Supporting Information

Visible-light-induced Hydroxycarboxylation of *α*-Trifluoromethylstyrenes to Construct Densely Functionalized *α*-CF3 Tertiary Alcohols

Min-Ming Lu,[a] Ning Deng,*[b] Shi-Yu Li,[a] Ren-Jie Tong,[a] Jun Xu,*[a] and Hua-Jian Xu*[a,b]

[a] School of Food and Biological Engineering, Hefei University of Technology, Hefei 230009, P. R. China

[b] School of Chemistry and Chemical Engineering, Hefei University of Technology, Hefei 230009, P. R. China

E-mail: hjxu@hfut.edu.cn (H.-J. Xu); junxu@hfut.edu.cn (J. Xu); ndeng@hfut.edu.cn (N. Deng)

Table of content

1 General Information

All the starting materials were obtained from commercial sources and used without further purification; reactions were carried out in flame-dried glassware unless otherwise stated. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on BRUKER 400 MHz or Keysight 600 MHz spectrometer in deuterated solvents. ^{1}H NMR chemical shifts are reported in ppm with the internal TMS signal at 0.0 ppm as a standard. The data is being reported as (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or unresolved, coupling constant(s) in Hz, integration). ^{13}C NMR spectra were recorded in deuterated solvent. GC measurements were conducted on Thermo Fisher Trace 1300. HRMS ESI-mass data were acquired on Thermo LTQ Orbitrap XL instrument equipped with an ESI source and controlled by Xcalibur software. Chromatographic purification of products was accomplished using forced-flow chromatography on silica gel (300-400 mesh). UV-Vis spectrum was measured by UV-3600. Photocatalytic reactions were conducted in photo-reactors, which comprise a circulating pump for cooling (approximately room temperature) and one 10W blue LED (purchased from Beijing Rogertech Ltd.) beads for each place. The average power output of the photo-reactor was ca. 6268.499uW/cm²/nm. The emission spectra of the blue LEDs were recorded on an OHSP-350UV spectrometer. The spectra were normalized to 1.0 at the maximum (455 nm). Melting point ranges were recorded by SGW®X-4 Melting-point Apparatus from Shanghai INESA.

2 Reaction Optimization Tables

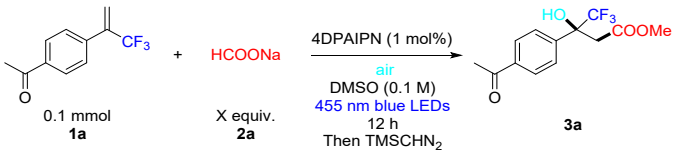
2.1 Optimization of solvents (Table S1)[a]

0.1 mmol **1a** | 3.0 equiv. **2a** | **3a**

Entry	Solvent	3a (%)[b]
1	**DMSO**	**45**
2	DMF	40
3	CH_3CN	<5
4	DCM	nd
5	ethyl acetate	nd
6	methanol	nd
7	THF	nd
8	DMAc	35
9	NMP	12
10	DMI	5

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.3 mmol) and 4DPAIPN (1 mol%, 0.001 mmol) in solvent (1 mL), irradiation with 10 W 455 nm blue LEDs at room temperature (r.t.) for 12 h, air. [b]Isolated yield.

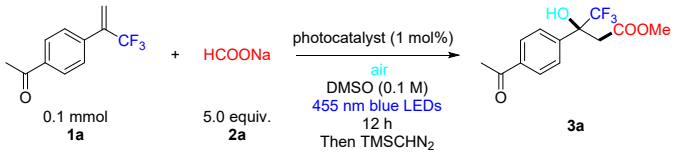
2.2 Optimization of HCOONa (Table S2) [a]



Entry	X equiv.	3a (%)[b]
1	1.0 equiv.	8
2	2.0 equiv.	35
3	3.0 equiv.	45
4	4.0 equiv.	63
5	**5.0 equiv.**	**76**
6	8.0 equiv.	78
7	10.0 equiv.	76

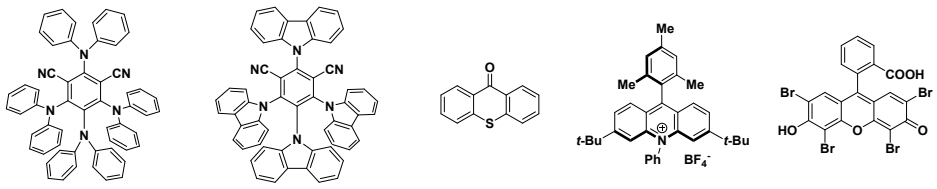
[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.1x mmol) and 4DPAIPN (1 mol%, 0.001 mmol) in DMSO (1 mL), irradiation with 10 W 455 nm blue LEDs at room temperature (r.t.) for 12 h, air. [b]Isolated yield.

2.3 Optimization of photocatalyst (Table S3) [a]

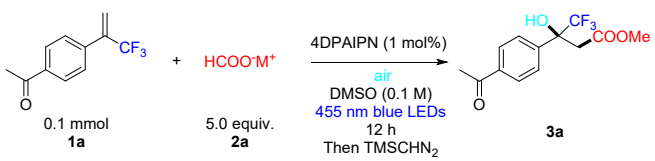


Entry[a]	Photocatalyst	3a (%)[b]
1	**4DPAIPN**	**76**
2	4CzIPN	70
3	TXO	8
4	Mes-Acr^{+}BF$_4^{-}$	36
5	Eosin Y	69

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.5 mmol) and photocatalyst (1 mol%, 0.001 mmol) in DMSO (1 mL), irradiation with 10 W 455 nm blue LEDs at room temperature (r.t.) for 12 h, air. [b]Isolated yield.



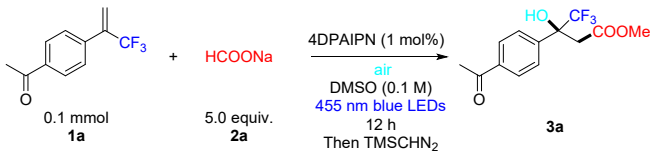
2.4 Optimization of formate salts (Table S4) [a]



Entry[a]	$HCOO^-M^+$	3a (%)[b]
1	HCOOLi	17
2	**HCOONa**	**76**
3	HCOOK	52
4	HCOOCs	35

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.5 mmol) and 4DPAIPN (1 mol%, 0.001 mmol) in DMSO (1 mL), irradiation with 10 W 455 nm blue LEDs at room temperature (r.t.) for 12 h, air. [b]Isolated yield.

2.5 Control experiments (Table S5) [a]

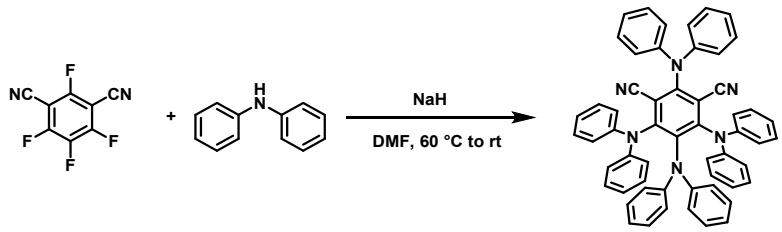


Entry[a]	Variation from the standard conditions	3a (%)[b]
1	**None**	**76**
2	Without 4DPAIPN	<5
3	Without HCOONa	nd
4[c]	Reaction in dark	<5
5[d]	365 nm	12
6	Reaction in nitrogen atmosphere	nd

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.5 mmol) and 4DPAIPN (1 mol%, 0.001 mmol) in DMSO (1 mL), irradiation with 10 W 455 nm blue LEDs at room temperature (r.t.) for 12 h, air. [b]Isolated yield. [c]Heated to 50 °C. [d]No 4DPAIPN but under 365 nm purple LEDs.

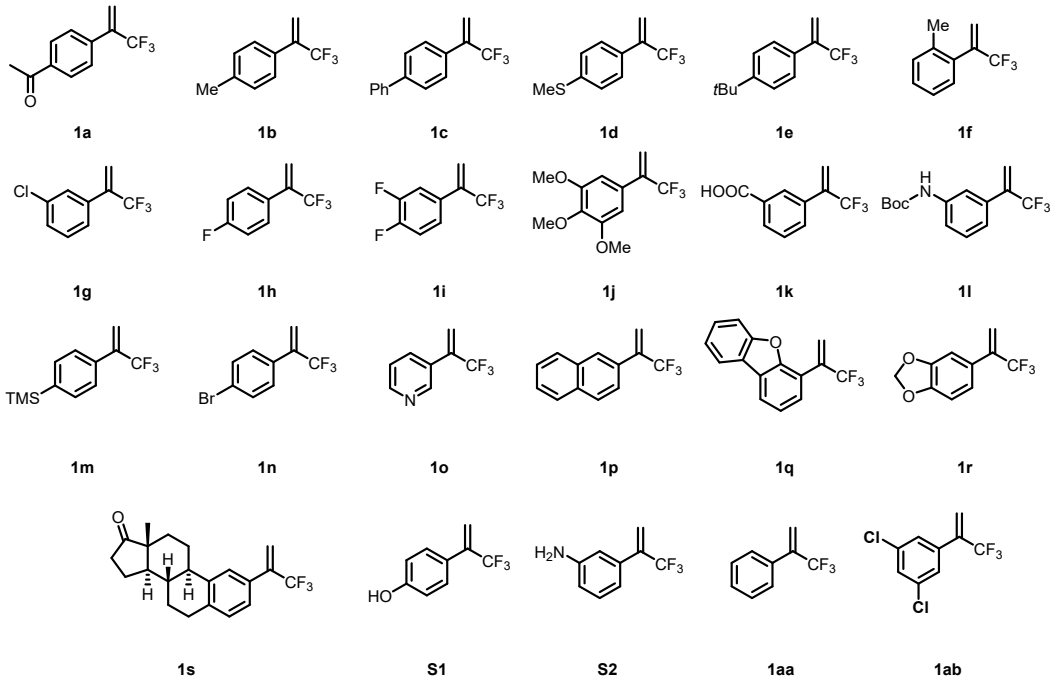
3 Synthesis of Substrates

3.1 Preparation of catalyst



2,4,5,6-tetrakis(diphenylamino)isophthalonitrile (4-DPAIPN) was prepared according to a previous published protocol[1]. NaH (60% dispersion, 3.00 g, 75.0 mmol, 7 equiv.) was added to a flame-dried flask under N_2. DMF (150 mL) was then added followed by slow addition of a solution of diphenylamine (8.46 g, 50.00 mmol, 5.00 equiv.) in DMF (25 mL). The mixture was then heated to 60 °C for 30 min. 2,4,5,6-tetrafluoroisophthalonitrile (2.00 g, 10.0 mmol, 1.00 equiv.) in DMF (25 mL) was then slowly added. The solution was allowed to stir at 40 °C for 12 h and rt for an additional 12 h. The reaction mixture was then cooled in an ice bath and 10 mL water was added slowly to quench residual NaH. The quenched mixture was then added to a flask containing 200 mL water. The precipitate was filtered off and concentrated. After redissolving in DCM, the product was filtered through a silica plug and then recrystallized from DCM/hexanes affording 4.92 g (6.17 mmol, 62% yield).

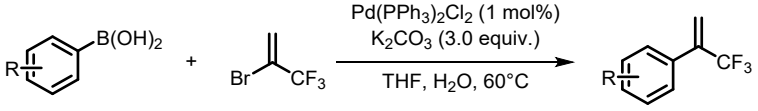
3.2 Preparation of trifluoromethyl alkenes



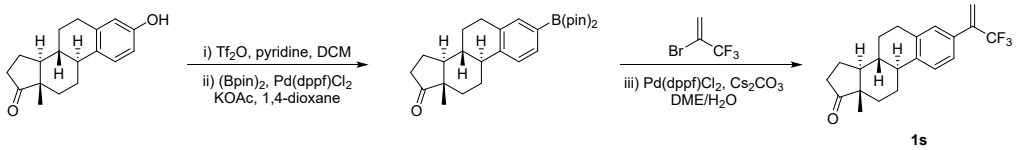
Scheme S1 Structures of trifluoromethyl alkenes

1-trifluoromethylalkenes were prepared following literature procedures[2]. The spectroscopic data of **1a-1r**[2], **S1-S2**[2] , **1aa-1ab**[2], **1t**[2], **1v**[2]and **1s**[3]were consistent with those reported in the literature.

General procedure A[2]**:** Synthesis of trifluoromethyl alkenes **(1a-1r, 1aa-1ab and S1-S3)**



To a Schlenk tube equipped a magnetic stir bar, boronic acid (5 mmol, 1.0 equiv.), $Pd(PPh_3)_2Cl_2$ (35.1 mg, 1 mol%) were added. The vessel was evacuated and filled with argon (three times), and then THF (15 mL) and aqueous K_2CO_3 (2.0 M, 10 mL) were added. After the addition of 2-bromo-3,3,3-trifluoropropene (1.0 mL, 10 mmol, 2.0 equiv.), the reaction mixture was stirred at 60 °C overnight under an argon atmosphere. The resultant mixture was cooled to room temperature, quenched with saturated aqueous NH_4Cl, and extracted with EtOAc (3 × 15 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (petroleum ether/ethyl acetate) to give the desired corresponding trifluoromethyl alkene.

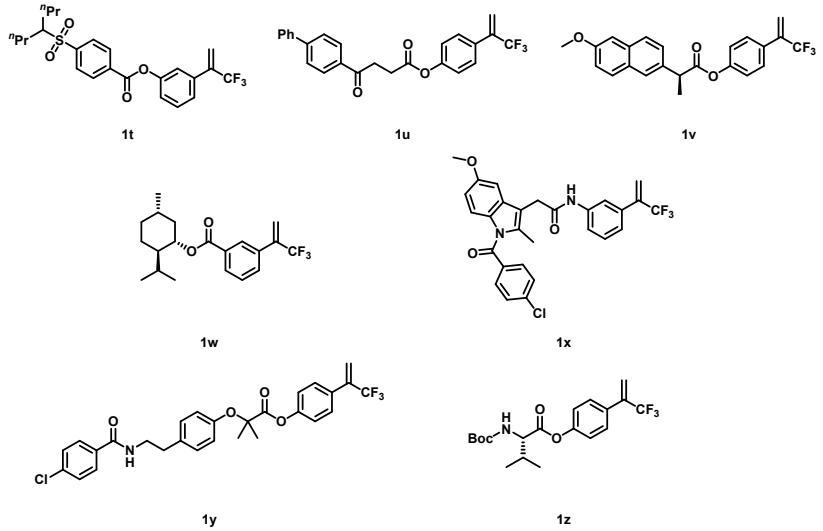


Synthesis of substrate 1s[3]**: :** i) Tf_2O (2.8 g, 10 mmol, 1.0 equiv.) was added dropwise to a solution of estrone (2.9 g, 11 mmol, 1.1 equiv.) and pyridine (2.8 mL, 20 mmol, 2.0 equiv.) in anhydrous DCM (25 mL) at 0 °C The mixture was stirred for 1 h, slowly warmed to room temperature and quenched by the addition of water. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (20 mL× 2), combined organic layers were dried over Na_2SO_4 and solvent was removed under reduced pressure. The crude mixture was purified by column chromatography (petroleum ether/ethyl acetate =

10:3) to give estrone trifluoromethanesulfonic ester (3.0 g, yield: 76%) which was used in the next step.

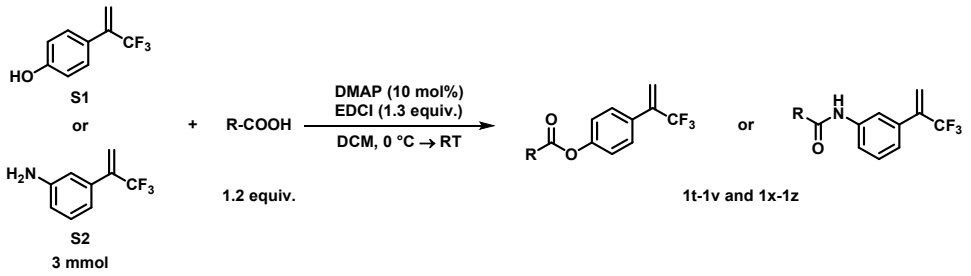
ii) A 100 mL Schlenk tube with a magnetic stir bar was charged with the above obtained estrone trifluoromethanesulfonic ester (2.0 g, 5.0 mmol, 1.0 equiv.), bis(pinacolato)diboron (2.5 g, 10 mmol, 2.0 equiv.), KOAc (1.5 g, 15 mmol, 3.0 equiv.), and Pd(dppf)Cl_2 (183.0 mg, 0.2 mmol, 4 mol%) under nitrogen, followed by dioxane (30.0 mL) with stirring. The Schlenk tube was heated to 120 ℃. After stirring for 8 hours, the reaction mixture was cooled to room temperature and diluted with THF, dried over Na_2SO_4, then filtered and concentrated. The crude product was purified by column chromatography (petroleum ether/ethyl acetate = 5:1) to give the desired boronate pinacol (1.5 g, yield: 78%) which was used in the next step.

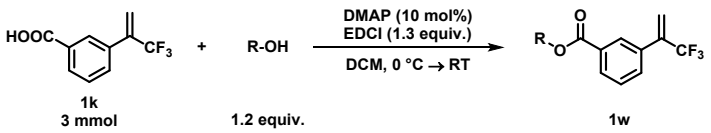
iii) To a 50 mL Schlenk tube was added boronate pinacol (1.5 g, 4.3 mmol, 1.0 equiv.), Cs_2CO_3 (1.69 g, 5.2 mmol, 1.2 equiv.), and Pd(dppf)Cl_2 (0.29 g, 0.40 mmol, 0.1 equiv.). The tube was sealed with a rubber septum and evacuated three times via branch, then purged with N_2. A mixture of degassed DME (20 mL) and degassed, deionized H_2O (7 mL) were added via syringe, followed by 2-bromo-3,3,3- trifluoroprop-1-ene (0.83 mL, 8.00 mmol, 2.0 equiv.). The tube was heated to 80 °C for 24 hours. Once completed, the reaction was cooled to room temperature and diluted in EtOAc (50 mL). The resultant crude product was purified by column chromatography (petroleum ether/ethyl acetate = 10:1) to give the desired trifluoromethyl alkene as a white solid (0.90 g, yield: 60%).



Scheme S2 Structures of trifluoromethyl alkenes derived from drugs

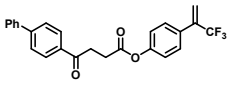
General procedure B[2]: Synthesis of substrate **(1t - 1z)**





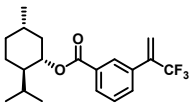
To a solution of carboxylic acid or **1k** (1.2 equiv., 3.6 mmol), 4-Dimethylaminopyridine (DMAP) (10 mol%, 0.3 mmol, 36.6 mg) and alcohol or **S1**/**S2** (1.0 equiv., 3 mmol) in DCM (10mL), 1-Ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDCI) (1.3 equiv., 3.9 mmol) was added at 0℃. The reaction mixture was slowly warmed to room temperature and stirred at room temperature for 12 hours (TLC tracking detection). Once complete, the reaction was quenched by water. The organic layer was then separated, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The mixture was purified by column chromatography to afford the corresponding trifluoromethyl alkenes (**1t - 1z**).

4-(3,3,3-trifluoroprop-1-en-2-yl)phenyl 4-([1,1'-biphenyl]-4-yl)-4-oxobutanoate (1u)



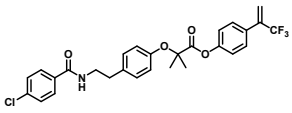
The product (66% yield determined by isolated yield) was purified with column chromatography (petroleum ether/EtOAc = 5:1) as a pink solid. **mp** = 82 – 86 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.09 (d, *J* = 8.5 Hz, 2H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.64 (d, *J* = 7.0 Hz, 1H), 7.51 – 7.46 (m, 4H), 7.44 – 7.39 (m, 1H), 7.17 (d, *J* = 8.7 Hz, 2H), 5.96 (q, *J* = 1.4 Hz, 1H), 5.76 (q, *J* = 1.7 Hz, 1H), 3.48 (t, *J* = 6.5 Hz, 2H), 3.05 (t, *J* = 6.5 Hz, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 197.5, 171.5, 151.3, 146.1, 139.8, 138.1 (q, *J* = 30.5 Hz), 135.1, 131.2, 129.0, 128.7, 128.6, 128.4, 127.3, 127.3, 123.2 (q, *J* = 274.7 Hz), 121.8, 120.7 (q, *J* = 5.8 Hz), 33.5, 28.5. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -64.82. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{25}H_{19}F_3O_3$ 424.1286, found: 424.1284.

(1*S*,2*R*,5*S*)-2-isopropyl-5-methylcyclohexyl 3-(3,3,3-trifluoroprop-1-en-2-yl)benzoate (1w)



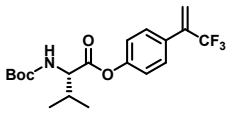
The product (87 % yield determined by isolated yield) was purified with column chromatography (petroleum ether/EtOAc = 5:1) as a colorless oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.95 (d, *J* = 1.9 Hz, 1H), 7.88 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.45 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.28 (t, *J* = 7.8 Hz, 1H), 5.84 (q, *J* = 1.4 Hz, 1H), 5.65 (q, *J* = 1.7 Hz, 1H), 4.77 (td, *J* = 10.9, 4.4 Hz, 1H), 2.00 – 1.88 (m, 1H), 1.76 (pd, *J* = 7.0, 2.7 Hz, 1H), 1.62 – 1.50 (m, 2H), 1.39 (ddt, *J* = 10.7, 9.1, 3.1 Hz, 2H), 1.02 – 0.87 (m, 2H), 0.74 (dd, *J* = 6.9, 4.0 Hz, 6H), 0.62 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 165.5, 138.2 (q, *J* = 30.3 Hz), 133.9, 131.4, 131.4, 130.0, 128.7, 123.2 (q, *J* = 273.9 Hz), 121.4 (q, *J* = 5.7 Hz), 75.2, 47.2, 40.9, 34.3, 31.5, 26.6, 23.7, 22.1, 20.7. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -64.85. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{20}H_{25}F_3O_2$ 355.1879, found 355.1878.

4-(3,3,3-trifluoroprop-1-en-2-yl)phenyl 2-(4-(2-(4-chlorobenzamido)ethyl)phenoxy)-2-methylpropanoate (1y)



The product (80% yield determined by isolated yield) was purified with column chromatography (petroleum ether/EtOAc = 3:1) as a white solid. **mp** = 79 – 82 °C. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.60 (dd, *J* = 8.5, 3.4 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 1H), 7.37 – 7.31 (m, 3H), 7.12 (dd, *J* = 8.4, 3.4 Hz, 2H), 7.04 (d, *J* = 8.7 Hz, 1H), 7.01 (d, *J* = 7.7 Hz, 1H), 6.92 (dd, *J* = 8.4, 3.8 Hz, 2H), 6.34 (s, 1H), 5.96 (d, *J* = 1.4 Hz, 1H), 5.75 (d, *J* = 1.7 Hz, 1H), 3.64 (d, *J* = 6.5 Hz, 2H), 2.86 (t, *J* = 6.9 Hz, 2H), 1.74 (s, 6H). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 172.8, 166.5, 154.0, 151.0, 137.8 (q, *J* = 30.2 Hz), 137.6, 132.9, 132.8, 129.7, 129.5, 128.8, 128.3, 126.2, 123.2 (q, *J* = 273.9 Hz), 121.5, 120.9 (q, *J* = 6.0 Hz), 119.4, 79.2, 41.3, 34.7, 25.4. **^{19}F NMR** (564 MHz, Chloroform-*d*) δ -64.87. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. For $C_{28}H_{25}ClF_3NO_4$ 532.1497, found: 532.1498.

4-(3,3,3-trifluoroprop-1-en-2-yl)phenyl (tert-butoxycarbonyl)-*L*-valinate (1z)



The product (74% yield determined by isolated yield) was purified with column chromatography (petroleum ether/EtOAc = 10:1) as a colorless oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.47 (d, *J* = 8.3 Hz, 2H), 7.12 (d, *J* = 8.7 Hz, 2H), 5.97 (d, *J* = 1.5 Hz, 1H), 5.76 (d, *J* = 1.7 Hz, 1H), 5.07 (d, *J* = 9.1 Hz, 1H), 4.46 (dd, *J* = 9.1, 4.9 Hz, 1H), 2.37 – 2.28 (m, 1H), 1.47 (s, 9H), 1.09 (d, *J* = 6.9 Hz, 3H), 1.03 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 171.0, 155.8, 150.9, 138.0 (q, *J* = 30.3 Hz), 131.5, 128.8, 123.2 (q, *J* = 273.9 Hz), 121.6, 120.8 (d, *J* = 6.1 Hz), 115.5, 80.1, 58.7, 31.3, 28.3, 19.1, 17.7. **^{19}F NMR** (564 MHz, DMSO-d_6) δ -69.70. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. For $C_{19}H_{24}F_3NO_4$ 388.1730, found: 388.1732.

4 Experimental Procedures and Characterization Data

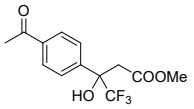
4.1 General procedure

To a 25 mL of Schlenk tube were added 4DPAIPN (1.5 mg, 0.002 mmol, 1 mol%), HCOONa (68.0 mg, 1.0 mmol, 5.0 equiv.), trifluoromethyl alkenes (0.2 mmol) and DMSO (2 mL). Then the reaction mixture was irradiated under blue LED strips (455nm, 10 W) for 12 h at room temperature with stirring under air atmosphere. The mixture was quenched with 3 mL HCl (1 M), extracted with EtOAc (3×10 mL) and the combined organic phase was washed with brine, dried by anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was dissolved in 4 mL MeOH/Et_2O (1/3), $TMSCH_2N_2$ (0.3

mL, 0.60 mmol, 2.0 M in hexane) was added drop wisely at 0 °C. The mixture was stirred at ambient temperature until the completion of the methylation reaction. The organic layers were concentrated under vacuo. The product was purified via flash column chromatography on silica gel.

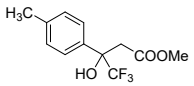
4.2 Characterization Data for Compounds 3a-3aa'

Methyl 3-(4-acetylphenyl)-4,4,4-trifluoro-3-hydroxybutanoate (3a)



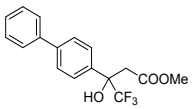
The product (76% yield) was purified with column chromatography (petroleum ether/EtOAc = 20:1) as a yellow oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.98 (d, *J* = 8.5 Hz, 2H), 7.69 (d, *J* = 8.3 Hz, 2H), 5.34 (s, 1H), 3.67 (s, 3H), 3.19 (s, 2H), 2.61 (s, 3H). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 197.6, 171.7, 141.9, 137.4, 128.4, 126.8, 124.2 (q, *J* = 285.4 Hz), 75.3 (q, *J* = 29.7 Hz), 52.7, 38.0, 26.7. **^{19}F NMR** (564 MHz, Chloroform-*d*) δ -80.19. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{13}H_{13}F_3O_4$ 291.0839, found 291.0840.

Methyl 4,4,4-trifluoro-3-hydroxy-3-(*p*-tolyl)butanoate (3b)



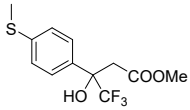
The product (80% yield determined by isolated yield) was purified with column chromatography (petroleum ether/EtOAc = 20:1) as a colorless oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.46 (d, *J* = 8.0 Hz, 2H), 7.21 (d, *J* = 8.7 Hz, 2H), 5.17 (s, 1H), 3.67 (s, 2H), 3.16 (m, 2H), 2.36 (s, 3H). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 171.9, 138.8, 134.0, 129.2, 126.2, 124.5 (q, *J* = 284.9 Hz), 75.2 (q, *J* = 29.3 Hz), 52.5, 38.1, 21.1. **^{19}F NMR** (564 MHz, Chloroform-*d*) δ -80.60. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{12}H_{13}F_3O_3$ 263.0890, found 263.0889.

Methyl 3-([1,1'-biphenyl]-4-yl)-4,4,4-trifluoro-3-hydroxybutanoate (3c)



The product (85% yield determined by isolated yield) was purified with column chromatography (petroleum ether/EtOAc = 20:1) as a white solid. **mp** = 98 – 100 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.67 – 7.62 (m, 4H), 7.60 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.37 (t, *J* = 7.3 Hz, 1H), 5.30 (s, 1H), 3.69 (s, 3H), 3.28 – 3.15 (m, 2H). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 171.9, 141.8, 140.2, 135.9, 128.8, 127.7, 127.2, 127.1, 126.8, 124.2 (q, *J* = 285.4 Hz), 75.2 (q, *J* = 30.2 Hz), 52.6, 38.1. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -80.35. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{17}H_{15}F_3O_3$ 325.1046, found 325.1043.

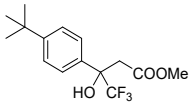
Methyl 4,4,4-trifluoro-3-hydroxy-3-(4-(methylthio)phenyl)butanoate (3d)



The product (89% yield determined by isolated yield) was purified column chromatography (petroleum ether/EtOAc = 10:1) as a yellow oil. **^{1}H NMR** (600

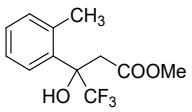
MHz, Chloroform-*d*) δ 7.48 (d, *J* = 8.3 Hz, 2H), 7.25 (d, *J* = 8.6 Hz, 2H), 5.22 (s, 1H), 3.66 (s, 3H), 3.21 – 3.10 (m, 2H), 2.48 (s, 3H). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 171.9, 139.9, 133.4, 126.8, 125.9, 124.4 (q, *J* = 285.0 Hz), 75.1 (q, *J* = 29.5 Hz), 52.5, 38.0, 15.2. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -80.59. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{12}H_{13}F_3O_3S$ 295.0610, found 295.0608.

Methyl 3-(4-(*tert*-butyl)phenyl)-4,4,4-trifluoro-3-hydroxybutanoate (3e)



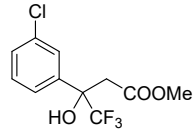
The product (61% yield determined by isolated yield) was purified with column chromatography (petroleum ether/EtOAc = 10:1) as a yellow oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.49 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 8.6 Hz, 2H), 5.25 (s, 1H), 3.68 (s, 3H), 3.21 – 3.13 (m, 2H), 1.32 (s, 9H). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 172.0, 151.9, 133.9, 126.0, 125.4, 124.6 (q, *J* = 285.0 Hz), 75.1 (q, *J* = 29.4 Hz), 52.5, 38.0, 34.5, 31.2. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -78.18. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{15}H_{19}F_3O_3$ 305.1359, found 305.1357.

Methyl 4,4,4-trifluoro-3-hydroxy-3-(*o*-tolyl)butanoate (3f)



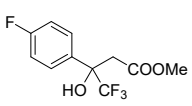
The product (46% yield determined by isolated yield) was purified with column chromatography (petroleum ether/EtOAc = 20:1) as a yellow oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.34 (d, *J* = 8.0 Hz, 1H), 7.27 – 7.22 (m, 1H), 7.18 (dd, *J* = 15.8, 7.7 Hz, 2H), 5.26 (s, 1H), 3.68 (s, 3H), 3.28 (dd, *J* = 151.5, 16.4 Hz, 2H), 2.63 (s, 3H). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 172.4, 138.6, 134.3, 133.6, 129.0, 127.7, 125.7, 125.0 (q, *J* = 285.6 Hz), 77.8 (q, *J* = 29.4 Hz), 52.5, 39.1, 22.9. **^{19}F NMR** (564 MHz, Chloroform-*d*) δ -79.62. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{12}H_{13}F_3O_3$ 263.0890, found 263.0893.

Methyl 3-(3-chlorophenyl)-4,4,4-trifluoro-3-hydroxybutanoate (3g)



The product (51% yield determined by isolated yield) was purified with flash column chromatography (petroleum ether/EtOAc = 20:1) as a yellow oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.61 (s, 1H), 7.44 (d, *J* = 7.9 Hz, 1H), 7.38 – 7.32 (m, 2H), 5.35 (s, 1H), 3.69 (s, 3H), 3.24 – 3.06 (m, 2H). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 171.7, 139.0, 134.7, 129.7, 129.3, 126.9, 124.5, 124.2 (q, *J* = 285.0 Hz), 75.0 (q, *J* = 29.6 Hz), 52.7, 38.0. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -80.32. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{11}H_{10}ClF_3O_3$ 283.0343, found 283.0341.

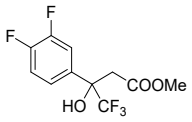
Methyl 4,4,4-trifluoro-3-(4-fluorophenyl)-3-hydroxybutanoate (3h)



The product (78% yield determined by isolated yield) was purified with column

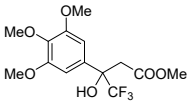
chromatography (petroleum ether/EtOAc = 20:1) as a yellow oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.56 (dd, *J* = 8.7, 5.3 Hz, 2H), 7.08 (t, *J* = 8.7 Hz, 2H), 5.29 (s, 1H), 3.68 (s, 3H), 3.15 (s, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 171.8, 163.1 (d, *J* = 248.4 Hz), 132.8 (d, *J* = 3.3 Hz), 128.4 (d, *J* = 8.5 Hz), 124.3 (q, *J* = 285.8 Hz), 115.5 (d, *J* = 21.6 Hz), 75.0 (q, *J* = 29.6 Hz), 52.6, 38.1. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -80.66, -112.99. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{11}H_{10}F_4O_3$ 267.0639, found 267.0640.

Methyl 3-(3,4-difluorophenyl)-4,4,4-trifluoro-3-hydroxybutanoate (3i)



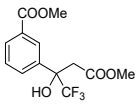
The product (86% yield determined by isolated yield) was purified with column chromatography (petroleum ether/EtOAc = 20:1) as a yellow oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.46 (ddd, *J* = 11.5, 7.5, 2.4 Hz, 1H), 7.30 – 7.27 (m, 1H), 7.18 (ddd, *J* = 9.9, 8.7, 7.9 Hz, 1H), 5.37 (s, 1H), 3.70 (s, 3H), 3.24 – 3.03 (m, 2H). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 171.6, 150.7 (dd, *J* = 250.7, 12.3 Hz), 150.2 (dd, *J* = 248.6, 12.3 Hz), 134.2 – 134.0 (m), 124.1 (q, *J* = 285.0 Hz), 122.7 – 122.6 (m), 117.3 (d, *J* = 17.5 Hz), 116.3 (d, *J* = 18.9 Hz), 74.7 (q, *J* = 30.4, 29.7 Hz), 52.7, 37.9. **^{19}F NMR** (564 MHz, Chloroform-*d*) δ -80.62, -136.47, -137.08. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{11}H_9F_5O_3$ 285.0545, found 285.0544.

Methyl 4,4,4-trifluoro-3-hydroxy-3-(3,4,5-trimethoxyphenyl)butanoate (3j)



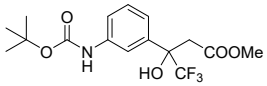
The product (73% yield determined by isolated yield) was purified with column chromatography (petroleum ether/EtOAc = 3:1) as a yellow oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.77 (s, 2H), 5.30 (s, 1H), 3.85 (d, *J* = 5.2 Hz, 9H), 3.68 (s, 3H), 3.19 – 3.08 (m, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 172.0, 153.0, 138.4, 132.4, 124.4 (q, *J* = 284.7 Hz), 103.7, 75.3 (q, *J* = 29.5 Hz), 60.8, 56.2, 52.7, 38.2. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -80.31. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{14}H_{17}F_3O_6$ 339.1050, found 339.1048.

Methyl 3-(1,1,1-trifluoro-2-hydroxy-4-methoxy-4-oxobutan-2-yl)benzoate (3k)



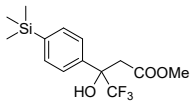
The product (47% yield determined by isolated yield) was purified with column chromatography (petroleum ether/EtOAc = 10:1) as a yellow oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 8.24 (s, 1H), 8.06 (d, *J* = 7.8 Hz, 1H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.49 (t, *J* = 7.8 Hz, 1H), 5.37 (s, 1H), 3.92 (s, 3H), 3.67 (s, 3H), 3.24 – 3.17 (m, 2H). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 171.8, 166.6, 137.6, 130.9, 130.5, 130.2, 128.7, 127.5, 124.3 (q, *J* = 285.0 Hz), 75.1 (q, *J* = 29.6 Hz), 52.6, 52.3, 38.0. **^{19}F NMR** (564 MHz, Chloroform-*d*) δ -81.16. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{13}H_{13}F_3O_5$ 307.0788, found 307.0791.

Methyl 3-(3-((*tert*-butoxycarbonyl)amino)phenyl)-4,4,4-trifluoro-3-hydroxybutanoate (3l)



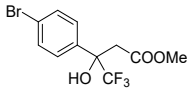
The product (70% yield determined by isolated yield) was purified with column chromatography (petroleum ether/EtOAc = 5:1) as a yellow oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.54 (d, *J* = 2.0 Hz, 1H), 7.29 (t, *J* = 8.0 Hz, 1H), 7.18 (d, *J* = 7.7 Hz, 1H), 6.77 (s, 1H), 5.31 (s, 1H), 3.65 (s, 3H), 3.14 (s, 2H), 1.50 (s, 9H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 171.9, 152.8, 138.8, 137.8, 129.1, 124.4 (q, *J* = 285.1 Hz), 120.7, 119.0, 116.7, 80.7, 75.2 (q, *J* = 29.4 Hz), 52.6, 38.1, 28.3. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -80.24. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{16}H_{20}F_3NO_5$ 364.1366, found 364.1368.

Methyl 4,4,4-trifluoro-3-hydroxy-3-(4-(trimethylsilyl)phenyl)butanoate (3m)



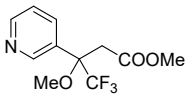
The product (73% yield determined by isolated yield) was purified with column chromatography (petroleum ether/EtOAc = 10:1) as a yellow oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.56 (d, *J* = 1.1 Hz, 4H), 5.27 (s, 1H), 3.68 (s, 3H), 3.28 – 3.14 (m, 2H), 0.28 (s, 9H). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 172.0, 141.5, 137.3, 133.5, 125.5, 124.5 (q, *J* = 285.0 Hz), 75.2 (q, *J* = 29.1 Hz), 52.5, 38.0, -1.2. **^{19}F NMR** (564 MHz, Chloroform-*d*) δ -80.31. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{14}H_{19}F_3O_3Si$ 321.1128, found 321.1125.

Methyl 3-(4-bromophenyl)-4,4,4-trifluoro-3-hydroxybutanoate (3n)



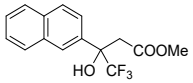
The product (64% yield determined by isolated yield) was purified with column chromatography (petroleum ether/EtOAc = 20:1) as a yellow oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.53 (d, *J* = 8.7 Hz, 2H), 7.46 (d, *J* = 8.6 Hz, 2H), 5.30 (s, 1H), 3.68 (s, 3H), 3.14 (s, 2H). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 171.7, 136.1, 131.7, 128.2, 124.2 (q, *J* = 285.0 Hz), 123.5, 75.1 (q, *J* = 29.5 Hz), 52.7, 37.9. **^{19}F NMR** (564 MHz, Chloroform-*d*) δ -80.53. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{11}H_{10}BrF_3O_3$ 326.9838, found 326.9841.

Methyl 4,4,4-trifluoro-3-methoxy-3-(pyridin-3-yl)butanoate (3o)



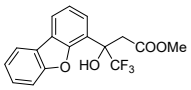
The product (62% yield determined by isolated yield) was purified with column chromatography (petroleum ether/EtOAc = 2:1) as a colorless oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 8.77 (s, 1H), 8.62 (dd, *J* = 4.9, 1.6 Hz, 2H), 7.97 (d, *J* = 8.1 Hz, 1H), 7.36 (dd, *J* = 8.1, 4.8 Hz, 1H), 3.67 (s, 4H), 3.23 – 3.14 (m, 3H), 2.98 (s, 4H). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 171.38, 150.02, 147.56, 134.71, 132.97, 124.51 (q, *J* = 286.9 Hz), 123.30 (d, *J* = 18.1 Hz), 74.34 (q, *J* = 29.9 Hz), 52.71, 42.63, 37.75. **^{19}F NMR** (564 MHz, Chloroform-*d*) δ -80.62. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{11}H_{12}F_3NO_3$ 264.0842, found 264.0835.

Methyl 4,4,4-trifluoro-3-hydroxy-3-(naphthalen-2-yl)butanoate (3p)



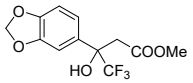
The product (60% yield determined by isolated yield) was purified with column chromatography (petroleum ether/EtOAc = 20:1) as a yellow solid. **mp** = 74 – 78 °C. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 8.13 (s, 2H), 7.92 – 7.85 (m, 3H), 7.69 (d, *J* = 8.2 Hz, 1H), 7.56 – 7.52 (m, 2H), 5.44 (s, 1H), 3.66 (s, 3H), 3.43 – 3.25 (m, 2H). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 172.0, 134.3, 133.3, 132.9, 128.6, 128.3, 127.6, 126.9, 126.5, 126.4, 124.6 (q, *J* = 285.0 Hz), 123.5, 75.5 (q, *J* = 29.4 Hz), 52.6, 38.2. **^{19}F NMR** (564 MHz, Chloroform-*d*) δ -80.11. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{15}H_{13}F_3O_3$ 299.0890, found 299.0887.

Methyl 3-(dibenzo[b,d]furan-4-yl)-4,4,4-trifluoro-3-hydroxybutanoate (3q)



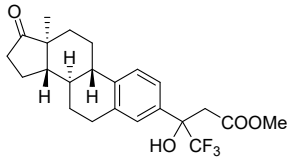
The product (84% yield determined by isolated yield) was purified with column chromatography (petroleum ether/EtOAc = 10:1) as a yellow oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 8.00 (d, *J* = 7.6 Hz, 1H), 7.97 (d, *J* = 7.4 Hz, 1H), 7.94 (d, *J* = 6.7 Hz, 1H), 7.61 (d, *J* = 8.2 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 5.52 (s, 1H), 4.10 – 3.50 (m, 2H), 3.62 (s, 3H). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 172.4, 155.7, 152.7, 127.5, 127.0, 125.1, 124.7 (q, *J* = 286.9 Hz), 123.6, 123.1, 123.0, 121.9, 121.1, 120.7, 111.7, 74.9 (q, *J* = 30.6 Hz), 52.4, 37.3. **^{19}F NMR** (564 MHz, Chloroform-*d*) δ -80.41. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{17}H_{13}F_3O_4$ 339.0839, found 339.0840.

Methyl 3-(benzo[*d*][1,3]dioxol-5-yl)-4,4,4-trifluoro-3-hydroxybutanoate (3r)



The product (75% yield determined by isolated yield) was purified with column chromatography (petroleum ether/EtOAc = 10:1) as a yellow oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.10 (s, 1H), 7.01 (d, *J* = 8.3 Hz, 1H), 6.80 (d, *J* = 8.2 Hz, 1H), 5.97 (s, 2H), 5.21 (s, 1H), 3.68 (s, 3H), 3.24 – 3.08 (m, 2H). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 171.9, 148.1, 147.9, 130.7, 124.4 (q, *J* = 284.8 Hz), 120.1, 108.0, 107.3, 101.4, 75.1 (q, *J* = 29.5 Hz), 52.5, 38.1. **^{19}F NMR** (564 MHz, Chloroform-*d*) δ -80.74. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{12}H_{11}F_3O_5$ 293.0631, found 293.0632.

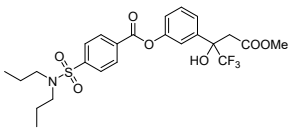
Methyl 4,4,4-trifluoro-3-hydroxy-3-((8*R*,9*S*,13*S*,14*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)butanoate (3s)



The product (74% yield determined by isolated yield) was purified with column chromatography (petroleum ether/EtOAc = 5:1) as a yellow oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.31 (d, *J* = 23.6 Hz, 3H), 5.20 (s,

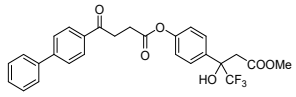
1H), 3.68 (s, 3H), 3.15 (d, *J* = 5.0 Hz, 2H), 2.97 – 2.90 (m, 2H), 2.54 – 2.38 (m, 2H), 2.29 (d, *J* = 10.6 Hz, 1H), 2.14 (dq, *J* = 14.7, 7.6, 6.5 Hz, 1H), 2.05 (tt, *J* = 11.3, 5.1 Hz, 2H), 1.96 (d, *J* = 12.2 Hz, 1H), 1.62 (q, *J* = 12.8, 12.3 Hz, 2H), 1.57 – 1.42 (m, 4H), 0.91 (s, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 172.0, 171.2, 140.6, 136.7, 134.3, 127.0, 125.4, 124.6 (q, *J* = 285.0 Hz), 123.5, 75.1 (q, *J* = 29.4 Hz), 52.5, 50.5, 48.0, 44.3, 38.0, 37.9, 35.8, 31.6, 29.5, 26.4, 25.5, 21.6, 13.8. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -80.36. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{23}H_{27}F_3O_4$ 425.1934, found 425.1936.

3-(1,1,1-trifluoro-2-hydroxy-4-methoxy-4-oxobutan-2-yl)phenyl 4-(*N*,*N*-dipropylsulfamoyl)benzoate (3t)



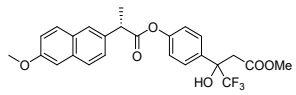
The product (39% yield determined by isolated yield) was purified with column chromatography (petroleum ether/EtOAc = 3:1) as a yellow oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.31 (d, *J* = 8.5 Hz, 2H), 7.95 (d, *J* = 8.7 Hz, 2H), 7.67 (d, *J* = 8.7 Hz, 2H), 7.28 (d, *J* = 8.8 Hz, 2H), 5.40 (s, 1H), 3.71 (s, 3H), 3.19 (s, 2H), 3.16 – 3.09 (m, 4H), 1.61 – 1.53 (m, 4H), 0.88 (t, *J* = 7.4 Hz, 6H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 171.9, 163.6, 151.1, 145.1, 135.0, 130.9, 127.9, 127.2, 124.3 (q, *J* = 286.9 Hz), 121.5, 75.1 (q, *J* = 29.5 Hz), 52.7, 50.0, 38.0, 22.0, 11.2. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -80.36. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{24}H_{28}F_3NO_7S$ 532.1611, found 532.1608.

Methyl 3-(4-((4-([1,1'-biphenyl]-4-yl)-4-oxobutanoyl)oxy)phenyl)-4,4,4-trifluoro-3-hydroxybutanoate (3u)



The product (50% yield determined by isolated yield) was purified with column chromatography (petroleum ether/EtOAc = 3:1) as a yellow oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 8.09 (d, *J* = 8.4 Hz, 2H), 7.71 (d, *J* = 8.5 Hz, 2H), 7.64 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.60 (d, *J* = 8.6 Hz, 2H), 7.50 – 7.46 (m, 2H), 7.43 – 7.39 (m, 1H), 7.18 (d, *J* = 8.8 Hz, 2H), 5.36 (s, 1H), 3.67 (s, 3H), 3.46 (t, *J* = 6.5 Hz, 2H), 3.15 (s, 2H), 3.04 (t, *J* = 6.4 Hz, 2H). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 197.4, 171.8, 171.4, 151.2, 146.1, 139.8, 135.1, 134.4, 129.0, 128.7, 128.3, 127.7, 127.3, 127.3, 126.3 (d, *J* = 285.1 Hz), 122.5 (q, *J* = 285.4 Hz), 121.6, 75.1 (q, *J* = 29.7 Hz), 52.6, 38.0, 33.4, 28.5. **^{19}F NMR** (564 MHz, Chloroform-*d*) δ -80.42. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{27}H_{23}F_3O_6$ 501.1519, found 501.1521.

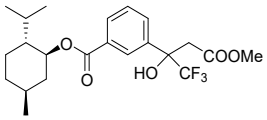
Methyl 4,4,4-trifluoro-3-hydroxy-3-(4-(((*S*)-2-(6-methoxynaphthalen-2-yl)propanoyl)oxy)phenyl)-butanoate (3v)



The product (54% yield determined by isolated yield) was purified with

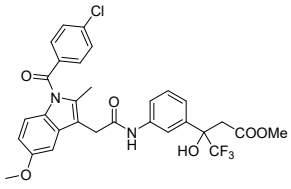
column chromatography (petroleum ether/EtOAc = 10:1) as a yellow oil. **^{1}H NMR** (600 MHz,) δ 7.79 – 7.71 (m, 3H), 7.54 (d, *J* = 8.7 Hz, 2H), 7.50 (dd, *J* = 8.4, 1.9 Hz, 1H), 7.17 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.15 (d, *J* = 2.5 Hz, 1H), 7.05 (dd, *J* = 8.7, 1.6 Hz, 2H), 5.31 (d, *J* = 3.6 Hz, 1H), 4.10 (q, *J* = 7.2 Hz, 1H), 3.92 (s, 3H), 3.65 (d, *J* = 2.7 Hz, 3H), 3.13 (s, 2H), 1.70 (dd, *J* = 7.1, 1.2 Hz, 3H). **^{13}C NMR** (151 MHz,) δ 172.9, 171.8, 157.8, 151.4, 135.0, 134.4, 133.9, 129.4, 129.0, 127.6, 127.5, 126.2, 126.1, 124.4 (q, *J* = 285.4 Hz), 121.4, 119.2, 105.7, 75.1 (q, *J* = 29.5 Hz), 55.4, 52.6, 45.6, 38.1, 18.4. **^{19}F NMR** (564 MHz, Chloroform-*d*) δ -80.47. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{25}H_{23}F_3O_6$ 477.1519, found 477.1518.

(1*S*,2*R*,5*S*)-2-isopropyl-5-methylcyclohexyl 3-(1,1,1-trifluoro-2-hydroxy-4-methoxy-4-oxobutan-2-yl)benzoate (3w)



The product (64% yield determined by isolated yield) was purified with column chromatography (petroleum ether/EtOAc = 10:1) as a yellow oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 8.23 (d, *J* = 8.3 Hz, 1H), 8.08 – 8.03 (m, 1H), 7.82 – 7.78 (m, 1H), 7.48 (t, *J* = 7.9 Hz, 1H), 5.38 (d, *J* = 25.8 Hz, 1H), 4.94 (tdd, *J* = 10.9, 4.5, 2.3 Hz, 1H), 3.66 (d, *J* = 6.9 Hz, 3H), 3.27 – 3.16 (m, 2H), 2.14 – 2.08 (m, 1H), 1.94 (dqd, *J* = 13.8, 6.8, 2.8 Hz, 1H), 1.73 (dp, *J* = 9.7, 2.9, 2.4 Hz, 2H), 1.56 (dddd, *J* = 11.7, 8.6, 5.9, 3.0 Hz, 2H), 1.20 – 1.06 (m, 2H), 0.91 (dd, *J* = 6.9, 5.4 Hz, 6H), 0.79 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (151 MHz,) δ 171.8, 165.6, 137.6, 131.3, 130.9, 130.2, 128.6, 127.5, 124.4 (q, *J* = 286.5 Hz), 75.3, 75.2 (q, *J* = 28.7 Hz), 52.6, 47.2, 40.9, 38.1, 34.3, 31.5, 26.6, 23.7, 22.0, 20.7, 16.6. **^{19}F NMR** (564 MHz, Chloroform-*d*) δ -80.35. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{22}H_{29}F_3O_5$ 431.2040, found 431.2039.

