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Synthesis of Tri(di)fluoroethylanilines via Copper-Catalyzed Coupling Reaction of Tri(di)fluoroethylamine with (Hetero)aromatic Bromides

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1. General information

All purchased reagents were used without further purification unless otherwise noted. All solvents were dried over activated 4Å molecular sieves. Analytical TLC was performed with 0.2 mm silica gel 60 F plates with 254 nm fluorescent indicator. TLC plates were visualized by ultraviolet light or by treatment with a spray off Pancaldi reagent {$Ce(SO_4)_2$}. Column chromatograph was performed on 200-300 mesh silica gal. NMR spectra were measured in $CDCl_3$ (TMS, ^1H $\delta = 0$; $CDCl_3$, ^1H $\delta =$ 7.26, ^{13}C $\delta = 77.16$) (^1H at 400 MHz, ^{13}C at 100 MHz, ^{19}F at 376 MHz) magnetic resonance spectrometer Chemical shifs (δ) are reported in ppm, and coupling constants (J) are in Hz. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. What should be noted is that all petroleum ether and ethyl acetate (EtOAc) used for flash column chromatography were redistilled twice before using, but the trace amount of residue of impurities such as H-grease and silicone grease could still be seen on NMR spectra of some products. *All the reactions were conducted in high pressure bottles with PTFE thread(resist 6 atm pressure) under the protection of a safety shield. In all the experiments, the solvent should never exceed the half volume of the high pressure bottle.*

2. General procedures

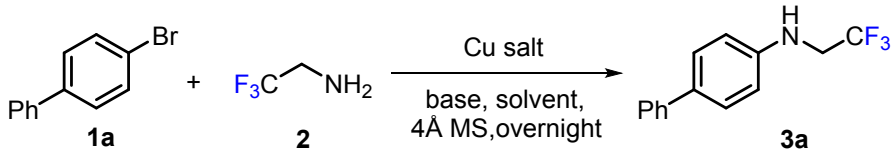
The general procedure for the Reaction of 2(6) with different bromobenzenes: A 10 mL high pressure bottle equipped with a magnetic stir bar was charged with bromobenzenes (0.5 mmol, 1 equiv), Cu_2O (7.1 mg, 0.05 mmol, 10 mol%), L14 (21.0 mg, 0.05 mmol, 10 mol%), K_2CO_3 (103.6mg, 0.75 mmol, 1.50 equiv), **2** (200 μL, 2.5 mmol, 5 equiv) [**6**, (70 μL, 1.0 mmol, 2 equiv)] and MeOH (2.0 mL). The reaction mixture was heated at 120 °C (**6**, 100°C) for 24 h under vigorous stirring. After removal of the solvent under vacuum, the residue was purified by column chromatography.

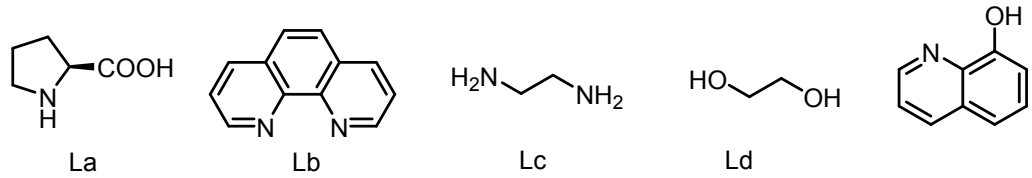
Gram-scale synthesis procedure: a 100 mL high pressure bottle equipped with a magnetic stir bar was charged with 1-bromo-4-methoxybenzene (6 mmol, 1.0 equiv), Cu_2O (42.9 mg, 0.3 mmol, 5 mol%), L14 (126.1 mg, 0.3 mmol, 5 mol%), K_2CO_3 (1.24 g, 9 mmol, 1.5 equiv), $CF_2HCH_2NH_2$ (0.85 mL, 12 mmol, 2 equiv) and MeOH (24 mL). The reaction mixture was heated at 100 °C for 24 h under vigorous stirring. After removal of the solvent under vacuum, the residue was purified by column chromatography.

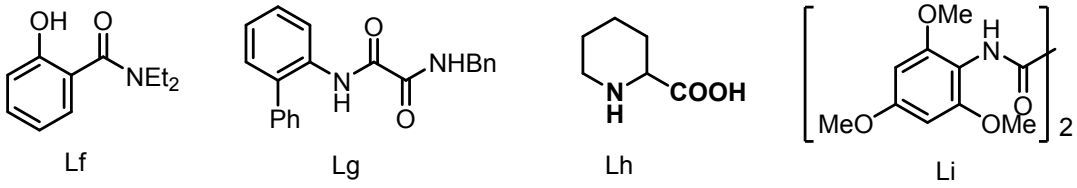
The procedure for competition reactions: A 10 mL high pressure bottle equipped with a magnetic stir bar was charged with bromobenzene (0.25 mmol, 1 equiv), Cu_2O (7.1 mg, 0.05 mmol, 20 mol%), L14 (21.0 mg, 0.05 mmol, 20 mol%), K_2CO_3 (52 mg, 0.375 mmol, 1.5 equiv), $CF_3CH_2NH_2$ (20 μL, 0.25 mmol, 1 equiv) or $CF_2HCH_2NH_2$ (17.5 μL, 0.25 mmol, 1 equiv) or 2-phenylethan-1-amine (31.5 μL, 0.25 mmol, 1 equiv) and MeOH (1.0 mL) . The reaction mixture was heated at 120 °C for 24 h under vigorous stirring. After removal of the solvent under vacuum, the ratio of the products is determined by the ^1H NMR.

3. Optimization of reactions

Table 1 Synthesis of fluoroalkylamine following relevant literatures.



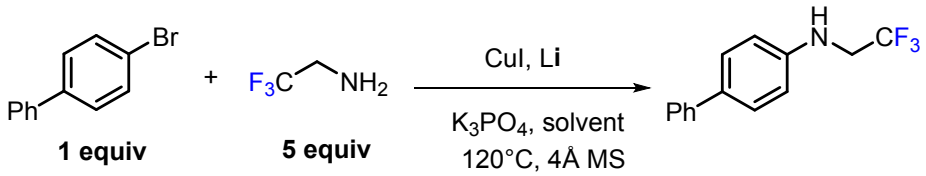




entry	Cu	Ligand	Base	solvent	T(℃)	Time(h)	Yield(%)
1[1]	CuI	La	K_2CO_3	DMSO	rt	17	0
2	CuI	Lb	^tBuOK	tuluene	115	3.5	0
3	CuI	Lc	K_3PO_4	dioxane	110	24	0
4	CuI	Ld	K_3PO_4	^iPrOH	90	24	0
5[2]	CuI	Le	Cs_2CO_3	^tBuOH	100	16	0
6[3]	CuI	Lf	K_3PO_4	DMF	90	22	0
7[4]	CuI	Lg	K_3PO_4	DMF	90	24	0
8[5]	CuI	Lh	K_2CO_3	DMF	110	24	0
9[6]	CuI	Li	K_3PO_4	DMSO	120	24	10

Condition: **1a** (0.25 mmol, 1 equiv), $CF_3CH_2NH_2$ (1.25 mmol, 5 equiv), CuI (0.05 mmol, 20 mol%), ligands (0.05 mmol, 20 mol%), bases (0,38 mmol, 1.5 equiv), 4Å MS, solvents (1.0 mL), T= 120 ºC, 24 h. Yields were determined by ^{19}F NMR spectroscopy using benzotrifluoride as an internal standard.

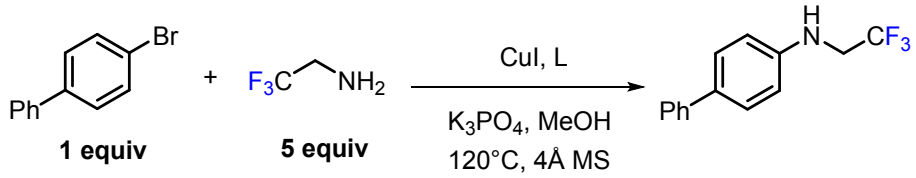
Table 2 The effect of solvents

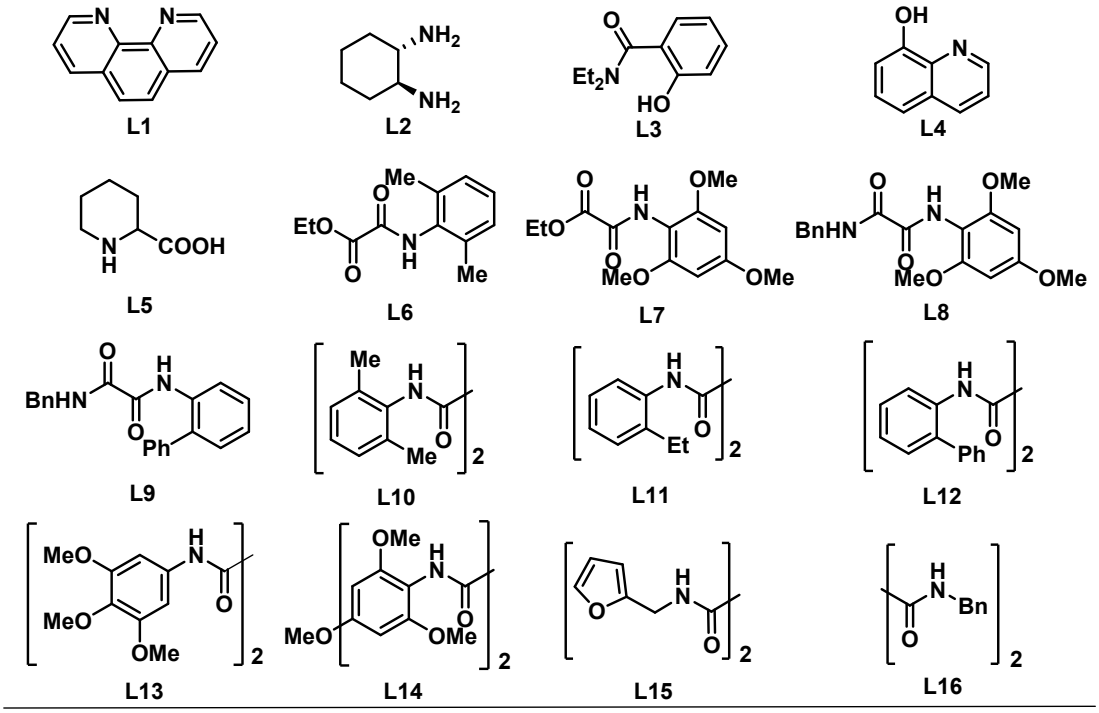


solvent	Yield(%)
DMSO	10%
DMSO(4Å MS)	20%
DMF	trace
MeCN	0
dioxane	0
DCE	0
toluene	0
NMP	0
MeOH	57%
EtOH	8%
^{i}PrOH	trace
^{t}BuOH	0
THF	0
acetone	trace
HFIP	trace

Condition: **1a** (0.25 mmol, 1 equiv), $CF_3CH_2NH_2$ (1.25 mmol, 5 equiv), CuI (0.05 mmol, 20 mol%), Li (0.05 mmol, 20 mol%), K_3PO_4 (0,38 mmol, 1.5 equiv), 4Å MS, solvents (1.0 mL), T= 120 ºC, 24 h. Yields were determined by ^{19}F NMR spectroscopy using benzotrifluoride as an internal standard.

Table 3 Ligand screen





ligand	yield	ligand	yield
L1	0	L9	24%
L2	trace	L10	20%
L3	trace	L11	17%
L4	trace	L12	5%
L5	trace	L13	18%
L6	28%	L14	57%
L7	33%	L15	27%
L8	51%	L16	15%

Condition: **1a** (0.25 mmol, 1 equiv), $CF_3CH_2NH_2$ (1.25 mmol, 5 equiv), CuI (0.05 mmol, 20 mol%), L (0.05 mmol, 20 mol%), MeOH (1.0 mL), T= 120 ºC, K_3PO_4 (0,38 mmol, 1.5 equiv), 4Å MS, 24 h. Yields were determined by ^{19}F NMR spectroscopy using benzotrifluoride as an internal standard.

Table 4 the effect of the base

base	Yield(%)
Cs_2CO_3	70%
K_2CO_3	75%
Na_2CO_3	48%
K_3PO_4	57%
NaOAc	0
TEA	0
^tBuONa	71%
TBAF(THF, 1 M)	66%

Condition: **1a** (0.25 mmol, 1 equiv), $CF_3CH_2NH_2$ (1.25 mmol, 5 equiv), CuI (0.05 mmol, 20 mol%), L14 (0.05 mmol, 20 mol%), MeOH (1.0 mL), T= 120 ºC, bases (0,38 mmol, 1.5 equiv), 4Å MS, 24 h. Yields were determined by ^{19}F NMR spectroscopy using benzotrifluoride as an internal standard.

Table 5 Evaluation of different copper salts

Cu salts	Yield(%)
CuI	69%
CuCl	78%
Cu_2O	90%
CuCN	64%
$CuCl_2$	64%
$Cu(OAc)_2$	53%
$CuBr_2$	42%
$Cu(acac)_2$	62%
$Cu(OTf)_2$	68%
CuBr	60%

Condition: **1a** (0.25 mmol, 1 equiv), $CF_3CH_2NH_2$ (1.25 mmol, 5 equiv), Cu salts (0.05 mmol, 20 mol%), L14 (0.05 mmol, 20 mol%), MeOH (1.0 mL), T= 120 ºC, K_2CO_3 (0,38 mmol, 1.5 equiv), 4Å MS, 24 h. Yields were determined by ^{19}F NMR spectroscopy using benzotrifluoride as an internal standard.

Table 6 The effect of temperature and the equivalent of $CF_3CH_2NH_2$

entry	T (°C)	$CF_3CH_2NH_2$(equiv)	yield[a]
1	80	5	0
2	90	5	0
3	100	5	3%
4	110	5	66%
5	120	5	90%
6	120	2	76%
7	120	5	93%[b]

Condition: Condition: **1a** (0.25 mmol, 1 equiv), **2** (X equiv), Cu_2O (0.05 mmol, 20 mol%), L14 (0.05 mmol, 20 mol%), MeOH (1.0 mL), T, K_2CO_3 (0,38 mmol, 1.5 equiv), 4Å MS, 24 h. a.Yields were determined by ^{19}F NMR spectroscopy using benzotrifluoride as an internal standard; b. no 4Å MS.

Table 7 The effect of temperature and the equivalent of $HCF_2CH_2NH_2$

Entry	T(℃)	$HCF_2CH_2NH_2$(equiv)	Yield
1	80	2	65%
2	90	2	81%
3	100	2	90%
4	100	5	95%
5	120	2	90%

Condition: **1a** (0.25 mmol, 1 equiv), **6** (X equiv), Cu_2O (0.05 mmol, 20 mol%), L14 (0.05 mmol, 20 mol%), MeOH (1.0 mL), T, K_2CO_3 (0,38 mmol, 1.5 equiv), 4Å MS, 24 h. Yields were determined by ^{19}F NMR spectroscopy using benzotrifluoride as an internal standard.

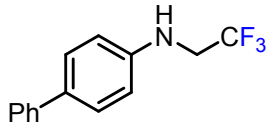
Table 8 The effect of water on the reaction

Entry	Variation conditions	Yield(%)
1	4Å MS	90%
2	no 4Å MS	93%
3	2 equiv H_2O	91%
4	no 2 equiv H_2O	95%
5	Untreated MeOH	95%

Condition: **1a** (0.25 mmol, 1 equiv), $CF_3CH_2NH_2$ (1.25 mmol, 5 equiv), Cu_2O (0.05 mmol, 20 mol%), L14 (0.05 mmol, 20 mol%), MeOH (1.0 mL), T= 120 ºC, K_2CO_3 (0,38 mmol, 1.5 equiv), 24 h. Yields were determined by ^{19}F NMR spectroscopy using benzotrifluoride as an internal standard.

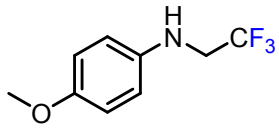
4. Characterization data of Compounds

_N_-(2,2,2-trifluoroethyl)-[1,1'-biphenyl]-4-amine (3a)



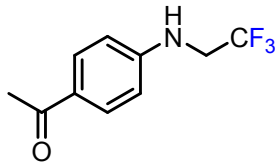
Purified by flash column chromatography (petroleum ether/AcOEt = 100:1), white solid (111.8 mg, 89% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.67 – 7.56 (m, 2H), 7.52 (d, *J* = 8.6 Hz, 2H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.40 – 7.30 (m, 1H), 6.92 – 6.67 (m, 2H), 3.85 (s, 1H), 3.82 (q, *J* = 8.9 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 145.7, 140.9, 132.1, 128.8, 128.2, 126.56, 126.53, 125.2 (q, *J* = 280.2 Hz), 113.5, 46.0 (q, *J* = 33.8 Hz). (Consistent with previous reported values[7].)

4-methoxy-_N_-(2,2,2-trifluoroethyl)aniline (3b)



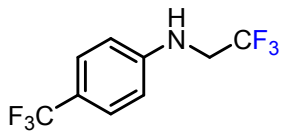
Purified by flash column chromatography (petroleum ether/AcOEt = 50:1), pale yellow liquid (90.3 mg, 88% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.83 (d, *J* = 9.0 Hz, 2H), 6.67 (d, *J* = 8.9 Hz, 2H), 3.77 (s, 3H), 3.71 (q, *J* = 9.0 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 153.2, 140.4, 125.3 (q, *J* = 279.9 Hz), 115.0, 114.8, 55.7, 47.1 (q, *J* = 33.0 Hz). (Consistent with previous reported values[7].)

