Electronic Supplementary Material (ESI) for Green Chemistry.

Supporting Information

Metal-Free Photocatalytic Trifluoromethylative Pyridylation of Unactivated Alkenes

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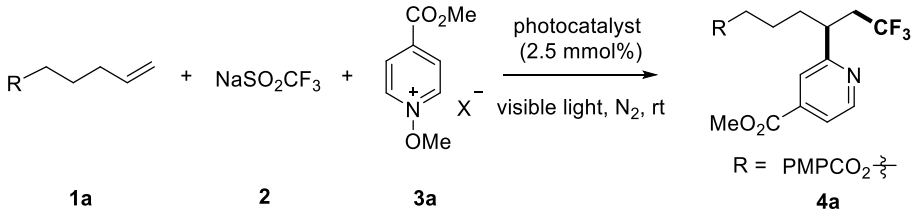
I. General Methods and Materials.

Unless stated otherwise, reactions were performed in flame-dried glassware. Analytical thin layer chromatography (TLC) was performed on precoated silica gel 60 F^{254} plates and visualization on TLC was achieved by UV light (254 and 365 nm). Flash column chromatography was undertaken on silica gel (400-630 mesh). ^{1}H NMR was recorded on 400 MHz or 600 MHz and chemical shifts were quoted in parts per million (ppm) referenced to the appropriate solvent peak. The following abbreviations were used to describe peak splitting patterns when appropriate: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet, td = triplet of doublet, ddd = doublet of doublet of doublet. Coupling constants, *J*, were reported in hertz unit (Hz). ^{13}C NMR was recorded on 100 MHz or 150 MHz and was fully decoupled by broad band proton decoupling. Chemical shifts of ^{13}C NMR were reported in ppm referenced to the centerline of a triplet at 77.0 ppm of $CDCl_3$. ^{19}F NMR was recorded on 376 MHz or 564 MHz and was fully coupled by broad band proton decoupling. High-resolution mass spectra were obtained by using EI or FAB method from Korea Basic Science Institute (Daegu), and ESI method from KAIST Basic Science Institute. Single crystal x-ray diffraction experiment with synchrotron radiation were performed at the BL2D-SMC in Pohang Accelerator Laboratory. Commercial grade reagents and solvents were used without further purification except as indicated below.

II. Optimization of the reaction conditions

Table S1[a]



Entry	Photocatalyst (2.5 mmol %)	X	Solvent	Yield[b]
1	$Ru(bpy)_3PF_6$	BF_4^-	MeCN	30%
2	$Ir(dF(CF_3)ppy_2(bpy)PF_6$	BF_4^-	MeCN	35%
3	$Ir(dF(CF_3)ppy_2(dtbpy)PF_6$	BF_4^-	MeCN	39%
4	*fac*-$Ir(ppy)_3$	BF_4^-	MeCN	44%
5	$Ir(F\text{-}ppy)_3$	BF_4^-	MeCN	59%
6	$Ir(F\text{-}ppy)_3$	BF_4^-	DMSO	79%
7	Mes-Acr+	BF_4^-	DMSO	10%

8	Eosin Y	BF_4^-	DMSO	84%
9	Eosin Y	BF_4^-	MeCN	40%
10	Eosin Y	BF_4^-	DMF	39%
11	Eosin Y	BF_4^-	DCM	29
12	Eosin Y	BF_4^-	toluene	trace
13	Eosin Y	BF_4^-	dioxane	30%
14	Eosin Y	BF_4^-	MeOH	30%
15[c]	Eosin Y	BF_4^-	DMSO	74%
16[d]	Eosin Y	BF_4^-	DMSO	11%
17[e]	Eosin Y	BF_4^-	DMSO	68%
18[f]	Eosin Y	BF_4^-	DMSO	78%
19[f]	Eosin Y	$CH_3OSO_3^-$	DMSO	77%
20[f]	Eosin Y	OTf^-	DMSO	79%
21	—	BF_4^-	DMSO	< 5%
22[g]	Eosin Y	BF_4^-	DMSO	0%
23[h]	Eosin Y	BF_4^-	DMSO	< 5%

[a] Unless otherwise noted, reactions were performed with mixtures of **1** (0.2 mmol), **2** (0.3 mmol), **3a** (0.4 mmol), photocatalyst (2.5 mol%) in solvent (2.0 mL) at rt under irradiation by blue LEDs for 4 h. [b] The isolated yields of products. [c] Under irradiation by white LED. [d] Under irradiation by red LEDs. [e] Under irradiation by 30 W CFL. [f] Under irradiation by green LED (7.5 W) for 8 h. [g] The reaction was carried out in the dark. [h] TEMPO (1.5 equiv) was added.

40W Kessil blue LED (25% intensity, 456nm): Eosin Y as a photocatalyst

time	15 min	30 min	60 min	2.0 h	4.0 h	6.0 h	8.0 h
yield	18%	32%	49%	68%	84%	85%	83%

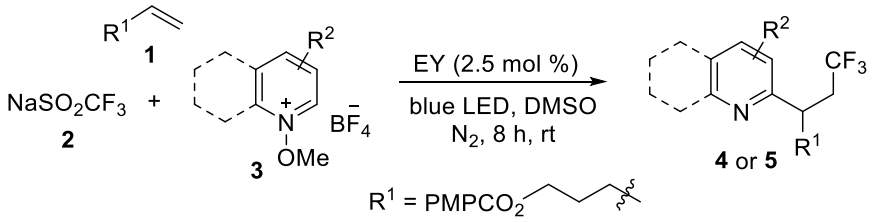
7.5 w blue LED: Eosin Y as a photocatalyst:

time	15 min	30 min	60 min	2.0 h	4.0 h	6.0 h	8.0 h
yield	11%	21%	36%	56%	72%	77%	79%

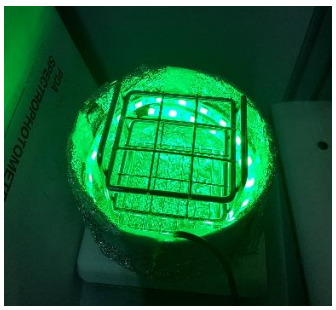
7.5 w green LED: Eosin Y as a photocatalyst:

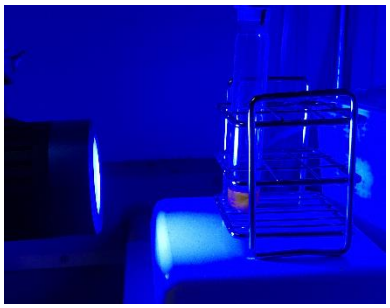
time	15 min	30 min	60 min	2.0 h	4.0 h	6.0 h	8.0 h
yield	4%	11%	21%	50%	62%	71%	78%

III. General experimental procedure



An oven-dried tube was charged with alkene **1** (0.2 mmol), N-methoxyheteroarenium salts **3** (0.4 mmol), CF_3SO_2Na (0.3 mmol), and Eosin Y (0.005 mmol). The tube was evacuated and backfilled with nitrogen (repeated three times). Then, dimethyl sulfoxide (2.0 mL) was added into the reaction via syringe. 7.5 W Green LEDs, or 40W Kessil blue LED with 25% intensity were used as light source. The reaction mixture was extracted by ethyl acetate, the combined organic layers were washed with saturated brine, dried over Na_2SO_4, concentrated in vacuumand purified by flash column chromatography on silica gel (hexanes/ethyl acetate or DCM/MeOH) to afford final the product **4**.





IV. Control Experiments

Quantum yield measurements (Green LED):

Determination of the light intensity at 515 nm

According to the procedure of Yoon[S1] the photon flux of the LED (λ_{max} = 515 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 H_2SO_4 (10 mL of a 0.05 M solution). A buffered solution of 1,10-phenanthroline was prepared by dissolving 1,10-phenanthroline (5.0 mg) and sodium acetate (1.13 g) in H_2SO_4 (5.0 mL of a 0.5 M solution). 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 90 seconds at λ_{max} = 515 nm. After irradiation, the phenanthroline solution (0.35 mL) was added to the cuvette and the mixture was allowed to stir in the dark for 1 h 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. Conversion was calculated using eq 1.

	Non-irrad	Irrad 01	Irrad 02	Irrad 03
$A_{510\ nm}$	0.3	2.992	3.096	3.175
		Average $A_{510\ nm}$ of irradiation samples		3.088

$$\text{mol of } Fe^{2+} = \frac{V \cdot \Delta A_{510\ nm}}{l \cdot \epsilon} = \frac{(0.00235\ L) \cdot (2.788)}{(1.00\ cm) \cdot (11{,}100 \frac{L}{mol} \cdot cm)} = 5.90 \times 10^{-7}\ mol \quad (1)$$

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 (1.00 cm), and ε is the molar absorptivity of the ferrioxalate actinometer at 510 nm (11,100 $Lmol^{-1}cm^{-1}$).[S2] The photon flux can be calculated using eq 2.

$$\text{Photon flux} = \frac{mol\ of\ Fe^{2+}}{\emptyset \cdot t \cdot f} = \frac{5.90 \times 10^{-7}\ mol}{(0.93) \cdot (90\ s) \cdot (0.489)} = 1.44 \times 10^{-8}\ einstein/s \quad (2)$$

Where Φ is the quantum yield for the ferrioxalate actinometer (0.93 at λ = 515 nm)[S3] is the irradiation time (90 s), and f is the fraction of light absorbed at 515 nm by the ferrioxalate actinometer. This value is calculated using eq 3 where $A_{515\ nm}$ is the absorbance of the ferrioxalate solution at 515 nm. An absorption spectrum gave an $A_{515\ nm}$ value of 0.489, indicating that the fraction of absorbed light (f) is 0.489.

$$f = 1 - 10^{-A_{515\ nm}} \quad (3)$$

The photon flux was thus calculated (average of three experiments) to be 1.44×10^{-8} einsteins s^{-1}

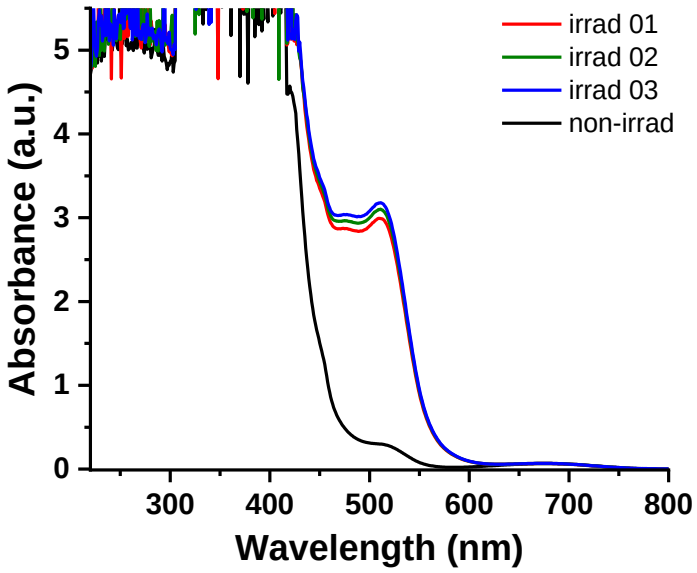
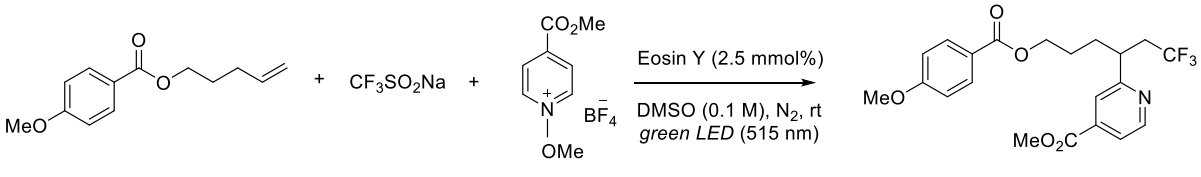


Figure S2. Absorption spectra of three irradiation experiments and non-irradiation experiment

Determination of the reaction quantum yield.



1a (0.2 mmol) **2** (1.5 equiv.) **3a** (2.0 equiv.) **4a**

The reaction mixture was stirred and irradiated by green LED (λ_{max} = 515 nm) for 3600 s. The yield of product was determined by ^{19}F NMR analysis using α,α,α-Trifluorotoluene as an internal standard. The yield of **4a** was determined to be 21% (0.042×10^{-3} mol of **4a**). The reaction quantum yield (Φ) was determined using eq 4 where the photon flux is 1.44×10^{-8} einsteins s^{-1} (determined by actinometry as described above), t is the reaction time (3600 s) and f is the fraction of incident light absorbed by the catalyst, determined using eq 3. An absorption spectrum of the catalyst (0.0025 M) gave an absorbance value of 3.817 at 515 nm (figure 3), indicating that the fraction of light absorbed by the photocatalyst (f) is 0.999.

$$\Phi = \frac{mol\ of\ product}{flux \cdot t \cdot f} \qquad (4)$$

$$60\ \text{min}: \ \Phi = \frac{0.042 \times 10^{-3}\ mol}{1.44 \times 10^{-8}\ einstein\ s^{-1} \cdot 3600\ s \cdot 0.999} = 0.81$$

The reaction quantum yield (Φ) was calculated to be 0.81

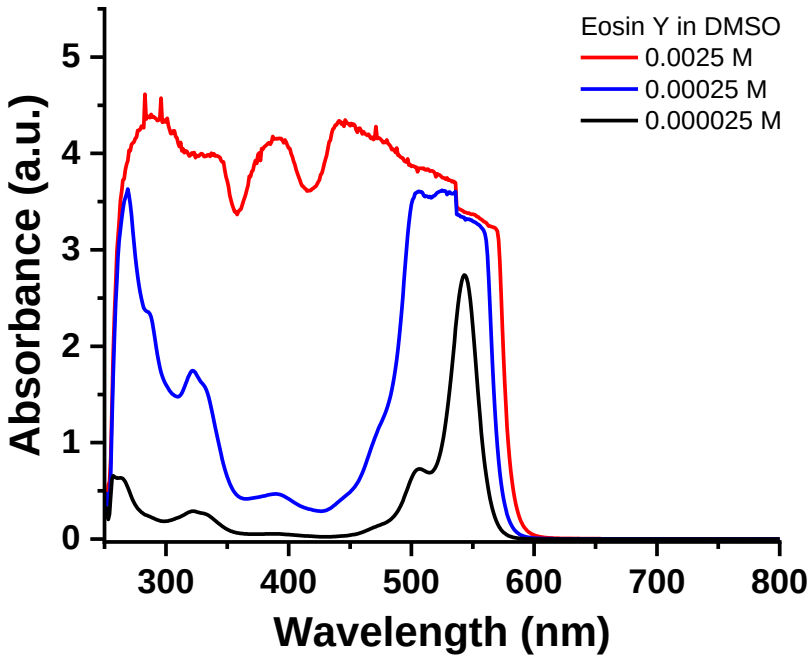


Figure S3. Absorption spectra of solution of eosin Y in DMSO

Quantum yield measurements (Blue LED):

Determination of the light intensity at 456 nm

Kessil LED (λ_{max} = 456 nm) was used with 25% intensity for measurement of quantum yield.

According to the procedure of Yoon [S1] the photon flux of the LED (λ_{max} = 456 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 H_2SO_4 (10 mL of a 0.05 M solution). A buffered solution of 1,10-phenanthroline was prepared by dissolving 1,10-phenanthroline (5.0 mg) and sodium acetate (1.13 g) in H_2SO_4 (5.0 mL of a 0.5 M solution). 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 90 seconds at λ_{max} = 456 nm. After irradiation, the phenanthroline solution (0.35 mL) was added to the cuvette and the mixture was allowed to stir in the dark for 1 h 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. Conversion was calculated using eq 1.

	Non-irrad	Irrad 01	Irrad 02	Irrad 03
$A_{510\ nm}$	1.195	2.494	2.500	2.476

	Average $A_{510\ nm}$ of irradiation samples	2.49

$$\text{mol of } Fe^{2+} = \frac{V \cdot \Delta A_{510\ nm}}{l \cdot \epsilon} = \frac{(0.00235\ L) \cdot (1.295)}{(1.00\ cm) \cdot (11{,}100 \frac{L}{mol} \cdot cm)} = 2.74 \times 10^{-7}\ mol \quad (1)$$

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 (1.00 cm), and ε is the molar absorptivity of the ferrioxalate actinometer at 510 nm (11,100 $Lmol^{-1}cm^{-1}$).[S2] The photon flux can be calculated using eq 2.

$$\text{Photon flux} = \frac{mol\ of\ Fe^{2+}}{\emptyset \cdot t \cdot f} = \frac{2.74 \times 10^{-7}\ mol}{(0.84) \cdot (90\ s) \cdot (0.998)} = 3.63 \times 10^{-9}\ einstein/s \quad (2)$$

Where Φ is the quantum yield for the ferrioxalate actinometer (0.84 at λ = 456 nm)[S3] is the irradiation time (90 s), and f is the fraction of light absorbed at 456 nm by the ferrioxalate actinometer. This value is calculated using eq 3 where $A_{456\ nm}$ is the absorbance of the ferrioxalate solution at 456 nm. An absorption spectrum gave an $A_{456\ nm}$ value of 2.742, indicating that the fraction of absorbed light (f) is 0.998.

$$f = 1 - 10^{-A_{456\ nm}} \quad (3)$$

The photon flux was thus calculated (average of three experiments) to be 3.63×10^{-9} einsteins s^{-1}

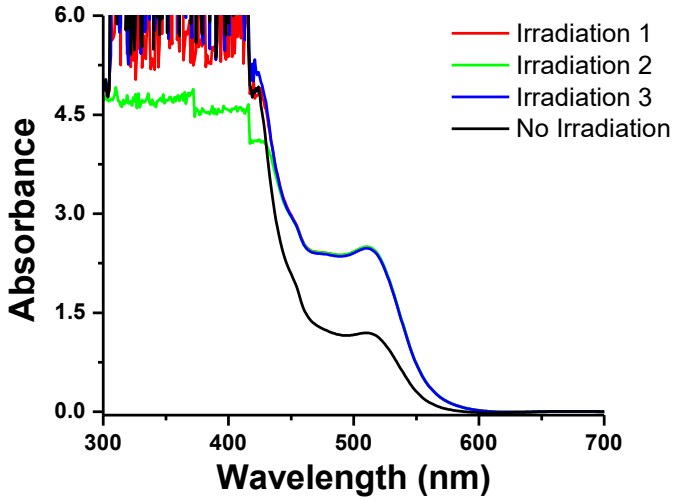
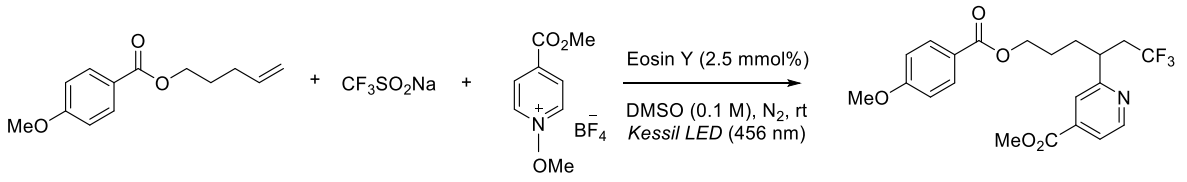


Figure S4. Absorption spectra of three irradiation experiments and non-irradiation experiment

Determination of the reaction quantum yield.



1a (0.2 mmol) **2** (1.5 equiv.) **3a** (2.0 equiv.) **4a**

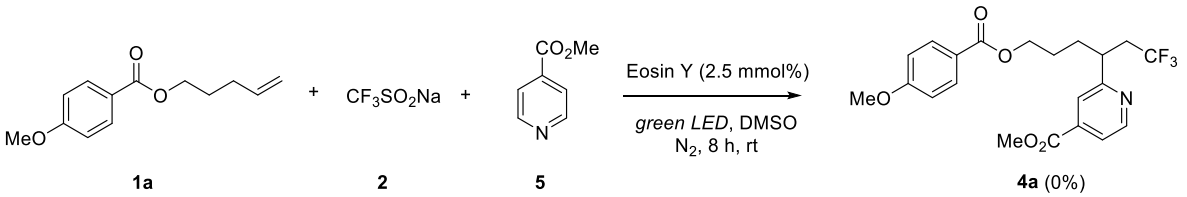
The reaction mixture was stirred and irradiated by 40W Kessil blue LED with 25% intensity (λ_{max} = 456 nm) for 3600 s. The yield of product was determined by ^{19}F NMR analysis using α,α,α-Trifluorotoluene as an internal standard. The yield of **4a** was determined to be 49% (0.098×10^{-3} mol of **4a**). The reaction quantum yield (Φ) was determined using eq 4 where the photon flux is 3.63×10^{-9} einsteins s^{-1} (determined by actinometry as described above), t is the reaction time (3600 s) and f is the fraction of incident light absorbed by the catalyst, determined using eq 3. An absorption spectrum of the catalyst (0.0025 M) gave an absorbance value of 4.219 at 456 nm (figure 3), indicating that the fraction of light absorbed by the photocatalyst (f) is 0.9999.

$$\Phi = \frac{mol\ of\ product}{flux \cdot t \cdot f} \qquad (4)$$

$$60\text{min: } \Phi = \frac{0.098 \times 10^{-3}\ mol}{3.63 \times 10^{-9}\ einstein\ s^{-1} \cdot 3600\ s \cdot 0.9999} = 7.51$$

The reaction quantum yield (Φ) was calculated to be 7.5

Pyridine 5 was used in the reaction

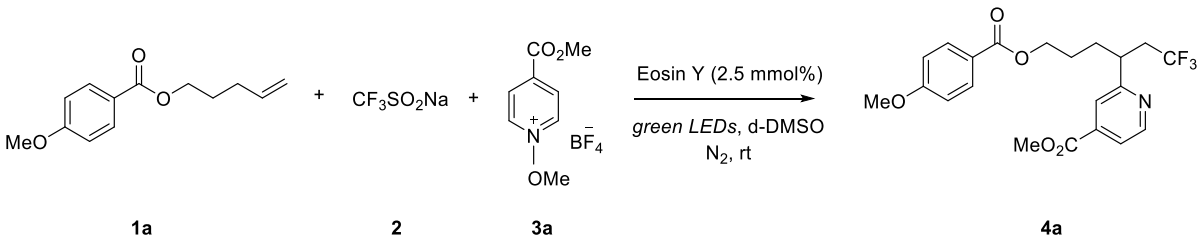


1a **2** **5** **4a** (0%)

NR: **1a** and **5** remained

An oven-dried tube was charged with alkene **1a** (0.2 mmol), CF_3SO_2Na (0.3 mmol), and Eosin Y (0.005 mmol). The tube was evacuated and backfilled with nitrogen (repeated three times). Then, pyridine **5** (0.4 mmol), and dimethyl sulfoxide (2.0 mL) was added into the reaction via syringe. The reaction mixture was stirring at room temperature under green LEDs for 8 h. After checked by TLC and NMR, no desired product was observed and starting material **1a** and **5** were fully remained.

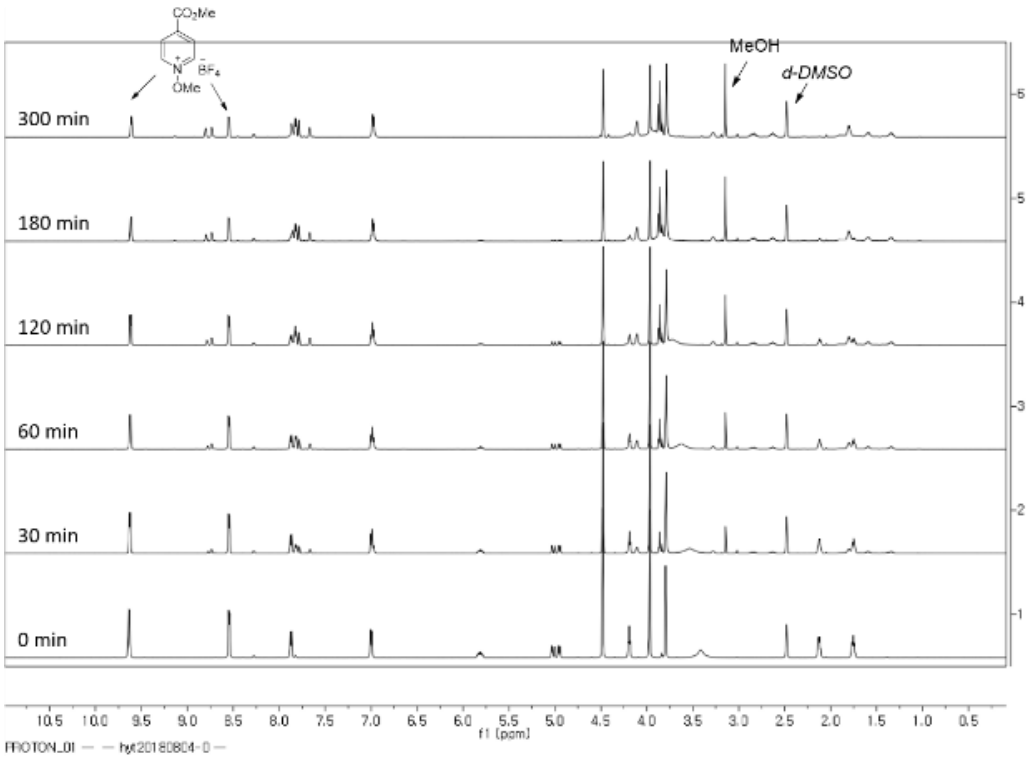
Transformation of 4a monitored by NMR spectroscopy

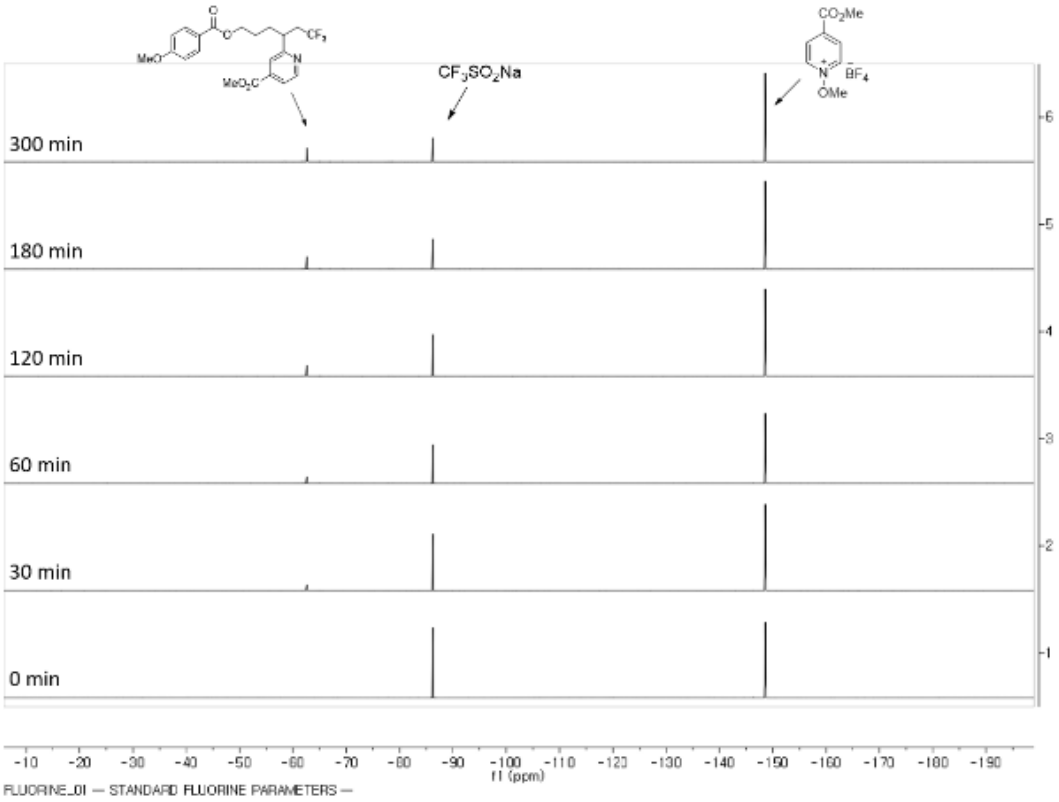


1a **2** **3a** **4a**

To gain insight into the fate of the methoxy radical in the OMe cleavage pathway, the transformation of **4a** was monitored by NMR spectroscopy. A NMR tube was charged with 22.0 mg (0.1 mmol) alkene **1a**, 51.0 mg (0.2 mmol) N-methoxyheteroarenium salts **3a**, 23.4 mg (0.15 mmol) CF_3SO_2Na, 1.62 mg (0.005 mmol) Eosin Y. The NMR tube was evacuated and backfilled with nitrogen. Then, d-DMSO were added into the tube. The reaction mixture was stirring at room temperature under green LEDs and checked by ^1H NMR and ^{19}H NMR. As shown in Figure 2 and Figure 3, signals of MeOH was observed by ^1H NMR, which indicated that the methoxy radical was not oxidized to formaldehyde by the action of related oxidant. No other F-containing byproduct was observed from ^{19}F NMR (Figure 3).

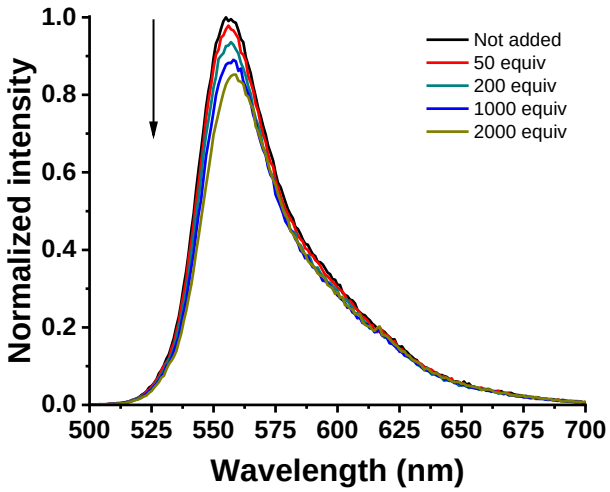
Figure S6. ^1H NMR spectroscopies.

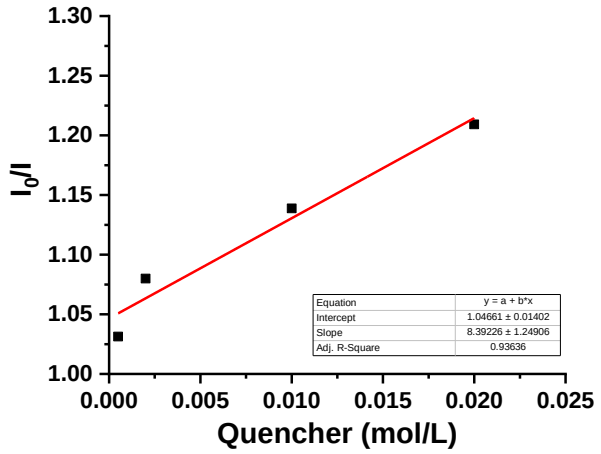




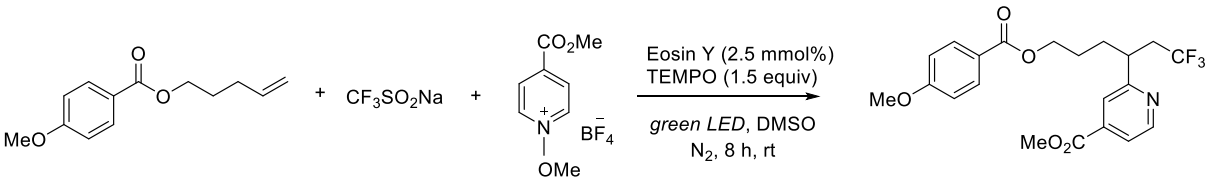
Stern–Volmer quenching experiment

Figure S7. Quenching of the Eosin Y emission (2×10^{-5} M in DMSO) in the presence of increasing amount of Langlois reagent. (Excitation wavelength: 400 nm, Ex bandwidth: 3.0 nm, Em bandwidth: 3.0 nm)





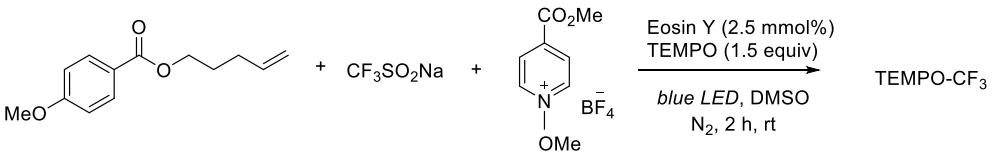
TEMPO experiment



1a **2** **3a** **4a** (< 5%)

An oven-dried tube was charged with alkene **1a** (0.2 mmol), N-methoxypyridinium salt **3a** (0.4 mmol), CF_3SO_2Na (0.3 mmol), TEMPO (0.3 mmol) and Eosin Y (0.005 mmol). The tube was evacuated and backfilled with nitrogen (repeated three times). Then, dimethyl sulfoxide (2.0 mL) was added into the reaction via syringe. The reaction mixture was stirring at room temperature under blue LEDs for 2 h. The desired product was observed in less than 5% yield determined by ^{19}F NMR based on benzotrifluoride as an internal standard.

Observation of TEMPO-CF_3



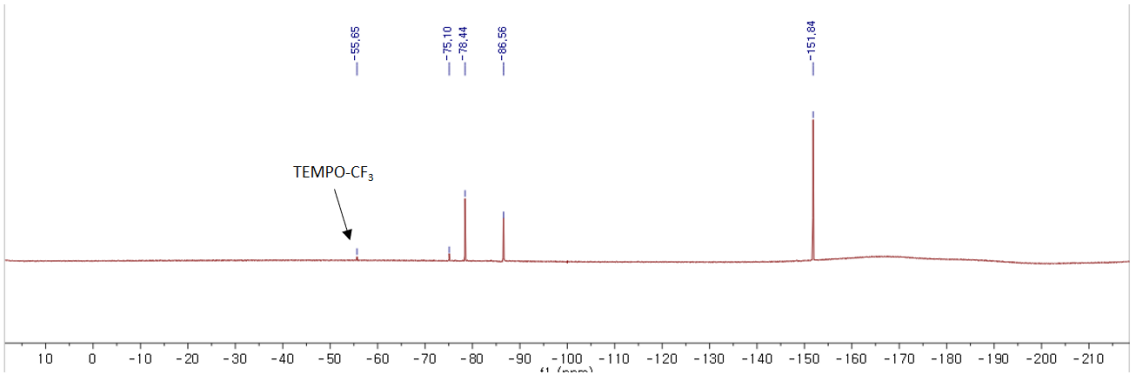
1a **2** **3a**

detected from ^{19}F NMR spectroscopy

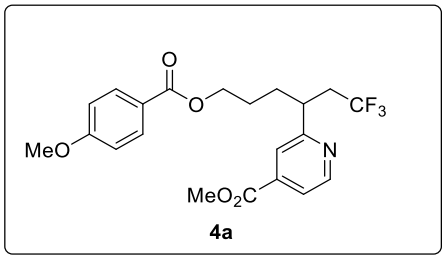
An oven-dried tube was charged with alkene **1a** (0.2 mmol), N-methoxypyridinium salt **3a** (0.4

mmol), CF_3SO_2Na (0.3 mmol), TEMPO (0.3 mmol) and Eosin Y (0.005 mmol). The tube was evacuated and backfilled with nitrogen (repeated three times). Then, deuterated dimethyl sulfoxide (2.0 mL) was added into the reaction via syringe. The reaction mixture was stirring at room temperature under 40W Kessil blue LED (25% intensity, 456nm) for 2 h. The crude mixture (0.04 mL) was diluted with $CDCl_3$ and TEMPO-CF_3 was detected in ^{19}F NMR spectroscopy. The chemical shift was well-matched with the reported literature.[S4]

Figure S8. ^{19}F NMR spectroscopy for TEMPO-CF_3



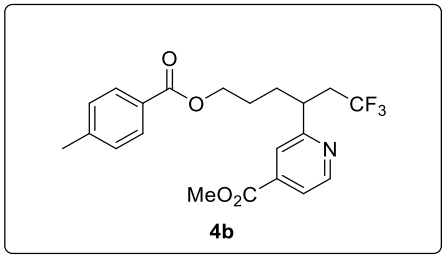
V. Compound Characterizations



4a

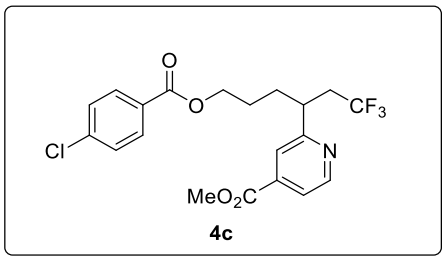
6,6,6-trifluoro-4-(4-methylpyridin-2-yl)hexyl 4-methoxybenzoate (4a). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 5 : 1). From 4-methoxyphenyl hex-5-enoate (44.0 mg, 0.2 mmol), compound **4a** (68.8 mg, 81%) was obtained. Colorless oil. ^1H NMR (599 MHz, Chloroform-d) δ 8.74 (d, *J* = 4.9 Hz, 1H), 7.96 (d, *J* = 8.9 Hz, 2H), 7.72 (d, *J* = 5.0 Hz, 1H), 7.70 (s, 1H), 6.91 (d, *J* = 8.9 Hz, 2H), 4.22 (t, *J* = 6.5 Hz, 2H), 3.96 (s, 3H), 3.86 (s, 3H), 3.24 – 3.21 (m, 1H), 2.85 – 2.82 (m, 1H), 2.47 – 2.45 (m, 1H), 1.98 – 1.96 (m, 1H), 1.91 – 1.89 (m, 1H), 1.69 – 1.66 (m, 1H), 1.50 – 1.48 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-d) δ 166.2, 165.5, 163.3, 162.9, 150.6, 137.8, 131.5, 126.6 (q, *J* = 277.3 Hz), 122.6, 122.4, 121.2, 113.6, 64.0, 55.4, 52.7, 41.3 (d, *J* = 2.6 Hz),

38.7 (q, *J* = 27.6 Hz), 32.1, 26.4. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.1 (t, *J* = 11.0 Hz). HRMS (ESI) Calcd for $C_{21}H_{22}F_3NO_5$: [M] + Na^+ = 448.1342. Found: 448.1364.



4b

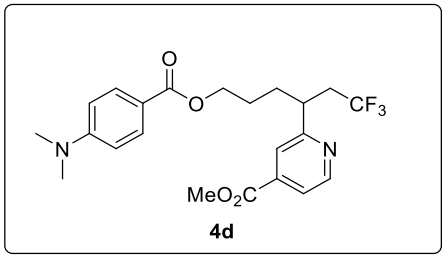
methyl 2-(1,1,1-trifluoro-6-((4-methylbenzoyl)oxy)hexan-3-yl)isonicotinate (4b). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 5 : 1). From pent-4-en-1-yl 4-methylbenzoate (40.8 mg, 0.2 mmol), compound **4b** (67.9 mg, 83%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.74 (d, *J* = 4.7 Hz, 1H), 7.89 (d, *J* = 8.1 Hz, 2H), 7.73 (d, *J* = 5.0 Hz, 1H), 7.71 (s, 1H), 7.23 (d, *J* = 7.9 Hz, 2H), 4.23 (t, *J* = 6.5 Hz, 2H), 3.96 (s, 3H), 3.24 – 3.21 (m, 1H), 2.85 – 2.83 (m, 1H), 2.48 – 2.45 (m, 1H), 2.41 (s, 3H), 1.99 – 1.96 (m, 1H), 1.92 – 1.90 (m, 1H), 1.70 – 1.66 (m, 1H), 1.51 – 1.48 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.5, 165.5, 162.8, 150.5, 143.6, 137.9, 129.5, 129.0, 127.5, 126.6 (d, *J* = 277.8 Hz), 122.4, 121.2, 64.1, 52.7, 41.3 (d, *J* = 2.7 Hz), 38.7 (q, *J* = 27.6 Hz), 32.1, 26.3, 21.6. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.1 (t, *J* = 11.0 Hz). HRMS (EI) Calcd for $C_{21}H_{22}F_3NO_4$: [M] = 409.1501. Found: 409.1504.



4c

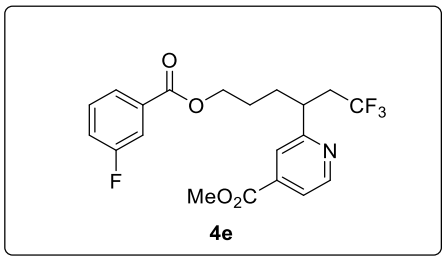
methyl 2-(6-((4-chlorobenzoyl)oxy)-1,1,1-trifluorohexan-3-yl)isonicotinate (4c). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 5 : 1). From pent-4-en-1-yl 4-chlorobenzoate (44.8 mg, 0.2 mmol), compound **4c** (71.2 mg, 83%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.73 (d, *J* = 5.0 Hz, 1H), 7.93 (d, *J* = 8.6 Hz, 2H), 7.72 (dd, *J* = 5.0, 1.5 Hz, 1H), 7.70 (s, 1H), 7.40 (d, *J* = 8.6 Hz, 2H), 4.24 (t, *J* = 6.5 Hz, 2H), 3.96 (s, 3H), 3.23 – 3.21 (m, 1H), 2.84 – 2.81 (m, 1H), 2.48 – 2.44 (m, 1H), 1.98 – 1.96 (m, 1H), 1.90 – 1.88 (m, 1H), 1.70 – 1.66 (m, 1H), 1.50 – 1.48 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 165.6, 165.5, 162.7, 150.6, 139.4, 137.9, 130.9, 128.7, 128.6, 126.5 (q, *J* = 277.3 Hz), 122.4, 121.2, 64.6, 52.7, 41.3 (q, *J* = 2.4 Hz),

38.7 (q, *J* = 27.7 Hz), 32.0, 26.3. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.0 (t, *J* = 10.9 Hz). HRMS (EI) Calcd for $C_{20}H_{19}ClF_3NO_4$: [M] = 429.0955. Found: 429.0951.



4d

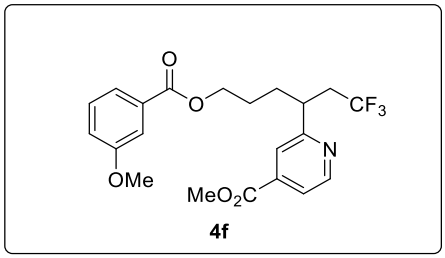
methyl 2-(6-((4-(dimethylamino)benzoyl)oxy)-1,1,1-trifluorohexan-3-yl)isonicotinate (4d). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 3 : 1). From pent-4-en-1-yl 4-(dimethylamino)benzoate (46.6 mg, 0.2 mmol), compound **4d** (52.6 mg, 60%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.74 (d, *J* = 4.9 Hz, 1H), 7.87 (d, *J* = 9.1 Hz, 2H), 7.72 (d, *J* = 9.8 Hz, 2H), 6.65 (d, *J* = 9.1 Hz, 2H), 4.20 (t, *J* = 6.0 Hz, 2H), 3.96 (s, 3H), 3.24 – 3.21 (m, 1H), 3.04 (s, 6H), 2.86 – 2.83 (m, 1H), 2.48 – 2.44 (m, 1H), 1.98 – 1.95 (m, 1H), 1.92 – 1.90 (m, 1H), 1.68 – 1.65 (m, 1H), 1.49 – 1.47 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.8, 165.5, 162.9, 153.3, 150.5, 137.9, 131.2, 126.6 (q, *J* = 277.1 Hz), 122.4, 121.2, 117.1, 110.8, 63.5, 52.7, 41.3, 40.1, 38.7 (q, *J* = 27.6 Hz), 32.2, 26.5. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.1 (t, *J* = 10.9 Hz). HRMS (EI) Calcd for $C_{22}H_{25}F_3N_2O_4$: [M] = 438.1766. Found: 438.1770.



4e

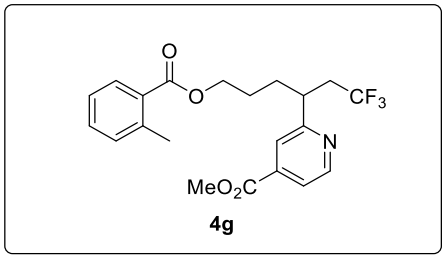
methyl 2-(1,1,1-trifluoro-6-((3-fluorobenzoyl)oxy)hexan-3-yl)isonicotinate (4e). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 5 : 1). From pent-4-en-1-yl 3-fluorobenzoate (41.6 mg, 0.2 mmol), compound **4e** (68.5 mg, 83%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-d) δ 8.73 (d, *J* = 4.9 Hz, 1H), 7.78 (d, *J* = 7.8 Hz, 1H), 7.72 – 7.70 (m, 2H), 7.66 – 7.64 (m, 1H), 7.41 – 7.38 (m, 1H), 7.25 – 7.24 (m, 1H), 4.24 (t, *J* = 6.5 Hz, 2H), 3.94 (s, 3H), 3.22 – 3.19 (m, 1H), 2.83 – 2.81 (m, 1H), 2.47 – 2.43 (m, 1H), 1.98 – 1.95 (m, 1H), 1.90 – 1.88 (m, 1H), 1.69 – 1.67 (m, 1H), 1.50 – 1.47 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-d) δ 165.5, 165.3 (d, *J* = 2.9 Hz), 162.7, 162.5 (d, *J* = 246.9 Hz), 150.6, 137.9, 132.3 (d, *J* = 7.4 Hz), 123.0 (d, *J* = 7.9

Hz), 126.5 (q, *J* = 277.3 Hz), 125.2 (d, *J* = 3.1 Hz), 122.4, 121.3, 120.0 (d, *J* = 21.2 Hz), 116.4 (d, *J* = 22.9 Hz), 64.7, 52.7, 41.3 (d, *J* = 2.4 Hz), 38.7 (q, *J* = 27.7 Hz), 31.9, 26.2. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.1 (t, *J* = 10.9 Hz), -112.4 (td, J = 8.9, 5.5 Hz). HRMS (ESI) Calcd for $C_{20}H_{19}F_4NO_4$: [M] + Na^+ = 436.1142. Found: 436.1142.



4f

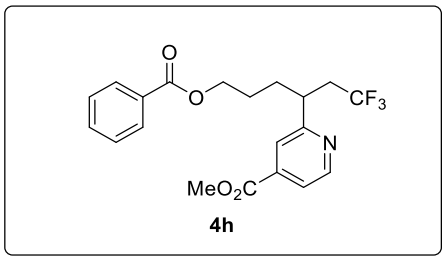
methyl 2-(1,1,1-trifluoro-6-((3-methoxybenzoyl)oxy)hexan-3-yl)isonicotinate (4f). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 4 : 1). From pent-4-en-1-yl 3-methoxybenzoate (44.0 mg, 0.2 mmol), compound **4f** (62.1 mg, 73%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.74 (d, *J* = 4.8 Hz, 1H), 7.73 – 7.71 (m, 2H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.52 (s, 1H), 7.34 (t, *J* = 7.9 Hz, 1H), 7.11 – 7.09 (m, 1H), 4.25 (t, *J* = 6.6 Hz, 2H), 3.96 (s, 3H), 3.85 (s, 3H), 3.23 – 3.21 (m, 1H), 2.85 – 2.82 (m, 1H), 2.48 – 2.45 (m, 1H), 1.99 – 1.96 (m, 1H), 1.92 – 1.90 (m, 1H), 1.70 – 1.67 (m, 1H), 1.51 – 1.49 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.3, 165.5, 162.8, 159.5, 150.6, 137.9, 131.5, 129.3, 126.6 (d, *J* = 2.5 Hz), 122.4, 121.9, 121.2, 119.3, 114.1, 64.4, 55.4, 52.7, 41.3 (d, *J* = 2.5 Hz), 38.7 (q, *J* = 277.8 Hz), 32.0, 26.3.^{19}F NMR (564 MHz, Chloroform-d) δ -64.0 (t, *J* = 11.0 Hz). HRMS (EI) Calcd for $C_{21}H_{22}F_3NO_5$: [M] = 425.1450. Found: 425.1447.



4g

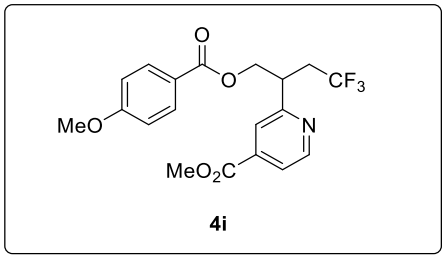
methyl 2-(1,1,1-trifluoro-6-((2-methylbenzoyl)oxy)hexan-3-yl)isonicotinate (4g). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 5 : 1). From pent-4-en-1-yl 2-methylbenzoate (40.8 mg, 0.2 mmol), compound **4g** (68.7 mg, 84%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.74 (d, *J* = 4.9 Hz, 1H), 7.86 (d, *J* = 8.2 Hz, 1H), 7.73 – 7.71 (m, 2H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.25 – 7.22 (m, 2H), 4.23 (t, *J* = 6.5 Hz, 2H), 3.96 (s, 3H), 3.25 – 3.22 (m,

1H), 2.85 – 2.83 (m, 1H), 2.57 (s, 3H), 2.48 – 2.45 (m, 1H), 2.00 – 1.98 (m, 1H), 1.93 – 1.90 (m, 1H), 1.70 – 1.67 (m, 1H), 1.51 – 1.49 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 167.5, 165.5, 162.8, 150.5, 140.1, 137.9, 131.9, 131.6, 130.5, 129.6, 126.6 (q, *J* = 277.8 Hz), 125.7, 122.4, 121.2, 64.1, 52.7, 41.3, 38.7 (q, *J* = 27.7 Hz), 32.1, 26.3, 21.7. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.1 (t, *J* = 10.9 Hz). HRMS (EI) Calcd for $C_{21}H_{22}F_3NO_4$: [M] = 409.1501. Found: 409.1499.



4h

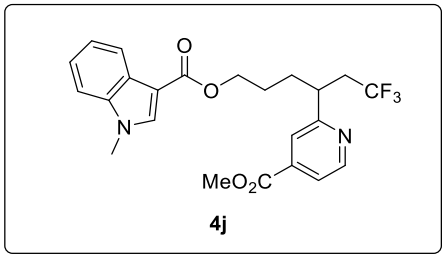
methyl 2-(6-(benzoyloxy)-1,1,1-trifluorohexan-3-yl)isonicotinate (4h). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 5 : 1). From pent-4-en-1-yl benzoate (38.0 mg, 0.2 mmol), compound **4h** (67.9 mg, 86%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.74 (d, *J* = 4.9 Hz, 1H), 8.00 (d, *J* = 7.1 Hz, 2H), 7.73 – 7.71 (m, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 2H), 4.25 (t, *J* = 6.5 Hz, 2H), 3.96 (s, 3H), 3.24 – 3.22 (m, 1H), 2.86 – 2.83 (m, 1H), 2.49 – 2.45 (m, 1H), 2.00 – 1.96 (m, 1H), 1.93 – 1.90 (m, 1H), 1.71 – 1.68 (m, 1H), 1.52 – 1.49 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.4, 165.5, 162.8, 150.5, 137.9, 132.9, 130.2, 129.5, 128.3, 126.6 (q, *J* = 277.8 Hz), 122.4, 121.2, 64.3, 52.7, 41.3 (d, *J* = 2.8 Hz), 38.7 (q, *J* = 27.7 Hz), 32.0, 26.3. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.1 (t, *J* = 10.9 Hz). HRMS (EI) Calcd for $C_{20}H_{20}F_3NO_4$: [M] = 395.1344. Found: 395.1347.



4i

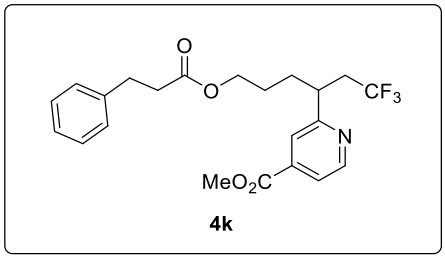
methyl 2-(4,4,4-trifluoro-1-((4-methoxybenzoyl)oxy)butan-2-yl)isonicotinate (4i). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 3 : 1). From allyl 4-methoxybenzoate (38.4 mg, 0.2 mmol), compound **4i** (49.2 mg, 62%) was obtained. White solid. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.75 (d, *J* = 5.0 Hz, 1H), 7.90 (d, *J* = 8.8 Hz, 2H), 7.83 (s, 1H), 7.76 (dd, *J* = 5.0, 1.5 Hz, 1H), 6.90 (d, *J* = 9.0 Hz, 2H), 4.53 (d, *J* = 7.0 Hz, 2H), 3.96 (s, 3H), 3.86 (s, 3H), 3.69 – 3.67 (m,

1H), 3.01 – 2.97 (m, 1H), 2.69 – 2.64 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 165.7, 165.4, 163.6, 160.0, 150.5, 138.0, 131.6, 126.5 (q, *J* = 276.8 Hz), 122.8, 122.0, 121.7, 113.7, 66.5, 55.4, 52.7, 41.1 (d, *J* = 2.8 Hz), 35.1 (q, *J* = 28.8 Hz). ^{19}F NMR (564 MHz, Chloroform-d) δ -64.1 (t, *J* = 10.9 Hz). HRMS (EI) Calcd for $C_{19}H_{18}F_3NO_5$: [M] = 397.1137. Found: 397.1138.



4j

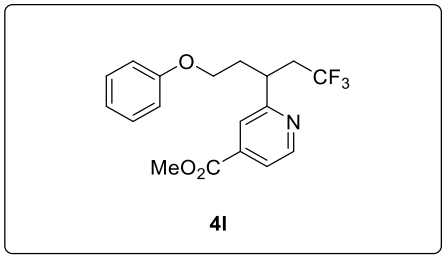
6,6,6-trifluoro-4-(4-(methoxycarbonyl)pyridin-2-yl)hexyl 1-methyl-1H-indole-3-carboxylate (4j). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 2 : 1). From pent-4-en-1-yl 1-methyl-1H-indole-3-carboxylate (48.6 mg, 0.2 mmol), compound **4j** (58.2 mg, 65%) was obtained. White solid. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.75 (d, *J* = 5.7 Hz, 1H), 8.12 (d, *J* = 6.7 Hz, 1H), 7.77 (s, 1H), 7.72 – 7.72 (m, 2H), 7.35 (d, *J* = 7.3 Hz, 1H), 7.32 – 7.27 (m, 2H), 4.27 – 4.26 (m, 2H), 3.95 (s, 3H), 3.84 (s, 3H), 3.27 – 3.24 (m, 1H), 2.86 – 2.84 (m, 1H), 2.49 – 2.46 (m, 1H), 2.03 – 1.99 (m, 1H), 1.96 – 1.94 (m, 1H), 1.73 – 1.70 (m, 1H), 1.55 – 1.53 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 165.6, 164.9, 163.0, 150.5, 137.8, 137.2, 135.2, 126.6 (q, *J* = 277.1 Hz), 126.6, 122.8, 122.4, 121.9, 121.6, 121.2, 109.7, 106.9, 63.1, 52.7, 41.4 (d, *J* = 2.8 Hz), 38.7 (q, *J* = 27.6 Hz), 33.4, 32.3, 26.6. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.0 (t, *J* = 10.9 Hz). HRMS (EI) Calcd for $C_{23}H_{23}F_3N_2O_4$: [M] = 448.1610. Found: 448.1611.



4k

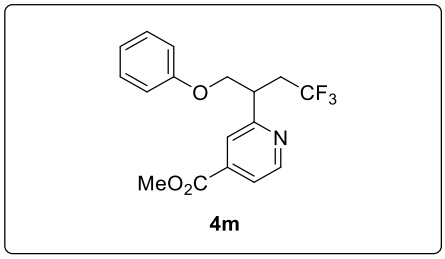
methyl 2-(1,1,1-trifluoro-6-((3-phenylpropanoyl)oxy)hexan-3-yl)isonicotinate (4k). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 5 : 1). From pent-4-en-1-yl 3-phenylpropanoate (43.6 mg, 0.2 mmol), compound **4k** (70.2 mg, 83%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.72 (d, *J* = 4.9 Hz, 1H), 7.71 (dd, *J* = 4.9, 1.7 Hz, 1H), 7.67 (s, 1H), 7.27 (t, *J* = 7.4 Hz, 2H), 7.19 (t, *J* = 8.1 Hz, 3H), 3.99 – 3.95 (m, 2H), 3.95 (s, 3H), 3.15 – 3.12 (m, 1H),

2.92 (t, *J* = 7.8 Hz, 2H), 2.81 – 2.76 (m, 1H), 2.60 (t, *J* = 7.8 Hz, 2H), 2.41 – 2.39 (m, 1H), 1.82 – 1.80 (m, 1H), 1.73 – 1.72 (m, 1H), 1.50 – 1.48 (m, 1H), 1.33 – 1.30 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 172.8, 165.5, 162.8, 150.5, 140.4, 137.8, 128.4, 128.2, 126.6 (q, *J* = 277.3 Hz), 126.2, 122.4, 121.2, 63.9, 52.7, 41.2 (d, *J* = 2.5 Hz), 38.7 (q, *J* = 27.7 Hz), 35.8, 32.0, 30.9, 26.2. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.1 (t, *J* = 10.9 Hz). HRMS (EI) Calcd for $C_{22}H_{24}F_3NO_4$: [M] = 423.1657. Found: 423.1660.



4l

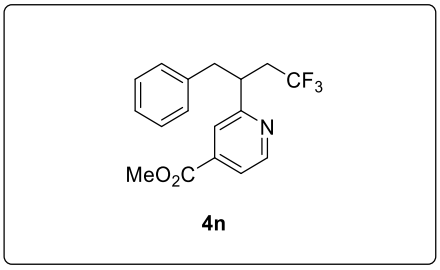
methyl 2-(1,1,1-trifluoro-5-phenoxypentan-3-yl)isonicotinate (4l). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 8 : 1). From (but-3-en-1-yloxy)benzene (29.6 mg, 0.2 mmol), compound **4l** (41.1 mg, 58%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.75 (d, *J* = 6.0 Hz, 1H), 7.72 – 7.72 (m, 2H), 7.25 (t, *J* = 8.0 Hz, 2H), 6.93 (t, *J* = 7.3 Hz, 1H), 6.80 (d, *J* = 7.7 Hz, 2H), 3.92 (s, 3H), 3.89 – 3.88 (m, 1H), 3.67 – 3.66 (m, 1H), 3.55 – 3.53 (m, 1H), 2.90 – 2.88 (m, 1H), 2.54 – 2.51(m, 1H), 2.28 – 2.26 (m, 2H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 165.5, 162.5, 158.6, 150.5, 137.9, 129.4, 126.6 (q, *J* = 277.3 Hz), 122.8, 121.2, 120.8, 114.5, 64.8, 52.6, 38.7 (q, *J* = 27.8 Hz), 38.4 (d, *J* = 2.7 Hz), 35.0. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.0 (t, *J* = 10.9 Hz). HRMS (EI) Calcd for $C_{18}H_{18}F_3NO_3$: [M] = 353.1239. Found: 4353.1241.



4m

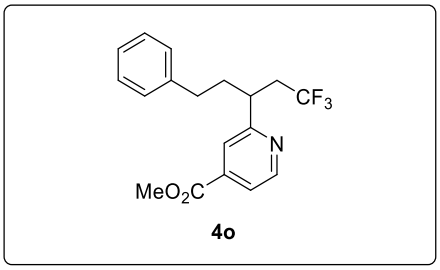
methyl 2-(4,4,4-trifluoro-1-phenoxybutan-2-yl)isonicotinate (4m). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 8 : 1). From (allyloxy)benzene (26.8 mg, 0.2 mmol), compound **4m** (37.2 mg, 55%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.73 (d, *J* = 5.1 Hz, 1H), 7.85 (s, 1H), 7.75 (d, *J* = 3.8 Hz, 1H), 7.27 – 7.24 (m, 2H), 6.95 (t, *J* = 7.3 Hz, 1H), 6.85 (d, *J* = 7.8 Hz, 2H), 4.21 (d, *J* = 6.8 Hz, 2H), 3.97 (s, 3H), 3.69 – 3.67 (m, 1H), 2.94 –

2.90 (m, 1H), 2.80 – 2.76 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 165.5, 160.4, 158.3, 150.3, 138.0, 129.5, 126.7 (q, *J* = 277.3 Hz), 123.0, 121.6, 121.3, 114.6, 70.1, 52.7, 41.7, 35.0 (*J* = 28.4 Hz). ^{19}F NMR (564 MHz, Chloroform-d) δ -64.0 (t, *J* = 10.9 Hz). HRMS (EI) Calcd for $C_{17}H_{16}F_3NO_3$: [M] = 339.1082. Found: 339.1084.



4n

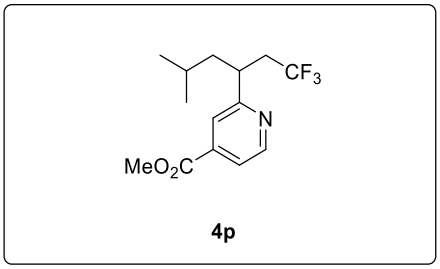
methyl 2-(4,4,4-trifluoro-1-phenylbutan-2-yl)isonicotinate (4n). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 8 : 1). From allylbenzene (23.6 mg, 0.2 mmol), compound **4n** (42.6 mg, 66%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.75 (d, *J* = 5.0 Hz, 1H), 7.69 (dd, *J* = 5.0, 1.4 Hz, 1H), 7.51 (s, 1H), 7.22 (t, *J* = 7.2 Hz, 2H), 7.17 (t, *J* = 7.3 Hz, 1H), 7.02 (d, *J* = 7.0 Hz, 2H), 3.92 (s, 3H), 3.46 – 3.44 (m, 1H), 3.08 (dd, *J* = 13.6, 8.0 Hz, 1H), 3.01 (dd, *J* = 13.6, 7.5 Hz, 1H), 2.90 – 2.88 (m, 1H), 2.48 – 2.44 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 165.5, 162.7, 150.2, 138.4, 137.6, 129.0, 128.5, 126.7 (q, *J* = 277.2 Hz), 126.5, 122.6, 121.1, 52.6, 43.5 (d, *J* = 2.4 Hz), 42.0, 37.5 (q, *J* = 27.7 Hz). ^{19}F NMR (564 MHz, Chloroform-d) δ -63.9 (t, *J* = 10.9 Hz). HRMS (EI) Calcd for $C_{17}H_{16}F_3NO_2$: [M] = 323.1133. Found: 323.1136.



4o

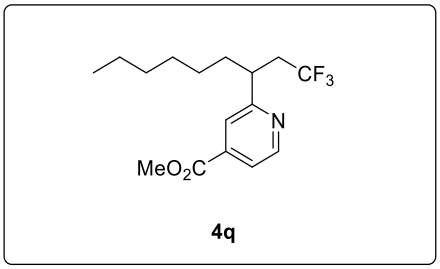
methyl 2-(1,1,1-trifluoro-5-phenylpentan-3-yl)isonicotinate (4o). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 8 : 1). From but-3-en-1-ylbenzene (26.4 mg, 0.2 mmol), compound **4o** (51.2 mg, 76%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.77 (d, *J* = 5.0 Hz, 1H), 7.74 (dd, *J* = 5.0, 1.6 Hz, 1H), 7.69 (s, 1H), 7.26 (t, *J* = 7.5 Hz, 2H), 7.18 (t, *J* = 7.3 Hz, 1H), 7.09 (d, *J* = 6.7 Hz, 2H), 3.98 (s, 3H), 3.22 – 3.20 (m, 1H), 2.86 – 2.84 (m, 1H), 2.48 – 2.45 (m, 2H), 2.42 – 2.39 (m, 1H), 2.19 – 2.17 (m, 1H), 2.09 – 2.07 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 165.6, 163.0, 150.5, 141.1, 137.8, 128.4, 128.2, 126.6 (q, *J* = 277.3 Hz), 126.0, 122.6,

121.1, 52.7, 41.2 (d, *J* = 2.8 Hz), 38.7 (q, *J* = 27.6 Hz), 37.2, 33.2. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.0 (t, *J* = 10.9 Hz). HRMS (EI) Calcd for $C_{18}H_{18}F_3NO_2$: [M] = 337.1290. Found: 337.1286.



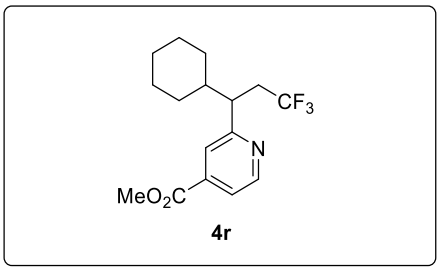
4p

methyl 2-(1,1,1-trifluoro-5-methylhexan-3-yl)isonicotinate (4p). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 8 : 1). From 4-methylpent-1-ene (16.8 mg, 0.2 mmol), compound **4p** (47.9 mg, 83%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.73 (d, *J* = 4.9 Hz, 1H), 7.71 – 7.69 (m, 2H), 3.97 (s, 3H), 3.27 – 3.25 (m, 1H), 2.81 – 2.75 (m, 1H), 2.40 – 2.37 (m, 1H), 1.78 – 1.74 (m, 1H), 1.53 – 1.49 (m, 1H), 1.28 – 1.23 (m, 1H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.84 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 165.6, 163.7, 150.3, 137.9, 126.7 (q, *J* = 277.4 Hz), 122.3, 121.0, 52.7, 45.0, 39.4 (d, *J* = 2.8 Hz), 38.9 (q, *J* = 27.5 Hz), 25.3, 23.0, 21.8. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.0 (t, *J* = 10.9 Hz). HRMS (EI) Calcd for $C_{14}H_{18}F_3NO_2$: [M] = 289.1290. Found: 289.1286.



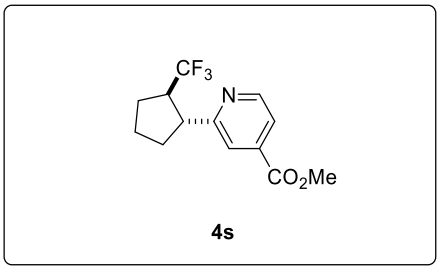
4q

methyl 2-(1,1,1-trifluorononan-3-yl)isonicotinate (4q). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 8 : 1). From oct-1-ene (22.4 mg, 0.2 mmol), compound **4q** (50.7 mg, 80%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.72 (d, *J* = 5.0 Hz, 1H), 7.70 (d, *J* = 4.9 Hz, 1H), 7.68 (s, 1H), 3.96 (s, 3H), 3.16 – 3.13 (m, 1H), 2.84 – 2.78 (m, 1H), 2.44 – 2.40 (m, 1H), 1.79 – 1.77 (m, 1H), 1.72 – 1.70 (m, 1H), 1.24 – 1.19 (m, 7H), 1.03 – 1.00 (m, 1H), 0.84 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 165.7, 163.7, 150.3, 137.7, 126.7 (q, *J* = 277.2 Hz), 122.3, 120.9, 52.7, 41.6 (d, *J* = 2.7 Hz), 38.6 (q, *J* = 27.3 Hz), 35.8, 31.6, 29.0, 27.0, 22.5, 14.0. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.1 (t, *J* = 11.0 Hz). HRMS (EI) Calcd for $C_{16}H_{22}F_3NO_2$: [M] = 317.1603. Found: 317.1604.



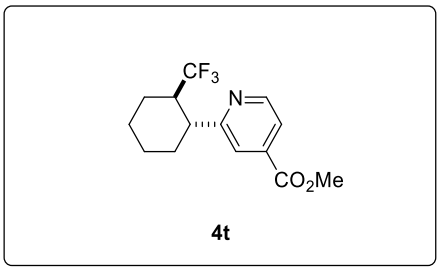
4r

methyl 2-(1-cyclohexyl-3,3,3-trifluoropropyl)isonicotinate (4r). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 8 : 1). From vinylcyclohexane (22.0 mg, 0.2 mmol), compound **4r** (43.0 mg, 68%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.73 (d, *J* = 4.9 Hz, 1H), 7.69 (d, *J* = 4.7 Hz, 1H), 7.65 (s, 1H), 3.96 (s, 3H), 2.95 – 2.90 (m, 2H), 2.57 – 2.49 (m, 1H), 1.89 (d, *J* = 12.8 Hz, 1H), 1.76 (d, *J* = 13.2 Hz, 1H), 1.67 – 1.63 (m, 3H), 1.30 – 1.21 (m, 2H), 1.14 – 1.07 (m, 2H), 0.96 – 0.86 (m, 2H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 165.8, 162.9, 150.0, 137.4, 127.1 (q, *J* = 277.5 Hz), 123.2, 120.8, 52.7, 47.2, 42.4, 35.4 (q, *J* = 27.3 Hz), 30.7 (d, *J* = 14.8 Hz), 26.2, 26.1. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.2 (t, *J* = 10.4 Hz). HRMS (EI) Calcd for $C_{16}H_{20}F_3NO_2$: [M] = 315.1446. Found: 315.1449.



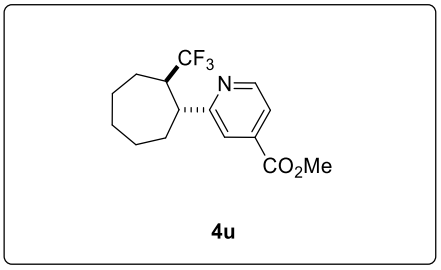
4s

methyl 2-(*trans*-2-(trifluoromethyl)cyclopentyl)isonicotinate (4s). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 8 : 1). From cyclopentene (13.6 mg, 0.2 mmol), compound **4s** (48.0 mg, 88%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.71 (d, *J* = 4.6 Hz, 1H), 7.73 (s, 1H), 7.69 (dd, *J* = 5.0, 1.7 Hz, 1H), 3.96 (s, 3H), 3.41 (q, *J* = 8.2 Hz, 1H), 3.28 – 3.22 (m, 1H), 2.18 – 2.11 (m, 2H), 1.95 – 1.88 (m, 3H), 1.82 – 1.79 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 165.7, 163.9, 150.4, 137.8, 128.5 (q, *J* = 277.8 Hz), 122.0, 120.8, 52.6, 48.5 (q, *J* = 27.2 Hz), 48.2 (d, *J* = 2.2 Hz), 35.6, 27.0 (d, *J* = 2.4 Hz), 25.7. ^{19}F NMR (564 MHz, Chloroform-*d*) δ -70.4 (d, *J* = 9.7 Hz). HRMS (EI) Calcd for $C_{13}H_{14}F_3NO_2$: [M] = 273.0977. Found: 273.0981.



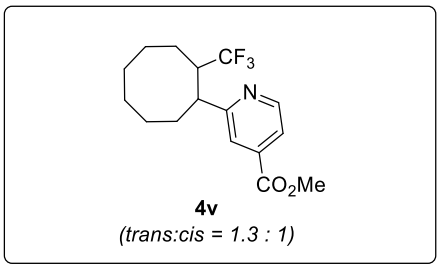
4t

methyl 2-(*trans*-2-(trifluoromethyl)cyclohexyl)isonicotinate (4t). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 8 : 1). From cyclohexene (16.4 mg, 0.2 mmol), compound **4t** (48.8 mg, 85%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.68 (d, *J* = 4.9 Hz, 1H), 7.70 – 7.64 (m, 2H), 3.94 (s, 3H), 2.90 – 2.87 (m, 1H), 2.77 – 2.75 (m, 1H), 2.13 – 2.11 (m, 1H), 1.88 – 1.85 (m, 3H), 1.71 – 1.68 (m, 1H), 1.44 – 1.38 (m, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 165.7, 164.7, 150.0, 137.8, 127.5 (q, *J* = 280.9 Hz), 121.6, 120.7, 52.6, 45.6, 45.0 (q, *J* = 24.2 Hz), 33.6, 25.5, 25.2 (q, *J* = 2.8 Hz), 24.5. ^{19}F NMR (564 MHz, Chloroform-*d*) δ -69.5 (d, *J* = 8.3 Hz). HRMS (EI) Calcd for $C_{14}H_{16}F_3NO_2$: [M] = 287.1133. Found: 287.1131.



4u

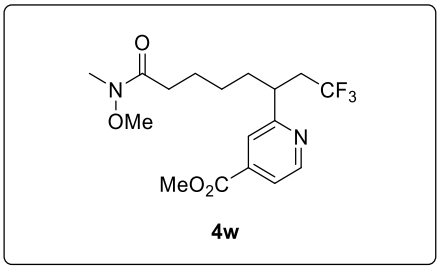
methyl 2-(*trans*-2-(trifluoromethyl)cycloheptyl)isonicotinate (4u). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 8 : 1). From cycloheptene (19.2 mg, 0.2 mmol), compound **4u** (50.0 mg, 83%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.68 (d, *J* = 5.0 Hz, 1H), 7.70 (s, 1H), 7.67 (d, *J* = 5.0 Hz, 1H), 3.95 (s, 3H), 3.39 – 3.35 (m, 1H), 3.30 – 3.28 (m, 1H), 2.04 – 2.01 (m, 1H), 1.89 – 1.85 (m, 4H), 1.75 – 1.73 (m, 1H), 1.66 – 1.62 (m, 2H), 1.57 – 1.53 (m, 1H), 1.50 – 1.47 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.2, 165.8, 149.6, 138.0, 128.7 (q, *J* = 281.1 Hz), 121.8, 120.4, 52.6, 46.3, 46.0 (q, *J* = 23.3 Hz), 34.5, 30.2, 26.8, 25.8 (d, *J* = 2.8 Hz), 25.6. ^{19}F NMR (564 MHz, Chloroform-*d*) δ -70.0 (d, *J* = 9.6 Hz). HRMS (EI) Calcd for $C_{15}H_{18}F_3NO_2$: [M] = 301.1290. Found: 301.1287.



4v

(trans:cis = 1.3 : 1)

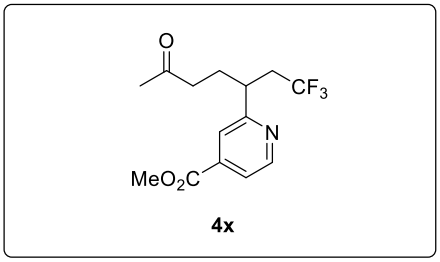
methyl 2-(2-(trifluoromethyl)cyclooctyl)isonicotinate (4v). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 8 : 1). From (Z)-cyclooctene (22.0 mg, 0.2 mmol), compound **4v** (56.7 mg, 90%) was obtained (*trans* : *cis* = 1.3 : 1). Colorless oil. *trans*: ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.67 (d, *J* = 4.7 Hz, 1H), 7.68 (s, 1H), 7.65 (d, *J* = 5.0 Hz, 1H), 3.95 (s, 3H), 3.08 – 3.05 (m, 1H), 2.41 – 2.32 (m, 1H), 2.13 – 2.09 (m, 1H), 2.02 – 2.00 (m, 2H), 1.91 – 1.82 (m, 5H), 1.67 – 1.60 (m, 4H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 168.5, 165.8, 149.8, 137.9, 128.8 (q, *J* = 279.4 Hz), 120.7, 120.5, 52.6, 46.7, 42.6 (q, *J* = 24.7 Hz), 32.8, 31.8, 25.6, 25.5, 25.4 (d, *J* = 2.4 Hz), 24.9. ^{19}F NMR (564 MHz, Chloroform-*d*) δ -73.1 (d, *J* = 9.8 Hz). *cis*: ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.66 (d, *J* = 4.5 Hz, 1H), 7.70 (s, 1H), 7.65 (d, *J* = 5.0 Hz, 1H), 3.95 (s, 3H), 3.02 – 3.01 (m, 1H), 2.35 – 2.32 (m, 1H), 2.13 – 2.09 (m, 1H), 1.98 – 1.96 (m, 2H), 1.91 – 1.82 (m, 5H), 1.67 – 1.60 (m, 4H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 168.4, 165.8, 149.8, 137.9, 128.7 (q, *J* = 280.9 Hz), 120.3, 120.2, 52.6, 45.5, 41.5 (q, *J* = 24.3 Hz), 32.6, 30.4, 25.5, 25.2 (d, *J* = 2.7 Hz), 25.1, 24.1 (d, *J* = 2.4 Hz). ^{19}F NMR (564 MHz, Chloroform-*d*) δ -73.2 (d, *J* = 9.7 Hz). HRMS (EI) Calcd for $C_{16}H_{20}F_3NO_2$: [M] = 315.1446. Found: 315.1445.



4w

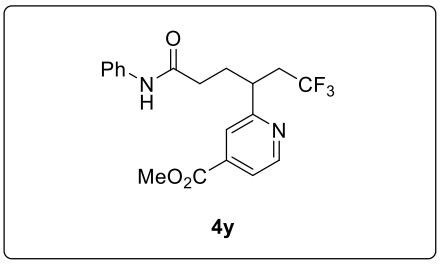
methyl 2-(1,1,1-trifluoro-8-(methoxy(methyl)amino)-8-oxooctan-3-yl)isonicotinate (4w). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 6 : 1). From N-methoxy-N-methylhept-6-enamide (34.2 mg, 0.2 mmol), compound **4w** (47.4 mg, 63%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.72 (d, *J* = 4.9 Hz, 1H), 7.69 (dd, *J* = 5.0, 1.6 Hz, 1H), 7.67 (s, 1H), 3.95 (s, 3H), 3.63 (s, 3H), 3.14 (s, 4H), 2.81 – 2.79 (m, 1H), 2.43 – 2.41 (m, 1H), 2.35 – 2.32 (m, 2H), 1.82 – 1.80 (m, 1H), 1.76 – 1.73 (m, 1H), 1.62 – 1.61 (m, 1H), 1.57 – 1.55 (m, 1H), 1.26 – 1.24 (m, 1H), 1.08 – 1.06 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.3, 165.6, 163.4, 150.4, 137.7,

126.7 (q, *J* = 277.3 Hz), 122.3, 121.0, 61.1, 52.6, 41.5 (d, *J* = 2.6 Hz), 38.6 (q, *J* = 27.5 Hz), 35.5, 32.1, 31.5, 26.8, 24.3. ^{19}F NMR (564 MHz, Chloroform-*d*) δ -64.1 (t, *J* = 10.9 Hz). HRMS (FAB) Calcd for $C_{17}H_{23}F_3N_2O_4$: [M] + H^+ = 377.1688. Found: 377.1689.



4x

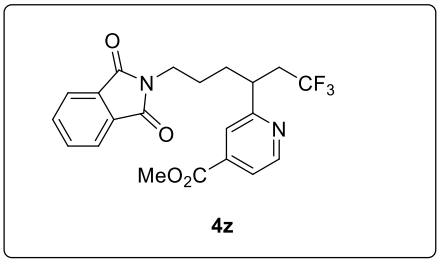
methyl 2-(1,1,1-trifluoro-6-oxoheptan-3-yl)isonicotinate (4x). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 8 : 1). From hex-5-en-2-one (19.6 mg, 0.2 mmol), compound **4x** (49.7 mg, 82%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.73 (d, *J* = 5.0 Hz, 1H), 7.72 (dd, *J* = 5.0, 1.5 Hz, 1H), 7.67 (s, 1H), 3.96 (s, 3H), 3.19 – 3.18 (m, 1H), 2.82 – 2.80 (m, 1H), 2.44 – 2.41 (m, 1H), 2.29 – 2.26 (m, 1H), 2.22 – 2.20 (m, 1H), 2.06 – 2.03 (s, 5H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 207.4, 165.5, 162.6, 150.6, 137.9, 126.5 (q, *J* = 277.4 Hz), 122.3, 121.3, 52.7, 40.7 (d, *J* = 2.6 Hz), 40.6, 38.7 (q, *J* = 27.7 Hz), 29.9, 29.3. ^{19}F NMR (564 MHz, Chloroform-*d*) δ -64.1 (t, *J* = 10.9 Hz). HRMS (EI) Calcd for $C_{14}H_{16}F_3NO_3$: [M] = 303.1082. Found: 303.1080.



4y

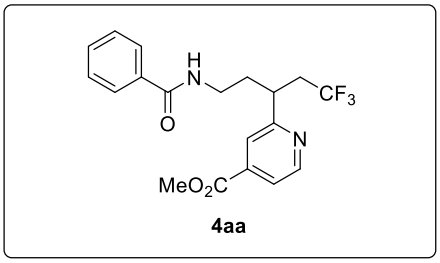
methyl 2-(1,1,1-trifluoro-6-oxo-6-(phenylamino)hexan-3-yl)isonicotinate (4y). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 8 : 1). From N-phenylpent-4-enamide (35.0 mg, 0.2 mmol), compound **4y** (66.1 mg, 87%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.74 (d, *J* = 5.5 Hz, 1H), 7.73 – 7.72 (m, 2H), 7.52 (s, 1H), 7.46 (d, *J* = 8.0 Hz, 2H), 7.30 (t, *J* = 7.9 Hz, 2H), 7.10 (t, *J* = 7.4 Hz, 1H), 3.94 (s, 3H), 3.32 – 3.29 (m, 1H), 2.84 – 2.80 (m, 1H), 2.47 – 2.43 (m, 1H), 2.20 – 2.14 (m, 4H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 170.0, 165.4, 162.4, 150.5, 138.0, 137.7, 128.9, 126.4 (q, *J* = 277.4 Hz), 124.3, 122.4, 121.4, 119.8, 52.71, 40.7 (d, *J* = 2.8

Hz), 38.7 (q, *J* = 27.8 Hz), 34.6, 31.1. ^{19}F NMR (564 MHz, Chloroform-*d*) δ -64.0 (t, *J* = 10.9 Hz). HRMS (EI) Calcd for $C_{19}H_{19}F_3N_2O_3$: [M] = 380.1348. Found: 380.1351.



4z

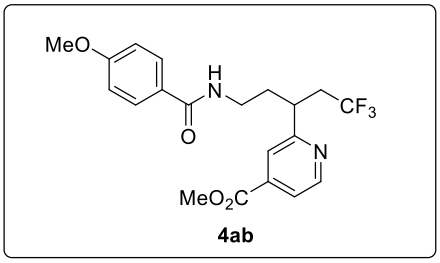
methyl 2-(6-(1,3-dioxoisoindolin-2-yl)-1,1,1-trifluorohexan-3-yl)isonicotinate (4z). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 4 : 1). From 2-(pent-4-en-1-yl)isoindoline-1,3-dione (43.0 mg, 0.2 mmol), compound **4z** (68.9 mg, 82%) was obtained. White solid. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.68 (d, *J* = 5.0 Hz, 1H), 7.81 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.71 – 7.69 (m, 3H), 7.67 (s, 1H), 3.94 (s, 3H), 3.62 (t, *J* = 7.2 Hz, 2H), 3.20 – 3.17 (m, 1H), 2.83 – 2.80 (m, 1H), 2.42 – 2.39 (m, 1H), 1.88 – 1.85 (m, 1H), 1.78 – 1.76 (m, 1H), 1.61 – 1.58 (m, 1H), 1.40 – 1.38 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 168.2, 165.5, 162.6, 150.5, 137.8, 133.9, 132.0, 126.5 (q, *J* = 277.3 Hz), 123.2, 122.4, 121.2, 52.6, 41.2 (d, *J* = 2.8 Hz), 38.6 (q, *J* = 27.6 Hz), 37.5, 32.8, 26.1. ^{19}F NMR (564 MHz, Chloroform-*d*) δ -64.1 (t, *J* = 10.9 Hz). HRMS (EI) Calcd for $C_{21}H_{19}F_3N_2O_4$: [M] = 420.1297. Found: 420.1299.



4aa

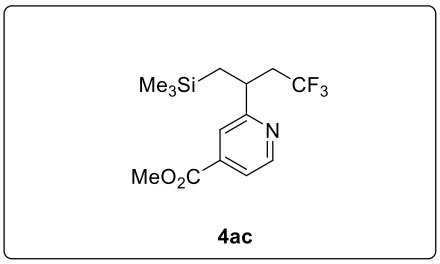
methyl 2-(5-benzamido-1,1,1-trifluoropentan-3-yl)isonicotinate (4aa). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 3 : 1). From N-(but-3-en-1-yl)benzamide (35.0 mg, 0.2 mmol), compound **4aa** (63.0 mg, 83%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.70 (d, *J* = 5.0 Hz, 1H), 7.75 (s, 1H), 7.71 – 7.68 (m, 3H), 7.47 (t, *J* = 7.4 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 2H), 6.54 (s, 1H), 3.94 (s, 3H), 3.34 – 3.28 (m, 3H), 2.80 – 2.78 (m, 1H), 2.50 – 2.46 (m, 1H), 2.14 – 2.10 (m, 2H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 167.4, 165.2, 162.4, 150.2, 138.3, 134.3, 131.4, 128.4, 126.8, 126.4 (q, *J* = 277.4 Hz), 122.3, 121.5, 52.7, 39.5 (d, *J* = 2.5 Hz), 38.7

(q, *J* = 27.9 Hz), 37.6, 35.0. ^{19}F NMR (564 MHz, Chloroform-*d*) δ -63.9 (t, *J* = 10.7 Hz). HRMS (ESI) Calcd for $C_{19}H_{19}F_3N_2O_3$: [M] + Na^+ = 403.1240. Found: 403.1231.