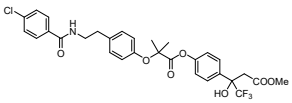
Methyl 3-(3-(2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)acetamido)phenyl)-4,4,4-trifluoro-3-hydroxybutanoate (3x)



The product (48% yield determined by isolated yield) was purified with column chromatography (petroleum ether/EtOAc = 10:1) as a yellow oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.66 (d, *J* = 8.4 Hz, 2H), 7.61 (d, *J* = 9.1 Hz, 1H), 7.53 (s, 1H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.42 (s, 1H), 7.32 (t, *J* = 8.0 Hz, 1H), 7.24 (d, *J* = 8.0 Hz, 1H), 6.87 (d, *J* = 9.0 Hz, 1H), 6.72 (d, *J* = 8.9 Hz, 1H), 5.30 (s, 1H), 3.81 (s, 5H), 3.66 (s, 3H), 3.17 – 3.08 (m, 2H), 2.45 (s, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 171.9, 168.4, 168.3, 156.4, 139.6, 137.9, 137.8, 136.8, 133.5, 131.2, 131.0, 130.2, 129.3, 129.1, 124.3 (q, *J* = 285.3 Hz), 122.3, 120.9, 118.2, 115.3, 112.5, 112.2, 100.8, 75.1 (q, *J* = 29.4 Hz), 55.8, 52.6, 38.0, 33.4, 13.4.**^{19}F NMR**

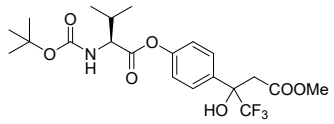
(564 MHz, Chloroform-*d*) δ -75.76. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{30}H_{26}ClF_3N_2O_6$ 603.1504, found 603.1506.

Methyl 3-(4-((2-(4-(2-(4-chlorobenzamido)ethyl)phenoxy)-2-methylpropanoyl)oxy)phenyl)-4,4,4-trifluoro-3-hydroxybutanoate (3y)



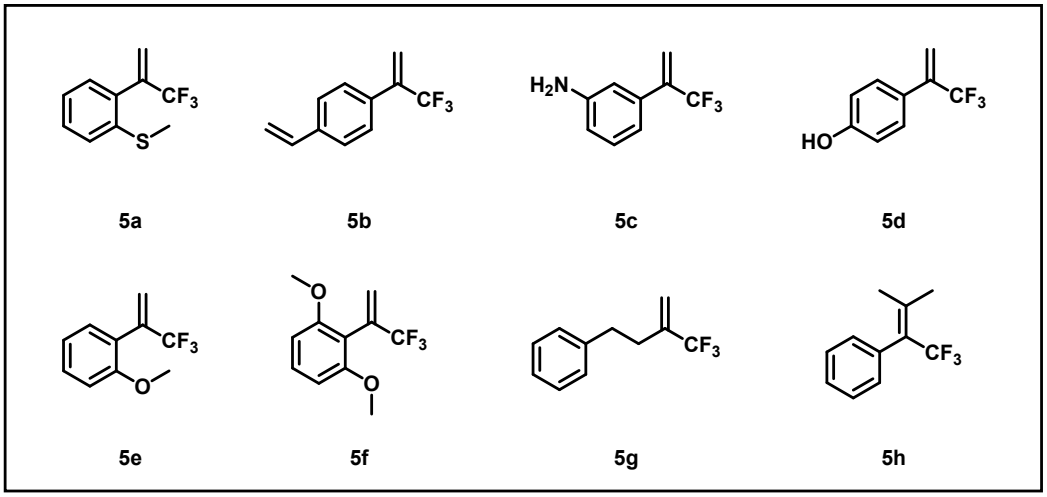
The product (69% yield determined by isolated yield) was purified with column chromatography (petroleum ether/EtOAc = 2:1) as a yellow oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 8.6 Hz, 2H), 7.58 (d, *J* = 8.8 Hz, 2H), 7.36 (d, *J* = 8.5 Hz, 2H), 7.13 (d, *J* = 8.5 Hz, 2H), 7.07 (d, *J* = 8.8 Hz, 2H), 6.91 (d, *J* = 8.5 Hz, 2H), 5.36 (s, 1H), 3.70 – 3.63 (m, 5H), 3.21 – 3.10 (m, 2H), 2.87 (t, *J* = 7.0 Hz, 2H), 1.74 (s, 6H). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 172.7, 171.8, 166.4, 154.0, 151.0, 137.6, 134.8, 132.9, 132.7, 129.7, 128.8, 128.2, 127.8, 124.3 (q, *J* = 285.0 Hz), 121.2, 119.4, 79.2, 75.0 (q, *J* = 29.7 Hz), 52.6, 41.3, 38.0, 34.8, 25.4. **^{19}F NMR** (564 MHz, Chloroform-*d*) δ -80.41. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{30}H_{29}ClF_3NO_7$ 608.1657, found 608.1654.

Methyl 3-(4-(((*tert*-butoxycarbonyl)-*L*-valyl)oxy)phenyl)-4,4,4-trifluoro-3-hydroxybutanoate (3z)



The product (67% yield determined by isolated yield) was purified with column chromatography (petroleum ether/EtOAc = 5:1) as a yellow oil. **^{1}H NMR** (600 MHz,) δ 7.59 (d, *J* = 8.4 Hz, 2H), 7.13 (d, *J* = 8.5 Hz, 2H), 5.35 (s, 1H), 5.08 (d, *J* = 9.1 Hz, 1H), 4.44 (dt, *J* = 9.1, 4.4 Hz, 1H), 3.67 (s, 3H), 3.14 (s, 2H), 2.35 – 2.27 (m, 1H), 1.46 (s, 9H), 1.07 (d, *J* = 6.9 Hz, 3H), 1.01 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 171.8, 170.9, 155.8, 150.9, 134.7, 127.8, 124.3 (q, *J* = 285.1 Hz), 121.4, 80.2, 75.0 (q, *J* = 29.7 Hz), 60.5, 58.8, 52.7, 38.0, 31.3, 28.3, 19.1, 17.7. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -80.43. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{21}H_{28}F_3NO_7$ 464.1891, found 464.1889.

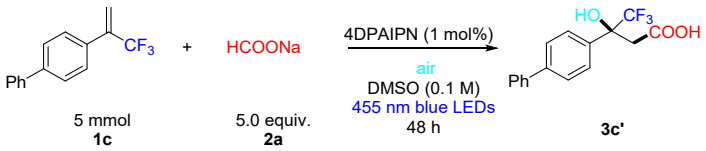
4.3 Unsuccessful Substrates



Scheme S3 Unsuccessful Substrates

5 Synthetic applications

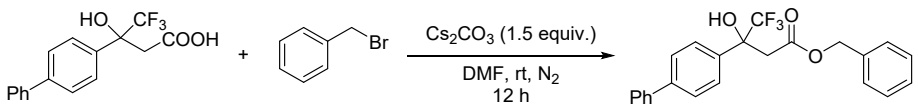
5.1 Gram-scale synthesis and derivatizations of 3c'



To a 250 mL of Schlenk tube were added 4DPAIPN (39.9 mg, 0.05 mmol, 1 mol%), HCOONa (1.73 g, 25 mmol, 5.0 equiv.), 4-(3,3,3-trifluoroprop-1-en-2-yl)-1,1'-biphenyl (1.24 g, 5 mmol) and DMSO (50 mL). Then the reaction mixture was irradiated under blue LED strips (455nm, 10 W) for 48 h at room temperature with stirring under air atmosphere. The mixture was quenched with 75 mL HCl (1 M), extracted with EtOAc (3×50 mL) and the combined organic phase was washed with brine, dried by anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The product was purified via flash column chromatography on silica gel using dichloromethane: methanol = 20:1 (0.5% AcOH) to afford the product in 72 % yield (white solid).

Figure S1. The device of gram-scale experiment

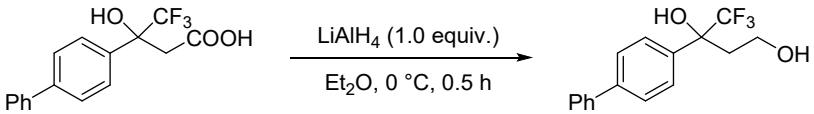
Synthesis of benzyl 3-([1,1'-biphenyl]-4-yl)-4,4,4-trifluoro-3-hydroxybutanoate (1)



3c', 0.2 mmol 1.5 equiv. **1**, 76%

To a solution of 3-([1,1'-biphenyl]-4-yl)-4,4,4-trifluoro-3-hydroxybutanoic acid **3c'** (62.1 mg, 0.2 mmol) in DMF (2 mL) was added Cs_2CO_3 (97.7 mg, 0.3 mmol, 1.5 equiv.) and benzyl bromide (0.036 mL, 0.3 mmol, 1.5 equiv.) under N_2. The reaction mixture was stirred overnight under N_2 at room temperature. After the reaction was complete (monitored by TLC), the reaction mixture was quenched with water (5 mL) and acidified with 2M HCl to pH 5. The mixture was extracted with ethyl acetate (5 mL × 3). The combined organic layers were washed with brine (10 mL) and dried over Na_2SO_4. The residue was concentrated under vacuum and purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 20:1) as eluent to afford **1** (60.9 mg, 76 %) as a white solid. **mp** = 98 – 101 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.68 (d, *J* = 8.3 Hz, 2H), 7.65 – 7.61 (m, 4H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.44 – 7.38 (m, 1H), 7.35 – 7.29 (m, 3H), 7.22 (dd, *J* = 6.6, 3.1 Hz, 2H), 5.26 (s, 1H), 5.17 – 5.08 (m, 2H), 3.38 – 3.22 (m, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 171.3, 141.8, 140.2, 135.8, 134.7, 128.9, 128.7, 128.4, 127.7, 127.2, 127.2, 127.0, 124.5 (q, *J* = 284.9 Hz), 75.4 (q, *J* = 29.4 Hz), 67.5, 38.6. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -80.31. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{23}H_{19}F_3O_3$ 401.1359, found: 401.1362.

Synthesis of 3-([1,1'-biphenyl]-4-yl)-4,4,4-trifluorobutane-1,3-diol (2)

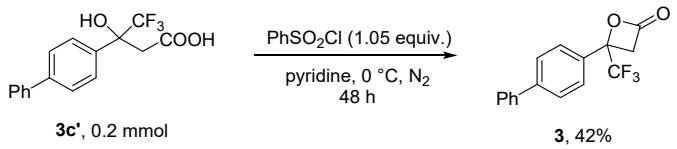


3c', 0.2 mmol **2**, 90%

3-([1,1'-biphenyl]-4-yl)-4,4,4-trifluoro-3-hydroxybutanoic acid **3c'** (62.1 mg, 0.2 mmol) was dissolved in Et_2O (2 mL) and cooled to 0 °C. Then $LiAlH_4$ (7.6 mg, 0.2 mmol, 1.0 equiv.) was added. The resulting mixture was stirred for 0.5 h at 0 °C. After full conversion of **3c'** monitored by TLC, the reaction was quenched by H_2O and extracted with Et_2O (10 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography using dichloromethane/methanol (30:1, v/v, 0.1% AcOH) as eluent to afford **2** (53.9 mg, 90%) as a colorless oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.73 – 7.60 (m, 6H), 7.47 (t, *J* = 7.1 Hz, 2H), 7.38 (d, *J* = 7.1 Hz, 1H), 6.58 (s, 1H), 3.49 (d, *J* = 9.2 Hz, 1H), 3.34 – 3.20 (m, 2H), 2.42 –

2.20 (m, 2H). **^{13}C NMR** (151 MHz, DMSO-d_6) δ 140.3, 140.0, 136.9, 129.4, 128.1 (q, J = 283.5 Hz), 128.1, 127.6, 127.2, 126.8, 75.6 (q, J = 27.1 Hz), 56.5, 36.8. **^{19}F NMR** (564 MHz, Chloroform-d) δ -78.54. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{16}H_{15}F_3O_2$ 297.1097, found: 297.1095.

Synthesis of 4-([1,1'-biphenyl]-4-yl)-4-(trifluoromethyl)oxetan-2-one (3)

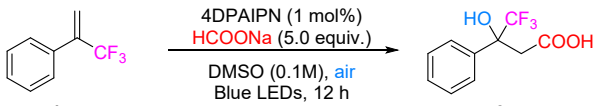


3c', 0.2 mmol — **3**, 42%

To a solution of 3-([1,1'-biphenyl]-4-yl)-4,4,4-trifluoro-3-hydroxybutanoic acid **3c'** (62.1 mg, 0.2 mmol) in dry pyridine (3 mL) was added benzenesulfonyl (0.077 mL, 0.21 mmol, 1.05 equiv.) at 0 °C under N_2. Then the reaction mixture was stirred at 0 °C for 48 h. After the reaction was complete, the reaction mixture was poured into crushed ice (5 mL) and stirred for 15 min. Then Et_2O (2 mL) was added and the layers were separated. The aqueous layer was extracted with Et_2O (5 mL × 3). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (3 mL × 2), 10 % aqueous $CuSO_4$ (5 mL × 4), water (5mL) and dried over Na_2SO_4. The residue was concentrated under vacuum and purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 10:1) as eluent to afford **3** (24.5 mg, 42 %) as a yellow oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.69 (d, J = 8.4 Hz, 2H), 7.64 – 7.57 (m, 2H), 7.54 (d, J = 8.1 Hz, 2H), 7.51 – 7.45 (m, 2H), 7.43 – 7.38 (m, 1H), 4.13 (d, J = 16.5 Hz, 1H), 3.78 (dd, J = 16.4, 1.1 Hz, 1H). **^{13}C NMR** (151 MHz, Chloroform-d) δ 163.5, 143.1, 139.8, 130.3, 129.0, 128.1, 127.5, 127.2, 127.2, 121.2 (q, J = 230.3 Hz), 75.1 (q, J = 24.2 Hz), 46.9. **^{19}F NMR** (564 MHz, Chloroform-d) δ -79.70. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{16}H_{11}F_3O_2$ 293.0784, found: 293.0779.

5.2 Synthesis of drug intermediates

Synthesis of intermediate of platelet-activating factor antagonists IV (3aa)

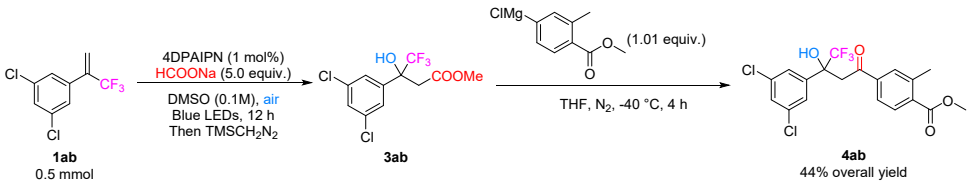


1aa 0.5 mmol — **3aa** 83%

To a 25 mL of Schlenk tube were added 4DPAIPN (3.8 mg, 0.002 mmol, 1 mol%), HCOONa (170.0 mg, 1.0 mmol, 5.0 equiv.), (3,3,3-trifluoroprop-1-en-2-yl)benzene (0.5 mmol, 86.1 mg) and DMSO (5

mL). Then the reaction mixture was irradiated under blue LED strips (455nm, 10 W) for 12 h at room temperature with stirring under air atmosphere. The mixture was quenched with 3 mL HCl (1 M), extracted with EtOAc (3×10 mL) and the combined organic phase was washed with brine, dried by anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was dissolved in 4 mL MeOH/Et_2O (1/3), $TMSCH_2N_2$ (0.75 mL, 0.60 mmol, 2.0 M in hexane) was added drop wisely at 0 °C. The mixture was stirred at ambient temperature until the completion of the methylation reaction. The organic layers were concentrated under vacuo. The product was purified via flash column chromatography on silica gel. The product was esterification of **3aa** with $TMSCHN_2$ (83% yield determined by isolated yield), it was purified with column chromatography (petroleum ether/EtOAc = 20:1) as a yellow oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.60 (d, *J* = 7.6 Hz, 2H), 7.48 – 7.35 (m, 3H), 5.29 (s, 1H), 3.66 (s, 3H), 3.31 – 3.12 (m, 2H). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 171.9, 137.0, 129.0, 128.4, 126.3, 124.5 (q, *J* = 284.9 Hz), 75.3 (q, *J* = 29.3 Hz), 52.5, 38.1. **^{19}F NMR** (564 MHz, Chloroform-*d*) δ -80.44. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{11}H_{11}F_3O_3$ 249.0733, found 249.0727.

Synthesis of intermediate of intermediate of Fluralaner (4ab)



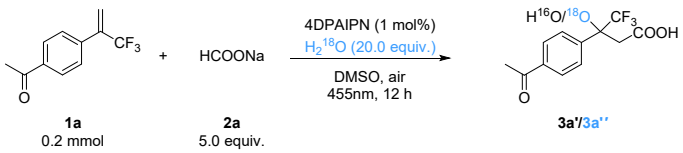
To a 25 mL of Schlenk tube were added 4DPAIPN (3.8 mg, 0.002 mmol, 1 mol%), HCOONa (170.0 mg, 1.0 mmol, 5.0 equiv.), 1,3-dichloro-5-(3,3,3-trifluoroprop-1-en-2-yl)benzene (0.5 mmol, 120.5mg) and DMSO (5 mL). Then the reaction mixture was irradiated under blue LED strips (455nm, 10 W) for 12 h at room temperature with stirring under air atmosphere. The mixture was quenched with 3 mL HCl (1 M), extracted with EtOAc (3×10 mL) and the combined organic phase was washed with brine, dried by anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was dissolved in 4 mL MeOH/Et_2O (1/3), $TMSCH_2N_2$ (0.75 mL, 0.60 mmol, 2.0 M in hexane) was added drop wisely at 0 °C. The mixture was stirred at ambient temperature until the completion of the methylation reaction. The organic layers were concentrated under vacuo. The product was purified via flash column chromatography on silica gel. The product was esterification of **3ab** with $TMSCHN_2$ (73% yield

determined by isolated yield), it was purified with column chromatography (petroleum ether/EtOAc = 10:1) as a yellow oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.47 (dd, *J* = 1.8, 0.8 Hz, 2H), 7.38 (t, *J* = 1.9 Hz, 1H), 5.45 (s, 1H), 3.72 (s, 3H), 3.27 – 2.95 (m, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 171.6, 140.5, 135.3, 129.4, 125.2, 124.0 (q, *J* = 285.3 Hz), 74.8 (q, *J* = 29.8 Hz), 52.9, 37.8. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -80.18. **HRMS (ESI)** m/z**:** $[M+H]^+$ Calcd. for $C_{11}H_9Cl_2F_3O_3$ 316.9954, found 316.9956.

To a 25 mL of Schlenk tube with rubber plug were added methyl 3-(3,5-dichlorophenyl)-4,4,4-trifluoro-3-hydroxybutanoate (113.8 mg, 0.36 mmol) and anhydrous THF (3 mL) in a glove box. The reaction tube containing the mixture was taken out and put on a balloon filled with nitrogen. Then cooling the mixture to -40 °C and (4-(methoxycarbonyl)-3-methylphenyl)magnesium chloride (182 μL, 2.0 M in THF, 1.01 equiv.) was added. The mixture was stirred at -40 ℃ for 4 hours and was quenched with 3 mL saturated NH_4Cl at -40 ℃, extracted with EtOAc (3×10 mL) and the combined organic phase was dried by anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The product was purified via flash column chromatography on silica gel to produce **4ab** (60% yield determined by isolated yield), it was purified with column chromatography (petroleum ether/EtOAc = 10:1) as a yellow oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.00 (d, *J* = 8.6 Hz, 1H), 7.80 – 7.76 (m, 2H), 7.49 (s, 2H), 7.36 – 7.34 (m, 1H), 5.63 (s, 1H), 3.94 (s, 3H), 3.90 – 3.84 (m, 1H), 3.77 – 3.71 (m, 1H), 2.66 (s, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 198.9, 167.0, 141.0, 140.9, 137.8, 135.4, 135.2, 131.2, 131.1, 129.2, 125.4, 125.1, 122.1 (q, *J* = 218.2 Hz), 73.7 (q, *J* = 22.2 Hz), 52.4, 40.5, 21.7. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -79.91.

6 Mechanistic Studies

6.1 Labelling Experiment by Adding H_2O^{18}



1a 0.2 mmol | **2a** 5.0 equiv. | **3a'/3a''**

To a 25 mL of Schlenk tube were added 4DPAIPN (1.5 mg, 0.002 mmol, 1 mol%), HCOONa (68.0 mg, 1.0 mmol, 5.0 equiv.), 1-(4-(3,3,3-trifluoroprop-1-en-2-yl)phenyl)ethan-1-one (42.8 mg, 0.2 mmol), $H_2{}^{18}O$ (80 μL, 4 mmol, 20.0 equiv.) and anhydrous DMSO (2 mL). Then the reaction mixture was irradiated under blue LED strips (455nm, 10 W) for 12 h at room temperature with stirring under air atmosphere. The mixture was quenched with 3 mL HCl (1 M), extracted with EtOAc (3×10 mL) and

the combined organic phase was washed with brine, dried by anhydrous Na_2SO_4, filtered, and concentrated in vacuo. As detected by LC-MS was performed (Figure S2), the desired labelled O^{18} product **3a''** was not obtained.

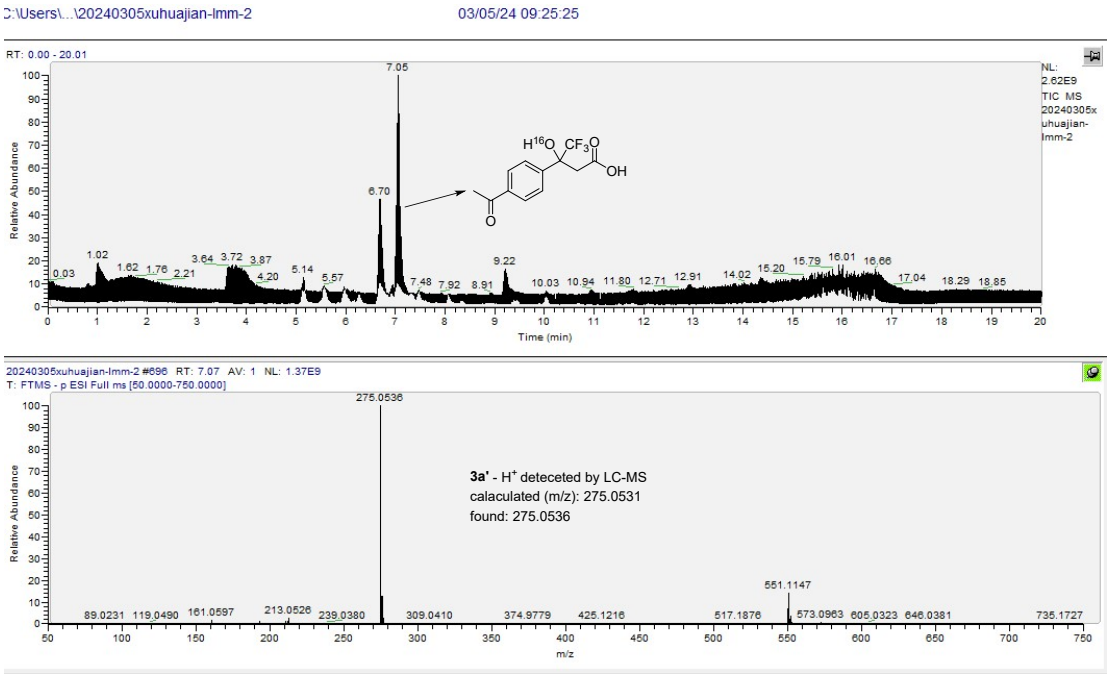
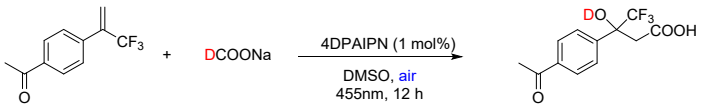


Figure S2. LC-MS of the labelling experiment by adding H_2O^{18}

6.2 Deuteration experiment



1a 0.2 mmol | **2a** 5.0 equiv. | **3a'-*d*** 57% yield, 93% D

To a 25 mL of Schlenk tube were added 4DPAIPN (1.5 mg, 0.002 mmol, 1 mol%), DCOONa (98% D; 69.0 mg, 1.0 mmol, 5.0 equiv.), 1-(4-(3,3,3-trifluoroprop-1-en-2-yl)phenyl)ethan-1-one (42.8 mg, 0.2 mmol) and anhydrous DMSO (2 mL). Then the reaction mixture was irradiated under blue LED strips (455nm, 10 W) for 12 h at room temperature with stirring under air atmosphere. The mixture was quenched with 3 mL HCl (1 M), extracted with EtOAc (3×10 mL) and the combined organic phase was washed with brine, dried by anhydrous Na_2SO_4, filtered, and concentrated in vacuo. Purified by flash column chromatography on silica gel (petroleum ether/EtOAc/AcOH = 1:1:0.25) as eluent to afford **3a'**.

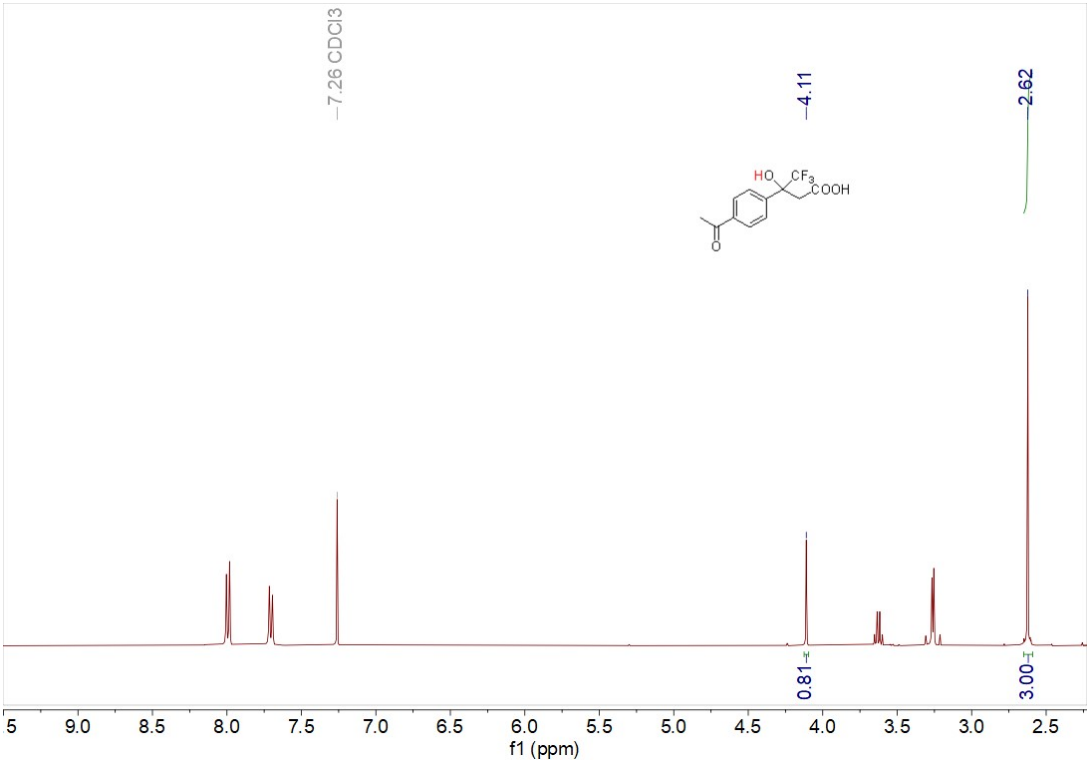


Figure S3. [1]H NMR spectra of **3a'**

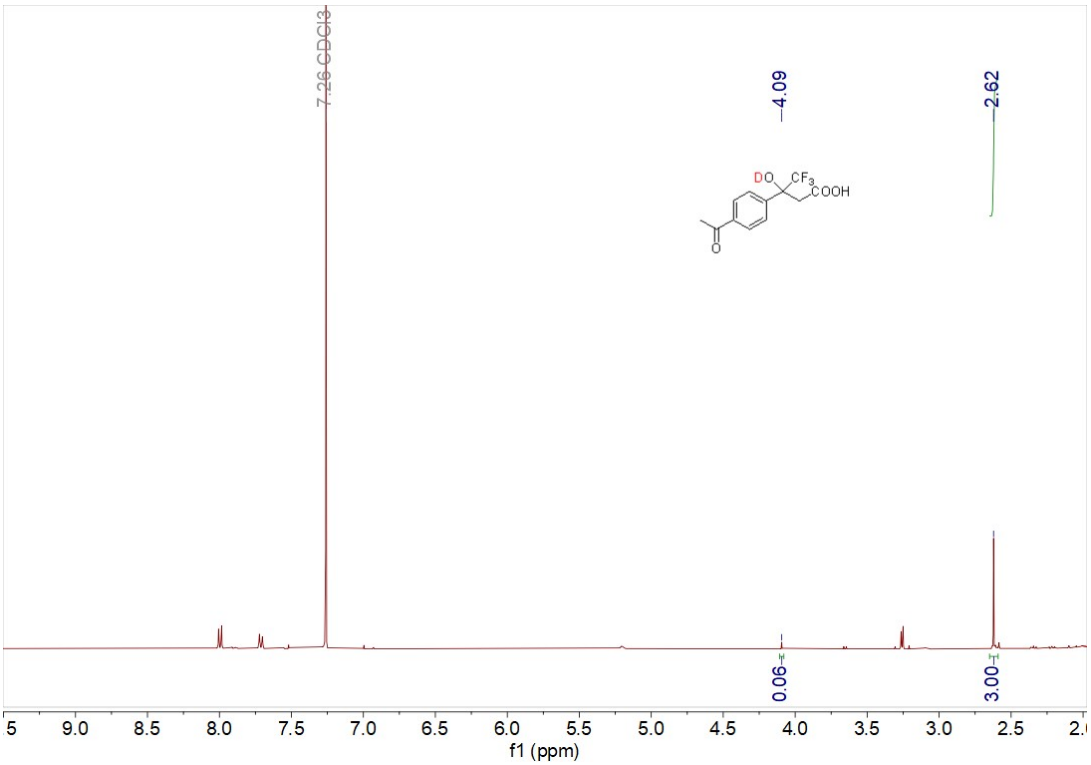
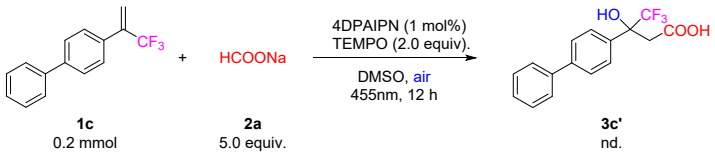


Figure S4. [1]H NMR spectra of **3a'-*d***

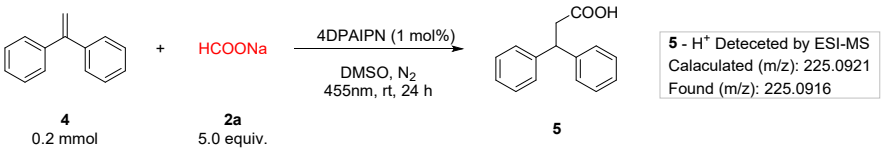
6.3 Radical inhibitor experiment

Radical inhibitor with TEMPO (2,2,6,6-tetramethylpiperidinooxy)



To a 25 mL of Schlenk tube were added 4DPAIPN (1.5 mg, 0.002 mmol, 1 mol%), HCOONa (68.0 mg, 1.0 mmol, 5.0 equiv.), 4-(3,3,3-trifluoroprop-1-en-2-yl)-1,1'-biphenyl (49.6 mg, 0.2 mmol), 2,2,6,6-Tetramethylpiperidinooxy (TEMPO) (62.4 mg, 0.2 mmol, 2.0 equiv.) and DMSO (2 mL). Then the reaction mixture was irradiated under blue LED strips (455nm, 40 W) for 12 h at room temperature with stirring under air atmosphere. The mixture was quenched with 3 mL HCl (1 M), extracted with EtOAc (3×10 mL) and the combined organic phase was washed with brine, dried by anhydrous Na_2SO_4, filtered, and concentrated in vacuo and the yield was then analyzed by ^1H NMR, the compound **3c'** were not detected by ^1H NMR.

6.4 $CO2^{-\cdot}$ generation and trapping



1,1-Diphenylethylene (1.0 equiv.,36.0 mg, 0.2 mmol), HCOONa (5.0 equiv., 68.0 mg, 1.0 mmol), 4DPAIPN (0.002 mmol, 1.6 mg, 1 mol%), were placed in a 25 mL transparent Schlenk tube equipped with a stirring bar. The tube was evacuated and filled with argon (repeated for three times). To this solid, anhydrous DMSO (2 mL) were added using a gastight syringe under argon atmosphere. The reaction mixture was stirred under the irradiation of 40W blue LEDs and stirred for 24 h at 30 °C. After 24 h, the mixture was quenched with 3 mL HCl (1 N), extracted with EtOAc (3×10 mL). The organic layers were combined and concentrated under vacuo. The reaction mixture was sent for ESI-HRMS analysis.

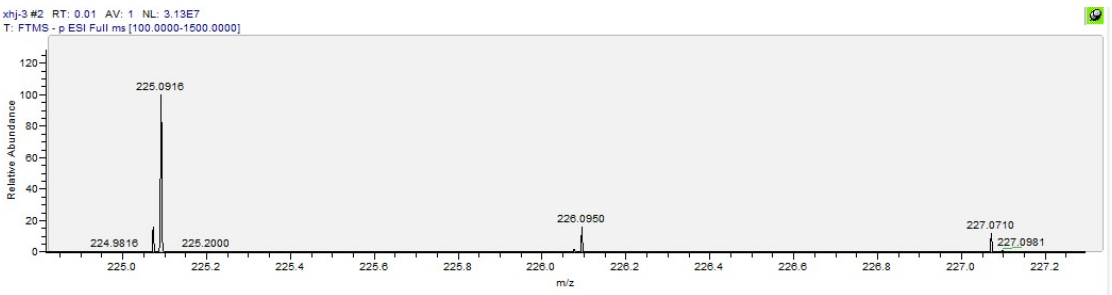


Figure S5. Crude ESI-HRMS of **5**

6.5 Stern-Volmer Quenching Experiments

Stern-Volmer quenching experiments were carried out using a 0.05 mM solution of 4DPAIPN and variable concentrations (0.1, 0.2, 0.3, 0.4, 0.5 mM) of 4-(3,3,3-trifluoroprop-1-en-2-yl)-1,1'-biphenyl (**1c**) and $HCOONH_4$ in DMSO. The samples were prepared in 4 mL quartz cuvettes, equipped with PTFE stoppers. The intensity of the emission peak at 523 nm (λex = 435 nm) expressed as the ratio I_0/I, where I_0 is the emission intensity of 4DPAIPN at 523 nm in the absence of a quencher and I is the observed intensity, as a function of the quencher concentration was measured. Fluorescence emission spectra and Stern-Volmer plots for each component are given in the Figures below.

Note: TBA-formate was used instead of Na-formate because of poor solubility of the sodium counter ion.

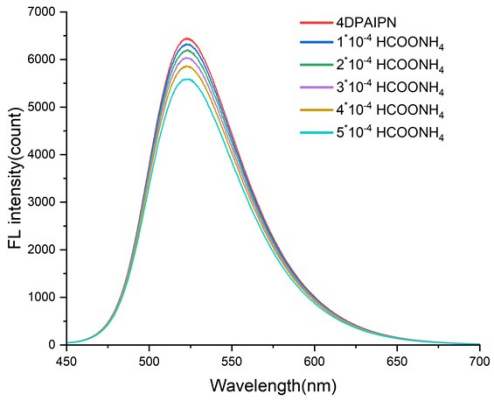


Figure S6. Emission spectra of 4DPAIPN (0.05 mM) at different concentrations of **$HCOONH_4$**.

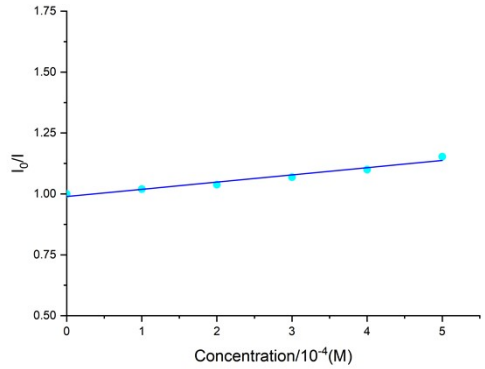


Figure S7. Stern-Volmer plot of 4DPAIPN (0.05 mM) at different concentrations of **$HCOONH_4$**.

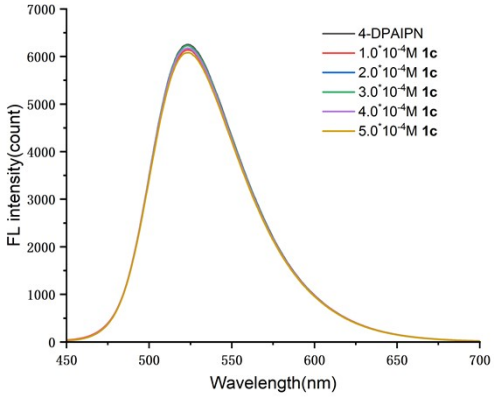


Figure S8. Stern-Volmer plot of 4DPAIPN (0.05 mM) at different concentrations of **1c**.

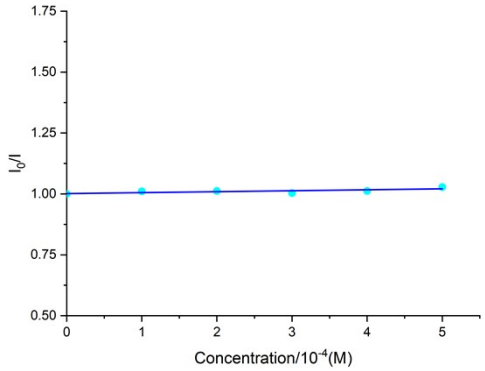


Figure S9. Stern-Volmer plot of 4DPAIPN (0.05 mM) at different concentrations of **1c**.

6.6 Measurement of Quantum Yield

Determination of the light intensity at 455 nm:

According to the previous reports[4,5], the photon flux of the LEDs (λ_{max} = 455 nm) was determined by standard ferrioxalate actinometry. A 0.15 M solution of ferrioxalate was prepared by dissolving potassium ferrioxalate hydrate (0.737 g) in 10 mL H_2SO_4 (0.05 M). A buffered solution of 1,10-phenanthroline was prepared by dissolving sodium acetate (5.63 g) and phenanthroline (25 mg) in 25 mL H_2SO_4 (0.5 M) at the same time. Both solutions were stored in the dark. To determine the photon flux of the LED, the ferrioxalate solution (2.0 mL) was placed in a cuvette and irradiated for 60 seconds at λ_{max} = 455 nm. After irradiation, the phenanthroline solution (0.35 mL) was added to the cuvette and the mixture was stirred in the dark for 1 hour to allow the ferrous ions to completely coordinate to the phenanthroline. The absorbance of the solution was measured at 510 nm. A non-irradiated sample was also prepared and the absorbance at 510 nm was measured. Using then the Beer's Law, the number of moles of Fe^{2+} produced by light irradiation is obtained

by:

$$\text{mol } Fe^{2+} = \frac{V \cdot \Delta A}{1 \cdot \varepsilon}$$

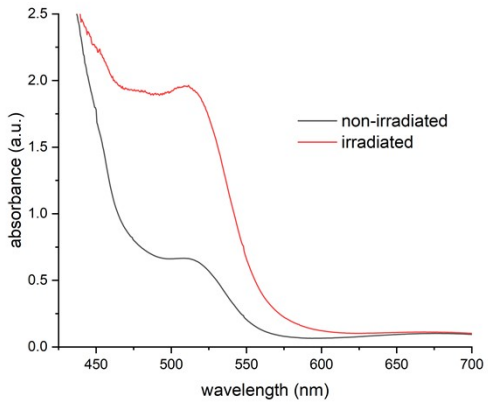


Figure S10. Absorbance of the ferrioxalate actinometer solution

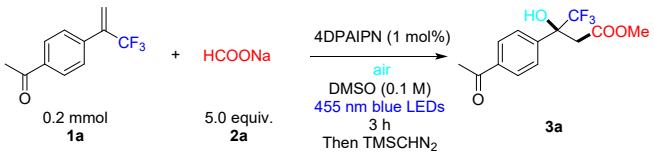
Where V is the total volume (0.00235 L) of the solution after addition of phenanthroline, ΔA is the difference in absorbance at 510 nm between the irradiated and non-irradiated solutions, l is the path length (1.000 cm), and ε is the molar absorptivity at 510 nm (11100 L $mol^{-1}cm^{-1}$).

The photon flux is obtained by using the following equation:

$$\text{photo flux} = \frac{\text{mol } Fe^{2+}}{\Phi \cdot t \cdot f}$$

Φ = quantum yield of ferrioxalate actinometer (0.92 at 455 nm);[6] t = time; *f* = fraction of light absorbed at λ = 468 nm (0.85). The average photon flux was calculated to be 6.46×10^{-9} einsteins s^{-1}

Determination of quantum yield:



To a 25 mL of Schlenk tube were added 4DPAIPN (1.5 mg, 0.002 mmol, 1 mol%), HCOONa (68.0 mg, 1.0 mmol, 5.0 equiv.) , 1-(4-(3,3,3-trifluoroprop-1-en-2-yl)phenyl)ethan-1-one (42.8 mg, 0.2 mmol) and DMSO (2 mL). Then the reaction mixture was irradiated under blue LED strips (455nm, 10 W) for 10800 s at room temperature with stirring under air atmosphere. The mixture was quenched with 3 mL HCl (1 M), extracted with EtOAc (3×10 mL) and the combined organic phase was washed with brine,

dried by

anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The yield of product formed was determined as 54% yield (0.02 mmol) by crude ^1H NMR based on a 1,3,5-trimethylbenzene standard. After 10800 s of light irradiation, 1.08 x 10^{-4} mol of product (**3a**) was obtained. The quantum yield of this reaction was calculated using the following equation:

$$\Phi = \frac{mol\ of\ product}{photon\ flux \cdot t \cdot f}$$

t = is the reaction time. The quantum yield (Φ) of the reaction is 2.02.

6.7 Light on / off experiment

Standard reactions were set up parallelly on a 0.2 mmol scale according to the general procedure for the preparation of **3a**. The reaction mixture was methyl esterified and the product was purified via flash column chromatography on silica gel. The reaction started with successive irradiation and black periods to study the influence of continuous irradiation of the visible-light for the progress. The reaction mixture was stirred with light-off for 2 h. All of the following yields were analyzed in the identical way after a 2 h light-on or light-off.

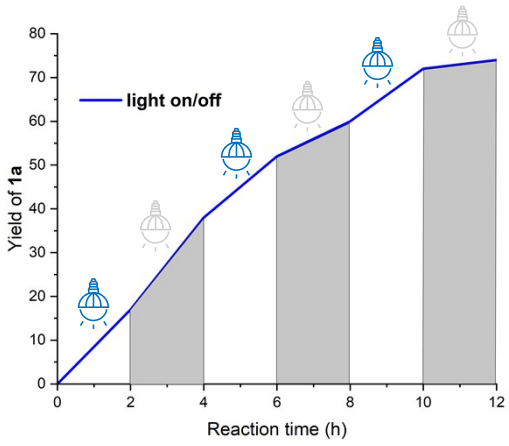


Figure S11. Line chart of light on-off experiments

6.8 Kinetic study

Order of the reaction w.r.t to α-trifluoromethylstyrene was obtained by different excess experiment and initial slope method. Two sets (**Run 1** and **Run 2**) of reactions were monitored in 0.1 mmol and 0.075 mmol scale respectively using 1-methyl-4-(3,3,3-trifluoroprop-1-en-2-yl)benzene (**1b**) as substrate.

Run	1b	4DPAIPN	HCOONa	DMSO

Run 1	**0.1 mmol**	0.001 mmol	0.5 mmol	1 mL
Run 2	**0.075 mmol**	0.001 mmol	0.5 mmol	1 mL

Procedure: To a 25 mL of Schlenk tube were added 4DPAIPN (0.8 mg, 0.001 mmol, 1 mol%), HCOONa (34.0 mg, 0.5 mmol, 5.0 equiv.), trifluoromethyl alkenes (**1b**) and DMSO (1 mL). Then the reaction mixture was irradiated under blue LED strips (455nm, 40 W) at room temperature with stirring under air atmosphere. After certain amount of time the reaction tubes were taken out, the mixture was quenched with 3 mL HCl (1 M), extracted with EtOAc (3×10 mL) and the combined organic phase was washed with brine, dried by anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was dissolved in 4 mL MeOH/Et_2O (1/3), $TMSCH_2N_2$ (0.15 mL, 0.30 mmol, 2.0 M in hexane) was added drop wisely at 0 °C. The mixture was stirred at ambient temperature for 3 h. Then the organic layers were concentrated under vacuo. The yields were measured using gas chromatography (GC) technique with 1,3-dimethoxybenzene as reference.

In each of the above "**Run**" the formation of the product was monitored at different time instant following the same procedure. The product formation profiles for both sets were shown below.

The rate of the reaction at a particular time instant is different for the two sets, which is contributed by the different initial concentration of the substrate. The initial rates for both the sets were calculated (initial-slope method).

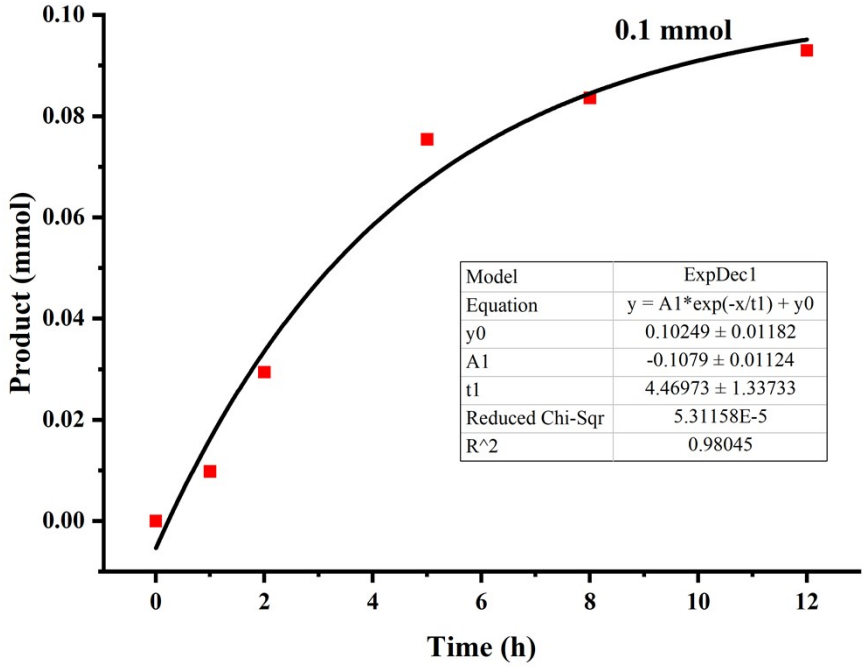


Figure S12. The variation curve of products over time in **Run1**

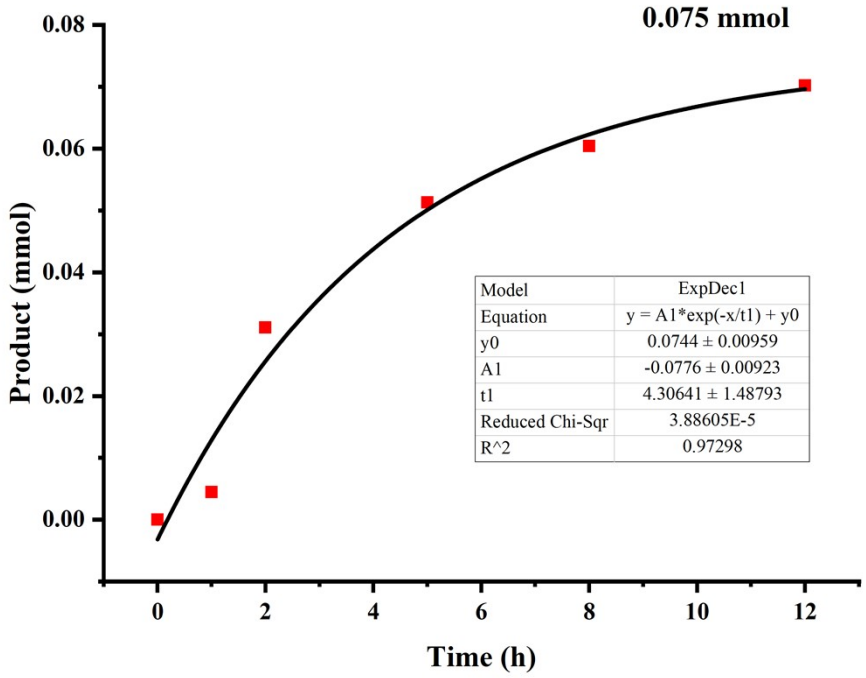


Figure S13. The variation curve of products over time in **Run2**

In case of **Run 1**

$$\text{Initial slope} = \text{Initial rate} = R_1 = 2.41 \times 10^{-2} \text{ mmol/h}$$

In case of **Run 2**

$$\text{Initial slope} = \text{Initial rate} = R_2 = 1.80 \times 10^{-2} \text{ mmol/h}$$

The simplified rate equation for the above reaction

Rate (R) = K $[Sub]^x$ $[HCOO^-]^y[O_2]^z$, where {K= Constant; x, y, z = order w.r.t the corresponding reagent

The applicability of such a simple rate reaction was verified from the linearity of the log(rate) *vs* **log(sub)** plot.

Applying the rate expression for above two sets

$$R_1 = K [Sub_1]^x [HCOO^-]^y[O_2]^z = 2.41 \times 10^{-2} \text{ ---------- (1)}$$

$$R_2 = K [Sub_2]^x [HCOO^-]^y[O_2]^z = 1.80 \times 10^{-2} \text{ ---------- (2)}$$

Taking the ratio of the equation (1) and equation (2)

$$R_1/R_2 = [Sub_1 / Sub_2]^x$$

$$\text{Therefore, } x = \log [R_1/R_2] / \log [Sub_1/Sub_2]$$

$$= \log [2.41 /1.80] / \log [0.1/0.075]$$

$$= 1.01 \cong 1$$

Hence, a first order rate dependency was observed for the α-trifluoromethylstyrene substrates.

