Supporting Information

Designer HF-Based Fluorination Reagent: Highly Regioselective Synthesis of Fluoroalkenes and *gem*-Difluoromethylene Compounds from Alkynes

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1. General

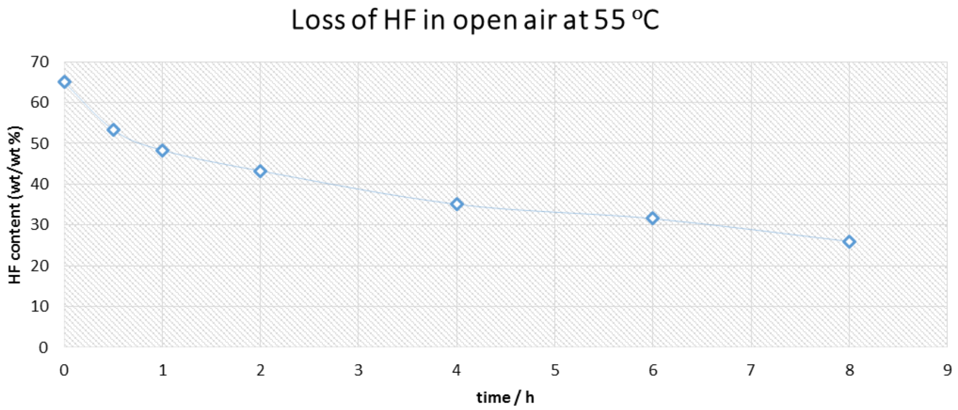
^1H and ^{13}C NMR spectra were recorded at 500 and 126 (or 400 and 101) MHz respectively, using $CDCl_3$ as a solvent. The chemical shifts are reported in δ (ppm) values (^1H and ^{13}C NMR relative to $CHCl_3$, δ 7.26 ppm for ^1H NMR and δ 77.0 ppm for ^{13}C NMR, multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (hextet), m (multiplet) and br (broad). Coupling constants, *J*, are reported in Hertz (Hz). All air and/or moisture sensitive reactions were carried out under argon atmosphere. Solvents (1,2-dichloroethane and dichloromethane) were chemically dried using a commercial solvent purification system. All other reagents and solvents were employed without further purification. The products were purified using a commercial flash chromatography system or a regular glass column. TLC was developed on Merck silica gel 60 F254 aluminum sheets.

Gold pre-catalyst (**Au-1**) was prepared using our published procedure.[1]

2. Preparation of DMPU/HF complex (HF 65% w/w)

DMPU (5 g) was added into a long Teflon tube, the Teflon tube was cooled to 0°C, and 9.3g of HF gas was condensed into the Teflon tube under stirring. The obtained liquid was stored in a 25 mL Teflon vial with a screw cap at room temperature.

The boiling point of DMPU/HF complex (HF 65% w/w) is around 50-120 °C. The boiling point is not well defined (HF evaporates continuously in the range of 50-120 °C).



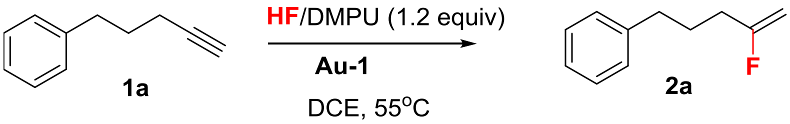
We also conducted HF loss experiment in open air at 55°C (the reaction temperature we used in our synthetic applications). In a well-vented fume hood, 1 gram of DMPU/HF complex (HF 65% w/w) was added to 5 mL polypropylene vial, the vial was heated to 55°C in open air (without cap), and we measured the weight of polypropylene vial periodically. We calculated the percent of HF left over time (we assumed evaporation of DMPU was negligible).

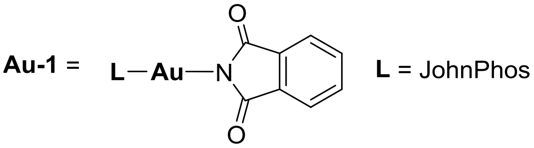
3. General Procedures for preparation of 2 and 3

Reactions were performed in 5 mL polypropylene vials with cone-lined caps. GC-MS and ^{19}F NMR analysis were used to monitor the progress of reactions.

General procedure for synthesis of fluoroalkene 2

Using synthesis of **2a** as an example:

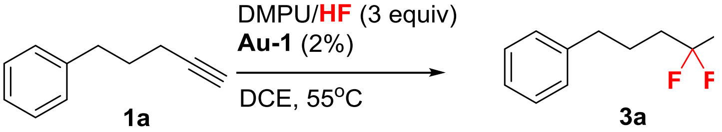




To a solution of 5-phenyl-1-pentyne **1a** (14.4 mg, 0.10 mmol) in DCE (0.5 mL) in a polypropylene vial, imidogold precatalyst **Au-1** (2 mol%, 0.01 M stock solution in DCE) was added at room temperature. The reaction mixture was stirred for 3 h at 55°C. Upon completion, the reaction was quenched with saturated sodium bicarbonate. The mixture was extracted with hexane and washed with brine; the organic layer was collected, dried over anhydrous $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was subjected to flash column chromatography purification (eluent: hexane) to give fluoroalkene **2a** as a colorless oil.

General procedure for synthesis of gem-difluoromethylene compounds 3

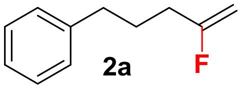
Using synthesis of **3a** as an example:



To a solution of 5-phenyl-1-pentyne (14.4 mg, 0.10 mmol) in DCE (0.5 mL), imidogold precatalyst **Au-1** (2 mol% from a 0.01 M solution in DCE), $KHSO_4$ (1.5 equiv) were added at room temperature. The mixture was stirred for 24 h at 55°C. Upon completion, the reaction was quenched with saturated sodium bicarbonate. The mixture was separated with hexane and washed with brine; the organic layer was collected, dried over anhydrous $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the residue was subjected to flash column chromatography purification (eluent: hexane) to give **3a** as a colorless oil.

4. Spectroscopic data of 2 and 3

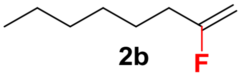
(4-fluoropent-4-en-1-yl) benzene (**2a**)



2a

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.18 (m, 5H), 4.52 (dd, J = 17.6, 2.6 Hz, 1H), 4.31 – 4.12 (m, 1H), 2.66 (t, J = 7.7 Hz, 2H), 2.27 – 2.13 (m, 2H), 1.92 – 1.78 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -94.91 (ddd, J = 50.0, 33.4, 16.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.62, 128.41, 128.34, 125.89, 89.80, 89.60, 34.89, 31.56, 31.38, 31.11, 27.60, 22.63. HRMS (EI +) for $C_{11}H_{13}F$ Cald = 164.1001, found 164.1001.

