Supporting Information

Selective and controllable amination and defluoroamidation of α-trifluoromethylstyrene

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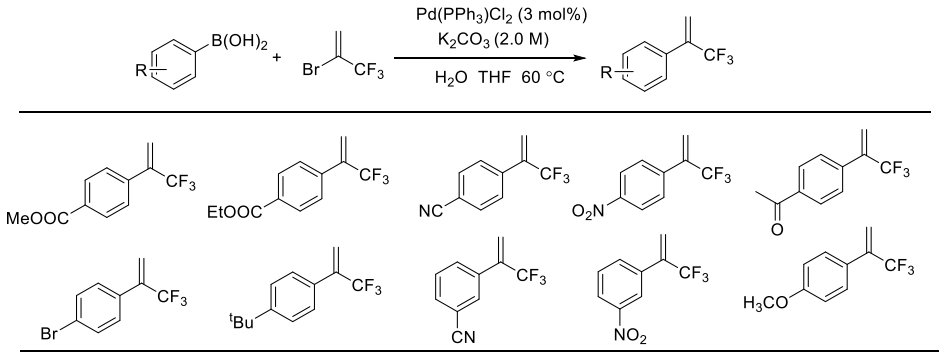
Content

1. General information

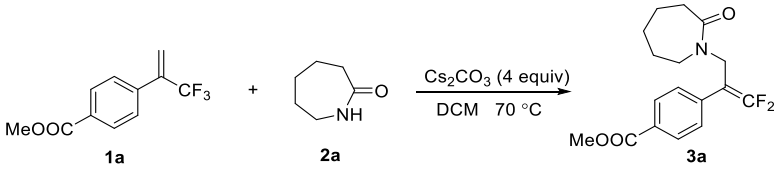
The starting materials were purchased by Energy and Aladdin and used as specified, without further purification. All reactions were performed in 25 mL dry pressure-resistant tubes at room temperature. Thin layer chromatography (TLC) was performed using silica gel GF254 precoated plates (0.5 mm). For column chromatography, 200-300 mesh silica gel. ^{1}H NMR and ^{13}C NMR spectra were measured on a 600 MHz Bruker Avance III NMR instrument using $CDCl_3$ or DMSO-d_6 as solvent, with tetramethylsilane (TMS) as internal standard, and chemical shifts (δ) were expressed in ppm. Preparation of α-(trifluoromethyl)styrene according to the procedure reported in the literature.

2. General procedure for the synthesis of the α-trifluoromethylstyrenes[1]



In a pressure-resistant tube equipped with a magnetic stirring bar, $Pd(PPh_3)Cl_2$ (105.15 mg, 3 mol%) , boric acid (5 mmol, 1.0 eq.) and K_2CO_3 (2.0 M, 10 mL) and THF (15 mL)were added to tube, and then 2-bromo-3,3,3-trifluoropropene (1.04 mL, 10 mmol, 2.0 equiv) was added by syringe, which was stirred overnight under nitrogen atmosphere at 60°C. The obtained mixture was cooled to room temperature and extracted with EtOAc (3 X 15 mL), the combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The mixture was then purified by silica gel column chromatography to obtain the desired corresponding trifluoromethyl olefin derivatives.

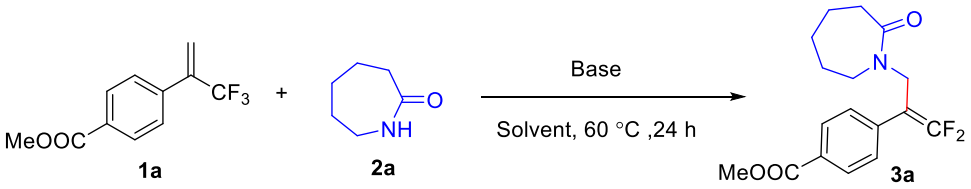
3. General procedure for the defluoroamidation of α-trifluoromethylstyrene



The general procedure for the aminolysis reaction: A pressure-resistant tube equipped with a stirring bar was charged with the base (0.8 mmol 4 equiv), p-methoxycarbonyl (trifluoromethyl)styrenes **1a** (0.4 mmol, 2 equiv), amide **2a** (0.2 mmol, 1 equiv) and DCM (0.5 mL), and then the vial evacuated under high vacuum and backfilled with N2 (10 times pumped gas). The resulting mixture was stirred at 70 °C for 24 hours. The residue was purified by flash column chromatography (silica gel, ethyl acetate/petroleum ether = 1:3 to 1:5 as eluent) to give the desired **3a** product.

4. Optimization of reaction conditions for the defluoroamidation of α-trifluoromethylstyrene

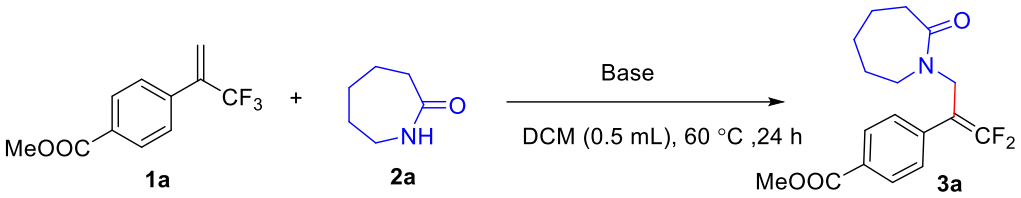
Table S1. The optimization of solvents [a]



Entry	Base	Solvent	Yield (%) [b]
1	Cs_2CO_3	MeCN	n.r.
2	Cs_2CO_3	DMF	11
3	Cs_2CO_3	DMA	n.r.
4	Cs_2CO_3	DMSO	n.r.
5	Cs_2CO_3	Acetone	n.r.
6	Cs_2CO_3	Benzene	16
7	Cs_2CO_3	$PhCF_3$	9
8	Cs_2CO_3	DCE	11
9	Cs_2CO_3	DCM	31
10	Cs_2CO_3	Hexane	18
11[c]	Cs_2CO_3	DCM	48
12[d]	Cs_2CO_3	DCM	35
13[e]	Cs_2CO_3	DCM	16

[a] Reaction conditions: **1a** (0.2 mmol 1 equiv), **2a** (0.4 mmol 2 equiv), base (2 equiv) in 25 mL Schlenk tube in the solvents (2 mL) at 60 ℃ under N_2 for 24 h. [b] Isolated yield. [c.]DCM (0.5 mL) [d.]DCM (1 mL) [e.]DCM (3 mL). n.r. = no reaction.

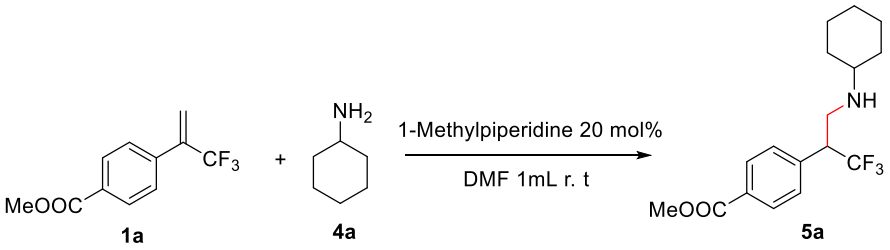
Table S2. The optimization of reaction condition [a]



Entry	Base	Solvent	Yiled(%)[b]
1	Cs_2CO_3	DCM	48
2	K^{t}OBu	DCM	6
3	Na^{t}OBu	DCM	18
4	Li^{t}OBu	DCM	46
5	NaOH	DCM	16
6	NaH	DCM	11
7	K_3PO_4	DCM	12
8	K_2HPO_4	DCM	-
9	Na_2CO_3	DCM	-
10	$NaHCO_3$	DCM	-
11	NEt_3	DCM	-
12	2,6-Lutidine	DCM	-
13	Collidine	DCM	-
14	TMG	DCM	-
15	DBU	DCM	16
16	DBN	DCM	-
17	DABCO	DCM	-
18	TMEDA	DCM	-
19	DIPEA	DCM	-
20[c]	Cs_2CO_3(3 equiv)	DCM	52
21[d]	Cs_2CO_3(4 equiv)	DCM	58
22[e]	Cs_2CO_3(5 equiv)	DCM	Trace
23[f]	Cs_2CO_3(4 equiv)	DCM	63
24[g]	Cs_2CO_3(4 equiv)	DCM	32
25[f,h]	Cs_2CO_3(4 equiv)	DCM	70
26[f,g,i]	Cs_2CO_3(4 equiv)	DCM	30

[a] Reaction conditions: **1a** (0.2 mmol 1 equiv), **2a** (0.4 mmol 2 equiv), base (2 equiv) in 25 mL Schlenk tube in DCM (0.5 mL) at 60 ℃ under N_2 for 24 h. [b] Isolated yield. [c]·Cs_2CO_3(3 equiv) [d]Cs_2CO_3(4 equiv) [e]Cs_2CO_3(5 equiv) [f]·**1a**:**2a**=2:1. [g]**1a**:**2a**=3:1[h]70 ºC [i]·80 ºC

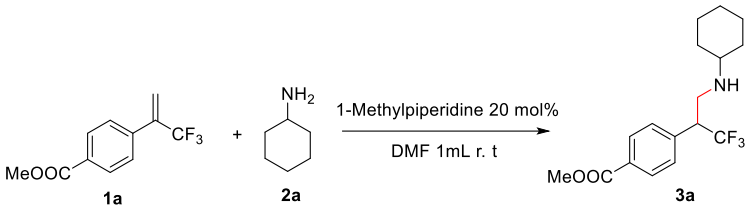
5. General procedure for the amination of α-trifluoromethylstyrene



A mixture of catalyst (N-methylpiperidine (20 mol%), *p*-Methoxycarbonyl (Trifluoromethyl)styrenes **1a** (0.2 mmol, 1 equiv), amine **4a** (0.4 mmol, 2 equiv) in DMF (1 mL) was added to a 25 mL oven-dried reaction tube and stirred at room temperature for 24 h. The residue was purified by flash column chromatography (silica gel, ethyl acetate/petroleum ether = 1:10 to 1:5 as eluent) to obtain the desired product.

6. Optimization of reaction conditions for the amination of α-trifluoromethylstyrene

Table S3. Screening of reaction conditions[a]

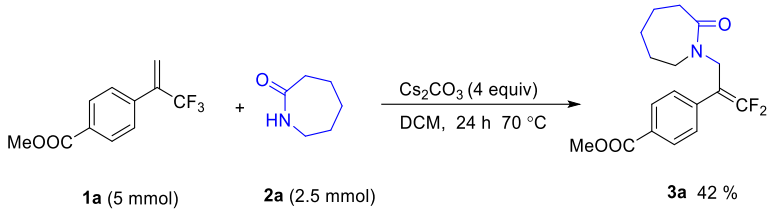


Entry	Base	Solvent	Yield%[b]
1	Cs_2CO_3	DMF	38
2	Cs_2CO_3	DMA	34
3	Cs_2CO_3	DMSO	27
4	Cs_2CO_3	Ethyl acetate	16
5	Cs_2CO_3	Benzene	22
6	Cs_2CO_3	Acetone	10
7	Cs_2CO_3	DCE	14
8	NaOH	DMF	37
9	Na_2CO_3	DMF	48
10	K_2CO_3	DMF	30
11	K_3PO_4	DMF	33
12	K_2HPO_4	DMF	54

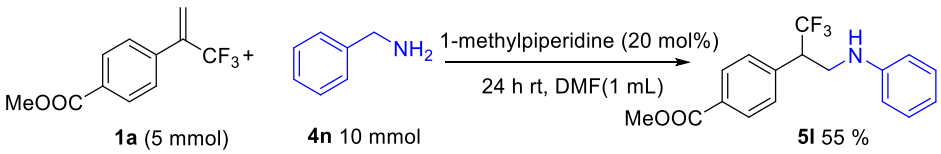
13	KH_2PO_4	DMF	65
14	2,6-Lutidine	DMF	56
15	DIPEA	DMF	62
16	Et_3N	DMF	61
17	N-Methylpiperidine	DMF	70
18	N-Methylpiperidine	DMF	85

[a] Reaction conditions:**1a** (0.2 mmol 1 equiv), **2a**(0.4 mmol), In solvent(1 mL) in a 25 mL Schlenk tube at room temperature for 24 h. [b]Isolated yield.

7. Gram-scale reaction



A pressure-resistant tube equipped with a stirring bar was charged with the base (0.8 mmol 4 equiv), *p*-methoxycarbonyl (trifluoromethyl)styrenes **1a** (5 mmol, 2 equiv.), amide **2a** (2.5 mmol, 1 equiv.) and DCM (6.5 mL), and then the vial evacuated under high vacuum and backfilled with N_2 (10 times pumped gas). The resulting mixture was stirred at 70 °C for 24 hours. The residue was purified by flash column chromatography (silica gel, ethyl acetate/petroleum ether = 1:3 to 1:5 as eluent) to give the desired **3a** product.



To a 50-mL oven-dried glass flask with magnetic stir bar were successively added catalyst (N-methylpiperidine (20 mol%), *p*-Methoxycarbonyl (Trifluoromethyl)styrenes **1a** (5 mmol, 1 equiv.), amine **4a** (10 mmol, 2equiv.) and DMF (10 mL), and then the resulted mixture was stirred at room temperature for 24 h. The residue was purified by flash column chromatography (silica gel, ethyl acetate/petroleum ether = 1:10 to 1:5 as eluent) to obtain the desired product.

8. Exploration of the reaction mechanism

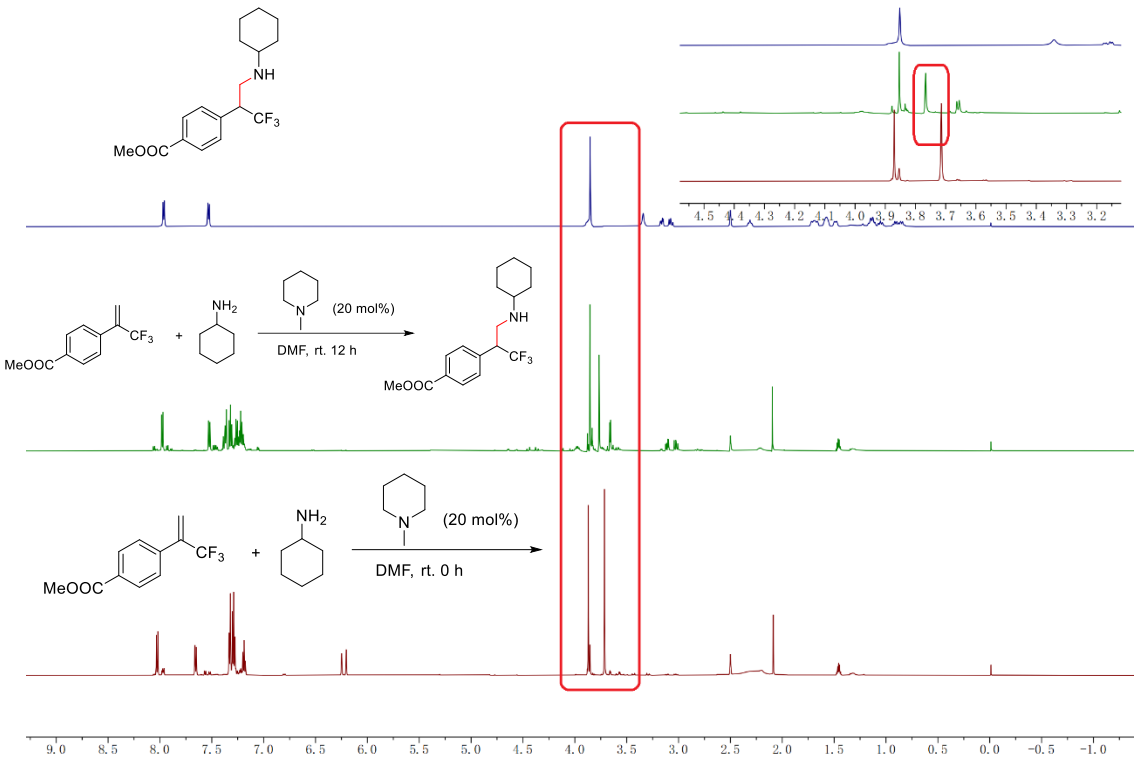
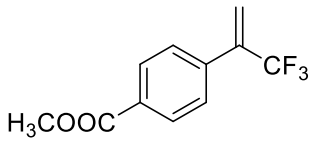


Figure S1 Exploration the mechanism of amine and α-(trifluoromethyl)styrenes

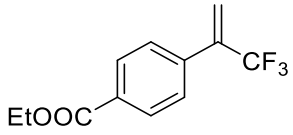
According to ^{1}H NMR experiments for mixtures of substrates and after reaction for 12 hours, the obvious changes of the chemical shifts of the methyl for 1-methylpiperidine was observed, and we hypothesized the changes may attributed to the hydrogen bond between 1-methylpiperidine and secondary amine, which increased the nucleophilicity of secondary amine.

Methyl 4-(3,3,3-trifluoroprop-1-en-2-yl)benzoate[2]



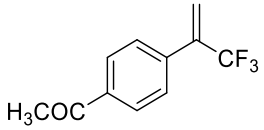
^{1}H NMR (600 MHz, $CDCl_3$) δ(ppm) = 8.05 (d, J = 8.4 Hz, 2H), 7.53 (d, J = 8.1 Hz, 2H), 6.04 (d, J = 2.0 Hz, 1H), 5.86 (d, J = 1.7 Hz, 1H), 3.93 (s, 3H). Data in accordance with the literature.

Ethyl 4-(3,3,3-trifluoroprop-1-en-2-yl)benzoate[3]



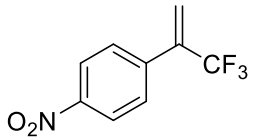
^{1}H NMR (600 MHz, $CDCl_3$) δ(ppm) = 8.08 – 8.04 (m, 2H), 7.53 (d, *J* = 8.2 Hz, 2H), 6.05 (t, *J* = 1.4 Hz, 1H), 5.86 (d, *J* = 1.7 Hz, 1H), 4.40 (q, *J* = 7.1 Hz, 2H), 1.40 (t, *J* = 7.1 Hz, 3H).

1-(4-(3,3,3-Trifluoroprop-1-en-2-yl)phenyl)ethan-1-one[4]



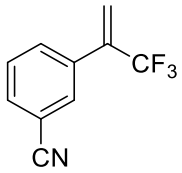
^{1}H NMR (600 MHz, $CDCl_3$) δ(ppm) = 7.87 (d, *J* = 8.4 Hz, 2H), 7.46 (d, *J* = 8.1 Hz, 2H), 5.96 (s, 1H), 5.78 (s, 1H), 2.52 (s, 3H).

1-Nitro-4-(3,3,3-trifluoroprop-1-en-2-yl)benzene[5]



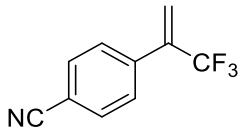
^{1}H NMR (600 MHz, $CDCl_3$) δ(ppm) = 8.26 (d, *J* = 8.8 Hz, 2H), 7.65 (d, *J* = 8.6 Hz, 2H), 6.16 (d, *J* = 1.8 Hz, 1H), 5.95 (d, *J* = 1.7 Hz, 1H).

3-(3,3,3-Trifluoroprop-1-en-2-yl)benzonitrile[6]



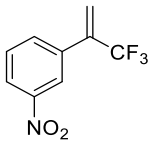
^{1}H NMR (600 MHz, $CDCl_3$) δ(ppm) = 7.74 (d, *J* = 1.7 Hz, 1H), 7.69 (dt, *J* = 8.0, 1.6 Hz, 2H), 7.53 (t, *J* = 7.8 Hz, 1H), 6.09 (d, *J* = 1.5 Hz, 1H), 5.85 (q, *J* = 1.7 Hz, 1H).

4-(3,3,3-Trifluoroprop-1-en-2-yl)benzonitrile[1]



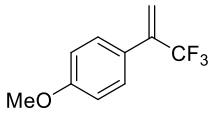
^{1}H NMR (600 MHz, $CDCl_3$) δ(ppm) = 7.69 (d, *J* = 8.3 Hz, 2H), 7.57 (d, *J* = 8.1 Hz, 2H), 6.11 (s, 1H), 5.92 – 5.86 (m, 1H).

1-Nitro-3-(3,3,3-trifluoroprop-1-en-2-yl)benzene



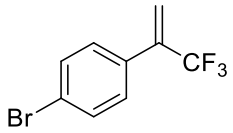
^{1}H NMR (600 MHz, $CDCl_3$) δ(ppm) = 8.33 (s, 1H), 8.26 (dd, *J* = 8.3, 2.2 Hz, 1H), 7.79 (d, *J* = 7.8 Hz, 1H), 7.60 (t, *J* = 8.0 Hz, 1H), 6.13 (d, *J* = 1.8 Hz, 1H), 5.92 (d, *J* = 2.1 Hz, 1H).

1-Methoxy-4-(3,3,3-trifluoroprop-1-en-2-yl)benzene[2]



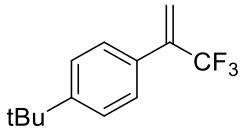
^{1}H NMR (600 MHz, $CDCl_3$) δ(ppm) = 7.40 (d, *J* = 8.2 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 5.86 (q, *J* = 1.4 Hz, 1H), 5.69 (q, *J* = 1.7 Hz, 1H), 3.82 (s, 3H).

1-Bromo-4-(3,3,3-trifluoroprop-1-en-2-yl)benzene[2]

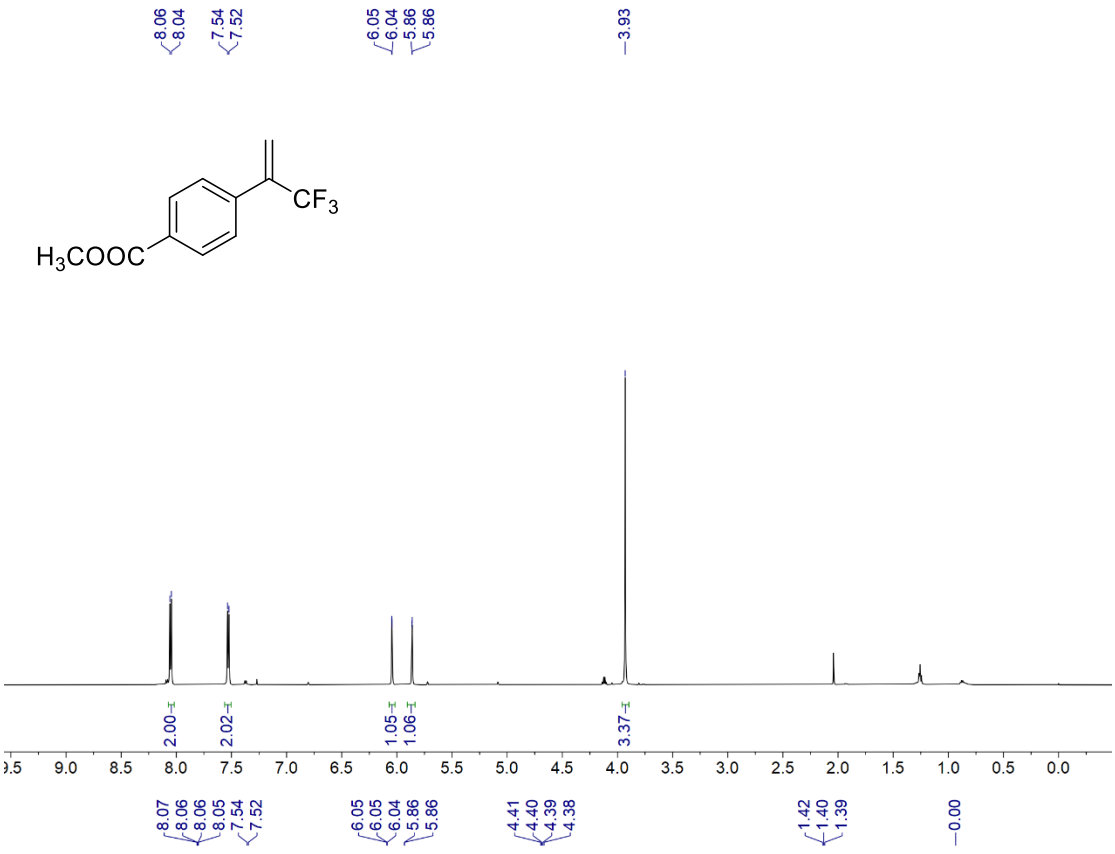


^{1}H NMR (600 MHz, $CDCl_3$) δ(ppm) = 7.52 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 5.98 (s, 1H), 5.77 (s, 1H).

1-(Tert-butyl)-4-(3,3,3-trifluoroprop-1-en-2-yl)benzene[2]



^{1}H NMR (600 MHz, $CDCl_3$) δ(ppm) = 7.40 (s, 4H), 5.91 (d, *J* = 1.3 Hz, 1H), 5.76 (d, *J* = 1.7 Hz, 1H), 1.33 (s, 9H).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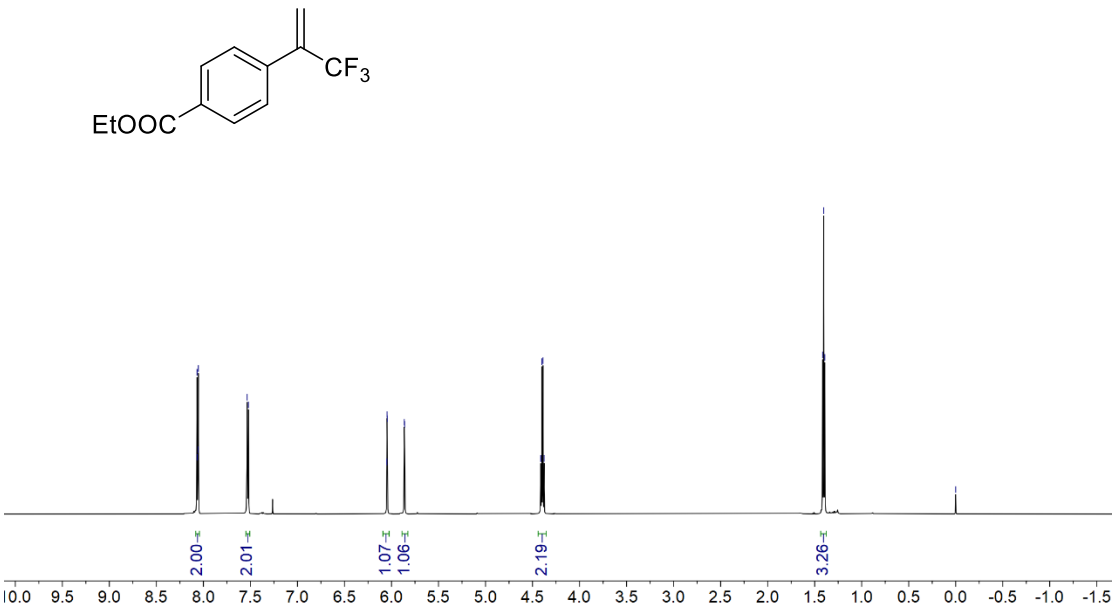
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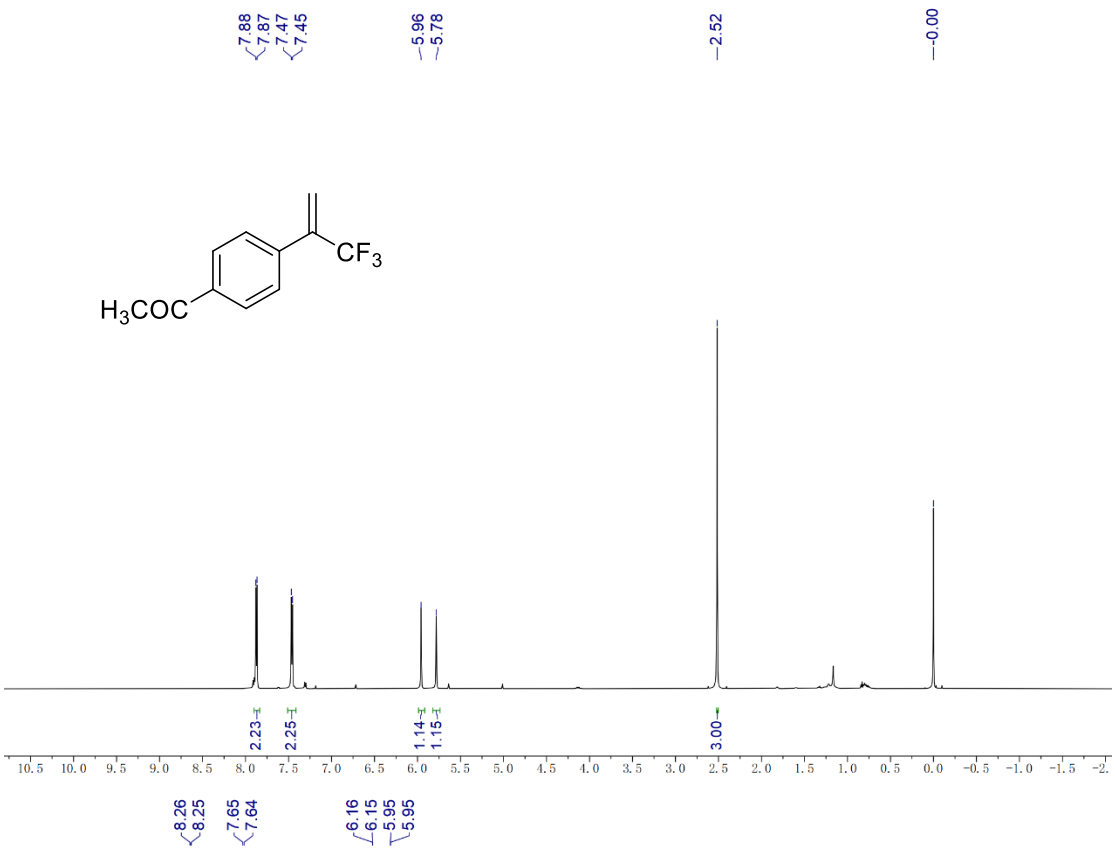
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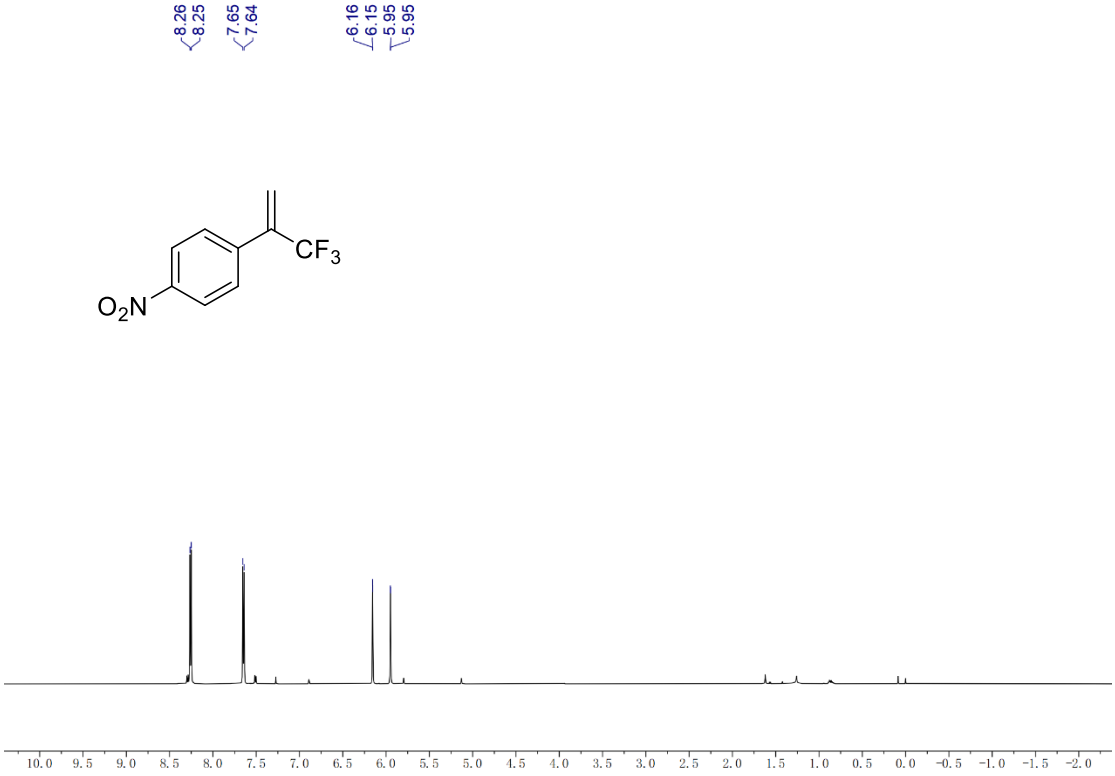
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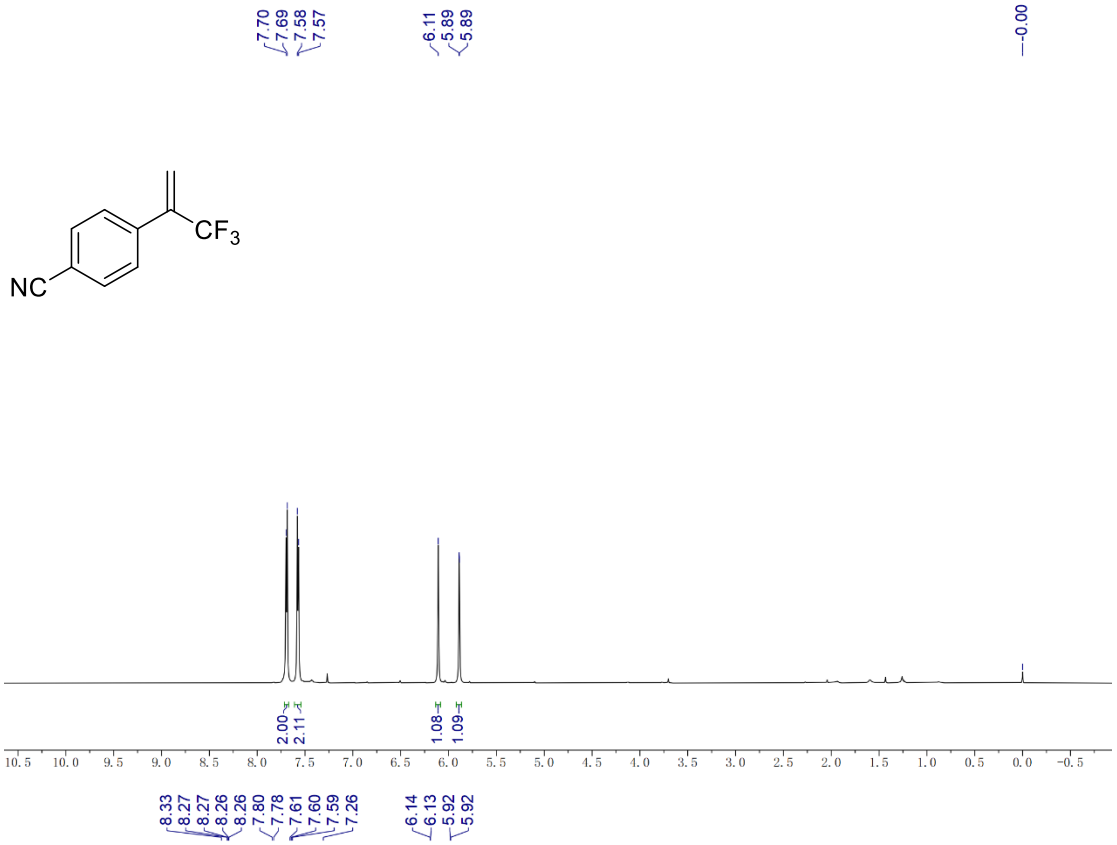
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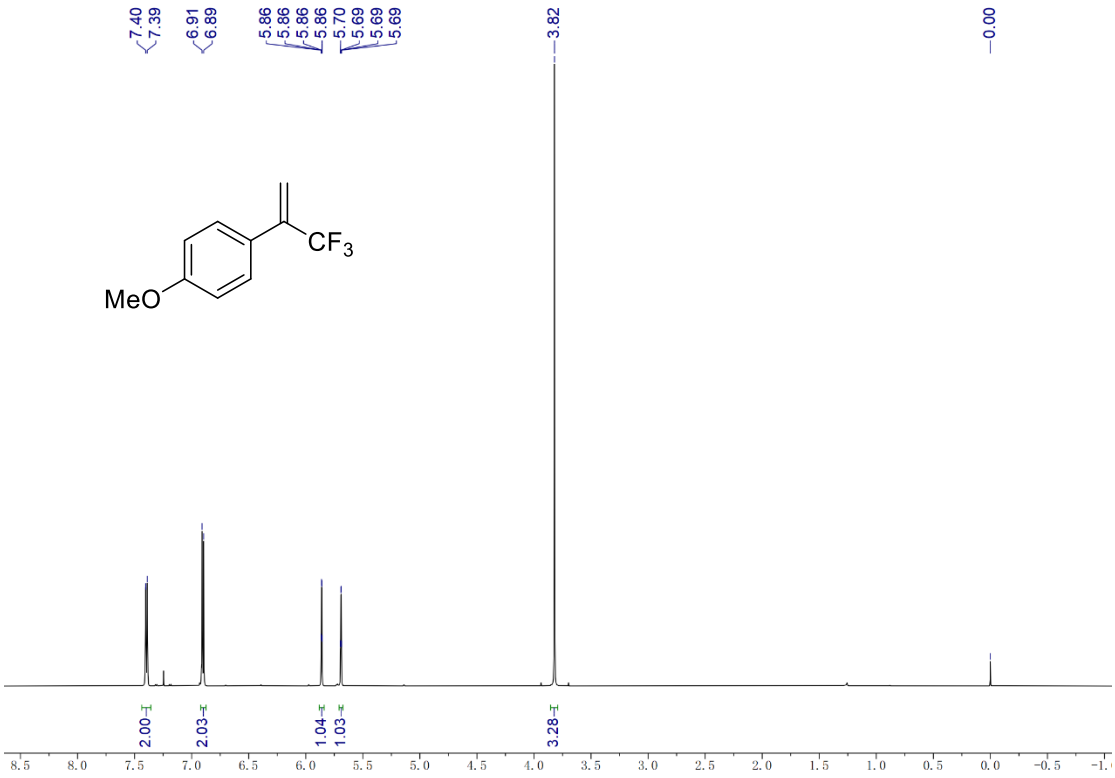
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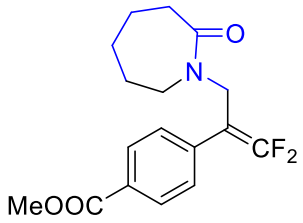
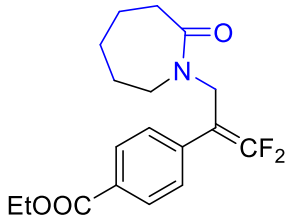
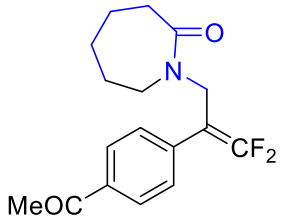
-0.5



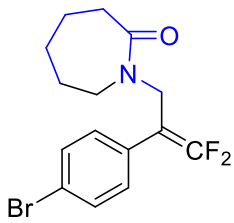
4-(1,1-difluoro-3-(2-oxoazepan-1-yl)prop-1-en-2-yl)phenyl acetate (3a) White solid, yield 70%. ^{1}H NMR (600 MHz, $CDCl_3$) δ(ppm) = 8.01 (d, *J* = 8.2 Hz, 2H), 7.48 (d, *J* = 8.1 Hz, 2H), 4.56 (t, *J* = 2.1 Hz, 2H), 3.91 (s, 3H), 3.21 – 3.17 (m, 2H), 2.42 – 2.39 (m, 2H), 1.57 – 1.53 (m, 2H), 1.46 – 1.43 (m, 2H), 1.38 – 1.36 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ(ppm) = 175.99, 166.65, 155.28 (dd, *J* = 296.5, 291.6 Hz), 135.92 (t, *J* = 3.9 Hz), 129.61, 129.31, 128.31 (t, *J* = 3.7 Hz), 90.36 (dd, *J* = 18.3, 11.6 Hz), 52.11, 47.57, 42.48, 37.04, 29.71, 27.81, 23.07. ^{19}F NMR (565 MHz, $CDCl_3$) δ(ppm) = -84.70 (d, *J* = 32.2 Hz, 1F), -87.44 (d, *J* = 32.1 Hz, 1F). HRMS (ESI) for $C_{17}H_{20}F_2NO_3^+$ [M+H] $^+$ calcd. 324.1406, found 324.1404



Ethyl 4-(1,1-difluoro-3-(2-oxoazepan-1-yl)prop-1-en-2-yl)benzoate (**3b**) White solid, yield 45%. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) = 8.02 (d, *J* = 8.5 Hz, 2H), 7.48 (d, *J* = 7.0 Hz, 2H), 4.56 (t, *J* = 2.1 Hz, 2H), 4.37 (q, *J* = 7.2 Hz, 2H), 3.28 – 3.13 (m, 2H), 2.53 – 2.29 (m, 2H), 1.61 – 1.55 (m, 2H), 1.49 – 1.43 (m, 2H), 1.42 – 1.35 (m, 5H). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm) = 175.97, 166.17, 155.29 (dd, *J* = 296.3, 291.5 Hz), 135.82 (t, *J* = 3.8 Hz), 129.72, 129.59, 128.30 (t, *J* = 3.7 Hz), 90.40 (dd, *J* = 18.3, 11.6 Hz), 77.21, 77.00, 76.79, 60.99, 47.61, 42.57, 37.06, 29.72, 27.84, 23.11, 14.28. ^{19}F NMR (565 MHz, $CDCl_3$) δ (ppm) = -84.81 (d, *J* = 32.1 Hz, 1F), -87.58 (d, *J* = 32.5 Hz, 1F). HRMS (ESI) for $C_{18}H_{22}F_2NO_3^+$ [M+H] $^+$ calcd. 338.1562, found 338.1550

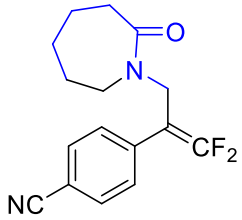


1-(2-(4-acetylphenyl)-3,3-difluoroallyl)azepan-2-one (3c) White solid, yield 42%. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) = 7.94 (d, *J* = 8.2 Hz, 2H), 7.52 (d, *J* = 7.8 Hz, 2H), 4.57 (s, 2H), 3.23 – 3.20 (m, 2H), 2.60 (s, 3H), 2.42 – 2.39 (m, 2H), 1.65 – 1.52 (m, 2H), 1.48 – 1.39 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm) = 197.53, 176.07,155.38 (dd, *J* = 296.7, 291.9 Hz), 136.18, 136.10, 128.53 (t, *J* = 3.3 Hz), 128.39, 90.37 (dd, *J* = 18.3, 11.4 Hz), 47.59, 42.47, 37.04, 29.72, 27.83, 26.56, 23.10. ^{19}F NMR (565 MHz, $CDCl_3$) δ (ppm) = -84.50 (d, *J* = 31.9 Hz, 1F), -87.28 (d, *J* = 31.8 Hz, 1F). HRMS (ESI) for $C_{17}H_{20}F_2NO_2^+$ [M+H] $^+$ calcd. 308.1457, found 308.1452.

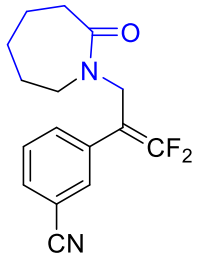


1-(2-(4-bromophenyl)-3,3-difluoroallyl)azepan-2-one (3d) White solid, Yield 28%. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) = 7.63 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 7.2 Hz, 2H), 4.54 (t, *J* = 2.2 Hz, 2H), 3.22 – 3.17 (m, 2H), 2.43 – 2.38 (m, 2H), 1.61 – 1.57 (m, 2H), 1.48 – 1.44 (m, 2H), 1.41 – 1.37 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm) = 176.08, 155.50 (dd, *J* = 297.6, 292.8 Hz), 136.10, 132.15, 129.03 (t, *J* = 3.8 Hz), 118.51, 111.49, 90.21 (dd, *J* = 18.8, 11.0 Hz), 47.60, 42.25, 36.99, 29.69,

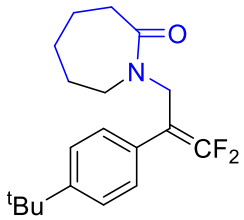
27.87, 23.11. ^{19}F NMR (565 MHz, $CDCl_3$) δ (ppm) = -83.61 (d, *J* = 30.0 Hz, 1F), -86.20 (d, *J* = 29.7 Hz, 1F). HRMS (ESI) for $C_{15}H_{17}BrF_2NO^+$ [M+H] $^+$ calcd. 344.0456, found 344.0451.



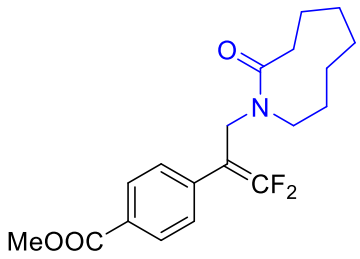
4-(1,1-difluoro-3-(2-oxoazepan-1-yl)prop-1-en-2-yl)benzonitrile (**3e**) White solid, Yield 38%. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) = 7.64 (d, *J* = 8.5 Hz, 2H), 7.54 (d, *J* = 7.1 Hz, 2H), 4.55 (t, *J* = 2.1 Hz, 2H), 3.22 – 3.18 (m, 2H), 2.44 – 2.39 (m, 2H), 1.62 – 1.56 (m, 2H), 1.50 – 1.43 (m, 2H), 1.43 – 1.36 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm) = 176.08, 155.50 (dd, *J* = 297.7, 292.7 Hz), 136.10 (t, *J* = 4.1 Hz), 132.15, 129.02 (t, *J* = 3.9 Hz), 118.51, 111.49, 90.31, 90.24, 90.18, 90.11, 77.21, 77.00, 76.79, 47.60, 42.24 (d, *J* = 3.2 Hz)., 36.99, 29.68, 27.87, 23.10. ^{19}F NMR (565 MHz, $CDCl_3$) δ (ppm) = -83.61 (d, *J* = 30.0 Hz, 1F), -86.20 (d, *J* = 30.0 Hz, 1F). HRMS (ESI) for $C_{16}H_{17}F_2N_2O^+$ [M+H] $^+$ calcd. 291.1303, found 291.1294.



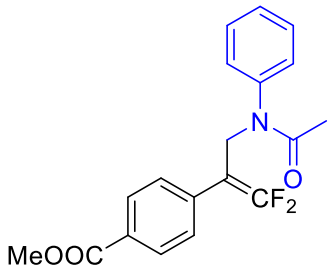
3-(1,1-difluoro-3-(2-oxoazepan-1-yl)prop-1-en-2-yl)benzonitrile (3f) White solid, yield 35%.^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) = 7.71 – 7.64 (m, 2H), 7.61 – 7.54 (m, 1H), 7.48 (t, *J* = 7.8 Hz, 1H), 4.52 (t, *J* = 2.2 Hz, 2H), 3.24 – 3.20 (m, 2H), 2.43 – 2.39 (m, 2H), 1.64 – 1.58 (m, 2H), 1.48 (p, *J* = 5.6, 5.1 Hz, 2H), 1.45 – 1.40 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm) = 176.01, 155.34 (dd, *J* = 295.9, 292.0 Hz), 132.71 (t, *J* = 3.3 Hz), 132.05 (dd, *J* = 5.2, 2.6 Hz), 131.29, 129.34, 118.38, 112.75, 89.60 (dd, *J* = 19.3, 11.6 Hz), 47.77, 42.61 (d, *J* = 3.3 Hz), 36.94, 29.68, 27.91, 23.12. ^{19}F NMR (565 MHz, $CDCl_3$) δ (ppm) = -84.99 (d, *J* = 32.0 Hz, 1F), -87.39 (d, *J* = 32.6 Hz, 1F). HRMS (ESI) for $C_{16}H_{17}F_2N_2O^+$ [M+H] $^+$ calcd. 291.1303, found 291.1304.



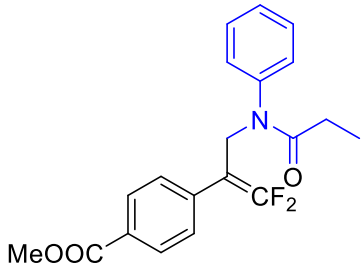
1-(2-(4-(tert-butyl)phenyl)-3,3-difluoroallyl)azepan-2-one (3g) White solid, yield 42%. H NMR (600 MHz, $CDCl_3$) δ (ppm) = 7.36 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.2 Hz, 2H), 4.51 (s, 2H), 3.20 – 3.18 (m, 2H), 2.44 – 2.41 (m, 2H), 1.60 – 1.53 (m, 2H), 1.50 – 1.43 (m, 2H), 1.42 – 1.35 (m, 2H), 1.30 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm) = 175.94, 154.99 (dd, *J* = 294.2, 289.8 Hz), 150.61, 127.88, 127.86 (t, *J* = 3.1 Hz), 125.28, 90.12 (dd, *J* = 17.4, 12.4 Hz), 47.41, 42.63, 37.11, 34.48, 31.17, 29.74, 27.61, 23.03. ^{19}F NMR (565 MHz, $CDCl_3$) δ (ppm) = -85.89 (d, *J* = 35.5 Hz, 1F), -88.72 (d, *J* = 35.3 Hz, 1F). HRMS (ESI) for $C_{19}H_{26}F_2NO^+$ [M+H] $^+$ calcd. 322.1977, found 322.1976.