6.9 By-product research

We selected **3f** and **3k** as model substrates to study the possible by-products in the reaction, and detected the by-products through GC-MS.

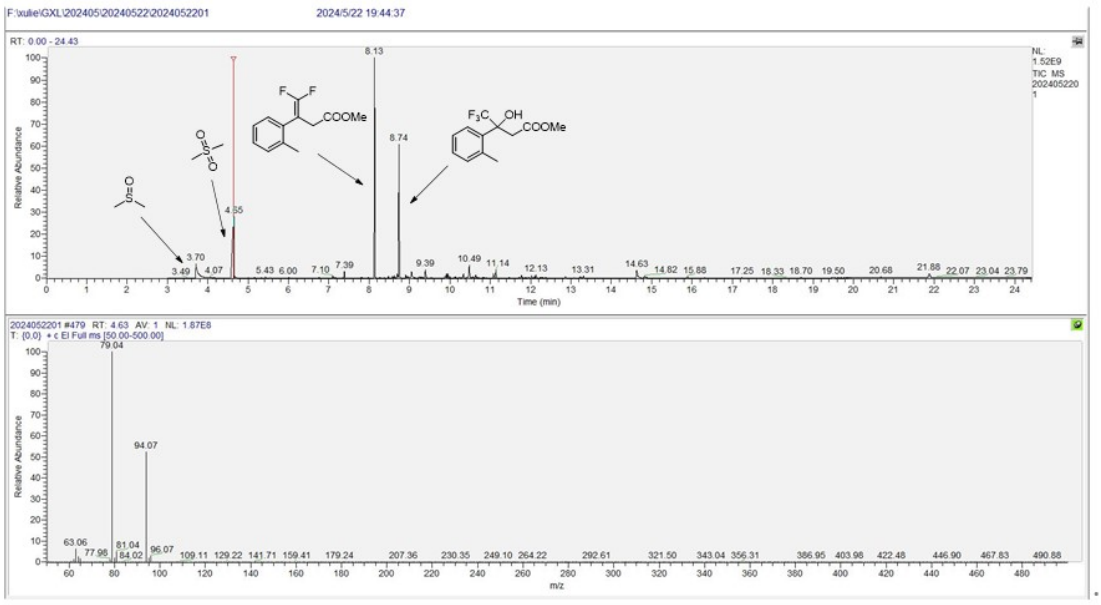


Figure S14. GC-MS spectrum of reaction solution of **3f**

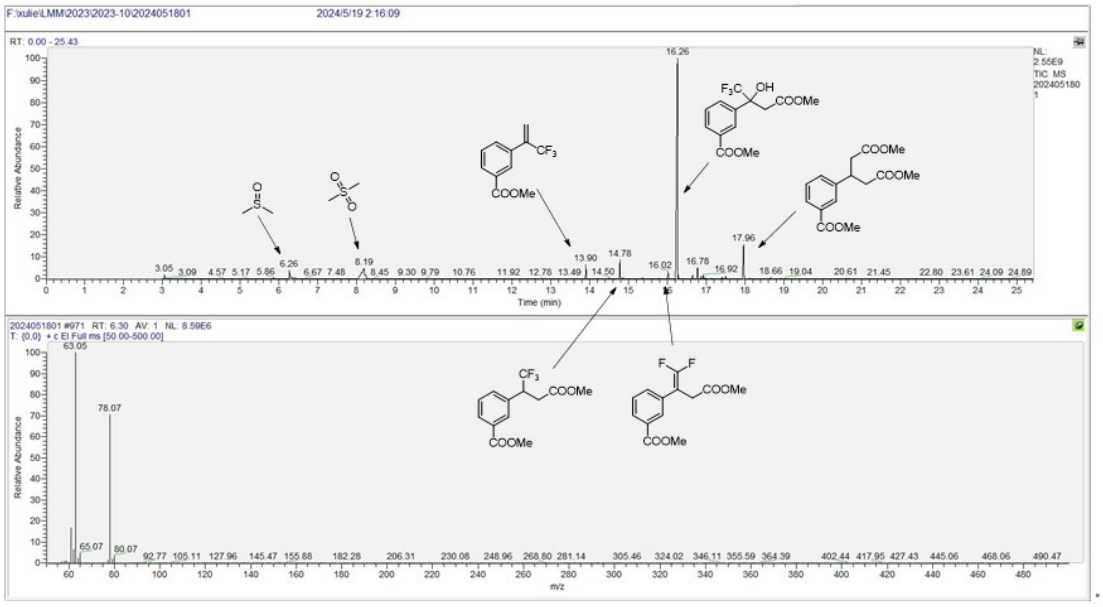


Figure S15. GC-MS spectrum of reaction solution of **3k**

7 References

(1) Alektiar, S. N.; Wickens, Z. K. *J. Am.Chem.Soc.* **2021**, *143*, 13022−13028.

(2) (a) G. Chen, L. Wang, X. Liu, P. Liu, *Adv. Synth. Catal.* **2020**, *362*, 2990–2996. (b) T. Ichitsuka, T. Fujita, J. Ichikawa, *ACS Catal.* **2015**, *5*, 5947−5950; (c) Y. Liu, Y. Zhou, Y. Zhao, J. Qu, *Org. Lett.* **2017**, *19*, 946-949; (d) Y. Lan, F. Yang, C. Wang, *ACS Catal.* **2018**, *8*, 9245−9251; (e) X. Lu, X.-X. Wang, T.-J. Gong, J.-J. Pi, S.-J. He, Y. Fu, *Chem. Sci.* **2019**, *10*, 809−814; (f) P.-J. Xia, Z.-P. Ye, Y.-Z. Hu, D. Song, H.-Y. Xiang, X.-Q. Chen, H. Yang, *Org. Lett.* **2019**, *21*, 2658−2662; (g) Pan, R.; Liu, X.; Deng, M., *J. Fluorine Chem.* **1999**, *95*, 167−170; (h) Z. Lin, Y. Lan, C. Wang, *ACS Catal.* **2019**, *9*,

775–780.

(3) J.-X. Wang, W. Ge, M.-C. Fu, Y. Fu, *Org. Lett.* **2022**, *24*, 1471−1475.

(4) Megan A. Cismesiaa, Tehshik P. Yoon, *Chem. Sci.* **2015**, *6*, 5426−5434.

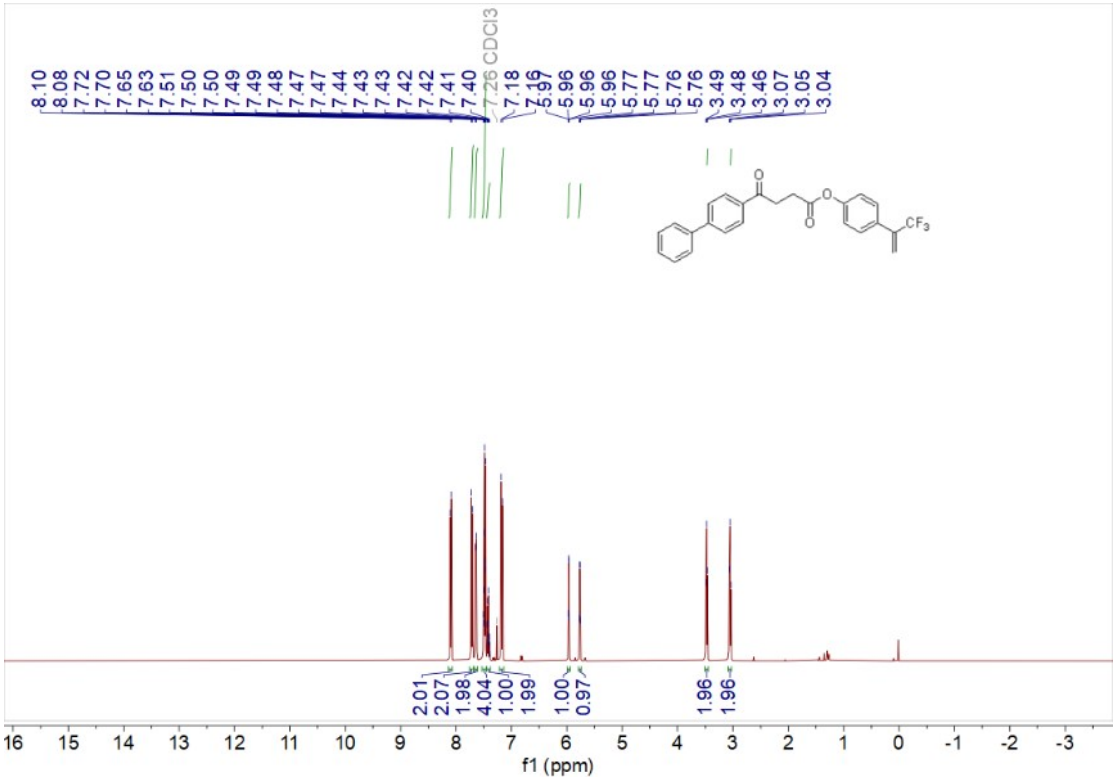
(5) J. Xu, J. W.Liu, R. Wang, J. Yang, K. K. Zhao, H. J. Xu, *ACS Catal.* **2023**, *13*, 7339−7346.

(6) Hatchard, C. G., Parker, C. A., *Proc. Roy. Soc.***1956**, *A235*, 518−536.

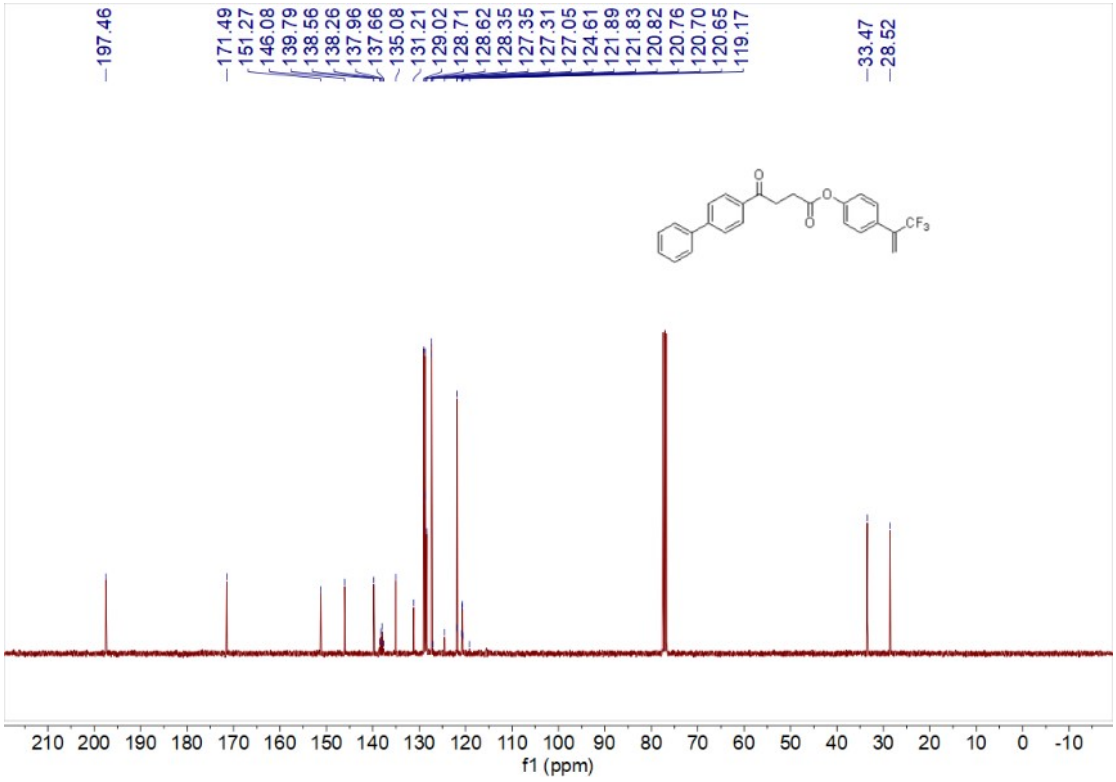
^{1}H NMR, ^{19}F NMR and ^{13}C NMR Spectra

4-(3,3,3-trifluoroprop-1-en-2-yl)phenyl 4-([1,1'-biphenyl]-4-yl)-4-oxobutanoate (1u)

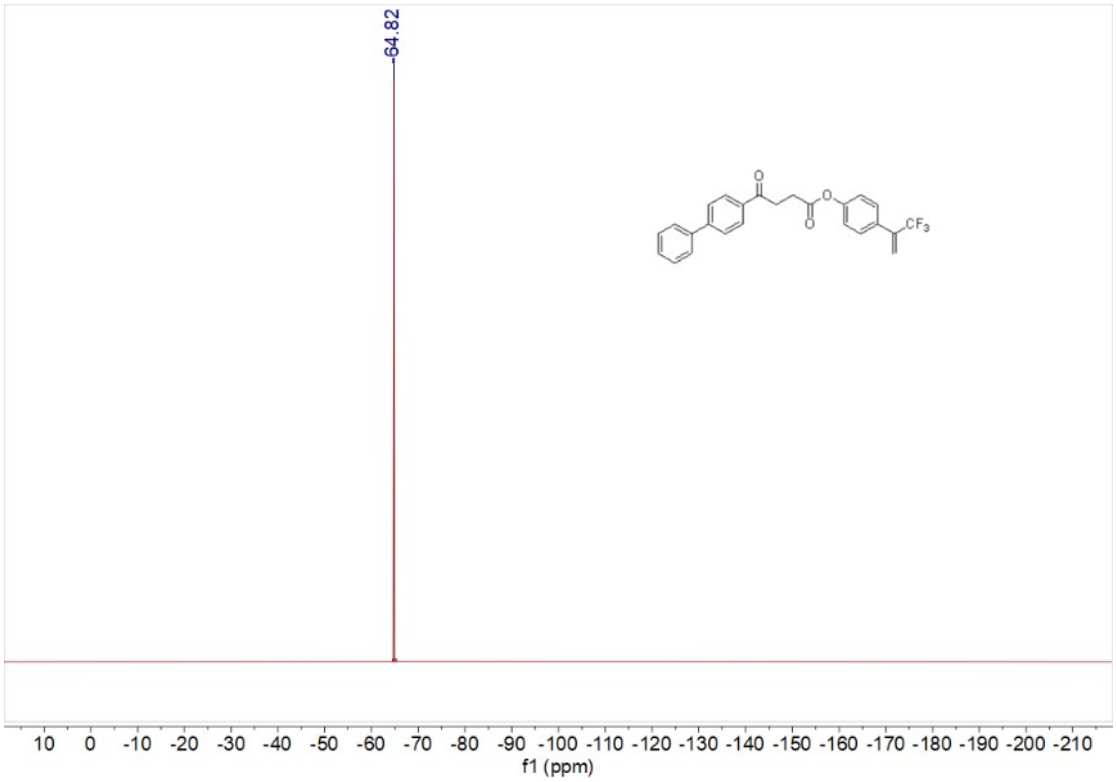
^{1}H NMR of 1u



^{13}C NMR of 1u

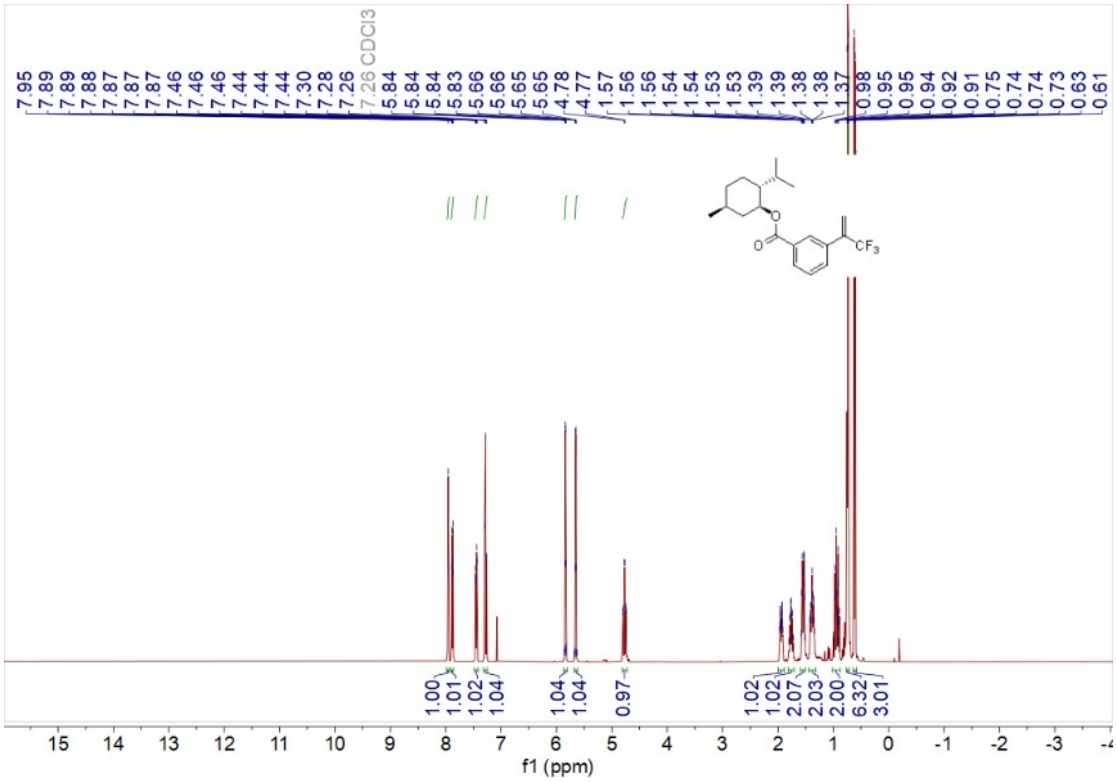


^{19}F NMR of 1u

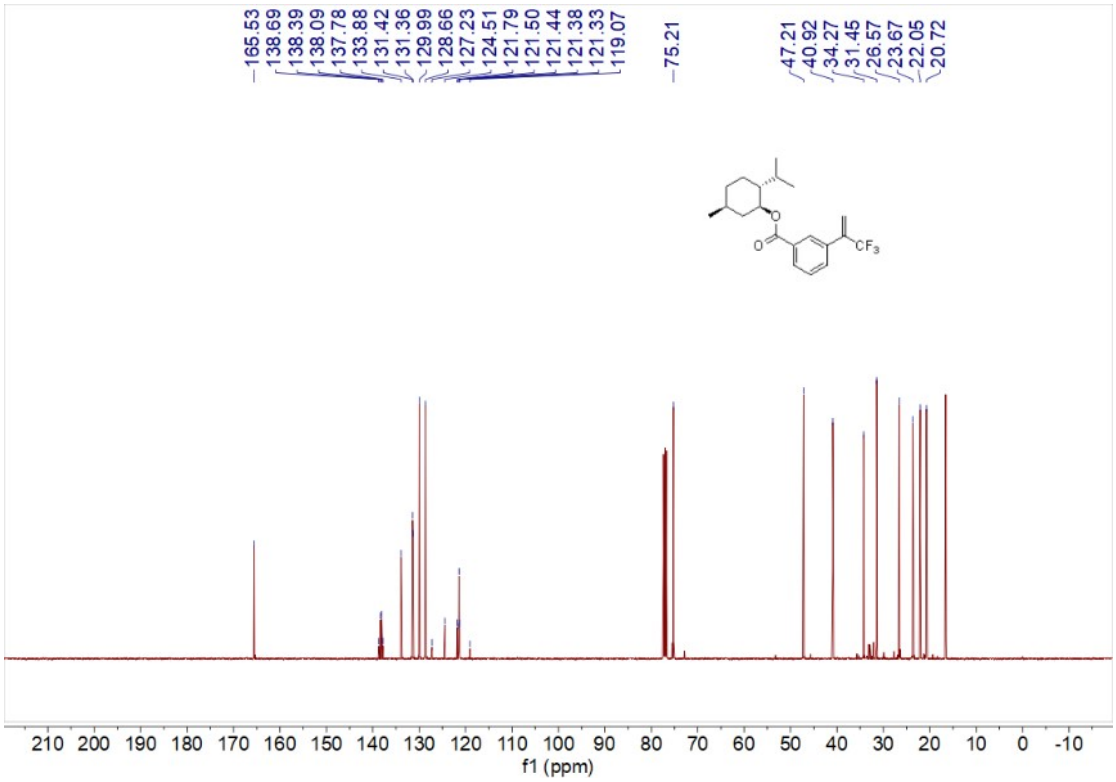


(1*S*,2*R*,5*S*)-2-isopropyl-5-methylcyclohexyl 3-(3,3,3-trifluoroprop-1-en-2-yl)benzoate (1w)

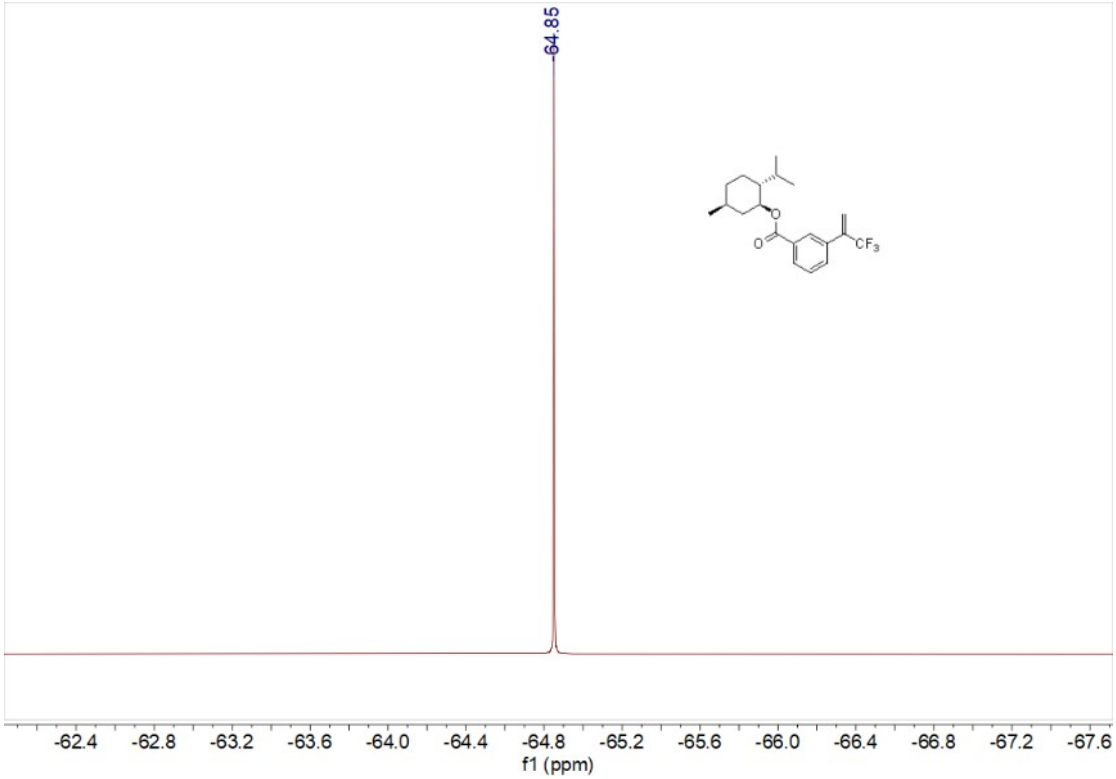
^{1}H NMR of 1w



^{13}C NMR of 1w

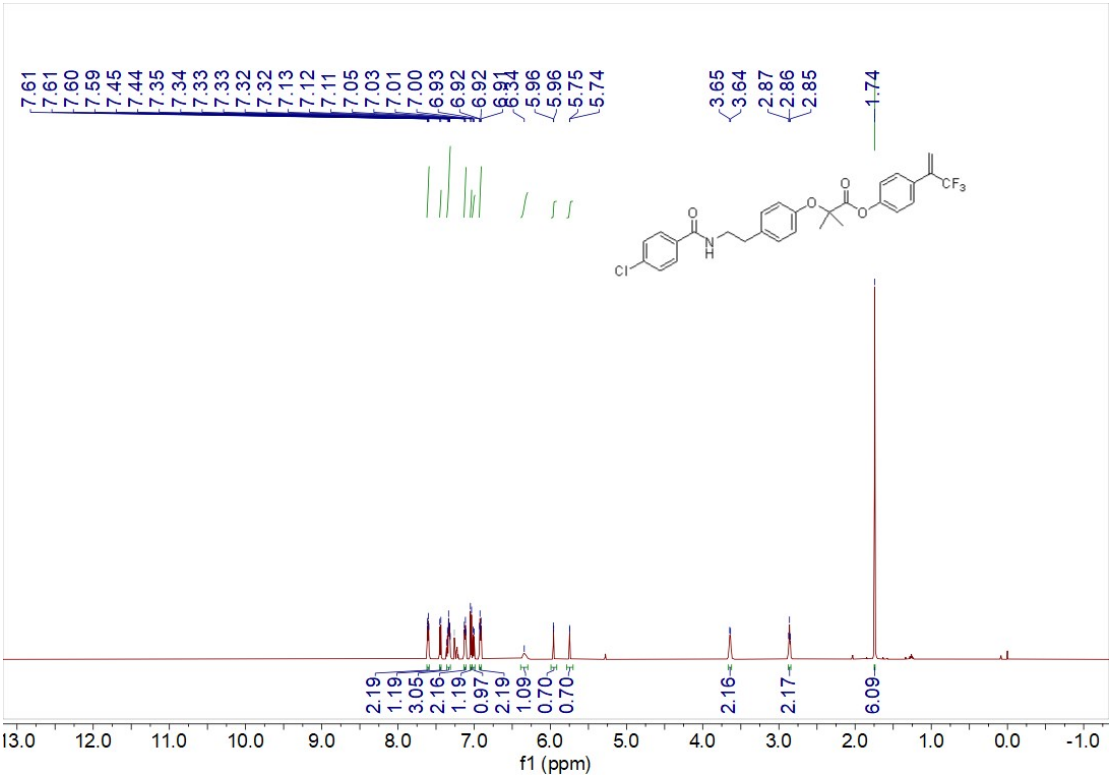


^{19}F NMR of 1w

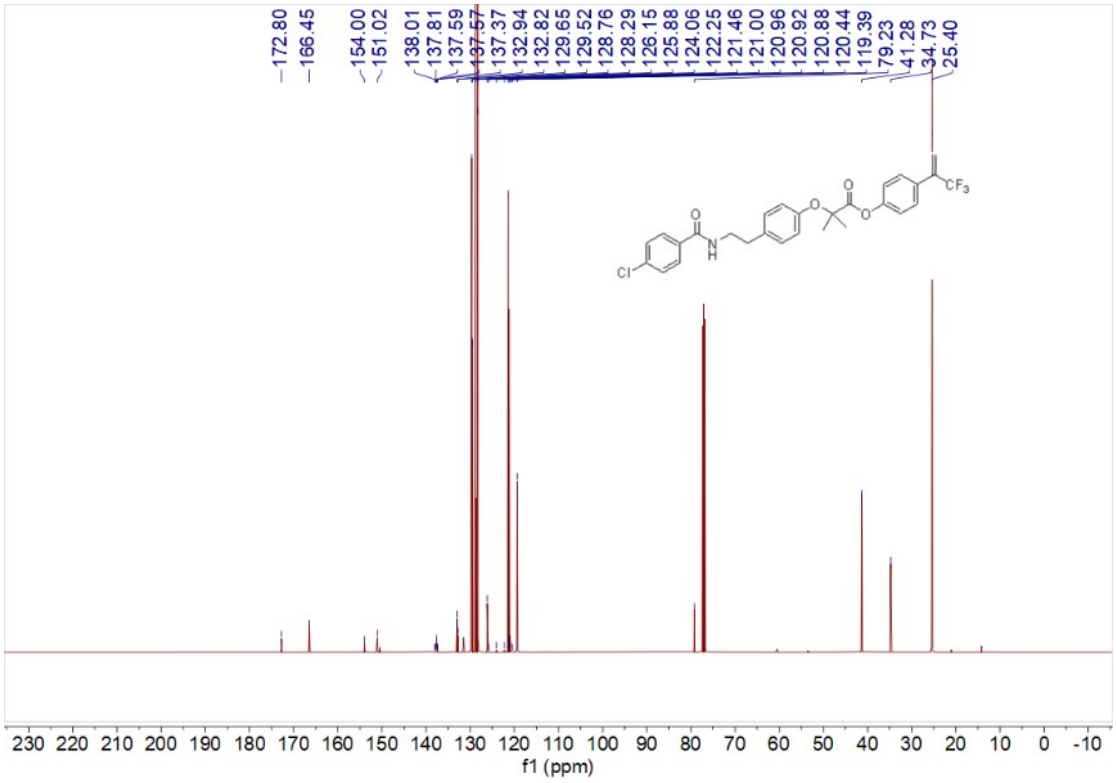


4-(3,3,3-trifluoroprop-1-en-2-yl)phenyl 2-(4-(2-(4-chlorobenzamido)ethyl)phenoxy)-2-methylpropanoate (1y)

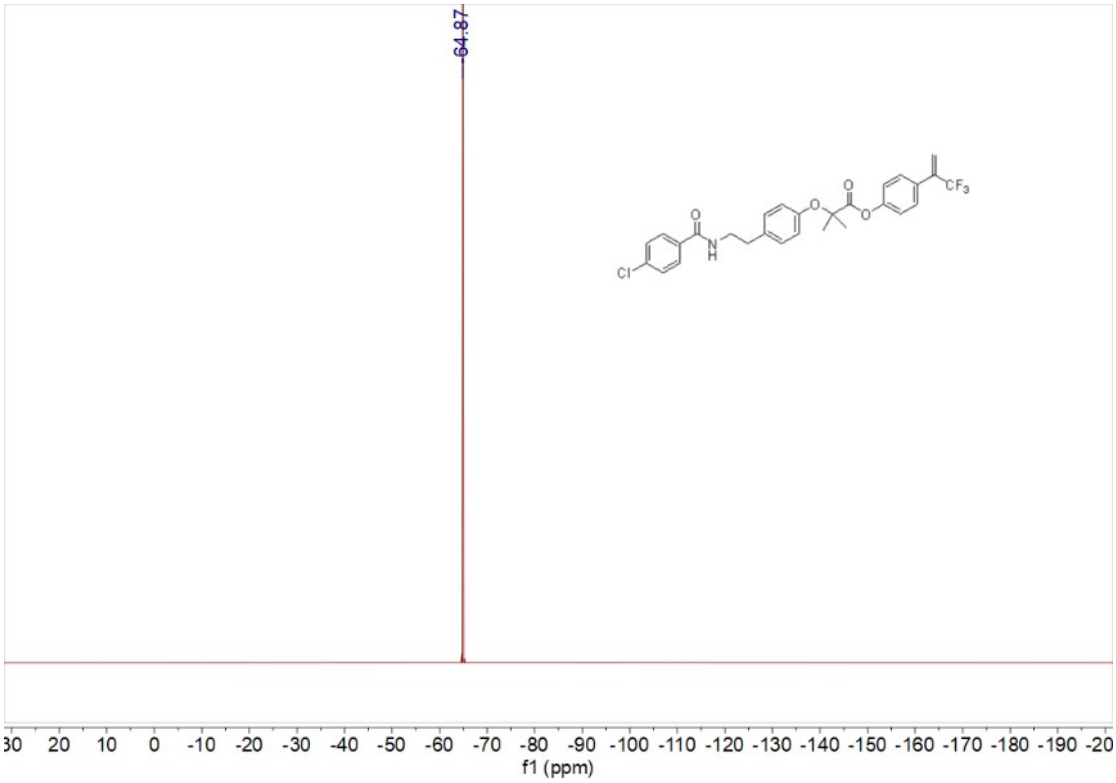
^{1}H NMR of 1y



^{13}C NMR of 1y

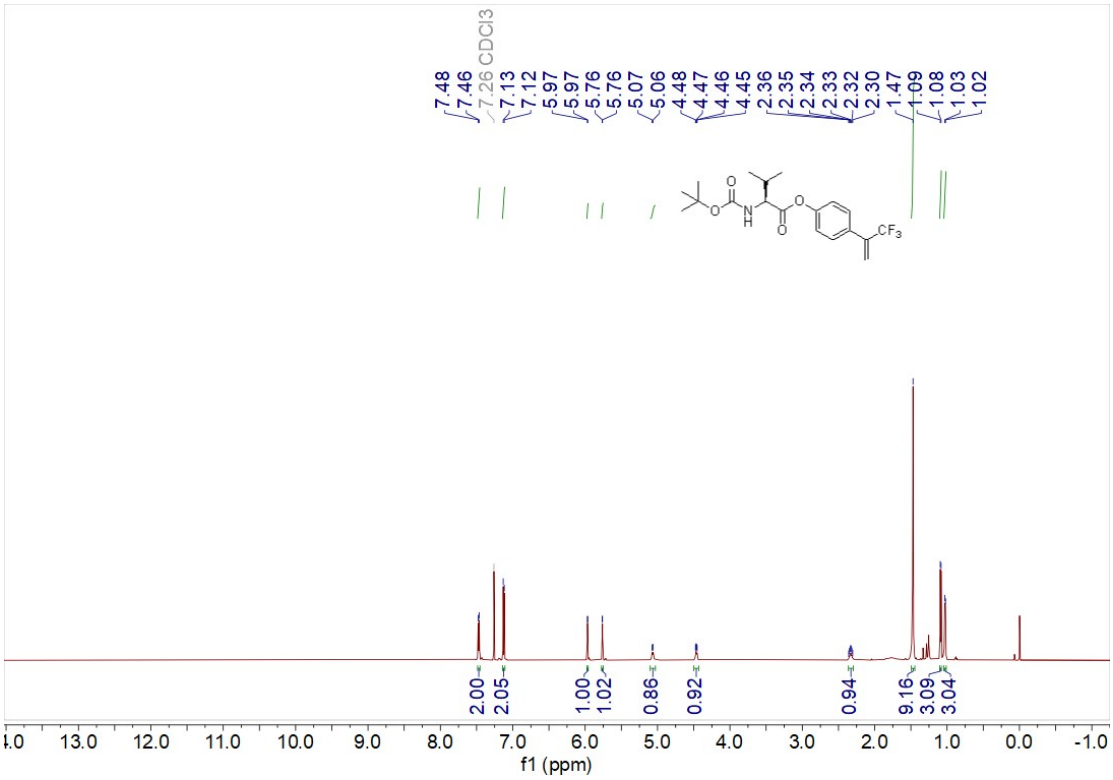


^{19}F NMR of 1y

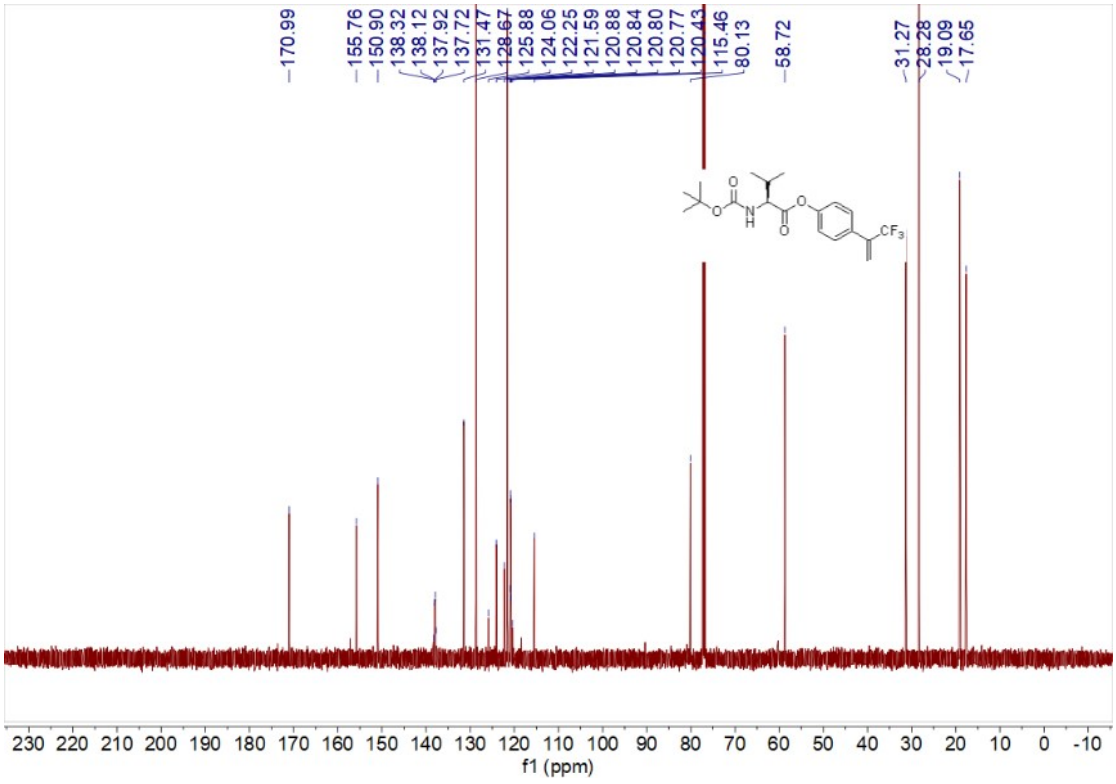


4-(3,3,3-trifluoroprop-1-en-2-yl)phenyl (tert-butoxycarbonyl)-*L*-valinate (1z)

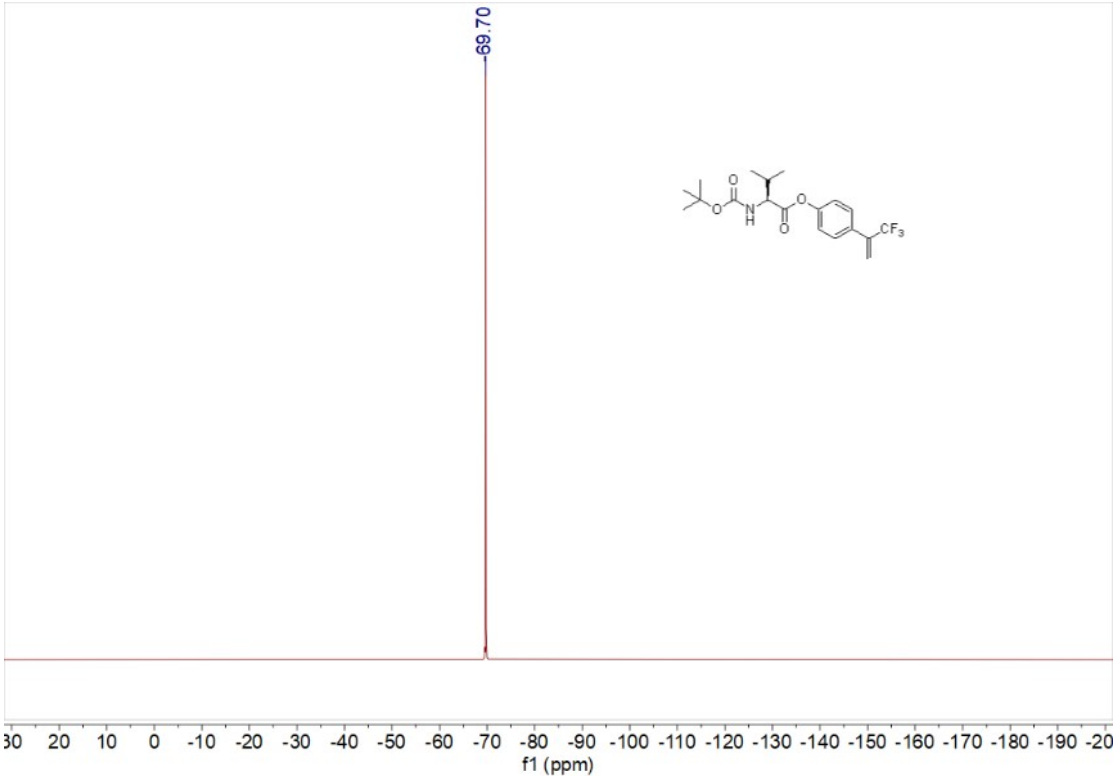
^{1}H NMR of 1z



^{13}C NMR of 1z

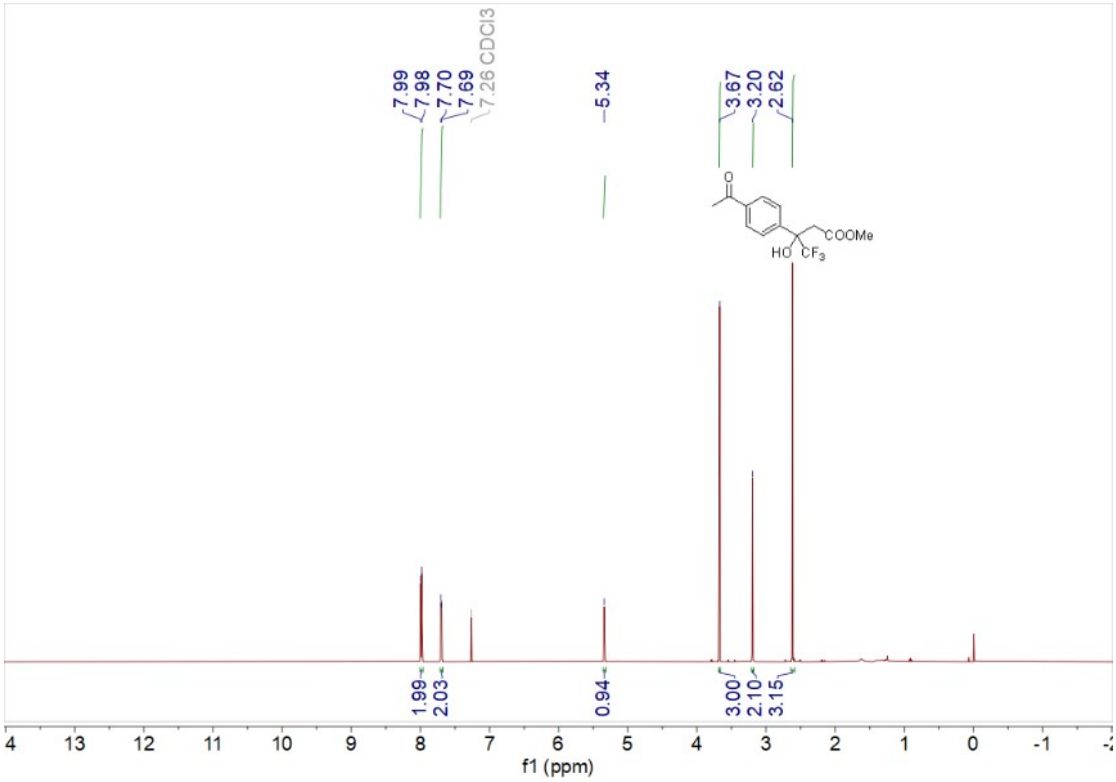


^{19}F NMR of 1z

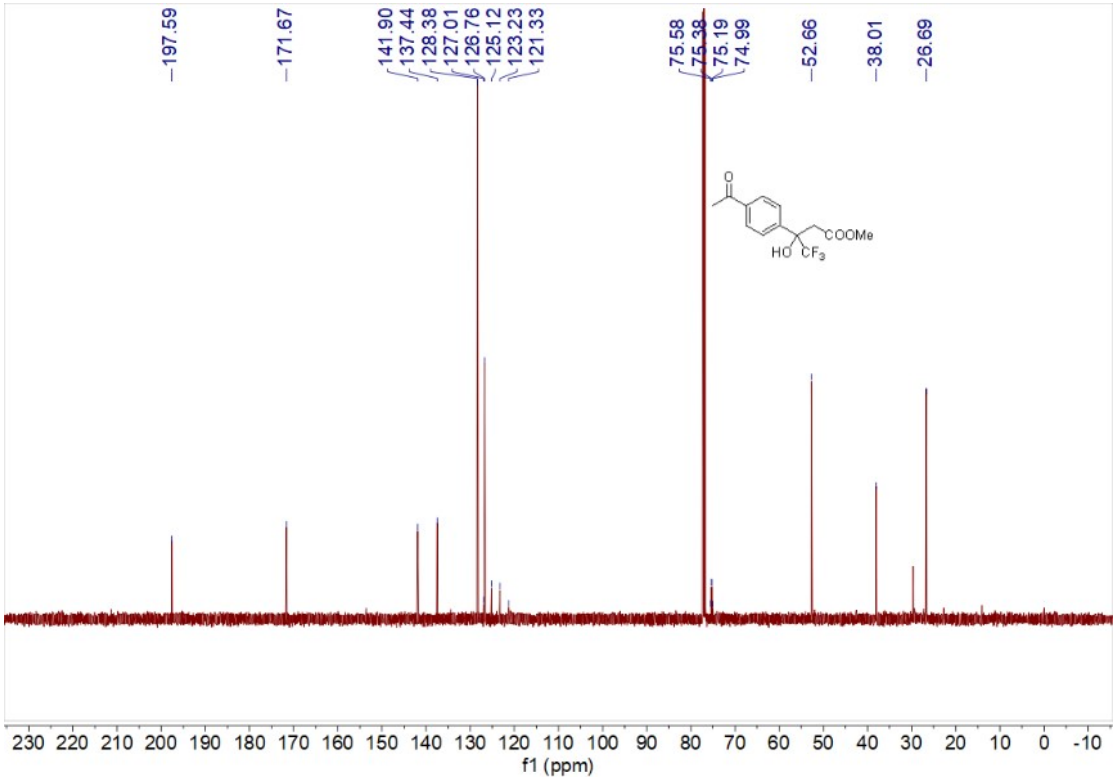


Methyl 3-(4-acetylphenyl)-4,4,4-trifluoro-3-hydroxybutanoate (3a)

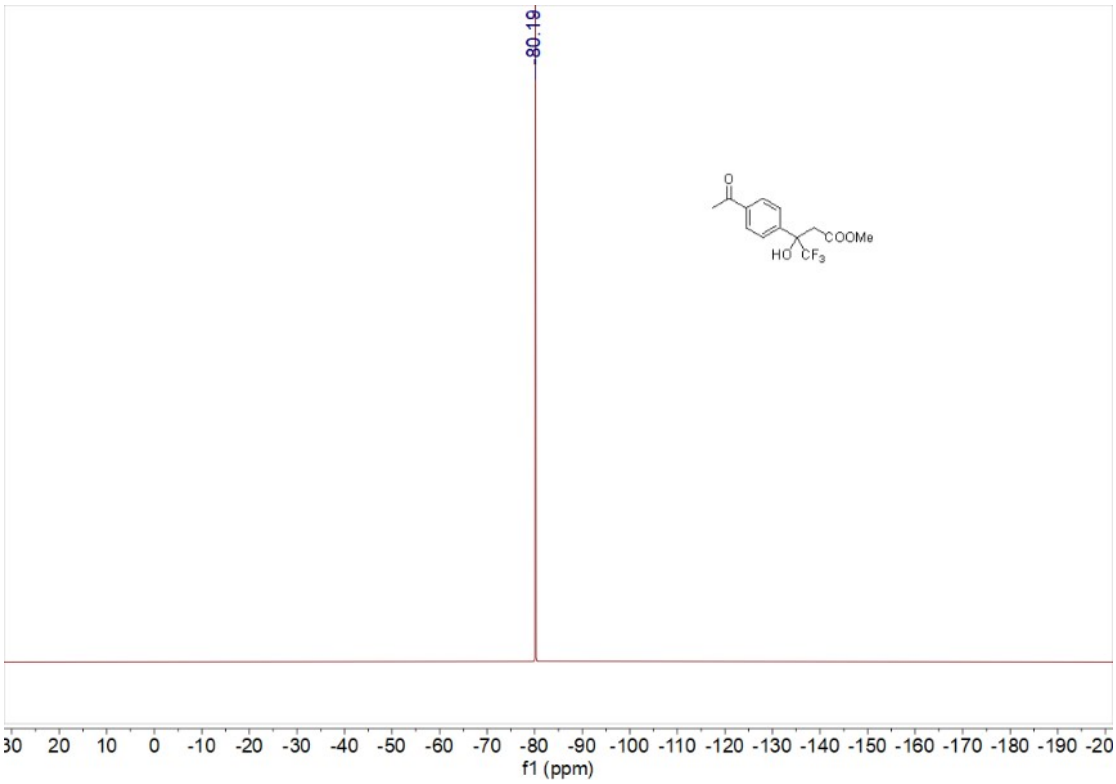
^{1}H NMR of 3a



^{13}C NMR of 3a

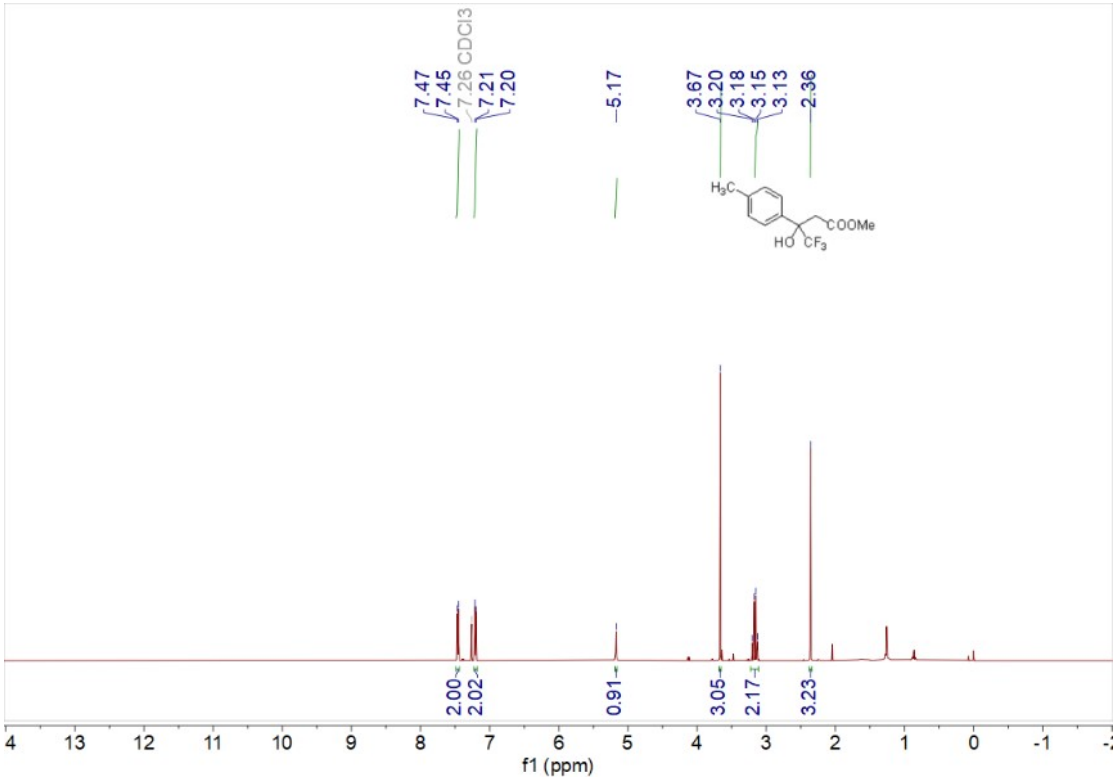


^{19}F NMR of 3a

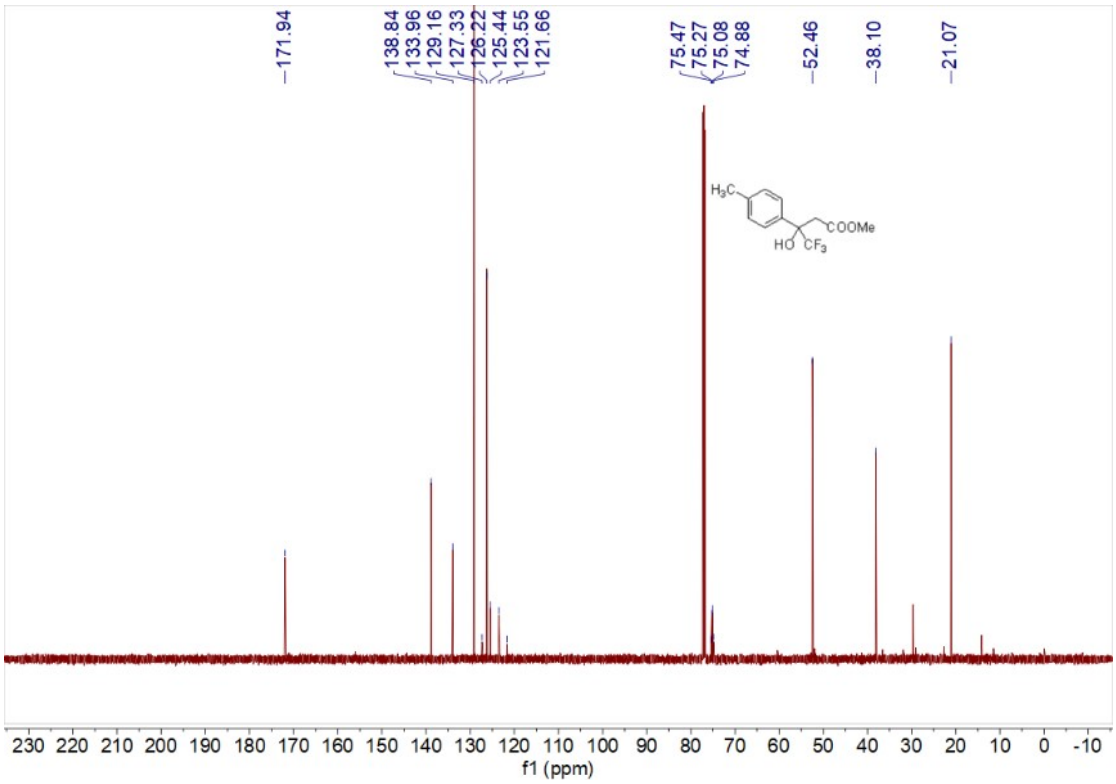


Methyl 4,4,4-trifluoro-3-hydroxy-3-(*p*-tolyl)butanoate (3b)

