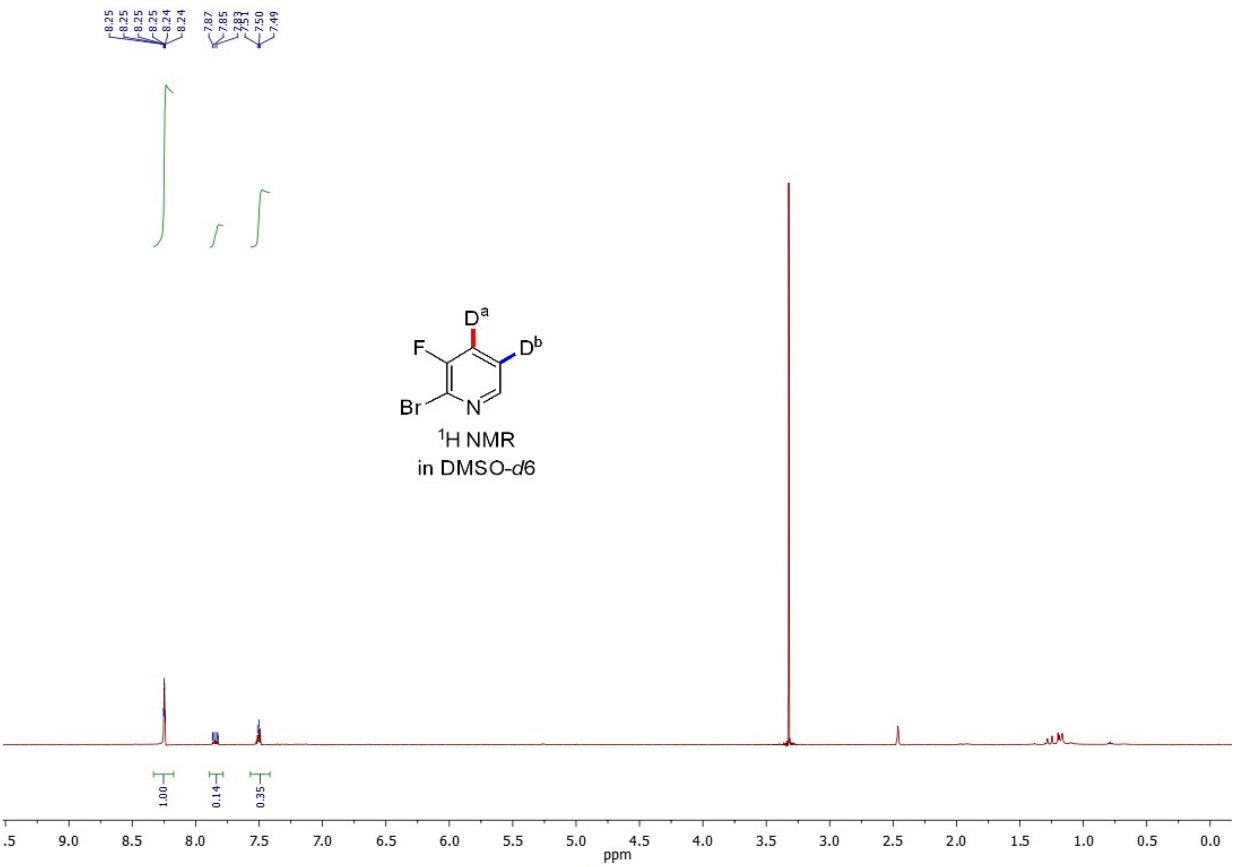

-68.41
-68.65
O
D
F
N
^{19}F NMR
0.31
0.69
-67 -68 -69 -70 -71 -7
ppm
0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -105 -115 -125 -135
ppm

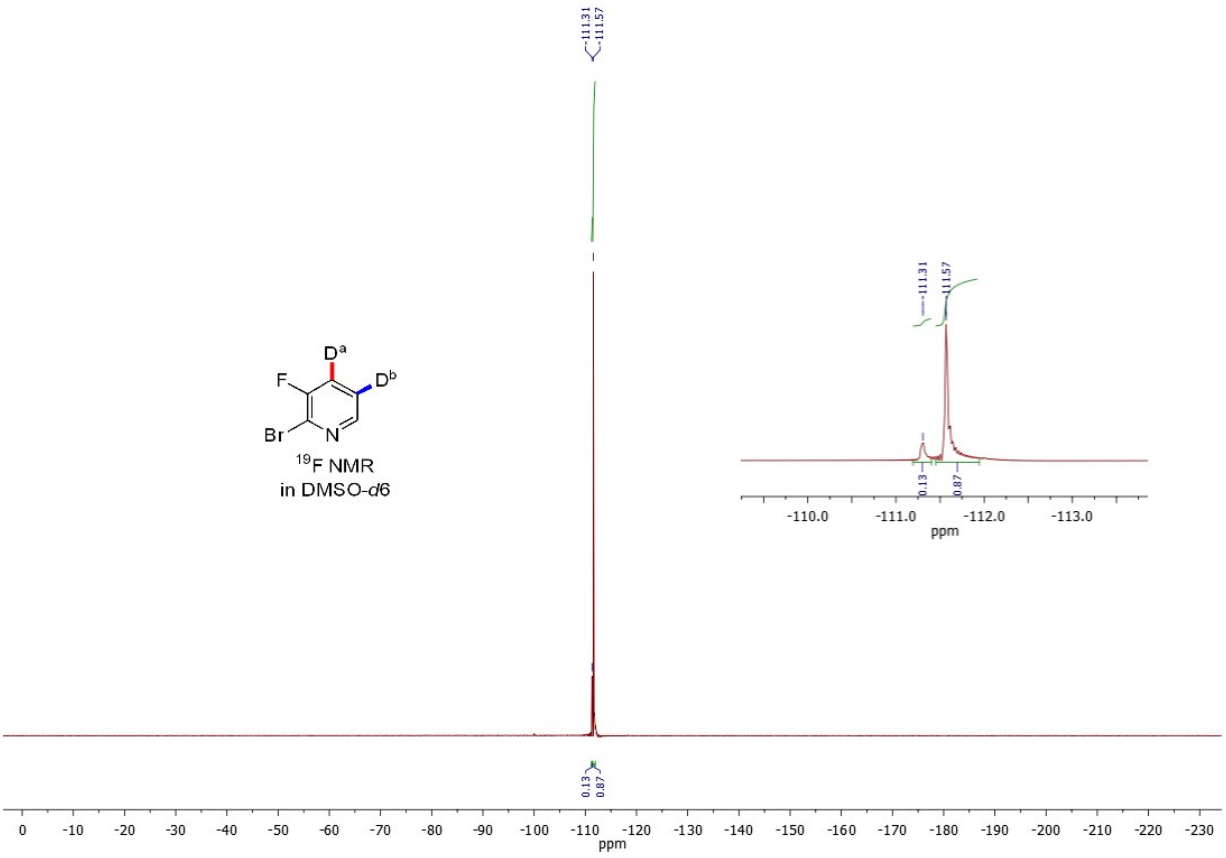

165.56
163.67
161.01
153.52
153.44
153.38
147.87
147.75
129.22
129.18
129.15
128.22
118.83
114.64
106.30
106.00
55.38
O
D
F
N
13C NMR
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

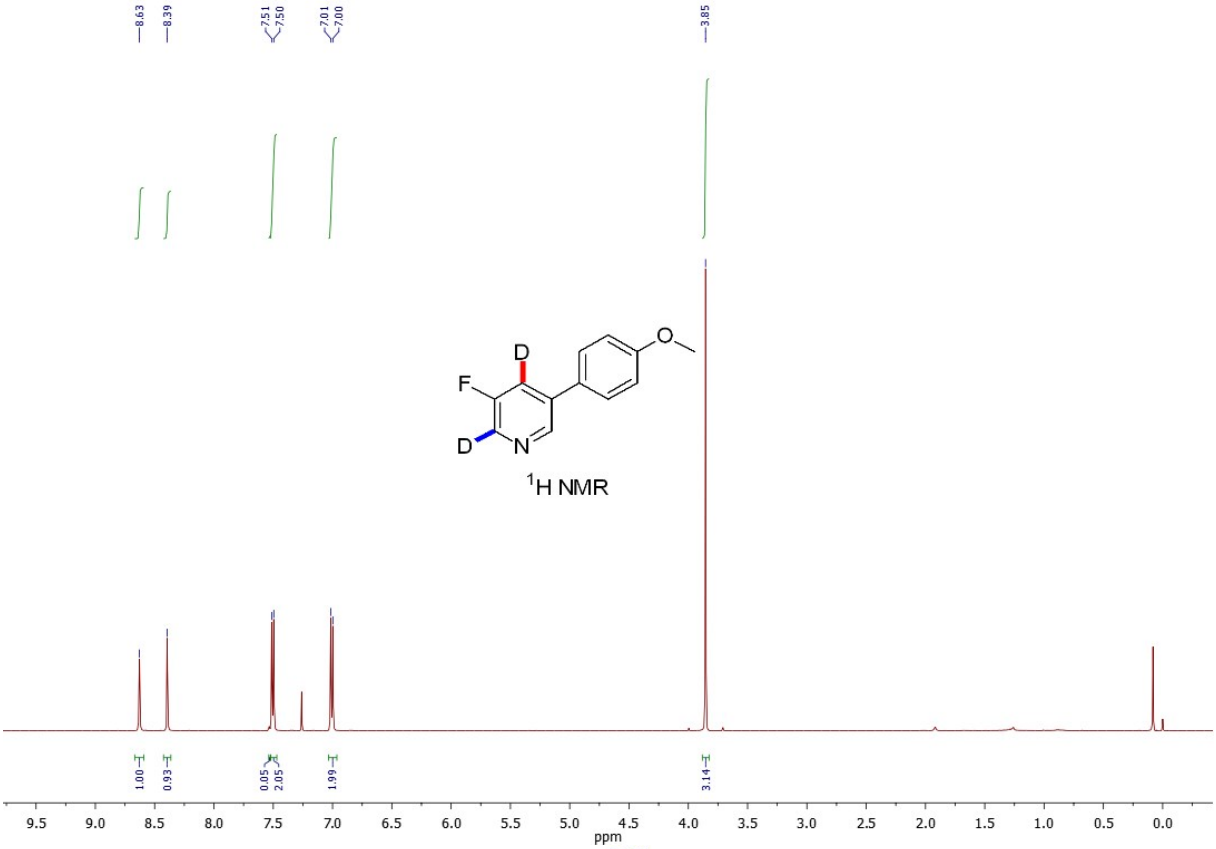

8.57
8.56
7.59
7.35
D
F
NC
N
1H NMR
1.00
0.94
0.03
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

