Supplementary Information

Metal- and Photosensitizer-Free Hydrodifluoromethylation of Unactivated Alkenes via Acetamide-Activated Difluoromethyl Aryl Sulfones

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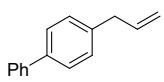
1. Supplementary Methods

All experiments were monitored by analytical thin-layer chromatography (TLC). TLC was performed on pre-coated plates. After elution, the plate was visualized under UV illumination at 254 nm for UV active material. Columns were packed as a slurry of silica gel in petroleum ether (PE) and equilibrated solution using the appropriate solvent system. All reagents were commercially available unless otherwise noted. All reactions were carried out under a nitrogen atmosphere in dried glassware. Air and moisture-sensitive liquids and solutions were transferred via a syringe. All solvents were dried and distilled by standard procedures. Solutions were concentrated under reduced pressure by rotary evaporation. Chromatographic purification of products was accomplished on silica gel Si 60® (300-400 mesh). Nuclear magnetic resonance spectra were acquired on a Bruker AMX 400 (400 MHz, 101 MHz and 377 MHz for ^{1}H, ^{13}C and ^{19}F respectively) and Bruker AMX 600 (600 MHz, and 151 MHz for ^{1}H, and ^{13}C respectively). All ^{1}H NMR spectra are reported in parts per million (ppm) downfield of TMS and were measured relative to the signals at 7.26 ppm ($CDCl_3$) or 2.50 ppm (DMSO). All ^{13}C NMR spectra were reported in ppm relative to $CDCl_3$ (77.16 ppm) or DMSO (35.92 ppm) with ^{1}H - decoupling. Data for ^{1}H-NMR and ^{19}F-NMR are reported as follows: chemical shift (δ in ppm), multiplicity (s = singlet; brs = broad singlet; vbs = vary broad singlet; d = doublet; t= triplet; q = quartet; quint = quintet; sext = sextet; m = multiplet), coupling constant (Hz), integration. Data for ^{13}C-NMR are reported in terms of chemical shift (δ in ppm), multiplicity, coupling constant (Hz). Melting points were measured on a WRS-1A digital. The light source used for the photocatalyzed experiments was a 40 W Blue LED (Kessil PR 160L-440 nm). It's about 2 cm from the light source to the irradiation vessel.

2. Supplementary Discussion

2.1 Substrate Preparations

2.1.1 Synthesis of olefins



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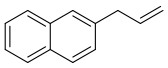

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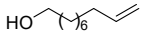

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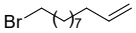

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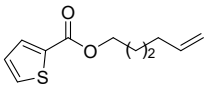

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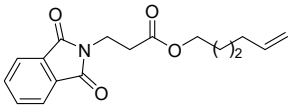

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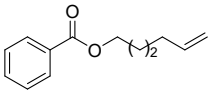

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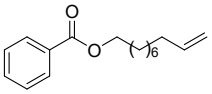

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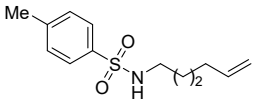

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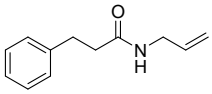

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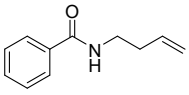

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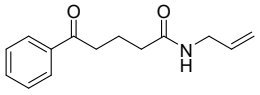

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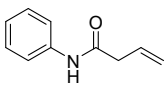

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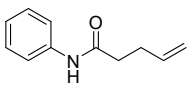

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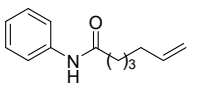

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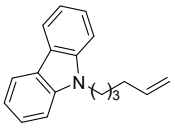

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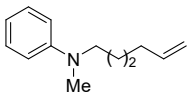

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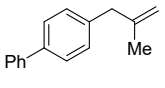

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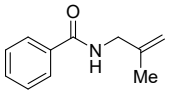

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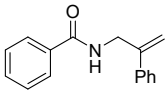

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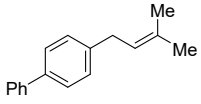

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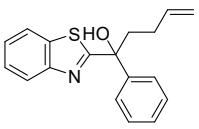

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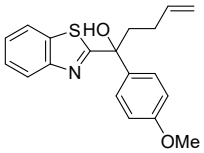

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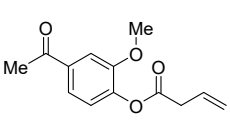

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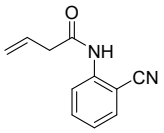

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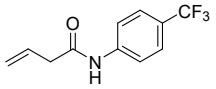

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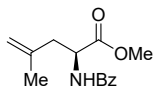

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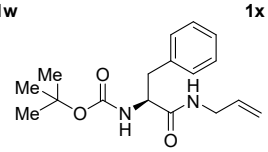

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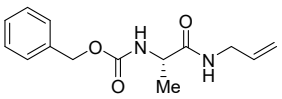

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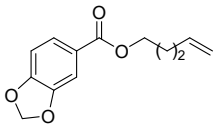

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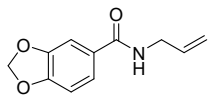

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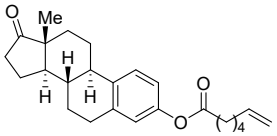

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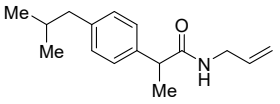

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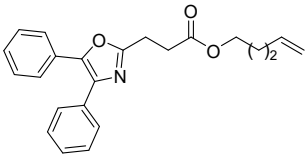

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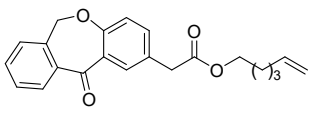

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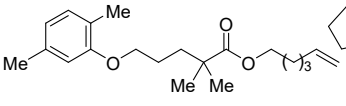

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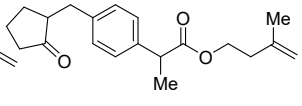

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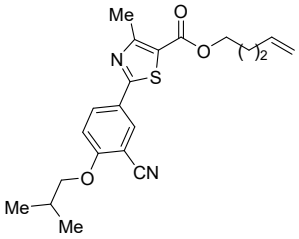

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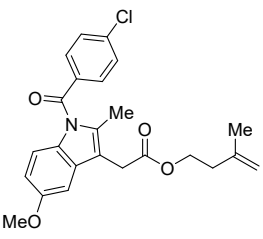

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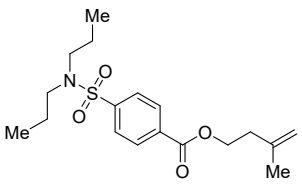

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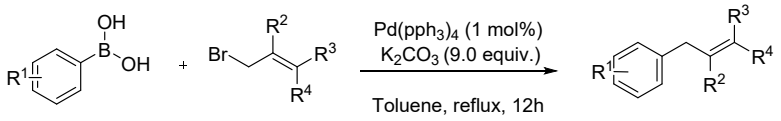
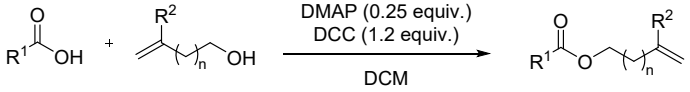
General procedure A



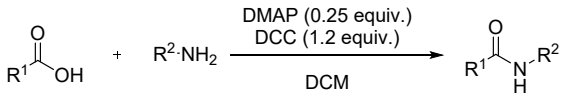
According to literature reports, alkenyl bromide (1.0 equiv.), $Pd(PPh_3)_4$ (1 mol%), K_2CO_3 (9.0 equiv.), arylboronic acid (1.25 equiv.) and dry toluene (30 mL) were placed in a two-necked round-bottom flask under nitrogen. The reaction mixture was heated at reflux for 12 h, monitoring by GC. Then hydrogen peroxide (10 mL) was added, the mixture was stirred at room temperature for 30 min and the toluene layer was separated. The aqueous layer was extracted three times with diethyl ether. The combined organic extracts were washed with brine and dried with $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by column chromatography on silica gel to give desired product.

General procedure B



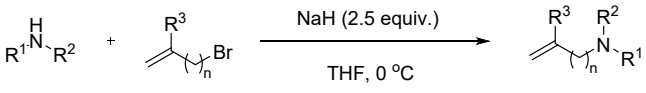
A solution of enol (1.0 equiv.) in DCM (10 mL) was slowly added via cannula to a solution of dicyclohexylcarbodiimide (DCC) (1.2 equiv.), 4-dimethylaminopyridine (DMAP) (0.25 equiv.) and carboxylic acid (1.05 equiv.) in DCM (100 mL) at room temperature. After stirring for 12 h at the same temperature, the reaction mixture was filtrated, and the filtrate was concentrated. The residue was subsequently purified by silica gel flash chromatography to provide compounds.

General procedure C



A solution of the corresponding amine (1.0 equiv.) in DCM (10 mL) was slowly added via cannula to a solution of dicyclohexylcarbodiimide (DCC) (1.2 equiv.), 4-dimethylaminopyridine (DMAP) (0.25 equiv.) and carboxylic acid (1.05 equiv.) in DCM (100 mL) at room temperature. After stirring for 12 h at the same temperature, the reaction mixture was filtrated, and the filtrate was concentrated. The residue was subsequently purified by silica gel flash chromatography to provide compounds.

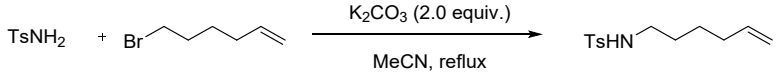
General procedure D



To an oven-dried 100 mL double-neck round bottom flask was added NaH (2.5 equiv.) and dry THF (0.25 M) under N_2 atmosphere. The mixture was further cooled to 0 °C and then the corresponding amine (1.0 equiv.)

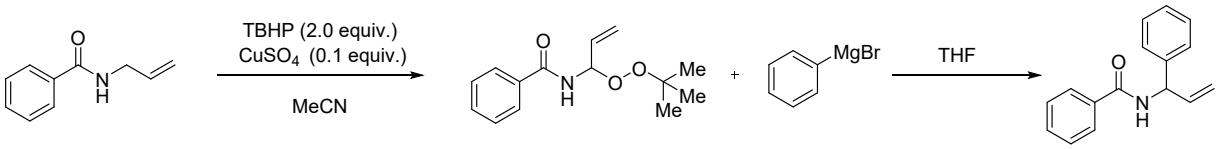
was added to this solution at 0 °C. The mixture was stirred for 30 min at 0 °C, and subsequently, respective alkenyl bromide (1.5 equiv.) was added. After the addition was complete, the solution was kept stirring by gradually increasing to room temperature and was stirred for 12 h. After the reaction completion, the mixture was extracted with EtOAc and dried before purified on a silica column to afford desire compound.

General procedure E



To a solution of 6-bromohex-1-ene (1.0 equiv.) in MeCN (0.5 M) were added K_2CO_3 (2.0 equiv.) and $TsNH_2$ (2.0 equiv.), and the reaction was heated to reflux. After 5 h, the reaction mixture was filtrated through Celite® and evaporated under vacuum to afford **1t** as a colorless oil after purification on silica gel.

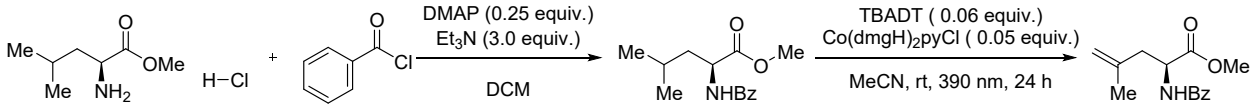
General procedure F



N-Allylbenzamide (1.0 equiv.), TBHP (70 % in H_2O, 2.0 equiv.) and $CuSO_4$ (0.1 equiv.) was dissolved in CH_3CN (20 mL) and the resultant solution was stirred for 4 h at same temperature. The reaction was monitored by TLC analysis until the starting material was consumed. After the reaction was extracted with EtOAc, dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum to get crude. The crude was purified by silica gel column chromatography using EtOAc: hexane as eluents to afford corresponding product *N*-(tert-Butylperoxy(phenyl)methyl)benzamide.

N-(tert-Butylperoxy(phenyl)methyl)benzamide (1.0 equiv.) was suspended in 10mL anhydrous THF under N_2, then Phenyl Grignard reagent (3.0 equiv.) was added at room temperature, and the mixture was stirred for 15 minutes until complete consumption of starting material as monitored by TLC. After the reaction was finished, the mixture was quenched with saturate ammonia chloride solution, then extracted with EtOAc, dried over anhydrous Na_2SO_4, and evaporated in vacuum. The residue was purified by flash column chromatography on silica gel to give the product.

General procedure G

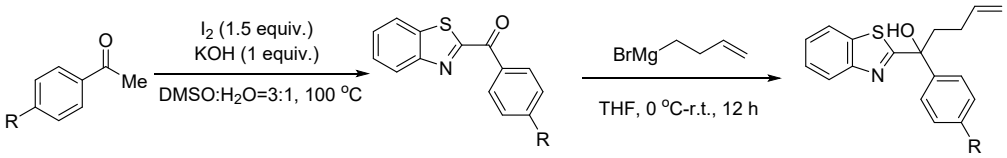


To a suspension of leucine methyl ester hydrochloride (1.0 equiv.) in DCM (55 mL) at room temperature was added triethylamine (Et_3N, 3.0 equiv.), 4-dimethylaminopyridine (DMAP, 0.25 equiv.) and benzoyl chloride (BzCl, 1.1 equiv.). The reaction mixture was stirred vigorously at room temperature overnight. Upon

completion, the reaction mixture was transferred to a separatory funnel. The organic layer was washed with sat. aqueous $NaHCO_3$ (2×20 mL), aqueous NH_4Cl (2×20 mL), water (20 mL), and brine (20 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The resultant crude residue was purified by flash column chromatography to give Bz-Leu-OMe as a white solid.

Into each of two 20×150 mm threaded borosilicate glass culture tubes charged with a PTFE-coated magnetic stir bar, amino acid (1.0 equiv.), TBADT (0.06 equiv.), $Co(dmgH)_2pyCl$ (0.05 equiv.) were subsequently added. The culture tubes were transferred into a nitrogen-filled purge box. Dry and degassed MeCN ($C_{amino\ acid}$ = 0.1 M) was added. The culture tubes were then capped with a polypropylene screw cap with a PTFE-faced silicone septum and removed from the purge box. The two culture tubes were placed 5 cm from 2 × UV LED Kessil lamps (390 nm) and stirred at 1000 rpm with cooling fans and a water bath. After 24 hours, the two crude reaction mixtures were combined and concentrated directly. The crude residue was purified by column chromatography to give the mixture of product and substrate. The isolated mixture was then purified with a prep-HPLC with acetonitrile and water as elutes to give the desired dehydrogenated product.

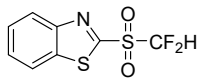
General procedure H



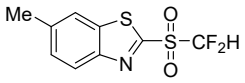
A mixture of acetophenone (1.0 equiv.), benzothiazole (1.5 equiv.), I_2 (1.5 equiv.), and KOH (1.0 equiv.) in solvent 40.0 mL (DMSO/H_2O = 3:1) was stirred at 100 °C (oil bath). After the disappearance of the reactant (monitored by TLC), 250 mL of water was added to the mixture, which was then extracted with ethyl acetate 3 times (3×100 mL). The extract was washed with $Na_2S_2O_3$ solution, dried over anhydrous Na_2SO_4, and evaporated. The residue was purified by column chromatography on silica gel and eluted with ethyl acetate/petroleum ether (1/50) to afford yellow solid in 78% yield.

To an oven-dried 100 mL double-neck round bottom flask, vinyl magnesium bromide (3.0 equiv.) was added dropwise to a solution of ketone (1.0 equiv.) in dry THF (0.2 M) under N_2 atmosphere at 0 °C (ice water bath). The resulting mixture was warmed gradually to room temperature and stirred for 6-8 h. After completion of the reaction, the reaction mixture was quenched with a saturated NH_4Cl solution, extracted with ethyl acetate, and dried before being purified on a silica column using an eluent of ethyl acetate/petroleum ether (1/20) to afford the desired product.

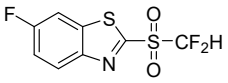
2.1.2 Synthesis of Difluoromethylsulfone



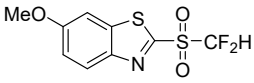
2a



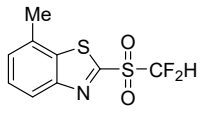
2b



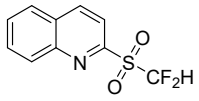
2c



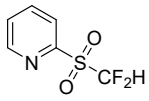
2d



2e

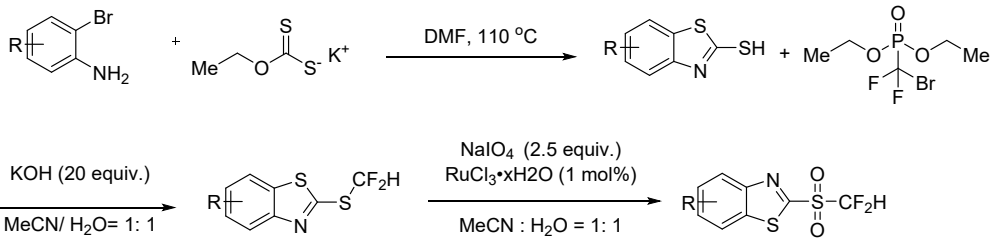


2f



2g

General Procedure I



A 25 mL Wattecs reaction tube was charged with 2-Bromoaniline (1.0 equiv.), potassium O-ethyl dithiocarbonate (3.0 equiv.), CuCl (0.1 equiv.), and DMF (30 mL). The reaction vessel was flushed with argon three times and sealed. Then the mixture was stirred electromagnetically in an oil bath at 110 °C for 12 h. The reaction process was monitored by TLC on silica gel. After the reaction was completed, the reaction mixture was cooled to room temperature, and then HCl (3 mol/L) was added and stirred for another 30 min. The reaction mixture solution was extracted by ethyl acetate (3×50 mL). Subsequently, the combined organic solutions were dried by anhydrous sodium sulfate and the target product was purified by chromatography on a silica gel column (eluent: ether/ethyl acetate) to give the corresponding pure product. The spectral data of the product were in agreement with those reported in the literature

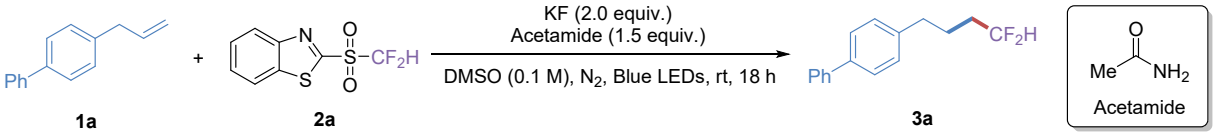
The starting material (1.0 equiv.) was added to a bottom holding 200 mL of a 1:1 mixture of acetonitrile/water and KOH (20.0 equiv.), which was cooled using an ice bath. The mixture was vigorously mixed for 30 min and then phosphonate (1.5 equiv.) was added to the mixture in one portion, and mixing and cooling was maintained for an additional 15-60 min, followed by~30 min-2.5 h at r.t.. The reaction mixture was then diluted with ether and the organic phase separated. The water phase was further washed with ether. The combined organic phase was dried over anhydrous Na_2SO_4 and the solvent evaporated to provide a crude product which was purified using column chromatography on silica gel.

To a solution of the above-obtained crude product in MeCN (200 mL)/H_2O (200 mL) was added $NaIO_4$ (2.5 equiv.) and $RuCl_3 \cdot xH_2O$ (10 mg). The reaction mixture was stirred at room temperature for 12 hours (the addition of some more water is necessary if solid precipitation makes it difficult to stir the reaction mixture).

Upon completion of the reaction as determined by ^{19}F NMR spectroscopy analysis, the reaction mixture was diluted with EtOAc (20 mL) and filtered to remove the solid. The filtrate was extracted with EtOAc (40 mL×3) and the combined organic phases were washed sequentially with saturated $NaHCO_3$ aqueous solution (10 mL), saturated $Na_2S_2O_3$ aqueous solution (10 mL) and water (10 mL). The so-obtained organic solution was dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was purified by flash column chromatography on silica gel with petroleum ether/EtOAc as the eluent to give **2** as white solid. The spectral data of the product were in agreement with those reported in the literature.

2.2 Optimization of Reaction Conditions

General Procedure 1 for Difluoromethylation



An oven-dried Schlenk tube containing a stirring bar was added alkene (**1a**, 0.2 mmol, 1.0 equiv.), 2-((difluoromethyl)sulfonyl)benzo[*d*]thiazole (**2a**, 0.4 mmol, 2.0 equiv.), Acetamide (0.3 mmol, 1.5 equiv.), KF (0.4 mmol, 2 equiv.). The tube was connected to a vacuum line where it was evacuated and back-filled with N_2 for three times. Then H_2O (1 mmol, 5.0 equiv.) and DMSO (2 mL) were added under N_2 atmosphere. Finally, the reaction mixture in sealed tube was stirred at room temperature for 18 h under continuous light irradiation from 40 W blue LED (λ = 440 nm). The solvent was removed under reduced pressure and the residue was purified by column chromatography to afford the pure product **3a**.

Figure S1. Photograph of the photocatalytic reactor

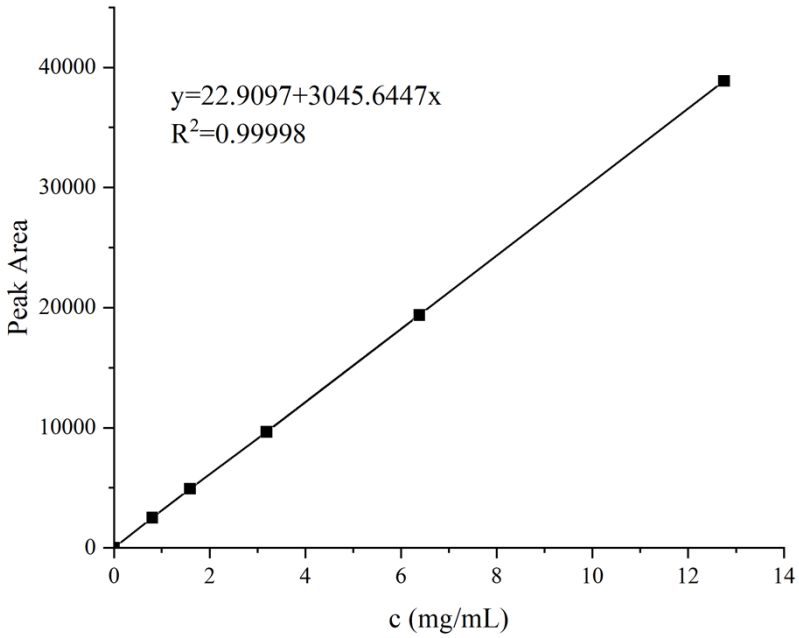
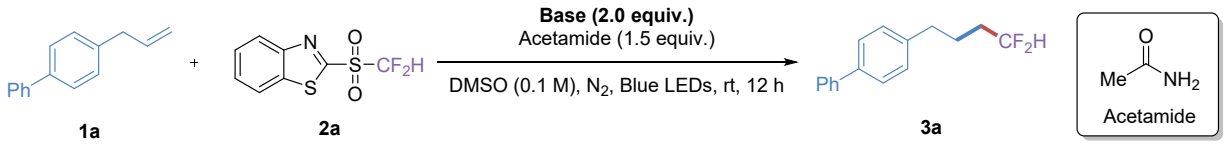


Figure S2. Gas-phase yield standard curve

Table S1. Screening of Bases

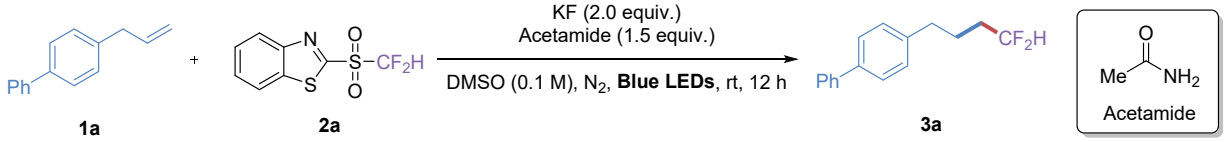


Entry	Deviation from standard conditions	Yield of **3a** [%]
1	Na_2CO_3	30
2	K_2CO_3	33
3	Cs_2CO_3	25
4	K_3PO_4	36
5	DMAP	15
6	DBU	5
7	**KF**	**42**
8	TMG	23
9	KOH	37
10	$KHCO_3$	34
11	K_2HPO_4	40
12	TBD	15

13	CsF	37

Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), Acetamide (0.3 mmol), base (0.4 mmol), DMSO (2 mL), blue LEDs (λ = 440 nm), rt, 12 h. Yields determined by GC analysis.

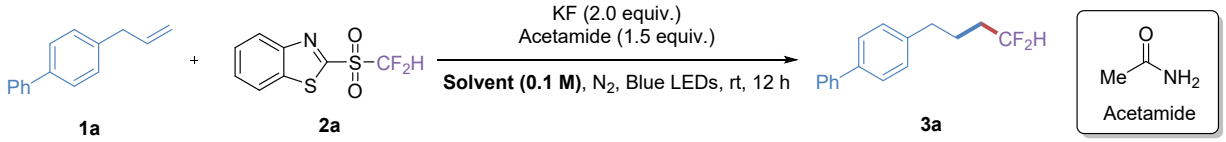
Table S2. Screening of Wavelengths



Entry	Deviation from standard conditions	Yield of **3a** [%]
1	Kessil 440 nm 40W	42
2	Kessil 390 nm 40W	26
3	Kessil 427 nm 40W	35
4	Kessil 456 nm 40W	30
5	Ring light 420-430 nm	38
6	Round light 420-430 nm	35
7	Round light 430-440 nm	0
8	Round light 465-470 nm	8

Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), Acetamide (0.3 mmol), KF (0.4 mmol), DMSO (2 mL), Blue LEDs (λ = x nm), rt, 12 h. Yields determined by GC analysis.

Table S3. Screening of Solvents

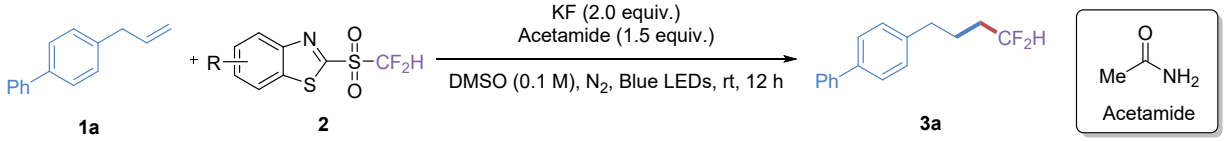


Entry	Deviation from standard conditions	Yield of **3a** [%]
1	DMF	23
2	MeCN	trace
3	1,4-Dioxane	trace
4	DMSO	42
5	DMSO : H_2O = 9:1	29
6	Isopropyl alcohol	trace
7	Ethanol	trace
8	Acetone	9

9	MeCN : H_2O = 1:1	trace

Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), Acetamide (0.3 mmol), KF (0.4 mmol), Solvent (2 mL), Blue LEDs (λ = 440 nm), rt, 12 h. Yields determined by GC analysis.

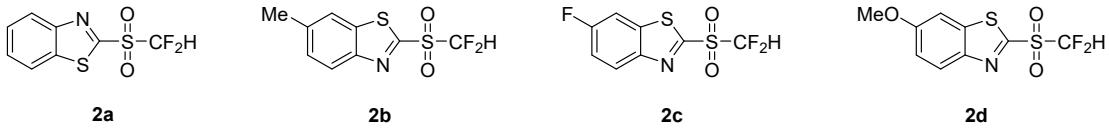
Table S4. Screening of 2



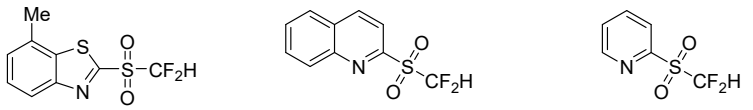
1a 2 3a

Entry	Deviation from standard conditions	Yield of **3a** [%]
1	**2a**	42
2	**2b**	38
3	**2c**	18
4	**2d**	32
5	**2e**	30
6	**2f**	7
7	**2g**	18

Reaction conditions: 1a (0.2 mmol), 2 (0.3 mmol), Acetamide (0.3 mmol), KF (0.4 mmol), DMSO (2 mL), Blue LEDs (λ = 440 nm), rt, 12 h. Yields determined by GC analysis.

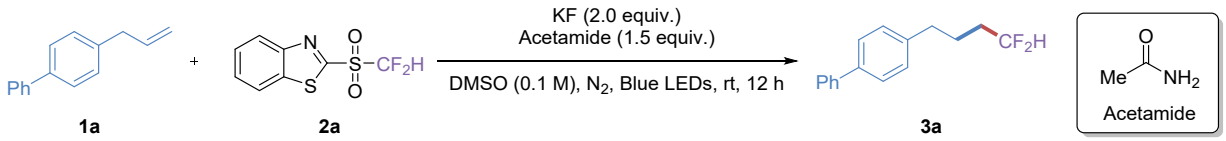


2a **2b** **2c** **2d**



2e **2f** **2g**

Table S5. Screening of equiv. of 2a



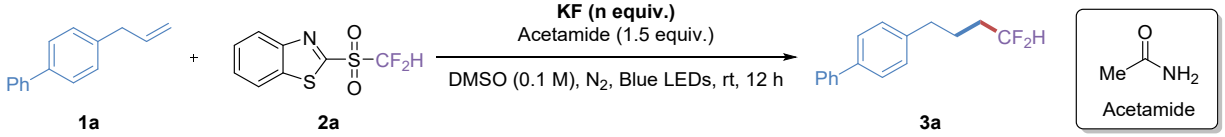
1a 2a 3a

Entry	Deviation from standard conditions	Yield of **3a** [%]
1	1.5	42
2	2	46
3	2.5	33

4	3	43

Reaction conditions: **1a** (0.2 mmol), **2a** (x mmol), Acetamide (0.3 mmol), KF (0.4 mmol), DMSO (2 mL), Blue LEDs (λ = 440 nm), rt, 12 h. Yields determined by GC analysis.

Table S6. Screening of equivalent of Base

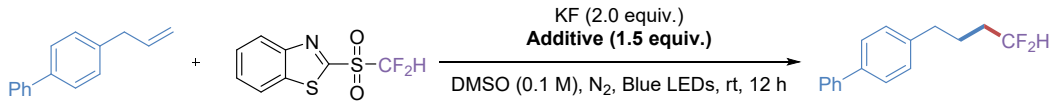


1a 2a 3a

Entry	Deviation from standard conditions	Yield of **3a** [%]
1	1.5	21
2	2	46
3	2.5	24
4	3	39
5	4	37

Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), Acetamide (0.3 mmol), KF (x mmol), DMSO (2 mL), Blue LEDs (λ = 440 nm), rt, 12 h. Yields determined by GC analysis.

Table S7. Screening of Additives



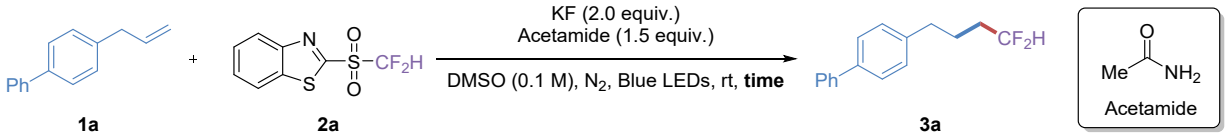
1a 2a 3a

Entry	Deviation from standard conditions	Yield of **3a** [%]
1	2-Chloro-*N*-methylacetamide	12
2	*N,N*-Dimethylbenzamide	43
3	2-Bromo-*N,N*-dimethylacetamide	4
4	Cyclohexanecarboxamide	21
5	*N*-Methylbenzamide	30
6	Acetamide	46
7	Benzanilide	24
8	*N*-Benzylbenzamide	36
9	Triethylamine	trace
10	Phenol	trace
11	Potassium ethylxanthate	trace

Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), Additive (0.3 mmol), KF (0.4 mmol), DMSO (2 mL), Blue

LEDs (λ = 440 nm), rt, 12 h. Yields determined by GC analysis.

Table S8. Screening of Times

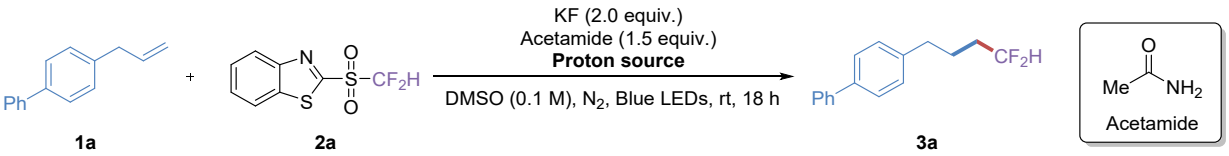


1a 2a 3a

Entry	Deviation from standard conditions	Yield of **3a** [%]
1	12	46
2	18	61

Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), Acetamide (0.3 mmol), KF (0.4 mmol), DMSO (2 mL), Blue LEDs (λ = 440 nm), rt. Yields determined by GC analysis.

Table S9. Screening of Proton source

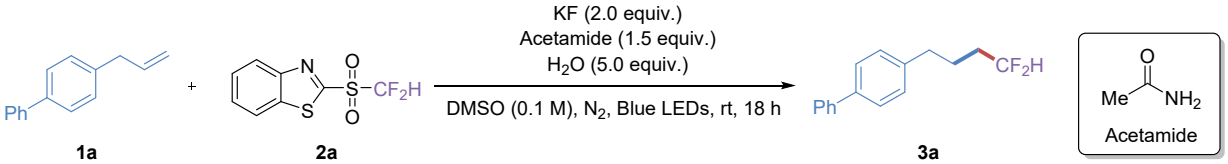


1a 2a 3a

Entry	Deviation from standard conditions	Yield of **3a** [%]
1	none	61
2	+ 5.0 equiv. H_2O	67
3	+ 5.0 equiv. MeOH	35
4	+ 5.0 equiv. EtOH	34
5	+ 5.0 equiv. 2,2,2-Trifluoroethanol	31
6	+ 5.0 equiv. 1,1,1,3,3,3-Hexafluoro-2-propanol	10

Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), Acetamide (0.3 mmol), KF (0.4 mmol), DMSO (2 mL), Blue LEDs (λ = 440 nm), rt, 18 h. Yields determined by GC analysis.

Table S10. Control Experiments



1a 2a 3a

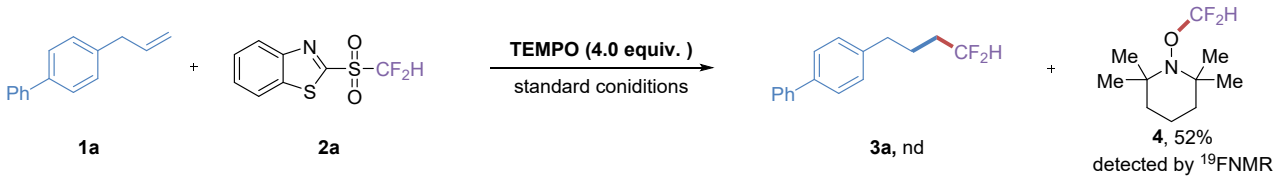
Entry	Deviation from standard conditions	Yield of **3a** [%]
1	None	67/ 75[a]
2	No Base	N. D.
3	No Additive	N. D.

4	Under Air	N. D.
5	No lights	N. D.

Standard condition: **1a** (0.2 mmol), **2a** (0.4 mmol), Acetamide (0.3 mmol), KF (0.4 mmol), DMSO (2 mL), Blue LEDs (λ = 440 nm), rt, 18 h. Yields determined by GC analysis. [a] Yield after isolations .

3. Mechanistic Studies

3.1 Radical Inhibition Experiments



An oven-dried Schlenk tube containing a stirring bar was added 4-allyl-1,1'-biphenyl (**1a**, 0.4 mmol, 1.0 equiv.), 2-((difluoromethyl)sulfonyl)benzo[d]thiazole (**2a**, 0.8 mmol, 2.0 equiv.), Acetamide (0.6 mmol, 1.5 equiv.), KF (0.8 mmol, 2.0 equiv.), TEMPO (1.6 mmol,4.0 equiv.). The tube was connected to a vacuum line where it was evacuated and back-filled with N_2 for three times. Then H_2O (2 mmol, 5.0 equiv.) and DMSO (4 mL) were added under N_2 atmosphere. Finally, the reaction mixture in sealed tube was stirred at room temperature for 18 h under continuous light irradiation from 40 W blue LED (λ = 440 nm).

To explore the reaction mechanism of this reaction, control experiments were conducted by adding the radical scavengers such as 2,2,6,6-tetramethylpiperidinooxy (TEMPO) to the reaction of **1a** and **2a** under standard conditions. The result showed that the reaction was completely inhibited by TEMPO suggest that the reaction might proceeded via a radical process. The compounds 4 was captured by NMR (**^{19}F NMR** (377 MHz, $CDCl_3$) δ -79.82) and the result same to previous report, which indicated that difluoromethyl radicals were generated in this reaction[1].

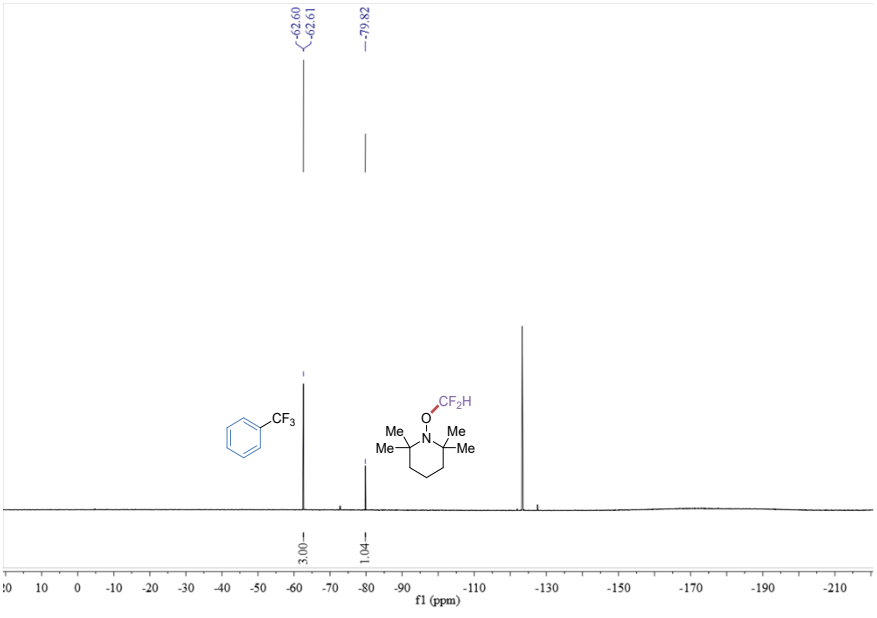
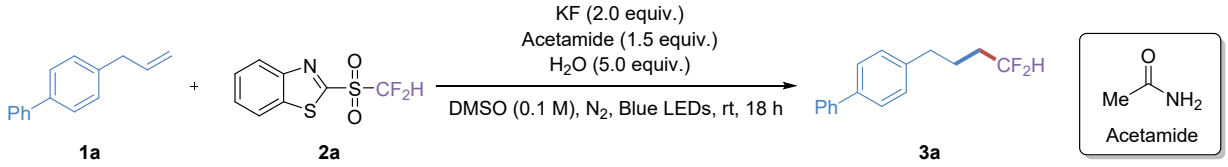


Figure S3. ^{19}F NMR spectrum of the radical trapping reaction

3.2 Light-On-Off Experiments



Parallel reactions were performed according to the **General Procedure 1**. The resulting residue was purified by silica gel column chromatography to afford the desired product **3a**. The white area indicates the light irradiation, while the grey area indicates time in the dark. The results of light on-off experiments indicated that the reaction proceeded only under the irradiation of light.

Figure S4. Light-on-off experiment of **3a**

3.3 UV/Vis Absorption Experiments

UV/vis absorption spectra between **2a** (0.1 M) and Acetamide (0.1 M) in DMSO were recorded in 1cm path quartz cuvettes using a X-6 Touch Screen UV-Vis Spectrophotometer. UV/vis absorption spectra between **2a** (0.1 M), Acetamide (0.1 M) and KF (0.1 M) in DMSO were recorded in 1cm path quartz cuvettes using a X-6 Touch Screen UV-Vis Spectrophotometer. When testing the UV/vis absorption of **2a**, Acetamide, KF and their mixture in DMSO, the mixture showed a bathochromic shift, which confirmed the existence of the electron donor-acceptor complex.

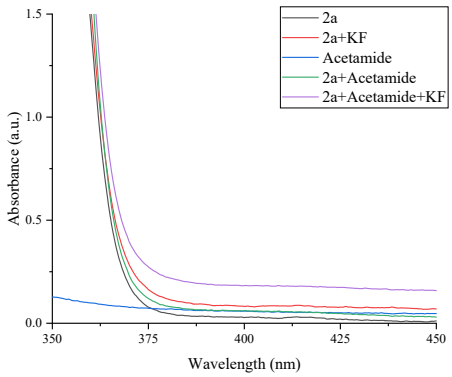


Figure S5. UV/vis absorption in DMSO

3.4 Stoichiometry of the EDA Complex in Solution

Using UV/vis spectroscopy, the absorbance values at 360 nm (corresponding to the EDA complex's absorption) were monitored and plotted as a function of molar fraction of the Acetamide. A parabolic curve with a maximum absorbance value at 50% molar fraction of Acetamide was obtained, indicating a 1:1 EDA complex between Acetamide and **2a**.

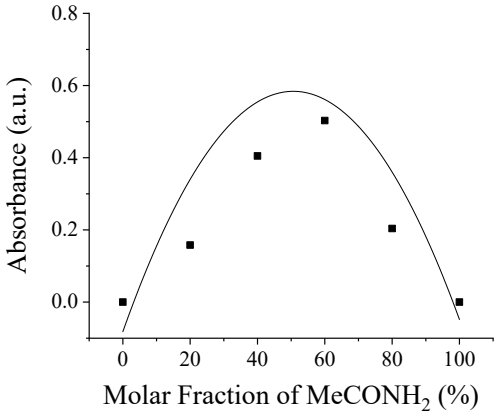


Figure S6. UV/vis absorption

3.5 ^{1}H NMR and ^{19}F NMR experiments

^{1}H NMR and ^{19}F NMR experiments were performed by the preparation of DMSO-d_6 solutions and revealed distinct chemical shift changes upon mixing Acetamide, **2a** and KF (1:1:1) compared to the individual components

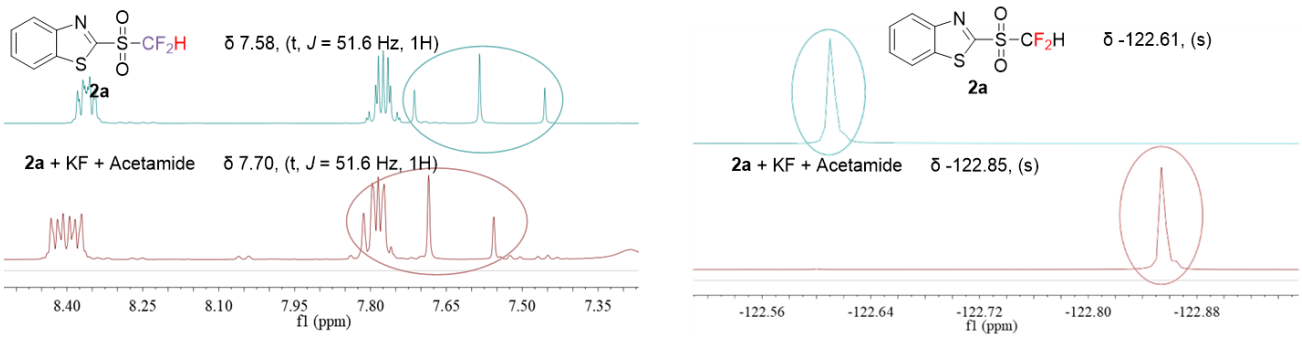
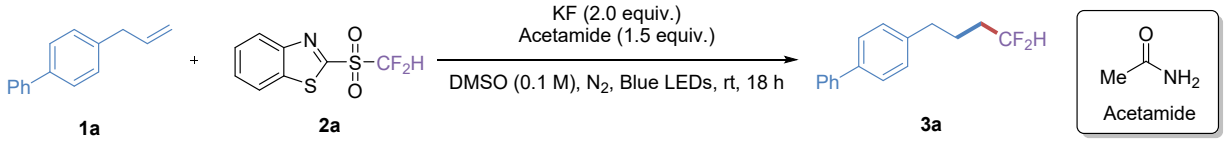


Figure S7. Evidence for the formation of EDA complex through ^{1}H NMR and ^{19}F NMR

3.6 Determination of Quantum Yield



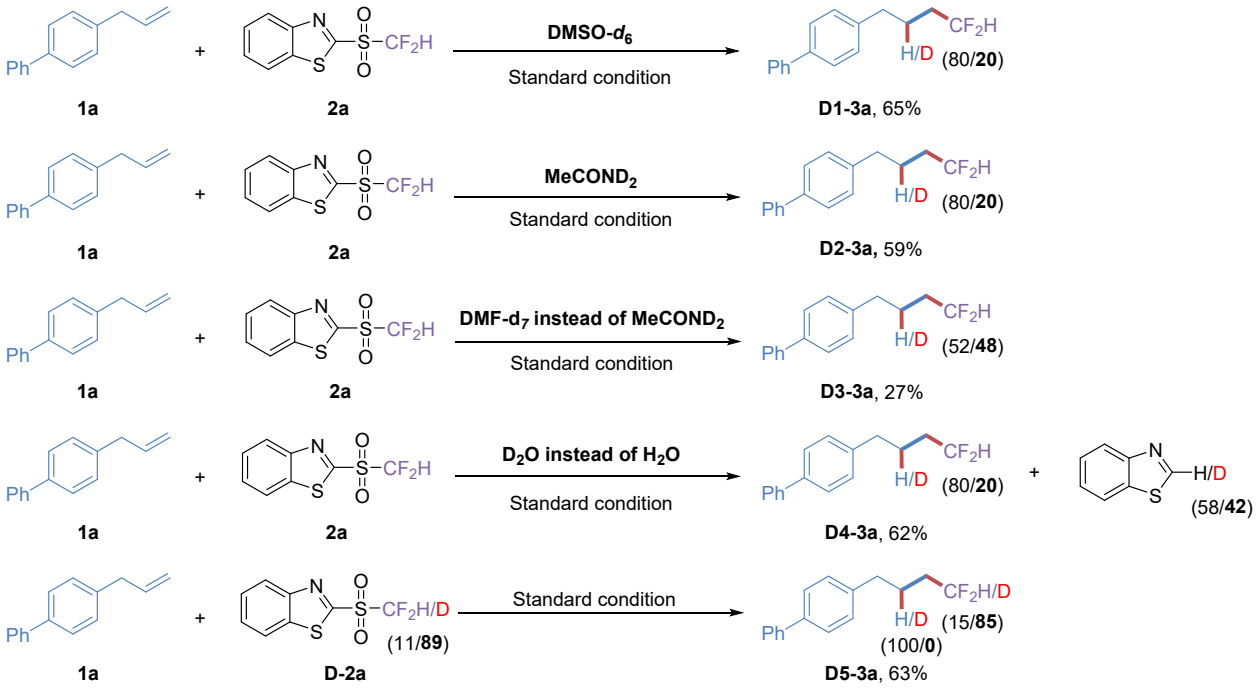
An oven-dried Schlenk tube containing a stirring bar was added 4-allyl-1,1'-biphenyl (**1a**, 0.2 mmol, 1.0 equiv.), 2-((difluoromethyl)sulfonyl)benzo[*d*]thiazole (**2a**, 0.4 mmol, 2.0 equiv.), Acetamide (0.3 mmol, 1.5 equiv.), KF (0.4 mmol, 2 equiv.), H_2O (1 mmol, 5.0 equiv.), DMSO (2 mL). The tube was sealed, the sample was irradiated (λ = 440 nm) for 7200 s. After irradiation, the residue was purified by column chromatography to calculate the yield.

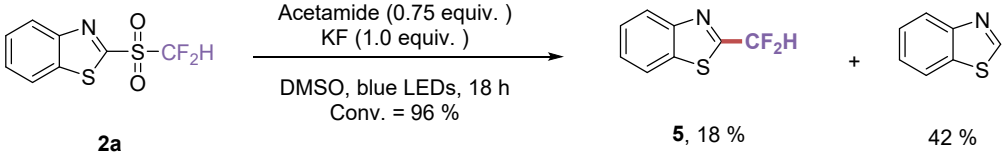
***Φ* = Mole number for product/Mole number for absorption of photons = 0.017**

$$\Phi = \frac{n_{3a}N_A/t}{fP\lambda/hc}$$

n_{3a}: the mole number of the product **3a**; t: reaction time (7200 s); N_A: 6.02×10^{23}/mol; f: $1\text{-}10^{-A}$ (440 nm, A = 0.2089); P: P = E*S (E: illumination intensity, E = 159 mW/cm^2; S: the area that irradiated S = 0.5 cm^2); λ: wavelength (λ = 4.40×10^{-7}m); h: planck constant (h = 6.626×10^{-34} J*s); c: velocity of light (c = 3×10^8 m/s). This result reveals that the radical chain process is not the main pathway.

3.7 Isotopic-labeling and control experiments

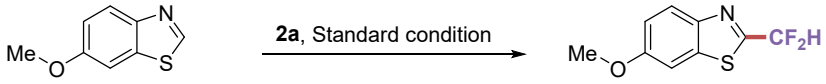




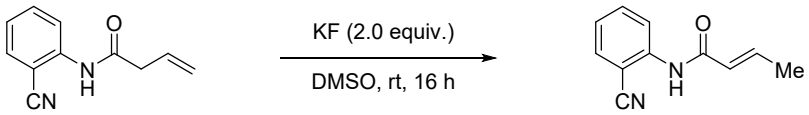
2a

5, 18 %

42 %

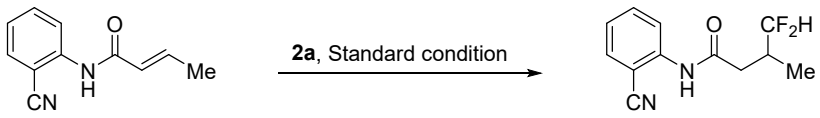


5b, 23%



1x

1xb, 85%

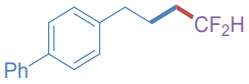


1xb

3x, 21%

4. Product Characterizations

4-(4,4-difluorobutyl)-1,1'-biphenyl (3a)



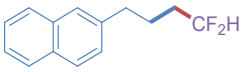
Colorless oil, 75%. Purified by flash chromatography on silica gel (hexane).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.56 (m, 2H), 7.55 – 7.49 (m, 2H), 7.43 (t, J = 7.6 Hz, 2H), 7.36 – 7.31 (m, 1H), 7.25 (d, J = 7.9 Hz, 2H), 5.99 – 5.64 (m, 1H), 2.72 (t, J = 7.2 Hz, 1H), 1.96 – 1.77 (m, 4H).

^{19}F NMR (377 MHz, $CDCl_3$) δ -114.54 (s).

The analytical data were in good agreement with the literature[2].

2-(4,4-difluorobutyl)naphthalene (3b)



Colorless oil, 39%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 100:1).

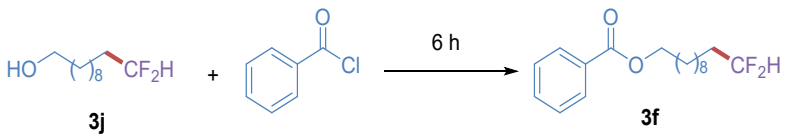
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.3 Hz, 1H), 7.91 (d, *J* = 7.7 Hz, 1H), 7.78 (d, *J* = 8.2 Hz, 1H), 7.58 – 7.50 (m, 2H), 7.45 (t, *J* = 15.2 Hz, 1H), 7.36 (d, *J* = 7.0 Hz, 1H), 5.87 (tt, J = 57.3, 4.1 Hz, 1H), 3.18 (t, *J* = 7.2 Hz, 2H), 2.03 – 1.93 (m, 4H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 137.5, 134.1, 131.9, 129.0, 127.1, 126.2, 126.1, 125.7, 125.6, 123.7, 117.4 (t, *J* = 239.0 Hz), 34.0 (t, *J* = 20.8 Hz), 32.40, 23.2 (t, *J* = 5.3 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -115.63 (d, *J* = 2.2 Hz).

HRMS (EI-TOF) m/z: [M] Calcd for $C_{14}H_{14}F_2$ 220.1064; Found 220.1063.

11,11-difluoroundecan-1-ol (3c)



Prepared according to standard conditions. Then benzoyl chloride and triethylamine are added and reacted at room temperature for 6 hours. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 100:1 to 50:1) as a colorless oil in 75% yield.

12-bromo-1,1-difluorododecane (3d)

Colorless oil, 70%. Purified by flash chromatography on silica gel (hexane).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.79 (tt, *J* = 57.0, 4.6 Hz, 1H), 3.40 (t, *J* = 6.9 Hz, 2H), 1.90 – 1.74 (m, 4H),

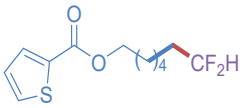
1.48 – 1.38 (m, 4H), 1.35 – 1.24 (m, 12H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 117.6 (t, *J* = 238.6 Hz), 34.2 (t, *J* = 20.5 Hz), 34.1, 33.0, 29.6, 29.5, 29.5, 29.5, 29.2, 28.9, 28.3, 22.2 (t, *J* = 5.5 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -115.55(s).

HRMS (EI-TOF) m/z: $[M-Br-]^+$ Calcd for $C_{12}H_{23}F_2$ 205.1768; Found 205.1764.

7,7-difluoroheptyl thiophene-2-carboxylate (3e)



Colorless oil, 49%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 25:1 to 10:1).

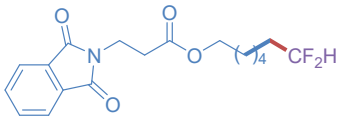
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (dd, J = 3.8, 1.3 Hz, 1H), 7.54 (dd, J = 5.0, 1.3 Hz, 1H), 7.09 (dd, J = 5.0, 3.8 Hz, 1H), 5.79 (tt, J = 56.9, 4.5 Hz, 1H), 4.29 (t, J = 6.6 Hz, 2H), 1.89 – 1.69 (m, 4H), 1.52 – 1.36 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4, 134.1, 133.4, 132.4, 127.8, 117.5 (t, *J* = 238.7 Hz), 65.1, 34.1 (t, *J* = 20.7 Hz), 28.8, 28.6, 25.9, 22.1 (t, *J* = 5.5 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -115.81(s).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{12}H_{17}F_2O_2S$ 263.0912; Found 263.0910.

7,7-difluoroheptyl 3-(1,3-dioxoisoindolin-2-yl)propanoate (3f)



Colorless oil, 59%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 25:1 to 10:1).

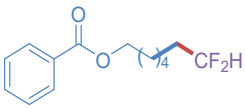
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (dd, J = 5.5, 3.0 Hz, 2H), 7.70 (dd, J = 5.5, 3.0 Hz, 2H), 5.77 (tt, J = 57.0, 4.5 Hz, 1H), 4.05 (t, J = 6.6 Hz, 2H), 3.98 (t, J = 7.2 Hz, 2H), 2.71 (t, J = 7.2 Hz, 2H), 1.85 – 1.71 (m, 2H), 1.63 – 1.54 (m, 2H), 1.44 – 1.36 (m, 2H), 1.36 – 1.26 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 168.1, 134.2, 132.1, 123.4, 117.4 (t, *J* = 238.7 Hz), 64.9, 34.0 (t, *J* = 20.6 Hz), 33.9, 33.8, 33.1, 28.7, 28.4, 25.8, 22.0 (t, *J* = 5.5 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -115.82(s).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{18}H_{22}F_2NO_4$ 354.1512; Found 354.1503.

7,7-difluoroheptyl benzoate (3g)



Colorless oil, 66%. Purified by flash chromatography on silica gel (hexane).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.9 Hz, 2H), 7.59 – 7.52 (m, 1H), 7.44 (t, *J* = 7.6 Hz, 2H), 5.80 (tt,

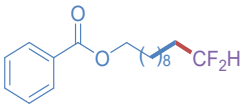
J = 56.9, 4.5 Hz, 1H), 4.32 (t, *J* = 6.6 Hz, 2H), 1.92 – 1.73 (m, 4H), 1.55 – 1.37 (m, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 166.8, 133.0, 130.6, 129.6, 128.5, 117.4 (t, *J* = 238.7 Hz), 65.0, 34.1 (t, *J* = 20.7 Hz), 28.8, 28.7, 26.0, 22.1 (t, *J* = 5.5 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -115.81(s).

HRMS (EI-TOF) m/z: [M] Calcd for $C_{14}H_{18}F_2O_2$ 256.1275; Found 256.1274.

11,11-difluoroundecyl benzoate (3h)



Colorless oil, 52%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 100:1 to 50:1).

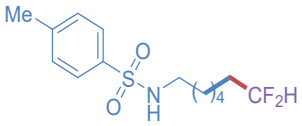
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 – 8.01 (m, 2H), 7.58 – 7.52 (m, 1H), 7.47 – 7.40 (m, 2H), 5.79 (tt, *J* = 57.0, 4.6 Hz, 1H), 4.32 (t, *J* = 6.7 Hz, 2H), 1.91 – 1.71 (m, 4H), 1.48 – 1.39 (m, 4H), 1.38 – 1.27 (m, 10H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 132.9, 130.7, 129.7, 128.5, 117.6 (t, *J* = 238.7 Hz), 65.2, 34.2 (t, *J* = 20.5 Hz), 29.6, 29.5, 29.4, 29.2, 28.8, 26.2, 22.2 (t, *J* = 5.5 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -115.72 (s).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{18}H_{27}F_2O_2$ 313.1974; Found 313.1966.

***N*-(7,7-difluoroheptyl)-4-methylbenzenesulfonamide (3i)**



Yellow oil, 78%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 10:1 to 5:1).

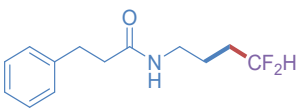
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.72 (m, 2H), 7.32 – 7.28 (m, 2H), 5.75 (tt, *J* = 56.9, 4.5 Hz, 1H), 4.82 (t, *J* = 6.2 Hz, 1H), 2.91 (q, J = 6.7 Hz, 2H), 2.42 (s, 3H), 1.83 – 1.68 (m, 2H), 1.48 – 1.40 (m, 2H), 1.39 – 1.31 (m, 2H), 1.31 – 1.21 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.4, 137.0, 129.7, 127.1, 117.3 (t, *J* = 238.7 Hz), 43.0, 33.9 (t, *J* = 20.7 Hz), 29.3, 28.5, 26.2, 21.9 (t, *J* = 5.5 Hz), 21.5.

^{19}F NMR (377 MHz, $CDCl_3$) δ -115.83 (s).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{30}F_2NO_4S$ 406.1858; Found 406.1853.

***N*-(4,4-difluorobutyl)-3-phenylpropanamide (3j)**



Colorless oil, 63%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 10:1 to 2:1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 – 7.26 (m, 2H), 7.22 – 7.17 (m, 3H), 5.77 (tt, J = 56.7, 4.2 Hz, 1H), 5.56

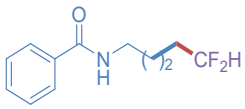
(s, 1H), 3.24 (q, J = 6.8 Hz, 2H), 2.95 (t, J = 7.6 Hz, 2H), 2.47 (t, J = 7.6 Hz, 2H), 1.76 – 1.64 (m, 2H), 1.58 (p, J = 7.2 Hz, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 172.4, 140.8, 128.7, 128.5, 126.4, 117.0 (t, *J* = 239.1 Hz), 38.7, 38.6, 31.8, 31.4 (t, *J* = 21.3 Hz), 22.4 (t, *J* = 5.3 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -116.05 (s).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{13}H_{18}F_2NO$ 242.1351; Found 242.1346.

O-(5,5-difluoropentyl)benzamide (3k)



Colorless oil, 56%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 10:1 to 5:1).

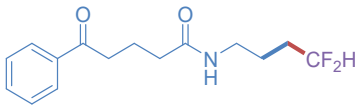
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.72 (m, 2H), 7.50 – 7.45 (m, 1H), 7.42 – 7.36 (m, 2H), 6.55 (s, 1H), 5.78 (tt, J = 56.8, 4.4 Hz, 1H), 3.43 (q, J = 7.0 Hz, 2H), 1.92 – 1.76 (m, 2H), 1.65 (p, J = 7.3 Hz, 2H), 1.55 – 1.46 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 134.6, 131.5, 128.6, 127.0, 117.2 (t, *J* = 238.9 Hz), 39.7, 33.7 (t, *J* = 20.9 Hz), 29.2, 19.6 (t, *J* = 5.6 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -115.97 (s).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{12}H_{16}F_2NO$ 228.1195; Found 228.1195.

O-(4,4-difluorobutyl)-5-oxo-5-phenylpentanamide (3l)



White solid, 65%, M.p. = 91-94 °C. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 10:1 to 2:1).

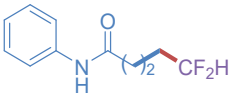
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.91 (m, 2H), 7.57 – 7.52 (m, 1H), 7.47 – 7.41 (m, 2H), 5.98 – 5.65 (m, 2H), 3.29 (q, *J* = 6.8 Hz, 2H), 3.04 (t, *J* = 6.8 Hz, 2H), 2.28 (t, *J* = 7.2 Hz, 2H), 2.06 (p, *J* = 7.4 Hz, 2H), 1.89 – 1.76 (m, 2H), 1.73 – 1.60 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 200.1, 172.8, 136.8, 133.3, 128.8, 128.1, 117.0 (t, *J* = 238.9 Hz), 38.7, 37.5, 35.6, 31.5 (t, *J* = 21.3 Hz), 22.5 (t, *J* = 5.3 Hz), 20.3.

^{19}F NMR (377 MHz, $CDCl_3$) δ -116.03 (s).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{15}H_{20}F_2NO_2$ 284.1457; Found 284.1453.

5,5-difluoro-*N*-phenylpentanamide (3m)



White solid, 55%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 10:1 to 5:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.45 (m, 3H), 7.31 (t, J = 15.8 Hz, 2H), 7.11 (t, J = 7.4 Hz, 1H), 5.83 (tt, J = 56.7, 4.0 Hz, 1H), 2.41 (t, J = 7.1 Hz, 2H), 1.97 – 1.83 (m, 4H).

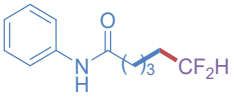
^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 137.8, 129.1, 124.6, 120.1, 117.2 (t, J = 239.1 Hz), 36.5, 33.3 (t, J = 21.1 Hz), 18.1 (t, J = 5.7 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -115.77 (s).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{11}H_{14}F_2NO$ 214.1038; Found 214.1031.

The analytical data were in good agreement with the literature[3].

6,6-difluoro-*N*-phenylhexanamide (3n)



White solid, 62%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 10:1 to 5:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.44 (m, 3H), 7.33 (t, J = 16.0 Hz, 2H), 7.12 (t, J = 14.8 Hz, 1H), 5.82 (tt, J = 56.8, 4.4 Hz, 1H), 2.39 (t, J = 7.4 Hz, 2H), 1.94 – 1.76 (m, 4H), 1.60 – 1.50 (m, 2H).

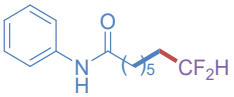
^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 137.8, 129.0, 124.4, 120.0, 117.1 (t, J = 238.9 Hz), 37.2, 33.8 (t, J = 20.9 Hz), 24.9, 21.7 (t, J = 5.5 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -115.90 (s).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{12}H_{16}F_2NO$ 228.1195; Found 228.1181.

The analytical data were in good agreement with the literature[3].

8,8-difluoro-*N*-phenyloctanamide (3o)



White solid, 58%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 10:1 to 5:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J = 7.9 Hz, 3H), 7.30 (t, J = 7.9 Hz, 2H), 7.09 (t, J = 7.4 Hz, 1H), 5.77 (tt, J = 56.9, 4.5 Hz, 1H), 2.34 (t, J = 7.5 Hz, 2H), 1.86 – 1.76 (m, 2H), 1.75 – 1.68 (m, 2H), 1.48 – 1.33 (m, 6H).

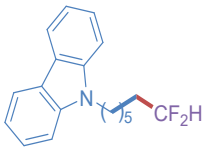
^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 138.1, 129.1, 124.3, 120.0, 117.5 (t, J = 238.7 Hz), 37.7, 34.1 (t, J = 20.7 Hz), 29.1, 28.9, 25.5, 22.0 (t, J = 5.6 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -115.73 (s).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{14}H_{20}F_2NO$ 256.1508; Found 256.1502.

The analytical data were in good agreement with the literature[3].

9-(7,7-difluoroheptyl)-9H-carbazole (3p)



Colorless oil, 66%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 100:1 to 50:1).

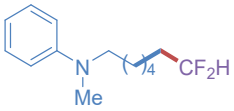
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (dt, *J* = 7.8, 1.1 Hz, 2H), 7.51 – 7.46 (m, 2H), 7.43 – 7.39 (m, 2H), 7.28 – 7.23 (m, 2H), 5.76 (tt, *J* = 57.0, 4.5 Hz, 1H), 4.32 (t, *J* = 7.1 Hz, 2H), 1.94 – 1.86 (m, 2H), 1.85 – 1.71 (m, 2H), 1.45 – 1.36 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 140.5, 125.7, 123.0, 120.5, 118.9, 117.4 (t, *J* = 238.7 Hz), 108.7, 43.0, 34.1 (t, *J* = 20.7 Hz), 29.0, 28.9, 27.2, 22.1 (t, *J* = 5.5 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -115.78 (s).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{22}F_2N$ 302.1715; Found 302.1710.

***N*-(7,7-difluoroheptyl)-*N*-methylaniline (3q)**



Colorless oil, 46%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 100:1 to 50:1).

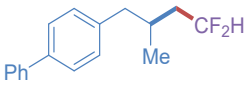
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.21 (m, 2H), 6.73 – 6.67 (m, 3H), 5.80 (tt, *J* = 57.0, 4.5 Hz, 1H), 3.32 (t, *J* = 7.6 Hz, 2H), 2.93 (s, 3H), 1.93 – 1.74 (m, 2H), 1.64 – 1.55 (m, 2H), 1.51 – 1.32 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 149.4, 129.2, 117.4 (t, *J* = 238.7 Hz), 116.0, 112.2, 52.7, 38.3, 34.0 (t, *J* = 20.7 Hz), 29.0, 27.0, 26.6, 22.1 (t, J = 5.5 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -115.76 (s).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{14}H_{22}F_2N$ 242.1715; Found 242.1707.

4-(4,4-difluoro-2-methylbutyl)-1,1'-biphenyl (3r)



Colorless oil, 77%. Purified by flash chromatography on silica gel (hexane).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.61 (m, 2H), 7.60 – 7.56 (m, 2H), 7.52 – 7.45 (m, 2H), 7.42 – 7.36 (m, 1H), 7.28 (d, *J* = 1.9 Hz, 2H), 5.92 (tt, *J* = 56.8, 5.3, 4.4 Hz, 1H), 2.74 (dd, *J* = 13.5, 6.7 Hz, 1H), 2.60 (dd, *J* = 13.6, 7.7 Hz, 1H), 2.21 – 2.08 (m, 1H), 2.08 – 1.90 (m, 1H), 1.84 – 1.65 (m, 1H), 1.06 (d, *J* = 6.7 Hz, 3H).

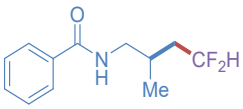
^{13}C NMR (151 MHz, $CDCl_3$) δ 141.1, 139.2, 139.2, 129.7, 128.9, 127.3, 127.2, 127.1, 117.1 (t, *J* = 238.6 Hz),

43.3, 40.5 (t, J = 19.9 Hz), 30.0 (t, J = 5.2 Hz), 19.8.

^{19}F NMR (377 MHz, $CDCl_3$) δ -114.52 (s).

HRMS (EI-TOF) m/z: [M] Calcd for $C_{17}H_{18}F_2$ 260.1377; Found 260.1369.

***N*-(4,4-difluoro-2-methylbutyl)benzamide (3s)**



Colorless oil, 83%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 10:1 to 5:1).

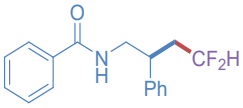
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.72 (m, 2H), 7.51 – 7.46 (m, 1H), 7.44 – 7.37 (m, 2H), 6.57 (s, 1H), 5.92 (tt, J = 56.7, 4.7 Hz, 1H), 3.36 (t, J = 6.7 Hz, 2H), 2.13 – 1.99 (m, 1H), 1.99 – 1.85 (m, 1H), 1.80 – 1.63 (m, 1H), 1.04 (d, J = 6.8 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 168.0, 134.6, 131.7, 128.8, 127.0, 116.8 (t, J = 238.8 Hz), 45.5, 38.5 (t, J = 20.6 Hz), 29.0, 18.1.

^{19}F NMR (377 MHz, $CDCl_3$) δ -114.54 (s).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{12}H_{16}F_2NO$ 228.1195; Found 228.1194.

***N*-(4,4-difluoro-2-phenylbutyl)benzamide (3t)**



White solid, 20%, M.p. = 105-109 °C. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 25:1 to 5:1).

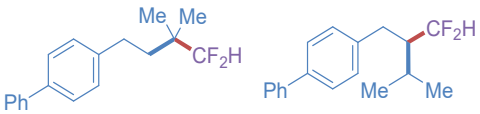
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.57 (m, 2H), 7.50 – 7.44 (m, 1H), 7.41 – 7.35 (m, 4H), 7.33 – 7.27 (m, 1H), 7.27 – 7.23 (m, 2H), 6.02 (s, 1H), 5.64 (tdd, J = 56.5, 6.4, 3.4 Hz, 1H), 3.99 – 3.88 (m, 1H),3.54 – 3.43 (m, 1H), 3.24 – 3.13 (m, 1H), 2.38 – 2.12 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.7, 140.5, 134.4, 131.7, 129.4, 128.7, 127.8, 127.7, 126.9, 116.3 (t, J = 238.7 Hz), 45.1, 40.6 – 40.4 (m), 38.0 (t, J = 21.4 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -115.16 (d, J = 284.3 Hz), -117.03 (d, J = 310.0 Hz).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{18}F_2NO$ 290.1351; Found 290.1353.

