Supporting Information

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2,2-Difluoroethylation of heteroatom nucleophiles via a hypervalent iodine strategy

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Abstract: The 2,2-difluoroethyl group is an important lipophilic hydrogen bond donor in medicinal chemistry, but its incorporation into small molecules is often challenging. Herein, we demonstrate electrophilic 2,2-difluoroethylation of thiol, amine and alcohol nucleophiles with a hypervalent iodine reagent, (2,2-difluoro-ethyl)(aryl)iodonium triflate, via a proposed ligand coupling mechanism. This transformation offers a complementary strategy to existing 2,2-difluoroethylation methods and allows access to a wide range of 2,2-difluoroethylated nucleophiles, including the drugs Captopril, Normorphine and Mefloquine.

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SUPPORTING INFORMATION

Table of Contents

1. General Information

All reactions were performed in oven dried apparatus with magnetic stirring under an inert atmosphere of argon. All solvents and chemicals were obtained from commercial suppliers and used as purchased, unless stated otherwise. All solvents were dried on a column of alumina prior to use. All reagents were used as supplied unless otherwise stated. *m*CPBA was dried at room temperature under vacuum for 4 hours prior to use (caution: dried *m*CPBA can be shock sensitive). 2,4,6-Triispropylthiophenol and 3-([1,1'-biphenyl]-2-yl)prop-2-yn-1-amine were synthesised following literature procedures.[1,2]

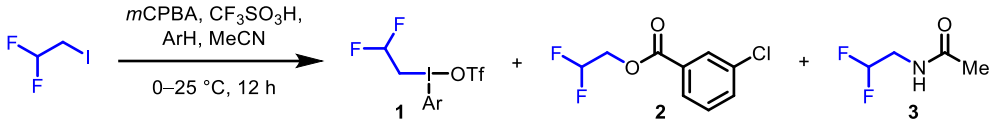
The reactions were followed by thin layer chromatography (TLC) carried out on aluminium-foil backed plates coated with silica gel (Polgram SIL G/UV254). The products were visualized using UV fluorescence (254 nm) or potassium permanganate stain. Manual silica flash column chromatography was performed over Fluorochem silica gel 60A (35–70 μm) using eluent systems as described for each experiment. Automated silica flash column chromatography was performed on a Teledyne NextGen 300 on RediSep Rf Disposable cartridges.

All NMR spectra were recorded on a Bruker AV 400 MHz spectrometer. NMR data were processed using MestReNova 14.2.1 software. Proton and carbon-13 NMR spectra are reported as chemical shifts (δ) in parts per million (ppm) relative to residual undeuterated solvent peak using the Bruker internal referencing procedure (edlock). Fluorine-19 NMR spectra are referenced relative to $CFCl_3$ in $CDCl_3$. Coupling constants (*J*) are reported in units of hertz (Hz) and are rounded to the nearest 0.5 Hz for ^{1}H and ^{19}F NMR and the nearest 1 Hz for ^{13}C NMR. The following abbreviations are used to describe multiplets: s (singlet), d (doublet), t (triplet), q (quartet), quin (quintet), hep (heptet), m (multiplet), br (broad signal). Where appropriate, COSY, HMQC and HMBC experiments were performed to aid structural assignment. High-resolution mass spectrometry (HRMS) measurements were carried out on Bruker micrOTOF II. Headspace GCMS measurements were carried out on a Thermo Single Quadrupole ITQ with Trace 1300 GC-MS with Triplus HS Headspace autosampler and analysed using Chromeleon 7.2. Infrared spectra were recorded on a Perkin–Elmer 1600 FTIR instrument as dilute chloroform solutions. Melting points were recorded on a Stuart manual melting point apparatus. Known compounds have been checked against literature references and only relevant analytical data are given. IUPAC names were generated using ChemDraw 20.1.1.125.

2. Reaction Development

2.1 Formation of (2,2-difluoroethyl)(4-methoxyphenyl)-λ³-iodane trifluoromethanesulfonate (1)

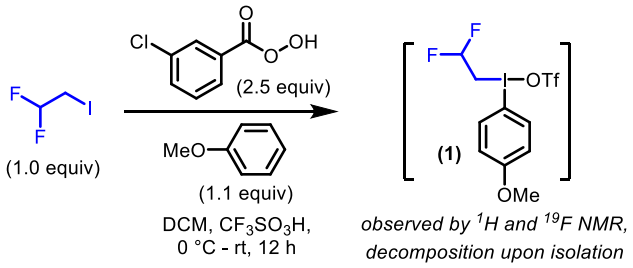
2.1.1 Reaction optimisation



Entry	Deviation from standard conditions[a]	HF_2CCH_2I [%][b]	**1** [%][b]	**2** [%][b]	**3** [%][b]
1	**None**	**40**	**59**	**1**	0
2	Solvent = DCM	20	77	0	0
3	ArH = benzene	67	33	0	0
4	ArH = methylbenzene	42	42	7	0
5	ArH = 2,4,6-trimethoxybenzene	100	0	0	0
6	ArH = nitrobenzene	23	23	55	0
7	Oxidant = Selectfluor (2 equiv.)	94	6	0	0
8	Oxidant = Urea.H_2O_2 (2 equiv.)	100	<1	<1	0
9	Open to air (no Ar atmosphere)	14	68	0	18
10	1 equiv. H_2O	14	51	0	33

Table S1. Reaction optimisation: *In-situ* formation of **1**. [a] Standard conditions (i) 1,1-difluoro-2-iodoethane (1.04 mmol), anisole (1.14 mmol), *m*CPBA (2.5 mmol), CF_3SO_3H (1.2 equiv.), MeCN (5 mL, 0.2 M), 0–25 °C, 12 h, Ar, exclusion of light (reaction wrapped in aluminium foil). [b] Product ratios were determined by ^{19}F NMR spectroscopy.

2.1.2 Optimised reaction conditions and analysis



Difluoroethyl(aryl)iodonium triflate **1** was synthesised via a modified literature procedure:[3] *m*CPBA (583 mg, 2.60 mmol, 2.5 equiv.) was added to an oven-dried pressure tube sealed with a rubber septum and dried under vacuum for 1–1.5 h until the reagent had the consistency of a free-flowing powder. (Caution: dried *m*CPBA can be shock sensitive.) The tube was flushed with argon and wrapped in aluminium foil to protect the reaction from light. Anhydrous DCM (5 mL, 0.2 M) was added, followed by 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol, 1.0 equiv.) and anisole (0.124 mL, 1.14 mmol, 1.1 equiv.). After stirring for 5–10 minutes, the reaction mixture was cooled to 0 °C and CF_3SO_3H (0.110 mL, 1.25 mmol, 1.2 equiv.) was added dropwise. The tube was removed from the ice bath, wrapped in aluminium foil to protect the reaction from light, and stirred at room temperature for 12 hours, after which NMR analysis of the crude mixture showed 59% conversion of 2-iodo-1,1-difluoroethane to intermediate **1**, with 35% of unreacted 2-iodo-1,1-difluoroethane remaining, as determined by integration of the corresponding R–$\underline{CH_2}CF_2H$ signals in the ^1H NMR (Figure S1). [Note: This reaction is sensitive to the purity of commercial *m*CPBA used, which we found to be extremely variable.]

^1H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.49 (m, 2H), 6.78 – 6.61 (m, 2H), 6.05 (tt, *J* = 54.0, 4.0 Hz, 1H), 4.59 (td, *J* = 12.5, 4.0 Hz, 2H), 3.78 (s, 3H); **$^{19}F\{^1H\}$ NMR** (376 MHz, $CDCl_3$) δ −74.13 (s, 3F, OTf), −126.51 (ad, *J* = 3.5 Hz, 1F).

SUPPORTING INFORMATION

Isolation of **1** was attempted by removing the reaction solvent *in vacuo*, precipitating the fluoroalkyl(aryl)iodonium reagent in Et_2O, and filtering the resulting white crystalline material, which rapidly decomposed, taking on a jelly-like consistency. ^{1}H NMR analysis of the decomposed product revealed iodoanisole as the main species (Fig. S2B), which confirms the formation and subsequent decomposition of fluoroalkyliodonium triflate **1**. Potential elimination pathways include *alpha*- and *beta*-elimination, or the reaction with weakly nucleophilic species in the reaction mixture such as *meta*-chlorobenzoic acid (*m*CBA) and MeCN (Fig. S2A). Formation of the corresponding products **2** and **3** was confirmed by ^{19}F NMR during optimisation.

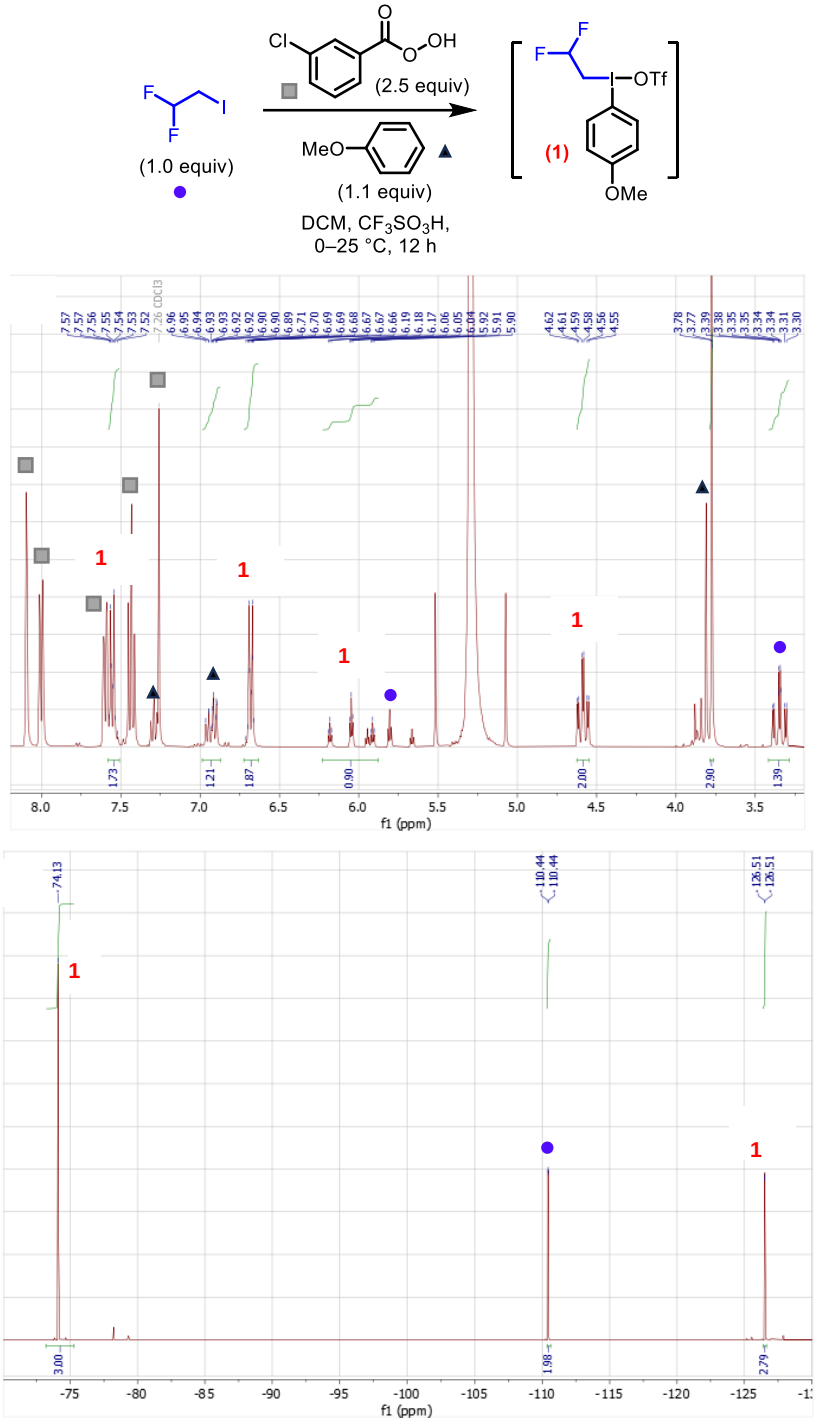


Figure S1. ^{1}H NMR (**A**) and ^{19}F NMR (**B**) analysis of the crude reaction mixture for *in-situ* formation of fluoroalkyl(aryl)iodonium intermediate **1**. The following species are labelled in the spectra: 2-iodo-1,1-difluoroethane (blue circle), *m*CPBA (grey square), anisole (black triangle) and the hypervalent fluoroalkyl(aryl)iodonium salt (red number **1**).

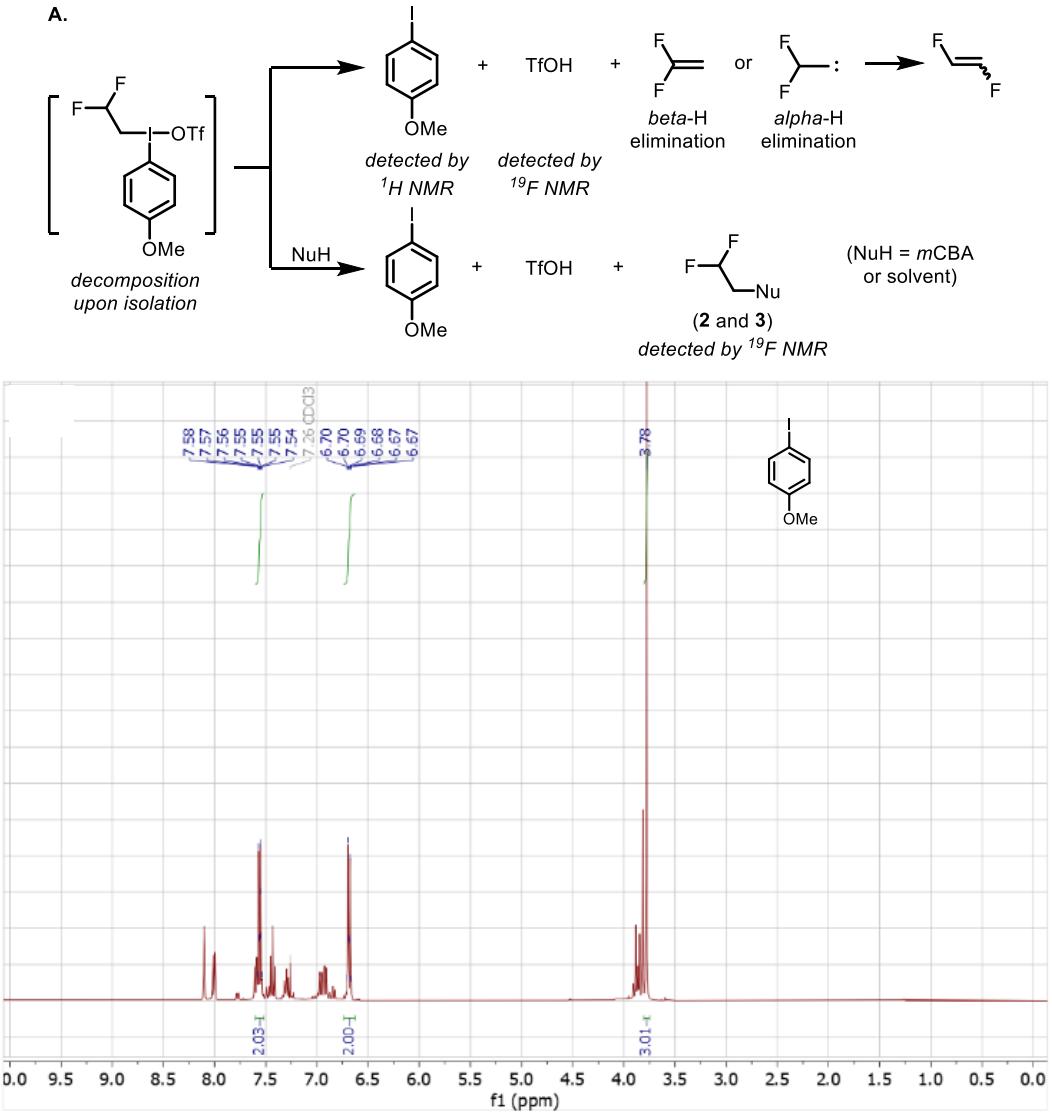
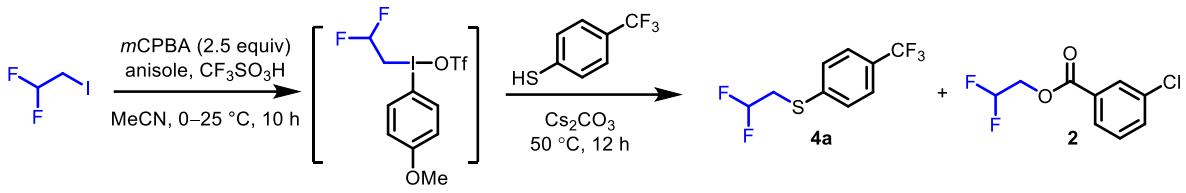


Figure S2. A. Proposed decomposition of fluoroalkyl(aryl)iodonium salt **1**. (*m*CBA = 3-chlorobenzoic acid) **B.** ^{1}H NMR of the product obtained from an attempt to isolate **1** by precipitation with Et_2O followed by filtration. The main species is iodoanisole, with traces of *meta*-chlorobenzoic acid and anisole.

2.2 Reaction optimisation: 2,2-Difluoroethylation of thiol nucleophiles

Extensive optimisation was carried out for the electrophilic 2,2-difluoroethylation of thiols with difluoroethyl(aryl)iodonium triflate **1**. A summary of our screening efforts is presented in Table S2 below.



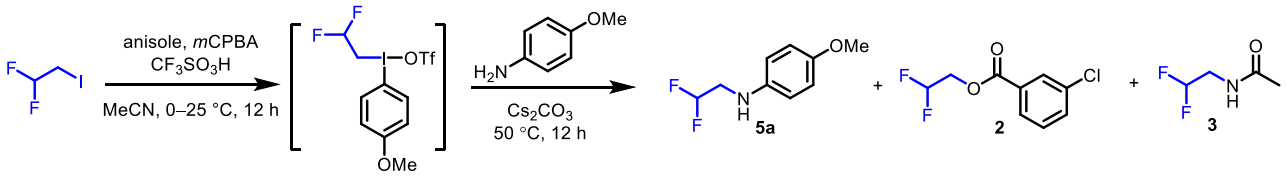
Entry	Deviation from standard conditions step 1[a]	Deviation from standard conditions step 2[a]	HF_2CCH_2I [%][b]	**4a** [%][b]	**2** [%][b]
1	None	None	**4**	**78**	**16**
2	ArH = benzene (instead of anisole) solvent = DCM	None	28	52	18
3	ArH= 4-methylbenzene solvent = DCM	None	51	38	11
4	ArH = 1,3,5-trimethylbenzene solvent = DCM	None	36	49	13
5	**ArH = 4-Methoxybenzene** solvent = DCM	None	**25**	**58**	**16**
6	ArH = 1,3,5-trimethoxybenzene solvent = DCM	None	94	<2	4
7	ArH = nitrobenzene solvent = DCM	None	82	11	5
8	ArH = thiophene solvent = DCM	None	56	33	10
(1)	**None (solvent = MeCN)**	None	**4**	**78**	**16**
9	Solvent = *n*BuOH	None	37	43	18
10	Solvent = EtOAc	None	26	60	14
11	Solvent = DCM + HFIP (1 mL)	None	18	65	17
12	Solvent = MeCN + HFIP (1 mL)	None	12	70	16
13	Oxidant = H_2O_2 (30% in H_2O) (1.5 equiv.)	None	85	6	9
14	Oxidant = $NaIO_4$[c] (2.0 equiv.)	None	75	18	6
15	Oxidant = Oxone[c] (2.0 equiv.)	None	81	12	5
16	Oxidant = mCPBA (1.5 equiv.)	None	30	58	10
17	Oxidant = mCPBA (2.1 equiv.)	None	15	73	11
(1)	**None (oxidant = mCPBA (2.5 equiv.))**	None	**4**	**78**	**16**
18	Oxidant = mCPBA (4.0 equiv.)	None	9	67	23
(1)	**None**	**None (base = Cs_2CO_3)**	**4**	**78**	**16**

19	None	Ag_2CO_3	68	trace	25
20	None	Li_2CO_3	51	28	20
21	None	Na_2CO_3	24	61	13
22	None	K_2CO_3	26	48	24
23	None	*t*BuOK	25	60	14
(1)	**None (t = 10 h)**	**None (t = 12 h, T = 50 °C)**	**4**	**78**	**16**
24	t = 4 h	None	61	30	7
25	None	t = 6 h	38	45	12
26	None	T = 40 °C	18	66	14
27	None	T = 60 °C	8	72	19

Table S2. Reaction optimisation: thiol nucleophiles. [a] Standard conditions: (i) 1,1-difluoro-2-iodoethane (1.04 mmol), 4-methoxybenzene (1.1 equiv.), *m*CPBA (2.5 equiv.), CF_3SO_3H (1.2 equiv.), MeCN (5 mL, 0.2 M), 0–25 °C, 10 h; (ii) thiol (1.1 equiv.), Cs_2CO_3 (2.0 equiv.), 50 °C, 12 h. [b] Crude ^{19}F NMR yields were determined relative to trifluorotoluene as the internal standard. [c] Poorly soluble in MeCN. [Note: anisole = 4-methpxybenzene, HFIP = hexafluoroisopropanol.]

2.3 Reaction optimisation: 2,2-Difluoroethylation of amine nucleophiles

We observed a range of by-products when less reactive nucleophiles were used to trap hypervalent iodine intermediate **1** (*e.g.* amines instead of thiols), due to the presence of competing nucleophiles in the reaction mixture. Reaction of the reduced oxidant, *meta*-chlorobenzoic acid, with difluoroethyl(aryl)iodonium intermediate **1** gave rise to 2,2-difluoroethyl benzoate **2**, and reaction with the solvent MeCN in the presence of water afforded the Ritter product **3**. Re-optimisation for amine nucleophiles (Table S3) afforded good 2,2-difluoroethylation yields when 1.5 equivalents of the nucleophile were used, and the reaction time of step 2 was increased to 24 hours (entry 2).

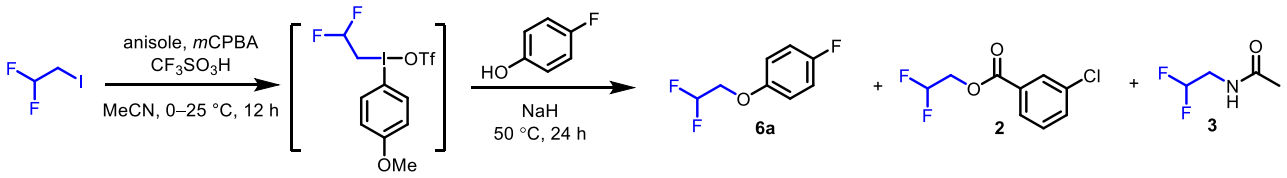


Entry	Deviation from standard conditions step 1[a]	Deviation from standard conditions step 2[a]	**5a** [%][b]
1	None	None (1.1 equiv. methoxyaniline, t = 12 h)	62
2	**None**	**1.5 equiv. 4-methoxyaniline, t = 24 h**	**71**
3	None	1.5 equiv. 4-methoxyaniline, t = 36 h	70
4	None	2.0 equiv. 4-methoxyaniline, t = 24 h	59
5	None	1.5 equiv. 4-methoxyaniline, t = 24 h, T = 60 °C	55
6	Solvent = DCM	1.5 equiv. 4-methoxyaniline, t = 24 h	26
7	Solvent = MeCN/HFIP	1.5 equiv. 4-methoxyaniline, t = 24 h	52
8	2.3 equiv. *m*CPBA	1.5 equiv. 4-methoxyaniline, t = 24 h	**72**
9	2.5 equiv. *m*CPBA	1.5 equiv. 4-methoxyaniline, t = 24 h	58
10	2.3 equiv. *m*CPBA	1.5 equiv. 4-methoxyaniline, t = 24 h, base = Li_2CO_3	67
11	2.3 equiv. *m*CPBA	1.5 equiv. 4-methoxyaniline, t = 24 h, base = Na_2CO_3	68
12	2.3 equiv. *m*CPBA	1.5 equiv. 4-methoxyaniline, t = 24 h, base = K_2CO_3	56
13	2.3 equiv. *m*CPBA	1.5 equiv. 4-methoxyaniline, t = 24 h, base = Ag_2CO_3	35
14	2.3 equiv. *m*CPBA	1.5 equiv. 4-methoxyaniline, t = 24 h, base = KHMDS	66
15	2.3 equiv. *m*CPBA	1.5 equiv. 4-methoxyaniline, t = 24 h, base = tBuOK	56

Table S3. Reaction optimisation: amine nucleophiles. [a] Standard conditions: (i) 1,1-difluoro-2-iodoethane (1.04 mmol), 4-methoxybenzene (1.1 equiv.), *m*CPBA (2.1 equiv.), CF_3SO_3H (1.2 equiv.), MeCN (5 mL, 0.2 M), 0–25 °C, 10 h; (ii) 4-methoxyaniline (1.1 equiv.), Cs_2CO_3 (2.0 equiv.), 50 °C, 12 h. [Note: HFIP = hexafluoroisopropanol.] [b] Crude ^{19}F NMR yields were determined relative to trifluorotoluene as the internal standard.

2.4 Reaction optimisation: 2,2-Difluoroethylation of alcohol nucleophiles

The choice of a fluorinated nucleophile for reaction screening was crucial, as the 2,2-difluoroethylether products **6** were indistinguishable from by-product **2** by ^{19}F NMR.

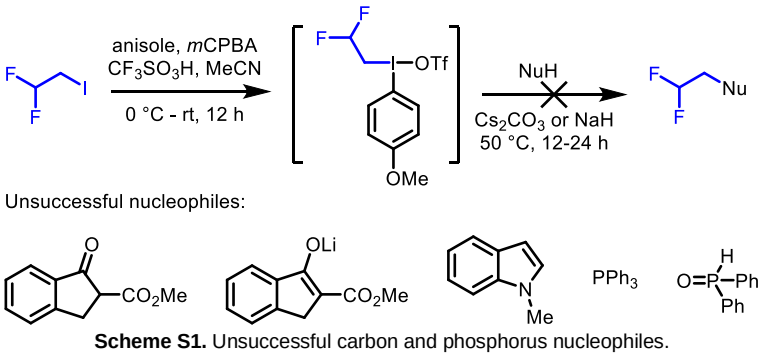


Entry	Deviation from standard conditions step 1[a]	Deviation from standard conditions step 2[a]	**6a** [%][b]
1	None	Base = Cs_2CO_3 (2.0 equiv.) 4-fluorophenol (1.1 equiv.)	24
2	ArH = benzene, t = 4 h	Base = $NaOH_{(aq)}$ (2.0 equiv.) 4-fluorophenol (1.1 equiv.) t = 4 h	46[c]
3	None	Base = NaH (2.0 equiv.) 4-fluorophenol (1.5 equiv.)	44
4	**None**	**None** **base = NaH (3.5 equiv.)** 4-fluorophenol (1.5 equiv.)	**47**

Table S4. Reaction optimisation: alcohol nucleophiles. [a] Standard conditions: (i) 1,1-difluoro-2-iodoethane (1.04 mmol), 4-methoxybenzene (1.1 equiv.), *m*CPBA (2.5 equiv.), CF_3SO_3H (1.2 equiv.), MeCN (5 mL, 0.2 M), 0–25 °C, 10 h; (ii) 4-fluorophenol (1.1 equiv.), NaH (3.5 equiv.), 50 °C, 12 h. [b] Crude ^{19}F NMR yields were determined relative to trifluorotoluene as the internal standard. [c] Reproducibility issues were encountered using these conditions.

2.5 Unsuccessful nucleophiles

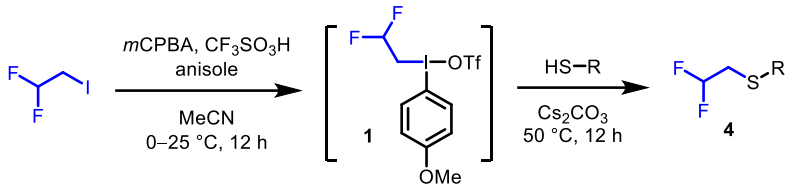
Attempts to 2,2-difluoroethylate carbon and phosphorus nucleophiles have so far proven unsuccessful under the conditions developed herein. In the case of the unsuccessful nucleophiles shown in Scheme S1 below, 2,2-difluoroethyl benzoate **2** was the main product observed.



Scheme S1. Unsuccessful carbon and phosphorus nucleophiles.

3. Experimental Procedures

3.1 General Procedure A for the 2,2-difluoroethylation of thiol nucleophiles



*m*CPBA (583 mg, 2.60 mmol, 2.5 equiv.) was added to an oven-dried pressure tube sealed with a rubber septum and dried under vacuum for 1–1.5 h until the reagent had the consistency of a free-flowing powder (Figure S3). (Caution: dried *m*CPBA can be shock sensitive.) The tube was flushed with argon and wrapped in aluminium foil to protect the reaction from light. Anhydrous CH_3CN (5 mL, 0.2 M) was added, followed by 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol, 1.0 equiv.) and anisole (0.12 mL, 1.14 mmol, 1.1 equiv.). After stirring for 5–10 minutes, the reaction mixture was cooled to 0 °C and CF_3SO_3H (0.11 mL, 1.25 mmol, 1.2 equiv.) was added dropwise. The tube was removed from the ice bath and stirred at room temperature for 12 hours. Next, the aluminium foil was removed and anhydrous Cs_2CO_3 (677 mg, 2.08 mmol, 2.0 equiv.) and the corresponding thiol nucleophile (1.14 mmol, 1.1 equiv.) were added to the reaction, which was then placed into an oil-bath pre-heated to 50 °C and stirred for 12 hours. The reaction was cooled to room temperature (r.t.) and partitioned between H_2O and EtOAc. The crude mixture was extracted 3 times with EtOAc, dried over $MgSO_4$ or Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (as described for each substrate) to give 2,2-difluoroethyl sulfides **4**.

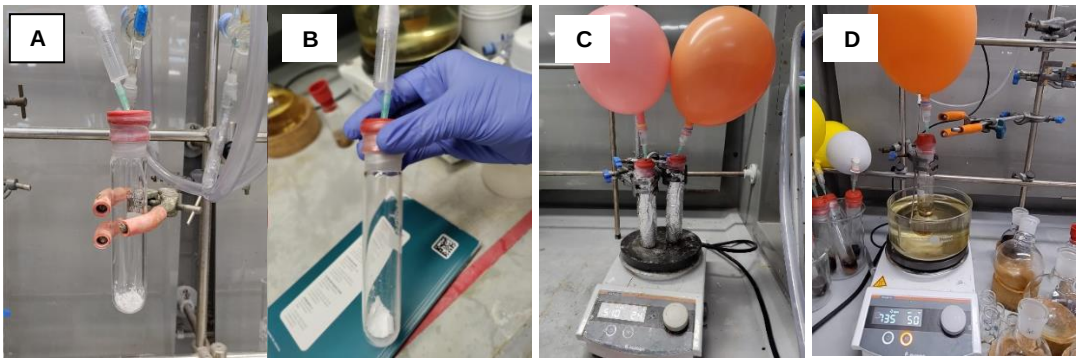
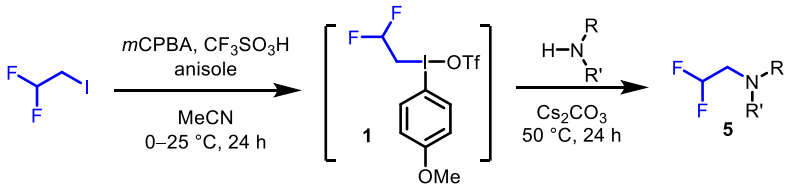


Figure S3. Reaction set up: **A.** *m*CPBA is pre-dried under vacuum for 1–1.5 h until the reagent has the consistency of a free-flowing powder (**B**). **C**: Step 1 is carried out at room temperature, protecting the reaction from light. **D**: Step 2 is carried out in an oil bath pre-heated to 50 °C.

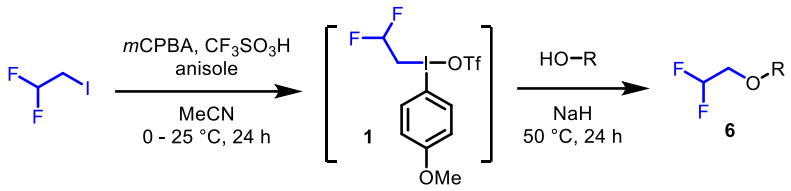
3.2 General Procedure B for the 2,2-difluoroethylation of amine nucleophiles



*m*CPBA (510 mg, 2.18 mmol, 2.1 equiv.) was added to an oven-dried pressure tube sealed with a rubber septum and dried under vacuum for 1–1.5 h until the reagent had the consistency of a free-flowing powder (Figure S3). (Caution: dried *m*CPBA can be shock sensitive.) The tube was flushed with argon and wrapped in aluminium foil to protect the reaction from light. Anhydrous CH_3CN (5 mL) was added, followed by 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol, 1.0 equiv.) and anisole (0.12 mL, 1.14 mmol, 1.1 equiv.). After stirring for 5–10 minutes, the reaction mixture was cooled to 0 °C and CF_3SO_3H (0.11 mL, 1.25 mmol, 1.2 equiv.) was added dropwise. The tube was removed from the ice bath and stirred at room temperature for 24 hours. Next, the aluminium foil was removed and anhydrous Cs_2CO_3 (677 mg, 2.08 mmol, 2.0 equiv.) and the corresponding amine nucleophile (1.56 mmol, 1.5 equiv.) were added to the reaction, which was then placed into an oil-bath pre-heated to 50 °C and stirred for 24 hours. The reaction was cooled to r.t. and partitioned between H_2O and EtOAc. The crude mixture was extracted 3 times with EtOAc, dried over $MgSO_4$ or Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (as described for each substrate) to give 2,2-difluoroethyl amines **5**.

[**Note**: As previously reported by Olofsson *et al.*,[4] the quality of the amine nucleophile can have an impact on the reaction outcome. It is recommended to use fresh amine reagents or to distil older batches before use.]

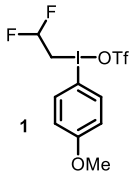
3.3 General Procedure C for the 2,2-difluoroethylation of alcohol nucleophiles



*m*CPBA (585 mg, 2.60 mmol, 2.5 equiv.) was added to an oven-dried pressure tube sealed with a rubber septum and dried under vacuum for 1–1.5 h until the reagent had the consistency of a free-flowing powder (Figure S1). (Caution: dried *m*CPBA can be shock sensitive.) The tube was flushed with argon and wrapped in aluminium foil to protect the reaction from light. Anhydrous CH_3CN (5 mL) was added, followed by 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol, 1.0 equiv.) and anisole (0.12 mL, 1.14 mmol, 1.1 equiv.). After stirring for 5–10 minutes, the reaction mixture was cooled to 0 °C and CF_3SO_3H (0.11 mL, 1.25 mmol, 1.2 equiv.) was added dropwise. The tube was removed from the ice bath and stirred at room temperature for 24 hours. Next, the aluminium foil was removed and NaH (60 % dispersion in mineral oil, 146 mg, 3.65 mmol, 3.5 equiv.) and the corresponding alcohol nucleophile (1.56 mmol, 1.5 equiv.) were added to the reaction, which was then placed into an oil-bath pre-heated to 50 °C and stirred for 24 hours. The reaction was cooled to r.t. and partitioned between H_2O and EtOAc. The crude mixture was extracted 3 times with EtOAc, dried over $MgSO_4$ or Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (as described for each substrate) to give 2,2-difluoroethyl ethers **6**.

4. Analytical Data

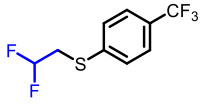
4.1 (2,2-Difluoroethyl)(4-methoxyphenyl)-λ³-iodane trifluoromethanesulfonate (1)



1 was synthesized as described on page 3 above. All isolation attempts of compound **1** failed in our hands. Crude analysis is provided below:
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.49 (m, 2H), 6.78 – 6.61 (m, 2H), 6.05 (tt, *J* = 54.0, 4.0 Hz, 1H), 4.59 (td, *J* = 12.5, 4.0 Hz, 2H), 3.78 (s, 3H); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −74.13 (s, 3F, OTf), −126.51 (ad, *J* = 3.5 Hz, 1F).

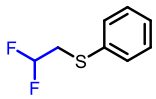
4.2 2,2-Difluoroethylsulfanes (4)

(2,2-Difluoroethyl)(4-(trifluoromethyl)phenyl)sulfane (4a)



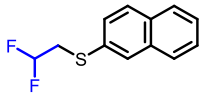
4a was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and 4-(trifluoromethyl)thiophenol (0.16 mL,1.14 mmol) following general procedure A. The crude product was purified by manual silica flash column chromatography (gradient: 100% pentane to 95:5 pentane/Et_2O) to give 179 mg (71% yield) of compound **4a** as a colourless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.5 Hz, 2H), 7.48 (d, *J* = 8.5 Hz, 2H), 5.92 (tt, *J* = 56.0, 4.5 Hz, 1H), 3.33 (td, *J* = 15.0, 4.5 Hz, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) 139.5, 129.3, 129.1 (q, *J* = 33 Hz), 126.1 (q, *J* = 4 Hz), 124.1 (q, *J* = 272 Hz), 115.1 (t, *J* = 243 Hz), 36.4 (t, *J* = 25 Hz); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −62.70 (s, 3F), −114.16 – −114.19 (m, 2F); **IR** *v* = 2972, 2926, 2851, 1742, 1608,1499, 1403, 1325, 1285, 1246, 1166, 1117, 1094, 1063, 1012, 826, 780, 702 cm^{-1}; **HRMS (APCI)** *m/z* calcd. for $C_9H_7F_5S$ $[M]^+$ 242.0189, found 242.0176.

(2,2-Difluoroethyl)(phenyl)sulfane (4b)



4b was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and thiophenol (0.13 mL,1.14 mmol) following general procedure A. The crude product was purified by manual silica flash column chromatography (gradient: 100% pentane to 95:5 pentane/Et_2O) to give 116 mg (64% yield) of compound **4b** as a colourless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50–7.46 (m, 2H), 7.36 (tt, *J* = 6.5, 1.0 Hz, 2H), 7.33–7.28 (m, 1H), 5.90 (tt, *J* = 56.5, 4.5 Hz, 1H), 3.28 (td, *J* = 15.0, 4.5 Hz, 2H); **^{13}C{^{1}H}** NMR (101 MHz, $CDCl_3$) δ 134.2, 131.0, 129.4, 127.6, 115.4 (t, *J* = 243 Hz), 37.6 (t, *J* = 24 Hz); **^{19}F{^{1}H}** NMR (376 MHz, $CDCl_3$) δ −114.41 (s, 2F); **IR** *v* = 3076, 3061, 2976, 2931, 2849, 1584, 1480, 1439, 1412, 1384, 1201, 1113, 1023, 1004, 834, 738, 689, 559 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_8H_{12}F_2NS[M+NH_4]^+$: 192.0659, found 192.0653.

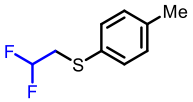
(2,2-Difluoroethyl)(naphthalen-2-yl)sulfane (4c)



4c was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and 2-napthalenethiol (190 mg, 1.14 mmol) following general procedure A**.** The crude product was purified by manual silica flash column chromatography (95:5 pentane/Et_2O) to give 118 mg (51% yield) of compound **4c** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (brs, 1H), 7.83–7.77 (m, 3H), 7.53–7.46 (m, 3H), 5.91 (tt, *J* = 56.5, 4.5 Hz, 1H), 3.33 (td, *J* = 15.0, 4.5 Hz, 2H); **^{13}C NMR{^{1}H}** (101 MHz, $CDCl_3$) δ 133.8, 132.5, 131.4, 129.7, 129.1, 128.3, 127.9, 127.5, 127.0, 126.6, 115.4 (t, *J* = 243 Hz), 37.6 (t, *J* = 24 Hz); **^{19}F NMR{^{1}H}** (376 MHz, $CDCl_3$) δ −114.33 (s, 2F); **IR** *v* = 3055, 2972, 2927, 2853, 1742, 1625, 1589, 1501, 1455, 1411, 1383, 1268, 1243, 1197, 1112, 1032, 1007, 943, 851, 811, 743, 632, 600, 473 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{12}H_{12}F_2S$ [M+H]$^+$: 226.0550, found 226.9513.

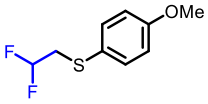
(2,2-Difluoroethyl)(4-methylphenyl)sulfane (4d)



4d was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and 4-methylthiophenol (142 mg, 1.14 mmol) following general procedure A. The crude product was purified by manual silica flash column chromatography (95:5 pentane/Et_2O) to give 113 mg (58% yield) of compound **4d** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.34 (m, 2H), 7.14 (d, *J* = 8.0 Hz, 2H), 5.84 (tt, *J* = 56.5, 4.5 Hz, 1H), 3.18 (td, *J* = 15.0, 4.5 Hz, 2H), 2.34 (s, 3H); **^{13}C NMR{^{1}H}** (101 MHz, $CDCl_3$) δ 138.0, 131.9, 130.4, 130.2, 115.5 (t, *J* = 243 Hz), 38.4 (t, *J* = 24 Hz), 21.2; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −114.60 (s, 2F); **IR** *v* = 3022, 2956, 2922, 2850, 1743, 1597, 1572, 1493, 1414, 1383, 1303, 1274, 1244, 1169, 1115, 1036, 1007, 835, 805, 747, 559 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_9H_{10}F_2S$ [M]$^+$: 188.0471, found 188.0877.

(2,2-Difluoroethyl)(4-methoxyphenyl)sulfane (4e)

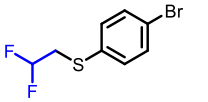


4e was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and 4-methoxythiophenol (140 mg,1.14 mmol) following general procedure A. The crude product was purified by manual silica flash column chromatography (95:5 pentane/Et_2O) to give 178 mg (84% yield) of compound **4e** as a colourless oil.

When the reaction was scaled up to 6.0 mmol (1.152 g 2-iodo-1,1-difluoroethane and 925 mg 4-methoxy-thiophenol), 1.059 g (86% yield) of compound **4e** was isolated as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46–7.40 (m, 2H), 6.88–6.58 (m, 2H), 5.83 (tt, *J* = 56.5, 4.5 Hz, 1H), 3.79 (s, 3H), 3.12 (td, *J* = 15.0, 4.5 Hz, 2H); **^{13}C NMR{^{1}H}** (101 MHz, $CDCl_3$) δ 159.9, 134.8, 124.3, 115.6 (t, *J* = 243 Hz), 114.9, 55.3, 39.3 (t, *J* = 24 Hz); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −114.74 (s, 2F); **IR** *v* = 3003, 2965, 2942, 2909, 2838, 1735, 1592, 1571, 1493, 1462, 1441, 1413, 1384, 1284, 1242, 1201, 1174, 1112, 1025, 823, 733, 638, 625, 524 cm^{-1}; **HRMS (APCI)** *m/z* calcd. for. $C_9H_{10}F_2OS$ [M]$^+$ 204.0420, found 204.0403.

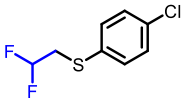
(2,2-Difluoroethyl) (4-bromophenyl)sulfane (4f)



4f was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and 4-bromothiophenol (216 mg,1.14 mmol) following general procedure A. The crude product was purified by manual silica flash column chromatography (gradient: 100% pentane to 95:5 pentane/Et_2O) to give 179 mg (68% yield) of compound **4f** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46–7.43 (m, 2H), 7.32–7.28 (m, 2H), 5.86 (tt, *J* = 56.5, 4.5 Hz, 1H), 3.22 (td, *J* = 15.0, 4.5 Hz, 2H); **^{13}C NMR{^{1}H}** (101 MHz, $CDCl_3$) δ 133.4, 132.7, 132.5, 121.8, 115.3 (t, *J* = 244 Hz), 37.8 (t, *J* = 24 Hz); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −114.31 (s, 2F); **IR** *v* = 2972, 2922, 2850, 1741, 1567, 1473, 1413, 1385, 1244, 1200, 1113, 1089, 1032, 1003, 808, 768, 726, 639, 559, 505 cm^{-1}; **HRMS (ESI/APCI)** not detected.

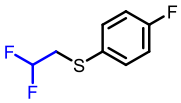
(2,2-Difluoroethyl)(4-chlorophenyl)sulfane (4g)



4g was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and 4-chlorothiophenol (165 mg,1.14 mmol) following general procedure A. The crude product was purified by manual silica flash column chromatography (gradient: 100% pentane to 95:5 pentane/Et_2O) to give 110 mg (51% yield) of compound **4g** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.35 (m, 2H), 7.31–7.27 (m, 2H), 5.87 (tt, *J* = 56.5, 4.5 Hz, 1H), 3.21 (td, *J* = 15.0, 4.5 Hz, 2H); **^{13}C NMR{^{1}H}** (101 MHz, $CDCl_3$) δ 133.8, 132.7, 132.5, 129.5, 115.3 (t, *J* = 243.4 Hz), 37.8 (t, *J* = 24.4 Hz); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −114.278 (s, 2F); **IR** *v* = 2922, 2851, 1744, 1644, 1608, 1576, 1494, 1477, 1326, 1299, 1274, 1170, 1124, 1095, 1039, 1012, 974, 899, 819, 745, 665, 501 cm^{-1}; **HRMS (ESI/APCI)** not detected.

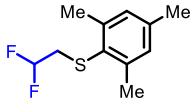
(2,2-Difluoroethyl)(4-fluorophenyl)sulfane (4h)



4h was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and 4-fluorothiophenol (0.15 mL,1.14 mmol) following general procedure A. The crude product was purified by manual silica flash column chromatography (gradient: 100% pentane to 95:5 pentane/Et_2O) to give 134 mg (67% yield) of compound **4h** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49–7.44 (m, 2H), 7.06–7.00 (m, 2H), 5.85 (tt, *J* = 56.5, 4.5 Hz, 1H), 3.17 (td, *J* = 15.0, 4.5 Hz, 2H); **^{13}C NMR{^{1}H}** (101 MHz, $CDCl_3$) δ 162.8 (d, *J* = 248 Hz), 134.4 (d, *J* = 8 Hz), 129.1 (d, *J* = 3 Hz), 116.5 (d, *J* = 22 Hz), 115.4 (t, *J* = 243 Hz), 38.8 (t, *J* = 24 Hz); **^{19}F{^{1}H}** NMR (376 MHz, $CDCl_3$) δ −113.32 (s, 1F), −114.53 (s, 2F); **IR** *v* = 2979, 2927, 2854, 1741, 1590, 1490, 1414, 1385, 1352, 1292, 1227, 1158, 1114, 1090, 1033, 1007, 825, 767, 629, 560 cm^{-1}; **HRMS (APCI)** *m/z* calcd. for. $C_8H_8F_3S$ [M+H]$^+$ 193.0293, found 193.0285.

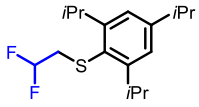
(2,2-Difluoroethyl)(2,4,6-trimethylphenyl)sulfane (4i)



4i was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and 2,4,6-trimethylthiophenol (0.17 mL,1.14 mmol) following general procedure A. The crude product was purified by manual silica flash column chromatography (gradient: 100% pentane to 95:5 pentane/Et_2O) to give 123 mg (55% yield) of compound **4i** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.97 (s, 2H), 5.75 (tt, *J* = 56.5, 4.5 Hz, 1H), 2.97 (td, *J* = 15.5, 4.5 Hz, 2H), 2.54 (s, 6H), 2.29 (s, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 143.0, 139.0, 129.4, 128.4, 115.7 (t, *J* = 243 Hz), 38.1 (t, *J* = 24 Hz), 21.9, 21.1; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −114.34 (s, 2F); **IR** *v* = 3023, 2972, 2926, 2856, 1743, 1602, 1461, 1377, 1244, 1201, 1114, 1032, 1005, 851, 766, 716, 555 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{11}H_{15}F_2S$ $[M+H]^+$ 217.0818; found 217.0817.

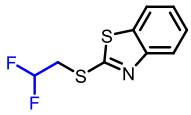
(2,2-Difluoroethyl)(2,4,6-triisopropylphenyl)sulfane (4j)



4j was synthesised from 2-iodo-1,1-difluoroethane (191 mg, 1.0 mmol) and 4-(trifluoromethyl)thiophenol (286 mg,1.3 mmol) following general procedure A. The crude product was purified by manual silica flash column chromatography (100% pentane) to give 160 mg (53% yield) of compound **4j** as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (s, 2H), 5.76 (tt, *J* = 56.5, 4.5 Hz, 1H), 3.89 (hept, *J* = 7.0 Hz, 2H), 2.95 (td, *J* = 15.5, 4.5 Hz, 2H), 2.88 (hept, *J* = 7.0 Hz, 1H), 1.25 (d, *J* = 7.0, 6H); 1.25 (d, *J* = 7.0 Hz, 12H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 153.2, 150.5, 126.6, 122.3, 115.5 (t, *J* = 243 Hz), 40.2 (t, *J* = 23 Hz), 34.4, 31.7, 24.6, 24.0; **^{19}F NMR** (376 MHz, $CDCl_3$) −114.39 (dt, J = 56.5 Hz, 15.5 Hz, 2F); **IR** v = 2968, 1456, 1382, 1115, 1037, 1013, 455 cm-$^{1;}$ **HRMS (APCI)** *m/z* calcd. for $C_{17}H_{26}F_2S$ $[M]^+$ 300.1723, found 300.1728.

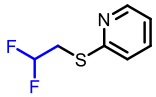
2-((2,2-Difluoroethyl)thio)benzo[*d*]thiazole (4k)



4k was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and 2-mercaptobenzothiazol (191 mg,1.14 mmol) following general procedure A. The crude product was purified by manual silica flash column chromatography (gradient: 100% pentane to 95:5 pentane/Et_2O) to give 166 mg (69% yield) of compound **4k** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90–7.88 (m, 1H), 7.77–7.75 (m, 1H), 7.44 (ddd, *J* = 8.5, 7.5, 1.5 Hz, 1H), 7.33 (ddd, *J* = 8.5, 7.5, 1.0 Hz, 1H), 6.21 (tt, *J* = 56.5, 4.5 Hz, 1H), 3.76 (td, *J* = 15.0, 4.5 Hz, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 164.2, 152.7, 135.5, 126.3, 124.7, 121.8, 121.2, 114.4 (t, *J* = 243 Hz), 35.0 (t, *J* = 26.2 Hz); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −115.09 (s, 2F); **IR** *v* = 3063, 2990, 2941, 1560, 1461, 1426, 1371, 1275, 1238, 1204, 1110, 1041, 1014, 994, 937, 852, 831, 752, 704, 676, 644, 598 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_9H_8F_2NS_2$ $[M+H]^+$ 232.0066, found 232.0060.

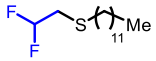
2-((2,2-Difluoroethyl)thio)pyridine (4l)



4l was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and 2-mercaptopyridine (127 mg,1.14 mmol) following general procedure A. The crude product was purified by manual silica flash column chromatography (gradient: 100% pentane to 95:5 pentane/Et_2O) to give 93 mg (51% yield) of compound **4l** as a colourless oil. The connectivity (i.e. *N*- versus S-fluoroalkylation) was confirmed by NOESY analysis and by the diagnostic signal at 156.4 ppm in the ^{13}C NMR spectrum,[5] and the diagnostic signal at −115.12 ppm in the ^{19}F NMR spectrum.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43–8.41 (m, 1H), 7.51 (td, *J* = 7.5, 2.0 Hz, 1H), 7.23–7.20 (m, 1H), 7.03 (ddd, *J* = 7.5, 5.0, 1.0 Hz, 1H), 6.01 (tt, *J* = 57.0, 4.5 Hz, 1H), 3.60 (td, *J* = 15.0, 4.5 Hz, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 156.4, 149.6, 136.4, 122.4, 120.2, 115.3 (t, *J* = 242 Hz), 32.3 (t, *J* = 26 Hz); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −115.12 (s, 2F); **IR** *v* = 3051, 2995, 2939, 1579, 1558, 1455, 1371, 1285, 1248, 1207, 1111, 1040, 1010, 987, 828, 781, 757, 653, 620, 557 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_7H_8F_2NS$ $[M+H]^+$ 176.0346, found 176.0335.

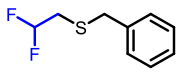
(2,2-Difluoroethyl)(dodecyl)sulfane (4m)



4m was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and dodecane-1-thiol (0.27 mL,1.14 mmol) following general procedure A. The crude product was purified by manual silica flash column chromatography (pentane/Et_2O = 95:5) to give 207 mg (75% yield) of compound **4m** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.84 (tt, *J* = 56.5, 4.5 Hz, 1H), 2.81 (td, *J* = 15.5, 4.5 Hz, 2H), 2.59 (t, *J* = 7.5 Hz, 2H), 1.65–1.50 (m, 2H), 1.41–1.26 (m, 18H), 0.87 (t, J = 7.0 Hz, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 116.9 (t, *J* = 243 Hz), 34.7 (t, *J* = 24 Hz), 33.0, 32.1, 29.79, 29.77, 29.73, 29.6, 29.5, 29.5, 29.3, 28.8, 22.8, 14.2; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ -112.61 (s, 2F); **IR** v = 2922, 2853, 1465, 1411, 1382, 1202, 1115, 1039, 843, 780, 721, 560, 456 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_4H_8F_2S[M+H]^+$: 126.1648, found 126.1648.

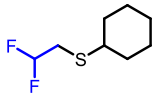
Benzyl(2,2-difluoroethyl)sulfane (4n)



4n was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and benzyl mercaptan (0.14 mL,1.14 mmol) following general procedure A. The crude product was purified by manual silica flash column chromatography (pentane/Et_2O 95:5) to give 115 mg (59% yield) of compound **4n** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.27 (m, 5H), 5.82 (tt, *J* = 56.5, 4.5 Hz, 1H), 3.81 (s, 2H), 2.73 (td, *J* = 15.5, 4.5 Hz, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 137.3, 129.3, 128.8, 127.5, 116.8 (t, *J* = 243 Hz), 36.6, 33.3 (t, *J* = 24 Hz); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −112.46 (s, 2F); **IR** *v* = 3085, 3062, 3030, 2970, 2926, 1602, 1494, 1454, 1410, 1382, 1349, 1240, 1202, 1112, 1071, 1027, 1005, 918, 802, 762, 699, 564 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_9H_{10}F_2S$ $[M]^+$: 188.0471, found 188.08875.

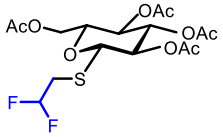
Cyclohexyl(2,2-difluoroethyl)sulfane (4o)



4o was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and cyclohexane thiol (0.14 mL,1.14 mmol) following general procedure A. The crude product was purified by manual silica flash column chromatography (pentane/Et_2O 95:5) to give 116 mg (62% yield) of compound **4o** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.83 (tt, *J* = 57.0, 4.6 Hz, 1H), 2.85 (td, *J* = 15.5, 4.5 Hz, 1H), 2.77–2.70 (m, 1H), 1.98–1.94 (m, 2H), 1.81–1.68 (m, 2H), 1.63–1.57 (m, 1H), 1.35–1.17 (m, 5H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 116.78 (t, *J* = 243 Hz), 44.1, 33.5, 32.77 (t, *J* = 24 Hz), 26.0, 25.8; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −112.95 (s, 2F); **IR** *v* = 2929, 2854, 1449, 1413, 1383, 1347, 1265, 1200, 1113, 1032, 994, 887, 775, 736, 559 cm^{-1}; **HRMS (APCI)** *m/z* calcd. for $C_{10}H_{15}F_2S$ [M+C_2H] 205.0857, found 205.0852.

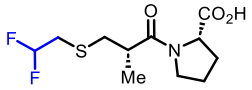
1-(2,2-Difluoroethyl)thio-β-D-glucose tetraacetate (4p)



4p was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and 1-thio-β-D-glucose tetraacetate (415 mg,1.14 mmol) following general procedure A. The crude product was purified by manual silica flash column chromatography (pentane/Et_2O = 95:5) to give 284 mg (64% yield) of compound **4p** as a white solid. Crystals for XRD analysis were obtained by recrystallisation from DCM at room temperature.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.94 (tt, *J* = 56.5, 4.5 Hz, 1H), 5.22 (t, *J* = 9.5 Hz, 1H), 5.04 (dt, *J* = 22.0, 9.5 Hz, 2H), 4.56 (d, *J* = 10.0 Hz, 1H), 4.18 (qd, *J* = 12.5, 3.5 Hz, 2H), 3.72 (ddd, *J* = 10.0, 5.0, 2.5 Hz, 1H), 3.29–3.02 (m, 1H), 2.86 (dddd, *J* = 19.5, 15.5, 12.0, 4.0 Hz, 1H), 2.08–2.05 (m, 6H), 2.02–2.00 (m, 6H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 170.7, 170.2, 169.6, 169.5, 116.1 (t, *J* = 243 Hz), 83.0, 76.2, 73.6, 69.8, 68.3, 62.0, 32.7 (t, *J* = 25 Hz), 20.75, 20.74, 20.69, 20.67; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −112.77 (d, *J* = 280.5 Hz, 1F), −114.77 (d, *J* = 280.5 Hz, 1F); **IR** *v* = 2947, 1748, 1433, 1414, 1371, 1221, 1115, 1091, 1038, 914, 816, 765, 749, 683, 600, 557 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{16}H_{22}F_2NaO_9S$ [M+Na]$^+$: 451.0850; found 451.0851; **mp** = 113–115 °C.

((S)-3-((2,2-difluoroethyl)thio)-2-methylpropanoyl)-L-proline (2,2-difluoroethyl-Captropril) (4q)

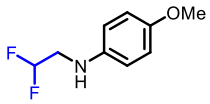


4q was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and *N*-[(S)-3-mercapto-2-methylpropionyl]-L-proline (Captopril) (249 mg,1.14 mmol) following a modified general procedure A. The reaction was quenched with 1 mL of 1M HCl, diluted with water (1 mL) and extracted with DCM (3 x 5 mL). The organics were combined, dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by automated silica flash column chromatography (gradient: 100% pentane to pentane/EtOAc 90/10) to give 127 mg (45% yield) of compound **4q** as a red-brown oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.91 (tt, *J* = 55.0, 4.0 Hz, 1H), 4.52 (dd, *J* = 8.5, 4.0 Hz, 1H), 4.41–4.19 (m, 2H), 3.70–3.66 (m, 2H), 3.24 – 2.90 (m, 2H), 2.61 (dd, *J* = 12.5, 4.0 Hz, 1H), 2.36–1.86 (m, 4H), 1.22 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.8, 171.5, 112.7 (t, *J* = 241 Hz), 62.9 (t, *J* = 29 Hz), 58.7, 47.1, 41.2, 37.9, 29.2, 25.0, 17.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ −125.18 (d, *J* = 297.0 Hz, 1F), −126.12 (d, *J* = 297.0 Hz, 1F); **IR** *v* = 3602, 3163, 3002, 2944, 2292, 2252, 1634, 1441, 1375, 1275, 1038, 918, 749 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{11}H_{17}F_2NO_3S$ [M+Na]$^+$ 451.0850; found 451.0851.

4.3 2,2-Difluoroethylamines (5)

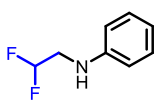
***N*-(2,2-Difluoroethyl)-4-methoxyaniline (5a)**



5a was synthesised form 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and 4-methoxyaniline (198 mg, 1.56 mmol) following general procedure B. The crude product was purified by manual silica flash column chromatography (gradient: 100% pentane to pentane/EtOAc 90/10) to give 134 mg (69% yield) of compound **5a** as a colourless oil. Analytical data matches that reported in the literature.[6]

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.83–6.79 (m, 2H), 6.66–6.62 (m, 2H), 5.91 (tt, *J* = 56.0, 4.5 Hz, 1H), 3.76 (s, 3H), 3.61 (brs, 1H, N*H*), 3.48 (ddt, *J* = 14.2, 9.6, 4.9 Hz, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 153.1, 140.9, 115.1, 114.9 (t, *J* = 242 Hz), 114.7, 55.9, 47.7 (t, *J* = 26 Hz); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −122.75 (s, 2F); **HRMS (ESI)** *m/z* calcd. for $C_9H_{12}F_2NO$ [M+H]$^+$ 188.0887, found 188.0879.

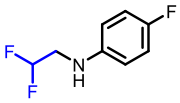
***N*-(2,2-Difluoroethyl)aniline (5b)**



5b was synthesised form 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and aniline (0.14 mL, 1.56 mmol) following general procedure B. The crude product was purified by automated silica flash column chromatography (gradient: 100% pentane to pentane/EtOAc 90/10) to give 90 mg (55% yield) of compound **5b** as a colourless oil. Analytical data matches that reported in the literature.[7]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25–7.20 (m, 2H), 6.82–6.78 (m, 1H), 6.70–6.66 (m, 2H), 5.93 (tt, *J* = 56.0, 4.5 Hz, 1H), 3.87 (brs, 1H, N*H*), 3.55 (tdd, *J* = 14.8, 7.0, 4.5 Hz, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 146.9, 129.6, 118.8, 114.7 (t, *J* = 242 Hz), 113.2, 46.57 (t, J = 26.1 Hz); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −122.65 (s, 2F); **HRMS (ESI)** *m/z* calcd. for $C_8H_{10}F_2N$ [M+H]$^+$ 158.0781, found 158.0772.

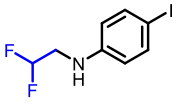
***N*-(2,2-Difluoroethyl)-4-fluoroaniline (5c)**



5c was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and 4-fluoroaniline (0.15 mL, 1.56 mmol) following general procedure B. The crude product was purified by automated silica flash column chromatography (gradient: 100% pentane to pentane/EtOAc 90/10) to give 80 mg (45% yield) of compound **5c** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.94–6.88 (m, 2H), 6.62–6.59 (m, 2H), 5.91 (tt, *J* = 56.0, 4.0 Hz, 1H), 3.50 (tdd, *J* = 14.5, 6.5, 4.0 Hz, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 156.6 (d, *J* = 237 Hz), 143.2, 116.1 (d, *J* = 23 Hz), 114.7 (t, *J* = 242 Hz), 114.3 (d, *J* = 7 Hz), 47.3 (t, *J* = 26 Hz); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −122.74 (s, 2F), −126.46 (s, 1F); **IR** *v* = 3421, 2979, 2931, 2866, 1717, 1609, 1511, 1459, 1441, 1404, 1367, 1311, 1259, 1220, 1118, 1091, 1062, 907, 887, 821, 767, 739, 567, 508 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_8H_9F_3N$ $[M+H]^+$ 176.0687, found 176.0683.

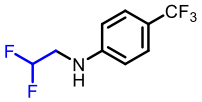
***N*-(2,2-Difluoroethyl)-4-iodoaniline (5d)**



5d was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and 4-iodoaniline (342 mg, 1.56 mmol) following general procedure B. The crude product was purified by automated silica flash column chromatography (gradient: 100% pentane to pentane/EtOAc 90/10) to give 54 mg (18% yield) of compound **5d** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47–7.43 (m, 2H), 6.47–6.43 (m, 2H), 5.89 (tt, *J* = 56.0, 4.0 Hz, 1H), 3.91 (brs, 1H, N*H*), 3.51 (tdd, *J* = 14.5, 6.0, 4.0 Hz, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 146.6, 138.2, 114.4 (t, *J* = 242 Hz), 115.4, 79.7, 46.4 (t, *J* = 26 Hz); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −122.60 (s, 2F); **IR** *v* = 3424, 2978, 2918, 2850, 1720, 1592, 1503, 1440, 1396, 1379, 1366, 1311, 1294, 1261, 1185, 1123, 1070, 997, 885, 811, 748, 695, 590, 504 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_8H_9F_2IN$ $[M+H]^+$ 283.9748, found 283.9739.

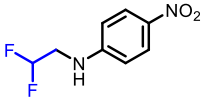
***N*-(2,2-Difluoroethyl)-4-(trifluoromethyl)aniline (5e)**



5e was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and 4-(trifluoromethyl)aniline (0.20 mL, 1.56 mmol) following general procedure B. The crude product was purified by automated silica flash column chromatography (gradient: 100% pentane to pentane/EtOAc 95/5) to give 11 mg (5% yield) of compound **5e** as a colourless oil. Analytical data matched that reported in the literature.[8]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.43 (m, 2H), 6.69–6.67 (m, 2H), 5.92 (tt, *J* = 56.0, 4.0 Hz, 1H), 4.20 (brs, 1H, N*H*), 3.59 (tdd, *J* = 14.5, 6.5, 4.0 Hz, 2H); **^{13}C{^{1}H} NMR** (101 MHz, CDCl3) δ 149.5, 127.0 (q, *J* = 4 Hz), (-CF_3 not detected), (-C-CF_3 not detected), 114.3 (t, *J* = 242 Hz), 112.4, 46.0 (t, *J* = 26 Hz); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −61.31 (s, 3F), −122.64 (s, 2F); **HRMS (ESI)** *m/z* calcd. for $C_9H_9F_5N$ $[M+H]^+$ 226.0655, found 226.0643.

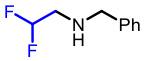
***N*-(2,2-Difluoroethyl)-4-nitroaniline (5f)**



5f was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and 4-nitroaniline (207mg, 1.56 mmol) following general procedure B, with a reaction time of 36 hours in step 2. Product **5f** was detected in 8% yield by ^{19}F NMR spectroscopy with trifluorotoluene (12 µL, 0.1 mmol, 0.1 equiv.) added as internal standard. Analytical data matched that reported in the literature.[8]

^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ −123.23 (s, 2F); **HRMS (ESI)** *m/z* calcd. for $C_8H_{10}F_2N_2O_2$ $[M+H]^+$ 203.0627, found 203.0631.

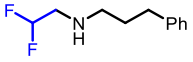
***N*-Benzyl-2,2-difluoroethan-1-amine (5g)**



5g was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and benzylamine (0.14 mL, 1.56 mmol) following general procedure B. The crude product was purified by automated silica flash column chromatography (gradient: 100% pentane to pentane/EtOAc 90/10) to give 119 mg (67% yield) of compound **5g** as a colourless oil. Analytical data matched that reported in the literature.[9]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.28 (m, 5H), 5.87 (tt, *J* = 56.5, 4.5 Hz, 1H), 3.87 (s, 2H), 2.98 (td, *J* = 15.0, 4.5 Hz, 2H), 1.61 (brs, 1H, N*H*); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 139.6, 128.6, 128.2, 127.4, 116.1 (t, *J* = 241 Hz), 53.7, 50.8 (t, *J* = 24 Hz); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −121.75 (s, 2F); **HRMS (ESI)** *m/z* calcd. for $C_9H_{12}F_2N$ $[M+H]^+$ 172.0938, found 172.0932.

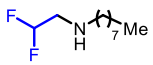
***N*-(2,2-Difluoroethyl)-3-phenylpropan-1-amine (5h)**



5h was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and 3-phenylpropan-1-amine (0.220 mL, 1.56 mmol) following general procedure B. The crude product was purified by automated silica flash column chromatography (gradient: 100% pentane to pentane/EtOAc 90/10) to give 123 mg (59% yield) of compound **5h** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.33 (m, 2H), 7.28–7.24 (m, 3H), 5.88 (tt, *J* = 56.5, 4.5 Hz, 1H), 3.00 (td, *J* = 15.0, 4.0 Hz, 2H), 2.77–2.71 (m, 4H), 1.91–1.84 (m, 2H), 1.35 (brs, 1H, –N*H*); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 141.9, 128.4, 125.9, 116.0 (t, *J* = 240 Hz), 51.6 (t, *J* = 24 Hz), 49.3, 33.4, 31.7; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −121.89 (s, 2F); **IR v =** 3084, 3062, 3026, 2933, 2855, 1603, 1512, 1495, 1454, 1364, 1287, 1245, 1179, 1116, 1033, 928, 893, 745, 697, 569 cm^{-1}; **HRMS (ESI)** m/z calcd. For $C_{11}H_{16}F_2N$ $[M+H]^+$ 200.1245; found 200.1248.

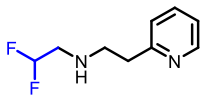
***N*-(2,2-Difluoroethyl)octan-1-amine (5i)**



5i was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and octan-1-amine (0.25 mL, 1.56 mmol) following general procedure B. The crude product was purified by automated silica flash column chromatography (gradient: 100% pentane to pentane/EtOAc 90/10) to give 124 mg (62% yield) of compound **5i** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.83 (ttd, *J* = 56.5, 4.5, 1.5 Hz, 1H), 2.94 (tdd, *J* = 15.0, 4.5, 1.5 Hz, 2H), 2.64 (t, *J* = 7.0 Hz, 2H), 1.46 (p, *J* = 7.0 Hz, 2H), 1.33–1.22 (m, 10H), 0.87 (t, *J* = 6.6 Hz, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 116.1(t, *J* = 240 Hz), 51.8 (t, *J* = 24 Hz), 50.1, 31.9, 30.2, 29.6, 29.4, 27.3, 22.8, 14.2; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ -121.99 (s, 2F); **IR** v = 2956, 2924, 2854, 1666, 1513, 1466, 1415, 1377, 1306, 1249, 1118, 1051, 893, 752, 723, 581 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{10}H_{21}F_2N$ $[M+H]^+$ 194.1715, found 194.1717.

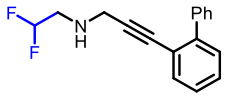
2,2-Difluoro-*N*-(2-(pyridin-2-yl)ethyl)ethan-1-amine (5j)



5j was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and 2-(2-pyridyl)ethylamine (0.19 mL, 1.56 mmol) following general procedure B. The crude product was purified by automated silica flash column chromatography (pentane/EtOAc 90/10) to give 132 mg (68% yield) of compound **5j** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, *J* = 5.0 Hz, 1H), 7.63–7.58 (m, 1H), 7.17–7.11 (m, 2H), 3.40 (brs, 1H, -N*H*), 5.85 (tt, J = 56.3, 4.3 Hz, 1H), 3.14–2.93 (m, 6H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 159.7, 149.3, 136.7, 123.5, 121.6, 115.8 (t, *J* = 240 Hz), 51.4 (t, *J* = 25 Hz), 49.2, 37.8; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −121.81 (s, 2F); **IR** v = 3526, 3164, 2999, 2944, 2292, 2252, 1631, 1440, 1375, 1272, 1156, 1119, 1035, 918, 750, 640 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_9H_{13}F_2N_2$ $[M+H]^+$ 187.1041, found 187.1041.

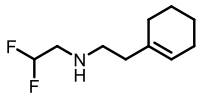
3-([1,1'-Biphenyl]-2-yl)-*N*-(2,2-difluoroethyl)prop-2-yn-1-amine (5k)



5k was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and 3-([1,1'-biphenyl]-2-yl)prop-2-yn-1-amine (0.323 mg, 1.56 mmol) following general procedure B. The crude product was purified by automated silica flash column chromatography (gradient: 100% pentane to pentane/EtOAc 90/10) to give 101 mg (36% yield) of compound **5k** as a brown-red oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55–7.51 (m, 3H), 7.44–7.36 (m, 5H), 7.32–7.27 (m, 1H), 5.77 (tt, *J* = 56.5, 4.5 Hz, 1H), 3.58 (s, 2H), 2.84 (td, *J* = 15.0, 4.5 Hz, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 144.2, 140.8, 133.0, 129.6, 129.3 (2C), 128.6, 128.1 (2C), 127.6, 127.2, 121.4, 115.9 (t, *J* = 240 Hz), 89.6, 84.0, 50.2 (t, *J* = 24.5 Hz), 39.2; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −121.89 (s, 2F); **IR** v = 3341, 3059, 3023, 2978, 2916, 2848, 1733, 1595, 1512, 1475, 1449, 1433, 1363, 1331, 1248, 1117, 1073, 955, 916, 756, 700, 565 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{17}H_{15}F_2NNa$ $[M+Na]^+$ 294.1065, found 294.1062.

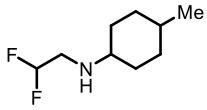
***N*-(2-(Cyclohex-1-en-1-yl)ethyl)-2,2-difluoroethan-1-amine (5l)**



5l was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and 1-isopropylpiperazine (0.24 ml, 1.56 mmol) following general procedure B. The crude product was purified by automated silica flash column chromatography (gradient: 100% pentane to pentane/EtOAc 90/10) to give 123 mg (63% yield) of compound **5l** as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.77 (tq, *J* = 56.6, 4.1 Hz, 1H), 5.40 (s, 1H), 2.90 (dtd, *J* = 15.1, 8.1, 4.2 Hz, 2H), 2.69–2.65 (m, 2H), 2.08–2.05 (m, 2H), 1.95–1.84 (m, 4H), 1.59–1.47 (m, 4H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 134.9, 123.1, 116.0 (t, *J* = 240 Hz), 51.5 (t, *J* = 24 Hz), 47.5, 38.3, 28.1, 25.2, 22.9, 22.4; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −121.90 (s, 2F); **IR** v = 2924, 2856, 2836, 1733, 1666, 1512, 1460, 1438, 1366, 1310, 1269, 1248, 1118, 1035, 919, 889, 799, 750 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_9H_{18}F_2N_2$ $[M+H]^+$ 190.1402, found 190.1401.

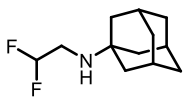
***N*-(2,2-Difluoroethyl)-4-methylcyclohexan-1-amine (5m)**



5m was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and 4-methylcyclohexan-1-amine (0.2 ml, 1.56 mmol) following general procedure B. The crude product was purified by automated silica flash column chromatography (gradient: 100% pentane to pentane/EtOAc 90/10) to give 90 mg (49% yield) of compound **5m** as a yellow oil.

1H NMR (400 MHz, CDCl3) δ 5.82 (tt, J = 56.5, 4.5 Hz, 1H), 2.93 (td, J = 15.0, 4.5 Hz, 2H), 2.69 (p, J = 5.0 Hz, 1H), 1.56–1.41 (m, 7H), 1.33–1.23 (m, 2H), 0.90 (d, J = 7.0 Hz, 3H); 13C{1H} NMR (101 MHz, CDCl3) δ 116.4 (t, J = 240 Hz), 53.7, 49.2 (t, J = 25 Hz), 30.6, 29.6, 29.4, 20.9; 19F{1H} NMR (376 MHz, CDCl3) δ -121.83 (s, 2F); IR v = 3351, 3336, 2925, 2852, 2035, 1724, 1607, 1574, 1513, 1455, 1374, 1258, 1169, 1102, 1033, 897, 830, 750 cm-1; HRMS (ESI) m/z calcd. for C9H18F2N [M+H]+ 178.1402, found 178.1401.

***N*-(2,2-difluoroethyl)adamantan-1-amine (5n)**

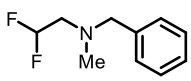


5n was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and (3s,5s,7s)-adamantan-1-amine (236 mg, 1.56 mmol) following general procedure B. The crude product was purified by automated silica flash column chromatography (gradient: 100% pentane to pentane/EtOAc 90/10) to give 120 mg (54% yield) of compound **5n** as a white solid. Crystals for XRD analysis were obtained by recrystallisation from DCM at room temperature.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.81 (tt, *J* = 57.0, 4.5 Hz, 1H), 2.95 (td, *J* = 15.0, 4.5 Hz, 2H), 2.07–2.09 (m, 3H), 1.70–1.59 (m, 12H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 117.0 (t, *J* = 240 Hz), 50.6, 43.4 (t, *J* = 25 Hz), 42.7, 36.7, 29.6; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ

−121.43 (s, 2F); **IR** v = 3346, 2904, 2849, 1739, 1623, 1556, 1452, 1407, 1358, 1245, 1185, 1124, 1098, 1057, 897, 829, 750 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{12}H_{20}F_2N$ $[M+H]^+$ 216.1558, found 216.1559; **melting point** = 210–215 °C.

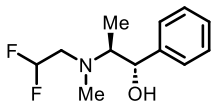
_N_-Benzyl-2,2-difluoro-N-methylethan-1-amine (5o)



5o was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and *N*-methyl-1-phenylmethanamine (0.2 mL, 1.56 mmol) following general procedure B. The crude product was purified by automated silica flash column chromatography (gradient: 100% pentane to pentane/EtOAc 90/10) to give 130 mg (68% yield) of compound **5o** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.26 (m, 5H), 5.88 (tt, *J* = 56.0, 4.5 Hz, 1H), 3.61 (s, 2H), 3.67 (s, 2H), 2.82 (td, *J* = 15.0, 4.5 Hz, 3H), 2.41 (s, 3H);**^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 138.4, 129.0, 128.5, 127.4, 116.2 (t, *J* = 241 Hz), 62.9, 58.7 (t, *J* = 25 Hz), 43.4; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −118.63 (s, 2F); **IR** v = 2954, 2919, 2849, 2787, 1719, 1606, 1579, 1512, 1454, 1366, 1279, 1258, 1169, 1102, 1075, 1027, 848, 770, 739, 699, 614 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{10}H_{14}F_2N$ $[M+H]^+$ 186.1089, found 186.1089.

(1S,2S)-2-((2,2-difluoroethyl)(methyl)amino)-1-phenylpropan-1-ol / _N_-2,2,-difluoro-Pseudoephedrin (5p)



5p was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and (1S,2S)-2-(methylamino)-1-phenylpropan-1-ol (257 mg, 1.56 mmol) following general procedure B. The crude product was purified by automated silica flash column chromatography (gradient: 100% pentane to pentane/EtOAc 90/10) to give 88 mg (37% yield) of compound **5p** as a colourless oil.

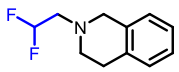
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.25 (m, 5H), 5.90 (tt, *J* = 56.0, 4.5 Hz, 1H), 4.54 (brs, 1H, –O*H*), 4.22 (d, *J* = 9.5 Hz, 1H), 2.98–2.63 (m, 3H), 2.41 (s, 3H), 0.75 (d, *J* = 6.5 Hz, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 141.3, 128.4, 128.0, 127.4, 115.8 (t, *J* = 242 Hz), 75.0, 67.0, 56.0 (t, *J* = 25 Hz), 37.9, 8.2; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −119.30 (d, *J* = 286.0 Hz, 1F), −120.27 (d, *J* = 286.0 Hz, 1F); **IR** v = 3422, 3407, 3064, 3032, 2972, 2812, 1736, 1605, 1494, 1454, 1401, 1372, 1322, 1284, 1251, 1200, 1123, 1039, 960, 879, 802, 758, 701, 638 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{12}H_{18}F_2NO$ $[M+H]^+$ 230.1351, found 230.1351.

_N_-Cyclohexyl-_N_-(2,2-difluoroethyl)cyclohexanamine (5q)

5q was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and dicyclohexylamine (0.30 mL, 1.56 mmol) following general procedure B. **5q** was detected in 2% yield by ^{19}F NMR yield, using trifluorotoluene as internal standard.

^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ −119.74 (s, 2F).

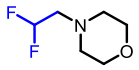
2-(2,2-Difluoroethyl)-1,2,3,4-tetrahydroisoquinoline (5r)



5r was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and 1,2,3,4-tetrahydroisoquinoline (0.2 mL, 1.56 mmol) following general procedure B. The crude product was purified by automated silica flash column chromatography (gradient: 100% pentane to pentane/EtOAc 95/5) to give 106 mg (52% yield) of compound **5r** as a colourless oil. Analytical data matched that reported in the literature.[10]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18–7.10 (m, 3 H), 7.03–7.01 (m, 1H), 5.98 (tt, *J* = 56.0, 4.5 Hz, 1H), 3.80 (s, 2H), 2.98–2.89 (m, 6H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 134., 133.9, 128.9, 126.7, 126.5, 125.9, 116.2 (t, *J* = 241 Hz), 59.9 (t, *J* = 25 Hz), 56.6, 51.9, 28.9; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ -118.16 (s, 2F); **HRMS (ESI)** *m/z* calcd. for $C_{11}H_{14}F_2N$ $[M+H]^+$ 198.1094, found 198.1086.

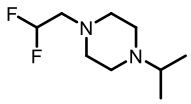
4-(2,2-Difluoroethyl)morpholine (5s)



5s was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and morpholine (0.14 mL, 1.56 mmol) following general procedure B. The crude product was purified by automated silica flash column chromatography (gradient: 100% pentane to pentane/EtOAc 95/5) to give 100 mg (64% yield) of compound **5s** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.87 (tt, *J* = 56.0, 4.5 Hz, 1H), 3.77–3.61 (m, 4H), 2.72 (td, *J* = 15.0, 4.5 Hz, 2H), 2.64–2.51 (m, 4H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 115.8 (t, *J* = 240.0 Hz), 67.0, 60.6 (t, *J* = 25 Hz), 54.4; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −118.34 (s, 2F); **IR** *v* = 3528, 3518, 3002, 2953, 2932, 2835, 1729, 1609, 1575, 1512, 1494, 1460, 1287, 1245, 1178, 1114, 1031, 831, 796, 753, 568 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_6H_{12}F_2NO$ $[M+H]^+$ 152.0887, found 152.0877.

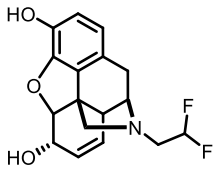
1-(2,2-Difluoroethyl)-4-isopropylpiperazine (5t)



5t was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and 1-isopropylpiperazine (0.23 ml, 1.56 mmol) following general procedure B. The crude product was purified by automated silica flash column chromatography (gradient: 100% pentane to pentane/EtOAc 90/10) to give 124 mg (62% yield) of compound **5t** as a brown oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.85 (tt, *J* = 56.0, 4.5 Hz, 1H), 2.71 (td, *J* = 15.0, 4.5 Hz, 2H), 2.65 – 2.52 (m, 9H), 1.03 (s, 3H), 1.01 (s, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 115.7 (t, *J* = 241 Hz), 60.3 (t, *J* = 25 Hz), 54.5, 54.3, 48.6, 18.6; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −118.31 (s, 2F); **IR** v = 2964, 2935, 2835, 2816, 1732, 1650, 1606, 1512, 1487, 1461, 1384, 1290, 1248, 1179, 1124, 1045, 982, 885, 866, 832, 753 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_9H_{19}F_2N_2$ $[M+H]^+$ 193.1511, found 193.1511.

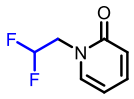
_N_-(2,2-Difluoroethyl)normorphine (5u)



5u was synthesised from 2-iodo-1,1-difluoroethane (96 mg, 0.5 mmol) and normorphine hydrochloride (230 mg, 0.78 mmol). Normorphine hydrochloride was stirred in a solution of sodium hydride (60% dispersion in mineral oil) (40 mg, 1.0 mmol) in anhydrous MeCN (2 mL), before being submitted to procedure C. The crude product was purified by silica flash column chromatography (100% pentane) to give 96 mg (29% yield) of compound **5u** as an off-white solid. *N*-Difluoroethylation was confirmed by NOESY analysis and the diagnostic signal at −118.38 ppm in the ^{19}F NMR spectrum.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.65 (d, *J* = 8.1 Hz, 1H), 6.51 (d, *J* = 8.1 Hz, 1H), 5.85 (tt, *J* = 56.2, 4.3 Hz, 1H), 5.70–5.67 (m, 1H), 5.25 (dt, *J* = 9.9, 2.7 Hz, 1H), 4.90 (dd, *J* = 6.5, 1.3 Hz, 1H), 4.22–4.19 (m, 1H), 3.42 (dd, *J* = 6.3, 3.2 Hz, 1H), 3.01– 2.69 (m, 6H), 2.62 (td, *J* = 12.1, 3.4 Hz, 1H), 2.45 (dd, *J* = 18.6, 6.4 Hz, 1H), 2.07 (td, *J* = 12.5, 5.5 Hz, 1H), 1.87–1.84 (m, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 145.2, 138.0, 133.0, 130.9, 128.6, 126.4, 120.2, 118.8, 116.9, 116.4 (t, *J* = 240 Hz), 91.7, 66.7, 59.1, 58.0 (t, *J* = 25 Hz), 46.0, 43.4, 40.7, 35.7, 23.4; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −118.38 (d, *J* = 284 Hz, 1F), −119.39 (d, *J* = 284 Hz, 1F); **IR** ν = 3328, 3033, 2917, 2849, 1728, 1613, 1502, 1459, 1383, 1317, 1243, 1162, 1117, 1092, 1032, 990, 953, 863, 835, 785,737, 645 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{17}H_{21}F_2N_2O_3$ $[M+NH_4]^+$ 336.1406, found 336.1401; **mp** = 238–247 °C.

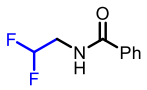
1-(2,2-Difluoroethyl)pyridin-2(1*H*)-one (5v)



5v was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and 2-pyridone (148 mg, 1.56 mmol) following general procedure B. The crude product was purified by automated silica flash column chromatography (gradient: 100% pentane to pentane/EtOAc 90/10) to give 38 mg (21% yield) of compound **5v** as a colourless oil. *N*-Difluoroethylation was confirmed by the diagnostic signals at and the diagnostic signal at 162.6 ppm in the ^{13}C NMR spectrum,[5] and the diagnostic signal at −118.38 ppm in the ^{19}F NMR spectrum.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.31 (m, 1H), 7.24–7.21 (m, 1H), 6.55–6.52 (m, 1H), 6.18–6.15 (m, 1H), 6.16 (tdd, *J* = 6.5, 2.5, 1.5 Hz, 1H), 4.20 (tdd, J = 13.5, 4.5, 2.5 Hz, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 162.6, 140.6, 138.3, 120.9, 112.5 (t, *J* = 243 Hz), 106.6, 51.6 (t, *J* = 28 Hz); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −122.92 (d, *J* = 4.0 Hz, 2F), **IR** ν = 3137, 3079, 2998, 2916, 1661, 1591, 1538, 1462, 1420, 1367, 1256, 1177, 1116, 1070, 1049, 897, 871, 844, 765, 731, 701, 577, 521, 561, 480 cm^{-1}; **HRMS (ESI)** *m/z* calcd. For $C_7H_7F_2NONa$ $[M+Na]^+$ 182.0339, found 182.0386.

***N*-(2,2-Difluoroethyl)benzamide (5w)**

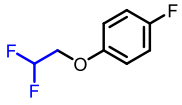


5w was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and benzamide (189mg, 1.56 mmol) following general procedure B. Product **5w** was detected in 6% yield by ^{19}F NMR with trifluorotoluene (12 µL, 0.1 mmol, 0.1 equiv.) added as an internal standard. Analytical data matched that reported in the literature.[11]

^{19}F NMR (376 MHz, $CDCl_3$) δ −123.32 (s, 2F); **HRMS (ESI)** *m/z* calcd. For $C_9H_9F_2NNaO$ $[M+Na]^+$ 208.0544, found 208.0537.

4.4 2,2-Difluoroethylethers (6)

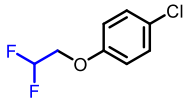
1-(2,2-Difluoroethoxy)-4-fluorobenzene (6a)



6a was synthesised from 2-iodo-1,1-difluoroethane (200 mg,1.04 mmol) and 4-fluorophenol (175 mg,1.56 mmol) following general procedure C. The crude product was purified by manual silica flash column chromatography (eluent: 100% pentane) to give 79 mg (44% yield) of compound **6a** as a colourless oil. Analytical data matched that reported in the literature.[12]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03–6.97 (m, 2H), 6.90–6.84 (m, 2H), 6.07 (tt, *J* = 55.0, 4.0 Hz, 1H), 4.15 (td, *J* = 13.0, 4.0 Hz, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 158.1 (d, *J* = 240 Hz), 154.0 (d, *J* = 2 Hz), 116.3 (d, *J* = 23 Hz), 116.0 (d, *J* = 8 Hz), 113.8 (t, *J* = 241 Hz), 68.2 (t, *J* = 29 Hz); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −122.25 (s, 1F), −125.34 (s, 2F); **HRMS (ESI)** *m/z* calcd. For $C_8H_8F_3O$ $[M+H]^+$ 176.0444, found 176.0447.

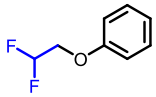
1-Chloro-4-(2,2-difluoroethoxy)benzene (6b)



6b was synthesised from 2-iodo-1,1-difluoroethane (200 mg,1.04 mmol) and 4-chlorophenol (200 mg,1.56 mmol) following general procedure C. The crude product was purified by manual silica flash column chromatography (eluent: 100% pentane) to give 99 mg (50% yield) of compound **6b** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.26 (m, 2H), 6.89–6.84 (m, 2H), 6.09 (tt, *J* = 55.0, 4.0 Hz, 1H), 4.17 (td, *J* = 13.0, 4.0 Hz, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 156.4, 129.7, 127.1, 116.1, 113.7 (t, *J* = 241 Hz), 67.7 (t, *J* = 30 Hz); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −125.29 (s, 2F), **IR** ν = 2987, 2938, 2887, 1596, 1585, 1491, 1370, 1325, 1285, 1245, 1172, 1132, 1062, 1008, 944, 913, 823, 741, 670, 638, 582, 506 cm^{-1}; **HRMS (ESI)** *m/z* calcd. For $C_8H_8ClF_2O$ $[M+H]^+$ 192.0148, found 192.0152.

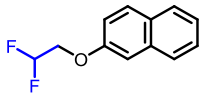
(2,2-Difluoroethoxy)benzene (6c)



6c was synthesised from 2-iodo-1,1-difluoroethane (200 mg,1.04 mmol) and phenol (146 mg,1.56 mmol) following general procedure C. The crude product was purified by manual silica flash column chromatography (eluent: 100% pentane) to give 96 mg (59% yield) of compound **6c** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.30 (m, 2H), 7.04–7.00 (m, 1H), 6.94–6.91 (m, 2H), 6.09 (tt, *J* = 55.0, 4.0 Hz, 1H), 4.19 (td, *J* = 13.0, 4.0 Hz, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ157.9, 129.8, 122.1, 114.8, 113.9 (t, *J* = 241 Hz), 67.4 (t, *J* = 30 Hz); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −125.24 (s, 2F), **IR** v = 2956, 2917, 2849,1727, 1721, 1462 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_8H_9F_2O$ $[M+H]^+$ 159.0616, found 159.0617.

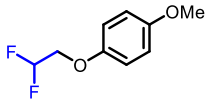
2-(2,2-Difluoroethoxy)naphthalene (6d)



6d was synthesised from 2-iodo-1,1-difluoroethane (192 mg, 1.00 mmol) and 2-napthol (216 mg, 1.50 mmol) following general procedure C. The crude product was purified by automated silica flash column chromatography (gradient: 100% pentane to 20% EtOAc in pentane), then manual flash column chromatography (100% pentane) to give 124 mg (60% yield) of compound **6q** as a white solid. Analytical data matched that reported in the literature.[13]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (q, J = 7.8, 3H), 7.58 (m, 1H), 7.49 (dt, J = 1.6, 8.1, 1H), 7.40 (dt, J = 1.3, 7.4, 1H), 7.20 (q, J = 2.42, 1H), 7.12 (d, J = 2.7 Hz, 1H), 6.16 (tt, J = 55.4, 4.1, 1H), 4.27, (dt, J = 17.4, 4.0 Hz, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 155.8, 134.4, 130.0, 129.60, 127.9, 127.0, 126.8, 124.4, 118.6, 113.9 (t, *J* = 241 Hz), 107.2, 67.4 (t, *J* = 30 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -125.08 (d, *J* = 55.0 Hz, 2F); **HRMS (ESI)** not detected.

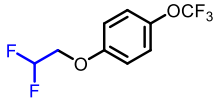
1-(2,2-Difluoroethoxy)-4-methoxybenzene (6e)



6e was synthesised from 2-iodo-1,1-difluoroethane (200 mg,1.04 mmol) and 4-methoxyphenol (194 mg,1.56 mmol) following general procedure C. The crude product was purified by manual silica flash column chromatography (eluent: 100% pentane) to give 158 mg (81% yield) of compound **6e** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.90–6.84 (m, 4H), 6.07 (tt, *J* = 55.0, 4.0 Hz, 1H), 4.142 (td, *J* = 13.5, 4.0 Hz, 2H), 3.78 (s, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 154.8, 152.0, 115.9, 114.8, 114.0 (t, *J* = 241 Hz), 68.1 (t, *J* = 30 Hz), 55.6; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −125.38 (s, 2F), **IR** v = 2997, 2953, 2939, 2837, 1594, 1506, 1458, 1370, 1231, 1129, 1065, 1033, 908, 824, 746, 582, 520 cm^{-1}; **HRMS (ESI)** *m/z* calcd. For $C_9H_{11}F_2O_2$ $[M+H]^+$ 189.0722, found 189.0731.

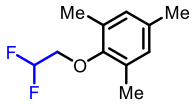
1-(2,2-Difluoroethoxy)-4-(trifluoromethoxy)benzene (6f)



6f was synthesised from 2-iodo-1,1-difluoroethane (200 mg,1.04 mmol) and 4-(trifluoromethoxy)phenol (0.20 mL,1.56 mmol) following general procedure C. The crude product was purified by manual silica flash column chromatography (eluent: 100% pentane) to give 171 mg (70% yield) of compound **6f** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20–7.15 (m, 2H), 6.94–6.90 (m, 2H), 6.08 (tt, *J* = 55.0, 4.0 Hz, 1H), 4.18 (td, *J* = 13.0, 4.0 Hz, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 156.3, 143.8, 122.8, 115.7, 113.6 (t, *J* = 241 Hz), 67.8 (t, *J* = 30 Hz); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ , − 58.41 (s, 3F), −125.31 (s, 2F); **IR** v = 2944, 2924, 2898, 2853, 1602, 1508, 1459, 1371, 1249, 1200, 1165, 1083, 915, 842, 828 cm^{-1}; **HRMS (APCI)** *m/z* calcd. For $C_9H_7F_5O_2$ $[M]^+$ 242.0366, found 242.0369.

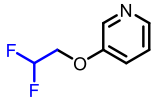
(2-(2,2-Difluoroethoxy)-1,3,5-trimethylbenzene) (6g)



6g was synthesised from 2-iodo-1,1-difluoroethane (200 mg,1.04 mmol) and 2,4,6-trimethylphenol (212 mg,1.56 mmol) following general procedure C. The crude product was purified by manual silica flash column chromatography (eluent: 100% pentane) to give 116 mg (56% yield) of compound **6g** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.91 (s, 2H), 6.14 (tt, *J* = 55.0, 4.0 Hz, 1H), 4.05 (td, *J* = 14.0, 4.0 Hz, 2H), 2.34 (s, 6H), 2.33 (s, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 152.9, 134.0, 130.2, 129.8, 114.2 (t, *J* = 241 Hz), 71.1 (t, *J* = 30 Hz), 20.7, 16.1; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −125.38 (s, 2F), **IR** v = 2979, 2950, 2925, 2863, 1600, 1484, 1461, 1445, 1377, 1309, 1215, 1129, 1053, 954, 932, 903, 854, 832, 782, 594, 517 cm^{-1}; **HRMS (ESI)** *m/z* calcd. For $C_{11}H_{15}F_2O$ $[M+H]^+$ 201.1591, found 201.1592.

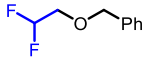
3-(2,2-difluoroethoxy)pyridine (6h)



6h was synthesised from 2-iodo-1,1-difluoroethane (200 mg,1.04 mmol) and 3-hydroxypyridine (148 mL, 1.56 mmol) following general procedure C. The crude product was purified by manual silica flash column chromatography (eluent: 100% pentane) to give 80 mg (48% yield) of compound **6h** as a colourless oil. The connectivity (i.e., *N*- versus *O*-fluoroalkylation) was confirmed by NOESY analysis and by the diagnostic signal at 154.1 ppm in the ^{13}C NMR spectrum,[5] and the diagnostic signal at −125.37 ppm in the ^{19}F NMR spectrum.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 2.0 Hz, 1H), 8.34 (dd, *J* = 4.0, 2.0 Hz, 1H), 7.32–7.26 (m, 2H), 6.15 (tt, *J* = 55.0, 4.0 Hz, 1H), 4.28 (td, *J* = 13.0, 4.0 Hz, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 154.1, 143.5, 138.0, 124.1, 121.6, 113.5 (t, *J* = 242 Hz), 67.6 (t, *J* = 30 Hz); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −125.37 (s, 2F); **IR** v = 3755, 2951, 2924, 2850, 1705, 1604, 1577, 1512, 1477, 1435, 1385, 1266, 1181, 1034, 967, 944, 903, 797, 763, 703, 631, 583, 531, 561, 473 cm^{-1}; **HRMS (ESI)** *m/z* calcd. For $C_{11}H_{15}F_2O$ $[M+H]^+$ 160.0568, found 160.0562.

((2,2-Difluoroethoxy)methyl)benzene (6i)

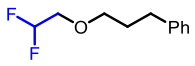


6i was synthesised from 2-iodo-1,1-difluoroethane (200 mg,1.04 mmol) and benzyl alcohol (0.14 mL,1.56 mmol) following general procedure C. The crude product was purified by manual silica flash column chromatography (eluent: 100% pentane) to give 96 mg (54% yield) of compound **6i** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.36 (m, 5H), 5.94 (tt, *J* = 55.5, 4.0 Hz, 1H), 4.66 (s, 2H), 3.73 (td, *J* = 14.0, 4.0 Hz, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 137.2, 128.6, 128.2, 128.0, 114.7 (t, *J* = 241 Hz), 73.9, 69.3 (t, *J* = 30 Hz); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$)

δ −124.80 (s, 2F), **IR** v = 3033, 2984, 2918, 2868, 1497, 1457, 1364, 1320, 1258, 1208, 1101, 1001, 903, 747, 698, 612, 515, 471 cm^{-1}; **HRMS (ESI)** *m/z* calcd. For $C_9H_{11}F_2O$ $[M+H]^+$ 173.0772, found 173.0773.

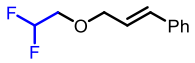
(3-(2,2-Difluoroethoxy)propyl)benzene (6j)



6j was synthesised from 2-iodo-1,1-difluoroethane (200 mg,1.04 mmol) and 3-phenyl-1-propanol (0.16 mL,1.56 mmol) following general procedure C. The crude product was purified by manual silica flash column chromatography (eluent: 100% pentane) to give 120 mg (58% yield) of compound **6j** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.33 (m, 2H), 7.27–7.24 (m, 3H), 5.91 (ttd, *J* = 55.5, 4.0, 2.5 Hz, 1H), 3.68 (tdd, *J* = 14.0, 4.0 Hz, 1.5 Hz, 2H), 3.58 (td, *J* = 6.5, 1.5 Hz, 2H), 2.76 (td, *J* = 8.0, 2.0 Hz, 2H), 2.02–1.94 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 141.7, 128.6, 128.5, 126.0, 114.7 (t, *J* = 241 Hz), 71.3, 70.2 (t, *J* = 27 Hz), 32.1, 31.2; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −124.87 (s, 2F), **IR** v = 3063, 3027, 2944, 2926, 2868, 1603, 1496, 1456, 1367, 1245, 1111, 1063, 902, 744, 698, 571, 515, 491 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{11}H_{22}F_2N_2O$ $[M+NH_4]^+$ 218.1351, found 218.1721.

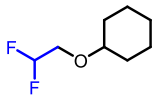
(*E*)-(3-(2,2-Difluoroethoxy)prop-1-en-1-yl)benzene (6k)



6k was synthesised from 2-iodo-1,1-difluoroethane (200 mg,1.04 mmol) and cinnamyl alcohol (209 mg,1.56 mmol) following general procedure C. The crude product was purified by manual silica flash column chromatography (eluent: 100% pentane) to give 87 mg (42% yield) of compound **6k** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.24 (m, 5H), 6.63 (d, *J* = 16.0 Hz, 1H), 6.26 (dt, *J* = 16.0, 6.0 Hz, 1H), 5.91 (tt, *J* = 55.5, 4.0 Hz, 1H), 4.26 (d, *J* = 6.0 Hz, 2H), 3.71 (td, *J* = 14.0, 4.0 Hz, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 136.4, 133.8, 128.8, 128.1, 126.7, 124.8, 114.7 (t, *J* = 241 Hz), 72.7, 69.3 (t, *J* = 27 Hz); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −124.85 (s, 2F), **IR** v = 3026, 2956, 2923, 2553, 1735, 1452, 1118, 1075, 967, 744, 692, 461 cm^{-1}; **HRMS (ESI)** not found.

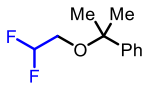
(2,2-Difluoroethoxy)cyclohexane) (6l)



6l was synthesised from 2-iodo-1,1-difluoroethane (200 mg,1.04 mmol) and cyclohexanol (0.16 mL,1.56 mmol) following a modified general procedure C (reaction time of step 2 was 16 h). The crude product was purified by manual silica flash column chromatography (eluent: 100% pentane) to give 116 mg (70% yield) of compound **6l** as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.81 (tt, *J* = 55.5, 4.0 Hz, 1H), 3.63 (td, *J* = 14.0, 4.0 Hz, 2H), 3.30 (td, *J* = 9.0, 4.0 Hz, 1H), 1.89–1.85 (m, 2H), 1.73–1.69 (m, 2H), 1.55–1.47 (m, 1H), 1.37–1.12 (m, 5H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 115.0 (t, *J* = 241 Hz), 78.9, 67.5 (t, *J* = 28 Hz), 35.6, 32.0 (2C), 25.7, 24.0; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −125.17 (s, 2F), **IR** v = 2933, 2858, 1592, 1552, 1451, 1364, 1313, 1244, 1106, 1068, 953, 905, 890, 745, 565, 513, 487 cm^{-1}; **HRMS (ESI)** *m/z* calcd. For $C_{10}H_{20}NF_2O$ $[M+C_2H_6N]^+$ 208.1519, found 208.1507.

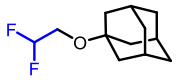
((2-(2,2-difluoroethoxy)propan-2-yl)benzene) (6m)



6m was synthesised from 2-iodo-1,1-difluoroethane (200 mg,1.04 mmol) and 2-phenylpropan-2-ol (212 mg,1.56 mmol) following general procedure C. The crude product was purified by manual silica flash column chromatography (eluent: 100% pentane), followed by a second manual column (eluent: 100% pentane) to give 127 mg (61% yield) of compound **6m** as a colourless oil. The product was 85% pure, with 15% unreacted 2-phenylpropan-2-ol remaining in the mixture, giving a corrected yield of 52% **6m**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.42 (m, 2H), 7.40–7.35 (m, 2H), 7.32–7.29 (m, 1H), 5.84 (tt, *J* = 55.5, 4.0 Hz, 1H), 3.40 (td, *J* = 14.0, 4.0 Hz, 2H), 1.60 (s, 6H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 145.0, 128.6, 127.5, 125.9, 115.1 (t, *J* = 241 Hz), 77.9, 63.1 (t, *J* = 28 Hz), 28.2; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −124.86 (s, 2F); **IR** v = 3087, 3060, 3027, 2979, 2931, 2880, 1603, 1494, 1447, 1365, 1322, 1260, 1131, 1069, 951, 911, 858, 758, 763, 698, 591, 573 cm^{-1}; **HRMS (APCI)** *m/z* calcd. For $C_{11}H_{15}F_2O$ $[M+H]^+$ 201.1091, found 201.1055.

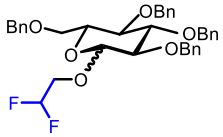
1-(2,2-Difluoroethoxy)adamantane) (6n)



6n was synthesised from 2-iodo-1,1-difluoroethane (200 mg,1.04 mmol) and 1-admantanol (237 mg,1.56 mmol) following general procedure C. The crude product was purified by manual silica flash column chromatography (gradient: 100% pentane) to give 138 mg (62% yield) of compound **6n** as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.79 (tt, *J* = 56.0, 4.5 Hz, 1H), 3.63 (td, *J* = 14.0, 4.5 Hz, 2H), 2.17–2.15 (m, 3H), 1.74–1.73 (m, 6H), 1.67–1.57 (m, 6H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 115.5 (t, *J* = 241 Hz), 73.5, 60.5 (t, *J* = 28 Hz), 41.3, 36.4, 30.6; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −124.82 (s, 2F), **IR** v = 2907, 2853, 1454, 1425, 1369, 1355, 1186, 1117, 1107, 1092, 1062, 972, 918, 814, 763, 750, 575, 504 cm^{-1}; **HRMS (ESI)** *m/z* calcd. For $C_{12}H_{18}F_2O$ $[M]^+$ 216.1557, found 216.1556; **melting point** = 200–205 °C.

