Supplementary Information (SI) for ChemComm.

Supplementary Information

Chemoselective Nickel-Catalyzed Difluoromethylation of Aryl Halides with (SIPr)AgCF$_2$H as Transmetalation Reagent

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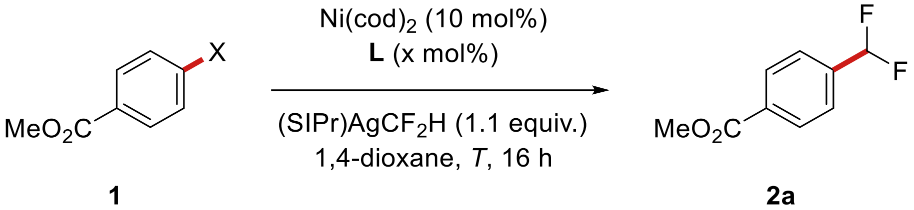
General Remarks

Reactions involving air- or moisture-sensitive compounds were conducted under an atmosphere of nitrogen using pre-dried glassware and standard Schlenk- or glovebox-techniques. Toluene and 1,4-dioxane were dried over Na/benzophenone, distilled under an atmosphere of nitrogen, degassed using three cycles of freeze-pump-thaw and stored over 3 Å molecular sieves inside a nitrogen-filled glovebox. THF was dried over Na/benzophenone and distilled under an atmosphere of nitrogen. Pentane was dried over CaH_2 and distilled under an atmosphere of nitrogen. Starting material **1a‘‘**[1], **1a‘‘‘**[2] and (SIPr)AgCl[3] were synthesized according to previously described methods. Styrene was distilled under an atmosphere of nitrogen and stored under an atmosphere of nitrogen inside a freezer. All other chemicals were obtained from commercial suppliers and used without further purification. If not otherwise noted, yields refer to isolated compounds, estimated to be >95% pure by GC and NMR. Analytical thin layer chromatography (TLC) was performed on Alugram Xtra SIL G UV254 from Machery-Nagel with detection at 254 nm. Preparative chromatographic separations were carried out on Machery-Nagel (0.04-0.063 mm) silica gel. Gas chromatographic analysis (GC) was performed on an Agilent 8860 GC System equipped with a flame-ionization detector (FID) using hydrogen as the carrier gas. Melting points (m.p.) were measured on Stuart SMP20 and values are uncorrected. Infrared (IR) spectra were recorded on a Agilent Technologies Cary 630 FT-IR spectrometer and values are reported in wavenumbers. Nuclear magnetic resonance (NMR) spectra were recorded on Bruker Avance II 400, Avance III 500 spectrometers. Chemical shifts (δ) are referenced using the residual proton or carbon solvent signal. Electrospray-ionization (ESI) and atmospheric pressure chemical ionization (APCI) mass spectra were obtained on Thermo Fisher Scientific Orbitrap XL instruments.

Optimization Studies

Table S-1. Optimization of Reaction Conditions.[a]



Entry	X	L (x mol%)	*T* / °C	Further deviations	Yield / %
1	I	Xantphos (10)	90	--	46
2	I	dppf (10)	90	--	27
3	I	dppe (10)	90	--	9
4	I	dtbbpy (10)	90	--	8
5	I	Xantphos (15)	90	--	67
6	I	Xantphos (15)	90	$Ni(cod)_2$ (15 mol%)	61
7	I	Xantphos (20)	90	--	79
8	I	Xantphos (15)	90	$(SIPr)AgCF_2H$ (1.5 equiv.)	56
9	I	Xantphos (15)	90	in 1,4-dioxane (0.05 M)	58
10	I	Xantphos (15)	90	in toluene (0.1 M)	80
11	I	Xantphos (11.3)	90	$Ni(cod)_2$ (7.5 mol%); in toluene (0.1 M)	76
12	I	Xantphos (7.5)	90	$Ni(cod)_2$ (5.0 mol%); in toluene (0.1 M)	60
13	**I**	**Xantphos (15)**	**60**	**in toluene (0.1 M)**	**89 (70)**
14	I	Xantphos (15)	40	in toluene (0.1 M)	84
15	I	Xantphos (15)	r.t.	in toluene (0.1 M)	68
16	Br	Xantphos (15)	60	in toluene (0.1 M)	63
17	OTf	Xantphos (15)	60	in toluene (0.1 M)	traces
18	ONf	Xantphos (15)	60	in toluene (0.1 M)	traces
19	I	--	60	in toluene (0.1 M)	n.d.

20	I	Xantphos (15)	60	w/o Ni(cod)$_2$; in toluene (0.1 M)	n.d.

[a] Reaction conditions: **1** (0.10 mmol), Ni(cod)$_2$ (5.0-10 mol%), **L** (7.5-20 mol%), (SIPr)AgCF$_2$H (0.11-0.15 mmol), 1,4-dioxane (1.0 mL), 16 h. Yields were determined by GC analysis with *n*-decane as internal standard. Isolated yield (0.20 mmol scale) is shown in parenthesis.

General Procedure for the Nickel-Catalyzed Difluoromethylation (GP1):

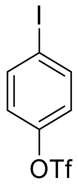
Inside a nitrogen-filled glovebox, a Schlenk-tube was charged with Ni(cod)$_2$ (5.5 mg, 20 µmol, 10.0 mol%), Xantphos (17.4 mg, 30 µmol, 15.0 mol%) and toluene (2.0 mL) and the mixture was stirred for 5 min at r.t. Afterwards, the corresponding aryl halide **1** (0.20 mmol, 1.00 equiv.) was added. Subsequently, (SIPr)AgCF$_2$H (121 mg, 0.22 mmol, 1.10 equiv.) was added, the Schlenk-tube sealed, removed from the glovebox and the mixture was heated to 60 °C for 16 h. The reaction mixture was diluted with DCM (ca. 2 mL) and filtered through a pad of Celite, which was thoroughly rinsed with DCM (ca. 15 mL). H_2O (20 mL) was added, the phases separated and the aqueous phase extracted with DCM (3 x 20 mL). The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the crude product by column chromatography on silica gel yielded products **2**.

General Procedure for the Nickel-Catalyzed Difluoromethylation of Volatile Compounds (GP2):

Inside a nitrogen-filled glovebox, a Schlenk-tube was charged with Ni(cod)$_2$ (2.8 mg, 10 µmol, 10.0 mol%), Xantphos (8.7 mg, 15 µmol, 15.0 mol%) and toluene (1.0 mL) and the mixture was stirred for 5 min at r.t. Afterwards, the corresponding aryl halide **1** (0.10 mmol, 1.00 equiv.) was added. Subsequently, (SIPr)AgCF$_2$H (60 mg, 0.11 mmol, 1.10 equiv.) was added, the Schlenk-tube sealed, removed from the glovebox and the mixture was heated to 60 °C for 16 h. After cooling to r.t., 4-fluorotoluene (7.5 µL, 0.068 mmol) was added. An aliquot (0.15 mL) was removed and filtered through a short plug of silica gel, which was rinsed with $CDCl_3$ (0.65 mL). The filtrate was analyzed by quantitative ^{19}F NMR spectroscopy to determine the yield of product **2**.

Synthesis of Starting Materials

4-Iodophenyl trifluoromethanesulfonate (1v)



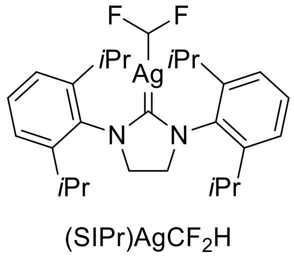
1v

A solution of 4-iodophenol (220 mg, 1.00 mmol, 1.00 equiv.) and pyridine (158 mg, 0.16 mL, 2.00 mmol, 2.00 equiv.) in DCM (3.0 mL) was cooled to 0 °C and trifluoromethanesulfonic anhydride (310 mg, 0.19 mL, 1.10 mmol, 1.10 equiv.) was added dropwise. Afterwards, the reaction mixture was allowed to warm to r.t. and stirred for 19 h. The reaction mixture was diluted with Et_2O (6 mL) and aq. HCl (1M, 2.5 mL) was added. The phases were separated and the aqueous phase extracted with Et_2O (3 x 6 mL). The combined organic phases were washed with sat. aq. $NaHCO_3$ solution (10 mL) and brine (5 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the crude product by column chromatography on silica gel (CyH/MTBE 30:1) yielded **1v** (271 mg, 0.77 mmol, 77%) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ/ppm = 7.78 (d, *J* = 9.0 Hz, 2H), 7.04 (d, *J* = 9.0 Hz, 2H).
^{19}F NMR (471 MHz, $CDCl_3$) δ/ppm = -72.71.
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ/ppm = 149.5, 139.6, 123.5, 118.8 (q, *J* = 320.8 Hz), 93.3.
HR-MS (APCI): *m/z* calcd for $C_7H_4F_3IO_3S^+$ $[M]^+$ 351.8872, found 351.8881.
IR (ATR): ṽ/cm^{-1} = 1476, 1421, 1203, 1132, 1055, 1007, 876, 825, 743, 697.
TLC: R_f = 0.43 (CyH/MTBE 30:1).

The analytical data are in accordance with those reported in the literature.[4]

[1,3-bis(2,6-diisopropylphenyl)imidazolidin-2-ylidene](difluoromethyl)silver ((SIPr)$AgCF_2H$)



(SIPr)$AgCF_2H$

(SIPr)AgCF$_2$H was synthesized following a modified literature procedure.[5]

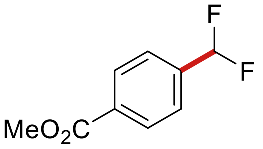
Under an atmosphere of nitrogen, a Schlenk-flask was charged with (SIPr)AgCl (910 mg, 1.70 mmol, 1.00 equiv.), sodium *tert*-butoxide (328 mg, 3.41 mmol, 2.00 equiv.) and THF (45 mL). Difluoromethyl(trimethyl)silane (423 mg, 3.41 mmol, 2.00 equiv.) was added dropwise and the reaction mixture was stirred at r.t. for 1.5 h. The mixture was filtered through a pad of Celite, which was rinsed with THF (15 mL), and all volatiles were removed from the filtrate under reduced pressure. THF (12 mL) and pentane (55 mL) were added, the precipitate filtered off *via* Schlenk-frit, washed with pentane (2 x 12 mL) and dried *in vacuo*. (SIPr)AgCF$_2$H (890 mg, 1.62 mmol, 95%) was obtained as an off-white to beige solid.

^{1}H NMR (500 MHz, THF-d_8) δ/ppm = 7.38 (t, J = 7.7 Hz, 2H), 7.27 (d, J = 7.7 Hz, 4H), 5.93 (td, J = 43.7, 14.1 Hz, 1H), 4.06 (s, 4H), 3.18 (hept, J = 6.9 Hz, 4H), 1.36 (d, J = 6.9 Hz, 12H), 1.33 (d, J = 6.9 Hz, 12H).
^{19}F NMR (471 MHz, THF-d_8) δ/ppm = -113.61 (pseudo-ddd, $J_{\text{F-109Ag}}$ = 62.9, $J_{\text{F-107Ag}}$ = 54.4, $J_{\text{F-H}}$ = 43.8 Hz, 2F).
^{13}C{^{1}H} NMR (126 MHz, THF-d_8) δ/ppm = 213.1 – 211.8 (m), 152.5 – 149.7 (m), 147.9, 136.3, 130.4, 125.3, 29.8, 25.7, 24.4.

The analytical data are in accordance with those reported in the literature.[5]

Characterization Data of Products 3 and 4

Methyl 4-(difluoromethyl)benzoate (2a)



2a

The General Procedure GP1 was followed using methyl 4-iodobenzoate (**1a**, 52.4 mg, 0.20 mmol). Purification by column chromatography on silica gel (pentane/Et_2O 40:1) yielded **2a** (26.1 mg, 0.14 mmol, 70%) as a white solid.

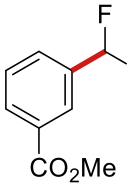
1.0 mmol scale reaction

Inside a nitrogen-filled glovebox, a Schlenk-tube was charged with $Ni(cod)_2$ (27.5 mg, 100 µmol, 10.0 mol%), Xantphos (86.8 mg, 150 µmol, 15.0 mol%) and toluene (10.0 mL) and the mixture was stirred for 5 min at r.t. Afterwards, methyl 4-iodobenzoate (**1a**, 262 mg, 1.00 mmol, 1.00 equiv.) was added. Subsequently, (SIPr)$AgCF_2H$ (604 mg, 1.10 mmol, 1.10 equiv.) was added, the Schlenk-tube sealed, removed from the glovebox and the mixture was heated to 60 °C for 16 h. The reaction mixture was filtered through a pad of Celite, which was thoroughly rinsed with DCM (ca. 50 mL). H_2O (50 mL) was added, the phases separated and the aqueous phase extracted with DCM (3 x 50 mL). The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. Purification by column chromatography on silica gel (pentane/Et_2O 40:1) yielded **2a** (156 mg, 0.84 mmol, 84%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ/ppm = 8.13 (d, *J* = 8.0 Hz, 2H), 7.59 (d, *J* = 8.0 Hz, 2H), 6.69 (t, *J* = 56.1 Hz, 1H), 3.94 (s, 3H).
^{19}F NMR (471 MHz, $CDCl_3$) δ/ppm = -112.27 (d, *J* = 56.2 Hz, 2F).
^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ/ppm = 166.4, 138.6 (t, *J* = 22.6 Hz), 132.5, 125.8 (t, *J* = 5.9 Hz), 114.2 (t, *J* = 239.8 Hz), 52.5.
HR-MS (APCI): *m/z* calcd for $C_9H_9F_2O_2^+$ $[M+H]^+$ 187.0565, found 187.0565.
IR (ATR): ṽ/cm^{-1} = 1716, 1439, 1275, 1213, 1110, 1070, 1009, 956, 768, 707.
TLC: R_f = 0.45 (pentane/Et_2O 10:1).
m.p.: 40-41 °C.

The analytical data are in accordance with those reported in the literature.[6]

Methyl 3-(difluoromethyl)benzoate (2b)



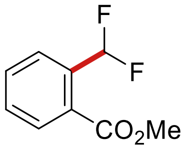
2b

The General Procedure GP1 was followed using methyl 3-iodobenzoate (**1b**, 52.4 mg, 0.20 mmol). Purification by column chromatography on silica gel (pentane/Et_2O 20:1) yielded **2b** (28.1 mg, 0.15 mmol, 75%) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ/ppm = 8.19 (s, 1H), 8.16 (d, *J* = 7.7 Hz, 1H), 7.71 (d, *J* = 7.6 Hz, 1H), 7.55 (t, *J* = 7.7 Hz, 1H), 6.69 (t, *J* = 56.2 Hz, 1H), 3.95 (s, 3H).
^{19}F NMR (471 MHz, $CDCl_3$) δ/ppm = -111.25 (d, *J* = 56.3 Hz, 2F).
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ/ppm = 166.3, 134.9 (t, *J* = 22.9 Hz), 131.9 (t, *J* = 1.9 Hz), 130.9, 130.0 (t, *J* = 5.7 Hz), 129.1, 127.1 (t, *J* = 6.3 Hz), 114.2 (t, *J* = 239.5 Hz), 52.5.
HR-MS (APCI): *m/z* calcd for $C_9H_9F_2O_2^+$ $[M+H]^+$ 187.0565, found 187.0567.
IR (ATR): ṽ/cm^{-1} = 1719, 1435, 1372, 1287, 1206, 1112, 1025, 981, 753, 708.
TLC: R_f = 0.50 (pentane/Et_2O 10:1).

The analytical data are in accordance with those reported in the literature.[7]

Methyl 2-(difluoromethyl)benzoate (2c)



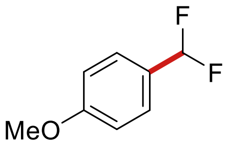
2c

The General Procedure GP1 was followed using methyl 2-iodobenzoate (**1c**, 52.4 mg, 29 µL, 0.20 mmol). **2c** (11%) was detected by quantitative ^{19}F NMR spectroscopy analysis of the crude reaction mixture with 4-fluorotoluene (15 µL, 0.136 mmol) as internal standard.

^{19}F NMR (471 MHz, $CDCl_3$) δ/ppm = -113.33 (d, *J* = 55.8 Hz, 2F).

The analytical data are in accordance with those reported in the literature.[8]

1-(Difluoromethyl)-4-methoxybenzene (2d)



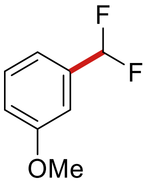
2d

The General Procedure GP2 was followed using 1-iodo-4-methoxybenzene (**1d**, 23.4 mg, 0.10 mmol). **2d** (45%) was detected by quantitative ^{19}F NMR spectroscopy.

^{19}F NMR (471 MHz, $CDCl_3$) δ/ppm = -107.86 (d, J = 56.7 Hz, 2F).

The analytical data are in accordance with those reported in the literature.[9]

1-(Difluoromethyl)-3-methoxybenzene (2e)



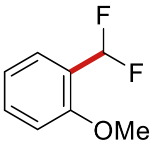
2e

The General Procedure GP2 was followed using 1-iodo-3-methoxybenzene (**1e**, 23.4 mg, 12 µL, 0.10 mmol). **2e** (31%) was detected by quantitative ^{19}F NMR spectroscopy.

^{19}F NMR (471 MHz, $CDCl_3$) δ/ppm = -110.26 (d, J = 56.4 Hz, 2F).

The analytical data are in accordance with those reported in the literature.[10]

1-(Difluoromethyl)-2-methoxybenzene (2f)



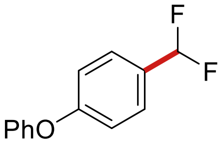
2f

The General Procedure GP2 was followed using 1-iodo-2-methoxybenzene (**1f**, 23.4 mg, 13 µL, 0.10 mmol). **2f** (30%) was detected by quantitative ^{19}F NMR spectroscopy.

^{19}F NMR (471 MHz, $CDCl_3$) δ/ppm = -114.97 (d, *J* = 55.7 Hz, 2F).

The analytical data are in accordance with those reported in the literature.[10]

1-(Difluoromethyl)-4-phenoxybenzene (2g)



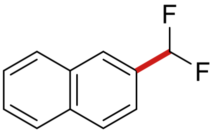
2g

The General Procedure GP1 was followed using 1-iodo-4-phenoxybenzene (**1g**, 59.2 mg, 0.20 mmol). Purification by column chromatography on silica gel (pentane) yielded **2g** (41.9 mg, 0.19 mmol, 75%) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ/ppm = 7.47 (d, *J* = 8.2 Hz, 2H), 7.43 – 7.31 (m, 2H), 7.17 (t, *J* = 7.4 Hz, 1H), 7.05 (d, *J* = 8.0 Hz, 4H), 6.63 (t, *J* = 56.7 Hz, 1H).
^{19}F NMR (471 MHz, $CDCl_3$) δ/ppm = -109.06 (d, *J* = 56.8 Hz, 2F).
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ/ppm = 159.8 (t, *J* = 2.2 Hz), 156.3, 130.1, 129.0 (t, *J* = 22.8 Hz), 127.5 (t, *J* = 5.9 Hz), 124.3, 119.8, 118.4, 114.7 (t, *J* = 238.0 Hz).
HR-MS (APCI): *m*/*z* calcd for $C_{13}H_{10}F_2O^+$ $[M]^+$ 220.0694, found 220.0695.
IR (ATR): $\tilde{\nu}$/cm^{-1} = 1588, 1486, 1232, 1167, 1066, 1019, 872, 831, 748, 690.
TLC: R_f = 0.34 (pentane).

The analytical data are in accordance with those reported in the literature.[11]

2-(Difluoromethyl)naphthalene (2h)



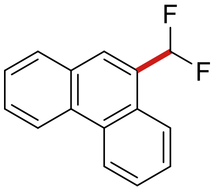
2h

The General Procedure GP1 was followed using 2-iodonaphthalene (**1h**, 50.8 mg, 0.20 mmol). Purification by column chromatography on silica gel (pentane) yielded **2h** (33.7 mg, 0.19 mmol, 95%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ/ppm = 7.98 (s, 1H), 7.94 (d, *J* = 8.6 Hz, 1H), 7.92 – 7.80 (m, 2H), 7.60 (d, *J* = 8.7 Hz, 1H), 7.59 – 7.51 (m, 2H), 6.81 (t, *J* = 56.4 Hz, 1H).
^{19}F NMR (471 MHz, $CDCl_3$) δ/ppm = -109.93 (d, *J* = 56.6 Hz, 2F).
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ/ppm = 134.5, 132.7, 131.8 (t, *J* = 22.2 Hz), 129.1, 128.7, 128.0, 127.6, 127.0, 126.0 (t, *J* = 7.6 Hz), 122.2 (t, *J* = 4.8 Hz), 115.2 (t, *J* = 238.5 Hz).
HR-MS (APCI): *m/z* calcd for $C_{11}H_8F_2^+$ [M]$^+$ 178.0589, found 178.0587.
IR (ATR): ṽ/cm^{-1} = 1400, 1336, 1174, 1011, 977, 903, 869, 830, 785, 749.
TLC: R_f = 0.43 (pentane).
m.p.: 76-77 °C.

The analytical data are in accordance with those reported in the literature.[5]

9-(Difluoromethyl)phenanthrene (2i)



2i

The General Procedure GP1 was followed using 9-iodophenanthrene (**1i**, 60.8 mg, 0.20 mmol). Purification by column chromatography on silica gel (pentane) yielded **2i** (11.0 mg, 0.05 mmol, 24%) as an off-white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ/ppm = 8.76 (d, *J* = 6.7 Hz, 1H), 8.70 (d, *J* = 8.4 Hz, 1H), 8.27 – 8.20 (m, 1H), 7.98 (s, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.79 – 7.62 (m, 5H), 7.16 (t, *J* = 55.0 Hz, 1H).
^{19}F NMR (471 MHz, $CDCl_3$) δ/ppm = -111.78 (d, *J* = 55.3 Hz, 2F).
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ/ppm = 131.6, 131.0, 130.3, 129.7, 128.5, 128.2 (t, *J* = 20.2 Hz), 128.1 (t, *J* = 1.8 Hz), 127.4, 127.3, 127.3, 127.0 (t, *J* = 9.4 Hz), 124.6 (t, *J* = 2.2 Hz), 123.4, 122.8, 115.8 (t, *J* = 238.6 Hz).
HR-MS (APCI): *m/z* calcd for $C_{15}H_{10}F_2^+$ [M]$^+$ 228.0745, found 228.0748.

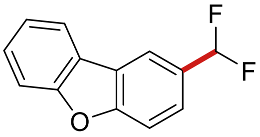
IR (ATR): ṽ/cm^{-1} = 1528, 1449, 1373, 1115, 1091, 1011, 898, 861, 746, 724.

TLC: R$_f$ = 0.42 (pentane).

m.p.: 54-55 °C.

The analytical data are in accordance with those reported in the literature.[12]

2-(Difluoromethyl)dibenzo[*b,d*]furan (2j)



2j

The General Procedure GP1 was followed using 2-iodo-dibenzo[*b,d*]furan (**1j**, 58.8 mg, 0.20 mmol). Purification by column chromatography on silica gel (pentane) yielded **2j** (34.1 mg, 0.16 mmol, 78%) as a white solid.

^{1}H NMR (500 MHz, CDCl$_3$) δ/ppm = 8.13 (s, 1H), 7.99 (d, *J* = 7.5 Hz, 1H), 7.68 – 7.58 (m, 3H), 7.51 (ddd, *J* = 8.5, 7.2, 1.3 Hz, 1H), 7.39 (td, *J* = 7.5, 1.0 Hz, 1H), 6.82 (t, *J* = 56.7 Hz, 1H).

^{19}F NMR (471 MHz, CDCl$_3$) δ/ppm = -107.9 (d, *J* = 56.7 Hz, 2F).

^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ/ppm = 157.4, 156.9, 129.3 (t, *J* = 22.6 Hz), 128.0, 124.8 (t, *J* = 6.0 Hz), 124.7, 123.7, 123.3, 121.0, 118.5 (t, *J* = 6.4 Hz), 115.2 (t, *J* = 238.6 Hz), 112.2, 112.1.

HR-MS (APCI): *m/z* calcd for $C_{13}H_8F_2O^+$ [M]$^+$ 218.0538, found 218.0538.

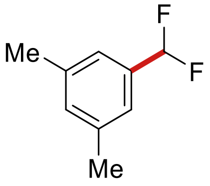
IR (ATR): ṽ/cm^{-1} = 1440, 1374, 1344, 1203, 1071, 1008, 890, 832, 748, 684.

TLC: R$_f$ = 0.29 (pentane).

m.p.: 90-91 °C.

The analytical data are in accordance with those reported in the literature.[13]

1-(Difluoromethyl)-3,5-dimethylbenzene (2k)



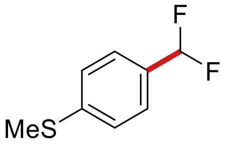
2k

The General Procedure GP1 was followed using 1-iodo-3,5-dimethylbenzene (**1k**, 46.4 mg, 29 µL, 0.20 mmol). Purification by column chromatography on silica gel (pentane) yielded a mixture of **2k**, **1k** and toluene. **2k** (23%) was detected by quantitative ^{19}F NMR spectroscopy analysis with 4-fluorotoluene (15 µL, 0.136 mmol) as internal standard.

^{19}F NMR (471 MHz, $CDCl_3$) δ/ppm = -109.89 (d, *J* = 56.5 Hz, 2F).
TLC: R_f = 0.79 (pentane).

The analytical data are in accordance with those reported in the literature.[10]

[4-(Difluoromethyl)phenyl](methyl)sulfane (2l)



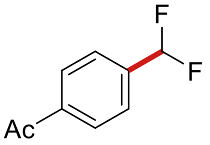
2l

The General Procedure GP1 was followed using 1-iodo-4-(methylthio)benzene (**1l**, 50.0 mg, 0.20 mmol). Purification by column chromatography on silica gel (pentane) yielded **2l** (26.5 mg, 0.15 mmol, 76%) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ/ppm = 7.41 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 6.61 (t, *J* = 56.6 Hz, 1H), 2.51 (s, 3H).
^{19}F NMR (471 MHz, $CDCl_3$) δ/ppm = -110.03 (d, *J* = 56.7 Hz, 2F).
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ/ppm = 142.4 (t, *J* = 2.3 Hz), 131.0 (t, *J* = 22.6 Hz), 126.2 (t, *J* = 6.2 Hz), 126.1, 114.8 (t, *J* = 238.3 Hz), 15.4.
HR-MS (APCI): *m/z* calcd for $C_8H_8F_2S^+$ $[M]^+$ 174.0309, found 174.0310.
IR (ATR): ṽ/cm^{-1} = 2921, 1603, 1372, 1218, 1067, 1014, 967, 850, 807, 731.
TLC: R_f = 0.32 (pentane).