4-(2-(difluoromethyl)-3-methylbutyl)-1,1'-biphenyl (3u)



2.5 : 1

Colorless oil, 19%. Purified by flash chromatography on silica gel (hexane).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.63 – 7.58 (m, 2H), 7.58 – 7.53 (m, 2H), 7.49 – 7.41 (m, 2H), 7.39 – 7.32 (m,

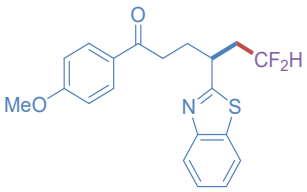
1H), 7.31 – 7.27 (m, 1.4H), 7.24 – 7.17 (m, 0.6H), 5.82 (td, *J* = 56.2, 3.1 Hz, 0.7H), 5.48 (td, *J* = 57.5, 7.0 Hz, 0.3H), 2.91 – 2.83 (m, 0.7H), 2.79 – 2.69 (m, 0.7H), 2.61 – 2.53 (m, 0.3H), 2.39 – 2.27 (m, 0.3H), 2.23 – 1.96 (m, 1.7H), 1.95 – 1.86 (m, 0.3H), 1.08 – 1.03 (m, 4.2H), 1.02 (d, *J* = 6.8 Hz, 0.9H), 0.81 (d, *J* = 6.7 Hz, 0.9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 140.9, 139.1, 139.1, 129.4, 128.8, 127.2, 127.2, 127.0, 118.2 (t, J = 242.4 Hz), 49.6 (t, *J* = 17.7 Hz), 30.5, 26.3, 20.2, 19.5. Peaks corresponding to the minor structure are present at δ 141.2, 140.8, 139.5, 128.8, 128.6, 127.0, 117.2, 46.9, 38.0 – 37.3 (m), 33.4, 20. 7, 20.5.

^{19}F NMR (377 MHz, $CDCl_3$) δ -120.85 (d, *J* = 281.0 Hz), -122.29 (d, *J* = 281.0 Hz). Peaks corresponding to the minor structure are present at δ -114.69 (d, *J* = 282.1 Hz), -118.10 (d, *J* = 282.0 Hz).

HRMS (EI-TOF) m/z：[M] Calcd for $C_{18}H_{20}F_2$ 274.1533; Found 274.1522.

4-(benzo[*d*]thiazol-2-yl)-6,6-difluoro-1-(4-methoxyphenyl)hexan-1-one (3v)



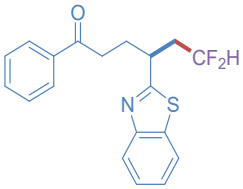
White solid, 37%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 100:1 to 20:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 – 7.96 (m, 1H), 7.91 – 7.81 (m, 3H), 7.54 – 7.44 (m, 1H), 7.44 – 7.33 (m, 1H), 6.87 (t, *J* = 8.2 Hz, 2H), 6.26 – 5.65 (m, 1H), 3.84 (s, 3H), 3.66 – 3.47 (m, 1H), 3.08 – 2.87 (m, 2H), 2.69 – 2.48 (m, 1H), 2.43 – 2.19 (m, 3H).

^{19}F NMR (377 MHz, $CDCl_3$) δ -114.87 (d, *J* = 285.1 Hz), -116.85 (d, *J* = 285.1 Hz).

The analytical data were in good agreement with the literature[4].

4-(benzo[*d*]thiazol-2-yl)-6,6-difluoro-1-phenylhexan-1-one (3w)



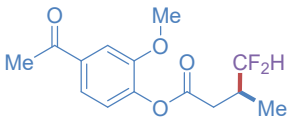
Colorless oil, 35%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 100:1 to 20:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 – 7.94 (m, 1H), 7.94 – 7.83 (m, 3H), 7.62 – 7.46 (m, 2H), 7.45 – 7.35 (m, 3H), 5.90 (tdd, J = 56.6, 6.0, 3.5 Hz, 1H), 3.75 – 3.36 (m, 1H), 3.17 – 2.88 (m, 2H), 2.78 – 2.45 (m, 1H), 2.45 – 2.13 (m, 3H).

^{19}F NMR (377 MHz, $CDCl_3$) δ -114.86 (d, *J* = 282.3 Hz), -116.86 (d, *J* = 276.0 Hz).

The analytical data were in good agreement with the literature[4].

4-acetyl-2-methoxyphenyl 4,4-difluoro-3-methylbutanoate (3x)



Yellow oil, 60%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 20:1 to 10:1).

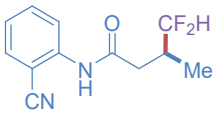
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 2.1 Hz, 1H), 7.57 (dd, J = 8.1, 2.0 Hz, 1H), 7.13 (d, J = 8.1 Hz, 1H), 5.86 (td, J = 56.7, 3.3 Hz, 1H), 3.90 (s, 3H), 2.91 – 2.83 (m, 1H), 2.65 – 2.55 (m, 5H), 1.20 (d, J = 6.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.0, 169.3, 151.4, 143.7, 136.2, 122.8, 122.1, 117.9 (t, J = 242.3 Hz), 111.5, 56.1, 34.8, 34.6, 34.5 – 34.3 (m), 26.6, 12.6 (t, J = 4.9 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -124.57 (s).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{14}H_{17}F_2O_4$ 287.1090; Found 287.1097.

N-(2-cyanophenyl)-4,4-difluoro-3-methylbutanamide (3y)



White solid, 44%, M.p. = 93-98 °C. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 100:1 to 5:1).

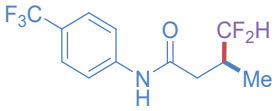
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, J = 8.9 Hz, 1H), 7.68 (s, 1H), 7.63 – 7.58 (m, 2H), 7.20 (td, J = 7.6, 1.2 Hz, 1H), 5.84 (td, J = 56.7, 3.3 Hz, 1H), 2.73 (dd, J = 15.3, 5.6 Hz, 1H), 2.69 – 2.54 (m, 1H), 2.43 – 2.36 (m, 1H), 1.15 (d, J = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.4, 140.3, 134.4, 132.5, 124.6, 121.7, 118.1 (t, J = 242.4 Hz), 116.4, 37.4, 34.6 (t, J = 20.6 Hz), 12.9 (t, J = 4.8 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -123.75 (d, J = 278.8 Hz), -124.95 (d, J = 278.8 Hz).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{12}H_{13}F_2N_2O$ 239.0991; Found 239.0986.

4,4-difluoro-3-methyl-N-(4-(trifluoromethyl)phenyl)butanamide (3z)



White solid, 58%, M.p. = 88-95 °C. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 100:1 to 5:1).

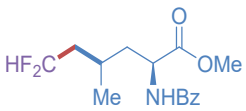
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 8.8 Hz, 3H), 7.56 (d, J = 8.8 Hz, 2H), 5.81 (td, J = 56.7, 3.0 Hz, 1H), 2.68 – 2.51 (m, 2H), 2.34 – 2.26 (m, 1H), 1.11 (d, J = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5, 140.7, 126.5, 126.5, 126.4, 126.4, 125.5, 122.8, 119.7, 118.2 (t, J = 242.5 Hz), 37.3 (t, J = 4.2 Hz), 34.6 (t, J = 20.3 Hz), 12.9 (dd, J = 5.8, 4.0 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -62.21(s), -123.53 (d, J = 278.1 Hz), -125.40 (d, J = 278.1 Hz).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{12}H_{13}F_5NO$ 282.0912; Found 282.0906.

methyl (2*S*)-2-benzamido-6,6-difluoro-4-methylhexanoate (3a')



Colorless oil, 88%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 20:1 to 10:1). At RT, this compound appears as an ~1.1:1 mixture of rotamers.

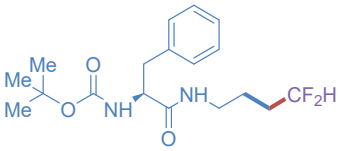
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.77 (m, 2H), 7.55 – 7.49 (m, 1H), 7.48 – 7.40 (m, 2H), 6.63 (dd, *J* = 31.1, 8.3 Hz, 1H), 6.05 – 5.70 (m, 1H), 4.96 – 4.83 (m, 1H), 3.78 (d, *J* = 3.7 Hz, 3H), 2.08 – 1.66 (m, 5H), 1.10 (dd, *J* = 9.1, 6.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 173.2, 167.1, 133.7, 131.9, 128.7, 127.1, 116.8 (t, *J* = 239.0 Hz), 77.24, 77.03, 76.82, 52.6, 50.6, 40.9 (t, *J* = 20.2 Hz), 40.4 – 39.9 (m), 25.0 (t, *J* = 5.2 Hz), 19.4. Peaks corresponding to the minor rotamer are present at δ 173.2, 167.3, 133.7, 131.9, 127.0, 116.6 (t, *J* = 239.0 Hz), 50.5, 24.9 (t, *J* = 5.2 Hz), 20.0.

^{19}F NMR (377 MHz, $CDCl_3$) δ -114.02 (d, *J* = 283.5 Hz), -114.92 (d, *J* = 283.4 Hz). Peaks corresponding to the minor rotamer are present at δ -114.30 (d, *J* = 283.5 Hz), -115.40 (d, *J* = 283.4 Hz).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{15}H_{20}F_2NO_3$ 300.1406; Found 300.1402.

tert-butyl (*S*)-(1-((4,4-difluorobutyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (3b')



White solid, 68%, M.p. = 117 126 °C. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 10:1 to 2:1).

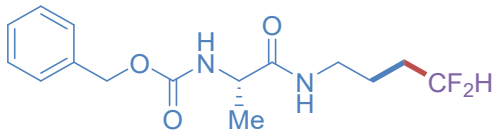
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.24 (m, 2H), 7.23 – 7.16 (m, 3H), 6.31 (s, 1H), 5.75 (tt, *J* = 56.7, 4.3 Hz, 1H), 5.30 (d, *J* = 8.3 Hz, 1H), 4.33 (d, *J* = 7.7 Hz, 1H), 3.29 – 3.18 (m, 1H), 3.15 (p, *J* = 6.7 Hz, 1H), 3.03 (d, *J* = 5.3 Hz, 2H), 1.79 – 1.60 (m, 2H), 1.52 (p, *J* = 6.8 Hz, 2H), 1.39 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 171.7, 155.7, 136.9, 129.4, 128.7, 127.0, 116.9 (t, *J* = 239.9 Hz), 80.1, 56.1, 38.8, 38.6, 31.3, 28.3, 22.1.

^{19}F NMR (377 MHz, $CDCl_3$) δ -116.05 (s).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{18}H_{27}F_2N_2O_3$ 357.1984; Found 357.1986.

benzyl (*S*)-(1-((4,4-difluorobutyl)amino)-1-oxopropan-2-yl)carbamate (3c')



White solid, 59%, M.p. = 111-118 °C. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 10:1 to 2:1).

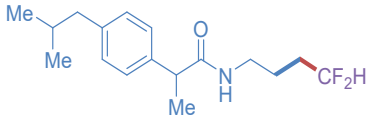
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.28 (m, 5H), 6.66 (s, 1H), 5.96 – 5.62 (m, 2H), 5.07 (s, 2H), 4.28 – 4.16 (m, 1H), 3.31 – 3.18 (m, 2H), 1.91 – 1.70 (m, 2H), 1.68-1.53 (m, 2H), 1.35 (d, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5, 156.2, 136.2, 133.9, 128.7, 128.4, 128.2, 116.9 (t, *J* = 238.9 Hz), 67.3, 50.7, 38.8, 31.4 (t, *J* = 21.3 Hz), 22.3 (t, *J* = 5.0 Hz), 18.5.

^{19}F NMR (377 MHz, $CDCl_3$) δ -116.06 (s).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{15}H_{21}F_2N_2O_3$ 315.1515; Found 315.1511.

***N*-(4,4-difluorobutyl)-2-(4-isobutylphenyl)propanamide (3d')**



Colorless oil, 60%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 10:1 to 5:1).

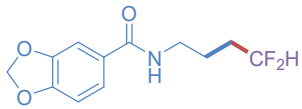
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.20 – 7.16 (m, 2H), 7.15 – 7.10 (m, 2H), 5.75 (tt, *J* = 56.7, 4.3 Hz, 1H), 5.42 (s, 1H), 3.52 (q, *J* = 7.2 Hz, 1H), 3.35 – 3.13 (m, 2H), 2.45 (d, *J* = 7.2 Hz, 2H), 1.91 – 1.79 (m, 1H), 1.78 – 1.65 (m, 2H), 1.63 – 1.55 (m, 2H), 1.51 (d, *J* = 5.6 Hz, 3H), 0.90 (d, *J* = 6.6 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.8, 141.0, 138.6, 129.8, 127.4, 116.9 (t, *J* = 239.0 Hz), 46.9, 45.1, 38.8, 31.4 (t, *J* = 21.3 Hz), 30.3, 22.5, 22.4 (t, *J* = 5.3 Hz), 18.5.

^{19}F NMR (377 MHz, $CDCl_3$) δ -116.06 (s).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{26}F_2NO$ 298.1977; Found 298.1968.

N-(4,4-difluorobutyl)benzo[*d*][1,3]dioxole-5-carboxamide (3e')



White solid, 48%, M.p. = 78-85 °C. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 10:1 to 5:1).

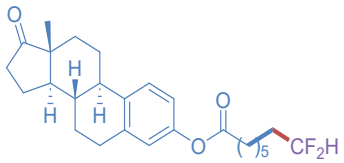
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.25 (d, *J* = 1.8 Hz, 1H), 6.79 (d, *J* = 8.1 Hz, 1H), 6.40 (s, 1H), 6.00 (s, 2H), 5.84 (tt, *J* = 56.7, 4.3 Hz, 1H), 3.45 (q, *J* = 6.7 Hz, 2H), 1.94 – 1.83 (m, 2H), 1.79 – 1.73 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 167.2, 150.4, 148.1, 128.7, 121.6, 117.0 (t, *J* = 238.9 Hz), 108.1, 107.6, 101.8, 39.3, 31.6, 22.5.

^{19}F NMR (377 MHz, $CDCl_3$) δ -115.95 (s).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{12}H_{14}F_2NO_3$ 258.0936; Found 258.0935.

(8*R*,9*S*,13*S*,14*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-3-yl 8,8-difluorooctanoate (3f')



Colorless oil, 55%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 10:1 to 5:1).

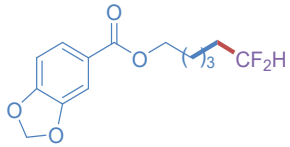
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.4 Hz, 1H), 6.84 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.80 (d, *J* = 2.5 Hz, 1H), 5.80 (tt, *J* = 57.0, 4.5 Hz, 1H), 2.94 – 2.85 (m, 2H), 2.56 – 2.44 (m, 3H), 2.43 – 2.35 (m, 1H), 2.32 – 2.22 (m, 1H), 2.18 – 2.08 (m, 1H), 2.07 – 1.91 (m, 3H), 1.89 – 1.68 (m, 5H), 1.67 – 1.54 (m, 3H), 1.53 – 1.35 (m, 10H), 0.90 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 172.5, 148.7, 138.1, 137.4, 126.5, 121.6, 118.8, 117.4 (t, *J* = 238.8 Hz), 50.5, 48.0, 44.2, 38.1, 35.9, 34.3, 34.1 (t, *J* = 20.7 Hz), 31.6, 29.5, 28.9, 28.8, 26.4, 25.8, 24.8, 21.7, 22.0 (t, *J* = 5.5 Hz), 13.9.

^{19}F NMR (377 MHz, $CDCl_3$) δ -115.76 (s).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{26}H_{35}F_2O_3$ 433.2549; Found 433.2548.

6,6-difluorohexyl benzo[*d*][1,3]dioxole-5-carboxylate (3g')



Colorless oil, 63%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 10:1 to 5:1).

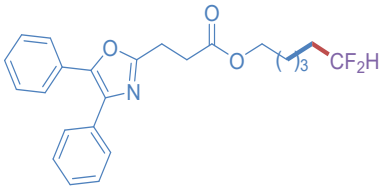
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.48 (d, *J* = 1.4 Hz, 1H), 6.85 (d, *J* = 8.2 Hz, 1H), 6.05 (s, 2H), 5.83 (tt, *J* = 56.9, 4.4 Hz, 1H), 4.30 (t, *J* = 6.5 Hz, 2H), 1.96 – 1.73 (m, 4H), 1.60 – 1.46 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7, 151.4, 147.5, 125.1, 124.2, 117.0 (t, *J* = 238.8 Hz), 109.2, 107.8, 101.6, 64.4, 33.8 (t, *J* = 20.8 Hz), 28.4, 25.4, 21.6 (t, *J* = 5.5 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -115.87 (s).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{14}H_{17}F_2O_4$ 287.1090; Found 287.1092.

6,6-difluorohexyl 3-(4,5-diphenyloxazol-2-yl)propanoate (3h')



Colorless oil, 56%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 10:1 to 5:1).

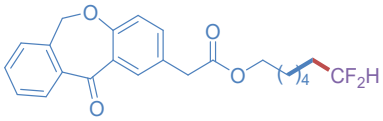
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.61 (m, 2H), 7.60 – 7.55 (m, 2H), 7.39 – 7.29 (m, 6H), 5.76 (tt, *J* = 56.8, 4.4 Hz, 1H), 4.13 (t, *J* = 6.5 Hz, 2H), 3.19 (t, *J* = 8.0, 6.9 Hz, 2H), 2.92 (t, *J* = 8.1 Hz, 2H), 1.85 – 1.70 (m, 2H), 1.69 – 1.61 (m, 2H), 1.49 – 1.35 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.1, 161.8, 145.4, 135.1, 132.5, 129.0, 128.7, 128.6, 128.5, 128.1, 127.9, 126.5, 117.2 (t, *J* = 238.7 Hz), 64.5, 33.9 (t, *J* = 20.7 Hz), 31.2, 28.4, 25.5, 23.6, 21.8 (t, *J* = 5.5 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -115.88 (s).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{24}H_{26}F_2NO_3$ 414.1875; Found 414.1865.

7,7-difluoroheptyl 2-(11-oxo-6,11-dihydrodibenzo[*b,e*]oxepin-2-yl)acetate (3i')



Colorless oil, 69%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 10:1 to 5:1).

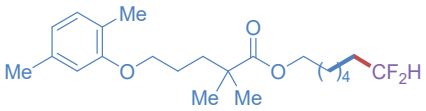
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 2.4 Hz, 1H), 7.88 (d, *J* = 7.7 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.50 – 7.39 (m, 2H), 7.35 (d, *J* = 7.4 Hz, 1H), 7.02 (d, *J* = 8.4 Hz, 1H), 5.76 (tt, *J* = 56.9, 4.5 Hz, 1H), 5.17 (s, 2H), 4.09 (t, *J* = 6.6 Hz, 2H), 3.63 (s, 2H), 1.86 – 1.68 (m, 2H), 1.67 – 1.57 (m, 2H), 1.47 – 1.37 (m, 2H), 1.37 – 1.28 (m, 4H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 190.9, 171.5, 160.5, 140.5, 136.4, 135.7, 132.9, 132.5, 129.5, 129.3, 128.0, 127.9, 125.2, 121.1, 117.4 (t, *J* = 238.8 Hz), 73.7, 65.0, 40.4, 34.0 (t, *J* = 20.5 Hz), 28.7, 28.4, 25.7, 22.0 (t, *J* = 5.4 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) δ -115.77 (s).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{25}F_2O_4$ 403.1716; Found 403.1710.

7,7-difluoroheptyl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (3j')



Colorless oil, 63%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 10:1 to 5:1).

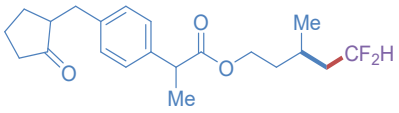
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 (d, *J* = 7.4 Hz, 1H), 6.66 (d, *J* = 7.5 Hz, 1H), 6.61 (s, 1H), 5.77 (tt, *J* = 56.9, 4.5 Hz, 1H), 4.07 (t, *J* = 6.6 Hz, 2H), 3.92 (t, *J* = 5.4 Hz, 2H), 2.31 (s, 3H), 2.18 (s, 3H), 1.88 – 1.69 (m, 6H), 1.67 – 1.59 (m, 2H), 1.50 – 1.34 (m, 6H), 1.23 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 178.0, 157.1, 136.6, 130.4, 123.7, 120.8, 117.4 (t, *J* = 238.9 Hz), 112.0, 68.1, 64.4, 42.2, 37.2, 34.1 (t, *J* = 20.7 Hz), 28.8, 28.6, 25.9, 25.3, 25.3, 22.1 (t, J = 5.5 Hz), 21.5, 15.9.

^{19}F NMR (377 MHz, $CDCl_3$) δ -115.81 (s).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{22}H_{35}F_2O_3$ 385.2549; Found 385.2541.

5,5-difluoro-3-methylpentyl 2-(4-((2-oxocyclopentyl)methyl)phenyl)propanoate (3k')



Colorless oil, 77%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 10:1 to 2:1).

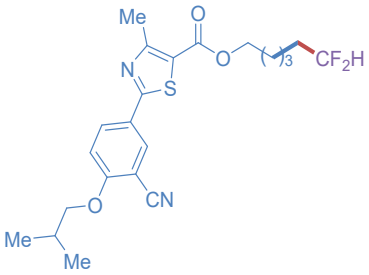
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 – 7.17 (m, 2H), 7.13 – 7.09 (m, 2H), 5.93 – 5.59 (m, 1H), 4.16 – 4.04 (m, 2H), 3.67 (q, *J* = 7.2 Hz, 1H), 3.11 (dd, *J* = 13.9, 4.1 Hz, 1H), 2.53 – 2.46 (m, 1H), 2.36 – 2.28 (m, 2H), 2.15 – 2.02 (m, 2H), 1.99 – 1.90 (m, 1H), 1.83 – 1.49 (m, 7H), 1.47 (d, *J* = 7.3 Hz, 3H), 0.92 (t, *J* = 6.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 220.2, 174.6, 139.0, 138.4, 129.2, 127.6, 116.8 (t, *J* = 238.8 Hz), 62.4, 51.0, 45.2, 40.7 (td, *J* = 19.6, 1.4 Hz), 38.2, 35.4, 35.2, 29.3, 25.1 (dd, *J* = 9.2, 5.3 Hz), 20.6, 19.5 (d, *J* = 3.1 Hz), 19.5, 18.4 (d, *J* = 1.5 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) -114.69 – -114.81 (m)

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{21}H_{28}F_2O_3$ 367.2080; Found 367.2083.

6,6-difluorohexyl 2-(3-cyano-4-isobutoxyphenyl)-4-methylthiazole-5-carboxylate (3l')



Colorless oil, 58%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 10:1 to 5:1).

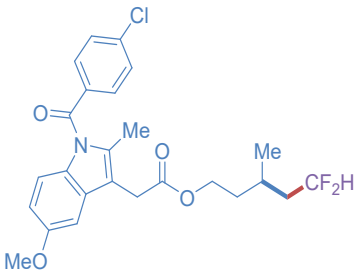
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 2.3 Hz, 1H), 8.08 (dd, *J* = 8.9, 2.4 Hz, 1H), 7.00 (d, *J* = 8.9 Hz, 1H), 5.82 (tt, *J* = 56.8, 4.4 Hz, 1H), 4.30 (t, *J* = 6.5 Hz, 2H), 3.89 (d, *J* = 6.5 Hz, 2H), 2.75 (s, 3H), 2.25 – 2.13 (m, 1H), 1.96 – 1.72 (m, 4H), 1.60 – 1.44 (m, 4H), 1.08 (d, *J* = 6.8 Hz, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 167.4, 162.6, 162.2, 161.4, 132.7, 132.2, 126.1, 121.9, 117.3 (t, *J* = 239.8 Hz), 112.8, 103.1, 75.8, 65.2, 34.1 (t, *J* = 21.0 Hz), 28.6, 28.3, 25.7, 21.9 (t, *J* = 5.5 Hz), 19.2, 17.6.

^{19}F NMR (377 MHz, $CDCl_3$) δ -115.89 (s).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{22}H_{27}F_2N_2O_3S$ 437.1705; Found 437.1706.

5,5-difluoro-3-methylpentyl 2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)acetate (3m')



Colorless oil, 79%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 10:1 to 2:1).

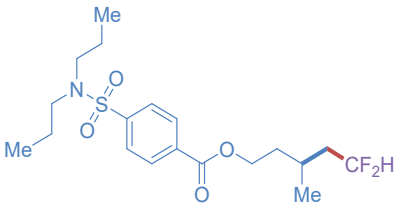
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.64 (m, 2H), 7.49 – 7.45 (m, 2H), 6.95 (d, *J* = 2.5 Hz, 1H), 6.86 (d, *J* = 9.0 Hz, 1H), 6.67 (dd, *J* = 9.1, 2.6 Hz, 1H), 5.94 – 5.61 (m, 1H), 4.19 – 4.11 (m, 2H), 3.83 (s, 3H), 3.66 (s, 2H), 2.38 (s, 3H), 1.84 – 1.77 (m, 1H), 1.76 – 1.59 (m, 3H), 1.57 – 1.46 (m, 1H), 0.95 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 168.4, 156.2, 139.4, 136.1, 134.0, 131.3, 130.9, 130.7, 129.2, 116.8 (t, *J* = 238.7 Hz), 115.1, 112.6, 111.7, 101.4, 62.8, 55.8, 40.8 (t, *J* = 20.3 Hz), 35.5, 30.5, 25.1 (t, *J* = 5.2 Hz), 19.6, 13.4.

^{19}F NMR (377 MHz, $CDCl_3$) δ -114.34 (d, *J* = 283.4 Hz), -115.15 (d, *J* = 283.3 Hz).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{25}H_{27}ClF_2NO_4$ 478.1591; Found 478.1582.

5,5-difluoro-3-methylpentyl 4-(N,N-dipropylsulfamoyl)benzoate (3n')



Colorless oil, 74%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 10:1 to 2:1).

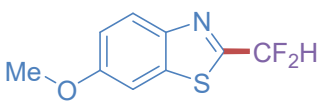
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 – 8.13 (m, 2H), 7.91 – 7.87 (m, 2H), 5.92 (tt, *J* = 56.7, 4.2 Hz, 1H), 4.46 – 4.39 (m, 2H), 3.14 – 3.09 (m, 4H), 2.03 – 1.96 (m, 1H), 1.96 – 1.86 (m, 2H), 1.85 – 1.74 (m, 1H), 1.74 – 1.68 (m, 1H), 1.61 – 1.51 (m, 4H), 1.11 – 1.08 (m, 3H), 0.88 (t, *J* = 7.4 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.3, 144.4, 133.6, 130.3, 127.1, 116.8 (t, *J* = 238.9 Hz), 63.4, 50.0, 40.8 (t, *J* = 20.2 Hz), 35.5, 25.3 (t, *J* = 5.3 Hz), 22.0, 19.7, 11.2.

^{19}F NMR (377 MHz, $CDCl_3$) δ -114.44 (d, *J* = 283.5 Hz), -115.31 (d, *J* = 283.6 Hz).

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{30}F_2NO_4S$ 406.1858; Found 406.1853.

2-(difluoromethyl)-6-methoxybenzo[d]thiazole (5b)



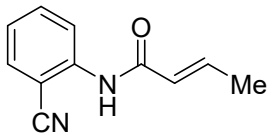
Colorless oil, yield 23%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 100:1 to 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 9.1 Hz, 1H), 7.38 (d, J = 2.6 Hz, 1H), 7.16 (dd, J = 9.0, 2.5 Hz, 1H), 6.91 (t, J = 54.7 Hz, 1H), 3.90 (s, 3H).

^{19}F NMR (377 MHz, $CDCl_3$) δ -109.28 (s).

The analytical data were in good agreement with the literature[5].

(E)-N-(2-cyanophenyl)but-2-enamide (1xb)



White soild, yield 85%. Purified by flash chromatography on silica gel (hexane/ethyl acetate = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 8.6 Hz, 1H), 7.66 – 7.58 (m, 3H), 7.19 (t, J = 7.0 Hz, 1H), 7.14 – 7.04 (m, 1H), 6.05 (dq, J = 15.1, 1.8 Hz, 1H), 1.98 (dd, J = 6.9, 1.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.9, 143.6, 140.7, 134.3, 132.2, 124.8, 124.0, 121.1, 116.4, 101.6, 18.0.

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{11}H_{10}N_2O$.

5. References

1. Zhang Z-Q, Sang Y-Q, Wang C-Q, Dai P, Xue X-S, Piper JL, Peng Z-H, Ma J-A, Zhang F-G, Wu J. Difluoromethylation of Unactivated Alkenes Using Freon-22 through Tertiary Amine-Borane-Triggered Halogen Atom Transfer. *Journal of the American Chemical Society*, **2022**, 144: 14288-14296.

2. Zhang Z, Chen K, Liu P, Dong G. Alkyl Fluoride Synthesis via Cu-Mediated Deacetylative Fluorination. *JAmChemSoc*, **2025**, 147: 20257-20264.

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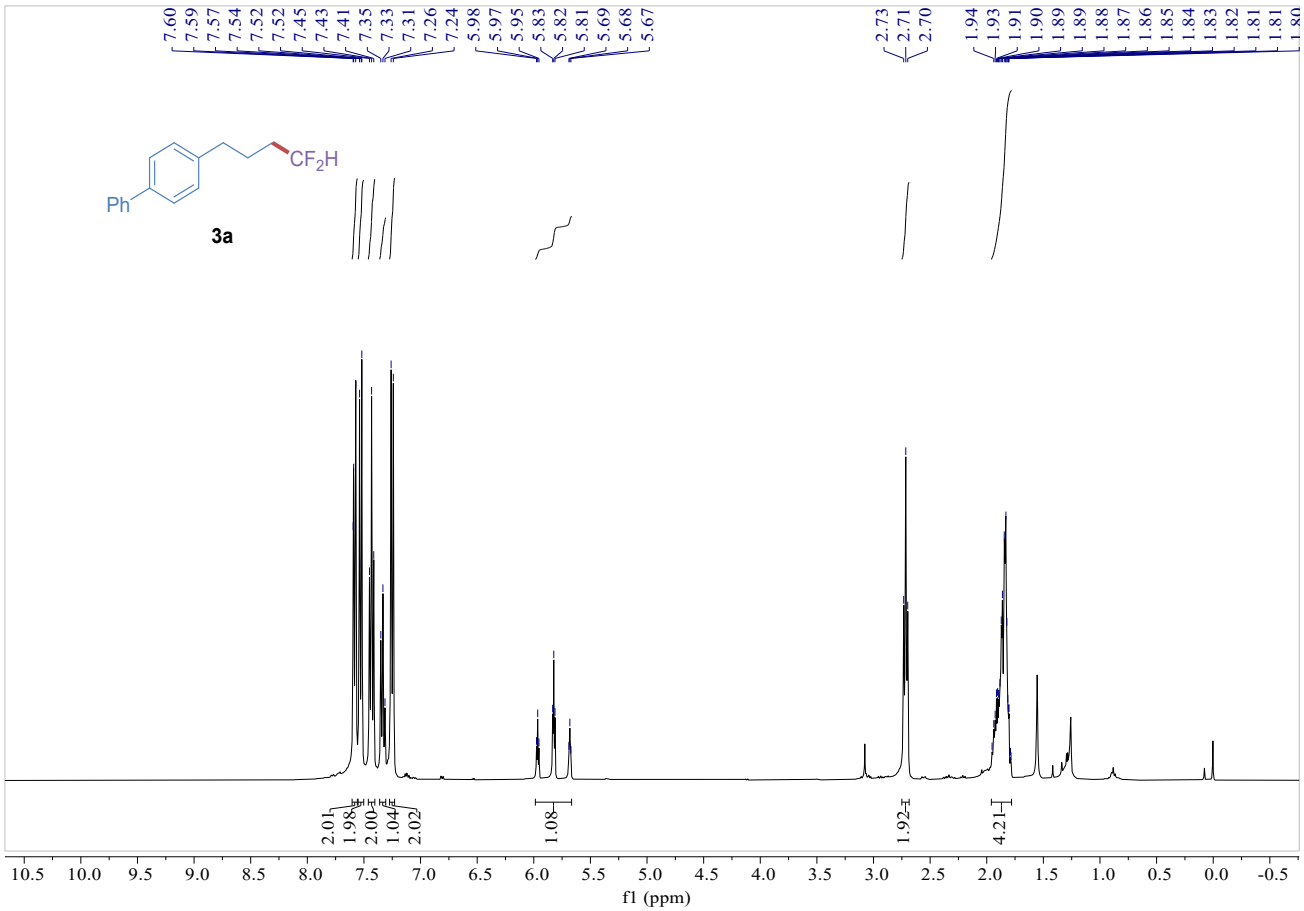
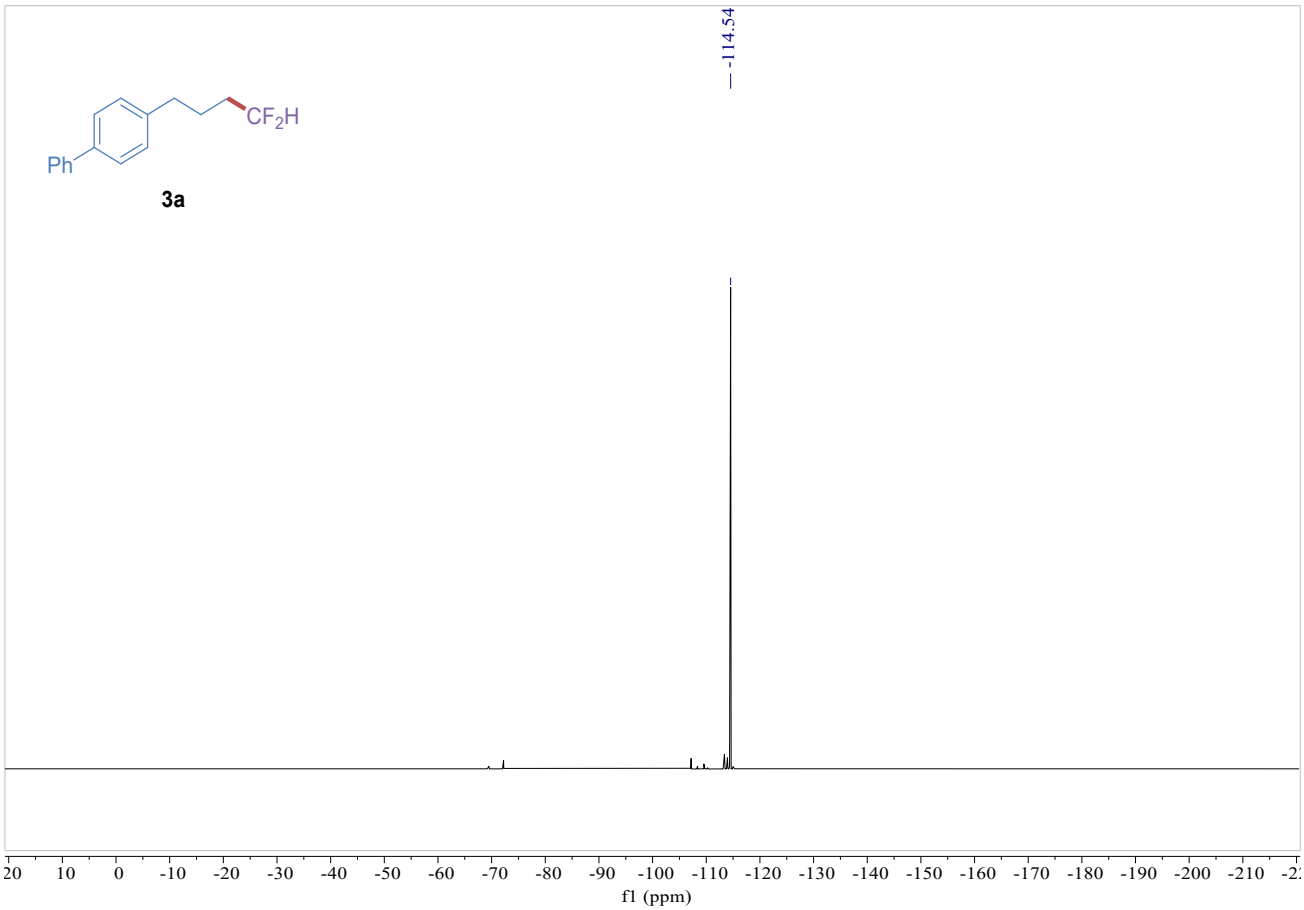
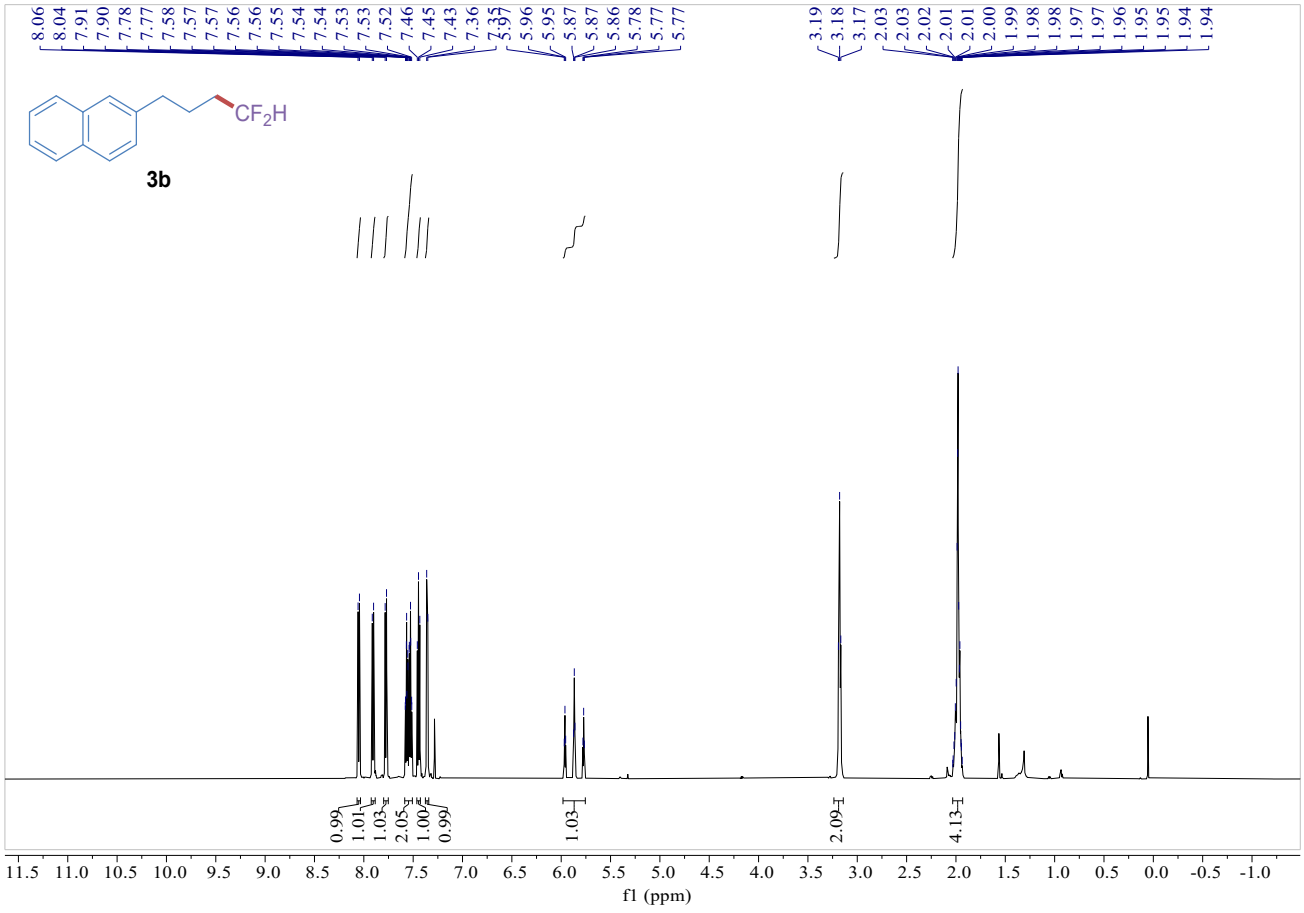
6. NMR Spectra



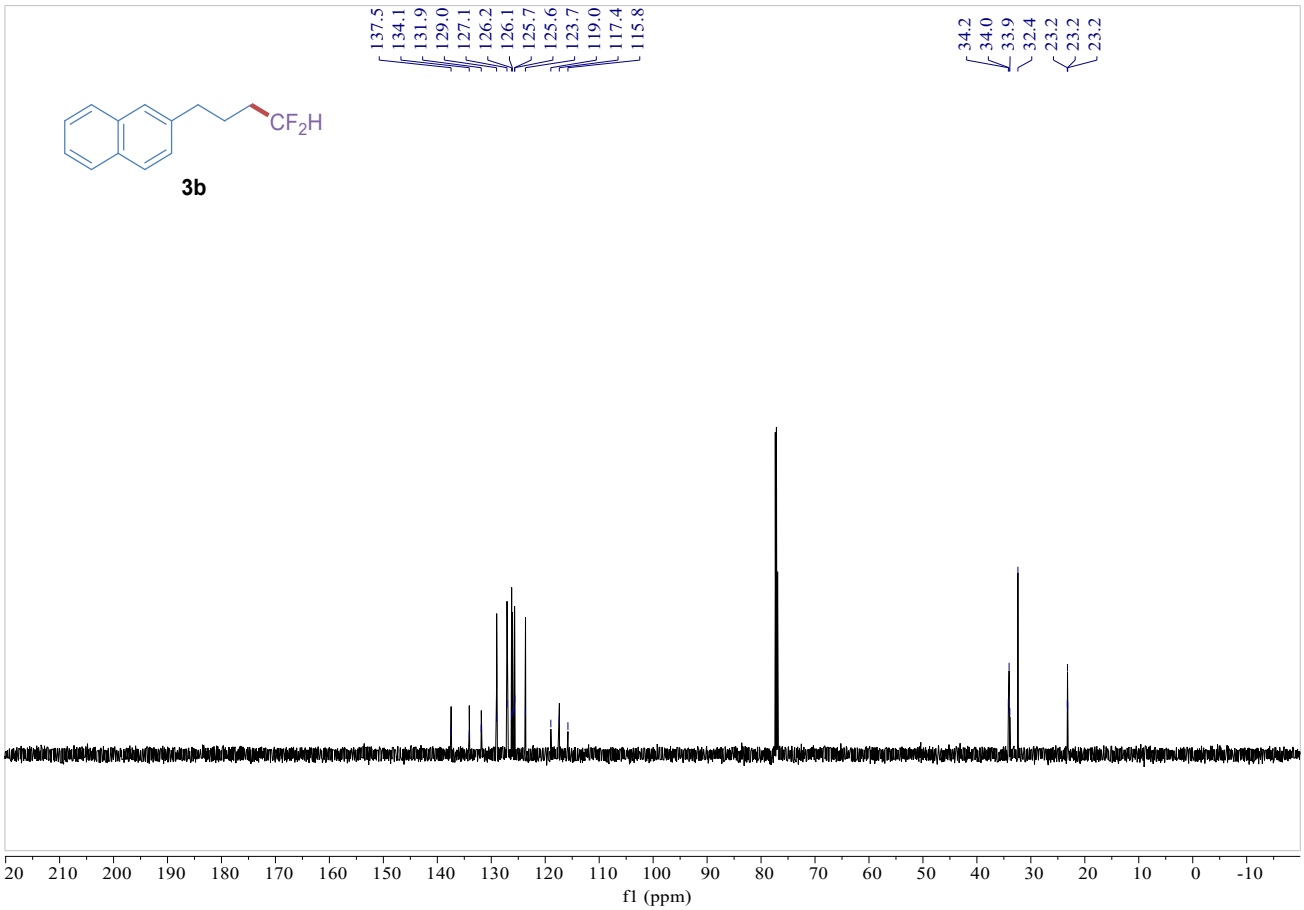
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3a**



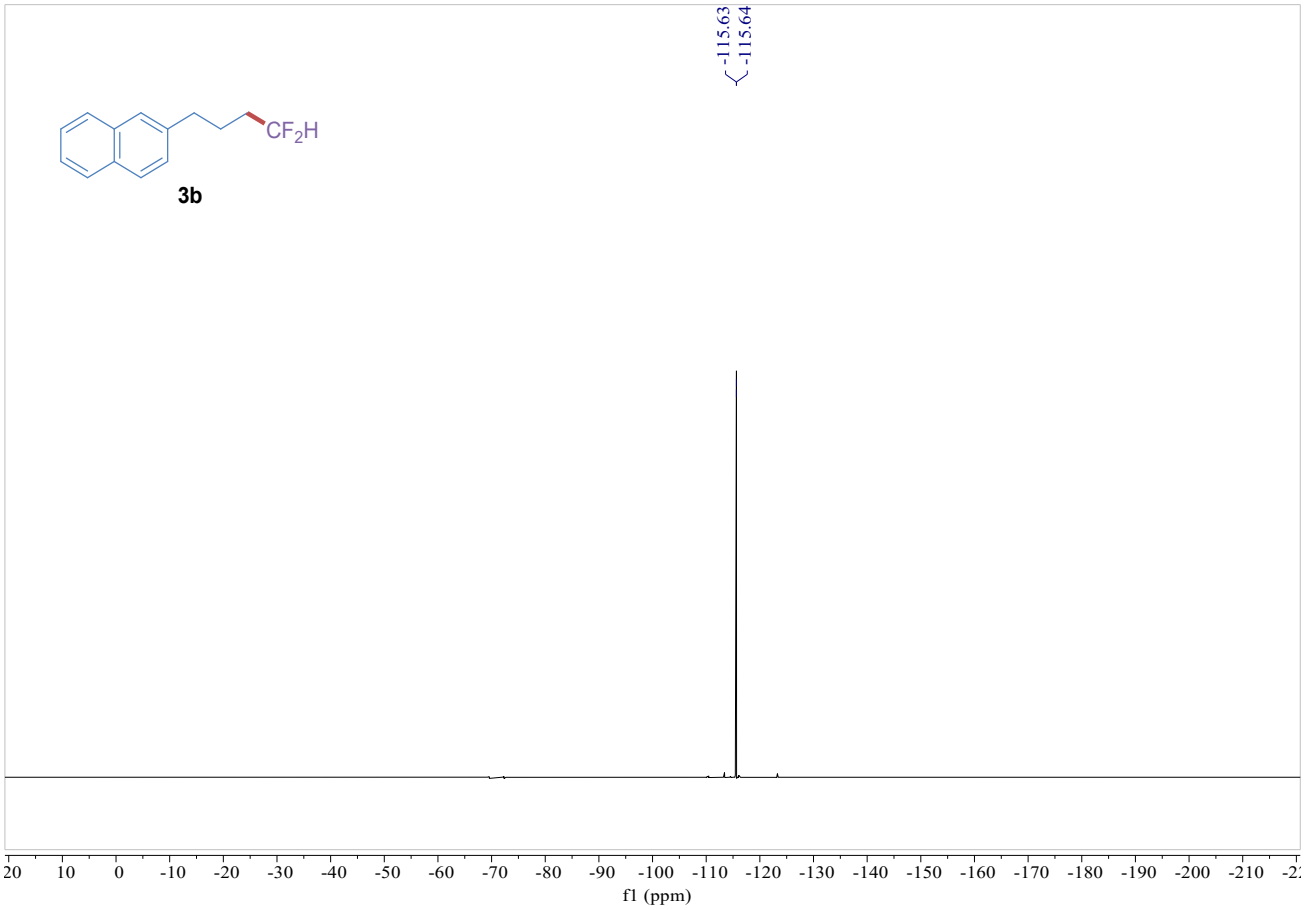
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3a**



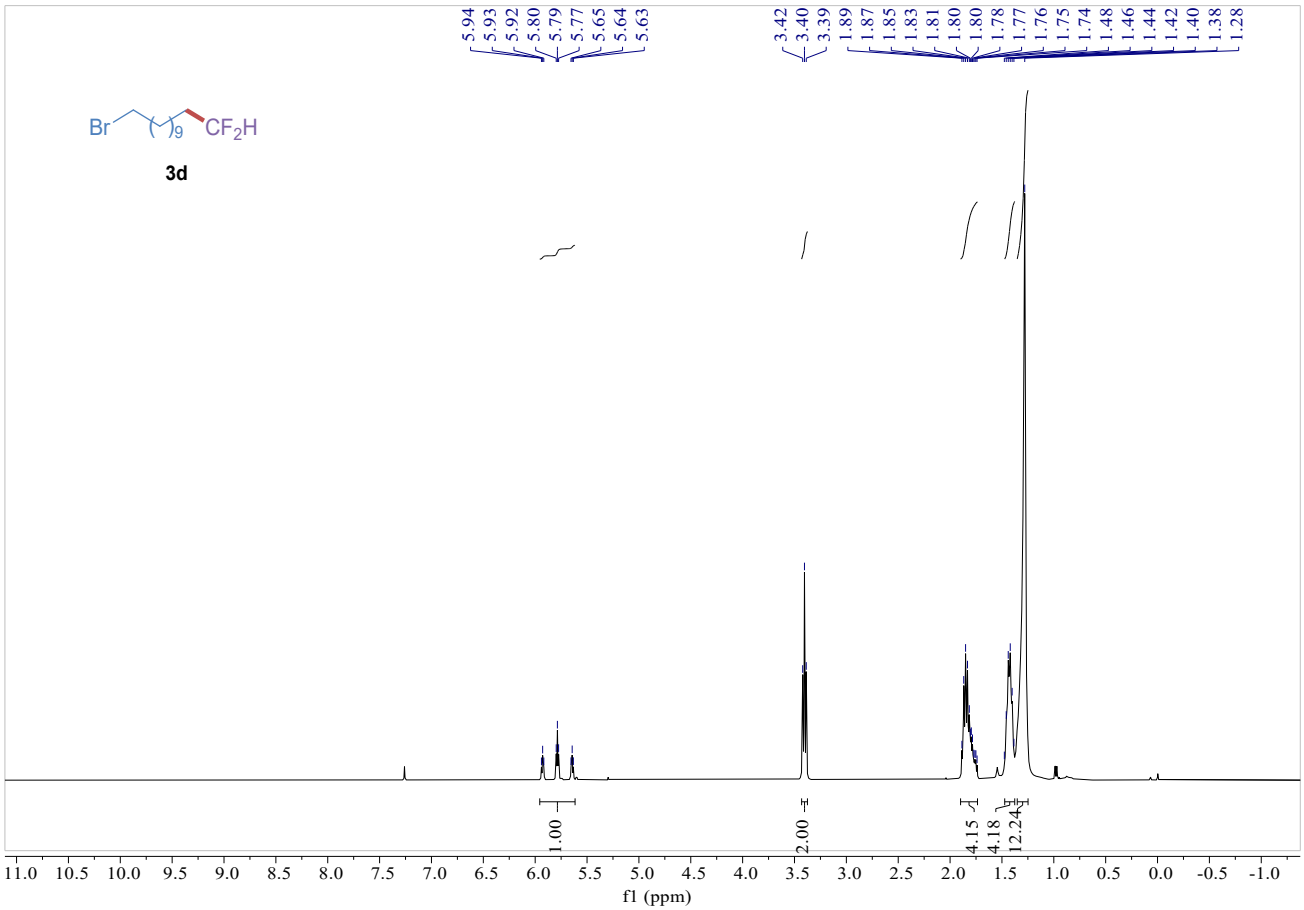
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound **3b**



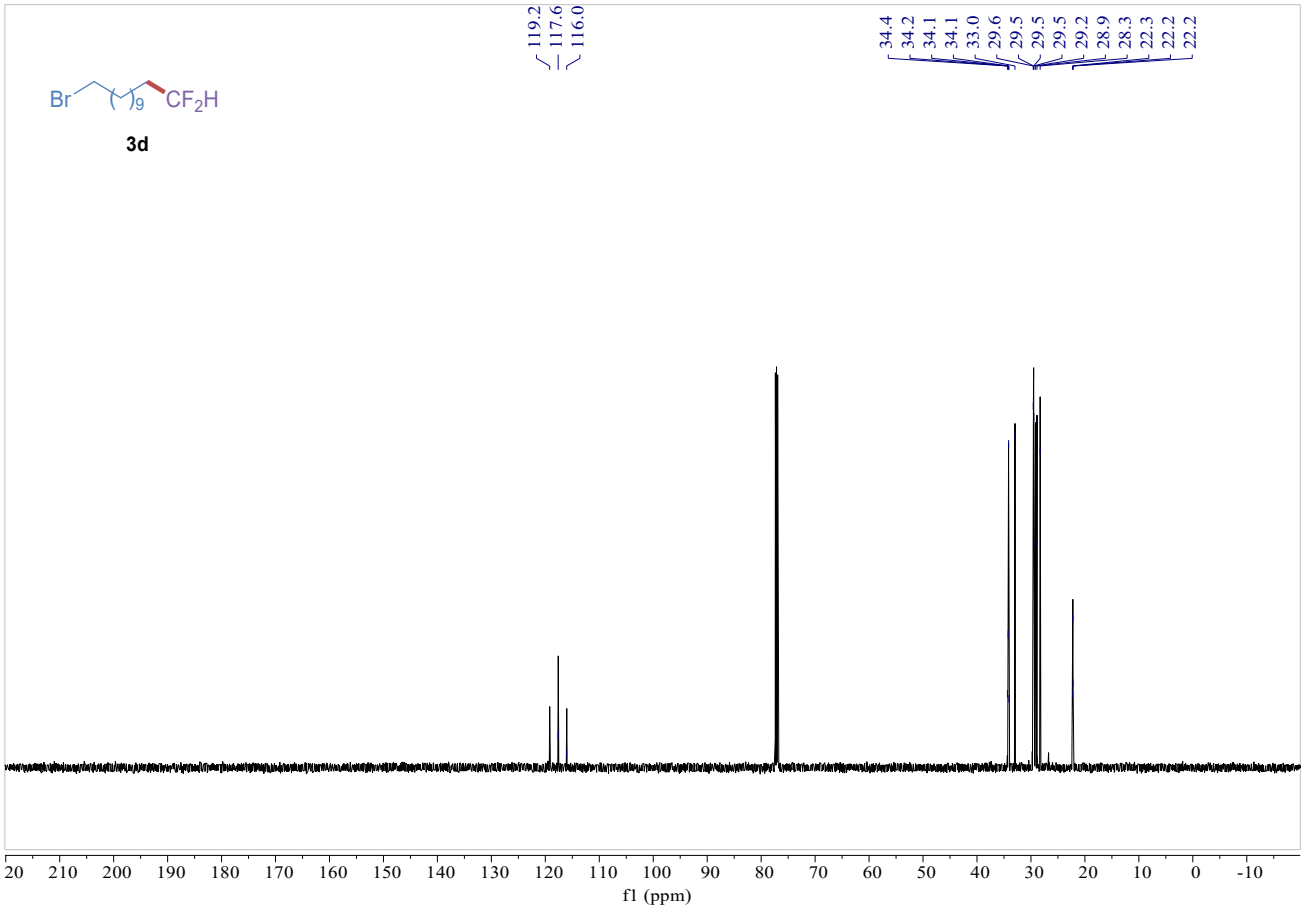
^{13}C NMR spectrum (151 MHz, $CDCl_3$) of compound **3b**



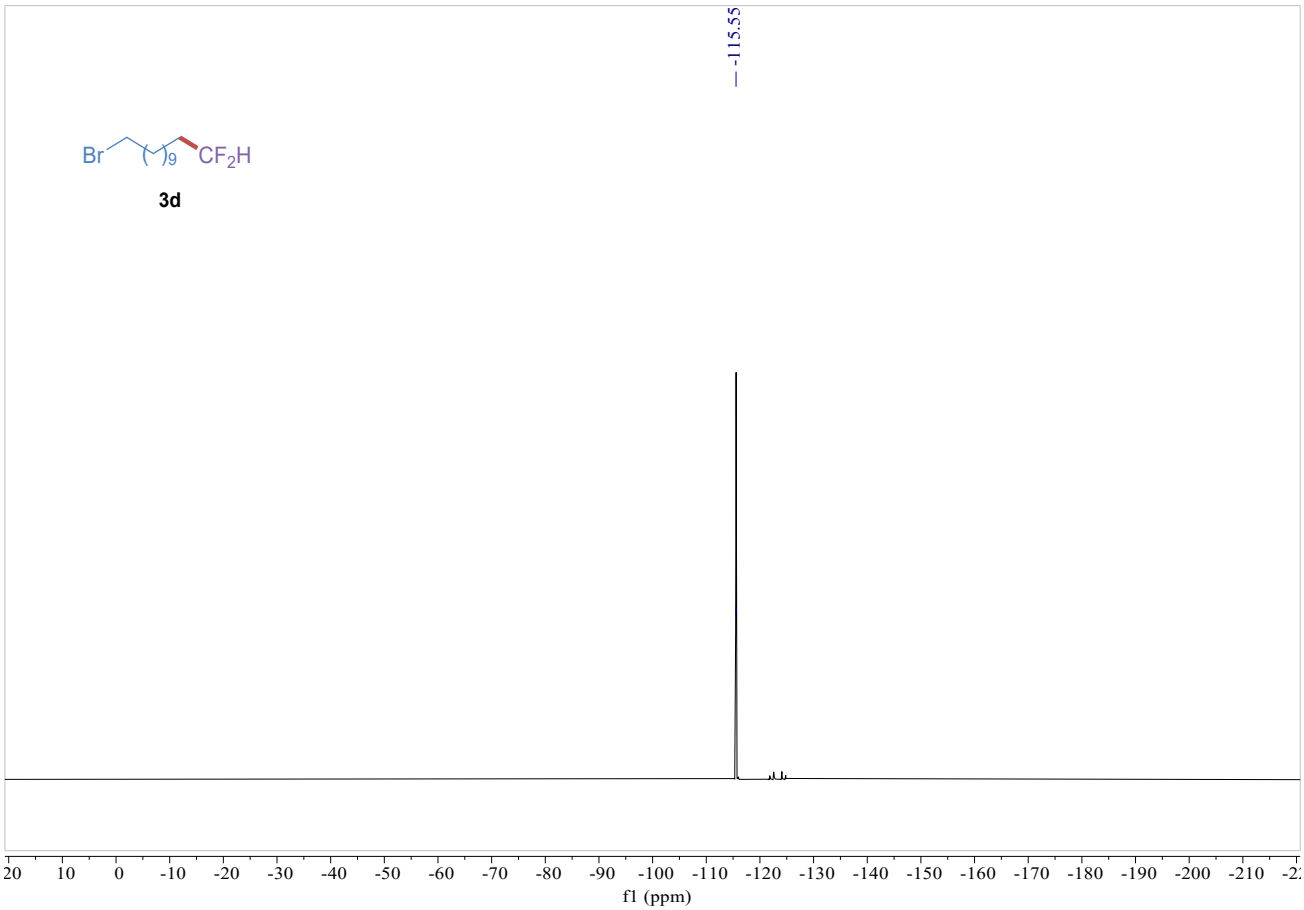
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3b**



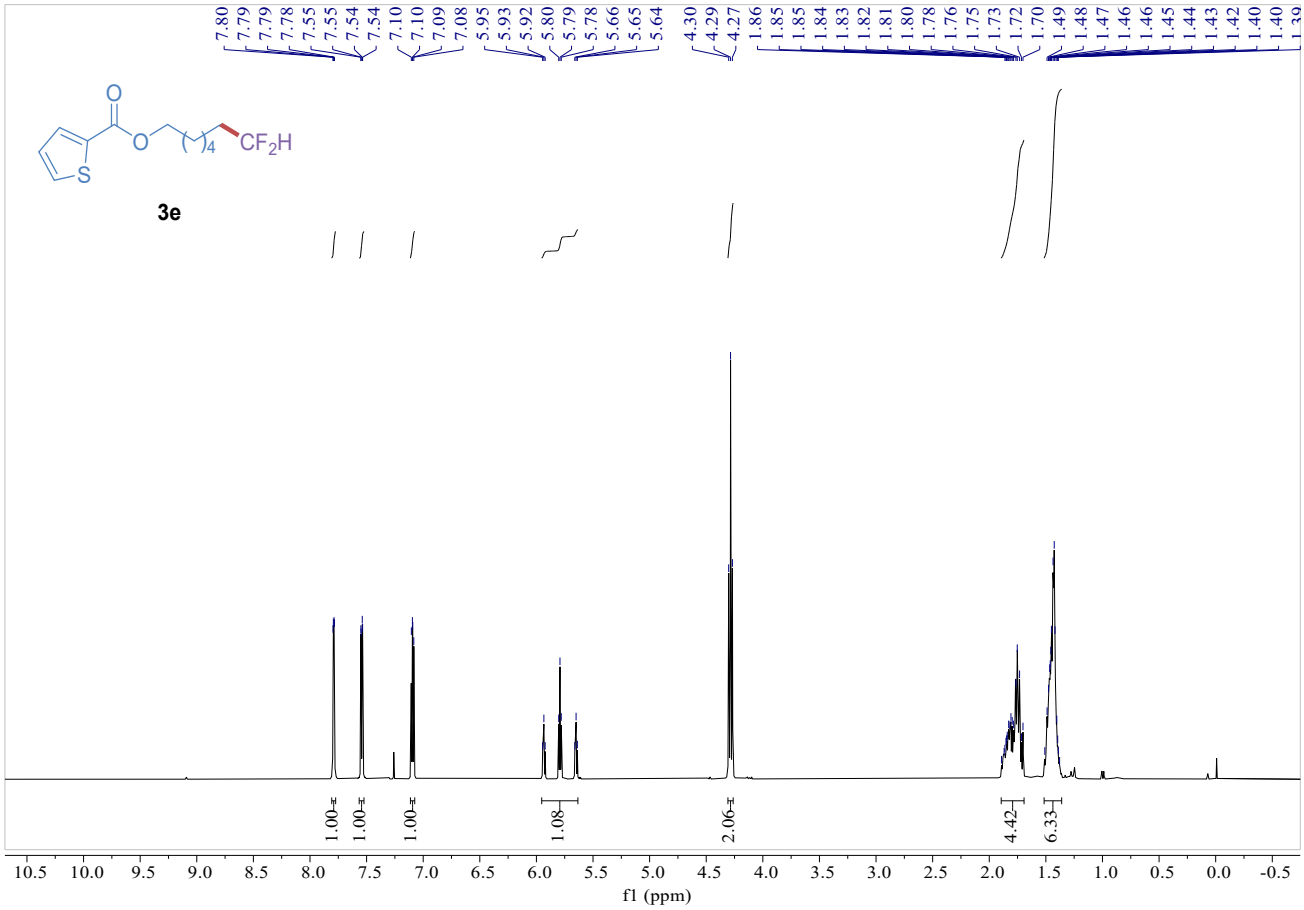
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3d**



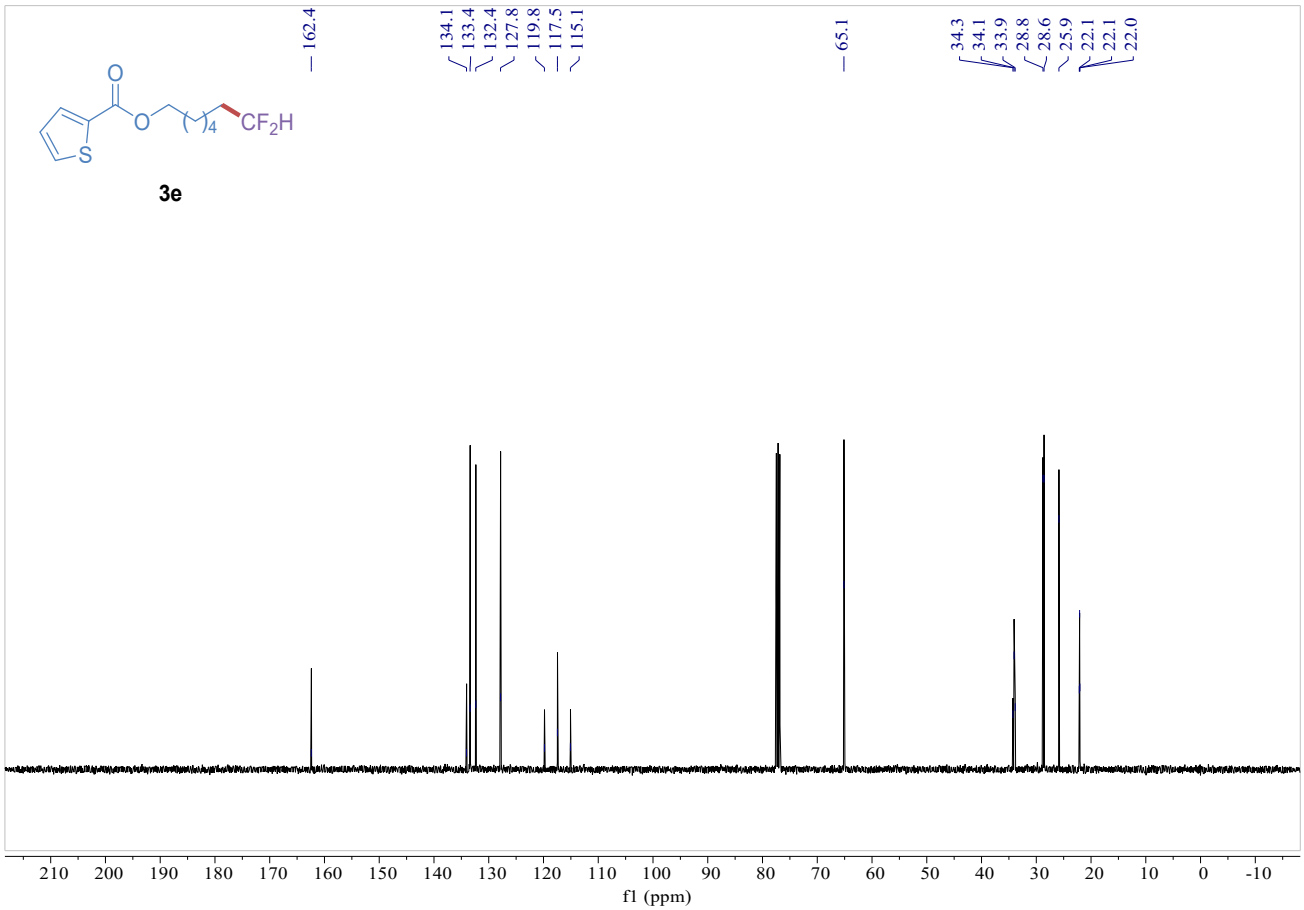
^{13}C NMR spectrum (151 MHz, $CDCl_3$) of compound **3d**



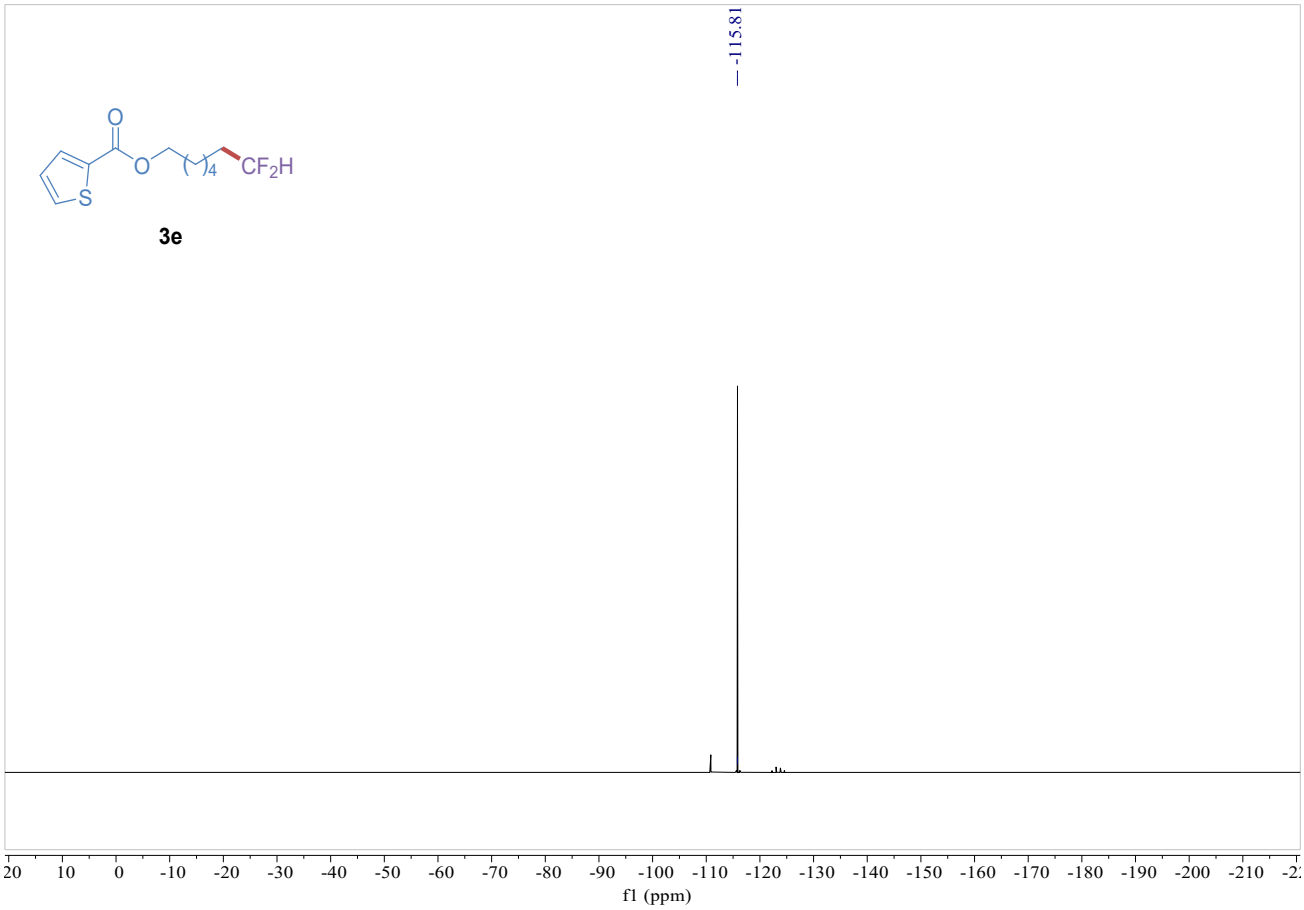
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3d**