2,2-Difluoroethyl-2,3,4,6-tetra-*O*-benzyl-D-α,β-glucopyranose (6o)

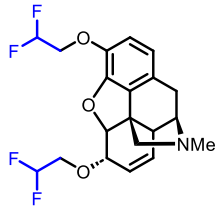


6o was synthesised from 2-iodo-1,1-difluoroethane (192 mg,1.00 mmol) and 2,3,4,6-tetra-*O*-benzyl-D-a,b-glucopyranose (811 mg,1.50 mmol) following general procedure C. The crude product was purified by automated silica flash column chromatography (gradient: 100% pentane to 100% EtOAc) to give 147 mg (27% yield) of compound **6o** as a yellow oil (ca. 1:1.2 mixture of a and b anomers).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.24 (m, 18H), 7.17–7.12 (m, 2H), 6.11–5.80 (m, 1H), 4.99–4.43 (m, 9H), 4.06–3.56 (m, 7H), 3.50–3.44 (m, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 138.8, 138.6, 138.3, 138.21, 138.16, 138.1, 137.9, 128.6,

128.5, 128.4, 128.2, 128.13, 128.08, 128.01, 127.95, 127.89, 127.85, 127.82, 127.7, 114.2 (t, *J* = 241 Hz), 114.3 (t, *J* = 241 Hz), 104.07, 98.09, 84.6, 82.1, 81.9, 79.9, 77.6, 77.51, 77.48, 77.2, 76.8, 75.9, 75.8, 75.2, 75.1, 75.0, 73.6, 70.8, 68.8, 68.7 (t, *J* = 29 Hz), 68.4, 67.3 (t, *J* = 29 Hz) [mixture of a and b anomers, some C signals overlap]; **^{19}F NMR** (376 MHz, $CDCl_3$) δ −124.32 (d, *J* = 295.0 Hz, 1Fα), −124.65 (d, J = 294.5 Hz, 1Fβ), −125.18 (d, *J* = 295.0 Hz, 1Fα), −125.76 (d, J = 294.5 Hz, 1Fβ); **IR** v = 3031, 2915, 2871,1496, 1452, 1362, 1119, 1067, 732, 696 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{36}H_{38}F_2NaO_6$ $[M+Na]^+$ 627.2528, found 627.2520.

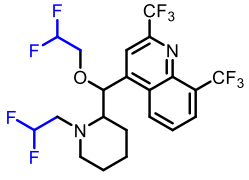
6,8-Bis(2,2-difluoroethoxy)morphine (6p)



6p was synthesised from 2-iodo-1,1-difluoroethane (200 mg,1.04 mmol) and morphine (445 mg,1.56 mmol) following general procedure C. The crude product was purified by Auto flash column chromatography (gradient: 100% EtOAc to EtOAc/MeOH 60/40) to give 74 mg (18% yield) of compound **6p** as an off-white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.71–6.66 (m, 1H), 6.54–6.51 (m, 1H), 6.21–5.80 (m, 1H), 5.74–5.66 (m, 1H), 5.44–5.33 (m, 1H), 4.96 (dd, *J* = 6.0, 1.5 Hz, 1H), 4.73–4.19 (m, 2H), 4.03–3.74 (m, 2H), 3.39–3.35 (m, 1H), 2.71–2.65 (m, 1H), 2.62 –2.57 (m, 1H), 2.44 (s, 3H), 2.42–2.35 (m, 1H), 2.33–2.26 (m, 1H), 2.08–2.00 (m, 1H), 1.92–1.87 (m, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 147.5, 140.1, 131.8, 129.9, 129.4, 127.8, 119.8, 118.0, 114.7 (t, *J* = 240 Hz), 114.2 (t, *J* = 241 Hz), 89.5, 88.7, 74.9, 69.8 (t, *J* = 29 Hz), 68.6 (t, *J* = 29 Hz), 59.0, 46.6, 43.2, 41.0, 20.7; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −124.74 (d, *J* = 295.0 Hz, 1F), −125.65 (d, *J* = 295.0 Hz, 1F), −125.27 (d, *J* = 295.0 Hz), −126.06 (d, *J* = 295.0 Hz); **IR** v = 3054, 2987, 2306, 2212, 1713, 1637, 1597, 1566, 1528, 1505, 1438, 1393, 1368, 1268, 1217, 1132, 1079, 987, 895, 807, 730, 702, 572, 552, 511 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{21}H_{24}F_4NO_3$ $[M+H]^+$ 414.1686, found 414.1683; **mp** 255–265 °C.

4-((2,2-Difluoroethoxy)(1-(2,2-difluoroethyl)piperidin-2-yl)methyl)-2,8 bis(trifluoromethyl)quinoline (6q)

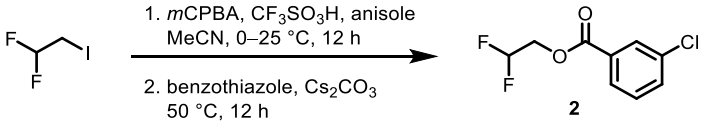


6q was synthesised from 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and Mefloquine (645 mg, 1.56 mmol) following general procedure B. The crude product was purified by automated silica flash column chromatography (gradient: 100% pentane to pentane/EtOAc 90/10) to give 190 mg (36% yield) of compound **6q** as a white solid. ^{19}F NMR of the crude reaction mixture also showed 6% of the *N*-difluoroethylated product (no difluoroethylation on the -OH group) relative to the internal standard trifluorotoluene.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.5 Hz, 1H), 8.20 (d, *J* = 7.0 Hz, 1H), 7.86 (s, 1H), 7.78 (t, *J* = 8.0 Hz, 1H), 5.95 (tt, *J* = 55.0, 4.0 Hz, 1H), 5.51 (tt, *J* = 56.0, 4.0 Hz, 1H), 5.41 (d, *J* = 4.5 Hz, 1H), 3.61 (td, *J* = 14.0, 4.0 Hz, 2H), 3.23–2.94 (m, 3H), 2.62 (ddd, *J* = 13.5, 8.5, 3.5 Hz, 1H), 1.85–1.72 (m, 2H), 1.63–1.34 (m, 3H), 1.28–1.24 (m, 1H), 0.88–0.83 (m, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 148.7, 148.3 (q, *J* = 36 Hz), 144.3, 129.9 (q, *J* = 30 Hz), 129.2 (q, *J* = 6 Hz), 127.7, 127.6, 127.5, 123.8 (q, *J* = 231 Hz), 121.1 (q, *J* = 232 Hz), 116.2 (t, *J* = 242 Hz), 115.9 (q, *J* = 3 Hz), 113.9 (t, *J* = 241 Hz), 80.7, 69.0 (t, *J* = 27 Hz), 64.7, 54.0 (t, *J* = 25 Hz), 52.4, 22.7, 21.3, 21.2; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −60.33 (s, 3F), −67.98 (s, 3F), −119.70 (d, *J* = 283.0 Hz, 1F), −120.72 (d, *J* = 283.0 Hz, 1F), −125.27 (ad, *J* = 2.0 Hz, 2F); **IR** v = 2933, 2861, 1602, 1585, 1517, 1431, 1371, 1310, 1274, 1144, 1110, 929, 900, 837, 768, 675 cm^{-1}; **HRMS (ESI)** *m/z* calcd. For $C_{21}H_{21}F_{10}N_2O$ $[M+H]^+$ 507.1489, found 507.1489; **mp** 240–245 °C.

5. Mechanistic Investigation and Control Reactions

5.1 By-product analysis: 2,2-Difluoroethyl 3-chlorobenzoate (2)

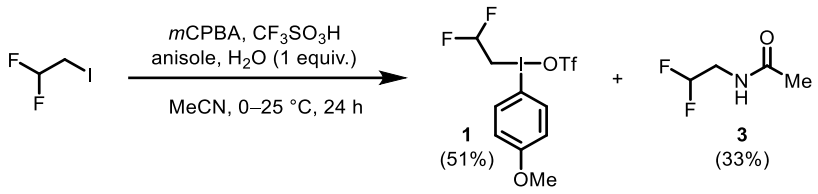


2 was observed as a by-product in the reaction of weak nucleophiles with fluoroalkyliodonium intermediate **1**. It is formed by reaction of **1** with the reduced oxidant, 3-chlorobenzoic acid (*m*CBA).

A reaction was set up following general procedure A with 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol) and benzothiazole (0.12 mL,1.14 mmol). The crude reaction mixture was purified by silica flash column chromatography (100% pentane to 95:5 pentane/Et_2O) and compound **2** (80 mg, 35% yield, colourless oil) was isolated as the main product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (t, *J* = 2.0 Hz, 1H), 7.93 (dt, *J* = 8.0, 1.5 Hz, 1H), 7.55 (ddd, *J* = 8.0, 2.0, 1.0 Hz, 1H), 7.38 (t, *J* = 8.0 Hz, 1H), 6.08 (tt, *J* = 55.0, 4.0 Hz, 1H), 4.51 (td, *J* = 13.5, 4.0 Hz, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 164.5, 134.8, 133.7, 130.7, 130.0 (2C), 128.1, 112.8 (t, *J* = 241 Hz), 63.2 (t, *J* = 30 Hz); **^{19}F{^{1}H}** NMR (376 MHz, $CDCl_3$) δ −125.55 (s, 2F); **IR** v = 3075, 2968,1730,1575,1475, 1428, 1428, 1369, 1328, 1281, 1250, 1073, 1009, 900, 744, 673 cm^{-1}; **HRMS (APCI)** *m/z* calcd. for $C_{10}H_8ClF_2O_2$ $[M+H]^+$ 221.0175, found 221.0164.

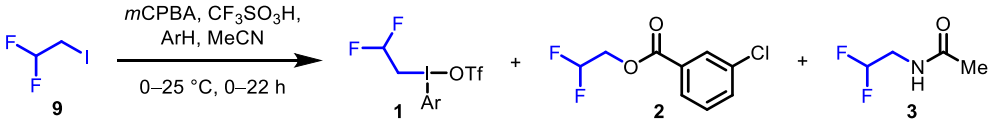
5.2 By-product analysis: *N*-(2,2-Difluoroethyl)acetamide (3)



3 was observed as a by-product when the formation of fluoroalkyliodonium intermediate **1** was attempted in wet MeCN (i.e. with traces of water in the reaction). It is formed by the reaction of **1** with MeCN in a Ritter-type reaction.
A reaction was set up as described in section 2.1 above with 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol), with the addition of 1 equivalent of water (18.6 µL, 1.04 mmol). Analysis of the crude reaction mixture by ^{1}H and ^{19}F NMR after 24 hours revealed the formation of 33% *N*-(2,2-difluoroethyl)acetamide **3** along with 51% fluoroalkyliodonium intermediate **1** and 14% unreacted 2-iodo-1,1-difluoroethane. Analytical data of **3** matched that reported in the literature.[14]
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.23 (brs, 1H, -N*H*), 5.84 (tt, *J* = 56.0, 4.0 Hz, 1H), 3.59 (tdd, *J* = 15.0, 6.0, 4.0 Hz, 2H), 2.02 (s, 3H);
^{19}F NMR (376 MHz, $CDCl_3$) δ −122.94 (dt, *J* = 56.0, 15.0 Hz, 2F).

5.3 Stability of (2,2-difluoroethyl)(4-methoxyphenyl)-λ^3-iodane trifluoromethanesulfonate (1) in solution

5.3.1 Stability of (2,2-difluoroethyl)(4-methoxyphenyl)-λ^3-iodane trifluoromethanesulfonate (1) at rt

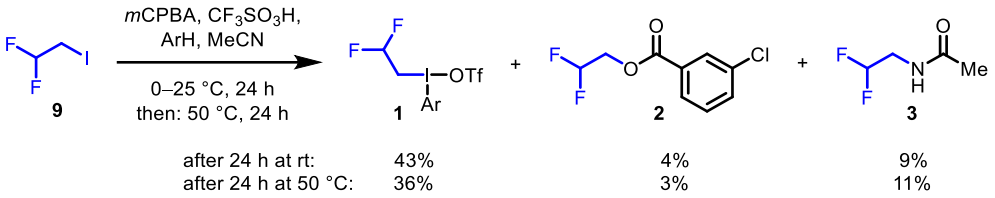


Formation of the hypervalent iodine reagent was set up as described in 2.1 above. The reaction was stirred at room temperature for 22 hours and aliquots were taken every 30 minutes for analysis by ^{19}F NMR spectroscopy. The hypervalent iodine intermediate was stable at room temperature over 24 hours (Table S5).

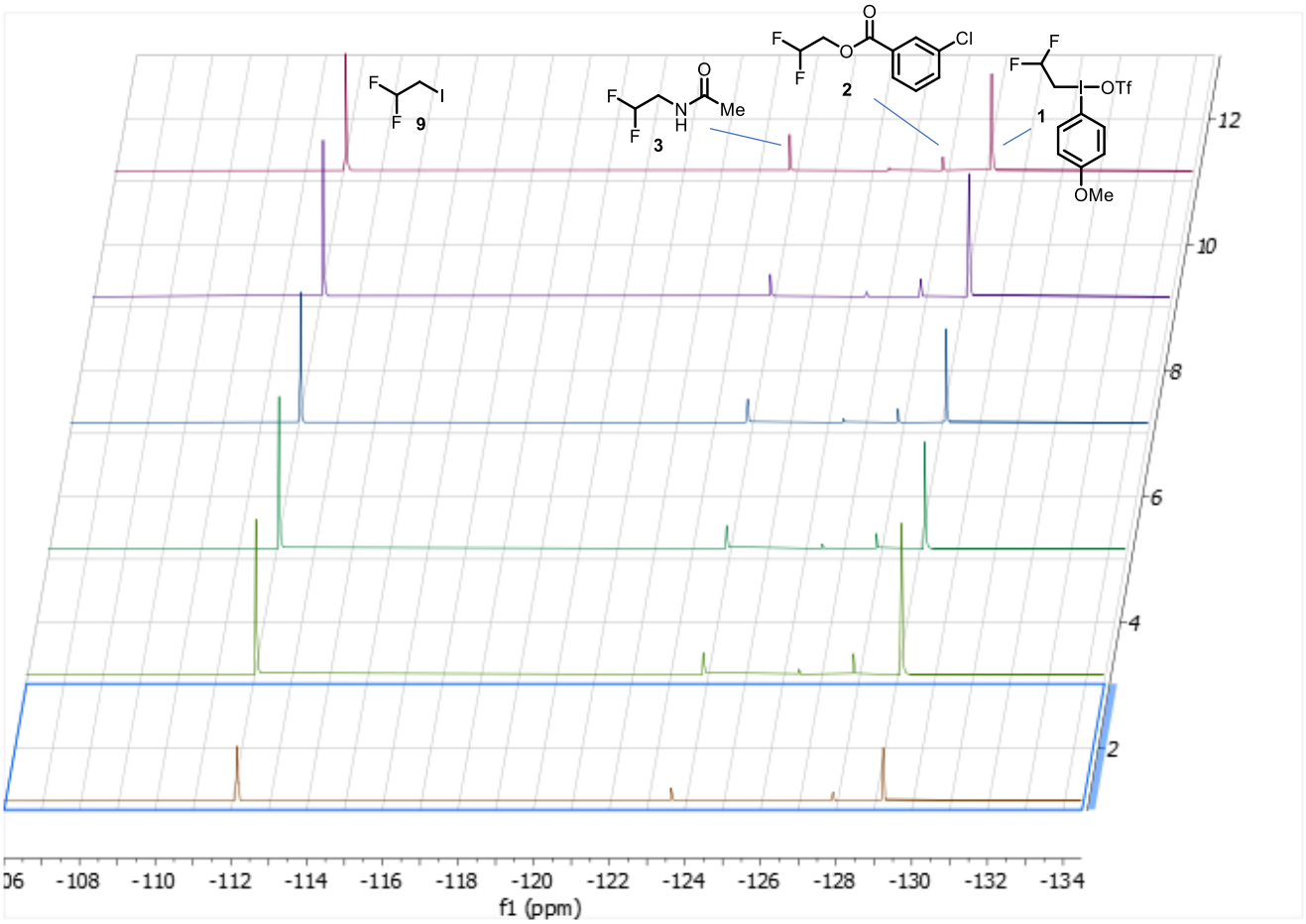
t (h)	Unreacted **9** (%)	Conversion **1** (%)	Conversion **2** (%)	Conversion **3** (%)
0.5	72%	24%	2%	5%
1	61%	36%	3%	6%
1.48	56%	42%	5%	9%
1.92	52%	41%	5%	10%
2.62	55%	41%	6%	9%
3.68	52%	41%	6%	10%
3.9	52%	42%	6%	9%
4.67	52%	41%	5%	7%
6.7	52%	41%	6%	11%
7.15	53%	43%	6%	8%
7.67	54%	42%	6%	10%
8.93	50%	41%	6%	11%
17.28	52%	42%	6%	11%
21.95	54%	42%	7%	7%

Table S5. Formation and stability of hypervalent iodine intermediate at rt.

5.3.2 Stability of (2,2-difluoroethyl)(4-methoxyphenyl)-λ³-iodane trifluoromethanesulfonate (1) at 50 °C



Formation of the hypervalent iodine reagent was set up as described in 2.1 above. After stirring for 24 hours at room temperature, the reaction was heated to 50 °C and stirred for a further 26 hours. Aliquots were taken at pre-determined time points and analysed by ^{19}F NMR spectroscopy. The distribution of products remained stable over 26 hours (Fig. S6).

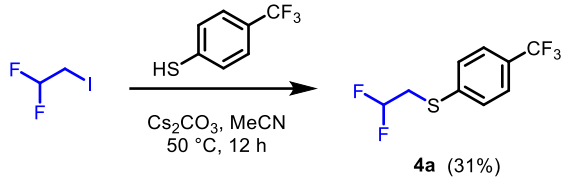


t (h)	Unreacted **9** (%)	Conversion **1** (%)	Conversion **2** (%)	Conversion **3** (%)
0.3	44	43	4	9
0.9	44	44	2	10
1.5	58	31	3	8
2.6	49	36	4	11
4.8	49	38	3	10
26.4	50	36	3	11

Table S6. Formation and stability of hypervalent iodine intermediate at 50 °C. Time refers to the time that passed between heating the reaction to 50 °C and the NMR acquisition.

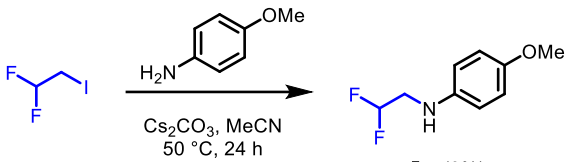
5.4 Control reactions: Direct nucleophilic attack on 1,1-difluoro-2-iodoethane

General procedure D for direct nucleophilic attack on 1,1-difluoro-2-iodoethane: 2-Iodo-1,1-difluoroethane (200 mg, 1.04 mmol, 1.0 equiv.), nucleophile (1.1–1.5 equiv.), base (2.0–3.5 equiv.) and anhydrous CH_3CN (5 mL, 0.2 M) were added to an oven-dried pressure tube and sealed with a rubber septum. The reaction was placed into an oil-bath pre-heated to 50 °C and stirred for 12–24 hours. The reaction was cooled to r.t. and partitioned between H_2O and EtOAc. The crude mixture was extracted 3 times with EtOAc, dried over $MgSO_4$ or Na_2SO_4, filtered, concentrated *in vacuo*, and analysed by ^{19}F NMR spectroscopy with trifluorotoluene as internal standard.



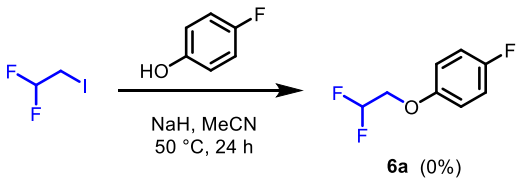
4a (31%)

General procedure D was carried out with 4-(trifluoromethyl)thiophenol (0.16 mL,1.14 mmol, 1.1 equiv.) and Cs_2CO_3 (677 mg, 2.08 mmol, 2.0 equiv.). Analysis by ^{19}F NMR spectroscopy after 12 hours revealed 31% of compound **4a** relative to the internal standard trifluorotoluene.



5a (0%)

General procedure D was carried out with 4-methoxyaniline (198 mg, 1.56 mmol, 1.5 equiv.) and Cs_2CO_3 (677 mg, 2.08 mmol, 2.0 equiv.). Analysis by ^{19}F NMR spectroscopy after 24 hours revealed 0% of compound **5a**.



6a (0%)

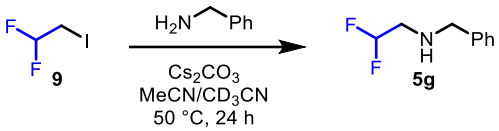
General procedure D was carried out with 4-fluorophenol (175 mg, 1.56 mmol, 1.5 equiv.) and NaH (60 % dispersion in mineral oil, 146 mg, 3.65 mmol, 3.5 equiv.). Analysis by ^{19}F NMR spectroscopy after 24 hours revealed 0% of compound **6a**.

5.5 Reaction kinetics

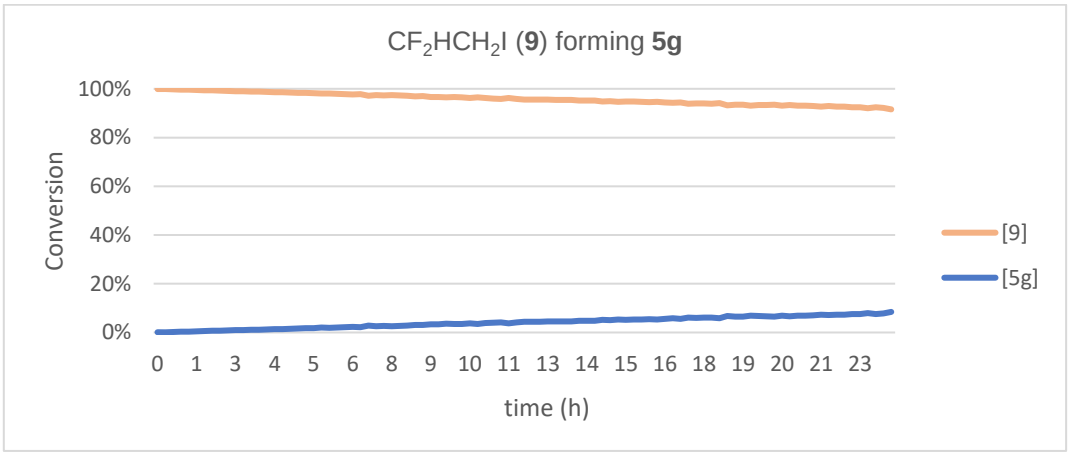
General procedure E for NMR experiments

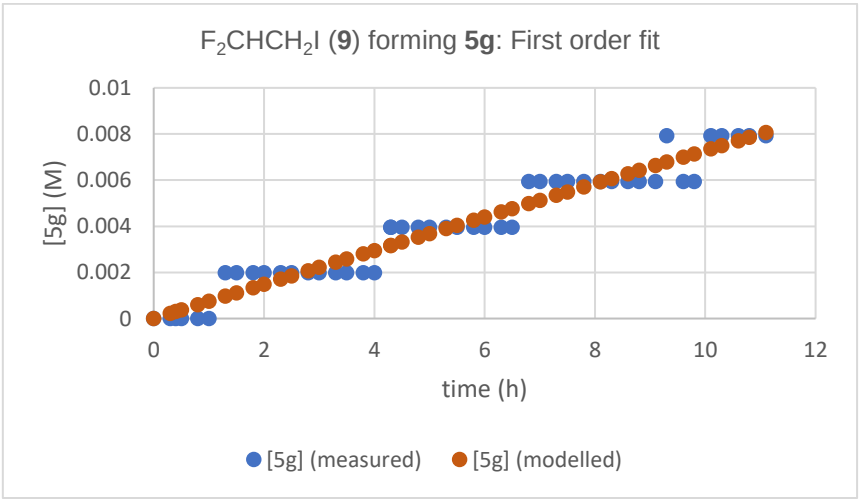
Prior to running kinetics NMR experiments, an inversion recovery experiment was run on a mixture of 2-iodo-1,1-difluoroethane (20 mg, 0.1 mmol) and 4,4'-bis(trifluoromethyl)-1,1'-biphenyl (0.3 mg, 0.01 mmol) in 0.5 mL MeCN/ CD_3CN (9:1). The relaxation time T_1 of the CF_2 signal was determined to be 4 seconds.
The reactions in this section were monitored by ^{19}F NMR on a Bruker AV 400 MHz. Where applicable, the probe was heated to 50 °C and left to equilibrate for 20–30 minutes before the sample was loaded into the magnet. On loading, an initial ^{19}F NMR spectrum was acquired with the transmitter frequency set to −100 ppm, spectral width of 120 ppm, the size of FID set to 256k points and a relaxation delay (d_1) of 1.5 seconds. Once the initial experiment had been run and checked, experiments were run every 15 minutes for 12–24 hours with d_1 set to 20 seconds. The data was analysed with MNova's Directory Spectra Stack script and Arrayed Data Analysis tools and exported to Excel. Conversions were determined relative to the internal standard 4,4'-bis(trifluoromethyl)-1,1'-biphenyl.

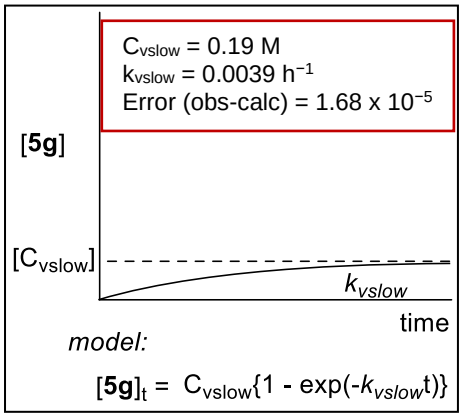
Reaction kinetics: Reaction of 2-iodo-1,1-difluoroethane with benzylamine



2-Iodo-1,1-difluoroethane **9** (200 mg, 1.04 mmol, 1.0 equiv., $[\mathbf{9}]_0$ = 0.198 M), benzylamine (0.14 mL, 1.56 mmol, 1.5 equiv., $[benzylamine]_0$ = 0.297 M), and 4,4'-bis(trifluoromethyl)-1,1'-biphenyl (30 mg, 0.1 mmol, 0.1 equiv.) were dissolved in a mixture of anhydrous MeCN (4.5 mL) and CD_3CN (0.5 mL) in an oven-dried Schlenk tube under an atmosphere of Ar. A 0.6 mL aliquot was transferred to a J Young NMR tube, Cs_2CO_3 (677 mg, 2.08 mmol, 2.0 equiv.) was added and the reaction was monitored for 24 hours at 50 °C by ^{19}F NMR on a Bruker AV 400 MHz as described in General Procedure E. Conversions were determined by integration of the relevant signals in the ^{19}F NMR spectra relative to the internal standard 4,4'-bis(trifluoromethyl)-1,1'-biphenyl.







time (h)	[9] (%)	[5g] (%)	[5g] (M)
0.3	100	0	0
0.4	100	0	0
0.5	100	0	0
0.8	100	0	0
1.0	100	0	0
1.3	99	1	0.001979
1.5	99	1	0.001979
1.8	99	1	0.001979
2.0	99	1	0.001979
2.3	99	1	0.001979
2.5	99	1	0.001979
2.8	99	1	0.001979
3.0	99	1	0.001979
3.3	99	1	0.001979
3.5	99	1	0.001979
3.8	99	1	0.001979
4.0	99	1	0.001979
4.3	98	2	0.003958
4.3	98	2	0.003958
4.5	98	2	0.003958
4.8	98	2	0.003958
5.0	98	2	0.003958
5.3	98	2	0.003958
5.5	98	2	0.003958
5.8	98	2	0.003958
6.0	98	2	0.003958
6.3	98	2	0.003958
6.5	98	2	0.003958
6.8	97	3	0.005938
7.0	97	3	0.005938
7.3	97	3	0.005938
7.5	97	3	0.005938

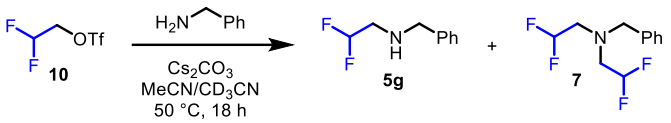
time (h)	[9] (%)	[5g] (%)	[5g] (M)
7.8	97	3	0.005938
8.1	97	3	0.005938
8.3	97	3	0.005938
8.6	97	3	0.005938
8.8	97	3	0.005938
9.1	97	3	0.005938
9.3	96	4	0.007917
9.6	97	3	0.005938
9.8	97	3	0.005938
10.1	96	4	0.007917
10.3	96	4	0.007917
10.6	96	4	0.007917
10.8	96	4	0.007917
11.1	96	4	0.007917
11.3	96	4	
11.6	96	4	
11.8	96	4	
12.1	96	4	
12.3	96	4	
12.6	96	4	
12.8	95	5	
13.1	95	5	
13.3	95	5	
13.6	95	5	
13.8	95	5	
14.1	95	5	
14.3	95	5	
14.6	95	5	
14.8	95	5	
15.1	95	5	
15.4	95	5	
15.6	95	5	

time (h)	[9] (%)	[5g] (%)	[5g] (M)
15.9	95%	5	
16.1	95%	5	
16.4	94%	6	
16.6	94%	6	
16.9	94%	6	
17.1	94%	6	
17.4	94%	6	
17.6	94%	6	
17.9	94%	6	
18.1	94%	6	
18.4	93%	7	
18.6	93%	7	
18.9	93%	7	
19.1	93%	7	
19.4	93%	7	
19.6	93%	7	
19.9	93%	7	
20.1	93%	7	
20.4	93%	7	
20.6	93%	7	
20.9	93%	7	
21.1	93%	7	
21.4	93%	7	
21.6	93%	7	
21.9	93%	7	
22.1	93%	7	
22.4	92%	8	
22.7	92%	8	
22.9	92%	8	
23.2	92%	8	
23.4	92%	8	
23.7	92%	8	

Table S7. Reaction kinetics. Conversion of 2-iodo-1,1-difluoroethane to *N*-benzyl-2,2-difluoroethan-1-amine **5g**, determined by ^{19}F NMR spectroscopy. Time (h) is defined as the time elapsed between addition of Cs_2CO_3 to the reaction and acquisition of the corresponding ^{19}F NMR spectrum.

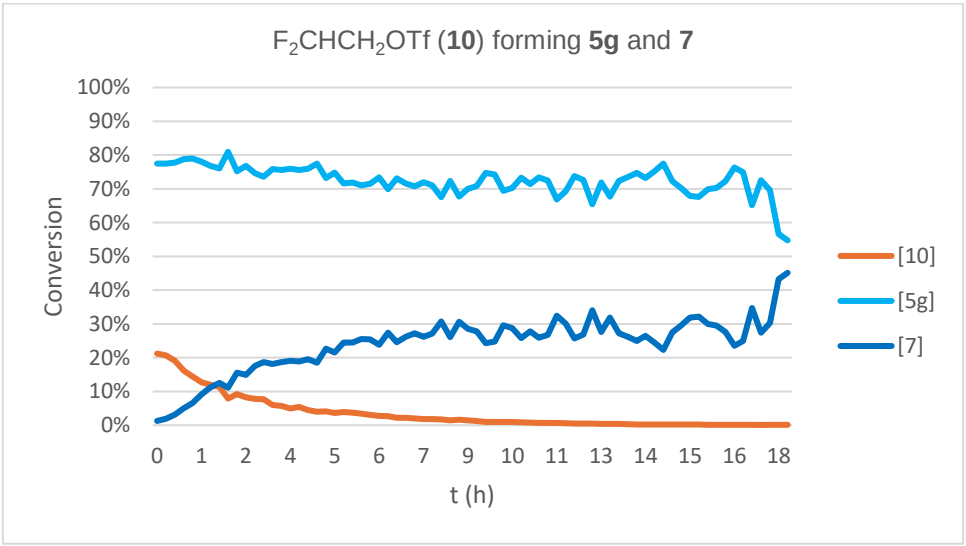
SUPPORTING INFORMATION

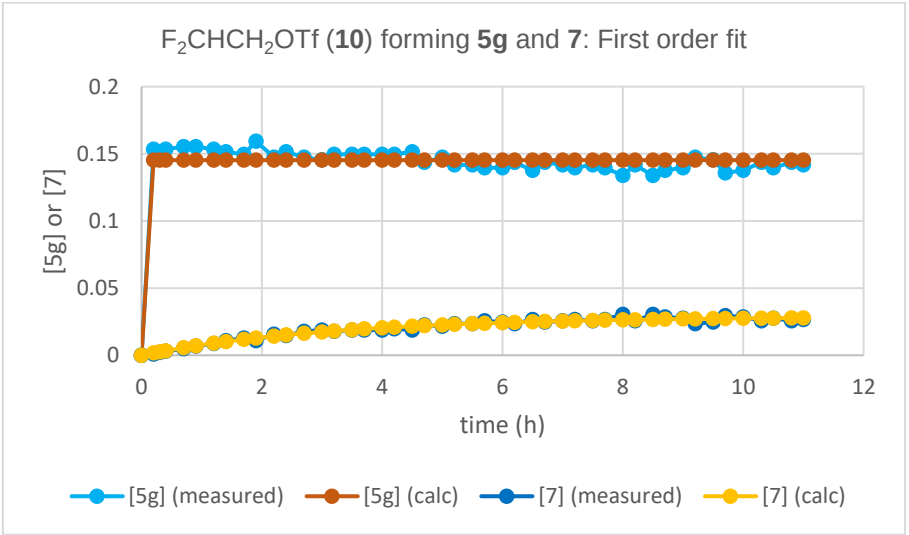
Reaction kinetics: Reaction of 2,2-difluoroethyl triflate with benzylamine

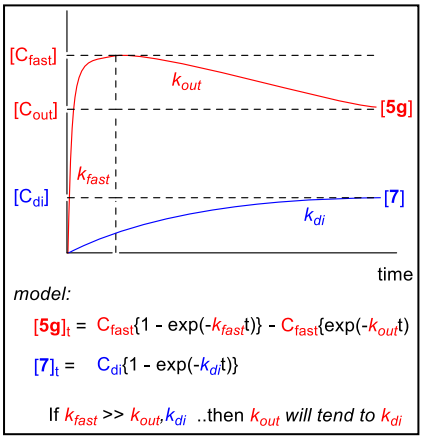


2,2-Difluoroethyl triflate **10** (200 mg, 1.04 mmol, 1.0 equiv., $[\mathbf{10}]_0$ = 0.181 M), benzylamine (0.14 mL, 1.56 mmol, 1.5 equiv., $[\text{benzylamine}]_0$ = 0.272 M), and 4,4'-bis(trifluoromethyl)-1,1'-biphenyl (30 mg, 0.1 mmol, 0.1 equiv.) were dissolved in a mixture of anhydrous MeCN (4.5 mL) and CD_3CN (0.5 mL) in an oven-dried Schlenk tube under an atmosphere of Ar. A 0.6 mL aliquot was transferred to a J Young NMR tube, anhydrous Cs_2CO_3 (677 mg, 2.08 mmol, 2.0 equiv.) was added and the reaction was monitored for 18 hours at 50 °C by ^{19}F NMR on a Bruker AV 400 MHz as described in General Procedure E. Conversions were determined by integration of the relevant signals in the ^{19}F NMR spectra relative to the internal standard 4,4'-bis(trifluoromethyl)-1,1'-biphenyl and plotted in Excel.

Analytical data for ***N*-benzyl-*N*-(2,2-difluoroethyl)-2,2-difluoroethan-1-amine** (**7**) was obtained by purification of the crude reaction mixture after 24 hours: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37–7.27 (m, 5H), 5.74 (tt, *J* = 56.0, 4.5 Hz, 2H), 3.87 (s, 2H), 3.01 (td, *J* = 14.5, 4.5 Hz, 4H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 138.2, 128.84, 128.76, 127.9, 116.2 (t, *J* = 242 Hz), 60.7, 57.0 (t, *J* = 25 Hz); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ −120.25 (s, 2F).







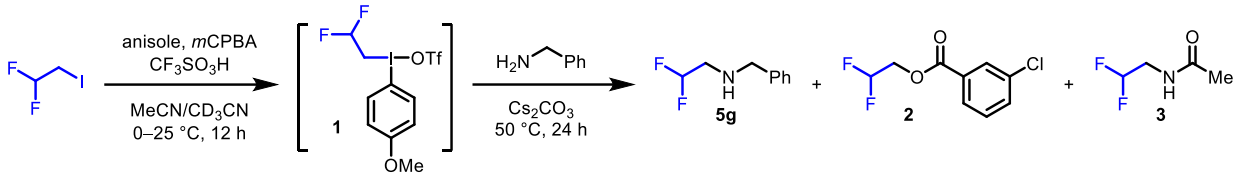
5g:	**7**:
C_{fast} = 0.145 M	C_{di} = 0.029 M
k_{fast} = 110.6744 h^{-1}	k_{di} = 0.3092 h^{-1}
k_{out} = 0.0105 h^{-1}	
Error (obs-calc) = 0.0018	

time (h)	[10] (%)	5g (%)	[5g] (M)	7 (%)	[7] (M)
0.2	21	78	0.153429	1	0.000984
0.3	21	77	0.151462	2	0.001967
0.4	19	78	0.153429	3	0.002951
0.7	16	79	0.155396	5	0.004918
0.9	14	79	0.155396	7	0.006885
1.2	13	78	0.153429	9	0.008852
1.4	12	77	0.151462	11	0.010819
1.7	11	76	0.149495	13	0.012786
1.9	8	81	0.15933	11	0.010819
2.2	9	75	0.147528	16	0.015736
2.4	8	77	0.151462	15	0.014753
2.7	8	75	0.147528	18	0.017703
3.0	8	74	0.145561	19	0.018687
3.2	6	76	0.149495	18	0.017703
3.5	6	76	0.149495	19	0.018687
3.7	5	76	0.149495	19	0.018687
4.0	5	76	0.149495	19	0.018687
4.2	4	76	0.149495	20	0.019670
4.5	4	77	0.151462	19	0.018687
4.7	4	73	0.143594	23	0.022621
5.0	4	75	0.147528	22	0.021637
5.2	4	72	0.141627	24	0.023605
5.5	4	72	0.141627	24	0.023605
5.7	3	71	0.13966	26	0.025572
6.0	3	71	0.13966	25	0.024588
6.2	3	73	0.143594	24	0.023605
6.5	3	70	0.137693	27	0.026555
6.7	2	73	0.143594	25	0.024588
7.0	2	72	0.141627	26	0.025572
7.2	2	71	0.13966	27	0.026555
7.5	2	72	0.141627	26	0.025572
7.7	2	71	0.13966	27	0.026555
8.0	2	68	0.133759	31	0.030489
8.2	1	72	0.141627	26	0.025572
8.5	2	68	0.133759	31	0.030489
8.7	1	70	0.137693	29	0.028522
9.0	1	71	0.13966	28	0.027539
9.2	1	75	0.147528	24	0.023605
9.5	1	74	0.145561	25	0.024588
9.7	1	69	0.135726	30	0.029506
10.0	1	70	0.137693	29	0.028522
10.3	1	73	0.143594	26	0.025572
10.5	1	71	0.13966	28	0.027539
10.8	1	73	0.143594	26	0.025572
11.0	1	72	0.141627	27	0.026555
11.3	1	67		32	
11.5	1	69		30	
11.8	1	74		26	
12.0	0	73		27	
12.3	1	65		34	
12.5	0	72		28	
12.8	0	68		32	
13.0	0	72		27	
13.3	0	73		26	
13.5	0	75		25	
13.8	0	73		26	
14.0	0	75		25	
14.3	0	77		22	
14.5	0	72		27	
14.8	0	70		30	
15.0	0	68		32	
15.3	0	68		32	
15.5	0	70		30	
15.8	0	70		30	
16.0	0	72		28	
16.3	0	76		24	
16.5	0	75		25	
16.8	0	65		35	
17.0	0	73		27	
17.3	0	70		30	
17.6	0	57		43	
17.8	0	55		45	

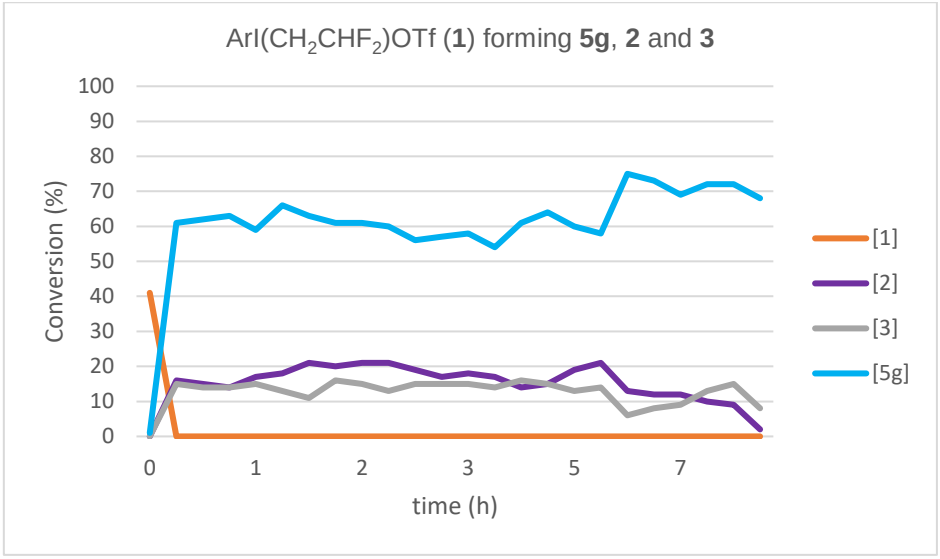
Table S8. Reaction kinetics. [a] Conversion of 2,2-difluoroethyl triflate to *N*-benzyl-2,2-difluoroethan-1-amine **5g** and *N*-benzyl-*N*-(2,2-difluoroethyl)-2,2-difluoroethan-1-amine **7**, determined by ^{19}F NMR spectroscopy. Time (h) is defined as the time elapsed between addition of Cs_2CO_3 to the reaction and acquisition of the corresponding ^{19}F NMR spectrum.

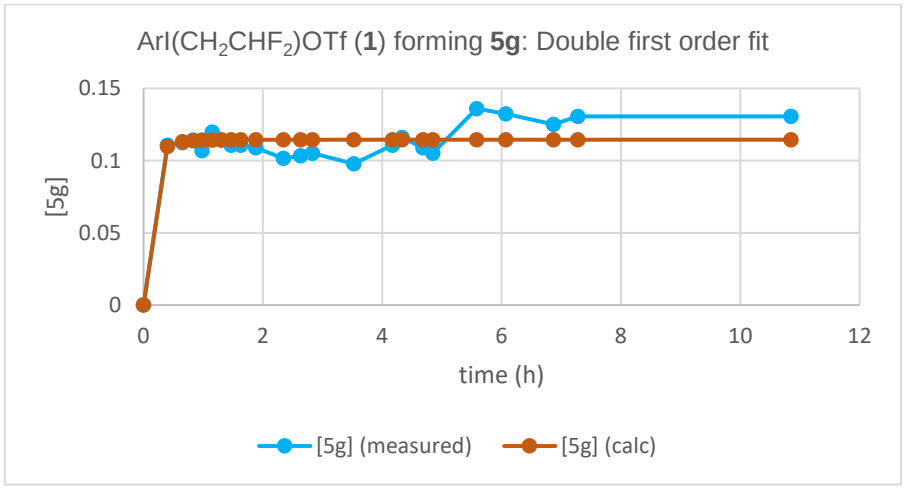
SUPPORTING INFORMATION

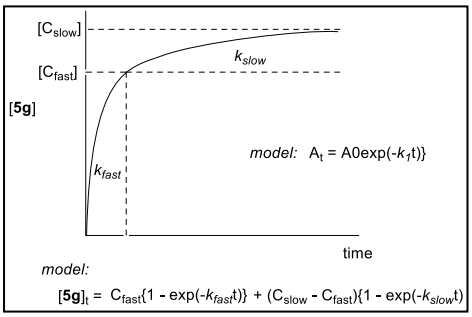
Reaction kinetics: Reaction of (2,2-difluoroethyl)(4-methoxyphenyl)iodonium triflate (1) with benzylamine



*m*CPBA (583 mg, 2.60 mmol, 2.5 equiv.) was added to an oven-dried pressure tube and dried under vacuum for 1–1.5 h. The tube was flushed with argon and wrapped in aluminium foil. Anhydrous CH_3CN (4.5 mL) and CD_3CN (0.4 mL) were added, followed by 2-iodo-1,1-difluoroethane (200 mg, 1.04 mmol, 1.0 equiv.), anisole (0.12 mL, 1.14 mmol, 1.1 equiv.) and 4,4'-bis(trifluoromethyl)-1,1'-biphenyl (30 mg, 0.1 mmol, 0.1 equiv.). After stirring for 5–10 minutes, the reaction mixture was cooled to 0 °C and CF_3SO_3H (0.11 mL, 1.25 mmol, 1.2 equiv.) was added dropwise. The tube was removed from the ice bath and stirred at room temperature for 12 hours. An aliquot was taken from the reaction and analysed by ^{19}F NMR to determine the conversion to hypervalent iodine intermediate **1** ($[\mathbf{1}]_0$ = 0.0743 M). Next, anhydrous Cs_2CO_3 (677 mg, 2.08 mmol, 2.0 equiv.) and benzylamine (0.14 mL, 1.56 mmol, 1.5 equiv., $[benzylamine]_0$ = 0.2720 M) were added to the reaction, which was placed into an oil-bath pre-heated to 50 °C and stirred for 24 hours. Manual aliquots were taken at predetermined time-points and analysed by ^{19}F NMR. Conversion was determined relative to the internal standard 4,4'-bis(trifluoromethyl)-1,1'-biphenyl. (No change in the amount of unreacted 2-iodo-1,1-difluoroethane was observed over the 24 hour time period during which the reaction was monitored.)







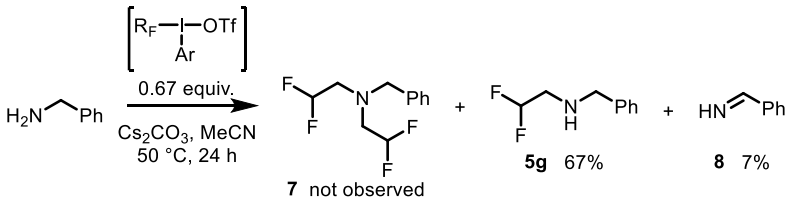
C_{fast} = 0.145 M C_{slow} = 0.114 M
k_{fast} = 10.7130 h^{-1} k_{slow} = 4.0072 h^{-1}
Error (obs-calc) = 0.0023

time (h)	[1] (%)	[5g] (%)	[5g] (M)	[2] (%)	[3] (%)
0	41	0	0	1	0
0.4	0	61	0.110604	16	15
0.65	0	62	0.112417	15	14
0.83	0	63	0.11423	14	14
0.98	0	59	0.106978	17	15
1.15	0	66	0.11967	18	13
1.3	0	63	0.11423	21	11
1.47	0	61	0.110604	20	16
1.63	0	61	0.110604	21	15
1.88	0	60	0.108791	21	13
2.34	0	56	0.101538	19	15
2.63	0	57	0.103351	17	15
2.83	0	58	0.105164	18	15
3.52	0	54	0.097912	17	14
4.17	0	61	0.110604	14	16
4.33	0	64	0.116044	15	15
4.68	0	60	0.108791	19	13
4.85	0	58	0.105164	21	14
5.58	0	75	0.135989	13	6
6.07	0	73	0.132362	12	8
6.87	0	69	0.125109	12	9
7.28	0	72	0.130549	10	13
10.85	0	72	0.130549	9	15
24.97	0	68	0.123296	2	8

Table S9. Reaction kinetics: Conversion of (2,2-difluoroethyl)(4-methoxyphenyl)iodonium triflate (**1**) to *N*-benzyl-2,2-difluoroethan-1-amine **5g**, determined by ^{19}F NMR spectroscopy. Time (h) is defined as the time elapsed between addition of benzylamine and Cs_2CO_3 to the reaction and acquisition of the corresponding ^{19}F NMR spectrum.

5.6 Mono- vs. bis-alkylation

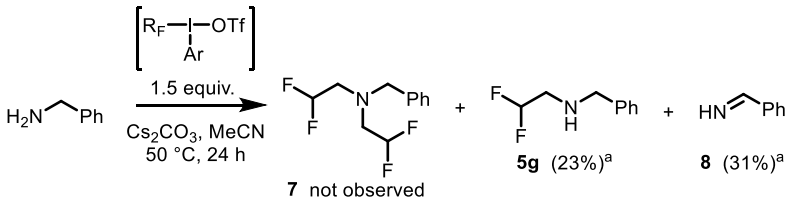
Reaction of benzylamine under standard conditions B



Phenylmethanimine (**8)** was formed in 7% isolated yield (8 mg) as a by-product in the synthesis of **5g**, when benzylamine (0.14 mL, 1.56 mmol) was submitted to general procedure B (see section 4.3 above). Analytical data for **8** matched that reported in the literature.[15]

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.02 (s, 1H), 7.90–7.86 (m, 2H), 7.66–7.61 (m, 1H), 7.56–7.51 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 192.5, 136.5, 134.6, 129.9, 129.1.

Reaction of benzylamine with an excess of hypervalent iodine reagent

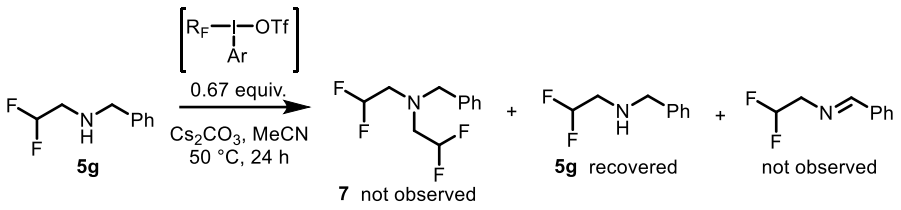


When benzylamine was reacted with an excess of the hypervalent iodine reagent, none of the bis-alkylated product **7** was observed. Instead, 31% phenylmethanimine **8** was detected in addition to 23% of the mono-alkylated product **5g**.

General procedure B was set up on double the scale outlined above [2-iodo-1,1-difluoroethane (400 mg, 2.08 mmol, 1.5 equiv.), *m*CPBA (1.02 g, 4.36 mmol, 2.8 equiv.), anisole (0.24 mL, 2.28 mmol, 1.5 equiv.), CF_3SO_3H (0.22 mL, 2.50 mmol, 1.6 equiv.), CH_3CN (10 mL)]. After stirring the reaction at room temperature for 24 hours, benzylamine (0.12 mL, 1.56 mmol, 1.0 equiv.) and Cs_2CO_3 (677 mg, 2.08 mmol, 2.0 equiv.) were added and the reaction was placed into an oil-bath pre-heated to 50 °C and stirred for 24 hours. After workup, the reaction was analysed by ^{19}F and ^1H NMR spectroscopy, with trifluorotoluene as internal standard.

SUPPORTING INFORMATION

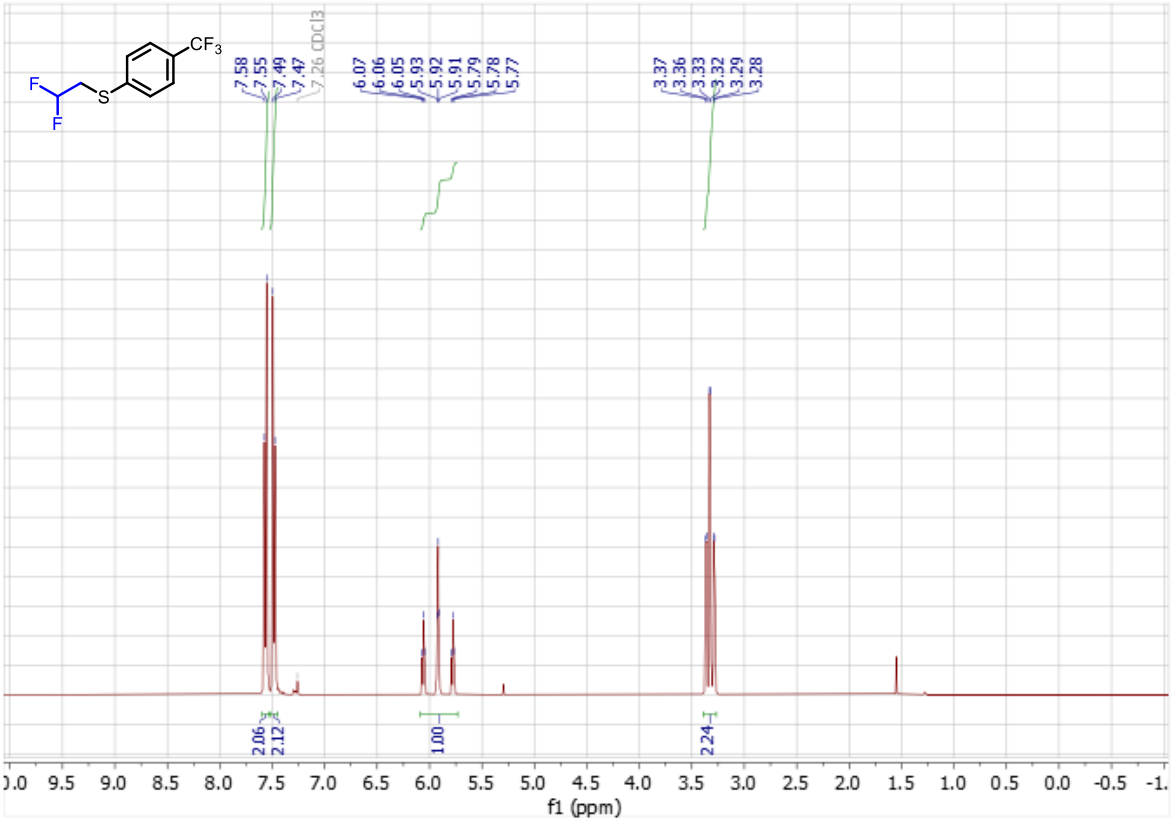
Reaction of 5g under standard conditions B

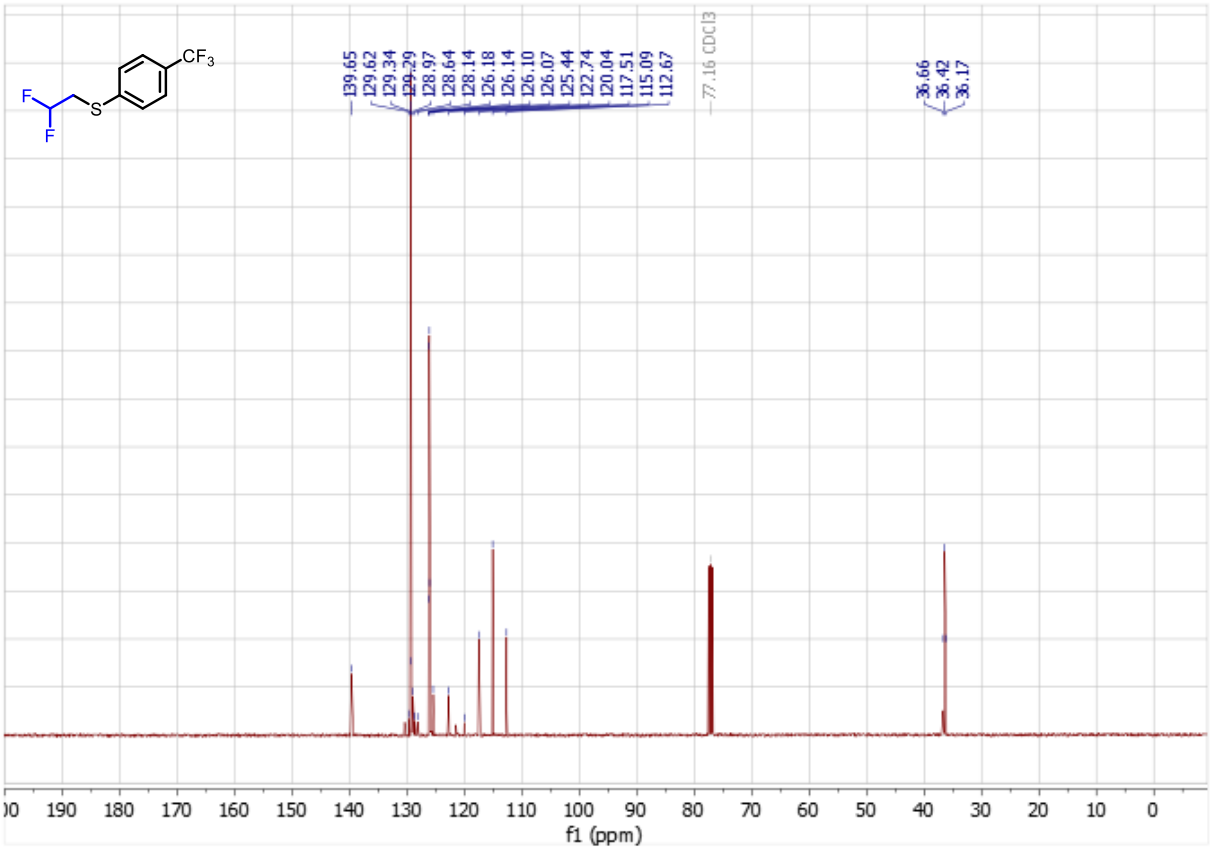


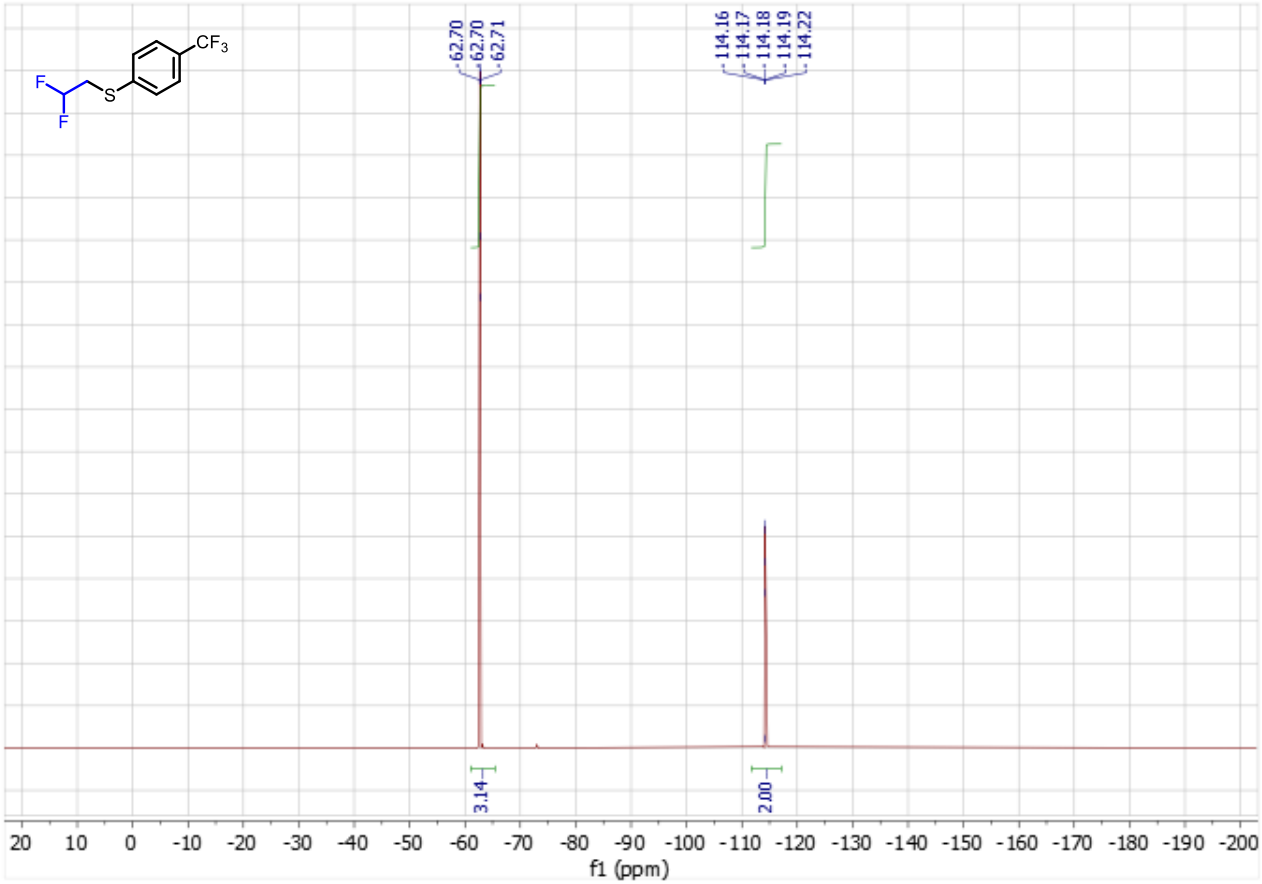
Similarly, when **5g** was isolated and re-submitted to general procedure B [2-iodo-1,1-difluoroethane (100 mg, 0.52 mmol, 1.0 equiv.), **5g** (133 mg, 0.78 mmol, 1.5 equiv.)], none of the bis-difluoroethylated product **7** was observed by ^{19}F NMR spectroscopy, and no oxidation product was observed. Instead, unreacted **5g** was observed in near quantitative yield relative to the internal standard trifluorotoluene.

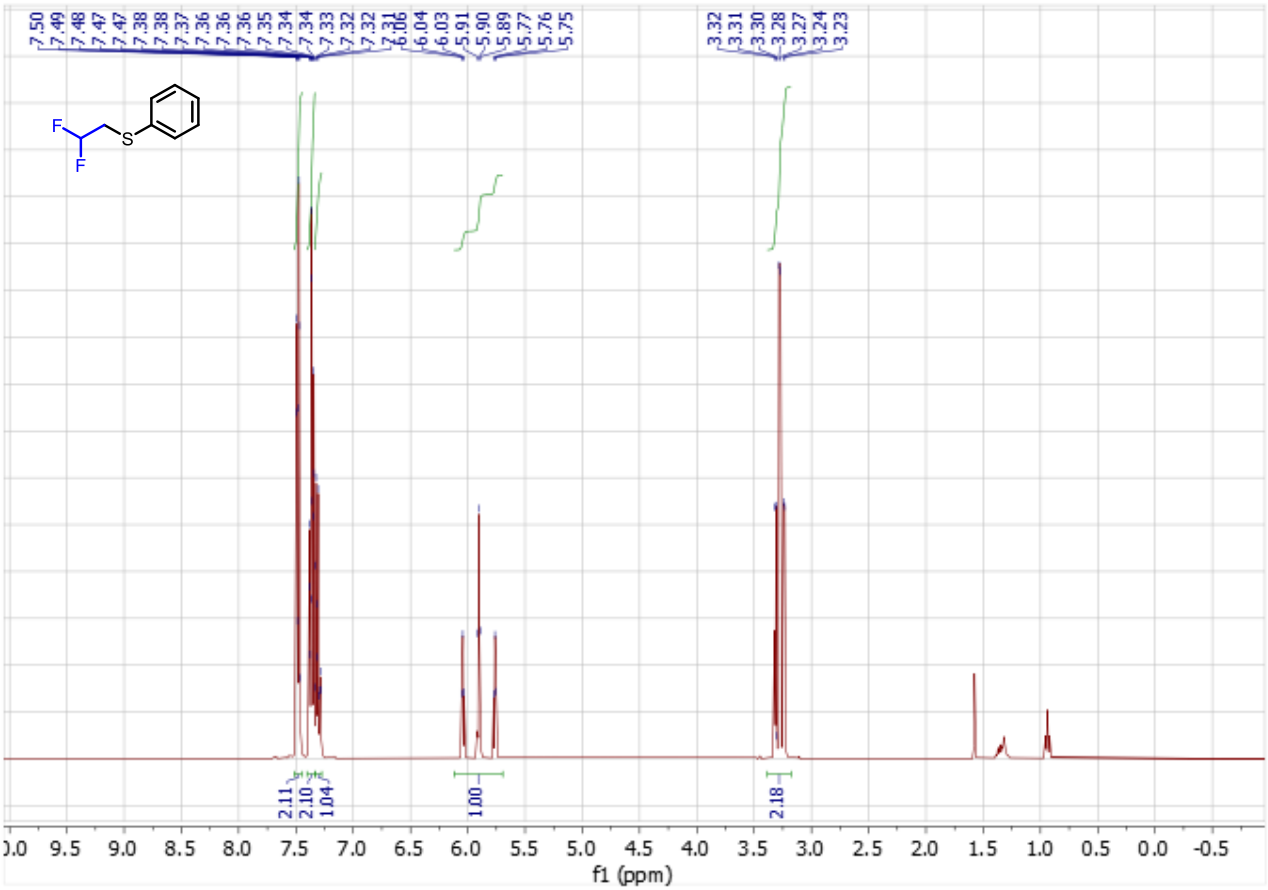
6. NMR Spectra

6.1 2,2-Difluoroethylsulfanes (4)






F
F
S
CF3
-62.70
-62.70
-62.71
-114.16
-114.17
-114.18
-114.19
-114.22
3.14
2.00
f1 (ppm)


F
F
S
7.50
7.49
7.48
7.47
7.47
7.38
7.38
7.37
7.36
7.36
7.36
7.35
7.34
7.34
7.33
7.32
7.32
7.31
6.06
6.04
6.03
5.91
5.90
5.89
5.77
5.76
5.75
3.32
3.31
3.30
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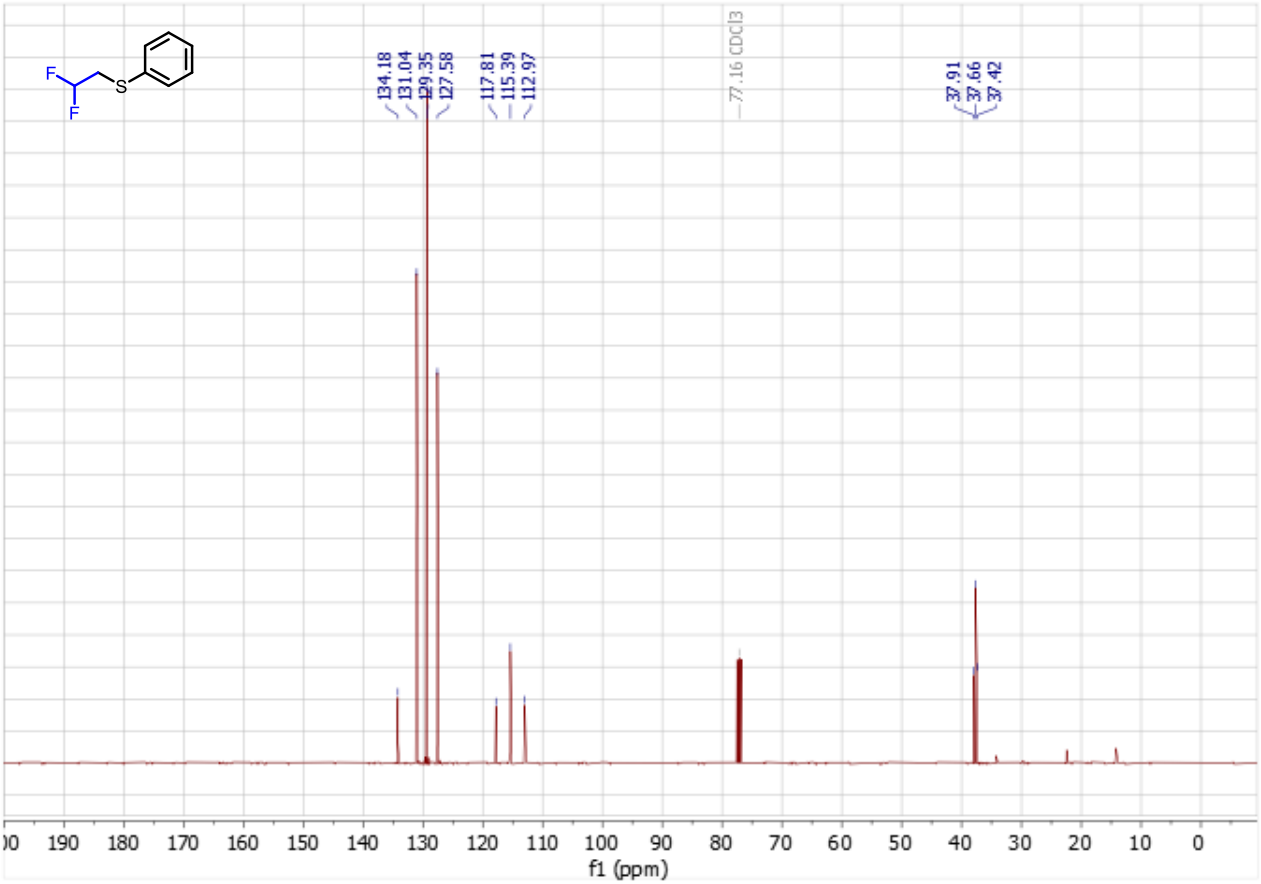
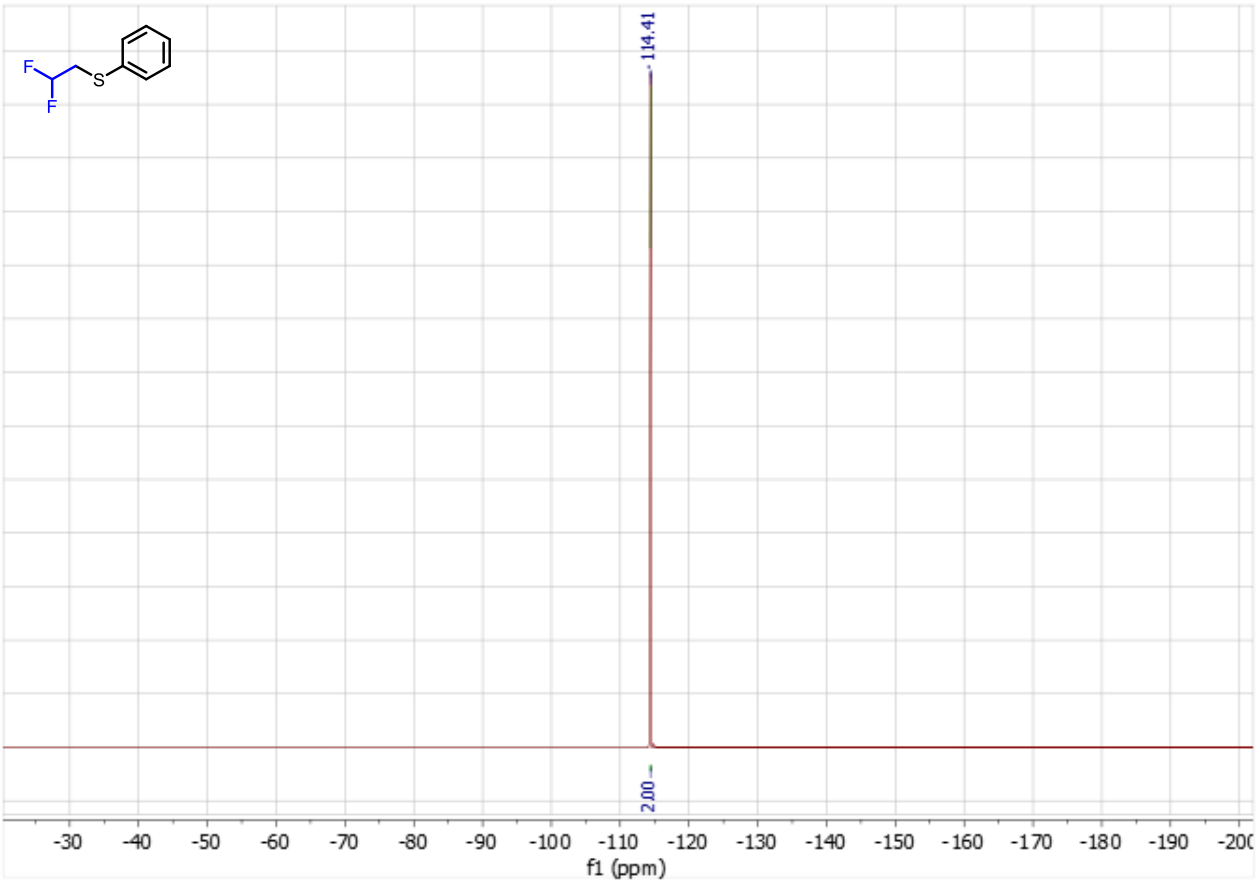
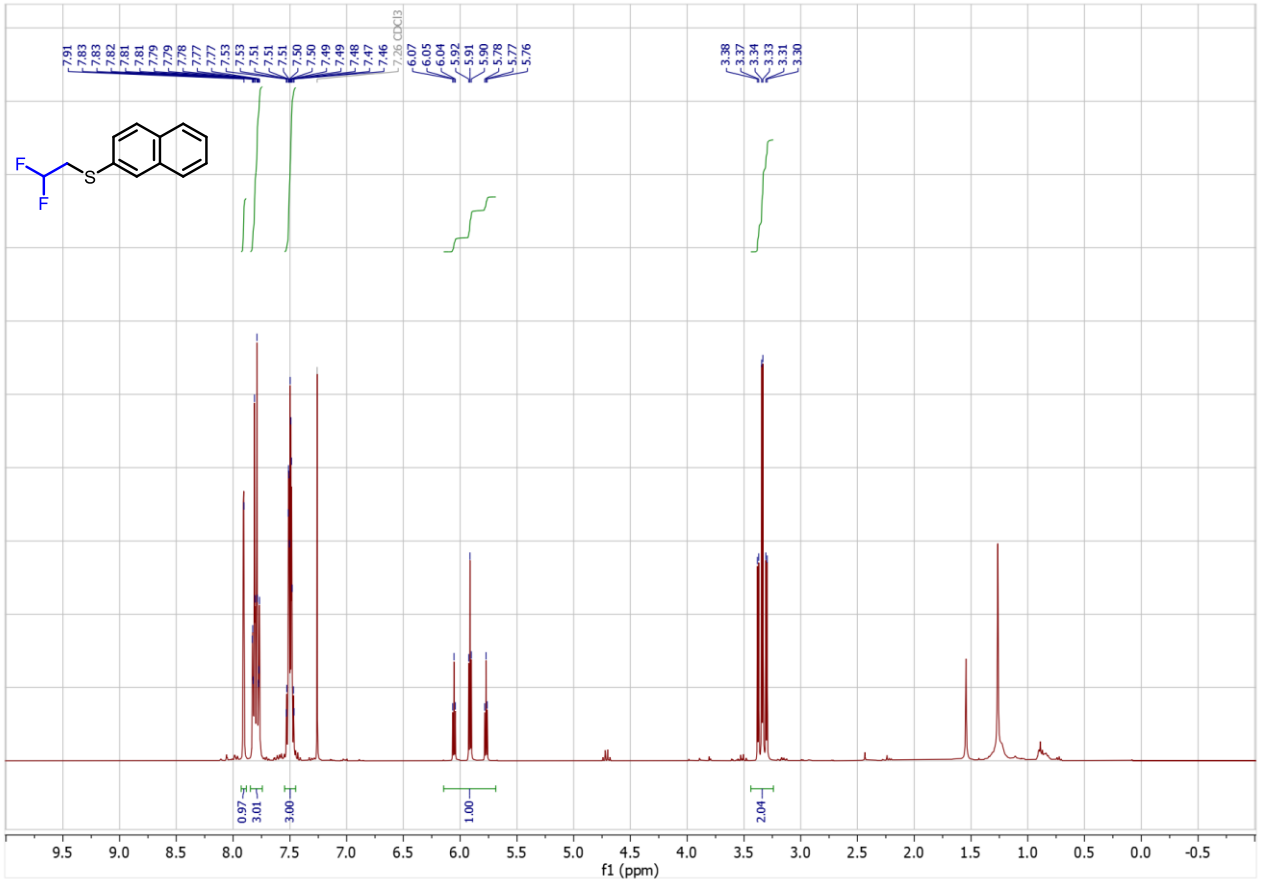
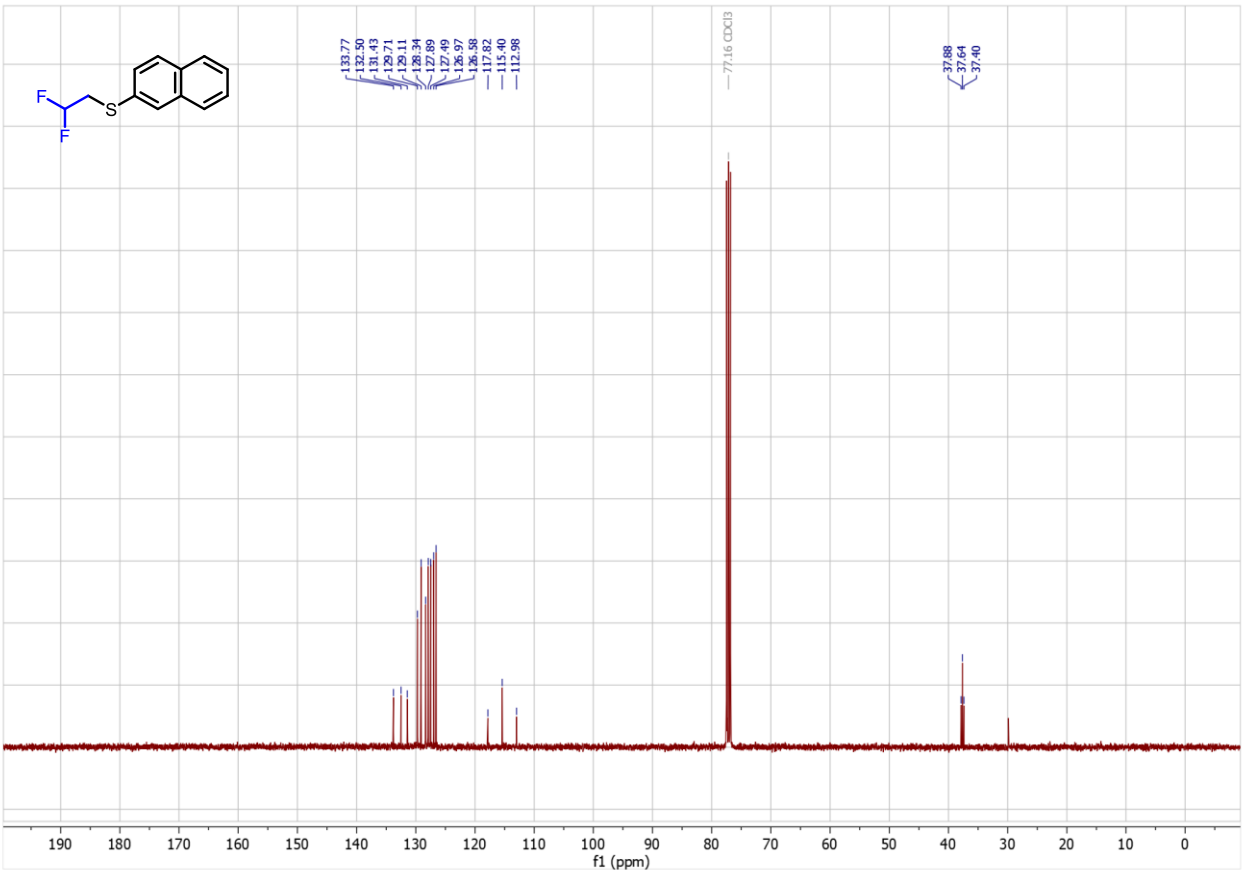
3.27
3.24
3.23
2.11
2.10
1.04
1.00
2.18
f1 (ppm)

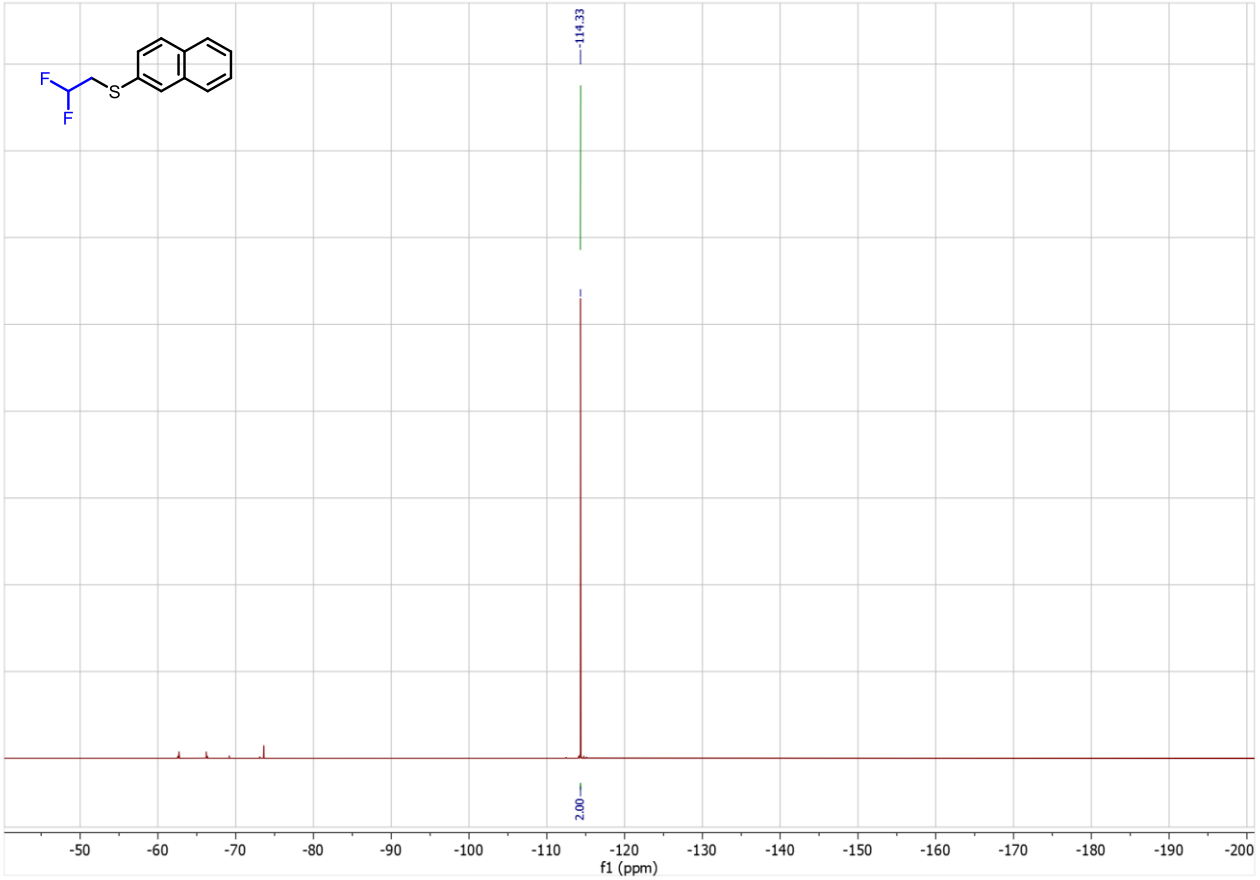

F
F
S
134.18
131.04
129.35
127.58
117.81
115.39
112.97
77.16 CDCl3
37.91
37.66
37.42
f1 (ppm)

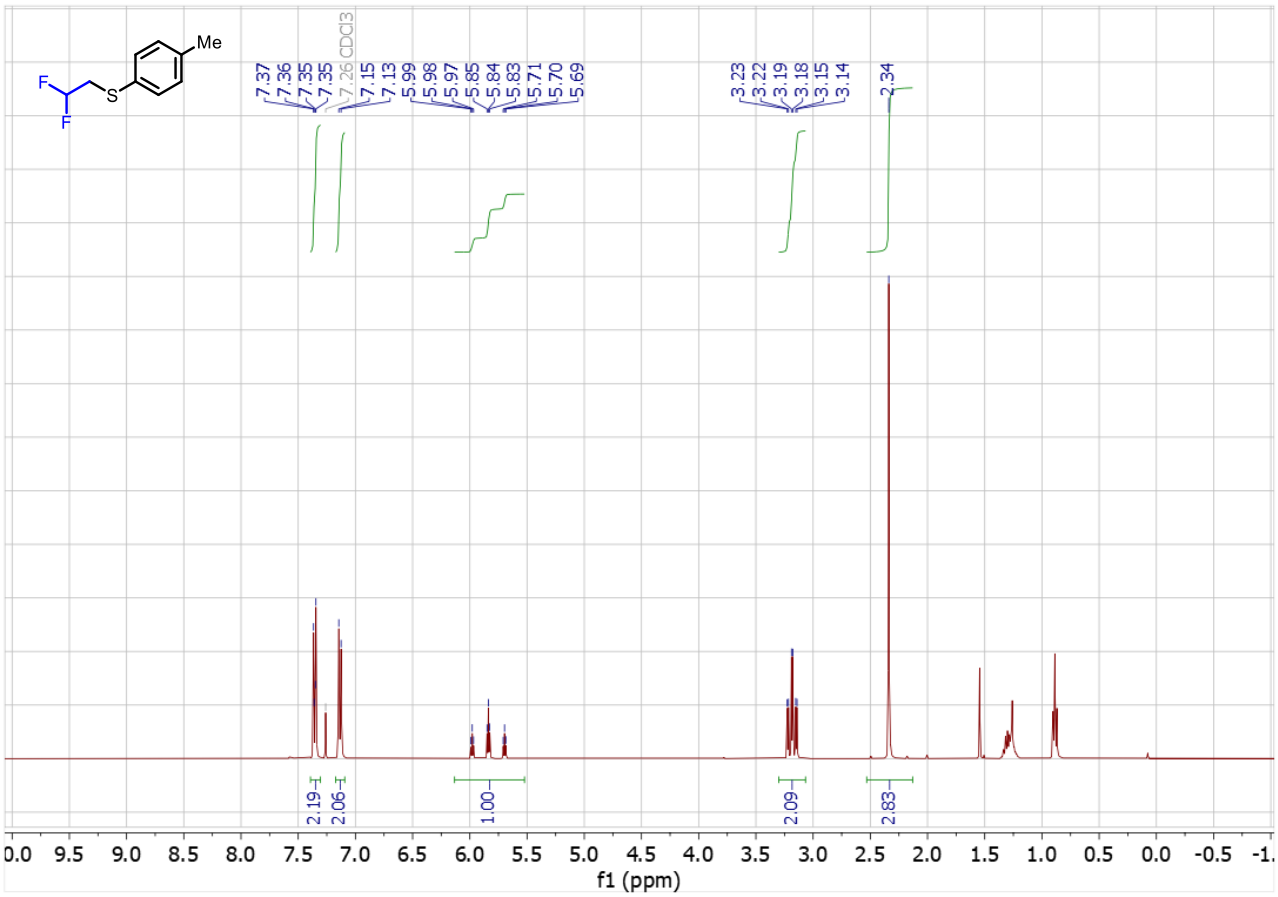

F
F
S
-114.41
2.00
f1 (ppm)

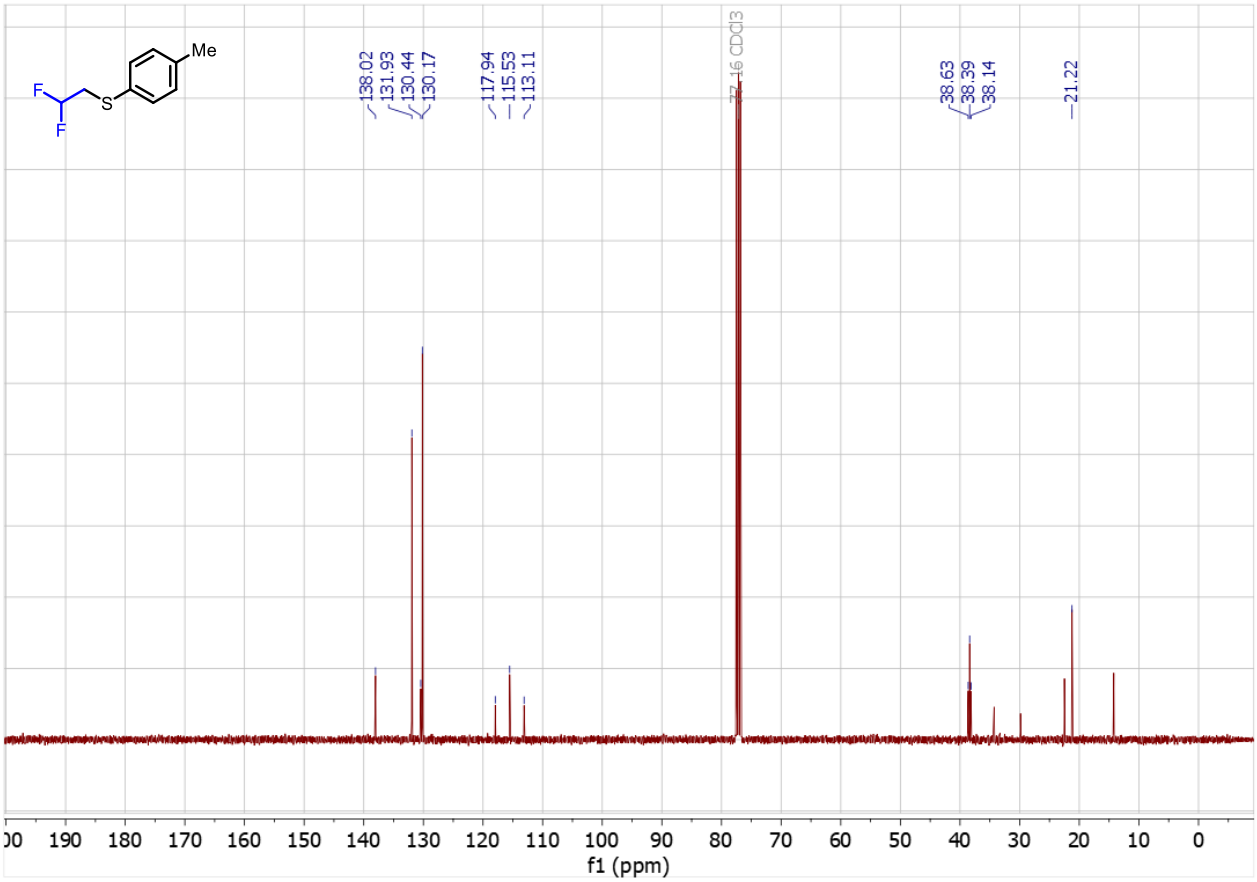

F
F
S
7.91
7.83
7.83
7.82
7.81
7.81
7.79
7.79
7.78
7.77
7.77
7.53
7.53
7.51
7.51
7.51
7.50
7.50
7.49
7.49
7.48
7.47
7.46
7.26 CDCl3
6.07
6.05
6.04
5.92
5.91
5.90
5.78
5.77
5.76
3.38
3.37
3.34
3.33
3.31
3.30
0.97
3.01
3.00
1.00
2.04
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

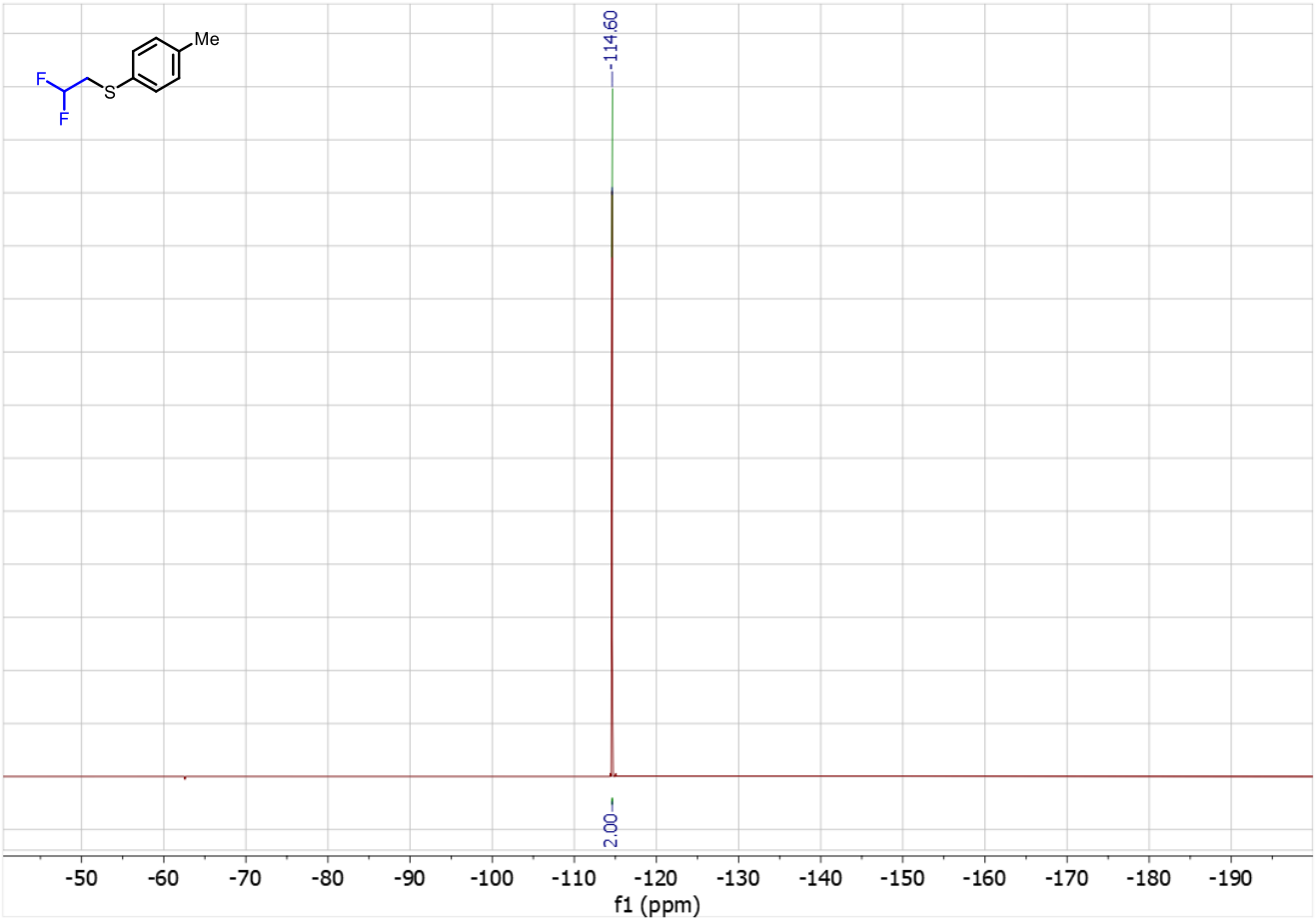

F
F
S
133.77
132.50
131.43
129.71
129.11
128.34
127.89
127.49
126.97
126.58
117.82
115.40
112.98
77.16 CDCl3
37.88
37.64
37.40
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

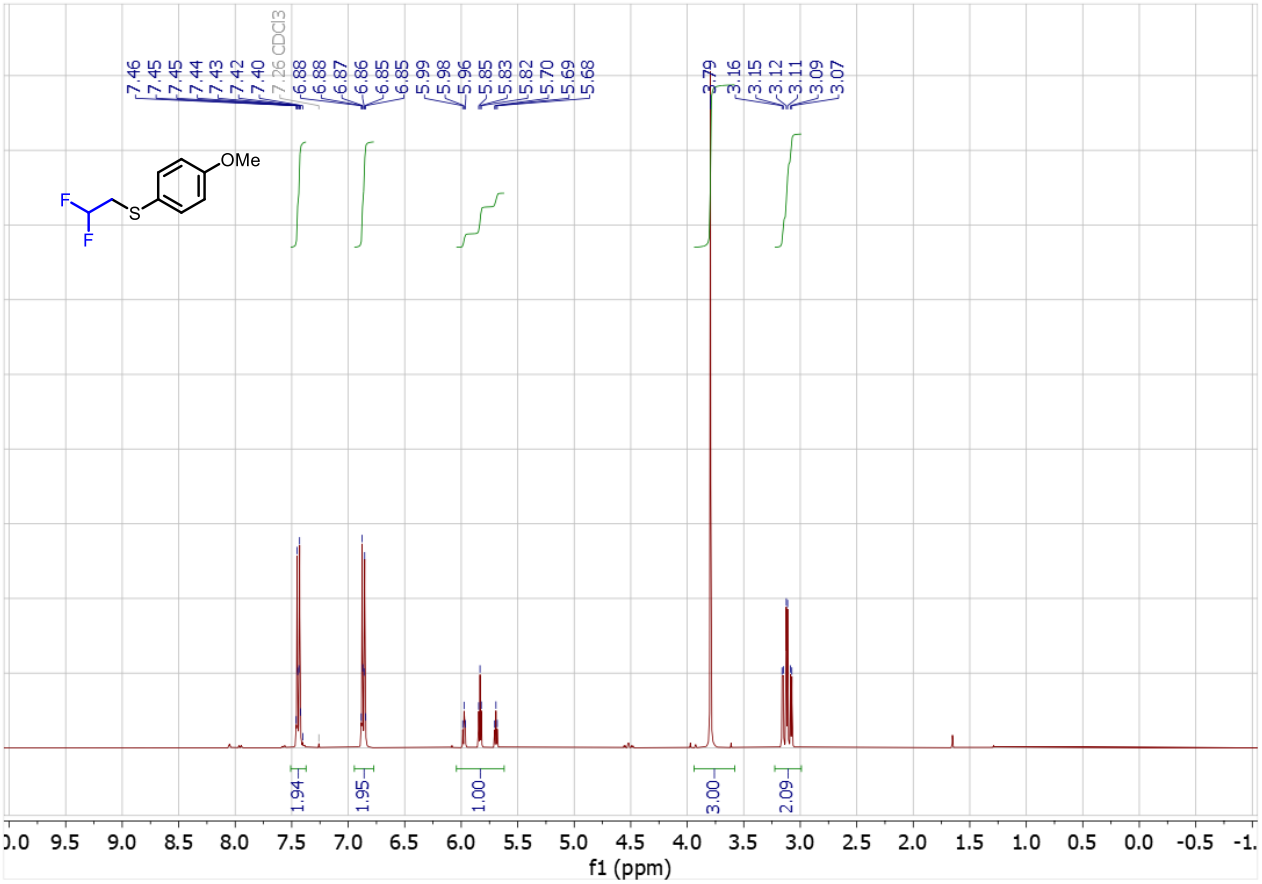
SUPPORTING INFORMATION

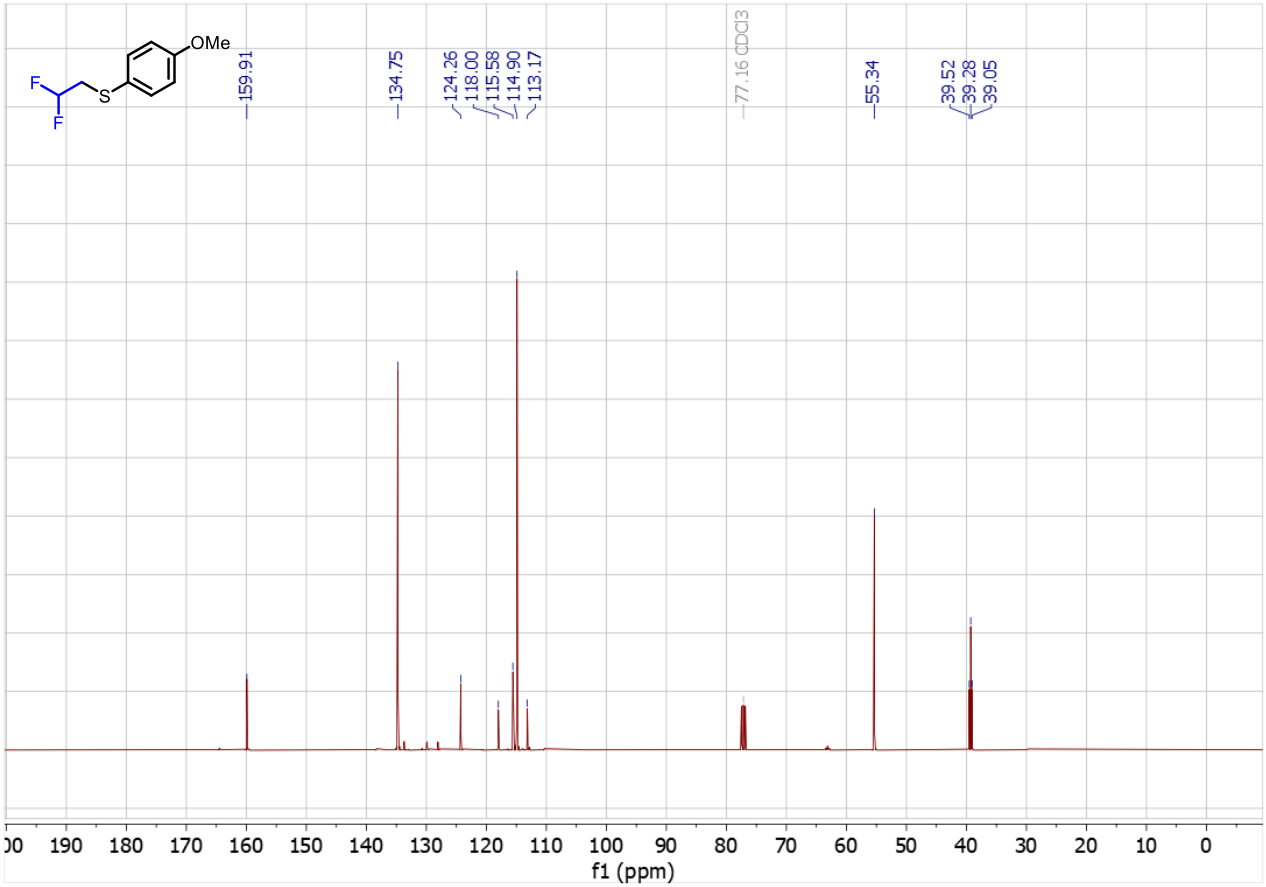


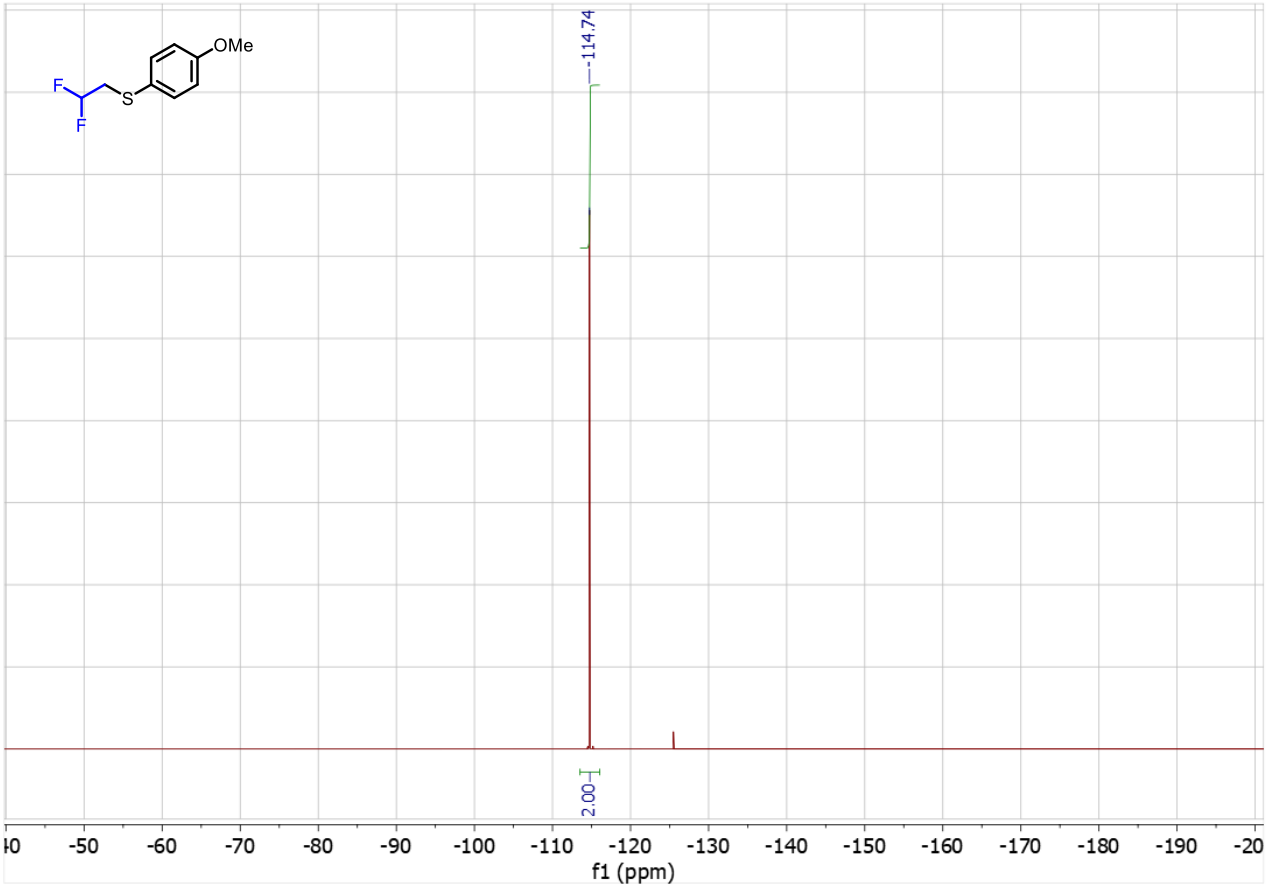


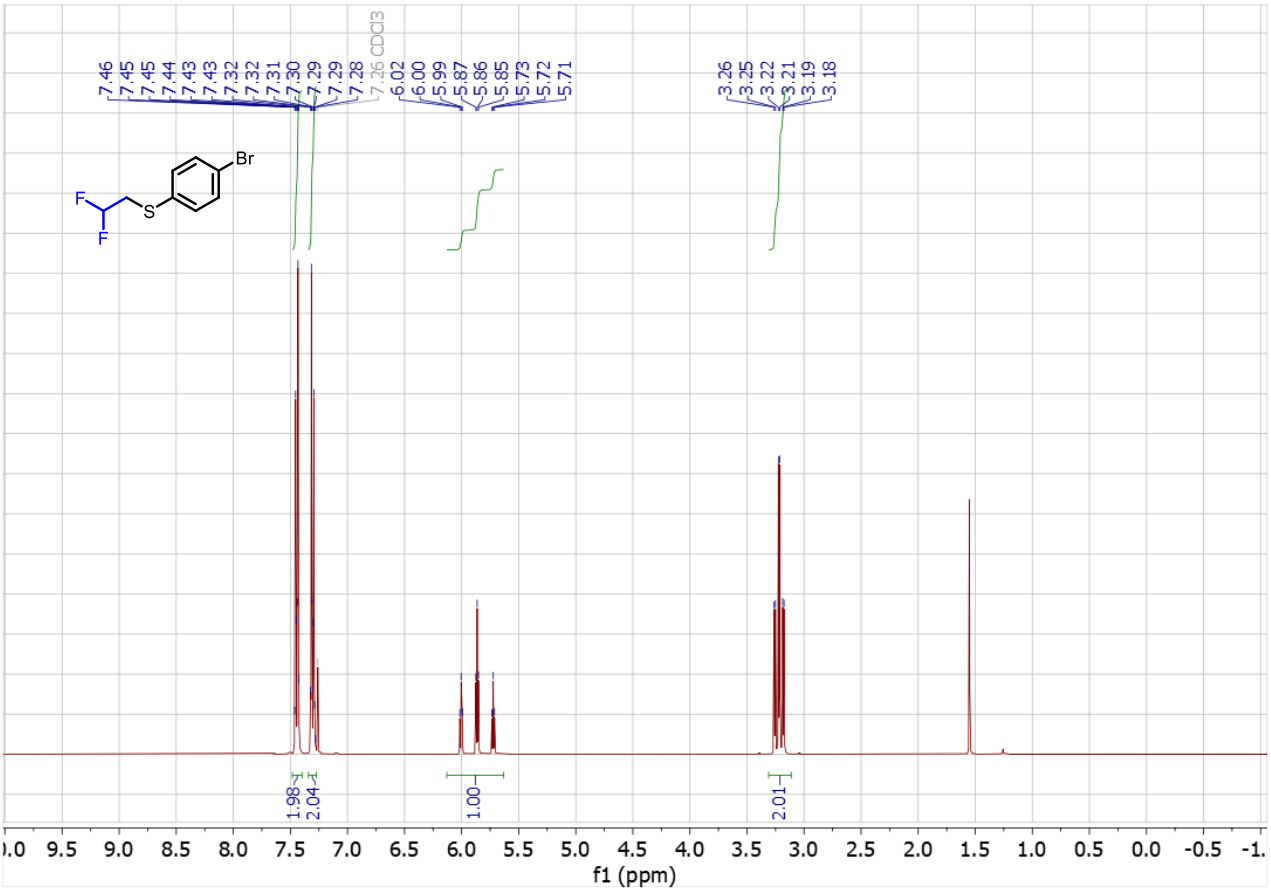

Me
F
S
F
138.02
131.93
130.44
130.17
117.94
115.53
113.11
77.16 CDCl3
38.63
38.39
38.14
21.22
f1 (ppm)