The analytical data are in accordance with those reported in the literature.[12]

1-[4-(Difluoromethyl)phenyl]ethan-1-one (2m)



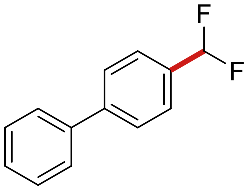
2m

The General Procedure GP1 was followed using 4'-iodoacetophenone (**1m**, 49.2 mg, 0.20 mmol). Purification by column chromatography on silica gel (pentane/Et_2O 10:1) yielded **2m** (25.6 mg, 0.15 mmol, 75%) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ/ppm = 8.04 (d, J = 8.0 Hz, 2H), 7.62 (d, J = 8.0 Hz, 2H), 6.69 (t, J = 56.1 Hz, 1H), 2.64 (s, 3H).
^{19}F NMR (471 MHz, $CDCl_3$) δ/ppm = -112.3 (d, J = 56.2 Hz, 2F).
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ/ppm = 197.5, 139.0 (t, J = 1.7 Hz), 138.7 (t, J = 22.4 Hz), 128.8, 126.1 (t, J = 6.1 Hz), 114.1 (t, J = 239.8 Hz), 26.9.
HR-MS (APCI): m/z calcd for $C_9H_9F_2O^+$ $[M+H]^+$ 171.0616, found 171.0615.
IR (ATR): ṽ/cm^{-1} = 1684, 1419, 1358, 1262, 1217, 1076, 1015, 957, 817, 722.
TLC: R_f = 0.27 (pentane/Et_2O 10:1).

The analytical data are in accordance with those reported in the literature.[9]

4-(Difluoromethyl)-1,1'-biphenyl (2n)



2n

The General Procedure GP1 was followed using 4-iodo-1,1'-biphenyl (**1n**, 56.0 mg, 0.20 mmol). Purification by column chromatography on silica gel (pentane) yielded **2n** (25.3 mg, 0.12 mmol, 62%) as a white solid.

^{1}H NMR (500 MHz, CDCl$_3$) δ/ppm = 7.68 (d, *J* = 7.9 Hz, 2H), 7.63 – 7.56 (m, 4H), 7.50 – 7.43 (m, 2H), 7.43 – 7.35 (m, 1H), 6.70 (t, *J* = 56.5 Hz, 1H).

^{19}F NMR (471 MHz, CDCl$_3$) δ/ppm = -110.4 (d, *J* = 56.6 Hz, 2F).

^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ/ppm = 143.9 (t, *J* = 1.9 Hz), 140.3, 133.5 (t, *J* = 22.4 Hz), 129.1, 128.1, 127.6, 127.4, 126.2 (t, *J* = 6.0 Hz), 114.9 (t, *J* = 238.6 Hz).

HR-MS (APCI): *m/z* calcd for $C_{13}H_{10}F_2^+$ $[M]^+$ 204.0745, found 204.0745.

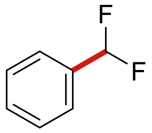
IR (ATR): ṽ/cm^{-1} = 1485, 1411, 1374, 1222, 1070, 1018, 834, 764, 736, 689.

TLC: R_f = 0.42 (pentane).

m.p.: 78-79 °C.

The analytical data are in accordance with those reported in the literature.[12]

Difluoromethylbenzene (2o)



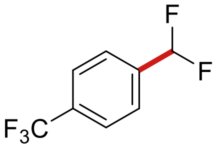
2o

The General Procedure GP2 was followed using iodobenzene (**1o**, 20.4 mg, 11 µL, 0.10 mmol). **2o** (58%) was detected by quantitative ^{19}F NMR spectroscopy.

^{19}F NMR (471 MHz, CDCl$_3$) δ/ppm = -110.20 (d, *J* = 56.4 Hz, 2F).

The analytical data are in accordance with those reported in the literature.[9]

1-(Difluoromethyl)-4-(trifluoromethyl)benzene (2p)



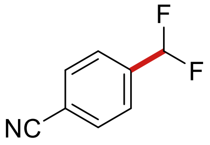
2p

The General Procedure GP2 was followed 1-iodo-4-(trifluoromethyl)benzene (**1p**, 27.2 mg, 15 µL, 0.10 mmol). **2p** (81%) was detected by quantitative ^{19}F NMR spectroscopy.

^{19}F NMR (471 MHz, CDCl$_3$) δ/ppm = -62.69 (s), -111.95 (d, *J* = 56.0 Hz).

The analytical data are in accordance with those reported in the literature.[12]

4-(Difluoromethyl)benzonitrile (2q)



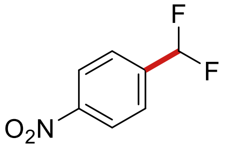
2q

The General Procedure GP2 was followed using 4-iodobenzonitrile (**1q**, 22.9 mg, 0.10 mmol). **2q** (26%) was detected by quantitative ^{19}F NMR spectroscopy.

^{19}F NMR (471 MHz, $CDCl_3$) δ/ppm = -112.67 (d, *J* = 56.3 Hz, 2F).

The analytical data are in accordance with those reported in the literature.[12]

1-(Difluoromethyl)-4-nitrobenzene (2r)



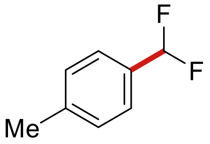
2r

The General Procedure GP1 was followed using 1-iodo-4-nitrobenzene (**1r**, 49.8 mg, 0.20 mmol). **2r** (11%) was detected by quantitative ^{19}F NMR spectroscopy analysis of the crude reaction mixture with 4-fluorotoluene (15 µL, 0.136 mmol) as internal standard.

^{19}F NMR (471 MHz, $CDCl_3$) δ/ppm = -112.36 (d, *J* = 55.8 Hz, 2F).

The analytical data are in accordance with those reported in the literature.[14]

4-(Difluoromethyl)toluene (2s)



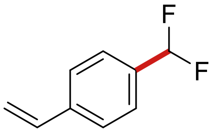
2s

The General Procedure GP2 was followed using 4-bromotoluene (**1s**, 17.1 mg, 12 µL, 0.10 mmol). **2s** (9%) was detected by quantitative ^{19}F NMR spectroscopy.

^{19}F NMR (471 MHz, $CDCl_3$) δ/ppm = -109.33 (d, *J* = 56.7 Hz, 2F).

The analytical data are in accordance with those reported in the literature.[6]

1-(Difluoromethyl)-4-vinylbenzene (2t)



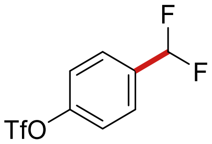
2t

The General Procedure GP2 was followed using 1-bromo-4-vinylbenzene (**1t**, 18.3 mg, 13 µL, 0.10 mmol). **2t** (8%) was detected by quantitative ^{19}F NMR spectroscopy.

^{19}F NMR (471 MHz, $CDCl_3$) δ/ppm = -110.05 (d, *J* = 56.9 Hz, 2F).

The analytical data are in accordance with those reported in the literature.[11]

4-(Difluoromethyl)phenyl trifluoromethanesulfonate (2v)



2v

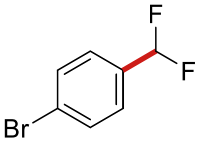
The General Procedure GP1 was followed using 4-iodophenyl trifluoromethanesulfonate (**1v**, 70.4 mg, 0.20 mmol). Purification by column chromatography on silica gel (pentane) yielded **2v** (28.5 mg, 0.10 mmol, 52%) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ/ppm = 7.63 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 8.4 Hz, 2H), 6.68 (t, *J* = 56.1 Hz, 1H).
^{19}F NMR (471 MHz, $CDCl_3$) δ/ppm = -72.75 (s, 3F), -111.54 (d, *J* = 56.1 Hz, 2F).
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ/ppm = 151.0 (t, *J* = 2.3 Hz), 134.8 (t, *J* = 23.1 Hz), 128.0 (t, *J* = 6.1 Hz), 122.0, 118.8 (q, *J* = 320.7 Hz), 113.6 (t, *J* = 240.0 Hz).
HR-MS (APCI): *m/z* calcd for $C_8H_5F_5O_3S^+$ $[M]^+$ 275.9874, found 275.9866.

IR (ATR): ṽ/cm^{-1} = 1505, 1421, 1375, 1208, 1135, 1075, 1033, 879, 817, 738.

TLC: R_f = 0.17 (pentane).

1-(Difluoromethyl)-4-bromobenzene (2w)



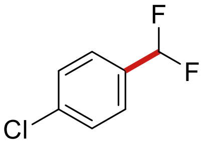
2w

The General Procedure GP2 was followed using 1-bromo-4-iodobenzene (**1w**, 28.3 mg, 0.10 mmol). **2w** (64%) 1,4-bis(difluoromethyl)benzene (traces) were detected by quantitative ^{19}F NMR spectroscopy. The structure of the product was further confirmed by GC-MS analysis.

^{19}F NMR (471 MHz, $CDCl_3$) δ/ppm = -110.72 (d, *J* = 56.4 Hz, 2F).

The analytical data are in accordance with those reported in the literature.[15]

1-Chloro-4-(difluoromethyl)benzene (2x)



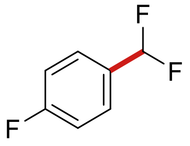
2x

The General Procedure GP2 was followed using 1-chloro-4-iodobenzene (**1x**, 23.8 mg, 0.10 mmol). **2x** (36%) and 1,4-bis(difluoromethyl)benzene (traces) were detected by quantitative ^{19}F NMR spectroscopy.

^{19}F NMR (471 MHz, $CDCl_3$) δ/ppm = -110.44 (d, *J* = 55.8 Hz, 2F).

The analytical data are in accordance with those reported in the literature.[12]

1-(Difluoromethyl)-4-fluorobenzene (2y)



2y

The General Procedure GP2 was followed using 1-fluoro-4-iodobenzene (**1y**, 22.2 mg, 12 µL, 0.10 mmol). **2y** (60%) was detected by quantitative ^{19}F NMR spectroscopy.

^{19}F NMR (471 MHz, $CDCl_3$) δ/ppm = -109.11 – -109.40 (m, 3F).

The analytical data are in accordance with those reported in the literature.[16]

Reactions with *in situ*-formed (SIPr)AgCF$_2$H

with (SIPr)AgCl (0.25 equiv.)

Inside a nitrogen-filled glovebox, a Schlenk-tube was charged with Ni(cod)$_2$ (5.5 mg, 20 µmol, 10.0 mol%), Xantphos (17.4 mg, 30 µmol, 15.0 mol%) and toluene (2.0 mL) and the mixture was stirred for 5 min at r.t. Afterwards, 2-iodonaphthalene (**1h**, 50.8 mg, 0.20 mmol, 1.00 equiv.) was added. Subsequently, (SIPr)AgCl (26.7 mg, 50 µmol, 0.25 equiv.), sodium *tert*-butoxide (38.4 mg, 0.40 mmol, 2.00 equiv.) and difluoromethyl(trimethyl)silane (49.7 mg, 57 µL, 0.40 mmol, 2.00 equiv.) were added, the Schlenk-tube sealed, removed from the glovebox and the mixture was heated to 60 °C for 16 h. After cooling to r.t., trifluorotoluene (15 µL, 0.12 mmol) was added. An aliquot (0.15 mL) was removed and filtered through a short plug of silica gel, which was rinsed with CDCl$_3$ (0.65 mL). (Difluoromethyl)naphthalene (**2h**) was detected in < 10% yield by ^{19}F NMR spectroscopy.

with (SIPr)AgCl (1.10 equiv.)

Inside a nitrogen-filled glovebox, a Schlenk-tube was charged with Ni(cod)$_2$ (5.5 mg, 20 µmol, 10.0 mol%), Xantphos (17.4 mg, 30 µmol, 15.0 mol%) and toluene (2.0 mL) and the mixture was stirred for 5 min at r.t. Afterwards, 2-iodonaphthalene (**1h**, 50.8 mg, 0.20 mmol, 1.00 equiv.) was added. Subsequently, (SIPr)AgCl (117 mg, 0.22 mmol, 1.10 equiv.), sodium *tert*-butoxide (38.4 mg, 0.40 mmol, 2.00 equiv.) and difluoromethyl(trimethyl)silane (49.7 mg, 57 µL, 0.40 mmol, 2.00 equiv.) were added, the Schlenk-tube sealed, removed from the glovebox and the mixture was heated to 60 °C for 16 h. The reaction mixture was diluted with DCM (ca. 2 mL) and filtered through a pad of Celite, which was thoroughly rinsed with DCM (ca. 15 mL). H_2O (20 mL) was added, the phases separated and the aqueous phase extracted with DCM (3 x 20 mL). The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the crude product by column chromatography on silica gel yielded 2-(difluoromethyl)naphthalene (**2h**, 12.2 mg, 0.07 mmol, 34%) as a white solid.

one-pot/two-step reaction

Inside a nitrogen-filled glovebox, a Schlenk-tube was charged with (SIPr)AgCl (117 mg, 0.22 mmol, 1.10 equiv.), sodium *tert*-butoxide (38.4 mg, 0.40 mmol, 2.00 equiv.), difluoromethyl(trimethyl)silane (49.7 mg, 57 µL, 0.40 mmol, 2.00 equiv.) and toluene (1.0 mL) or THF (1.0 mL). The reaction mixture was stirred for 2 h at r.t. A separate vial was charged with Ni(cod)$_2$ (5.5 mg, 20 µmol, 10.0 mol%), Xantphos (17.4 mg, 30 µmol, 15.0 mol%) and toluene (1.0 mL) or THF (1.0 mL) and the resulting solution was stirred for 5 min at r.t. Afterwards, 2-iodonaphthalene (**1h**, 50.8 mg, 0.20 mmol, 1.00 equiv.) was added and the solution was transferred to the Schlenk-tube via syringe. The Schlenk-tube was sealed, removed from the glovebox and the mixture was heated to 60 °C for 16 h. The reaction mixture was diluted with DCM (ca. 2 mL) and filtered through a pad of Celite, which was thoroughly rinsed with DCM (ca. 15 mL). H_2O (20 mL) was added, the phases separated and the aqueous phase extracted with DCM (3 x 20 mL). The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the crude product by column chromatography on silica gel yielded 2-(difluoromethyl)naphthalene (**2h**, in toluene: 9.5 mg, 0.05 mmol, 27%; in THF: 22.5 mg, 0.13 mmol, 63%) as a white solid.

Reactions in the presence of styrene and benzonitrile

Inside a nitrogen-filled glovebox, a Schlenk-tube was charged with Ni(cod)$_2$ (2.8 mg, 10 µmol, 10.0 mol%), Xantphos (8.7 mg, 15 µmol, 15.0 mol%) and toluene (1.0 mL) and the mixture was stirred for 5 min at r.t. Afterwards, methyl 4-iodobenzoate (**1a**, 26.2 mg, 0.10 mmol, 1.0 equiv.) was added. Subsequently, (SIPr)AgCF$_2$H (60 mg, 0.22 mmol, 1.10 equiv.) and styrene (5.2 mg, 6 µL, 50 µmol, 0.50 equiv.) or benzonitrile (5.2 mg, 5 µL, 50 µmol, 0.50 equiv.) were added, the Schlenk-tube sealed, removed from the glovebox and the mixture was heated to 60 °C for 16 h. After cooling to r.t., *n*-decane (10 µL) was added and the reaction mixture was analyzed by gas chromatography.

Entry	**Additive**	**Yield of 2a / %**
1	--	89
2	styrene	77
3	benzonitrile	54

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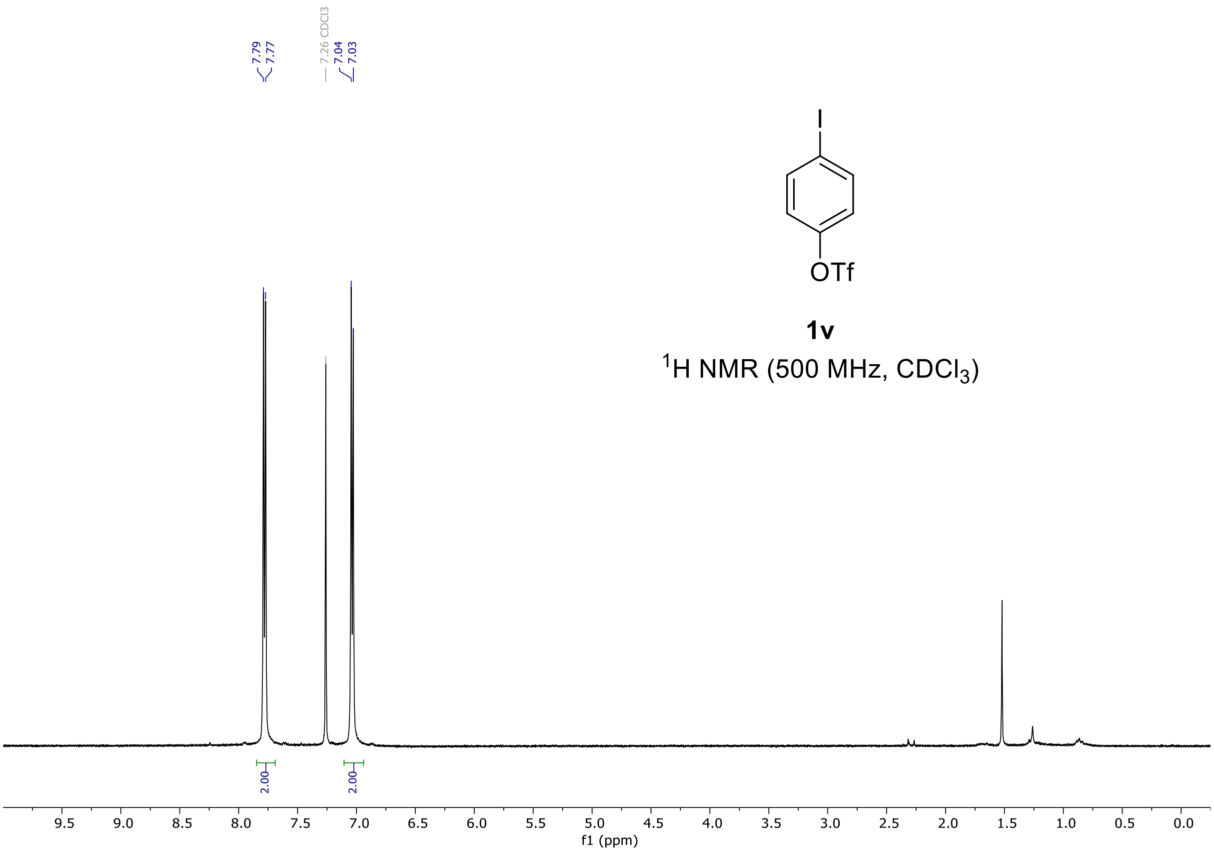
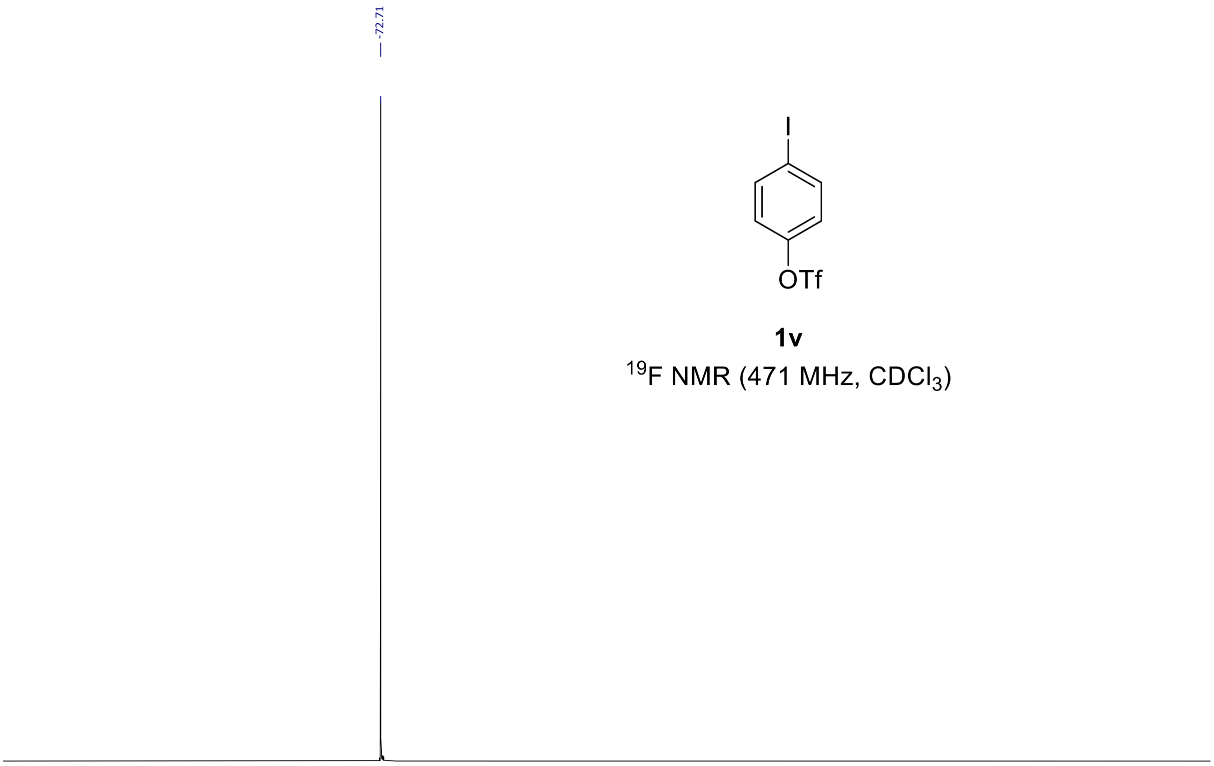
NMR Spectra



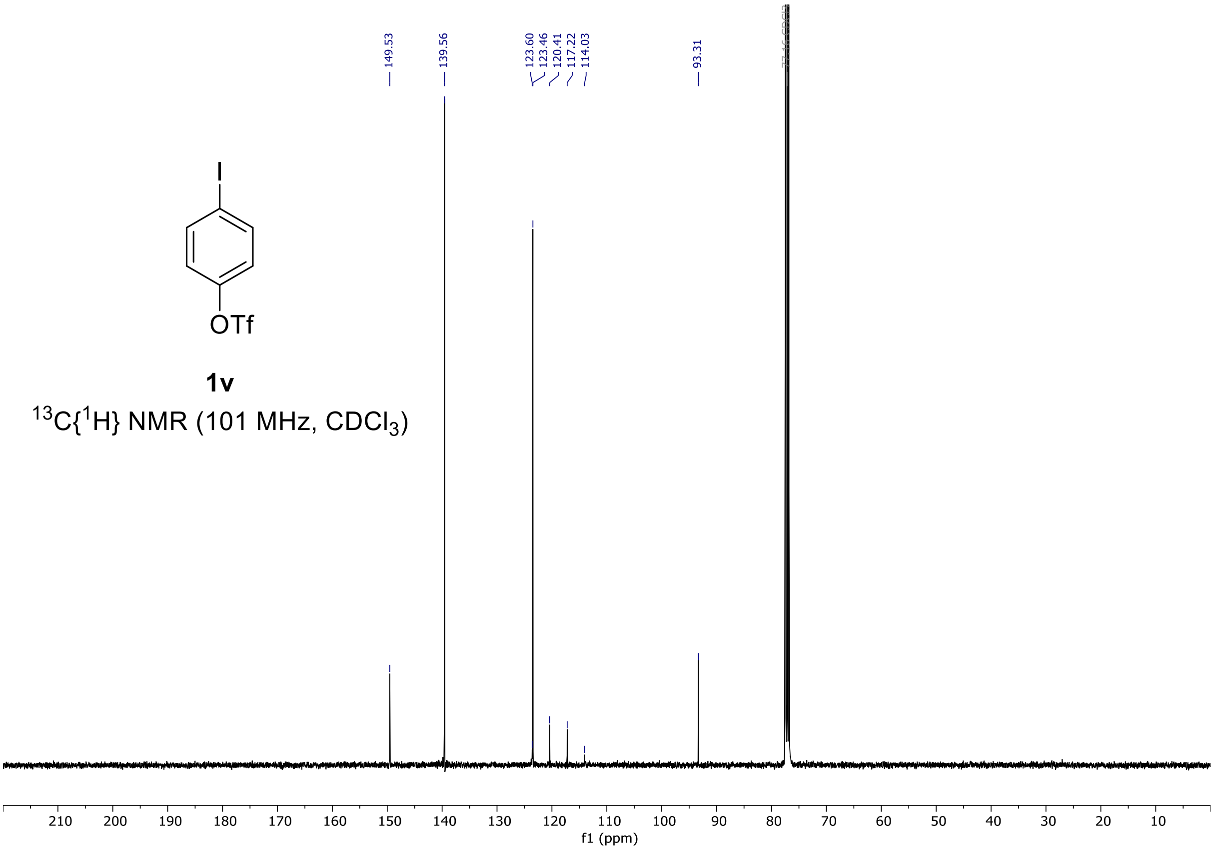
1v

^{1}H NMR (500 MHz, CDCl$_3$)