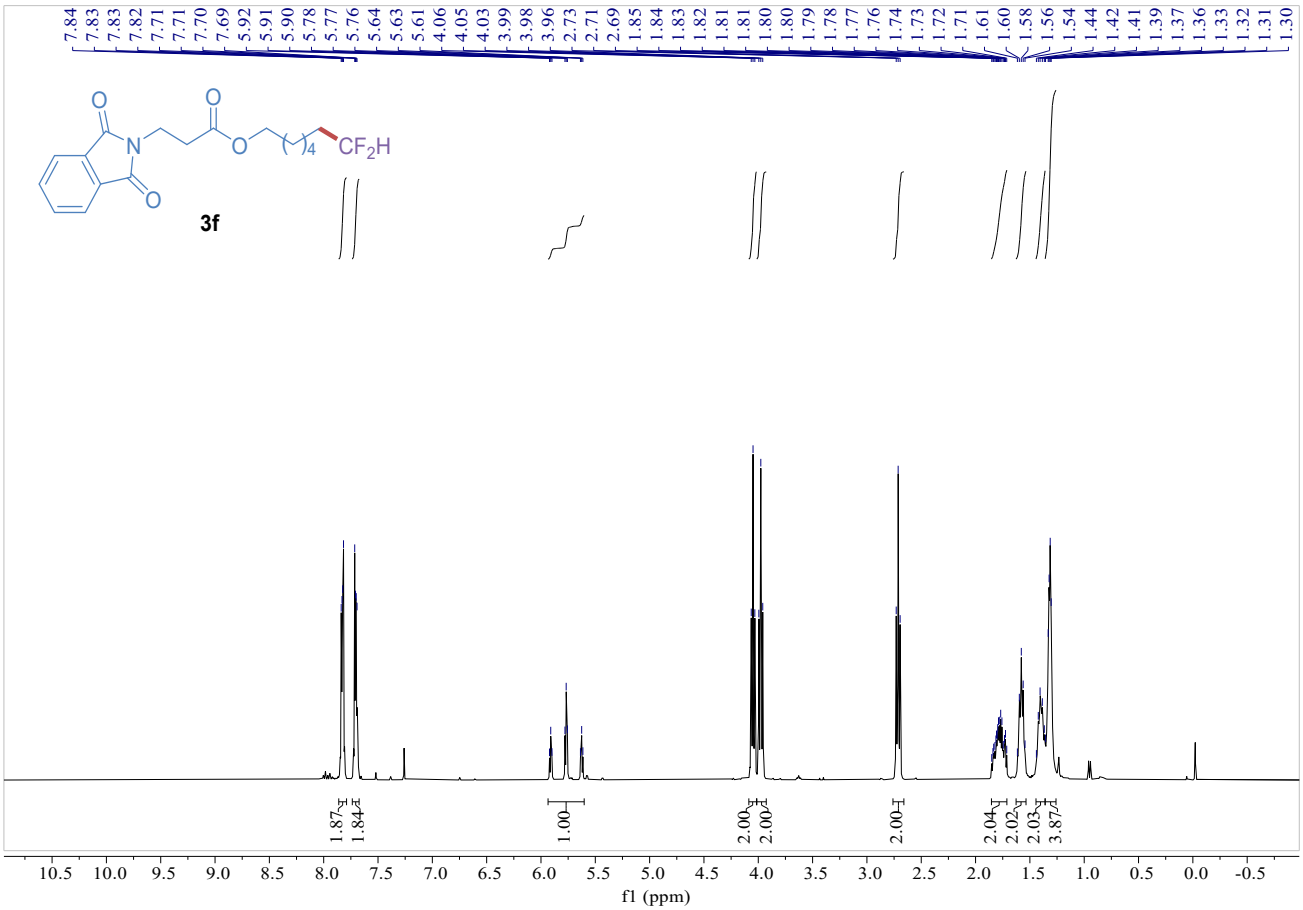
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3e**



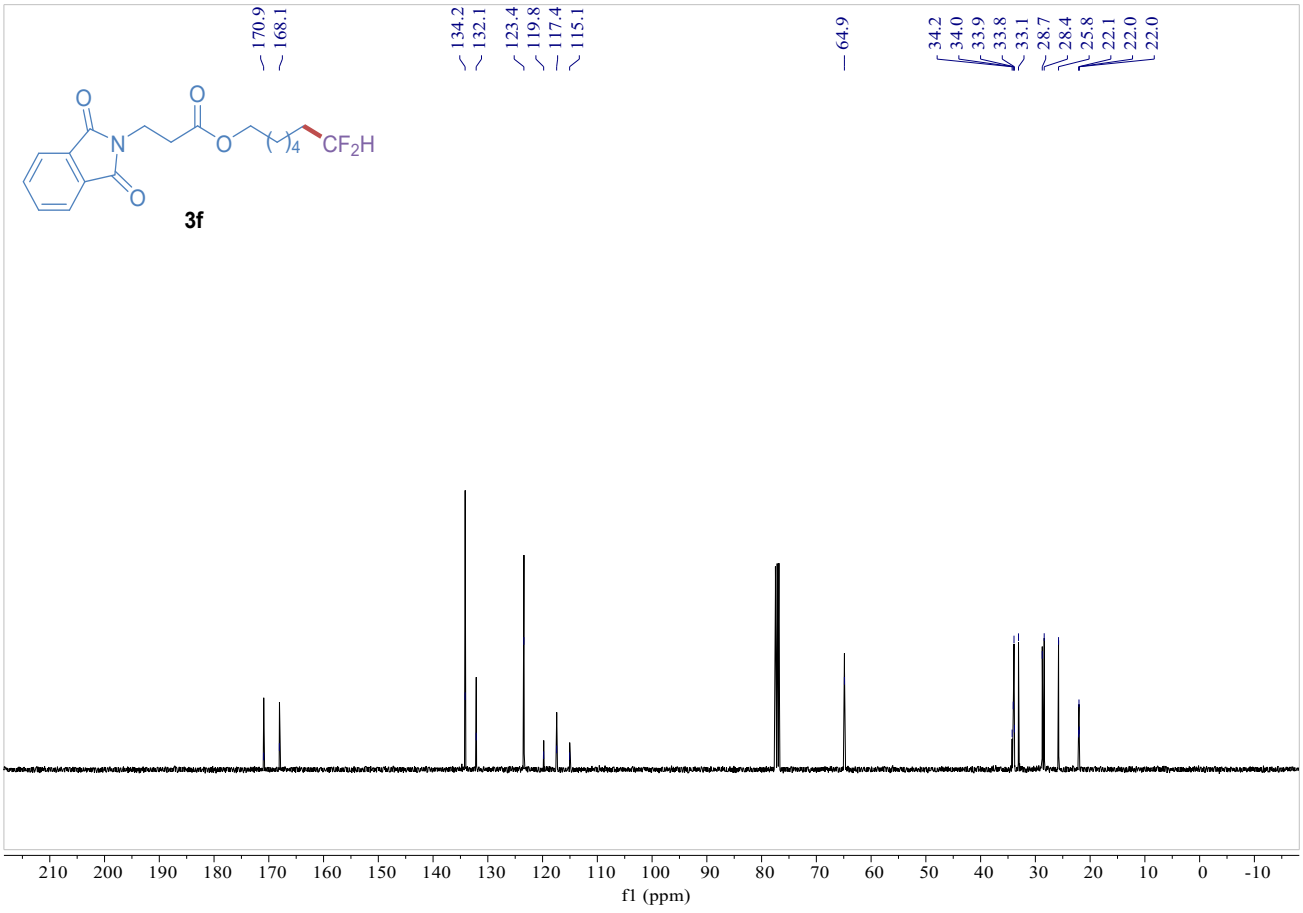
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **3e**



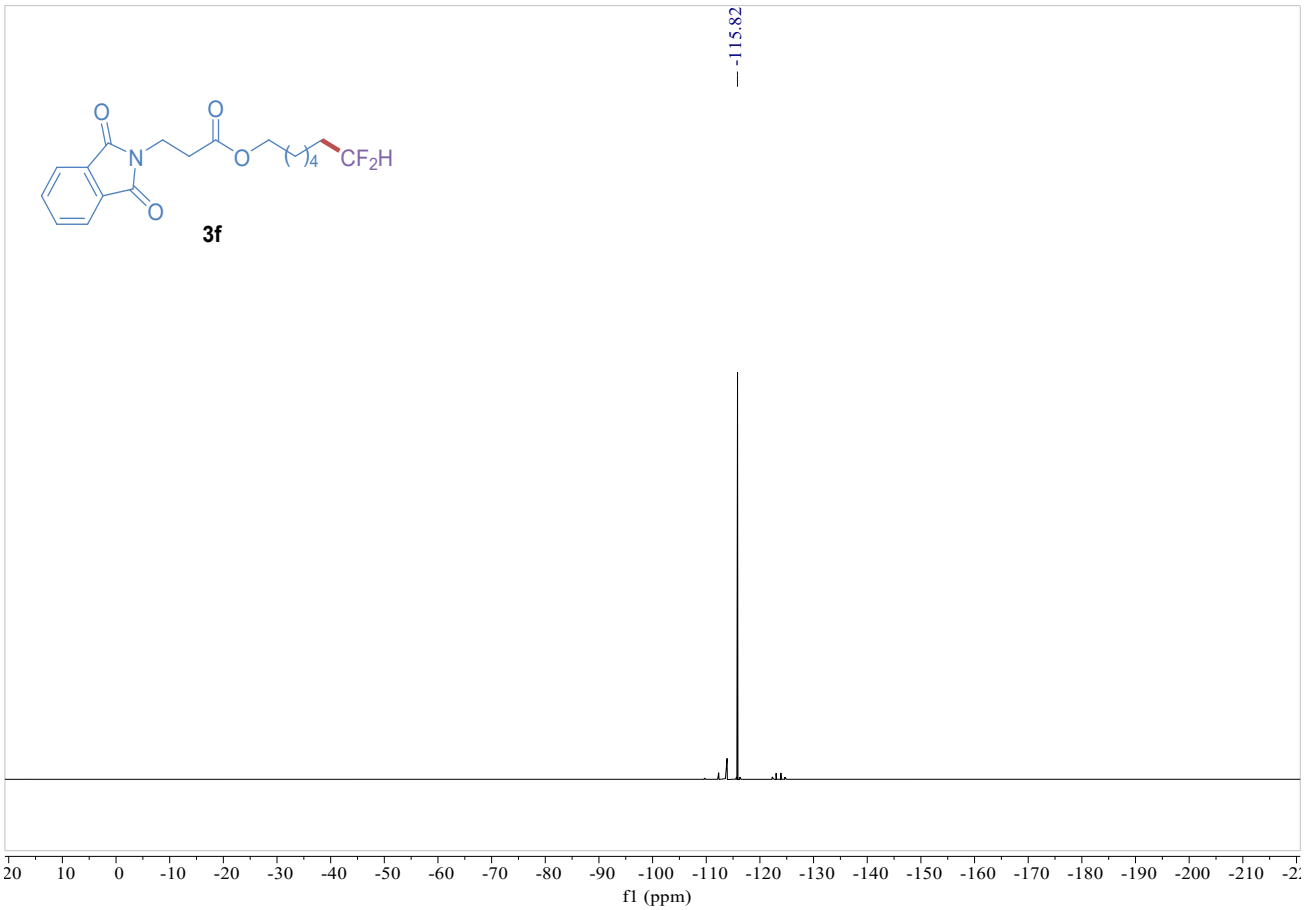
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3e**



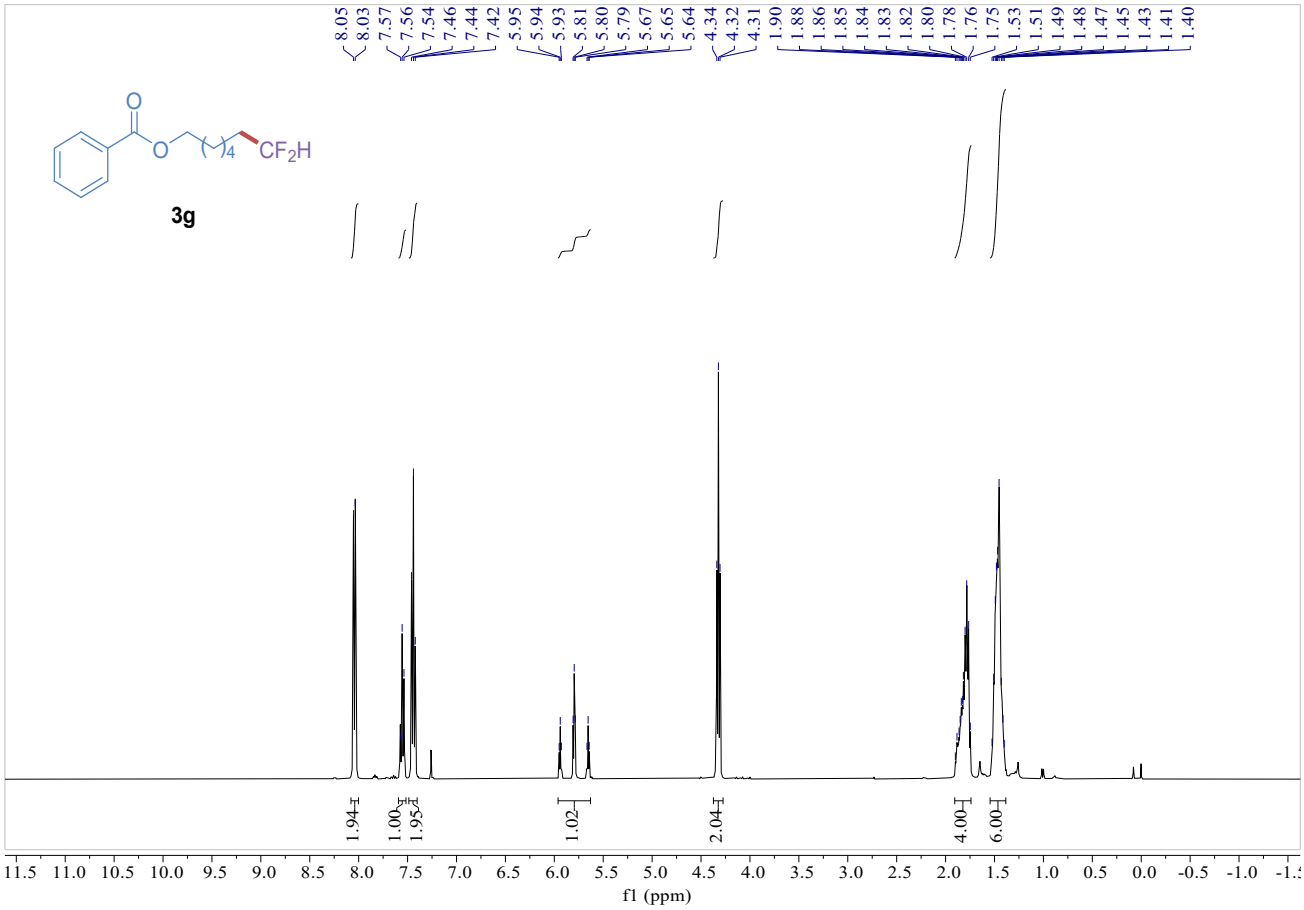
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3f**



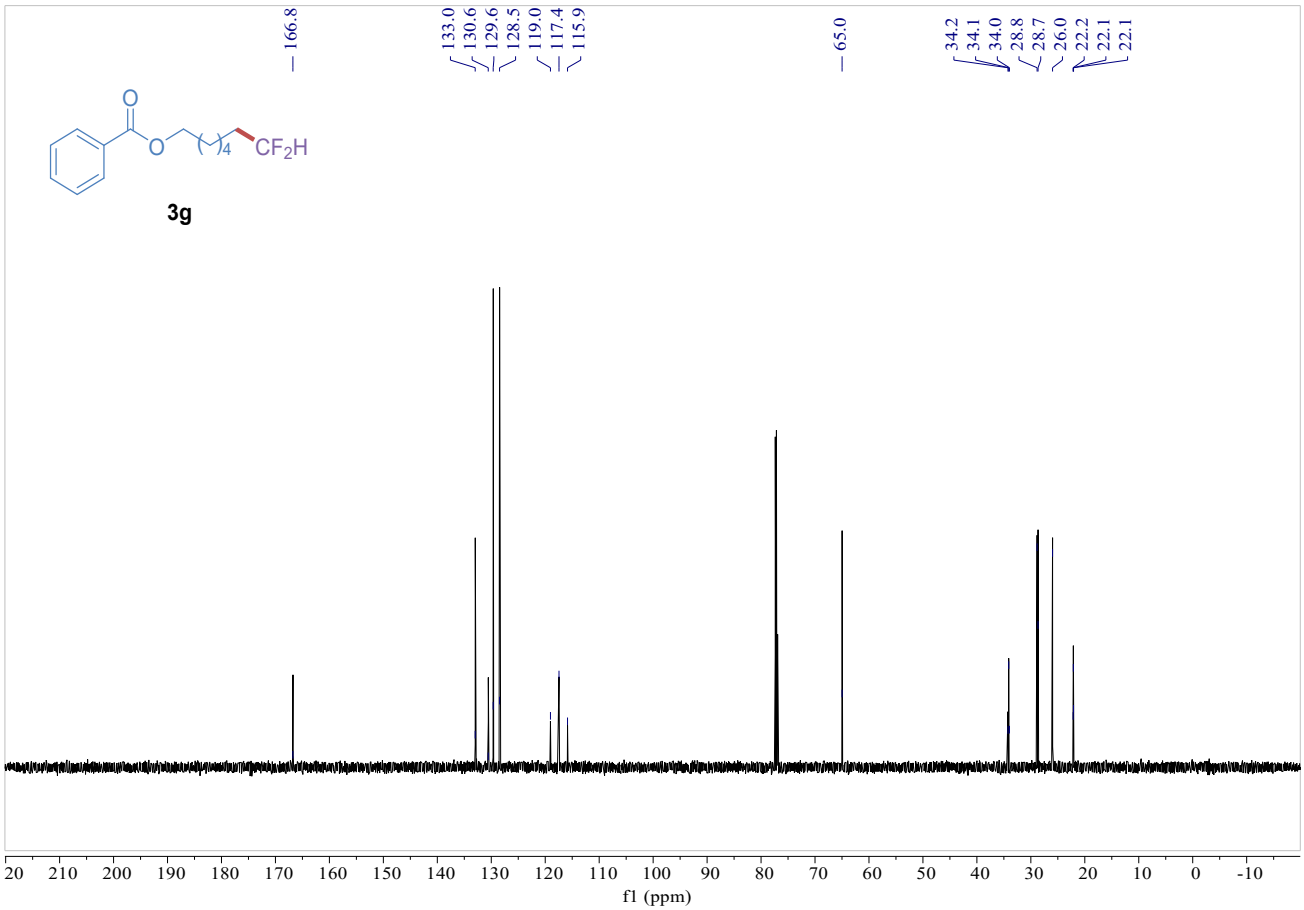
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **3f**



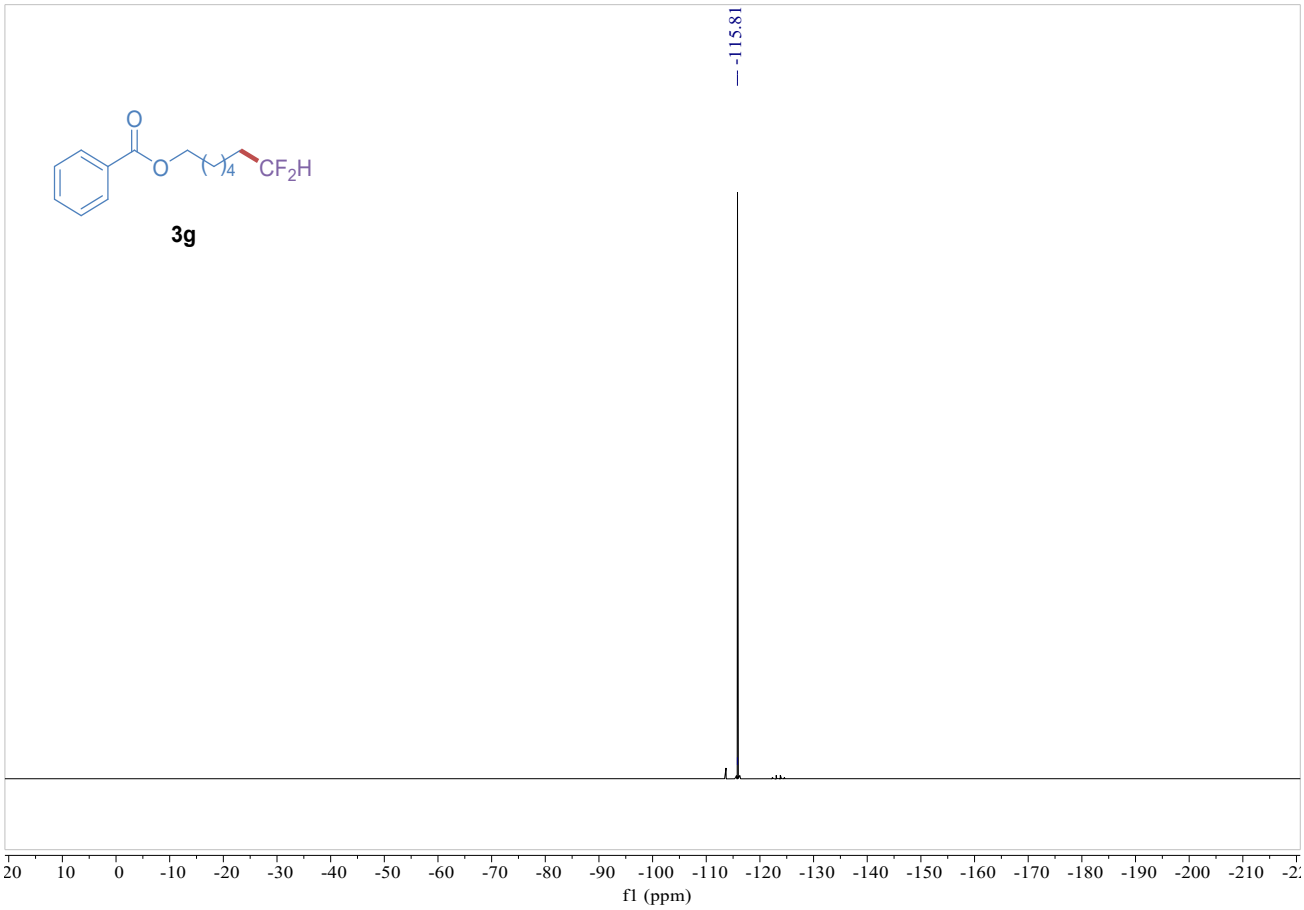
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3f**



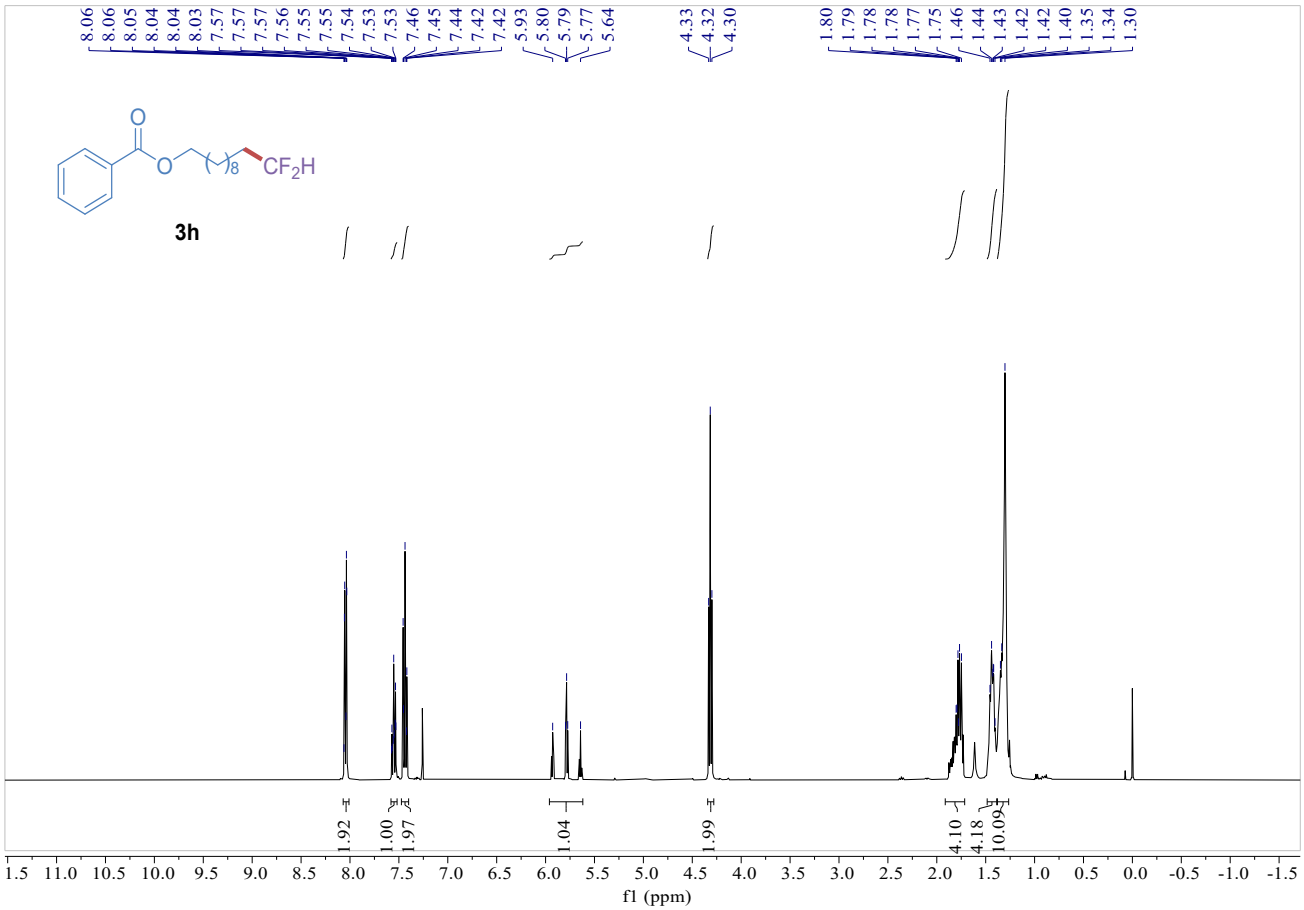
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3g**



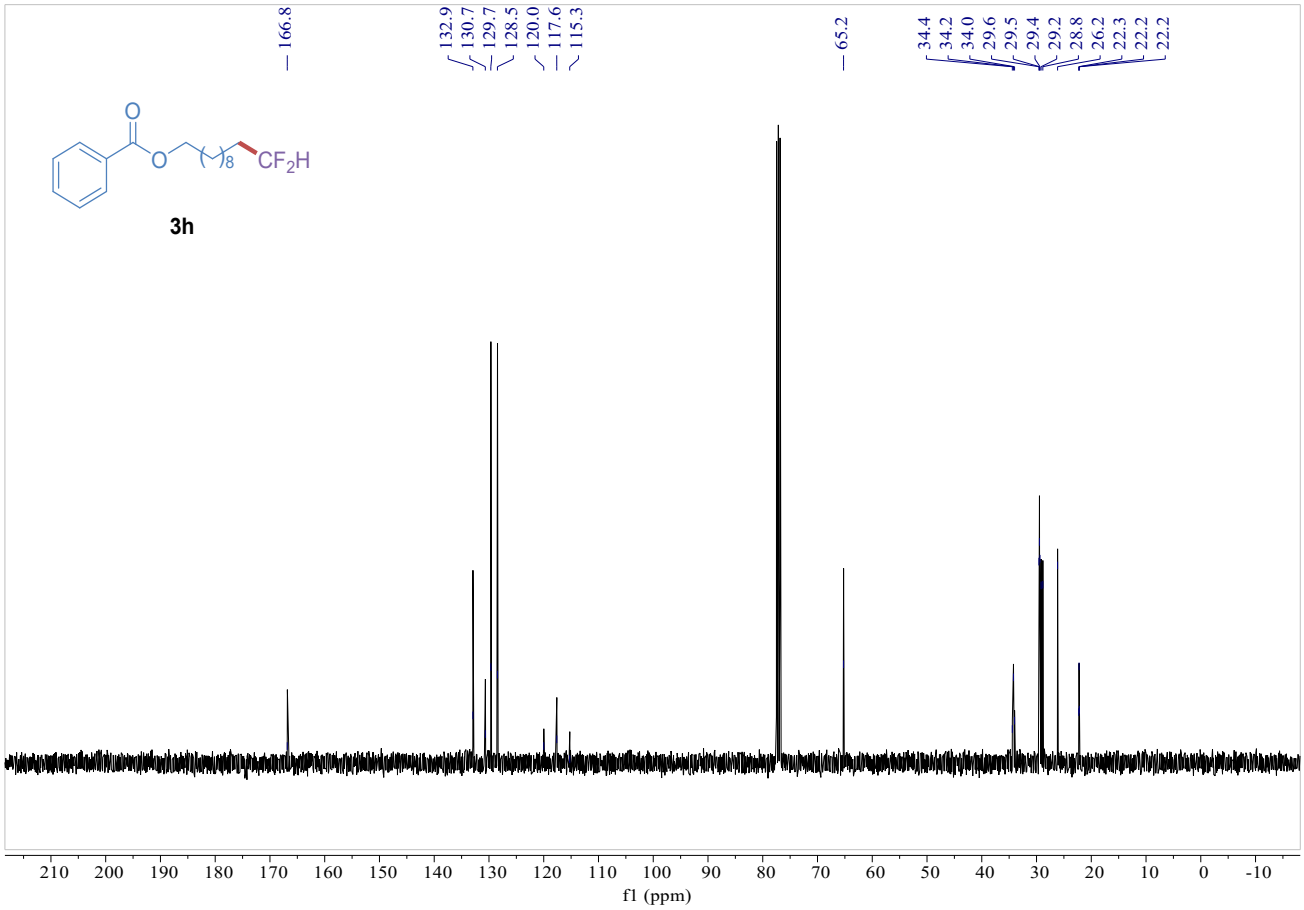
^{13}C NMR spectrum (151 MHz, $CDCl_3$) of compound **3g**



^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3g**



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3h**



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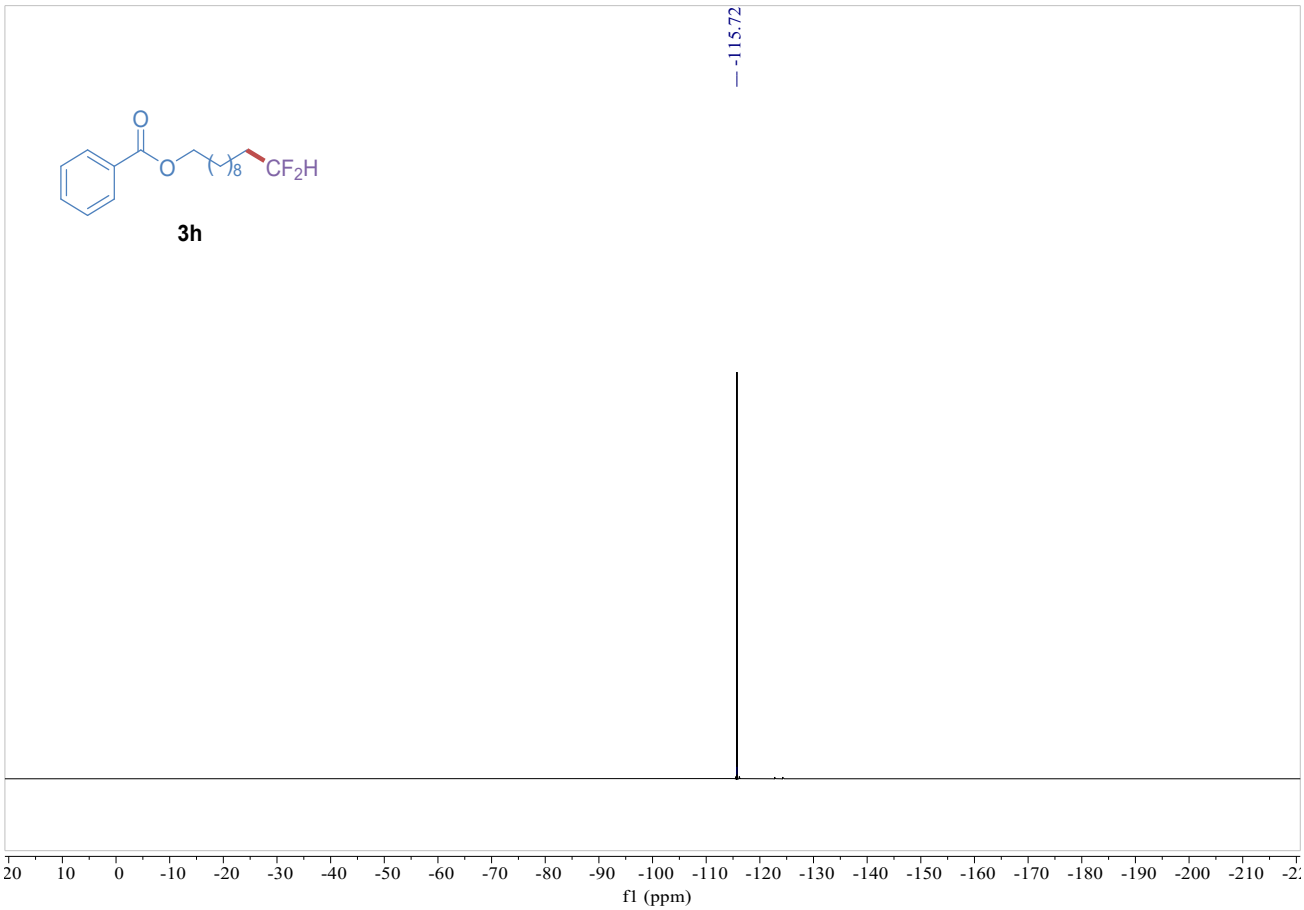

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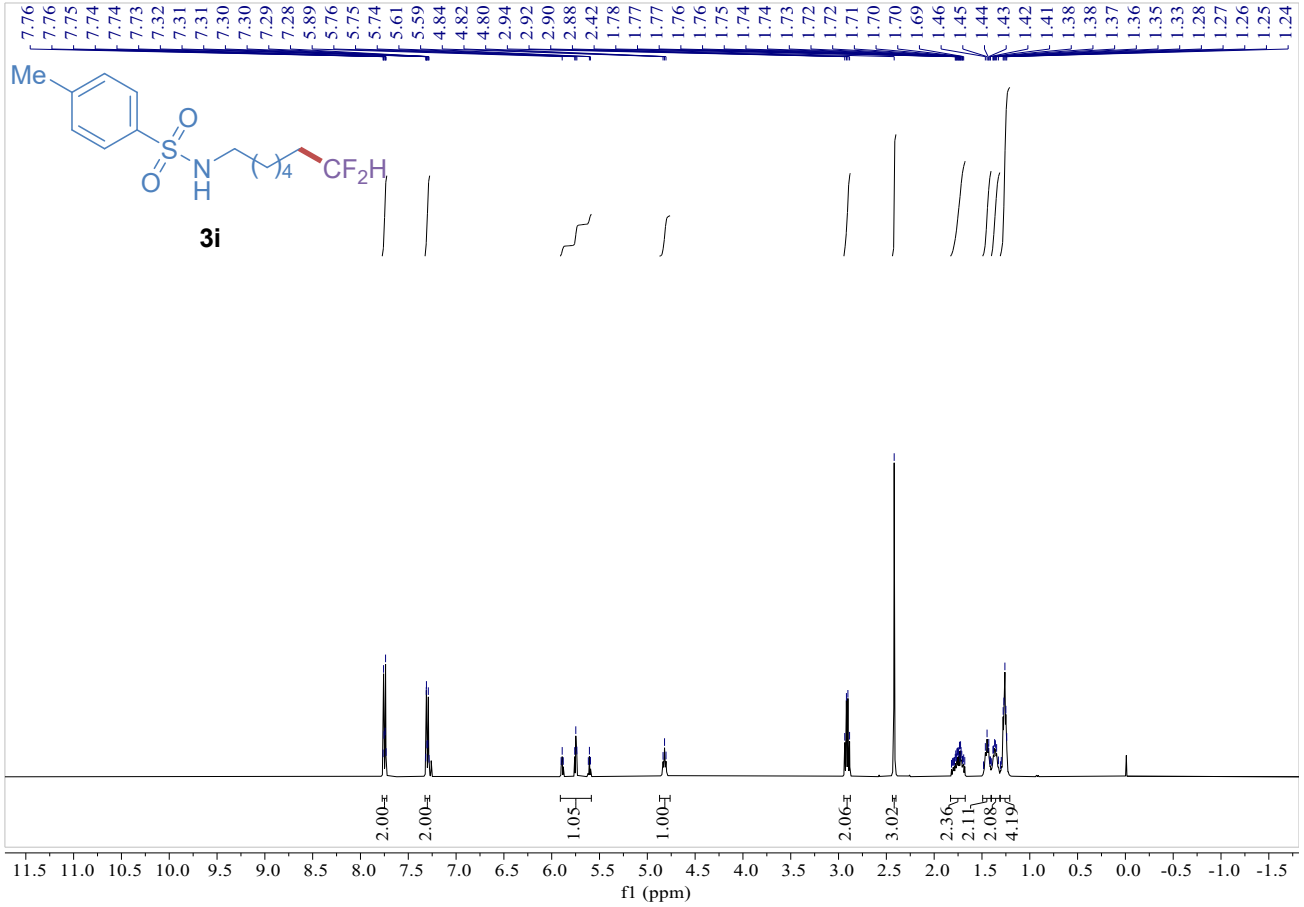
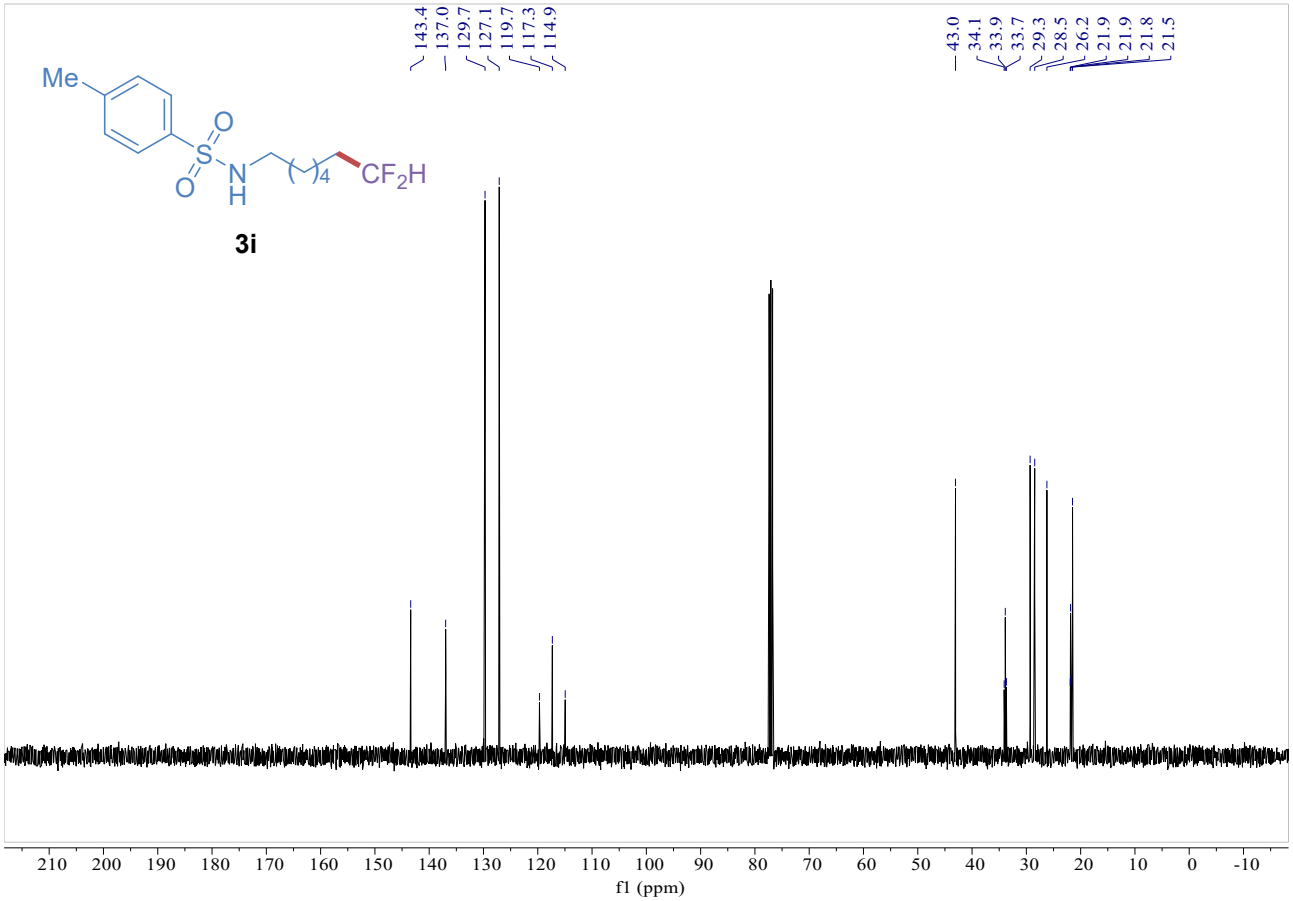


^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3i**



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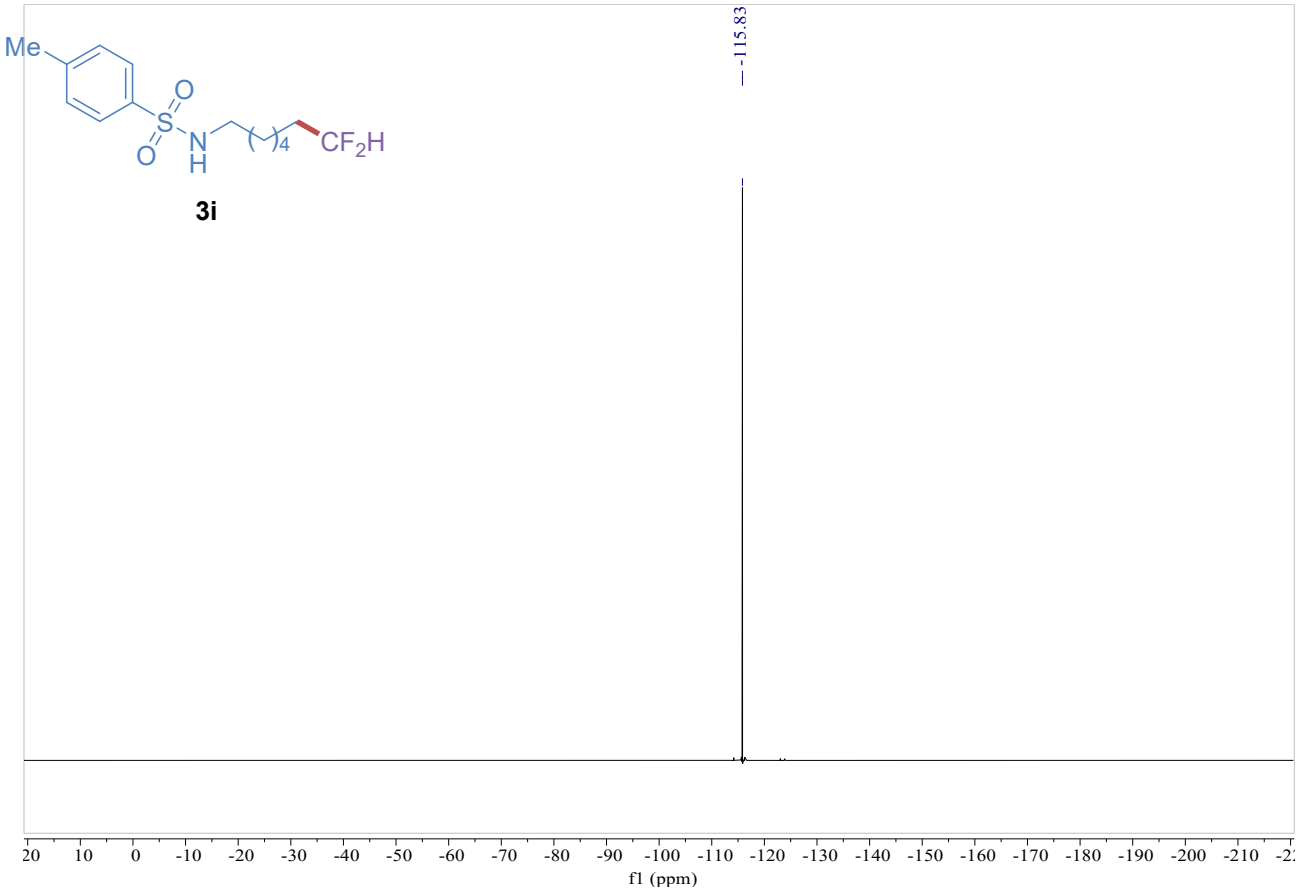

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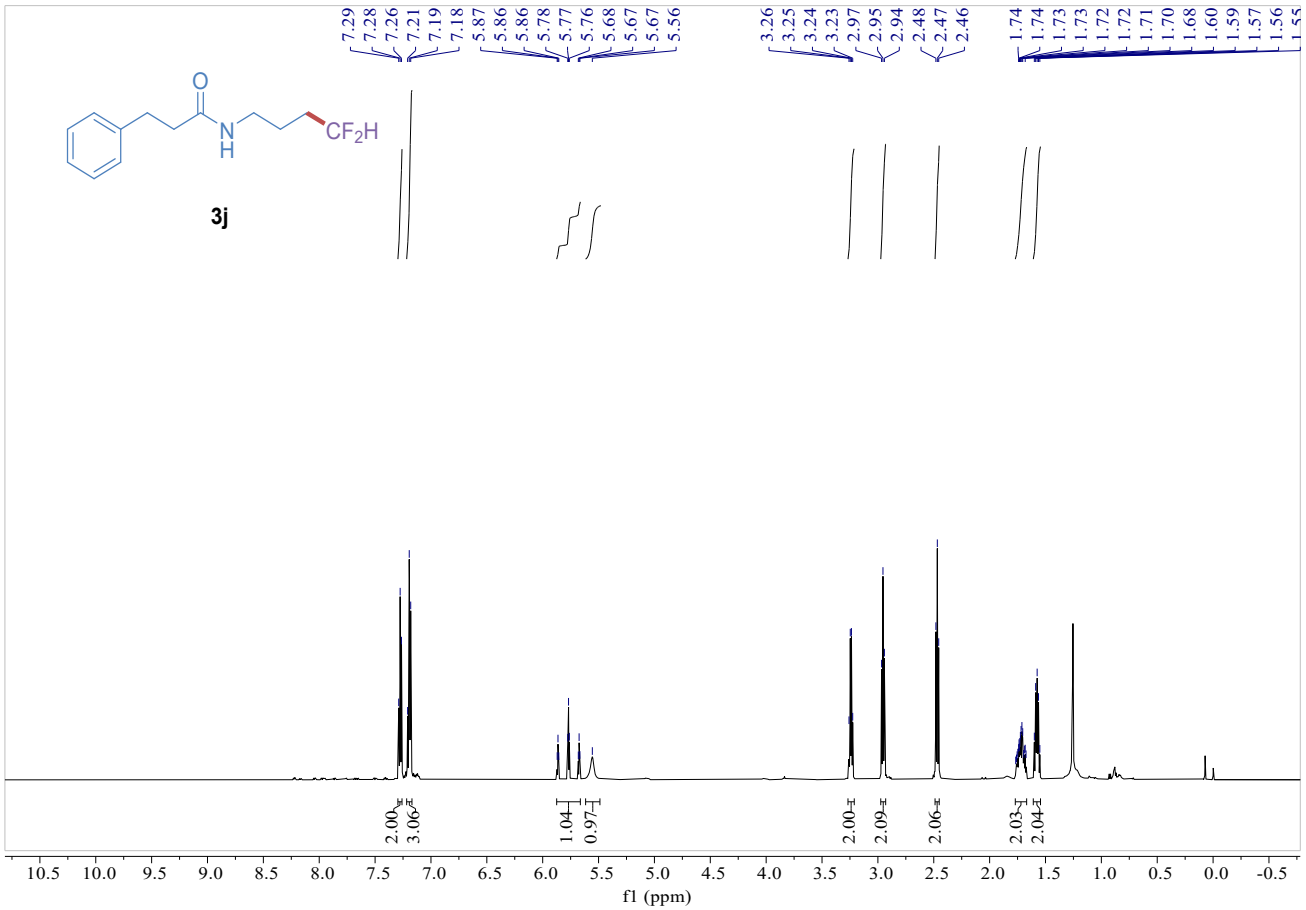
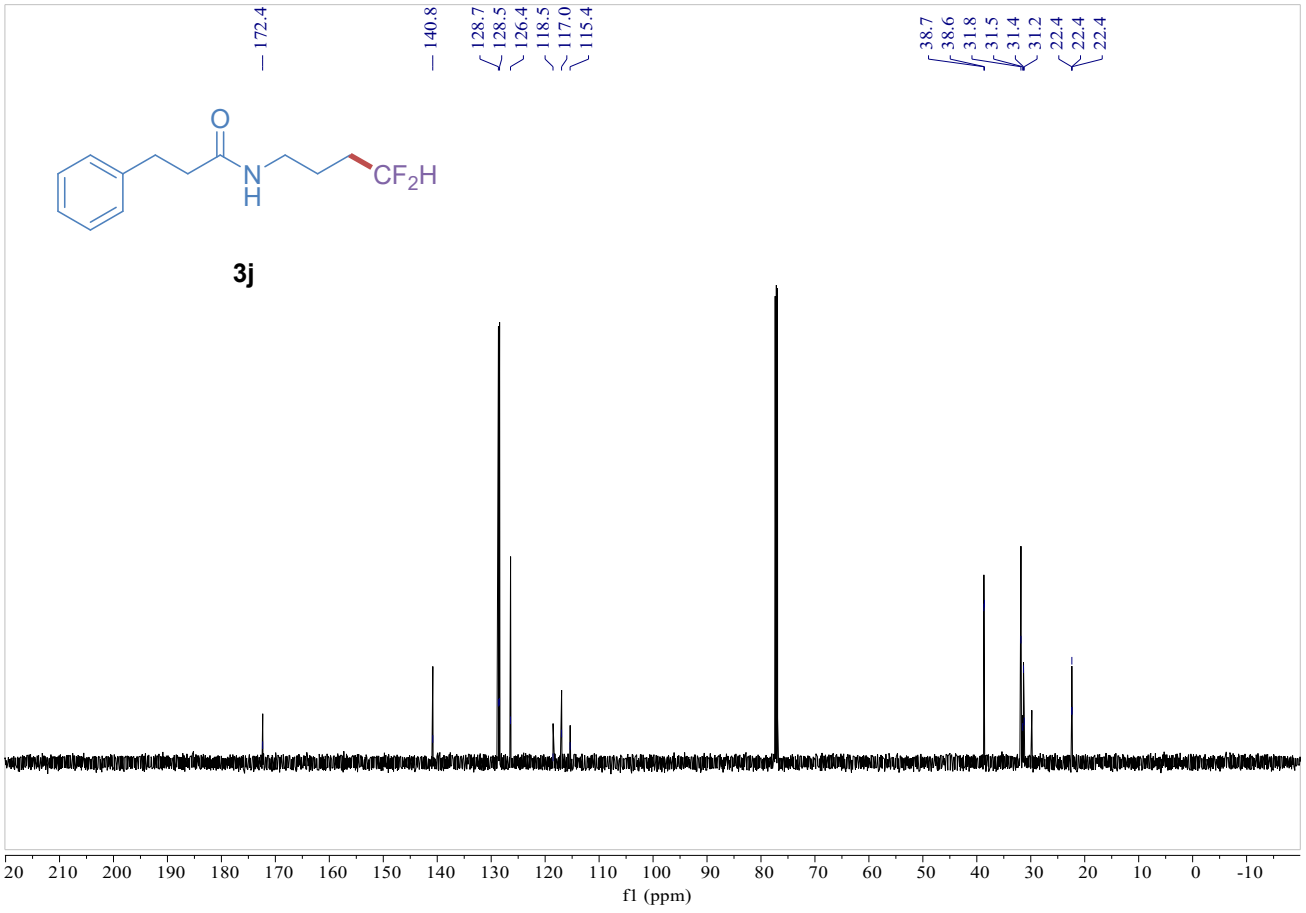
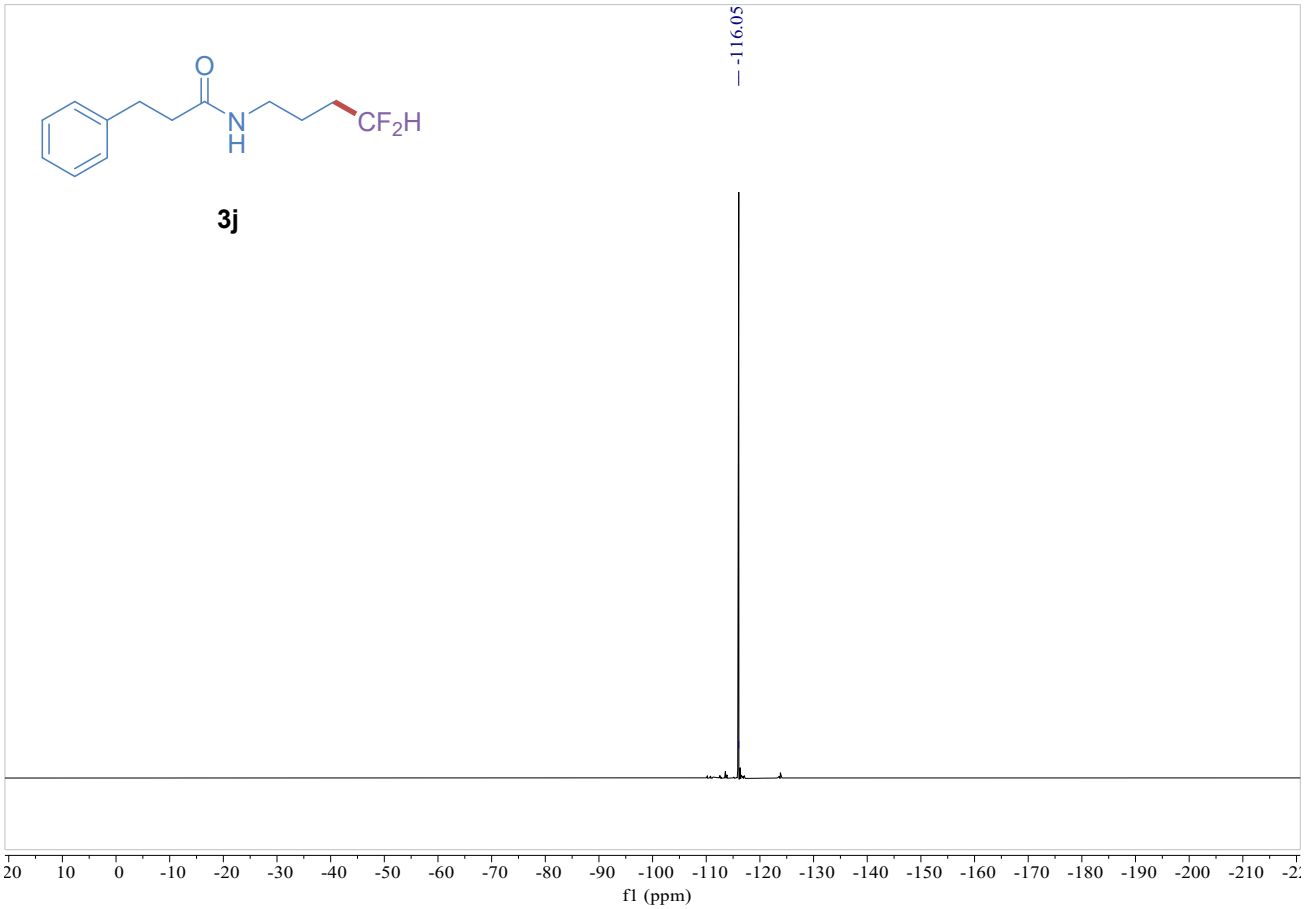


^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound **3j**



^{13}C NMR spectrum (151 MHz, $CDCl_3$) of compound **3j**



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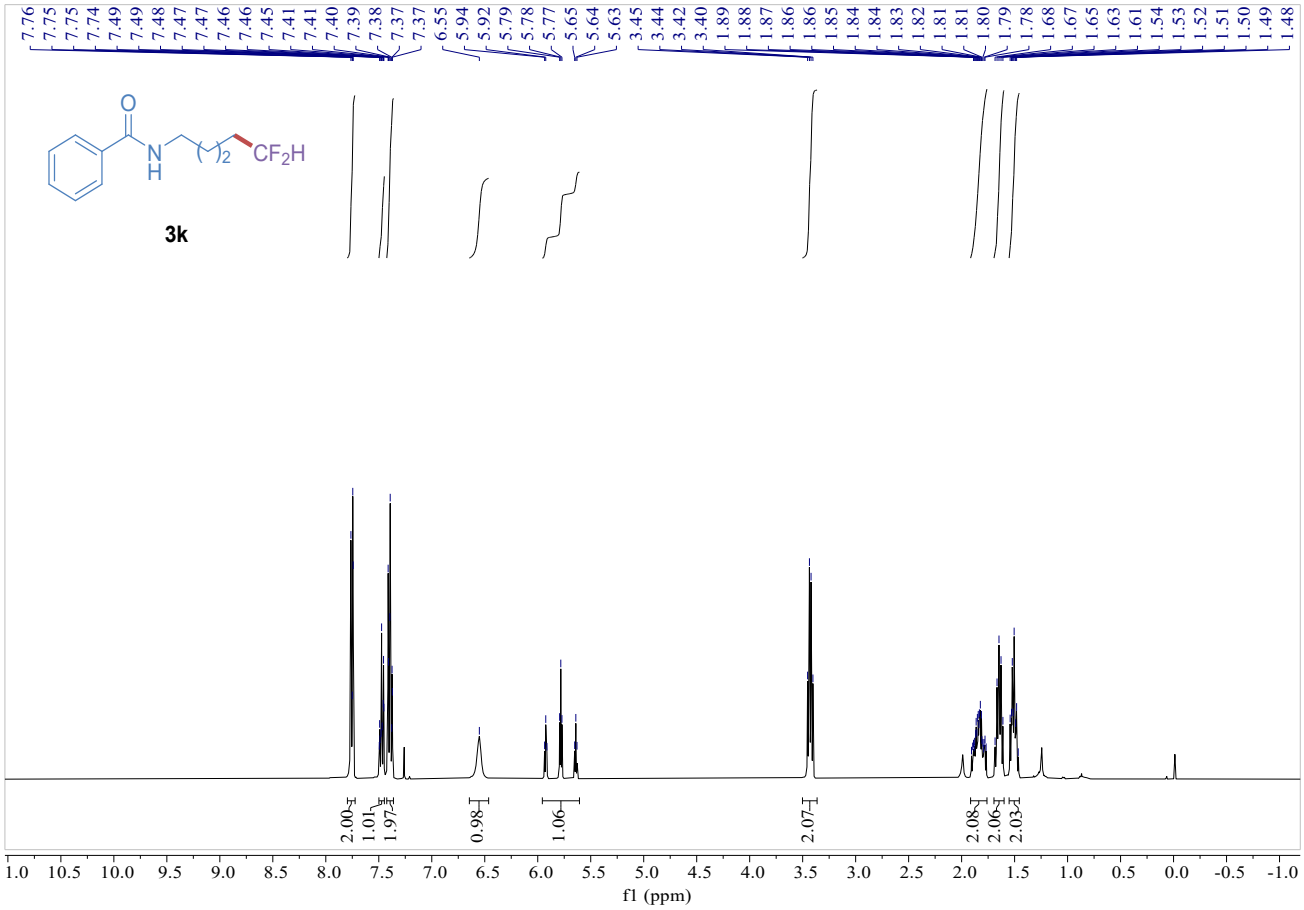

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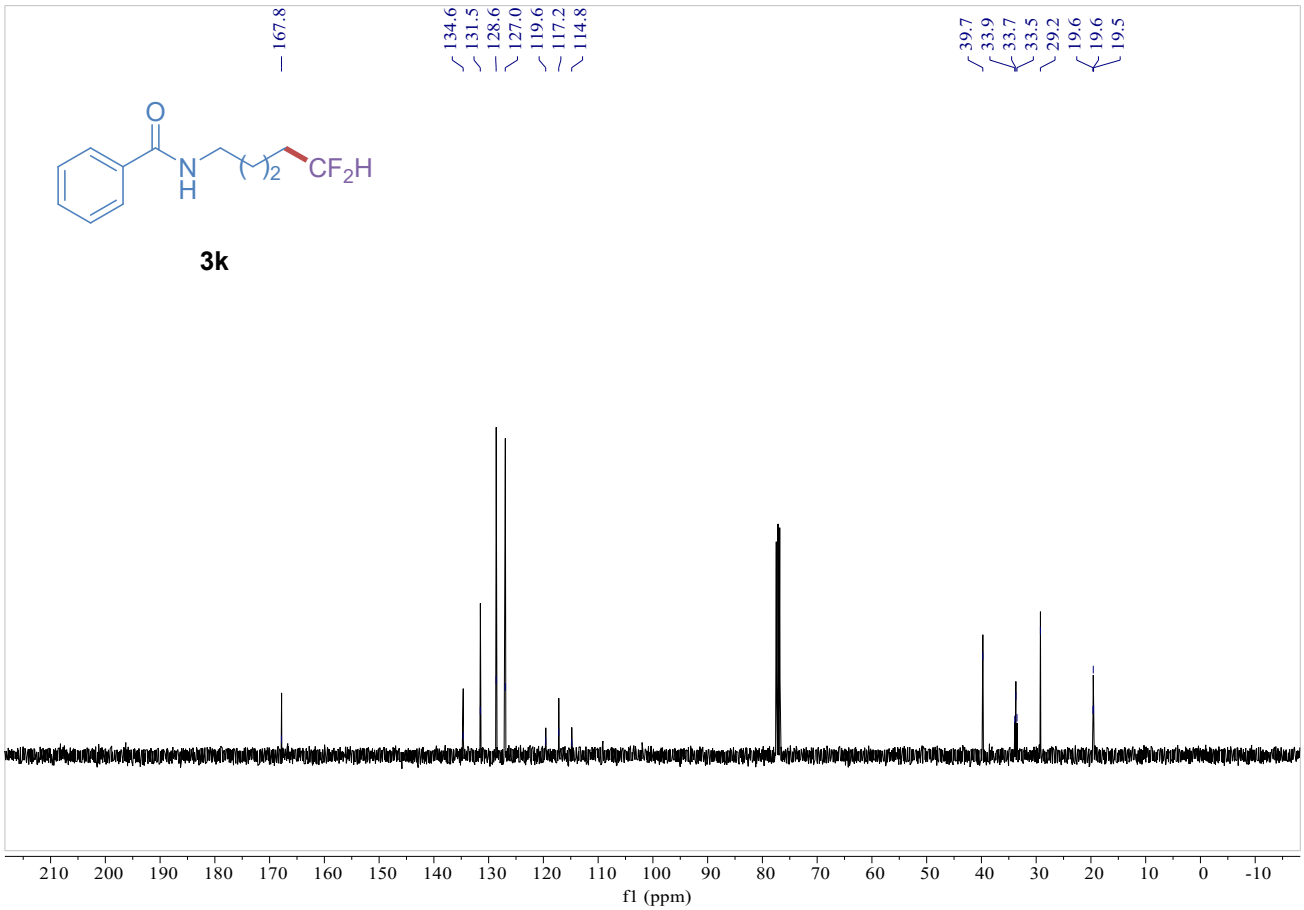
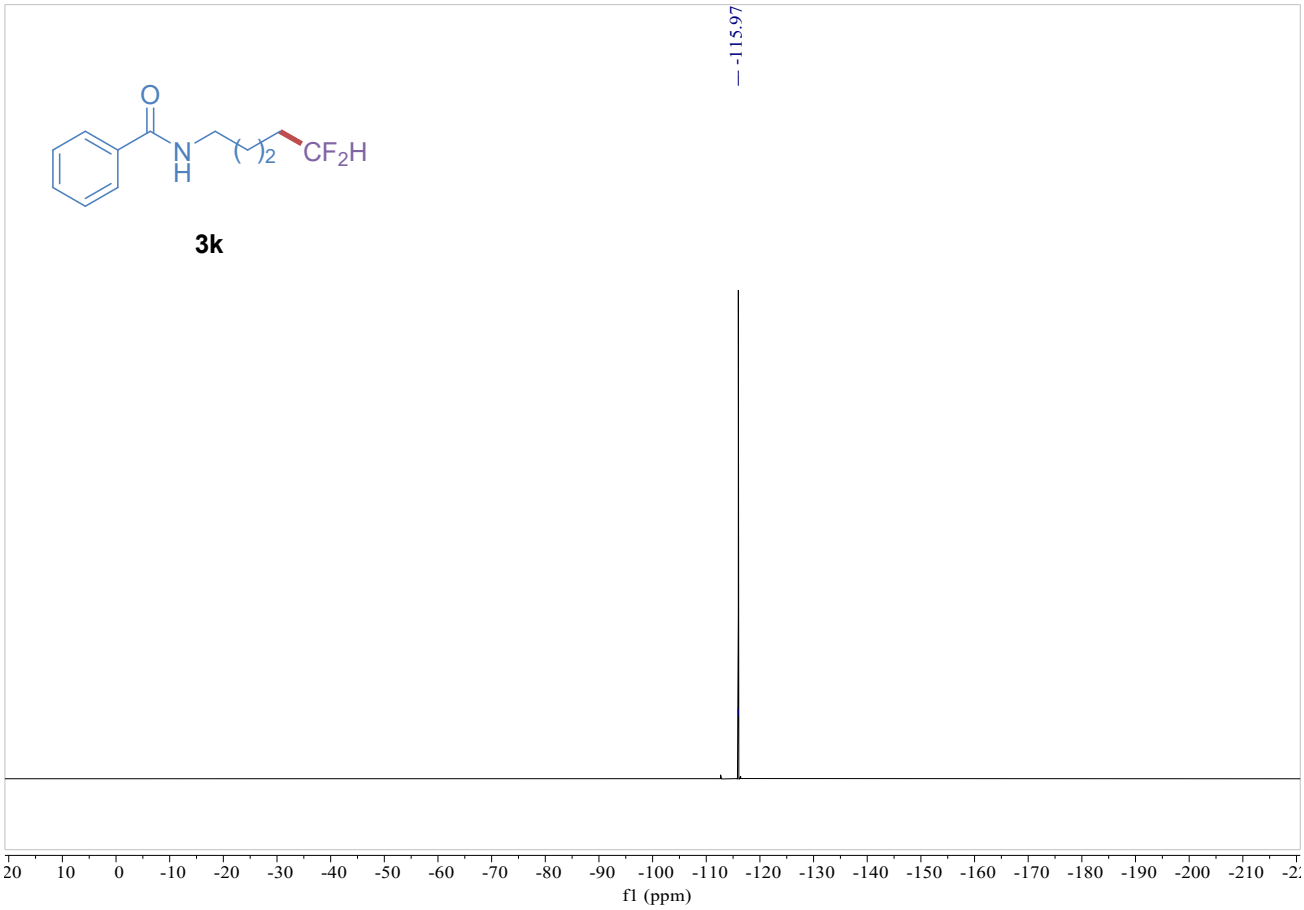
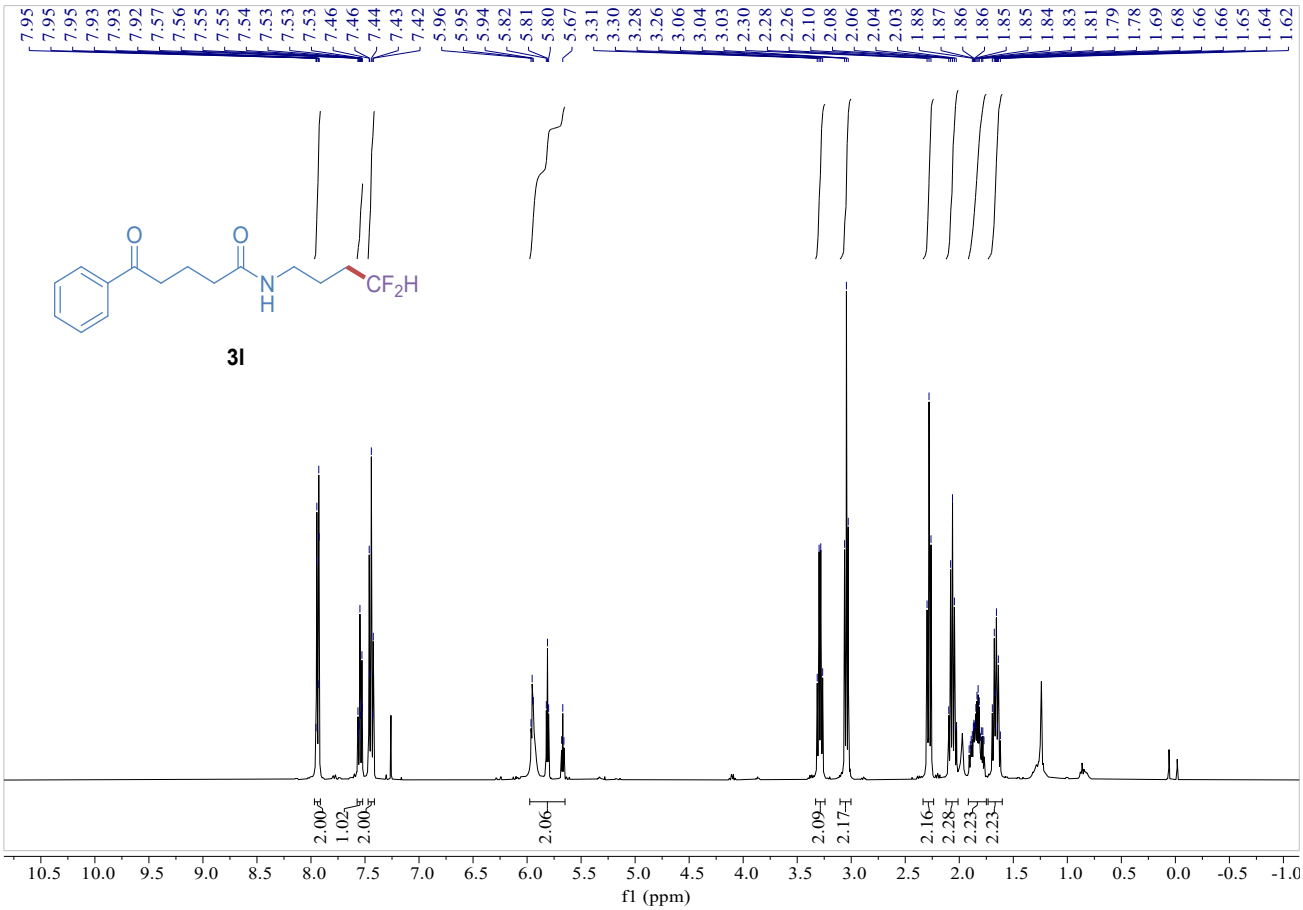