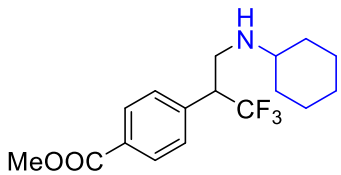
4-(1,1-difluoro-3-(2-oxoazonan-1-yl)prop-1-en-2-yl)phenyl acetate (3h) brown Solid, yield 23%.^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) = 8.00 (d, *J* = 8.2 Hz, 2H), 7.47 (d, *J* = 7.9 Hz, 2H), 4.56 (s, 2H), 3.91 (s, 3H), 3.33 (t, *J* = 5.9 Hz, 2H), 2.39 – 2.34 (m, 2H), 1.75 (s, 2H), 1.63 (s, 2H), 1.44 (d, *J* = 15.7 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm) = 175.77, 166.59,155.18 (dd, *J* = 296.0, 291.7 Hz), 135.89, 129.57, 129.26, 128.22 (t, *J* = 3.3 Hz), 89.64 (dd, *J* = 18.8, 12.3 Hz), 52.05, 46.02, 39.06, 34.84, 28.32, 26.03, 25.59, 24.60, 21.41. ^{19}F NMR (565 MHz, $CDCl_3$) δ (ppm) = -84.52 (d, *J* = 32.1 Hz, 1F), -87.23 (d, *J* = 32.1 Hz, 1F). HRMS (ESI) for $C_{19}H_{24}F_2NO_3^+$ [M+H] $^+$ calcd. 352.1719, found 352.1723.



4-(1,1-difluoro-3-(N-phenylacetamido)prop-1-en-2-yl)phenyl acetate (3i) White liquid, yield 38%. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) = 7.94 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 7.0 Hz, 2H), 7.27 – 7.24 (m, 3H), 6.77 (dd, *J* = 6.6, 3.0 Hz, 2H), 4.85 (s, 2H), 3.86 (s, 3H), 1.65 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm) = 170.58, 166.72, 155.41 (dd, *J* = 296.5, 292.7 Hz), 141.22, 136.14 (t, *J* = 4.2 Hz), 129.69, 129.57, 129.31, 128.35, 128.32, 128.29, 128.11, 89.71 (dd, *J* = 18.6, 12.9 Hz), 52.16, 43.65, 22.62. ^{19}F NMR (ppm) = (565 MHz, $CDCl_3$) δ -85.04 (d, *J* = 28.7 Hz, 1F), -86.40 (d, *J* = 28.6 Hz, 1F). HRMS (ESI) for $C_{19}H_{18}F_2NO_3^+$ [M+H] $^+$ calcd. 346.1249, found 346.1251.

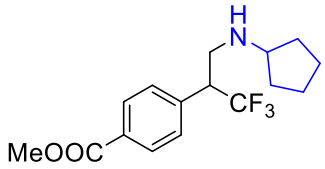


4-(1,1-difluoro-3-(N-phenylpropionamido)prop-1-en-2-yl)phenyl acetate (3j) Yellow solid yield 36%. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) = 8.02 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.33 – 7.31 (m, 3H), 6.84 – 6.81 (m, 2H), 4.92 (t, *J* = 2.1 Hz, 2H), 3.93 (s, 3H), 1.91 (q, *J* = 7.4 Hz, 2H), 0.95 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm) = 173.96, 166.68,155.32 (dd, *J* = 296.5, 292.5 Hz), 140.87, 136.18 (t, *J* = 4.0 Hz), 129.61, 129.49, 129.22, 128.30 (d, *J* = 3.0 Hz), 128.25, 128.19, 89.74 (dd, *J* = 18.8, 12.6 Hz), 52.10, 43.87, 27.70, 9.44. ^{19}F NMR (565 MHz, $CDCl_3$) δ (ppm) = -85.13 (d, *J* = 28.9 Hz, 1F), -86.42 (d, *J* = 29.0 Hz, 1F). HRMS (ESI) for $C_{20}H_{20}F_2NO_3^+$ [M+H] $^+$ calcd. 360.1406, found 360.1390.

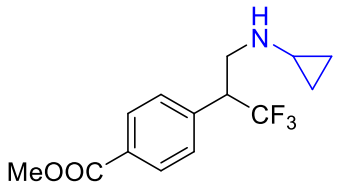


4-(3-(cyclohexylamino)-1,1,1-trifluoropropan-2-yl)phenyl acetate (**5a**). Yellow oil, yield 85% ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm) = 7.97 (d, *J* = 8.0 Hz, 2H), 7.54 (d, *J* = 8.0 Hz, 2H), 3.91 – 3.85 (m, 4H), 3.17 (dd, *J* = 12.1, 4.7 Hz, 1H), 3.08 (dd, *J* = 12.1, 9.6 Hz, 1H), 2.35 – 2.29 (m, 1H), 1.74 – 1.48

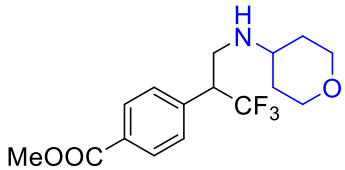
(m, 5H), 1.33 (s, 1H), 1.19 – 1.02 (m, 3H), 0.96 – 0.82 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ (ppm) =165.91, 139.61, 129.59, 129.35, 129.25, 126.52 (q, J = 280.4 Hz), 55.50, 52.13, 49.20 (q, J = 24.5 Hz), 44.82, 32.87, 32.49, 25.69, 24.30, 24.21. ^{19}F NMR (565 MHz, DMSO-d_6) δ (ppm) = -66.76. HRMS (ESI) for $C_{17}H_{23}F_3NO_2^+$ [M+H] $^+$ calcd. 360.1406, found 360.1390.



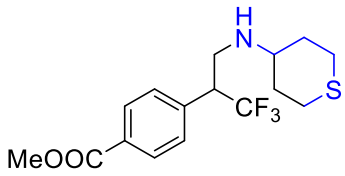
4-(3-(cyclopentylamino)-1,1,1-trifluoropropan-2-yl)phenyl acetate (**5b**). Yellow oil, yield 70%**.** ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm) = 7.96 (d, J = 8.2 Hz, 2H), 7.53 (d, J = 8.1 Hz, 2H), 3.91 – 3.87 (m, 1H), 3.85 (s, 3H), 3.11 (dd, J = 12.1, 4.7 Hz, 1H), 3.03 (dd, J = 12.1, 9.6 Hz, 1H), 2.97 – 2.93 (m, 1H), 1.66 – 1.60 (m, 2H), 1.54 – 1.36 (m, 5H), 1.19 – 1.11 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ (ppm) = 165.94, 139.60, 129.60, 129.39, 129.29, 126.53 (q, J = 280.4 Hz), 58.82, 52.15, 49.06 (q, J = 24.5 Hz), 46.39, 32.41, 32.21, 23.40, 23.37. ^{19}F NMR (565 MHz, $CDCl_3$) δ (ppm) = -62.45. HRMS (ESI) for $C_{16}H_{21}F_3NO_2^+$ [M+H] $^+$ calcd. 316.1519, found 316.1507.



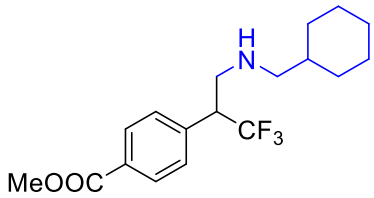
Methyl 4-(3-(cyclopropylamino)-1,1,1-trifluoropropan-2-yl)benzoate (5c) Yellow oil, yield 84%. ^{1}H NMR (600 MHz, $CDCl_3$) δ(ppm) = 8.06 (d, J = 8.4 Hz, 2H), 7.41 (d, J = 8.1 Hz, 2H), 3.93 (s, 3H), 3.65 – 3.51 (m, 1H), 3.35 (dd, J = 12.6, 4.9 Hz, 1H), 3.21 (dd, J = 12.6, 9.6 Hz, 1H), 2.10 – 2.03 (m, 1H), 1.54 (s, 1H), 0.46 – 0.37 (m, 2H), 0.32 – 0.23 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ(ppm) = 166.54, 138.73, 138.72, 130.34, 130.05, 129.16, 126.11 (q, J = 280.2 Hz), 52.16, 50.17 (q, J = 25.9 Hz), 48.05 (q, J = 2.5 Hz), 29.87, 6.56, 6.13. ^{19}F NMR (565 MHz, DMSO-d_6) δ (ppm) = -66.68. HRMS (ESI) for $C_{14}H_{17}F_3NO_2^+$ [M+H] $^+$ calcd. 288.1206, found 288.1207.



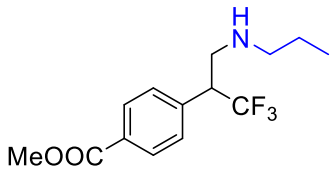
Methyl 4-(1,1,1-trifluoro-3-((tetrahydro-2H-pyran-4-yl)amino)propan-2-yl) benzoate (**5d**). Yellow oil, yield 83 %. ^{1}H NMR (600 MHz, DMSO-d_6) δ(ppm) = 7.98 (d, J = 8.3 Hz, 2H), 7.55 (d, J = 8.1 Hz, 2H), 3.94 – 3.88 (m, 1H), 3.87 (s, 3H), 3.78 – 3.72 (m, 2H), 3.25 – 3.07 (m, 3H), 3.10 (dd, J = 12.2, 9.5 Hz, 1H), 2.59 – 2.54 (m, 1H), 1.66 (t, J = 14.8 Hz, 2H), 1.19 – 1.04 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ(ppm) = 165.91, 139.58, 129.60, 129.37, 129.26, 126.51 (q, J = 280.6 Hz), 65.69, 65.65, 52.79, 52.12, 49.16 (q, J = 24.6 Hz), 44.43, 44.41, 33.11, 32.80. ^{19}F NMR (565 MHz, DMSO-d_6) δ (ppm) = -66.72. HRMS (ESI) for $C_{16}H_{21}F_3NO_3^+$ [M+H] $^+$ calcd. 332.1468, found 332.1468.



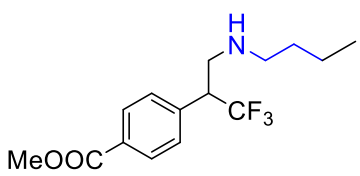
Methyl 4-(1,1,1-trifluoro-3-((tetrahydro-2H-thiopyran-4-yl)amino)propan-2-yl)benzoate.(**5e**). Yellow oil, yield 81%**.** ^{1}H NMR (600 MHz, DMSO-d_6) δ(ppm) = 7.98 (d, *J* = 8.3 Hz, 2H), 7.55 (d, *J* = 8.1 Hz, 2H), 3.91 – 3.86 (m, 4H), 3.18 (dd, *J* = 12.2, 4.8 Hz, 1H), 3.09 (dd, *J* = 12.2, 9.5 Hz, 1H), 2.61 – 2.53 (m, 2H), 2.50 – 2.36 (m, 3H), 2.00 – 1.93 (m, 2H), 1.50 (s, 1H), 1.37 – 1.21 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ = 165.90, 139.59, 129.58, 129.34, 129.23, 126.49 (q, *J* = 280.7 Hz), 54.36, 52.11, 49.19 (q, *J* = 24.4 Hz), 44.57, 33.89, 33.48, 26.24, 26.16. ^{19}F NMR (565 MHz, DMSO-d_6) δ (ppm) = -66.76. HRMS (ESI) for $C_{16}H_{21}F_3NO_2S^+$ [M+H] $^+$ calcd. 348.1240, found 348.1239.



Methyl 4-(3-((cyclohexylmethyl)amino)-1,1,1-trifluoropropan-2-yl)benzoate (**5f**). Yellow oil, yield 85% ^{1}H NMR (600 MHz, DMSO-d_6) δ(ppm) = 7.98 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 8.1 Hz, 2H), 3.96 – 3.92 (m, 1H), 3.87 (s, 3H), 3.12 (dd, *J* = 12.3, 4.9 Hz, 1H), 3.05 (dd, *J* = 12.2, 9.5 Hz, 1H), 2.35 – 2.25 (m, 2H), 1.64 – 1.52 (m, 5H), 1.43 (s, 1H), 1.31 – 1.20 (m, 1H), 1.16 – 1.02 (m, 3H), 0.81 – 0.68 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ(ppm) = 165.89, 139.60, 129.55, 129.32, 129.21, 126.52 (q, *J* = 280.4 Hz), 55.56, 52.08, 48.73 (q, *J* = 24.5 Hz), 47.98, 47.96, 37.22, 30.82, 30.77, 26.20, 25.48, 25.44. ^{19}F NMR (565 MHz, $CDCl_3$) δ (ppm) = -62.21. HRMS (ESI) for $C_{18}H_{25}F_3NO_2^+$ [M+H] $^+$ calcd. 344.1832, found 344.1840.

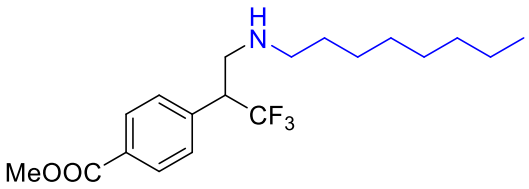


Methyl 4-(1,1,1-trifluoro-3-(propylamino)propan-2-yl)benzoate (**5g**). Yellow oil, yield 65%. ^{1}H NMR (600 MHz, DMSO-d_6) δ(ppm) = 7.98 (d, *J* = 8.3 Hz, 2H), 7.55 (d, *J* = 8.1 Hz, 2H), 3.96 – 3.91 (m, 1H), 3.86 (s, 3H), 3.13 (dd, *J* = 12.2, 4.9 Hz, 1H), 3.06 (dd, *J* = 12.2, 9.5 Hz, 1H), 2.48 – 2.36 (m, 2H), 1.35 – 1.26 (m, 2H), 0.76 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ(ppm) = 165.91, 139.61, 129.59, 129.36, 129.25, 126.53 (q, *J* = 280.4 Hz), 52.12, 50.71, 48.78 (q, *J* = 24.6 Hz), 47.69, 22.33, 11.52. ^{19}F NMR (565 MHz, $CDCl_3$) δ (ppm) = -62.41. HRMS (ESI) for $C_{14}H_{19}F_3NO_2^+$ [M+H] $^+$ calcd. 290.1362, found 290.1363.

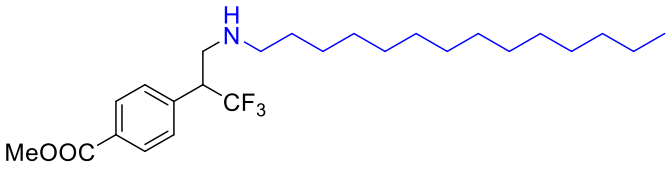


Methyl 4-(3-(butylamino)-1,1,1-trifluoropropan-2-yl)benzoate (**5h**). Yellow oil, yield 75%. ^{1}H NMR (600 MHz, DMSO-d_6) δ(ppm) = 7.97 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 8.1 Hz, 2H), 3.95 – 3.90 (m, 1H), 3.86 (s, 3H), 3.12 (dd, *J* = 12.2, 4.9 Hz, 1H), 3.06 (dd, *J* = 12.2, 9.5 Hz, 1H), 2.50 – 2.39 (m, 2H), 1.52 (s, 1H), 1.29 – 1.17 (m, 4H), 0.80 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ(ppm) = 165.91, 139.60, 129.58, 129.35, 129.24, 126.53 (q, *J* = 280.4 Hz), 52.13,

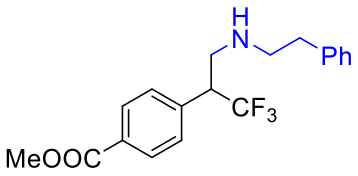
48.75 (q, *J* = 24.5 Hz), 48.47, 47.78, 31.38, 19.74, 13.74. ^{19}F NMR (565 MHz, DMSO-d_6) δ (ppm) = -66.78. HRMS (ESI) for $C_{15}H_{21}F_3NO_2^+$ [M+H] $^+$ calcd. 304.1519, found 304.1512.



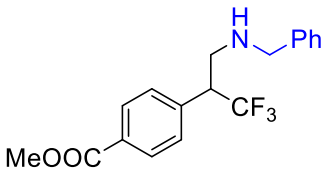
Methyl 4-(1,1,1-trifluoro-3-(octylamino)propan-2-yl)benzoate (5i) Yellow oil, yield 42%**.** ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm) = 7.97 (d, *J* = 8.1 Hz, 2H), 7.54 (d, *J* = 8.0 Hz, 2H), 3.95 – 3.91 (m, 1H), 3.86 (s, 3H), 3.12 (dd, *J* = 12.2, 4.8 Hz, 1H), 3.06 (dd, *J* = 12.2, 9.6 Hz, 1H), 2.49 – 2.37 (m, 2H), 1.44 (s, 1H), 1.31 – 1.11 (m, 12H), 0.84 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ (ppm) = 165.88, 139.59, 129.57, 129.33, 129.22, 126.52 (q, *J* = 280.5 Hz), 52.09, 52.07, 48.79 (d, *J* = 24.9 Hz), 48.71, 47.71, , 31.19, 29.17, 28.79, 28.66, 26.59, 22.03, 13.83, 13.82. ^{19}F NMR (565 MHz, DMSO-d_6) δ (ppm) = -66.82. HRMS (ESI) for $C_{19}H_{29}F_3NO_2^+$ [M+H] $^+$ calcd. 360.2145, found 360.2146.



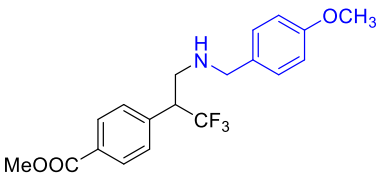
Methyl 4-(1,1,1-trifluoro-3-(tetradecylamino)propan-2-yl)benzoate (5j) Yellow oil, yield 39%. ^{1}H NMR (600 MHz, DMSO-d_6) δ(ppm) = 7.96 (d, *J* = 8.1 Hz, 2H), 7.53 (d, *J* = 8.1 Hz, 2H), 3.93 – 3.89 (m, 1H), 3.85 (s, 3H), 3.11 (dd, *J* = 12.2, 4.9 Hz, 1H), 3.04 (dd, *J* = 12.2, 9.6 Hz, 1H), 2.47 – 2.37 (m, 2H), 1.50 (s, 1H), 1.27 – 1.13 (m, 24H), 0.84 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ (ppm) = 165.88, 139.58, 129.58, 129.33, 129.22, 126.51 (q, *J* = 280.5 Hz), 52.11, 48.75 (q, *J* = 24.2 Hz), 48.69, 47.69, 31.25, 29.13, 28.99, 28.97, 28.96, 28.91, 28.79, 28.65, 26.55, 22.04, 13.88. ^{19}F NMR (565 MHz, $CDCl_3$) δ (ppm) = -62.51. HRMS (ESI) for $C_{24}H_{39}F_3NO_2^+$ [M+H] $^+$ calcd. 444.3084, found 444.3094.



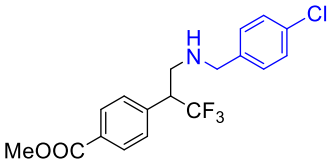
Methyl 4-(1,1,1-trifluoro-3-(phenethylamino)propan-2-yl)benzoate (5k). Yellow oil, yield 82 % ^{1}H NMR (600 MHz, DMSO-d_6) δ = 7.97 (d, *J* = 8.1 Hz, 2H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.22 (t, *J* = 7.4 Hz, 2H), 7.17 – 7.09 (m, 3H), 3.98 – 3.93 (m, 1H), 3.87 (s, 3H), 3.17 (dd, *J* = 12.3, 4.9 Hz, 1H), 3.12 (dd, *J* = 12.2, 9.5 Hz, 1H), 2.79 – 2.57 (m, 4H), 1.50 (s, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ = 165.91, 140.07, 139.43, 129.56, 129.37, 129.27, 128.46, 128.09, 126.50 (q, *J* = 280.0 Hz), 125.72, 52.11, 50.32, 48.71 (q, *J* = 24.6 Hz), 47.54, 47.52, 35.53. ^{19}F NMR (565 MHz, $CDCl_3$) δ (ppm) = -62.39. HRMS (ESI) for $C_{19}H_{21}F_3NO_2^+$ [M+H] $^+$ calcd. 352.1519 found 352.1515.



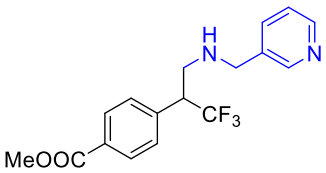
Methyl 4-(3-(benzylamino)-1,1,1-trifluoropropan-2-yl)benzoate (**5l**). Yellow oil, yield 89%. ^{1}H NMR (600 MHz, DMSO-d_6) δ(ppm) = 7.99 (d, J = 8.3 Hz, 2H), 7.54 (d, J = 8.1 Hz, 2H), 7.28 (t, J = 7.4 Hz, 2H), 7.26 – 7.19 (m, 3H), 4.03 – 3.97 (m, 1H), 3.87 (s, 3H), 3.68 (dd, J = 22.0, 14.1 Hz, 2H), 3.13 (dd, J = 12.2, 4.9 Hz, 1H), 3.04 (dd, J = 12.2, 9.6 Hz, 1H), 2.11 (s, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ(ppm) = 165.91, 140.24, 139.54, 129.58, 129.39, 129.26, 128.06, 127.82, 126.60, 126.50 (q, J = 280.4 Hz), 52.33, 52.10, 48.70 (q, J = 24.6 Hz), 46.91. ^{19}F NMR (565 MHz, $CDCl_3$) δ (ppm) = -62.44. HRMS (ESI) for $C_{18}H_{19}F_3NO_2^+$ [M+H] $^+$ calcd. 338.1362 found 338.1363.



Methyl 4-(1,1,1-trifluoro-3-((4-methoxybenzyl)amino)propan-2-yl)benzoate (**5m**). Yellow oil, yield 80%. ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm) = 7.98 (d, J = 8.3 Hz, 2H), 7.53 (d, J = 8.1 Hz, 2H), 7.14 (d, J = 8.6 Hz, 2H), 6.84 (d, J = 8.6 Hz, 2H), 3.99 – 3.95 (m, 1H), 3.87 (s, 3H), 3.72 (s, 5H), 3.59 (dd, J = 20.6, 13.4 Hz, 2H), 3.09 (dd, J = 12.2, 4.9 Hz, 1H), 3.01 (dd, J = 12.2, 9.6 Hz, 1H), 2.01 (s, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ(ppm) = 165.93, 158.08, 139.56, 132.12, 129.59, 129.38, 129.27, 129.02, 126.52 (q, J = 280.4 Hz), 113.49, 54.93, 52.13, 51.71, 48.65 (q, J = 24.5 Hz), 46.74. ^{19}F NMR (565 MHz, DMSO-d_6) δ (ppm) = -66.70. HRMS (ESI) for $C_{19}H_{21}F_3NO_3^+$ [M+H] $^+$ calcd. 368.1468 found 368.1470.

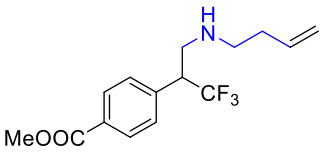


Methyl 4-(3-((4-chlorobenzyl)amino)-1,1,1-trifluoropropan-2-yl)benzoate (**5n**). Yellow oil, yield 72%. ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm) = 7.98 (d, J = 8.4 Hz, 2H), 7.53 (d, J = 8.2 Hz, 2H), 7.35 – 7.31 (m, 2H), 7.27 – 7.23 (m, 2H), 4.04 – 3.93 (m, 1H), 3.87 (s, 3H), 3.65 (dd, J = 20.7, 14.0 Hz, 2H), 3.09 (dd, J = 12.2, 4.9 Hz, 1H), 3.01 (dd, J = 12.2, 9.5 Hz, 1H), 2.22 (s, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ(ppm) = 165.91, 139.50, 139.36, 131.09, 129.62, 129.58, 129.38, 129.26, 128.01, 126.48 (q, J = 280.3 Hz), 52.13, 51.43, 48.65 (q, J = 24.7 Hz), 46.82. ^{19}F NMR (565 MHz, DMSO-d_6) δ (ppm) = -66.68. HRMS (ESI) for $C_{18}H_{18}ClF_3NO_2^+$ [M+H] $^+$ calcd. 372.0973 found 372.0974.

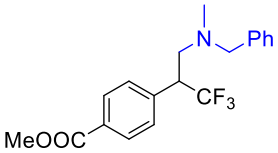


Methyl 4-(1,1,1-trifluoro-3-((pyridin-3-ylmethyl)amino)propan-2-yl)benzoate (**5o**). Yellow oil, yield 65 %. ^{1}H NMR (600 MHz, DMSO-d_6) δ(ppm) = 8.44 – 8.41 (m, 2H), 7.98 (d, J = 8.4 Hz, 2H), 7.64 – 7.59 (m, 1H), 7.54 (d, J = 8.2 Hz, 2H), 7.30 (dd, J = 7.7, 4.8 Hz, 1H), 4.03 – 3.97 (m, 1H), 3.87 (s, 3H), 3.74 – 3.65 (m, 2H), 3.11 (dd, J = 12.3, 4.9 Hz, 1H), 3.03 (dd, J = 12.2, 9.5 Hz,

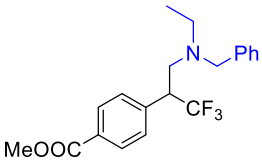
1H), 2.28 (s, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ(ppm) = 165.92, 149.32, 147.96, 139.49, 135.58, 135.51, 129.60, 129.39, 129.27, 126.48 (q, J = 280.5 Hz), 123.26, 52.14, 49.59, 48.64 (q, J = 24.7 Hz), 46.89, 46.87. ^{19}F NMR (565 MHz, DMSO-d_6) δ (ppm) = -66.74. HRMS (ESI) for $C_{17}H_{18}F_3N_2O_2^+$ [M+H] $^+$ calcd. 339.1315 found 339.1314.



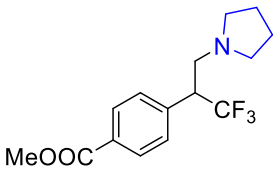
Methyl 4-(3-(but-3-en-1-ylamino)-1,1,1-trifluoropropan-2-yl)benzoate (**5p**) Yellow oil, yield 68%. ^{1}H NMR (600 MHz, DMSO-d_6) δ = 7.97 (d, J = 8.4 Hz, 2H), 7.55 (d, J = 8.1 Hz, 2H), 5.69 (ddt, J = 17.0, 10.2, 6.8 Hz, 1H), 5.01 – 4.87 (m, 2H), 3.97 – 3.92 (m, 1H), 3.86 (s, 3H), 3.18 – 3.06 (m, 2H), 2.62 – 2.46 (m, 2H), 2.09 – 2.02 (m, 2H), 1.55 (s, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ (ppm) = 165.91, 139.49, 136.70, 129.61, 129.38, 129.27, 126.51 (q, J = 280.6 Hz), 115.75, 52.15, 48.69 (q, J = 24.6 Hz), 48.06, 47.53, 33.59. ^{19}F NMR (565 MHz, DMSO-d_6) δ (ppm) = -66.77. HRMS (ESI) for $C_{15}H_{19}F_3NO_2^+$ [M+H] $^+$ calcd. 302.1362 found 302.1360.



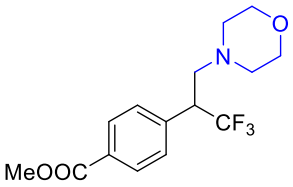
Methyl 4-(3-(benzyl(methyl)amino)-1,1,1-trifluoropropan-2-yl)benzoate (**5q**). Yellow oil, yield 66%. ^{1}H NMR (600 MHz, DMSO-d_6) δ(ppm) = 7.97 (d, J = 8.4 Hz, 2H), 7.52 (d, J = 8.0 Hz, 2H), 7.28 – 7.18 (m, 3H), 7.10 – 7.02 (m, 2H), 4.24 – 4.20 (m, 1H), 3.88 (s, 3H), 3.58 (d, J = 13.2 Hz, 1H), 3.38 (d, J = 3.2 Hz, 1H), 3.04 (dd, J = 12.6, 10.3 Hz, 1H), 2.83 (dd, J = 12.6, 4.9 Hz, 1H), 2.10 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ(ppm) = 165.94, 139.73, 138.35, 129.64, 129.26, 129.03, 128.59, 127.97, 126.87,126.53 (q, J = 280.4 Hz), 61.11, 54.94, 52.09, 46.57 (q, J = 24.5 Hz), 41.67. ^{19}F NMR (565 MHz, DMSO-d_6) δ(ppm) = 66.75. HRMS (ESI) for $C_{19}H_{21}F_3NO_2^+$ [M+H] $^+$ calcd. 352.1519 found 352.1518.



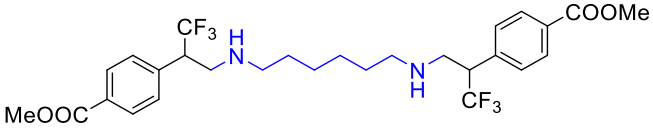
Methyl 4-(3-(benzyl(ethyl)amino)-1,1,1-trifluoropropan-2-yl)benzoate (5r) Yellow oil, yield 63%. ^{1}H NMR (600 MHz, DMSO-d_6) δ(ppm) = 7.98 (d, J = 8.3 Hz, 2H), 7.55 (d, J = 8.2 Hz, 2H), 7.23 (t, J = 7.5 Hz, 2H), 7.14 (t, J = 7.3 Hz, 1H), 7.10 (d, J = 7.2 Hz, 2H), 3.95 – 3.89 (m, 1H), 3.86 (s, 3H), 3.13 (dd, J = 12.2, 4.8 Hz, 1H), 3.06 (dd, J = 12.1, 9.7 Hz, 1H), 2.48 (t, J = 7.5 Hz, 2H), 1.65 – 1.50 (m, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ(ppm) = 166.42, 142.49, 140.12, 130.09, 129.85, 129.76, 128.67, 128.62, 127.02 (d, J = 280.5 Hz), 126.02, 52.62, 49.38 (q, J = 24.6 Hz), 48.69, 48.23, 33.16, 31.47. ^{19}F NMR (565 MHz, DMSO-d_6) δ(ppm) = -66.72. HRMS (ESI) for $C_{20}H_{23}F_3NO_2^+$ [M+H] $^+$ calcd. 366.1675 found 366.1667.



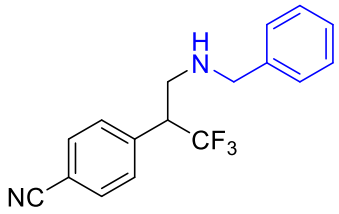
4-(1,1,1-trifluoro-3-(pyrrolidin-1-yl)propan-2-yl)phenyl acetate (**5s**). Yellow oil, yield 75%. ^{1}H NMR (600 MHz, DMSO-d_6) δ(ppm) = 7.97 (d, J = 8.3 Hz, 2H), 7.59 (d, J = 8.1 Hz, 2H), 4.08 – 4.03 (m, 1H), 3.86 (s, 3H), 3.15 (dd, J = 12.2, 10.2 Hz, 1H), 2.85 (dd, J = 12.2, 4.6 Hz, 1H), 2.49 – 2.43 (m, 2H), 2.40 – 2.31 (m, 2H), 1.63 – 1.52 (m, 4H). ^{13}C NMR (151 MHz, DMSO-d_6) δ(ppm) = 165.97, 139.63, 129.64, 129.39, 129.30,126.57 (q, J = 280.4 Hz), 52.19, 50.73, 48.79 (q, J = 24.6 Hz), 22.35, 11.58. ^{19}F NMR (565 MHz, $CDCl_3$) δ(ppm) = -62.59. HRMS (ESI) for $C_{15}H_{19}F_3NO_2^+$ [M+H] $^+$ calcd. 302.1362 found 302.1361.



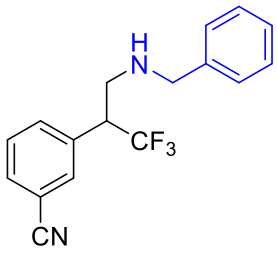
Methyl 4-(1,1,1-trifluoro-3-morpholinopropan-2-yl)benzoate (5t) Yellow oil, yield 85%**.** ^{1}H NMR (600 MHz, DMSO-d_6) δ(ppm) = 7.96 (d, J = 8.3 Hz, 2H), 7.57 (d, J = 8.1 Hz, 2H), 4.19 – 4.15 (m, 1H), 3.85 (s, 3H), 3.45 – 3.35 (m, 4H), 2.95 (dd, J = 12.7, 9.6 Hz, 1H), 2.81 (dd, J = 12.7, 5.0 Hz, 1H), 2.48 – 2.39 (m, 2H), 2.34 – 2.24 (m, 2H). ^{13}CNMR (151 MHz, DMSO-d_6) δ 165.92, 139.83, 129.56, 129.33, 129.15, 126.54 (q, J = 280.6 Hz), 65.97, 56.62, 53.08, 52.11, 45.71 (q, J = 24.6 Hz). ^{19}F NMR (565 MHz, DMSO-d_6) δ(ppm) = -66.74. HRMS (ESI) for $C_{15}H_{19}F_3NO_3^+$ [M+H] $^+$ calcd. 318.1312 found 318.1312.



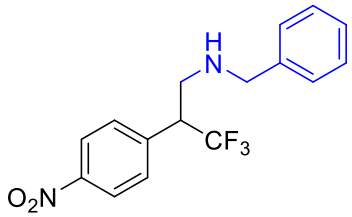
Dimethyl 4,4'-((hexane-1,6-diylbis(azanediyl))bis(3,3,3-trifluoropropane-1,2-diyl))dibenzoat (**5u**). Yellow oil, yield 25%. ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm) =7.96 (d, J = 8.1 Hz, 2H), 7.53 (d, J = 8.1 Hz, 2H), 3.93 – 3.89 (m, 1H), 3.85 (s, 3H), 3.10 (dd, J = 12.2, 4.9 Hz, 1H), 3.04 (dd, J = 12.2, 9.5 Hz, 1H), 2.44 – 2.34 (m, 2H), 1.55 (s, 1H), 1.29 – 1.16 (m, 3H), 1.16 – 1.02 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ (ppm) = 165.91, 139.59, 129.59, 129.34, 129.24, 126.52 (q, J = 280.3 Hz), 52.13,48.74 (q, J = 24.6 Hz), 48.70, 47.71, 29.15, 26.44. ^{19}F NMR (565 MHz, $CDCl_3$) δ(ppm) = -62.50. HRMS (ESI) for $C_{28}H_{35}F_6N_2O_4^+$ [M+H] $^+$ calcd. 577.2496 found 577.2493.



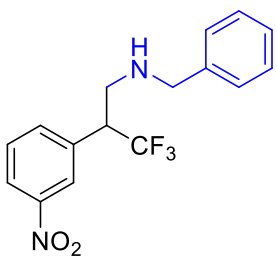
4-(3-(Benzylamino)-1,1,1-trifluoropropan-2-yl)benzonitrile (6a) white oil, yield 91%. ^{1}H NMR (600 MHz, DMSO-d_6) δ(ppm) = 7.87 (d, J = 8.0 Hz, 2H), 7.60 (d, J = 7.8 Hz, 2H), 7.31 – 7.19 (m, 5H), 4.09 – 3.96 (m, 1H), 3.66 (dd, J = 22.1, 12.4 Hz, 2H), 3.11 (dd, J = 11.9, 4.0 Hz, 1H), 3.04 (t, J = 10.9 Hz, 1H), 2.22 (s, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ(ppm) = 147.84, 142.33, 140.69, 131.14, 128.57, 128.34, 127.11, 126.78 (d, J = 280.7 Hz), 123.96, 52.76,48.90 (q, J = 24.4 Hz), 47.29. ^{19}F NMR (565 MHz, DMSO-d_6) δ(ppm) = -66.69. HRMS (ESI) for $C_{17}H_{16}F_3N_2^+$ [M+H] $^+$ calcd. 305.1260 found 305.1262.



3-(3-(Benzylamino)-1,1,1-trifluoropropan-2-yl)benzonitrile (6b) white oil, yield 70%. ^{1}H NMR (600 MHz, $CDCl_3$) δ(ppm) = 7.66 (d, J = 7.5 Hz, 1H), 7.57 (s, 1H), 7.55 – 7.47 (m, 2H), 7.32 (t, J = 7.4 Hz, 2H), 7.29 – 7.25 (m, 1H), 7.23 – 7.18 (m, 2H), 3.77 (dd, J = 13.4 Hz, 2H), 3.62 – 3.54 (m, 1H), 3.26 (dd, J = 12.5, 4.8 Hz, 1H), 3.10 (dd, J = 12.5, 9.5 Hz, 1H).^{13}C NMR (151 MHz, DMSO-d_6) δ(ppm) = 140.75, 136.26, 134.69, 133.42, 132.38, 130.24, 128.57, 128.34, 127.12, 126.86 (q, J = 280.5 Hz), 119.01, 112.09, 66.83, 52.67, 48.64 (q, J = 24.9 Hz), 46.83. ^{19}F NMR (565 MHz, DMSO-d_6) δ(ppm) = -67.00. HRMS (ESI) for $C_{17}H_{16}F_3N_2^+$ [M+H] $^+$ calcd. 305.1260 found 305.1270.

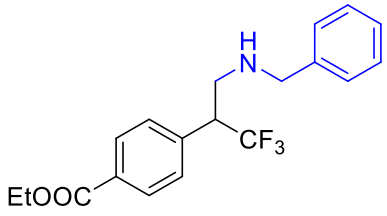


N-benzyl-3,3,3-trifluoro-2-(4-nitrophenyl)propan-1-amine (6c) red oil, yield 91%. ^{1}H NMR (600 MHz, DMSO-d_6) δ(ppm) = 8.26 (d, J = 8.2 Hz, 2H), 7.68 (d, J = 8.1 Hz, 2H), 7.31 – 7.19 (m, 5H), 4.15 – 4.08 (m, 1H), 3.67 (dd, J = 23.1, 5.0 Hz, 2H), 3.13 (dd, J = 12.0, 4.0 Hz, 1H), 3.06 (t, J = 10.9 Hz, 1H), 2.29 (s, 1H).^{13}C NMR (151 MHz, DMSO-d_6) δ(ppm) = 140.68, 140.29, 132.84, 130.80, 128.57, 128.34, 127.12, 126.84 (q, J = 280.6 Hz), 119.01, 111.52, 52.74,49.13 (q, J = 24.3 Hz), 47.16. ^{19}F NMR (565 MHz, DMSO-d_6) δ(ppm) = -66.62. HRMS (ESI) for $C_{16}H_{16}F_3N_2O_2^+$ [M+H] $^+$ calcd. 325.1158 found 325.1162.

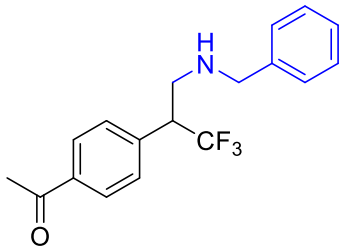


N-benzyl-3,3,3-trifluoro-2-(3-nitrophenyl)propan-1-amine (6d) white oil, yield 75%.^{1}H NMR (600 MHz, $CDCl_3$) δ(ppm) = 8.22 (d, J = 8.8 Hz, 1H), 8.18 (s, 1H), 7.63 (d, J = 7.7 Hz, 1H), 7.56 (t, J = 7.9 Hz, 1H), 7.30 (t, J = 7.2 Hz, 2H), 7.27 – 7.23 (m, 1H), 7.22 – 7.19 (m, 2H), 3.77 (q, J = 13.4 Hz, 2H), 3.71 – 3.63 (m, 1H), 3.30 (dd, J = 12.5, 4.8 Hz, 1H), 3.16 (dd, J = 12.5, 9.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ(ppm) = 148.45, 139.17, 135.72, 135.28,

129.77, 128.50, 127.97, 127.30, 125.77 (d, J = 280.7 Hz), 124.10, 123.49, 53.57, 50.23 (q, J = 25.9 Hz), 47.38. ^{19}F NMR (565 MHz, DMSO-d_6) δ(ppm) = -66.75. HRMS (ESI) for $C_{16}H_{16}F_3N_2O_2^+$ [M+H] $^+$ calcd. 325.1158 found 325.1153.

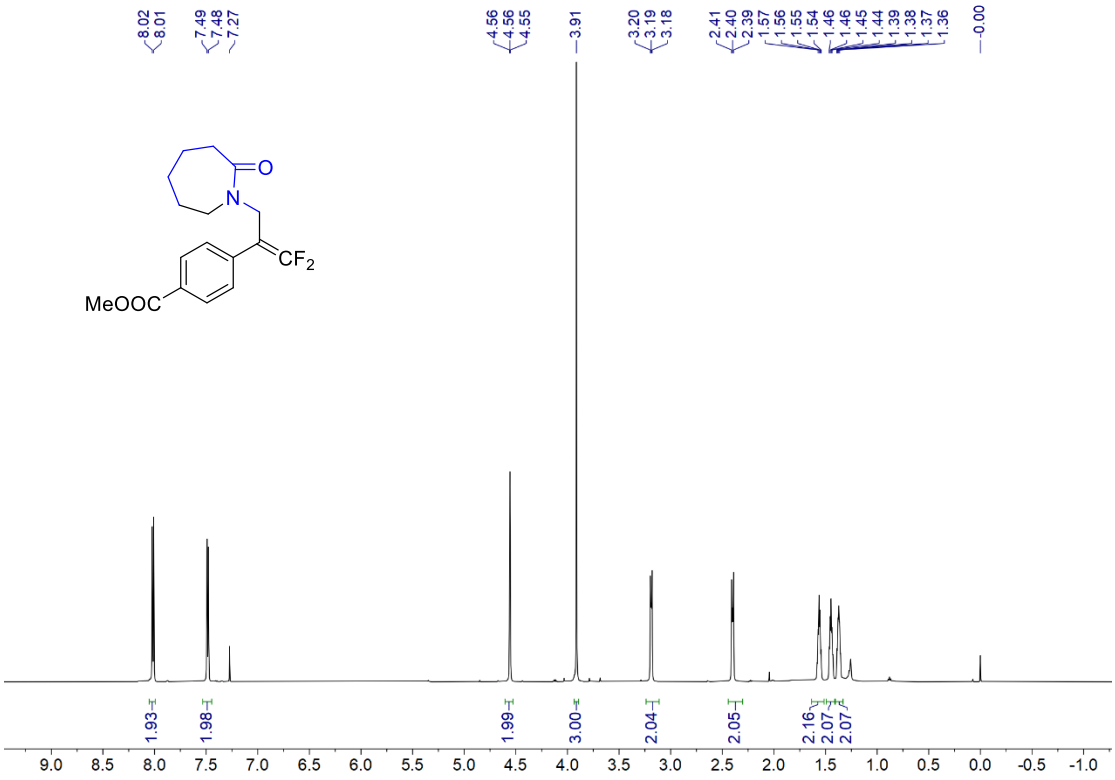


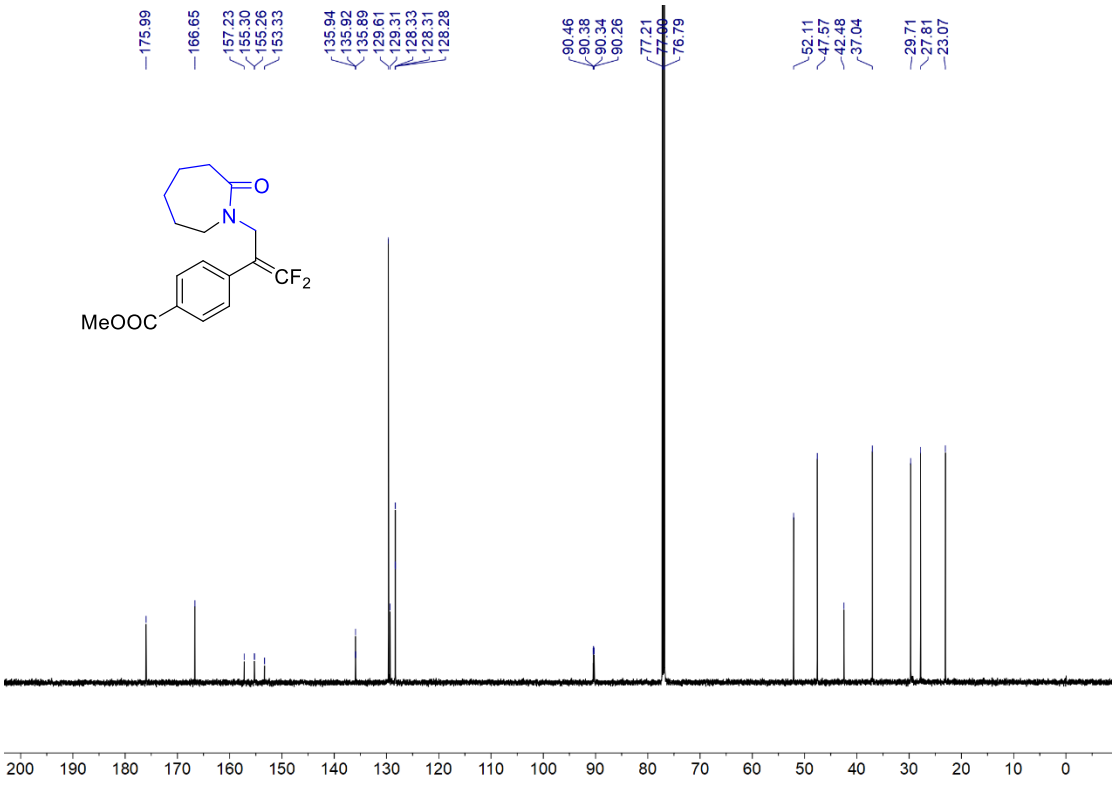
Ethyl 4-(3-(benzylamino)-1,1,1-trifluoropropan-2-yl)benzoate (6e) Yellow oil, yield 88%. ^{1}H NMR (600 MHz, DMSO-d_6) δ(ppm) = 8.01 (d, J = 8.1 Hz, 2H), 7.56 (d, J = 7.9 Hz, 2H), 7.34 – 7.21 (m, 5H), 4.36 (q, J = 7.0 Hz, 2H), 4.03 – 3.98 (m, 1H), 3.76 – 3.65 (m, 2H), 3.15 (dd, J = 12.1, 4.7 Hz, 1H), 3.06 (dd, J = 13.1, 9.8 Hz, 1H), 2.18 (s, 1H), 1.35 (t, J = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ(ppm) = 166.33, 141.14, 140.36, 130.60, 130.48, 130.14, 128.99, 128.75, 127.53,127.42 (d, J = 280.5 Hz), 61.65, 53.24, 49.60 (q, J = 24.2 Hz), 47.83, 15.03. ^{19}F NMR (565 MHz, DMSO-d_6) δ(ppm) = -66.71. HRMS (ESI) for $C_{19}H_{21}F_3NO_2^+$ [M+H] $^+$ calcd. 352.1519 found 352.1516.

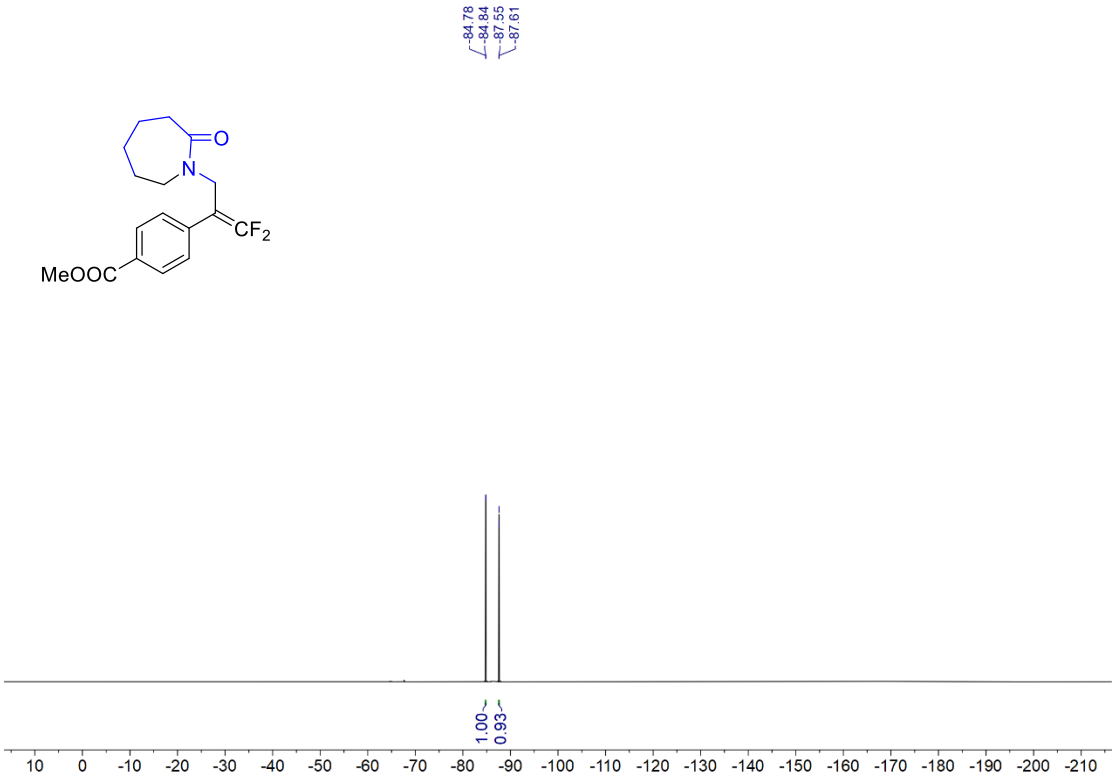


1-(4-(3-(Benzylamino)-1,1,1-trifluoropropan-2-yl)phenyl)ethan-1-one (6f) Yellow oil, yield 85%. ^{1}H NMR (600 MHz, Chloroform-d) δ 7.96 (d, J = 8.2 Hz, 2H), 7.40 (d, J = 8.0 Hz, 2H), 7.32 – 7.17 (m, 5H), 3.75 (dd, J = 20.1, 13.2 Hz, 2H), 3.69 – 3.59 (m, 1H), 3.26 (dd, J = 12.3, 4.7 Hz, 1H), 3.14 (dd, J = 12.0, 9.9 Hz, 1H), 2.60 (s, 3H), 1.32 (s, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 198.00, 140.74, 139.84, 137.01, 129.99, 128.80, 128.57, 128.33, 127.10, 127.02 (q, J = 280.5 Hz), 52.85,49.19 (q, J = 24.3 Hz), 47.41, 27.16. ^{19}F NMR (565 MHz, $CDCl_3$) δ -64.95. HRMS (ESI) for $C_{18}H_{19}F_3NO^+$ [M+H] $^+$ calcd. 322.1413 found 322.1413.