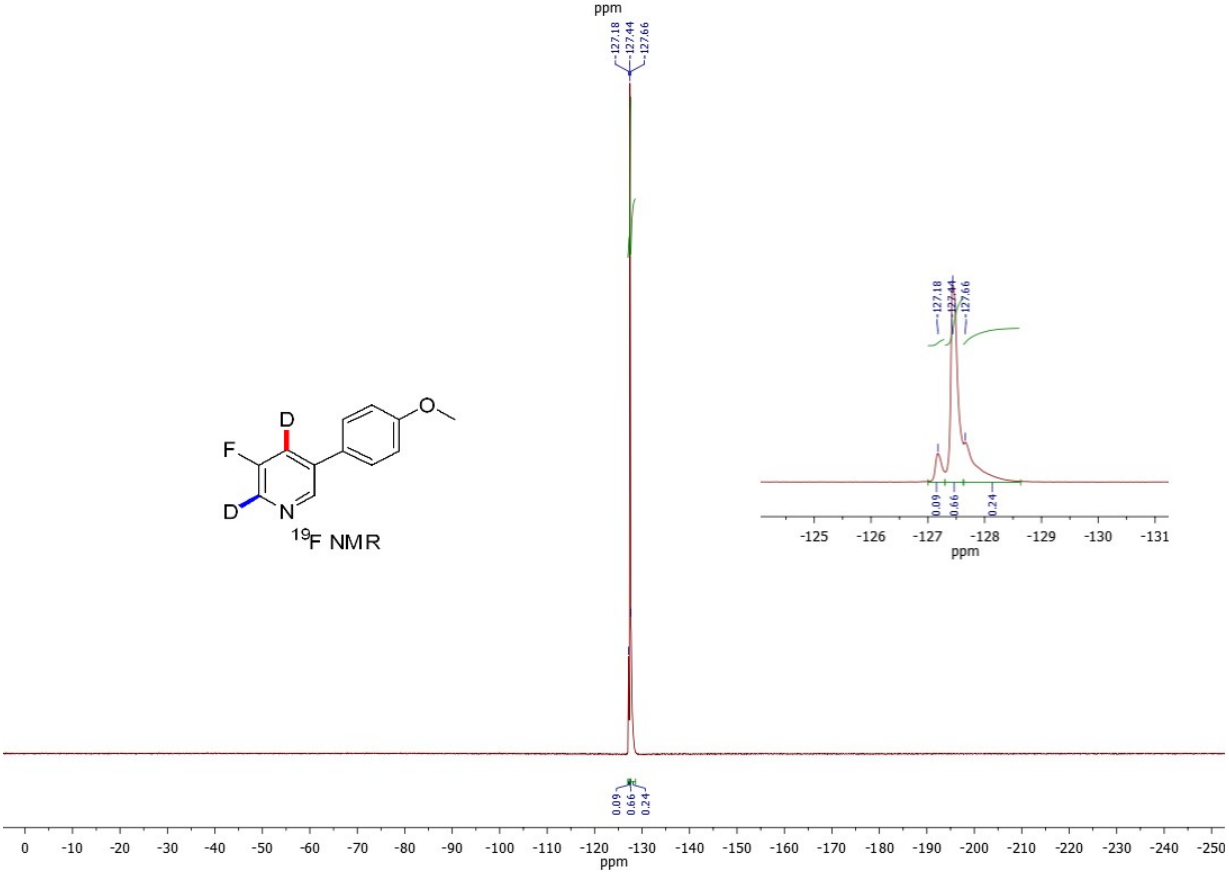

D
F
NC
N
19F NMR
-114.88
-115.12
0.02
0.98
ppm


D
F
NC
N
13C NMR
ppm

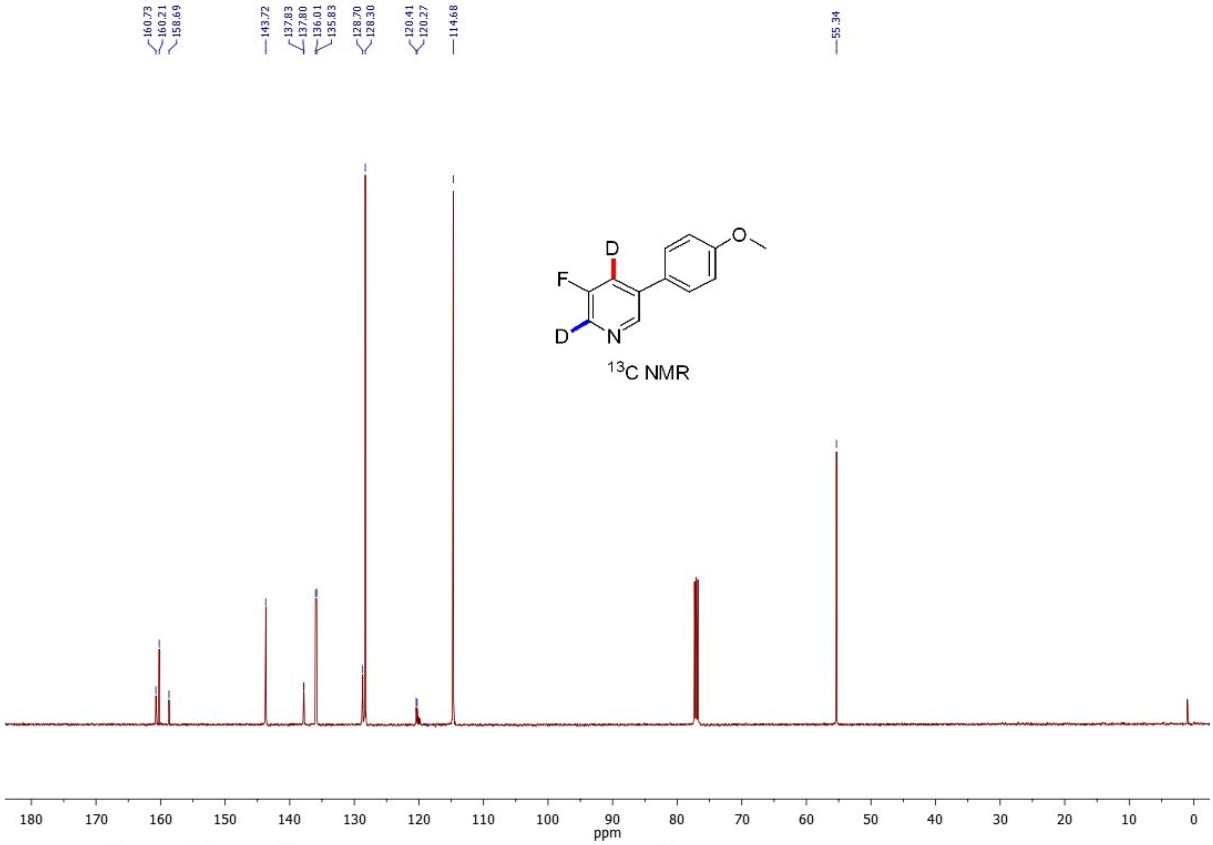

8.25
8.25
8.25
8.25
8.24
8.24
7.87
7.85
7.83
7.81
7.50
7.49
D^a
F
D^b
Br
N
1H NMR
in DMSO-d6
1.00
0.14
0.35
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

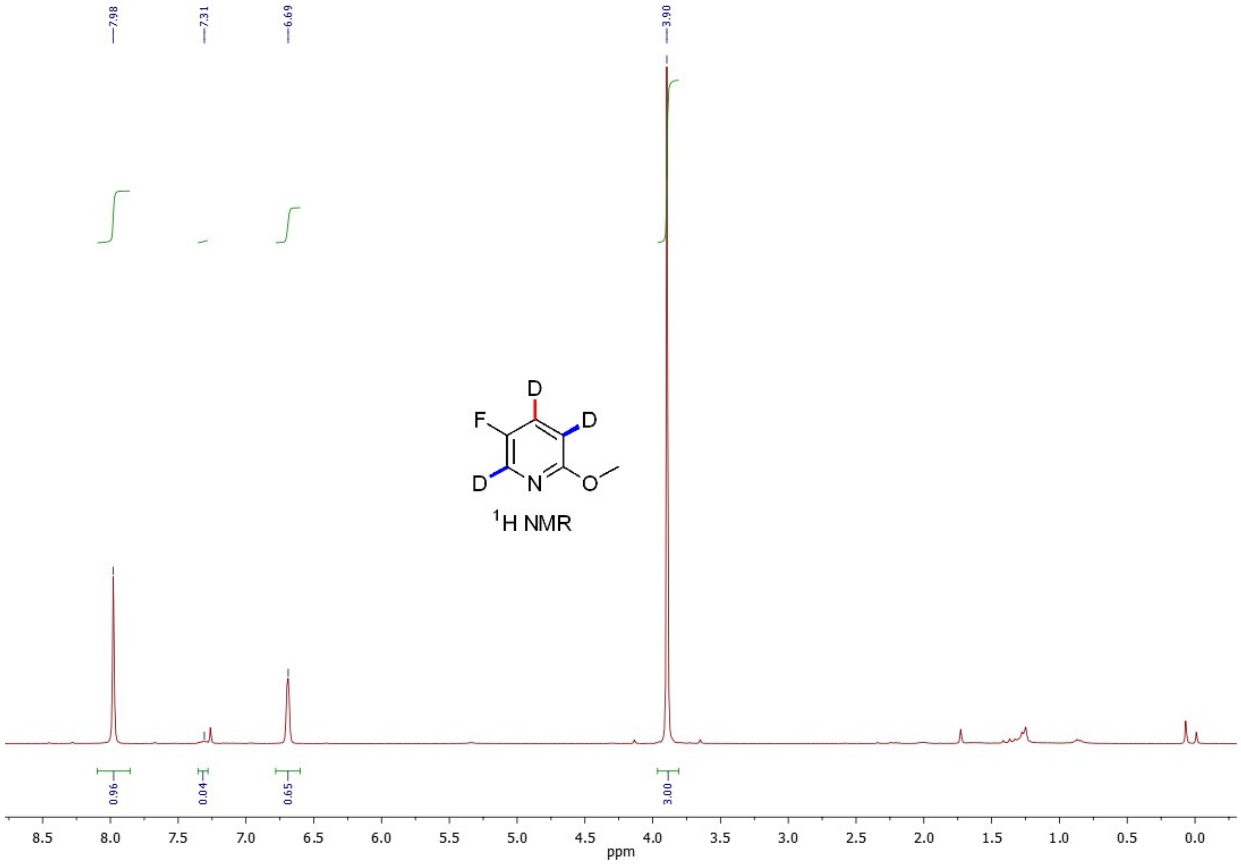

-111.31
-111.57
D^a
F
D^b
Br
N
19F NMR
in DMSO-d6
0.13
0.87
-110.0
-111.0
-112.0
-113.0
ppm
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
ppm

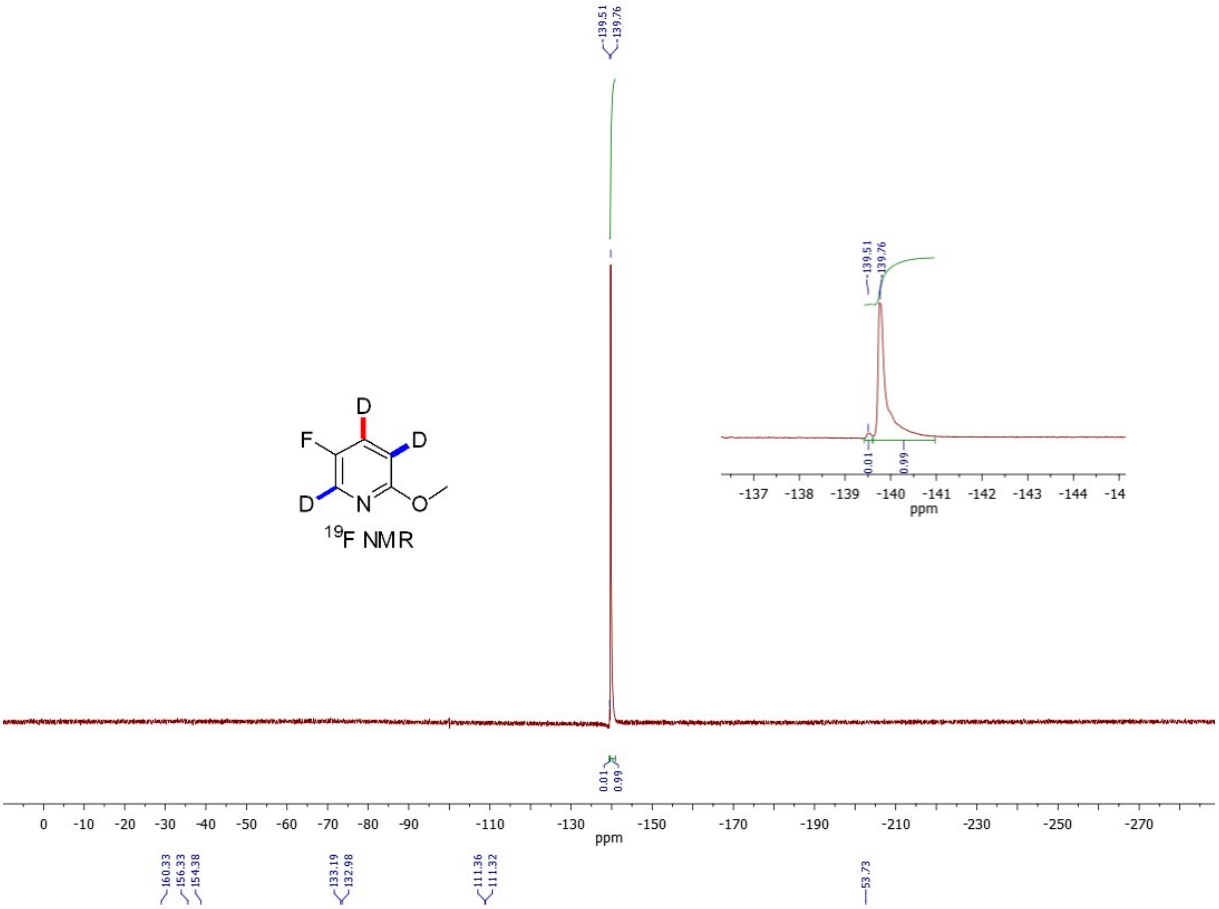

8.63
8.39
7.51
7.50
7.01
7.00
3.85
D
F
D
N
O
1H NMR
1.00
0.93
0.05
2.05
1.99
3.14
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