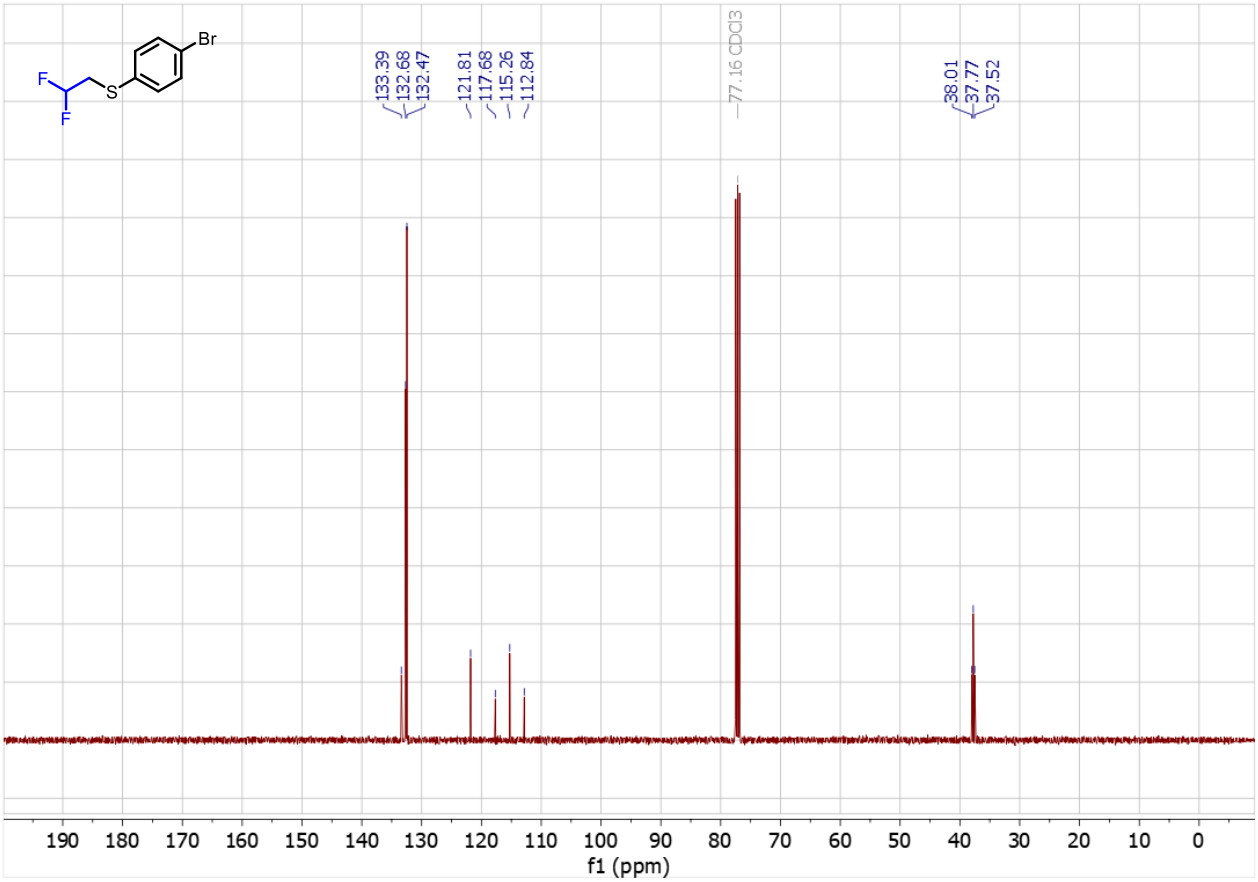

Me
F
S
F
-114.60
2.00
f1 (ppm)

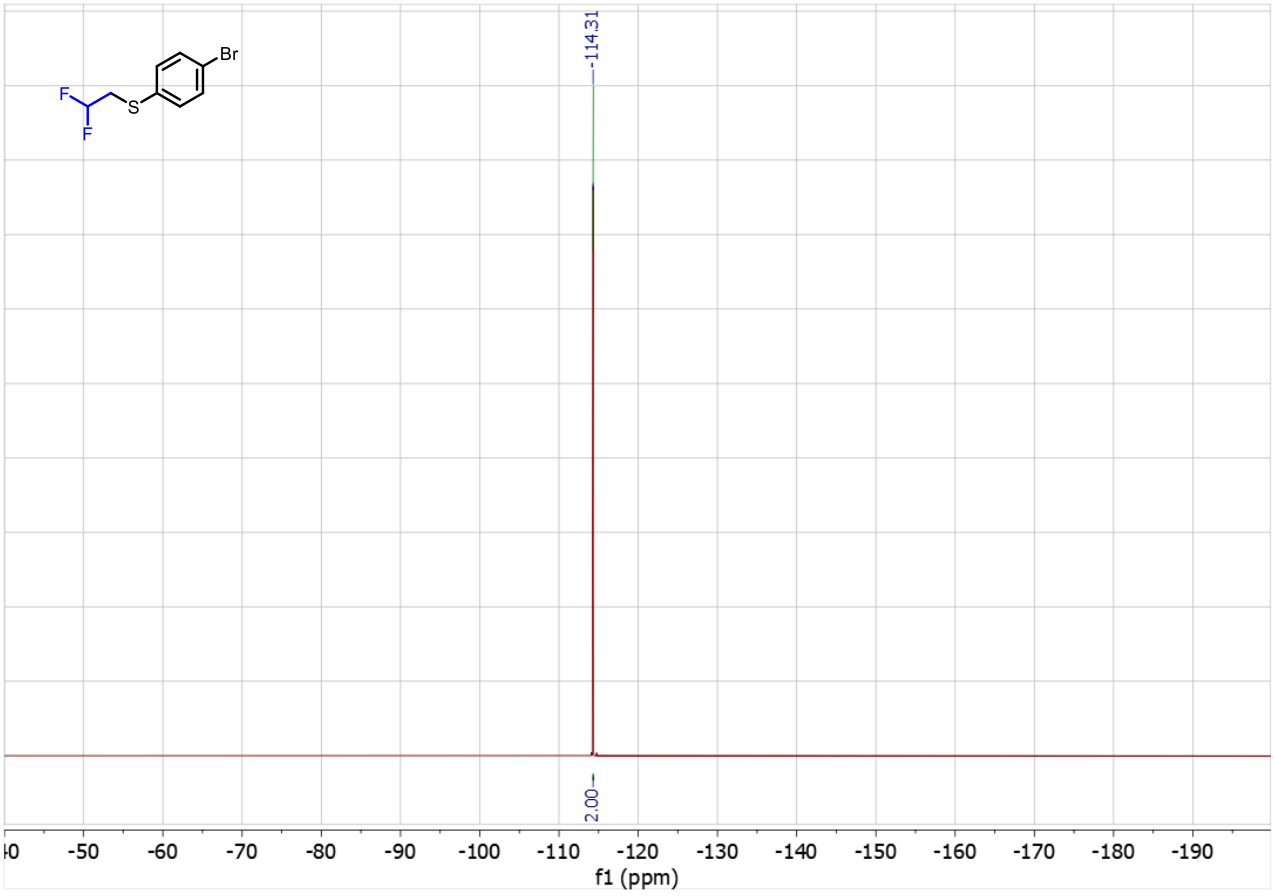

7.46
7.45
7.45
7.44
7.43
7.42
7.40
7.26 CDCl3
6.88
6.88
6.87
6.86
6.86
6.85
6.85
5.99
5.98
5.96
5.85
5.83
5.82
5.70
5.69
5.68
3.79
3.16
3.15
3.12
3.11
3.09
3.07
OMe
F
F
S
1.94
1.95
1.00
3.00
2.09
f1 (ppm)

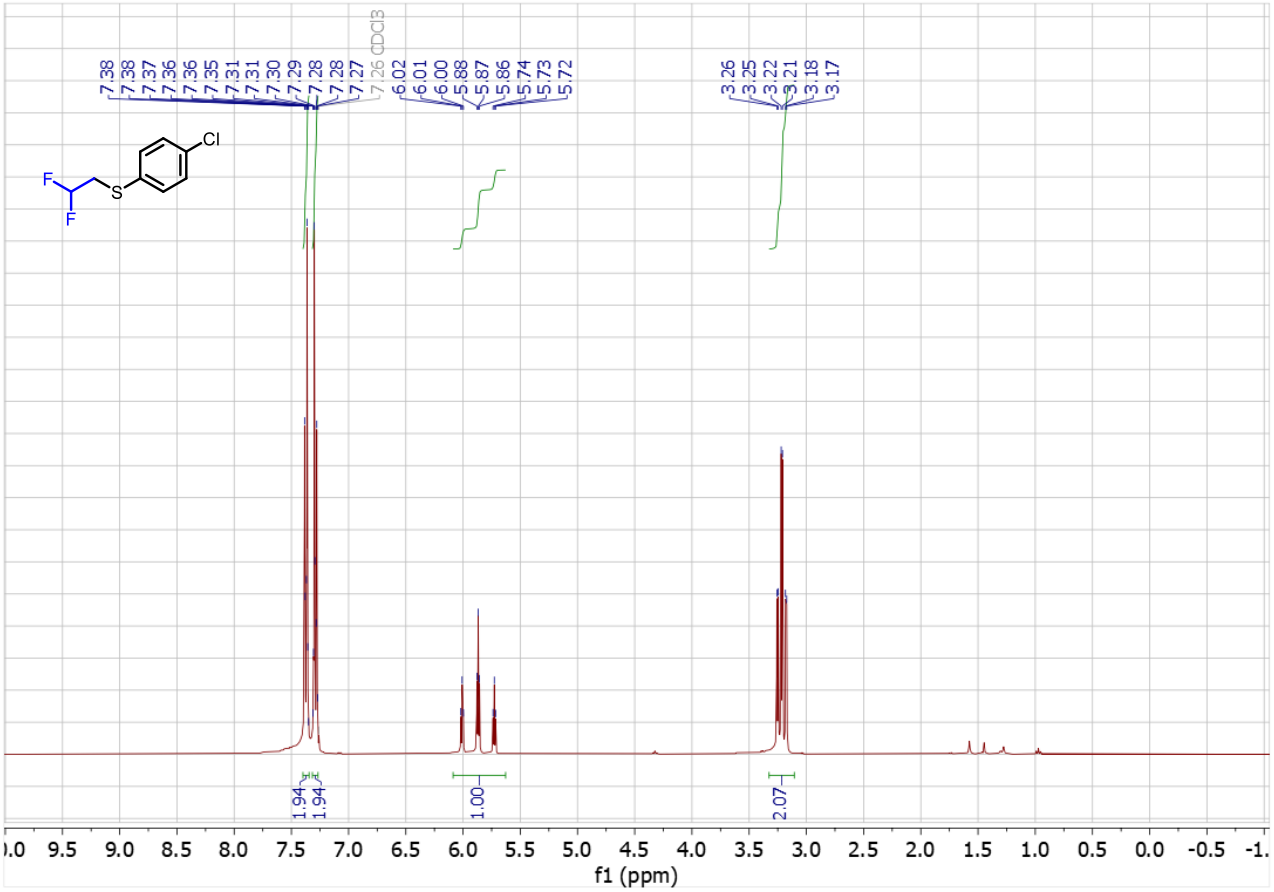

OMe
F
F
S
159.91
134.75
124.26
118.00
115.58
114.90
113.17
77.16 CDCl3
55.34
39.52
39.28
39.05
f1 (ppm)

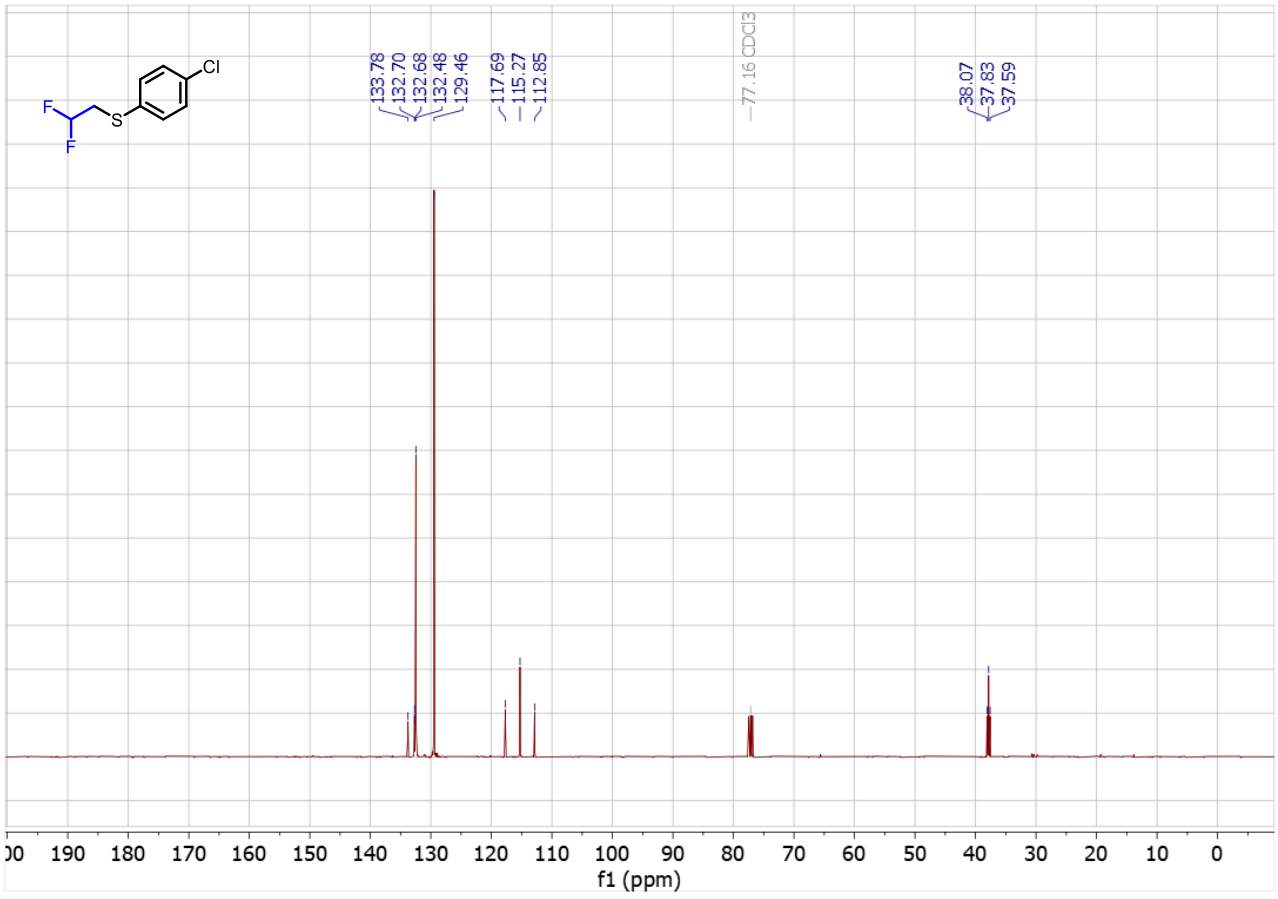

OMe
F
F
S
-114.74
2.00
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-20
f1 (ppm)


7.46
7.45
7.45
7.44
7.43
7.43
7.32
7.32
7.31
7.30
7.29
7.29
7.28
7.26 CDCl3
6.02
6.00
5.99
5.87
5.86
5.85
5.73
5.72
5.71
3.26
3.25
3.22
3.21
3.19
3.18
Br
F
F
S
1.98
2.04
1.00
2.01
10.0
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
-0.5
f1 (ppm)

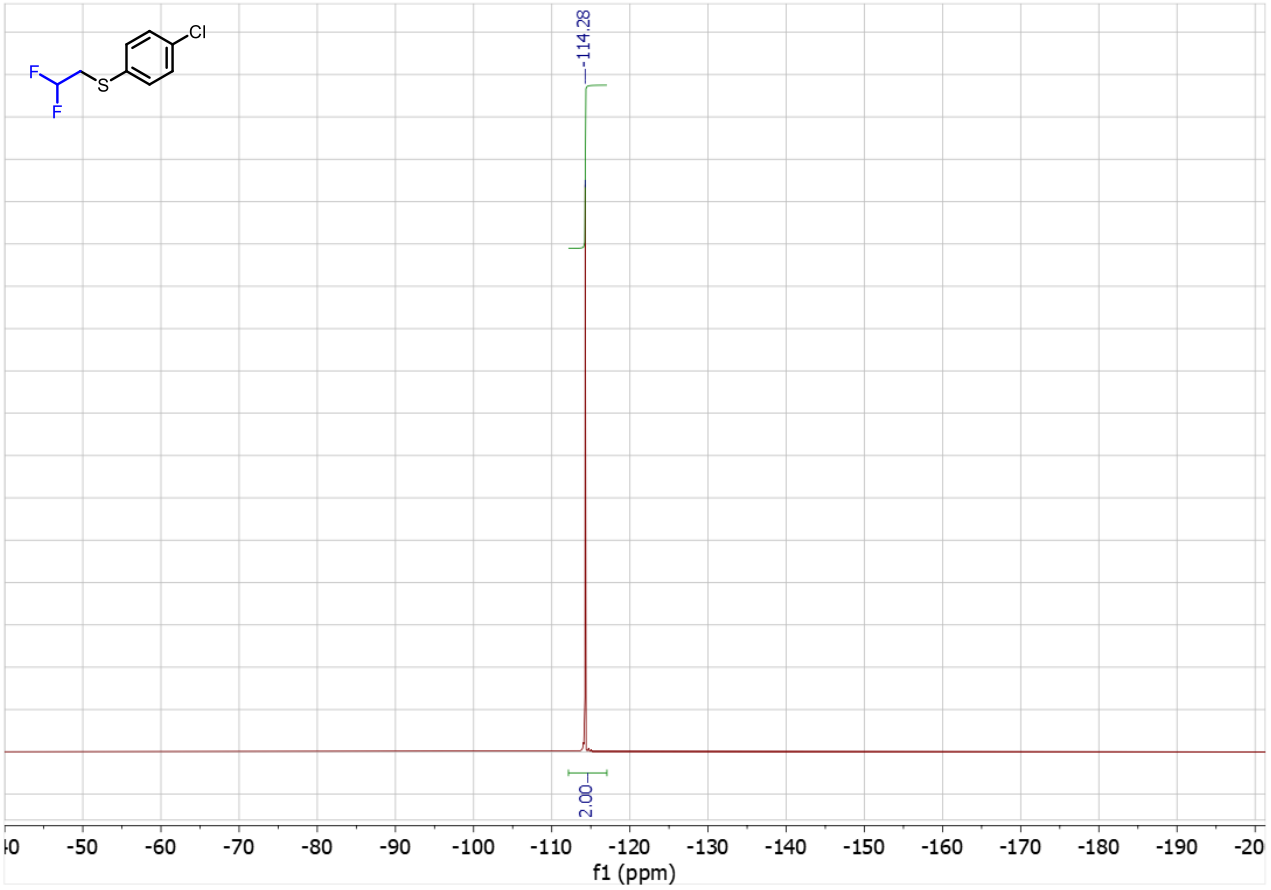

Br
F
F
S
133.39
132.68
132.47
121.81
117.68
115.26
112.84
77.16 CDCl3
38.01
37.77
37.52
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

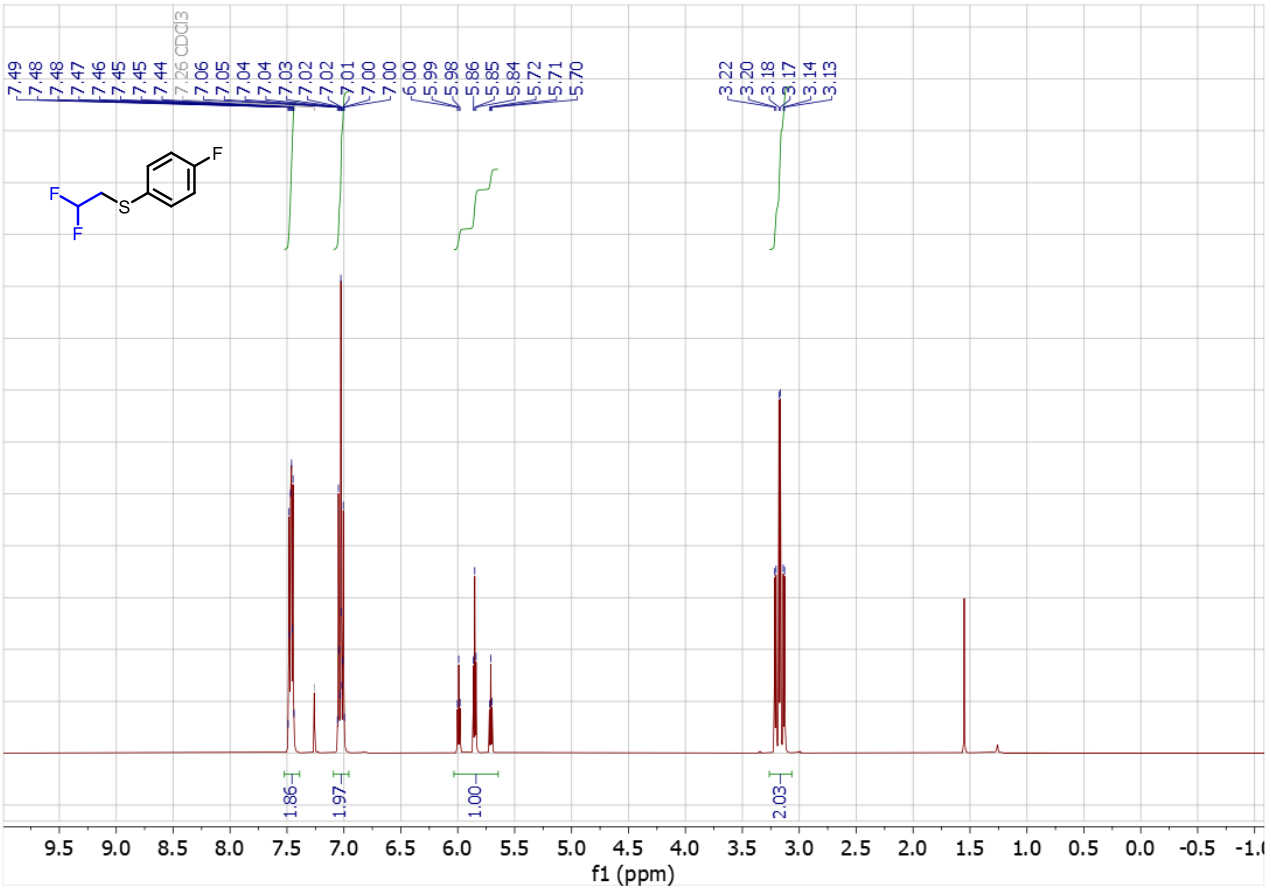

Br
F
F
S
-114.31
2.00
-50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

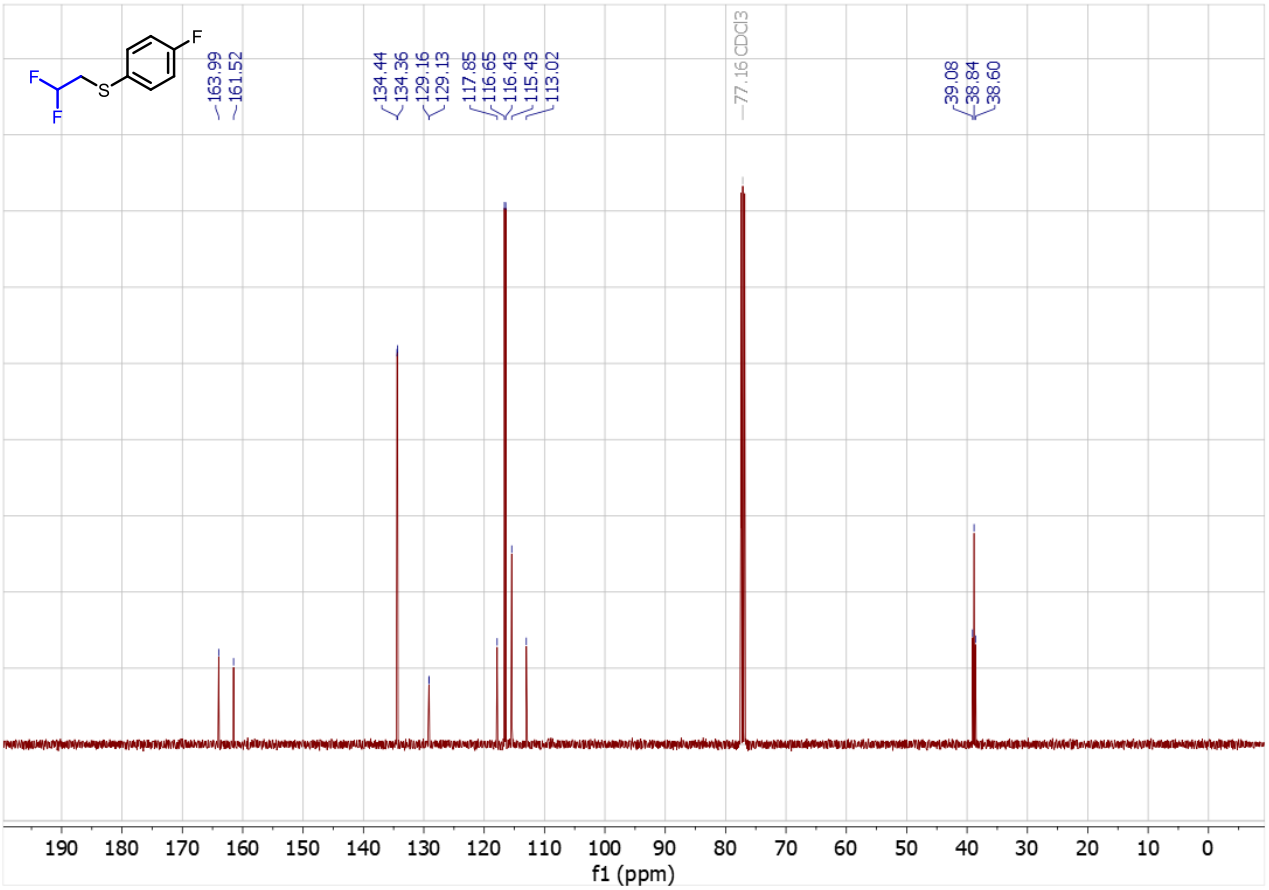

7.38
7.38
7.37
7.36
7.36
7.35
7.31
7.31
7.30
7.29
7.28
7.28
7.27
7.26 CDCl3
6.02
6.01
6.00
5.88
5.87
5.86
5.74
5.73
5.72
3.26
3.25
3.22
3.21
3.18
3.17
Cl
F
F
S
1.94
1.94
1.00
2.07
f1 (ppm)

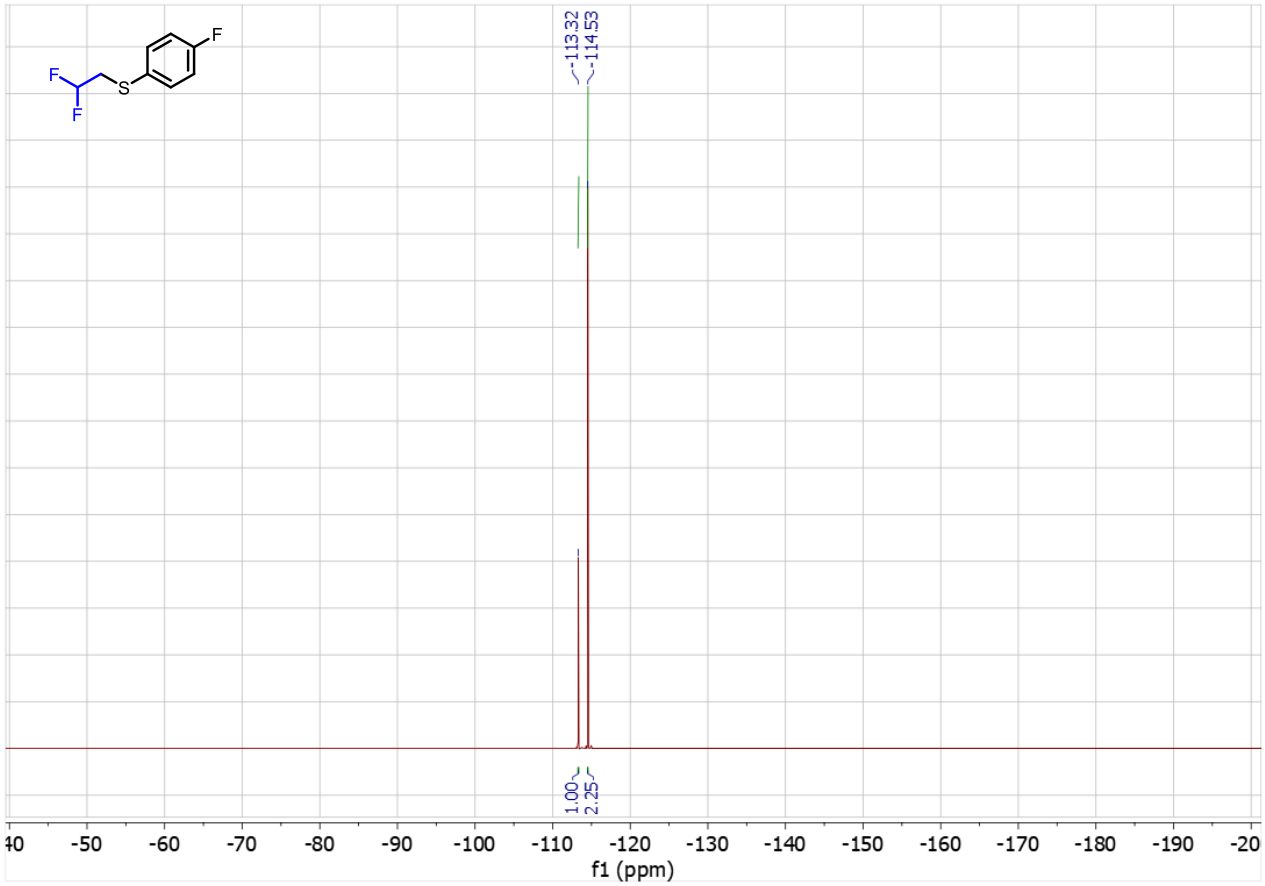

133.78
132.70
132.68
132.48
129.46
117.69
115.27
112.85
77.16 CDCl3
38.07
37.83
37.59
Cl
F
F
S
f1 (ppm)

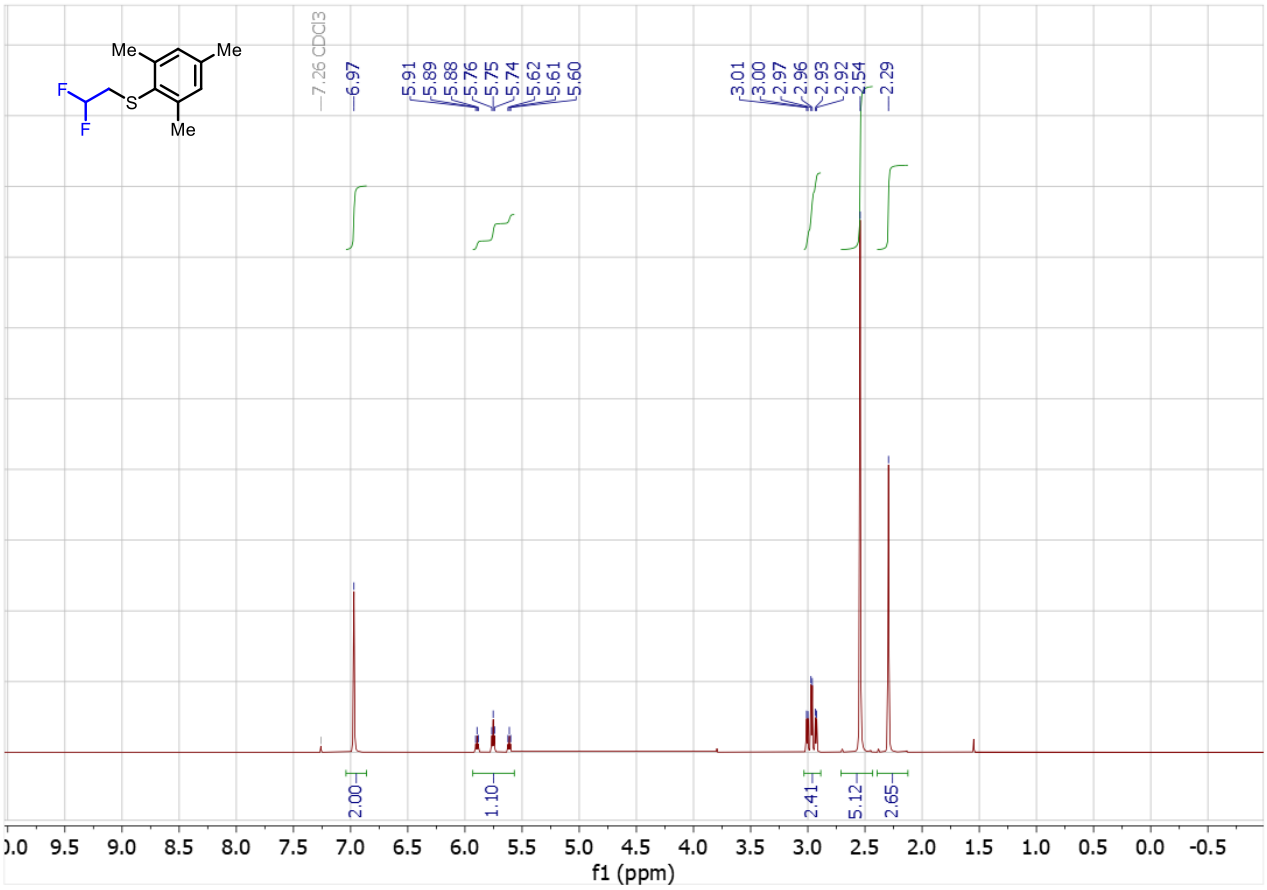
SUPPORTING INFORMATION

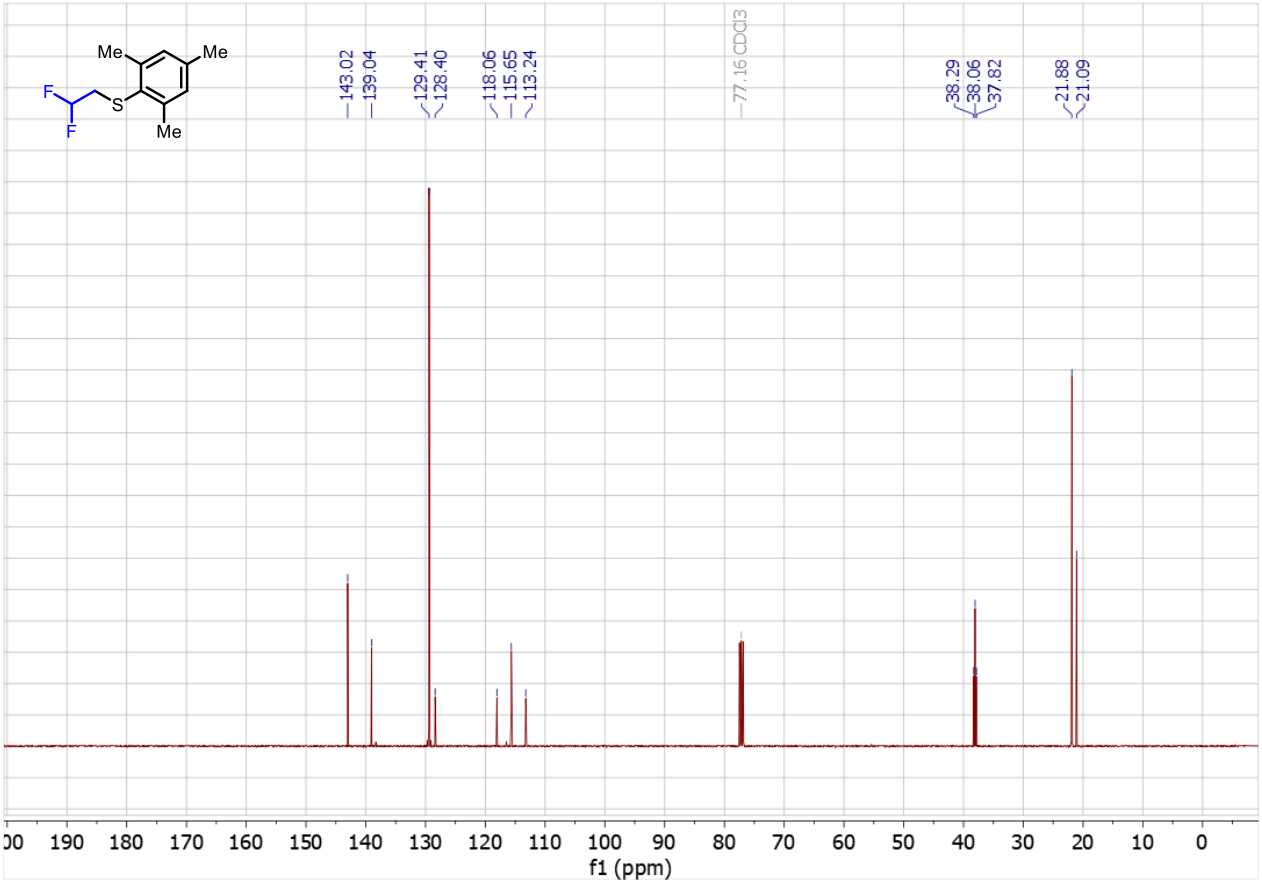


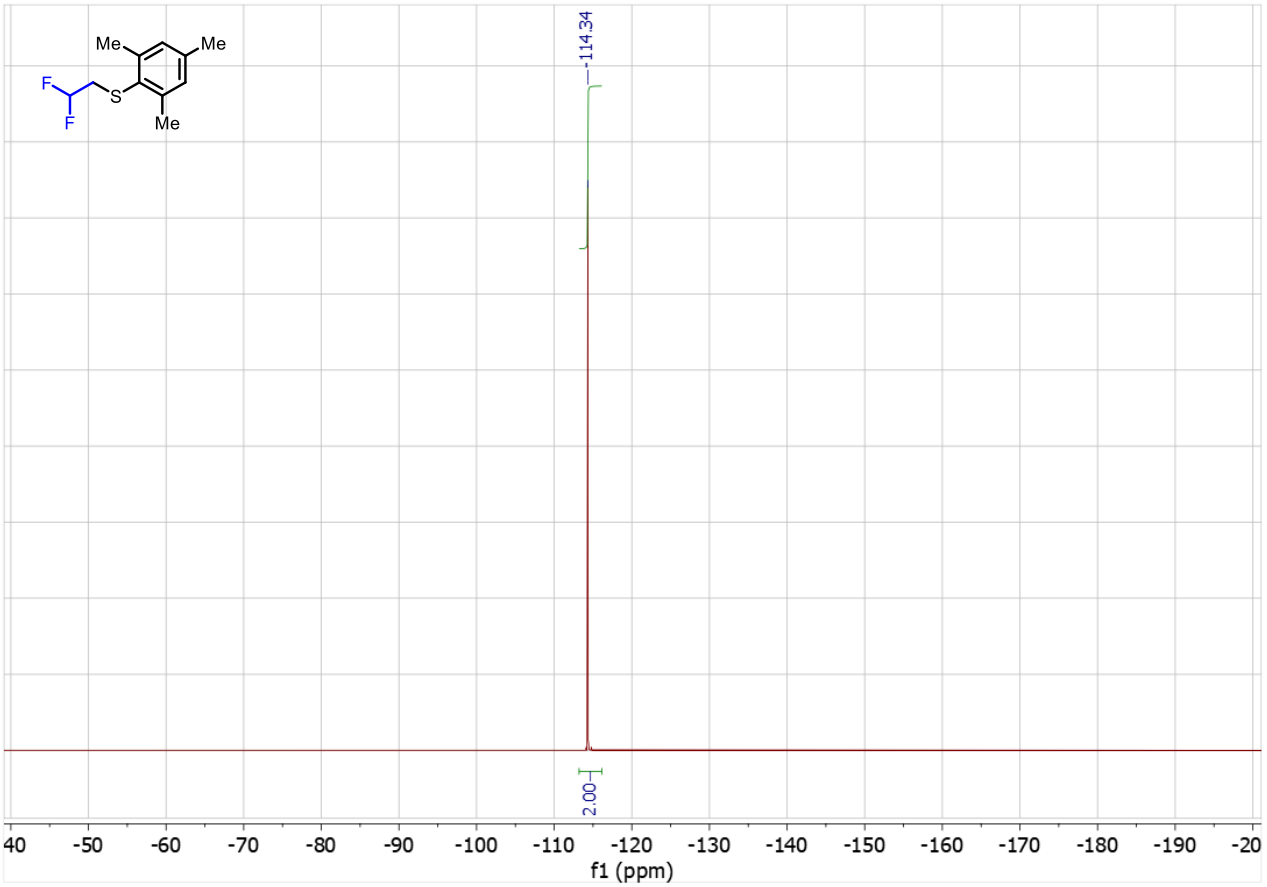


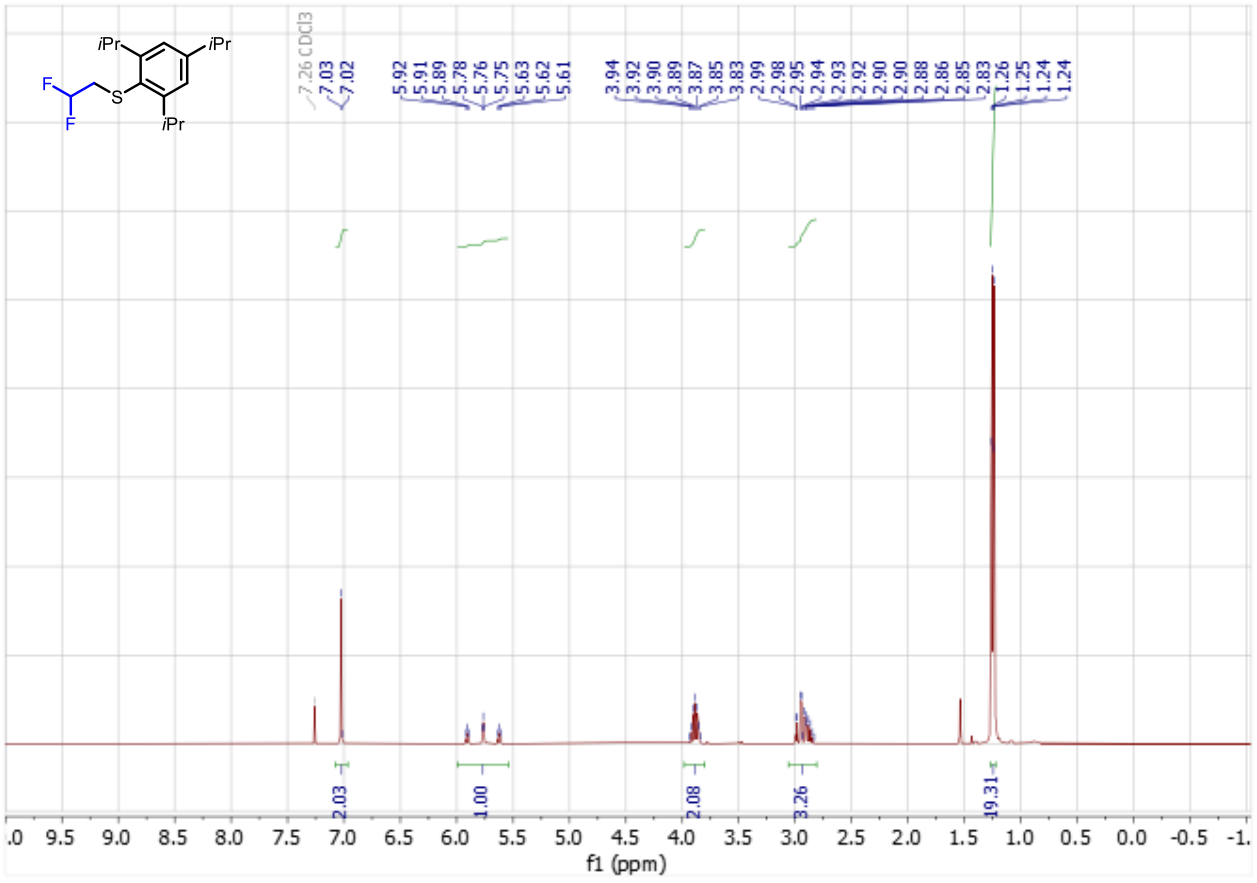

F
F
F
S
163.99
161.52
134.44
134.36
129.16
129.13
117.85
116.65
116.43
115.43
113.02
77.16 CDCl3
39.08
38.84
38.60
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

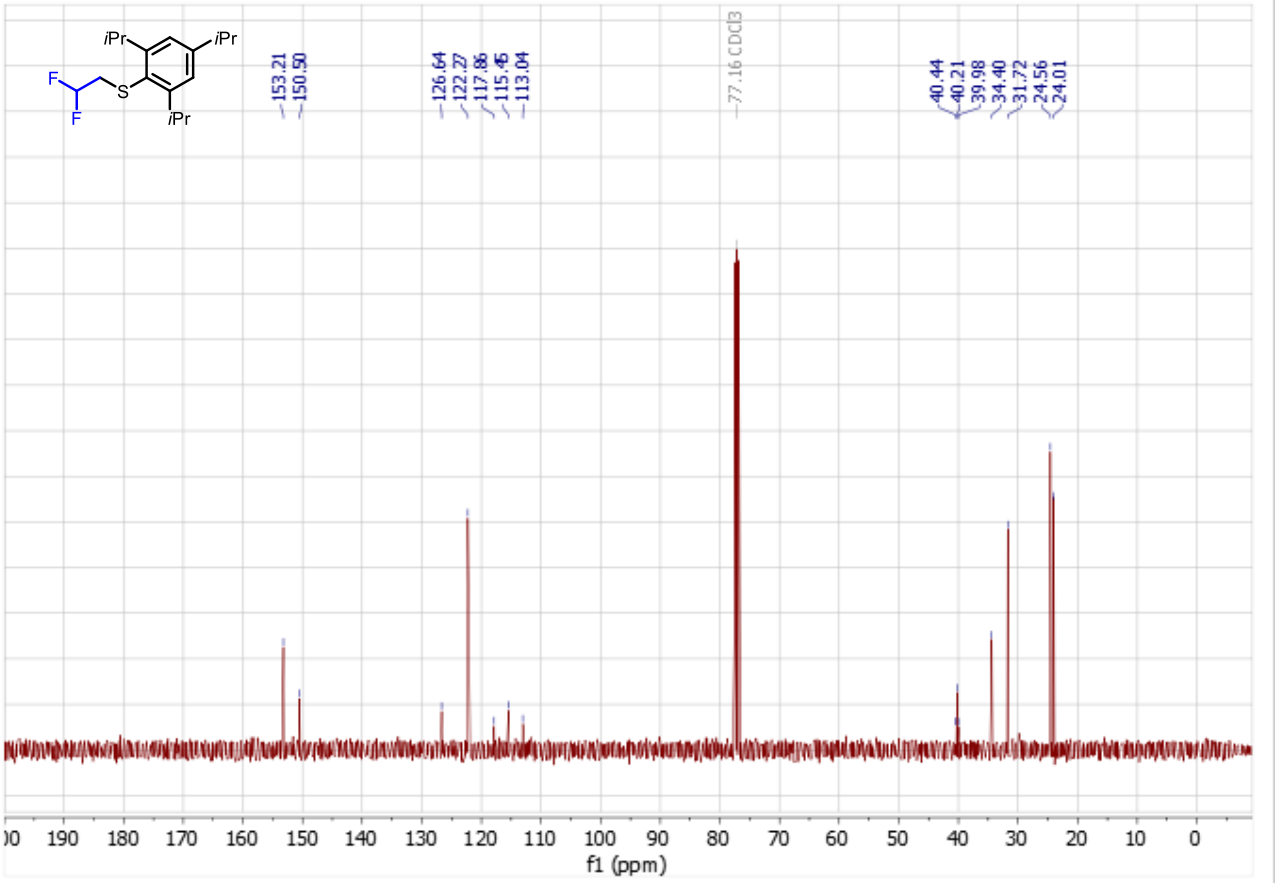

F
F
F
S
-113.32
-114.53
1.00
2.25
-40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -20
f1 (ppm)

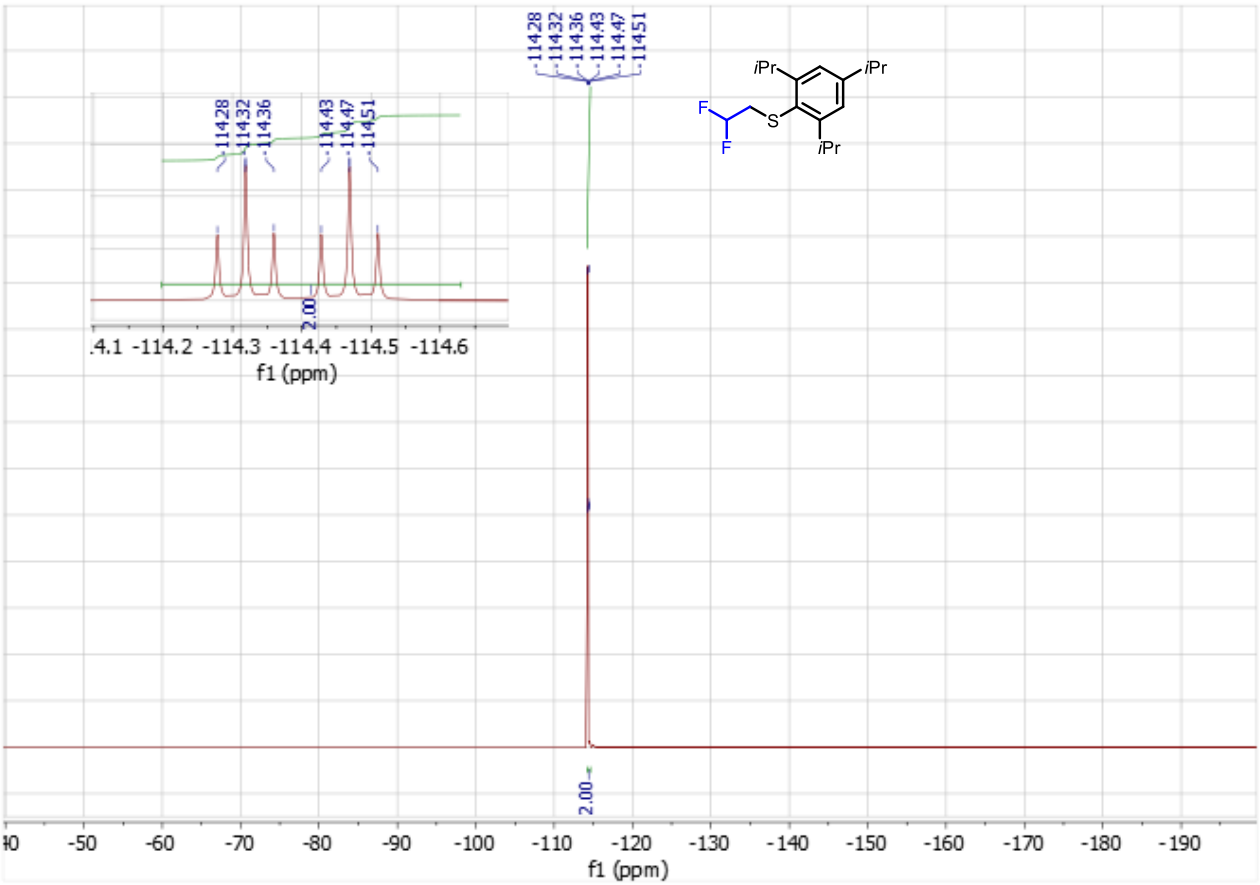

Me
Me
F
S
F
Me
7.26 CDCl3
6.97
5.91
5.89
5.88
5.76
5.75
5.74
5.62
5.61
5.60
3.01
3.00
2.97
2.96
2.93
2.92
2.54
2.29
2.00
1.10
2.41
5.12
2.65
f1 (ppm)

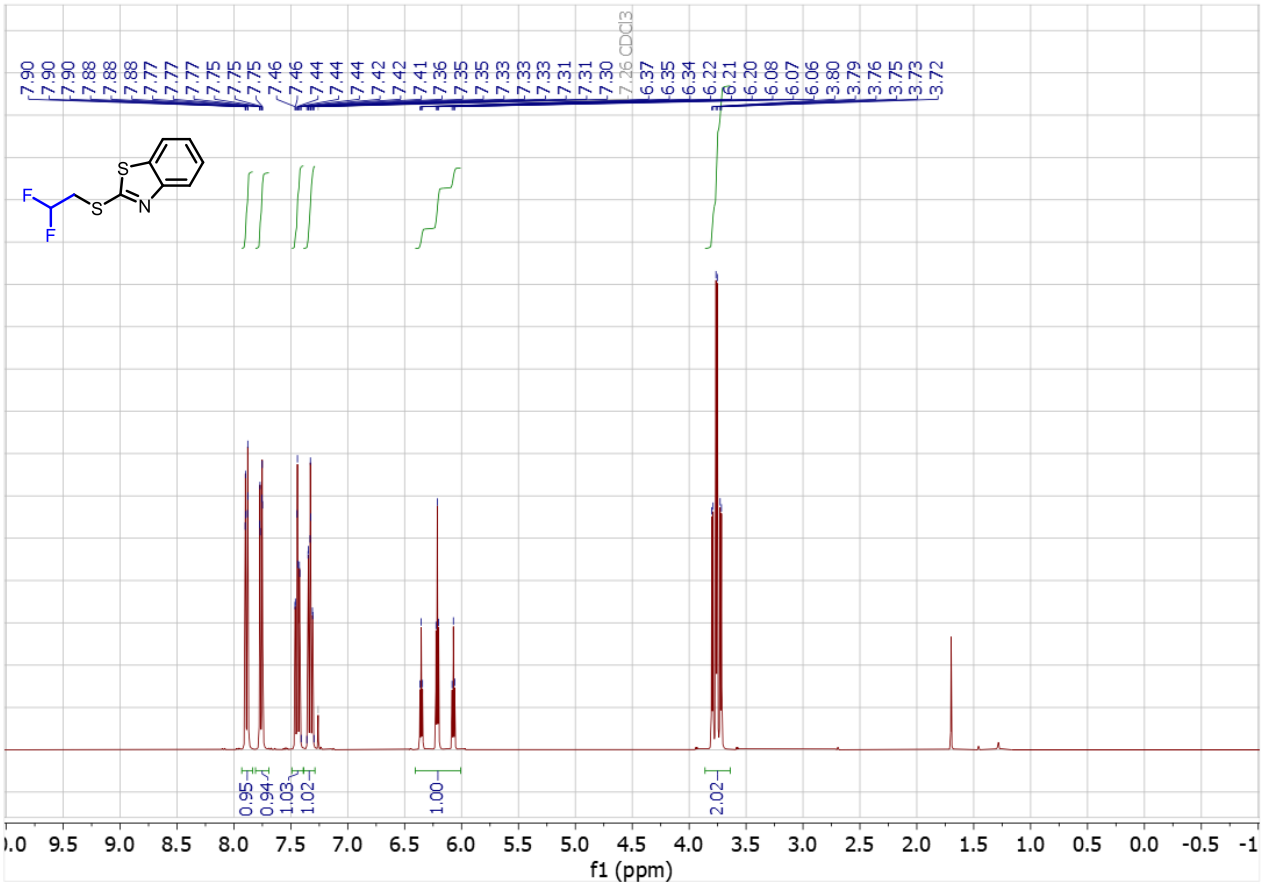

Me
Me
F
S
F
Me
143.02
139.04
129.41
128.40
118.06
115.65
113.24
77.16 CDCl3
38.29
38.06
37.82
21.88
21.09
f1 (ppm)

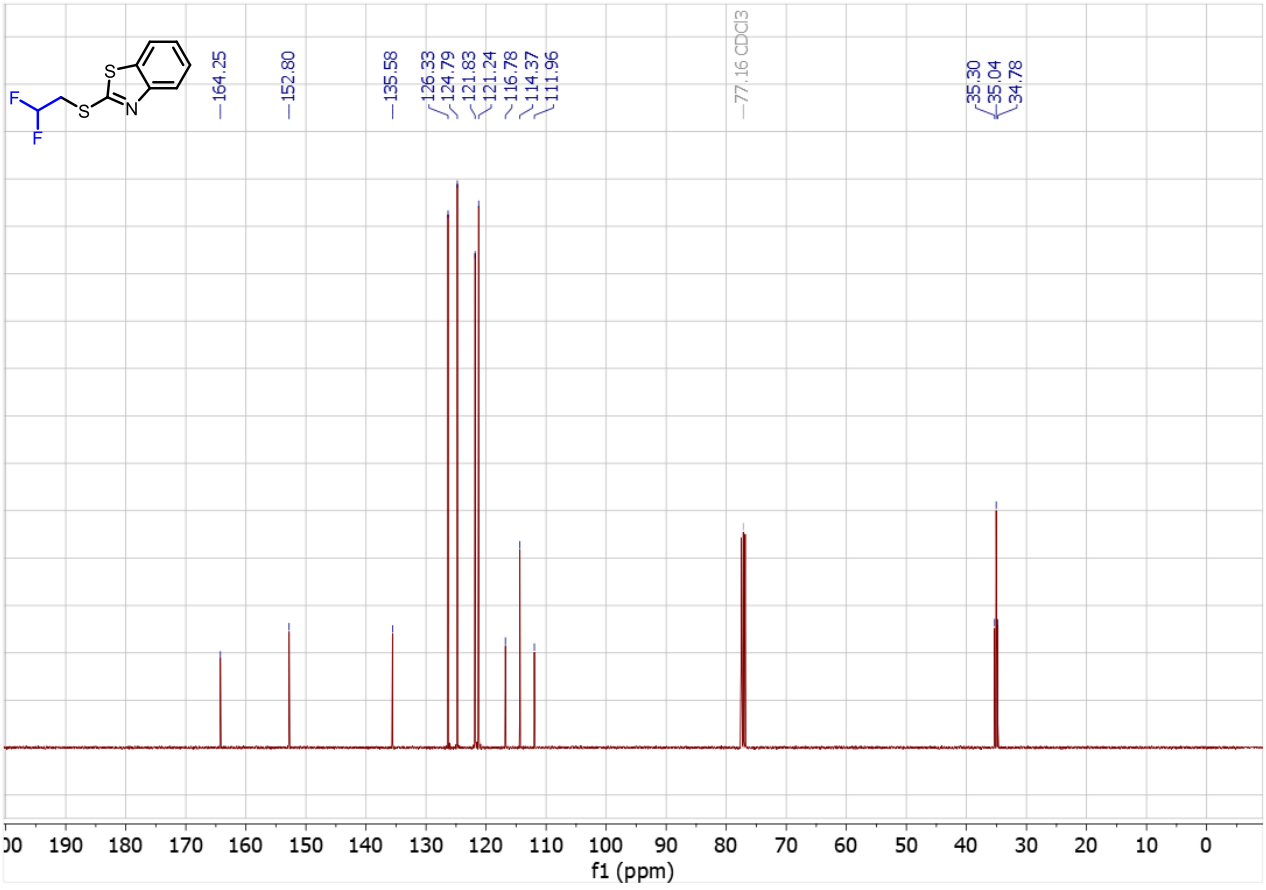

Me
Me
F
S
F
Me
-114.34
2.00
40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -20
f1 (ppm)

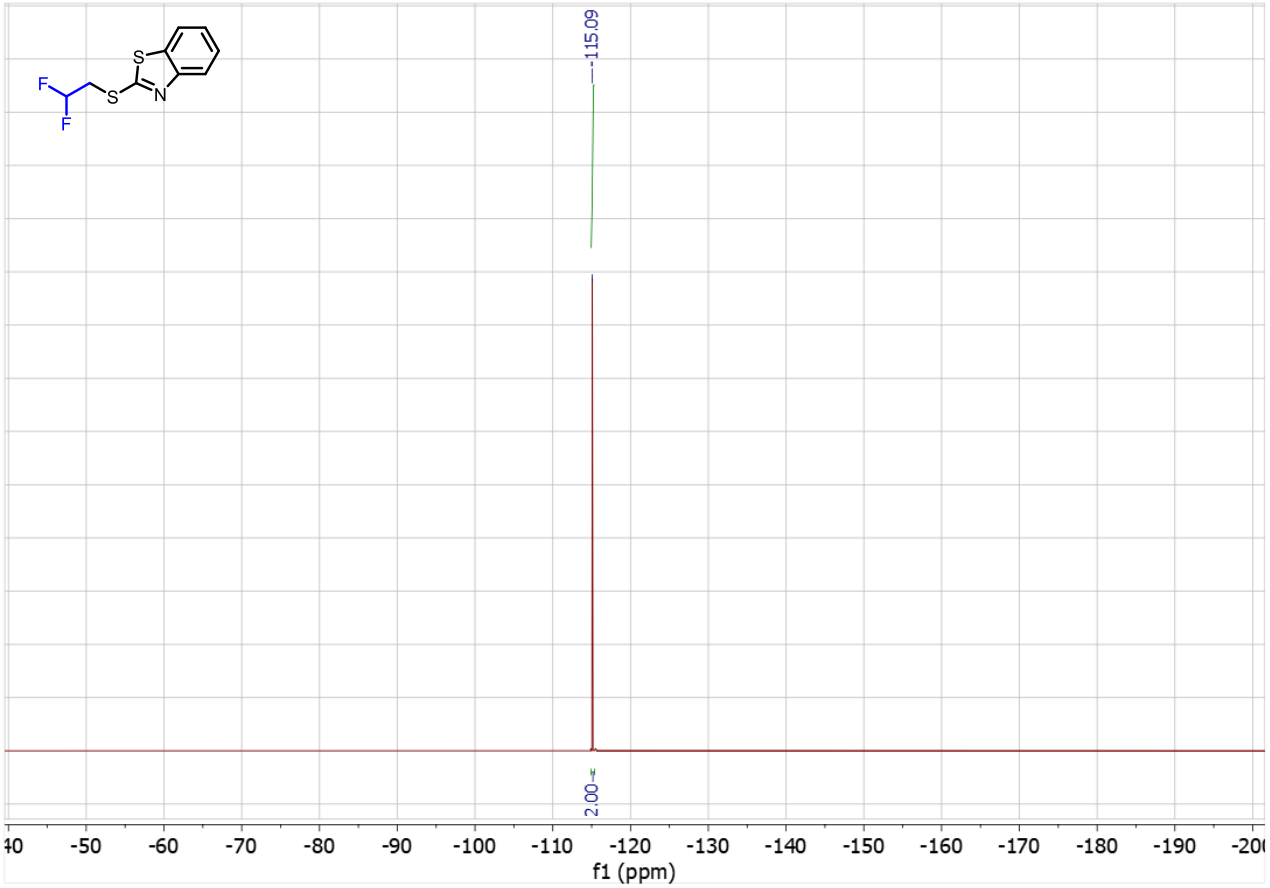

iPr
iPr
F
S
F
iPr
7.26 CDCl3
7.03
7.02
5.92
5.91
5.89
5.78
5.76
5.75
5.63
5.62
5.61
3.94
3.92
3.90
3.89
3.87
3.85
3.83
2.99
2.98
2.95
2.94
2.93
2.92
2.90
2.90
2.88
2.86
2.85
2.83
1.26
1.25
1.24
1.24
2.03
1.00
2.08
3.26
19.31
.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

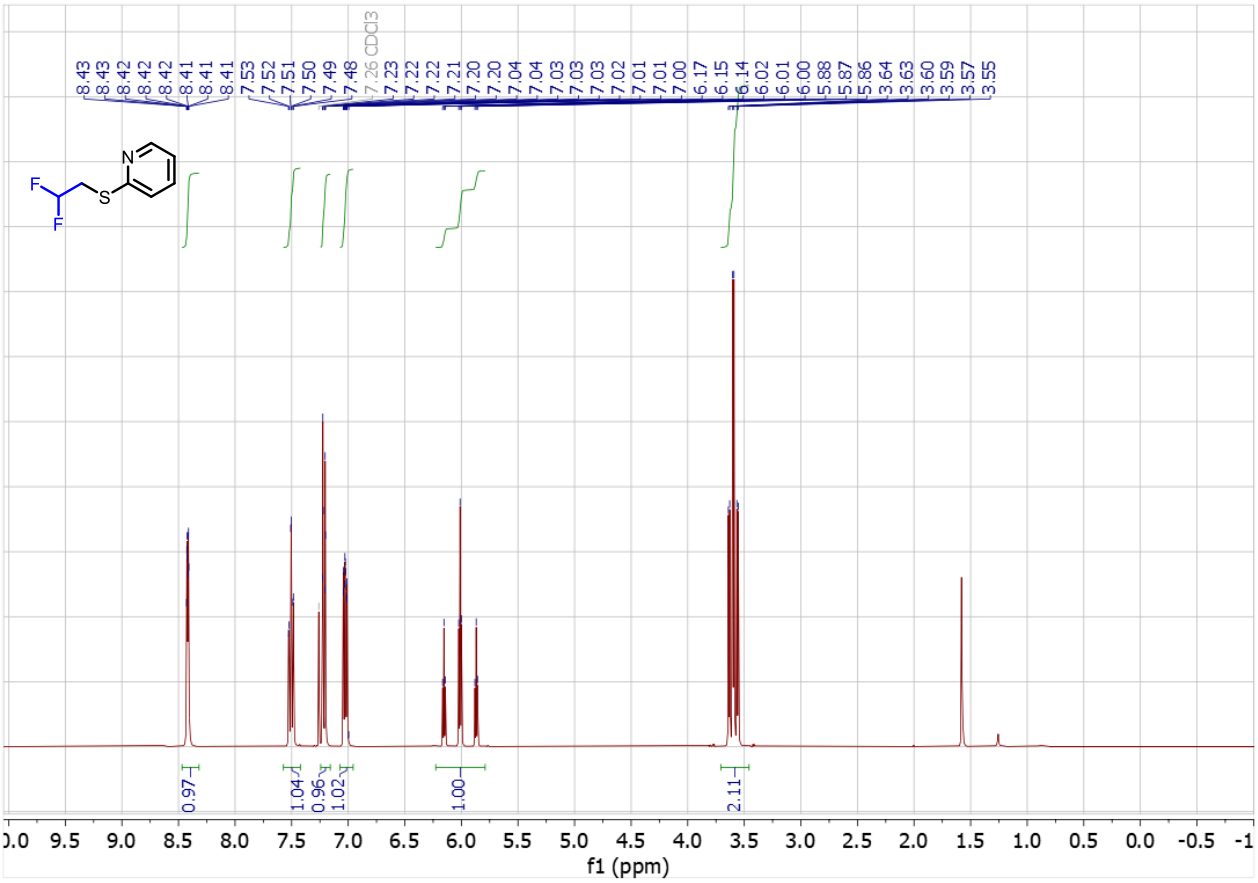

iPr
iPr
iPr
F
F
S
153.21
150.50
126.64
122.27
117.86
115.45
113.04
77.16 CDCl3
40.44
40.21
39.98
34.40
31.72
24.56
24.01
f1 (ppm)

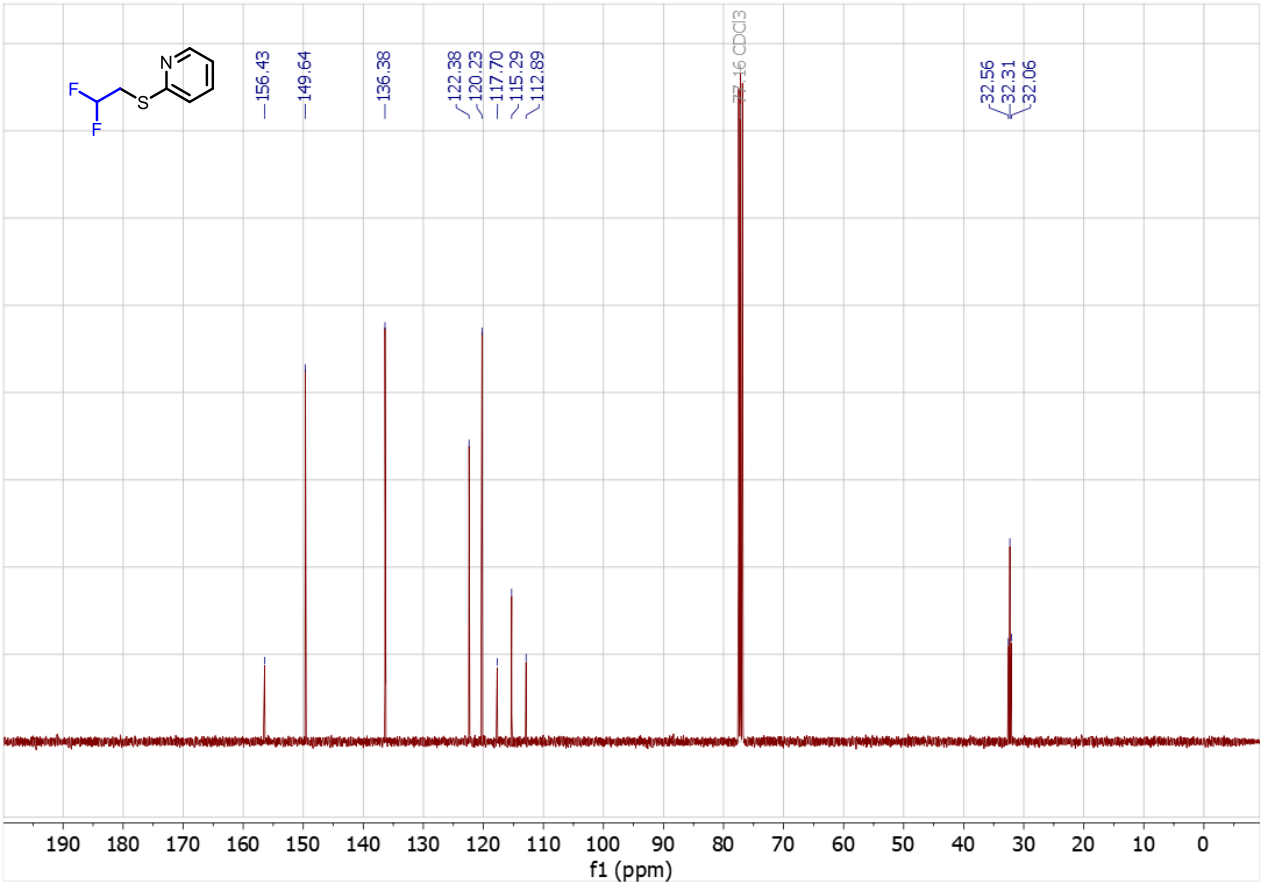

114.28
114.32
114.36
114.43
114.47
114.51
iPr
iPr
iPr
F
F
S
2.00
f1 (ppm)
2.00
f1 (ppm)

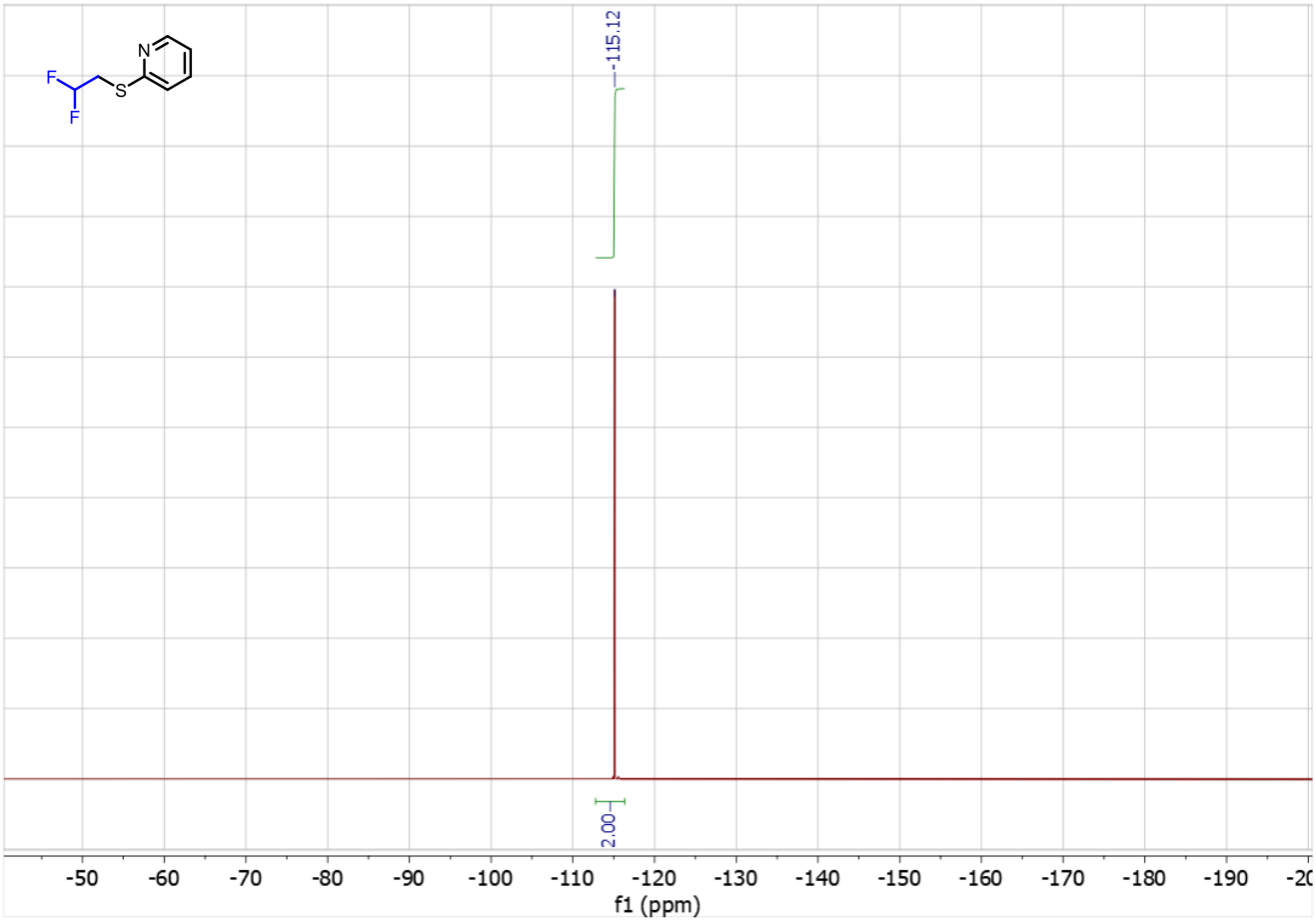

7.90
7.90
7.88
7.88
7.77
7.77
7.75
7.75
7.46
7.44
7.44
7.42
7.42
7.41
7.36
7.35
7.35
7.33
7.33
7.31
7.31
7.30
7.26 CDCl3
6.37
6.35
6.34
6.22
6.21
6.20
6.08
6.07
6.06
3.80
3.79
3.76
3.75
3.73
3.72
F
F
S
S
N
0.95
0.94
1.03
1.02
1.00
2.02
f1 (ppm)

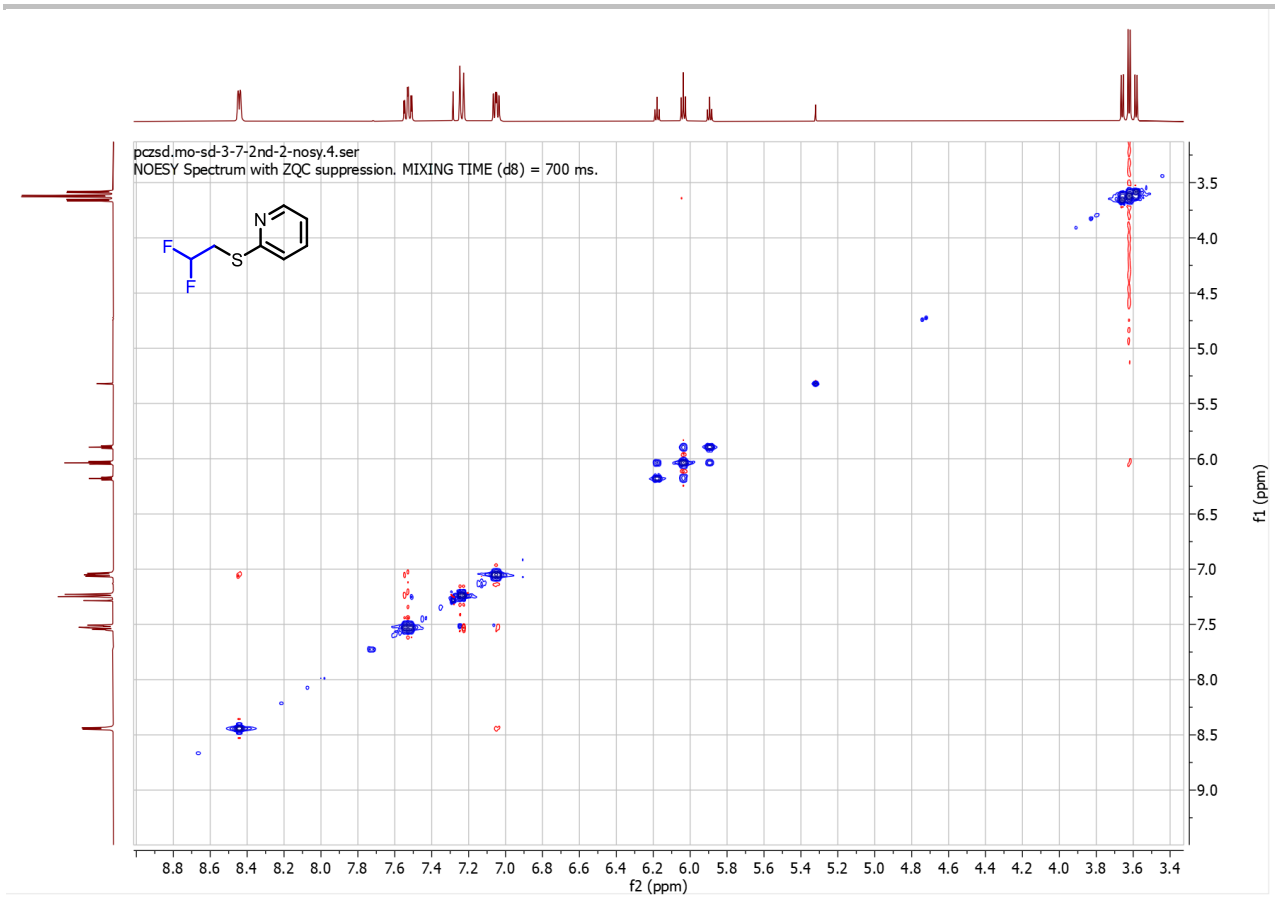

F
F
S
S
N
164.25
152.80
135.58
126.33
124.79
121.83
121.24
116.78
114.37
111.96
77.16 CDCl3
35.30
35.04
34.78
f1 (ppm)

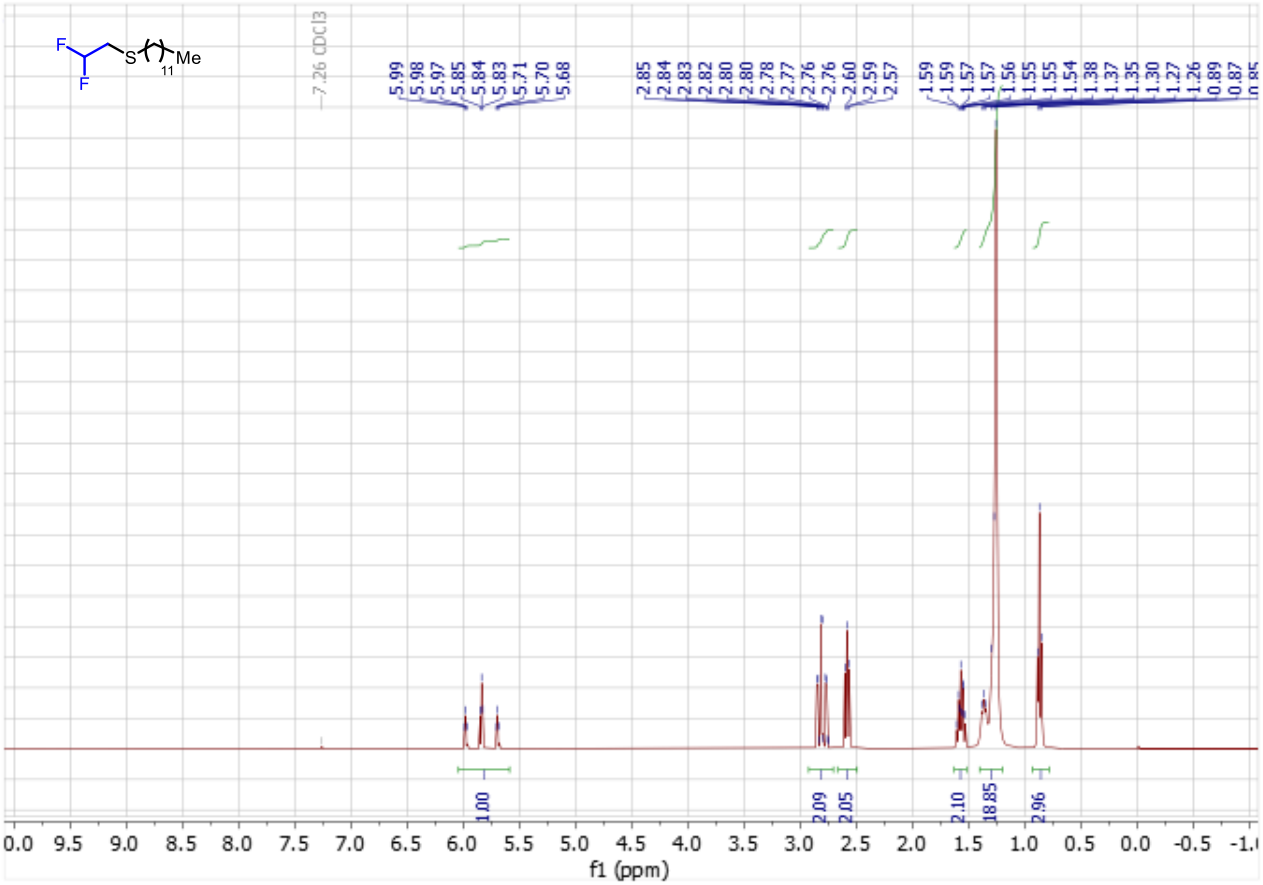

F
F
S
S
N
-115.09
2.00
f1 (ppm)

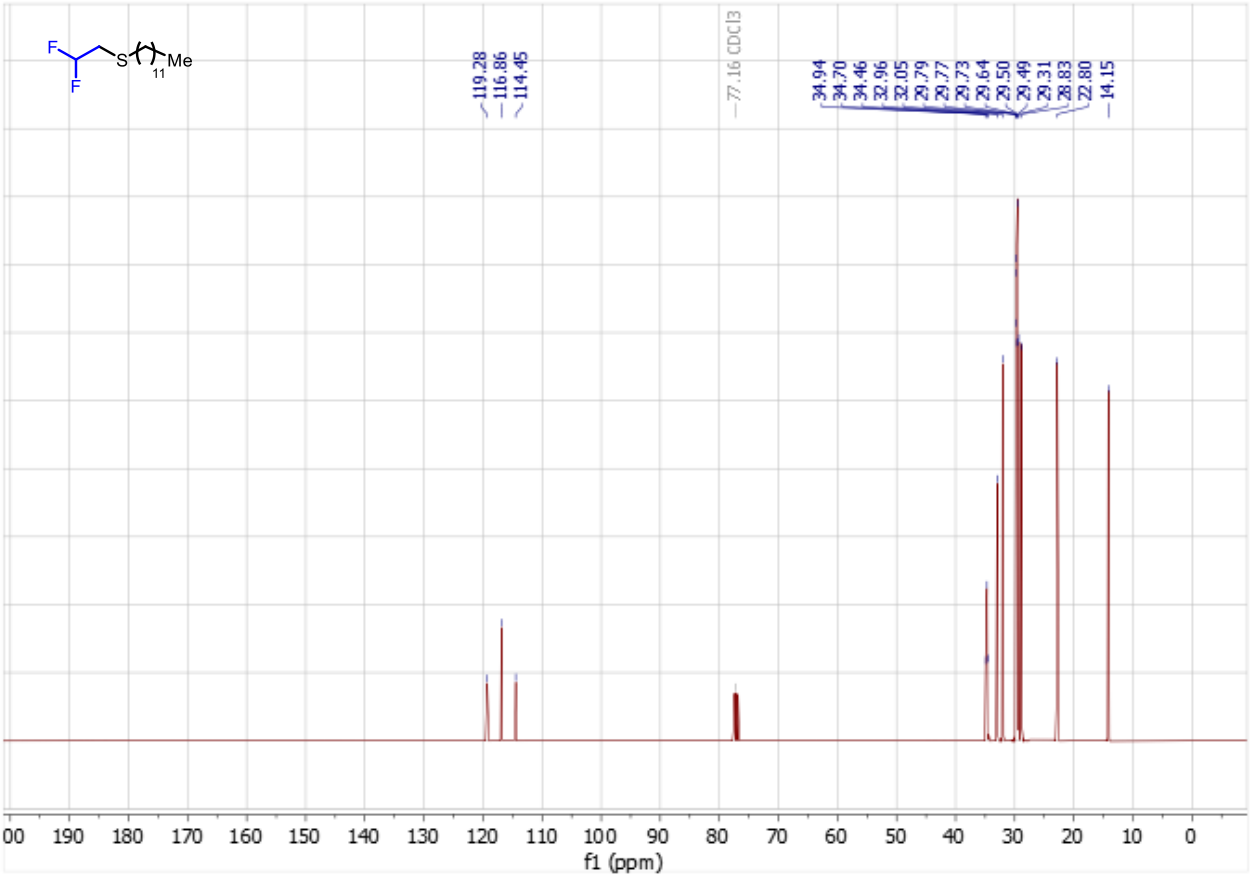

8.43
8.43
8.42
8.42
8.42
8.41
8.41
8.41
7.53
7.52
7.51
7.50
7.49
7.48
7.26 CDCl3
7.23
7.22
7.22
7.21
7.20
7.20
7.04
7.04
7.03
7.03
7.03
7.02
7.01
7.01
7.00
6.17
6.15
6.14
6.02
6.01
6.00
5.88
5.87
5.86
3.64
3.63
3.60
3.59
3.57
3.55
N
F
F
S
0.97
1.04
0.96
1.02
1.00
2.11
f1 (ppm)

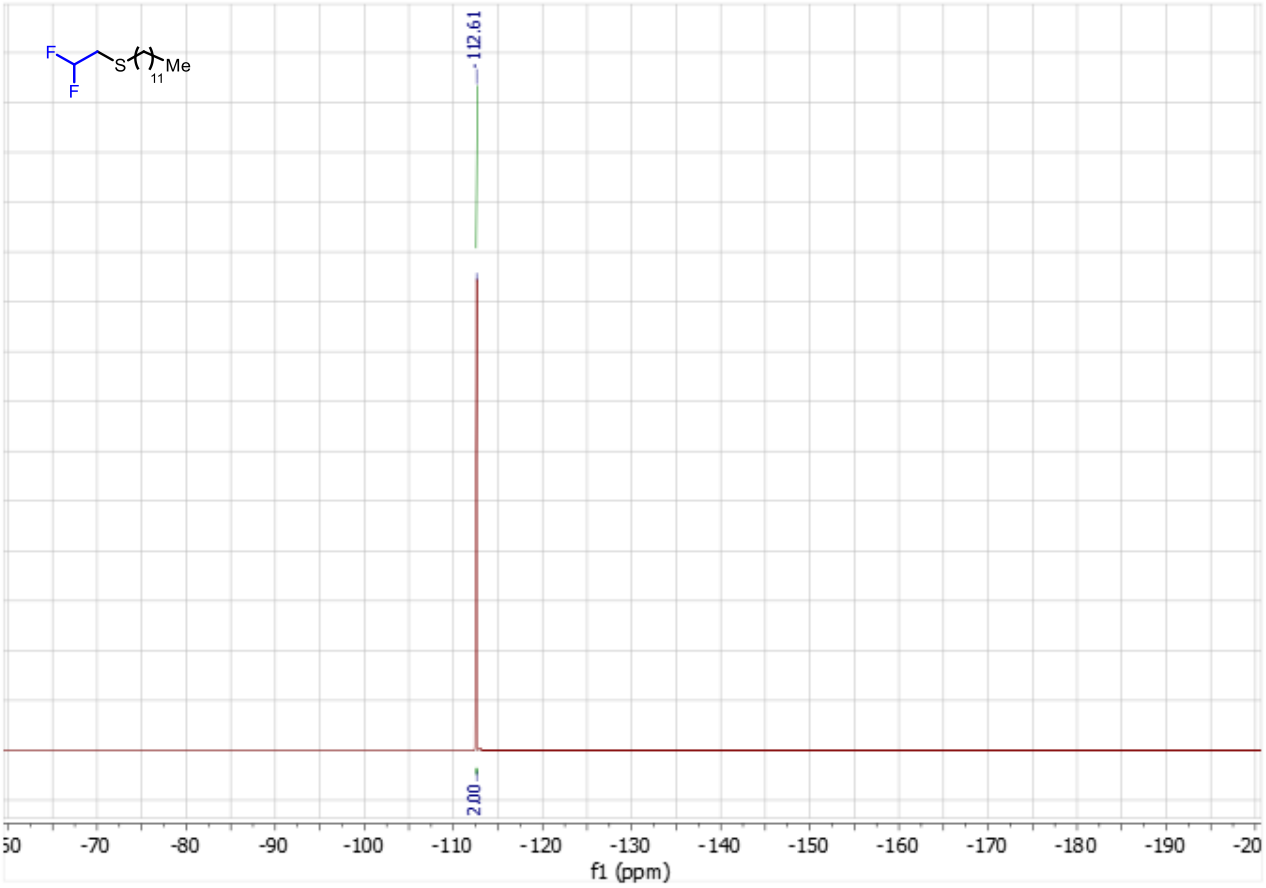

156.43
149.64
136.38
122.38
120.23
117.70
115.29
112.89
77.16 CDCl3
32.56
32.31
32.06
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

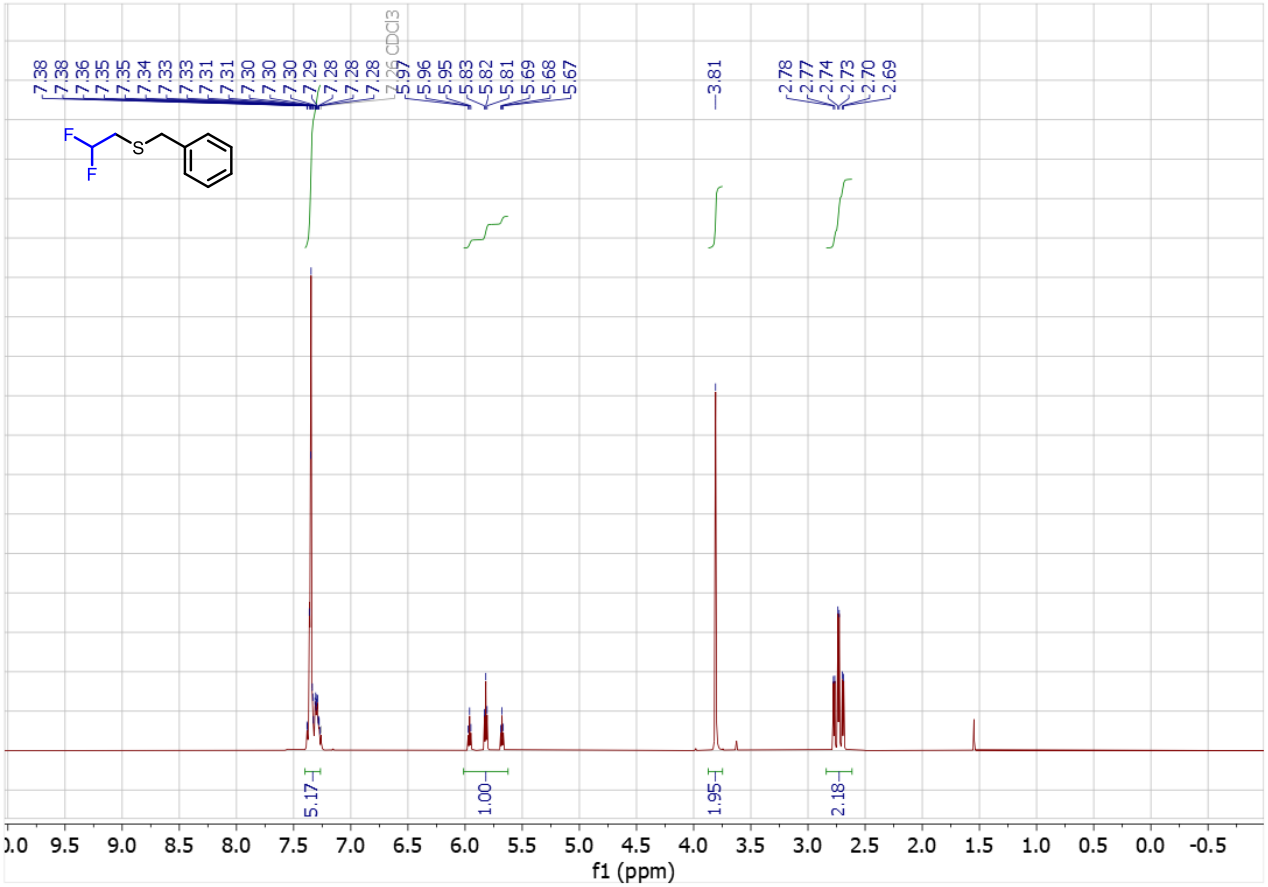

-115.12
2.00
-50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

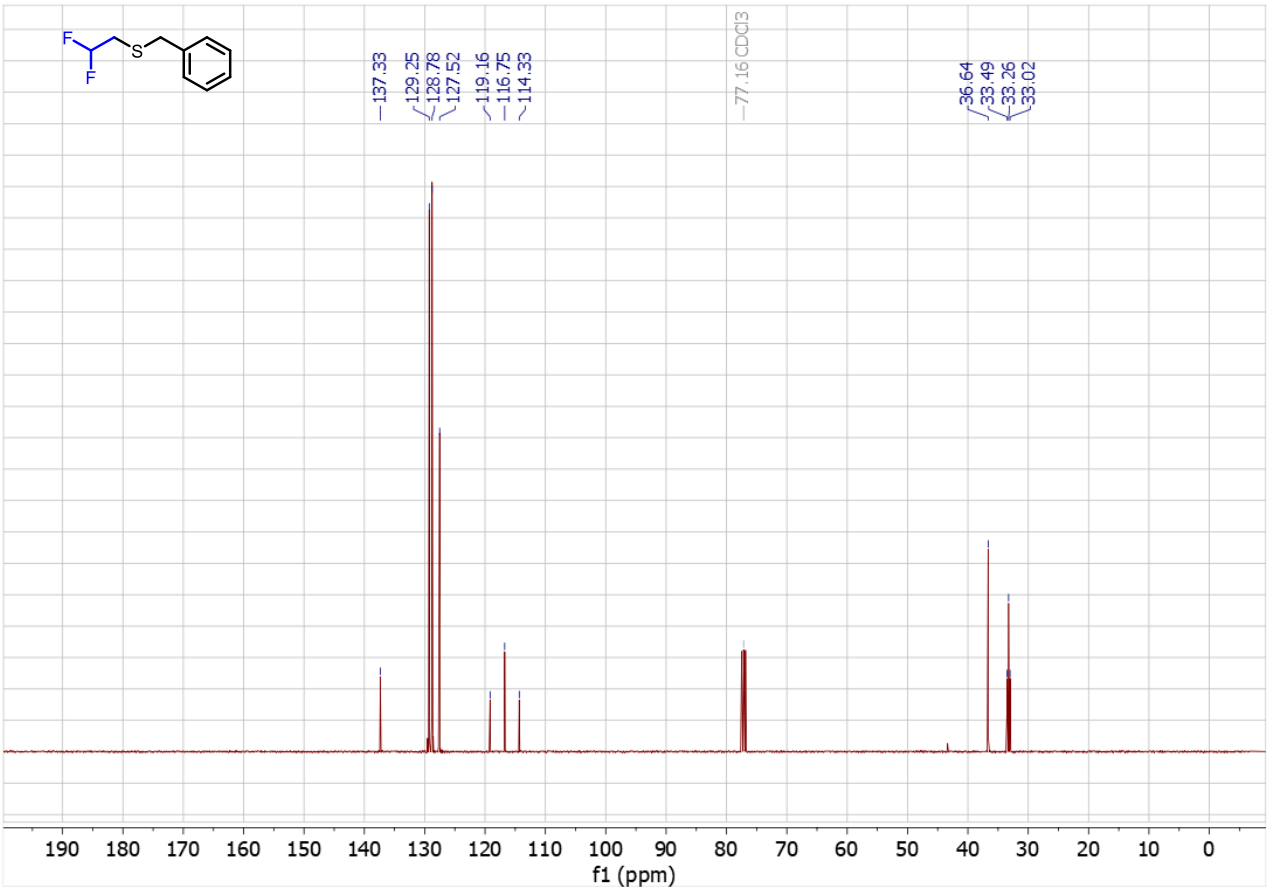

pczsd.mo-sd-3-7-2nd-2-nosy.4.ser
NOESY Spectrum with ZQC suppression. MIXING TIME (d8) = 700 ms.
F
F
S
N
f2 (ppm)
f1 (ppm)