4ab

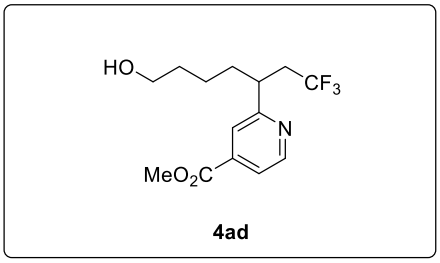
methyl 2-(1,1,1-trifluoro-5-(4-methoxybenzamido)pentan-3-yl)isonicotinate (4ab). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 3 : 1). From N-(but-3-en-1-yl)-4-methoxybenzamide (41.0 mg, 0.2 mmol), compound **4ab** (75.4 mg, 92%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.71 (d, *J* = 4.9 Hz, 1H), 7.73 (s, 1H), 7.70 (d, *J* = 4.9 Hz, 1H), 7.65 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 8.9 Hz, 2H), 6.32 (s, 1H), 3.94 (s, 3H), 3.83 (s, 3H), 3.31 – 3.25 (m, 3H), 2.82 – 2.76 (m, 1H), 2.49 – 2.45 (m, 1H), 2.12 – 2.09 (m, 2H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.9, 165.4, 162.6, 162.1, 150.5, 138.1, 128.6, 126.6, 126.4 (q, *J* = 277.4 Hz), 122.2, 121.3, 113.7, 55.3, 52.7, 39.6 (d, *J* = 2.5 Hz), 38.7 (q, *J* = 27.7 Hz), 37.6, 35.1. ^{19}F NMR (564 MHz, Chloroform-*d*) δ -63.9 (t, *J* = 10.8 Hz). HRMS (ESI) Calcd for $C_{20}H_{21}F_3N_2O_4$: [M] = 410.1453. Found: 410.1451.



4ac

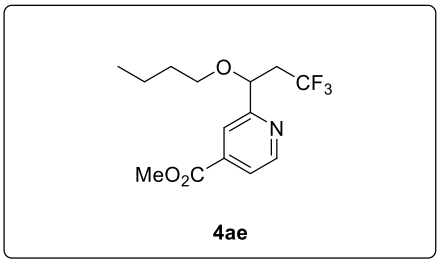
methyl 2-(4,4,4-trifluoro-1-(trimethylsilyl)butan-2-yl)isonicotinate (4ac). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 8 : 1). From allyltrimethylsilane (22.8 mg, 0.2 mmol), compound **4ac** (56.1 mg, 88%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.71 (d, *J* = 4.8 Hz, 1H), 7.69 (d, *J* = 4.6 Hz, 2H), 3.96 (s, 3H), 3.33 – 3.30 (m, 1H), 2.82 – 2.79 (m, 1H), 2.42 – 2.38 (m, 1H), 1.21 (dd, *J* = 14.6, 10.0 Hz, 1H), 1.01 (dd, *J* = 14.7, 5.3 Hz, 1H), -0.19 (s, 9H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 165.6, 164.8, 150.3, 137.8, 126.4 (q, *J* = 277.7 Hz), 121.8, 121.0, 52.7, 42.0 (q, *J* = 26.8 Hz), 38.1 (q, *J* = 2.5 Hz), 24.4, -1.4. ^{19}F NMR (564 MHz,

Chloroform-*d*) δ -64.1 (t, *J* = 10.9 Hz). HRMS (EI) Calcd for $C_{14}H_{20}F_3NO_2Si$: [M] = 319.1215. Found: 319.1212.



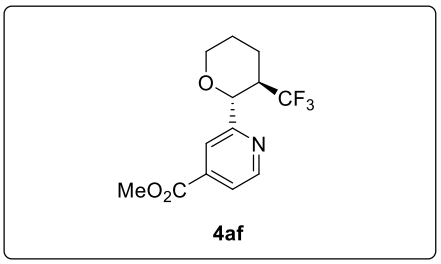
4ad

methyl 2-(1,1,1-trifluoro-7-hydroxyheptan-3-yl)isonicotinate (4ad). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 1 : 1). From hex-5-en-1-ol (20.0 mg, 0.2 mmol), compound **4ad** (41.5 mg, 68%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.72 (d, *J* = 4.9 Hz, 1H), 7.70 (dd, *J* = 5.1, 1.6 Hz, 1H), 7.68 (s, 1H), 3.96 (s, 3H), 3.58 – 3.56 (m, 2H), 3.17 – 3.14 (m, 1H), 2.80 – 2.78 (m, 1H), 2.44 – 2.41 (m, 1H), 1.85 – 1.82 (m, 1H), 1.76 – 1.74 (m, 1H), 1.55 – 1.49 (m, 2H), 1.29 – 1.26 (m, 1H), 1.11 – 1.10 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 165.6, 163.3, 150.4, 137.8, 126.6 (q, *J* = 277.4 Hz), 122.4, 121.0, 62.5, 52.7, 41.6 (d, *J* = 2.5 Hz), 38.7 (q, *J* = 27.6 Hz), 35.5, 32.4, 23.3. ^{19}F NMR (564 MHz, Chloroform-*d*) δ -64.1 (t, *J* = 11.0 Hz). HRMS (EI) Calcd for $C_{14}H_{18}F_3NO_3$: [M] = 305.1239 Found: 305.1240.



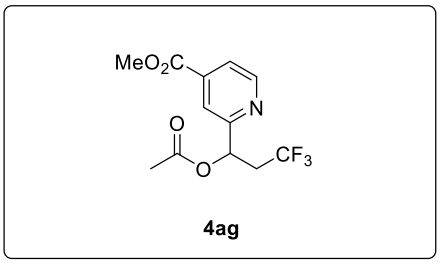
4ae

methyl 2-(1-butoxy-3,3,3-trifluoropropyl)isonicotinate (4ae). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 6 : 1). From 1-(vinyloxy)butane (20.0 mg, 0.2 mmol), compound **4ae** (50.6 mg, 83%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.74 (d, *J* = 4.8 Hz, 1H), 8.00 (s, 1H), 7.79 (d, *J* = 5.0 Hz, 1H), 4.76 (dd, *J* = 8.2, 4.5 Hz, 1H), 3.98 (s, 3H), 3.44 (t, *J* = 6.5 Hz, 2H), 2.64 – 2.62 (m, 2H), 1.60 – 1.58 (m, 2H), 1.42 – 1.38 (m, 2H), 0.91 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 165.5, 161.5, 150.3, 138.4, 125.8 (q, *J* = 277.4 Hz), 122.2, 119.9, 77.1 (q, *J* = 3.1 Hz), 69.9, 52.8, 40.3 (q, *J* = 28.0 Hz), 31.7, 19.1, 13.7. ^{19}F NMR (564 MHz, Chloroform-*d*) δ -63.5 (t, *J* = 10.5 Hz). HRMS (FAB) Calcd for $C_{14}H_{18}F_3NO_3$: [M] + H^+ = 306.1317. Found: 306.1320.



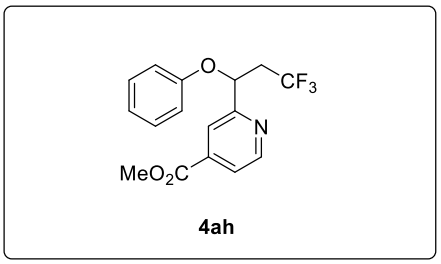
4af

methyl 2-((2R,3R)-3-(trifluoromethyl)tetrahydro-2H-pyran-2-yl)isonicotinate (4af). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 6 : 1). From 3,4-dihydro-2H-pyran (16.8 mg, 0.2 mmol), compound **4af** (46.8 mg, 81%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.78 (d, *J* = 5.0 Hz, 1H), 7.89 (s, 1H), 7.80 (d, *J* = 5.0 Hz, 1H), 4.57 (d, *J* = 9.5 Hz, 1H), 4.12 (d, *J* = 11.2 Hz, 1H), 3.96 (s, 3H), 3.60 (t, *J* = 11.5 Hz, 1H), 2.91 – 2.88 (m, 1H), 2.25 – 2.23 (m, 1H), 1.89 – 1.86 (m, 1H), 1.82 – 1.79 (m, 2H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 165.4, 159.4, 150.3, 138.1, 126.1 (q, *J* = 279.9 Hz), 122.6, 122.0 , 79.7, 68.2, 52.7, 44.1 (q, *J* = 24.7 Hz), 24.1, 22.9 (q, *J* = 2.9 Hz). ^{19}F NMR (564 MHz, Chloroform-*d*) δ -68.4 (d, *J* = 8.2 Hz). HRMS (EI) Calcd for $C_{13}H_{14}F_3NO_3$: [M] = 289.0926. Found: 289.0929.



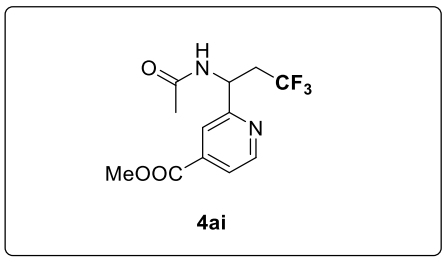
4ag

methyl 2-(1-acetoxy-3,3,3-trifluoropropyl)isonicotinate (4ag). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 6 : 1). From vinyl acetate (17.2 mg, 0.2 mmol), compound **4ag** (41.9 mg, 72%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.76 (d, *J* = 4.9 Hz, 1H), 7.91 (s, 1H), 7.82 (d, *J* = 4.8 Hz, 1H), 6.24 (dd, *J* = 8.3, 4.4 Hz, 1H), 3.97 (s, 3H), 2.92 – 2.87 (m, 2H), 2.17 (s, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 169.7, 165.1, 158.1, 150.4, 138.5, 125.4 (q, *J* = 277.8 Hz), 122.7, 120.6, 69.7 (q, *J* = 3.2 Hz), 52.8, 38.1 (q, *J* = 28.8 Hz), 20.8. ^{19}F NMR (564 MHz, Chloroform-*d*) δ -63.8 (d, *J* = 10.3 Hz). HRMS (ESI) Calcd for $C_{12}H_{12}F_3NO_4$: [M] + Na^+ = 314.0611. Found: 314.0606.



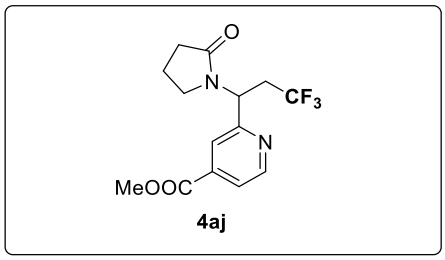
4ah

methyl 2-(3,3,3-trifluoro-1-phenoxypropyl)isonicotinate (4ah). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 6 : 1). From (vinyloxy)benzene (24.0 mg, 0.2 mmol), compound **4ah** (49.4 mg, 76%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.76 (d, *J* = 4.9 Hz, 1H), 7.91 (s, 1H), 7.82 (d, *J* = 4.8 Hz, 1H), 6.24 (dd, *J* = 8.3, 4.4 Hz, 1H), 3.97 (s, 3H), 2.92 – 2.87 (m, 2H), 2.17 (s, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 169.7, 165.1, 158.1, 150.4, 138.5, 125.4 (q, *J* = 277.8 Hz), 122.7, 120.6, 69.7 (q, *J* = 3.2 Hz), 52.8, 38.1 (q, *J* = 28.8 Hz), 20.8. ^{19}F NMR (564 MHz, Chloroform-*d*) δ -63.8 (d, *J* = 10.3 Hz). HRMS (ESI) Calcd for $C_{16}H_{14}F_3NO_3$: [M] + Na^+ = 348.0818. Found: 348.0822.



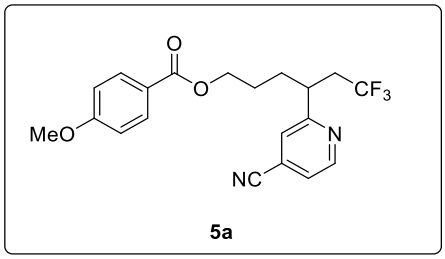
4ai

methyl 2-(1-acetamido-3,3,3-trifluoropropyl)isonicotinate (4ai). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 4 : 1). From N-vinylacetamide (17.0 mg, 0.2 mmol), compound **4ai** (41.2mg, 71%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.72 (d, *J* = 4.8 Hz, 1H), 7.86 (s, 1H), 7.80 (d, *J* = 4.9 Hz, 1H), 6.65 (d, *J* = 8.1 Hz, 1H), 5.50 (q, *J* = 7.2 Hz, 1H), 3.96 (s, 3H), 2.79 – 2.74 (m, 2H), 2.03 (s, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 169.3, 165.1, 158.9, 150.3, 138.5, 125.5 (q, *J* = 277.5 Hz), 122.4, 121.6, 52.8, 48.9 (q, *J* = 3.0 Hz), 38.8 (q, *J* = 27.6 Hz), 23.2. ^{19}F NMR (564 MHz, Chloroform-*d*) δ -63.1 (t, *J* = 10.5 Hz). HRMS (EI) Calcd for $C_{12}H_{13}F_3N_2O_3$: [M] = 290.0878. Found: 290.0877.



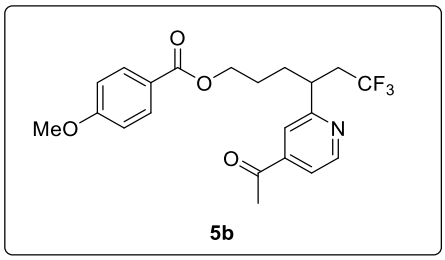
4aj

methyl 2-(3,3,3-trifluoro-1-(2-oxopyrrolidin-1-yl)propyl)isonicotinatee (4aj). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 4 : 1). From 1-vinylpyrrolidin-2-one (22.2 mg, 0.2 mmol), compound **4aj** (51.8 mg, 82%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-d) δ 8.69 (d, *J* = 5.1 Hz, 1H), 7.85 (s, 1H), 7.79 (d, *J* = 4.6 Hz, 1H), 5.81 – 5.78 (m, 1H), 3.94 (s, 3H), 3.47 – 3.45 (m, 1H), 3.17 – 3.14 (m, 1H), 3.08 – 3.05 (m, 1H), 2.95 – 2.91 (m, 1H), 2.44 – 2.38 (m, 2H), 2.04 – 2.02 (m, 1H), 1.95 – 1.93 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.9, 165.2, 157.7, 149.8, 138.7, 126.1 (q, *J* = 277.0 Hz), 122.3, 122.0, 52.8, 50.2 (d, *J* = 3.3 Hz), 43.1, 33.3 (q, *J* = 28.5 Hz), 30.9, 18.2. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.5 (t, *J* = 10.4 Hz). HRMS (EI) Calcd for $C_{14}H_{15}F_3N_2O_3$: [M] = 316.1035. Found: 316.1034.



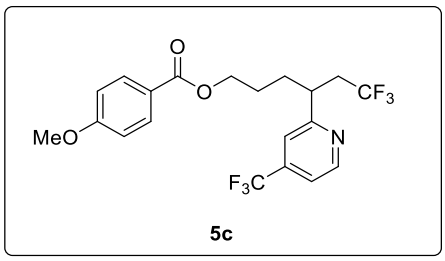
5a

4-(4-cyanopyridin-2-yl)-6,6,6-trifluorohexyl 4-methoxybenzoate (5a). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 6 : 1). From 4-methoxyphenyl hex-5-enoate (44.0 mg, 0.2 mmol), compound **5a** (66.6 mg, 85%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.77 (d, *J* = 4.9 Hz, 1H), 7.96 (d, *J* = 8.5 Hz, 2H), 7.40 (d, *J* = 4.9 Hz, 1H), 7.38 (s, 1H), 6.92 (d, *J* = 8.5 Hz, 2H), 4.24 (t, *J* = 6.5 Hz, 2H), 3.87 (s, 3H), 3.21 – 3.18 (m, 1H), 2.86 – 2.80 (m, 1H), 2.48 – 2.44 (m, 1H), 1.97 – 1.94 (m, 1H), 1.90 – 1.88 (m, 1H), 1.70 – 1.67 (m, 1H), 1.50 – 1.47 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.2, 163.4, 150.8, 131.5, 126.4 (q, *J* = 277.2 Hz), 124.8, 123.5, 122.5, 120.9, 116.3, 113.6, 63.8, 55.4, 41.3 (q, *J* = 2.5 Hz), 38.5 (q, *J* = 27.8 Hz), 32.0, 26.3. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.1 (t, *J* = 10.7 Hz). HRMS (EI) Calcd for $C_{20}H_{19}F_3N_2O_3$: [M] = 392.1348. Found: 392.1346.



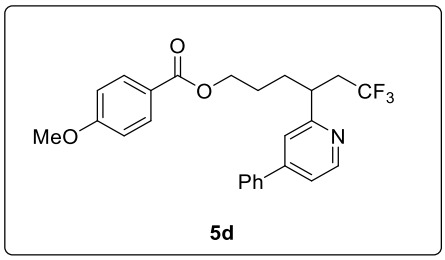
5b

4-(4-acetylpyridin-2-yl)-6,6,6-trifluorohexyl 4-methoxybenzoate (5b). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 6 : 1). From 4-methoxyphenyl hex-5-enoate (44.0 mg, 0.2 mmol), compound **5b** (63.0 mg, 77%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.77 (d, *J* = 4.9 Hz, 1H), 7.95 (d, *J* = 8.5 Hz, 2H), 7.60 – 7.58 (m, 2H), 6.91 (d, *J* = 8.4 Hz, 2H), 4.22 (t, *J* = 6.5 Hz, 2H), 3.86 (s, 3H), 3.24 – 3.22 (m, 1H), 2.85 – 2.81 (m, 1H), 2.62 (s, 3H), 2.48 – 2.45 (m, 1H), 1.98 – 1.96 (m, 1H), 1.91 – 1.89 (m, 1H), 1.69 – 1.66 (m, 1H), 1.51 – 1.49 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 197.3, 166.2, 163.4, 163.2, 150.9, 143.4, 131.5, 126.6 (q, *J* = 277.2 Hz), 122.6, 120.7, 119.7, 113.6, 64.0, 55.4, 41.4 (d, *J* = 2.5 Hz), 38.7 (q, *J* = 27.7 Hz), 32.1, 26.7, 26.4. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.0 (t, *J* = 10.9 Hz). HRMS (EI) Calcd for $C_{21}H_{22}F_3NO_4$: [M] = 409.1501. Found: 409.1505.



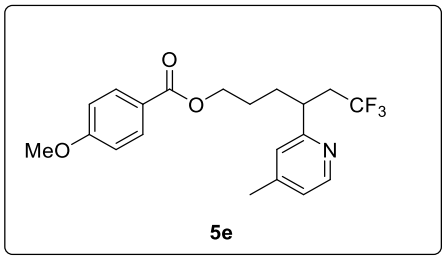
5c

6,6,6-trifluoro-4-(4-(trifluoromethyl)pyridin-2-yl)hexyl 4-methoxybenzoate (5c). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 6 : 1). From 4-methoxyphenyl hex-5-enoate (44.0 mg, 0.2 mmol), compound **5c** (74.0 mg, 85%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.77 (d, *J* = 5.0 Hz, 1H), 7.96 (d, *J* = 8.7 Hz, 2H), 7.40 (d, *J* = 4.9 Hz, 1H), 7.37 (s, 1H), 6.92 (d, *J* = 8.7 Hz, 2H), 4.24 (t, *J* = 6.5 Hz, 2H), 3.86 (s, 3H), 3.24 – 3.21 (m, 1H), 2.87 – 2.81 (m, 1H), 2.49 – 2.46 (m, 1H), 1.99 – 1.97 (m, 1H), 1.92 – 1.89 (m, 1H), 1.71 – 1.67 (m, 1H), 1.53 – 1.49 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.2, 163.4, 163.4, 150.7, 138.8 (q, *J* = 34.1 Hz), 131.5, 126.5 (q, *J* = 277.8 Hz), 126.7 (q, *J* = 274.8 Hz), 122.6, 118.8, 117.7, 113.6, 64.0, 55.4, 41.4 (d, *J* = 2.8 Hz), 38.6 (q, *J* = 27.8 Hz), 32.1, 26.3. ^{19}F NMR (564 MHz, Chloroform-*d*) δ -64.1 (t, *J* = 10.9 Hz), -64.8. HRMS (EI) Calcd for $C_{20}H_{19}F_6NO_3$: [M] = 435.1269. Found: 435.1272.



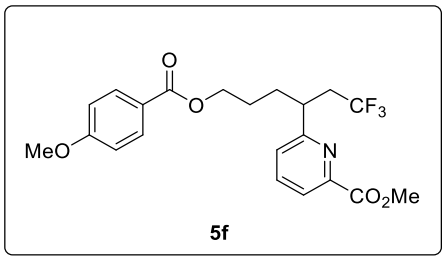
5d

6,6,6-trifluoro-4-(4-phenylpyridin-2-yl)hexyl 4-methoxybenzoate (5d). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 6 : 1). From 4-methoxyphenyl hex-5-enoate (44.0 mg, 0.2 mmol), compound **5d** (53.6 mg, 61%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.63 (d, *J* = 5.1 Hz, 1H), 7.97 (d, *J* = 8.8 Hz, 2H), 7.64 (d, *J* = 6.7 Hz, 2H), 7.49 (t, *J* = 7.3 Hz, 2H), 7.45 (t, *J* = 7.3 Hz, 1H), 7.39 (d, *J* = 5.1 Hz, 1H), 7.37 (s, 1H), 6.90 (d, *J* = 8.9 Hz, 2H), 4.26 (t, *J* = 6.5 Hz, 2H), 3.85 (s, 3H), 3.22 – 3.19 (m, 1H), 2.90 – 2.84 (m, 1H), 2.51 – 2.46 (m, 1H), 2.04 – 2.01 (m, 1H), 1.95 – 1.91 (m, 1H), 1.73 – 1.69 (m, 1H), 1.60 – 1.56 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.2, 163.3, 162.1, 150.1, 148.9, 138.1, 131.5, 129.1, 127.0, 126.8 (q, *J* = 277.3 Hz), 122.7, 121.3, 120.0, 113.6, 64.2, 55.4, 41.3 (q, *J* = 2.5 Hz), 38.8 (q, *J* = 27.5 Hz), 32.0, 26.4. ^{19}F NMR (564 MHz, Chloroform-*d*) δ -64.0 (t, *J* = 11.0 Hz). HRMS (EI) Calcd for $C_{25}H_{24}F_3NO_3$: [M] = 443.1708. Found: 443.1711.



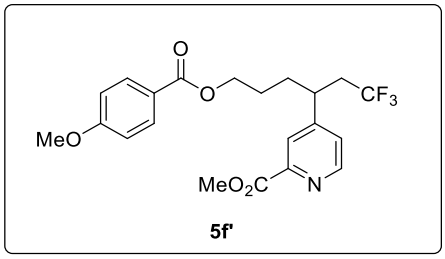
5e

6,6,6-trifluoro-4-(4-methylpyridin-2-yl)hexyl 4-methoxybenzoate (5e). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 5 : 1). From 4-methoxyphenyl hex-5-enoate (44.0 mg, 0.2 mmol), compound **5e** (38.1 mg, 50%) was obtained. White solid. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.43 (d, *J* = 4.9 Hz, 1H), 7.97 (d, *J* = 8.5 Hz, 2H), 6.97 (d, *J* = 5.1 Hz, 1H), 6.95 (s, 1H), 6.91 (d, *J* = 8.5 Hz, 2H), 4.22 (t, *J* = 6.5 Hz, 2H), 3.86 (s, 3H), 3.06 – 3.04 (m, 1H), 2.80 – 2.78 (m, 1H), 2.44 – 2.41 (m, 1H), 2.33 (s, 3H), 1.96 – 1.93 (m, 1H), 1.88 – 1.86 (m, 1H), 1.65 – 1.63 (m, 1H), 1.52 – 1.50 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.3, 163.3, 161.4, 149.4, 147.5, 131.5, 126.8 (q, *J* = 277.2 Hz), 124.3, 122.9, 122.7, 113.6, 64.2, 55.4, 41.0 (d, *J* = 2.9 Hz), 38.8 (q, *J* = 27.6 Hz), 32.0, 26.4, 21.0. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.1 (t, *J* = 10.9 Hz), HRMS (ESI) Calcd for $C_{20}H_{22}F_3NO_3$: [M] + Na^+ = 404.1444. Found: 404.1442.



5f

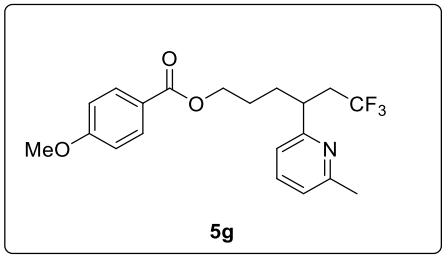
methyl 6-(1,1,1-trifluoro-6-((4-methoxybenzoyl)oxy)hexan-3-yl)picolinate (5f). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 4 : 1). From 4-methoxyphenyl hex-5-enoate (44.0 mg, 0.2 mmol), compound **5f** (18.7 mg, 22%) (minor) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 7.97 (d, *J* = 7.7 Hz, 1H), 7.95 (d, *J* = 8.9 Hz, 2H), 7.76 (t, *J* = 7.7 Hz, 1H), 7.32 (d, *J* = 7.7 Hz, 1H), 6.91 (d, *J* = 8.9 Hz, 2H), 4.22 (t, *J* = 6.5 Hz, 2H), 3.98 (s, 3H), 3.86 (s, 3H), 3.24 – 3.22 (m, 1H), 2.93 – 2.87 (m, 1H), 2.51 – 2.46 (m, 1H), 2.03 – 1.99 (m, 1H), 1.93 – 1.89 (m, 1H), 1.69 – 1.66 (m, 1H), 1.54 – 1.50 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.2, 165.8, 163.3, 162.2, 148.2, 137.2, 131.5, 126.7 (q, *J* = 277.2 Hz), 126.3, 123.4, 122.6, 113.6, 64.1, 55.4, 52.7, 41.2 (d, *J* = 2.6 Hz), 38.6 (q, *J* = 27.6 Hz), 31.9, 26.4. ^{19}F NMR (564 MHz, Chloroform-d) δ -63.9 (t, *J* = 11.0 Hz). HRMS (EI) Calcd for $C_{21}H_{22}F_3NO_5$: [M] = 425.1450. Found: 425.1449.



5f'

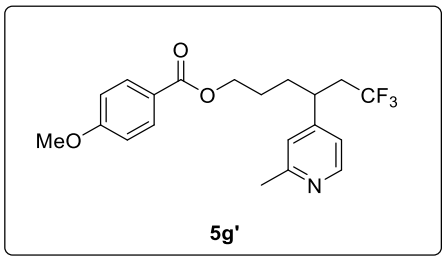
methyl 4-(1,1,1-trifluoro-6-((4-methoxybenzoyl)oxy)hexan-3-yl)picolinate (5f'). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 2 : 1). From 4-methoxyphenyl hex-5-enoate (44.0 mg, 0.2 mmol), compound **5f'** (47.6 mg, 56%) (major) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.68 (d, *J* = 4.9 Hz, 1H), 7.99 (s, 1H), 7.93 (d, *J* = 8.9 Hz, 2H), 7.30 (d, *J* = 4.8 Hz, 1H), 6.90 (d, *J* = 8.9 Hz, 2H), 4.21 (t, *J* = 6.4 Hz, 2H), 4.00 (s, 3H), 3.84 (s, 3H), 3.08 – 3.06 (m, 1H), 2.51 – 2.47 (m, 2H), 1.96 – 1.92 (m, 1H), 1.83 – 1.79 (m, 1H), 1.66 – 1.61 (m, 1H), 1.53 – 1.48 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.1, 165.5, 163.4, 153.2, 150.2, 148.5, 131.5, 126.1, 125.9 (q, *J* = 277.5 Hz), 123.8, 122.4, 113.6, 63.6, 55.4, 52.9, 39.7 (q, *J* = 27.9 Hz), 39.2 (d, *J* =

2.4 Hz), 32.3, 26.3. ^{19}F NMR (564 MHz, Chloroform-d) δ -63.7 (t, *J* = 10.5 Hz). HRMS (EI) Calcd for $C_{21}H_{22}F_3NO_5$: [M] = 425.1450. Found: 425.1445.



5g

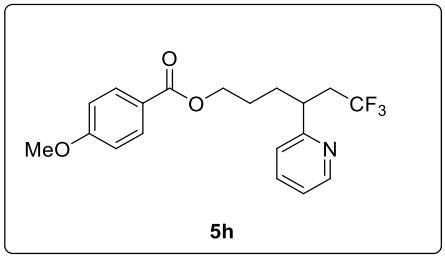
6,6,6-trifluoro-4-(6-methylpyridin-2-yl)hexyl 4-methoxybenzoate (5g). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 5 : 1). From 4-methoxyphenyl hex-5-enoate (44.0 mg, 0.2 mmol), compound **5g** (24.3 mg, 32%) (major) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 7.97 (d, *J* = 8.9 Hz, 2H), 7.48 (t, *J* = 7.6 Hz, 1H), 6.99 (d, *J* = 7.6 Hz, 1H), 6.93 – 6.91 (m, 3H), 4.22 (t, *J* = 6.6 Hz, 2H), 3.86 (s, 3H), 3.08 – 3.06 (m, 1H), 2.82 – 2.80 (m, 1H), 2.52 (s, 3H), 2.44 – 2.42 (m, 1H), 1.96 – 1.93 (m, 1H), 1.87 – 1.84 (m, 1H), 1.67 – 1.64 (m, 1H), 1.54 – 1.51 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.3, 163.3, 160.9, 158.4, 136.4, 131.5, 126.9 (q, *J* = 277.3 Hz), 122.8, 121.3, 120.0, 113.6, 64.2, 55.4, 41.1 (d, *J* = 2.6 Hz), 38.8 (q, *J* = 27.3 Hz), 31.9, 26.4, 24.6. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.0 (t, *J* = 11.1 Hz). HRMS (EI) Calcd for $C_{20}H_{22}F_3NO_3$: [M] = 381.1552. Found: 381.1553.



5g'

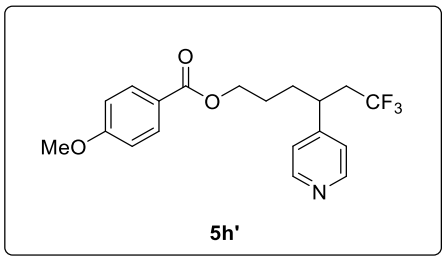
6,6,6-trifluoro-4-(2-methylpyridin-4-yl)hexyl 4-methoxybenzoate (5g'). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 2 : 1). From 4-methoxyphenyl hex-5-enoate (44.0 mg, 0.2 mmol), compound **5g'** (16.0 mg, 21%) (minor) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.44 (d, *J* = 5.1 Hz, 1H), 7.96 (d, *J* = 8.5 Hz, 2H), 6.98 (s, 1H), 6.93 – 6.91 (m, 3H), 4.23 (t, *J* = 6.4 Hz, 2H), 3.86 (s, 3H), 2.94 – 2.92 (m, 1H), 2.55 (s, 3H), 2.45 – 2.42 (m, 2H), 1.90 – 1.88 (m, 1H), 1.78 – 1.74 (m, 1H), 1.65 – 1.62 (m, 1H), 1.56 – 1.53 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.2, 163.4, 159.0, 151.9, 149.6, 131.5, 122.6, 122.3, 119.7, 113.6, 63.8, 55.4, 39.9

(q, *J* = 27.7 Hz), 39.1 (q, *J* = 2.6 Hz), 32.2, 26.4, 24.4. ^{19}F NMR (564 MHz, Chloroform-d) δ -63.7 (t, *J* = 10.6 Hz). HRMS (EI) Calcd for $C_{20}H_{22}F_3NO_3$: [M] = 381.1552. Found: 381.1548.



5h

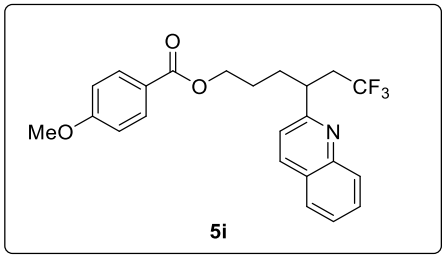
6,6,6-trifluoro-4-(pyridin-2-yl)hexyl 4-methoxybenzoate (5h). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 5 : 1). From 4-methoxyphenyl hex-5-enoate (44.0 mg, 0.2 mmol), compound **5h** (34.1 mg, 47%) (major) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.59 (d, *J* = 4.0 Hz, 1H), 7.96 (d, *J* = 8.8 Hz, 2H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.17 – 7.14 (m, 2H), 6.91 (d, *J* = 8.9 Hz, 2H), 4.22 (t, *J* = 6.5 Hz, 2H), 3.86 (s, 3H), 3.13 – 3.10 (m, 1H), 2.84 – 2.78 (m, 1H), 2.46 – 2.41 (m, 1H), 1.98 – 1.94 (m, 1H), 1.90 – 1.87 (m, 1H), 1.67 – 1.63 (m, 1H), 1.53 – 1.49 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.2, 163.3, 161.6, 149.8, 136.4, 131.5, 126.7 (q, *J* = 277.3 Hz), 123.4, 122.7, 121.9, 113.6, 64.2, 55.4, 41.2 (d, *J* = 2.6 Hz), 38.8 (q, *J* = 27.5 Hz), 32.0, 26.4. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.1 (t, *J* = 11.1 Hz). HRMS (EI) Calcd for $C_{19}H_{20}F_3NO_3$: [M] = 367.1395. Found: 367.1394.



5h'

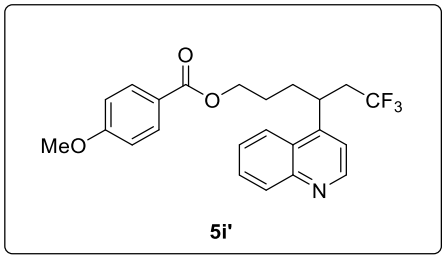
6,6,6-trifluoro-4-(pyridin-4-yl)hexyl 4-methoxybenzoate (5h'). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 2 : 1). From 4-methoxyphenyl hex-5-enoate (44.0 mg, 0.2 mmol), compound **5h'** (18.0 mg, 25%) (minor) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.57 (d, *J* = 5.0 Hz, 2H), 7.96 (d, *J* = 8.9 Hz, 2H), 7.13 (d, *J* = 6.1 Hz, 2H), 6.93 (d, *J* = 8.9 Hz, 2H), 4.24 (t, *J* = 6.4 Hz, 2H), 3.87 (s, 3H), 3.00 – 2.97 (m, 1H), 2.48 – 2.45 (m, 2H), 1.95 – 1.91 (m, 1H), 1.80 – 1.77 (m, 1H), 1.65 – 1.62 (m, 1H), 1.57 – 1.53 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.2, 163.5, 151.6, 150.3, 131.5, 126.1 (q, *J* = 277.8 Hz), 122.7, 122.5, 113.7, 63.8,

55.4, 40.0 (q, *J* = 27.8 Hz), 39.2 (q, *J* = 2.5 Hz), 32.3, 26.4. ^{19}F NMR (564 MHz, Chloroform-d) δ -63.7 (t, *J* = 10.6 Hz). HRMS (EI) Calcd for $C_{19}H_{20}F_3NO_3$: [M] = 367.1395. Found: 367.1391.



5i

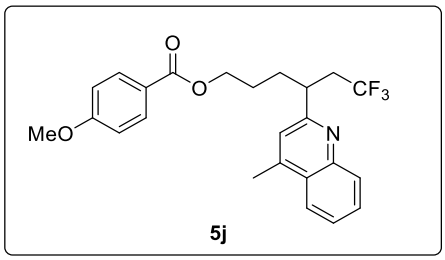
6,6,6-trifluoro-4-(quinolin-2-yl)hexyl 4-methoxybenzoate (5i). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 5 : 1). From 4-methoxyphenyl hex-5-enoate (44.0 mg, 0.2 mmol), compound **5i** (35.9 mg, 43%) (major) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.11 (d, *J* = 8.4 Hz, 1H), 8.06 (d, *J* = 8.4 Hz, 1H), 7.95 (d, *J* = 8.9 Hz, 2H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.71 (t, *J* = 7.7 Hz, 1H), 7.52 (t, *J* = 7.8 Hz, 1H), 7.29 (d, *J* = 8.4 Hz, 1H), 6.90 (d, *J* = 8.9 Hz, 2H), 4.24 (t, *J* = 6.5 Hz, 2H), 3.86 (s, 3H), 3.36 – 3.34 (m, 1H), 3.04 – 2.99 (m, 1H), 2.57 – 2.53 (m, 1H), 2.10 – 2.08 (m, 1H), 2.00 – 1.98 (m, 1H), 1.74 – 1.71 (m, 1H), 1.60 – 1.57 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.2, 163.3, 162.1, 148.1, 136.5, 131.5, 129.4, 129.2, 127.5, 127.1, 126.8 (q, *J* = 277.4 Hz), 126.1, 122.7, 121.3, 113.6, 64.2, 55.4, 41.7 (d, *J* = 2.4 Hz), 38.6 (q, *J* = 27.6 Hz), 32.2, 26.3. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.0 (t, *J* = 11.0 Hz). HRMS (EI) Calcd for $C_{23}H_{22}F_3NO_3$: [M] = 417.1552. Found: 417.1553.



5i'

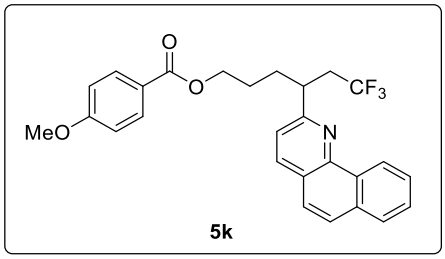
6,6,6-trifluoro-4-(quinolin-4-yl)hexyl 4-methoxybenzoate (5i'). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 1 : 1). From 4-methoxyphenyl hex-5-enoate (44.0 mg, 0.2 mmol), compound **5i'** (30.0 mg, 36%) (minor) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.90 (d, *J* = 4.5 Hz, 1H), 8.17 (d, *J* = 8.4 Hz, 1H), 7.92 (d, *J* = 8.9 Hz, 2H), 7.75 (t, *J* = 7.6 Hz, 1H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 4.6 Hz, 1H), 6.90 (d, *J* = 8.9 Hz, 2H), 4.21 (q, *J* = 6.4 Hz, 2H), 3.98 – 3.96 (m, 1H), 3.85 (s, 3H), 2.62 – 2.59 (m, 2H), 2.13 – 2.11 (m, 1H), 2.01 – 2.01 (m, 1H), 1.66 – 1.64 (m, 1H), 1.58 – 1.55 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.2, 163.4,

150.0, 148.9, 148.7, 131.5, 130.7, 129.4, 127.0, 126.3 (q, *J* = 277.5 Hz), 122.5, 122.3, 113.6, 63.8, 55.4, 39.8 (q, *J* = 28.0 Hz), 32.1, 26.3. ^{19}F NMR (564 MHz, Chloroform-d) δ -63.8 (s). HRMS (EI) Calcd for $C_{23}H_{22}F_3NO_3$: [M] = 417.1552. Found: 417.1550.



5j

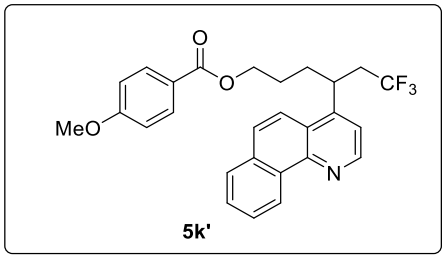
6,6,6-trifluoro-4-(4-methylquinolin-2-yl)hexyl 4-methoxybenzoate (5j). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 5 : 1). From 4-methoxyphenyl hex-5-enoate (44.0 mg, 0.2 mmol), compound **5j** (48.3 mg, 56%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.06 (d, *J* = 8.5 Hz, 1H), 7.98 – 7.95 (m, 3H), 7.70 (t, *J* = 7.5 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.12 (s, 1H), 6.91 (d, *J* = 8.4 Hz, 2H), 4.24 (t, *J* = 6.5 Hz, 2H), 3.86 (s, 3H), 3.31 – 3.28 (m, 1H), 3.02 – 2.97 (m, 1H), 2.70 (s, 3H), 2.56 – 2.52 (m, 1H), 2.09 – 2.06 (m, 1H), 1.99 – 1.95 (m, 1H), 1.74 – 1.71 (m, 1H), 1.61 – 1.58 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.2, 163.3, 161.8, 147.9, 144.6, 131.5, 129.8, 129.1, 127.2, 126.9 (q, *J* = 277.3 Hz), 125.8, 123.6, 122.7, 121.9, 113.6, 64.2, 55.4, 41.6 (d, *J* = 2.5 Hz), 38.5 (q, *J* = 27.6 Hz), 32.1, 26.4, 18.7. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.0 (t, *J* = 11.1 Hz). HRMS (EI) Calcd for $C_{24}H_{24}F_3NO_3$: [M] = 431.1708. Found: 431.1710.



5k

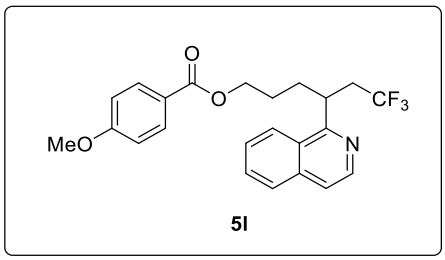
4-(benzo[h]quinolin-2-yl)-6,6,6-trifluorohexyl 4-methoxybenzoate (5k). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 5 : 1). From 4-methoxyphenyl hex-5-enoate (44.0 mg, 0.2 mmol), compound **5k** (48.9 mg, 52.4%) (major) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 9.37 (d, *J* = 8.5 Hz, 1H), 8.12 (d, *J* = 8.0 Hz, 1H), 7.92 (d, *J* = 8.6 Hz, 3H), 7.79 (d, *J* = 8.7 Hz, 1H), 7.75 – 7.68 (m, 3H), 7.40 (d, *J* = 8.1 Hz, 1H), 6.84 (d, *J* = 8.8 Hz, 2H), 4.26 (t, *J* = 6.1 Hz, 2H), 3.84 (s, 3H), 3.43 – 3.40 (m, 1H), 3.17 – 3.12 (m, 1H), 2.67 – 2.62 (m, 1H), 2.26 – 2.22 (m, 1H), 2.07 – 2.01 (m, 1H), 1.78 – 1.73 (m, 1H), 1.63 – 1.59 (m, 1H). ^{13}C NMR (151 MHz,

Chloroform-*d*) δ 166.2, 163.3, 160.6, 146.2, 136.2, 133.8, 131.5, 131.4, 128.1, 127.7, 127.2, 127.0 (q, *J* = 277.4 Hz), 126.8, 125.1, 125.0, 124.5, 122.7, 122.0, 113.5, 64.2, 55.4, 41.6 (d, *J* = 2.5 Hz), 39.1 (q, *J* = 27.4 Hz), 32.5, 26.3. ^{19}F NMR (564 MHz, Chloroform-d) δ -63.8 (t, *J* = 11.1 Hz). HRMS (EI) Calcd for $C_{27}H_{24}F_3NO_3$: [M] = 467.1708. Found: 467.1711.



5k'

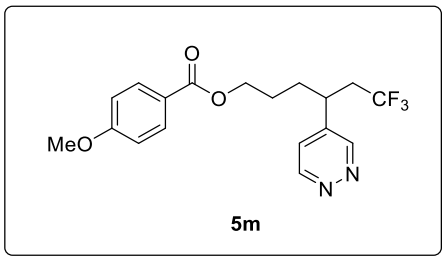
4-(benzo[h]quinolin-4-yl)-6,6,6-trifluorohexyl 4-methoxybenzoate (5k'). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 1 : 1). From 4-methoxyphenyl hex-5-enoate (44.0 mg, 0.2 mmol), compound **5k'** (25.8 mg, 27.6%) (minor) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 9.36 (d, *J* = 8.1 Hz, 1H), 9.00 (d, *J* = 4.6 Hz, 1H), 8.00 (d, *J* = 9.2 Hz, 1H), 7.93 – 7.87 (m, 4H), 7.76 (t, *J* = 7.5 Hz, 1H), 7.72 (t, *J* = 7.3 Hz, 1H), 7.42 (d, *J* = 4.7 Hz, 1H), 6.87 (d, *J* = 8.5 Hz, 2H), 4.23 – 4.21 (m, 2H), 4.06 (s, 1H), 3.84 (s, 3H), 2.66 – 2.63 (m, 2H), 2.16 – 2.14 (m, 1H), 2.03 (s, 1H), 1.68 – 1.66 (m, 1H), 1.59 – 1.54 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.2, 163.4, 148.7, 148.4, 147.0, 133.2, 132.0, 131.5, 128.4, 128.2, 127.6, 127.3, 126.3 (q, *J* = 277.6 Hz), 125.0 , 124.9, 122.5, 119.7, 118.6, 113.6, 63.8, 55.4, 40.0 (q, *J* = 27.8 Hz), 32.3, 26.3. ^{19}F NMR (564 MHz, Chloroform-d) δ -63.7 (s). HRMS (EI) Calcd for $C_{27}H_{24}F_3NO_3$: [M] = 467.1708. Found: 467.1707.



5l

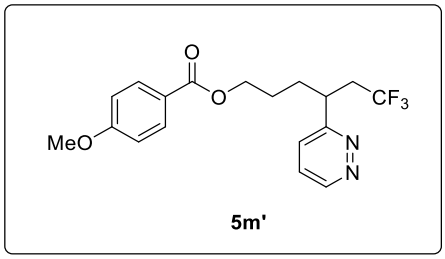
6,6,6-trifluoro-4-(isoquinolin-1-yl)hexyl 4-methoxybenzoate (5l). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 4 : 1). From 4-methoxyphenyl hex-5-enoate (44.0 mg, 0.2 mmol), compound **5l** (45.7 mg, 55%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.52 (d, *J* = 5.6 Hz, 1H), 8.22 (d, *J* = 8.6 Hz, 1H), 7.93 (d, *J* = 8.4 Hz, 2H), 7.86 (d, *J* = 8.2 Hz, 1H), 7.70 (t, *J* = 7.6 Hz, 1H), 7.62 (t, *J* = 7.7 Hz, 1H), 7.56 (d, *J* = 5.7 Hz, 1H), 6.90 (d, *J* = 8.4 Hz, 2H), 4.21 – 4.15 (m, 3H), 3.85 (s, 3H), 3.13 – 3.07 (m, 1H), 2.62 – 2.59 (m, 1H), 2.19 – 2.14

(m, 1H), 2.04 – 2.01 (m, 1H), 1.69 – 1.66 (m, 1H), 1.52 – 1.49 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.2, 163.3, 161.5, 141.8, 136.5, 131.5, 130.0, 127.7, 127.5, 127.1, 126.9 (q, *J* = 277.8 Hz), 122.7, 119.7, 113.5, 64.1, 55.4, 38.5 (q, *J* = 27.6 Hz), 34.8, 32.3, 26.3. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.3 (t, *J* = 11.1 Hz). HRMS (EI) Calcd for $C_{23}H_{22}F_3NO_3$: [M] = 417.1552. Found: 417.1550.



5m

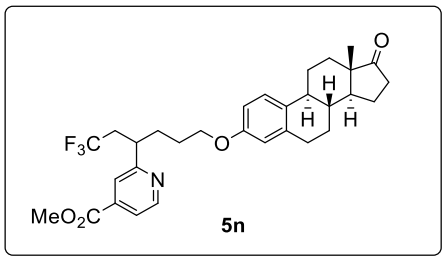
6,6,6-trifluoro-4-(pyridazin-4-yl)hexyl 4-methoxybenzoate (5m). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 1 : 1). From 4-methoxyphenyl hex-5-enoate (44.0 mg, 0.2 mmol), compound **5m** (54.5 mg, 74%) (major) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 9.15 (d, *J* = 5.2 Hz, 1H), 9.11 (s, 1H), 7.94 (d, *J* = 7.9 Hz, 2H), 7.32 (d, *J* = 6.5 Hz, 1H), 6.92 (d, *J* = 7.9 Hz, 2H), 4.25 (t, *J* = 6.4 Hz, 2H), 3.86 (s, 3H), 3.05 – 3.01 (m, 1H), 2.55 – 2.50 (m, 2H), 1.97 – 1.94 (m, 1H), 1.84 – 1.82 (m, 1H), 1.69 – 1.66 (m, 1H), 1.58 – 1.54 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.12 , 163.49 , 151.55 , 151.21 , 141.93 , 131.51 , 125.78 (q, *J* = 277.4 Hz), 125.01 , 122.28 , 113.68 , 63.44 , 55.42 , 39.32 (q, *J* = 28.3 Hz), 37.15 (d, *J* = 2.7 Hz), 32.12 , 26.32 . ^{19}F NMR (564 MHz, Chloroform-d) δ -64.0 (t, *J* = 10.3 Hz). HRMS (FAB) Calcd for $C_{18}H_{19}F_3N_2O_3$: [M] + H^+ = 369.1426. Found: 369.1424.



5m'

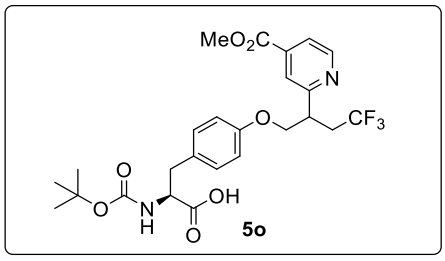
6,6,6-trifluoro-4-(pyridazin-3-yl)hexyl 4-methoxybenzoate (5m'). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 1 : 1). From 4-methoxyphenyl hex-5-enoate (44.0 mg, 0.2 mmol), compound **5m'** (9.6 mg, 13%) (minor) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 9.06 (d, *J* = 4.8 Hz, 1H), 7.90 (d, *J* = 7.0 Hz, 2H), 7.39 – 7.37 (m, 1H), 7.27 (d, *J* = 8.4 Hz, 1H), 6.86 (d, *J* = 8.2 Hz, 2H), 4.19 (t, *J* = 6.3 Hz, 2H), 3.81 (s, 3H), 3.23 – 3.21 (m, 1H), 2.94 –

2.92 (m, 1H), 2.54 – 2.51 (m, 1H), 2.05 – 2.03 (m, 1H), 1.95 – 1.93 (m, 1H), 1.65 – 1.62 (m, 1H), 1.52 – 1.49 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.2, 163.8, 163.4, 150.2, 131.5, 126.6, 126.5, 126.5 (q, *J* = 277.8 Hz), 122.5, 113.6, 63.9, 55.4, 40.3 (d, *J* = 2.2 Hz), 38.6 (q, *J* = 28.2 Hz), 32.1, 26.3. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.0 (t, *J* = 10.9 Hz). HRMS (EI) Calcd for $C_{18}H_{19}F_3N_2O_3$: [M] = 368.1348. Found: 368.1346.



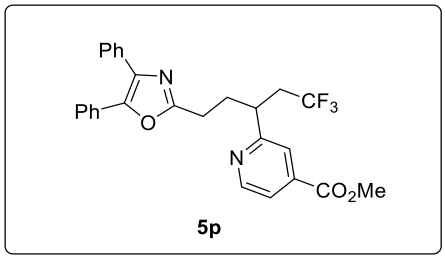
5n

methyl 2-(1,1,1-trifluoro-6-(((8R,9S,13S,14S)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-3-yl)oxy)hexan-3-yl)isonicotinate (5n). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 3 : 1). From (8R,9S,13S,14S)-13-methyl-3-(pent-4-en-1-yloxy)-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one (67.6 mg, 0.2 mmol), compound **5n** (80.4 mg, 74%) was obtained. White solid. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.74 (d, *J* = 6.0 Hz, 1H), 7.72 (d, *J* = 4.5 Hz, 2H), 7.18 (d, *J* = 8.6 Hz, 1H), 6.66 (d, *J* = 8.5 Hz, 1H), 6.60 (s, 1H), 3.97 (s, 3H), 3.87 (t, *J* = 6.2 Hz, 2H), 3.25 – 3.23 (m, 1H), 2.88 – 2.84 (m, 3H), 2.51 – 2.48 (m, 2H), 2.39 (d, *J* = 10.7 Hz, 1H), 2.24 (t, *J* = 8.5 Hz, 1H), 2.16 – 2.13 (m, 1H), 2.08 – 2.05 (m, 1H), 2.00 – 1.94 (m, 4H), 1.69 – 1.66 (m, 1H), 1.62 – 1.57 (m, 2H), 1.53 – 1.49 (m, 4H), 1.45 – 1.41 (m, 1H), 0.91 (s, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 220.8, 165.5, 163.0, 156.8, 150.4, 137.8, 137.7, 132.1, 126.6 (q, *J* = 277.3 Hz), 126.3, 122.5, 121.1, 114.4, 112.0, 67.3, 52.7, 50.4, 48.0 , 43.9, 41.3 (d, *J* = 2.9 Hz), 38.7 (q, *J* = 27.6 Hz), 38.3, 35.8, 32.3, 31.6, 29.6, 26.8, 26.5, 25.9, 21.5, 13.8. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.0 (t, *J* = 10.9 Hz). HRMS (EI) Calcd for $C_{31}H_{36}F_3NO_4$: [M] = 543.2596. Found: 543.2598.



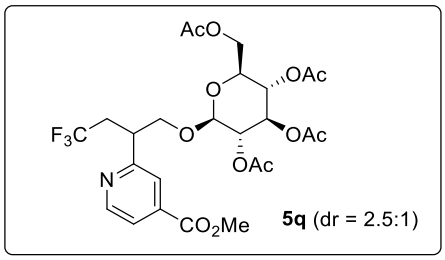
5o

(2S)-2-((tert-butoxycarbonyl)amino)-3-(4-(4,4,4-trifluoro-2-(4-(methoxycarbonyl)pyridin-2-yl)butoxy)phenyl)propanoic acid (5o). Purified by flash column chromatography on silica gel (dichloromethane/MeOH = 10 : 1). From (S)-3-(4-(allyloxy)phenyl)-2-((tert-butoxycarbonyl)amino)propanoic acid (64.2 mg, 0.2 mmol), compound **5o** (61.0 mg, 58%) was obtained. White solid. ^{1}H NMR (599 MHz, Methanol-d_4) δ 8.72 (d, J = 5.2 Hz, 1H), 7.92 (s, 1H), 7.80 (dd, J = 5.0, 1.6 Hz, 1H), 7.10 (d, J = 8.4 Hz, 2H), 6.74 (d, J = 8.2 Hz, 2H), 4.20 – 4.15 (m, 3H), 3.96 (s, 3H), 3.70 – 3.68 (m, 1H), 3.07 (dd, J = 13.7, 4.6 Hz, 1H), 2.96 – 2.92 (m, 1H), 2.84 – 2.78 (m, 2H), 1.36 (s, 9H), 1.27 (s, 1H). ^{13}C NMR (151 MHz, Methanol-d_4) δ 166.9, 162.3, 158.6, 157.4, 151.5, 139.8, 132.5, 131.8, 128.5 (q, J = 276.0 Hz), 124.3, 122.9, 115.6, 115.5, 80.1, 71.6, 53.4, 43.2, 39.1, 35.8 (q, J = 28.4 Hz), 28.9, 28.6. ^{19}F NMR (564 MHz, Chloroform-d) δ -65.4 (t, J = 11.0 Hz). HRMS (EI) Calcd for $C_{25}H_{29}F_3N_2O_7$: [M] + Na^+ = 549.1819. Found: 549.1800.



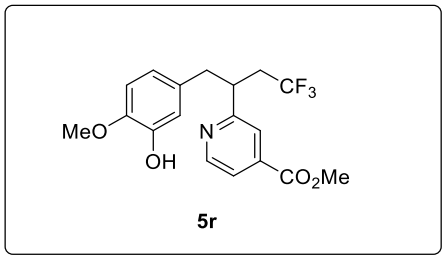
5p

methyl 2-(5-(4,5-diphenyloxazol-2-yl)-1,1,1-trifluoropentan-3-yl)isonicotinate (5p). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 3 : 1). From (2-(but-3-en-1-yl)-4,5-diphenyloxazole (55.0 mg, 0.2 mmol), compound **5p** (49.0 mg, 51%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-d) δ 8.72 (d, J = 5.0 Hz, 1H), 7.74 (s, 1H), 7.69 (d, J = 5.0 Hz, 1H), 7.61 (d, J = 7.3 Hz, 2H), 7.54 (d, J = 7.0 Hz, 2H), 7.37 – 7.32 (m, 6H), 3.90 (s, 3H), 3.37 – 3.34 (m, 1H), 2.91 – 2.88 (m, 1H), 2.74 – 2.69 (m, 2H), 2.55 – 2.51 (m, 1H), 2.44 – 2.42 (m, 1H), 2.36 – 2.34 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-d) δ 165.4, 162.1, 162.1, 150.6, 145.2, 137.8, 135.0, 132.4, 128.9, 128.6, 128.5, 128.4, 128.0, 127.8, 126.5 (q, J = 277.4 Hz), 126.4, 122.7, 121.3, 52.6, 41.1 (d, J = 2.9 Hz), 38.8 (q, J = 27.6 Hz), 32.5, 25.8. ^{19}F NMR (564 MHz, Chloroform-d) δ -64.0 (t, J = 10.9 Hz). HRMS (EI) Calcd for $C_{27}H_{23}F_3N_2O_3$: [M] + Na^+ = 503.1553. Found: 503.1550.



5q (dr = 2.5:1)

(2S,3S,4R,5S,6S)-2-(acetoxymethyl)-6-(4,4,4-trifluoro-2-(4-(methoxycarbonyl)pyridin-2-yl)butoxy)tetrahydro-2H-pyran-3,4,5-triyl triacetate (5q). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 1 : 1). From Allyl-2,3,4,6-tetra-O-acetyl-*β*-D-glucopyranoside (77.6 mg, 0.2 mmol), compound **5q** (88.9 mg, 75%) (dr = 2.5:1) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.67 (d, *J* = 4.3 Hz, 1H), 7.72 – 7.70 (m, 2H), 5.10 (t, *J* = 9.5 Hz, 1H), 5.02 (t, *J* = 9.7 Hz, 1H), 4.88 (dd, *J* = 9.6, 8.0 Hz, 1H), 4.41 (d, *J* = 8.0 Hz, 1H), 4.22 (dd, *J* = 12.3, 4.8 Hz, 1H), 4.09 – 4.04 (m, 2H), 3.93 (s, 3H), 3.77 – 3.73 (m, 1H), 3.65 – 3.63 (m, 1H), 3.46 – 3.44 (m, 1H), 2.76 – 2.72 (m, 1H), 2.53 – 2.49 (m, 1H), 2.06 (s, 3H), 1.98 (s, 3H), 1.94 (s, 3H), 1.79 (s, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 170.5, 170.1, 169.3, 168.8, 165.4, 160.4, 150.1, 137.8, 126.5 (q, *J* = 276.9 Hz), 123.2, 121.4, 100.6, 72.6, 71.8, 71.7, 70.9, 68.3, 61.8, 52.6, 41.7 (d, *J* = 2.5 Hz), 34.7 (q, *J* = 28.5 Hz), 20.6, 20.4, 20.4, 20.2. ^{19}F NMR (564 MHz, Chloroform-*d*) δ -64.1 (t, *J* = 10.8 Hz). *Isomer*: ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.66 (d, *J* = 4.6 Hz, 1H), 7.72 – 7.70 (m, 2H), 5.15 (t, *J* = 9.5 Hz, 1H), 5.02 (t, *J* = 9.7 Hz, 1H), 4.95 (dd, *J* = 9.7, 8.0 Hz, 1H), 4.50 (d, *J* = 7.9 Hz, 1H), 4.18 (dd, *J* = 12.3, 4.8 Hz, 1H), 4.09 – 4.04 (m, 2H), 3.93 (s, 3H), 3.77 – 3.73 (m, 1H), 3.65 – 3.63 (m, 1H), 3.46 – 3.44 (m, 1H), 2.74 – 2.72 (m, 1H), 2.63 – 2.58 (m, 1H), 2.04 (s, 3H), 1.99 (s, 3H), 1.97 (s, 3H), 1.97 (s, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 170.5, 170.1, 169.2, 169.0, 165.4, 160.1, 150.2, 137.9, 126.6 (q, *J* = 276.3 Hz), 122.7, 121.5, 100.9, 72.6, 71.9, 71.8, 71.0, 68.3, 61.8, 52.6, 41.9 (d, *J* = 2.2 Hz), 34.7 (q, *J* = 28.5 Hz), 20.5, 20.4, 20.4, 20.3. ^{19}F NMR (564 MHz, Chloroform-*d*) δ -64.0 (t, *J* = 11.3 Hz). HRMS (EI) Calcd for $C_{25}H_{30}F_3NO_{12}$: [M] + Na^+ = 616.1612. Found: 616.1611.



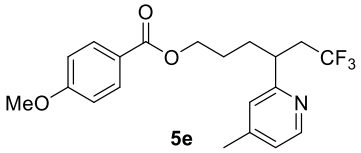
5r

methyl 2-(4,4,4-trifluoro-1-(3-hydroxy-4-methoxyphenyl)butan-2-yl)isonicotinate (5r). Purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 2 : 1). From Eugenol (32.8 mg, 0.2 mmol), compound **5r** (35.4 mg, 48%) was obtained. Colorless oil. ^{1}H NMR (599 MHz, Chloroform-d) δ 8.75 (d, *J* = 5.0 Hz, 1H), 7.69 (dd, *J* = 5.0, 1.6 Hz, 1H), 7.53 (s, 1H), 6.76 (d, *J* = 8.1 Hz, 1H), 6.52 (dd, *J* = 8.0, 1.9 Hz, 1H), 6.46 (d, *J* = 1.9 Hz, 1H), 5.65 (s, 1H), 3.93 (s, 3H), 3.76 (s, 3H), 3.41 – 3.39 (m, 1H), 3.02 – 2.99 (m, 1H), 2.93 – 2.83 (m, 2H), 2.47 – 2.43 (m, 1H). ^{13}C NMR (151 MHz, Chloroform-d) δ 165.5, 162.8, 150.2, 146.4, 144.2, 137.6, 130.3, 126.7 (q, *J* = 277.4 Hz), 122.7, 121.8, 121.0, 114.4, 111.4, 55.8, 52.6, 43.7 (d, *J* = 2.5 Hz), 41.7, 37.5 (q, *J* = 27.7 Hz). ^{19}F NMR (564 MHz,

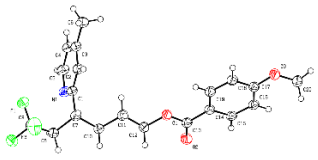
Chloroform-*d*) δ -63.9 (t, *J* = 10.9 Hz). HRMS (EI) Calcd for $C_{18}H_{18}F_3NO_4$: [M] + Na^+ = 392.1080. Found: 392.1077.

VI. Crystallographic Data of 5e

A crystal of **P027_002M** was coated with parabar oil and the diffraction data measured at 100 K with synchrotron radiation (λ = 0.70000 Å) on a Rayonix MX225HS detector at BL2D-SMC with a silicon (111) double crystal monochromator (DCM) at the Pohang Accelerator Laboratory, Korea. The PAL BL2D-SMDC program was used for data collection (detector distance is 66 mm, omega scan; Δω = 1º, exposure time is 1 sec per frame) and HKL3000sm (Ver. 716.7) was used for cell refinement, reduction and absorption correction. The crystal structure of **P027_002M** was solved by SHELX structure solution program and refined by full-matrix least-squares calculations with the SHELXL.



5e



Datablock: P027_002M

Bond precision:	C-C = 0.0021 A		Wavelength=0.70000
Cell:	a=8.3180(17)	b=11.515(2)	c=11.539(2)
	alpha=61.60(3)	beta=78.05(3)	gamma=75.08(3)
Temperature:	100 K		

	Calculated	Reported
Volume	934.8(4)	934.8(4)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C20 H22 F3 N O3	?
Sum formula	C20 H22 F3 N O3	C20 H22 F3 N O3
Mr	381.39	381.38
Dx,g cm-3	1.355	1.355
Z	2	2
Mu (mm-1)	0.105	0.105
F000	400.0	400.0
F000'	400.24	
h,k,lmax	11,15,15	11,15,15
Nref	4732	4586
Tmin,Tmax	0.995,0.996	0.863,1.000
Tmin'	0.995	

Correction method= # Reported T Limits: Tmin=0.863 Tmax=1.000 AbsCorr = EMPIRICAL

Data completeness= 0.969 Theta(max)= 27.998
R(reflections)= 0.0624(3876) wR2(reflections)= 0.1927(4586)
S = 1.125 Npar= 246

VII. Computational Details

All calculations were conducted using DFT[S5] as implemented in Gaussian 09 software[S6] of ab initio quantum chemistry programs with Minnesota functional M06 including Grimme's D3 dispersion correction levels of theory. [S7, S8] Geometry optimization of all species was carried out using the 6-31G** basis set. Frequency analysis was performed to ensure the stationary point as minimum. The orbital energy levels of the optimized structures were reevaluated by additional single point calculations on each geometry using M06 including Grimme's D3 dispersion correction and Dunning's correlation consistent triple-ζ basis set cc-pVTZ.[S9]

- Cartesian coordinates of optimized structures (Å)

1a (alkenyl substrate)

Lowest three frequencies(cm^{-1}): 25.3295, 29.4851, 46.2267

C	3.75546300	-0.64219600	0.01286800
C	3.60668500	0.74620500	0.06357200
C	2.62557800	-1.46755800	-0.03996800
H	4.47214400	1.40030900	0.10411600
H	2.77753400	-2.54284200	-0.07791800
C	2.33091500	1.29165300	0.06090600
C	1.36211000	-0.91183500	-0.04298300
H	2.18946500	2.36873600	0.09980600
H	0.48279200	-1.54840300	-0.08306600
C	1.20114300	0.47860700	0.00782300
O	4.94622400	-1.28070900	0.01134900
C	6.11440700	-0.49510200	0.05495000
H	6.18676600	0.16894100	-0.81751500
H	6.15860500	0.11275000	0.96925800
H	6.95591900	-1.18984000	0.04660800
C	-0.12237900	1.13256300	0.00672600
O	-0.30171100	2.32974100	0.06006500
O	-1.13215800	0.24326500	-0.06225500
C	-2.44373300	0.80899200	-0.06767400
H	-2.53455700	1.50912800	-0.90993600
H	-2.58983700	1.39677400	0.84927100
C	-3.43568600	-0.32210100	-0.17076900
H	-3.23263600	-0.89946300	-1.08423200
H	-3.29554600	-1.01293600	0.67169200
C	-4.87133800	0.19547300	-0.18469300

H	-4.98475500	0.90382600	-1.02145100
H	-5.07305800	0.76711500	0.73341100
C	-5.87037000	-0.90752800	-0.31726800
H	-5.78143100	-1.52675500	-1.21371100
C	-6.81689900	-1.18288800	0.57373400
H	-6.92916800	-0.58828500	1.47964200
H	-7.51645600	-2.00313800	0.43741400

1-methoxy-4-methylpyridinium salt

Lowest three frequencies(cm^{-1}): 48.2023, 96.5337, 105.4065

C	-1.80003500	0.00170300	0.05104800
C	-1.08200500	-1.19986000	-0.04427400
C	0.28256700	-1.18565400	-0.21522000
N	0.91974500	-0.00031000	-0.28547300
C	0.28444300	1.18540300	-0.21569800
C	-1.08055700	1.20158800	-0.04426900
H	-1.59392400	-2.15654100	0.00774700
H	0.91128100	-2.06465300	-0.31590600
H	0.91404900	2.06371800	-0.31694800
H	-1.59087700	2.15897900	0.00776300
C	-3.27290400	0.00041700	0.26097400
H	-3.49361100	-0.08790800	1.33272800
H	-3.73397000	0.92570900	-0.09328000
H	-3.74985600	-0.84839300	-0.23697400
O	2.26401000	-0.00143300	-0.53229200
C	3.02047700	0.00001400	0.69661400
H	2.80745700	0.90253300	1.28005600
H	2.80607700	-0.90023900	1.28302800
H	4.06116400	-0.00123000	0.37338700

Trifluoromethyl radical

Lowest three frequencies(cm^{-1}): 512.7667, 512.8168, 710.0702

C	0.00000000	0.00000000	0.32773500
F	0.00000000	1.25208200	-0.07283000
F	1.08433500	-0.62604100	-0.07283000
F	-1.08433500	-0.62604100	-0.07283000

A (alkyl radical intermediate)

Lowest three frequencies(cm^{-1}): 22.0838, 28.5634, 33.6473

C	5.52786800	-0.89695100	-0.00006800
C	5.55196900	0.49642800	-0.10205800
C	4.30452400	-1.57347300	0.08410600
H	6.49108800	1.03661200	-0.17104100

H	4.32212300	-2.65718300	0.16065700
C	4.35410700	1.19653200	-0.11378100
C	3.12023000	-0.86503300	0.07036500
H	4.34551000	2.28094500	-0.18995700
H	2.17007400	-1.38697300	0.13735600
C	3.13249700	0.53210300	-0.02823000
O	6.62891800	-1.67902800	0.02672900
C	7.88800100	-1.05441000	-0.06448300
H	8.00840200	-0.52546200	-1.02007700
H	8.04823600	-0.34450000	0.75857900
H	8.63297800	-1.84923200	0.00000700
C	1.90145300	1.34569900	-0.04222400
O	1.87106600	2.55443100	-0.12035300
O	0.78745300	0.59096500	0.04424400
C	-0.44116100	1.31731200	0.04503900
H	-0.52291800	1.89708800	-0.88511100
H	-0.43537300	2.04243000	0.87071800
C	-1.56344100	0.32028500	0.18515600
H	-1.51955500	-0.40025600	-0.64268400
H	-1.42018400	-0.25630000	1.10984600
C	-2.92395800	1.00239200	0.20776100
H	-3.06302900	1.59485300	-0.71465200
H	-2.93911300	1.75468500	1.02187000
C	-4.04751700	0.04796200	0.36299900
H	-3.85315600	-0.95278500	0.74832400
C	-5.45583000	0.49911300	0.24541900
H	-5.56398700	1.27329600	-0.52758300
H	-5.83807800	0.94540800	1.18053300
C	-6.39417600	-0.62267200	-0.10691100
F	-6.35397100	-1.60026800	0.80904200
F	-7.65835000	-0.19102300	-0.17779500
F	-6.08655600	-1.17040900	-1.28683400

VIII. References

[S1] Cismesia, M. A.; Yoon, T. P. *Chem. Sci.*, **2015**, *6*, 5426.

[S2] Kuhn, H. J.; Braslavsky, S. E.; Schmidt, R. *Pure Appl. Chem.*, **2004**, *76*, 2105.

[S3] Demas, J. N.; Bowman, W. D.; Zalewski, E. F.; Velapoldi, R. A. *J. Phys. Chem.*, **1981**, *85*, 2766.

[S4] Konik, Y. A.; Kudrjashova, M.; Konrad, N.; Kaabel, S.; Järving, I.; Lopp, M.; Kananovich, D. G. *Org. Biomol. Chem.* **2017**, *15*, 4635.

[S5] Parr, R.G.; Yang, W. Density Functional Theory of Atoms and Molecules. Oxford University Press: New York, **1989**.

[S6] Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.;

Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Keith, T.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian 09, revision D.01; Gaussian, Inc.: Wallingford CT, **2013**.

[S7] Zhao, Y.; Truhlar, D. G. Theor. Chem. Acc. **2008**, *120*, 215.

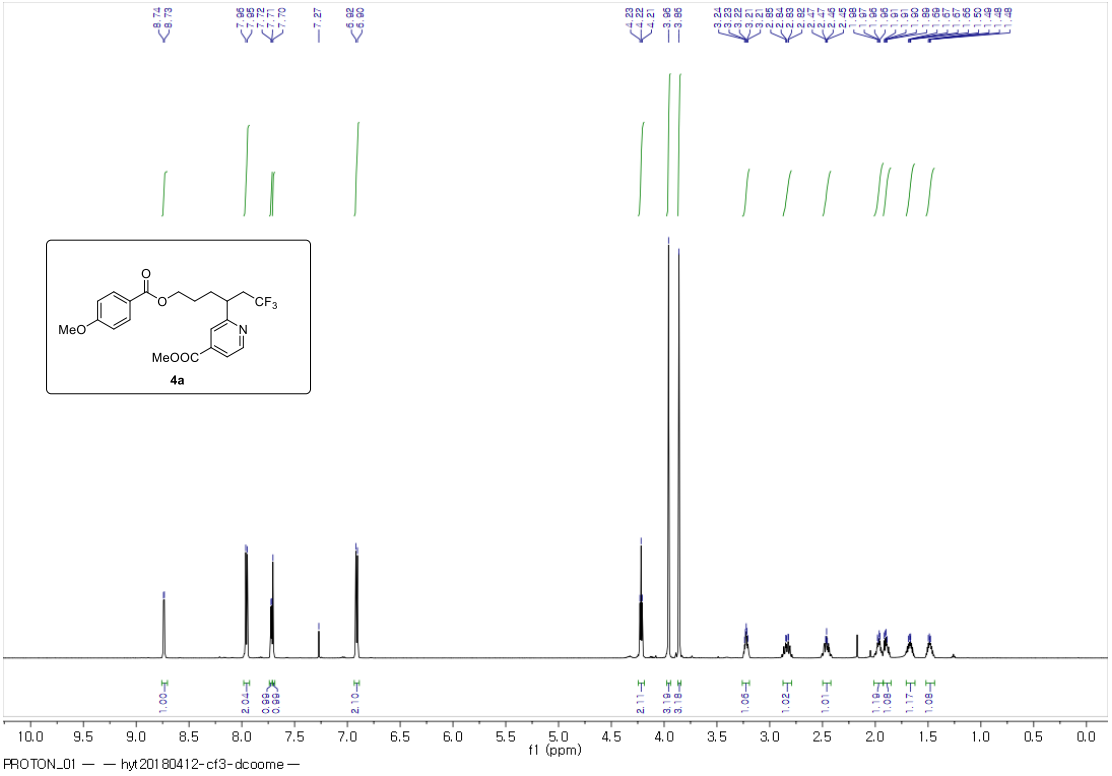
[S8] Grimme, S.; Antony, J.; Ehrlich, S.; Krieg, S. *J. Chem. Phys.* **2010**, *132*, 154104.

[S9] Dunning, T. H., Jr. *J. Chem. Phys.* **1989**, *90*, 1007.

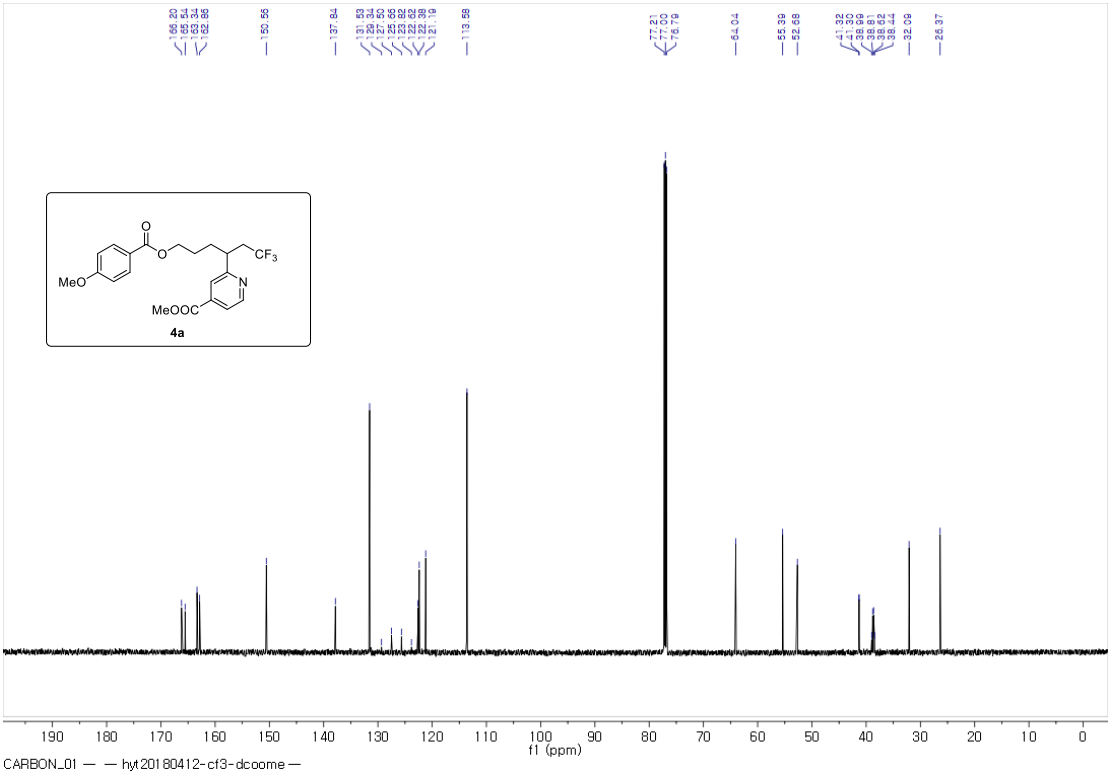
Appendix I

Spectral Copies of ^{1}H, ^{13}C and ^{19}F NMR Data Obtained in this Study

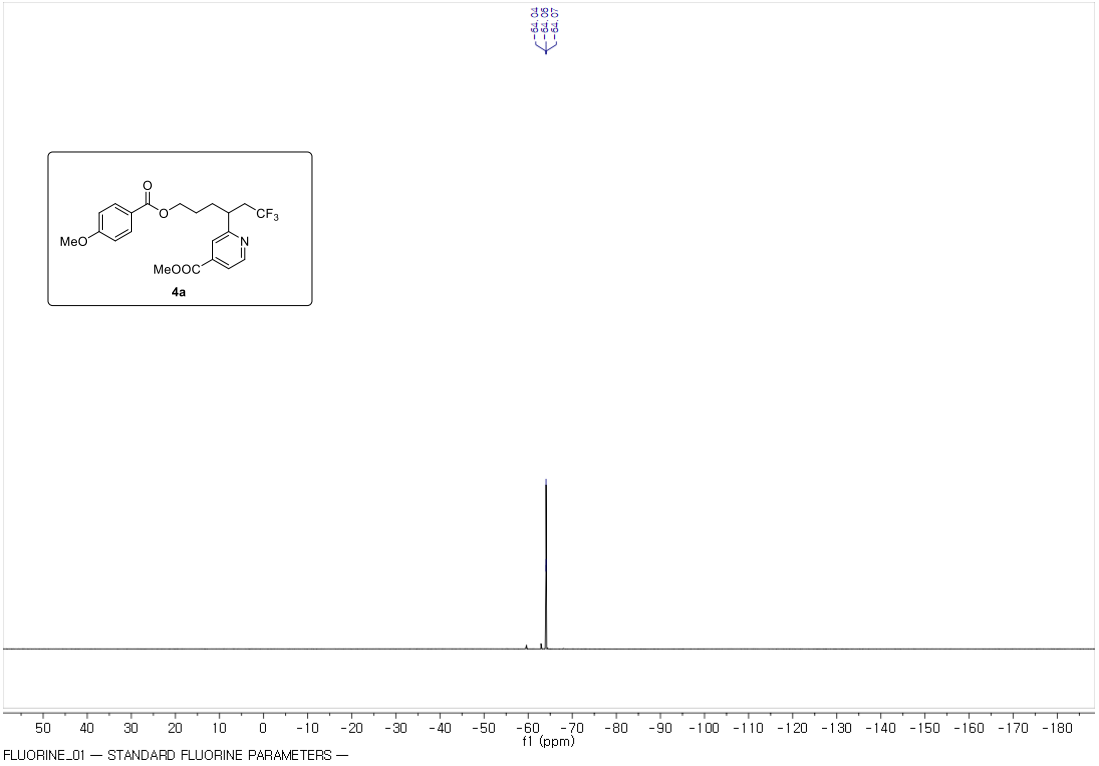
6,6,6-trifluoro-4-(4-methylpyridin-2-yl)hexyl 4-methoxybenzoate (4a).



599 MHz, ^{1}H NMR in $CDCl_3$

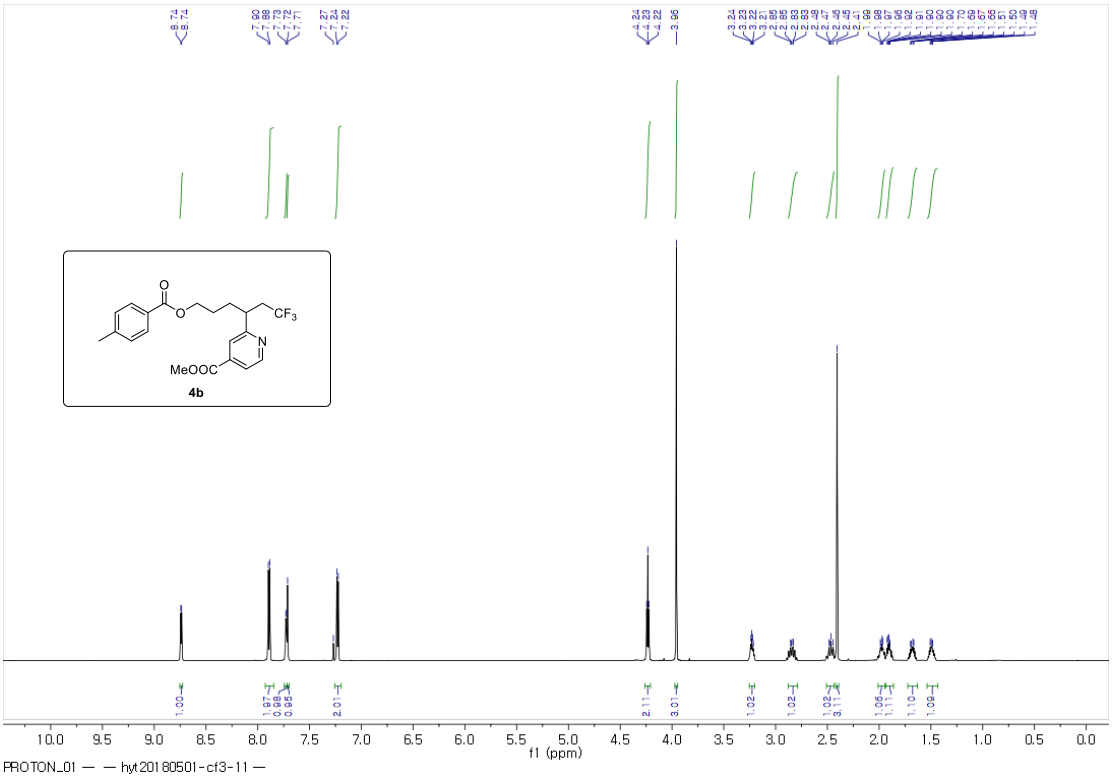


151 MHz, ^{13}C NMR in $CDCl_3$

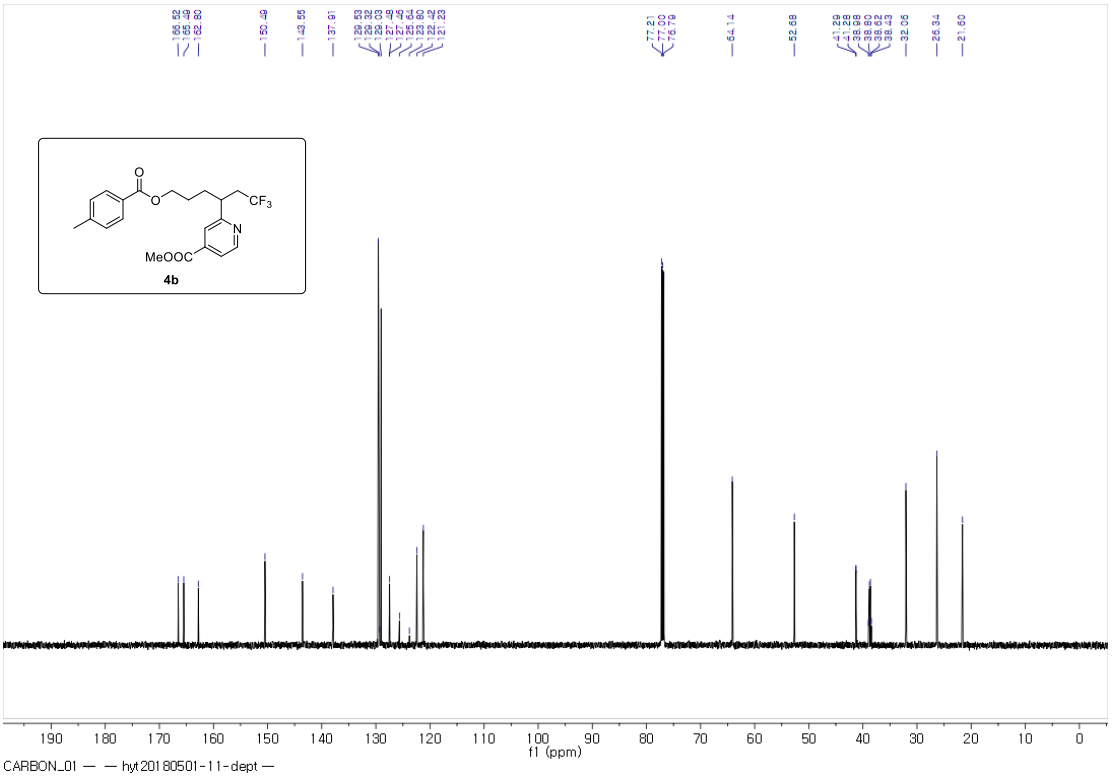


564 MHz, ^{19}F NMR in $CDCl_3$

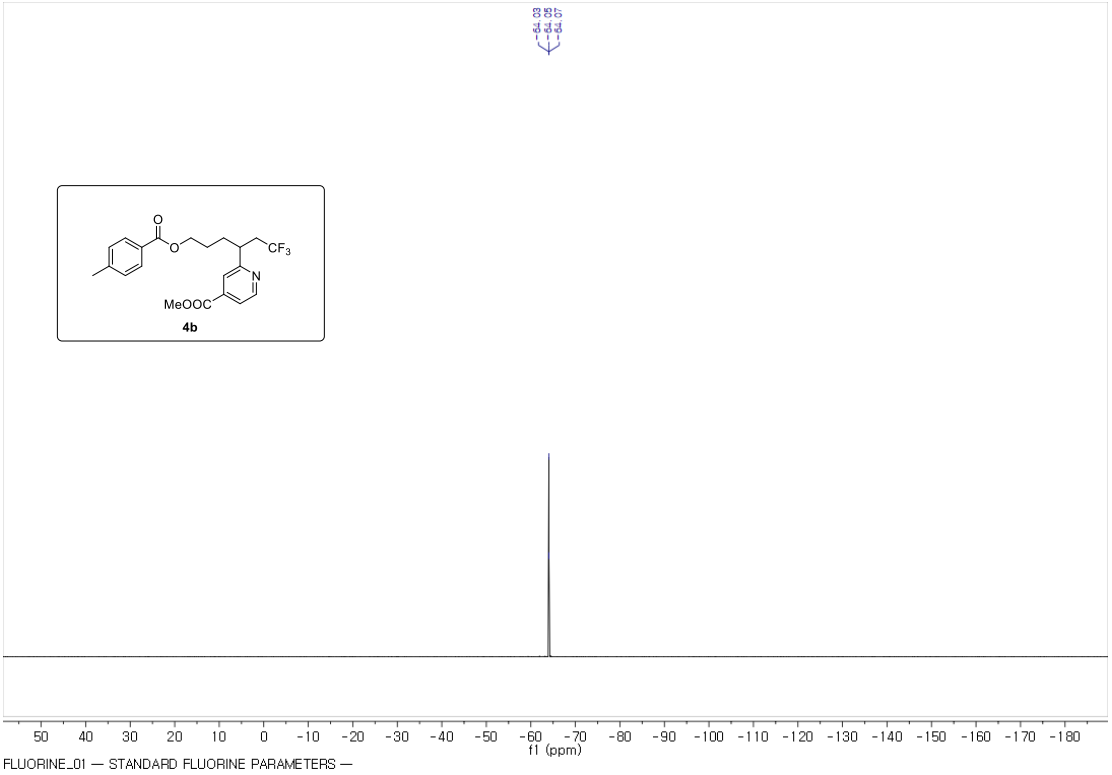
methyl 2-(1,1,1-trifluoro-6-((4-methylbenzoyl)oxy)hexan-3-yl)isonicotinate (4b).