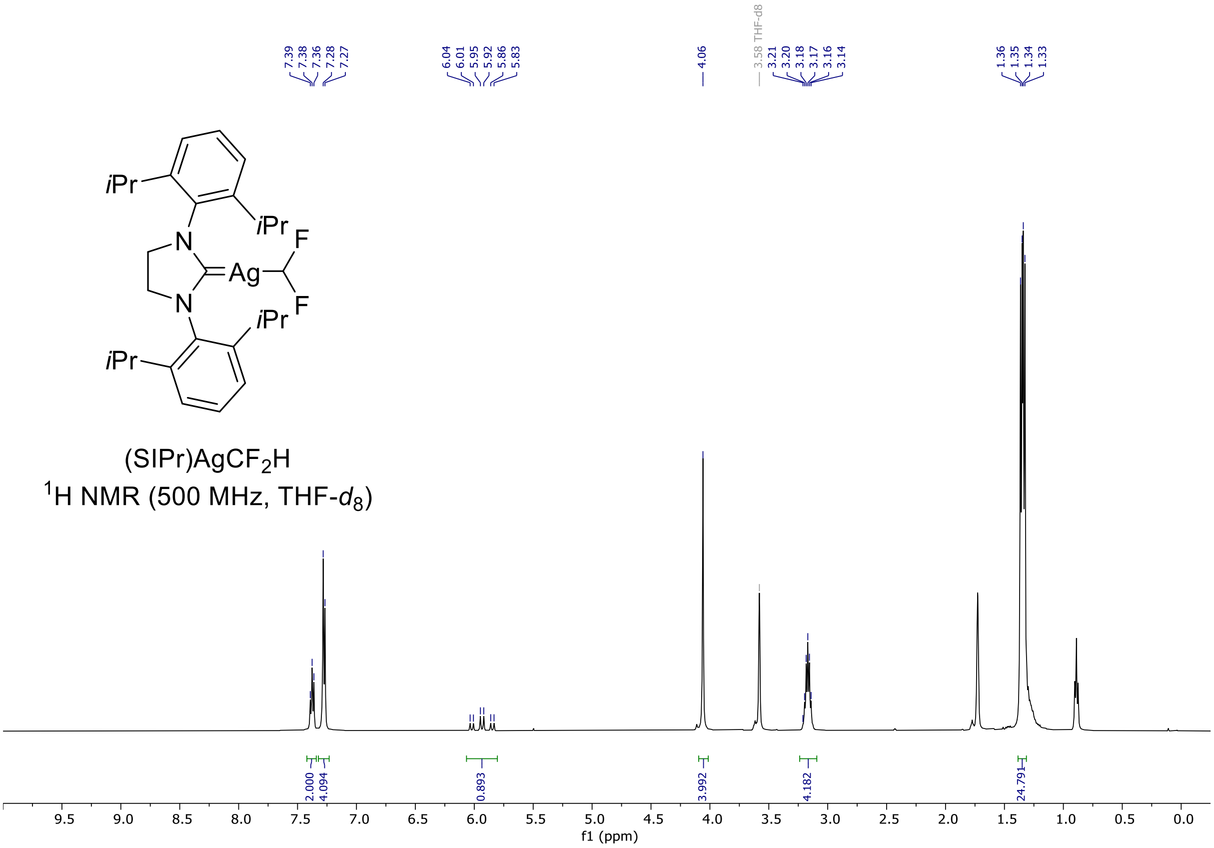
1v

^{19}F NMR (471 MHz, CDCl$_3$)



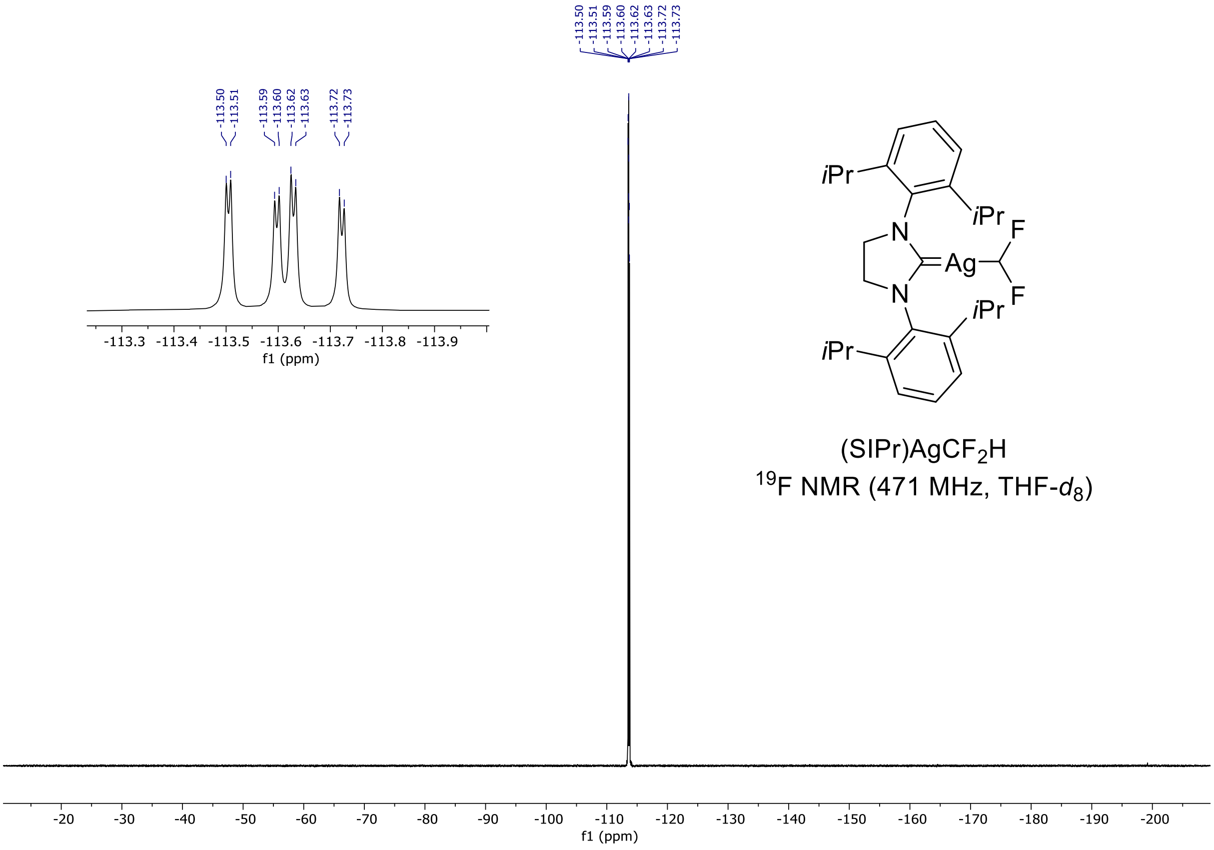
1v

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$)



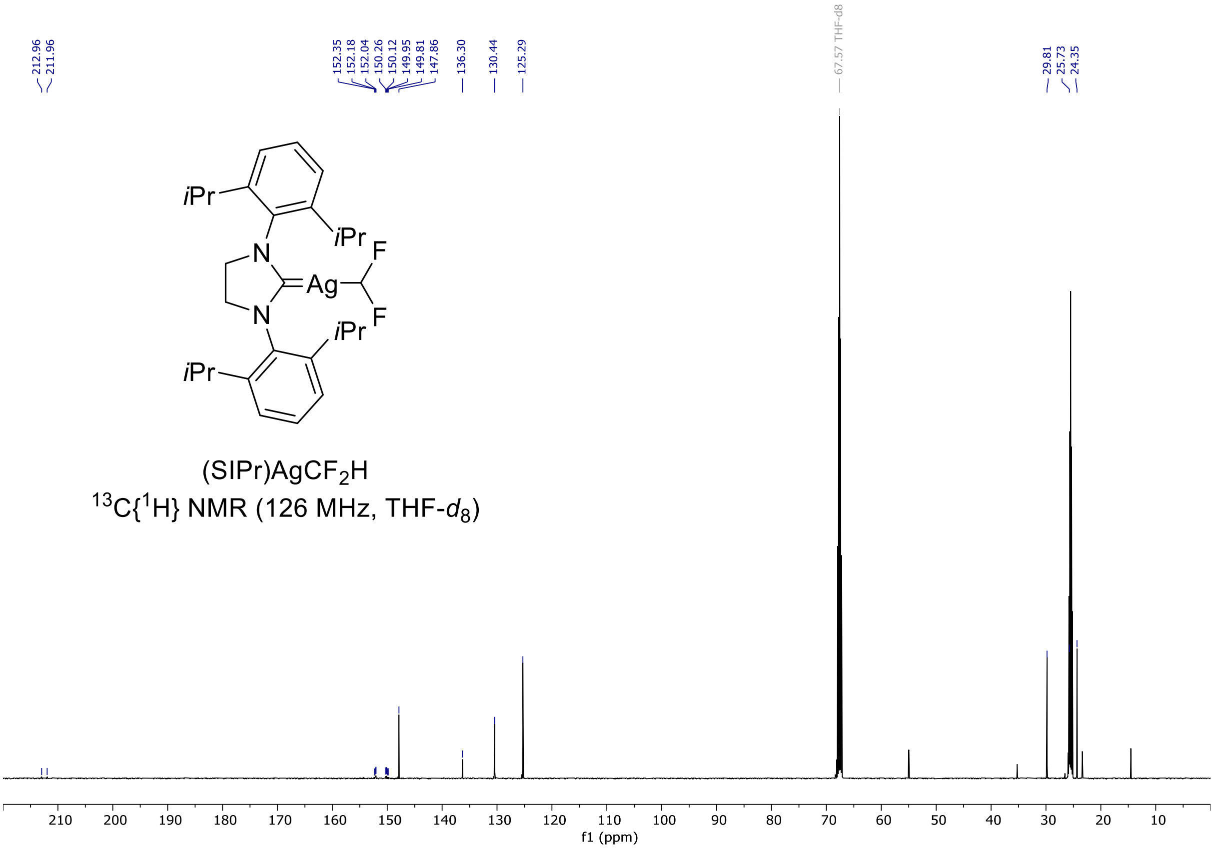
(SIPr)$AgCF_2H$

^1H NMR (500 MHz, THF-d_8)



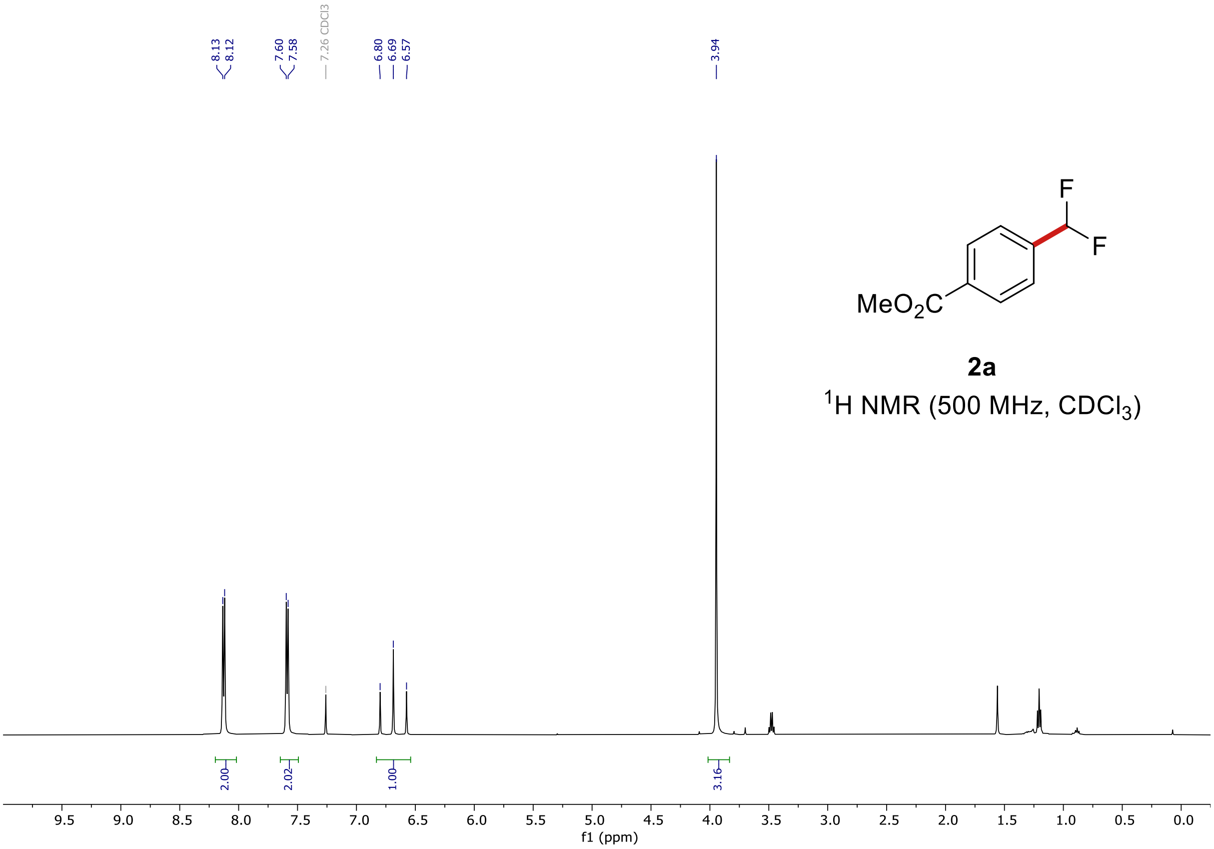
(SIPr)AgCF$_2$H

^{19}F NMR (471 MHz, THF-d_8)



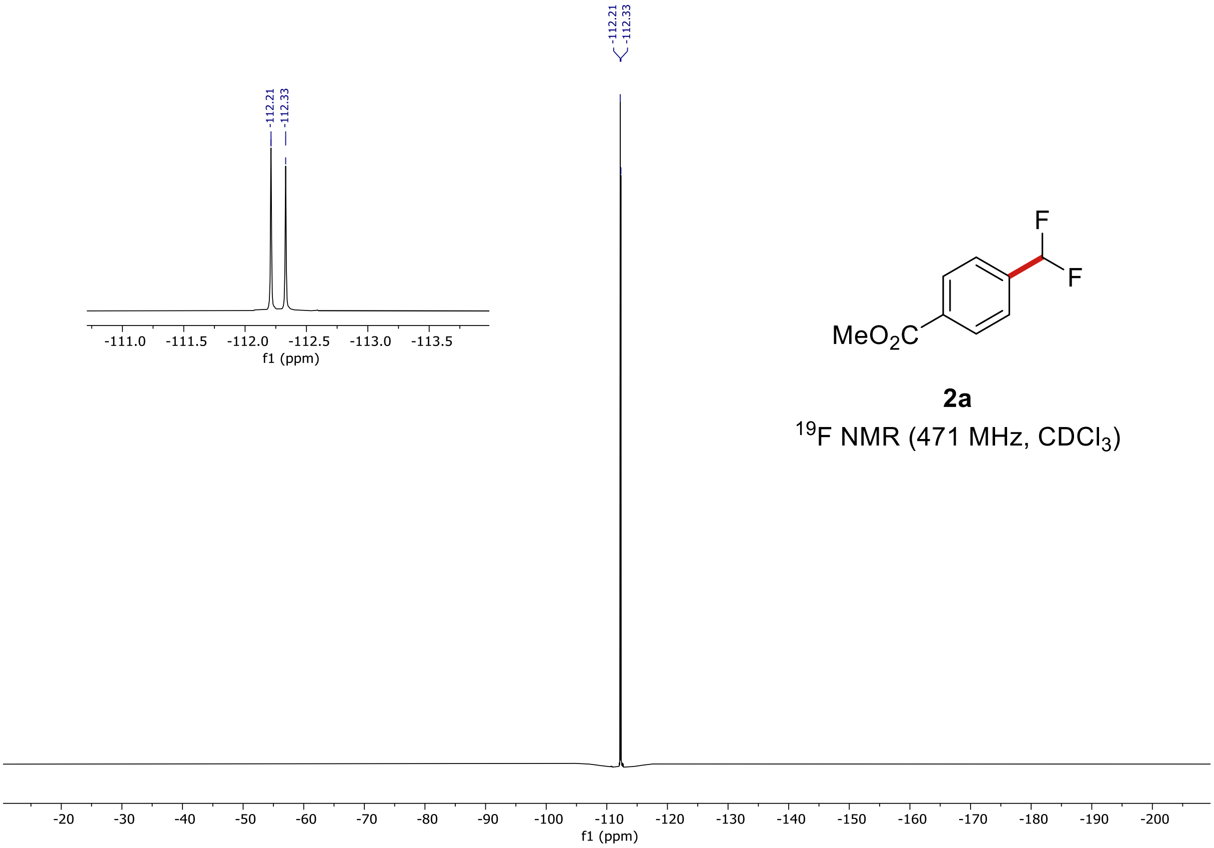
(SIPr)AgCF$_2$H

^{13}C{^{1}H} NMR (126 MHz, THF-d_8)



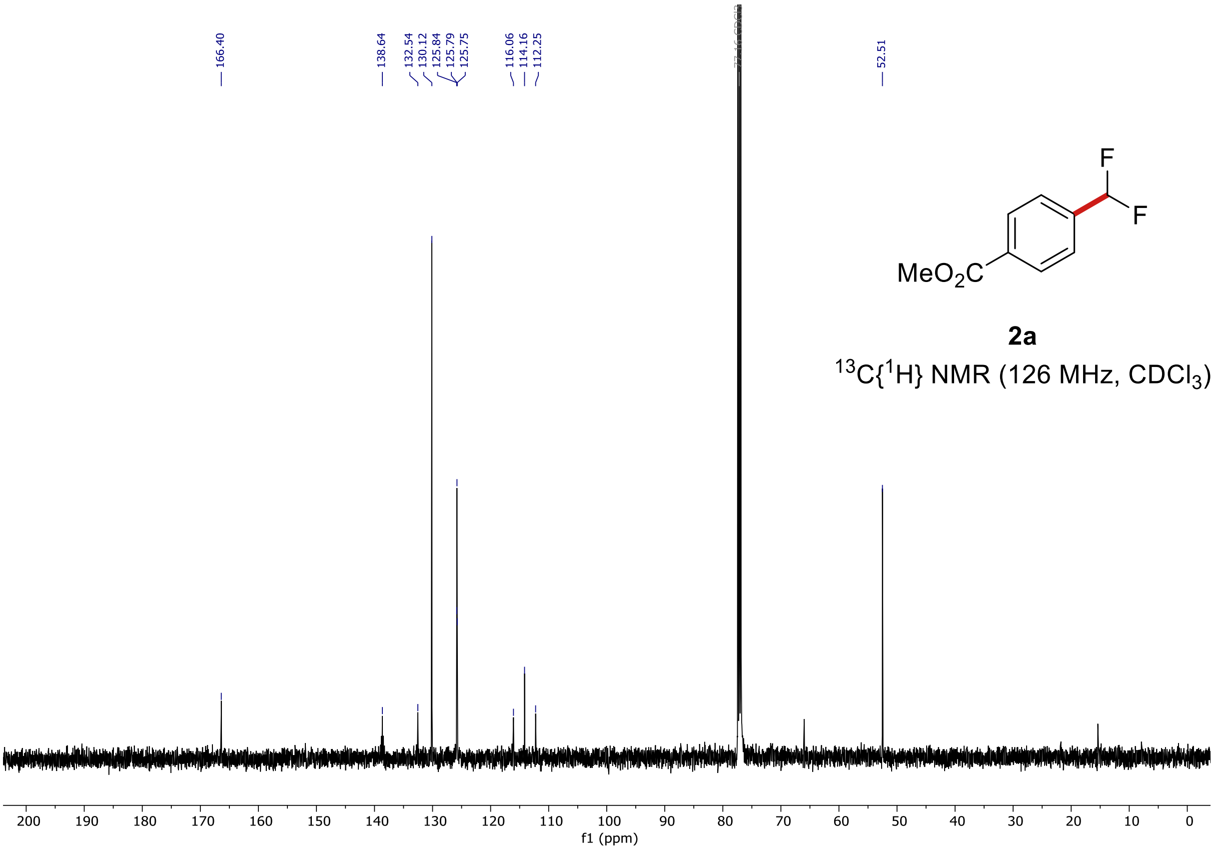
2a

^{1}H NMR (500 MHz, $CDCl_3$)



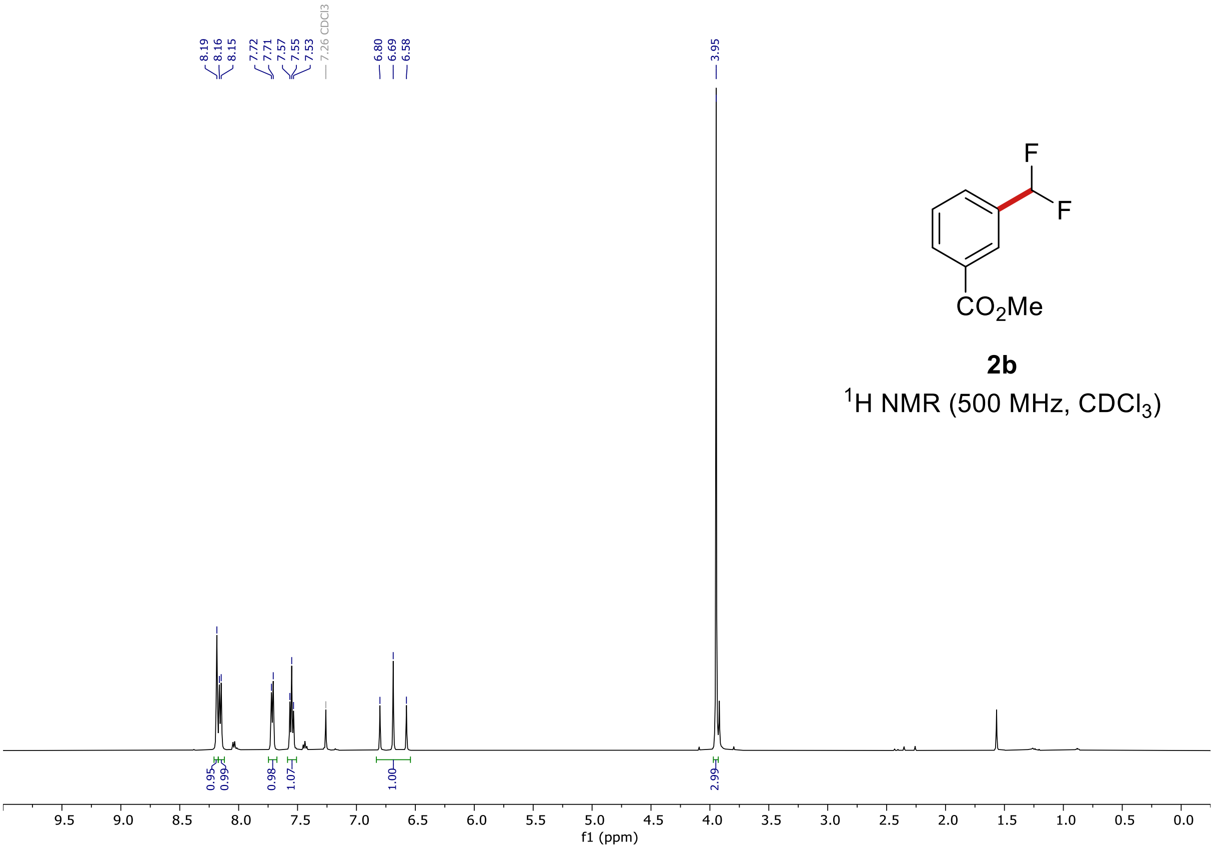
2a

^{19}F NMR (471 MHz, $CDCl_3$)



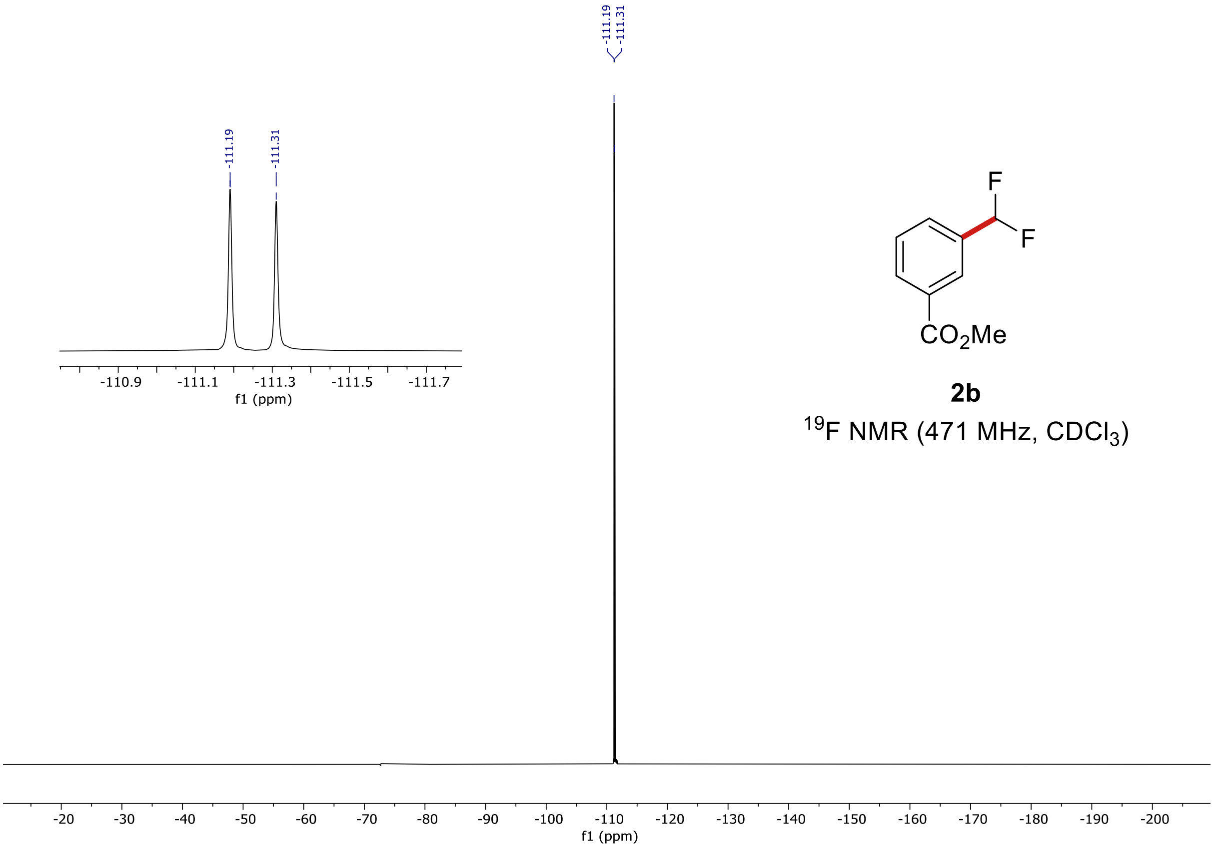
2a

$^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$)