^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **3k**



^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3k**



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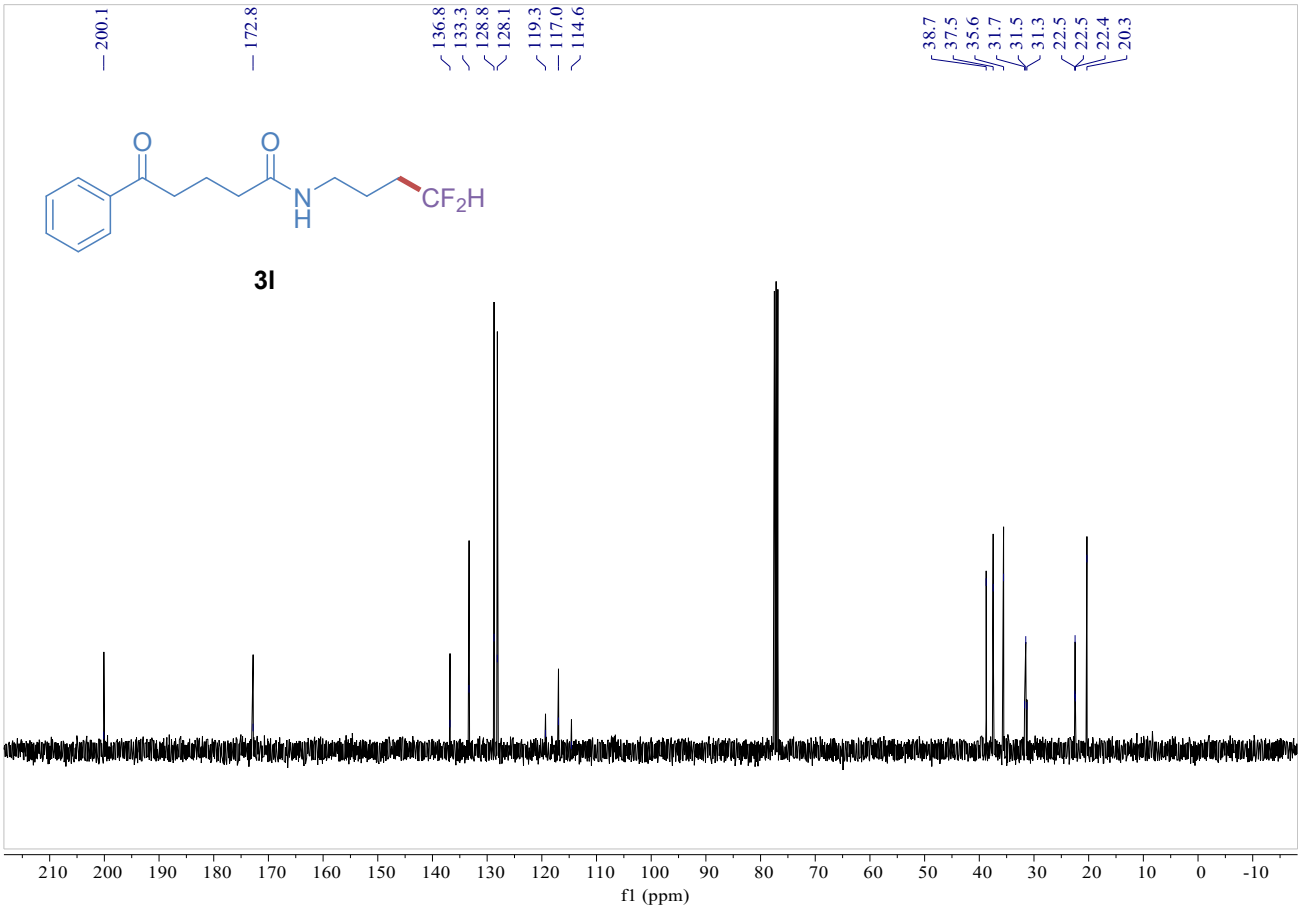

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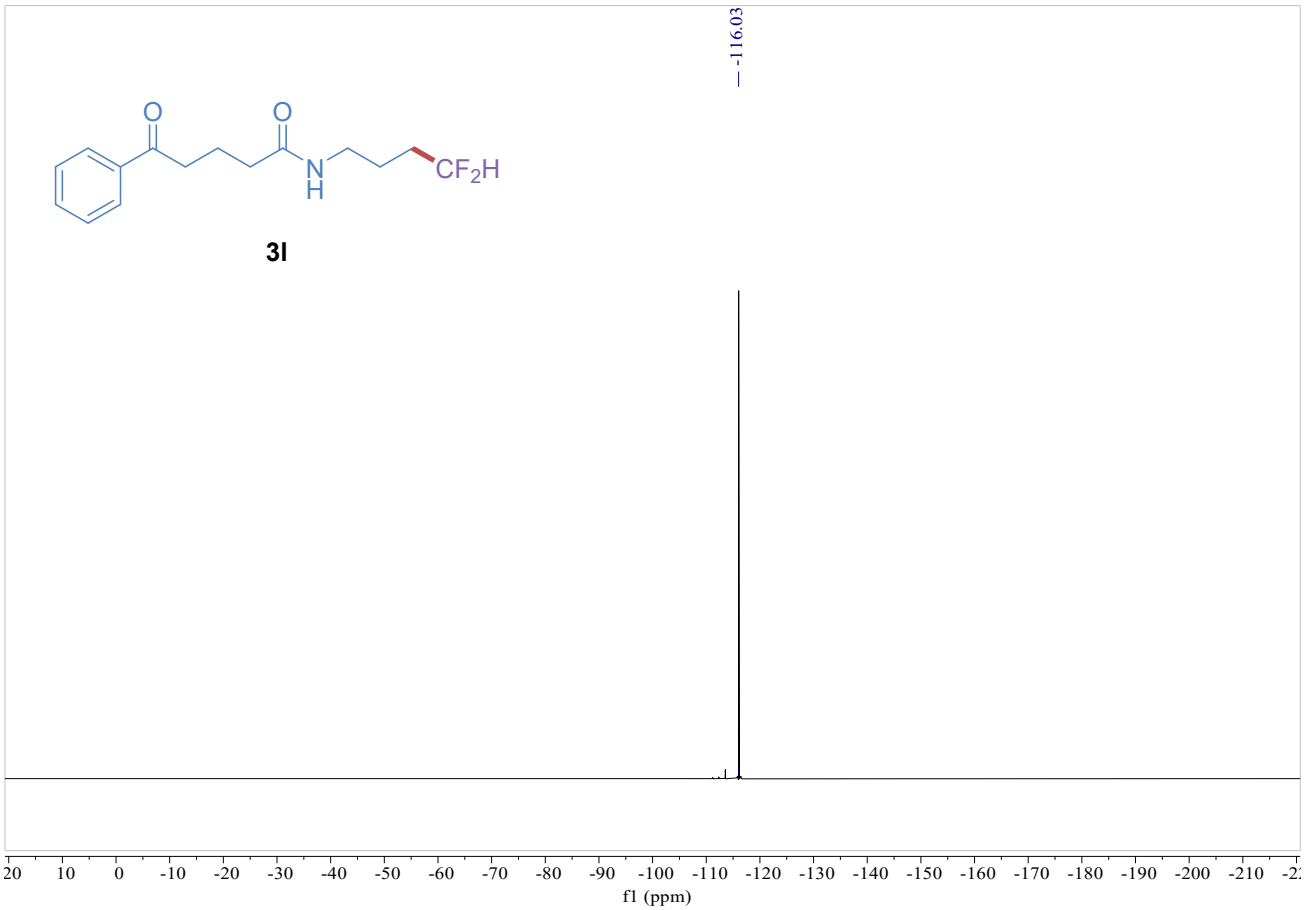

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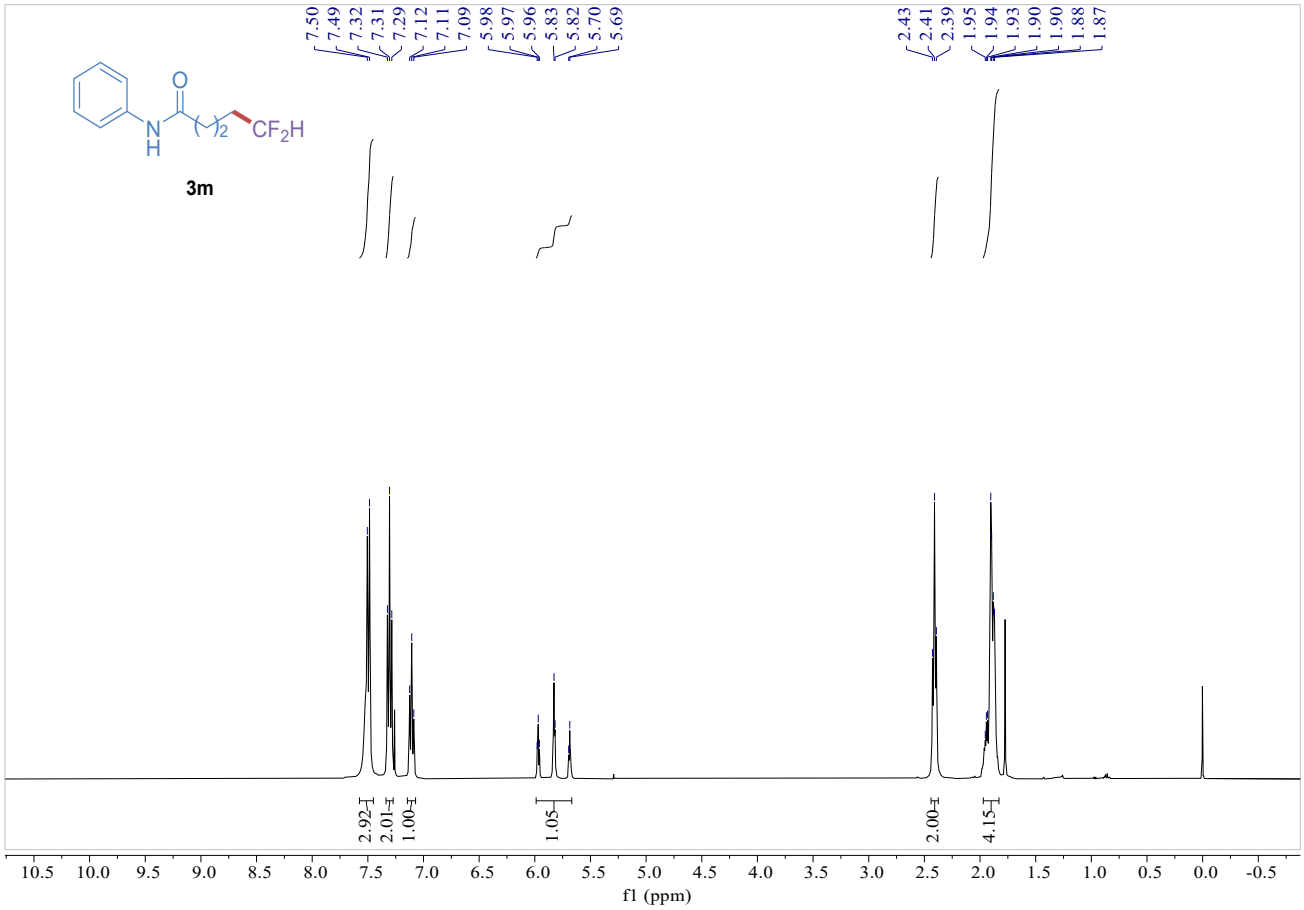

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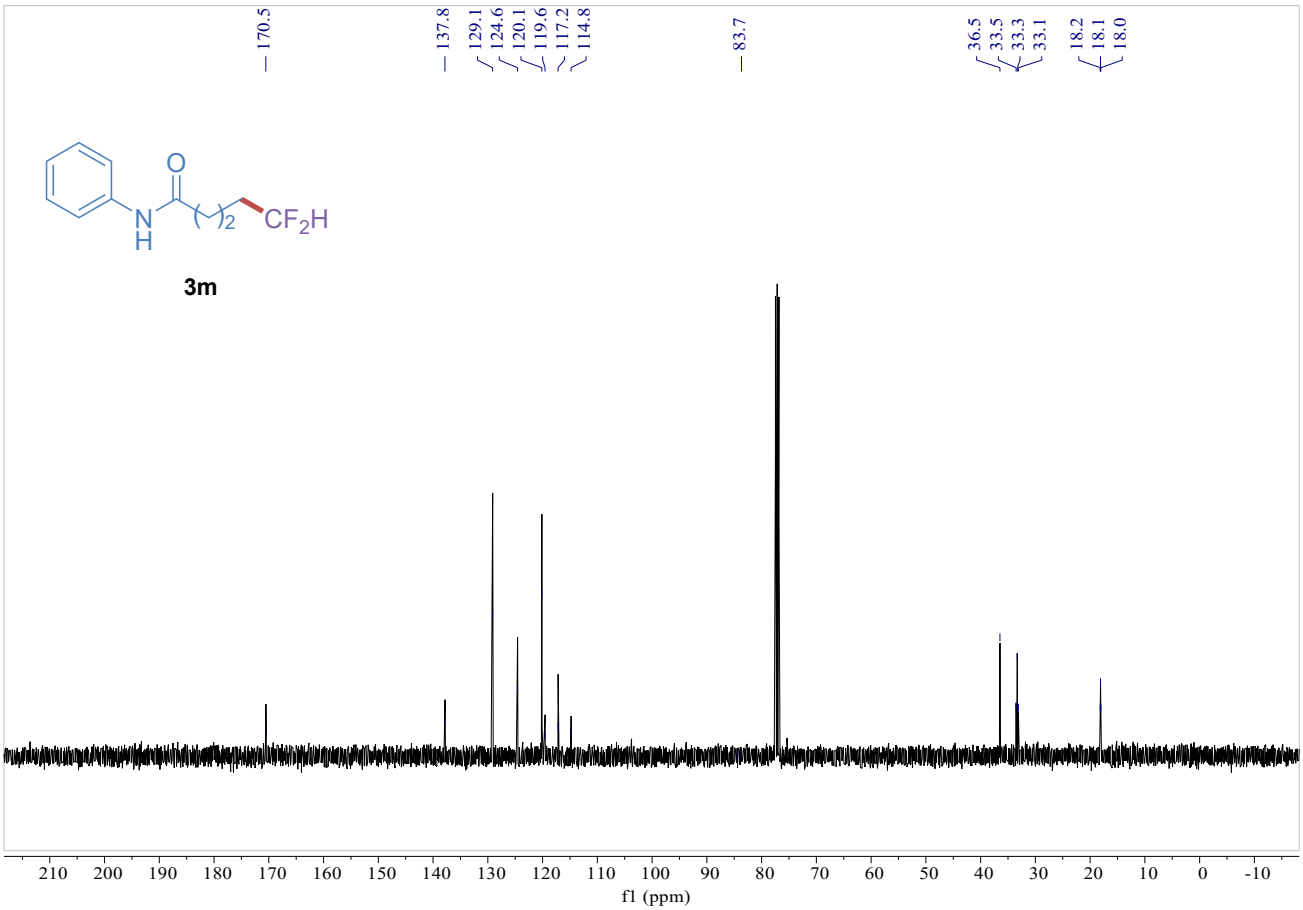

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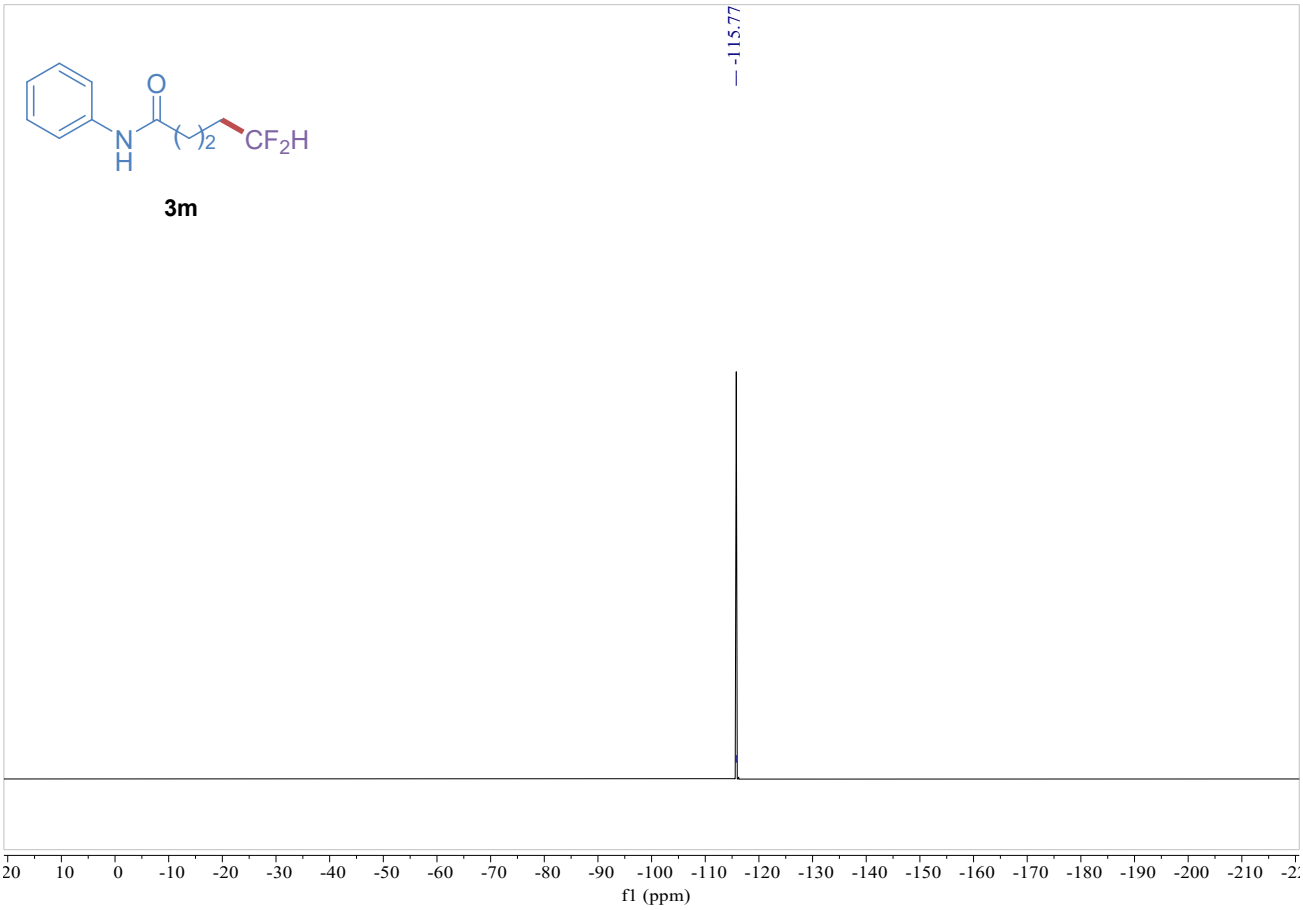

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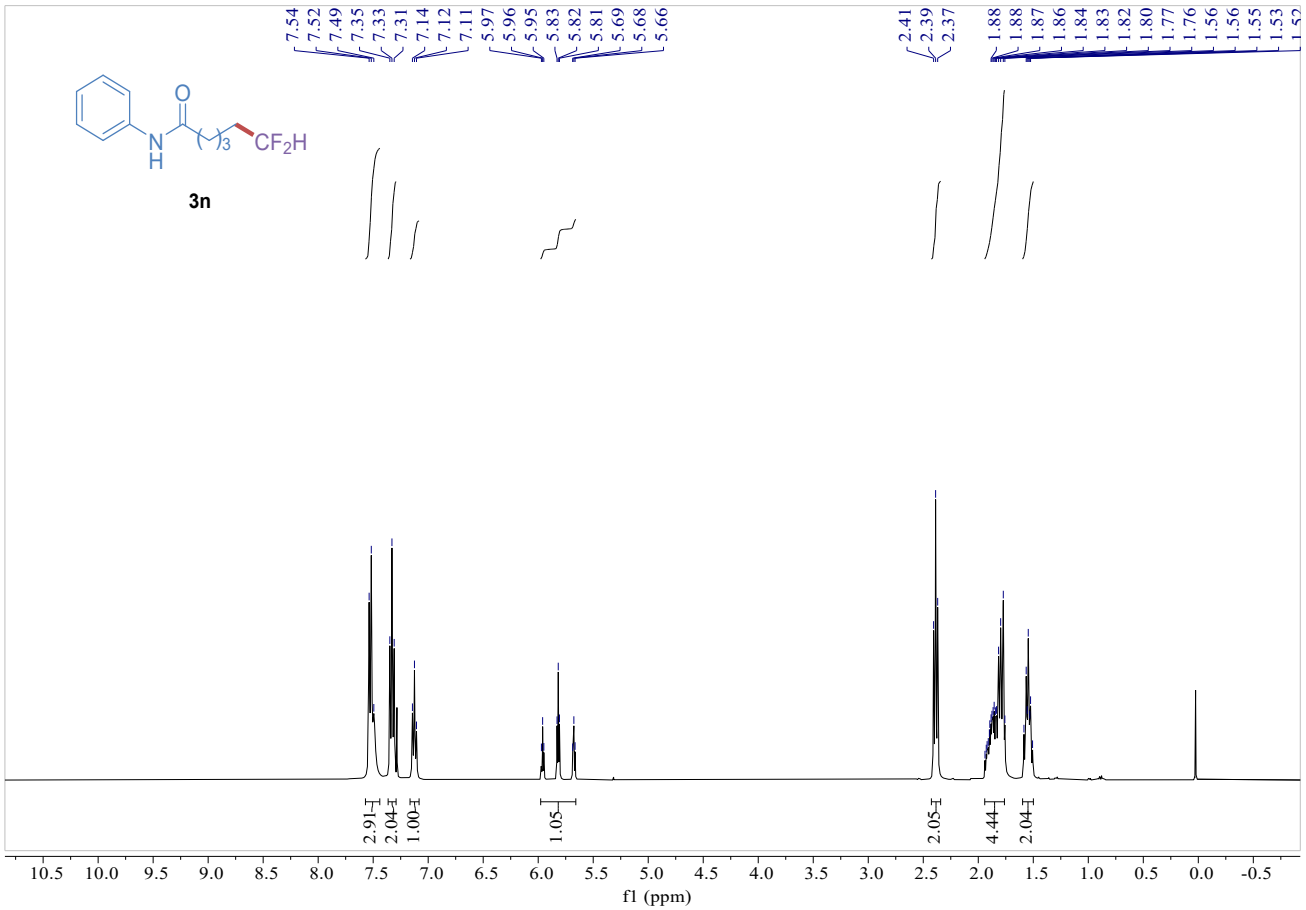

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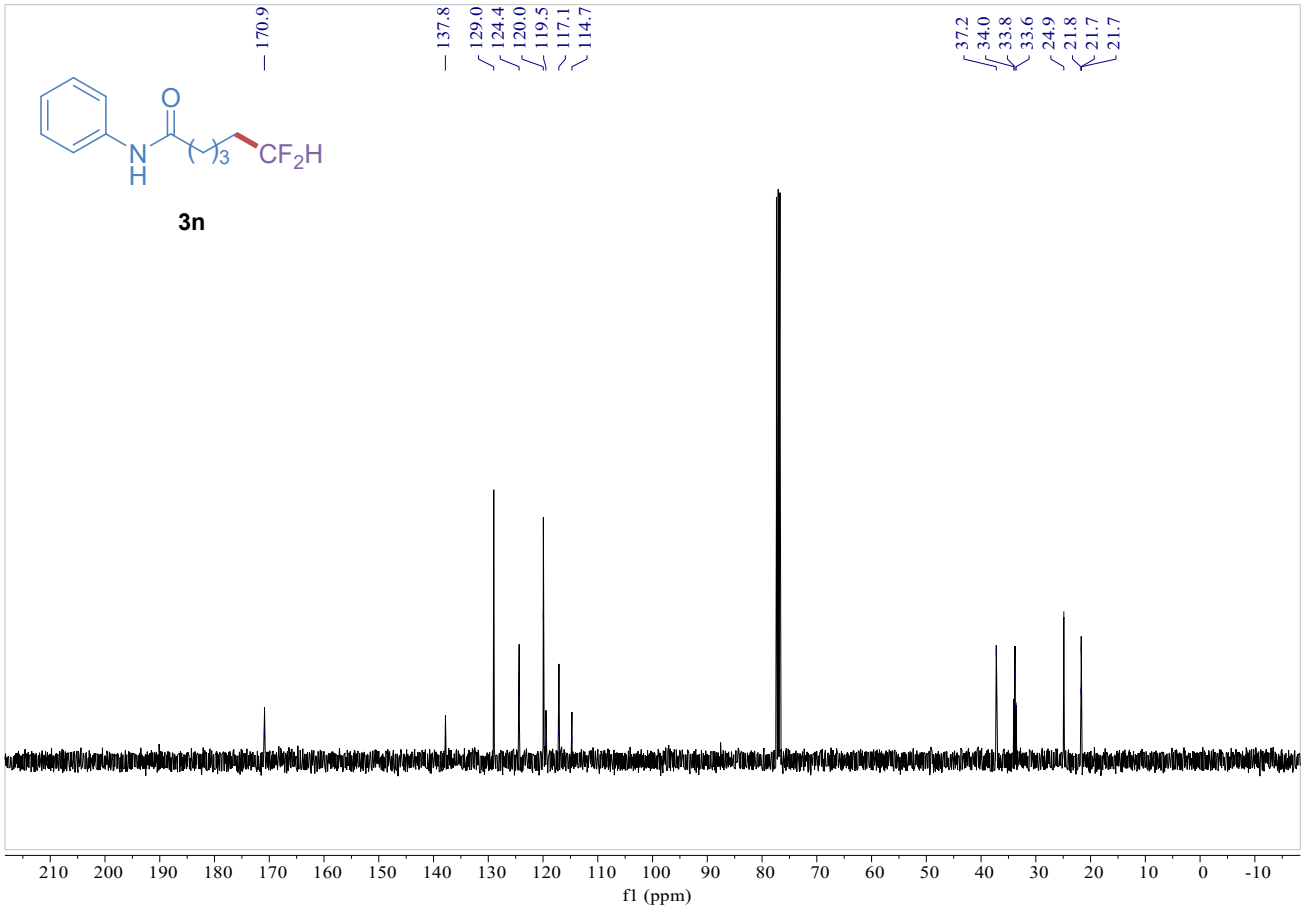

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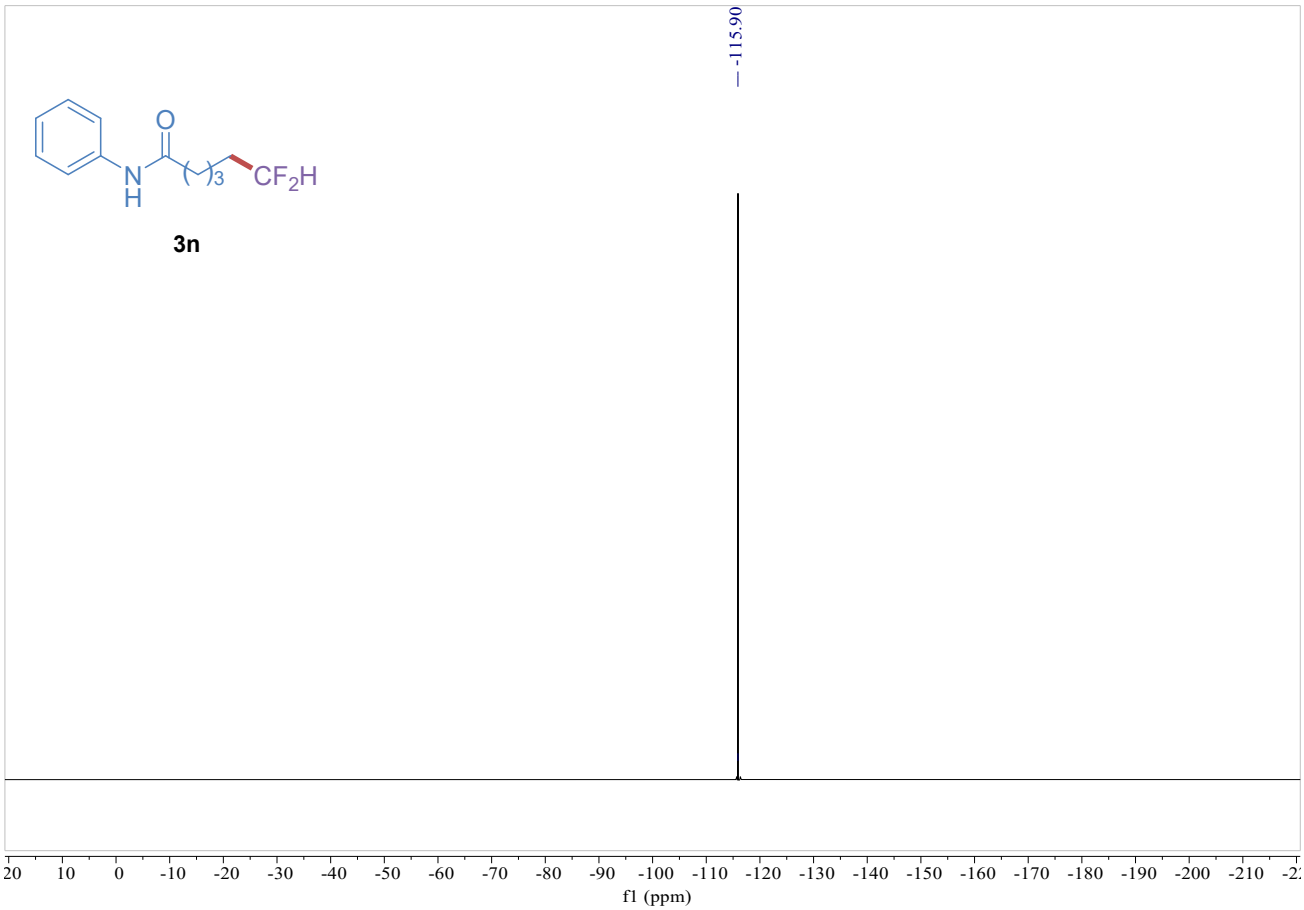

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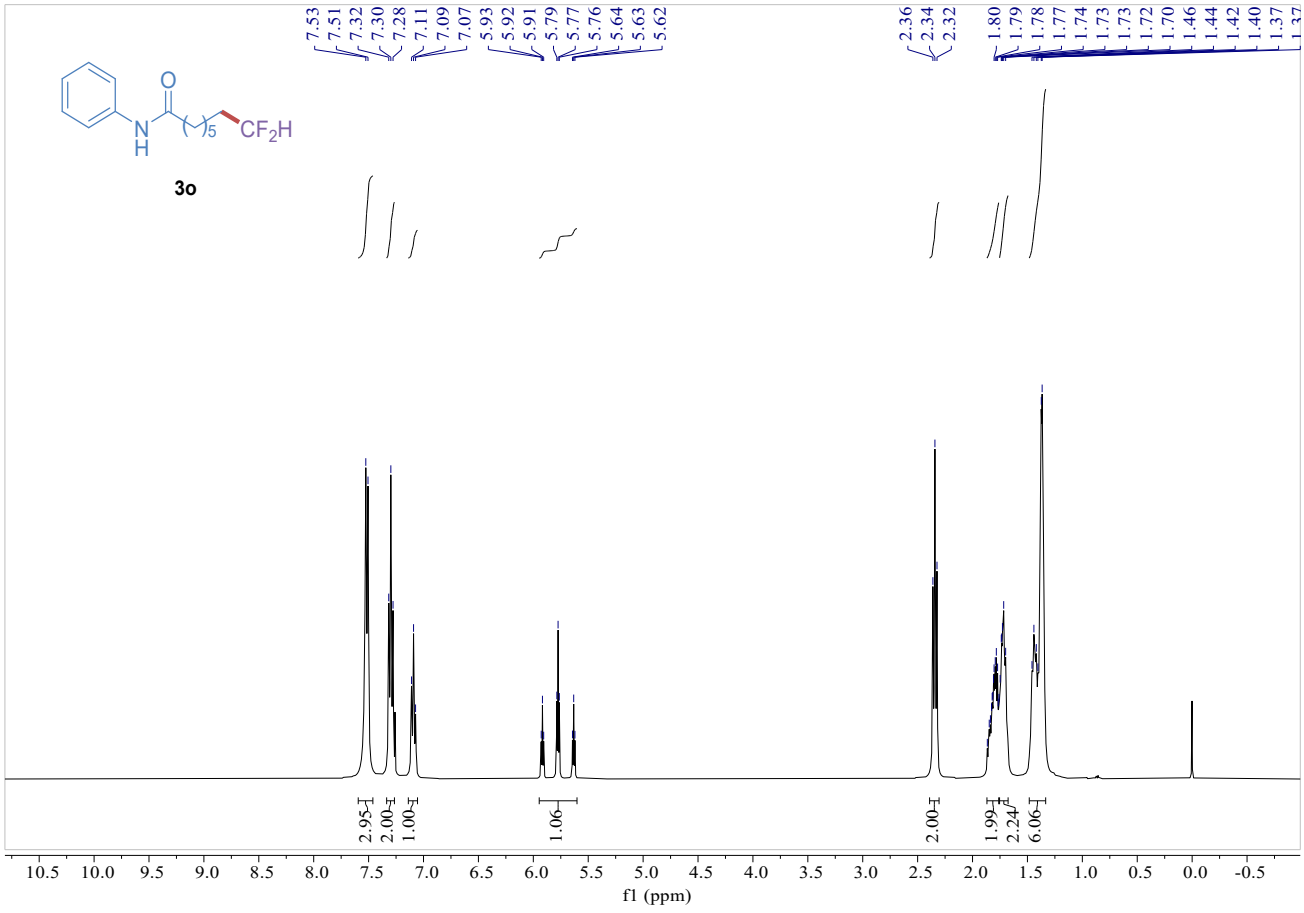

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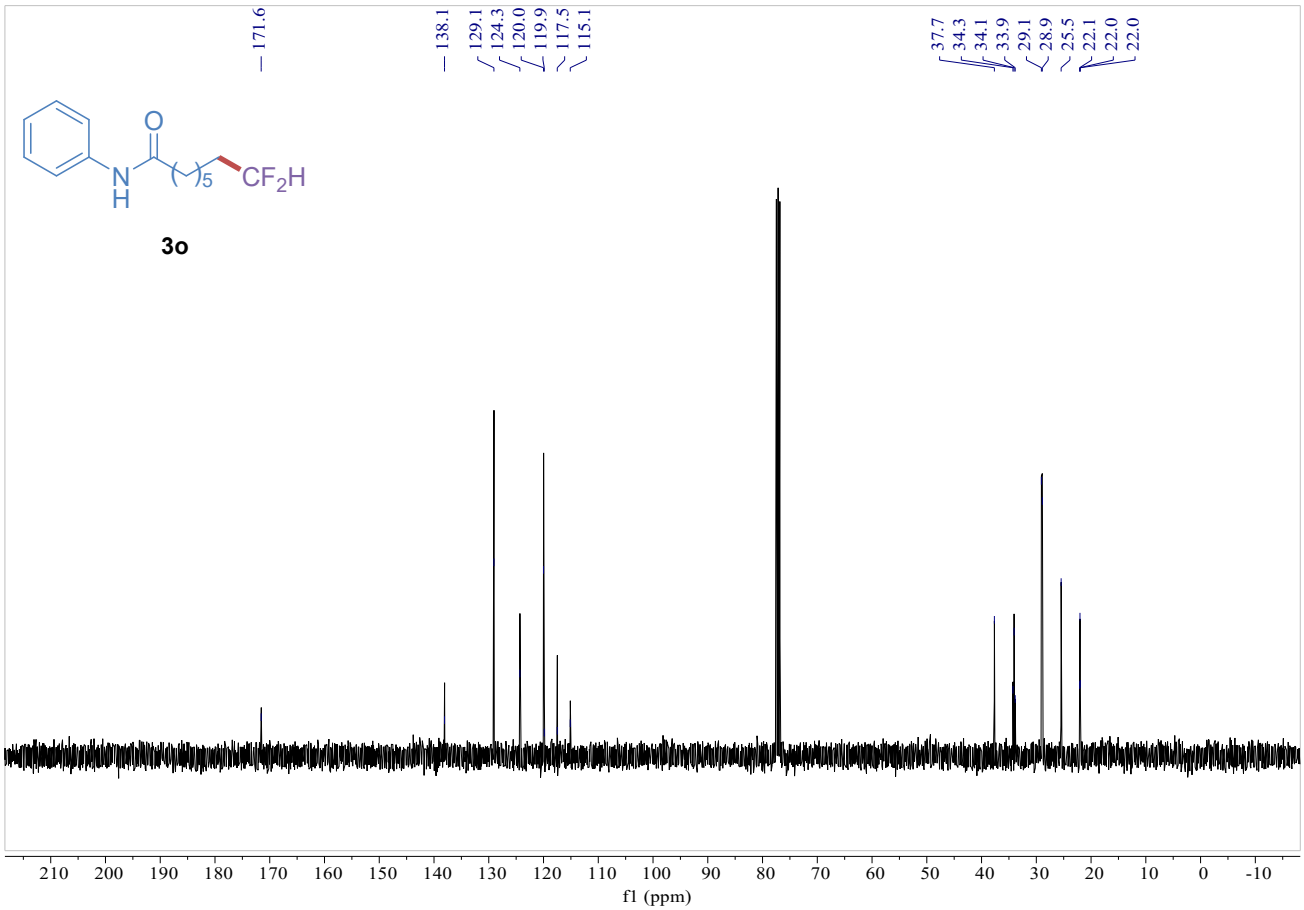

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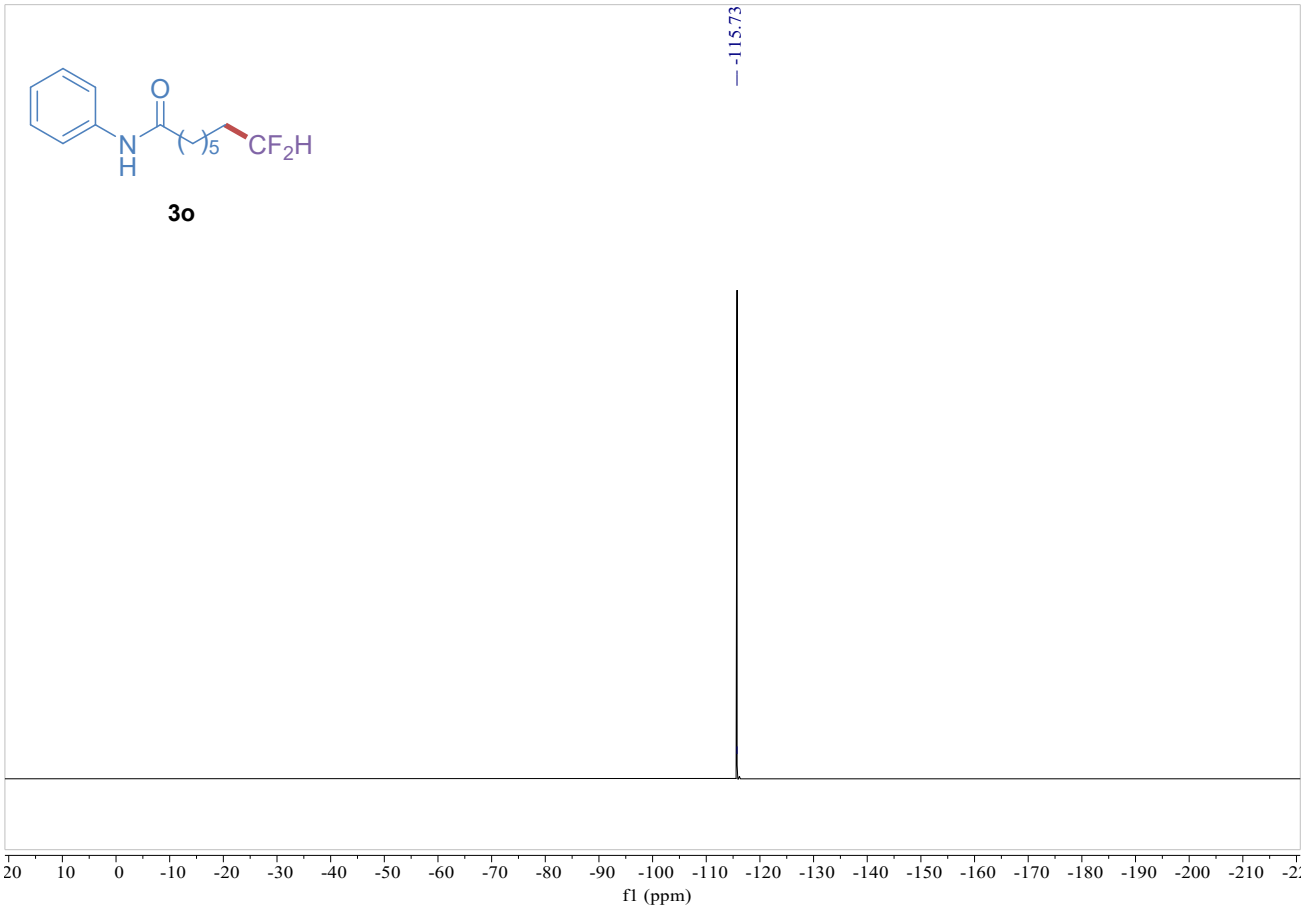

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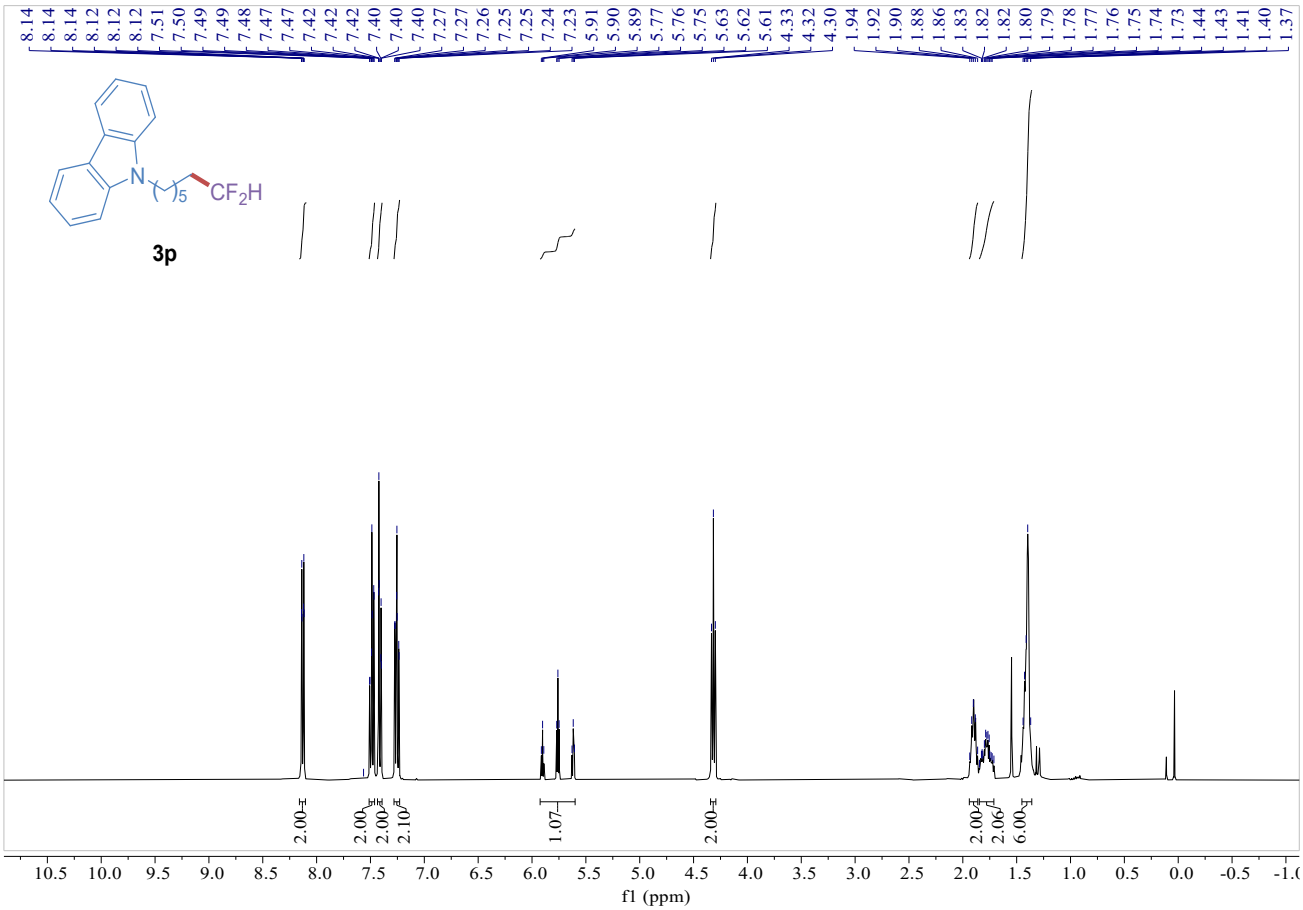

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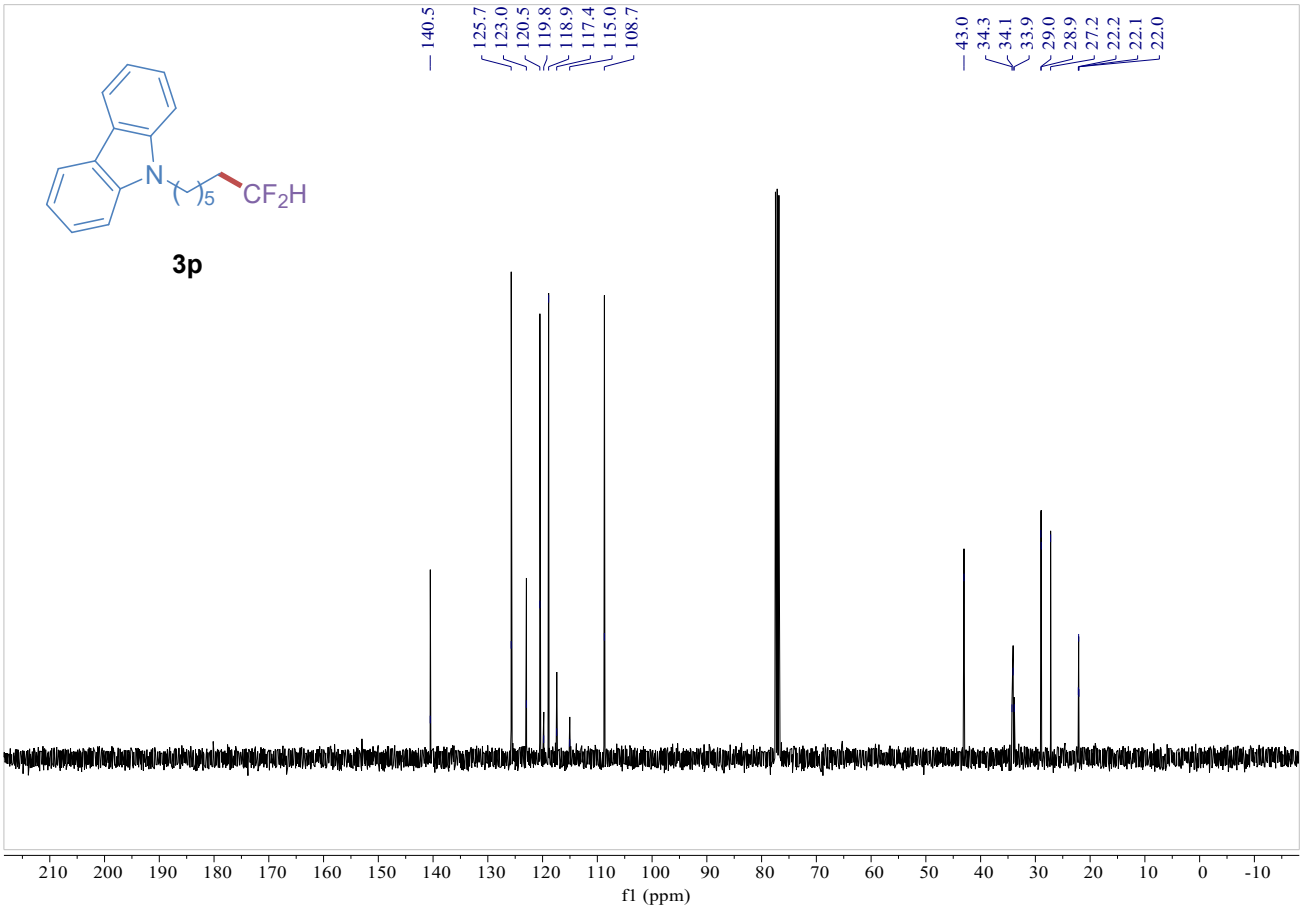

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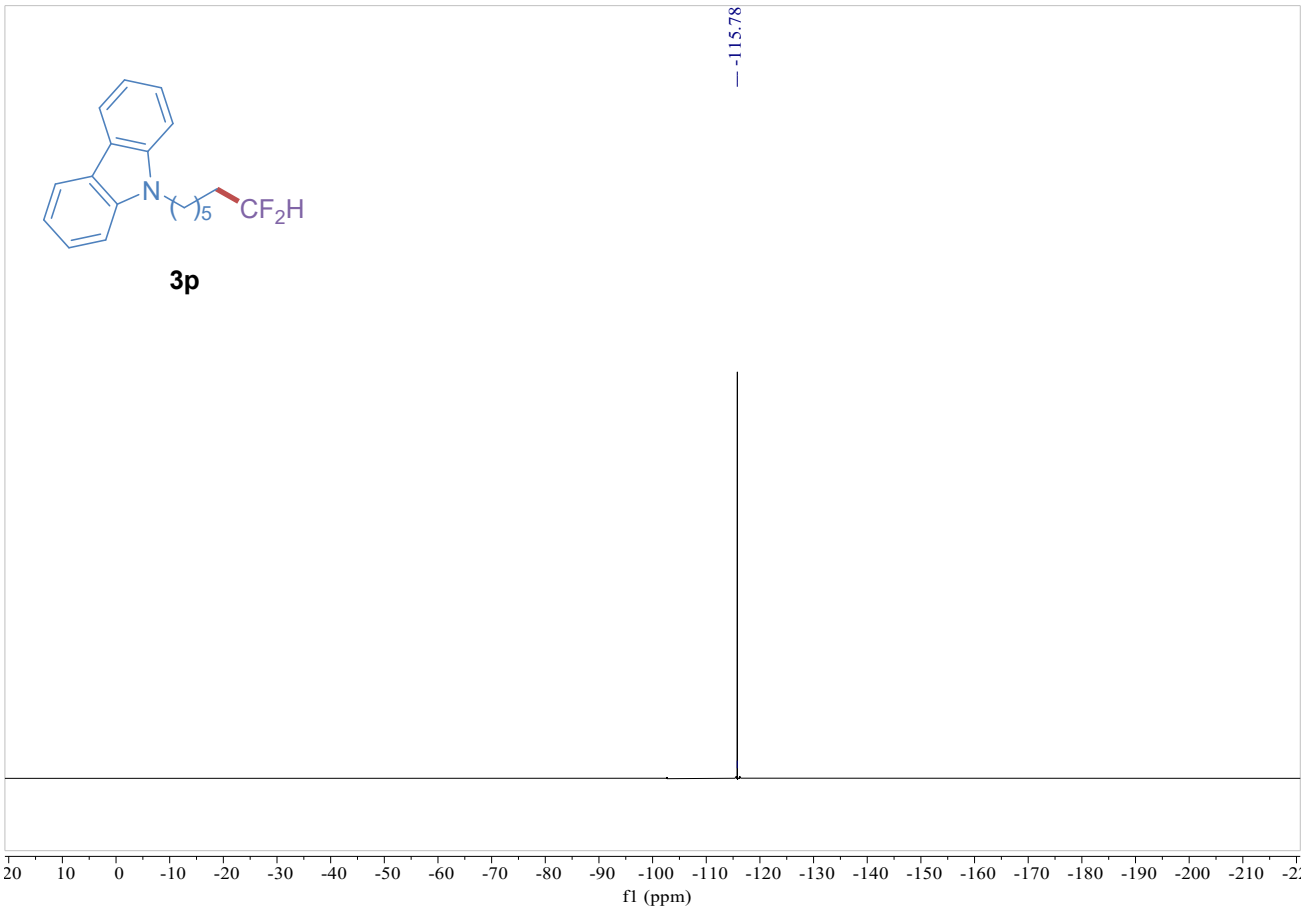

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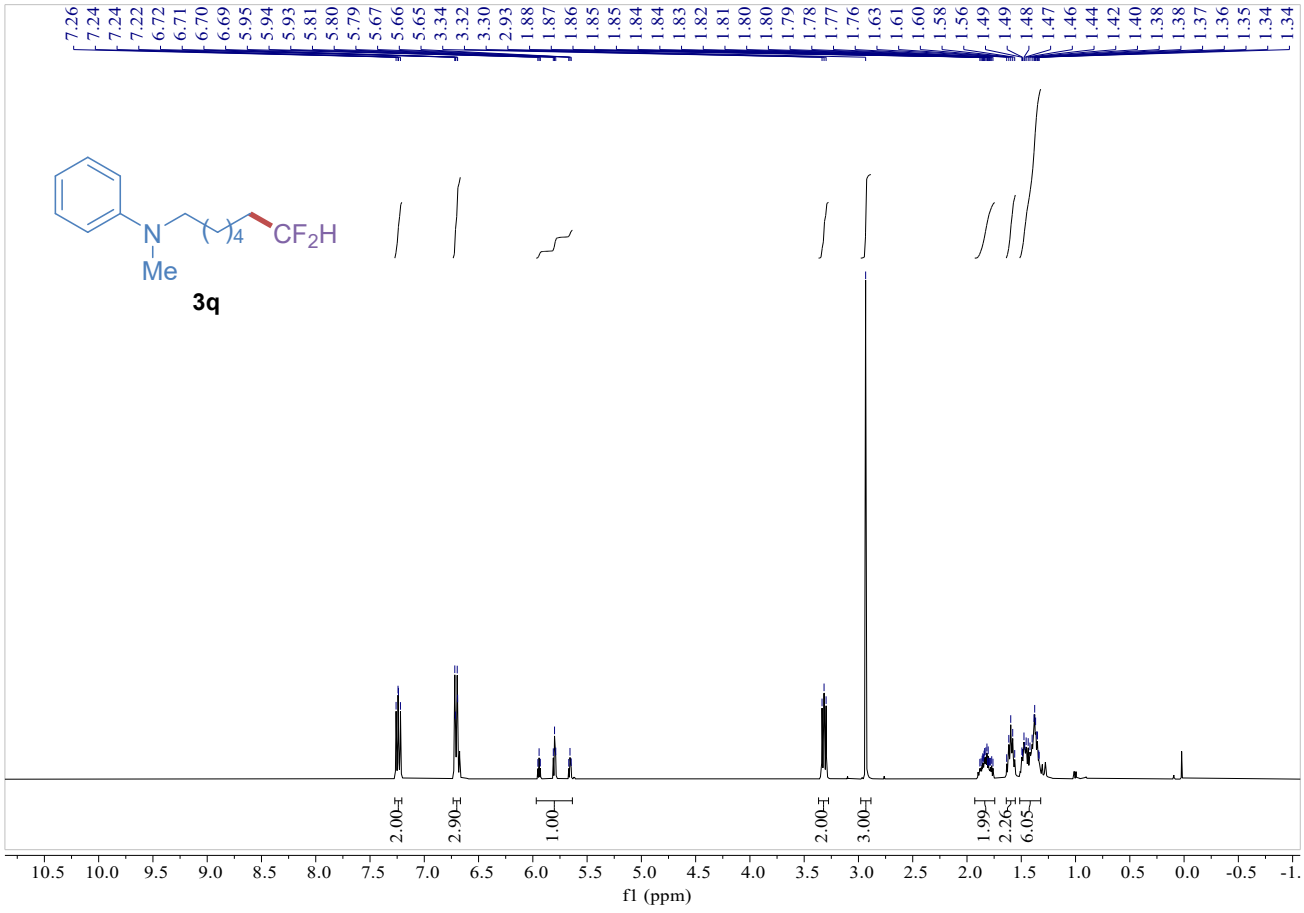

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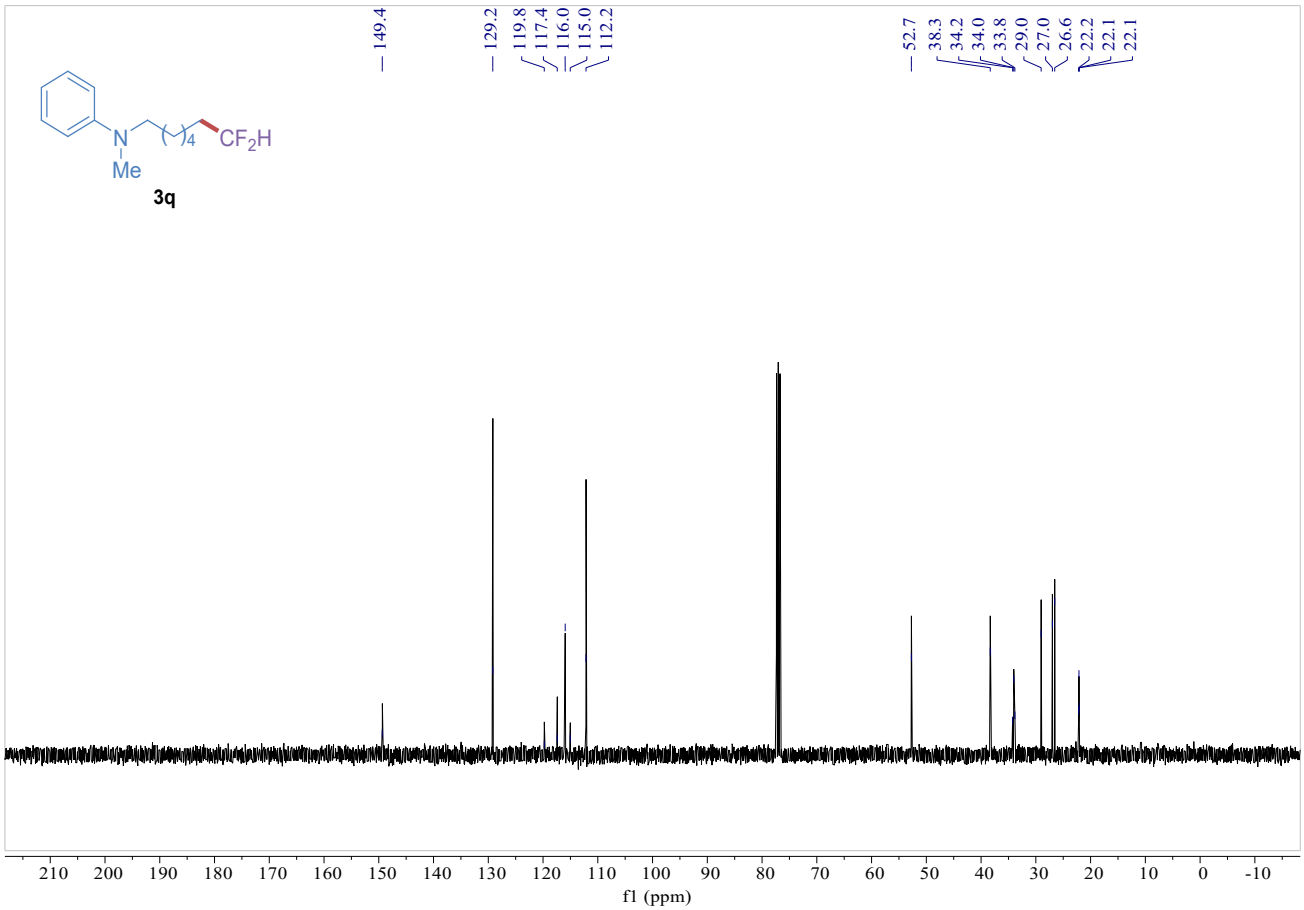
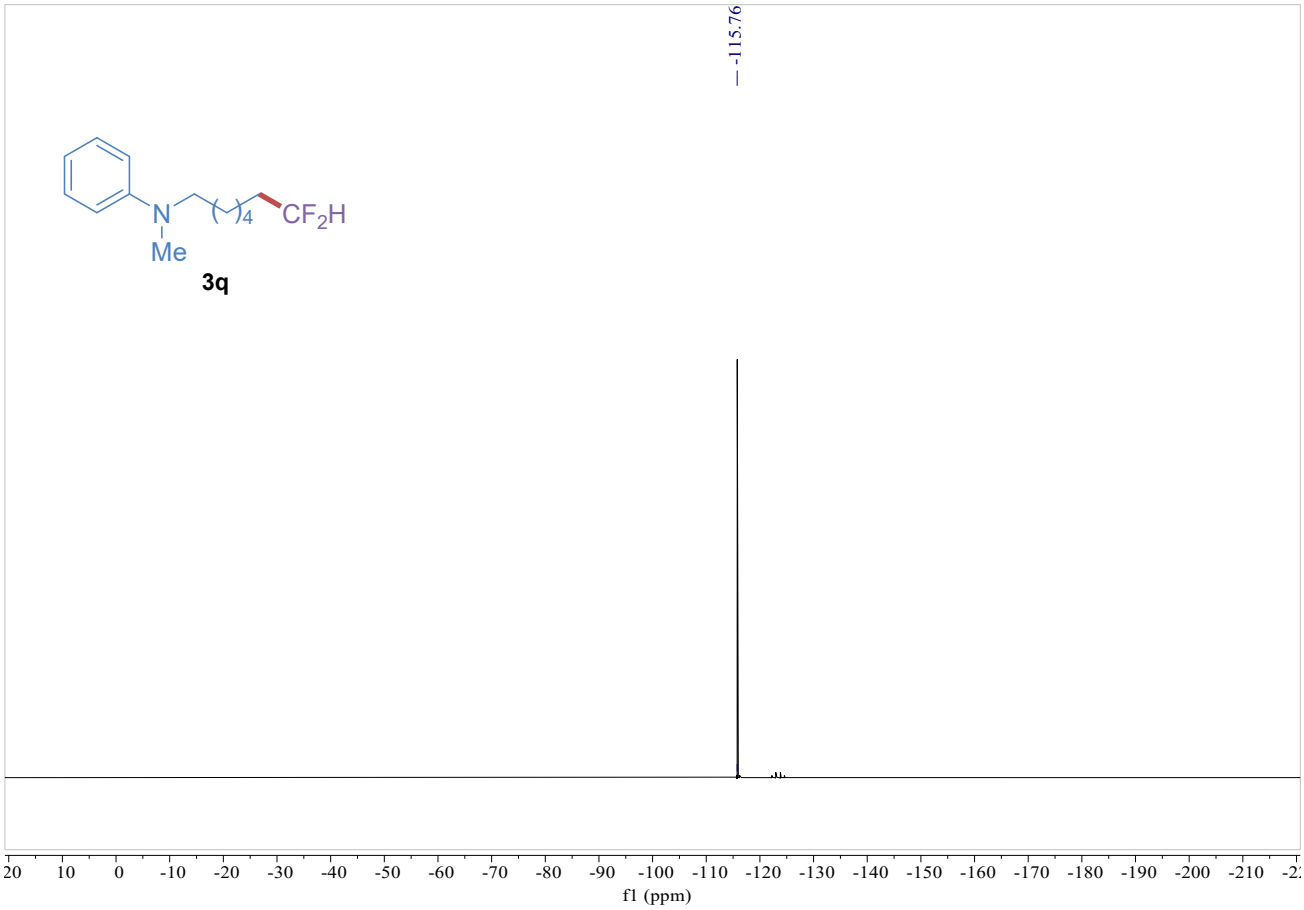
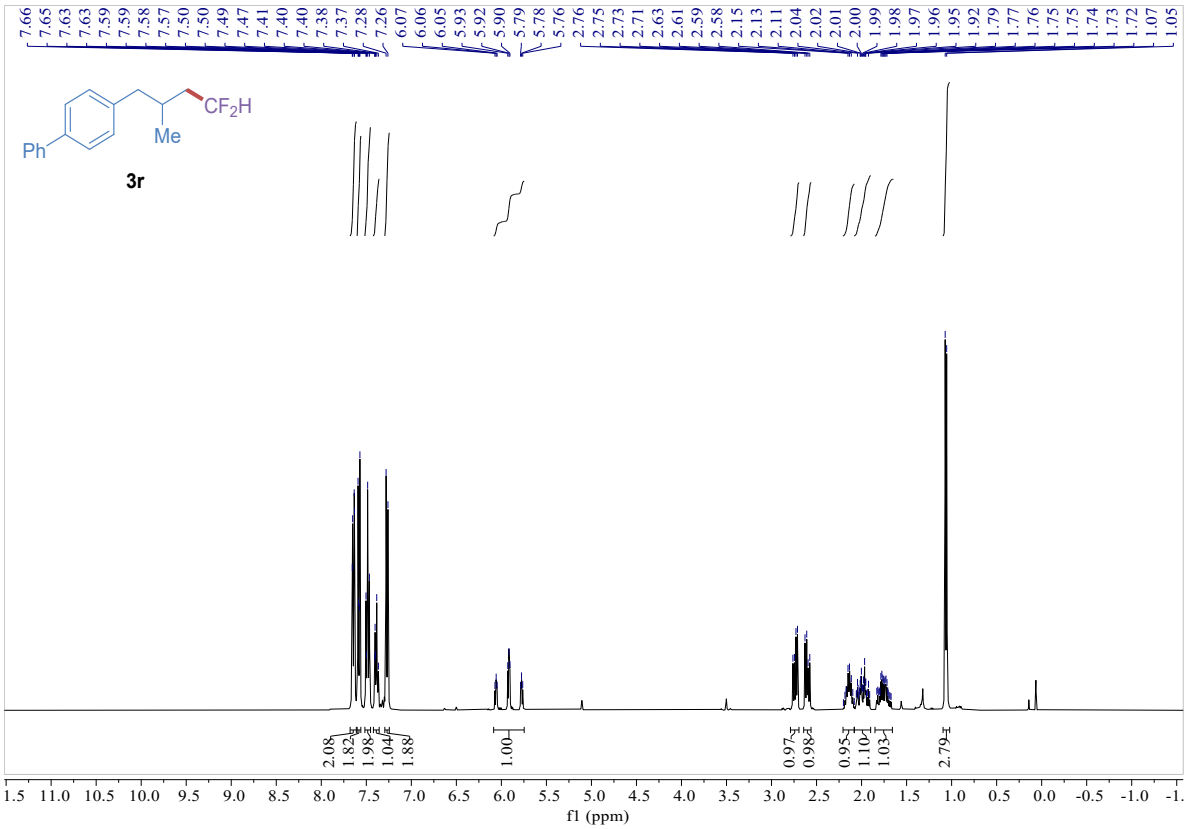