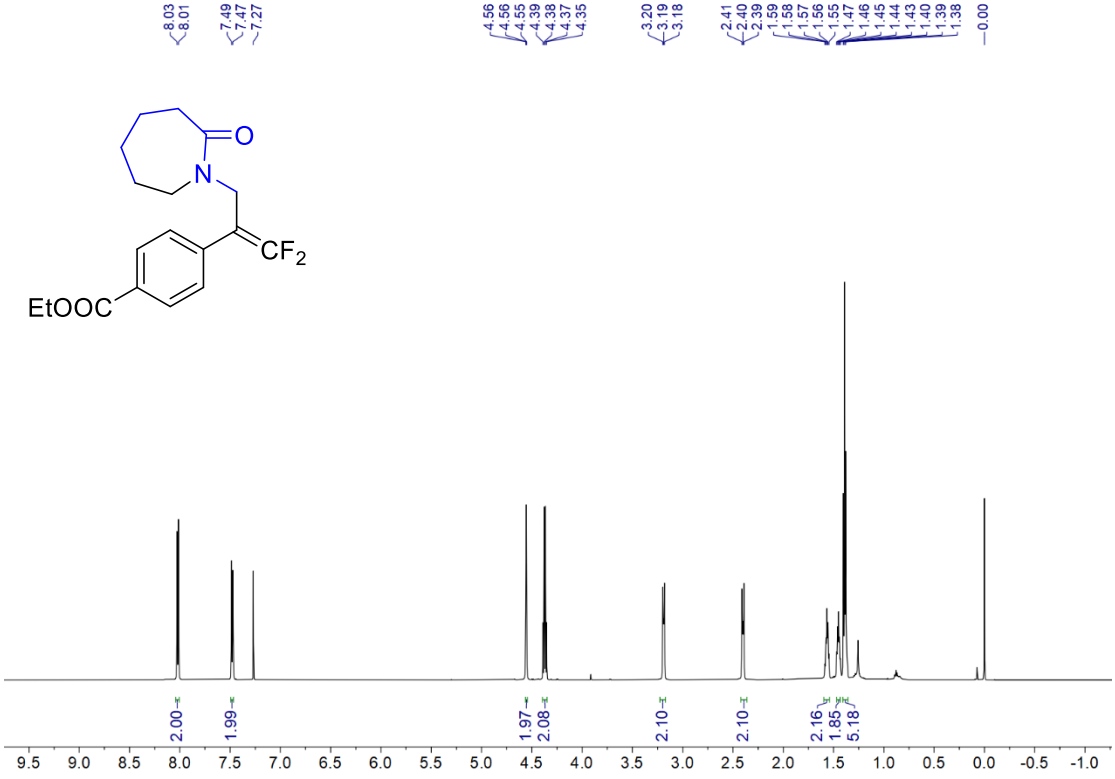
4-(1,1-difluoro-3-(2-oxoazepan-1-yl)prop-1-en-2-yl)phenyl acetate (**1a**)

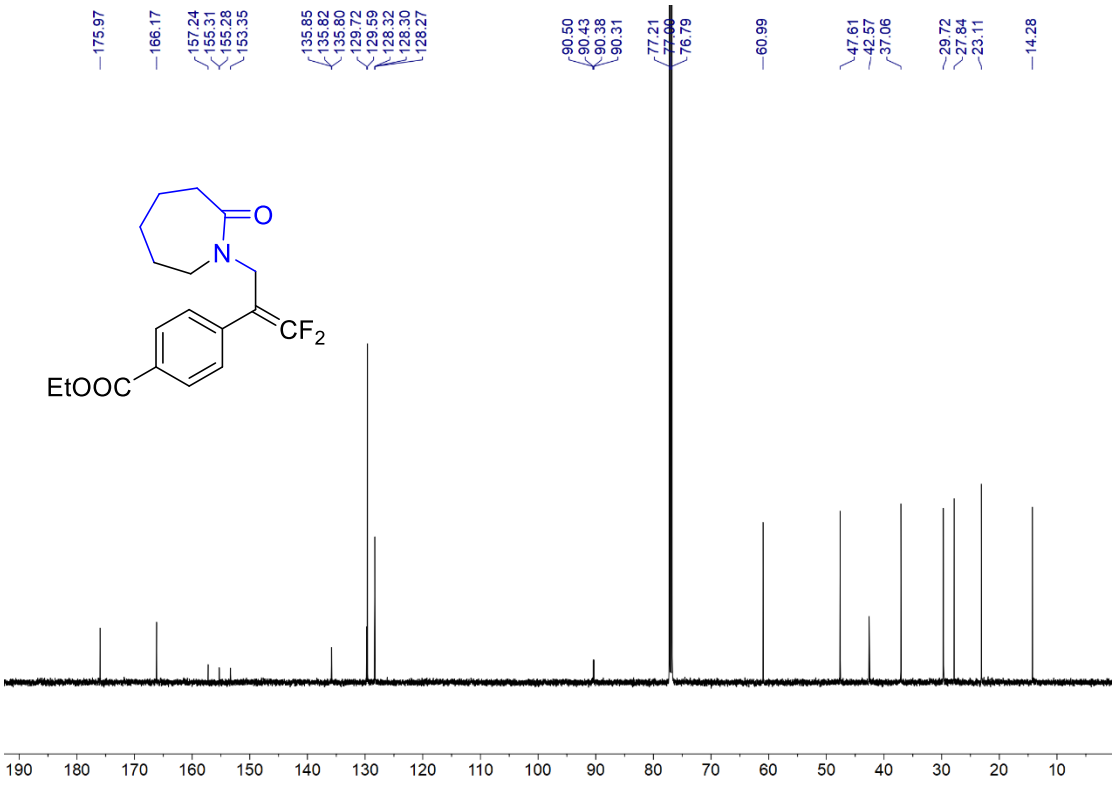






ethyl 4-(1,1-difluoro-3-(2-oxoazepan-1-yl)prop-1-en-2-yl)benzoate (**3b**)

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135.82
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128.32
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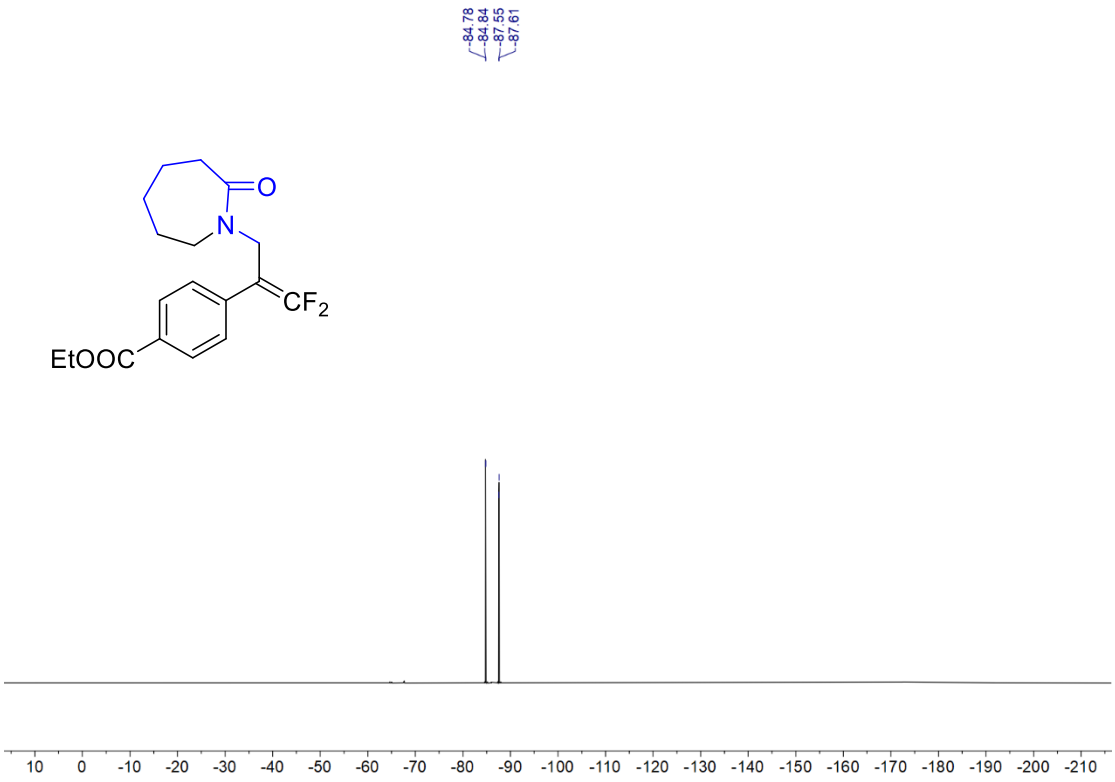
128.27
90.50
90.43
90.38
90.31
77.21
77.00
76.79
60.99
47.61
42.57
37.06
29.72
27.84
23.11
14.28
O
N
CF2
EtOOC
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10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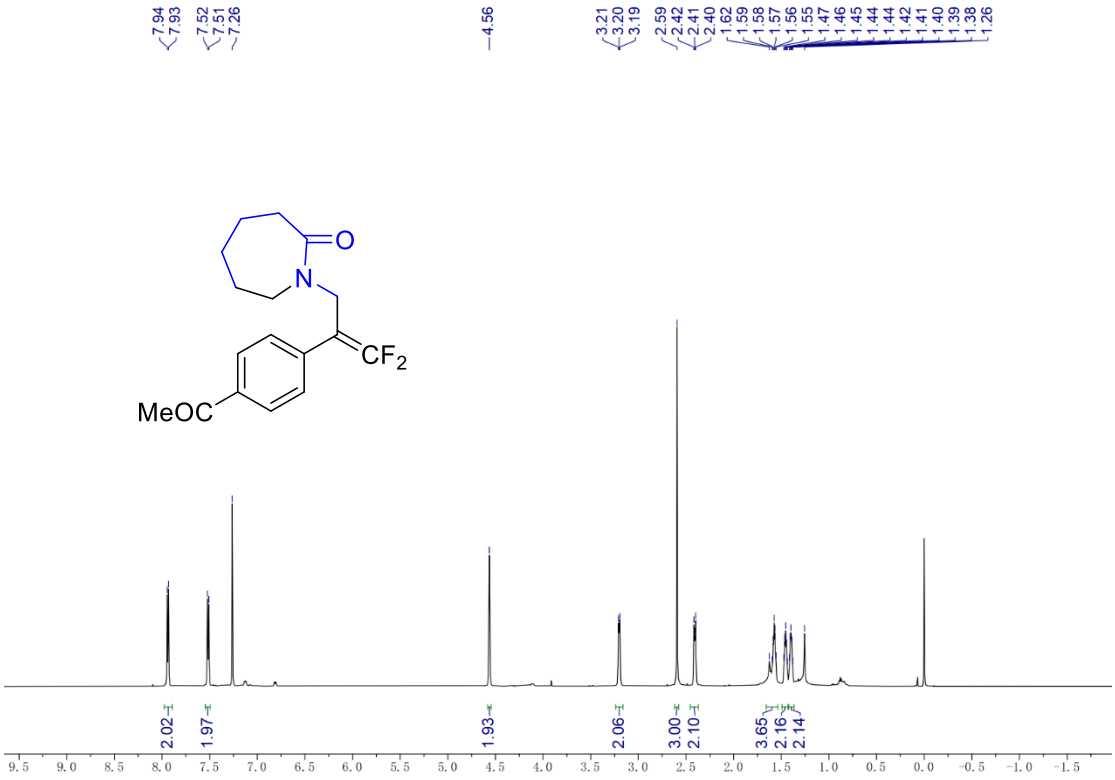
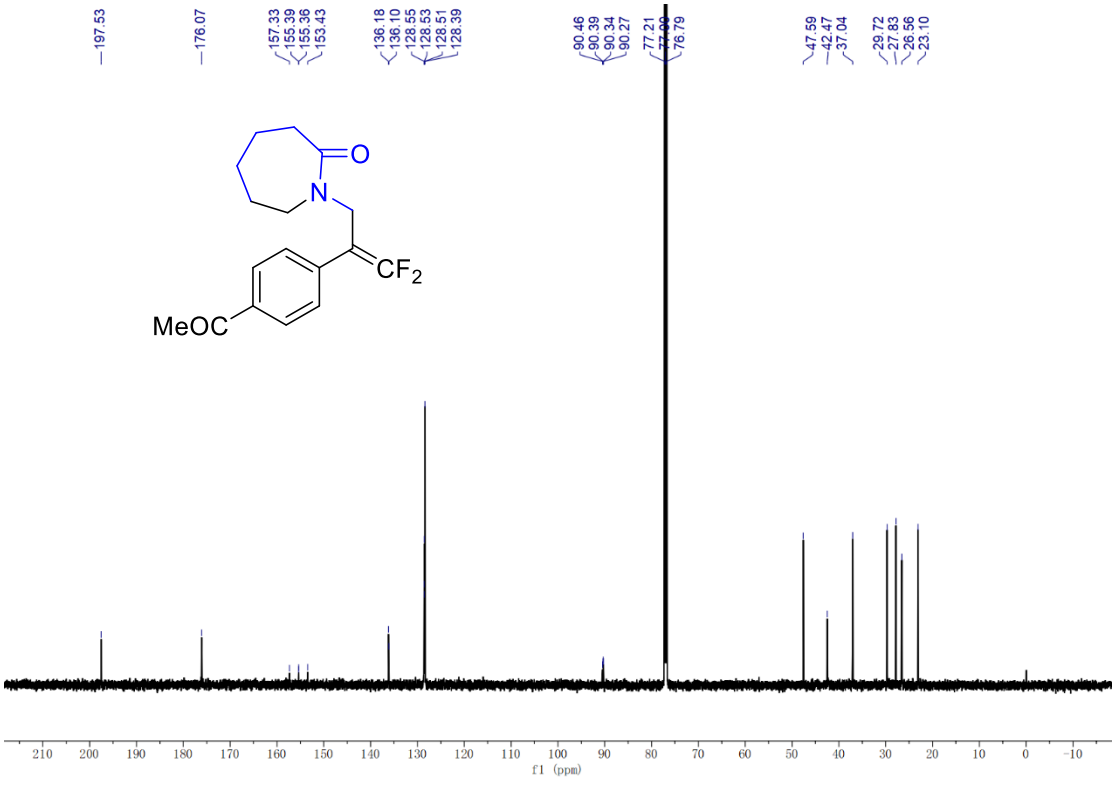
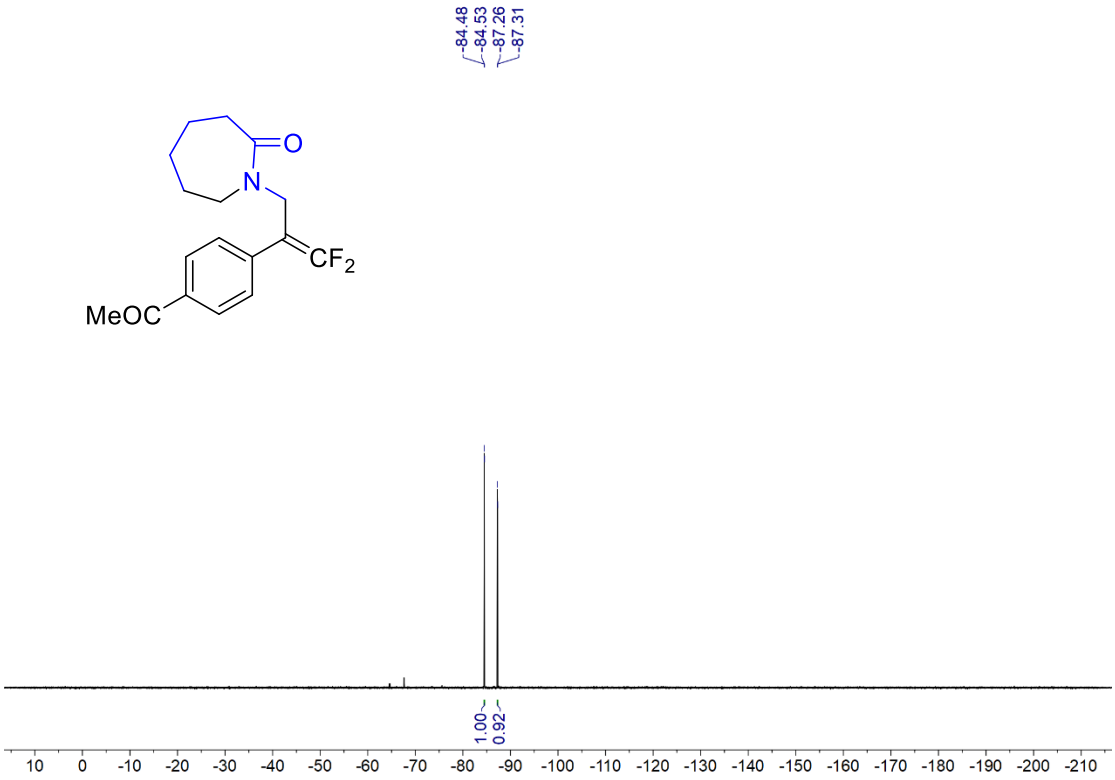
84.84
87.55
87.61
O
N
CF2
EtOOC
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210

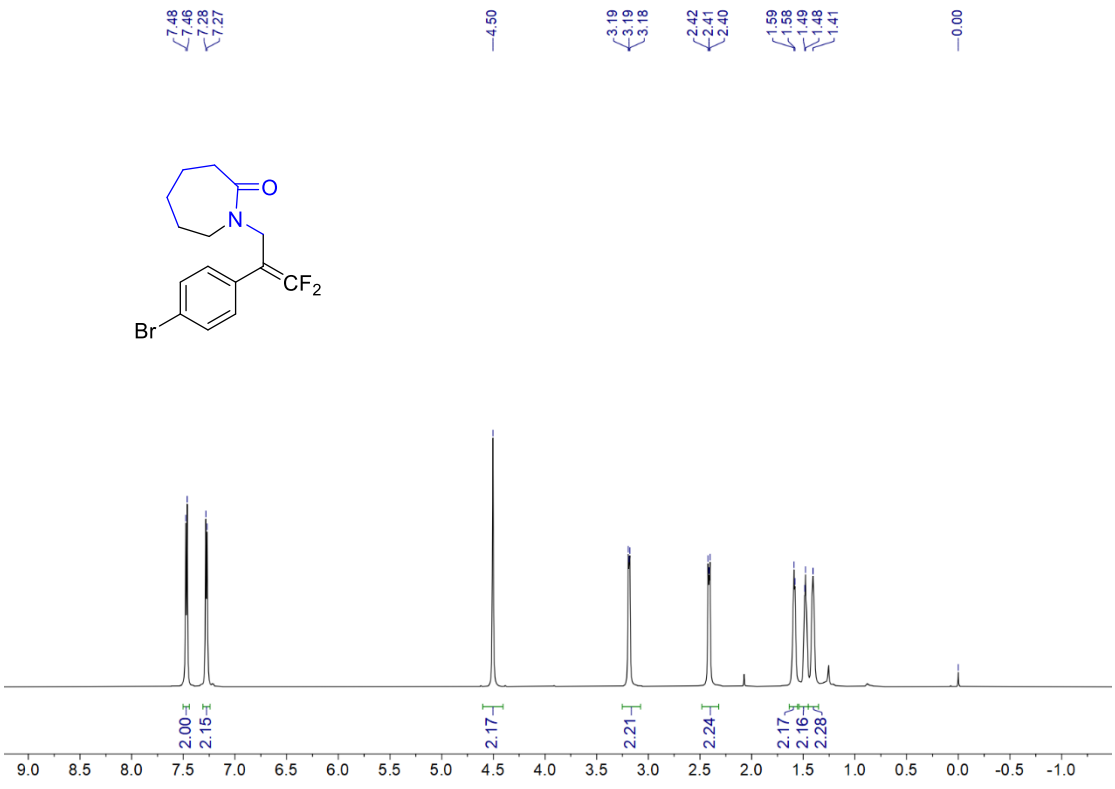
1-(2-(4-acetylphenyl)-3,3-difluoroallyl)azepan-2-one (3c)

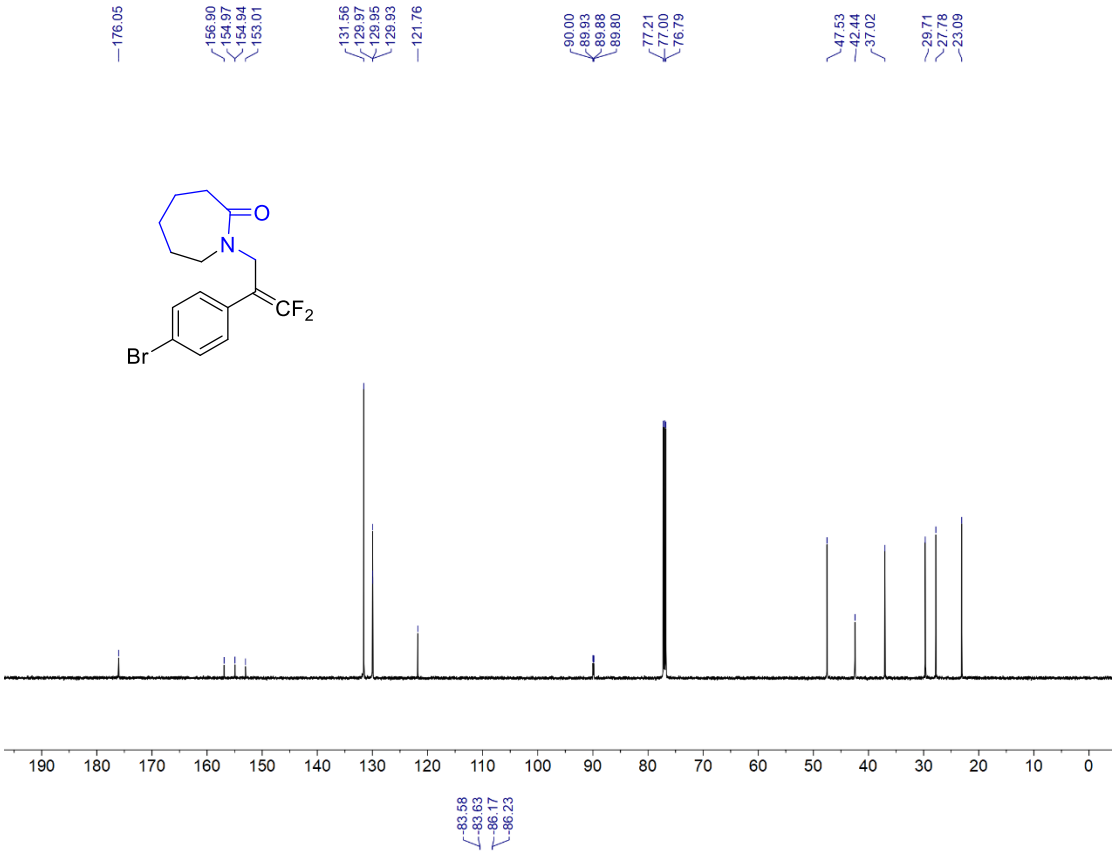






1-(2-(4-bromophenyl)-3,3-difluoroallyl)azepan-2-one (3e)

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131.56
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129.95
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89.93
89.88
89.80
77.21
77.00
76.79
47.53
42.44
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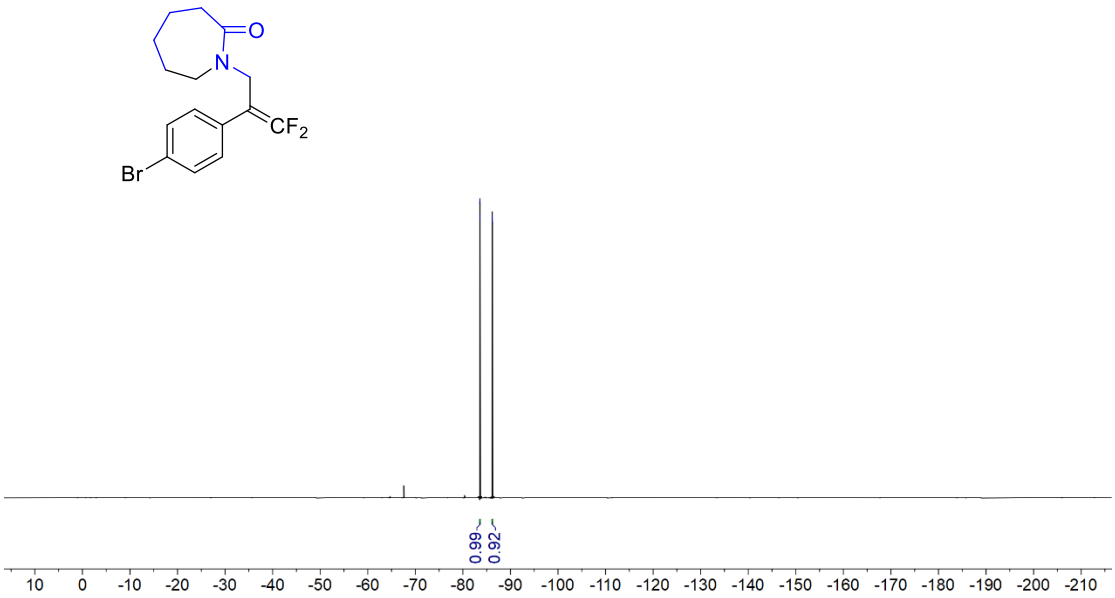
29.71
27.78
23.09
O
N
CF2
Br
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0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O
N
CF2
Br
0.99
0.92
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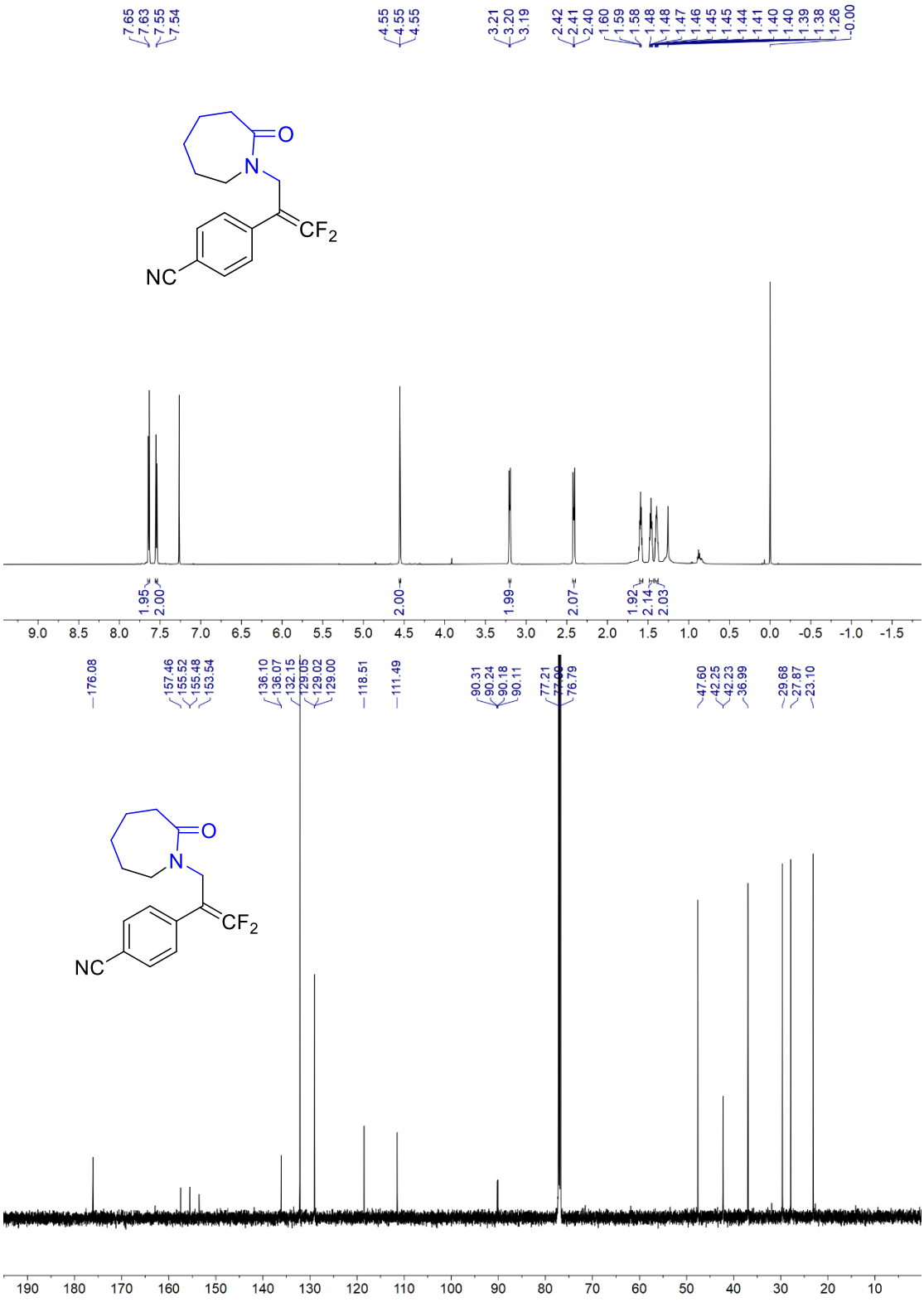
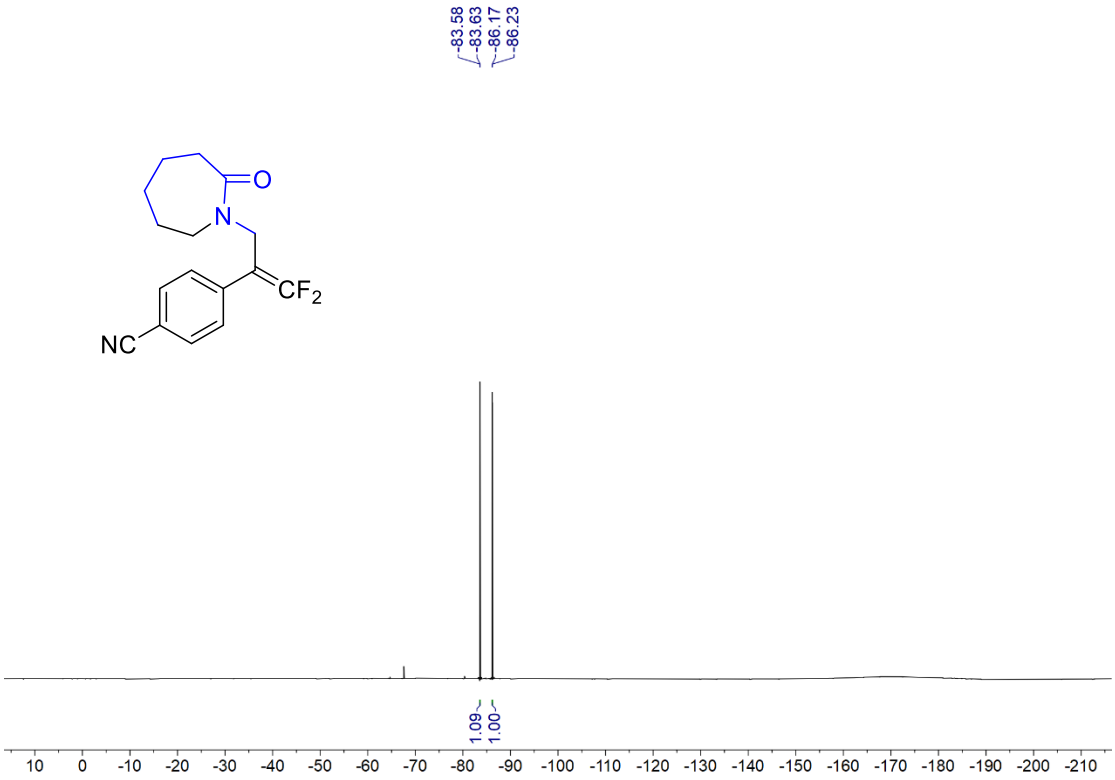
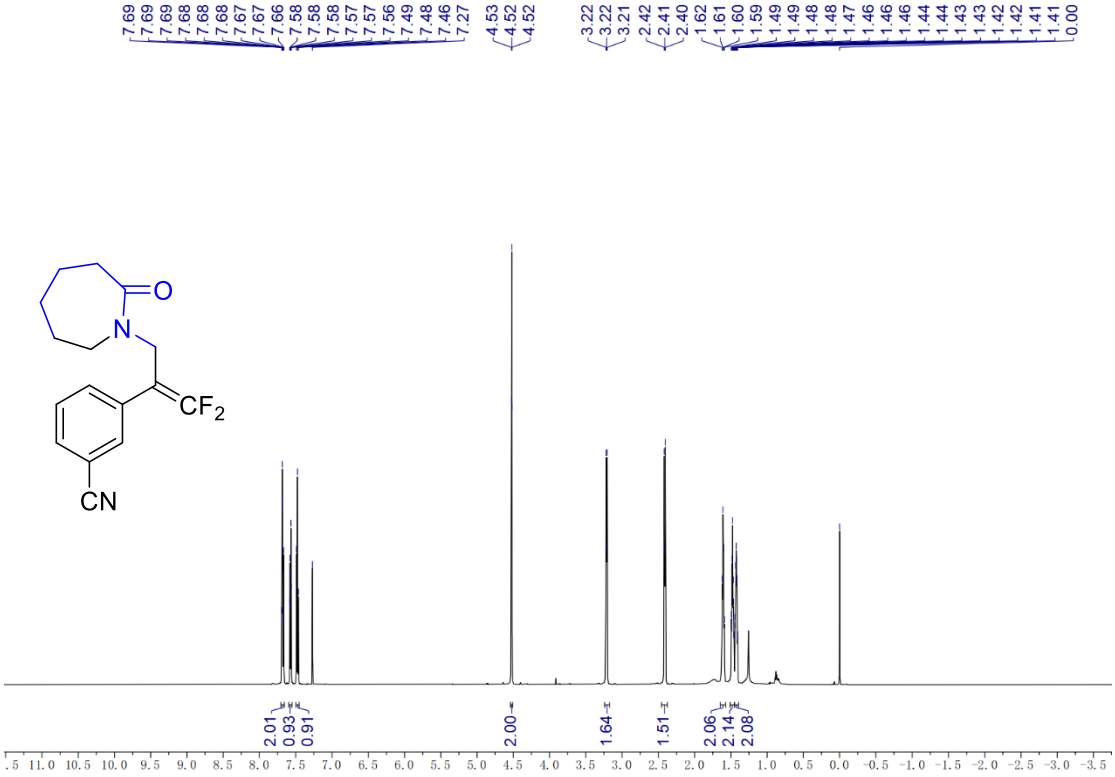
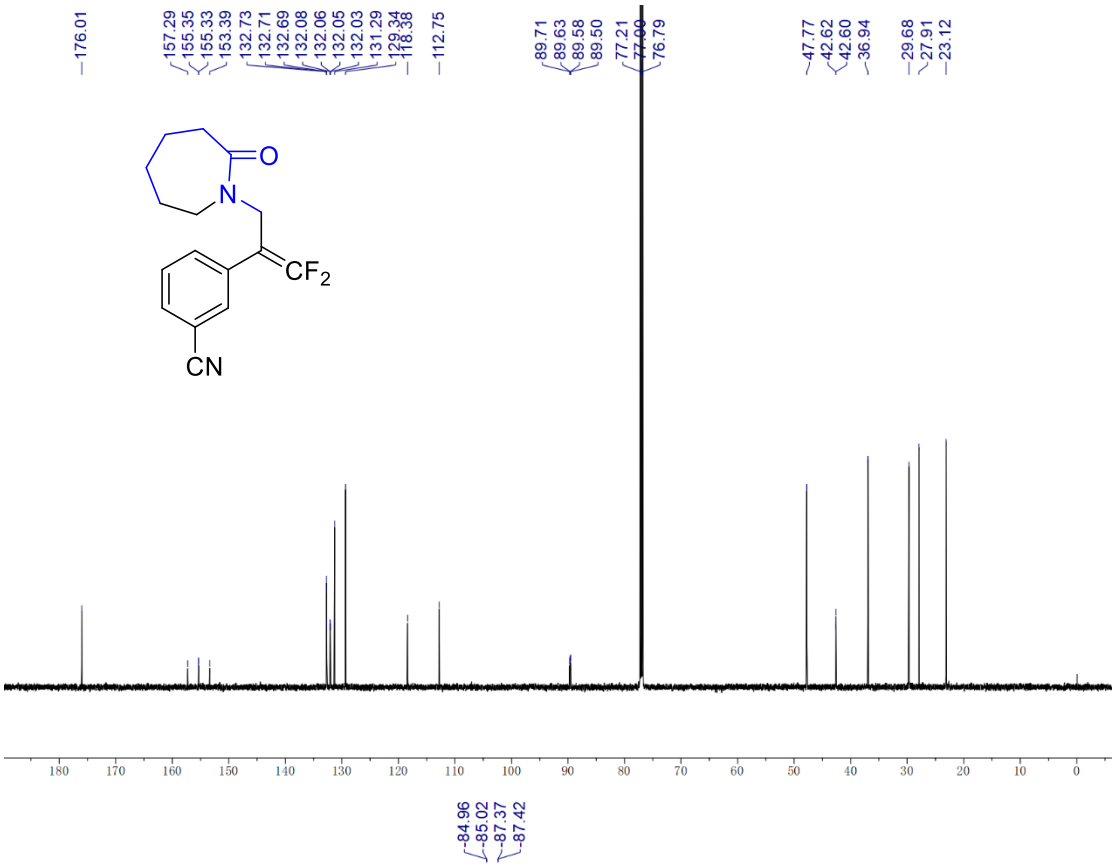
4-(1,1-difluoro-3-(2-oxoazepan-1-yl)prop-1-en-2-yl)benzonitrile (3f)





3-(1,1-difluoro-3-(2-oxoazepan-1-yl)prop-1-en-2-yl)benzonitrile (3g)

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132.71
132.69
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132.05
132.03
131.29
129.34
118.38
112.75
89.71
89.63
89.58
89.50
77.21
77.00
76.79
47.77
42.62
42.60
36.94
29.68
27.91
23.12
O
N
CF2
CN
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150
140
130
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110
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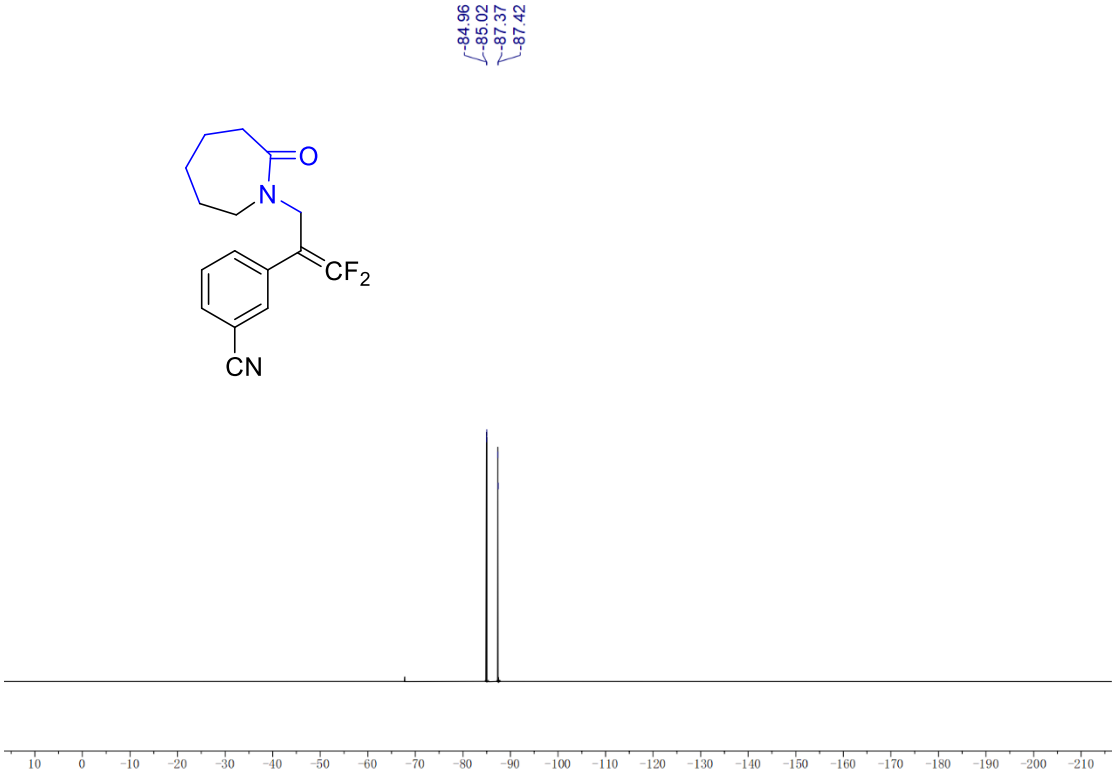
90
80
70
60
50
40
30
20
10
0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O
N
CF2
CN
10
0
-10
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-30
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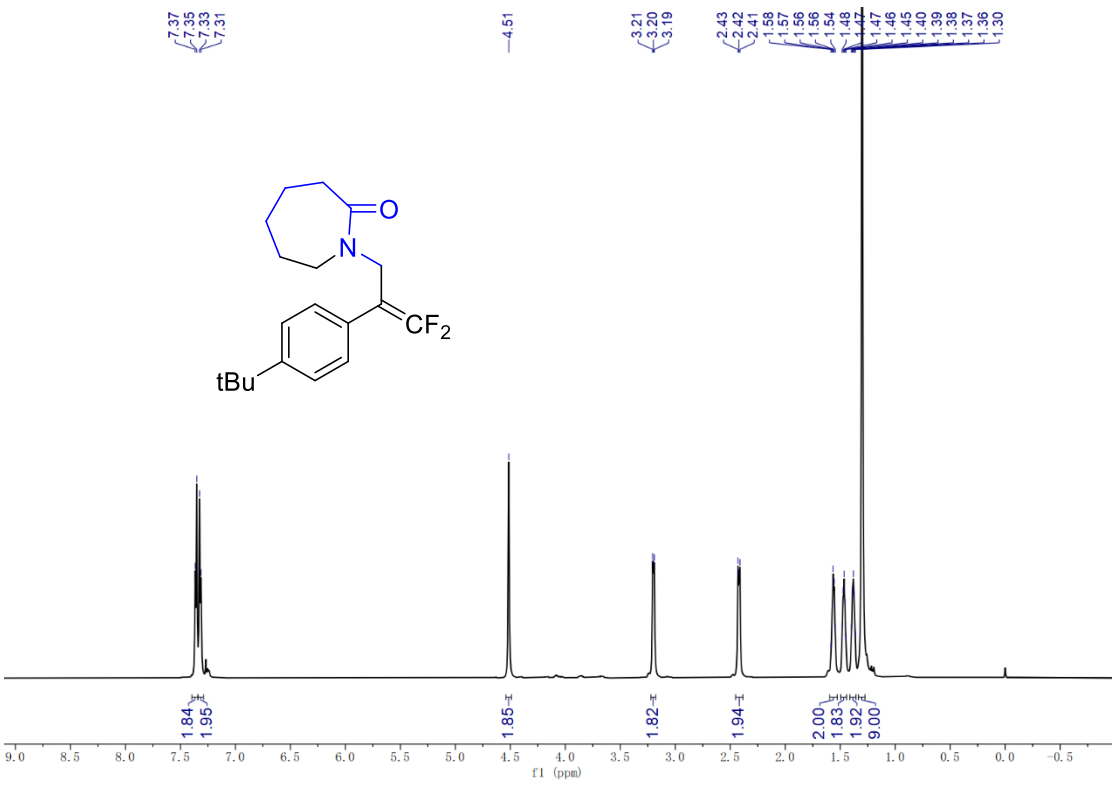
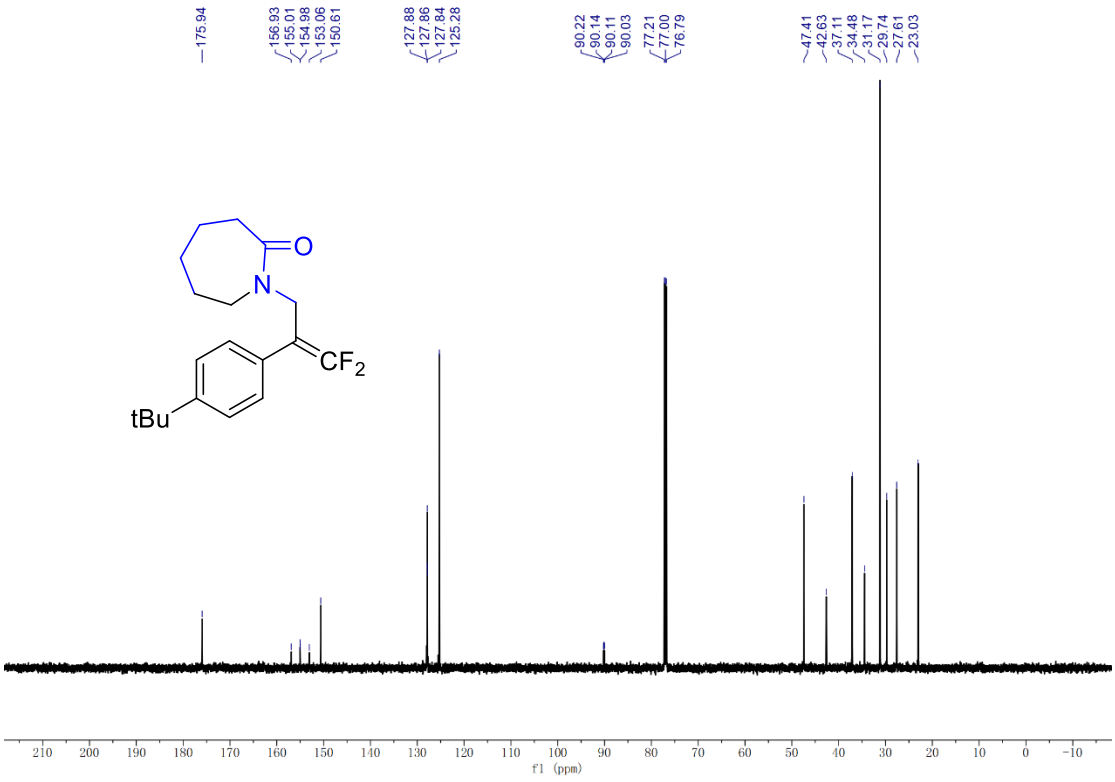
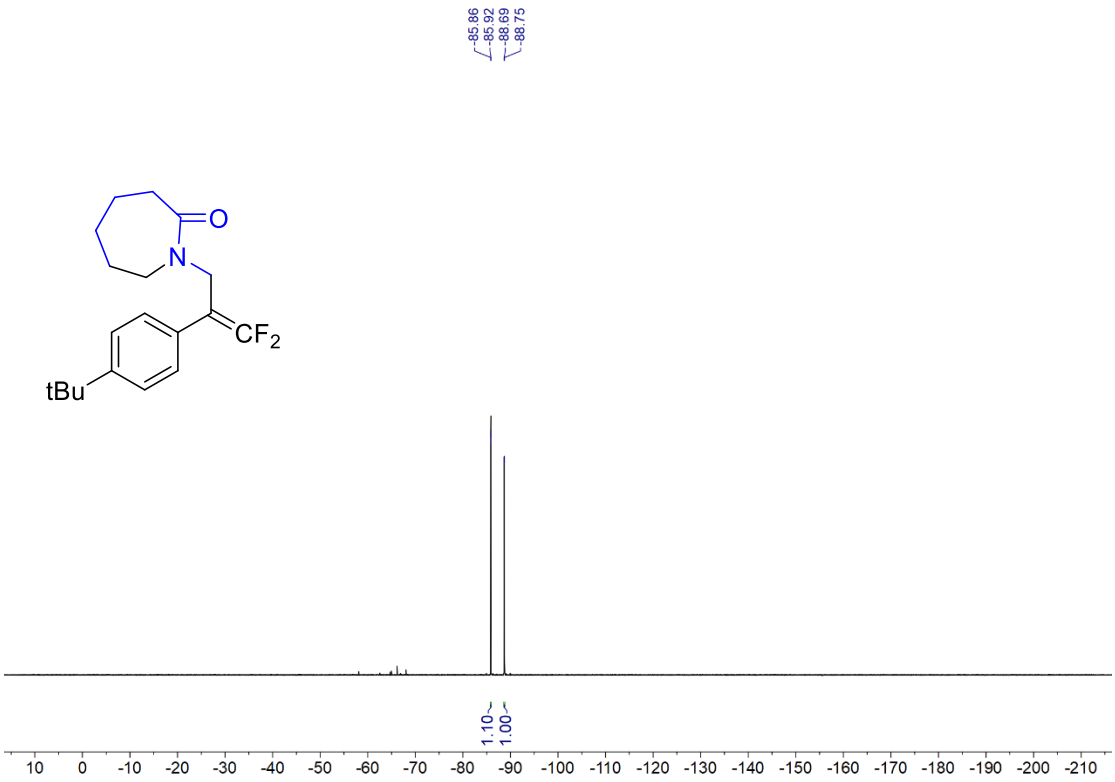
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210

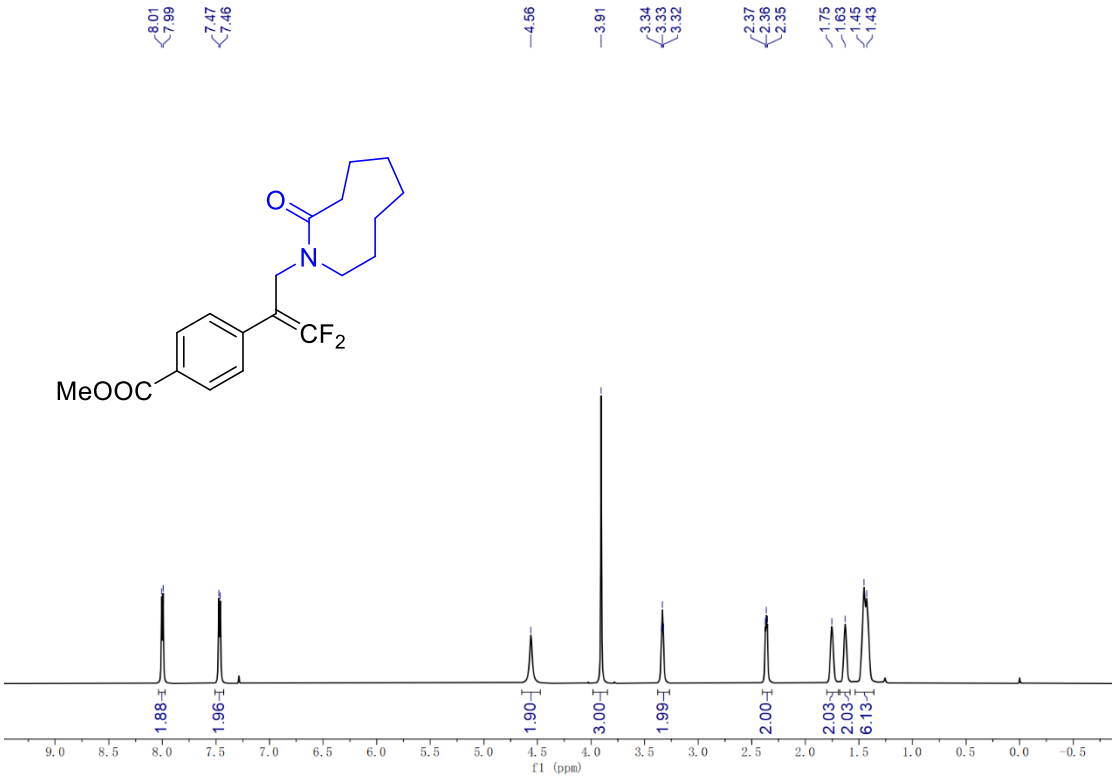
1-(2-(4-(tert-butyl)phenyl)-3,3-difluoroallyl)azepan-2-one (3h)

