Supplementary Information

Synthesis of (benzenesulfonyl)difluoromethyl thioethers from ((difluoromethyl)sulfonyl)benzene and organothiocyanates generated in situ

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General.

All manipulations of oxygen- and moisture-sensitive materials were conducted with a standard schlenk technique under an argon atmosphere or in a glove box under a nitrogen atmosphere. During the experiment, the low temperature conditions were provided by the PSL-1810 type low temperature reactor. Analytical thin layer chromatography (TLC) was performed on Merck TLC silica gel 60 F_{254} (0.25 mm) plates. Visualization was accomplished with UV light (254 nm) and/or an aqueous alkaline $KMnO_4$ solution followed by heating.

Apparatus.

Analysis of crude reaction mixture was done on an GC-MS (Thermo, ISQ LT-Single Quadrupole Mass Spectrometer; TRACE 1300-Gas Chromatograph). Proton and carbon nuclear magnetic resonance spectra (^{1}H and ^{13}C NMR) were recorded on a Bruker AV 400 and Bruker AV 600 (^{1}H NMR, 400 MHz; ^{13}C NMR 101 MHz and ^{1}H NMR, 600 MHz; ^{13}C NMR 151 MHz) spectrometer with solvent resonance as the internal standard (^{1}H NMR, $CDCl_3$ at 7.26 ppm, C_6D_6 at 7.16 ppm; ^{13}C NMR, $CDCl_3$ at 77.16 ppm, C_6D_6 at 128.0 ppm). NMR data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, sept = septet, br = broad, m = multiplet), coupling constants (Hz), and integration. High-resolution mass spectra were obtained with Thermo Scientific Exactive (APCI).

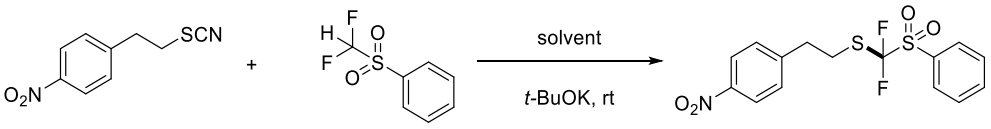
Chemicals.

Unless otherwise noted, commercially available chemicals were distilled and degassed before use. If commercially available chemicals are solids, the chemicals are used without purification. Anhydrous toluene and 1,4-dioxane purchased from Wako were used without purification. Besides, the THF is sensitive in our reaction and which we used is new purchased from aladdin.

Optimization of the Reaction Conditions.

The reaction conditions were studied using 1-nitro-4-(2-thiocyanatoethyl)benzene **1a** (0.2 mmol) and (difluoromethyl) sulfonyl benzene **2** (0.3 mmol) as substrates.

Table S1: Study on the effect of **solvent** on reaction [a,b]

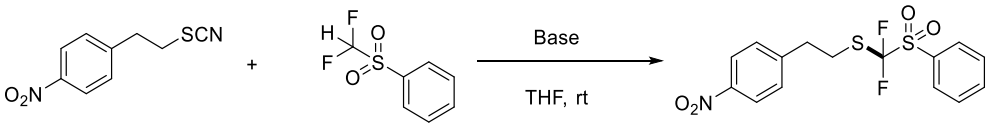


1a **2** **3a**

Entry	Solvent	Yeild (%)
1	DMF	0
2	DMSO	0
3	Acetone	0
4	NMP	0
5	CH_3CN	0
6	CH_3OH	0
7	Toluene	trace
8	DCE	trace
9	1,4-dioxane	12
10	THF	24

[a] Reaction conditions: At room temperature, 1-nitro-4-(2-thiocyanatoethyl)benzene **1a** (0.2 mmol) and ((difluoromethyl)sulfonyl)benzene **2** (0.3 mmol) were dissolved in **solvent** (1 mL), Drop *t*-BuOK (0.4 mL in 5min, 1 mmol / mL in THF) gradually to the reaction. After that, stir for 20 min. [b] Yields were determined by GC analysis with biphenyl as internal standard.

Table S2: Study on the effect of **base** on reaction [a,b]



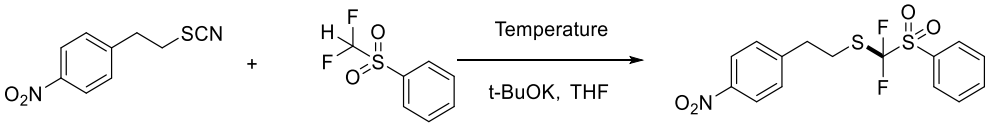
1a **2** **3a**

Entry	Base	Yeild (%)
1	DBU	0
2	DMAP	0
3	Pyridine	0
4	Et_3N	0
5	CsF	trace
6	K_2CO_3	trace
7	KOH	0
8	*t*-BuOK	24
9	NaH	16

[a] Reaction conditions: At room temperature, 1-nitro-4-(2-thiocyanatoethyl)benzene **1a** (0.2

mmol) and ((difluoromethyl)sulfonyl)benzene **2** (0.3 mmol) were dissolved in THF (1 mL), Drop **base** (0.4 mL in min, 1 mmol / mL in THF) gradually to the reaction. After dropwise, stir for 20 min. [b] Yields were determined by GC analysis with biphenyl as internal standard.

Table S3: Study on the effect of **temperature** on reaction [a,b]

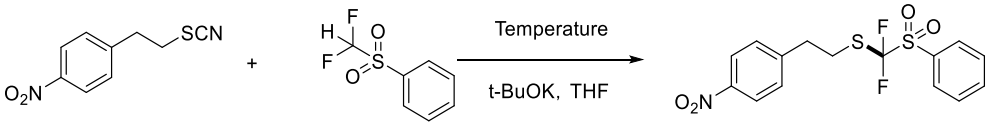


1a **2** **3a**

Entry	Temperature (^{o}C)	Yeild (%)
1	60	0
2	40	0
3	rt	24
4	0	36
5	-10	61
6	-20	80
7	-40	87
8	-50	92
9	-60	91
10	-70	91

[a] Reaction conditions: 1-nitro-4-(2-thiocyanatoethyl)benzene **1a** (0.2 mmol) and ((difluoromethyl)sulfonyl)benzene **2** (0.3 mmol) were dissolved in THF (1 mL), the reaction was then placed in a reactor at a set **temperature**. Drop *t*-BuOK (0.4 mL in 5 min, 1 mmol / mL in THF) gradually to the reaction. After drop wise, stir for 20 min. [b] Yields were determined by GC analysis with biphenyl as internal standard.

Table S4: Influence of the **sequence** of t-BuOK on the reaction [a,b]



1a **2** **3a**

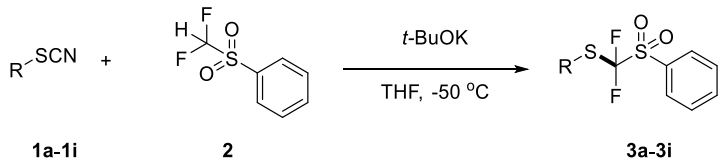
Entry	The sequence of *t*-BuOK	Yeild (%)
1	Together with **1a**, then add **2**	35
2	Having added **1a** and **2**, then Pour *t*-BuOK into the reaction	46
3	No change	92

[a] Reaction conditions: (1) entry 1: 1-nitro-4-(2-thiocyanatoethyl)benzene **1a** (0.2 mmol) and *t*-BuOK, cooling to -50 ^{o}C under low temperature reactor stirring, then add in ((difluoromethyl)sulfonyl)benzene **2** (0.3 mmol), stir for 20 min; (2) entry 2:

1-nitro-4-(2-thiocyanatoethyl)benzene **1a** (0.2 mmol) and ((difluoromethyl)sulfonyl)benzene **2** (0.3 mmol) were dissolved in THF (1 mL), cooling to -50 ^{o}C under low temperature reactor stirring. Pour *t*-BuOK (0.4 mL, 1 mmol / mL in THF) into the reaction. Stir for 20 min; (3) entry 3: 1-nitro-4-(2-thiocyanatoethyl)benzene **1a** (0.2 mmol) and ((difluoromethyl)sulfonyl)benzene **2** (0.3 mmol) were dissolved in THF (1 mL), cooling to -50 ^{o}C under low temperature reactor stirring. Drop *t*-BuOK (0.4 mL in 5min, 1 mmol / mL in THF) gradually to the reaction. After dropwise, stir for 20 min. [b] Yields were determined by GC analysis with biphenyl as internal standard.

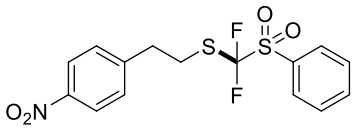
General procedures for Scheme S1.

Scheme S1. Scope of (Benzenesulfonyl)Difluoromethyl Thioethers



1a-1i **2** **3a-3i**

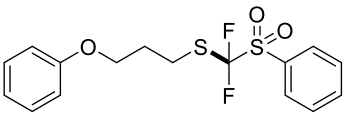
A 25ml vial was charged with organothiocyanate (0.2 mmol) **1**, 0.3 mmol of ((difluoromethyl)sulfonyl)benzene **2**, cooling to -50 ^{o}C under low - temperature reactor stirring, then add drop wise *t*-BuOK (4mL in 5 min, 1 mmol / mL in THF). After drop wise, stir for 20 min. The resulting mixture was purified by flash chromatography (Polarity is given below) to get the product. All the products are confirmed by the NMR and all new compounds were identified by high resolution mass spectrometry. By this method, we obtain product **3a**-**3i**, and the relevant data are shown below：



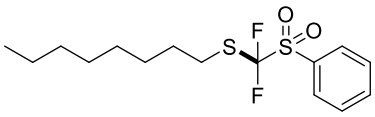
(difluoro(phenylsulfonyl)methyl)(4-nitrophenethyl)-sulfane (**3a**) Light yellow oil, R_f 0.35 (petroleum ether : ethyl acetate =5:1) (67.14 mg, 90% yield). ^{1}H NMR (600 MHz, CDCl^{3}): δ 8.19 (d, J = 9.0 Hz, 2H), 7.99 (d, J = 8.8 Hz, 2H), 7.79 (t, J = 7.7 Hz, 1H), 7.63 (t, J = 8.2 Hz, 2H), 7.40 (d, J = 9.1 Hz, 2H), 3.40 – 3.33 (m, 2H), 3.16 (t, J = 8.1 Hz, 2H). ^{13}C NMR (151 MHz, CDCl^{3}): δ 147.19, 146.36, 135.78, 132.26, 130.98, 129.72, 129.58, 129.50 (t, J = 323.1 Hz), 124.07, 36.02, 31.35 (t, J = 3.4 Hz). ^{19}F NMR (564 MHz, $CDCl_3$): δ -80.20. HRMS m/z (EI) calculated for $C_{15}H_{13}F_2NO_4S_2$ [M]+:373.0254, found:373.0250

Benzyl(difluoro(phenylsulfonyl)methyl)sulfane (**3b**) Light yellow oil, R_f 0.5 (petroleum ether : ethyl acetate =10:1) (59.66 mg, 95% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.03 (d, J = 7.8 Hz, 2H), 7.77 (t, J = 7.5 Hz, 1H), 7.63 (t, J = 7.8 Hz, 2H), 7.38 (d, J = 7.3 Hz, 2H), 7.34 (t, J = 7.3 Hz, 2H), 7.30 (t, J = 7.1 Hz, 1H), 4.34 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 135.65, 134.73, 132.41, 130.93, 129.50, 129.29, 129.25 (t, J =

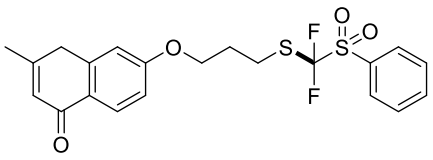
323.6 Hz), 128.97, 128.19, 35.19 (t, J = 3.7 Hz). ^{19}F NMR (564 MHz, $CDCl_3$): δ -80.46. The characterization data was consistent with the previous report[1].



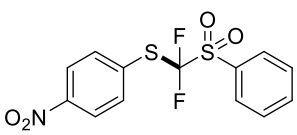
(difluoro(phenylsulfonyl)methyl)(3-phenoxypropyl)-sulfane (**3c**) Colorless oil, R_f 0.6 (petroleum ether : ethyl acetate =10:1) (66.59 mg, 93% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.00 (d, J = 9.1 Hz, 3H), 7.79 – 7.73 (m, 1H), 7.62 (dd, J = 8.6, 7.6 Hz, 2H), 7.33 – 7.27 (m, 2H), 6.99 – 6.94 (m, 1H), 6.90 (dd, J = 8.9, 1.1 Hz, 2H), 4.08 (t, J = 6.0 Hz, 2H), 3.29 (t, J = 7.4 Hz, 2H), 2.24 – 2.17 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 158.72, 135.63, 132.52, 131.02, 129.74(t, J = 322.7 Hz), 129.64, 129.51, 121.13, 114.67, 65.52, 29.76, 27.68(t, J = 3.8 Hz). ^{19}F NMR (564 MHz, $CDCl_3$): δ -79.98. HRMS m/z (EI) calculated for $C_{16}H_{16}F_2O_3S_2$ [M]+:358.0509, found:358.0504.



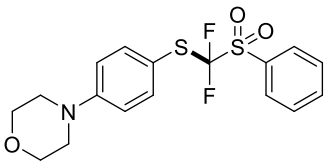
(difluoro(phenylsulfonyl)methyl)(octyl)sulfane (**3d**) Colorless oil, R_f 0.85 (petroleum ether : ethyl acetate =20:1) (63.17 mg, 94% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.99 (d, J = 7.8 Hz, 2H), 7.75 (t, J = 7.5 Hz, 1H), 7.61 (t, J = 7.6 Hz, 2H), 3.06 (t, J = 7.4 Hz, 2H), 1.67 (dd, J = 14.9, 7.4 Hz, 2H), 1.38 (dd, J = 14.0, 6.7 Hz, 2H), 1.27 (dd, J = 17.5, 9.9 Hz, 8H), 0.86 (t, J = 6.7 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 135.54, 132.44, 130.90, 129.75 (t, J = 322.2 Hz), 129.43, 31.81, 30.83(t, J = 3.1 Hz), 29.62, 29.15, 29.02, 28.61, 22.71, 14.18. ^{19}F NMR (564 MHz, $CDCl_3$): δ -80.21. HRMS m/z (EI) calculated for $C_{15}H_{22}F_2O_2S_2$ [M]+:336.1029, found:336.1025.



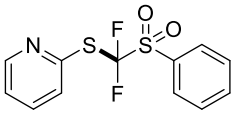
6-(4-((difluoro(phenylsulfonyl)methyl)thio)-butyl)-3-methyln aphthalen-1(4H)-one (**3e**) Light yellow solid, R_f 0.7 (petroleum ether : ethyl acetate =2:1) (70.08 mg, 80% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, J = 7.7 Hz, 2H), 7.76 (t, J = 7.5 Hz, 1H), 7.61 (t, J = 7.8 Hz, 2H), 7.47 (d, J = 8.8 Hz, 1H), 6.83 (dd, J = 8.8, 2.4 Hz, 1H), 6.76 (d, J = 2.3 Hz, 1H), 6.10 (s, 1H), 4.03 (t, J = 5.3 Hz, 2H), 3.15 (t, J = 6.5 Hz, 2H), 2.37 (s, 3H), 1.97 – 1.89 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 161.93, 161.30, 155.32, 152.64, 135.61, 132.40, 130.90, 129.66 (t, J = 322.6 Hz), 129.48, 125.67, 113.70, 112.58, 112.02, 101.47, 67.69, 30.46(t, J = 3.3 Hz), 27.87, 26.52, 18.72. ^{19}F NMR (376 MHz, $CDCl_3$): δ -80.00. HRMS m/z (EI) calculated for $C_{21}H_{20}F_2O_4S_2$ [M]+:438.0771, found:438.0768.



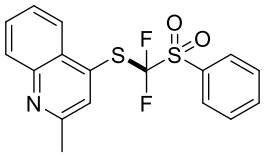
(difluoro(phenylsulfonyl)methyl)(4-nitrophenyl)sulfane (**3f**) Light yellow solid, Rf 0.6 (petroleum ether : ethyl acetate =5:1) (55.89 mg, 81% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.23 (d, J = 8.3 Hz, 2H), 7.95 (d, J = 8.0 Hz, 2H), 7.88 (d, J = 8.6 Hz, 2H), 7.78 (t, J = 7.5 Hz, 1H), 7.62 (t, J = 7.7 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 149.35, 137.59, 135.99, 131.99 – 131.78 (m), 130.91, 129.65, 127.89 (t, *J* = 326.9 Hz), 124.13. ^{19}F NMR (564 MHz, $CDCl_3$): δ -78.21. The characterization data was consistent with the previous report[1].



4-(4-((difluoro(phenylsulfonyl)methyl)thio)phenyl)-morpholine (3g) Light yellow oil, R_f 0.8 (petroleum ether : ethyl acetate =2:1) (53.91 mg, 70% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.97 (d, J = 7.5 Hz, 2H), 7.74 (t, J = 7.5 Hz, 1H), 7.59 (t, J = 7.6 Hz, 2H), 7.55 (d, J = 8.9 Hz, 2H), 6.86 (d, J = 9.0 Hz, 2H), 3.85 – 3.82 (m, 4H), 3.24 – 3.21 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 152.91, 138.85, 135.47, 132.89, 130.90, 129.41, 128.22 (t, *J* = 324.3 Hz), 115.19, 111.25, 66.70, 47.99. ^{19}F NMR (564 MHz, $CDCl_3$): δ -79.34. HRMS m/z (EI) calculated for $C_{17}H_{17}F_2NO_3S_2$ [M]+:385.0618, found:385.0615.



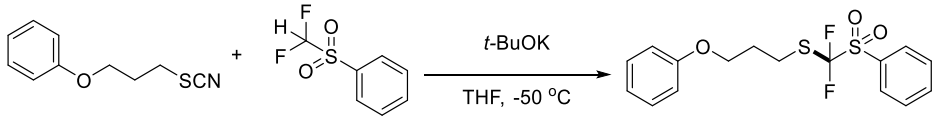
2-((difluoro(phenylsulfonyl)methyl)thio)pyridine (3h) Light yellow oil, R_f 0.8 (petroleum ether : ethyl acetate =5:1) (51.17 mg, 85% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.58 (s, 1H), 7.98 (d, J = 7.9 Hz, 2H), 7.76 – 7.67 (m, 3H), 7.58 (t, J = 7.9 Hz, 2H), 7.34 – 7.29 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 150.77, 148.32, 137.71, 135.77, 132.25, 131.04, 130.94, 129.52, 128.67 (t, *J* = 326.3 Hz), 124.53. ^{19}F NMR (564 MHz, $CDCl_3$): δ -77.68. The characterization data was consistent with the previous report[1].



4-((difluoro(phenylsulfonyl)methyl)thio)-2-methylquinoline (3i) Light yellow oil, R_f 0.75 (petroleum ether : ethyl acetate =5:1) (55.48 mg, 76% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.35 (d, J = 8.3 Hz, 1H), 8.06 (d, J = 8.3 Hz, 1H), 7.98 (d, J = 7.8 Hz, 2H), 7.79 – 7.69 (m, 3H), 7.59 (dd, J = 13.3, 6.3 Hz, 3H), 2.76 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 158.60, 148.61, 135.90, 132.30, 132.17, 131.73, 131.06, 130.46, 129.60, 129.35, 128.50 (t, *J* = 327.6 Hz), 128.45, 127.31, 125.54, 25.25. ^{19}F NMR (564 MHz, $CDCl_3$): δ -76.28. HRMS m/z (EI) calculated for $C_{17}H_{13}F_2NO_2S_2$ [M]+:365.0356, found:365.0353.

General procedures for Scheme S2.

Scheme S2. Studies on Gram-level Reaction



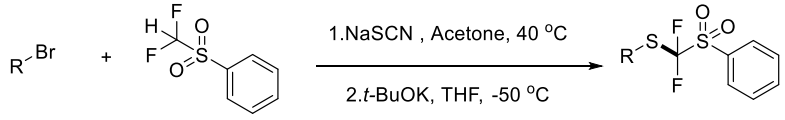
1.93 g **3.84 g** **2.61 g (73 %)**

A 25ml vial was charged with (3-thiocyanatopropoxy)benzene **3c** (10 mmol) and ((difluoromethyl)sulfonyl)benzene 2 (20 mmol), cooling to -50 °C under low - temperature reactor stirring, then add drop wise *t*-BuOK (30 mL in 40min , 1 mmol / mL in THF). After drop wise, stir for 6h. Evaporation solvent and then dissolved with ethyl acetate. Add water and separate liquid to take organic phase.

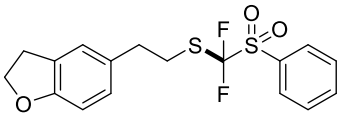
The resulting mixture was purified by flash chromatography (Polarity is given below) to get the corresponding product (difluoro(phenylsulfonyl)methyl)(3-phenoxypropyl)-sulfane **3a**, yield 73% (2.61g).

General procedures for Scheme S3.

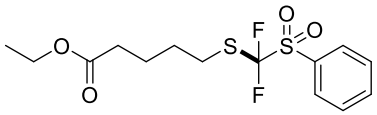
Scheme S3. Synthesis of (Benzenesulfonyl)Difluoromethyl Thioethers by one-pot method of alkyl halides



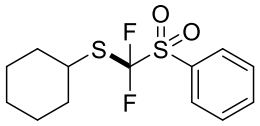
According to the literature[2]. Add alkyl halides (0.2 mmol), NaSCN (0.24 mmol) and acetone (1.5 mL) in a vial, then heat it to 45 °C for 5 hours. When the reaction is complete， acetone was evaporated. Then add in ((difluoromethyl)sulfonyl)benzene **2** (0.3 mmol) and THF (1 mL), cooling to -50℃.Finally, add drop wise *t*-BuOK (0.4 mL in 5min, 1 mmol / mL in THF) . After drop wise, stir for 20 min. The resulting mixture was purified by flash chromatography (Polarity is given below) to get the product. All the products are confirmed by the NMR and all new compounds were identified by high resolution mass spectrometry. By this method, we obtain product **3j-3o**, and the relevant data are shown below：



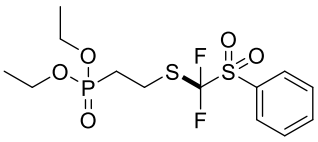
5-(2-((difluoro(phenylsulfonyl)methyl)thio)ethyl)-2,3-dihydrobenzofuran (3j) Light yellow oil, R_f 0.55 (petroleum ether : ethyl acetate =10:1) (55.5 mg, 75% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.00 (d, J = 9.7 Hz, 2H), 7.77 (t, J = 7.6 Hz, 1H), 7.65 – 7.58 (m, 2H), 7.05 (s, 1H), 6.94 (d, J = 10.5 Hz, 1H), 6.72 (d, J = 8.3 Hz, 1H), 4.56 (t, J = 8.8 Hz, 2H), 3.33 – 3.26 (m, 2H), 3.19 (t, J = 9.0 Hz, 2H), 2.98 – 2.90 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 159.20, 135.57, 132.55, 130.97, 130.92, 129.85 (t, *J* = 322.6 Hz), 129.47, 128.26, 127.55, 125.25, 109.35, 71.37, 35.64, 32.54 (t, *J* = 3.3 Hz), 29.83. ^{19}F NMR (564 MHz, $CDCl_3$): δ -79.86. HRMS m/z (EI) calculated for $C_{17}H_{16}F_2O_3S_2$ [M]+:370.0509, found:370.0504.