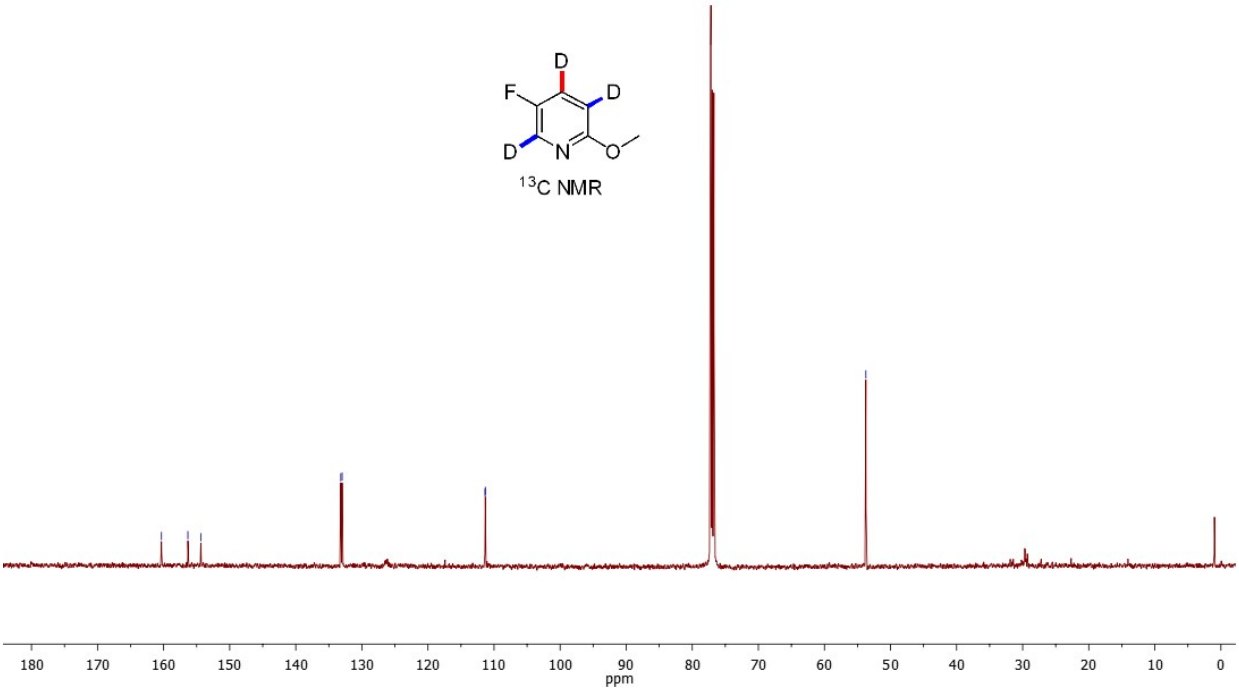

-127.18
-127.44
-127.66
D
F
D
N
O
19F NMR
0.09
0.66
0.24
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240 -250
ppm

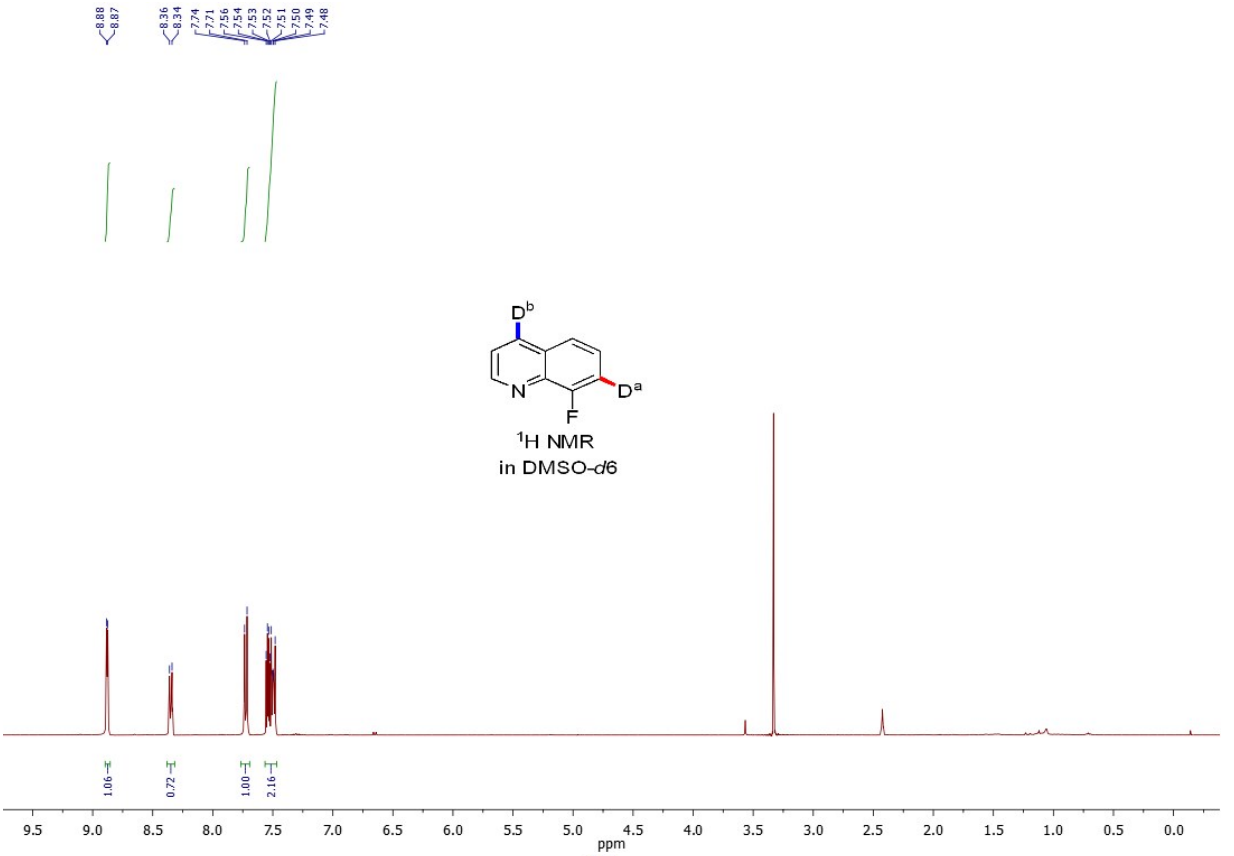
-127.18
-127.44
-127.66
0.09
0.66
0.24
-125 -126 -127 -128 -129 -130 -131
ppm

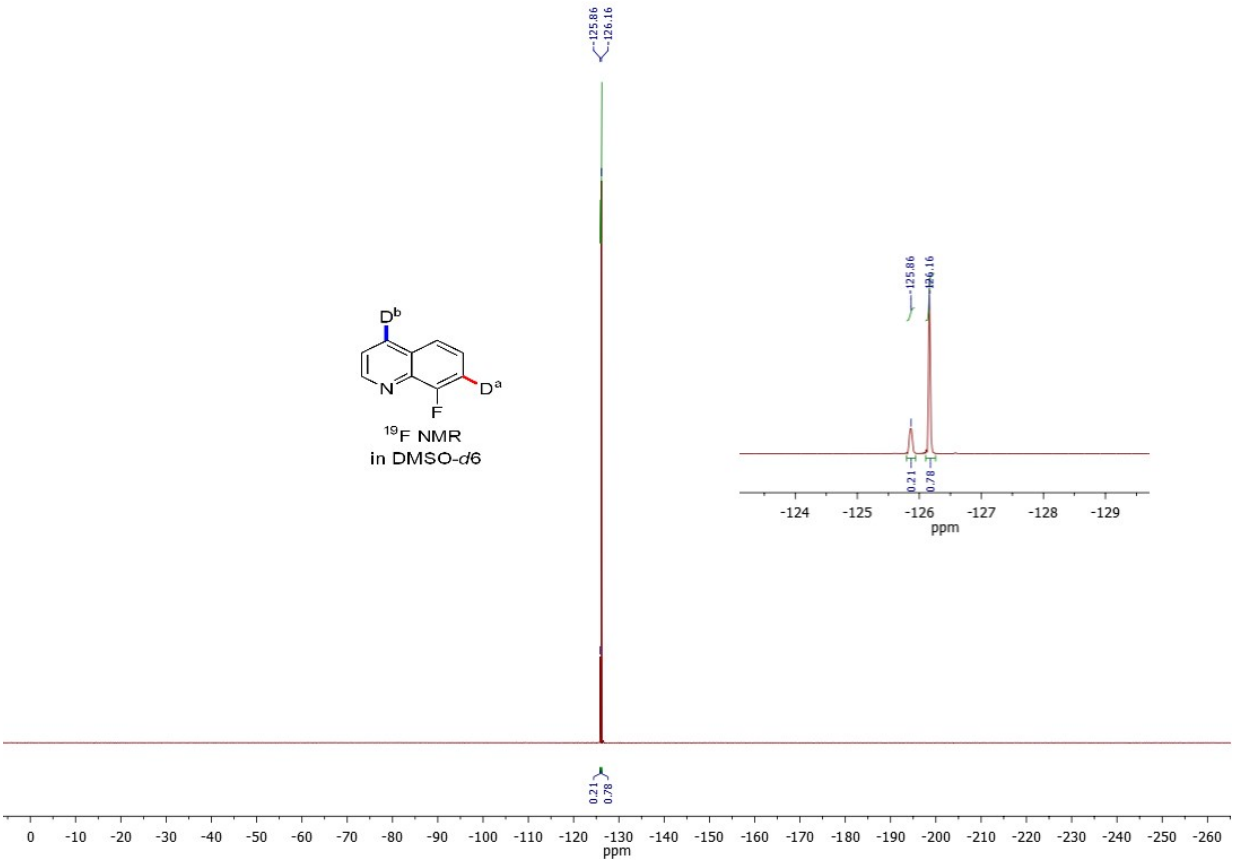

160.73
160.21
158.69
143.72
137.83
137.80
136.01
135.83
128.70
128.30
120.41
120.27
114.68
55.34
D
F
D
N
O
^{13}C NMR
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm

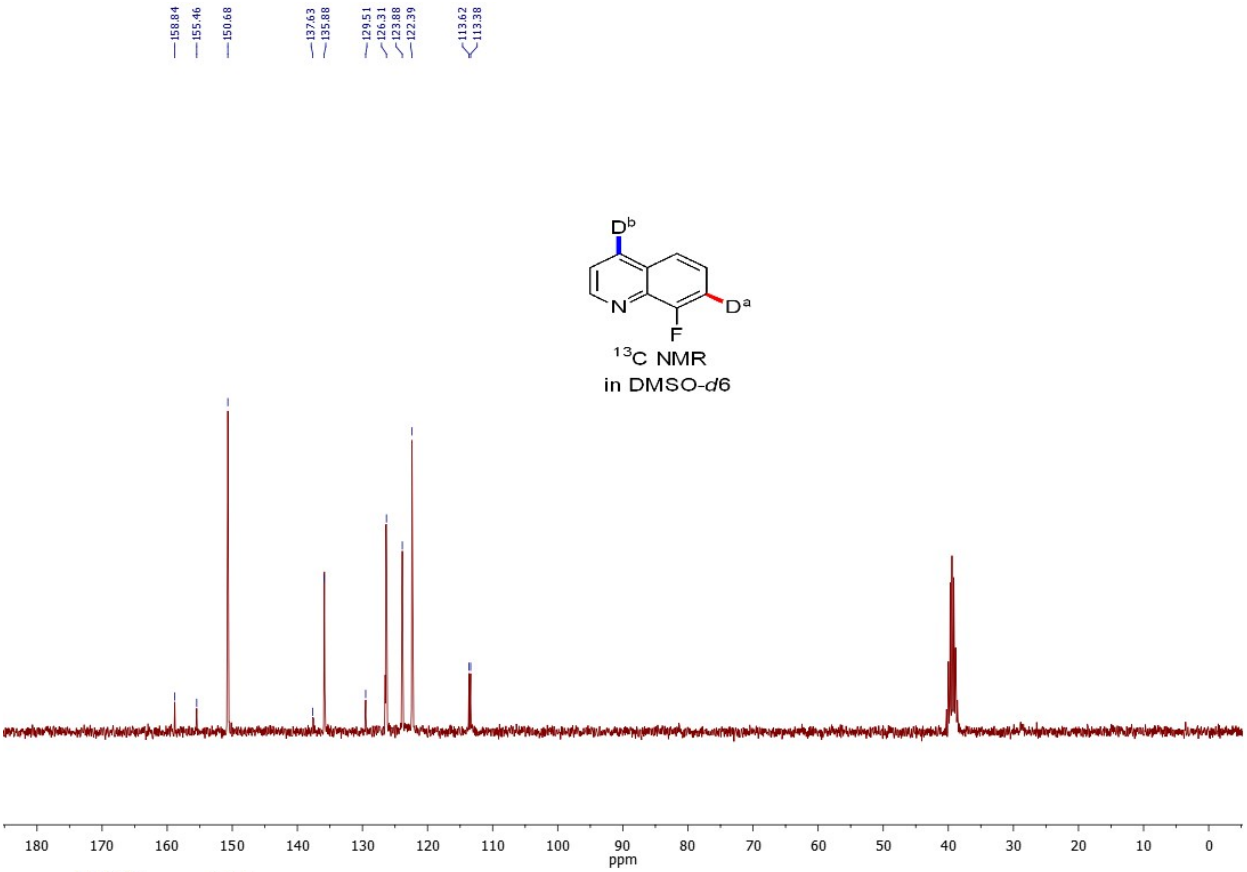

7.98
7.31
6.69
3.90
D
F
D
D
N
O
^{1}H NMR
0.96
0.04
0.65
3.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm