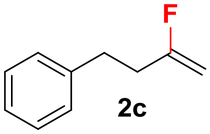
2-fluorooct-1-ene (**2b**)



2b

^{19}F NMR (CCl_4) 93.5 ppm ($CFCl_3$) (m). Its spectroscopic data is consistent with a literature report.[2]

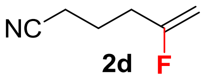
(3-fluorobut-3-en-1-yl) benzene (**2c**)



2c

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.46-2.62 (m, 2H), 2.48-2.92 (m, 2H), 4.45 (dd, $^2J_{H\text{-}F}$ = 50.0 Hz, J = 2.5 Hz, 1H), 4.61 (dd, $^2J_{H\text{-}F}$ = 18.0 Hz, J = 2.5 Hz, 1H), 7.22-7.33 (m, 3H), 7.47-7.55 ppm (m, 2H); ^{19}F NMR (470 MHz, $CDCl_3$): d = -95.5 ppm (dq, $^3J_{F\text{-}H(olefin)}$=49.8 Hz, $^3J_{F\text{-}H}$ = $^3J_{F\text{-}Hcis(olefin)}$ =17.4 Hz, 1F,). Its spectroscopic data is consistent with a literature report.[3]

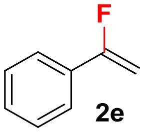
5-fluorohex-5-enenitrile (**2d**)



2d

^{1}H NMR (400 MHz, CDCl$_3$) δ 4.59 (dd, *J* = 17.2, 3.0 Hz, 1H), 4.31 (dd, *J* = 49.7, 2.9 Hz, 1H), 2.48 – 2.28 (m, 4H), 1.87 (m, 2H).^{19}F NMR (376 MHz, CDCl$_3$) δ -97.09 (m, 1F).^{13}C NMR (100 MHz, CDCl$_3$) δ 165.25, 162.69, 118.95, 91.68, 91.48, 30.71, 30.43, 21.83, 16.16. HRMS (ESI +) Calcd. for C_6H_9FN 114. 0719, found 114.0720.

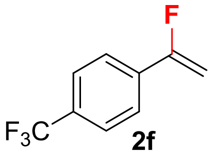
(1-fluorovinyl) benzene (**2e**)



2e

Following general procedure for synthesis of **2** except ratio of phenylacetylene and DMPU/HF is 2:1. ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.57-7.55 (m, 2H), 7.38-7.37 (m, 3H), 5.04 (dd, 1H, *J* = 49.7; 3.4 Hz), 4.85 (dd, 1H, *J* = 17.7, 3.4 Hz). ^{19}F NMR (282 MHz, CDCl$_3$): δ –108.47 (dd, $^3J_{HF}$ = 51.9; 18.3 Hz). Its spectroscopic data is consistent with a literature report.[3]

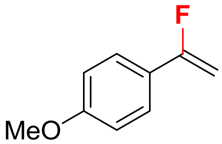
1-(1-fluorovinyl)-4-(trifluoromethyl)benzene (**2f**)



2f

^{1}H NMR (CDCl$_3$, 300 MHz): δ 4.98 (dd, 1 H, *J* = 17.5, 3.7 Hz), 5.14 (dd, 1H, *J* = 48.9, 3.7 Hz, H$_B$), 7.58–7.70 (m, 4H). ^{19}F NMR (CDCl$_3$, 282 MHz): d 63.42 (s, 3F, CF$_3$), 108.72 (dd, 1F, *J* = 50.8, 17.7 Hz, 1-CF). Its spectroscopic data is consistent with a literature report.[4]

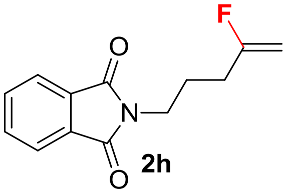
1-(1-fluorovinyl)-4-methoxybenzene (**2g**)



2g

Following general procedure for synthesis of **2** except ratio of phenylacetylene and DMPU/HF is 2:1. ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.50 (d, *J* = 8.8 Hz, 2 H), 6.90 (d, *J* = 8.7 Hz, 2 H), 4.89 (dd, *J* = 3.4, 50.2 Hz, 1 H), 4.74 (dd, *J* = 3.4, 18.1 Hz, 1 H), 3.84 (s, 3 H) ppm. ^{19}F NMR (CDCl$_3$, 376 MHz) δ –107.2 (dd, $^3J_{F–H}$ = 18.1, 50.0 Hz, 1F). Its spectroscopic data is consistent with a literature report.[5]

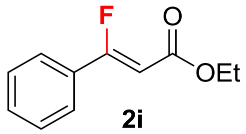
2-(4-fluoropent-4-en-1-yl)isoindoline-1,3-dione (**2h**)



2h

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.89 – 7.80 (m, 2H), 7.72 (dt, *J* = 4.5, 3.6 Hz, 2H), 4.52 (dd, *J* = 17.5, 2.2 Hz, 1H),4.28 (dd, *J* = 50.2, 2.1 Hz, 1H), 3.73 (t, *J* = 7.1 Hz, 2H), 2.25 (dt, *J* = 15.3, 7.6 Hz, 2H), 1.99 – 1.83 (m, 2H).^{19}F NMR (376 MHz, CDCl$_3$) δ -95.15 (m, 1F).^{13}C NMR (101 MHz, CDCl$_3$) δ 168.31, 166.63, 164.08, 133.96, 132.02, 123.23, 90.28, 90.08, 77.32,77.00, 76.68, 37.16, 29.45, 29.17, 25.04. HRMS (CI +) calcd. for $C_{13}H_{13}FNO_2$ 234. 0930, found 234. 0930.

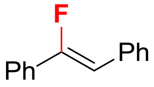
(Z)-ethyl 3-fluoro-3-phenylacrylate (**2i**)



2i

^{1}H NMR (400 MHz, CDCl$_3$), δ 7.62 (d, *J* = 7.6 Hz, 2H), 7.38-7.47 (m, 3H), 5.88 (d, *J* = 33.4 Hz, 1H), 4.23 (q, *J* = 7.2 Hz, 2H), 1.30 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 166.1 (d, *J* = 275.9 Hz), 163.90 (d, *J* = 2.3 Hz), 125.5 (d, *J* = 8.0 Hz), 97.1 (d, *J* = 6.8 Hz), 60.3, 14.1. ^{19}F NMR (376 MHz, CDCl$_3$) δ 96.16 (d, *J* = 33 Hz, 1F). Its spectroscopic data is consistent with a literature report.[6]

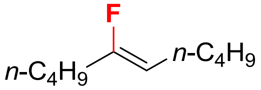
(Z)- (1-fluoroethene-1,2-diyl)dibenzene (**2j**)



2j

^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.67–7.69 (m, 4 H), 7.37–7.46 (m, 5 H), 7.27–7.31 (m, 1 H), 6.34 (d, *J* = 39.5 Hz, 1 H) ppm. ^{19}F NMR (CDCl$_3$, 376 MHz) δ –114.2 (d, $^3J_{F–H}$ = 39.9 Hz). Its spectroscopic data is consistent with literature report.[7]

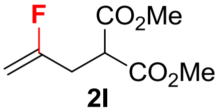
(Z)-5-fluorodec-5-ene (**2k**)



2k

^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.46 (dt, J = 38.4, 7.2 Hz, 1H), 2.14 (dt, J = 17.2, 7.2 Hz, 2H), 2.08-2.03 (m, 2 H), 1.51-1.43 (m, 2H), 1.39-1.28 (m, 6H),0.95-0.88 (m, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ –110.7 (dt, J = 38.4, 16.9 Hz). Its spectroscopic data is consistent with a literature report.[8]

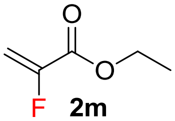
Dimethyl 2-(2-fluoroallyl)malonate (**2l**)



2l

^{1}H NMR (700 MHz, $CDCl_3$) δ 4.59 (dd, J = 17.0, 2.6 Hz, 1H), 4.33 (dd, J = 49.4, 2.8 Hz, 1H), 3.73 (s, 3H), 3.65 (s, 3H), 2.81 (dd, J = 17.0, 7.6 Hz, 2H).^{19}F NMR (470 MHz, $CDCl_3$) δ -97.34 (m, 1F). ^{13}C NMR (176 MHz, $CDCl_3$) δ 168.58, 166.89, 92.34, 92.23, 52.78, 52.53, 48.80, 41.10, 31.47, 31.31. EI-HR MS (ESI +) Calcd for $C_8H_{11}FO_4$ 190.0641, found: 190.0639.