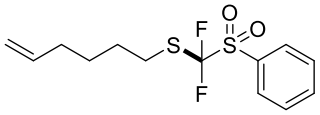
Ethyl-5-((difluoro(phenylsulfonyl)methyl)thio)-pentanoate (**3k**) Light yellow oil, R_f 0.4 (petroleum ether : ethyl acetate =2:1) (51.39 mg, 73% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.97 (d, J = 7.9 Hz, 2H), 7.75 (t, J = 7.5 Hz, 1H), 7.60 (t, J = 7.8 Hz, 2H), 4.11 (q, J = 7.1 Hz, 2H), 3.06 (t, J = 6.1 Hz, 2H), 2.31 (t, J = 6.5 Hz, 2H), 1.73 (dt, J = 6.6, 3.5 Hz, 4H), 1.23 (t, J = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 173.09, 135.58, 132.48, 130.93, 129.68 (t, *J* = 322.5 Hz), 129.47, 60.51, 33.65, 30.40 (t, *J* = 3.2 Hz), 29.19, 23.86, 14.32. ^{19}F NMR (564 MHz, $CDCl_3$): δ -80.18. HRMS m/z (EI) calculated for $C_{14}H_{18}F_2O_4S_2$ [M]+:352.0615, found:352.0613.



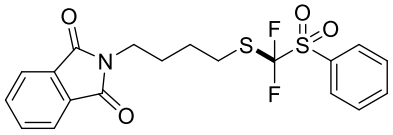
Cyclohexyl(difluoro(phenylsulfonyl)methyl)sulfane (3l) Light yellow oil, R_f 0.85 (petroleum ether : ethyl acetate =10:1) (37.94 mg, 62% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.00 (d, J = 9.0 Hz, 2H), 7.76 (t, J = 8.0 Hz, 1H), 7.61 (t, J = 8.4 Hz, 2H), 3.63 – 3.45 (m, 1H), 2.09 (d, J = 18.0 Hz, 2H), 1.74 (d, J = 14.6 Hz, 2H), 1.64 – 1.10 (m, 6H). ^{13}C NMR (151 MHz, CDC_3): δ 135.48, 132.71, 130.99, 130.31 (t, *J* = 322.7 Hz), 129.42, 45.24(t, *J* = 2.0 Hz), 34.69, 25.58, 25.12. ^{19}F NMR (564 MHz, $CDCl_3$): δ -77.80. HRMS m/z (EI) calculated for $C_{13}H_{16}F_2O_2S_2$ [M]+:306.0560, found:306.0558.



Diethyl(2-((difluoro(phenylsulfonyl)methyl)thio)ethyl)-phosphonate (**3m**) Light yellow oil, R_c 0.25(petroleum ether : ethyl acetate =2:1) (47.34 mg, 61% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.98 (d, J = 7.8 Hz, 2H), 7.77 (t, J = 7.5 Hz, 1H), 7.62 (t, J = 7.6 Hz, 2H), 4.11 (dd, J = 15.6, 7.6 Hz, 4H), 3.27 (dd, J = 17.0, 9.4 Hz, 2H), 2.23 – 2.17 (m, 2H), 1.33 (t, J = 7.0 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 135.72, 132.23, 130.97, 129.54, 129.44 (t, *J* = 323.4 Hz, 1H), 62.19 (d, *J* = 6.5 Hz), 27.87, 26.96, 24.37(dd, *J* = 6.7, 3.8 Hz), 16.52(d, *J* = 5.9 Hz). 19F NMR (564 MHz, CDCl3): δ -80.54. HRMS m/z (EI) calculated for $C_{13}H_{19}F_2O_5PS_2$ [M]+:388.0380, found:388.0378.



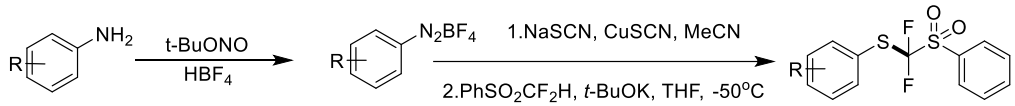
(difluoro(phenylsulfonyl)methyl)(hex-5-en-1-yl)sulfane (3n): Colorless oil, R_f 0.95(petroleum ether : ethyl acetate =10:1) (45.90 mg, 75% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.00 (d, J = 7.6 Hz, 2H), 7.77 (t, J = 7.5 Hz, 1H), 7.64 – 7.60 (m, 2H), 5.78 (ddt, J = 17.0, 10.2, 6.7 Hz, 1H), 5.06 – 4.95 (m, 2H), 3.08 (t, J = 7.4 Hz, 2H), 2.08 (dd, J = 14.2, 7.2 Hz, 2H), 1.72 (dt, J = 15.2, 7.5 Hz, 2H), 1.54 – 1.49 (m, 2H). ^{13}C NMR (151 MHz, CDCl3): δ 138.09, 135.56, 132.65, 131.00, 129.83 (t, *J* = 322.5 Hz), 129.48, 115.23, 33.14, 30.69 (t, *J* = 3.5 Hz), 29.12, 27.81. ^{19}F NMR (565 MHz, CDCl3): δ -79.98. HRMS m/z (EI) calculated for $C_{13}H_{16}F_2O_2S_2$ [M]+:306.0560, found:306.0558.



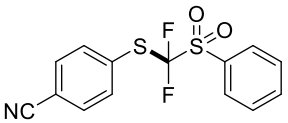
2-**(4-((difluoro(phenylsulfonyl)methyl)thio)butyl)isoindoline-1,3-dione (3o)** Light yellow oil, R_f 0.25(petroleum ether : ethyl acetate =5:1) (64.60 mg, 76% yield). ^{1}H NMR (600 MHz, CDCl3): δ 7.97 (d, J = 8.9 Hz, 2H), 7.82 (dd, J = 5.6, 3.1 Hz, 2H), 7.75 (t, J = 7.6 Hz, 1H), 7.70 (dd, J = 5.6, 3.1 Hz, 2H), 7.60 (t, J = 8.6 Hz, 2H), 3.70 (t, J = 7.4 Hz, 2H), 3.09 (t, J = 7.8 Hz, 2H), 1.81 (dd, J = 15.7, 7.1 Hz, 2H), 1.73 (dd, J = 15.5, 7.6 Hz, 2H). ^{13}C NMR (151 MHz, CDCl3): δ 168.37, 135.54, 134.07, 132.41, 132.10, 130.91, 129.60 (t, *J* = 323.0 Hz), 129.43, 123.32, 37.18, 30.20(t, *J* = 3.7 Hz), 27.53, 27.07. ^{19}F NMR (564 MHz, CDCl3): δ -80.13. HRMS m/z (EI) calculated for $C_{19}H_{17}F_2NO_4S_2$ [M]+:425.0567, found:425.0564.

General procedures for Scheme S4

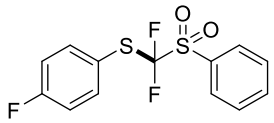
Scheme S4. Synthesis of (Benzenesulfonyl)Difluoromethyl Thioethers by one-pot method of aryl diazonium saults



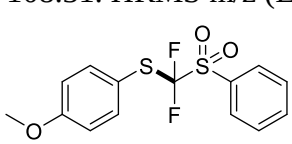
According to the literature[2,3]. Add arylamine (2 mmol), tetrafluoroboric acid (2.4 mmol) and ethanol (4 ml) in a vial, cooling to -0 ^{o}C. Next, add drop wise *t*-BuONO (3 mL, 1 mmol / mL in H_2O) in 5min and react for 2 h after dropping wise. Add ether and then extract the corresponding arenediazonium tetrafluoroborate. Next, add arenediazonium tetrafluoroborate (1.5mmol), NaSCN (3 mmol), CuSCN (2 mmol) and MeCN (4 mL) in a glass bottle to reaction at room temperature for 2 hours. When the reaction is complete, MeCN was evaporated. Add in THF (2 mL) and ((difluoromethyl)sulfonyl)benzene (1.5 mmol), cooling to -50℃. Finally, add *t*-BuOK (2 mL in 4min, 1 mmol / mL in THF) drop wise. After drop wise, stirring for 1 hour. The resulting mixture was purified by flash chromatography (Polarity is given below) to get the product. All the products are confirmed by the NMR and all new compounds were identified by high resolution mass spectrometry. By this method, we obtain product **3p**-**3q**, and the relevant data are shown below：



4-((difluoro(phenylsulfonyl)methyl)thio)benzonitrile (3p) Brown solid, Rf 0.45(petroleum ether : ethyl acetate =5:1) (37.05 mg, 57%yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.94 (d, J = 6.8 Hz, 2H), 7.82 – 7.66 (m, 5H), 7.61 (t, J = 7.8 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 137.43, 135.94, 133.63, 132.77, 132.03, 130.94, 129.64, 128.89, 127.94 (t, *J* = 326.8 Hz), 114.19. ^{19}F NMR (564 MHz, $CDCl_3$): δ -78.11. HRMS m/z (EI) calculated for $C_{14}H_9F_2NO_2S_2$ [M]+:325.0043, found:325.0039.



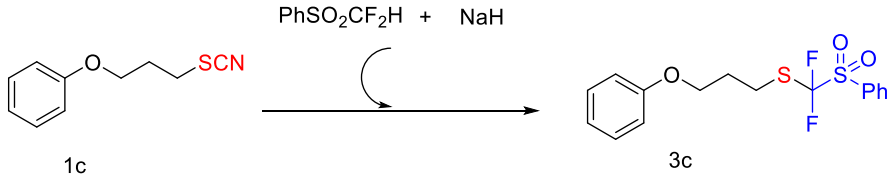
(difluoro(phenylsulfonyl)methyl)(4-fluorophenyl)sulfane (3q) Light yellow oil, R_f 0.75(petroleum ether : ethyl acetate =5:1) (32.44 mg, 51% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.97 (d, J = 7.9 Hz, 2H), 7.76 (t, J = 7.4 Hz, 1H), 7.69 (dd, J = 7.7, 5.9 Hz, 2H), 7.61 (t, J = 7.7 Hz, 2H), 7.09 (t, J = 8.4 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 165.56, 163.89, 139.73(d, *J* = 9.0 Hz), 135.70, 132.54, 130.94, 129.53, 128.04 (t, *J* = 325.2 Hz, 1H), 116.78 (d, *J* = 22.3 Hz). ^{19}F NMR (564 MHz, $CDCl_3$): δ -79.05, -108.31. HRMS m/z (EI) calculated for $C_{13}H_9F_3O_2S_2$ [M]+:317.9996, found:317.9992.



(difluoro(phenylsulfonyl)methyl)(4-methoxyphenyl)-sulfane (3r) Light yellow oil, R_f 0.65(petroleum ether : ethyl acetate =5:1) (28.38 mg, 43% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.97 (d, J = 9.1 Hz, 2H), 7.75 (t, J = 7.9 Hz, 1H), 7.60 (t, J = 8.9 Hz, 4H), 6.91 (d, J = 9.2 Hz, 2H), 3.82 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 162.09, 139.23, 135.54, 132.77, 130.93, 129.47, 128.17 (t, *J* = 324.6 Hz), 115.03, 113.71, 55.55. ^{19}F NMR (564 MHz, $CDCl_3$): δ -79.37. HRMS m/z (EI) calculated for C14H12F2O3S2 [M]+:330.0196, found:330.0190.

General procedures for Scheme S5.

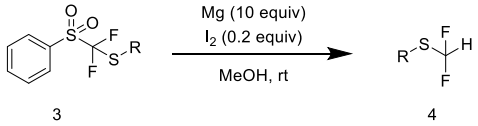
Scheme S5. Study on the mechanism of reaction.



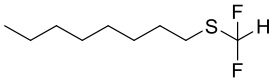
First, add 2 mmol ((difluoromethyl)sulfonyl)benzene to 5 ml of THF, Stir for 5min at -50 ℃, then add 2 mmol sodium hydride (dissolved in 10mL THF), react for 10min, the solution gradually turns into a white suspension. Then take a 100mL reaction flask, add in 1.5mol **3c** and 10 ml THF, stir for 5min at -50 ℃, add the suspension, and react for 1h. Yield was 41% which determination by meteorological chromatography with diphenyl (154 mg, 1 mmol) as an internal standard.

General procedures for Scheme S6.

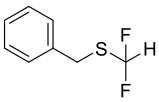
Scheme S6. Reduction of (benzenesulfonyl)difluoromethyl thioethers.



According to the literature[1,2], we used magnesium and methanol to convert our products **3b** and **3d** into **4a** and **4b**. Firse, add benzenesulfonyl)difluoromethyl thioethers (1mmol of **3b** / **3d**), iodine (0.2 equiv) and magnesium (10equiv and which was activated by hydrochloric acid) into a 25ml vail, then drop in methanol (5ml). Keep the reaction for 10 hours. When the reaction is finished, quenching the reaction with dilute hydrochloric acid. The resulting mixture was purified by flash chromatography (Polarity is given below) to get the product. The yield was determination by Meteorological Chromatography with diphenyl (154 mg, 1 mmol) as an internal standard. All the products are confirmed by the NMR and all new compounds were identified by high resolution mass spectrometry. By this method, we obtain product **4a** and **4b**, and the relevant data are shown below：



(**difluoromethyl)(octyl)sulfane** (**4a**) Colorless oil, R_f 0.85 (petroleum ether) (126.72 mg, 64% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.80 (t, J = 56.6 Hz, 1H), 2.85 – 2.75 (m, 2H), 1.73 – 1.62 (m, 2H), 1.56 – 1.25 (m, 10H), 0.88 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, CDCl3): δ 120.95 (t, J = 272.2 Hz), 31.92, 30.26, 29.20, 29.16, 28.85, 27.40 (t, J = 3.0 Hz), 22.77, 14.20. ^{19}F NMR (376 MHz, $CDCl_3$): δ -92.77. HRMS m/z (EI) calculated for $C_9H_{18}F_2S$ [M]+:196.1097, found:196.1092.



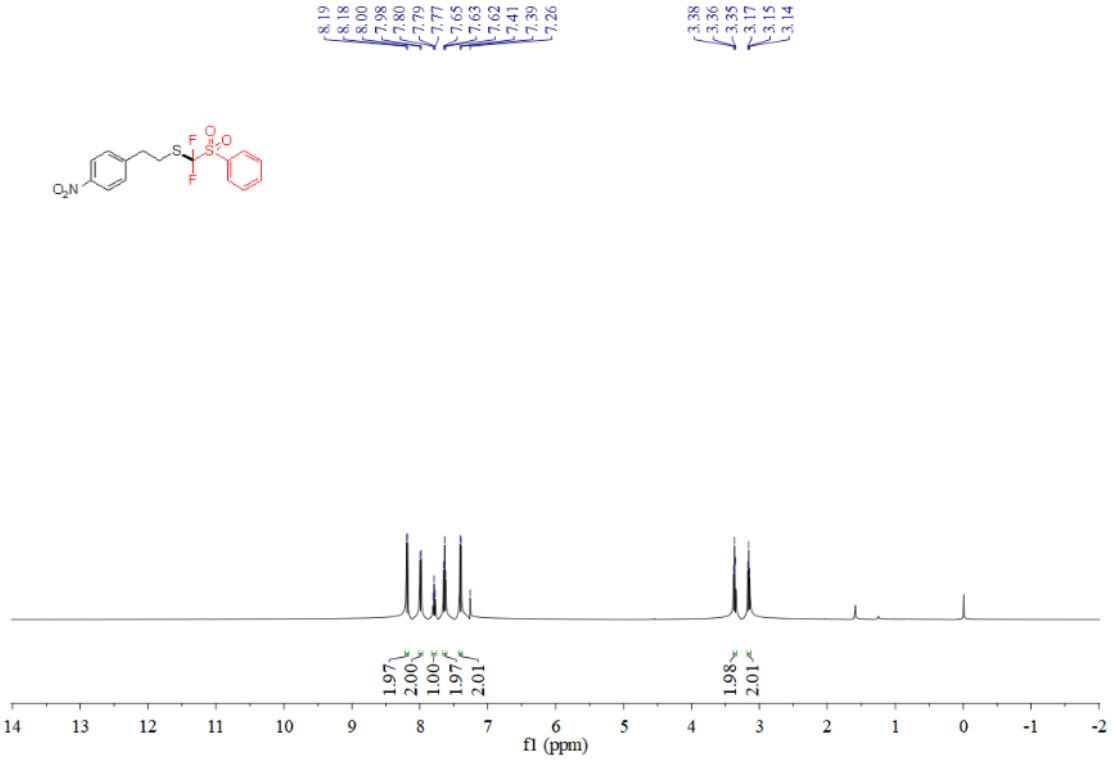
benzyl(difluoromethyl)sulfane (**4b**) Colorless oil, R_f 0.75 (petroleum ether : ethyl acetate =40:1) (118.32 mg, 68% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.39 – 7.33 (m, 5H), 6.74 (t, J = 56.6 Hz, 1H), 4.03 (s, 2H).^{13}C NMR (151 MHz, $CDCl_3$): δ 136.50, 129.13, 129.03, 127.89, 120.49 (t, J = 272.9 Hz), 31.99 (t, J = 3.8 Hz, 6H). ^{19}F NMR (565 MHz, $CDCl_3$): δ -94.25, -94.35. The characterization data was consistent with the previous report[2].

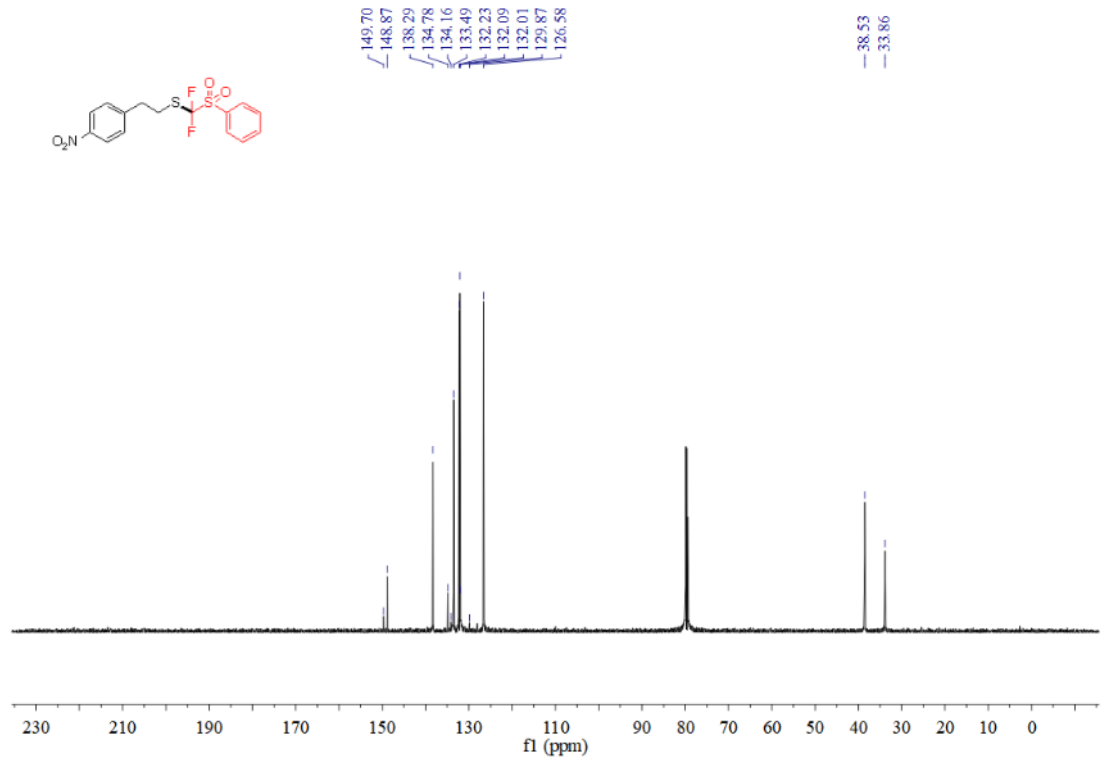
References

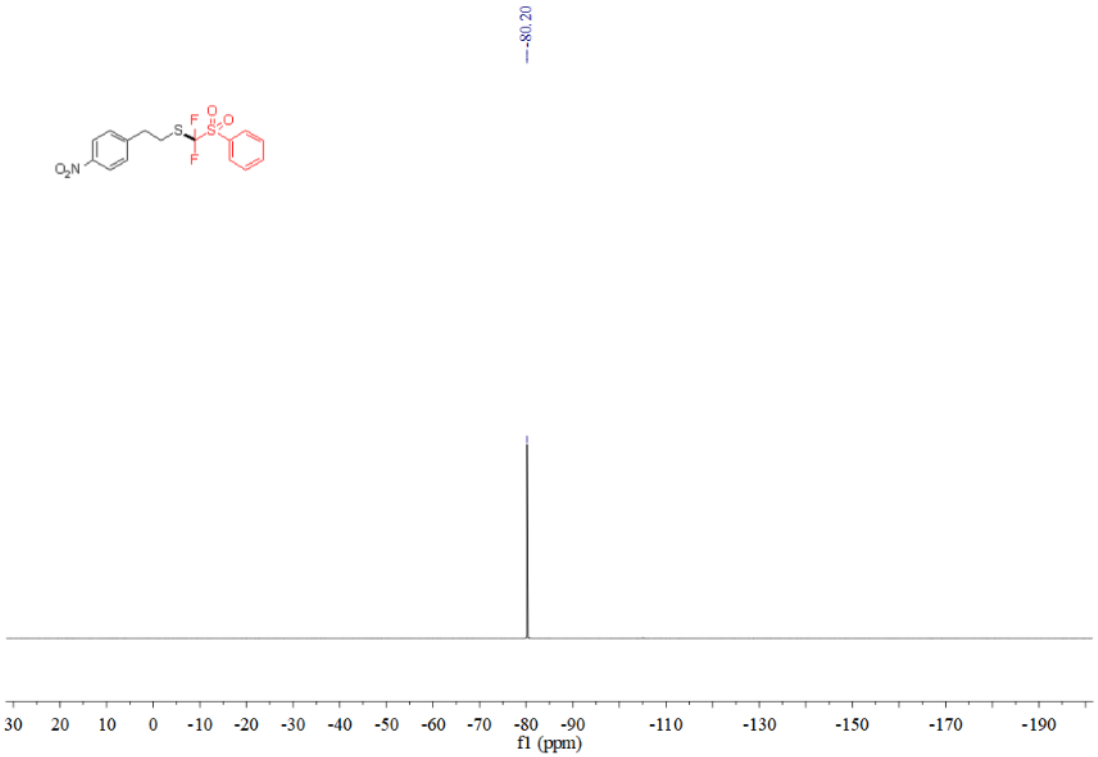
1. W. Zhang, J. Zhu, J. Hu, *Tetrahedron Letters*. 2008, **49**, 5006-5008.
2. B. Bayarmagnai, C. Matheis, K. Jouvin, L. J. Goossen, *Angew. Chem., Int. Ed*. 2015, **54**, 5753-5756.
3. P. Wang, Z. Yang, Z. Wang, C. Xu, L. Huang, S. Wang, H. Zhang, A. Lei, *Angew. Chem., Int. Ed*. 2019, **58**, 15747-15751.
4. T. Billard, S. Large, B. R. Langlois, *Tetrahedron Letters*. 1997, **38**, 65-68.