139.51
139.76
D
F
D
D
N
O
^{19}F NMR
0.01
0.99
ppm
160.33
156.33
154.38
133.19
132.98
111.36
111.32
53.73

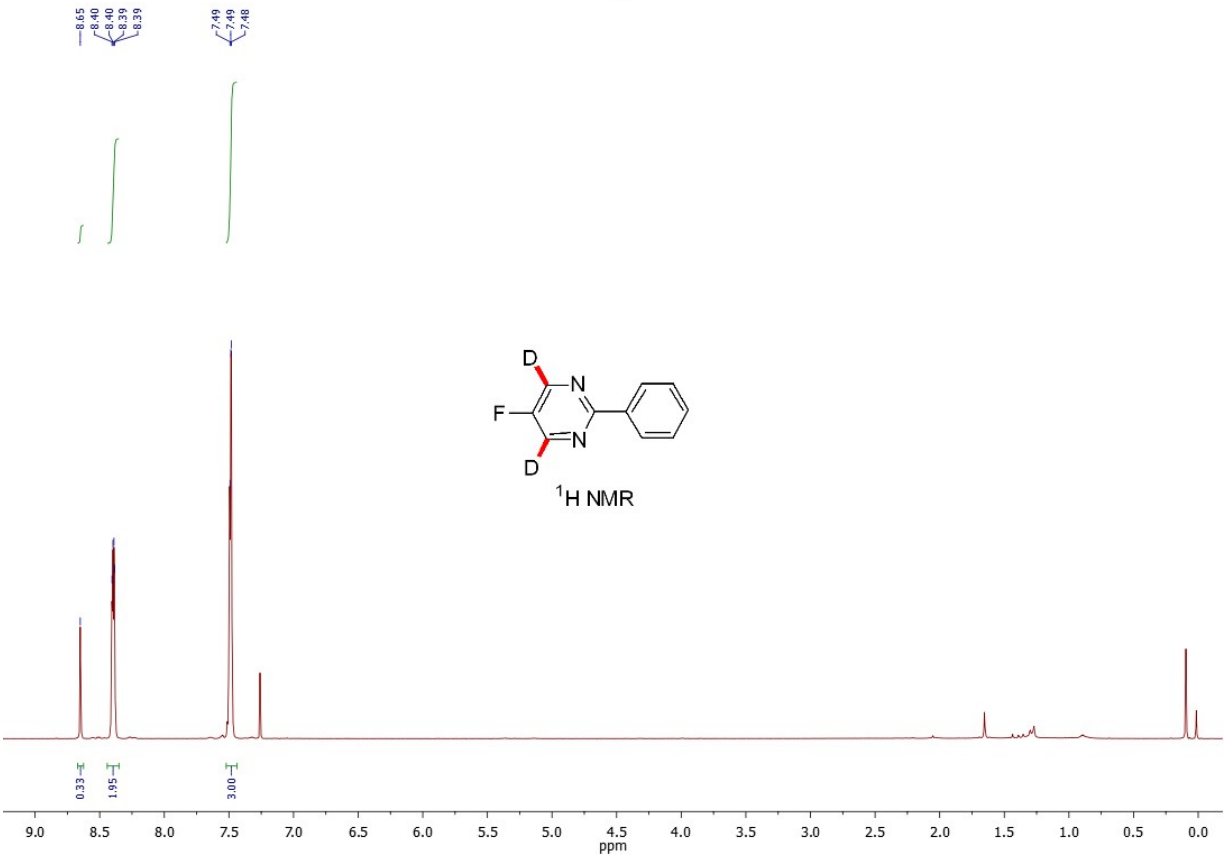

D
F
D
D
N
O
^{13}C NMR
ppm


8.88
8.87
8.36
8.34
7.74
7.71
7.56
7.54
7.53
7.52
7.51
7.50
7.49
7.48
D^b
D^a
N
F
1H NMR
in DMSO-d6
1.06
0.72
1.00
2.16
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

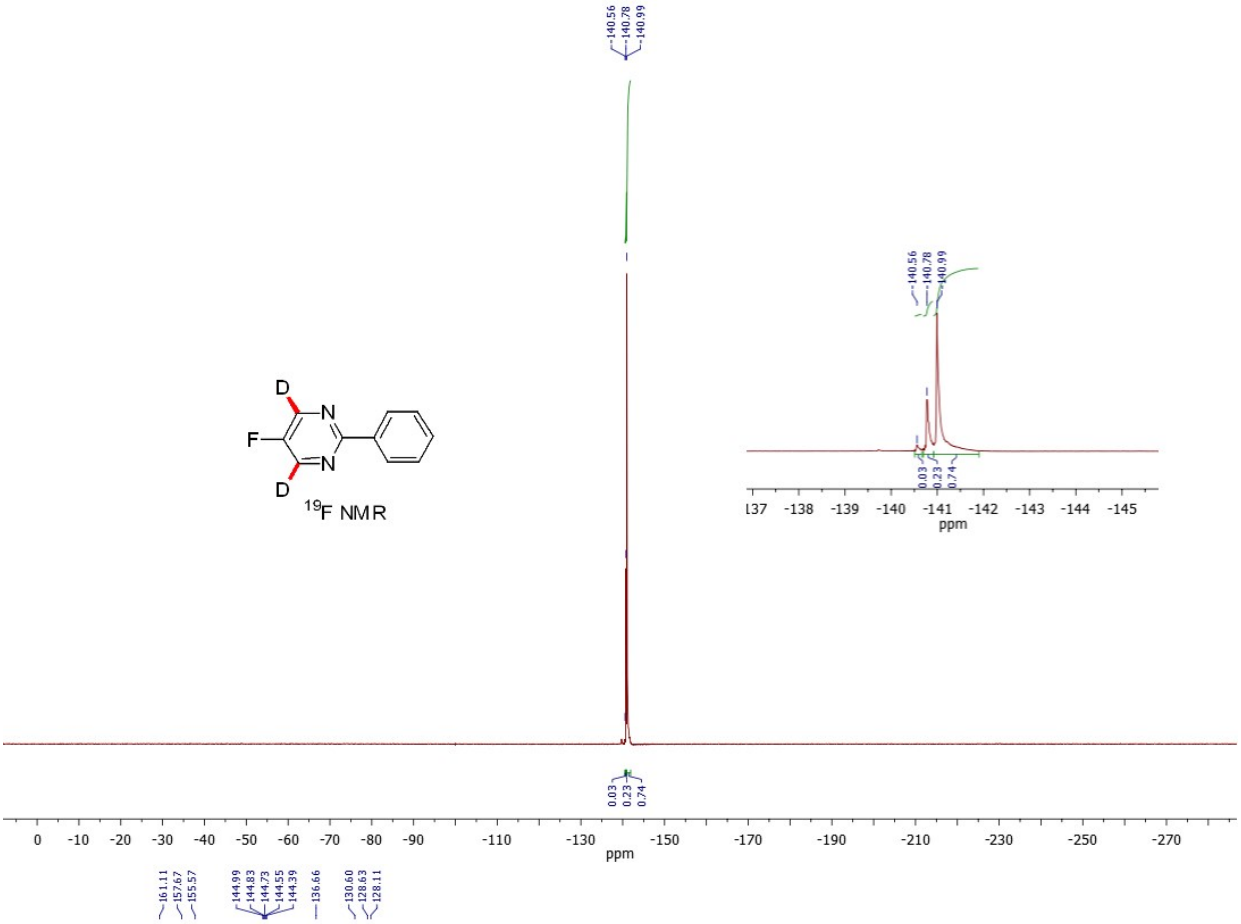

-125.86
-126.16
D^b
D^a
N
F
19F NMR
in DMSO-d6
0.21
0.78
-124 -125 -126 -127 -128 -129
ppm
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240 -250 -260
ppm