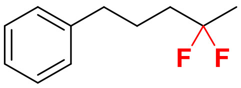
Ethyl 2-fluoroacrylate (**2m**)



2m

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.67 (dd, 1H, J = 43.5, 3.4 Hz), 5.31 (dd, 1H, J = 13.2, 3.4 Hz), 4.30 (q, 2H, J = 7.2 Hz), 1.34 (t, 3H, J = 7.1 Hz). ^{19}F NMR (282 MHz, $CDCl_3$): δ –117.72 (d, $^3J_{HF}$ = 42.7 Hz). Its spectroscopic data is consistent with literature report.[9] Pure **2m** was not isolated due to its volatility.

(4, 4-Difluoropentyl)benzene (**3a**)

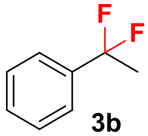


3a

^{19}F NMR (376 MHz, $CDCl_3$) δ -90.529 (m, 1F). HRMS (EI +) calcd. for $C_{11}H_{14}F_2$ 184.1064;

found 184.1064. Note: The product **3a** is very volatile and usually cyclizes on silica gel chromatography, so analytically pure **3a** couldn't be obtained.

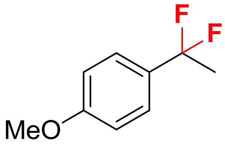
(1,1-Difluoroethyl)benzene (**3b**)



3b

^{19}F NMR (376 MHz, $CDCl_3$) δ -87.16 (q, J =18.6 Hz). Its spectroscopic data is consistent with a literature report.[10]

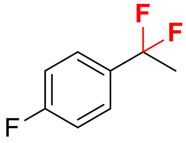
1-(1,1-Difluoroethyl)-4-methoxybenzene (**3c**)



3c

^{19}F NMR (376 MHz, $CDCl_3$) δ -86.4 (q, J =18.6 Hz). Its spectroscopic data is consistent with a literature report.[11]

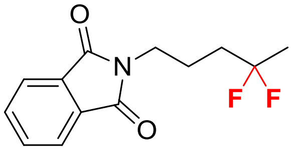
1-(1,1-difluoroethyl)-4-fluorobenzene (**3d**)



3d

^{19}F NMR (376 MHz, $CDCl_3$) δ -86.08 (q, J = 19.0 Hz, 2F), -113.17 (m, 1F). Its spectroscopic data is consistent with a literature report.[12]

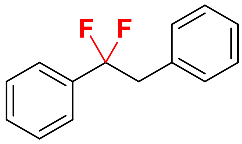
2-(4,4-difluoropentyl)isoindoline-1,3-dione (**3e**)



3e

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88-7.83 (m, 2H), 7.76-7.70 (m, 2H), 3.74 (t, J = 6.6 Hz, 2H), 1.93-1.87 (m, 4H), 1.59 (t, J_{HF} = 18.4 Hz, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ - 91.4 (m). Its spectroscopic data is consistent with a literature report.[13]

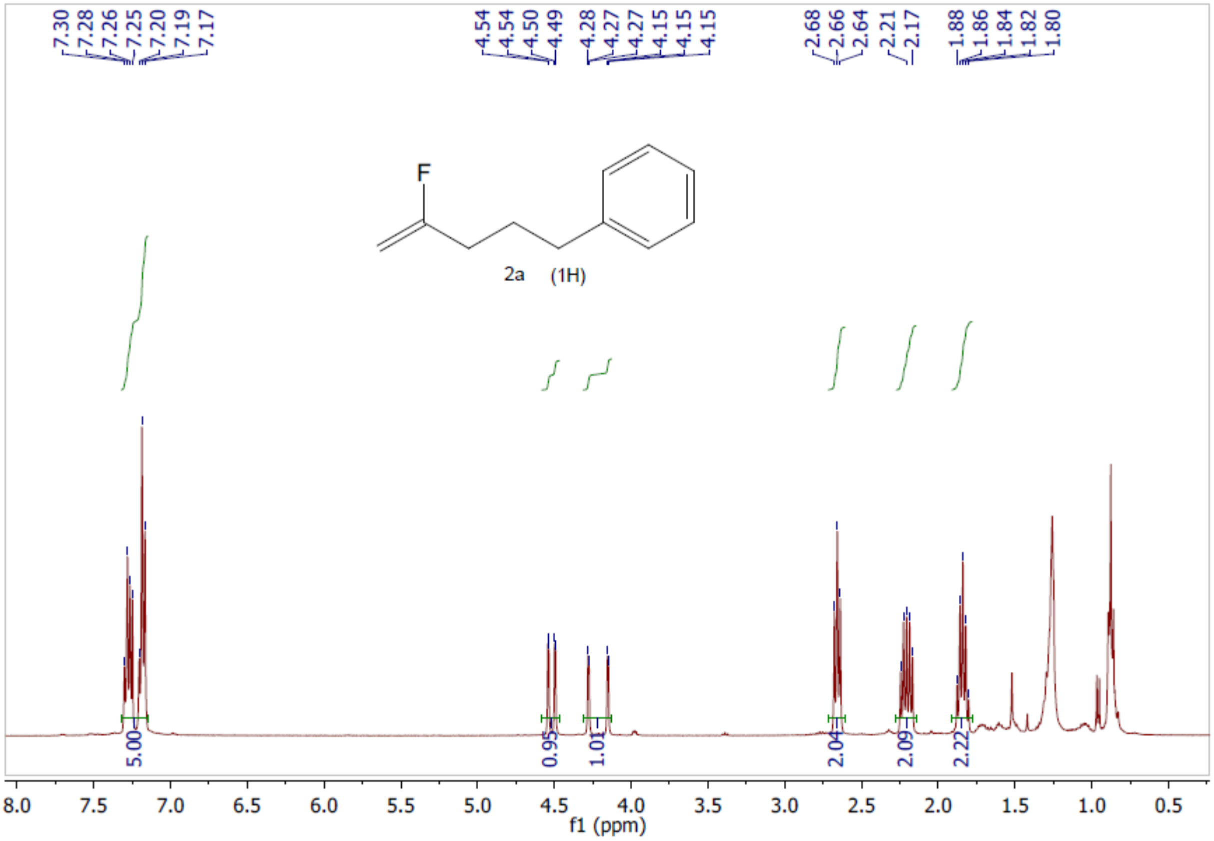
(1,1-difluoroethane-1,2-diyl)dibenzene (**3f**)