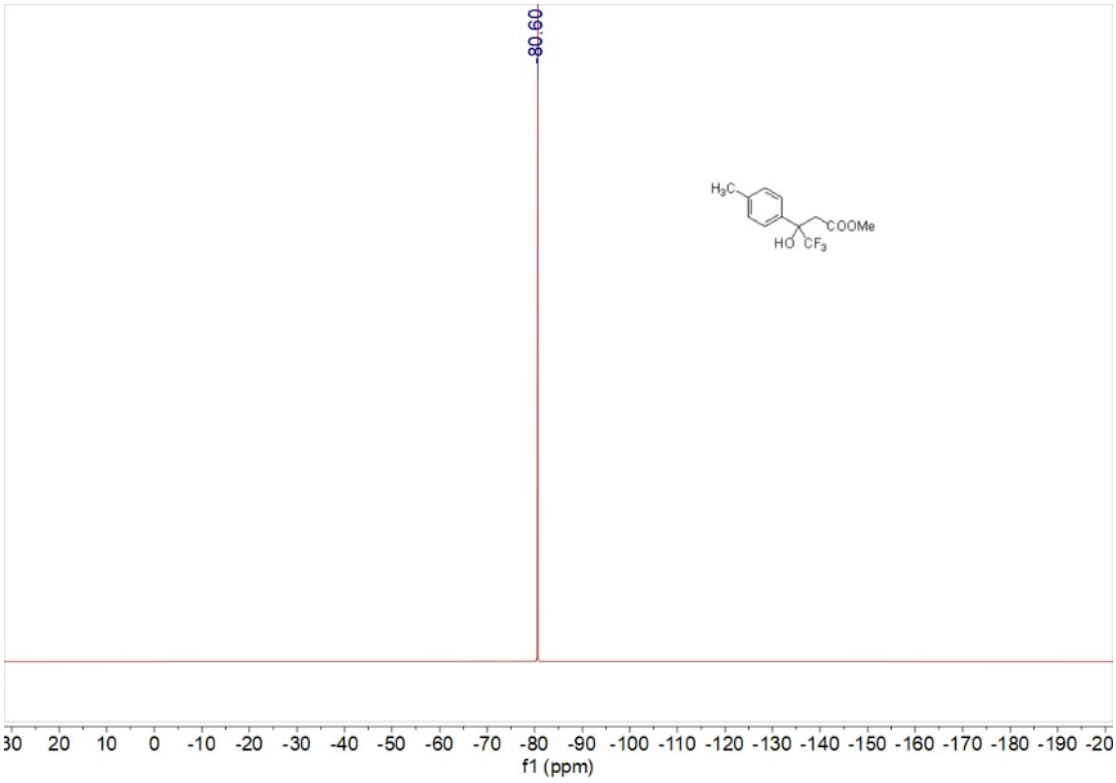
^{1}H NMR of 3b



^{13}C NMR of 3b

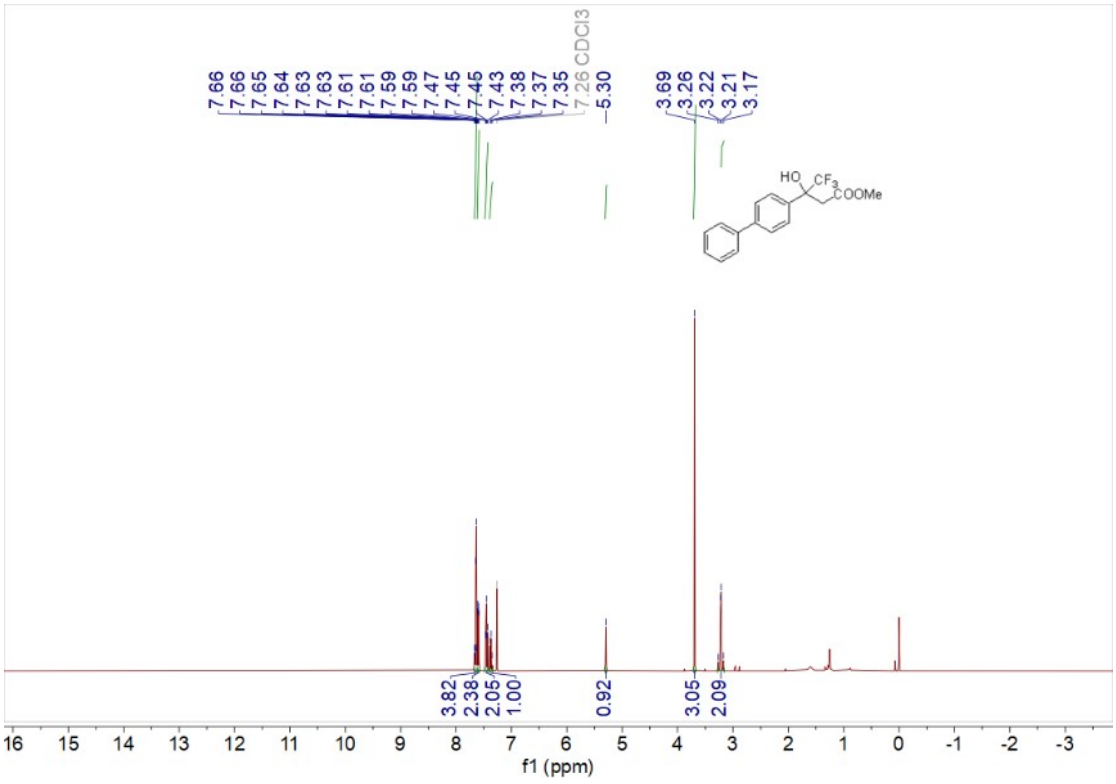


^{19}F NMR of 3b

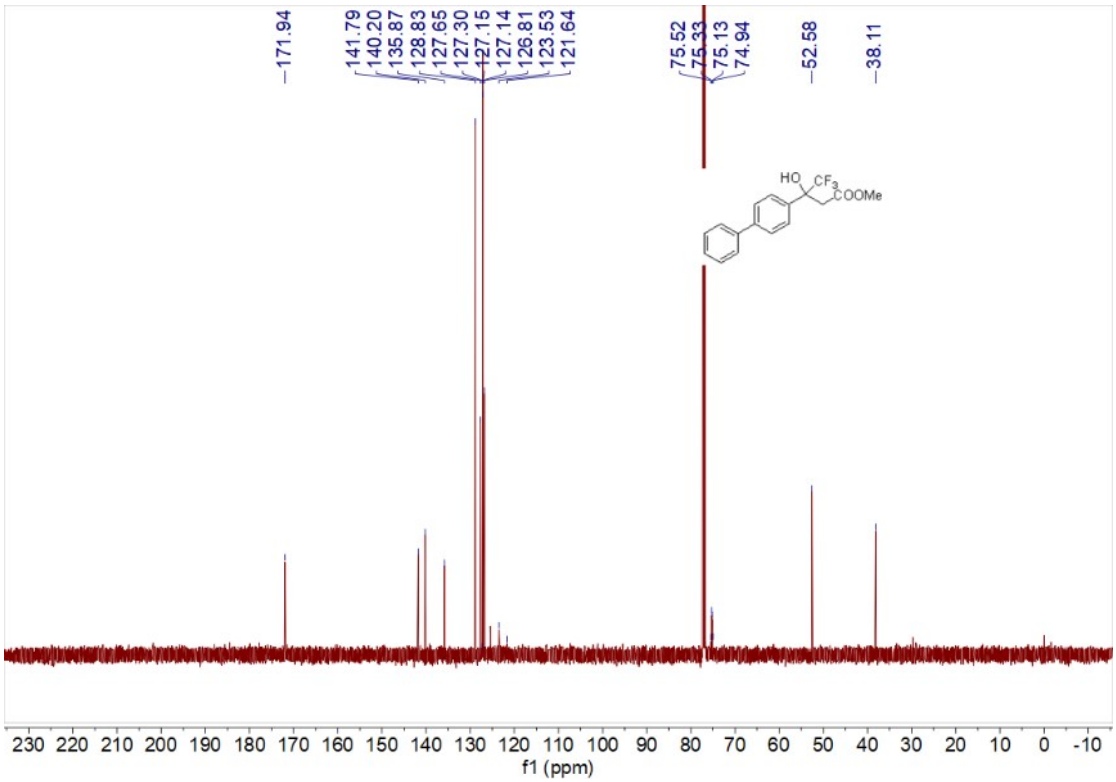


Methyl 3-([1,1'-biphenyl]-4-yl)-4,4,4-trifluoro-3-hydroxybutanoate (3c)

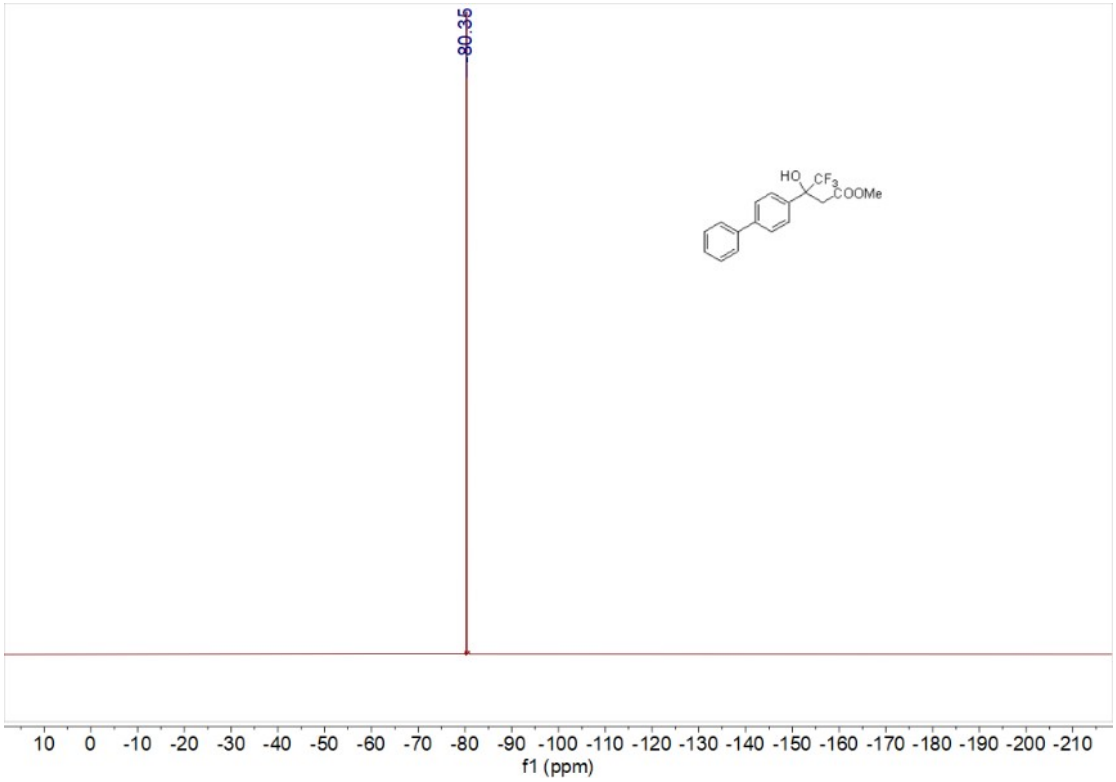
^{1}H NMR of 3c



^{13}C NMR of 3c

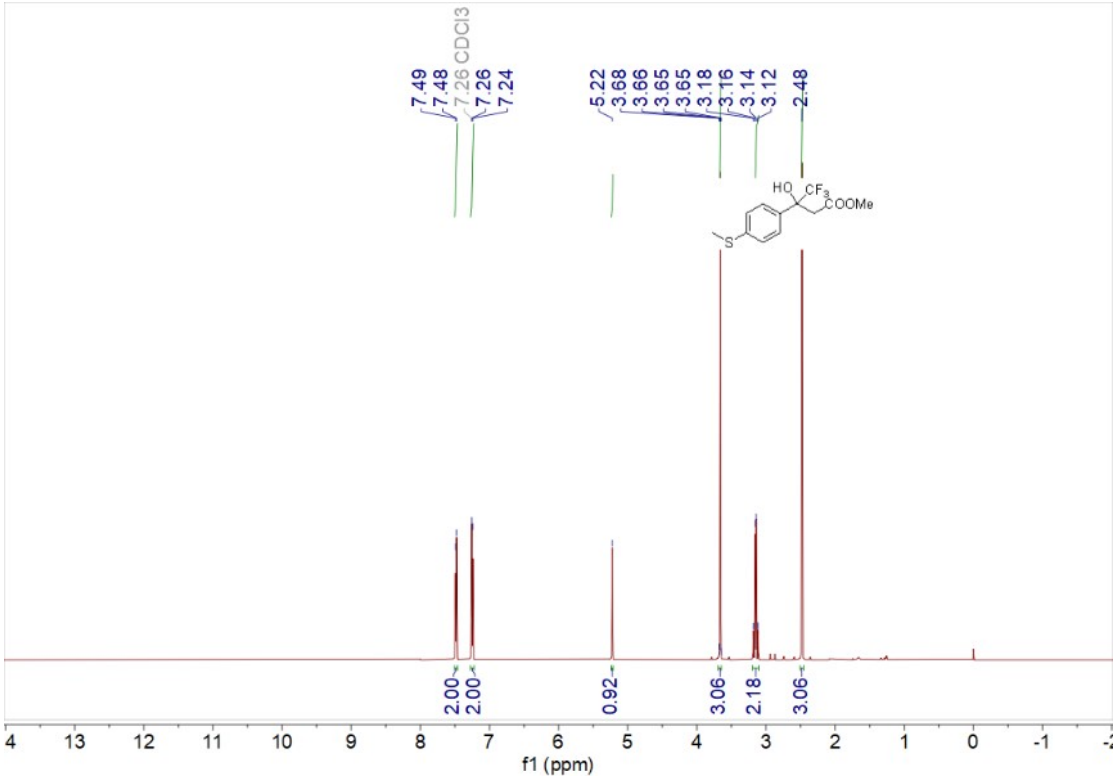


^{19}F NMR of 3c

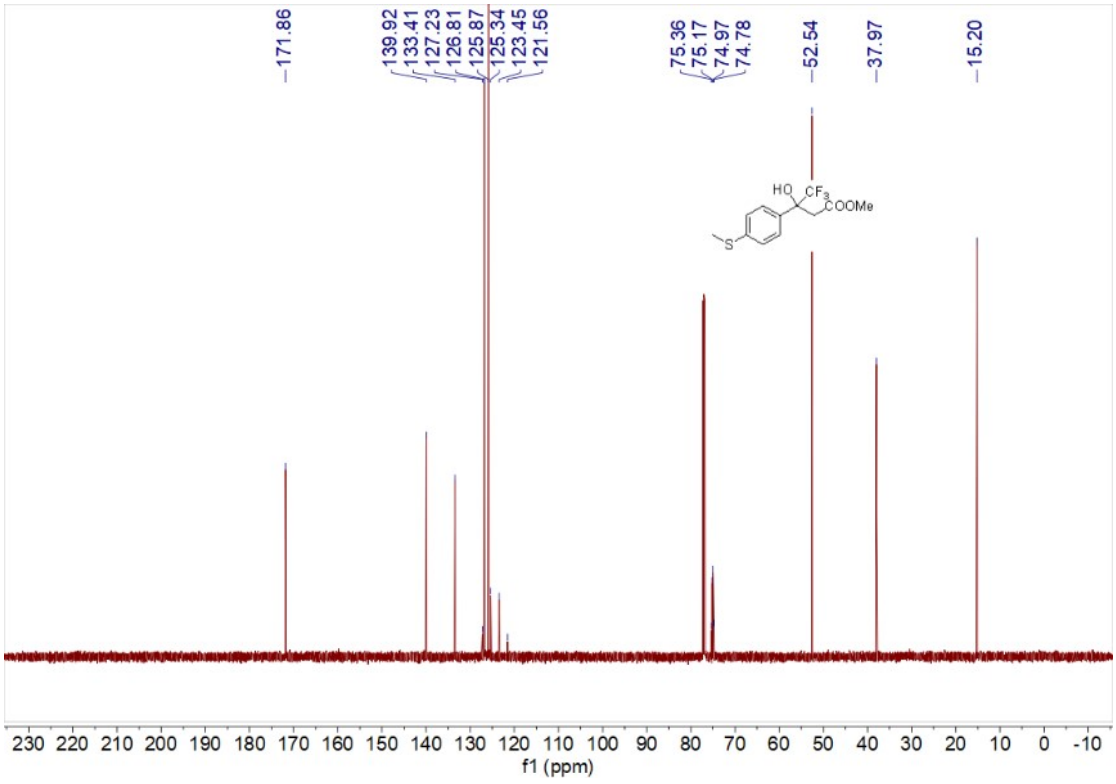


Methyl 4,4,4-trifluoro-3-hydroxy-3-(4-(methylthio)phenyl)butanoate (3d)

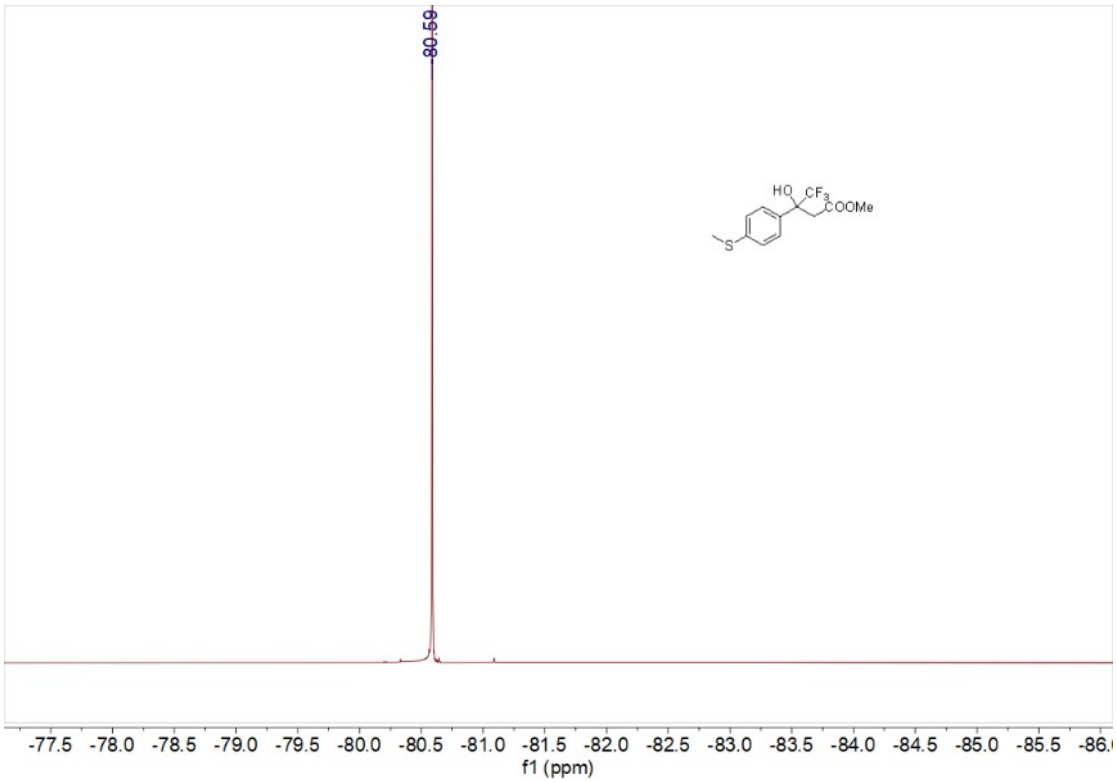
^{1}H NMR of 3d



^{13}C NMR of 3d

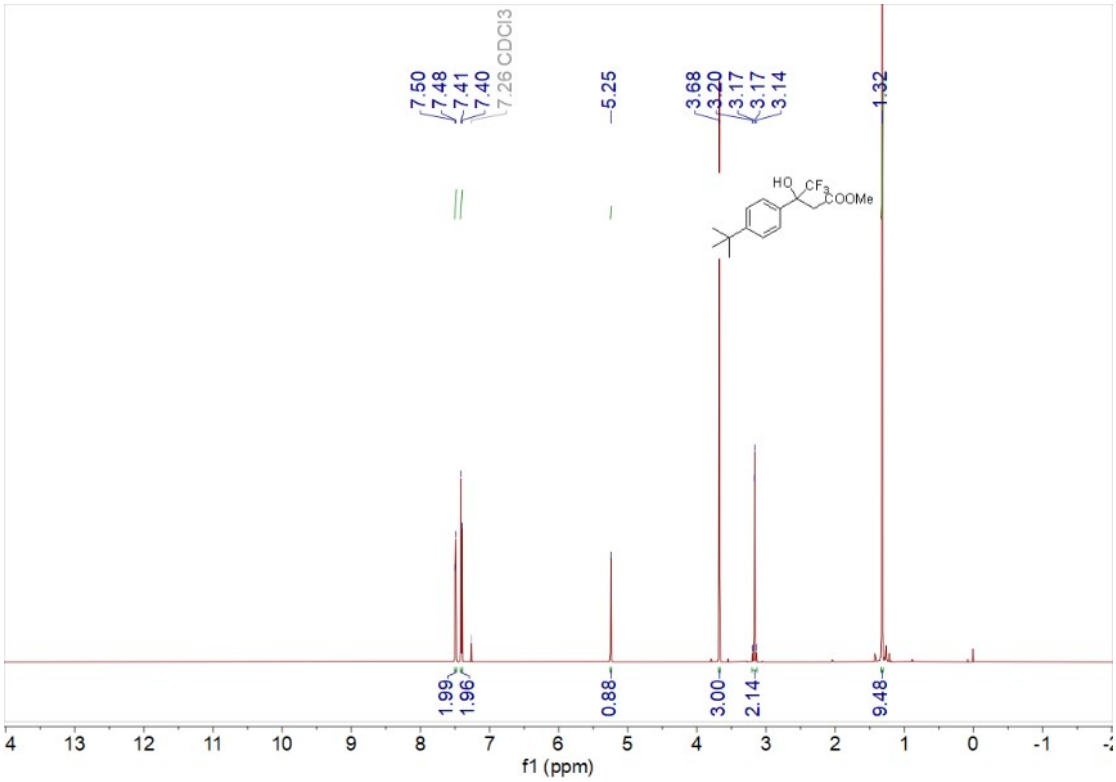


^{19}F NMR of 3d

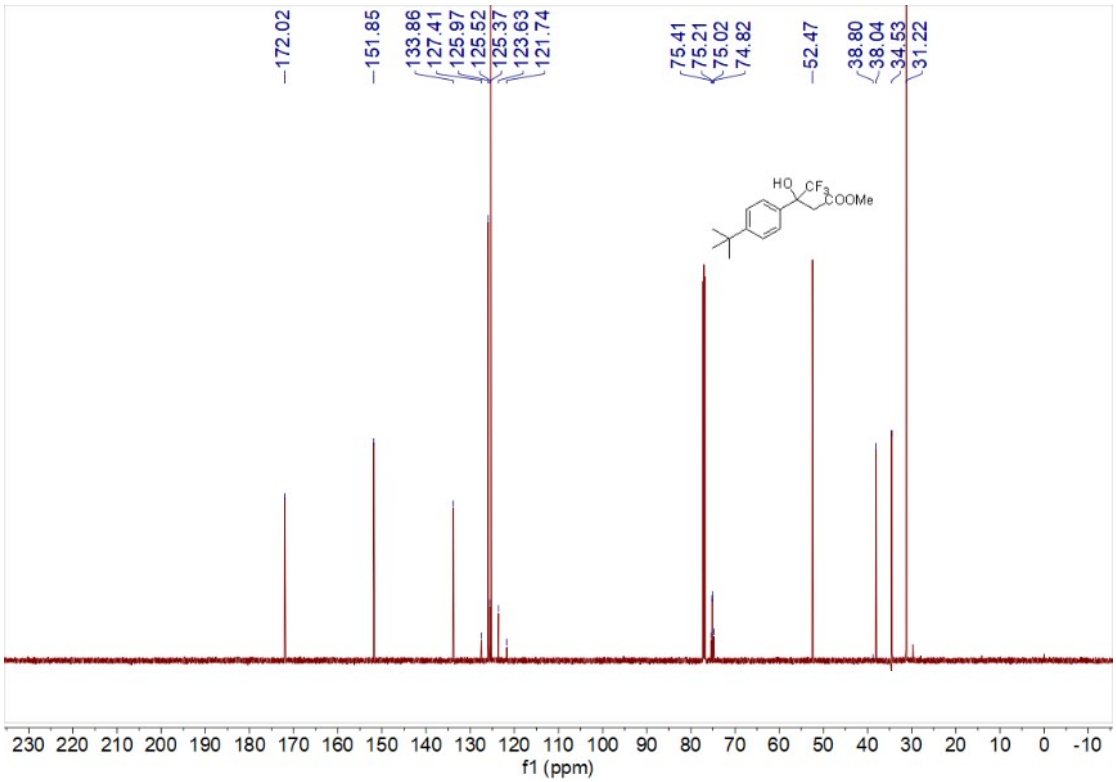


Methyl 3-(4-(*tert*-butyl)phenyl)-4,4,4-trifluoro-3-hydroxybutanoate (3e)

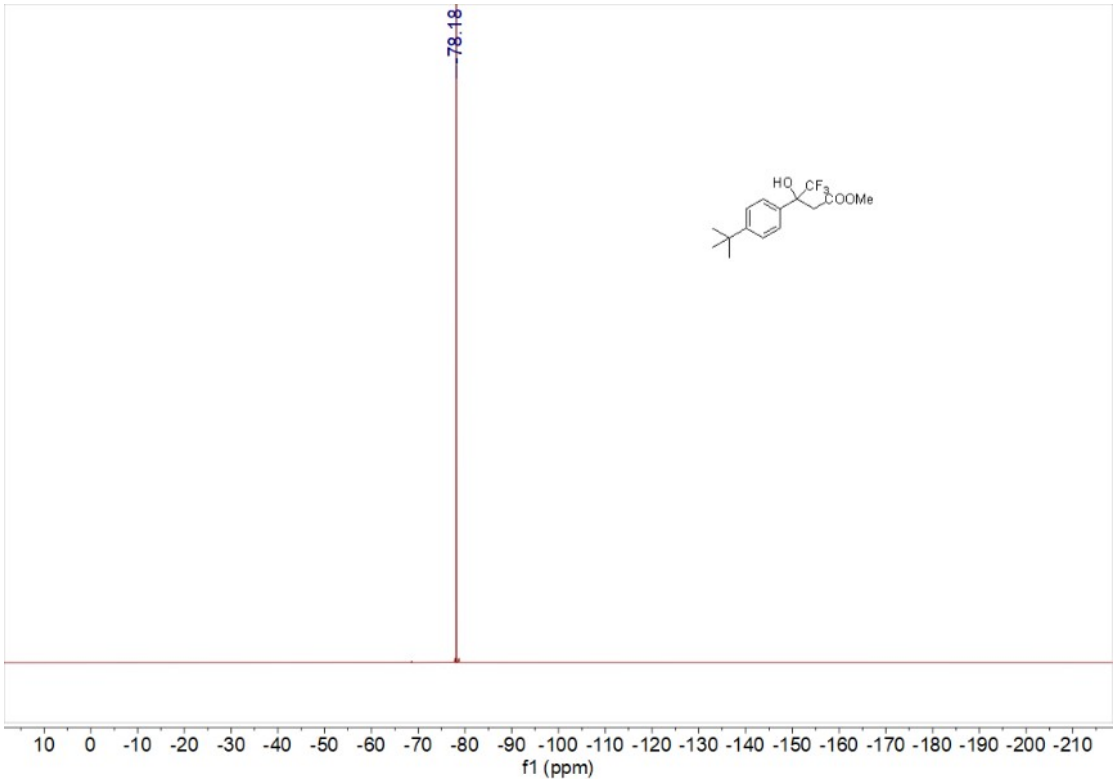
^{1}H NMR of 3e



^{13}C NMR of 3e

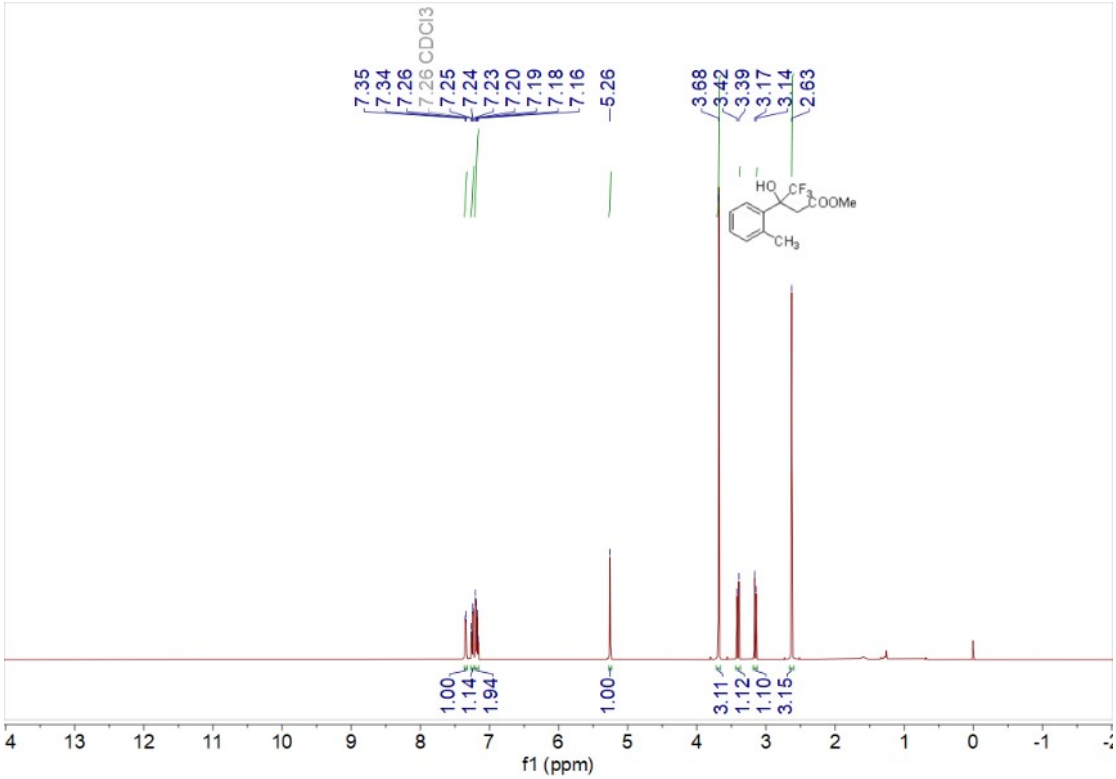


^{19}F NMR of 3e

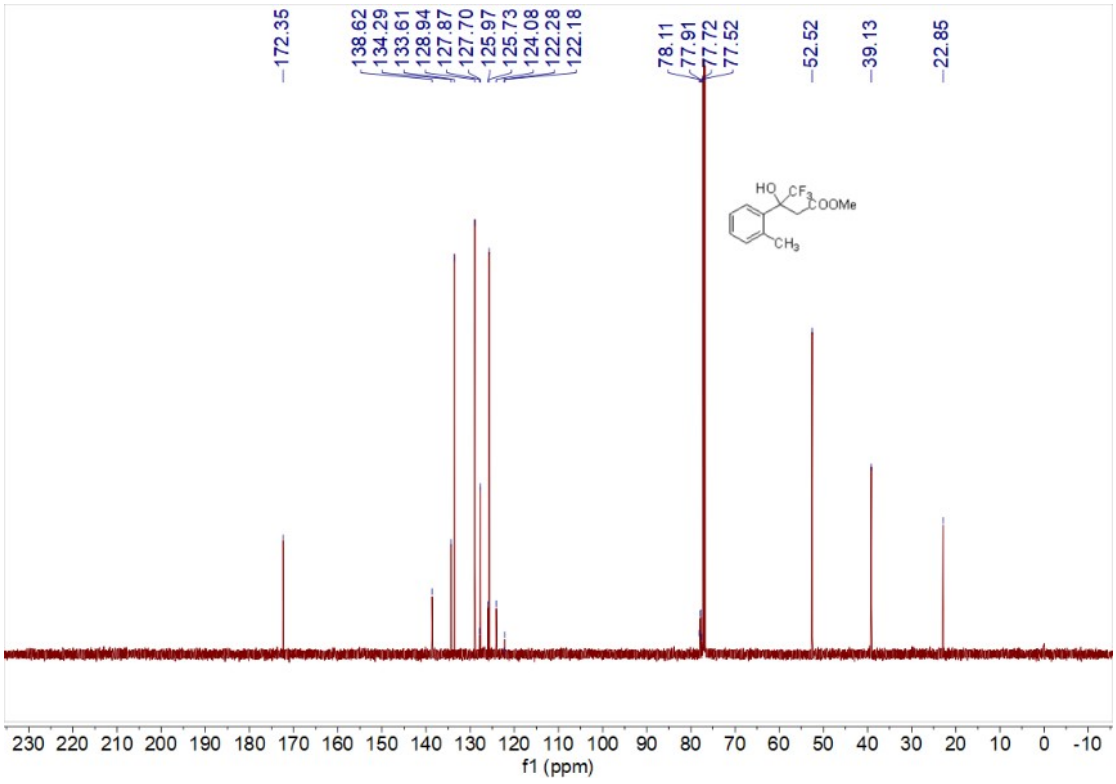


Methyl 4,4,4-trifluoro-3-hydroxy-3-(*o*-tolyl)butanoate (3f)

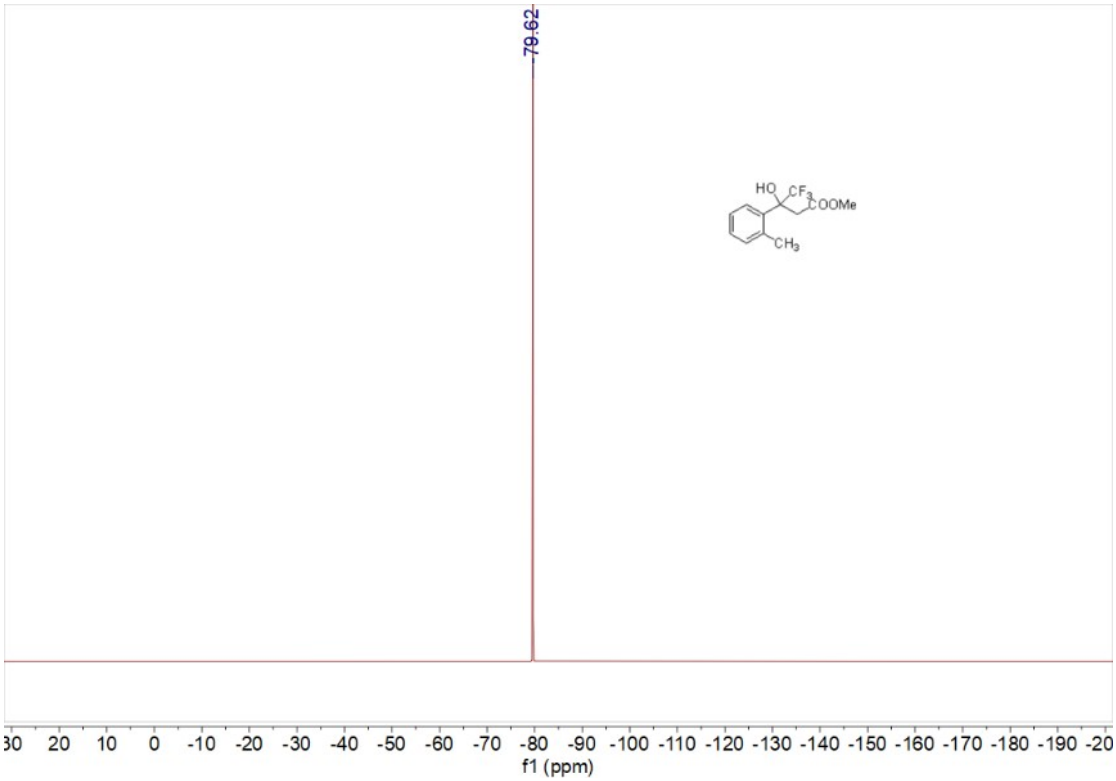
^{1}H NMR of 3f



^{13}C NMR of 3f

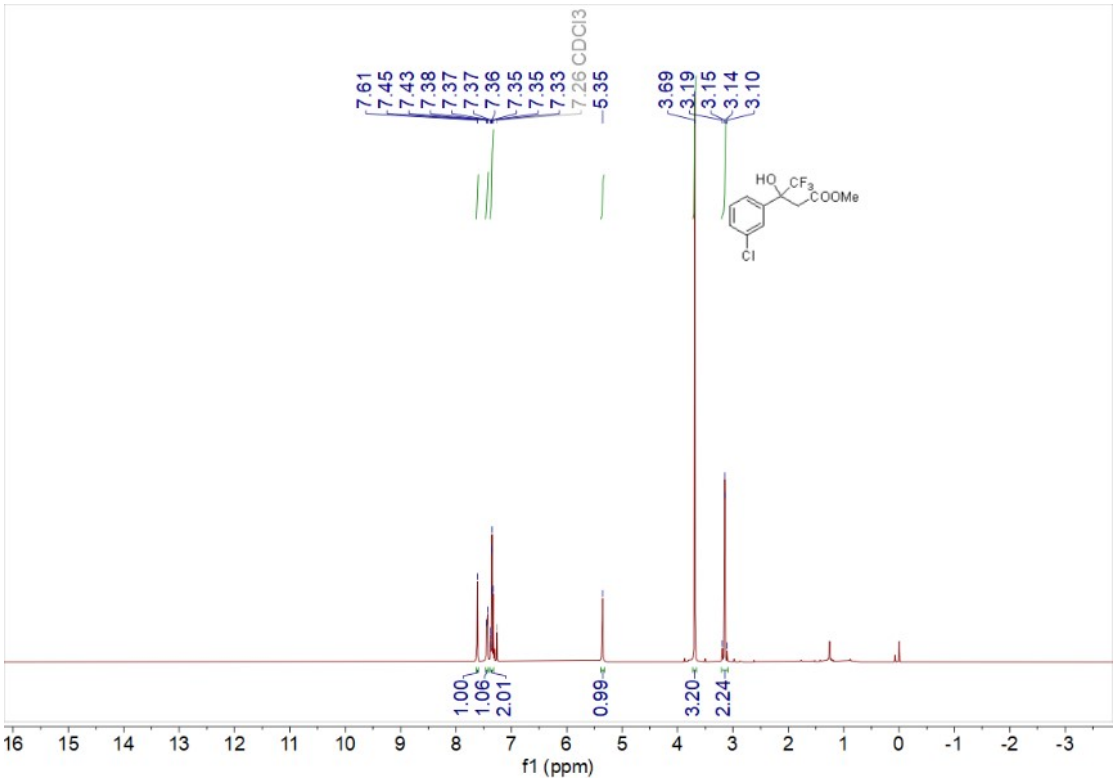


^{19}F NMR of 3f

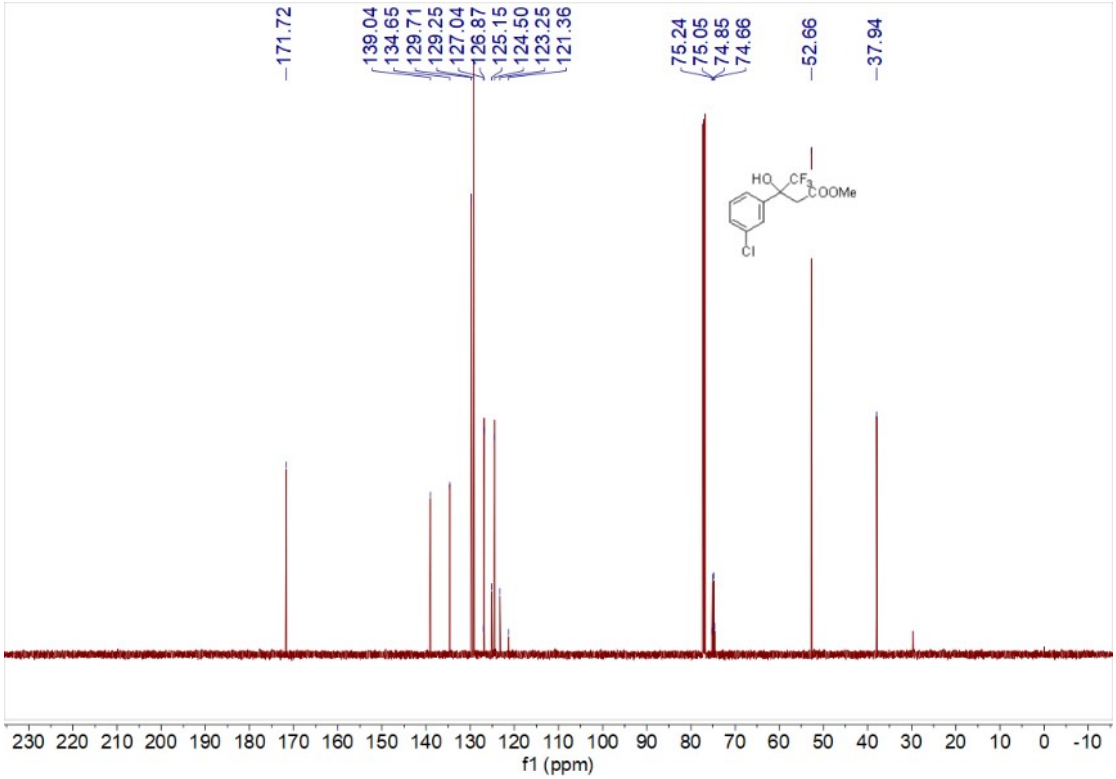


Methyl 3-(3-chlorophenyl)-4,4,4-trifluoro-3-hydroxybutanoate (3g)

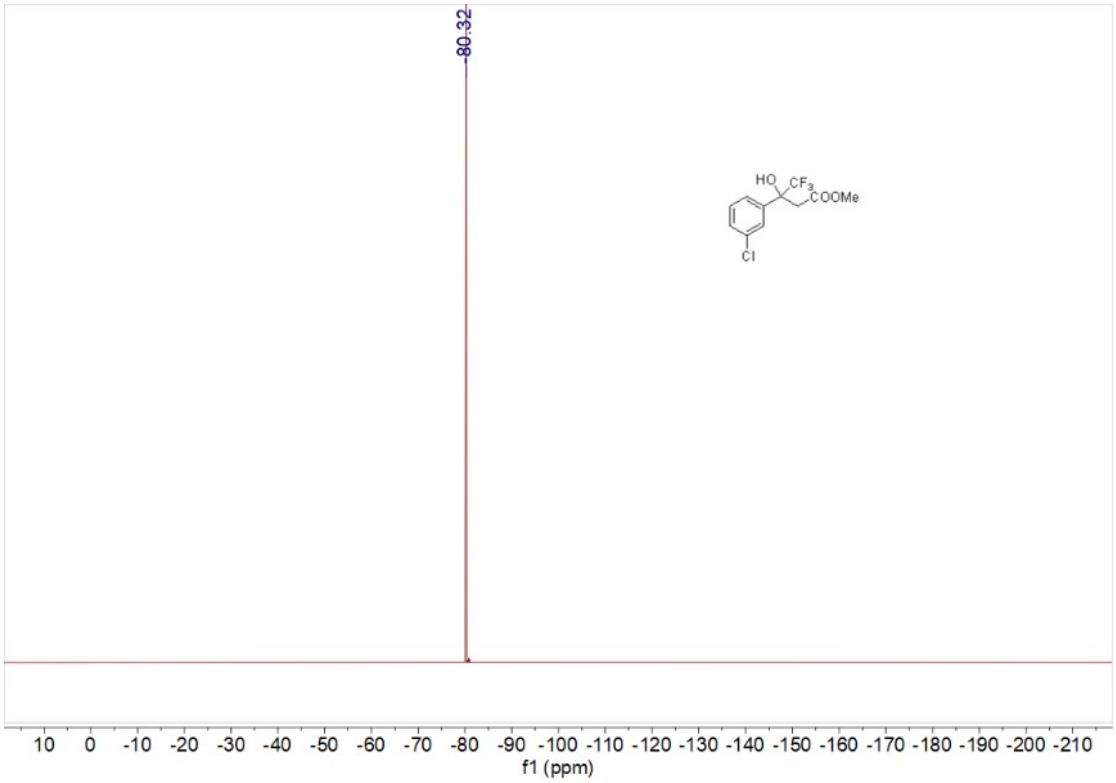
^{1}H NMR of 3g



^{13}C NMR of 3g

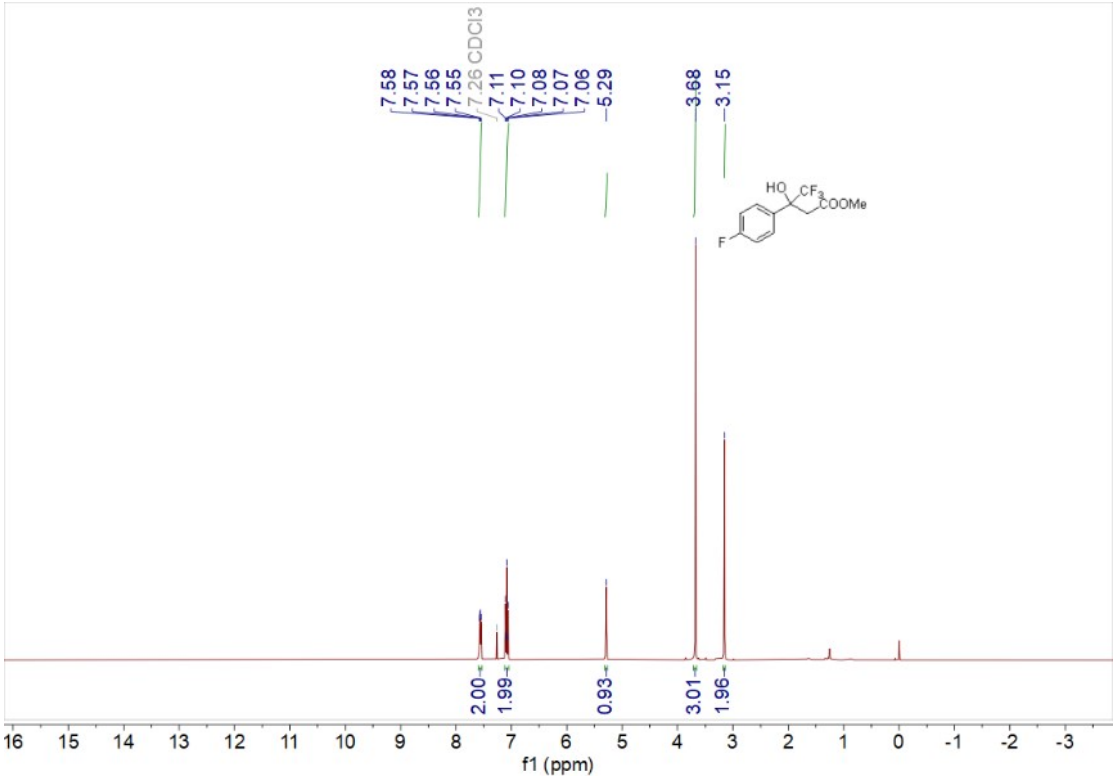


^{19}F NMR of 3g

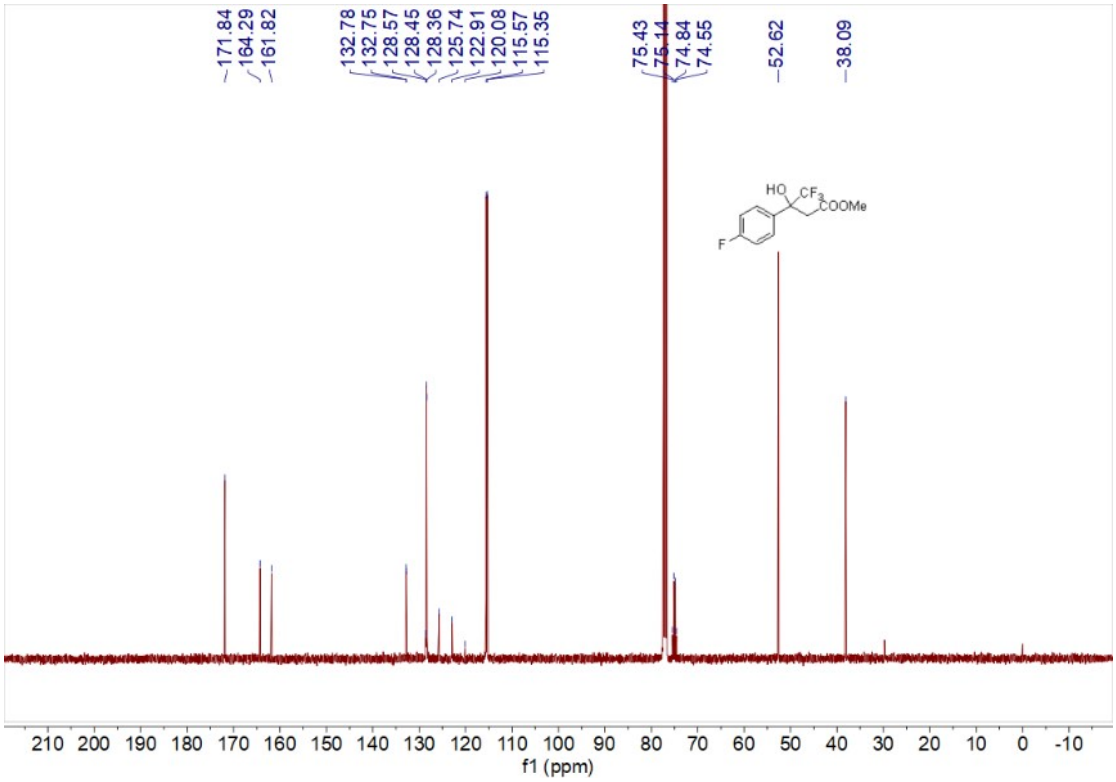


Methyl 4,4,4-trifluoro-3-(4-fluorophenyl)-3-hydroxybutanoate (3h)