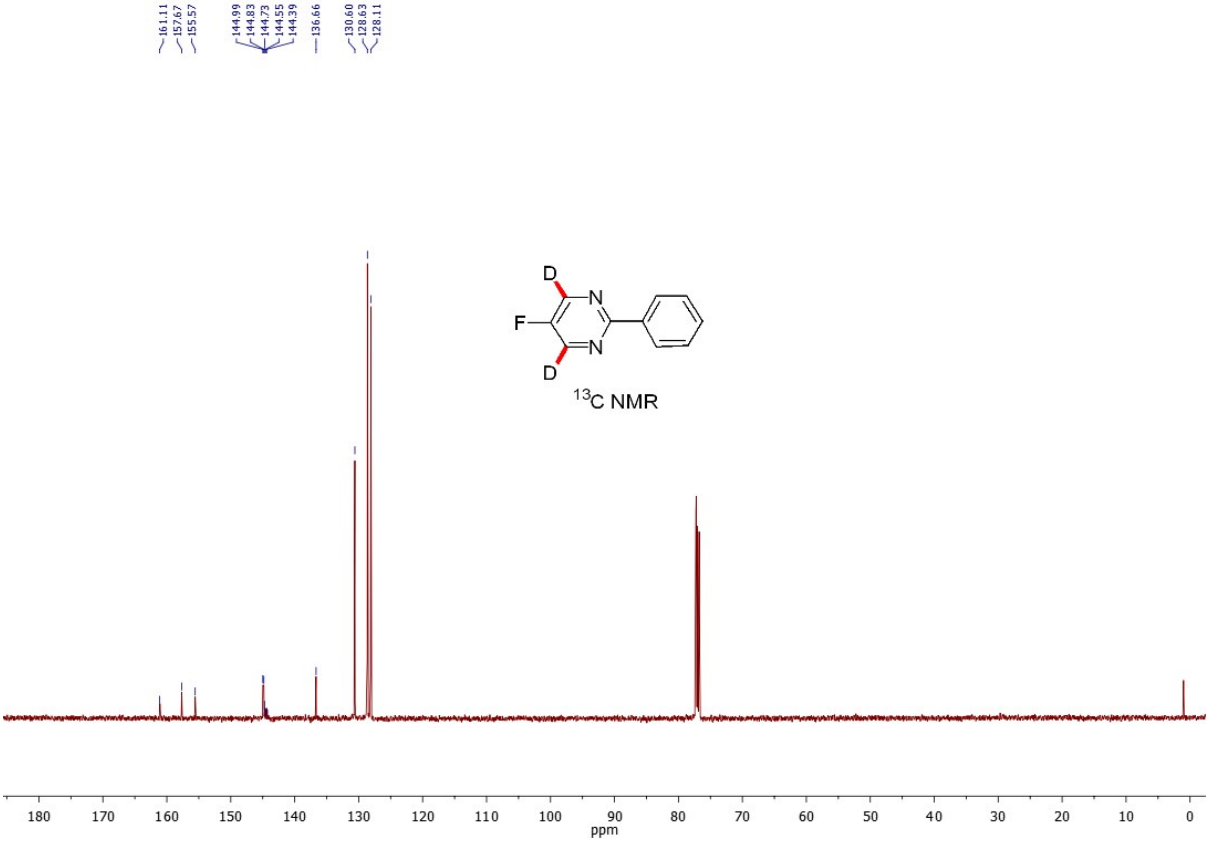


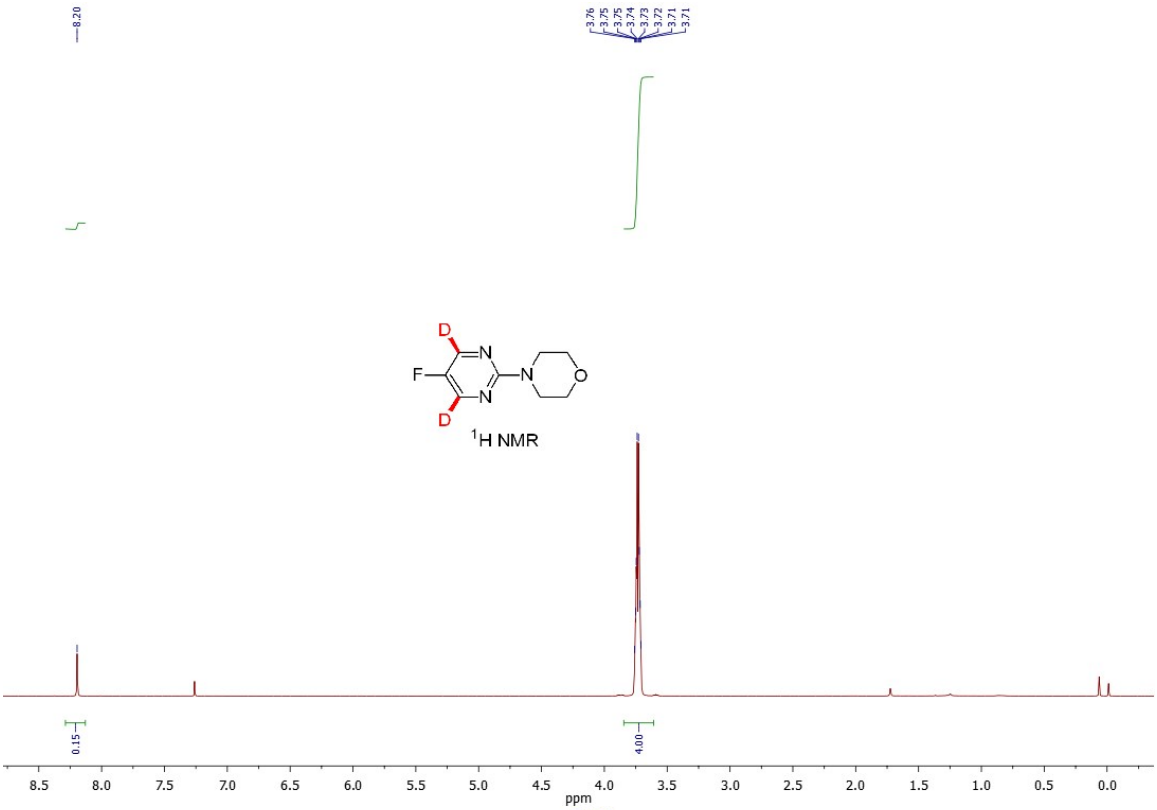
^{13}C NMR
in DMSO-*d*6

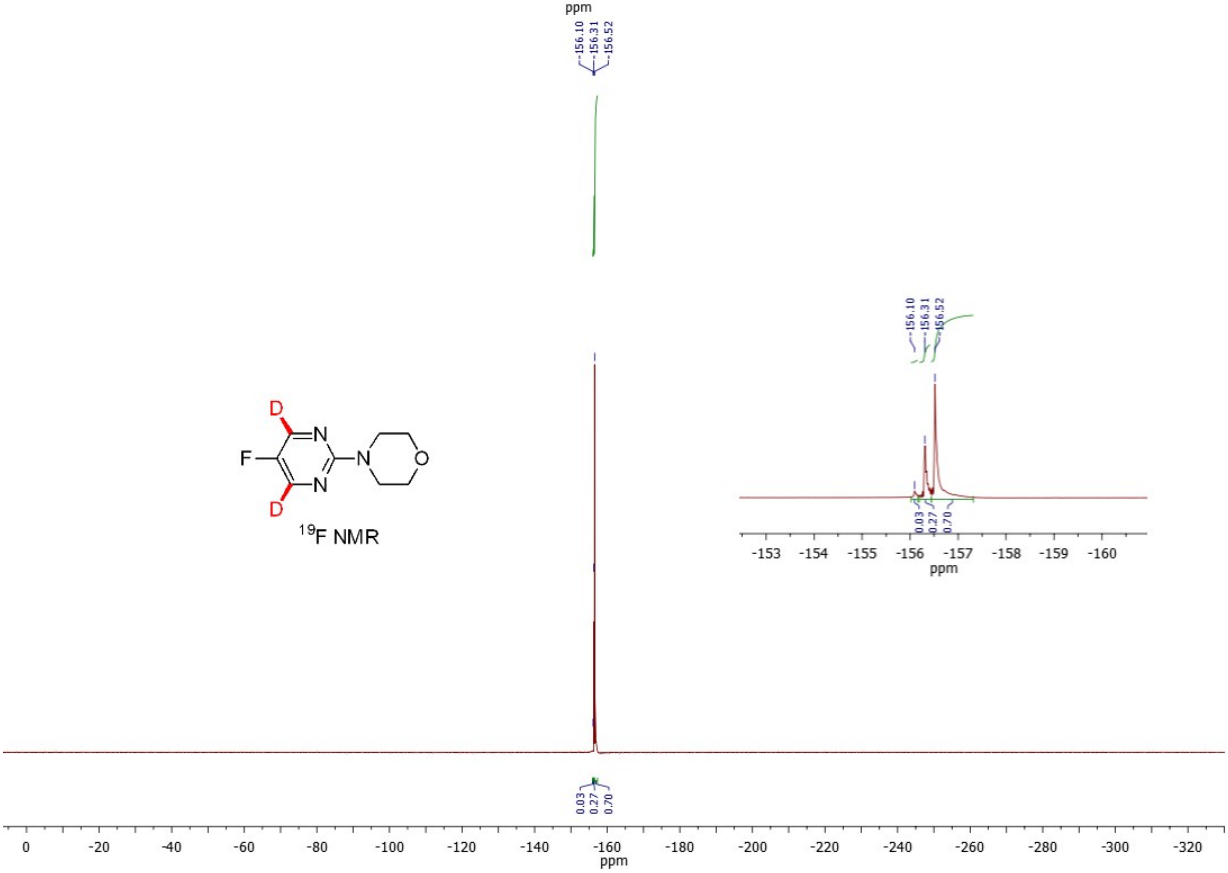


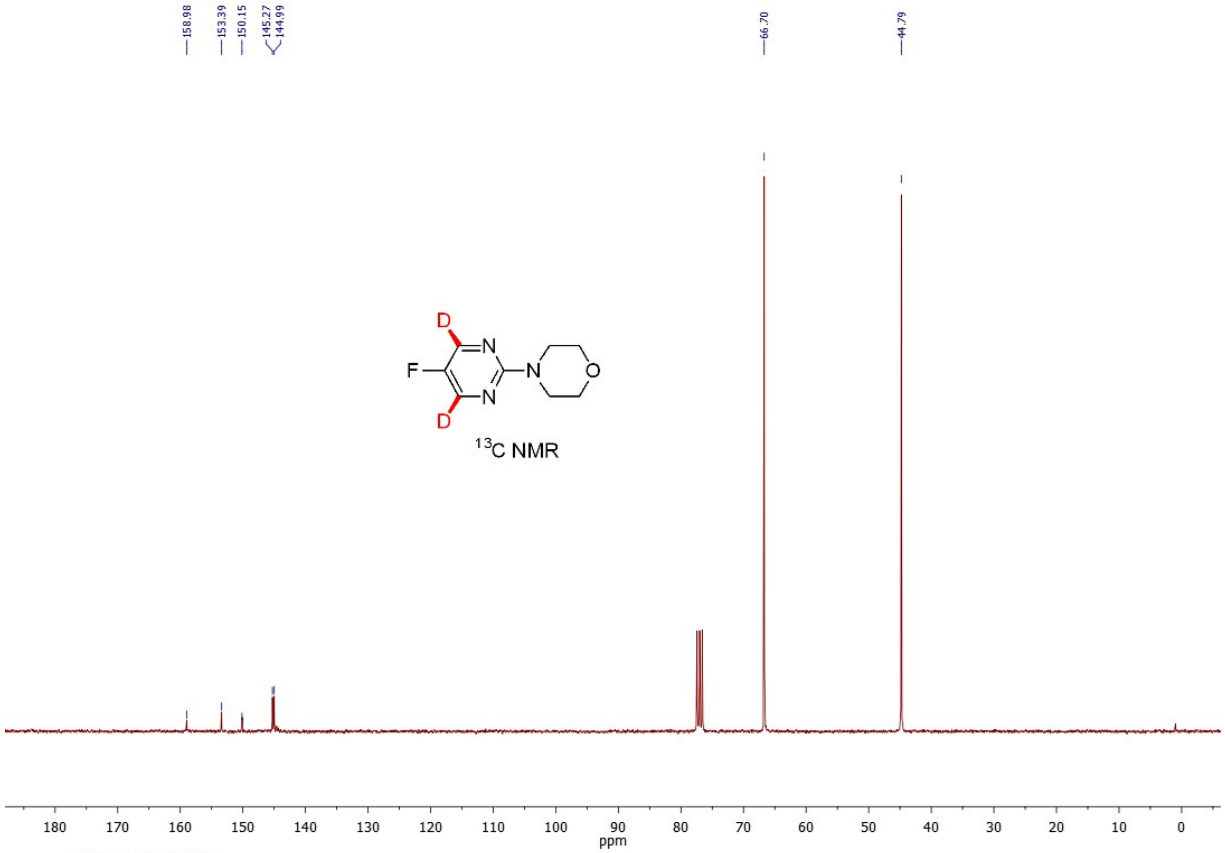
^{1}H NMR

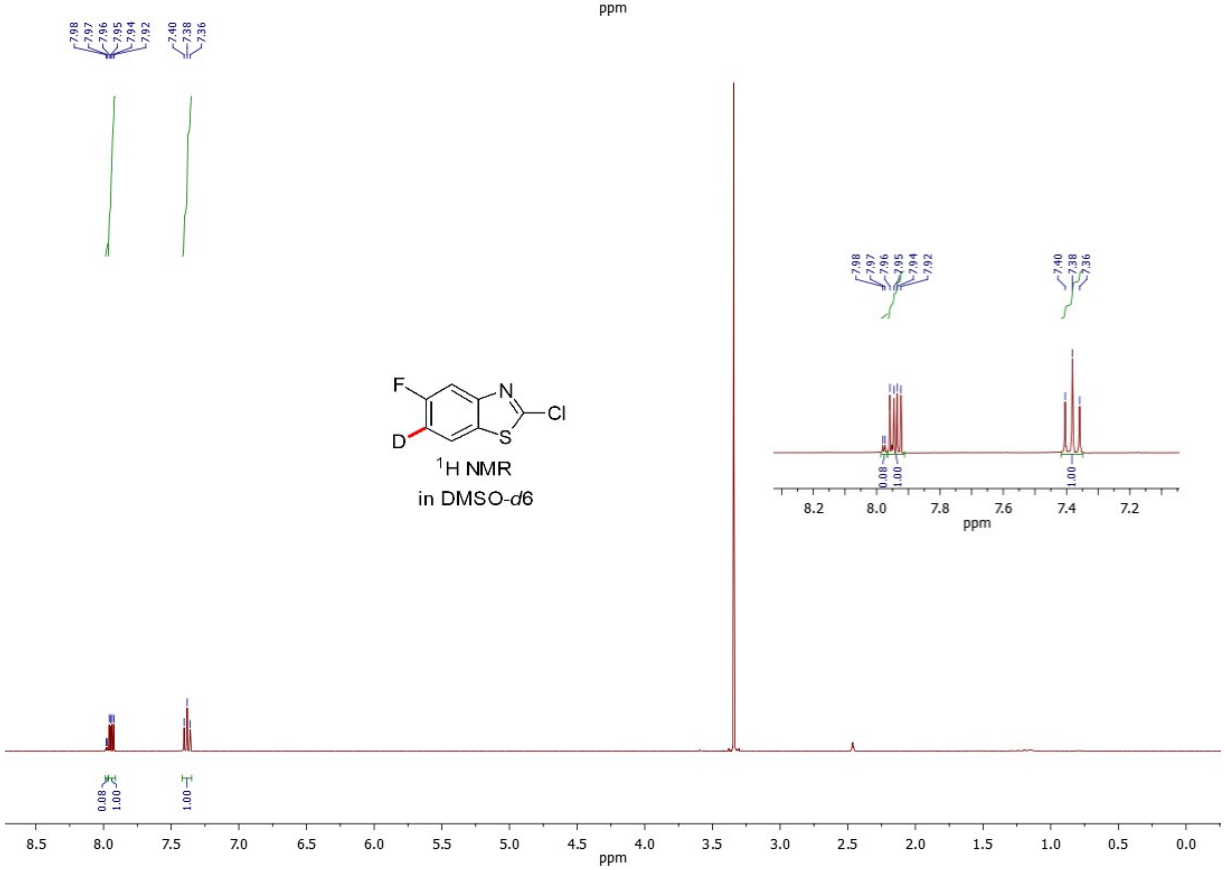

D
N
F
N
D
19F NMR
140.56
140.78
140.99
0.03
0.23
0.74
137 -138 -139 -140 -141 -142 -143 -144 -145
ppm
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 -130 -150 -170 -190 -210 -230 -250 -270
ppm