599 MHz, ^{1}H NMR in $CDCl_3$

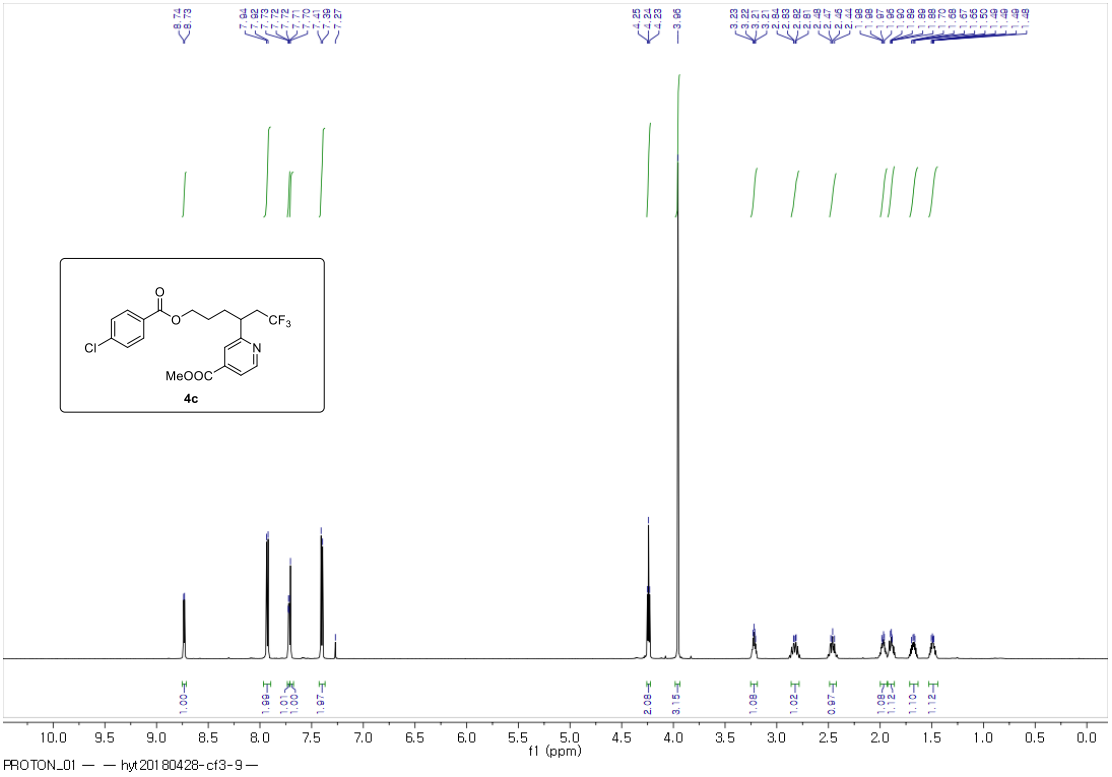


151 MHz, ^{13}C NMR in $CDCl_3$

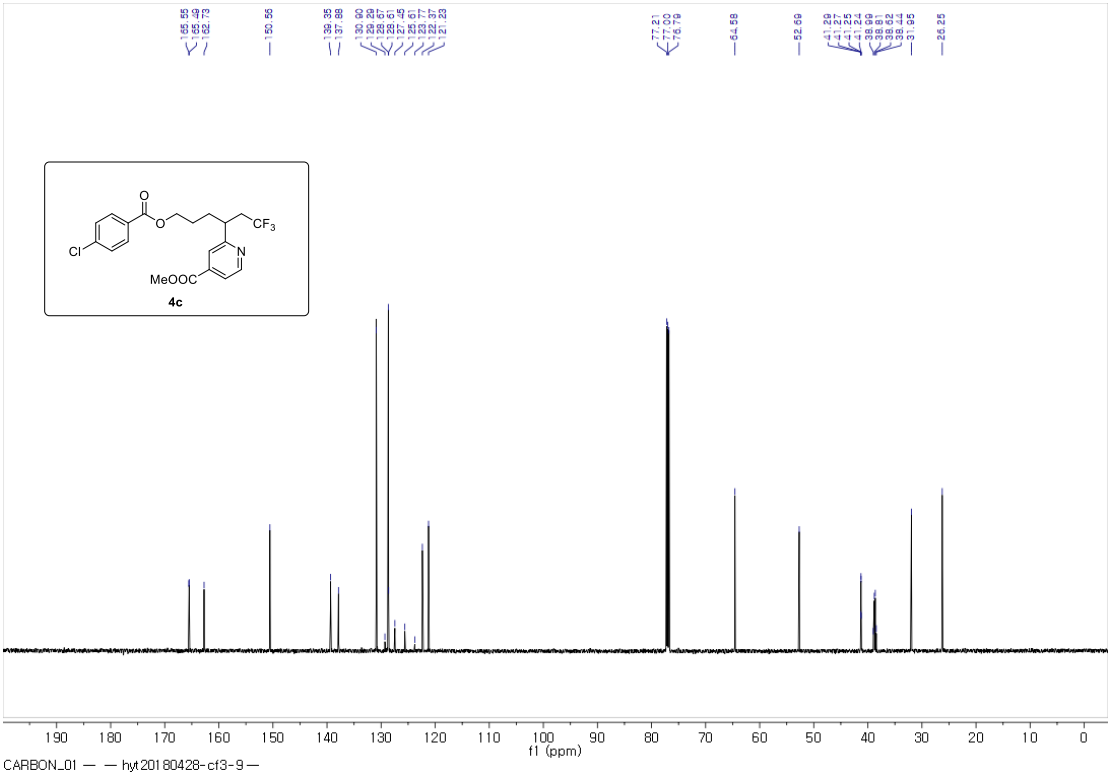


564 MHz, ^{19}F NMR in $CDCl_3$

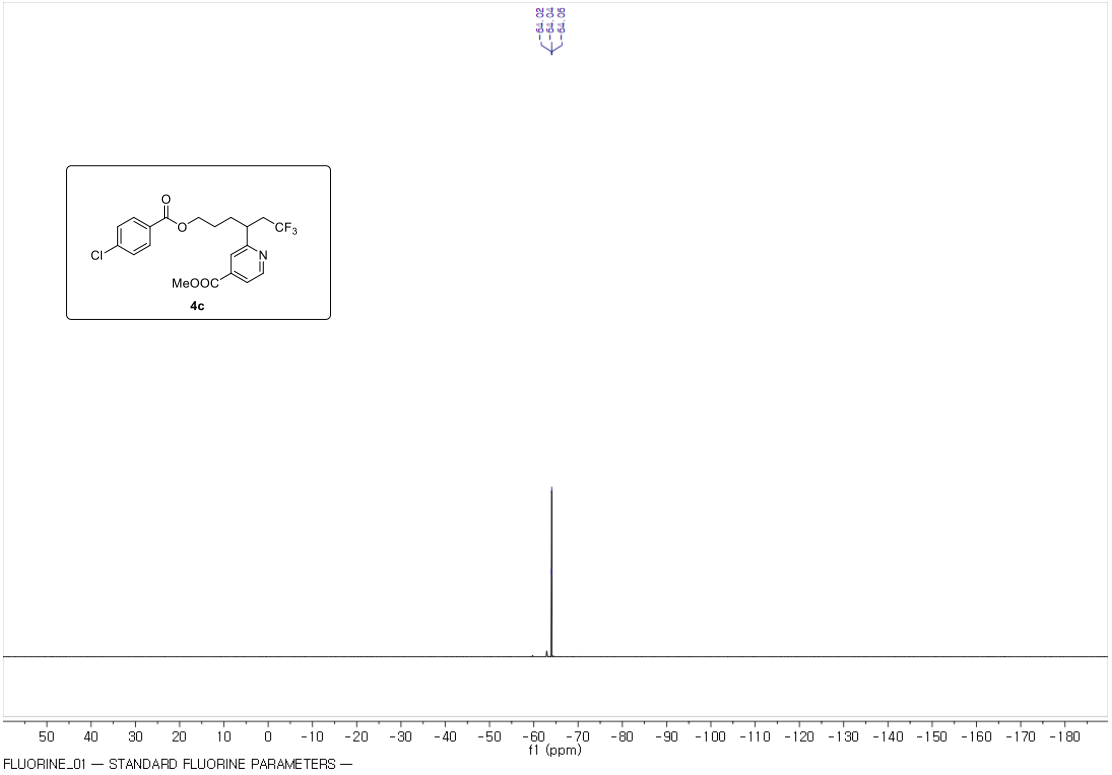
methyl 2-(6-((4-chlorobenzoyl)oxy)-1,1,1-trifluorohexan-3-yl)isonicotinate (4c).



599 MHz, ^{1}H NMR in $CDCl_3$

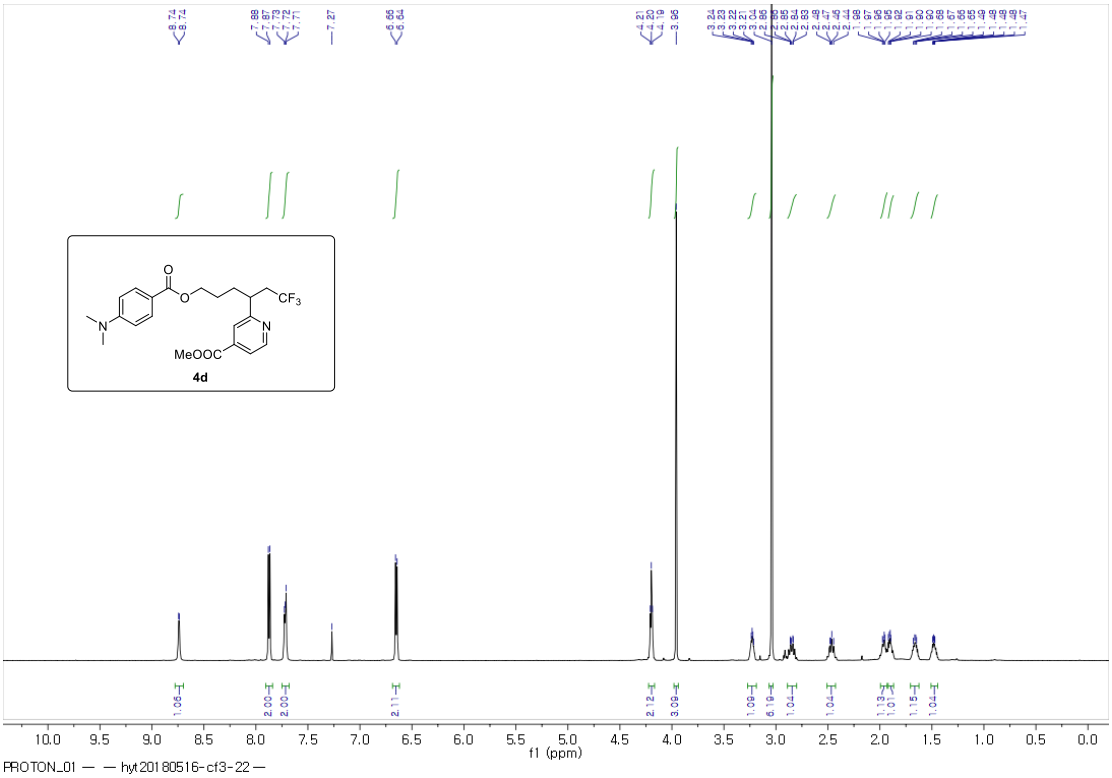


151 MHz, ^{13}C NMR in $CDCl_3$

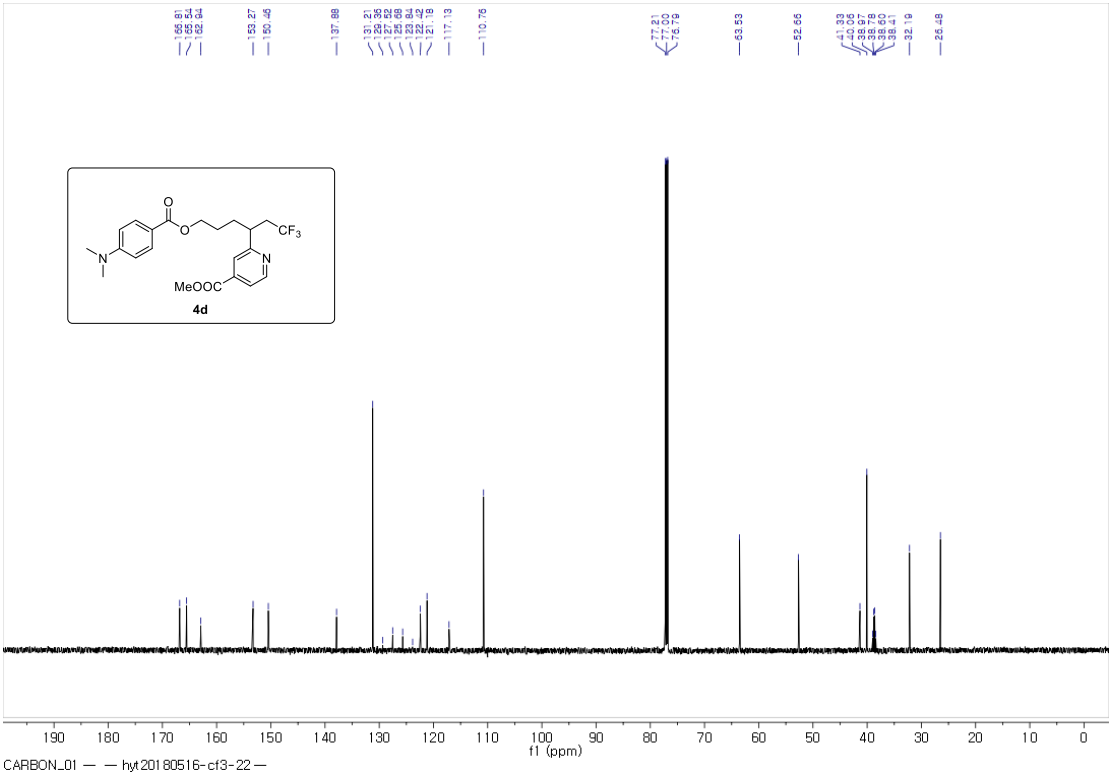


564 MHz, ^{19}F NMR in $CDCl_3$

methyl 2-(6-((4-(dimethylamino)benzoyl)oxy)-1,1,1-trifluorohexan-3-yl)isonicotinate (4d).



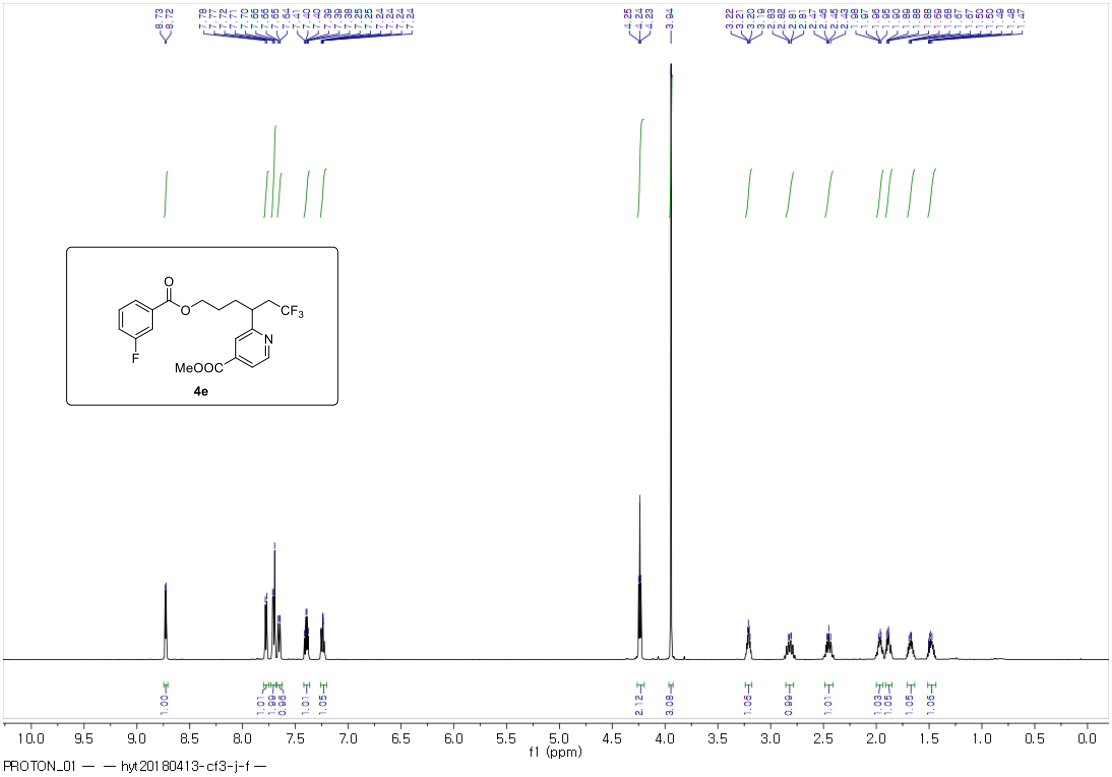
599 MHz, ^{1}H NMR in $CDCl_3$



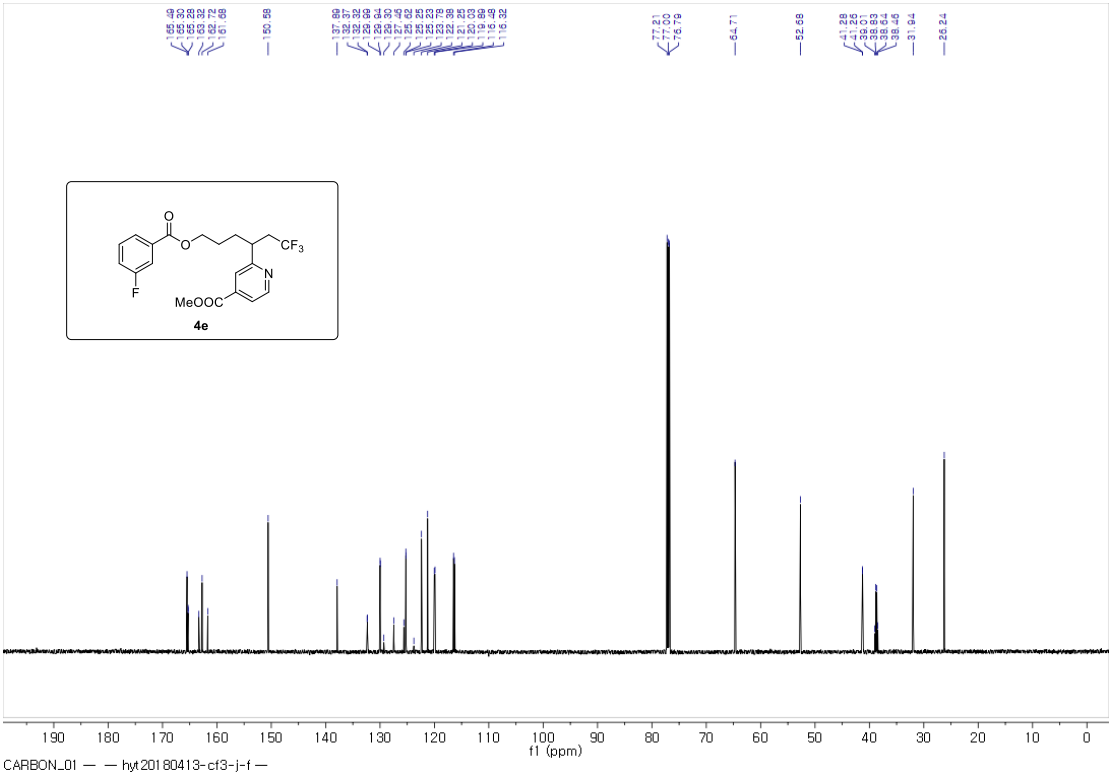
151 MHz, ^{13}C NMR in $CDCl_3$

564 MHz, ^{19}F NMR in $CDCl_3$

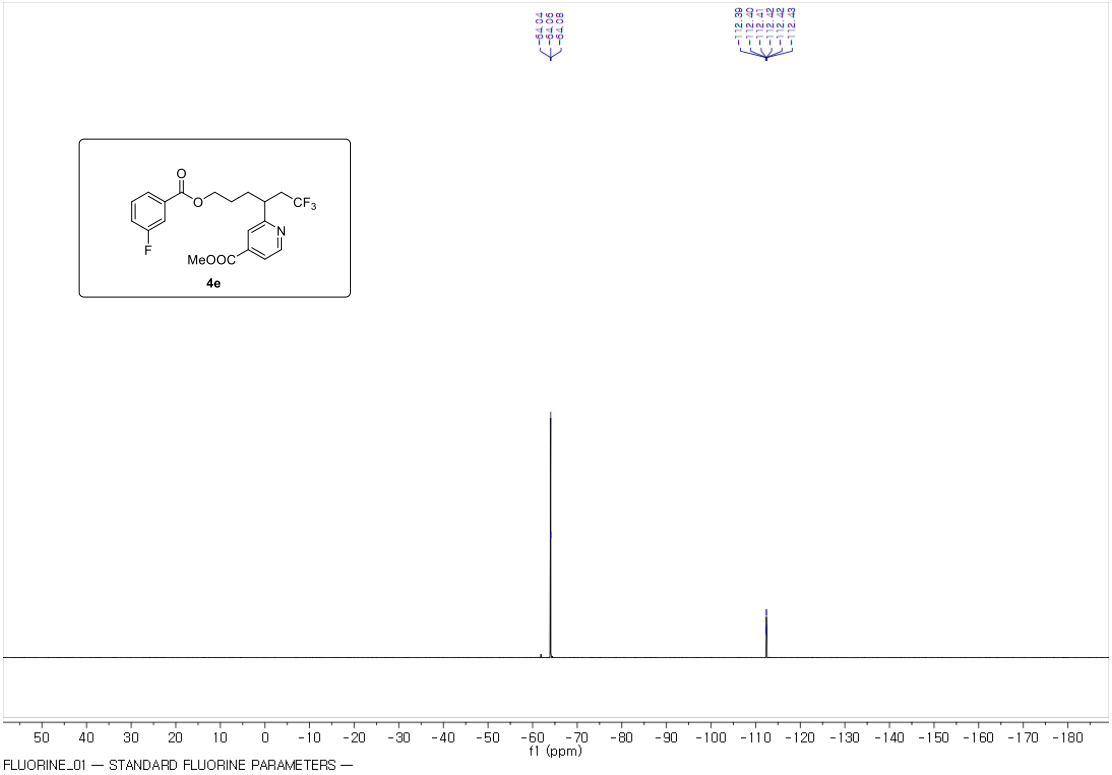
methyl 2-(1,1,1-trifluoro-6-((3-fluorobenzoyl)oxy)hexan-3-yl)isonicotinate (4e).



599 MHz, ^{1}H NMR in $CDCl_3$

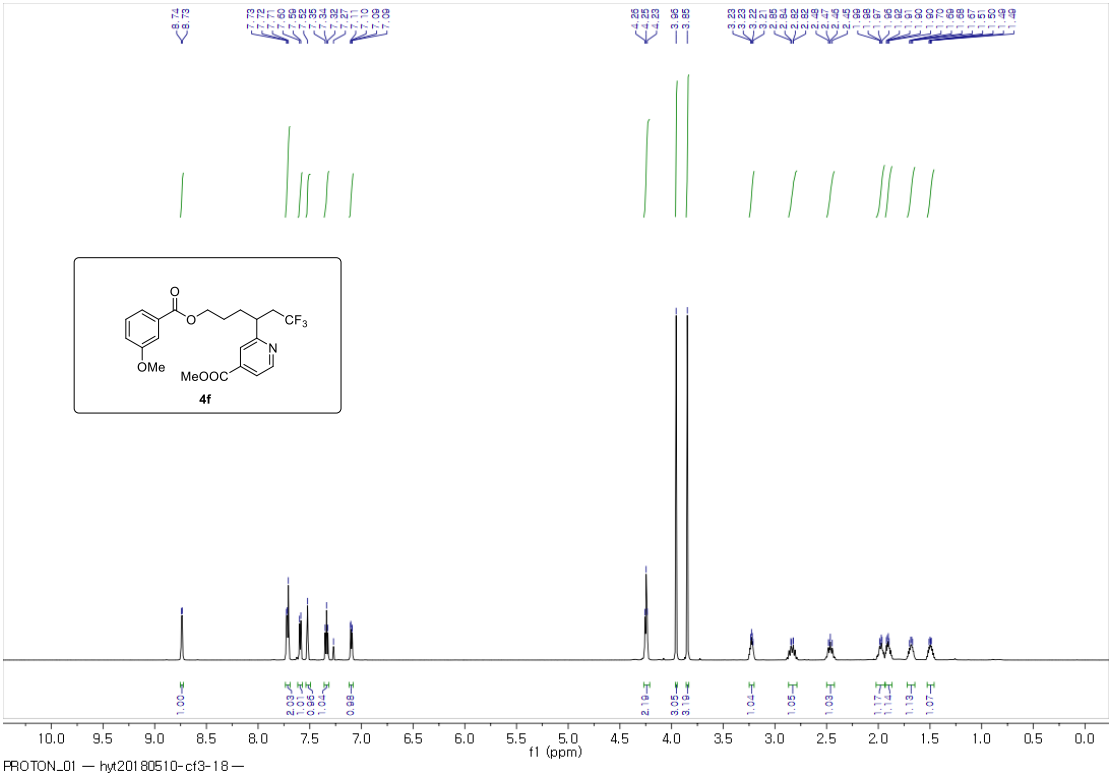


151 MHz, ^{13}C NMR in $CDCl_3$

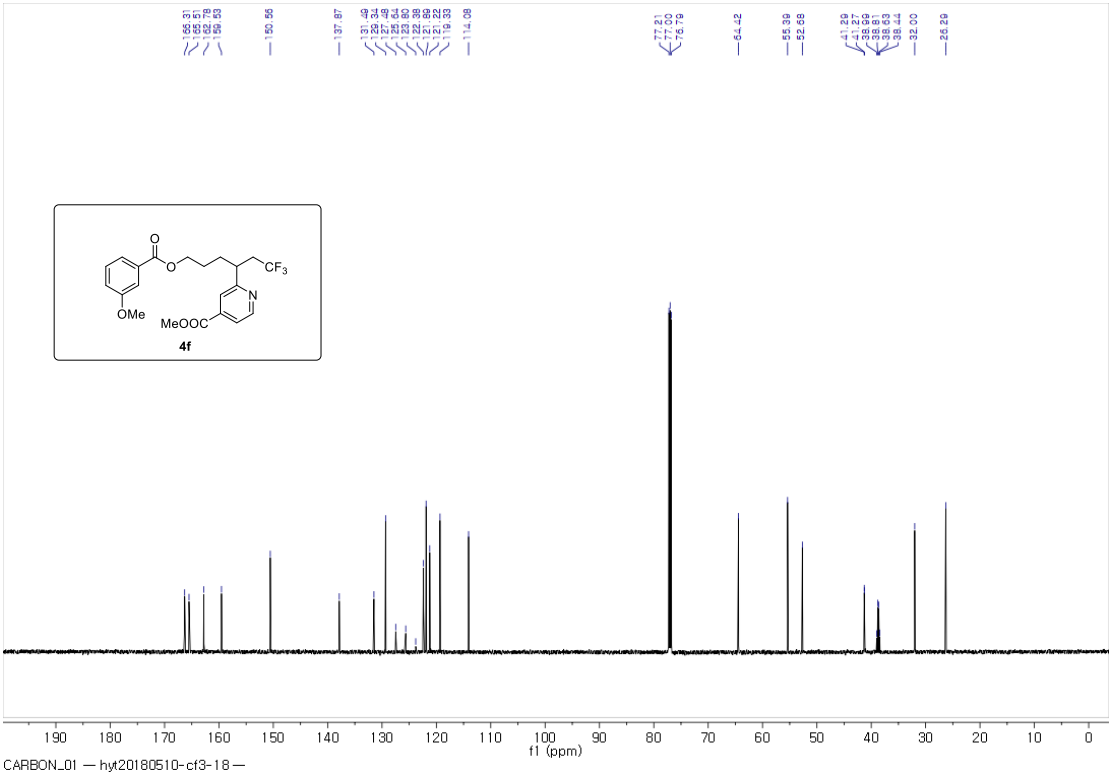


564 MHz, ^{19}F NMR in $CDCl_3$

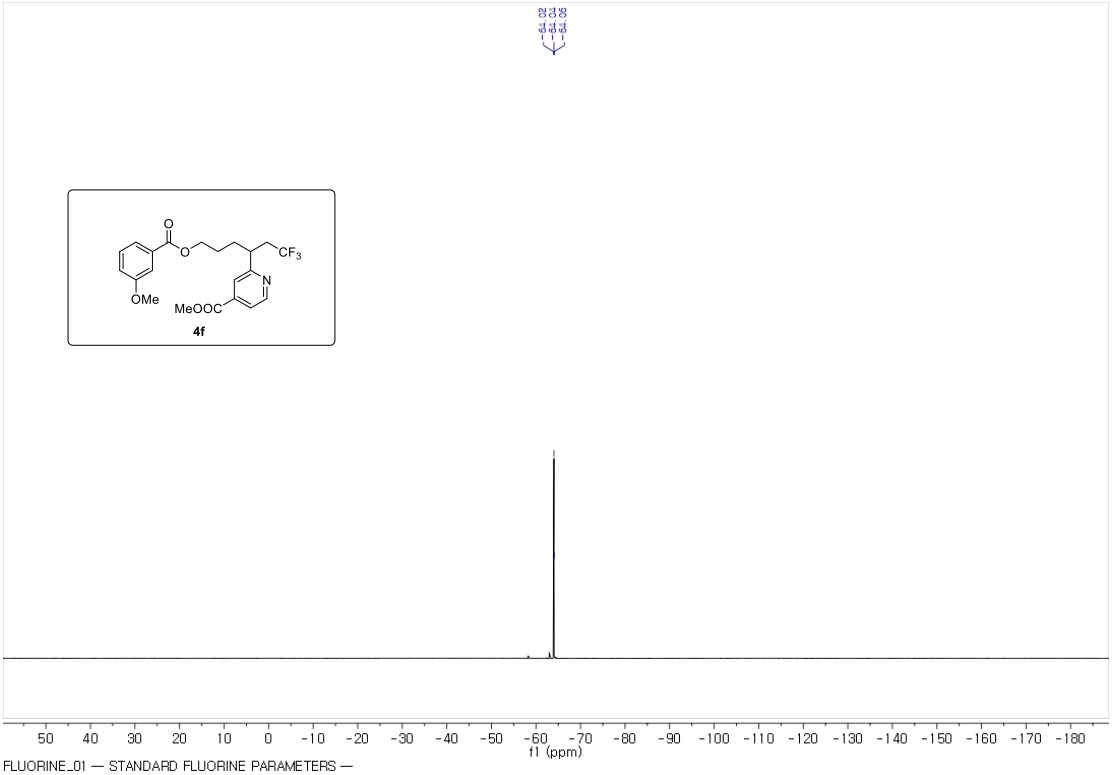
methyl 2-(1,1,1-trifluoro-6-((3-methoxybenzoyl)oxy)hexan-3-yl)isonicotinate (4f).



599 MHz, ^{1}H NMR in $CDCl_3$

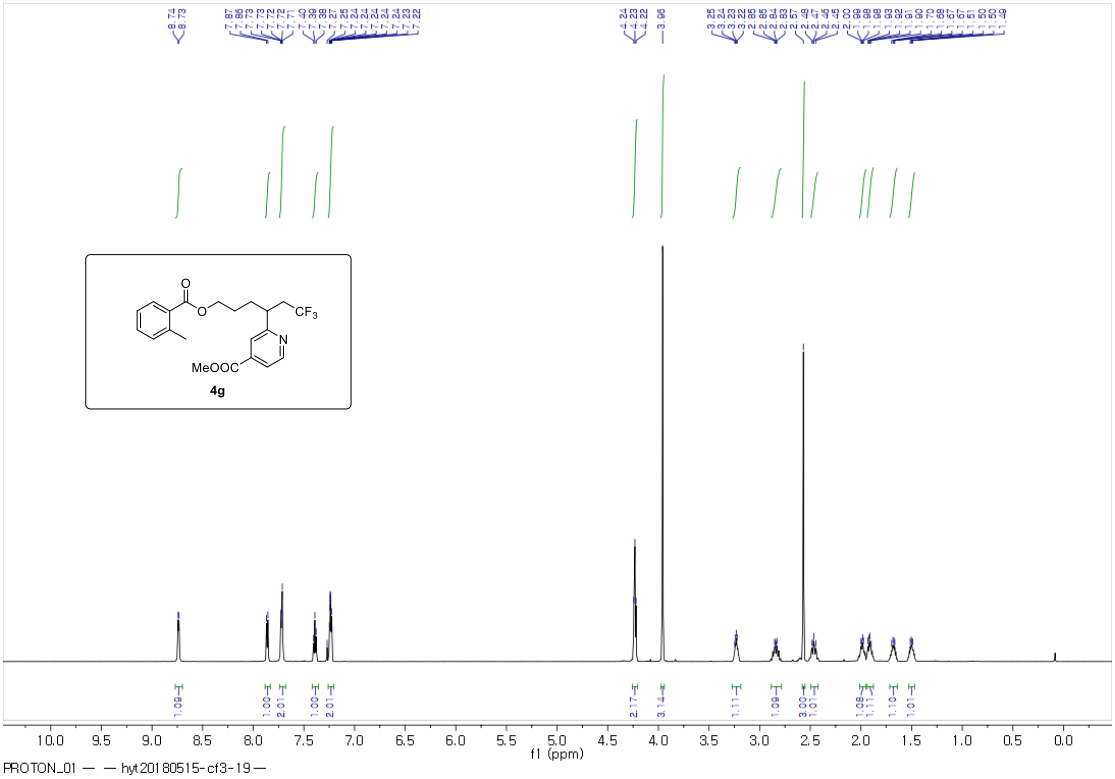


151 MHz, ^{13}C NMR in $CDCl_3$

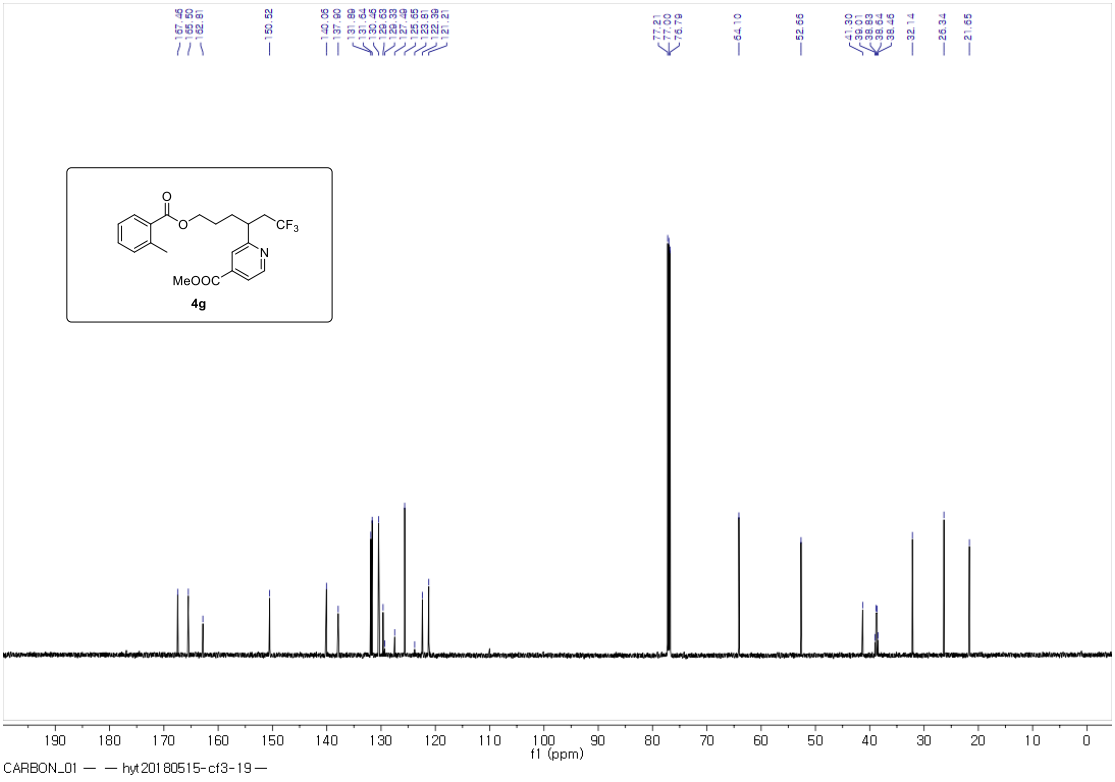


564 MHz, ^{19}F NMR in $CDCl_3$

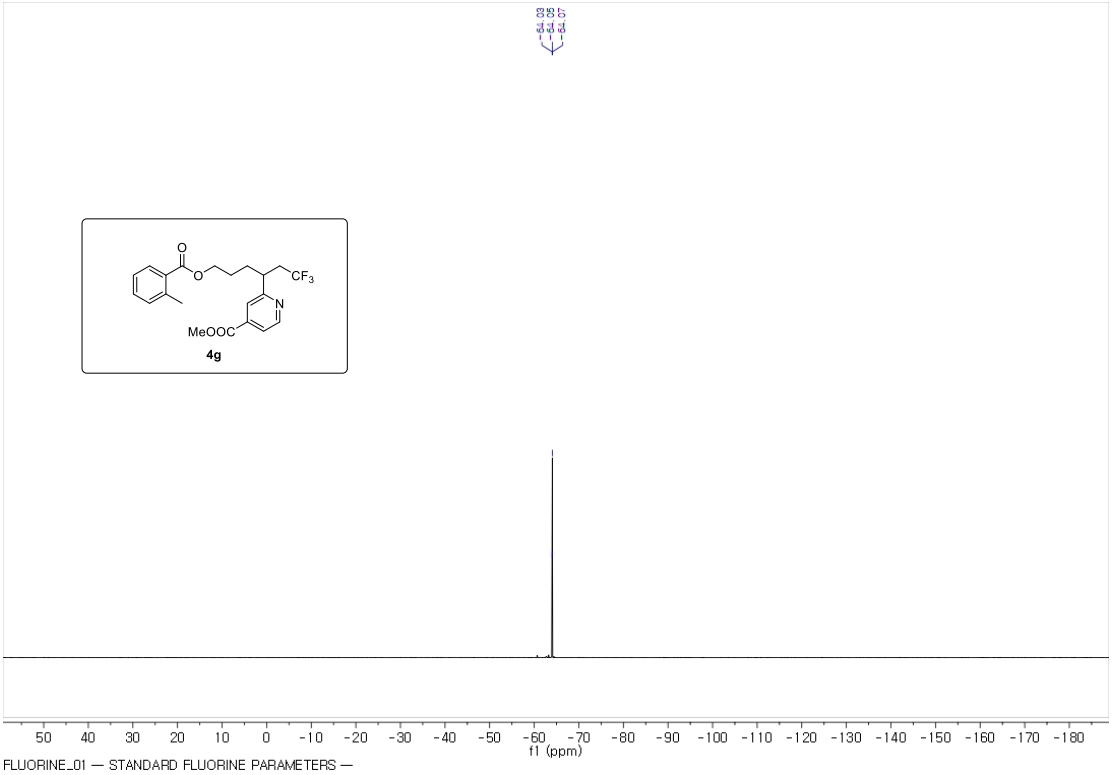
methyl 2-(1,1,1-trifluoro-6-((2-methylbenzoyl)oxy)hexan-3-yl)isonicotinate (4g).



599 MHz, ^{1}H NMR in $CDCl_3$

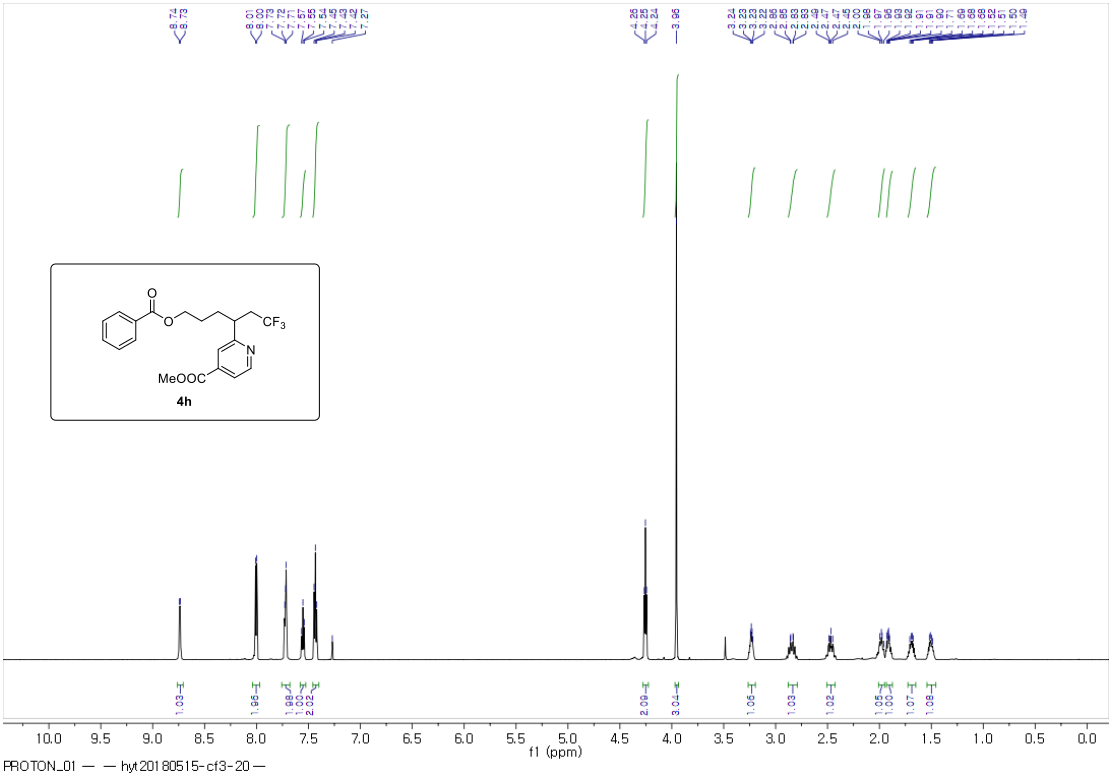


151 MHz, ^{13}C NMR in $CDCl_3$

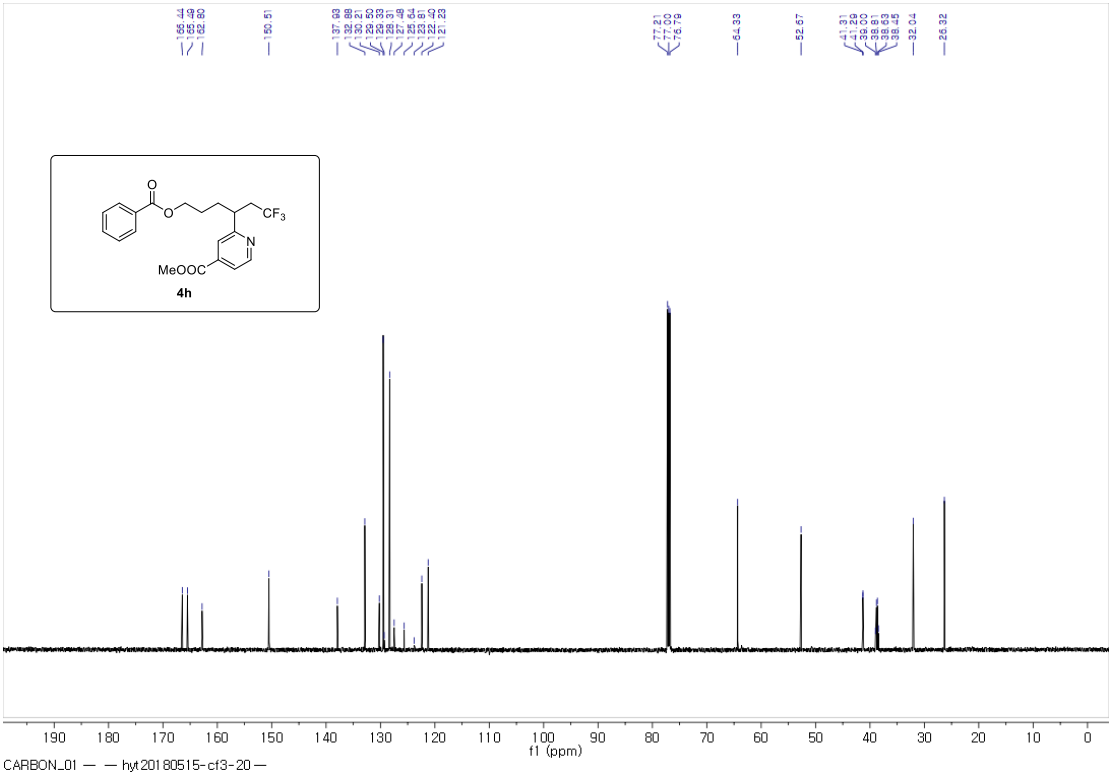


564 MHz, ^{19}F NMR in $CDCl_3$

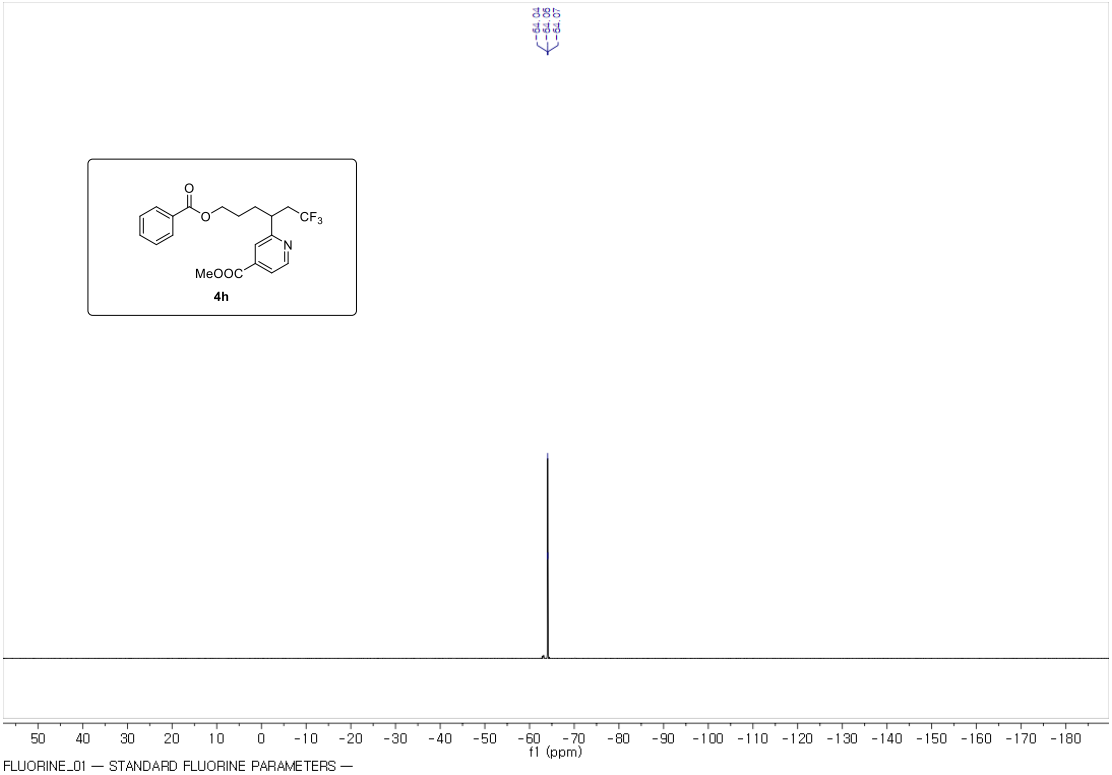
methyl 2-(6-(benzoyloxy)-1,1,1-trifluorohexan-3-yl)isonicotinate (4h).



599 MHz, ^{1}H NMR in $CDCl_3$

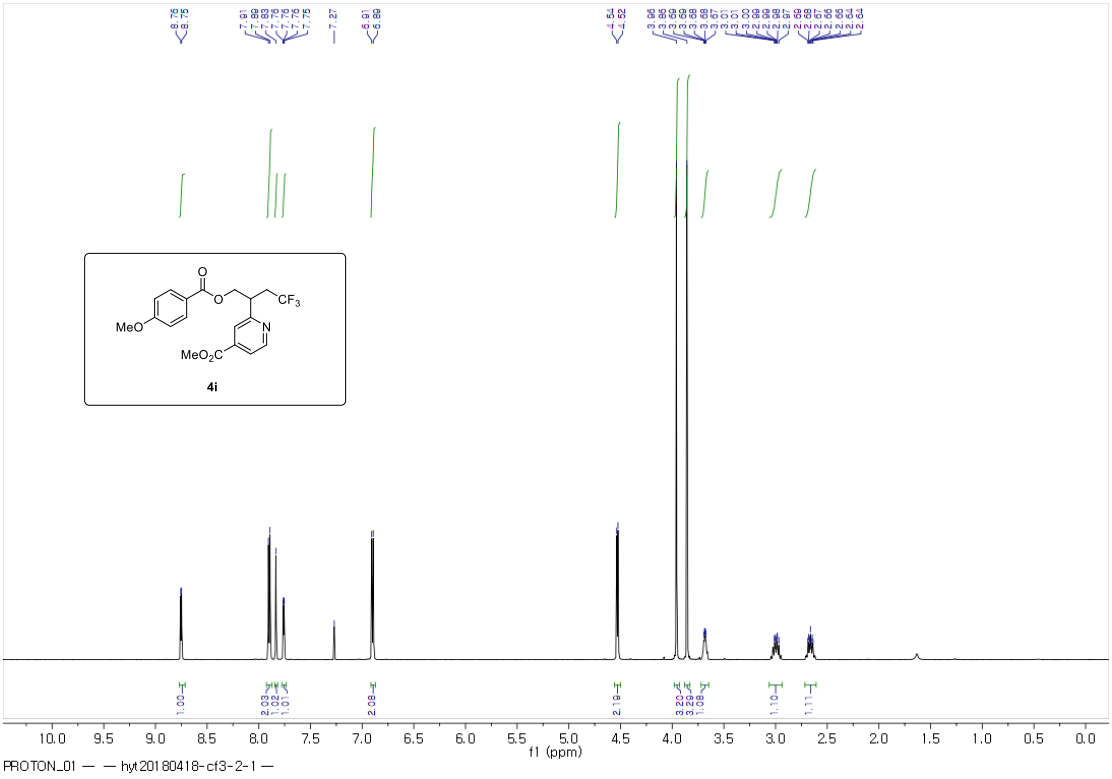


151 MHz, ^{13}C NMR in $CDCl_3$

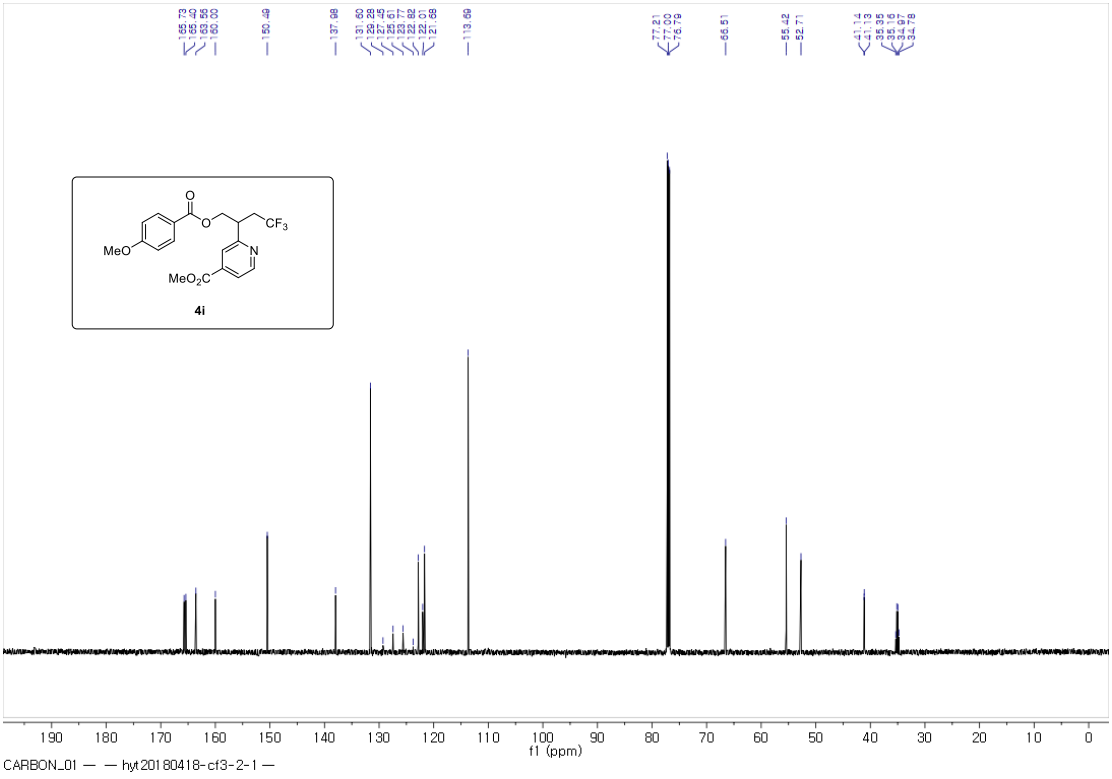


564 MHz, ^{19}F NMR in $CDCl_3$

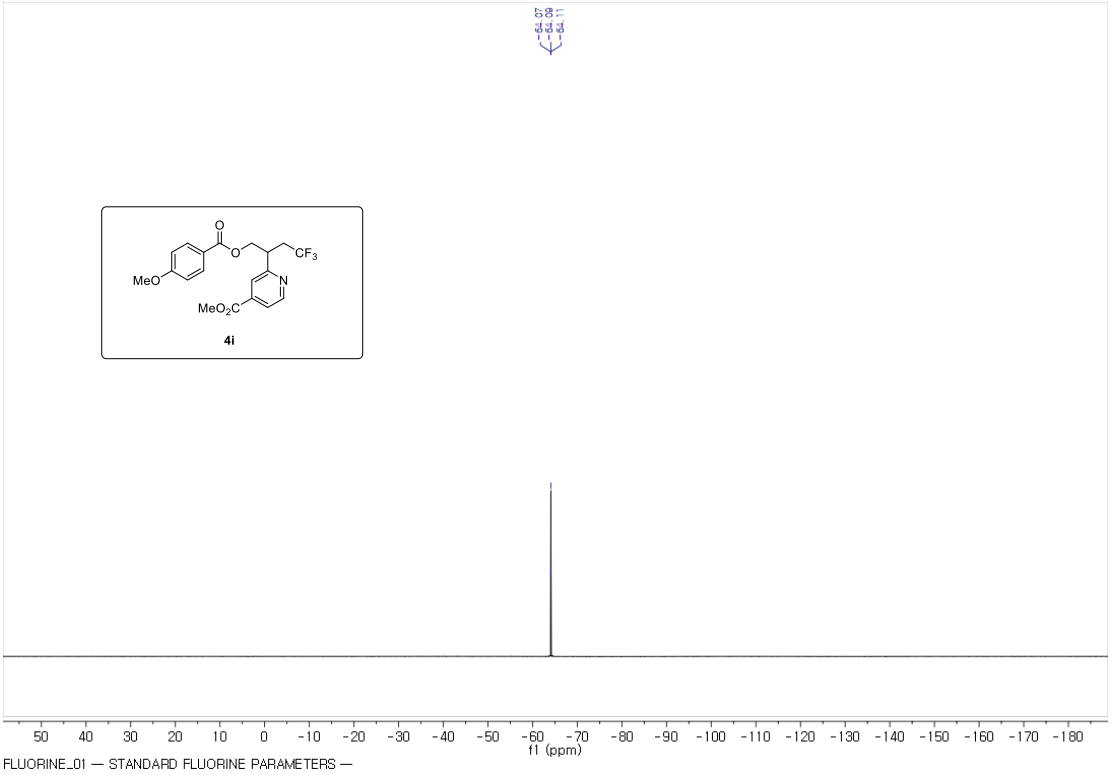
methyl 2-(4,4,4-trifluoro-1-((4-methoxybenzoyl)oxy)butan-2-yl)isonicotinate (4i).



599 MHz, ^{1}H NMR in $CDCl_3$

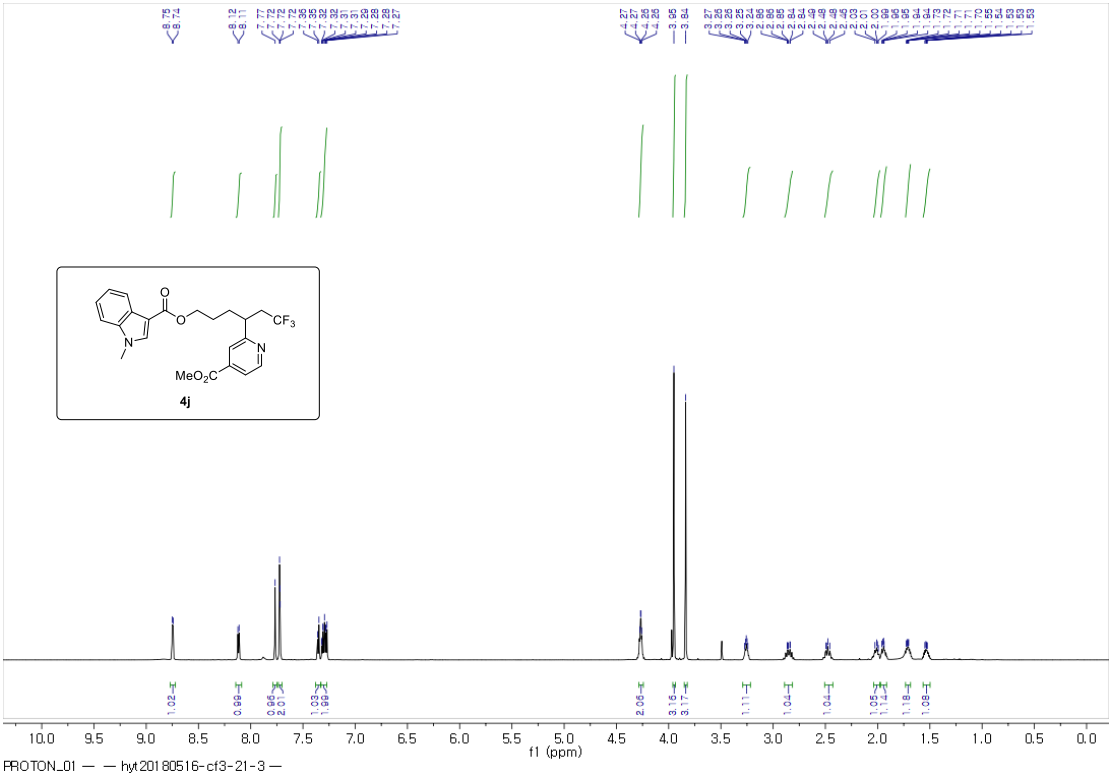


151 MHz, ^{13}C NMR in $CDCl_3$

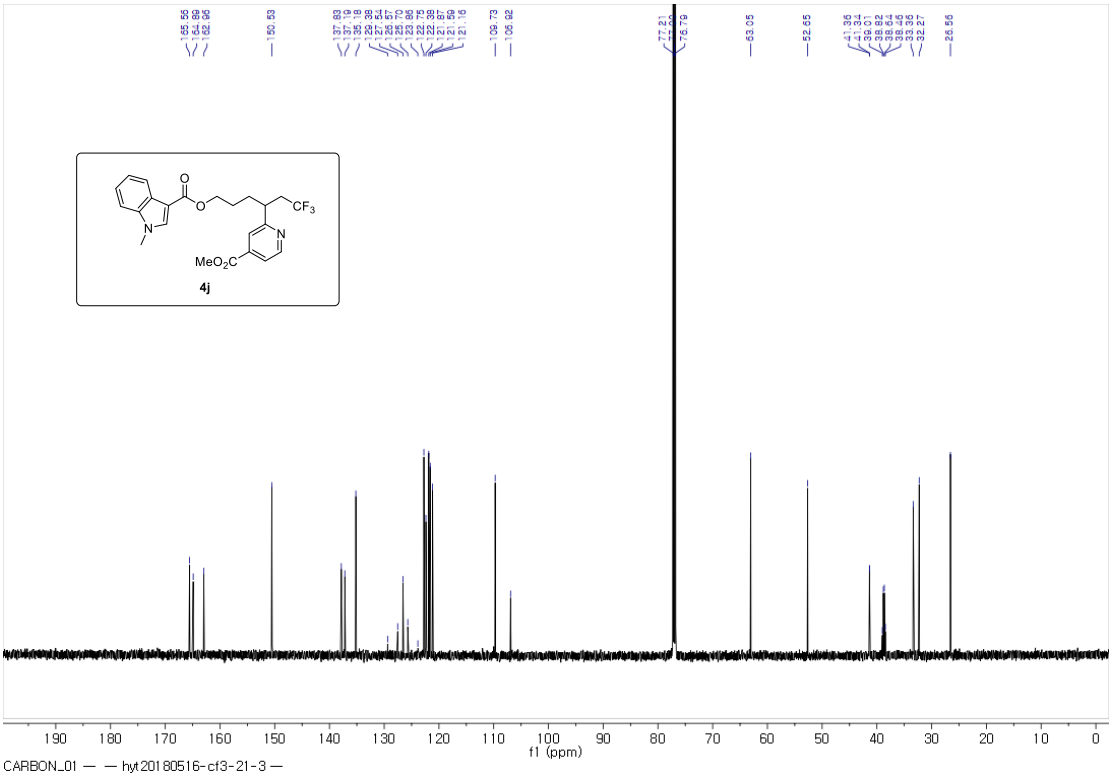


564 MHz, ^{19}F NMR in $CDCl_3$

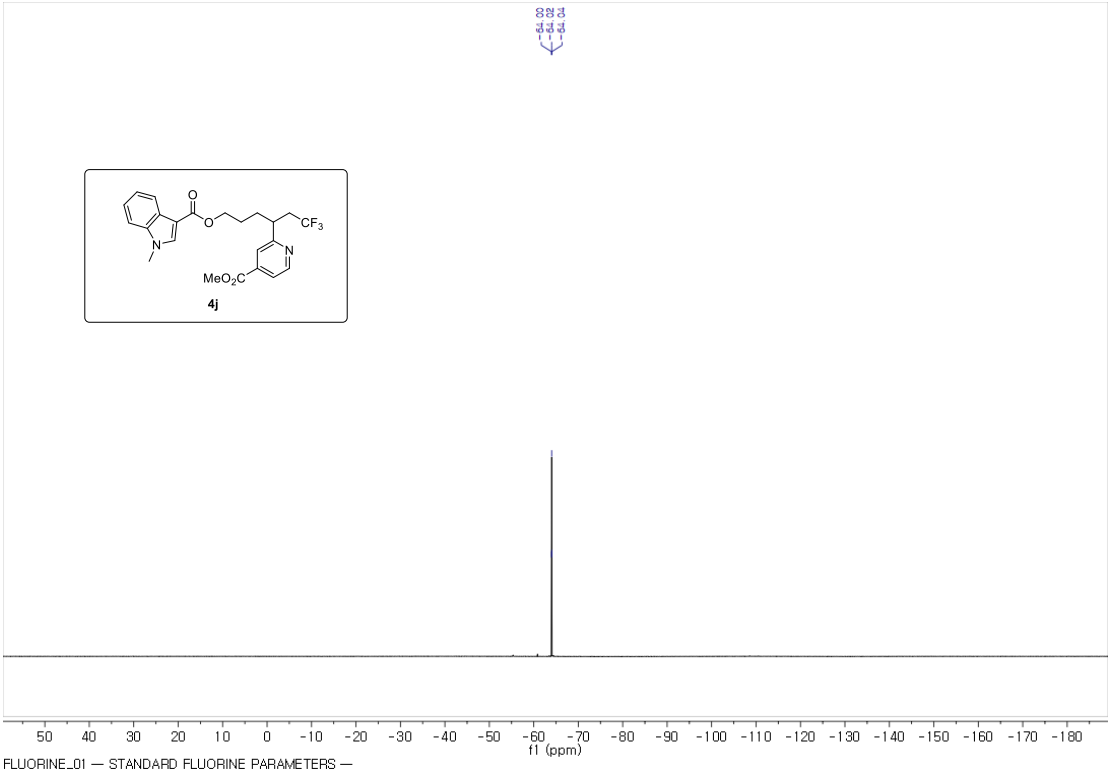
6,6,6-trifluoro-4-(4-(methoxycarbonyl)pyridin-2-yl)hexyl 1-methyl-1H-indole-3-carboxylate (4j).



599 MHz, ^{1}H NMR in $CDCl_3$

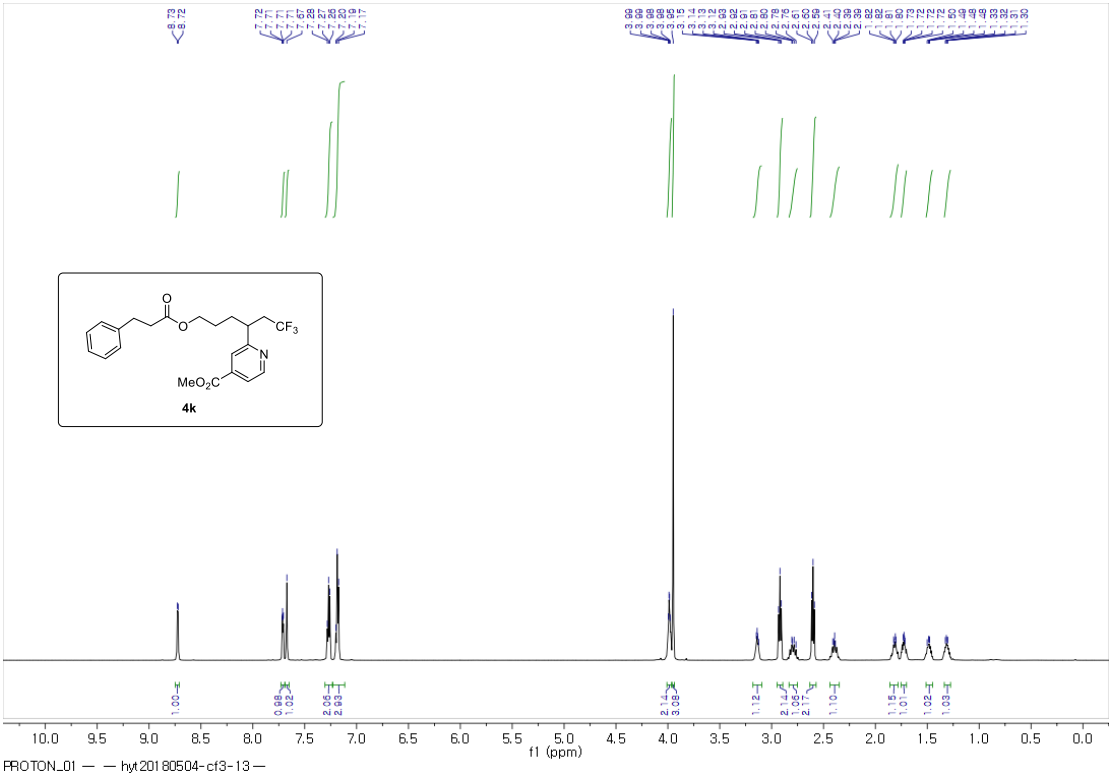


151 MHz, ^{13}C NMR in $CDCl_3$

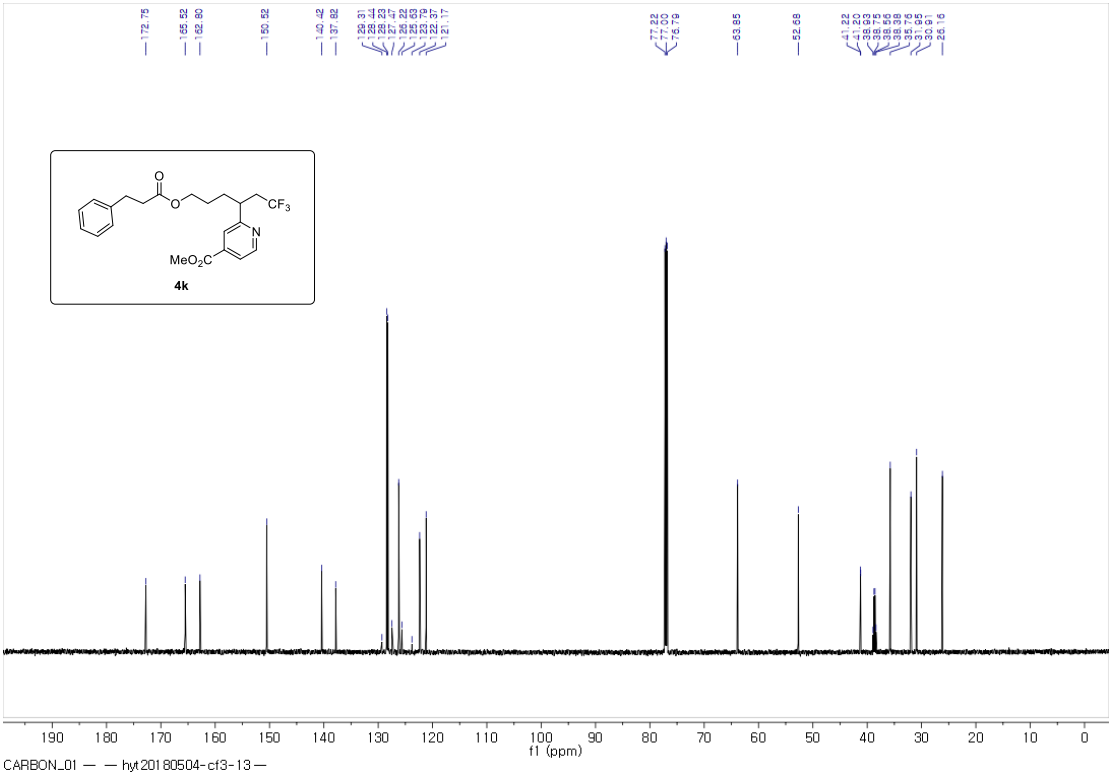


564 MHz, ^{19}F NMR in $CDCl_3$

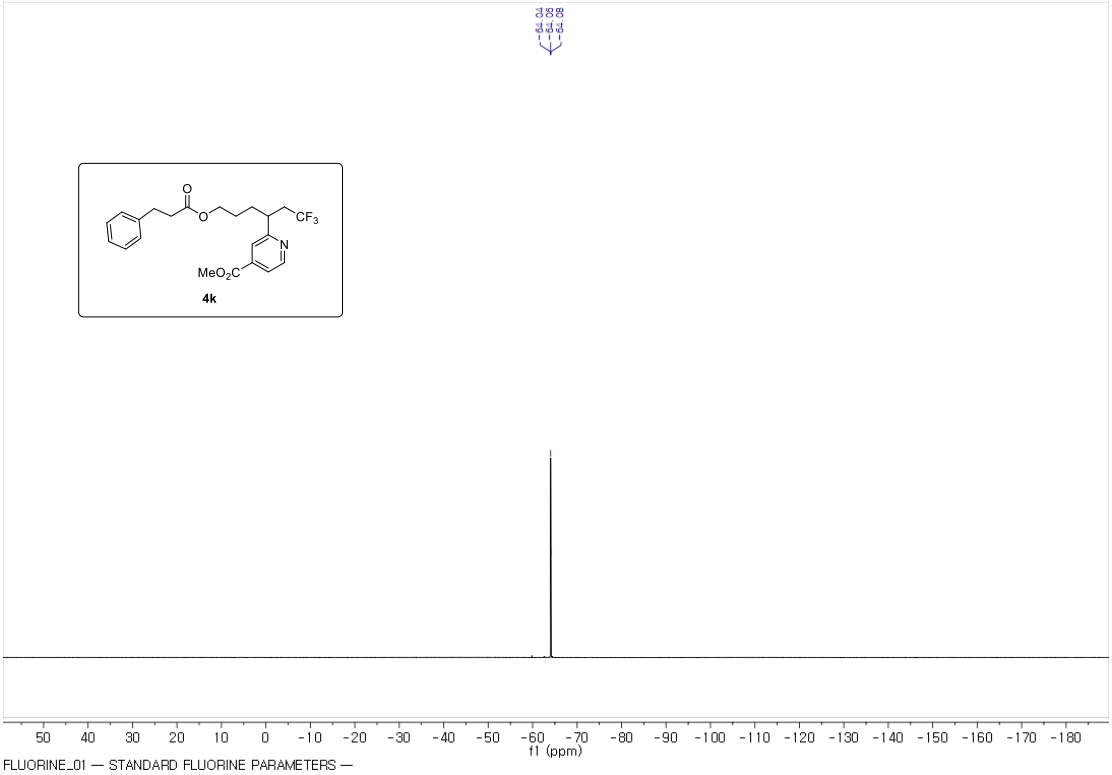
methyl 2-(1,1,1-trifluoro-6-((3-phenylpropanoyl)oxy)hexan-3-yl)isonicotinate (4k).



599 MHz, ^{1}H NMR in $CDCl_3$

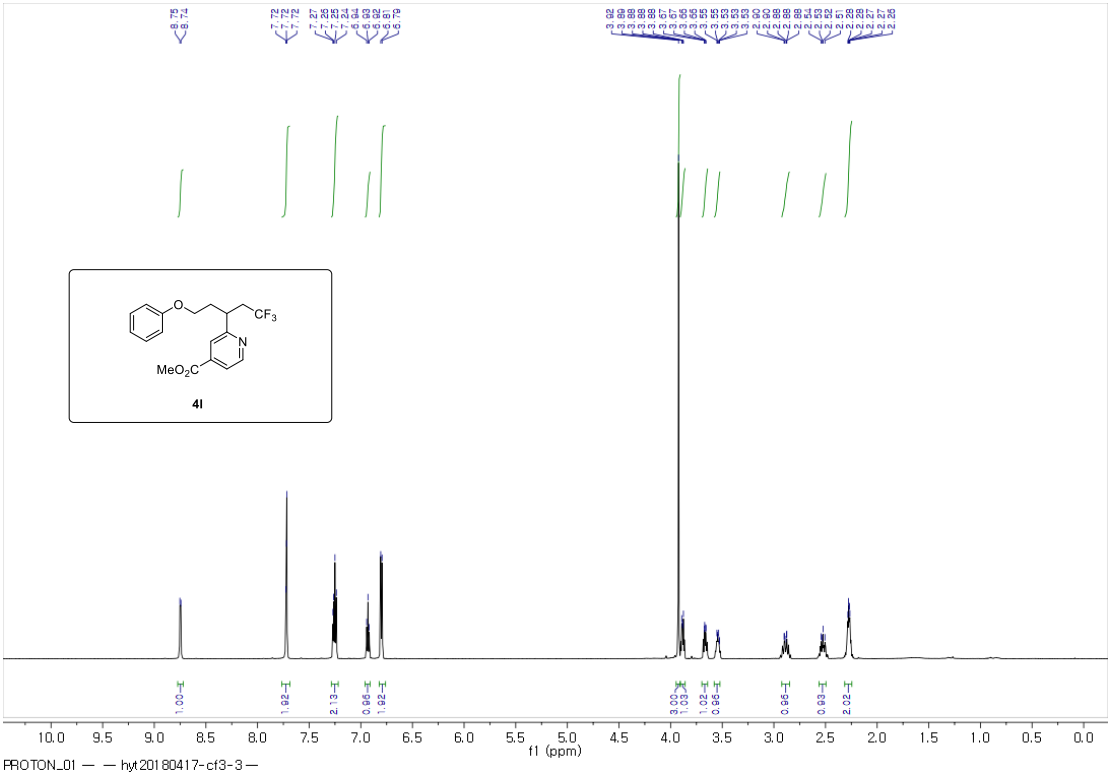


151 MHz, ^{13}C NMR in $CDCl_3$

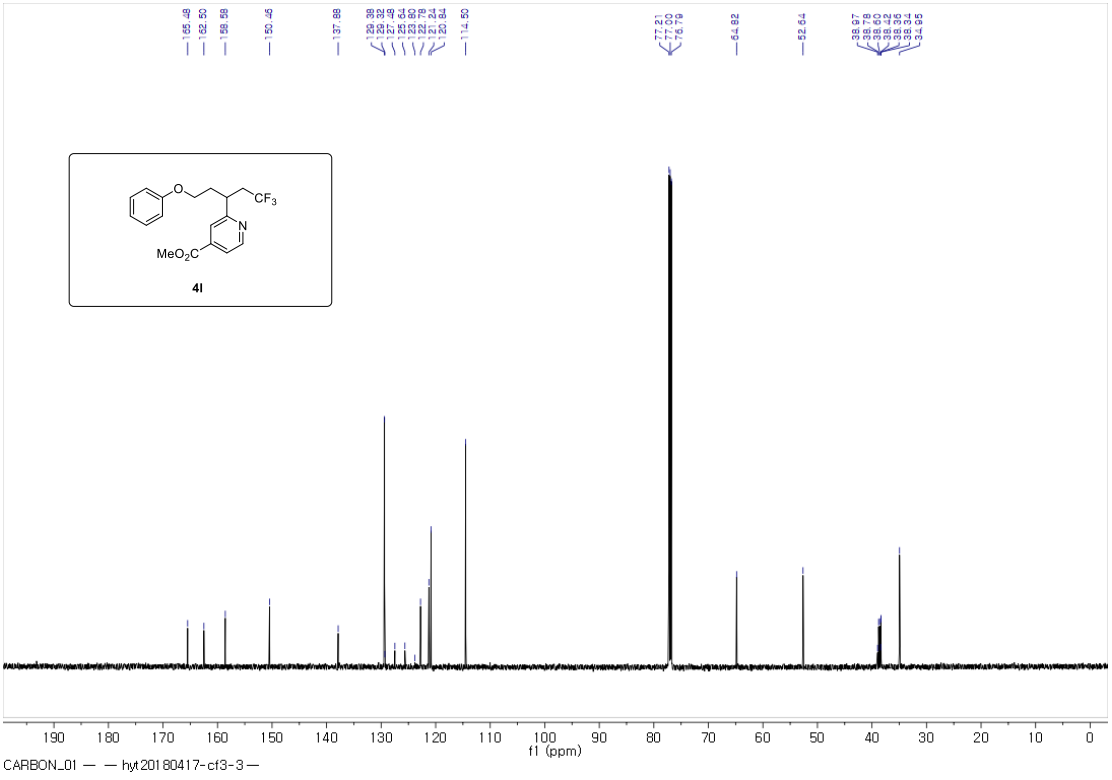


564 MHz, ^{19}F NMR in $CDCl_3$

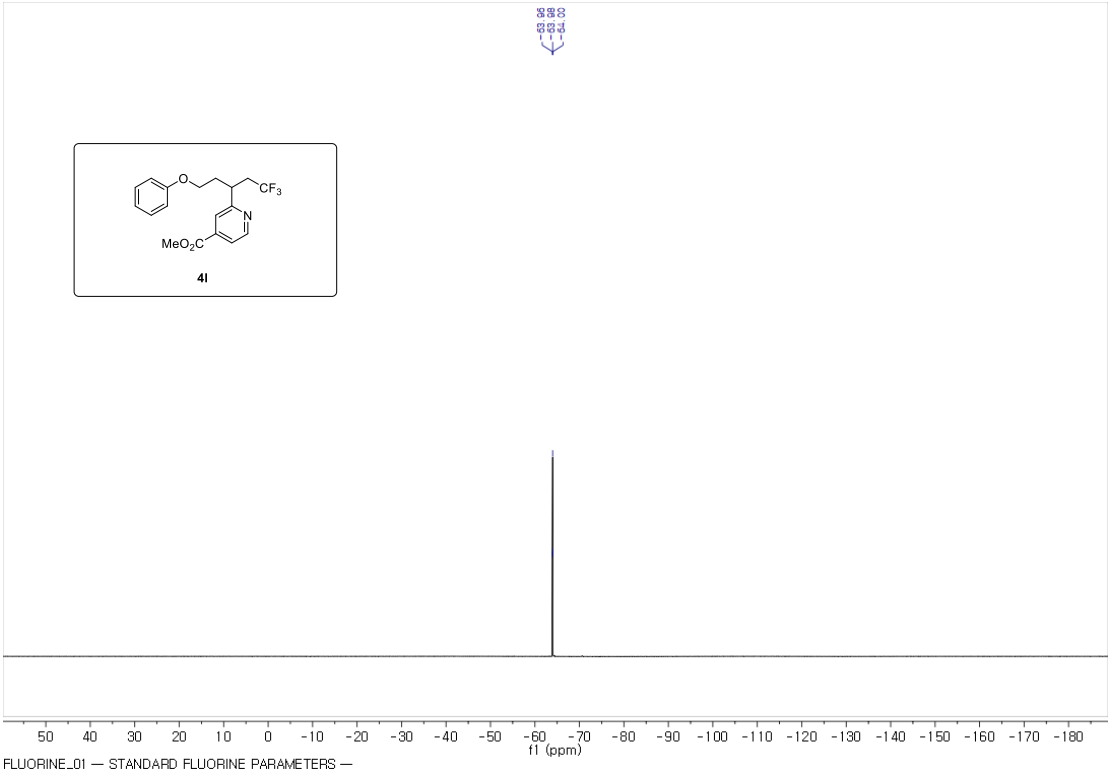
methyl 2-(1,1,1-trifluoro-5-phenoxypentan-3-yl)isonicotinate (4l).