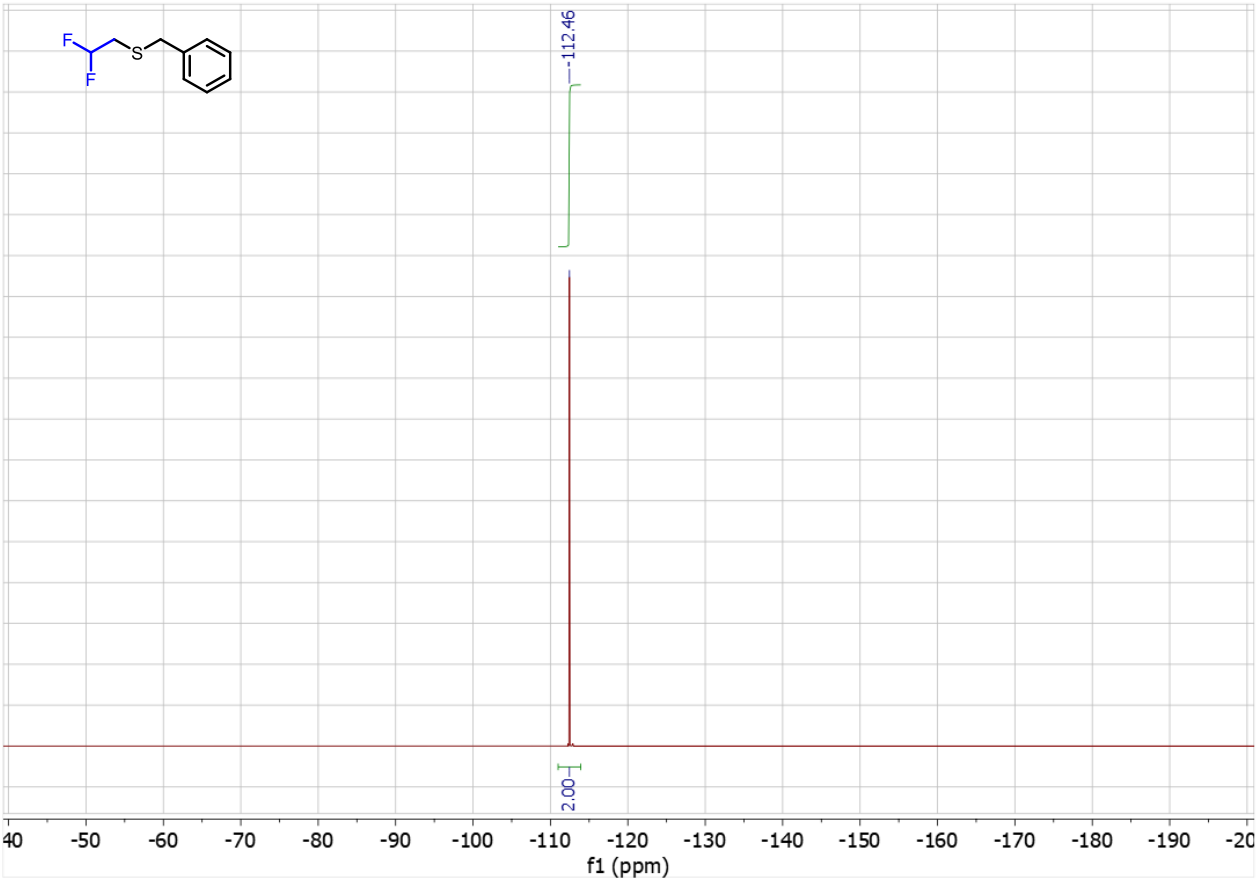

F
F
S
11
Me
7.26 CDCl3
5.99
5.98
5.97
5.85
5.84
5.83
5.71
5.70
5.68
2.85
2.84
2.83
2.82
2.80
2.80
2.78
2.77
2.76
2.76
2.60
2.59
2.57
1.59
1.59
1.57
1.57
1.56
1.55
1.55
1.54
1.38
1.37
1.35
1.30
1.27
1.26
0.89
0.87
1.00
2.09
2.05
2.10
18.85
2.96
f1 (ppm)

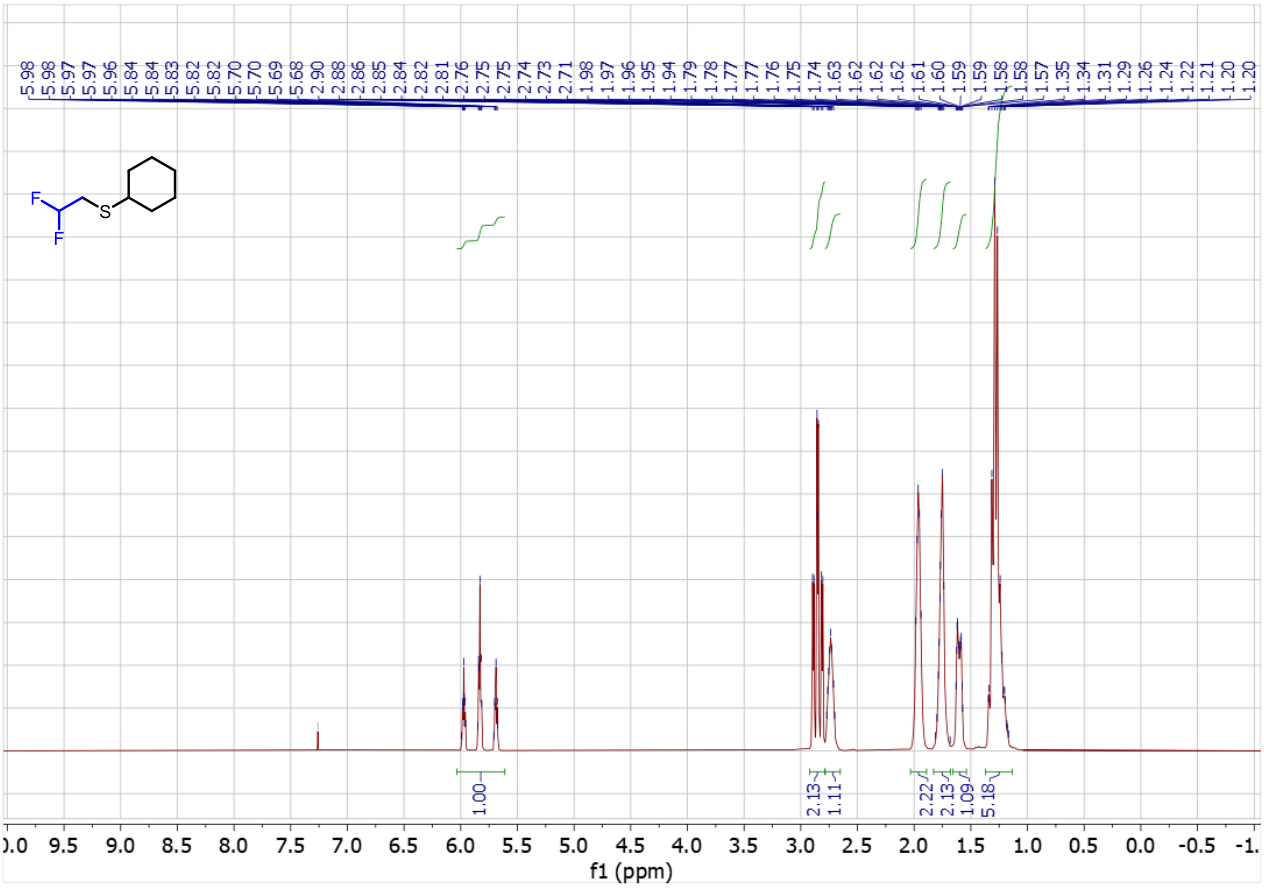

F
F
S
11
Me
119.28
116.86
114.45
77.16 CDCl3
34.94
34.70
34.46
32.96
32.05
29.79
29.77
29.73
29.64
29.50
29.49
29.31
28.83
22.80
14.15
f1 (ppm)

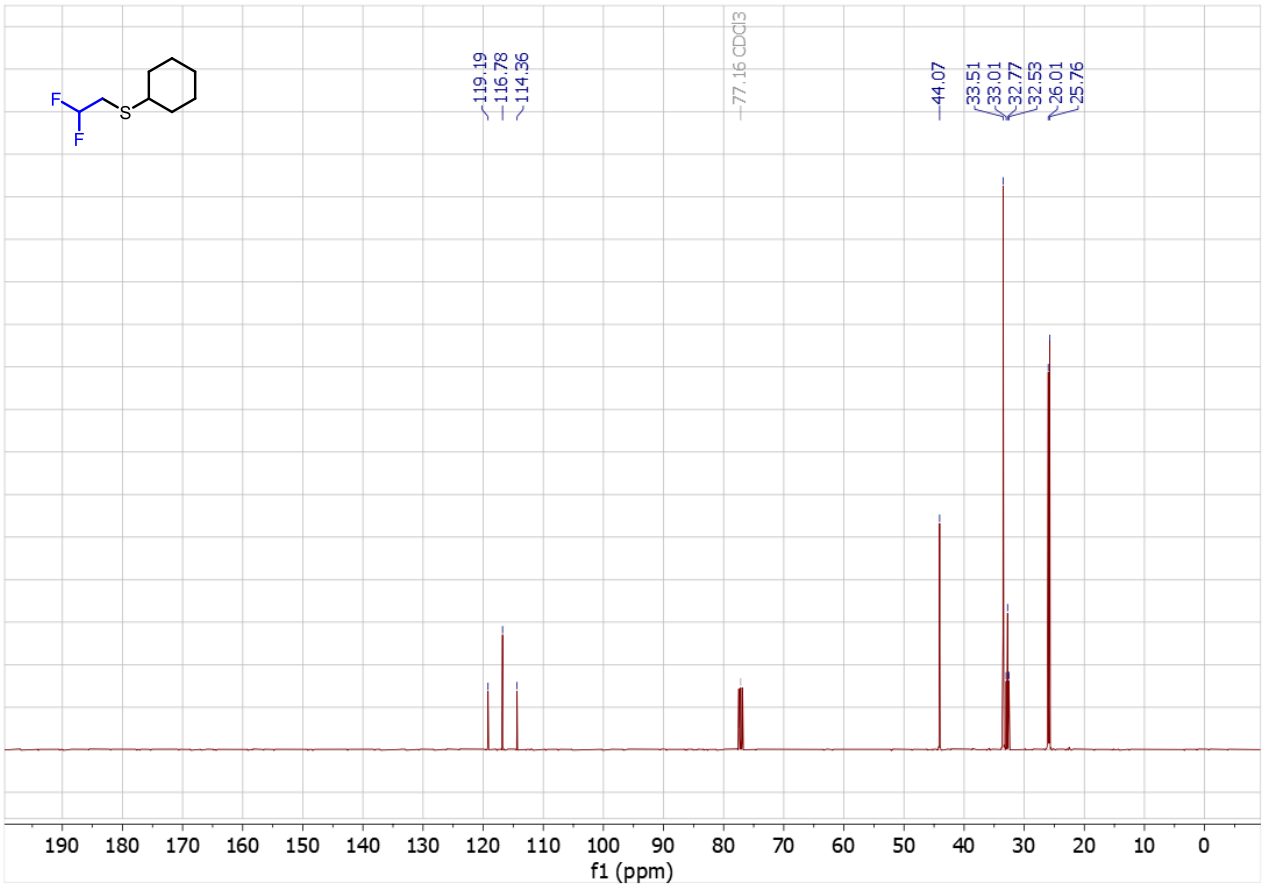

F
F
S
11
Me
-112.61
2.00
f1 (ppm)

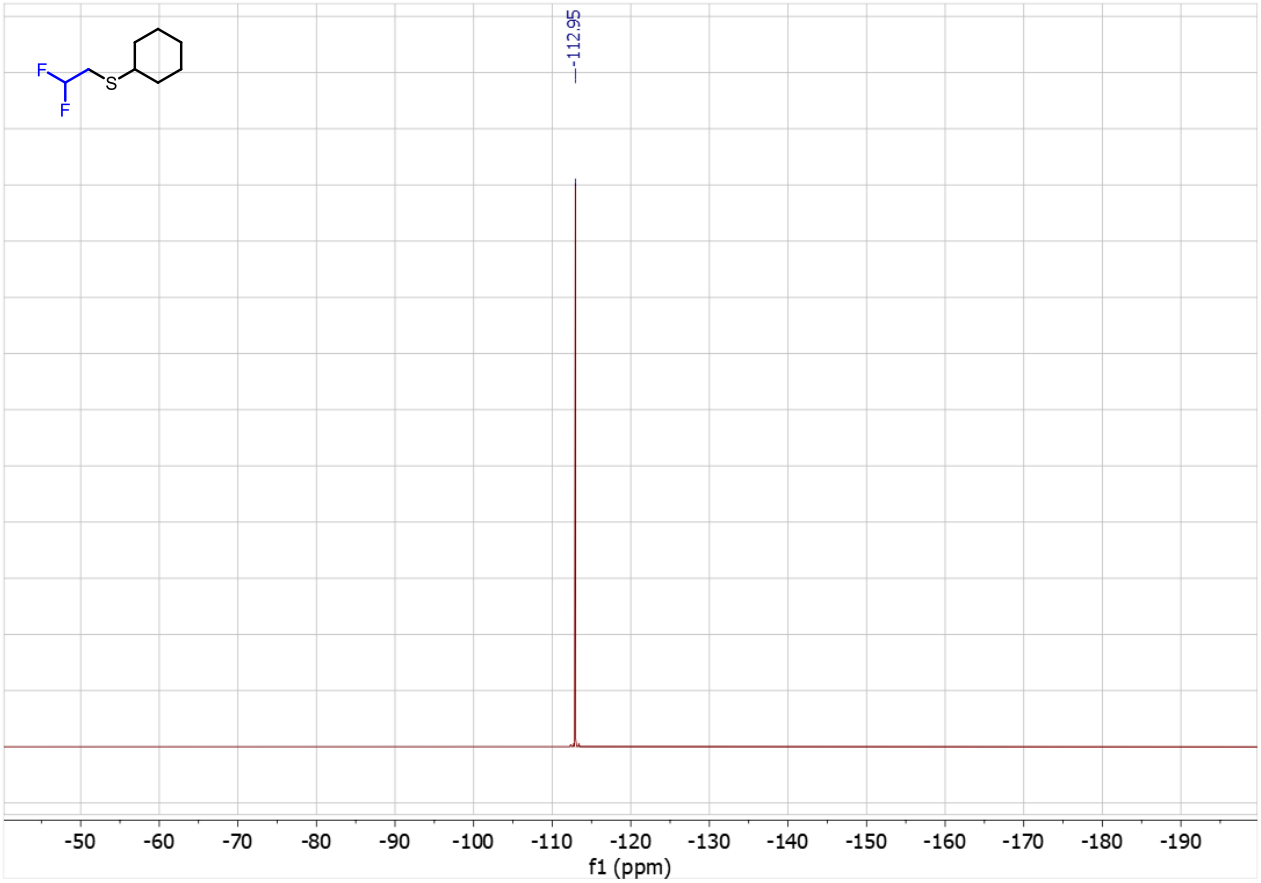

7.38
7.38
7.36
7.35
7.35
7.34
7.33
7.33
7.31
7.31
7.30
7.30
7.30
7.29
7.28
7.28
7.28
5.97
5.96
5.95
5.83
5.82
5.81
5.69
5.68
5.67
3.81
2.78
2.77
2.74
2.73
2.70
2.69
5.17
1.00
1.95
2.18
f1 (ppm)

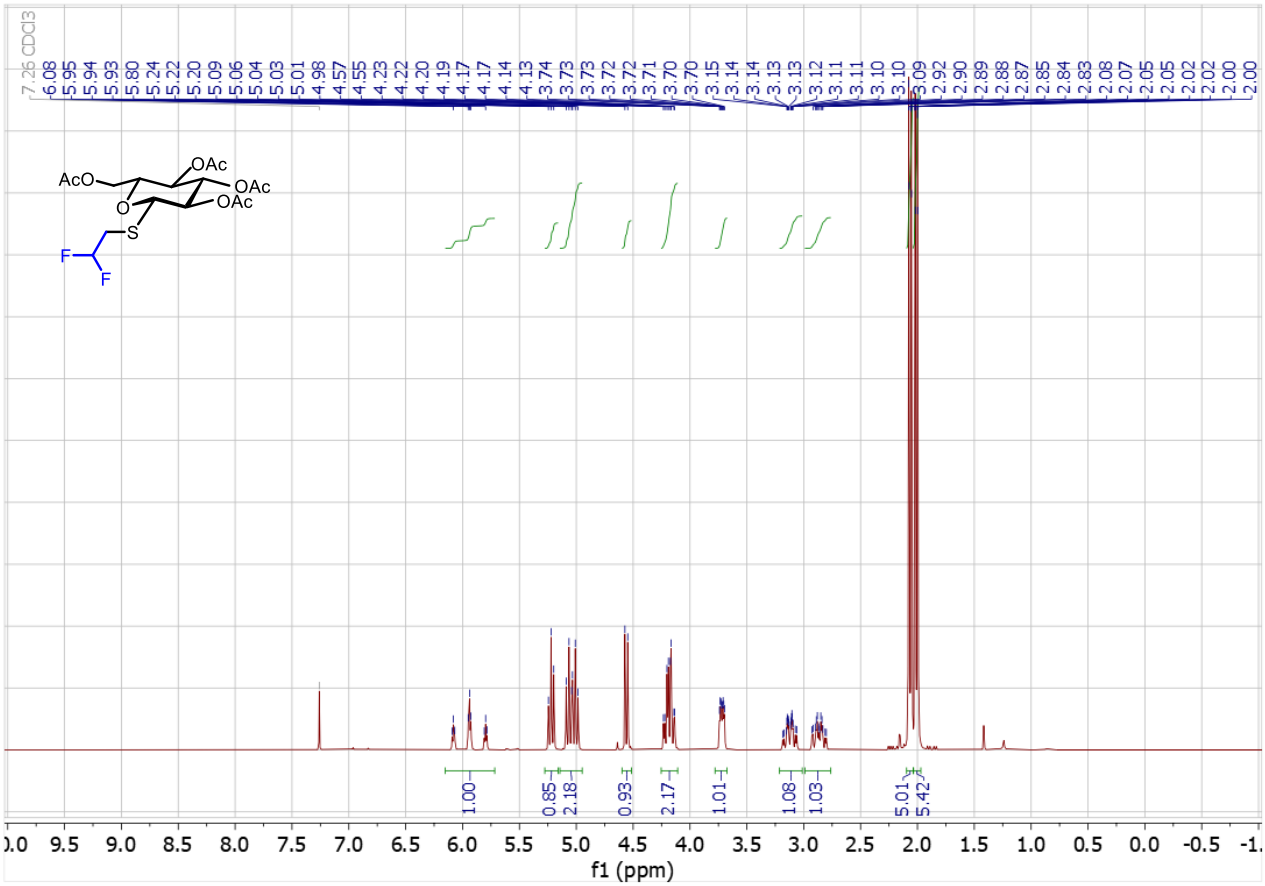

137.33
129.25
128.78
127.52
119.16
116.75
114.33
77.16 CDCl3
36.64
33.49
33.26
33.02
f1 (ppm)

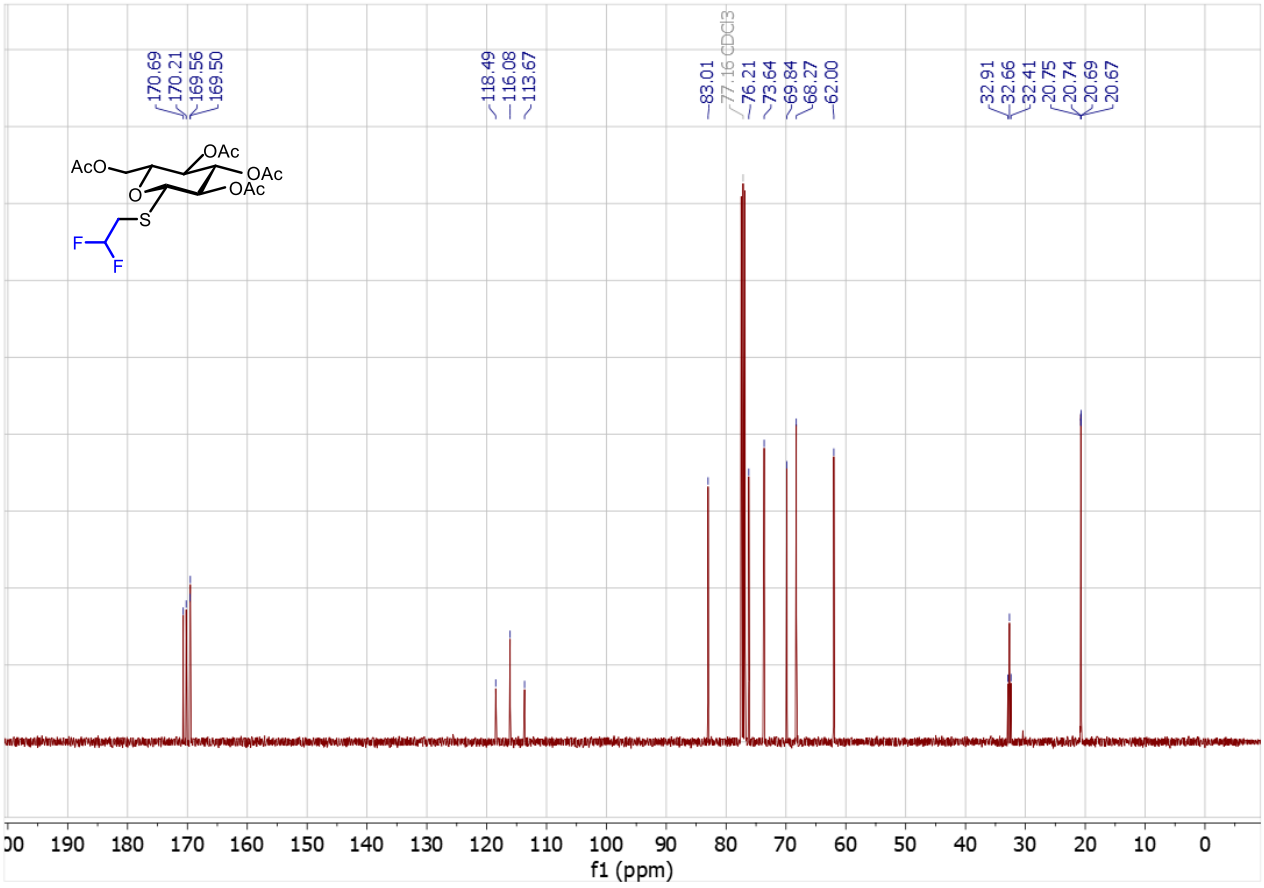

F
F
S
-112.46
2.00
40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -20
f1 (ppm)

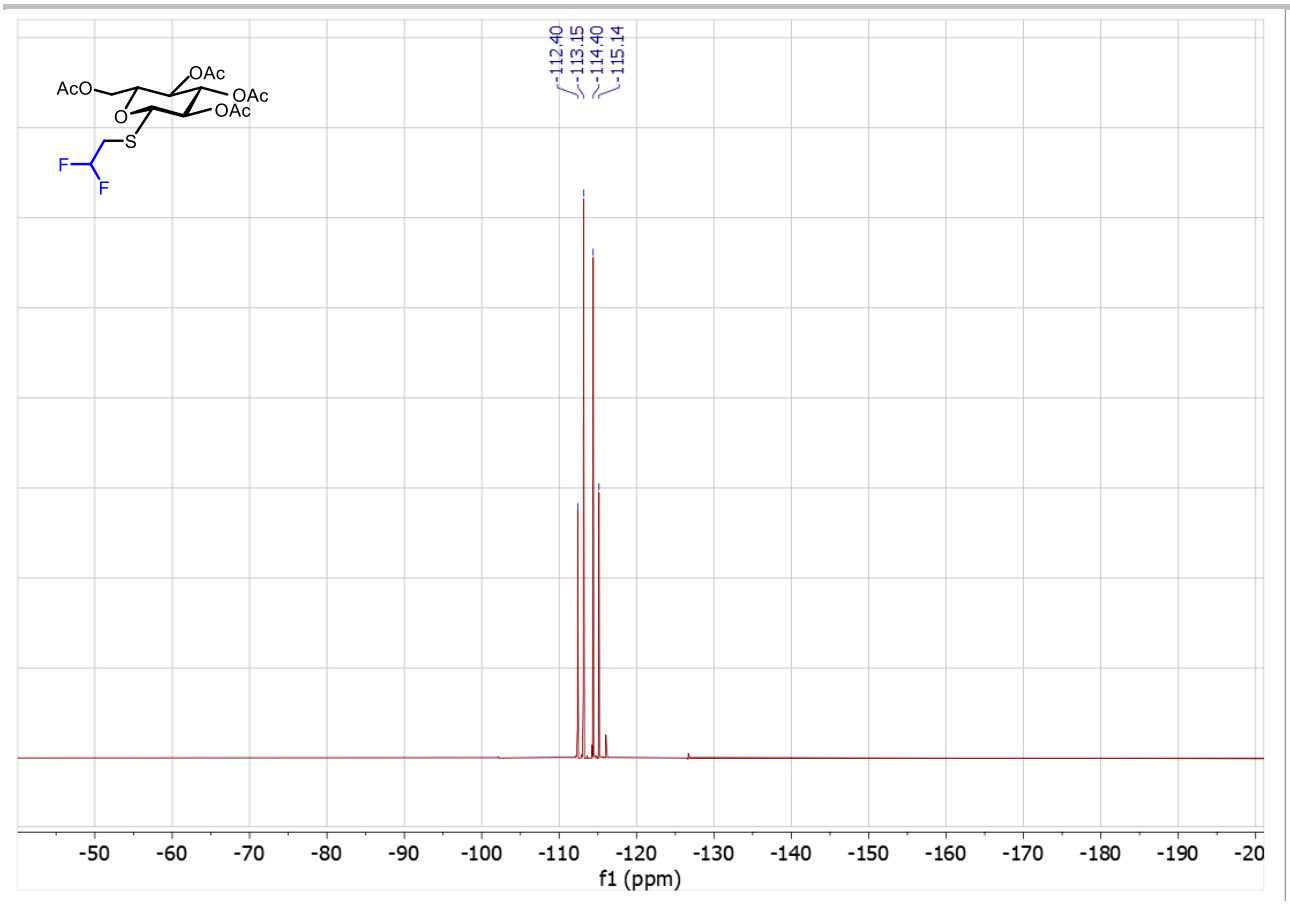

F
F
S
1.00
2.13
1.11
2.22
2.13
1.09
5.18
f1 (ppm)

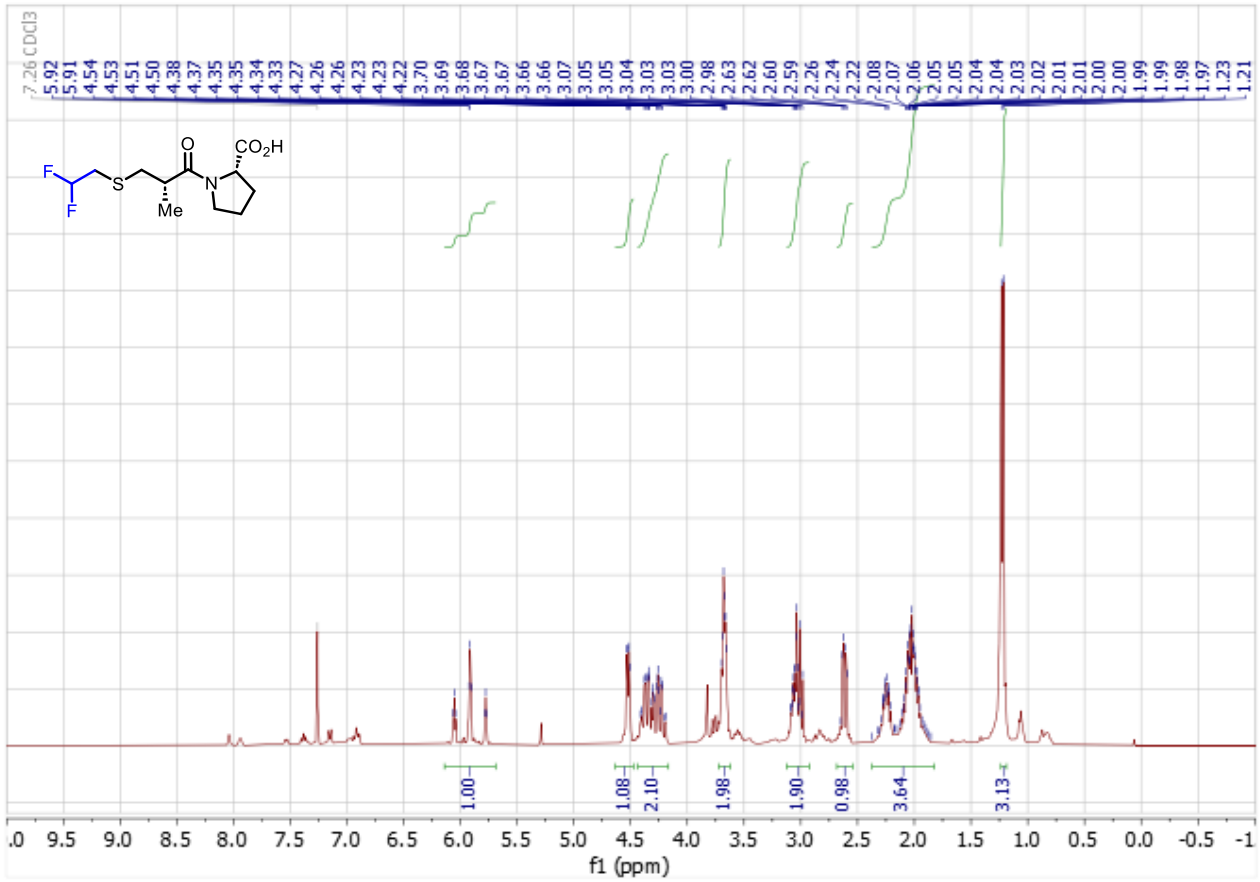

F
F
S
119.19
116.78
114.36
77.16 CDCl3
44.07
33.51
33.01
32.77
32.53
26.01
25.76
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

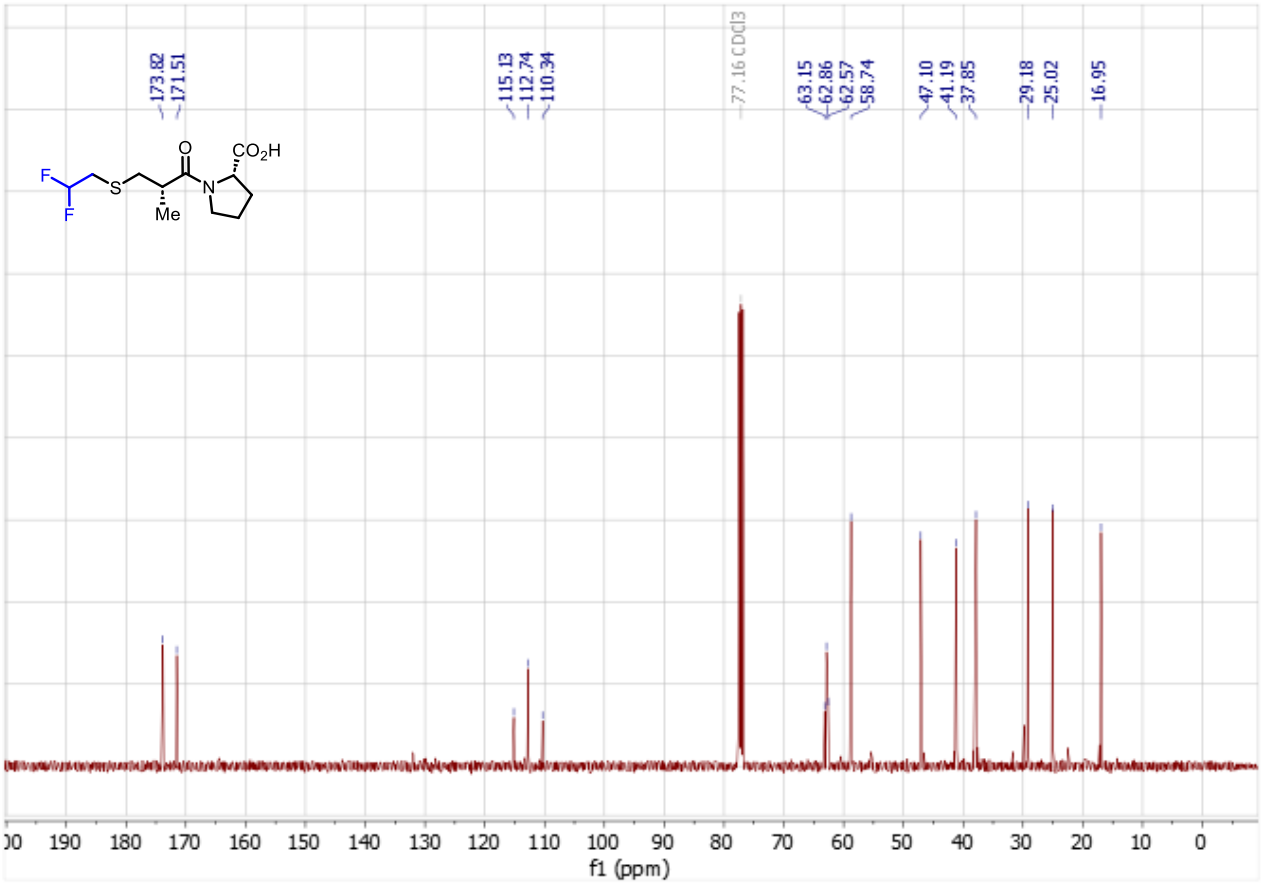

F
F
S
-112.95
-50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

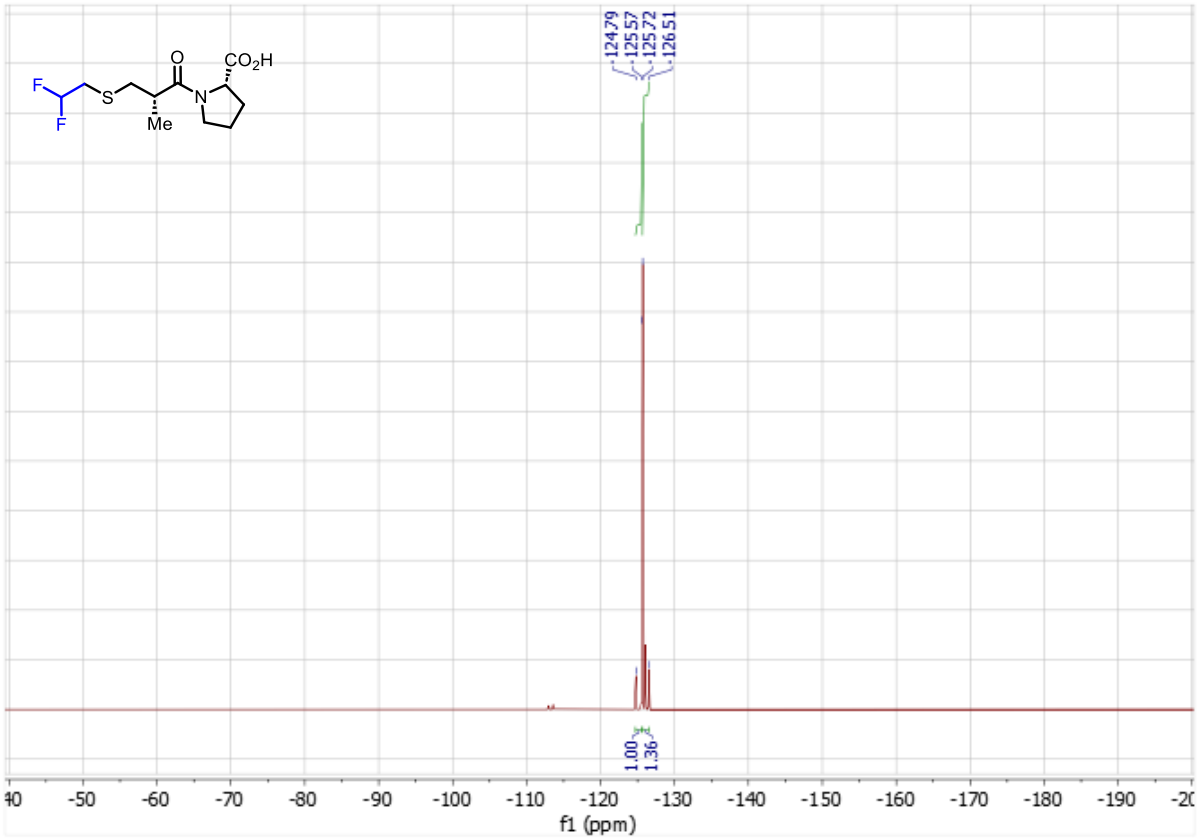

7.26 CDCl3
6.08 5.95 5.94 5.93 5.80 5.24 5.22 5.20 5.09 5.06 5.04 5.03 5.01 4.98 4.57 4.55 4.23 4.22 4.20 4.19 4.17 4.17 4.14 4.13 3.74 3.73 3.73 3.72 3.72 3.71 3.70 3.70 3.15 3.14 3.14 3.13 3.13 3.12 3.11 3.11 3.10 3.10 3.09 2.92 2.90 2.89 2.88 2.87 2.85 2.84 2.83 2.08 2.07 2.05 2.05 2.02 2.02 2.00 2.00
AcO
OAc
OAc
OAc
O
S
F
F
1.00 0.85 2.18 0.93 2.17 1.01 1.08 1.03 5.01 5.42
f1 (ppm)


170.69 170.21 169.56 169.50
118.49 116.08 113.67
83.01 77.16 CDCl3 76.21 73.64 69.84 68.27 62.00
32.91 32.66 32.41 20.75 20.74 20.69 20.67
AcO
OAc
OAc
OAc
O
S
F
F
f1 (ppm)

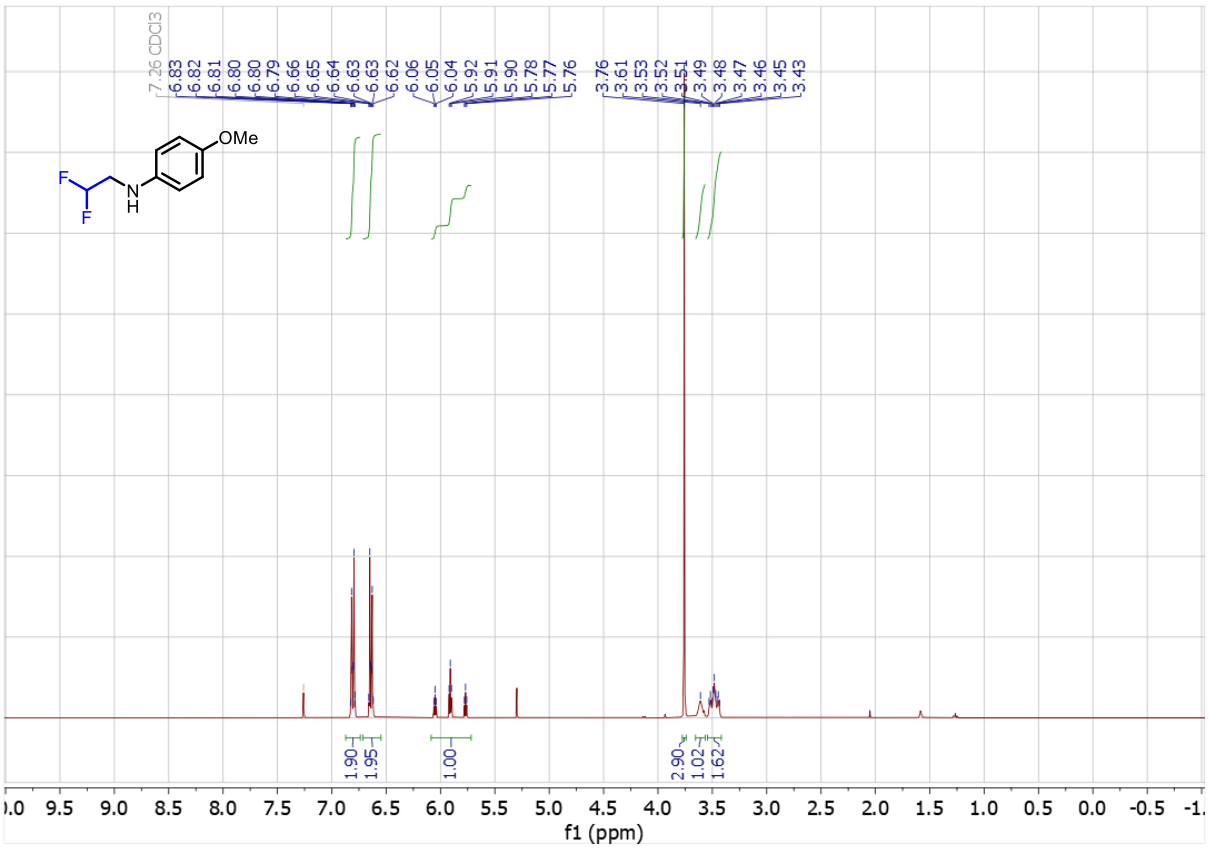

AcO
OAc
OAc
OAc
O
S
F
F
-112.40
-113.15
-114.40
-115.14
-50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -20
f1 (ppm)

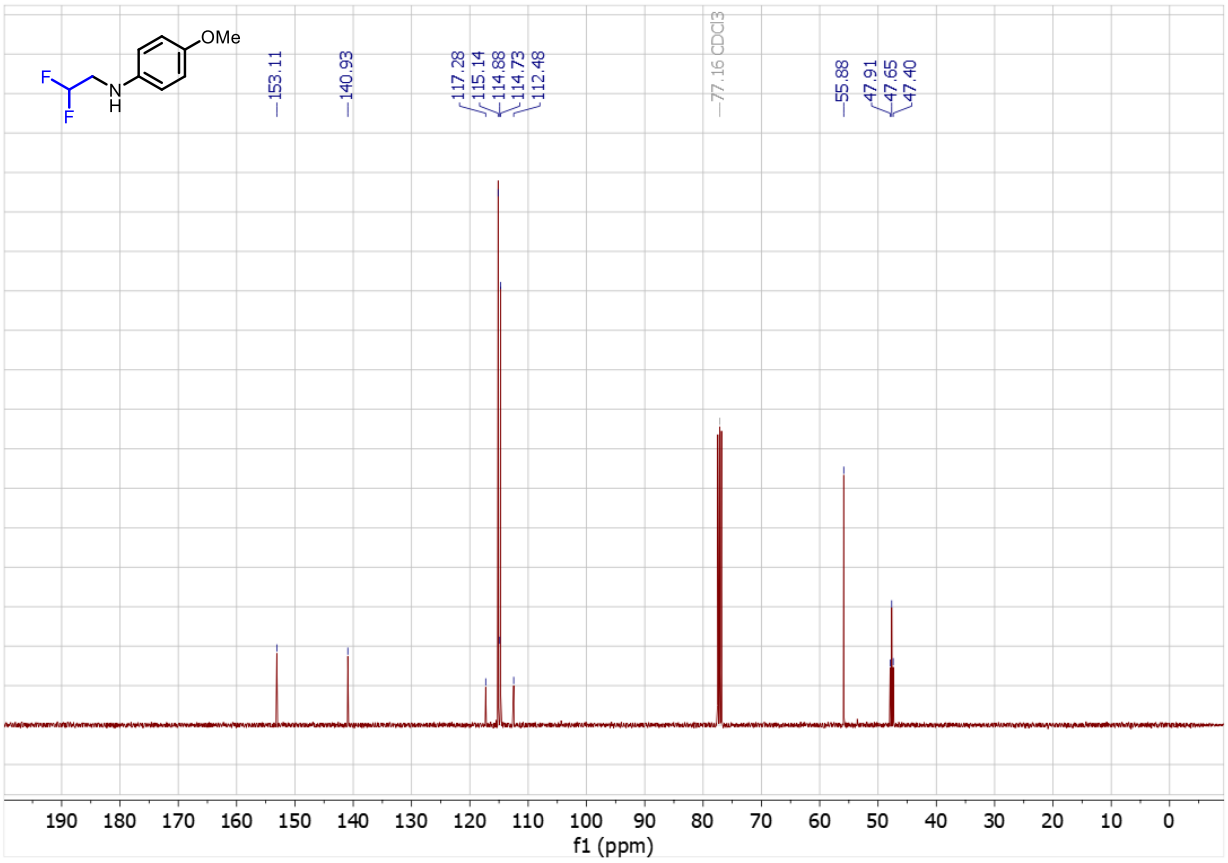

7.26 CDCl3
F
F
S
O
N
CO2H
Me
1.00
1.08
2.10
1.98
1.90
0.98
3.64
3.13
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

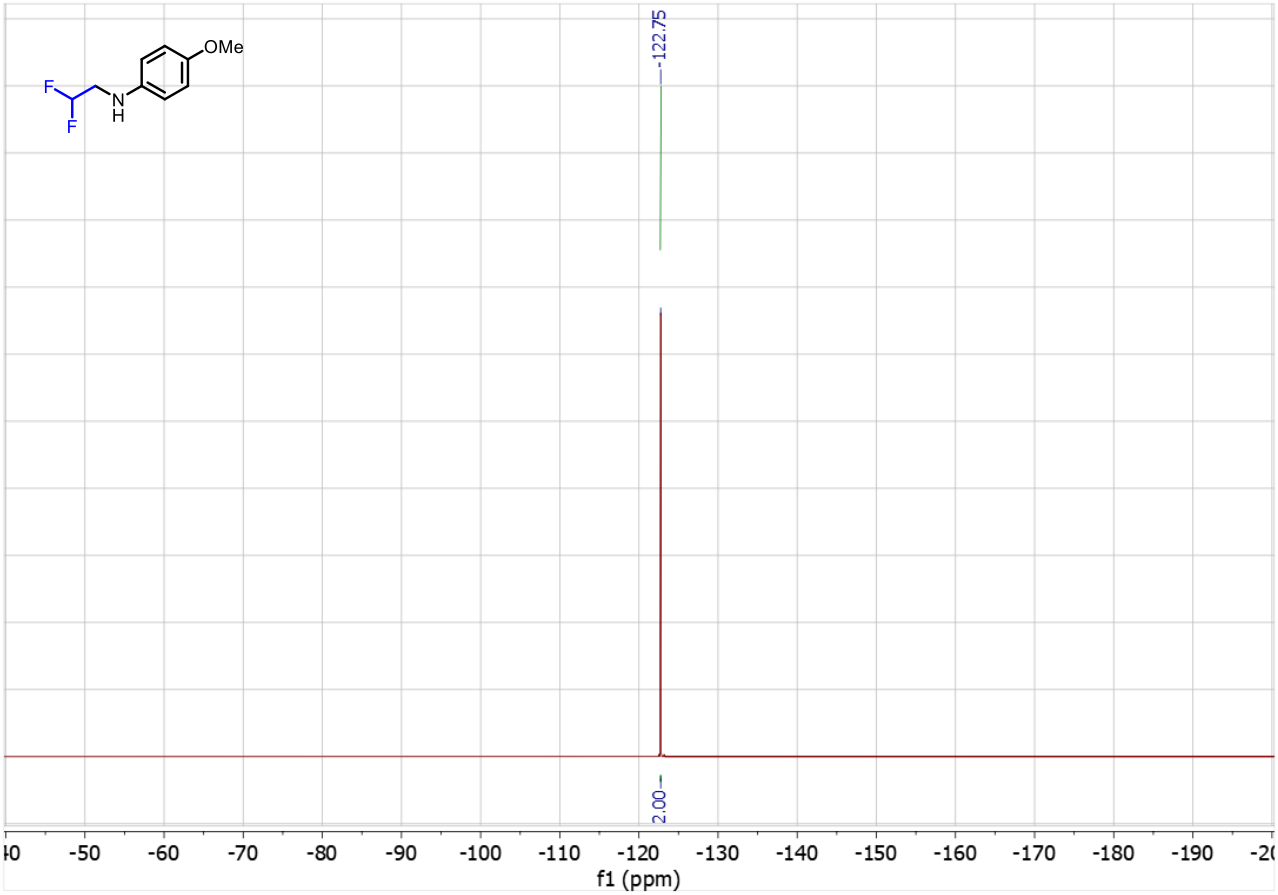

173.82
171.51
115.13
112.74
110.34
77.16 CDCl3
63.15
62.86
62.57
58.74
47.10
41.19
37.85
29.18
25.02
16.95
CO2H
F
F
S
O
N
Me
f1 (ppm)

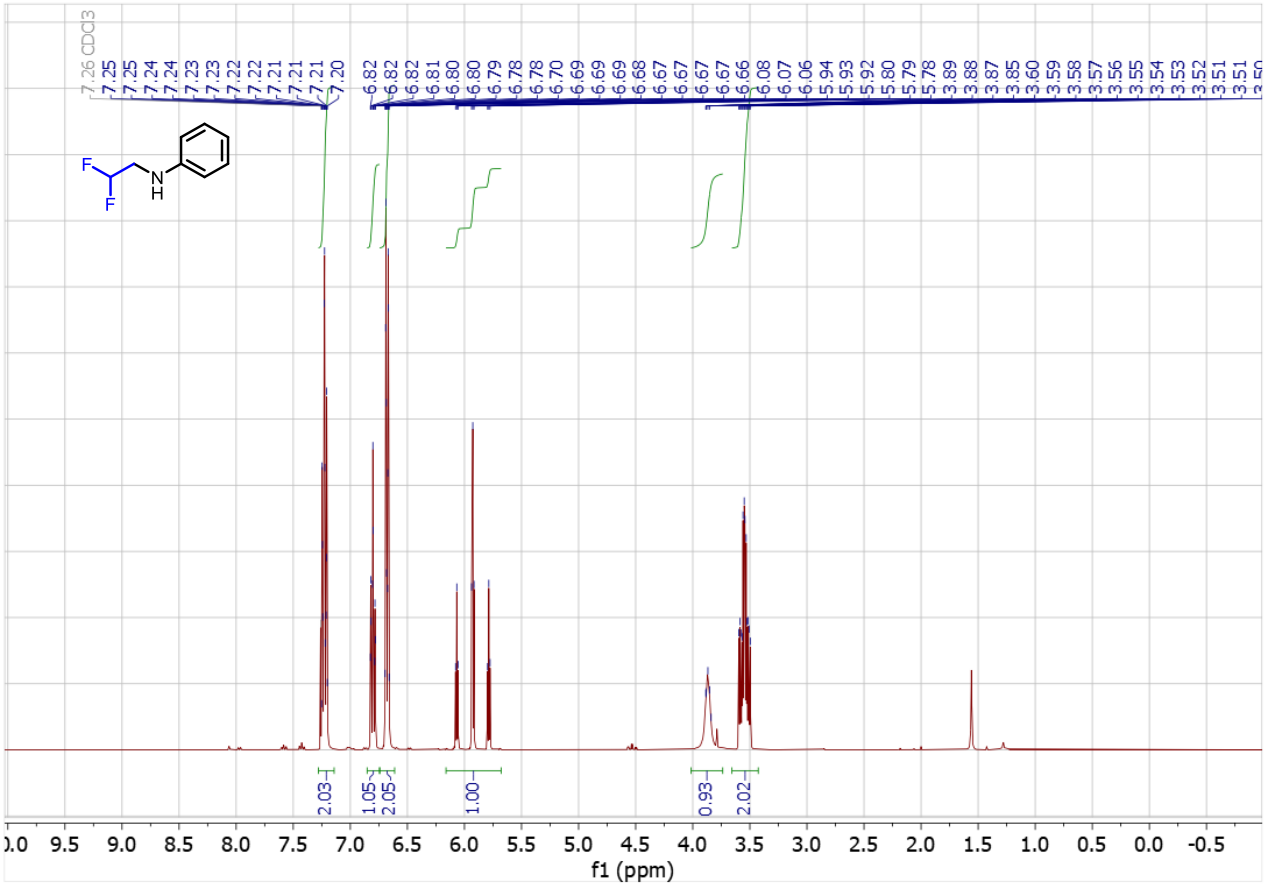

124.79
125.57
125.72
126.51
CO2H
F
F
S
O
N
Me
1.00
1.36
f1 (ppm)

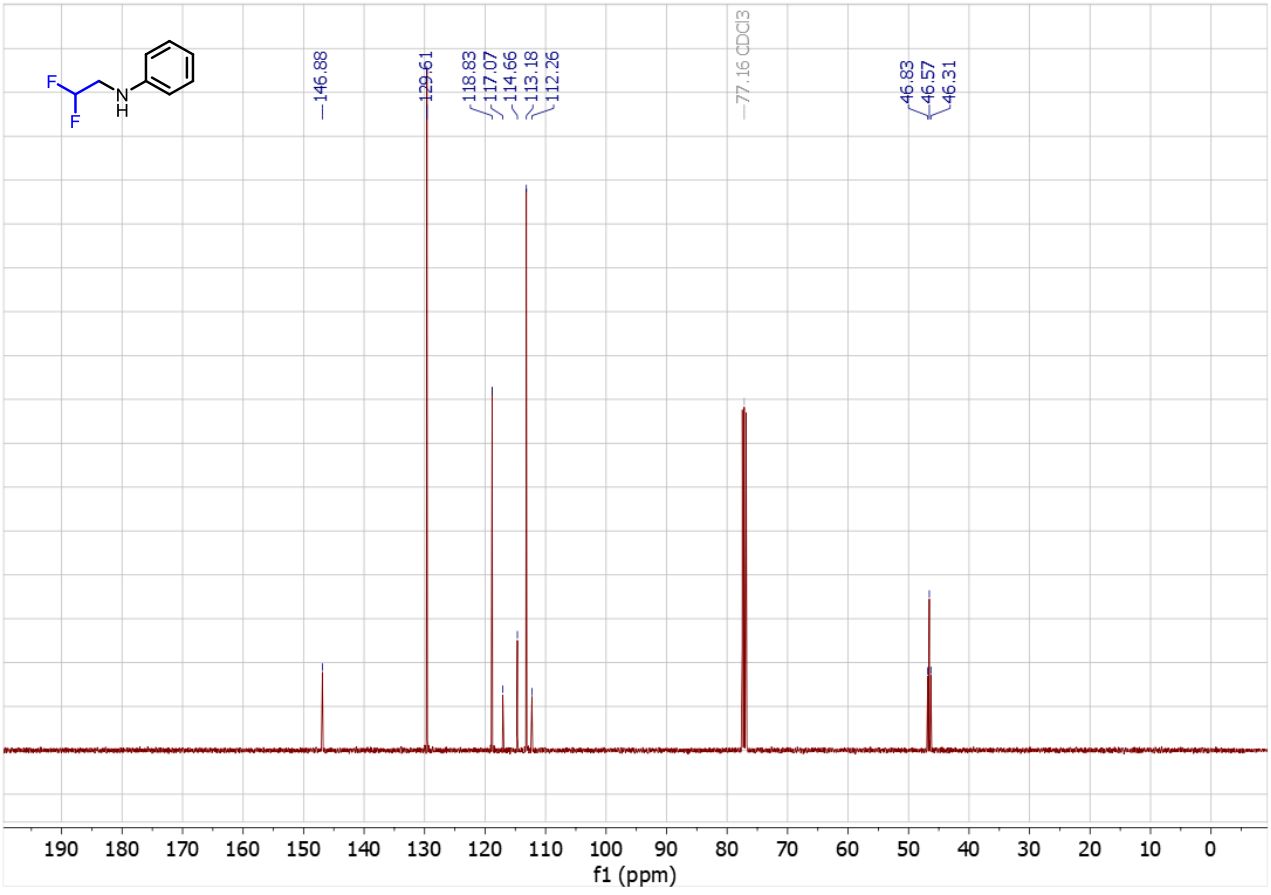
6.2 2,2-Difluoroethylamines (5)

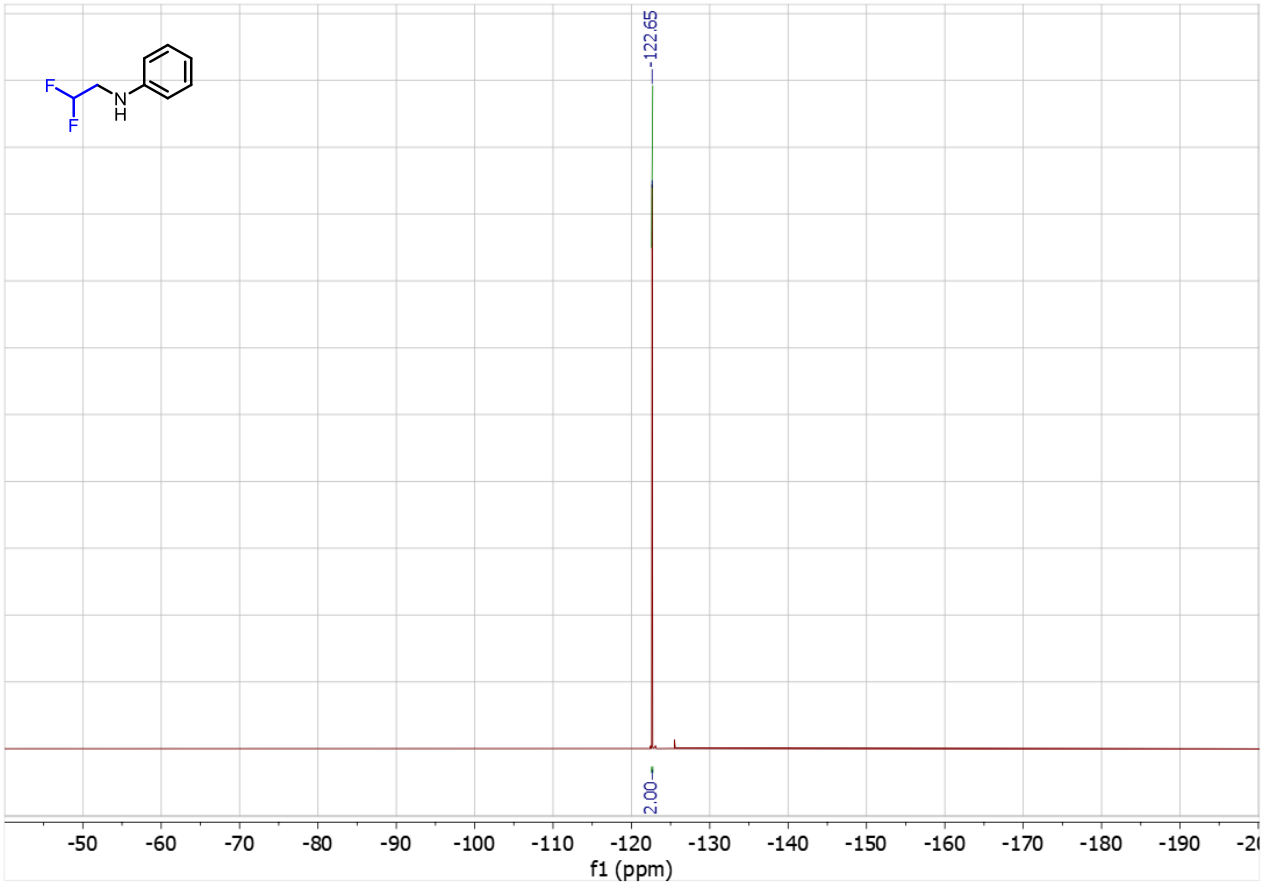


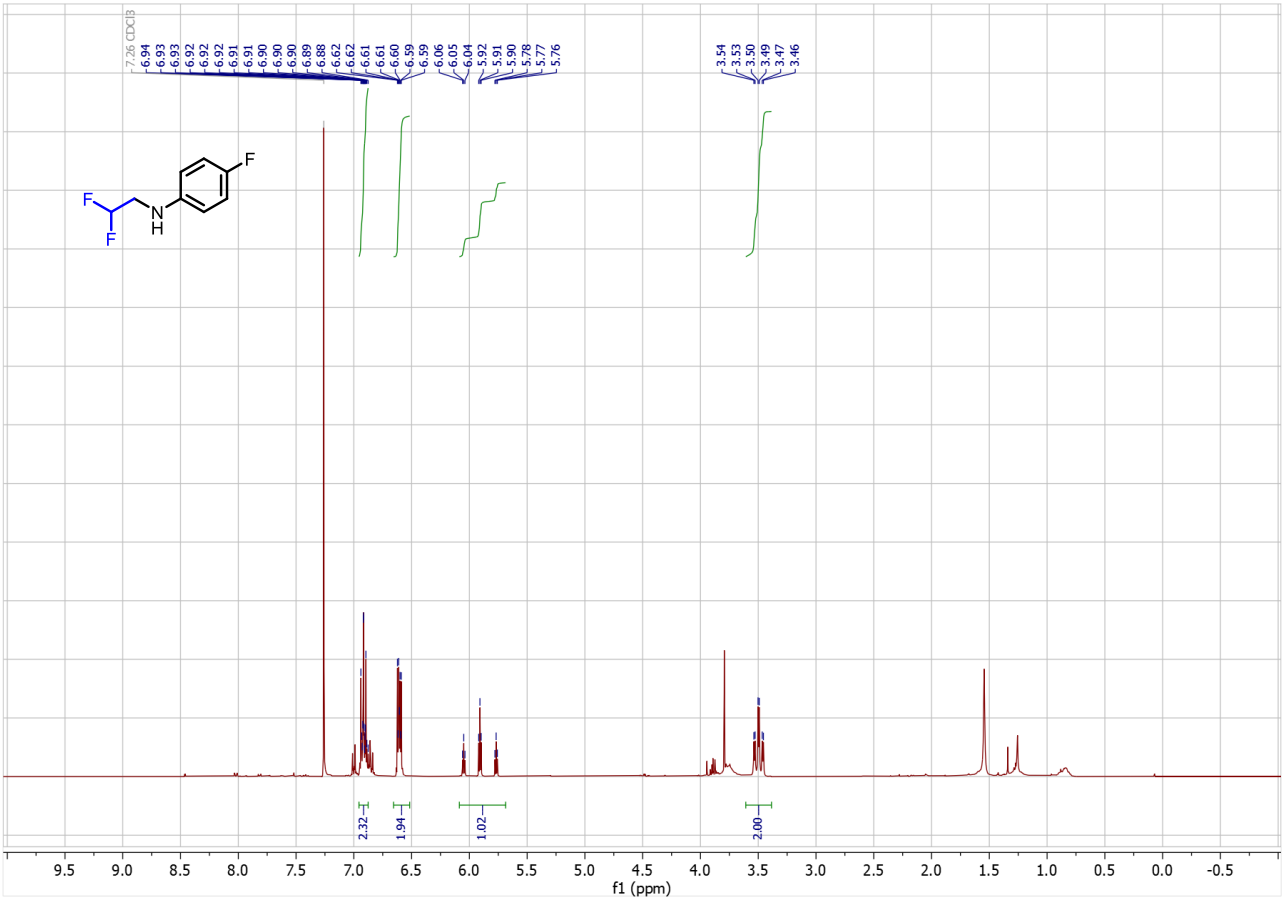


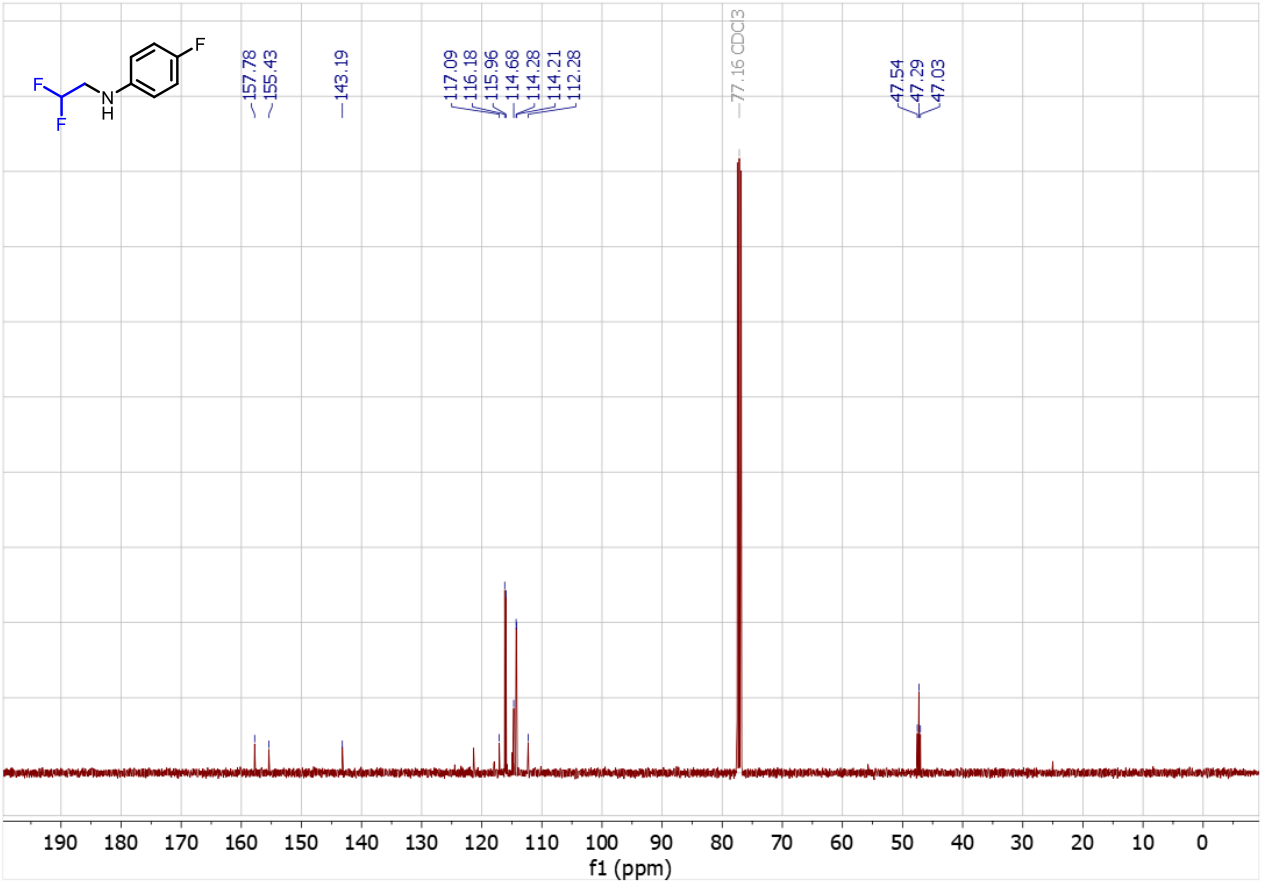

OMe
F
F
N
H
-122.75
2.00
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

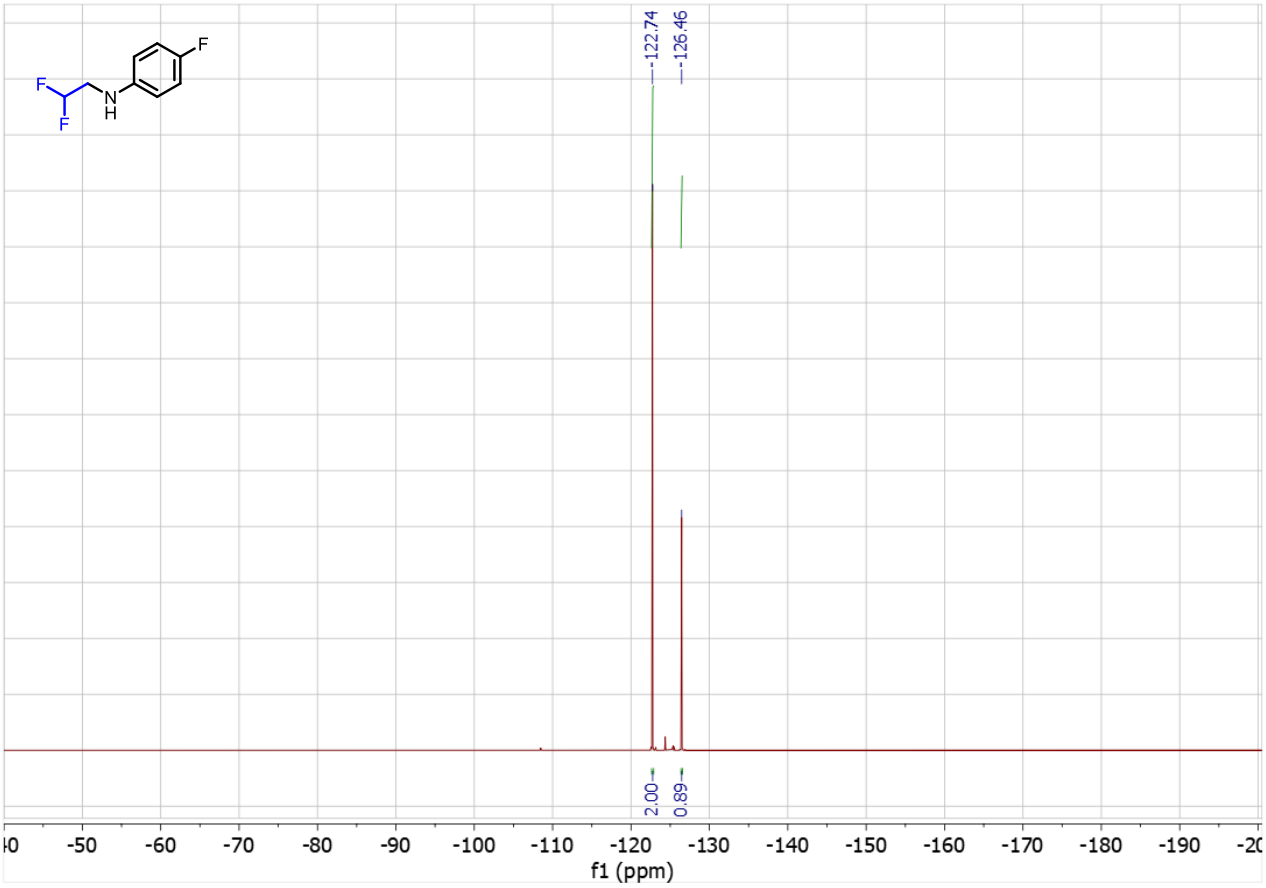

7.26 CDCl3
7.25
7.25
7.24
7.24
7.23
7.23
7.22
7.22
7.21
7.21
7.21
7.20
6.82
6.82
6.82
6.81
6.80
6.80
6.79
6.78
6.78
6.70
6.69
6.69
6.69
6.68
6.67
6.67
6.67
6.67
6.66
6.08
6.07
6.06
5.94
5.93
5.92
5.80
5.79
5.78
3.89
3.88
3.87
3.85
3.60
3.59
3.58
3.57
3.56
3.55
3.54
3.53
3.52
3.51
3.51
F
F
N
H
2.03
1.05
2.05
1.00
0.93
2.02
f1 (ppm)

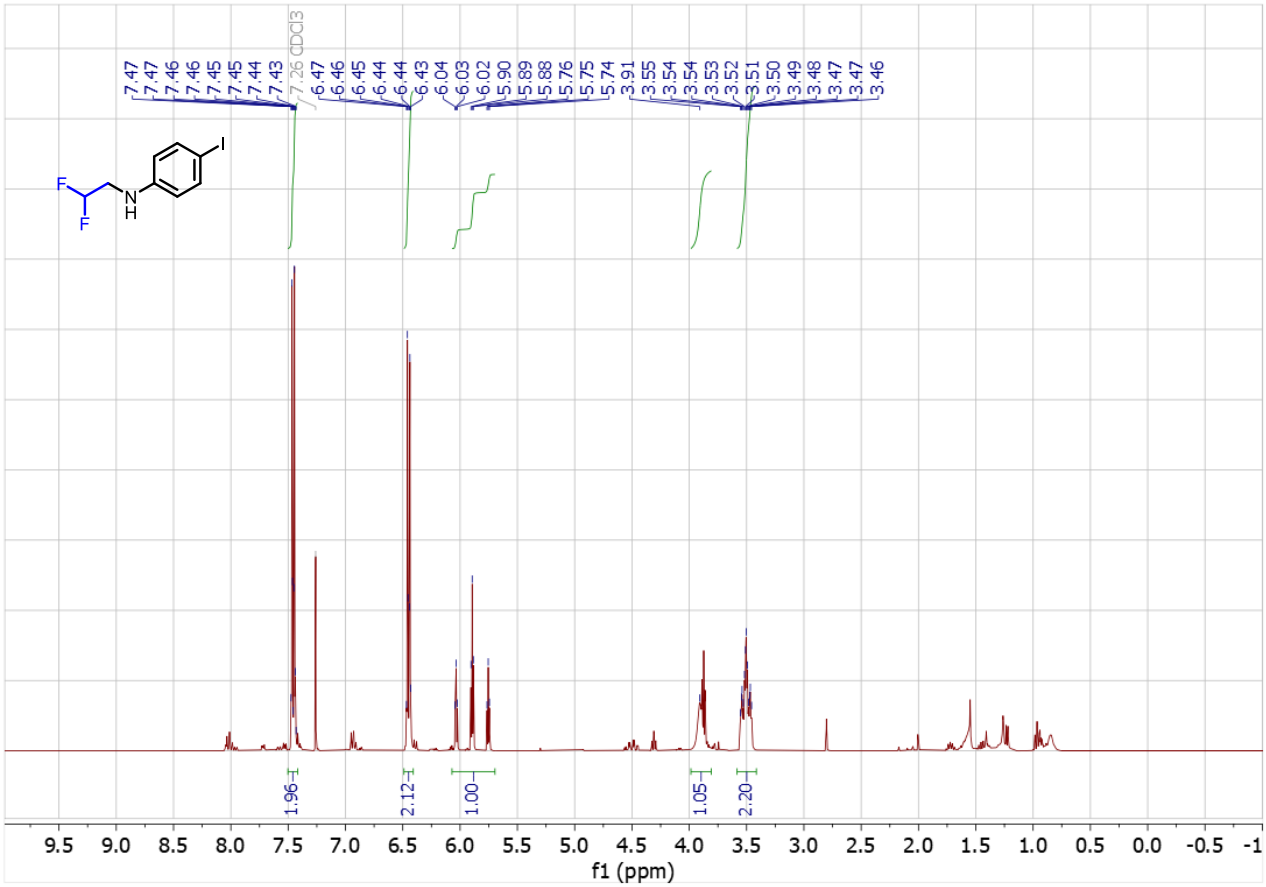

F
F
N
H
146.88
129.61
118.83
117.07
114.66
113.18
112.26
77.16 CDCl3
46.83
46.57
46.31
f1 (ppm)

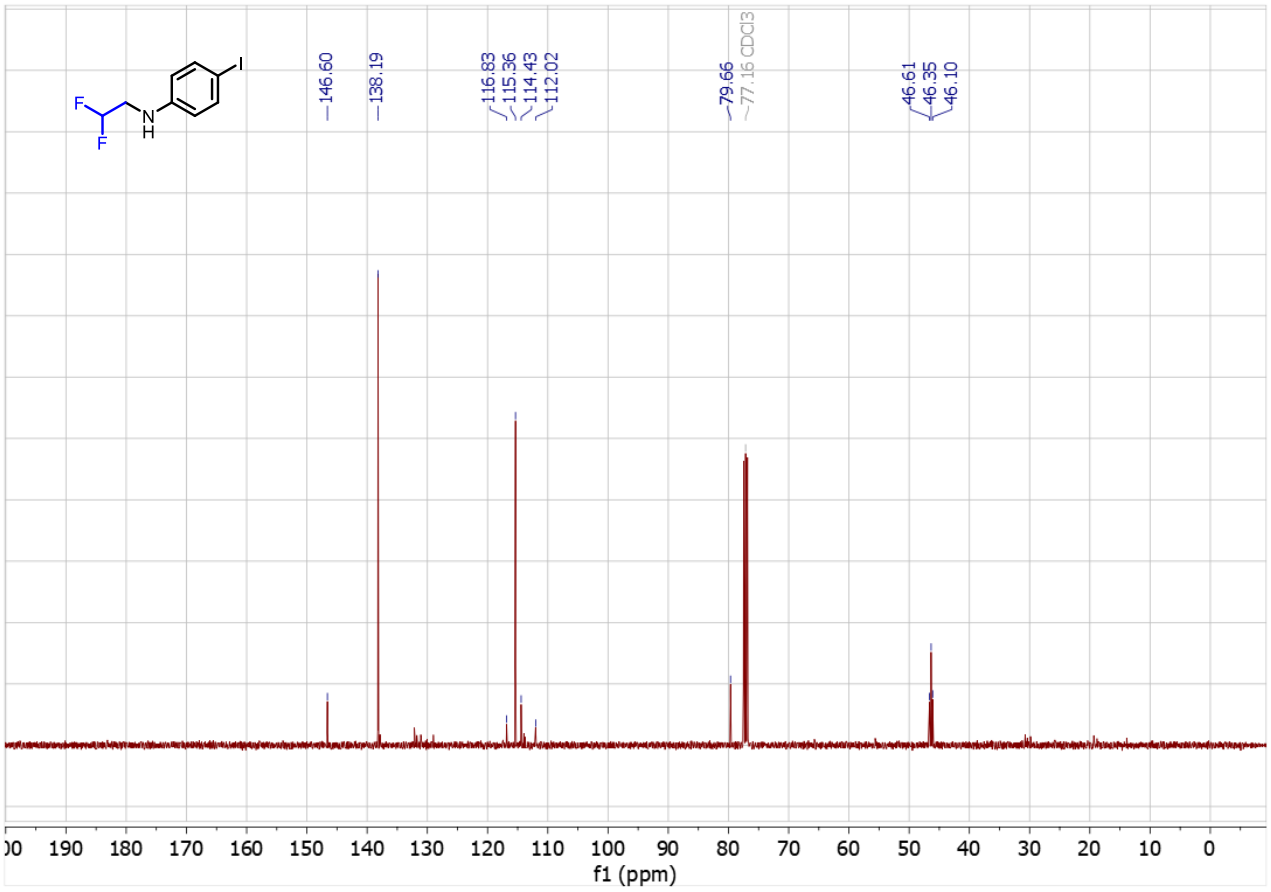

F
F
N
H
-122.65
2.00
-50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

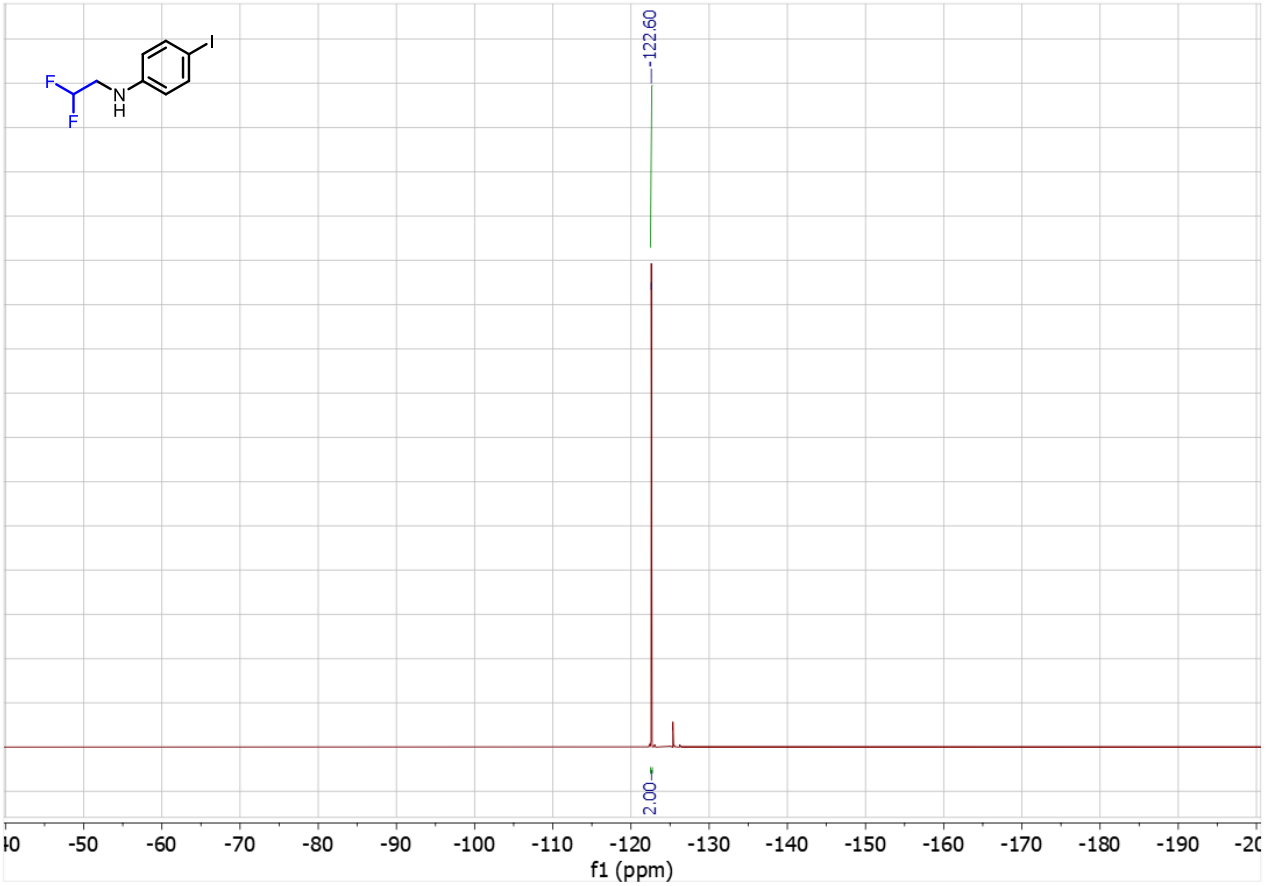

7.26 CDCl3
6.94 6.93 6.93 6.92 6.92 6.92 6.91 6.91 6.90 6.90 6.90 6.89 6.88 6.62 6.61 6.61 6.60 6.59 6.59 6.06 6.05 6.04 5.92 5.91 5.90 5.78 5.77 5.76
3.54 3.53 3.50 3.49 3.47 3.46
F
F
N
H
F
2.32
1.94
1.02
2.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

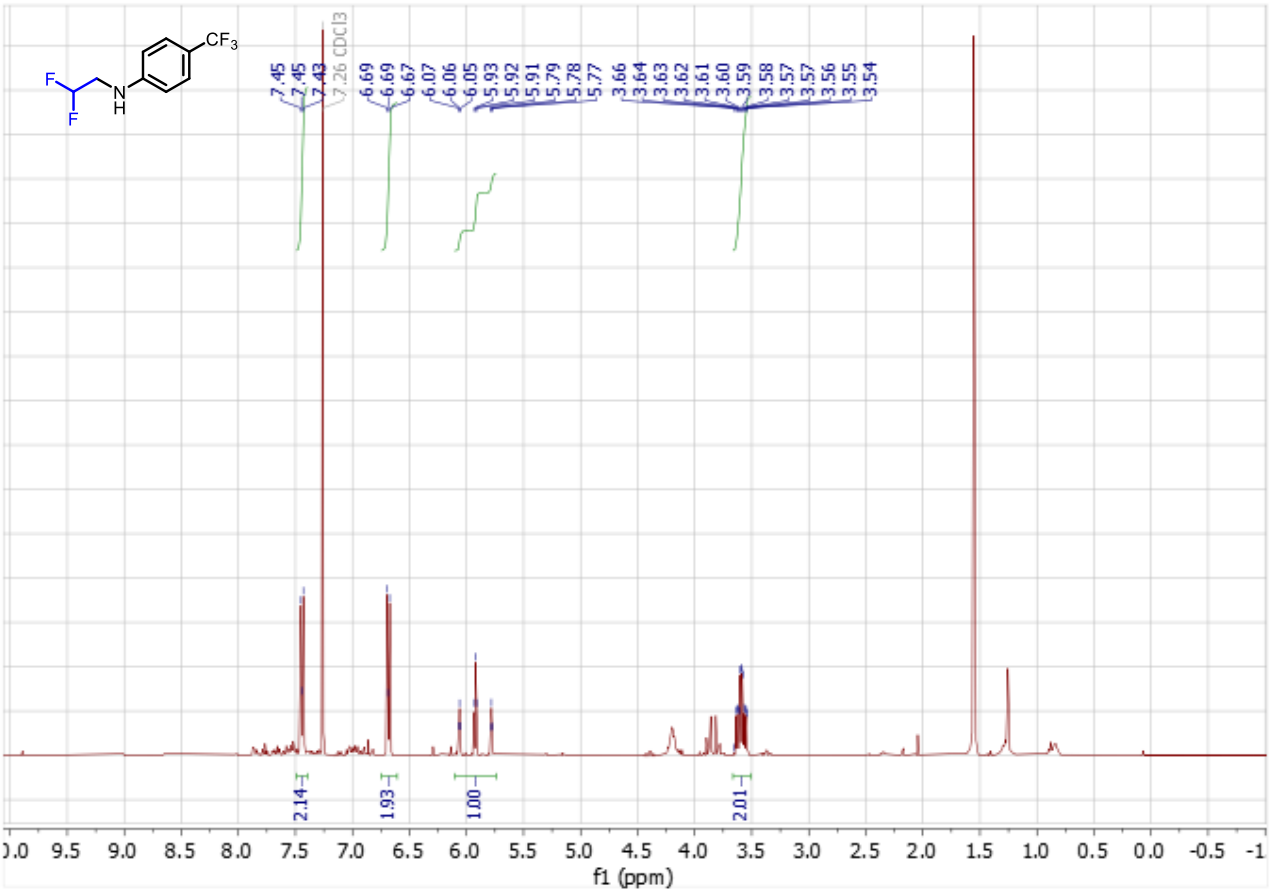

F
F
F
N
H
157.78
155.43
143.19
117.09
116.18
115.96
114.68
114.28
114.21
112.28
77.16 CDCl3
47.54
47.29
47.03
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

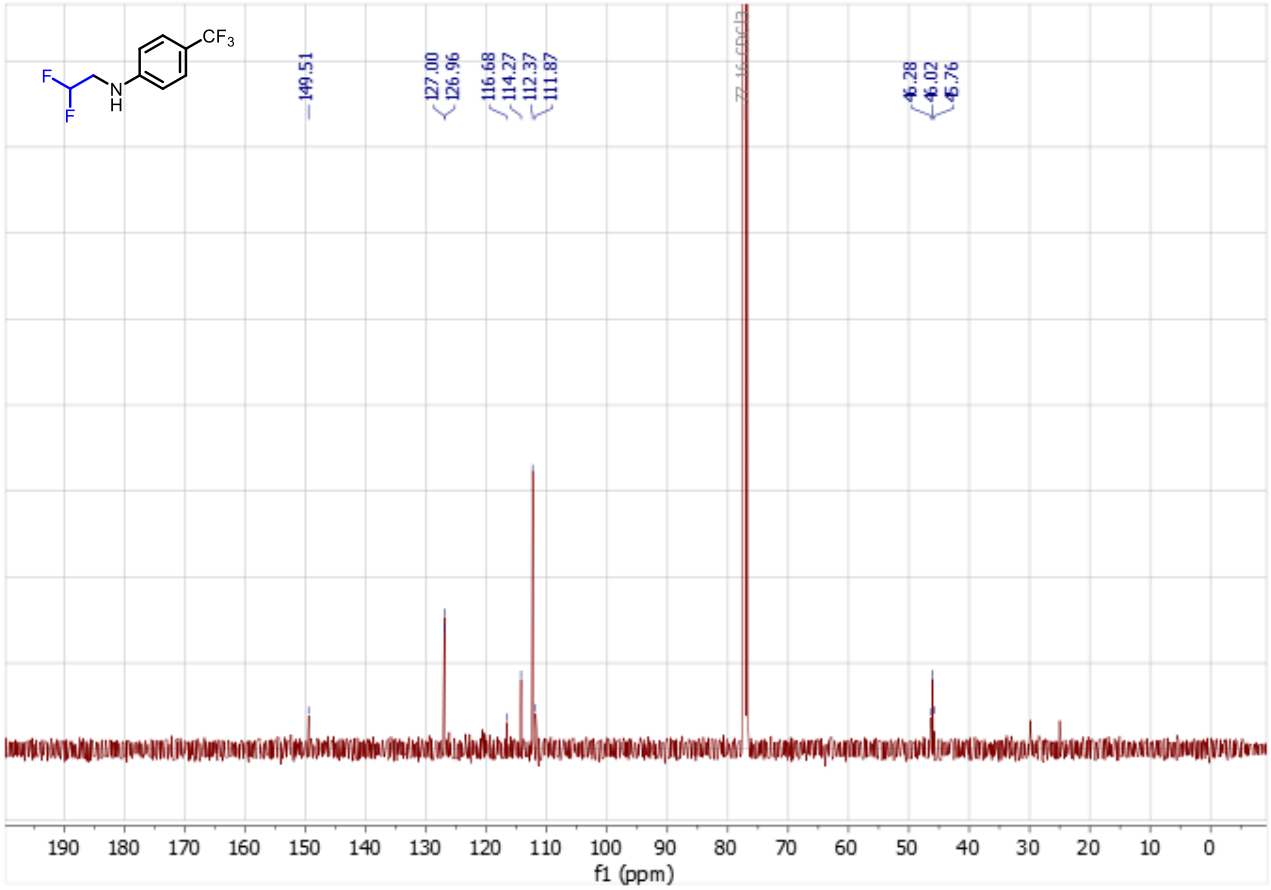

F
F
F
N
H
-122.74
-126.46
2.00
0.89
-50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

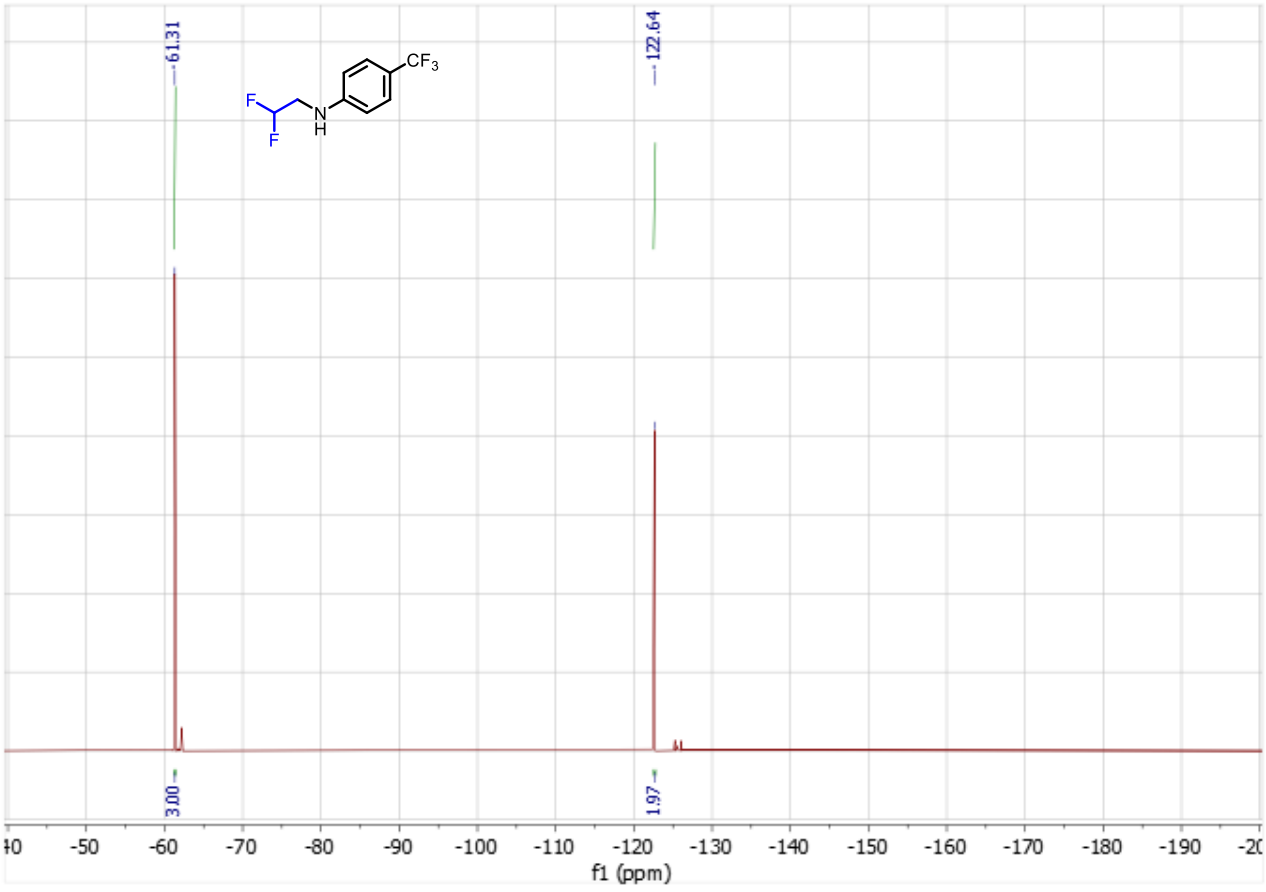

7.47
7.47
7.46
7.46
7.45
7.45
7.44
7.43
7.26 CDCl3
6.47
6.46
6.45
6.44
6.44
6.43
6.04
6.03
6.02
5.90
5.89
5.88
5.76
5.75
5.74
3.91
3.55
3.54
3.54
3.53
3.52
3.51
3.50
3.49
3.48
3.47
3.47
3.46
F
F
N
H
I
1.96
2.12
1.00
1.05
2.20
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

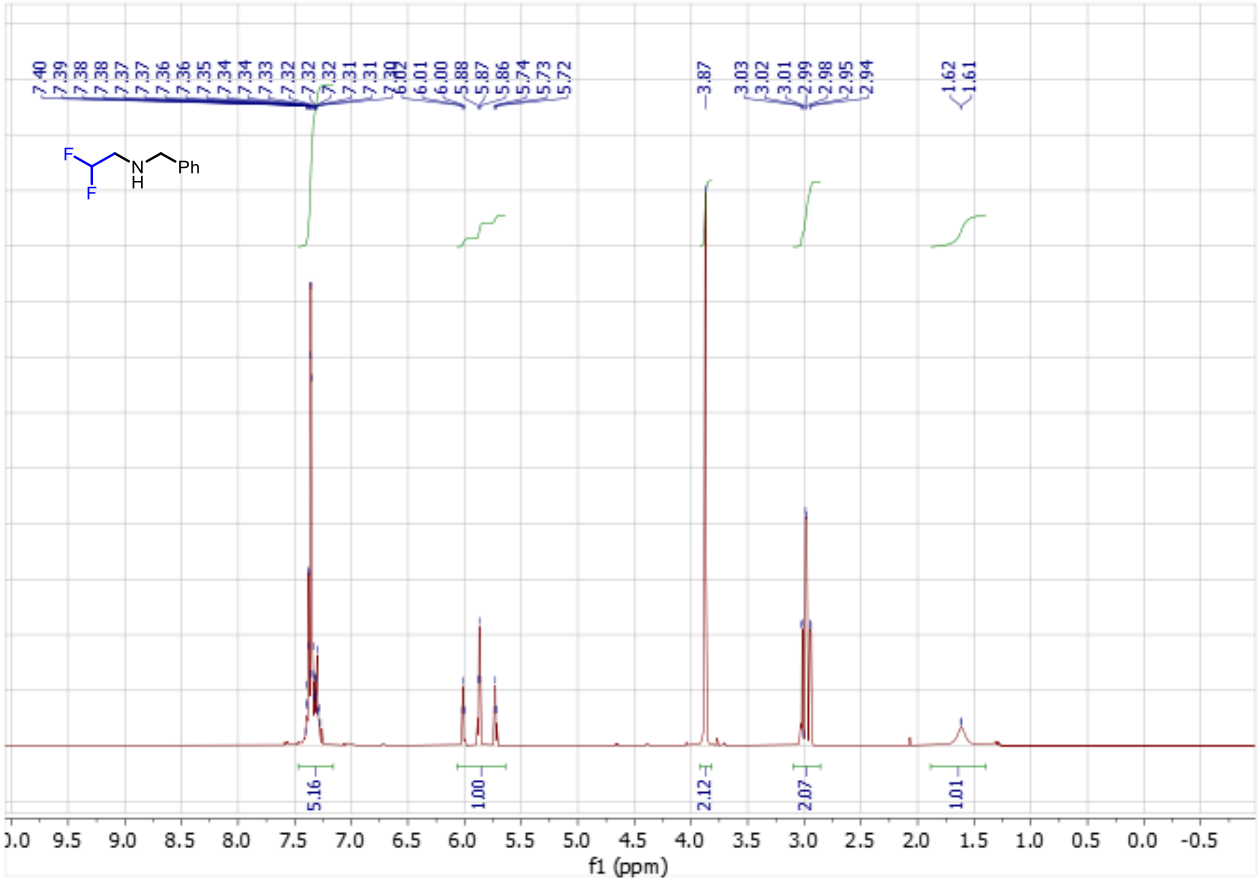

F
F
N
H
I
146.60
138.19
116.83
115.36
114.43
112.02
79.66
77.16 CDCl3
46.61
46.35
46.10
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

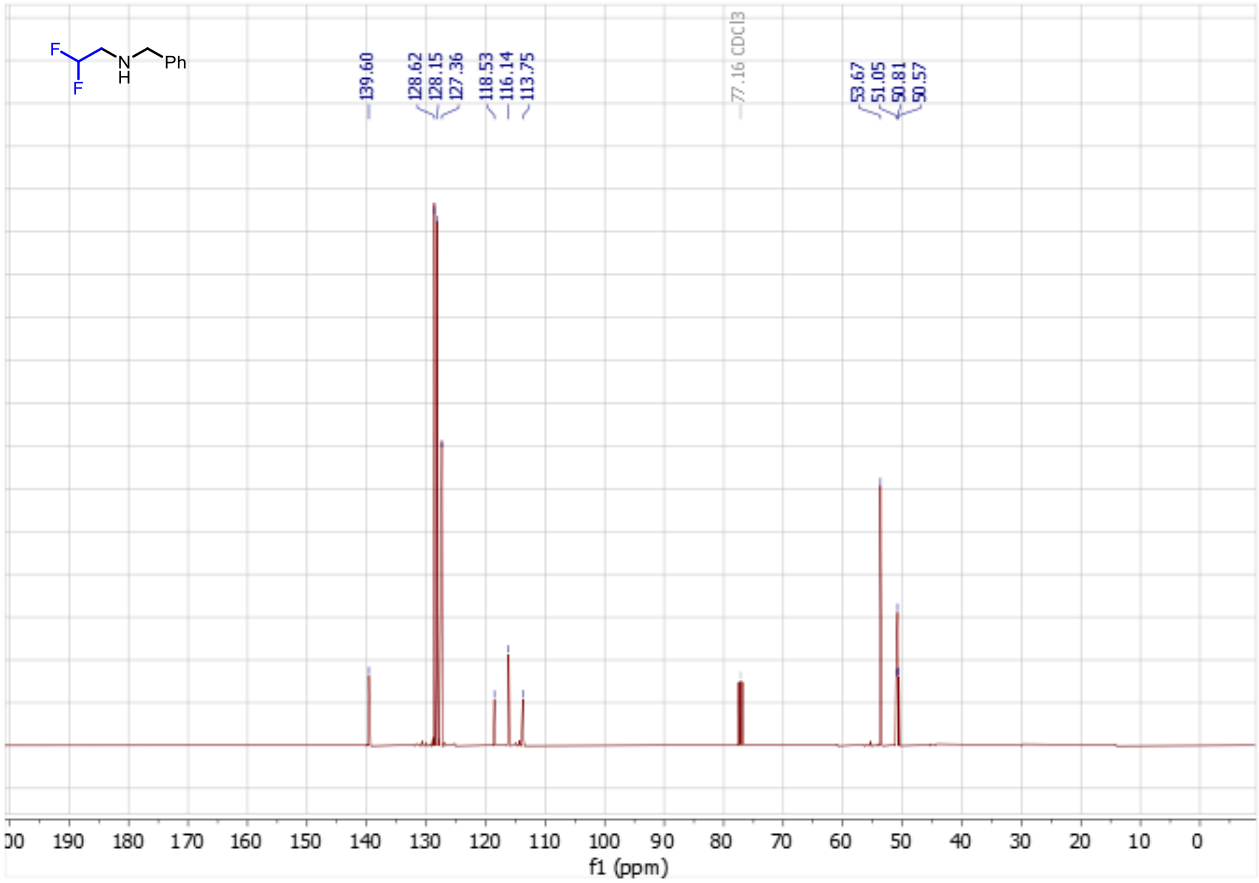

F
F
N
H
I
-122.60
2.00
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

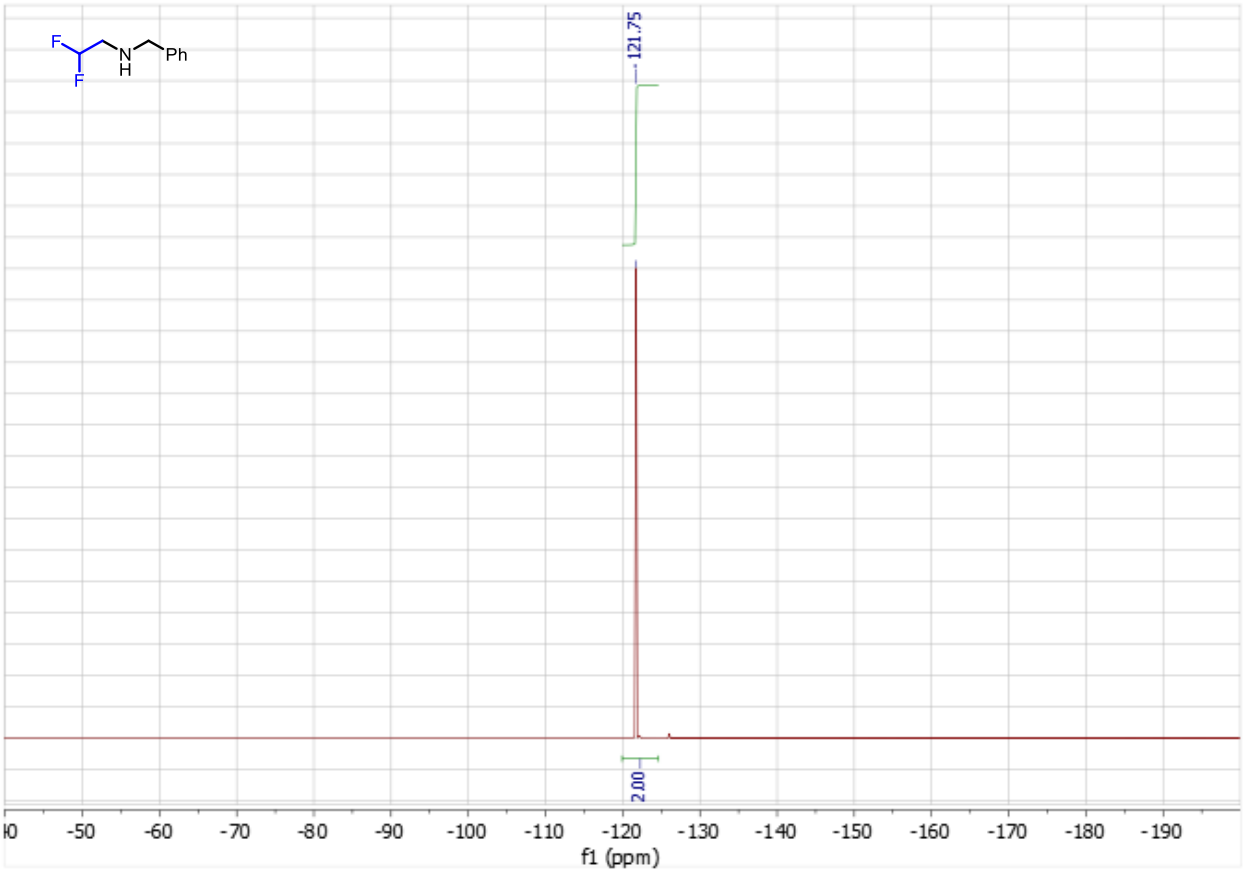

F
F
N
H
CF3
7.45
7.45
7.43
7.26 CDCl3
6.69
6.69
6.67
6.07
6.06
6.05
5.93
5.92
5.91
5.79
5.78
5.77
3.66
3.64
3.63
3.62
3.61
3.60
3.59
3.58
3.57
3.57
3.56
3.55
3.54
2.14
1.93
1.00
2.01
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