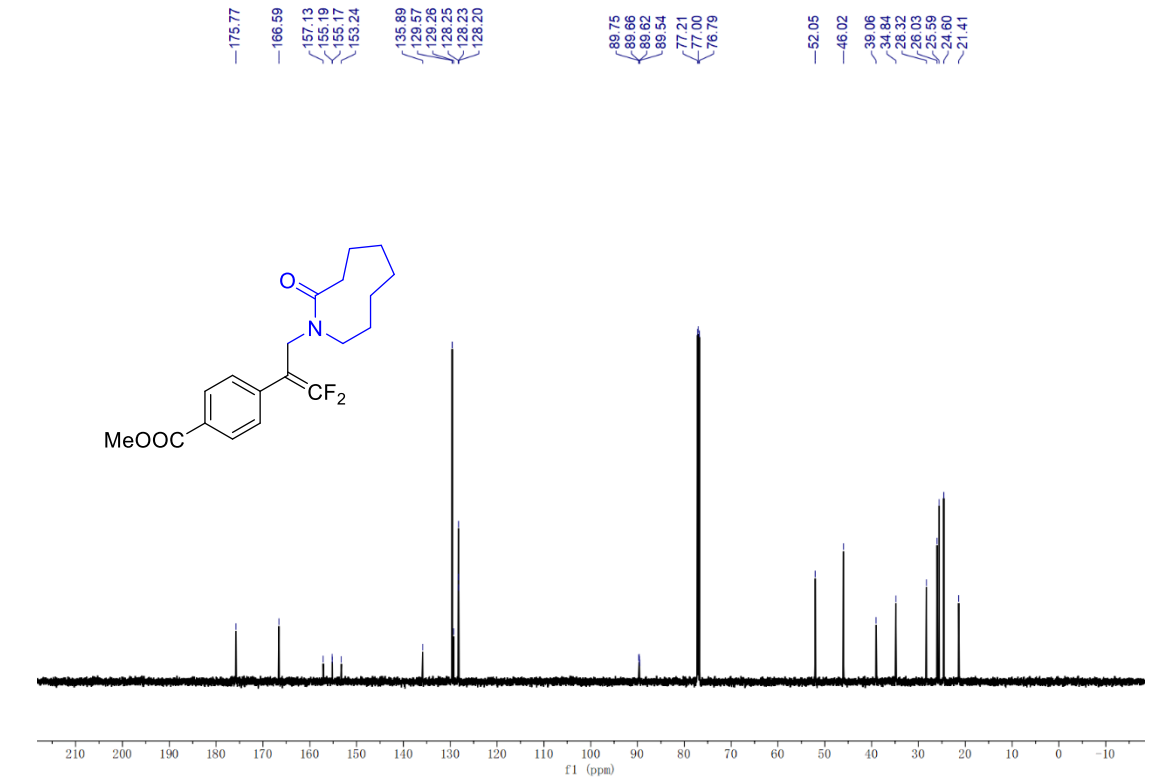






4-(1,1-difluoro-3-(2-oxoazonan-1-yl)prop-1-en-2-yl)phenyl acetate (3h)

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135.89
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128.23
128.20
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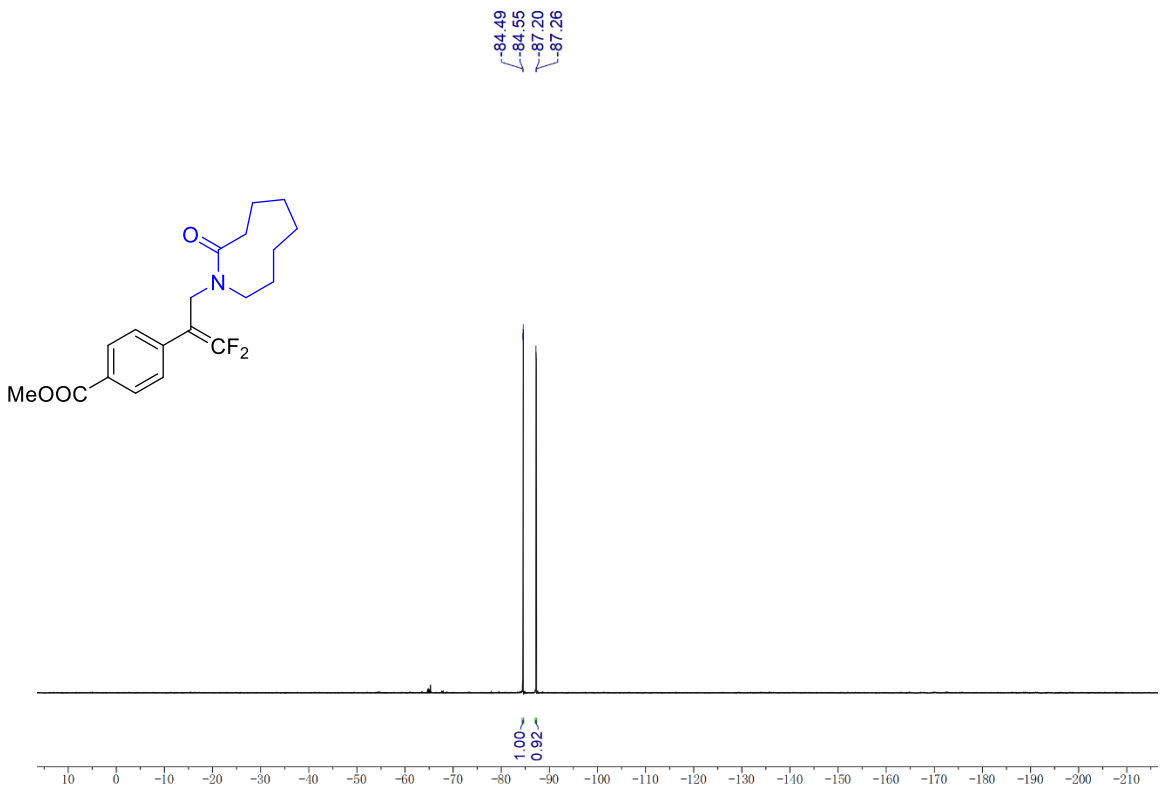
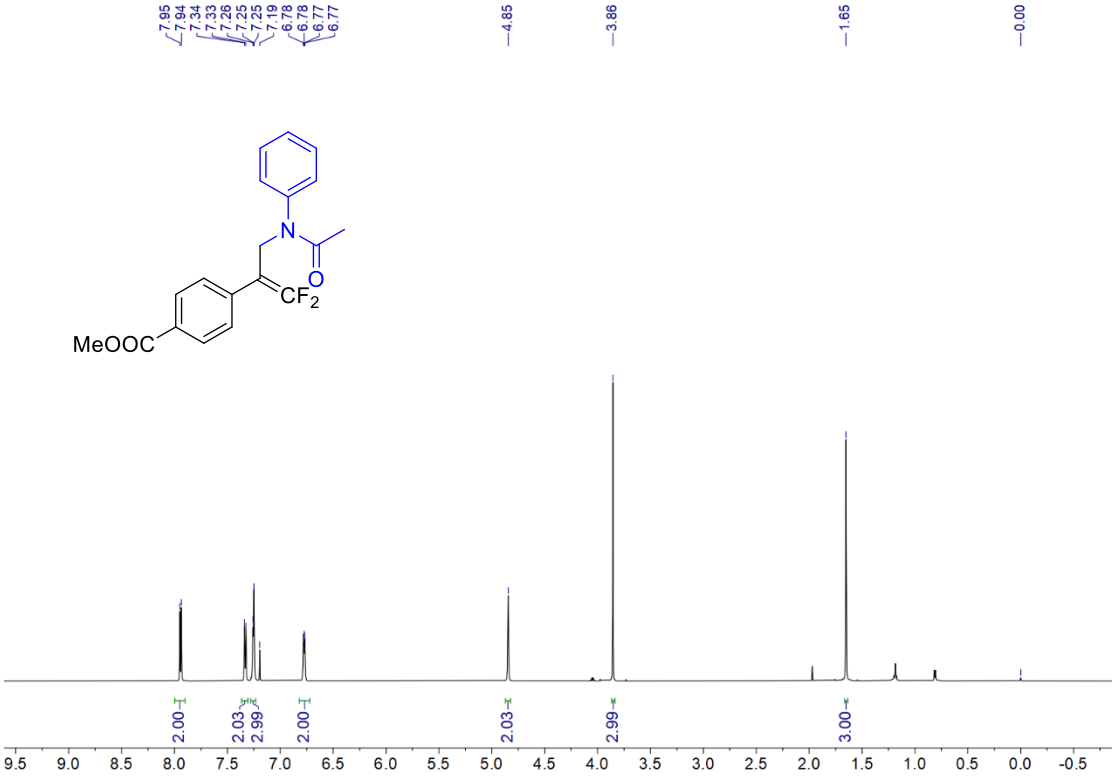
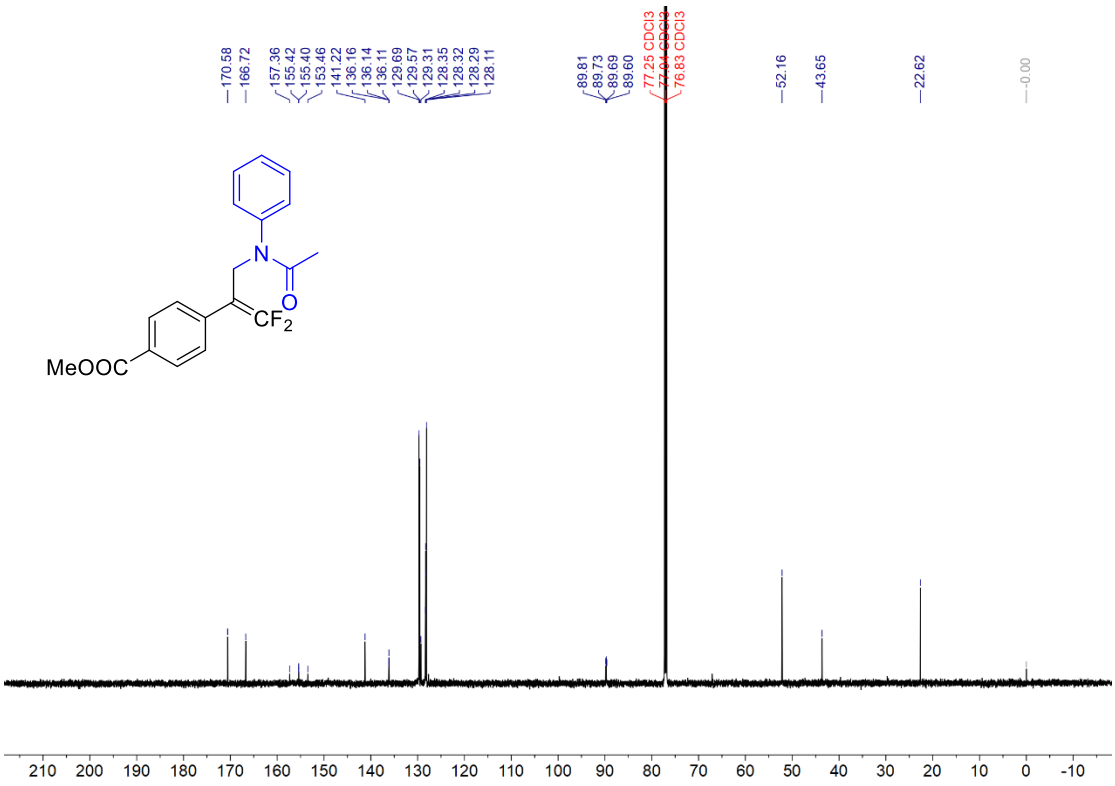
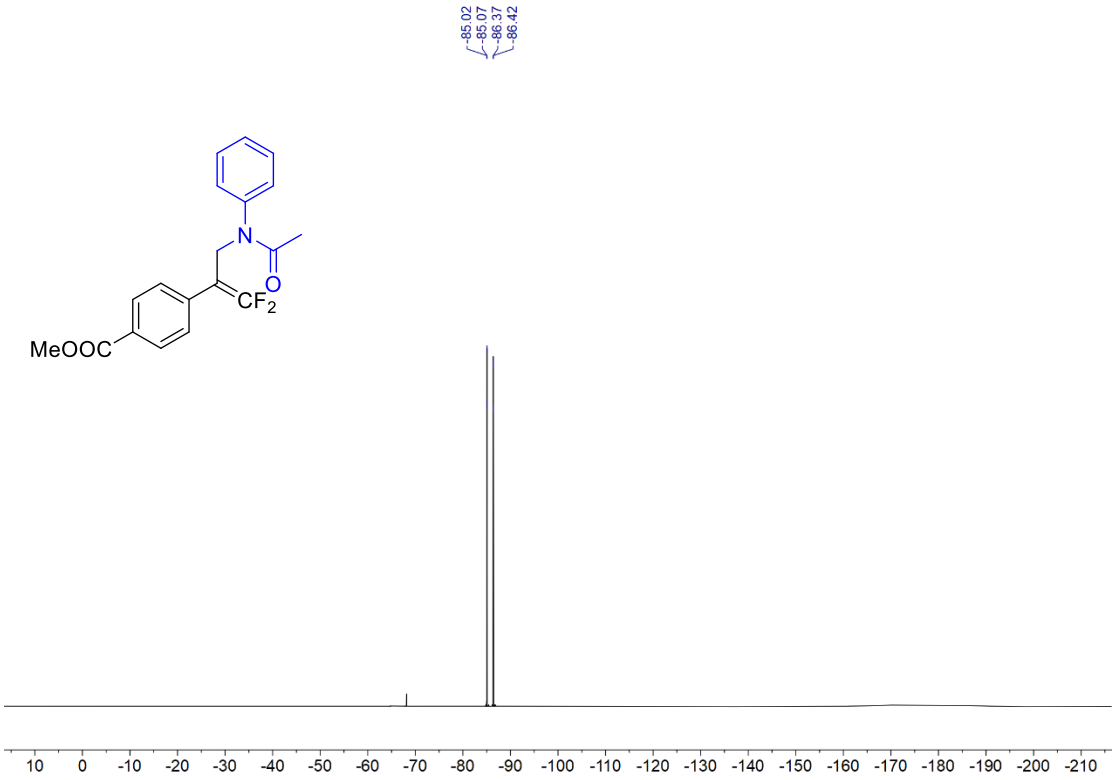
89.66
89.62
89.54
77.21
77.00
76.79
52.05
46.02
39.06
34.84
28.32
26.03
25.59
24.60
21.41
O
N
CF2
MeOOC
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


-84.49
-84.55
-87.20
-87.26
O
N
CF2
MeOOC
1.00
0.92
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210

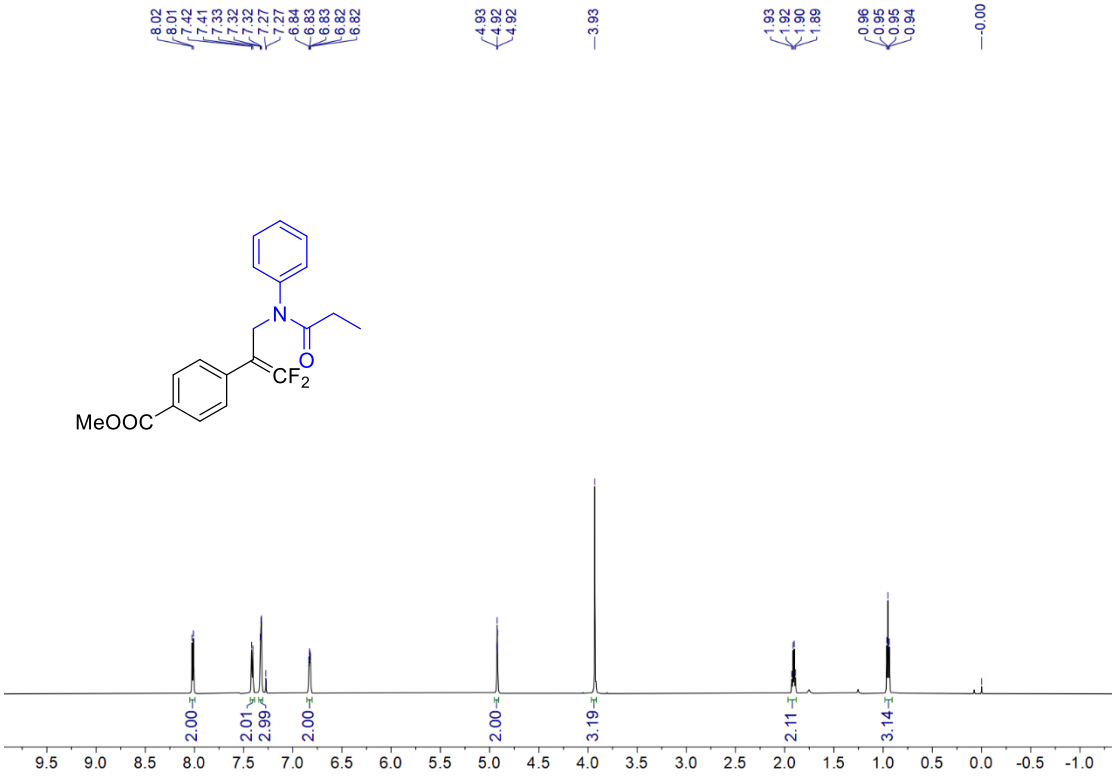
4-(1,1-difluoro-3-(N-phenylacetamido)prop-1-en-2-yl)phenyl acetate (3k)

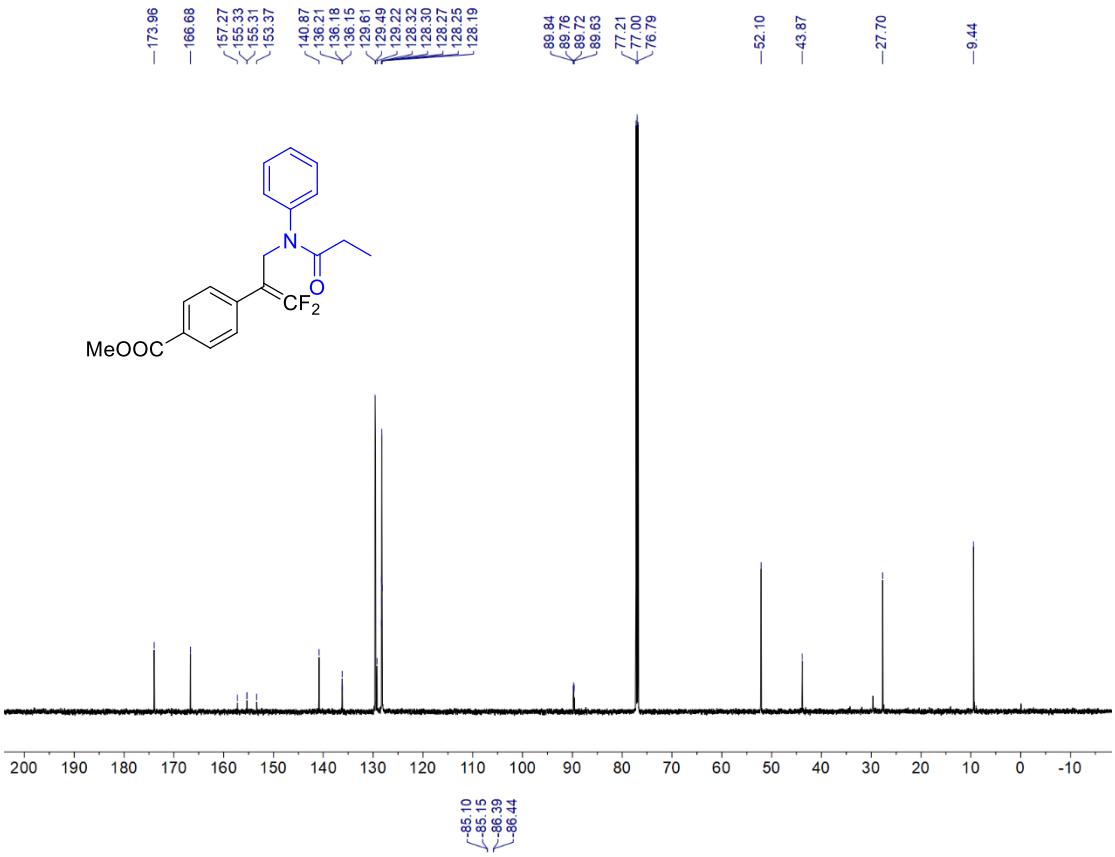


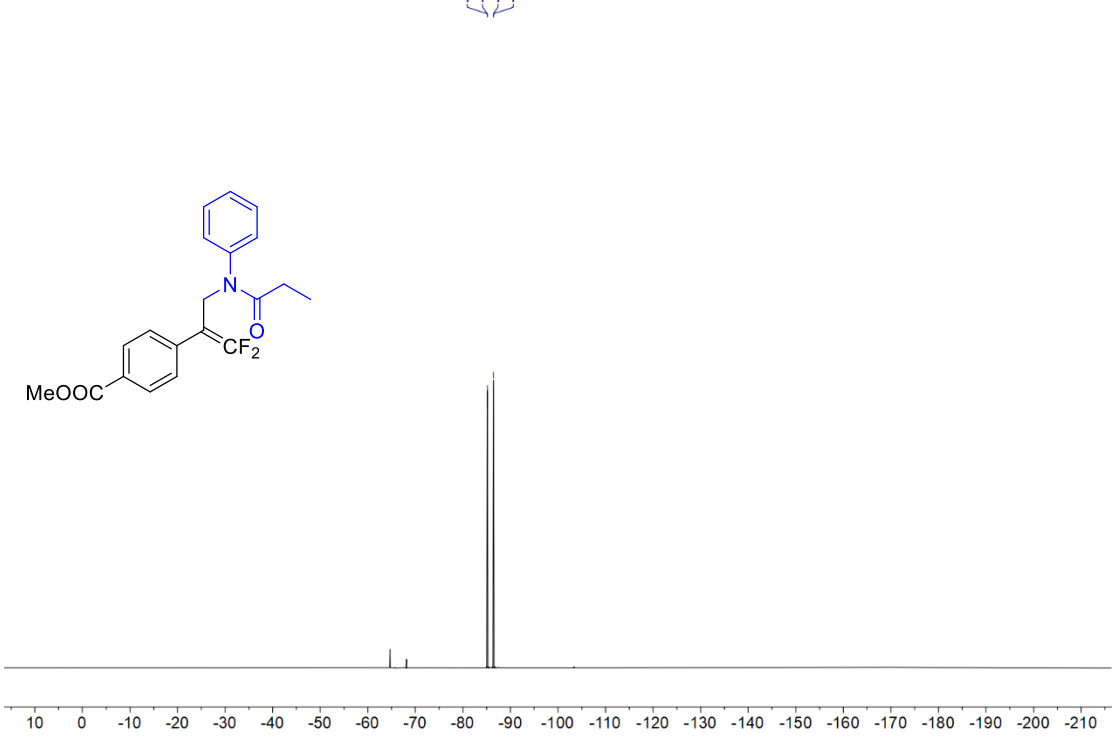




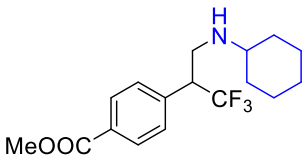
4-(1,1-difluoro-3-(N-phenylpropionamido)prop-1-en-2-yl)phenyl acetate (3l)

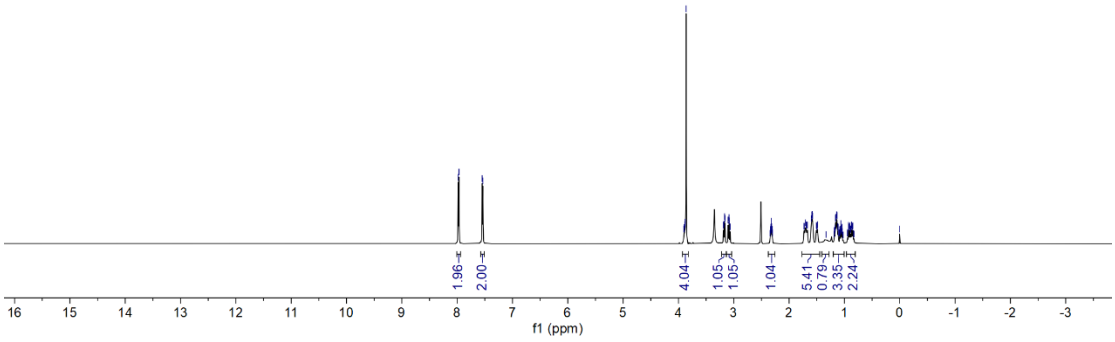


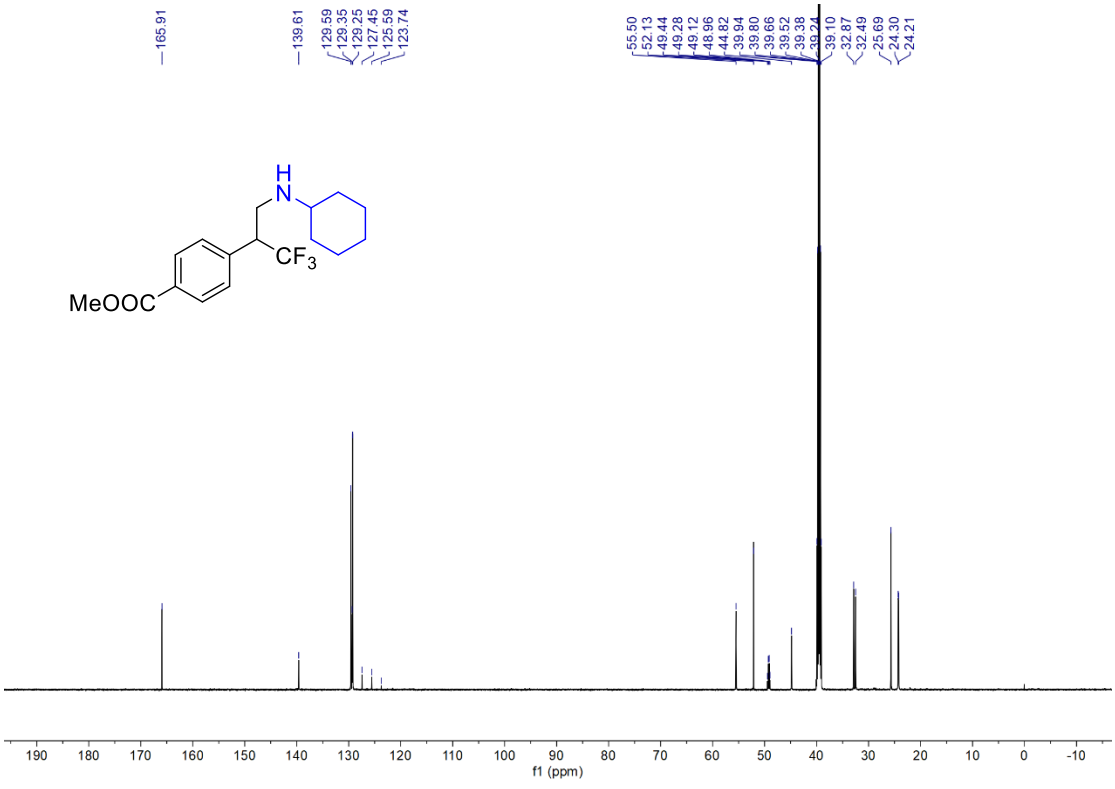

173.96
166.68
157.27
155.33
155.31
153.37
140.87
136.21
136.18
136.15
129.61
129.49
129.22
128.32
128.30
128.27
128.25
128.19
89.84
89.76
89.72
89.63
77.21
77.00
76.79
52.10
43.87
27.70
9.44
N
O
CF2
MeOOC
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

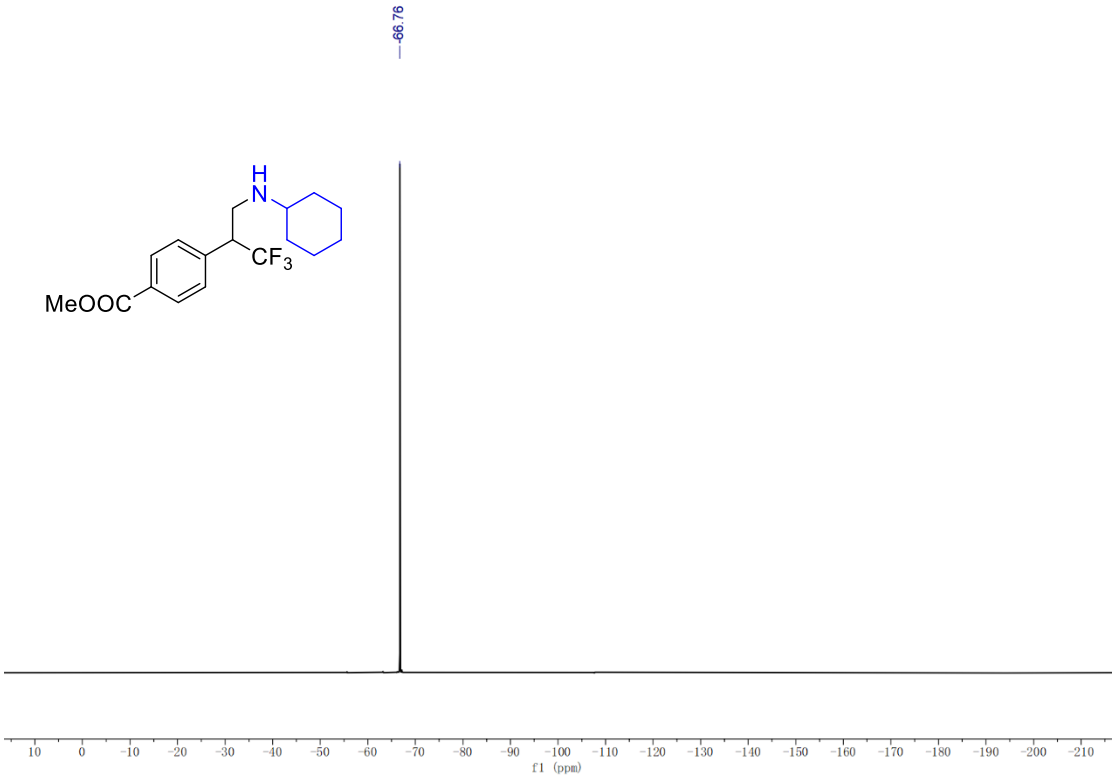

85.10
85.15
86.39
86.44
N
O
CF2
MeOOC
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210

4-(3-(cyclohexylamino)-1,1,1-trifluoropropan-2-yl)phenyl acetate (5a)

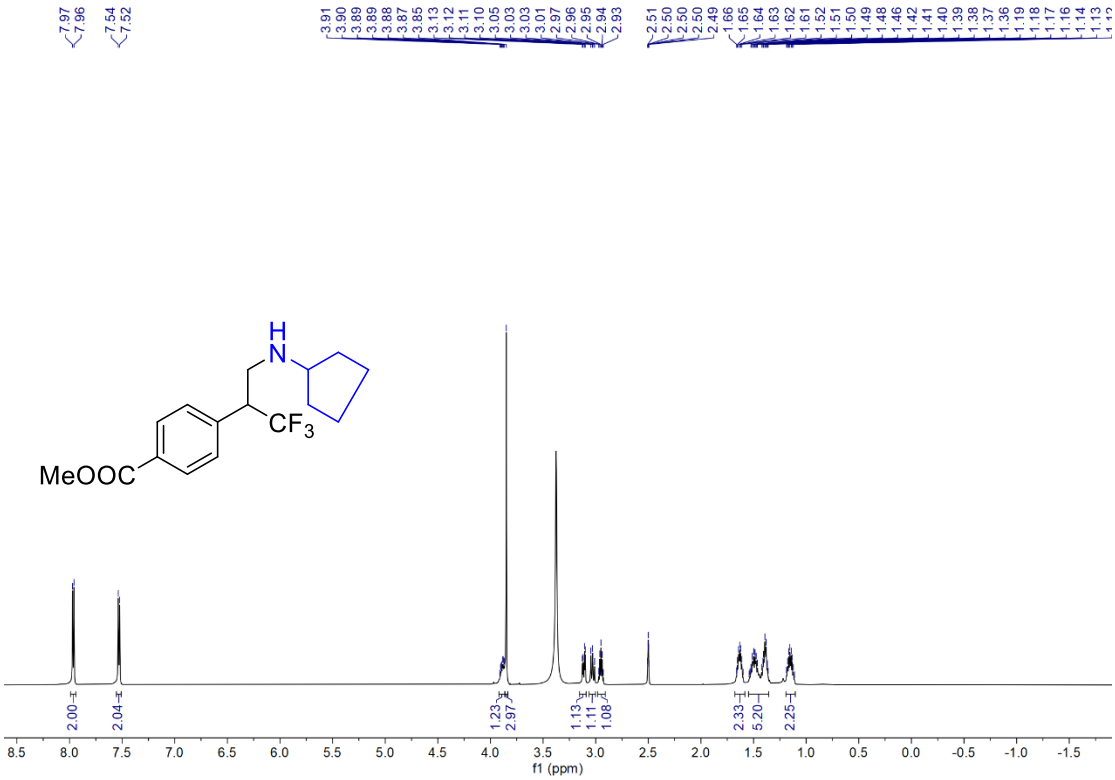


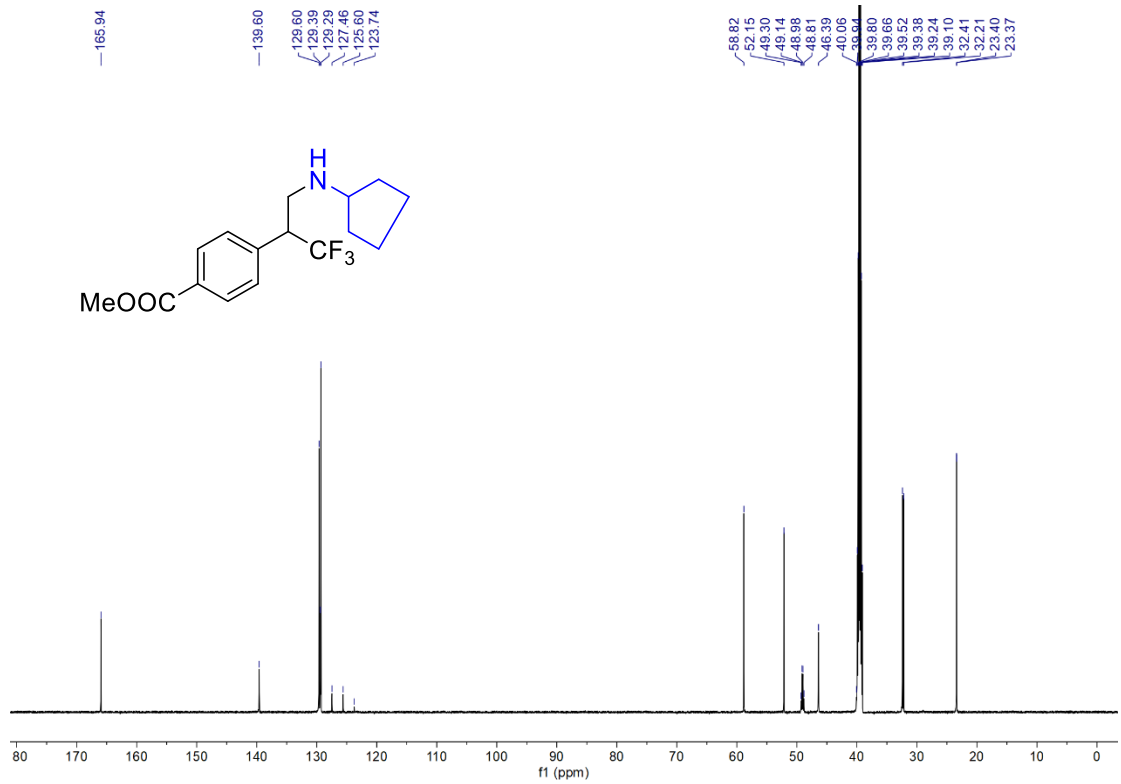


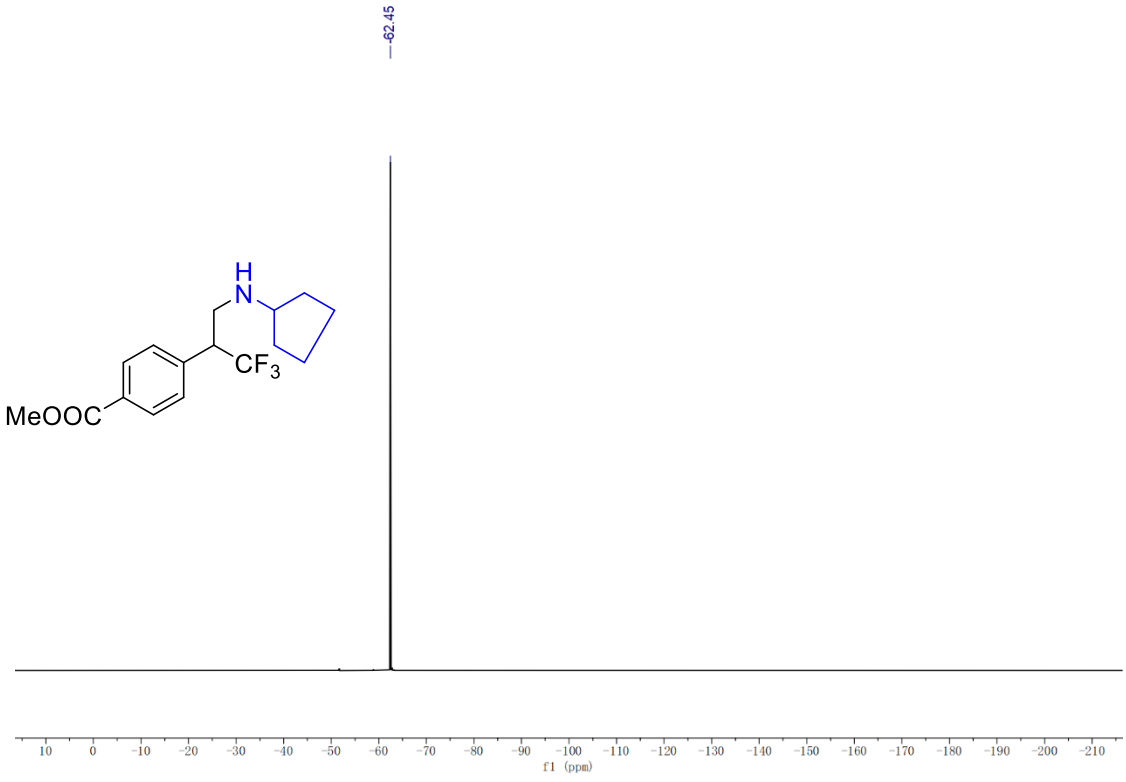




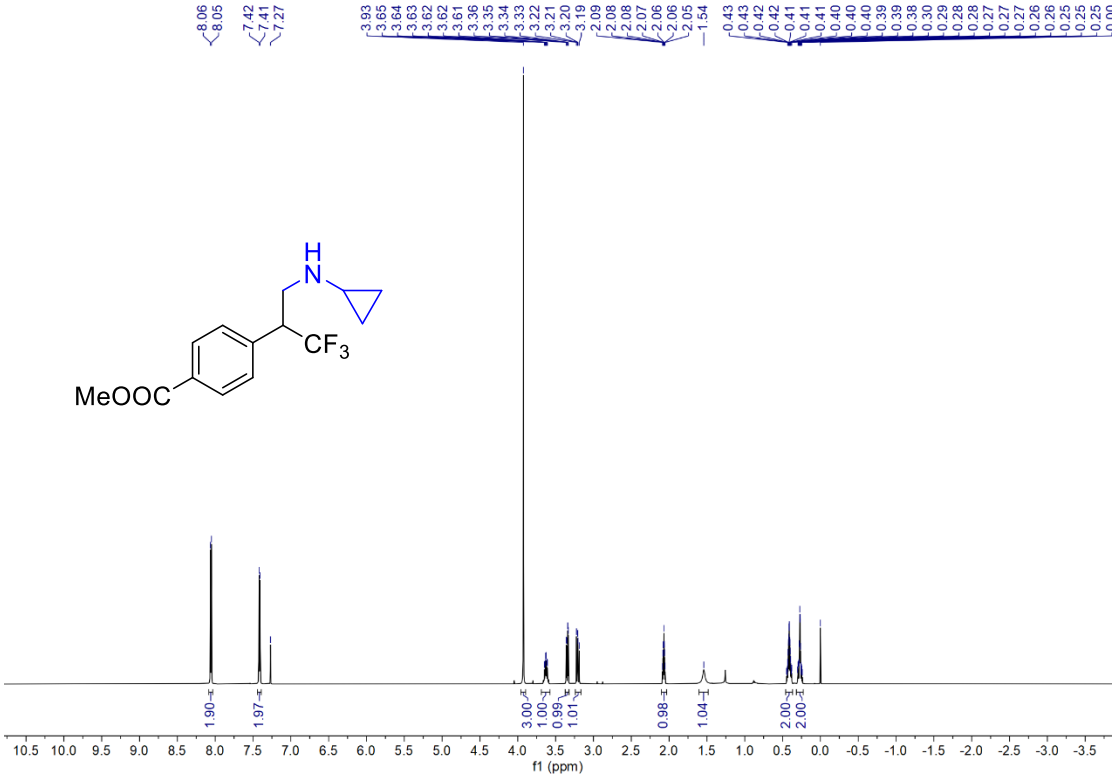
4-(3-(cyclopentylamino)-1,1,1-trifluoropropan-2-yl)phenyl acetate (5b)

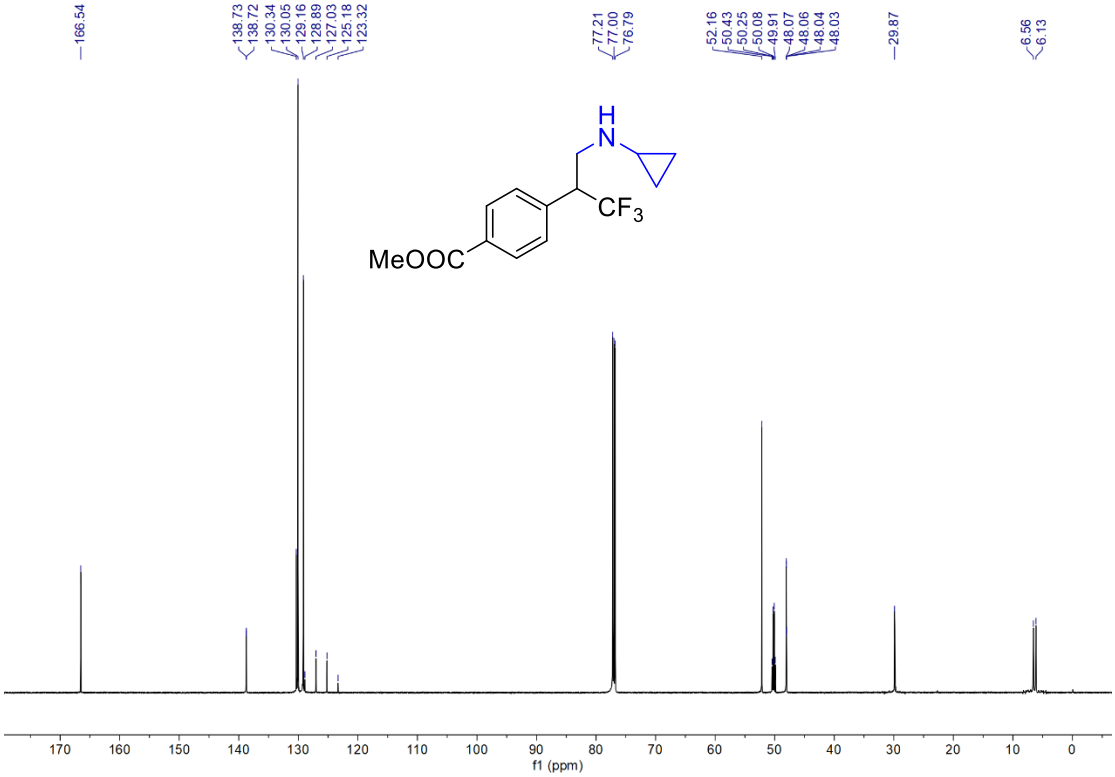


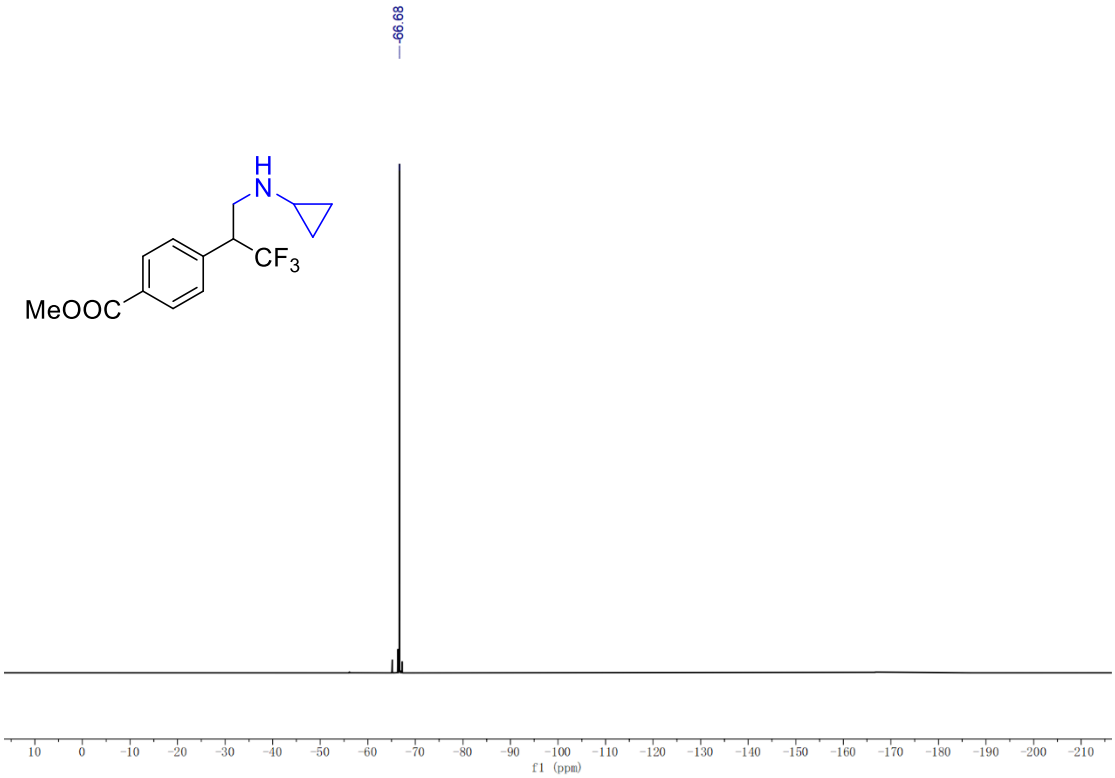

165.94
139.60
129.60
129.39
129.29
127.46
125.60
123.74
58.82
52.15
49.30
49.14
48.98
48.81
46.39
40.06
39.94
39.80
39.66
39.52
39.38
39.24
39.10
32.41
32.21
23.40
23.37
H
N
CF3
MeOOC
80 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


62.45
H
N
CF3
MeOOC
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

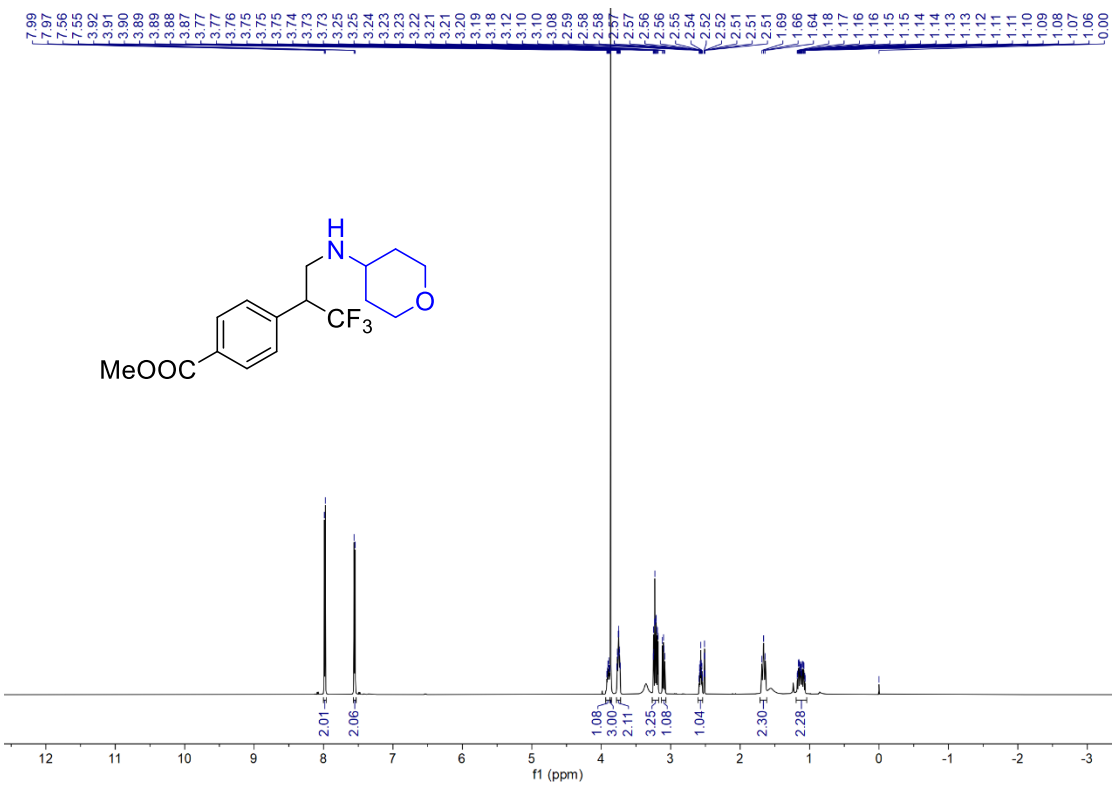
4-(3-(cyclopropylamino)-1,1,1-trifluoropropan-2-yl)phenyl acetate (5c)