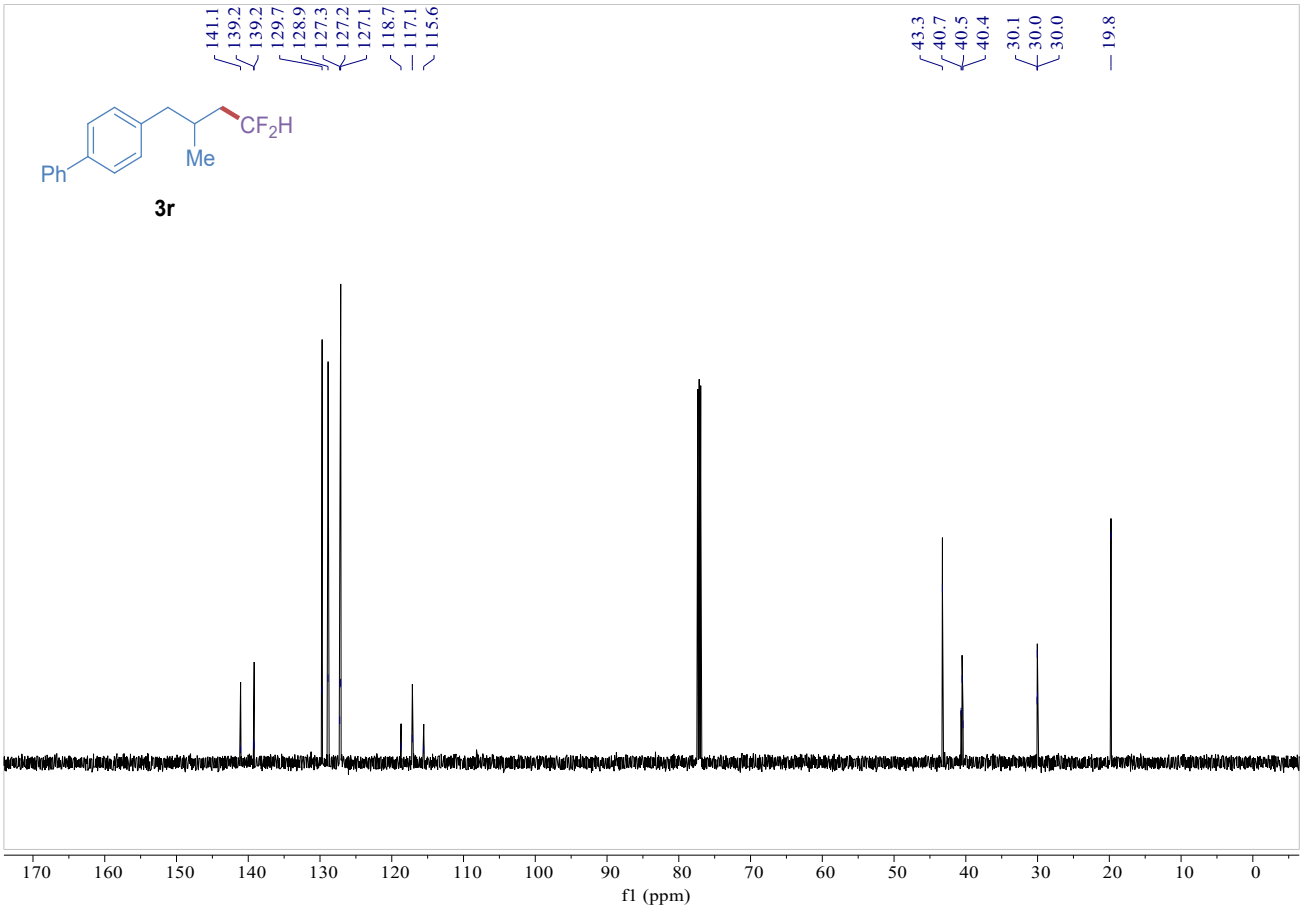
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **3q**



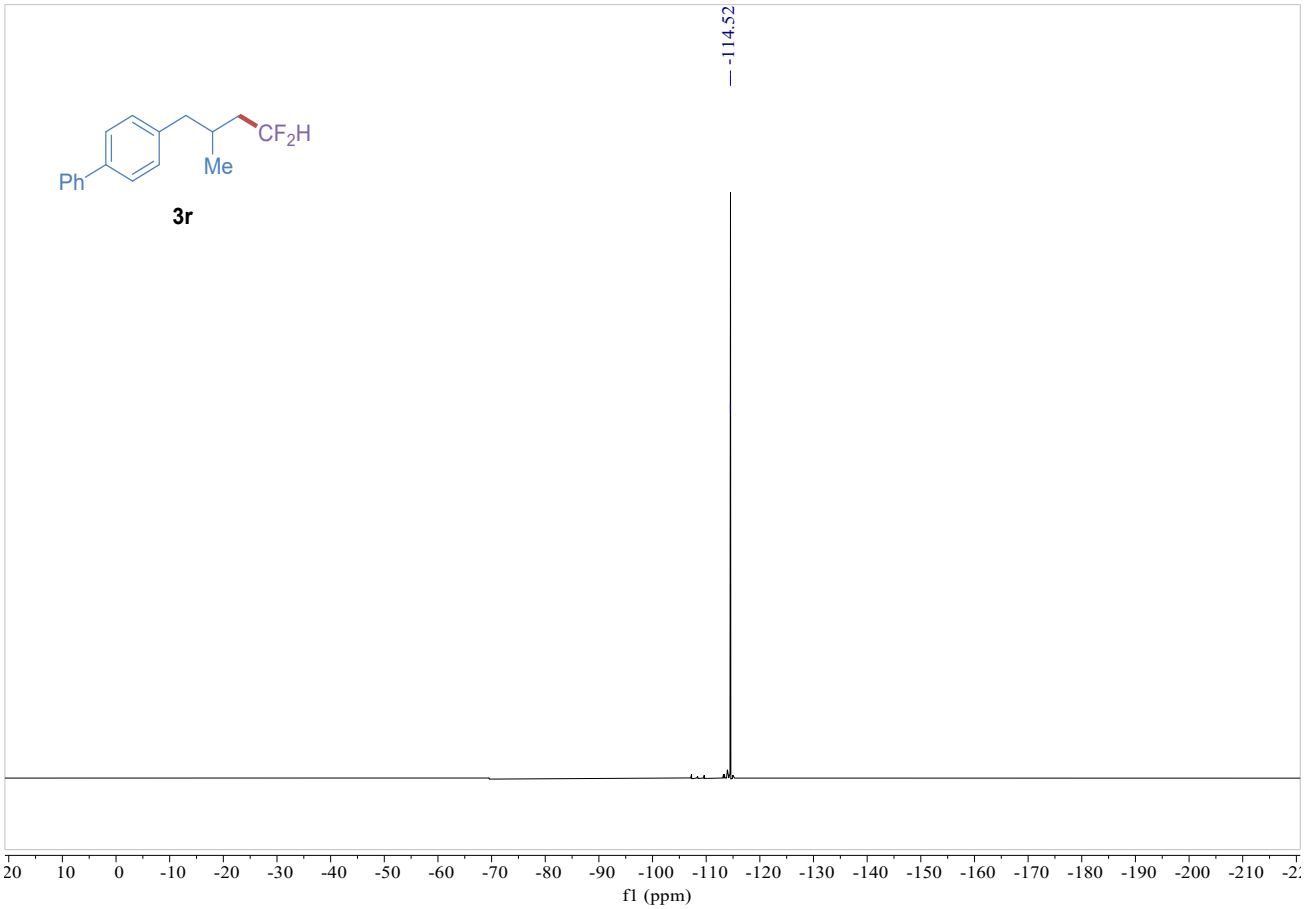
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3q**



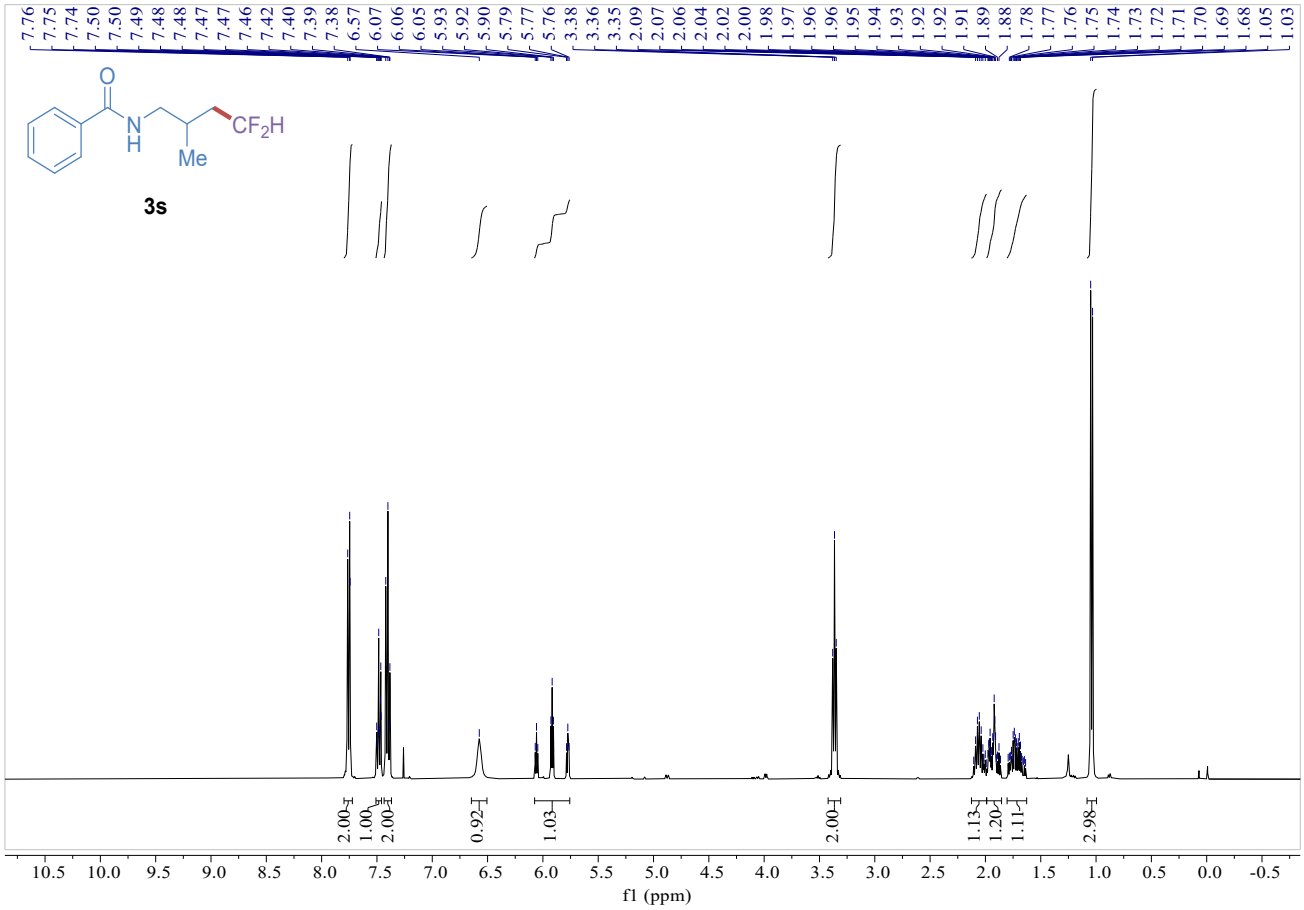
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3r**



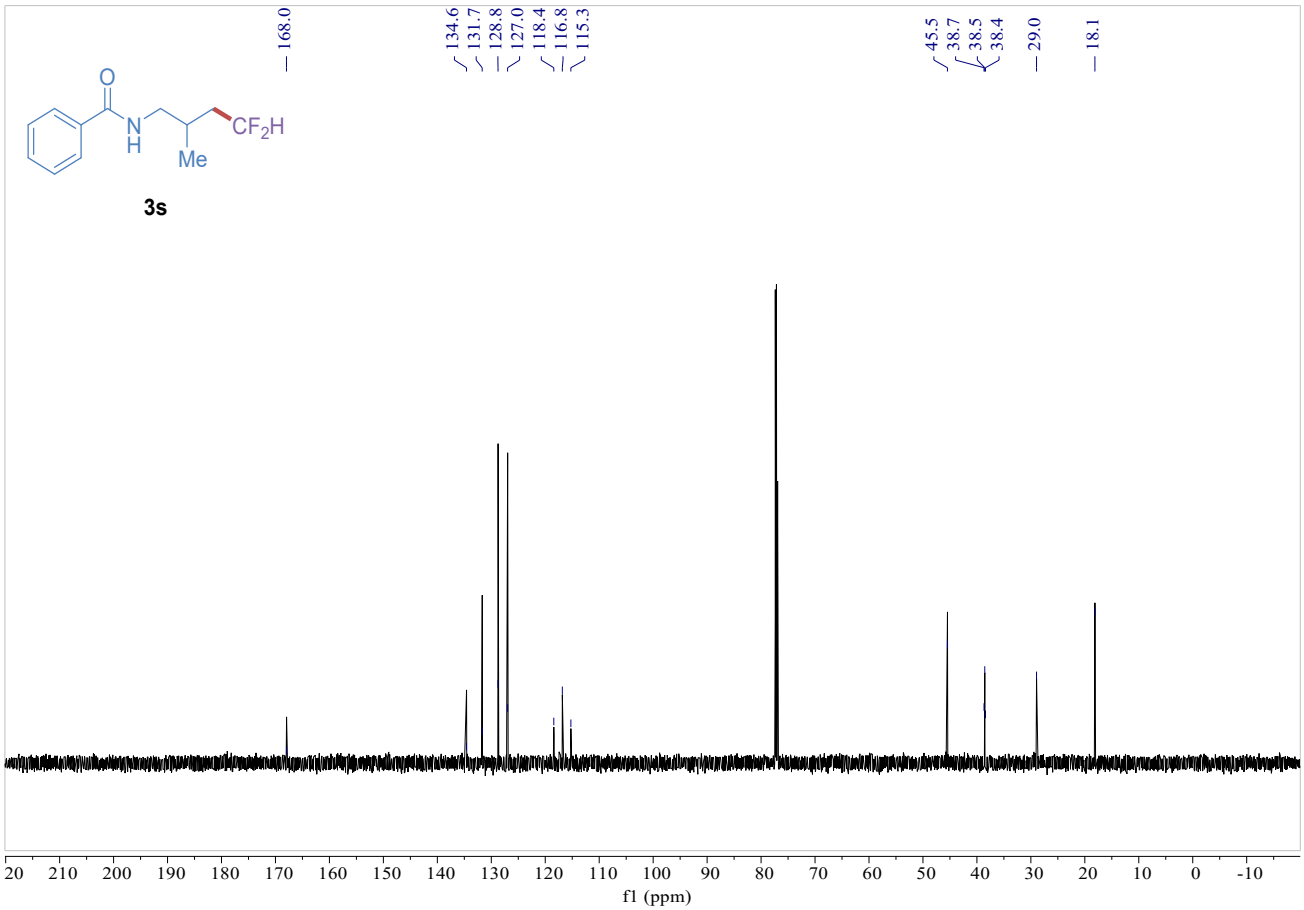
^{13}C NMR spectrum (151 MHz, $CDCl_3$) of compound **3r**



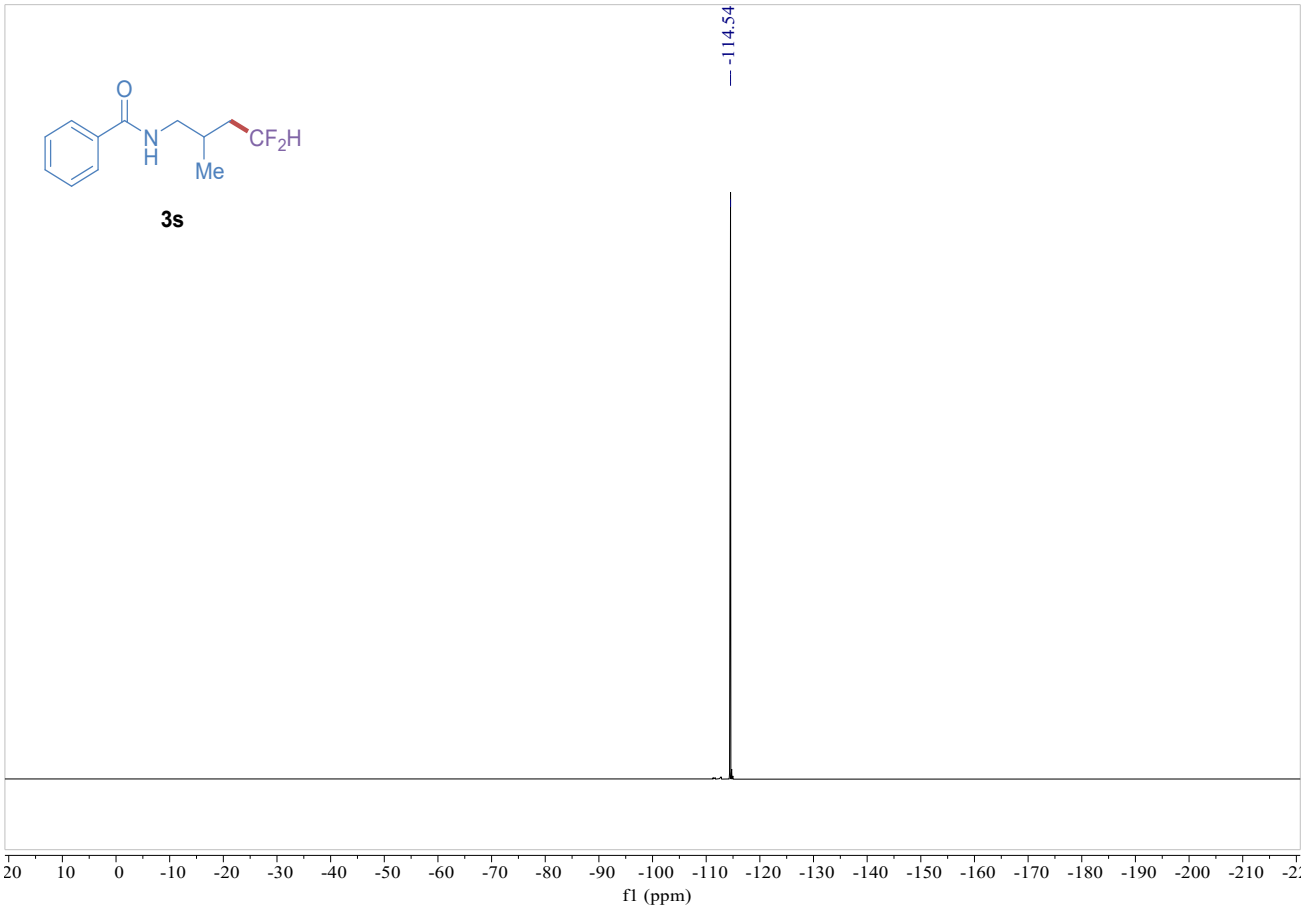
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3r**



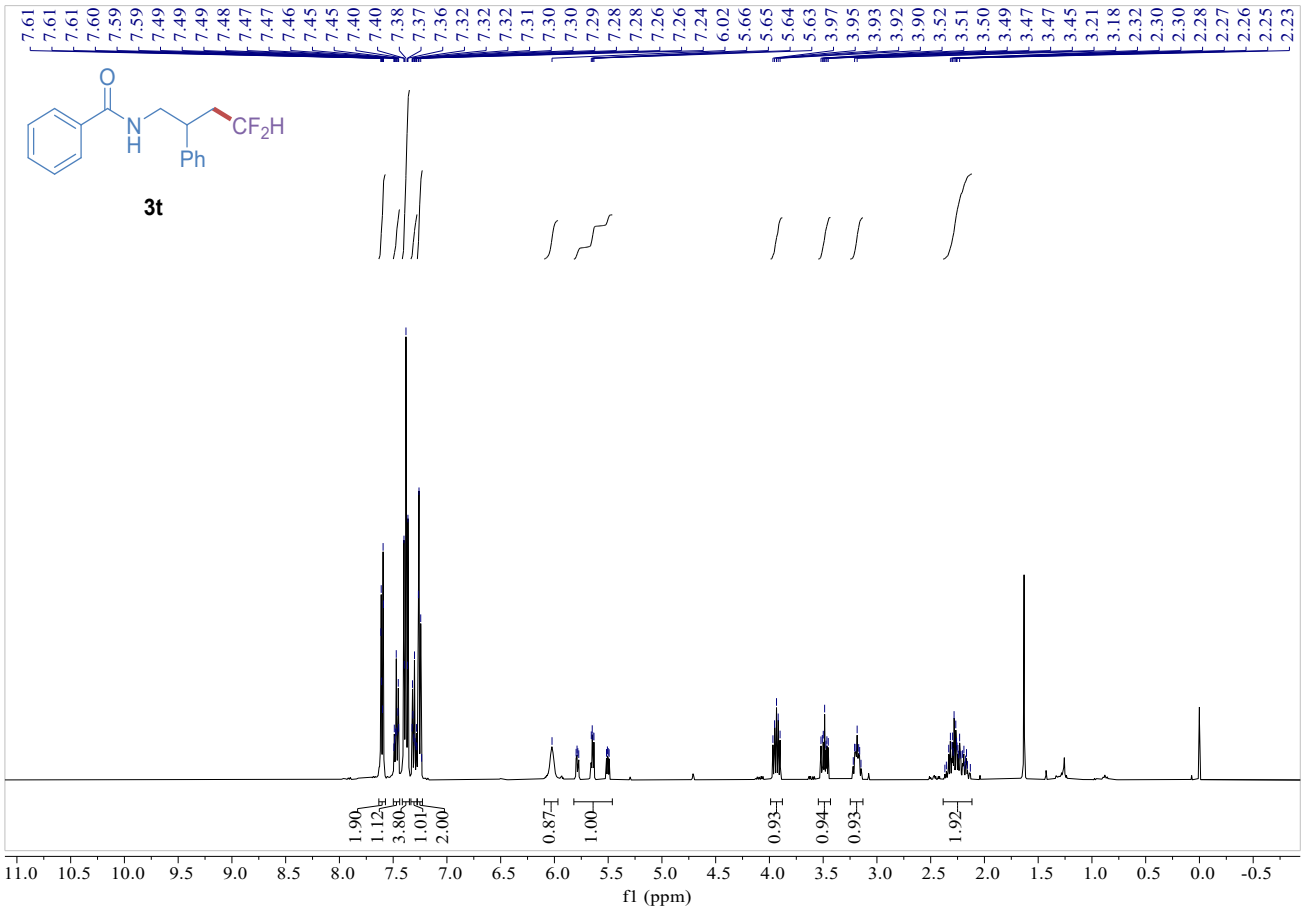
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3s**



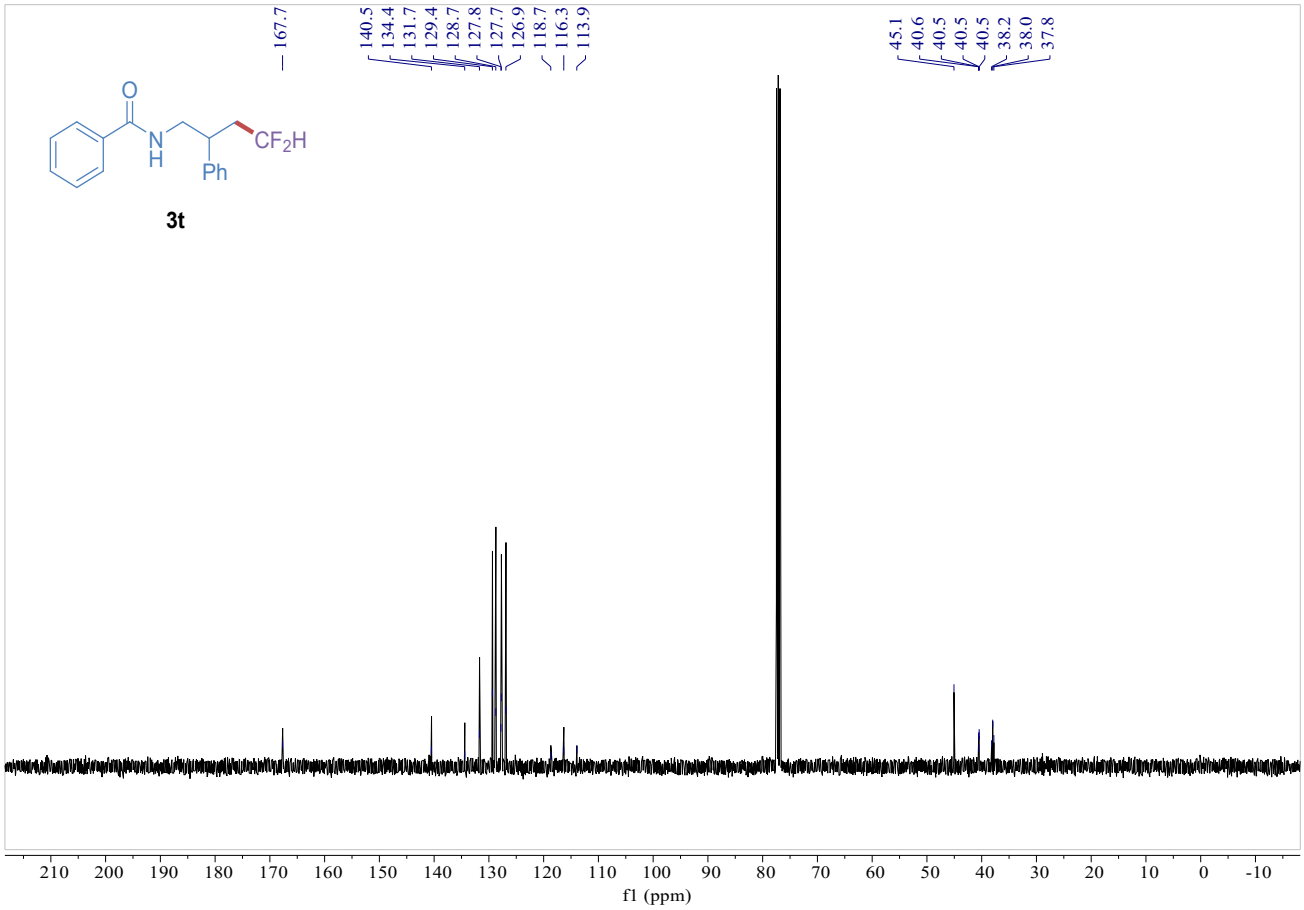
^{13}C NMR spectrum (151 MHz, $CDCl_3$) of compound **3s**



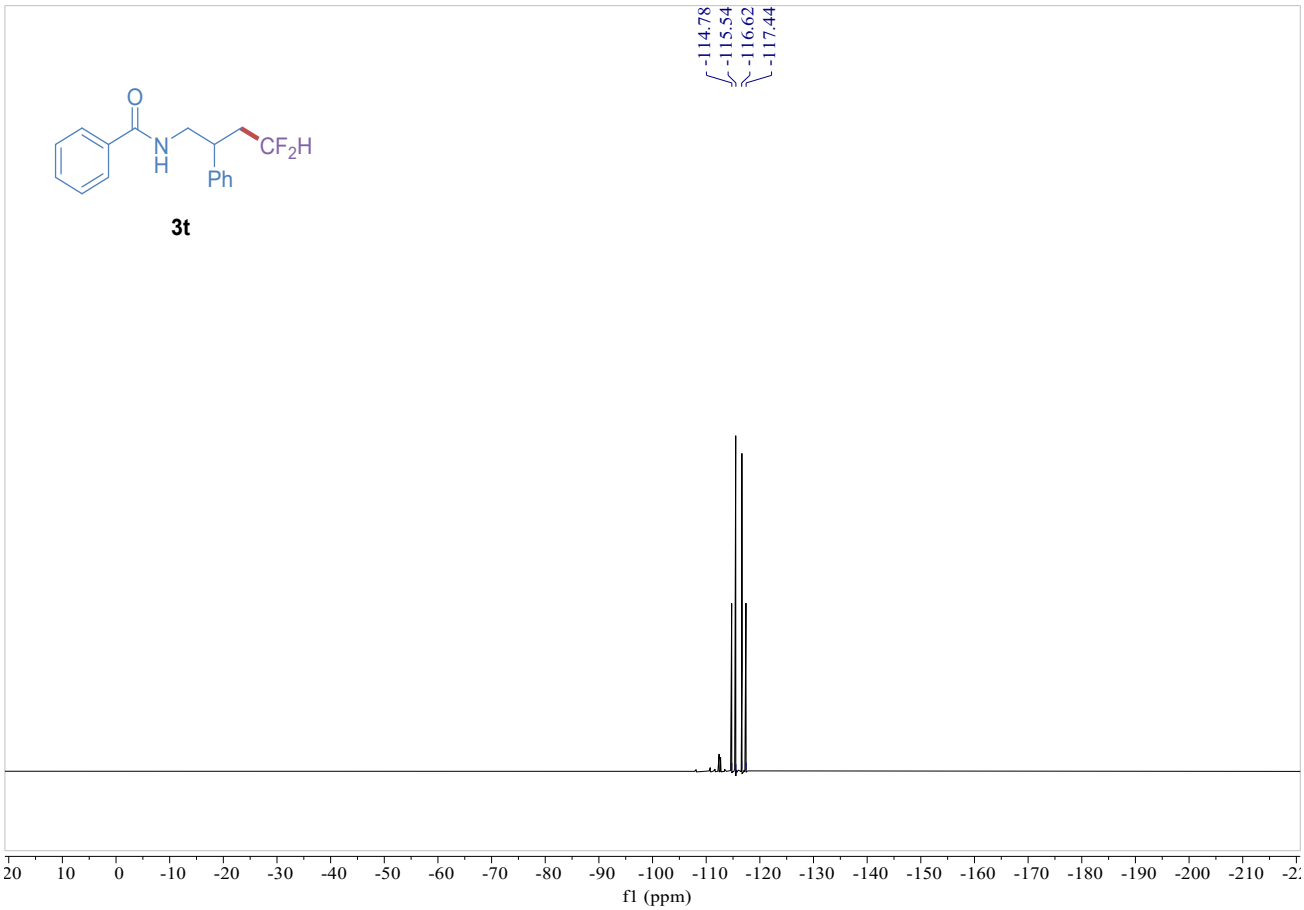
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3s**



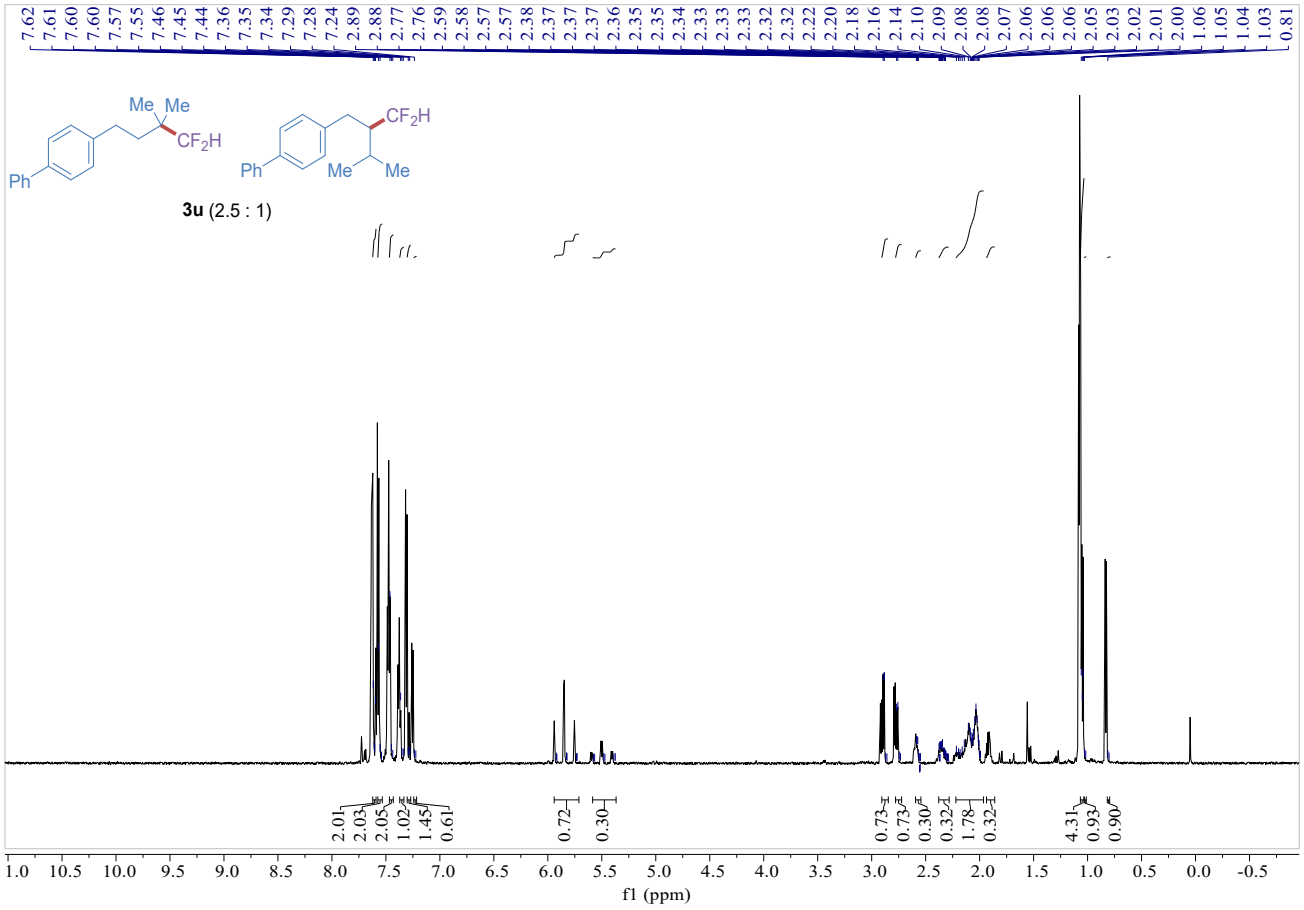
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3t**



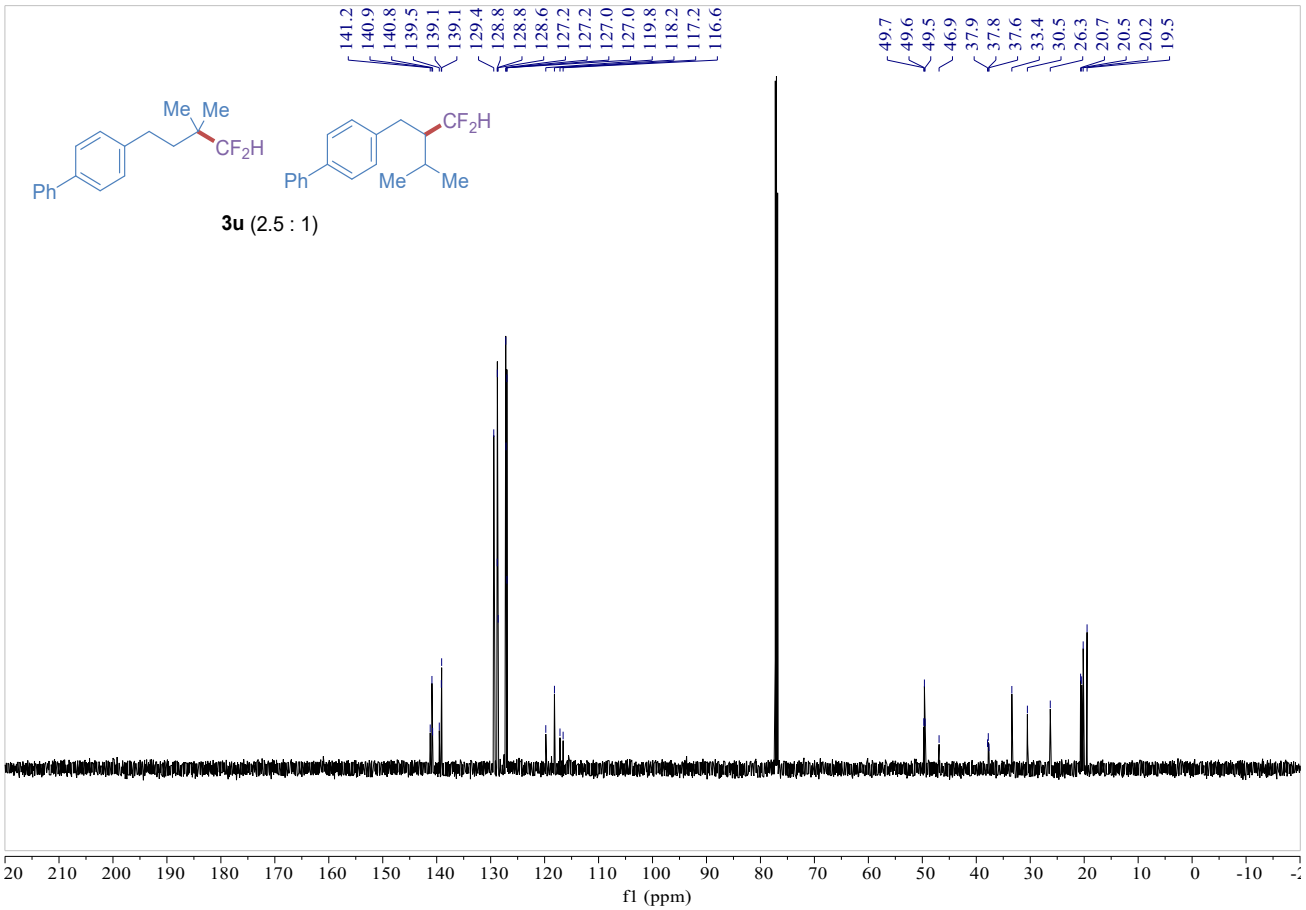
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **3t**



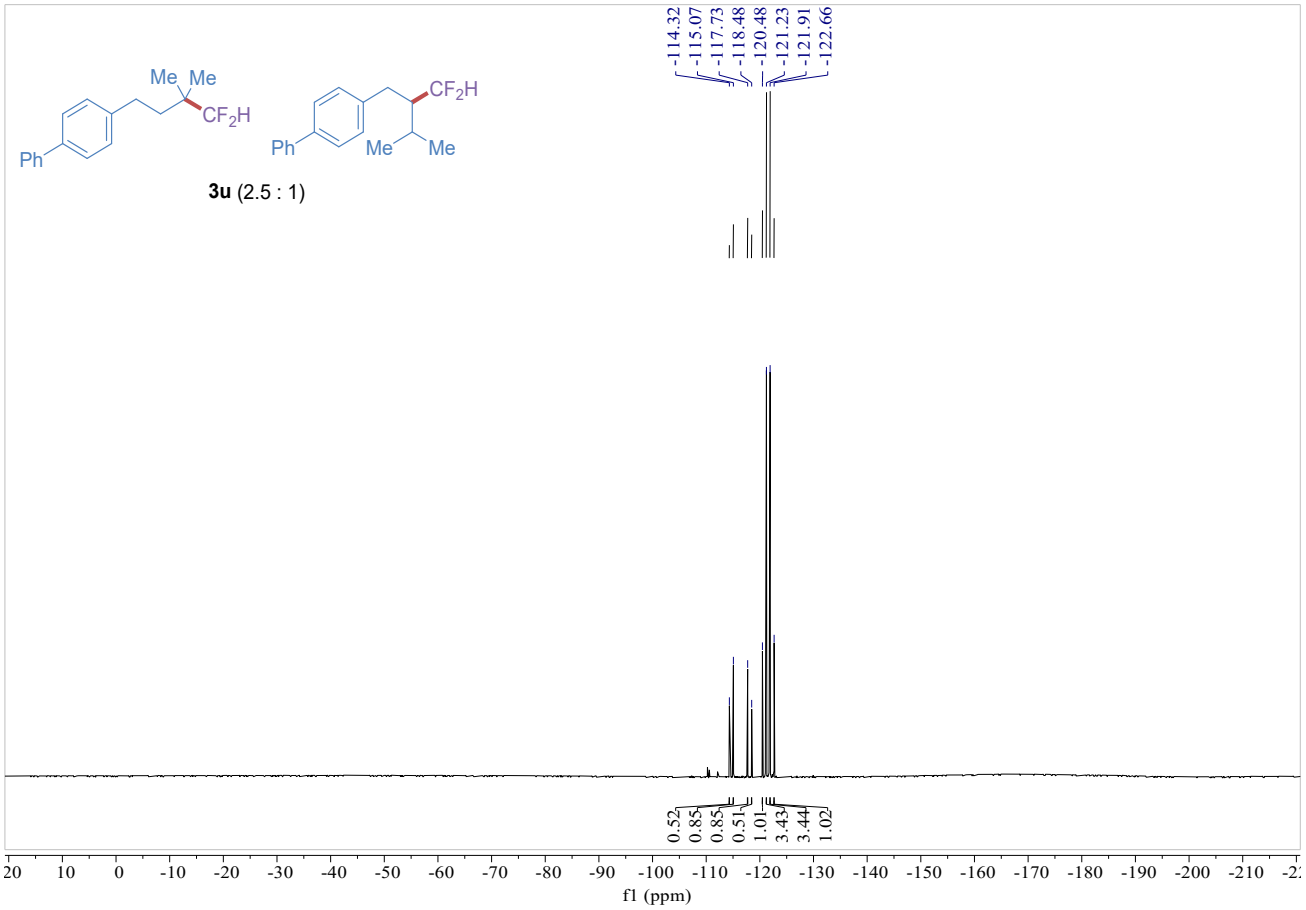
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3t**



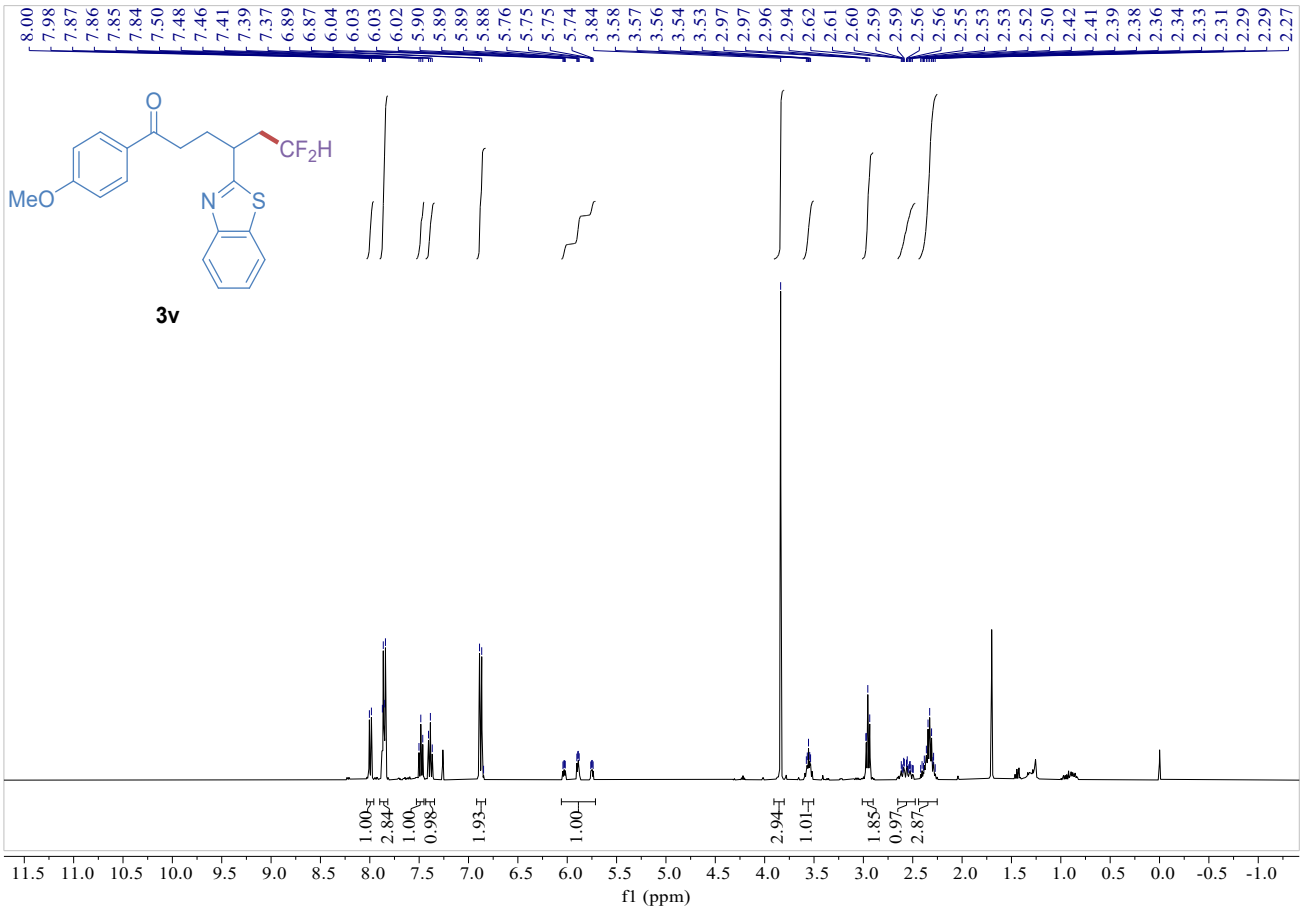
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound **3u**



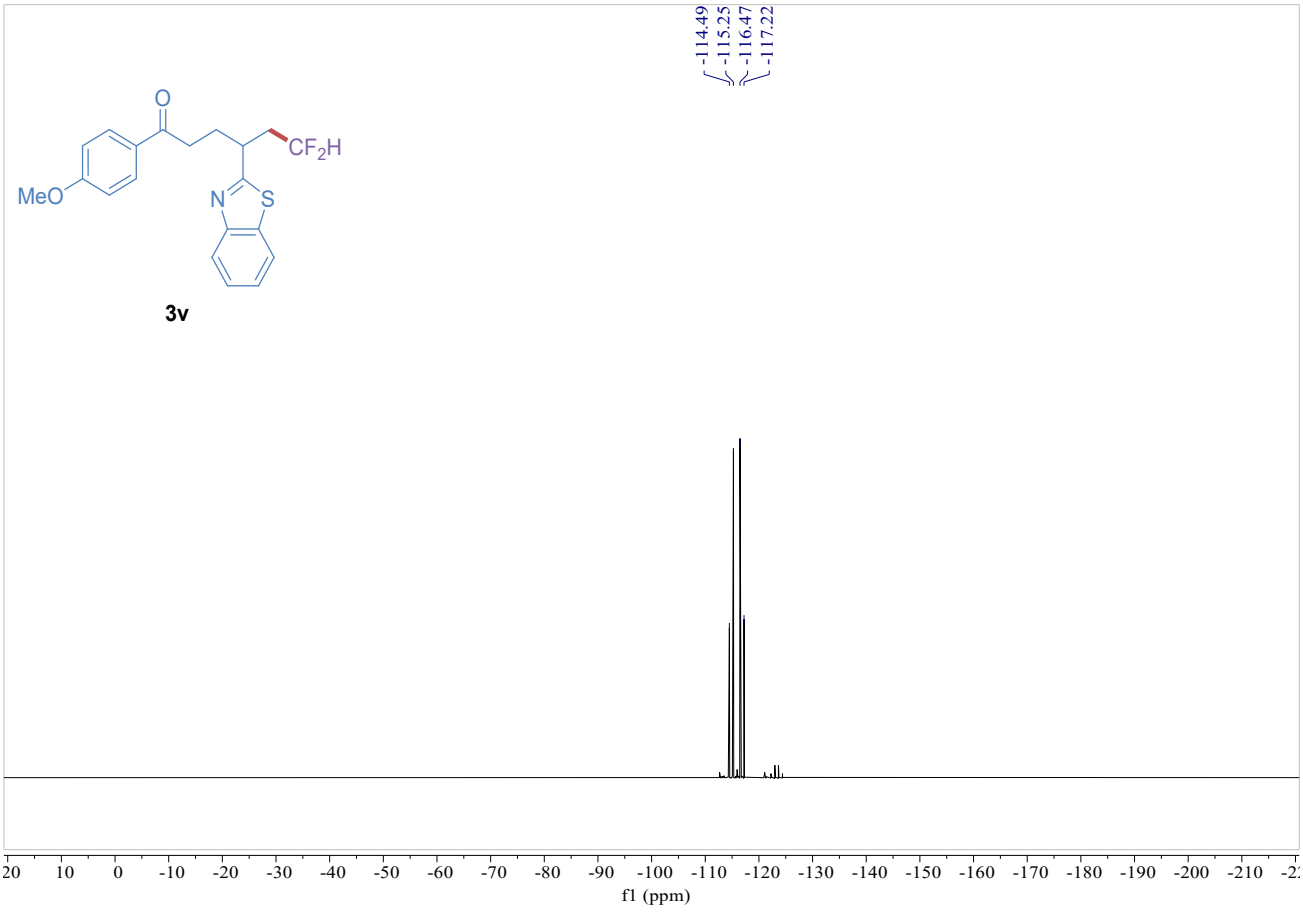
^{13}C NMR spectrum (151 MHz, $CDCl_3$) of compound **3u**



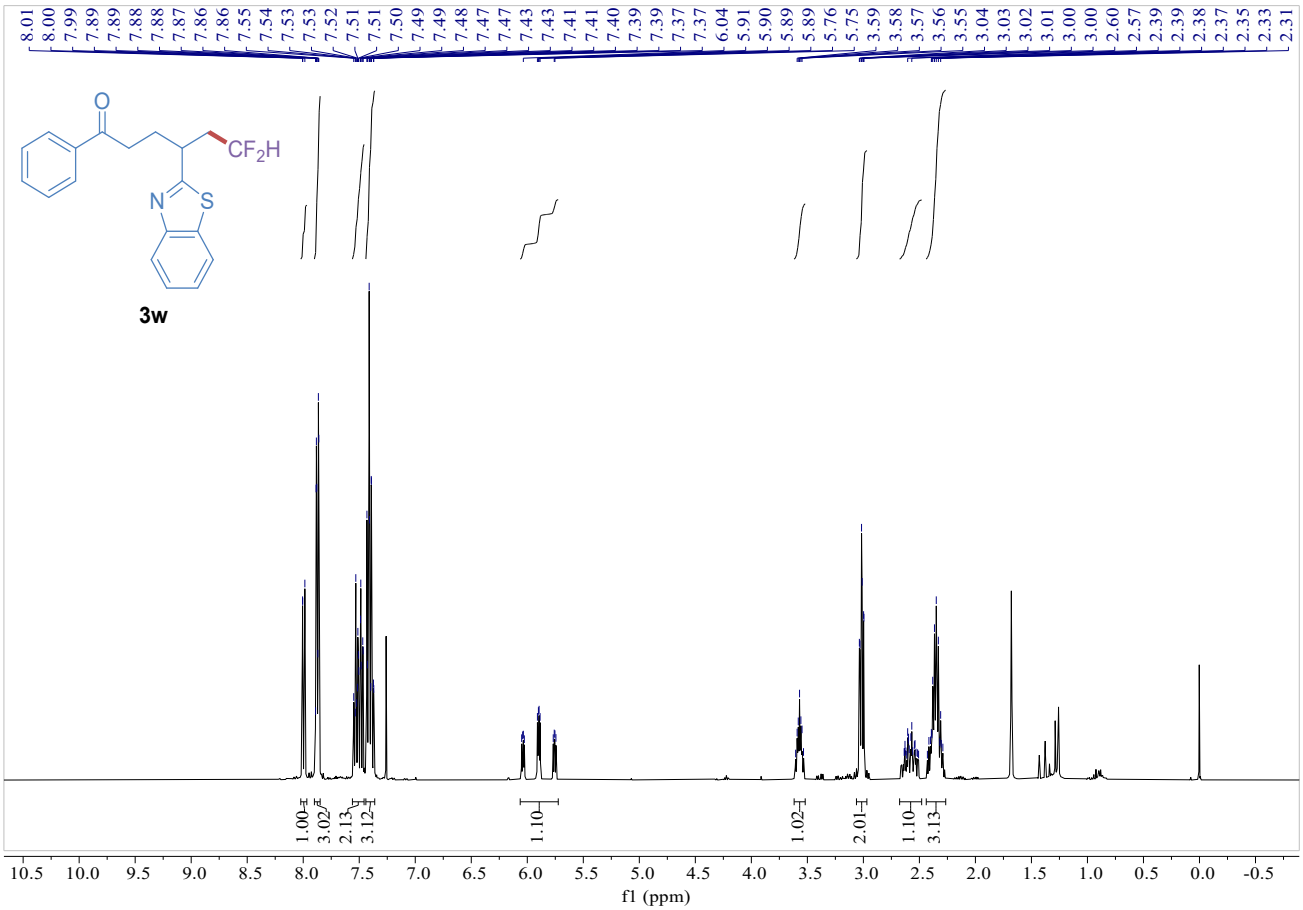
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3u**



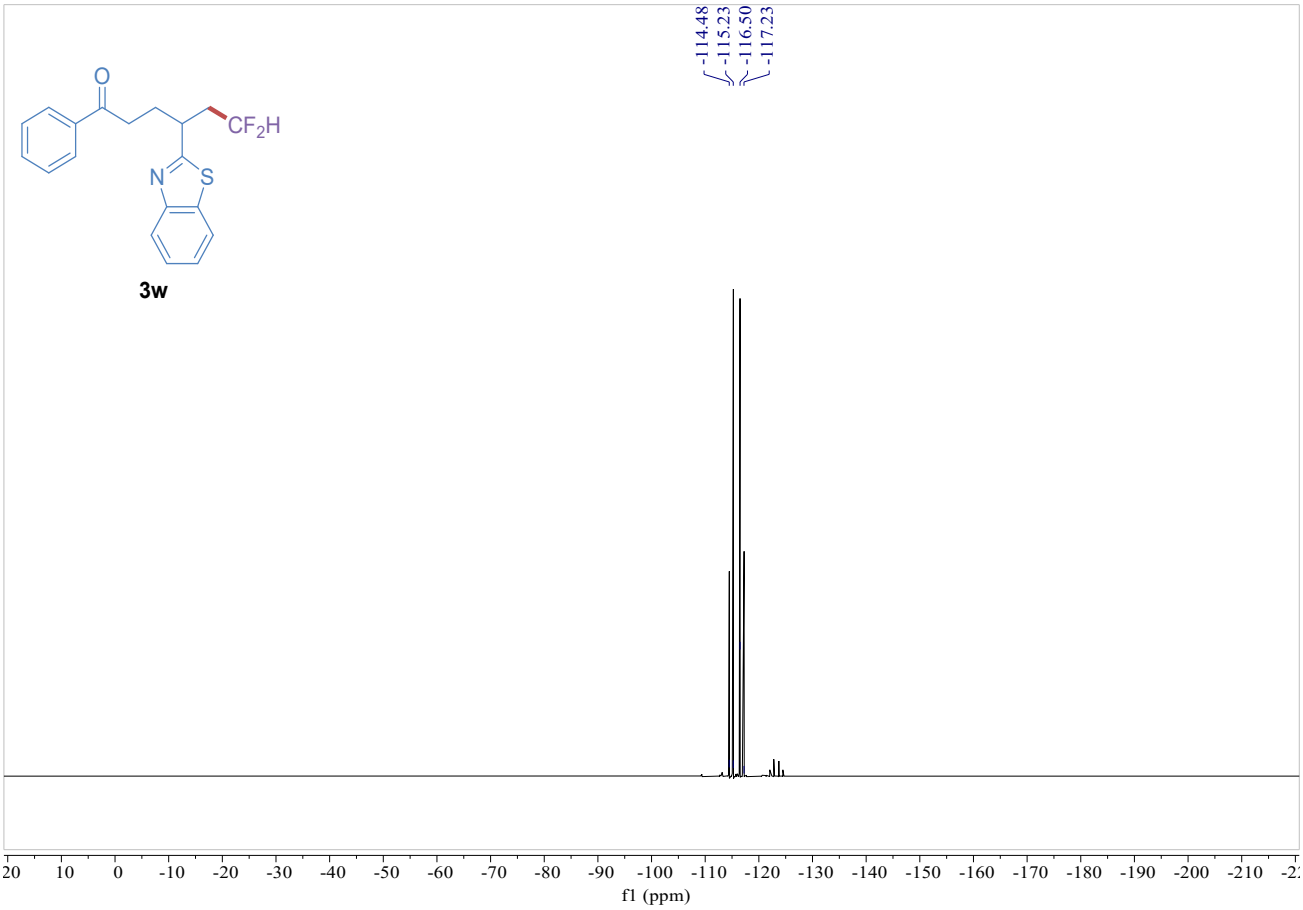
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3v**



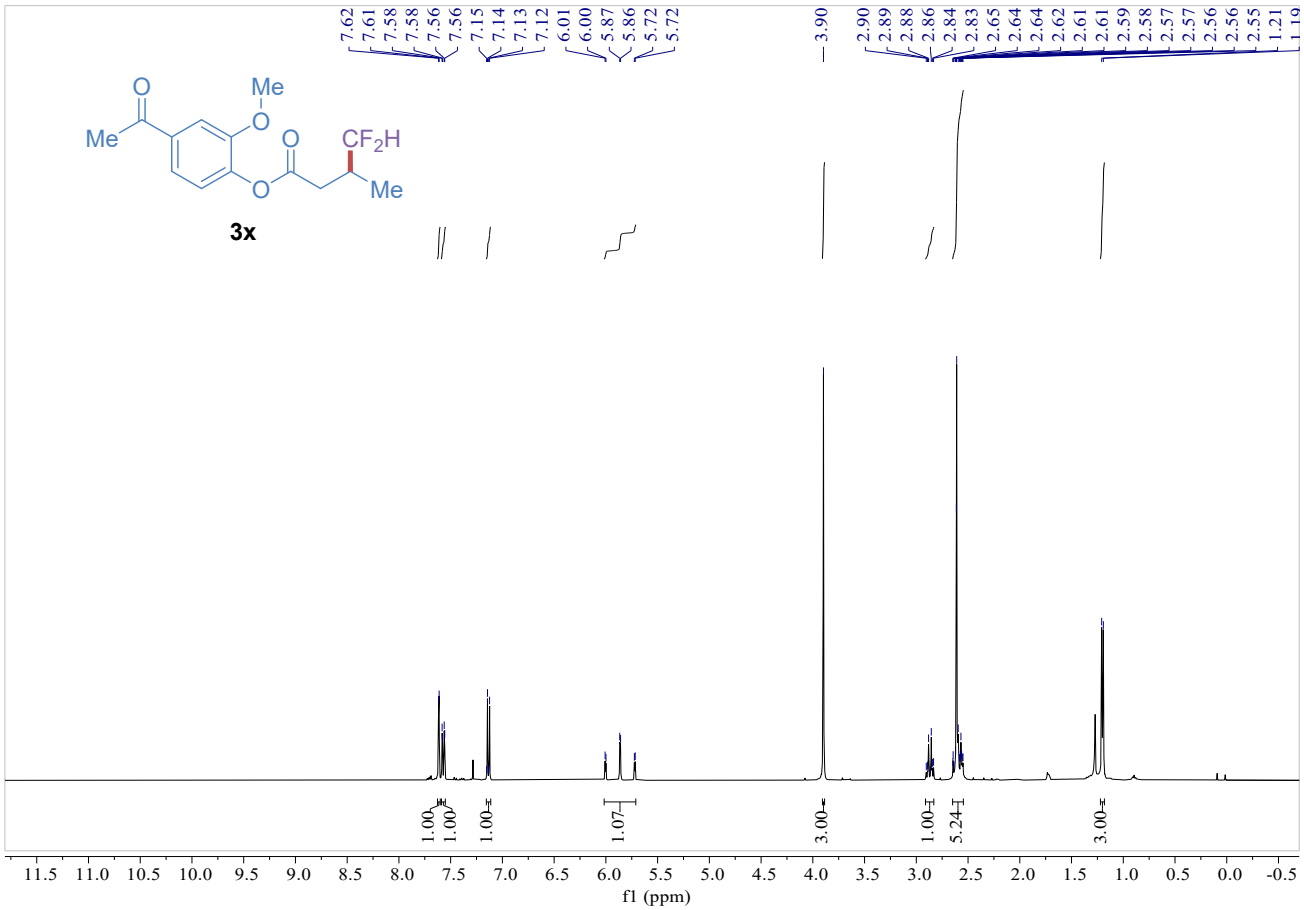
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3v**



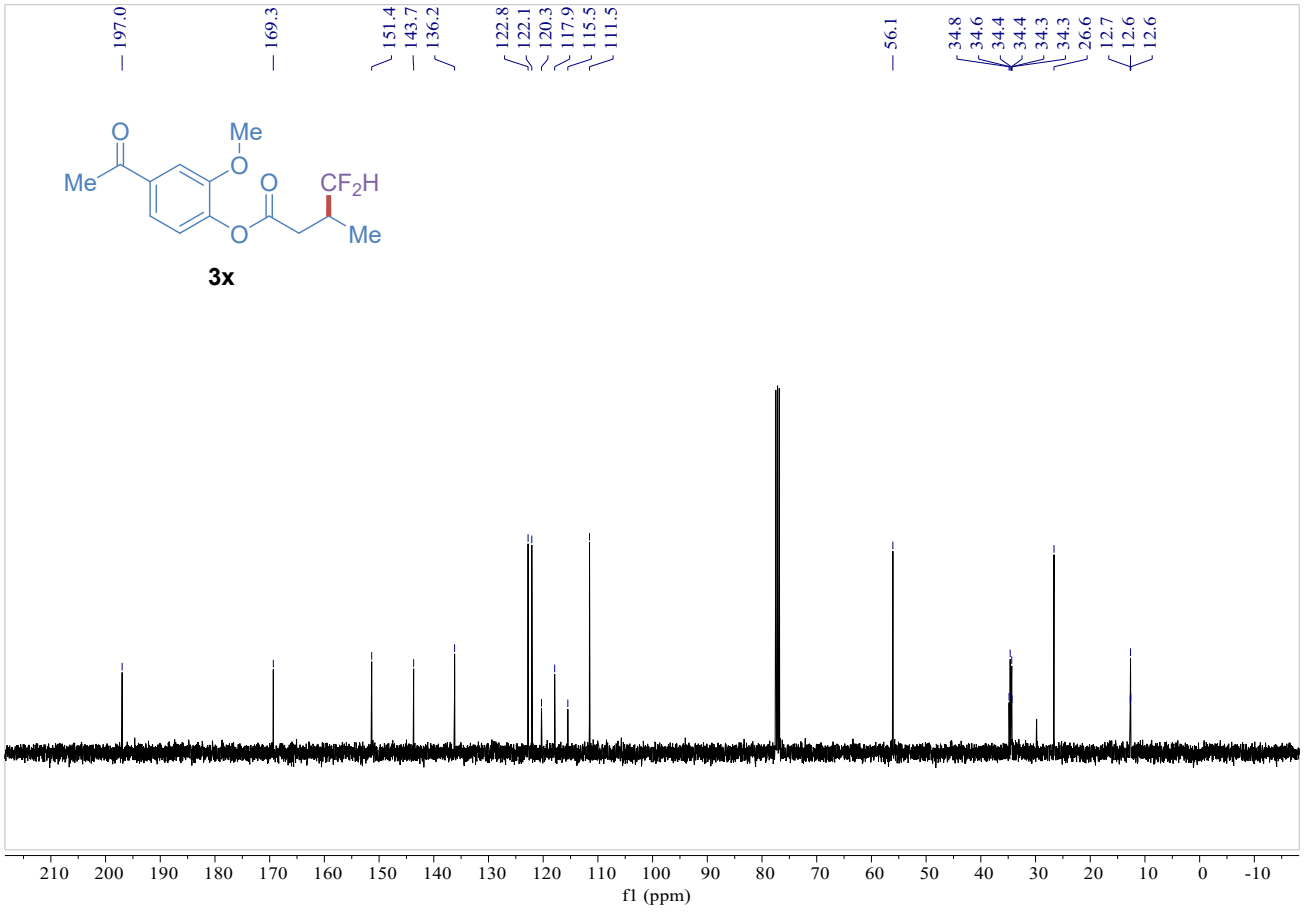
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3w**



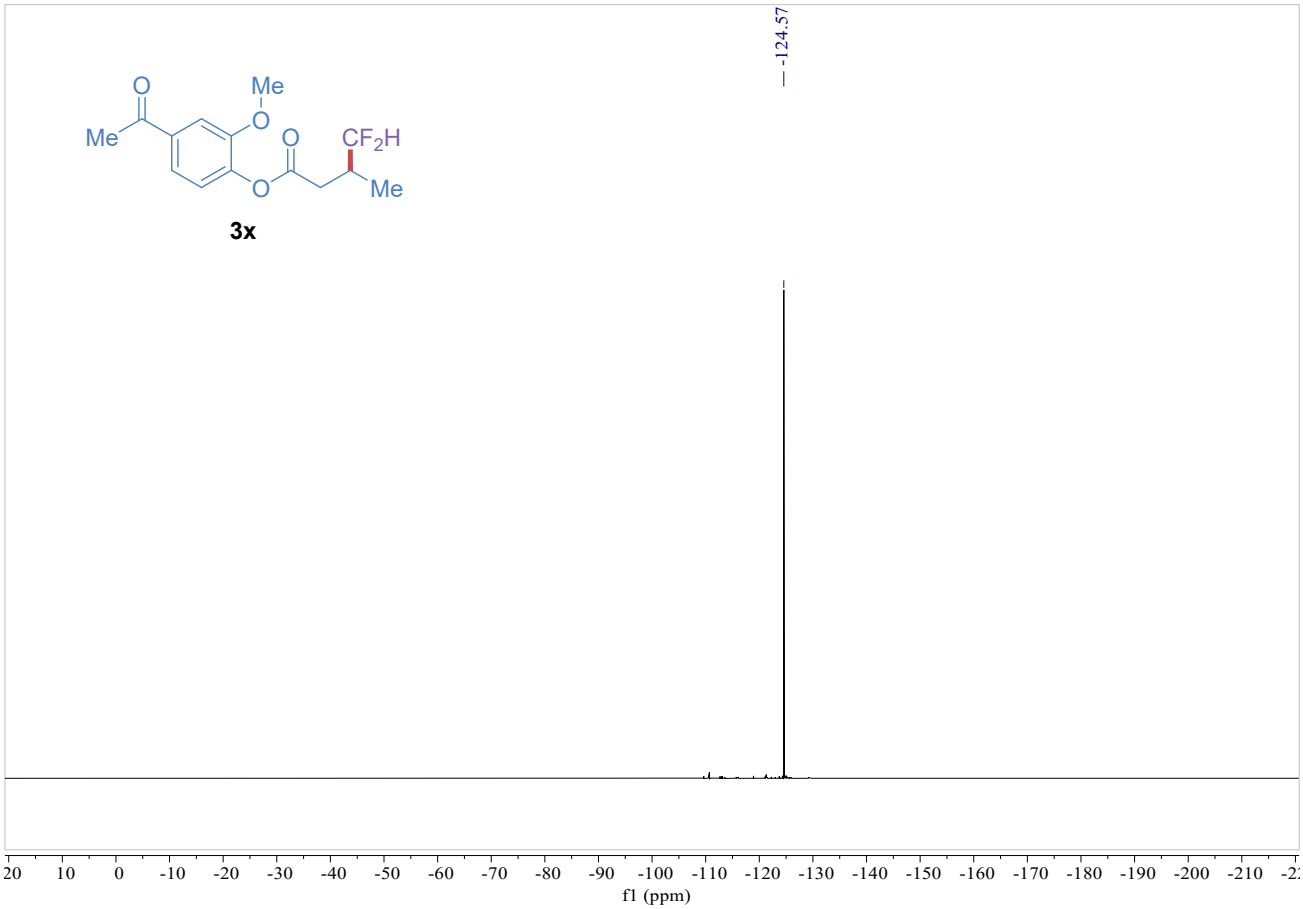
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3w**



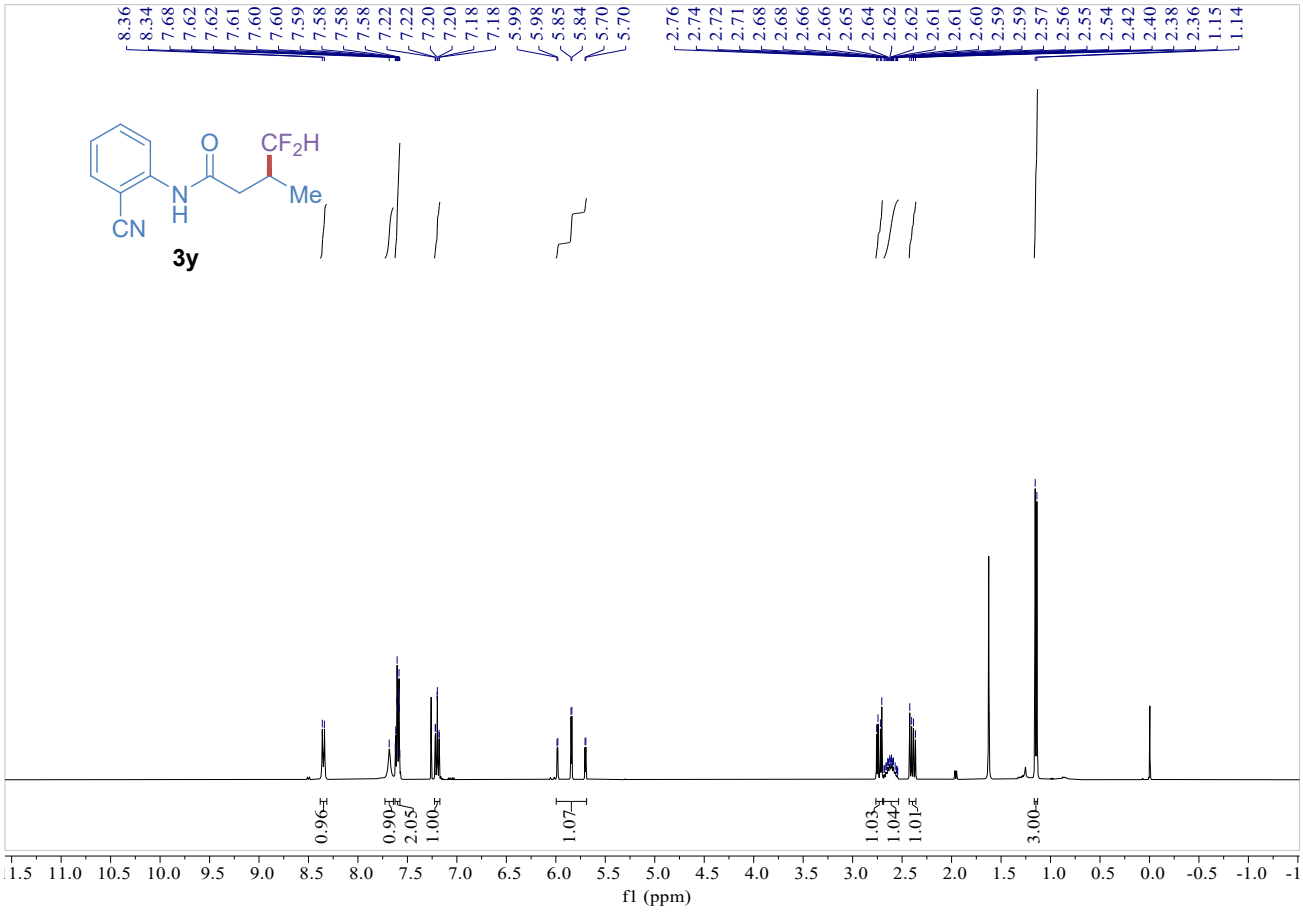
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3x**