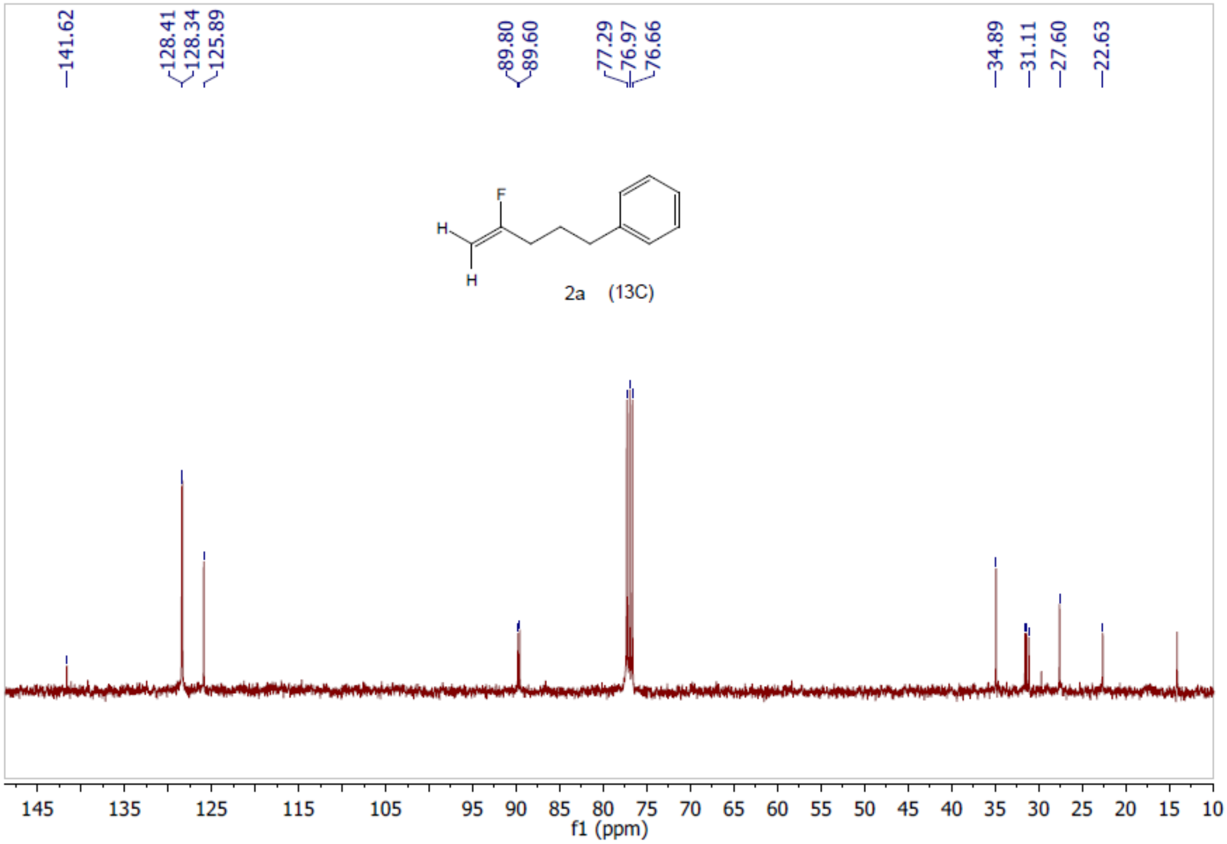


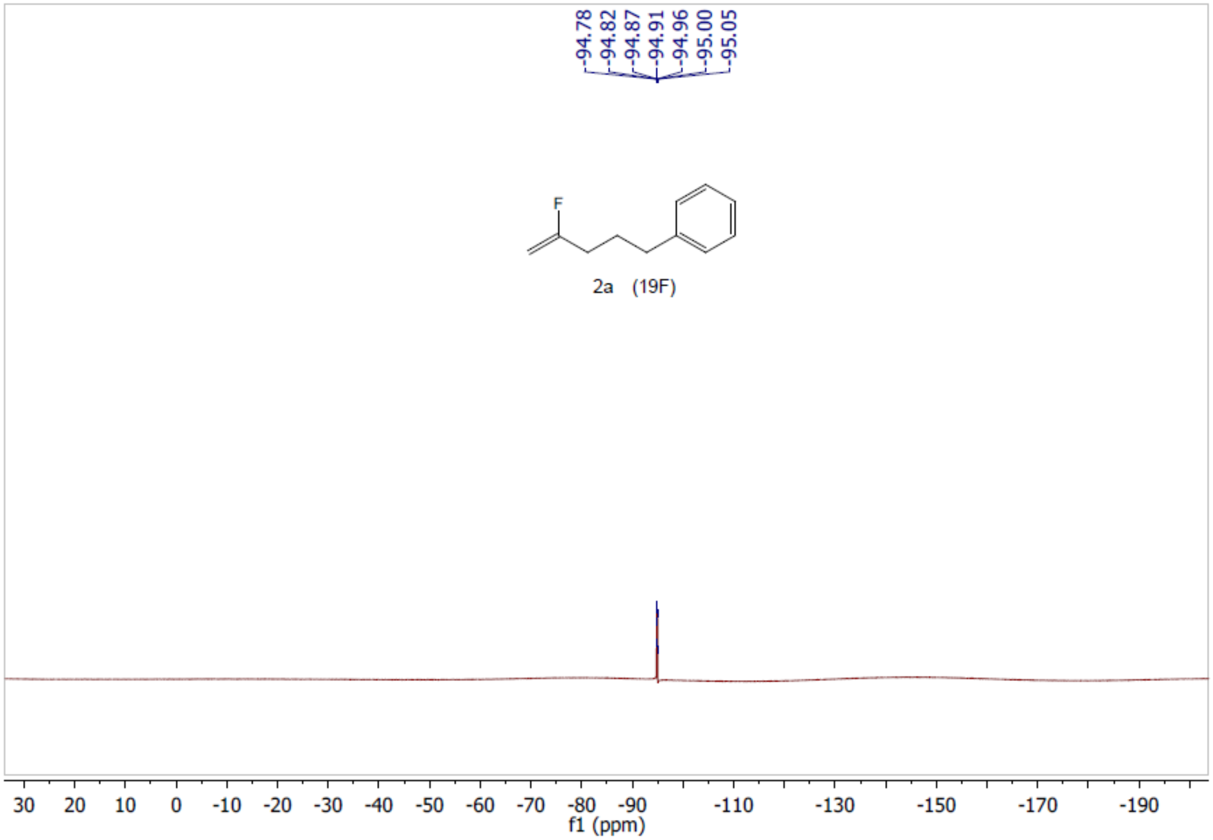
3f

^{1}H NMR δ: 3.46 (t, 2H, J = 15.8 Hz), 7.13-7.16 (m, 2H), 7.28-7.30 (m, 3H), 7.37-7.42 (m, 5H), ^{19}F NMR δ: -94.7 (t, 2F, J = 15.8 Hz). Its spectroscopic data is consistent with a literature report.[14]

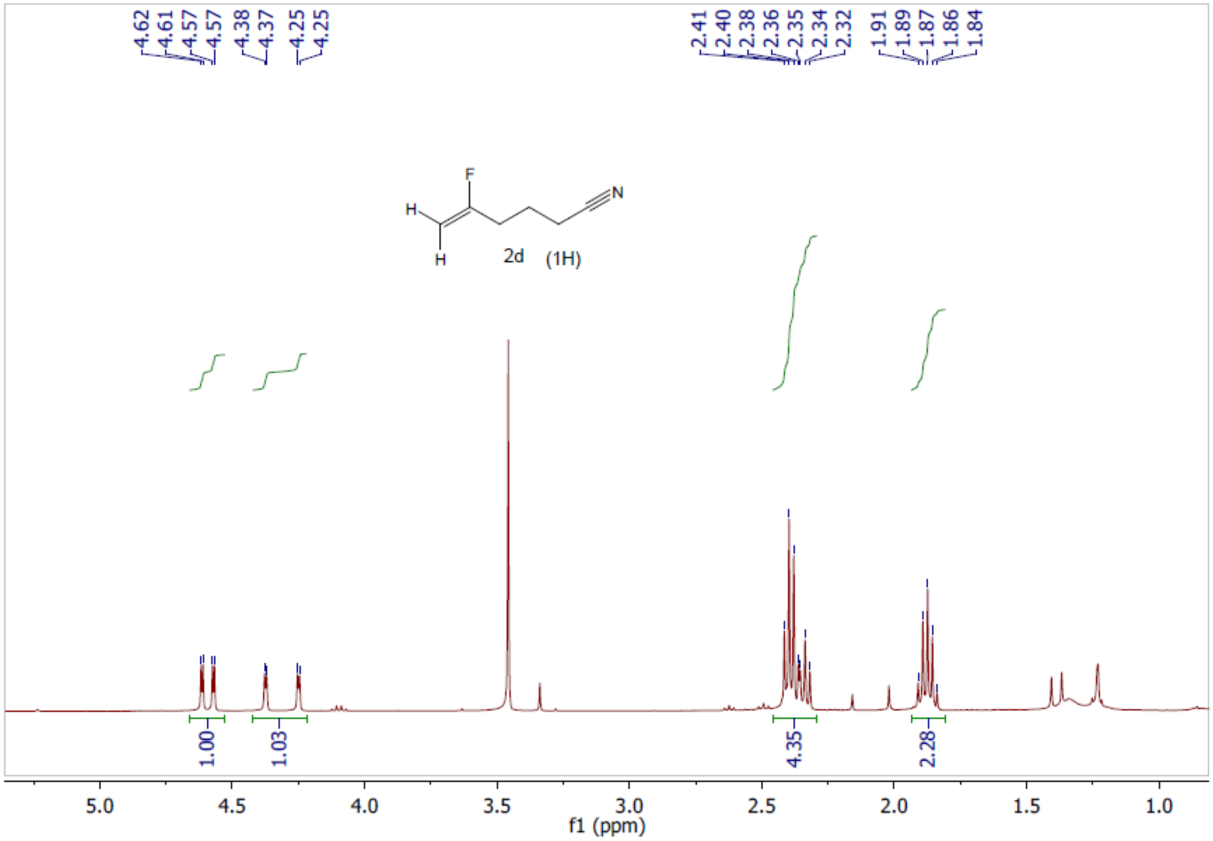
5. Copies of NMR spectra for compounds 2 and 3