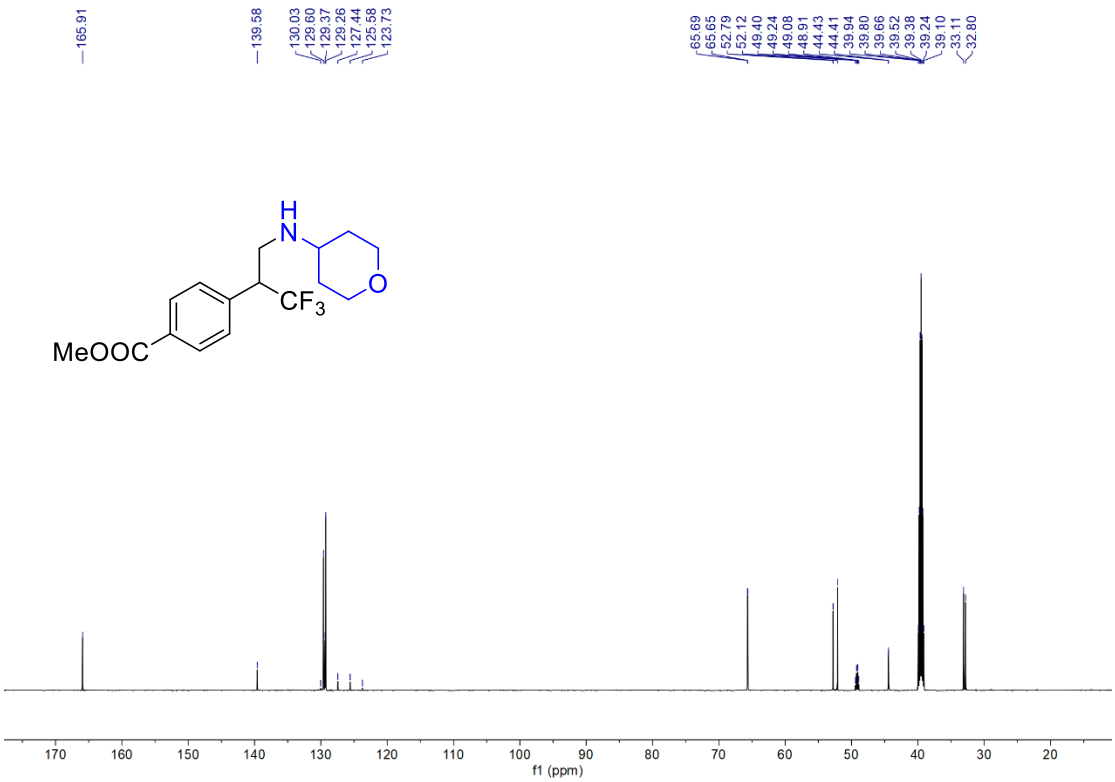


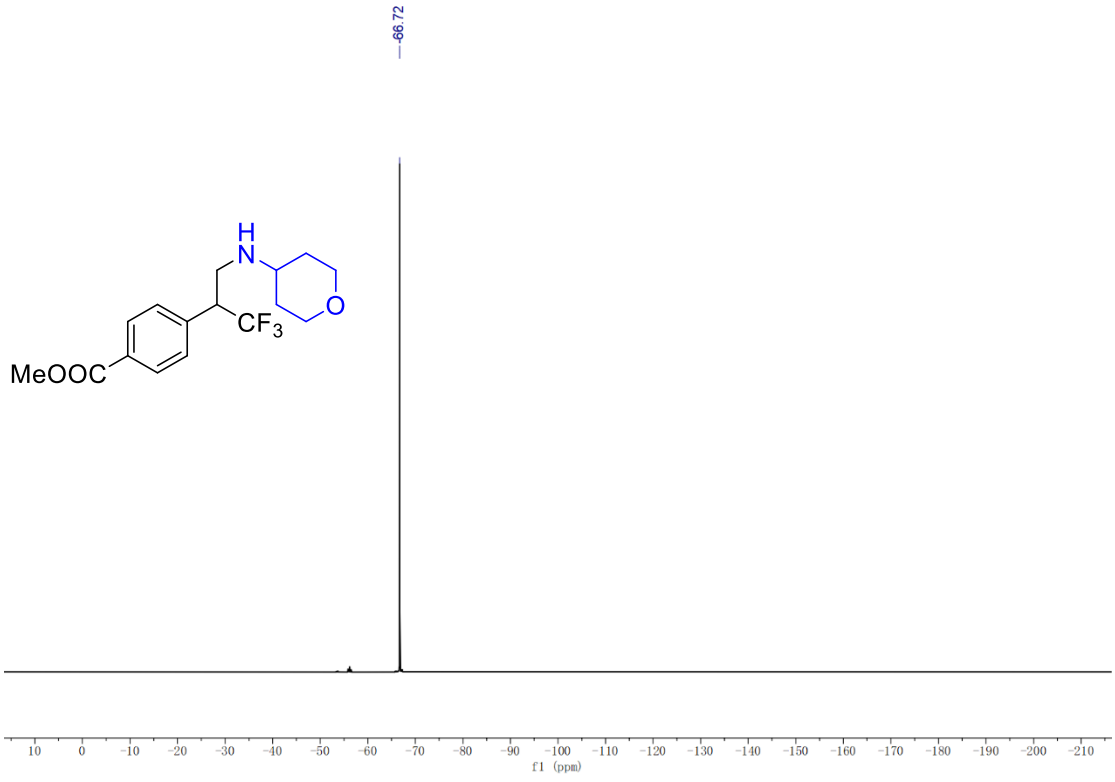




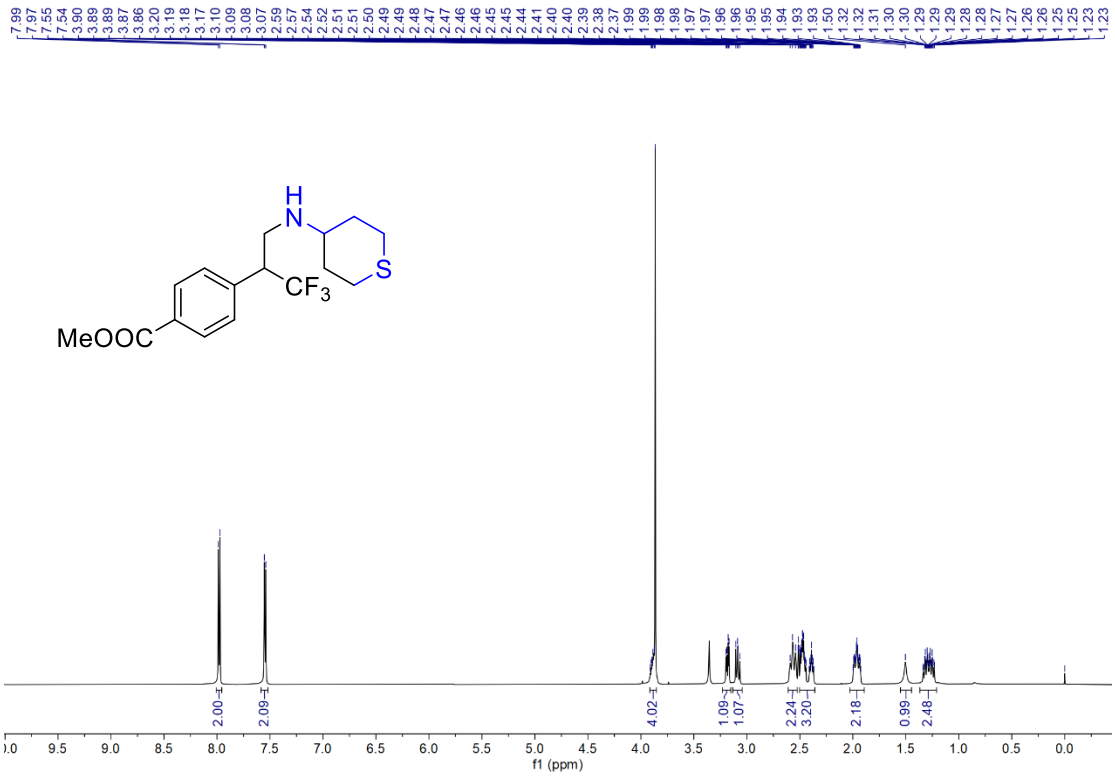
methyl 4-(1,1,1-trifluoro-3-((tetrahydro-2H-pyran-4-yl)amino)propan-2-yl)benzoate (5d)

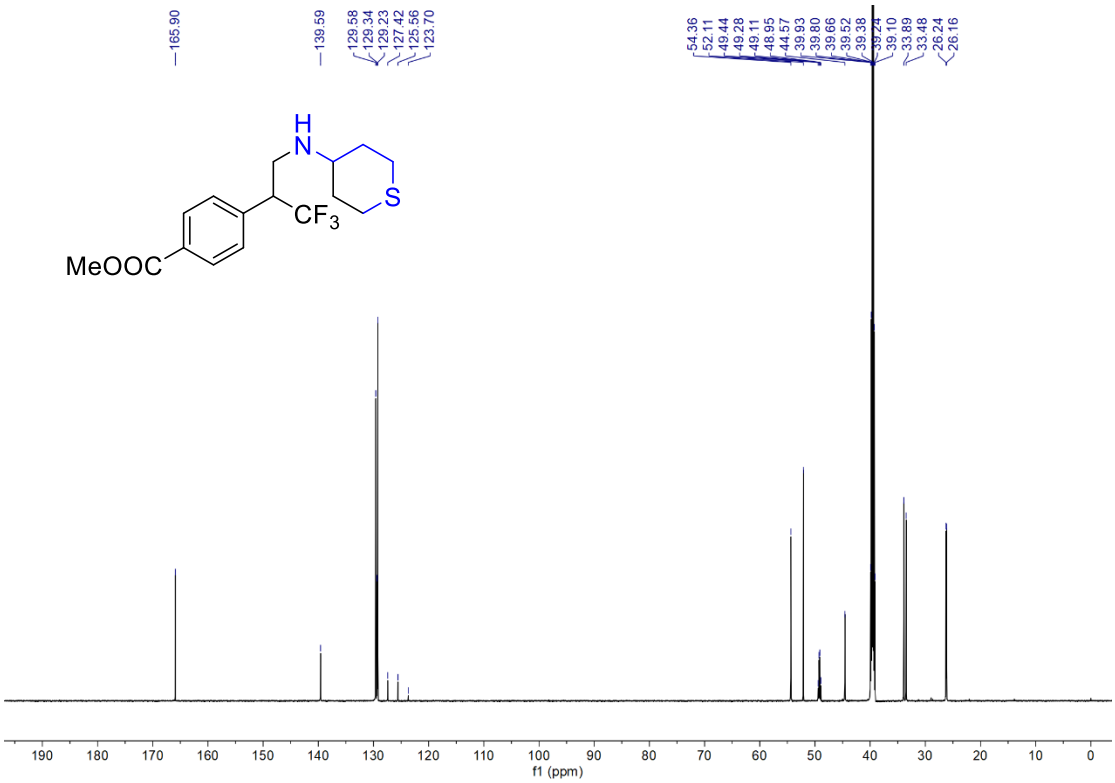


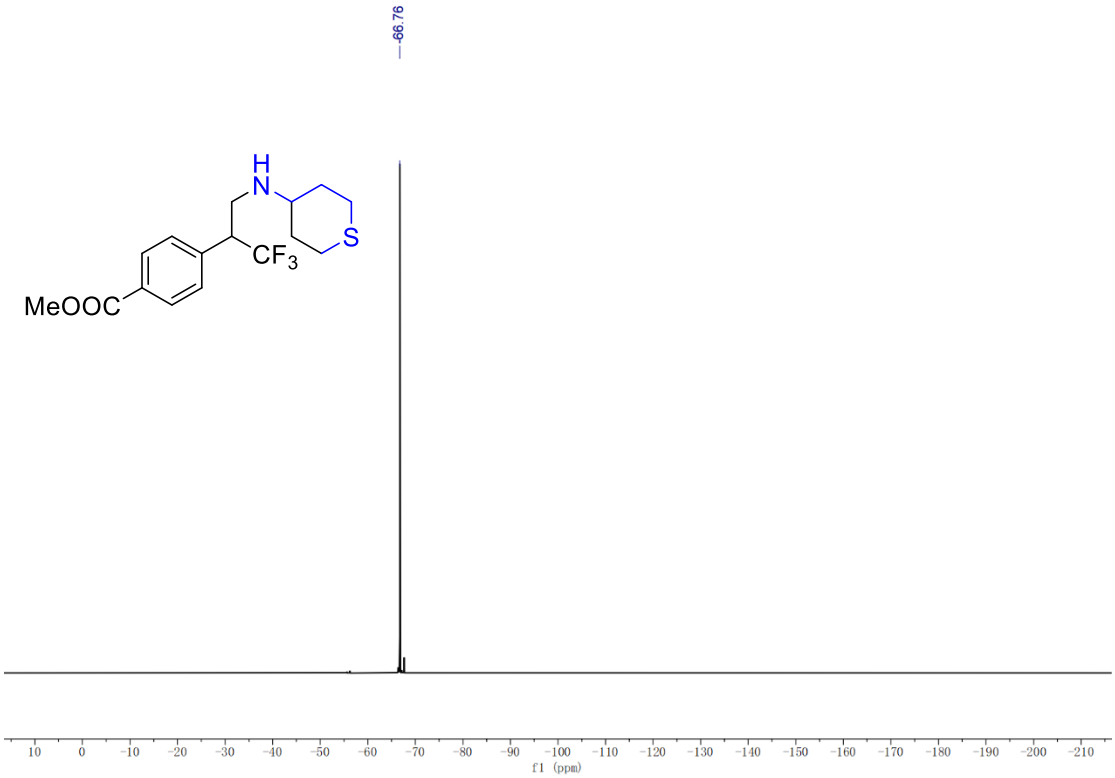

165.91
139.58
130.03
129.60
129.37
129.26
127.44
125.58
123.73
65.69
65.65
52.79
52.12
49.40
49.24
49.08
48.91
44.43
44.41
39.94
39.80
39.66
39.52
39.38
39.24
39.10
33.11
32.80
H
N
O
CF3
MeOOC
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)


-66.72
H
N
O
CF3
MeOOC
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

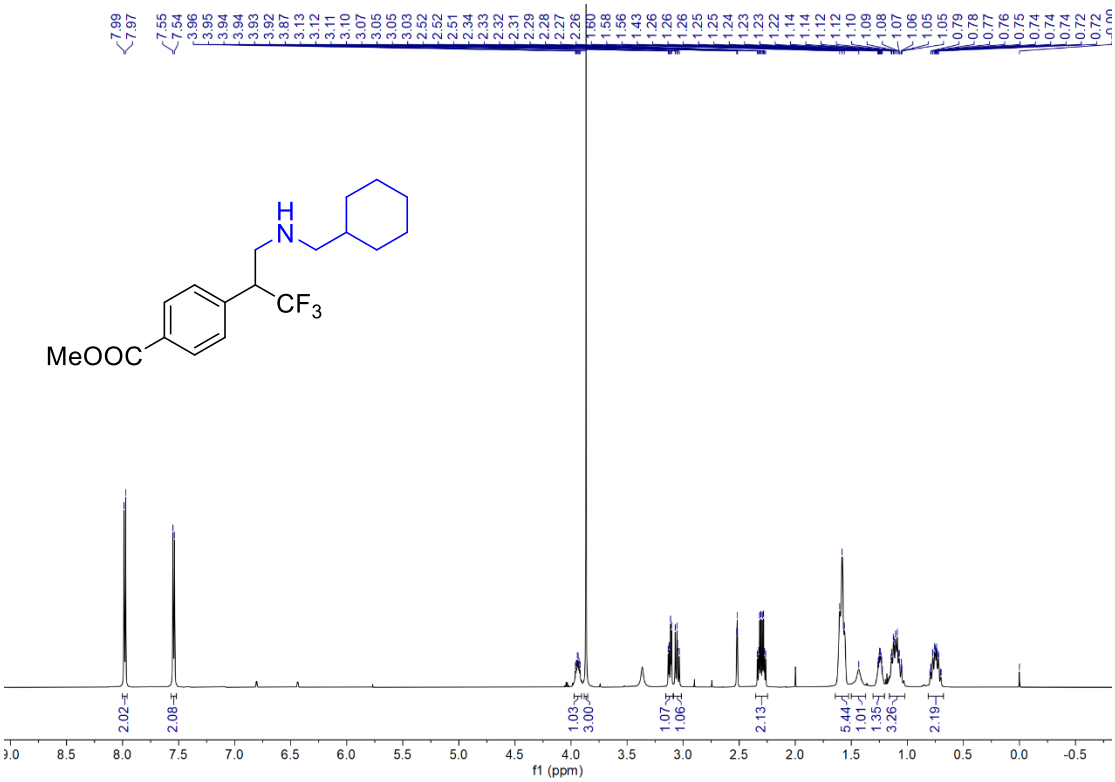
methyl 4-(1,1,1-trifluoro-3-((tetrahydro-2H-thiopyran-4-yl)amino)propan-2-yl)benzoate (**5e**)

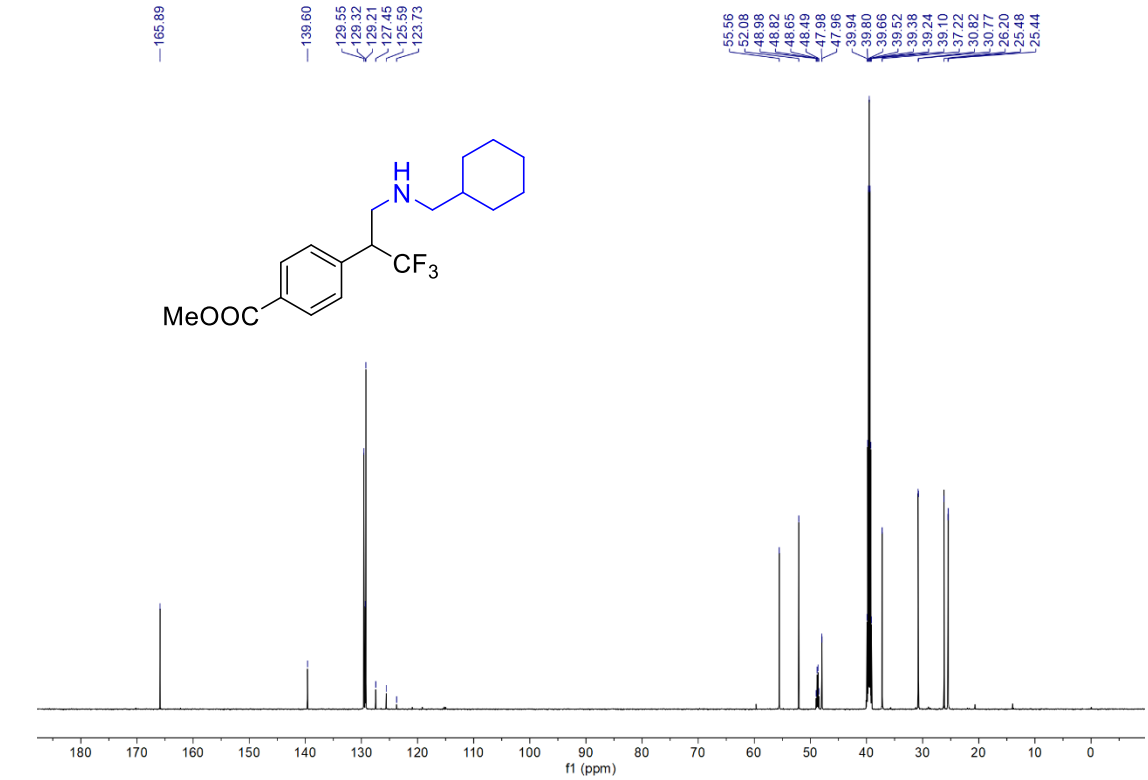


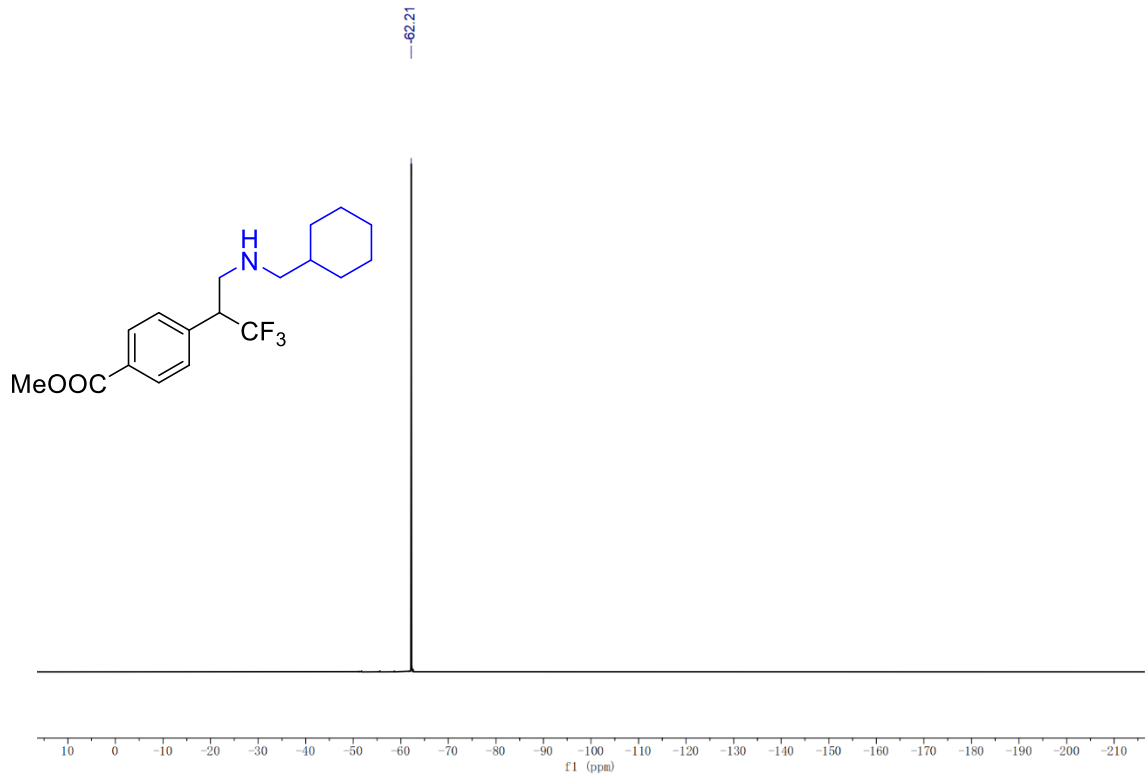




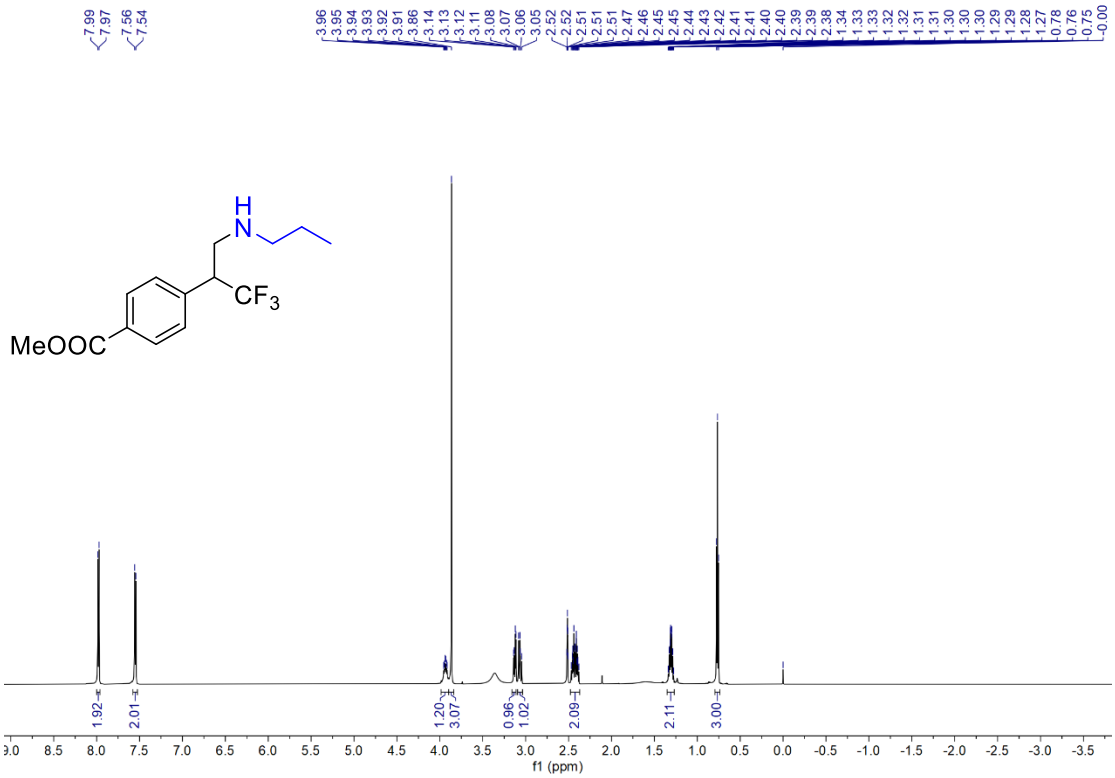
methyl 4-(3-((cyclohexylmethyl)amino)-1,1,1-trifluoropropan-2-yl)benzoate (**5f**)

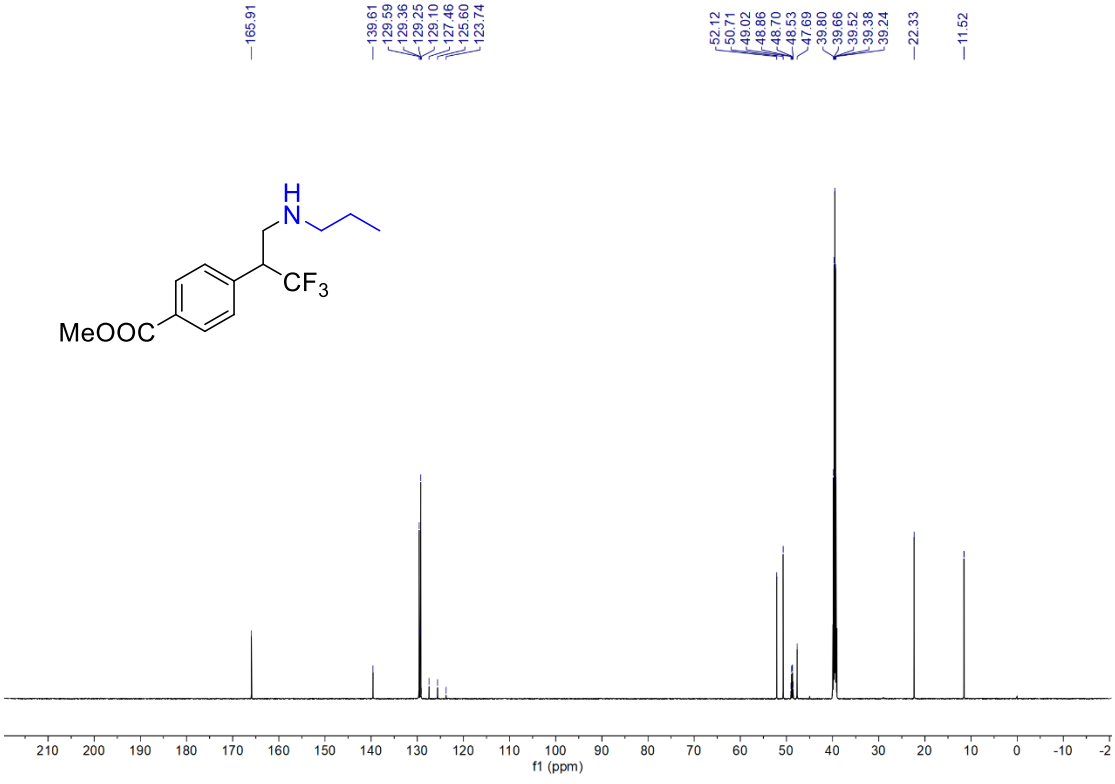


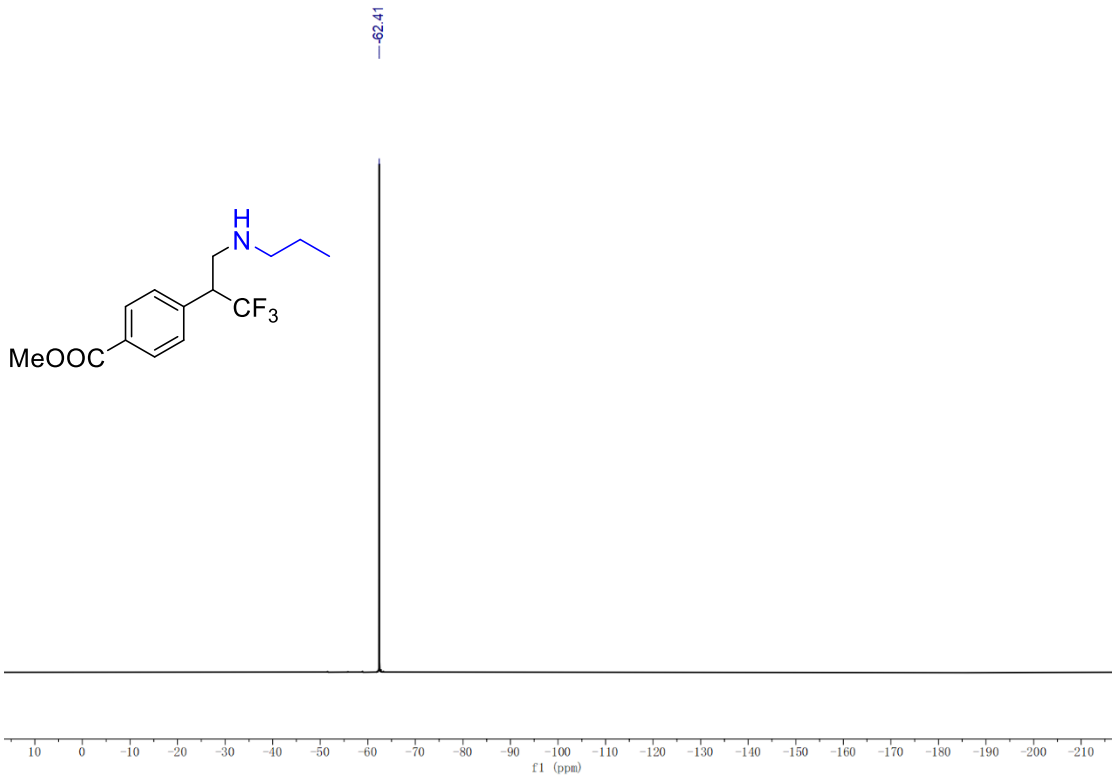

165.89
139.60
129.55
129.32
129.21
127.45
125.59
123.73
55.56
52.08
48.98
48.82
48.65
48.49
47.98
47.96
39.94
39.80
39.66
39.52
39.38
39.24
39.10
37.22
30.82
30.77
26.20
25.48
25.44
H
N
CF3
MeOOC
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


62.21
H
N
CF3
MeOOC
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

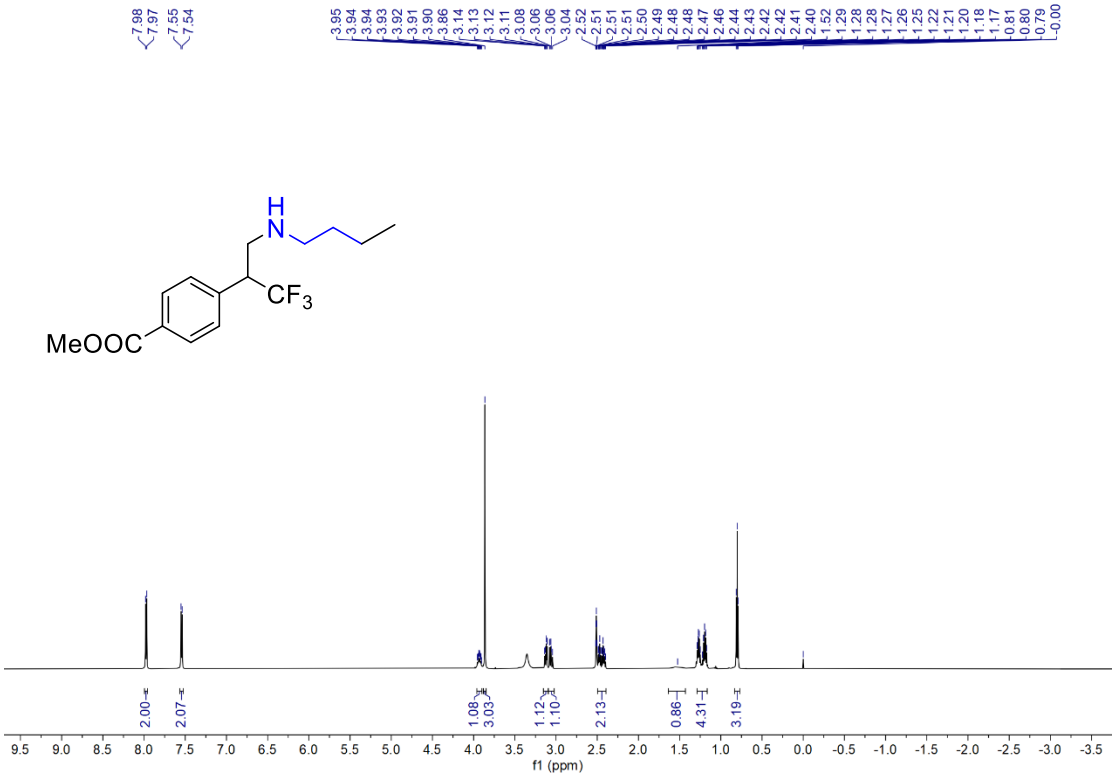
methyl 4-(1,1,1-trifluoro-3-(propylamino)propan-2-yl)benzoate (**5g**)

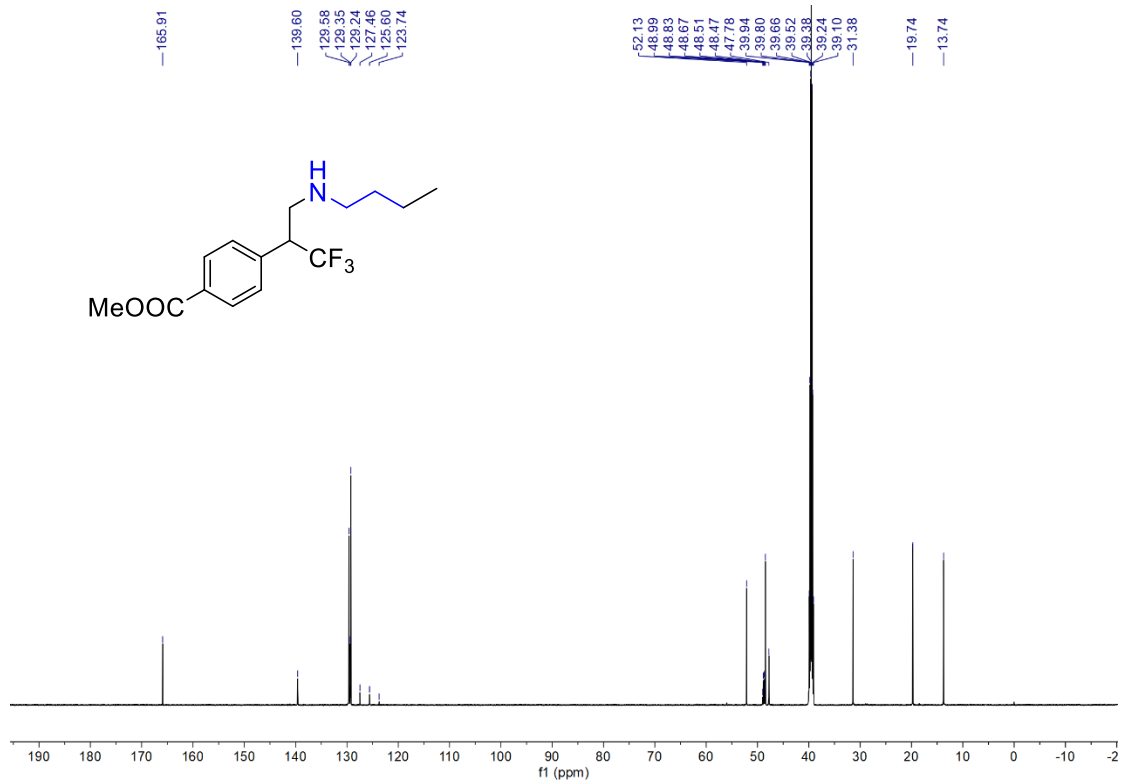


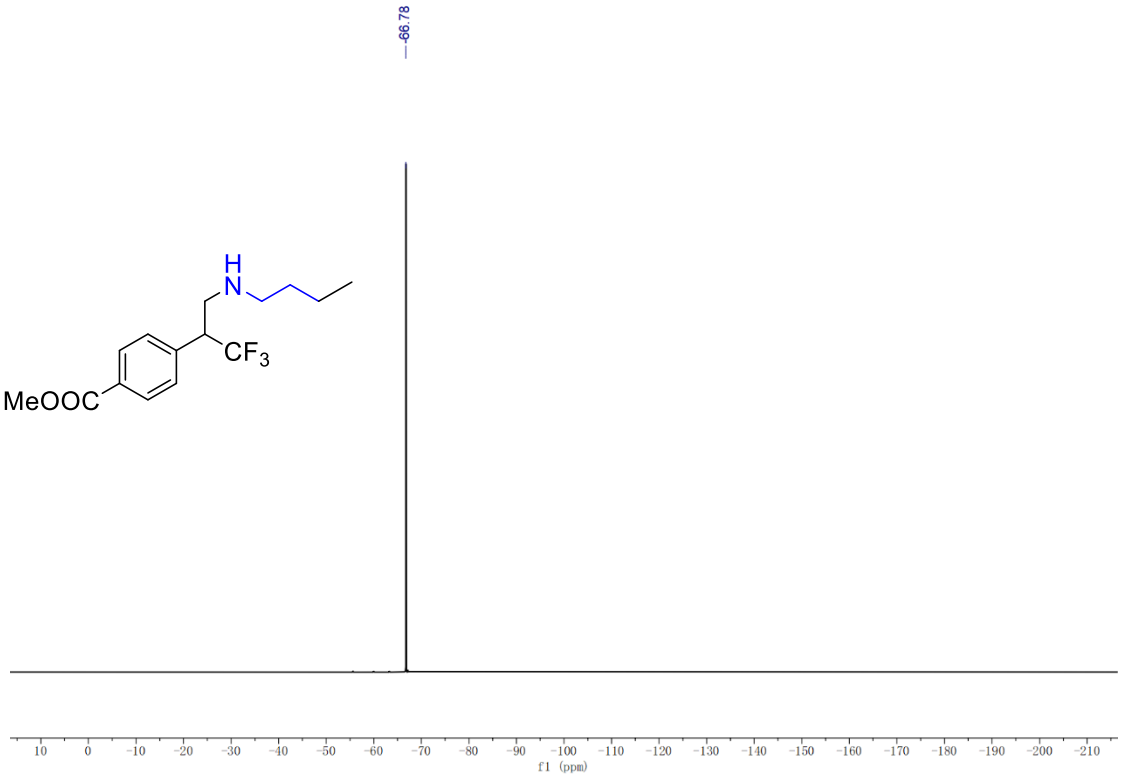




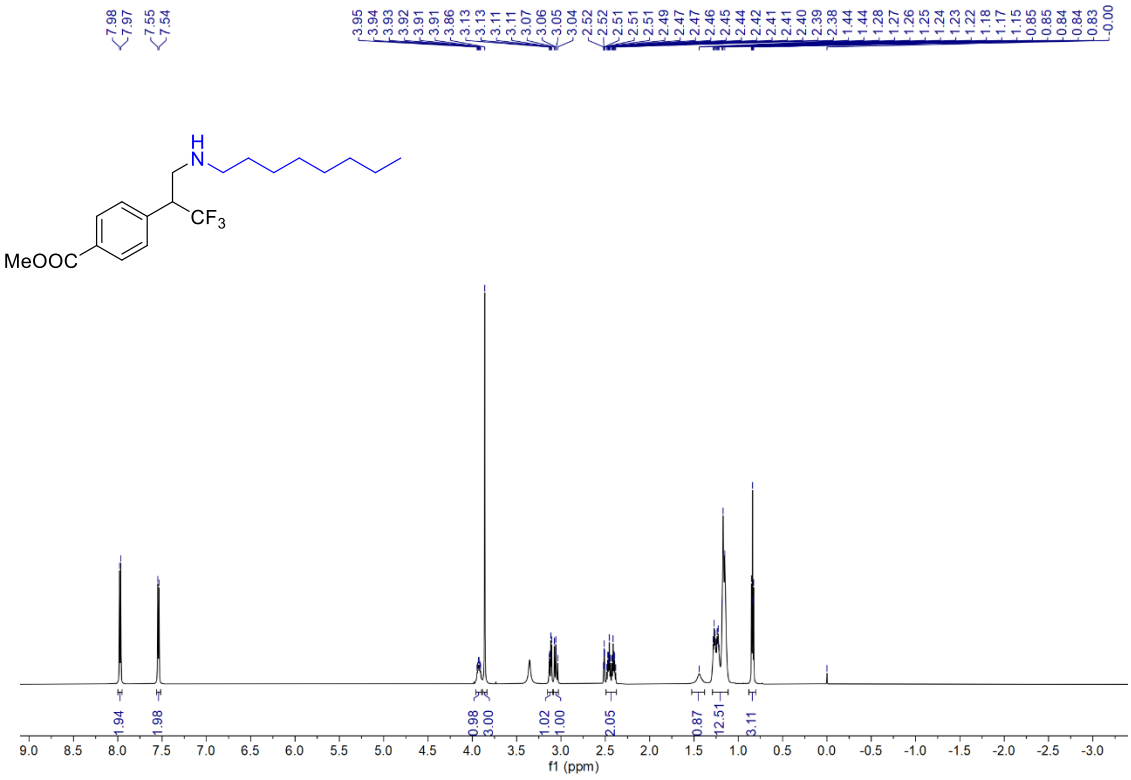
methyl 4-(3-(butylamino)-1,1,1-trifluoropropan-2-yl)benzoate (**5h**)

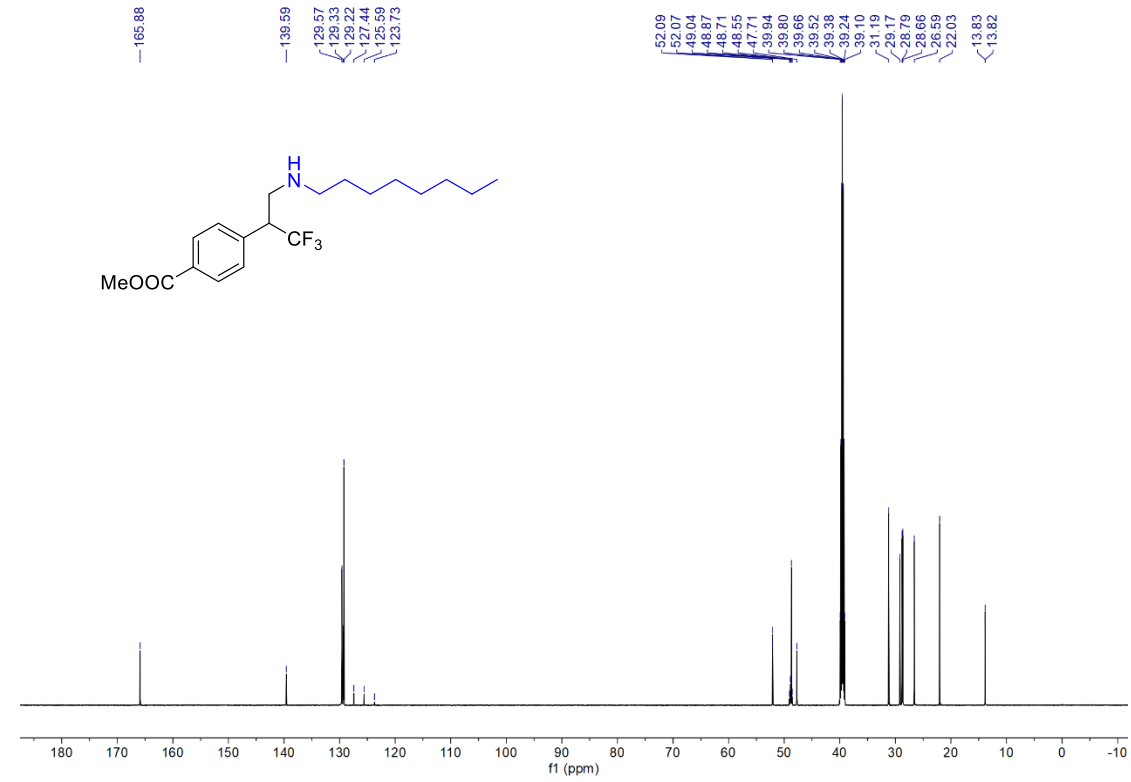


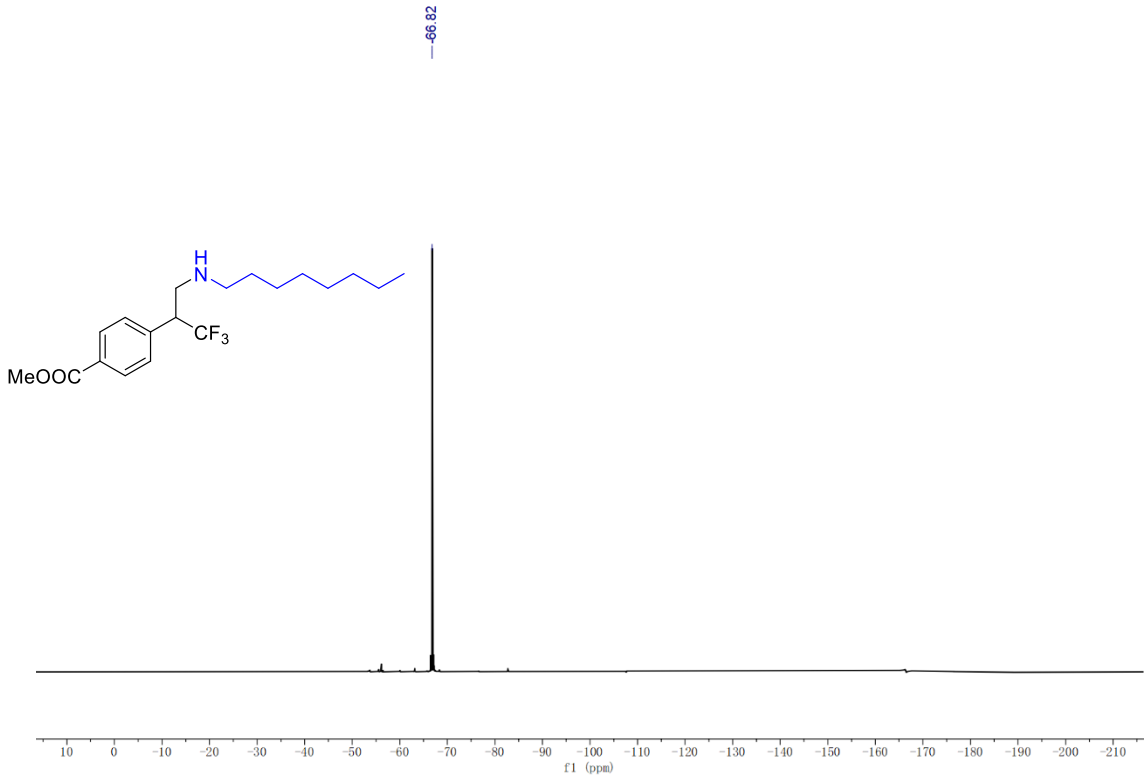

165.91
139.60
129.58
129.35
129.24
127.46
125.60
123.74
52.13
48.99
48.83
48.67
48.51
48.47
47.78
39.94
39.80
39.66
39.52
39.38
39.24
39.10
31.38
19.74
13.74
H
N
CF3
MeOOC
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -2
f1 (ppm)