1-(4-((2,2,2-trifluoroethyl)amino)phenyl)ethan-1-one (3c)



Purified by flash column chromatography (petroleum ether/AcOEt = 10:1), white solid (93.1 mg, 85% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.8 Hz, 2H), 6.68 (d, *J* = 8.8 Hz, 2H), 4.76 (s, 1H), 3.94 – 3.68 (m, 2H), 2.51 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 196.7, 150.5, 130.9, 128.5, 124.8 (q, *J* = 280.2 Hz), 112.1, 45.3 (q, *J* = 34.1 Hz), 26.3. (Consistent with previous reported values[8].)

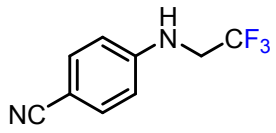
_N_-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)aniline (3d)



Purified by flash column chromatography (petroleum ether/AcOEt = 50:1), colorless and transparent liquid (84 mg, 69% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.5 Hz, 2H), 6.72 (d, *J* = 8.5 Hz, 2H),

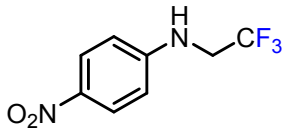
4.21 (s, 1H), 3.81 (q, J = 8.8 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 148.9, 126.9 (q, J = 3.8 Hz), 124.9 (q, J = 280.4 Hz), 124.8 (q, J = 270.0 Hz), 121.0 (q, J = 32.7 Hz), 112.5, 45.5 (q, J = 34.0 Hz). (Consistent with previous reported values[7].)

4-((2,2,2-trifluoroethyl)amino)benzonitrile (3e)



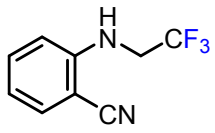
Purified by flash column chromatography (petroleum ether/AcOEt = 10:1), white solid (74 mg, 74% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 (d, J = 8.8 Hz, 2H), 6.69 (d, J = 8.8 Hz, 2H), 4.64 (s, 1H), 3.82 (dq, J = 8.0, 6.2 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.9, 133.9, 124.7 (q, J = 280.3 Hz), 120.0, 112.9, 101.0, 45.1 (q, J = 34.3 Hz). (Consistent with previous reported values[8].)

4-nitro-*N*-(2,2,2-trifluoroethyl)aniline (3f)



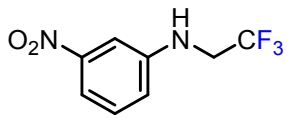
Purified by flash column chromatography (petroleum ether / AcOEt = 5:1), yellow solid (64.9 mg, 59% yield), m.p. 113-114 ℃; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.12 (d, J = 9.2 Hz, 2H), 6.69 (d, J = 9.2 Hz, 2H), 4.84 (s, 1H), 4.04 – 3.75 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 151.8, 139.8, 126.4, 124.5 (q, J = 280.3 Hz), 112.0, 45.2 (q, J = 34.5 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -72.05 (t, J = 8.7 Hz); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ -72.05 (s); **HRMS (ESI)**: calcd. for $C_8H_8F_3N_2O_2^+$ $[M+H]^+$ 221.0532, found 221.0524.

2-((2,2,2-trifluoroethyl)amino)benzonitrile (3g)



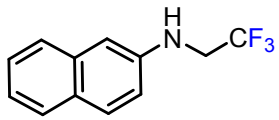
Purified by flash column chromatography (petroleum ether/AcOEt = 10:1),white solid (42.8 mg, 43% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.45 (ddd, J = 7.4, 4.4, 2.6 Hz, 2H), 6.87 – 6.75 (m, 2H), 4.94 (s, 1H), 3.88 (qd, J = 8.7, 6.9 Hz, 2H); **^{13}C NMR** (100MHz, $CDCl_3$) δ 148.8, 134.5, 133.0, 124.6 (q, J = 280.3 Hz), 118.7, 117.4, 111.0 (q, J = 1.6 Hz), 97.3, 45.2 (q, J = 34.6 Hz). (Consistent with previous reported values[8].)

3-nitro-*N*-(2,2,2-trifluoroethyl)aniline (3h)



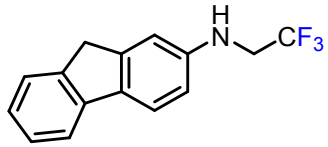
Purified by flash column chromatography (petroleum ether / Dichloromethane = 5:1), yellow solid (103.6 mg, 94% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.51 (t, *J* = 2.3 Hz, 1H), 7.35 (t, *J* = 8.1 Hz, 1H), 6.98 (dd, *J* = 8.2, 2.5 Hz, 1H), 4.36 (s, 1H), 3.85 (q, *J* = 9.1 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.4, 147.2, 130.2, 124.8 (q, *J* = 280.1 Hz), 119.1, 113.9, 107.1, 45.7 (q, *J* = 34.2 Hz). (Consistent with previous reported values[7].)

_N_-(2,2,2-trifluoroethyl)naphthalen-2-amine (3i)



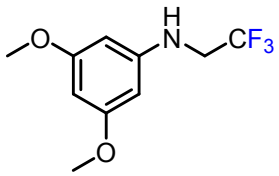
Purified by flash column chromatography (petroleum ether/AcOEt = 50:1), white solid (105.4 mg, 93% yield), m.p. 96-97 ℃; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 – 7.62 (m, 3H), 7.45 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.31 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 6.99 – 6.87 (m, 2H), 4.00 (s, 1H), 3.87 (q, *J* = 9.0 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 144.0, 134.9, 129.4, 128.3, 127.8, 126.7, 126.3, 125.2 (q, *J* = 280.4 Hz), 123.0, 117.5, 105.7, 46.1 (q, *J* = 33.7 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -71.97 (t, *J* = 8.9 Hz); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) *δ* -71.97 (s); **HRMS (ESI)**: calcd. for $C_{12}H_{11}F_3N^+$ $[M+H]^+$ 226.0838, found 226.0832.

_N_-(2,2,2-trifluoroethyl)-9*H*-fluoren-2-amine (3j)



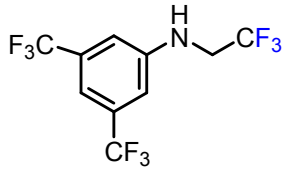
Purified by flash column chromatography (petroleum ether/AcOEt = 50:1), white solid (131.6 mg, 92% yield), m.p. 119-120 ℃; **^{1}H NMR** (400 MHz, $CDCl_3$) δ7.67 (d, *J* = 7.6 Hz, 1H), 7.62 (d, *J* = 8.2 Hz, 1H), 7.49 (d, *J* = 7.4 Hz, 1H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.23 (td, *J* = 7.4, 1.2 Hz, 1H), 6.88 (d, *J* = 2.2 Hz, 1H), 6.71 (dd, *J* = 8.3, 2.2 Hz, 1H), 3.99 (s, 1H), 3.89 – 3.74 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 145.8, 145.4, 142.4, 142.0, 133.7, 126.8, 125.4, 125.2 (q, *J* = 280.1 Hz), 124.9, 120.8, 118.9, 112.5, 109.9, 46.5 (q, *J* = 33.4 Hz), 37.1; **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -72.19 (t, *J* = 8.8 Hz); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) *δ* -72.19 (s); **HRMS (ESI)**: calcd. for $C_{15}H_{13}F_3N^+$ $[M+H]^+$ 264.0995, found 264.0988.

3,5-dimethoxy-_N_-(2,2,2-trifluoroethyl)aniline (3k)



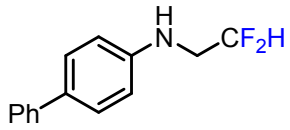
Purified by flash column chromatography (petroleum ether/AcOEt = 20:1), colorless liquid (102.3 mg, 87% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.97 (s, 1H), 5.86 (d, *J* = 2.0 Hz, 2H), 3.76 (s, 6H), 3.75 – 3.69 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.9, 148.4, 125.0 (q, *J* = 279.9 Hz), 92.2, 91.2, 55.3 , 46.1 (q, *J* = 33.8 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -72.28 (t, *J* = 8.9 Hz); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) *δ* -72.28(s); **HRMS (ESI)**: calcd. for $C_{10}H_{13}F_3NO_2^+$ $[M+H]^+$ 236.0893, found 236.0888.

***N*-(2,2,2-trifluoroethyl)-3,5-bis(trifluoromethyl)aniline (3l)**



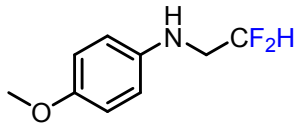
Purified by flash column chromatography (petroleum ether/AcOEt = 50:1), pale yellow liquid (113.4 mg, 73% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.28 (s, 1H), 7.06 (s, 2H), 4.40 (s, 1H), 3.85 (q, *J* = 8.7 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 146.2, 131.9 (q, *J* = 33.0 Hz), 123.7 (q, *J* =280.5 Hz), 122.5 (q, *J* =272.7 Hz), 111.6 (d, *J* = 4.1 Hz), 111.52 – 111.27 (m), 44.57 (q, *J* = 34.3 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -63.30(s) , -72.22 (t, *J* = 8.8 Hz); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) *δ* -63.30(s) , -72.22(s) ; **HRMS (ESI)**: calcd. for $C_{10}H_7F_9N^+$ $[M+H]^+$ 312.0429, found 312.0426.

***N*-(2,2-difluoroethyl)-[1,1'-biphenyl]-4-amine (7a)**



Purified by flash column chromatography (petroleum ether/AcOEt = 100:1),white solid (100.3 mg, 86% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.58 – 7.51 (m, 2H), 7.48 (d, *J* = 8.2 Hz, 2H), 7.41 (t, *J* = 7.7 Hz, 2H), 7.33 – 7.23 (m, 1H), 6.79 (d, *J* = 8.2 Hz, 2H), 5.98 (tt, *J* = 56.0, 4.1 Hz, 1H), 3.60 (td, *J* = 14.3, 4.1 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 145.7, 140.9, 132.3, 128.9, 128.2 , 126.58, 126.56, 114.5 (t, *J* = 240.8 Hz), 113.9, 46.8 (t, *J* = 26.1 Hz). (Consistent with previous reported values[9].)

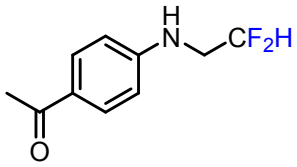
***N*-(2,2-difluoroethyl)-4-methoxyaniline (7b)**



Purified by flash column chromatography (petroleum ether / EtOAc = 50:1), pale yellow liquid (87.8 mg, 93% yield); **^{1}H NMR** (400 MHz,

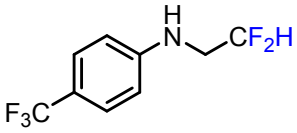
$CDCl_3$) δ 6.80 (d, *J* = 8.9 Hz, 2H), 6.64 (d, *J* = 8.9 Hz, 2H), 5.91 (tt, *J* = 56.2, 4.3 Hz, 1H), 3.76 (s, 3H), 3.48 (td, *J* = 14.4, 4.3 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 153.1, 140.9, 115.2, 114.9 (t, *J* = 240.5 Hz), 114.8, 55.9, 47.7 (t, *J* = 25.7 Hz). (Consistent with previous reported values[8].)

1-(4-((2,2-difluoroethyl)amino)phenyl)ethan-1-one (7c)



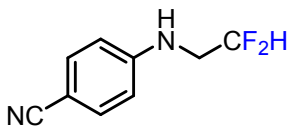
Purified by flash column chromatography (petroleum ether / EtOAc = 5:1), white solid (77.1 mg, 77% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.8 Hz, 2H), 6.64 (d, *J* = 8.8 Hz, 2H), 5.92 (tt, *J* = 55.8, 4.0 Hz, 1H), 4.39 (s, 1H), 3.61 (td, *J* = 14.5, 4.0 Hz, 2H), 2.50 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 196.7, 151.2, 130.9, 127.9, 114.2 (t, *J* = 241.0 Hz), 111.9, 45.7 (t, *J* = 26.0 Hz), 26.1. (Consistent with previous reported values[9].)

***N*-(2,2-difluoroethyl)-4-(trifluoromethyl)aniline (7d)**



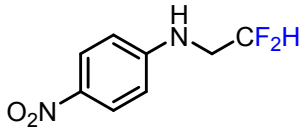
Purified by flash column chromatography (petroleum ether / EtOAc = 50:1), tawny liquid (85 mg, 75% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.4 Hz, 2H), 6.68 (d, *J* = 8.4 Hz, 2H), 5.92 (tt, *J* = 55.8, 4.0 Hz, 1H), 4.21 (s, 1H), 3.59 (tdd, *J* = 14.5, 6.7, 4.0 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.5, 127.0 (q, *J* = 3.8 Hz), 124.9 (q, *J* = 270.4 Hz), 120.4 (q, *J* = 32.8 Hz), 114.3 (t, *J* = 242.3 Hz), 112.4, 46.0 (t, *J* = 26.1 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -61.27 (s) , -122.67 (dt, *J* = 55.8, 14.5 Hz); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) *δ* -61.27 (s) , -122.67 (s) ; **HRMS (ESI)**: calcd. for $C_9H_9F_5N^+$ $[M+H]^+$ 226.0650, found 226.0643.

4-((2,2-difluoroethyl)amino)benzonitrile (7e)



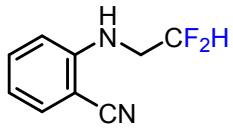
Purified by flash column chromatography (petroleum ether / EtOAc = 8:1), white solid (66 mg, 72% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.8 Hz, 2H), 6.65 (d, *J* = 8.8 Hz, 2H), 5.92 (tt, *J* = 55.6, 3.9 Hz, 1H), 4.36 (s, 1H), 3.60 (td, *J* = 14.5, 3.9 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.3, 134.0, 120.0, 114.0 (t, *J* = 241.2 Hz), 112.7, 100.8, 45.6 (t, *J* = 25.8 Hz). (Consistent with previous reported values[8].)

***N*-(2,2-difluoroethyl)-4-nitroaniline (7f)**



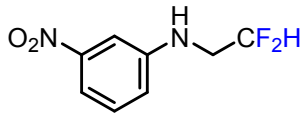
Purified by flash column chromatography (petroleum ether / EtOAc = 5:1), yellow solid (42.4 mg, 42% yield), m.p. 110-111 ℃; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 9.2 Hz, 2H), 6.64 (d, *J* = 9.2 Hz, 2H), 5.95 (tt, *J* = 55.5, 3.8 Hz, 1H), 4.80 (t, *J* = 6.7 Hz, 1H), 3.66 (tdd, *J* = 14.6, 6.6, 3.8 Hz, 2H); **^{13}C NMR** (100MHz, $CDCl_3$) δ 152.5, 139.2, 126.5, 114.0 (t, *J* = 242.8 Hz), 111.7, 45.7 (t, *J* = 25.9 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -122.51 (dt, *J* = 55.7, 14.6 Hz); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ -122.51 (s); **HRMS (ESI)**: calcd. for $C_8H_9F_2N_2O_2^+$ $[M+H]^+$ 203.0627, found 203.0626.

2-((2,2-difluoroethyl)amino)benzonitrile (7g)



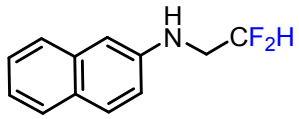
Purified by flash column chromatography (petroleum ether/AcOEt = 10:1), colorless and transparent liquid (47.2 mg, 51% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43 (ddd, *J* = 8.1, 6.7, 1.7 Hz, 2H), 6.88 – 6.63 (m, 2H), 5.93 (tt, *J* = 55.6, 4.0 Hz, 1H), 4.78 (s, 1H), 3.66 (td, *J* = 14.2, 4.0 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.3, 134.5, 133.2, 118.2, 114.2 (t, *J* = 243.0 Hz), 110.8, 97.1, 45.8 (t, *J* = 26.6 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -122.17 (dt, *J* = 55.5, 14.2 Hz); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) *δ* -122.17 (s); **HRMS (ESI)**: calcd. for $C_9H_9F_2N_2^+$ $[M+H]^+$ 183.0728, found 183.0727.

***N*-(2,2-difluoroethyl)-3-nitroaniline (7h)**



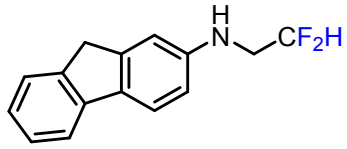
Purified by flash column chromatography (petroleum ether / EtOAc = 10:1), yellow solid (92.4 mg, 90% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.67 – 7.55 (m, 1H), 7.48 (t, *J* = 2.3 Hz, 1H), 7.33 (t, *J* = 8.2 Hz, 1H), 6.95 (dd, *J* = 8.0, 2.4 Hz, 1H), 5.95 (tt, *J* = 55.7, 3.9 Hz, 1H), 4.25 (s, 1H), 3.63 (dddd, *J* = 14.6, 10.7, 6.7, 3.3 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.6, 147.9, 130.2, 119.2, 114.2 (t, *J* = 242.4 Hz), 113.5, 106.8, 46.2 (t, *J* = 25.8 Hz). (Consistent with previous reported values[9].)

***N*-(2,2-difluoroethyl)naphthalen-2-amine (7i)**



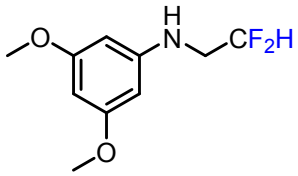
Purified by flash column chromatography (petroleum ether/AcOEt = 50:1),white solid (99.1 mg, 95% yield), m.p. 93-94 ℃; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 – 7.58 (m, 3H), 7.39 (ddd, *J* = 8.2, 6.8, 1.4 Hz, 1H), 7.28 – 7.18 (m, 1H), 6.91 – 6.83 (m, 2H), 5.97 (tt, *J* = 56.1, 4.2 Hz, 1H), 3.93 (s, 1H), 3.61 (td, *J* = 14.4, 4.3 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 144.5, 135.0 , 129.5, 128.15, 127.8, 126.78, 126.2 , 122.8, 117.8, 117.49 – 110.91 (m), 105.1, 46.5 (t, *J* = 26.1 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -122.42 (dt, *J* = 56.0, 14.4 Hz); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) *δ* -122.42(s); **HRMS (ESI)**: calcd. for $C_{12}H_{12}F_2N^+$ $[M+H]^+$ 208.0932, found 208.0933.