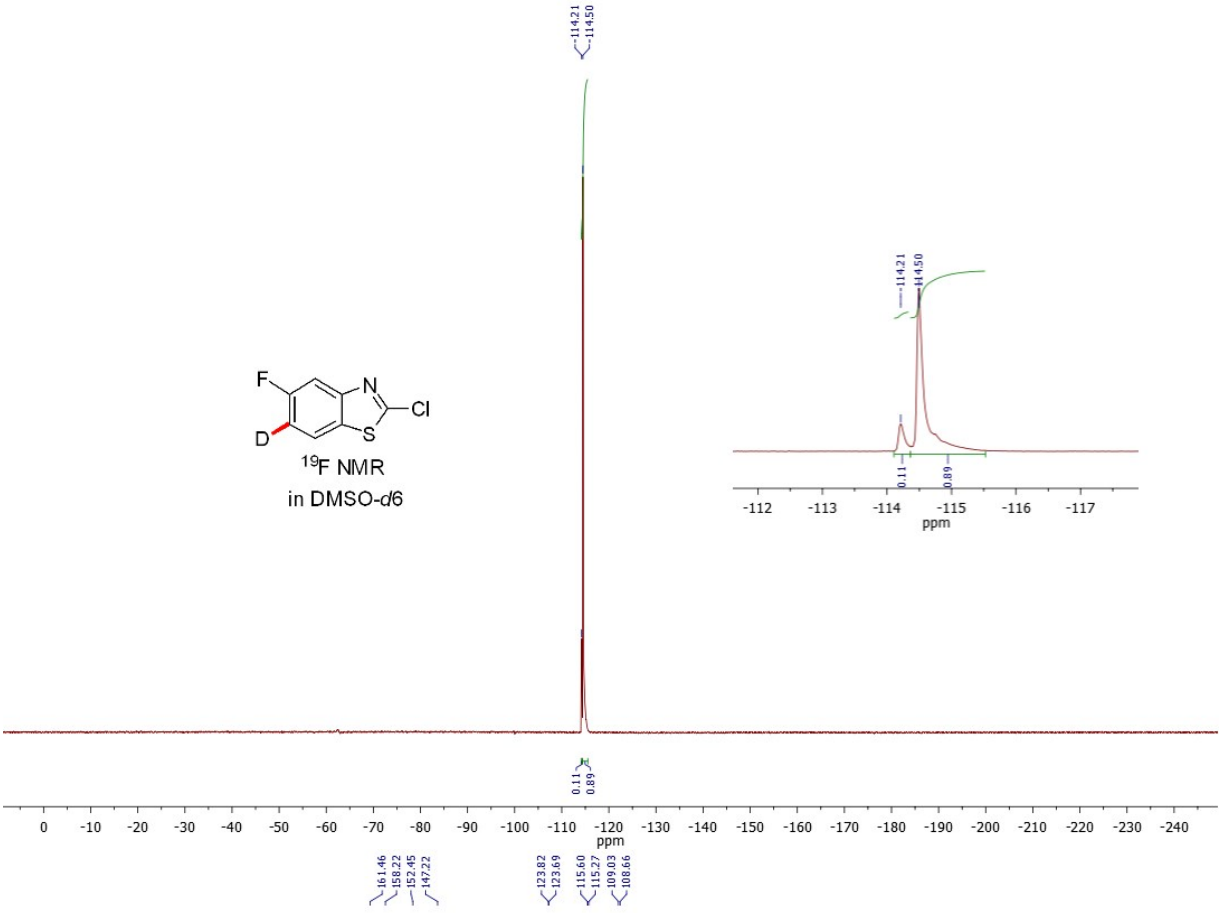

161.11
157.67
155.57
144.99
144.83
144.73
144.55
144.39
136.66
130.60
128.63
128.11
D
N
F
N
D
13C NMR
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm

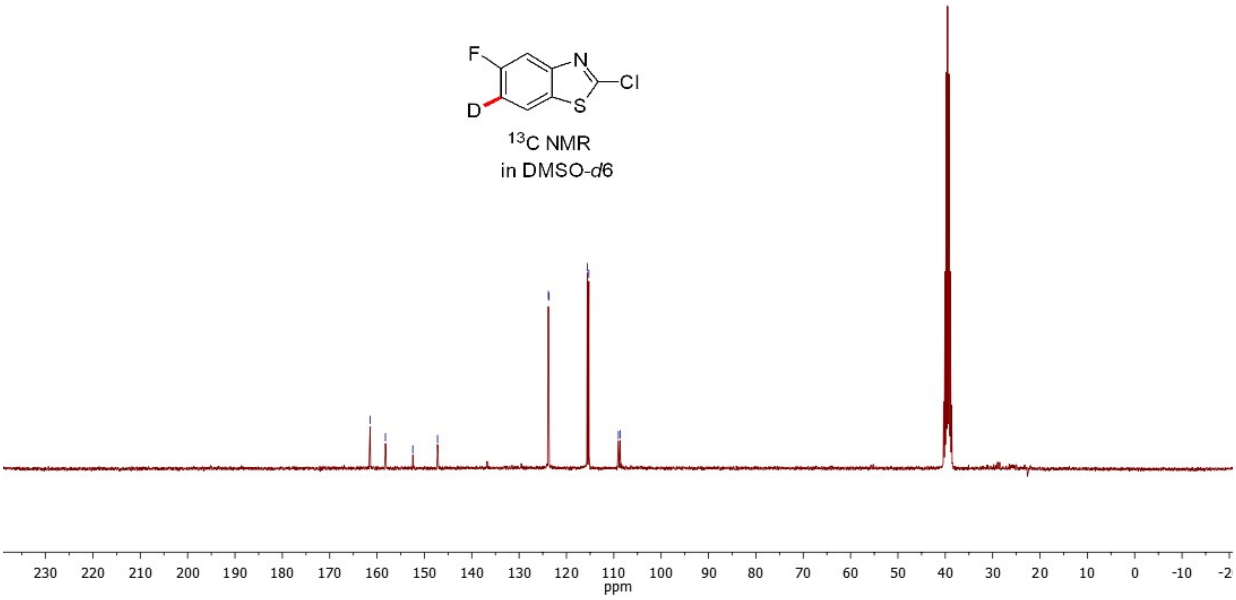

8.20
3.76
3.75
3.75
3.74
3.73
3.72
3.71
3.71
D
N
F
N
N
O
D
^{1}H NMR
0.15
4.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

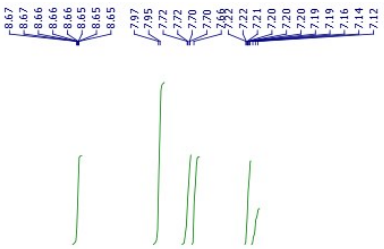

156.10
156.31
156.52
D
N
F
N
N
O
D
^{19}F NMR
156.10
156.31
156.52
0.03
0.27
0.70
-153
-154
-155
-156
-157
-158
-159
-160
ppm
0.03
0.27
0.70
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-240
-260
-280
-300
-320
ppm

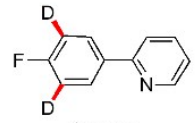

158.98
153.39
150.15
145.27
144.99
66.70
44.79
D
N
F
N
O
N
D
^{13}C NMR
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm


7.98
7.97
7.96
7.95
7.94
7.92
7.40
7.38
7.36
F
N
Cl
D
S
^{1}H NMR
in DMSO-*d*6
0.08
1.00
1.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm
8.2 8.0 7.8 7.6 7.4 7.2
ppm

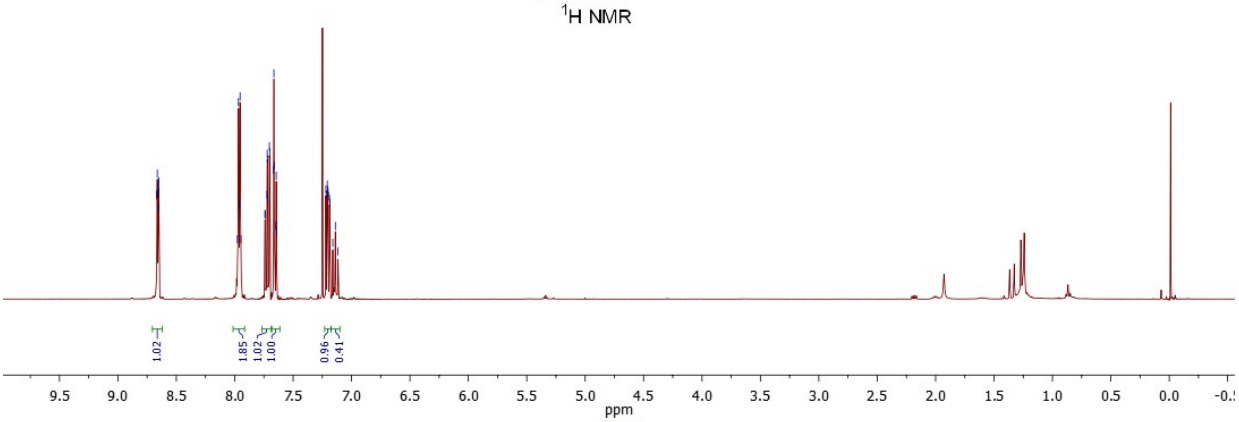

F
N
Cl
D
S
^{19}F NMR
in DMSO-*d*6
-114.21
-114.50
0.11
0.89
-112
-113
-114
-115
-116
-117
ppm
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
-240
ppm
161.46
158.22
152.45
147.22
123.82
123.69
115.60
115.27
109.03
108.66

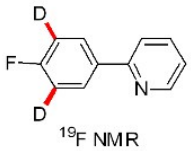

F
N
Cl
D
S
^{13}C NMR
in DMSO-*d*6
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-2
ppm