66.78
H
N
CF3
MeOOC
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

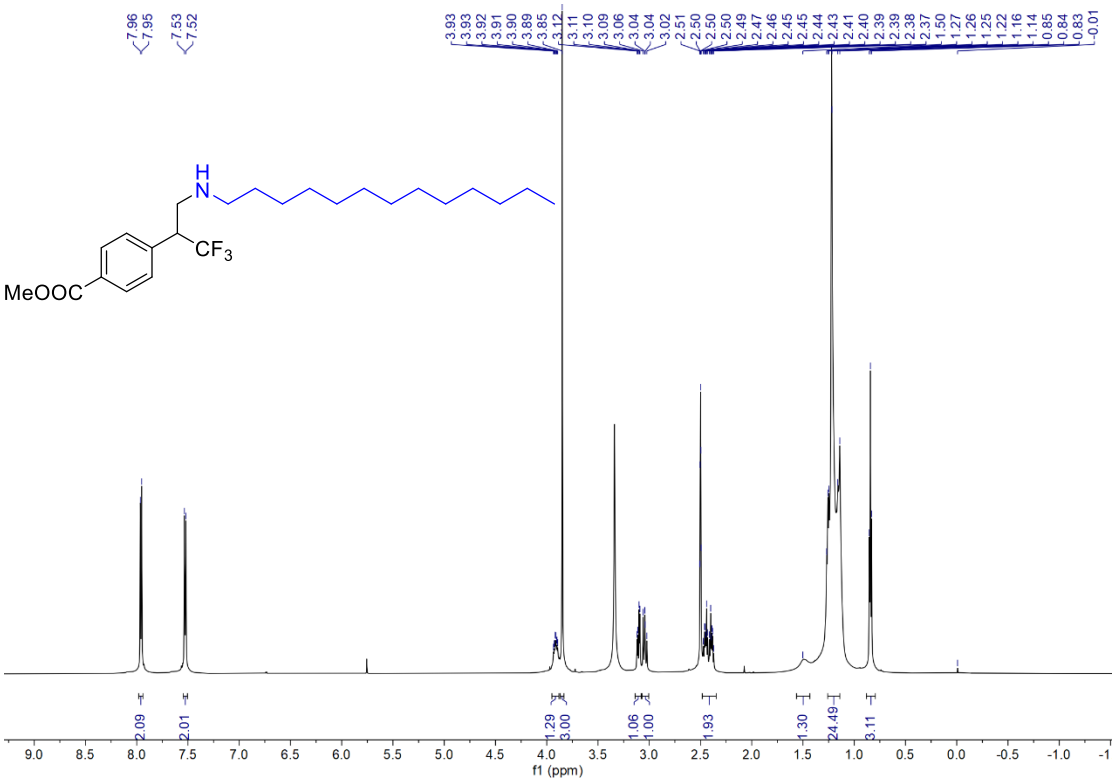
methyl 4-(1,1,1-trifluoro-3-(octylamino)propan-2-yl)benzoate (**5i**)

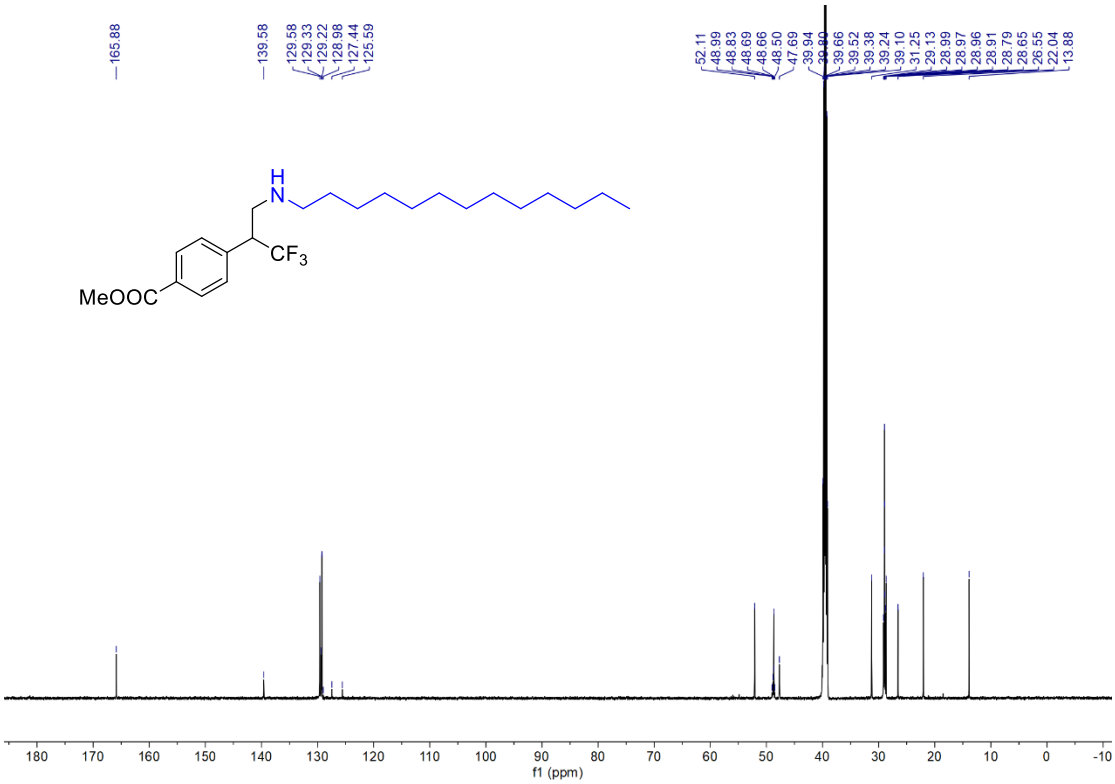


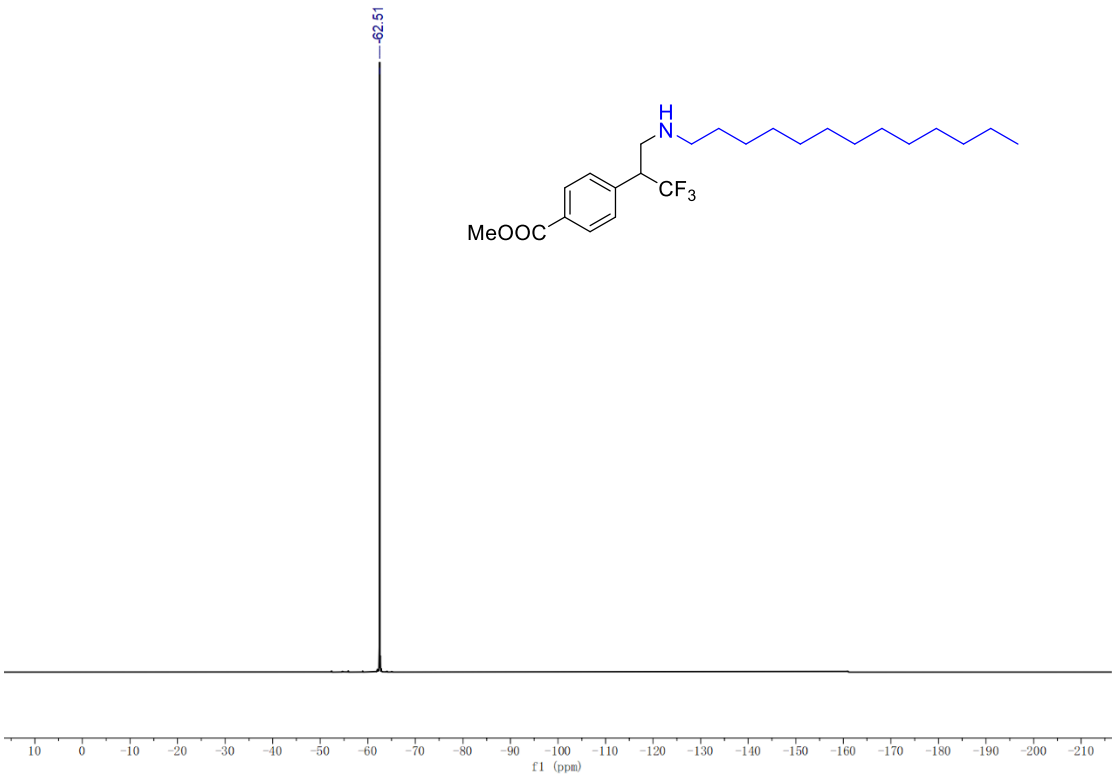




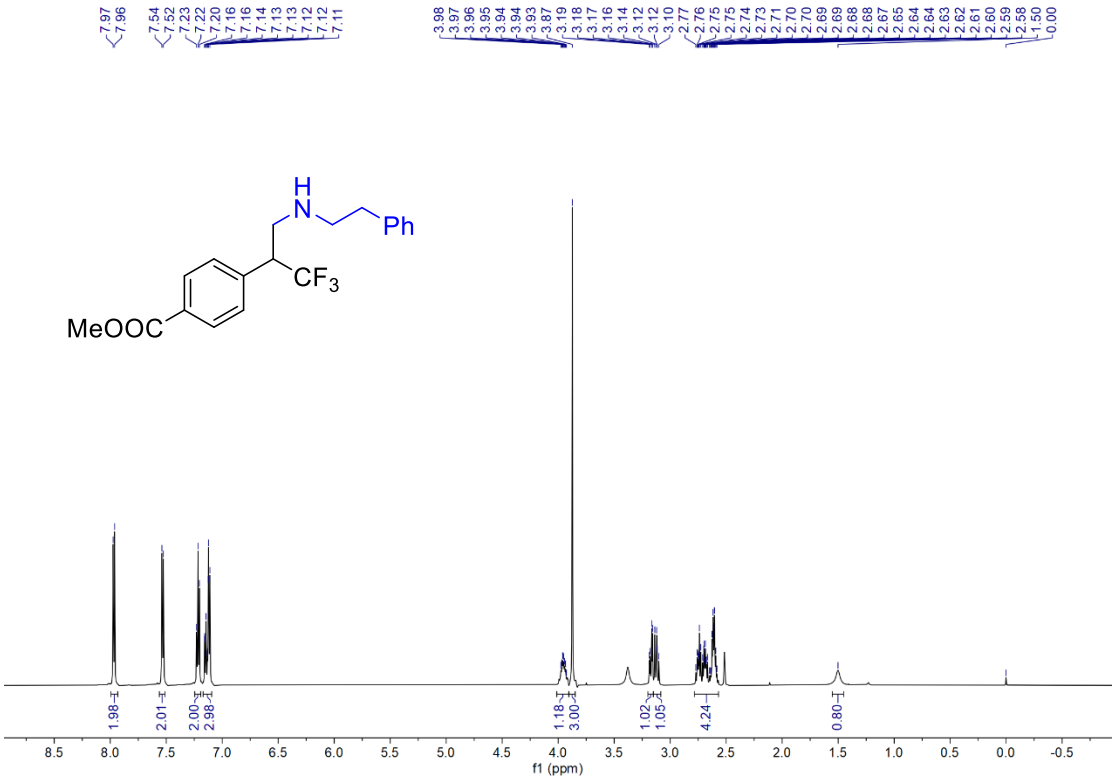
methyl 4-(1,1,1-trifluoro-3-(tridecylamino)propan-2-yl)benzoate (**5j**)

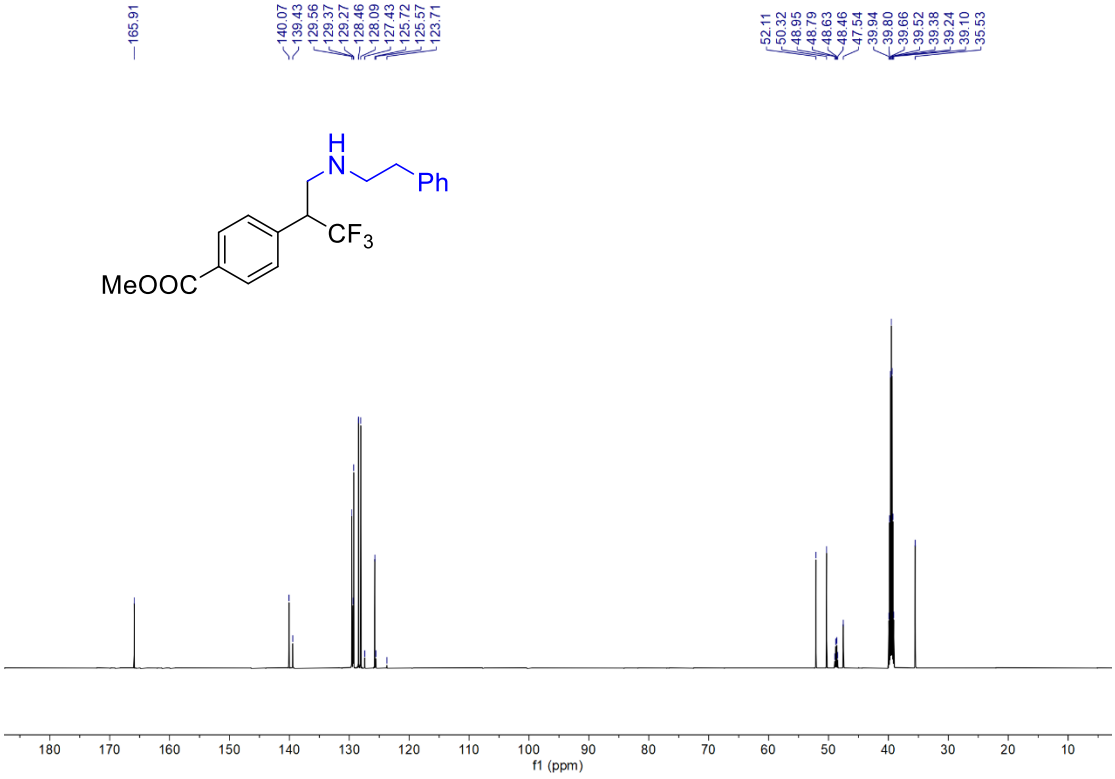


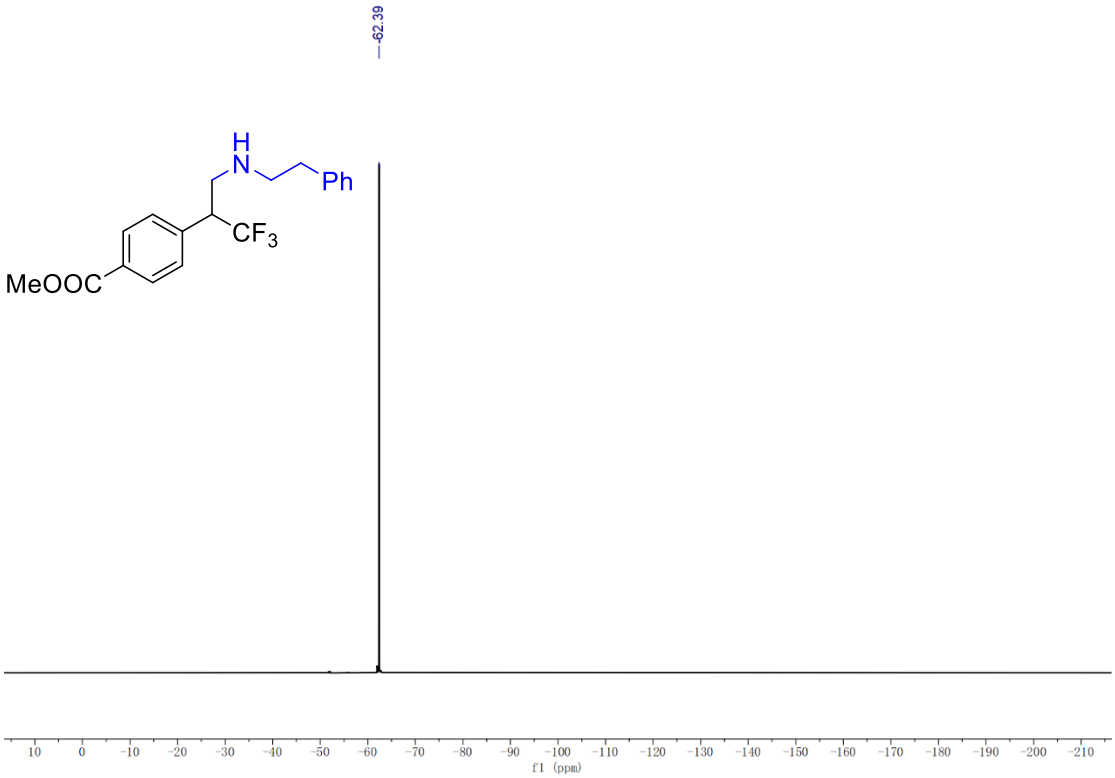

165.88
139.58
129.58
129.33
129.22
128.98
127.44
125.59
52.11
48.99
48.83
48.69
48.66
48.50
47.69
39.94
39.80
39.66
39.52
39.38
39.24
39.10
31.25
29.13
28.99
28.97
28.96
28.91
28.79
28.65
26.55
22.04
13.88
H
N
CF3
MeOOC
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


62.51
H
N
CF3
MeOOC
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

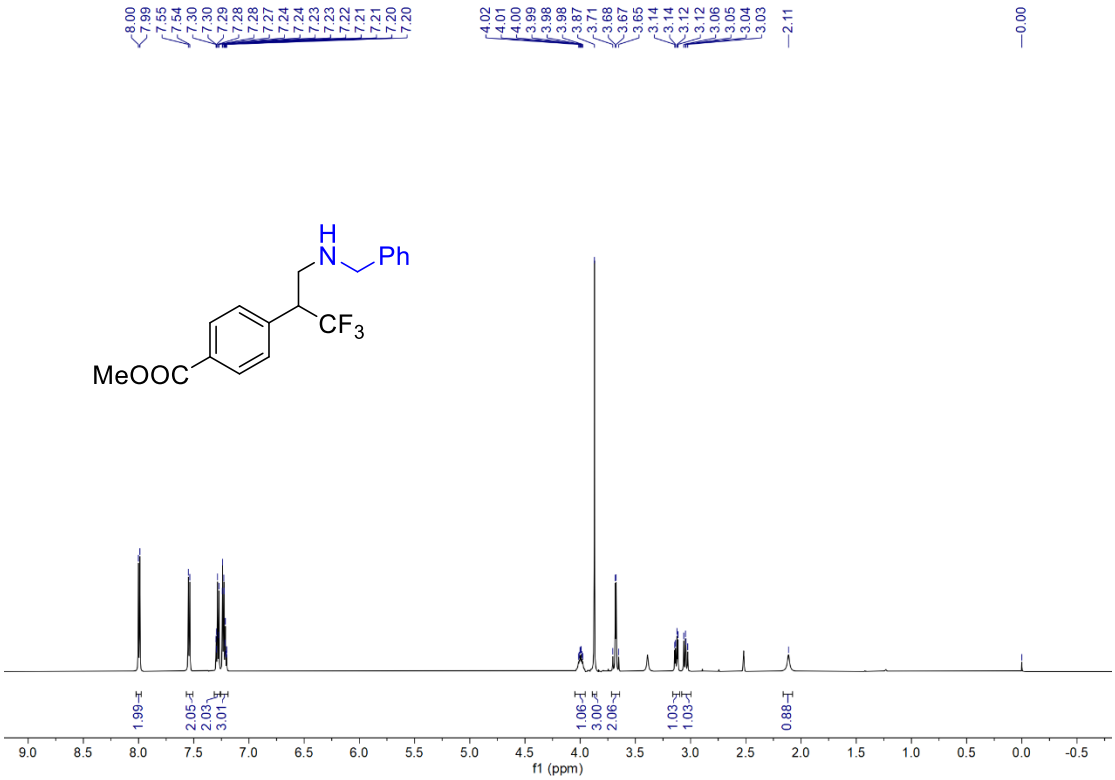
methyl 4-(1,1,1-trifluoro-3-(phenethylamino)propan-2-yl)benzoate (**5k**)

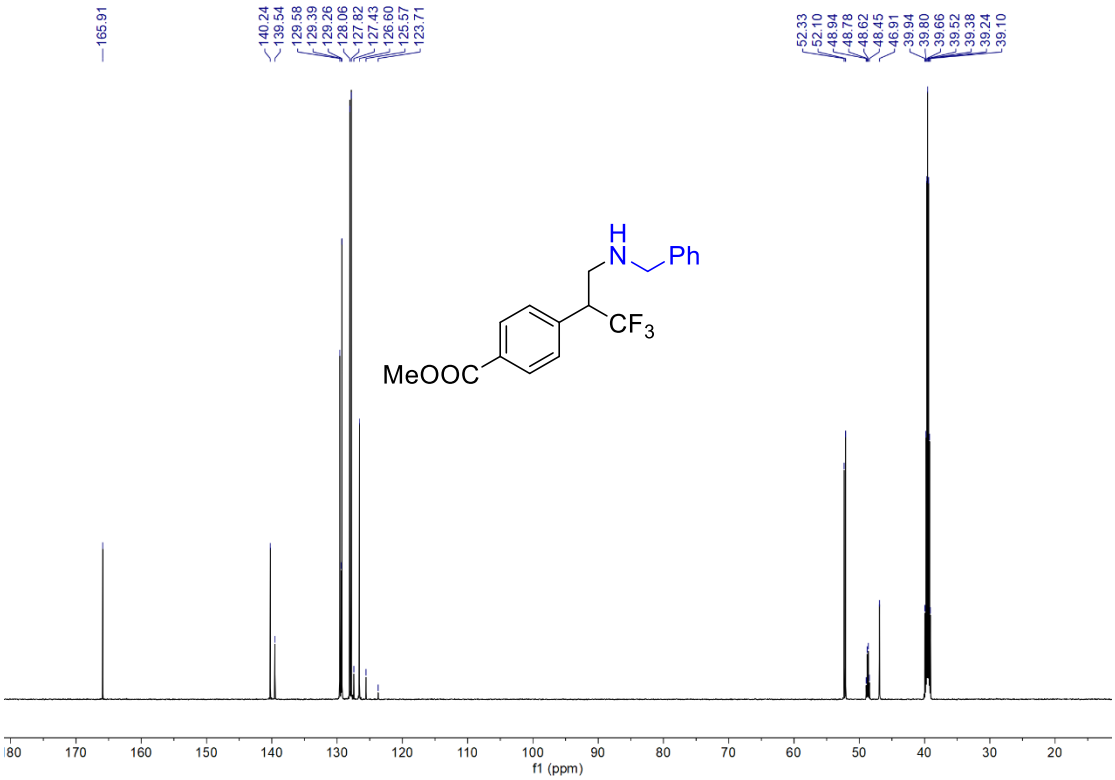


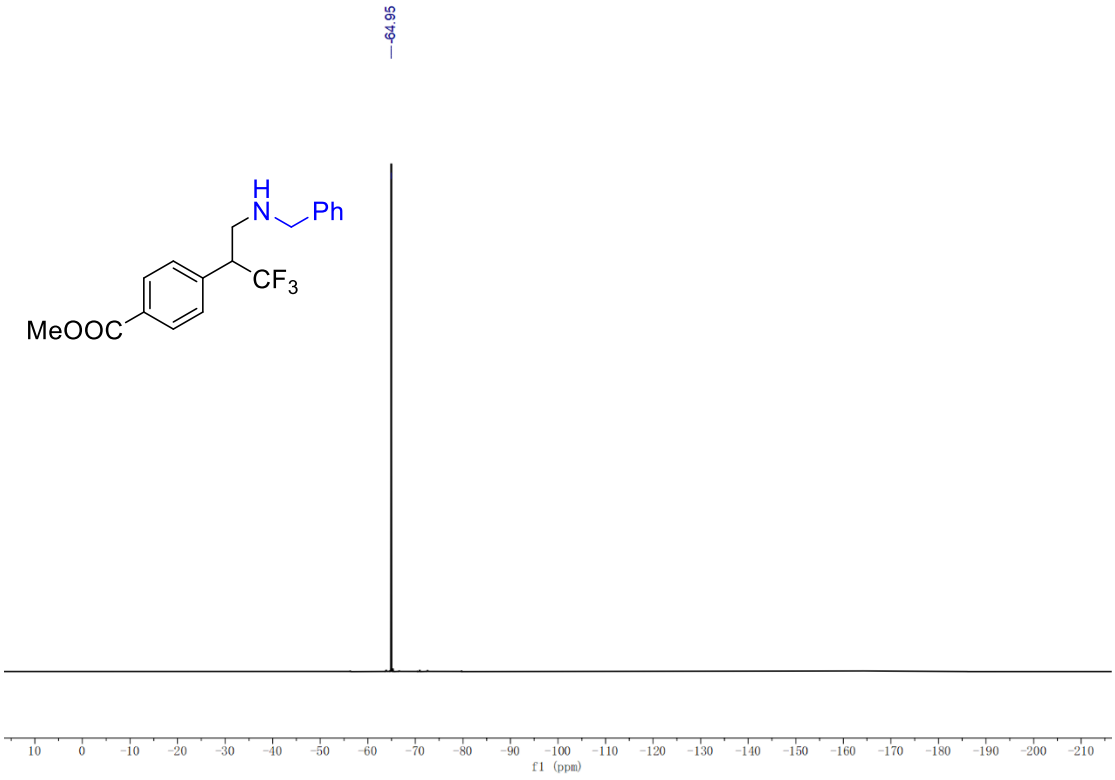




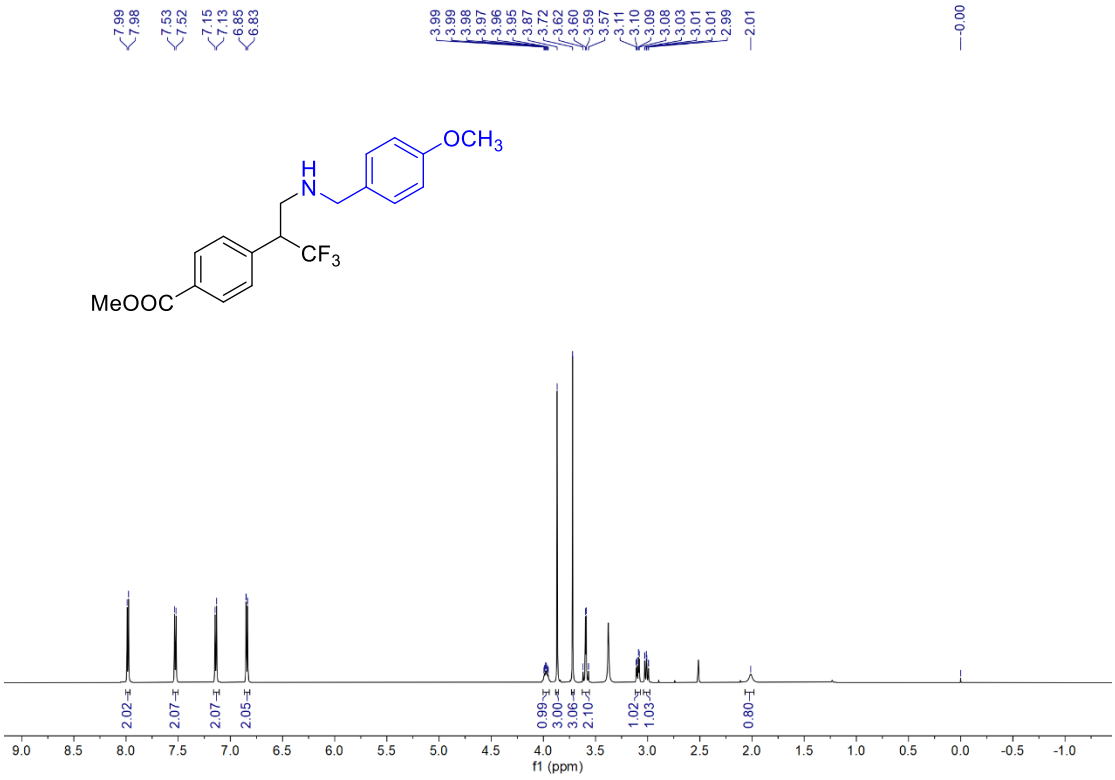
methyl 4-(3-(benzylamino)-1,1,1-trifluoropropan-2-yl)benzoate (**5l**)

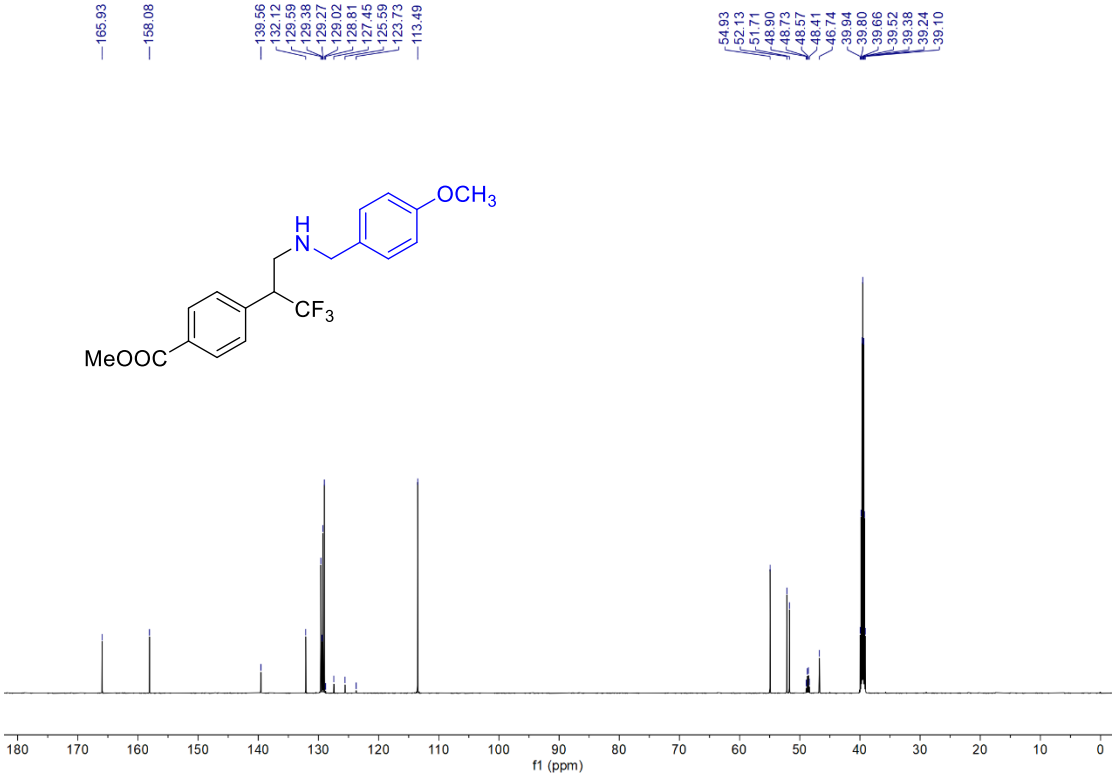


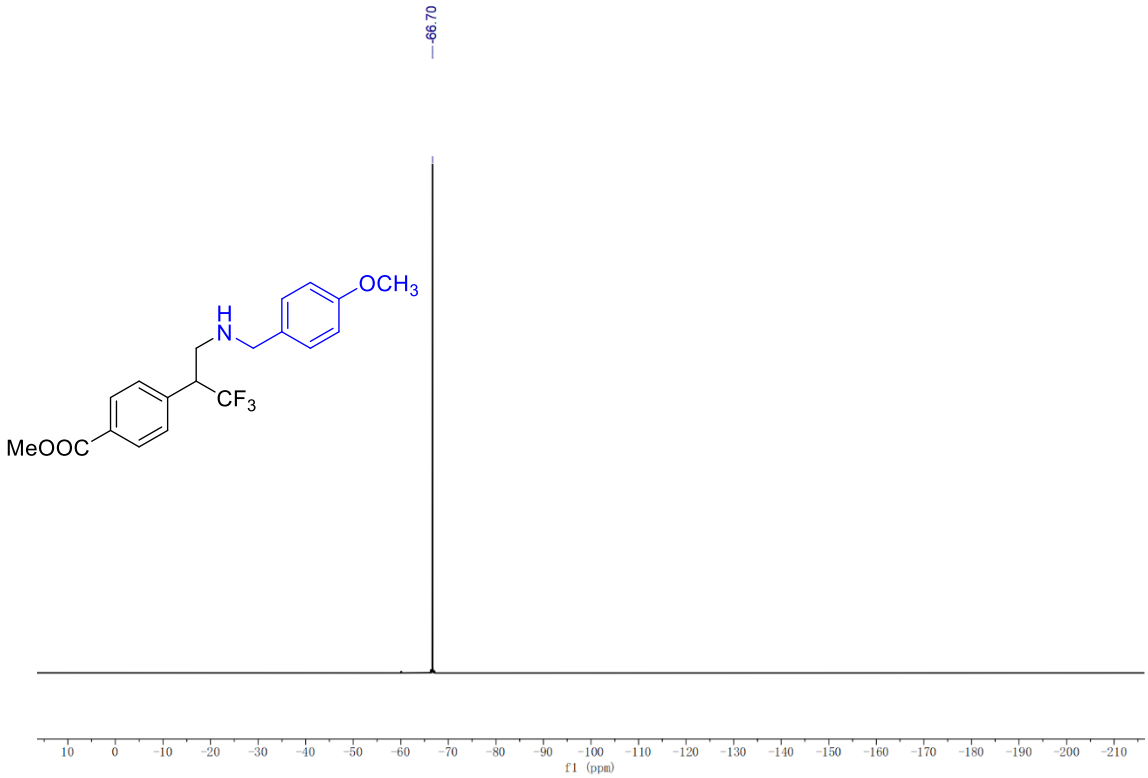

165.91
140.24
139.54
129.58
129.39
129.26
128.06
127.82
127.43
126.60
125.57
123.71
52.33
52.10
48.94
48.78
48.62
48.45
46.91
39.94
39.80
39.66
39.52
39.38
39.24
39.10
H
N
Ph
CF3
MeOOC
f1 (ppm)


-64.95
H
N
Ph
CF3
MeOOC
f1 (ppm)

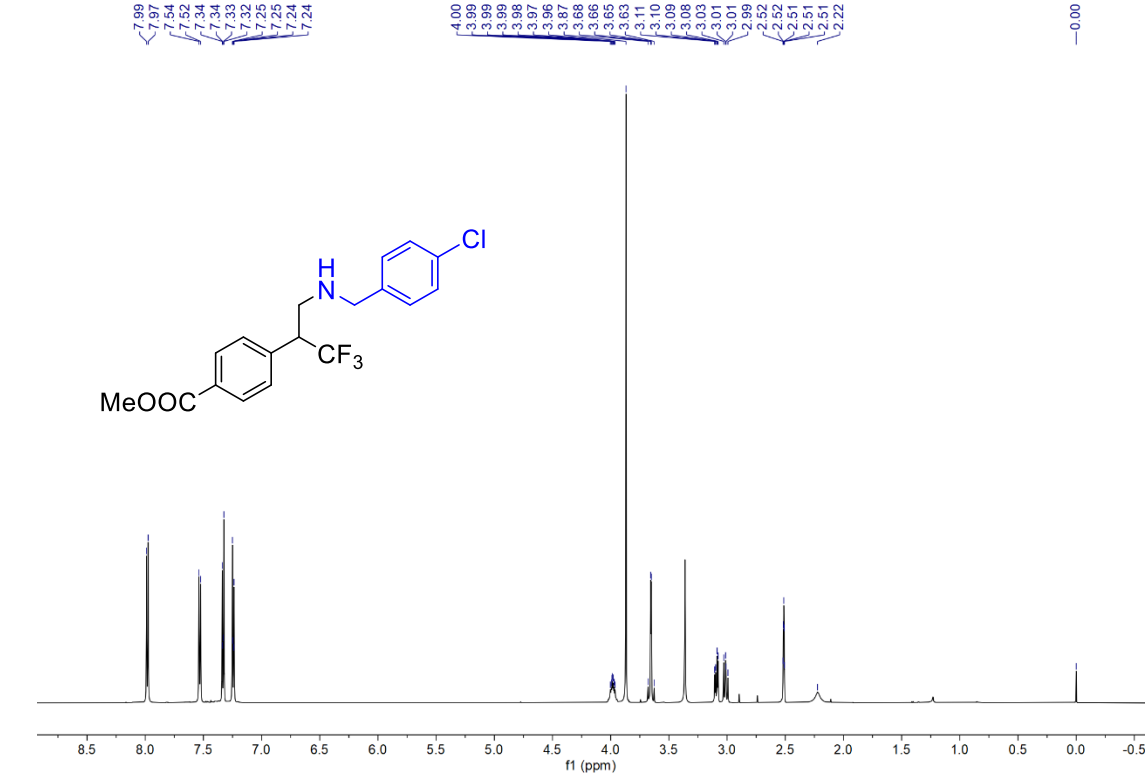
methyl 4-(1,1,1-trifluoro-3-((4-methoxybenzyl)amino)propan-2-yl)benzoate (**5m**)

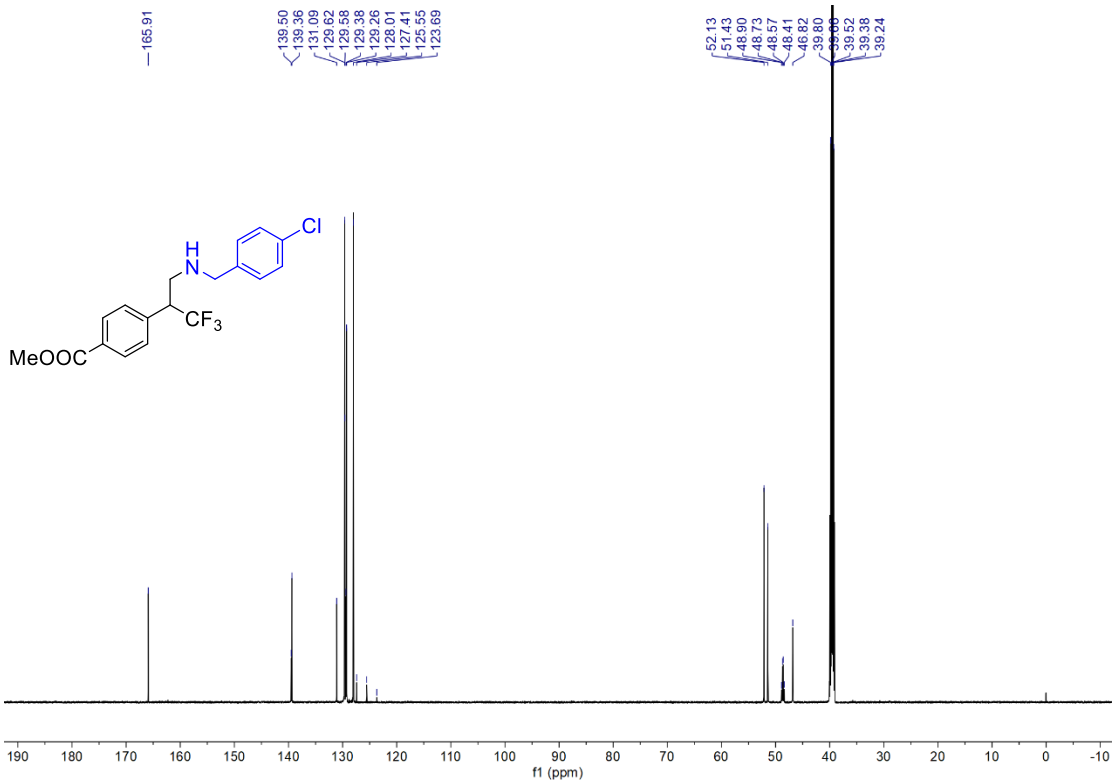


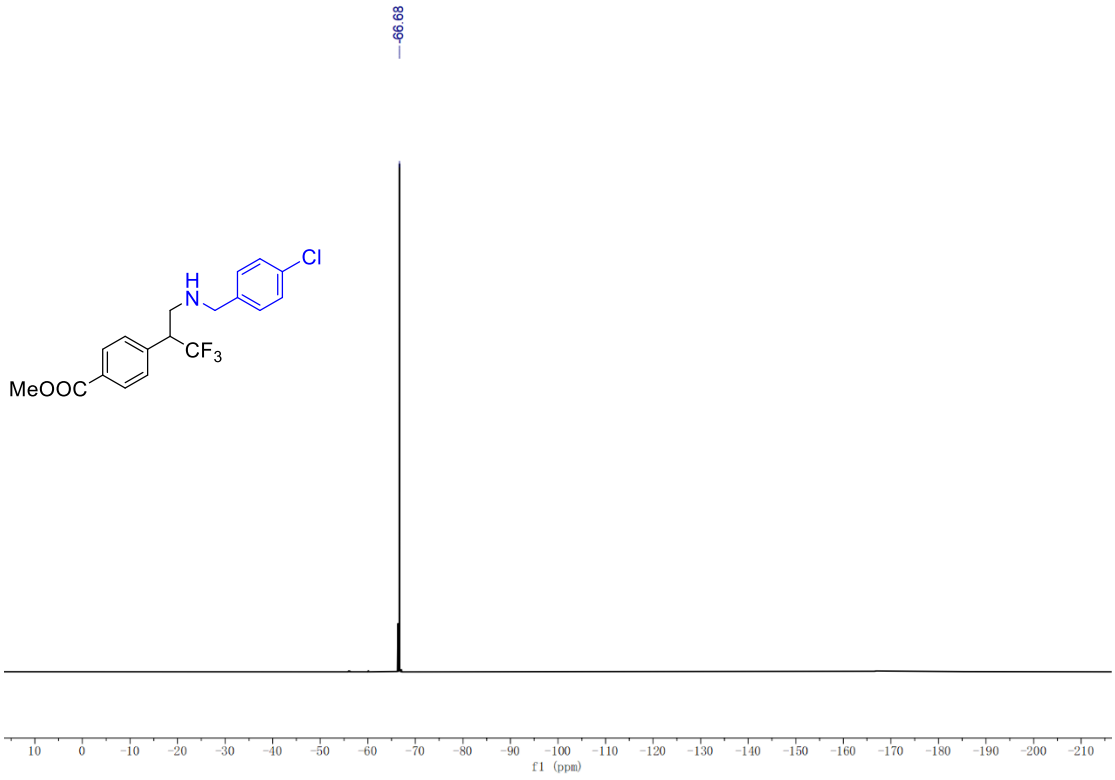




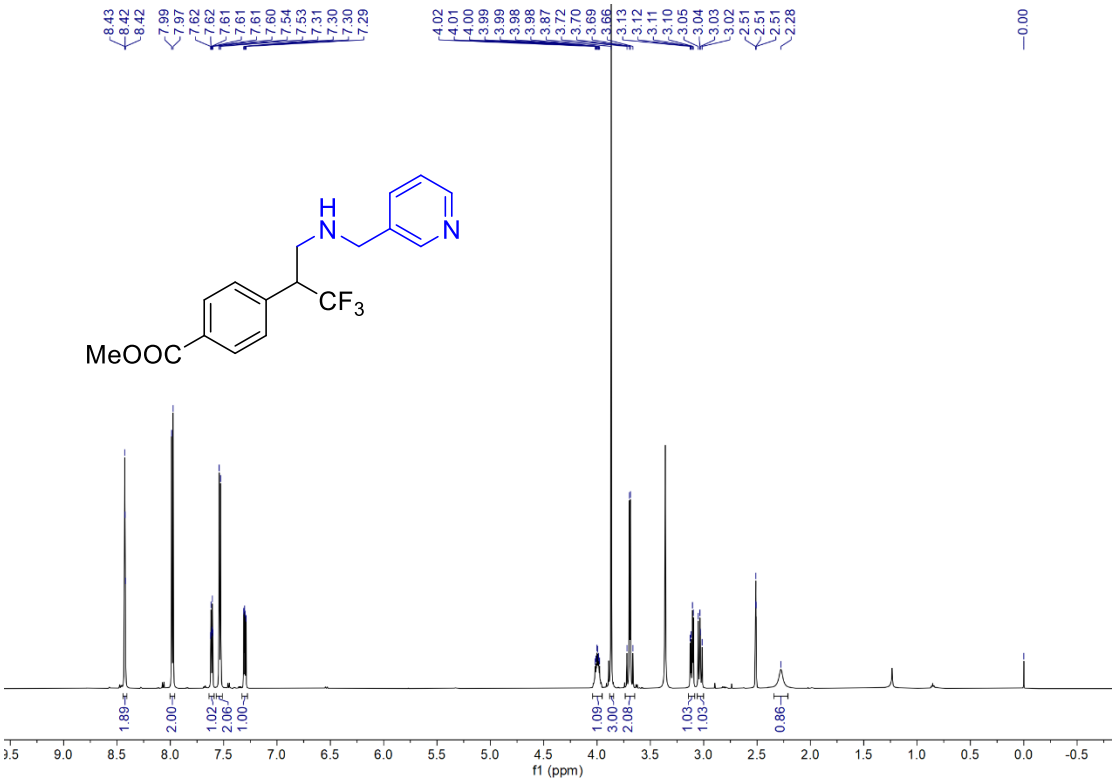
methyl 4-(3-((4-chlorobenzyl)amino)-1,1,1-trifluoropropan-2-yl)benzoate (**5n**)

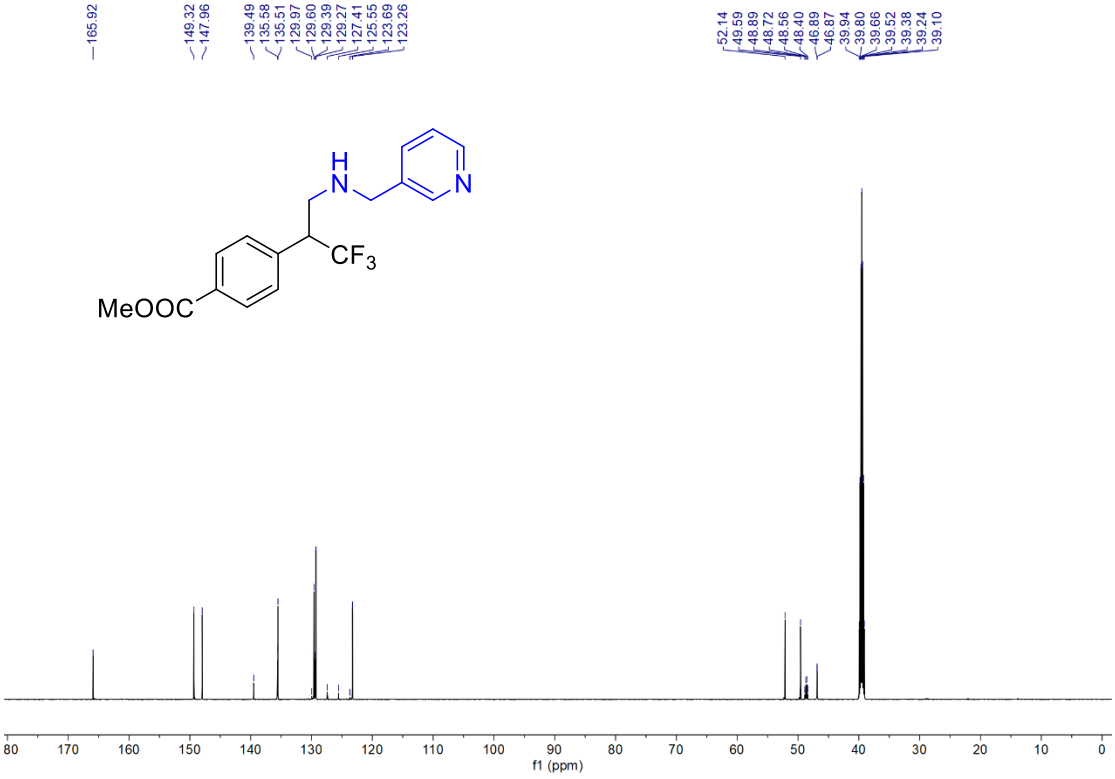


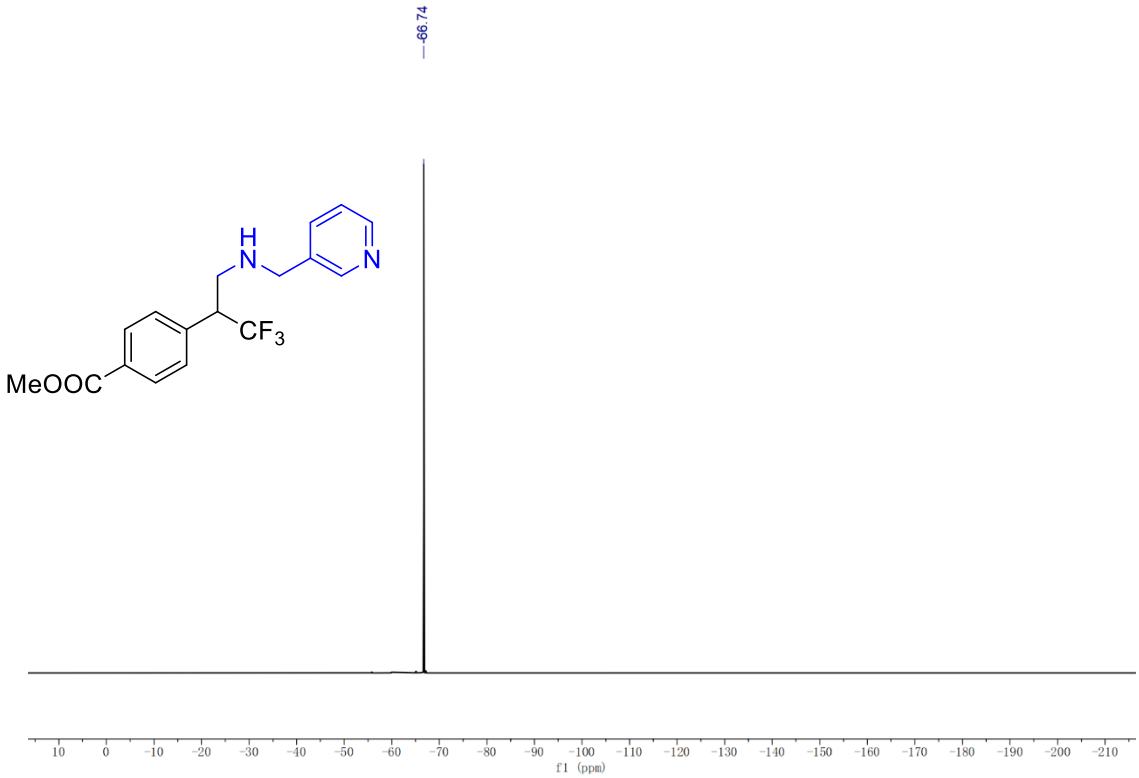

165.91
139.50
139.36
131.09
129.62
129.58
129.38
129.26
128.01
127.41
125.55
123.69
52.13
51.43
48.90
48.73
48.57
48.41
46.82
39.80
39.66
39.52
39.38
39.24
Cl
H
N
CF3
MeOOC
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