***N*-(2,2-difluoroethyl)-9H-fluoren-2-amine (7j)**



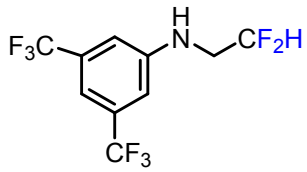
Purified by flash column chromatography (petroleum ether/AcOEt = 50:1),white solid (104.6 mg, 85% yield), m.p. 117-118 ℃; **^{1}H NMR** (400 MHz, $CDCl_3$) δ, 7.65 (d, *J* = 7.6 Hz, 1H), 7.61 (d, *J* = 8.2 Hz, 1H), 7.48 (d, *J* = 7.4 Hz, 1H), 7.33 (t, *J* = 7.5 Hz, 1H), 7.21 (td, *J* = 7.5, 1.2 Hz, 1H), 6.89 – 6.82 (m, 1H), 6.69 (dd, *J* = 8.2, 2.2 Hz, 1H), 5.97 (tt, *J* = 56.1, 4.3 Hz, 1H), 3.96 (s, 1H), 3.83 (s, 2H), 3.60 (td, *J* = 14.4, 4.3 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 146.3, 145.4, 142.4, 142.1, 133.3, 126.8, 125.4, 124.9, 120.9, 118.8, 114.7 (t, *J* = 240.8 Hz), 112.4, 109.7, 46.9 (t, *J* = 26.0 Hz), 37.1; **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -122.57 (dt, *J* = 56.3, 14.3 Hz); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) *δ* -122.57 (s); **HRMS (ESI)**: calcd. for $C_{15}H_{14}F_2N^+$ $[M+H]^+$ 246.1089, found 246.1082.

***N*-(2,2-difluoroethyl)-3,5-dimethoxyaniline (7k)**



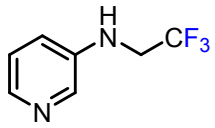
Purified by flash column chromatography (petroleum ether / EtOAc = 20:1), colorless liquid (99.8 mg, 92% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.95 (tt, *J* = 56.2, 2.1 Hz, 1H), 5.91 (t, *J* = 4.2 Hz, 1H), 5.84 (d, *J* = 2.1 Hz, 2H), 3.76 (s, 6H), 3.49 (td, *J* = 14.4, 4.2 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.9, 148.8, 120.2 – 109.6 (m), 92.1, 90.8, 55.24, 55.19, 46.45 (t, *J* = 26.3 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -122.60 (dt, *J* = 56.0, 14.4 Hz); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) *δ* -122.60 (s); **HRMS (ESI)**: calcd. for $C_{10}H_{14}F_2NO_2^+$ $[M+H]^+$ 218.0987, found 218.0985.

***N*-(2,2-difluoroethyl)-3,5-bis(trifluoromethyl)aniline (7l)**



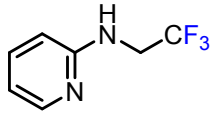
Purified by flash column chromatography (petroleum ether / EtOAc = 30:1), pale yellow liquid (120.8 mg, 83% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.24 (s, 1H), 7.02 (s, 2H), 5.95 (tt, *J* = 55.5, 3.8 Hz, 1H), 4.32 (s, 1H), 3.62 (td, *J* = 14.6, 3.8 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 147.8, 132.9 (q, *J* = 32.9 Hz), 123.5 (q, *J* = 272.8 Hz), 114.1 (q, *J* = 242.5 Hz), 112.4 (d, *J* = 4.2 Hz), 112.0 – 111.8 (m), 46.0 (t, *J* = 25.7 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -63.26 (s) , -122.73 (dt, *J* = 55.6, 14.4 Hz); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) *δ* -63.26 (s) , -122.73(s); **HRMS (ESI)**: calcd. for $C_{10}H_8F_8N^+$ $[M+H]^+$ 294.0524, found 294.0527.

***N*-(2,2,2-trifluoroethyl)pyridin-3-amine (9a)**



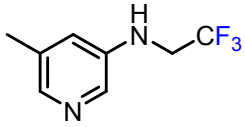
Purified by flash column chromatography (petroleum ether / EtOAc = 1:1), white solid (35.7 mg, 81% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 2.9 Hz, 1H), 8.06 (d, *J* = 4.7 Hz, 1H), 7.14 (dd, *J* = 8.3, 4.6 Hz, 1H), 6.99 (ddd, *J* = 8.4, 3.0, 1.3 Hz, 1H), 4.21 (s, 1H), 3.78 (qd, *J* = 8.8, 7.0 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 142.5, 140.5, 136.4, 124.9 (q, *J* = 280.0 Hz), 123.9, 119.1, 45.7 (q, *J* = 34.0 Hz). (Consistent with previous reported values[8].)

***N*-(2,2,2-trifluoroethyl)pyridin-2-amine (9b)**



Purified by flash column chromatography (petroleum ether / EtOAc = 20:1), white solid (27.4 mg, 62% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.12 (dd, *J* = 5.1, 1.8 Hz, 1H), 7.45 (ddd, *J* = 8.7, 7.2, 1.9 Hz, 1H), 6.68 (ddd, *J* = 7.3, 5.0, 1.0 Hz, 1H), 6.49 (d, *J* = 8.3 Hz, 1H), 4.62 (s, 1H), 4.11 (qd, *J* = 9.2, 6.8 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.0, 148.0, 137.8, 125.1 (q, *J* = 279.3 Hz), 114.7, 108.3, 43.0 (q, *J* = 33.8 Hz). (Consistent with previous reported values[8].)

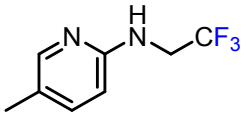
5-methyl-*N*-(2,2,2-trifluoroethyl)pyridin-3-amine (9c)



Purified by flash column chromatography (petroleum ether / EtOAc = 1:1), white solid (39.6 mg, 83% yield), m.p. 46-47 ℃; **^{1}H NMR** (400 MHz,

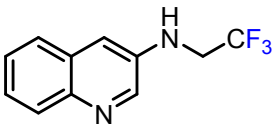
$CDCl_3$) δ 7.93 (d, *J* = 23.4 Hz, 2H), 6.82 (s, 1H), 4.22 (s, 1H), 3.89 – 3.63 (m, 2H), 2.28 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 140.7, 133.4, 125.0 (q, *J* = 280.0 Hz), 120.1 , 45.7 (q, *J* = 33.9 Hz), 18.6; **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -72.28 (t, *J* = 8.8 Hz); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) *δ* -72.28 (s); **HRMS (ESI)**: calcd. for $C_8H_{10}F_3N_2^+$ $[M+H]^+$ 191.0791, found 191.0787.

5-methyl-*N*-(2,2,2-trifluoroethyl)pyridin-2-amine (9d)



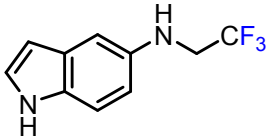
Purified by flash column chromatography (petroleum ether / EtOAc = 5:1), white solid (33.6 mg, 70% yield), m.p. 60-61 ℃; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.30 (dd, *J* = 8.4, 2.3 Hz, 1H), 6.45 (d, *J* = 8.4 Hz, 1H), 4.66 (s, 1H), 4.06 (qd, *J* = 9.1, 6.8 Hz, 2H), 2.20 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 155.1, 147.1, 139.2, 125.1 (q, *J* = 279.5 Hz), 123.6, 108.0 , 43.3 (q, *J* = 34.0 Hz), 17.6; **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -72.67 (t, *J* = 9.1 Hz); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) *δ* -72.67 (s); **HRMS (ESI)**: calcd. for $C_8H_{10}F_3N_2^+$ $[M+H]^+$ 191.0791, found 191.0785.

***N*-(2,2,2-trifluoroethyl)quinolin-3-amine (9e)**



Purified by flash column chromatography (petroleum ether / EtOAc = 3:1), white solid (42.6 mg, 75% yield), m.p. 78-79 ℃; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.51 (d, *J* = 2.9 Hz, 1H), 8.02 – 7.94 (m, 1H), 7.71 – 7.59 (m, 1H), 7.54 – 7.40 (m, 2H), 7.18 (d, *J* = 2.8 Hz, 1H), 4.54 (s, 1H), 3.88 (qd, *J* = 8.8, 6.9 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 142.8, 142.7, 139.8, 129.04, 128.98, 127.4, 126.3, 126.1, 125.0 (q, *J* = 281.1 Hz), 111.7, 45.7 (q, *J* = 34.1 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -71.87 (t, *J* = 8.8 Hz); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ -71.87(s); **HRMS (ESI)**: calcd. for $C_{11}H_{10}F_3N_2^+$ $[M+H]^+$ 227.0791, found 227.0784.

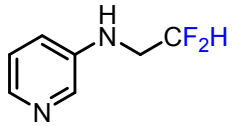
***N*-(2,2,2-trifluoroethyl)-*1H*-indol-5-amine (9f)**



Purified by flash column chromatography (petroleum ether / AcOEt = 5:1), white solid (45.0 mg, 84% yield), m.p. 126-127 ℃; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.29 – 7.21 (m, 1H), 7.15 (t, *J* = 2.8 Hz, 1H), 6.95 (d, *J* = 2.3 Hz, 1H), 6.68 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.52 – 6.36 (m, 1H), 3.79 (q, *J* = 9.1

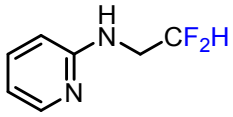
Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 140.4, 130.9, 128.8, 125.5 (q, *J* = 279.8 Hz), 125.0, 112.2, 111.9, 103.5, 102.0, 47.9 (q, *J* = 33.0 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -72.10 (t, *J* = 8.9 Hz); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) *δ* -72.10 (s); **HRMS (ESI)**: calcd. for $C_{10}H_{10}F_3N_2^+$ $[M+H]^+$ 215.0791, found 215.0783.

***N*-(2,2-difluoroethyl)pyridin-3-amine (10a)**



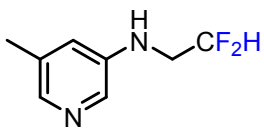
Purified by flash column chromatography (petroleum ether / EtOAc = 2:3), brown liquid (33.2 mg, 84% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.20 – 7.89 (m, 2H), 7.12 (dd, *J* = 8.3, 4.6 Hz, 1H), 6.95 (ddd, *J* = 8.3, 3.0, 1.3 Hz, 1H), 5.92 (tt, *J* = 55.8, 4.0 Hz, 1H), 4.09 (s, 1H), 3.55 (tdd, *J* = 14.5, 6.7, 4.0 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 143.1, 140.1, 136.3, 123.9, 119.1, 114.4 (t, *J* = 242.2 Hz), 46.1 (t, *J* = 26.0 Hz). (Consistent with previous reported values[8].)

***N*-(2,2-difluoroethyl)pyridin-2-amine (10b)**



Purified by flash column chromatography (petroleum ether / EtOAc = 20:1), colorless and transparent liquid (22.5 mg, 57% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 4.4 Hz, 1H), 7.42 (ddd, *J* = 8.7, 7.1, 1.9 Hz, 1H), 6.64 (ddd, *J* = 7.2, 5.1, 1.0 Hz, 1H), 6.46 (dd, *J* = 8.3, 1.0 Hz, 1H), 5.97 (tt, *J* = 56.6, 4.3 Hz, 1H), 4.66 (s, 1H), 3.78 (tdd, *J* = 14.6, 6.5, 4.3 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.6, 148.0, 137.6, 114.6 (t, *J* = 241.7 Hz), 114.1, 108.4, 44.1 (t, *J* = 26.6 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -123.14 (dt, *J* = 56.5, 14.7 Hz); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) *δ* -123.14 (s); **HRMS (ESI)**: calcd. for $C_7H_9F_2N_2^+$ $[M+H]^+$ 159.0728, found 159.0726.

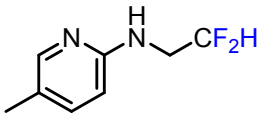
***N*-(2,2-difluoroethyl)-5-methylpyridin-3-amine (10c)**



Purified by flash column chromatography (petroleum ether / EtOAc = 1:1), white solid (40.2 mg, 93% yield), m.p. 43-44 ℃; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 – 7.80 (m, 2H), 6.76 (t, *J* = 2.1 Hz, 1H), 5.91 (tt, *J* = 55.8, 4.1 Hz, 1H), 4.08 (s, 1H), 3.53 (tdd, *J* = 14.5, 6.5, 4.1 Hz, 2H), 2.26 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 142.8, 140.7, 133.7, 133.5, 119.9, 114.5 (t, *J* = 242.1 Hz), 46.1 (t, *J* = 26.0 Hz),

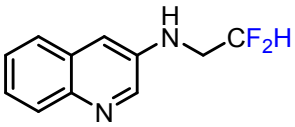
18.6; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -122.65 (dt, J = 55.6, 14.2 Hz); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ -122.65 (s); **HRMS (ESI)**: calcd. for $C_8H_{11}F_2N_2^+$ $[M+H]^+$ 173.0885, found 173.0884.

***N*-(2,2-difluoroethyl)-5-methylpyridin-2-amine (10d)**



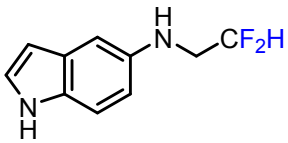
Purified by flash column chromatography (petroleum ether / EtOAc = 5:1), pale yellow liquid (34.8 mg, 81% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.25 (dd, J = 8.3, 2.4 Hz, 1H), 6.39 (d, J = 8.4 Hz, 1H), 5.95 (tt, J = 56.6, 4.3 Hz, 1H), 4.60 (s, 1H), 3.73 (tdd, J = 14.6, 6.5, 4.3 Hz, 2H), 2.17 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 155.7 147.3, 138.7, 122.9, 114.7 (t, J = 241.2 Hz), 108.1, 44.3 (t, J = 26.5 Hz), 17.5; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -123.11 (dt, J = 56.6, 14.7 Hz); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ -123.11 (s); **HRMS (ESI)**: calcd. for $C_8H_{11}F_2N_2^+$ $[M+H]^+$ 173.0885, found 173.0882.

***N*-(2,2-difluoroethyl)quinolin-3-amine (10e)**



Purified by flash column chromatography (petroleum ether / EtOAc = 3:1), white solid (40.5 mg, 77% yield), m.p. 73-74 ℃; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.47 (d, J = 2.9 Hz, 1H), 7.96 (dd, J = 6.2, 3.4 Hz, 1H), 7.62 (dd, J = 6.2, 3.4 Hz, 1H), 7.45 (dt, J = 6.3, 3.5 Hz, 2H), 7.10 (d, J = 2.8 Hz, 1H), 5.98 (tt, J = 55.8, 4.1 Hz, 1H), 4.42 (s, 1H), 3.62 (tdd, J = 14.5, 6.6, 4.1 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 143.1, 142.7, 140.4, 129.1, 129.1, 126.2, 125.8, 114.4 (t, J = 242.3 Hz), 111.0 , 46.1 (t, J = 26.1 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -122.23 (dt, J = 55.8, 14.5 Hz); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ -122.23(s); **HRMS (ESI)**: calcd. for $C_{11}H_{11}F_2N_2^+$ $[M+H]^+$ 209.0885, found 209.0879.

***N*-(2,2-difluoroethyl)-*1H*-indol-5-amine (10f)**

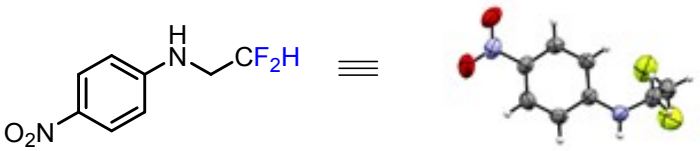


Purified by flash column chromatography (petroleum ether / EtOAc = 5:1), brown solid (39.4 mg, 80% yield), m.p. 111-112 ℃; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.23 (d, J = 8.6 Hz, 1H), 7.15 (t, J = 2.8 Hz, 1H), 6.92 (d, J = 2.3 Hz, 1H), 6.67 (dd, J = 8.6, 2.3 Hz, 1H), 6.43 (t, J = 2.8 Hz, 1H), 5.98 (tt, J = 56.4, 4.3 Hz, 1H), 3.57 (td, J = 14.4, 4.4 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 140.8,

130.8, 128.8, 125.0 , 115.0 (t, J = 241.3 Hz), 112.4, 112.0, 103.1, 102.0, 48.1 (t, J = 25.8 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -122.70 (dt, J = 56.3, 14.4 Hz); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ -122.70(s); **HRMS (ESI)**: calcd. for $C_{10}H_{11}F_2N_2^+$ $[M+H]^+$ 197.0885, found 197.0881.