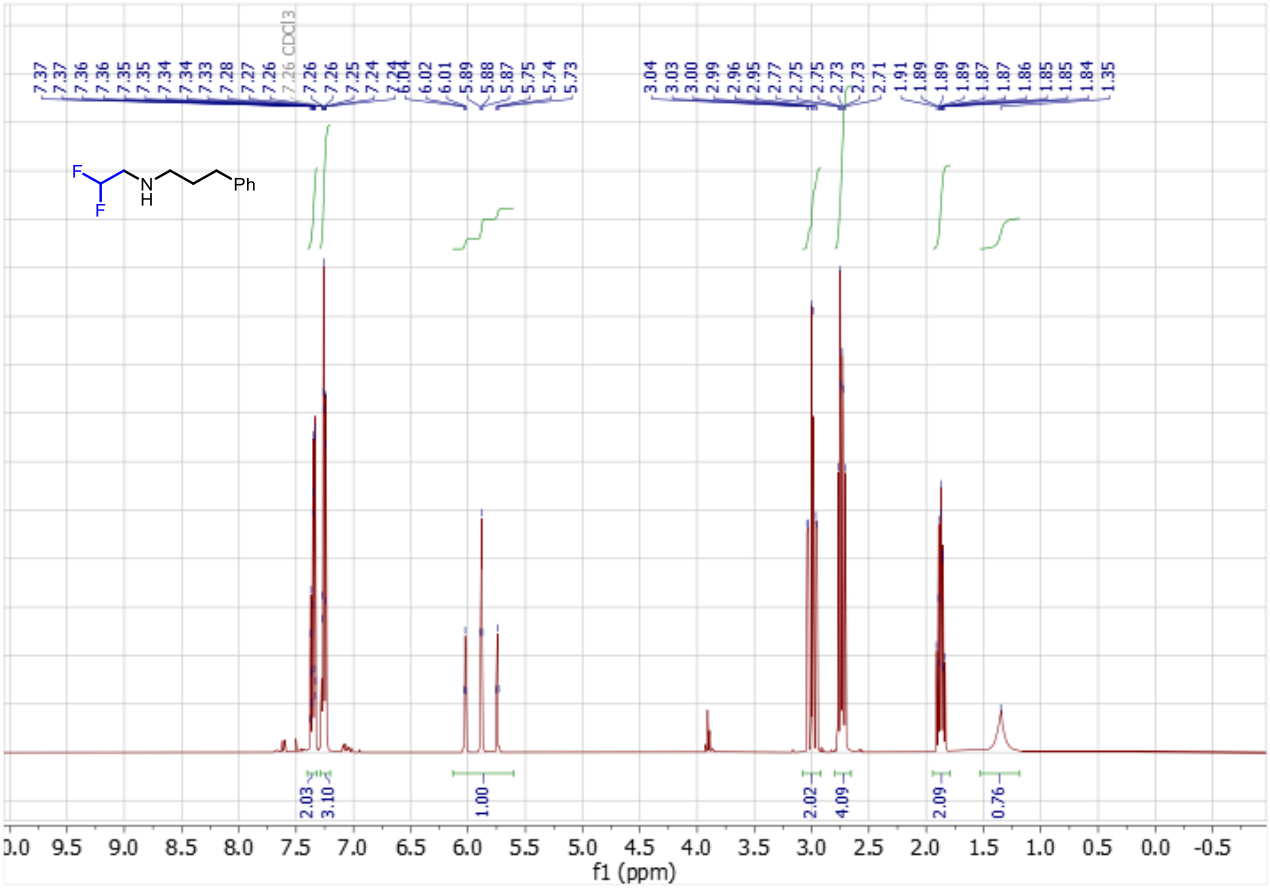

F
F
N
H
CF3
149.51
127.00
126.96
116.68
114.27
112.37
111.87
77.16 CDCl3
46.28
46.02
45.76
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

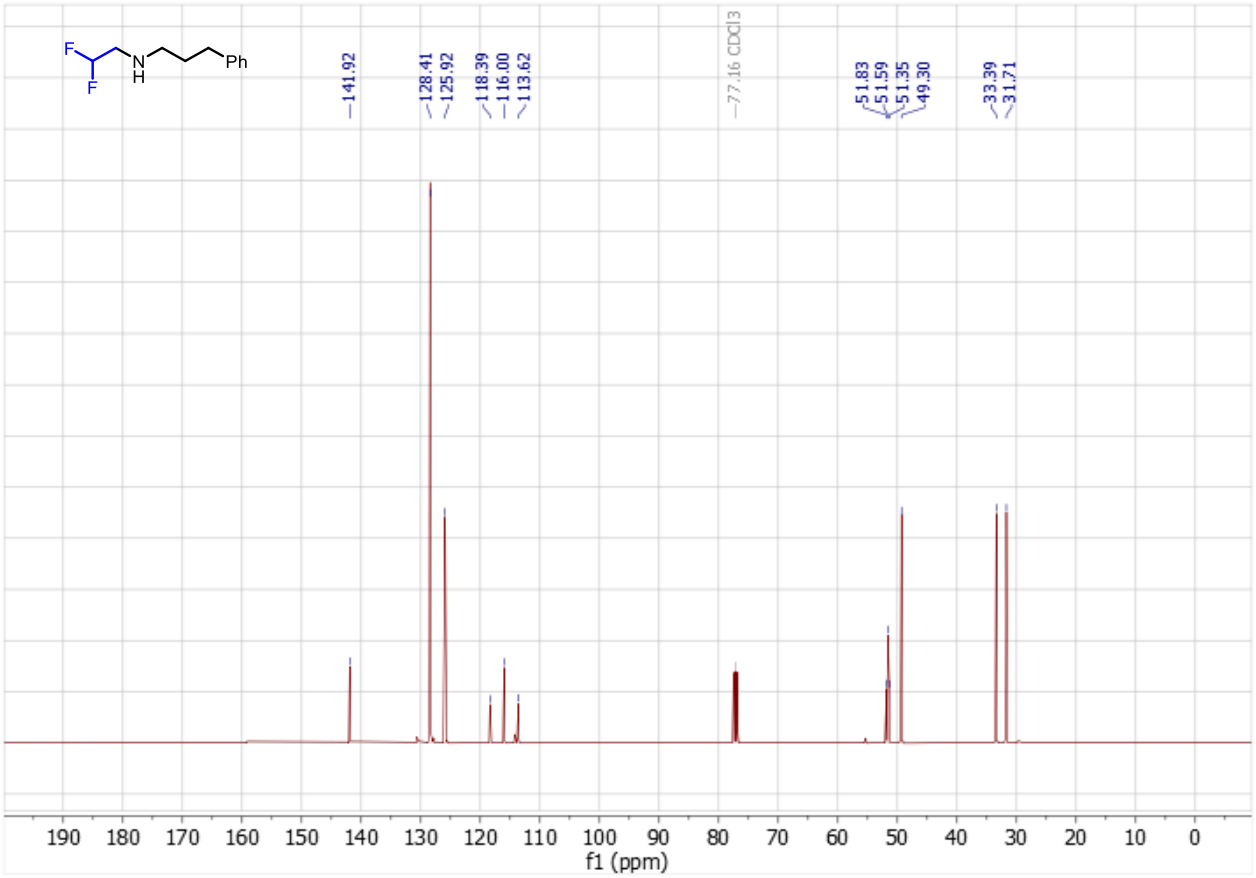

F
F
N
H
CF3
-61.31
-122.64
3.00
1.97
-50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

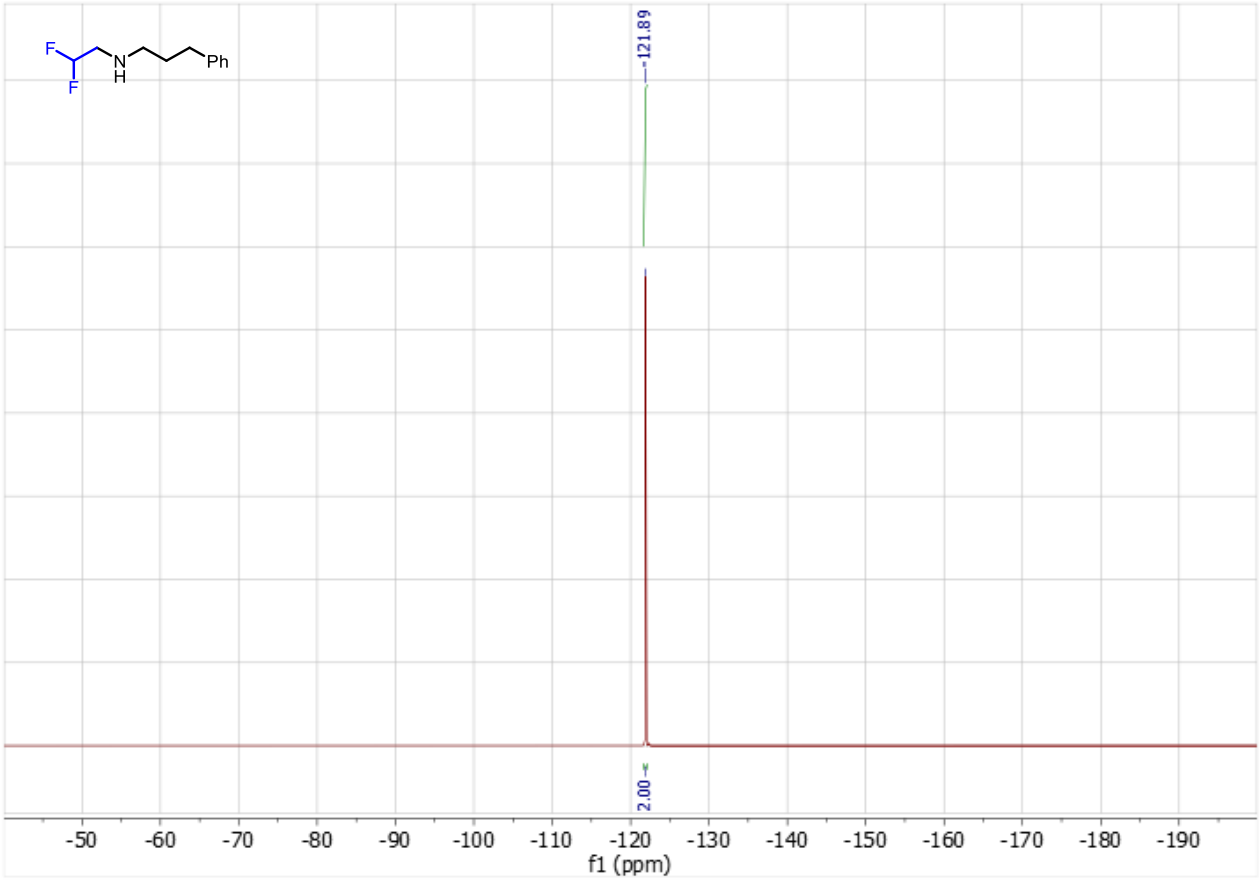

7.40
7.39
7.38
7.38
7.37
7.37
7.36
7.36
7.35
7.34
7.34
7.33
7.32
7.32
7.32
7.31
7.31
6.02
6.01
6.00
5.88
5.87
5.86
5.74
5.73
5.72
3.87
3.03
3.02
3.01
2.99
2.98
2.95
2.94
1.62
1.61
F
F
N
H
Ph
5.16
1.00
2.12
2.07
1.01
f1 (ppm)

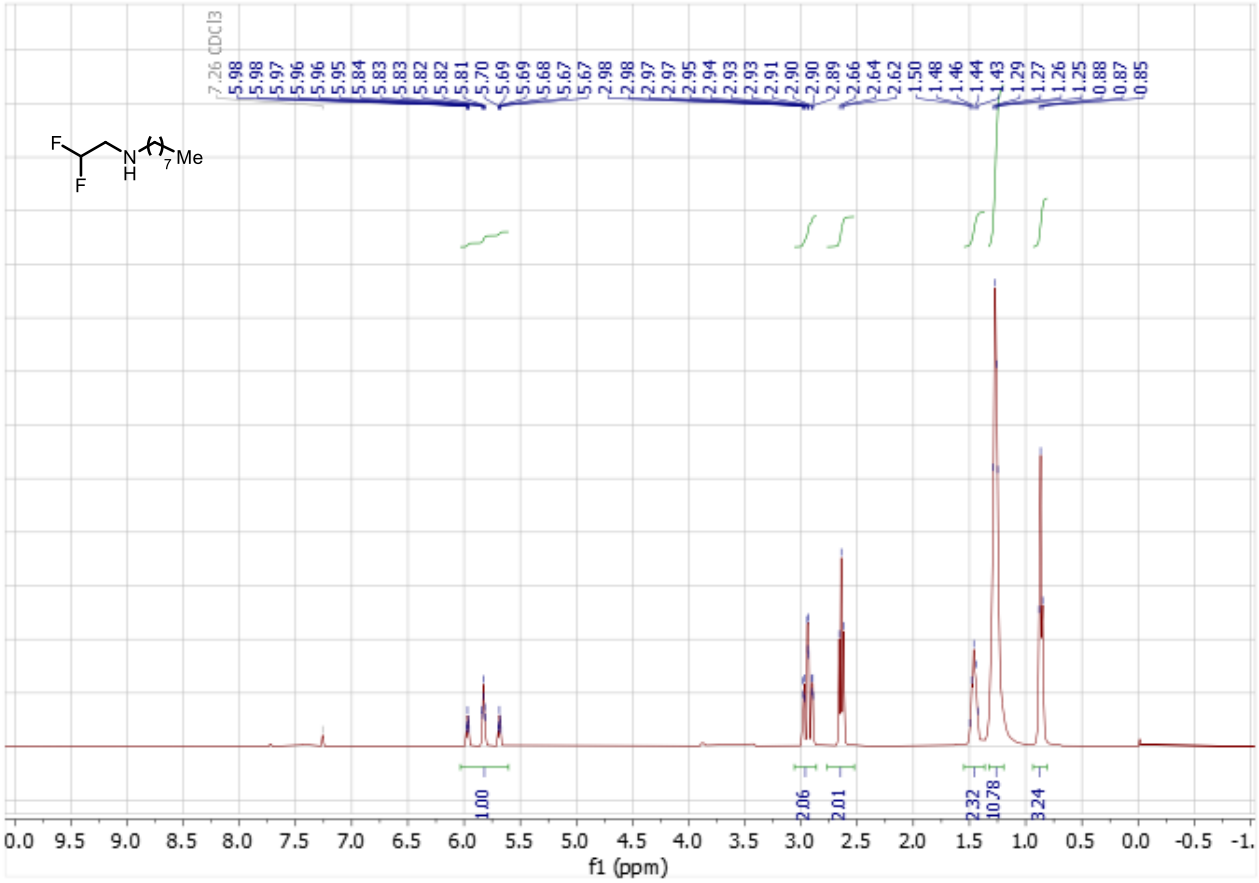

F
F
N
H
Ph
139.60
128.62
128.15
127.36
118.53
116.14
113.75
77.16 CDCl3
53.67
51.05
50.81
50.57
f1 (ppm)

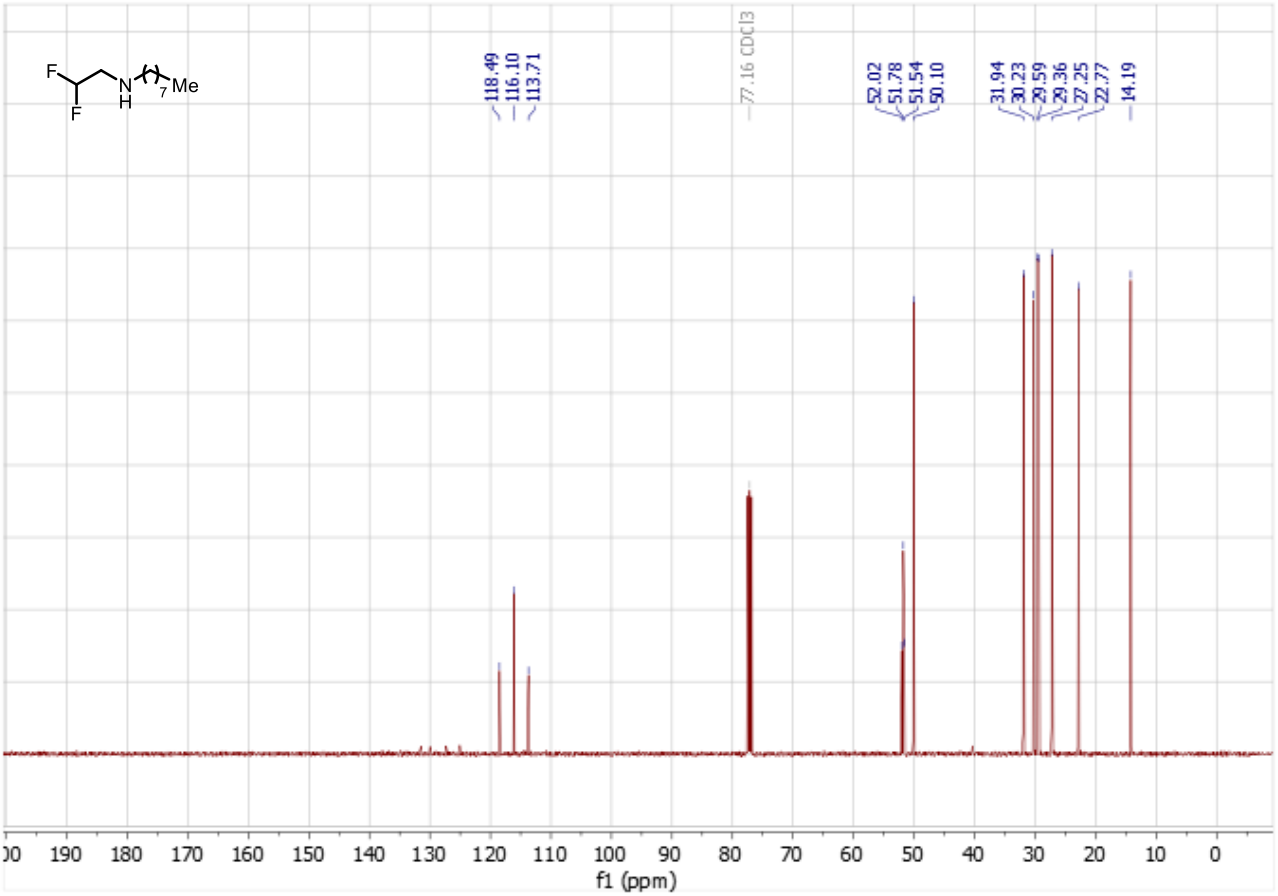

F
F
N
H
Ph
121.75
2.00
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)


7.37
7.37
7.36
7.36
7.35
7.35
7.34
7.34
7.33
7.28
7.27
7.26
7.26 CDCl3
7.26
7.26
7.25
7.24
7.04
6.04
6.02
6.01
5.89
5.88
5.87
5.75
5.74
5.73
3.04
3.03
3.00
2.99
2.96
2.95
2.77
2.75
2.75
2.73
2.73
2.71
1.91
1.89
1.89
1.89
1.87
1.87
1.86
1.85
1.85
1.84
1.35
F
F
N
H
Ph
2.03
3.10
1.00
2.02
4.09
2.09
0.76
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
-0.5
f1 (ppm)

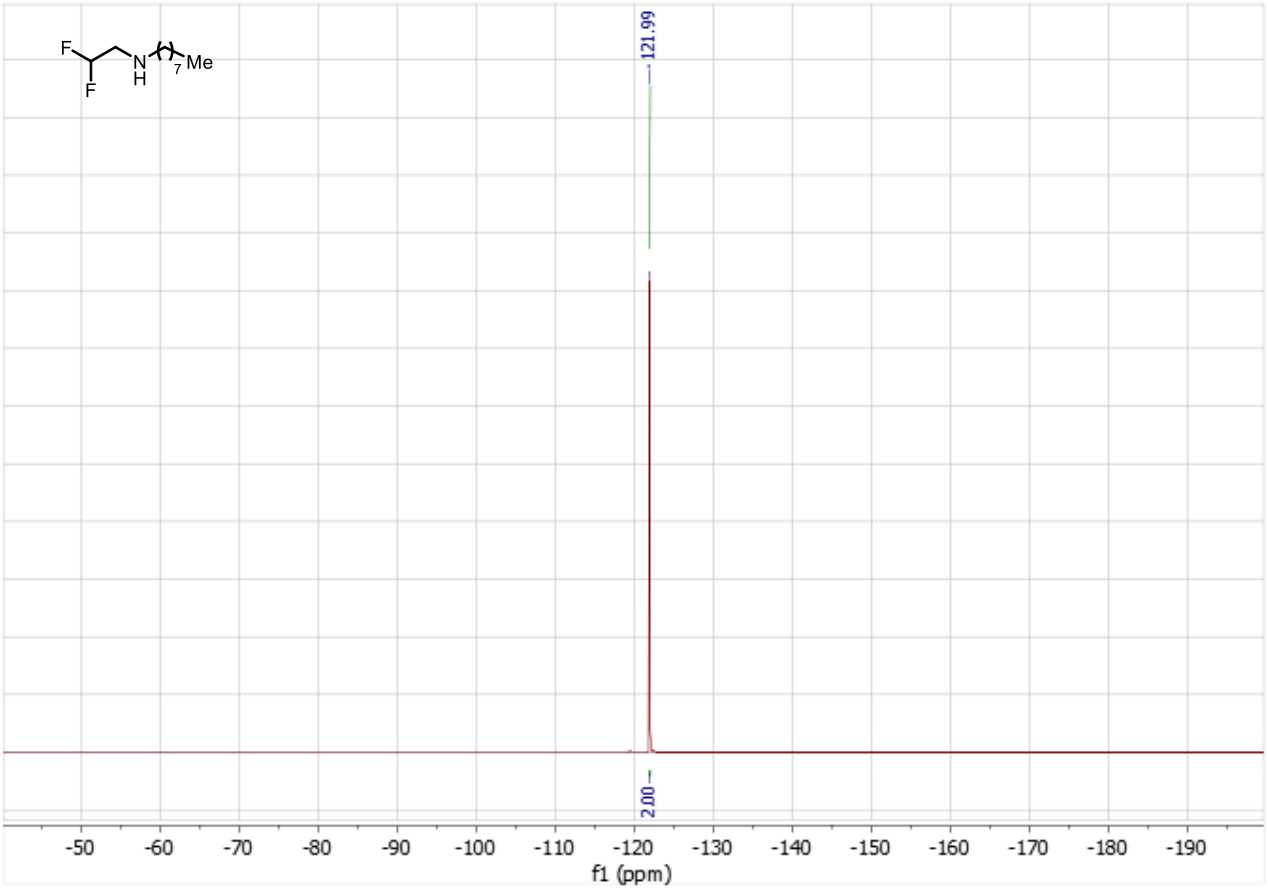

F
F
N
H
Ph
141.92
128.41
125.92
118.39
116.00
113.62
77.16 CDCl3
51.83
51.59
51.35
49.30
33.39
31.71
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

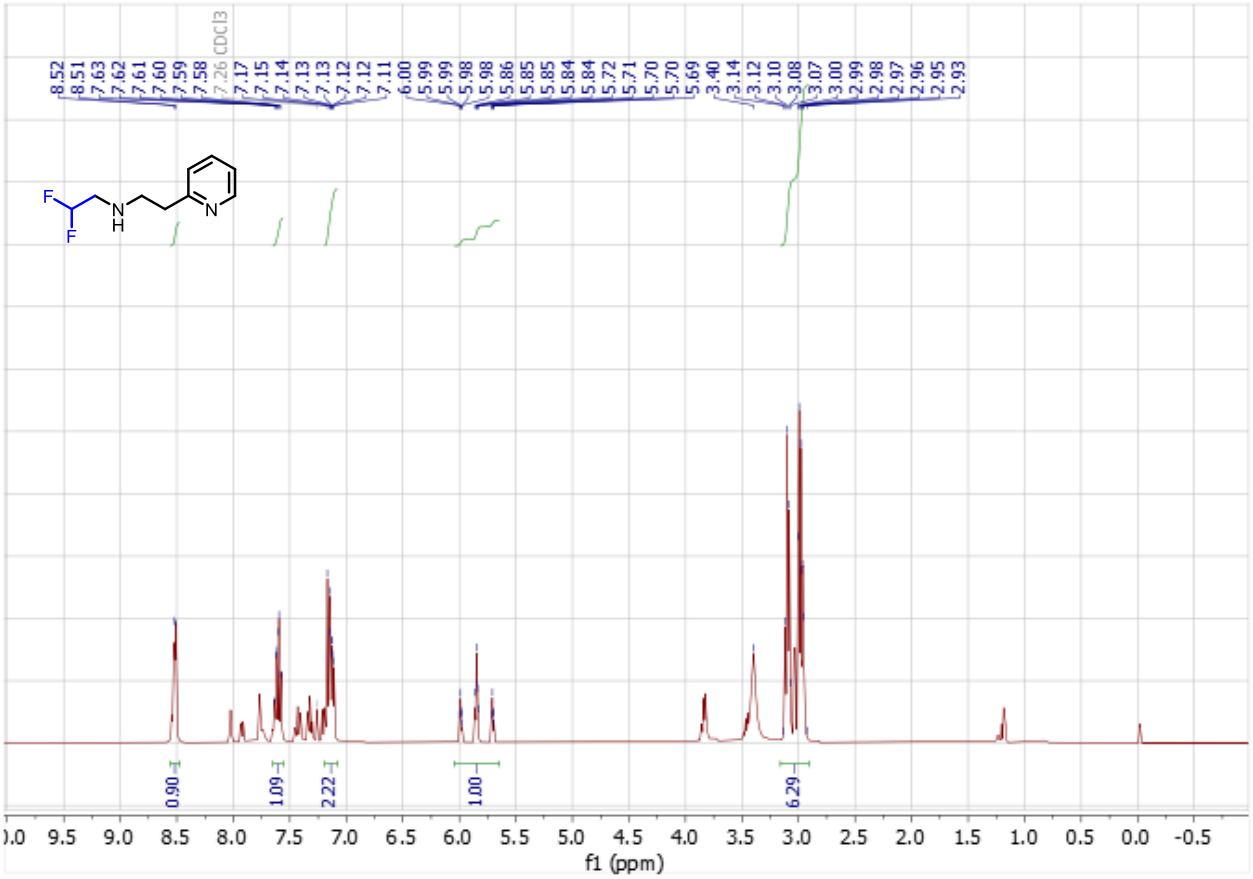

F
F
N
H
Ph
-121.89
2.00
-50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

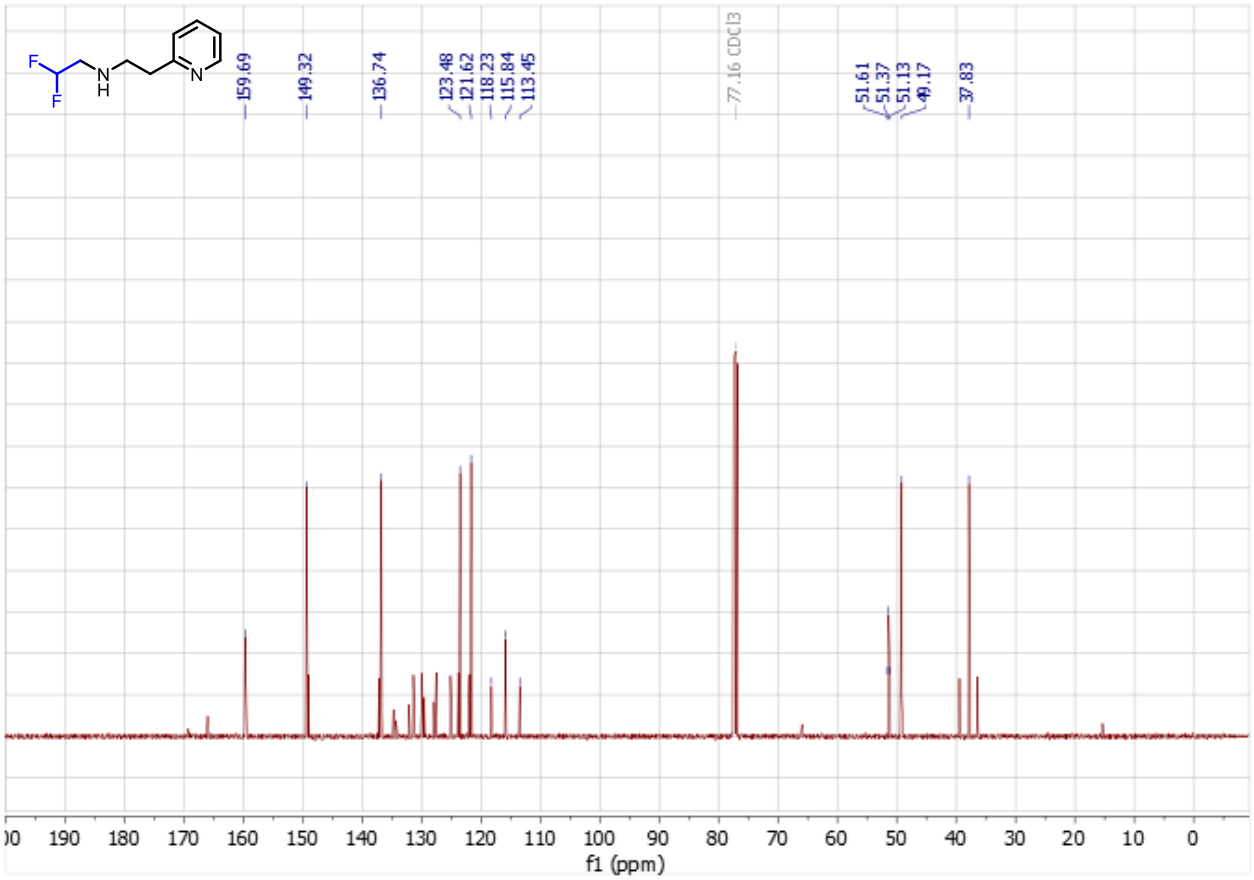

7.26 CDCl3
5.98 5.98 5.97 5.96 5.96 5.95 5.84 5.83 5.83 5.82 5.82 5.81 5.70 5.69 5.69 5.68 5.67 5.67 2.98 2.98 2.97 2.97 2.95 2.94 2.93 2.93 2.91 2.90 2.90 2.89 2.66 2.64 2.62 1.50 1.48 1.46 1.44 1.43 1.29 1.27 1.26 1.25 0.88 0.87 0.85
F
F
N
H
7
Me
1.00
2.06
2.01
2.32
10.78
3.24
0.0 9.5 9.0 8.5 8.0 7.5 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 -0.5 -1.
f1 (ppm)

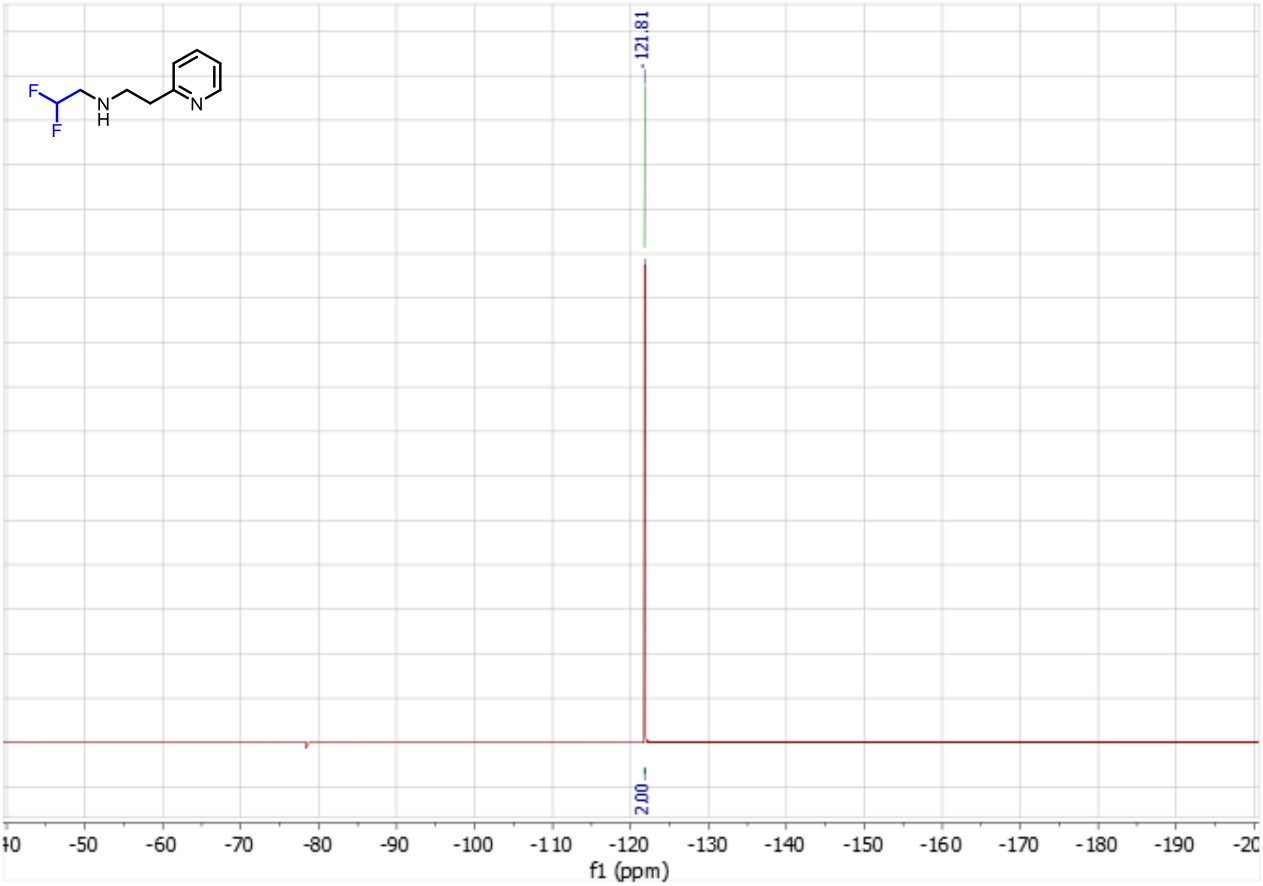

F
F
N
H
7
Me
118.49
116.10
113.71
77.16 CDCl3
52.02
51.78
51.54
50.10
31.94
30.23
29.59
29.36
27.25
22.77
14.19
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

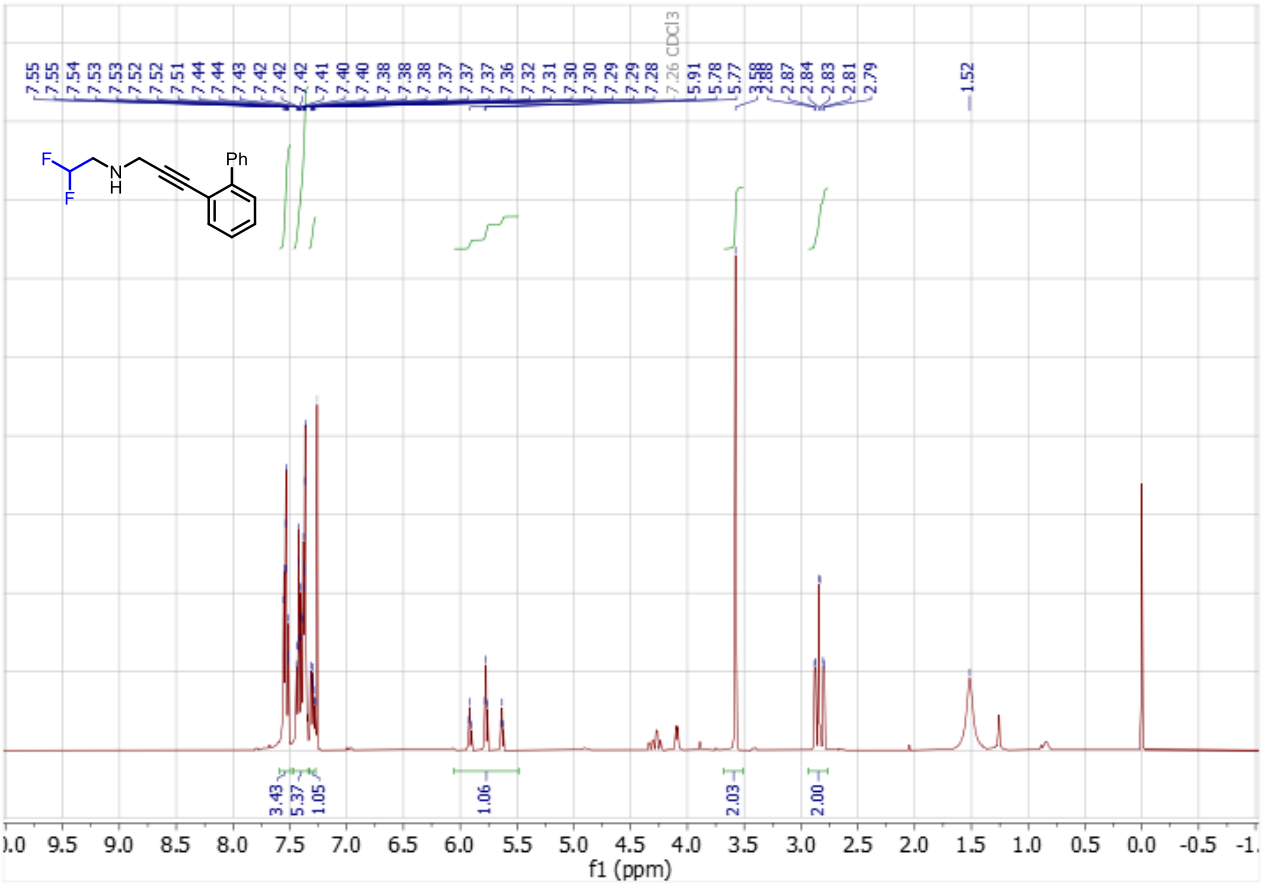
SUPPORTING INFORMATION

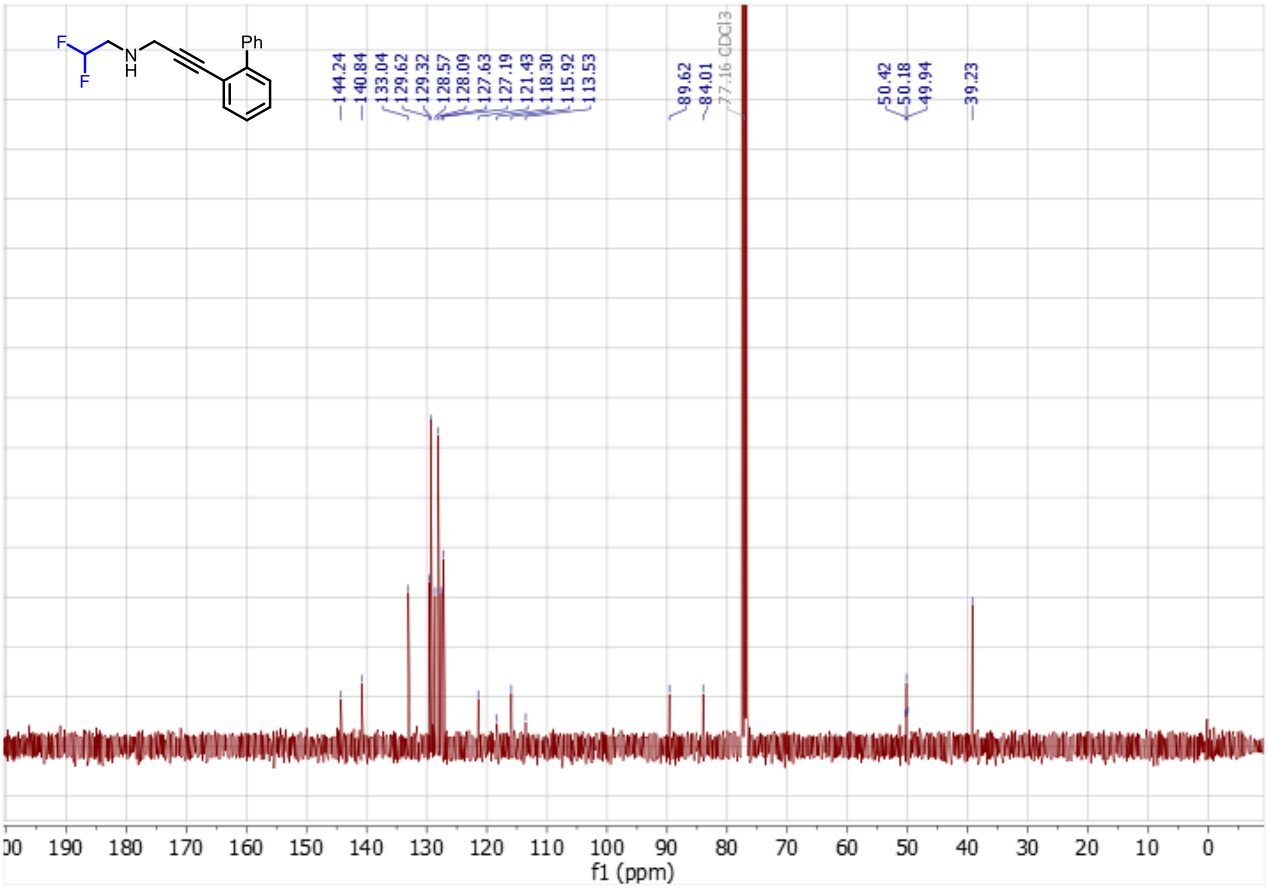


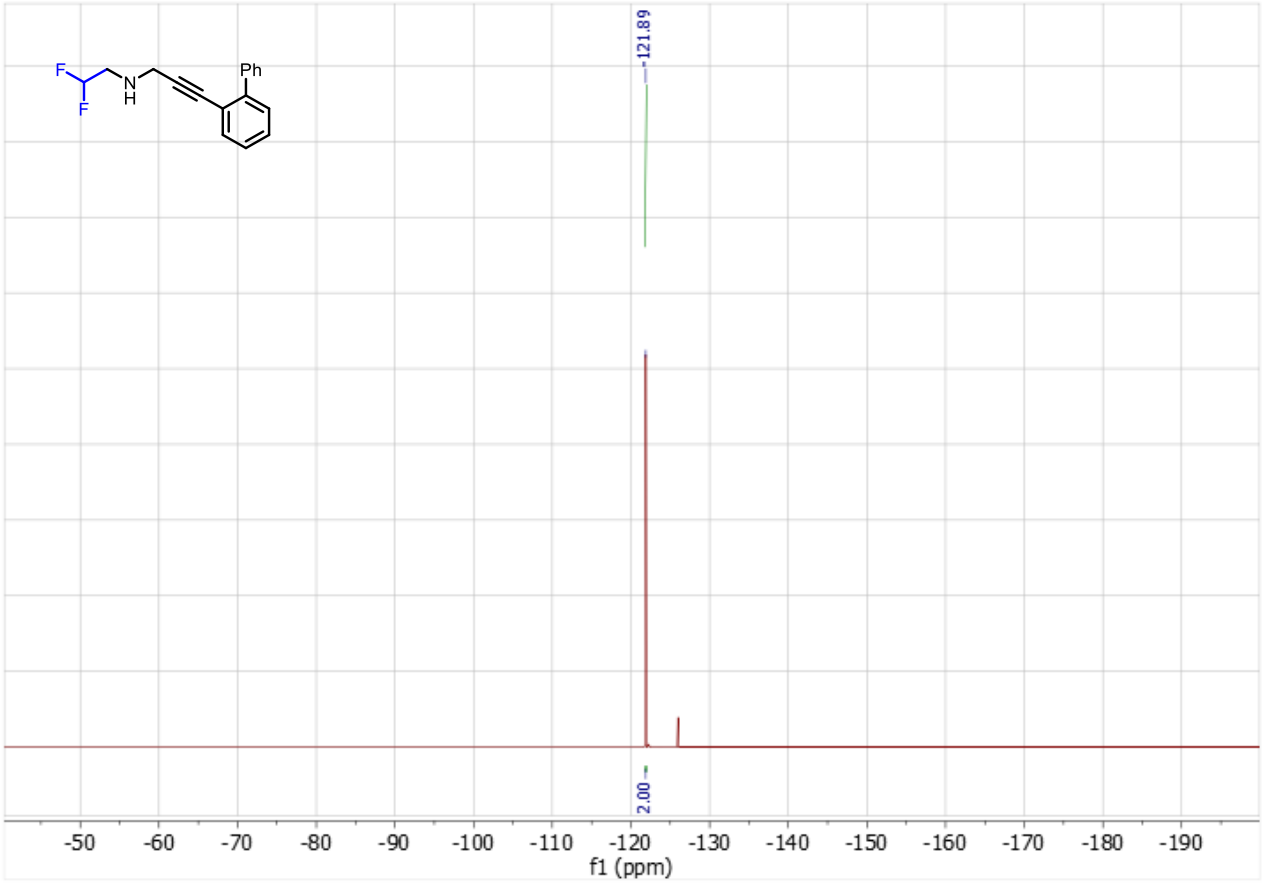


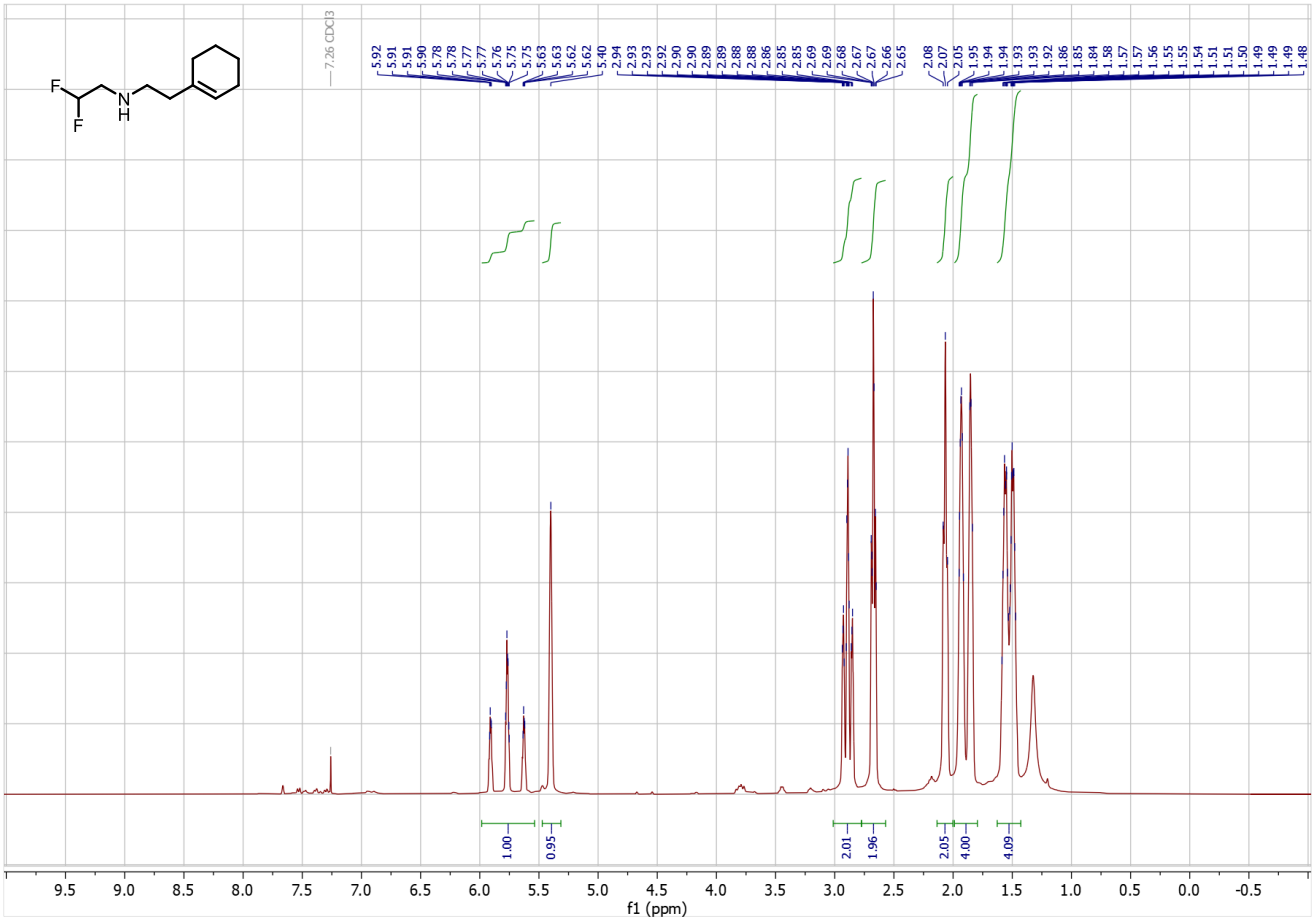

159.69
149.32
136.74
123.48
121.62
118.23
115.84
113.45
77.16 CDCl3
51.61
51.37
51.13
49.17
37.83
f1 (ppm)

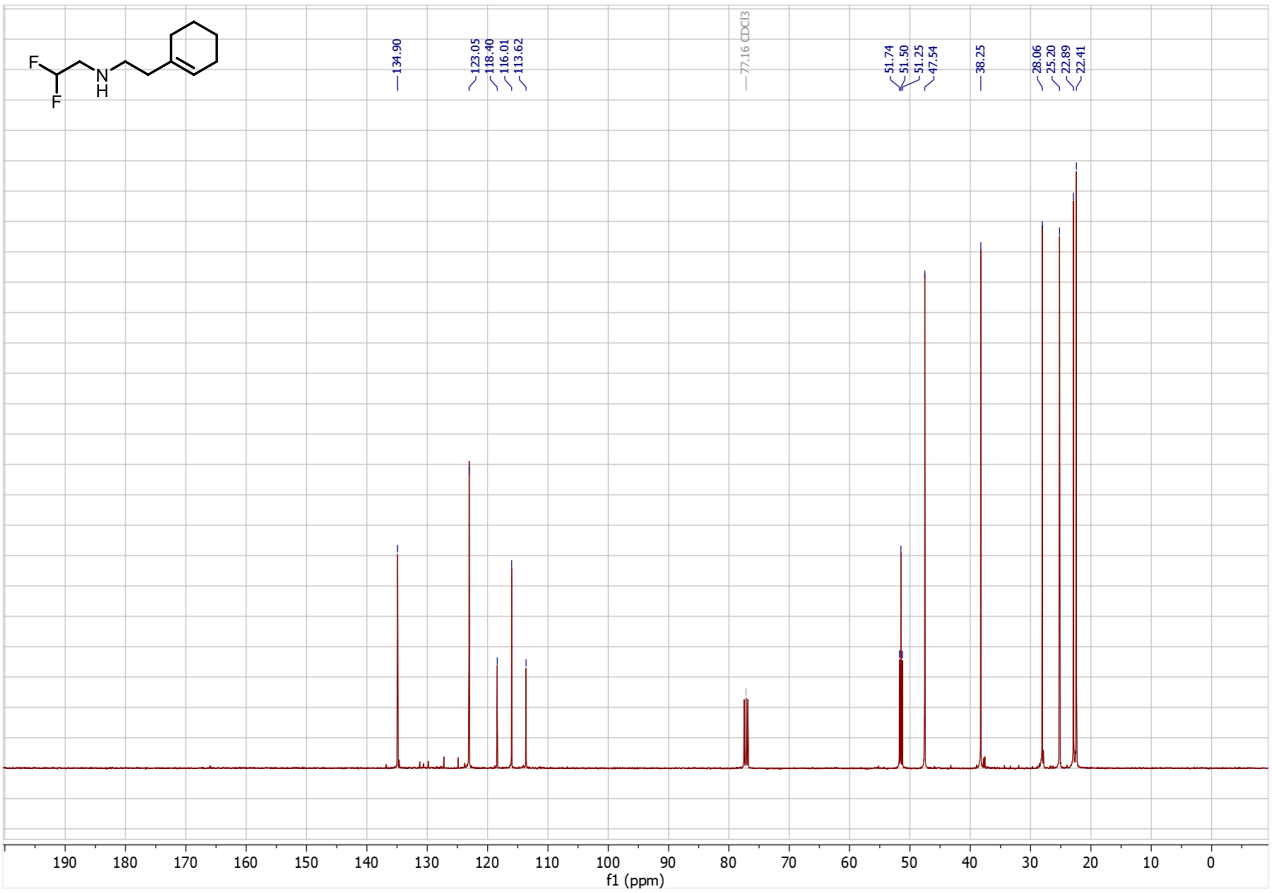

-121.81
2.00
f1 (ppm)

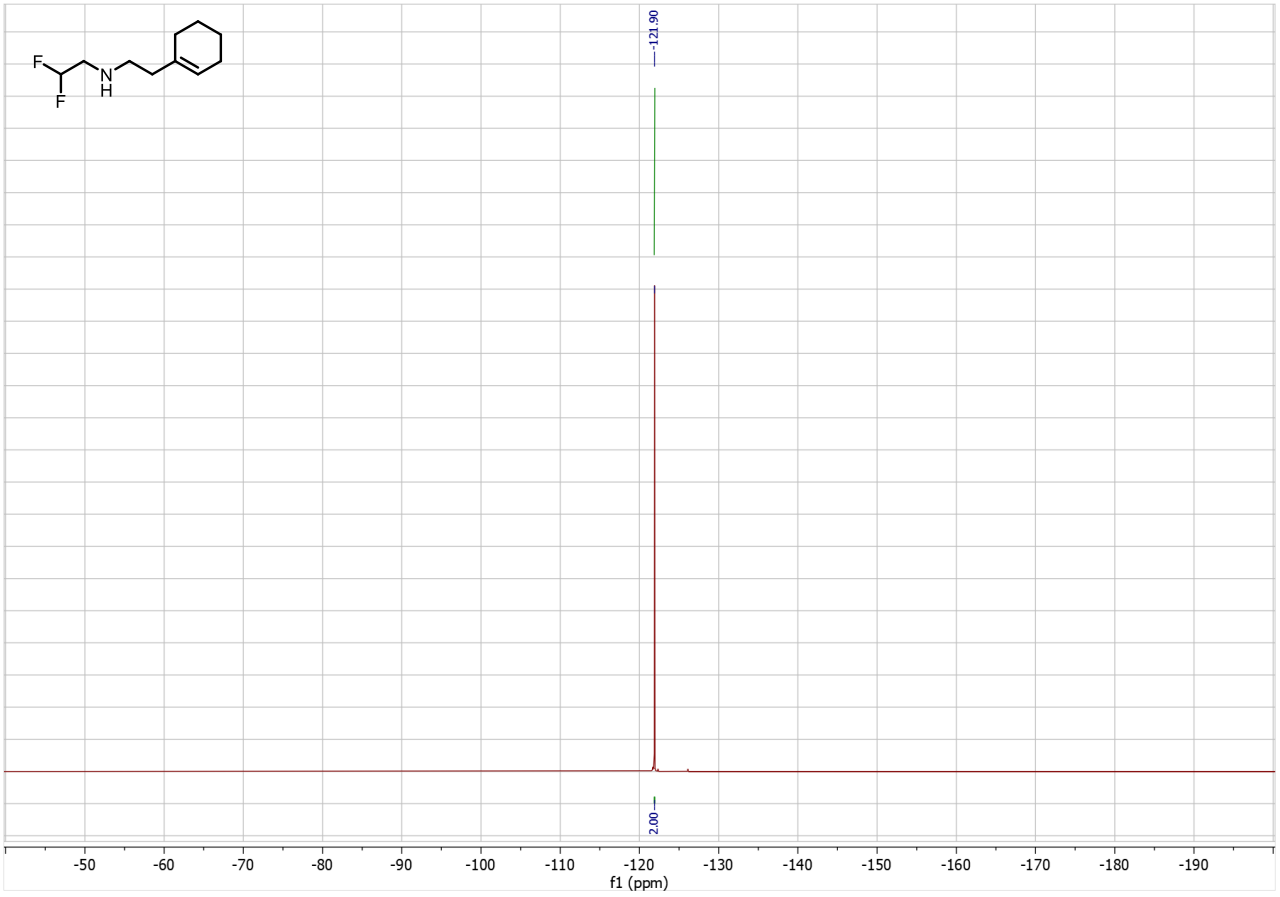

F
F
N
H
Ph
7.55 7.55 7.54 7.53 7.53 7.52 7.52 7.51 7.44 7.44 7.43 7.42 7.42 7.42 7.41 7.40 7.40 7.38 7.38 7.37 7.37 7.37 7.36 7.32 7.31 7.30 7.30 7.29 7.29 7.28 7.26 CDCl3 5.91 5.78 5.77 3.88 2.87 2.84 2.83 2.81 2.79 1.52
3.43 5.37 1.05 1.06 2.03 2.00
f1 (ppm)

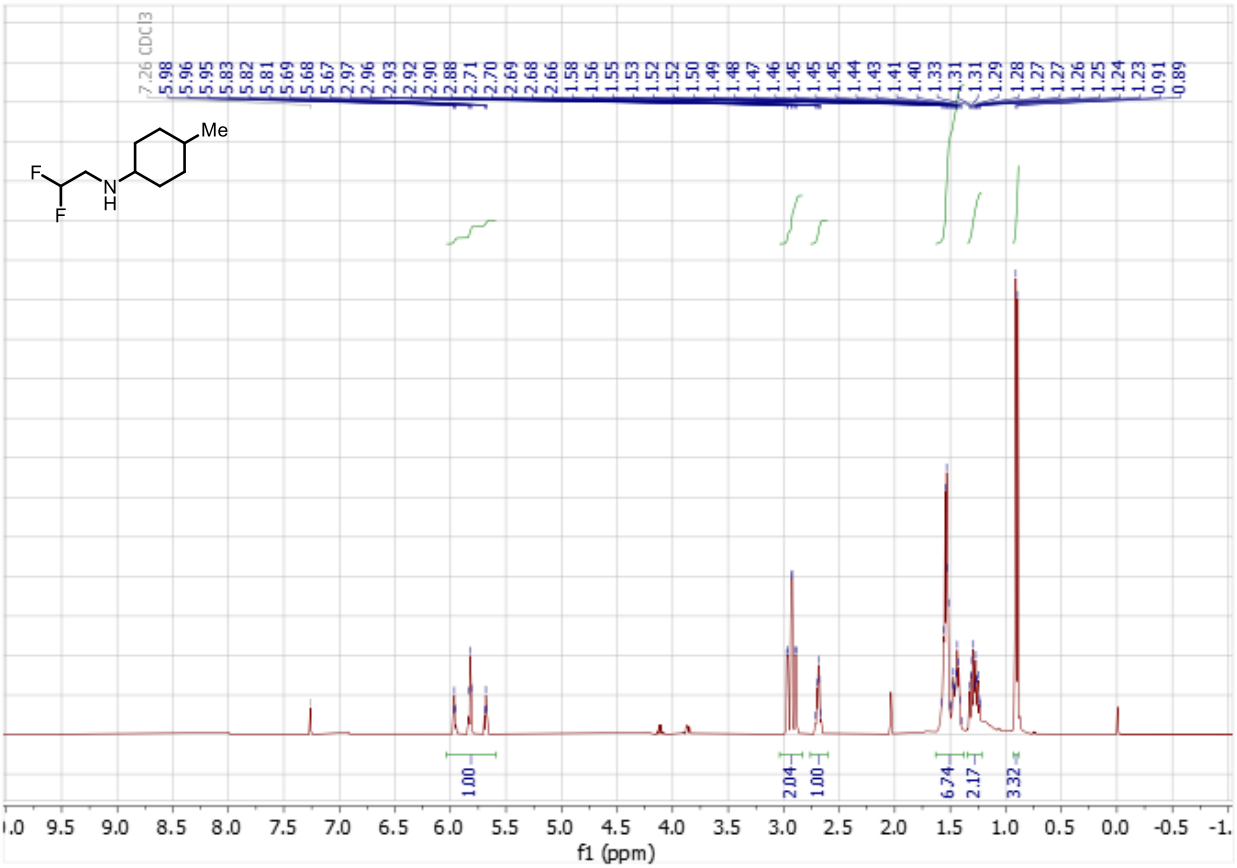

F
F
N
H
Ph
144.24 140.84 133.04 129.62 129.32 128.57 128.09 127.63 127.19 121.43 118.30 115.92 113.53
89.62 84.01 77.16 CDCl3
50.42 50.18 49.94 39.23
f1 (ppm)

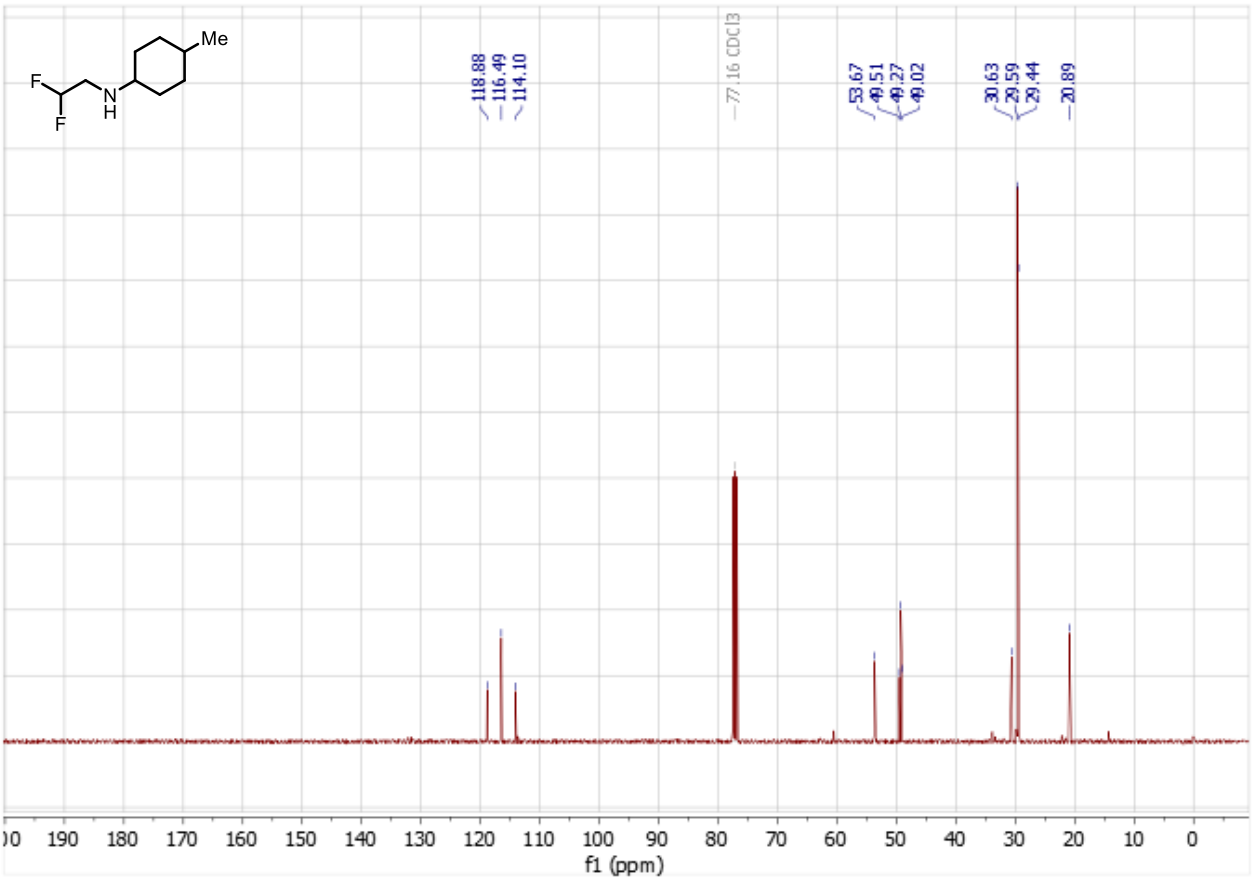

F
F
N
H
Ph
-121.89
2.00
-50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

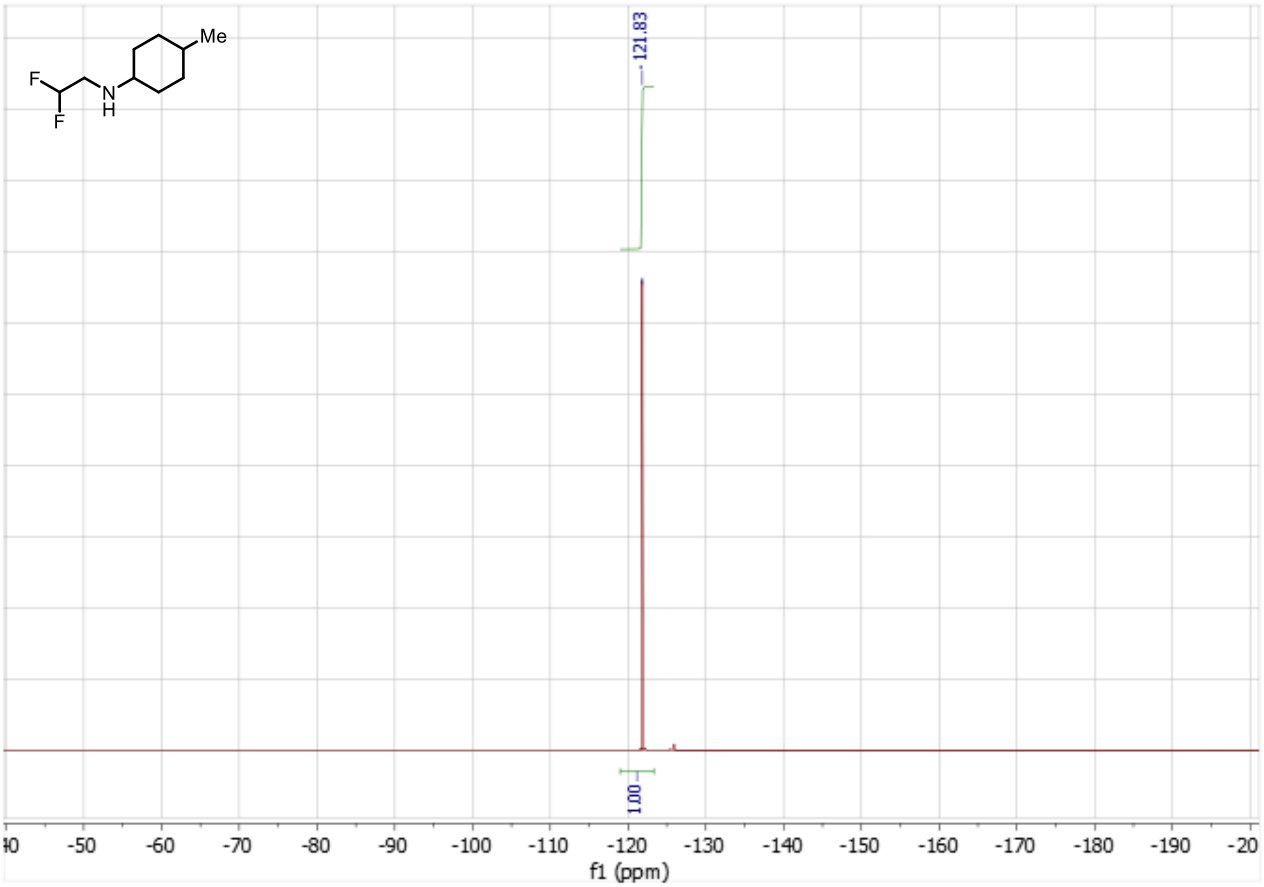

F
F
N
H
7.26 CDCl3
1.00
0.95
2.01
1.96
2.05
4.00
4.09
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

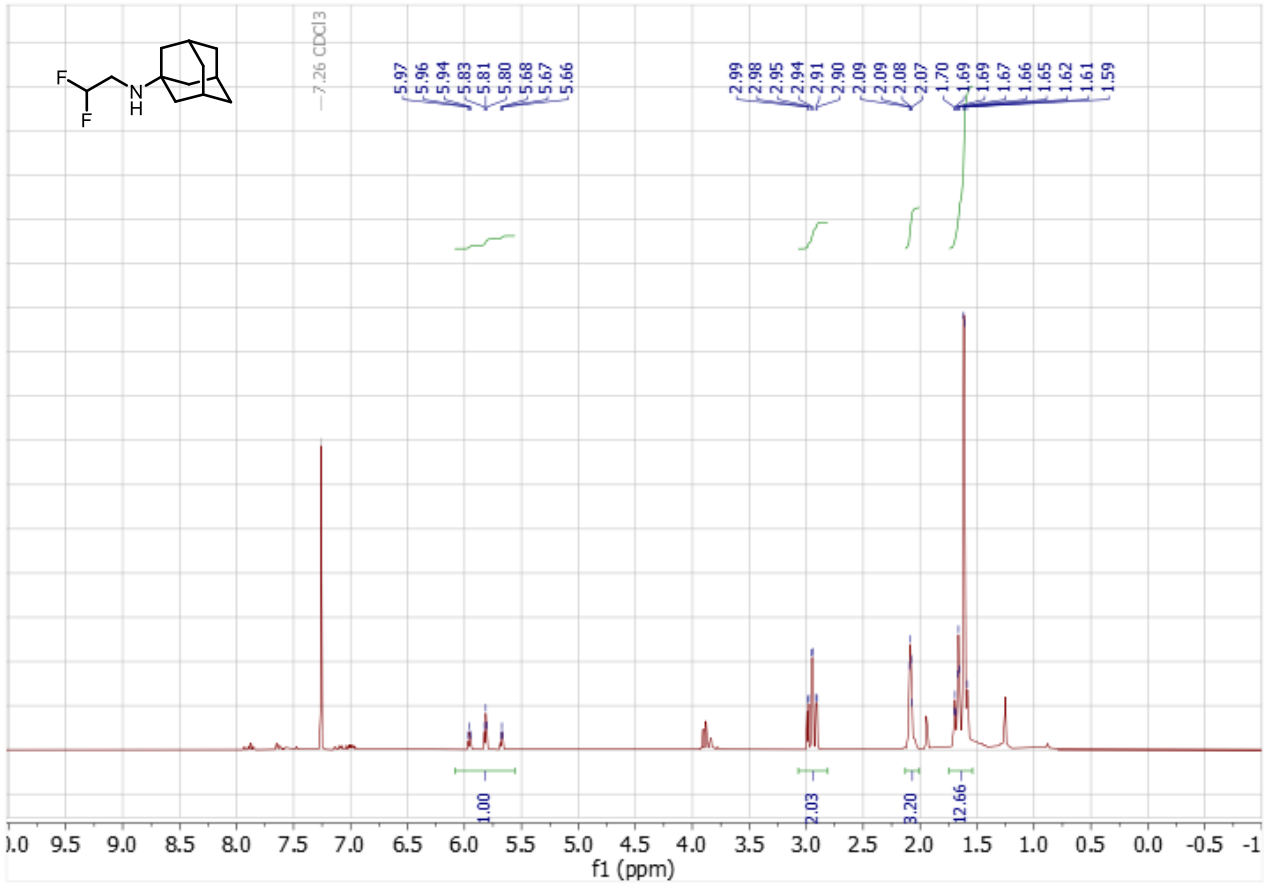

F
F
N
H
134.90
123.05
118.40
116.01
113.62
77.16 CDCl3
51.74
51.50
51.25
47.54
38.25
28.06
25.20
22.89
22.41
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

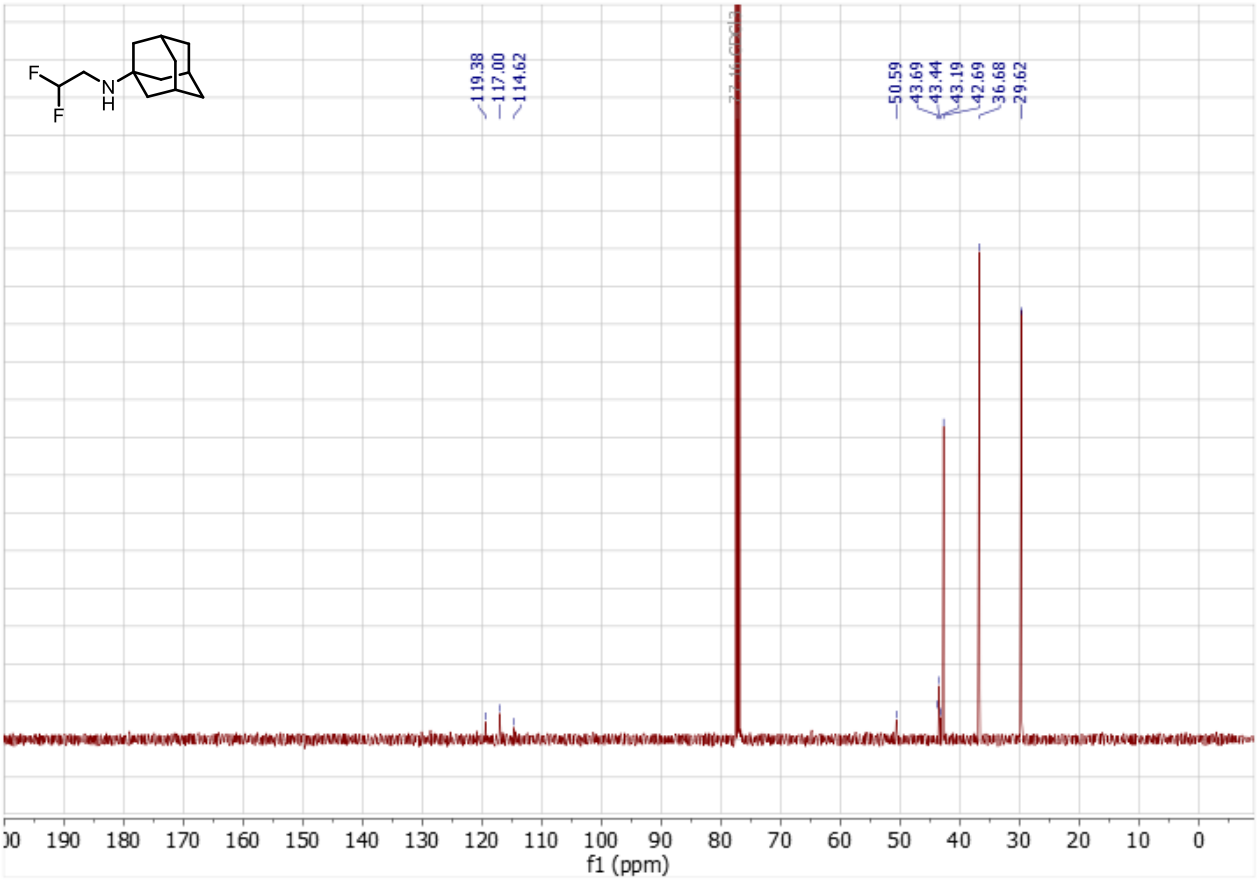

F
F
N
H
-121.90
2.00
-50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

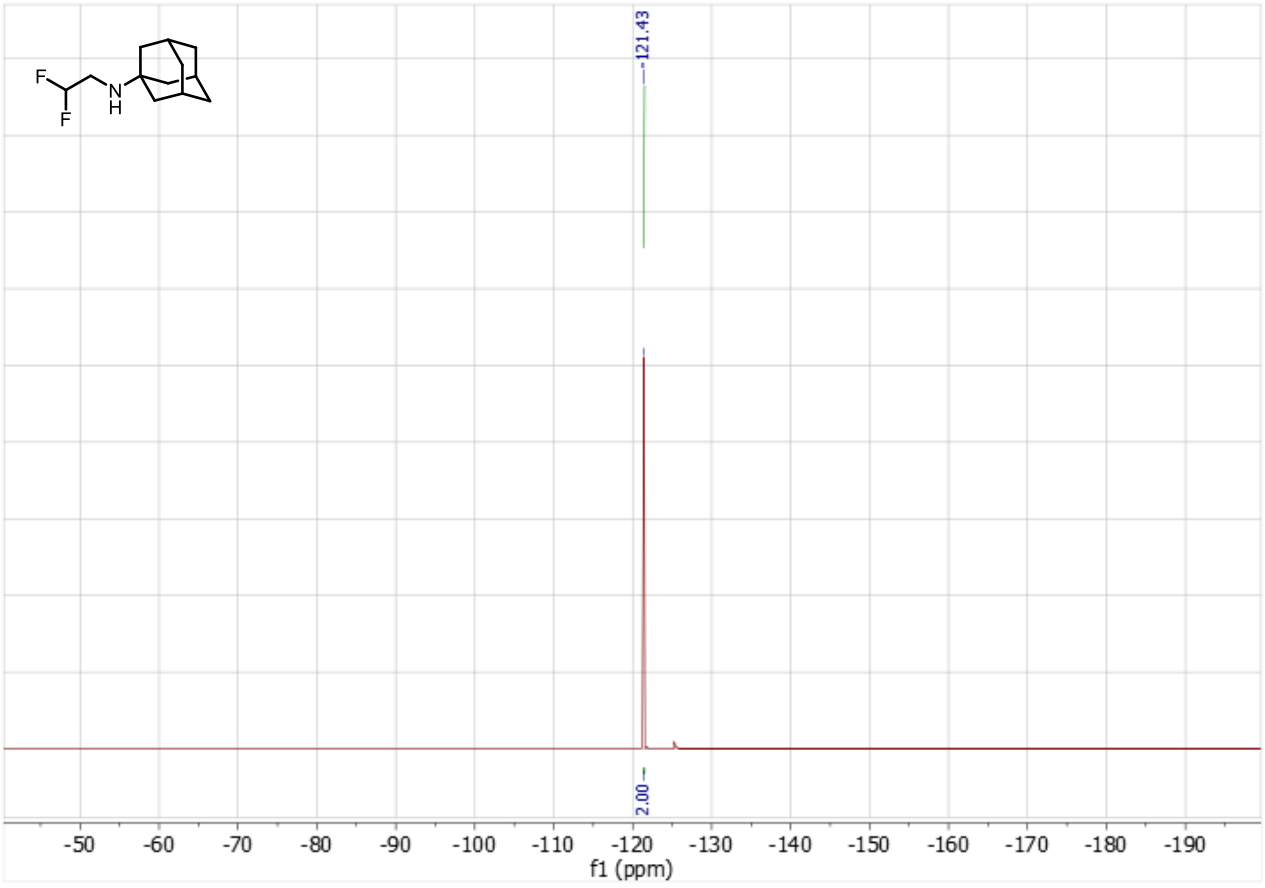

Me
F
F
N
H
7.26 CDCl3
5.98
5.96
5.95
5.83
5.82
5.81
5.69
5.68
5.67
2.97
2.96
2.93
2.92
2.90
2.88
2.71
2.70
2.69
2.68
2.66
1.58
1.56
1.55
1.53
1.52
1.52
1.50
1.49
1.48
1.47
1.46
1.45
1.45
1.45
1.44
1.43
1.41
1.40
1.33
1.31
1.31
1.29
1.28
1.27
1.27
1.26
1.25
1.24
1.23
0.91
0.89
1.00
2.04
1.00
6.74
2.17
3.32
f1 (ppm)

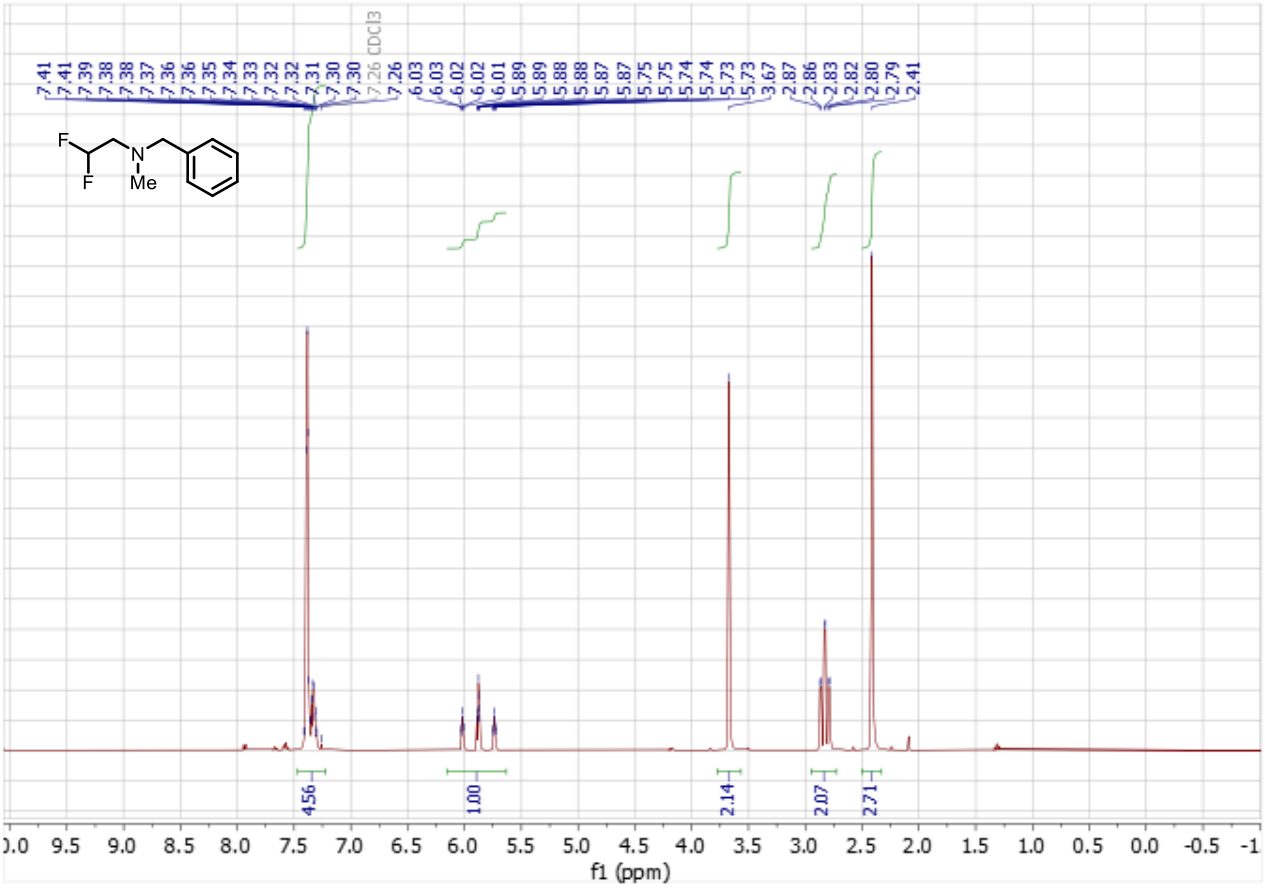

Me
F
F
N
H
118.88
116.49
114.10
77.16 CDCl3
53.67
49.51
49.27
49.02
30.63
29.59
29.44
20.89
f1 (ppm)

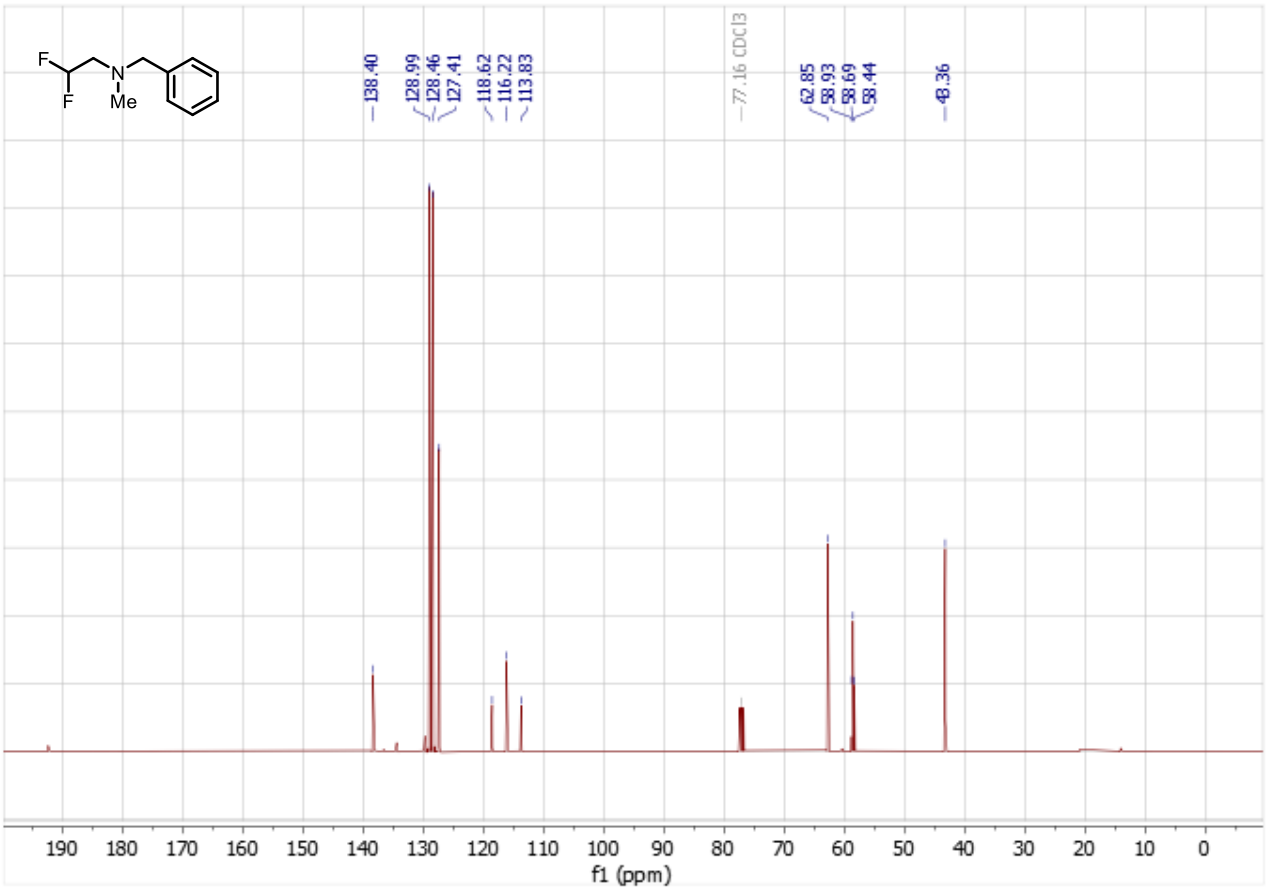

Me
F
F
N
H
121.83
1.00
-40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -20
f1 (ppm)

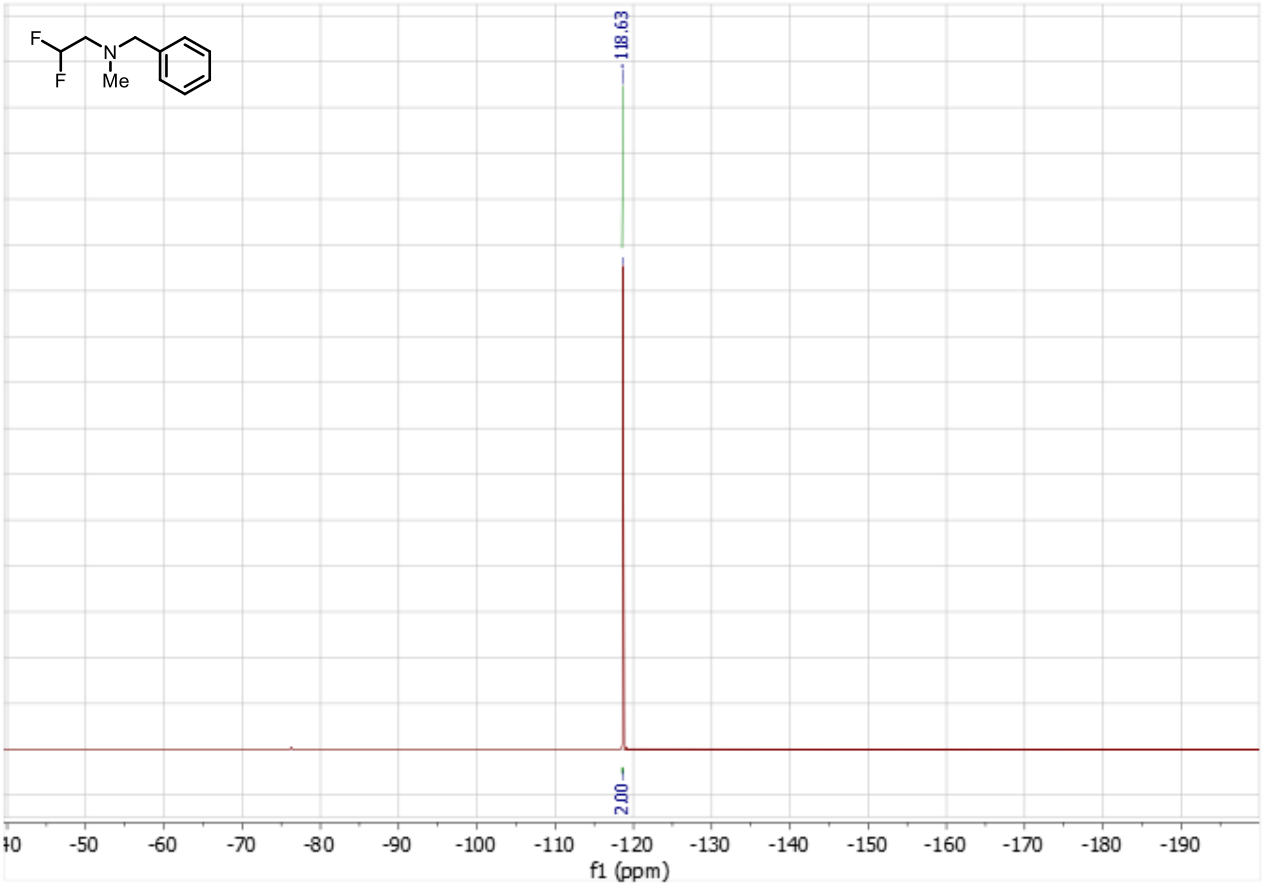

F
F
N
H
7.26 CDCl3
5.97 5.96 5.94 5.83 5.81 5.80 5.68 5.67 5.66
2.99 2.98 2.95 2.94 2.91 2.90 2.09 2.09 2.08 2.07 1.70 1.69 1.69 1.67 1.66 1.65 1.62 1.61 1.59
1.00
2.03
3.20
12.66
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

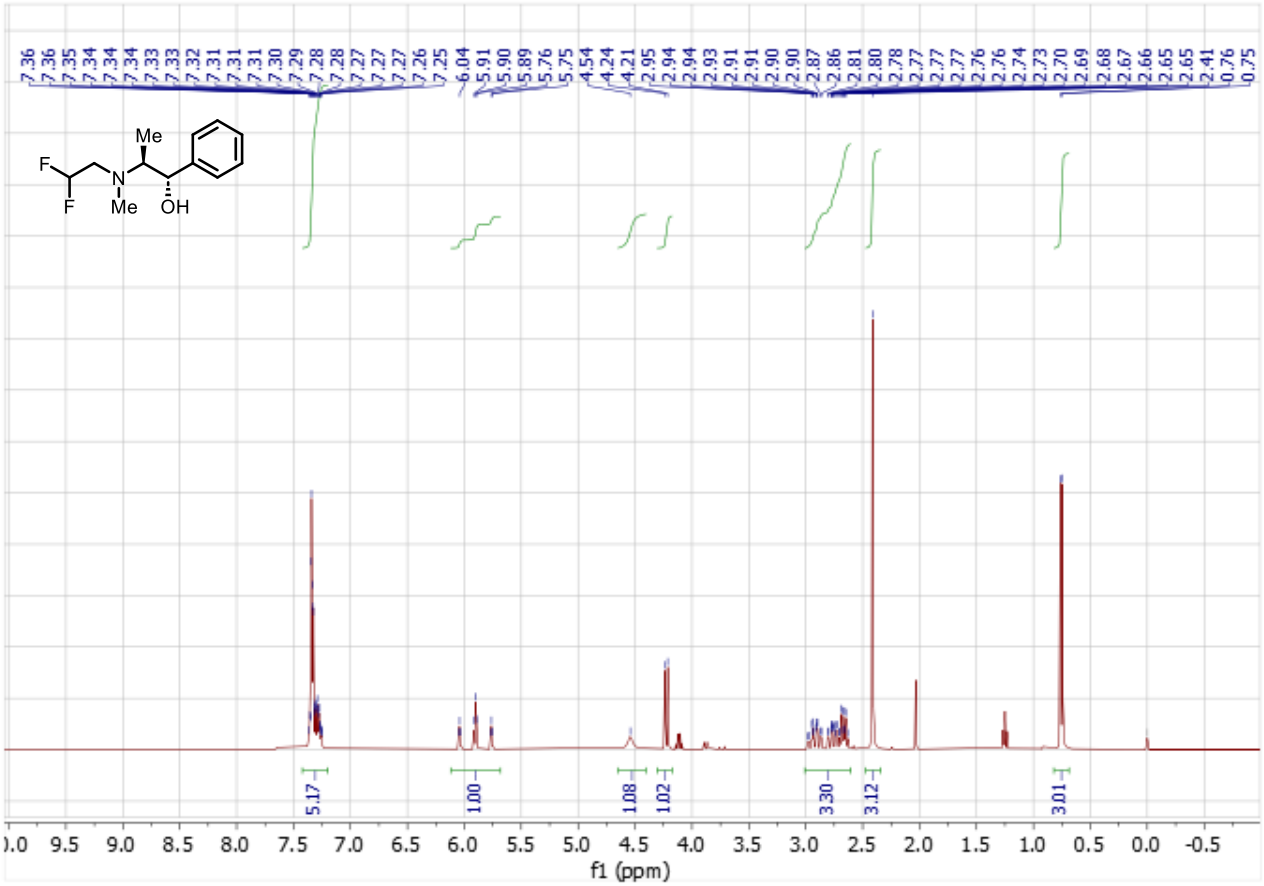

F
F
N
H
119.38
117.00
114.62
77.48
50.59
43.69
43.44
43.19
42.69
36.68
29.62
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


F
F
N
H
-121.43
2.00
-50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)


F
F
N
Me
7.41
7.41
7.39
7.38
7.38
7.37
7.36
7.36
7.35
7.34
7.33
7.32
7.32
7.31
7.30
7.30
7.26 CDCl3
7.26
6.03
6.03
6.02
6.02
6.01
5.89
5.89
5.88
5.88
5.87
5.87
5.75
5.75
5.74
5.74
5.73
5.73
3.67
2.87
2.86
2.83
2.82
2.80
2.79
2.41
4.56
1.00
2.14
2.07
2.71
f1 (ppm)


F
F
N
Me
138.40
128.99
128.46
127.41
118.62
116.22
113.83
77.16 CDCl3
62.85
58.93
58.69
58.44
48.36
f1 (ppm)


F
F
N
Me
118.63
2.00
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)


F
F
N
Me
Me
OH
7.36
7.36
7.35
7.34
7.34
7.34
7.33
7.33
7.32
7.31
7.31
7.31
7.30
7.29
7.28
7.28
7.27
7.27
7.27
7.26
7.25
6.04
5.91
5.90
5.89
5.76
5.75
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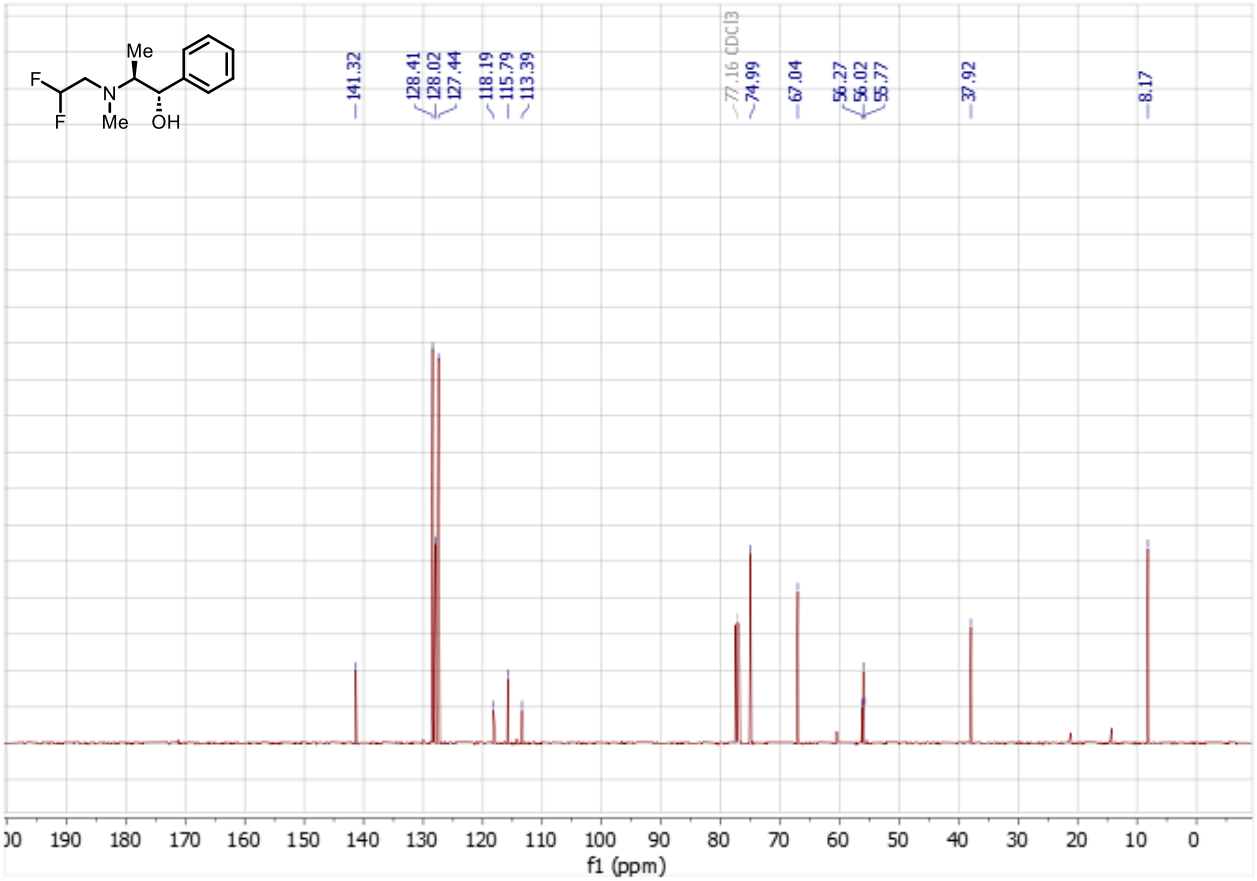
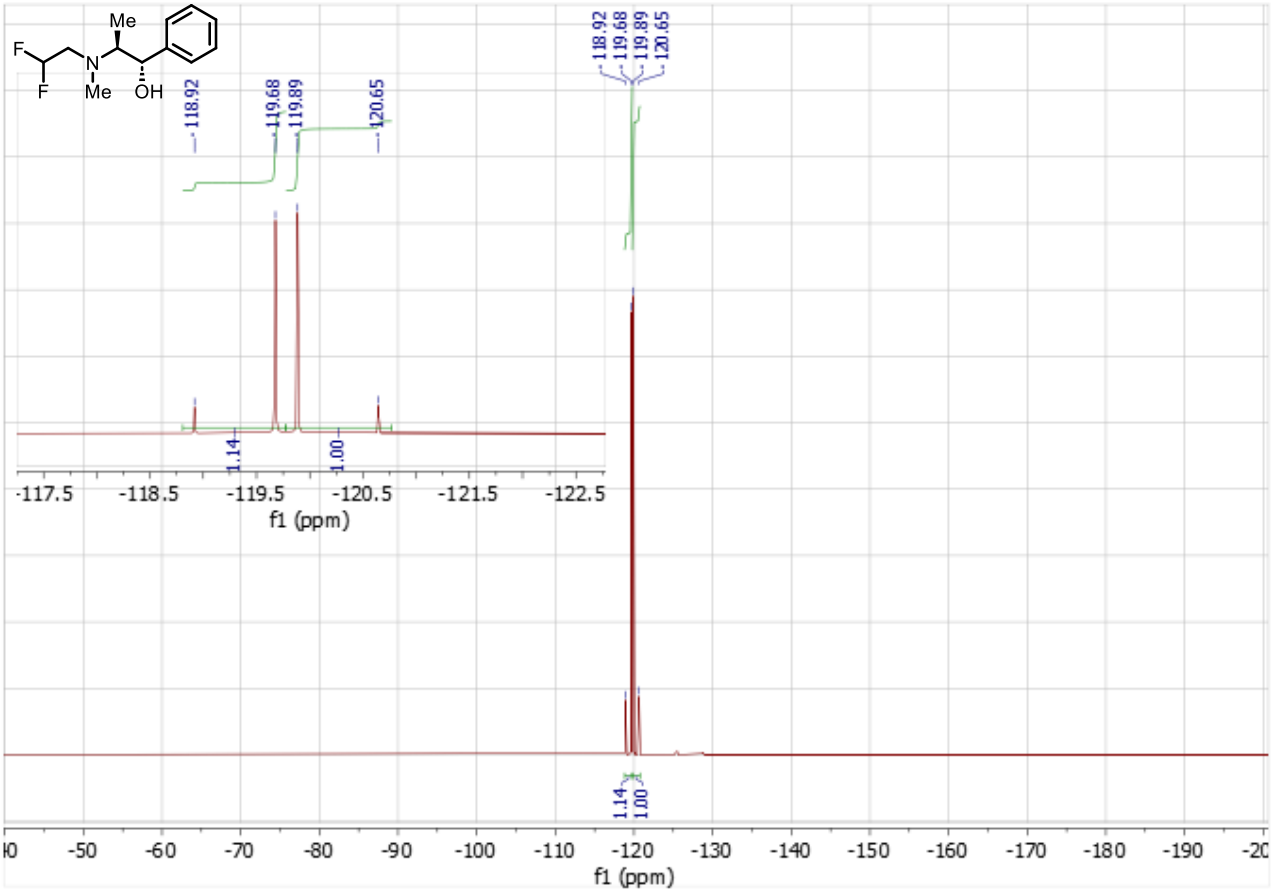
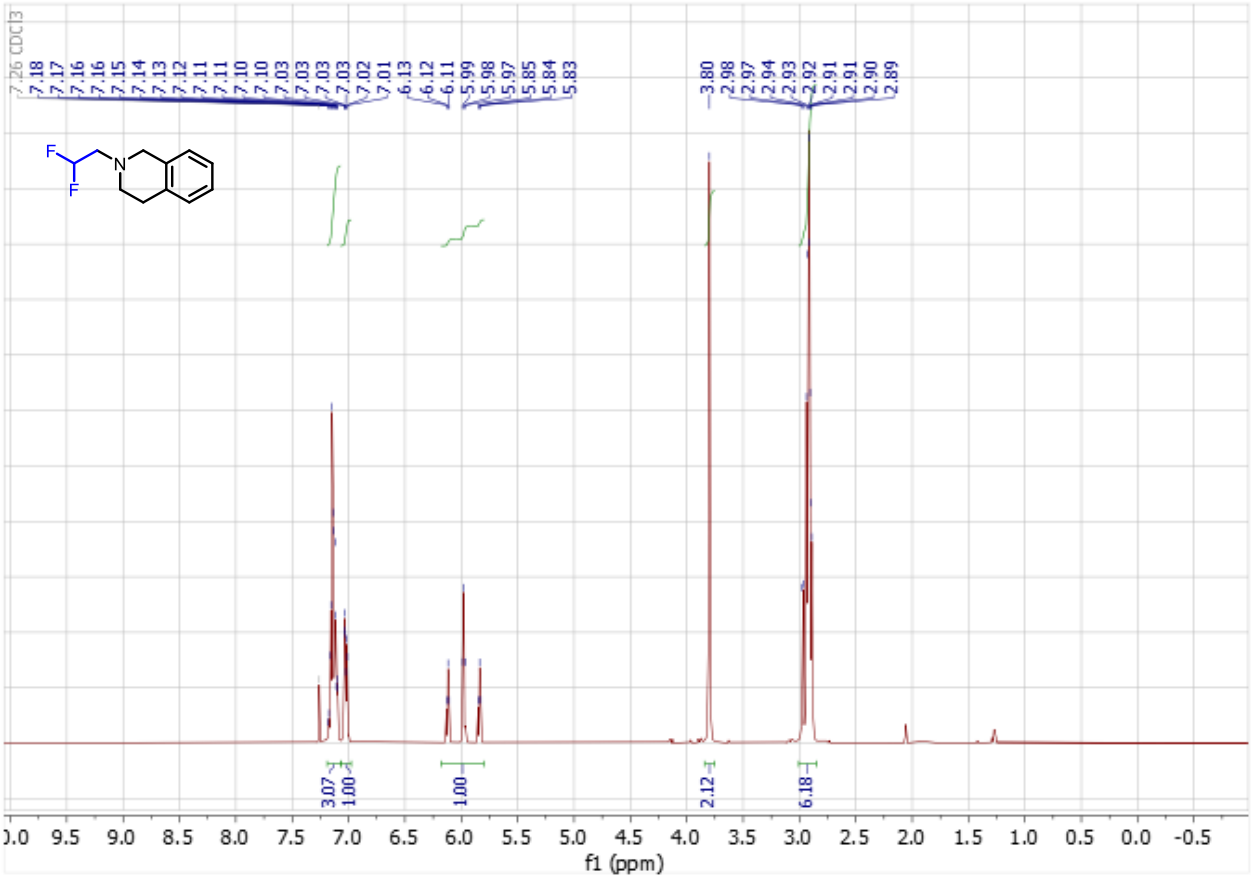
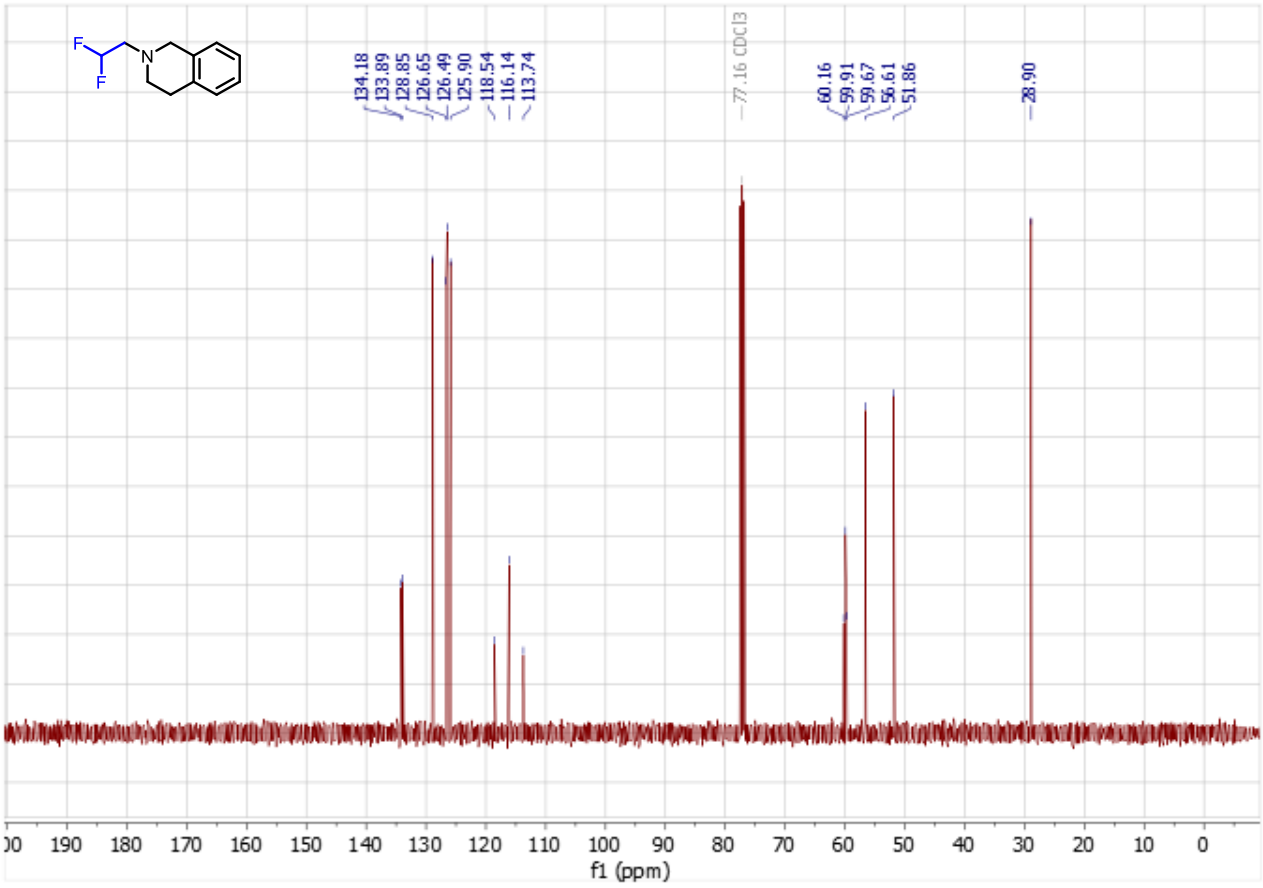
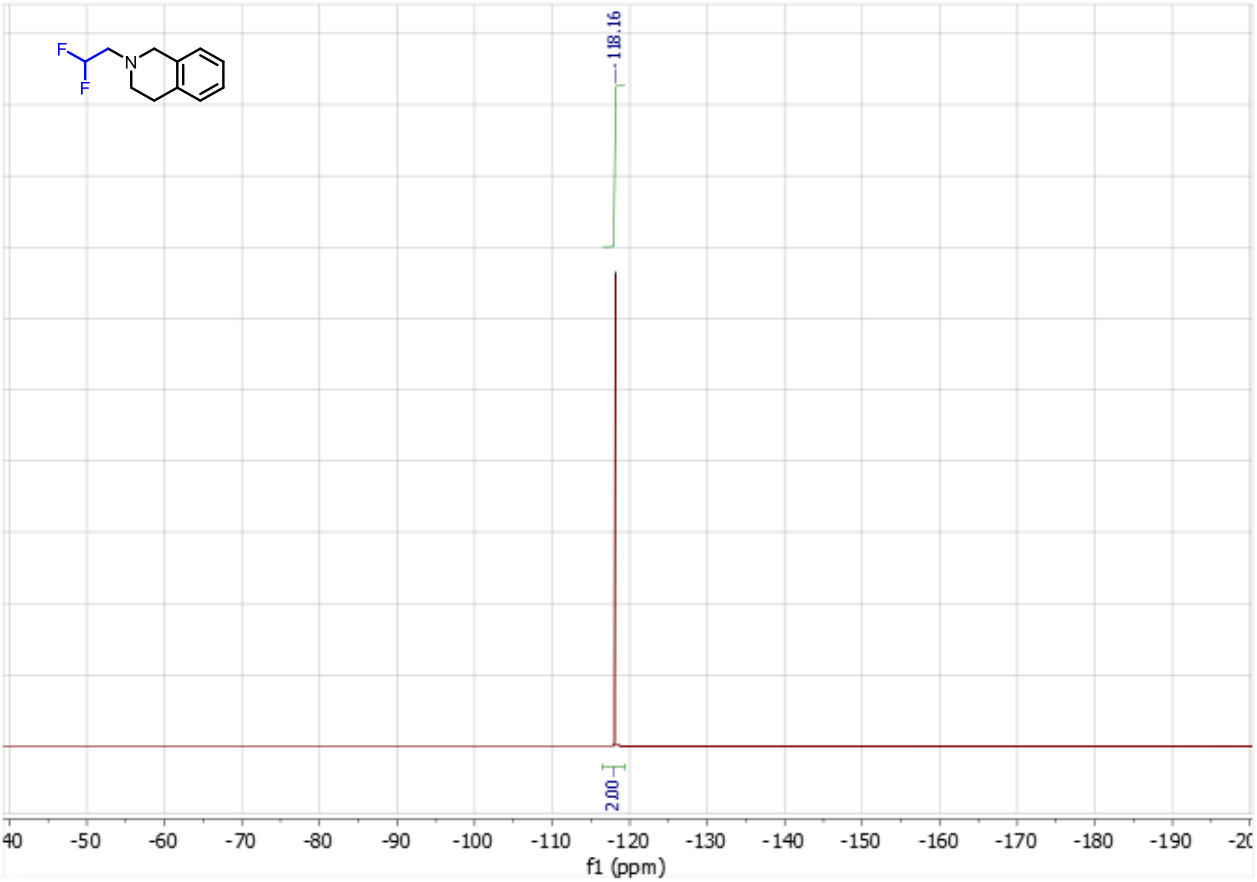
4.24
4.21
2.95
2.94
2.94
2.93
2.91
2.91
2.90
2.90
2.87
2.86
2.81
2.80
2.78
2.77
2.77
2.77
2.76
2.76
2.74
2.73
2.70
2.69
2.68
2.67
2.66
2.65
2.65
2.41
0.76
0.75
5.17
1.00
1.08
1.02
3.30
3.12
3.01
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