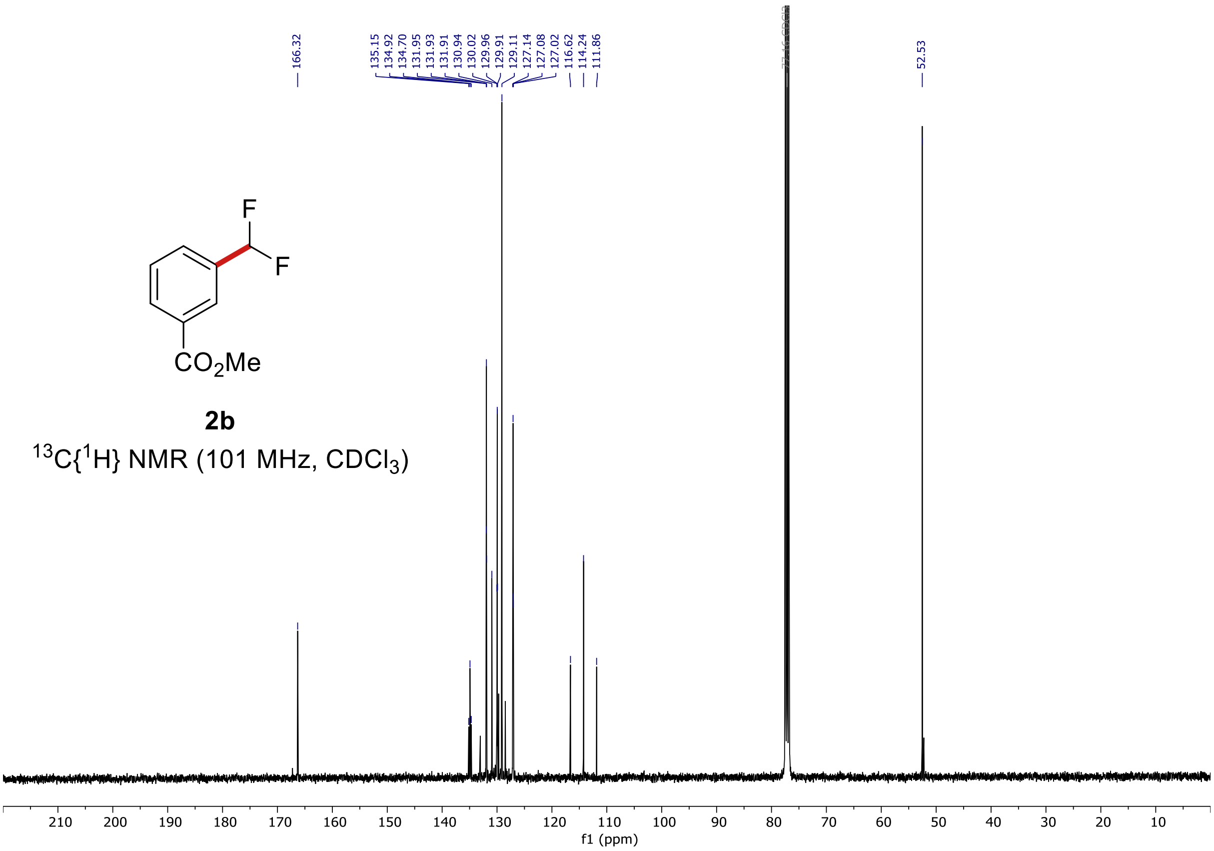
2b

^1H NMR (500 MHz, $CDCl_3$)



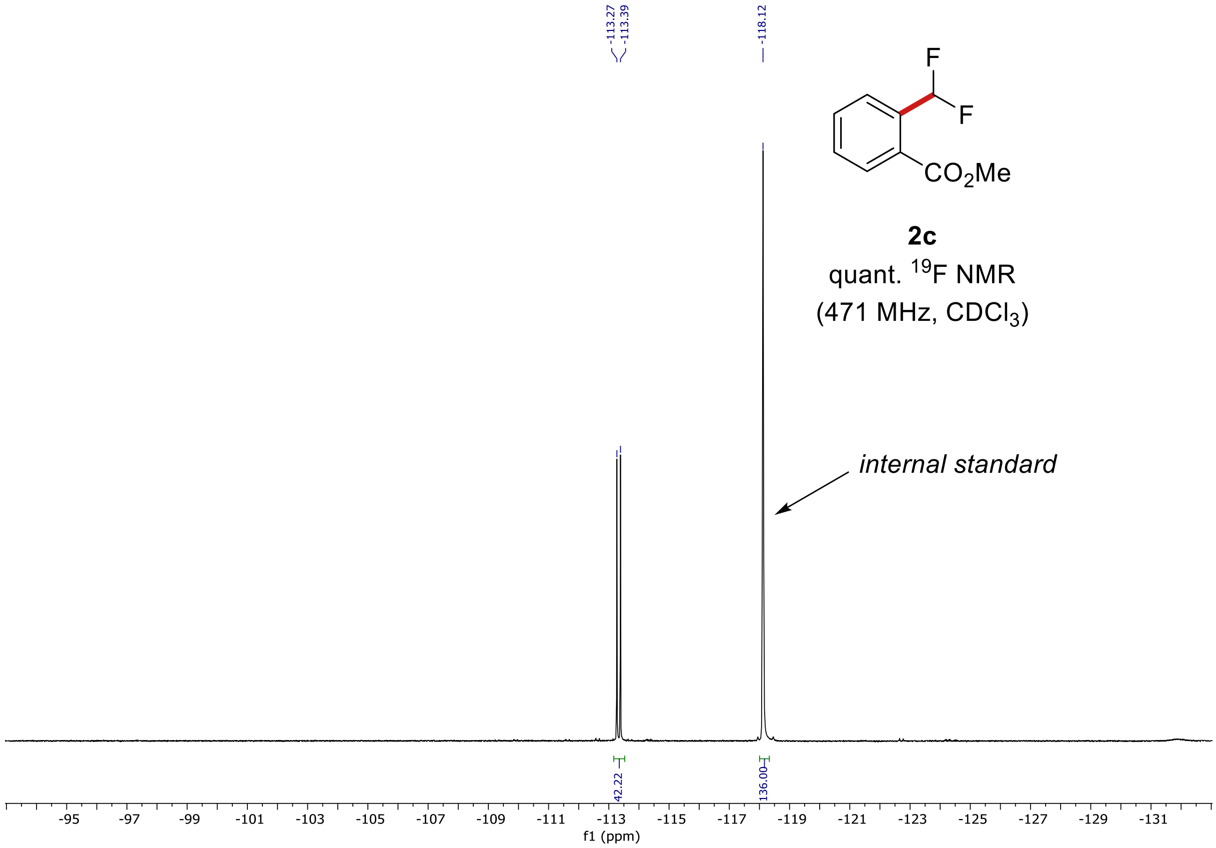
2b

^{19}F NMR (471 MHz, CDCl$_3$)

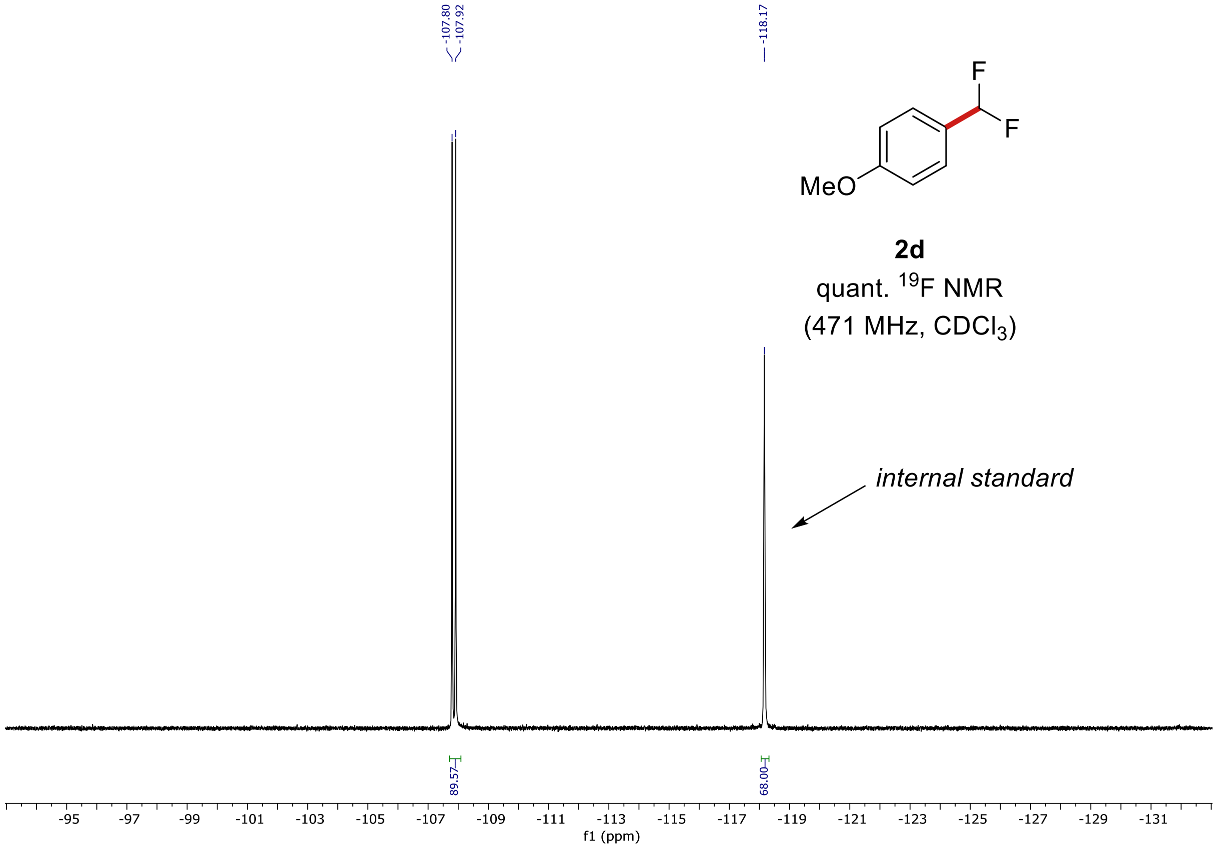


2b

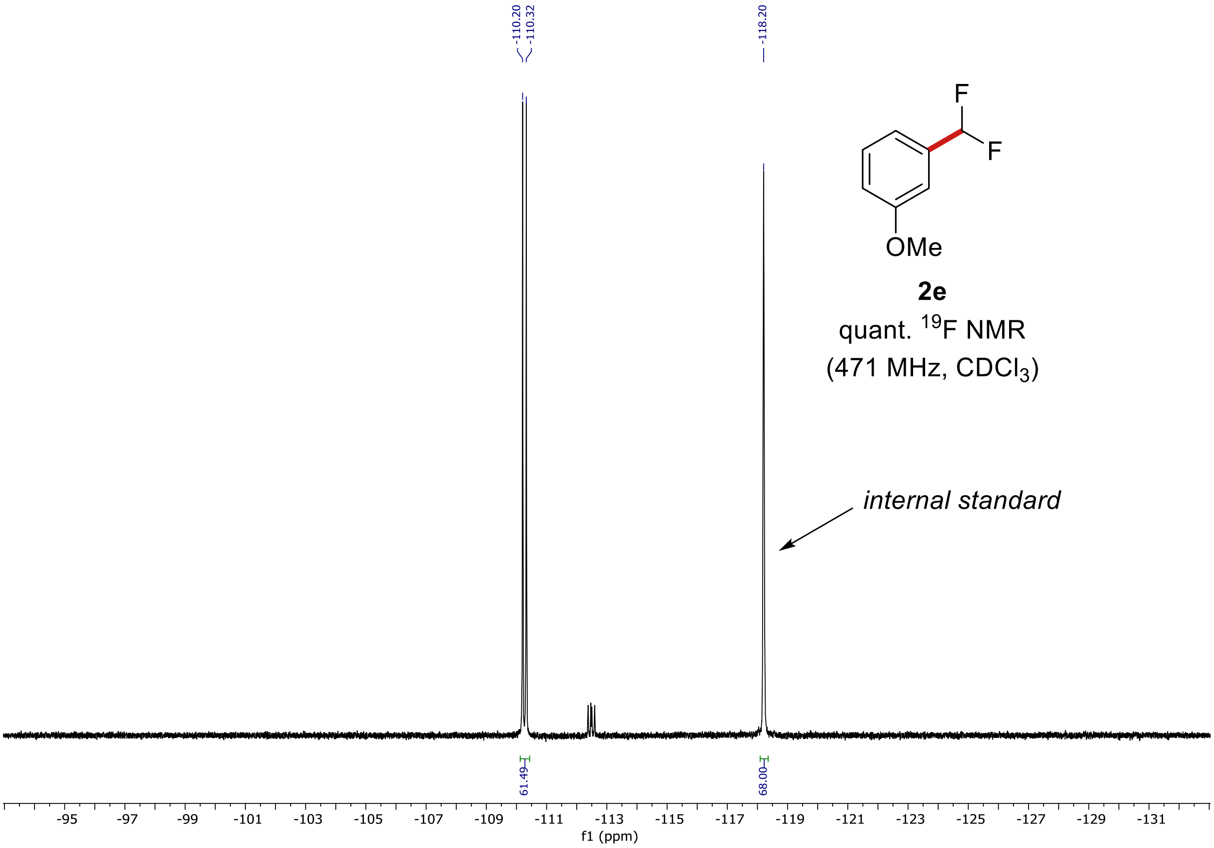
^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$)



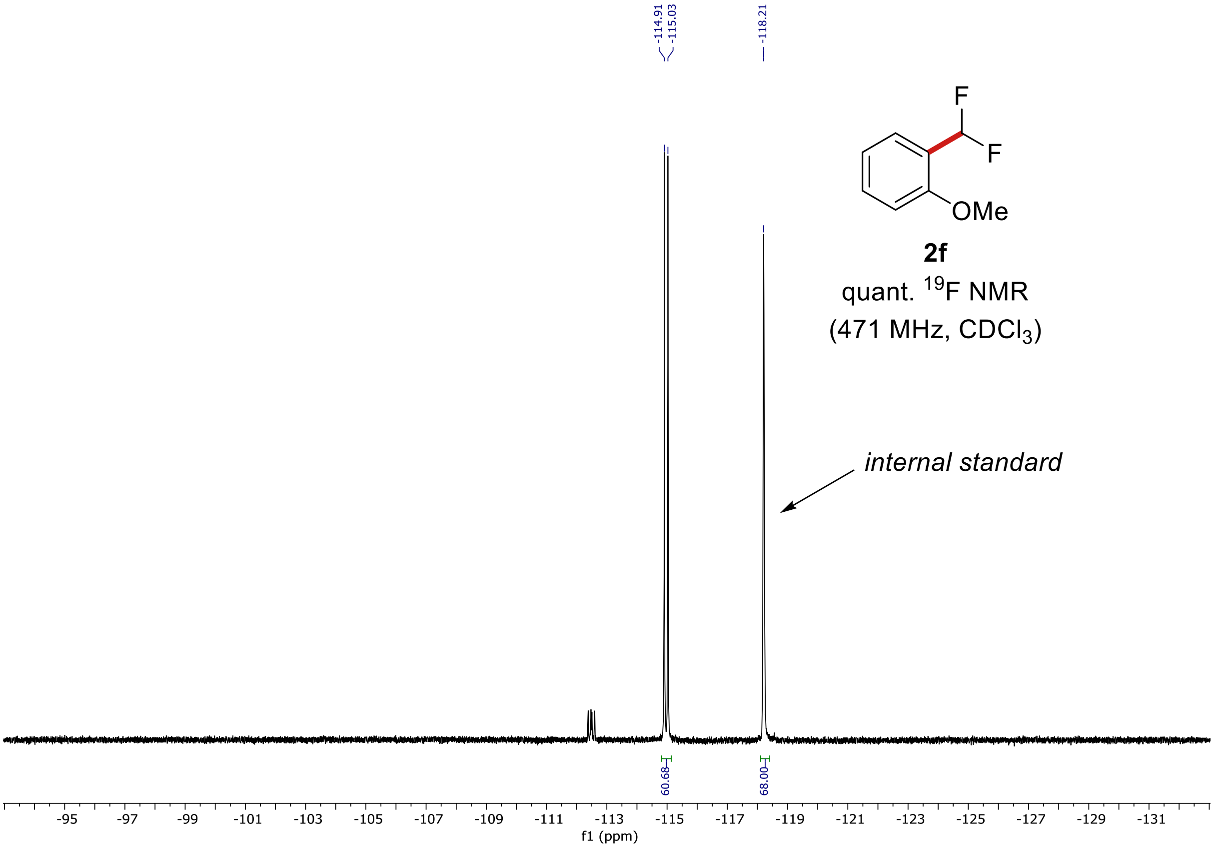
2c
quant. ^{19}F NMR
(471 MHz, $CDCl_3$)



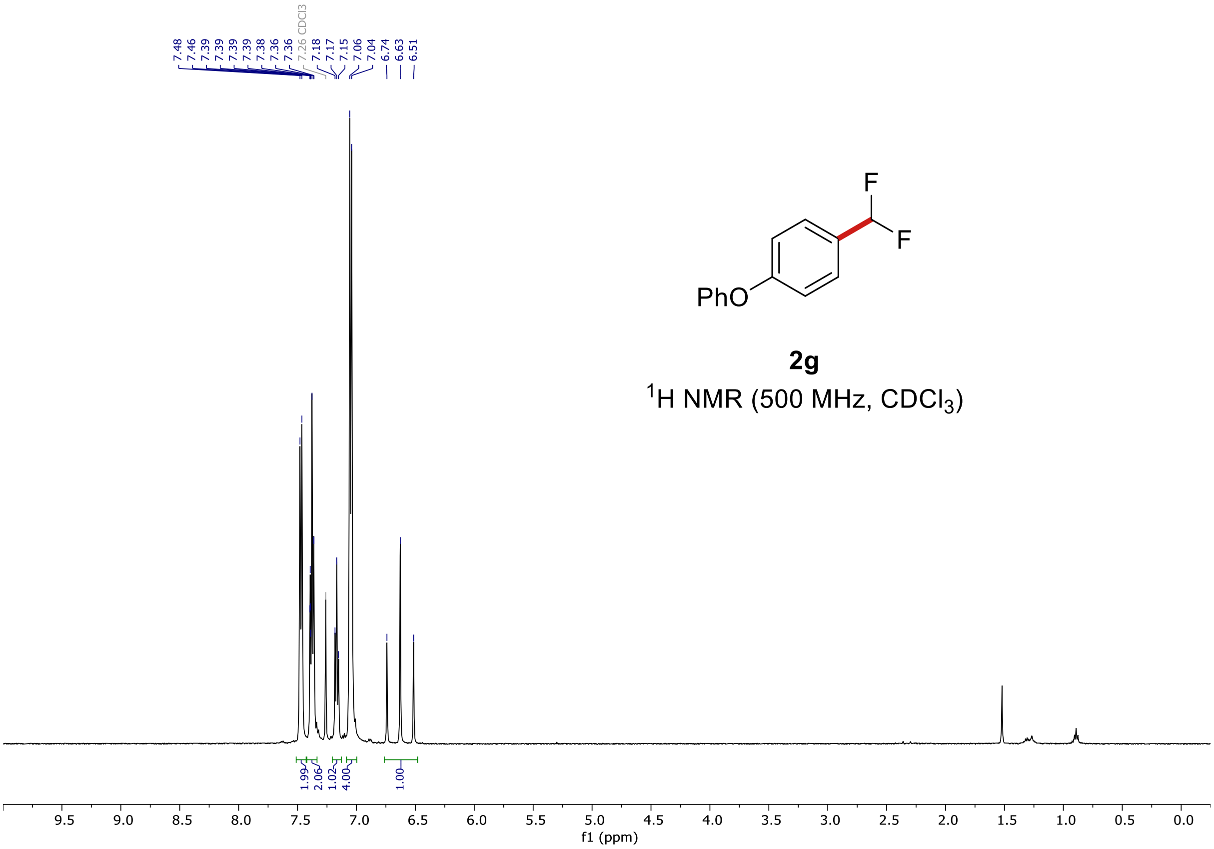
2d
quant. ^{19}F NMR
(471 MHz, $CDCl_3$)



2e
quant. ^{19}F NMR
(471 MHz, $CDCl_3$)

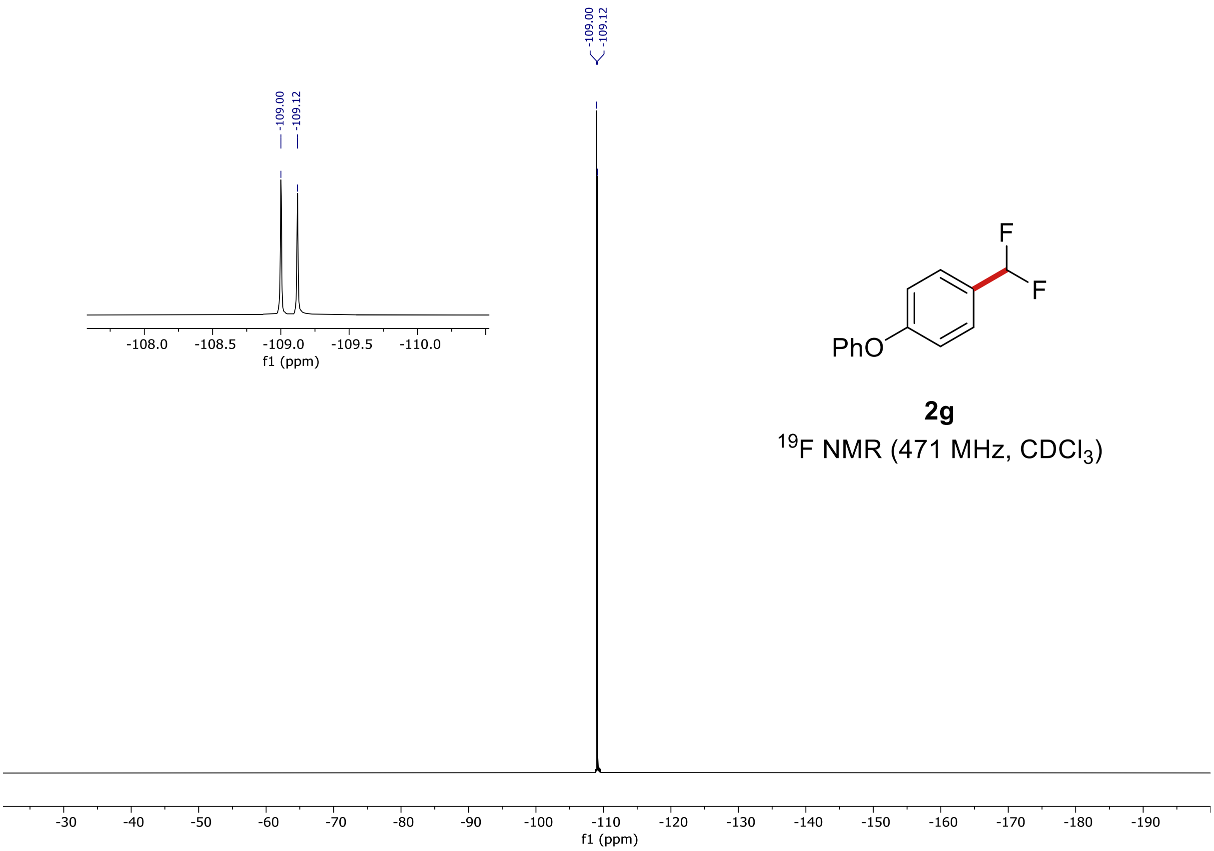


2f
quant. ^{19}F NMR
(471 MHz, $CDCl_3$)



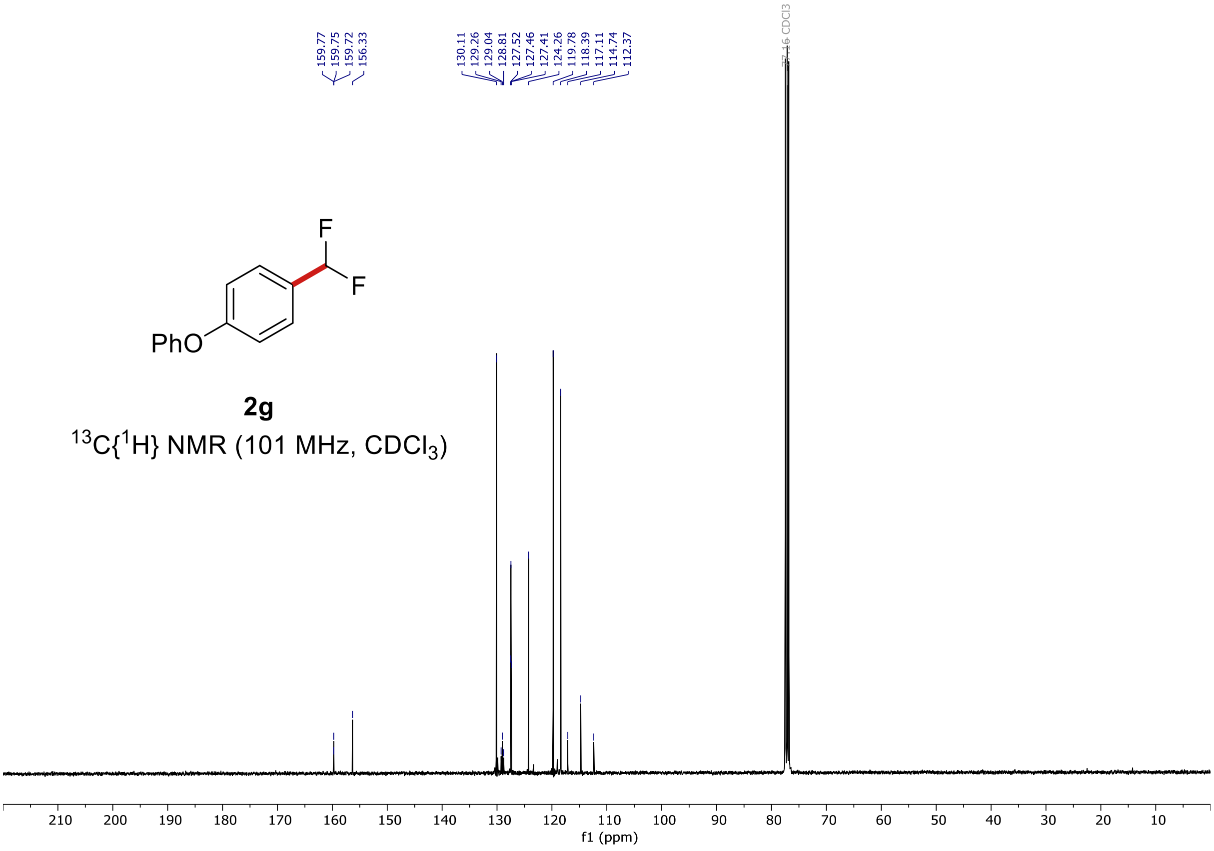
2g

^{1}H NMR (500 MHz, $CDCl_3$)