5. X-ray structures of 7f and 9e

compound 7f (CCDC 1914999)



compound 9e (CCDC 1915000)

6. Reference

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2. S. Ueda and S. L. Buchwald, Angew. Chem. Int. Ed. , 2012, 51, 10364-10367.
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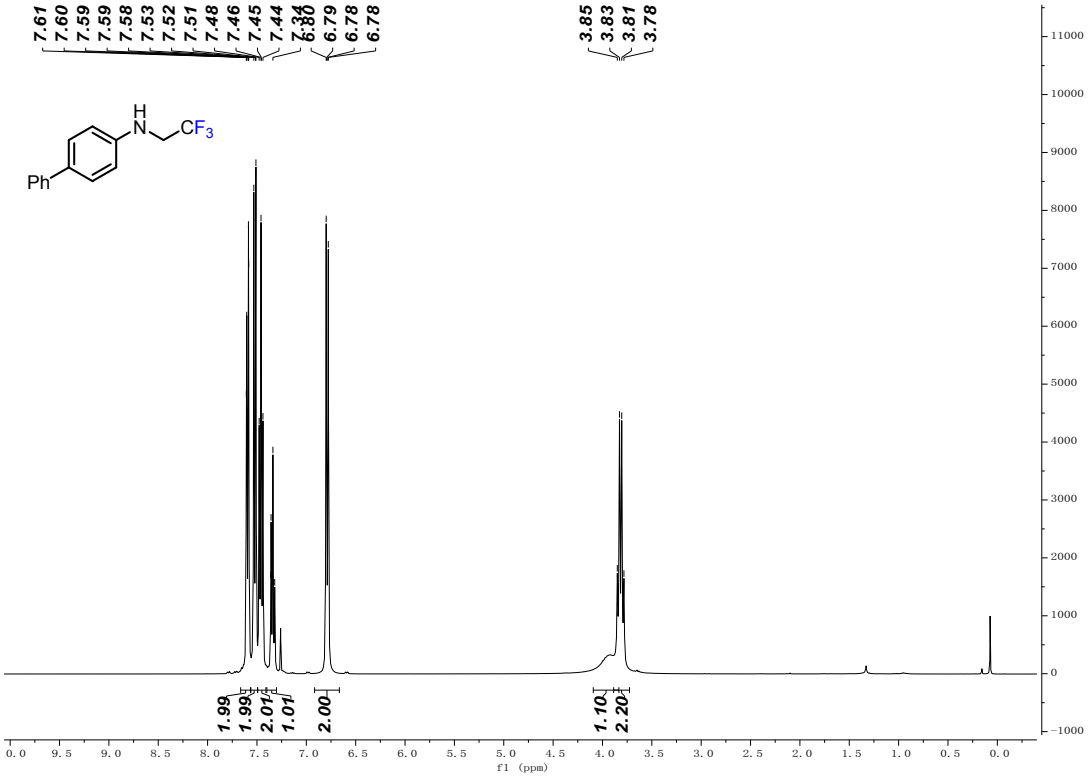
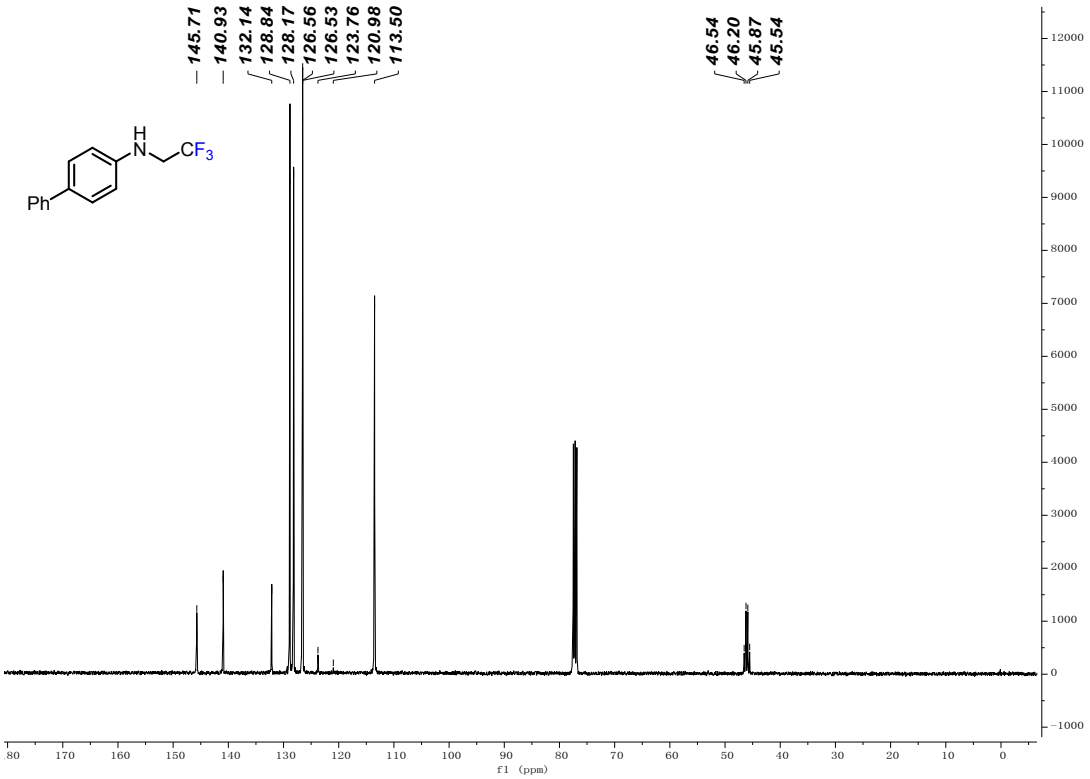
7. NMR spectra of novel compounds

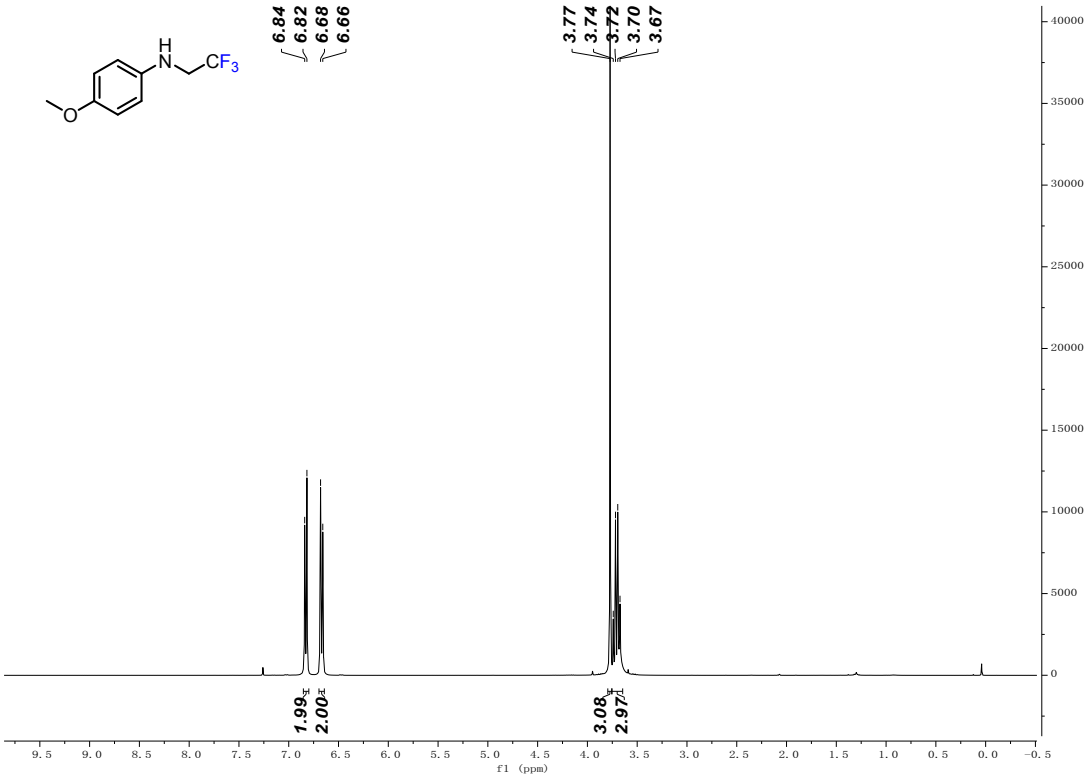
^{1}H NMR ($CDCl_3$, 400 MHz) of **3a**



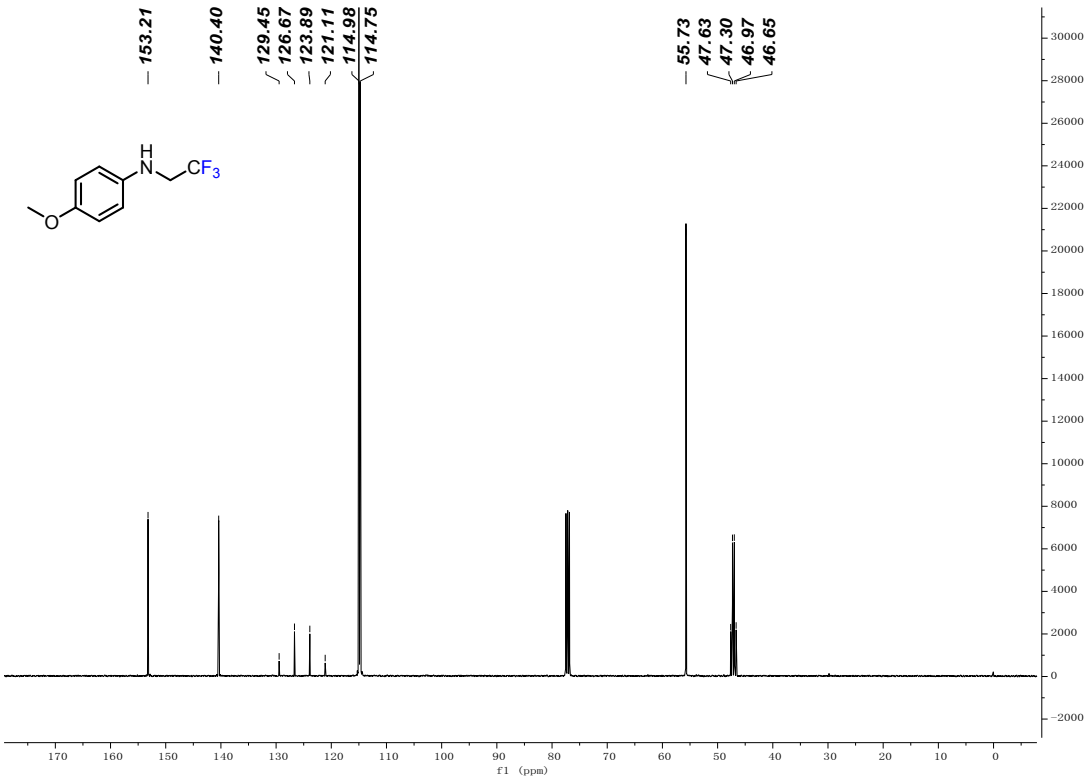
^{13}C NMR ($CDCl_3$, 400 MHz) of **3a**



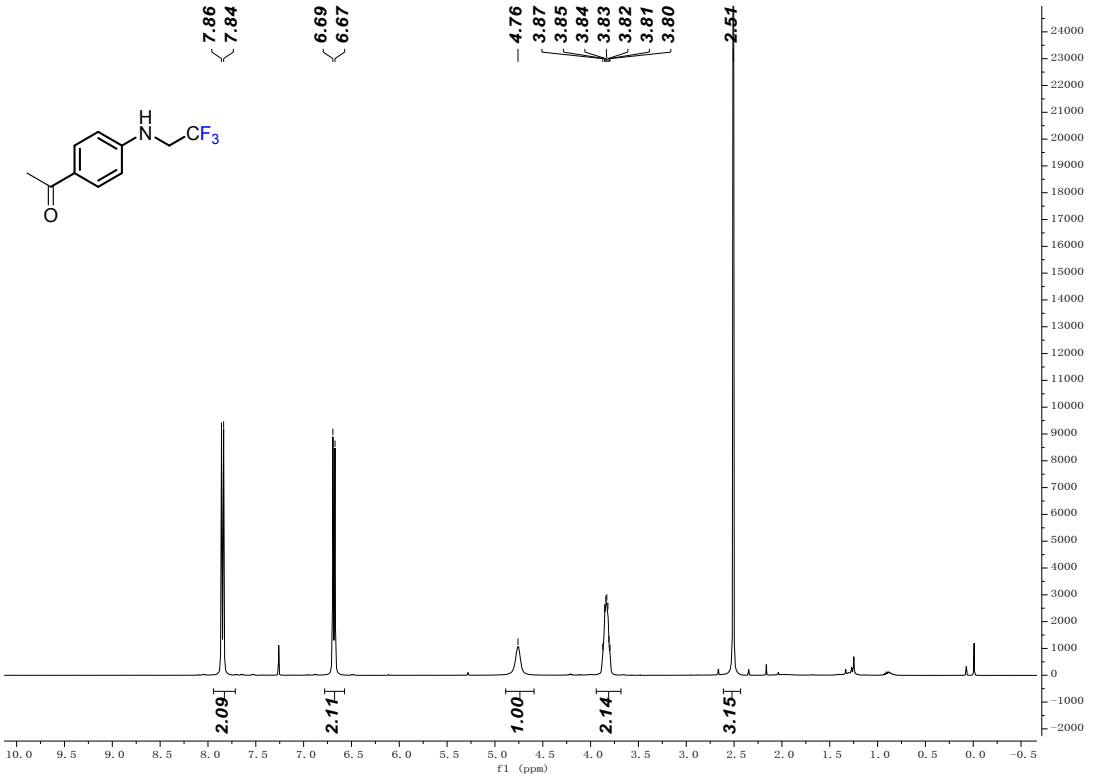
^{1}H NMR ($CDCl_3$, 400 MHz) of **3b**



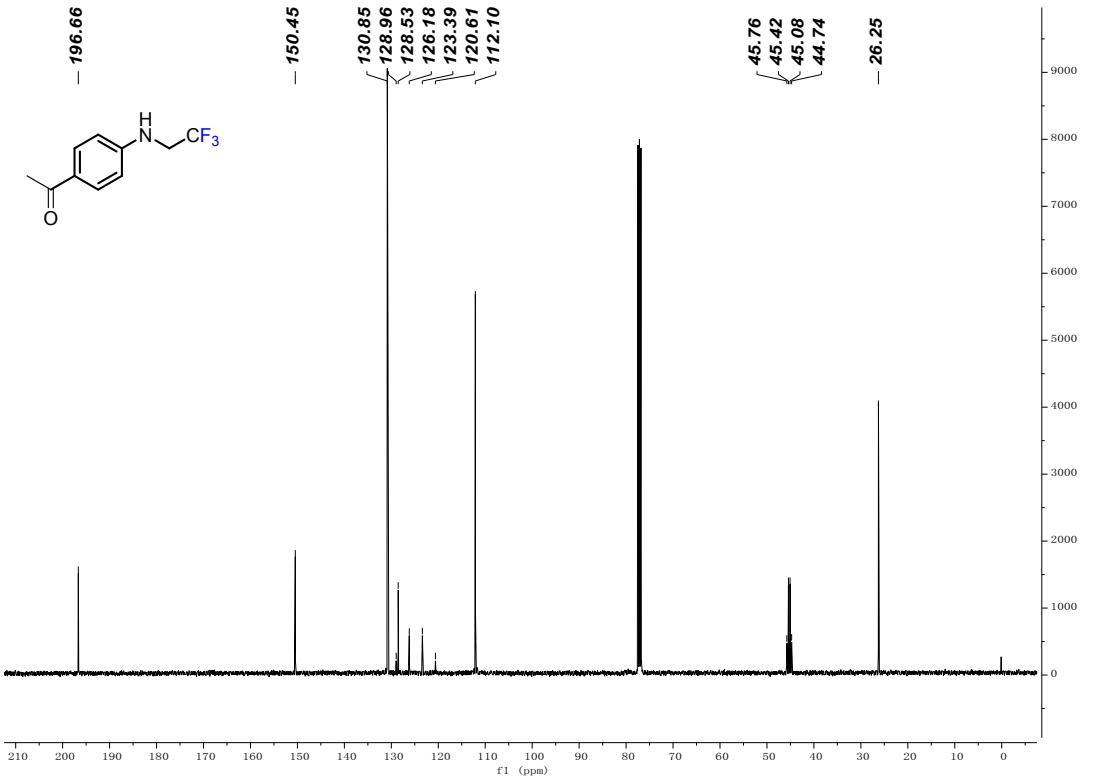
^{13}C NMR ($CDCl_3$, 400 MHz) of **3b**