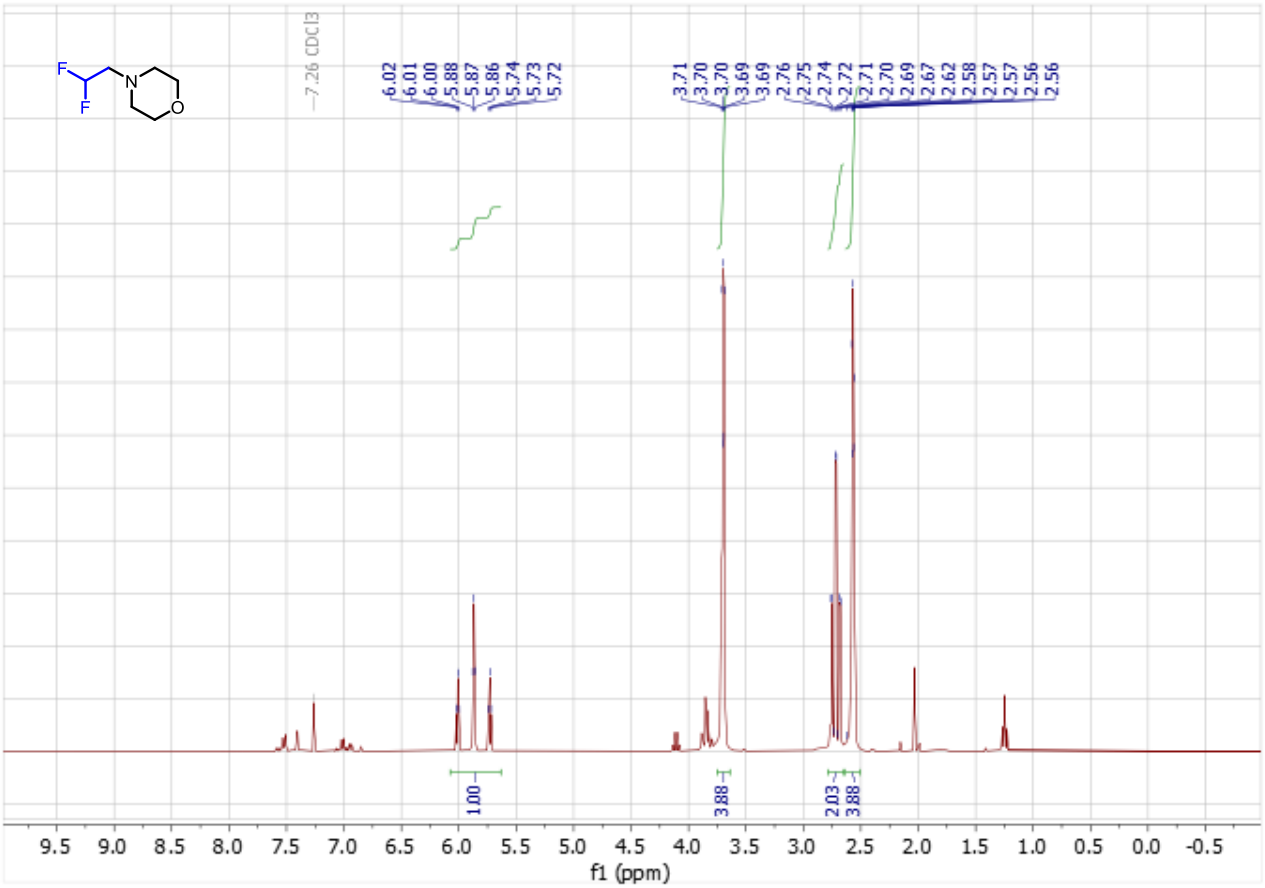

Me
F
N
F
Me
OH
141.32
128.41
128.02
127.44
118.19
115.79
113.39
77.16 CDCl3
74.99
67.04
56.27
56.02
55.77
37.92
8.17
f1 (ppm)

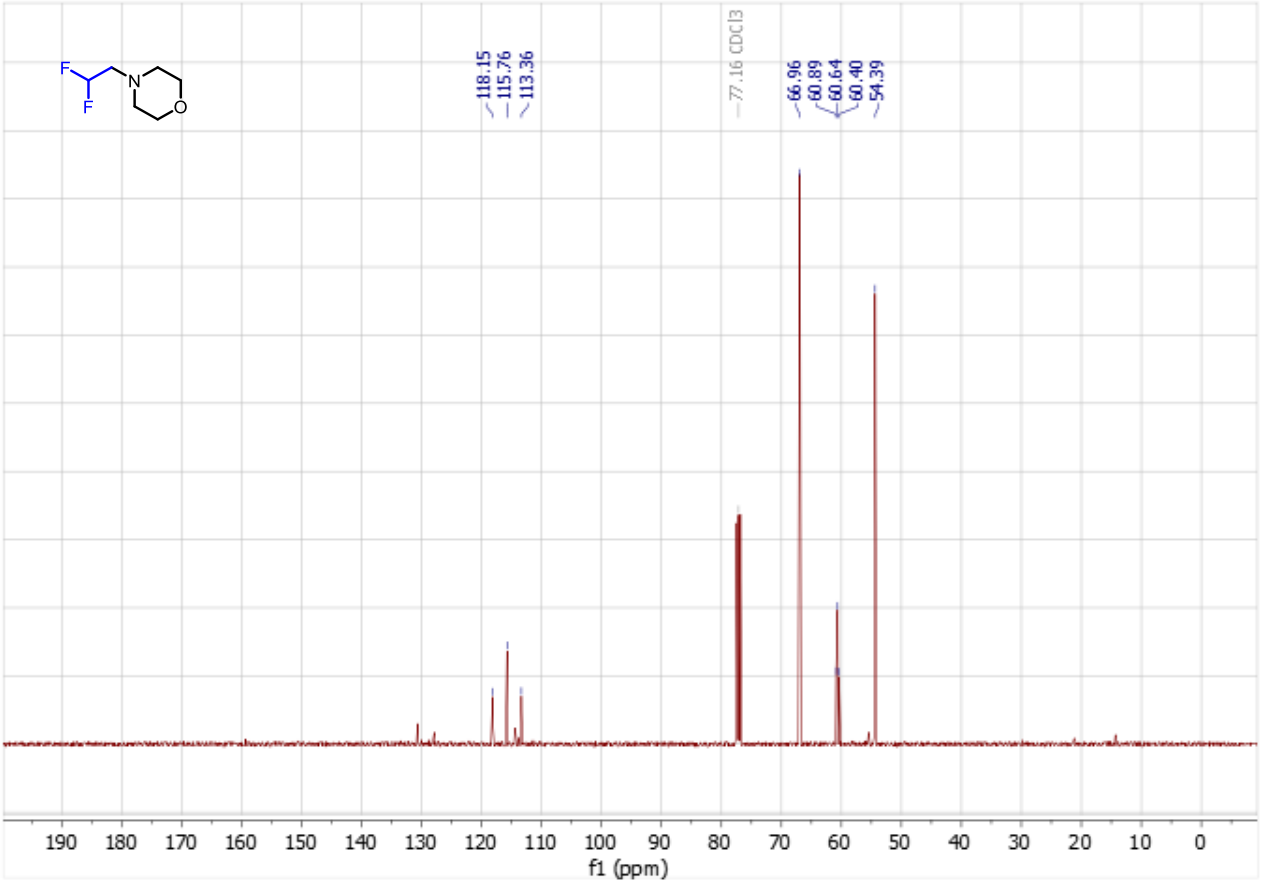

Me
F
N
F
Me
OH
118.92
119.68
119.89
120.65
1.14
1.00
f1 (ppm)

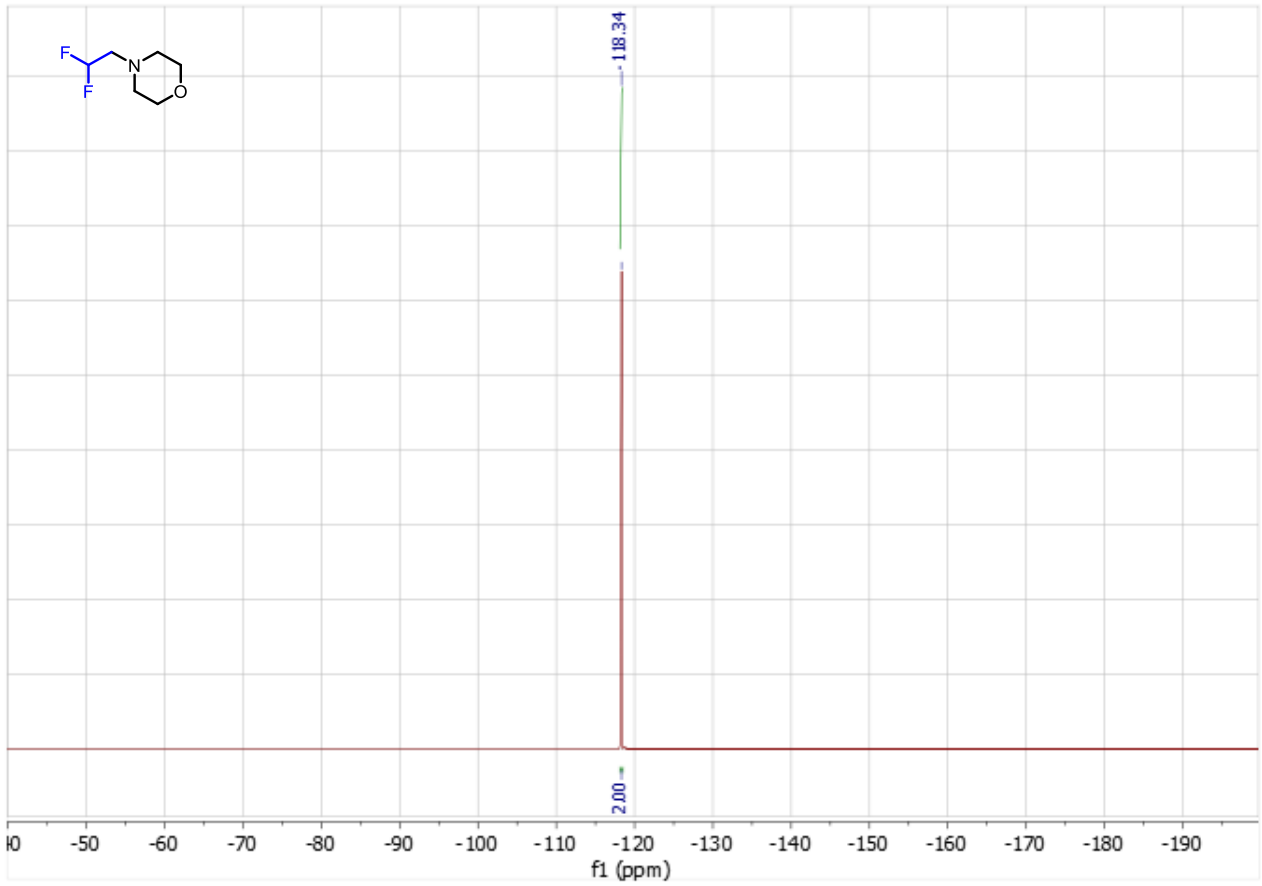

7.26 CDCl3
7.18
7.17
7.16
7.16
7.15
7.14
7.13
7.12
7.11
7.11
7.10
7.10
7.03
7.03
7.03
7.03
7.02
7.01
6.13
6.12
6.11
5.99
5.98
5.97
5.85
5.84
5.83
3.80
2.98
2.97
2.94
2.93
2.92
2.91
2.91
2.90
2.89
F
F
N
3.07
1.00
1.00
2.12
6.18
f1 (ppm)

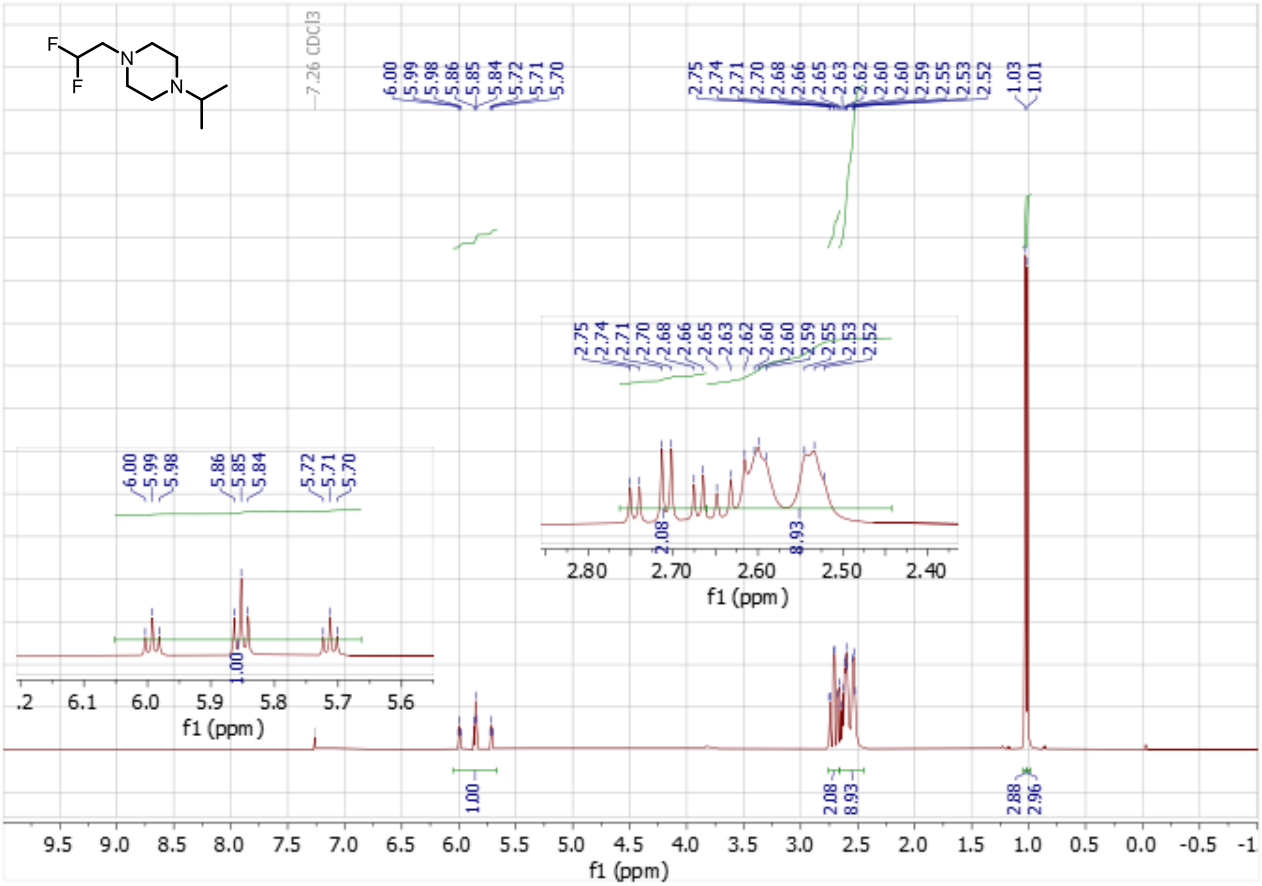

F
F
N
134.18
133.89
128.85
126.65
126.49
125.90
118.54
116.14
113.74
77.16 CDCl3
60.16
59.91
59.67
56.61
51.86
28.90
f1 (ppm)

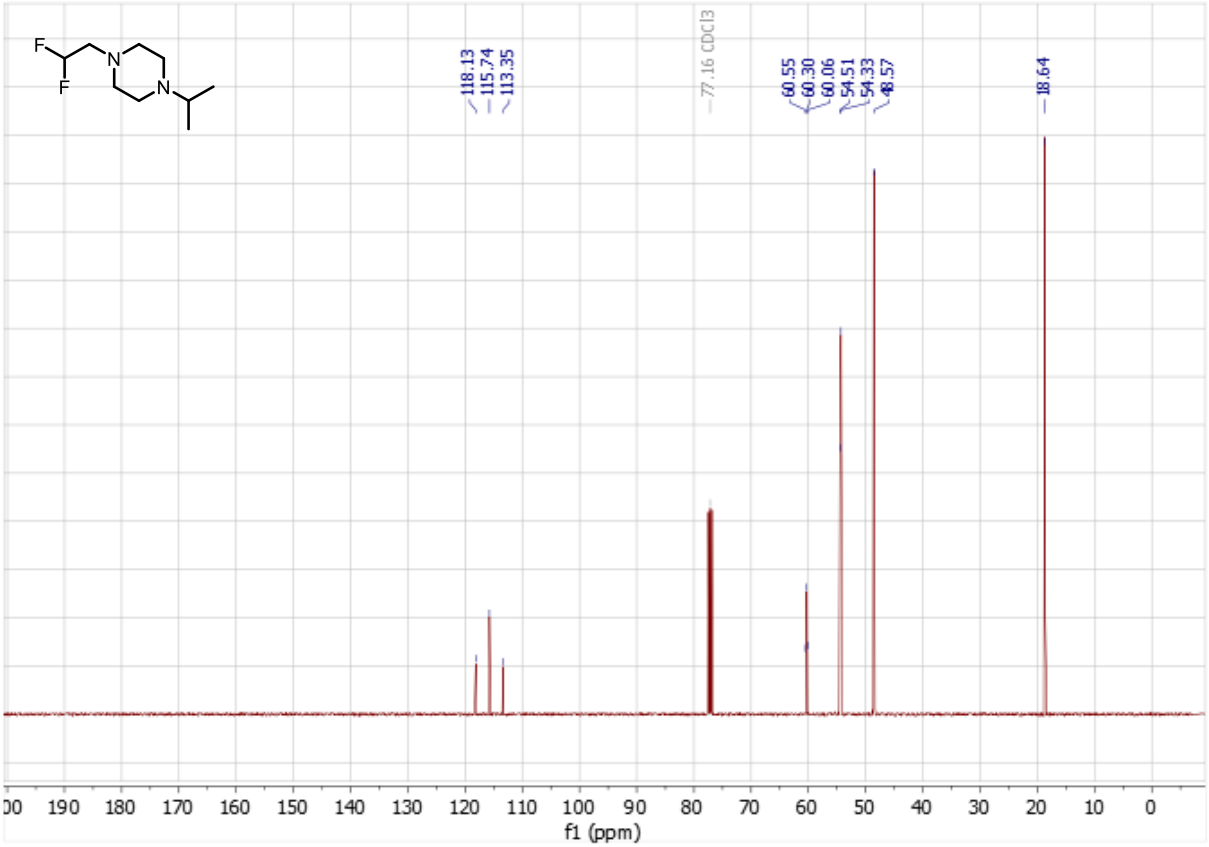

F
F
N
118.16
2.00
40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -20
f1 (ppm)

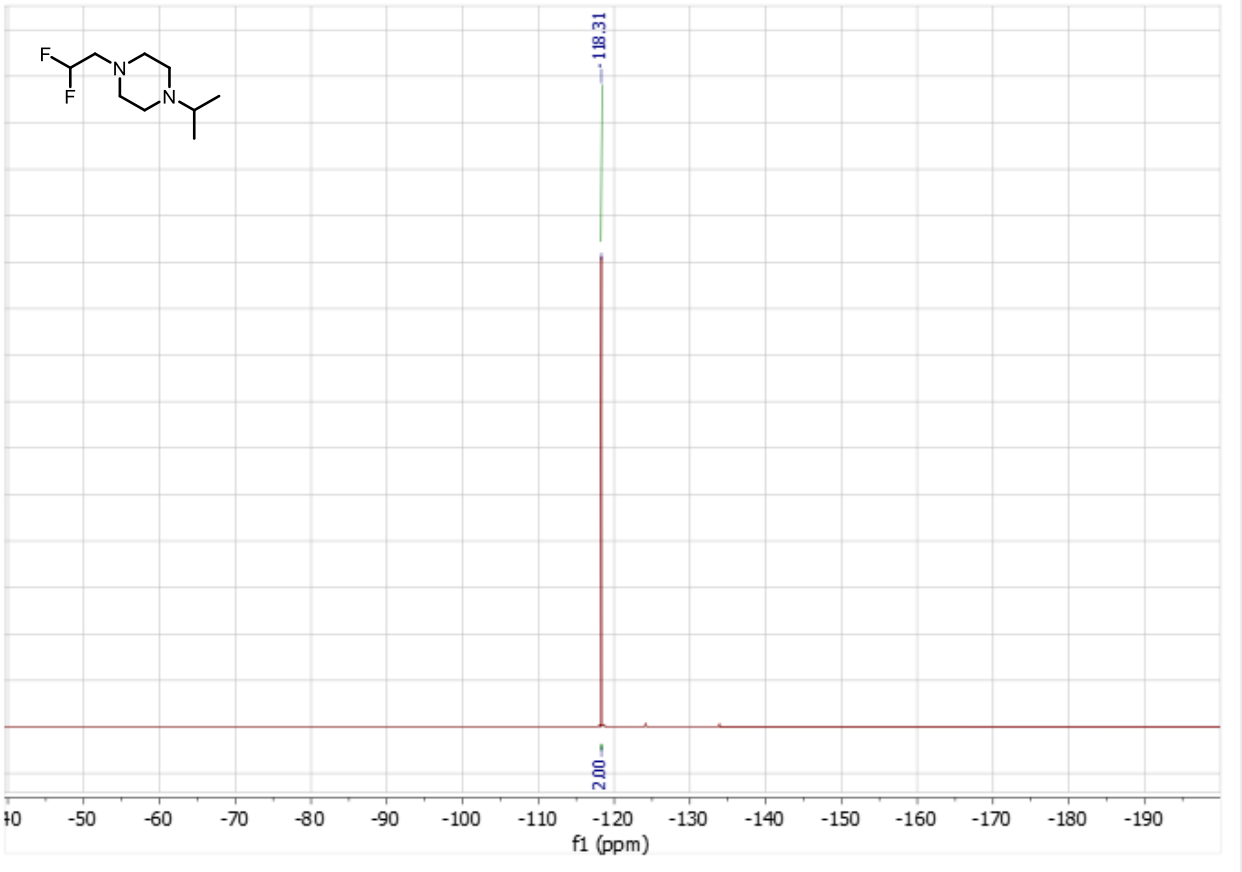

F
F
N
O
7.26 CDCl3
6.02
6.01
6.00
5.88
5.87
5.86
5.74
5.73
5.72
3.71
3.70
3.70
3.69
2.76
2.75
2.74
2.72
2.71
2.70
2.69
2.67
2.62
2.58
2.57
2.57
2.56
2.56
1.00
3.88
2.03
3.88
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

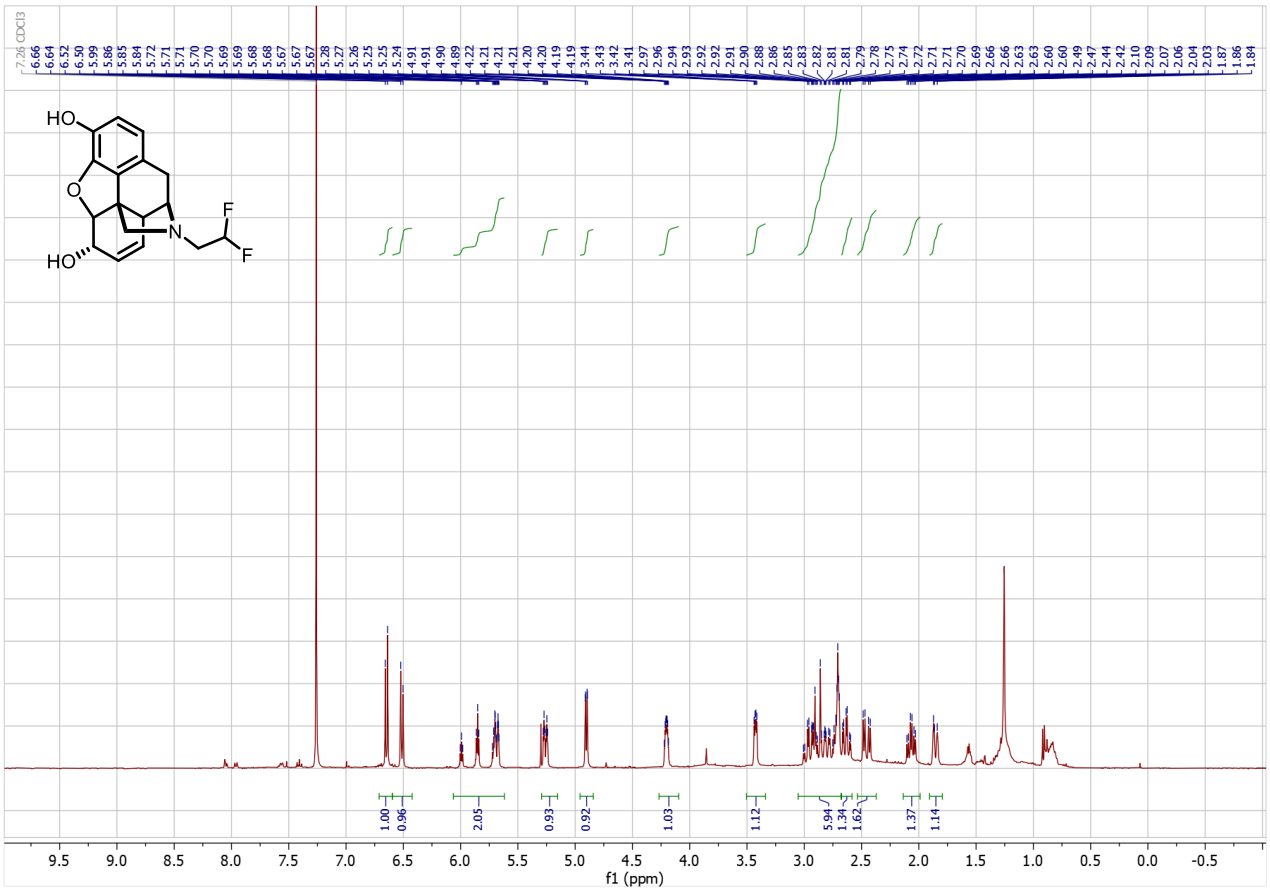

F
F
N
O
118.15
115.76
113.36
77.16 CDCl3
66.96
60.89
60.64
60.40
54.39
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


F
F
N
O
118.34
2.00
-50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

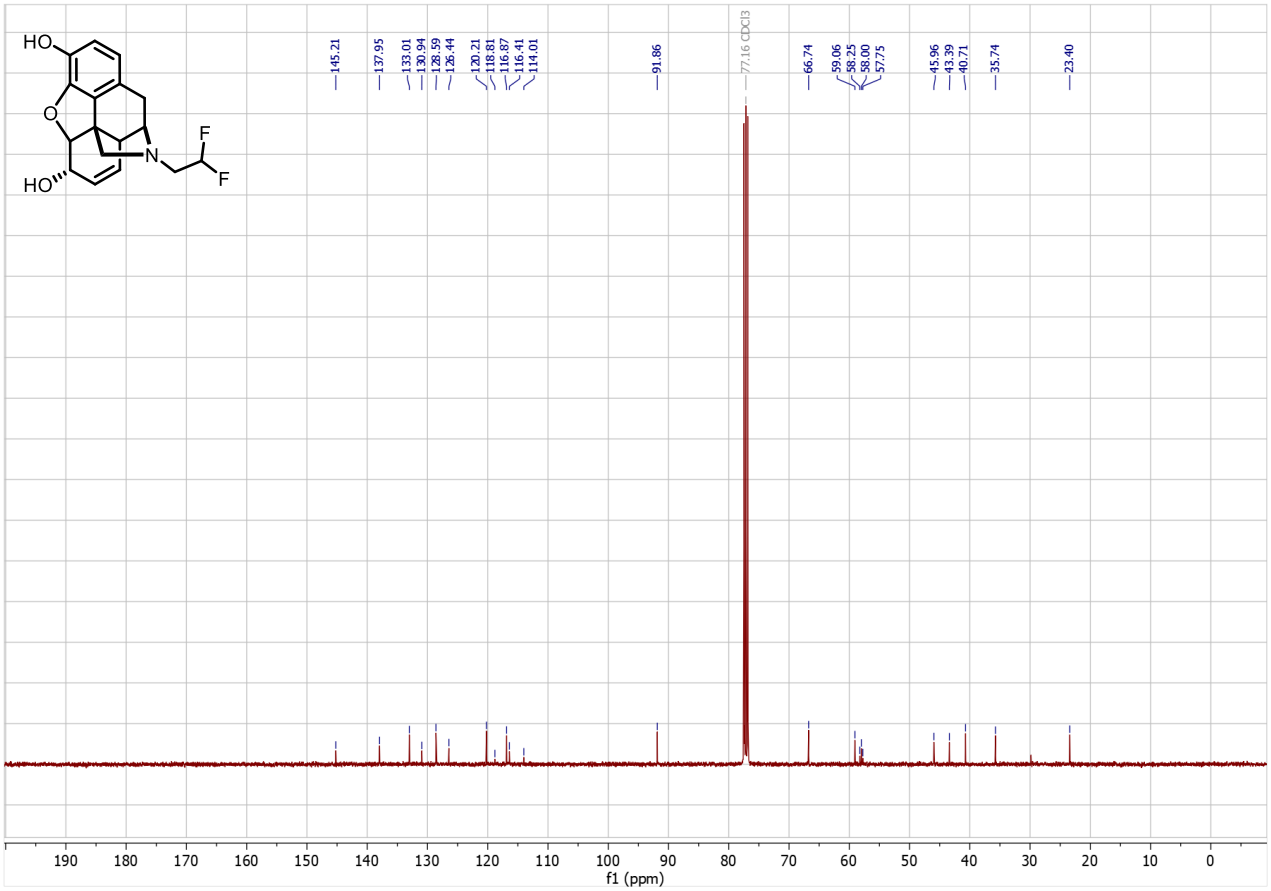

F
F
N
N
7.26 CDCl3
6.00
5.99
5.98
5.86
5.85
5.84
5.72
5.71
5.70
2.75
2.74
2.71
2.70
2.68
2.66
2.65
2.63
2.62
2.60
2.60
2.59
2.55
2.53
2.52
1.03
1.01
1.00
2.08
8.93
2.88
2.96
f1 (ppm)

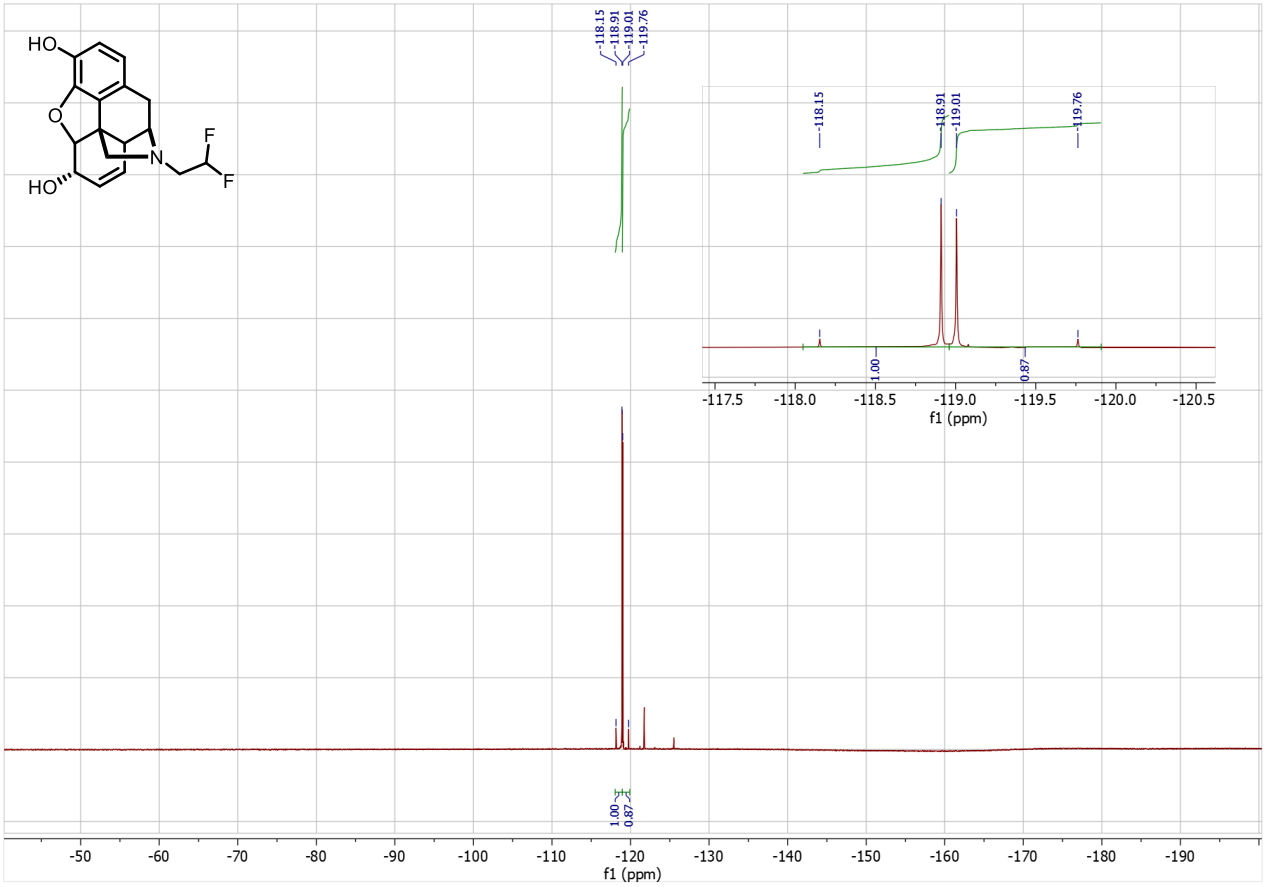

F
F
N
N
118.13
115.74
113.35
77.16 CDCl3
60.55
60.30
60.06
54.51
54.33
18.64
f1 (ppm)

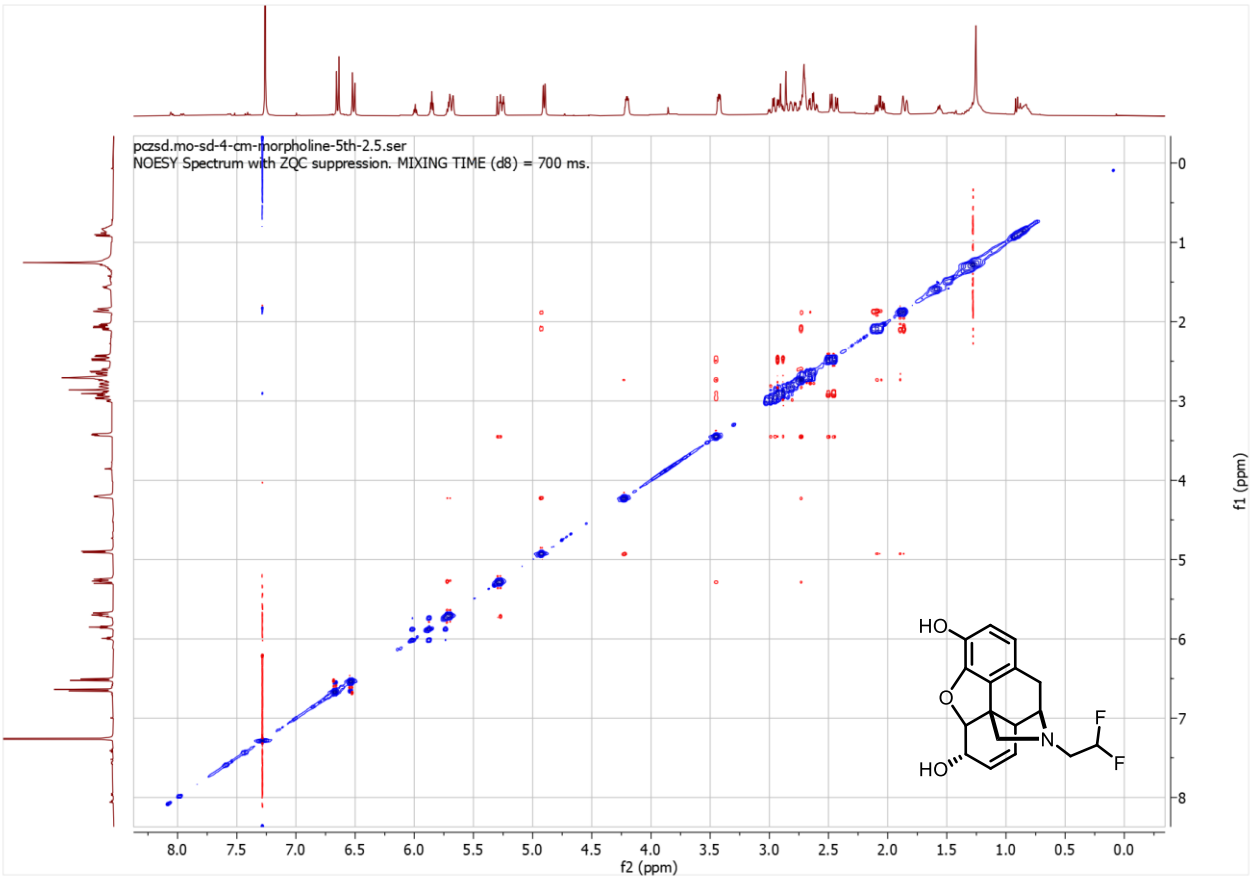

F
F
N
N
118.31
2.00
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

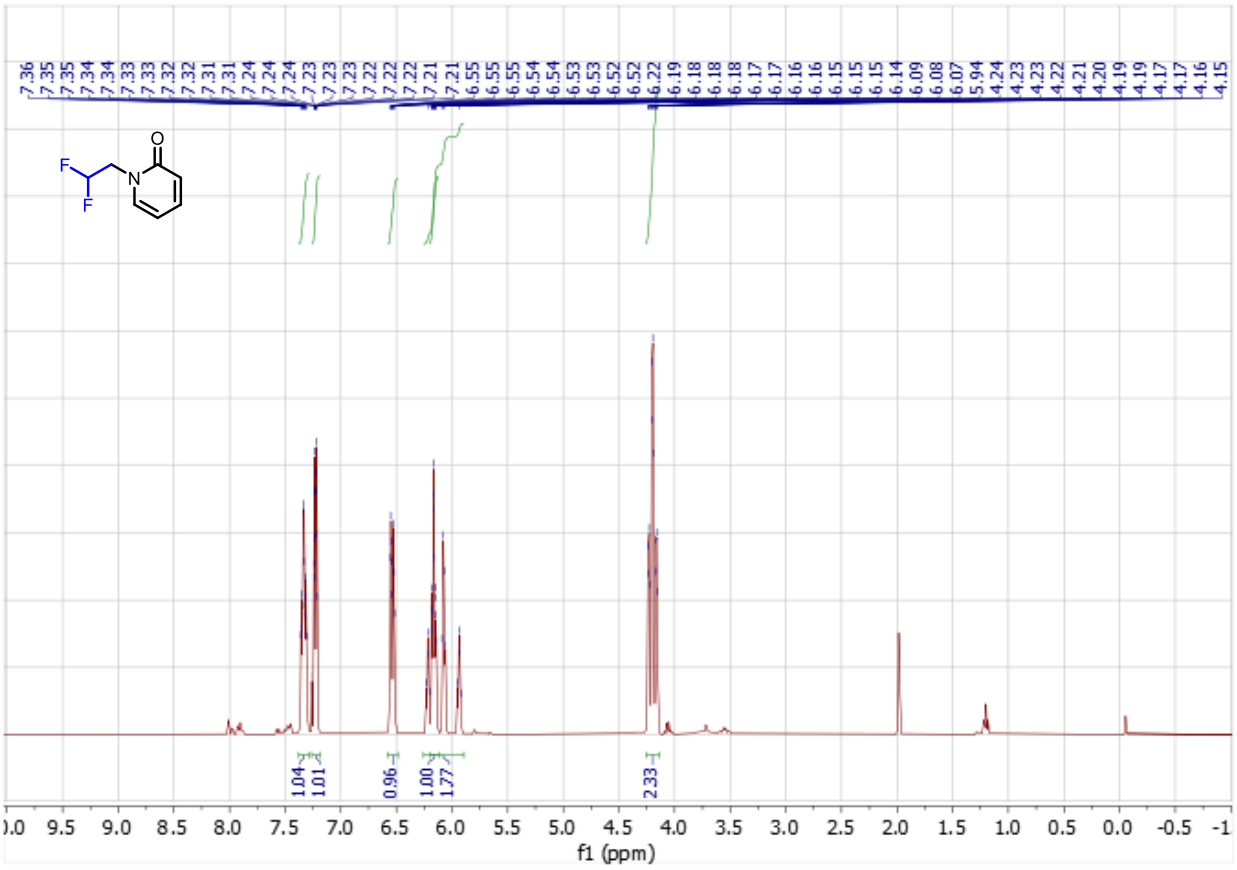

HO
O
N
F
F
HO
7.26 CDCl3
1.00
0.96
2.05
0.93
0.92
1.03
1.12
5.94
1.34
1.62
1.37
1.14
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

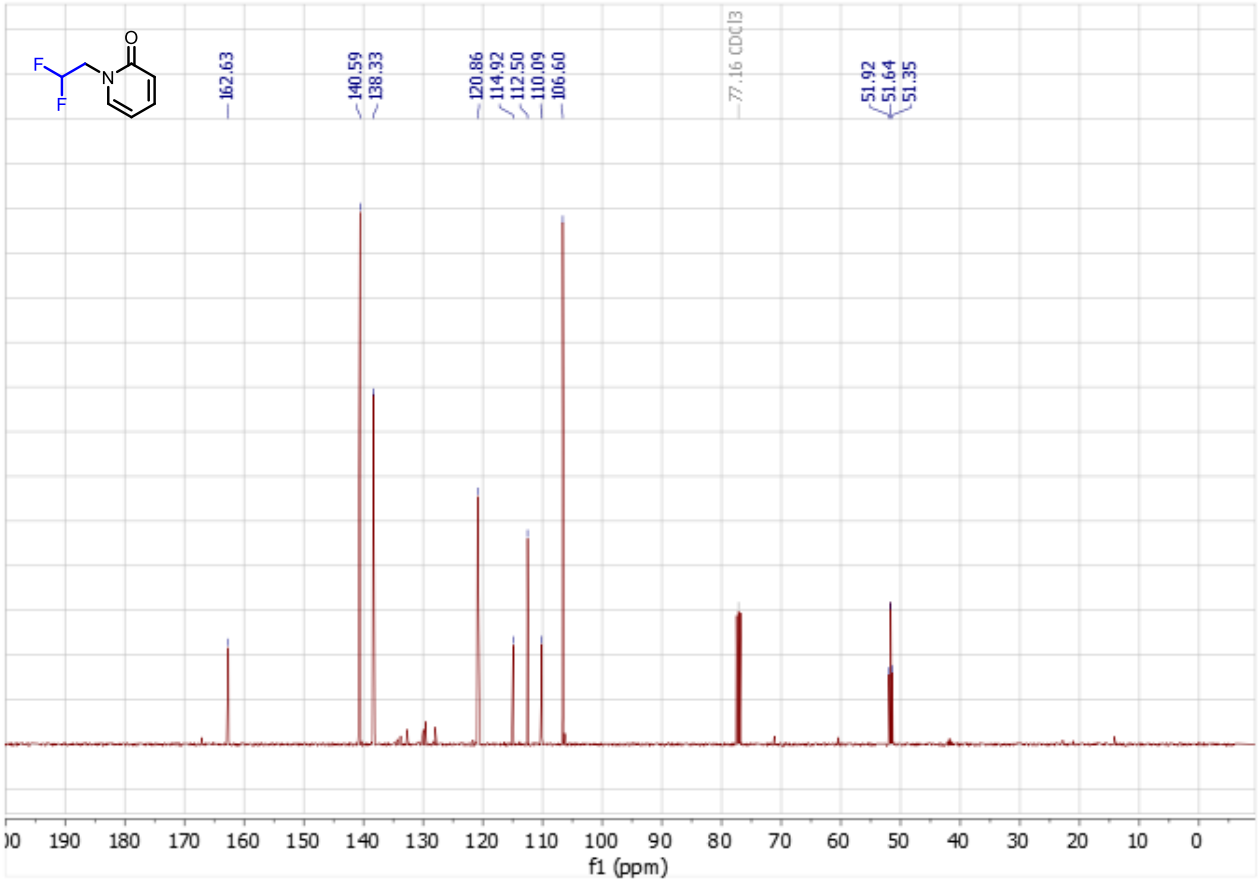
SUPPORTING INFORMATION

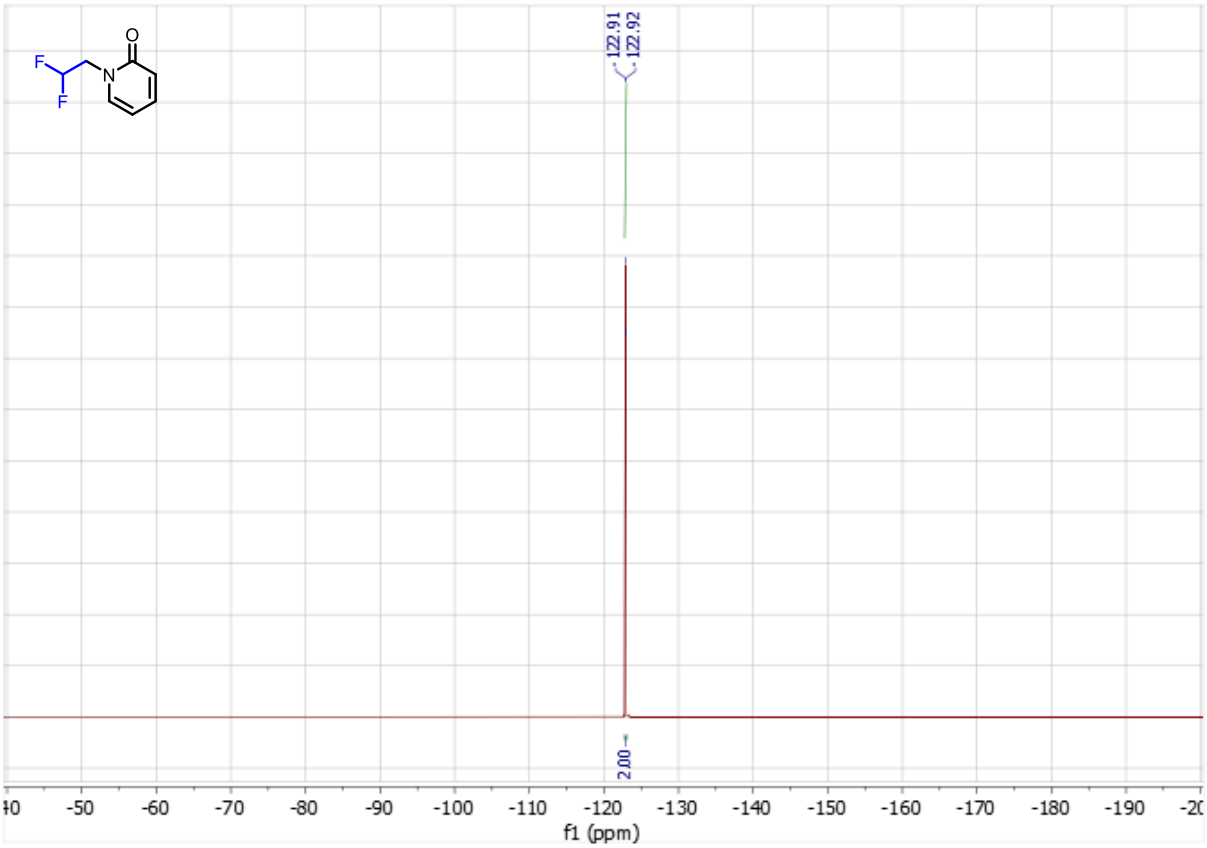


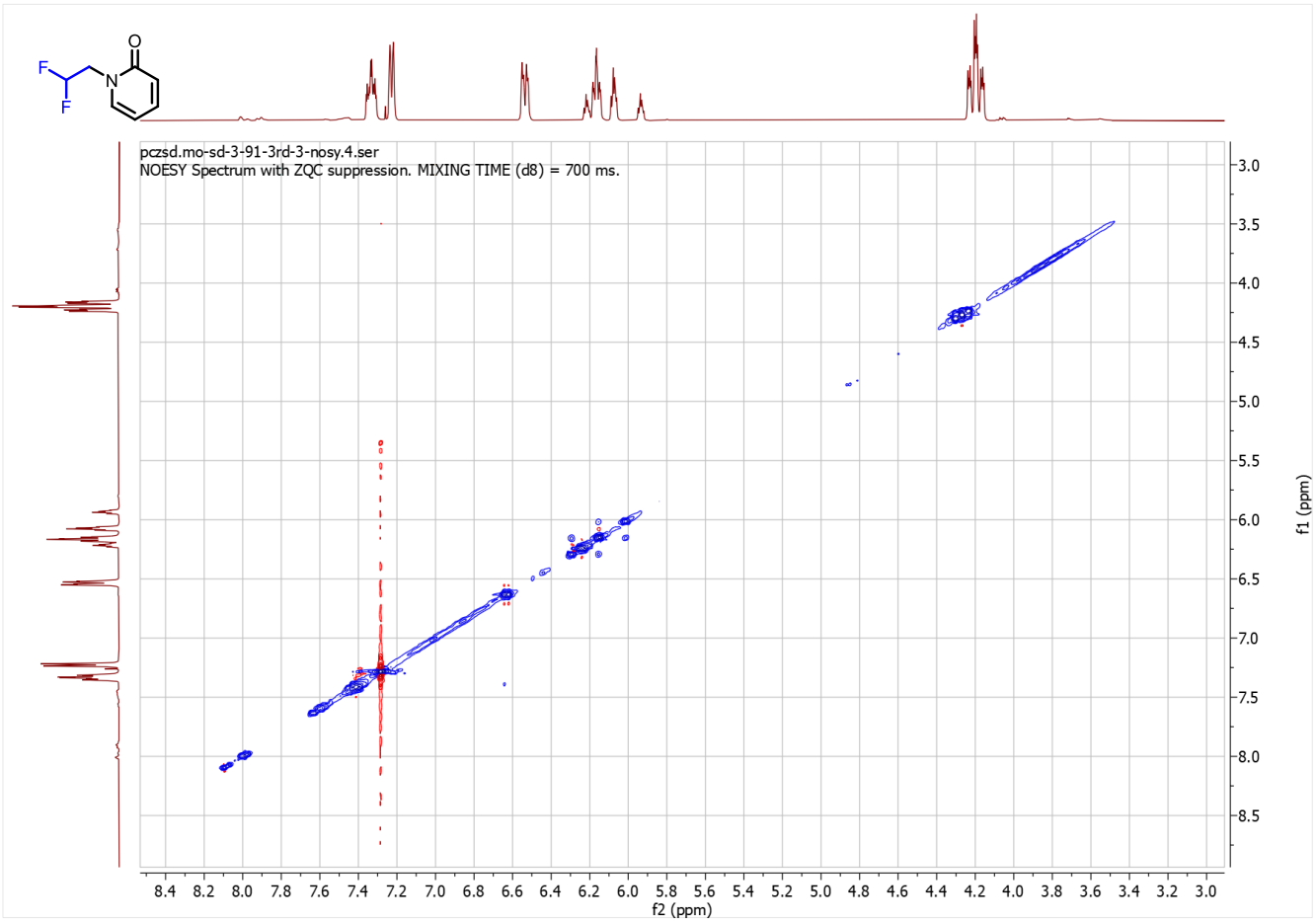



pczsd.mo-sd-4-cm-morpholine-5th-2.5.ser
NOESY Spectrum with ZQC suppression. MIXING TIME (d8) = 700 ms.
f2 (ppm)
f1 (ppm)
HO
O
HO
N
F
F

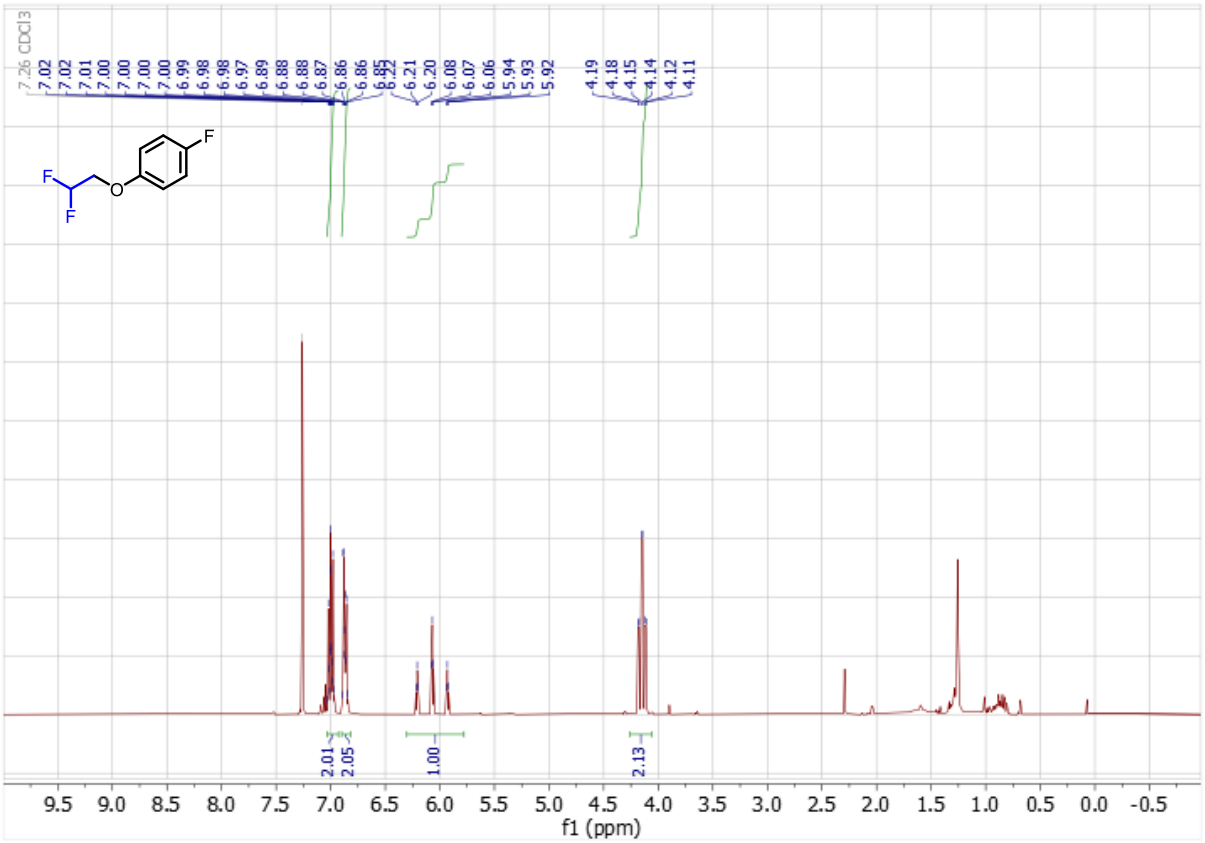

O
F
F
N
1.04
1.01
0.96
1.00
1.77
2.33
f1 (ppm)

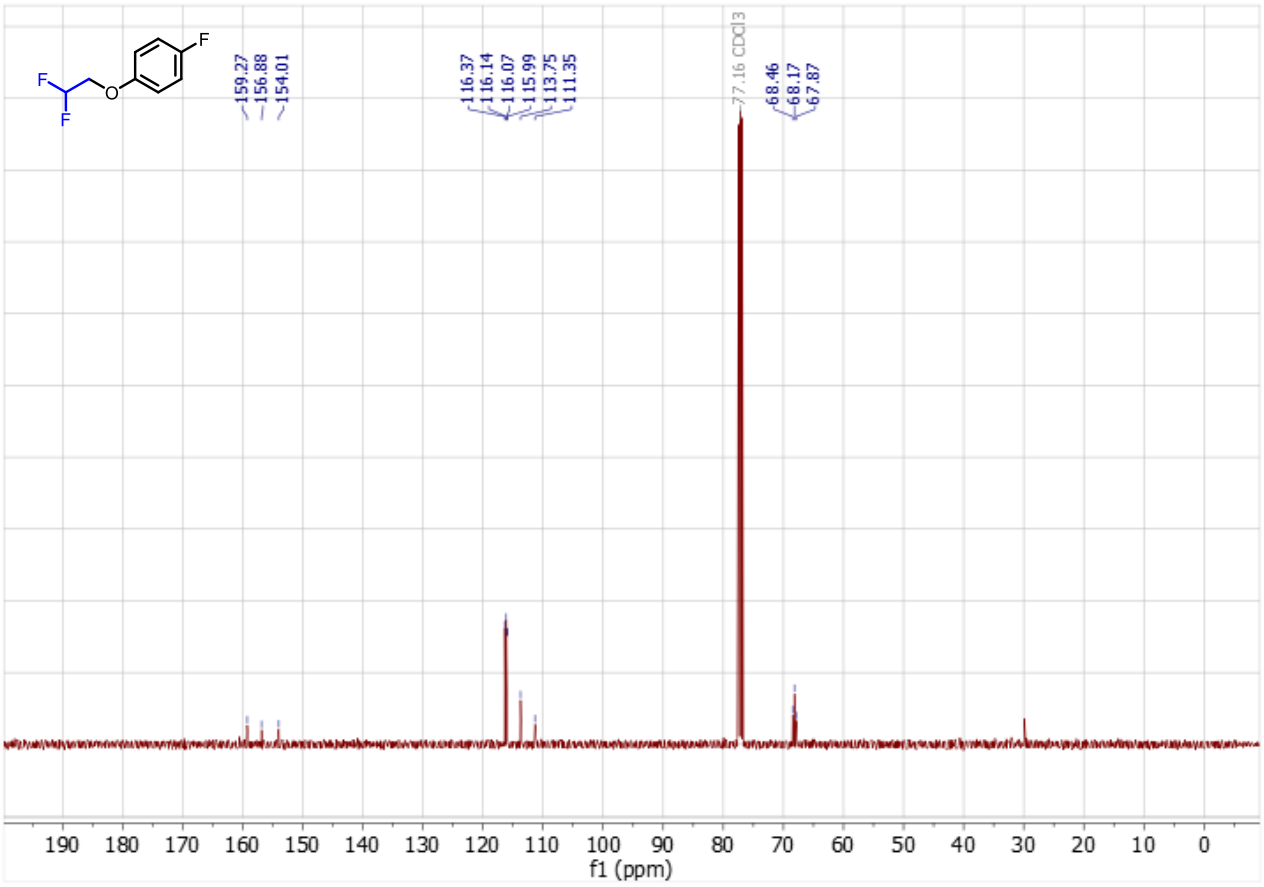

F
F
N
O
162.63
140.59
138.33
120.86
114.92
112.50
110.09
106.60
77.16 CDCl3
51.92
51.64
51.35
f1 (ppm)

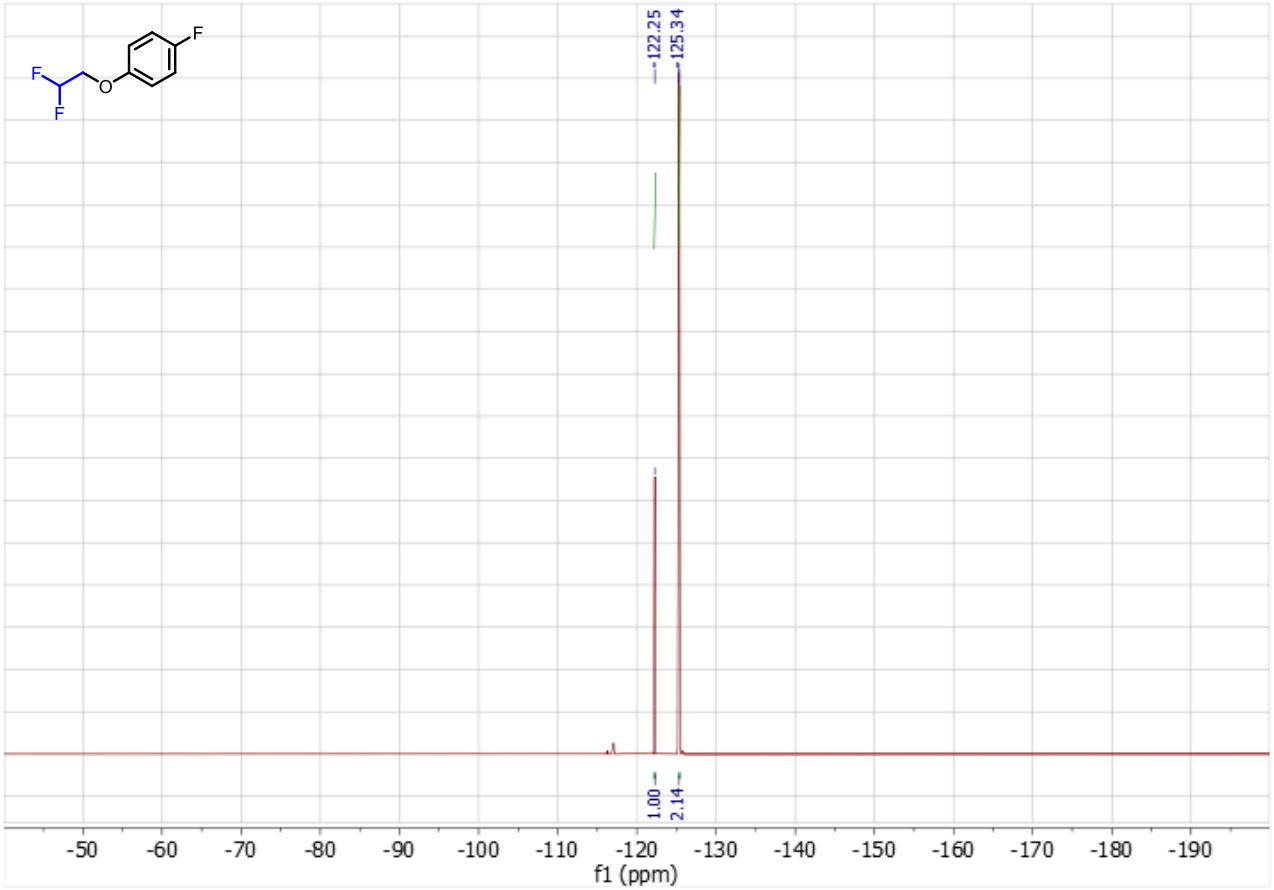

F
F
N
O
122.91
122.92
2.00
f1 (ppm)

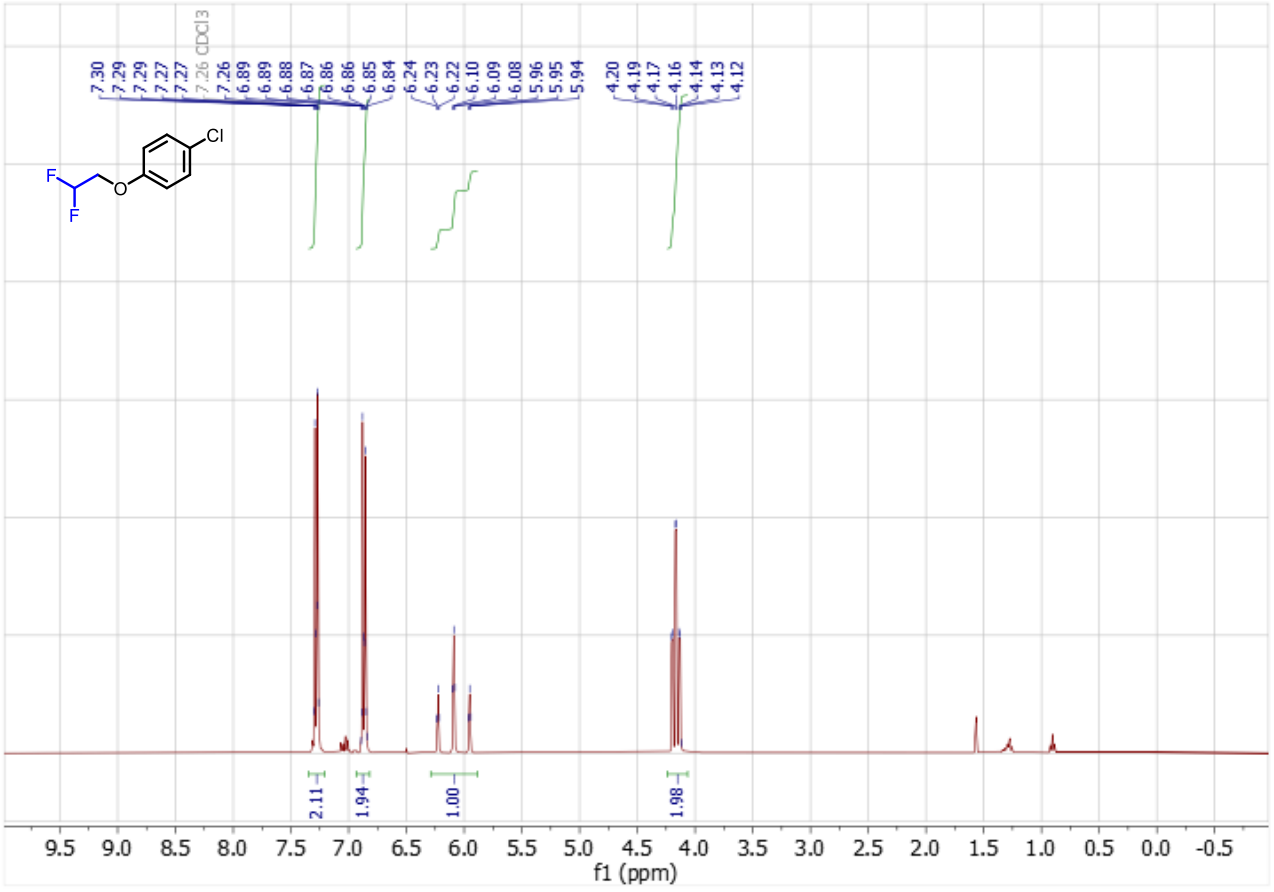

pczsd.mo-sd-3-91-3rd-3-nosy.4.ser
NOESY Spectrum with ZQC suppression. MIXING TIME (d8) = 700 ms.
f2 (ppm)
f1 (ppm)

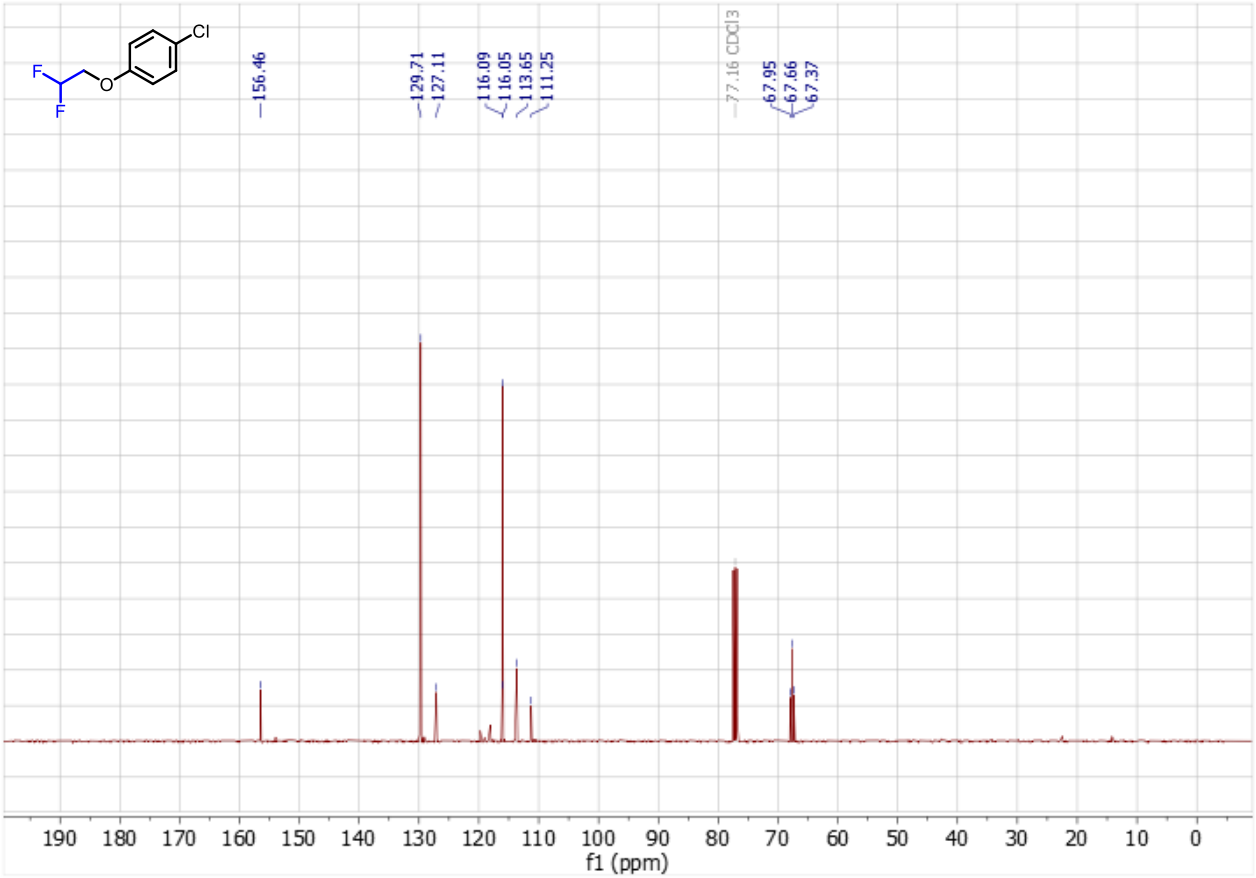
6.3 2,2-Difluoroethylethers (6)

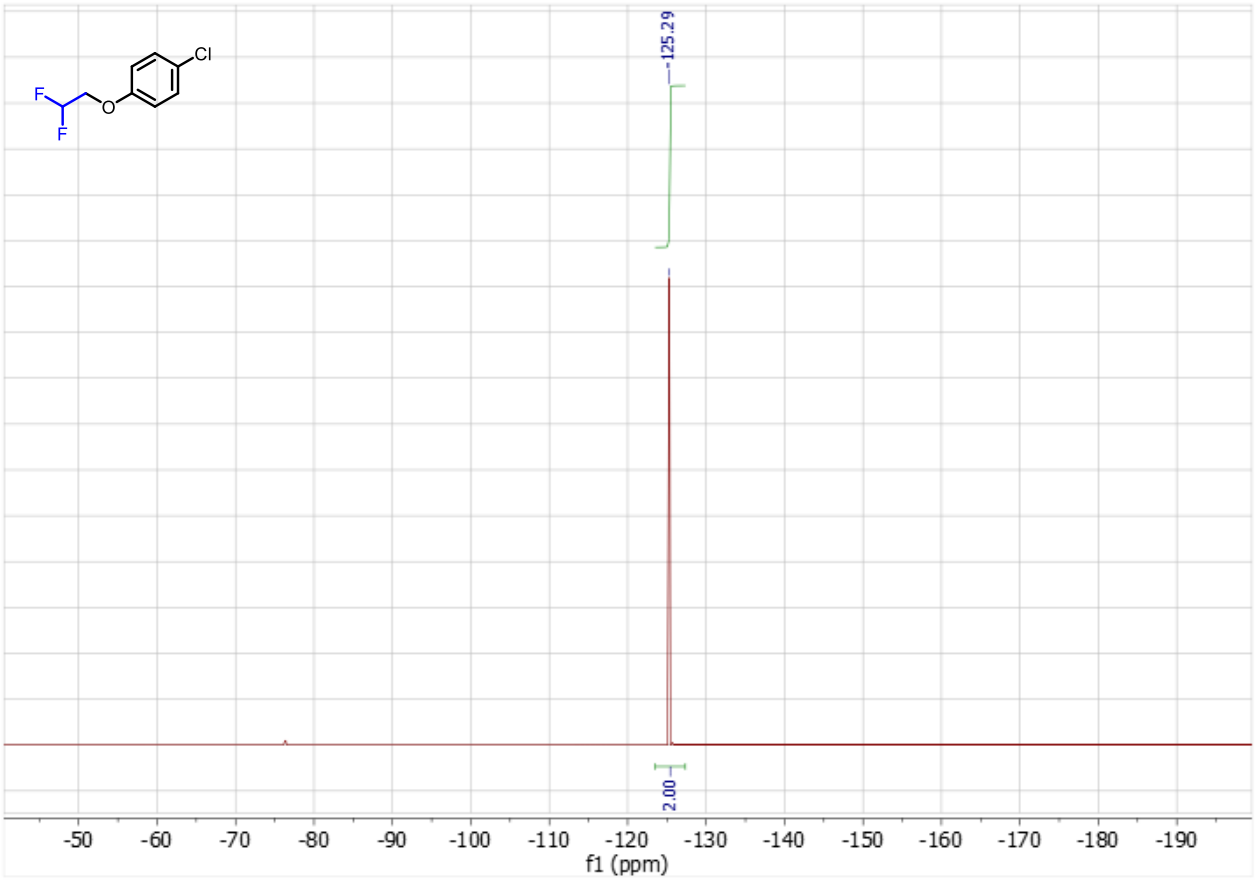


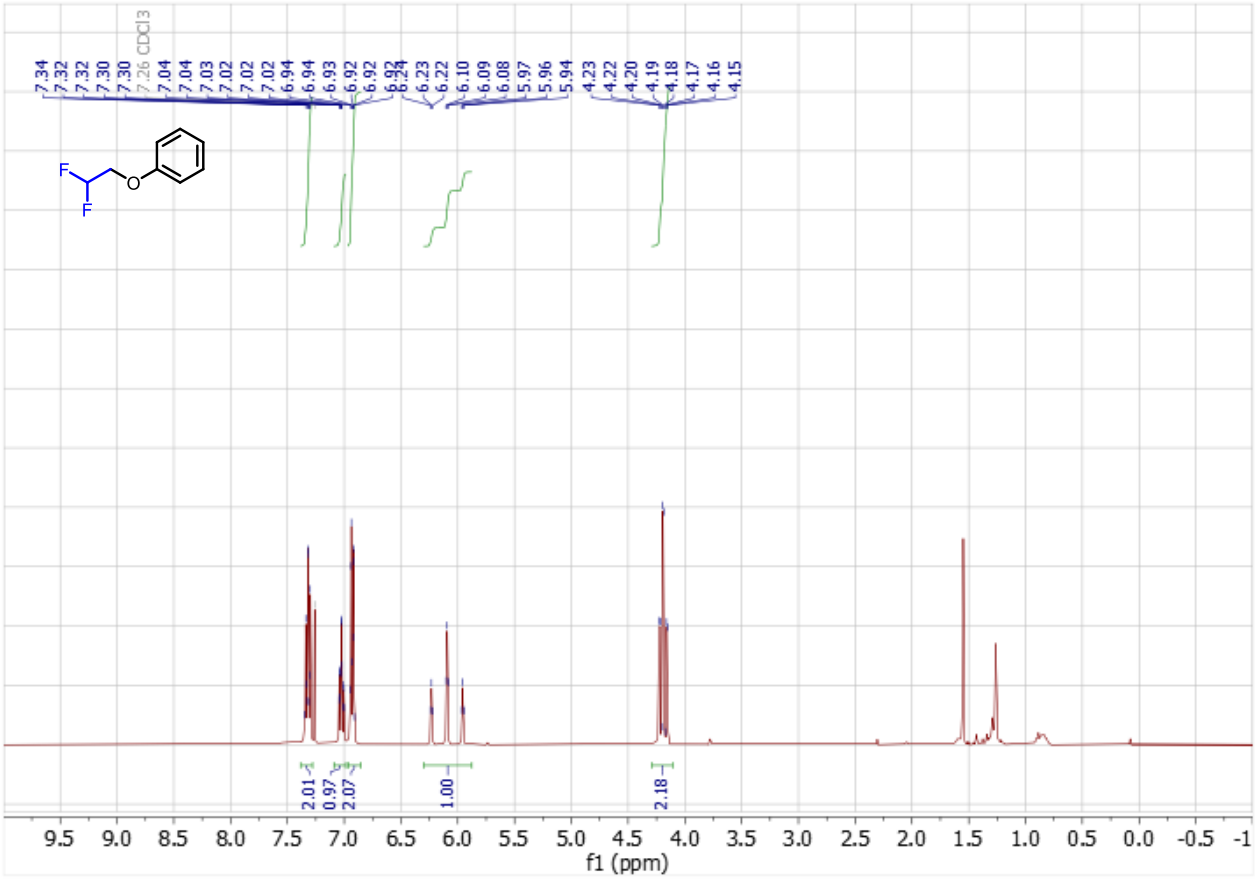


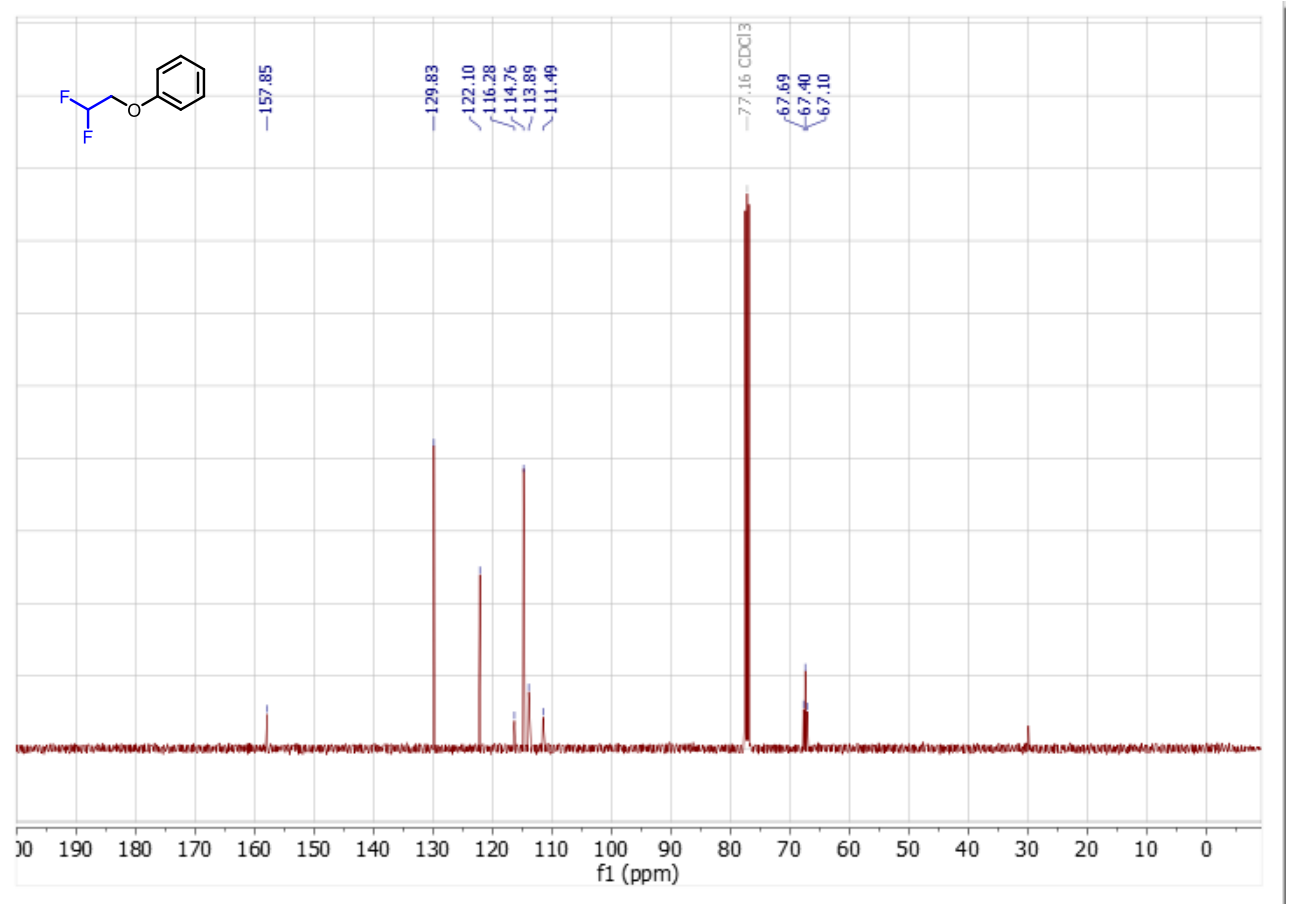

F
F
F
O
122.25
125.34
1.00
2.14
-50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

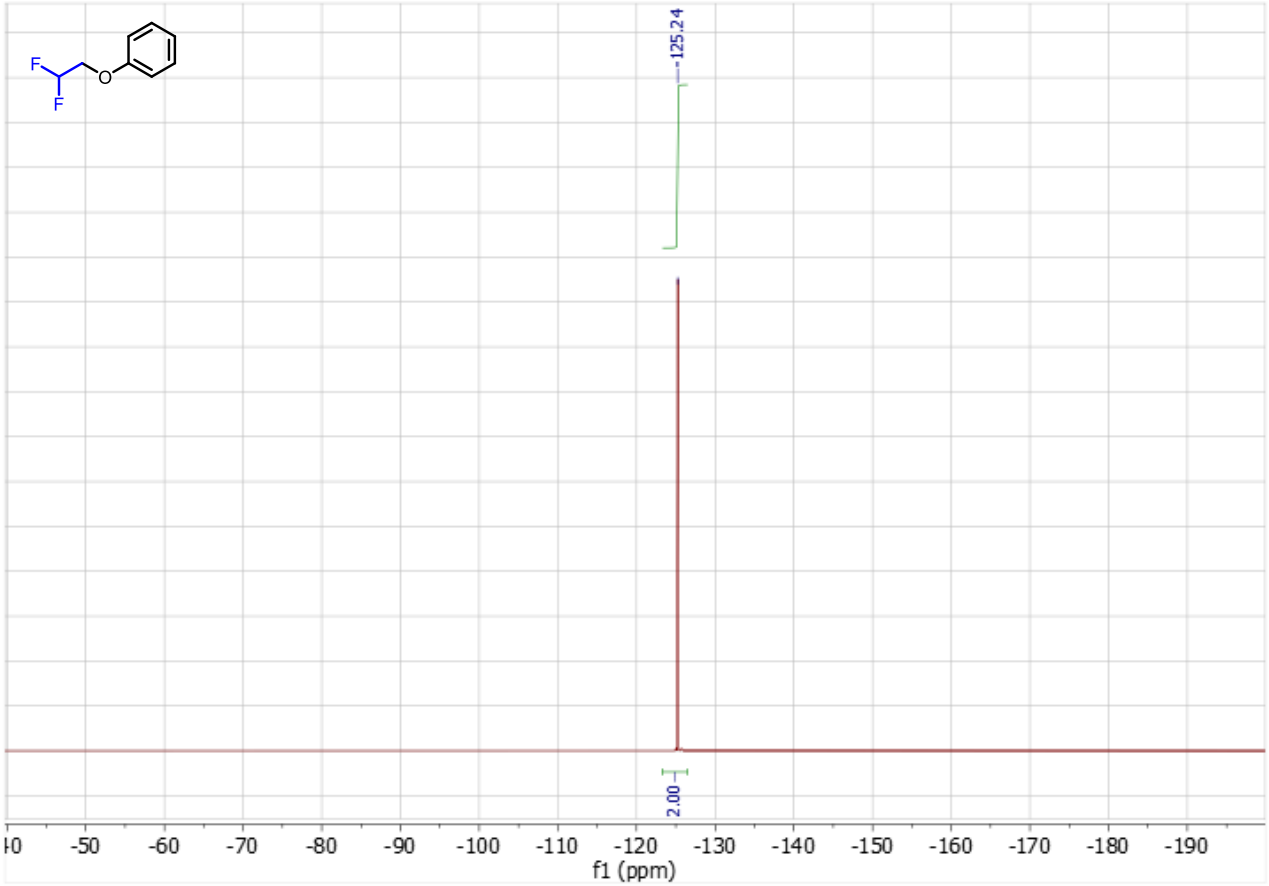

7.30 7.29 7.29 7.27 7.27 7.26 CDCl3 7.26 6.89 6.89 6.88 6.87 6.86 6.86 6.85 6.84
6.24 6.23 6.22 6.10 6.09 6.08 5.96 5.95 5.94
4.20 4.19 4.17 4.16 4.14 4.13 4.12
Cl
F
F
O
2.11
1.94
1.00
1.98
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

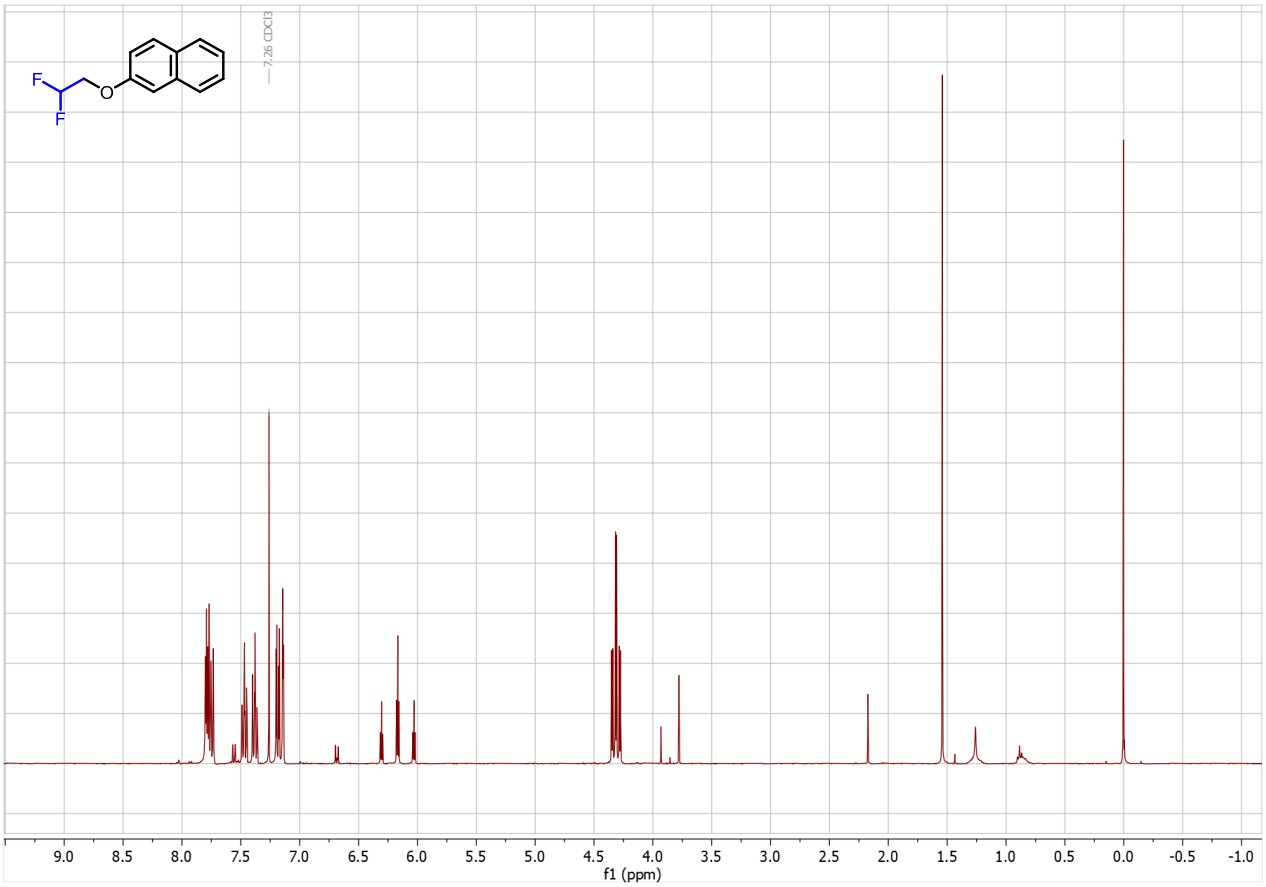

Cl
F
F
O
156.46
129.71
127.11
116.09
116.05
113.65
111.25
77.16 CDCl3
67.95
67.66
67.37
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

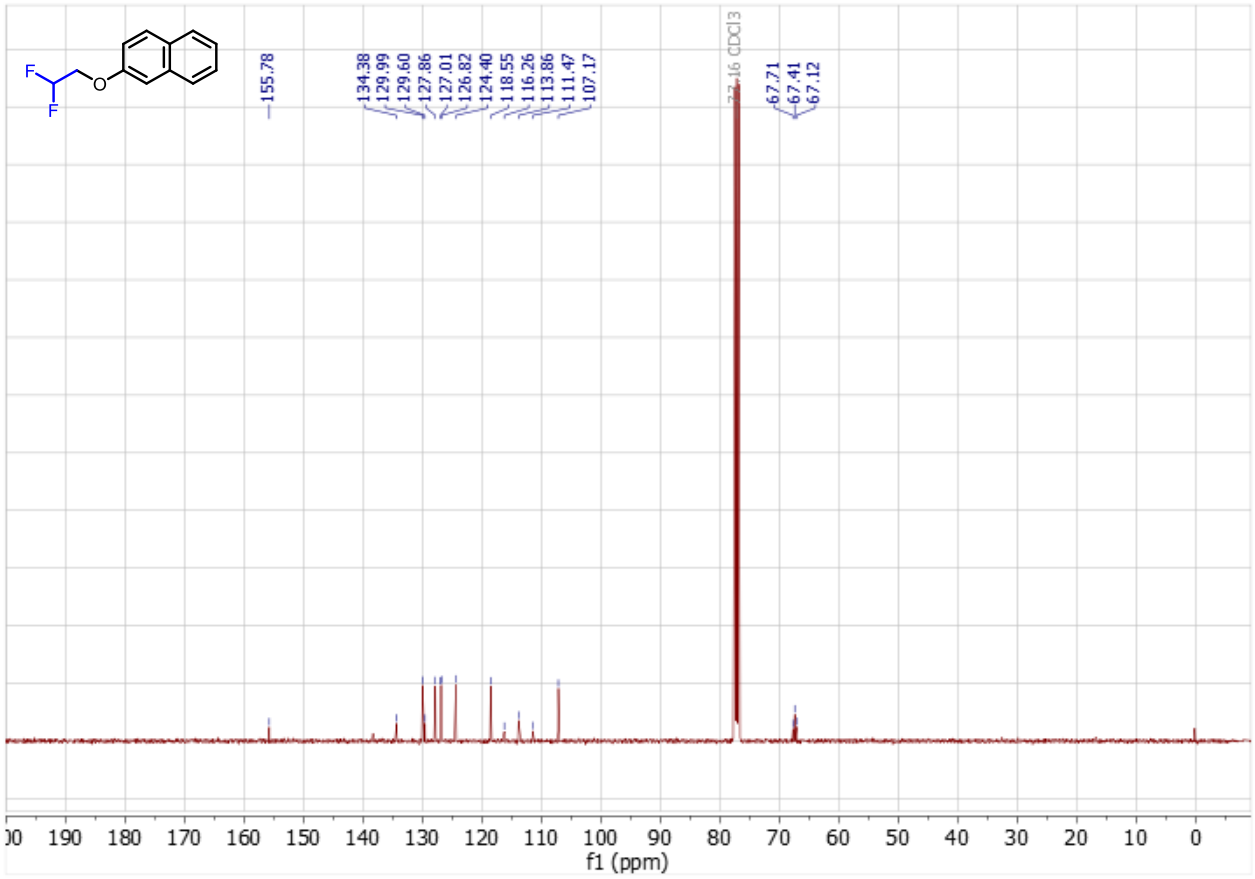

Cl
F
F
O
125.29
2.00
-50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

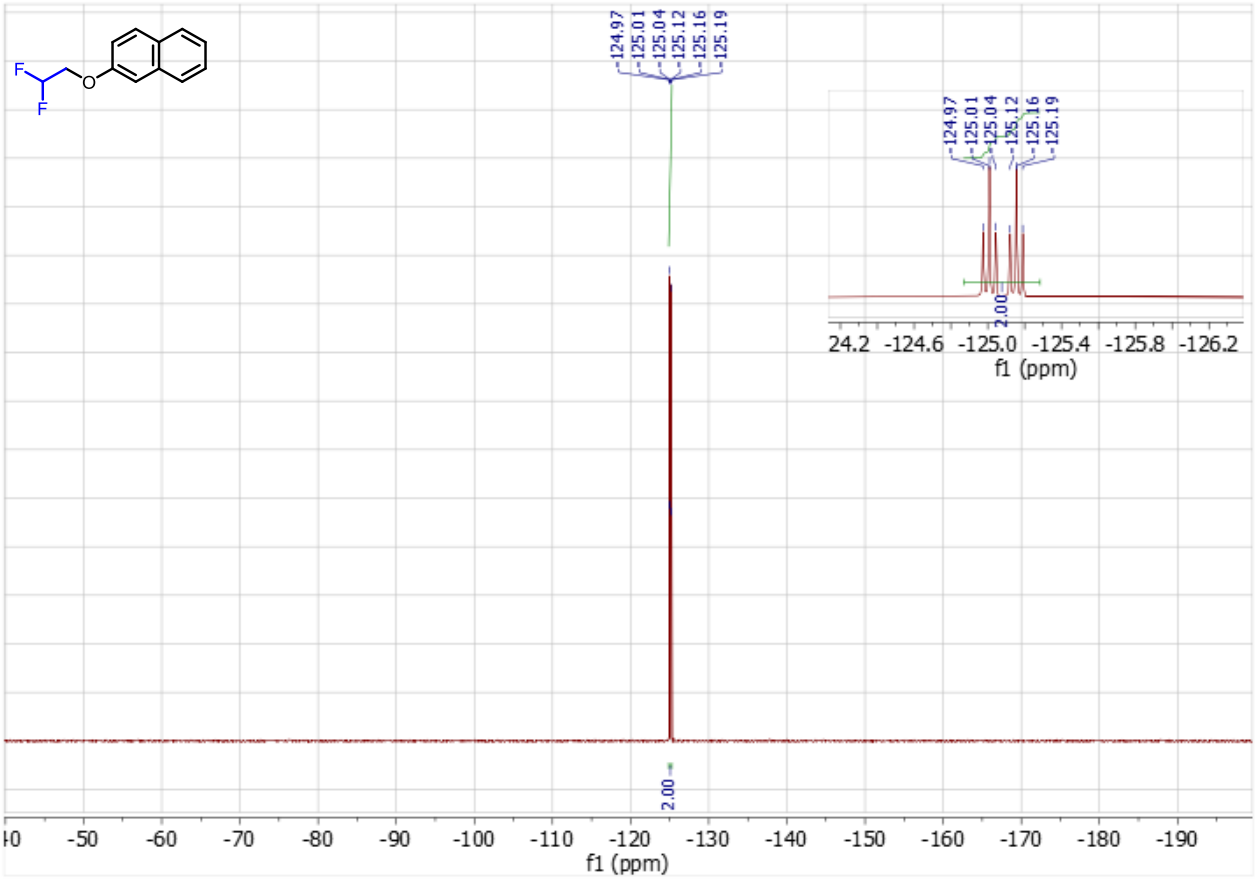

7.34
7.32
7.32
7.30
7.30
7.26 CDCl3
7.04
7.04
7.03
7.02
7.02
7.02
6.94
6.94
6.93
6.92
6.92
6.24
6.23
6.22
6.10
6.09
6.08
5.97
5.96
5.94
4.23
4.22
4.20
4.19
4.18
4.17
4.16
4.15
F
F
O
2.01
0.97
2.07
1.00
2.18
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