599 MHz, ^{1}H NMR in $CDCl_3$

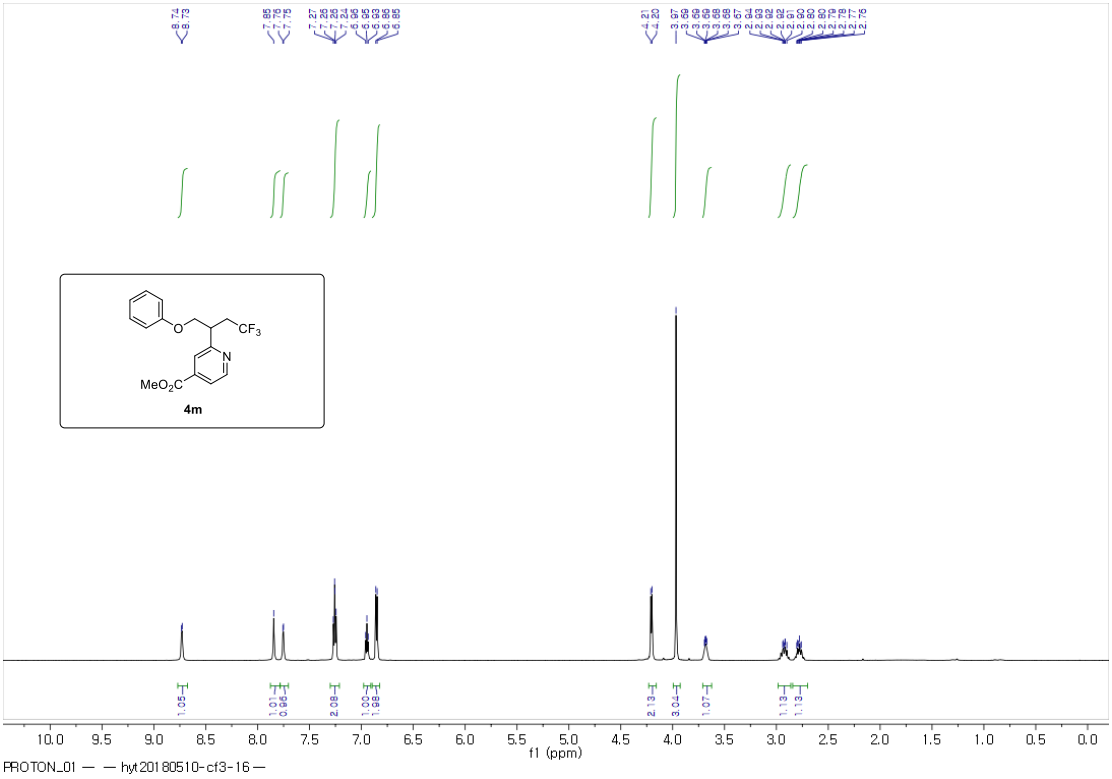


151 MHz, ^{13}C NMR in $CDCl_3$

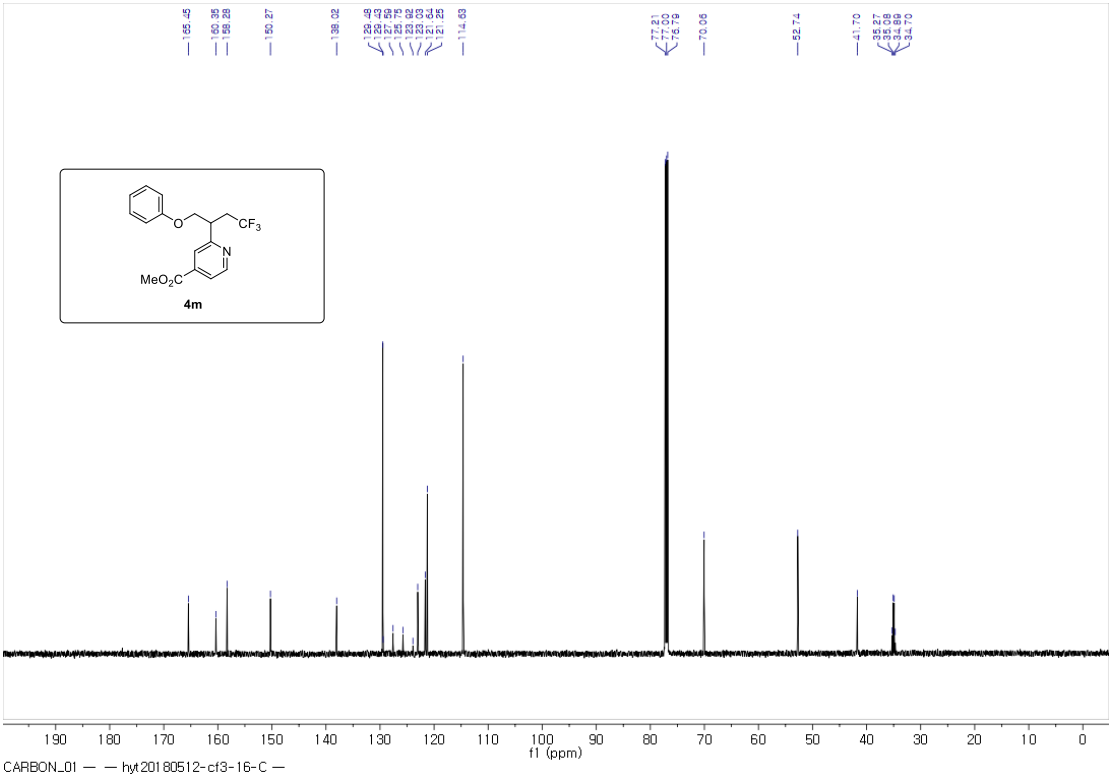


564 MHz, ^{19}F NMR in $CDCl_3$

methyl 2-(4,4,4-trifluoro-1-phenoxybutan-2-yl)isonicotinate (4m).



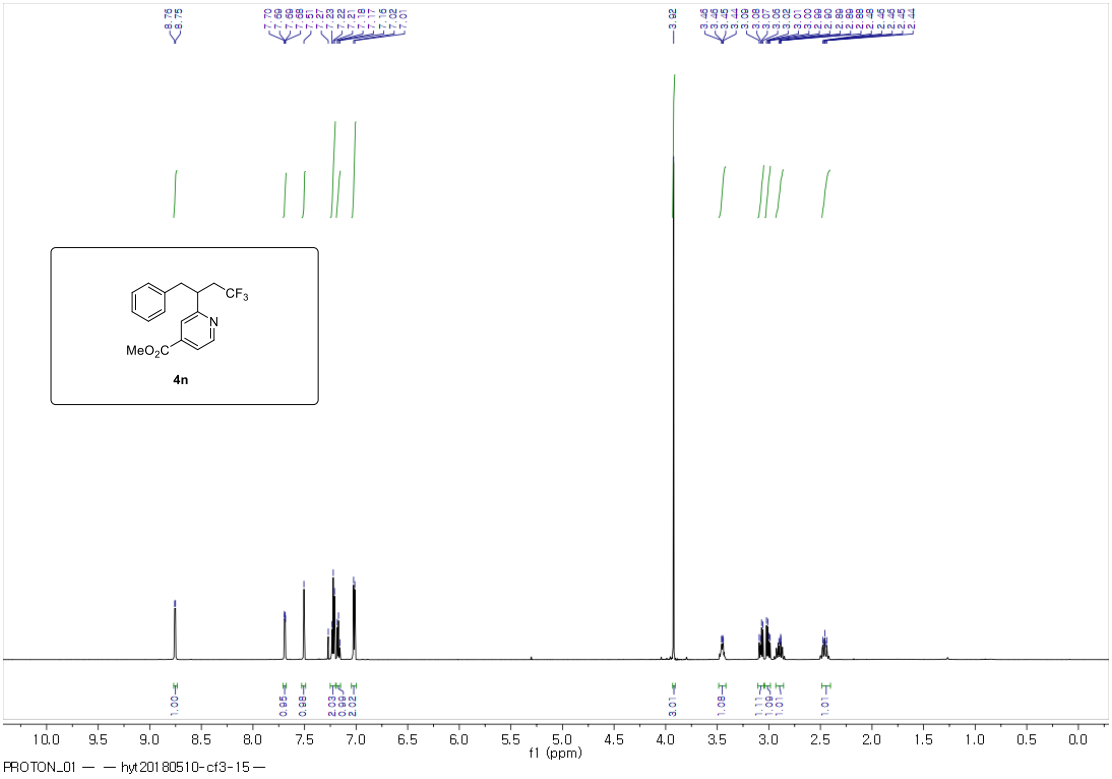
599 MHz, ^{1}H NMR in $CDCl_3$



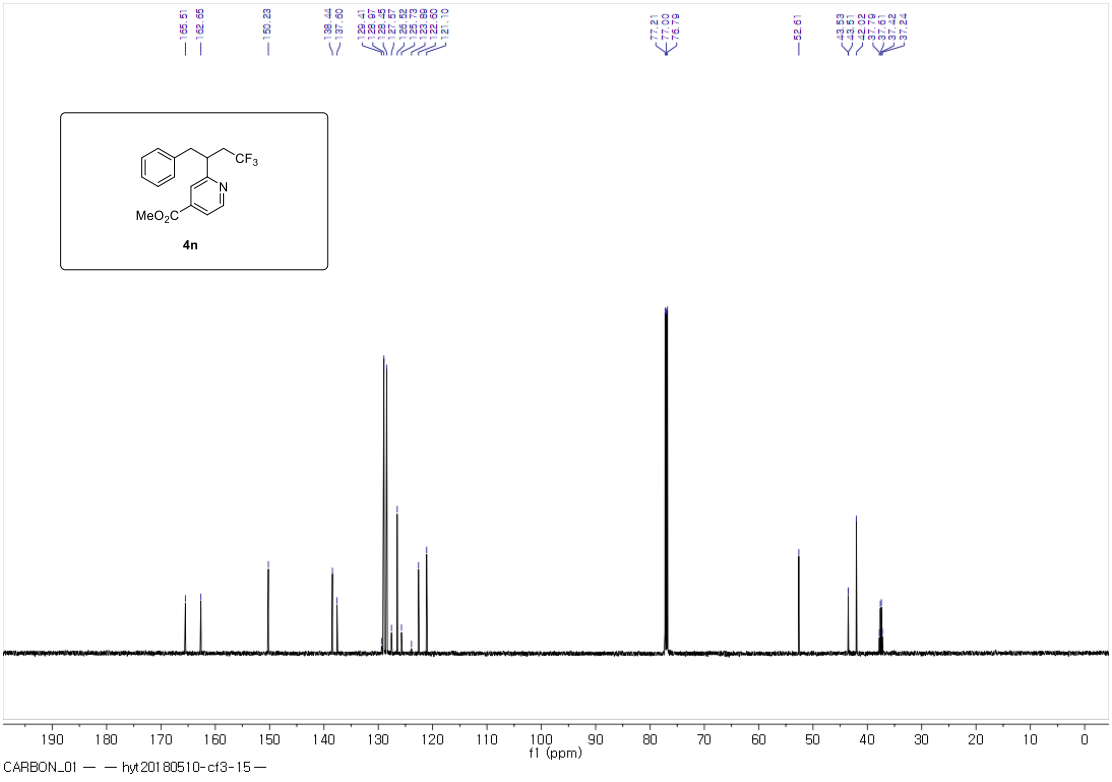
151 MHz, ^{13}C NMR in $CDCl_3$

564 MHz, ^{19}F NMR in $CDCl_3$

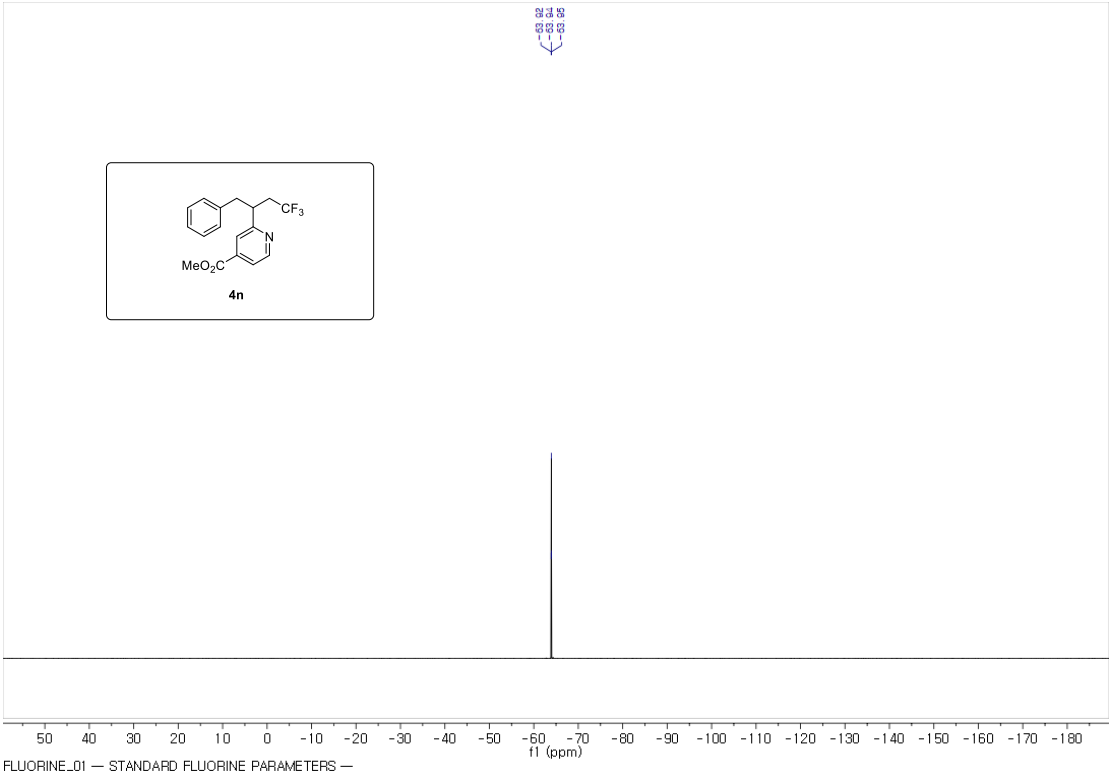
methyl 2-(4,4,4-trifluoro-1-phenylbutan-2-yl)isonicotinate (4n).



599 MHz, ^{1}H NMR in $CDCl_3$

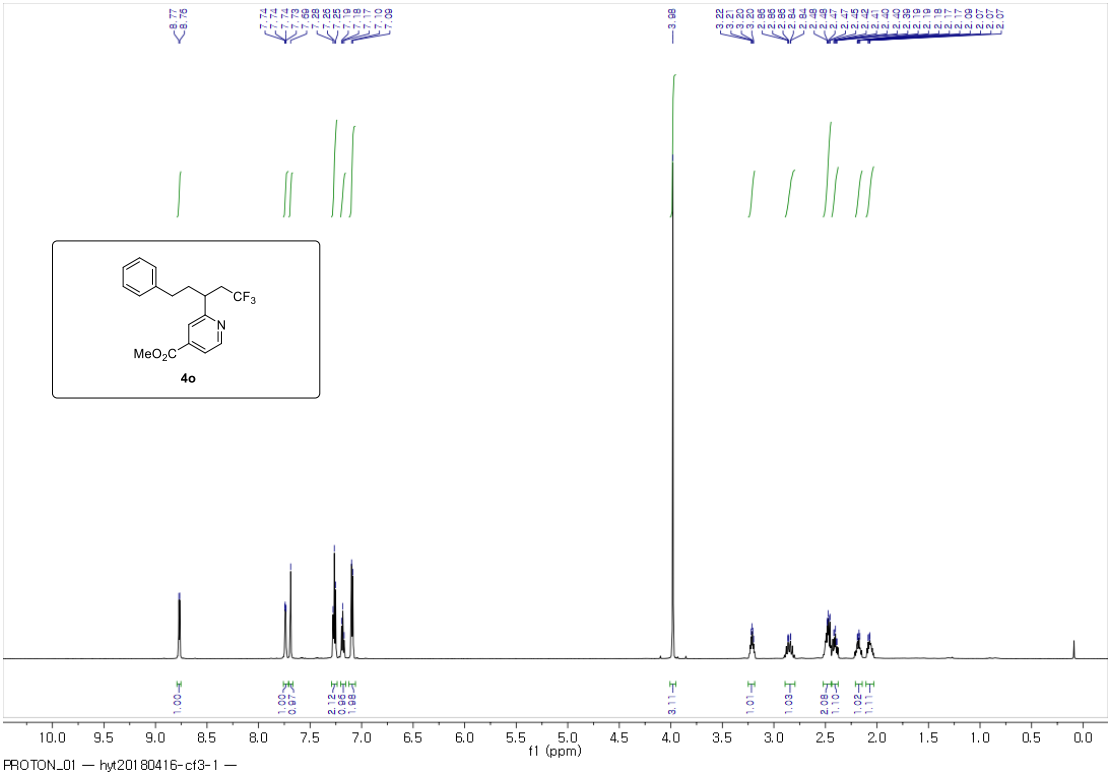


151 MHz, ^{13}C NMR in $CDCl_3$

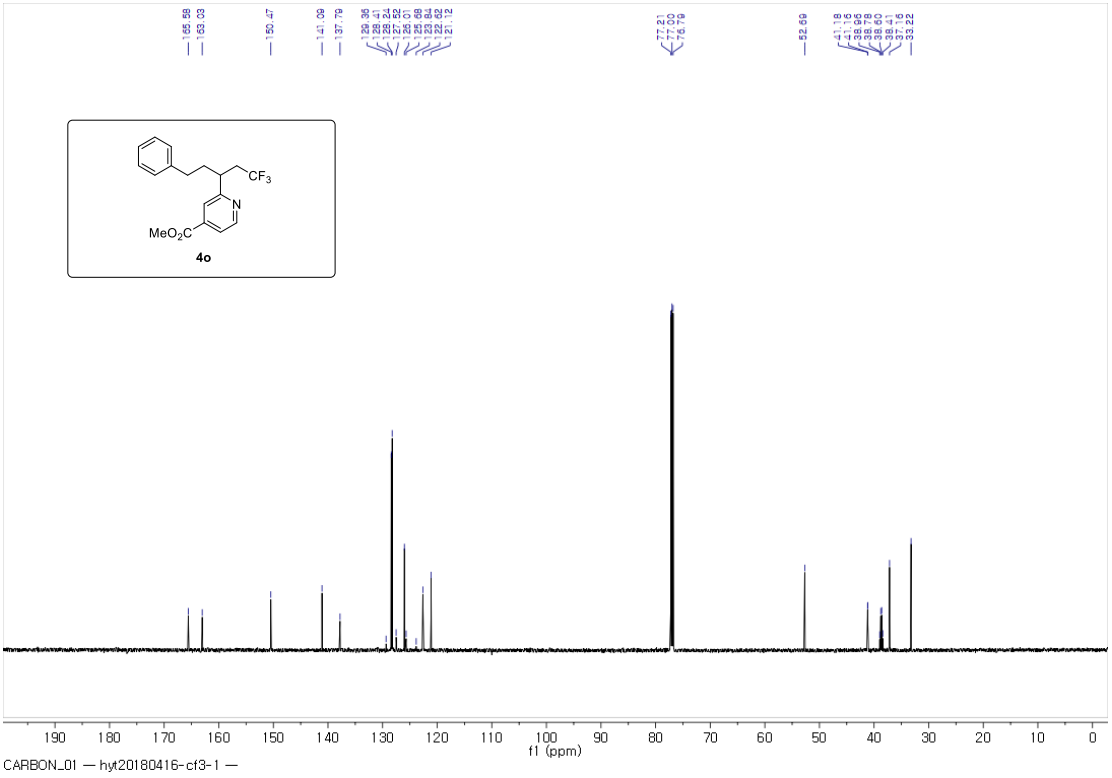


564 MHz, ^{19}F NMR in $CDCl_3$

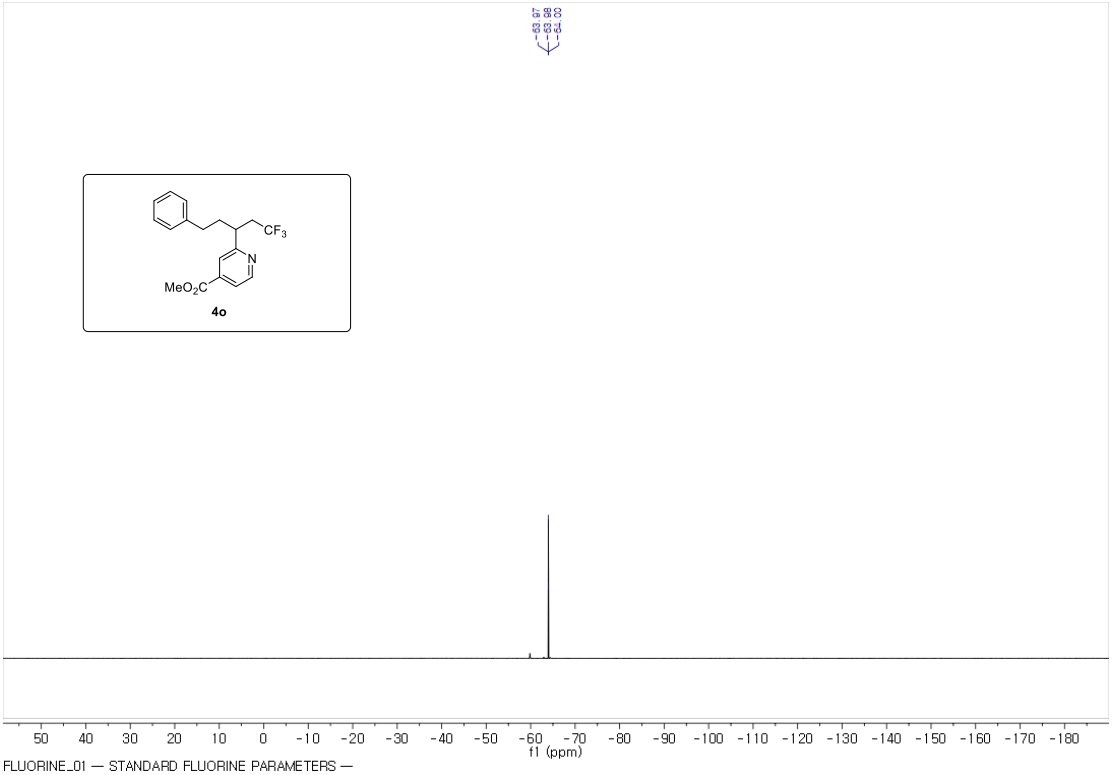
methyl 2-(1,1,1-trifluoro-5-phenylpentan-3-yl)isonicotinate (4o).



599 MHz, ^{1}H NMR in $CDCl_3$

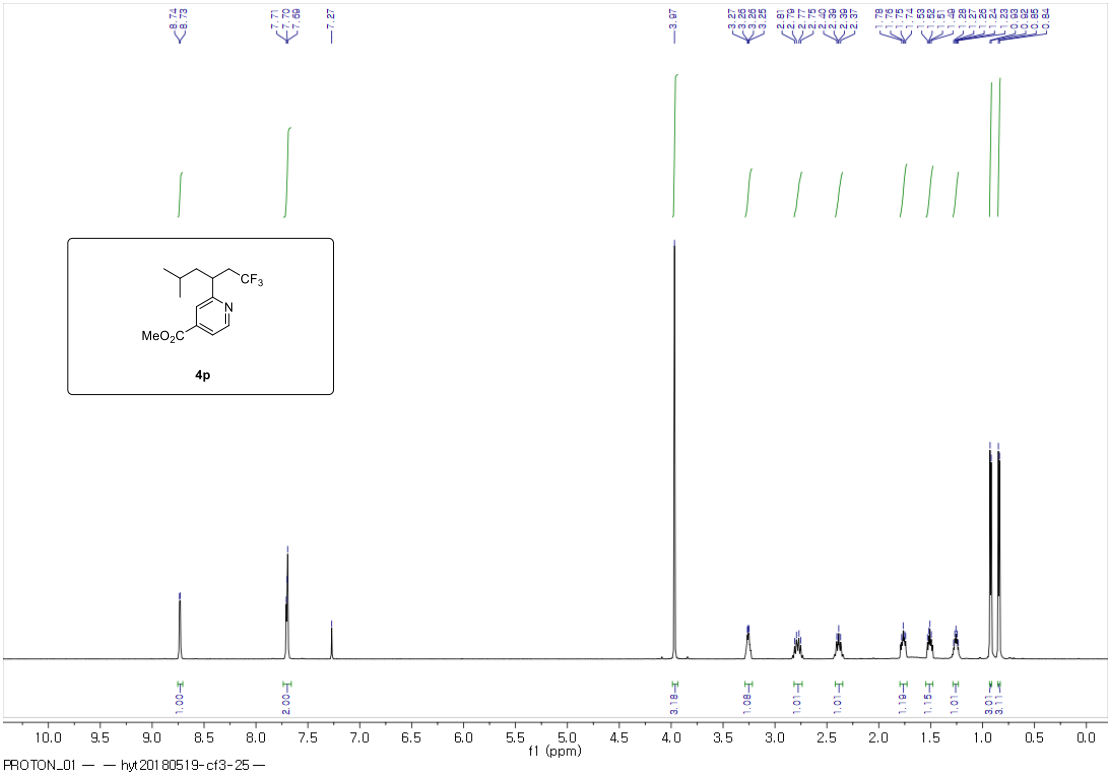


151 MHz, ^{13}C NMR in $CDCl_3$

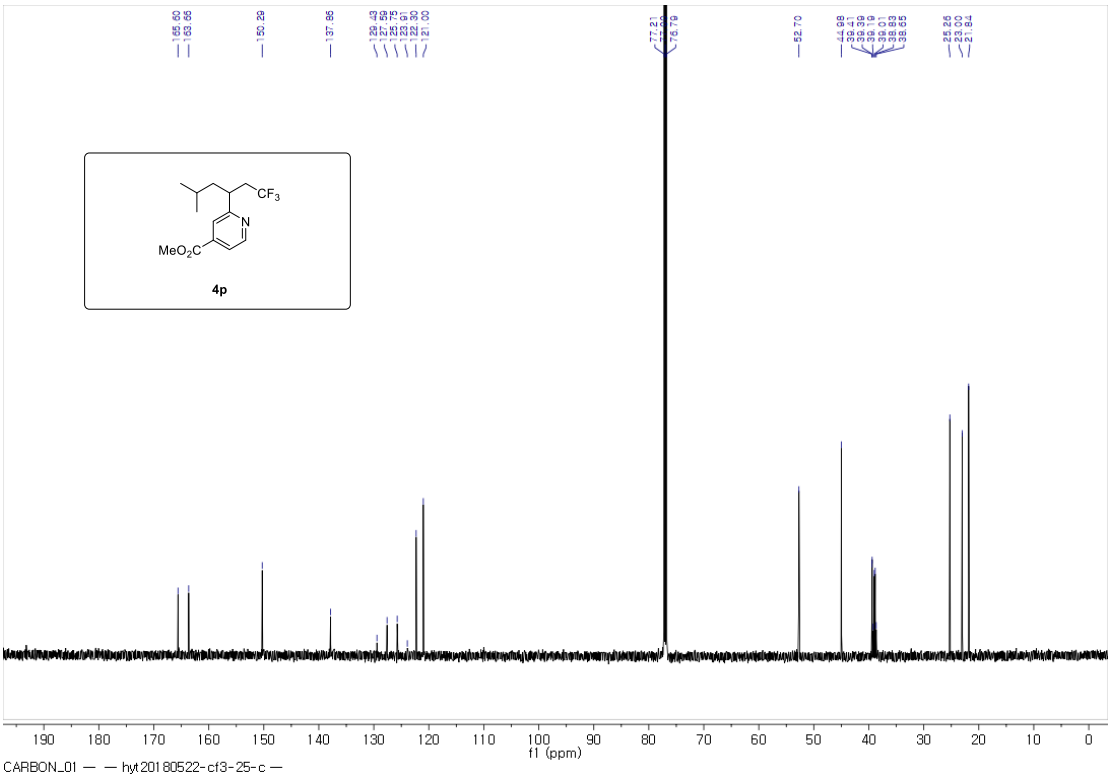


564 MHz, ^{19}F NMR in $CDCl_3$

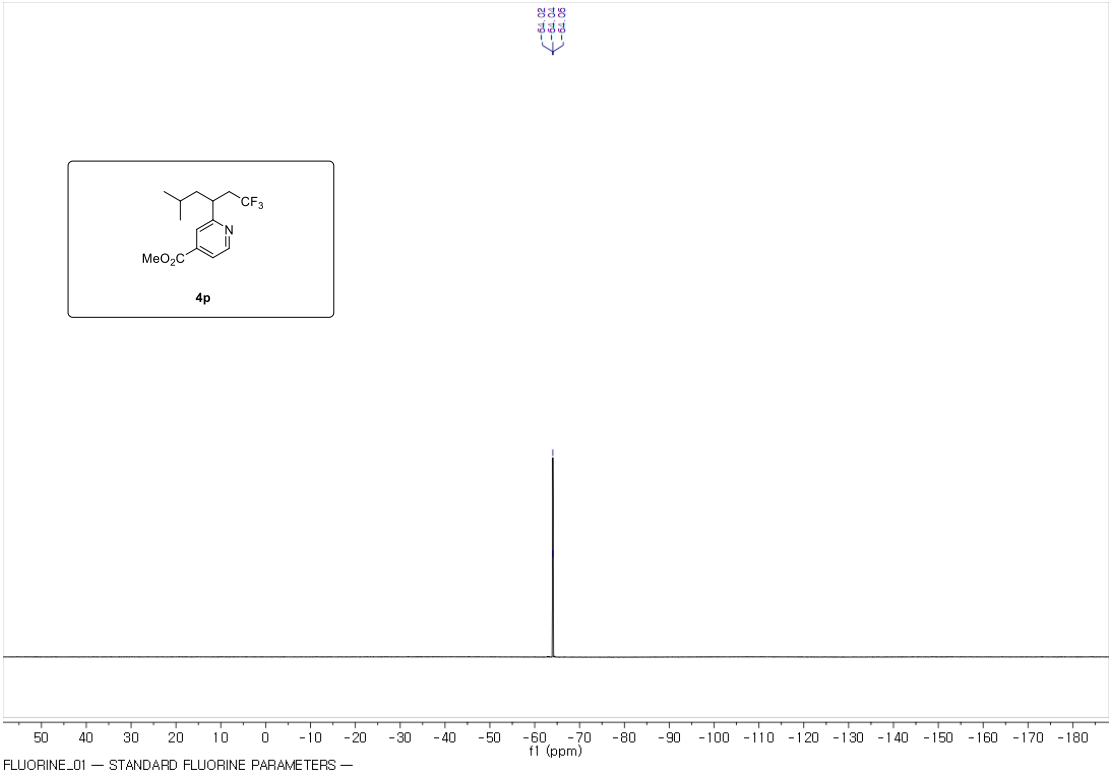
methyl 2-(1,1,1-trifluoro-5-methylhexan-3-yl)isonicotinate (4p).



599 MHz, ^{1}H NMR in $CDCl_3$

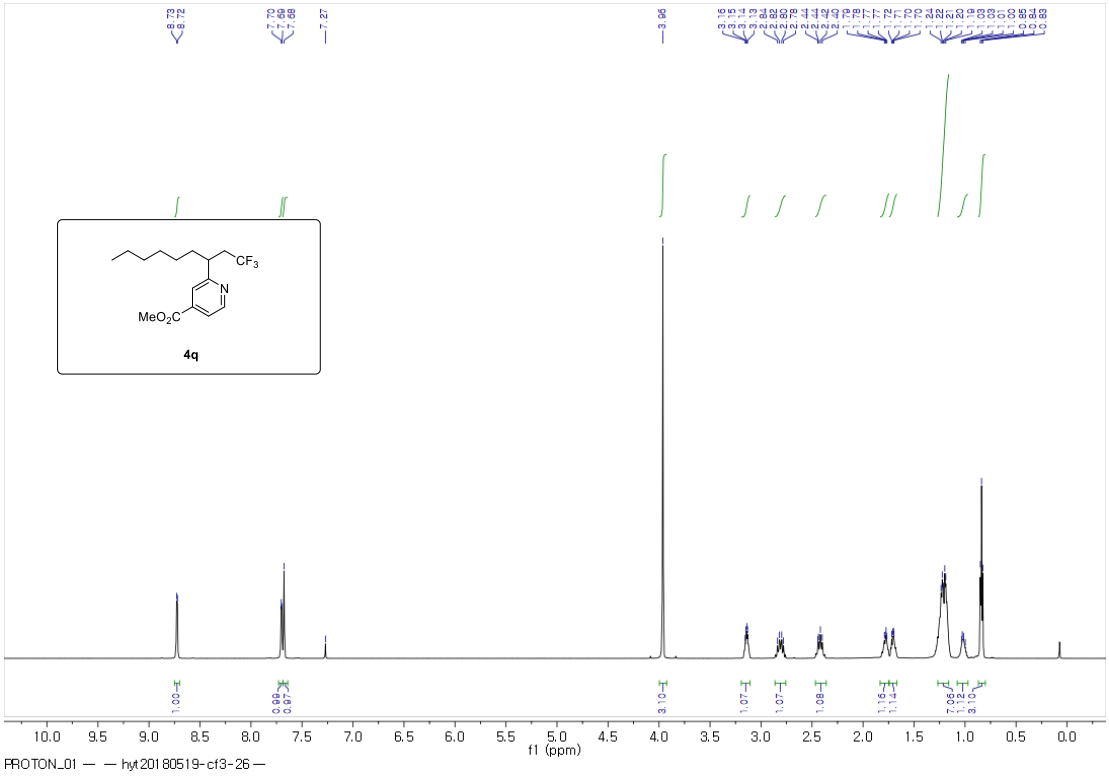


151 MHz, ^{13}C NMR in $CDCl_3$

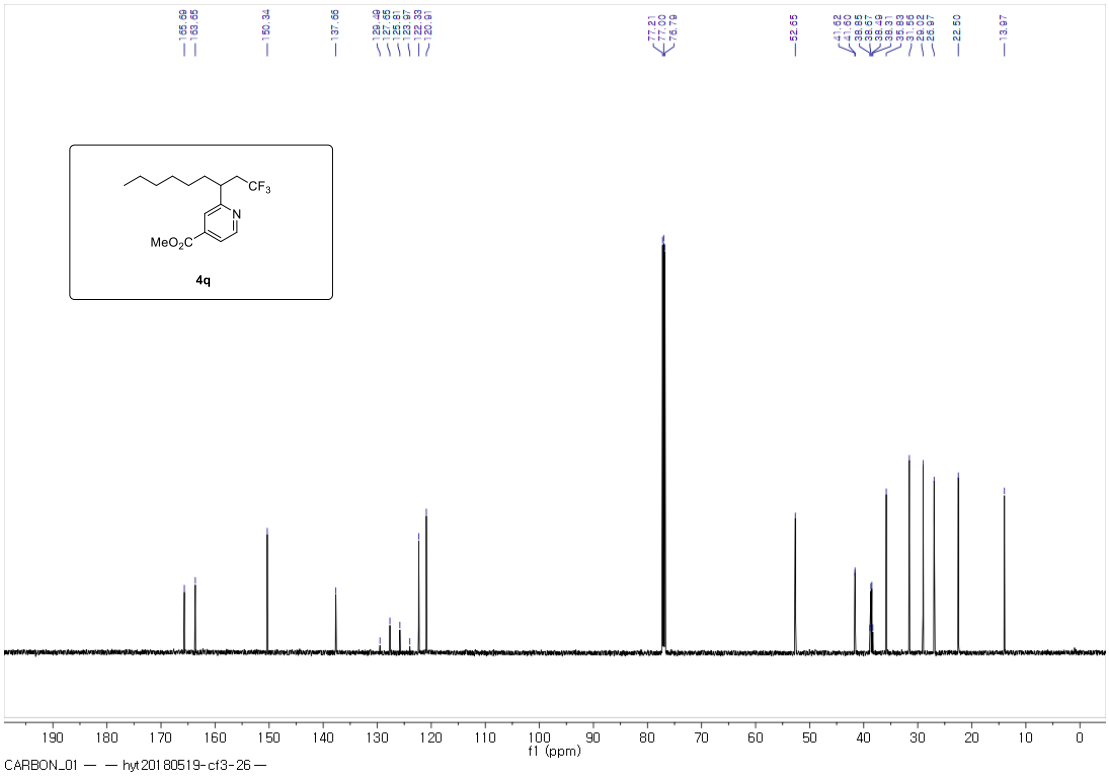


564 MHz, ^{19}F NMR in $CDCl_3$

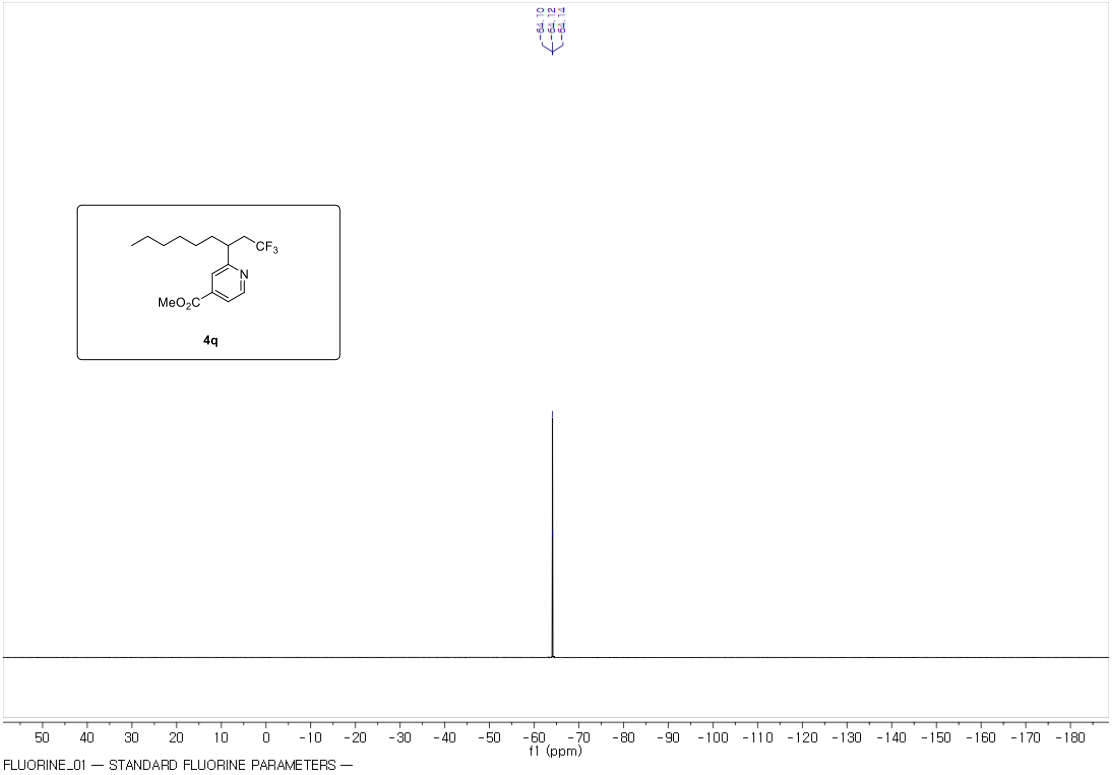
methyl 2-(1,1,1-trifluorononan-3-yl)isonicotinate (4q).



599 MHz, ^{1}H NMR in $CDCl_3$

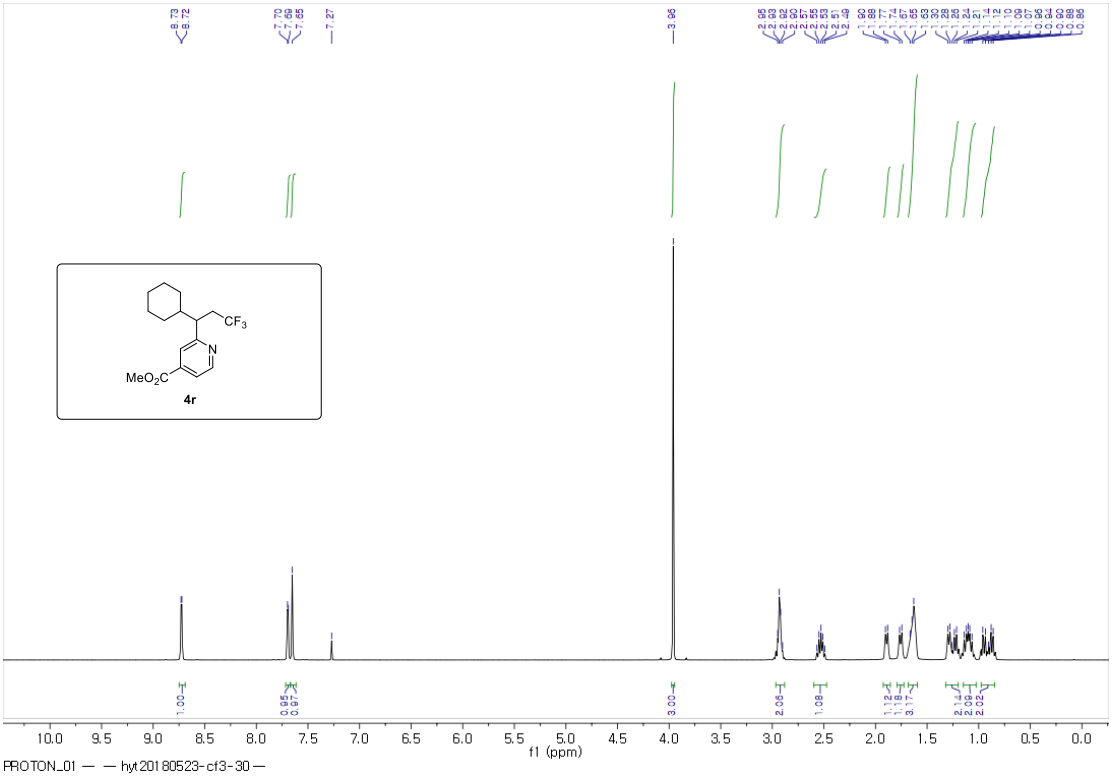


151 MHz, ^{13}C NMR in $CDCl_3$

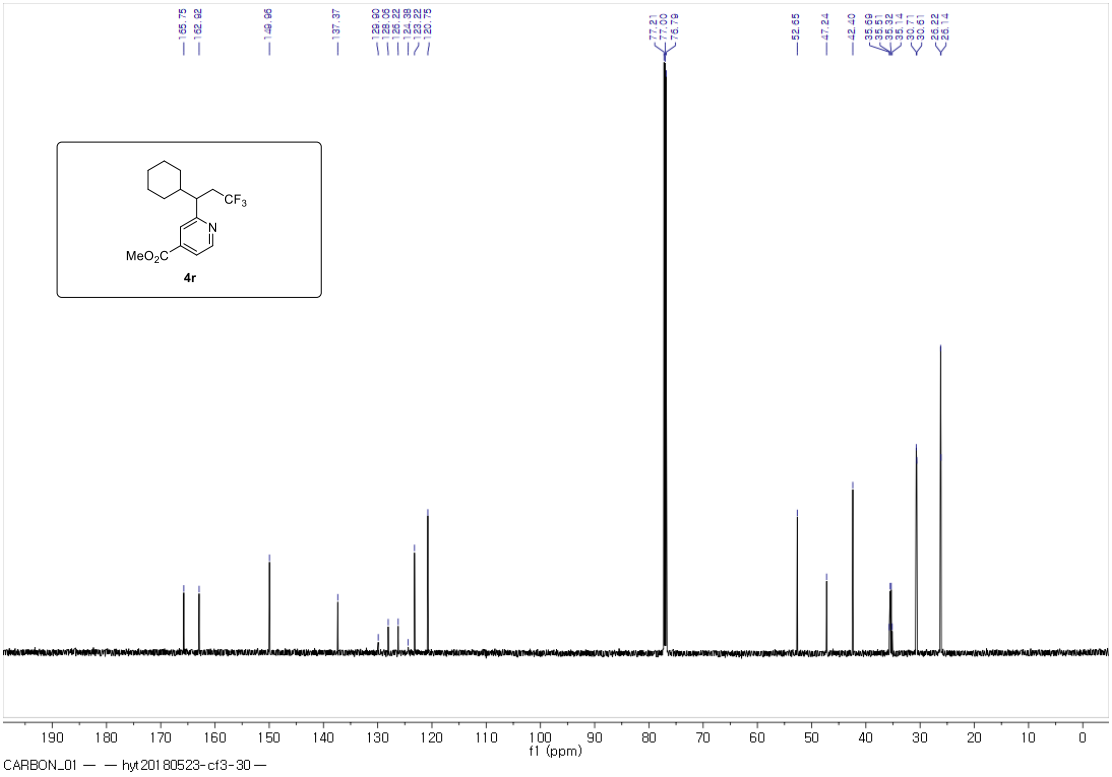


564 MHz, ^{19}F NMR in $CDCl_3$

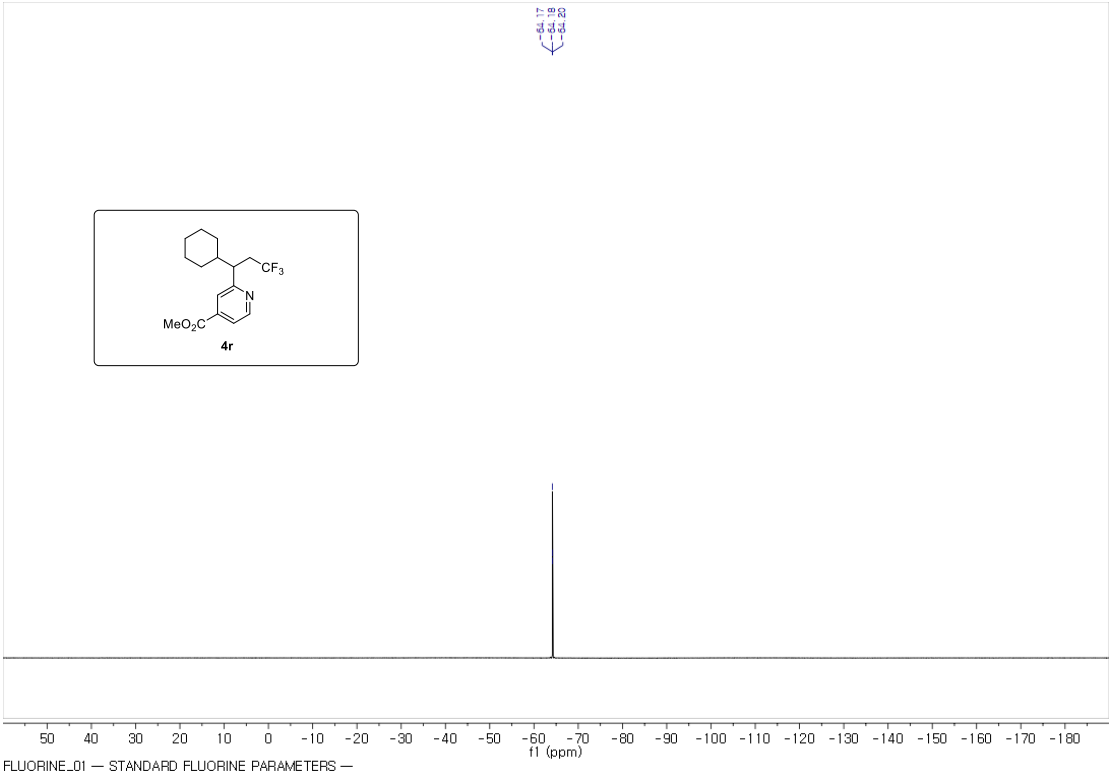
methyl 2-(1-cyclohexyl-3,3,3-trifluoropropyl)isonicotinate (4r).



599 MHz, ^{1}H NMR in $CDCl_3$

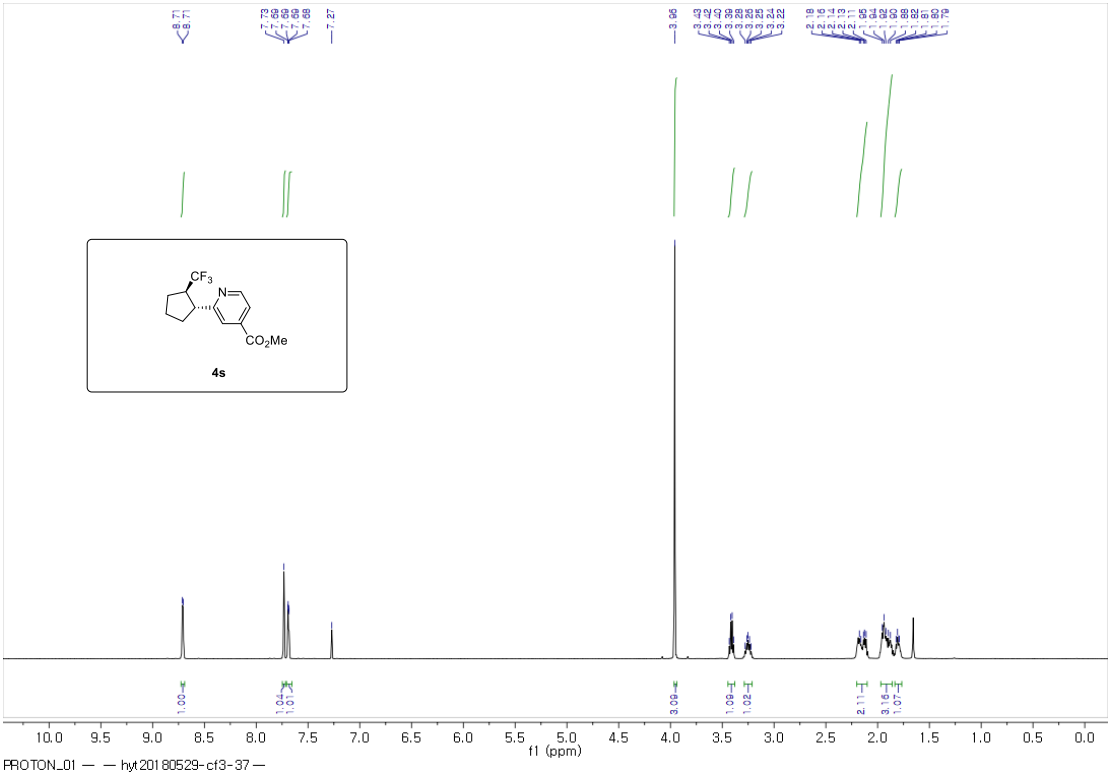


151 MHz, ^{13}C NMR in $CDCl_3$

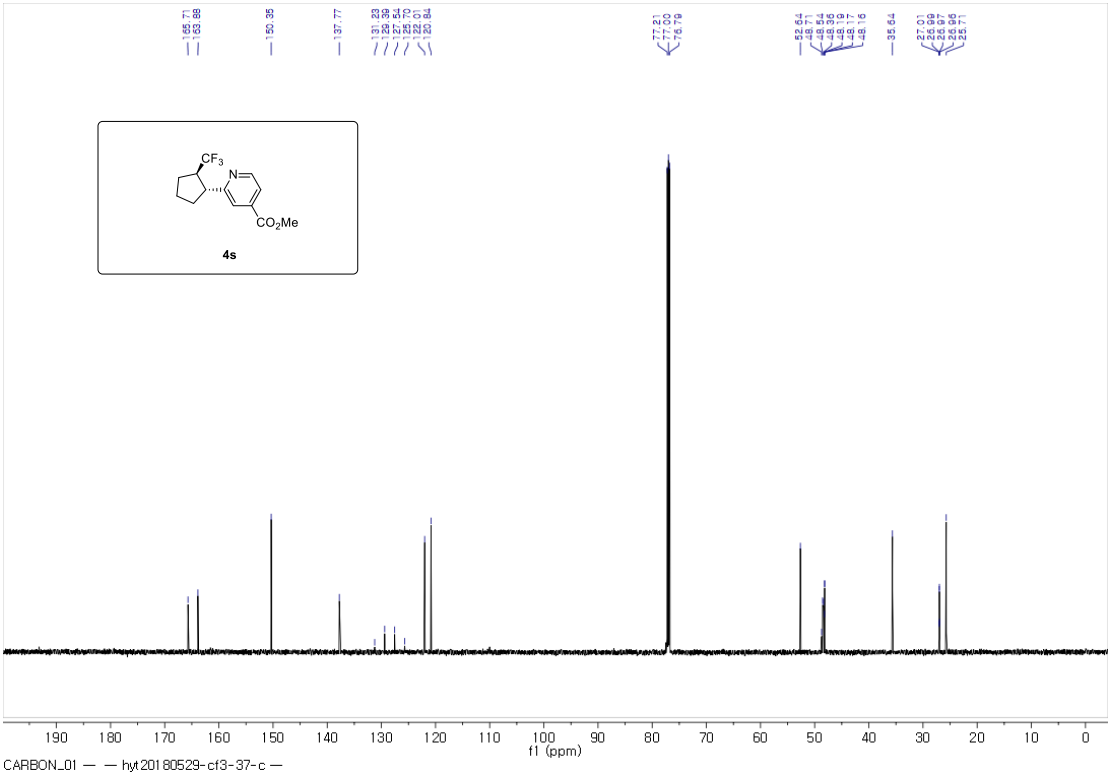


564 MHz, ^{19}F NMR in $CDCl_3$

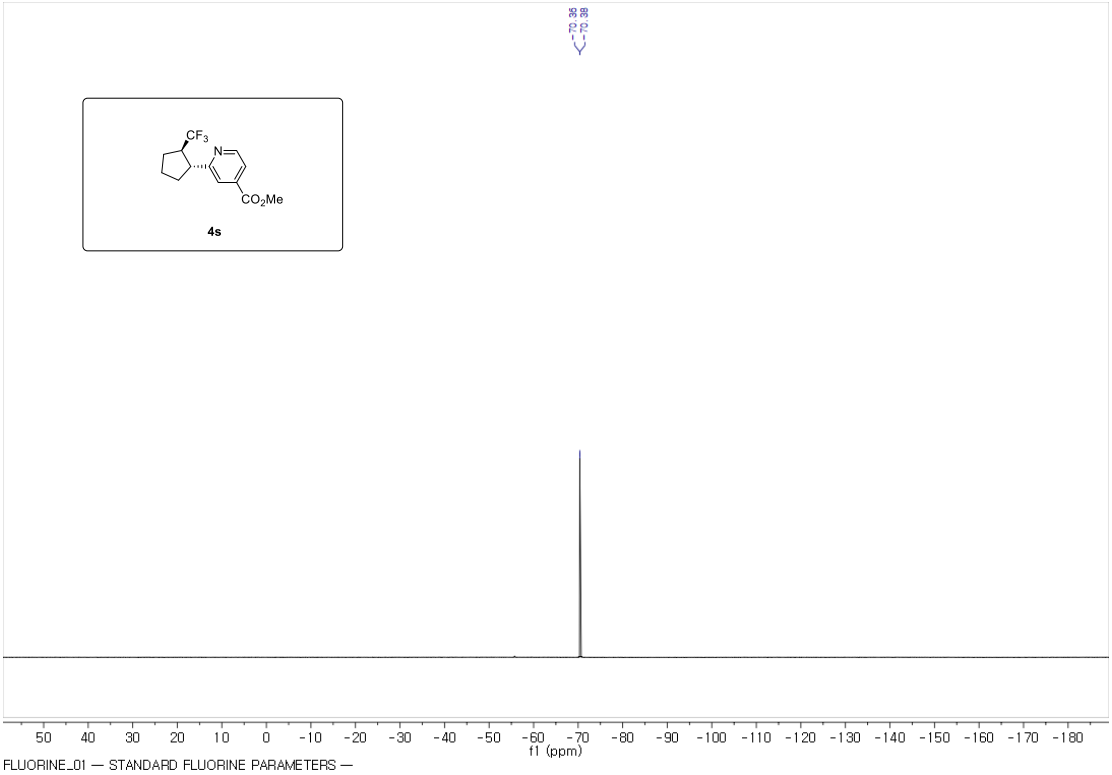
methyl 2-((1R,2R)-2-(trifluoromethyl)cyclopentyl)isonicotinate (4s).



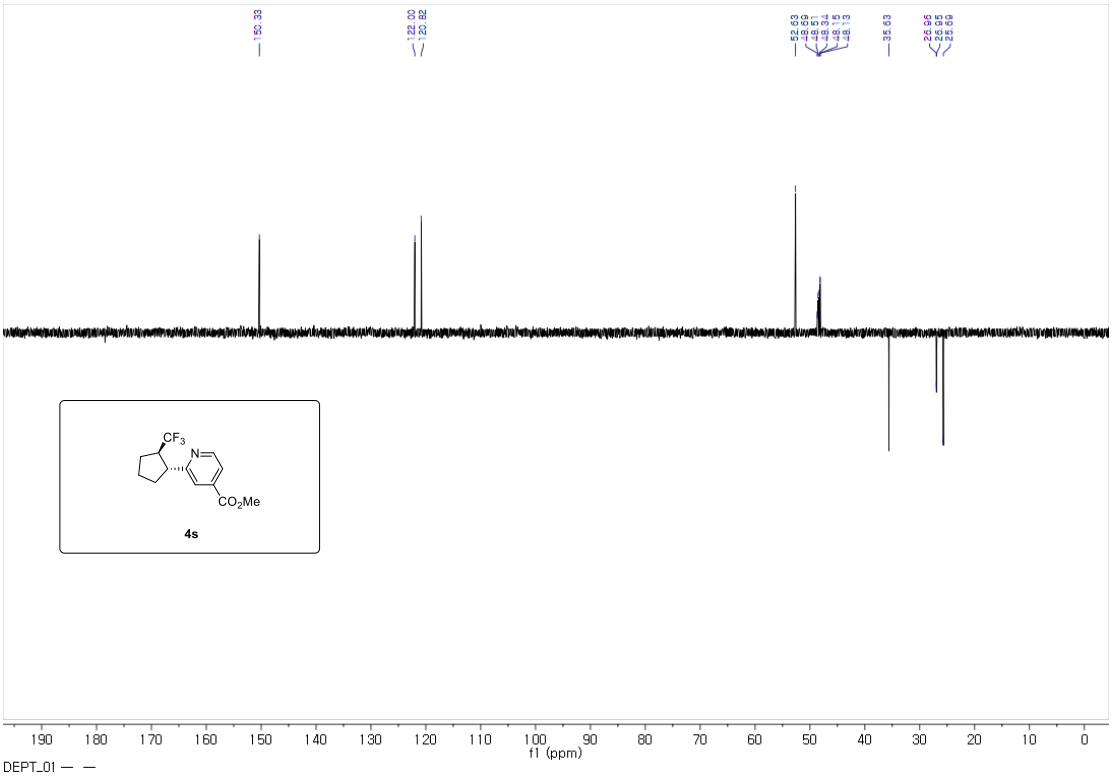
599 MHz, ^{1}H NMR in $CDCl_3$



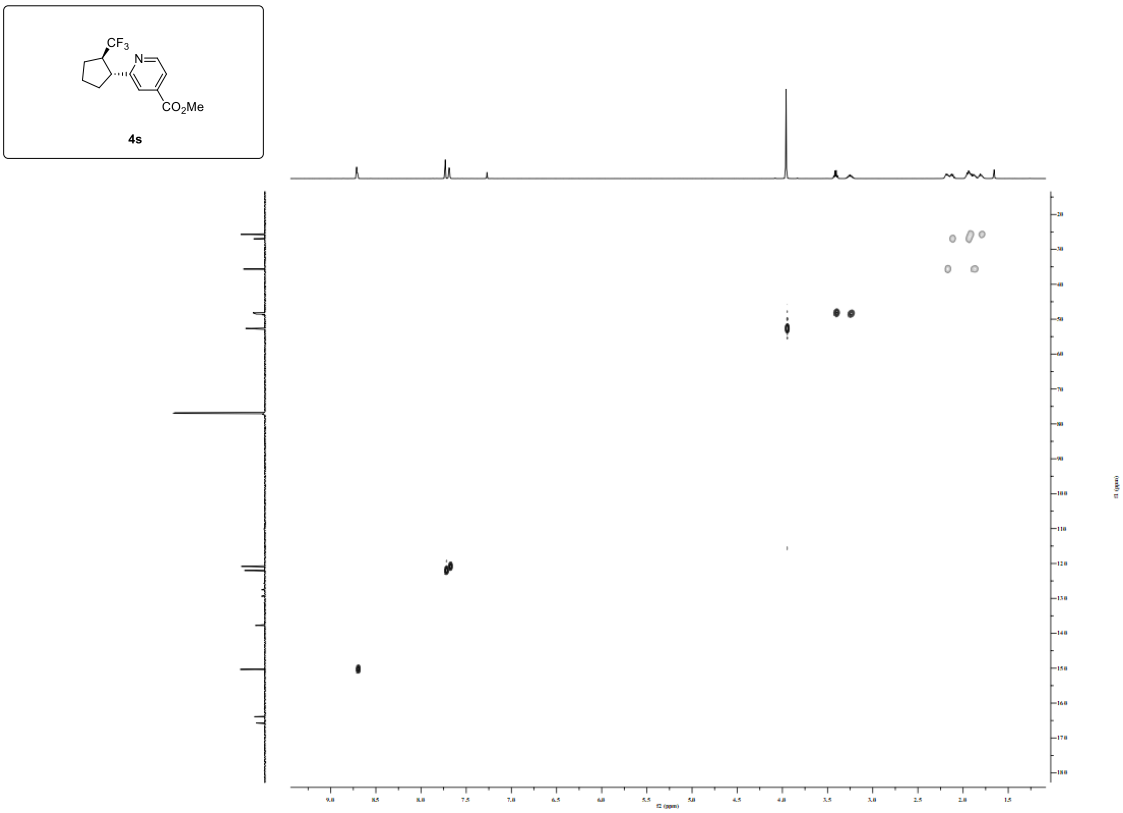
151 MHz, ^{13}C NMR in $CDCl_3$



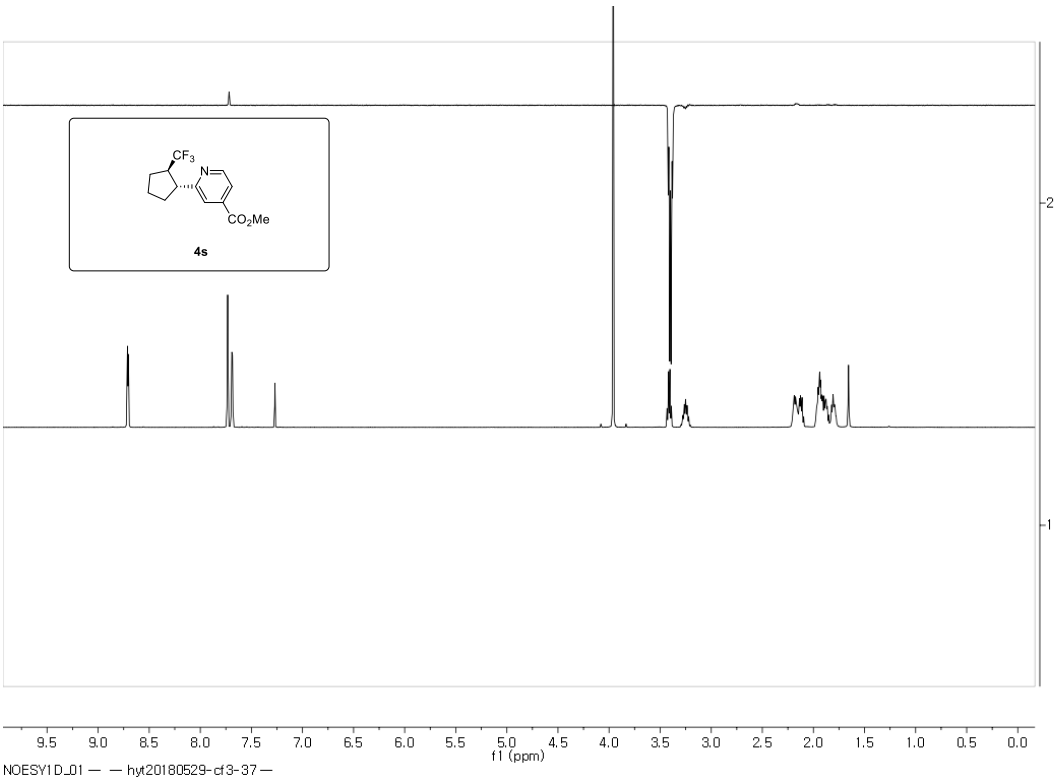
564 MHz, ^{19}F NMR in $CDCl_3$



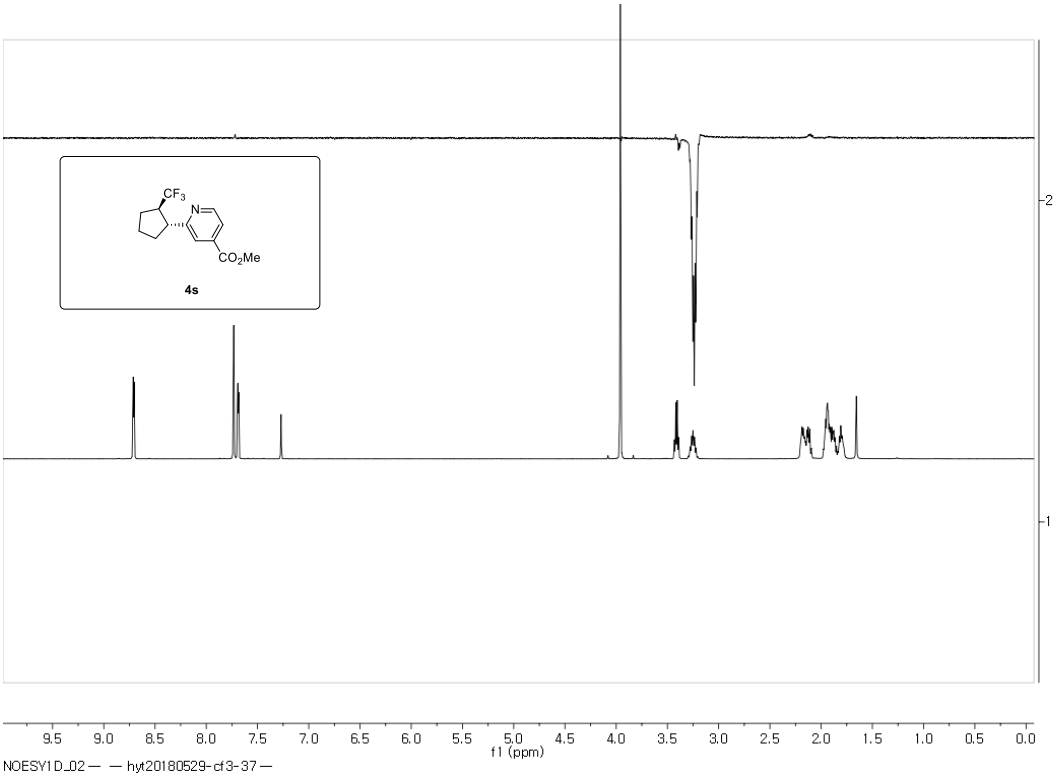
DEPT135 in $CDCl_3$



HSQC in $CDCl_3$

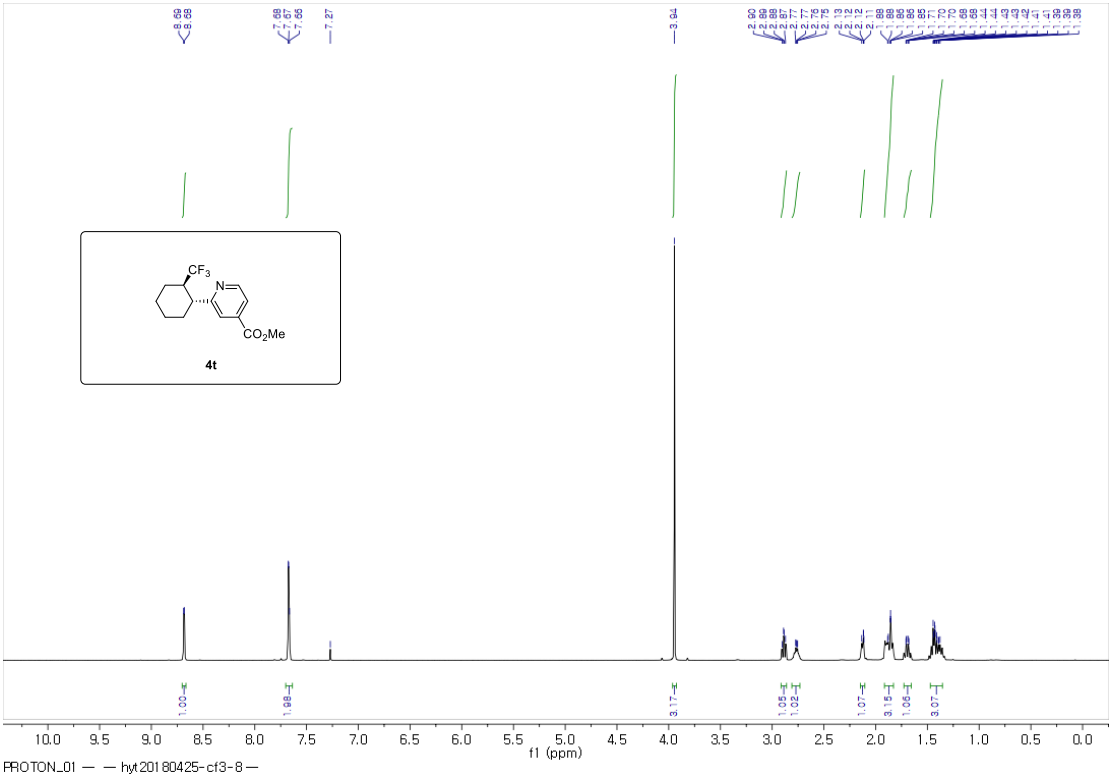


NOESY 1D in $CDCl_3$

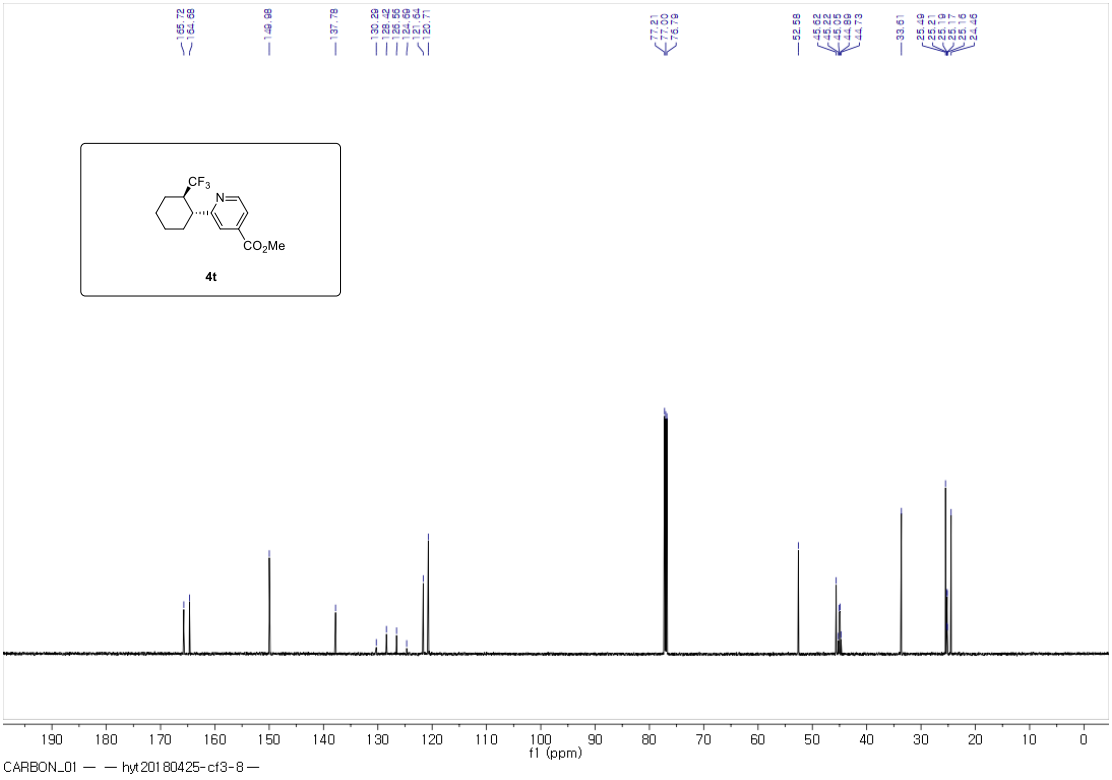


NOESY 1D in $CDCl_3$

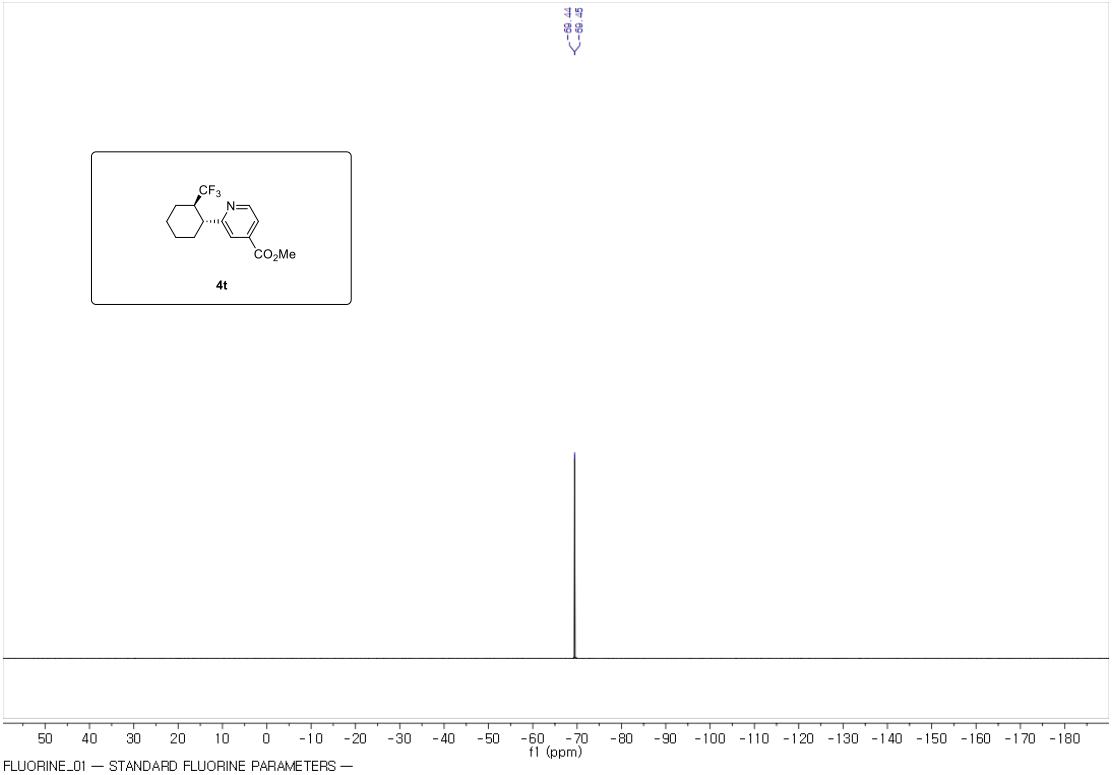
methyl 2-((1R,2R)-2-(trifluoromethyl)cyclohexyl)isonicotinate (4t).



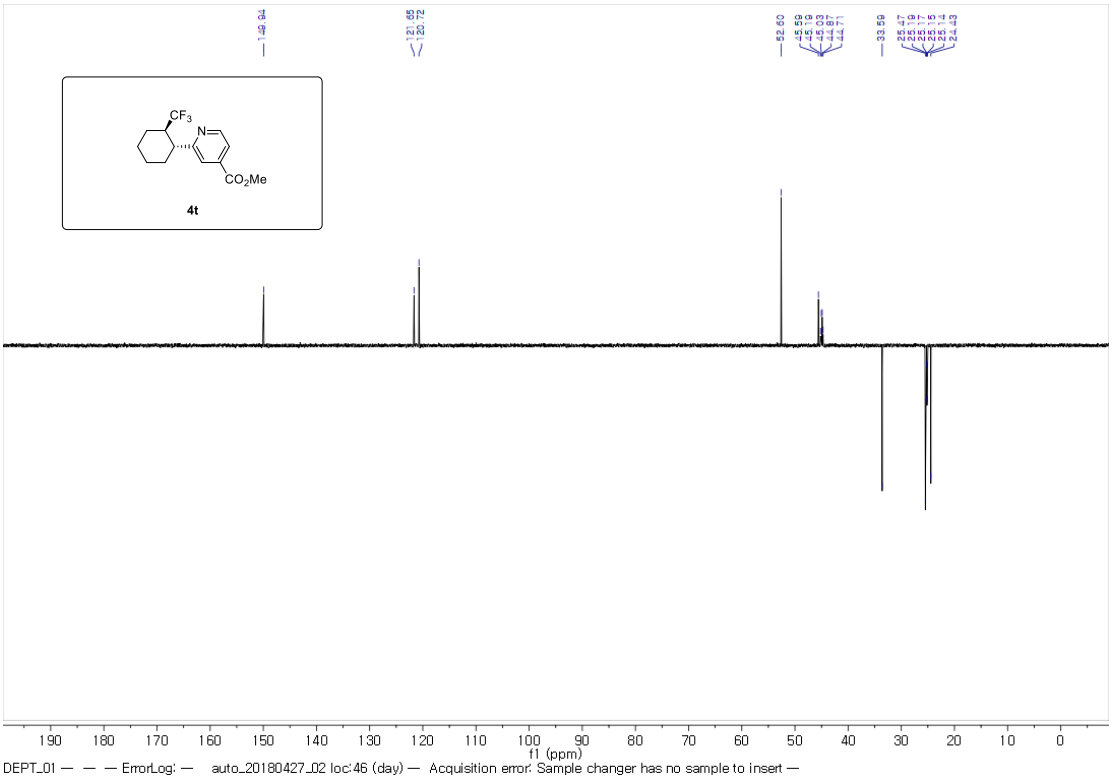
599 MHz, ^{1}H NMR in $CDCl_3$



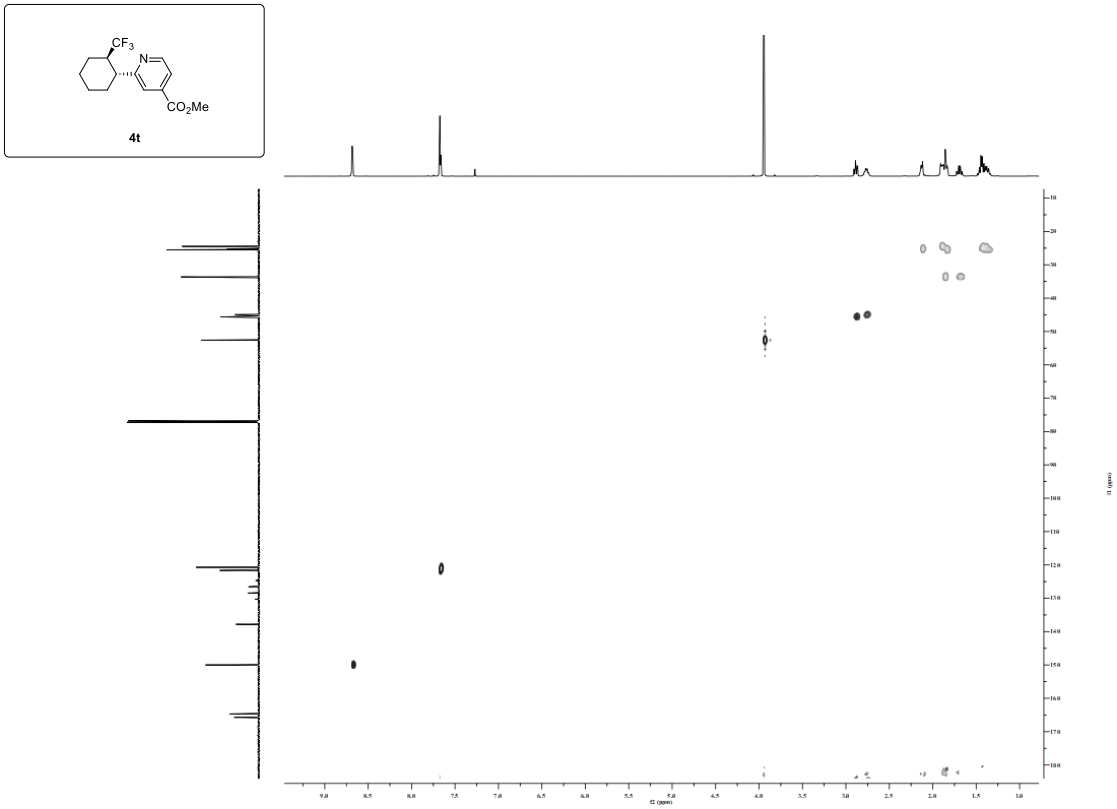
151 MHz, ^{13}C NMR in $CDCl_3$



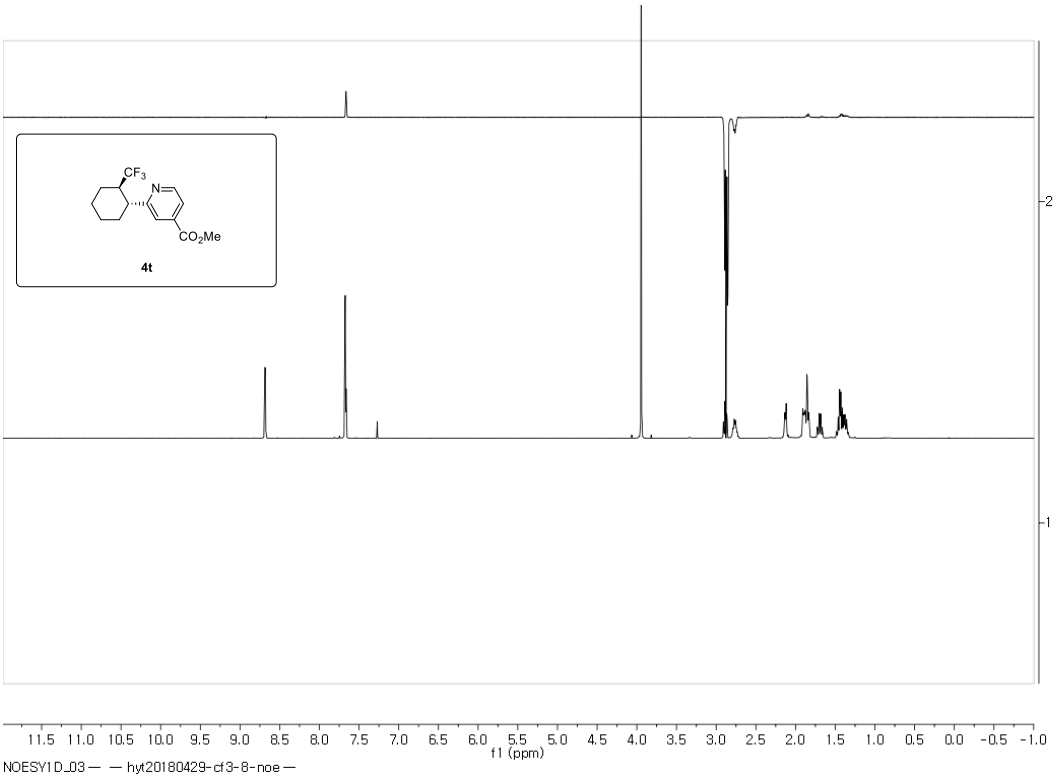
564 MHz, ^{19}F NMR in $CDCl_3$



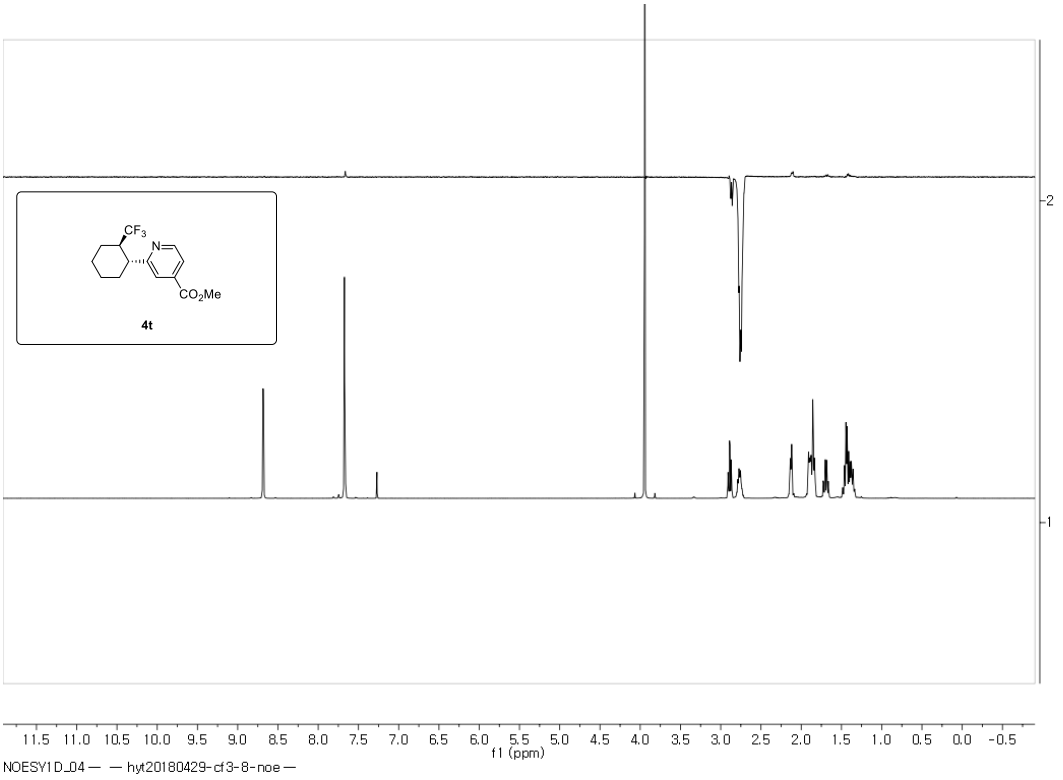
DEPT135 in $CDCl_3$



HSQC in $CDCl_3$

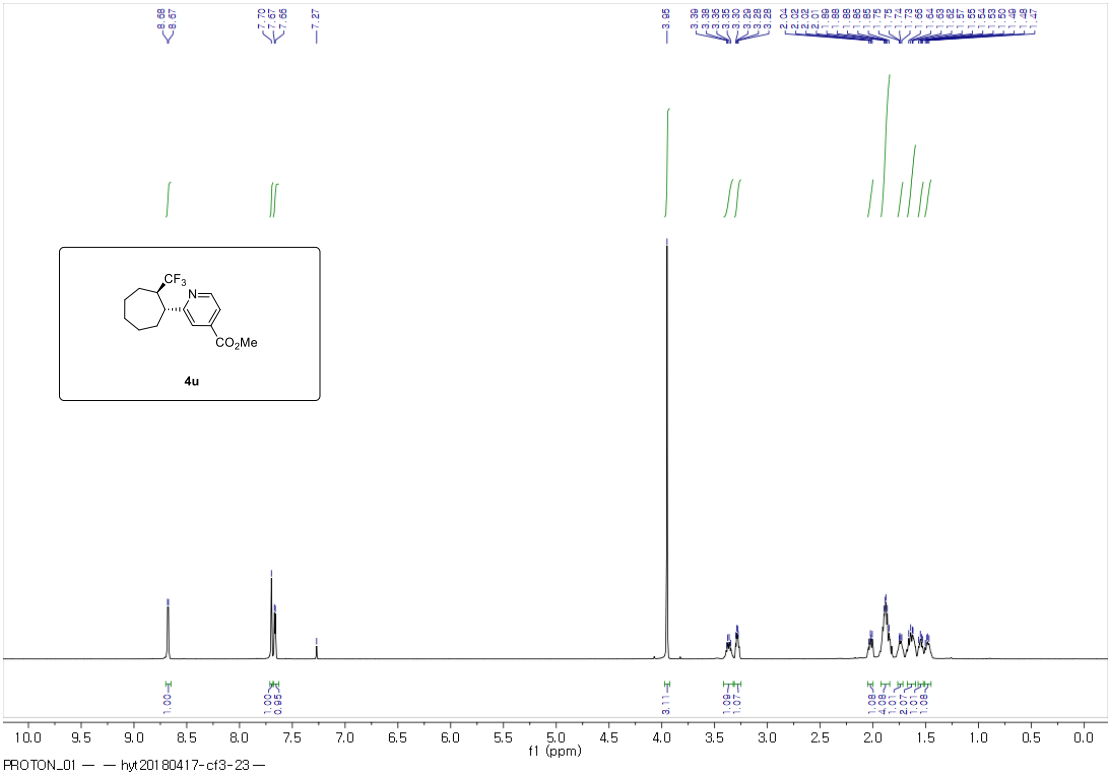


NOESY 1D in $CDCl_3$

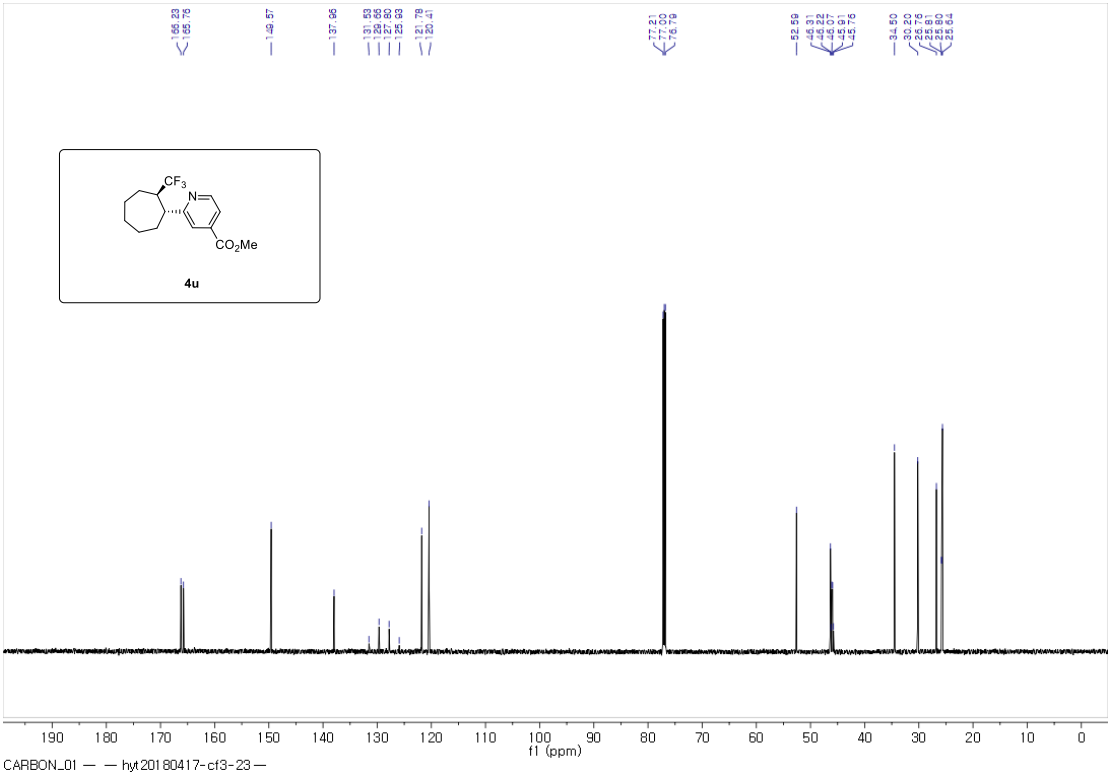


NOESY 1D in $CDCl_3$

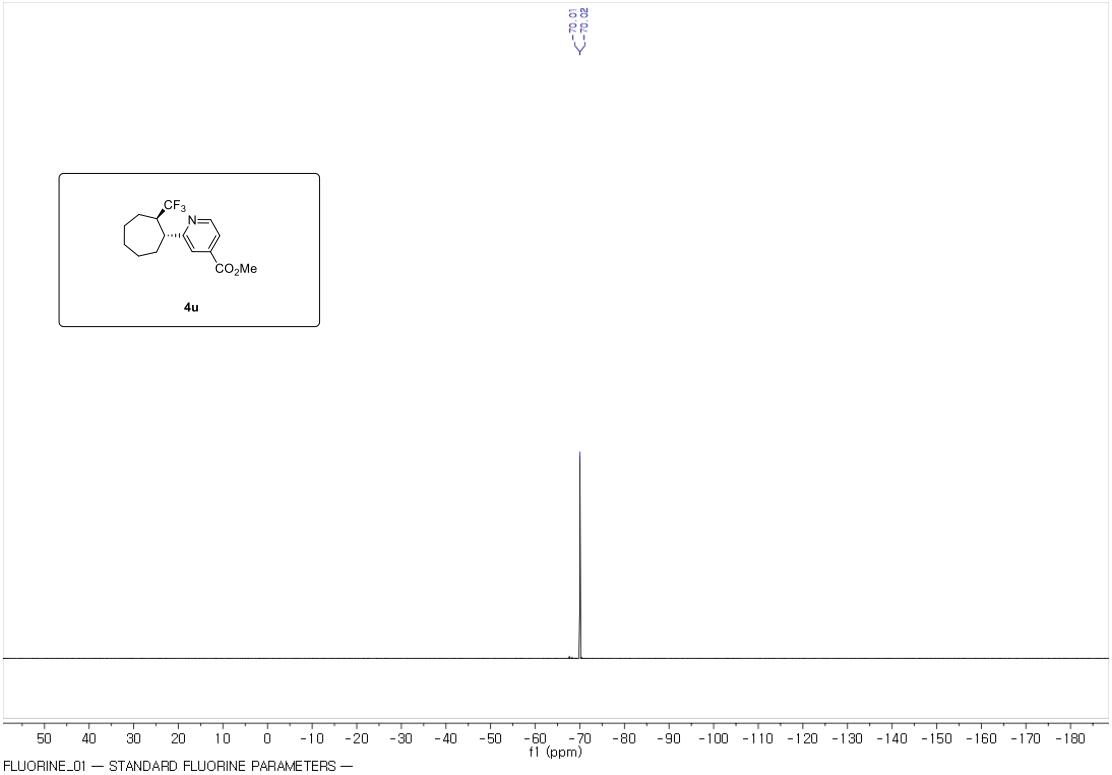
methyl 2-((1R,2R)-2-(trifluoromethyl)cycloheptyl)isonicotinate (4u).