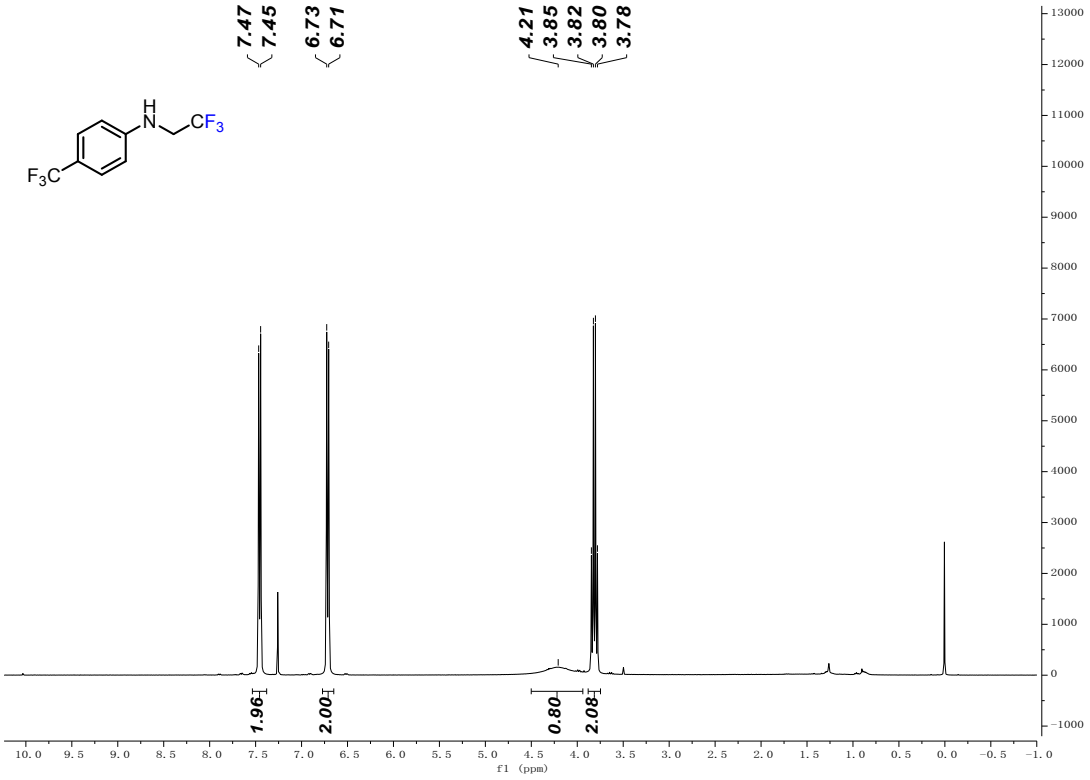
^{1}H NMR ($CDCl_3$, 400 MHz) of **3c**



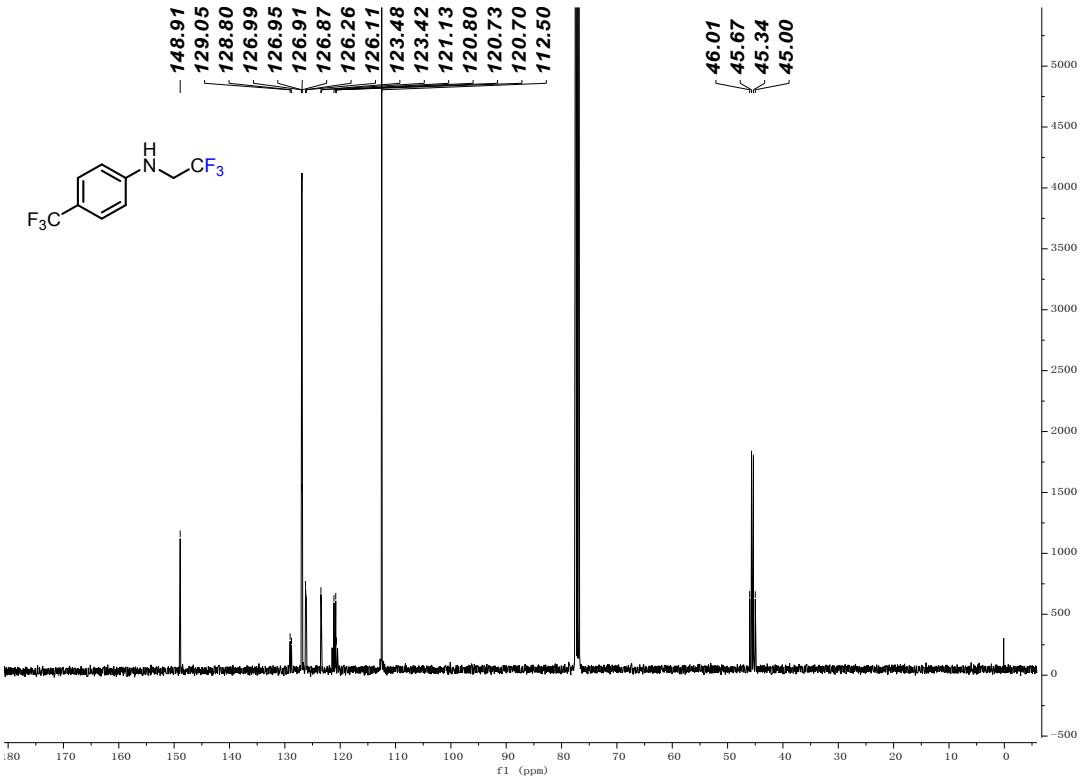
^{13}C NMR ($CDCl_3$, 400 MHz) of **3c**



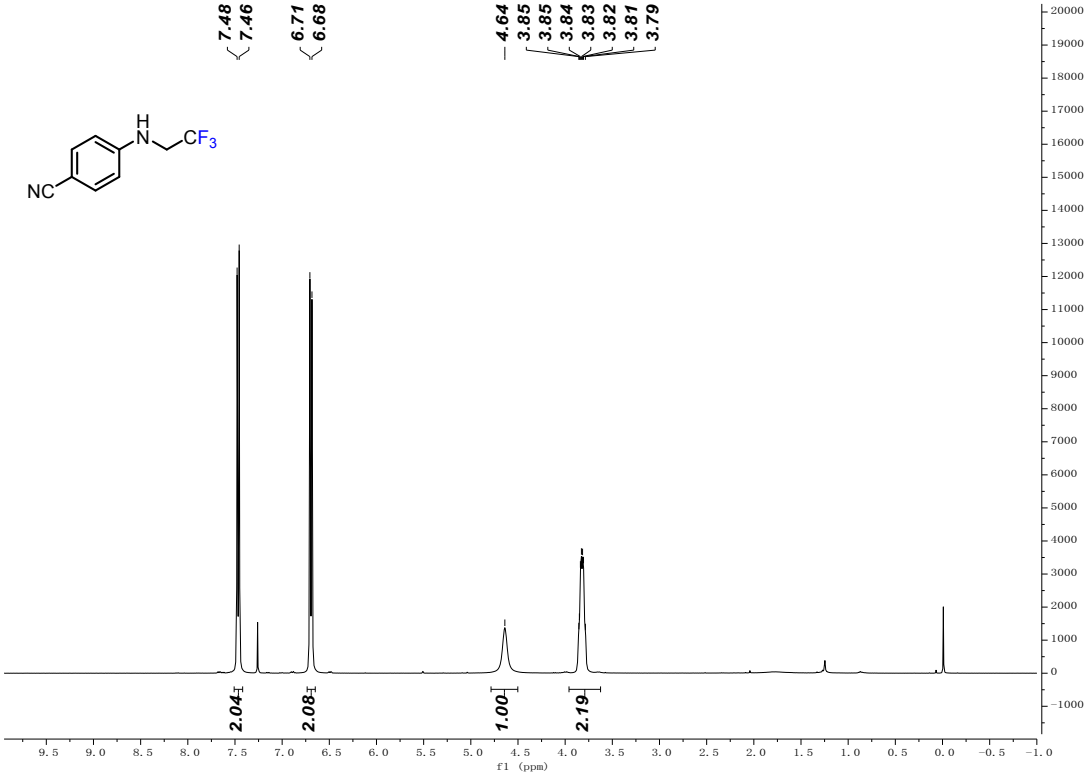
^{1}H NMR ($CDCl_3$, 400 MHz) of **3d**



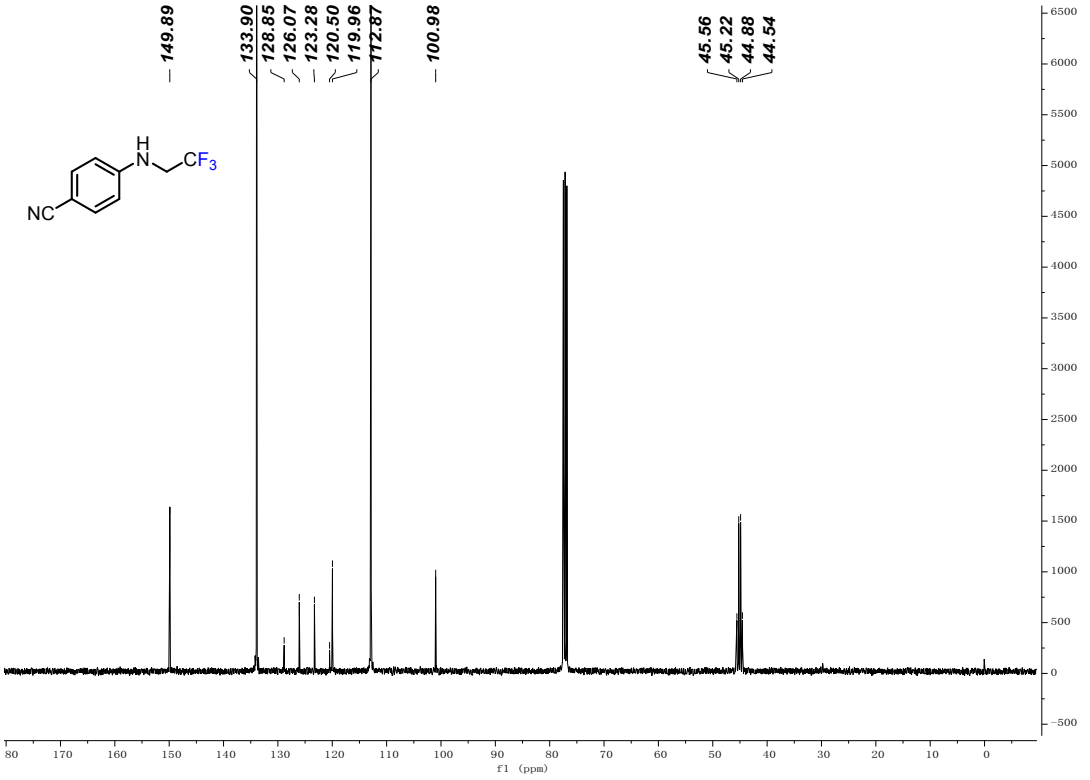
^{13}C NMR ($CDCl_3$, 400 MHz) of **3d**



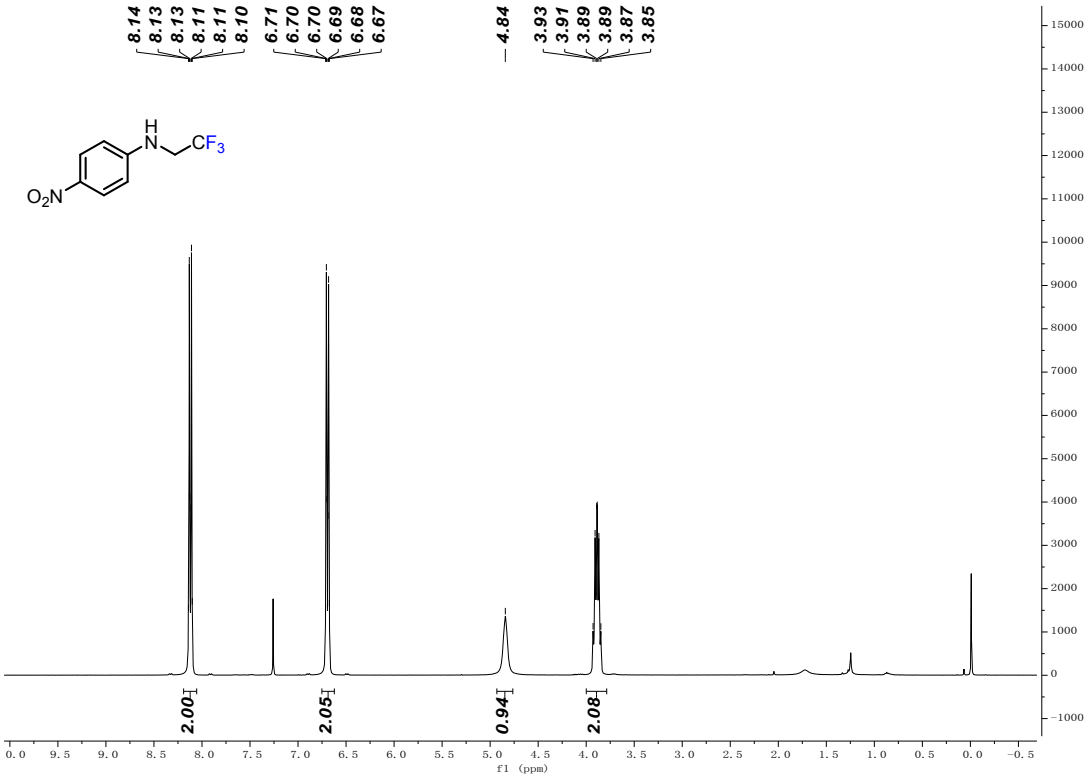
^{1}H NMR ($CDCl_3$, 400 MHz) of **3e**



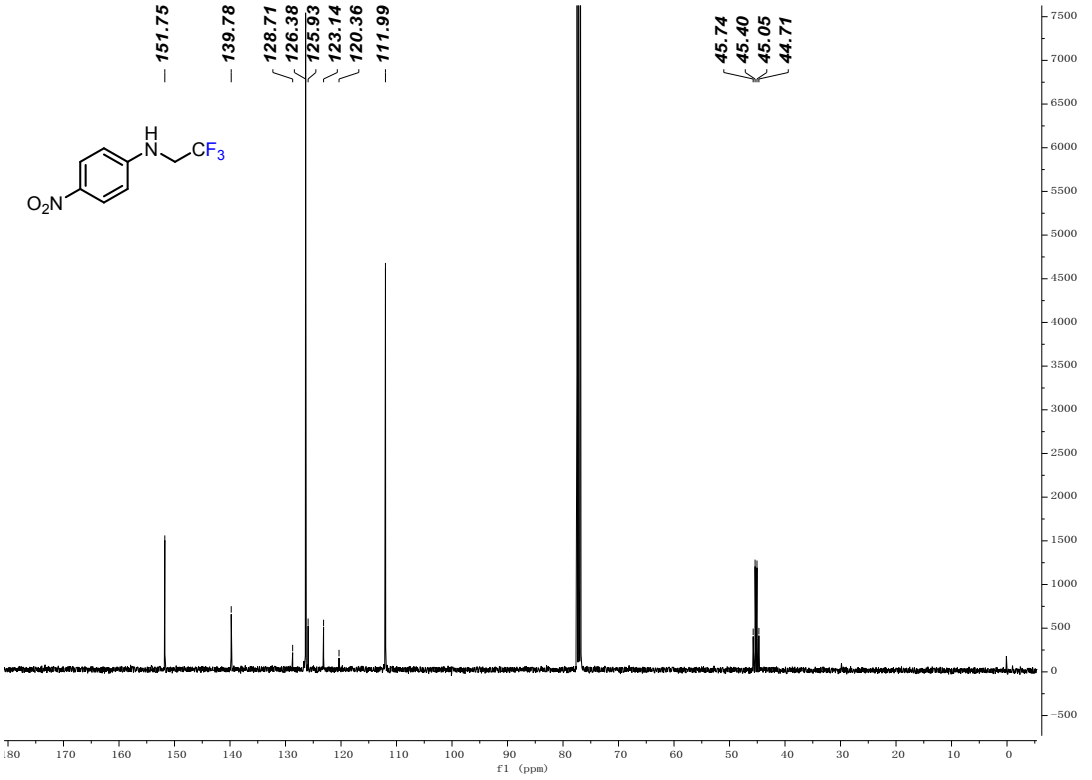
^{13}C NMR ($CDCl_3$, 400 MHz) of **3e**