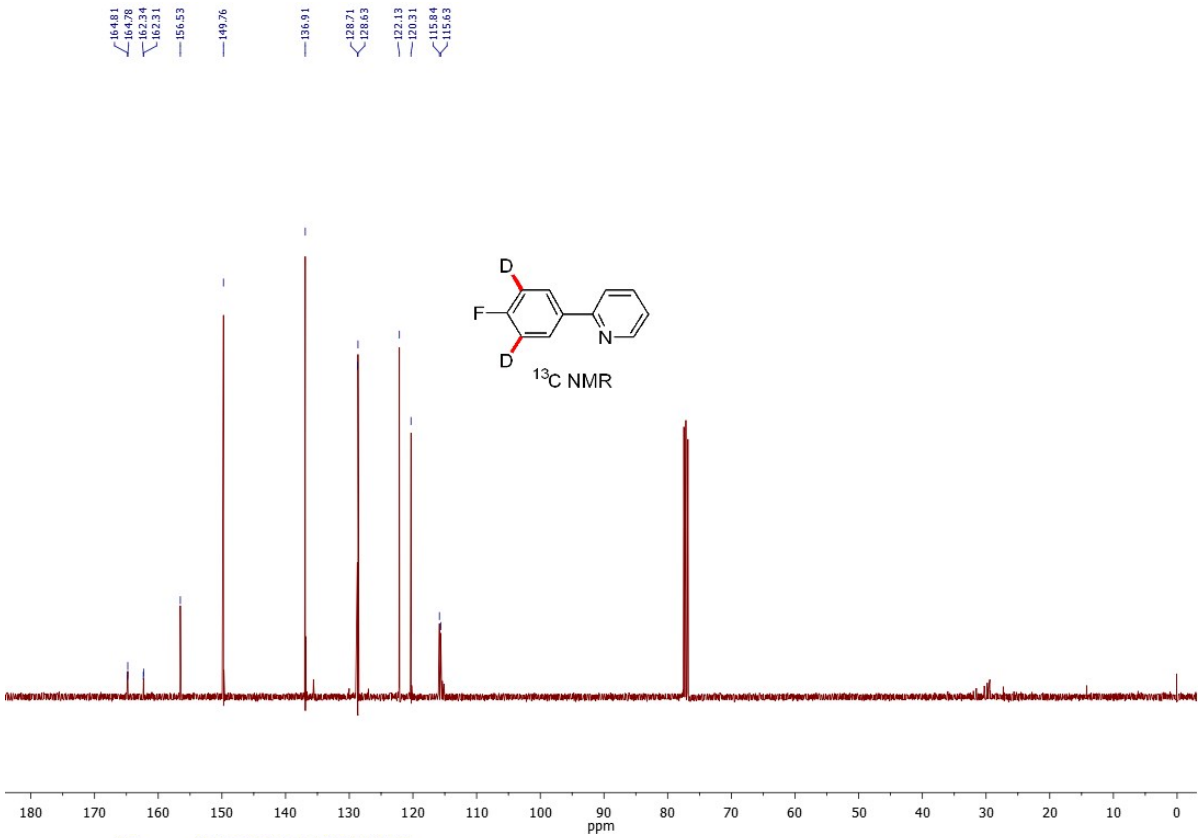


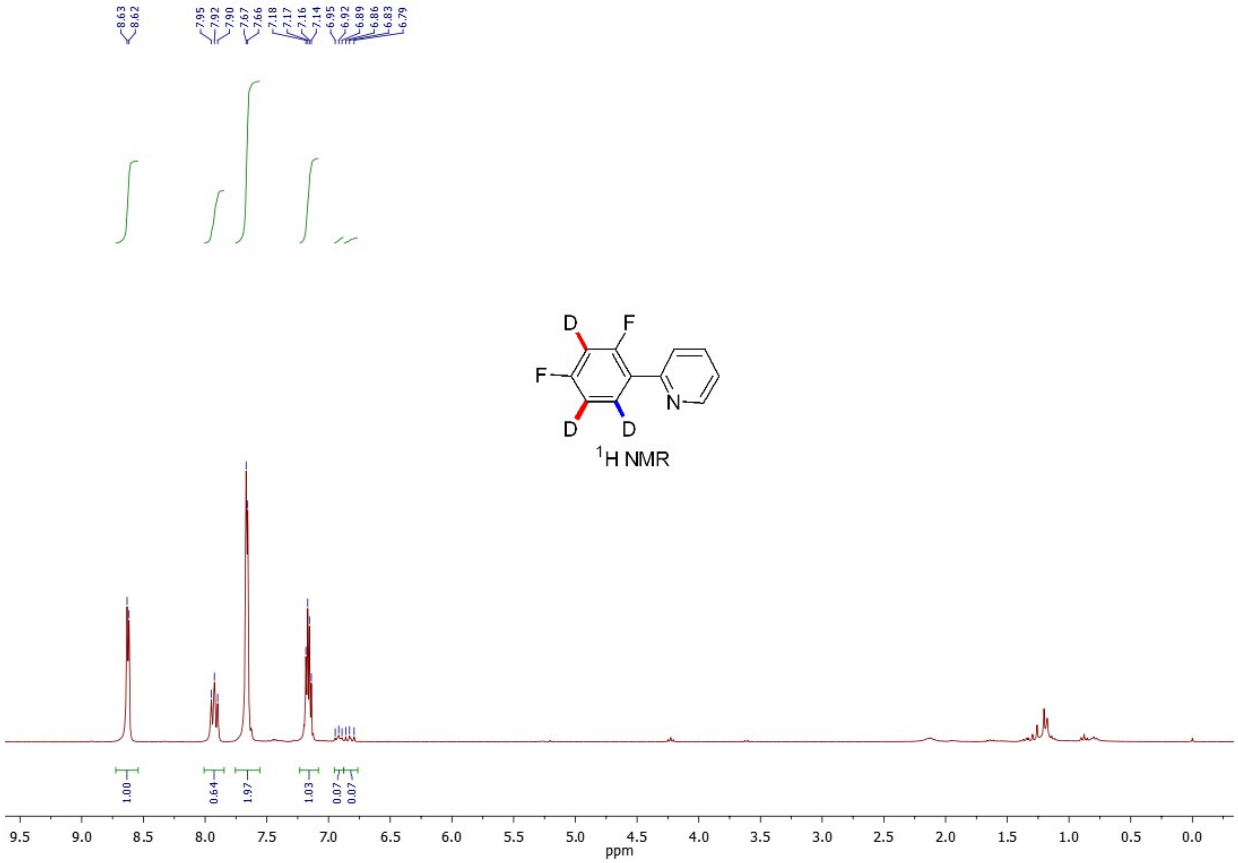
^{1}H NMR

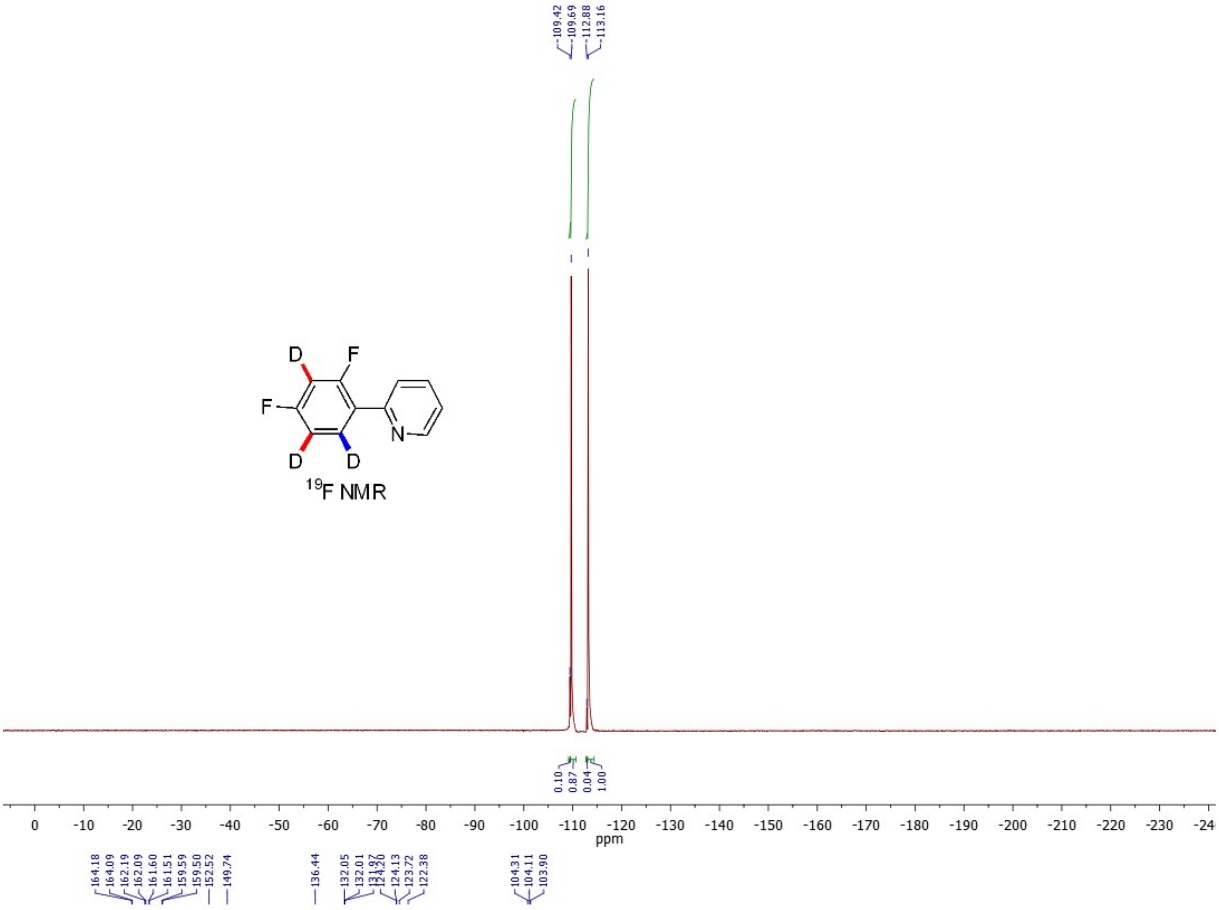


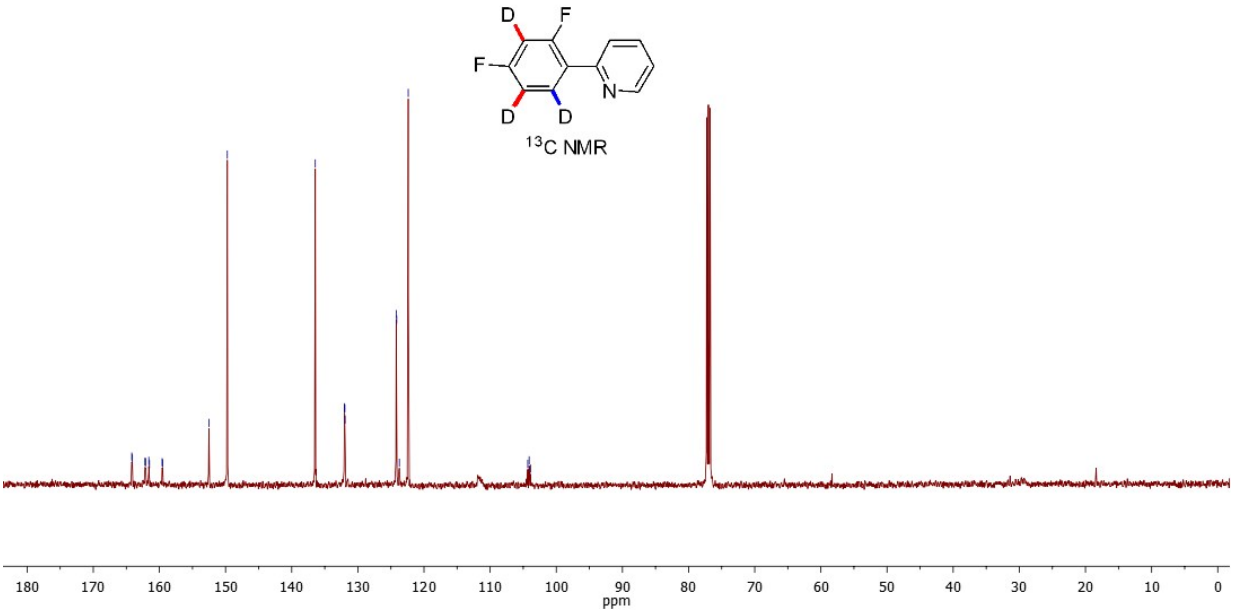


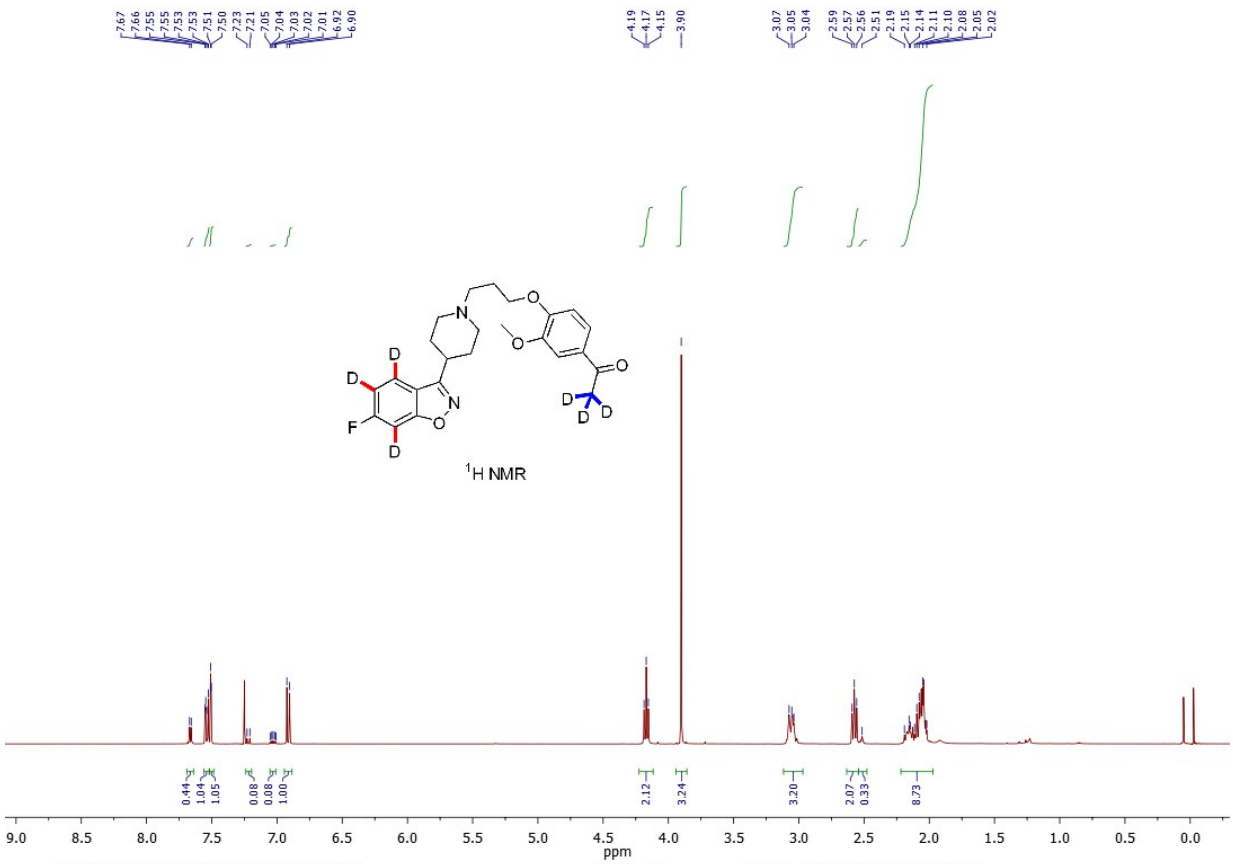
^{19}F NMR

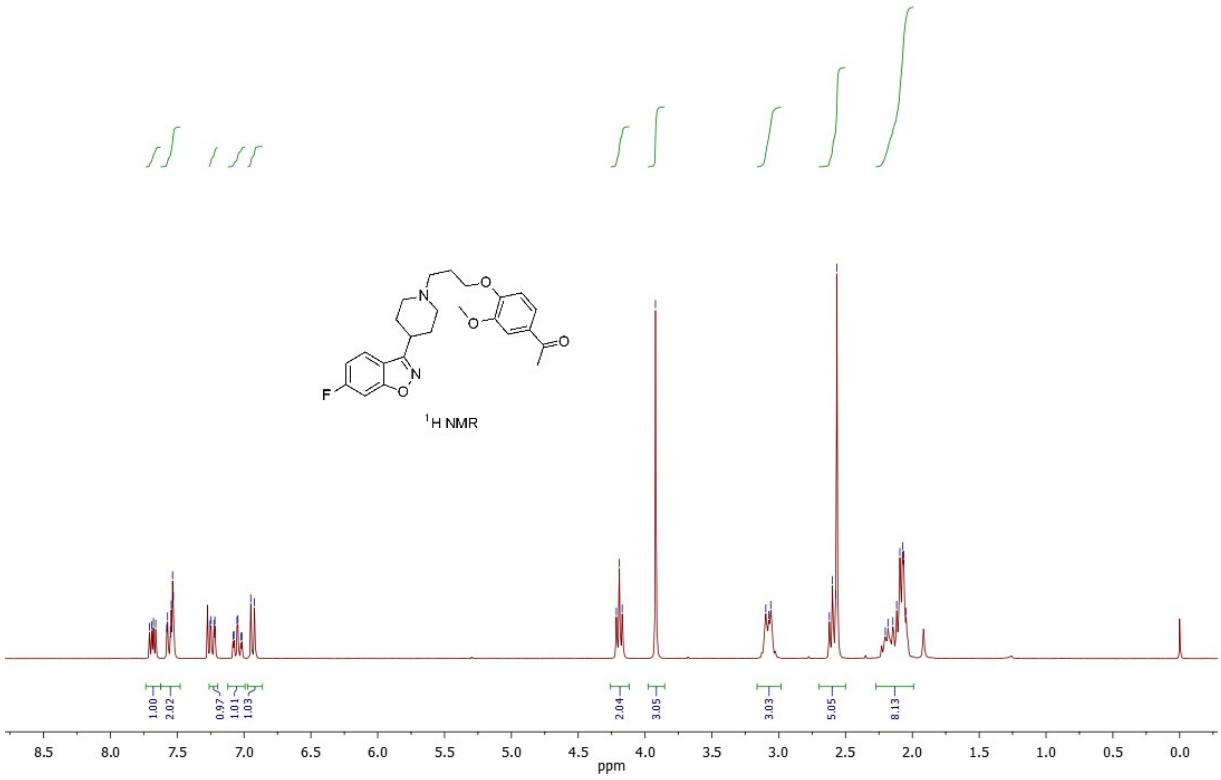

164.81
164.78
162.34
162.31
156.53
149.76
136.91
128.71
128.63
122.13
120.31
115.84
115.63
D
F
D
N
^{13}C NMR
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm

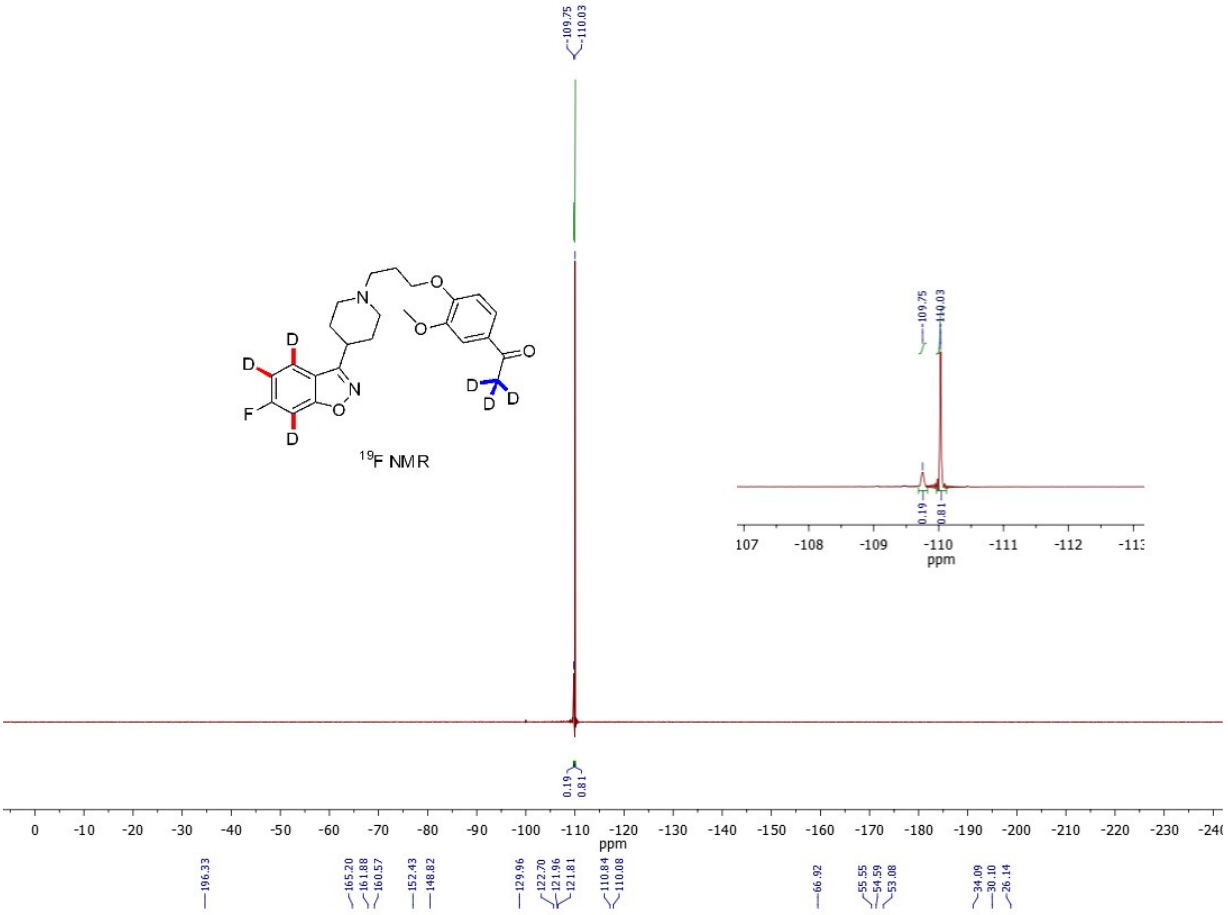

8.63
8.62
7.95
7.92
7.90
7.67
7.66
7.18
7.17
7.16
7.14
6.95
6.92
6.89
6.86
6.83
6.79
D
F
F
N
D
D
^{1}H NMR
1.00
0.64
1.97
1.03
0.07
0.07
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

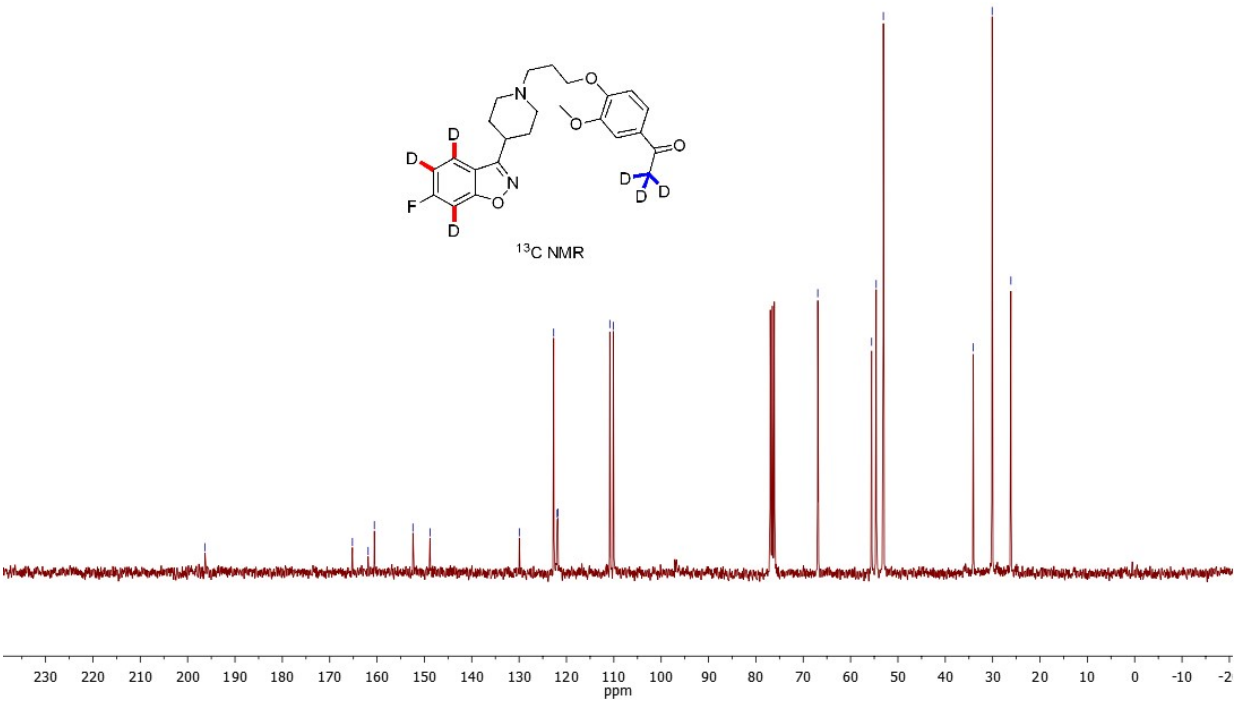

109.42
109.69
112.88
113.16
D
F
F
N
D
D
19F NMR
0.10
0.87
0.04
1.00
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
-24
ppm
164.18
164.09
162.19
162.09
161.60
161.51
159.59
159.50
152.52
149.74
136.44
132.05
132.01
124.13
123.72
122.38
104.31
104.11
103.90


D
F
F
N
D
D
13C NMR
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


D
D
F
D
N
O
N
O
O
D
D
D
^{1}H NMR
ppm


N
O
O
O
F
N
O
^{1}H NMR
ppm


109.75
110.03
D
D
F
D
N
O
O
O
D
D
D
19F NMR
109.75
110.03
0.19
0.81
107
-108
-109
-110
-111
-112
-113
ppm
0.19
0.81
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
-240
ppm


196.33
165.20
161.88
160.57
152.43
148.82
129.96
122.70
121.96
121.81
110.84
110.08
66.92
55.55
54.59
53.08
34.09
30.10
26.14
D
D
F
D
N
O
O
O
D
D
D
13C NMR
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-2
ppm