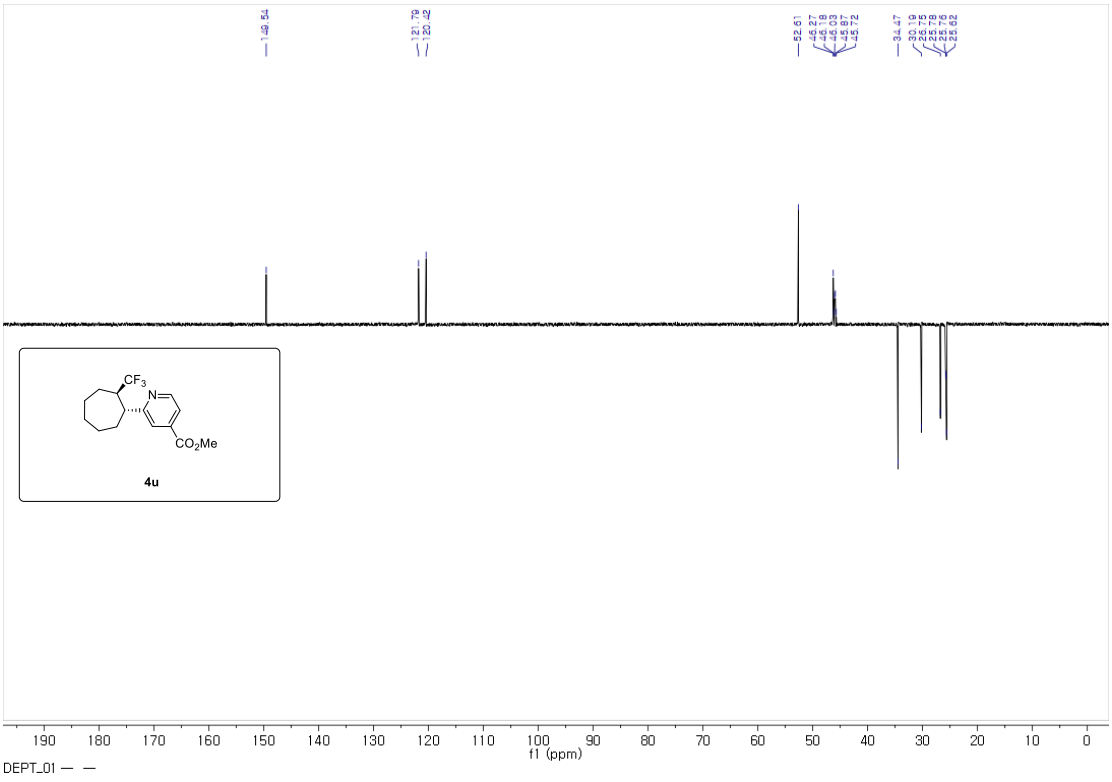
599 MHz, ^{1}H NMR in $CDCl_3$



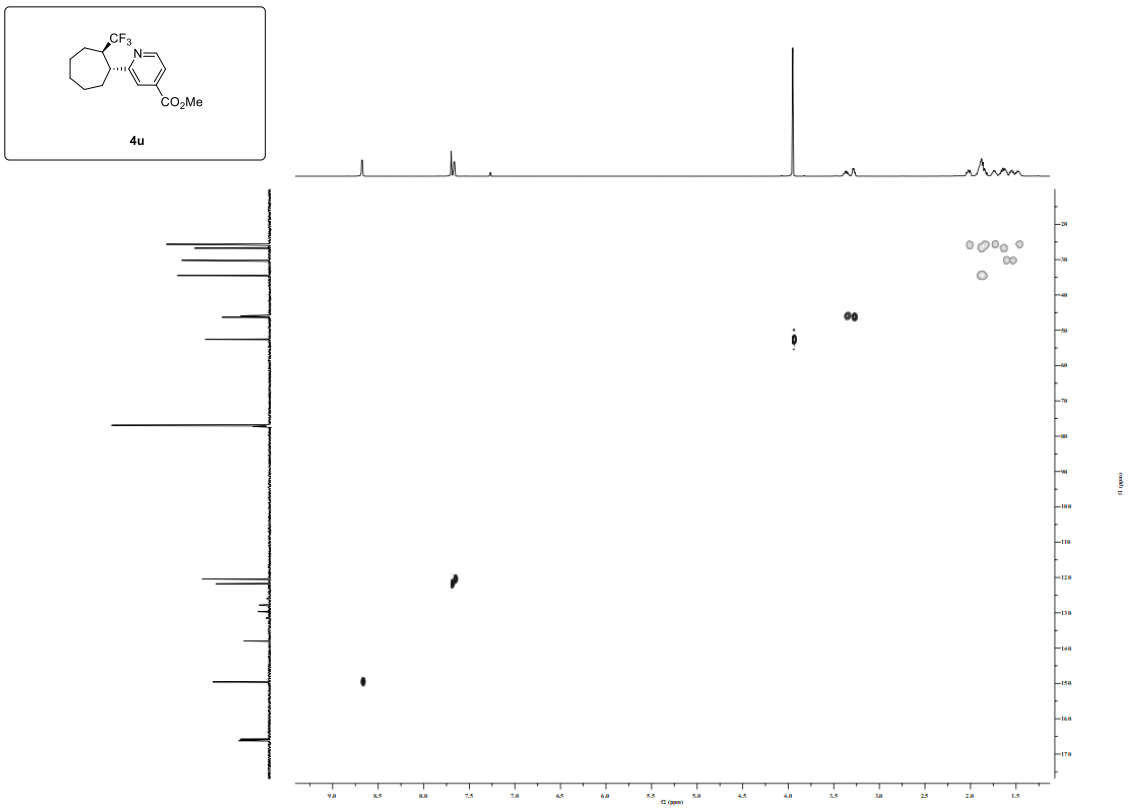
151 MHz, ^{13}C NMR in $CDCl_3$



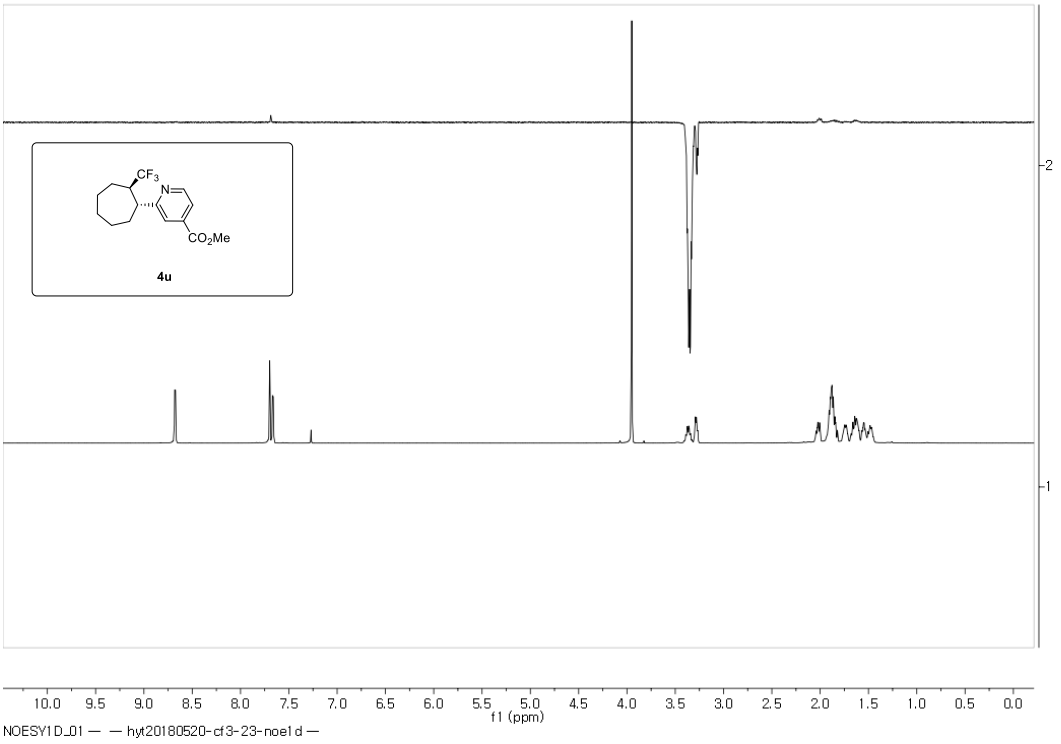
564 MHz, ^{19}F NMR in $CDCl_3$



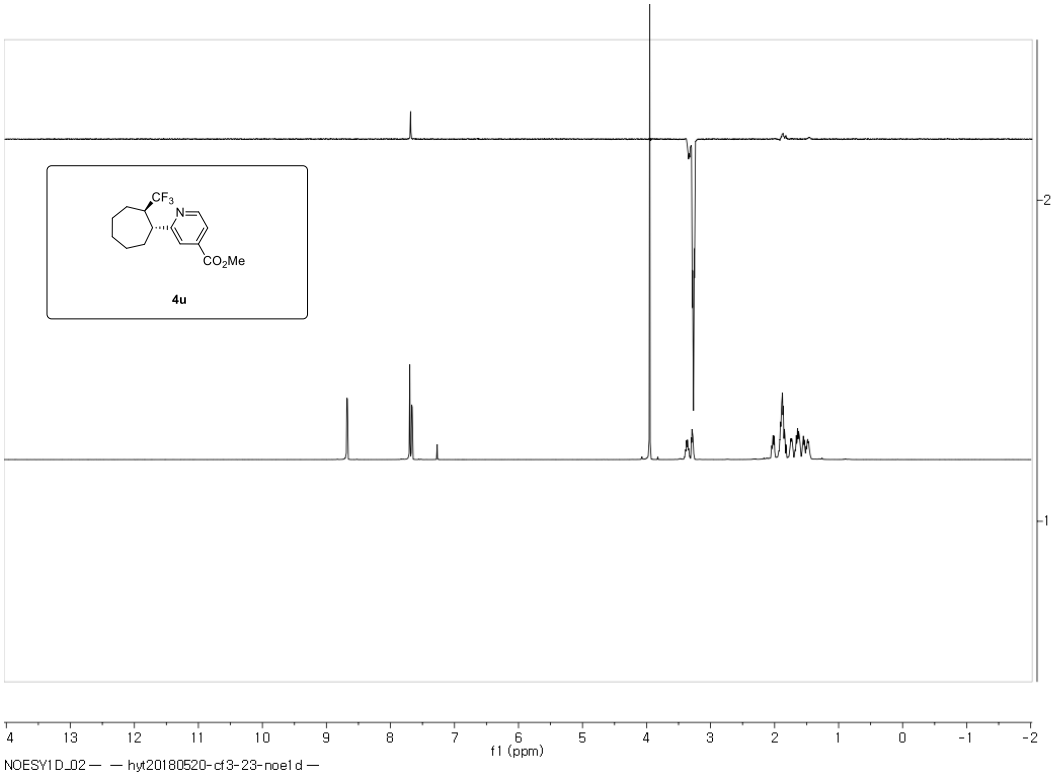
DEPT135 in $CDCl_3$



HSQC in $CDCl_3$

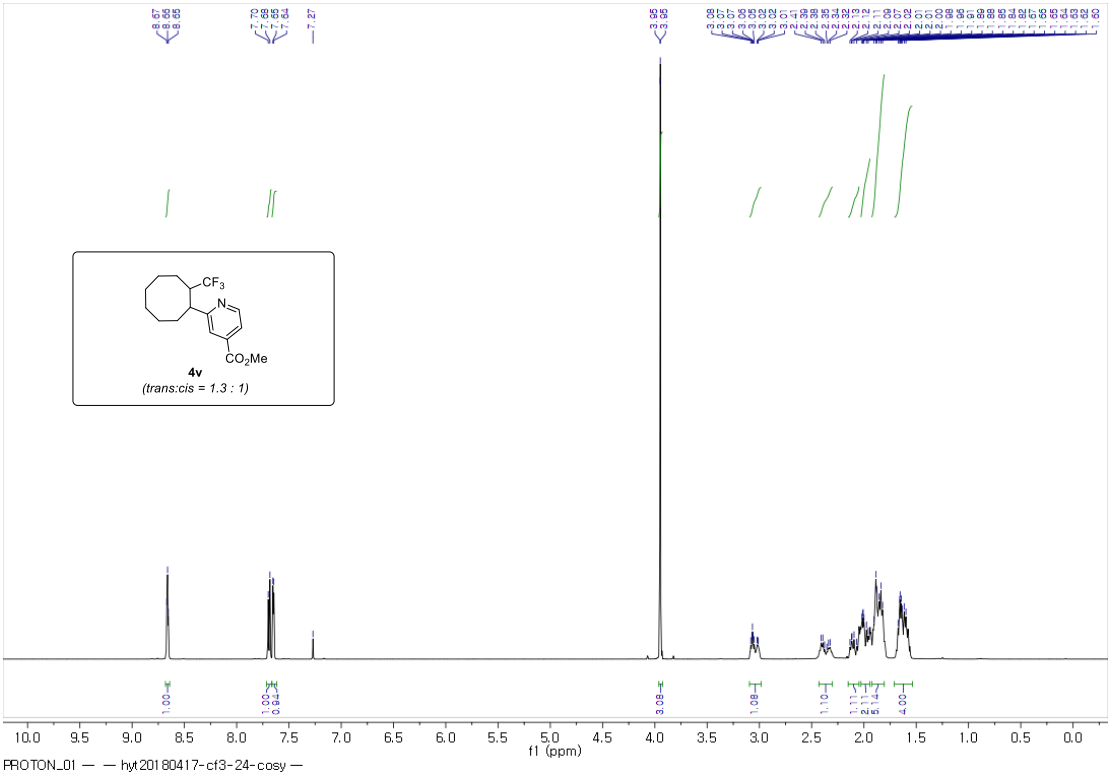


NOESY 1D in $CDCl_3$

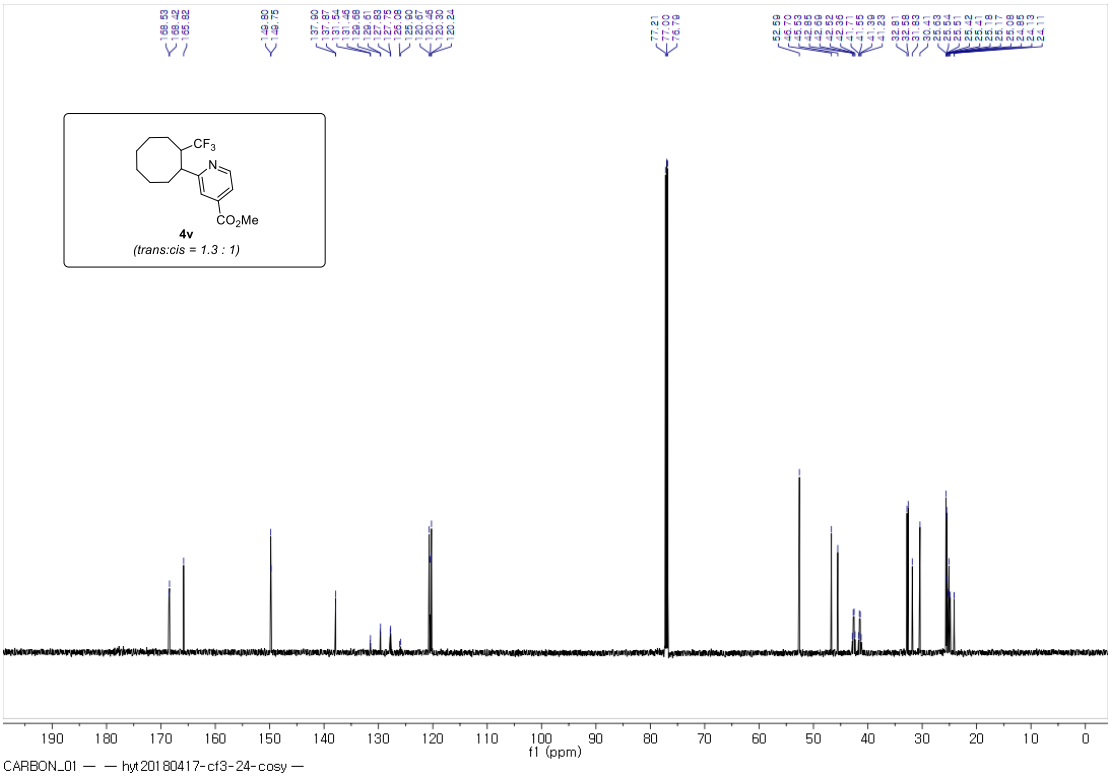


NOESY 1D in $CDCl_3$

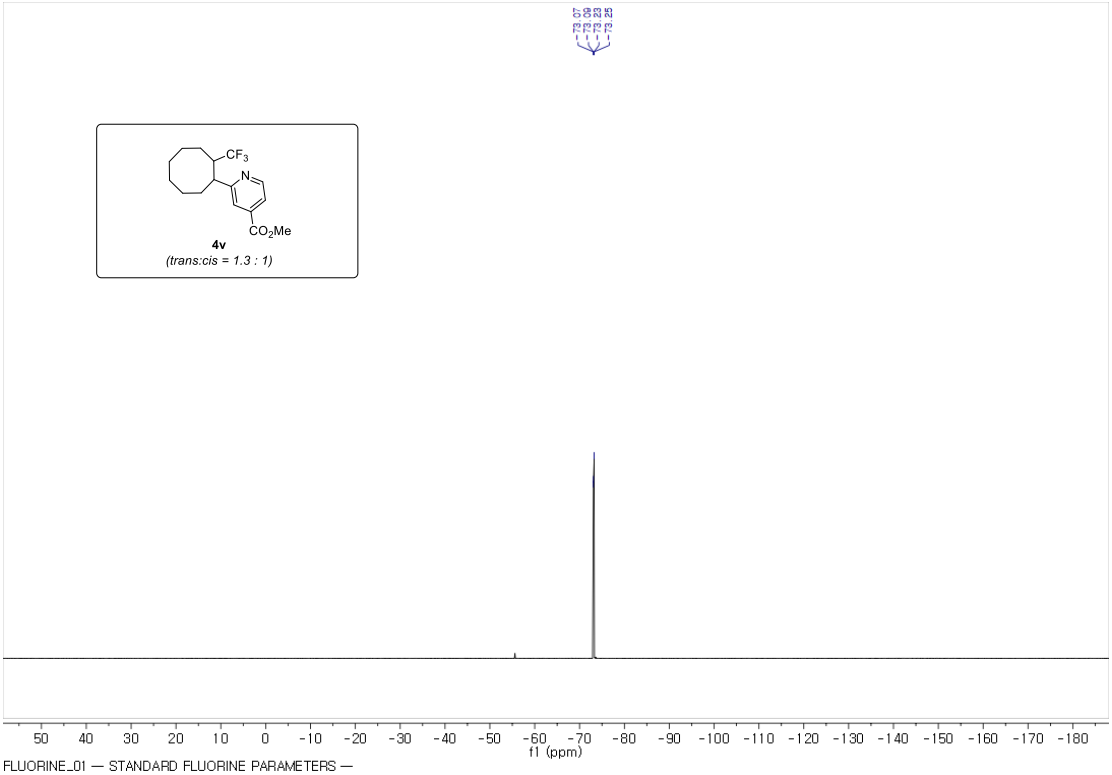
methyl 2-(2-(trifluoromethyl)cyclooctyl)isonicotinate (4v).



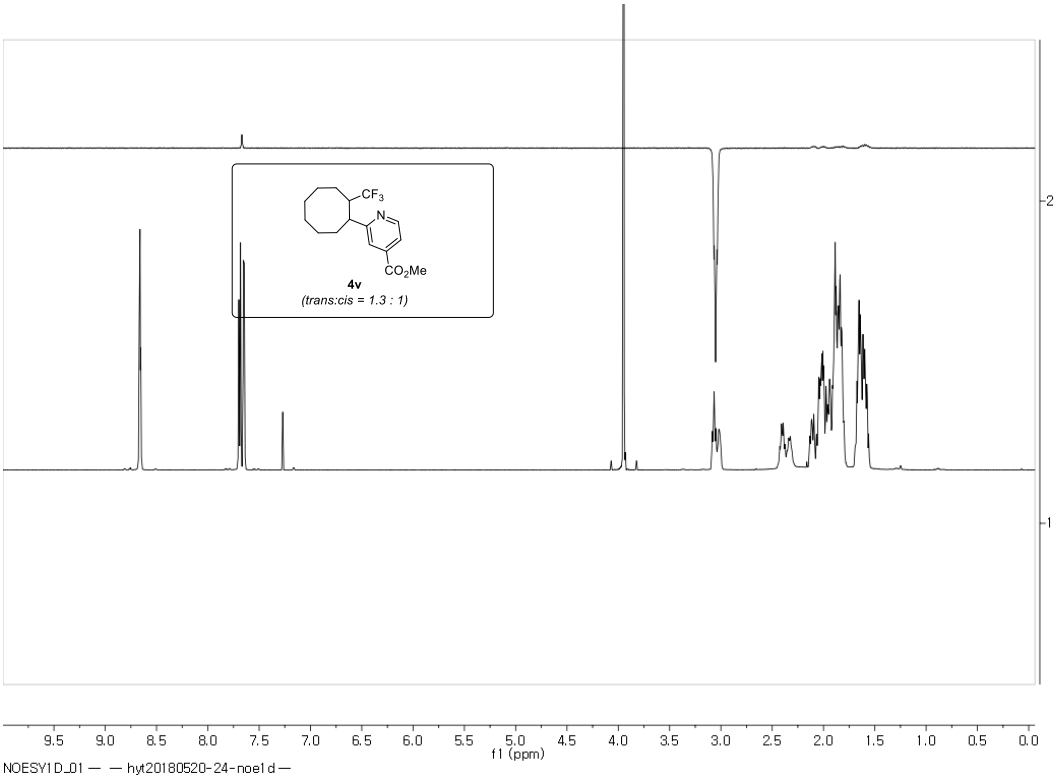
599 MHz, ^{1}H NMR in $CDCl_3$



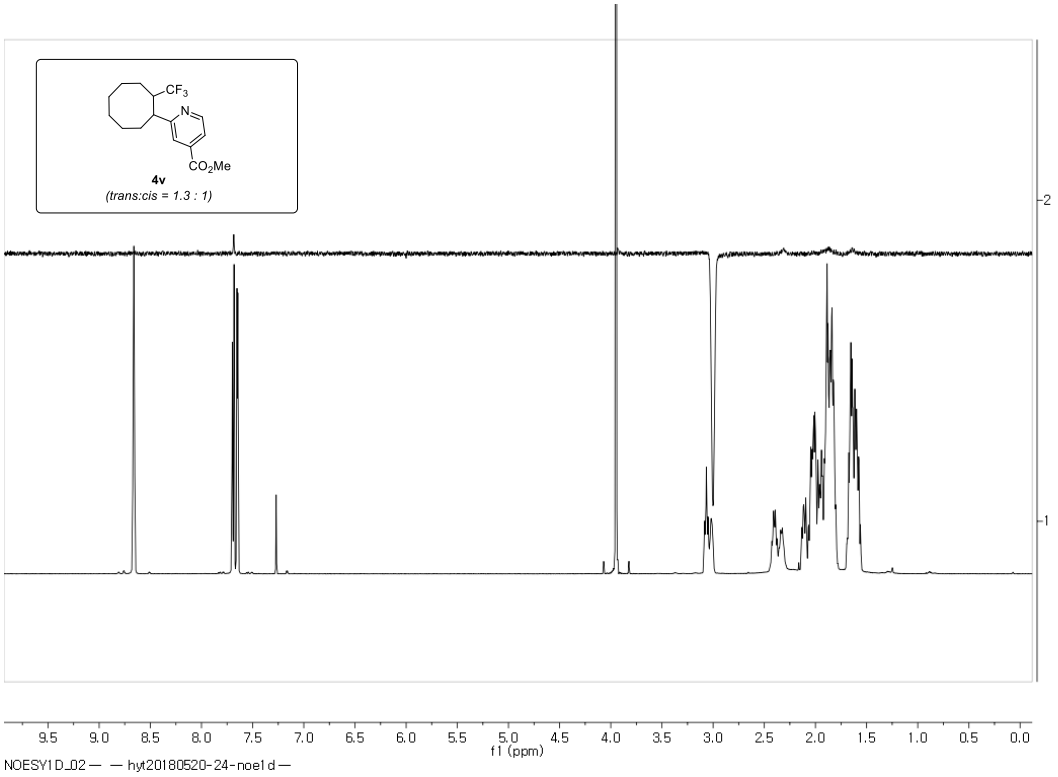
151 MHz, ^{13}C NMR in $CDCl_3$



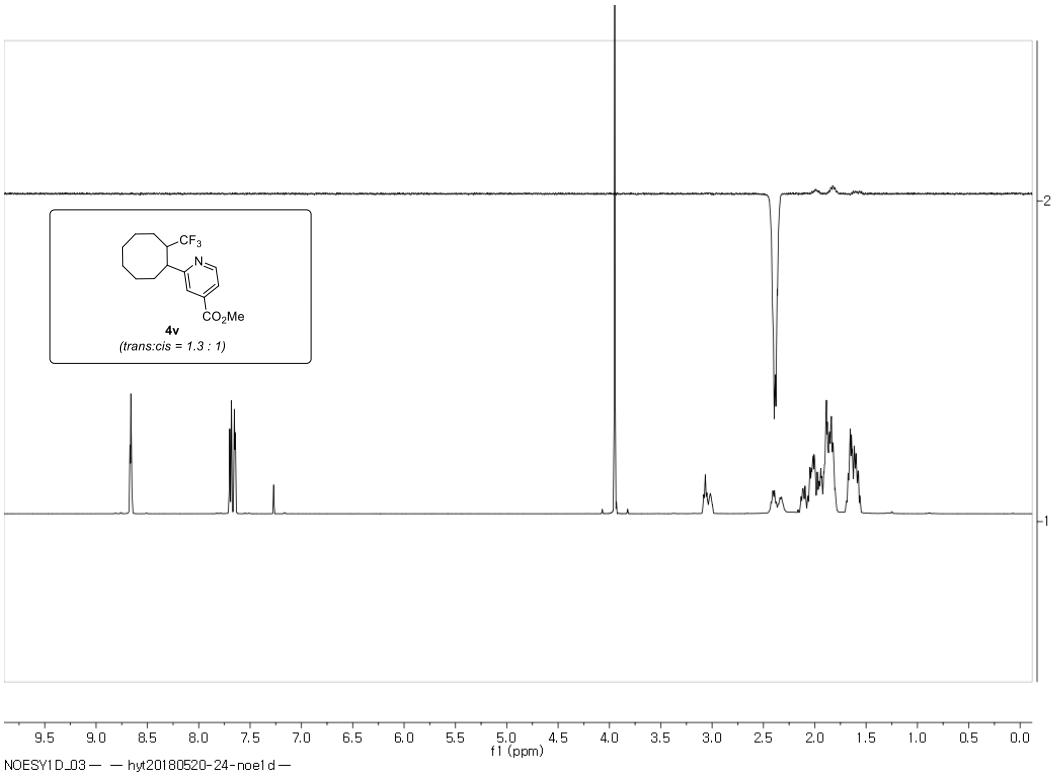
564 MHz, ^{19}F NMR in $CDCl_3$



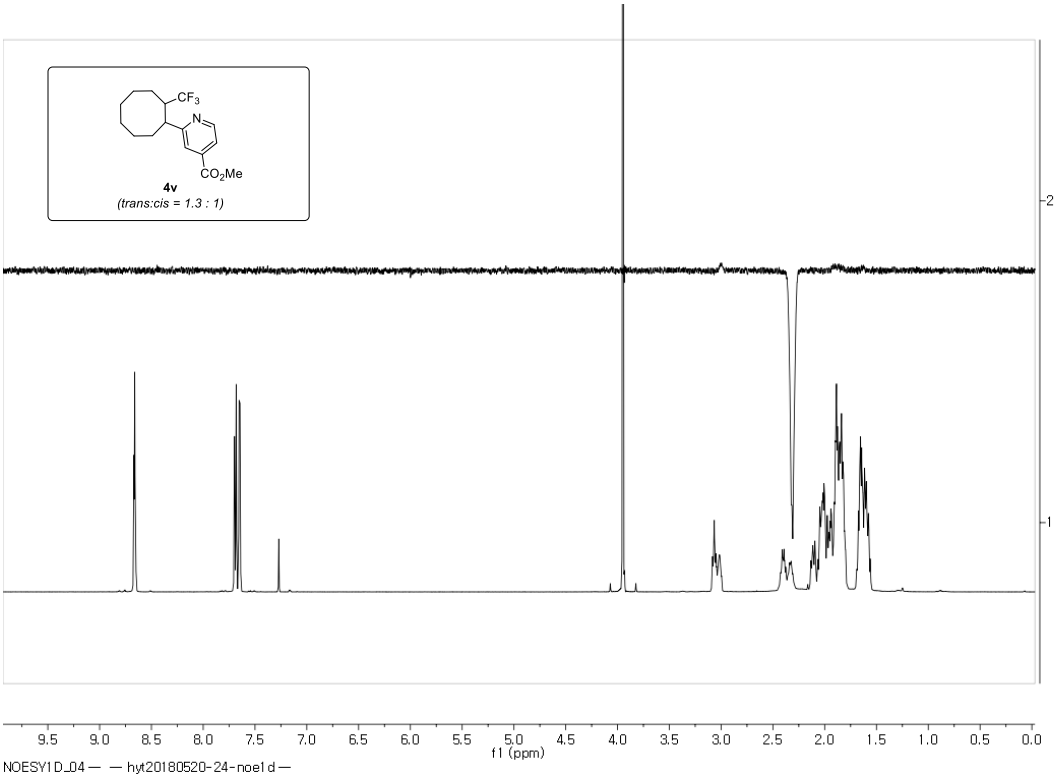
NOESY 1D in $CDCl_3$



NOESY 1D in $CDCl_3$

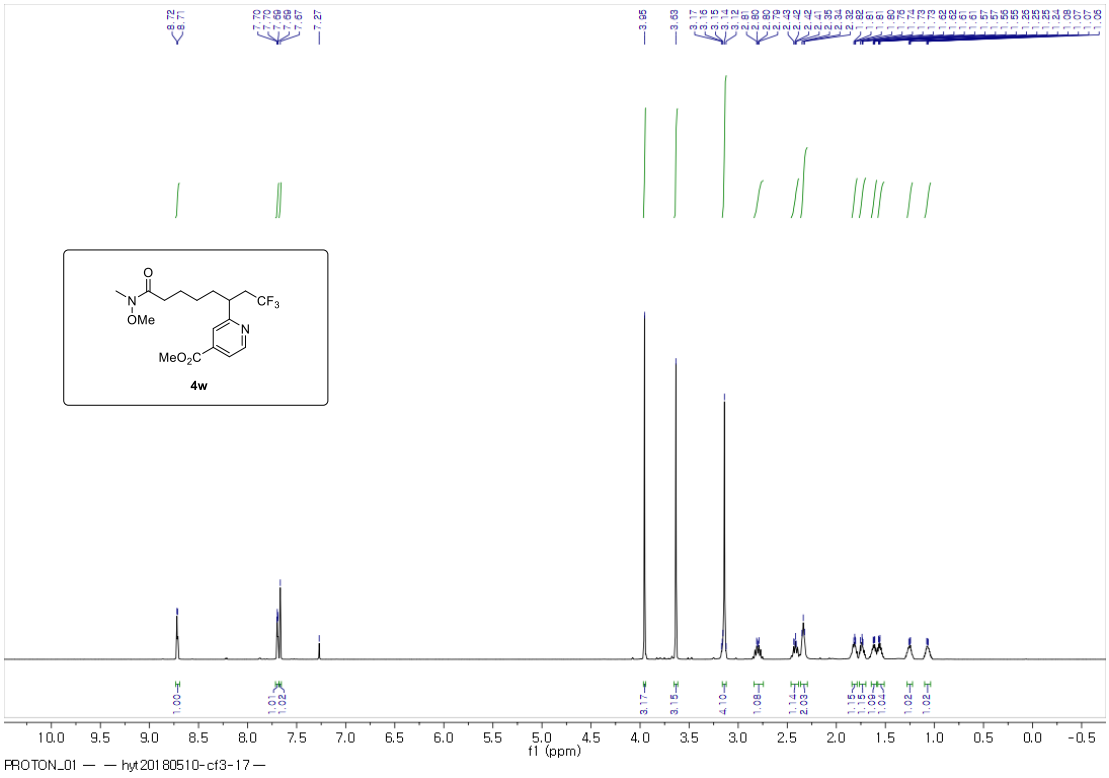


NOESY 1D in $CDCl_3$

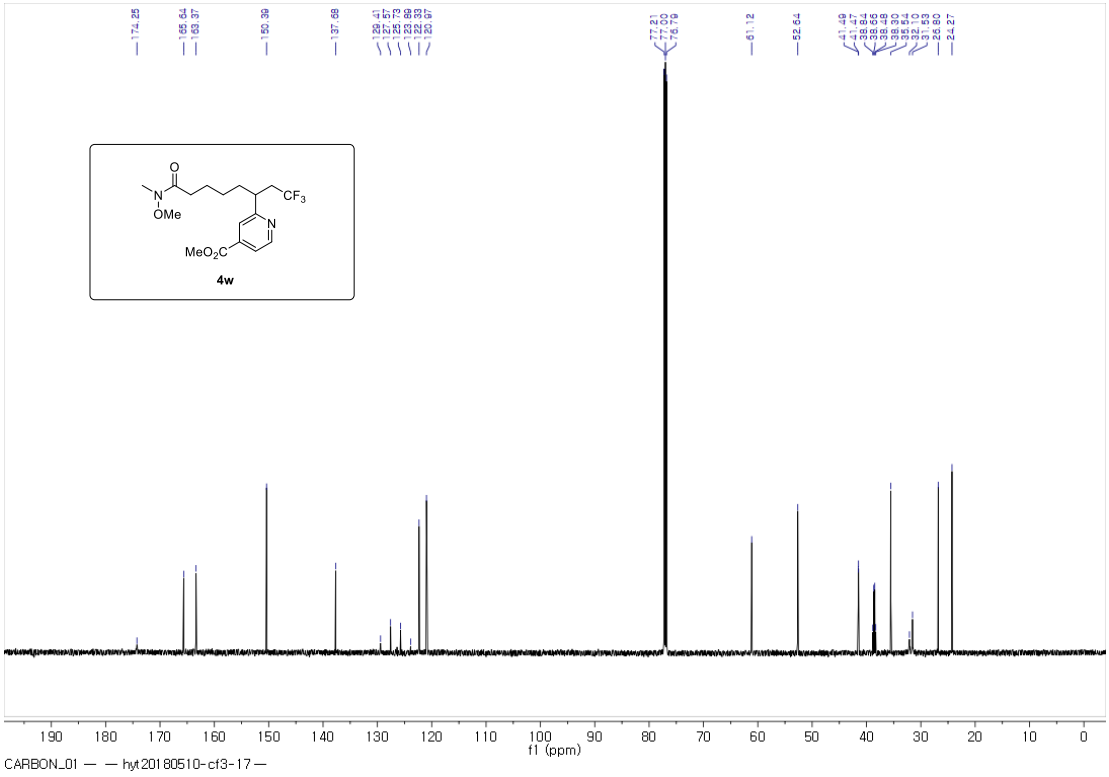


NOESY 1D in $CDCl_3$

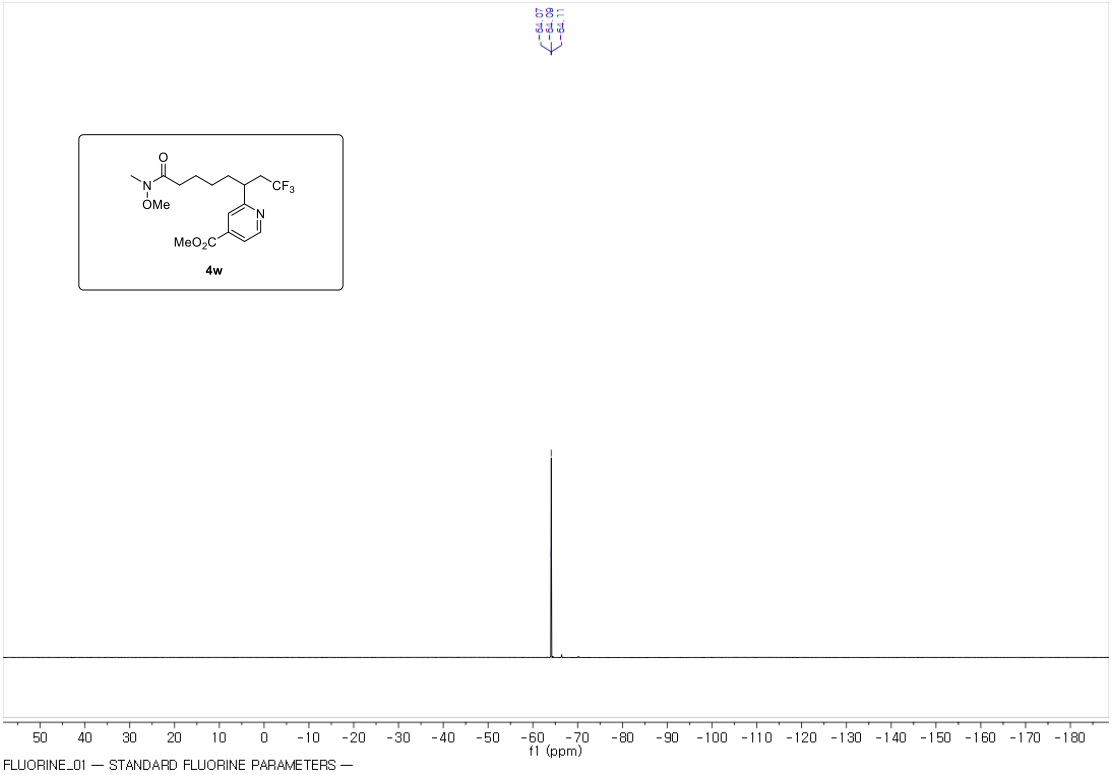
methyl 2-(1,1,1-trifluoro-8-(methoxy(methyl)amino)-8-oxooctan-3-yl)isonicotinate (4w).



599 MHz, ^{1}H NMR in $CDCl_3$

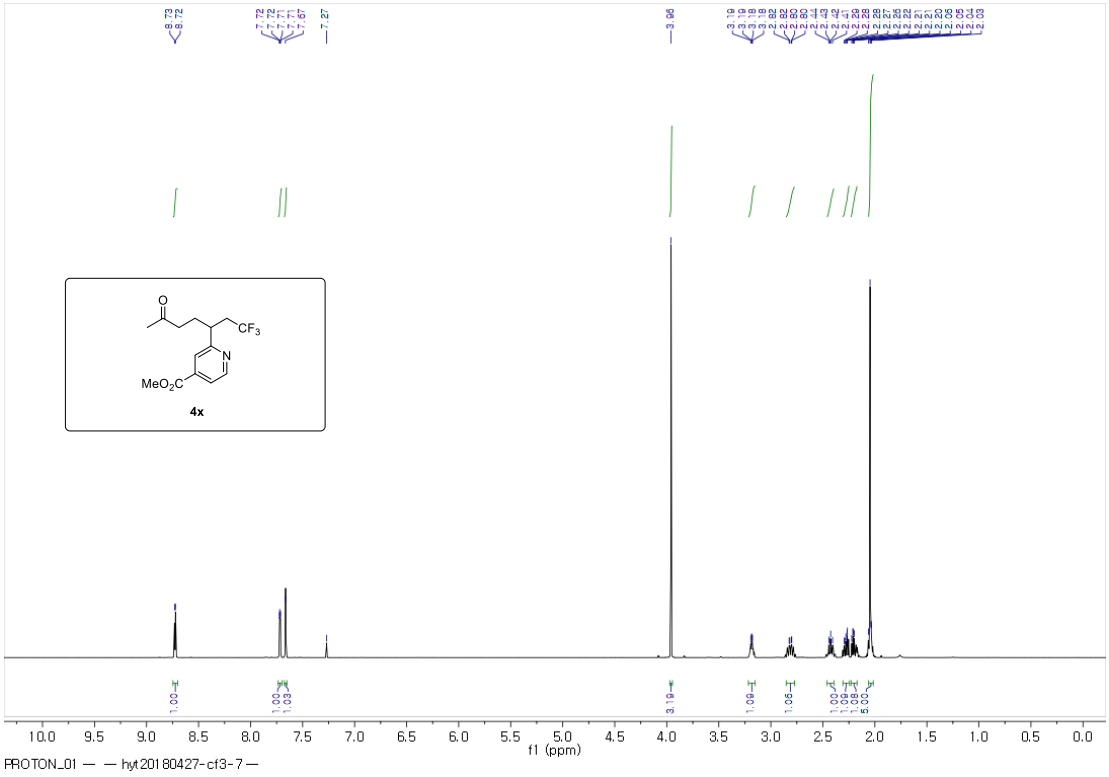


151 MHz, ^{13}C NMR in $CDCl_3$

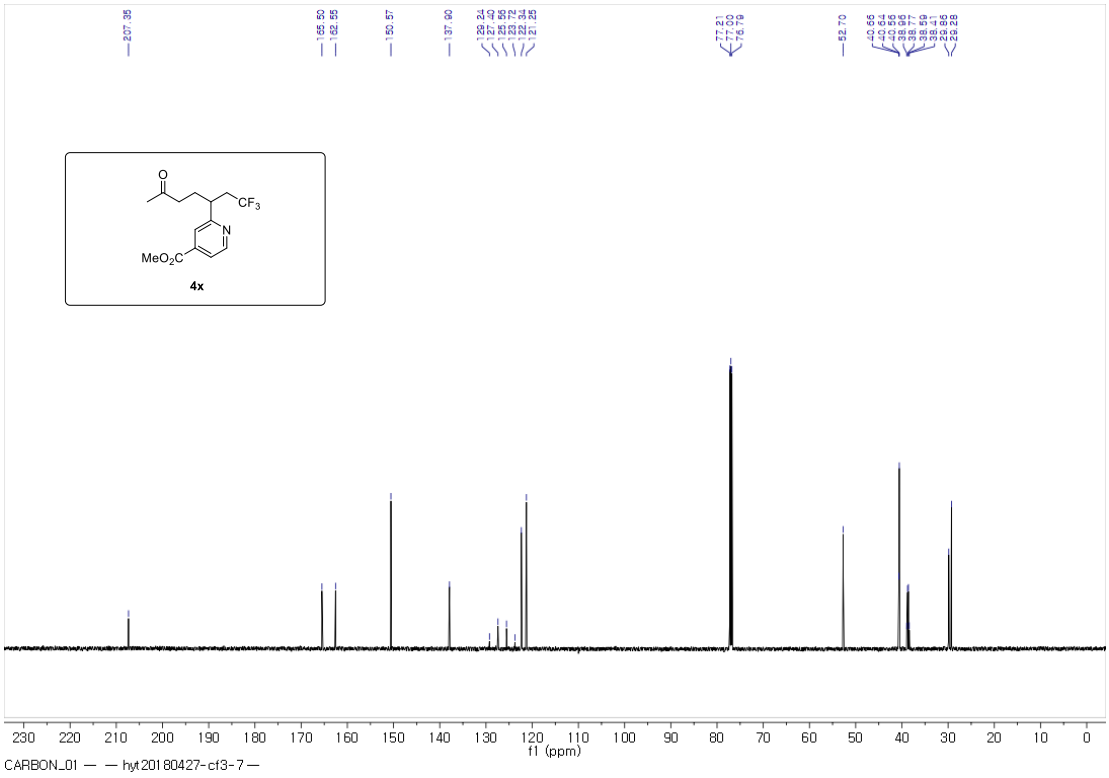


564 MHz, ^{19}F NMR in $CDCl_3$

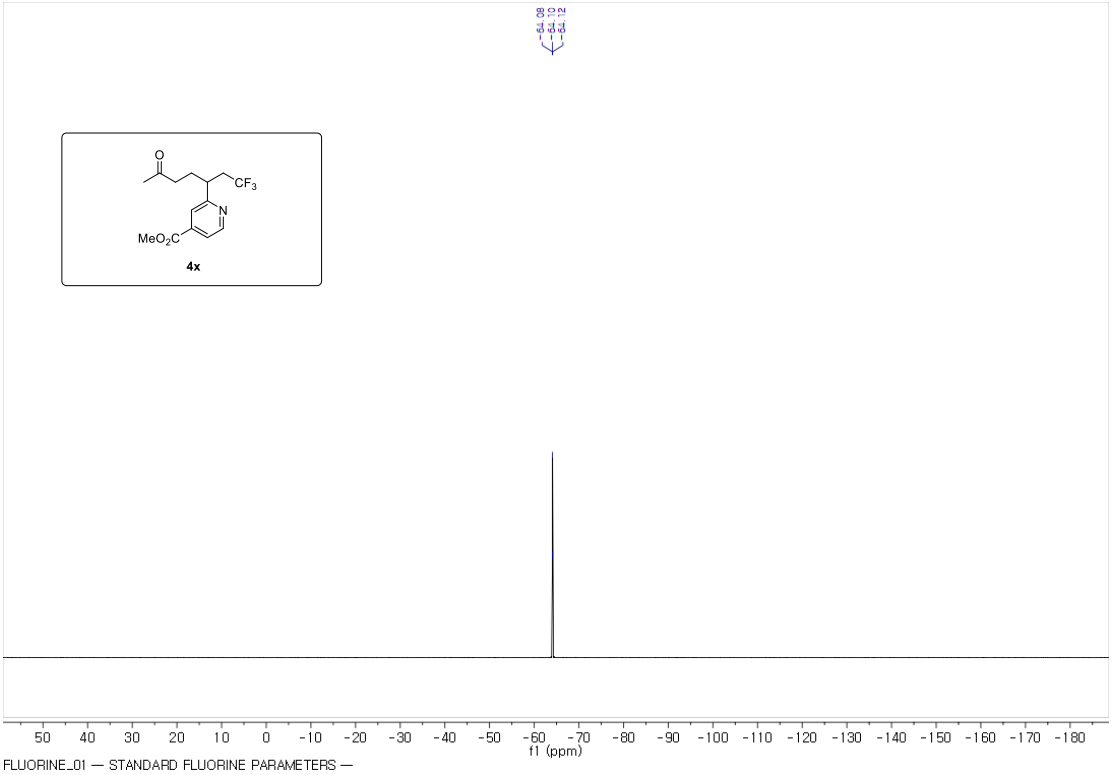
methyl 2-(1,1,1-trifluoro-6-oxoheptan-3-yl)isonicotinate (4x).



599 MHz, ^{1}H NMR in $CDCl_3$

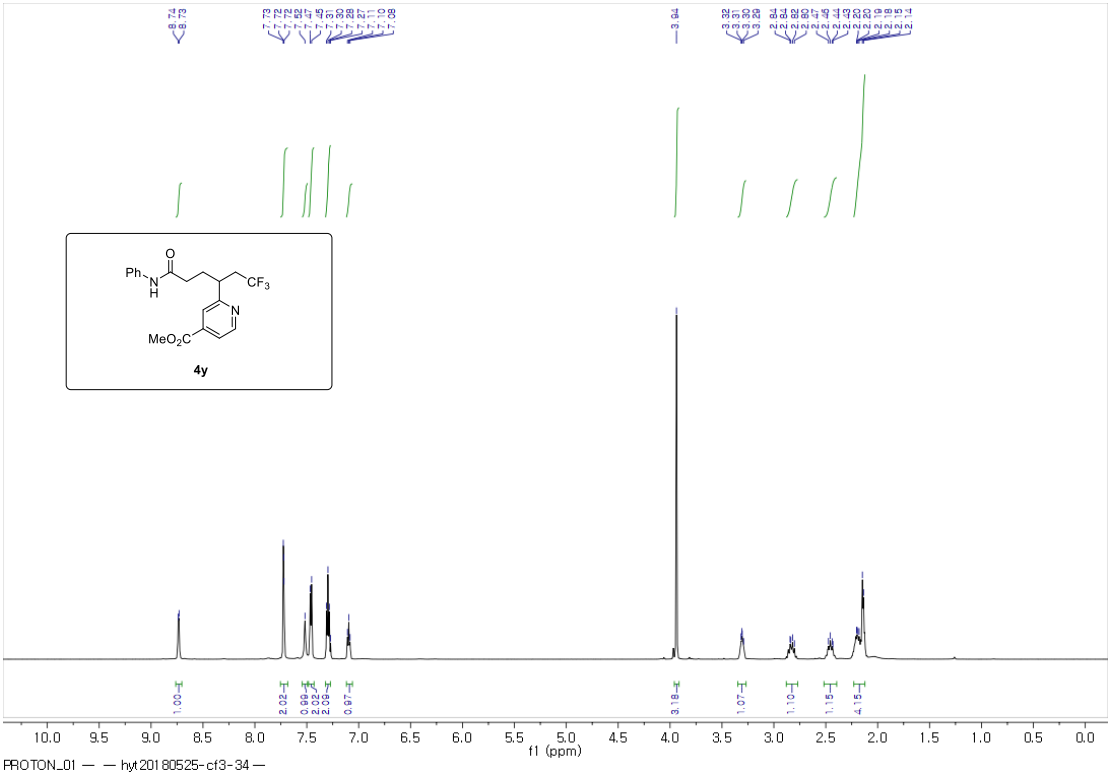


151 MHz, ^{13}C NMR in $CDCl_3$

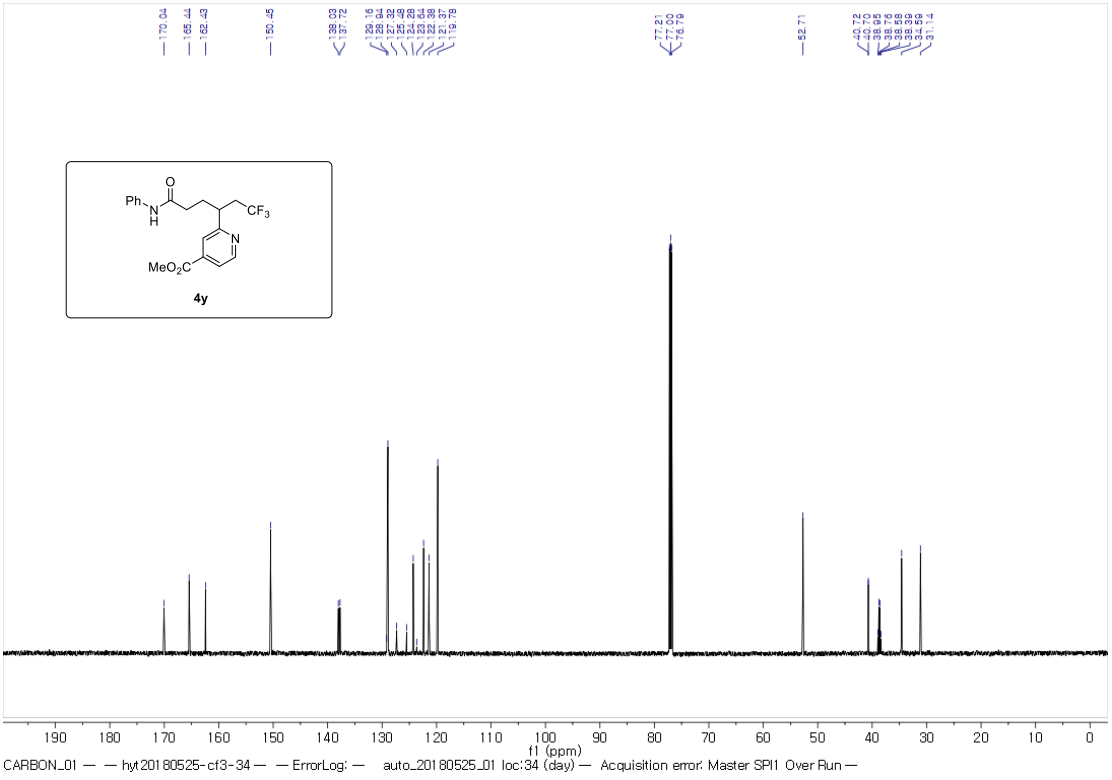


564 MHz, ^{19}F NMR in $CDCl_3$

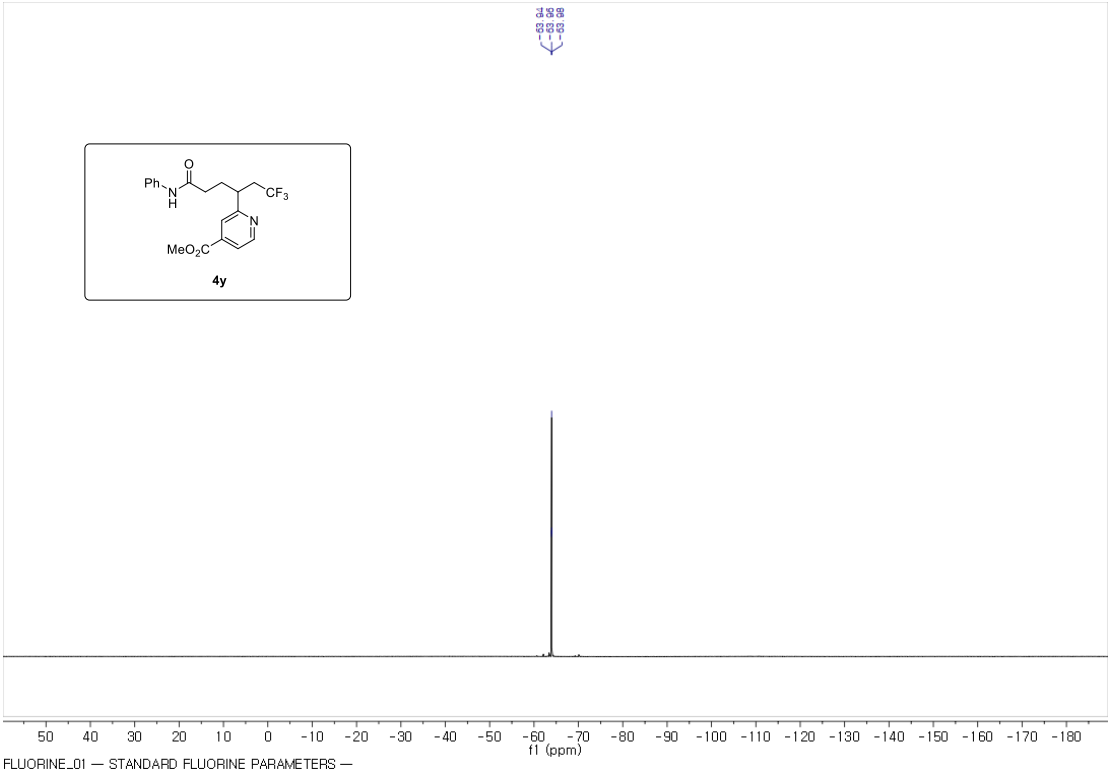
methyl 2-(1,1,1-trifluoro-6-oxo-6-(phenylamino)hexan-3-yl)isonicotinate (4y).



599 MHz, ^{1}H NMR in $CDCl_3$

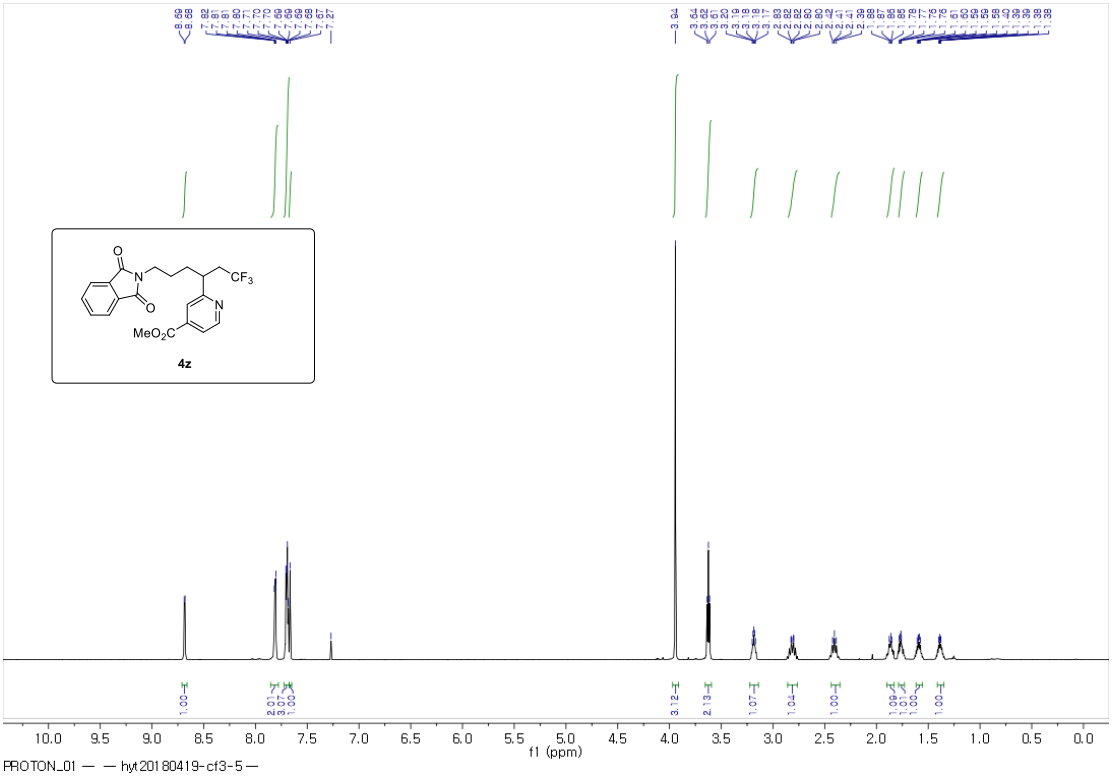


151 MHz, ^{13}C NMR in $CDCl_3$

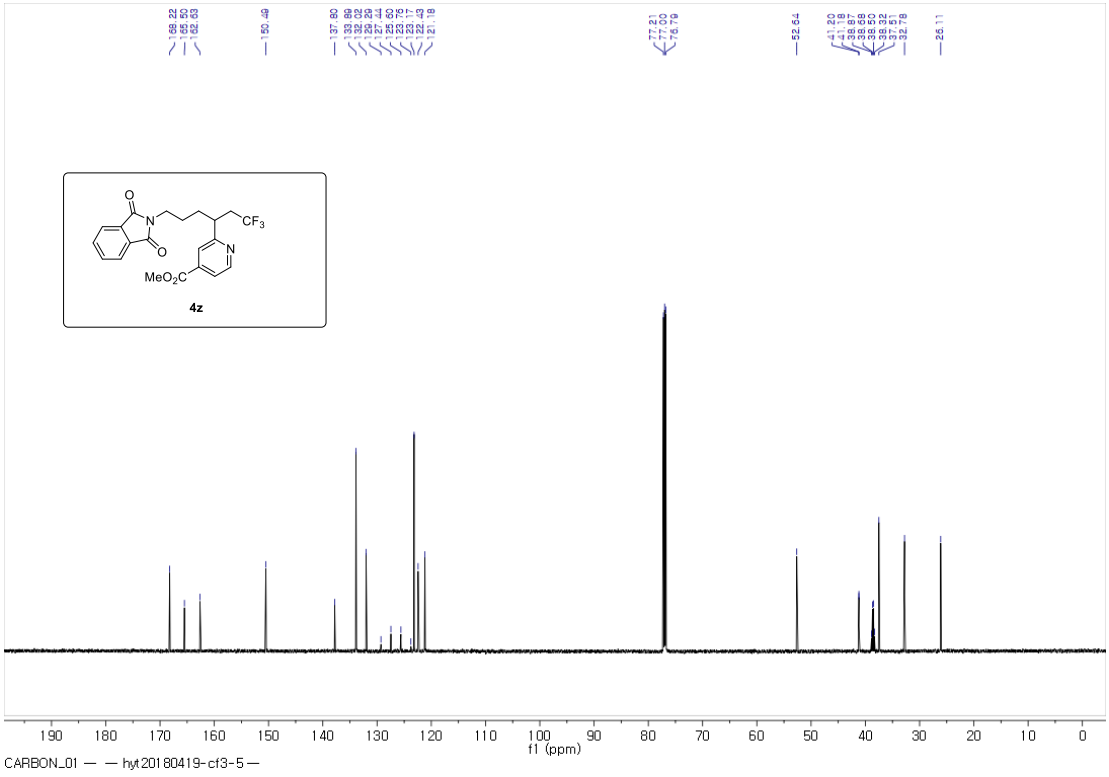


564 MHz, ^{19}F NMR in $CDCl_3$

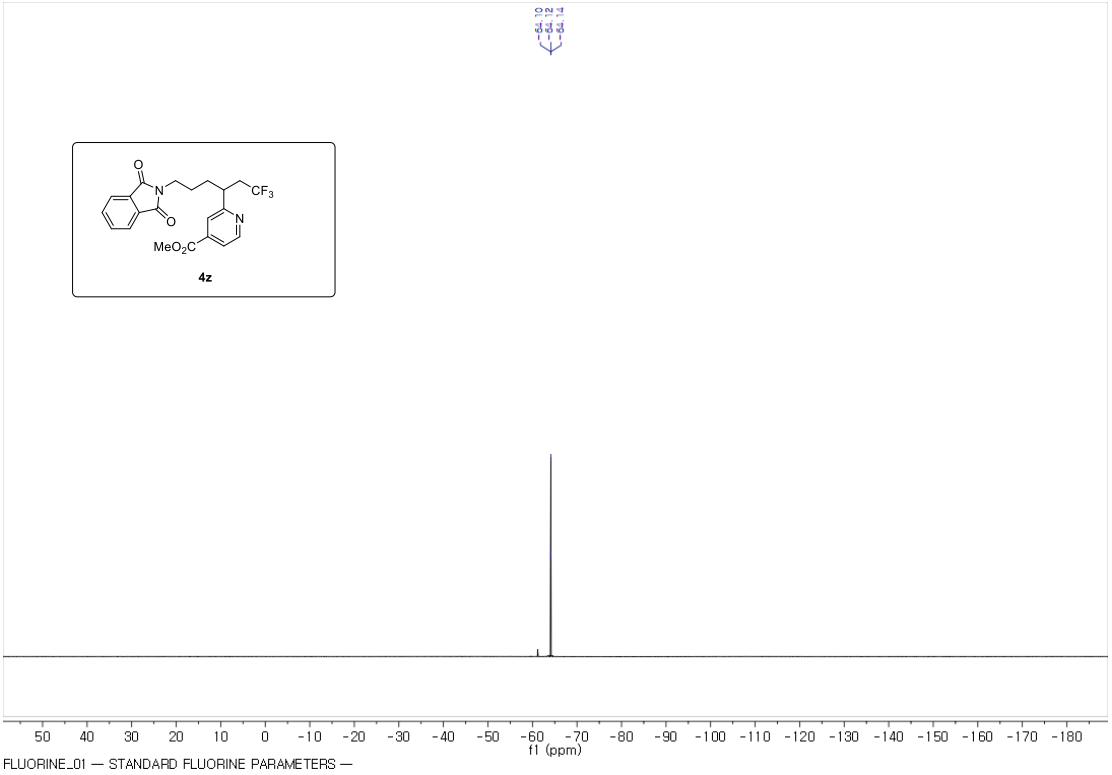
methyl 2-(6-(1,3-dioxoisoindolin-2-yl)-1,1,1-trifluorohexan-3-yl)isonicotinate (4z).



599 MHz, ^{1}H NMR in $CDCl_3$

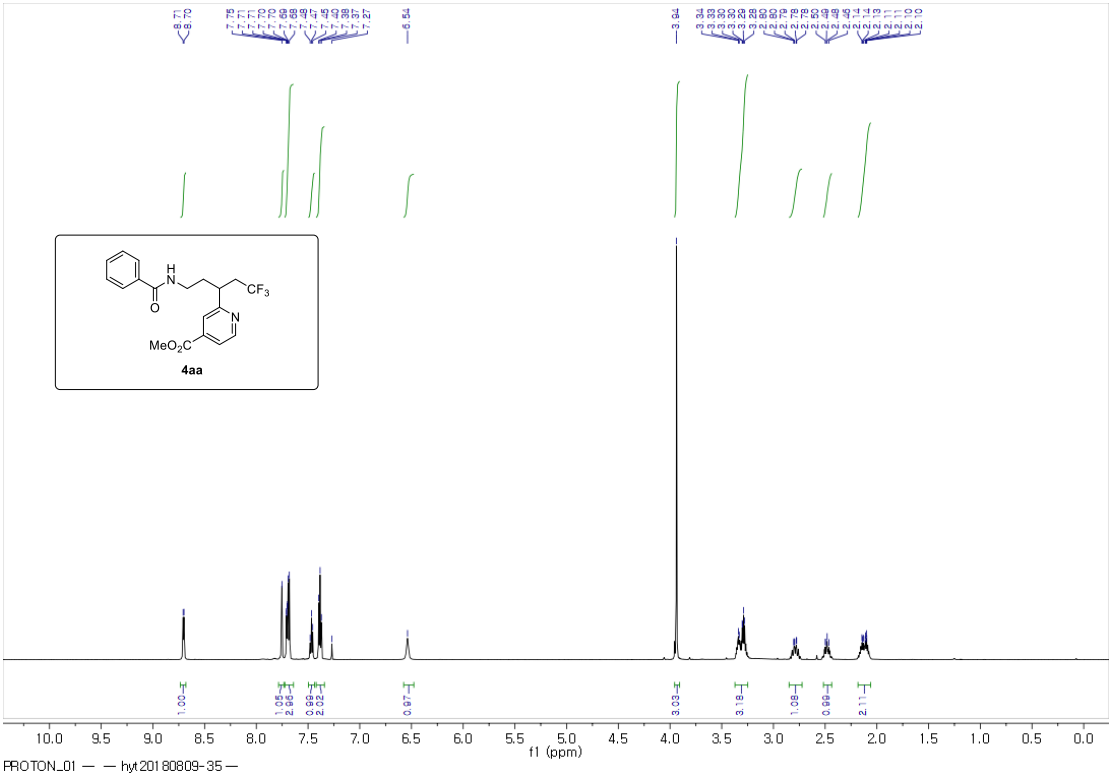


151 MHz, ^{13}C NMR in $CDCl_3$

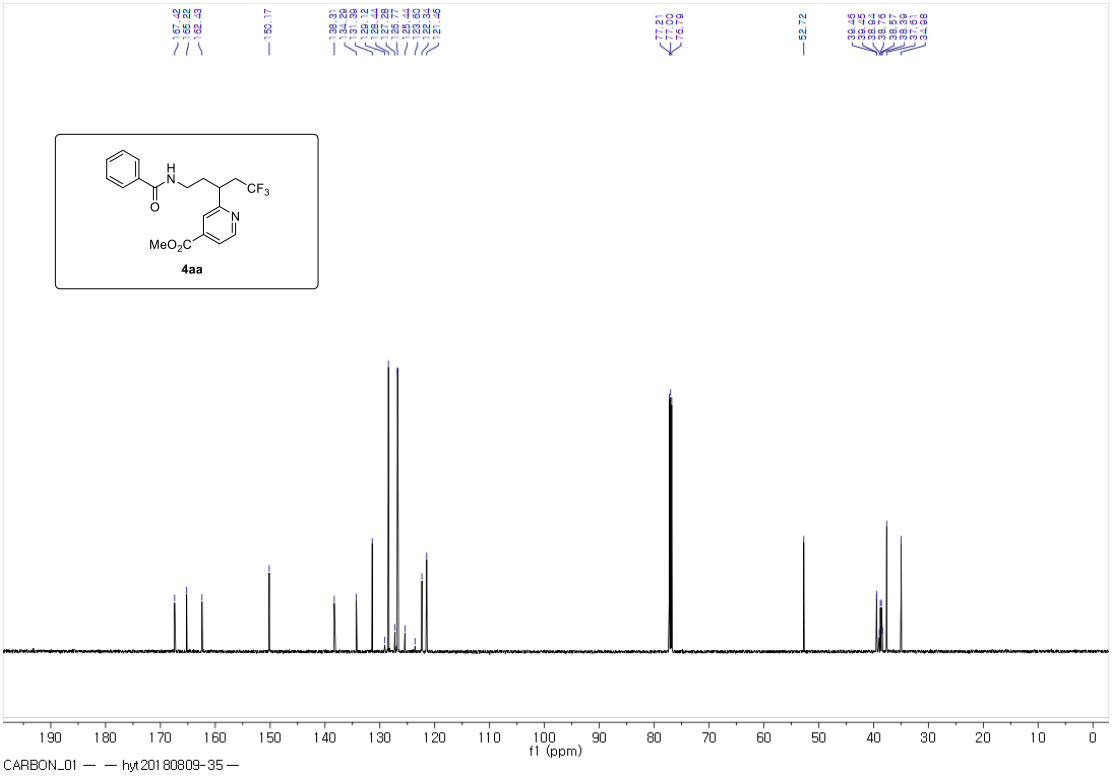


564 MHz, ^{19}F NMR in $CDCl_3$

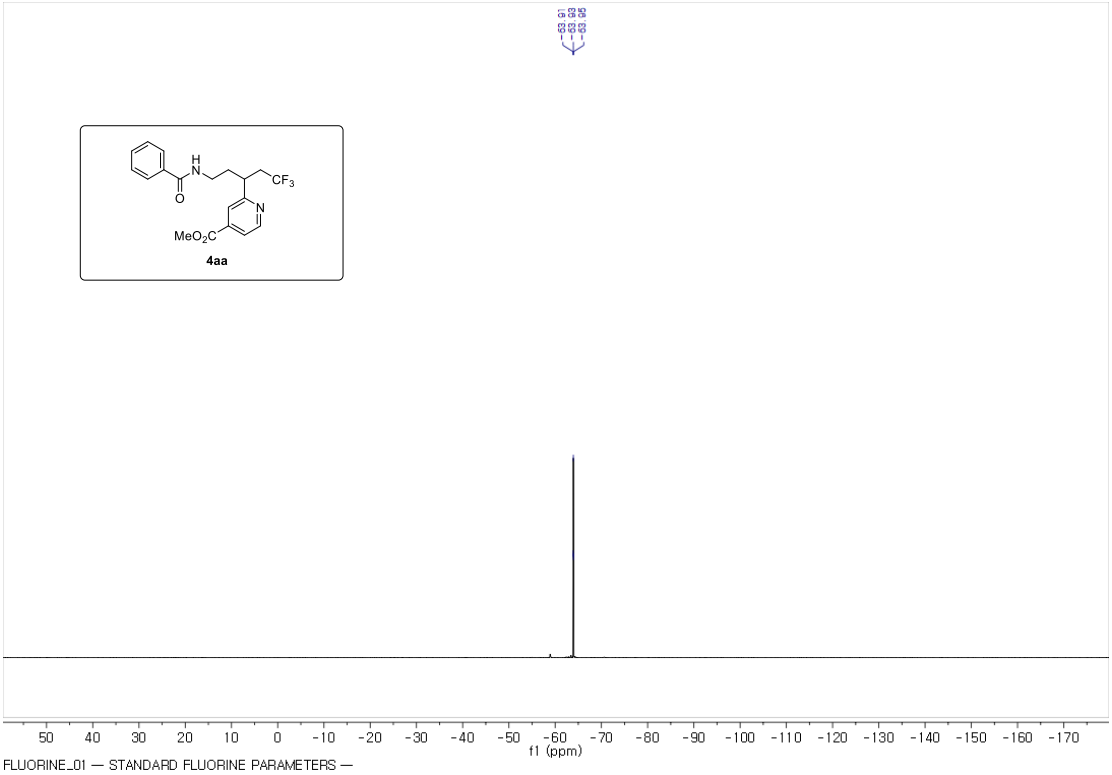
methyl 2-(5-benzamido-1,1,1-trifluoropentan-3-yl)isonicotinate (4aa).



599 MHz, ^{1}H NMR in $CDCl_3$

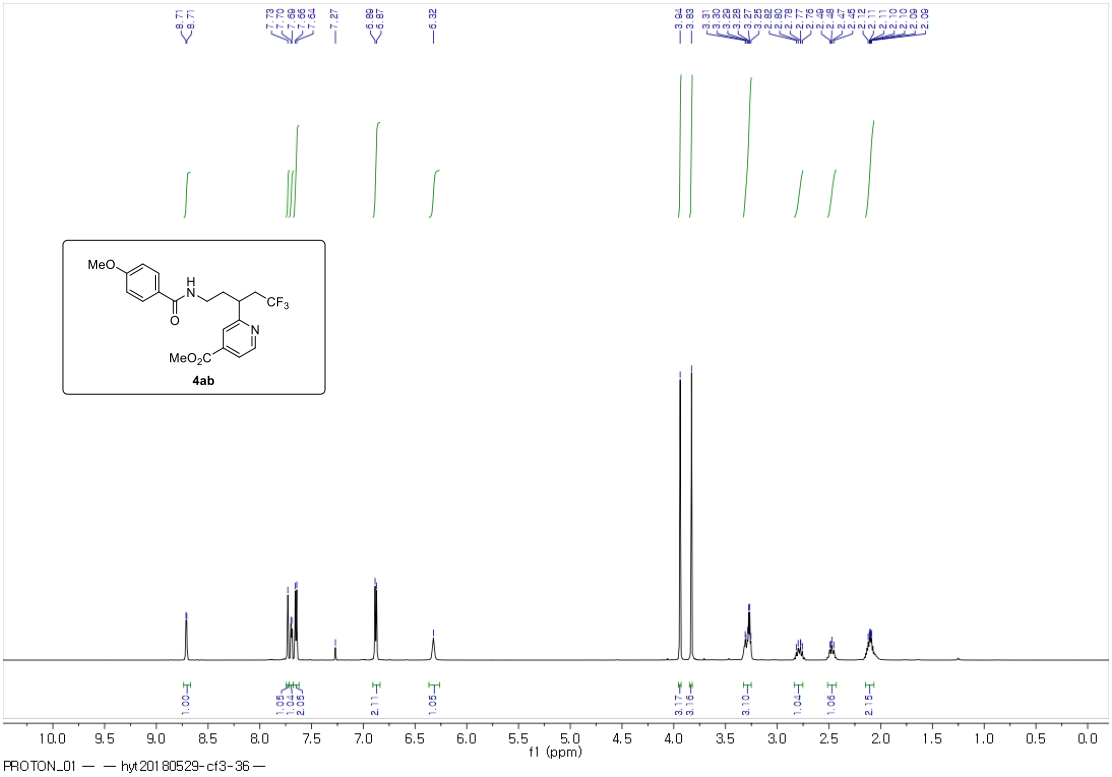


151 MHz, ^{13}C NMR in $CDCl_3$

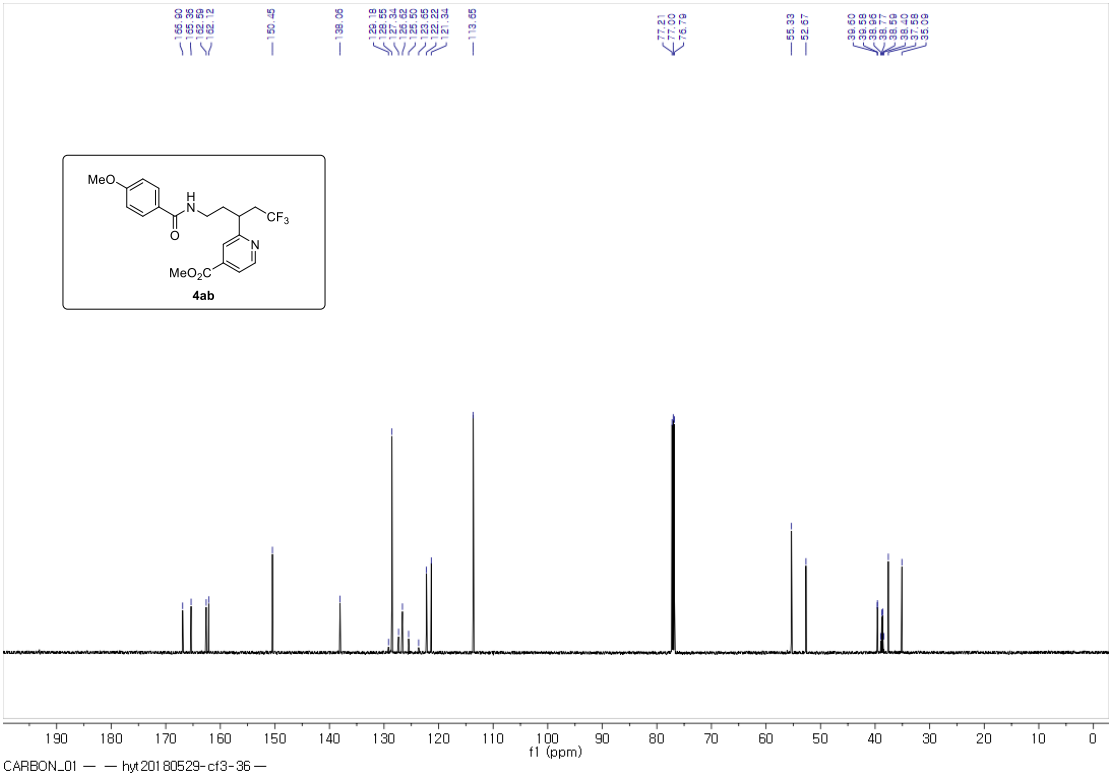


564 MHz, ^{19}F NMR in $CDCl_3$

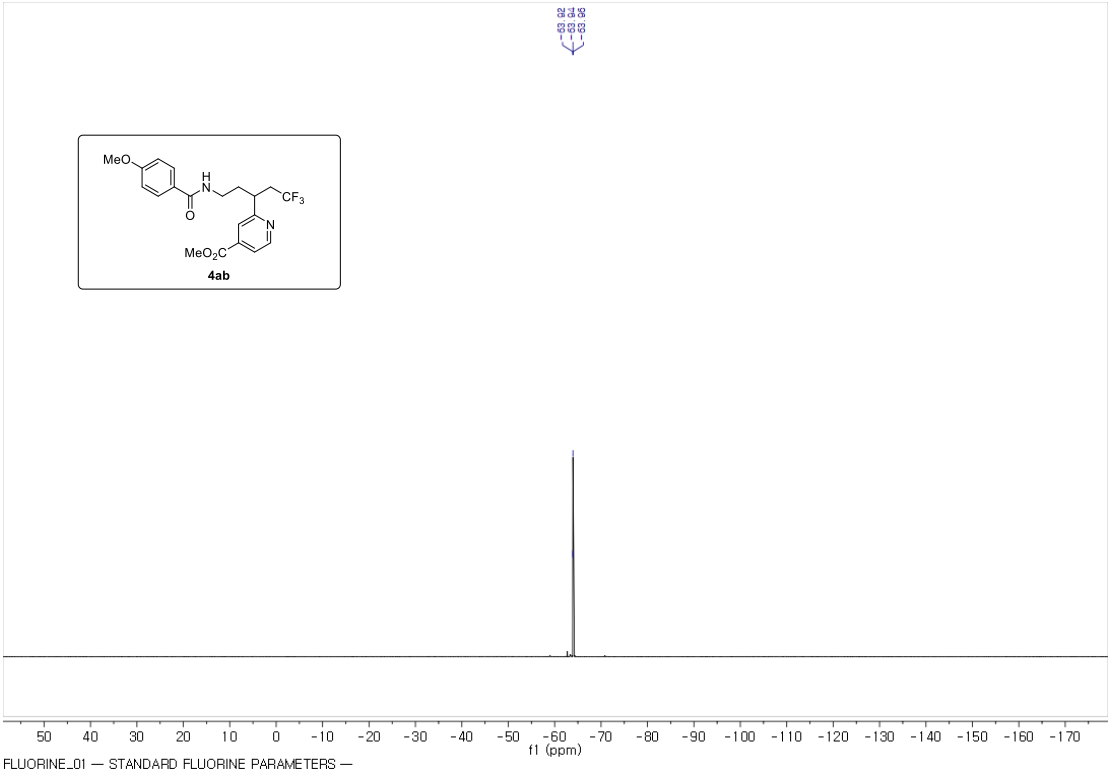
methyl 2-(1,1,1-trifluoro-5-(4-methoxybenzamido)pentan-3-yl)isonicotinate (4ab).