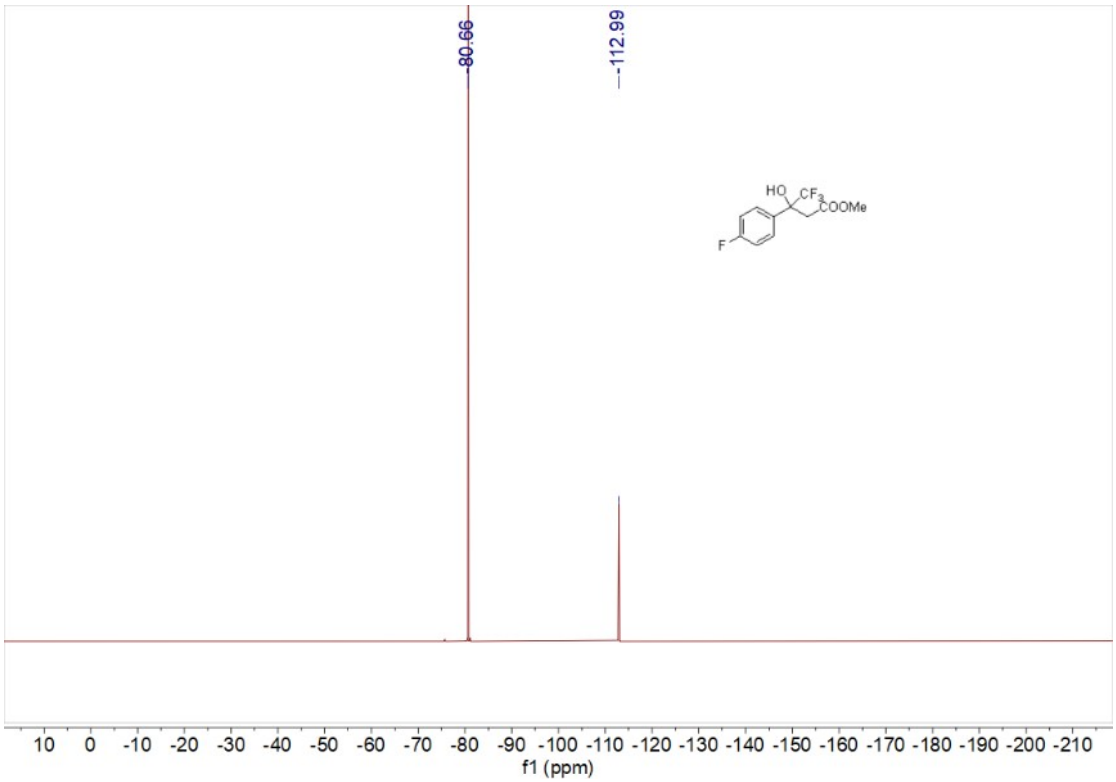
^{1}H NMR of 3h



^{13}C NMR of 3h

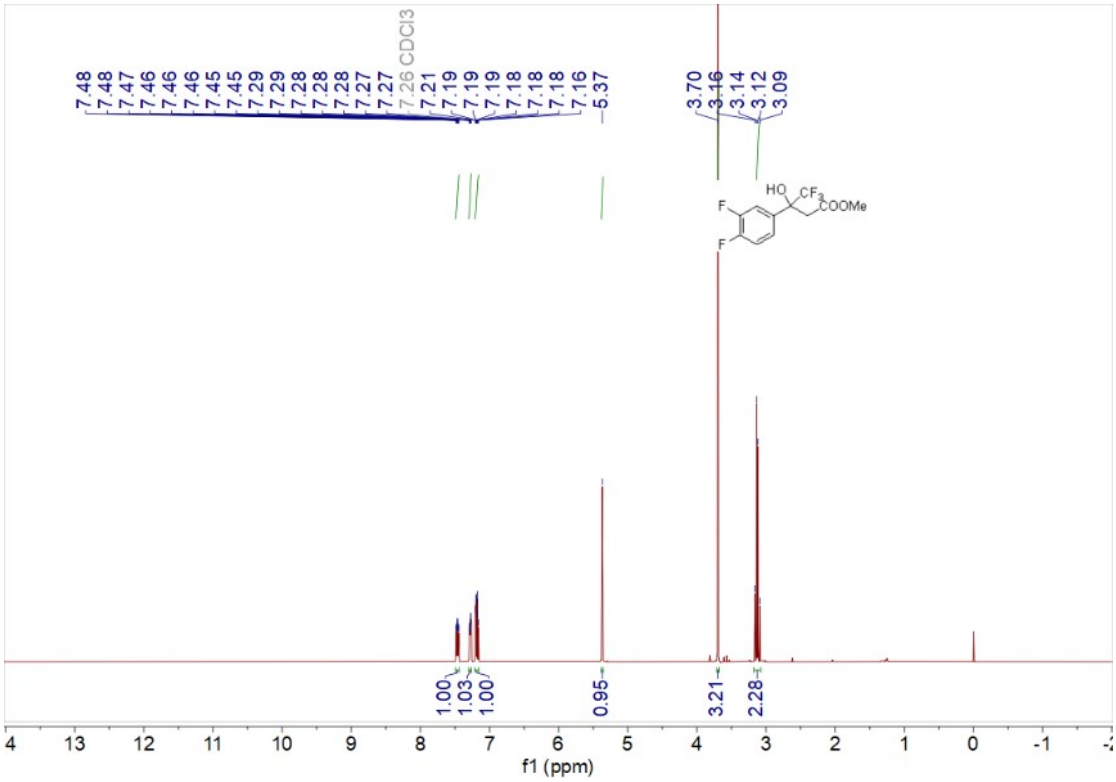


^{19}F NMR of 3h

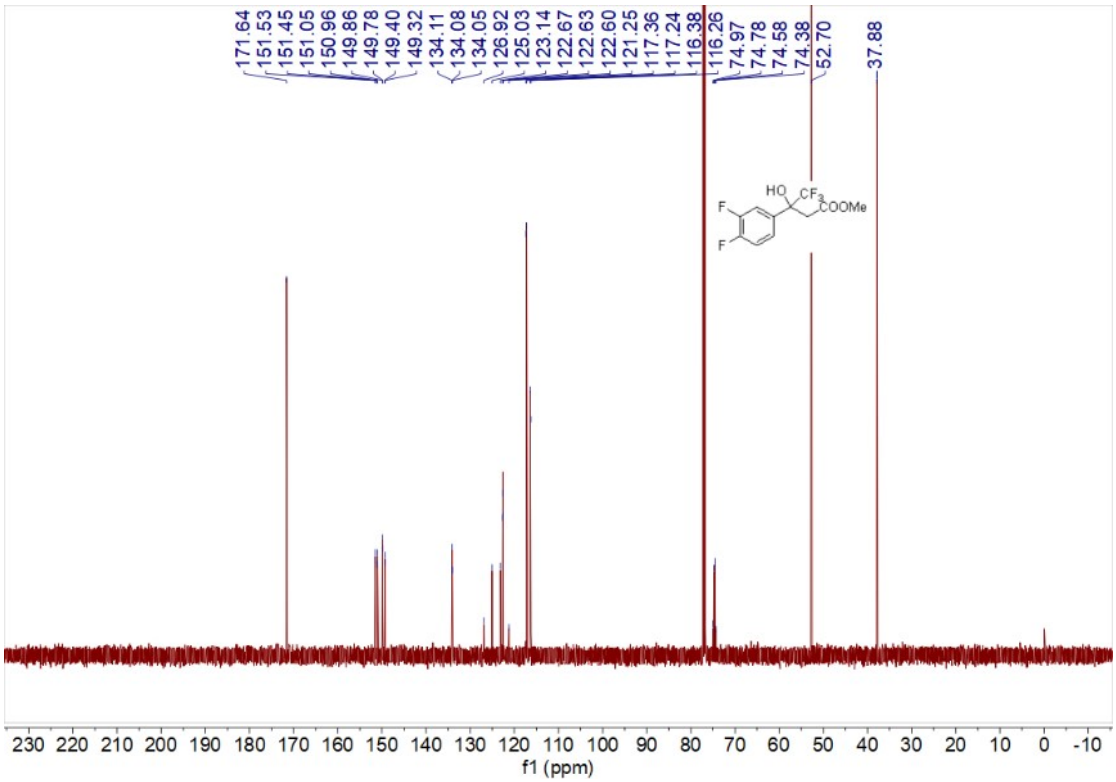


Methyl 3-(3,4-difluorophenyl)-4,4,4-trifluoro-3-hydroxybutanoate (3i)

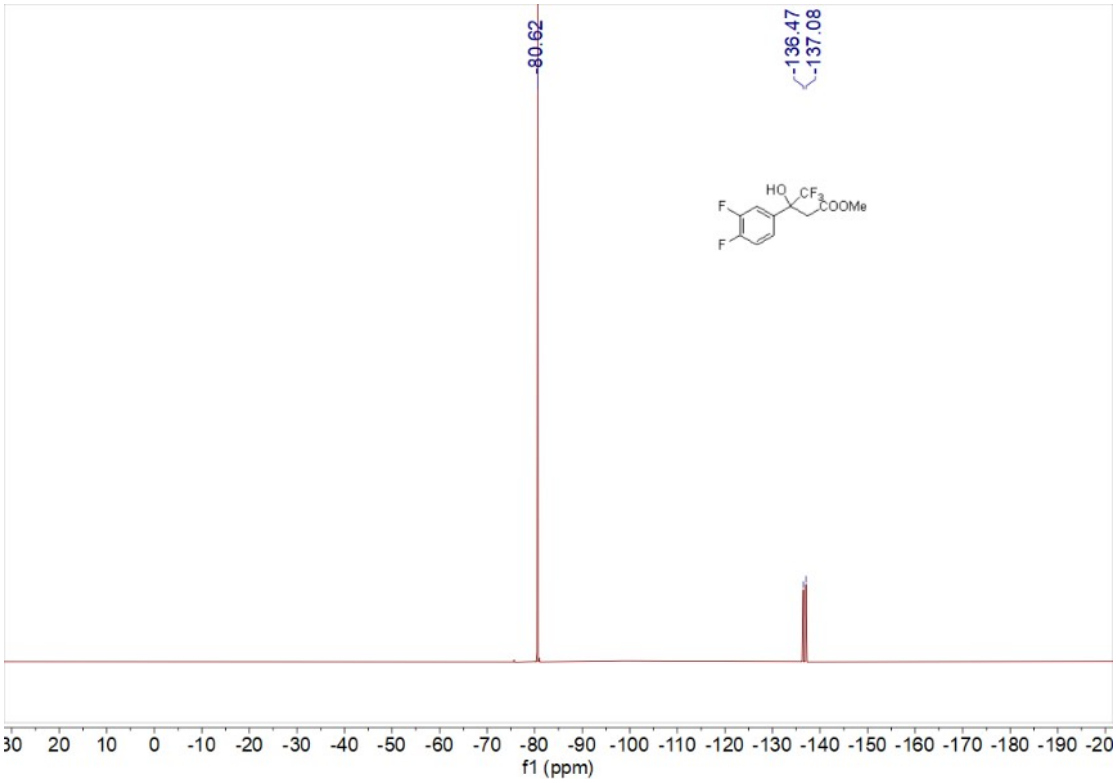
^{1}H NMR of 3i



^{13}C NMR of 3i

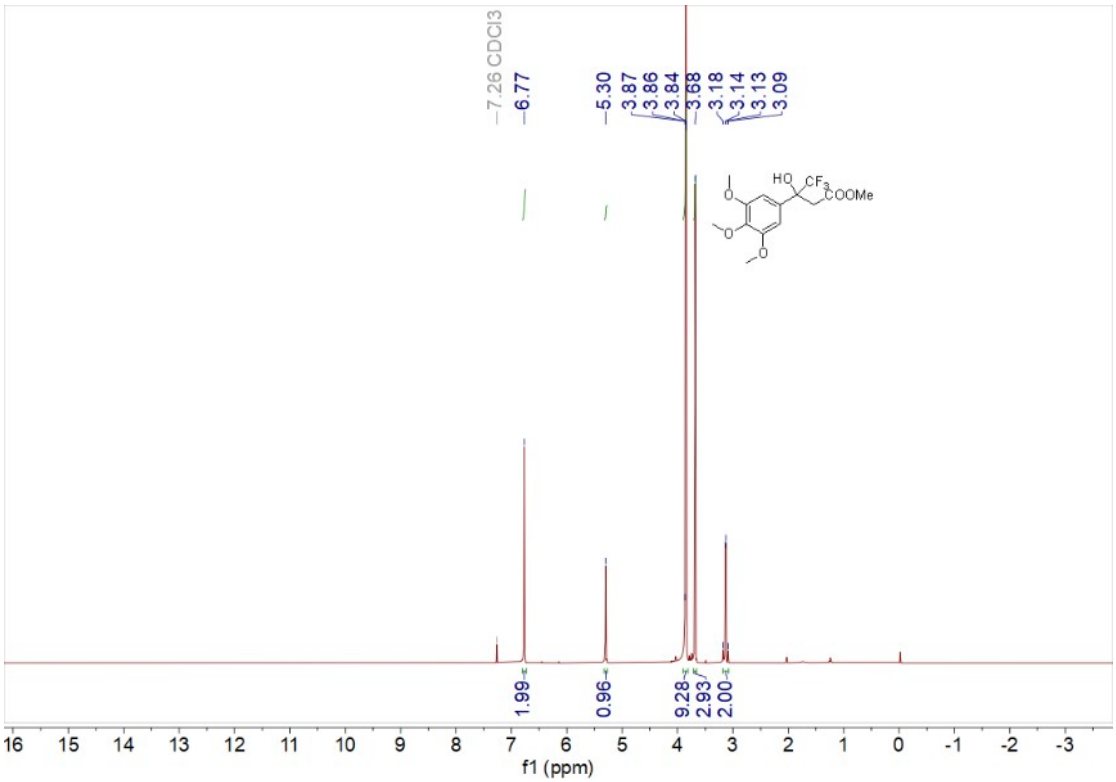


^{19}F NMR of 3i

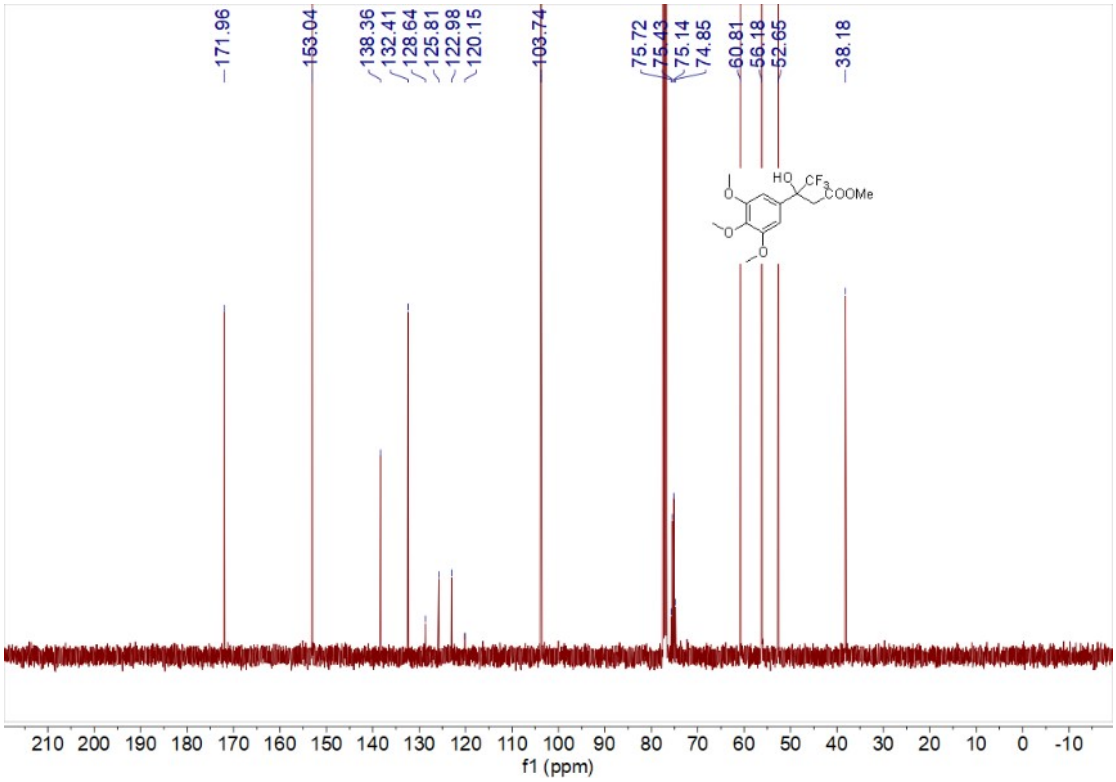


Methyl 4,4,4-trifluoro-3-hydroxy-3-(3,4,5-trimethoxyphenyl)butanoate (3j)

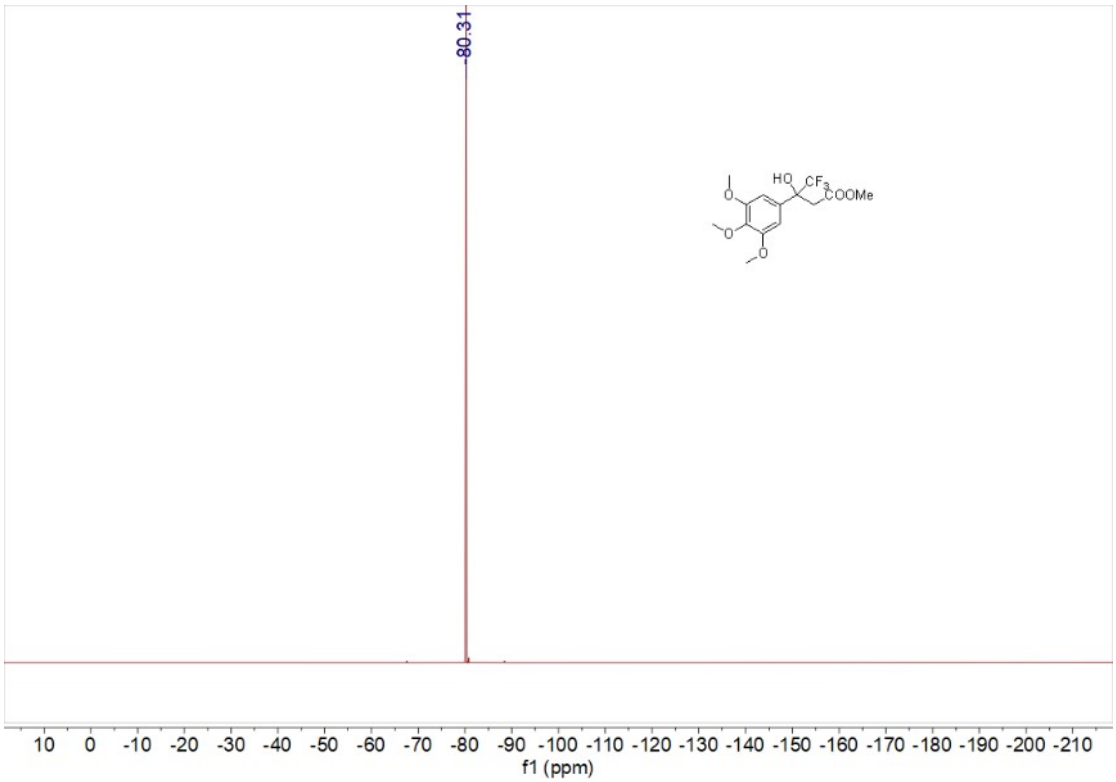
^{1}H NMR of 3j



^{13}C NMR of 3j

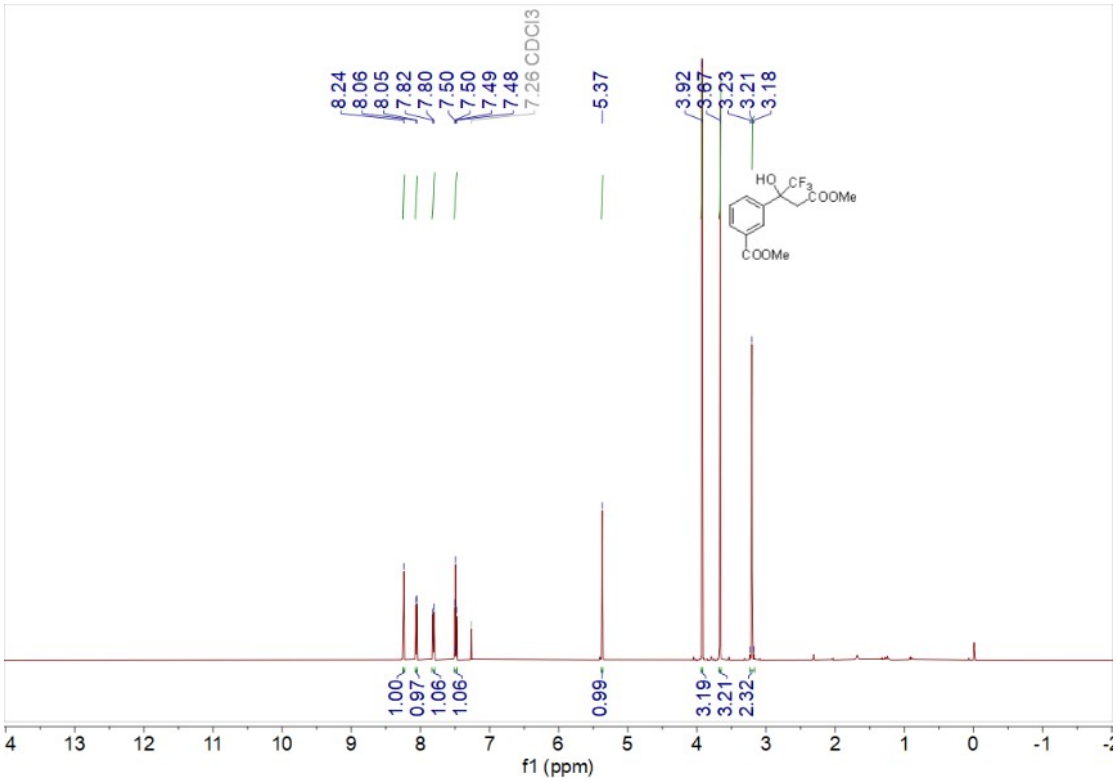


^{19}F NMR of 3j

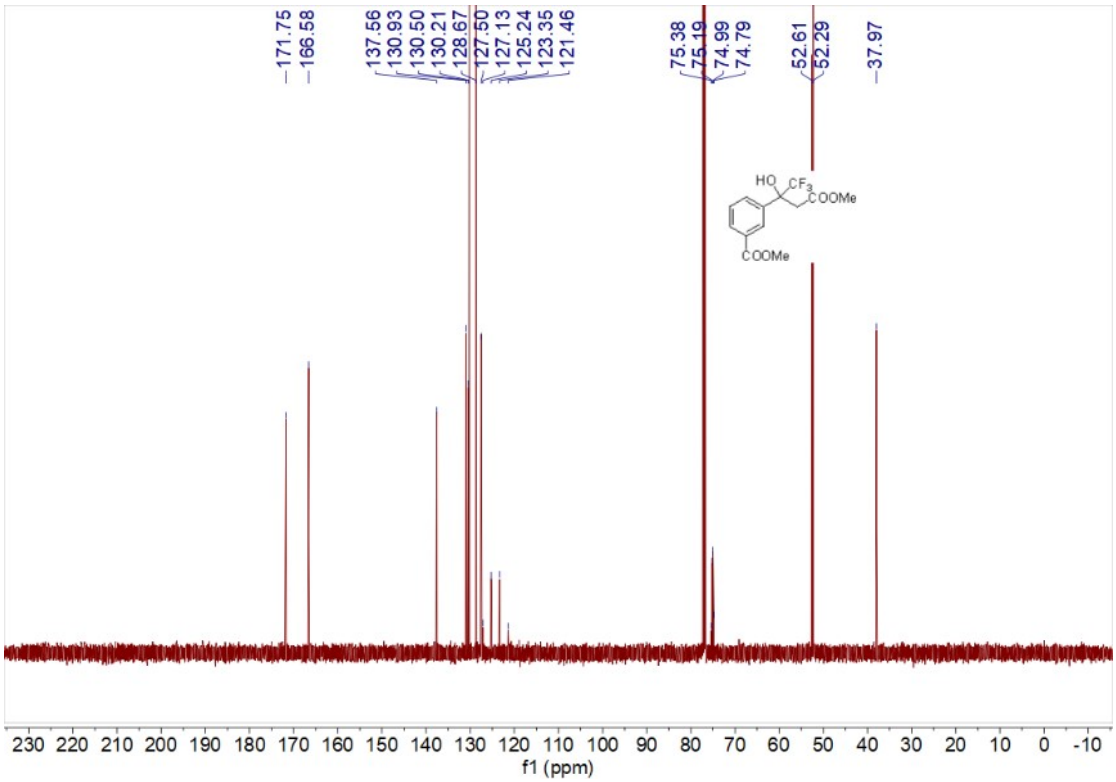


Methyl 3-(1,1,1-trifluoro-2-hydroxy-4-methoxy-4-oxobutan-2-yl)benzoate (3k)

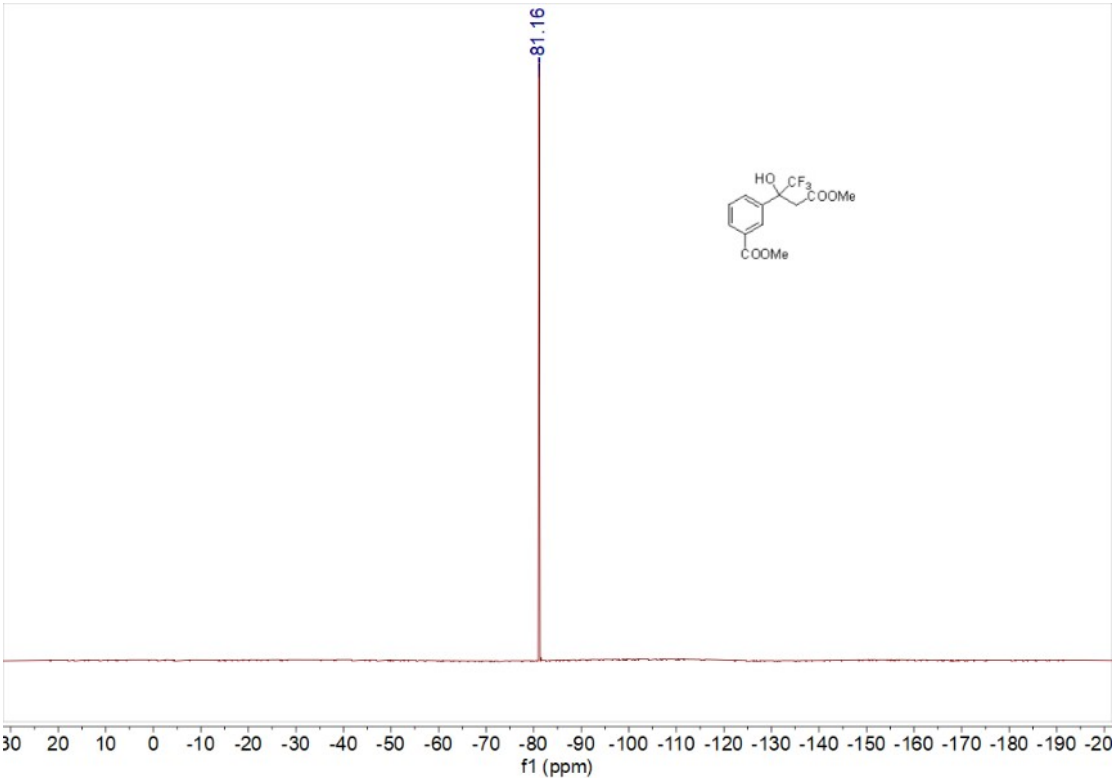
^{1}H NMR of 3k



^{13}C NMR of 3k

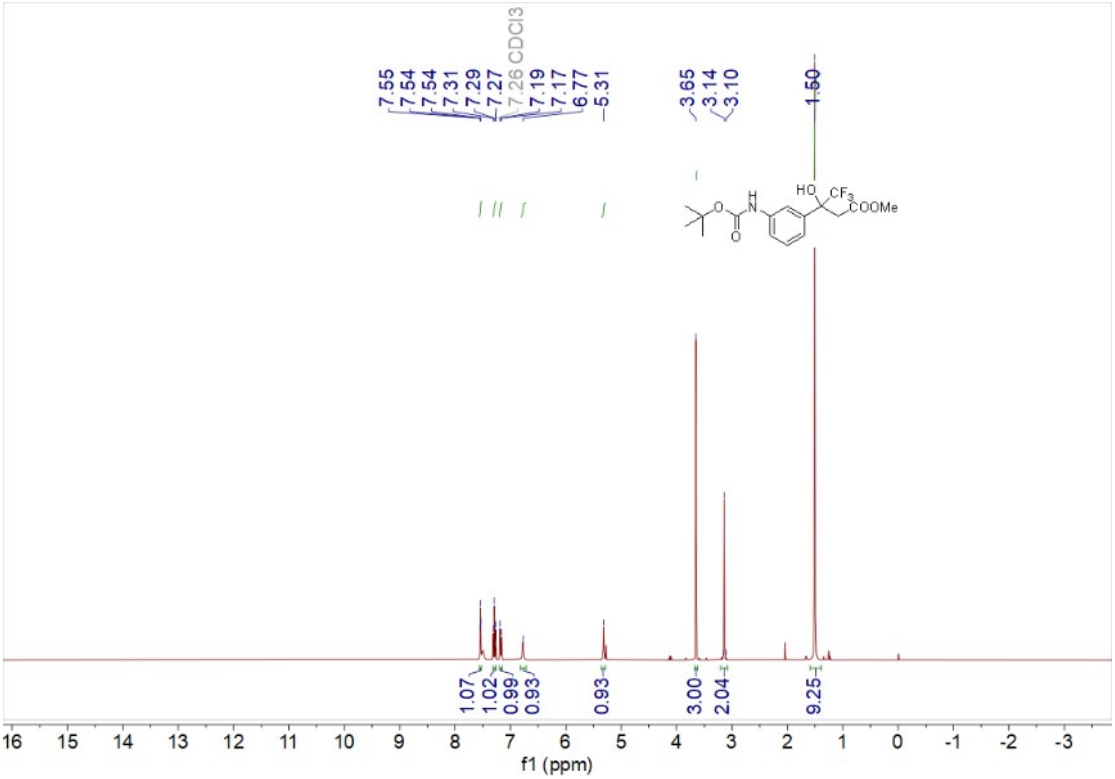


^{19}F NMR of 3k

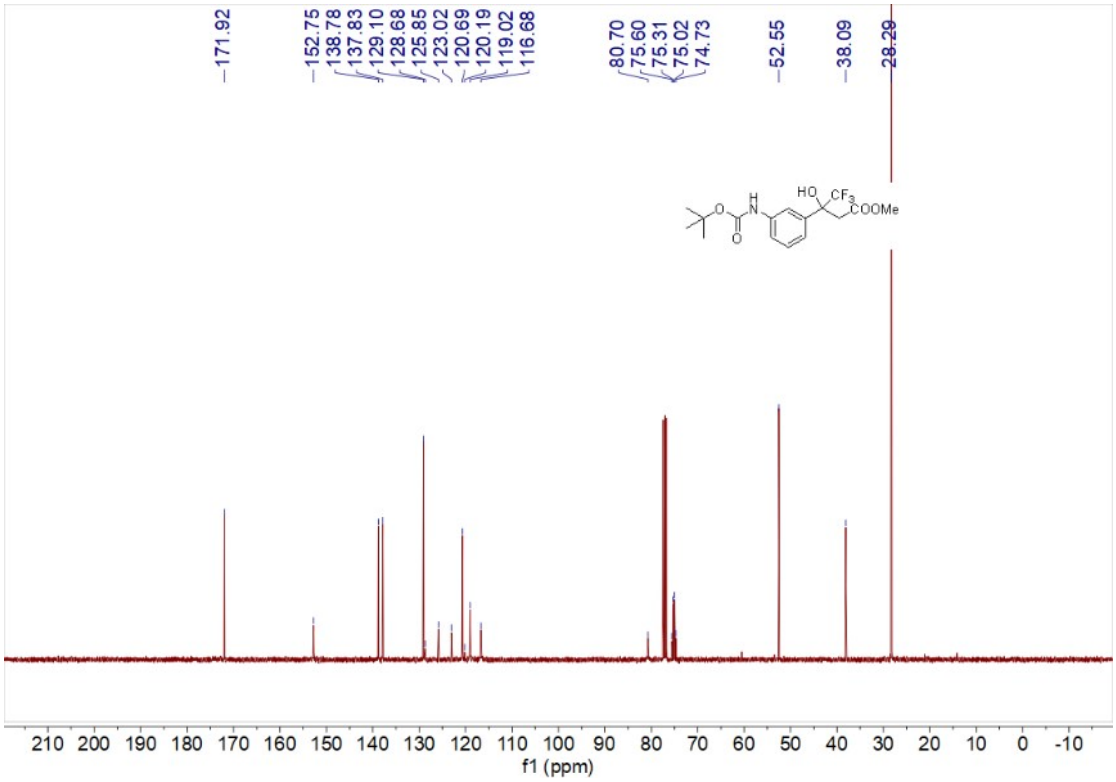


Methyl 3-(3-((*tert*-butoxycarbonyl)amino)phenyl)-4,4,4-trifluoro-3-hydroxybutanoate (3l)

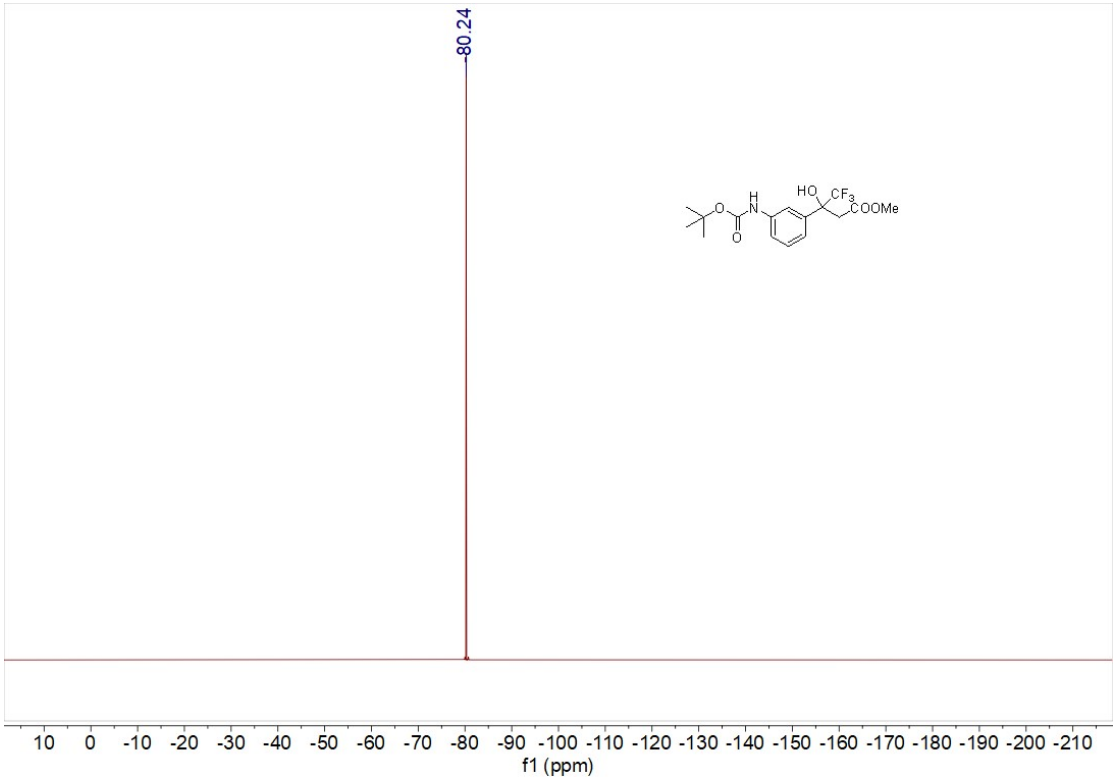
^{1}H NMR of 3l



^{13}C NMR of 3l

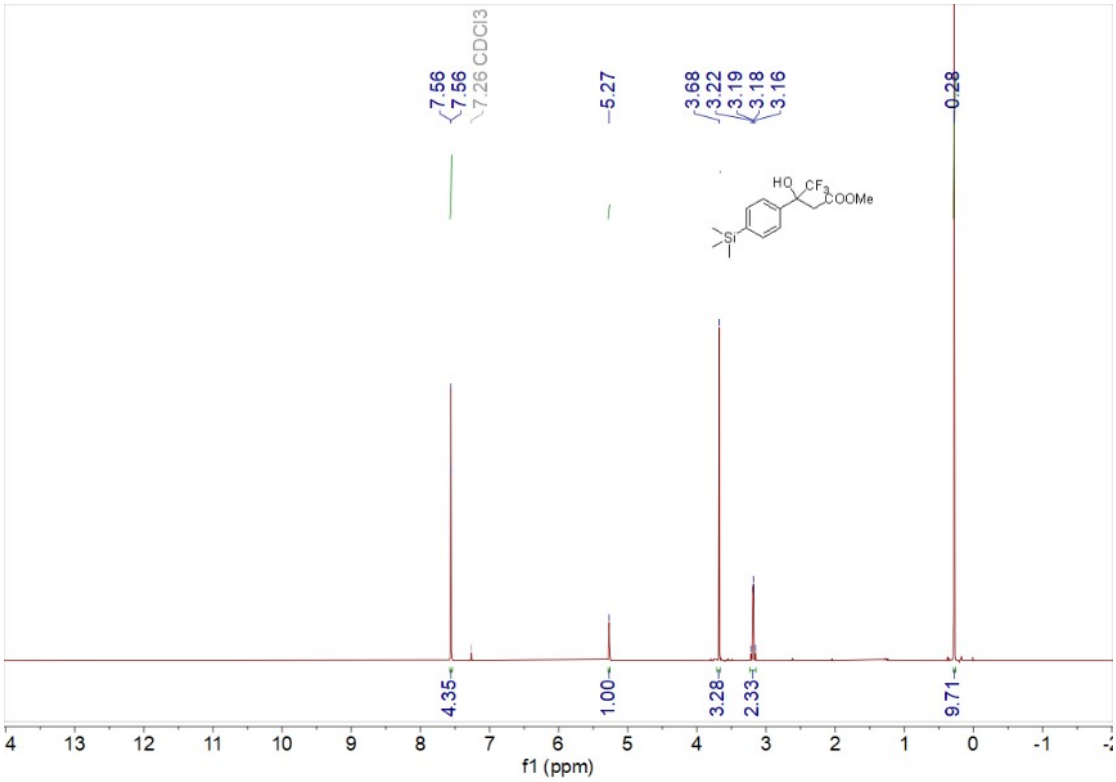


^{19}F NMR of 3l

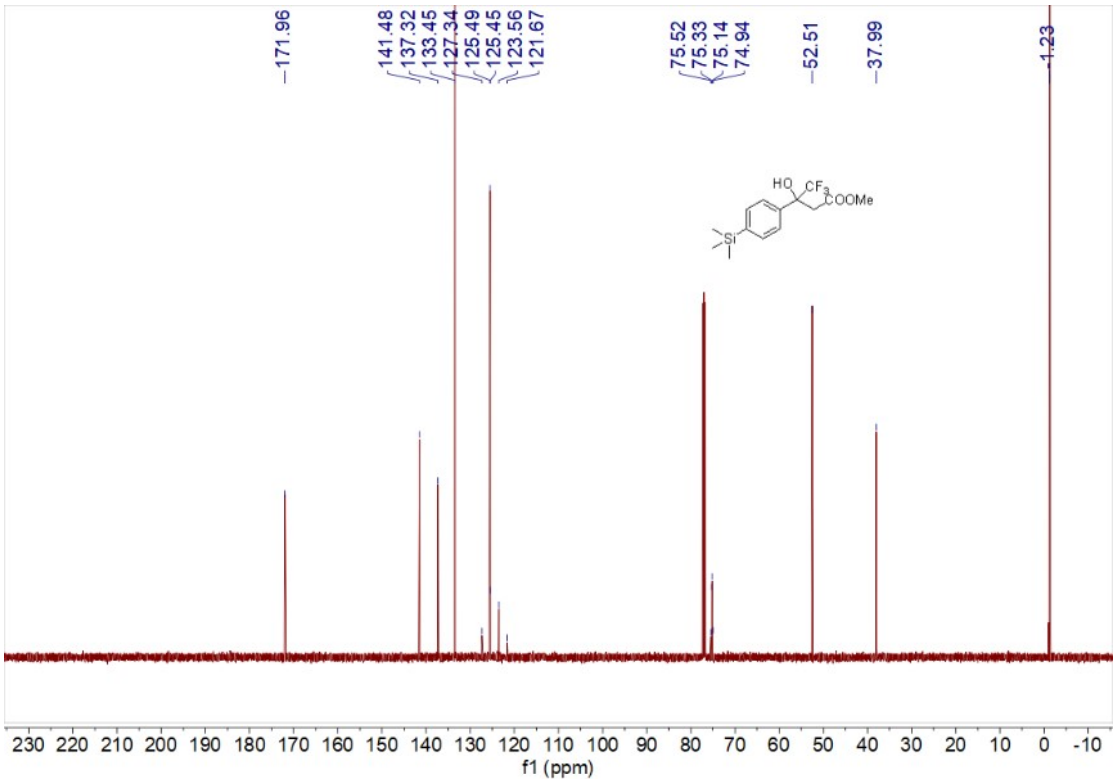


Methyl 4,4,4-trifluoro-3-hydroxy-3-(4-(trimethylsilyl)phenyl)butanoate (3m)

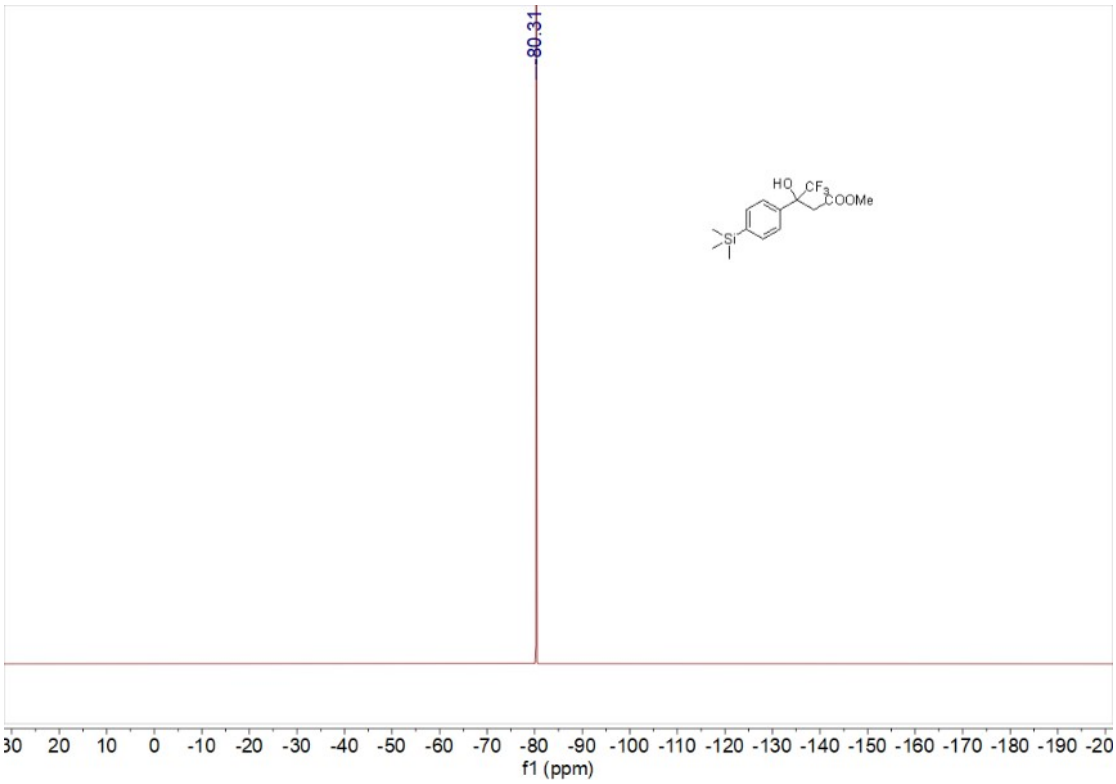
^{1}H NMR of 3m



^{13}C NMR of 3m

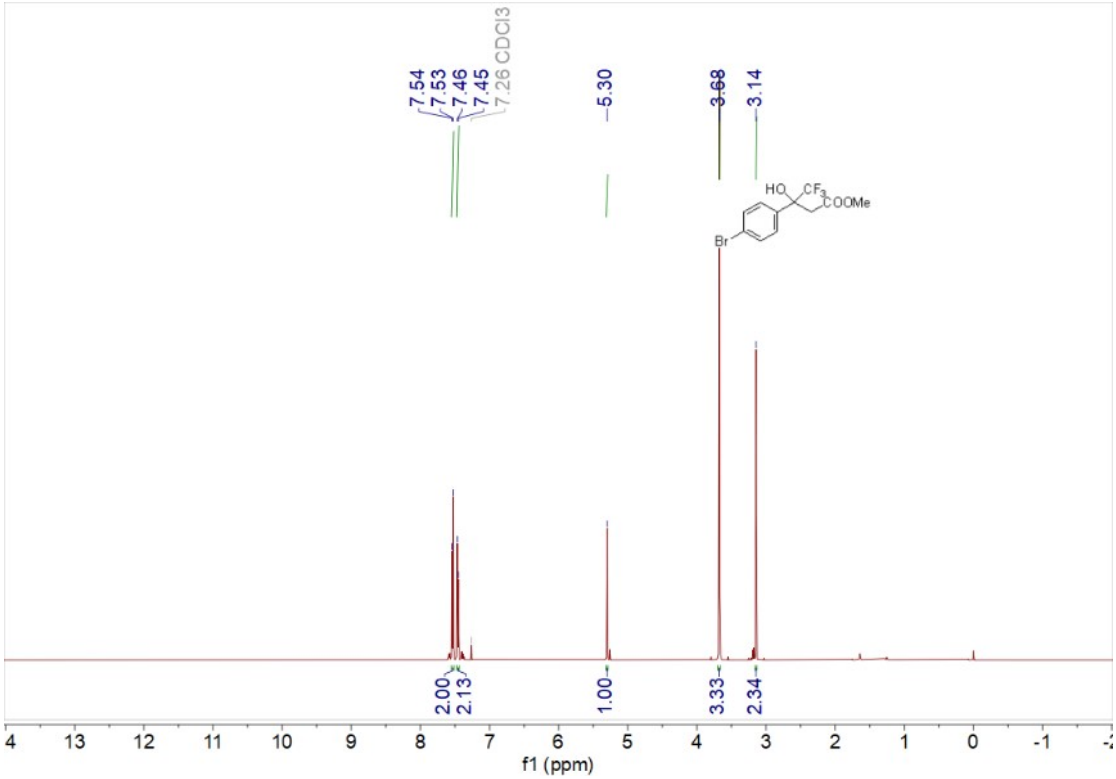


^{19}F NMR of 3m

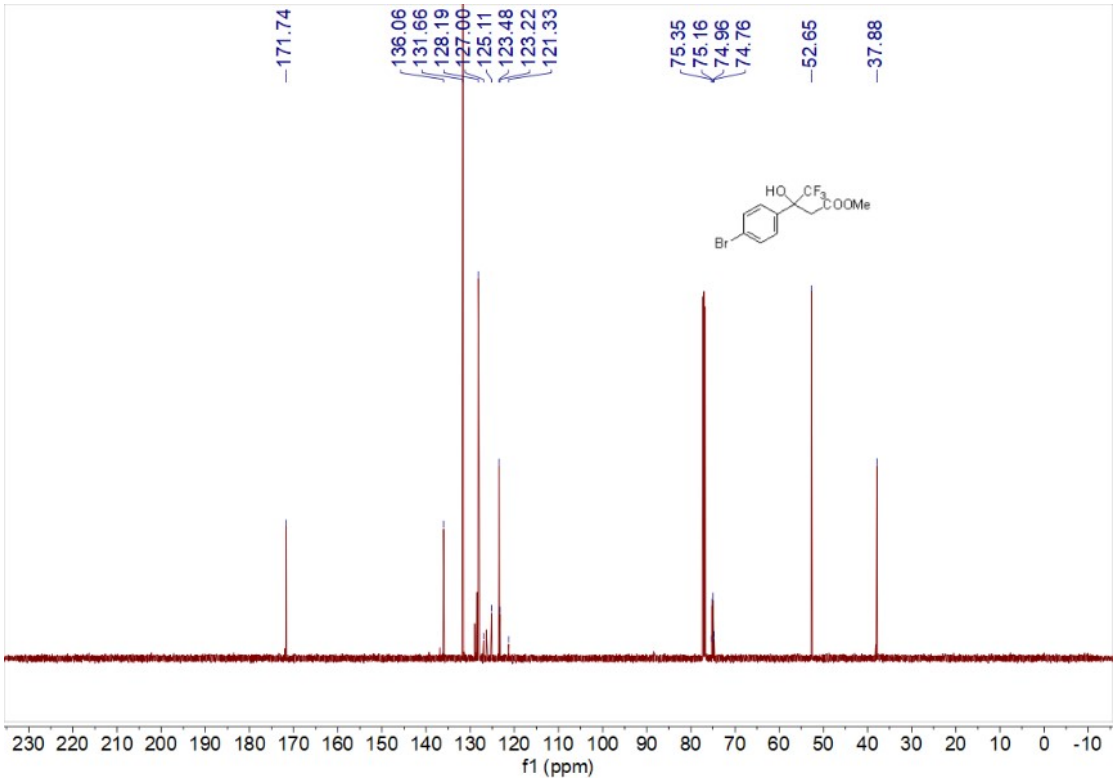


Methyl 3-(4-bromophenyl)-4,4,4-trifluoro-3-hydroxybutanoate (3n)