NMR spectra

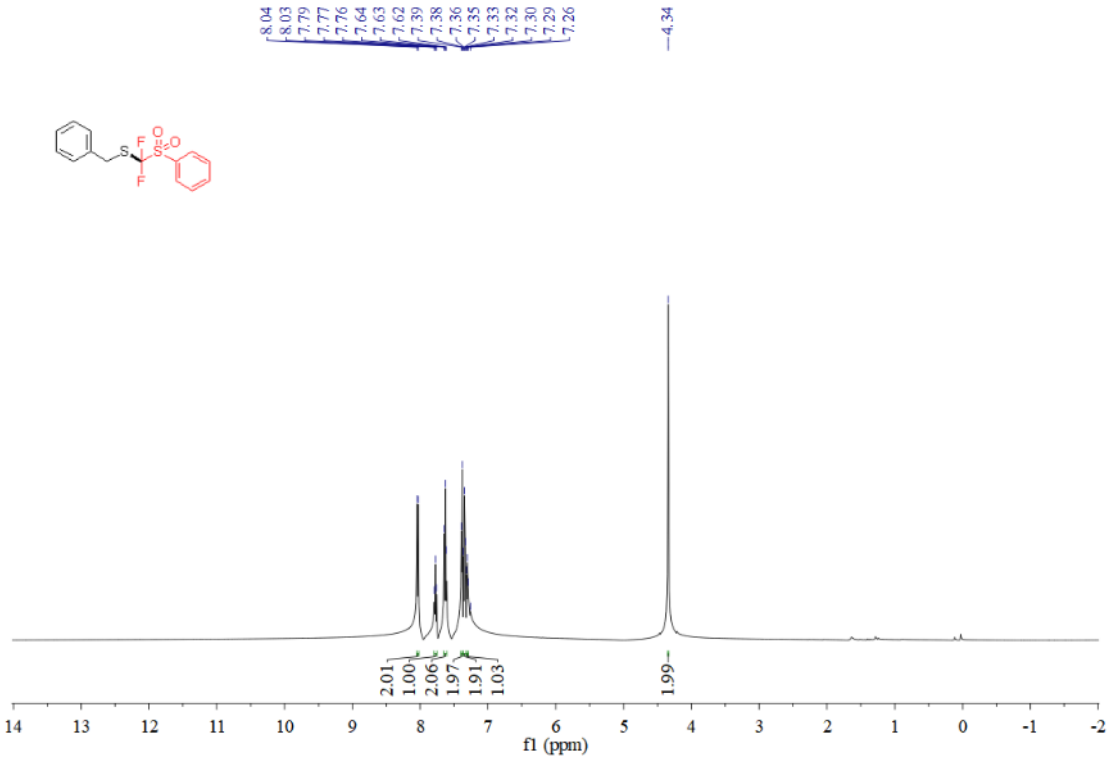
(difluoro(phenylsulfonyl)methyl)(4-nitrophenethyl)sulfane (3a)

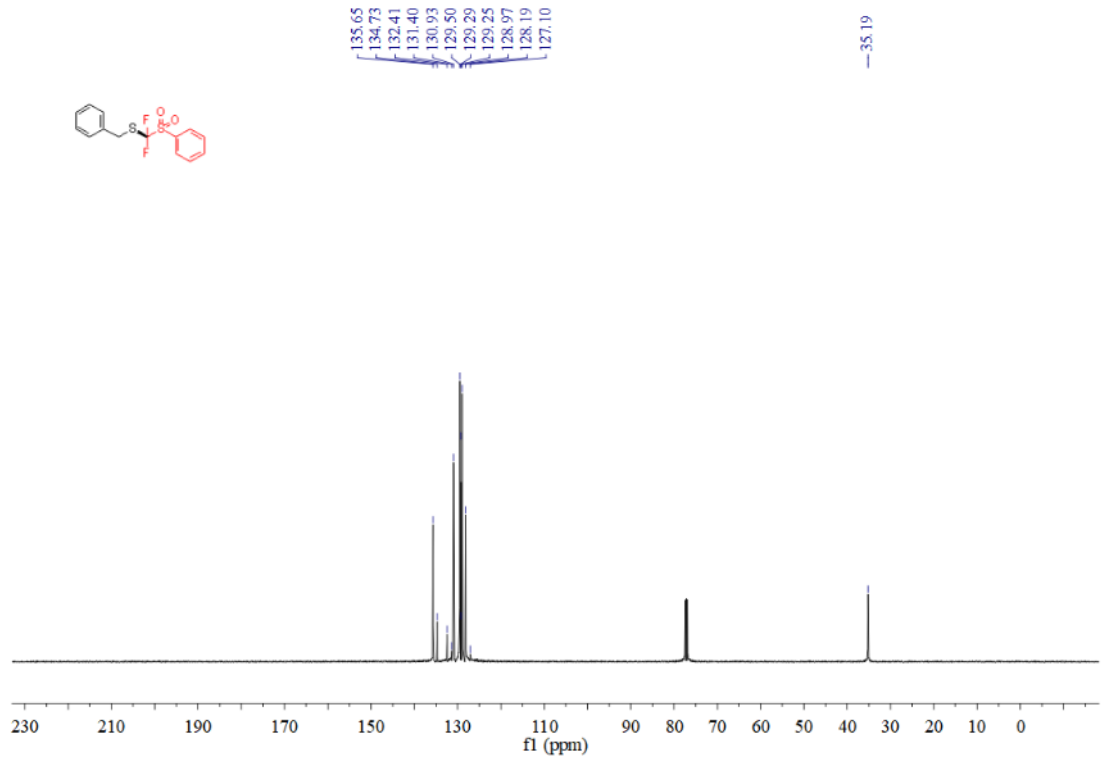


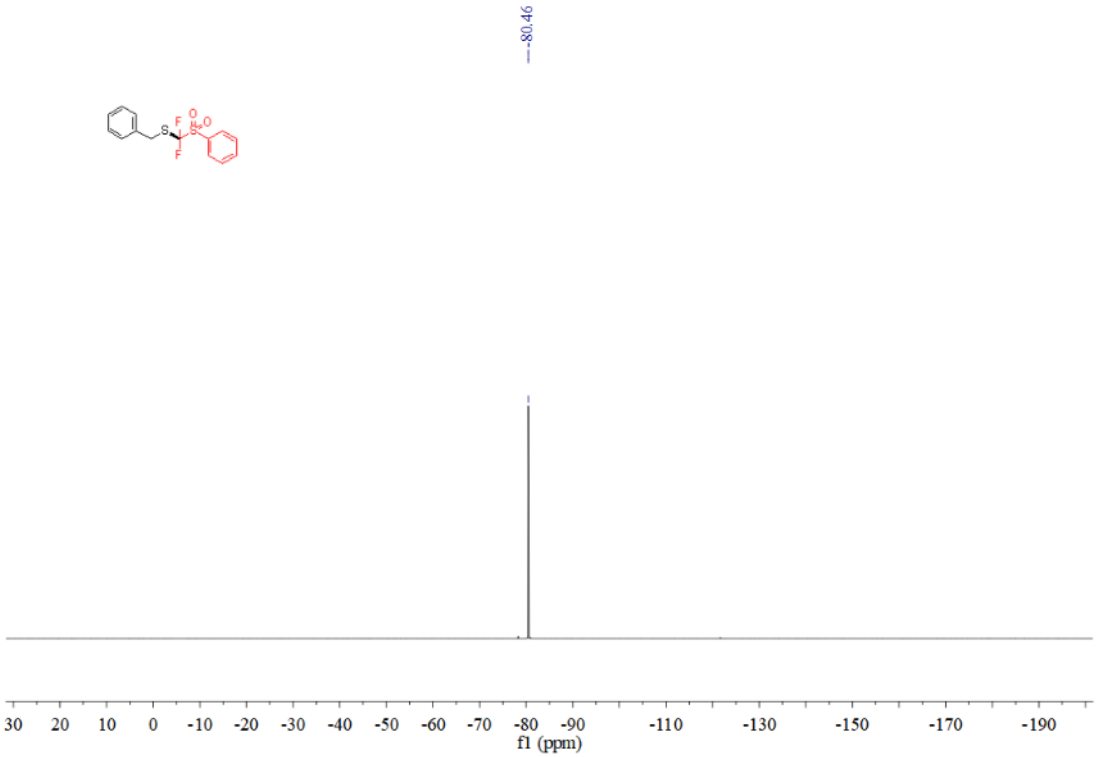



-80.20
O2N
S
F
F
O
S
O
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 -130 -150 -170 -190
f1 (ppm)

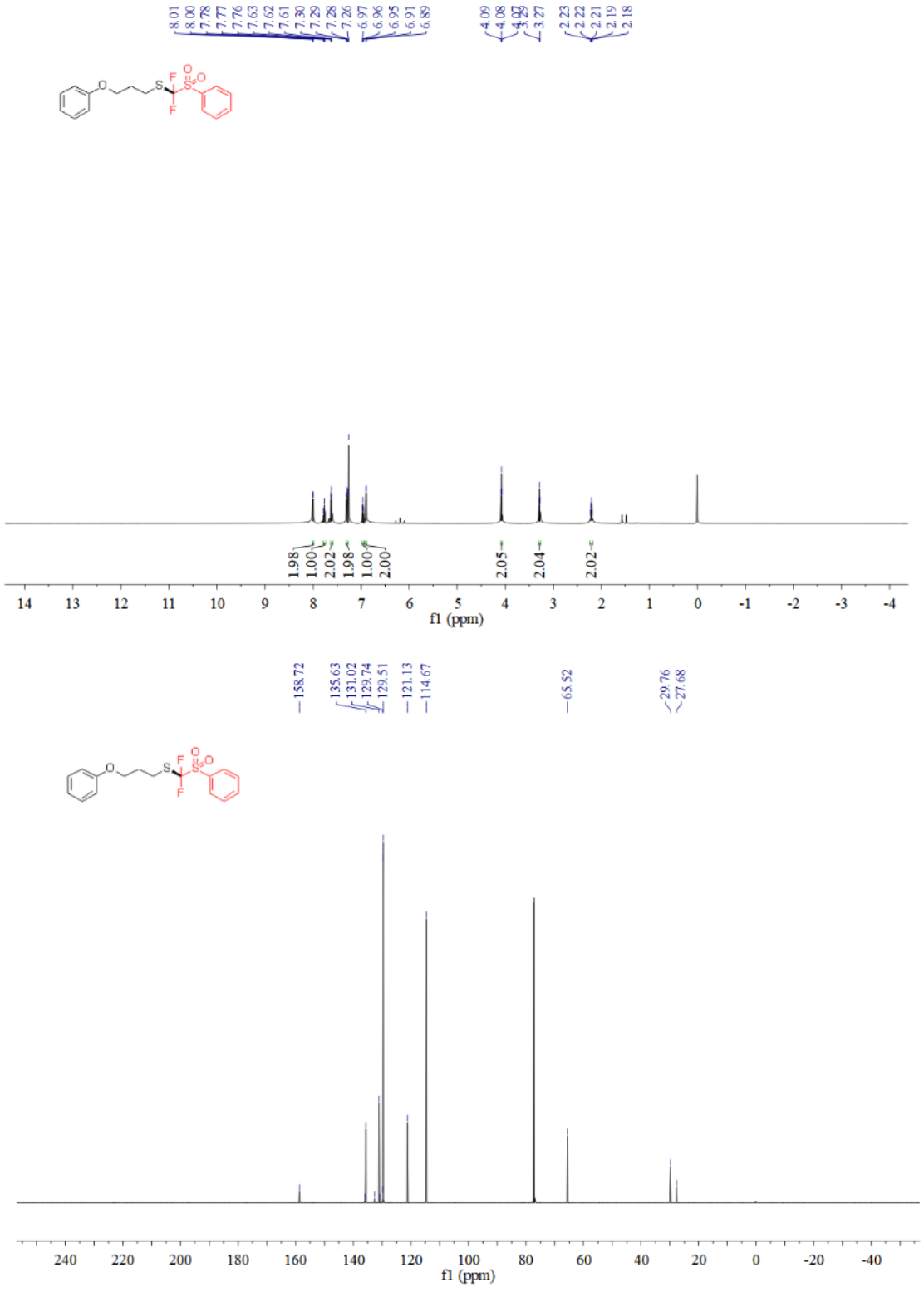
benzyl(difluoro(phenylsulfonyl)methyl)sulfane (3b)

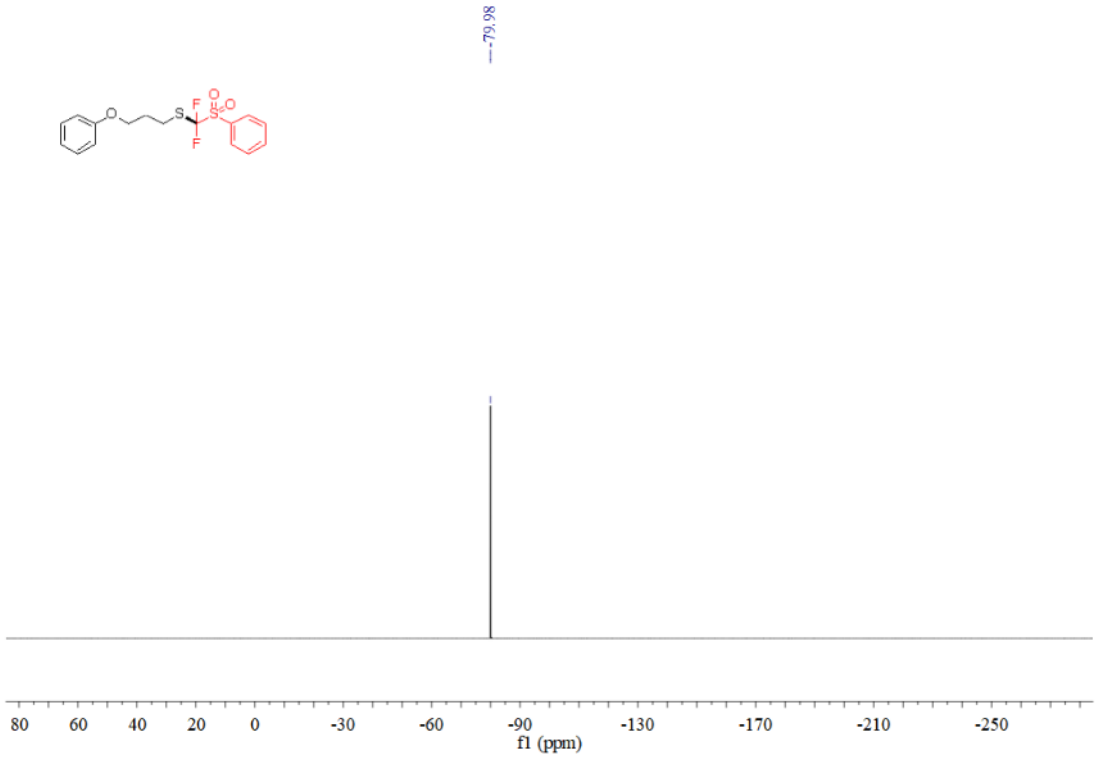




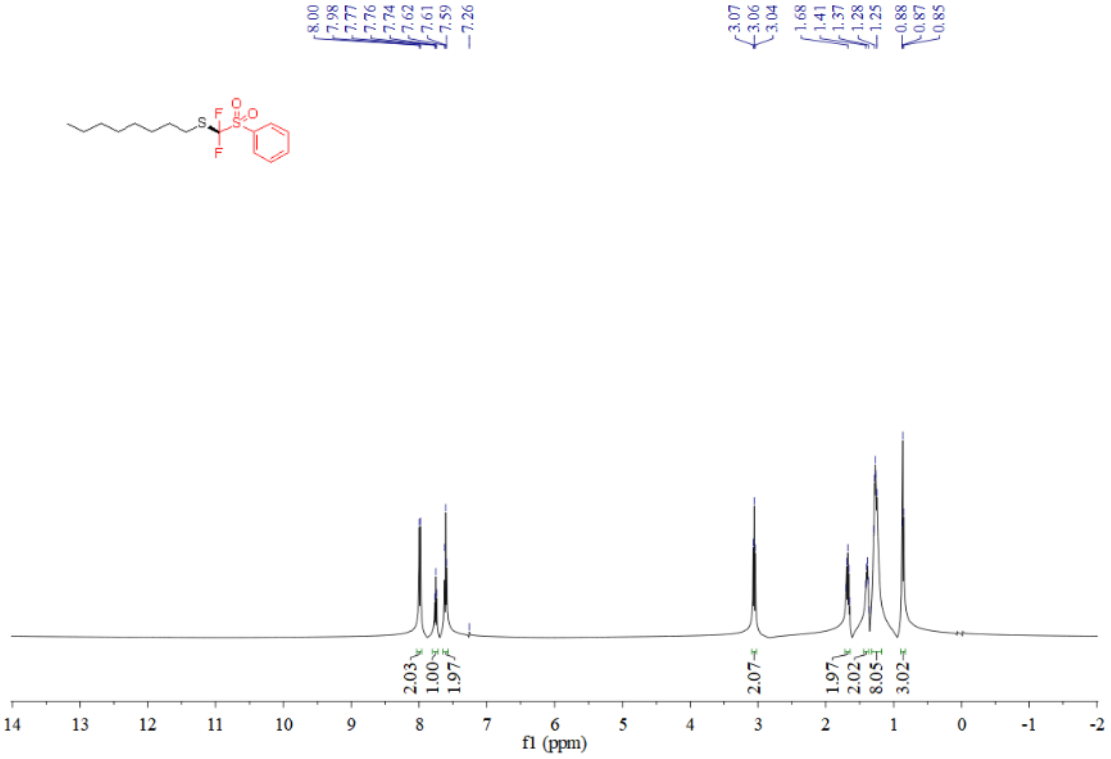

-80.46
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 -130 -150 -170 -190
f1 (ppm)

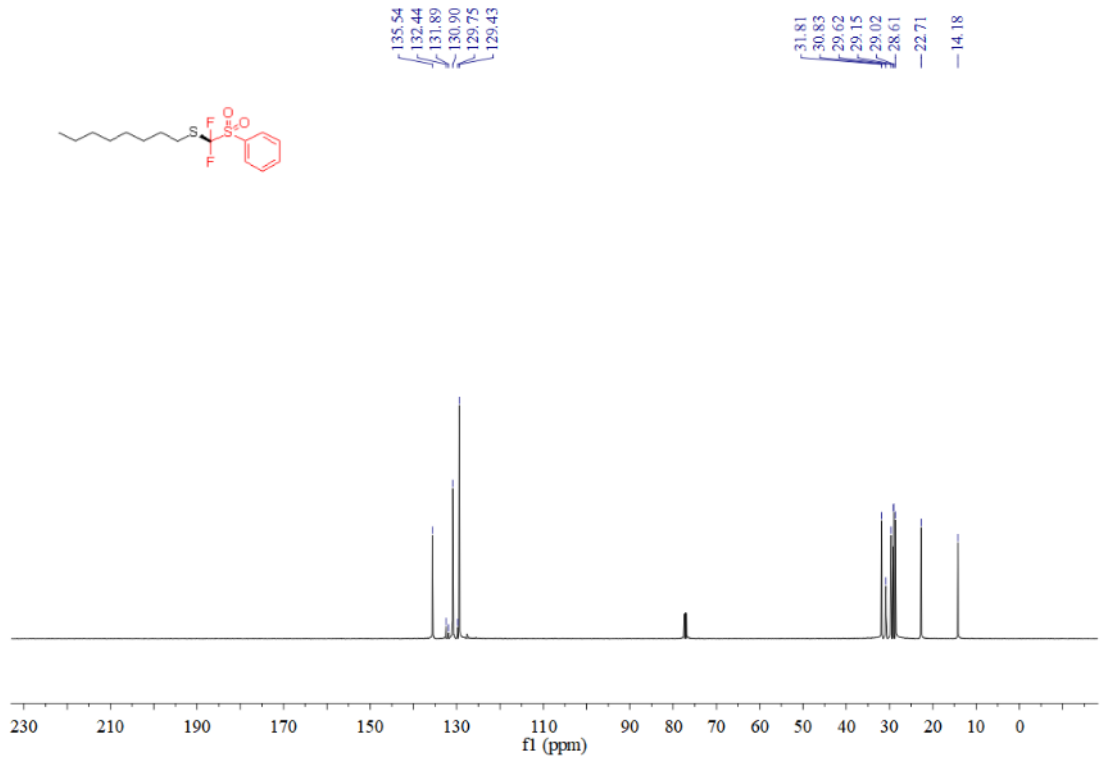
(difluoro(phenylsulfonyl)methyl)(3-phenoxypropyl)sulfan (3c)