599 MHz, ^{1}H NMR in $CDCl_3$

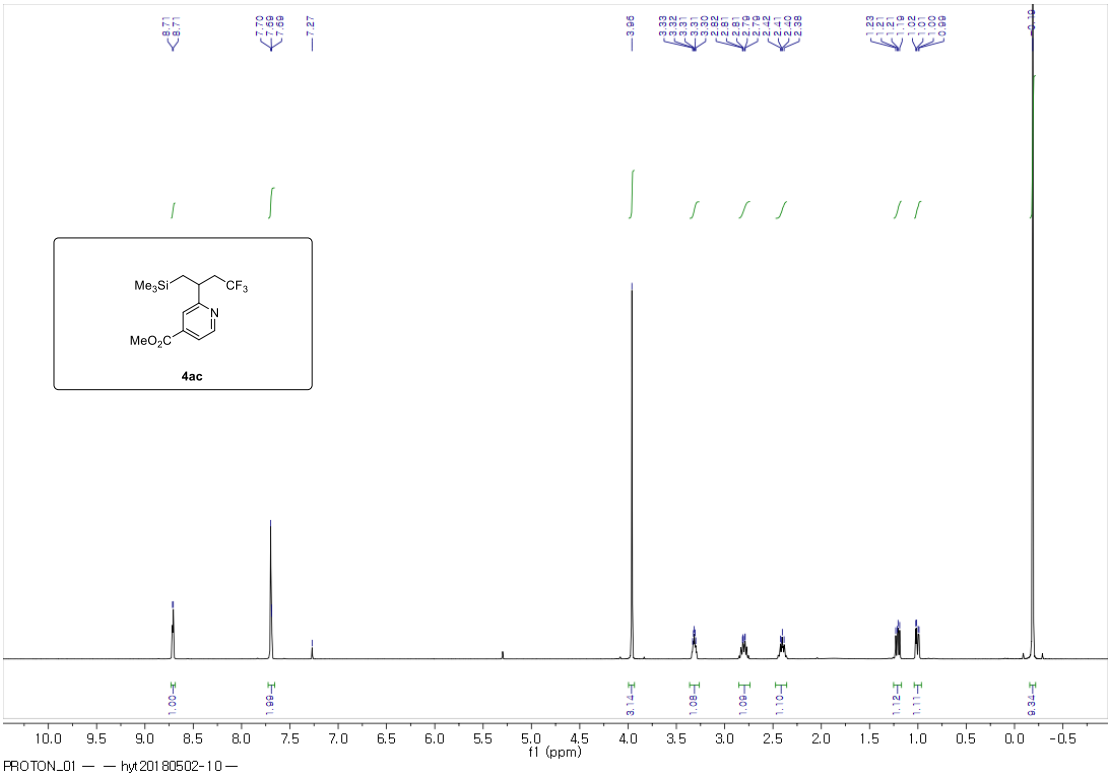


151 MHz, ^{13}C NMR in $CDCl_3$

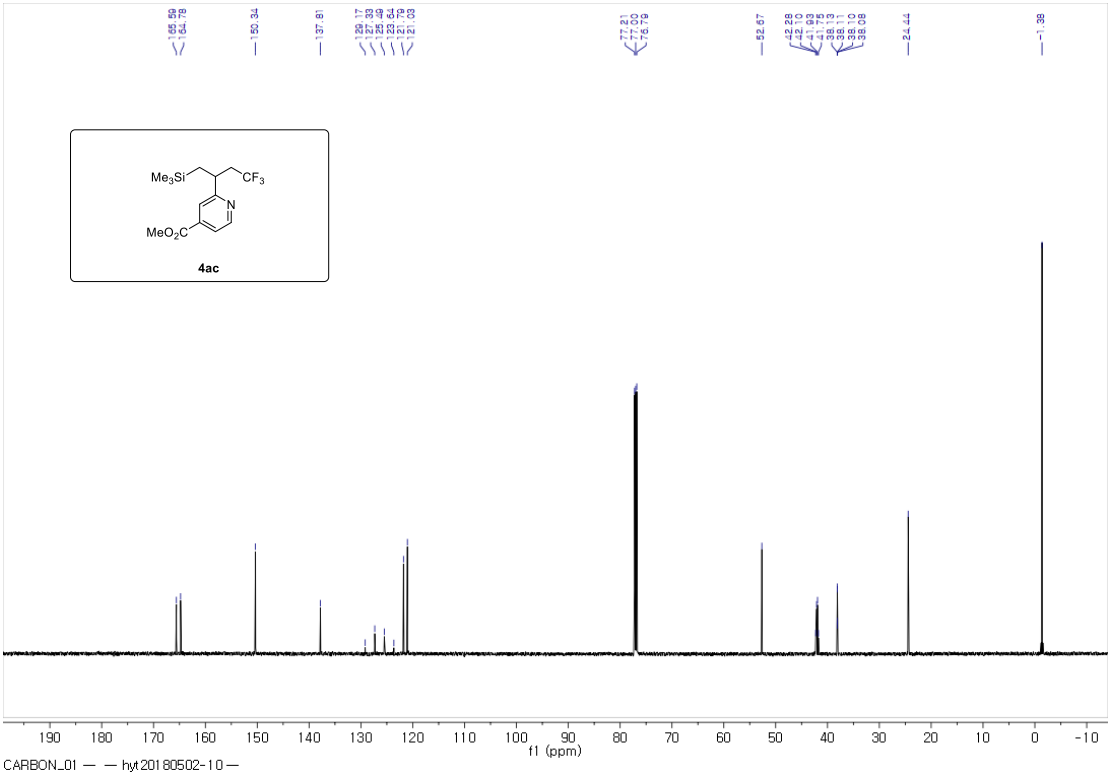


564 MHz, ^{19}F NMR in $CDCl_3$

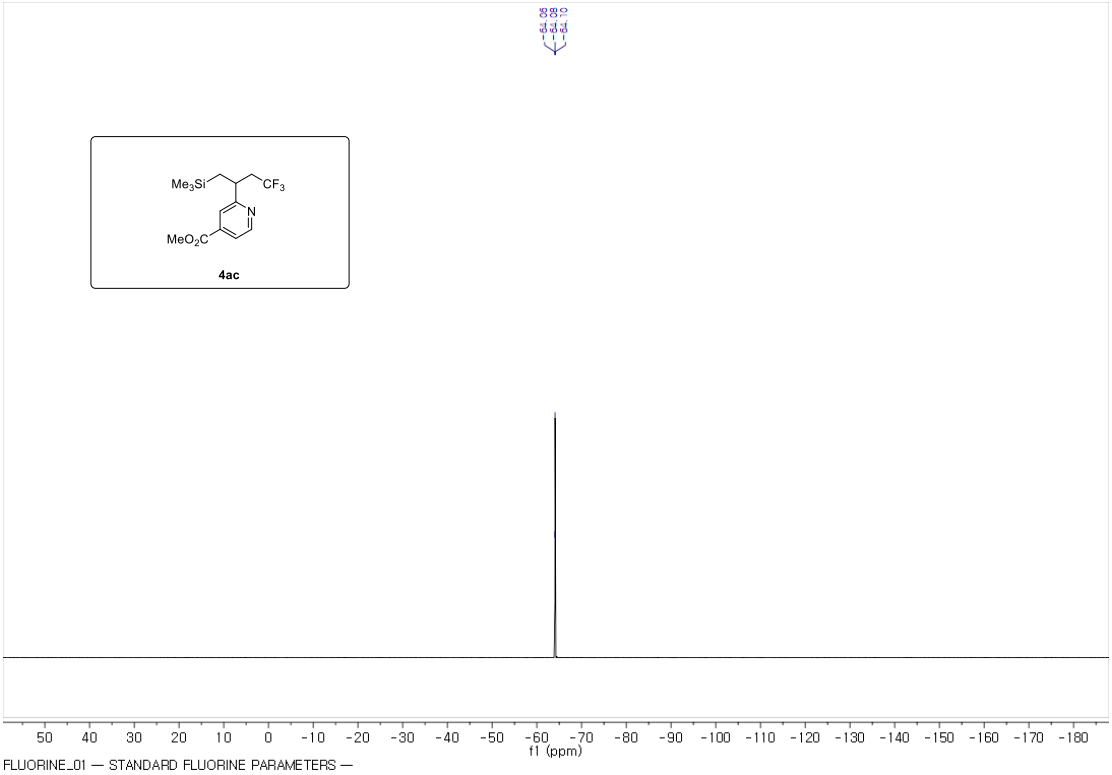
methyl 2-(4,4,4-trifluoro-1-(trimethylsilyl)butan-2-yl)isonicotinate (4ac).



599 MHz, ^{1}H NMR in $CDCl_3$

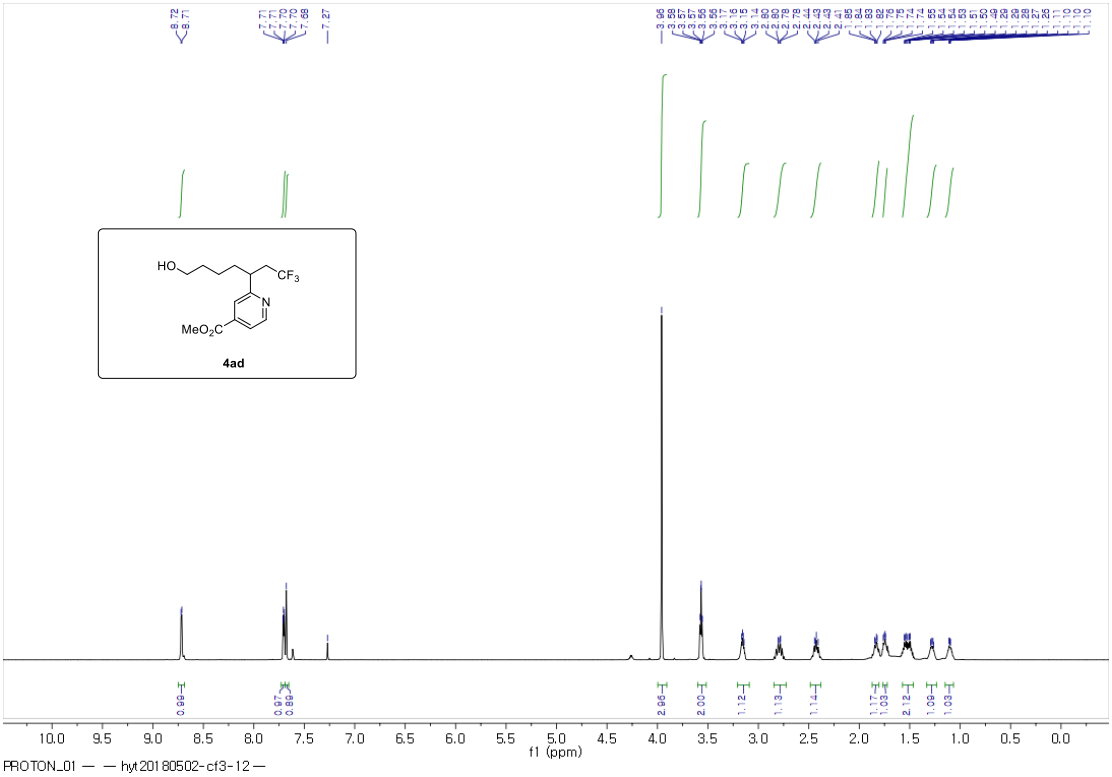


151 MHz, ^{13}C NMR in $CDCl_3$

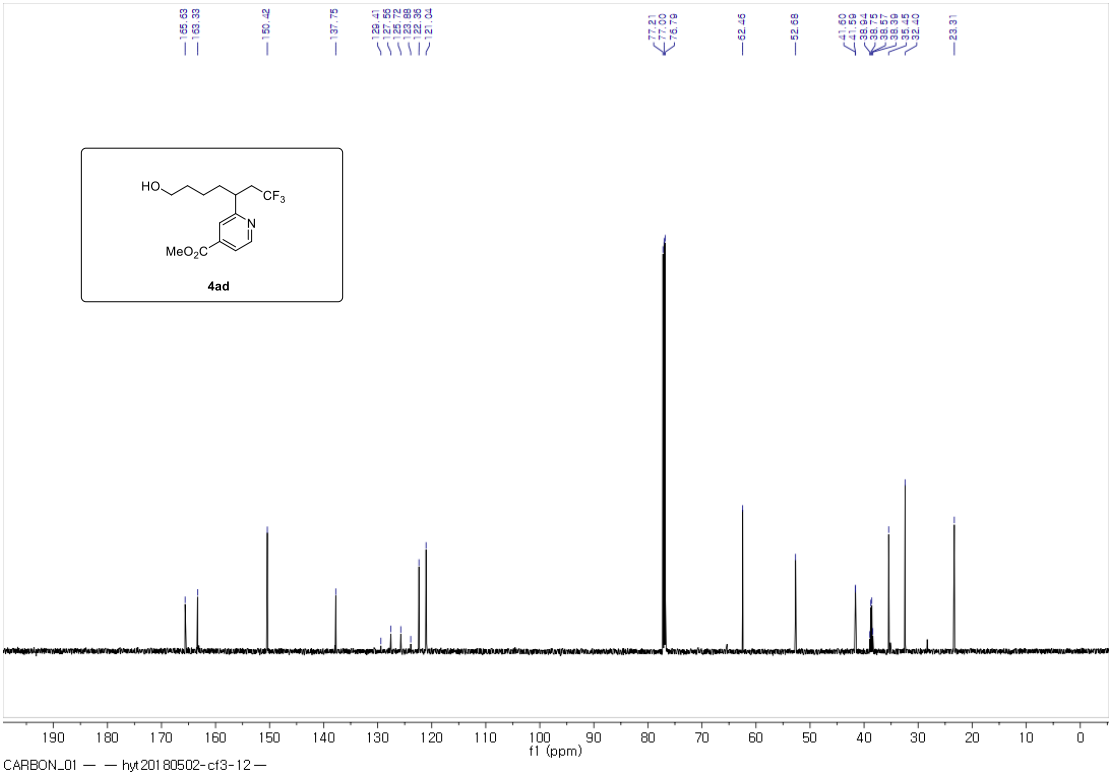


564 MHz, ^{19}F NMR in $CDCl_3$

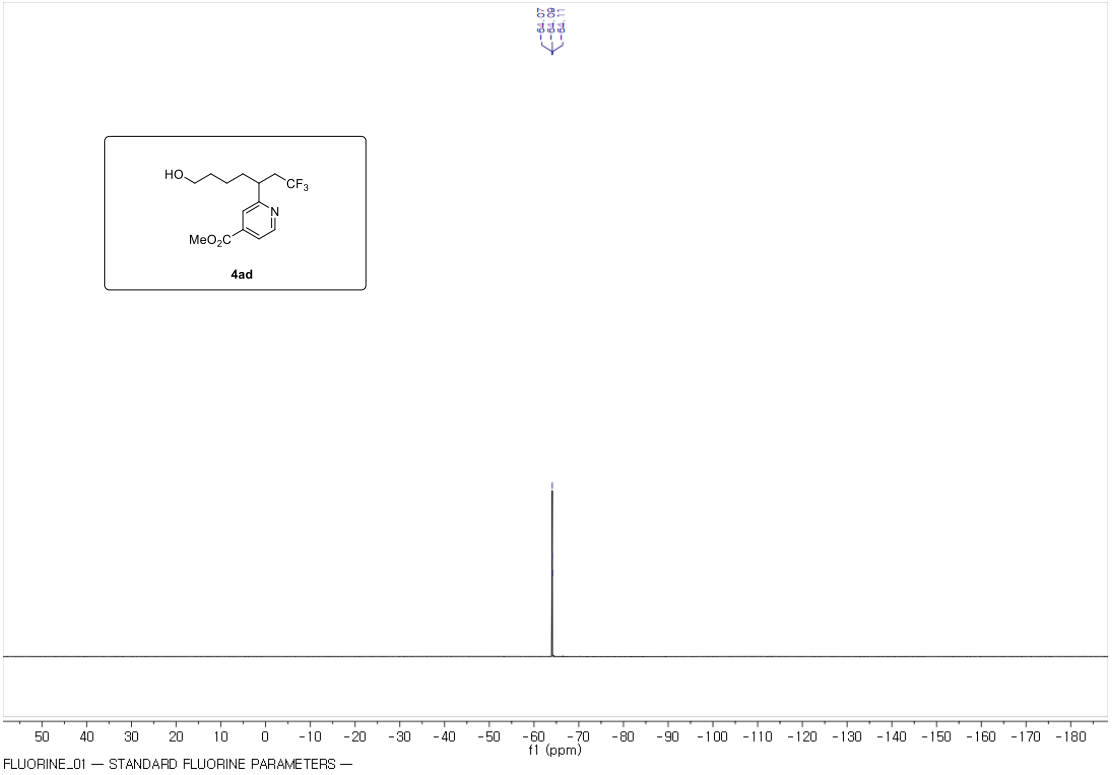
methyl 2-(1,1,1-trifluoro-7-hydroxyheptan-3-yl)isonicotinate (4ad).



599 MHz, ^{1}H NMR in $CDCl_3$

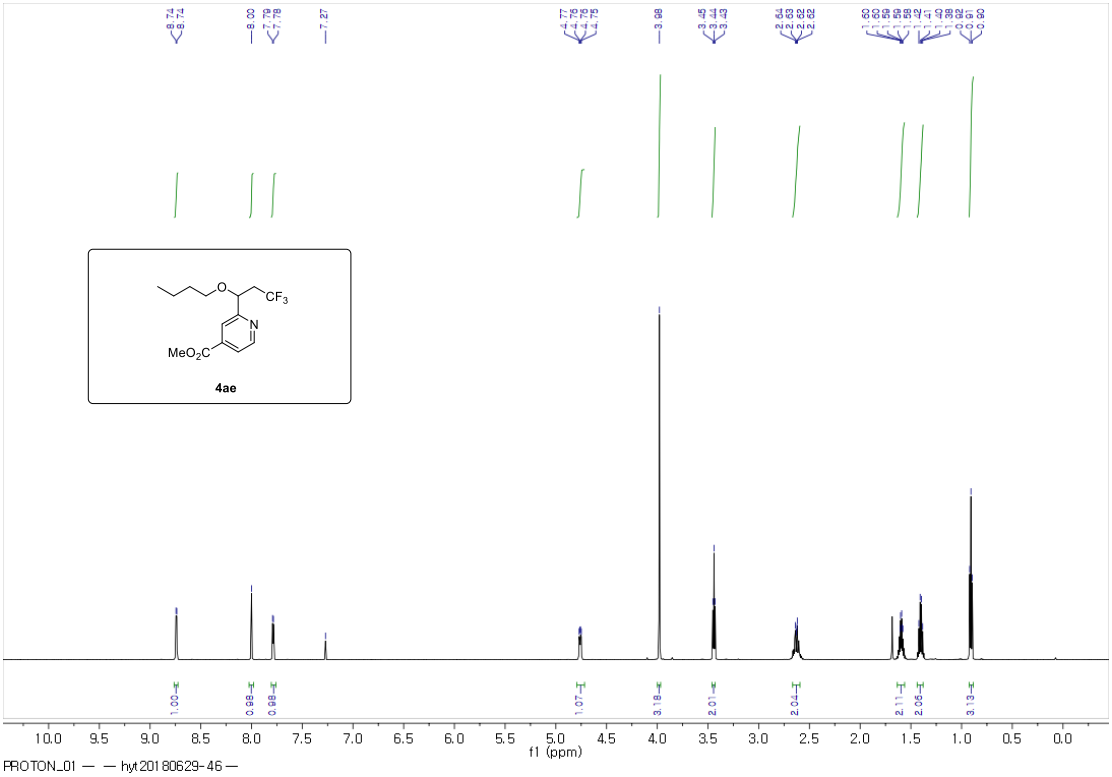


151 MHz, ^{13}C NMR in $CDCl_3$

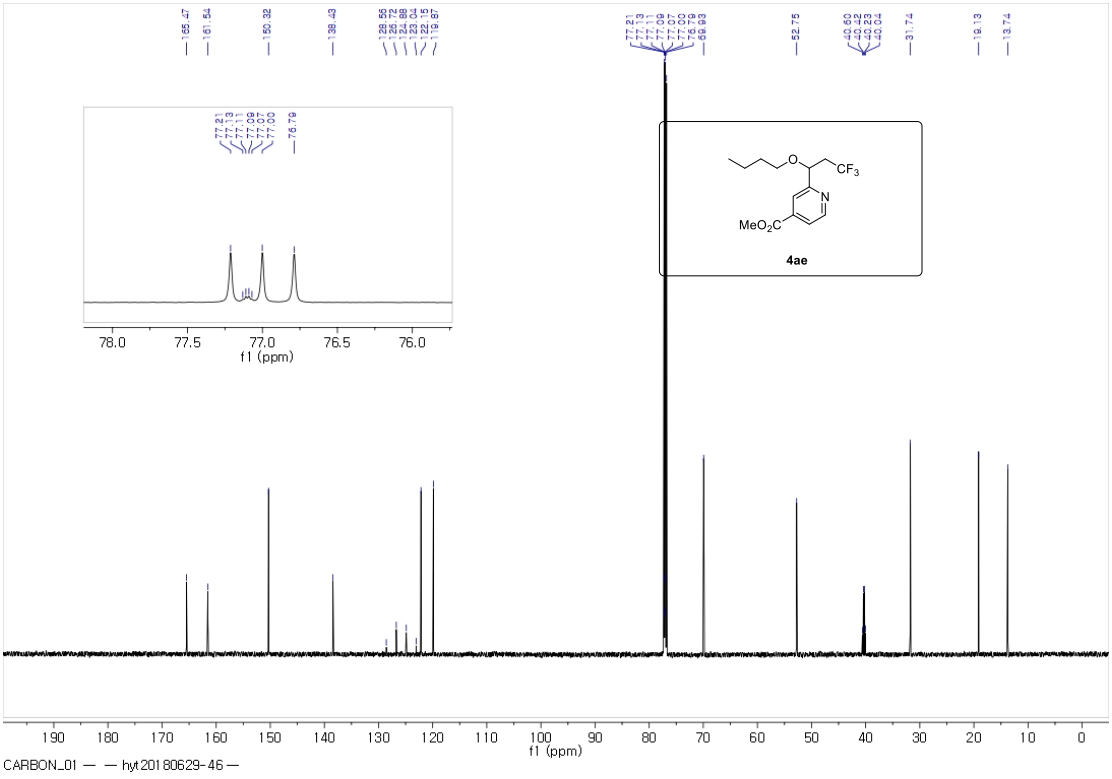


564 MHz, ^{19}F NMR in $CDCl_3$

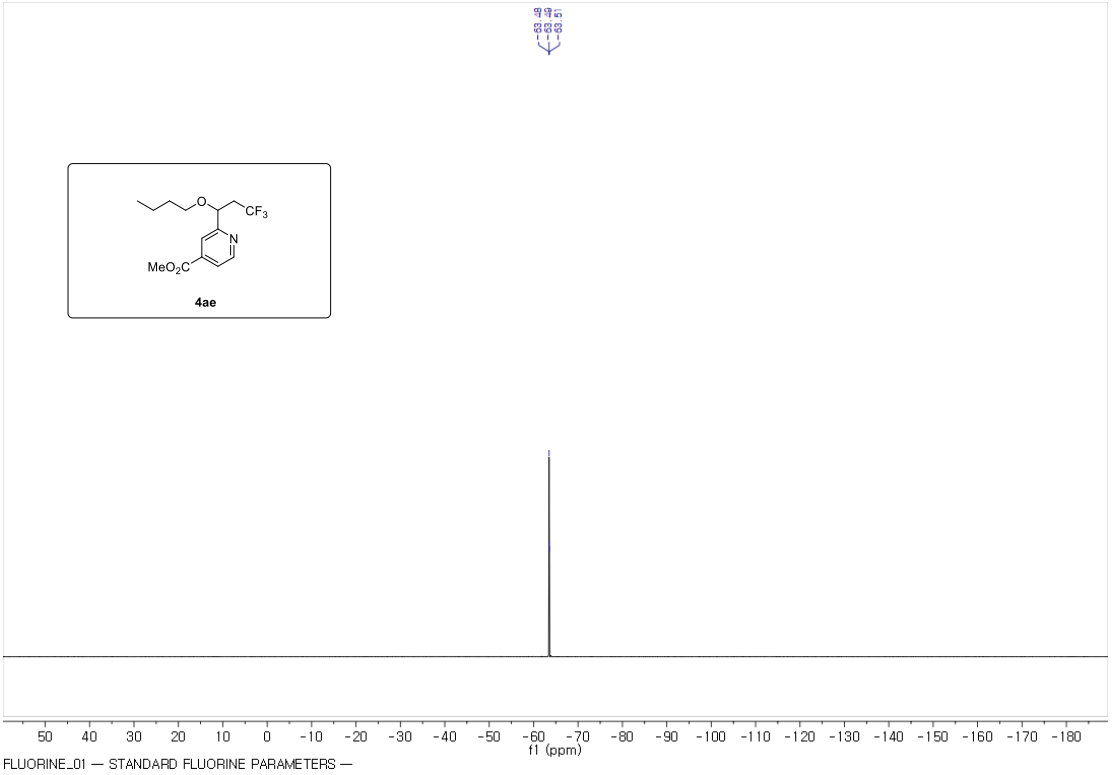
methyl 2-(1-butoxy-3,3,3-trifluoropropyl)isonicotinate (4ae).



599 MHz, ^{1}H NMR in $CDCl_3$

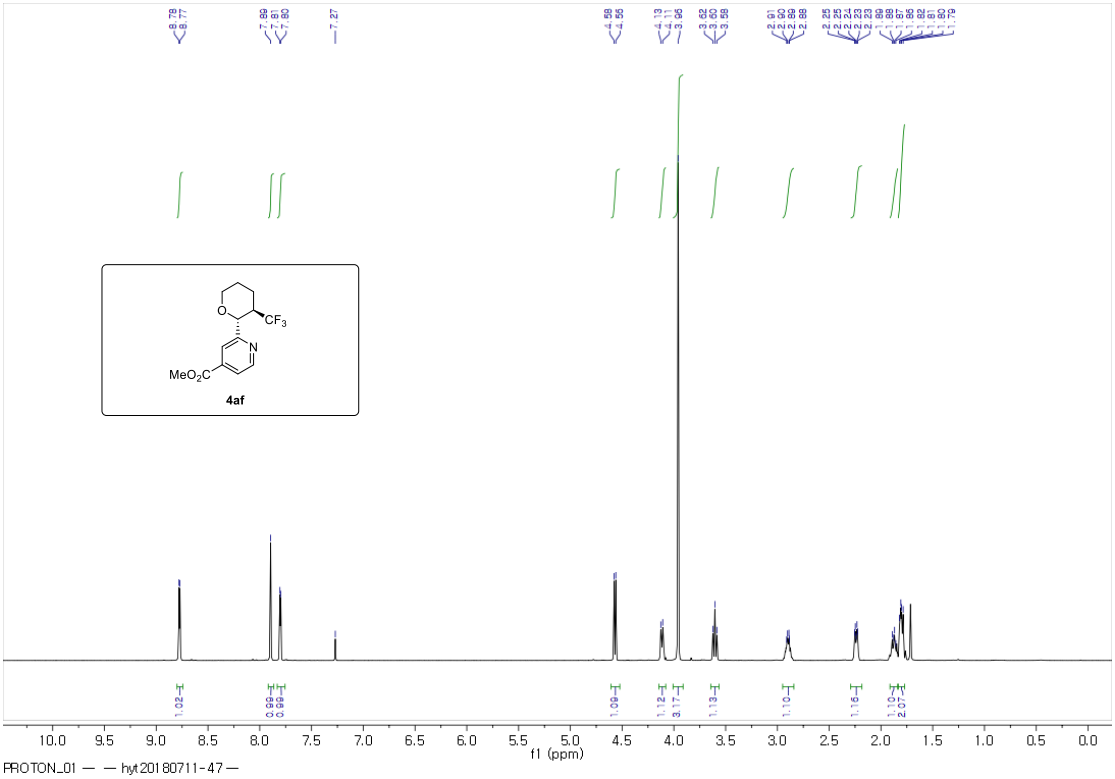


151 MHz, ^{13}C NMR in $CDCl_3$

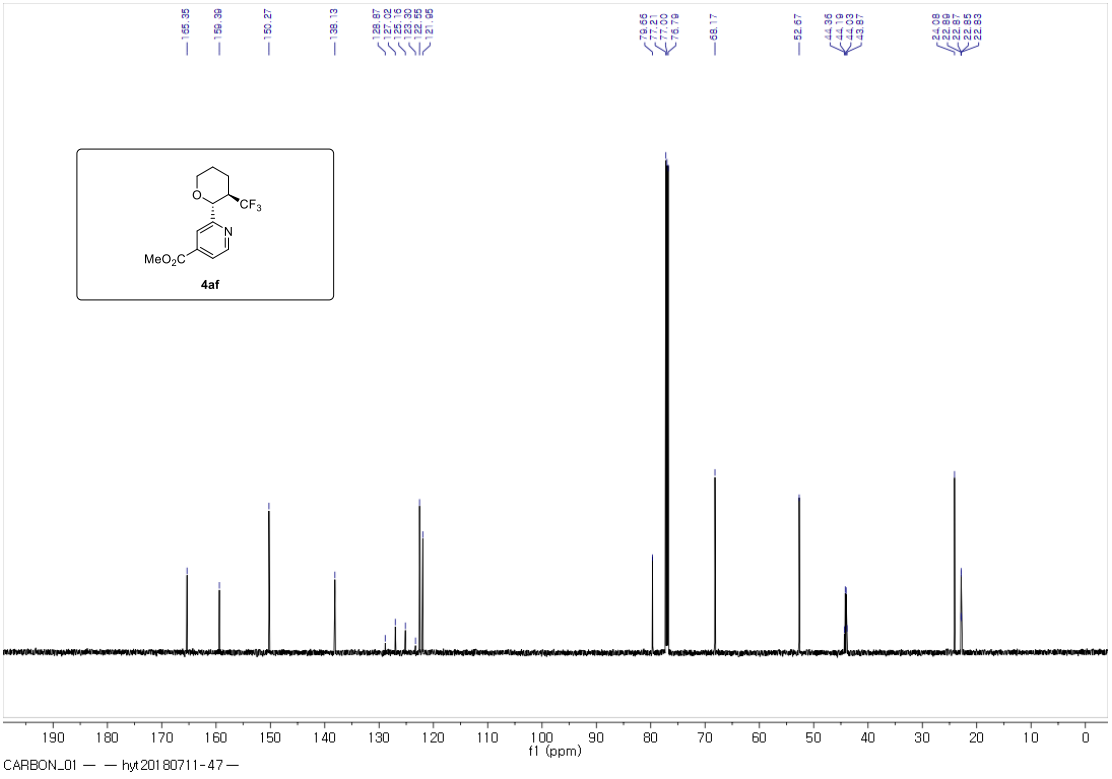


564 MHz, ^{19}F NMR in $CDCl_3$

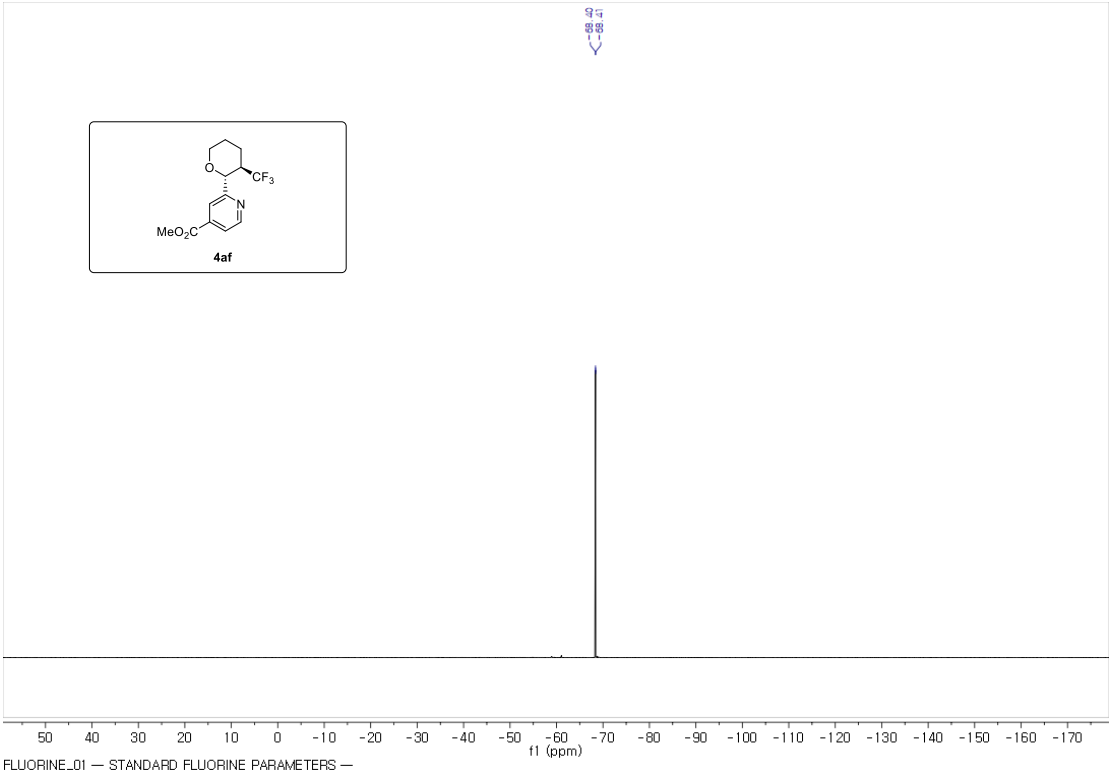
methyl 2-((2R,3R)-3-(trifluoromethyl)tetrahydro-2H-pyran-2-yl)isonicotinate (4af).



599 MHz, ^{1}H NMR in $CDCl_3$

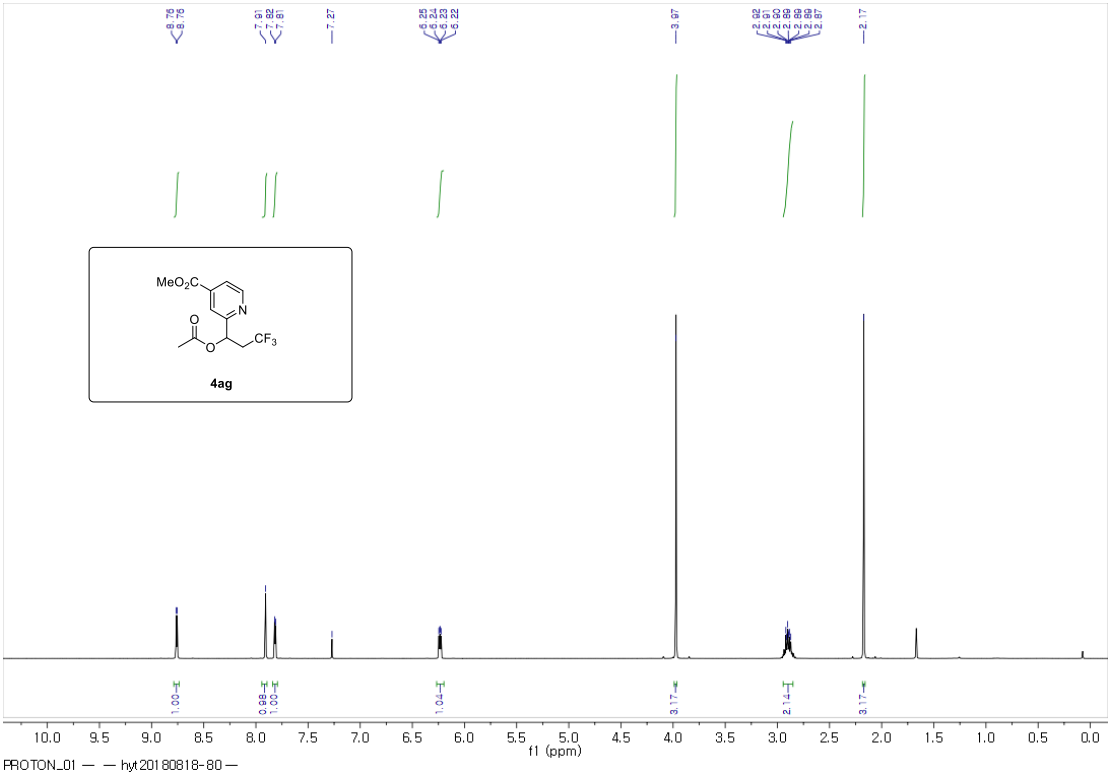


151 MHz, ^{13}C NMR in $CDCl_3$

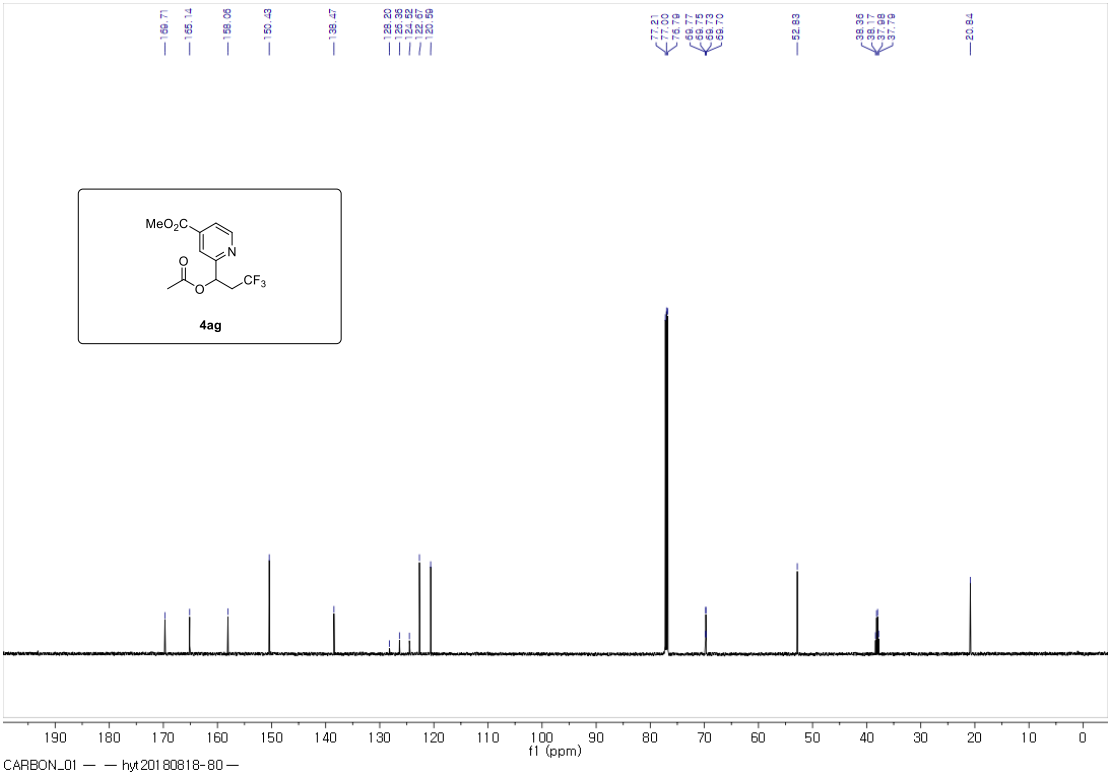


564 MHz, ^{19}F NMR in $CDCl_3$

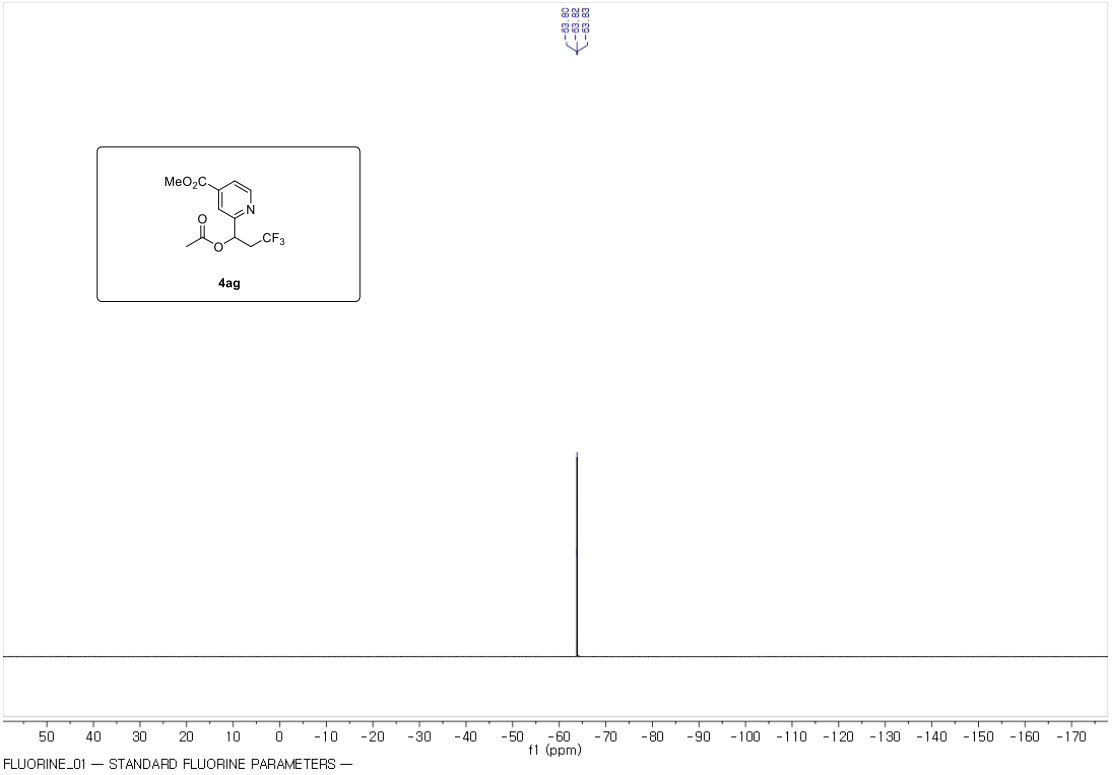
methyl 2-(1-acetoxy-3,3,3-trifluoropropyl)isonicotinate (4ag).



599 MHz, ^{1}H NMR in $CDCl_3$

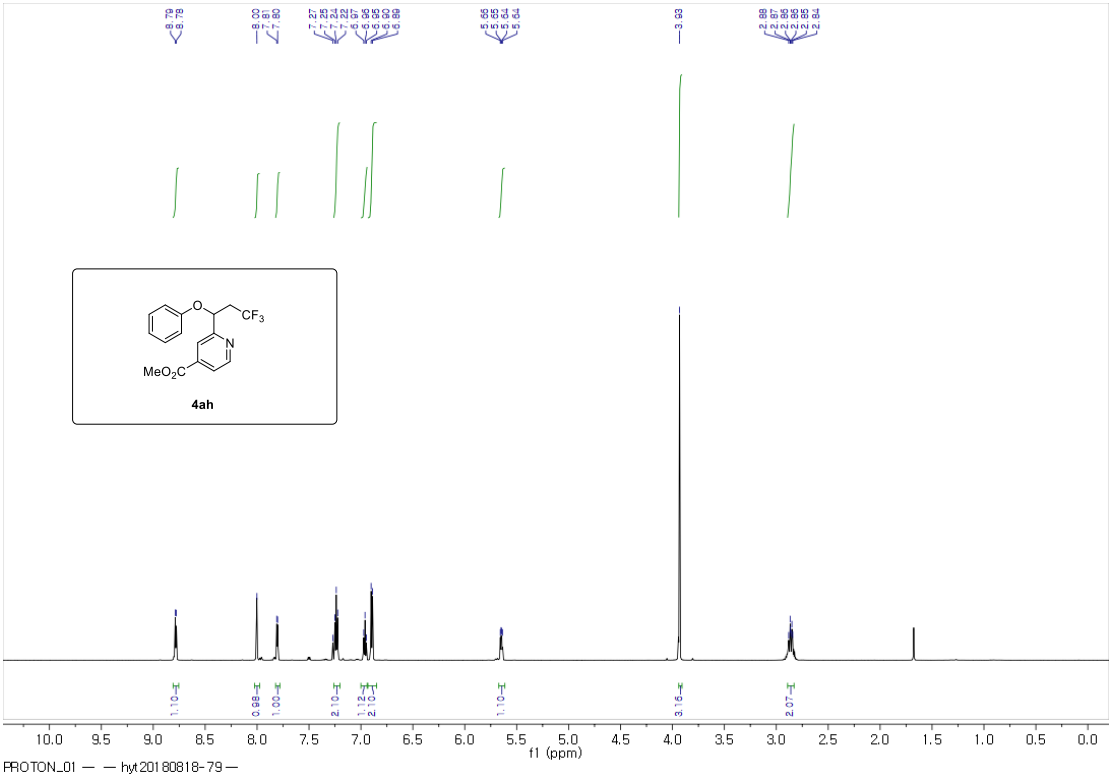


151 MHz, ^{13}C NMR in $CDCl_3$

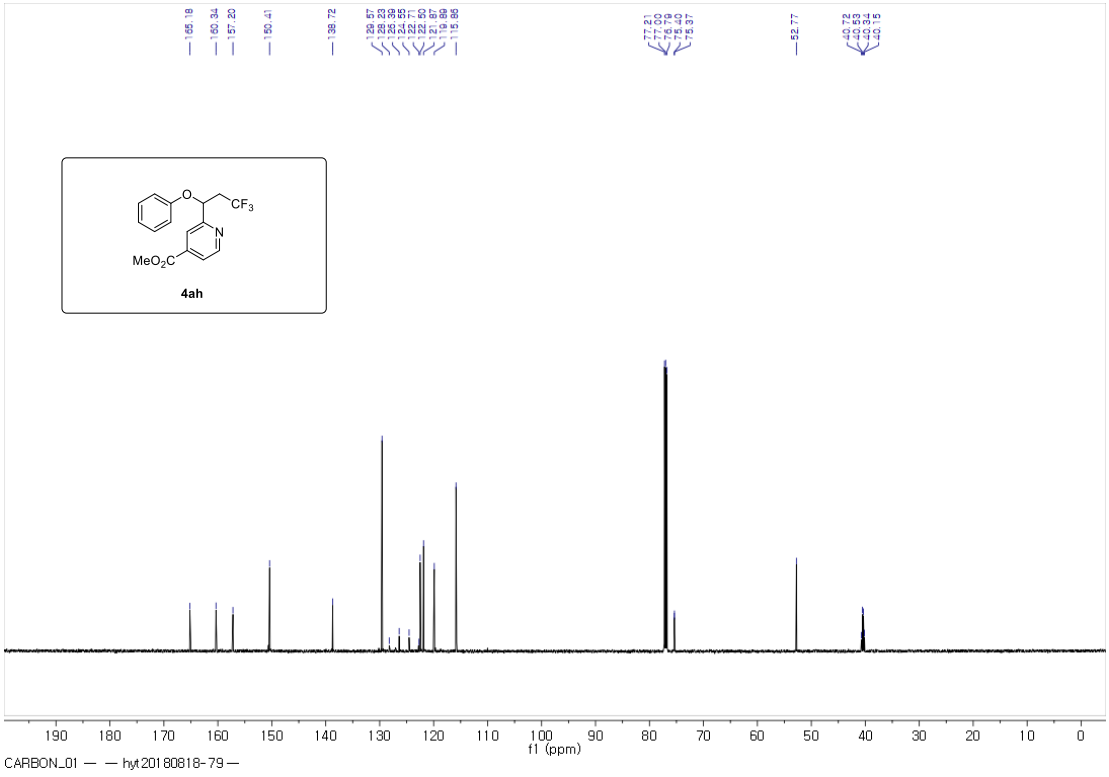


564 MHz, ^{19}F NMR in $CDCl_3$

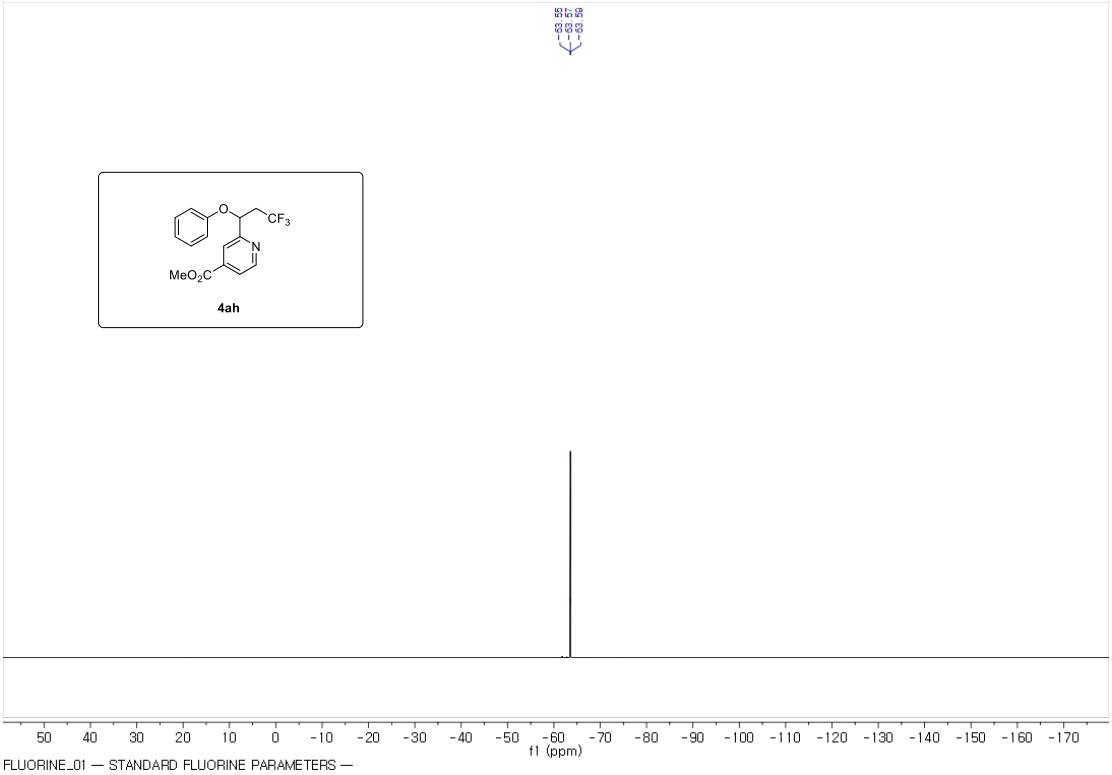
methyl 2-(3,3,3-trifluoro-1-phenoxypropyl)isonicotinate (4ah).



599 MHz, ^{1}H NMR in $CDCl_3$

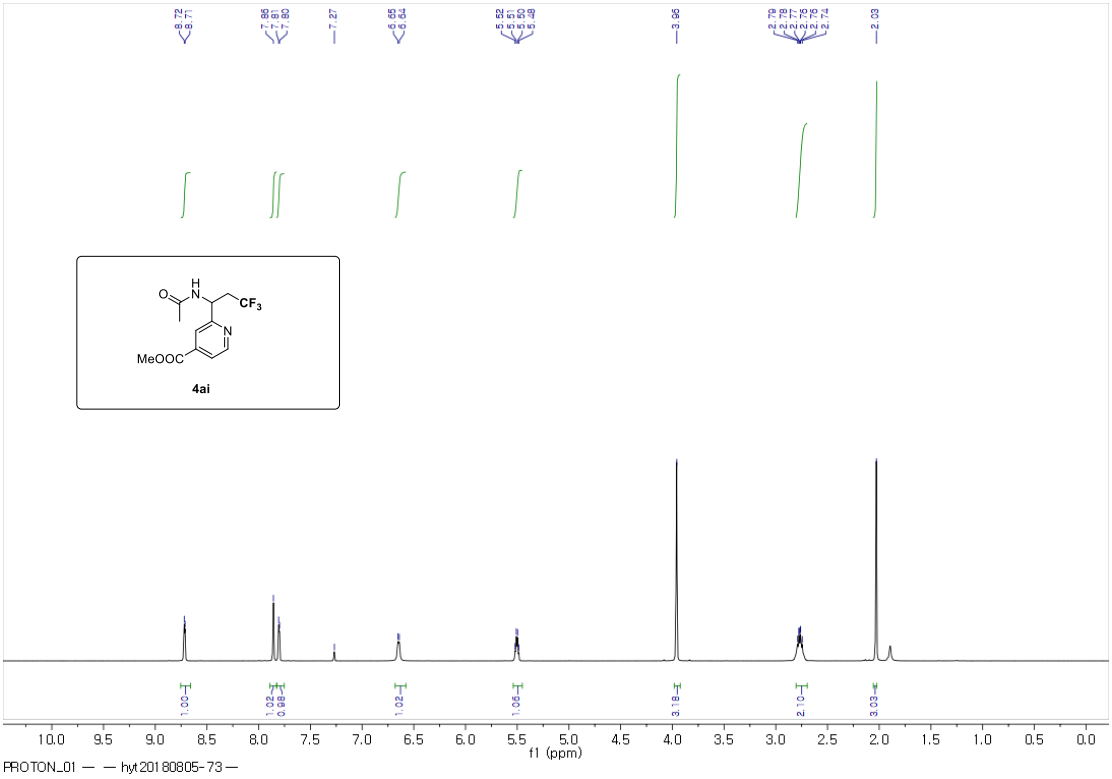


151 MHz, ^{13}C NMR in $CDCl_3$

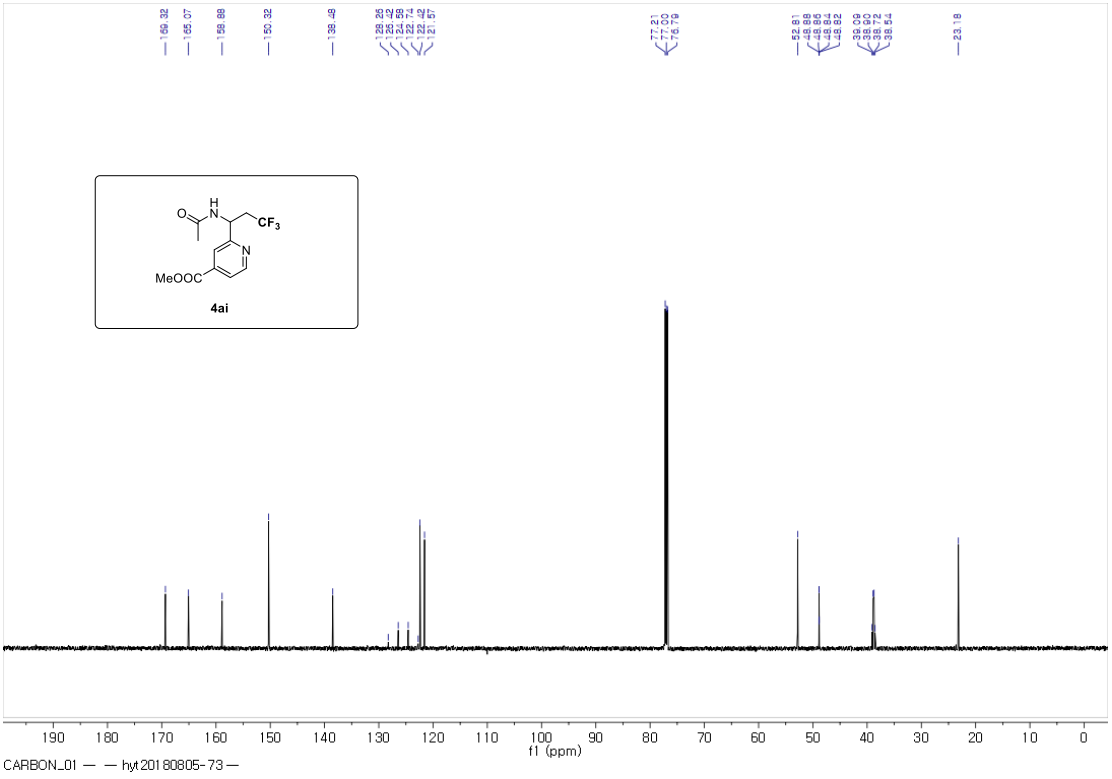


564 MHz, ^{19}F NMR in $CDCl_3$

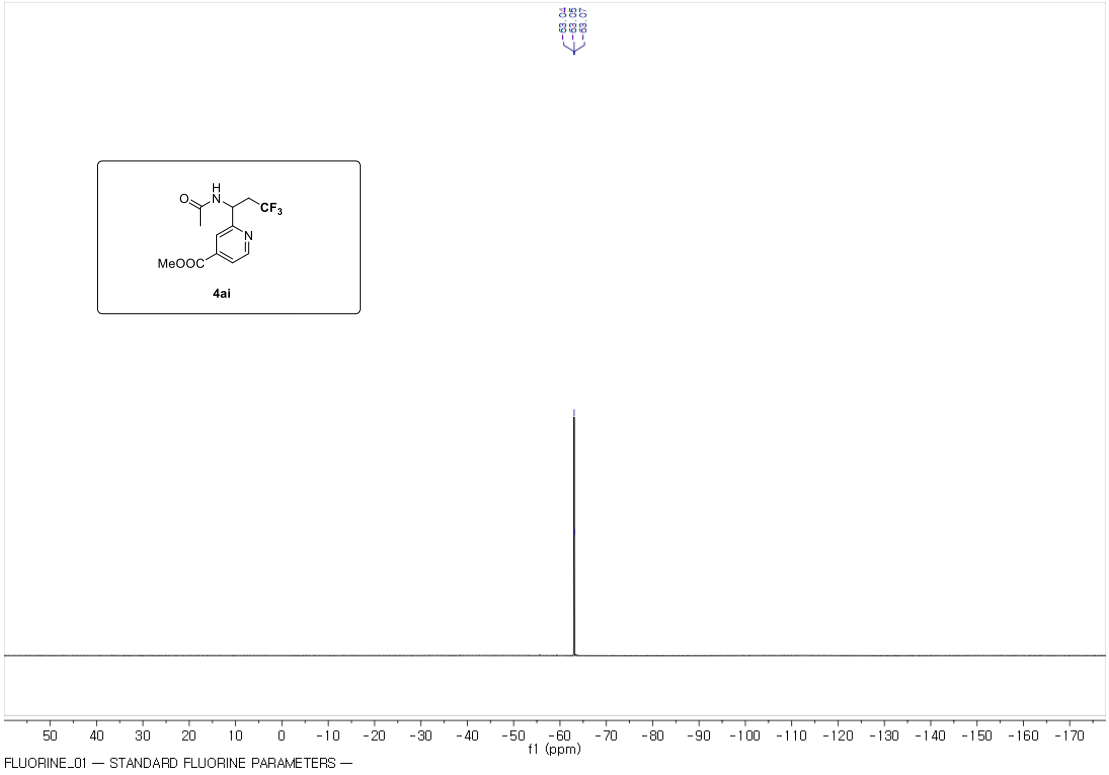
methyl 2-(1-acetamido-3,3,3-trifluoropropyl)isonicotinate (4ai).



599 MHz, ^{1}H NMR in $CDCl_3$

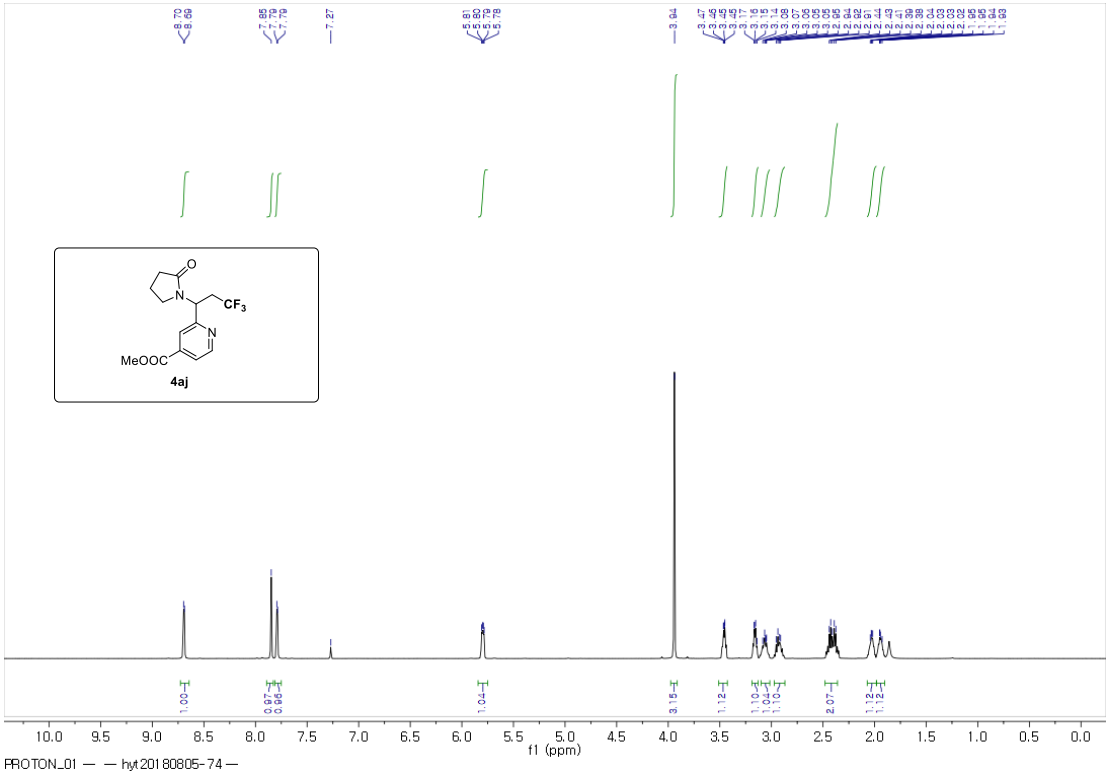


151 MHz, ^{13}C NMR in $CDCl_3$

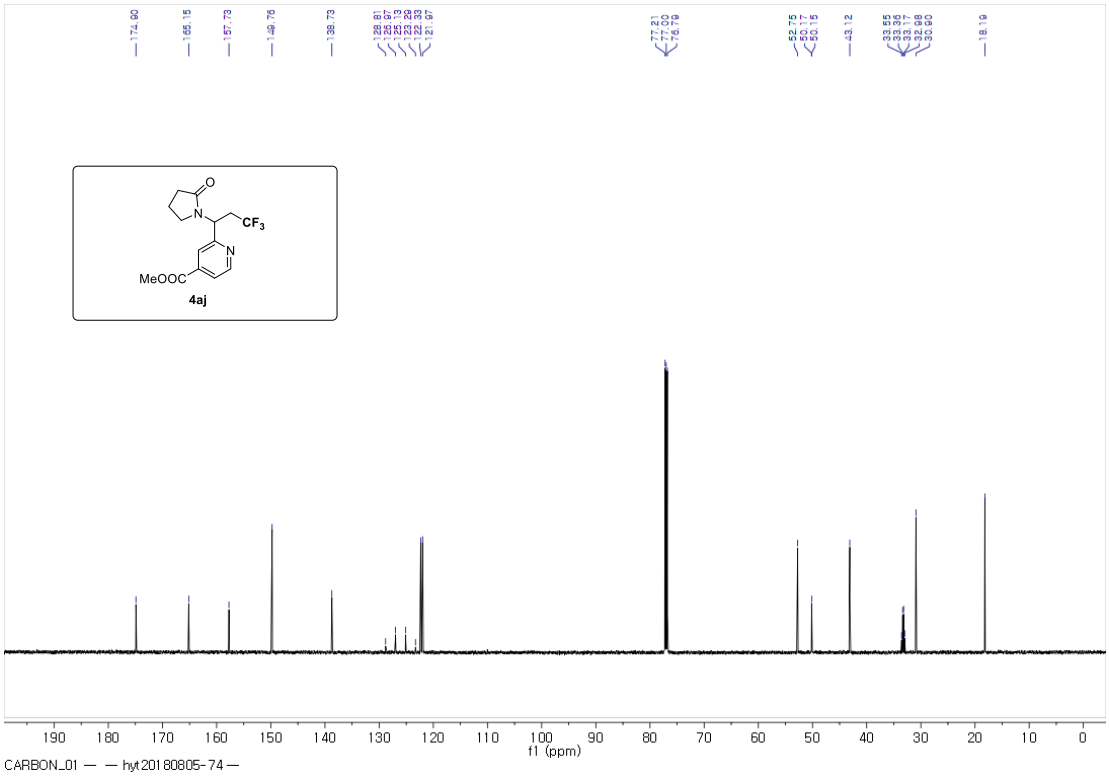


564 MHz, ^{19}F NMR in $CDCl_3$

methyl 2-(3,3,3-trifluoro-1-(2-oxopyrrolidin-1-yl)propyl)isonicotinatee (4aj).



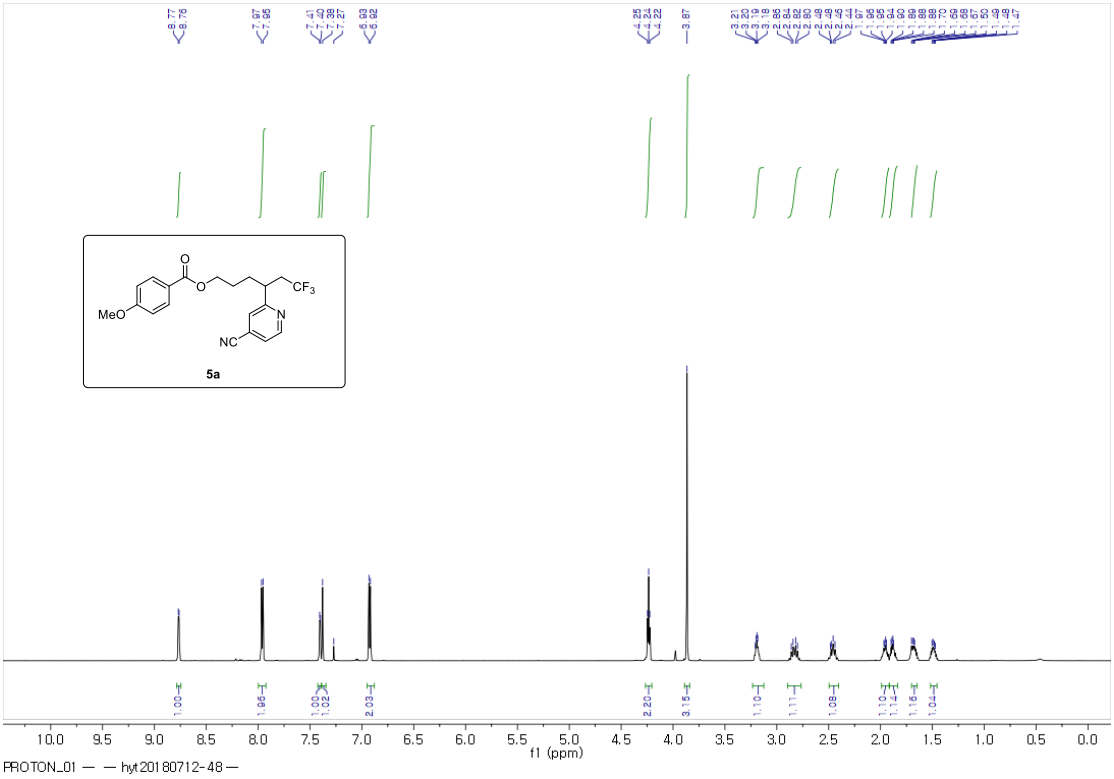
599 MHz, ^{1}H NMR in $CDCl_3$



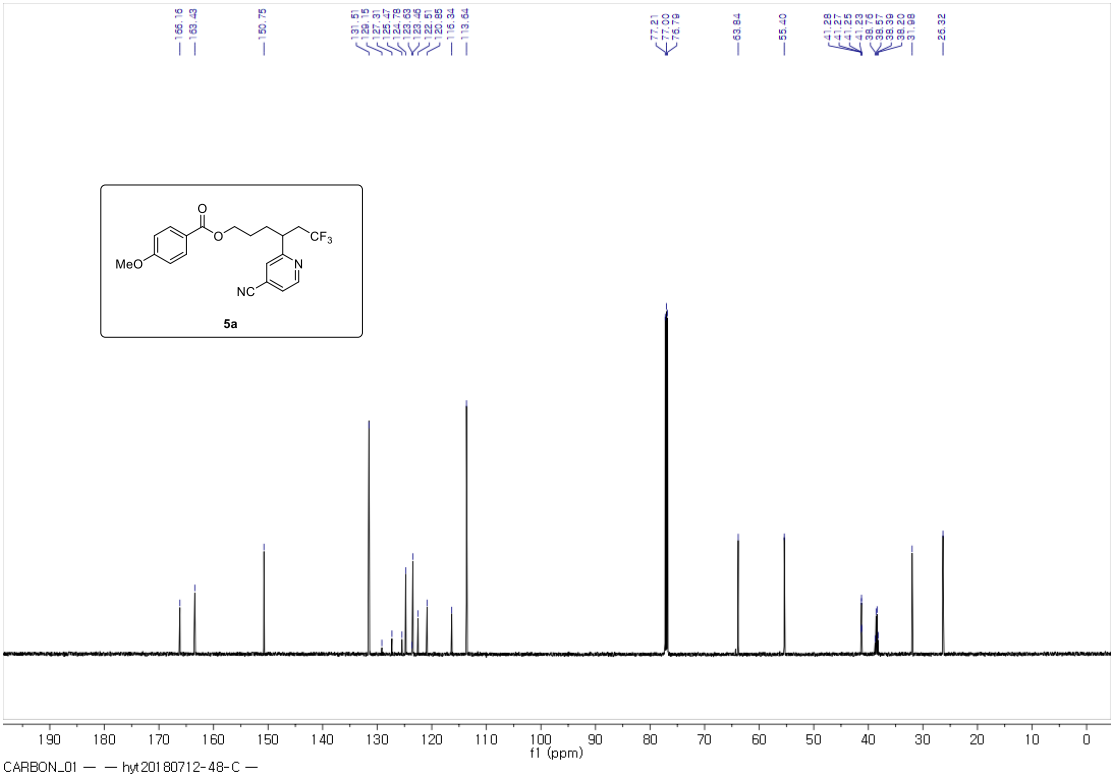
151 MHz, ^{13}C NMR in $CDCl_3$

564 MHz, ^{19}F NMR in $CDCl_3$

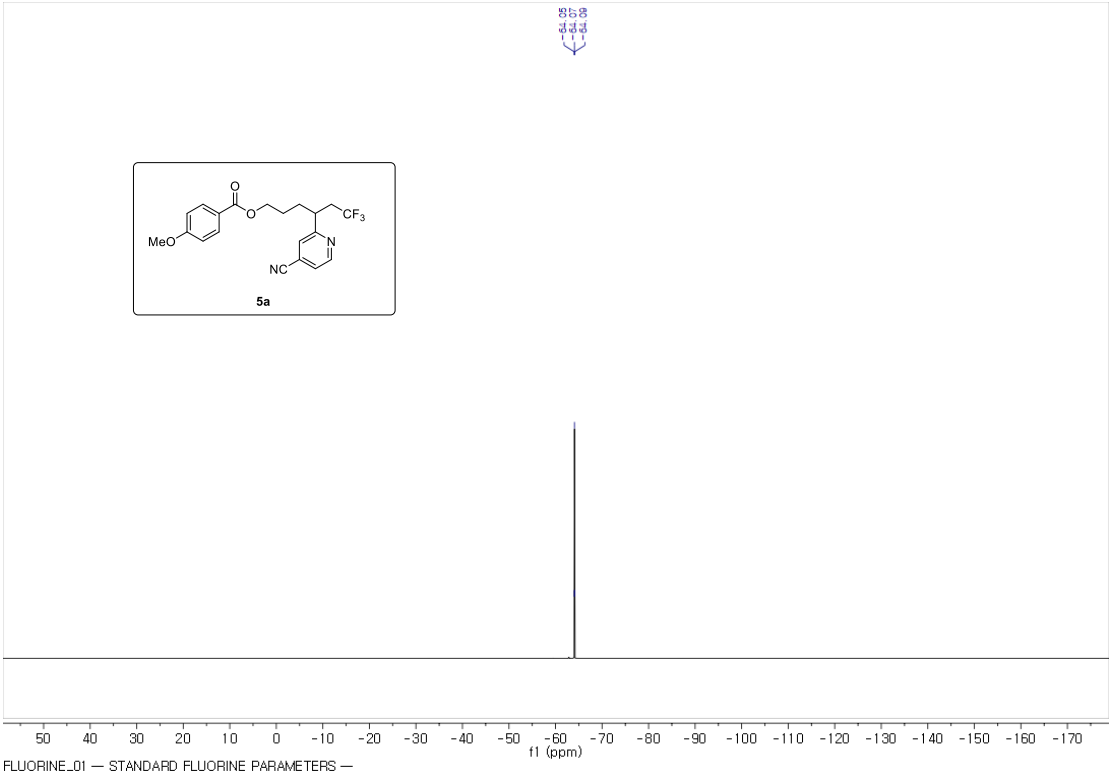
4-(4-cyanopyridin-2-yl)-6,6,6-trifluorohexyl 4-methoxybenzoate (5a).



599 MHz, ^{1}H NMR in $CDCl_3$

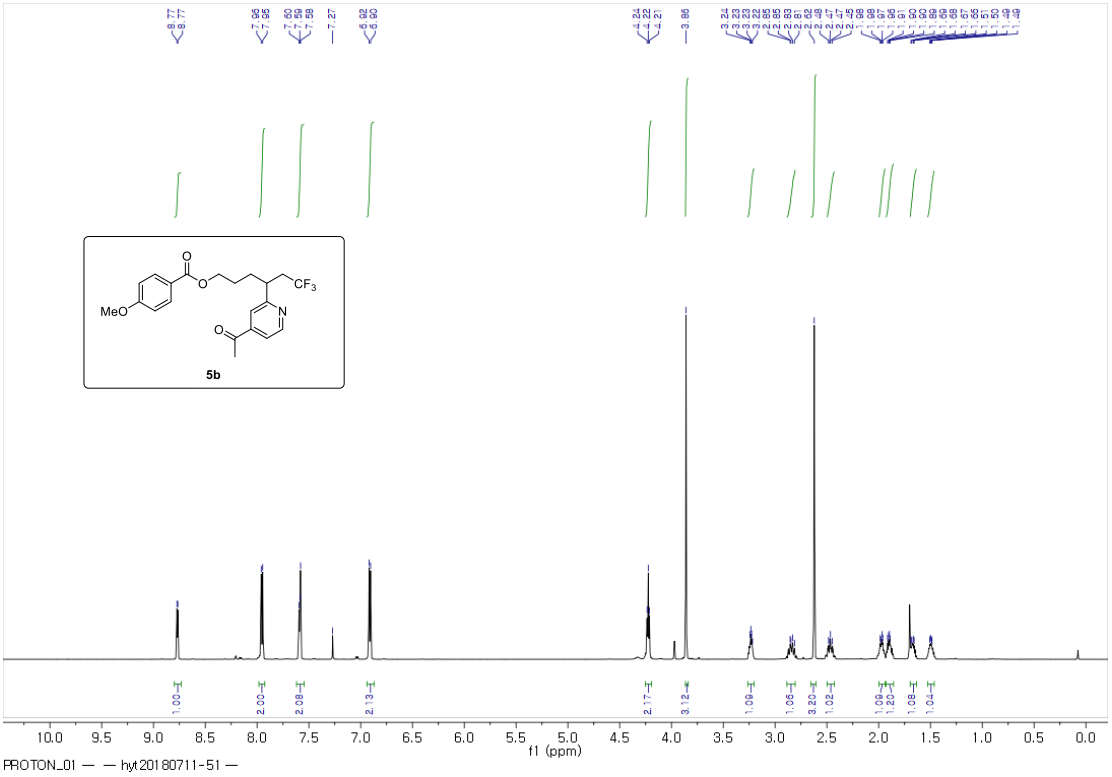


151 MHz, ^{13}C NMR in $CDCl_3$

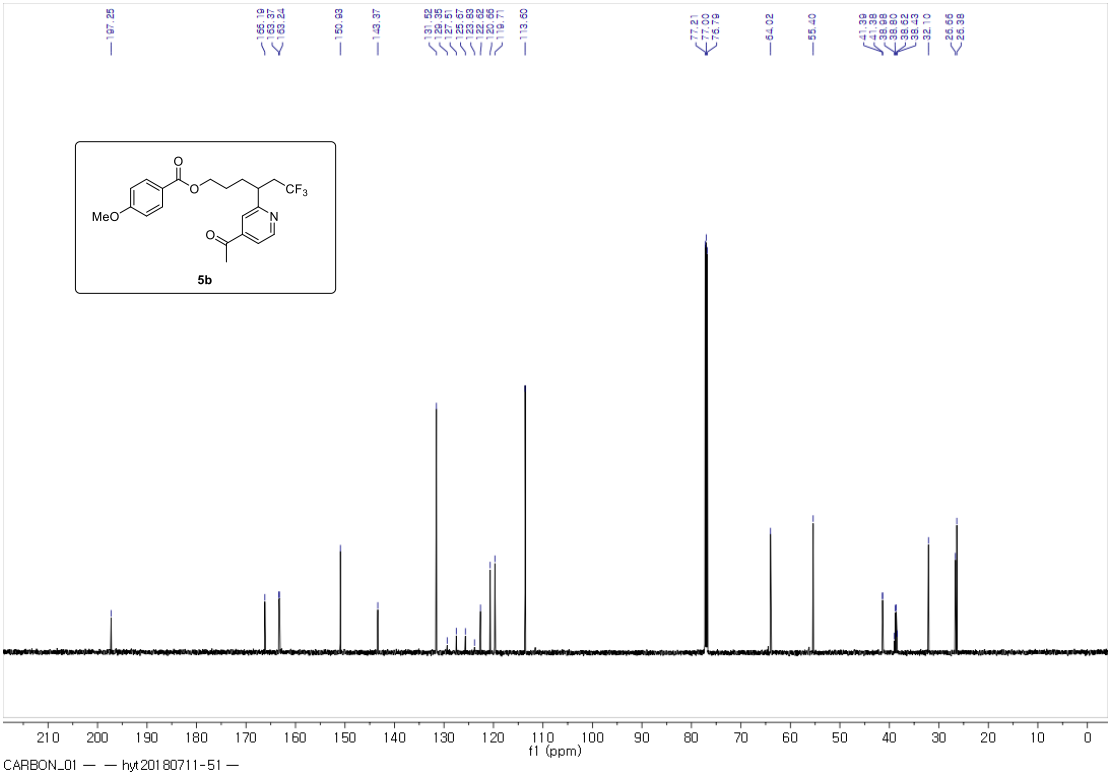


564 MHz, ^{19}F NMR in $CDCl_3$

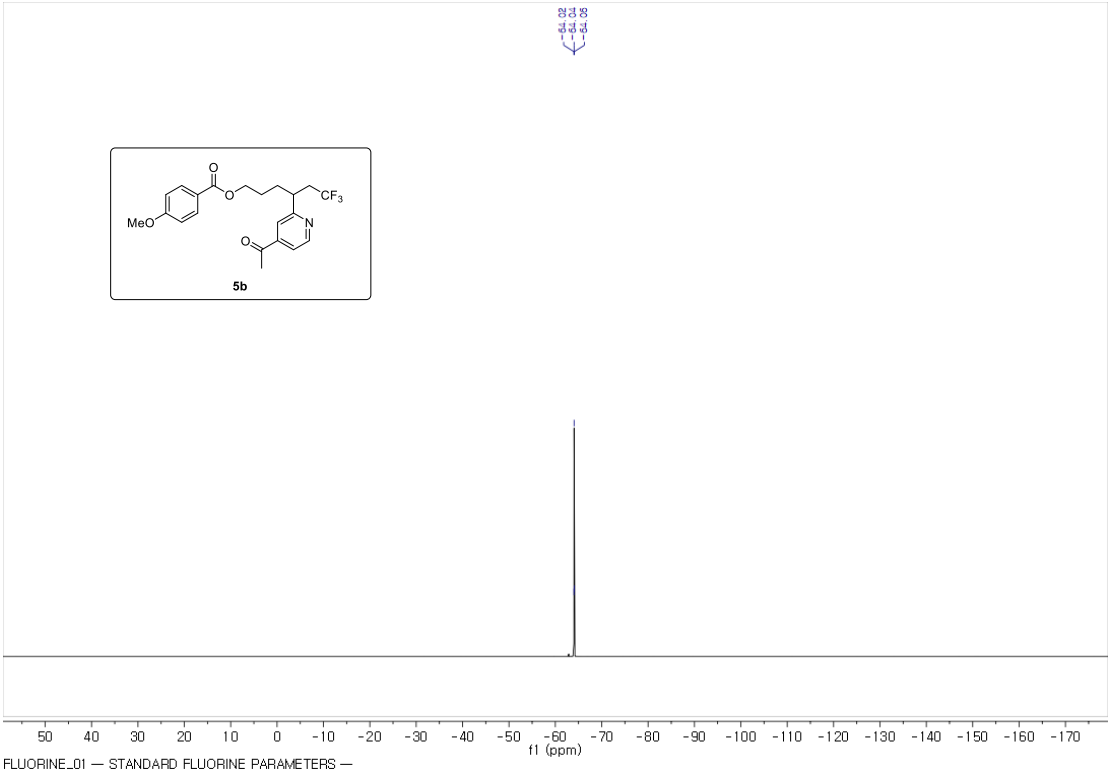
4-(4-acetylpyridin-2-yl)-6,6,6-trifluorohexyl 4-methoxybenzoate (5b).