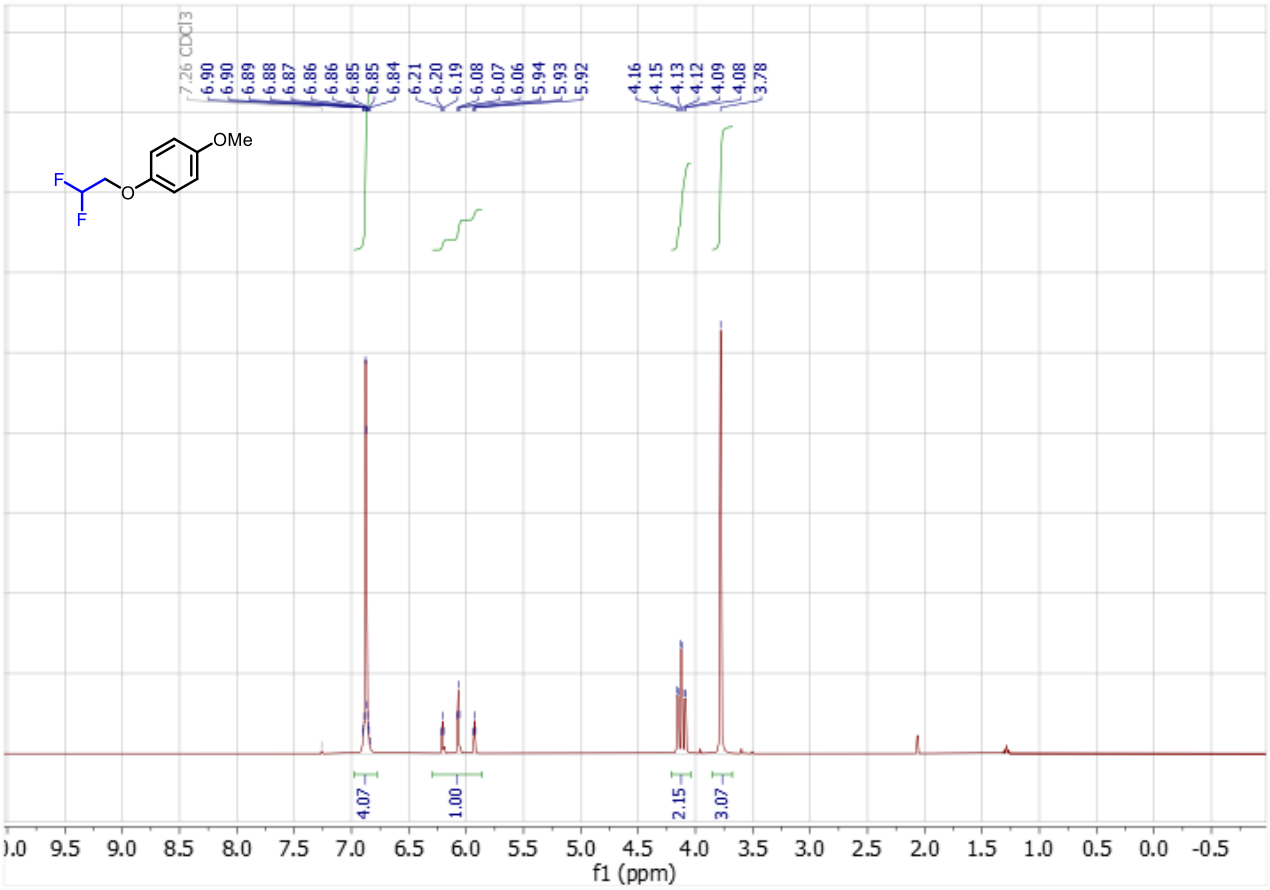

F
F
O
157.85
129.83
122.10
116.28
114.76
113.89
111.49
77.16 CDCl3
67.69
67.40
67.10
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

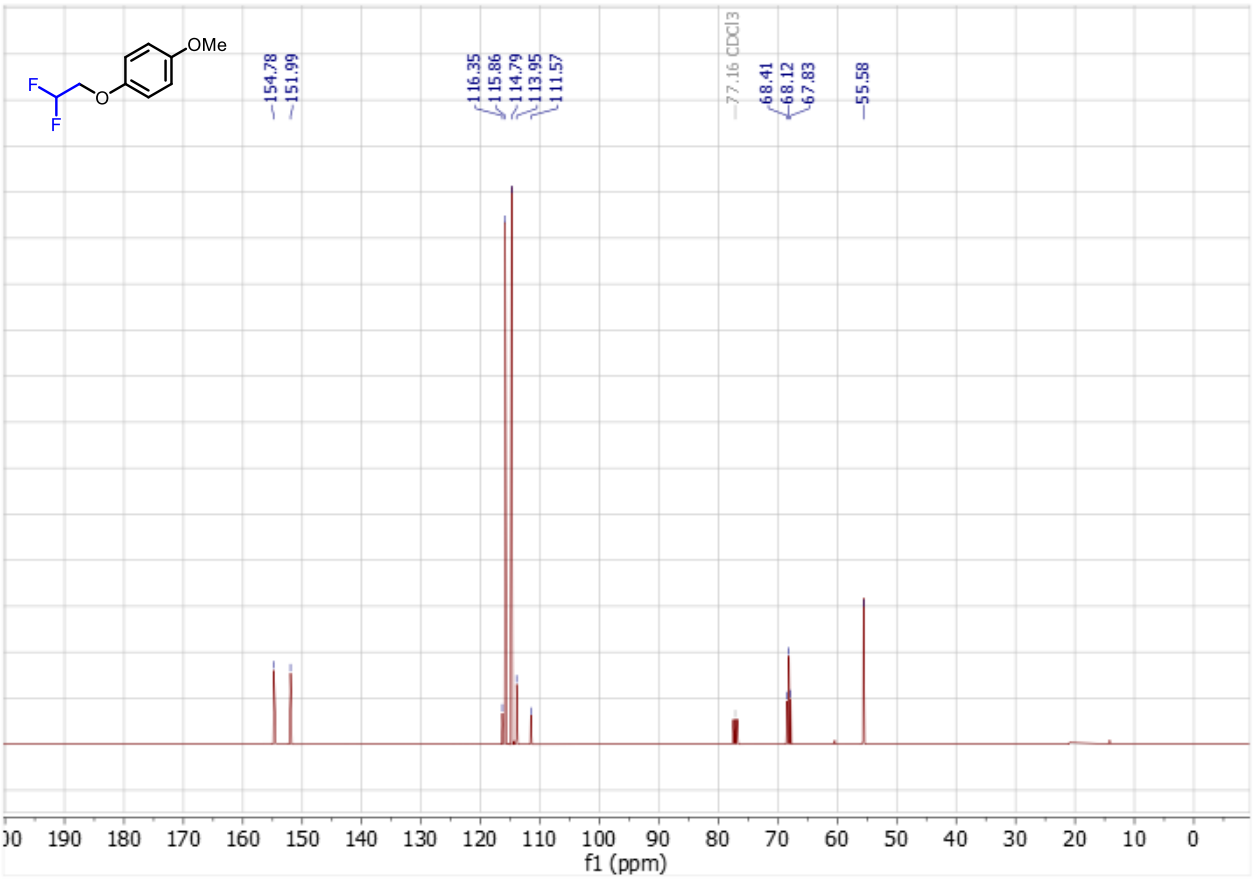

F
F
O
-125.24
2.00
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

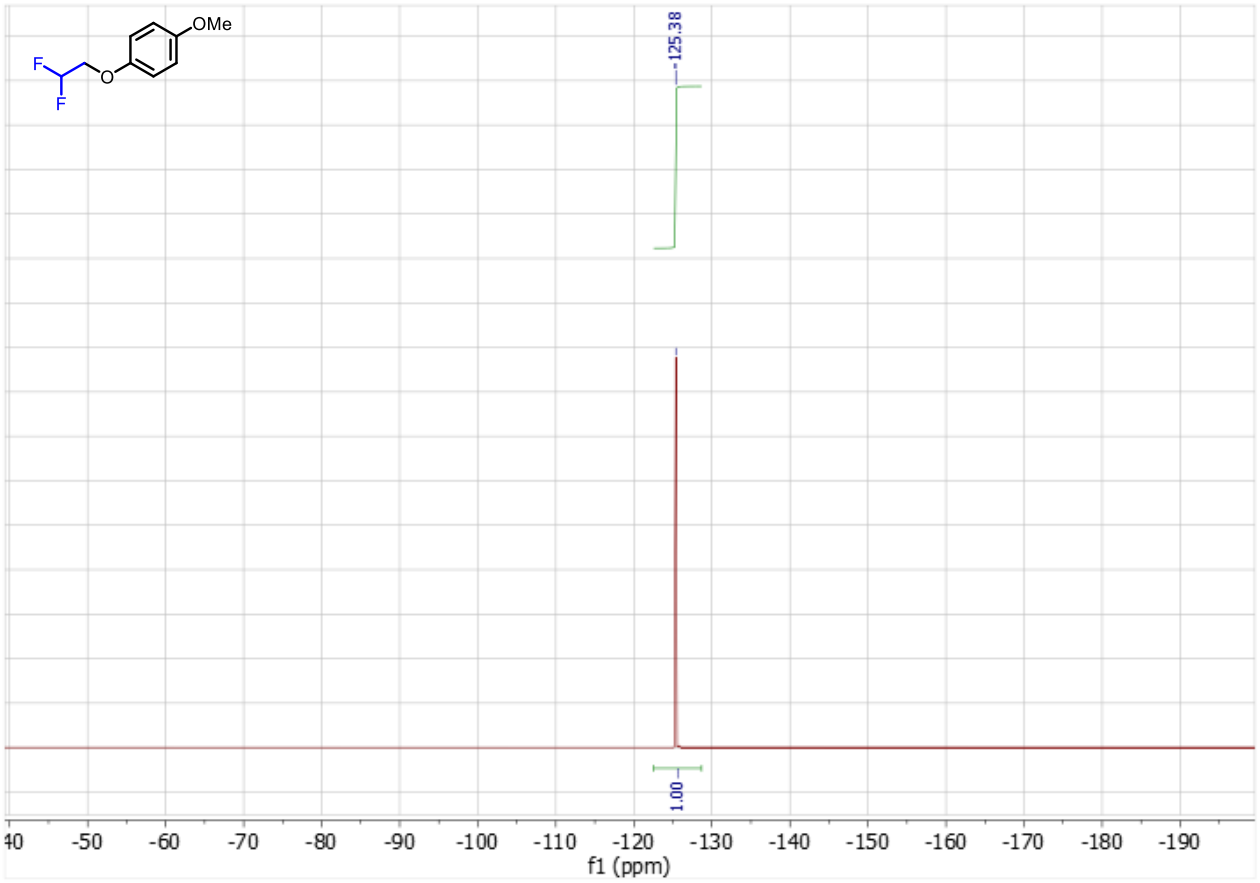

F
F
O
7.26 CDCl3
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

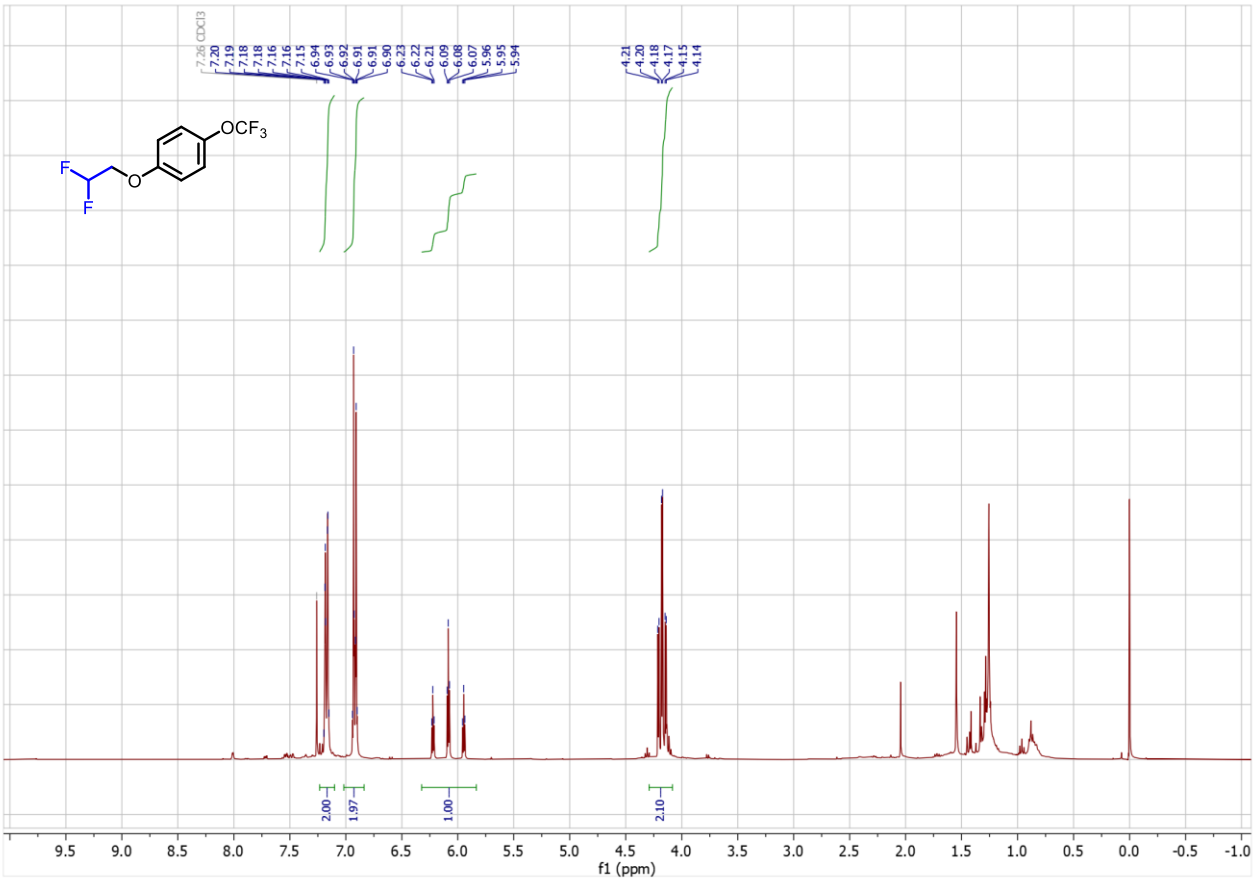

F
F
O
155.78
134.38
129.99
129.60
127.86
127.01
126.82
124.40
118.55
116.26
113.86
111.47
107.17
77.16 CDCl3
67.71
67.41
67.12
f1 (ppm)

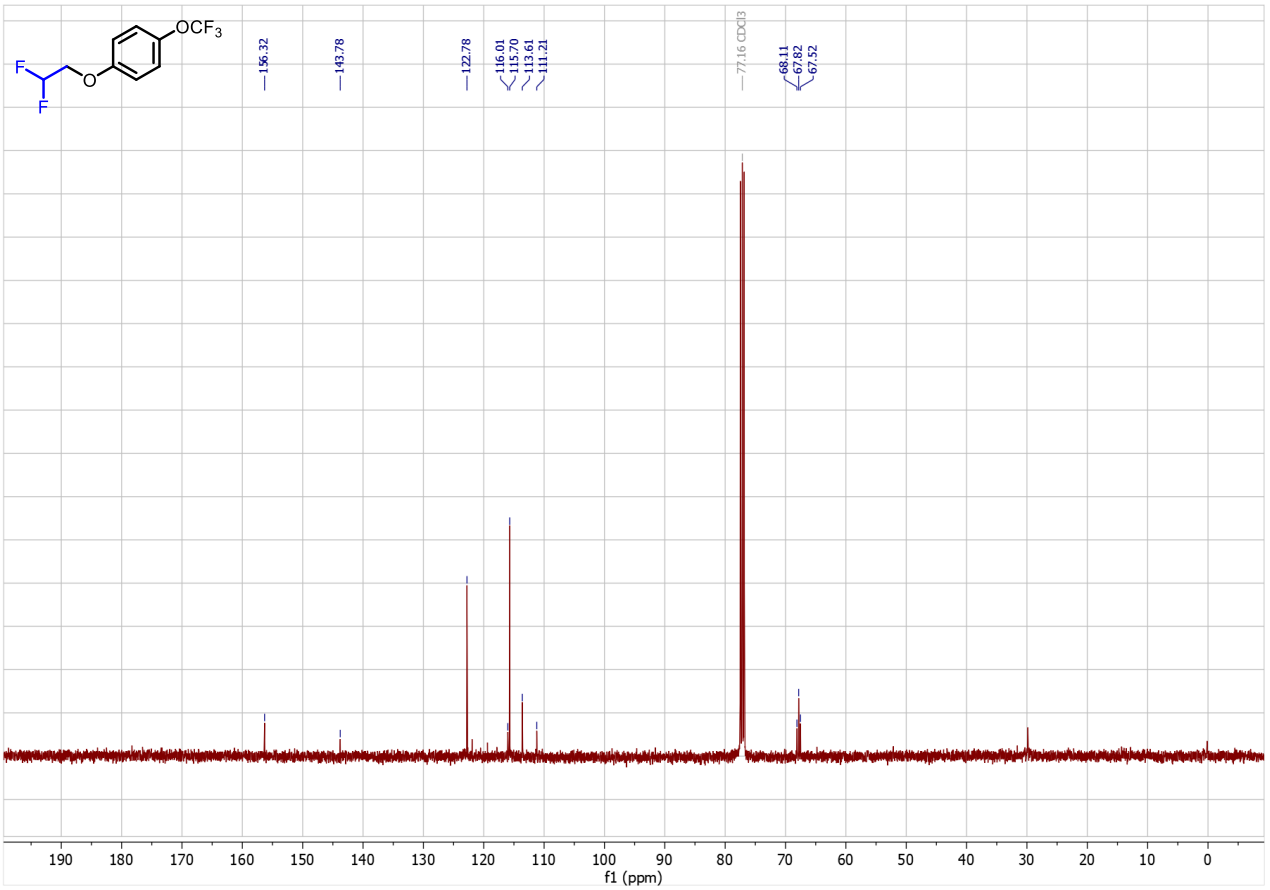

F
F
O
-124.97
-125.01
-125.04
-125.12
-125.16
-125.19
2.00
f1 (ppm)

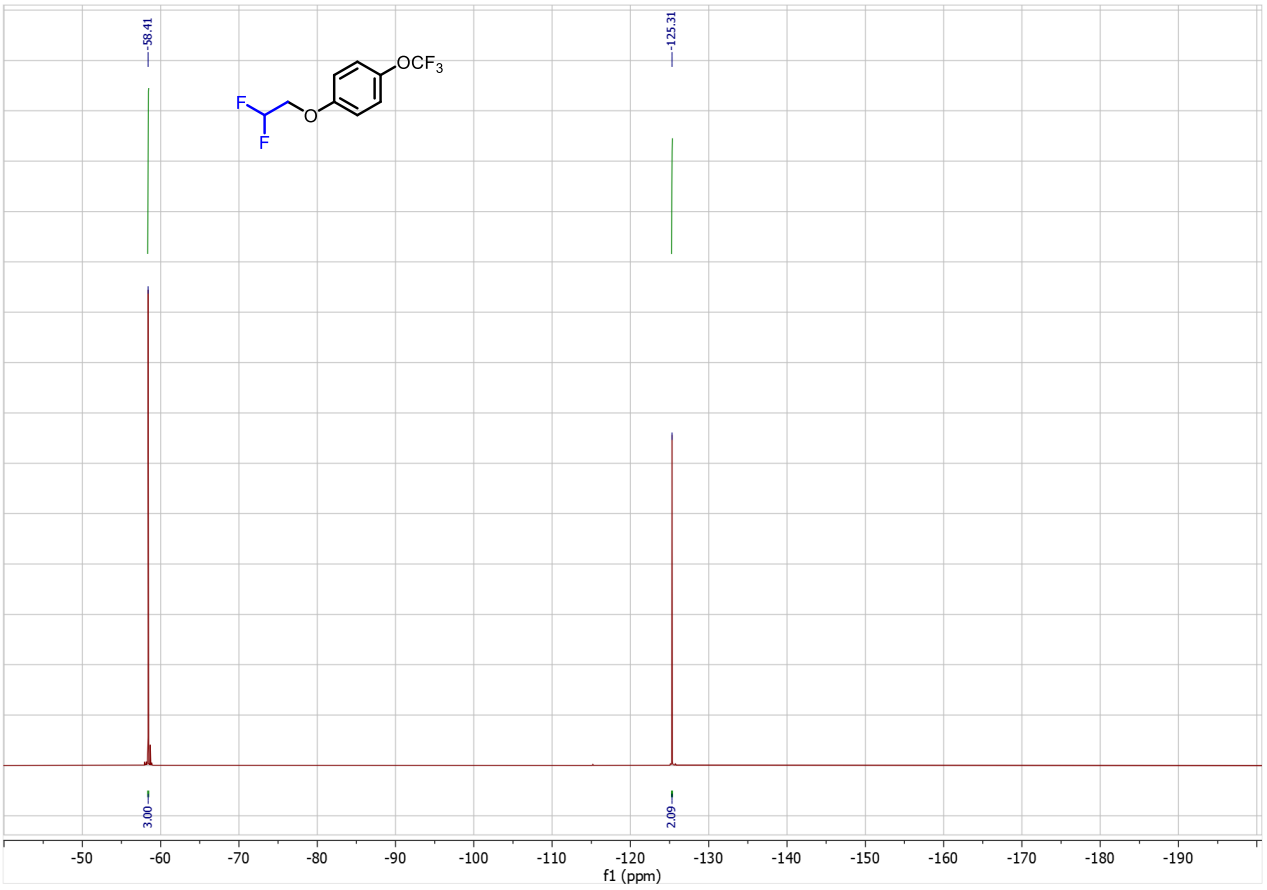

7.26 CDCl3
6.90
6.90
6.89
6.88
6.87
6.86
6.86
6.85
6.85
6.84
6.21
6.20
6.19
6.08
6.07
6.06
5.94
5.93
5.92
4.16
4.15
4.13
4.12
4.09
4.08
3.78
OMe
F
F
O
4.07
1.00
2.15
3.07
f1 (ppm)

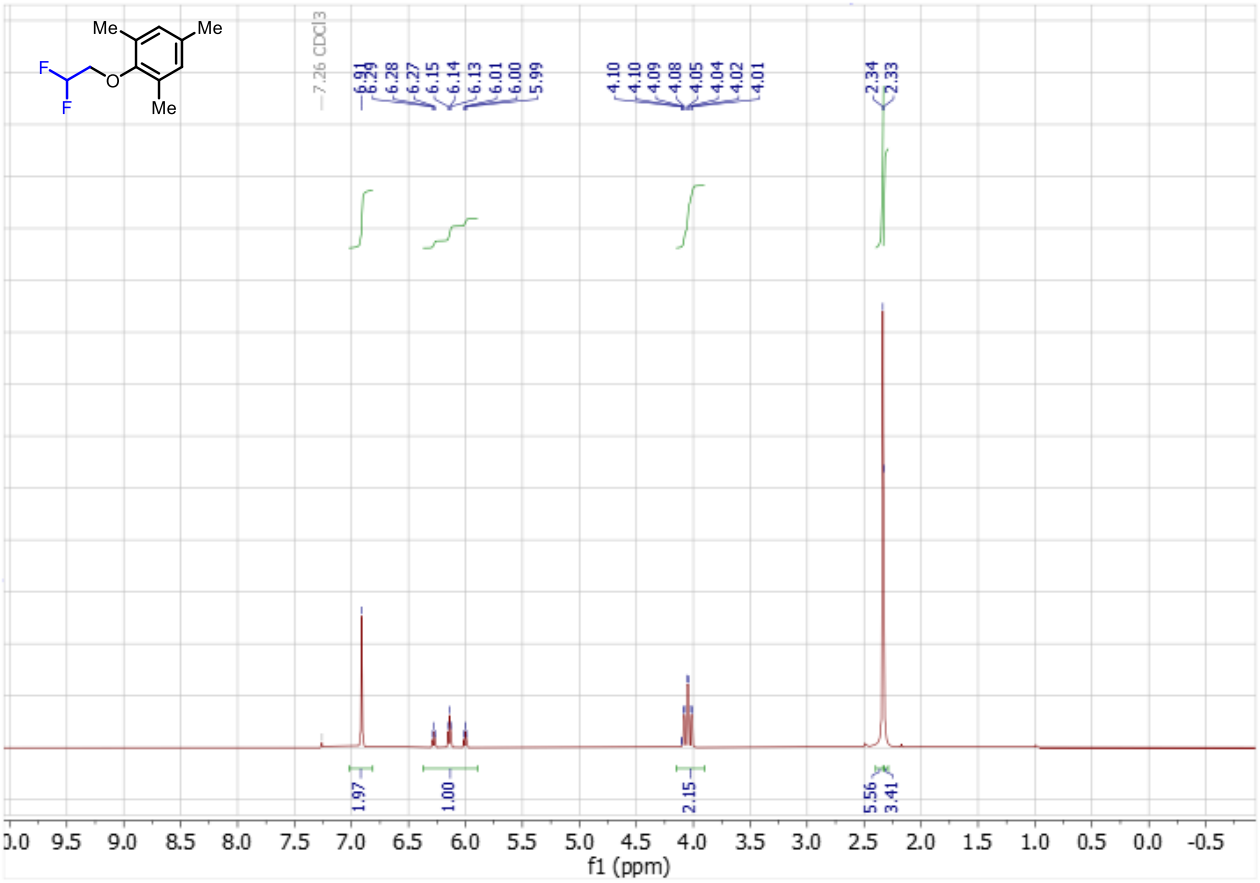

OMe
F
F
O
154.78
151.99
116.35
115.86
114.79
113.95
111.57
77.16 CDCl3
68.41
68.12
67.83
55.58
f1 (ppm)

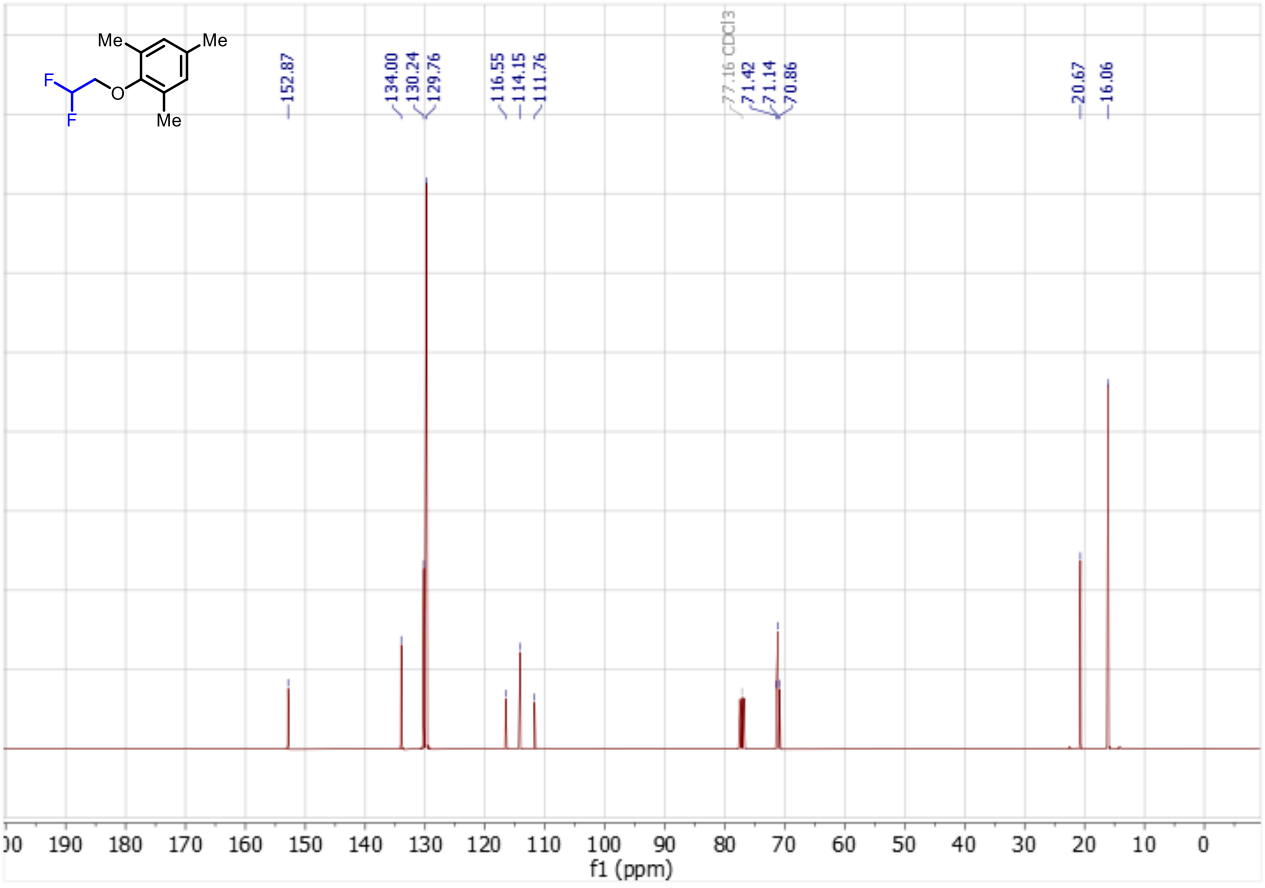

OMe
F
F
O
-125.38
1.00
40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

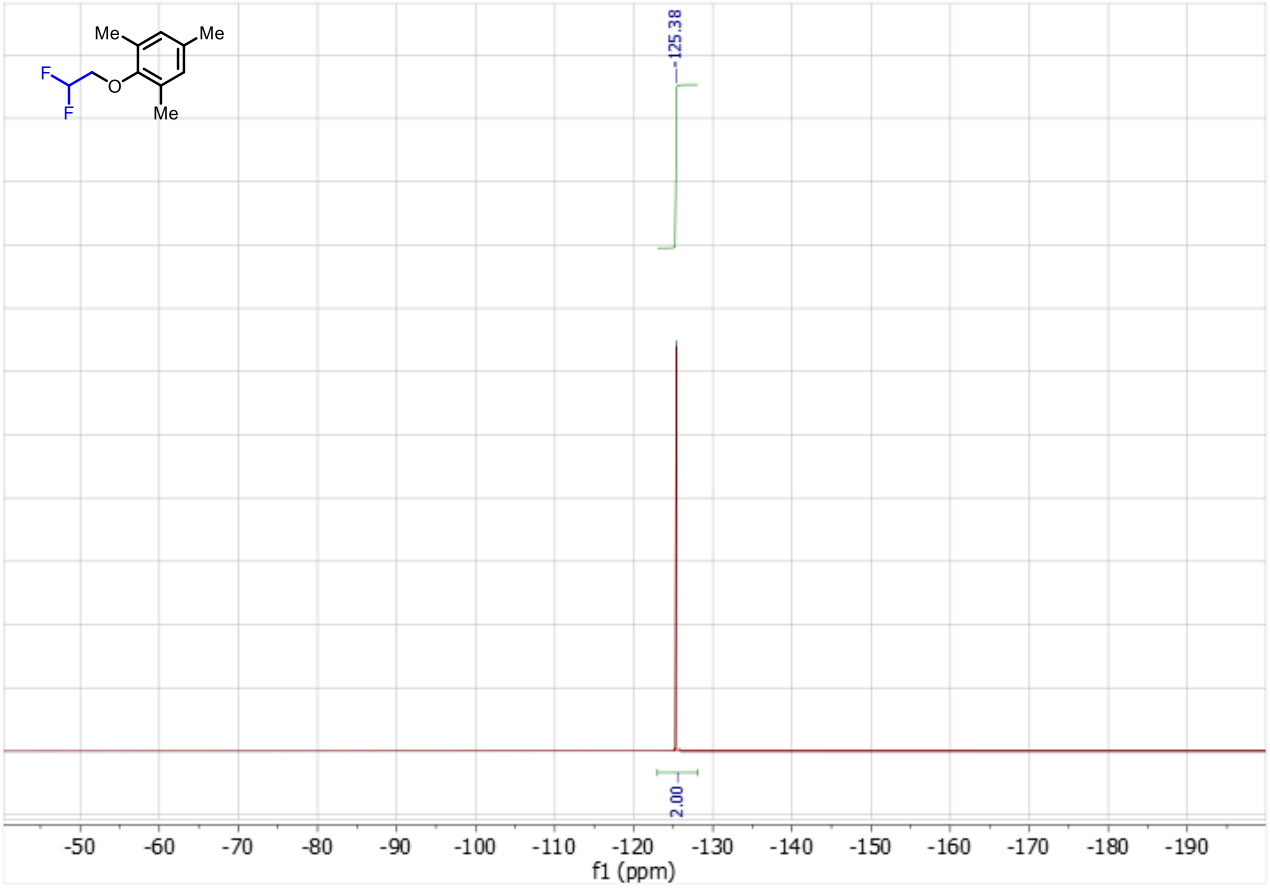

OCF3
F
F
O
2.00
1.97
1.00
2.10
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

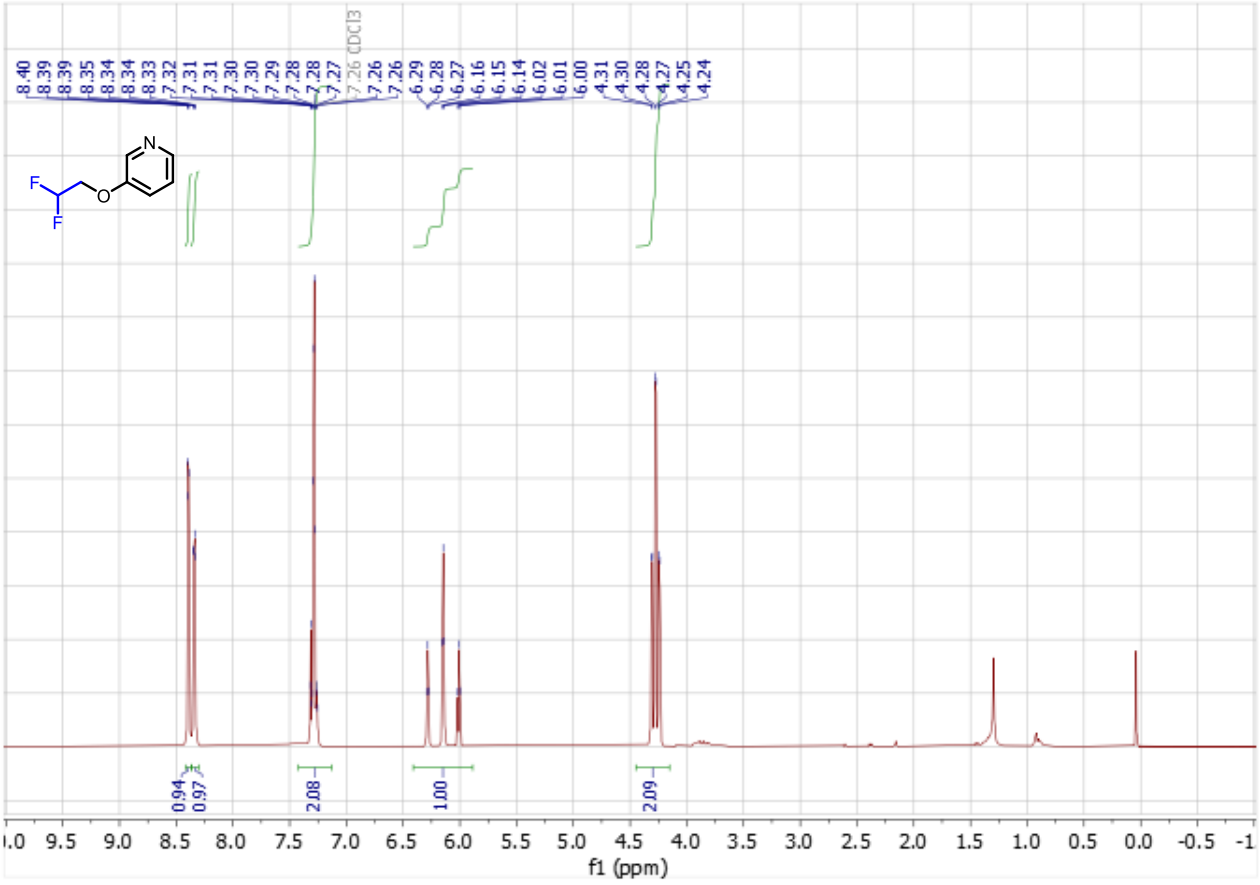

OCF3
F
F
O
156.32
143.78
122.78
116.01
115.70
113.61
111.21
77.16 CDCl3
68.11
67.82
67.52
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

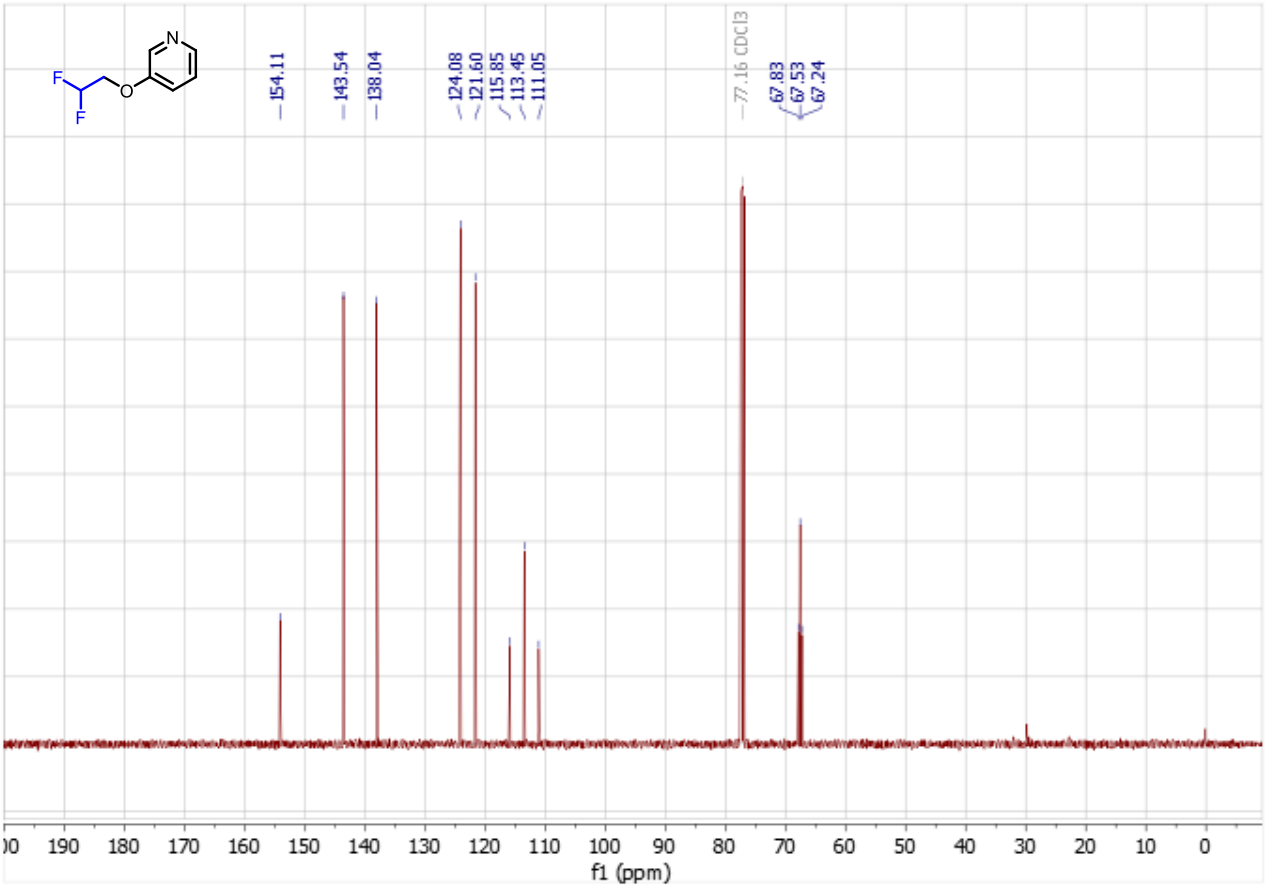

-58.41
-125.31
OCF3
F
F
O
3.00
2.09
-50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

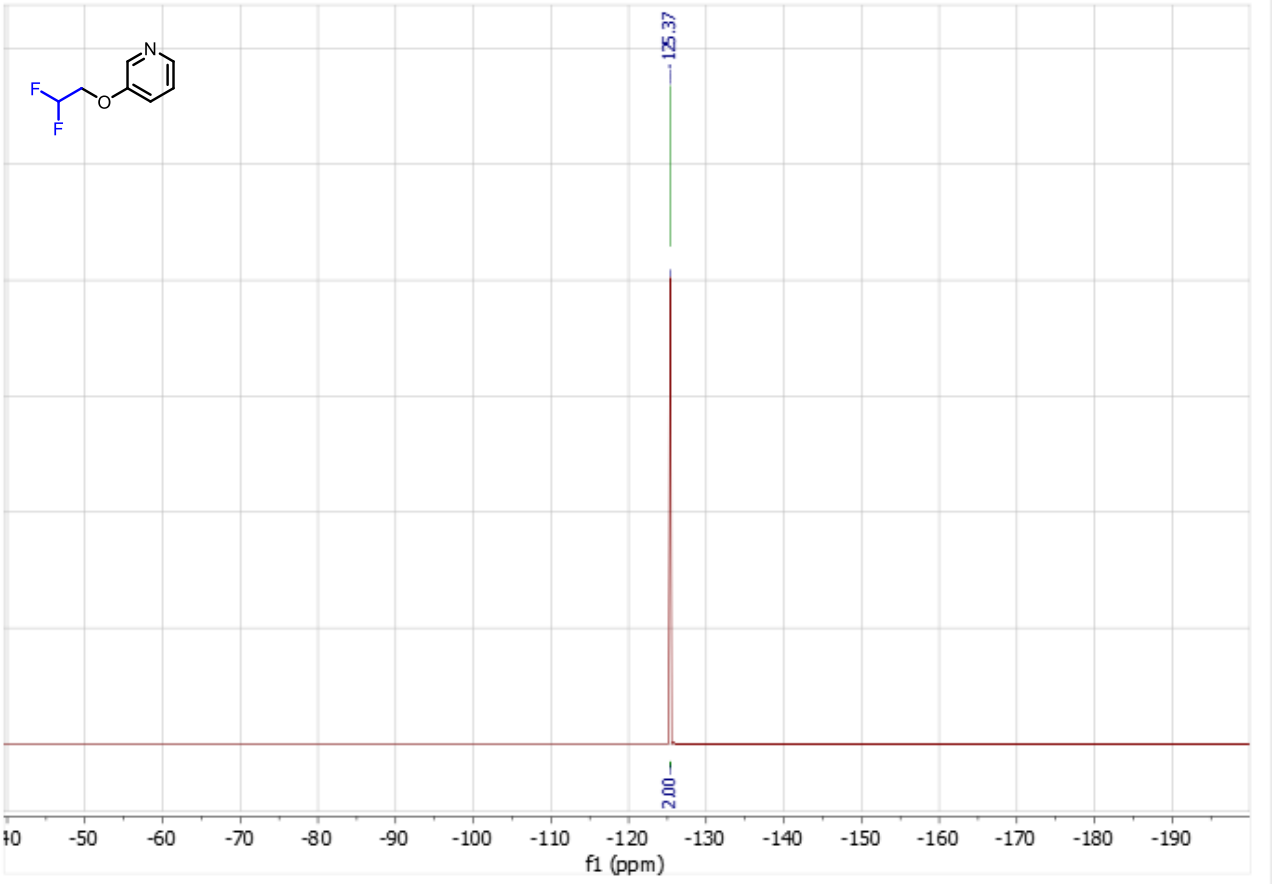

Me
Me
F
O
F
Me
7.26 CDCl3
6.31
6.29
6.28
6.27
6.15
6.14
6.13
6.01
6.00
5.99
4.10
4.10
4.09
4.08
4.05
4.04
4.02
4.01
2.34
2.33
1.97
1.00
2.15
5.56
3.41
f1 (ppm)

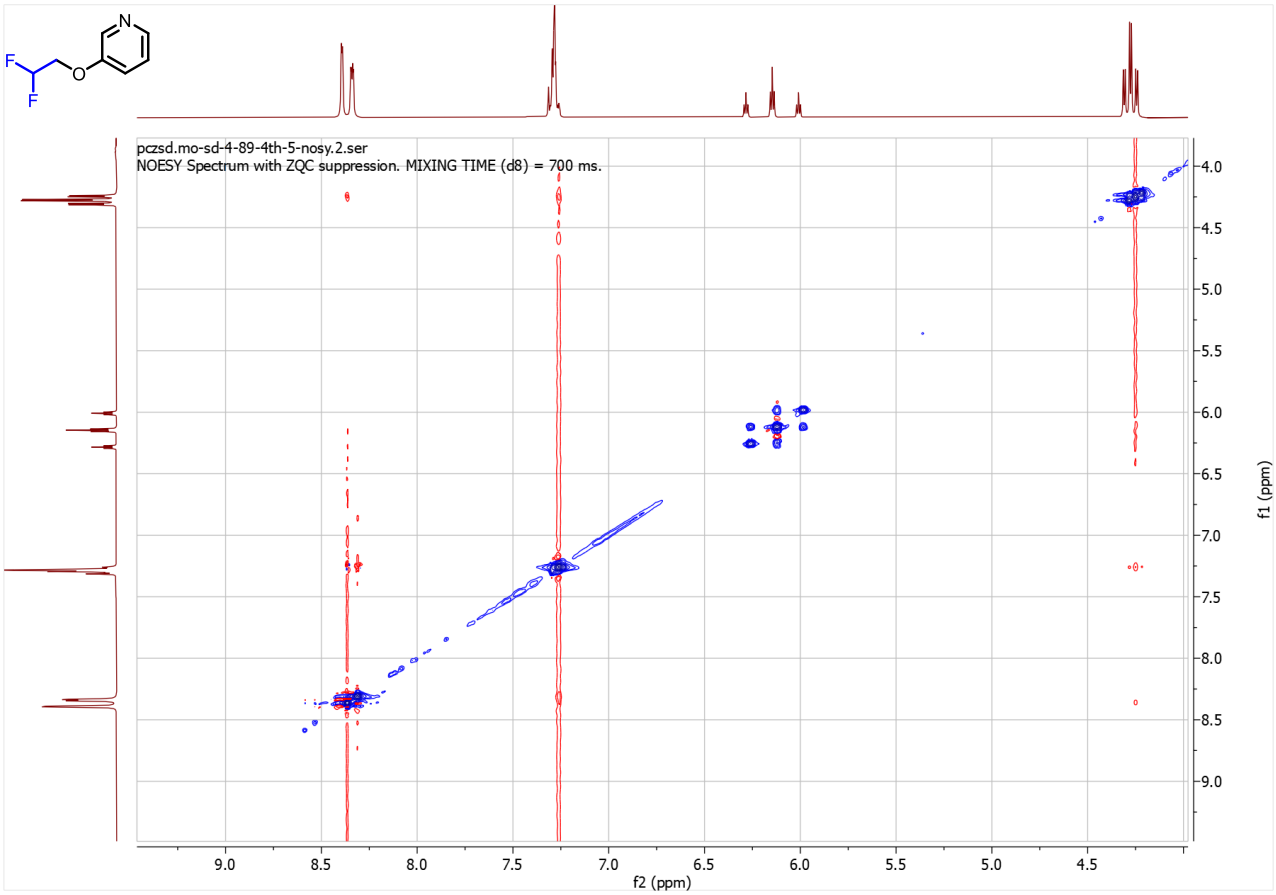

Me
Me
F
O
F
Me
152.87
134.00
130.24
129.76
116.55
114.15
111.76
77.16 CDCl3
71.42
71.14
70.86
20.67
16.06
f1 (ppm)

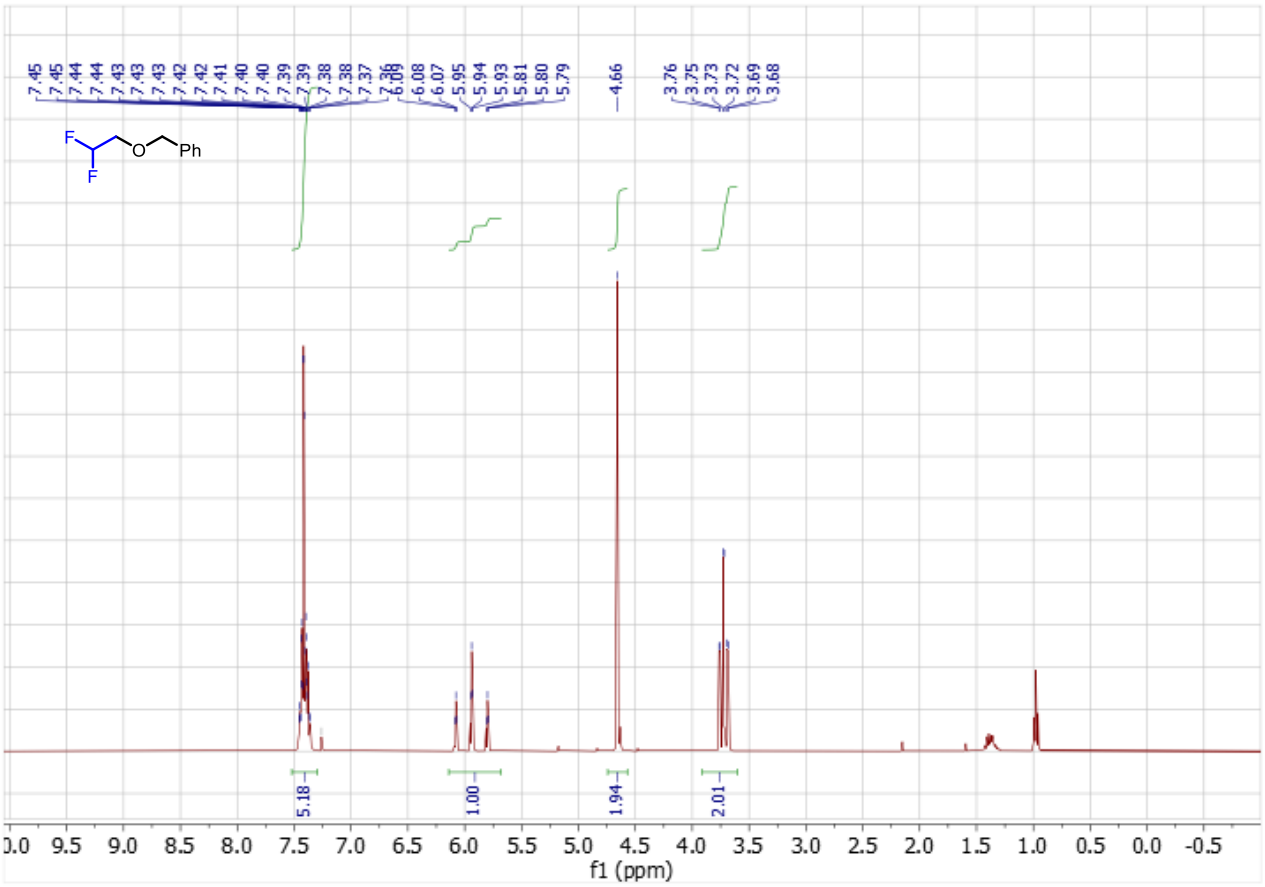

Me
Me
F
F
O
Me
-125.38
2.00
-50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

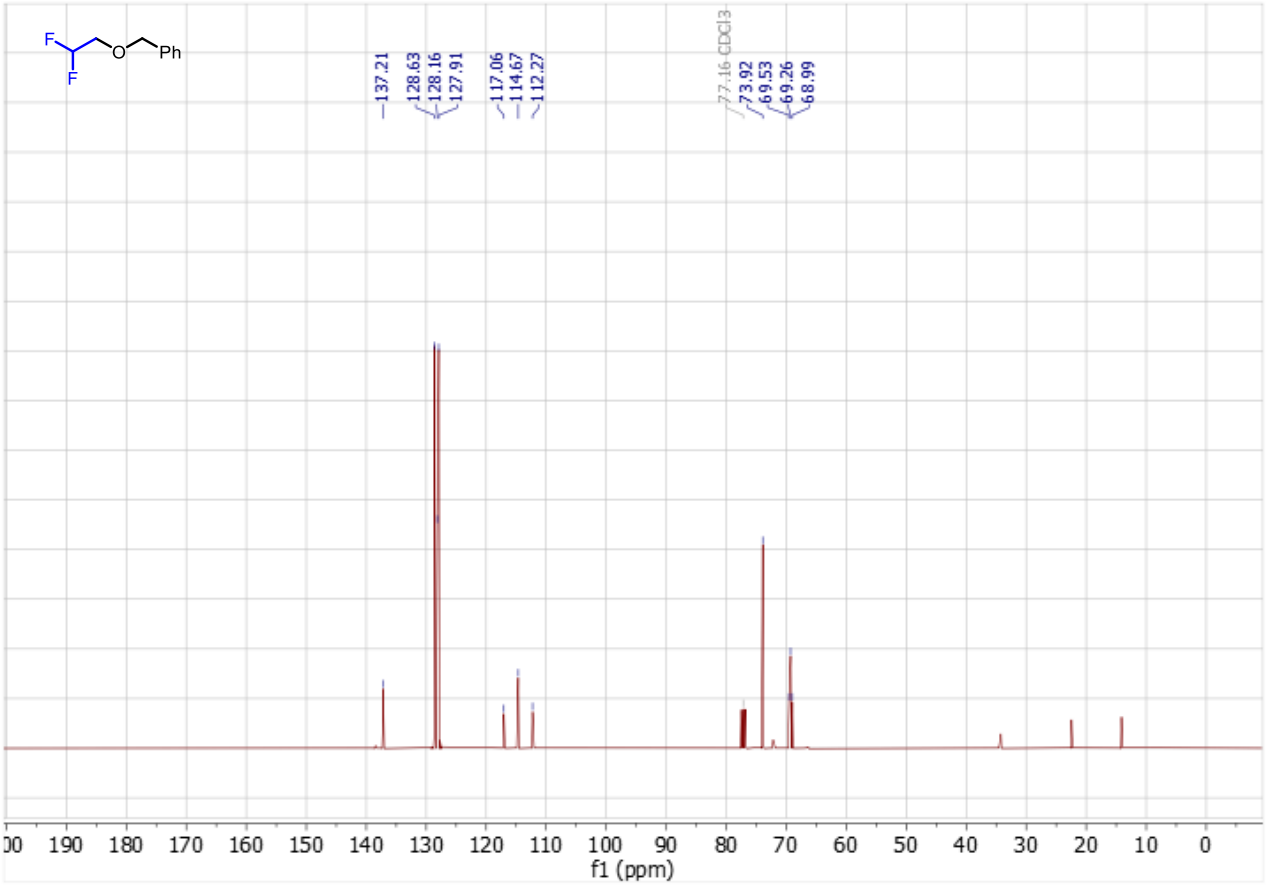

8.40 8.39 8.39 8.35 8.34 8.34 8.33 7.32 7.31 7.31 7.30 7.30 7.29 7.28 7.28 7.27 7.26 CDCl3 7.26 7.26 6.29 6.28 6.27 6.16 6.15 6.14 6.02 6.01 6.00 4.31 4.30 4.28 4.27 4.25 4.24
N
F
F
O
0.94
0.97
2.08
1.00
2.09
f1 (ppm)

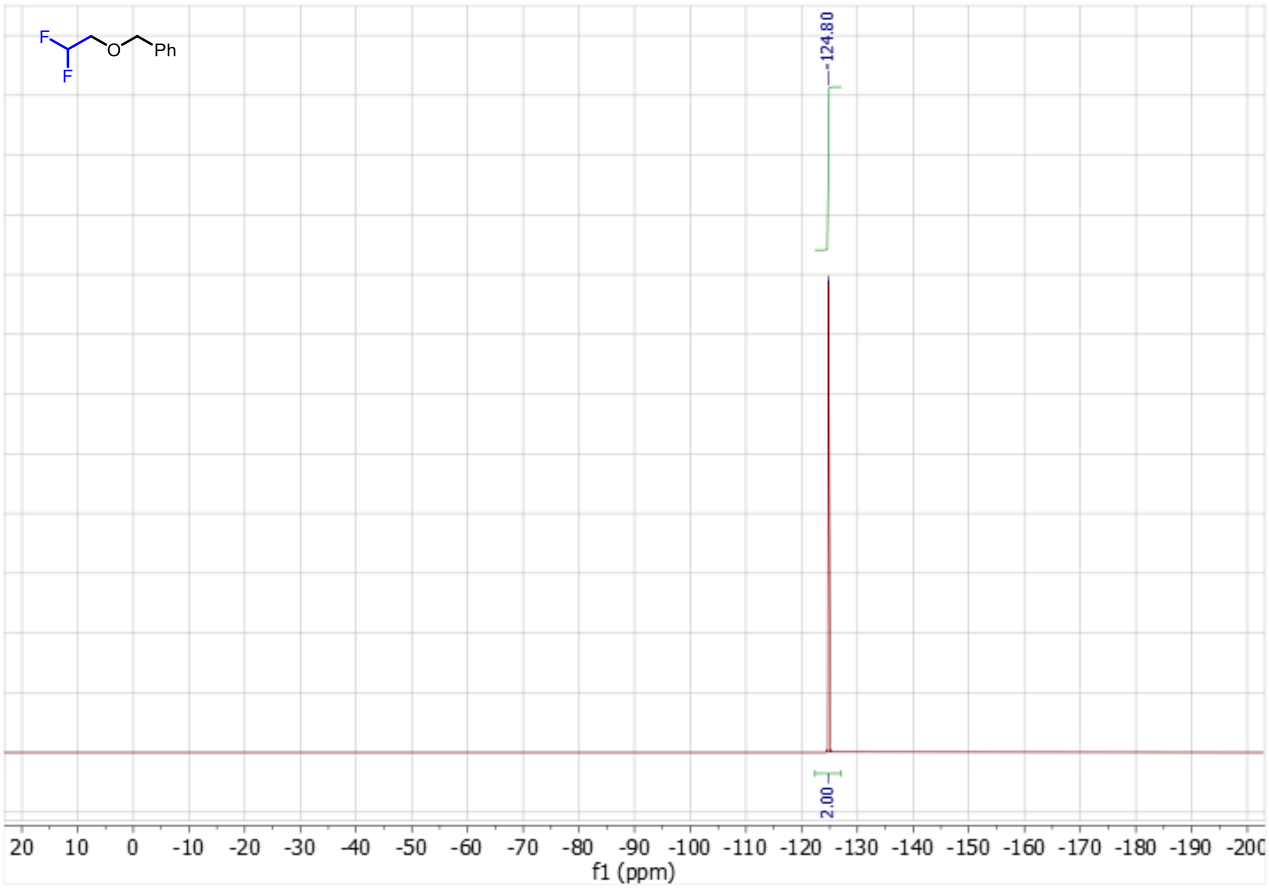

154.11
143.54
138.04
124.08
121.60
115.85
113.45
111.05
77.16 CDCl3
67.83
67.53
67.24
f1 (ppm)

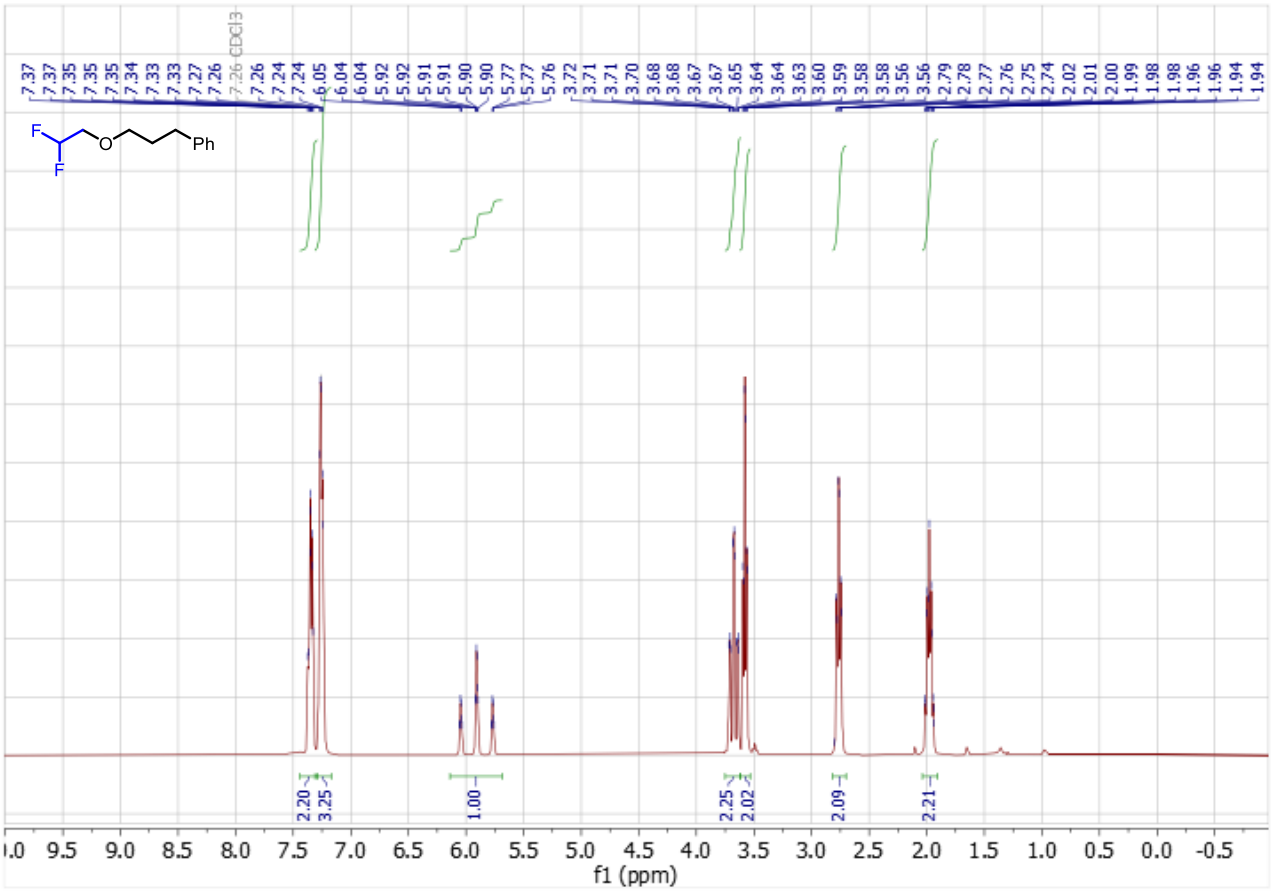

125.37
2.00
f1 (ppm)

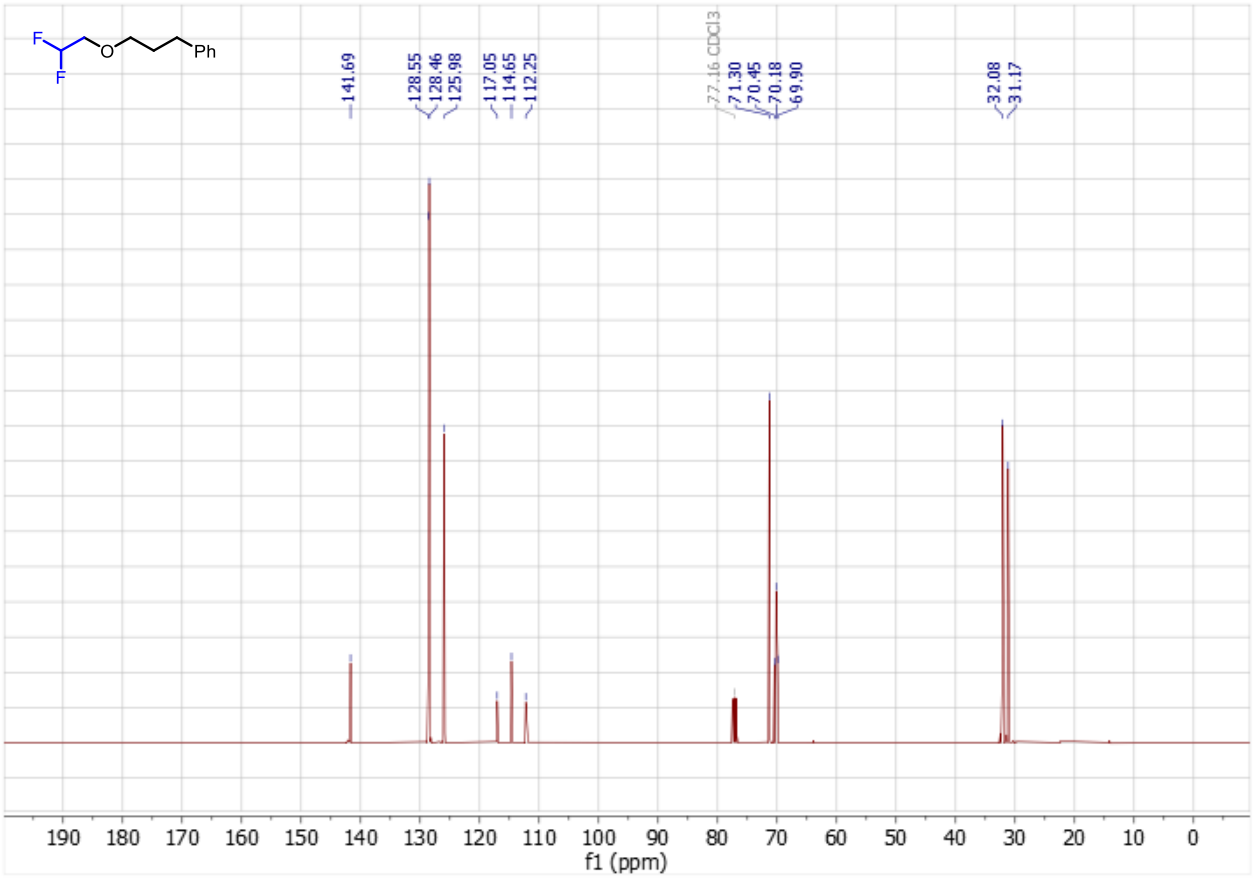

pczsd.mo-sd-4-89-4th-5-nosy.2.ser
NOESY Spectrum with ZQC suppression. MIXING TIME (d8) = 700 ms.
f2 (ppm)
f1 (ppm)

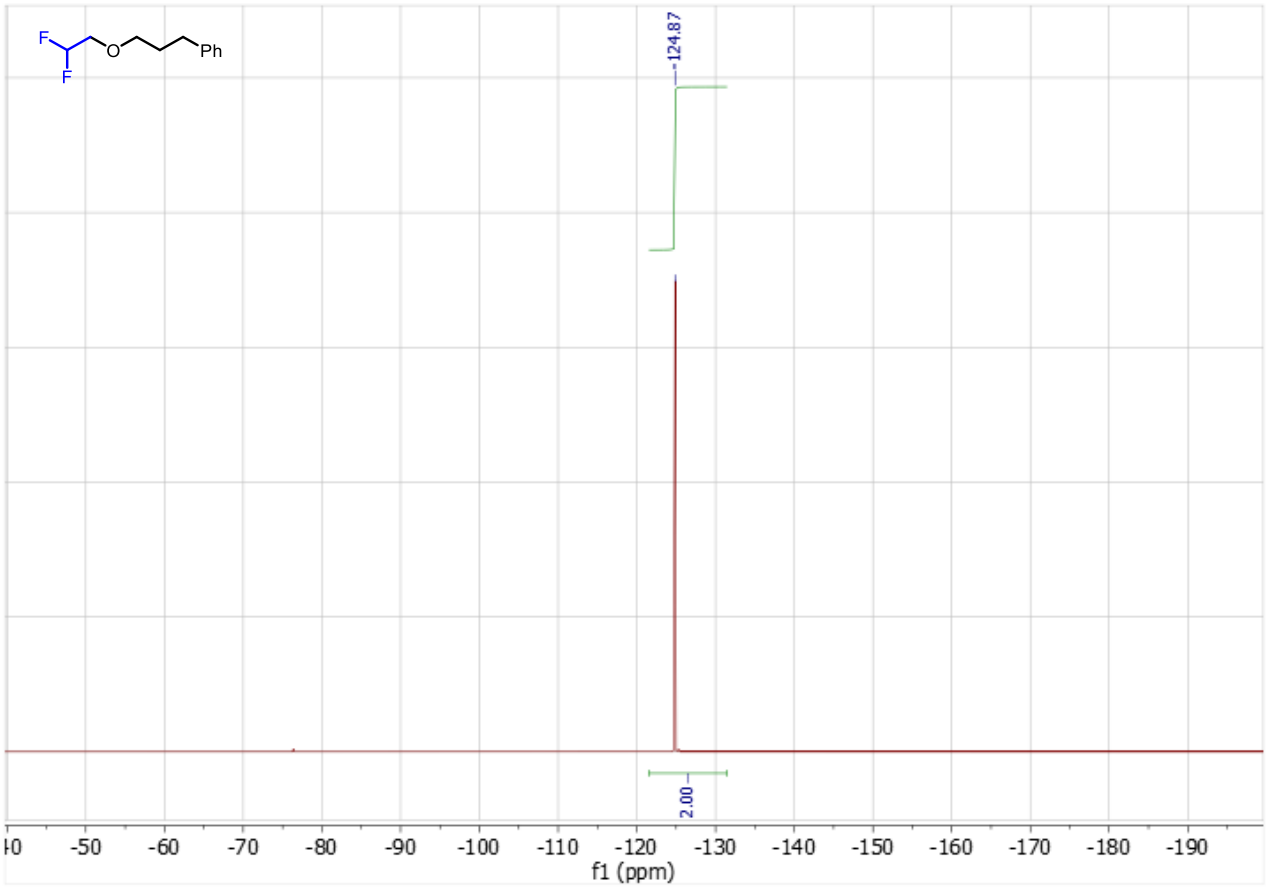

7.45
7.45
7.44
7.44
7.43
7.43
7.43
7.42
7.42
7.41
7.40
7.40
7.39
7.39
7.38
7.38
7.37
7.36
6.09
6.08
6.07
5.95
5.94
5.93
5.81
5.80
5.79
4.66
3.76
3.75
3.73
3.72
3.69
3.68
Ph
5.18
1.00
1.94
2.01
f1 (ppm)

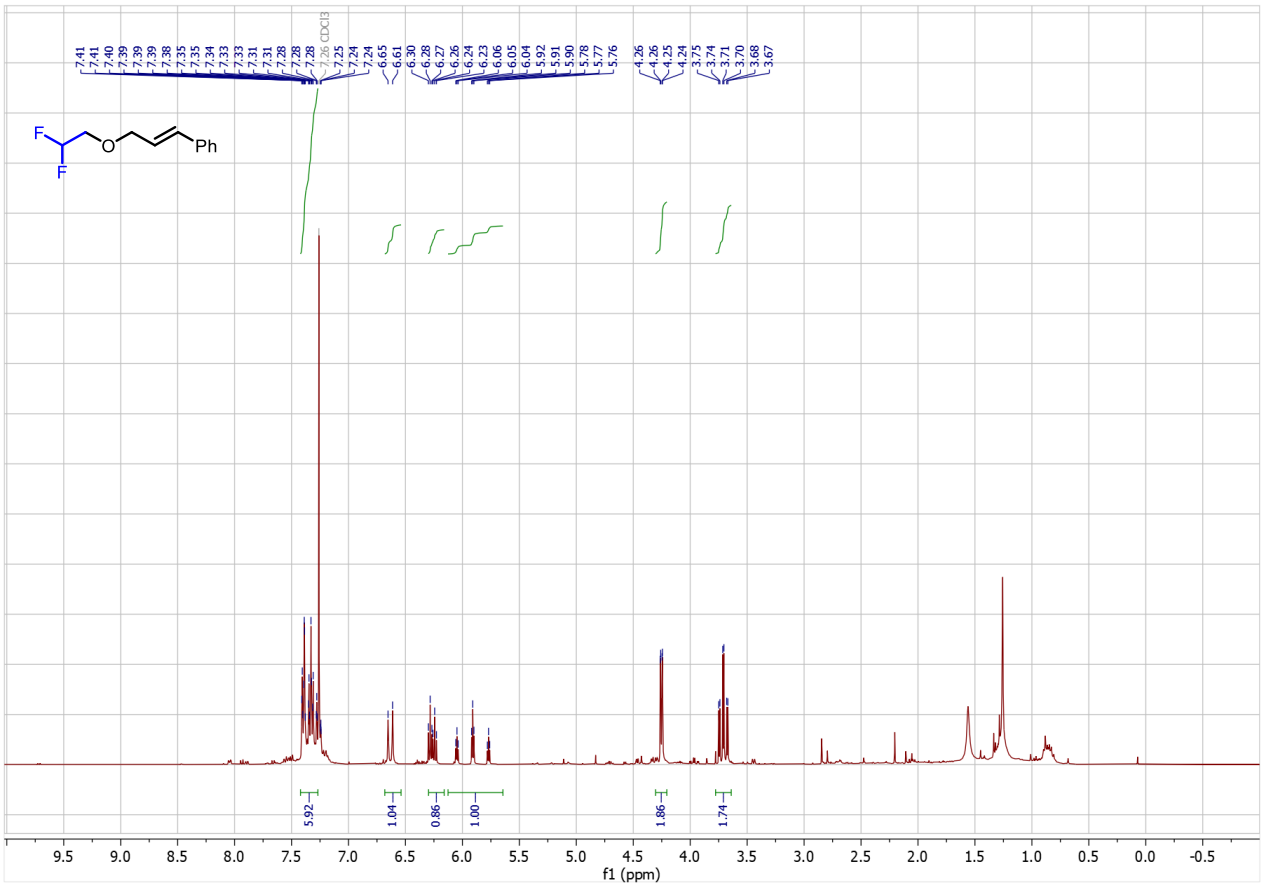

F
F
O
Ph
137.21
128.63
128.16
127.91
117.06
114.67
112.27
77.16 CDCl3
73.92
69.53
69.26
68.99
f1 (ppm)

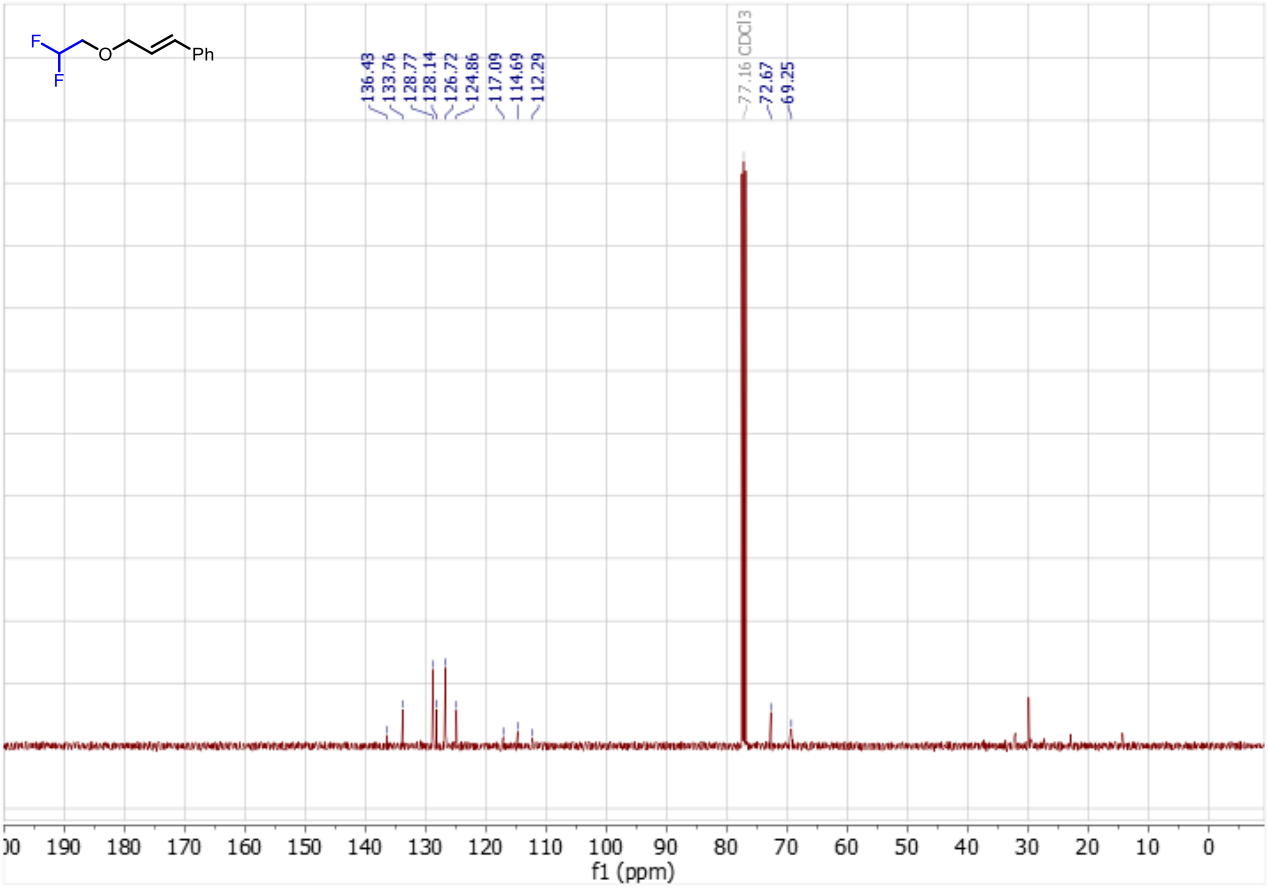

F
F
O
Ph
-124.80
2.00
f1 (ppm)

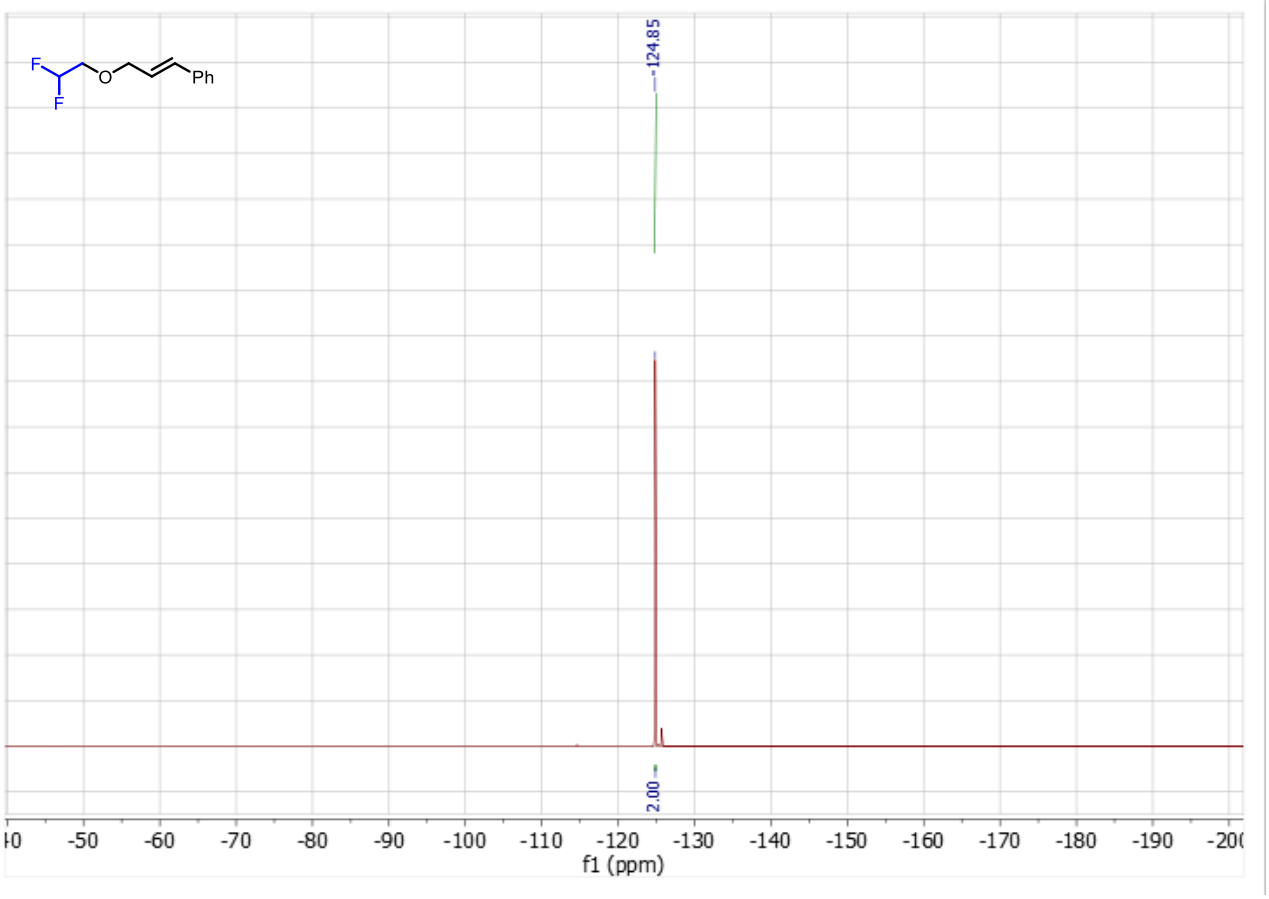

F
F
O
Ph
7.37 7.37 7.35 7.35 7.35 7.34 7.33 7.33 7.27 7.26 7.26 CDCl3 7.26 7.24 7.24 6.05 6.04 6.04 5.92 5.92 5.91 5.91 5.90 5.90 5.77 5.77 5.76 3.72 3.71 3.71 3.70 3.68 3.68 3.67 3.67 3.65 3.64 3.64 3.63 3.60 3.59 3.58 3.58 3.56 3.56 2.79 2.78 2.77 2.76 2.75 2.74 2.02 2.01 2.00 1.99 1.98 1.98 1.96 1.96 1.94 1.94
2.20
3.25
1.00
2.25
2.02
2.09
2.21
f1 (ppm)

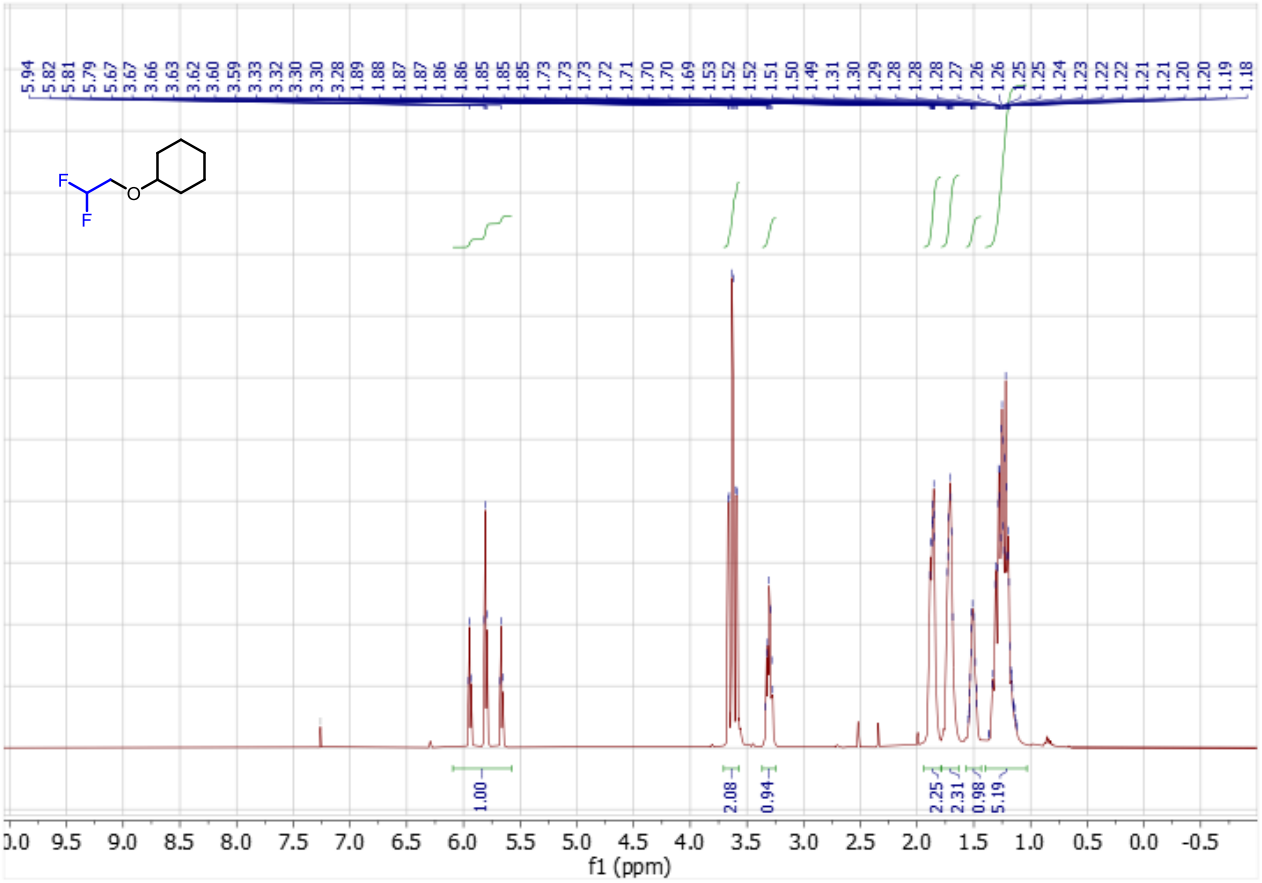

F
F
O
Ph
141.69
128.55
128.46
125.98
117.05
114.65
112.25
77.16 CDCl3
71.30
70.45
70.18
69.90
32.08
31.17
f1 (ppm)

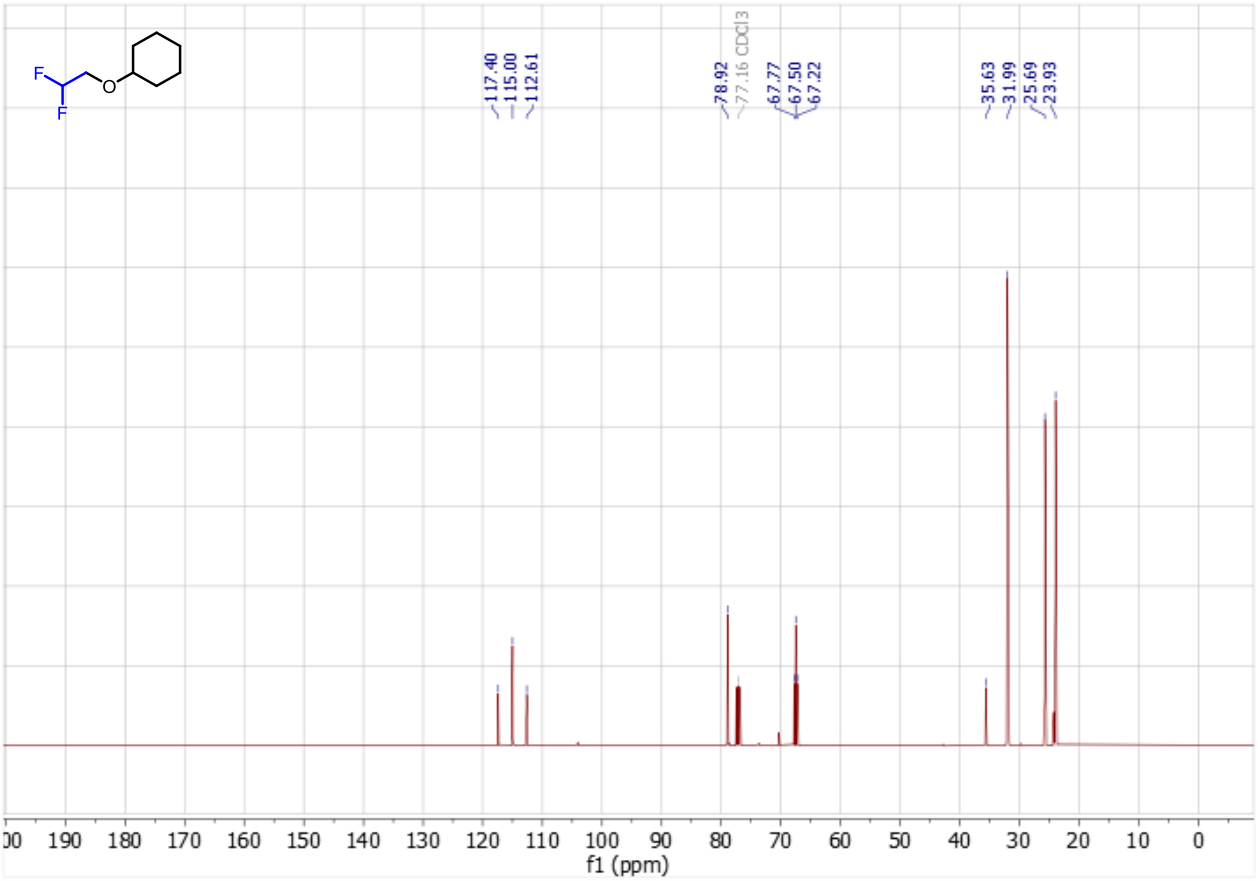

F
F
O
Ph
-124.87
2.00
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

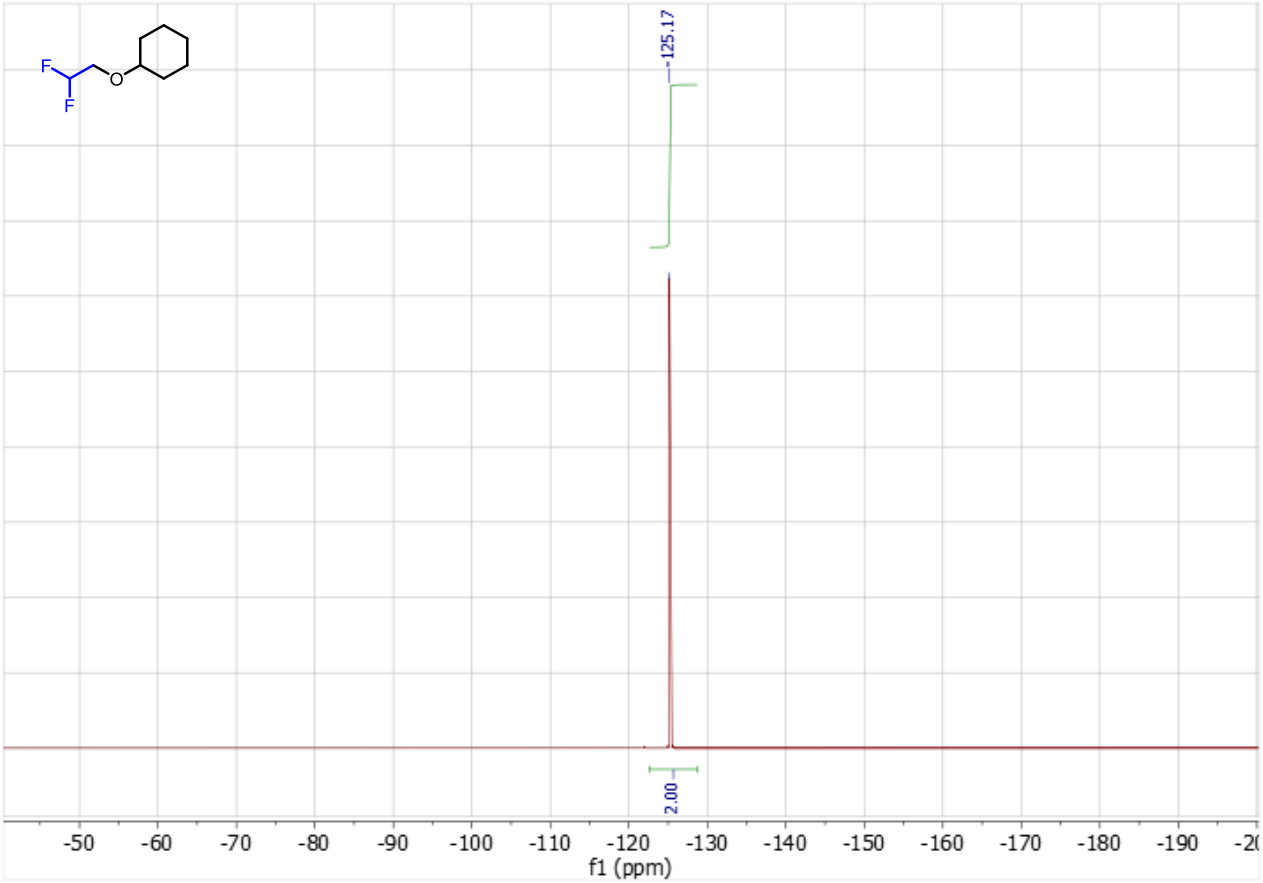

F
F
O
Ph
5.92
1.04
0.86
1.00
1.86
1.74
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

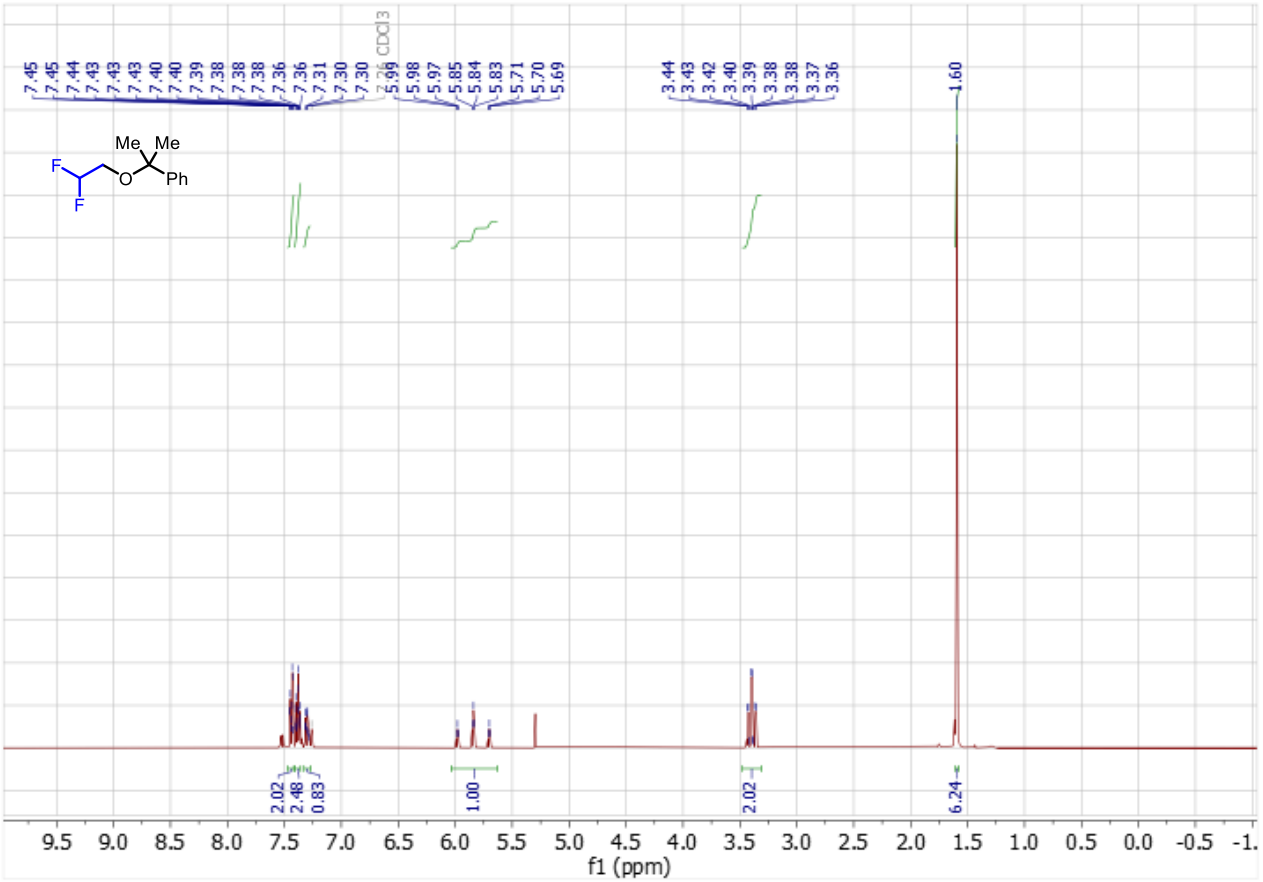

F
F
O
Ph
136.43
133.76
128.77
128.14
126.72
124.86
117.09
114.69
112.29
77.16 CDCl3
72.67
69.25
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

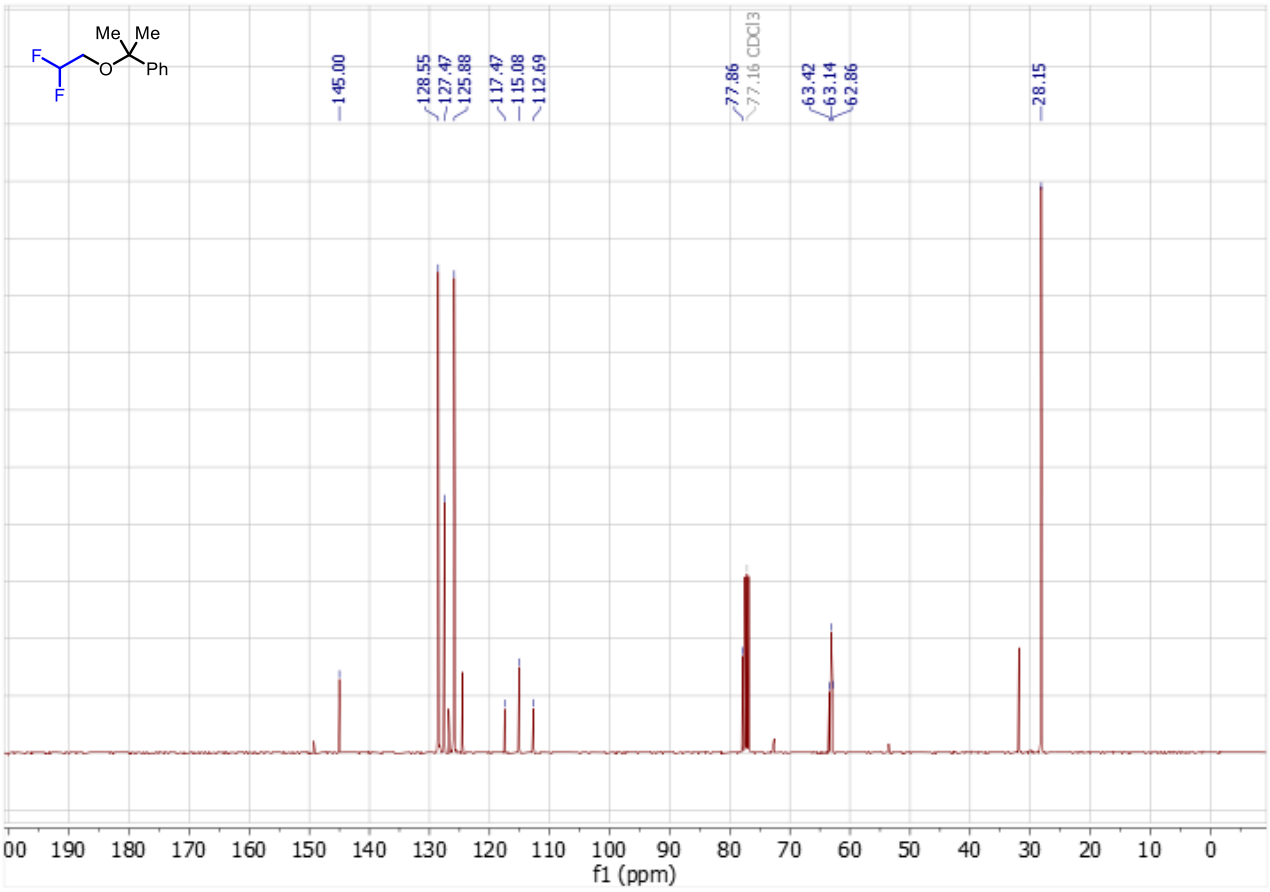

F
F
O
Ph
124.85
2.00
-50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

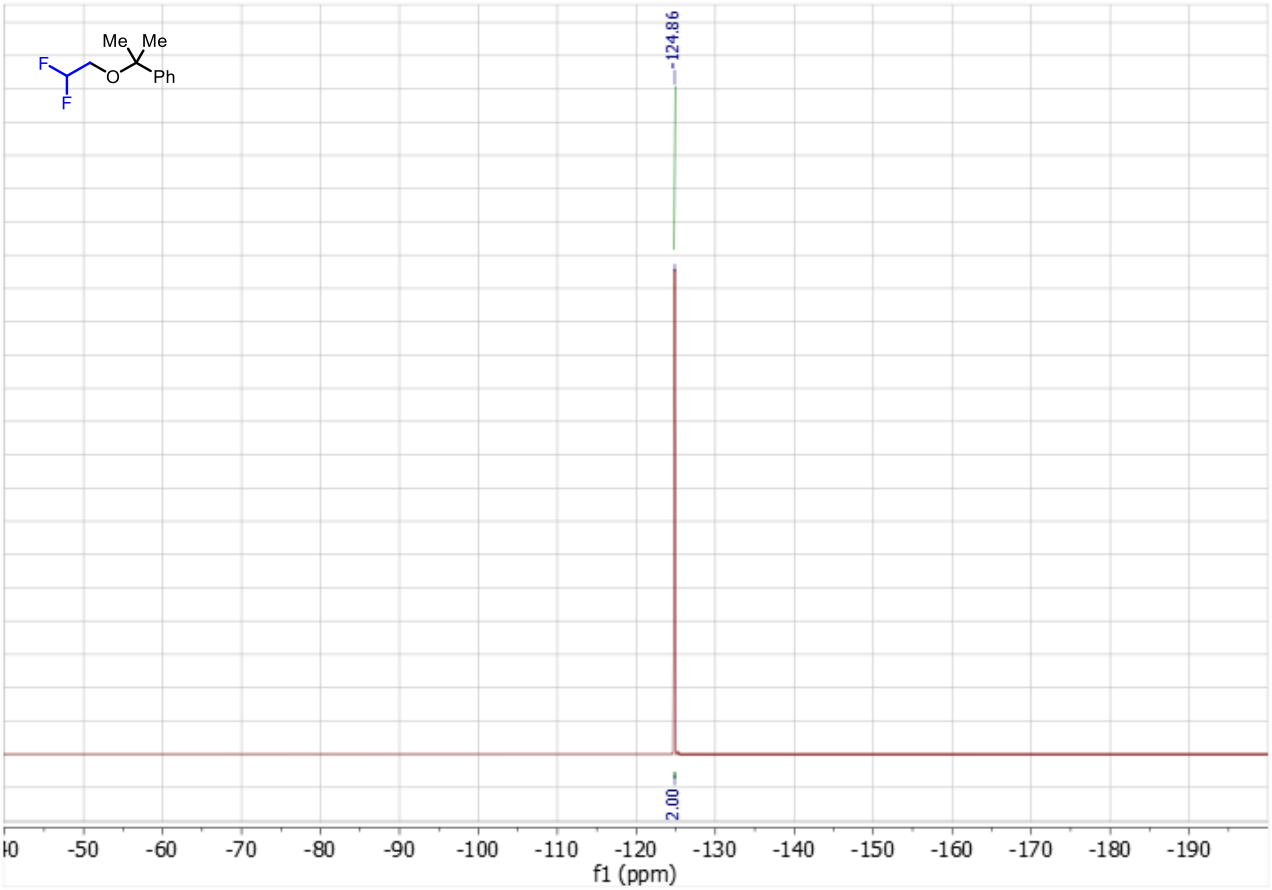

5.94 5.82 5.81 5.79 5.67 3.67 3.66 3.63 3.62 3.60 3.59 3.33 3.32 3.30 3.30 3.28 1.89 1.88 1.87 1.87 1.86 1.86 1.85 1.85 1.85 1.73 1.73 1.73 1.72 1.71 1.70 1.70 1.69 1.53 1.52 1.52 1.51 1.50 1.49 1.31 1.30 1.29 1.28 1.28 1.28 1.27 1.26 1.26 1.25 1.25 1.24 1.23 1.22 1.22 1.21 1.21 1.20 1.20 1.19 1.18
F
F
O
1.00
2.08
0.94
2.25
2.31
0.98
5.19
f1 (ppm)