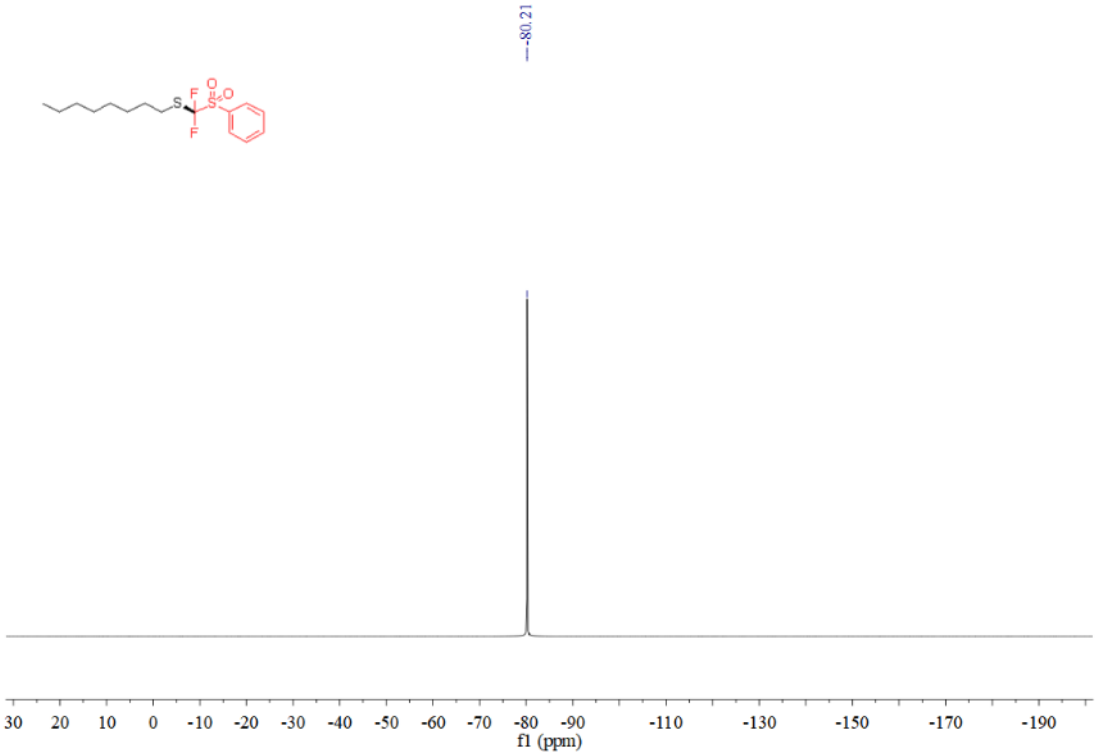



-79.98
80
60
40
20
0
-30
-60
-90
-130
-170
-210
-250
f1 (ppm)

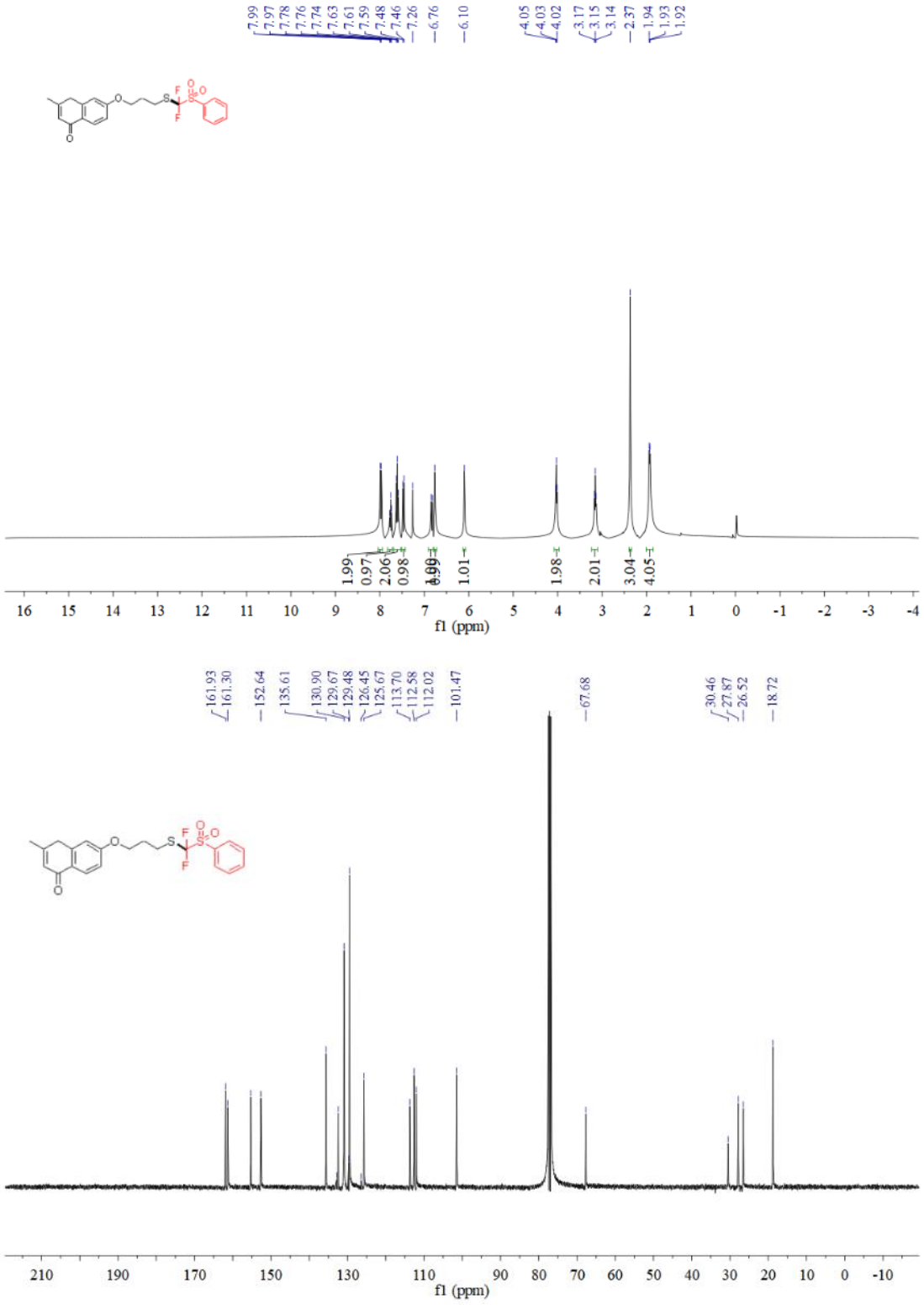
(difluoro(phenylsulfonyl)methyl)(octyl)sulfan (3d)

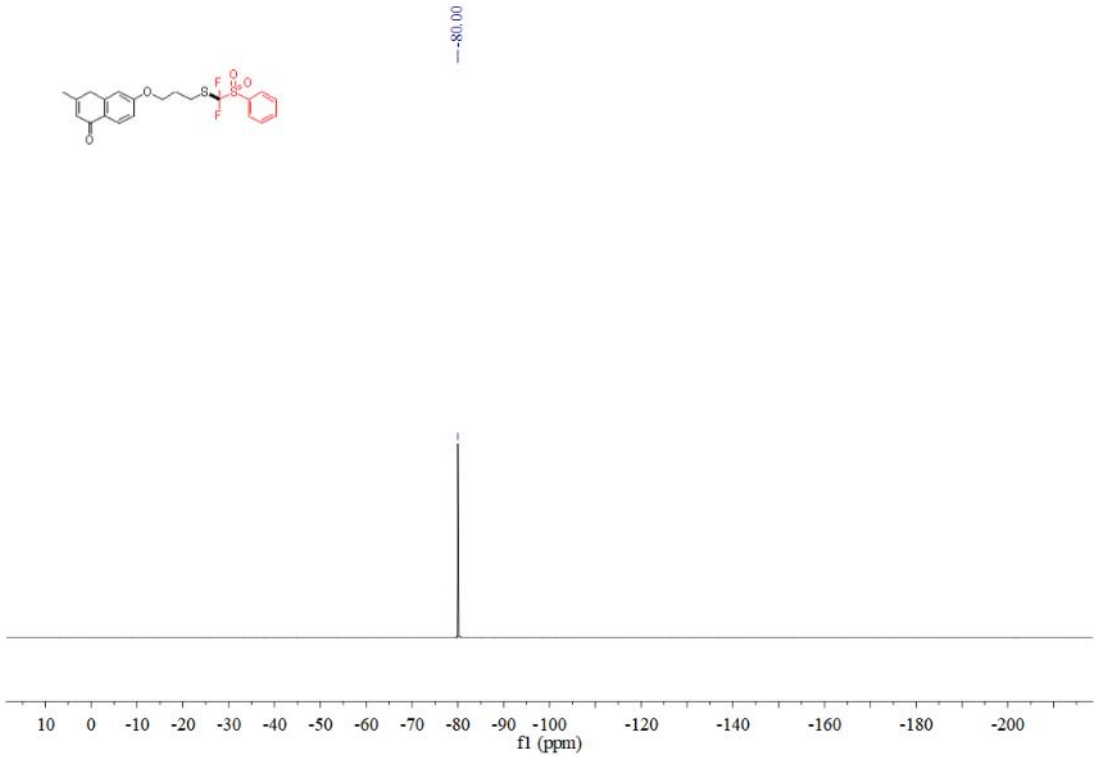




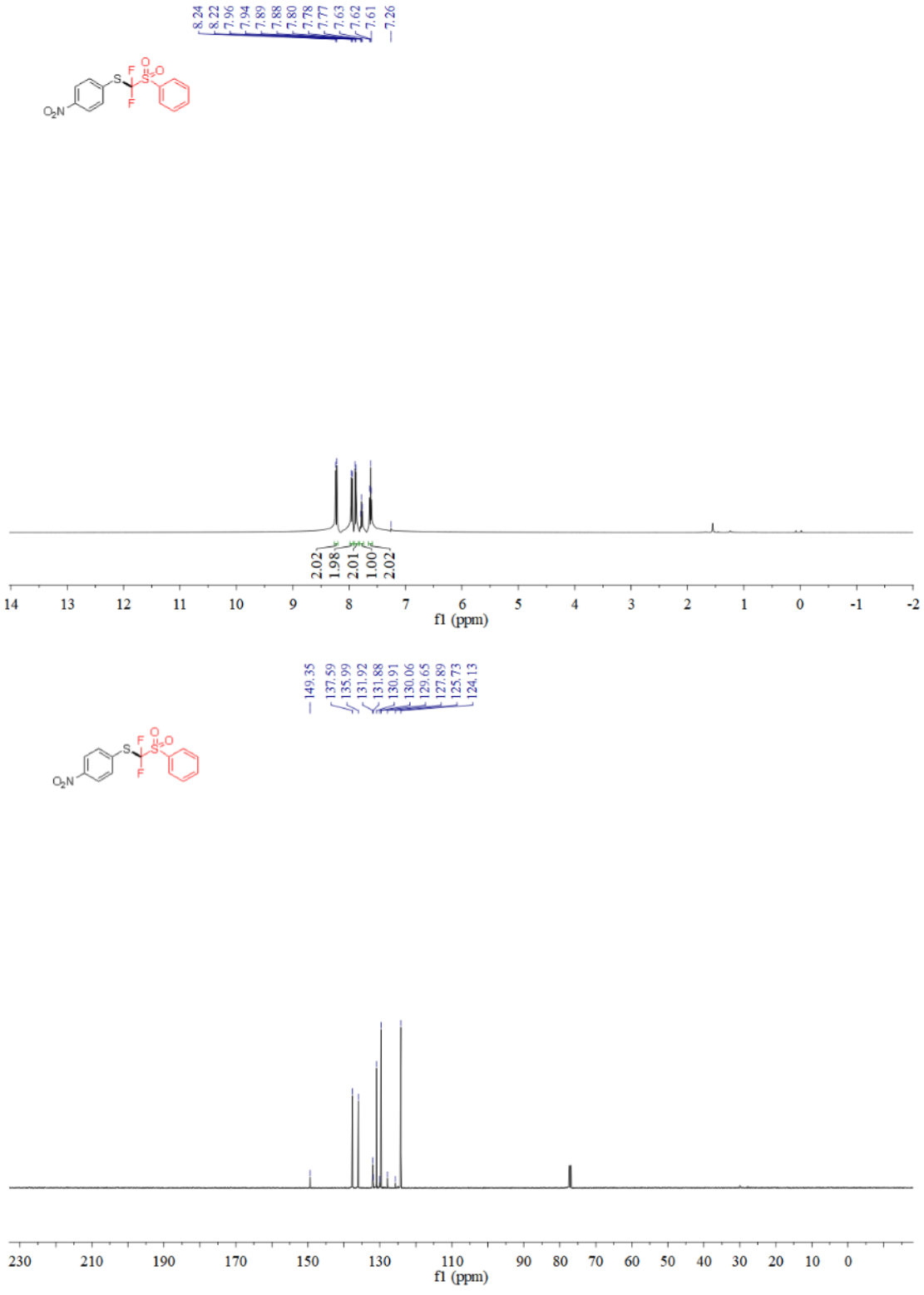

-80.21
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 -130 -150 -170 -190
f1 (ppm)

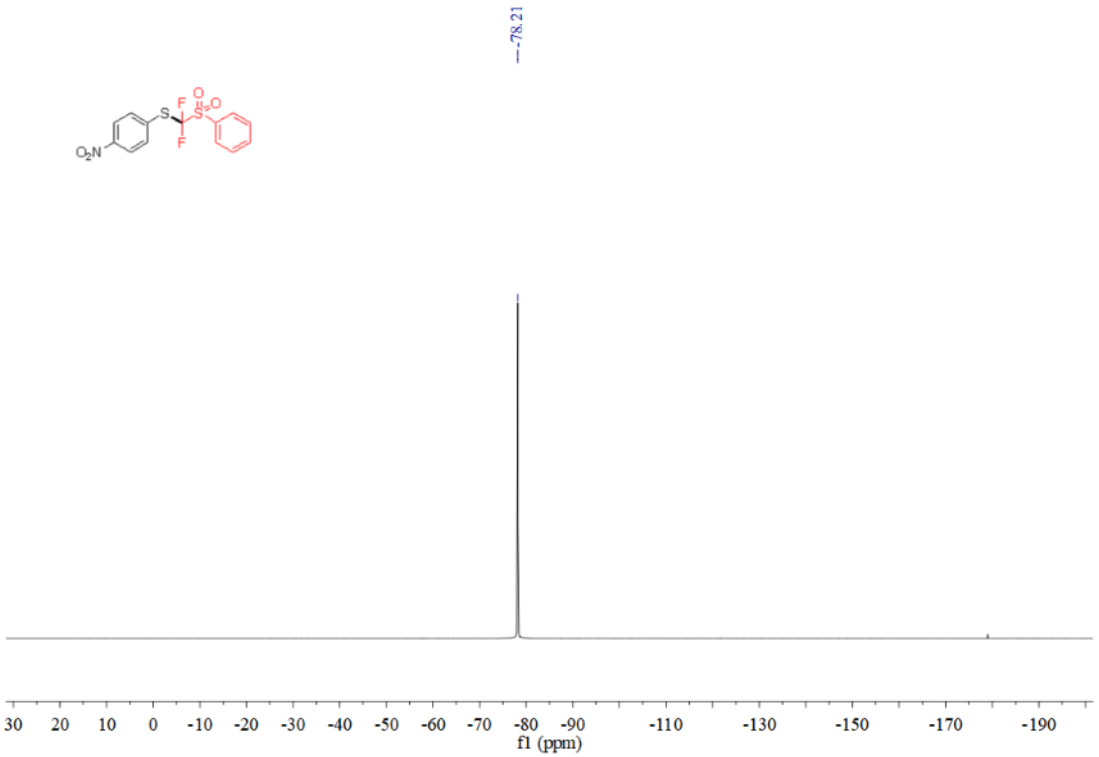
6-(4-((difluoro(phenylsulfonyl)methyl)thio)butyl)-3-methylnaphthalen-1(4H)-one (3e)



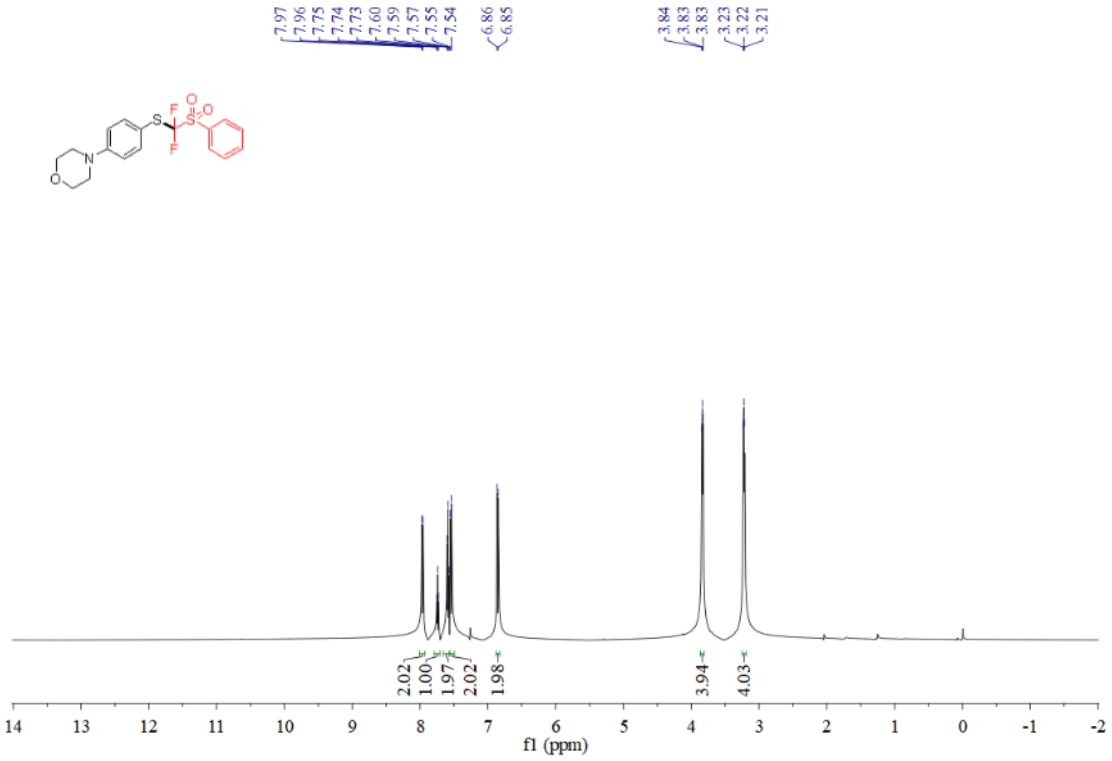

-80.00
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
-200
f1 (ppm)

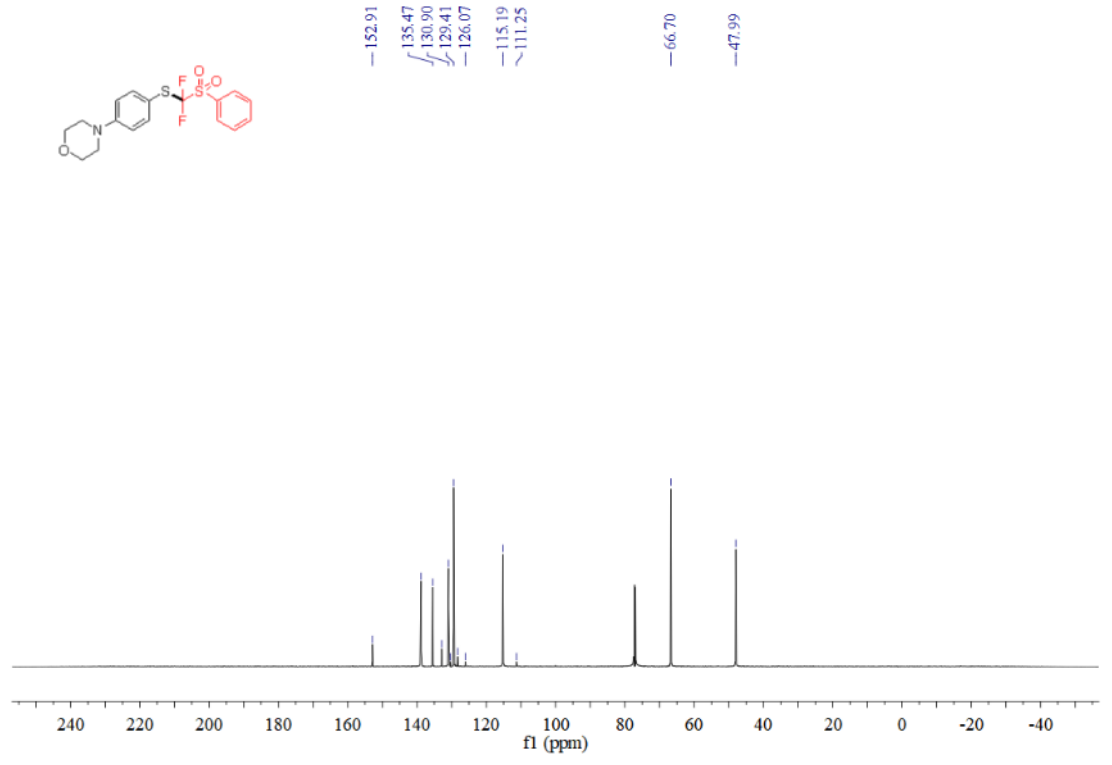
(difluoro(phenylsulfonyl)methyl)(4-nitrophenyl)sulfane (3f)