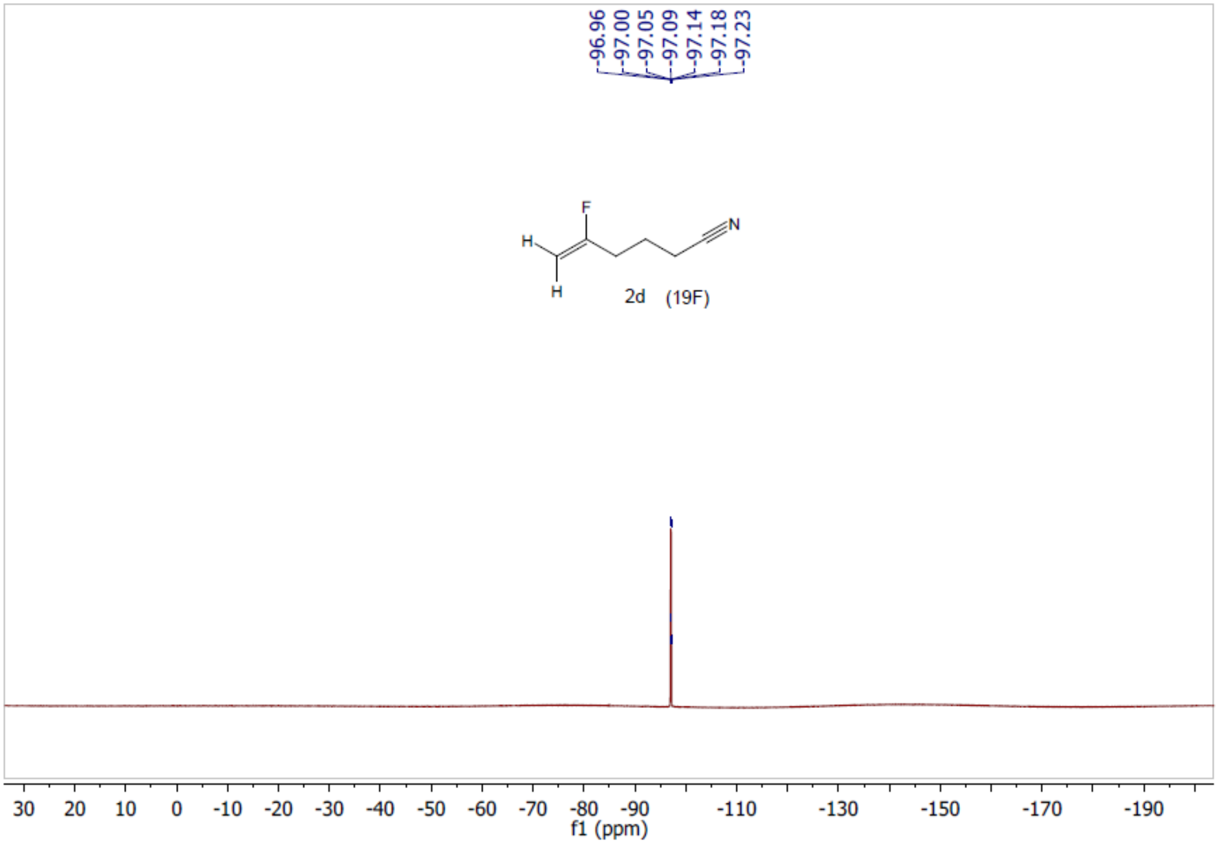


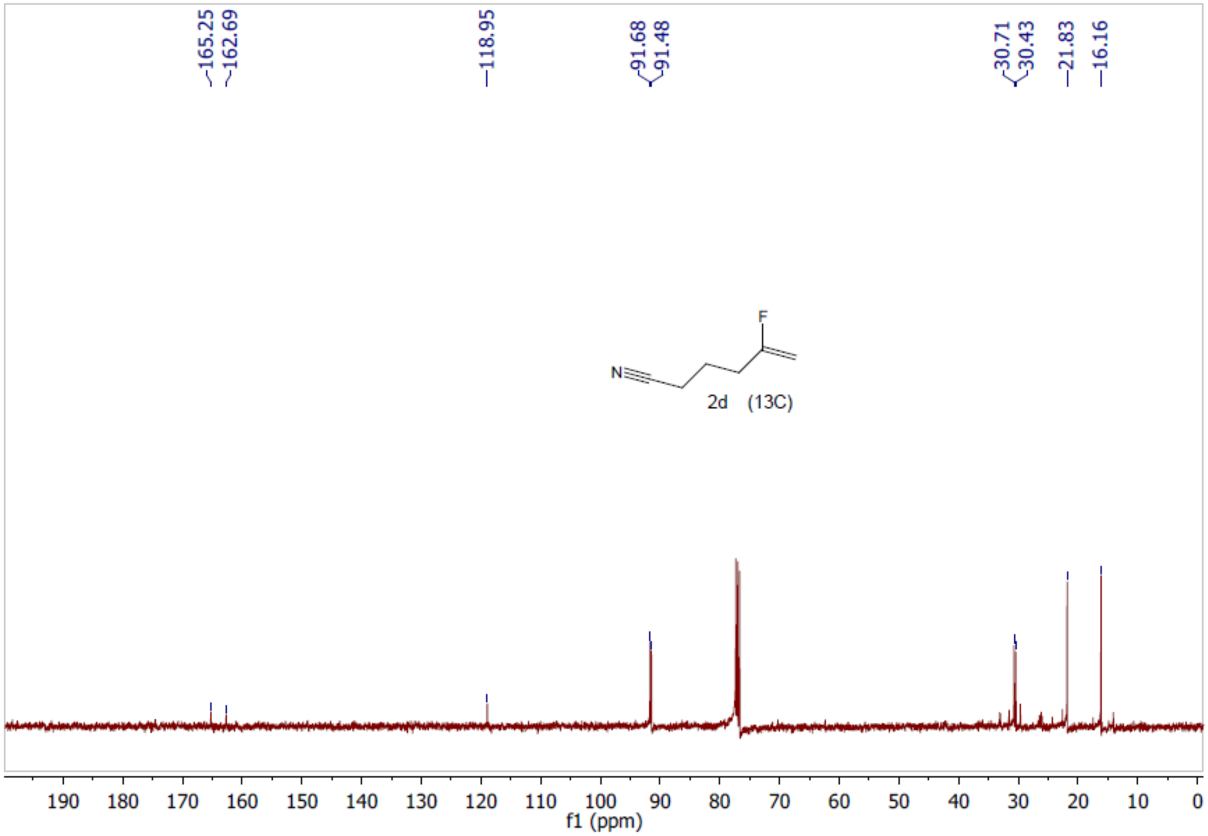

141.62
128.41
128.34
125.89
89.80
89.60
77.29
76.97
76.66
34.89
31.11
27.60
22.63
F
H
H
2a (13C)
145
135
125
115
105
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
f1 (ppm)