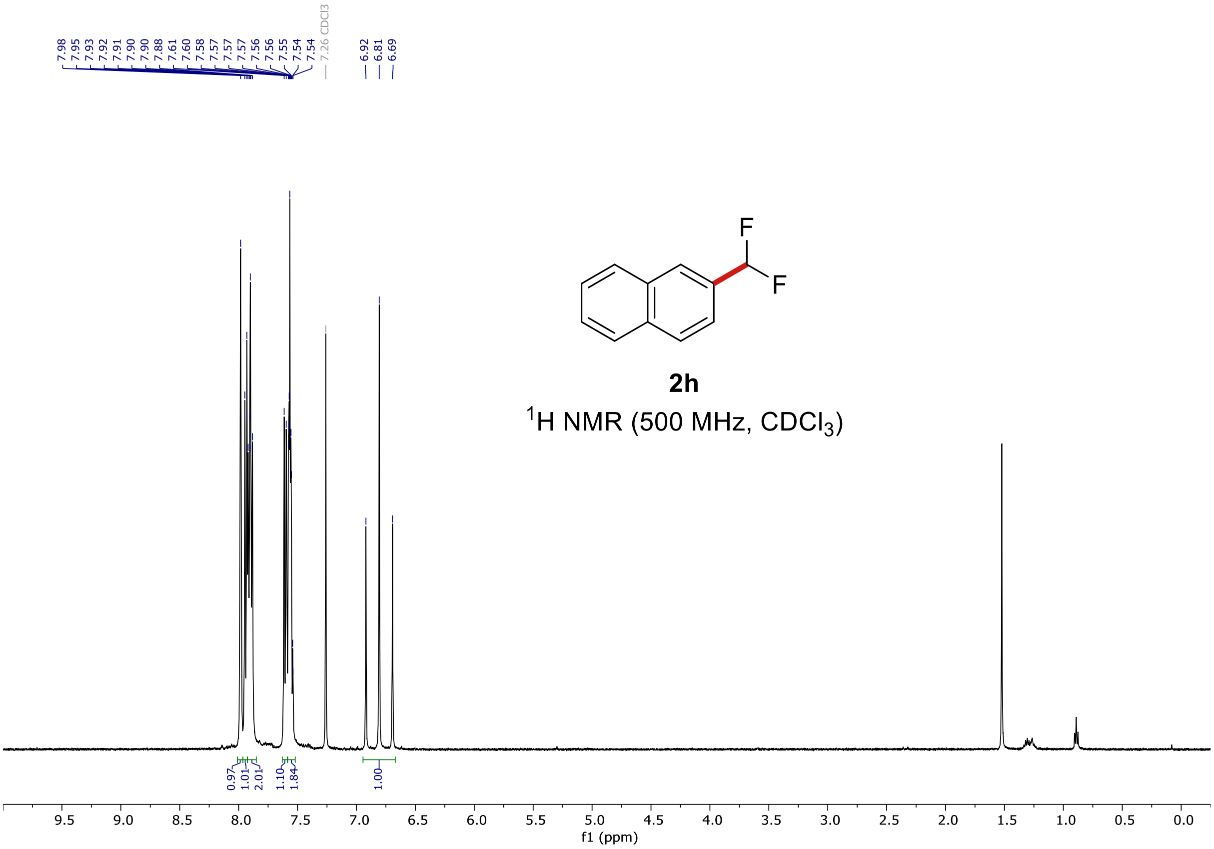
2g

^{19}F NMR (471 MHz, $CDCl_3$)



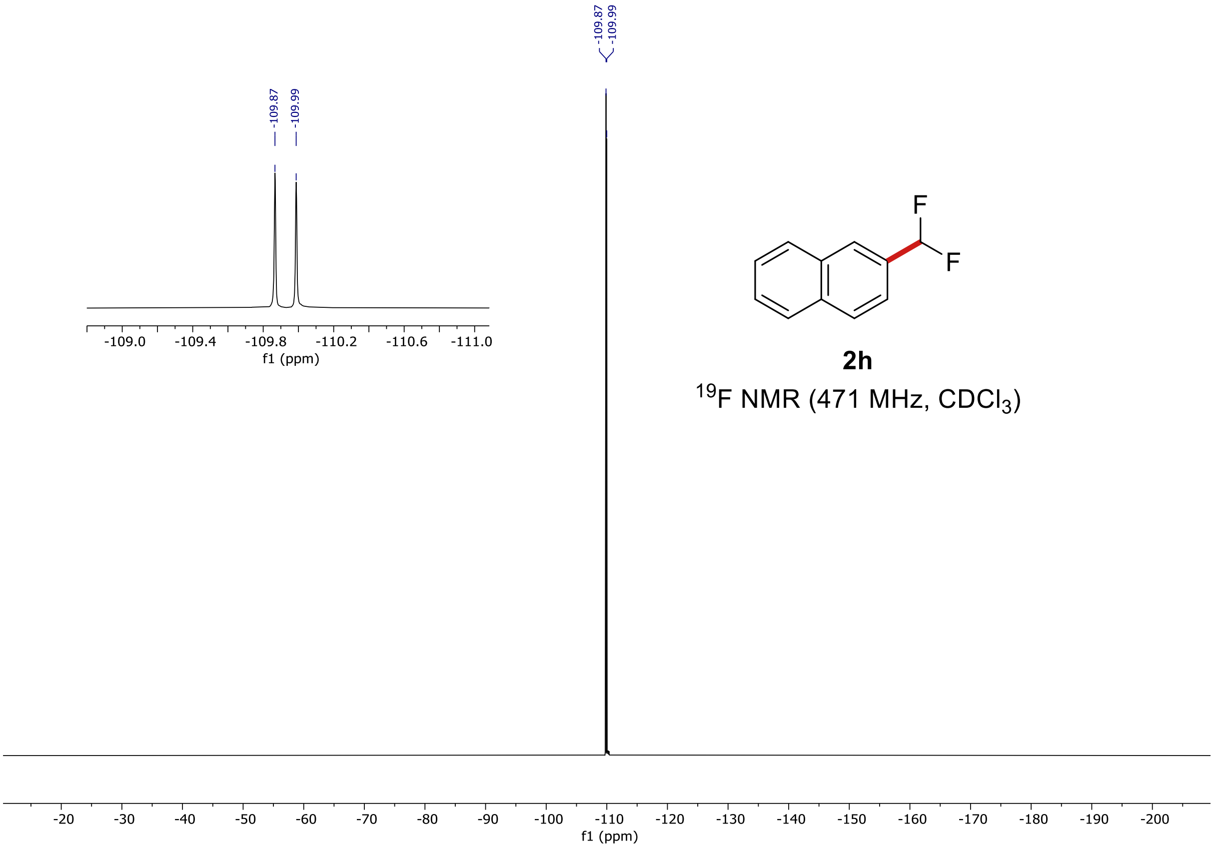
2g

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$)



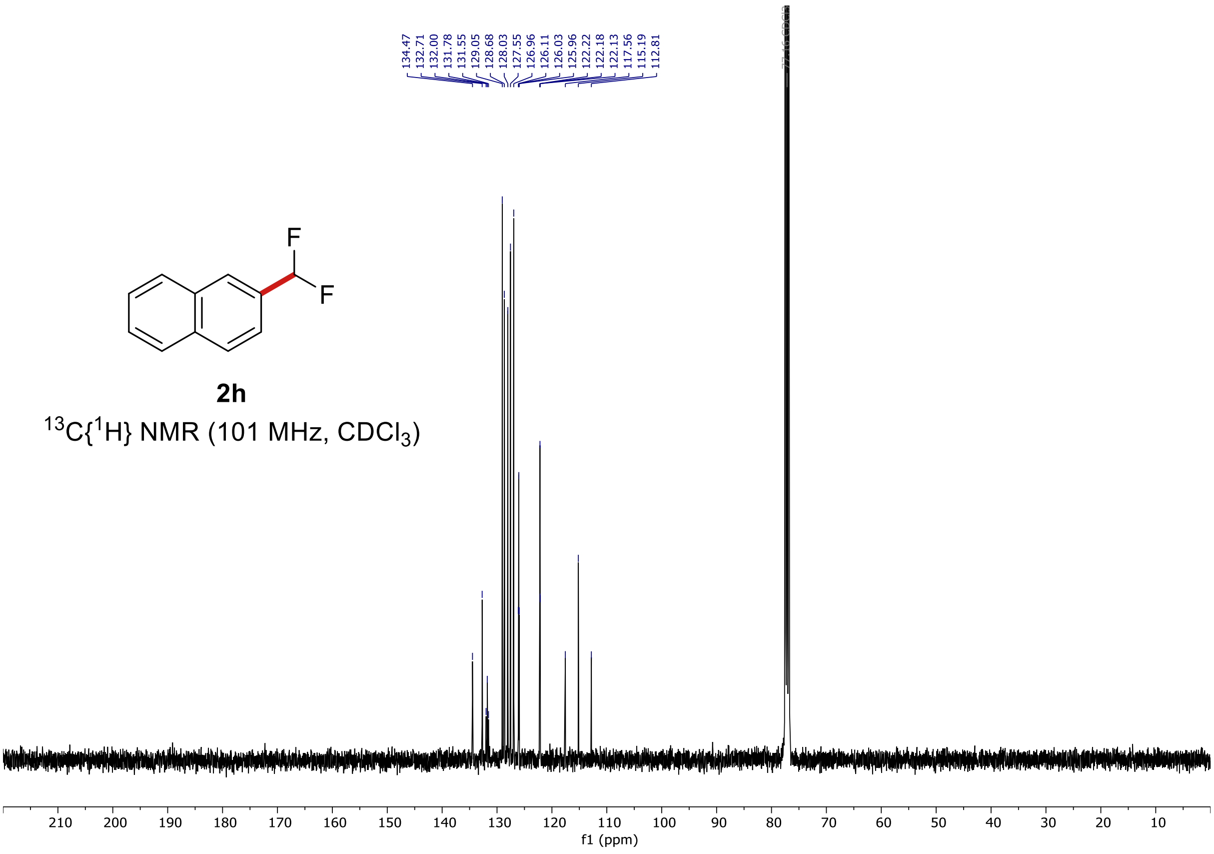
2h

^1H NMR (500 MHz, $CDCl_3$)



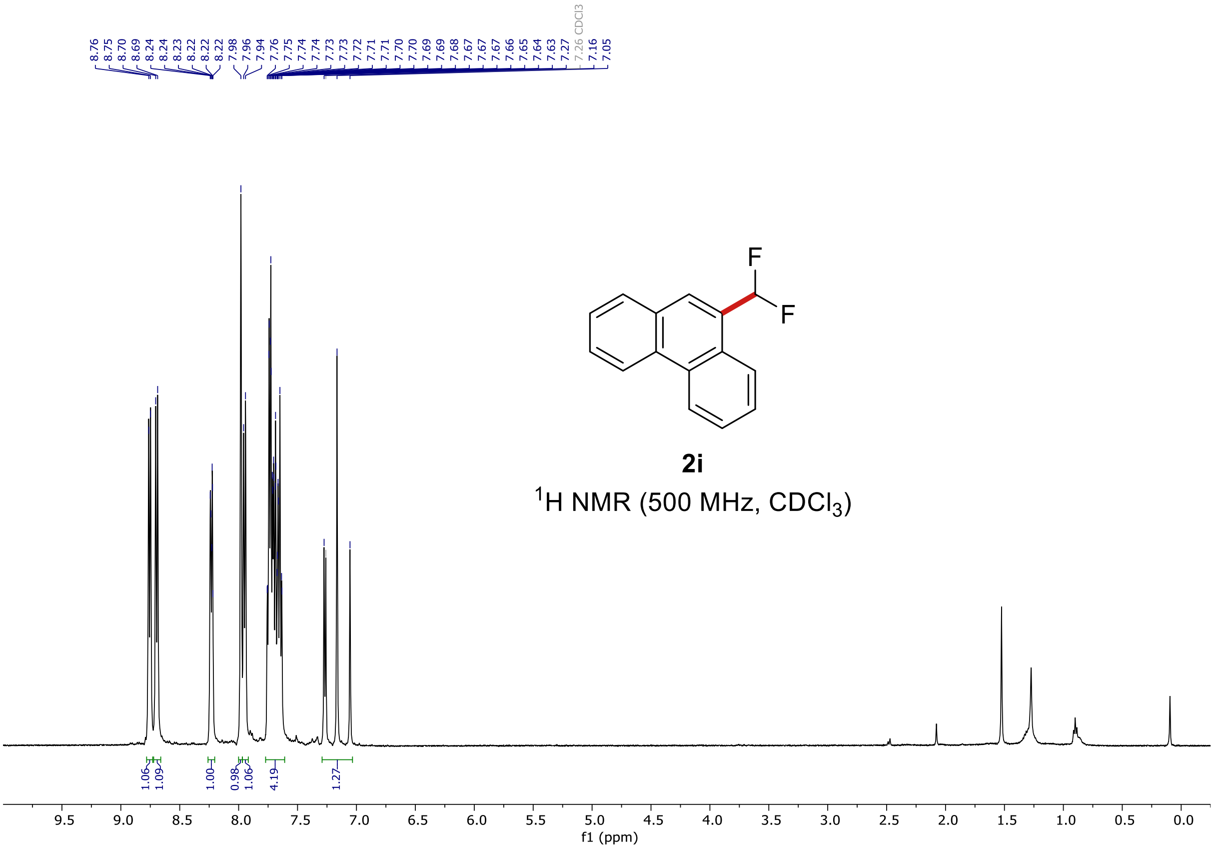
2h

^{19}F NMR (471 MHz, CDCl$_3$)



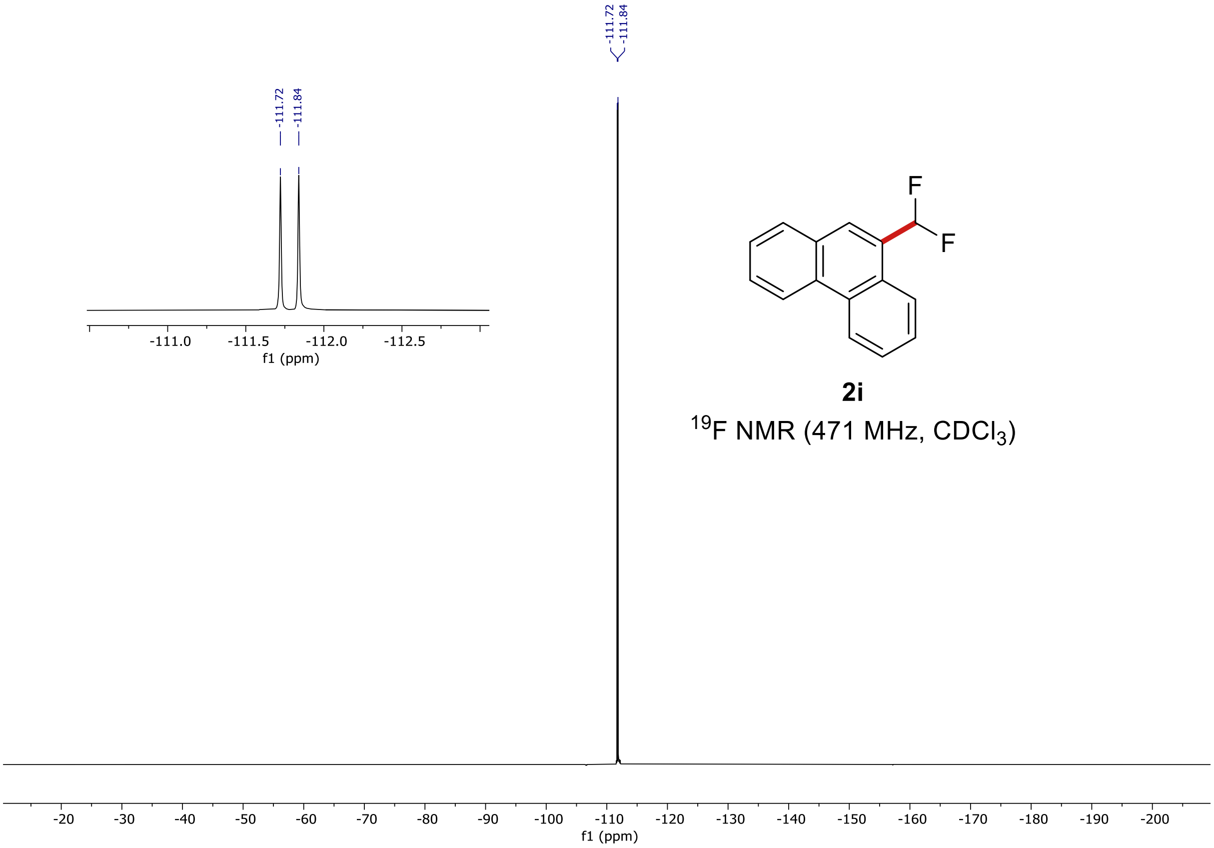
2h

^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$)



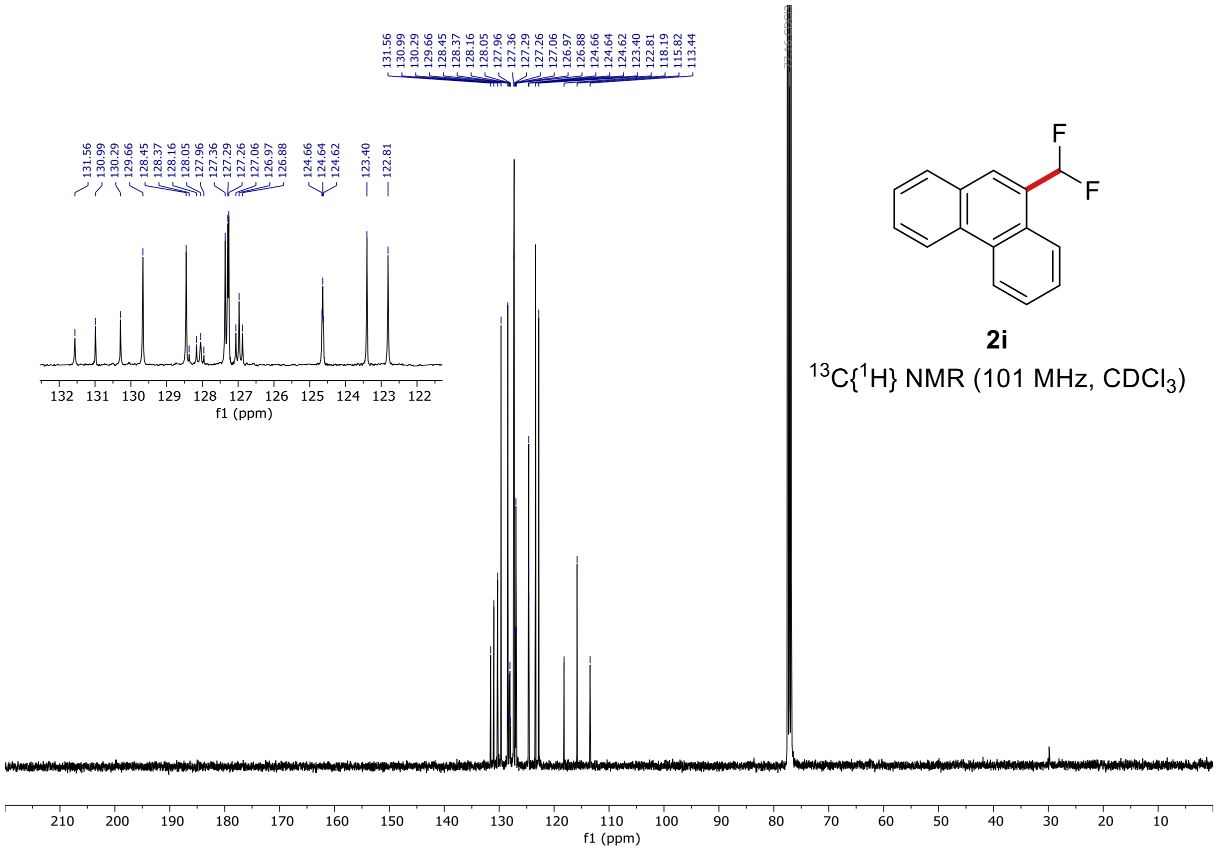
2i

^1H NMR (500 MHz, $CDCl_3$)



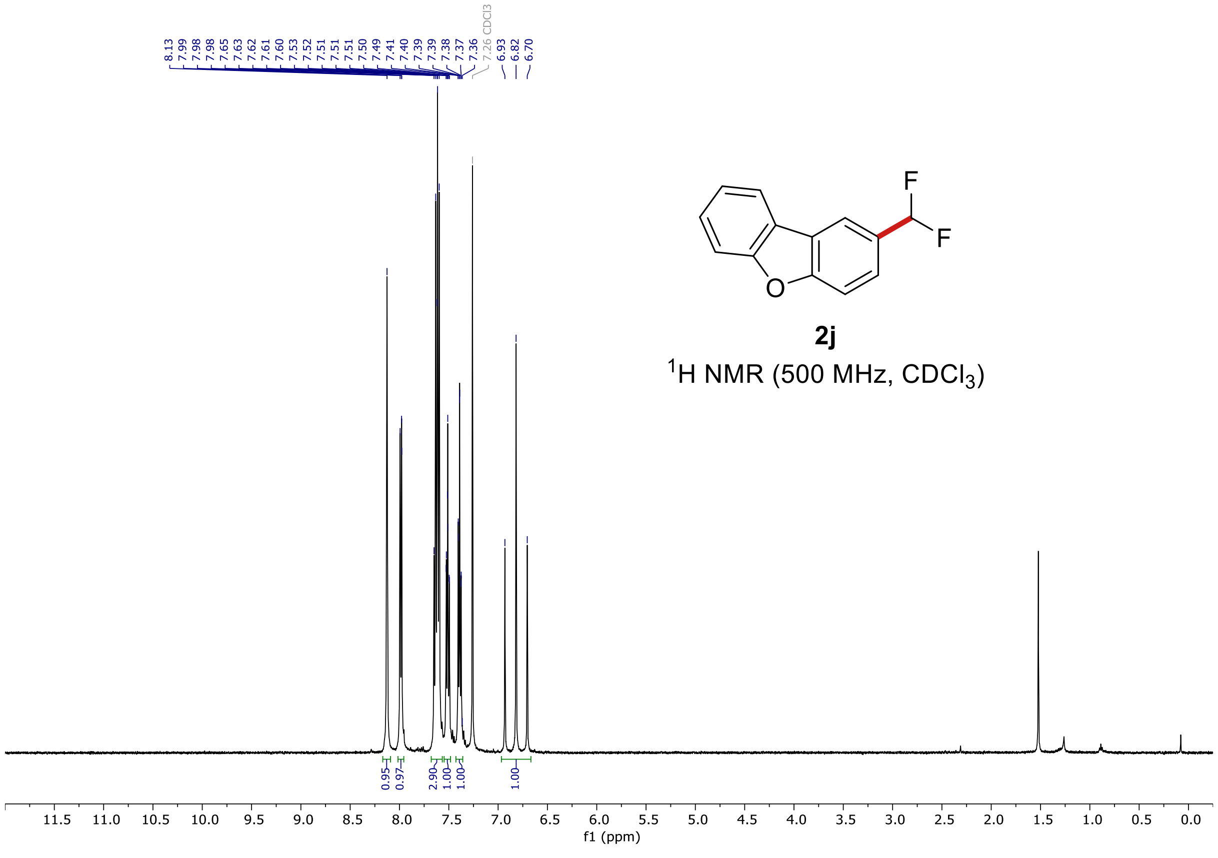
2i

^{19}F NMR (471 MHz, $CDCl_3$)



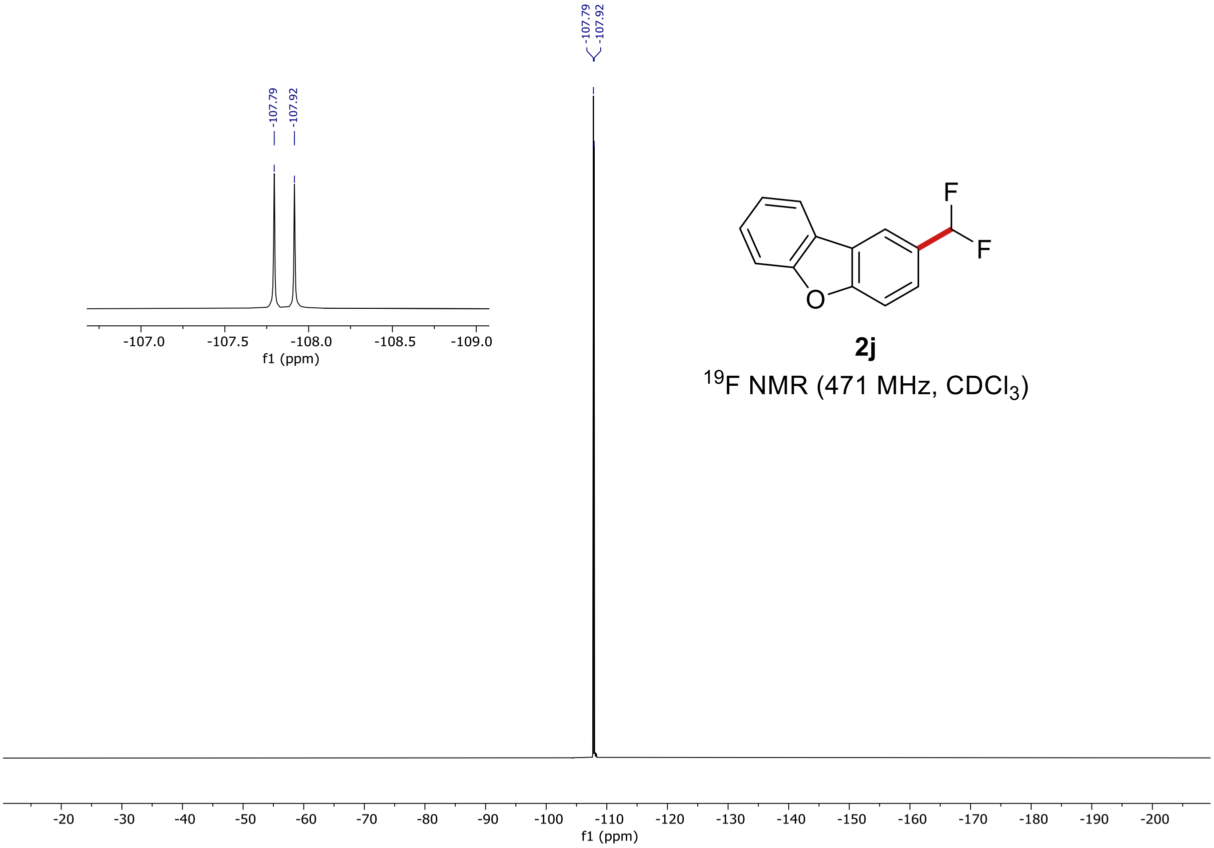
2i

$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)