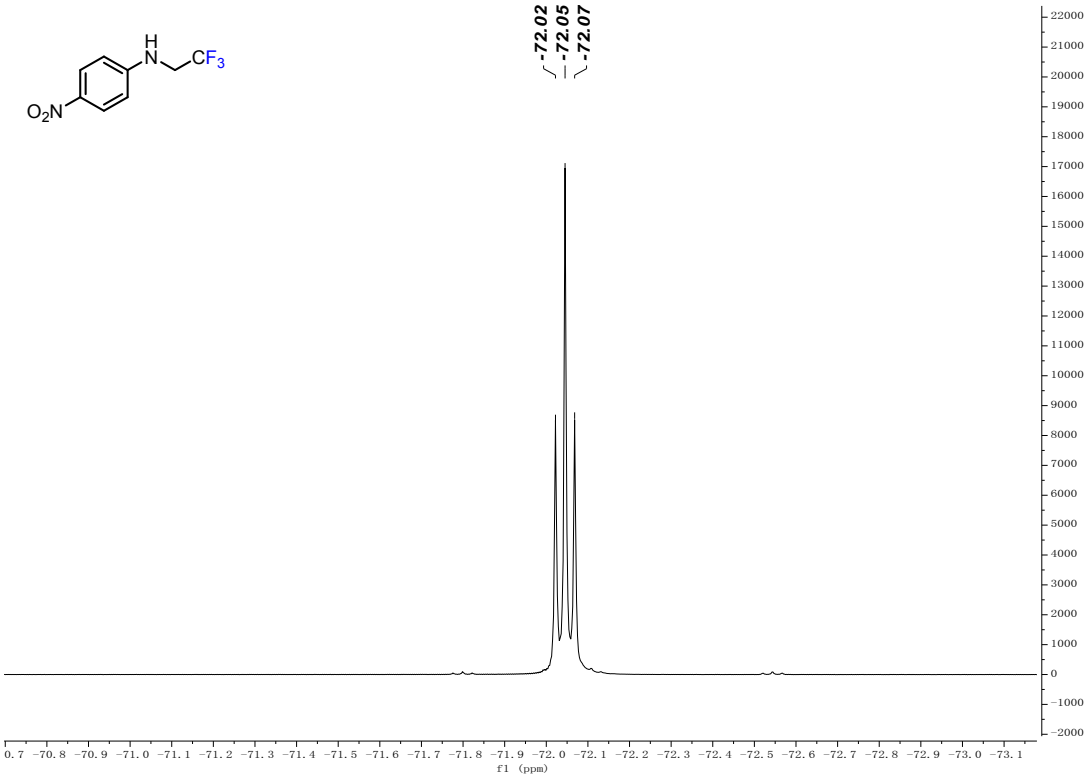
^{1}H NMR ($CDCl_3$, 400 MHz) of **3f**



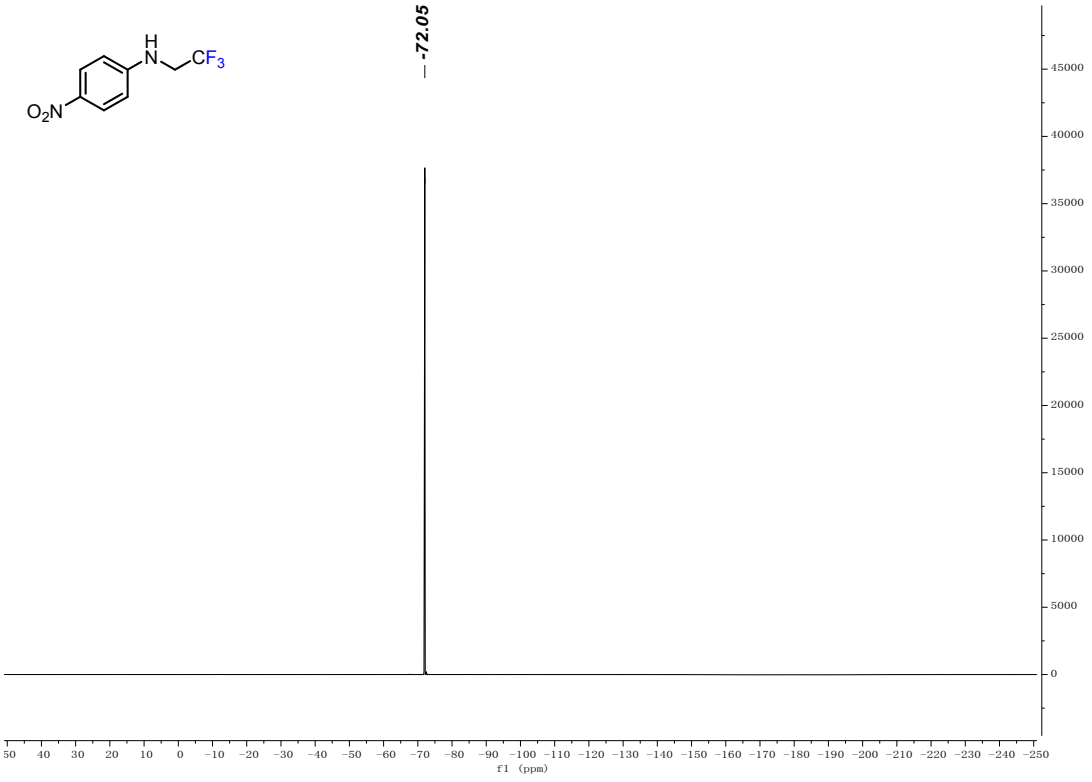
^{13}C NMR ($CDCl_3$, 400 MHz) of **3f**



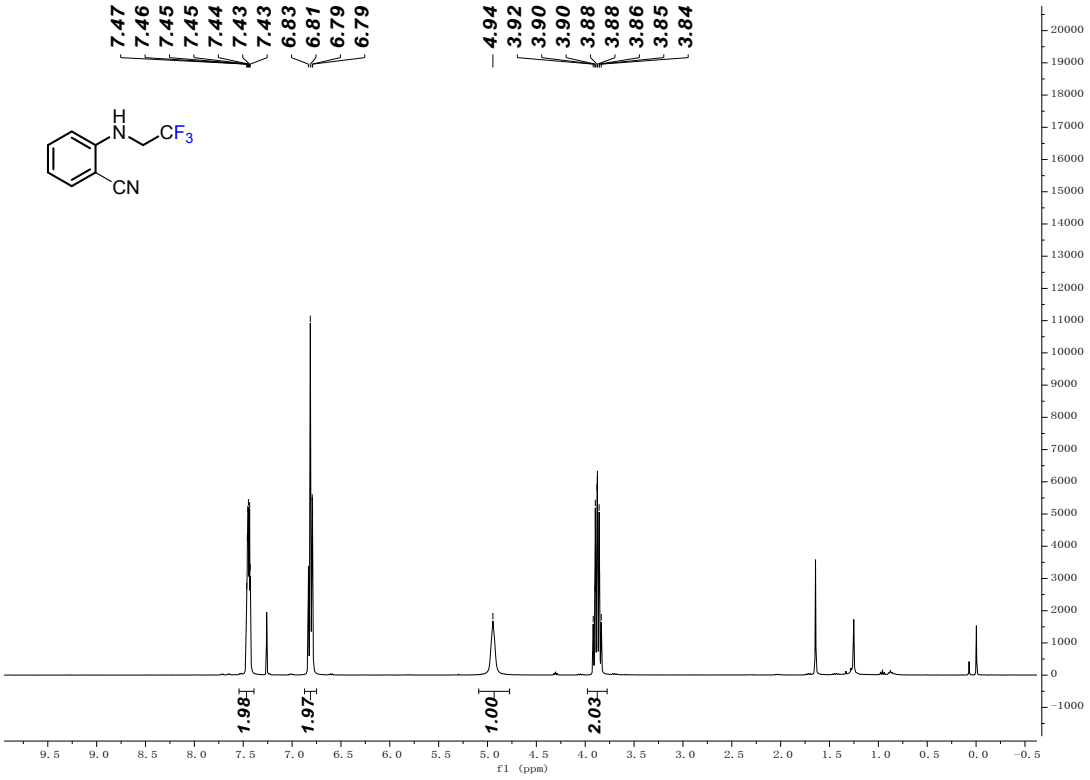
^{19}F NMR ($CDCl_3$, 376 MHz) of **3f**



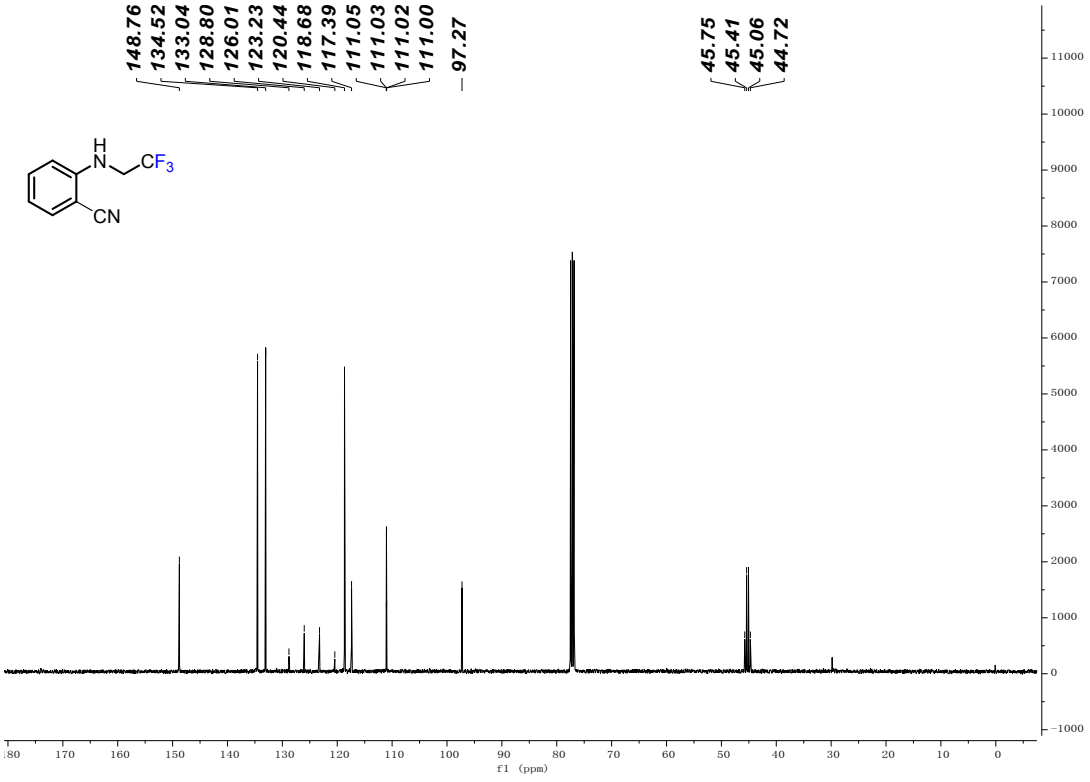
^{19}F {^{1}H} NMR ($CDCl_3$, 376 MHz) of **3f**



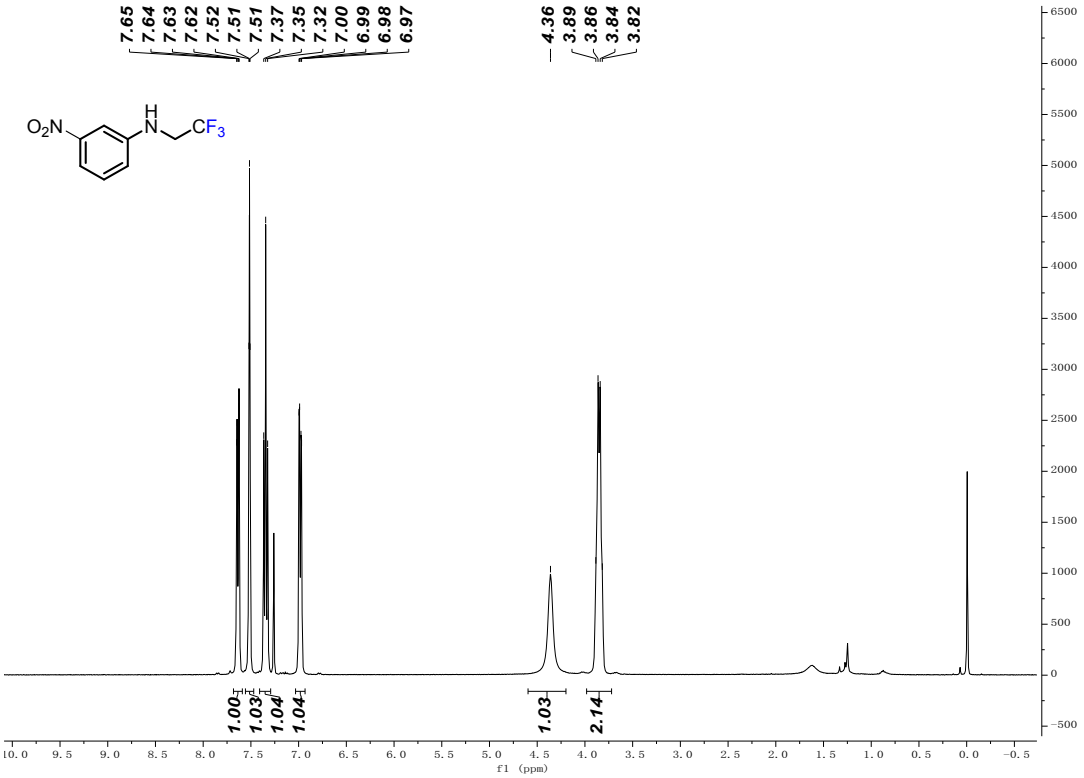
^{1}H NMR ($CDCl_3$, 400 MHz) of **3g**



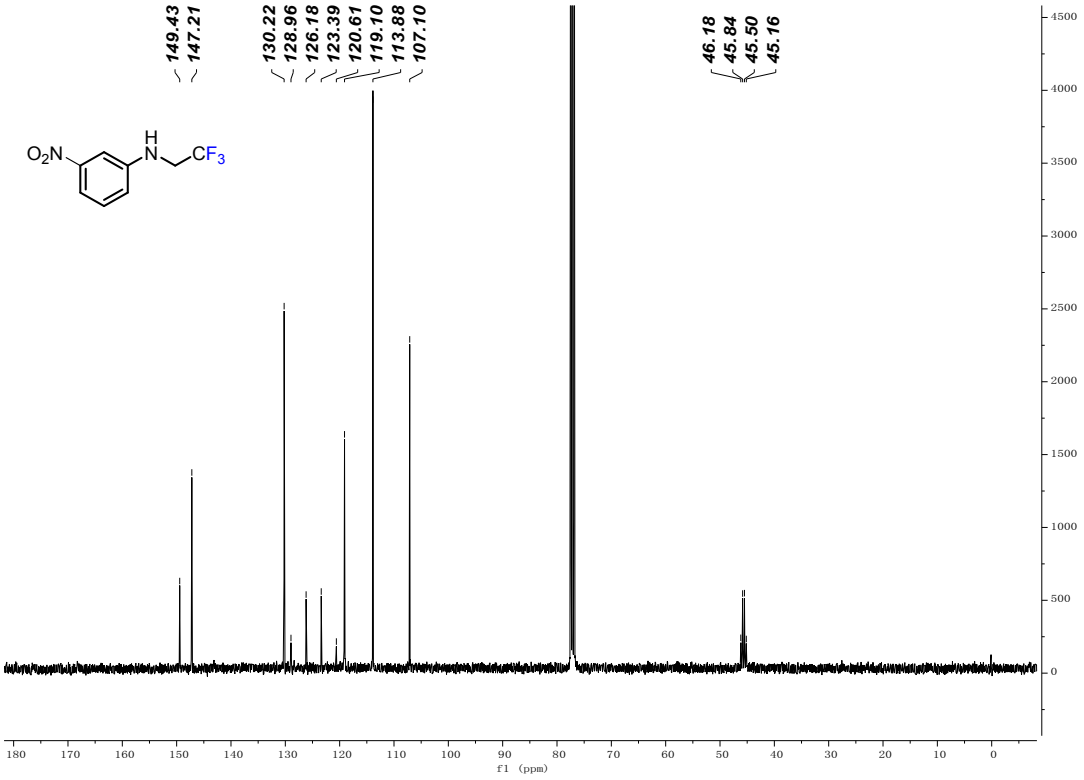
^{13}C NMR ($CDCl_3$, 400 MHz) of **3g**



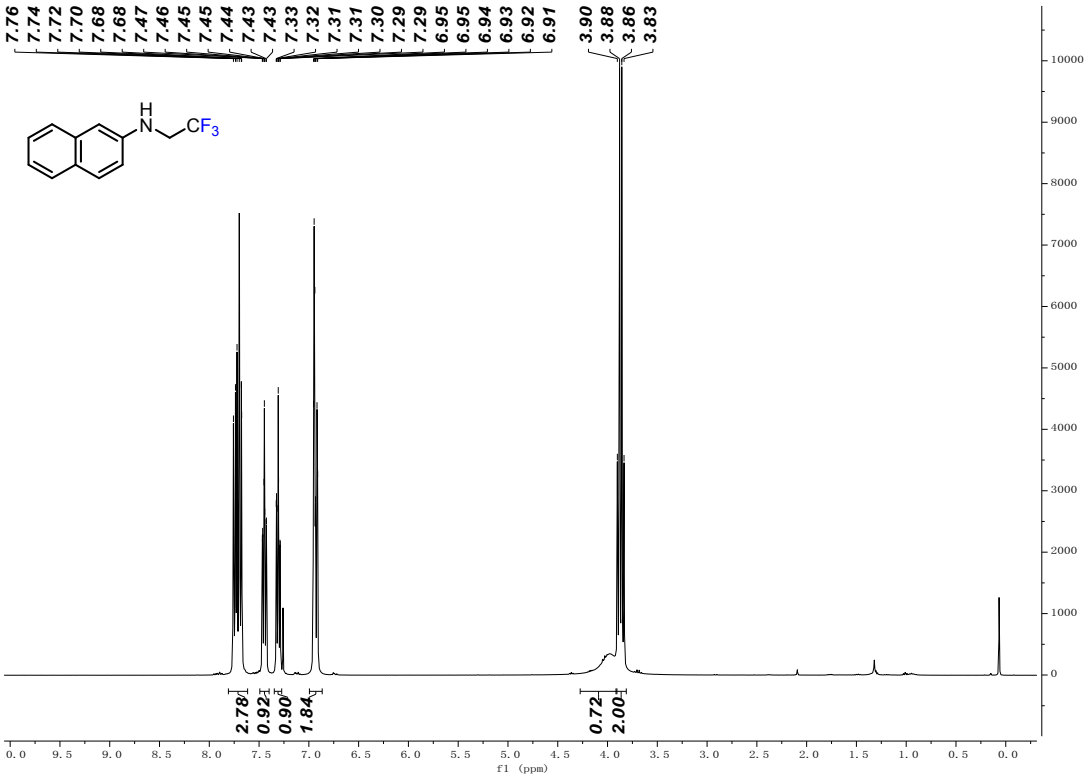
^{1}H NMR ($CDCl_3$, 400 MHz) of **3h**



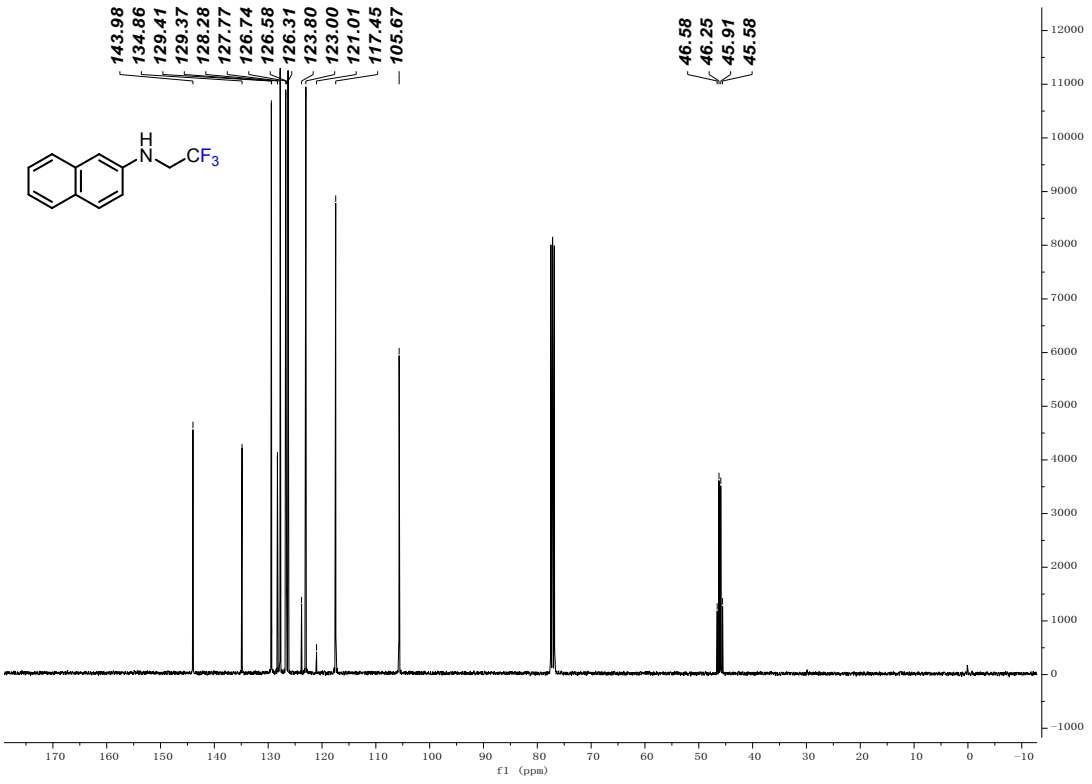
^{13}C NMR ($CDCl_3$, 400 MHz) of **3h**