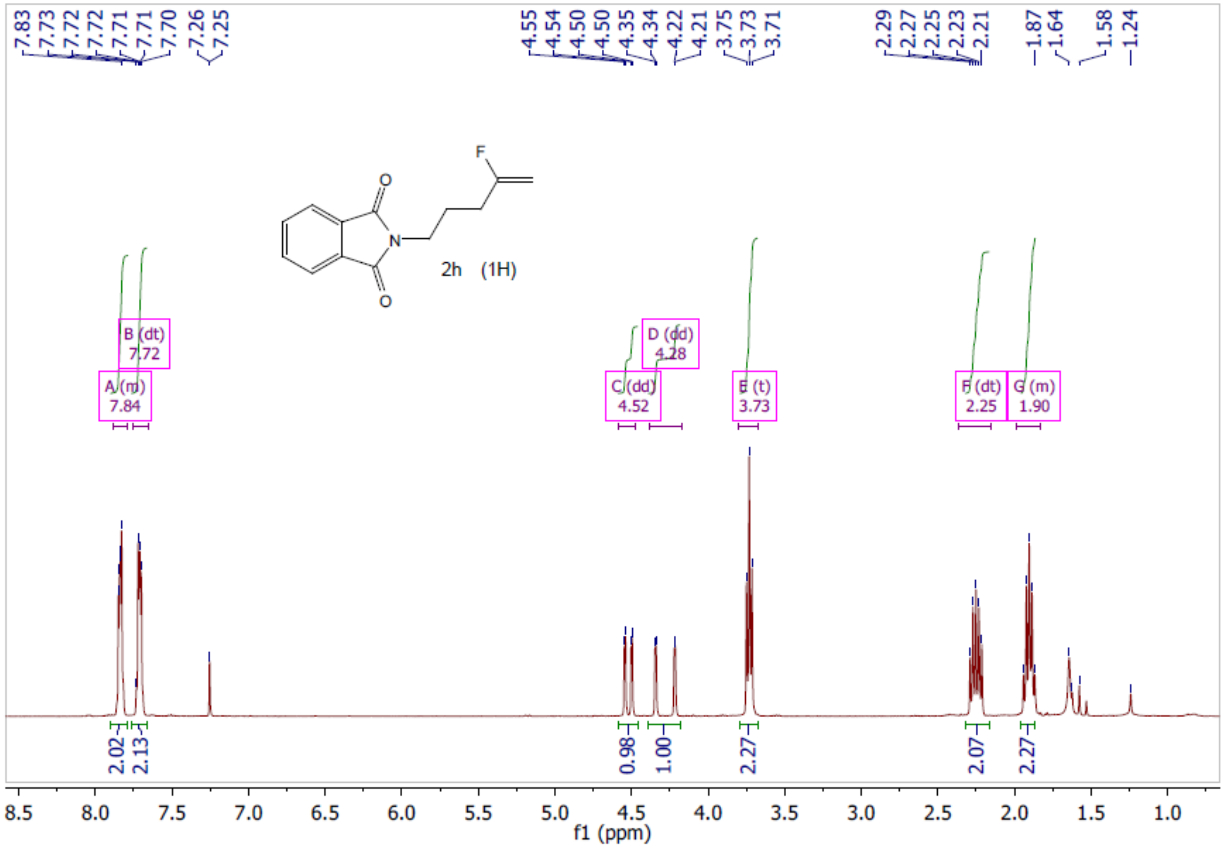

2a (19F)

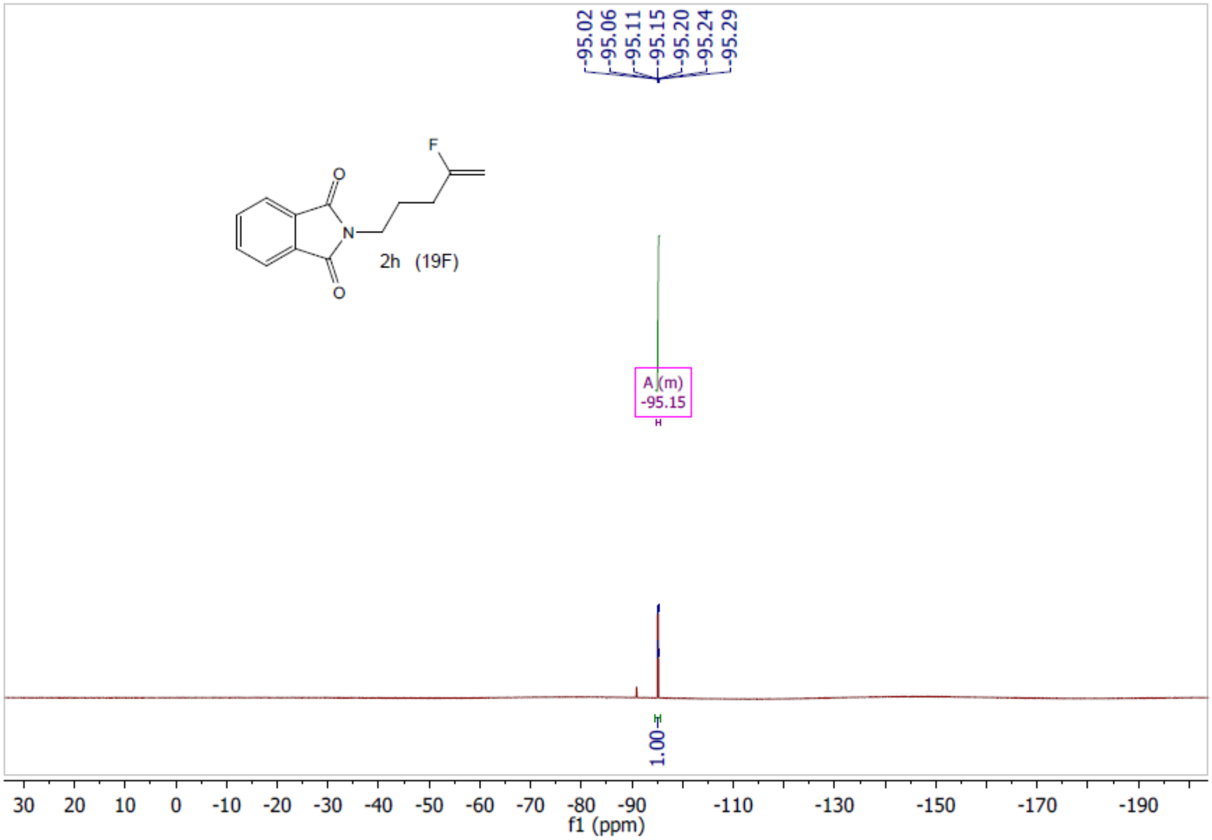
-94.78
-94.82
-94.87
-94.91
-94.96
-95.00
-95.05
F
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-110
-130
-150
-170
-190
f1 (ppm)