599 MHz, ^{1}H NMR in $CDCl_3$

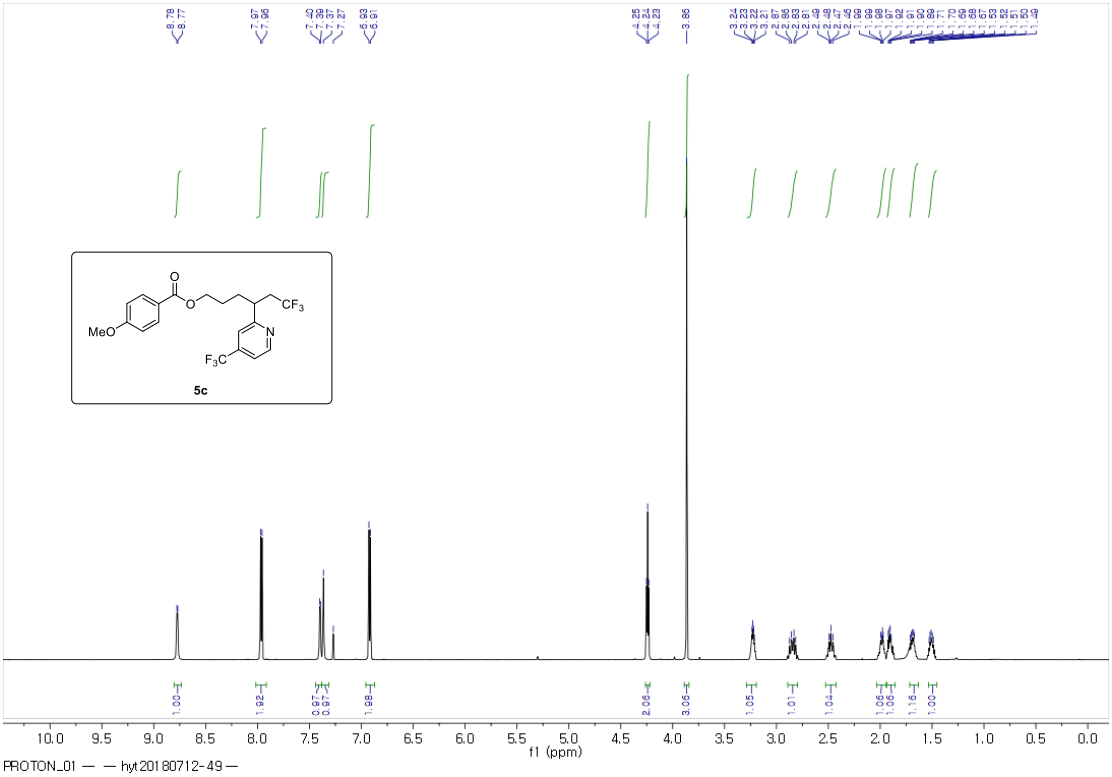


151 MHz, ^{13}C NMR in $CDCl_3$

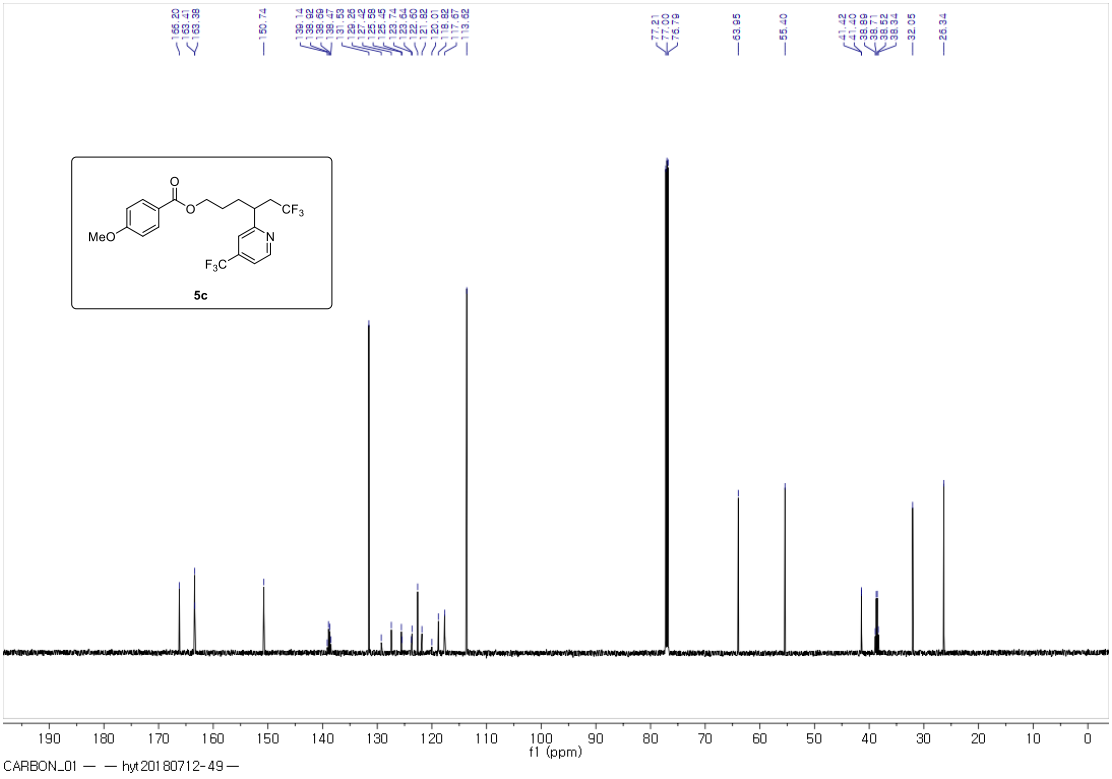


564 MHz, ^{19}F NMR in $CDCl_3$

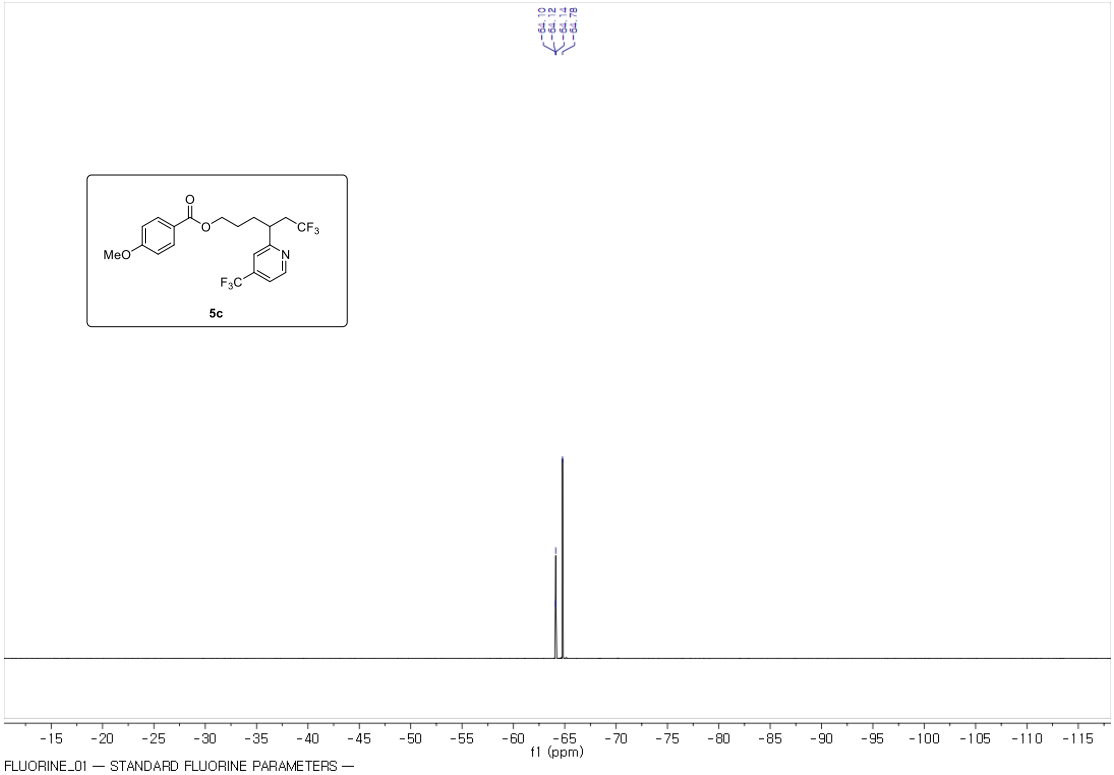
6,6,6-trifluoro-4-(4-(trifluoromethyl)pyridin-2-yl)hexyl 4-methoxybenzoate (5c).



599 MHz, ^{1}H NMR in $CDCl_3$

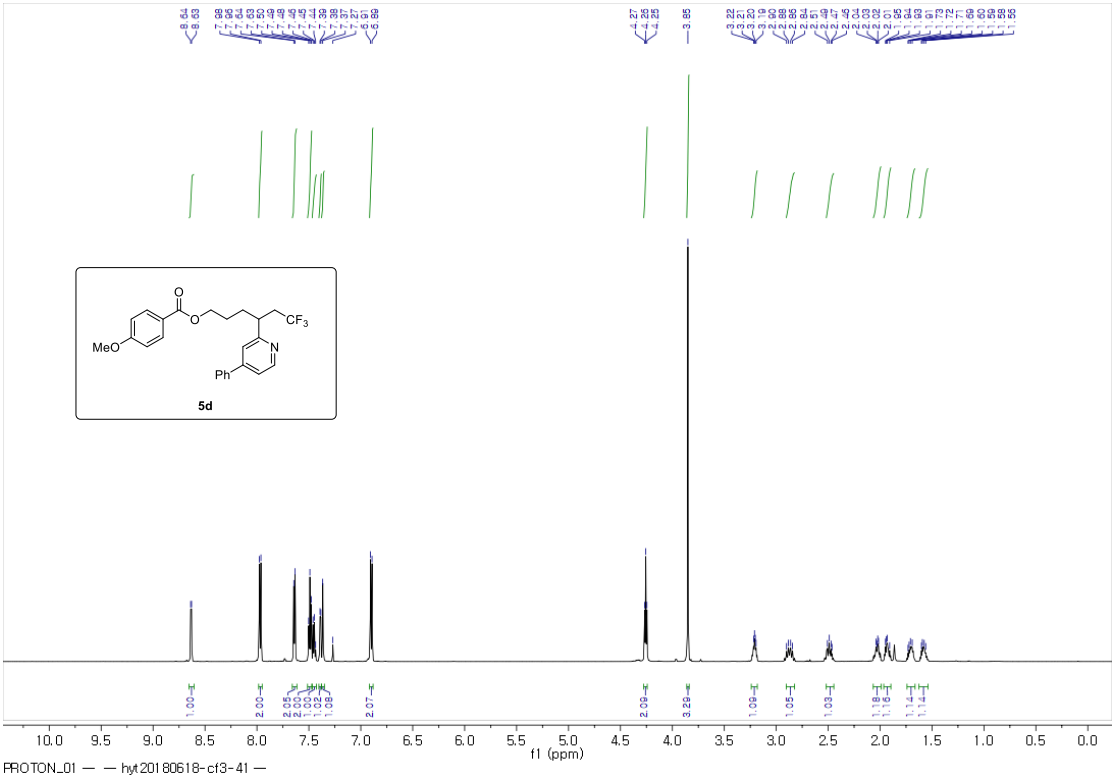


151 MHz, ^{13}C NMR in $CDCl_3$

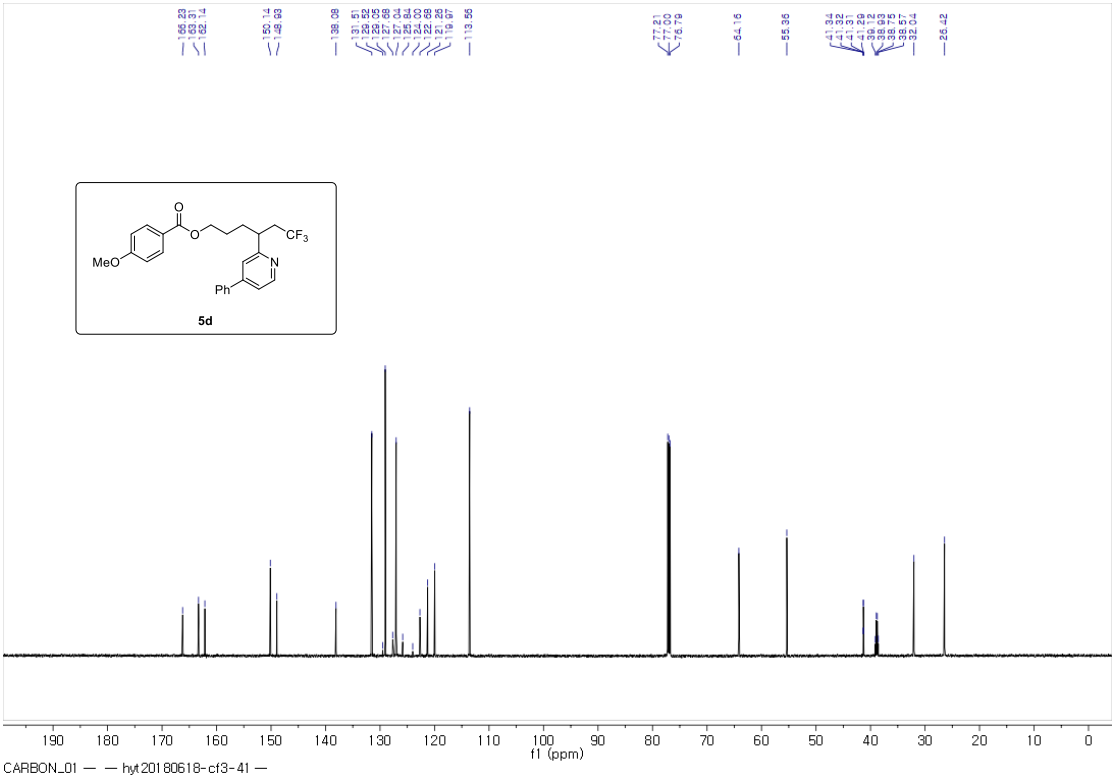


564 MHz, ^{19}F NMR in $CDCl_3$

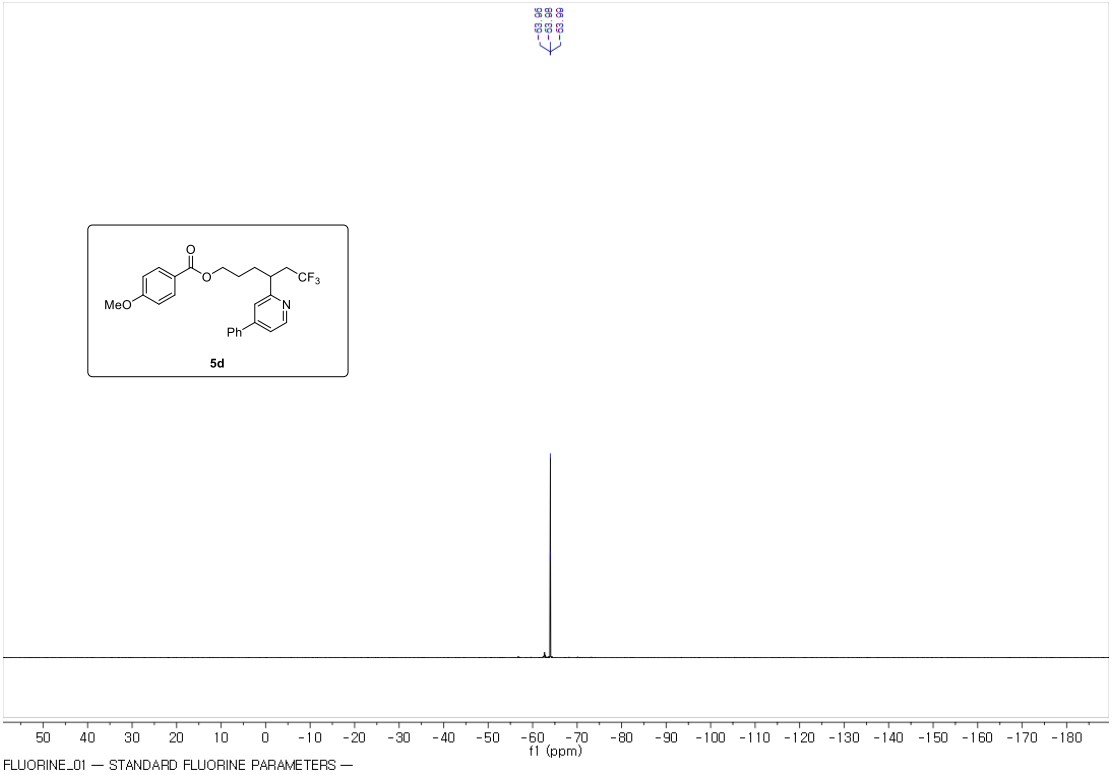
6,6,6-trifluoro-4-(4-phenylpyridin-2-yl)hexyl 4-methoxybenzoate (5d).



599 MHz, ^{1}H NMR in $CDCl_3$

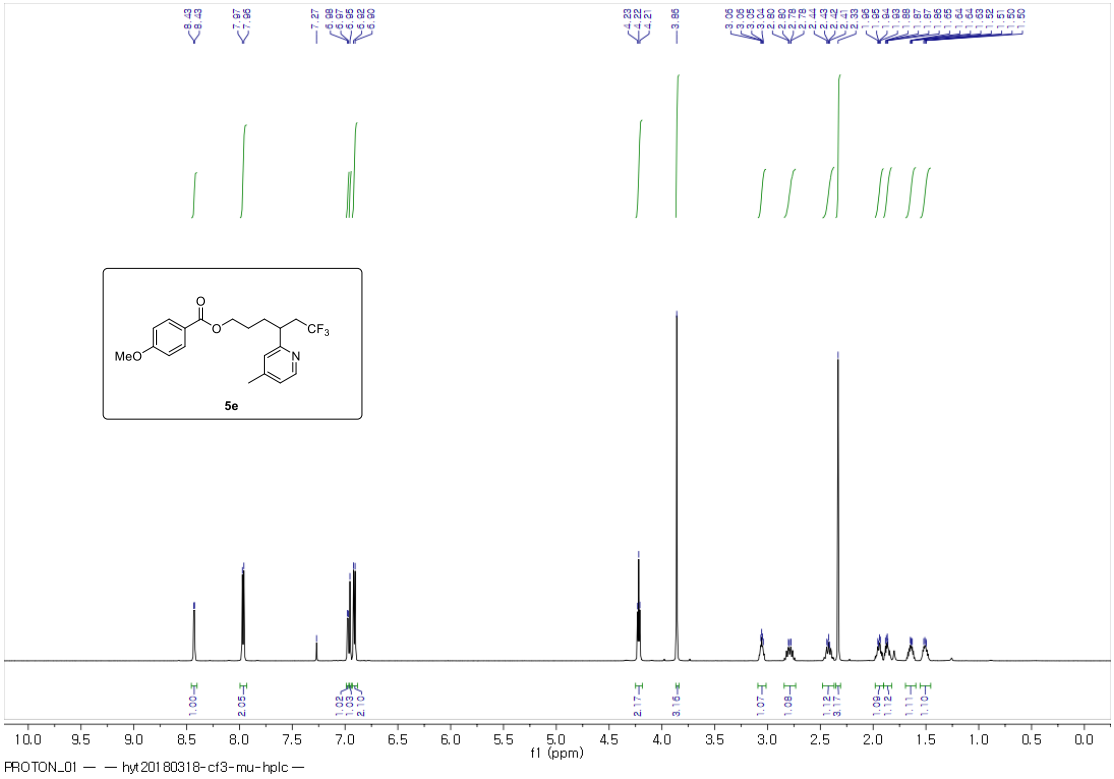


151 MHz, ^{13}C NMR in $CDCl_3$

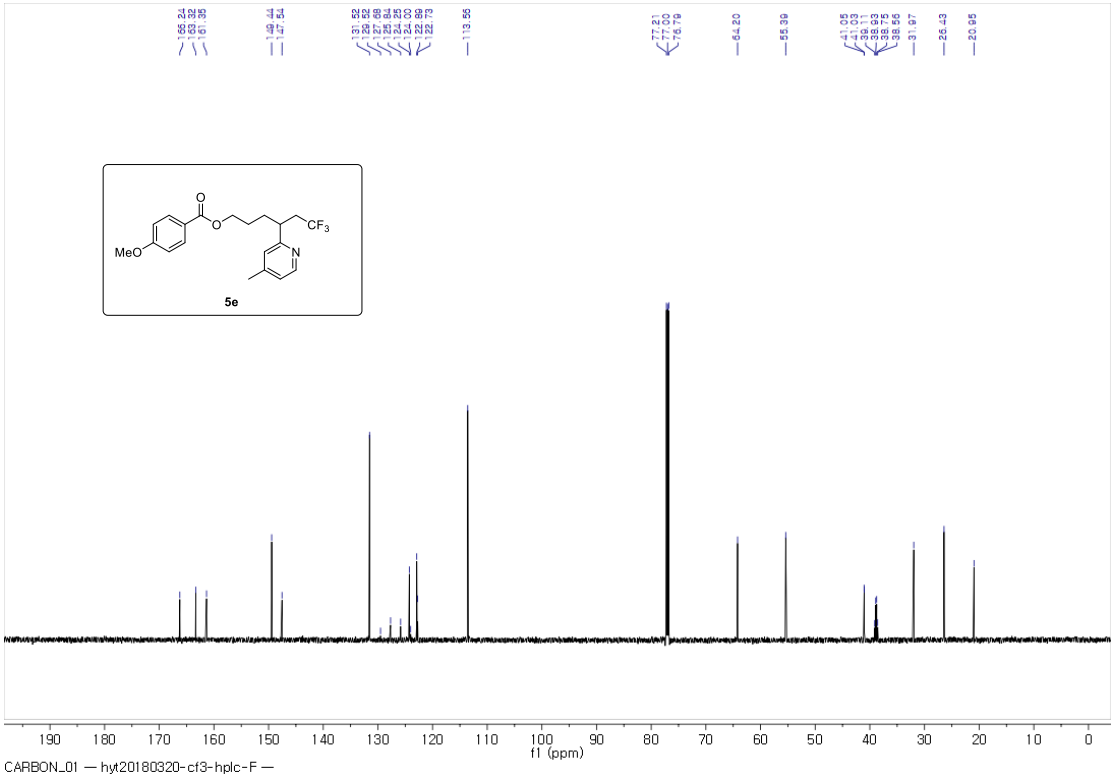


564 MHz, ^{19}F NMR in $CDCl_3$

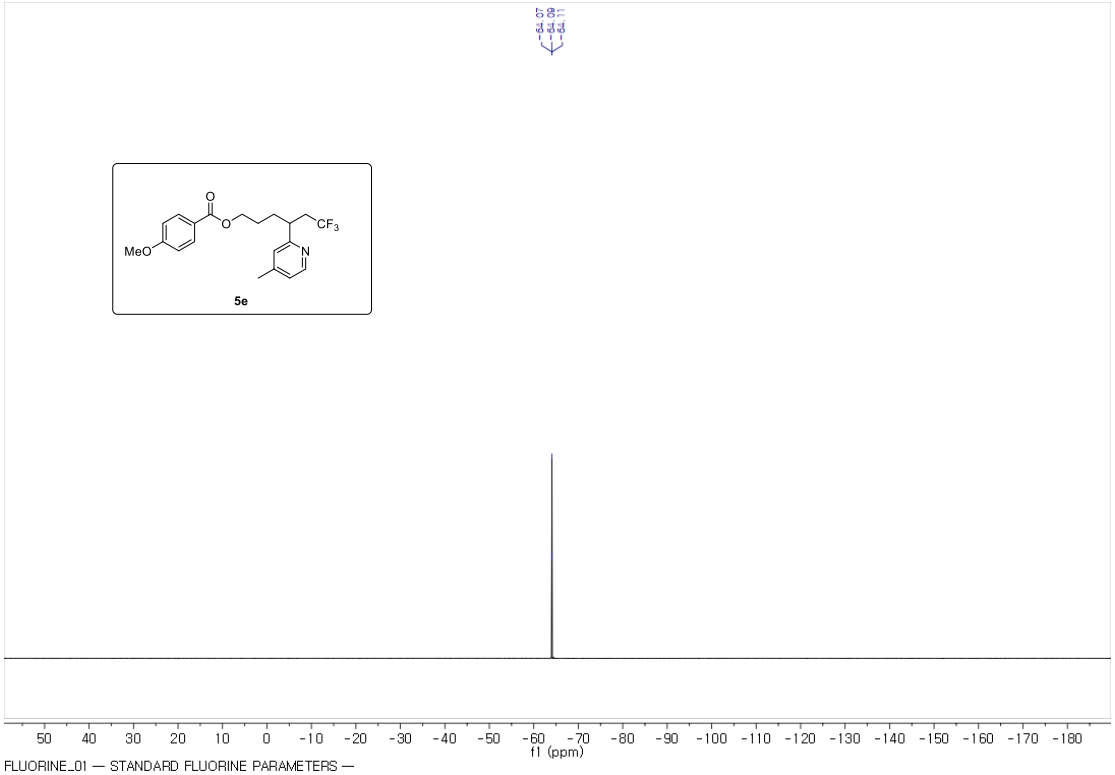
6,6,6-trifluoro-4-(4-methylpyridin-2-yl)hexyl 4-methoxybenzoate (5e).



599 MHz, ^{1}H NMR in $CDCl_3$

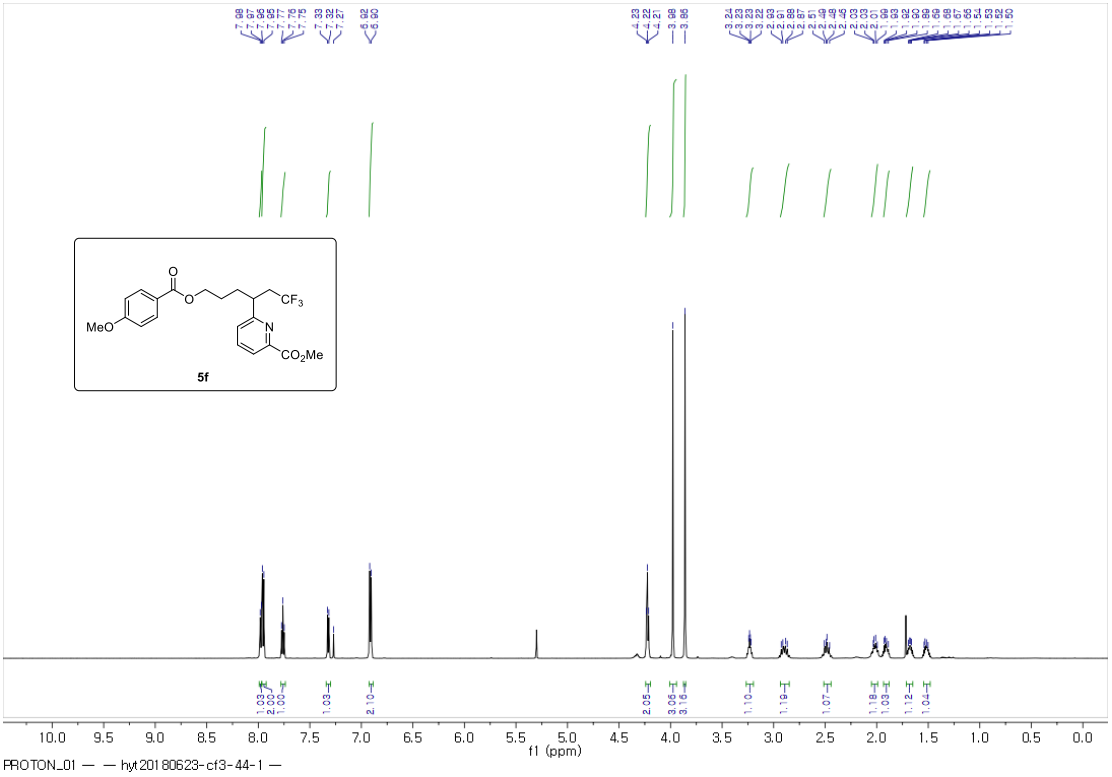


151 MHz, ^{13}C NMR in $CDCl_3$

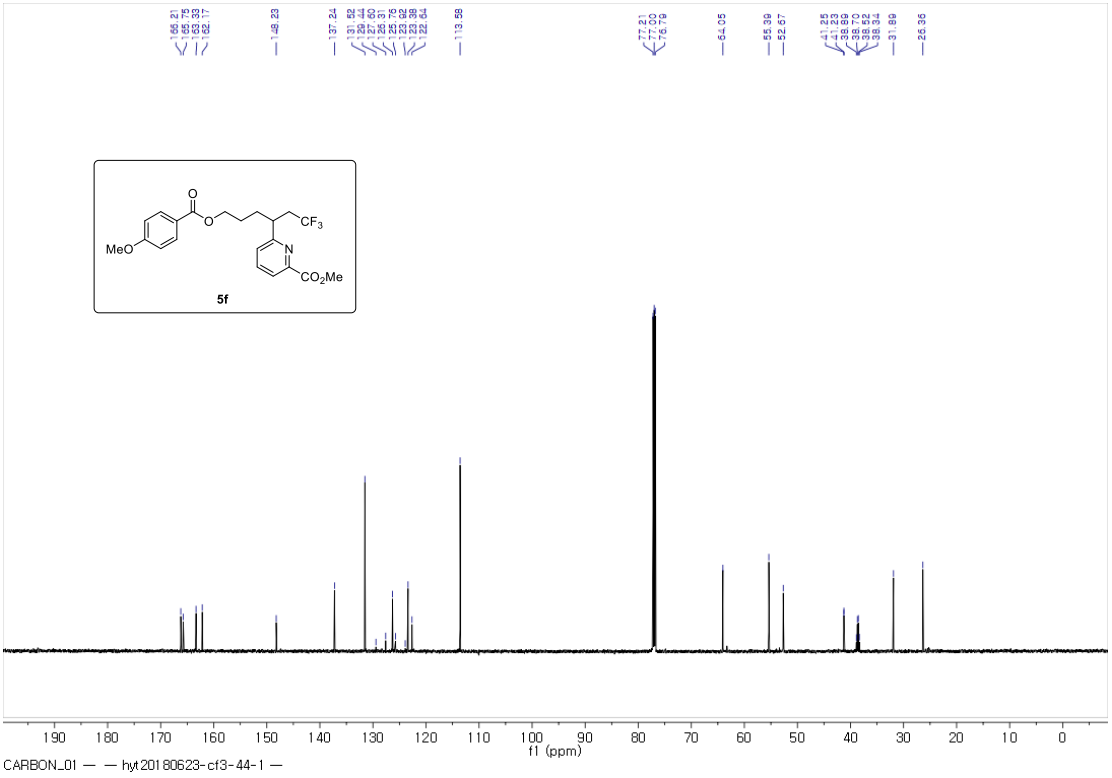


564 MHz, ^{19}F NMR in $CDCl_3$

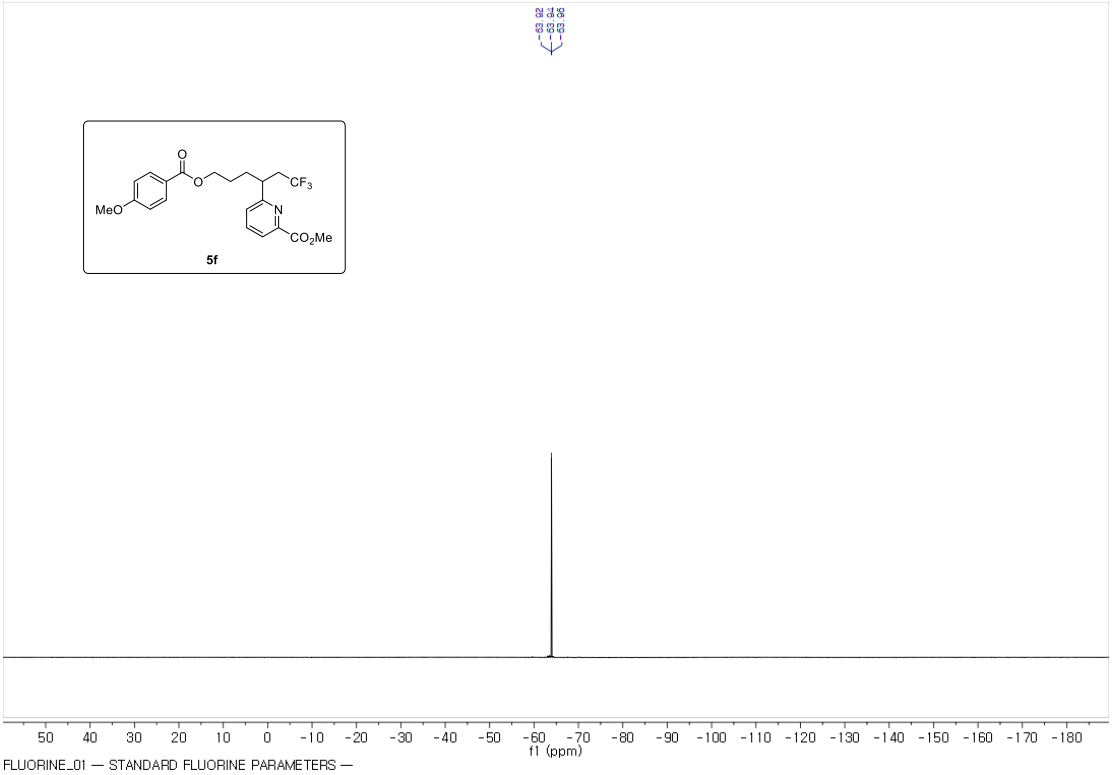
methyl 6-(1,1,1-trifluoro-6-((4-methoxybenzoyl)oxy)hexan-3-yl)picolinate (5f).



599 MHz, ^{1}H NMR in $CDCl_3$

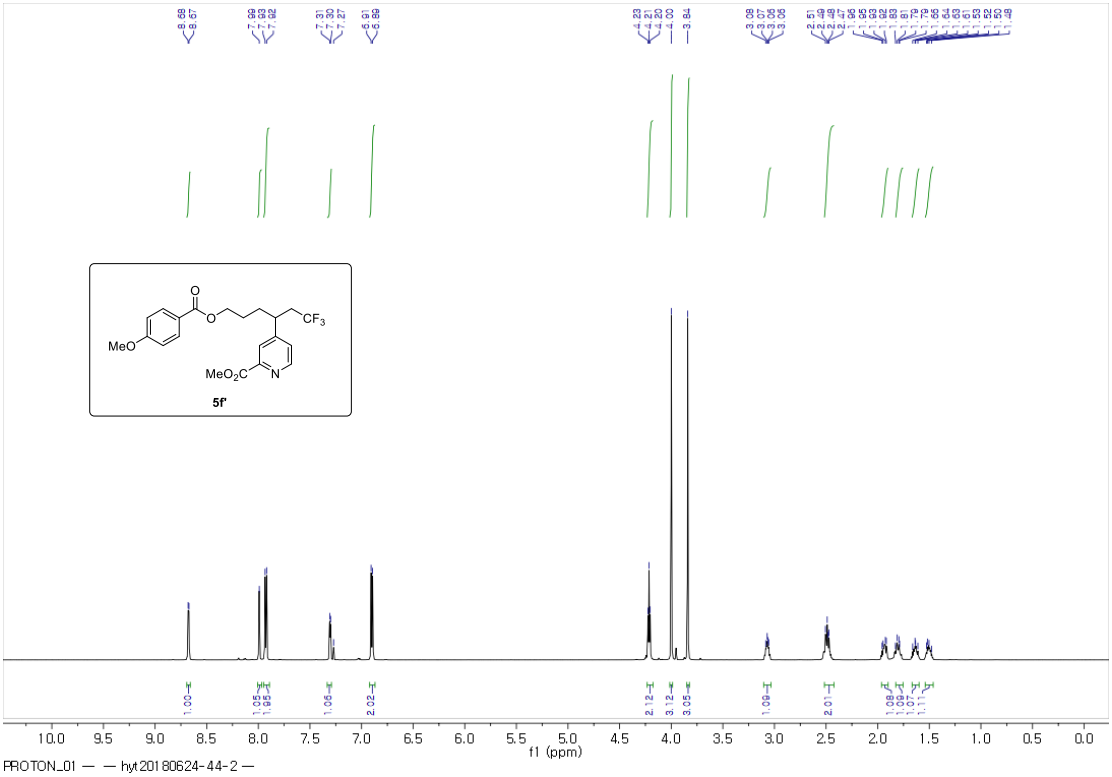


151 MHz, ^{13}C NMR in $CDCl_3$

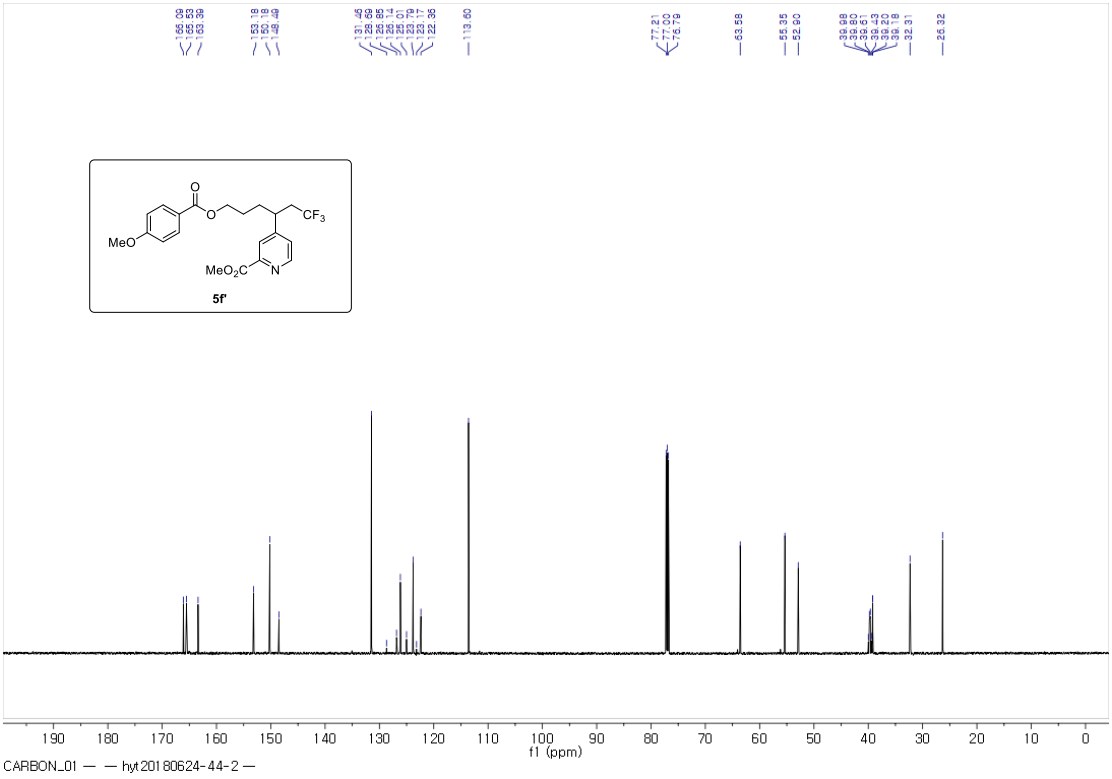


564 MHz, ^{19}F NMR in $CDCl_3$

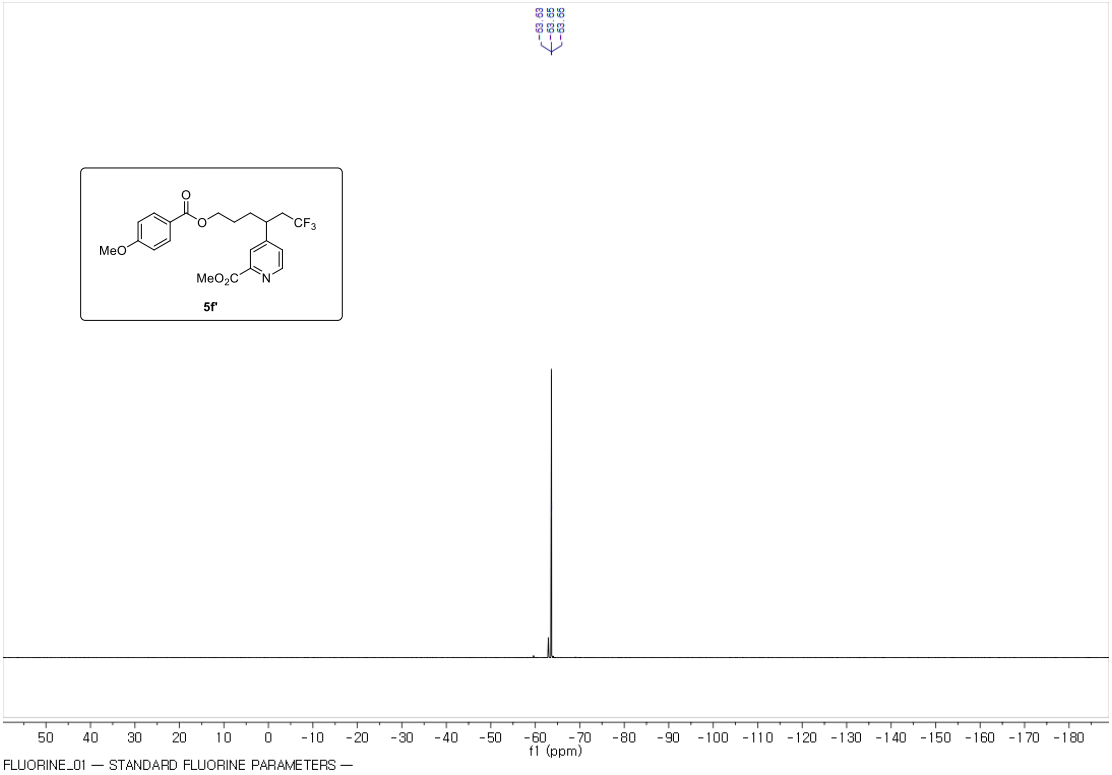
methyl 4-(1,1,1-trifluoro-6-((4-methoxybenzoyl)oxy)hexan-3-yl)picolinate (5f').



599 MHz, ^{1}H NMR in $CDCl_3$

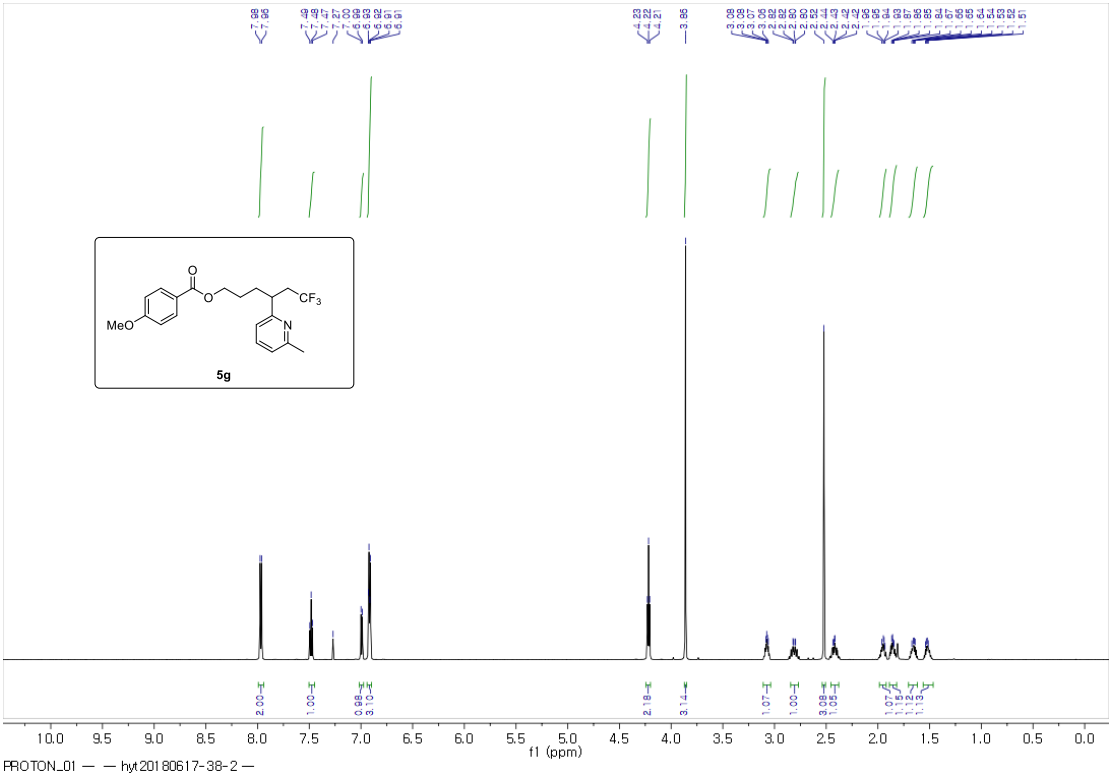


151 MHz, ^{13}C NMR in $CDCl_3$

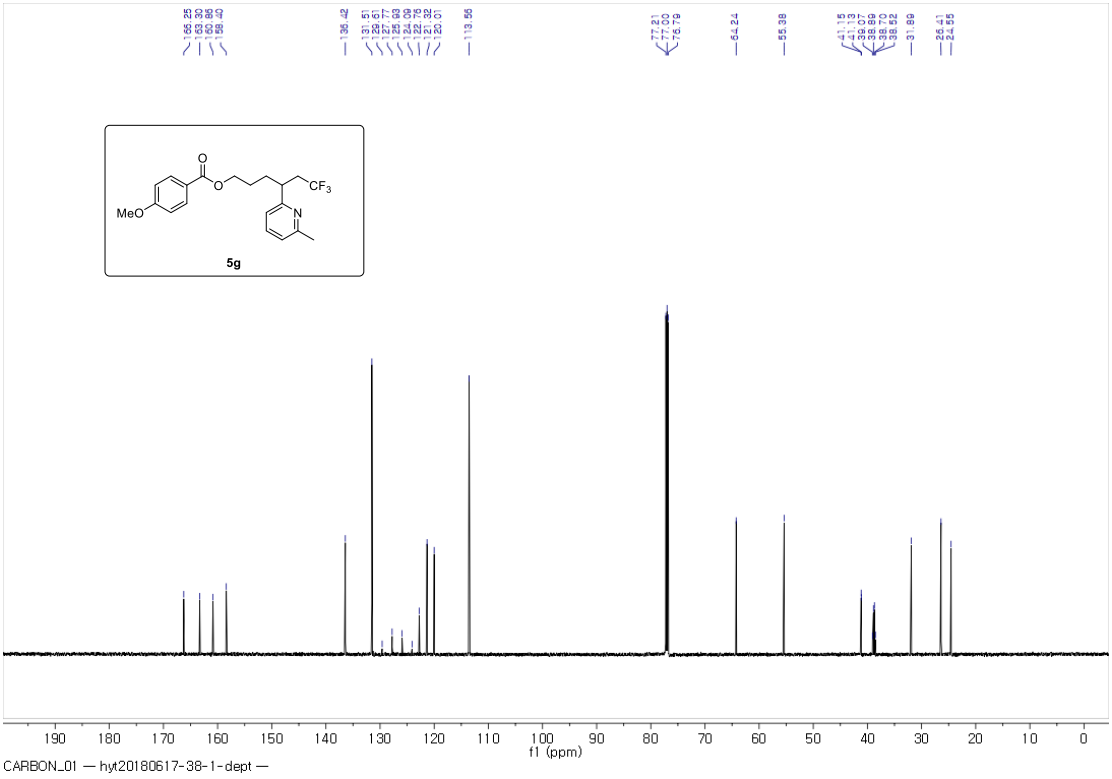


564 MHz, ^{19}F NMR in $CDCl_3$

6,6,6-trifluoro-4-(6-methylpyridin-2-yl)hexyl 4-methoxybenzoate (5g).



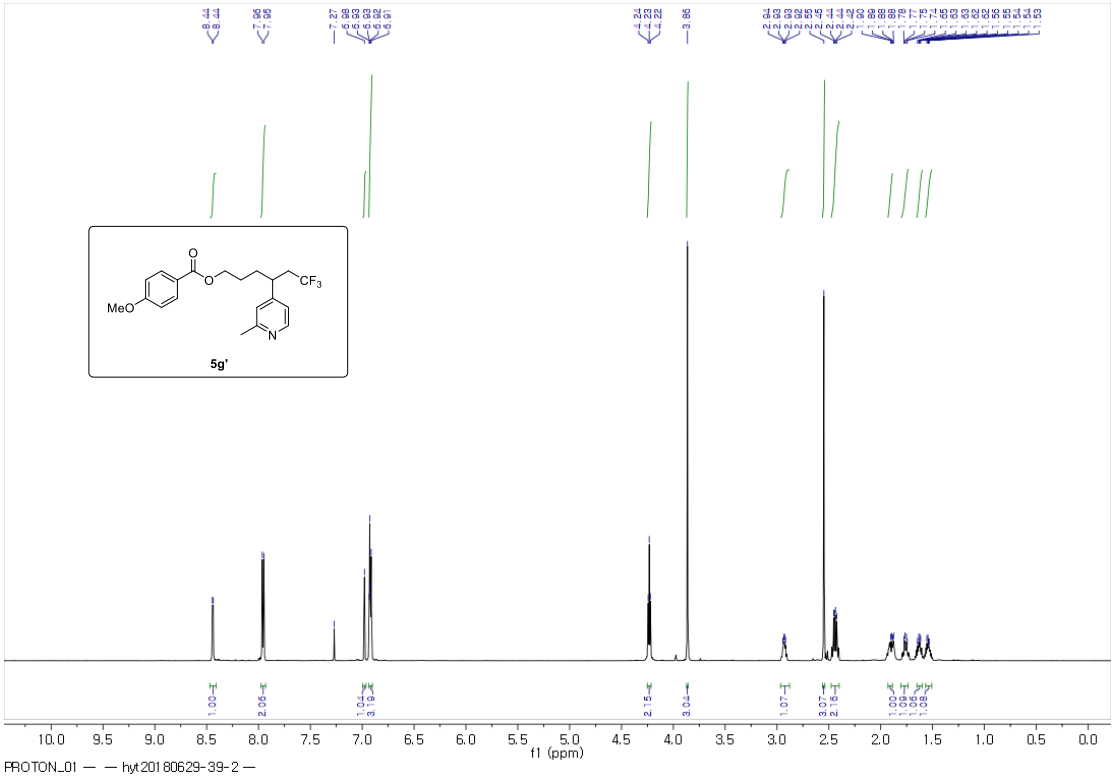
599 MHz, ^{1}H NMR in $CDCl_3$



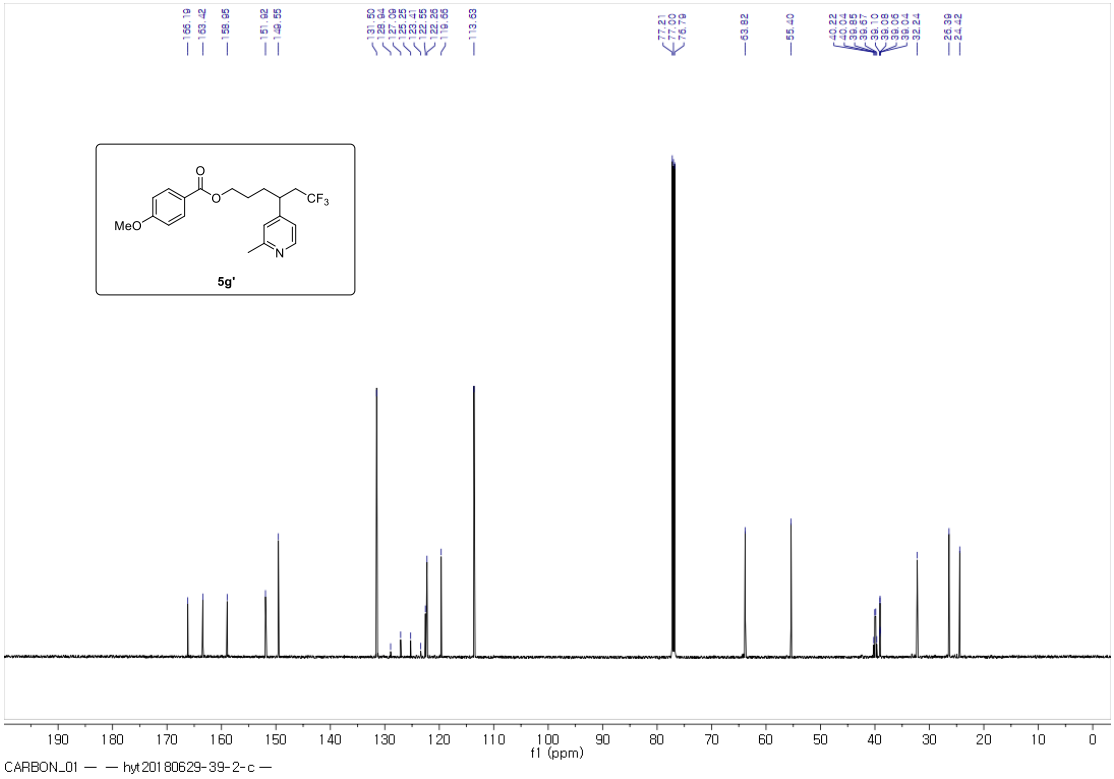
151 MHz, ^{13}C NMR in $CDCl_3$

564 MHz, ^{19}F NMR in $CDCl_3$

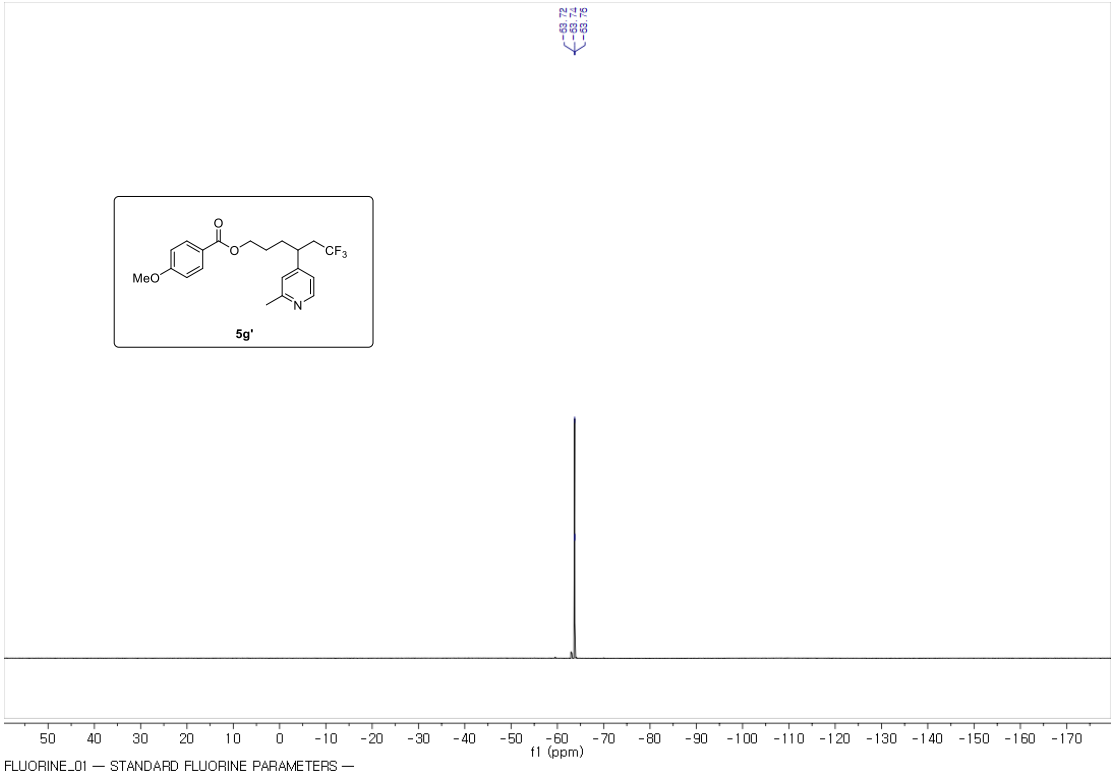
6,6,6-trifluoro-4-(2-methylpyridin-4-yl)hexyl 4-methoxybenzoate (5g').



599 MHz, ^{1}H NMR in $CDCl_3$

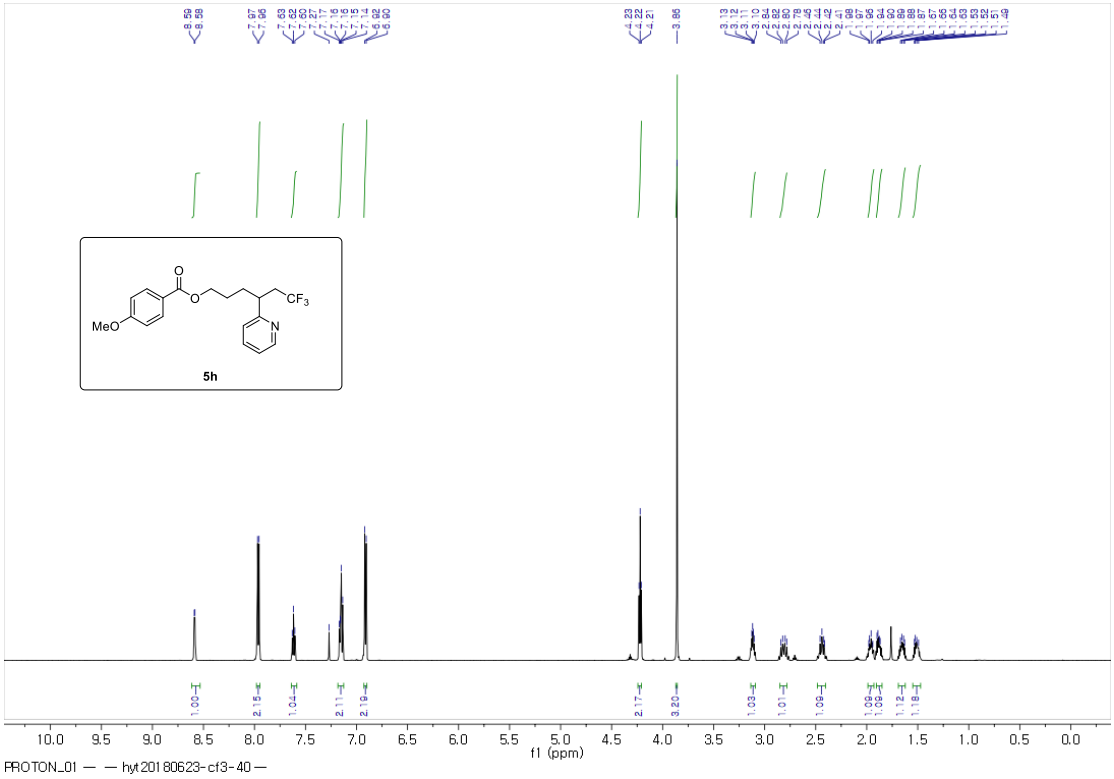


151 MHz, ^{13}C NMR in $CDCl_3$

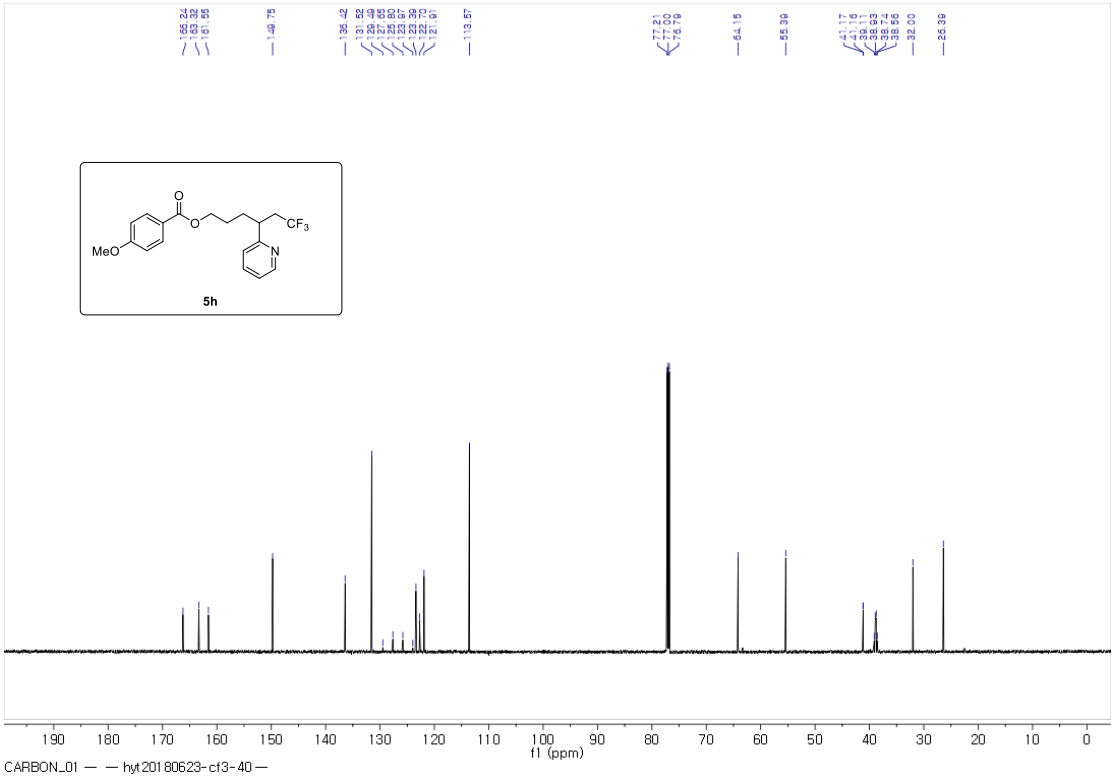


564 MHz, ^{19}F NMR in $CDCl_3$

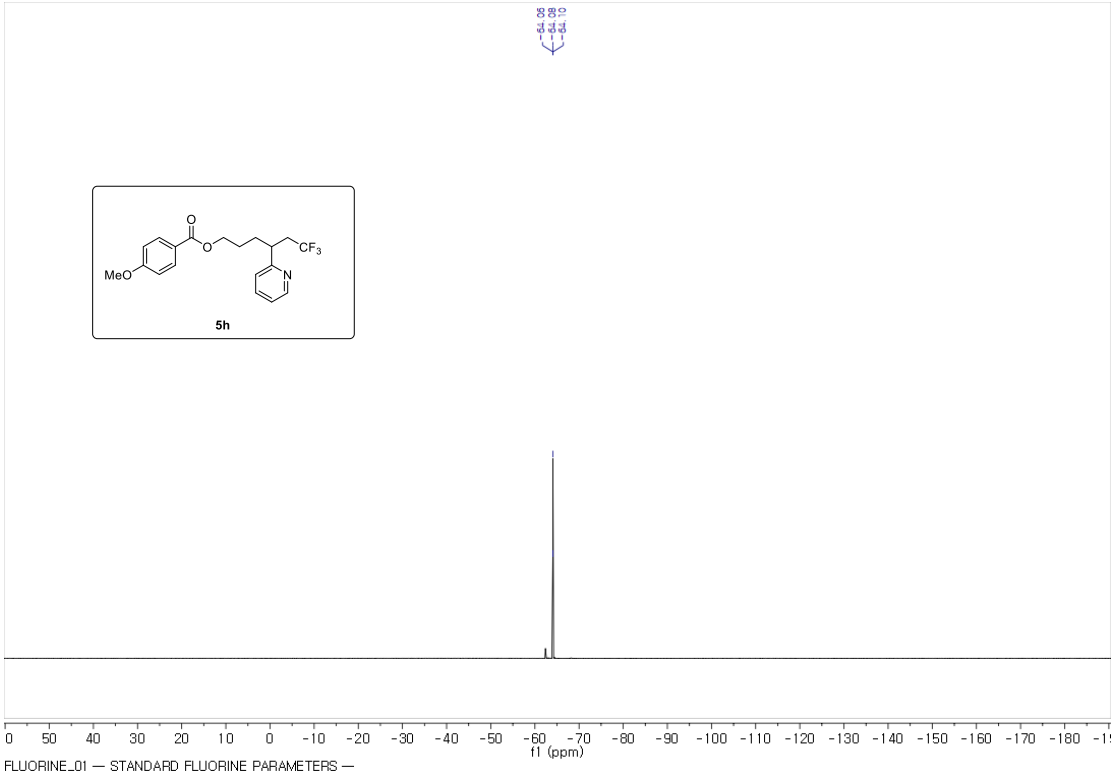
6,6,6-trifluoro-4-(pyridin-2-yl)hexyl 4-methoxybenzoate (5h).



599 MHz, ^{1}H NMR in $CDCl_3$

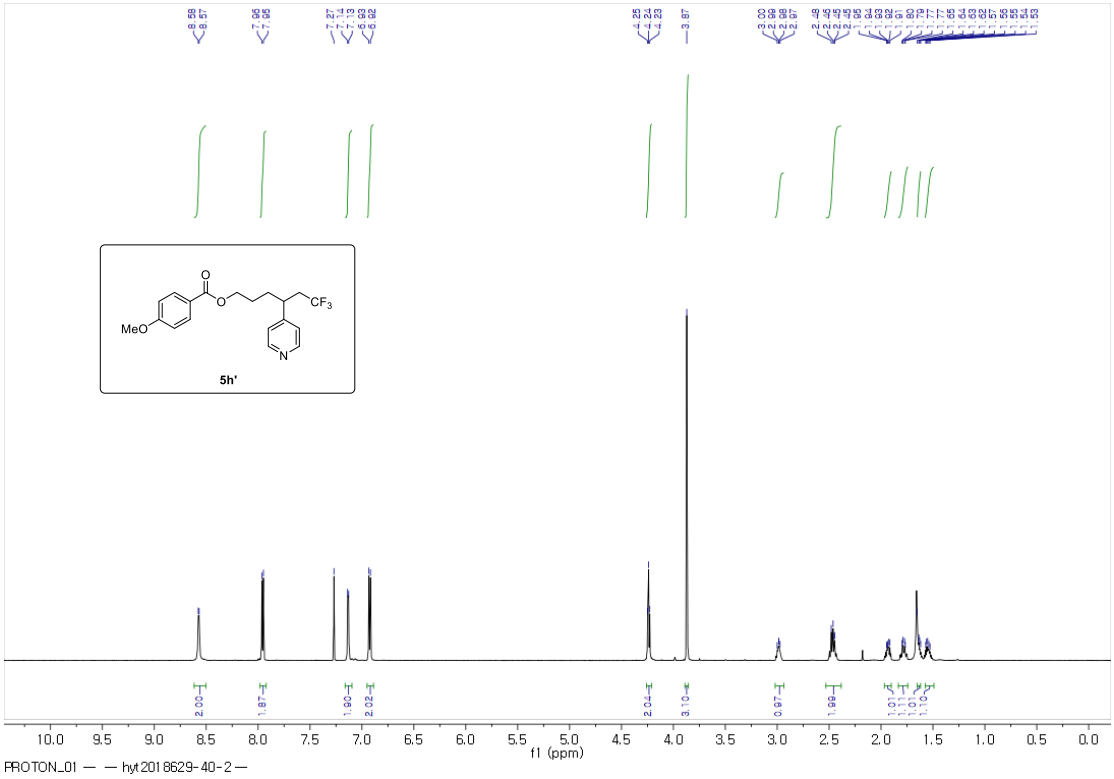


151 MHz, ^{13}C NMR in $CDCl_3$

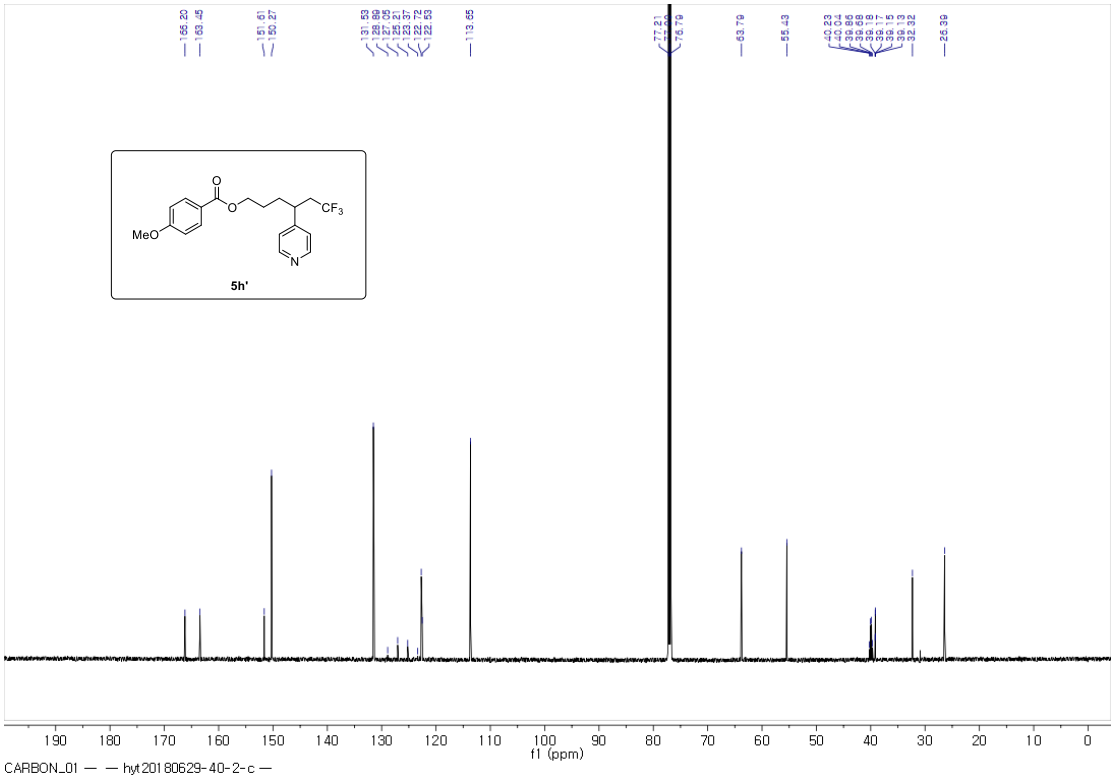


564 MHz, ^{19}F NMR in $CDCl_3$

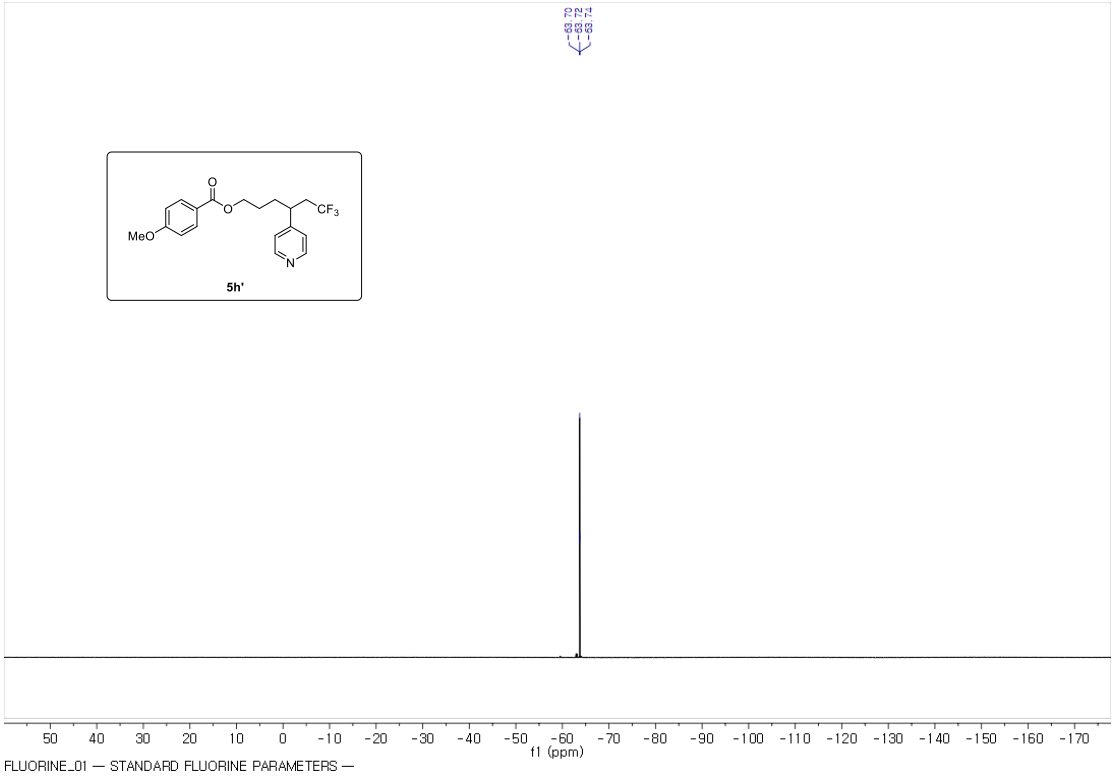
6,6,6-trifluoro-4-(pyridin-4-yl)hexyl 4-methoxybenzoate (5h').



599 MHz, ^{1}H NMR in $CDCl_3$

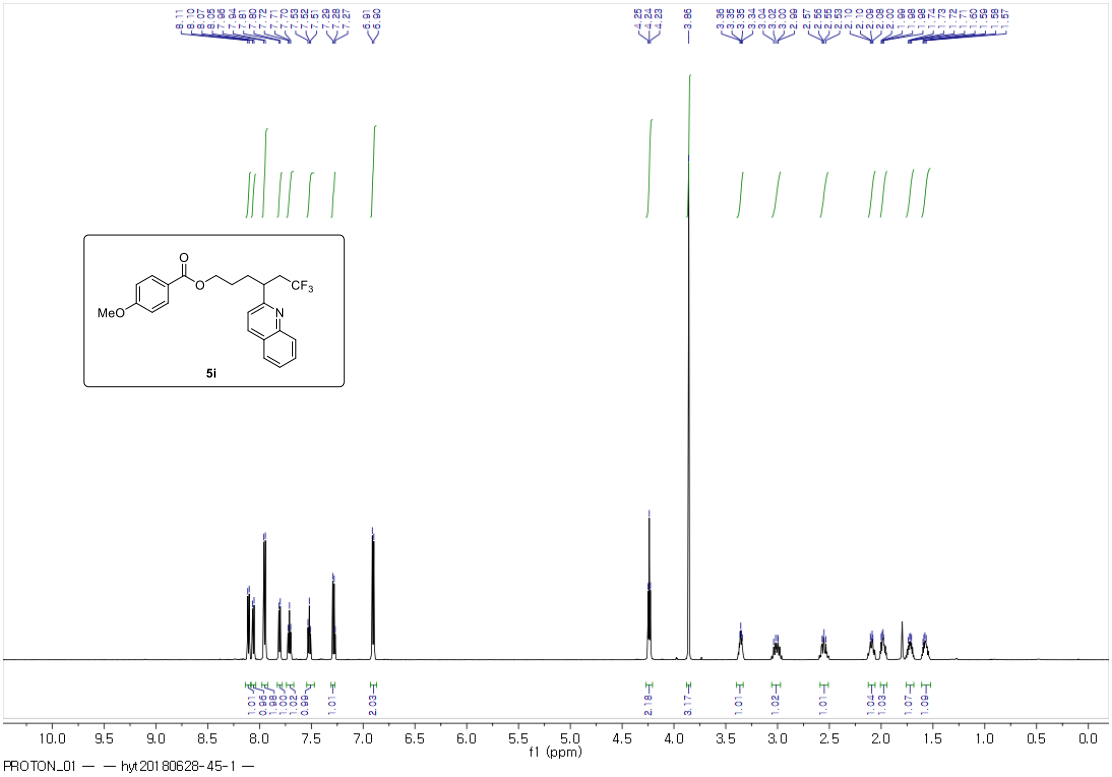


151 MHz, ^{13}C NMR in $CDCl_3$

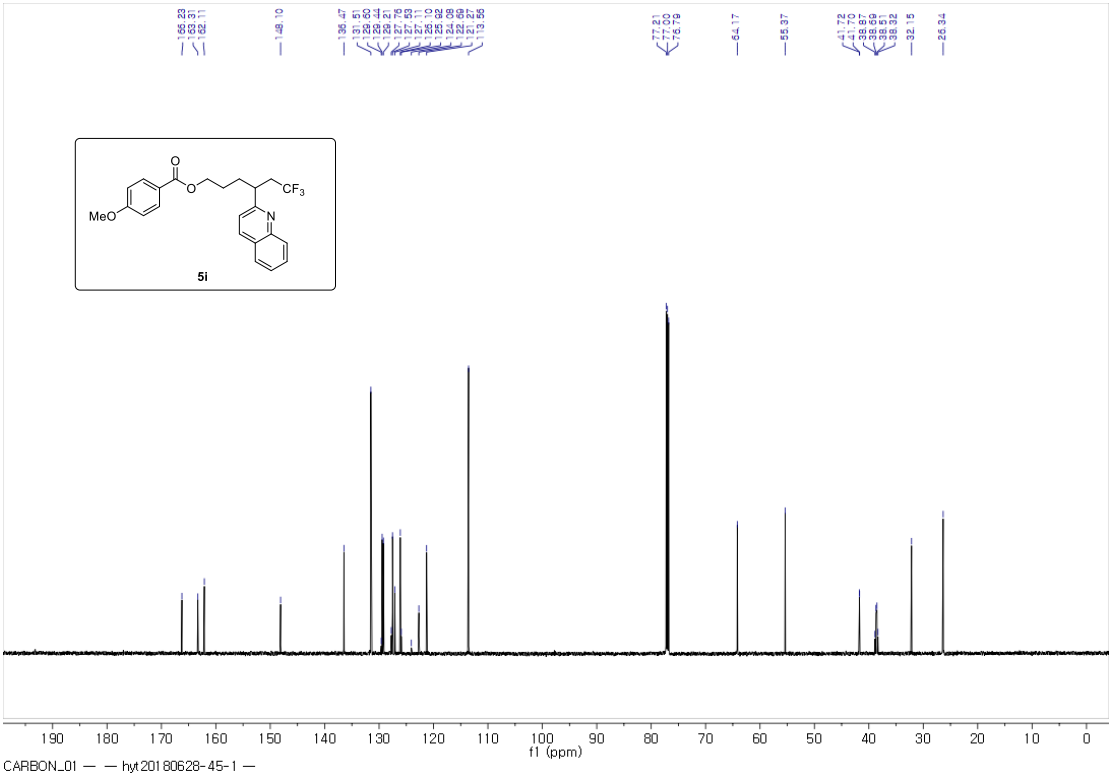


564 MHz, ^{19}F NMR in $CDCl_3$

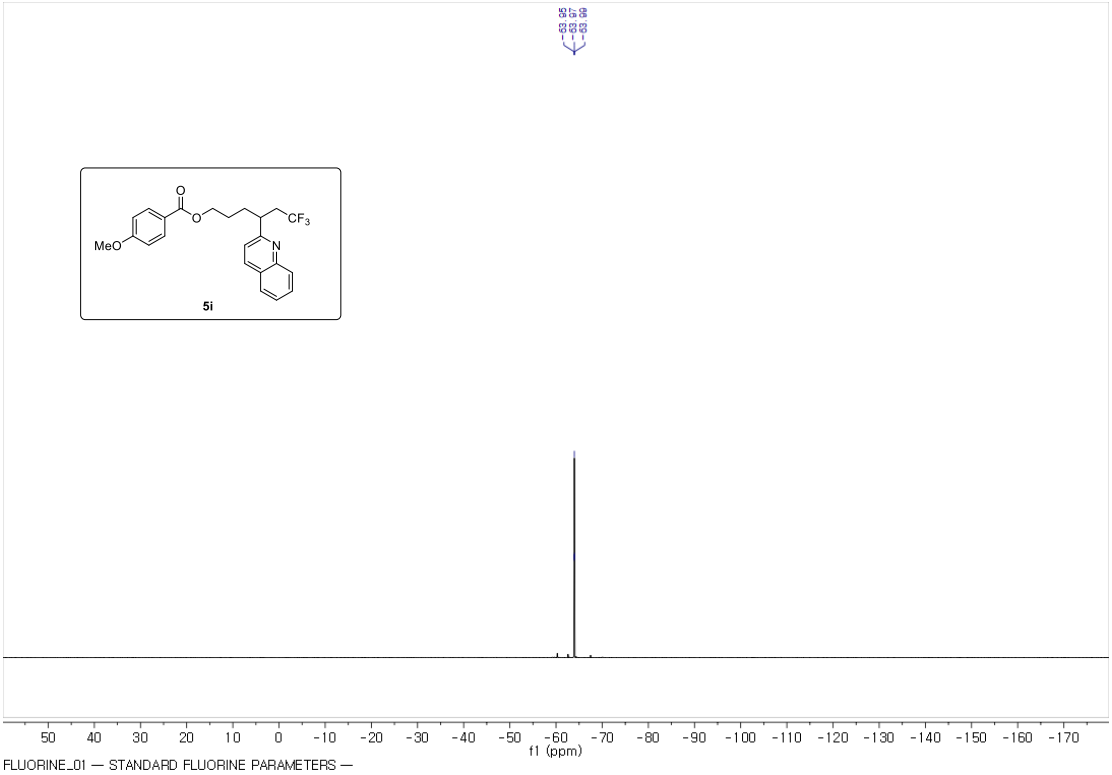
6,6,6-trifluoro-4-(quinolin-2-yl)hexyl 4-methoxybenzoate (5i).



599 MHz, ^{1}H NMR in $CDCl_3$

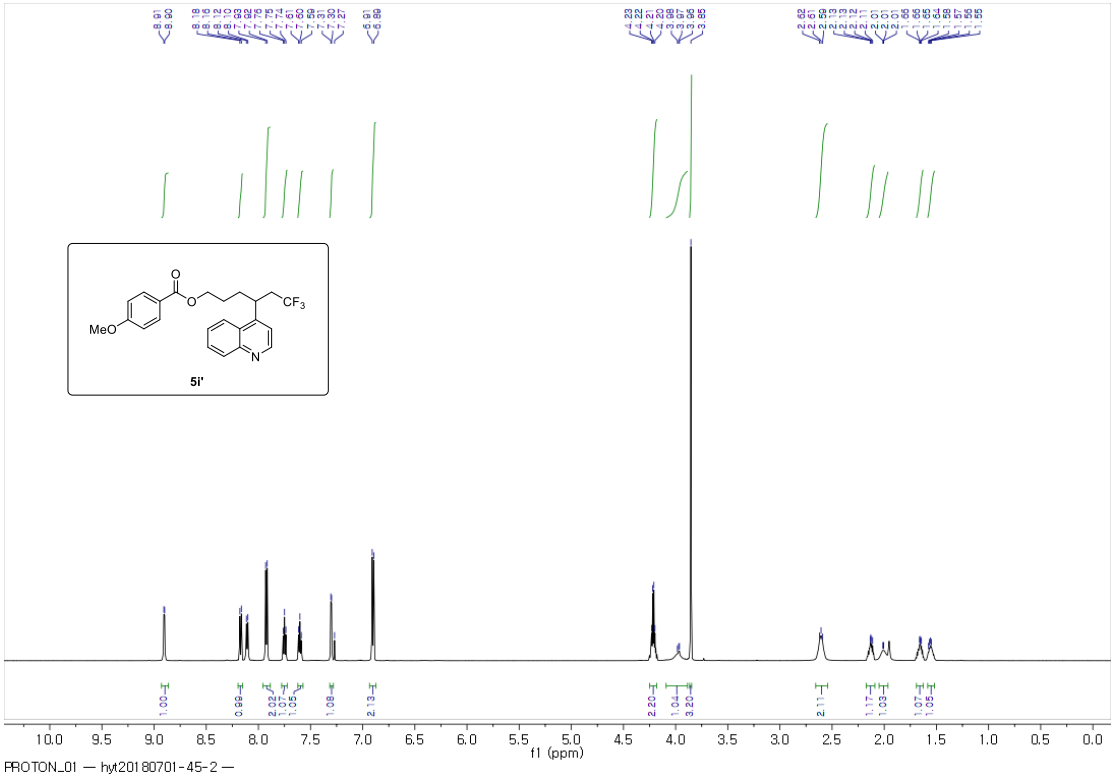


151 MHz, ^{13}C NMR in $CDCl_3$

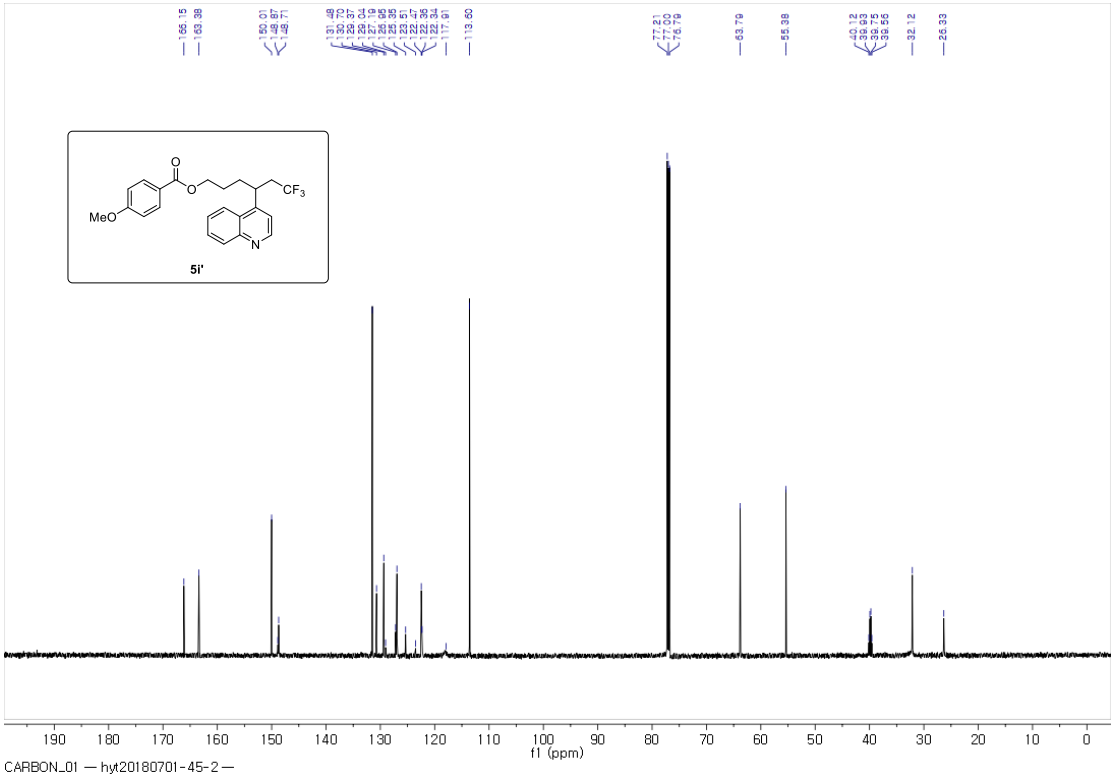


564 MHz, ^{19}F NMR in $CDCl_3$

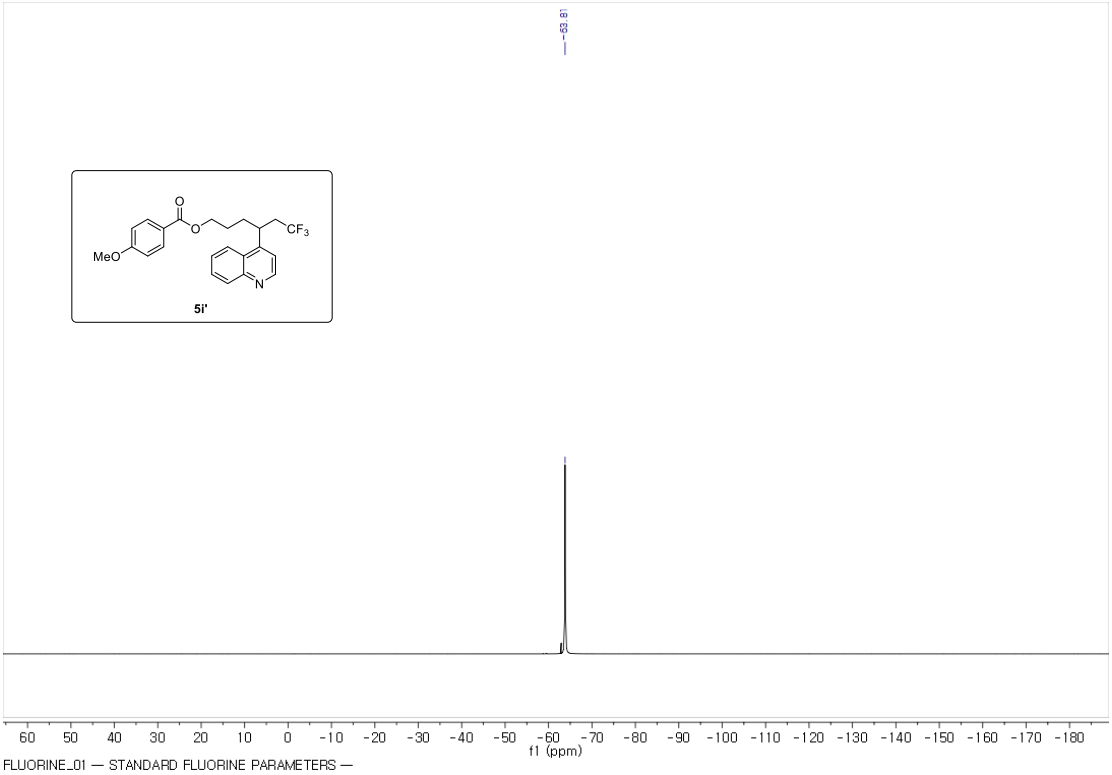
6,6,6-trifluoro-4-(quinolin-4-yl)hexyl 4-methoxybenzoate (5i').