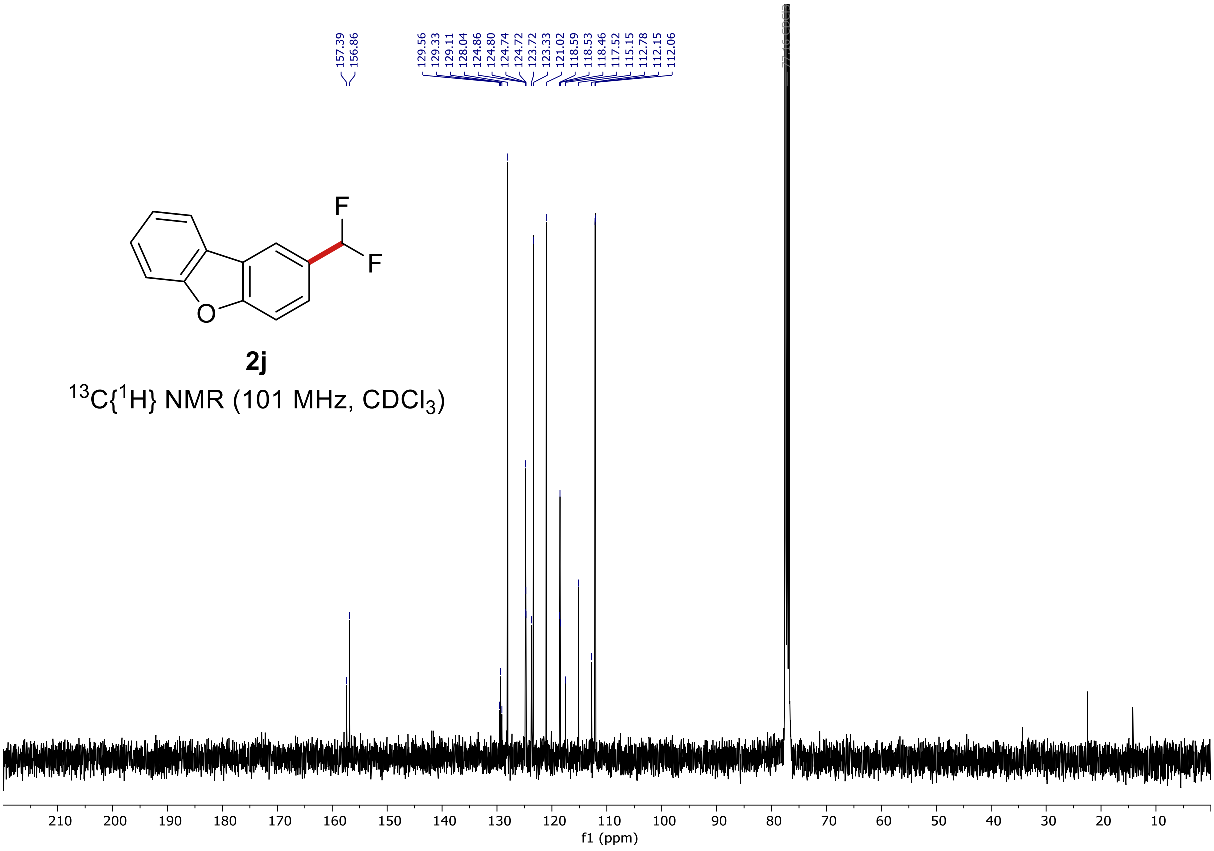
2j

^{1}H NMR (500 MHz, $CDCl_3$)



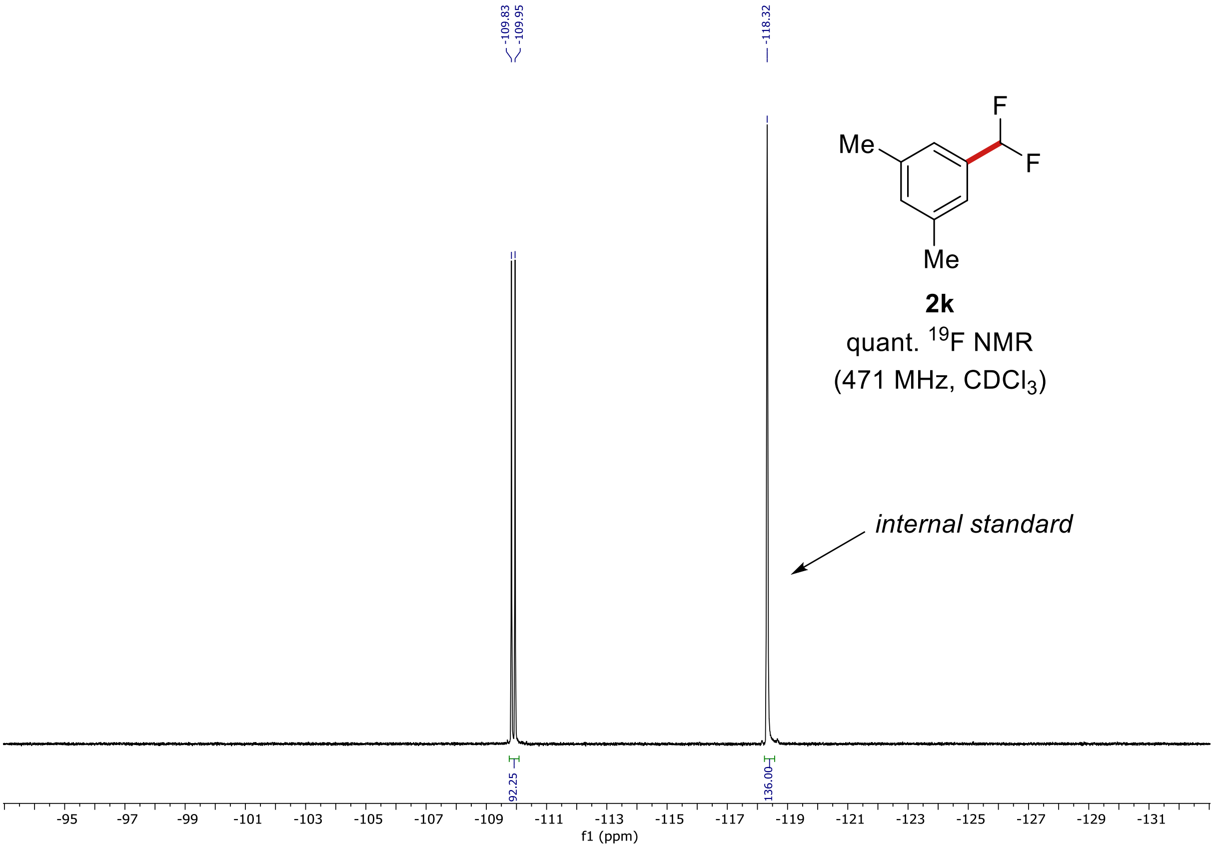
2j

^{19}F NMR (471 MHz, $CDCl_3$)



2j

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$)

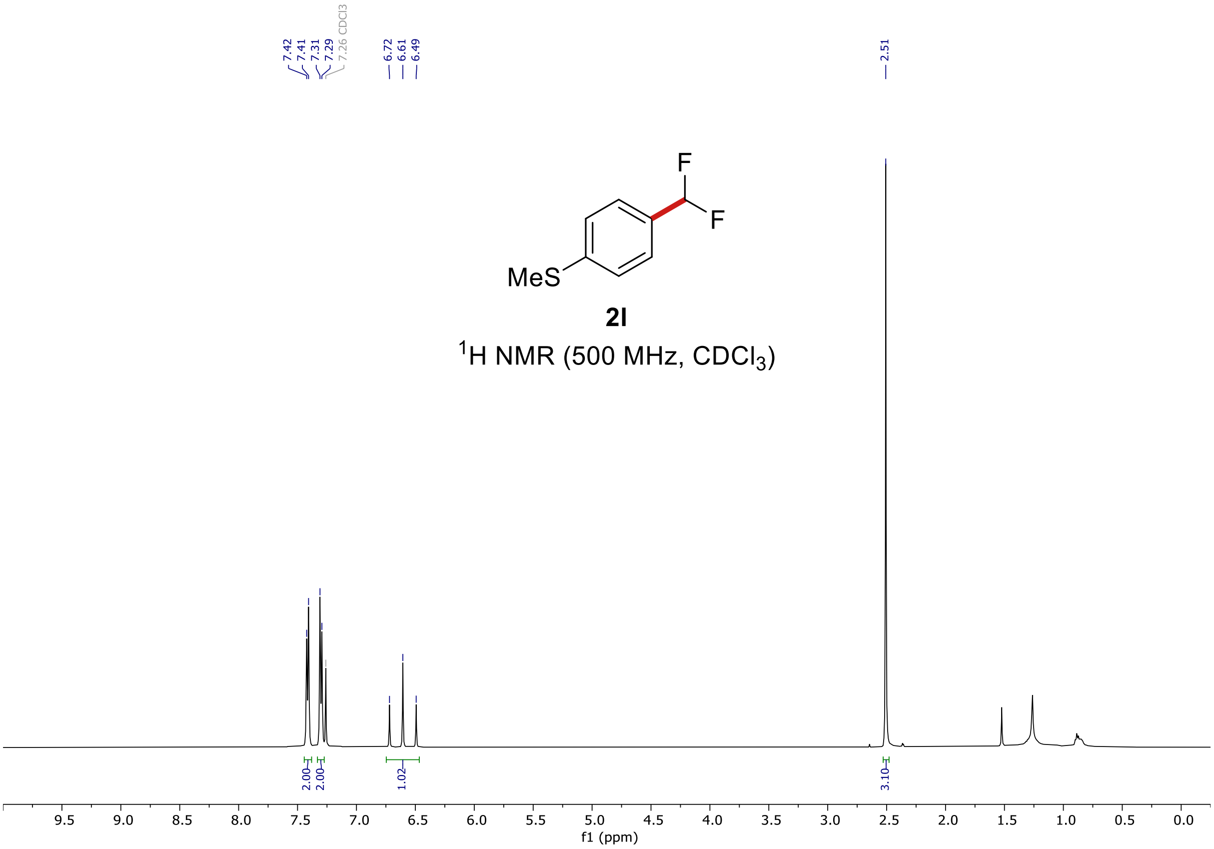


2k

quant. ^{19}F NMR

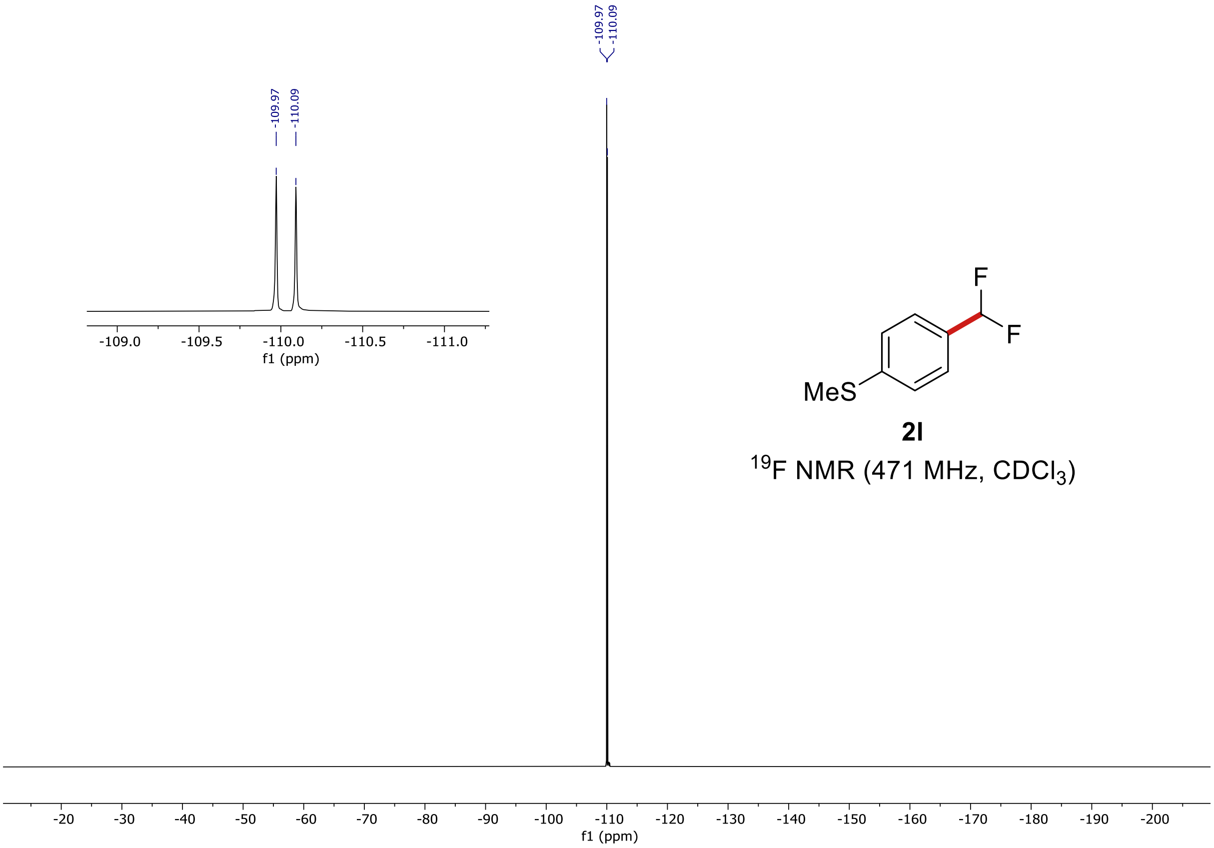
(471 MHz, CDCl$_3$)

internal standard



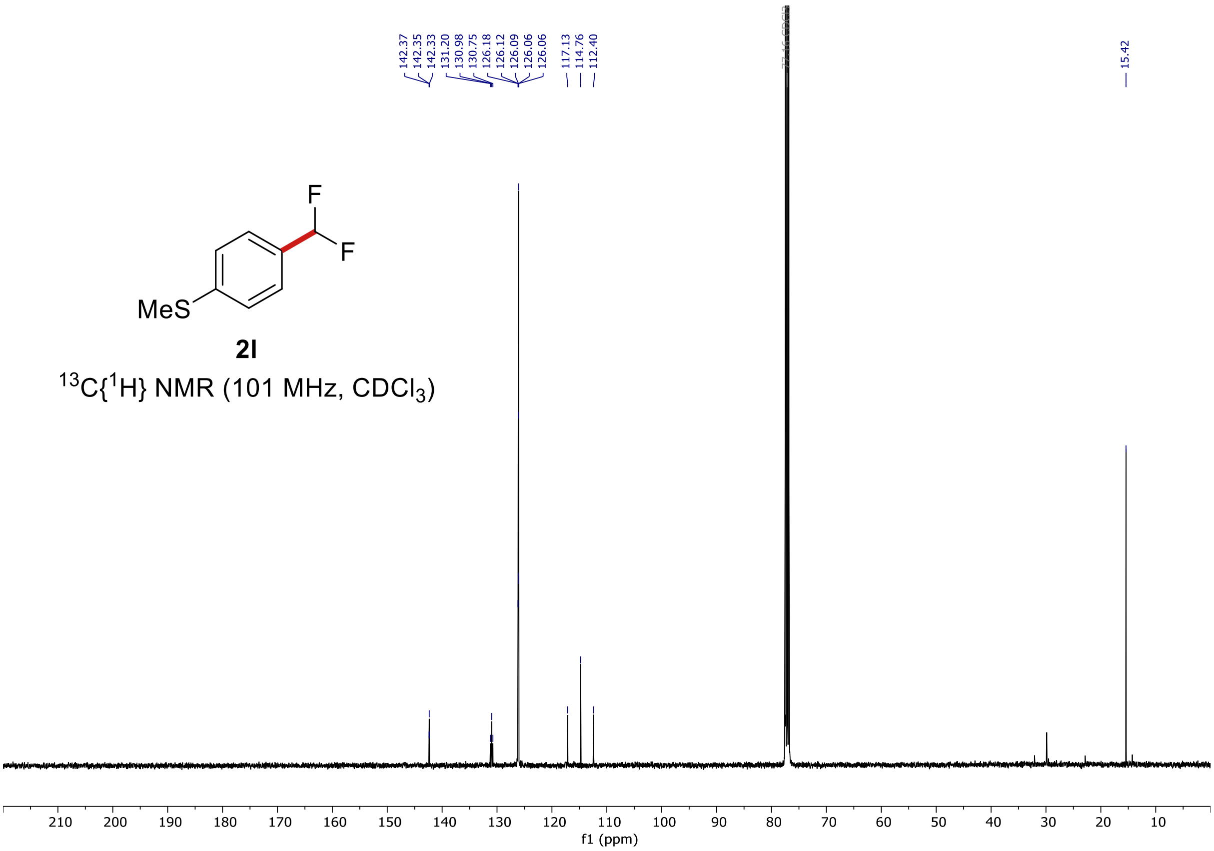
2l

^{1}H NMR (500 MHz, CDCl$_3$)



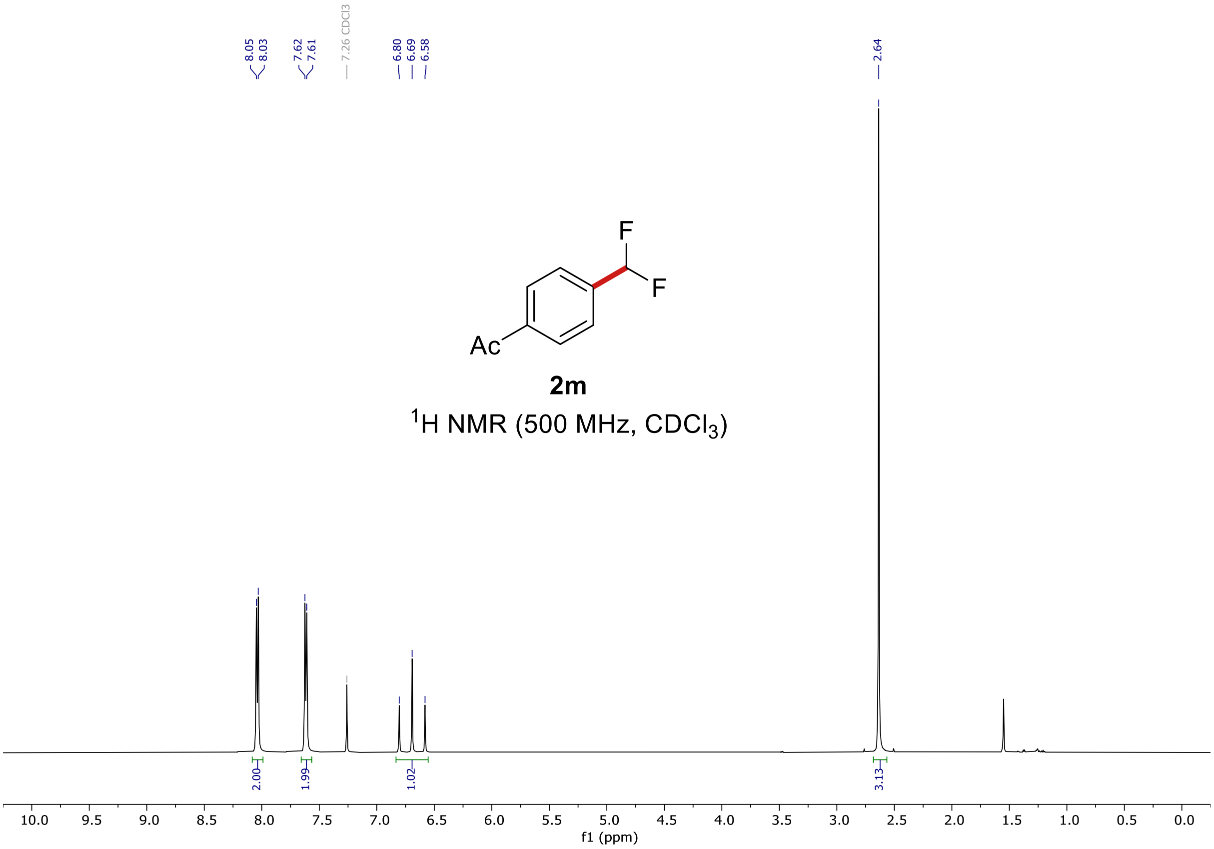
2l

^{19}F NMR (471 MHz, $CDCl_3$)



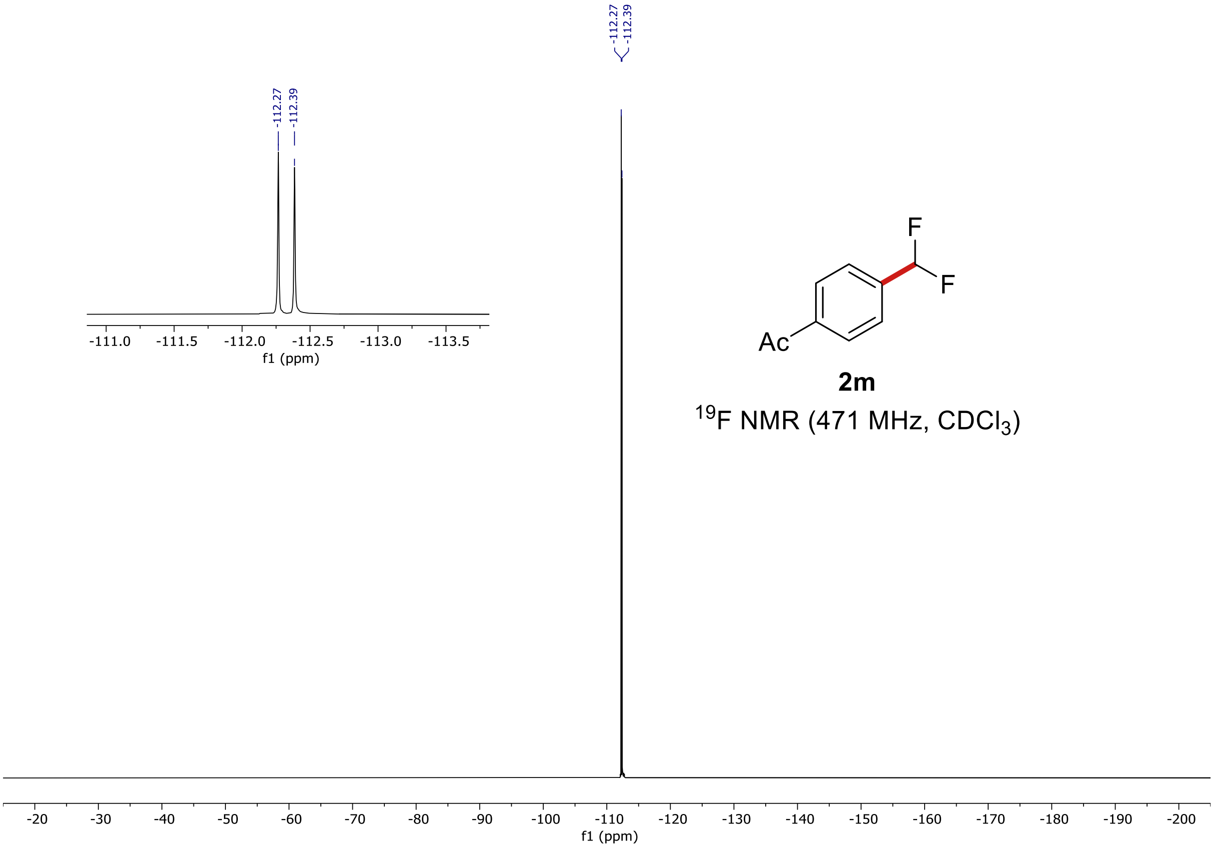
2l

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



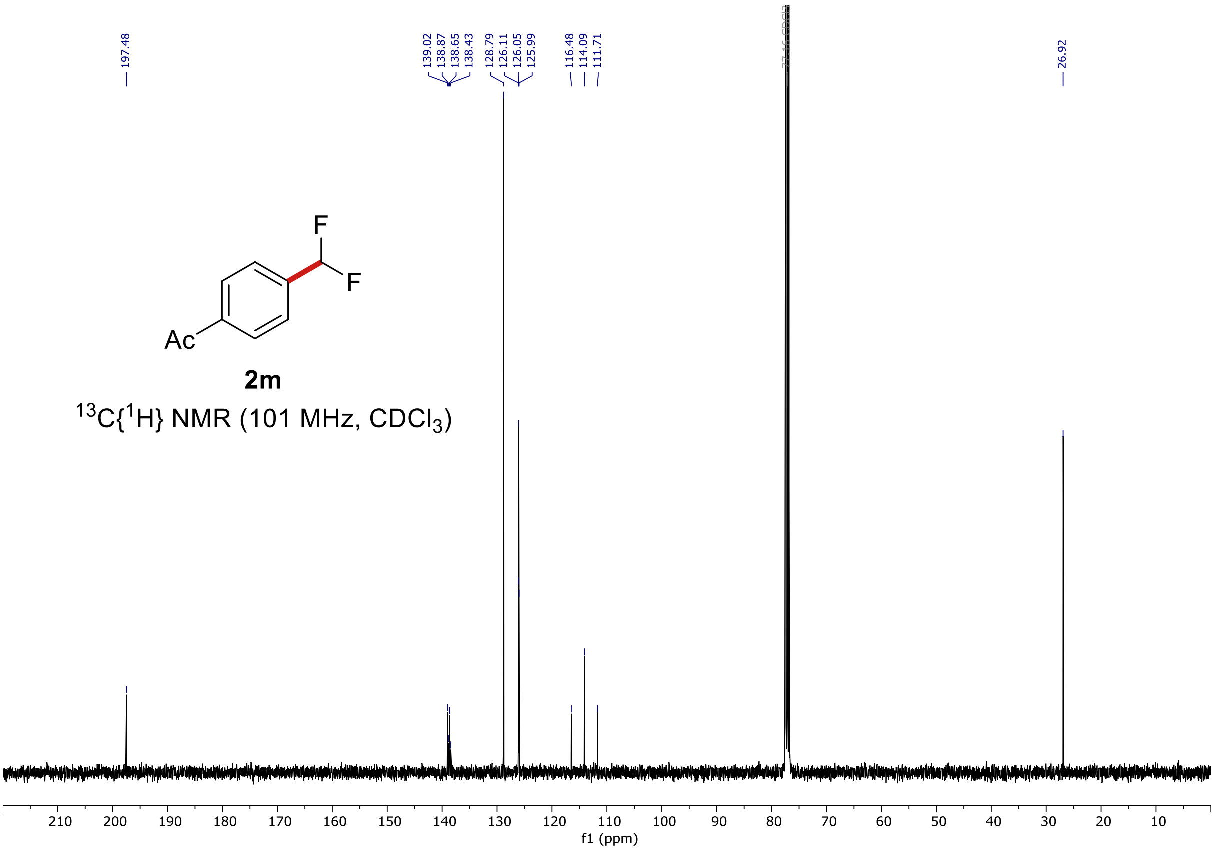
2m

^{1}H NMR (500 MHz, $CDCl_3$)