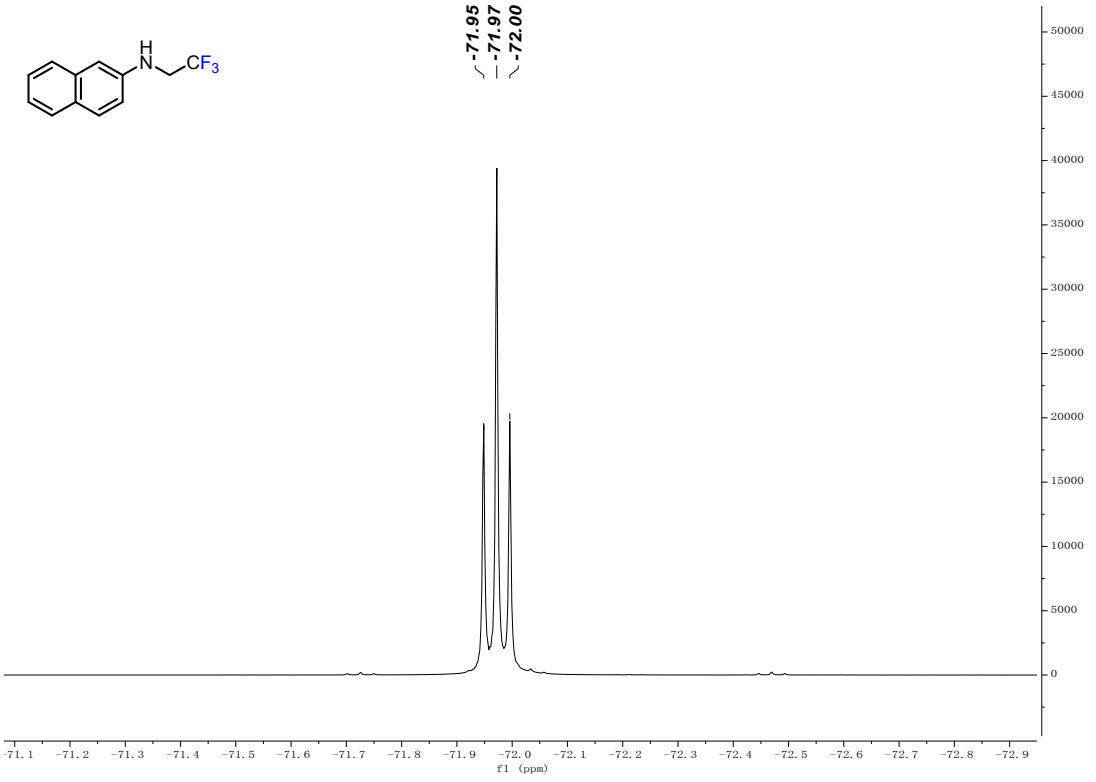
^{1}H NMR ($CDCl_3$, 400 MHz) of **3i**



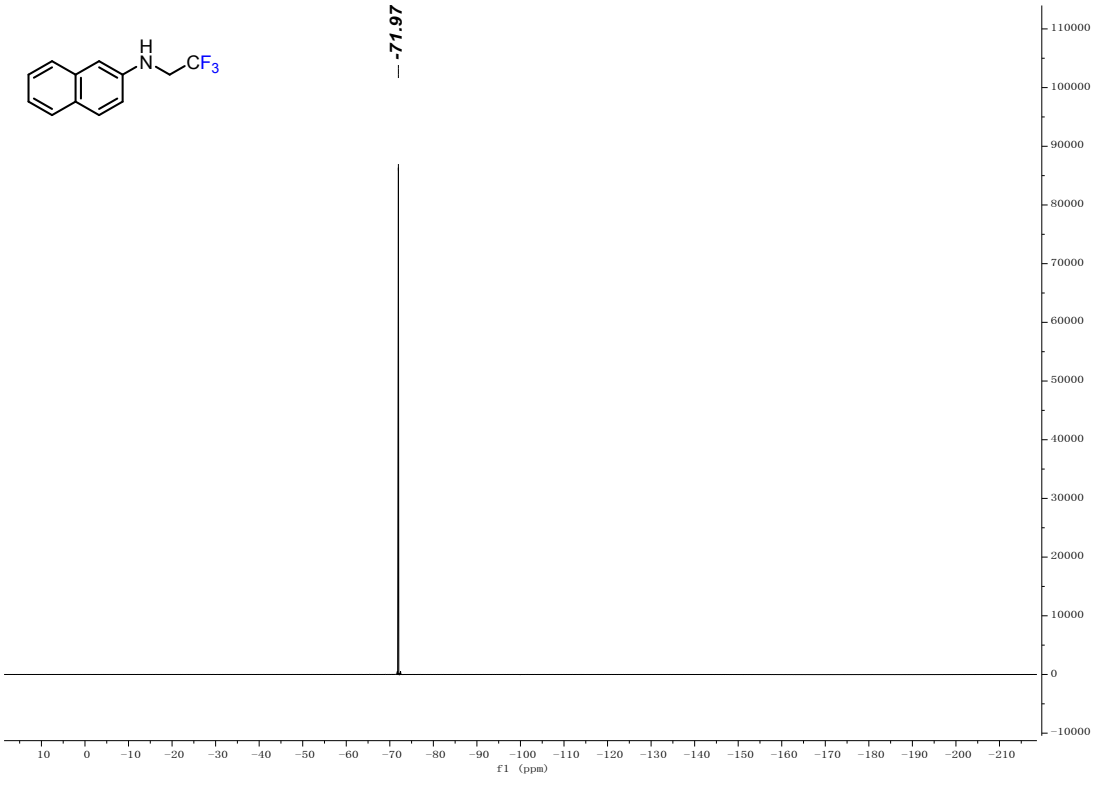
^{13}C NMR ($CDCl_3$, 400 MHz) of **3i**



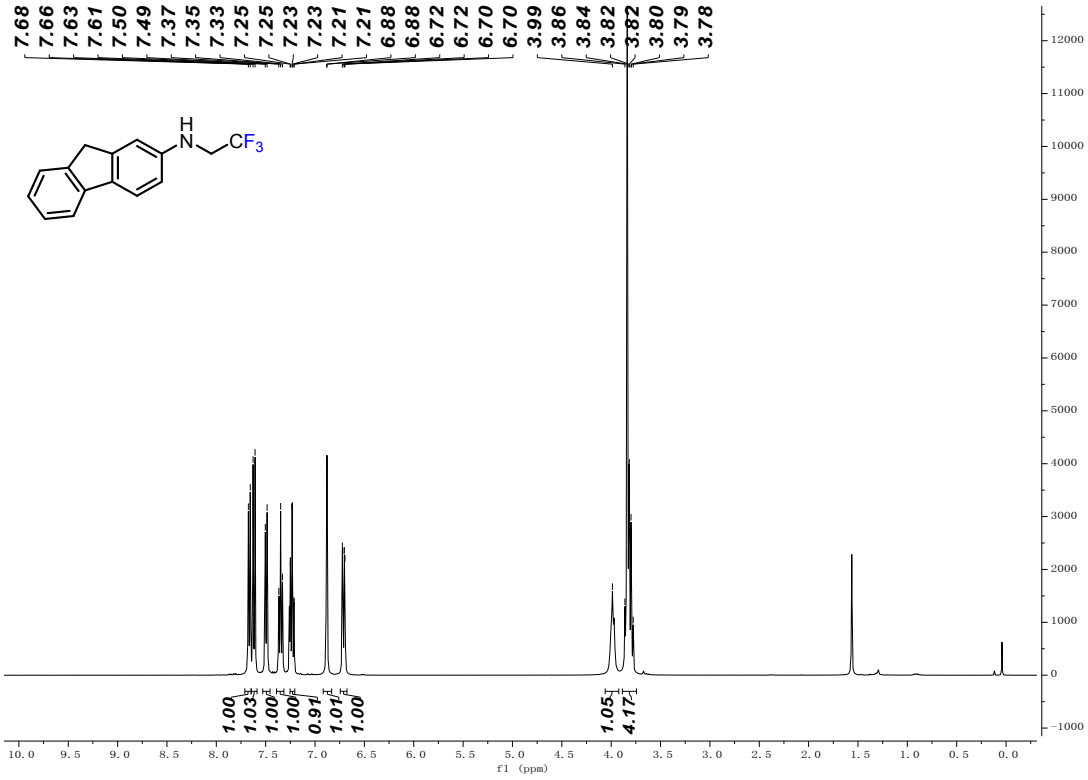
^{19}F NMR ($CDCl_3$, 376 MHz) of **3i**



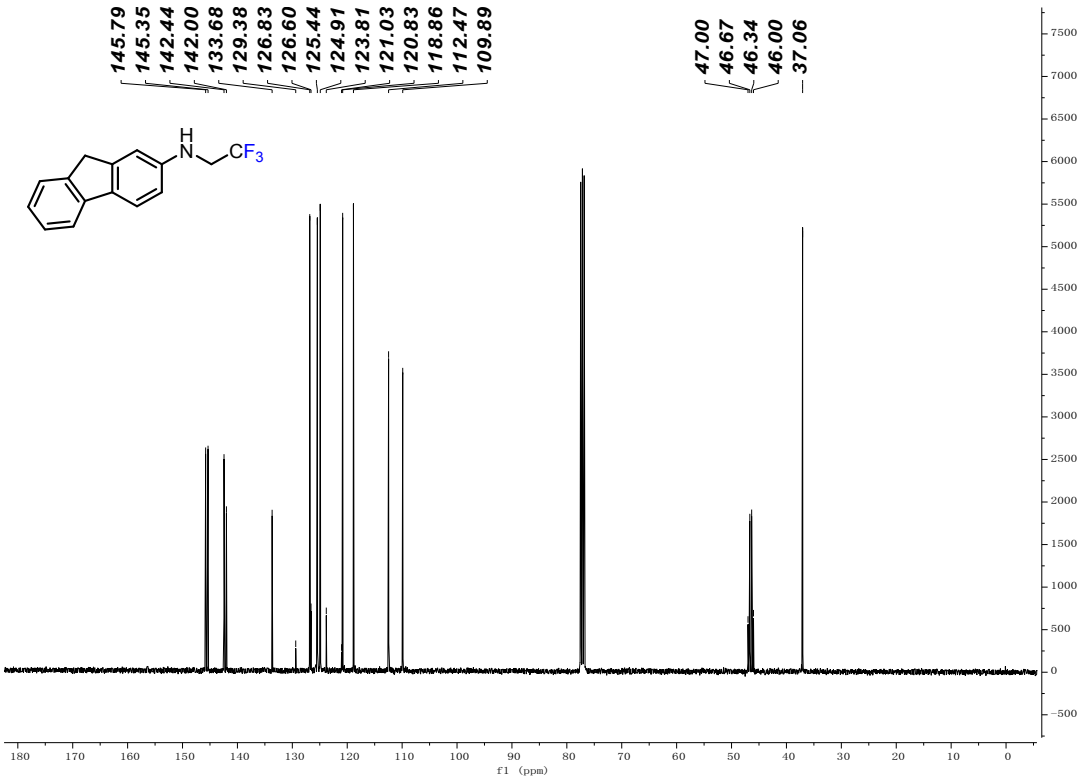
^{19}F {^{1}H} NMR ($CDCl_3$, 376 MHz) of **3i**



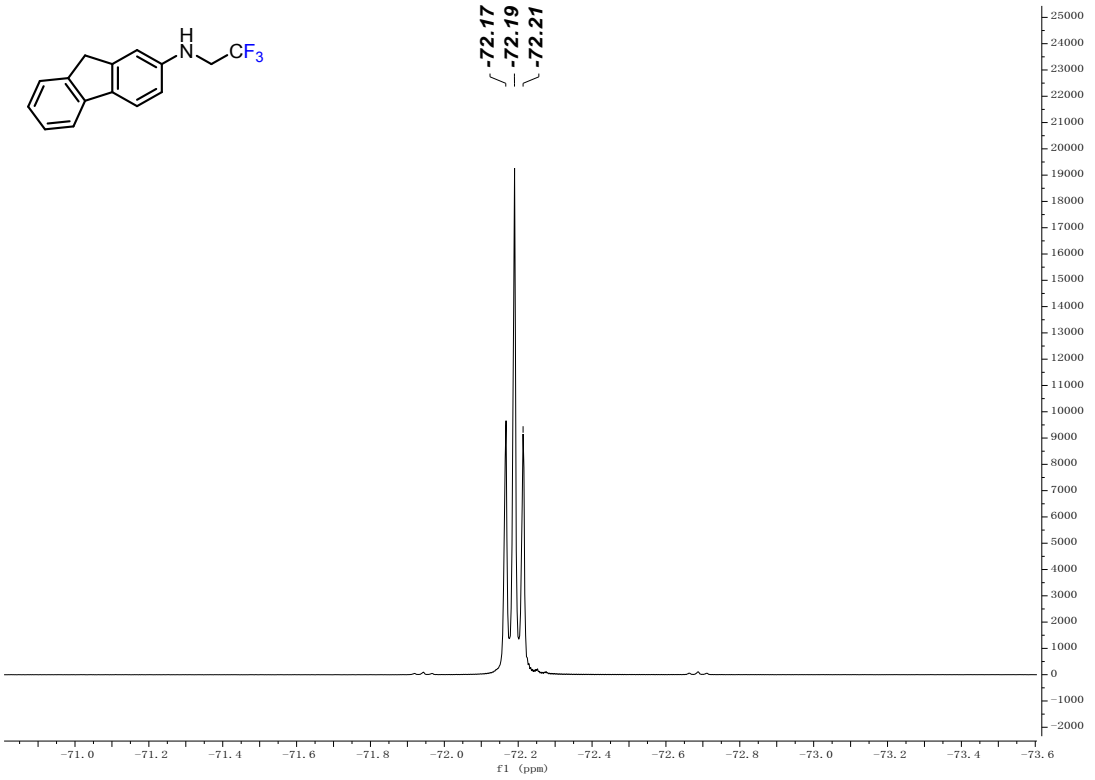
^{1}H NMR ($CDCl_3$, 400 MHz) of **3j**



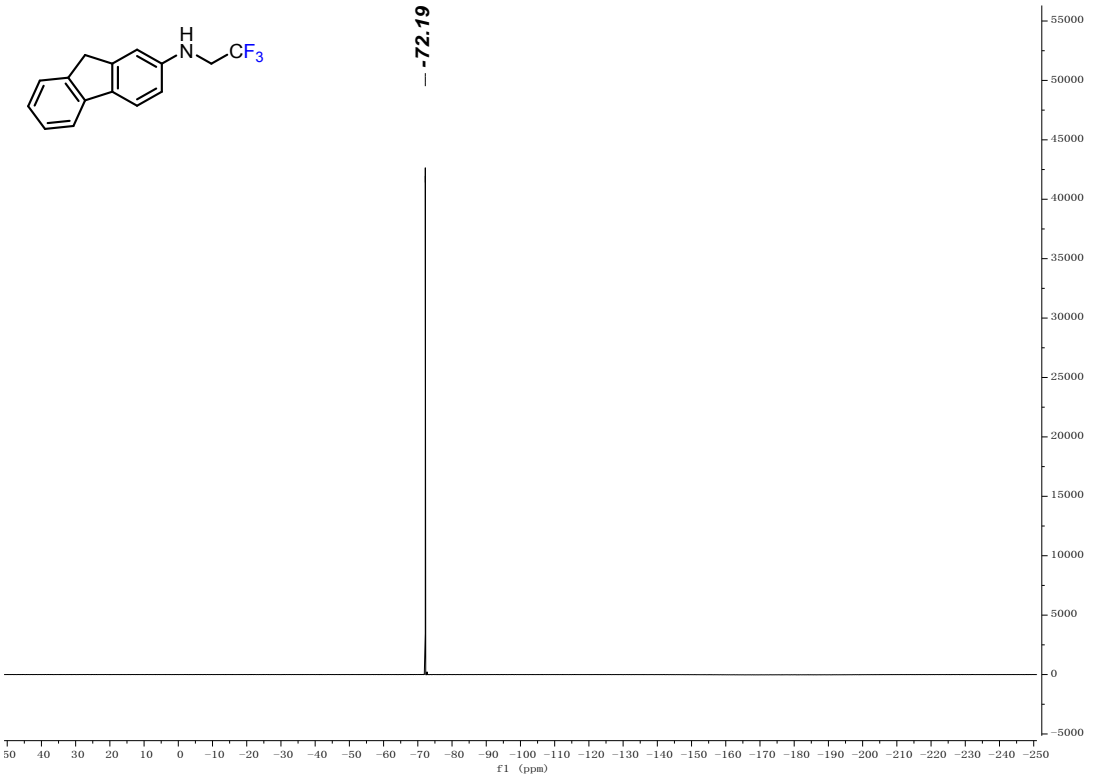
^{13}C NMR ($CDCl_3$, 400 MHz) of **3j**