599 MHz, ^{1}H NMR in $CDCl_3$

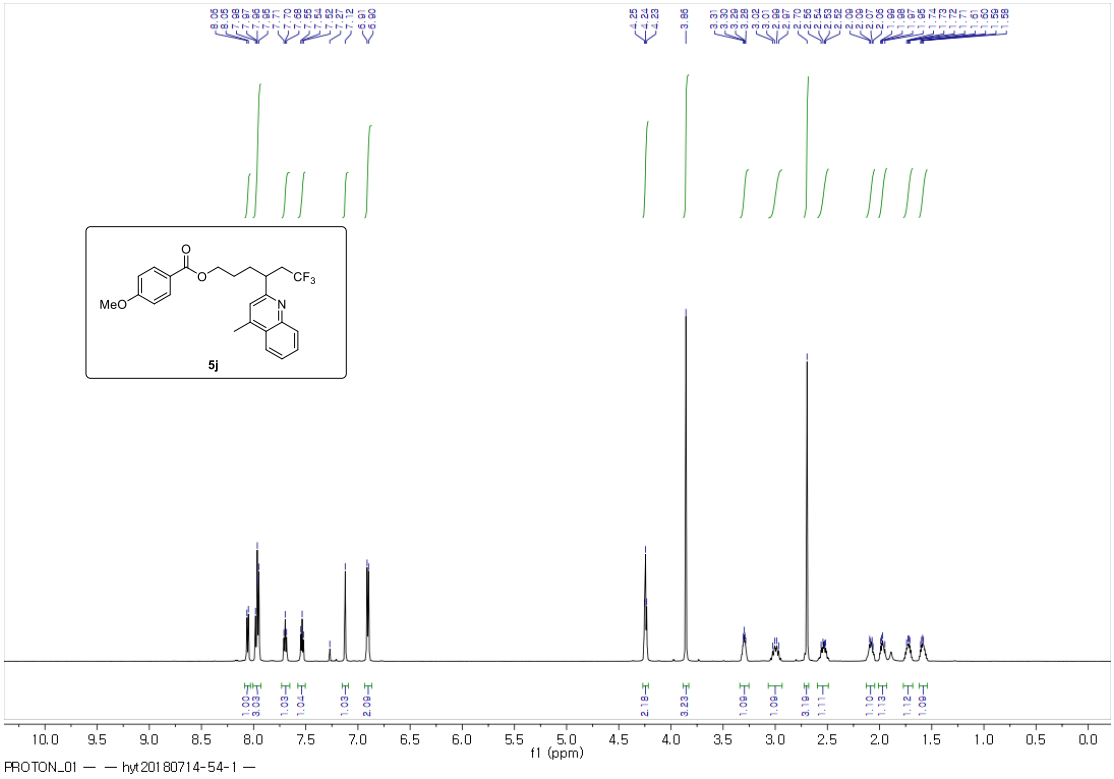


151 MHz, ^{13}C NMR in $CDCl_3$

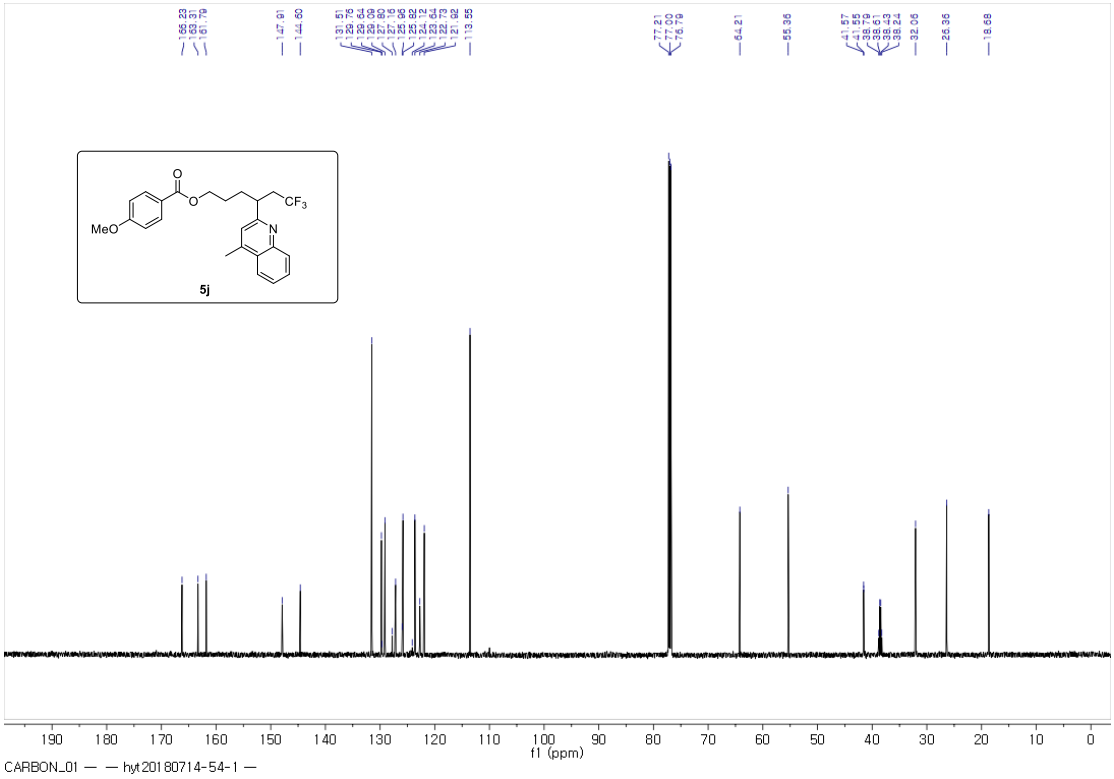


564 MHz, ^{19}F NMR in $CDCl_3$

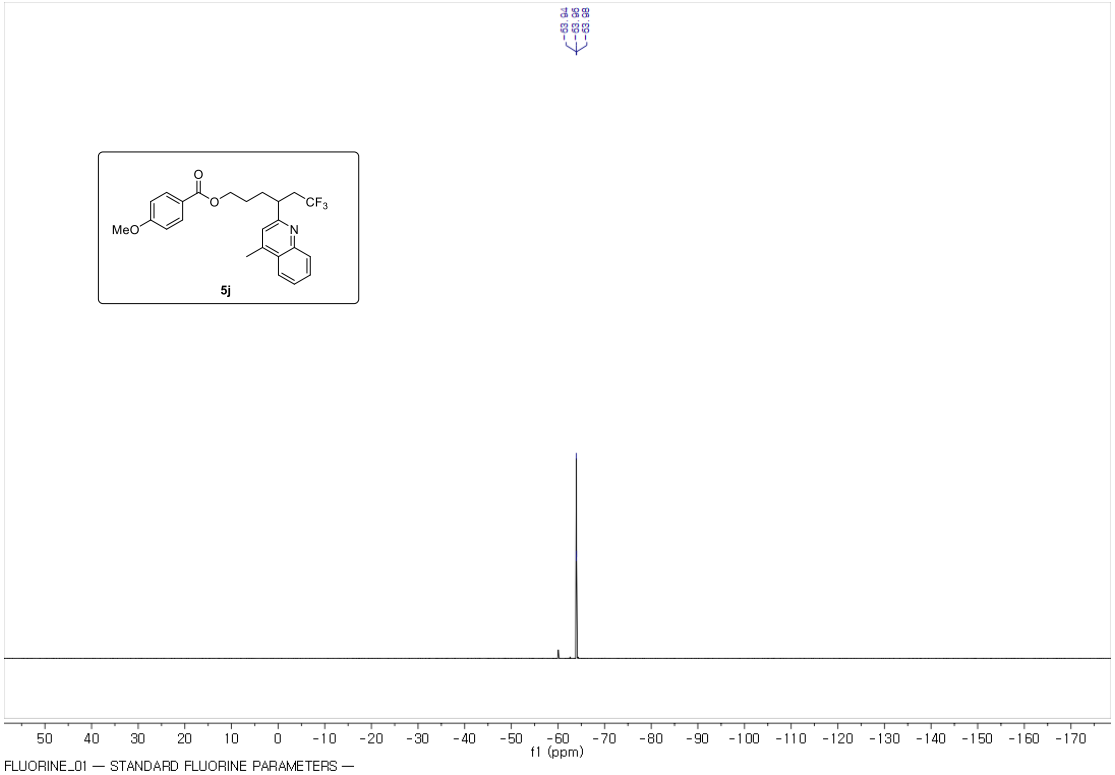
6,6,6-trifluoro-4-(4-methylquinolin-2-yl)hexyl 4-methoxybenzoate (5j).



599 MHz, ^{1}H NMR in $CDCl_3$

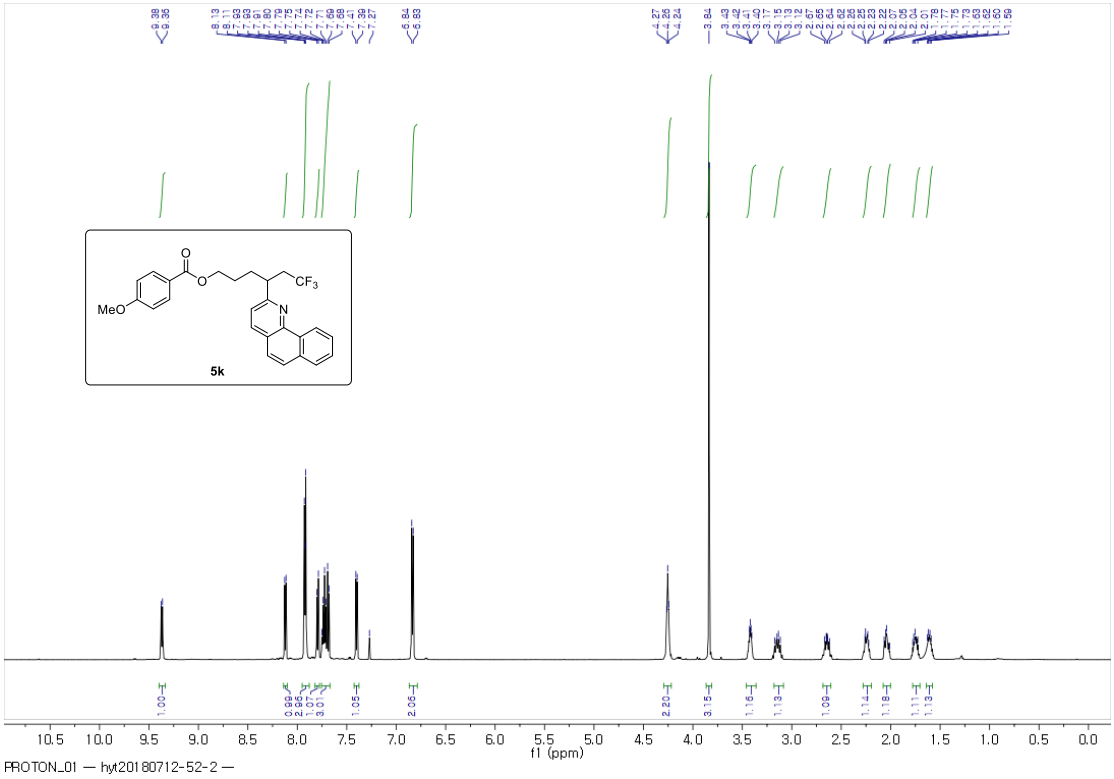


151 MHz, ^{13}C NMR in $CDCl_3$

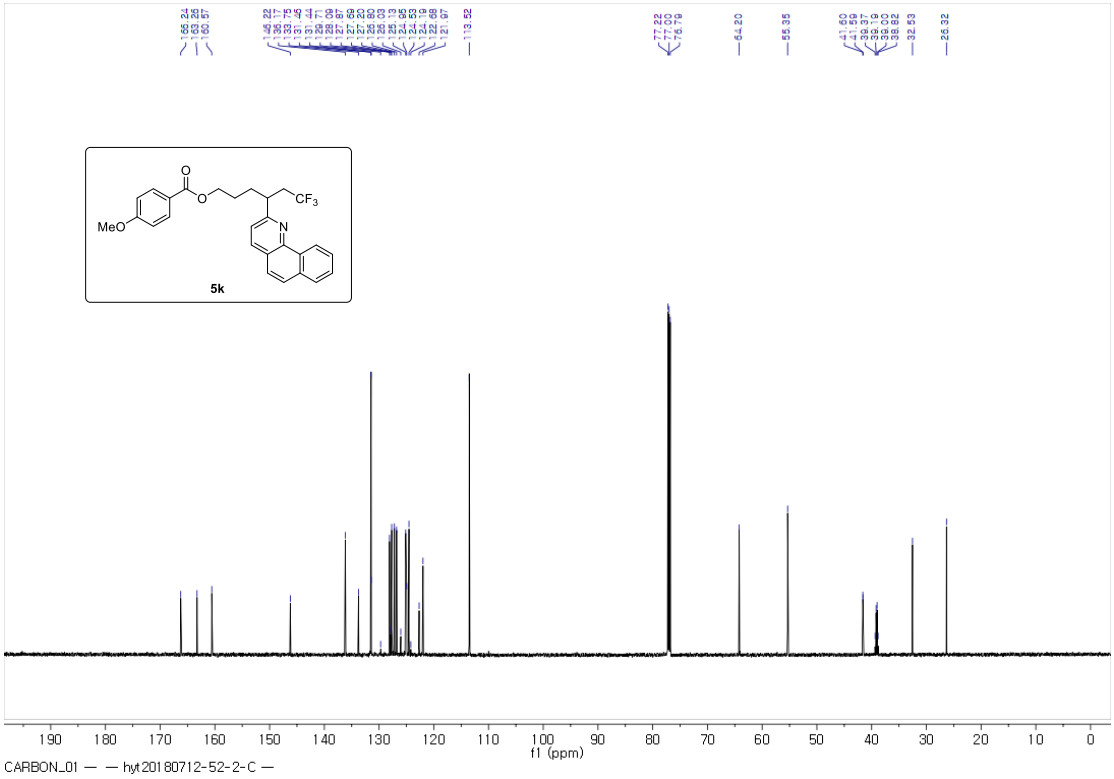


564 MHz, ^{19}F NMR in $CDCl_3$

4-(benzo[h]quinolin-2-yl)-6,6,6-trifluorohexyl 4-methoxybenzoate (5k).



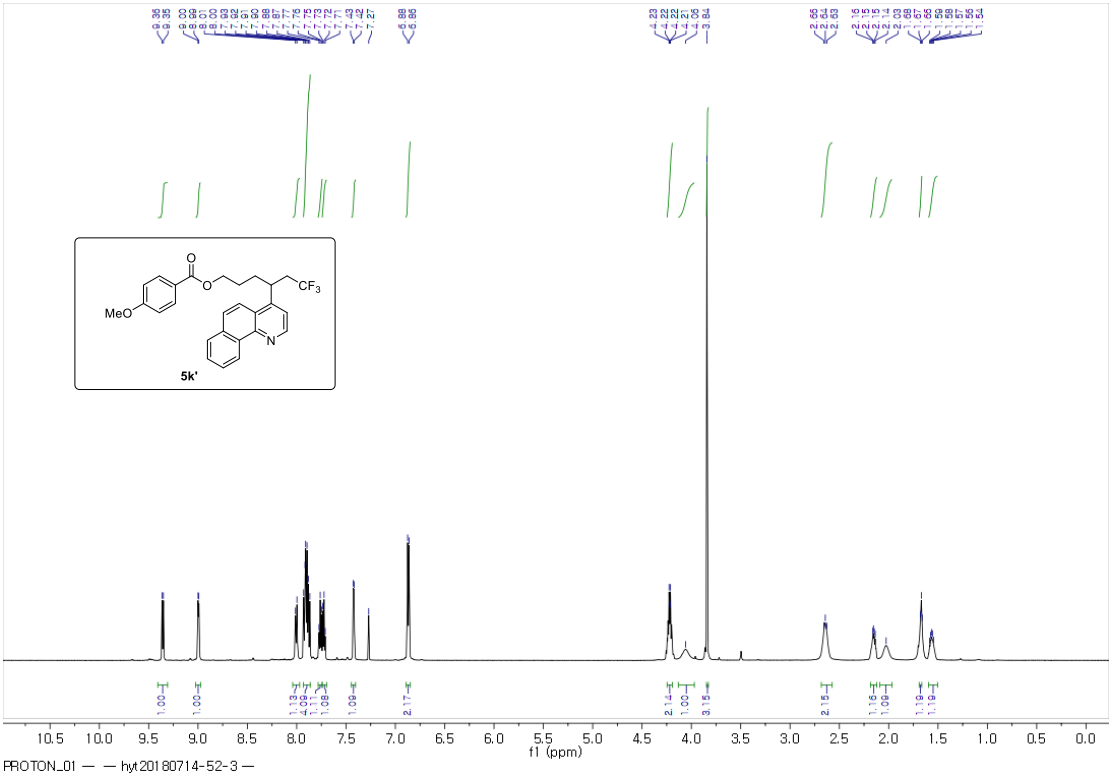
599 MHz, ^{1}H NMR in $CDCl_3$



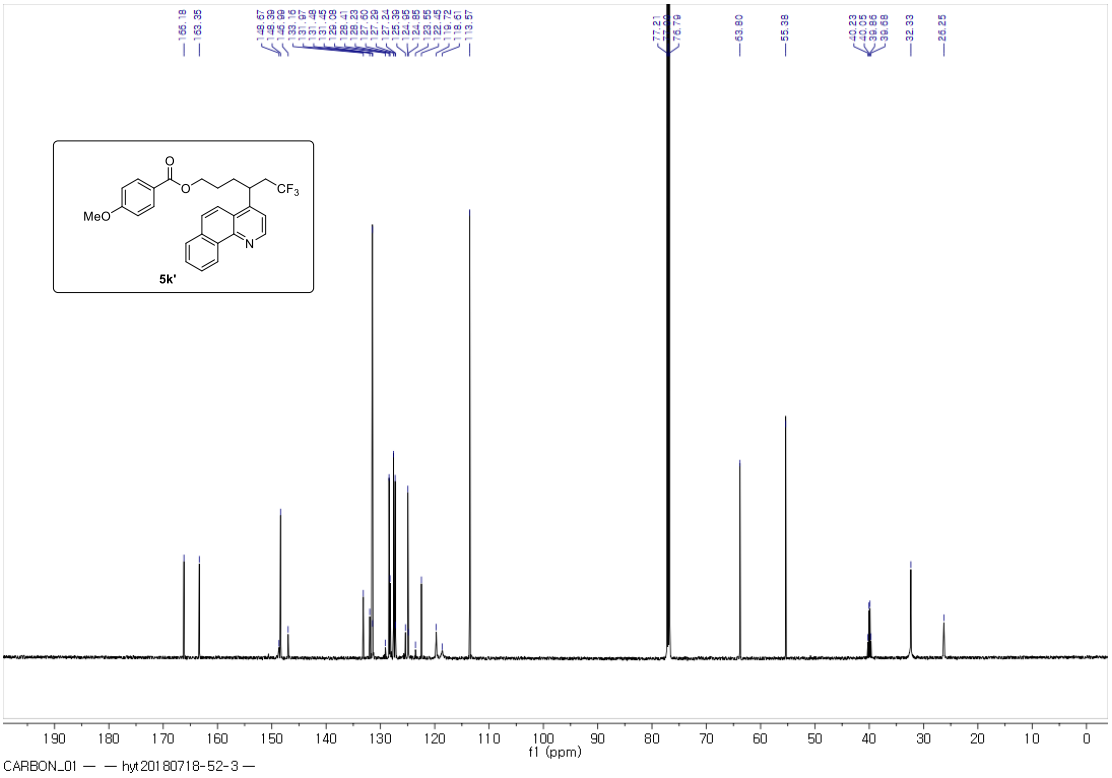
151 MHz, ^{13}C NMR in $CDCl_3$

564 MHz, ^{19}F NMR in $CDCl_3$

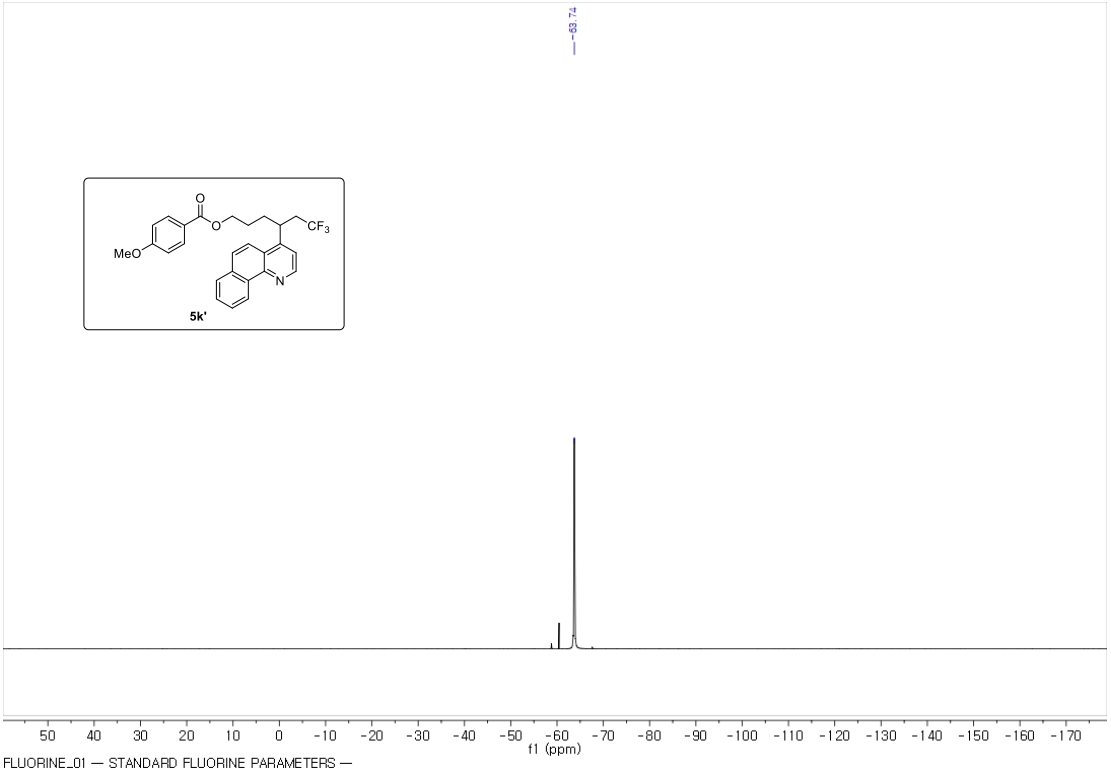
4-(benzo[h]quinolin-4-yl)-6,6,6-trifluorohexyl 4-methoxybenzoate (5k').



599 MHz, ^{1}H NMR in $CDCl_3$

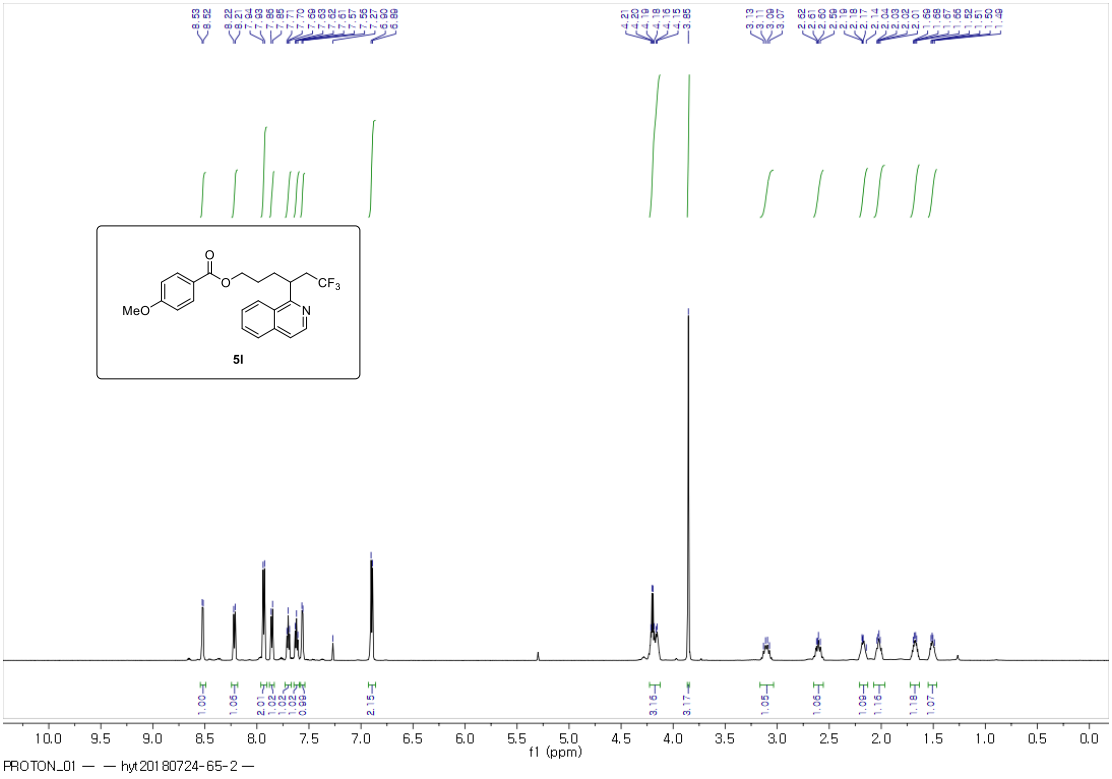


151 MHz, ^{13}C NMR in $CDCl_3$

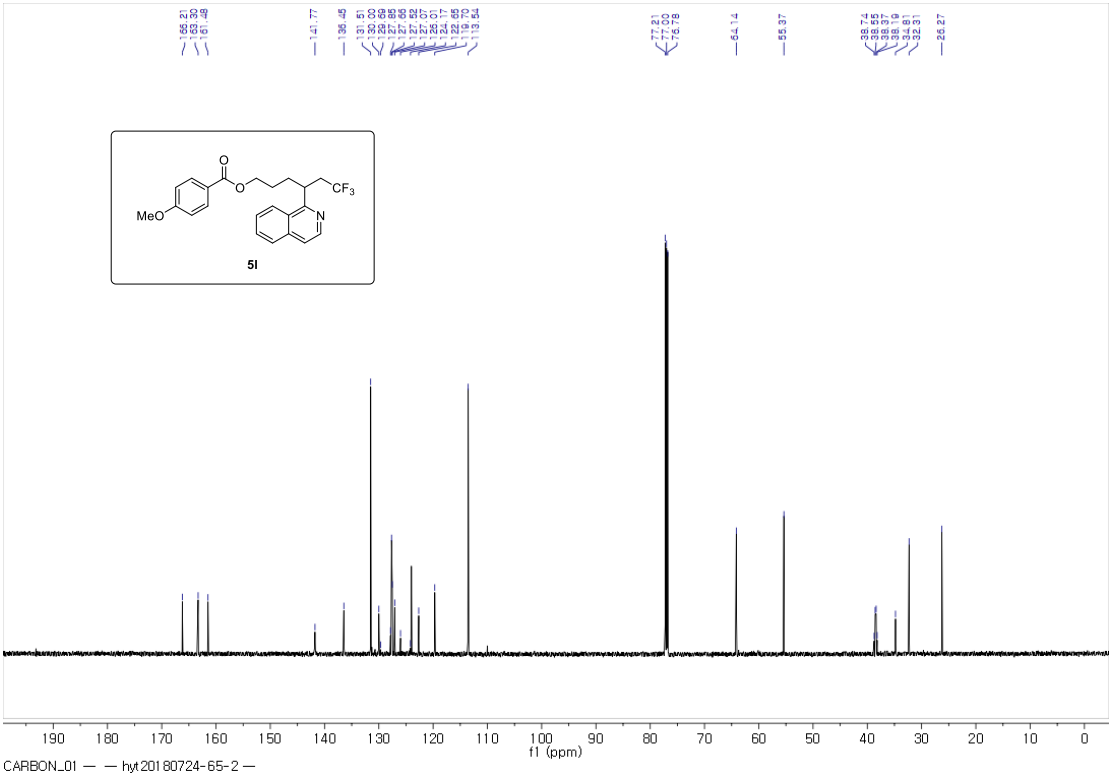


564 MHz, ^{19}F NMR in $CDCl_3$

6,6,6-trifluoro-4-(isoquinolin-1-yl)hexyl 4-methoxybenzoate (5l).



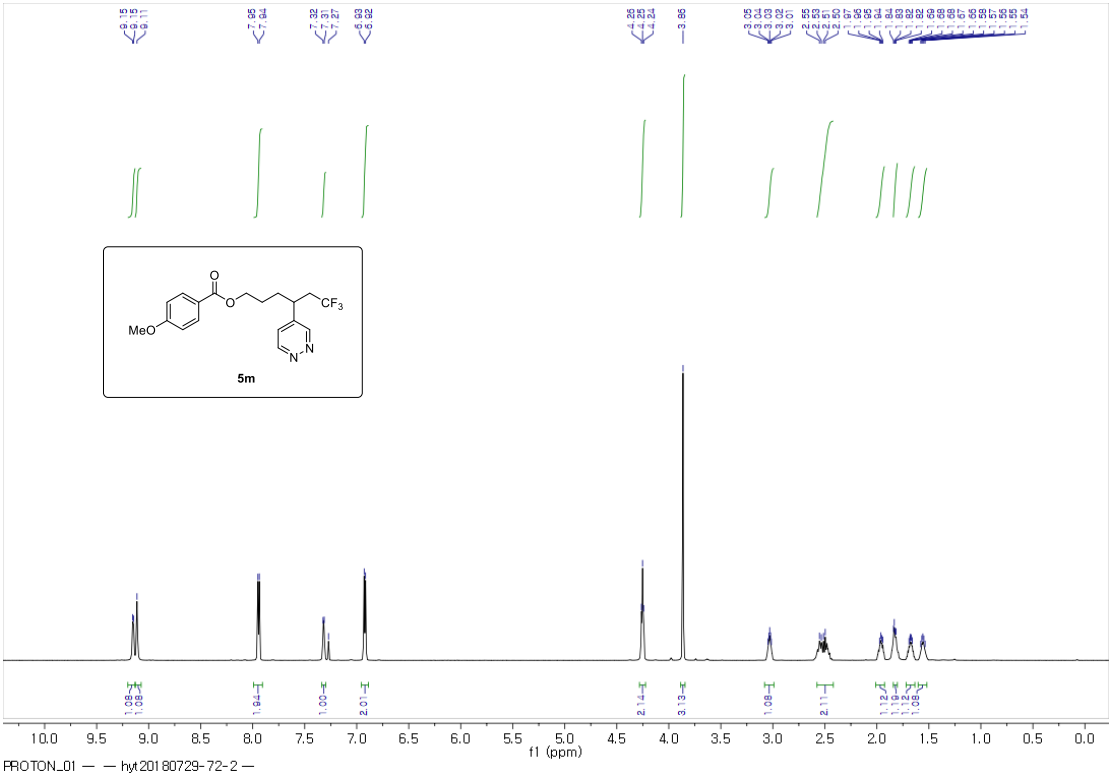
599 MHz, ^{1}H NMR in $CDCl_3$



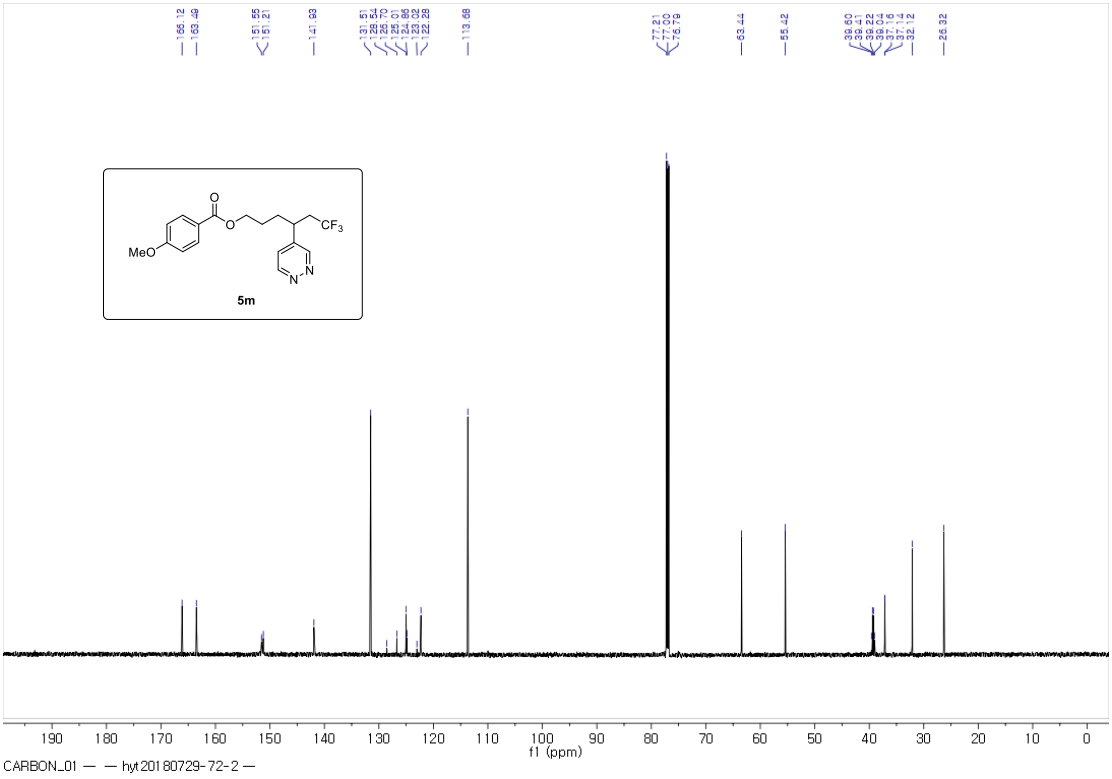
151 MHz, ^{13}C NMR in $CDCl_3$

564 MHz, ^{19}F NMR in $CDCl_3$

6,6,6-trifluoro-4-(pyridazin-4-yl)hexyl 4-methoxybenzoate (5m).



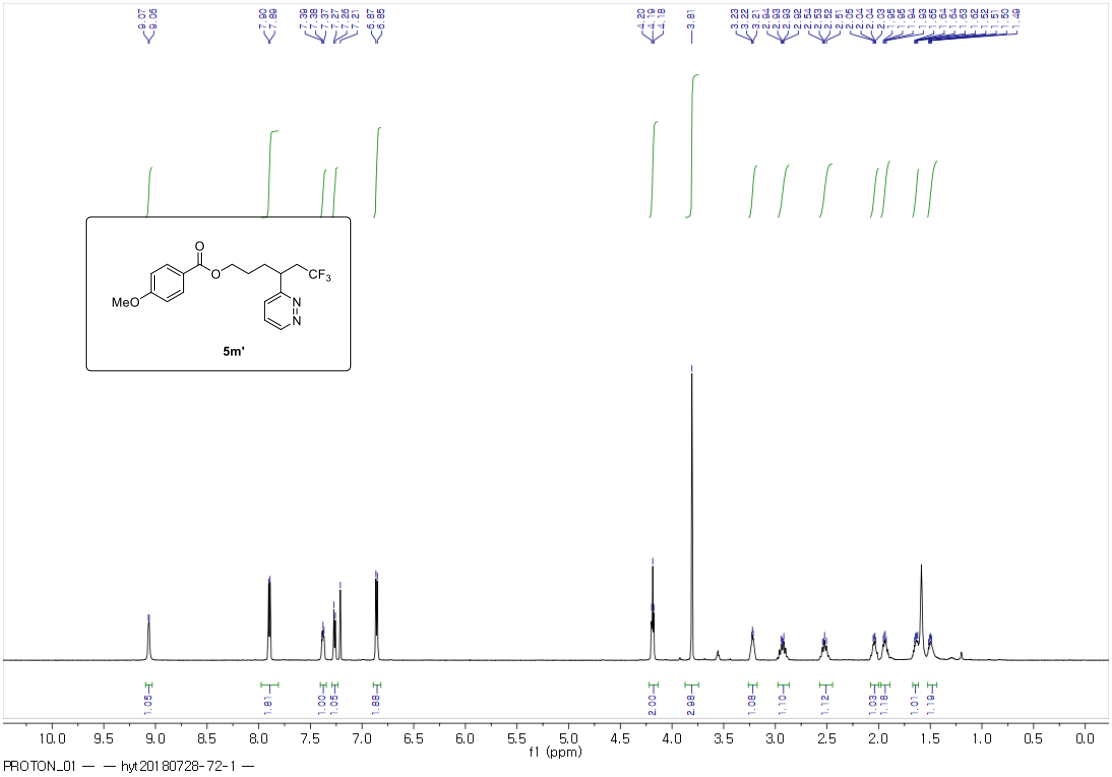
599 MHz, ^{1}H NMR in $CDCl_3$



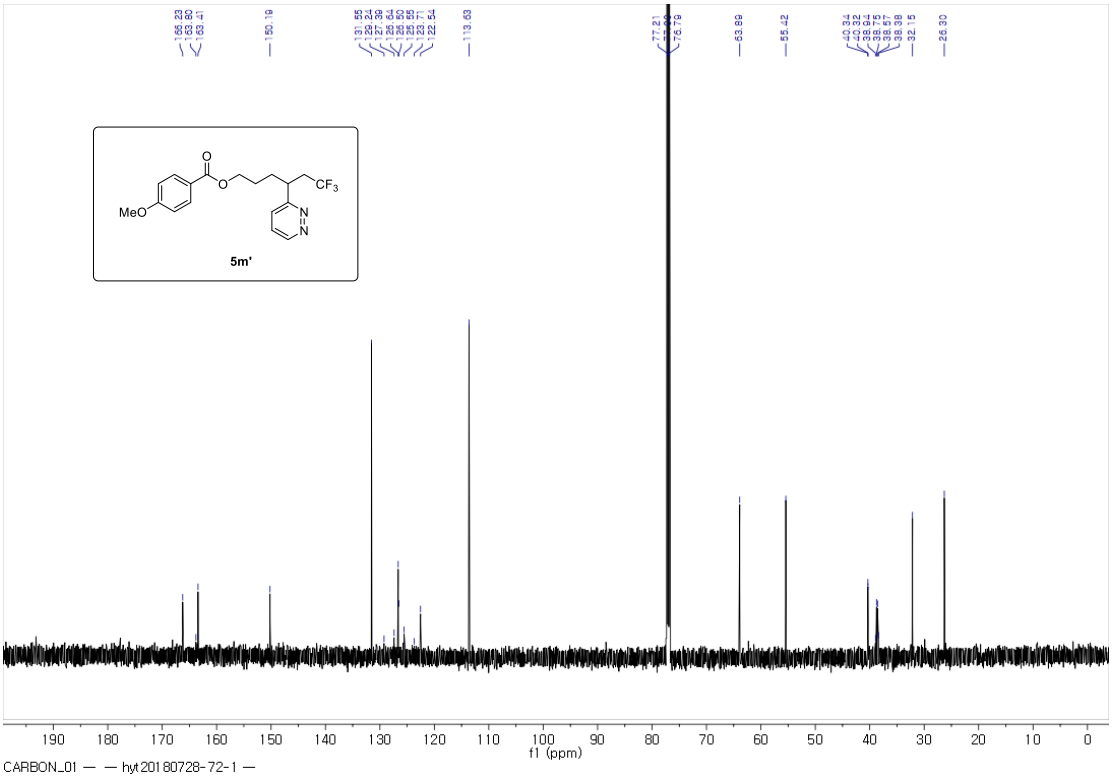
151 MHz, ^{13}C NMR in $CDCl_3$

564 MHz, ^{19}F NMR in $CDCl_3$

6,6,6-trifluoro-4-(pyridazin-3-yl)hexyl 4-methoxybenzoate (5m').



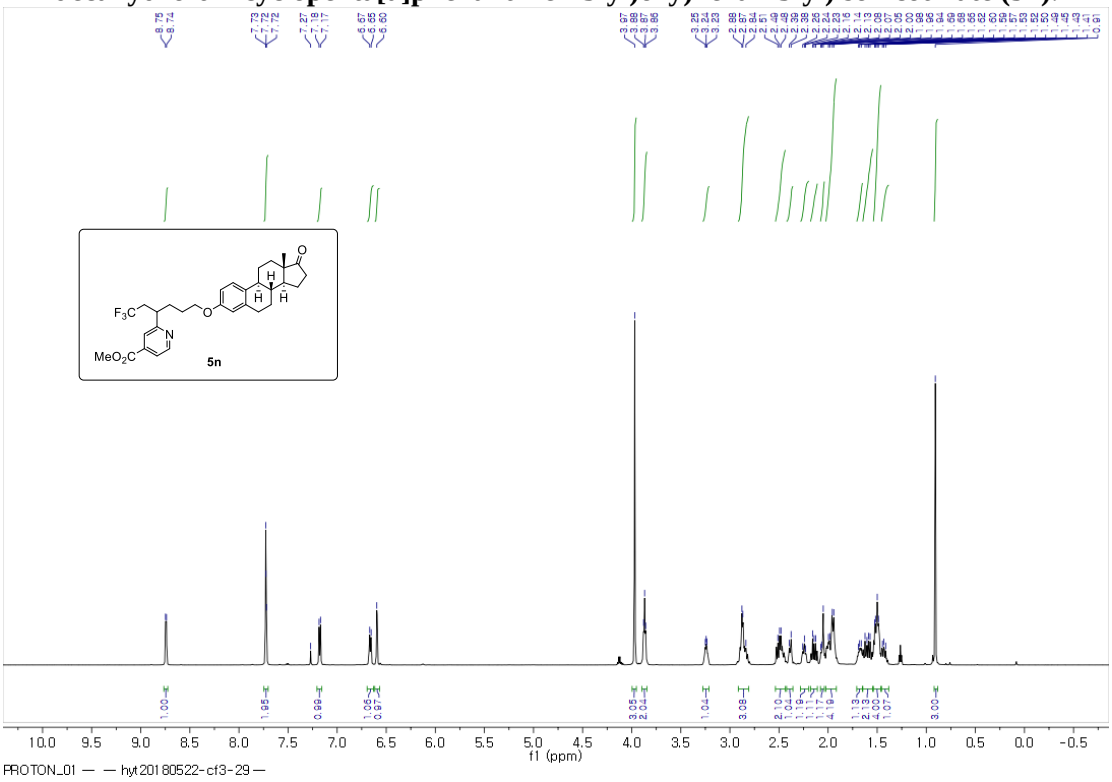
599 MHz, ^{1}H NMR in $CDCl_3$



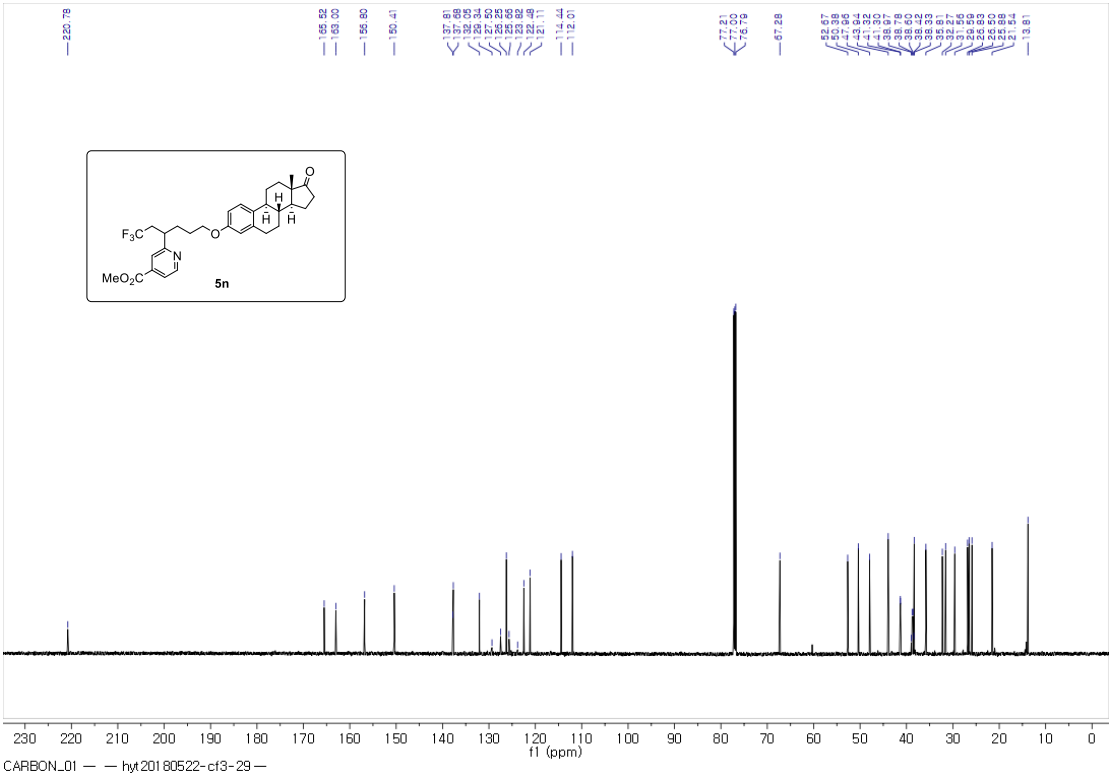
151 MHz, ^{13}C NMR in $CDCl_3$

564 MHz, ^{19}F NMR in $CDCl_3$

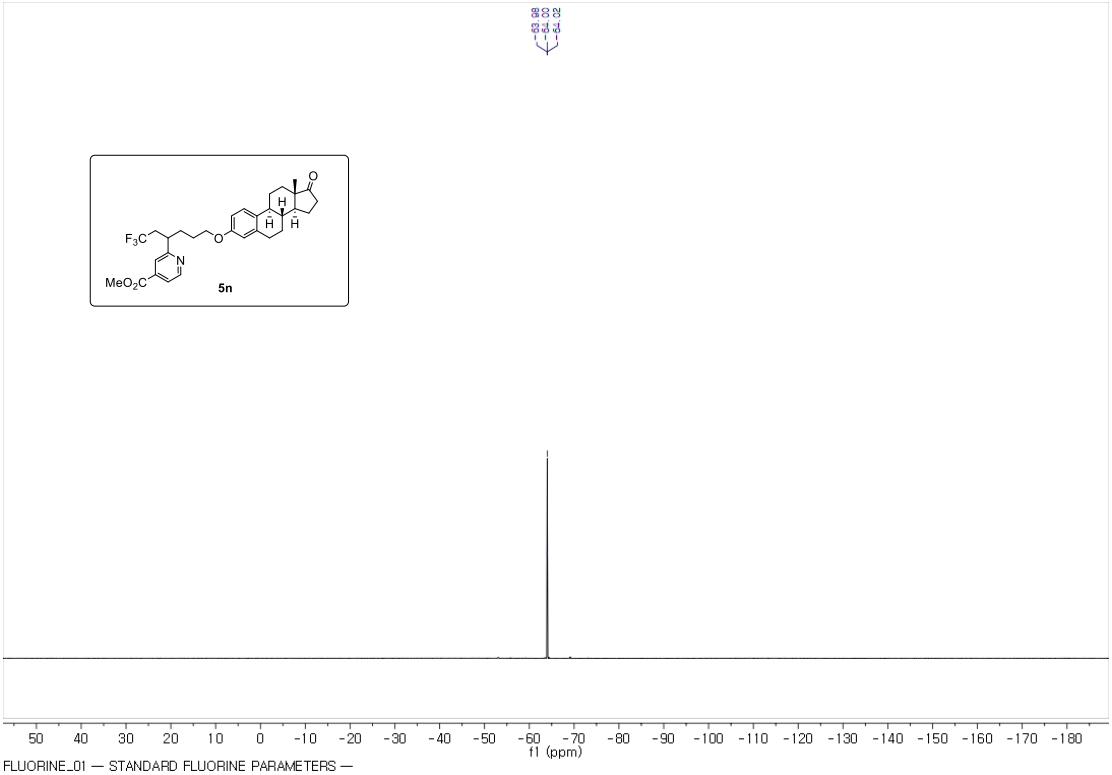
methyl 2-(1,1,1-trifluoro-6-(((8R,9S,13S,14S)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-3-yl)oxy)hexan-3-yl)isonicotinate (5n).



599 MHz, ^{1}H NMR in $CDCl_3$

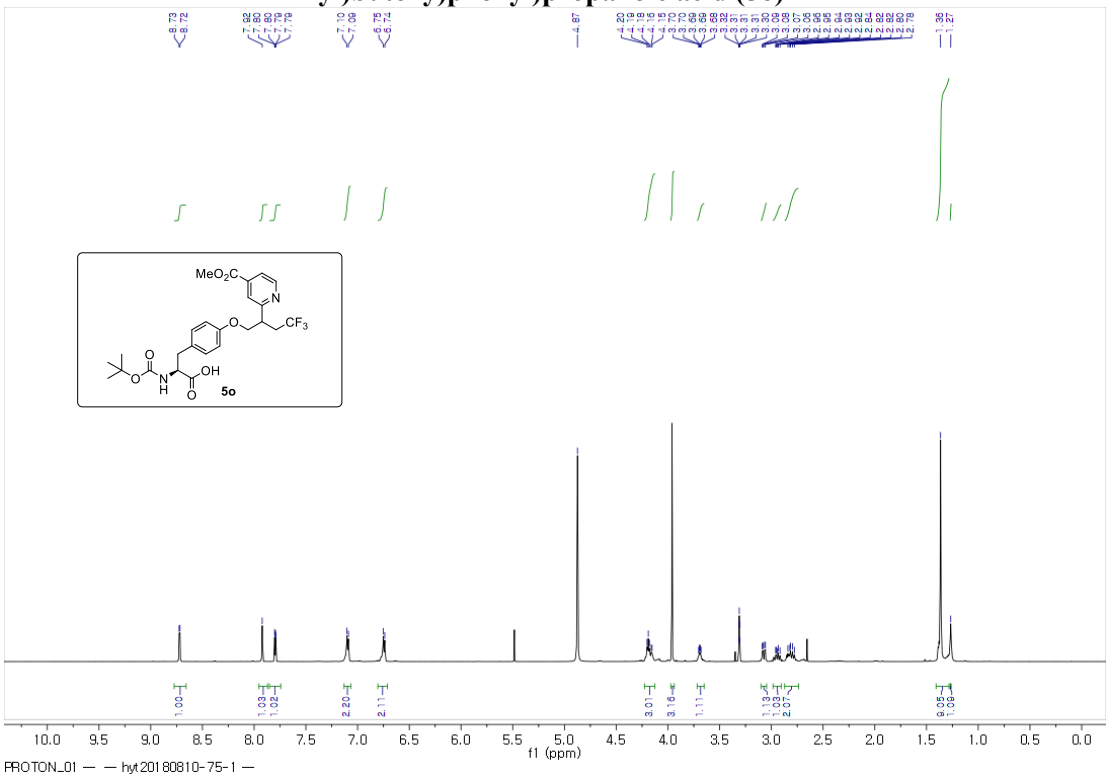


151 MHz, ^{13}C NMR in $CDCl_3$

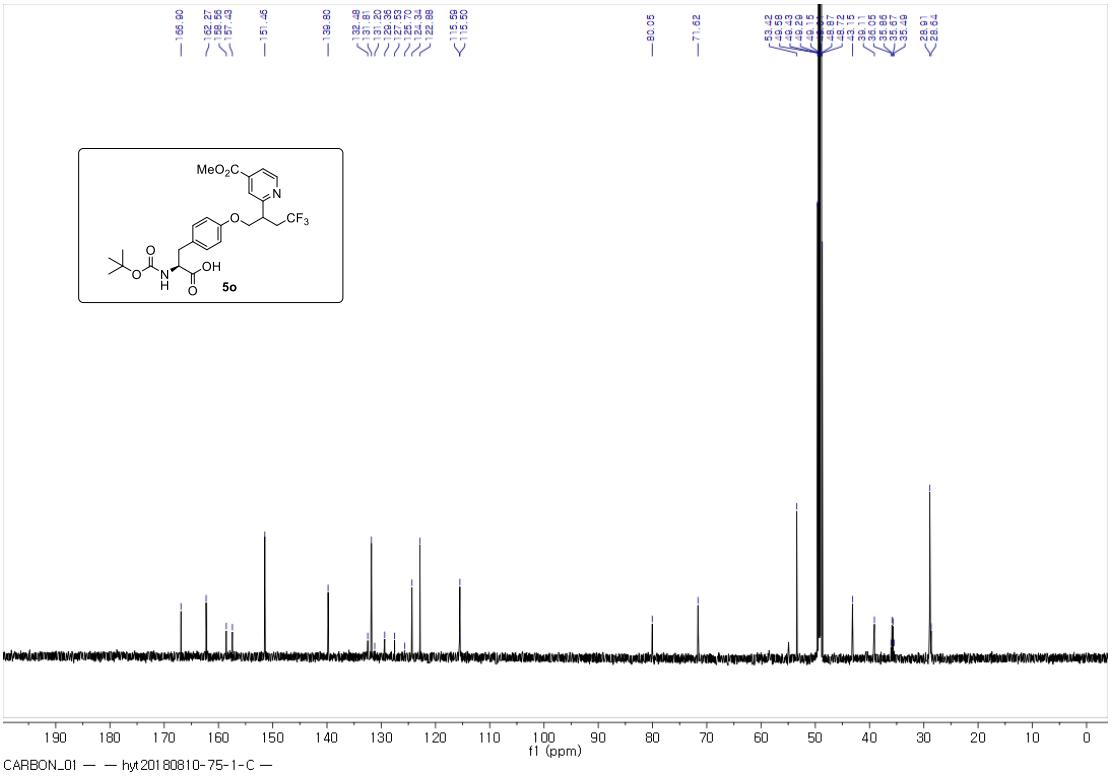


564 MHz, ^{19}F NMR in $CDCl_3$

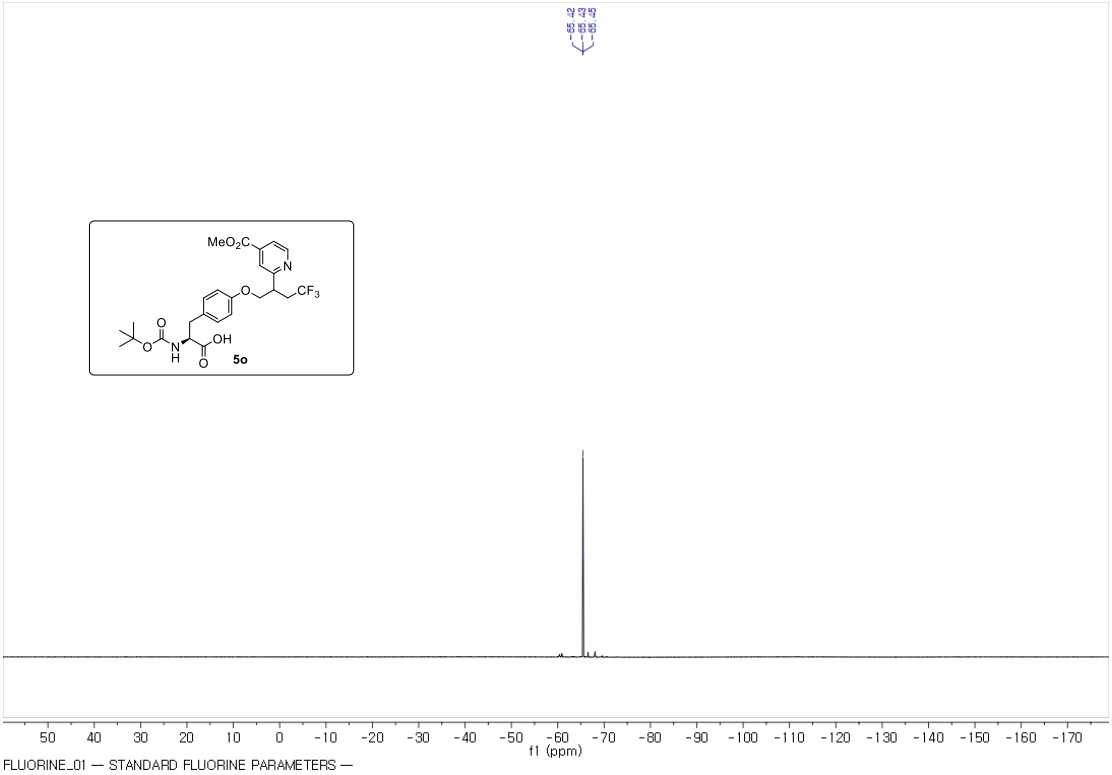
(2S)-2-((tert-butoxycarbonyl)amino)-3-(4-(4,4,4-trifluoro-2-(4-(methoxycarbonyl)pyridin-2-yl)butoxy)phenyl)propanoic acid (5o).



599 MHz, ^{1}H NMR in $CDCl_3$

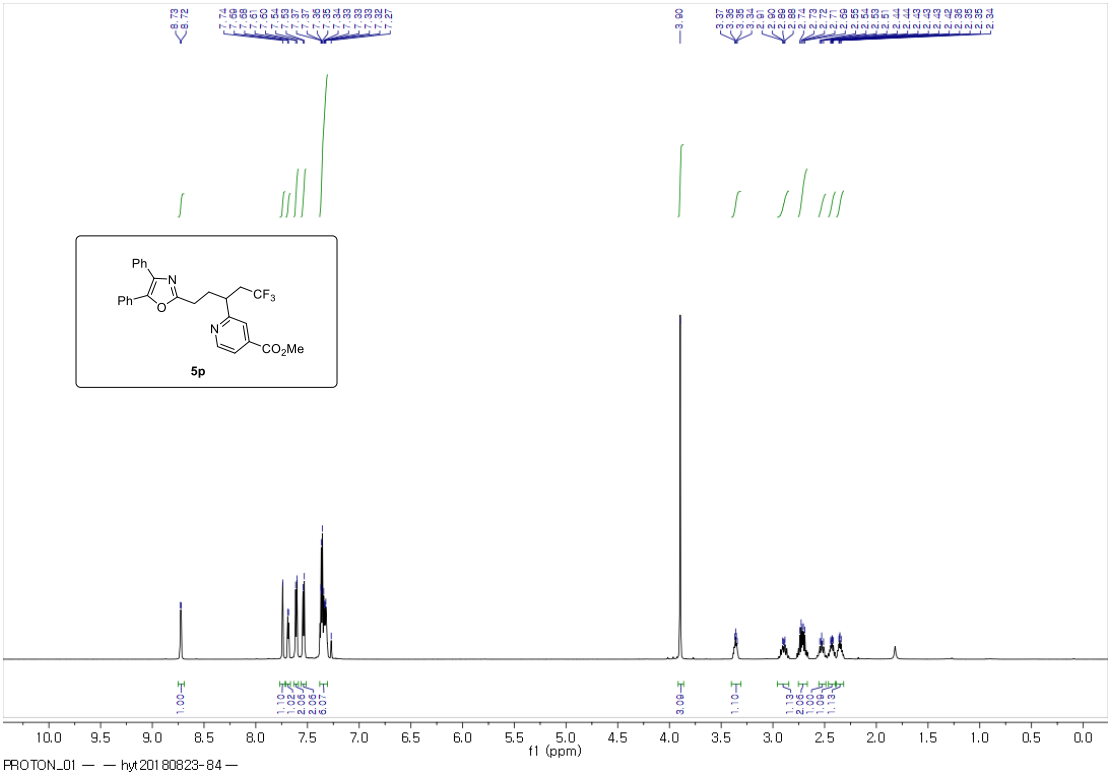


151 MHz, ^{13}C NMR in $CDCl_3$

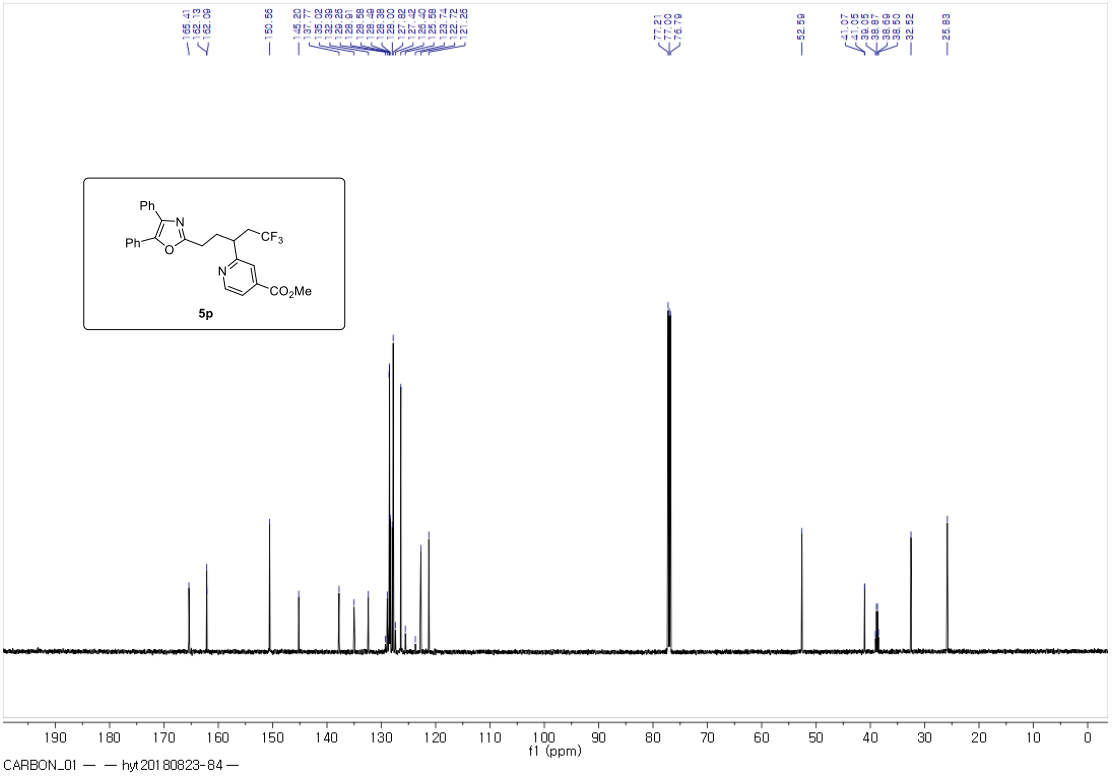


564 MHz, ^{19}F NMR in $CDCl_3$

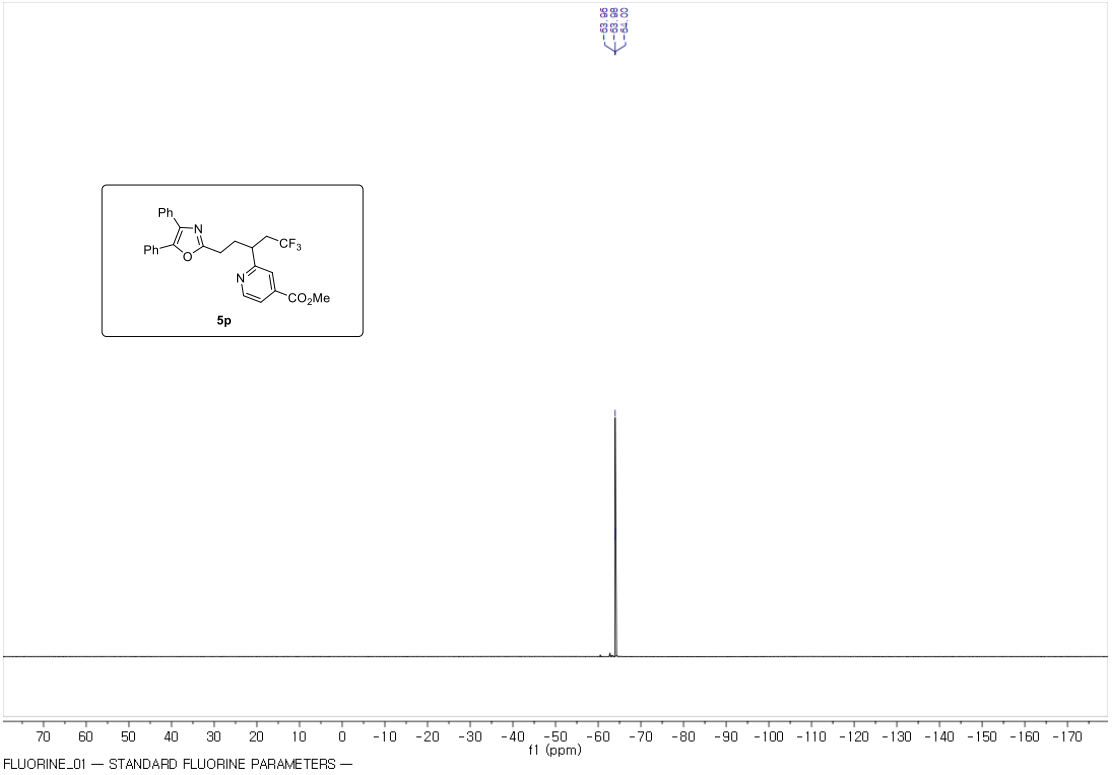
methyl 2-(5-(4,5-diphenyloxazol-2-yl)-1,1,1-trifluoropentan-3-yl)isonicotinate (5p).



599 MHz, ^{1}H NMR in $CDCl_3$

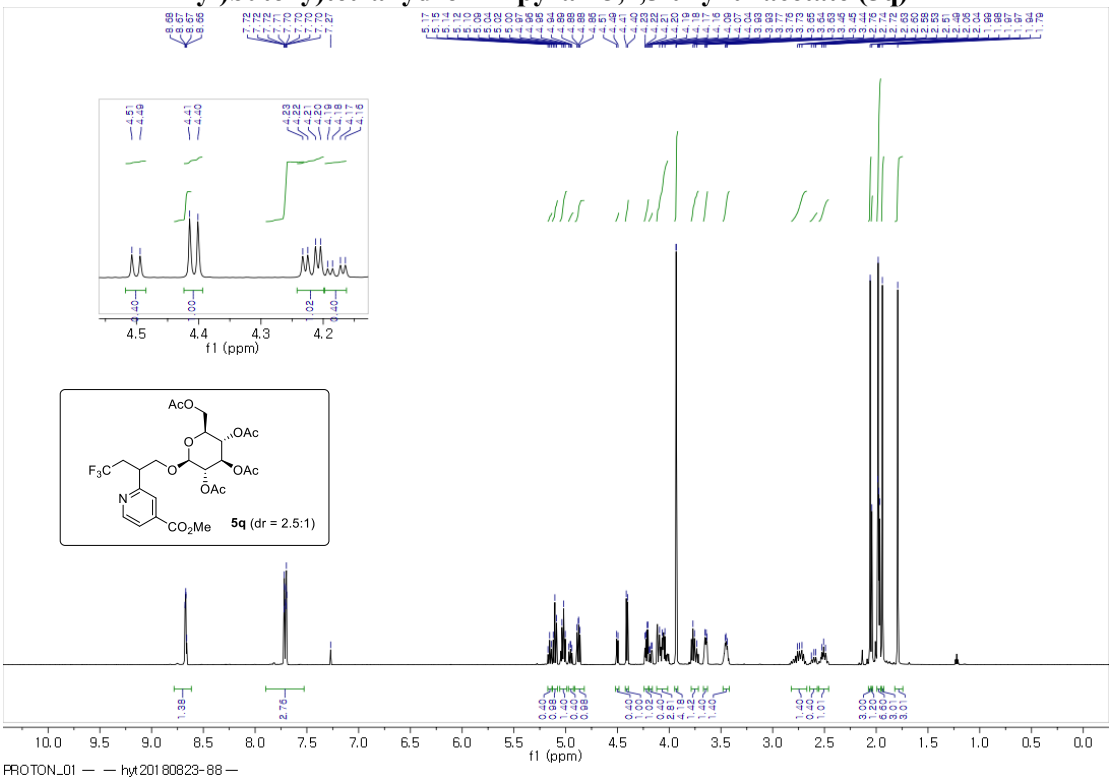


151 MHz, ^{13}C NMR in $CDCl_3$

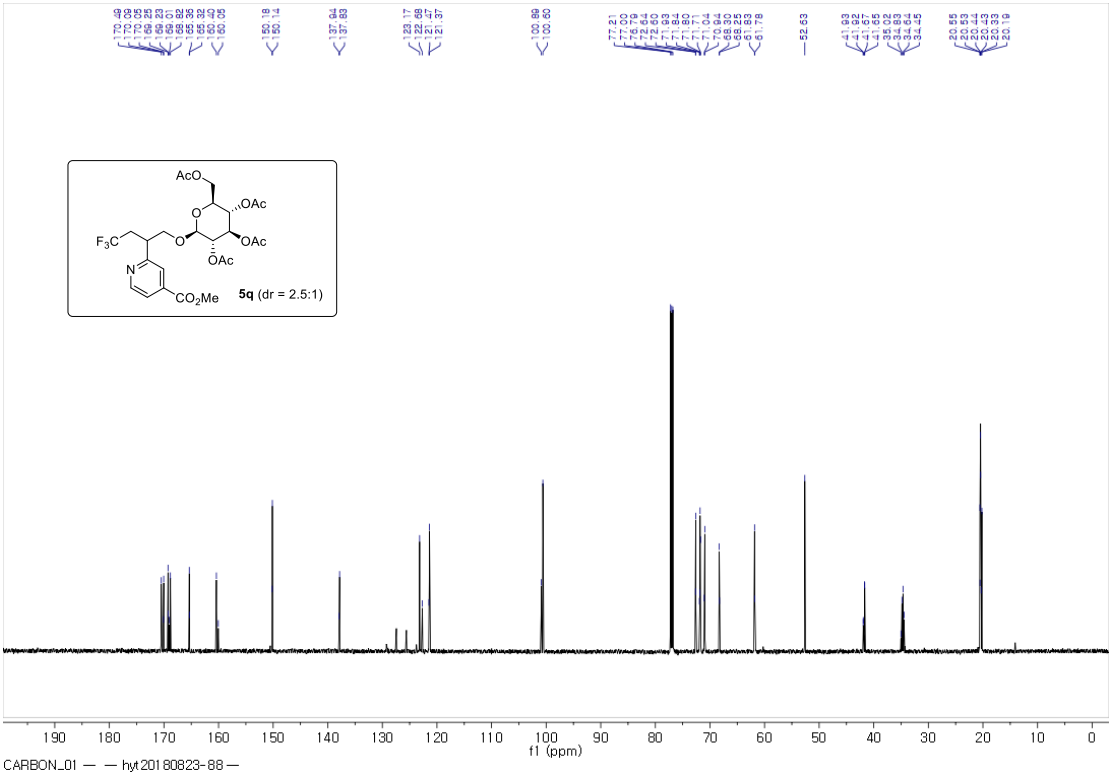


564 MHz, ^{19}F NMR in $CDCl_3$

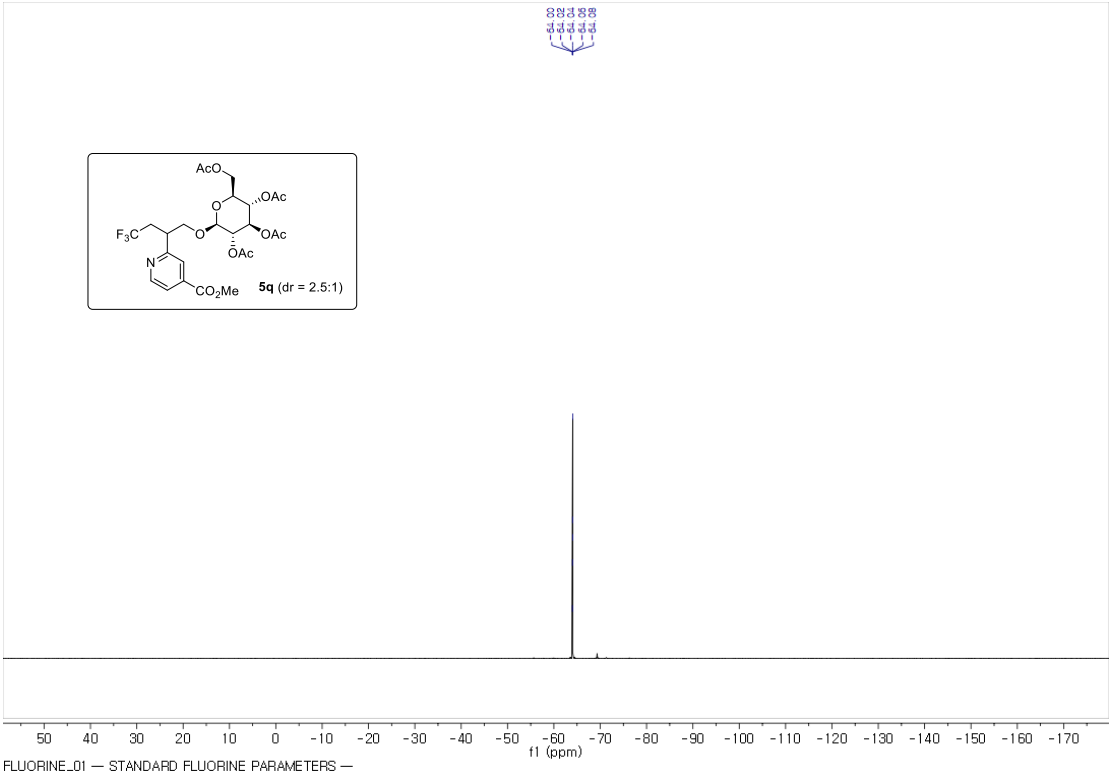
(2S,3S,4R,5S,6S)-2-(acetoxymethyl)-6-(4,4,4-trifluoro-2-(4-(methoxycarbonyl)pyridin-2-yl)butoxy)tetrahydro-2H-pyran-3,4,5-triyl triacetate (5q).



599 MHz, ^{1}H NMR in $CDCl_3$

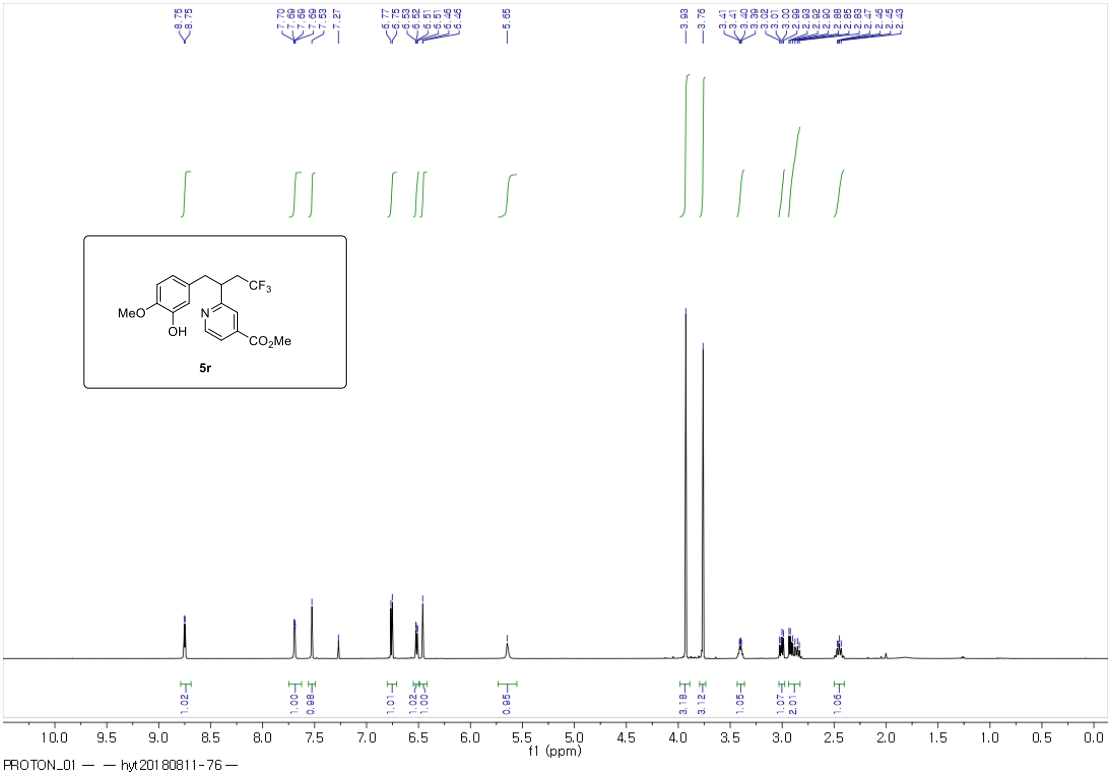


151 MHz, ^{13}C NMR in $CDCl_3$

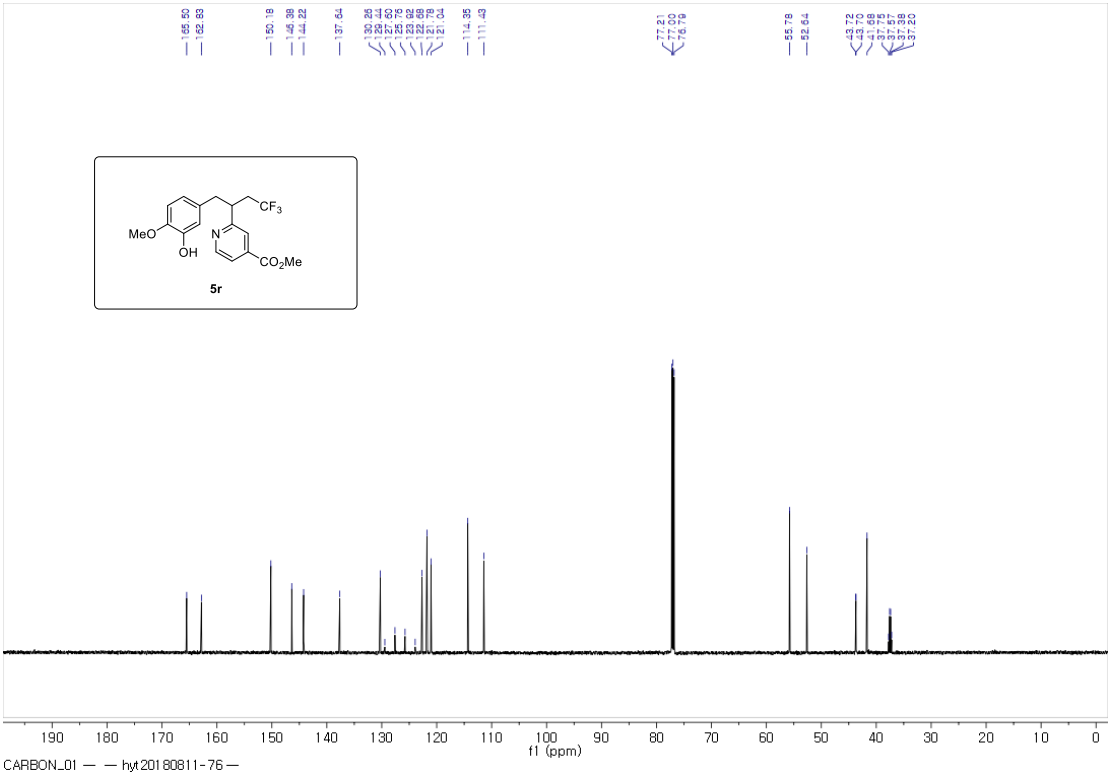


564 MHz, ^{19}F NMR in $CDCl_3$

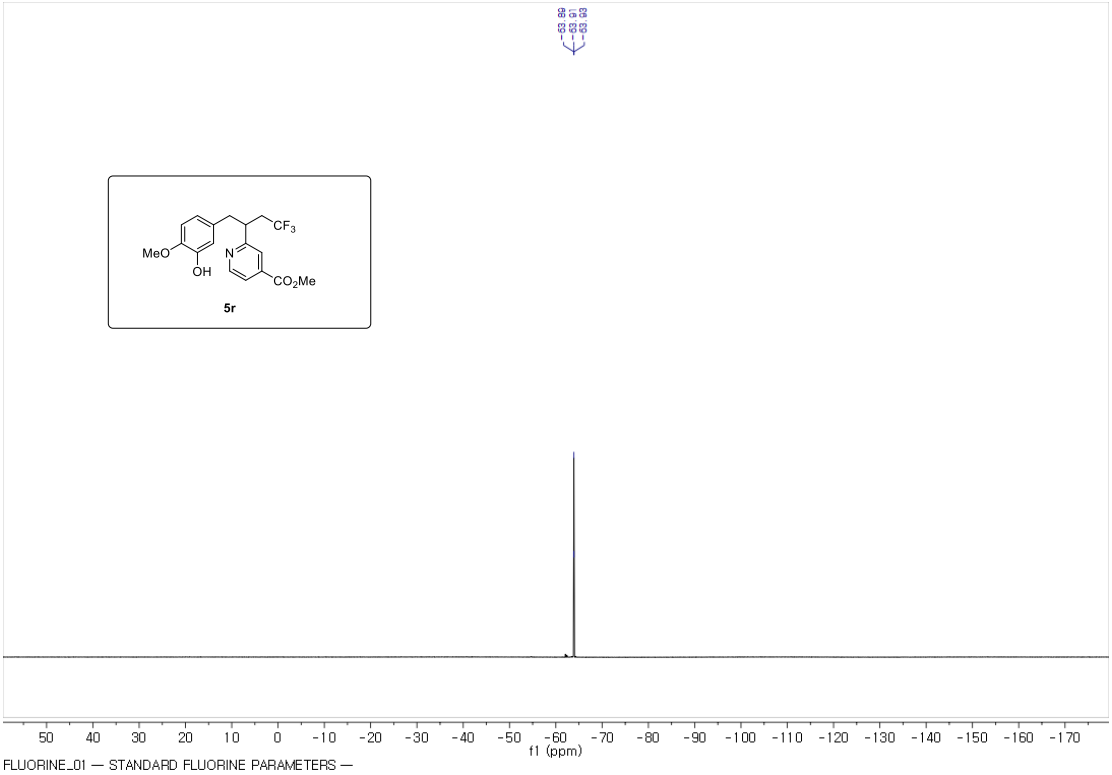
methyl 2-(4,4,4-trifluoro-1-(3-hydroxy-4-methoxyphenyl)butan-2-yl)isonicotinate (5r).



599 MHz, ^{1}H NMR in $CDCl_3$



151 MHz, ^{13}C NMR in $CDCl_3$



564 MHz, ^{19}F NMR in $CDCl_3$