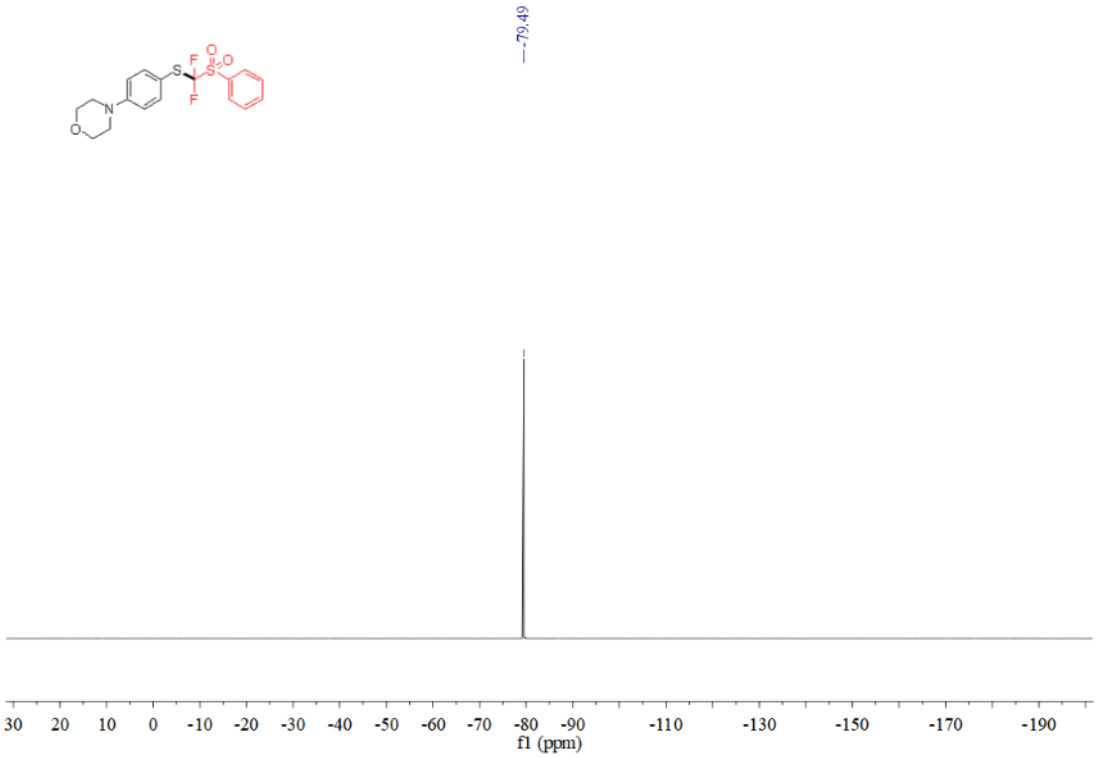



-78.21
O2N
S
F
F
O
S
O
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-110
-130
-150
-170
-190
f1 (ppm)

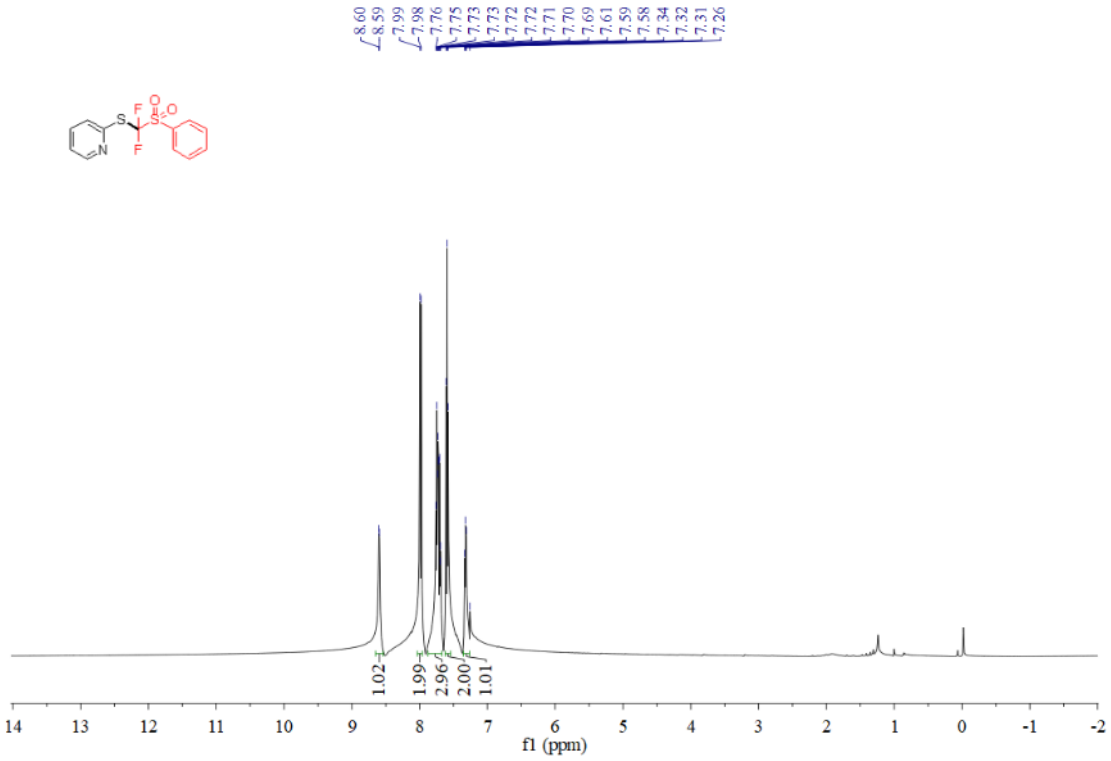
4-(4-((difluoro(phenylsulfonyl)methyl)thio)phenyl)morpholine (3g)

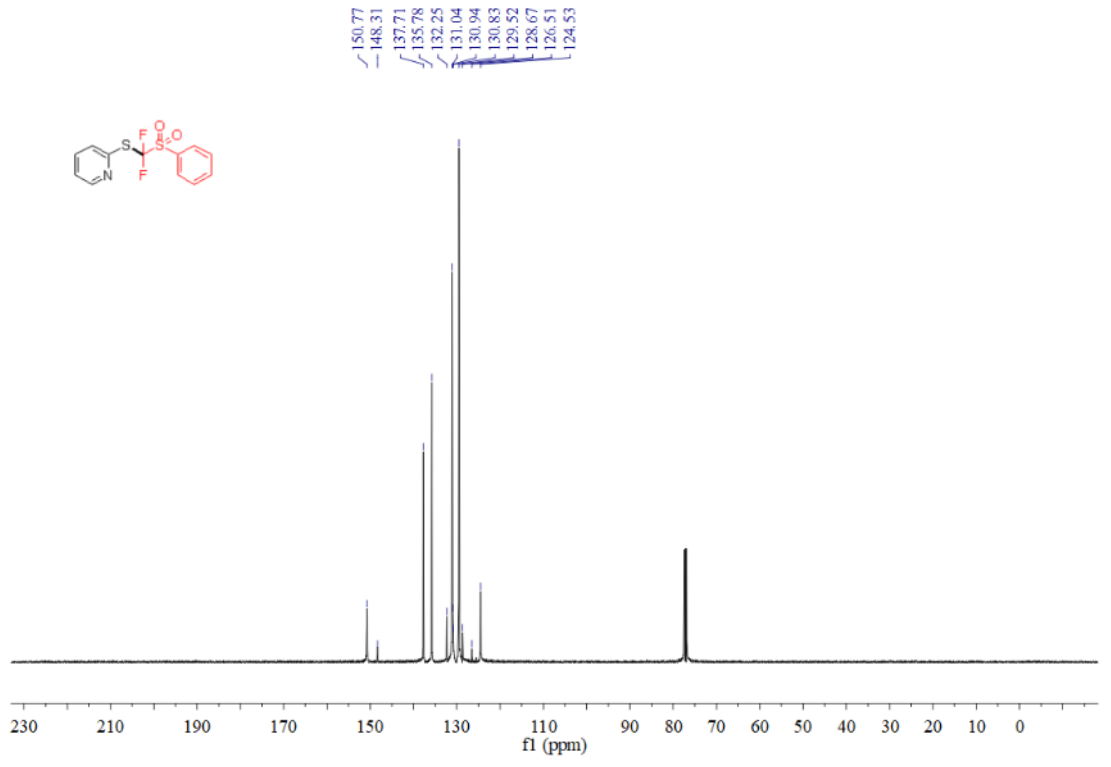


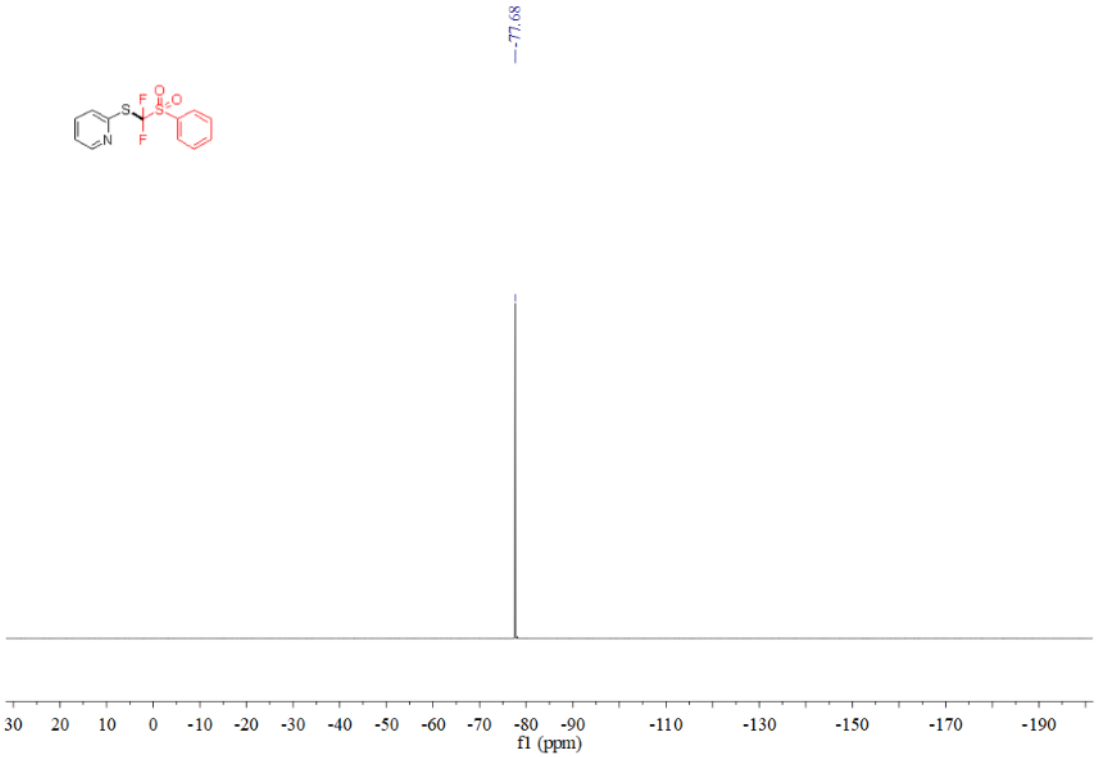



-79.49
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 -130 -150 -170 -190
f1 (ppm)

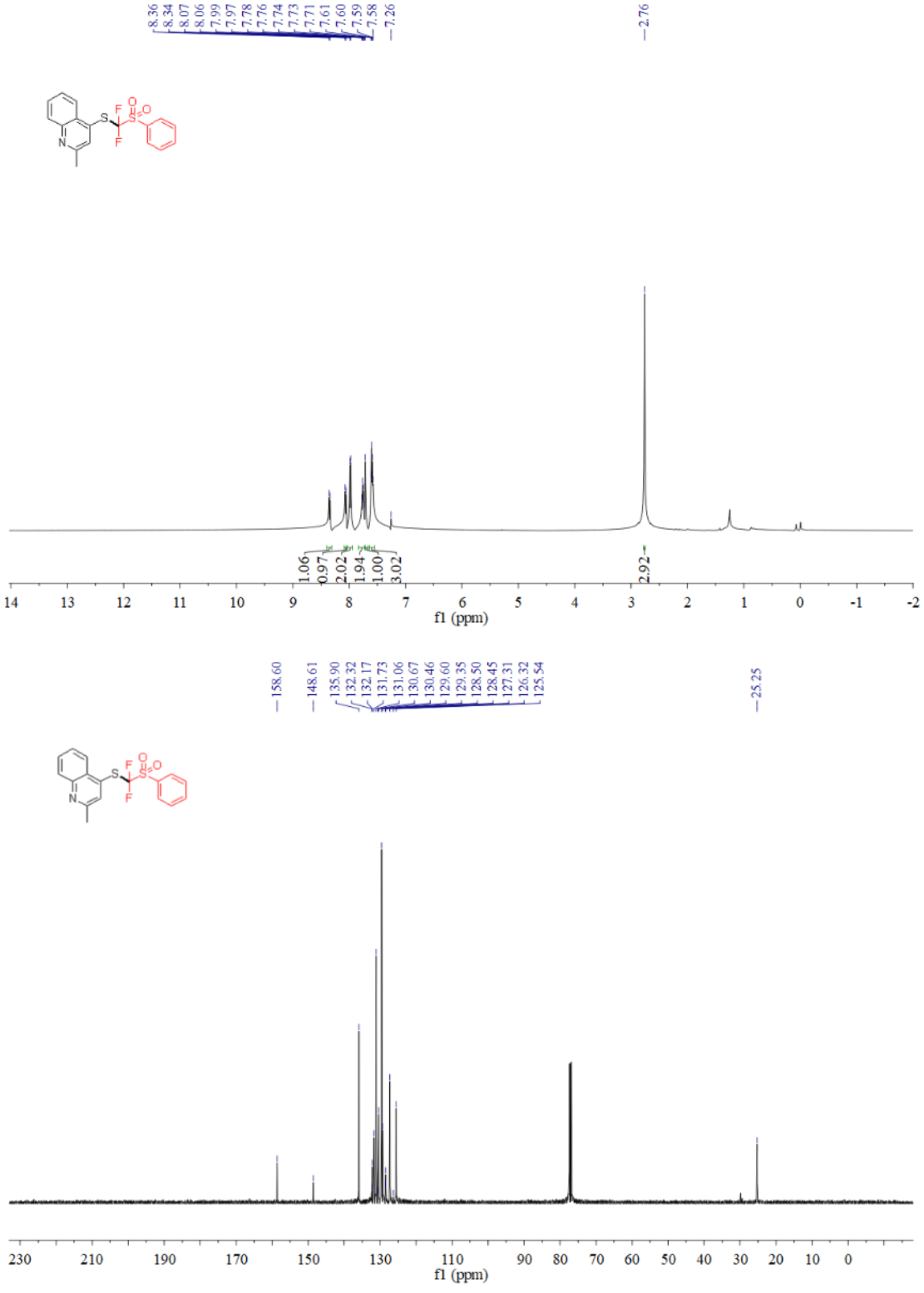
2-((difluoro(phenylsulfonyl)methyl)thio)pyridine (3h)

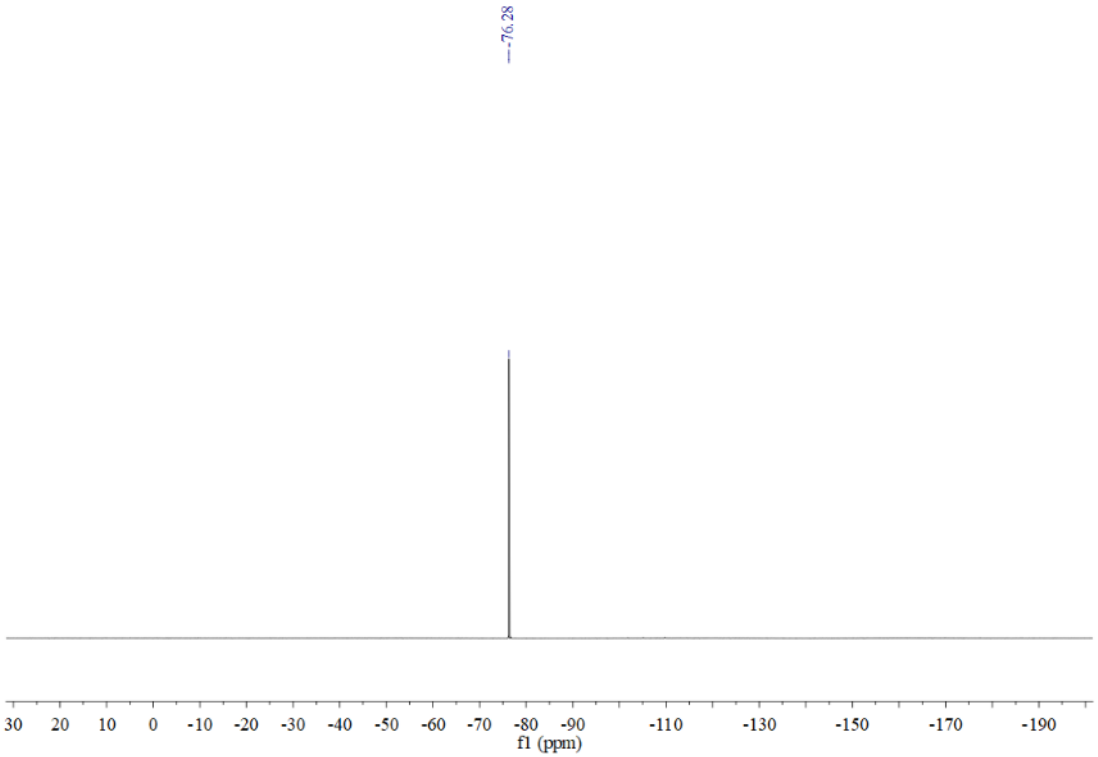




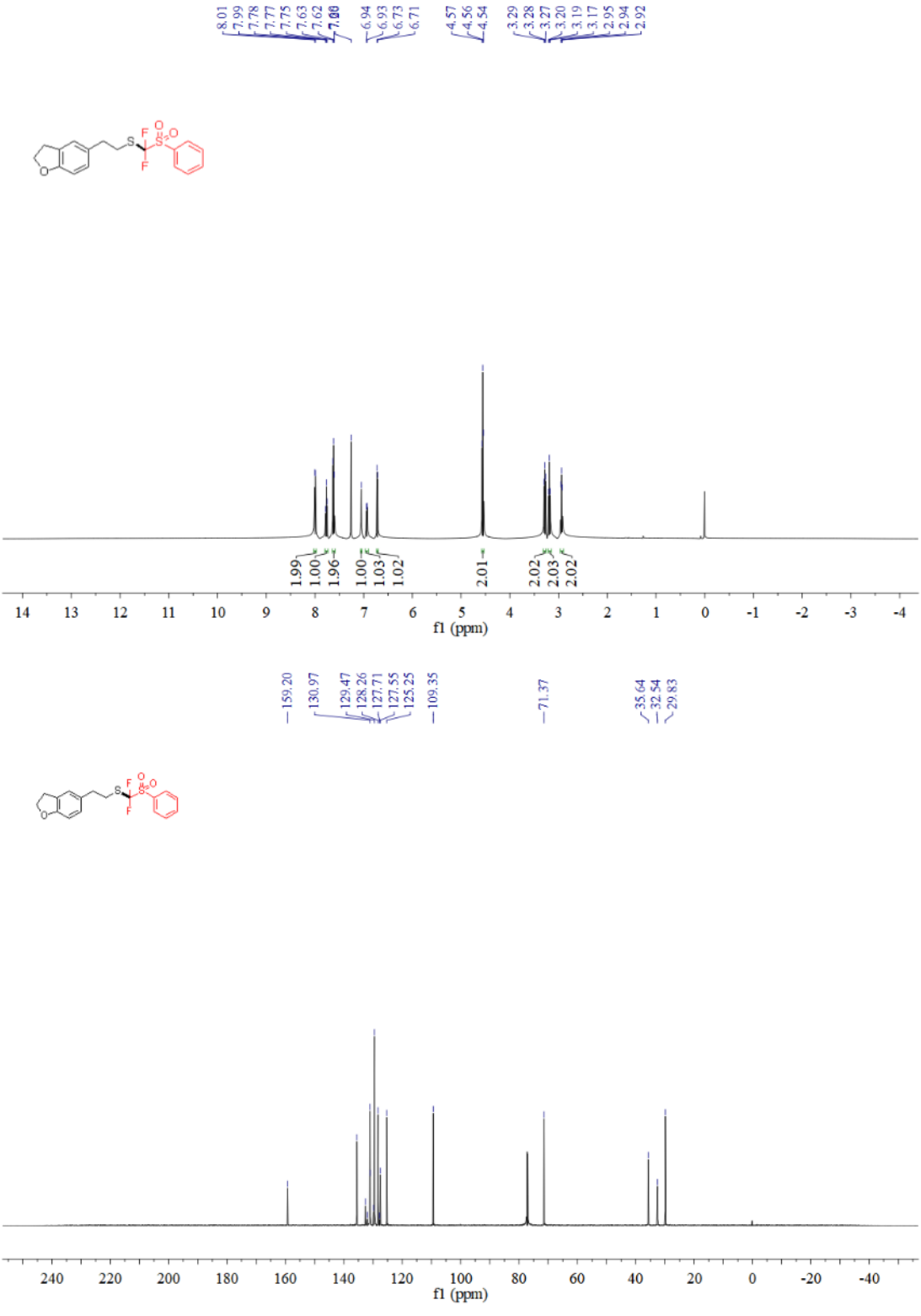

-77.68
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 -130 -150 -170 -190
f1 (ppm)