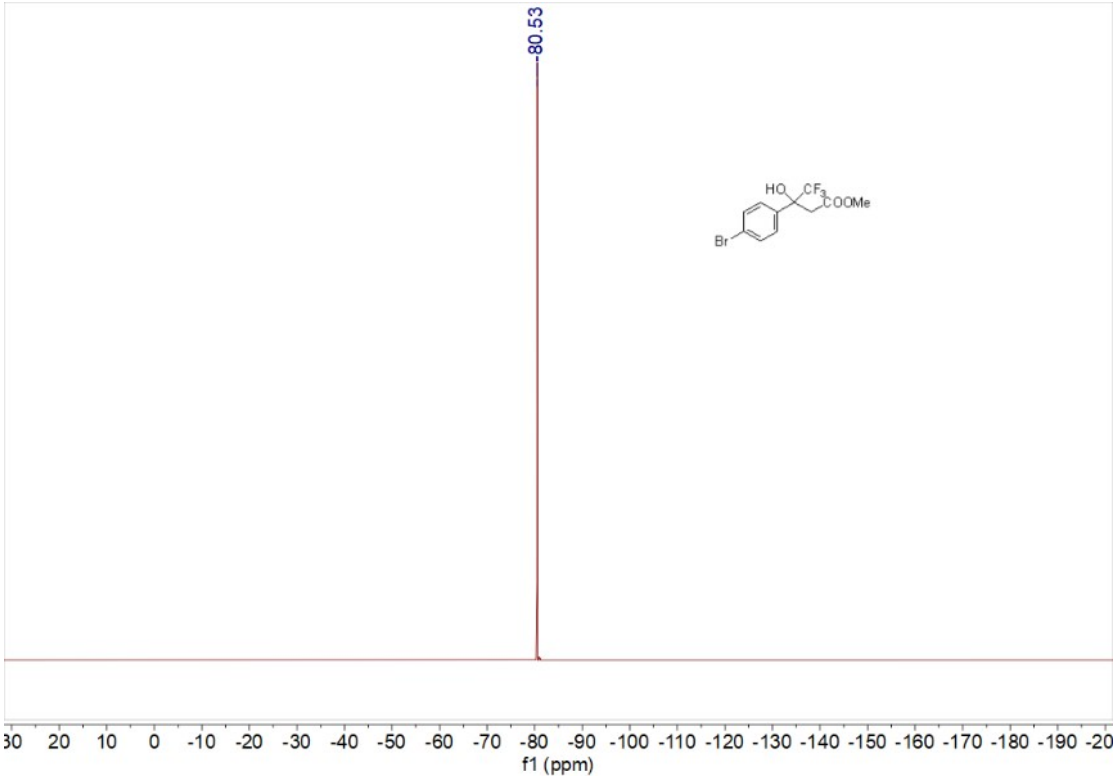
^{1}H NMR of 3n



^{13}C NMR of 3n

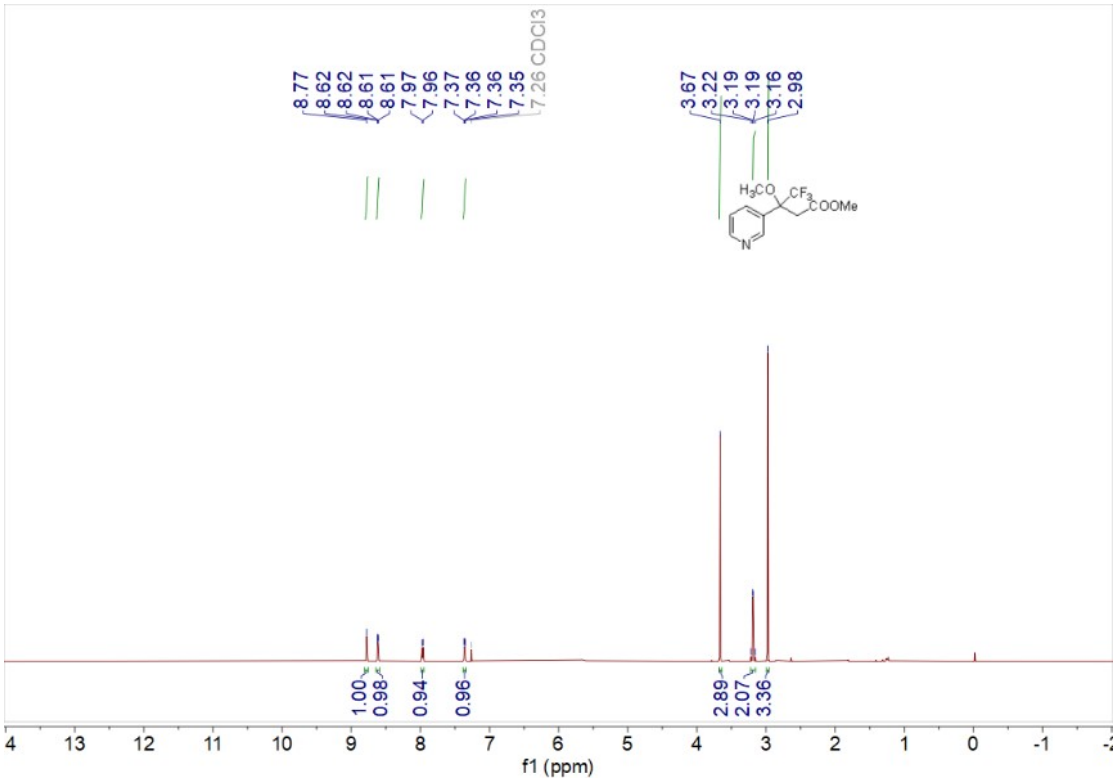


^{19}F NMR of 3n

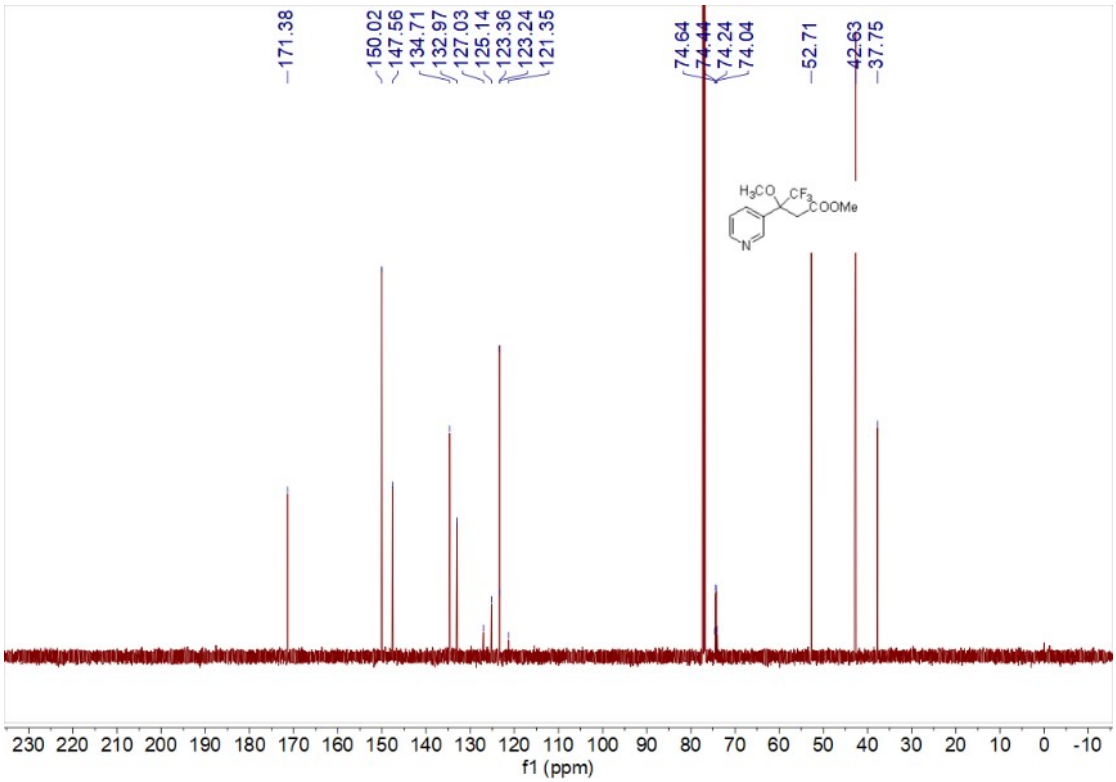


Methyl 4,4,4-trifluoro-3-hydroxy-3-(pyridin-4-yl)butanoate (3o)

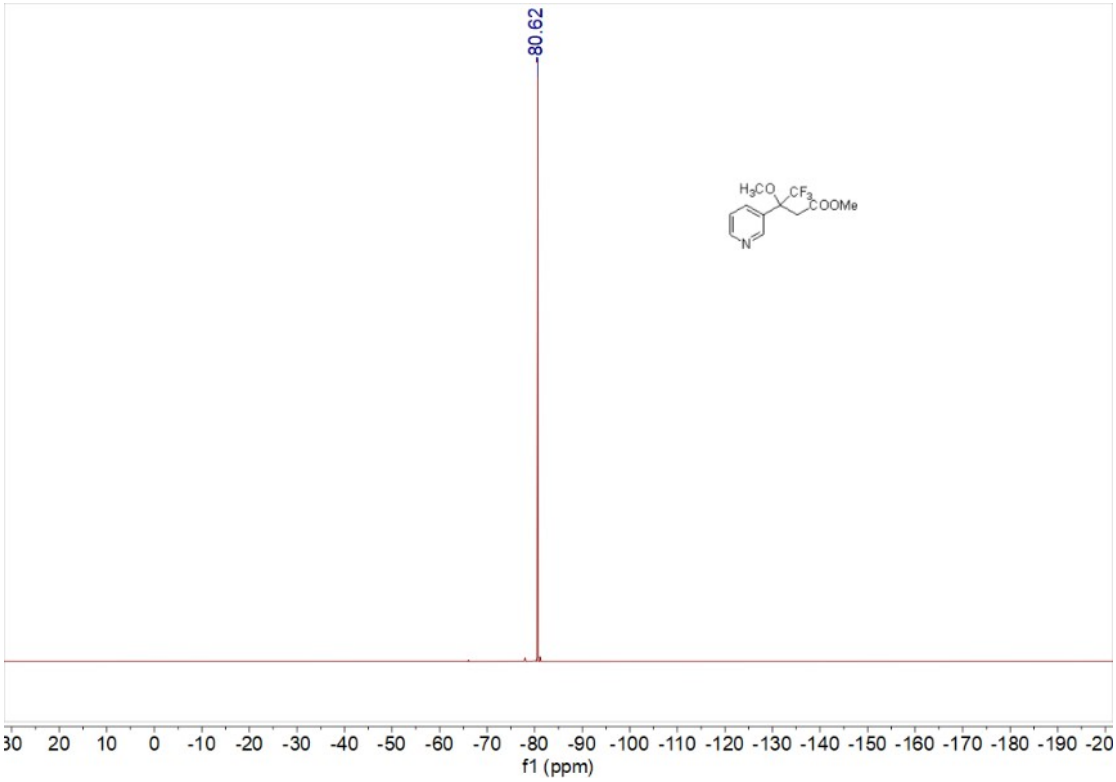
^{1}H NMR of 3o



^{13}C NMR of 3o

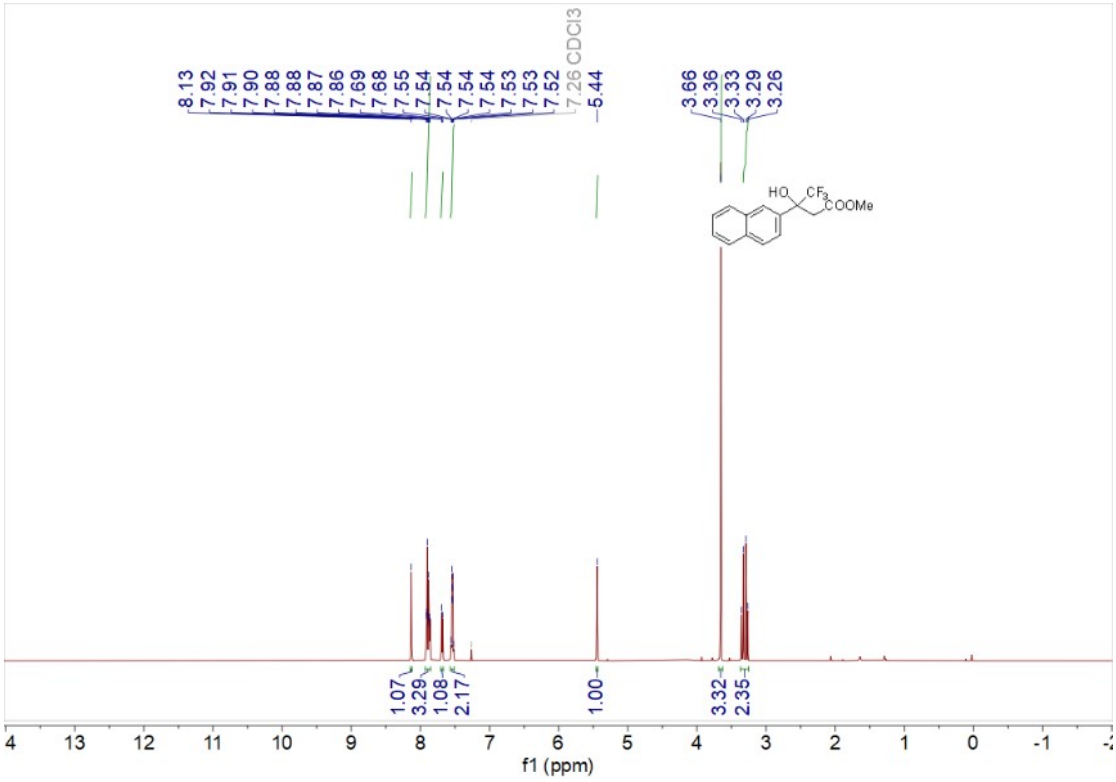


^{19}F NMR of 3o

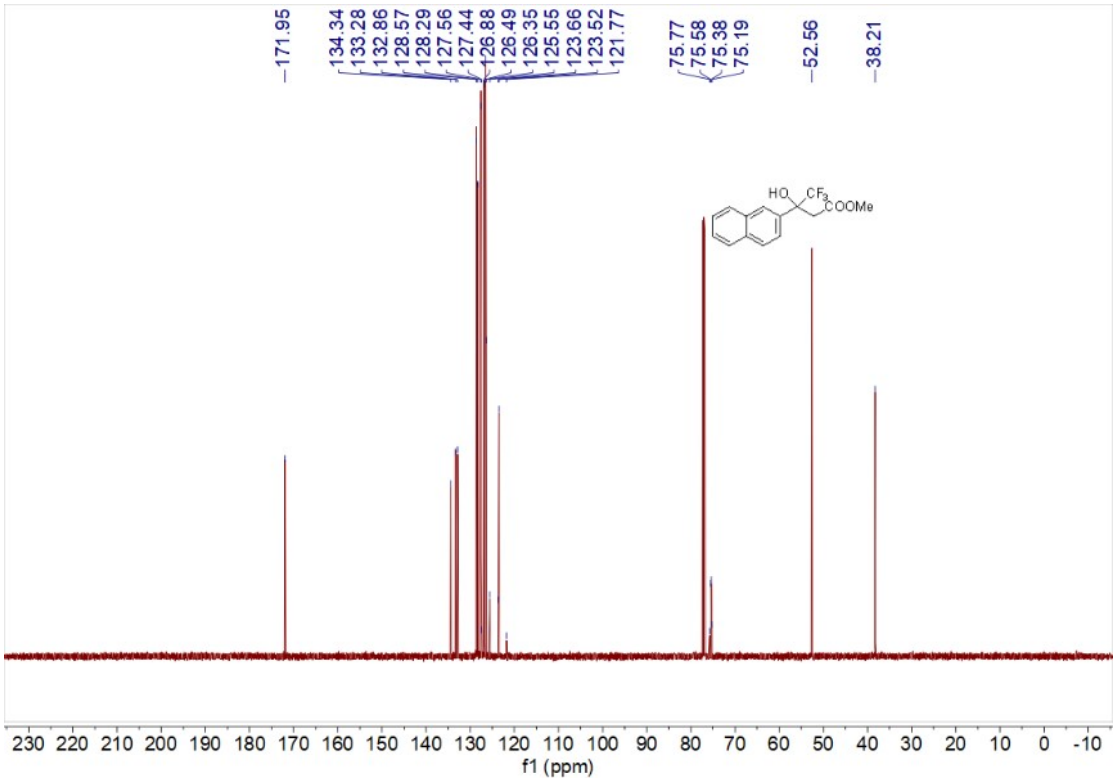


Methyl 4,4,4-trifluoro-3-hydroxy-3-(naphthalen-2-yl)butanoate (3p)

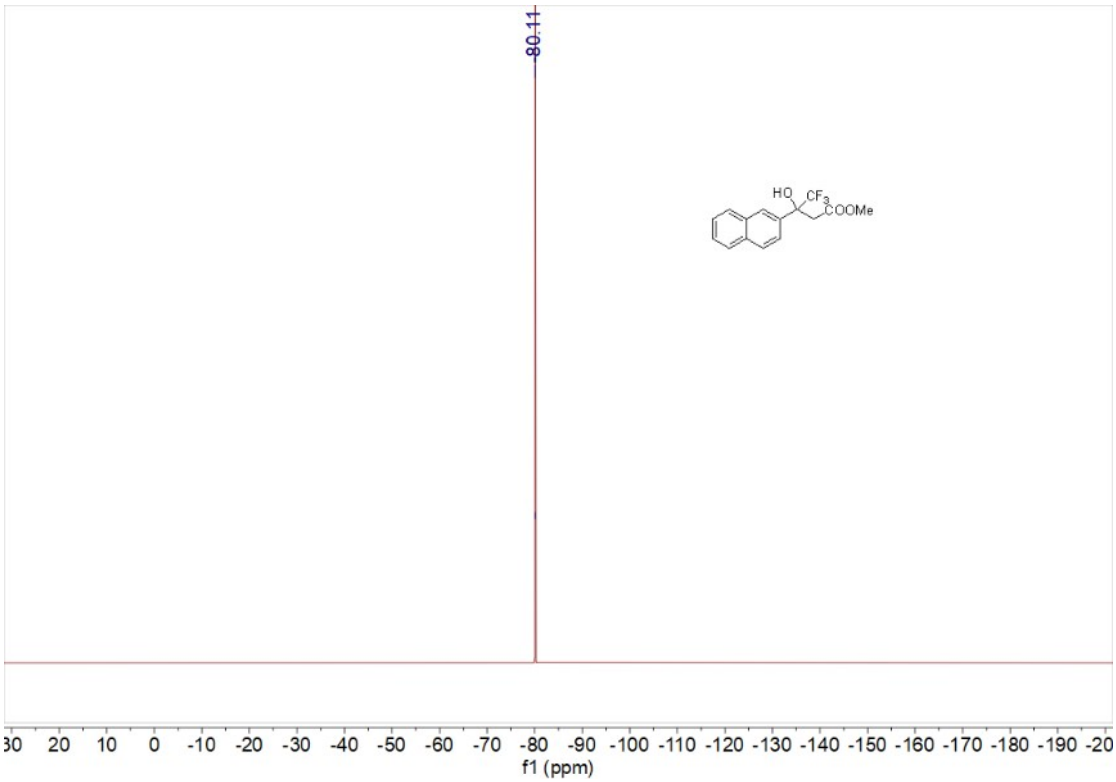
^{1}H NMR of 3p



^{13}C NMR of 3p

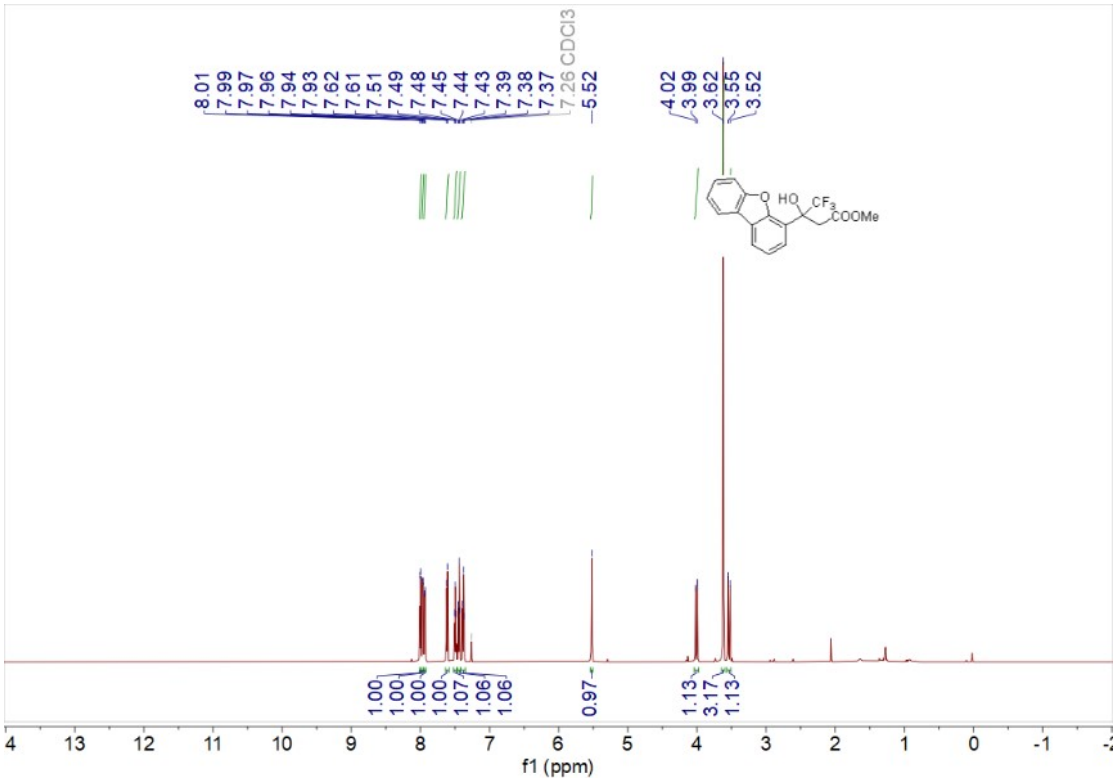


^{19}F NMR of 3p

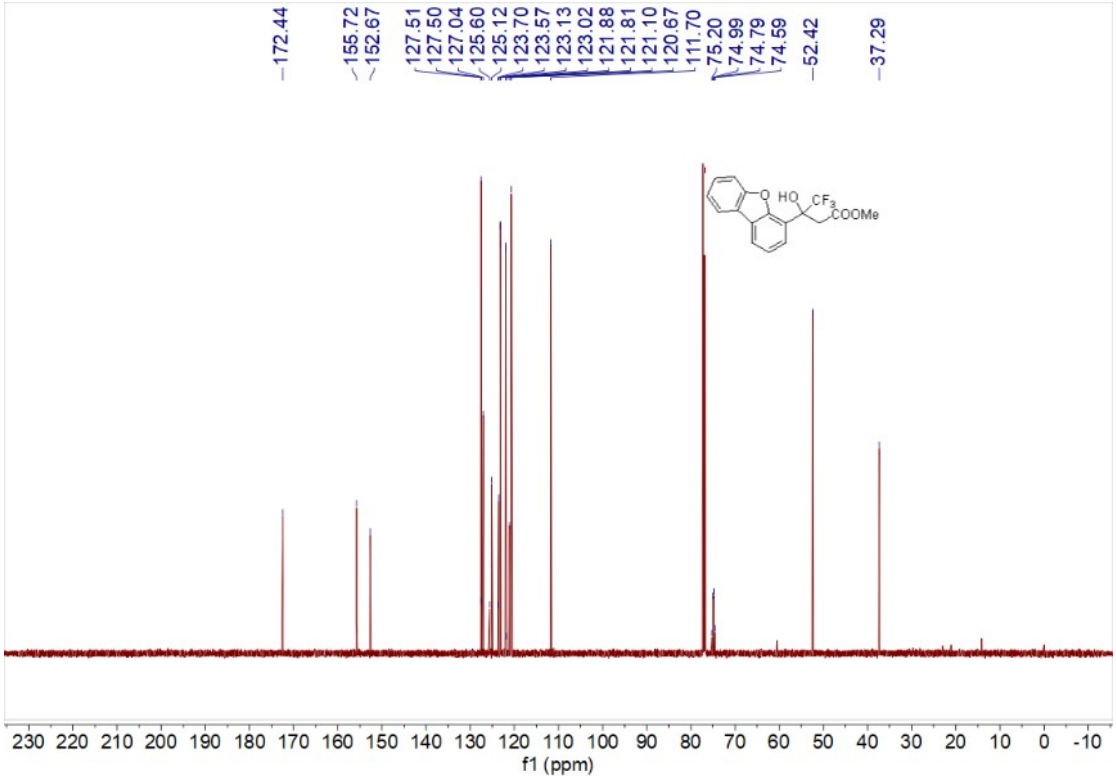


Methyl 3-(dibenzo[b,d]furan-4-yl)-4,4,4-trifluoro-3-hydroxybutanoate (3q)

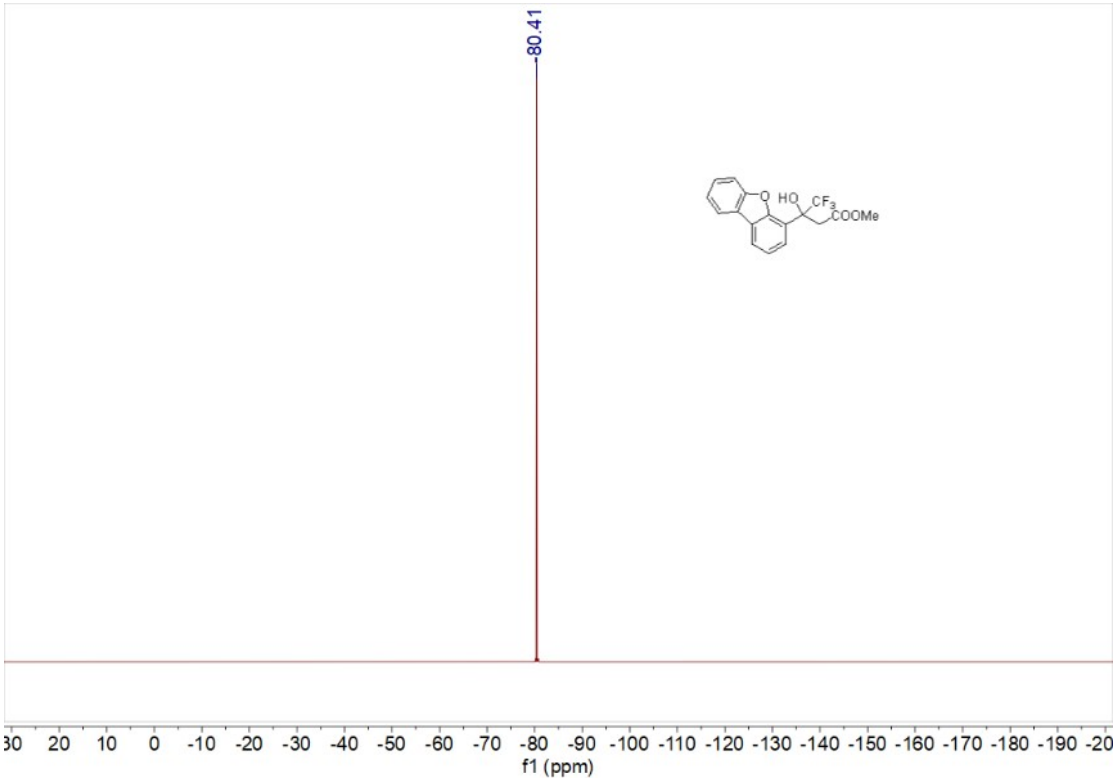
^{1}H NMR of 3q



^{13}C NMR of 3q

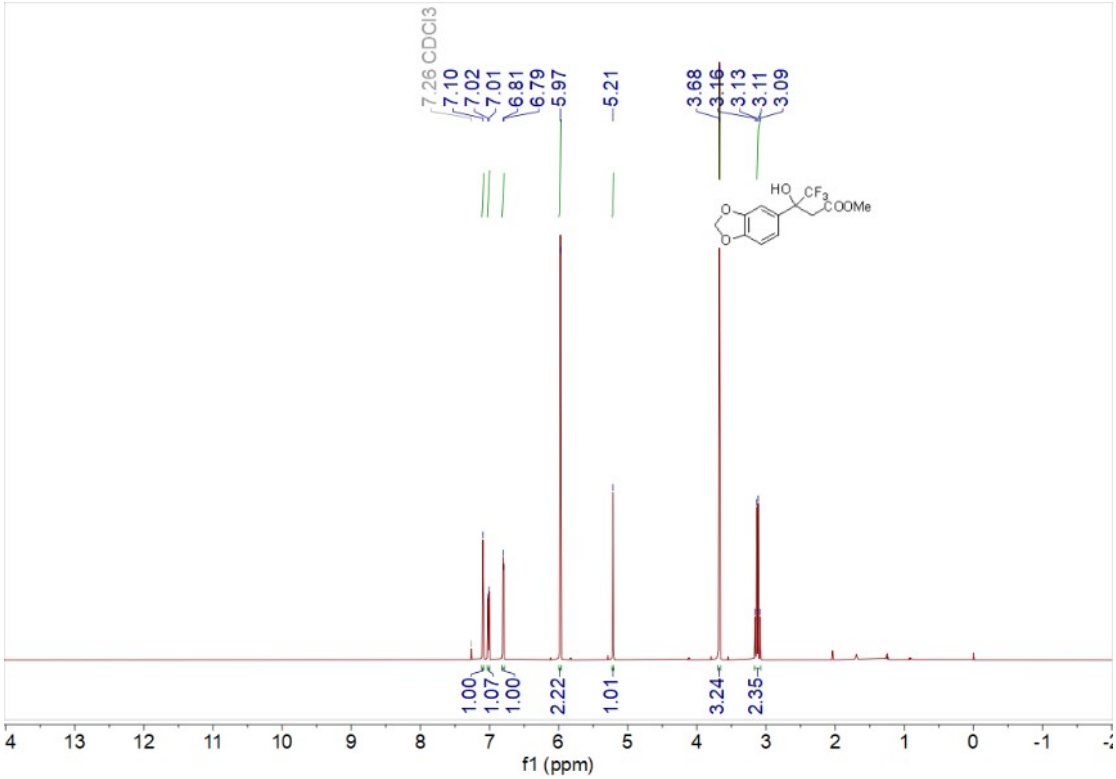


^{19}F NMR of 3q

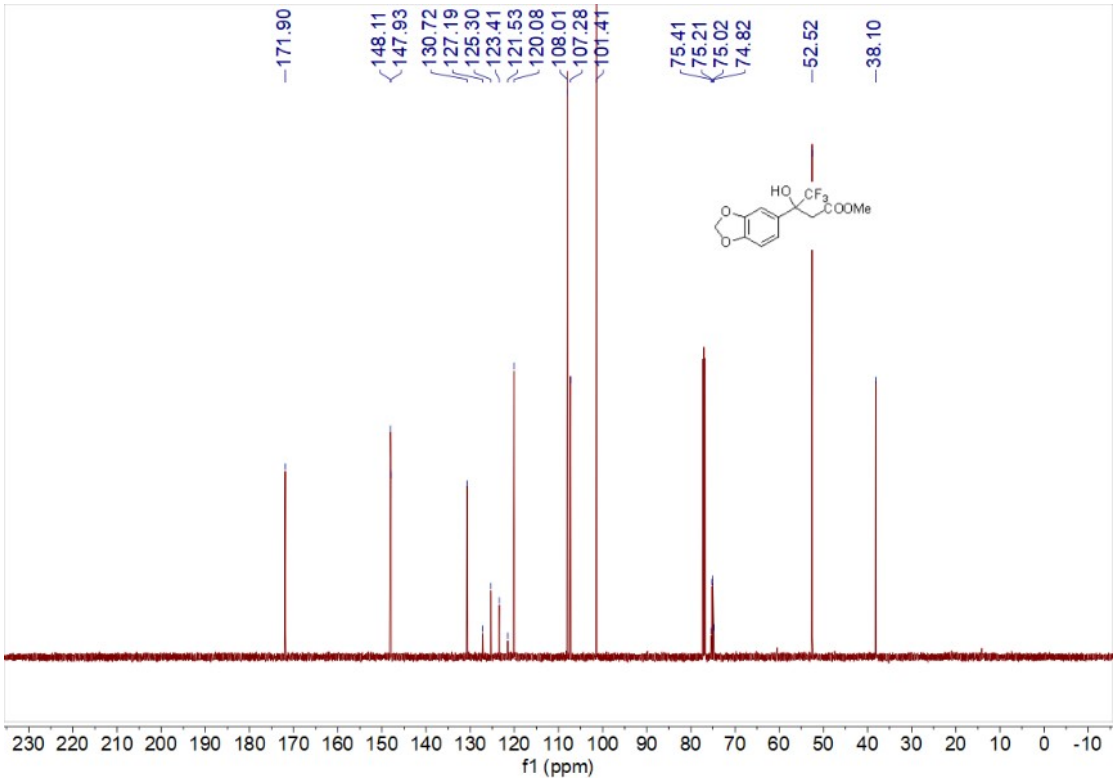


Methyl 3-(benzo[*d*][1,3]dioxol-5-yl)-4,4,4-trifluoro-3-hydroxybutanoate (3r)

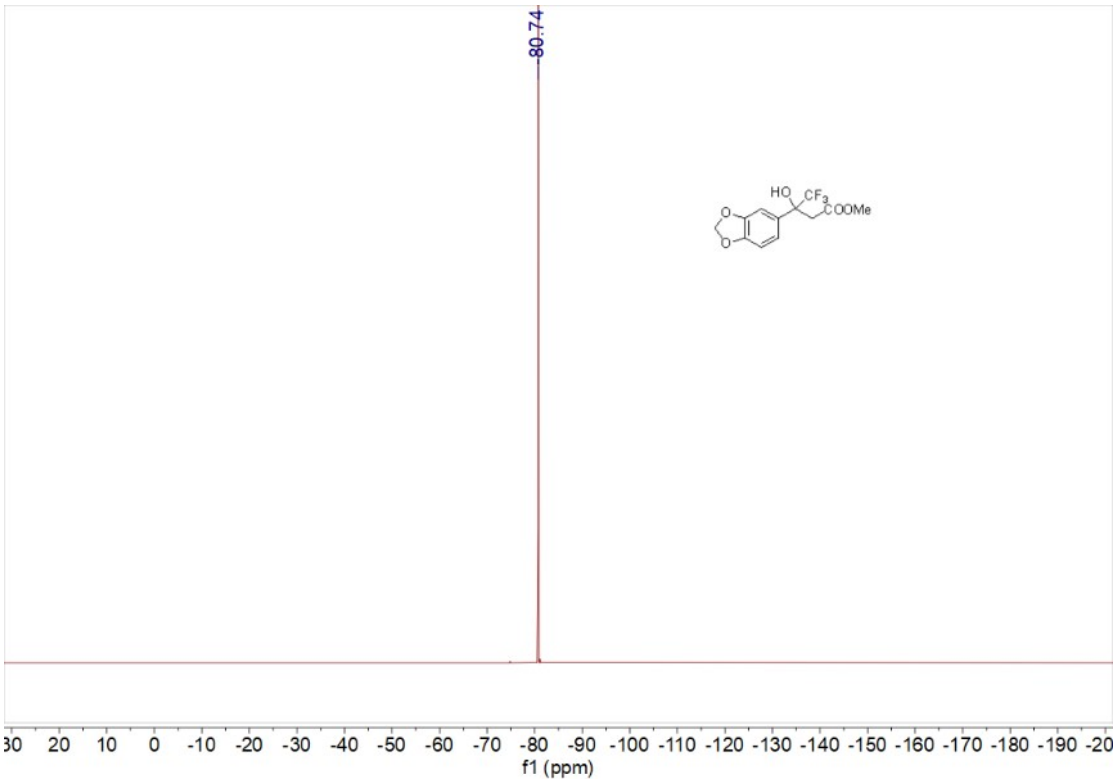
^{1}H NMR of 3r



^{13}C NMR of 3r

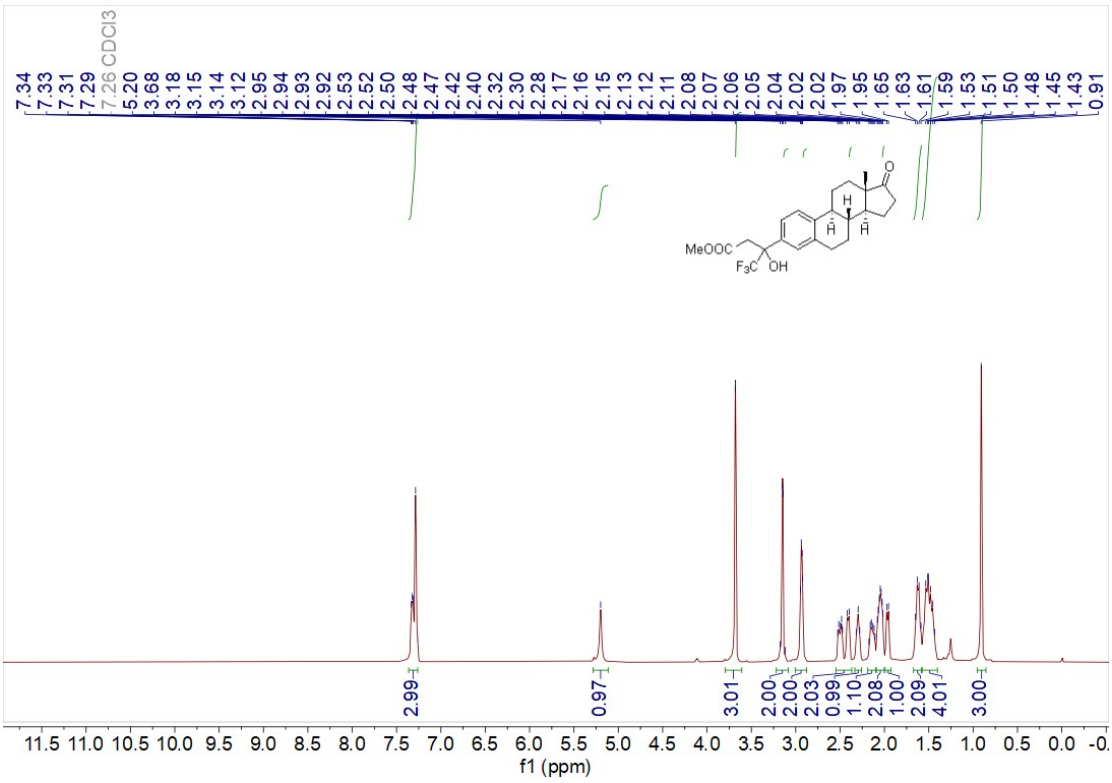


^{19}F NMR of 3r

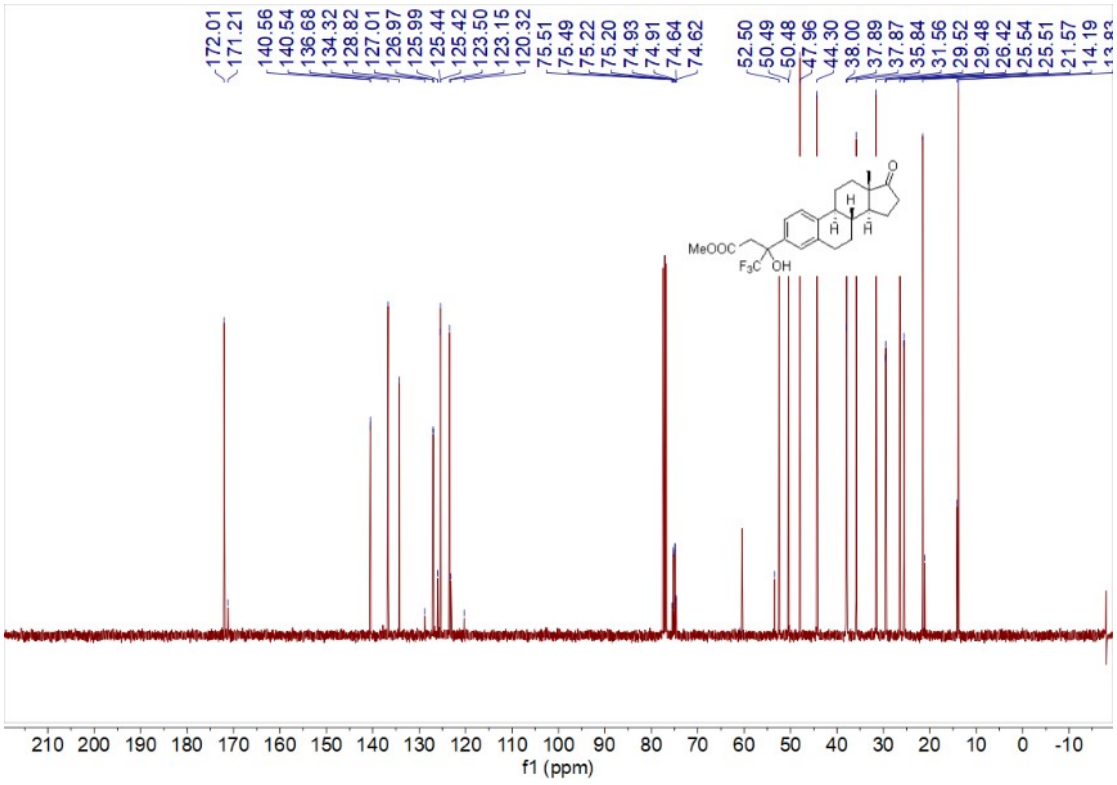


Methyl 4,4,4-trifluoro-3-hydroxy-3-((8*R*,9*S*,13*S*,14*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)butanoate (3s)

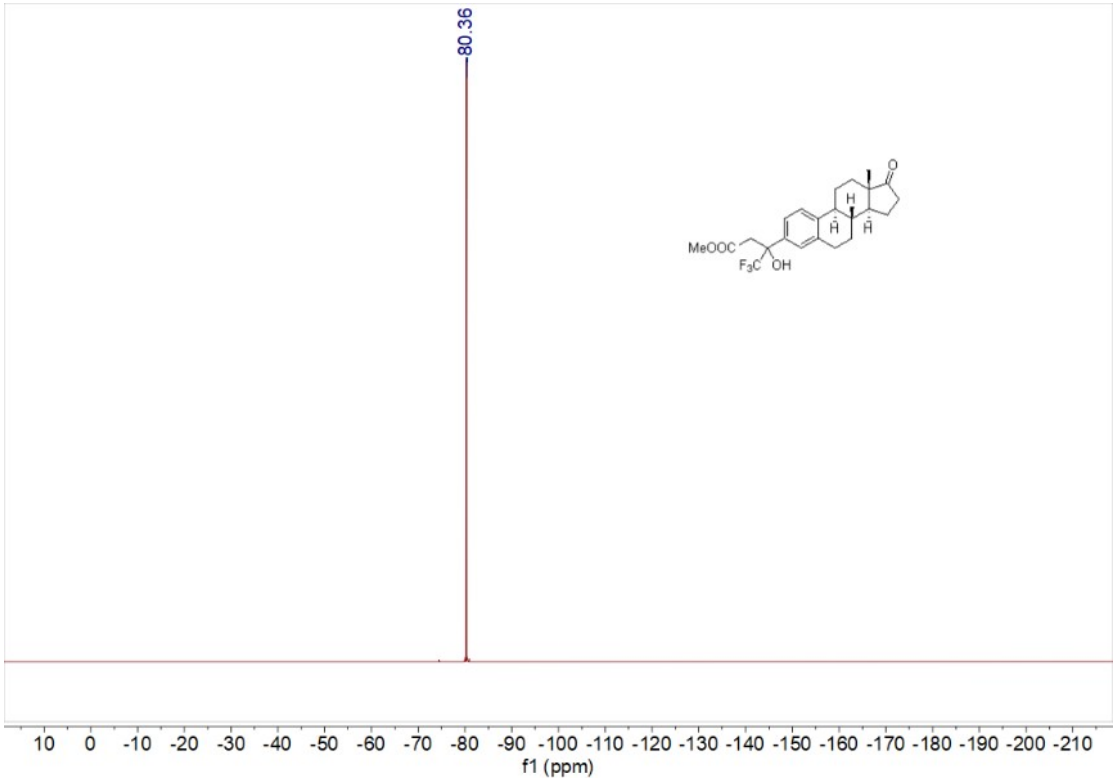
^{1}H NMR of 3s



^{13}C NMR of 3s

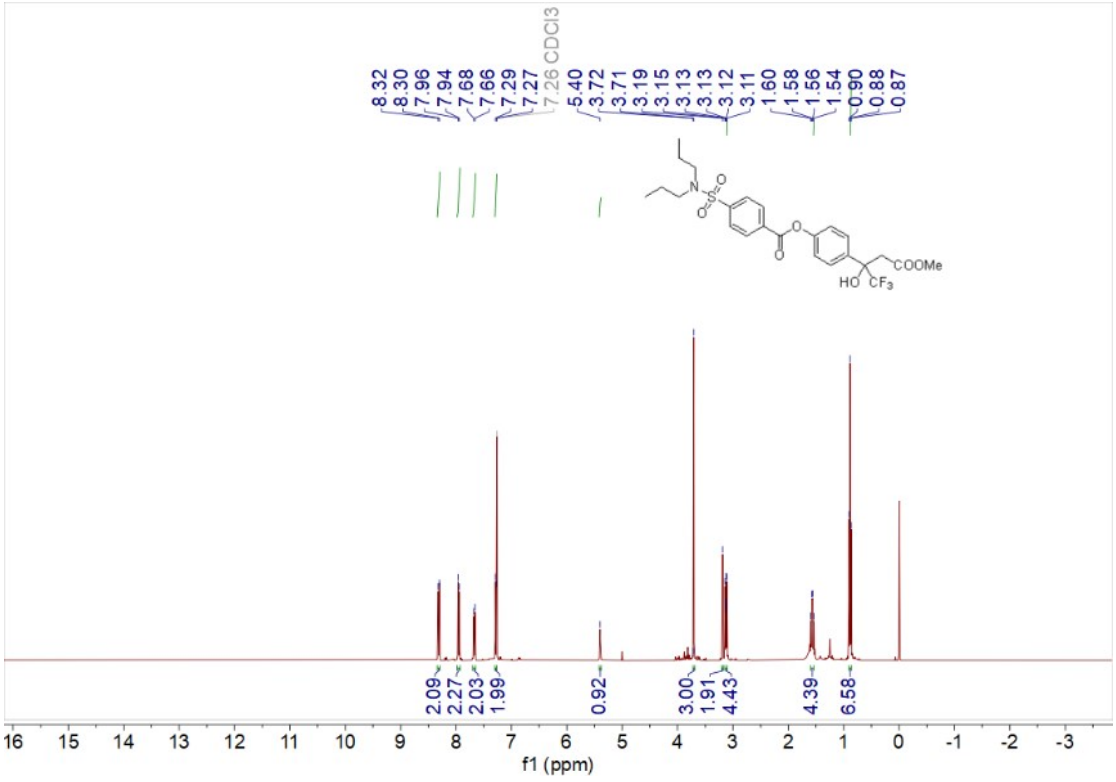


^{19}F NMR of 3s

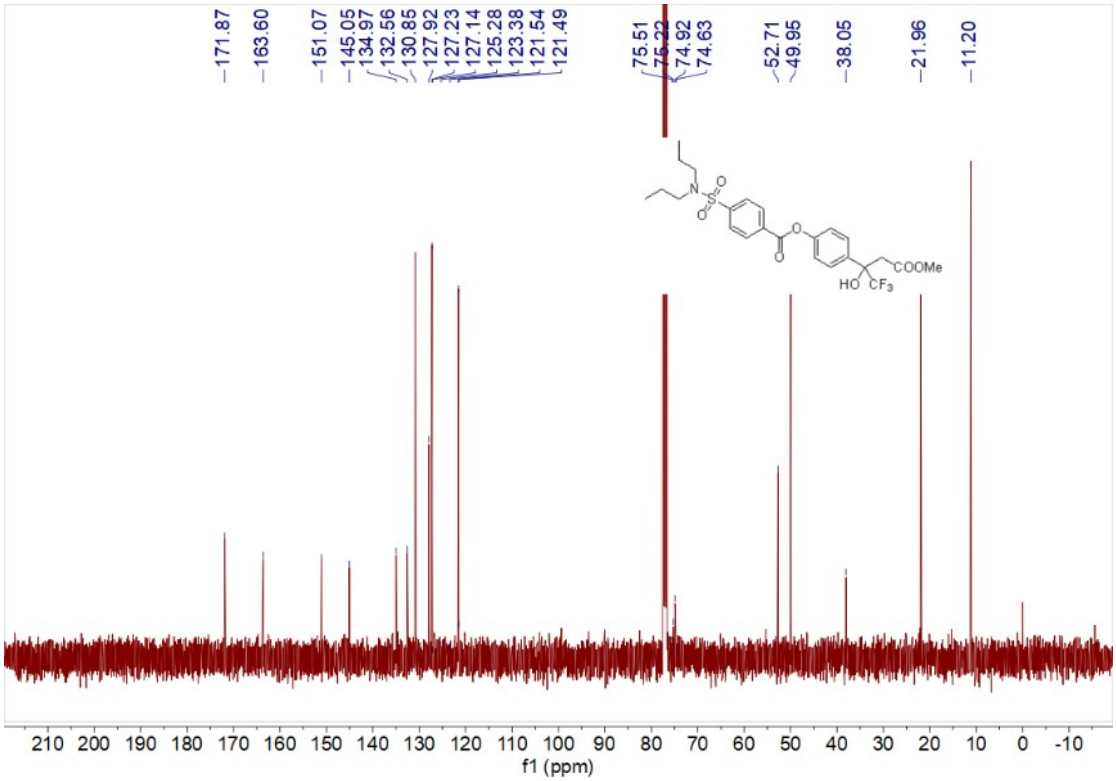


3-(1,1,1-trifluoro-2-hydroxy-4-methoxy-4-oxobutan-2-yl)phenyl 4-(*N*,*N*-dipropylsulfamoyl)benzoate (3t)