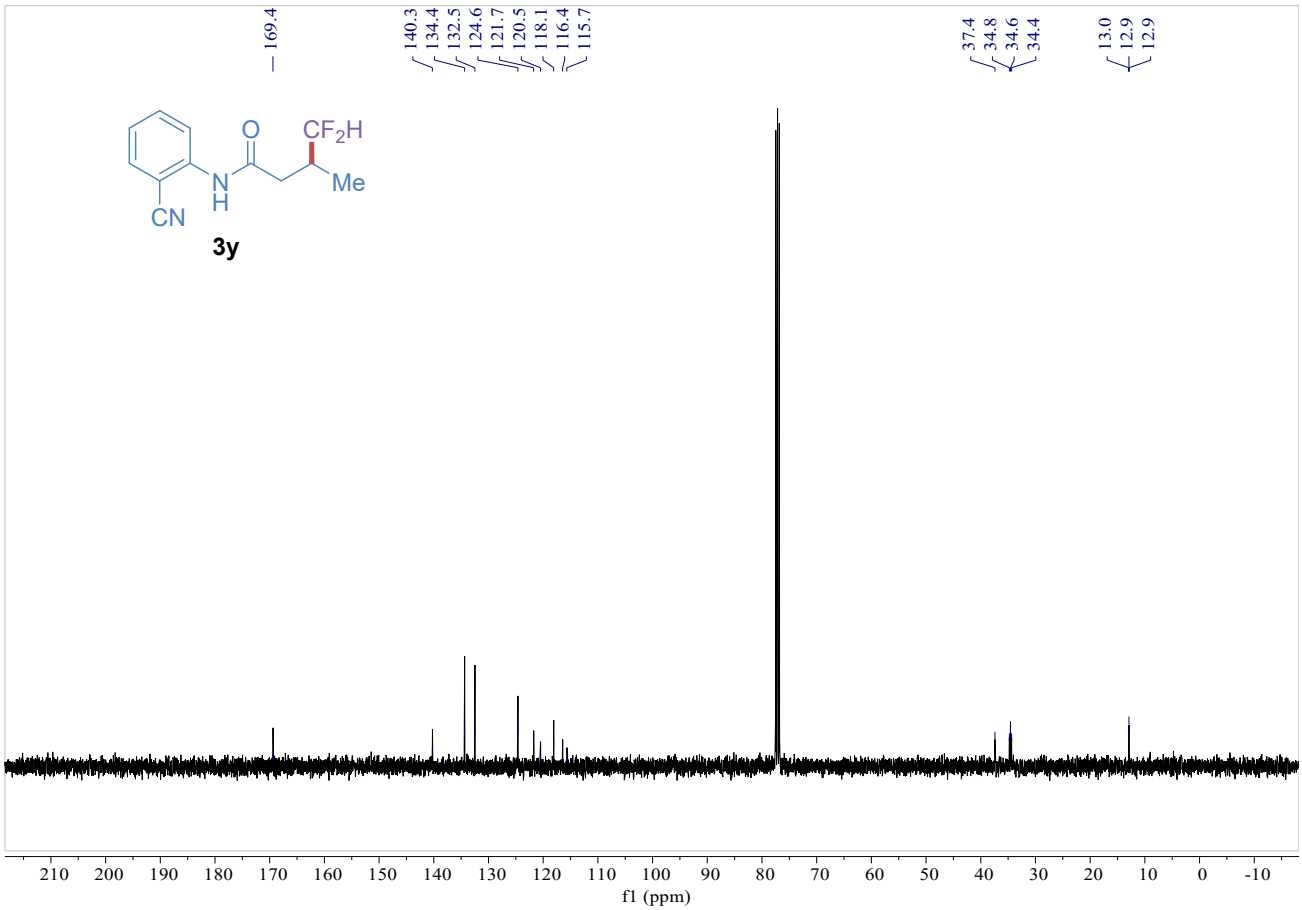
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **3x**



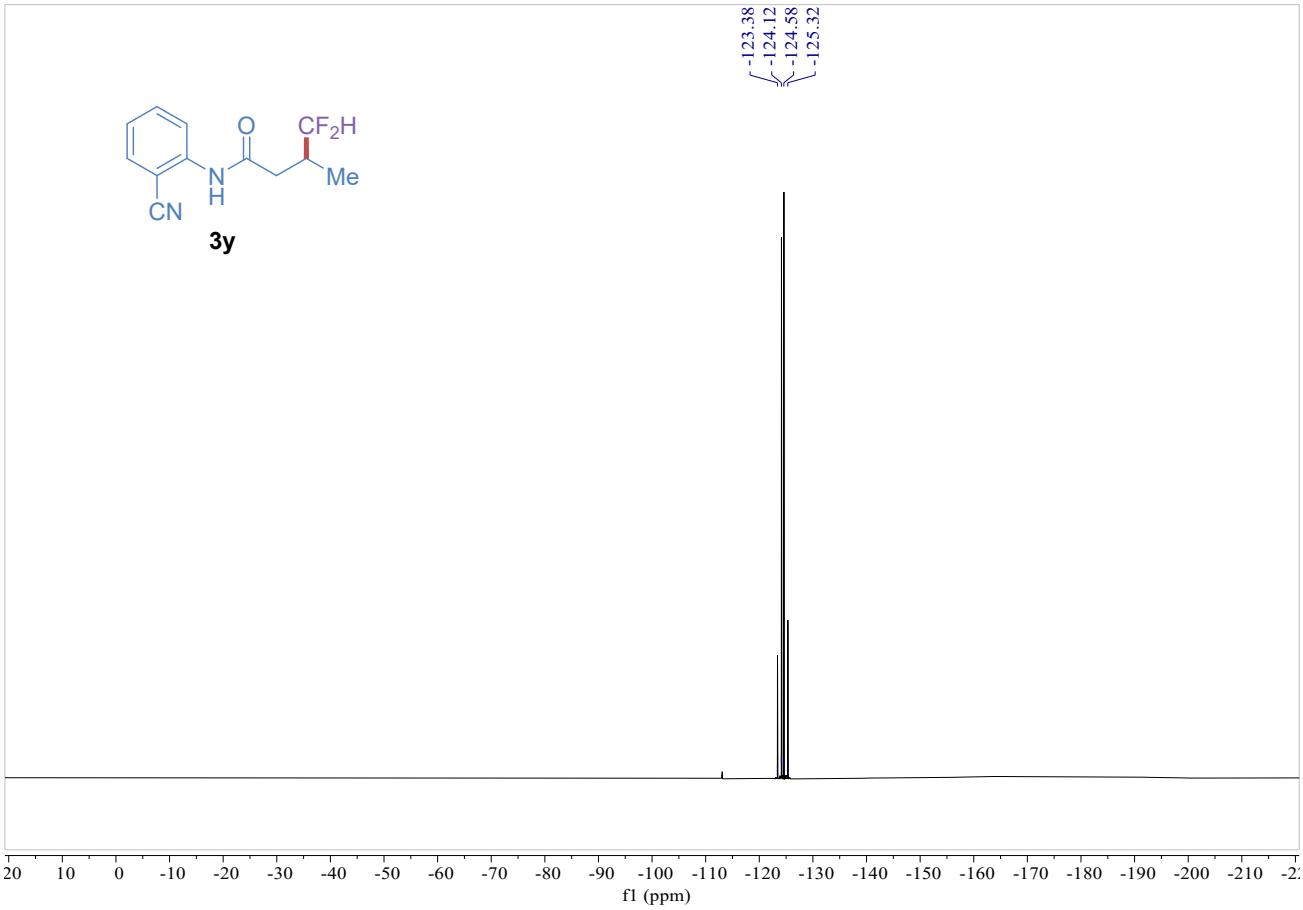
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3x**



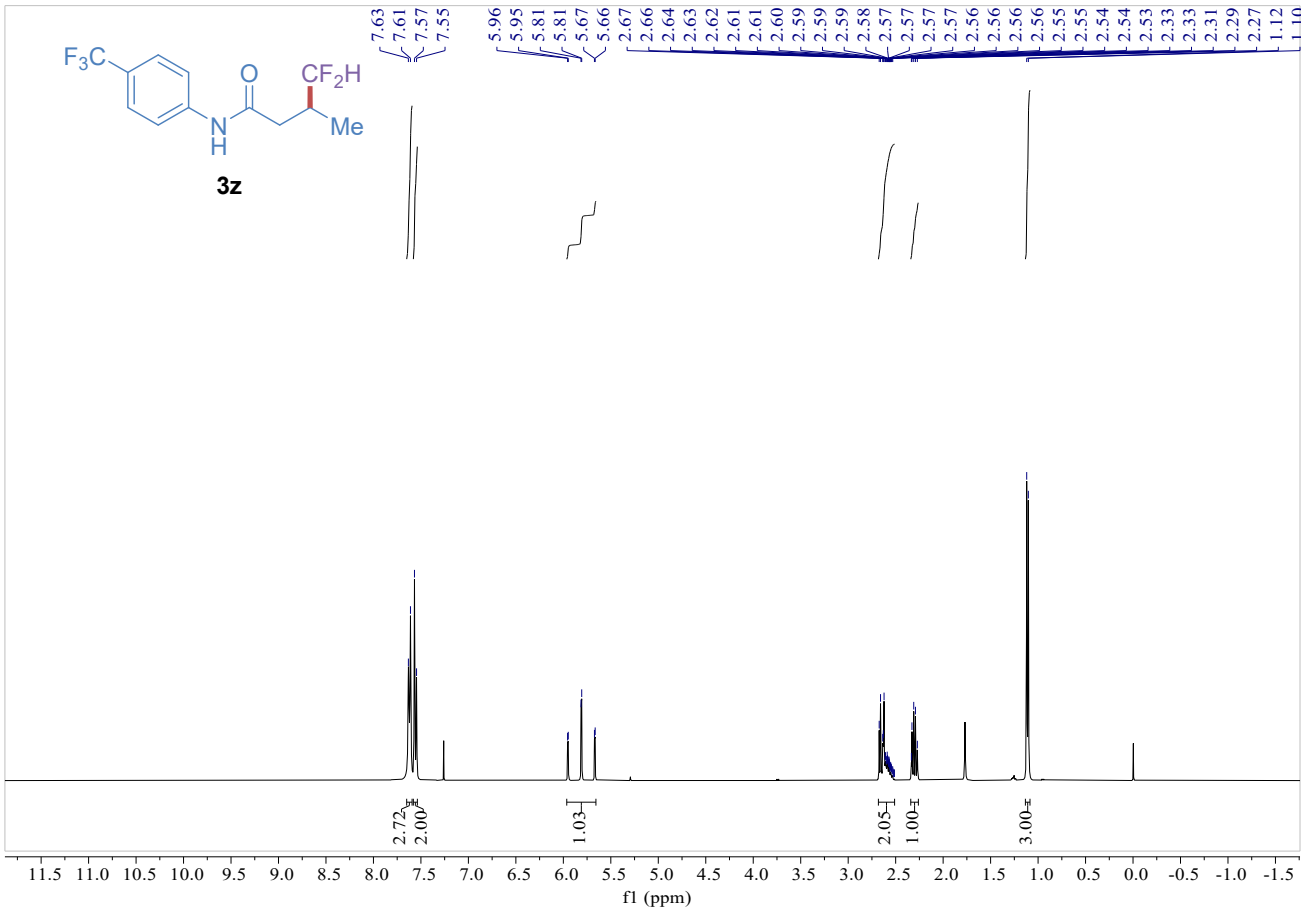
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3y**



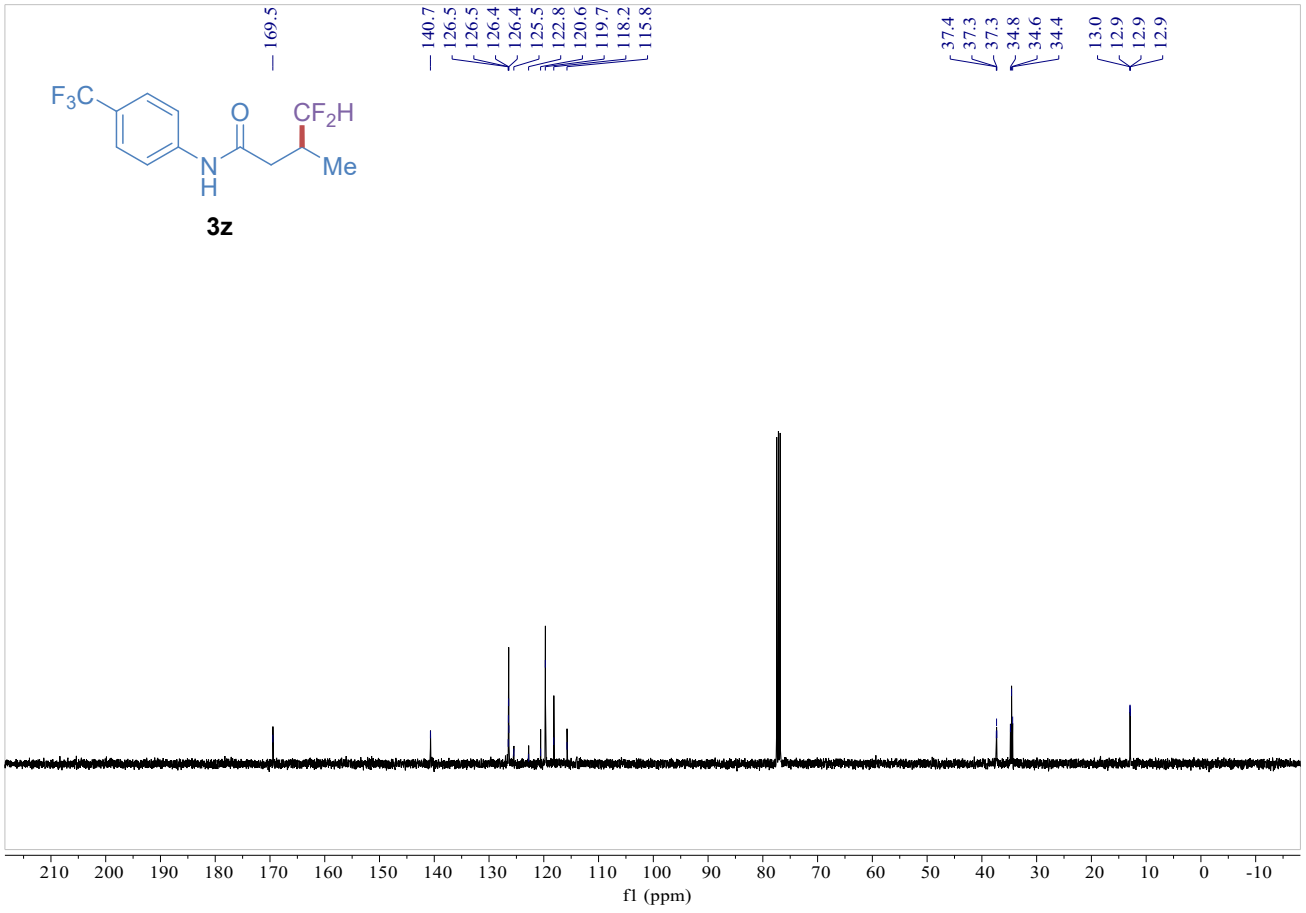
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **3y**



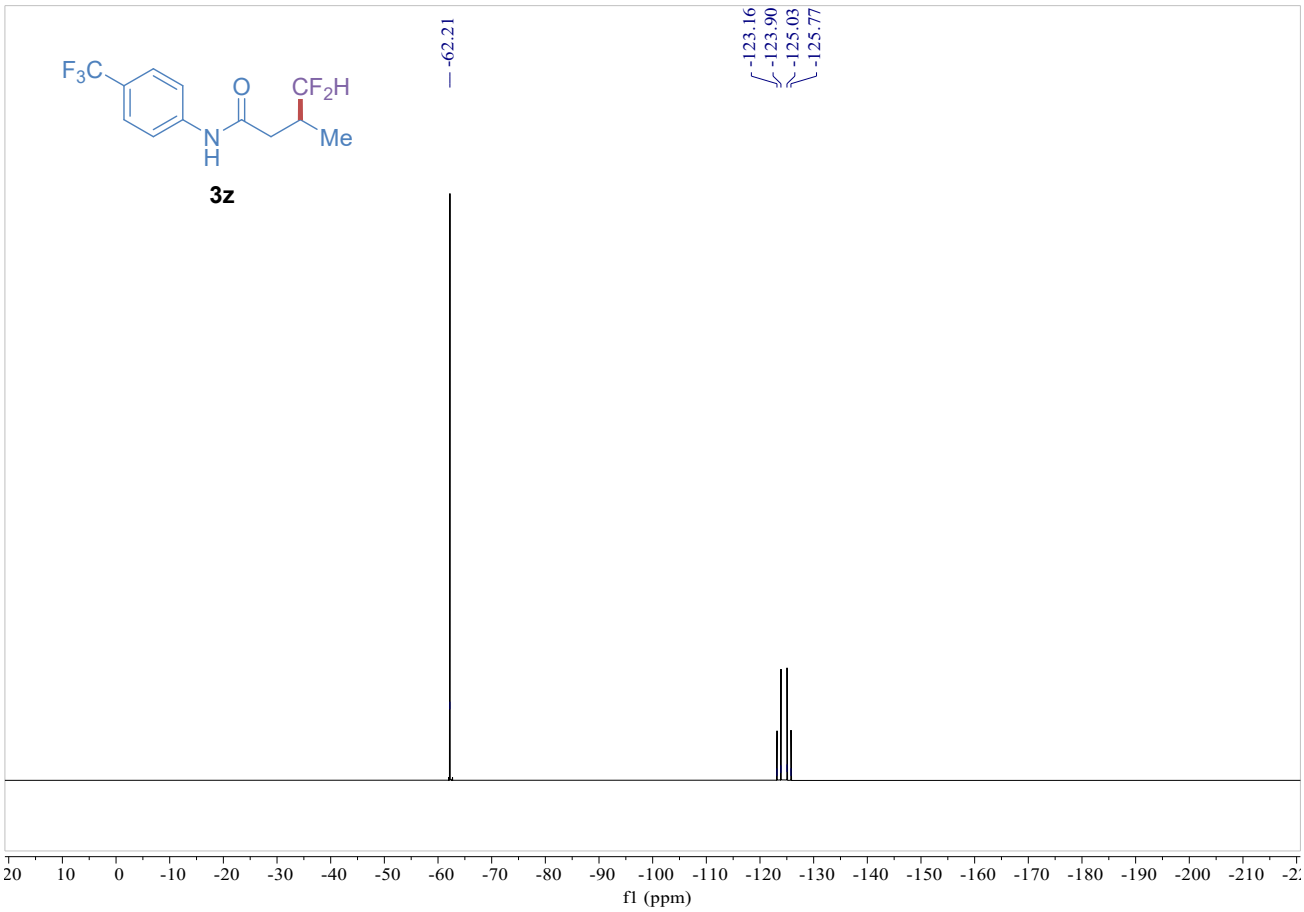
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3y**



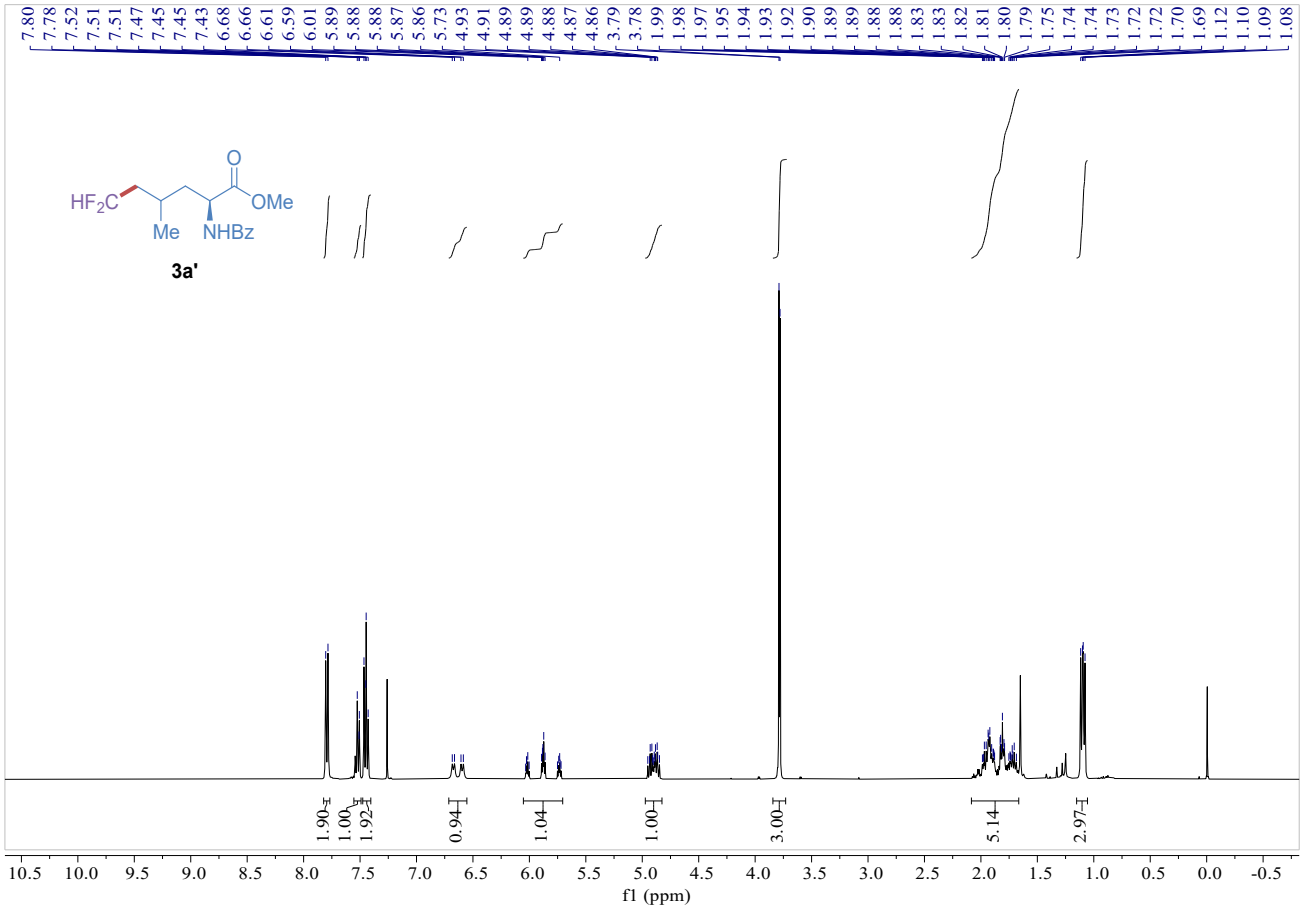
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3z**



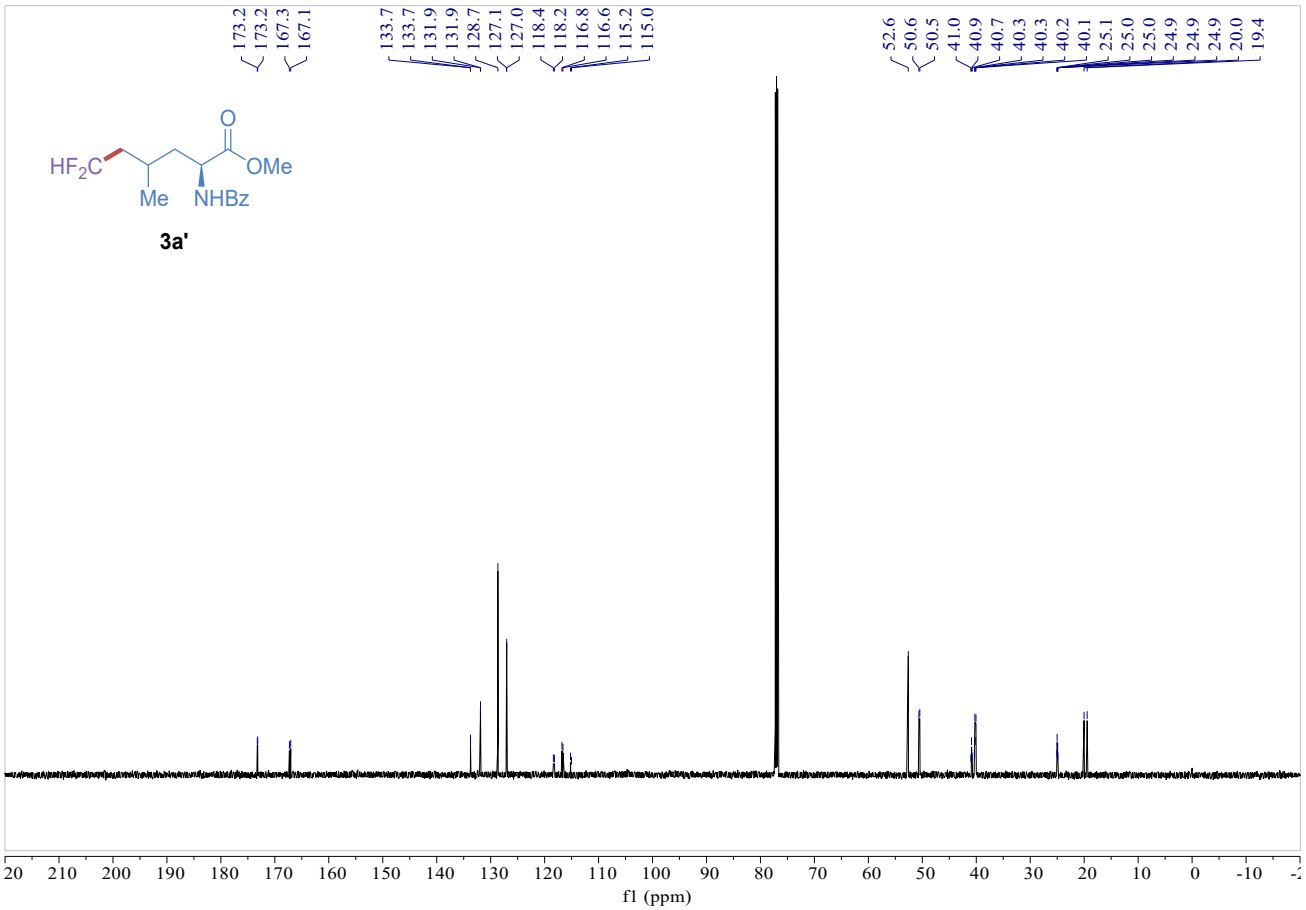
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **3z**



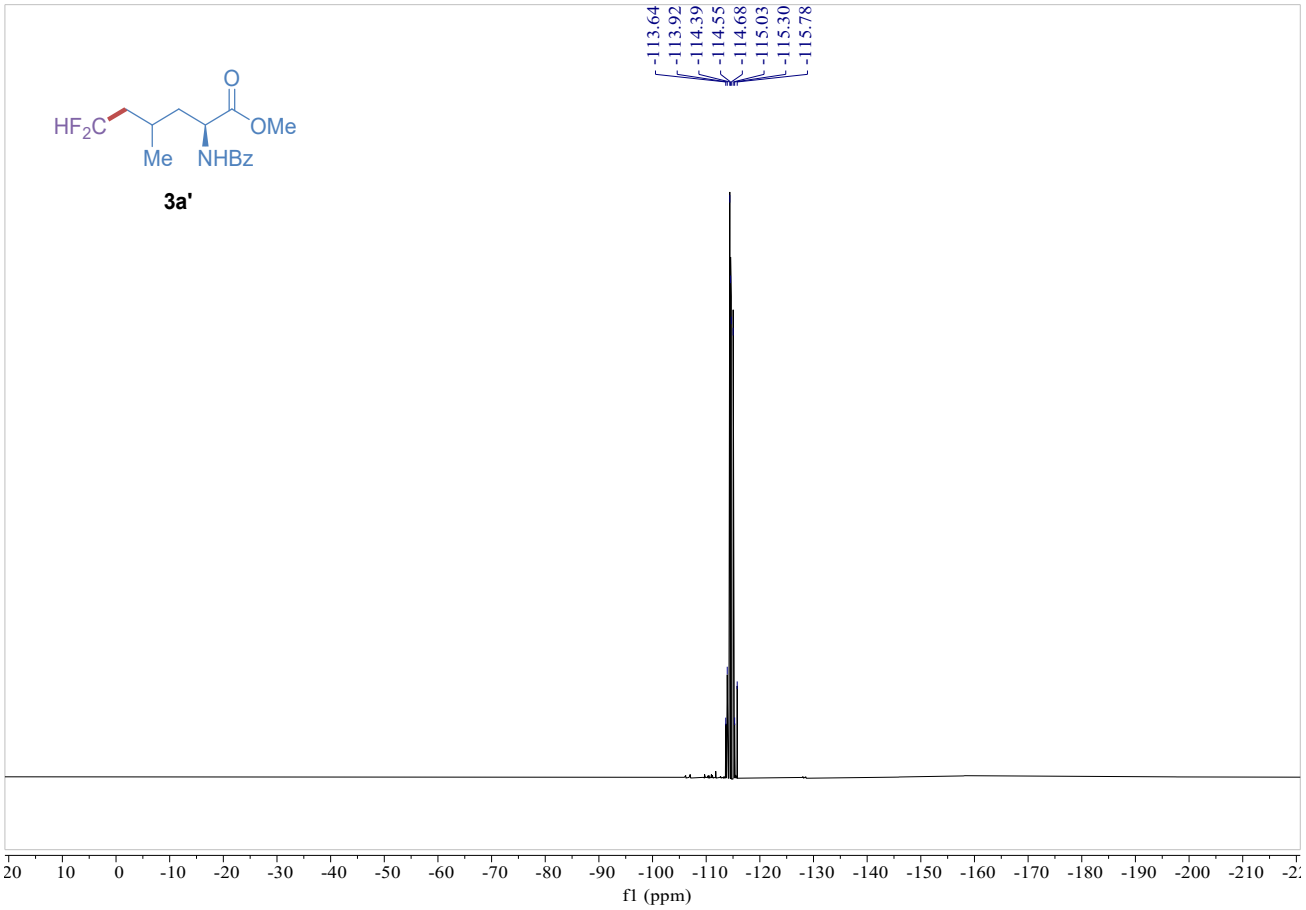
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3z**



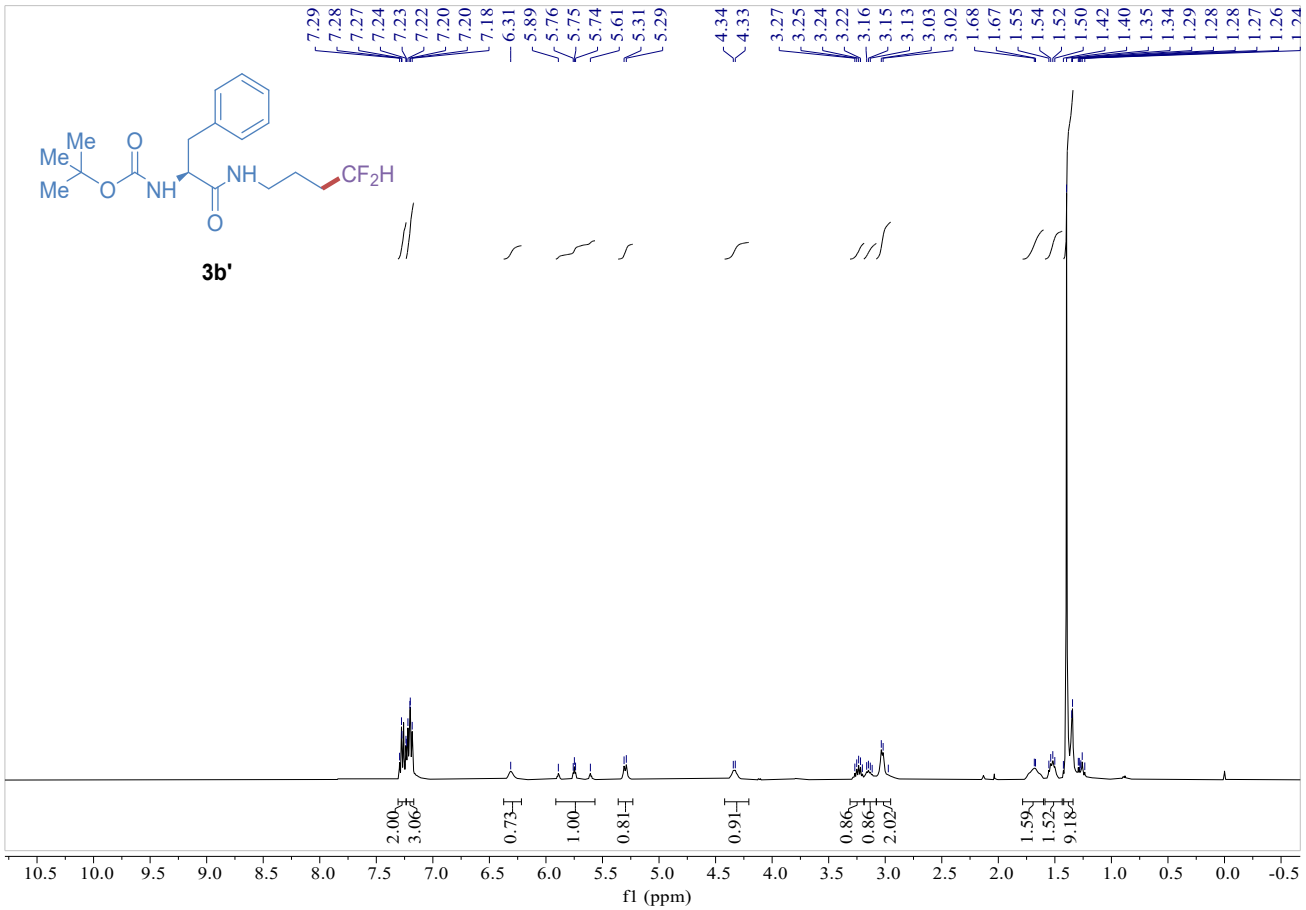
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3a'**



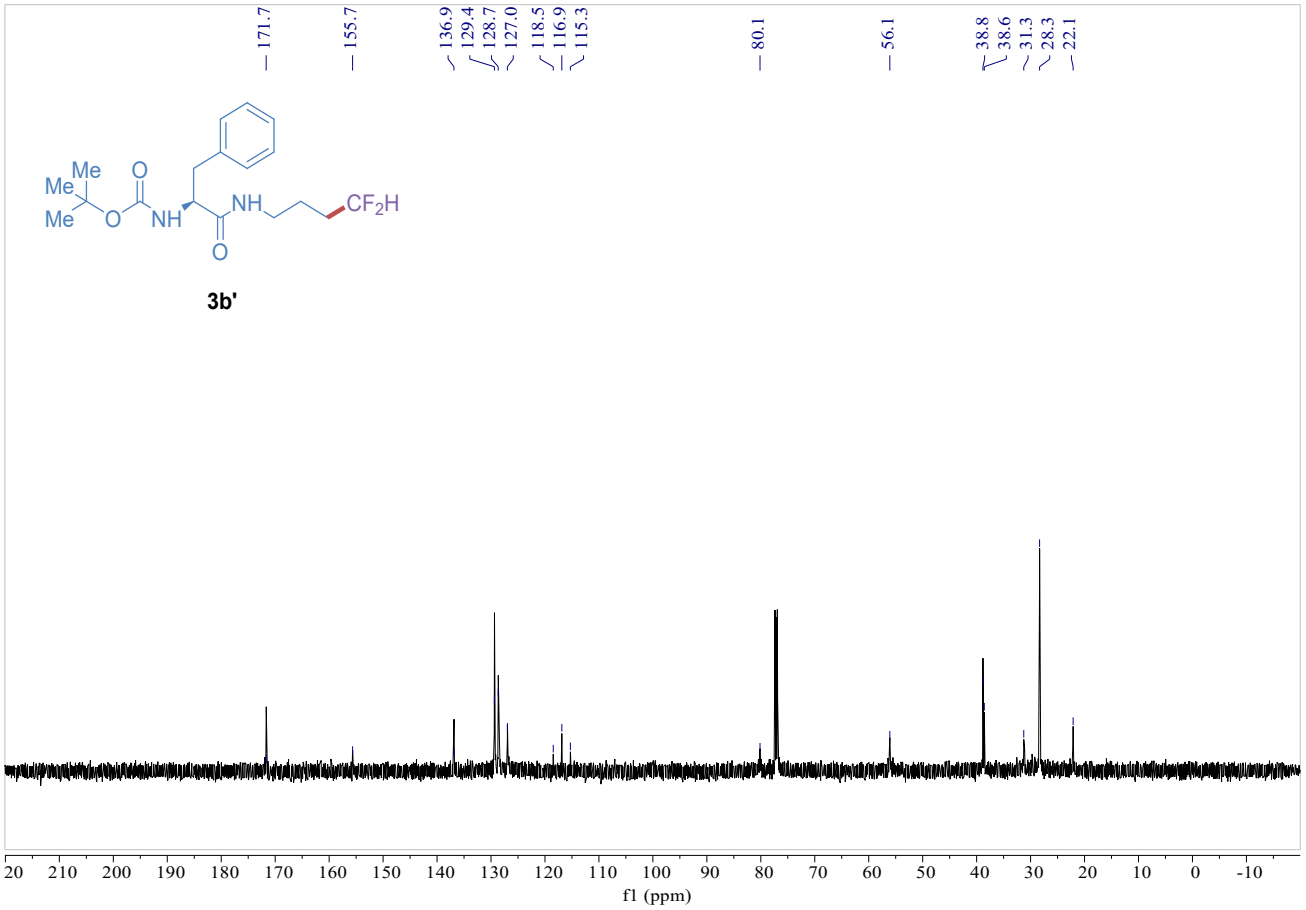
^{13}C NMR spectrum (151 MHz, $CDCl_3$) of compound **3a'**



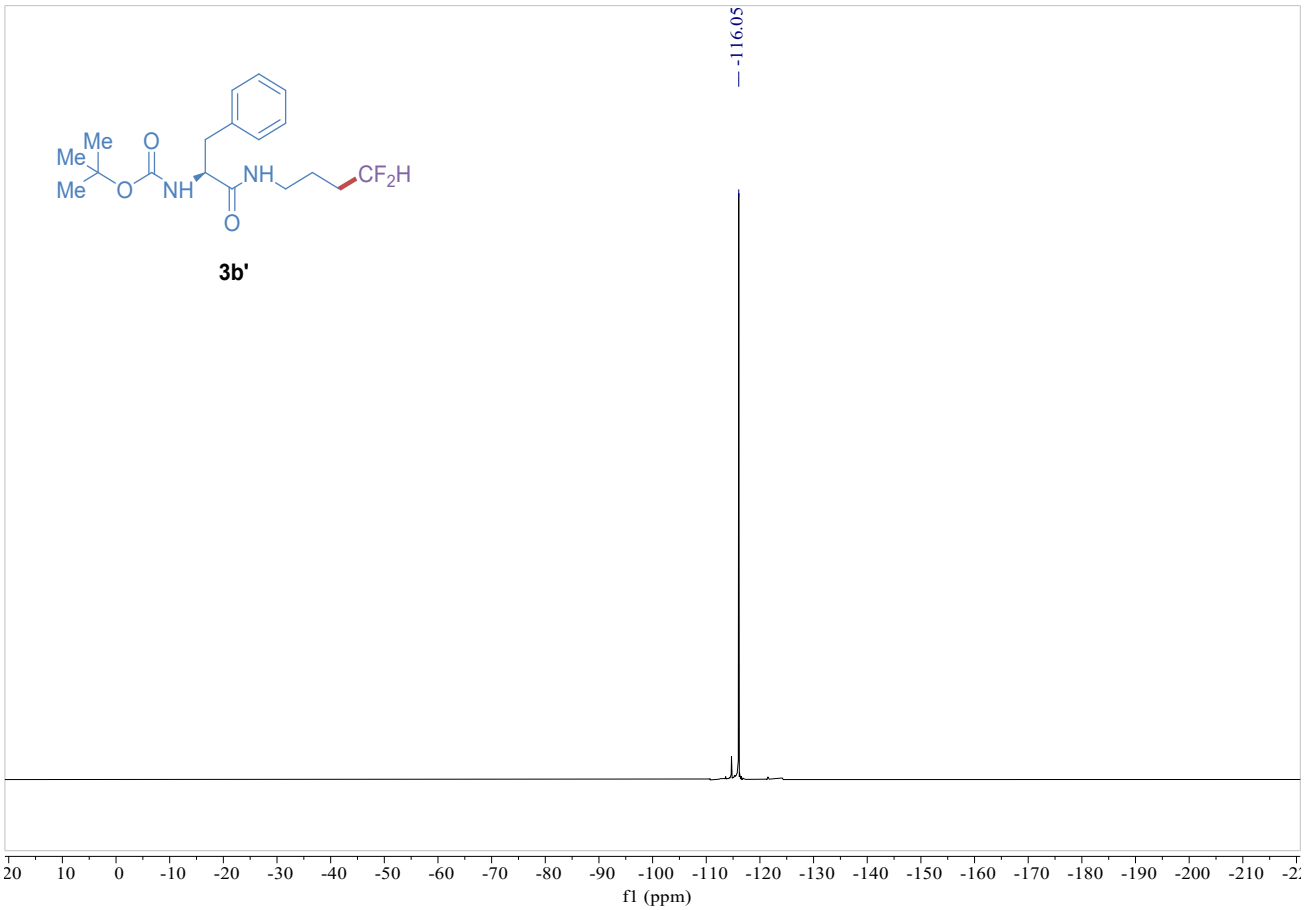
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3a'**



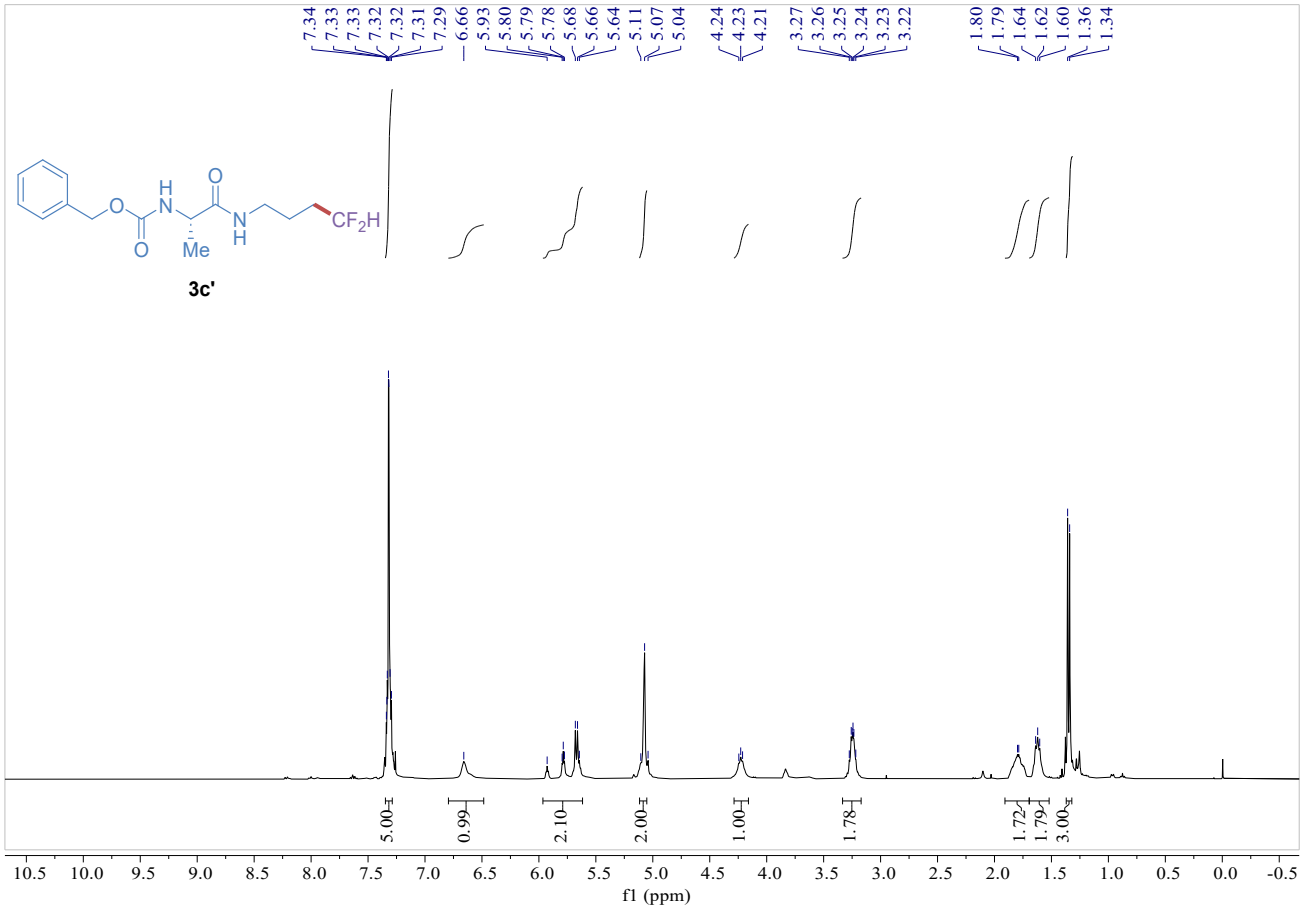
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3b'**



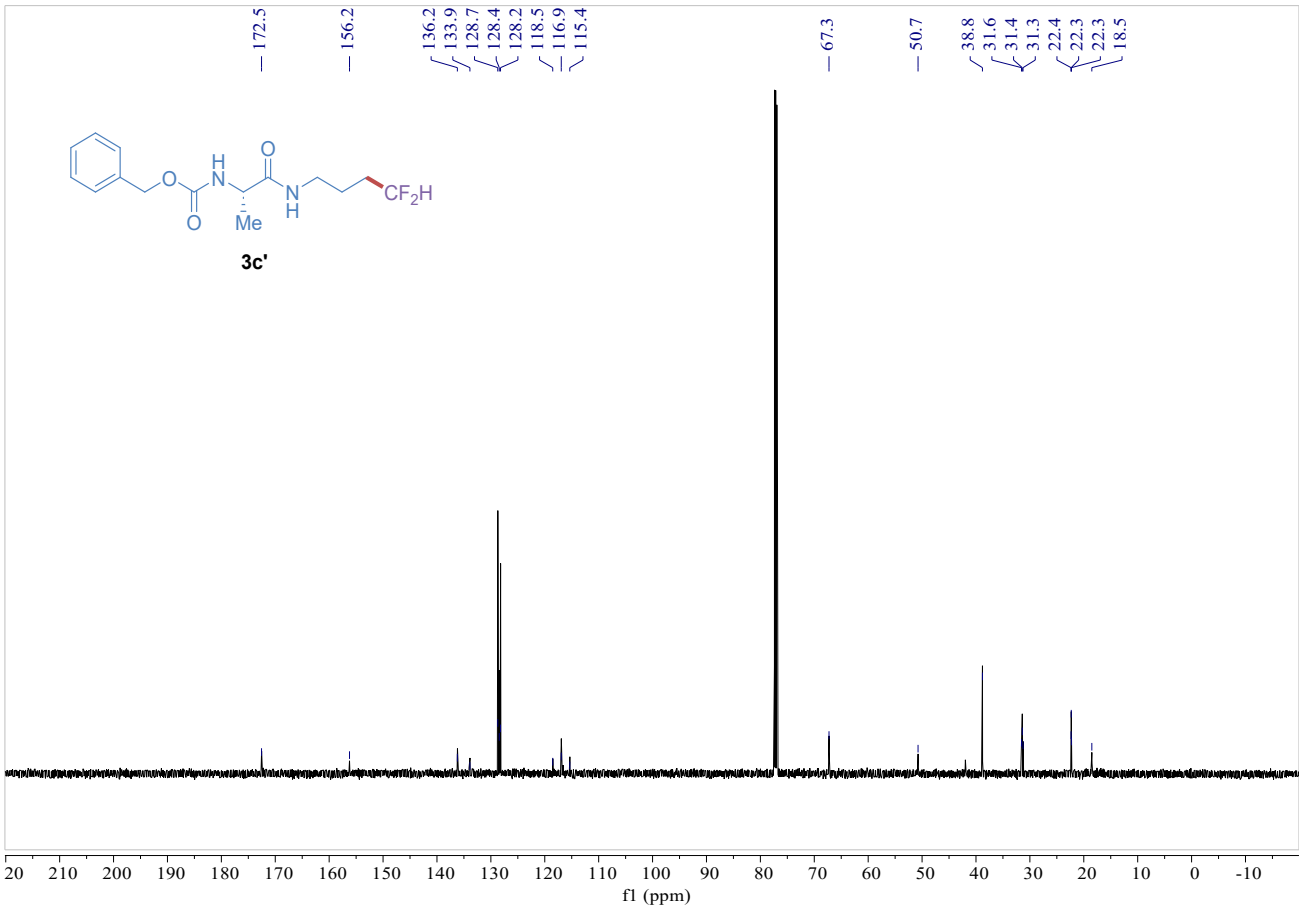
^{13}C NMR spectrum (151 MHz, $CDCl_3$) of compound **3b'**



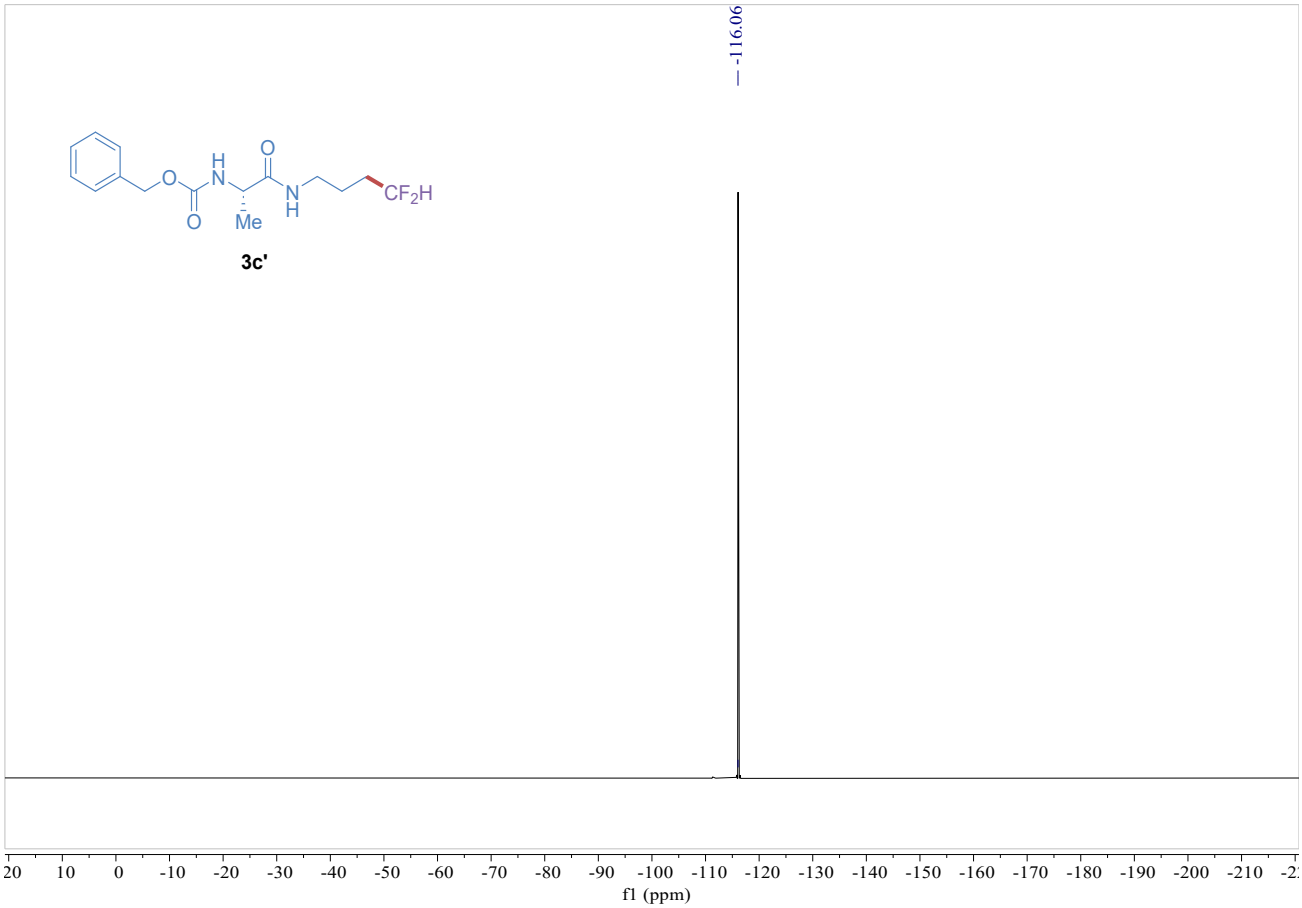
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3b'**



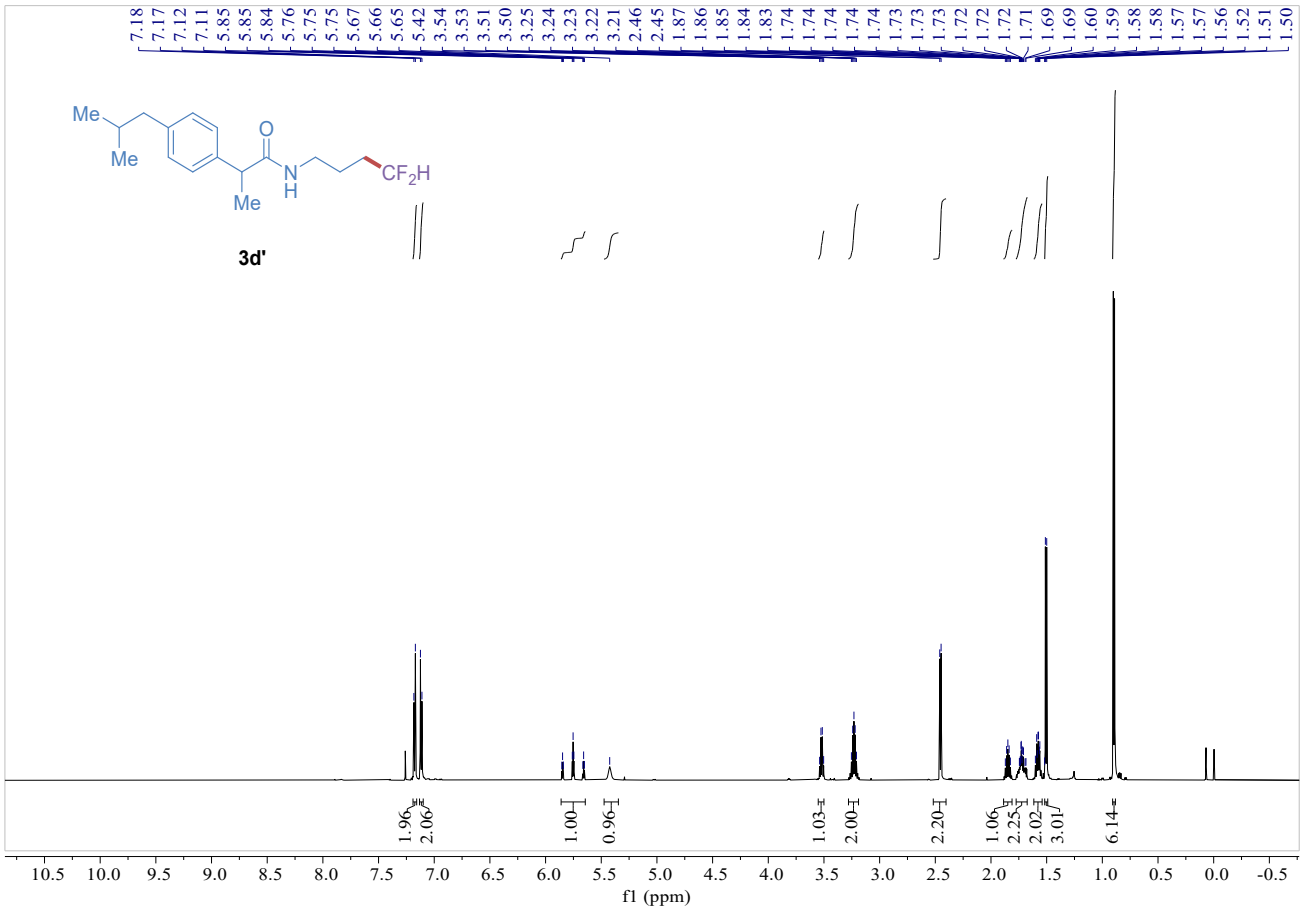
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3c'**



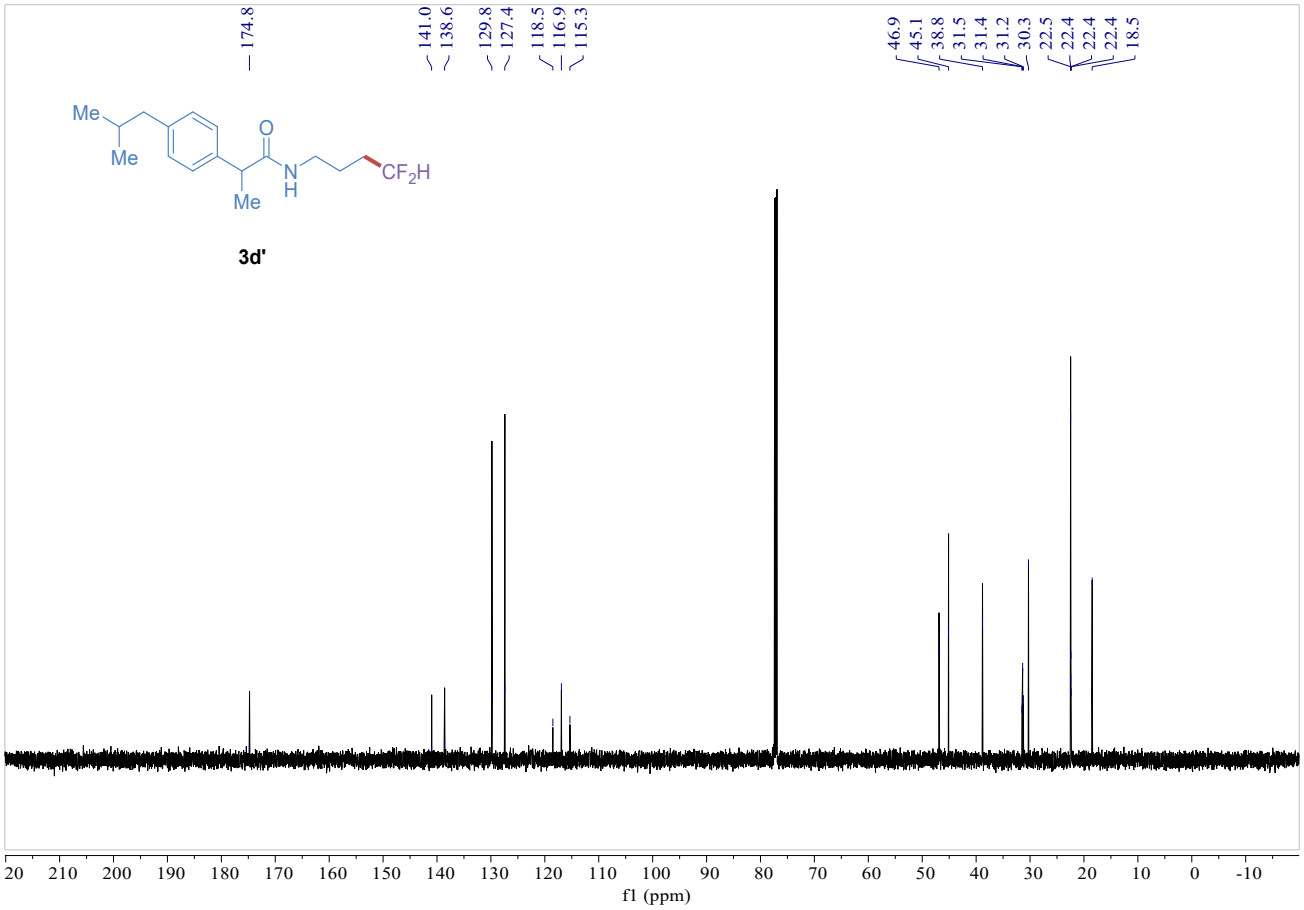
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **3c'**



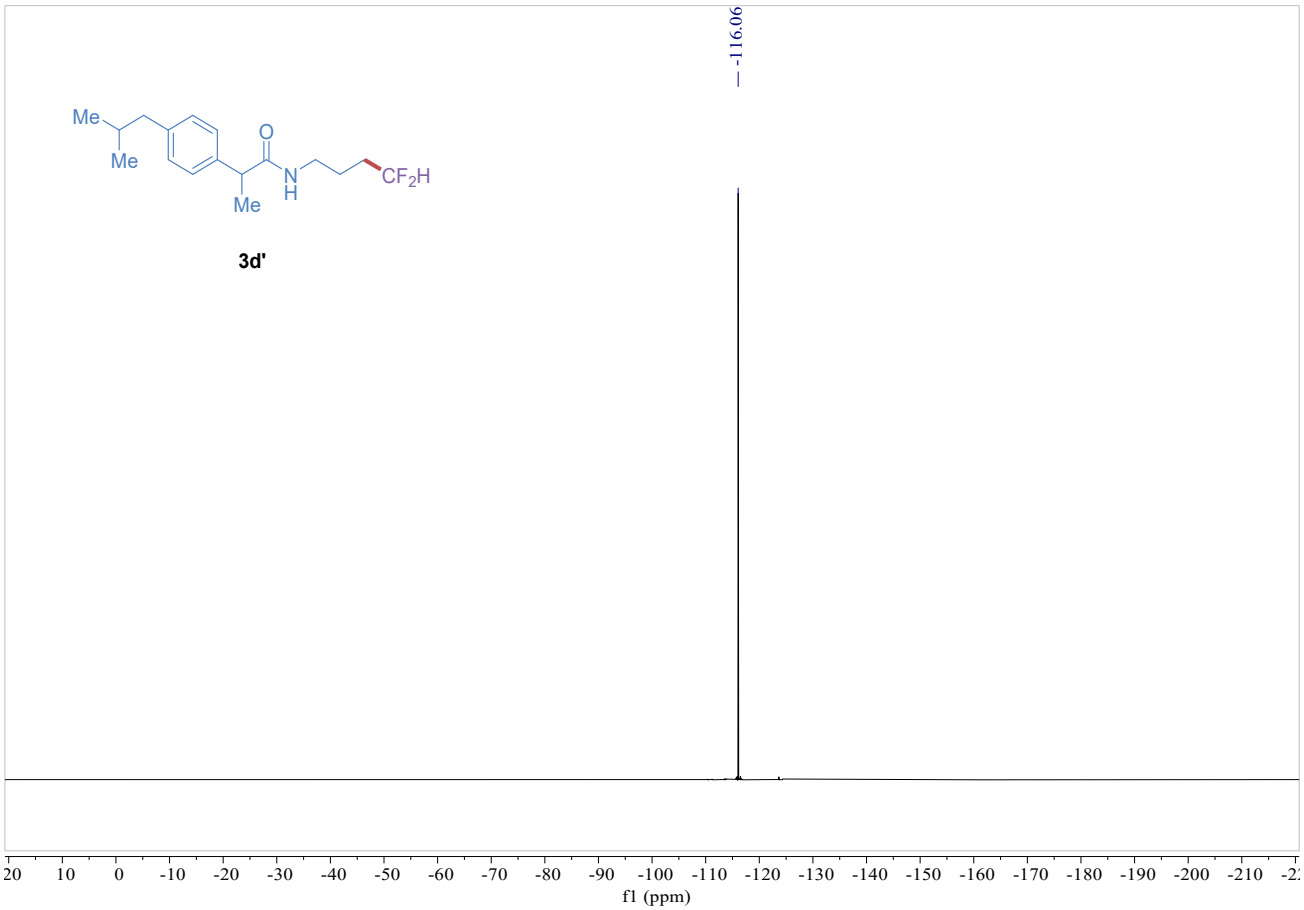
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3c'**



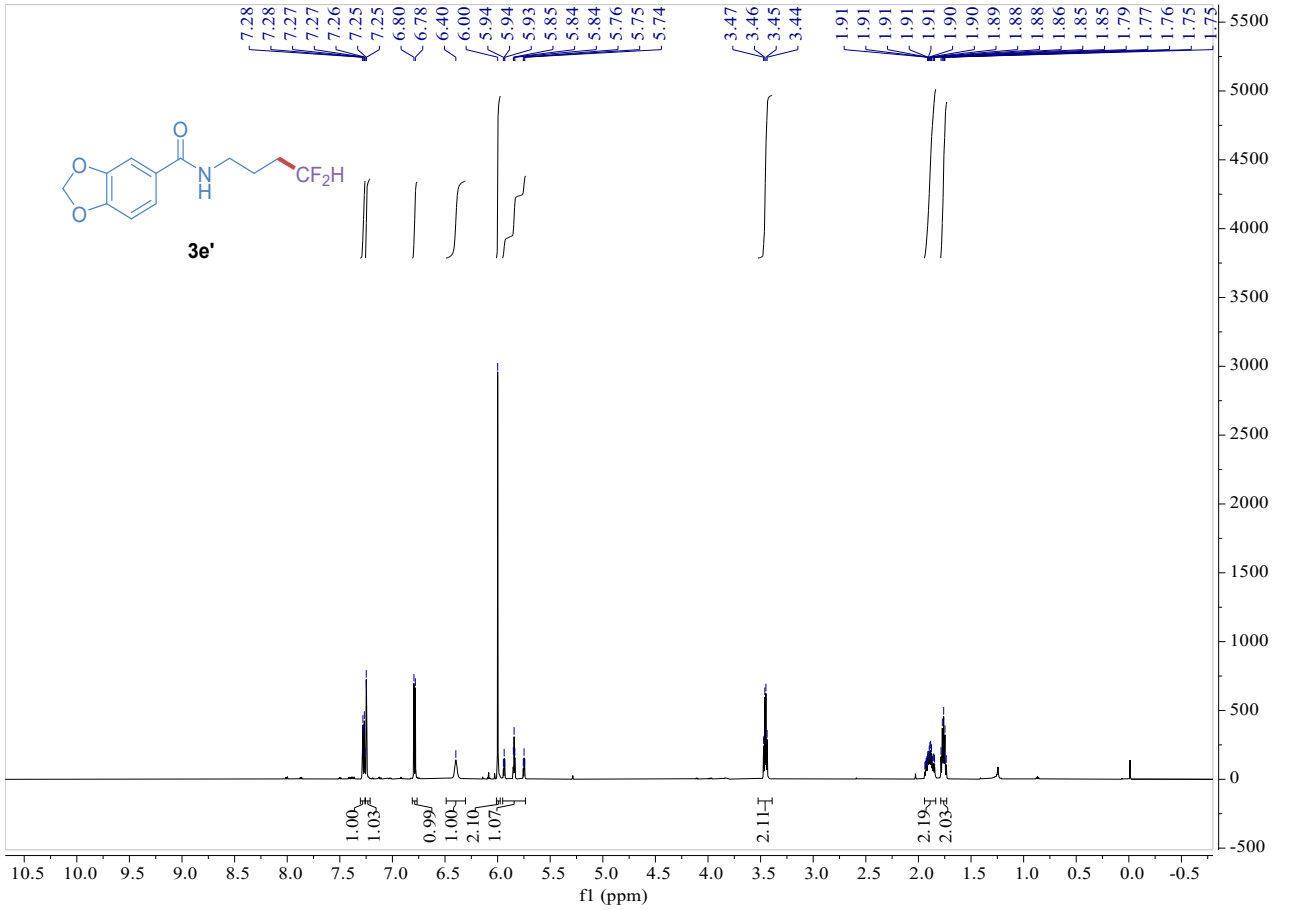
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound **3d'**



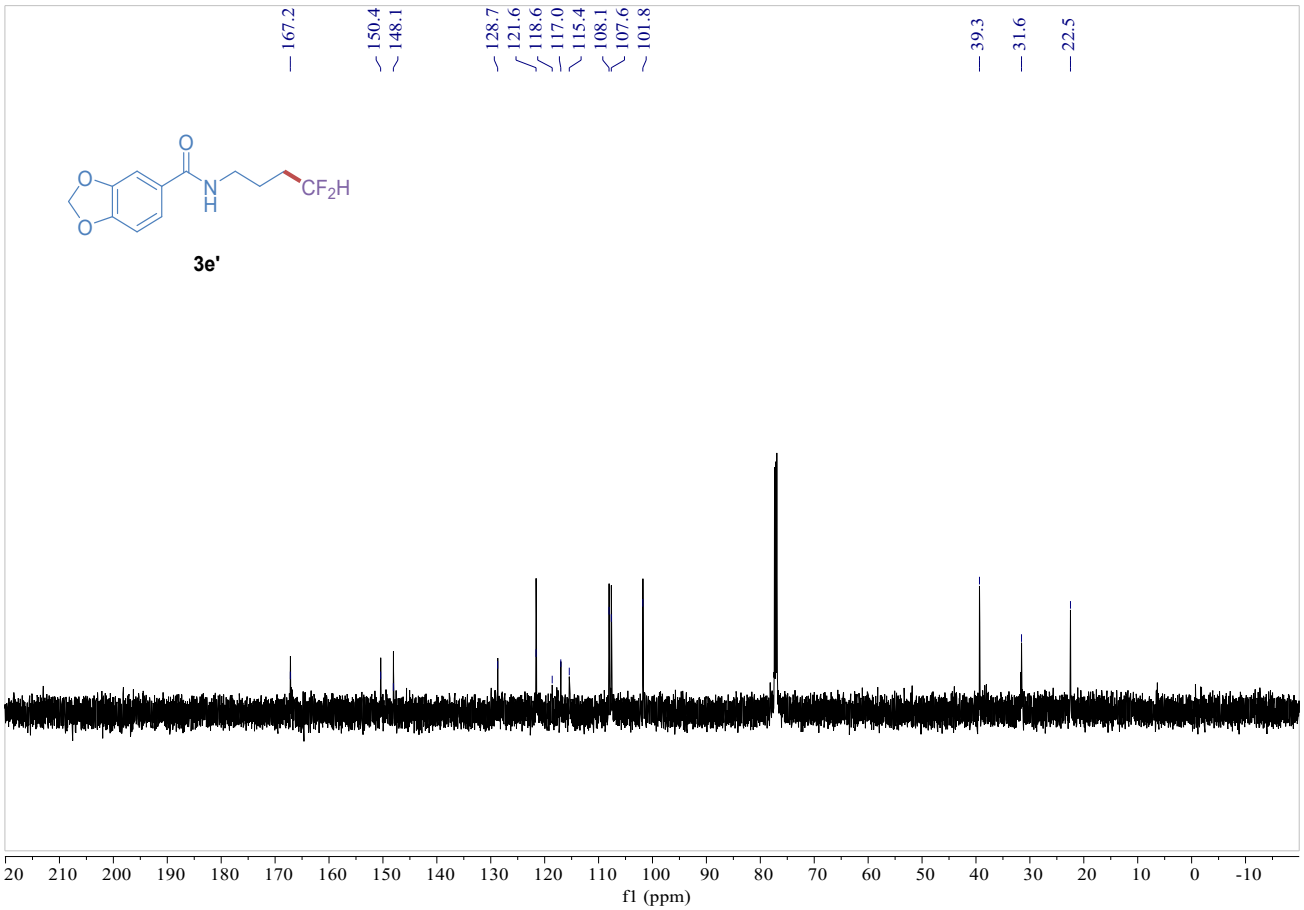
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **3d'**