-66.68
Cl
H
N
CF3
MeOOC
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

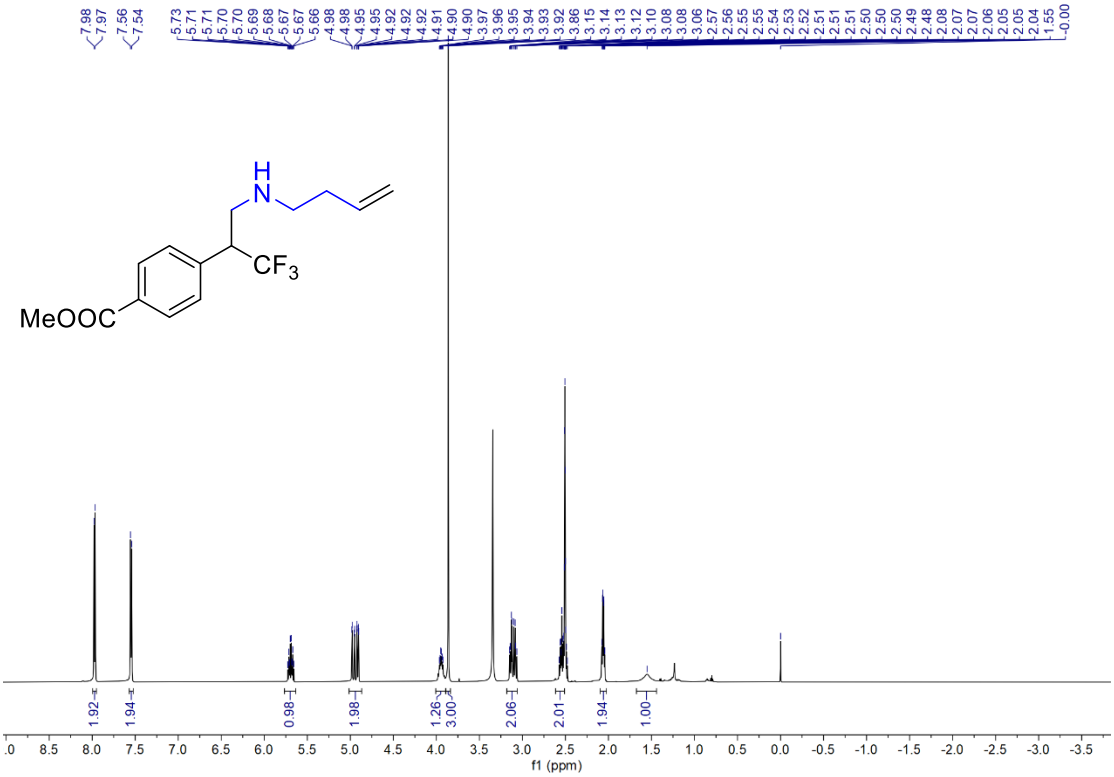
methyl 4-(1,1,1-trifluoro-3-((pyridin-3-ylmethyl)amino)propan-2-yl)benzoate (**5o**)

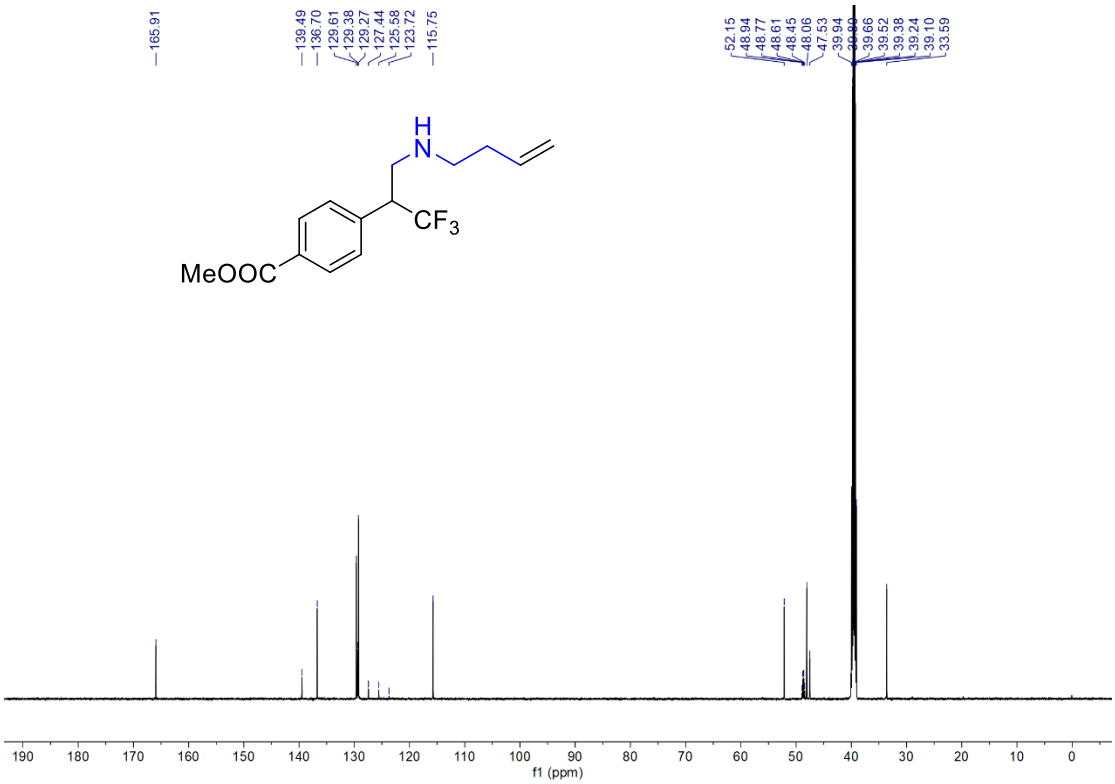


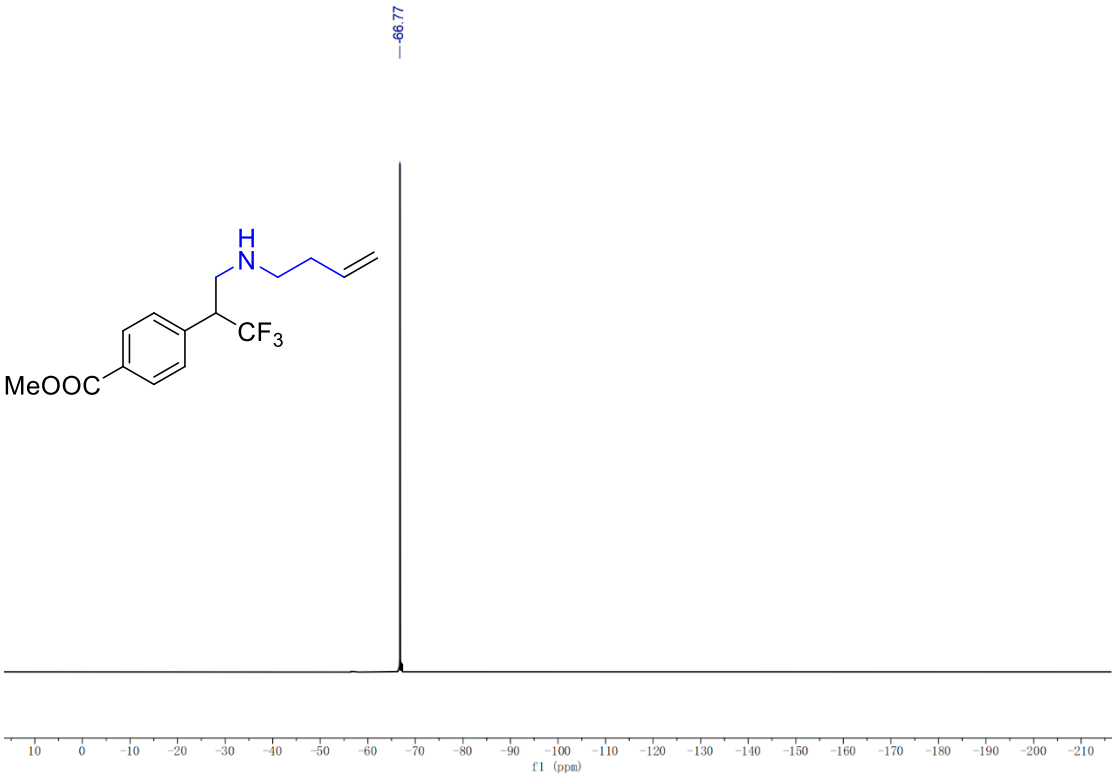




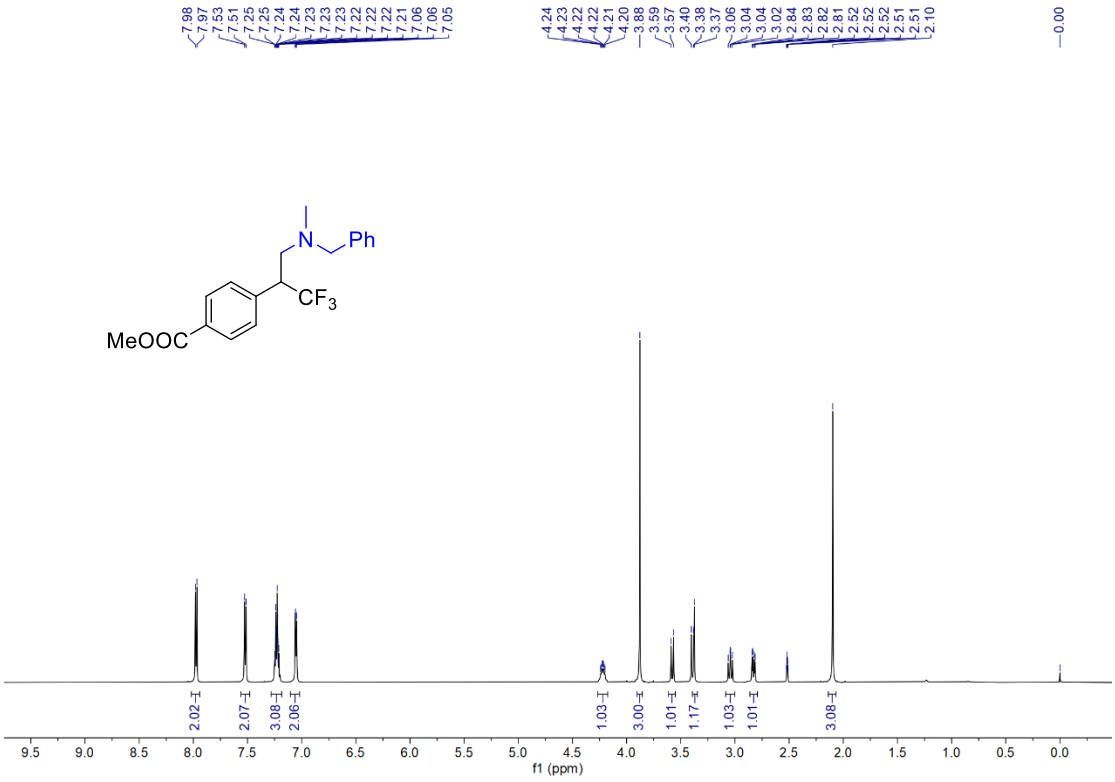
methyl 4-(3-(but-3-en-1-ylamino)-1,1,1-trifluoropropan-2-yl)benzoate (**5p**)

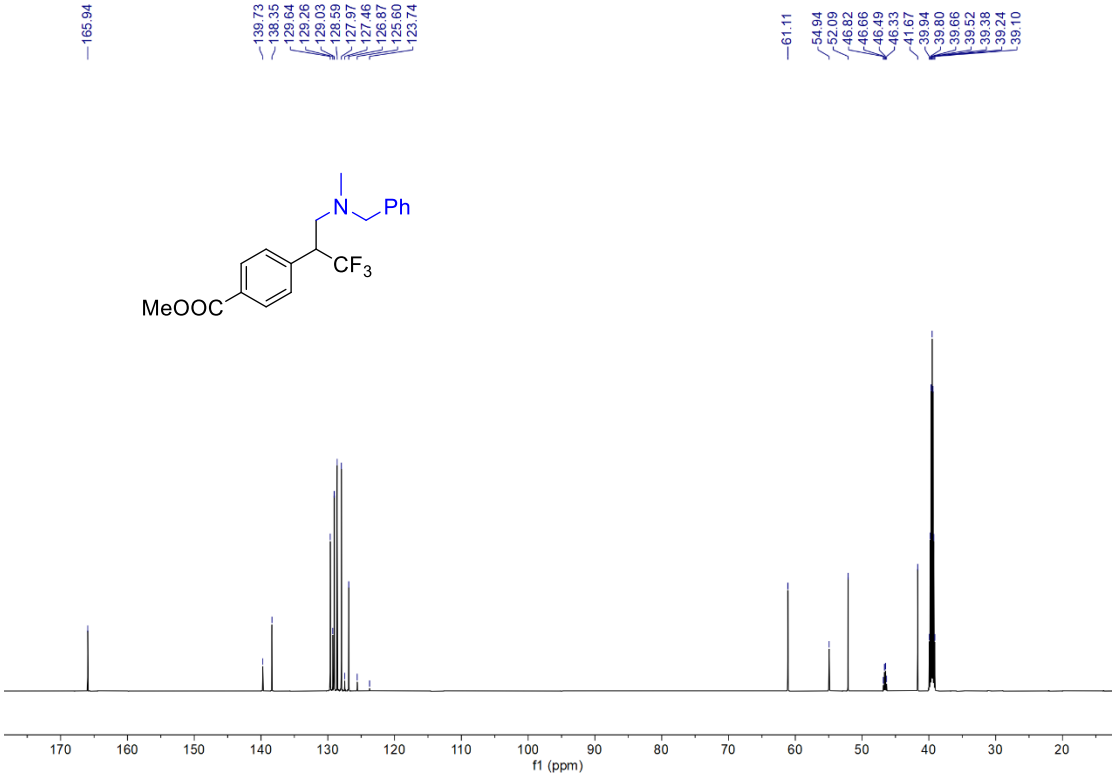


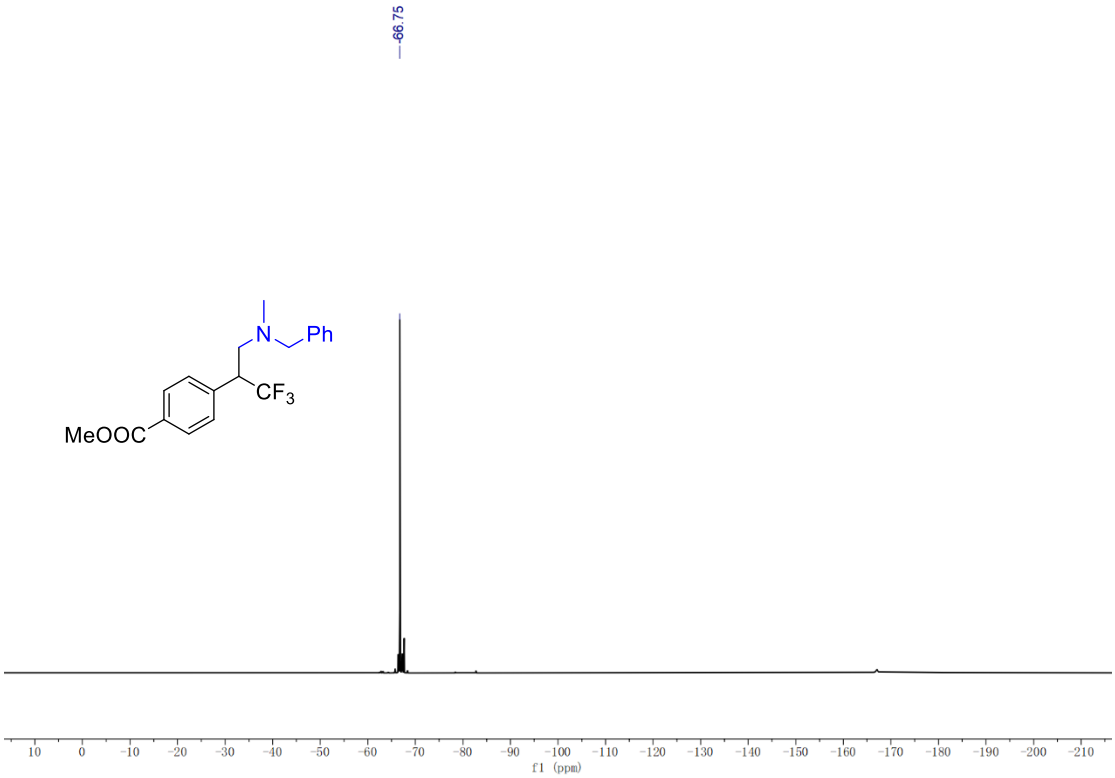

165.91
139.49
136.70
129.61
129.38
129.27
127.44
125.58
123.72
115.75
52.15
48.94
48.77
48.61
48.45
48.06
47.53
39.94
39.80
39.66
39.52
39.38
39.24
39.10
33.59
H
N
CF3
MeOOC
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-66.77
H
N
CF3
MeOOC
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

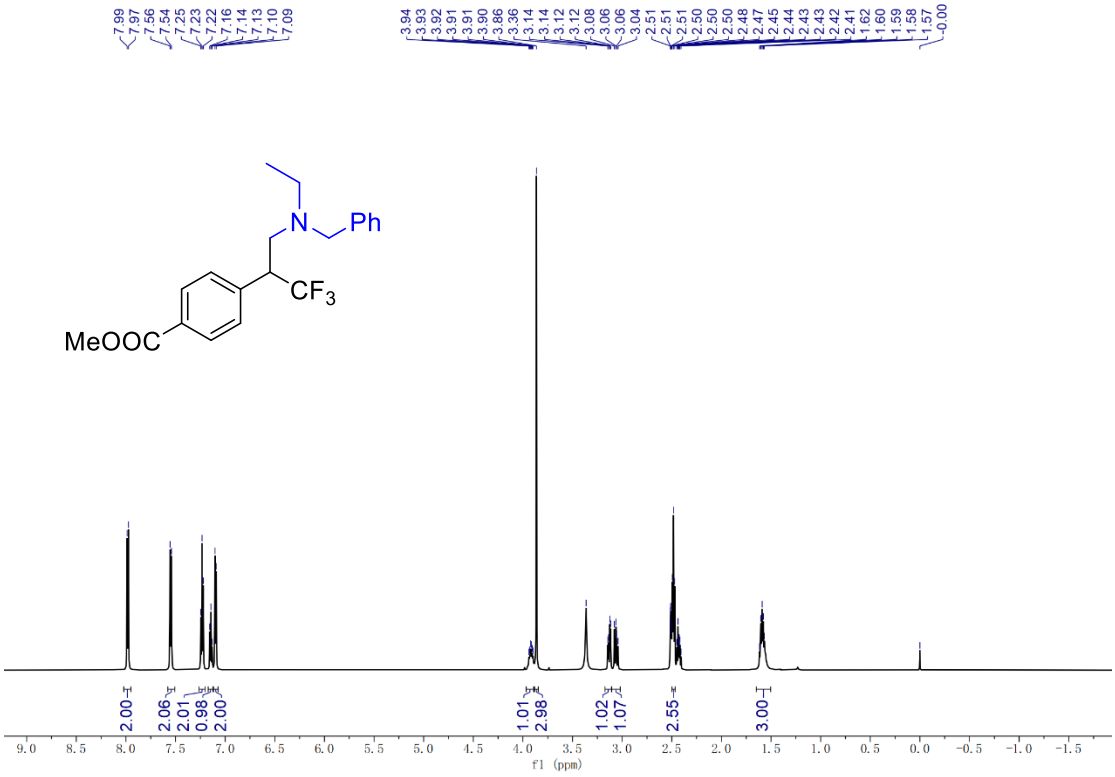
methyl 4-(3-(benzyl(methyl)amino)-1,1,1-trifluoropropan-2-yl)benzoate (**5q**)

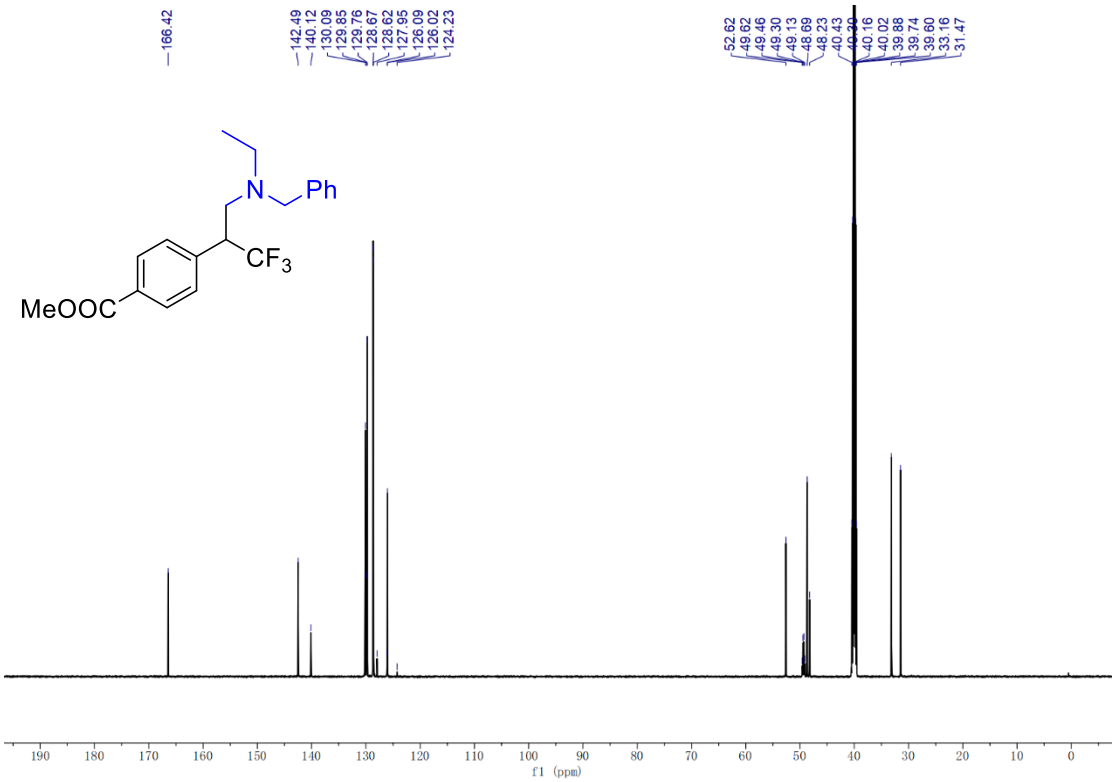


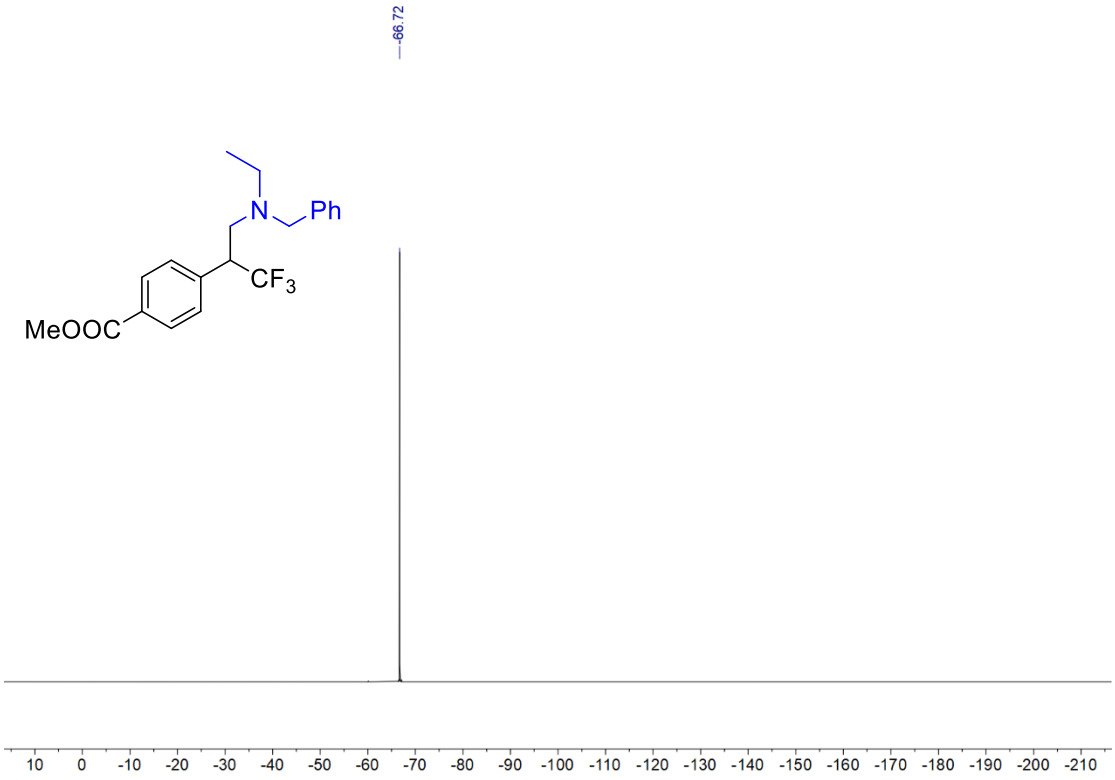




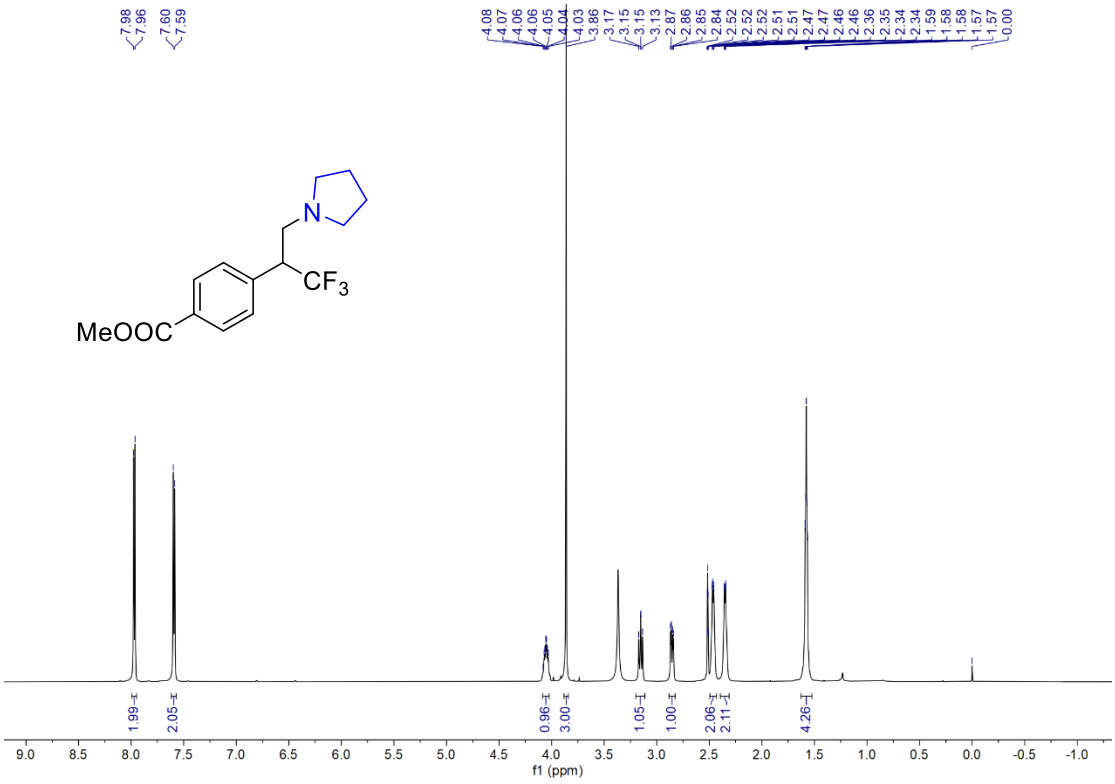
methyl 4-(3-(benzyl(ethyl)amino)-1,1,1-trifluoropropan-2-yl)benzoate (**5r**)

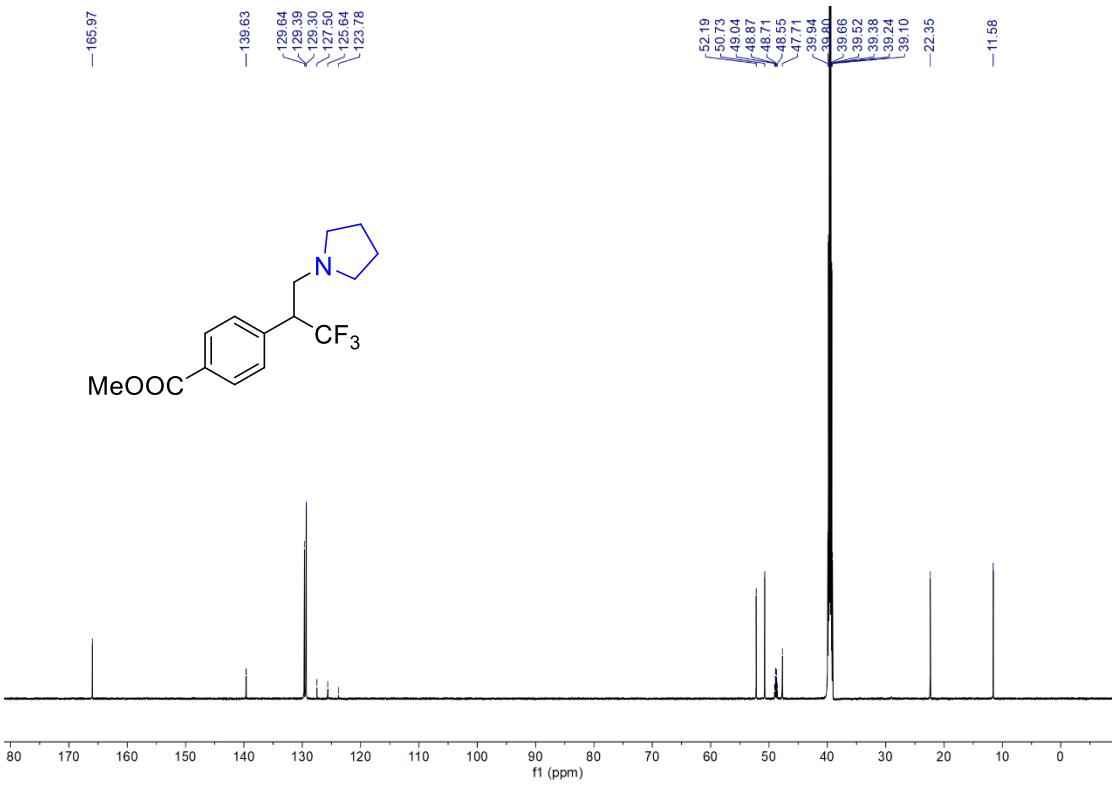


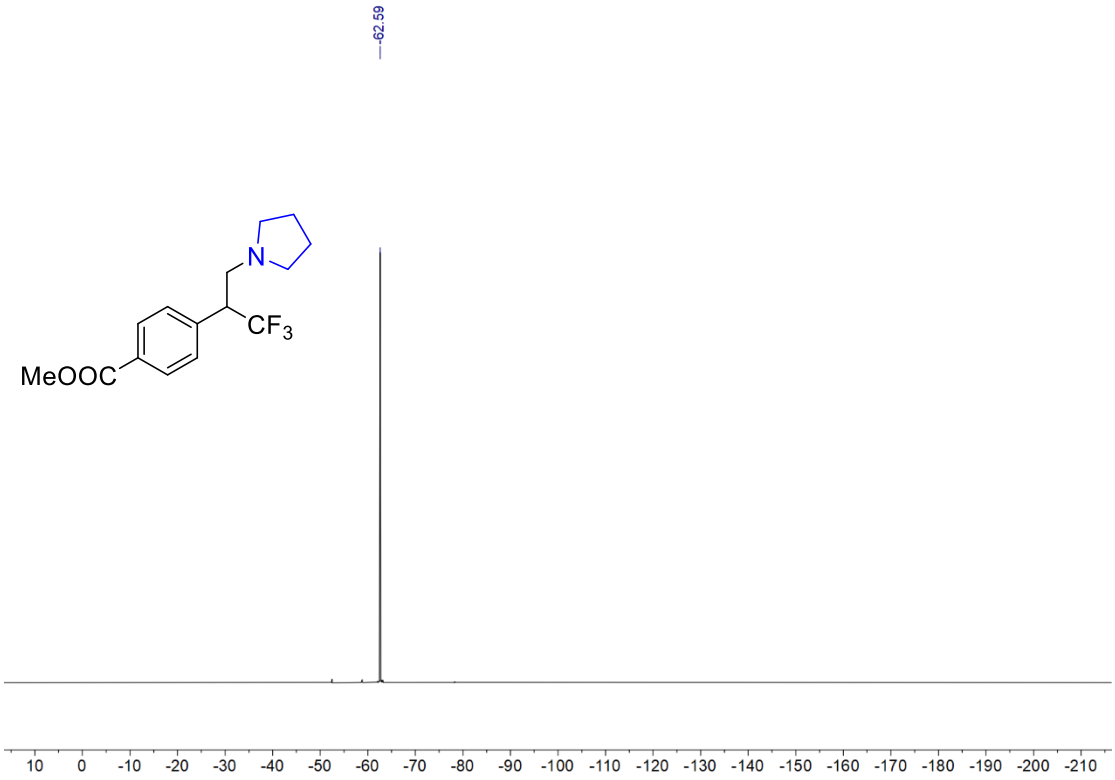

166.42
142.49
140.12
130.09
129.85
129.76
128.67
128.62
127.95
126.09
126.02
124.23
52.62
49.62
49.46
49.30
49.13
48.89
48.23
40.43
40.30
40.16
40.02
39.88
39.74
39.60
33.16
31.47
N
Ph
CF3
MeOOC
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-66.72
N
Ph
CF3
MeOOC
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210

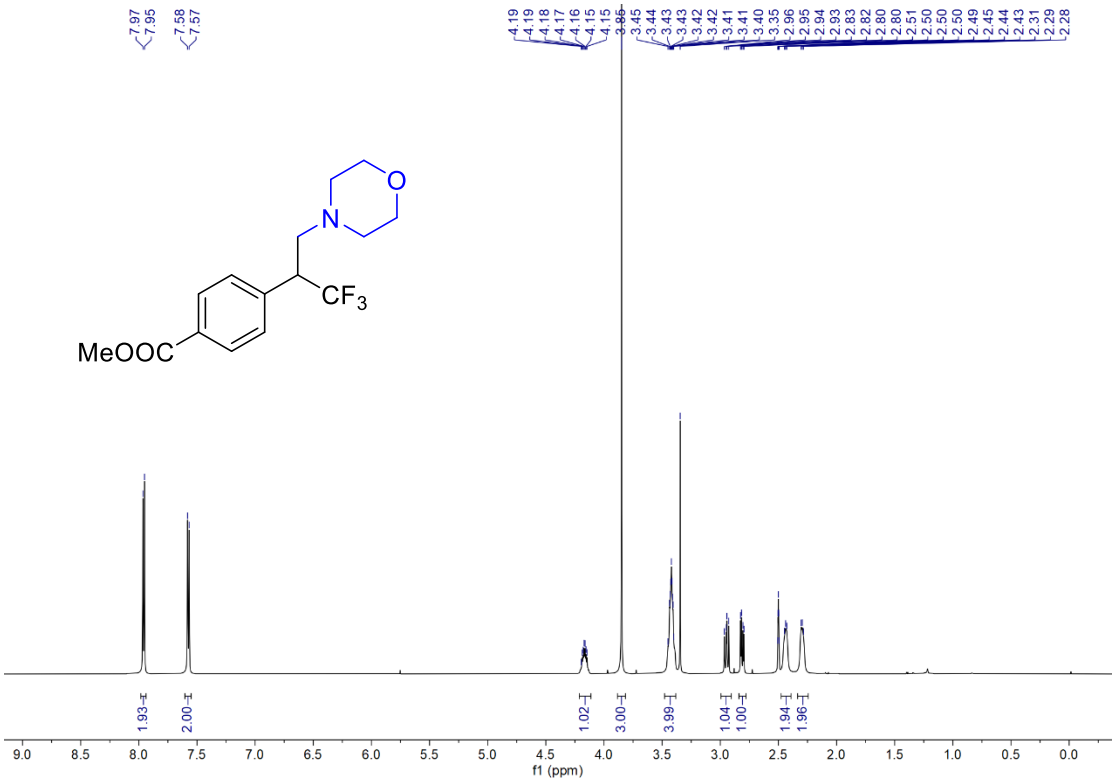
4-(1,1,1-trifluoro-3-(pyrrolidin-1-yl)propan-2-yl)phenyl acetate (**5s**)

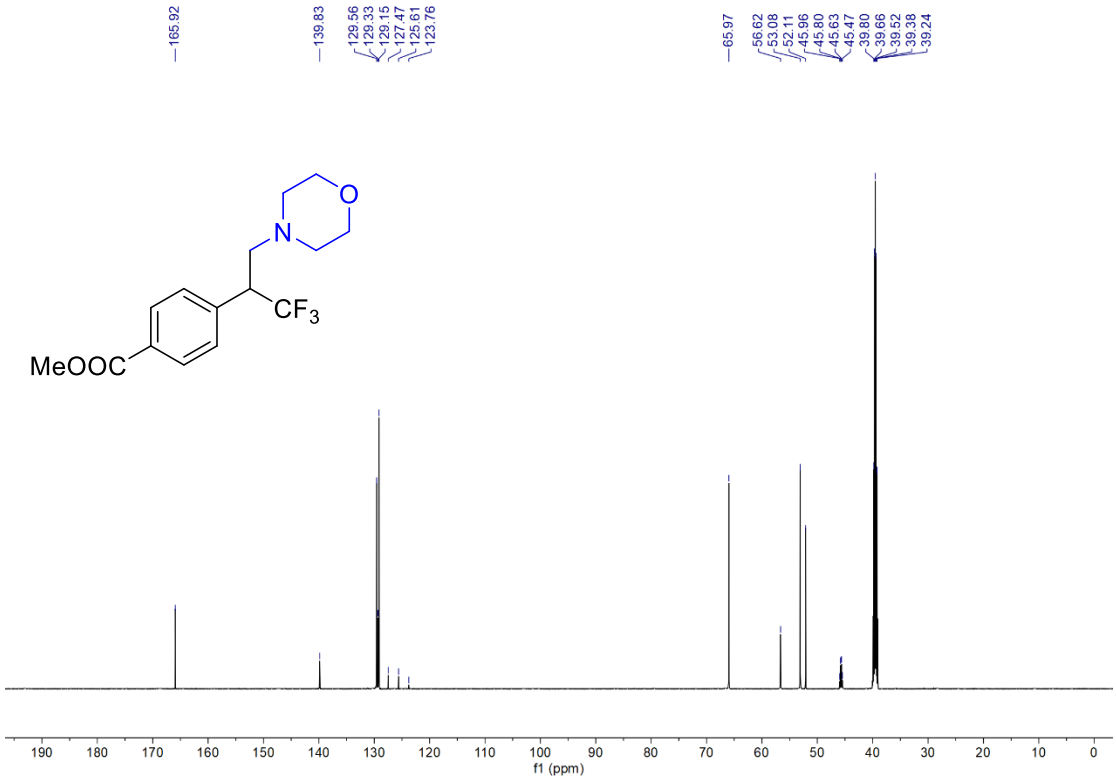


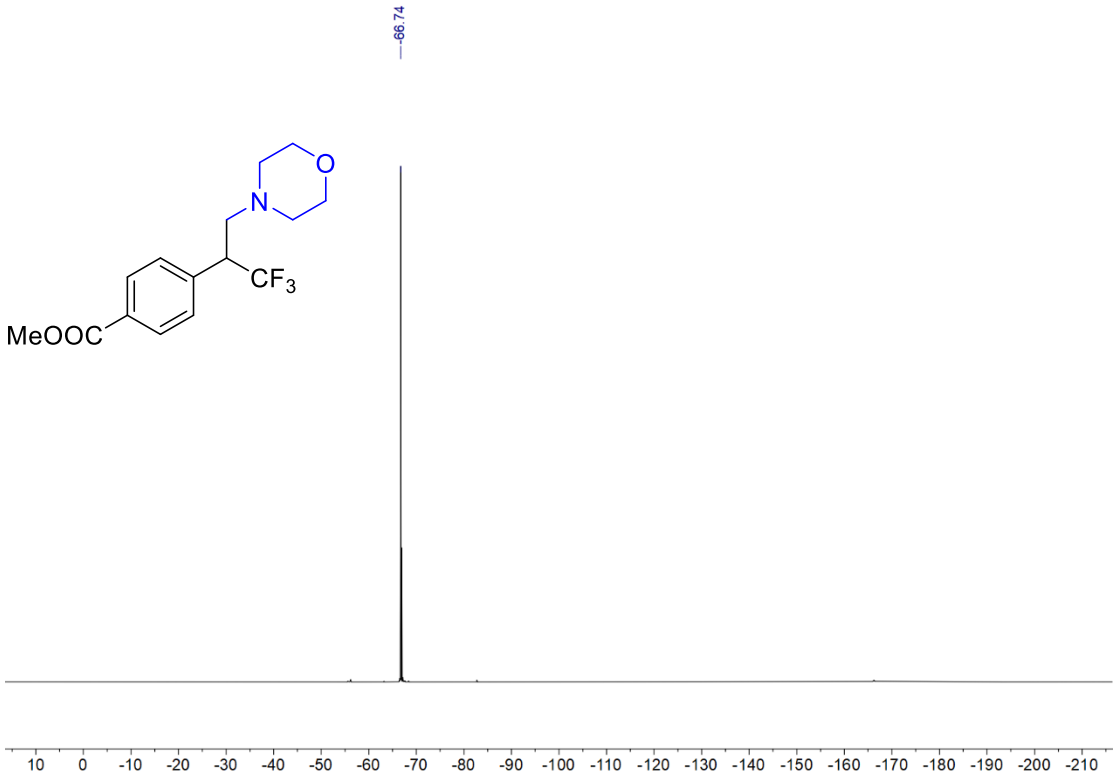




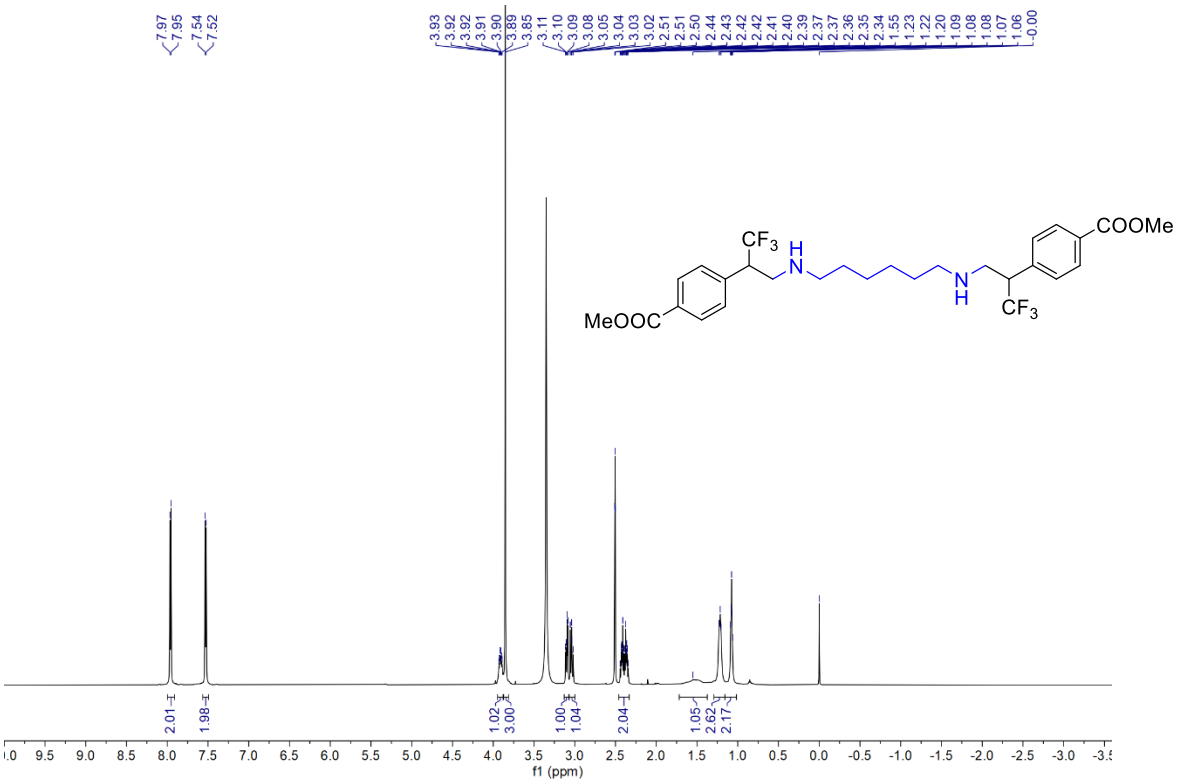
methyl 4-(1,1,1-trifluoro-3-morpholinopropan-2-yl)benzoate (**5t**)

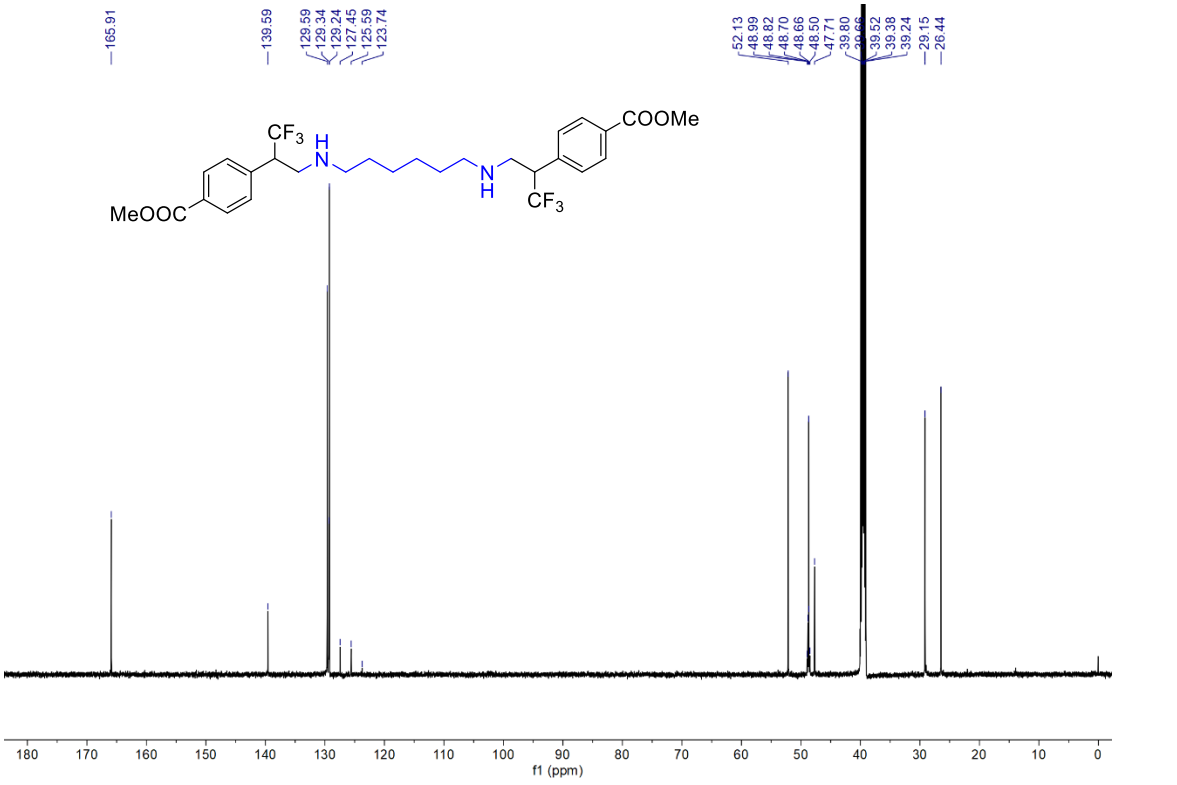


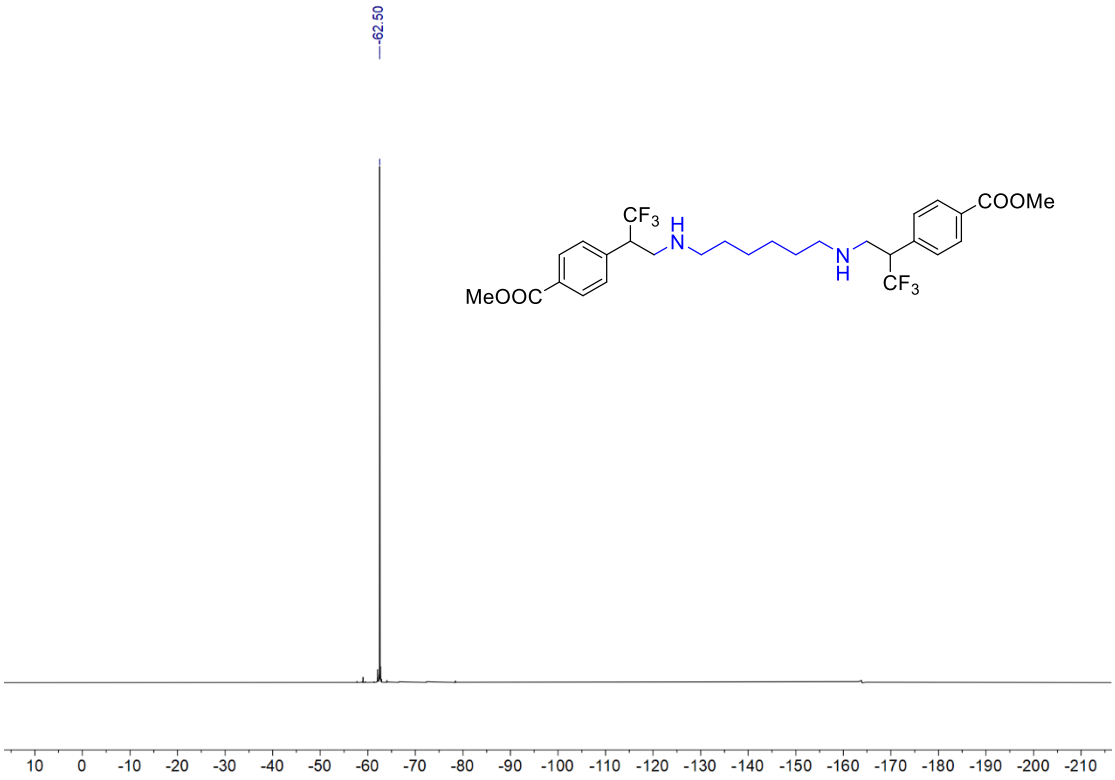

165.92
139.83
129.56
129.33
129.15
127.47
125.61
123.76
65.97
56.62
53.08
52.11
45.96
45.80
45.63
45.47
39.80
39.66
39.52
39.38
39.24
O
N
CF3
MeOOC
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-66.74
O
N
CF3
MeOOC
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210