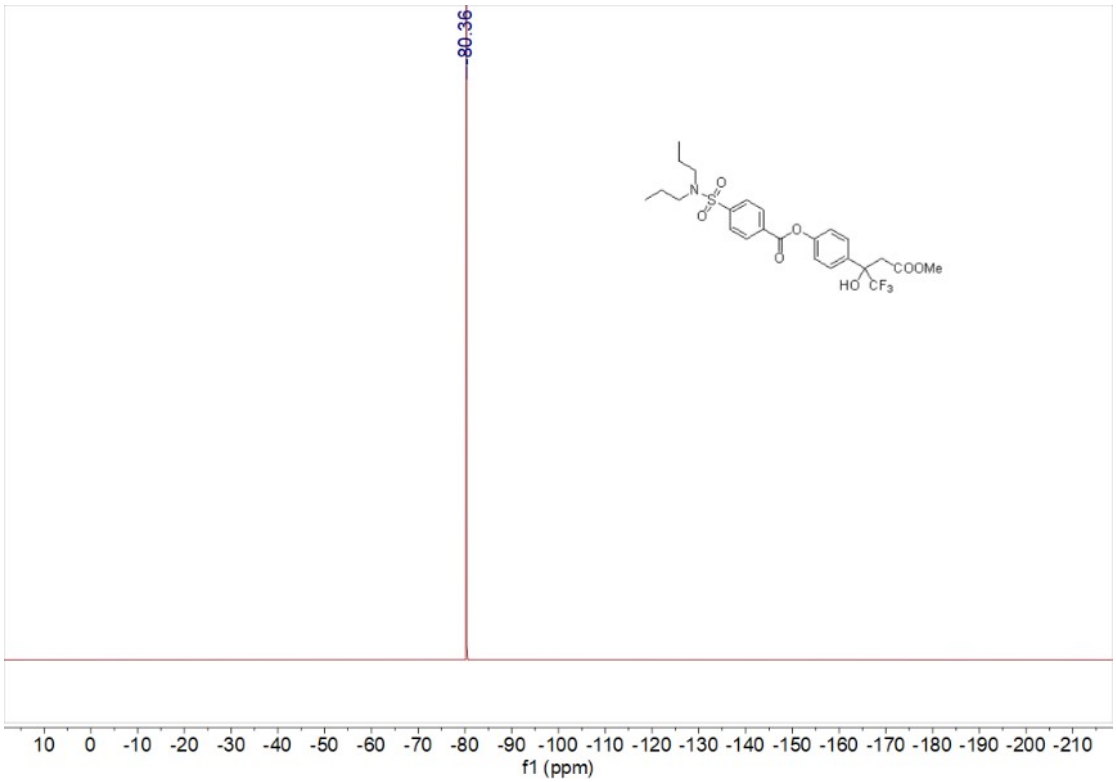
^{1}H NMR of 3t



^{13}C NMR of 3t

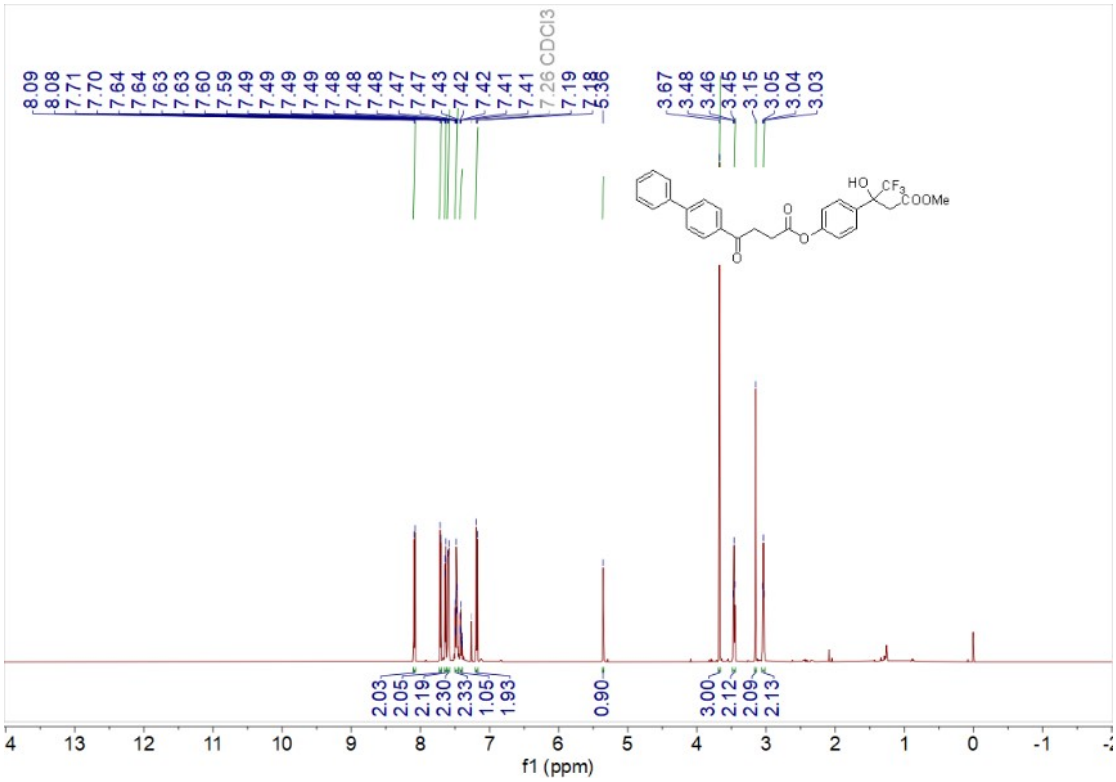


^{19}F NMR of 3t

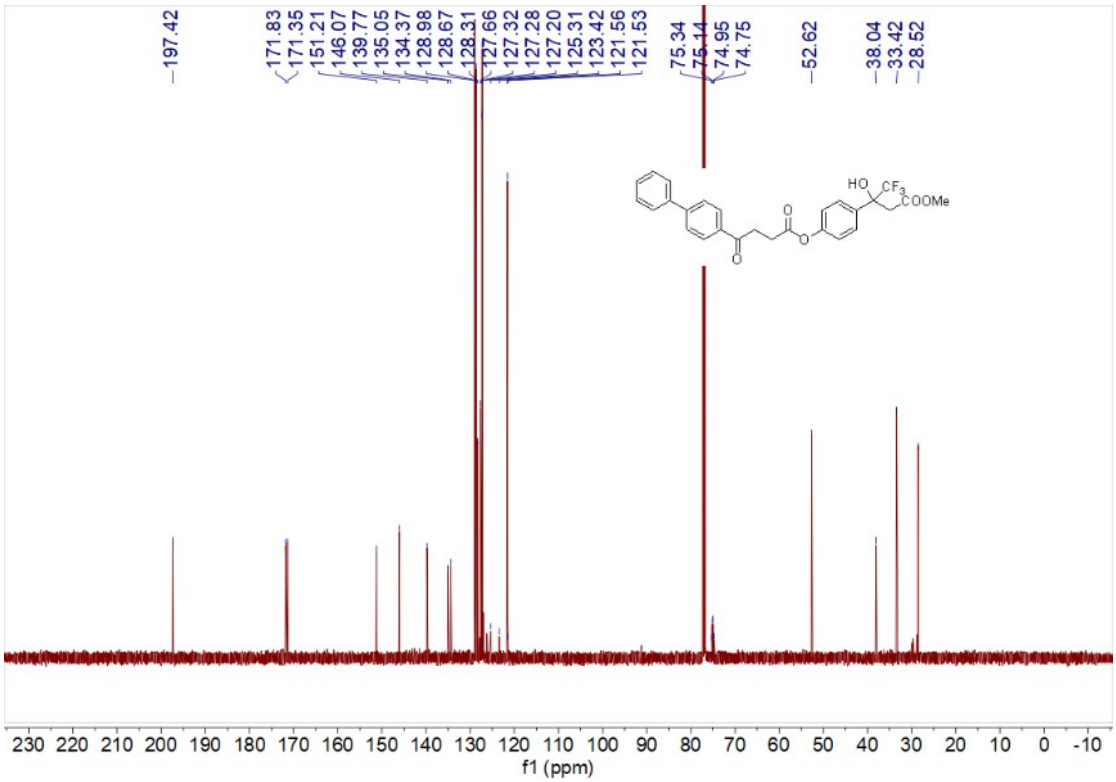


Methyl 3-(4-((4-([1,1'-biphenyl]-4-yl)-4-oxobutanoyl)oxy)phenyl)-4,4,4-trifluoro-3-hydroxybutanoate (3u)

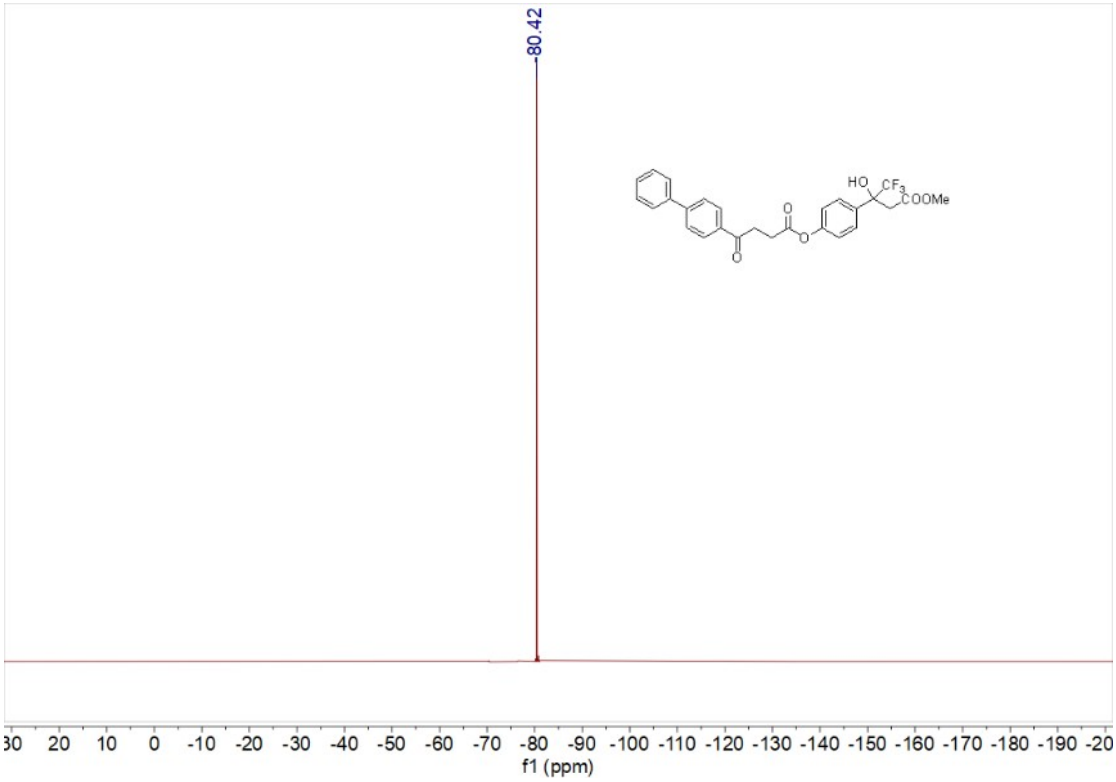
^{1}H NMR of 3u



^{13}C NMR of 3u

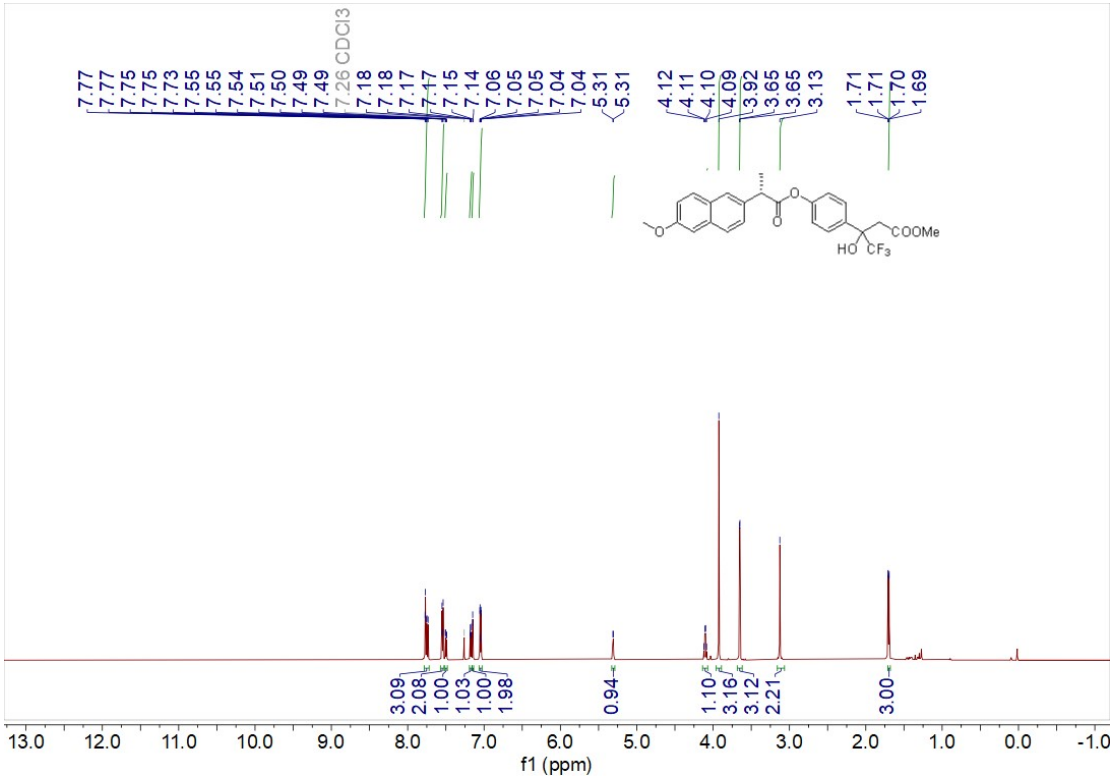


^{19}F NMR of 3u

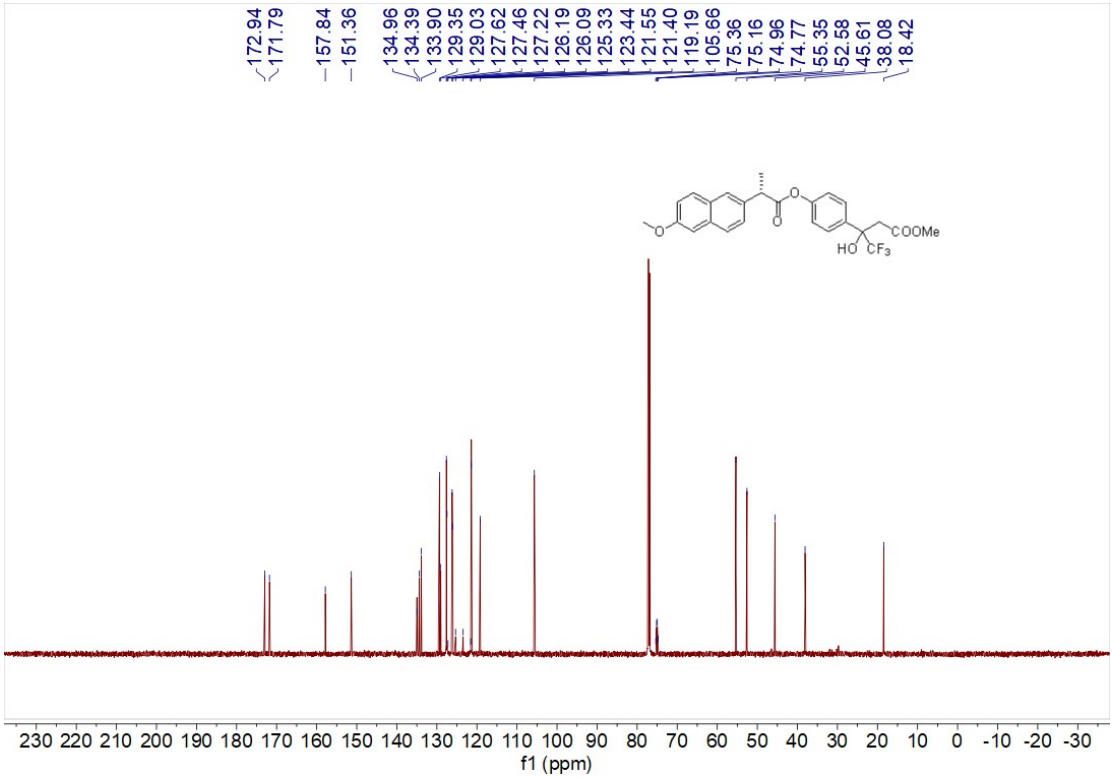


Methyl 4,4,4-trifluoro-3-hydroxy-3-(4-(((*S*)-2-(6-methoxynaphthalen-2-yl)propanoyl)oxy)phenyl)-butanoate (3v)

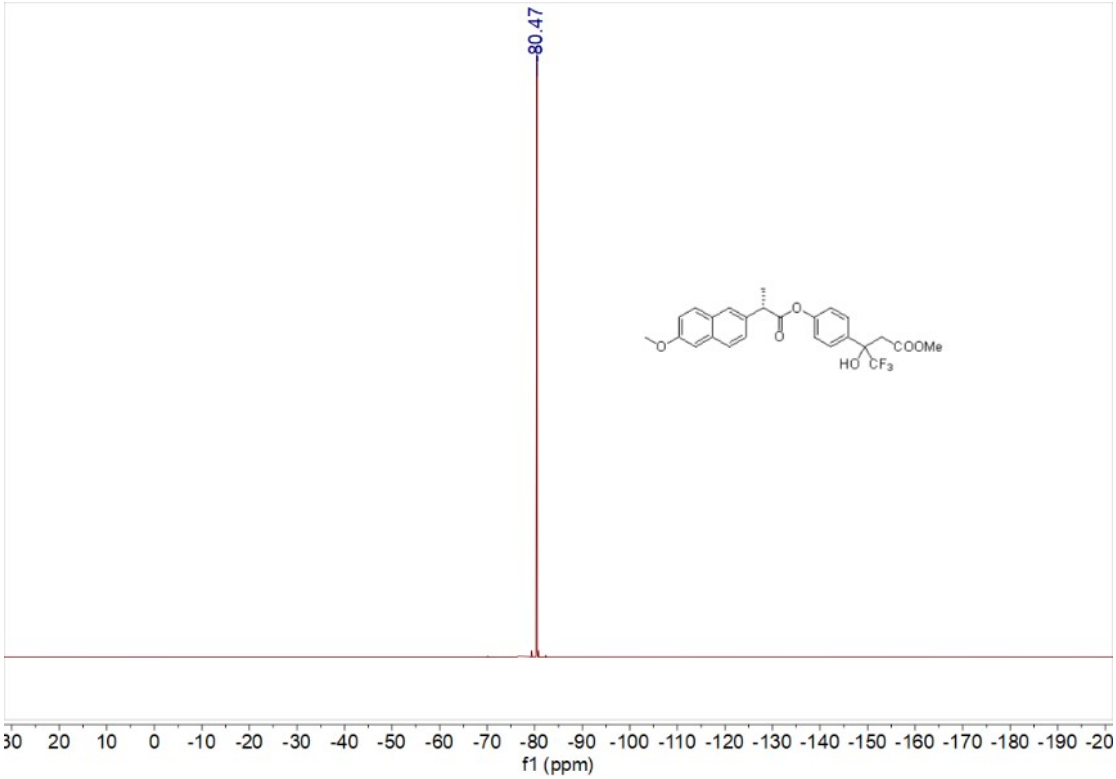
^{1}H NMR of 3v



^{13}C NMR of 3v

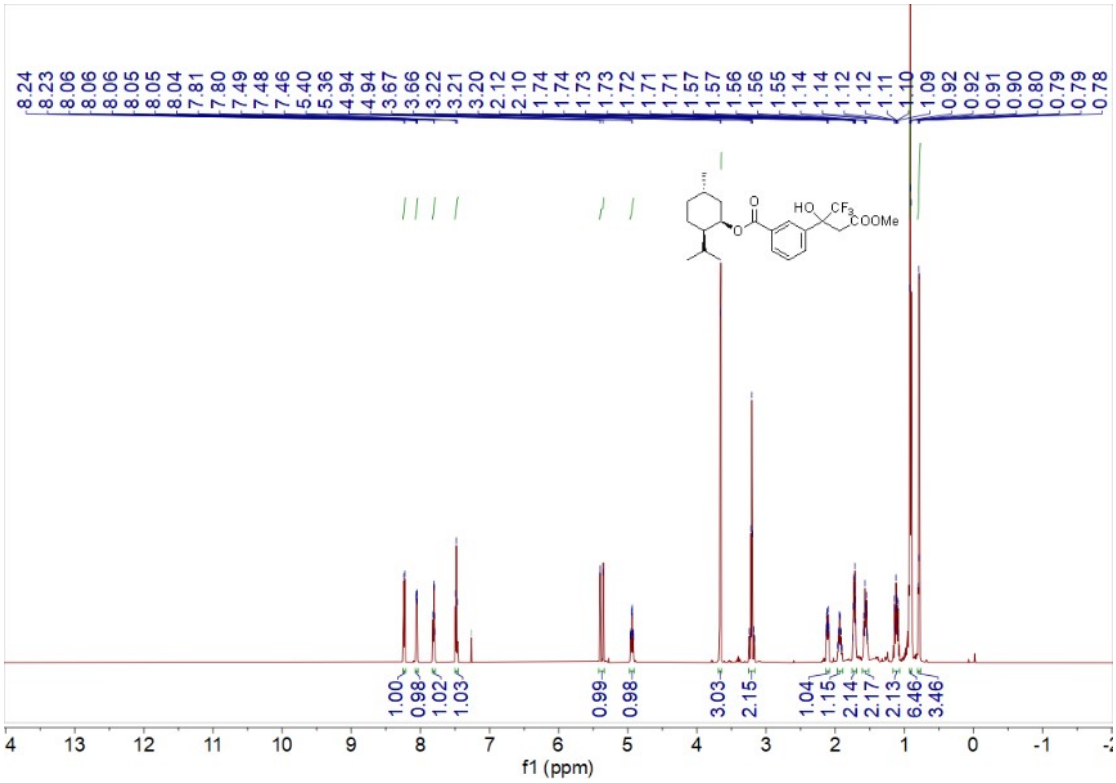


^{19}F NMR of 3v

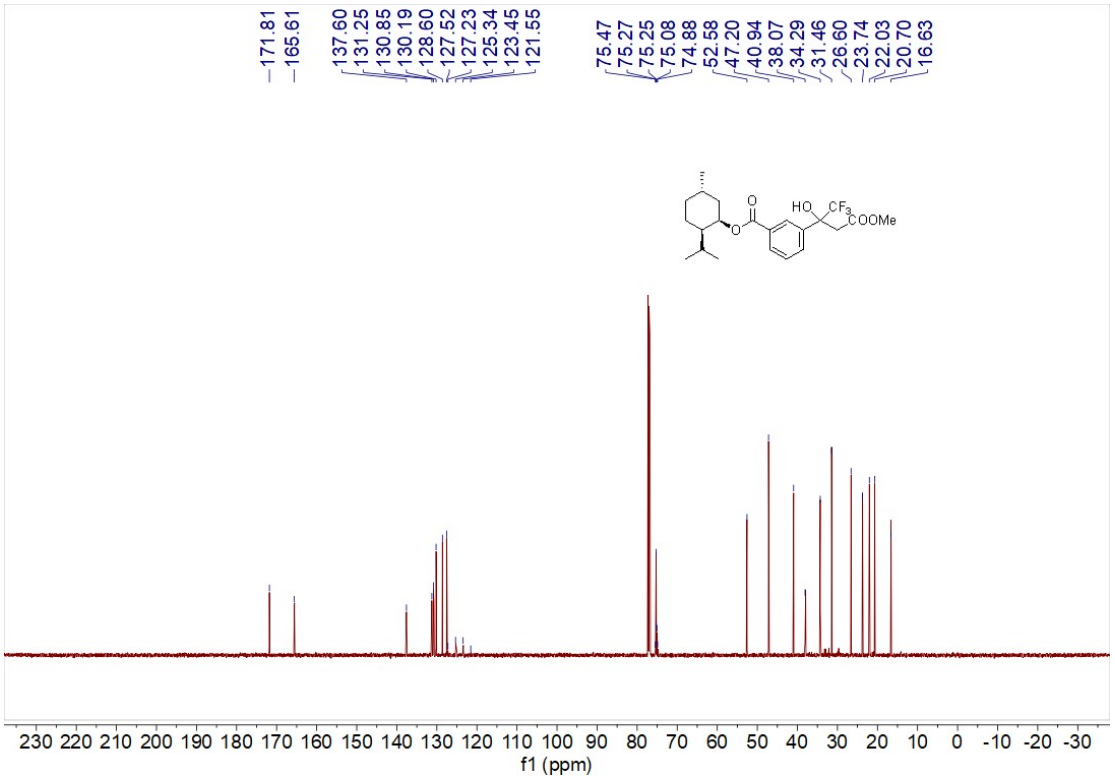


(1*S*,2*R*,5*S*)-2-isopropyl-5-methylcyclohexyl 3-(1,1,1-trifluoro-2-hydroxy-4-methoxy-4-oxobutan-2-yl)benzoate (3w)

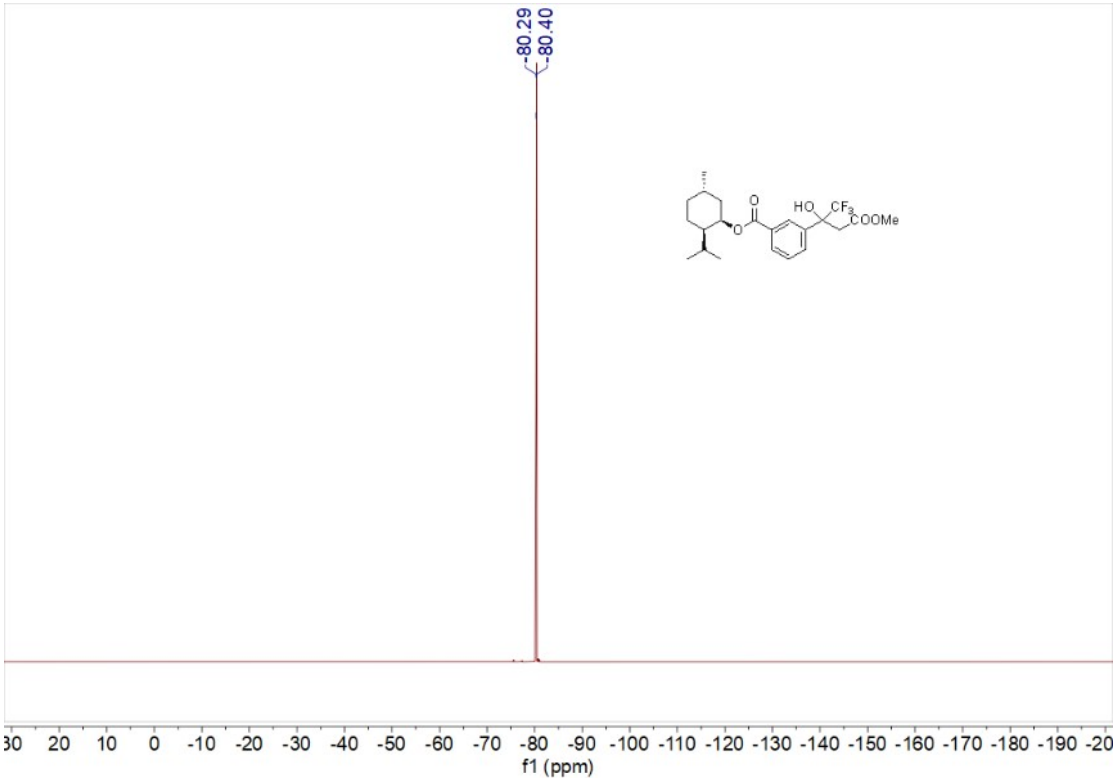
^{1}H NMR of 3w



^{13}C NMR of 3w

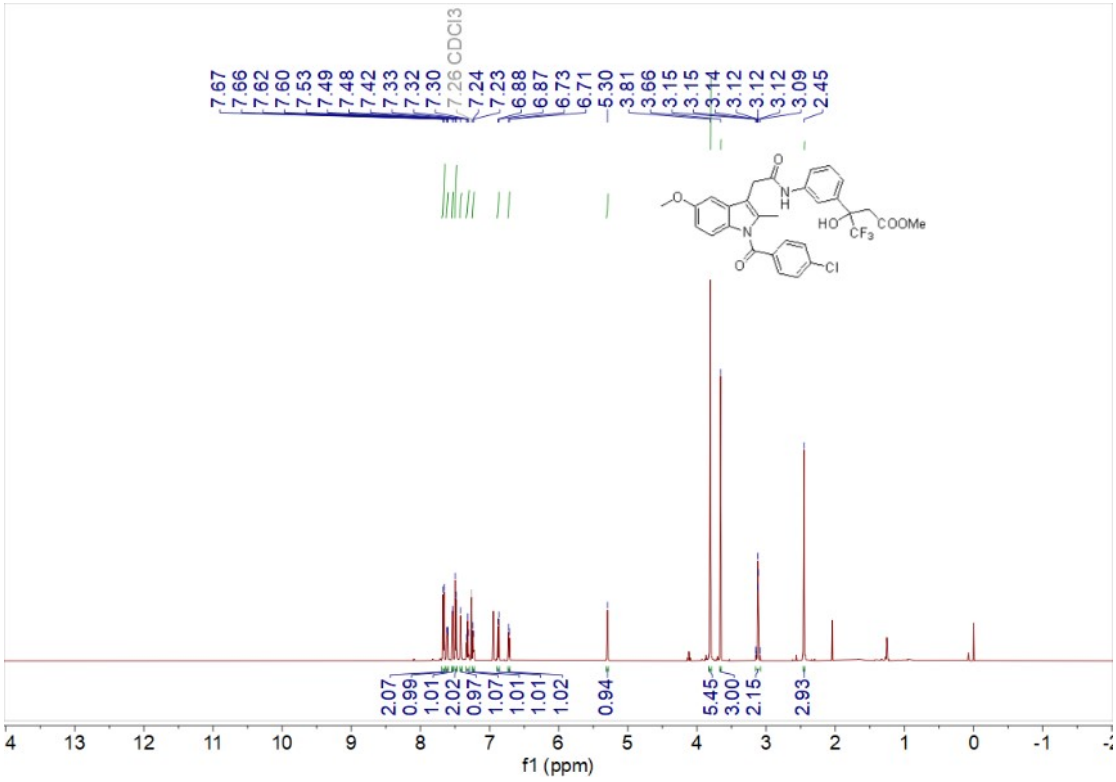


^{19}F NMR of 3w

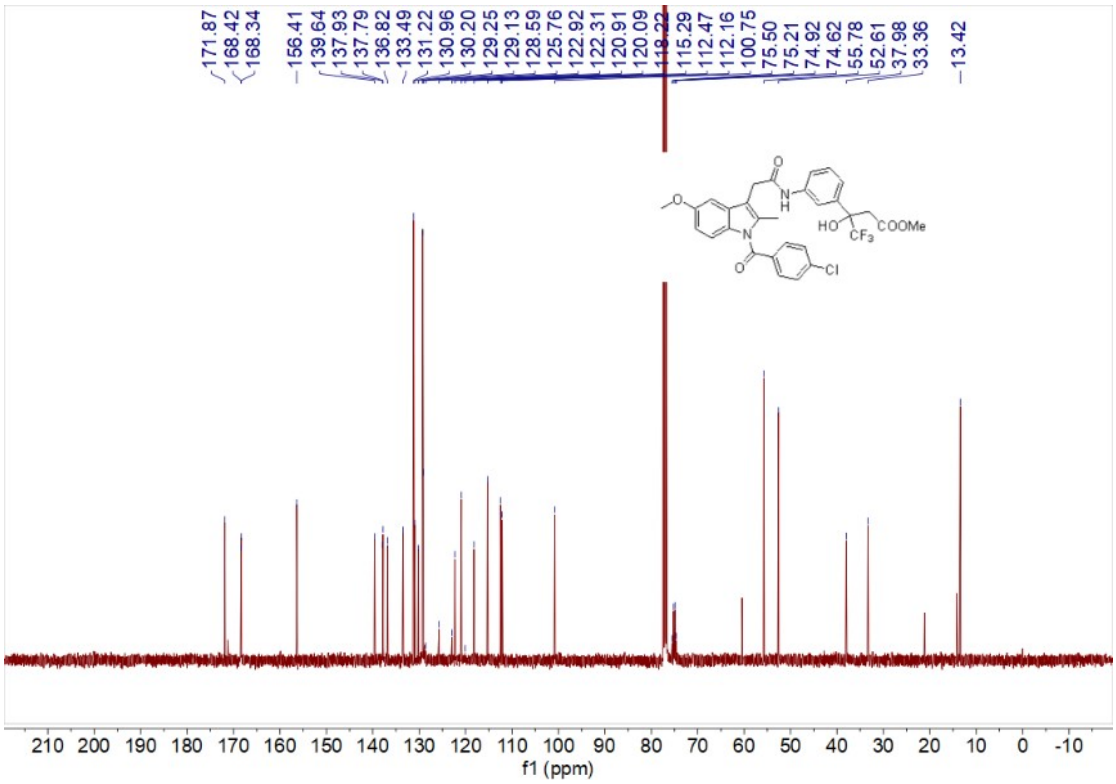


Methyl 3-(3-(2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)acetamido)phenyl)-4,4,4-trifluoro-3-hydroxybutanoate (3x)

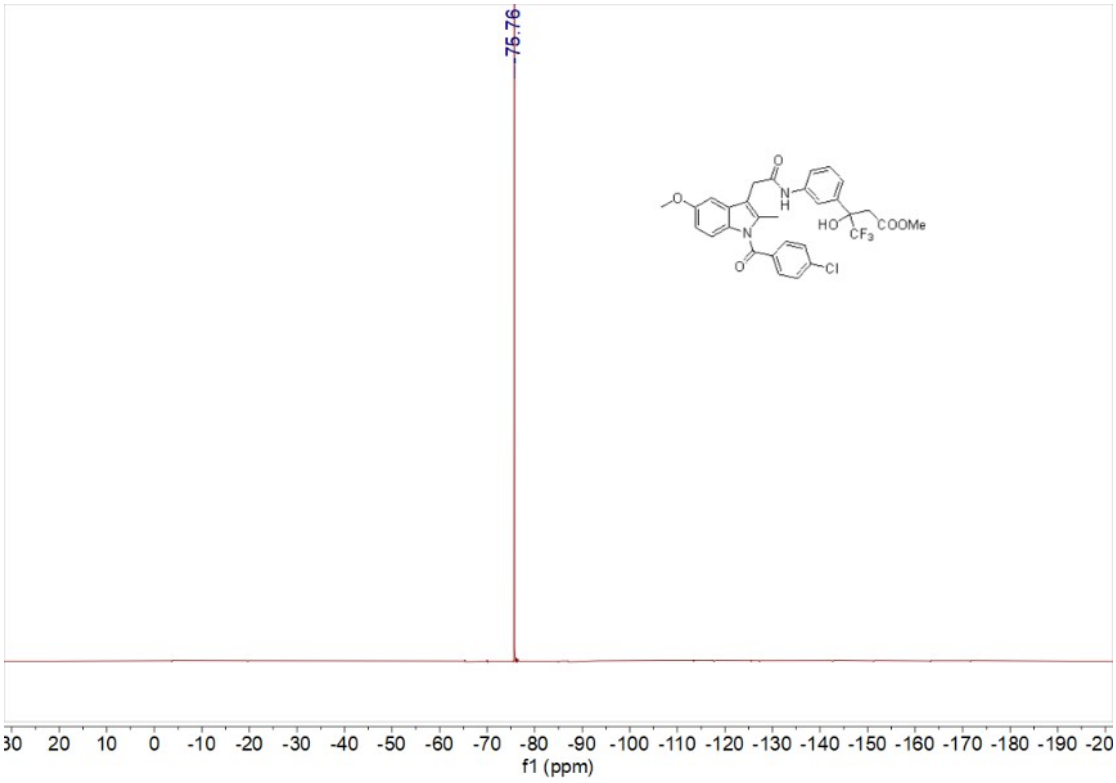
^{1}H NMR of 3x



^{13}C NMR of 3x

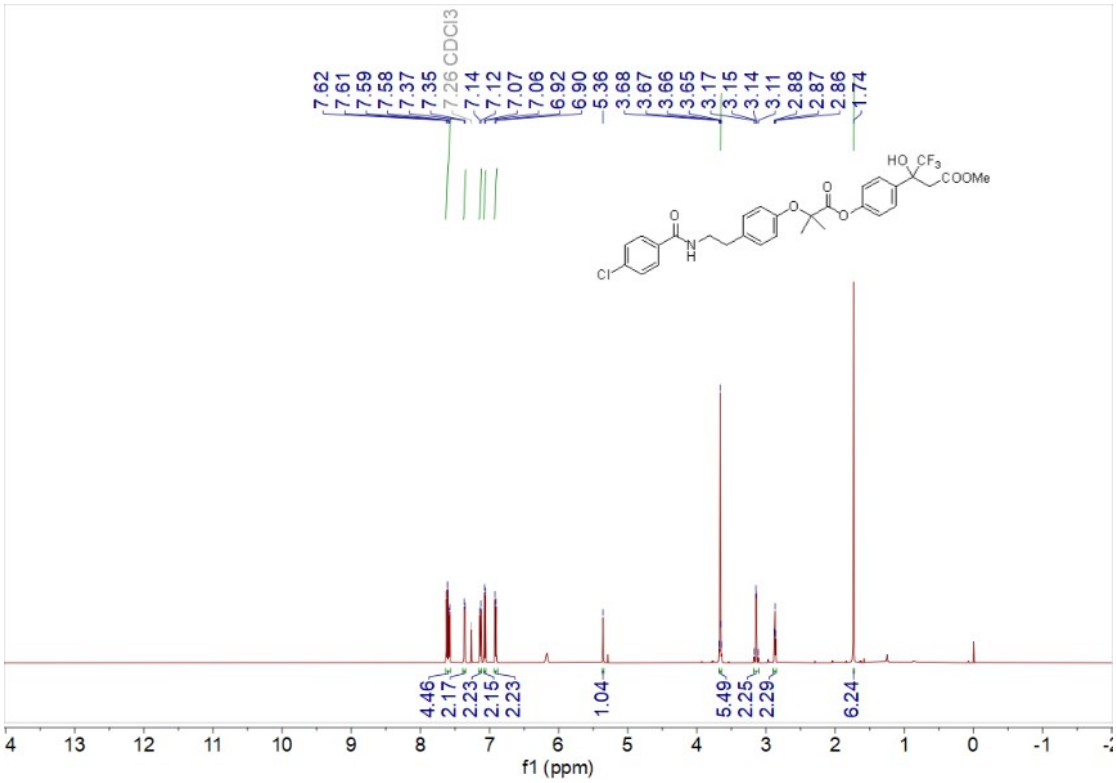


^{19}F NMR of 3x

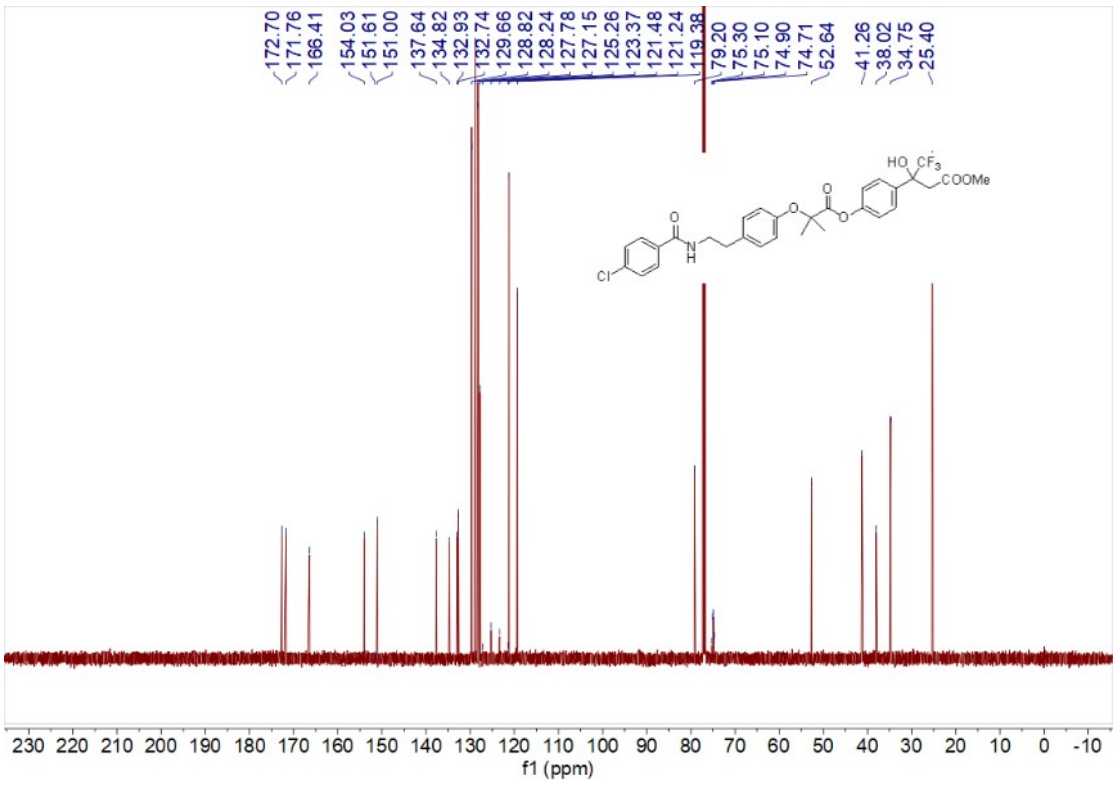


Methyl 3-(4-((2-(4-(2-(4-chlorobenzamido)ethyl)phenoxy)-2-methylpropanoyl)oxy)phenyl)-4,4,4-trifluoro-3-hydroxybutanoate (3y)

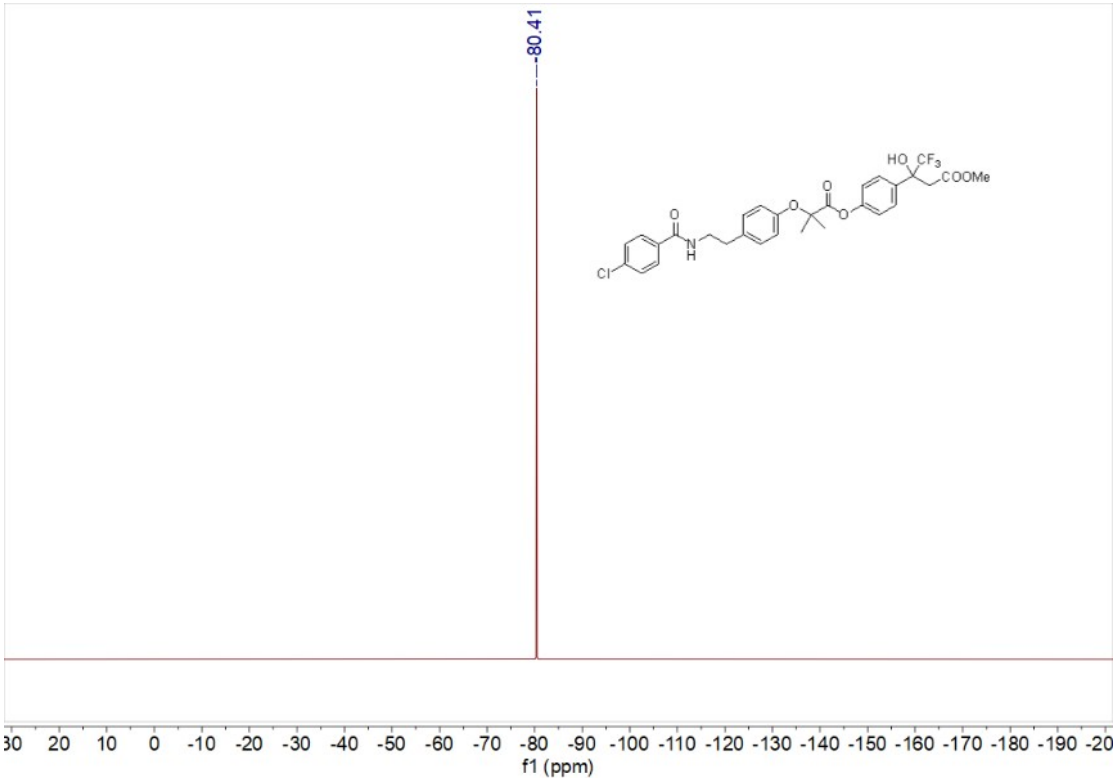
^{1}H NMR of 3y



^{13}C NMR of 3y

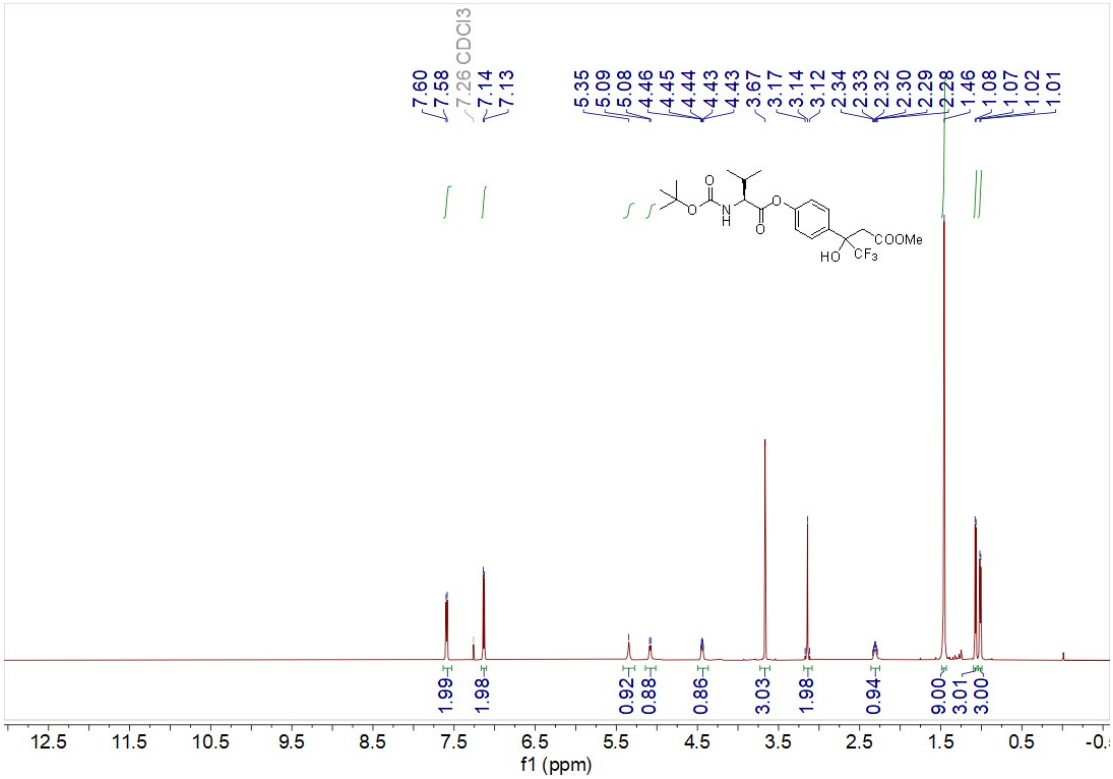


^{19}F NMR of 3y

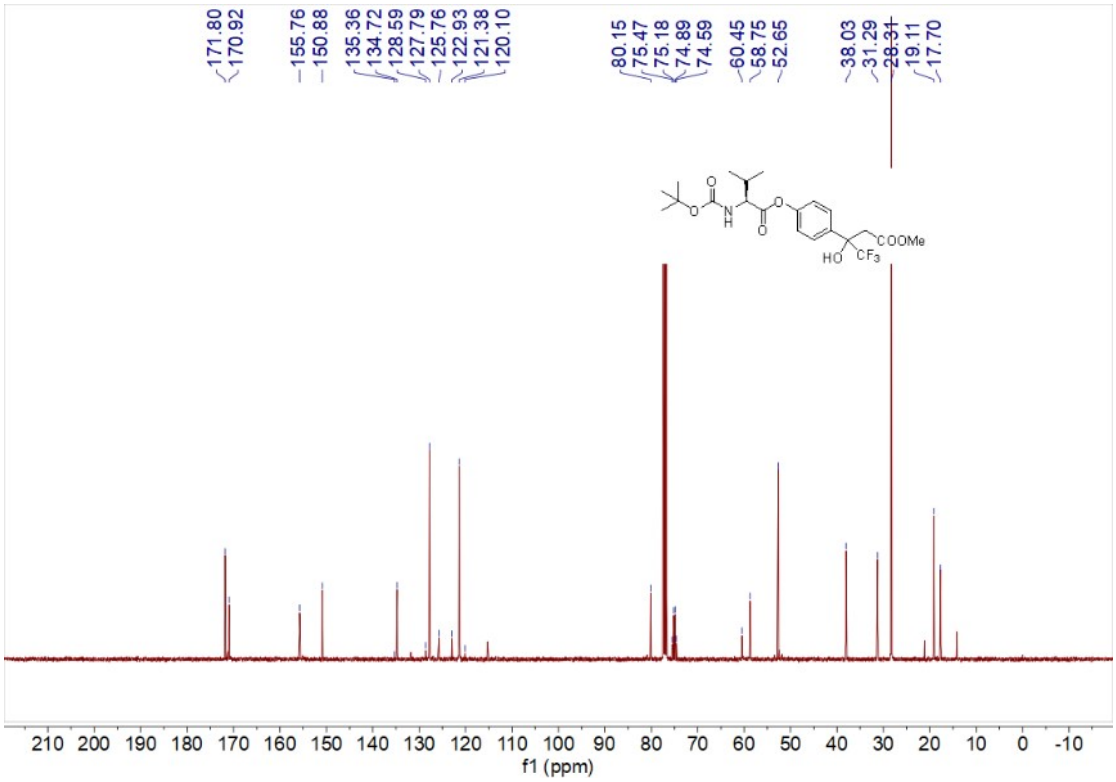


Methyl 3-(4-(((*tert*-butoxycarbonyl)-*L*-valyl)oxy)phenyl)-4,4,4-trifluoro-3-hydroxybutanoate (3z)