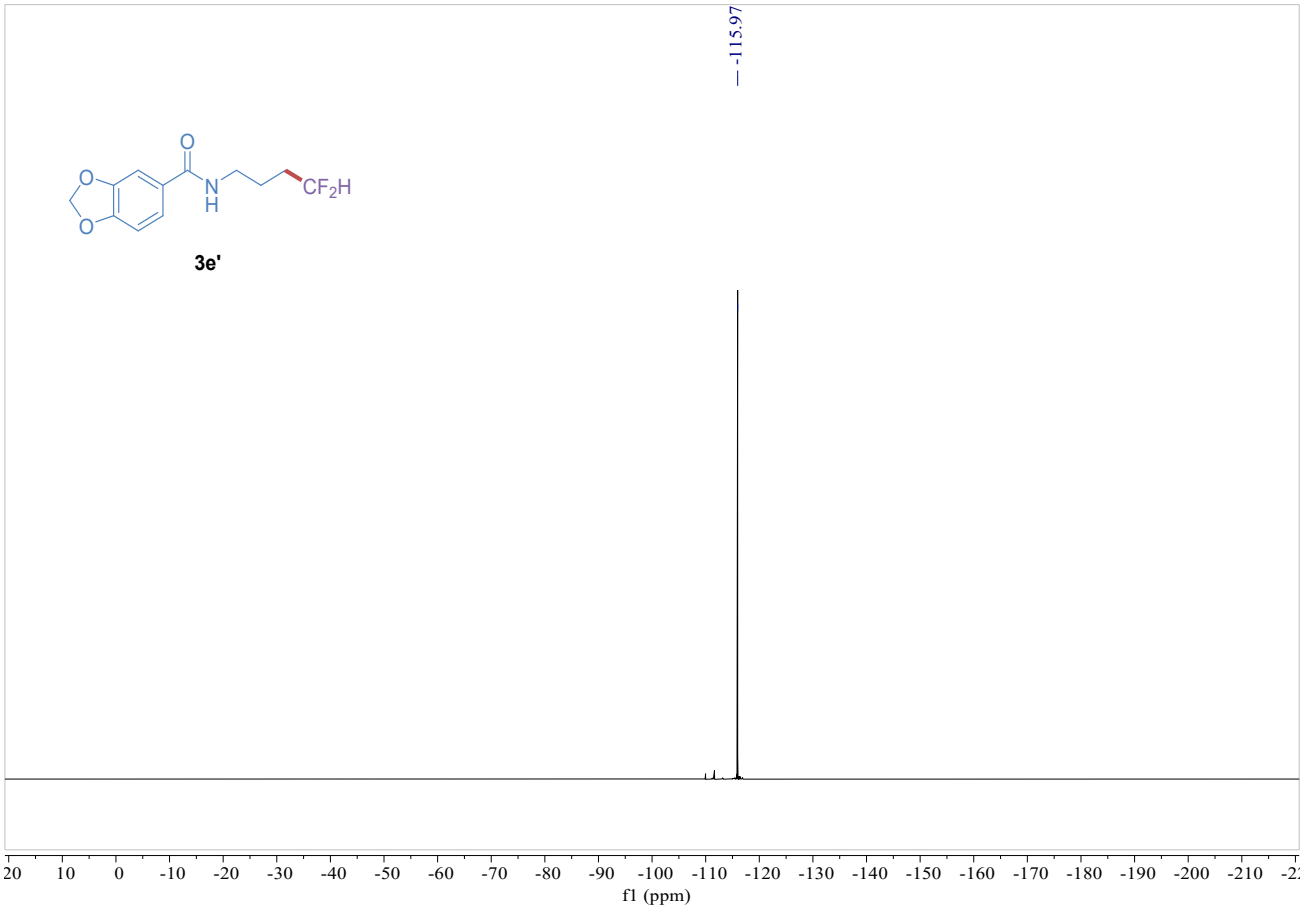
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3d'**



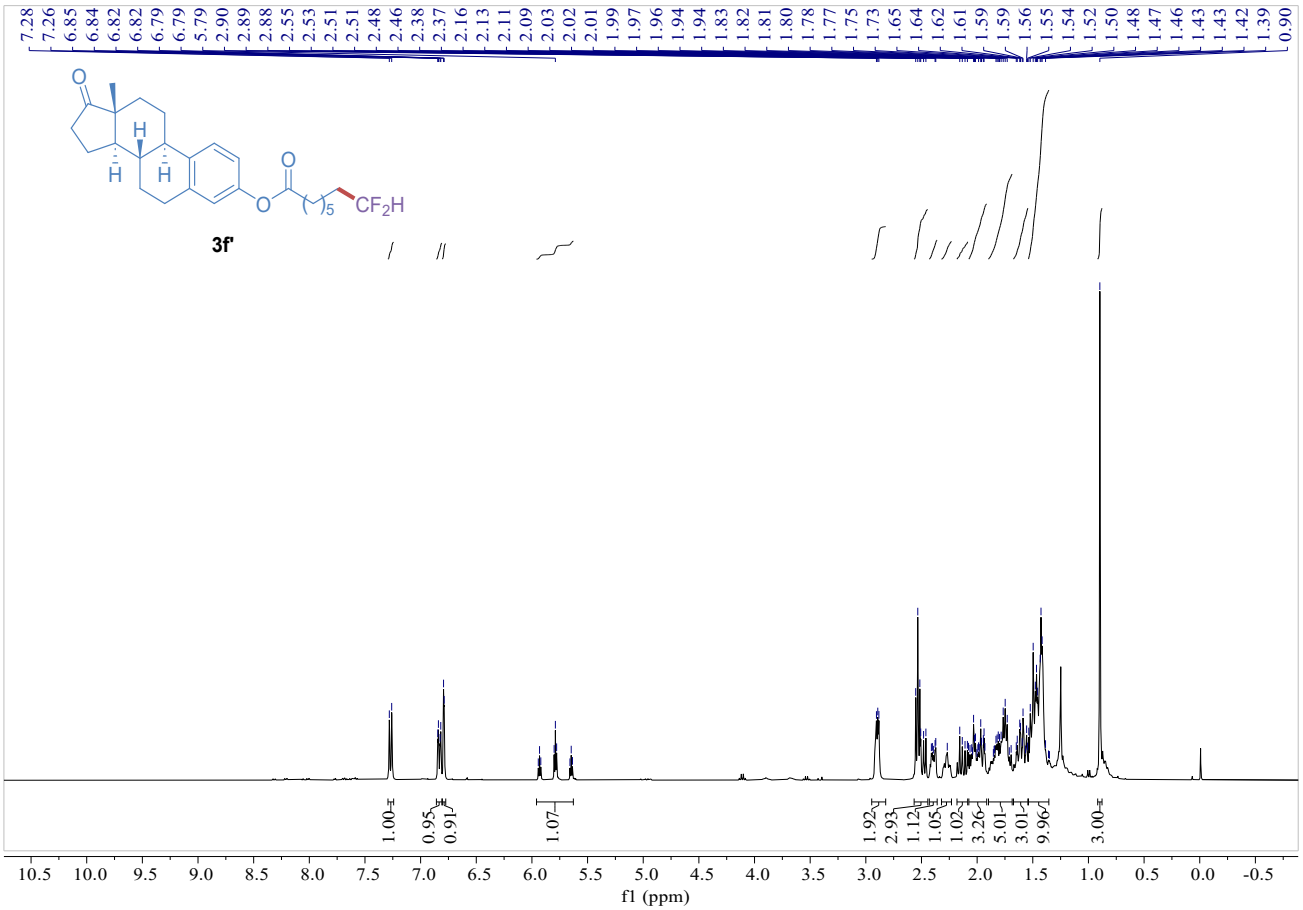
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound **3e'**



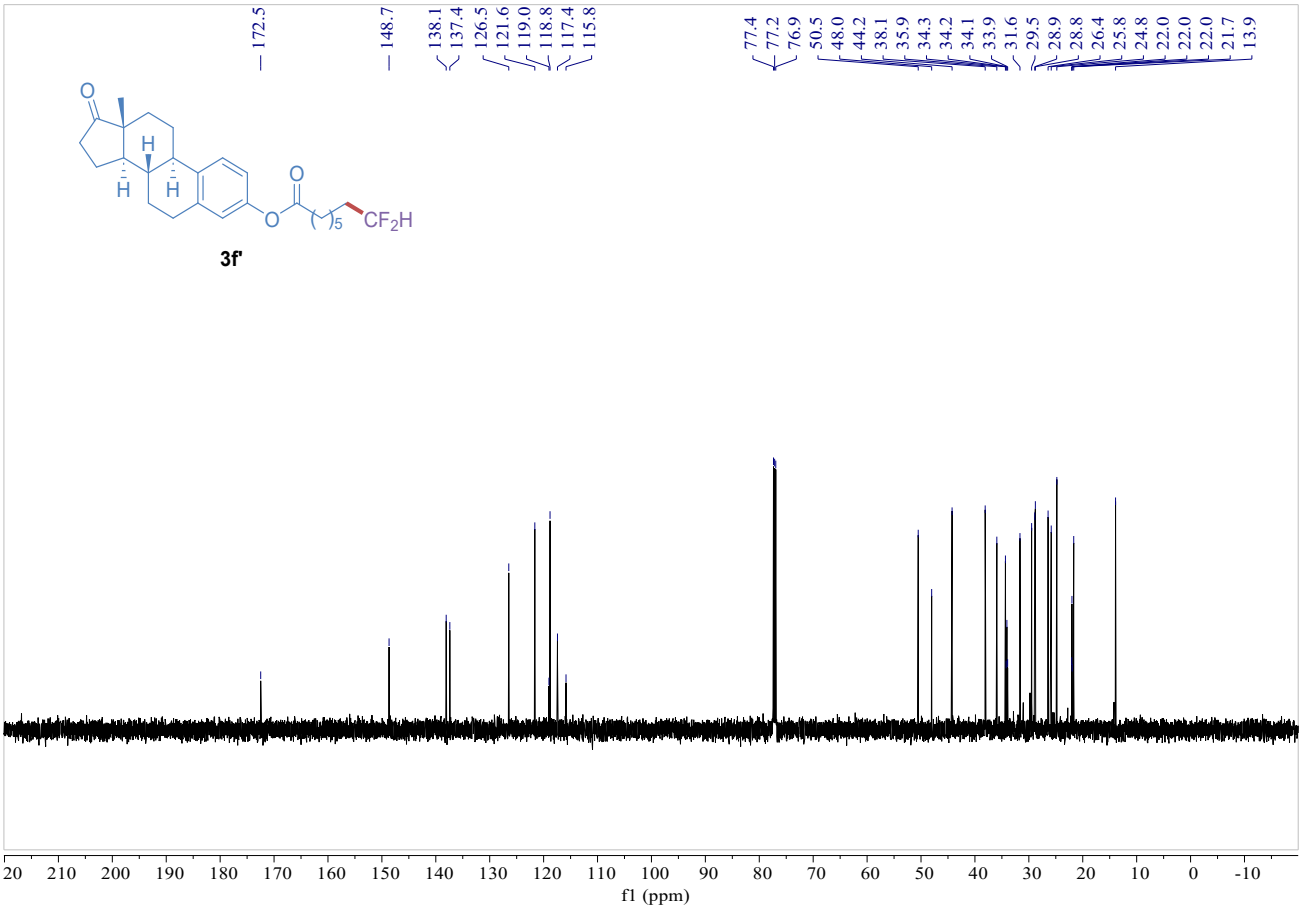
^{13}C NMR spectrum (151 MHz, $CDCl_3$) of compound **3e'**



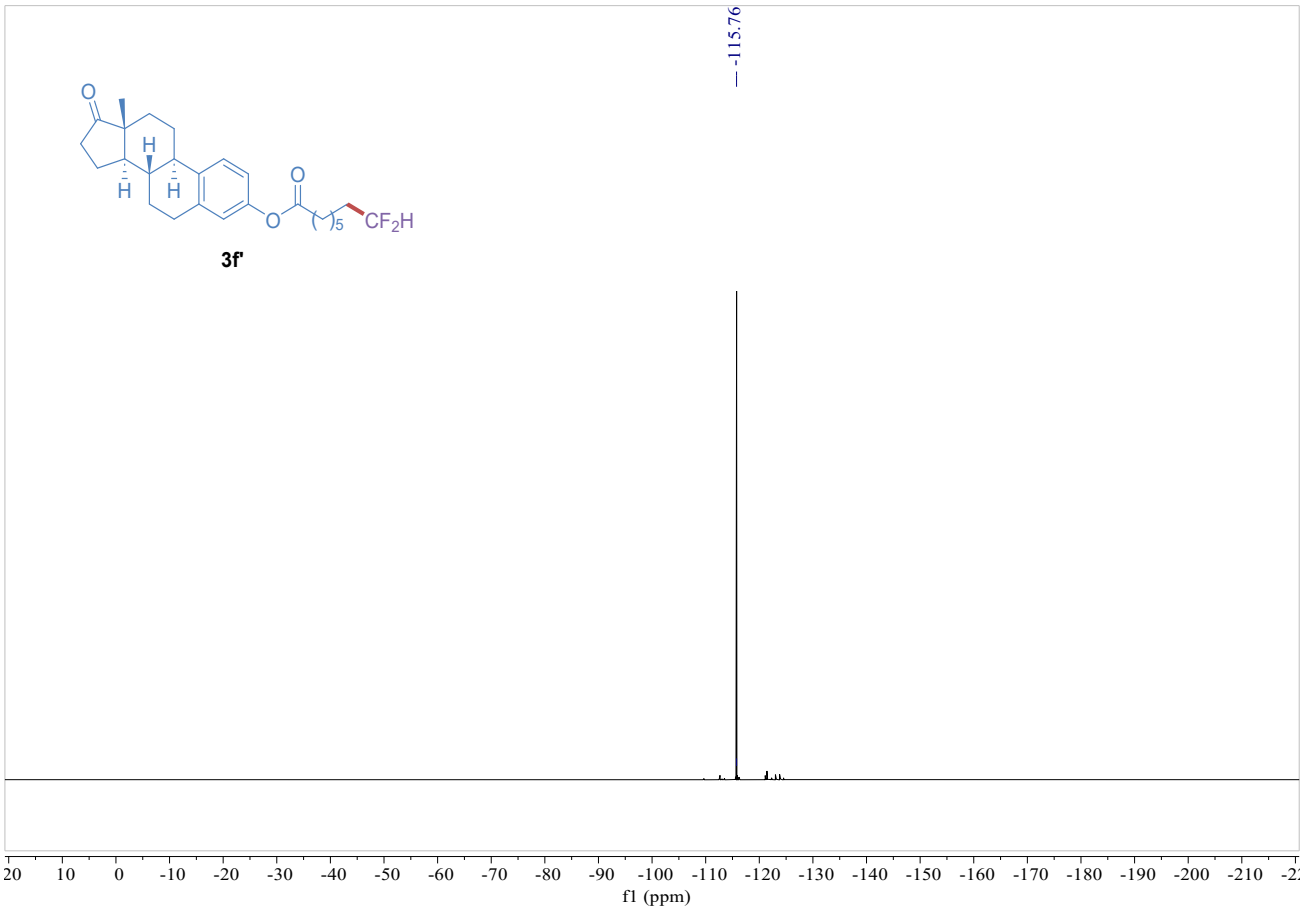
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3e'**



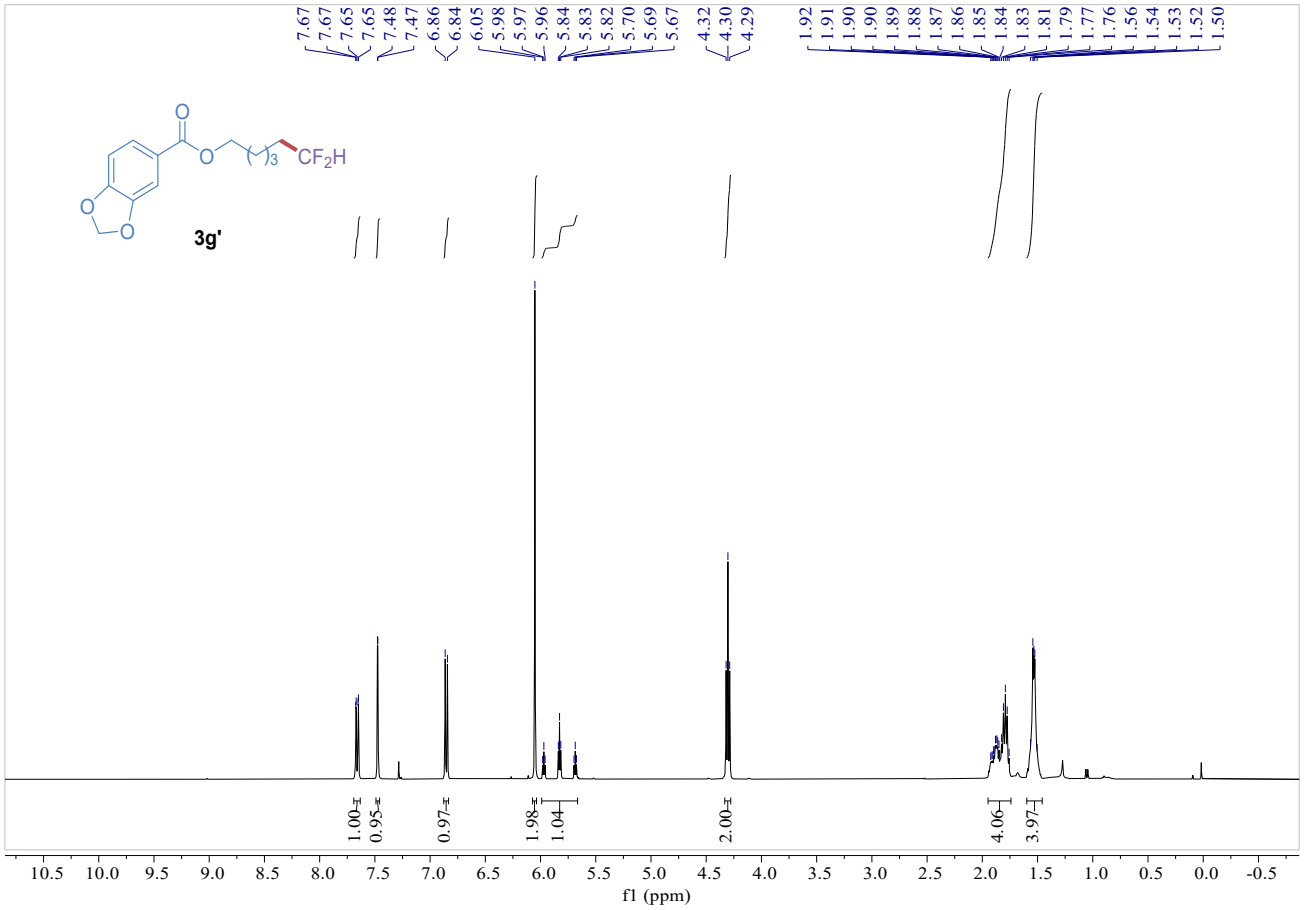
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3f'**



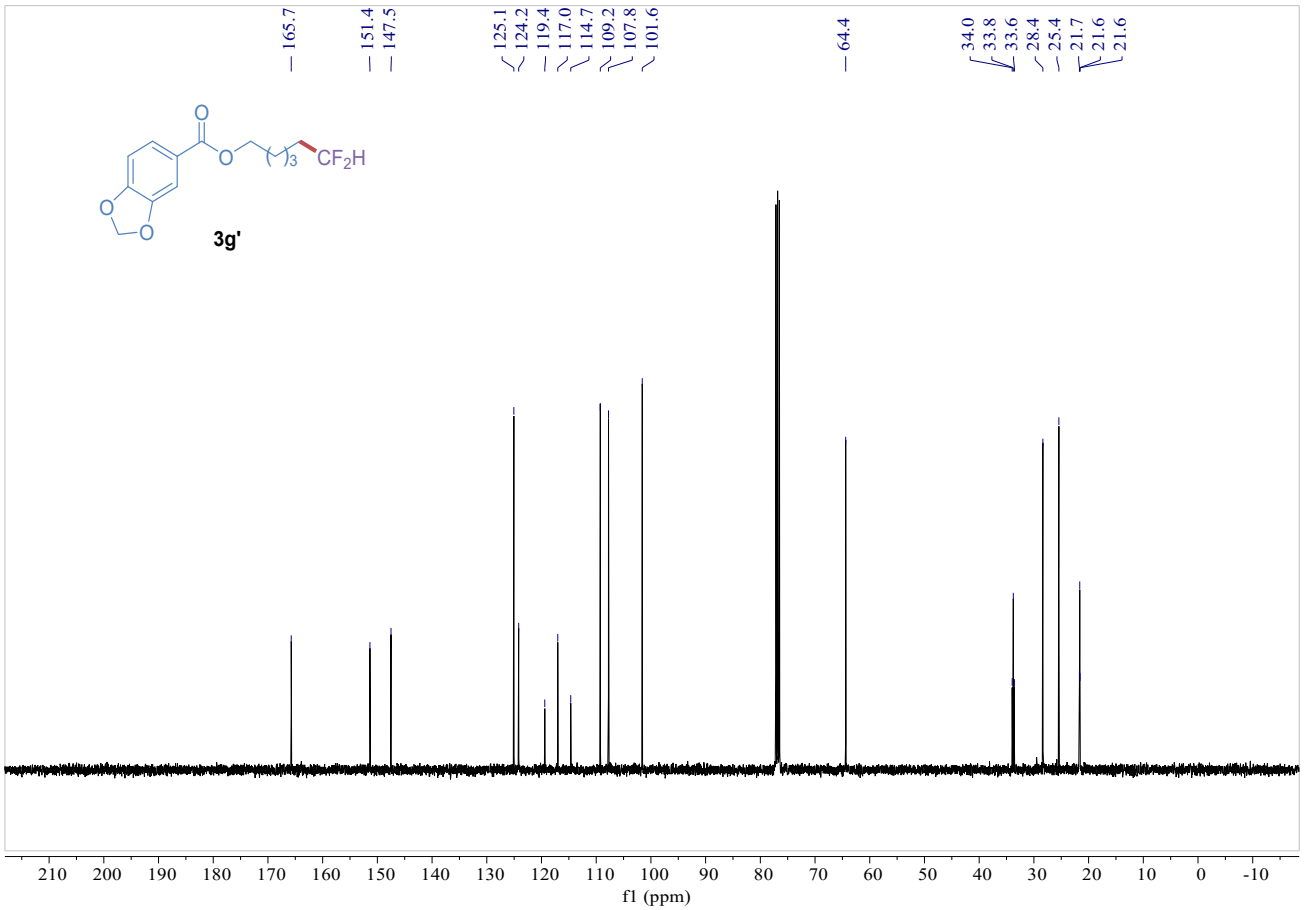
^{13}C NMR spectrum (151 MHz, $CDCl_3$) of compound **3f'**



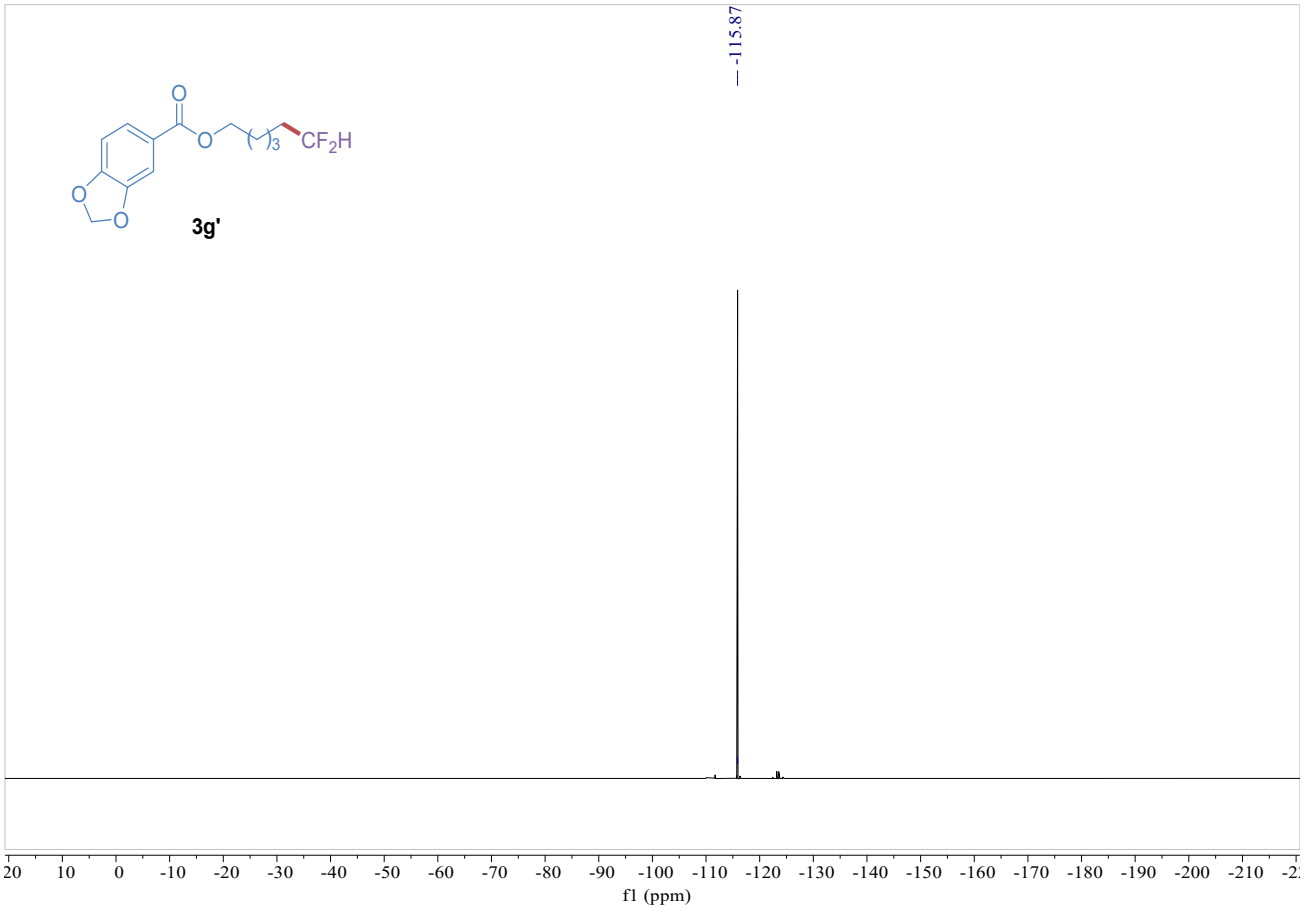
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3f'**



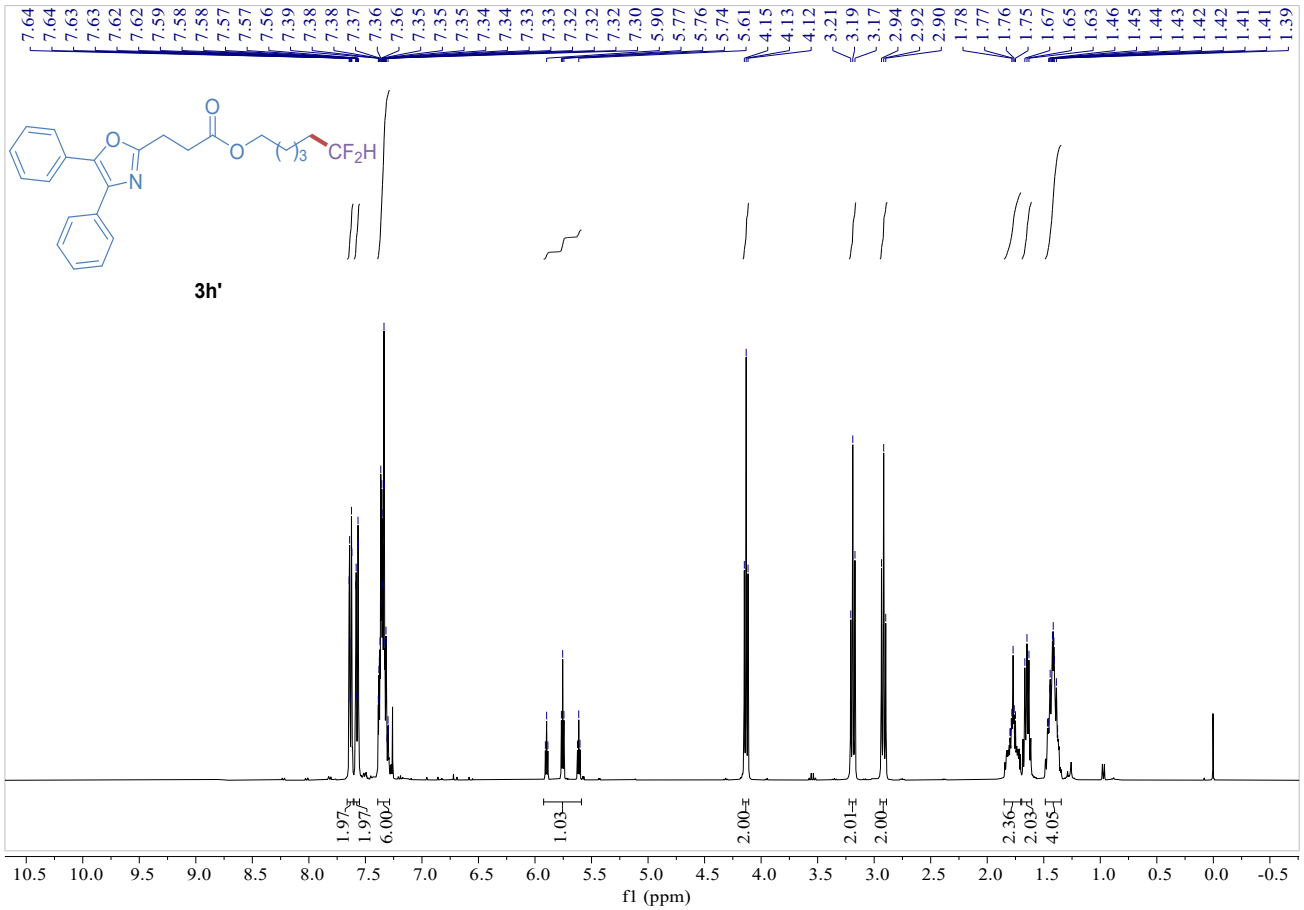
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3g'**



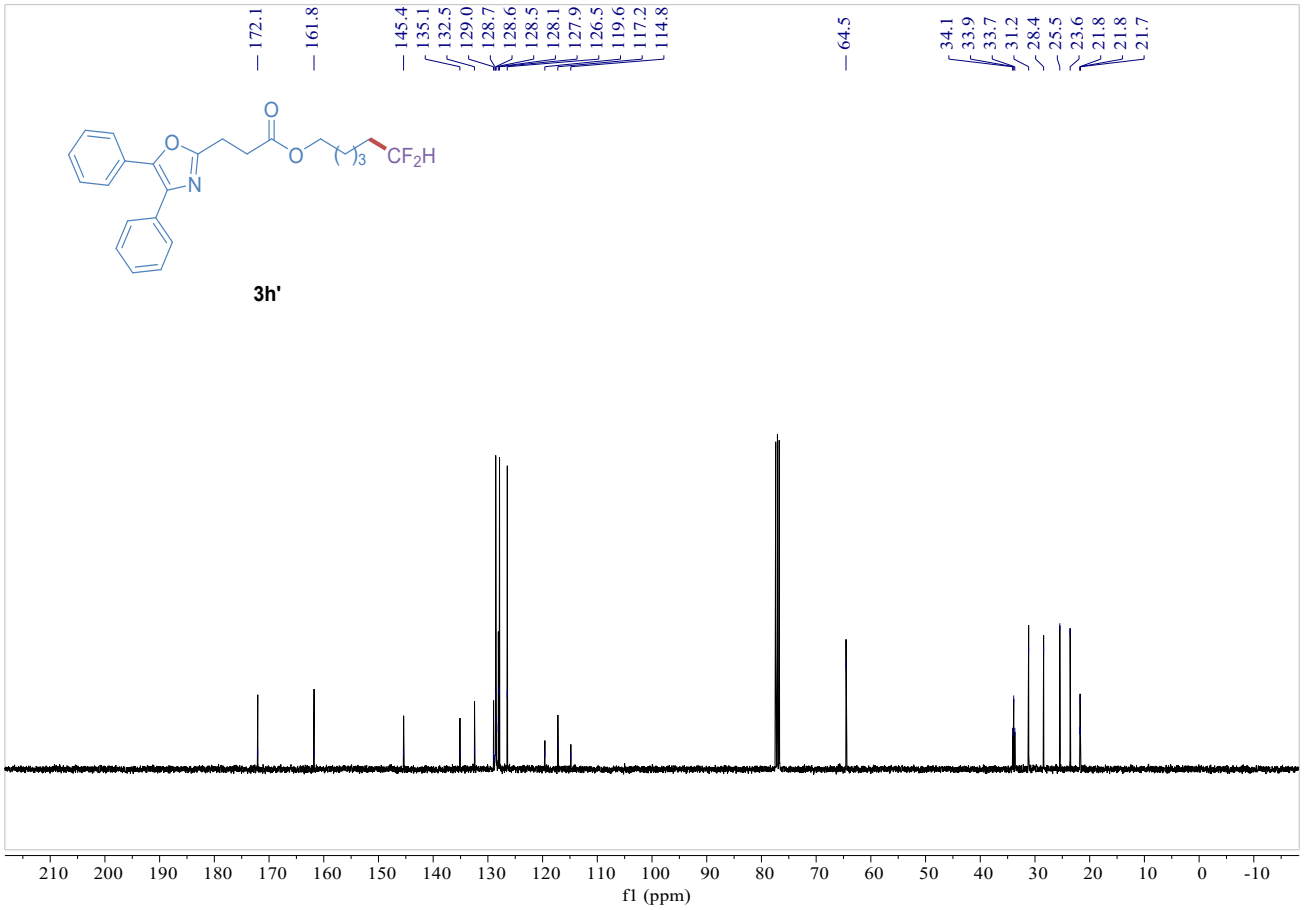
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **3g'**



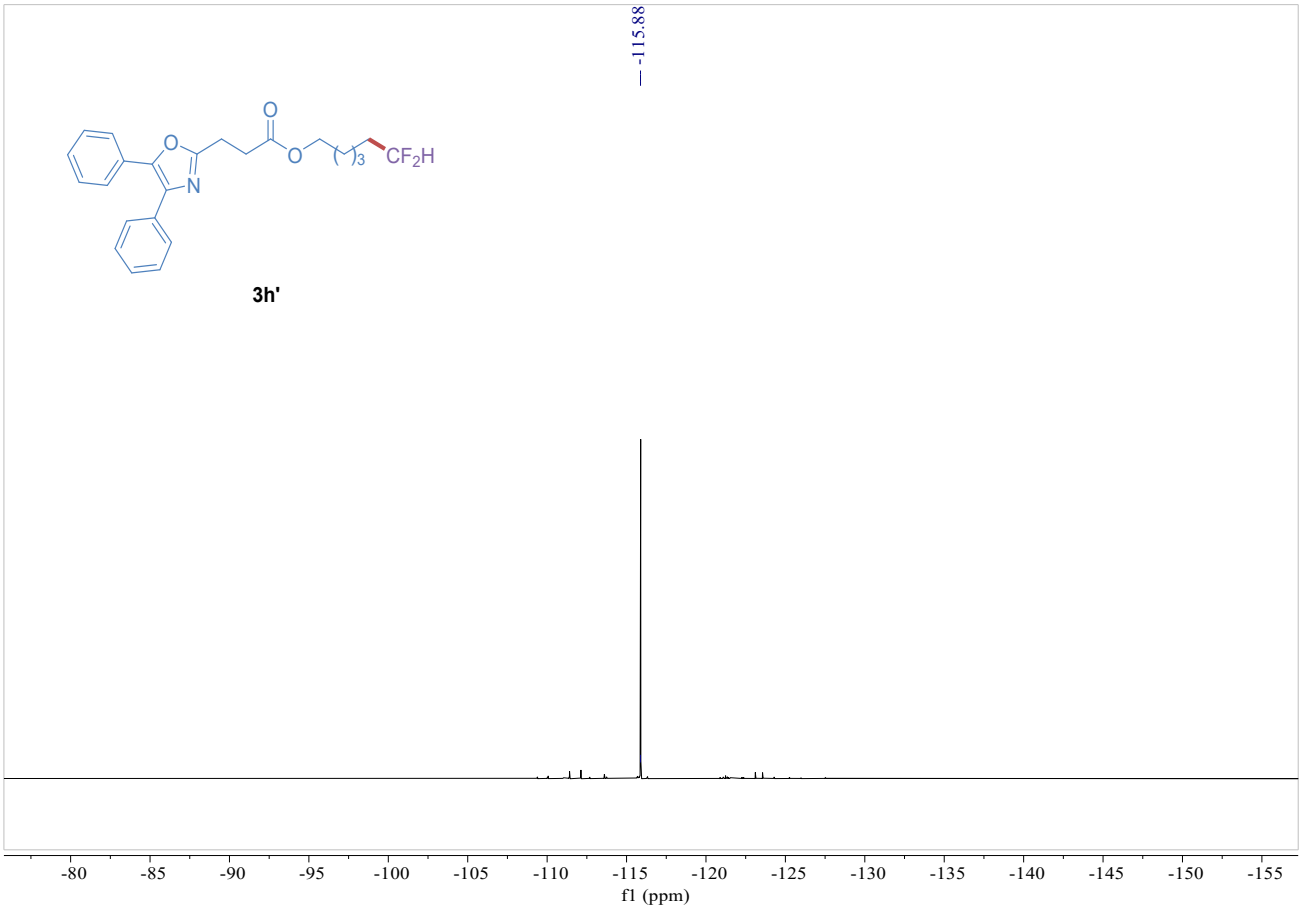
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3g'**



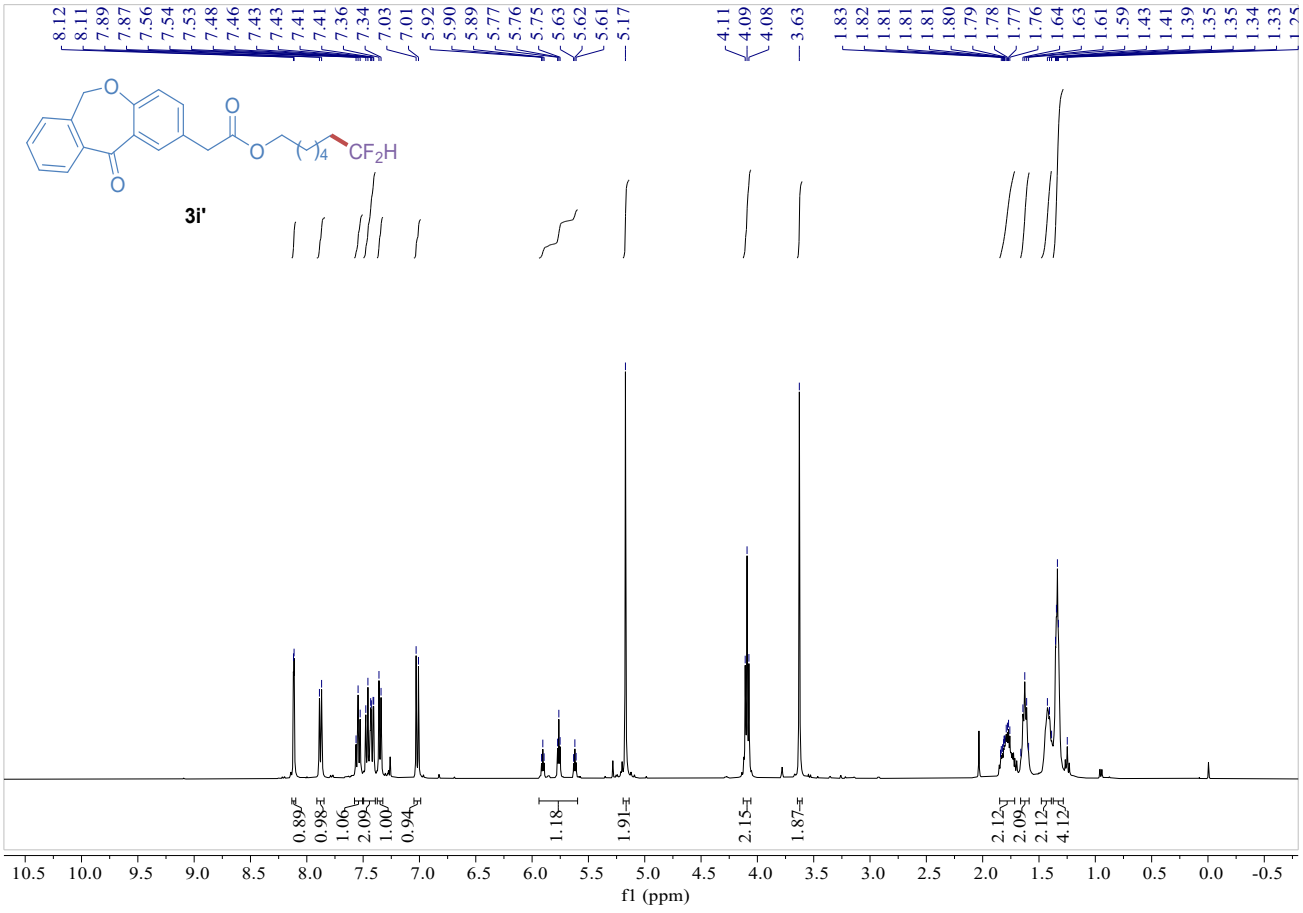
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3h'**



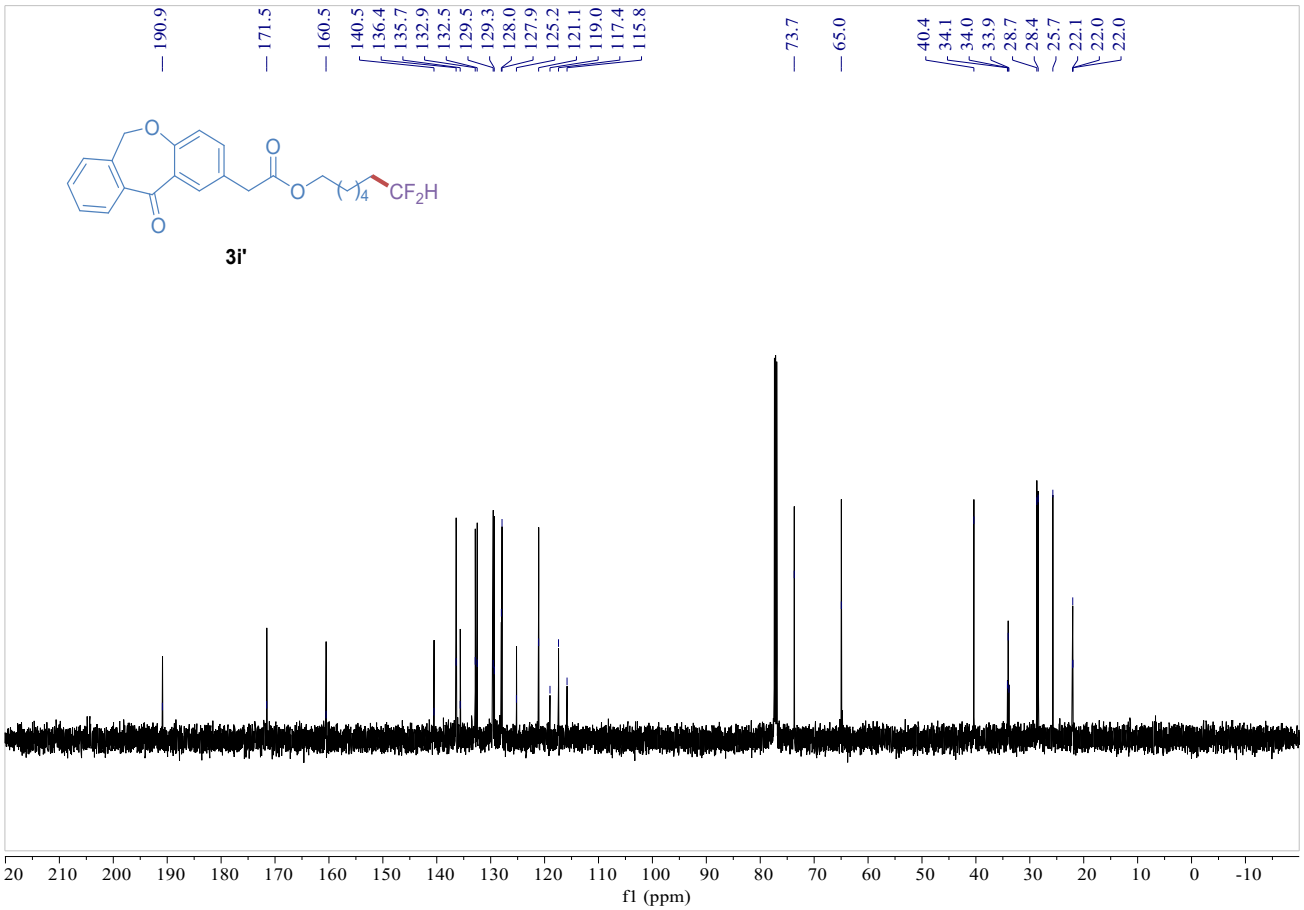
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **3h'**



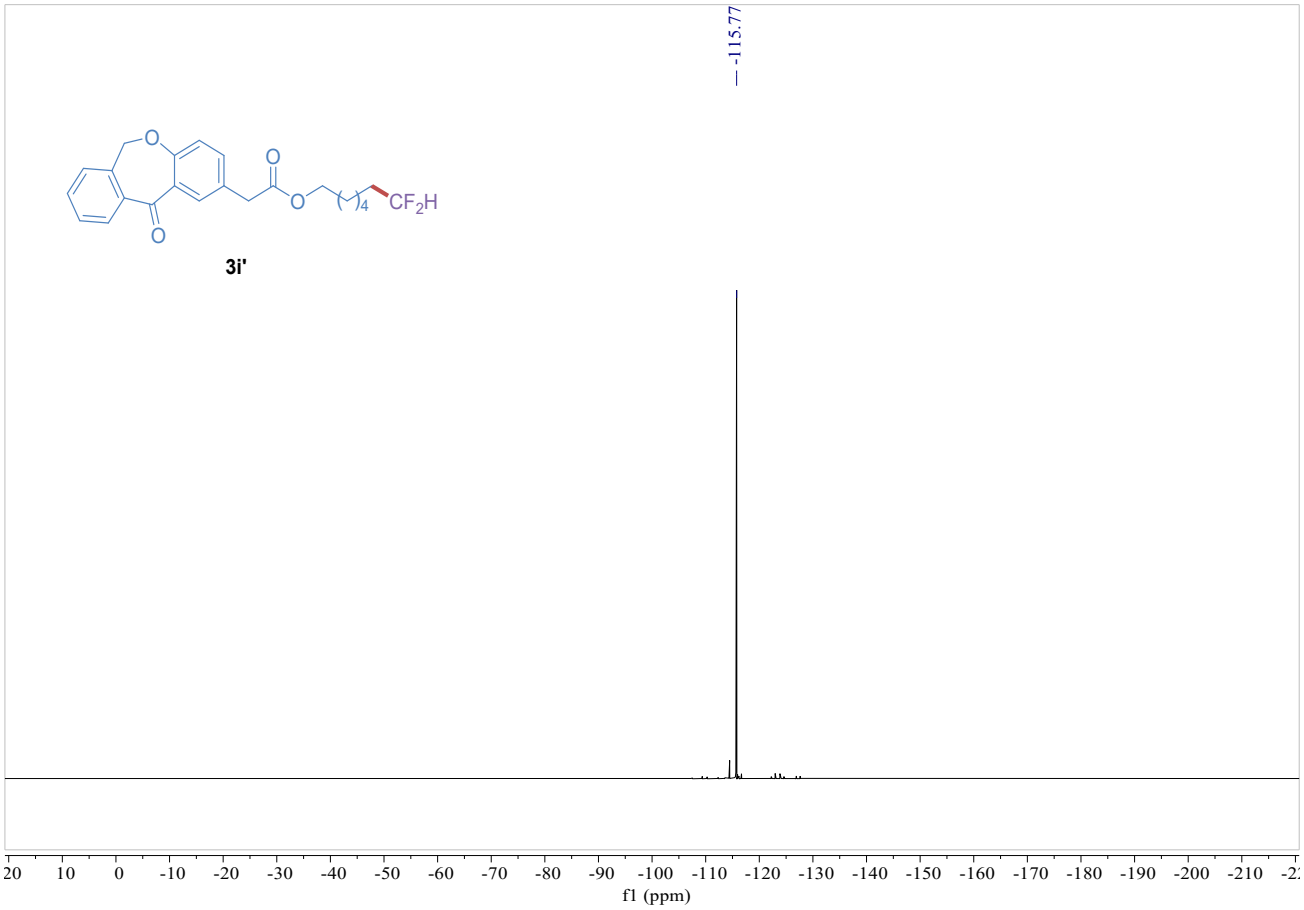
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3h'**



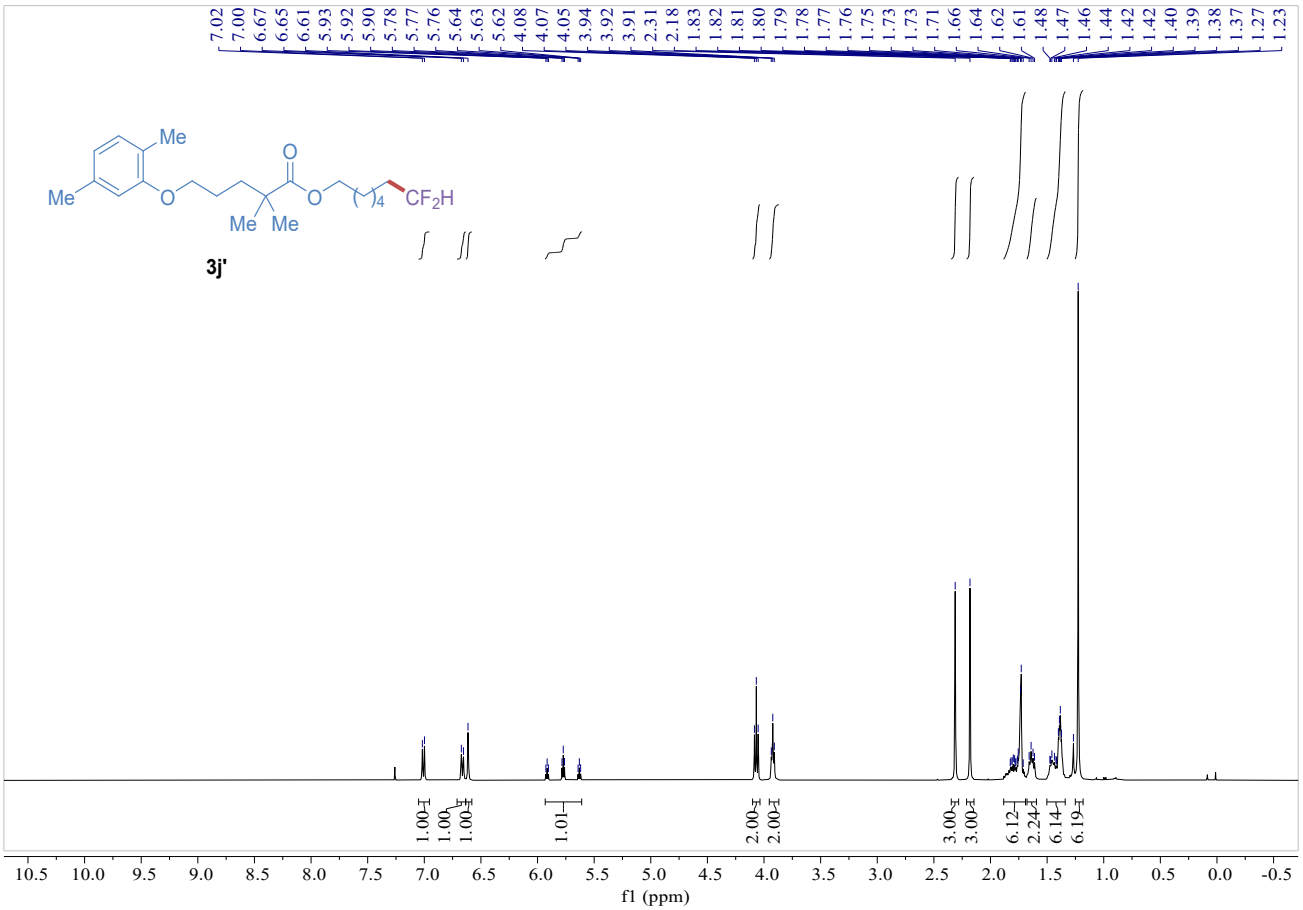
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3i'**



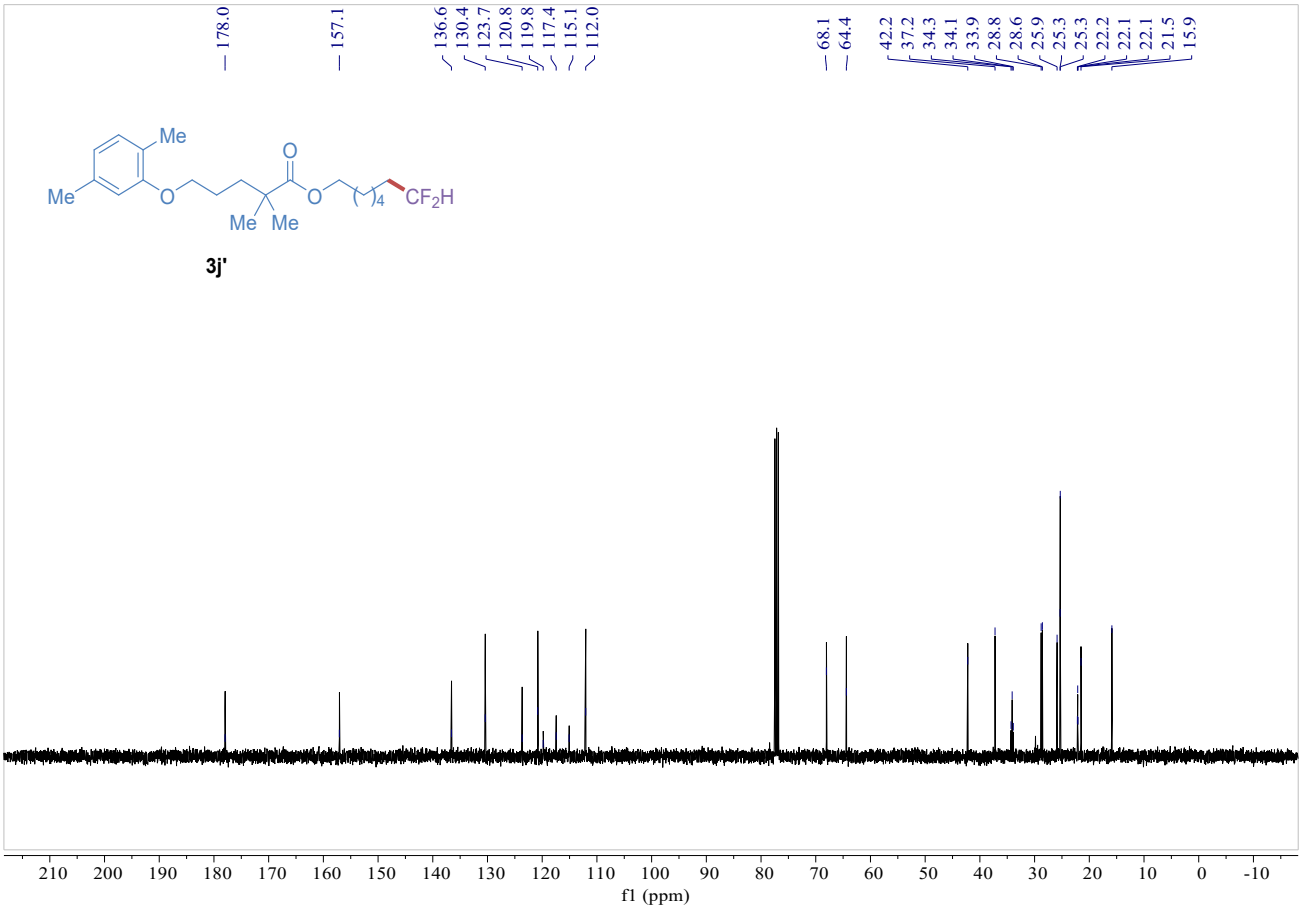
^{13}C NMR spectrum (151 MHz, $CDCl_3$) of compound **3i'**



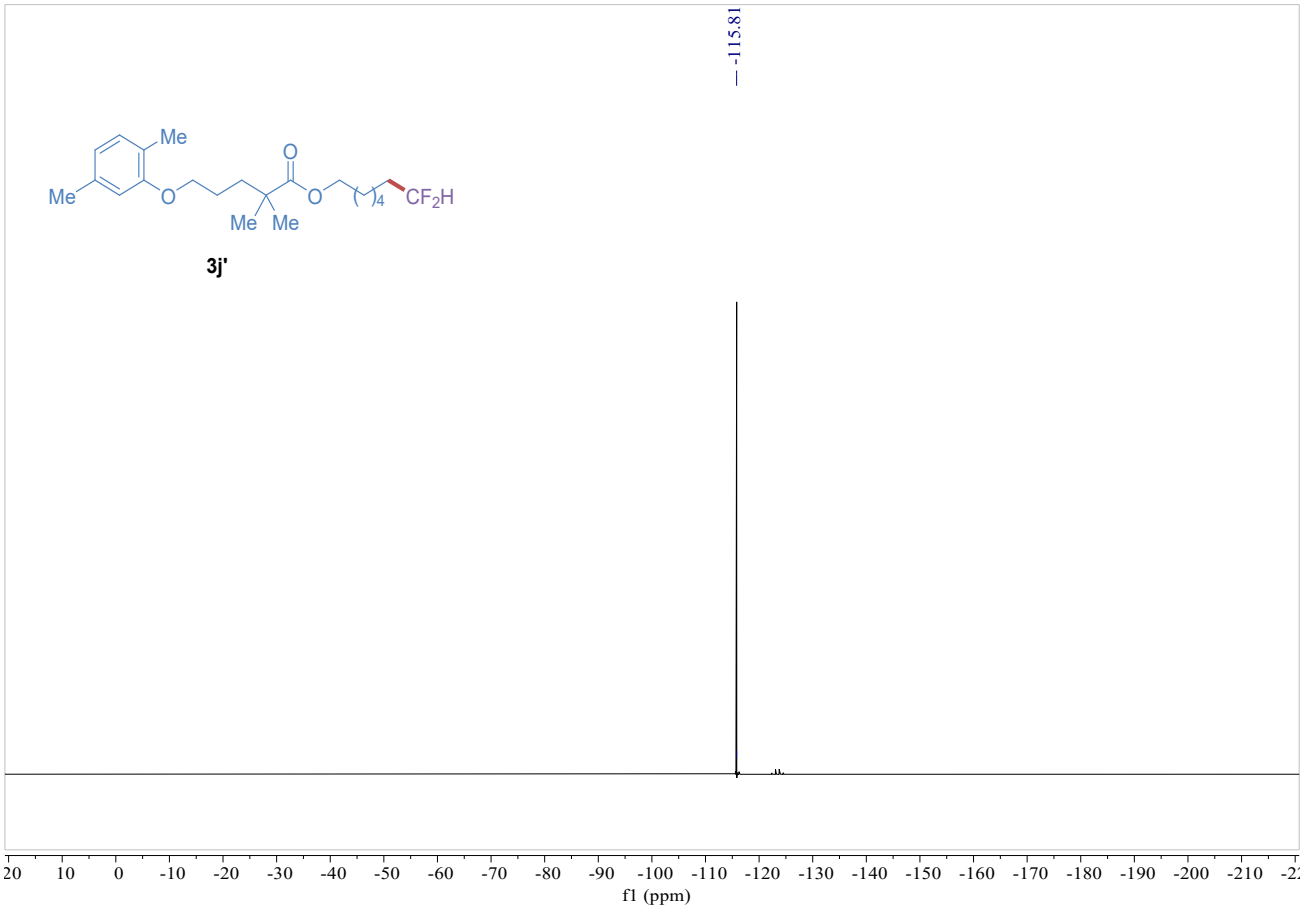
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3i'**



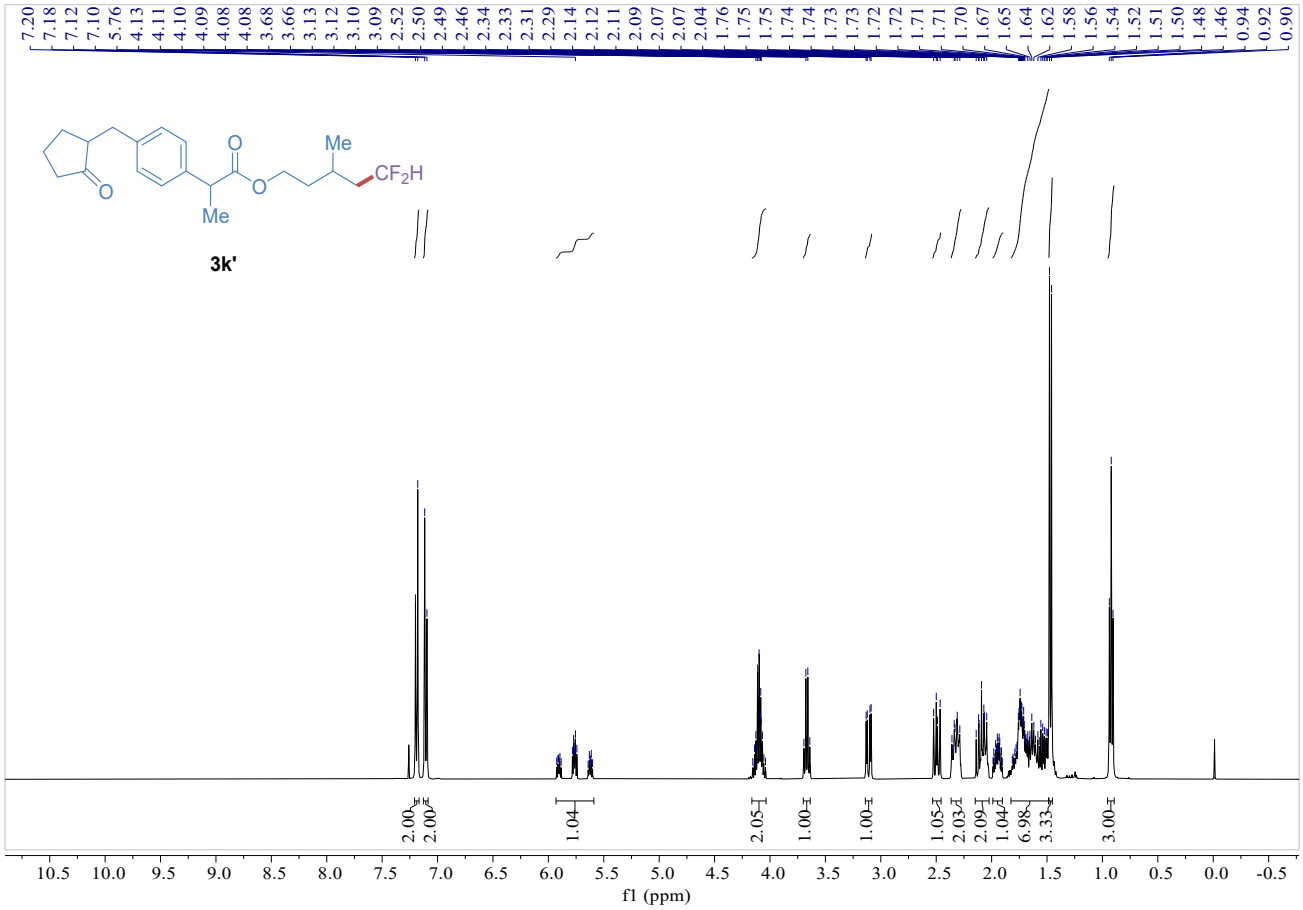
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3j'**



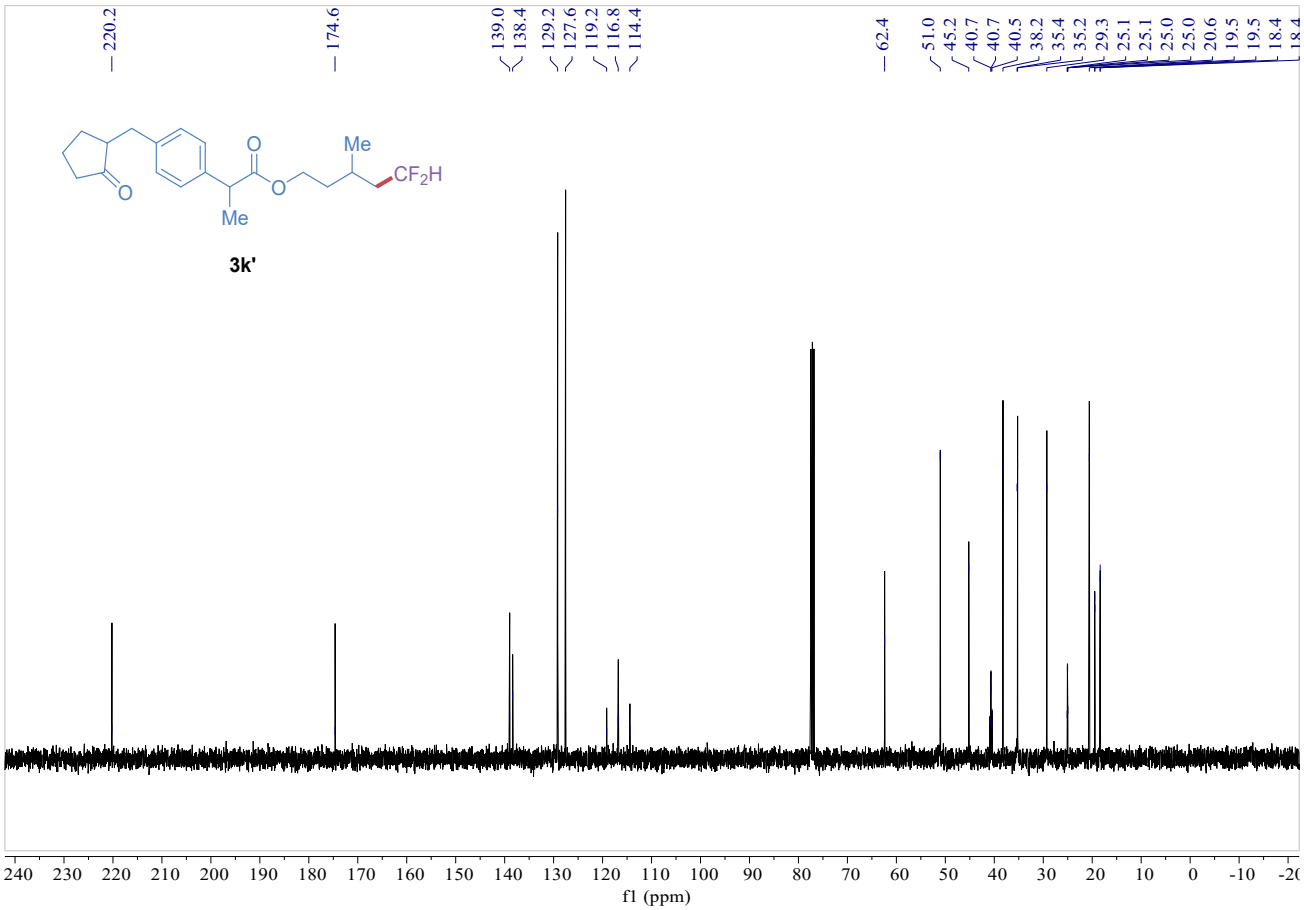
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **3j'**