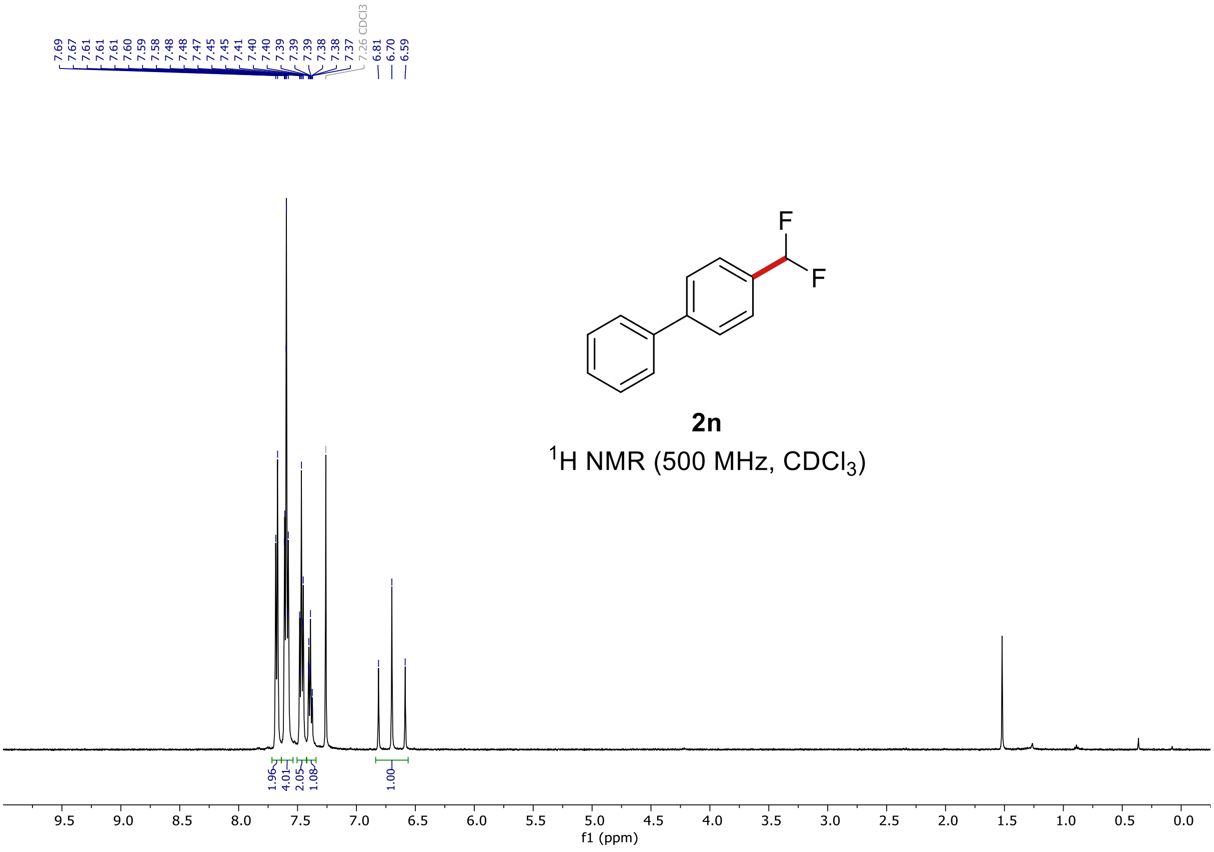
2m

^{19}F NMR (471 MHz, $CDCl_3$)



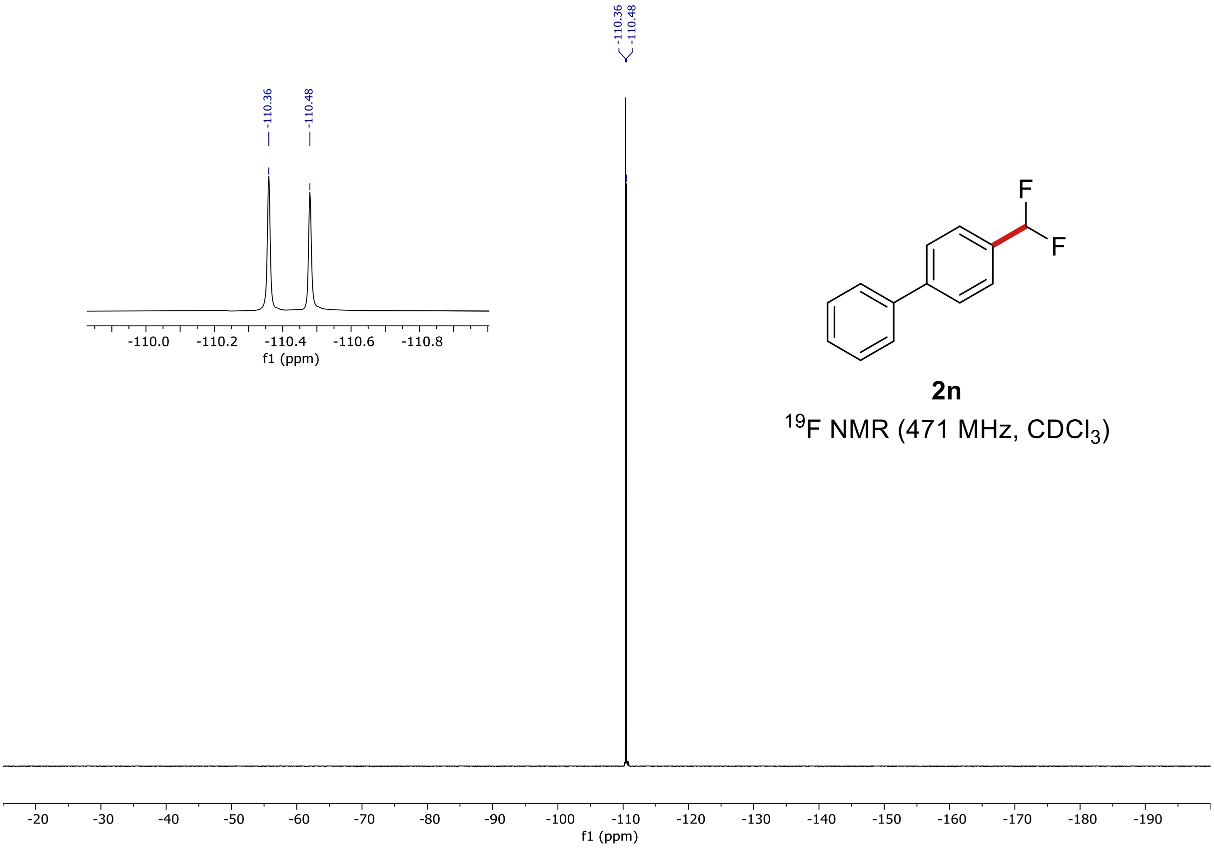
2m

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$)



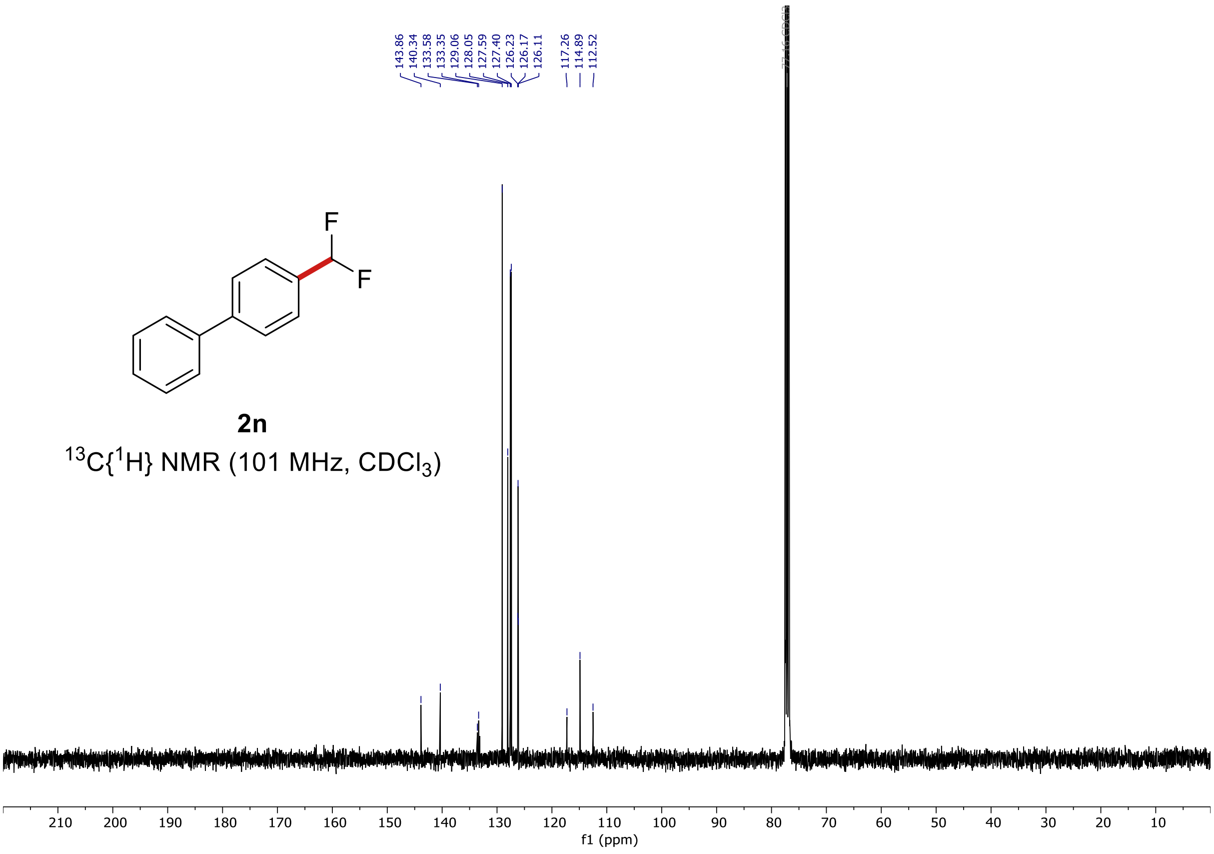
2n

^1H NMR (500 MHz, $CDCl_3$)



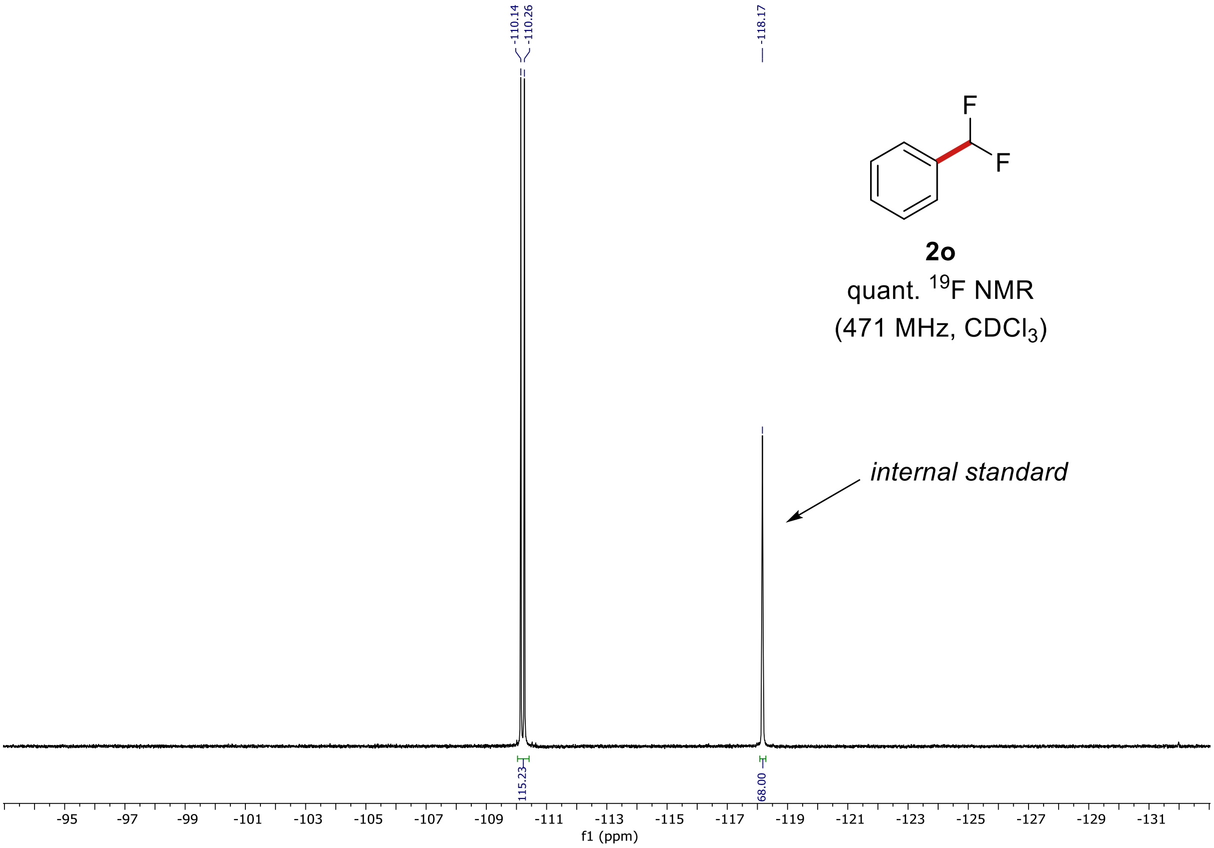
2n

^{19}F NMR (471 MHz, CDCl$_3$)



2n

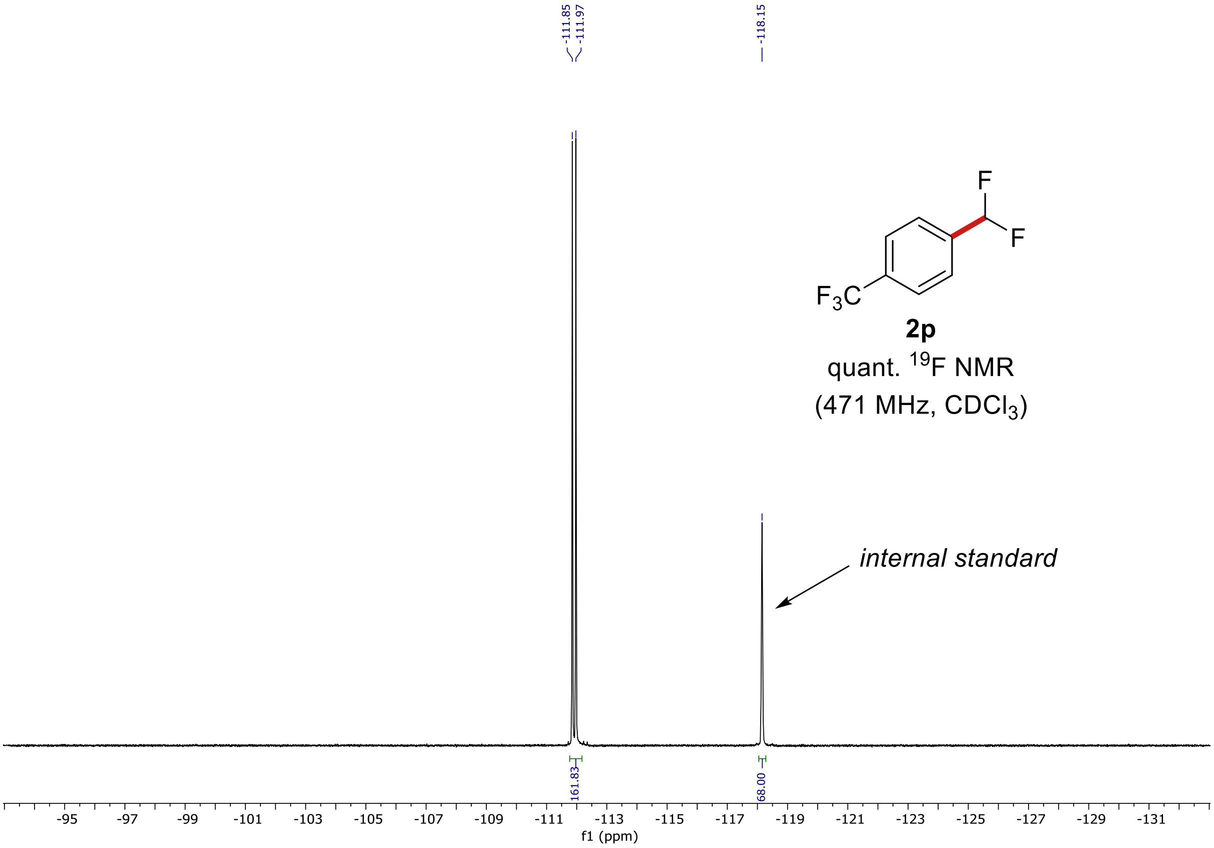
^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$)



2o

quant. ^{19}F NMR

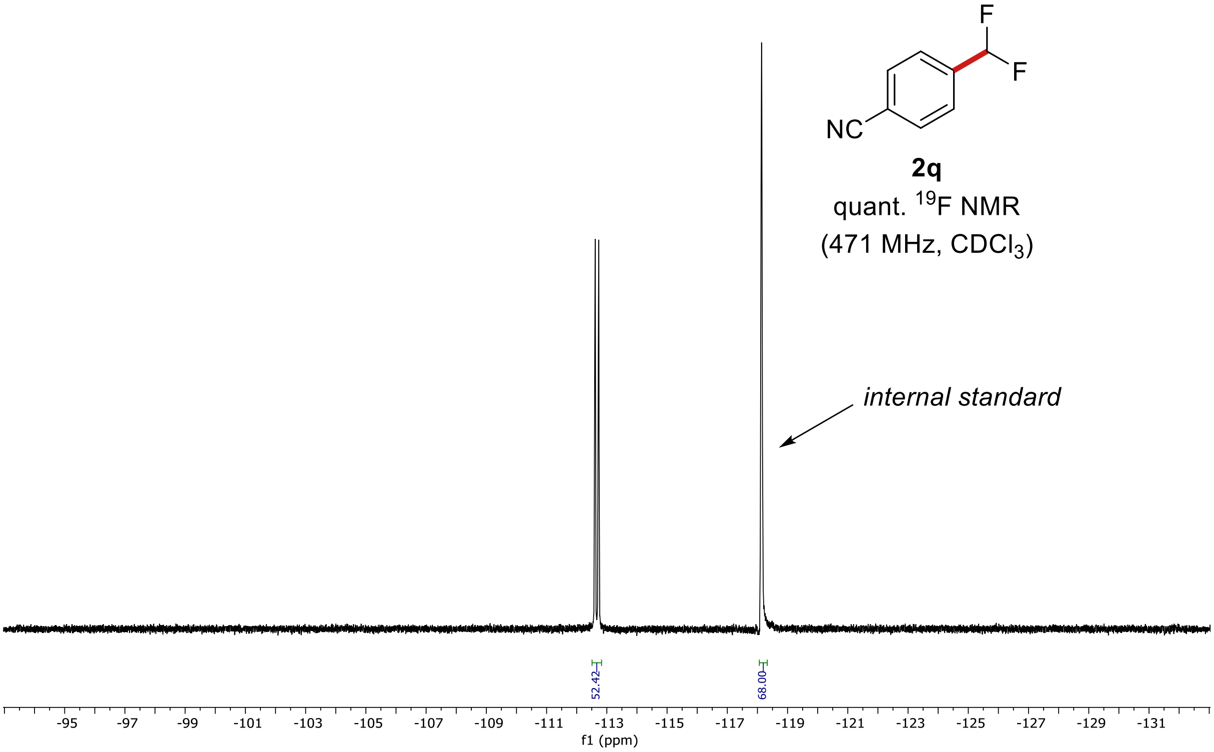
(471 MHz, $CDCl_3$)



2p

quant. ^{19}F NMR

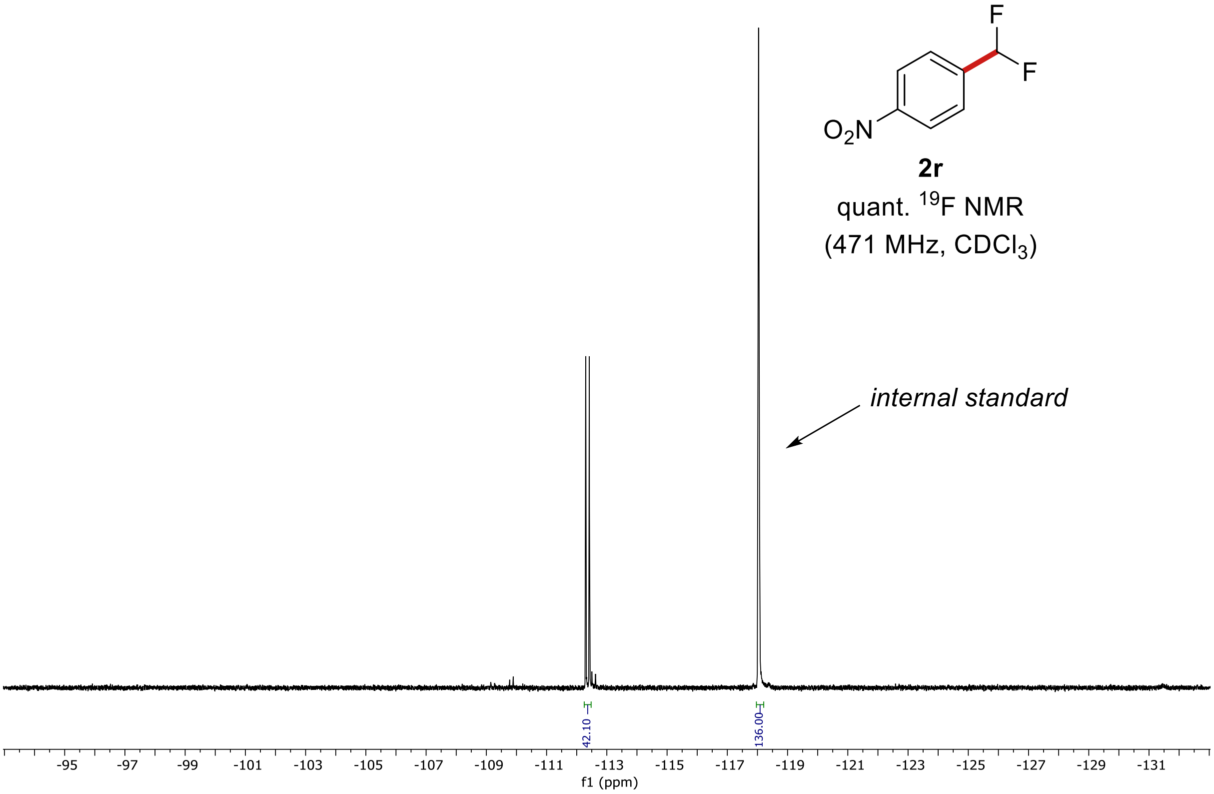
(471 MHz, $CDCl_3$)