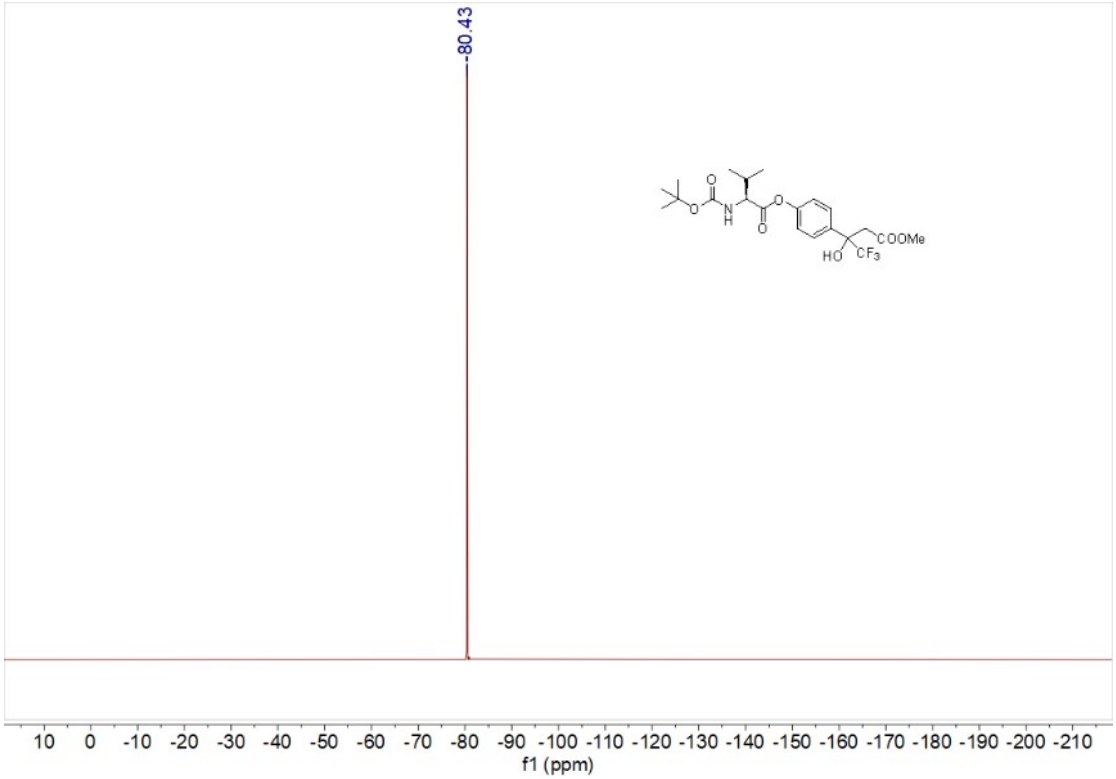
^{1}H NMR of 3z



^{13}C NMR of 3z

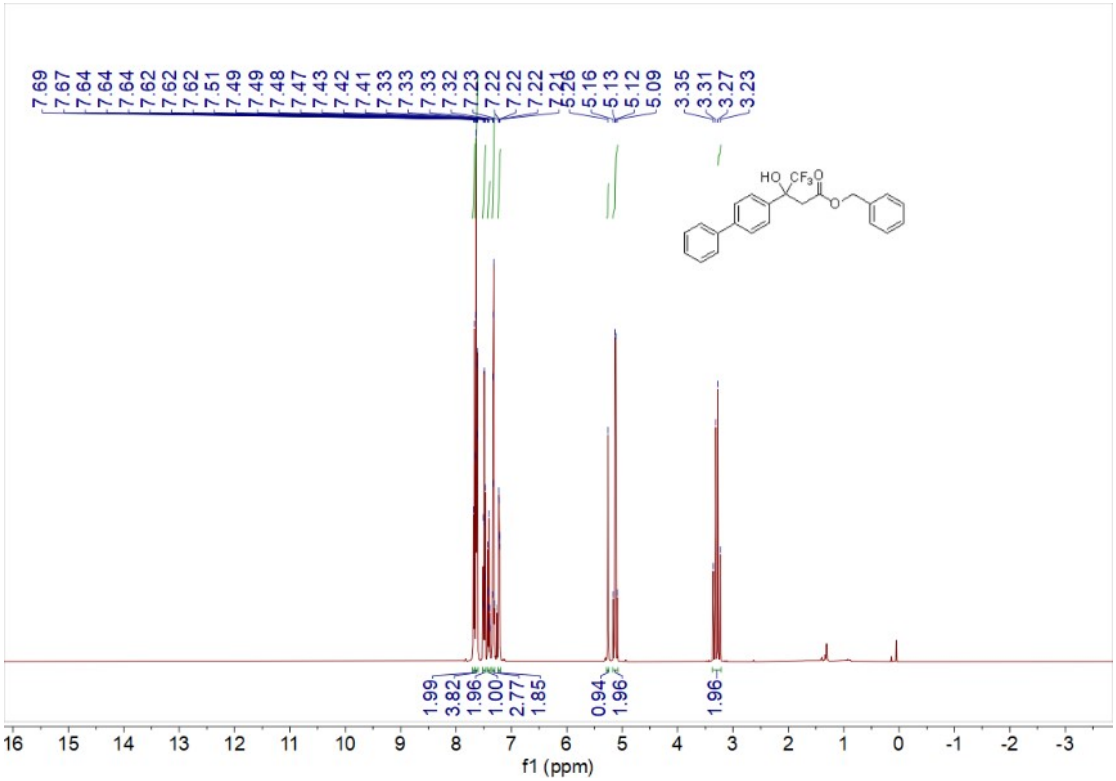


^{19}F NMR of 3z

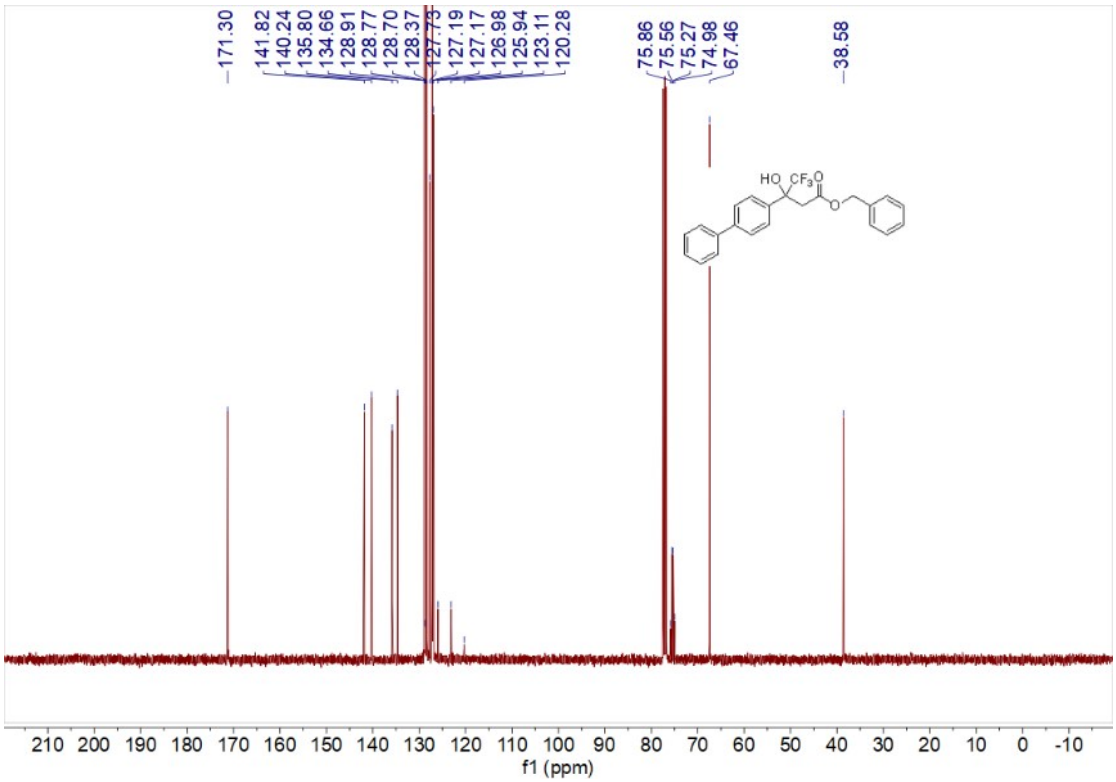


Benzyl 3-([1,1'-biphenyl]-4-yl)-4,4,4-trifluoro-3-hydroxybutanoate (1)

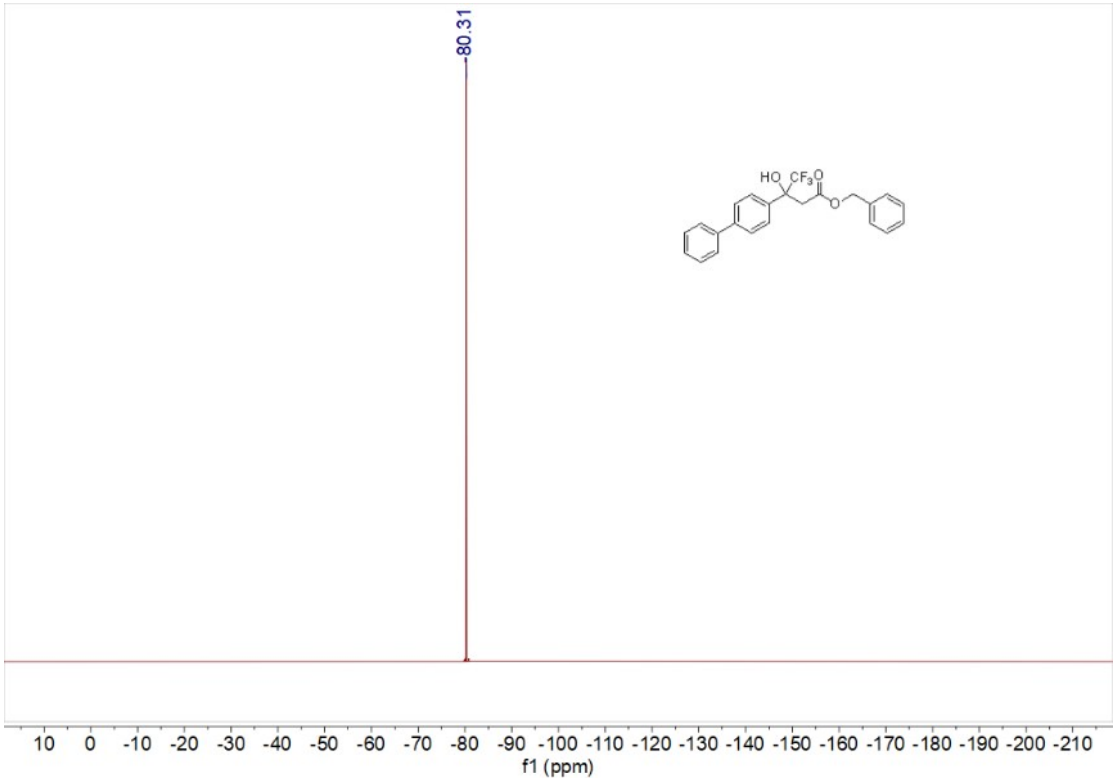
^{1}H NMR of 1



^{13}C NMR of 1

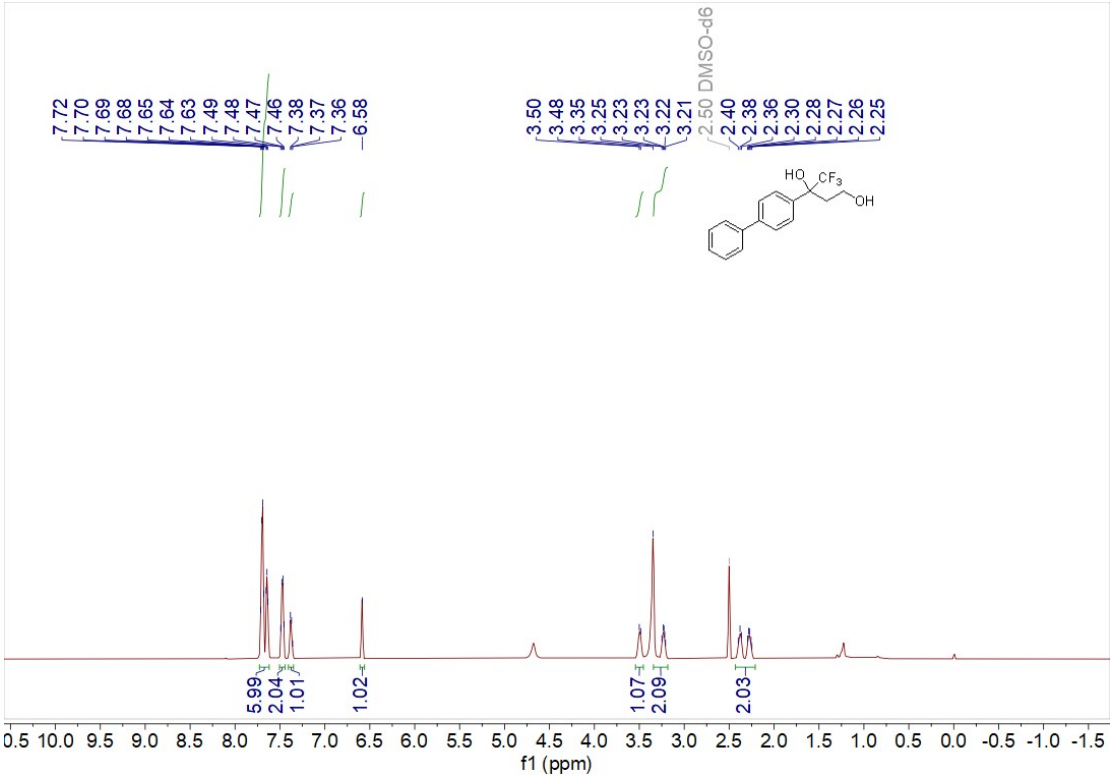


^{19}F NMR of 1

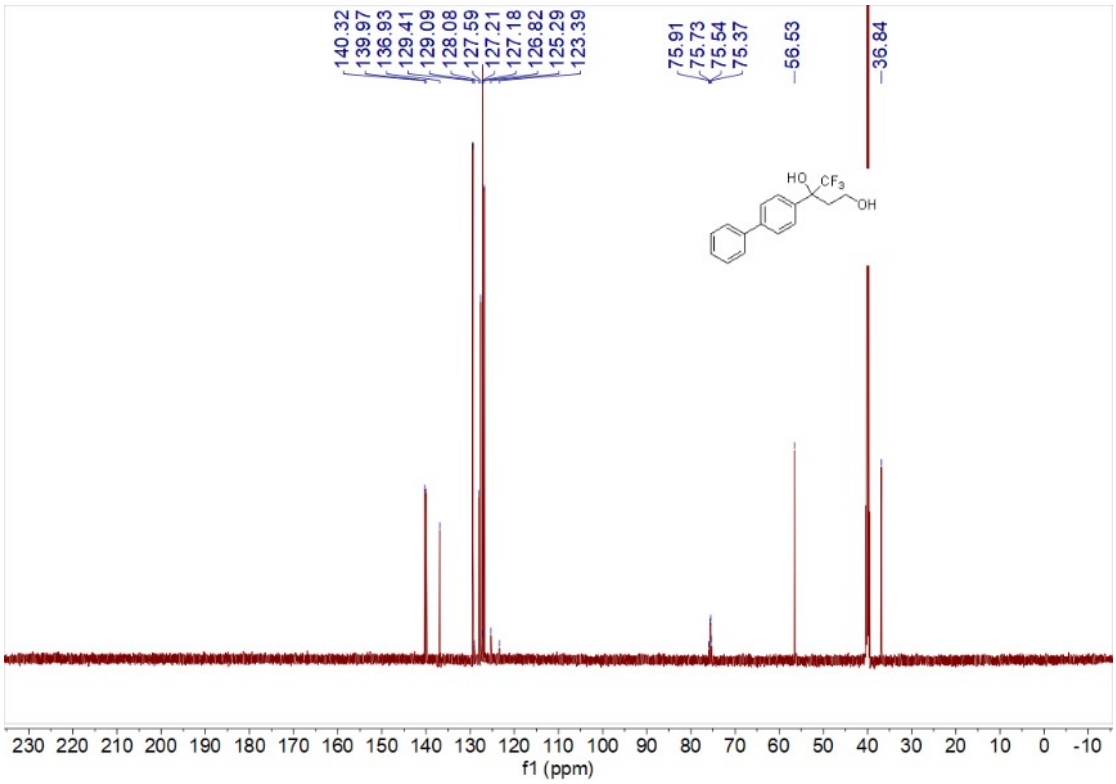


3-([1,1'-Biphenyl]-4-yl)-4,4,4-trifluorobutane-1,3-diol (2)

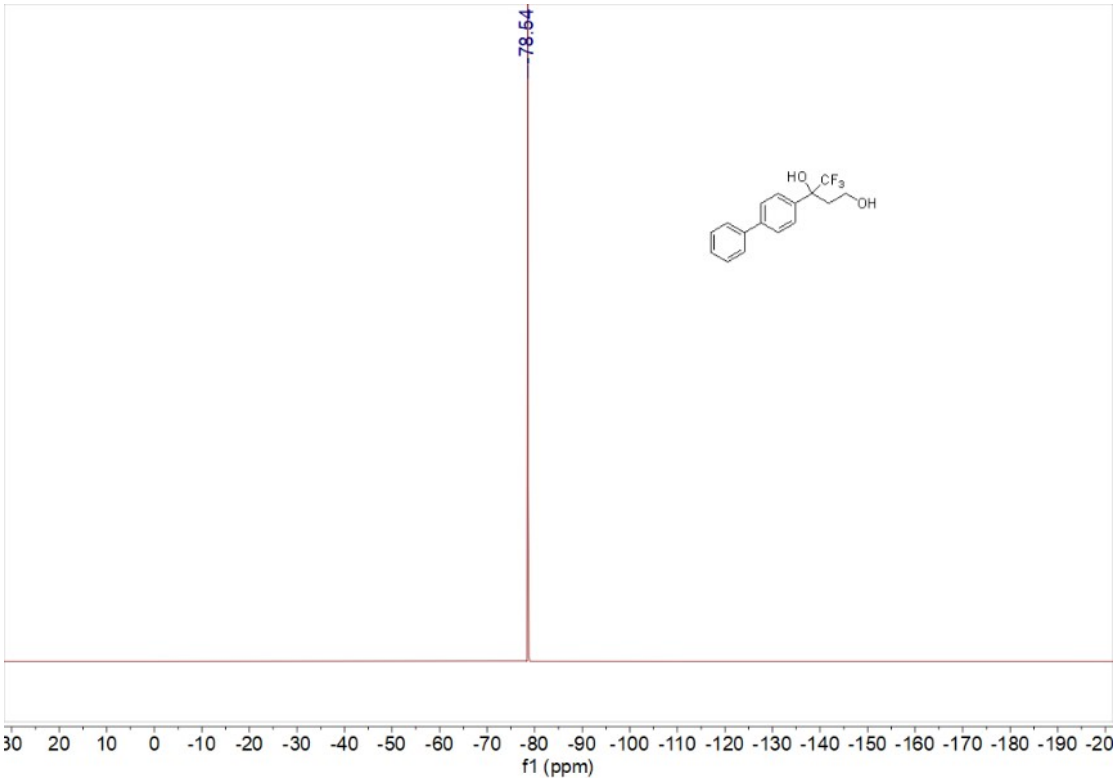
^{1}H NMR of 2



^{13}C NMR of 2

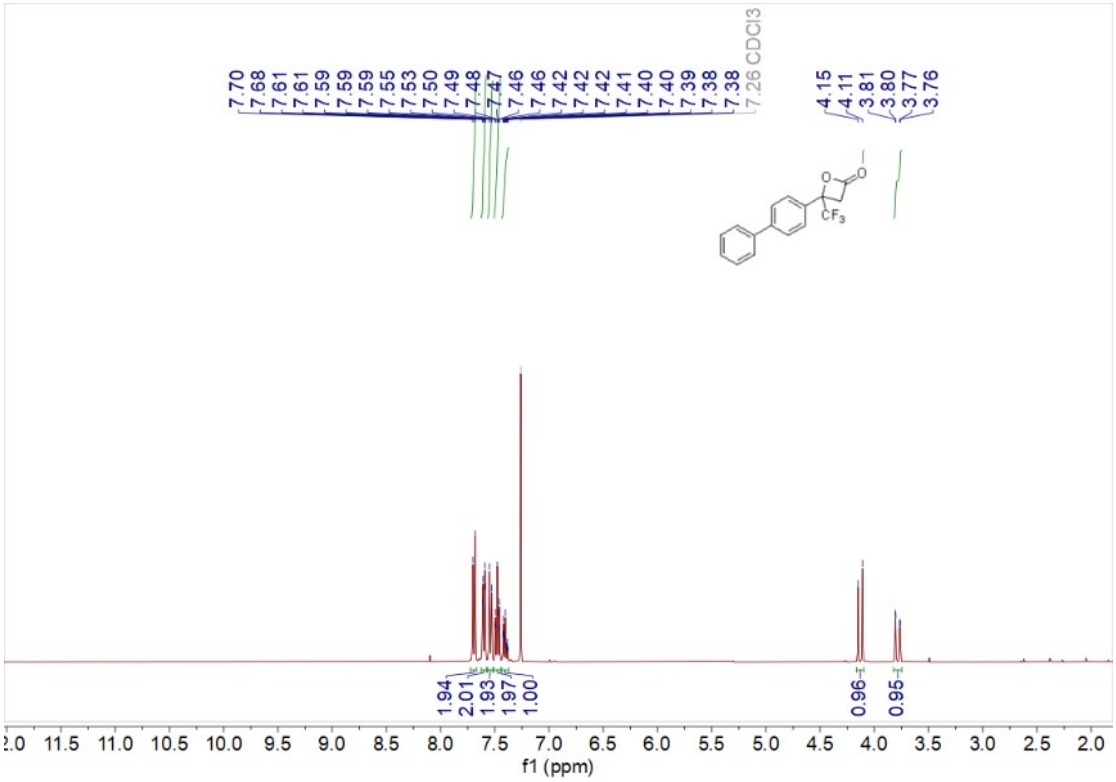


^{19}F NMR of 2

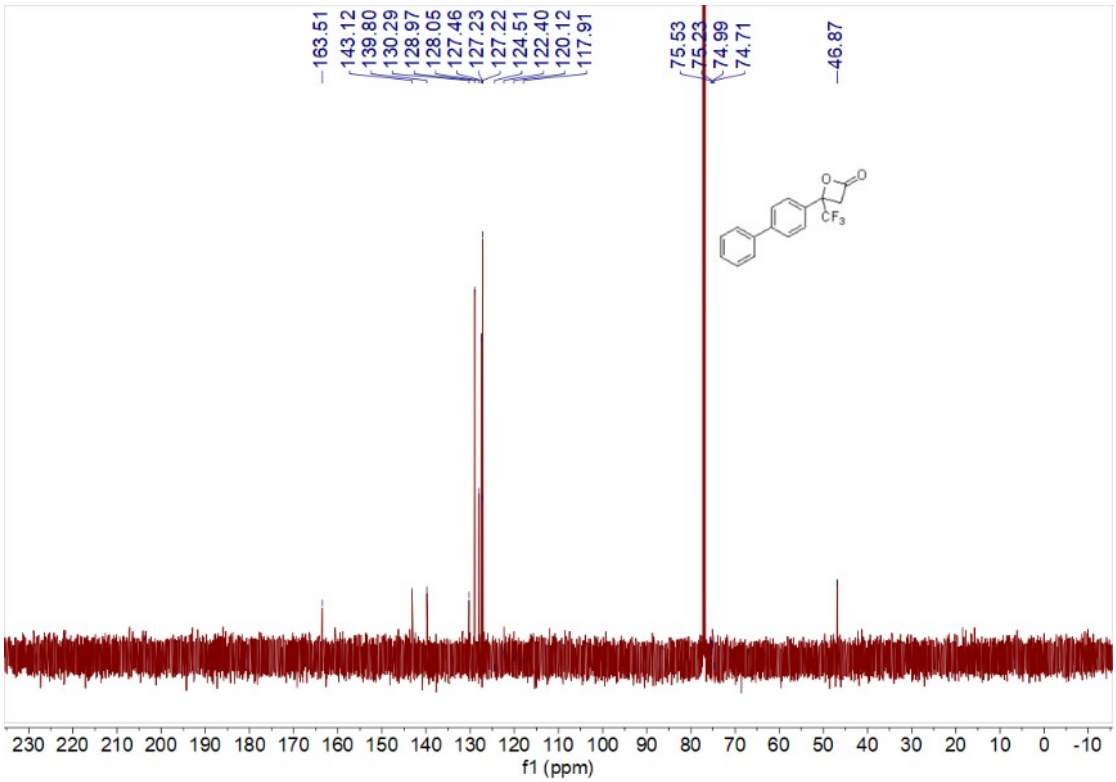


4-([1,1'-Biphenyl]-4-yl)-4-(trifluoromethyl)oxetan-2-one (3)

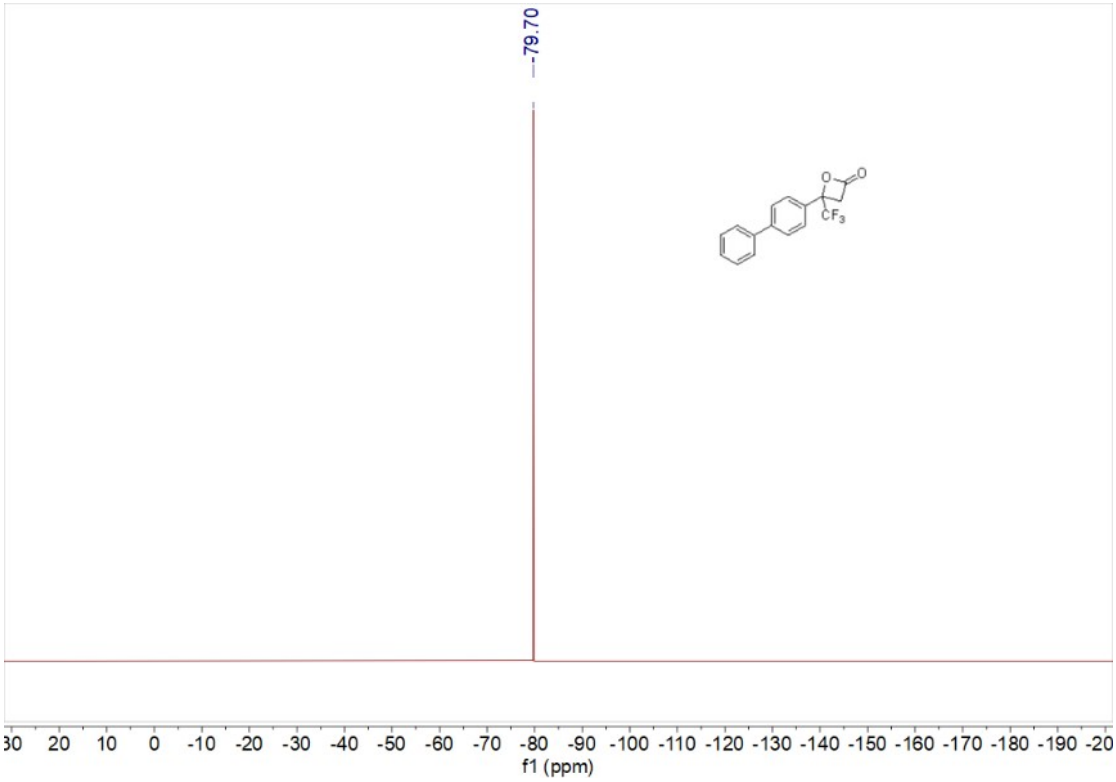
^{1}H NMR of 3



^{13}C NMR of 3

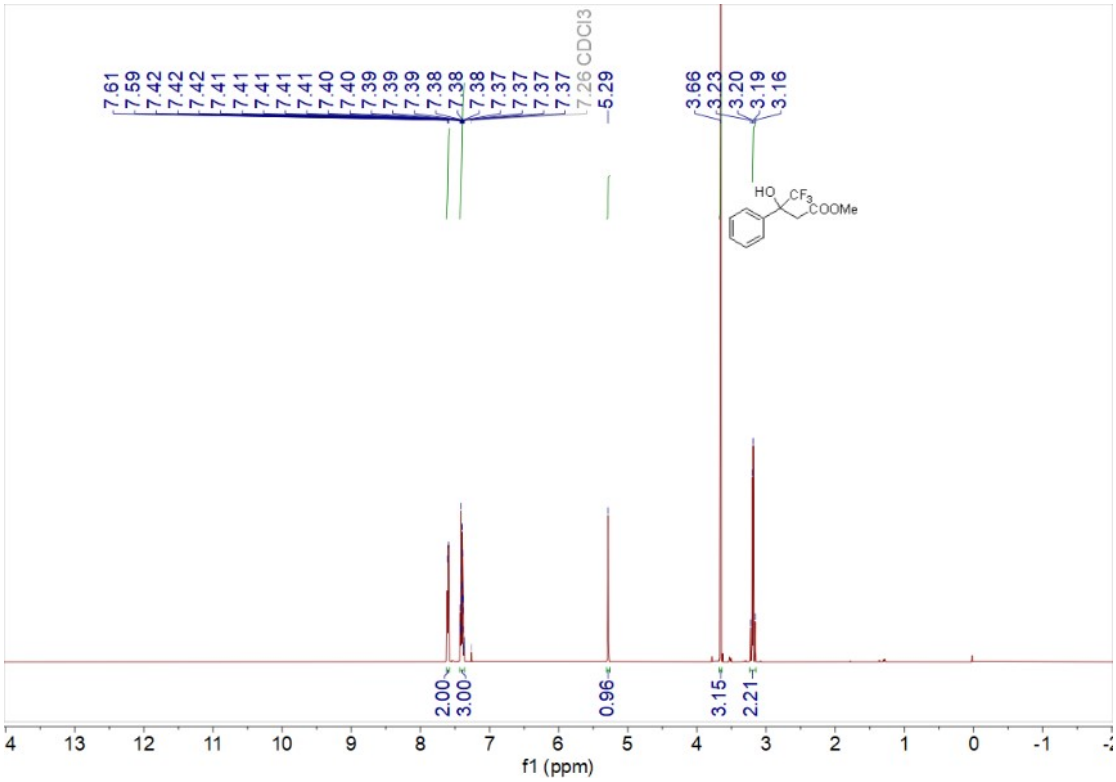


^{19}F NMR of 3

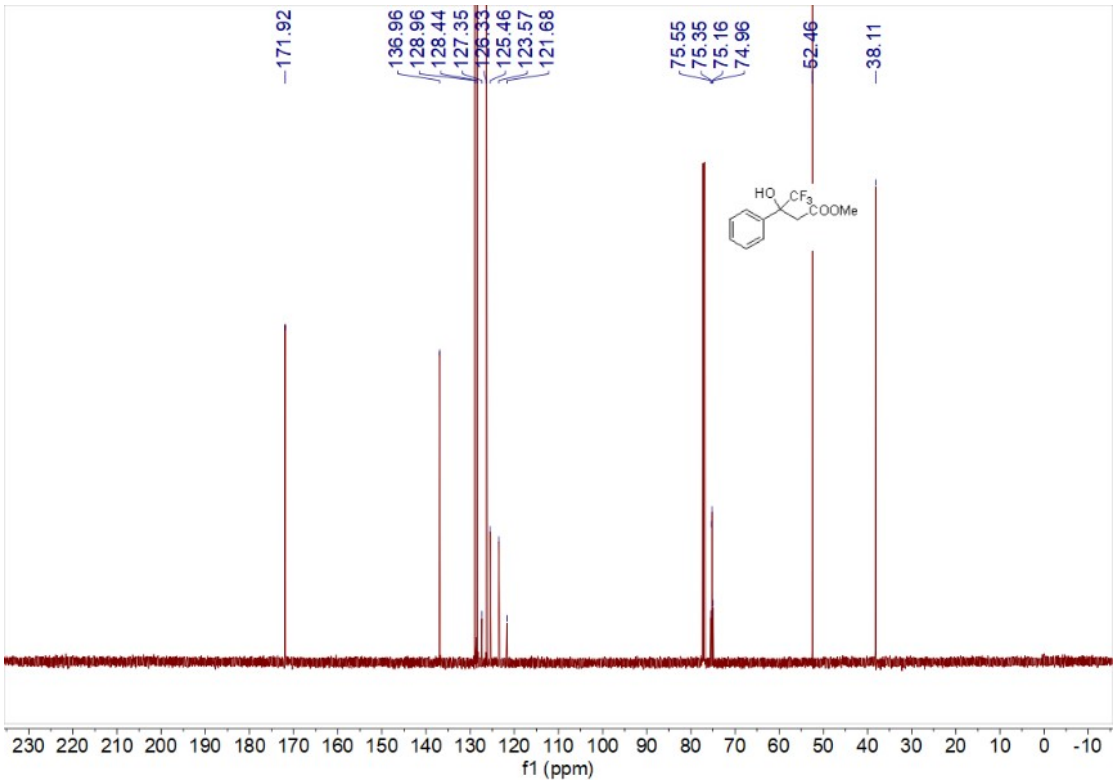


Methyl 4,4,4-trifluoro-3-hydroxy-3-phenylbutanoate (3aa')

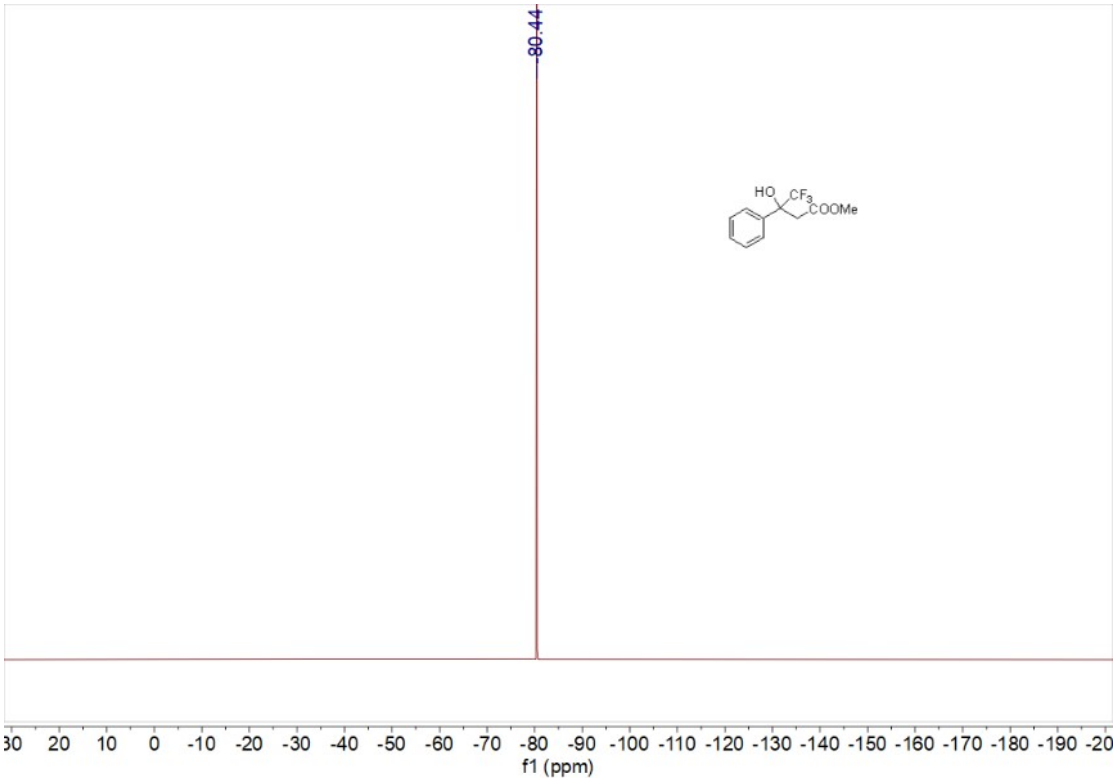
^{1}H NMR of 3aa'



^{13}C NMR of 3aa'

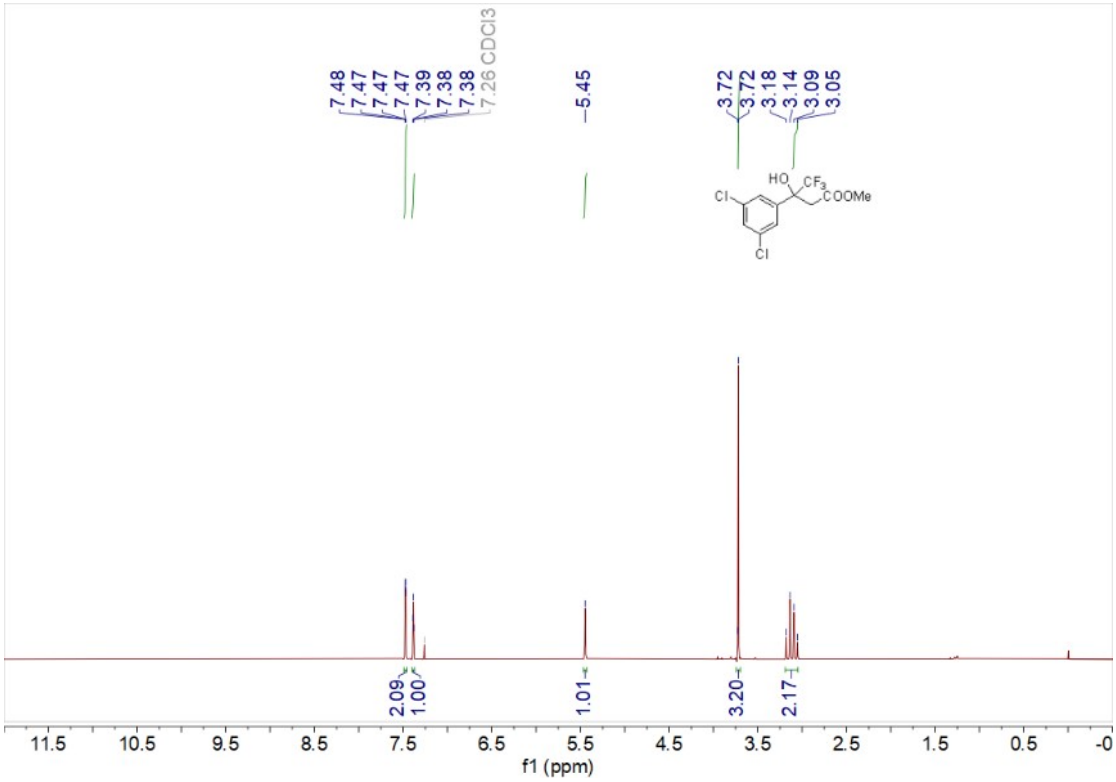


^{19}F NMR of 3aa'

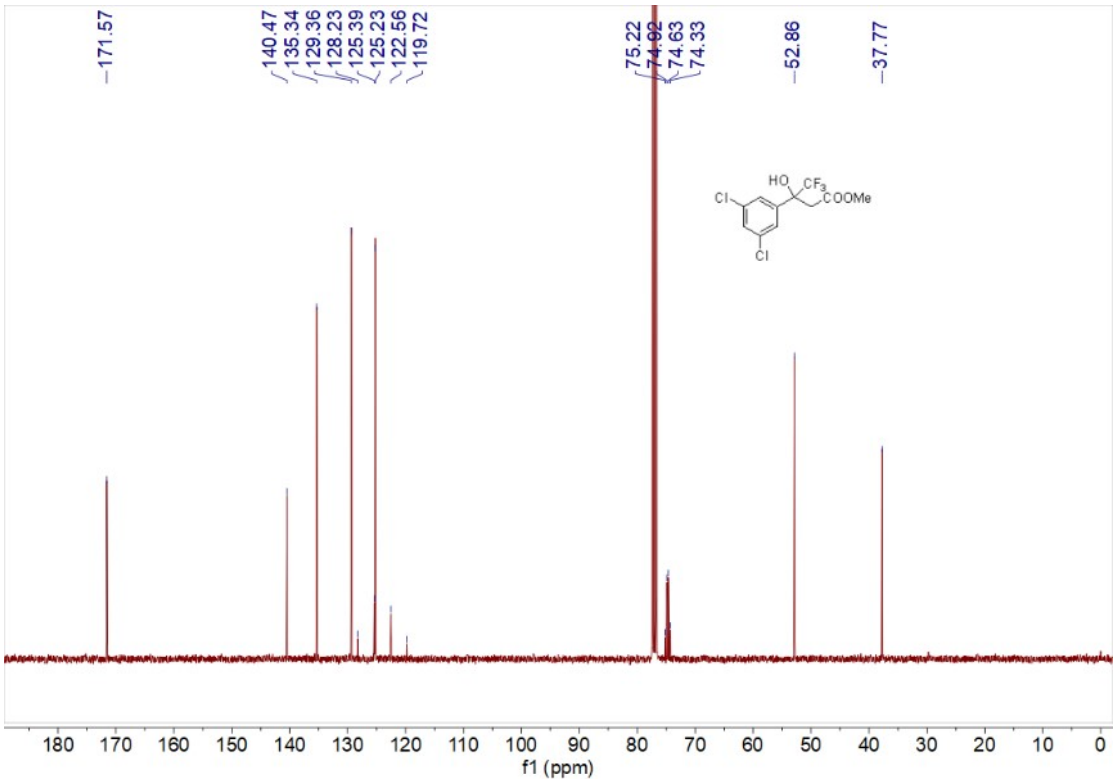


Methyl 3-(3,5-dichlorophenyl)-4,4,4-trifluoro-3-hydroxybutanoate (3ab)

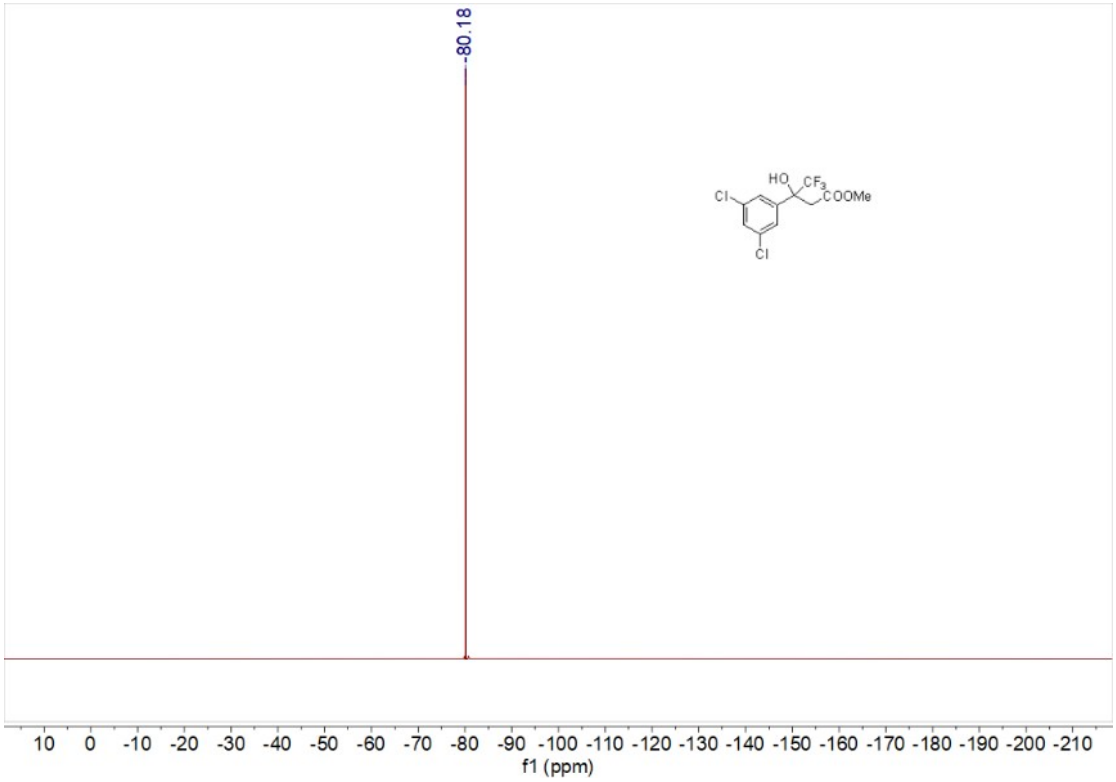
^{1}H NMR of 3ab



^{13}C NMR of 3ab

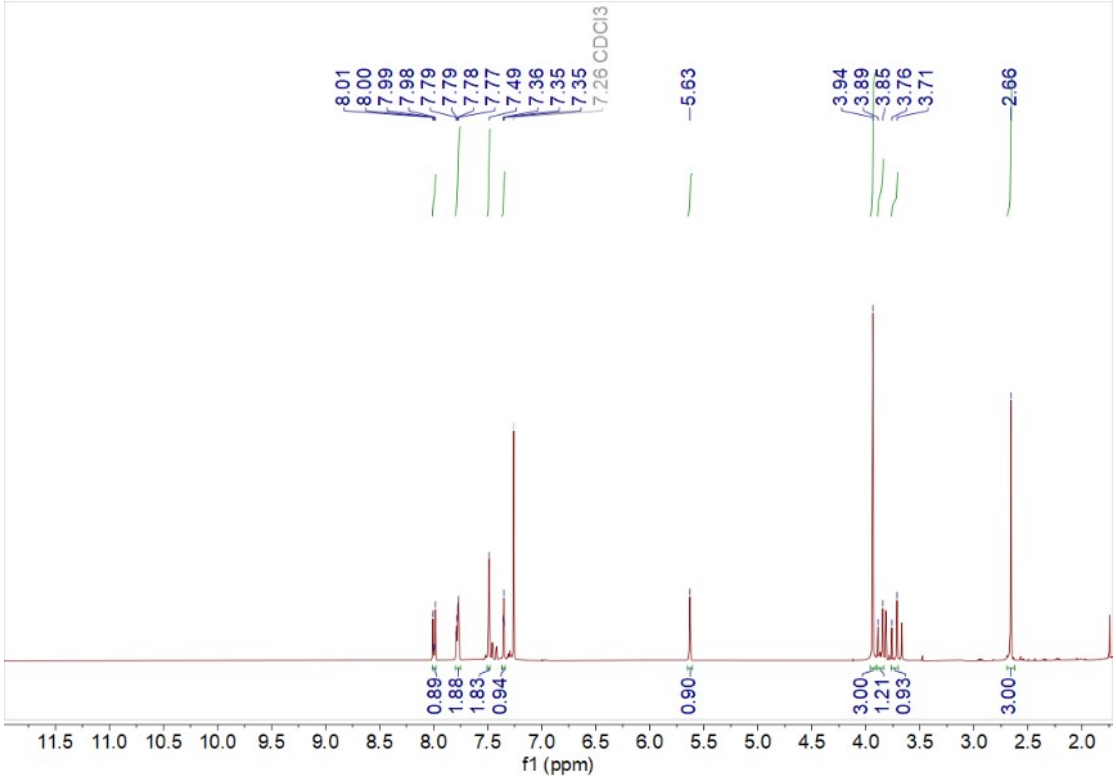


^{19}F NMR of 3ab

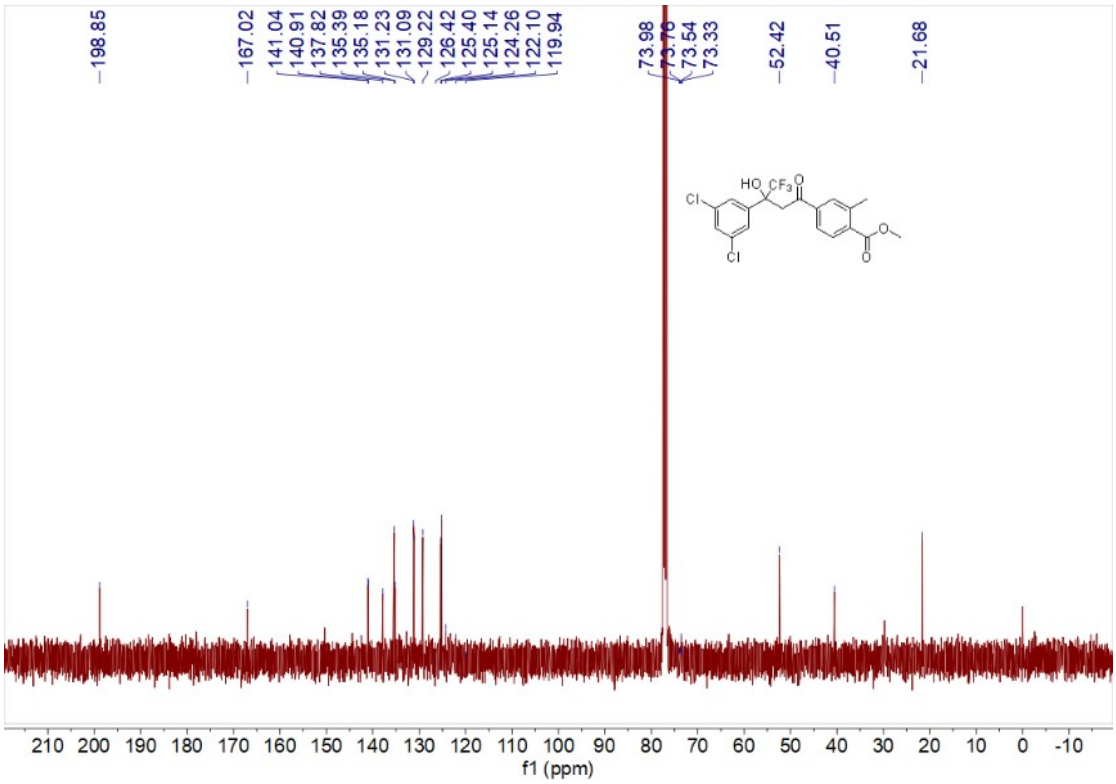


Methyl 4-(3-(3,5-dichlorophenyl)-4,4,4-trifluoro-3-hydroxybutanoyl)-2-methylbenzoate (4ab)

^{1}H NMR of 4ab



^{13}C NMR of 4ab



^{19}F NMR of 4ab