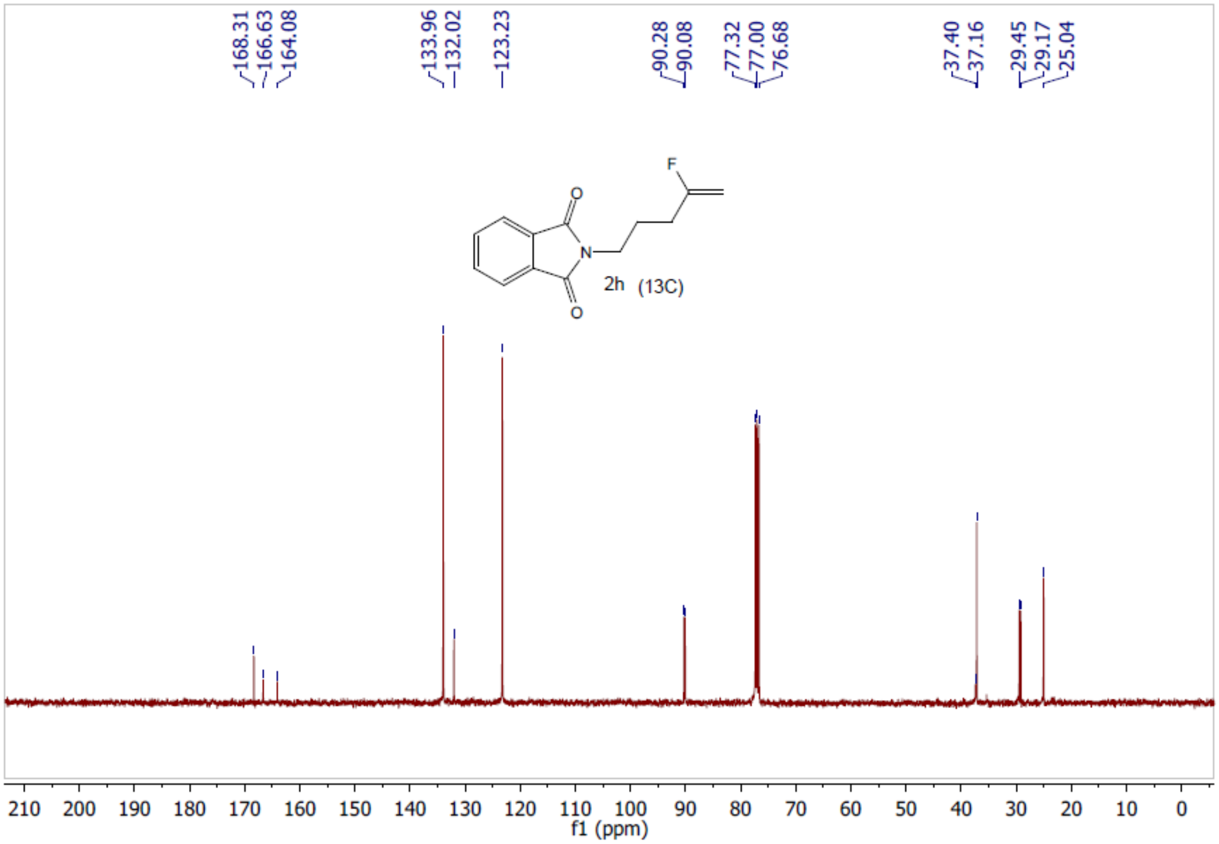

4.62
4.61
4.57
4.57
4.38
4.37
4.25
4.25
2.41
2.40
2.38
2.36
2.35
2.34
2.32
1.91
1.89
1.87
1.86
1.84
F
H
N
H
2d
(1H)
1.00
1.03
4.35
2.28
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

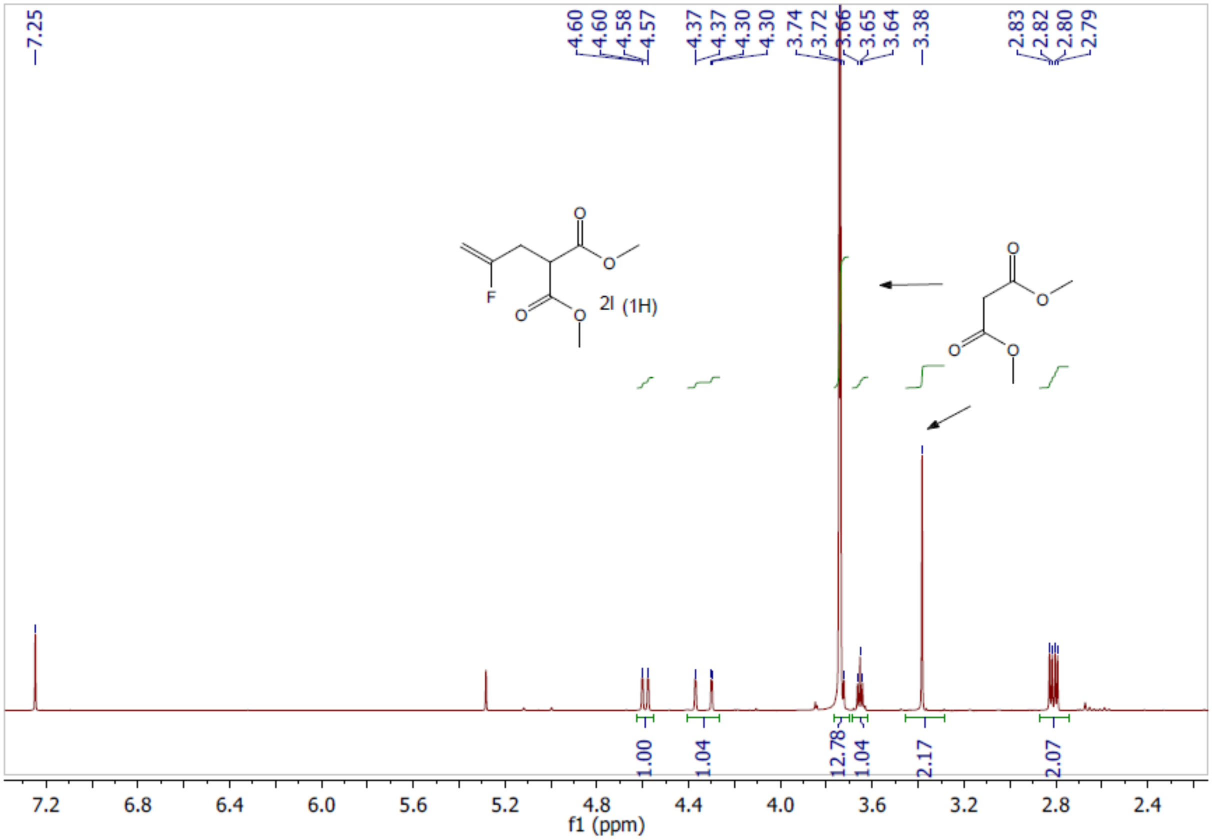

-96.96
-97.00
-97.05
-97.09
-97.14
-97.18
-97.23
F
H
H
N
2d (19F)
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-110
-130
-150
-170
-190
f1 (ppm)


165.25
162.69
118.95
91.68
91.48
30.71
30.43
21.83
16.16
F
N
2d (13C)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