2q

quant. ^{19}F NMR

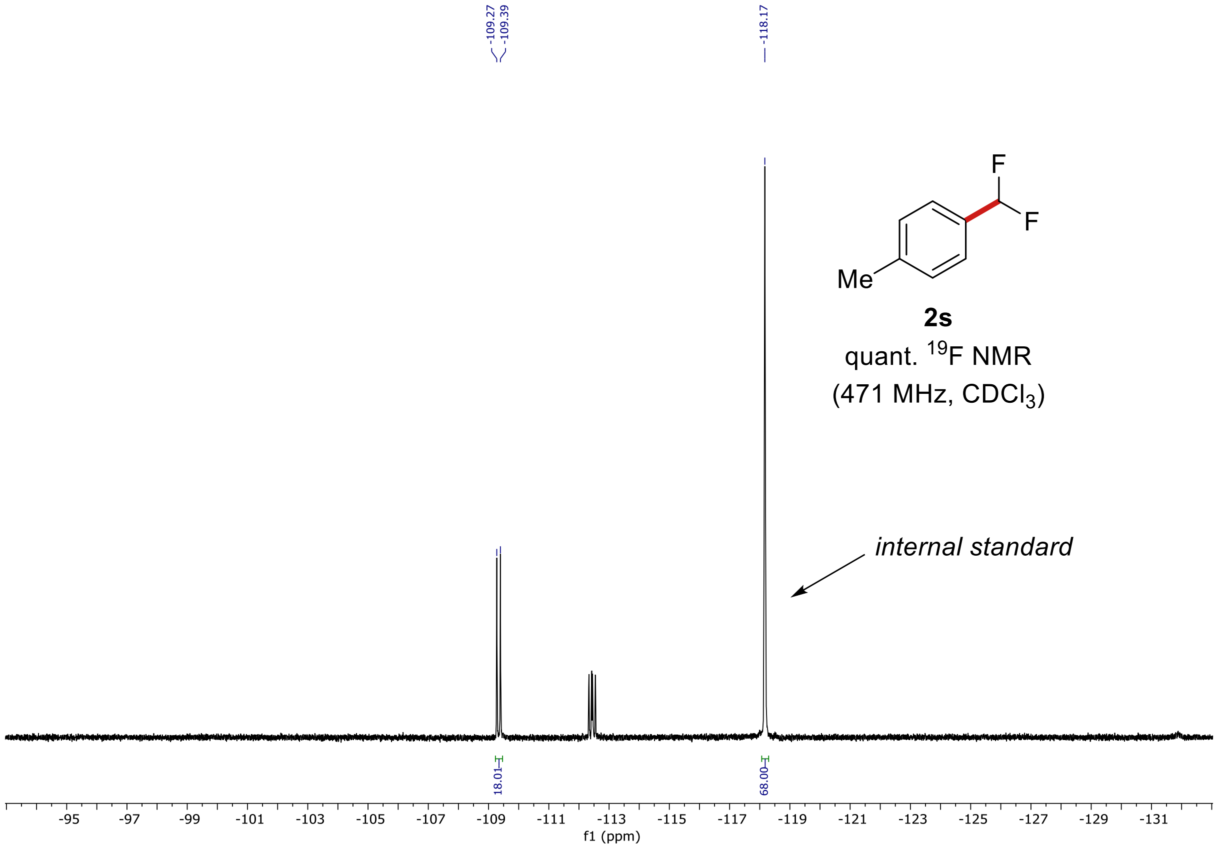
(471 MHz, $CDCl_3$)

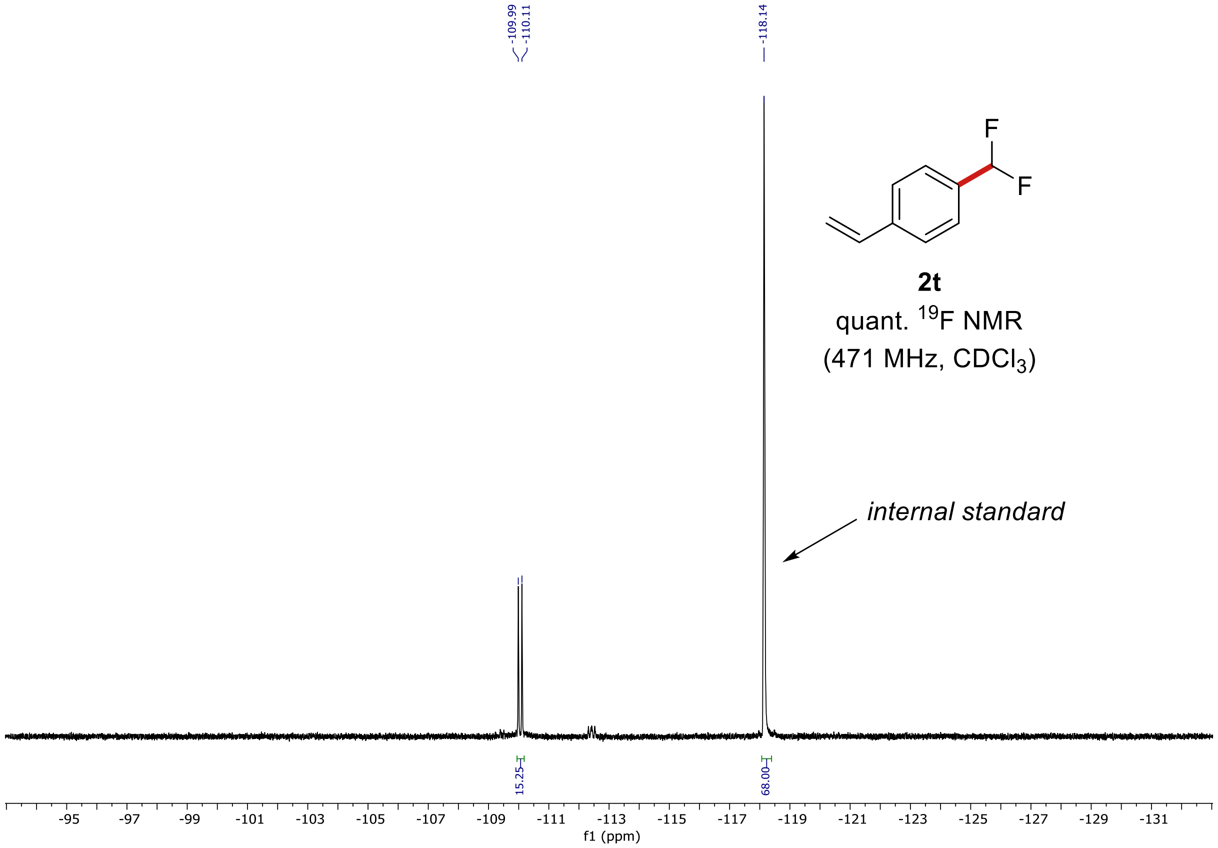


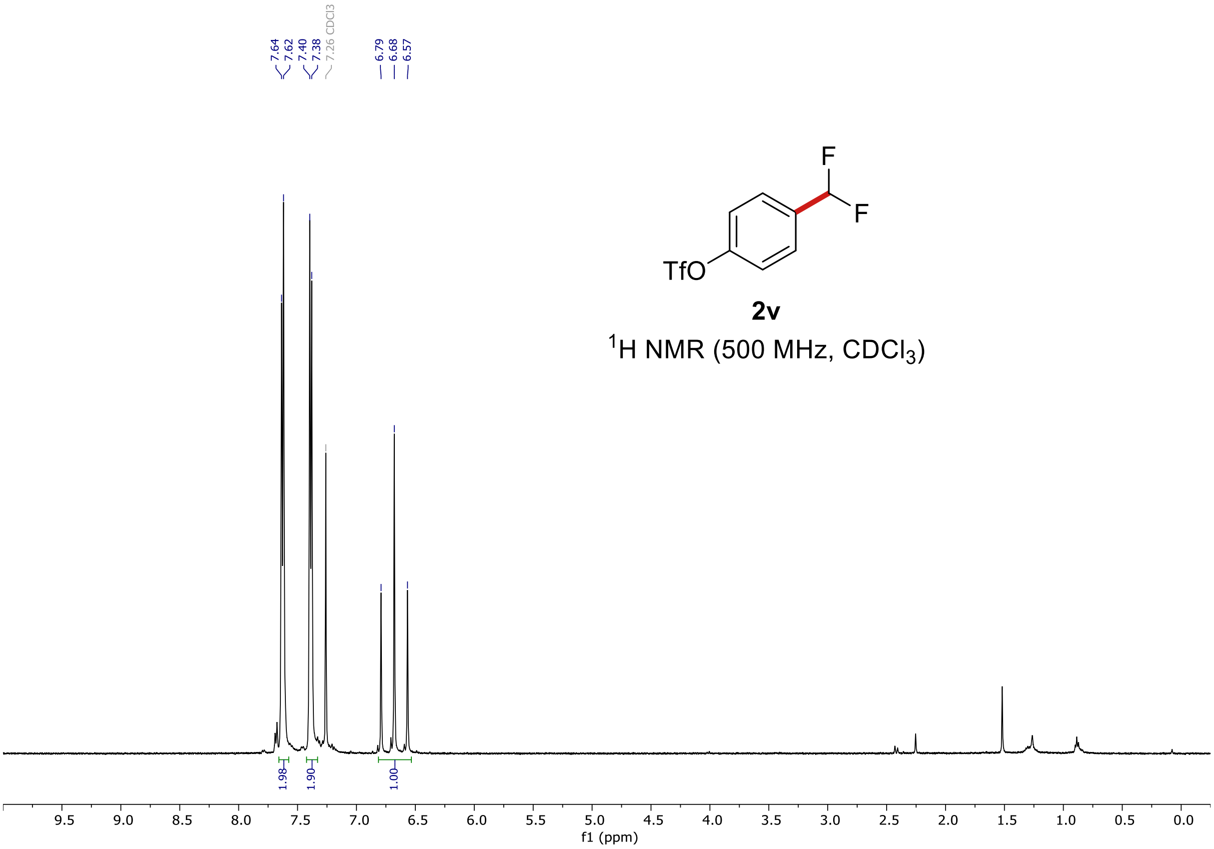
2r

quant. ^{19}F NMR

(471 MHz, $CDCl_3$)

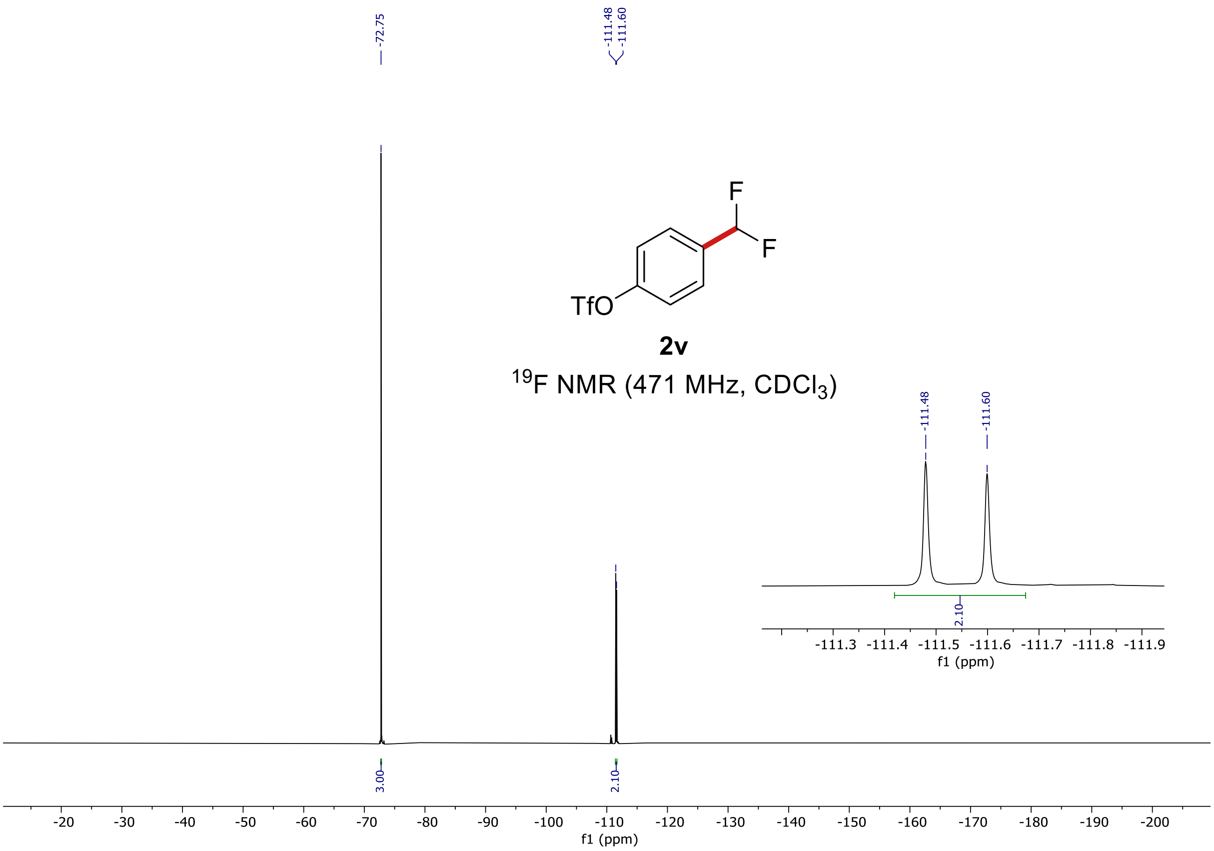

-109.27
-109.39
-118.17
Me
F
F
2s
quant. ^{19}F NMR
(471 MHz, CDCl$_3$)
internal standard
18.01
68.00
-95
-97
-99
-101
-103
-105
-107
-109
-111
-113
-115
-117
-119
-121
-123
-125
-127
-129
-131
f1 (ppm)


-109.99
-110.11
-118.14
F
F
2t
quant. ^{19}F NMR
(471 MHz, CDCl$_3$)
internal standard
15.25
68.00
-95
-97
-99
-101
-103
-105
-107
-109
-111
-113
-115
-117
-119
-121
-123
-125
-127
-129
-131
f1 (ppm)



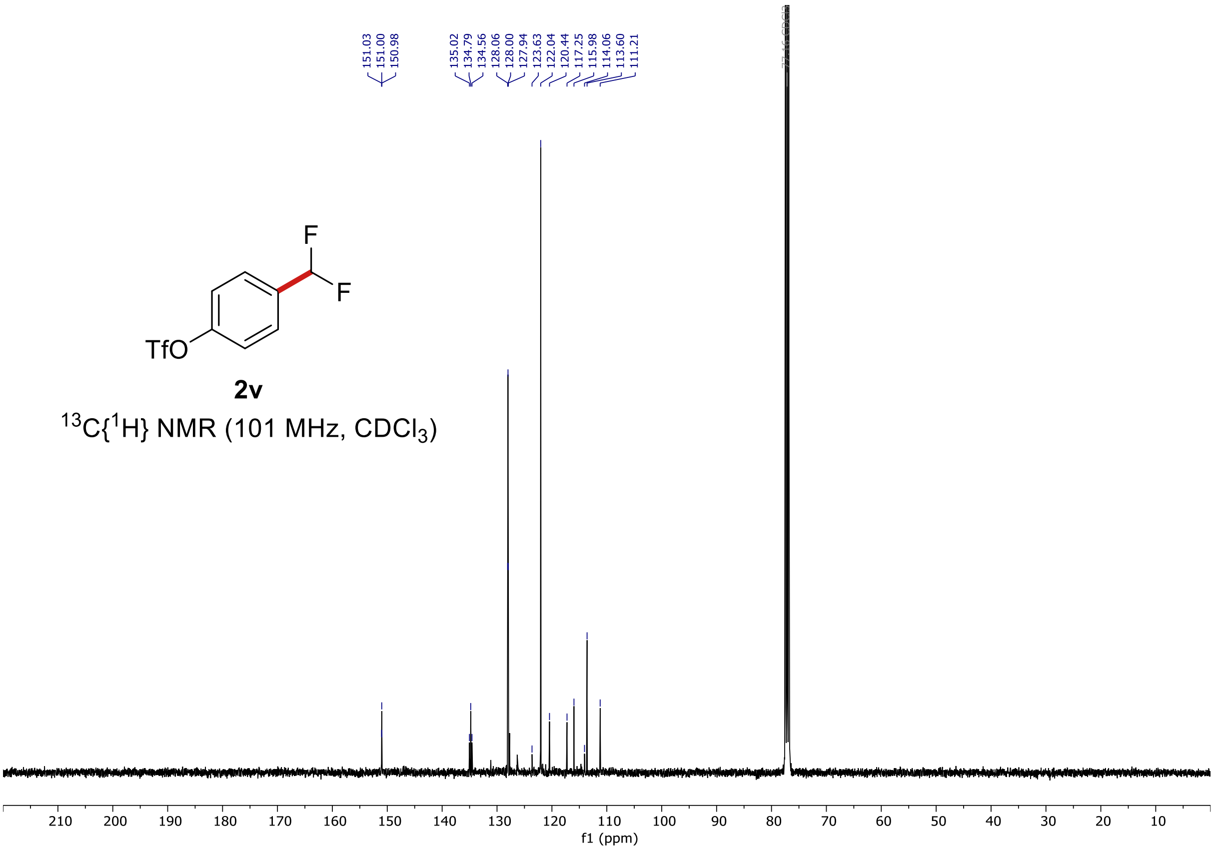
2v

^{1}H NMR (500 MHz, CDCl$_3$)



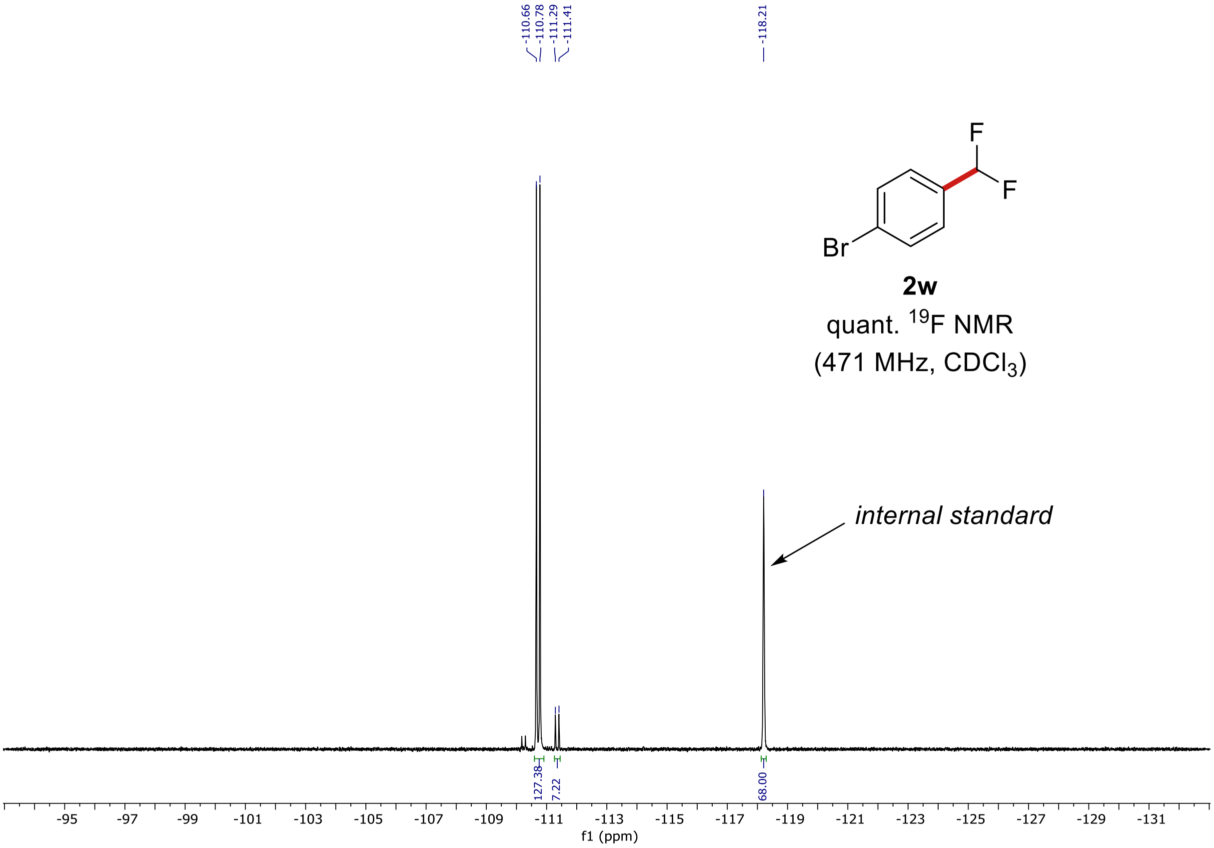
2v

^{19}F NMR (471 MHz, CDCl$_3$)



2v

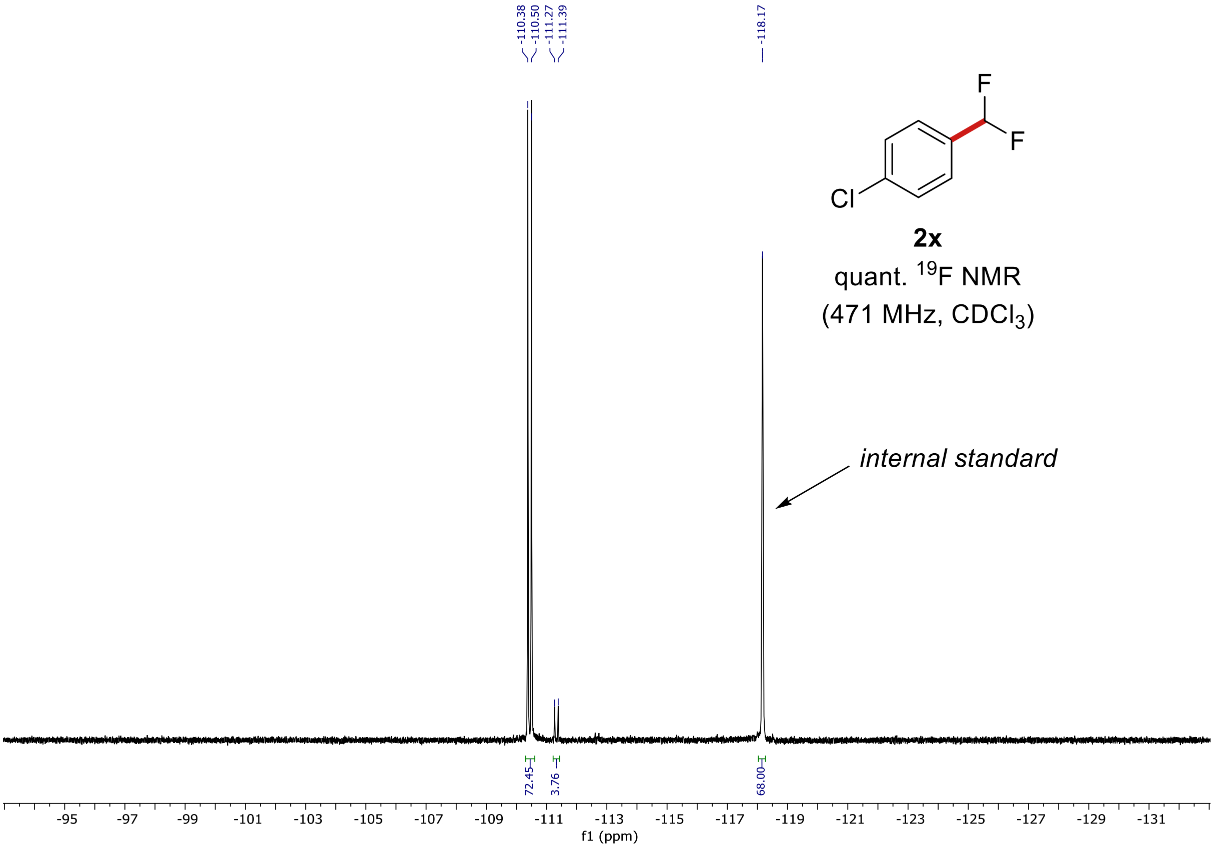
$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$)



2w

quant. ^{19}F NMR

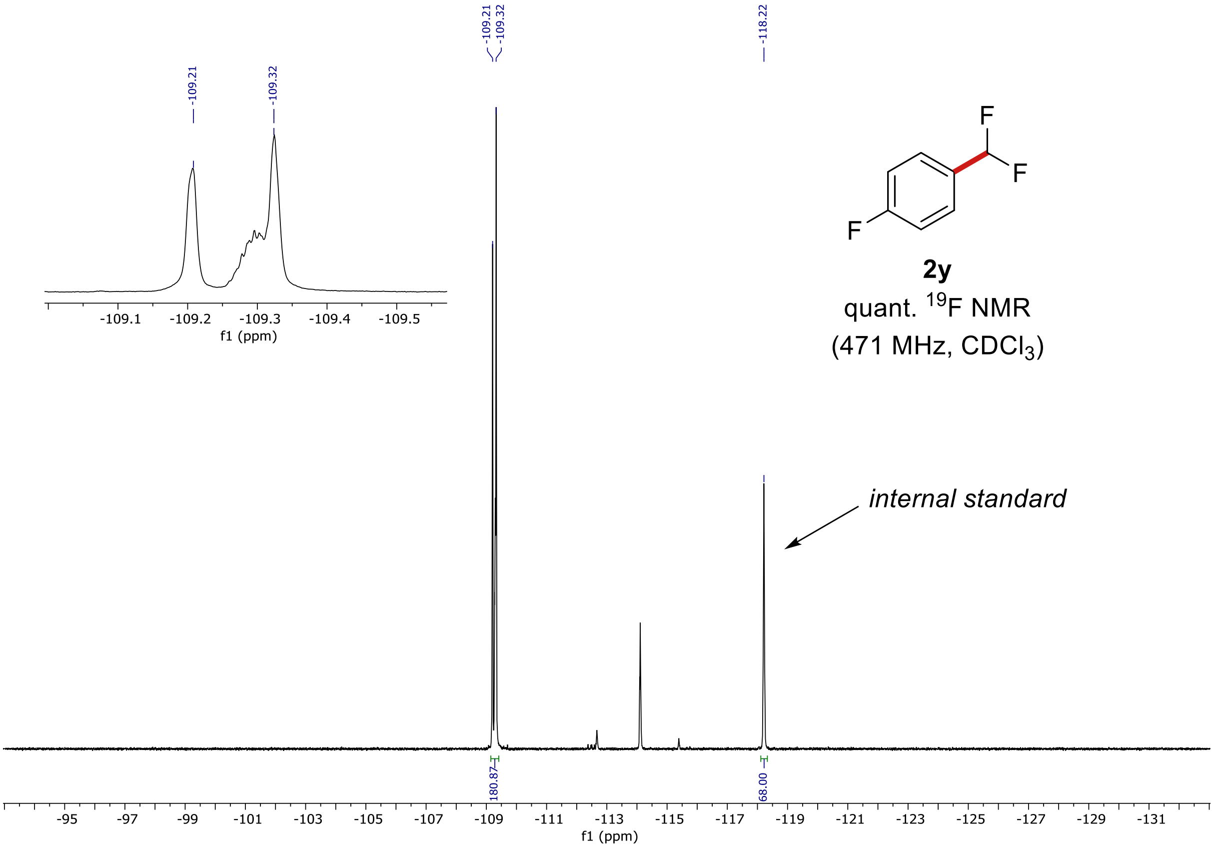
(471 MHz, $CDCl_3$)



2x

quant. ^{19}F NMR

(471 MHz, CDCl$_3$)



2y

quant. ^{19}F NMR

(471 MHz, CDCl$_3$)