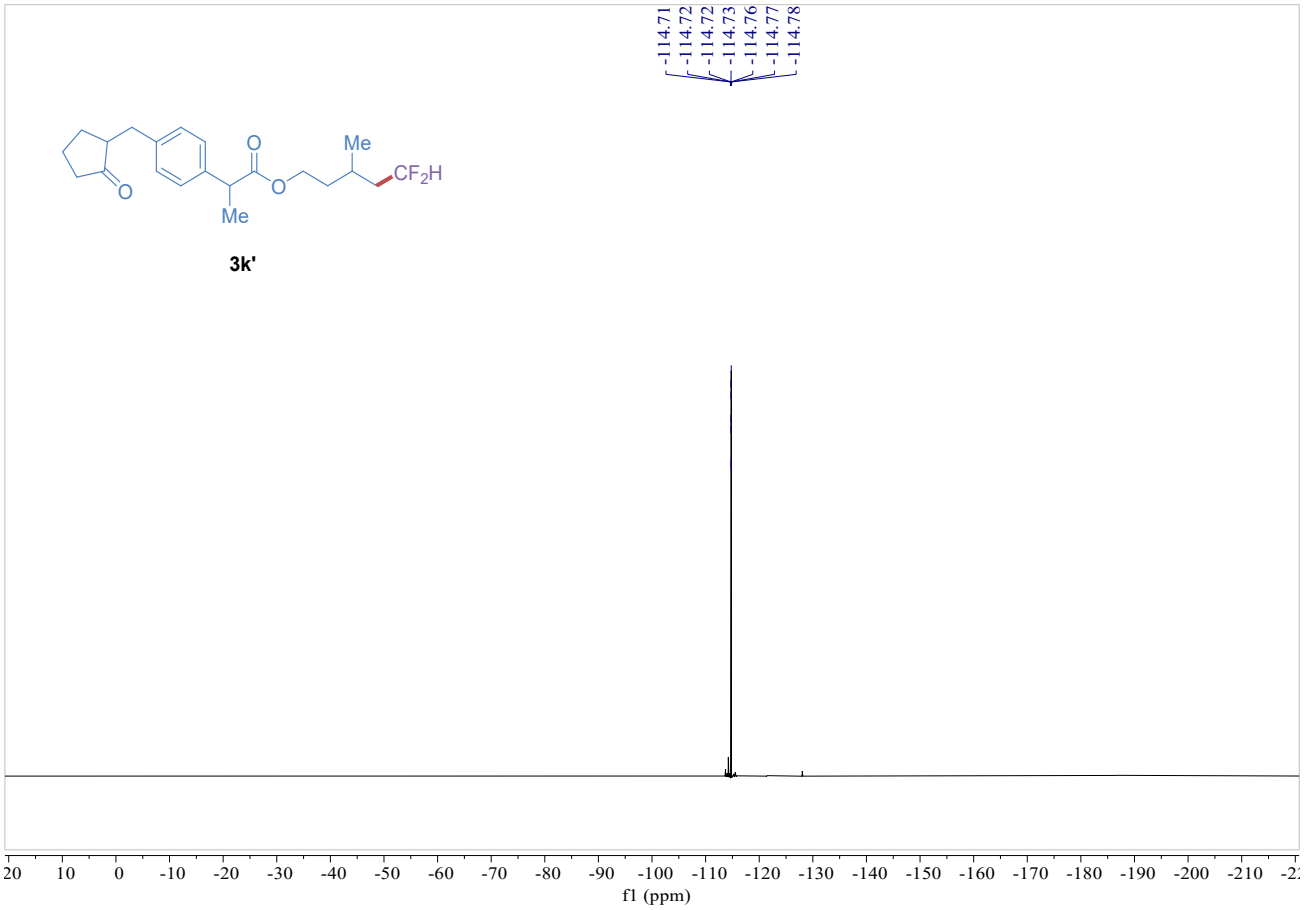
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3j'**



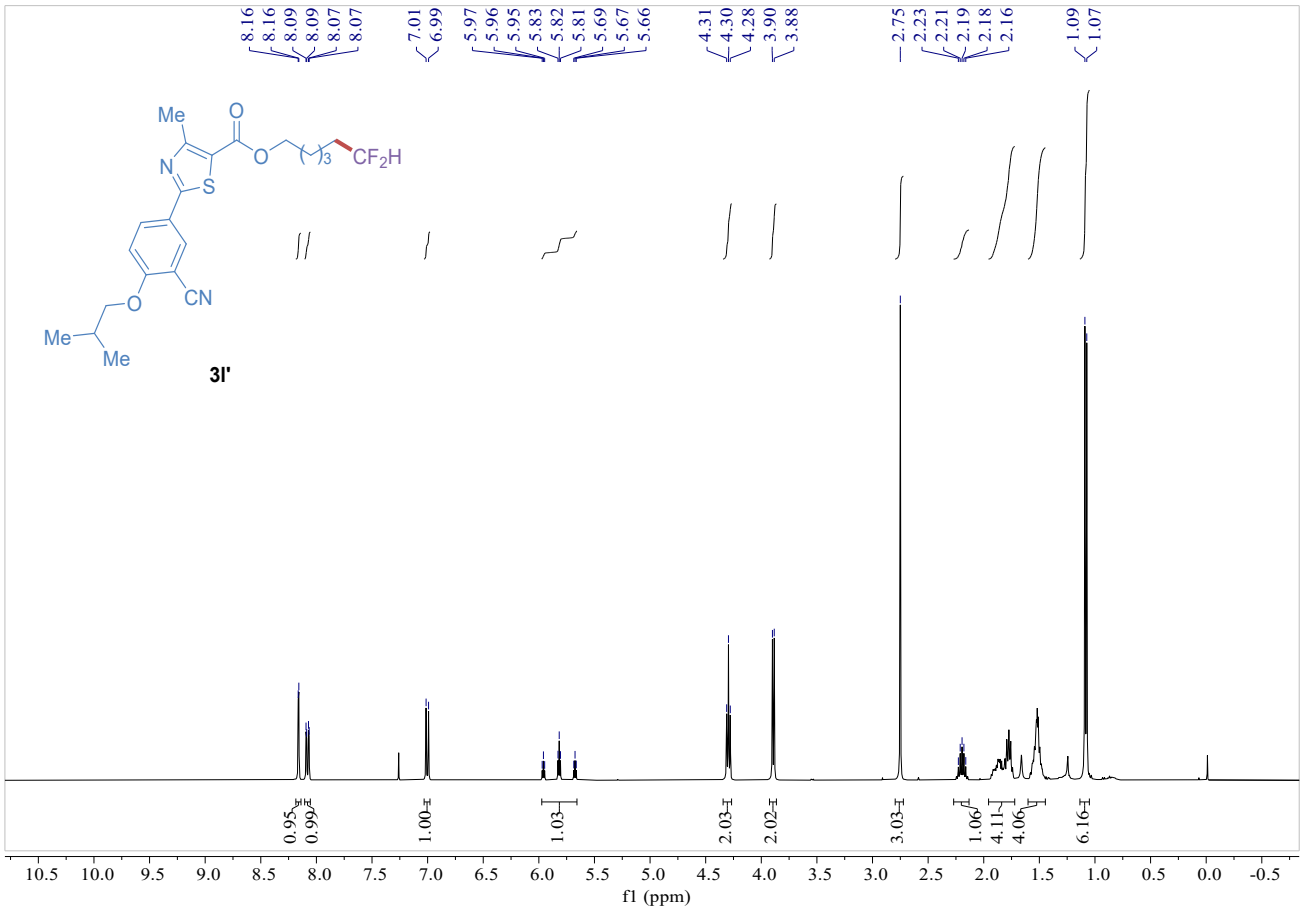
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3k'**



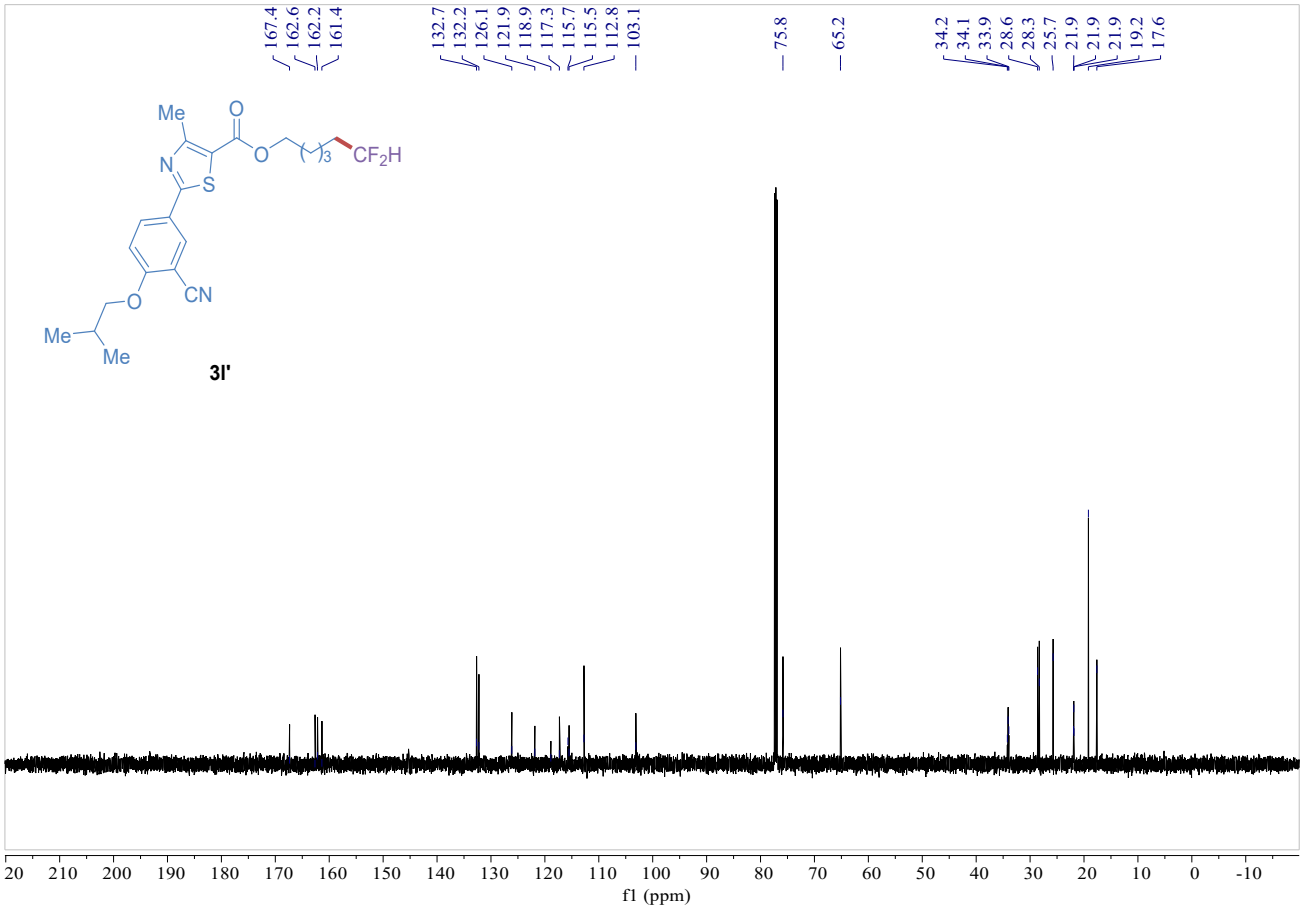
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **3k'**



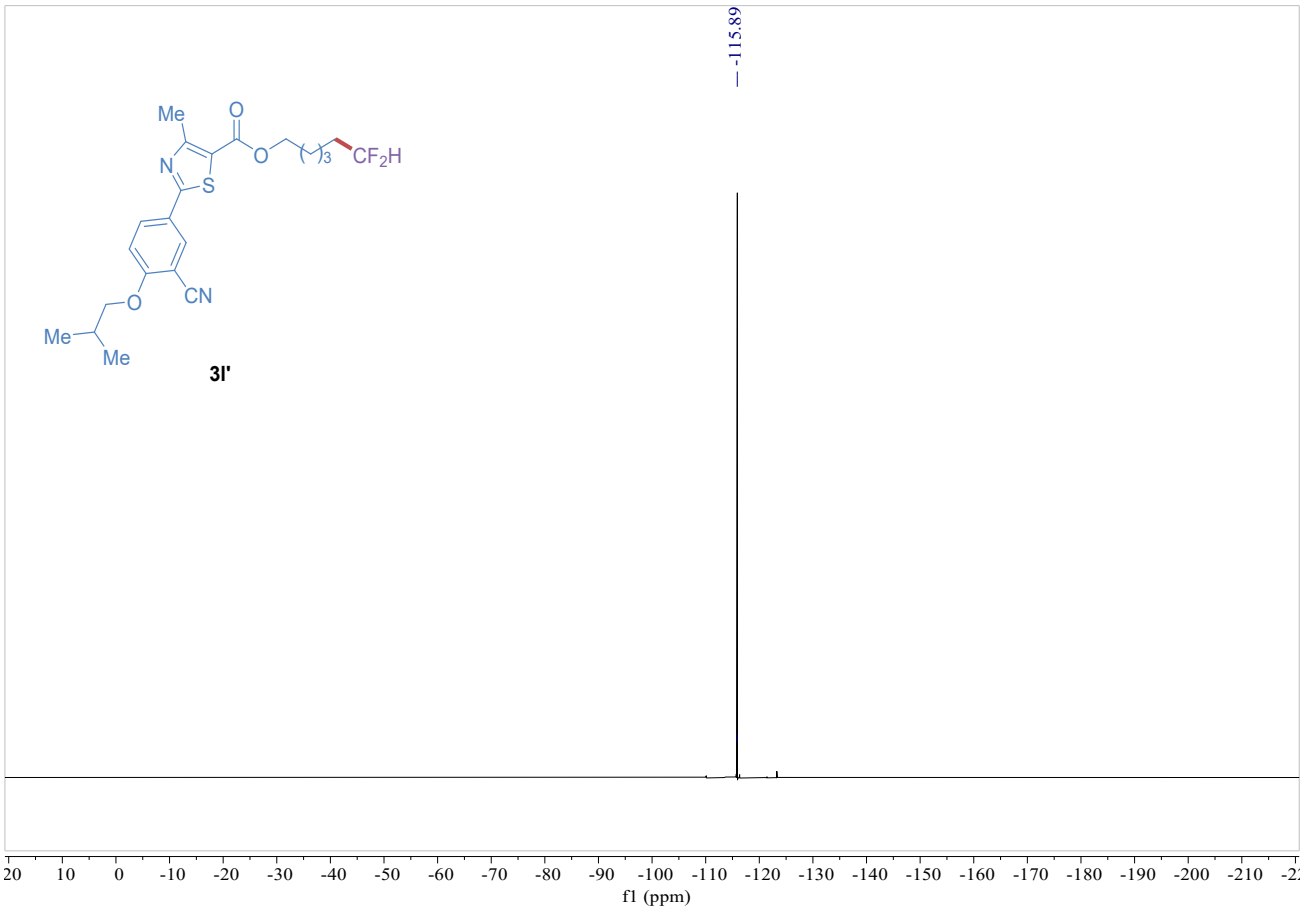
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3k'**



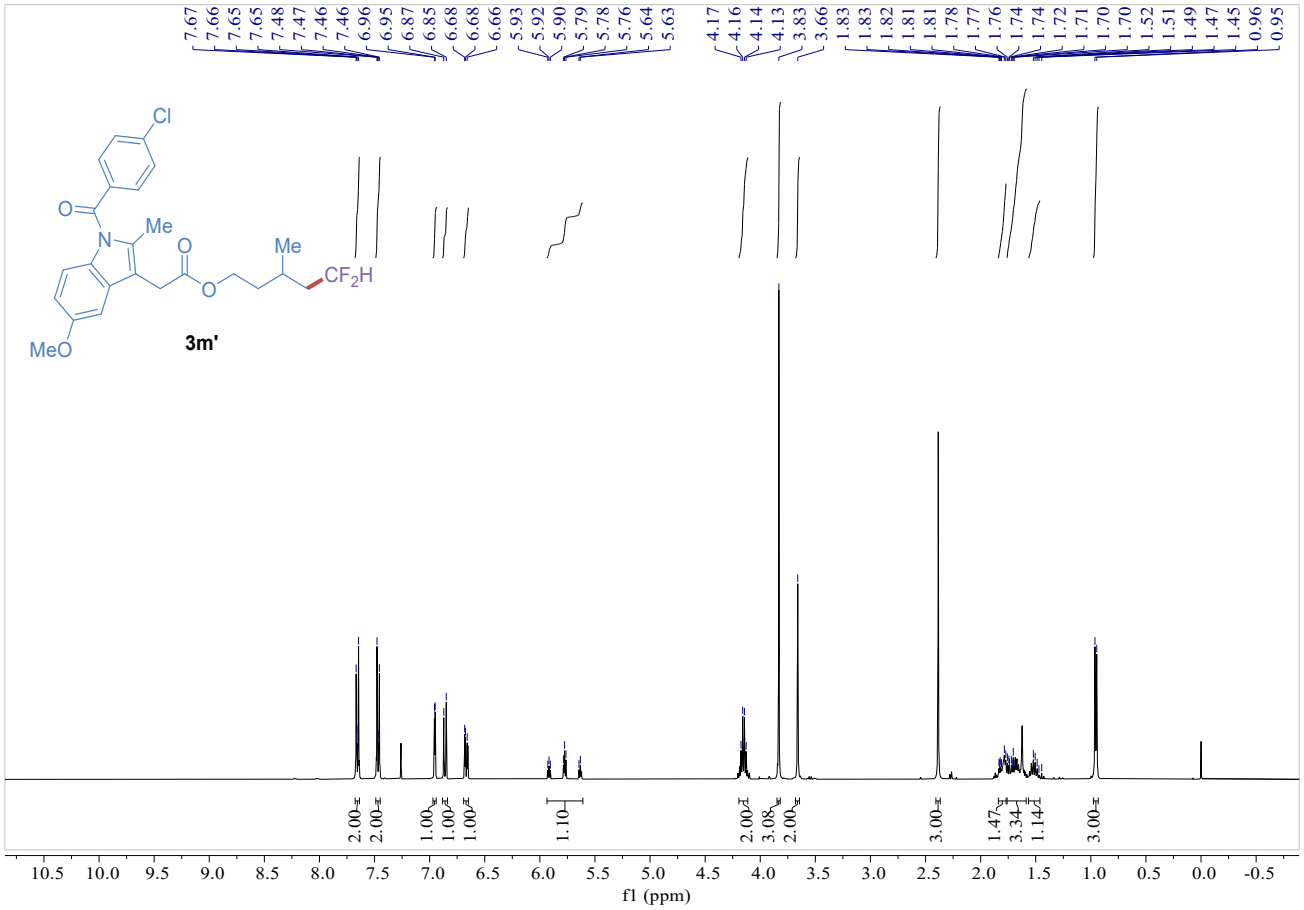
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3l'**



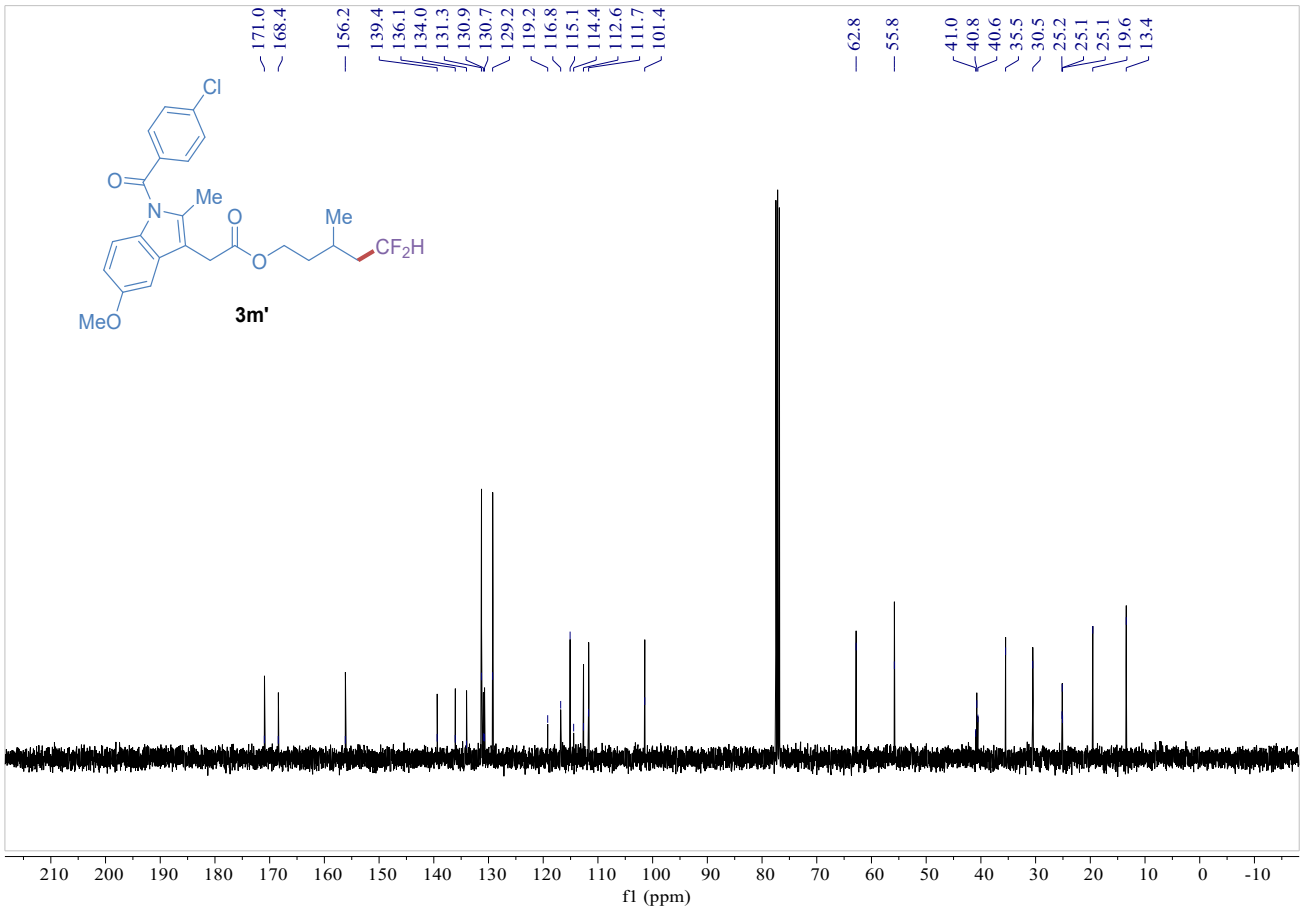
^{13}C NMR spectrum (151 MHz, $CDCl_3$) of compound **3l'**



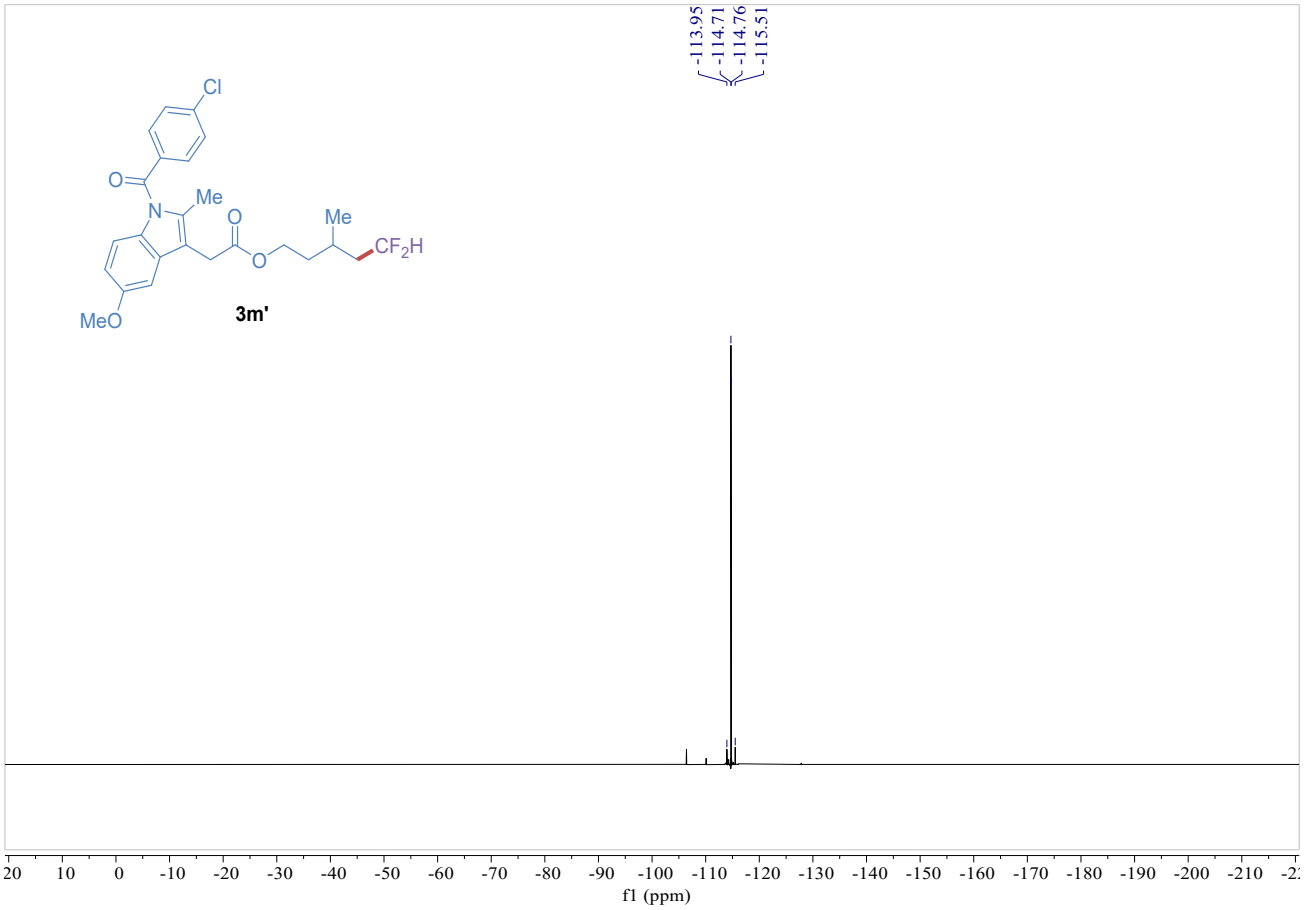
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3l'**



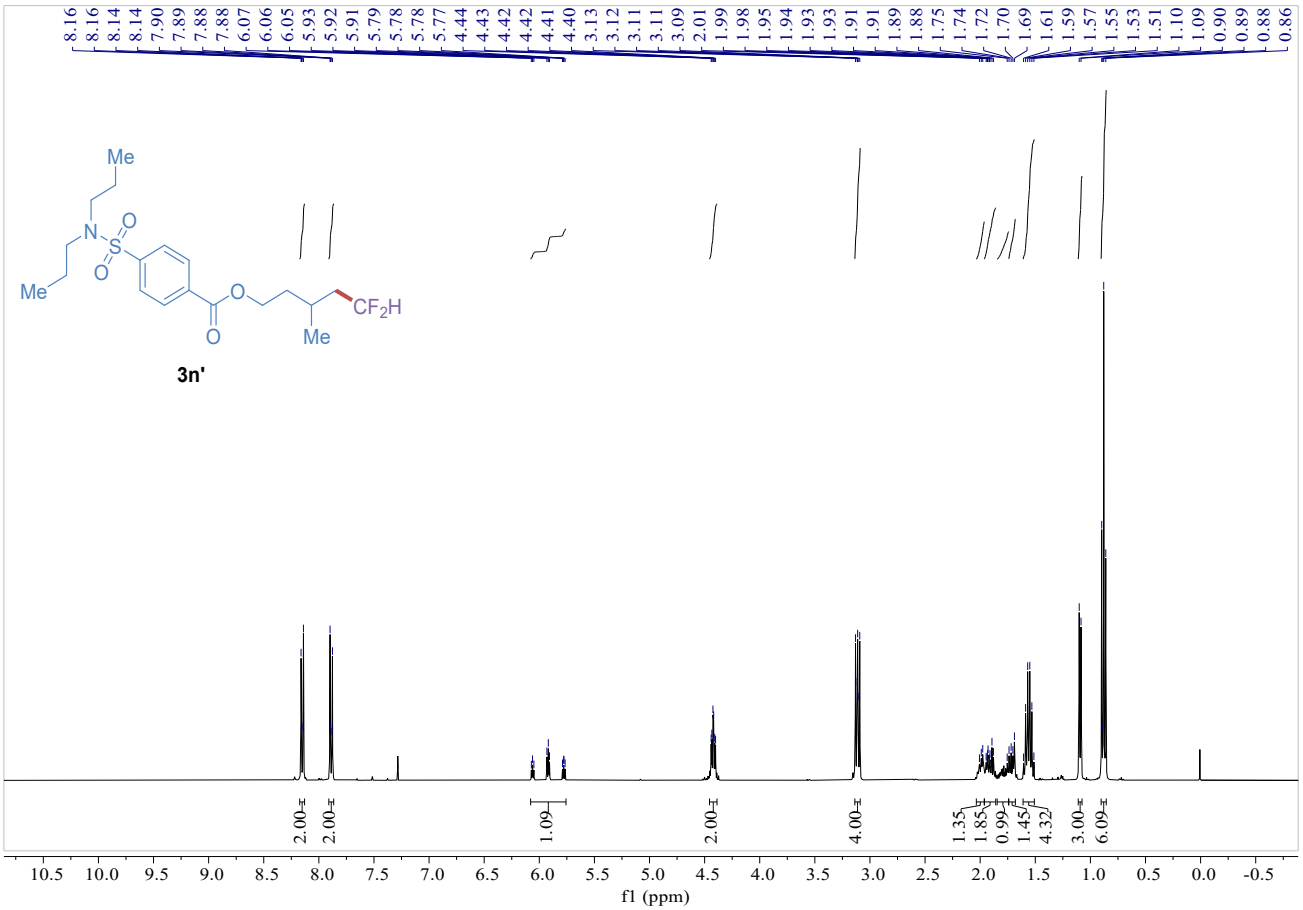
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3m'**



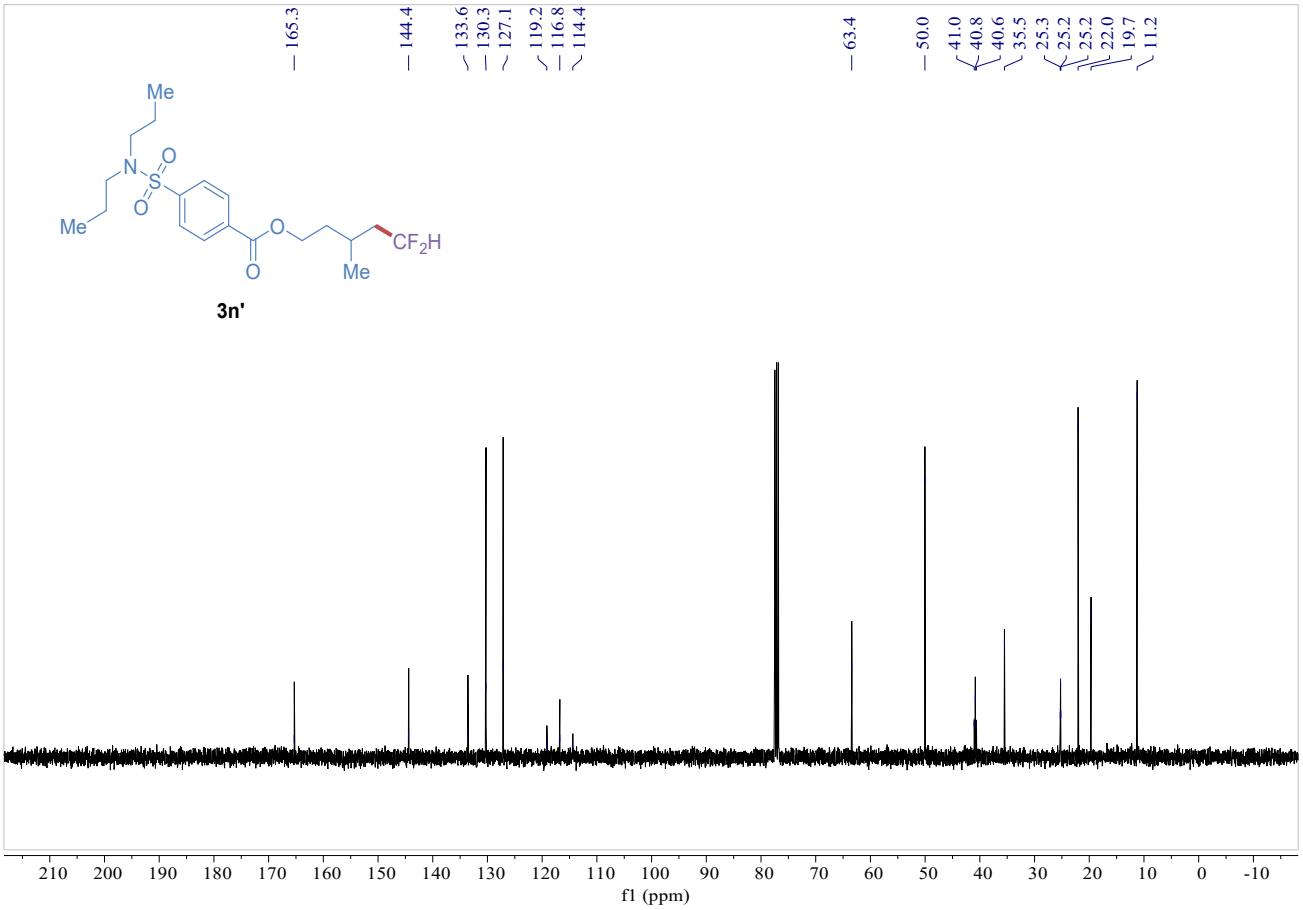
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **3m'**



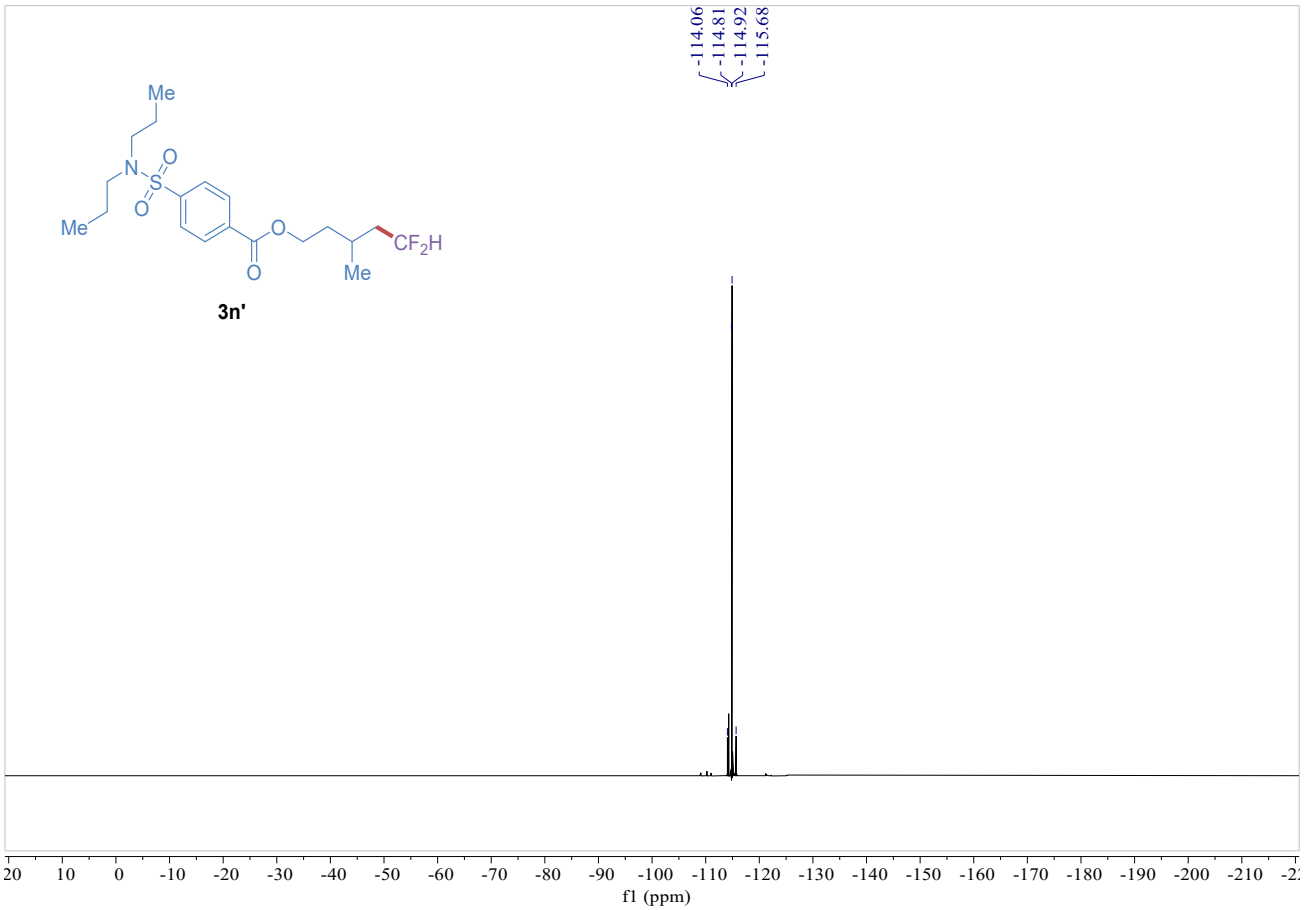
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3m'**



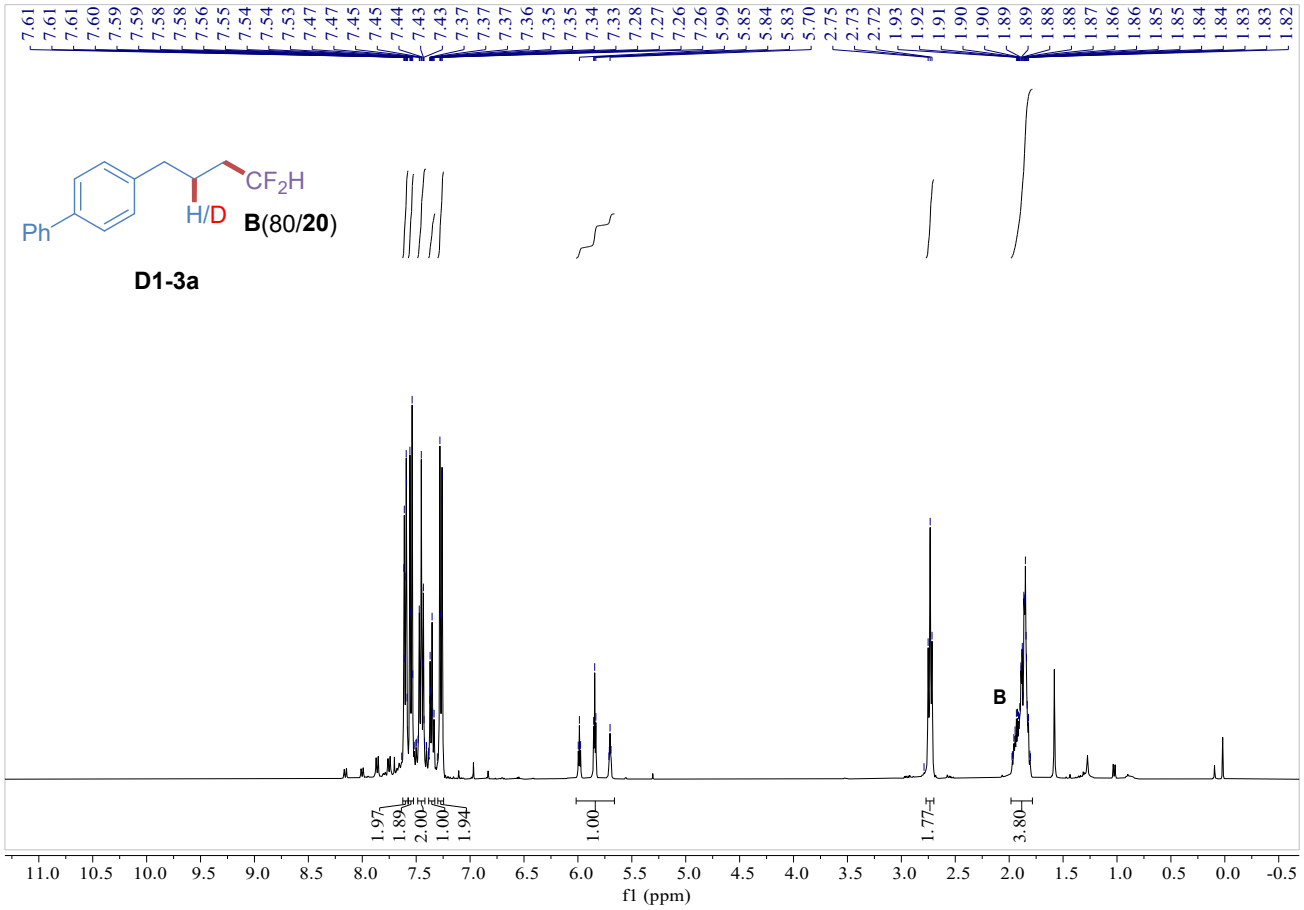
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3n'**



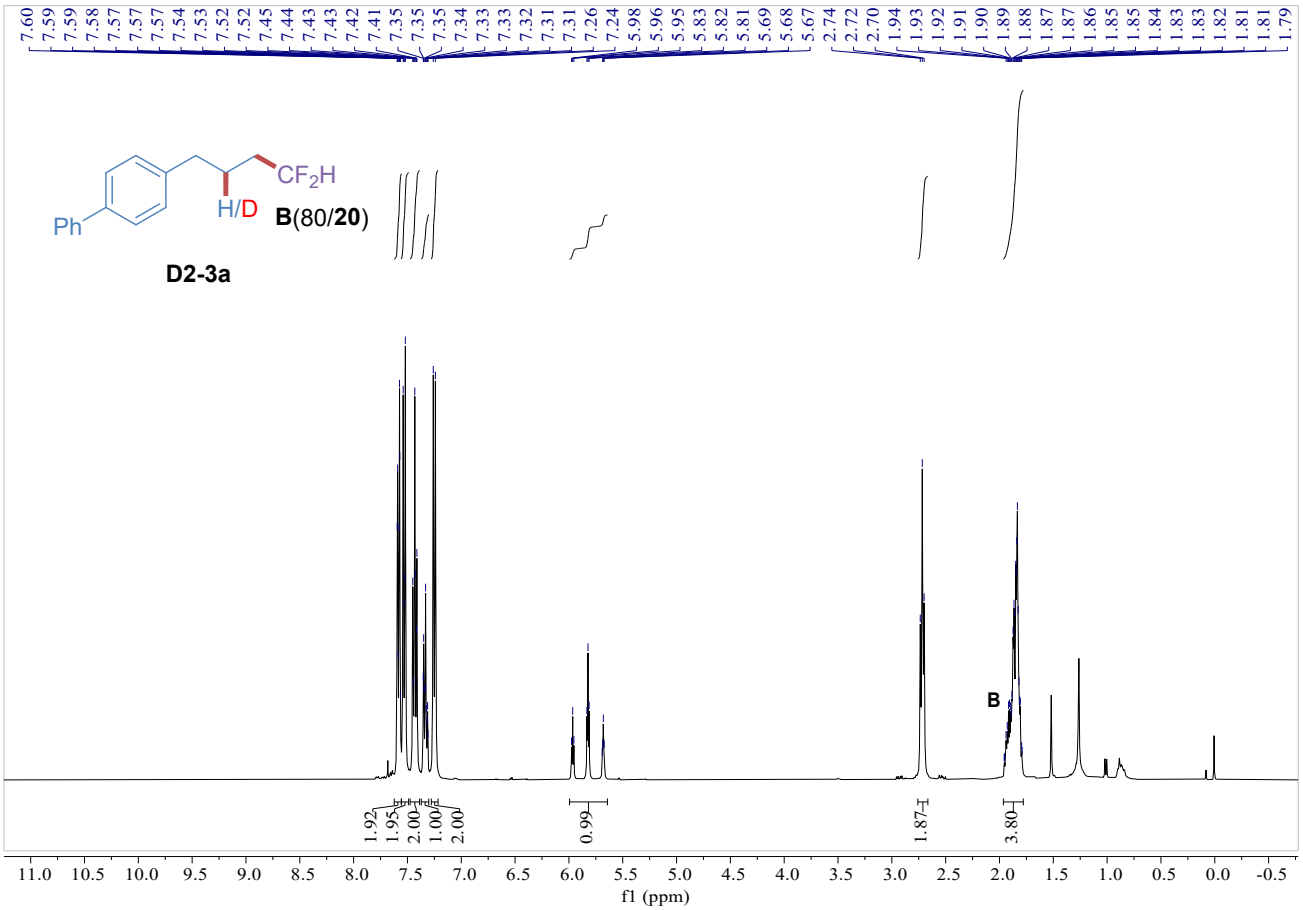
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **3n'**



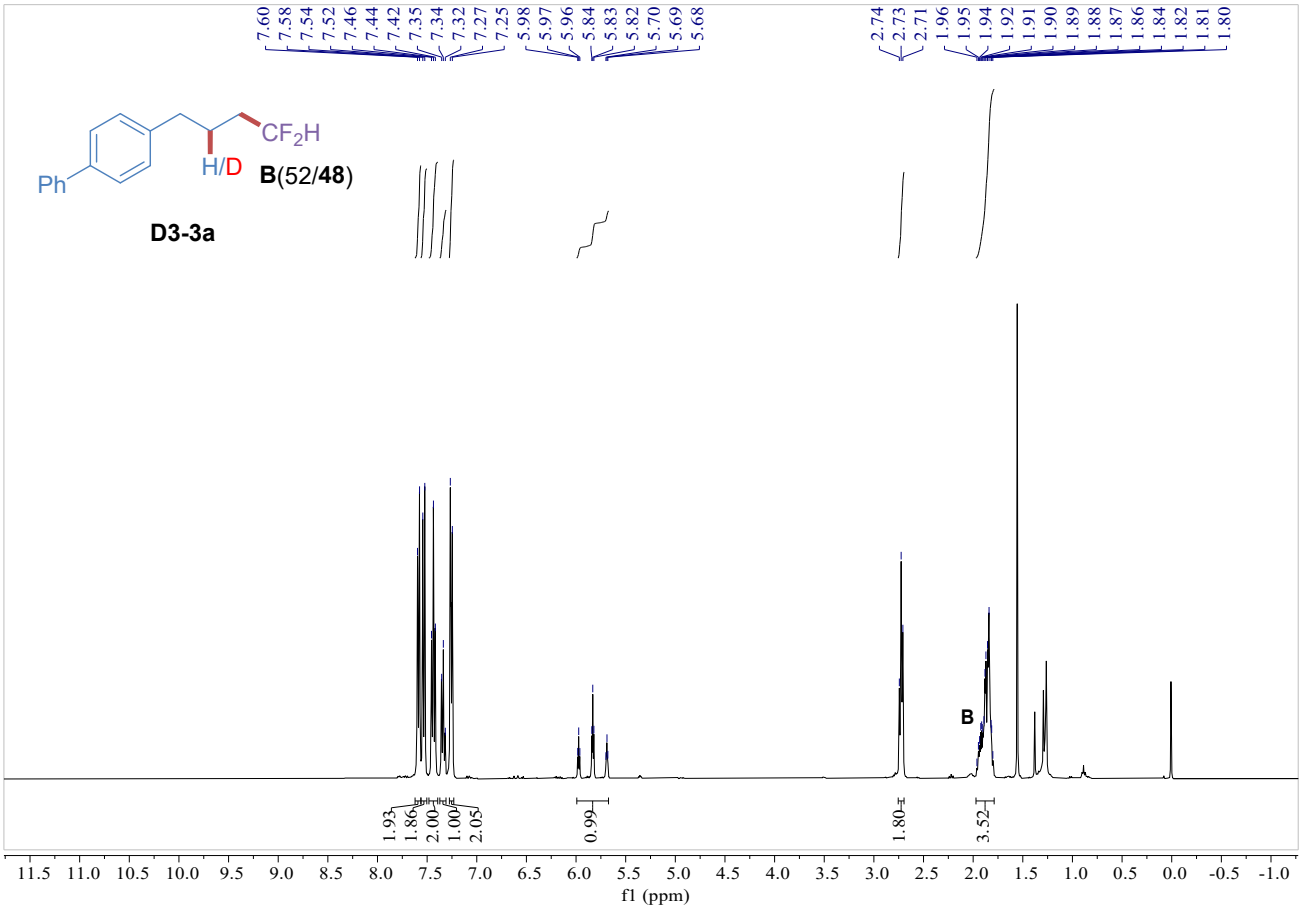
^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **3n'**



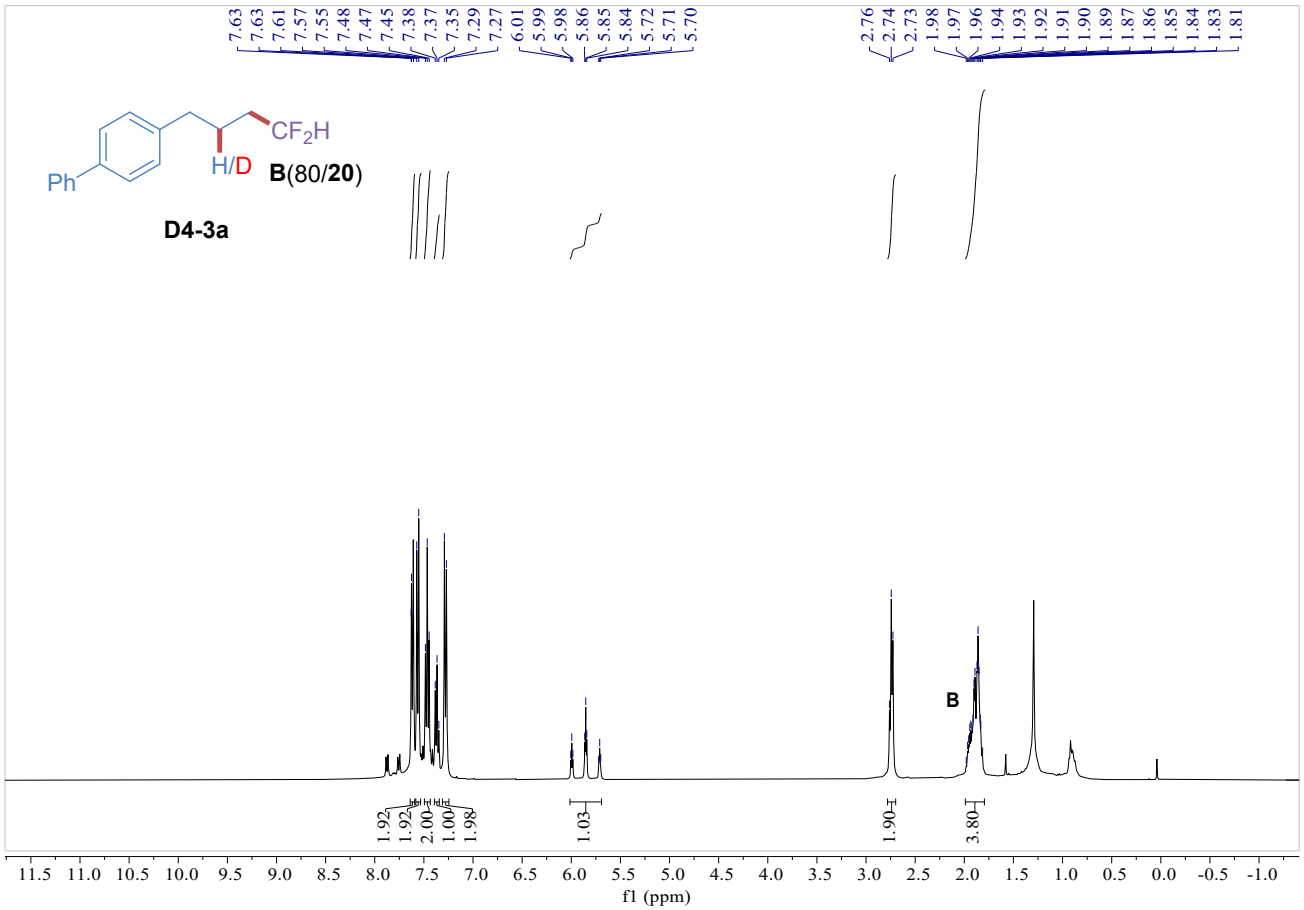
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **D1-3a**



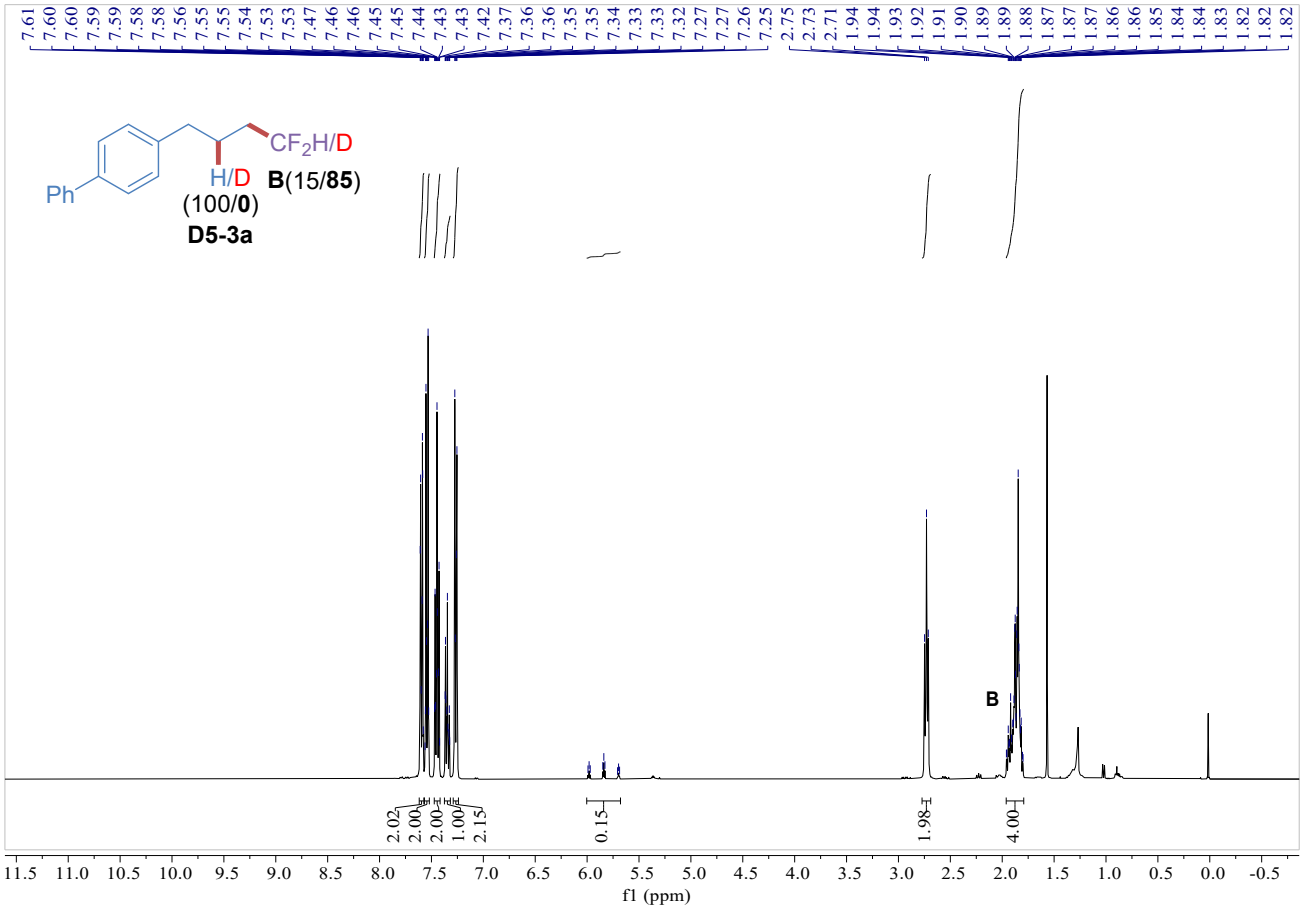
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **D2-3a**



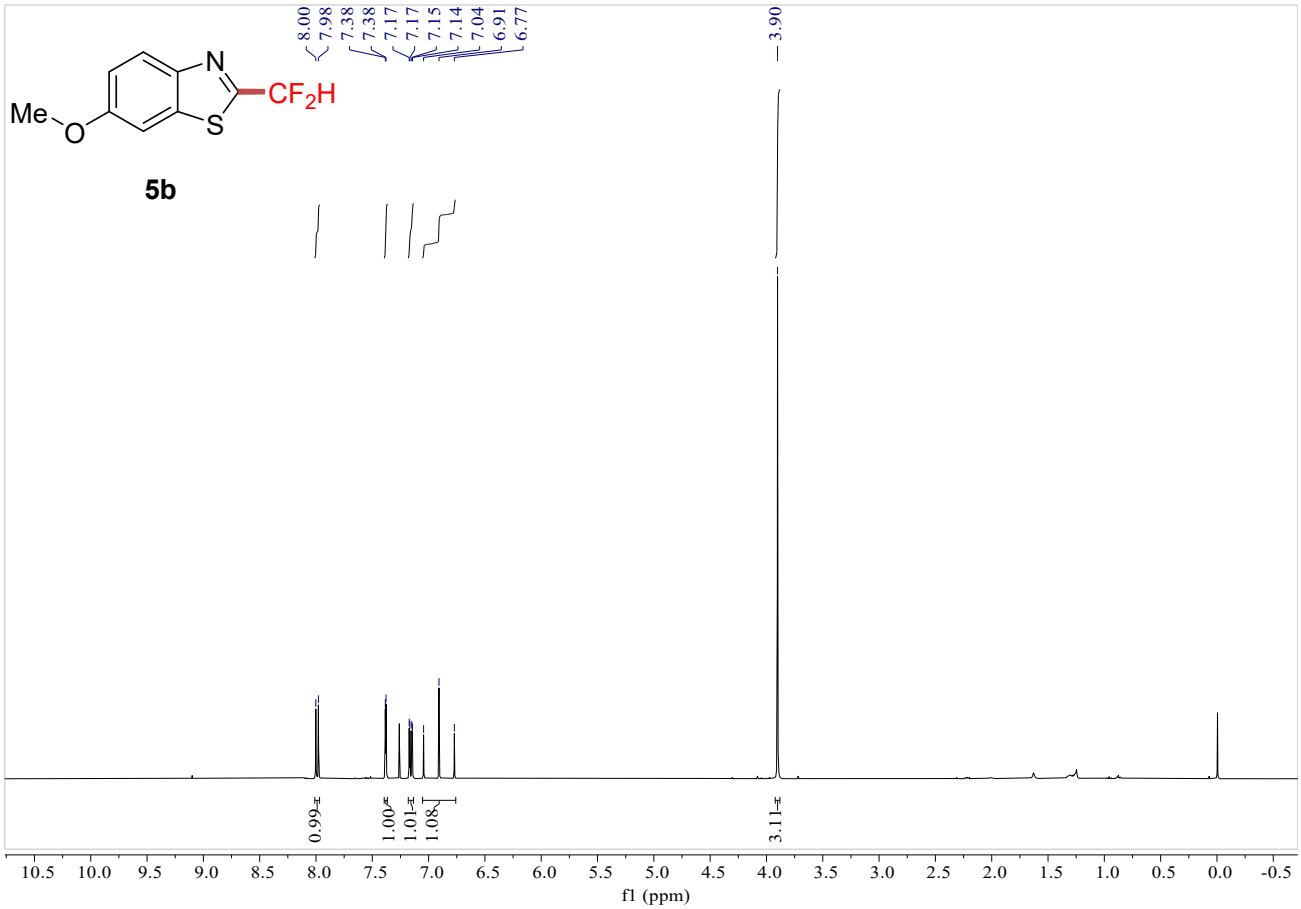
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **D3-3a**



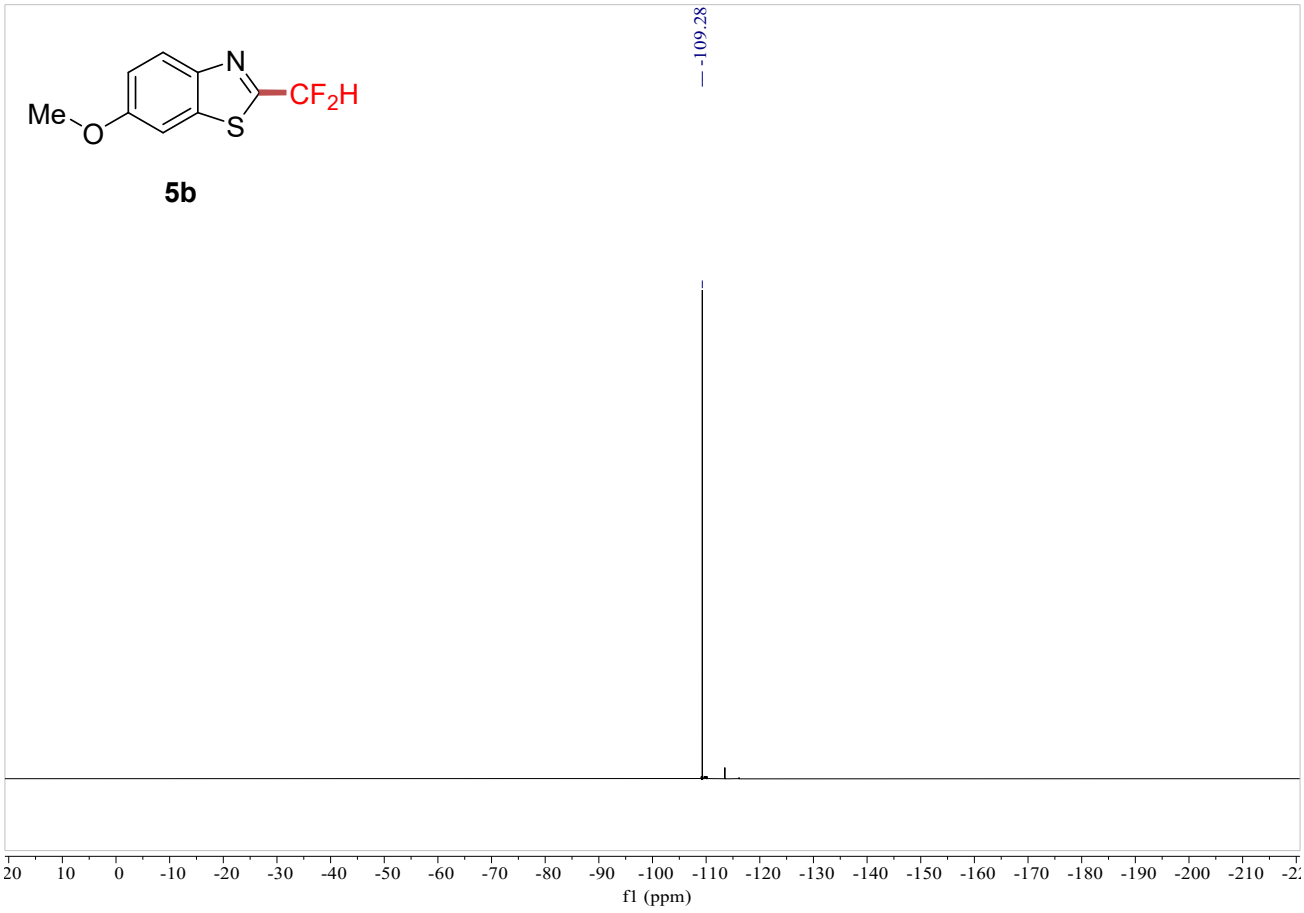
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **D4-3a**



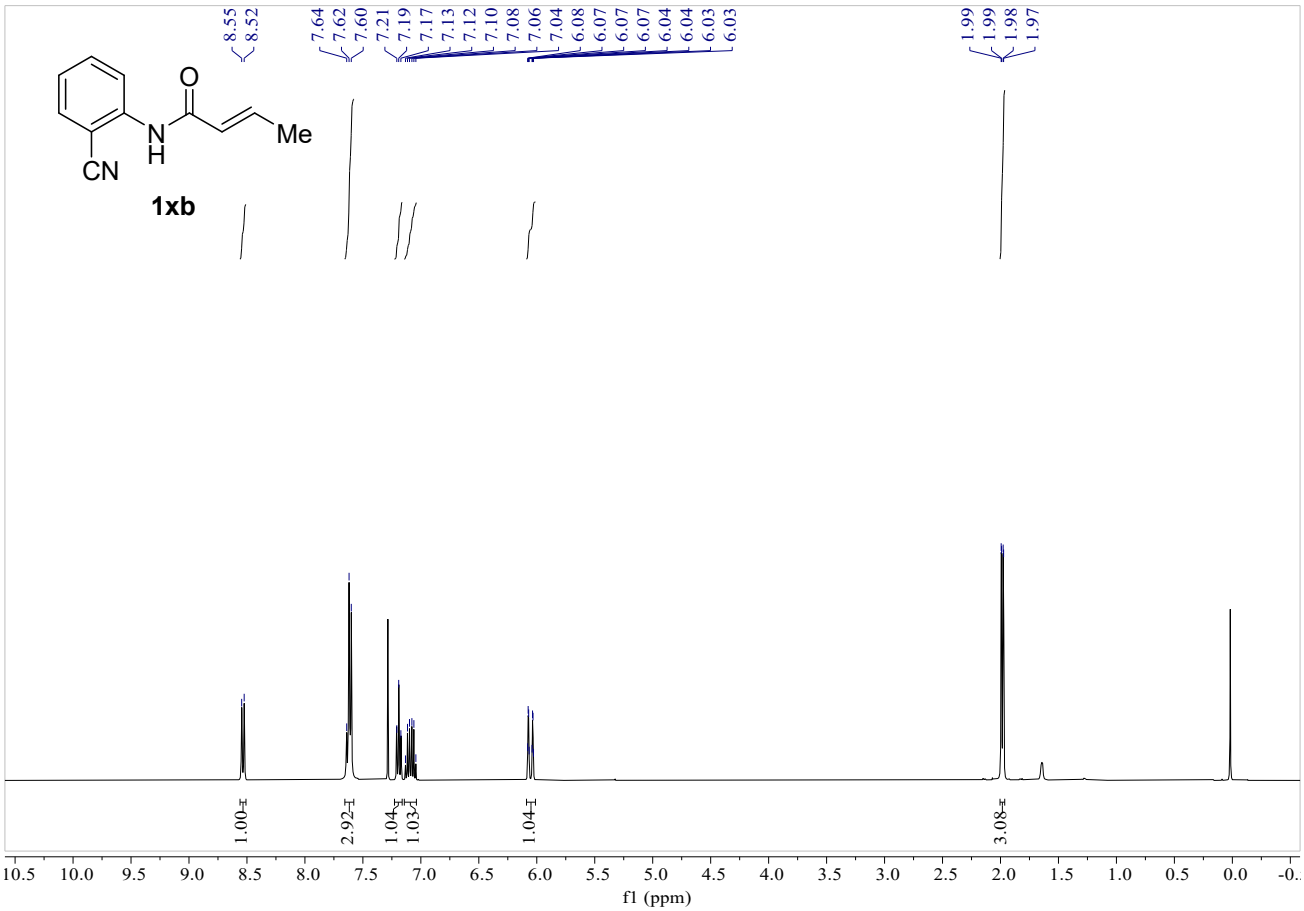
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **D5-3a**



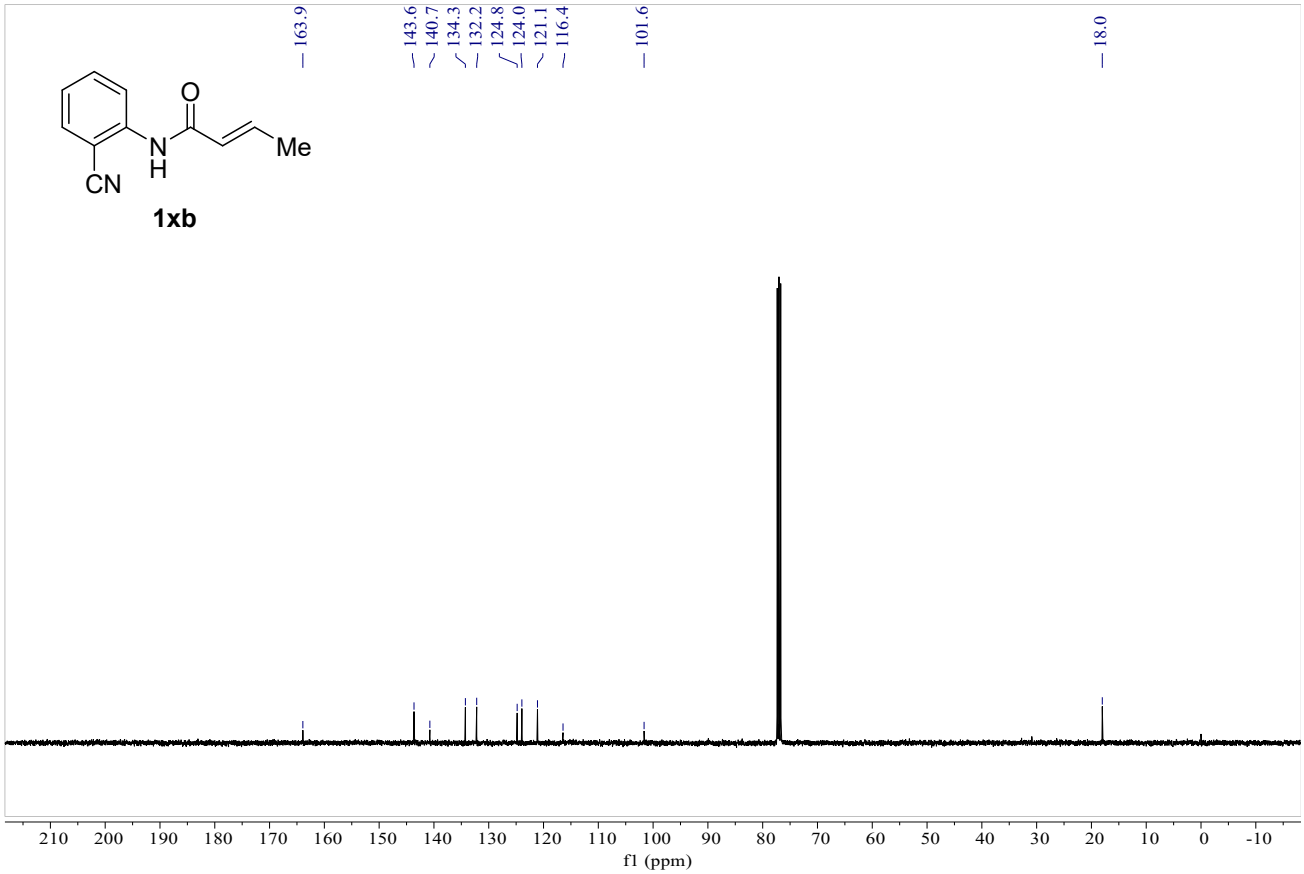
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **5b**



^{19}F NMR spectrum (377 MHz, $CDCl_3$) of compound **5b**



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **1xb**



^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **1xb**