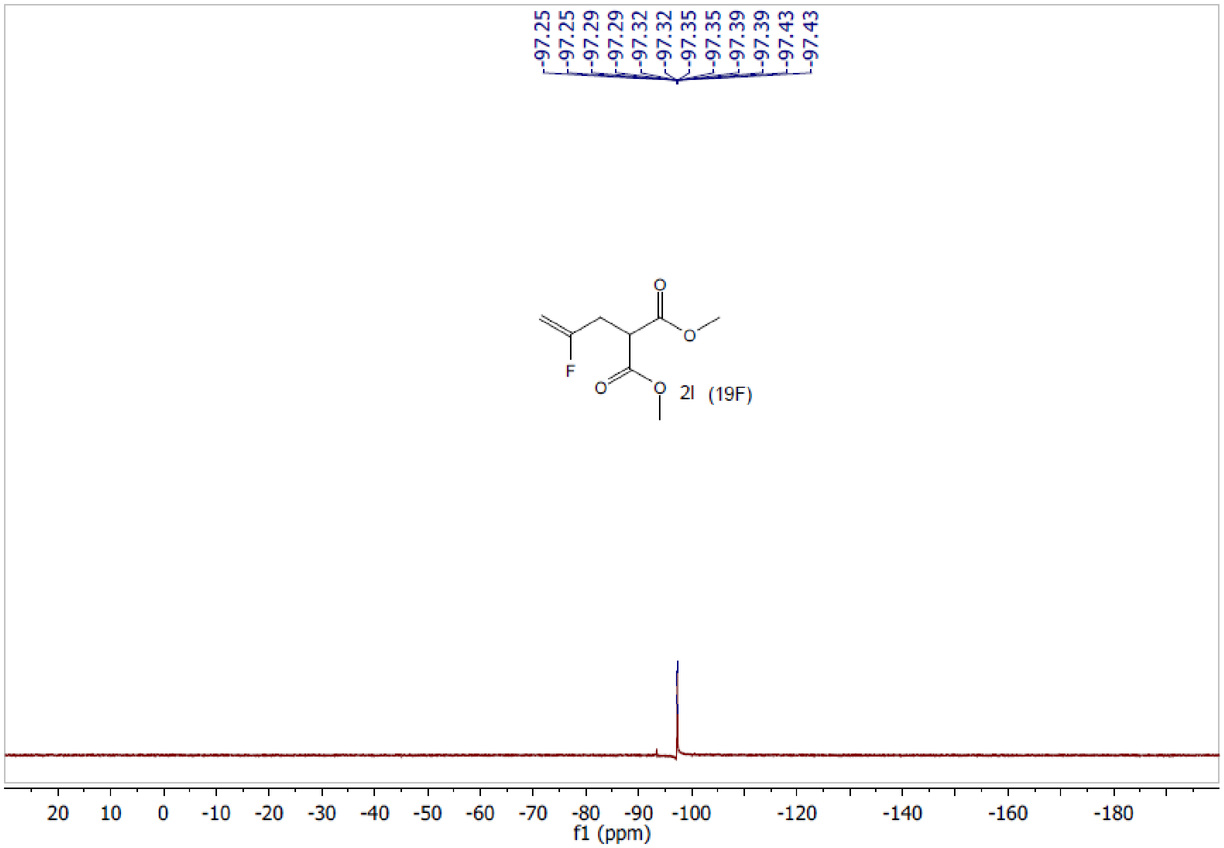

7.83
7.73
7.72
7.72
7.71
7.71
7.70
7.26
7.25
4.55
4.54
4.50
4.50
4.35
4.34
4.22
4.21
3.75
3.73
3.71
2.29
2.27
2.25
2.23
2.21
1.87
1.64
1.58
1.24
F
O
N
O
2h (1H)
B (dt)
7.72
A (m)
7.84
C (dd)
4.52
D (dd)
4.28
E (t)
3.73
F (dt)
2.25
G (m)
1.90
2.02
2.13
0.98
1.00
2.27
2.07
2.27
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

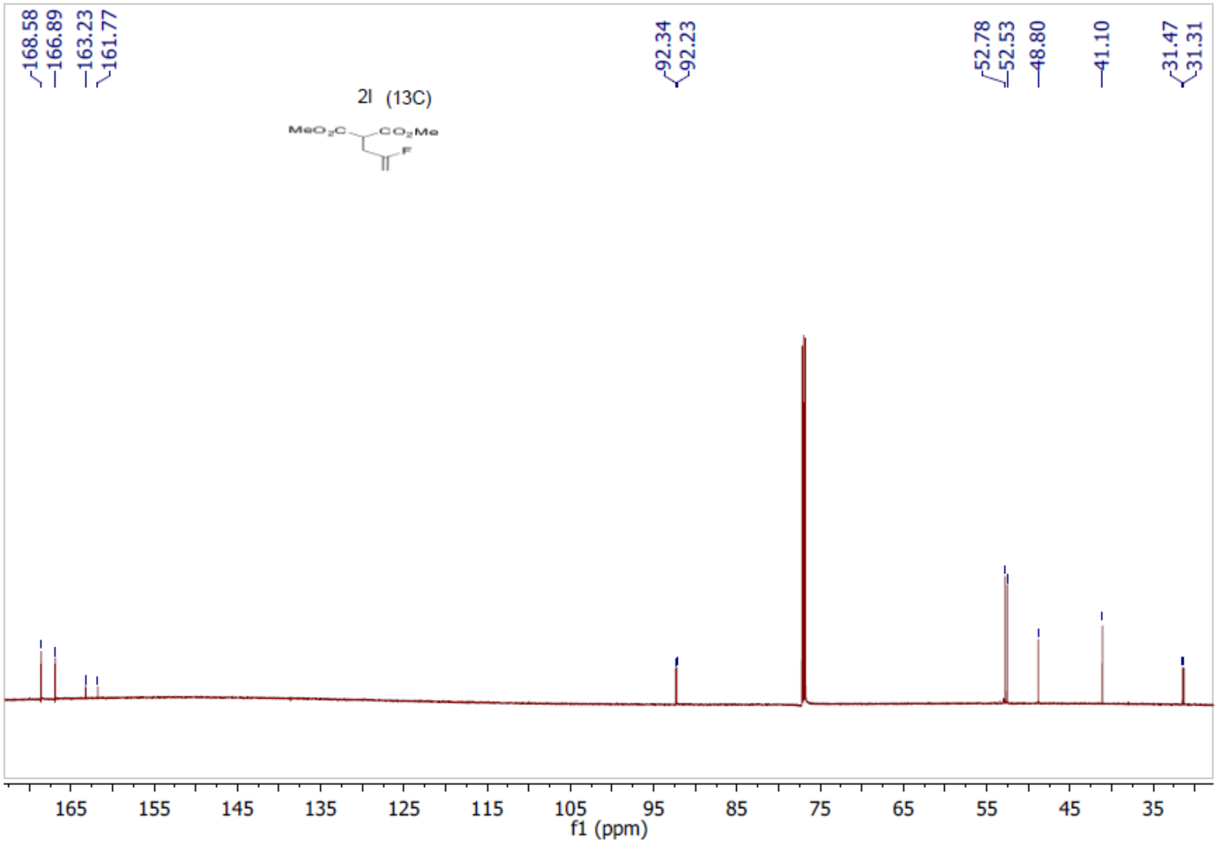

-95.02
-95.06
-95.11
-95.15
-95.20
-95.24
-95.29
F
O
N
O
2h (19F)
A (m)
-95.15
1.00
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-110
-130
-150
-170
-190
f1 (ppm)


168.31
166.63
164.08
133.96
132.02
123.23
90.28
90.08
77.32
77.00
76.68
37.40
37.16
29.45
29.17
25.04
F
O
N
O
2h (13C)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



7.25
4.60
4.60
4.58
4.57
4.37
4.37
4.30
4.30
3.74
3.72
3.66
3.65
3.64
3.38
2.83
2.82
2.80
2.79
O
O
O
O
F
2l (1H)
O
O
O
O
1.00
1.04
12.78
1.04
2.17
2.07
7.2
6.8
6.4
6.0
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
f1 (ppm)


-97.25
-97.25
-97.29
-97.29
-97.32
-97.32
-97.35
-97.35
-97.39
-97.39
-97.43
-97.43
O
O
F
O
O
2l (19F)
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
f1 (ppm)



168.58
166.89
163.23
161.77
92.34
92.23
52.78
52.53
48.80
41.10
31.47
31.31
2l (13C)
MeO₂C
CO₂Me
F
165
155
145
135
125
115
105
95
85
75
65
55
45
35
f1 (ppm)

6. Reference

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