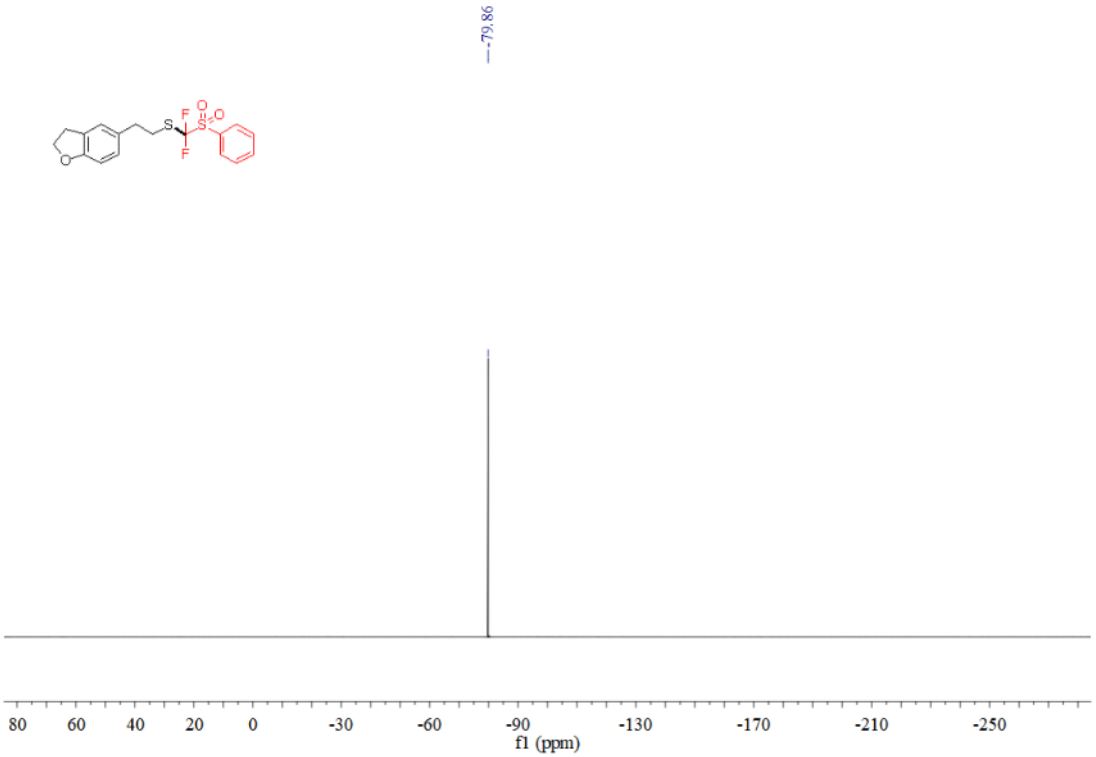
4-((difluoro(phenylsulfonyl)methyl)thio)-2-methylquinoline (3i)



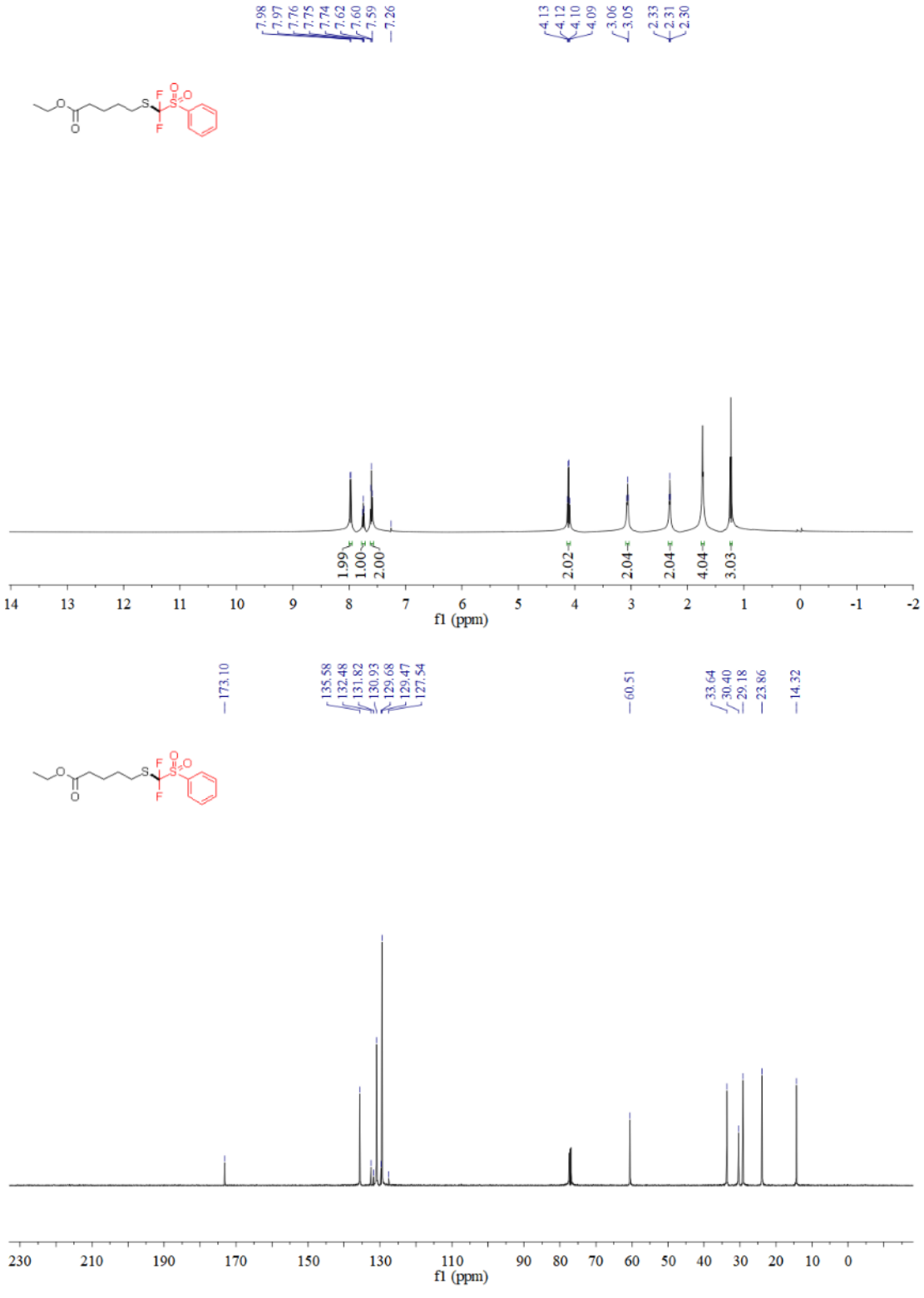

-76.28
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 -130 -150 -170 -190
f1 (ppm)

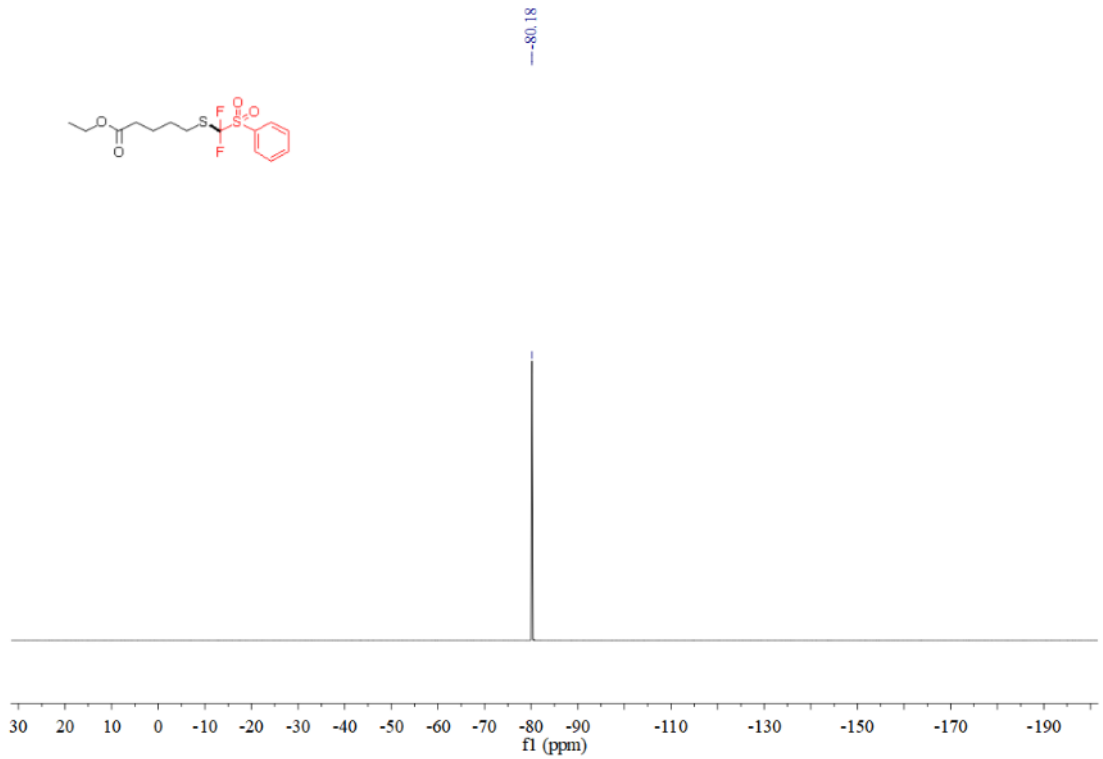
5-(2-((difluoro(phenylsulfonyl)methyl)thio)ethyl)-2,3-dihydrobenzofuran (3j)



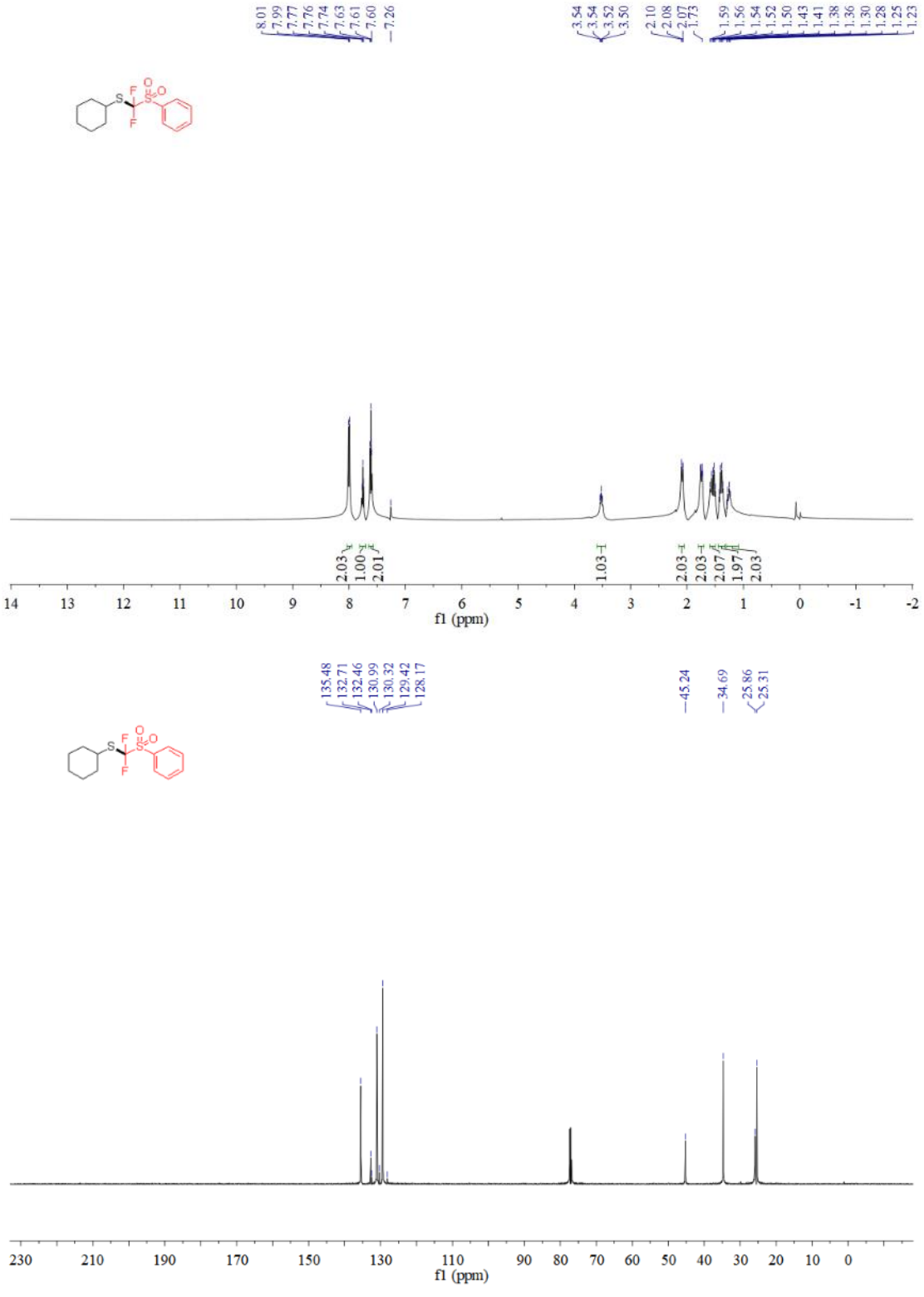

-79.86
80
60
40
20
0
-30
-60
-90
-130
-170
-210
-250
f1 (ppm)

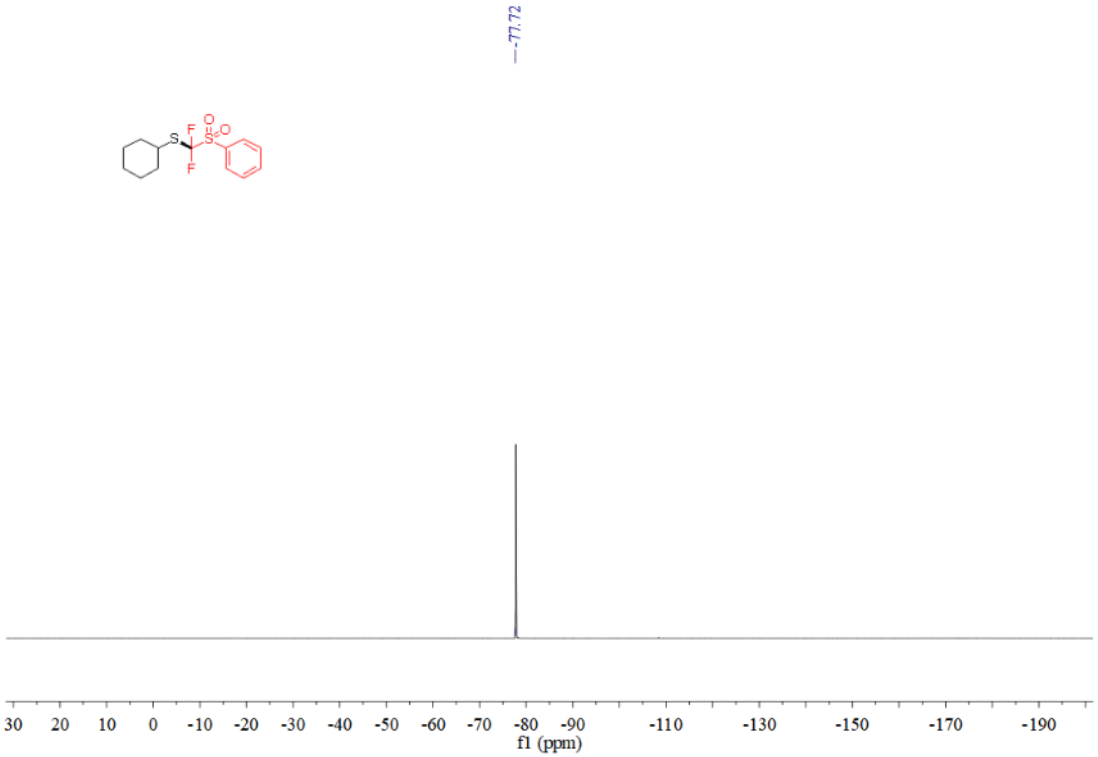
ethyl 5-((difluoro(phenylsulfonyl)methyl)thio)pentanoate (3k)



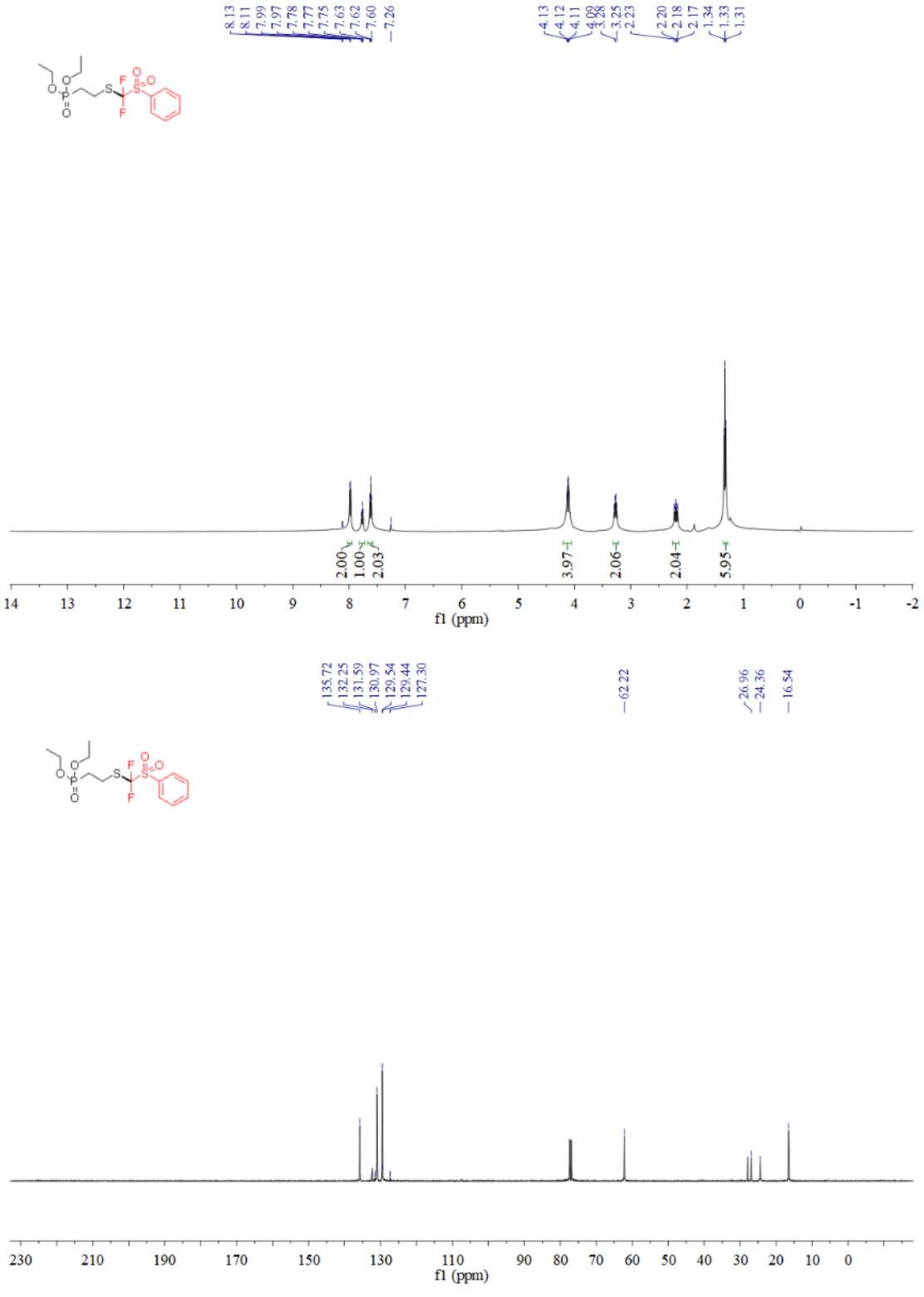

-80.18
O
O
S
F
F
O
O
S
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 -130 -150 -170 -190
f1 (ppm)

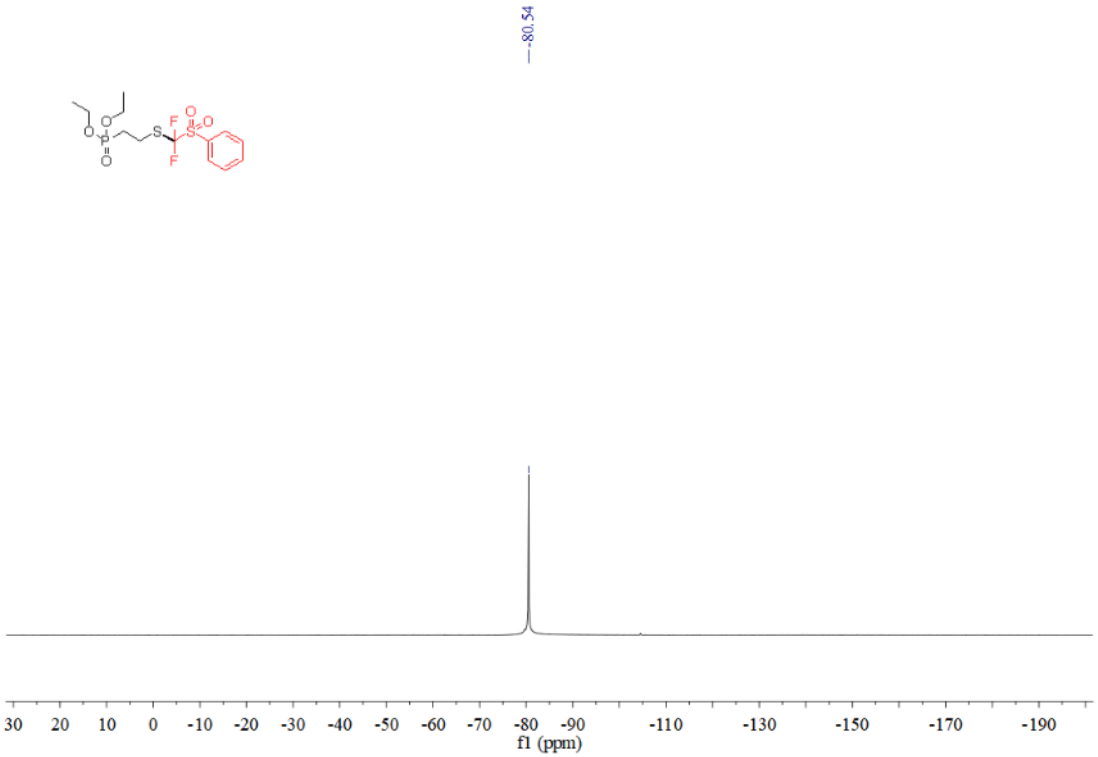
cyclohexyl(difluoro(phenylsulfonyl)methyl)sulfane (3l)



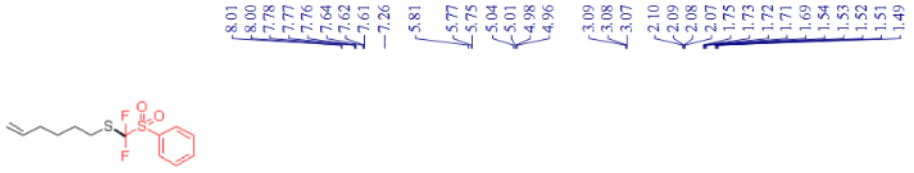

-77.72
S
F
F
O
S
O
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-110
-130
-150
-170
-190
f1 (ppm)