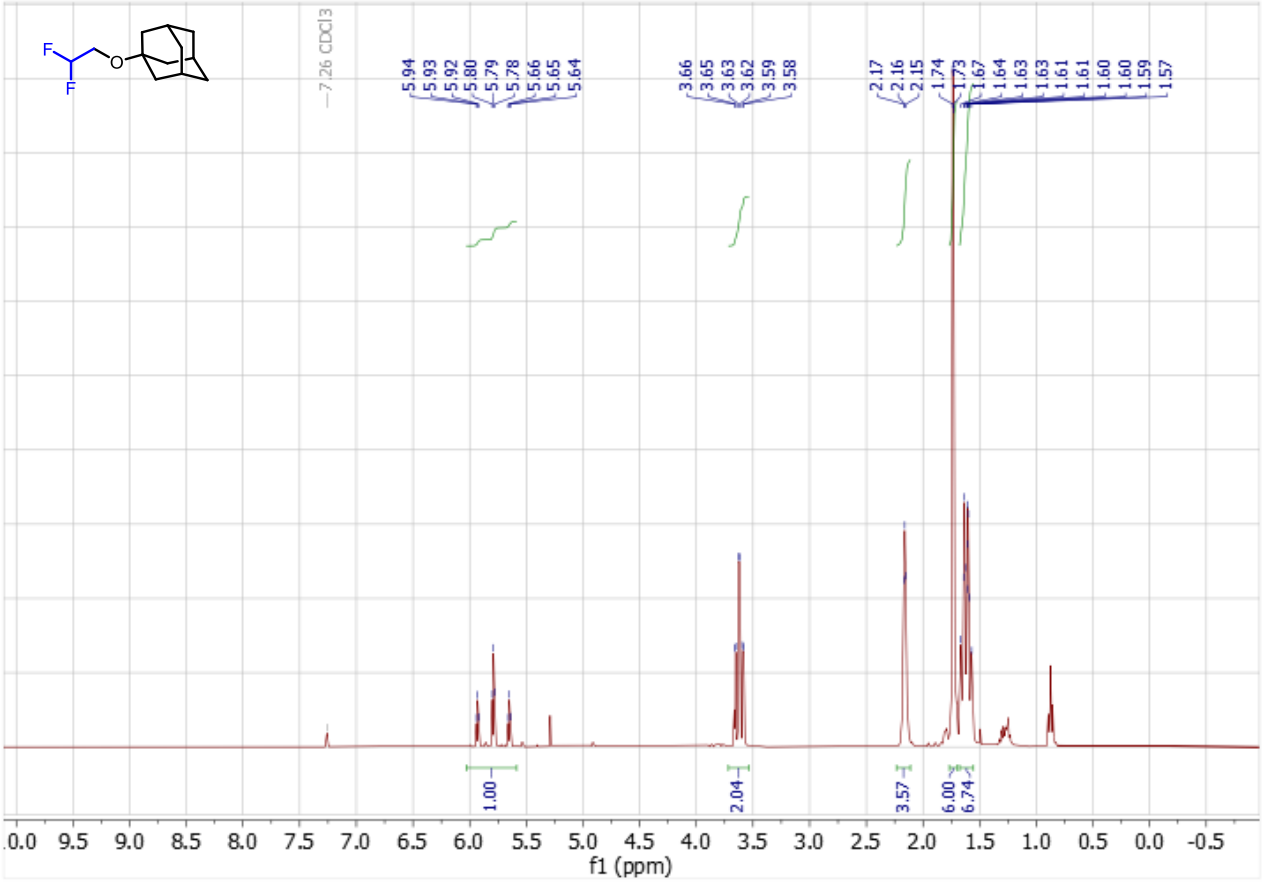

F
F
O
117.40
115.00
112.61
78.92
77.16 CDCl3
67.77
67.50
67.22
35.63
31.99
25.69
23.93
f1 (ppm)

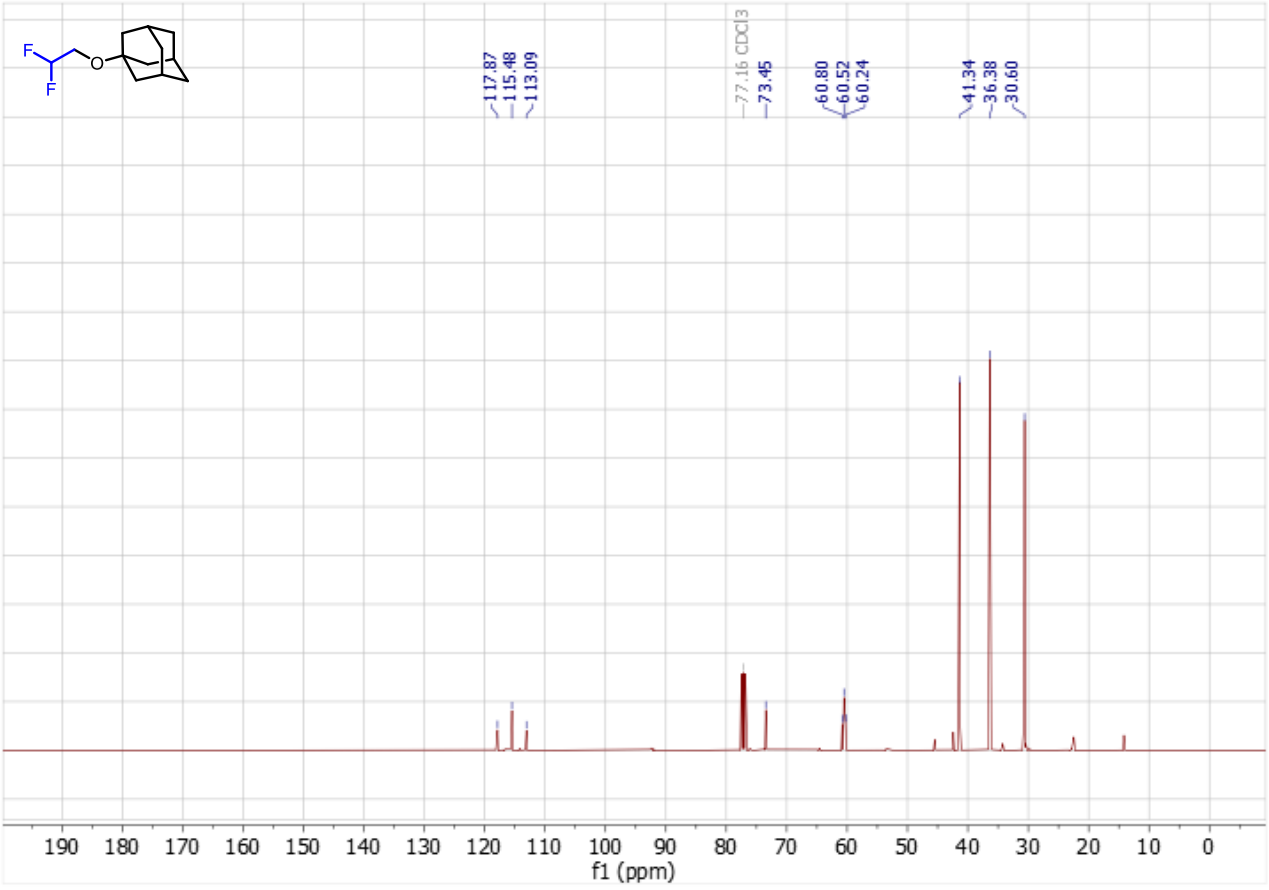

F
F
O
-125.17
2.00
-50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

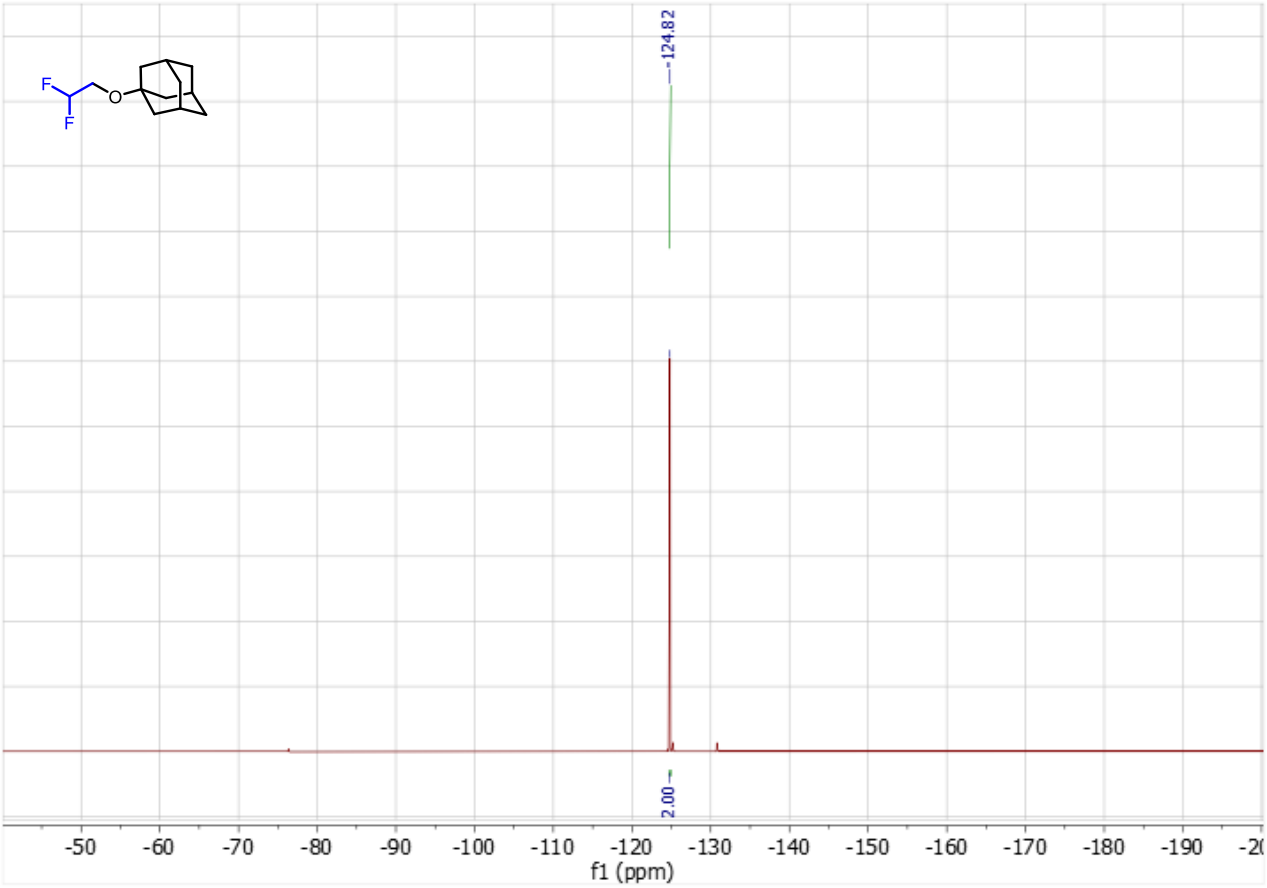

7.45 7.45 7.44 7.43 7.43 7.43 7.40 7.40 7.39 7.38 7.38 7.38 7.36 7.36 7.31 7.30 7.30
CDCl3
5.99 5.98 5.97 5.85 5.84 5.83 5.71 5.70 5.69
3.44 3.43 3.42 3.40 3.39 3.38 3.38 3.37 3.36
1.60
Me Me
Ph
F
F
O
2.02 2.48 0.83
1.00
2.02
6.24
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

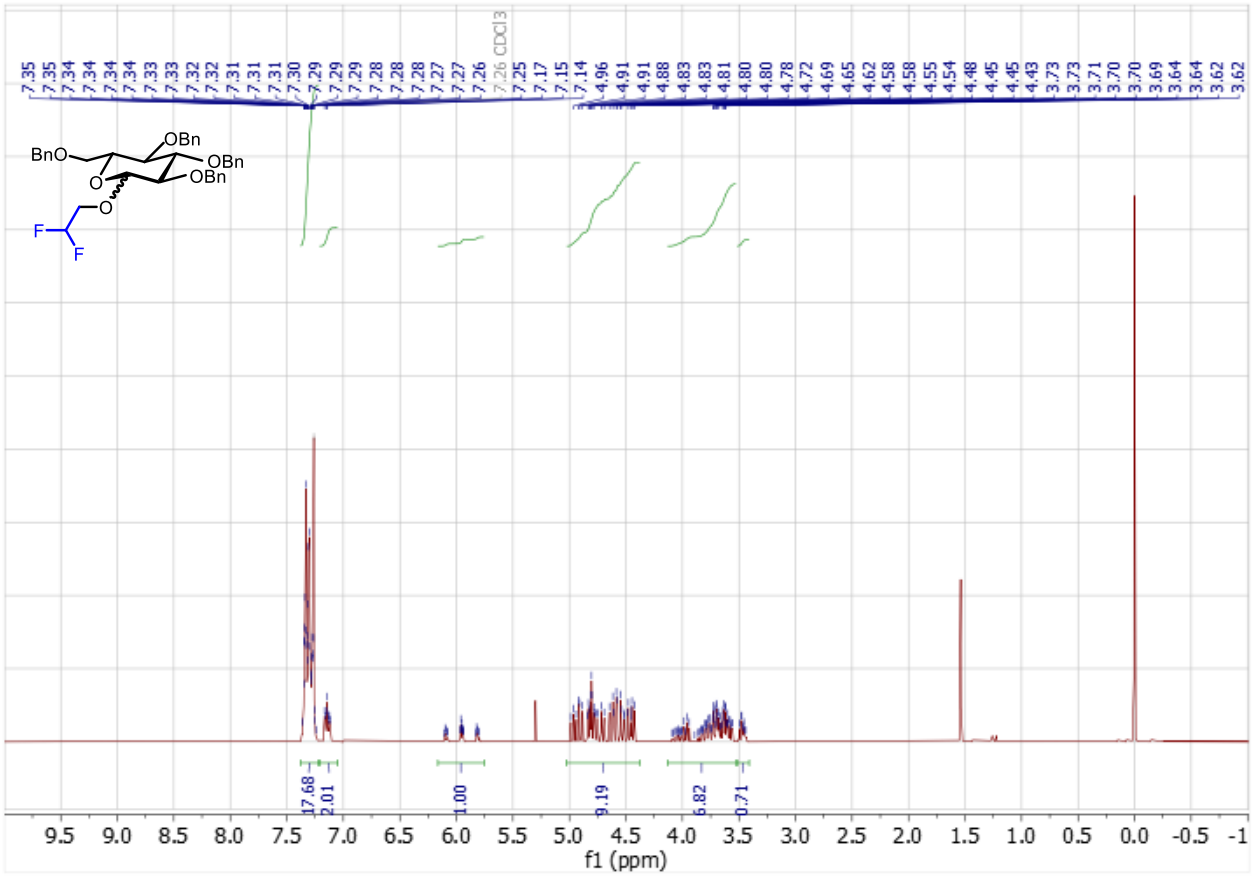

Me
Me
F
O
Ph
F
145.00
128.55
127.47
125.88
117.47
115.08
112.69
77.86
77.16 CDCl3
63.42
63.14
62.86
28.15
f1 (ppm)

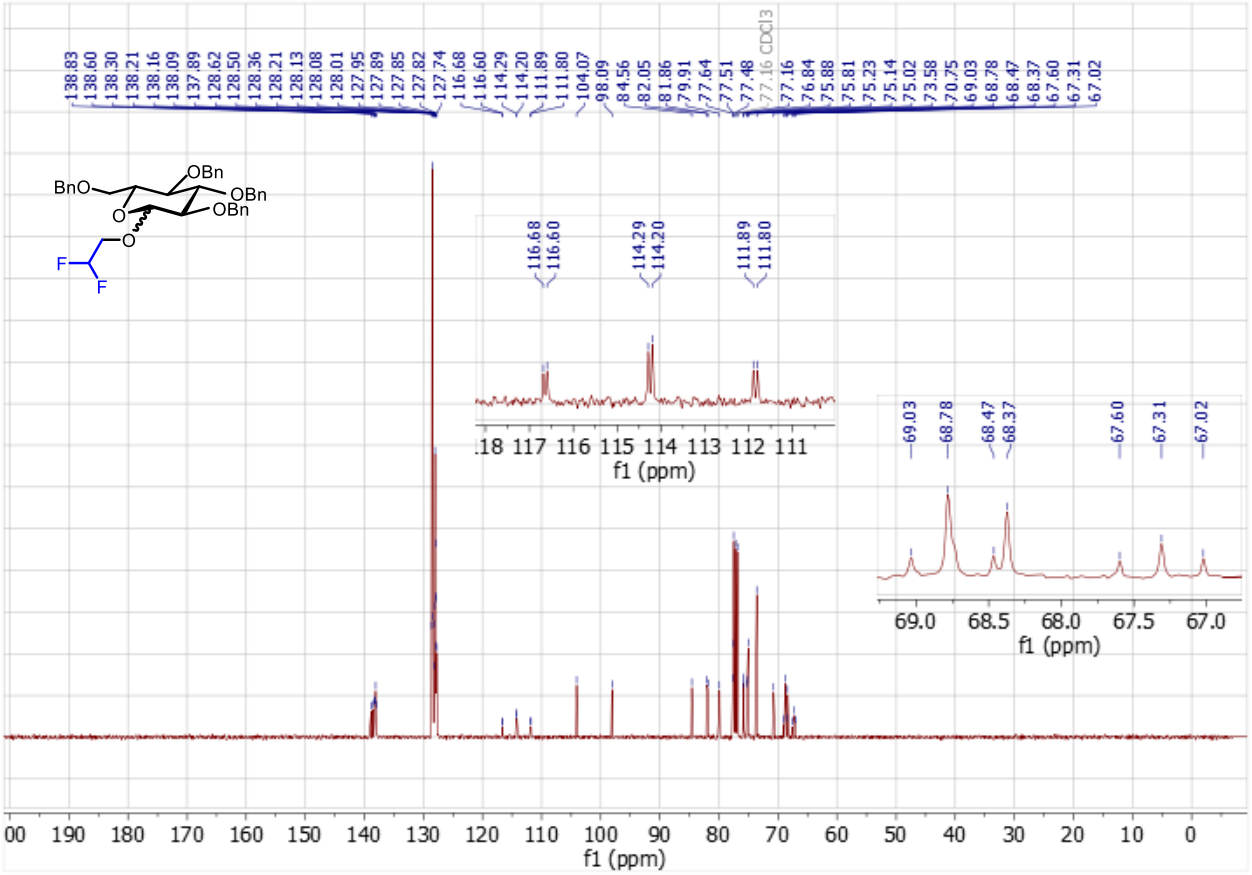

Me
Me
F
O
Ph
F
-124.86
2.00
f1 (ppm)

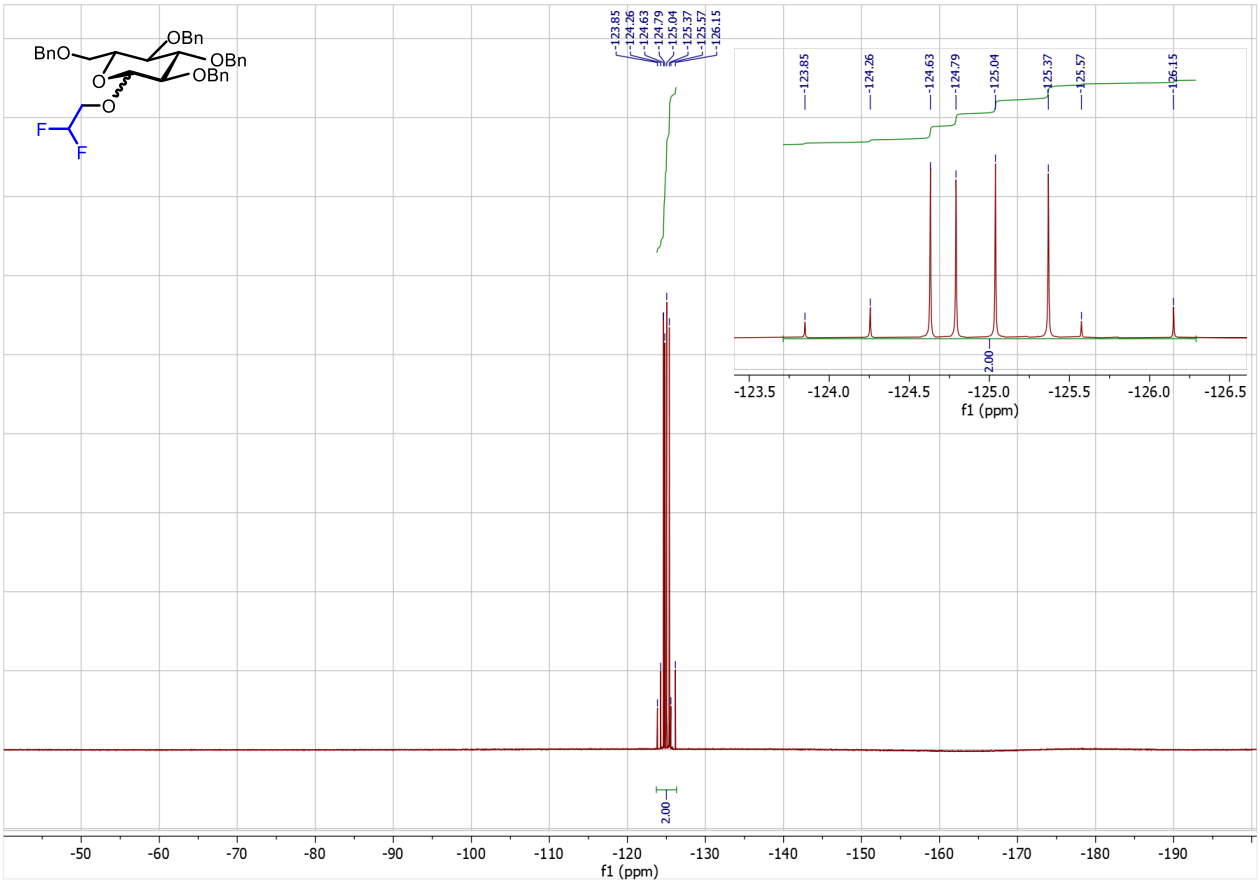

F
F
O
7.26 CDCl3
5.94
5.93
5.92
5.80
5.79
5.78
5.66
5.65
5.64
3.66
3.65
3.63
3.62
3.59
3.58
2.17
2.16
2.15
1.74
1.73
1.67
1.64
1.63
1.63
1.61
1.61
1.60
1.60
1.59
1.57
1.00
2.04
3.57
6.00
6.74
f1 (ppm)

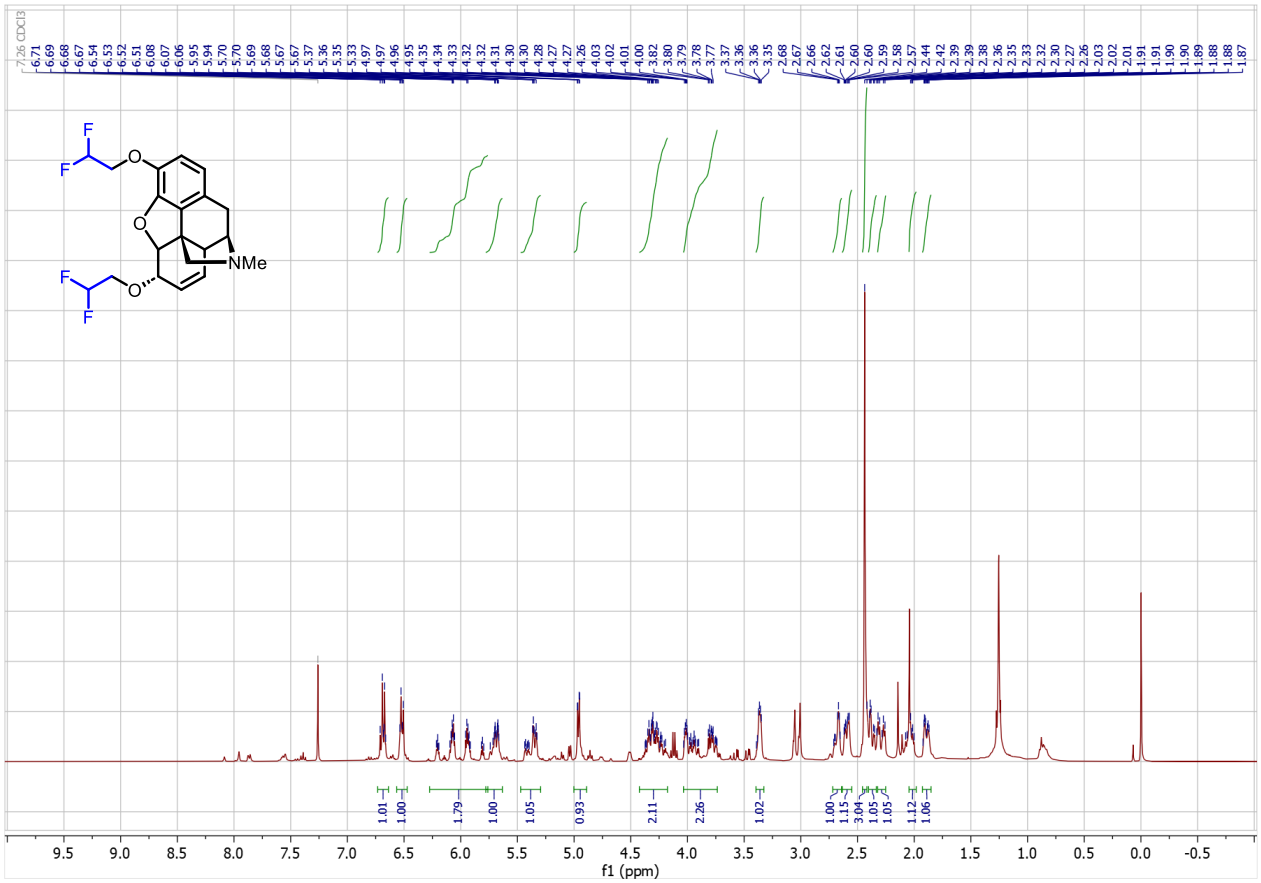

F
F
O
117.87
115.48
113.09
77.16 CDCl3
73.45
60.80
60.52
60.24
41.34
36.38
30.60
f1 (ppm)

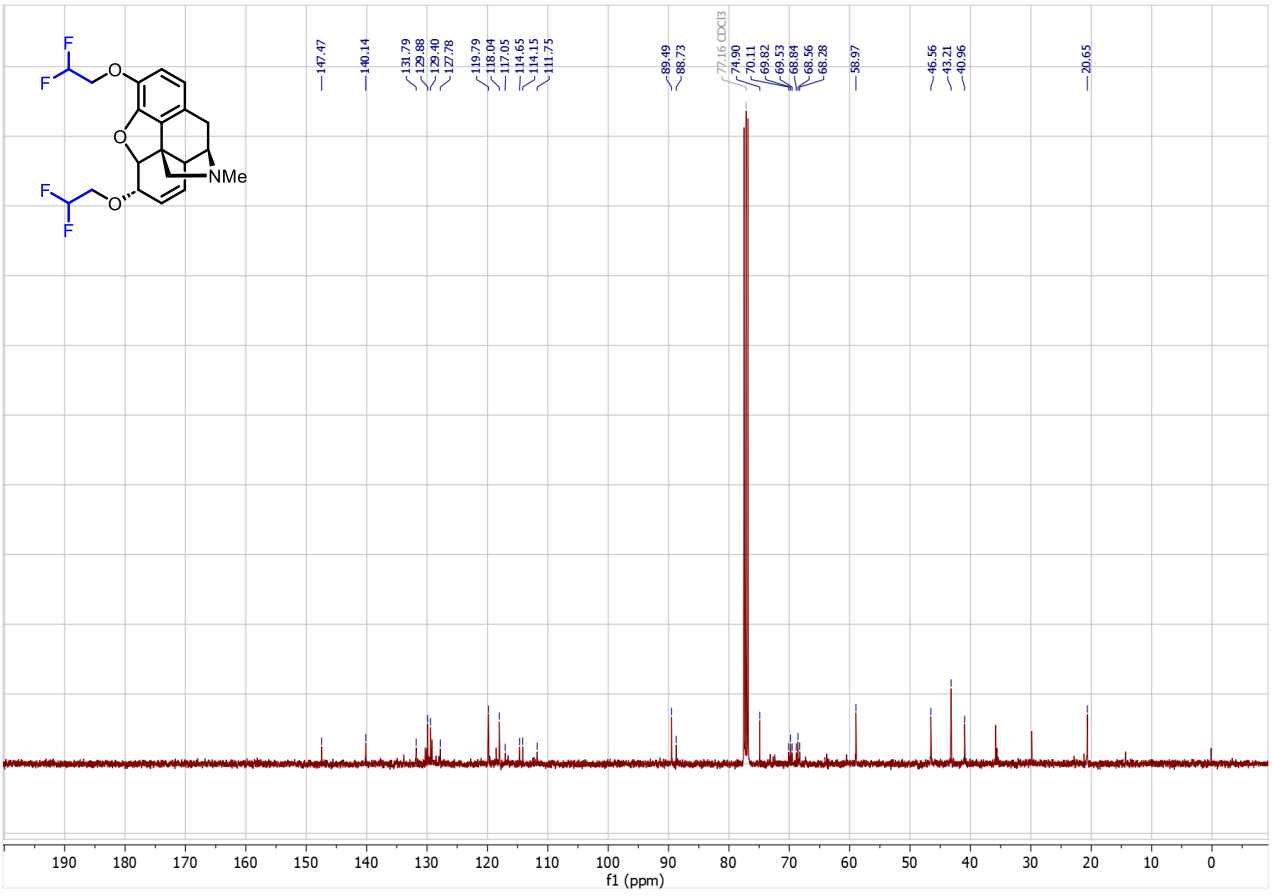

F
F
O
124.82
2.00
-50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

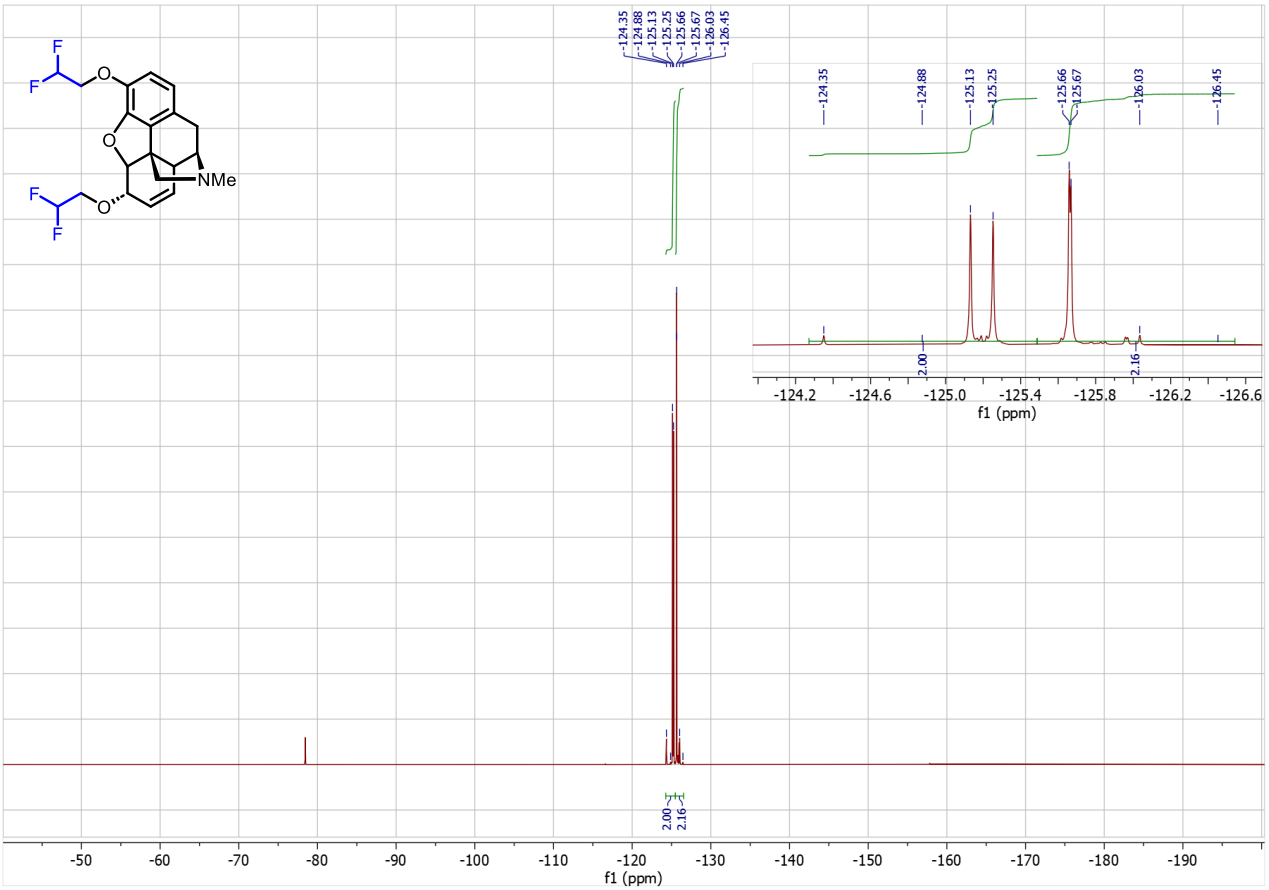

BnO
OBn
OBn
OBn
O
O
F
F
7.35 7.35 7.34 7.34 7.34 7.34 7.33 7.33 7.32 7.32 7.31 7.31 7.31 7.30 7.29 7.29 7.29 7.29 7.28 7.28 7.28 7.27 7.27 7.27 7.26 7.26 CDCl3 7.25 7.17 7.15 7.14 4.96 4.91 4.91 4.88 4.83 4.83 4.81 4.80 4.80 4.78 4.72 4.69 4.65 4.62 4.58 4.58 4.55 4.54 4.48 4.45 4.45 4.43 3.73 3.73 3.71 3.70 3.70 3.69 3.64 3.64 3.62 3.62
17.68
2.01
1.00
9.19
6.82
0.71
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 -0.5 -1
f1 (ppm)

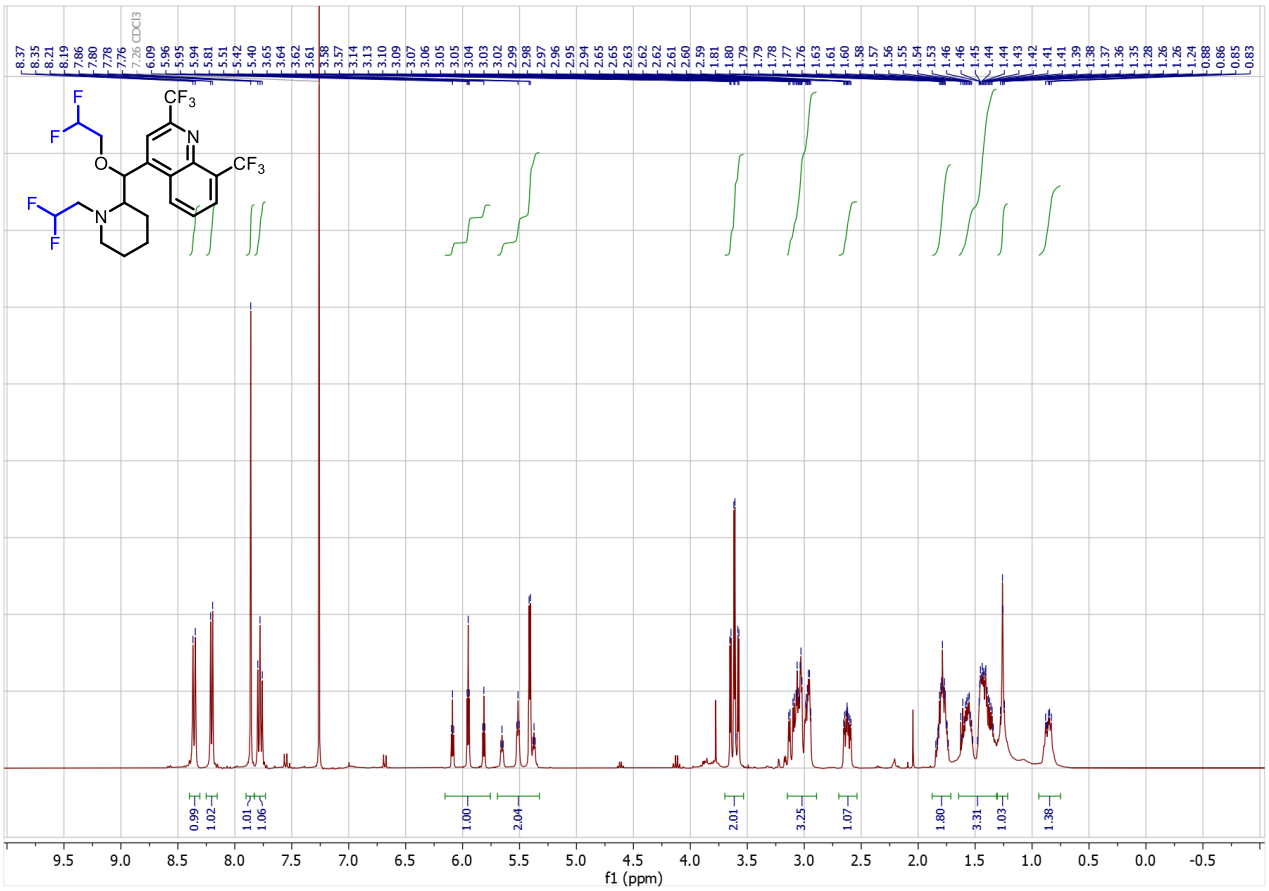

138.83
138.60
138.30
138.21
138.16
138.09
137.89
128.62
128.50
128.36
128.21
128.13
128.08
128.01
127.95
127.89
127.85
127.82
127.74
116.68
116.60
114.29
114.20
111.89
111.80
104.07
98.09
84.56
82.05
81.86
79.91
77.64
77.51
77.48
77.16 CDCl3
77.16
76.84
75.88
75.81
75.23
75.14
75.02
73.58
70.75
69.03
68.78
68.47
68.37
67.60
67.31
67.02
BnO
OBn
OBn
OBn
O
O
F
F
f1 (ppm)
f1 (ppm)

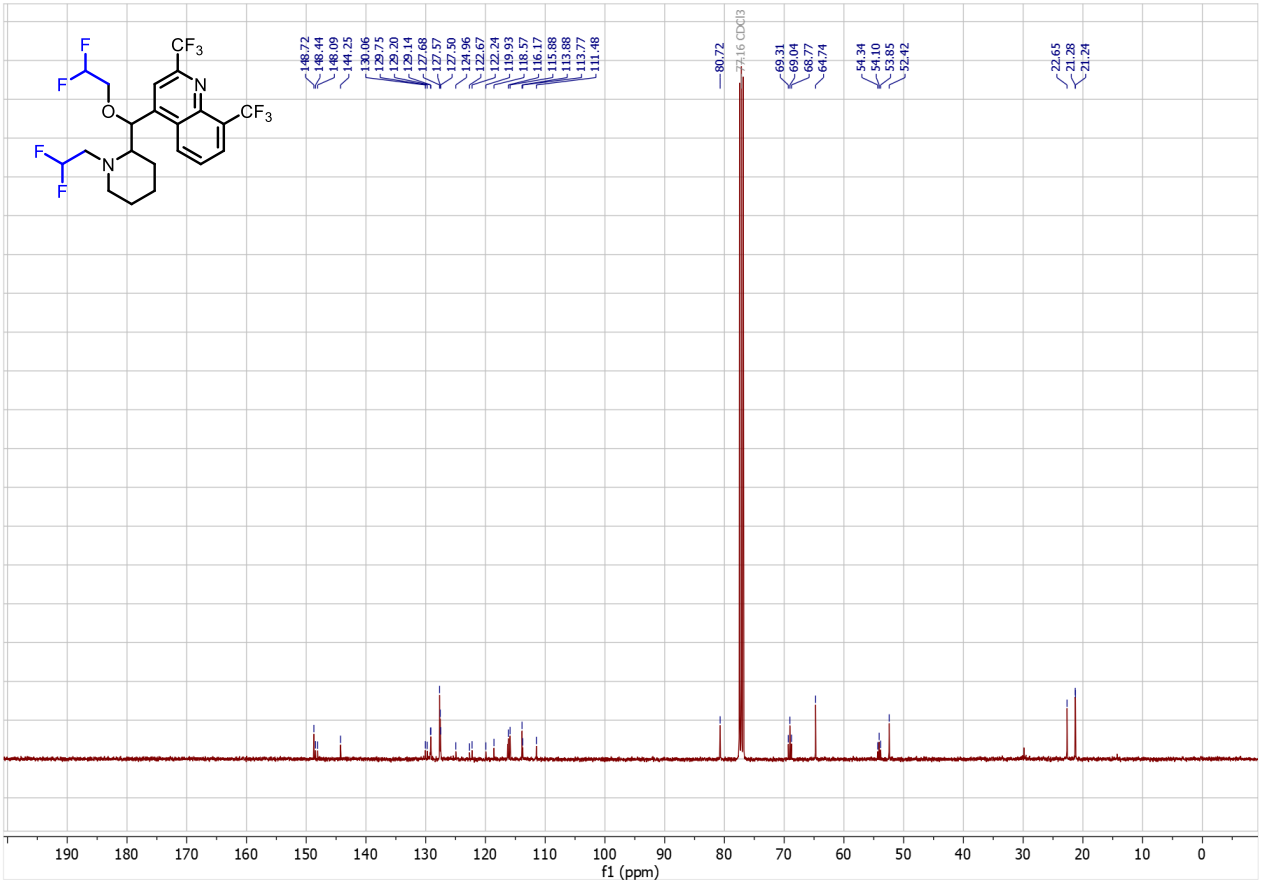

BnO
OBn
OBn
OBn
O
O
F
F
-123.85
-124.26
-124.63
-124.79
-125.04
-125.37
-125.57
-126.15
2.00
f1 (ppm)
f1 (ppm)

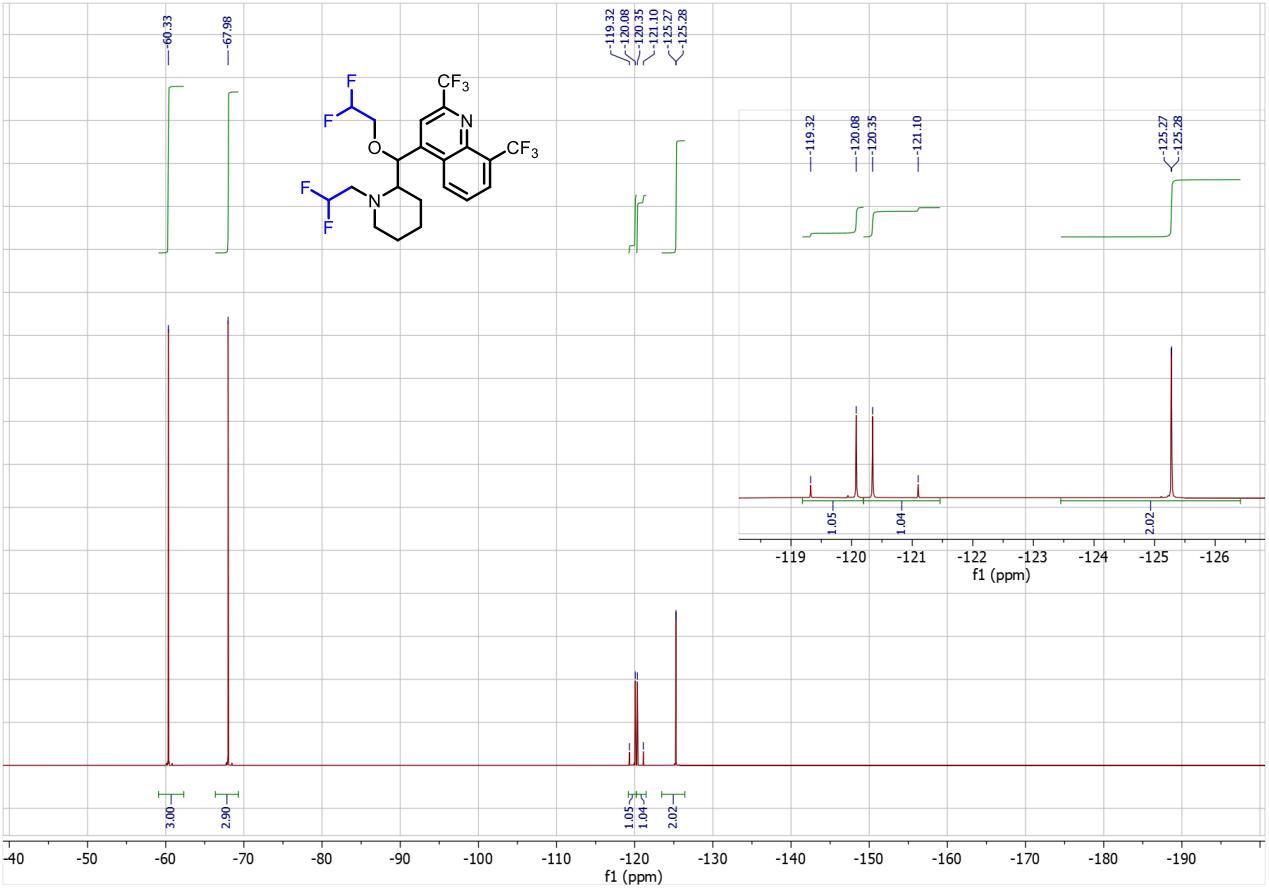

F
F
O
O
NMe
F
F
O
7.26 CDCl3
6.71 6.69 6.68 6.67 6.54 6.53 6.52 6.51 6.08 6.07 6.06 5.95 5.94 5.70 5.70 5.69 5.68 5.67 5.67 5.37 5.36 5.35 5.33 4.97 4.97 4.96 4.95 4.35 4.34 4.33 4.32 4.31 4.30 4.30 4.28 4.27 4.27 4.26 4.03 4.02 4.01 4.00 3.82 3.80 3.79 3.78 3.77 3.37 3.36 3.36 3.35 2.68 2.67 2.66 2.62 2.61 2.60 2.60 2.60 2.59 2.58 2.57 2.44 2.42 2.39 2.39 2.38 2.36 2.35 2.33 2.32 2.30 2.27 2.26 2.03 2.02 2.01 1.91 1.91 1.90 1.90 1.89 1.88 1.88 1.87
1.01 1.00 1.79 1.00 1.05 0.93 2.11 2.26 1.02 1.00 1.15 3.04 1.05 1.05 1.12 1.06
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 -0.5
f1 (ppm)


F
F
O
O
NMe
F
F
O
147.47 140.14 131.79 129.88 129.40 127.78 119.79 118.04 117.05 114.65 114.15 111.75
89.49 88.73
77.16 CDCl3
74.90 70.11 69.82 69.53 68.84 68.56 68.28
58.97
46.56 43.21 40.96
20.65
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

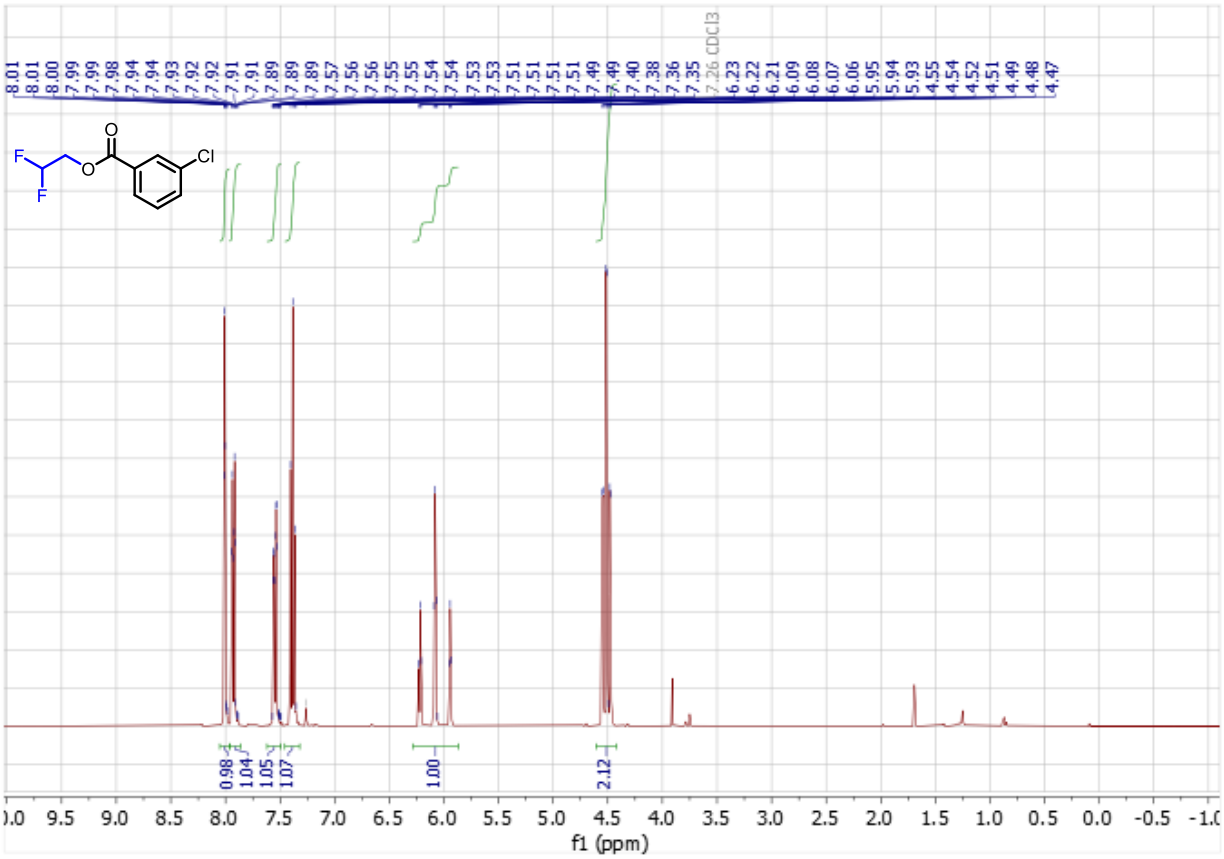

F
F
O
O
NMe
F
F
O
-124.35
-124.88
-125.13
-125.25
-125.66
-125.67
-126.03
-126.45
2.00
2.16
-124.2
-124.6
-125.0
-125.4
-125.8
-126.2
-126.6
f1 (ppm)
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

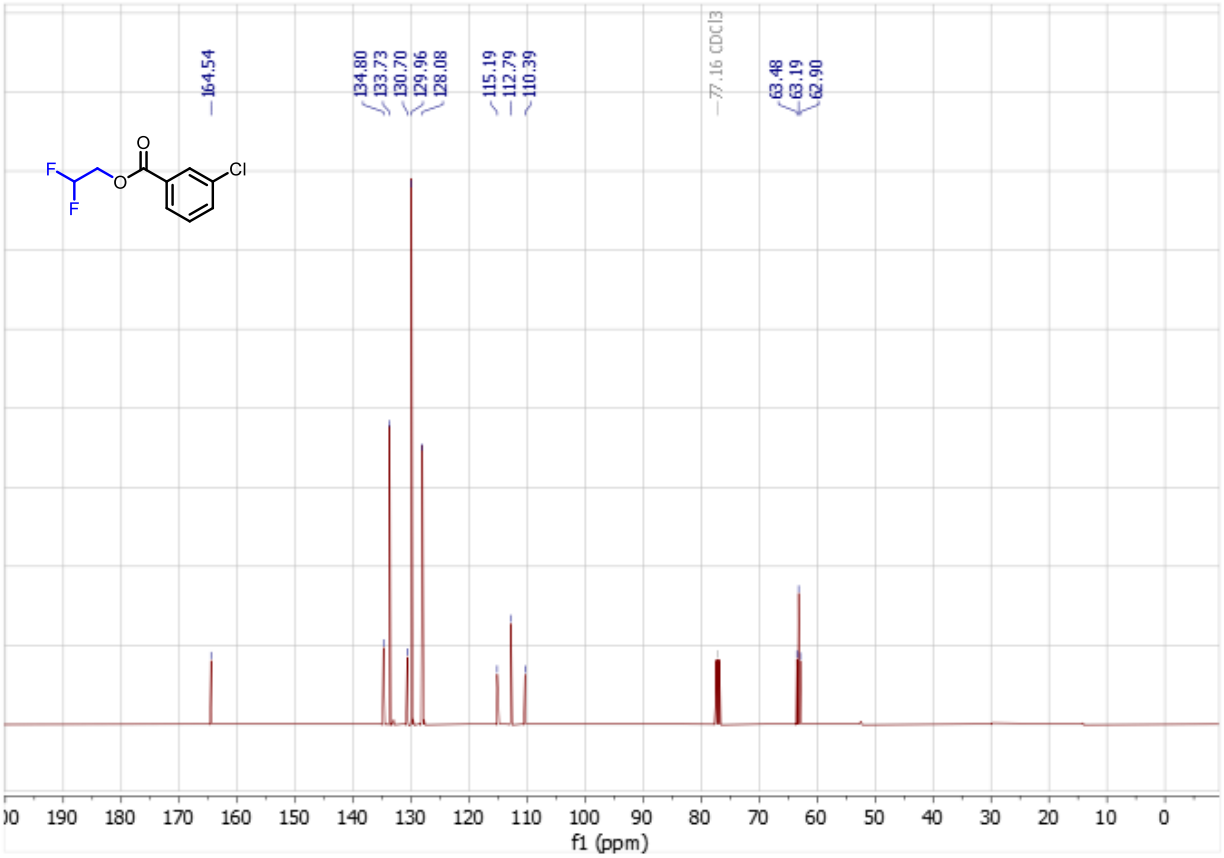

F
F
O
CF3
N
CF3
F
F
N
0.99
1.02
1.01
1.06
1.00
2.04
2.01
3.25
1.07
1.80
3.31
1.03
1.38
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

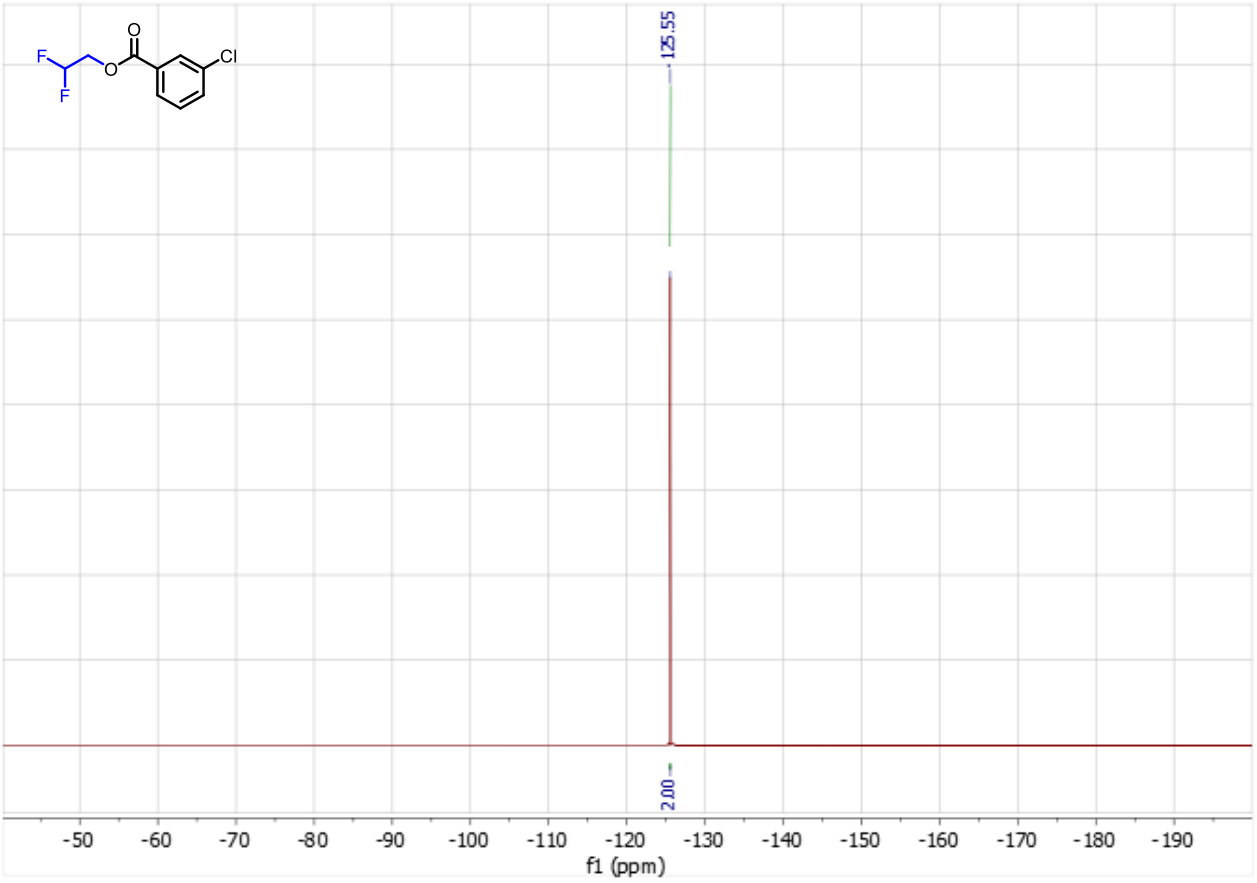

148.72
148.44
148.09
144.25
130.06
129.75
129.20
129.14
127.68
127.57
127.50
124.96
122.67
122.24
119.93
118.57
116.17
115.88
113.88
113.77
111.48
80.72
77.16 CDCl3
69.31
69.04
68.77
64.74
54.34
54.10
53.85
52.42
22.65
21.28
21.24
f1 (ppm)

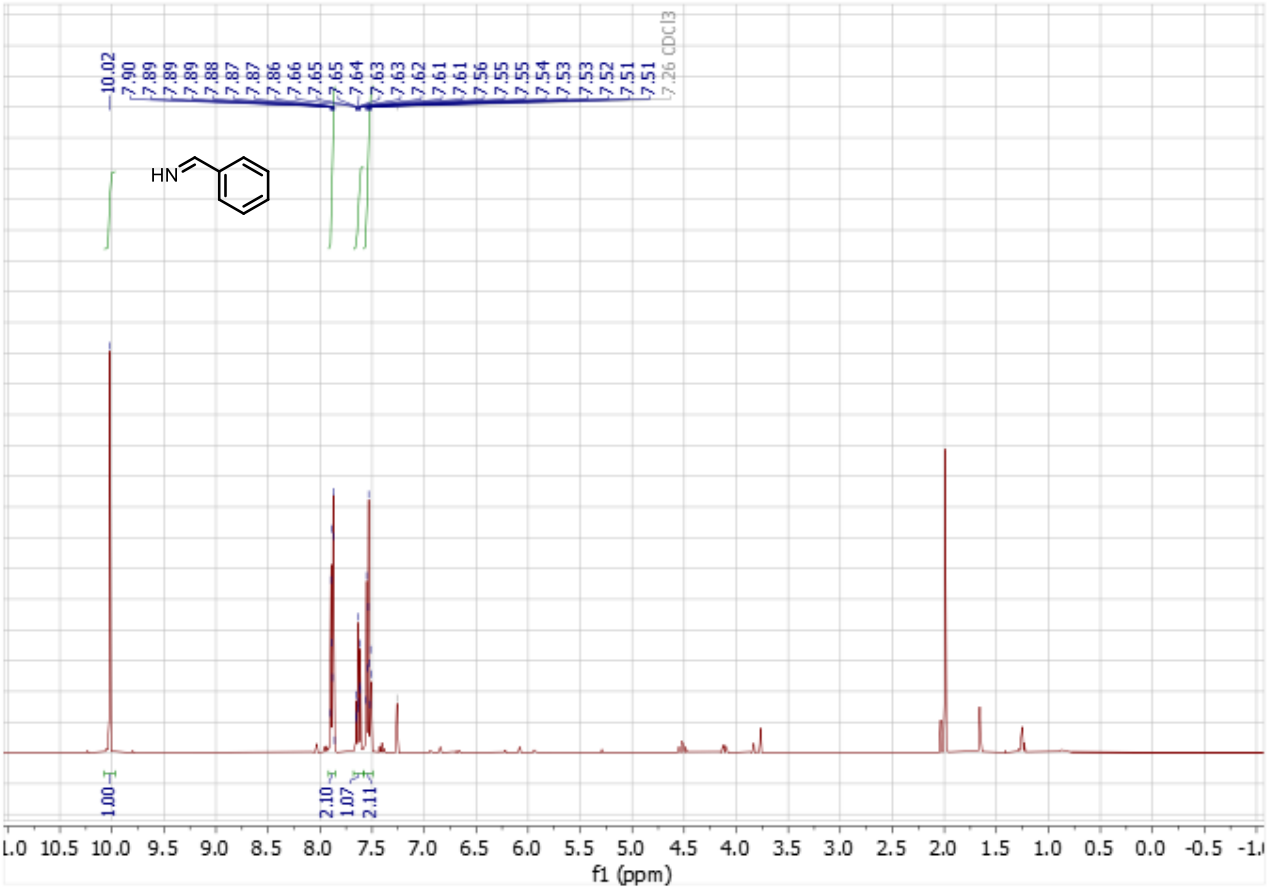

-60.33
-67.98
-119.32
-120.08
-120.35
-121.10
-125.27
-125.28
3.00
2.90
1.05
1.04
2.02
f1 (ppm)

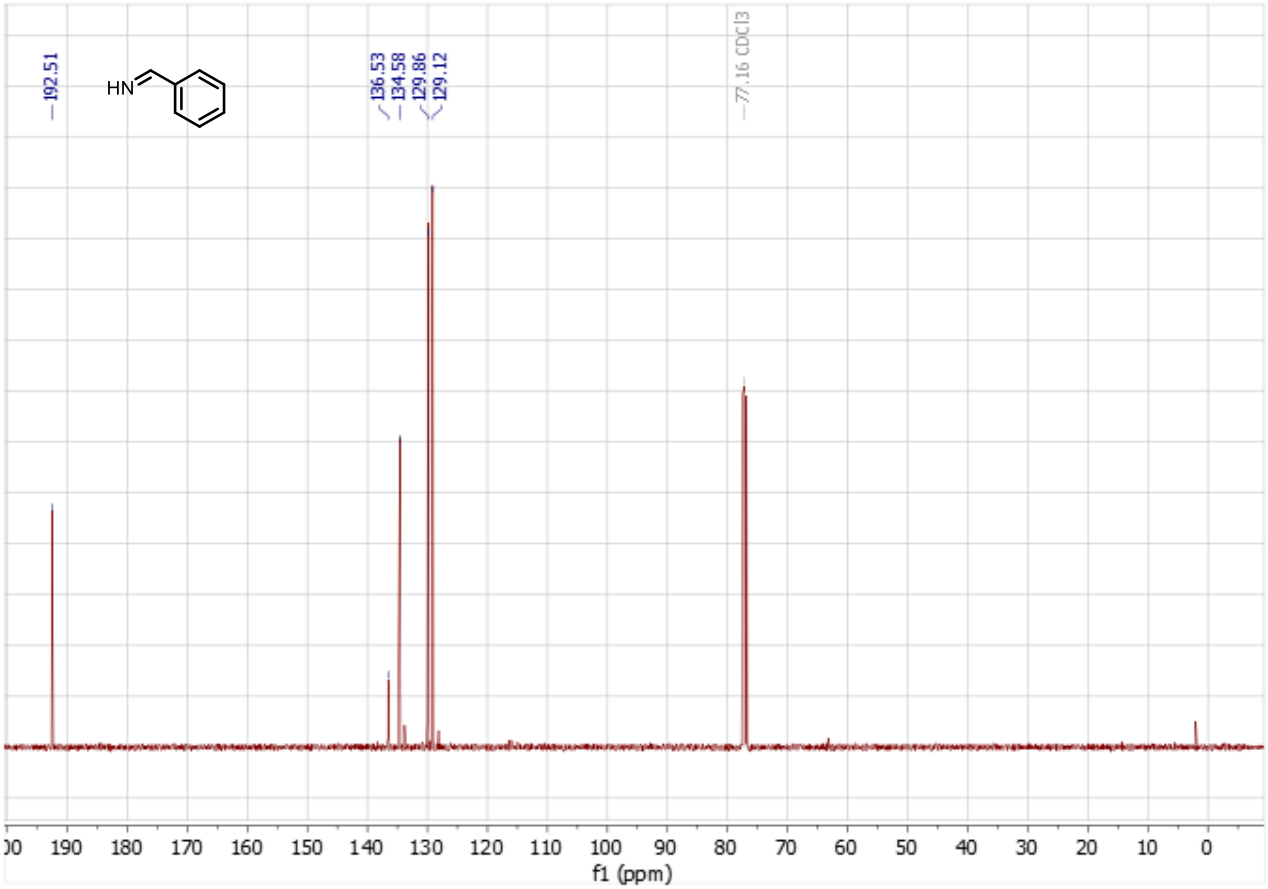
6.4 Miscellaneous

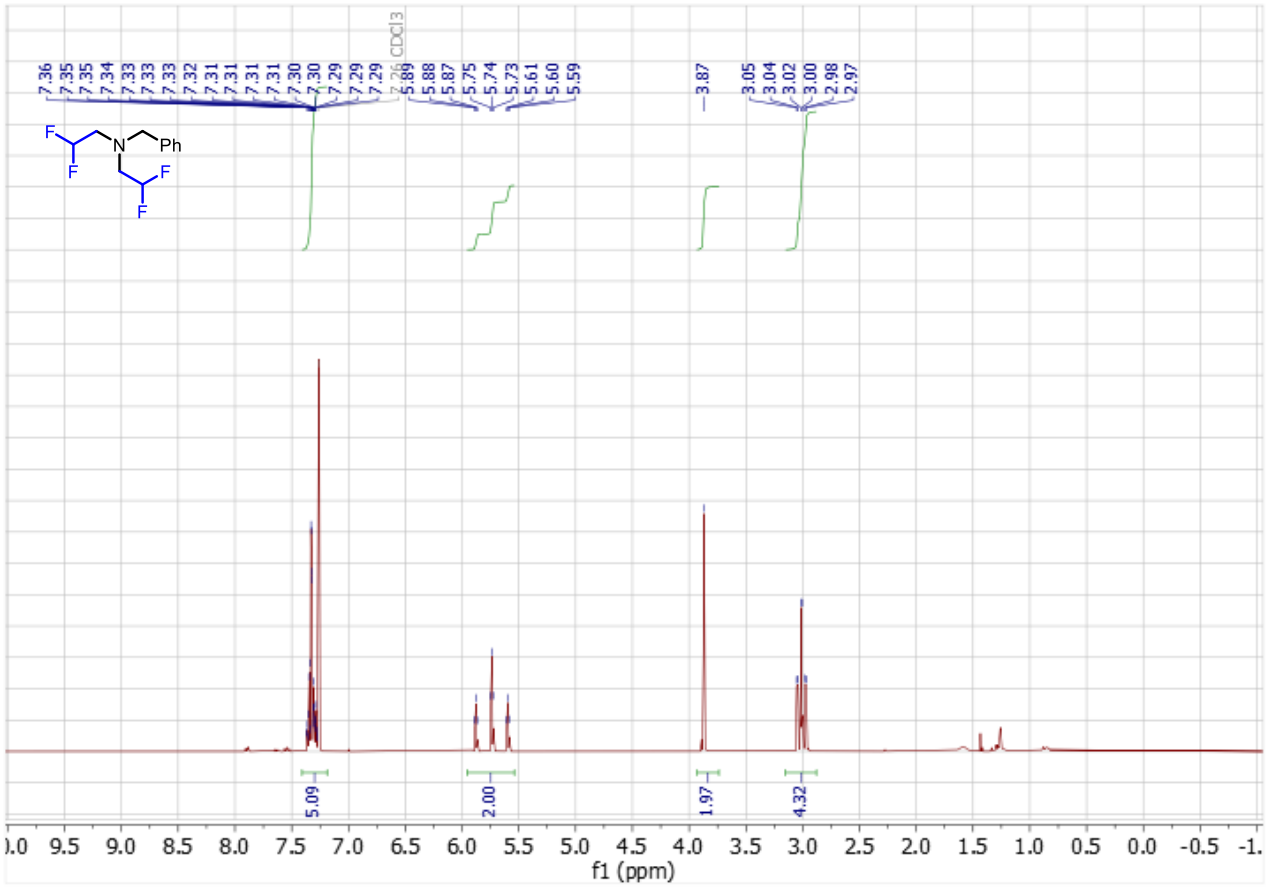


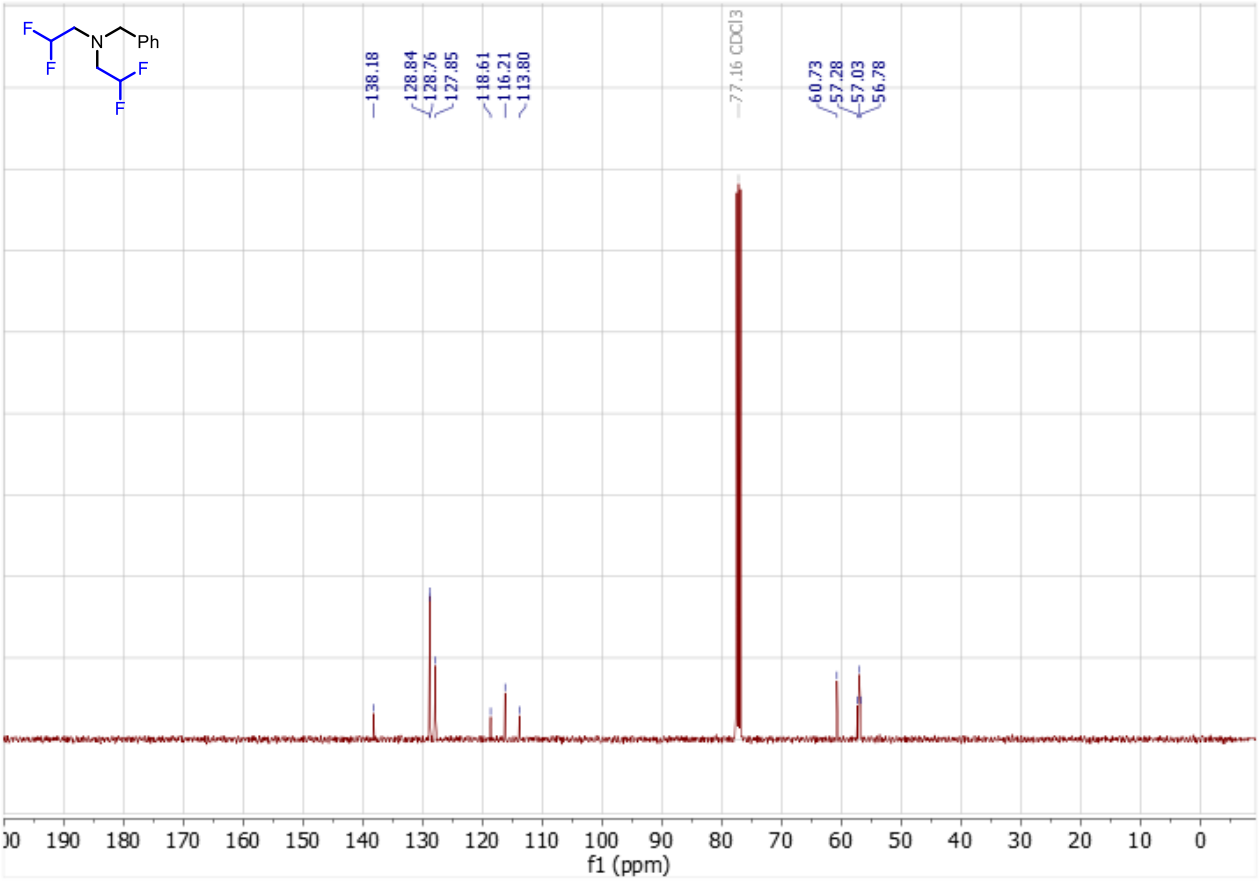


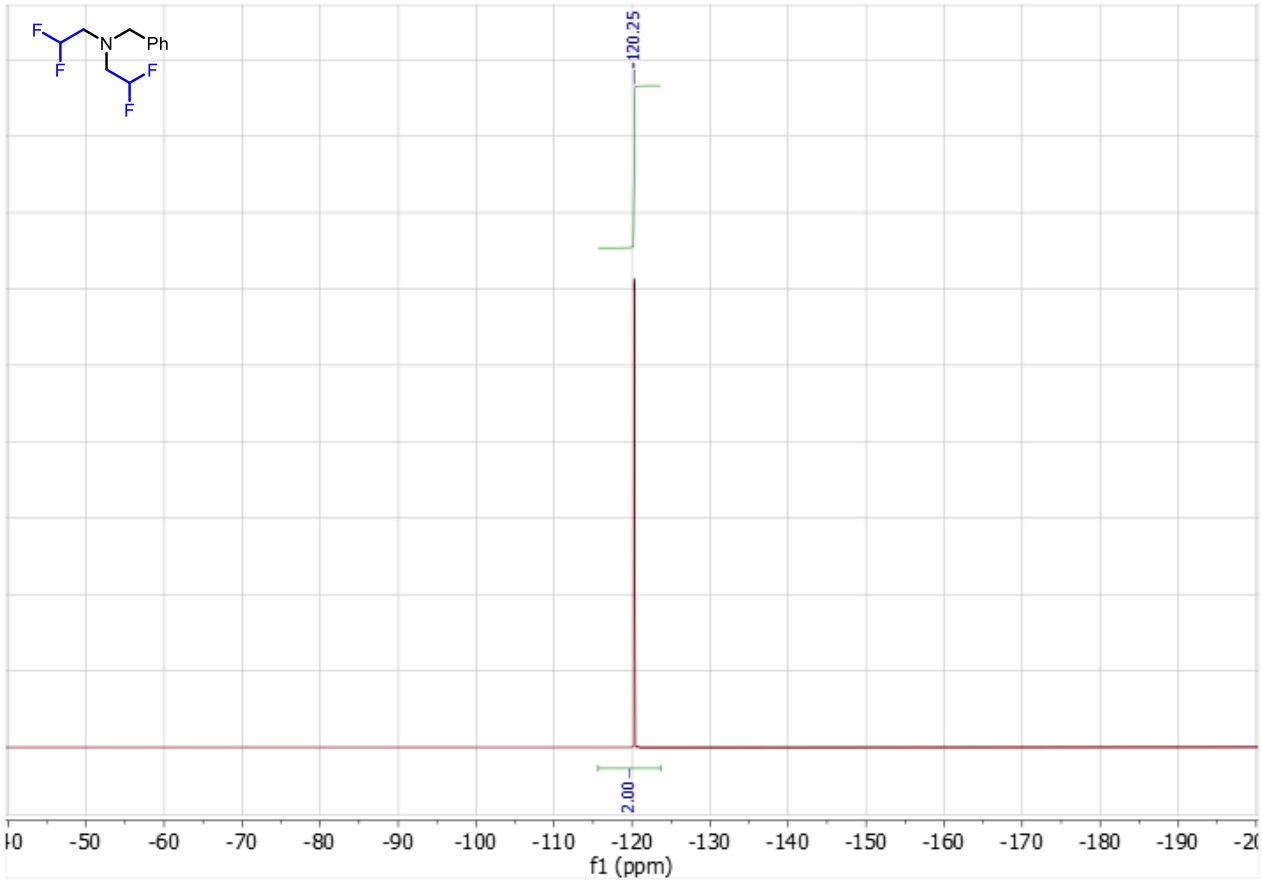

F
F
O
O
Cl
125.55
2.00
-50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)


10.02
7.90
7.89
7.89
7.89
7.88
7.87
7.87
7.86
7.66
7.65
7.65
7.64
7.63
7.63
7.62
7.61
7.61
7.56
7.55
7.55
7.54
7.53
7.53
7.52
7.51
7.51
7.26 CDCl3
HN
1.00
2.10
1.07
2.11
10.5 10.0 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 -0.5
f1 (ppm)


192.51
HN
136.53
134.58
129.86
129.12
77.16 CDCl3
f1 (ppm)


7.36
7.35
7.35
7.34
7.33
7.33
7.32
7.31
7.31
7.31
7.30
7.30
7.29
7.29
7.29
7.26 CDCl3
5.89
5.88
5.87
5.75
5.74
5.73
5.61
5.60
5.59
3.87
3.05
3.04
3.02
3.00
2.98
2.97
F
F
N
Ph
F
F
5.09
2.00
1.97
4.32
f1 (ppm)

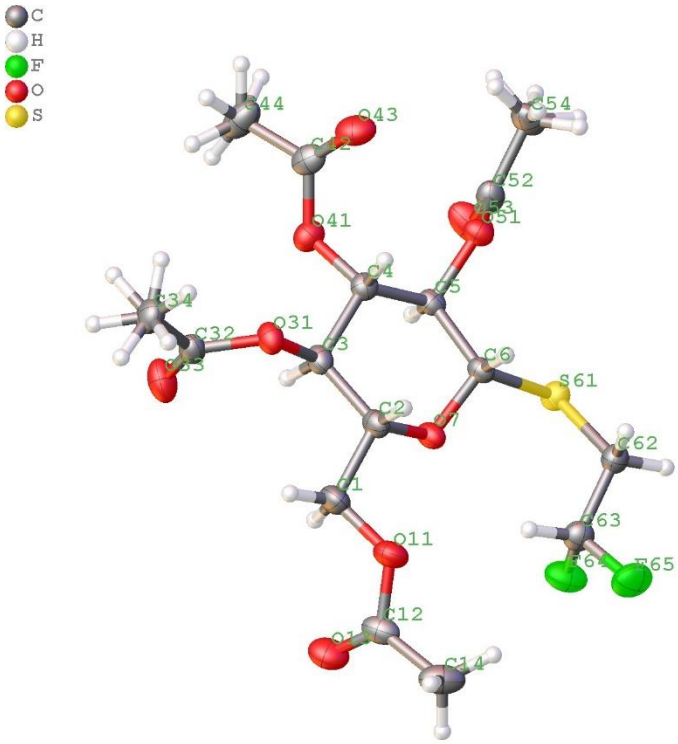

F
F
N
Ph
F
F
138.18
128.84
128.76
127.85
118.61
116.21
113.80
77.16 CDCl3
60.73
57.28
57.03
56.78
f1 (ppm)


F
F
N
Ph
F
F
120.25
2.00
f1 (ppm)

7. XRD Data

Single crystals were selected and mounted using Fomblin® (YR-1800 perfluoropolyether oil) on a polymer-tipped MiTeGen MicroMountTM and cooled rapidly to 120 K in a stream of cold N_2 using an Oxford Cryosystems open flow cryostat.[16] Single crystal X-ray diffraction data were collected on an Oxford Diffraction GV1000 (TitanS2 CCD area detector, mirror-monochromated Cu-Kα radiation source; λ = 1.54184 Å, ω scans). Cell parameters were refined from the observed positions of all strong reflections and absorption corrections were applied using a Gaussian numerical method with beam profile correction (CrysAlisPro).[17] Structures were solved within Olex2[18] by dual space iterative methods (SHELXT)[19] and all non-hydrogen atoms refined by full-matrix least-squares on all unique F2 values with anisotropic displacement parameters (SHELXL).[20] Hydrogen atoms were refined with constrained riding geometries and thermal parameters linked to Uiso of their parent atoms. Structures were checked with checkCIF (http://checkcif.iucr.or). CCDC deposition numbers 2320482 and 2336551 contain the supplementary data for **4p** and **5n** respectively. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

7.1 XRD Data (4p)



All hydrogen atoms were observed in the electron density map. The hydrogen atoms of methyl groups C34, C44 and C54 are disordered over two conformations rotated approximately 60 degrees from one another. The pairs of conformations are modelled as idealised rigid groups riding on the carbon atoms with their respective occupancies refined and constrained to sum to unity (AFIX 123). The occupancies of the major disorder components for methyl hydrogen atoms of C34, C44 and C54 components refine to values of 0.61(3), 0.74(3) and 0.67(3) respectively. All other hydrogen atoms were geometrically placed and refined with a riding model.

Table S10. Crystal data and structure refinement.

Identification code	SDMODJ
Empirical formula	$C_{16}H_{22}F_2O_9S$
Formula weight	428.39
Temperature/K	120(2)
Crystal system	monoclinic
Space group	$P2_1$
a/Å	7.16590(10)
b/Å	10.9372(2)

c/Å	12.7434(2)
α/°	90
β/°	93.5710(10)
γ/°	90
Volume/Å^3	996.82(3)
Z	2
ρ_{calc}g/cm^3	1.427
μ/mm^{-1}	2.037
F(000)	448.0
Crystal size/mm^3	0.393 × 0.216 × 0.043
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	6.95 to 144.446
Index ranges	-8 ≤ h ≤ 8, -13 ≤ k ≤ 11, -15 ≤ l ≤ 15
Reflections collected	15351
Independent reflections	3622 [R_{int} = 0.0249, R_{sigma} = 0.0196]
Data/restraints/parameters	3622/1/257
Goodness-of-fit on F^2	1.094
Final R indexes [I>=2σ (I)]	R_1 = 0.0244, wR_2 = 0.0637
Final R indexes [all data]	R_1 = 0.0250, wR_2 = 0.0641
Largest diff. peak/hole / e Å^{-3}	0.24/-0.18
Flack parameter	0.003(11)

Table S11. Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3). U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
C1	6654(4)	3463(2)	3127.4(19)	36.1(5)
C2	5574(3)	4637(2)	3006.6(15)	26.6(4)
C3	4080(3)	4730(2)	3806.7(15)	25.6(4)
C4	2834(3)	5831(2)	3570.3(14)	23.5(4)
C5	2106(3)	5898.3(19)	2421.8(15)	22.1(4)
C6	3726(3)	5733(2)	1709.5(14)	22.7(4)
O7	4633(2)	4605.0(14)	1980.8(10)	25.1(3)
O11	8158(2)	3518.6(16)	2420.5(13)	34.4(4)
C12	8740(3)	2451(2)	2034.2(19)	31.5(5)
O13	8068(3)	1479.6(18)	2243.9(14)	41.4(4)
C14	10308(3)	2646(3)	1330(2)	43.2(6)
O31	4975(2)	4940.3(15)	4839.9(11)	28.0(3)
C32	4750(3)	4093(2)	5600.4(16)	27.6(5)
O33	3974(3)	3140.9(18)	5447.1(14)	42.5(4)
C34	5601(3)	4527(3)	6637.6(17)	36.7(6)
O41	1270.7(19)	5699.9(17)	4219.8(10)	29.3(3)
C42	706(3)	6701(2)	4741.7(16)	30.4(5)
O43	1329(2)	7705.8(18)	4625.5(14)	39.5(4)
C44	-760(3)	6352(3)	5465.6(19)	44.1(7)
O51	1331.4(18)	7101.7(14)	2271.0(11)	23.8(3)
C52	-486(3)	7212(2)	1925.7(16)	27.6(5)
O53	-1435(2)	6358.5(19)	1638.6(17)	49.3(5)
C54	-1109(3)	8503(3)	1984(2)	37.1(6)
S61	2869.1(6)	5659.3(5)	357.3(3)	26.05(12)
C62	5057(3)	5818(2)	-270.4(15)	27.7(4)
C63	6273(3)	4712(2)	-177.2(17)	29.9(5)
F64	5399(2)	3726.5(14)	-640.2(13)	43.8(4)
F65	7802(2)	4907.4(16)	-752.0(13)	47.0(4)

Table S12. Anisotropic Displacement Parameters ($Å^2×10^3$). The Anisotropic displacement factor exponent takes the form: $-2π^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+…]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C1	44.1(13)	30.2(14)	34.1(11)	5.0(10)	2.1(10)	12.8(11)
C2	31.4(10)	25.0(12)	22.7(9)	1.3(8)	-4.2(8)	5.1(9)
C3	31.4(10)	22.3(12)	22.2(9)	-0.1(8)	-4.3(8)	-0.8(8)
C4	23.7(8)	22.9(12)	23.8(8)	-1.1(8)	-0.4(7)	-2.4(8)
C5	22.0(8)	18.5(12)	25.3(9)	-0.6(8)	-2.5(7)	-1.7(7)
C6	23.7(8)	20.6(11)	23.4(8)	-0.4(8)	-3.0(6)	2.3(9)
O7	29.9(7)	21.7(8)	23.1(6)	-1.1(6)	-4.2(5)	4.4(6)
O11	36.3(8)	26.5(9)	40.3(8)	-2.2(7)	1.4(7)	8.8(7)
C12	29.0(11)	28.2(14)	35.5(11)	-8.9(10)	-12.3(8)	5.0(10)
O13	45.0(9)	29.4(11)	49.2(10)	-9.1(8)	-2.9(7)	1.9(8)
C14	31.2(12)	37.4(16)	60.8(16)	-17.7(13)	1.2(11)	2.2(11)
O31	34.7(7)	26.2(9)	22.4(7)	2.2(6)	-4.6(5)	-1.5(6)
C32	25.6(9)	30.2(14)	27.2(10)	5.3(9)	2.2(8)	3.2(9)
O33	47.9(10)	37.8(12)	40.6(9)	13.0(8)	-5.9(7)	-9.6(9)
C34	41.0(12)	45.1(16)	23.8(10)	4.6(10)	0.7(9)	3.1(11)
O41	27.0(6)	33.1(9)	27.9(6)	-2.9(7)	3.2(5)	-4.1(7)
C42	23.8(9)	43.0(16)	23.3(9)	-5.5(9)	-6.2(7)	3.7(10)
O43	39.6(9)	39.3(12)	39.2(9)	-13.6(7)	0.3(7)	3.3(8)
C44	29.5(11)	73(2)	29.7(11)	-2.2(12)	2.2(9)	6.1(12)
O51	20.1(6)	21.9(8)	28.7(7)	-1.4(6)	-3.5(5)	1.0(6)
C52	20.0(9)	33.9(14)	28.8(10)	5.5(9)	0.0(7)	0.8(9)
O53	30.1(8)	36.3(11)	78.5(13)	4.1(10)	-19.2(8)	-6.1(8)
C54	28.5(11)	35.1(15)	47.6(14)	7.7(11)	2.3(10)	9.4(10)
S61	23.0(2)	32.5(3)	22.0(2)	-1.2(2)	-3.36(15)	1.7(2)
C62	29.4(9)	28.3(13)	25.5(9)	1.3(9)	3.8(7)	-0.2(9)
C63	25.3(10)	33.2(14)	31.3(10)	0.5(9)	2.2(8)	1.2(9)
F64	42.3(8)	28.2(9)	61.1(9)	-7.8(7)	4.2(7)	1.0(6)
F65	34.7(7)	51.2(10)	57.0(9)	-2.2(7)	18.2(6)	1.8(7)

Table S13. Bond Lengths.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C1	C2	1.502(3)	C12	C14	1.497(4)
C1	O11	1.448(3)	O31	C32	1.358(3)
C2	C3	1.527(3)	C32	O33	1.190(3)
C2	O7	1.434(2)	C32	C34	1.498(3)
C3	C4	1.519(3)	O41	C42	1.356(3)
C3	O31	1.447(2)	C42	O43	1.198(3)
C4	C5	1.525(3)	C42	C44	1.490(3)
C4	O41	1.441(2)	O51	C52	1.354(2)
C5	C6	1.529(3)	C52	O53	1.198(3)
C5	O51	1.437(2)	C52	C54	1.485(4)
C6	O7	1.427(3)	S61	C62	1.8122(19)
C6	S61	1.7947(18)	C62	C63	1.491(3)
O11	C12	1.343(3)	C63	F64	1.363(3)
C12	O13	1.204(3)	C63	F65	1.372(3)

Table S14. Bond Angles.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
O11	C1	C2	107.40(19)	O13	C12	O11	123.2(2)
C1	C2	C3	111.47(19)	O13	C12	C14	125.8(2)
O7	C2	C1	106.41(18)	C32	O31	C3	118.37(17)
O7	C2	C3	107.50(16)	O31	C32	C34	110.7(2)
C4	C3	C2	110.37(17)	O33	C32	O31	123.7(2)
O31	C3	C2	109.19(17)	O33	C32	C34	125.6(2)
O31	C3	C4	106.03(16)	C42	O41	C4	117.89(18)
C3	C4	C5	112.99(16)	O41	C42	C44	109.8(2)
O41	C4	C3	106.00(17)	O43	C42	O41	123.7(2)
O41	C4	C5	108.93(15)	O43	C42	C44	126.5(2)
C4	C5	C6	109.70(15)	C52	O51	C5	118.72(16)
O51	C5	C4	106.19(16)	O51	C52	C54	110.7(2)
O51	C5	C6	109.29(16)	O53	C52	O51	123.1(2)
C5	C6	S61	110.39(12)	O53	C52	C54	126.1(2)
O7	C6	C5	108.05(16)	C6	S61	C62	99.54(9)
O7	C6	S61	108.50(14)	C63	C62	S61	113.88(16)
C6	O7	C2	112.40(16)	F64	C63	C62	110.90(18)
C12	O11	C1	116.9(2)	F64	C63	F65	104.63(18)
O11	C12	C14	111.0(2)	F65	C63	C62	108.29(19)

Table S15. Torsion Angles.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
C1	C2	C3	C4	-171.97(19)	C5	C4	O41	C42	-102.80(19)
C1	C2	C3	O31	71.9(2)	C5	C6	O7	C2	-67.90(19)
C1	C2	O7	C6	-172.98(17)	C5	C6	S61	C62	167.69(16)
C1	O11	C12	O13	0.4(3)	C5	O51	C52	O53	-7.7(3)
C1	O11	C12	C14	-179.30(19)	C5	O51	C52	C54	170.78(17)
C2	C1	O11	C12	-150.36(19)	C6	C5	O51	C52	119.67(18)
C2	C3	C4	C5	49.4(2)	C6	S61	C62	C63	72.54(17)
C2	C3	C4	O41	168.65(16)	O7	C2	C3	C4	-55.7(2)
C2	C3	O31	C32	-118.3(2)	O7	C2	C3	O31	-171.89(18)
C3	C2	O7	C6	67.5(2)	O7	C6	S61	C62	-74.09(15)
C3	C4	C5	C6	-49.1(2)	O11	C1	C2	C3	-173.83(18)
C3	C4	C5	O51	-167.14(16)	O11	C1	C2	O7	69.2(2)
C3	C4	O41	C42	135.33(17)	O31	C3	C4	C5	167.55(16)
C3	O31	C32	O33	5.8(3)	O31	C3	C4	O41	-73.22(19)
C3	O31	C32	C34	-174.04(18)	O41	C4	C5	C6	-166.67(18)
C4	C3	O31	C32	122.74(19)	O41	C4	C5	O51	75.3(2)
C4	C5	C6	O7	55.9(2)	O51	C5	C6	O7	171.92(14)
C4	C5	C6	S61	174.37(15)	O51	C5	C6	S61	-69.58(18)
C4	C5	O51	C52	-122.06(18)	S61	C6	O7	C2	172.40(13)
C4	O41	C42	O43	6.4(3)	S61	C62	C63	F64	60.9(2)
C4	O41	C42	C44	-173.14(17)	S61	C62	C63	F65	175.13(14)

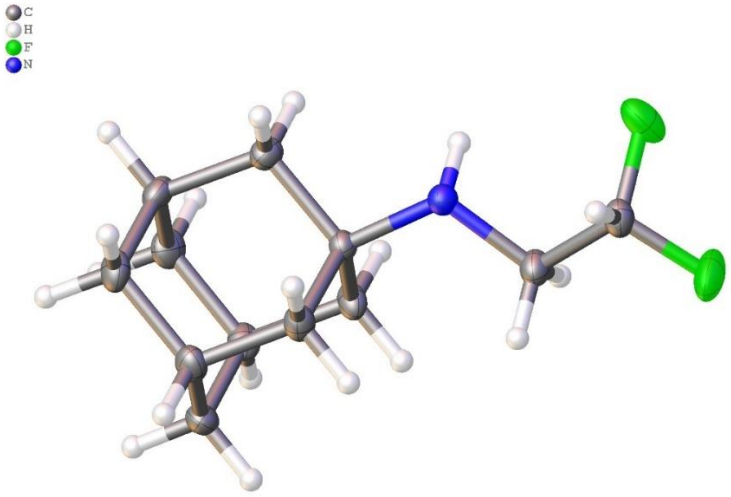
Table S16. Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3).

Atom	*x*	*y*	*z*	U(eq)
H1A	7166.58	3367.68	3862.26	43
H1B	5828.18	2758.2	2947.96	43
H2	6439.43	5354.41	3071.91	32
H3	3316.57	3964.21	3803.64	31
H4	3533.4	6597.08	3766.17	28
H5	1125.1	5261.84	2266.63	27
H6	4629.8	6425.33	1813.51	27
H14A	10001.73	3329.66	852.27	65
H14B	10492.11	1903.19	918.89	65
H14C	11457.76	2833.4	1756.43	65
H34A	6151.55	5338.47	6551.78	44
H34B	4632.49	4573.46	7145.99	44
H34C	6577.03	3953.35	6893.47	44
H34D	5422.5	3905.05	7175.71	44
H34E	6941.55	4670.06	6581.5	44
H34F	4997.02	5290.18	6834.02	44
H44A	-1007.19	5472.32	5404.15	53
H44B	-325.7	6545.82	6190.85	53
H44C	-1911.12	6806.26	5277.77	53
H44D	-1155.49	7077.27	5844.36	53
H44E	-1836.97	6003.78	5057.66	53
H44F	-251.55	5743.34	5970.74	53
H54A	-56.77	9015.05	2244.88	45
H54B	-1558.59	8782.5	1282.98	45
H54C	-2121.4	8564.82	2464.27	45
H54D	-2434.4	8559.86	1749.87	45
H54E	-932.59	8792.41	2711.77	45
H54F	-369.77	9010.09	1530.49	45
H62A	4780.92	6001.12	-1024.88	33
H62B	5752.5	6522.48	46.35	33
H63	6661.75	4538.2	575.17	36

Table S17. Atomic Occupancy.

Atom	*Occupancy*	Atom	*Occupancy*	Atom	*Occupancy*
H34A	0.39(3)	H34B	0.39(3)	H34C	0.39(3)
H34D	0.61(3)	H34E	0.61(3)	H34F	0.61(3)
H44A	0.26(3)	H44B	0.26(3)	H44C	0.26(3)
H44D	0.74(3)	H44E	0.74(3)	H44F	0.74(3)
H54A	0.34(3)	H54B	0.34(3)	H54C	0.34(3)
H54D	0.66(3)	H54E	0.66(3)	H54F	0.66(3)

7.2 XRD Data (5n)



Secondary amine hydrogen atom H1 is refined with the N-H bond restrained to have target value of 0.91 %A (DFIX, esd 0.02 %A). All other hydrogen atoms in the structure were observed in the electron difference map before being geometrically placed and refined with a riding model. A twin law of (-1 0 0 0 -1 0 -0.139 -0.732 1) was suggested by PLATON TwinRotMat, however, neither refinement against an HKLF5 file nor inclusion of the twin law directly in the structure model file resulted in a lower R1 value or a non-zero refined batch scale factor for the twin fraction, hence, the possibility of twinning was not pursued further.

Table S18. Crystal data and structure refinement.

Identification code	SDMODL1
Empirical formula	$C_{12}H_{19}NF_2$
Formula weight	215.28
Temperature/K	120(2)
Crystal system	triclinic
Space group	P-1
a/Å	6.8157(3)
b/Å	7.8824(3)
c/Å	10.6959(6)
α/°	74.294(4)
β/°	87.151(4)
γ/°	88.828(3)
Volume/Å^3	552.47(5)
Z	2
ρ_{calc}g/cm^3	1.294
μ/mm^{-1}	0.818
F(000)	232.0
Crystal size/mm^3	0.152 × 0.137 × 0.061
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	8.596 to 148.228
Index ranges	-7 ≤ h ≤ 8, -9 ≤ k ≤ 9, -13 ≤ l ≤ 13
Reflections collected	11966
Independent reflections	2237 [R_{int} = 0.0227, R_{sigma} = 0.0154]
Data/restraints/parameters	2237/1/139
Goodness-of-fit on F^2	1.262
Final R indexes [I>=2σ (I)]	R_1 = 0.0622, wR_2 = 0.1697
Final R indexes [all data]	R_1 = 0.0649, wR_2 = 0.1708
Largest diff. peak/hole / e Å^{-3}	0.34/-0.26

Table S19. Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3). U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
N1	7369(3)	8799(3)	3997(2)	19.0(5)
C2	7615(4)	7776(4)	5341(3)	23.4(6)
C3	7003(4)	8914(4)	6215(3)	22.8(6)
F4	8162(3)	10392(2)	5916.0(18)	34.9(5)
F5	7354(3)	8054(3)	7476.8(17)	39.9(5)
C6	7426(4)	7807(3)	3000(2)	16.8(5)
C7	5513(4)	6784(4)	3090(3)	21.6(6)
C8	5498(4)	5872(4)	1987(3)	23.5(6)
C9	7248(5)	4597(4)	2096(3)	25.0(6)
C10	9166(4)	5621(4)	1982(3)	22.8(6)
C11	9179(4)	6526(4)	3090(3)	21.5(6)
C12	7578(4)	9188(4)	1683(3)	21.3(6)
C13	5657(4)	7267(4)	676(3)	24.9(6)
C14	9316(4)	7026(4)	673(3)	24.2(6)
C15	7565(4)	8294(4)	571(3)	22.0(6)

Table S20. Anisotropic Displacement Parameters (Å^2×10^3). The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
N1	23.4(12)	17.3(11)	16.5(11)	-5.1(9)	-1.2(9)	-0.2(9)
C2	30.6(15)	22.4(14)	18.7(13)	-7.8(11)	-4.8(11)	3.5(11)
C3	25.0(14)	26.0(14)	19.4(13)	-8.9(11)	-4.0(11)	0.7(11)
F4	35.0(10)	34.8(10)	42.2(11)	-23.5(8)	5.6(8)	-10.1(8)
F5	61.4(13)	42.0(11)	18.9(9)	-12.3(8)	-11.0(8)	14.4(9)
C6	19.7(13)	16.2(12)	15.3(12)	-5.6(10)	-2.0(9)	0.6(10)
C7	21.1(13)	25.9(14)	18.4(13)	-7.1(11)	-0.2(10)	-3.5(11)
C8	24.0(14)	26.1(14)	21.9(13)	-8.3(11)	-2.7(11)	-5.9(11)
C9	37.7(17)	16.9(13)	21.8(13)	-6.9(10)	-4.0(12)	-1.9(11)
C10	26.3(14)	21.9(14)	22.5(14)	-9.8(11)	-5.4(11)	7.3(11)
C11	23.3(14)	22.2(13)	21.6(13)	-9.7(11)	-8.0(10)	5.3(11)
C12	25.6(14)	19.3(13)	18.2(13)	-4.1(10)	-0.1(10)	1.4(11)
C13	26.1(15)	31.1(15)	19.3(13)	-9.1(11)	-6.5(11)	3.9(12)
C14	25.1(14)	28.8(15)	20.7(13)	-10.7(11)	3.1(11)	1.3(11)
C15	29.8(15)	20.4(13)	14.0(12)	-2.1(10)	-0.7(10)	3.4(11)

Table S21. Bond Lengths.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
N1	C2	1.461(3)	C8	C9	1.532(4)
N1	C6	1.482(3)	C8	C13	1.530(4)
C2	C3	1.501(4)	C9	C10	1.533(4)
C3	F4	1.376(3)	C10	C11	1.540(4)
C3	F5	1.367(3)	C10	C14	1.533(4)
C6	C7	1.532(4)	C12	C15	1.538(4)
C6	C11	1.538(4)	C13	C15	1.529(4)
C6	C12	1.530(3)	C14	C15	1.530(4)
C7	C8	1.540(4)			

Table S22. Bond Angles.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C2	N1	C6	116.8(2)	C13	C8	C7	109.3(2)
N1	C2	C3	108.1(2)	C13	C8	C9	109.5(2)
F4	C3	C2	109.3(2)	C8	C9	C10	109.5(2)
F5	C3	C2	110.0(2)	C9	C10	C11	109.1(2)
F5	C3	F4	105.6(2)	C14	C10	C9	109.7(2)
N1	C6	C7	110.0(2)	C14	C10	C11	109.2(2)
N1	C6	C11	113.9(2)	C6	C11	C10	110.1(2)
N1	C6	C12	106.1(2)	C6	C12	C15	110.3(2)
C7	C6	C11	109.2(2)	C15	C13	C8	109.6(2)
C12	C6	C7	108.7(2)	C15	C14	C10	109.5(2)
C12	C6	C11	108.8(2)	C13	C15	C12	109.5(2)
C6	C7	C8	110.2(2)	C13	C15	C14	109.5(2)
C9	C8	C7	109.4(2)	C14	C15	C12	109.3(2)

Table S23. Torsion Angles.

A	B	C	D	Angle/˚	A	B	C	D	Angle/˚
N1	C2	C3	F4	-59.9(3)	C8	C9	C10	C11	60.3(3)
N1	C2	C3	F5	-175.3(2)	C8	C9	C10	C14	-59.3(3)
N1	C6	C7	C8	175.5(2)	C8	C13	C15	C12	-59.5(3)
N1	C6	C11	C10	-177.4(2)	C8	C13	C15	C14	60.3(3)
N1	C6	C12	C15	-177.7(2)	C9	C8	C13	C15	-60.1(3)
C2	N1	C6	C7	74.3(3)	C9	C10	C11	C6	-60.0(3)
C2	N1	C6	C11	-48.7(3)	C9	C10	C14	C15	59.5(3)
C2	N1	C6	C12	-168.3(2)	C10	C14	C15	C12	60.0(3)
C6	N1	C2	C3	-165.7(2)	C10	C14	C15	C13	-59.9(3)
C6	C7	C8	C9	59.7(3)	C11	C6	C7	C8	-58.9(3)
C6	C7	C8	C13	-60.2(3)	C11	C6	C12	C15	59.4(3)
C6	C12	C15	C13	59.8(3)	C11	C10	C14	C15	-60.1(3)
C6	C12	C15	C14	-60.1(3)	C12	C6	C7	C8	59.7(3)
C7	C6	C11	C10	59.1(3)	C12	C6	C11	C10	-59.4(3)
C7	C6	C12	C15	-59.4(3)	C13	C8	C9	C10	59.5(3)
C7	C8	C9	C10	-60.2(3)	C14	C10	C11	C6	60.0(3)
C7	C8	C13	C15	59.7(3)					

Table S24. Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3).

Atom	*x*	*y*	*z*	U(eq)
H1	8330(40)	9610(40)	3810(30)	23
H2A	9004.78	7407.16	5467.03	28
H2B	6793.8	6705.61	5548.19	28
H3	5584.34	9250.58	6122.16	27
H7A	4378.38	7603.43	3026.44	26
H7B	5389.34	5889.45	3941.2	26
H8	4246.33	5205.84	2055.75	28
H9A	7234.87	3994.16	1396.05	30
H9B	7150.04	3690.79	2942.46	30
H10	10308.86	4789.97	2048.82	27
H11A	9100.22	5624.06	3939.12	26

Table S24. Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3).

Atom	*x*	*y*	*z*	U(eq)
H11B	10420.64	7178.75	3029.47	26
H12A	8807.51	9862.43	1612.32	26
H12B	6458.99	10024.31	1613.32	26
H13A	5640.51	6691.38	-38.89	30
H13B	4519.81	8085.86	596.91	30
H14A	10555.7	7685.32	598.05	29
H14B	9324.15	6453.74	-45.56	29
H15	7661.25	9209.85	-283.11	26

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9. Author Contributions

SD – led experimental investigation, data curation and analysis, validation, writing of original draft
CMcI – experimental investigation, data curation and analysis, validation
AG – supporting experimental investigation
CS – supporting experimental investigation
SPA – XRD analysis and refinement
MOD – design and development of project idea, funding acquisition, project administration, data analysis, writing of original draft.