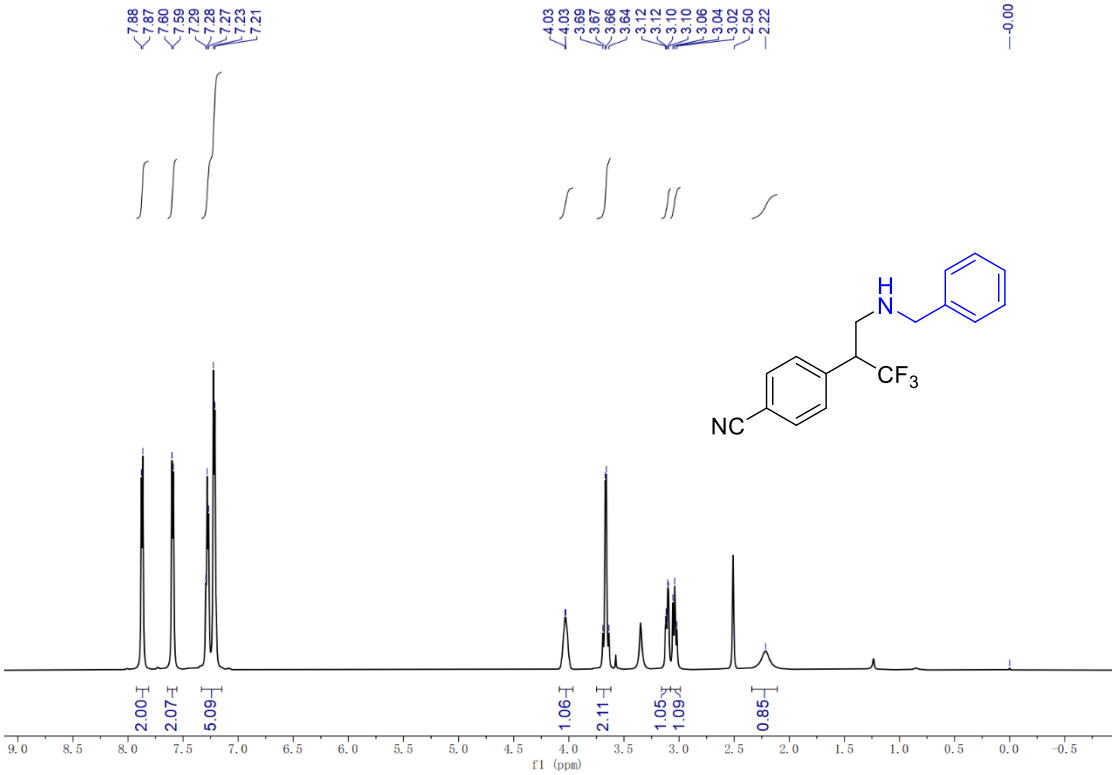
dimethyl 4,4'-((hexane-1,6-diylbis(azanediyl))bis(3,3,3-trifluoropropane-1,2-diyl))dibenzoate (**5u**)

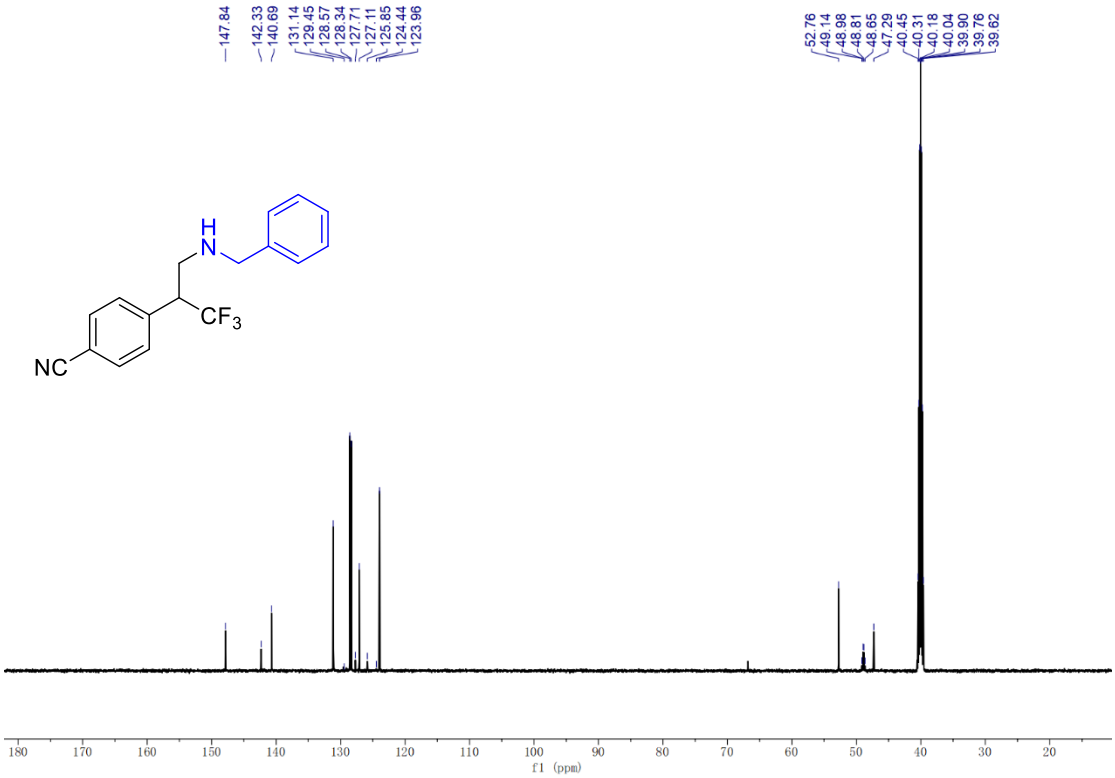


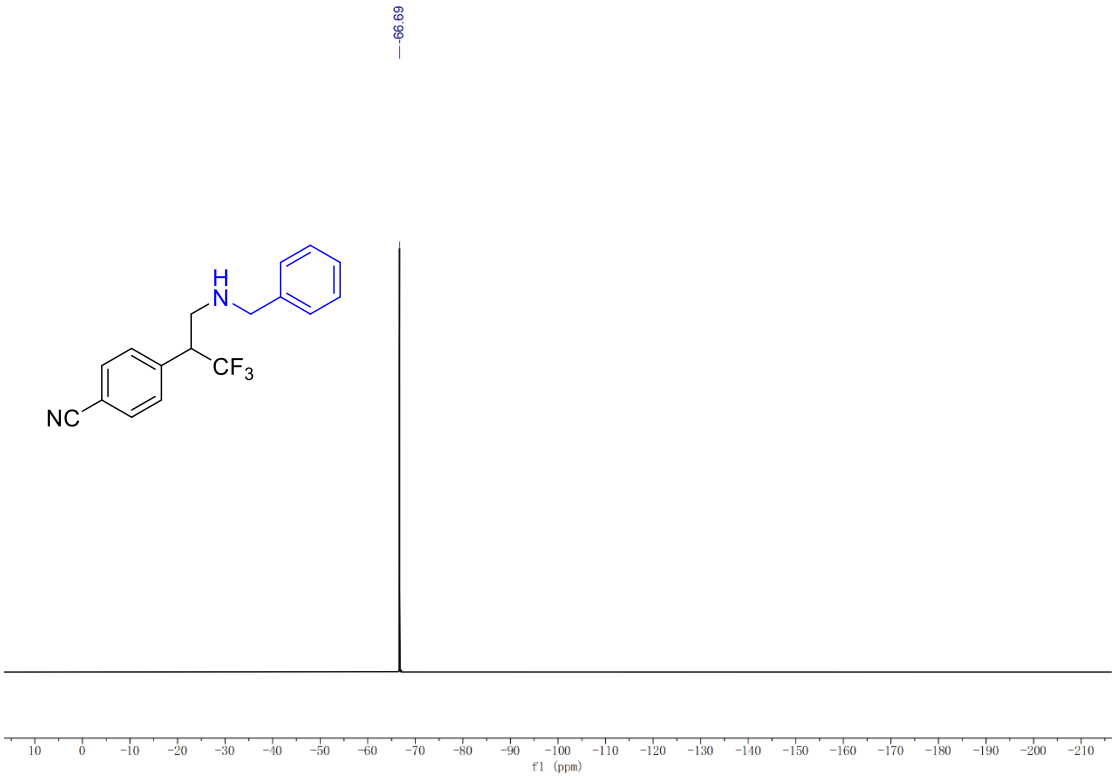




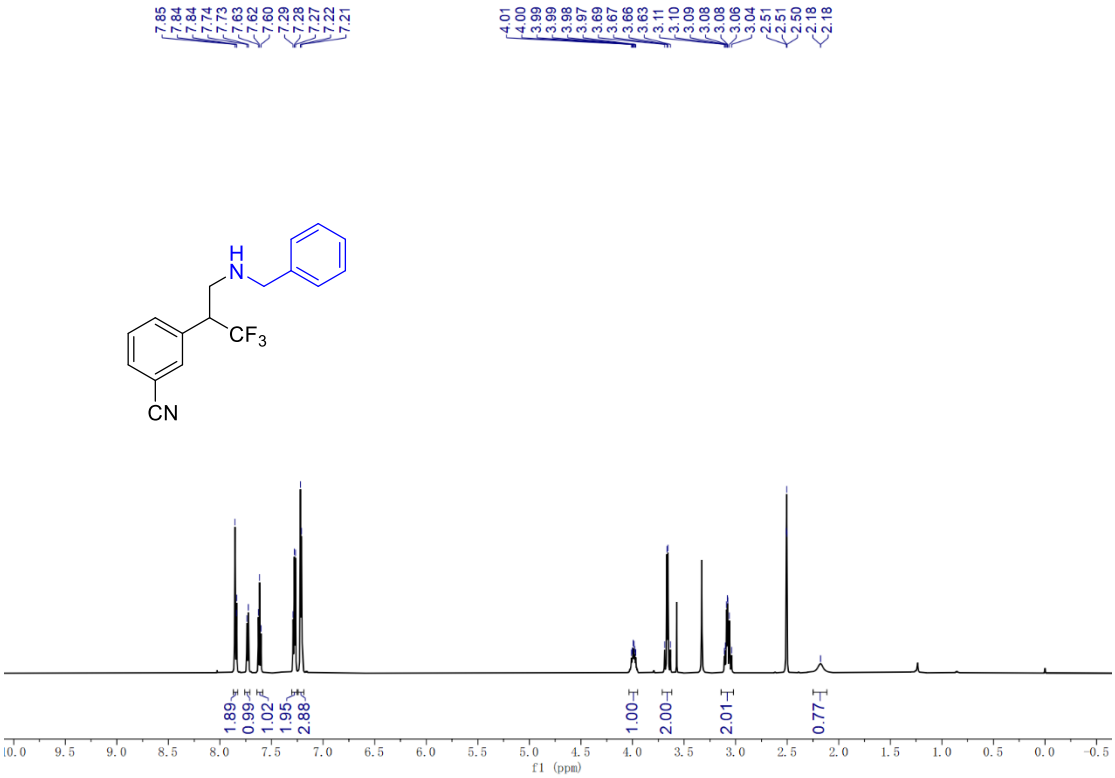
4-(3-(benzylamino)-1,1,1-trifluoropropan-2-yl)benzonitrile (**6a**)

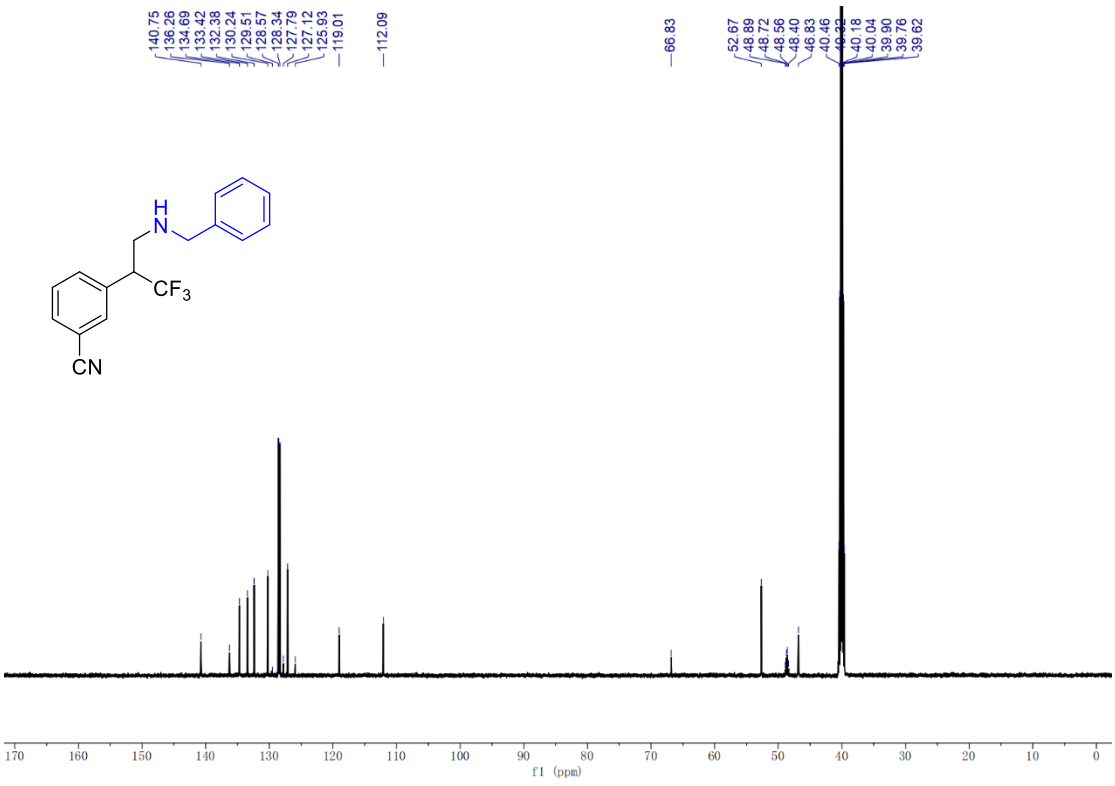


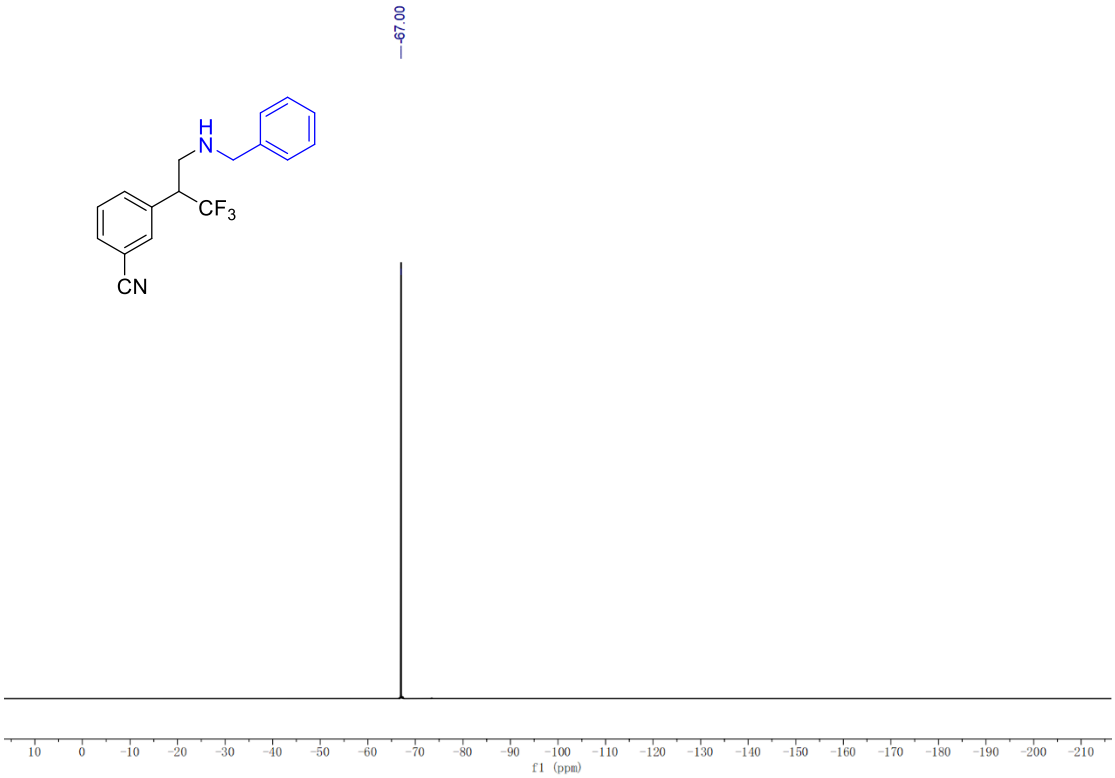

147.84
142.33
140.69
131.14
129.45
128.57
128.34
127.71
127.11
125.85
124.44
123.96
52.76
49.14
48.98
48.81
48.65
47.29
40.45
40.31
40.18
40.04
39.90
39.76
39.62
H
N
CF3
NC
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
f1 (ppm)


-66.69
H
N
CF3
NC
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

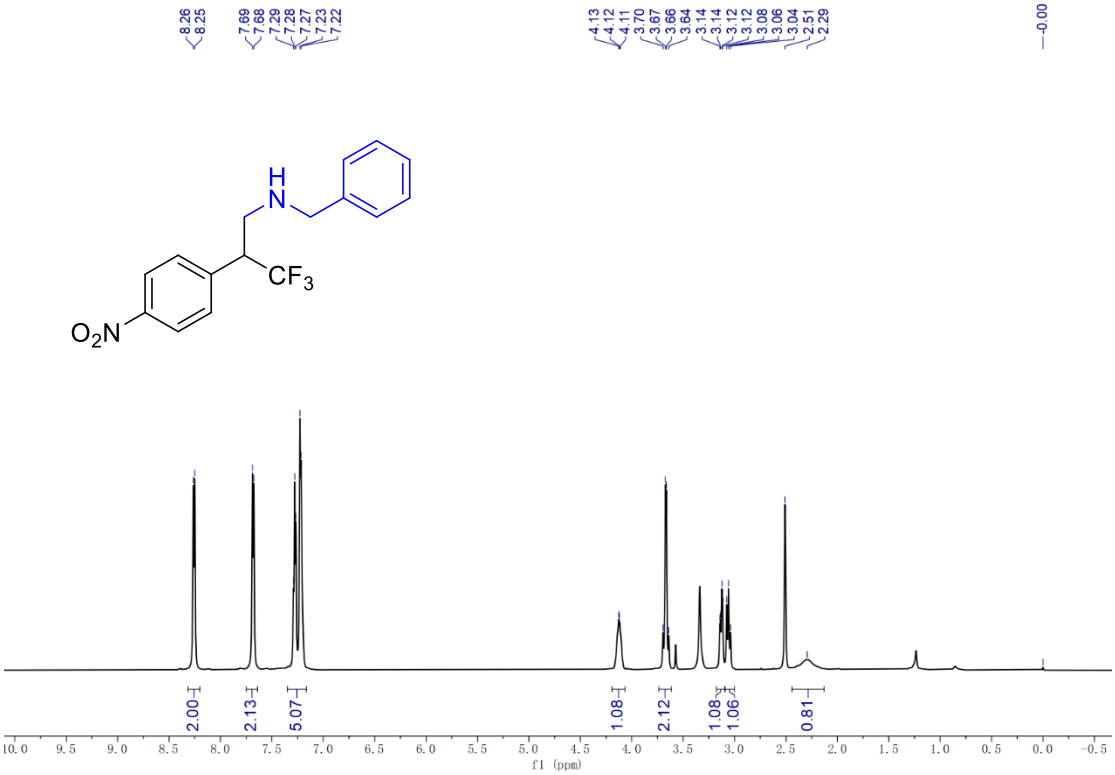
3-(3-(benzylamino)-1,1,1-trifluoropropan-2-yl)benzonitrile (**6b**)

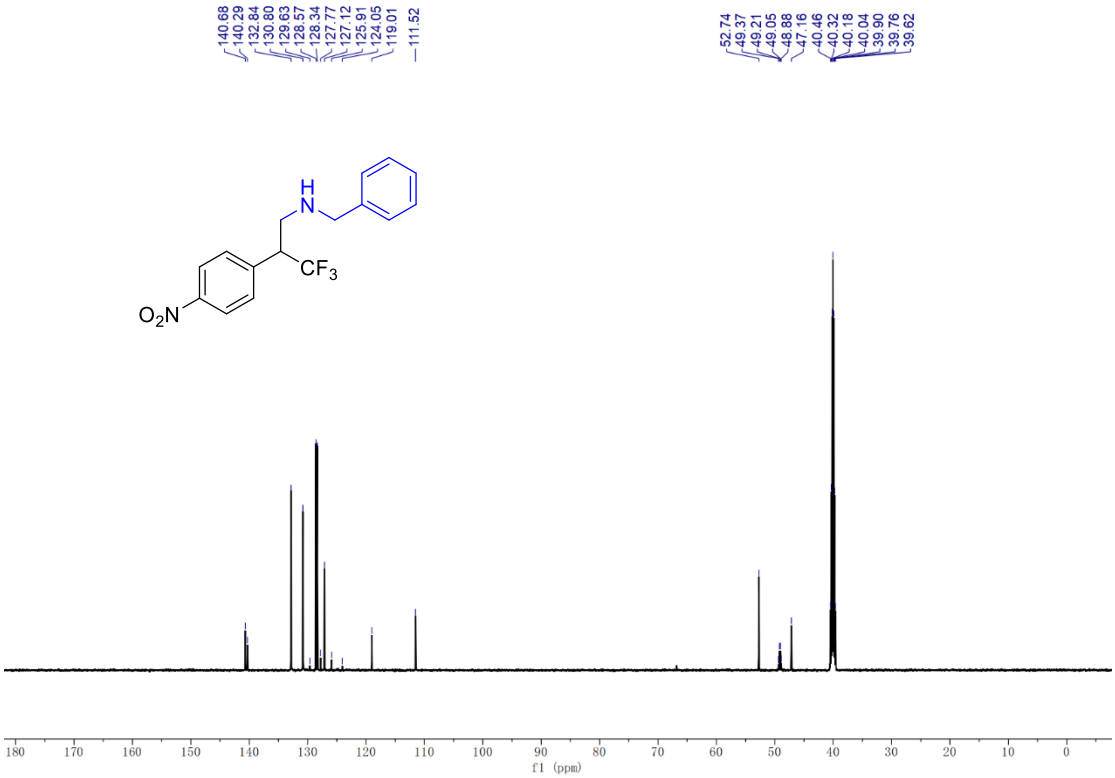


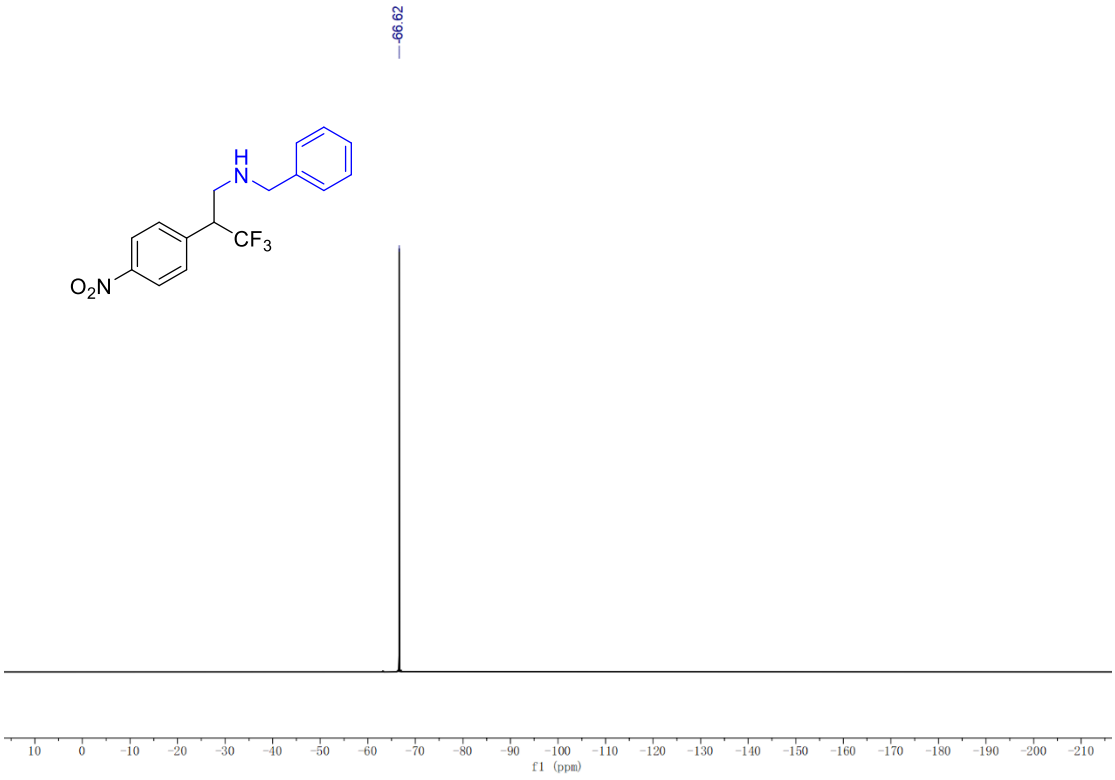




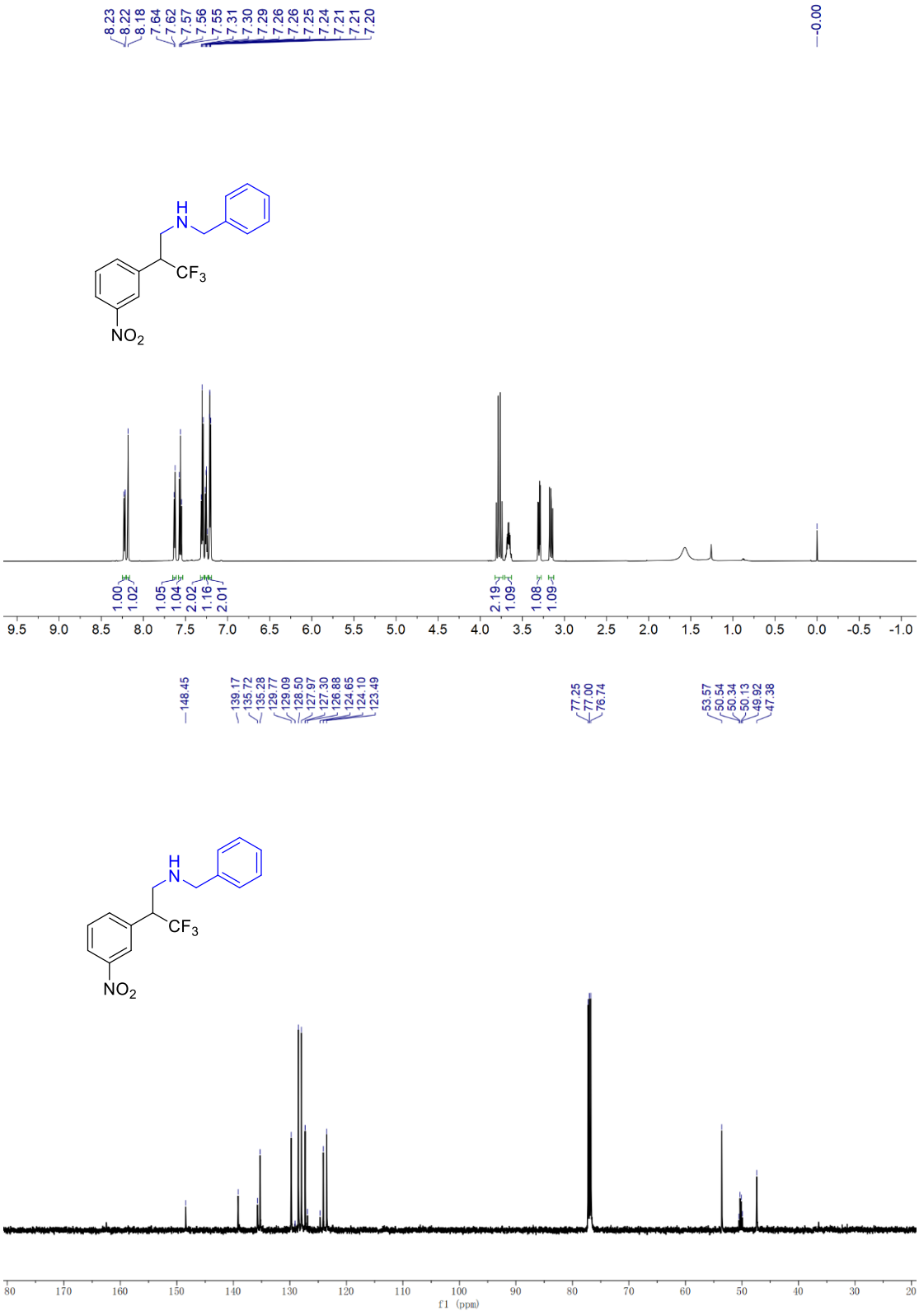
N-benzyl-3,3,3-trifluoro-2-(4-nitrophenyl)propan-1-amine (**6c**)

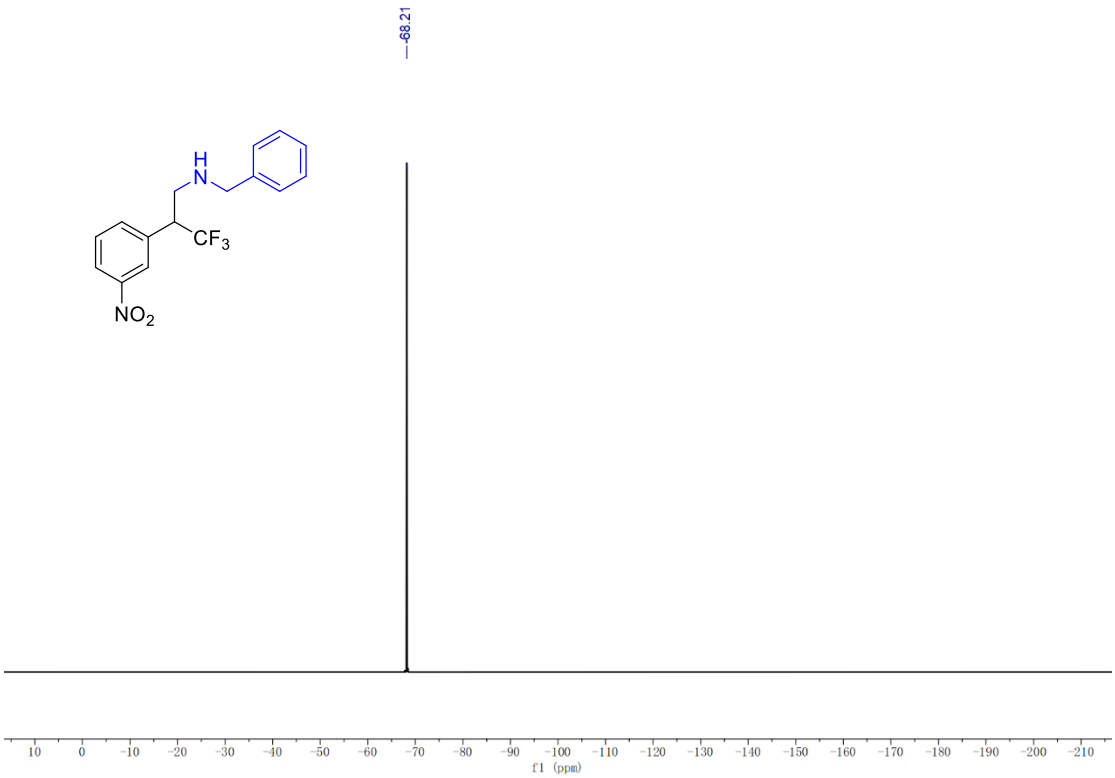



140.68
140.29
132.84
130.80
129.63
128.57
128.34
127.77
127.12
125.91
124.05
119.01
111.52
52.74
49.37
49.21
49.05
48.88
47.16
40.46
40.32
40.18
40.04
39.90
39.76
39.62
H
N
CF3
O2N
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

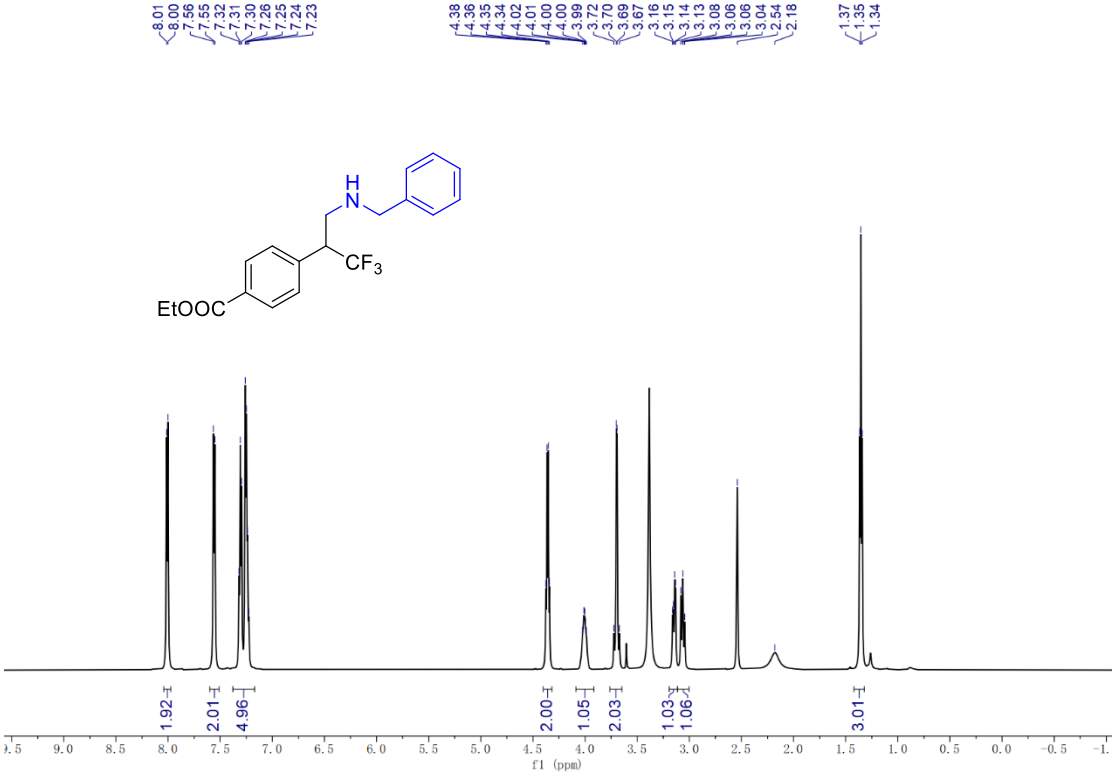

-66.62
H
N
CF3
O2N
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

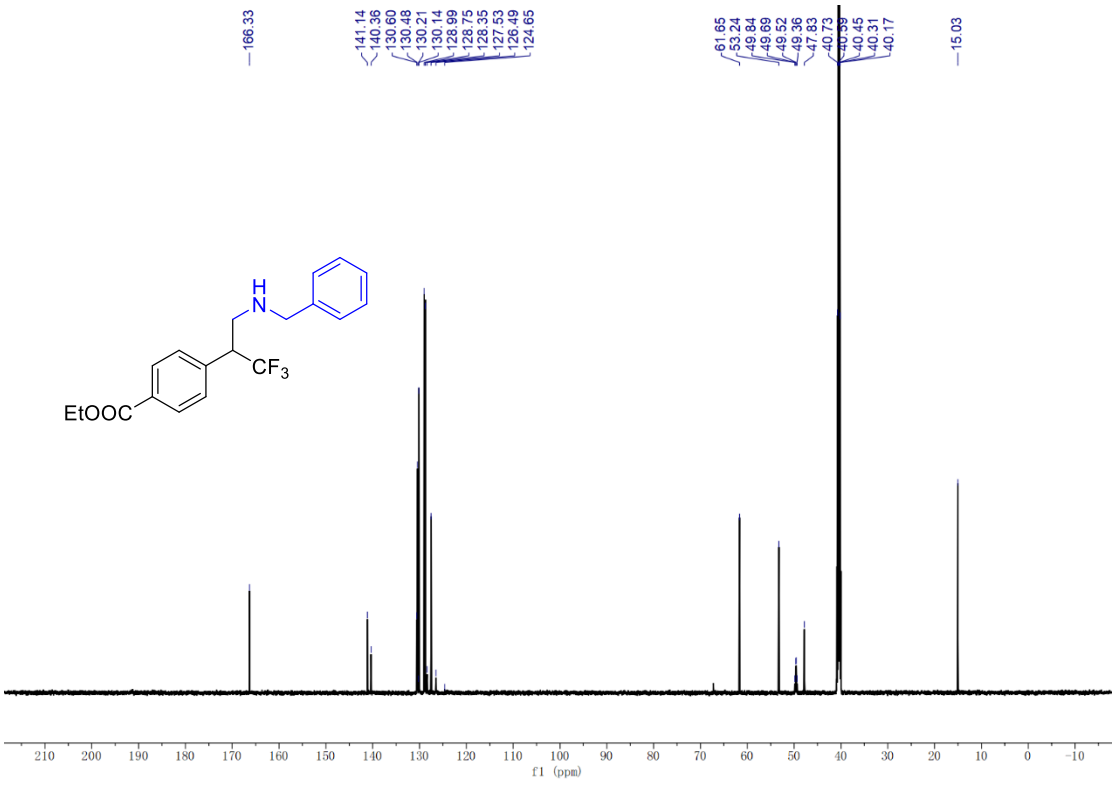
N-benzyl-3,3,3-trifluoro-2-(3-nitrophenyl)propan-1-amine (**6d**)

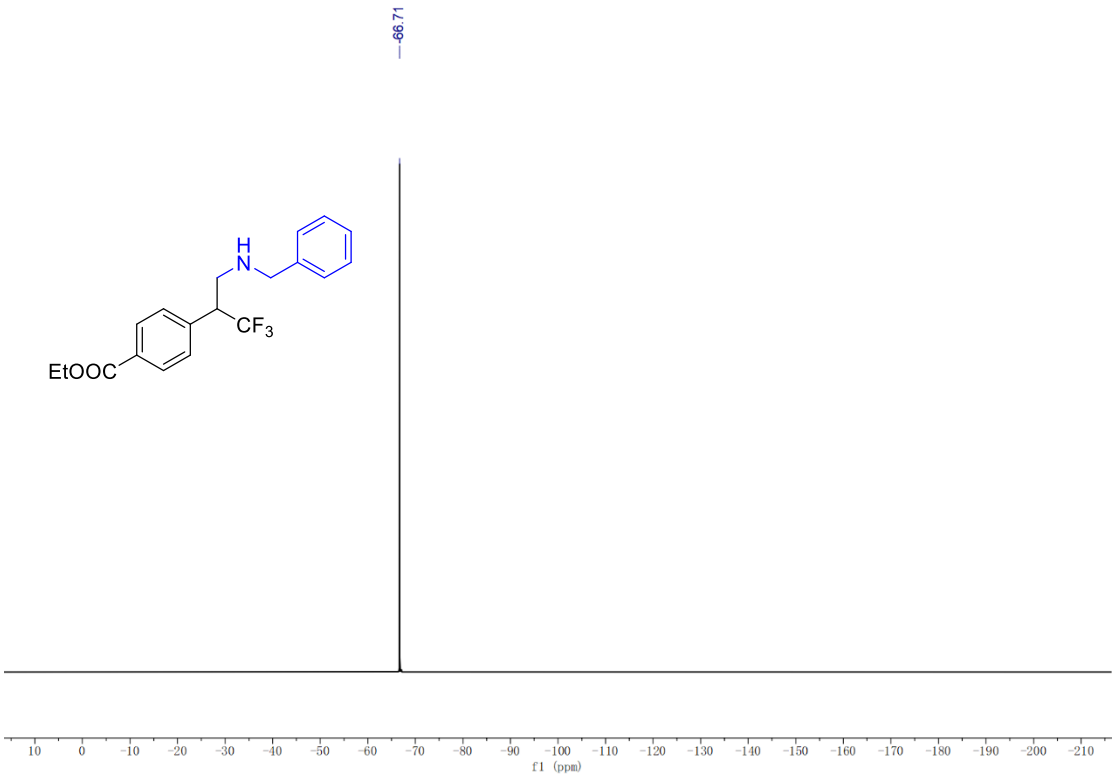




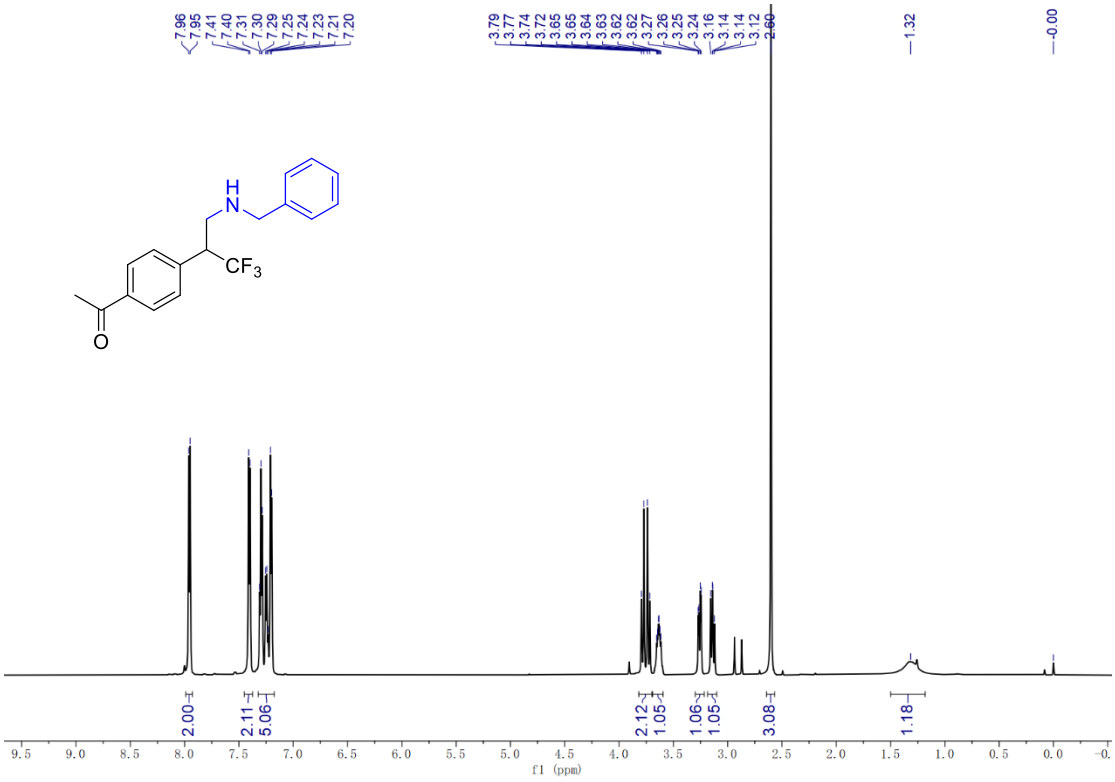
ethyl 4-(3-(benzylamino)-1,1,1-trifluoropropan-2-yl)benzoate (**6e**)

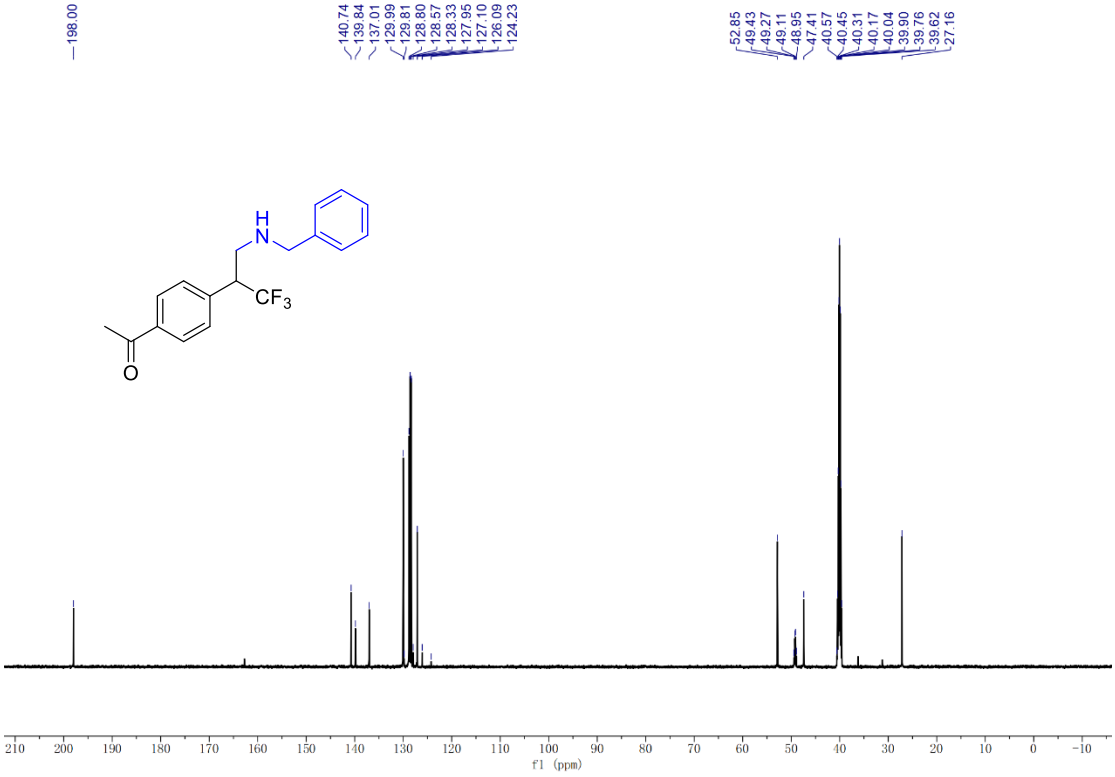


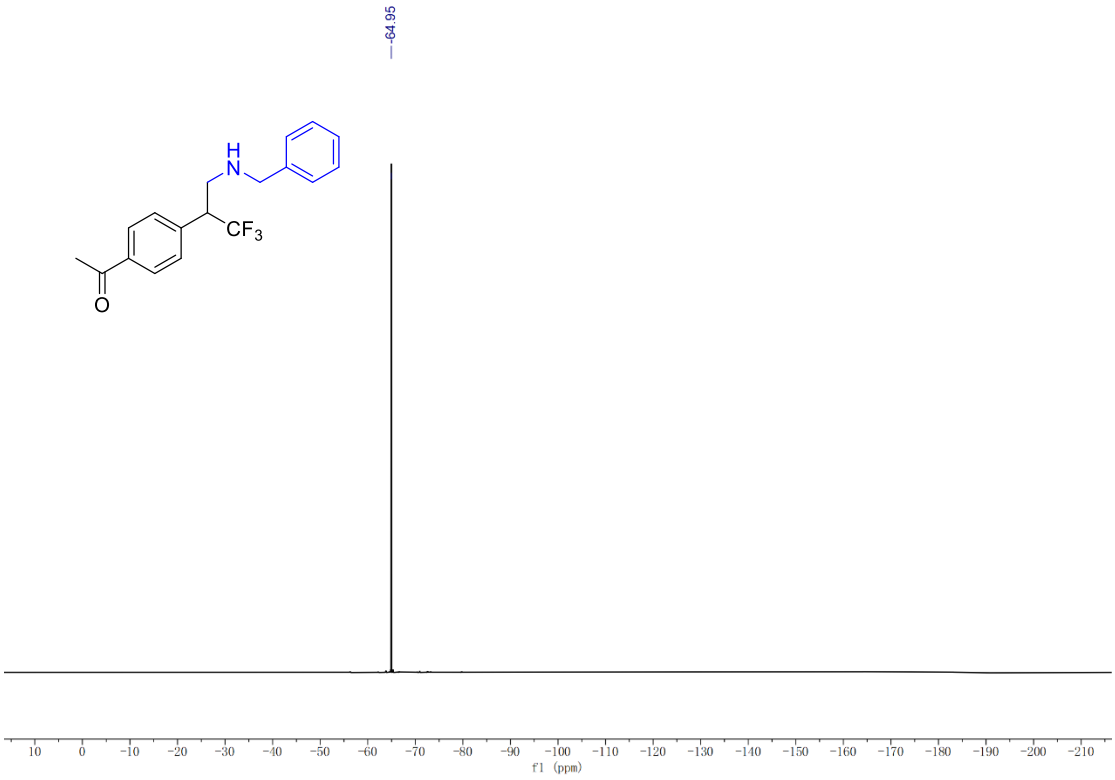

166.33
141.14
140.36
130.60
130.48
130.21
130.14
128.99
128.75
128.35
127.53
126.49
124.65
61.65
53.24
49.84
49.69
49.52
49.36
47.83
40.73
40.59
40.45
40.31
40.17
15.03
H
N
CF3
EtOOC
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


-66.71
H
N
CF3
EtOOC
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

1-(4-(3-(benzylamino)-1,1,1-trifluoropropan-2-yl)phenyl)ethan-1-one (**6f**)







1. P. Fan, C. Zhang, Y. Lan, Z. Lin, L. Zhang and C. Wang, *Chem. Commun.*, 2019, **55**, 12691.
2. Y. X. Chen, Z. J. Wang, J. A. Xiao, K. Chen, H. Y. Xiang and H. Yang, *Org. Lett.*, 2021, **23**, 6558.
3. X. Lu, X. X. Wang, T. J. Gong, J. J. Pi, S. J. He and Y. Fu, *Chem. Sci.*, 2019, **10**, 809.
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