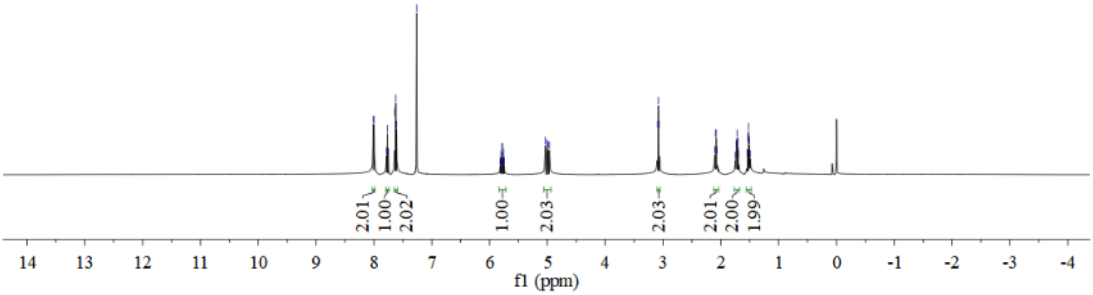
Diethyl(2-((difluoro(phenylsulfonyl)methyl)thio)ethyl)phosphonate (3m)

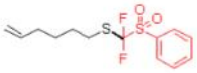


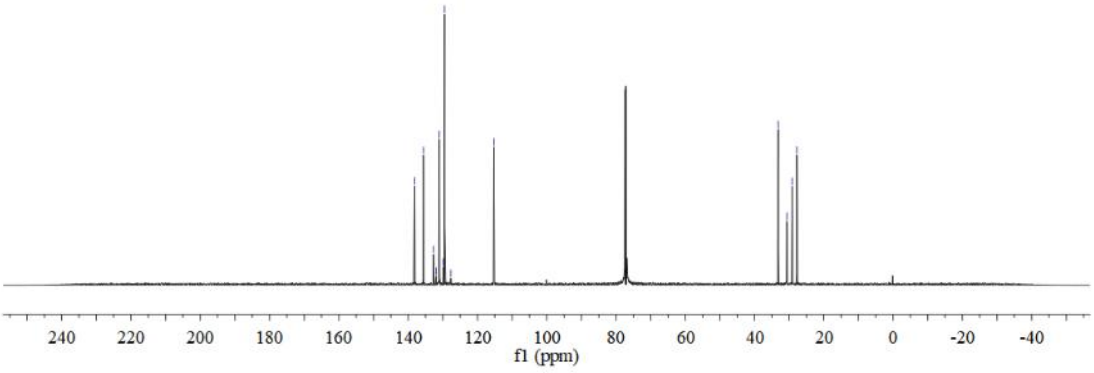

-80.54
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 -130 -150 -170 -190
f1 (ppm)

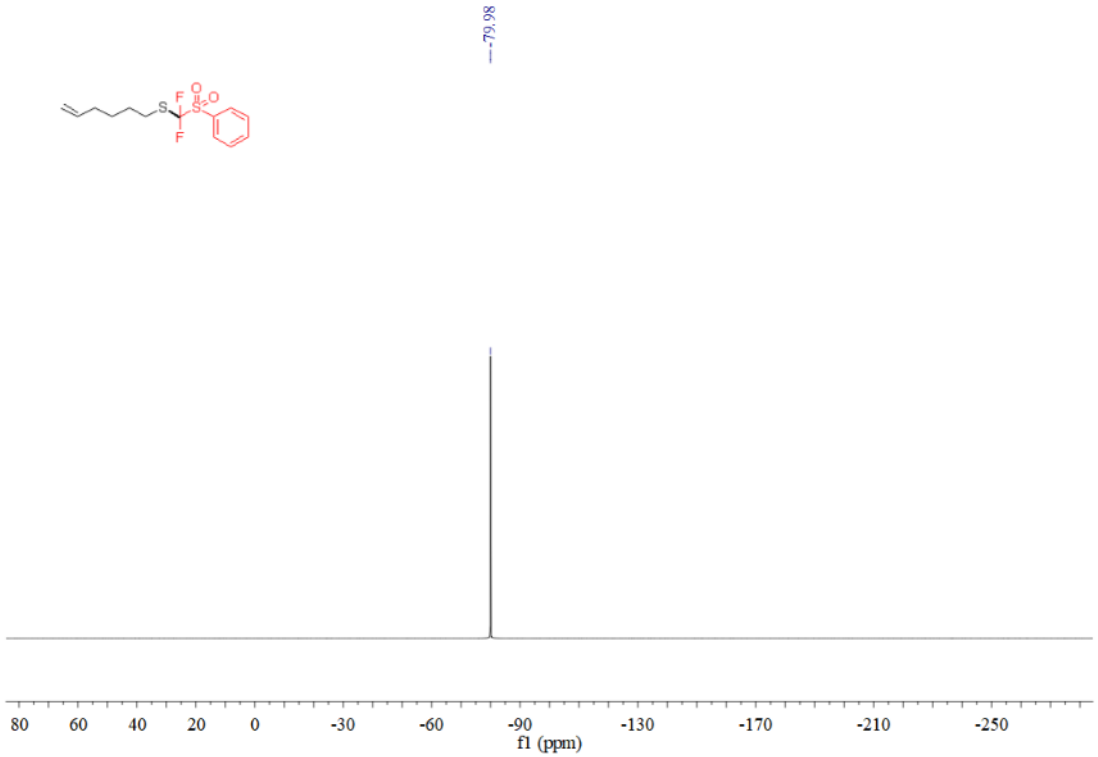
(difluoro(phenylsulfonyl)methyl)(hex-5-en-1-yl)sulfane (3n)



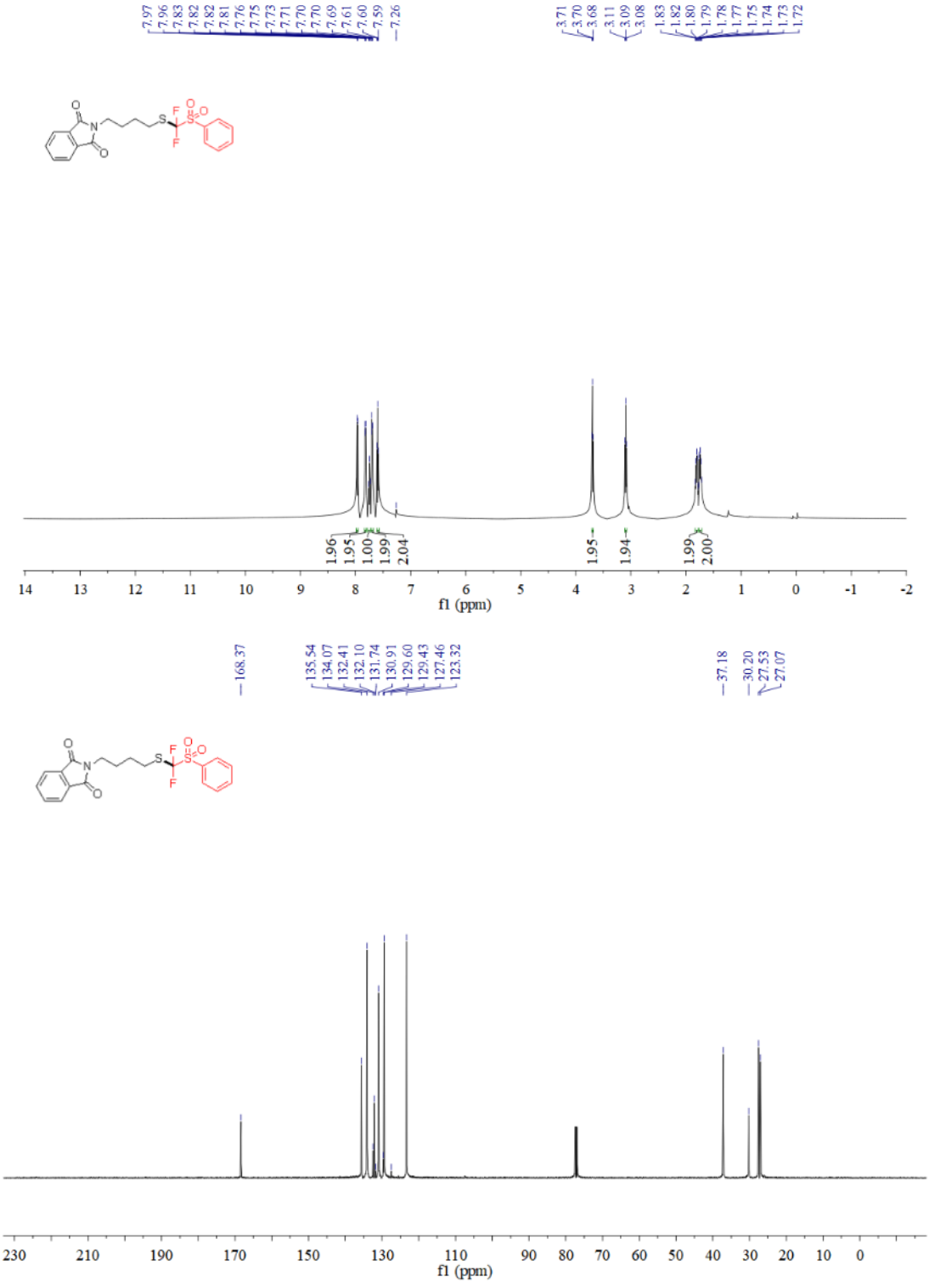


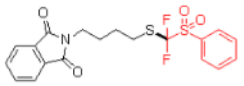





-79.98
80
60
40
20
0
-30
-60
-90
-130
-170
-210
-250
f1 (ppm)

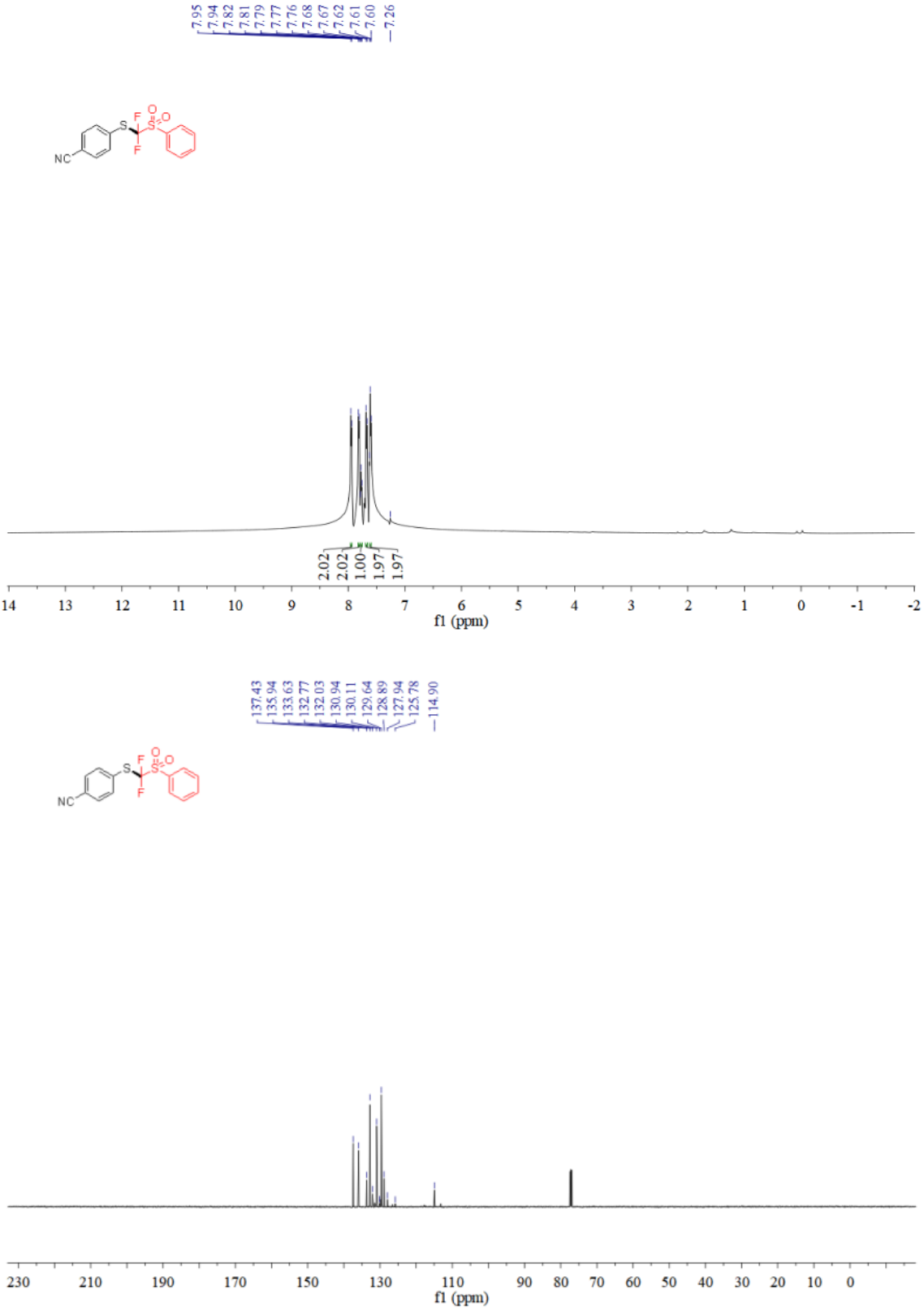
2-(4-((difluoro(phenylsulfonyl)methyl)thio)butyl)isoindoline-1,3-dione (3o)

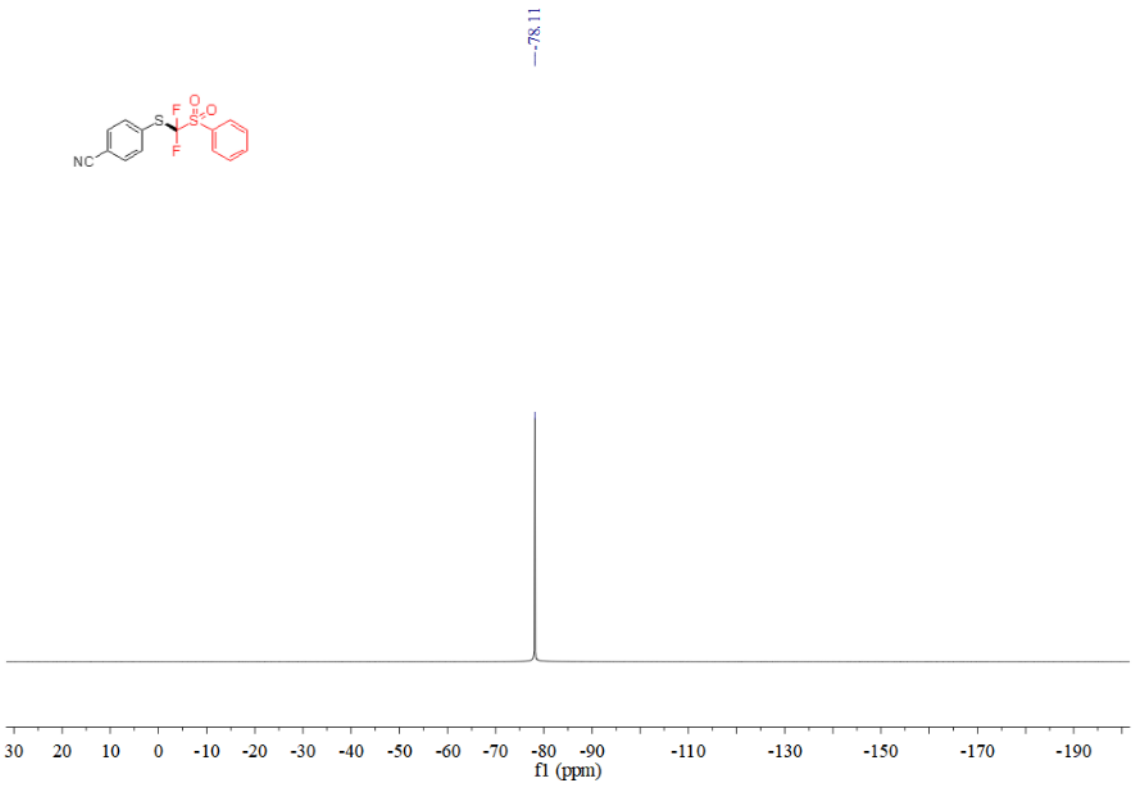




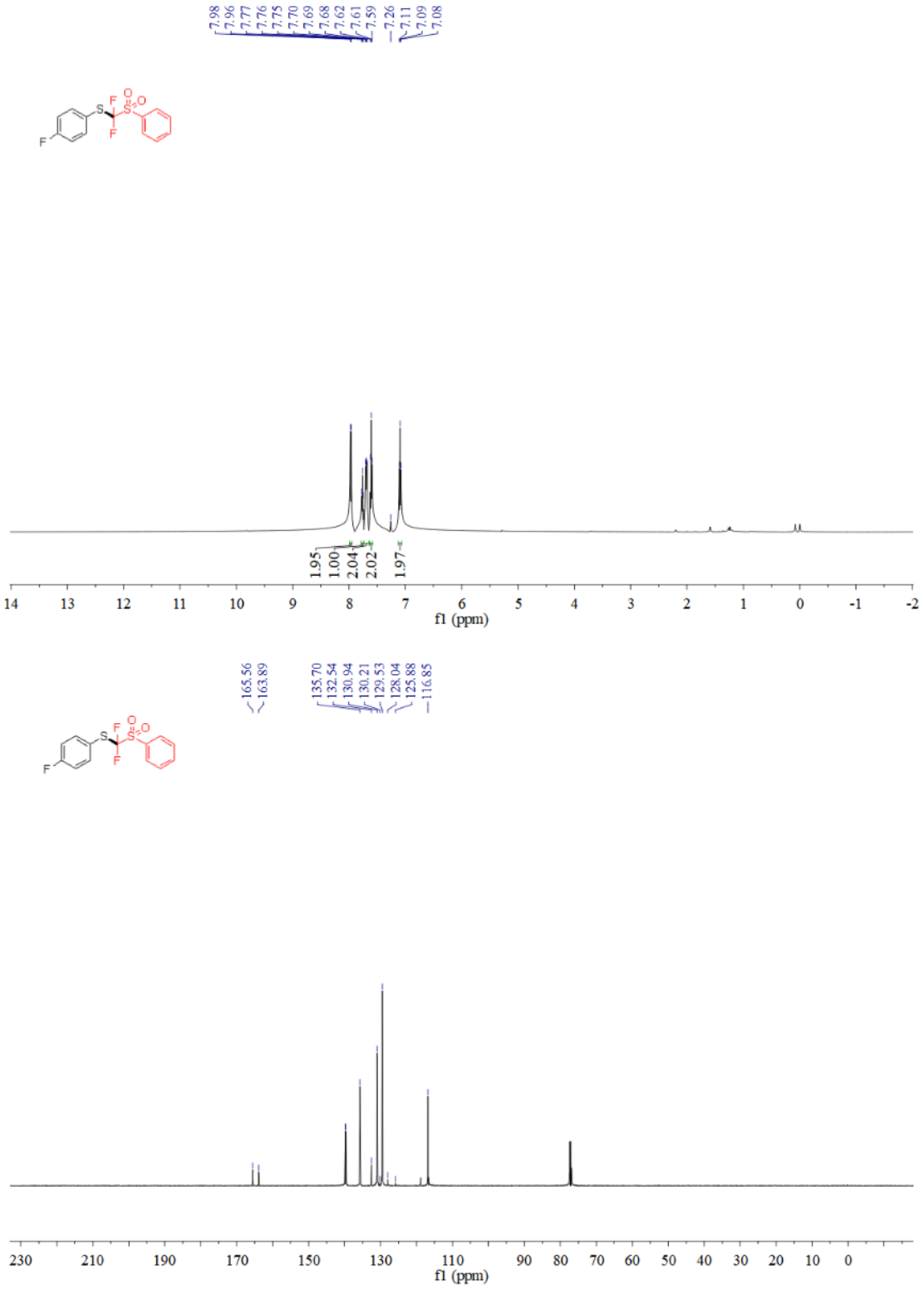
-80.13
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 -130 -150 -170 -190
f1 (ppm)

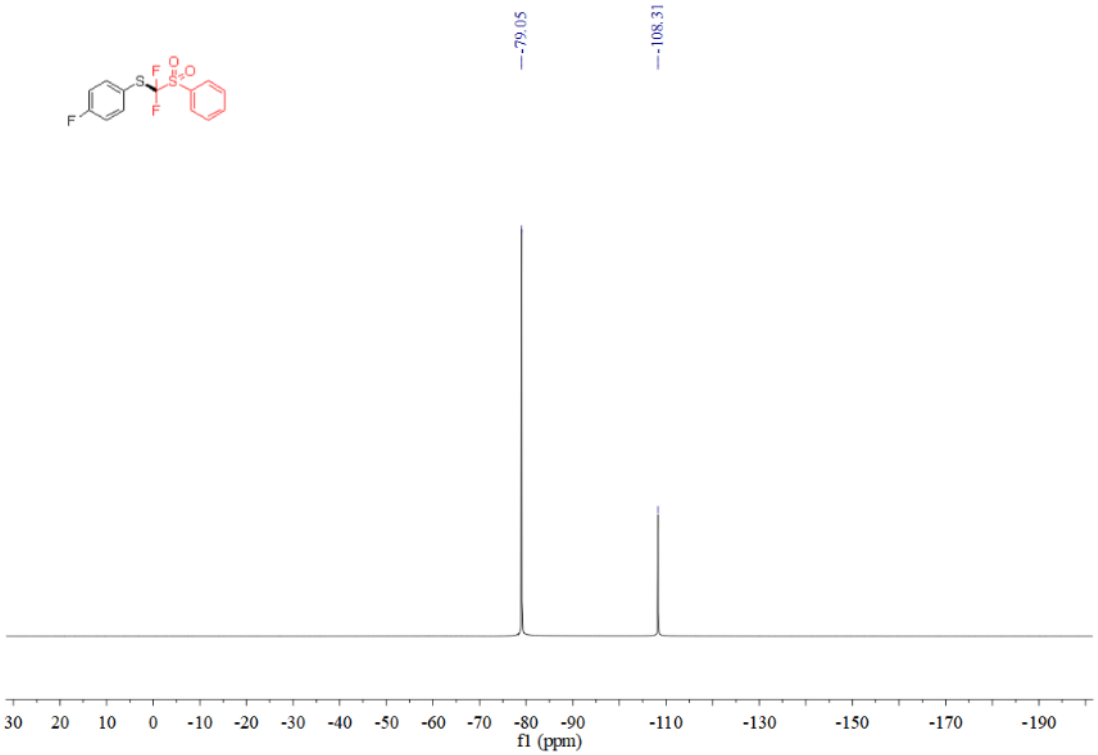
4-((difluoro(phenylsulfonyl)methyl)thio)benzonitrile (3p)



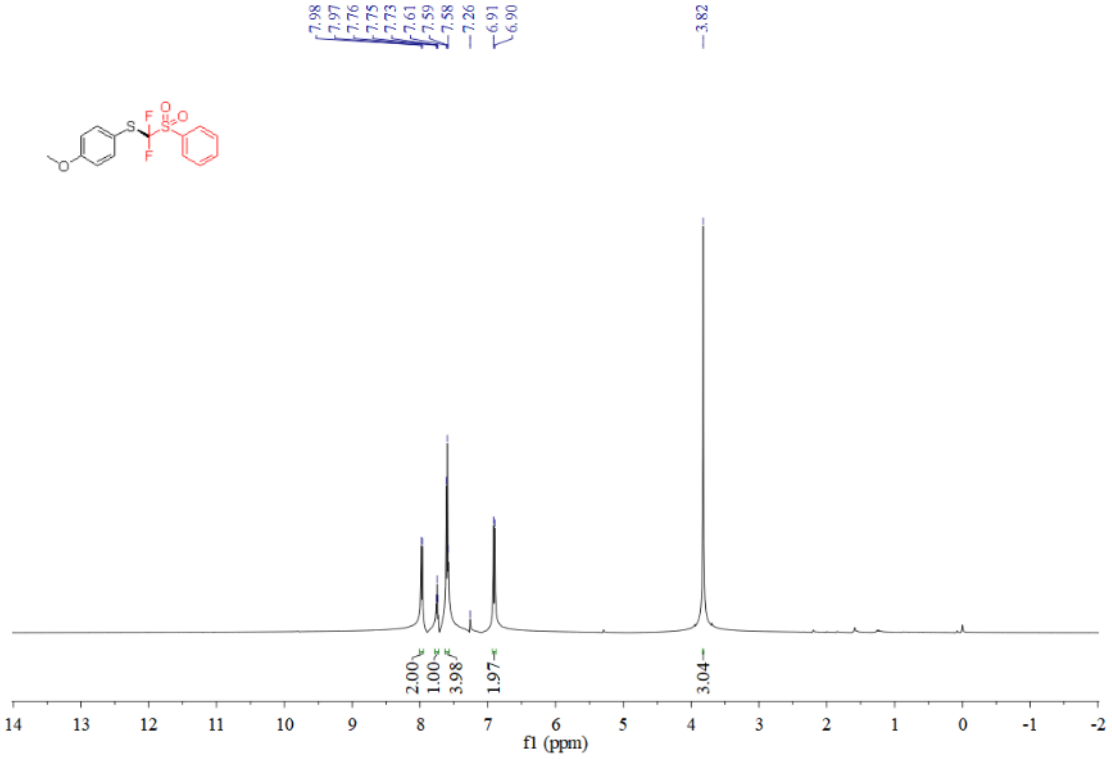

-78.11
NC
S
F
F
O
S
O
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-110
-130
-150
-170
-190
f1 (ppm)

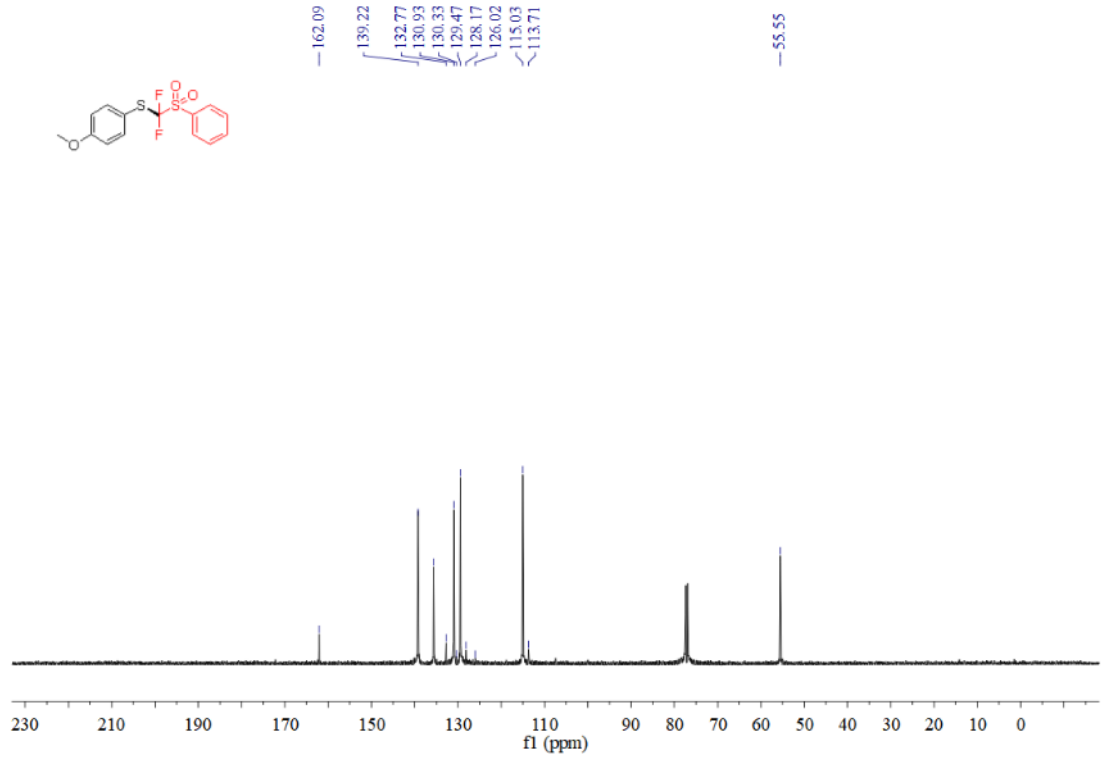
(difluoro(phenylsulfonyl)methyl)(4-fluorophenyl)sulfane (3q)

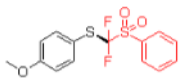



-79.05
-108.31
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 -130 -150 -170 -190
f1 (ppm)

(difluoro(phenylsulfonyl)methyl)(4-methoxyphenyl)sulfane (3r)

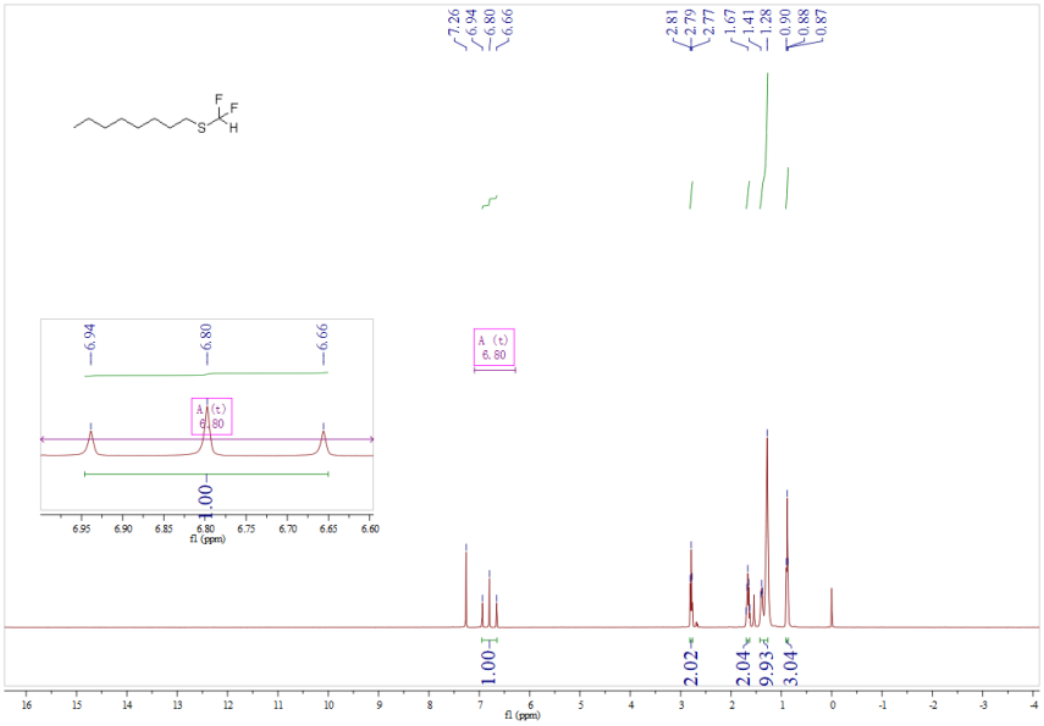


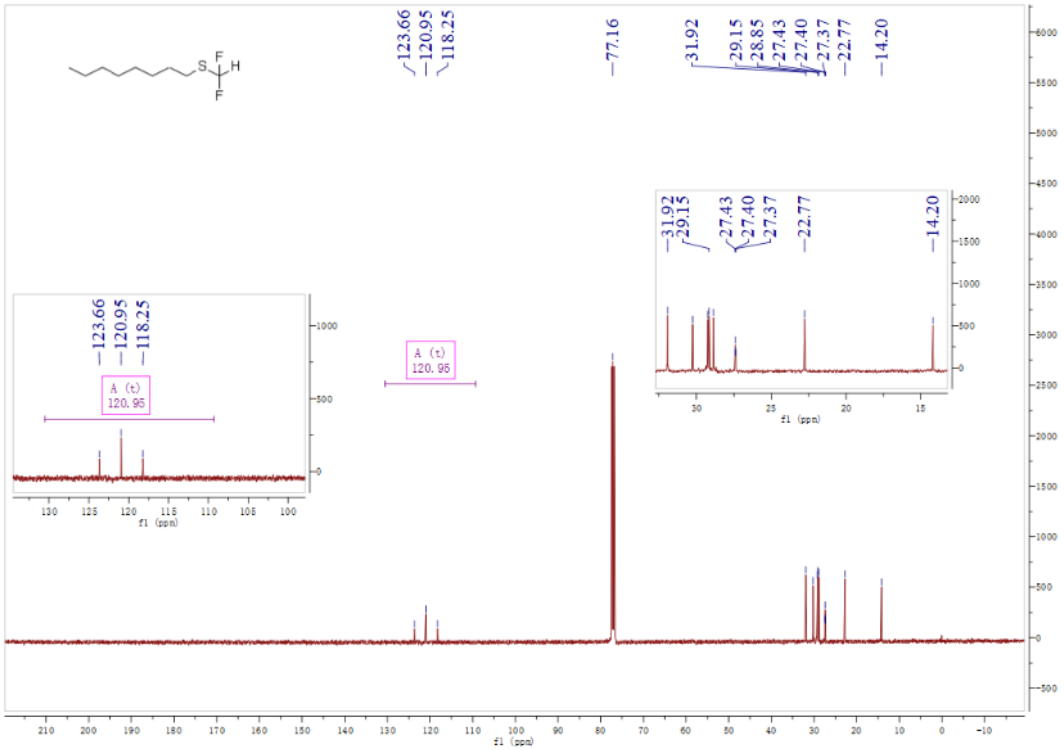


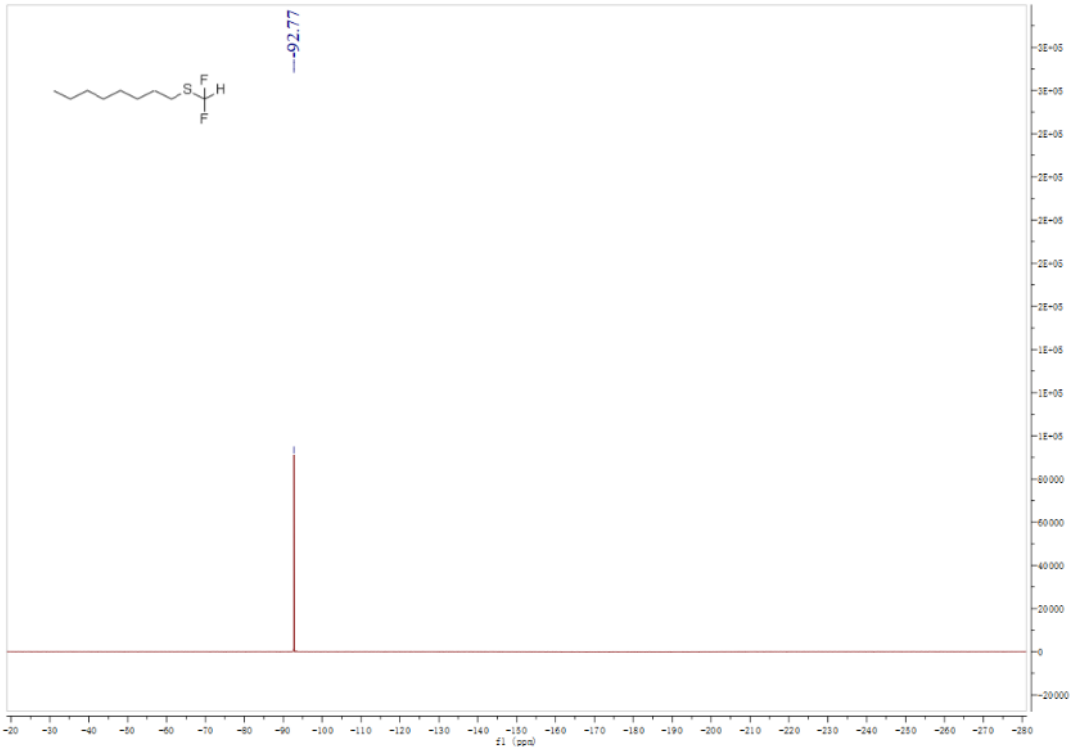

O
F
S
O
S
F
O

-79.37
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 -130 -150 -170 -190
f1 (ppm)

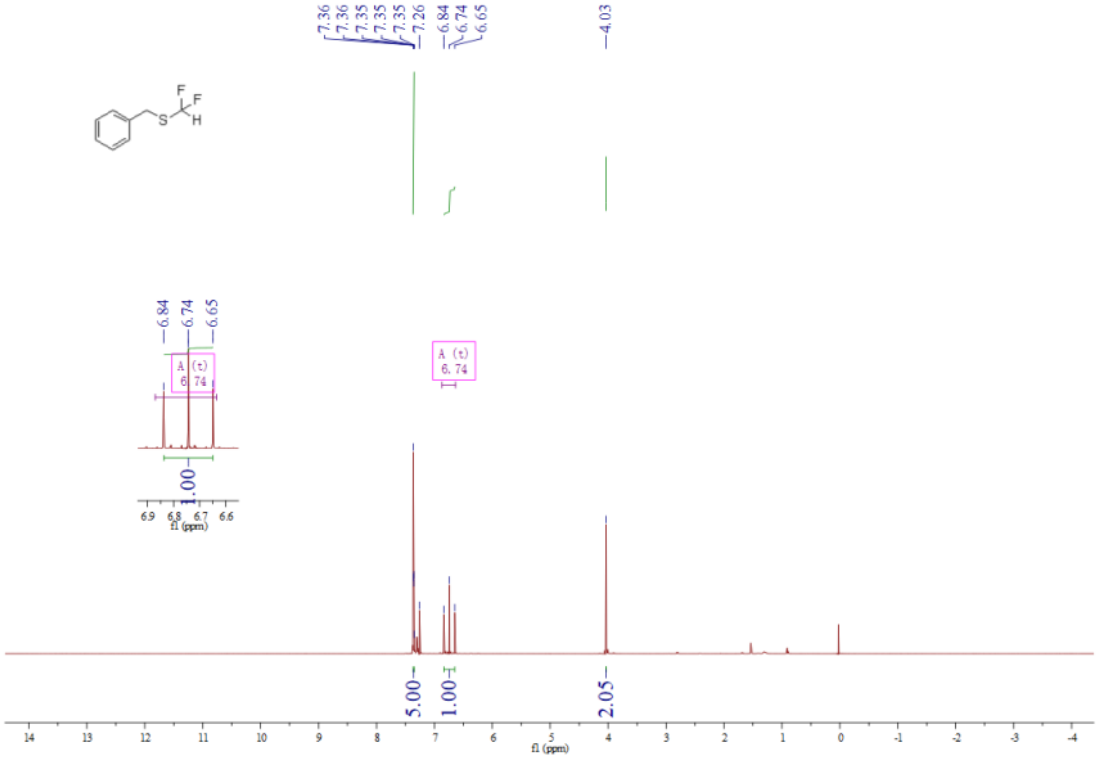
(difluoromethyl)(octyl)sulfane **(4a)**

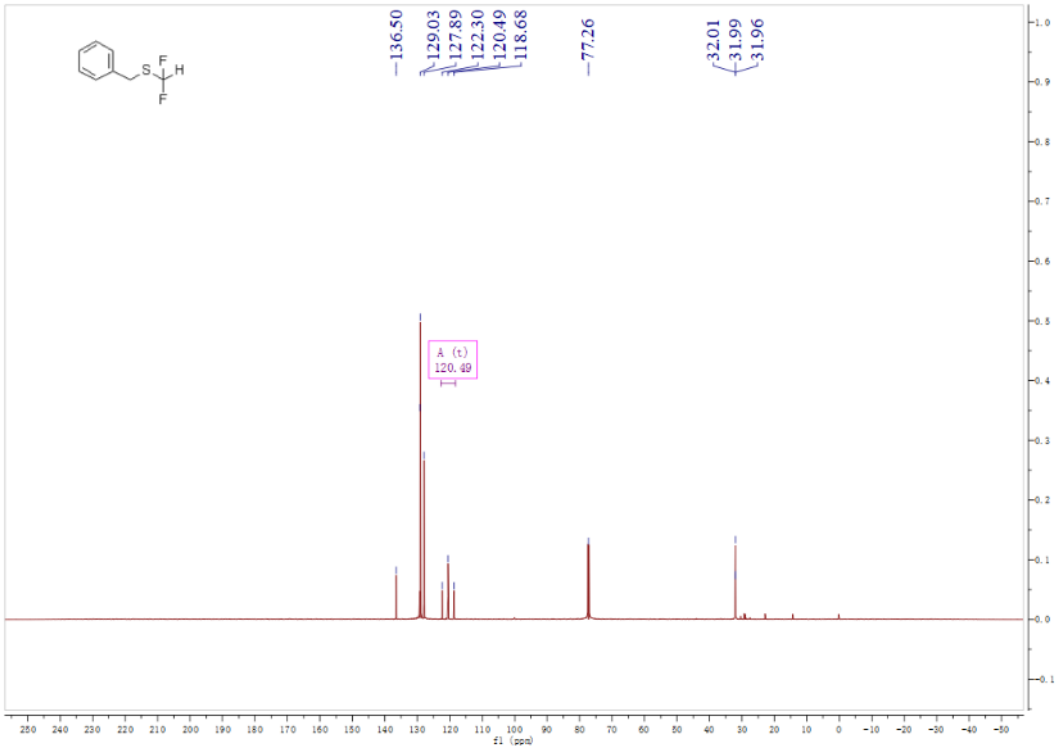


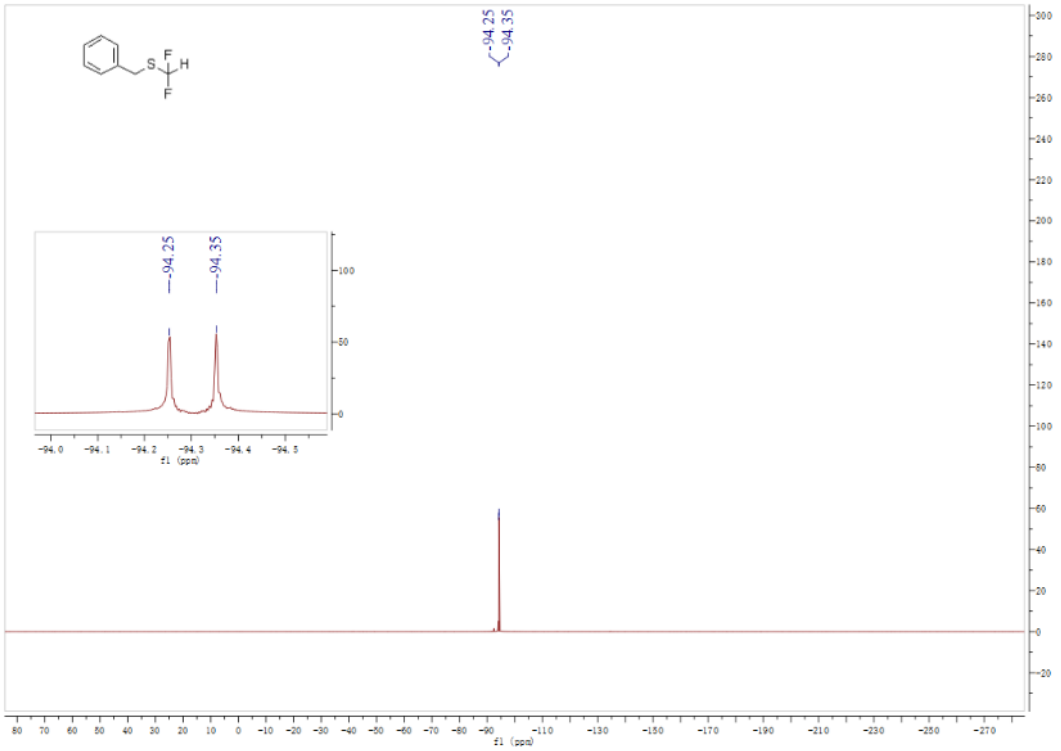



-92.77
S
F
H
F
3E+05
3E+05
2E+05
2E+05
2E+05
2E+05
2E+05
2E+05
1E+05
1E+05
1E+05
80000
60000
40000
20000
0
-20000
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
-240
-250
-260
-270
-280
f1 (ppm)

benzyl(difluoromethyl)sulfane (**4b**)






-94.25
-94.35
S
F
H
F
-94.25
-94.35
f1 (ppm)
f1 (ppm)