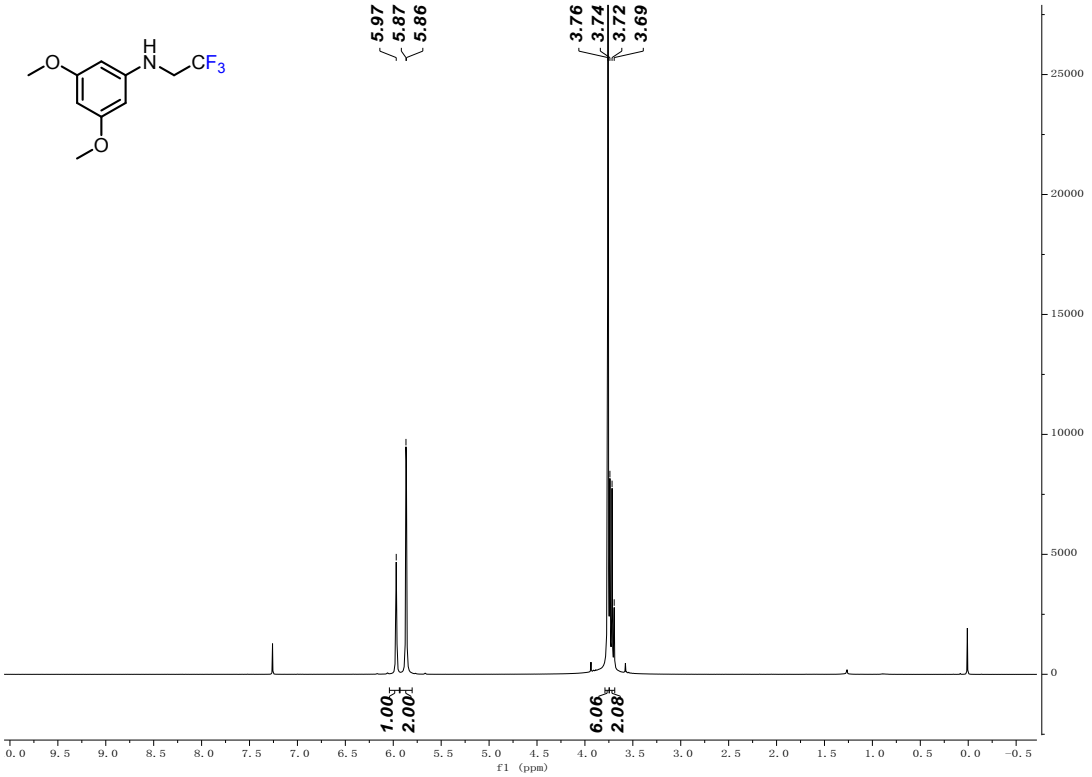
^{19}F NMR ($CDCl_3$, 376 MHz) of **3j**



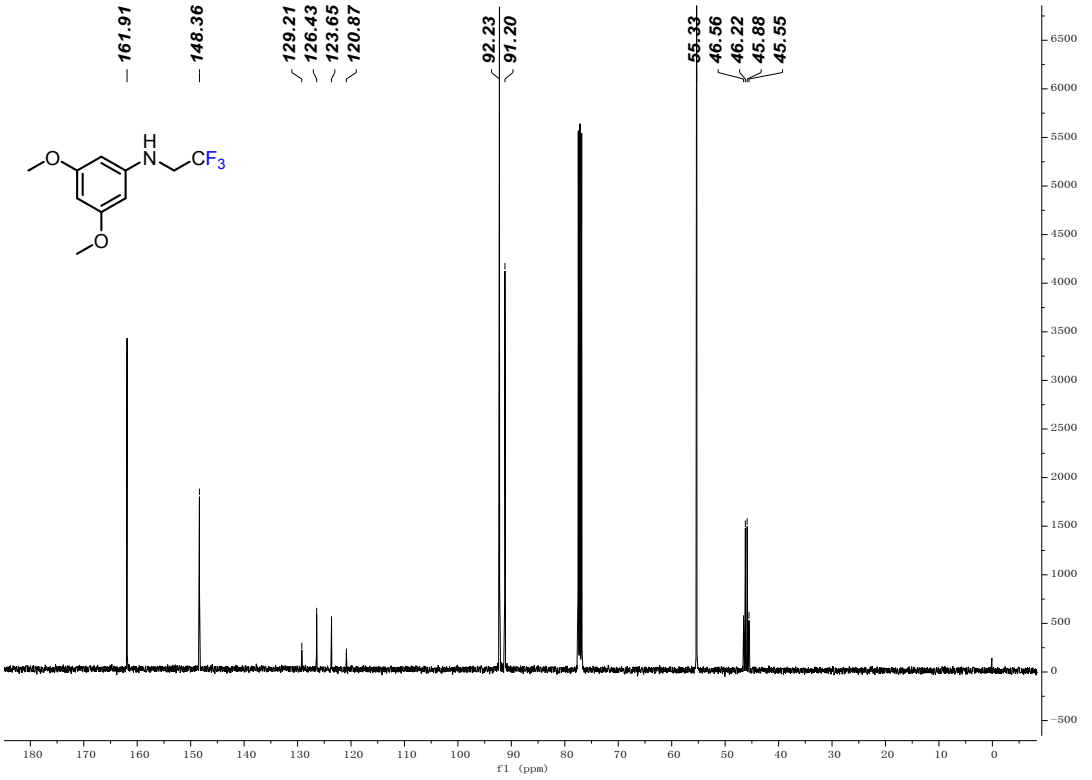
^{19}F {^{1}H} NMR ($CDCl_3$, 376 MHz) of **3j**



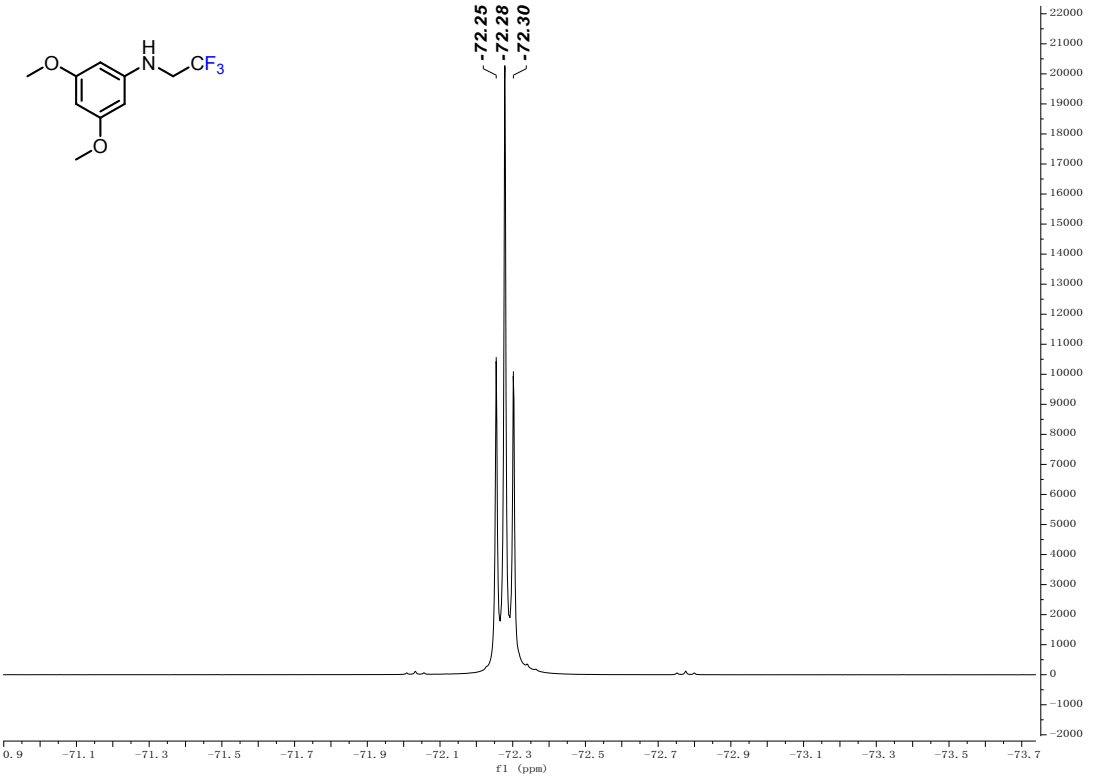
^{1}H NMR ($CDCl_3$, 400 MHz) of **3k**



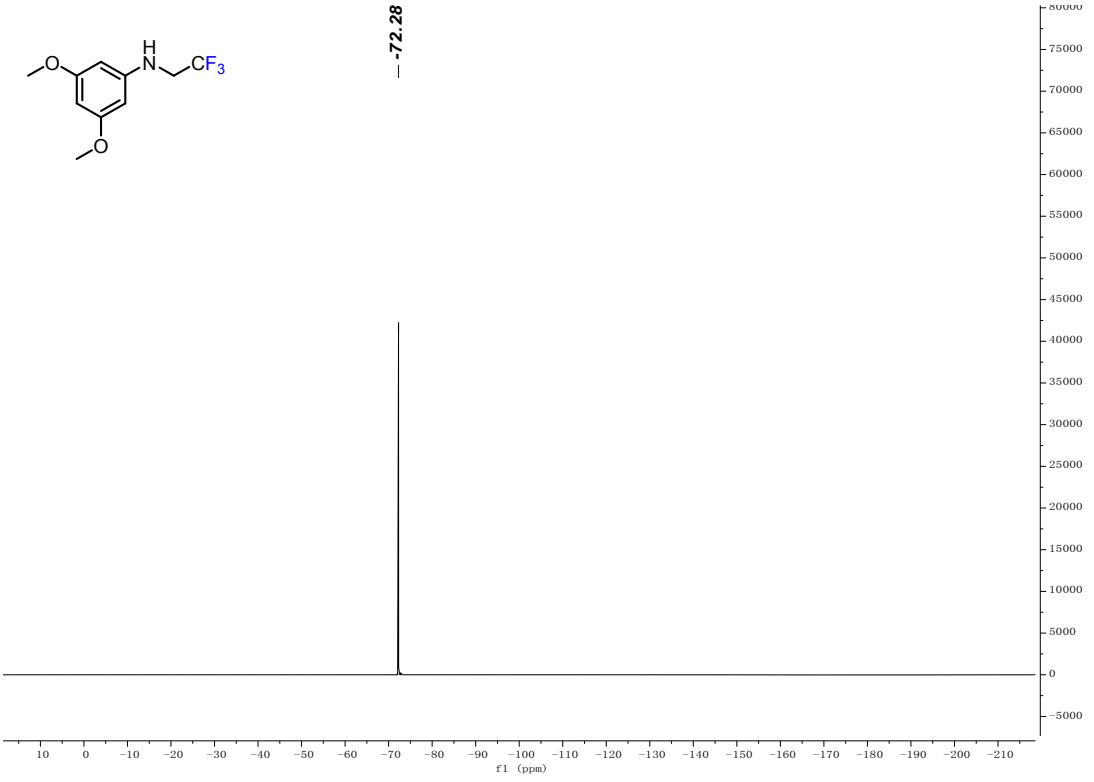
^{13}C NMR ($CDCl_3$, 400 MHz) of **3k**



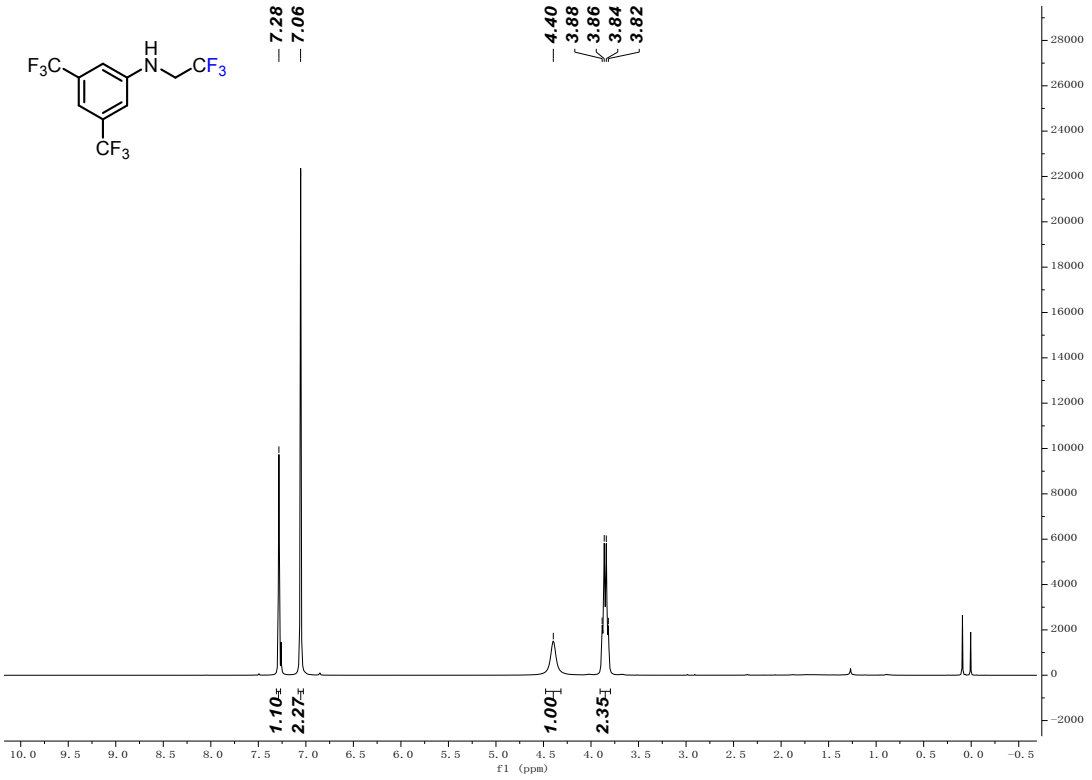
^{19}F NMR ($CDCl_3$, 376 MHz) of **3k**



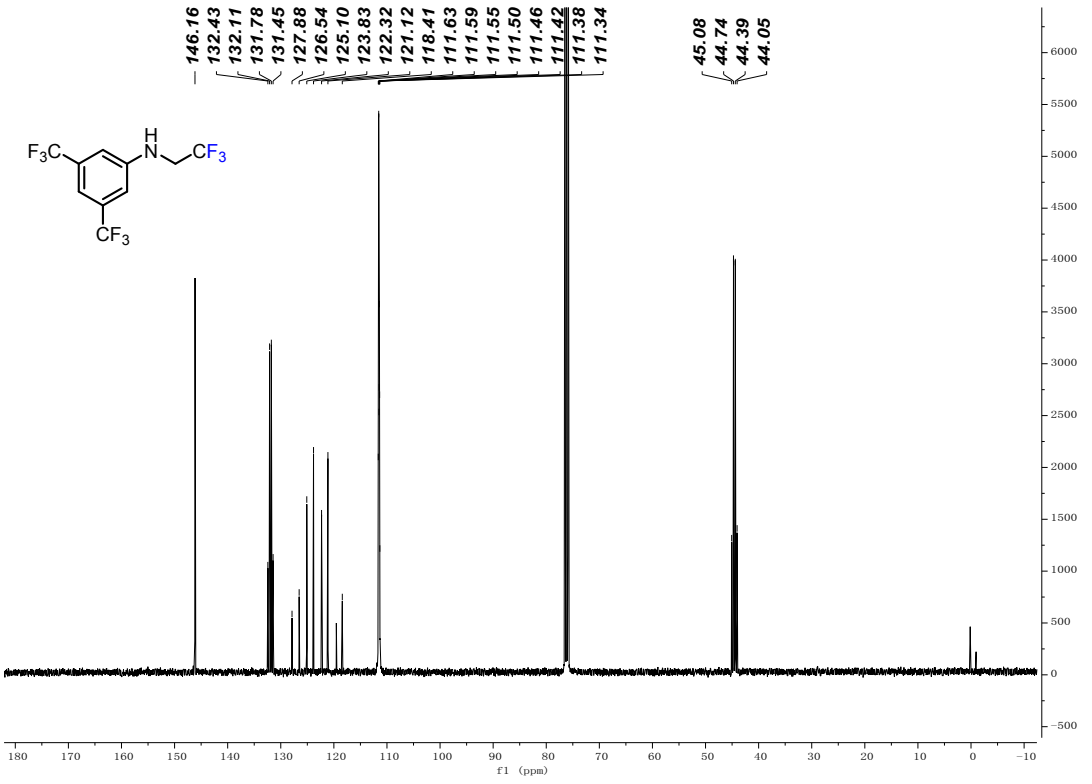
^{19}F {^{1}H} NMR ($CDCl_3$, 376 MHz) of **3k**



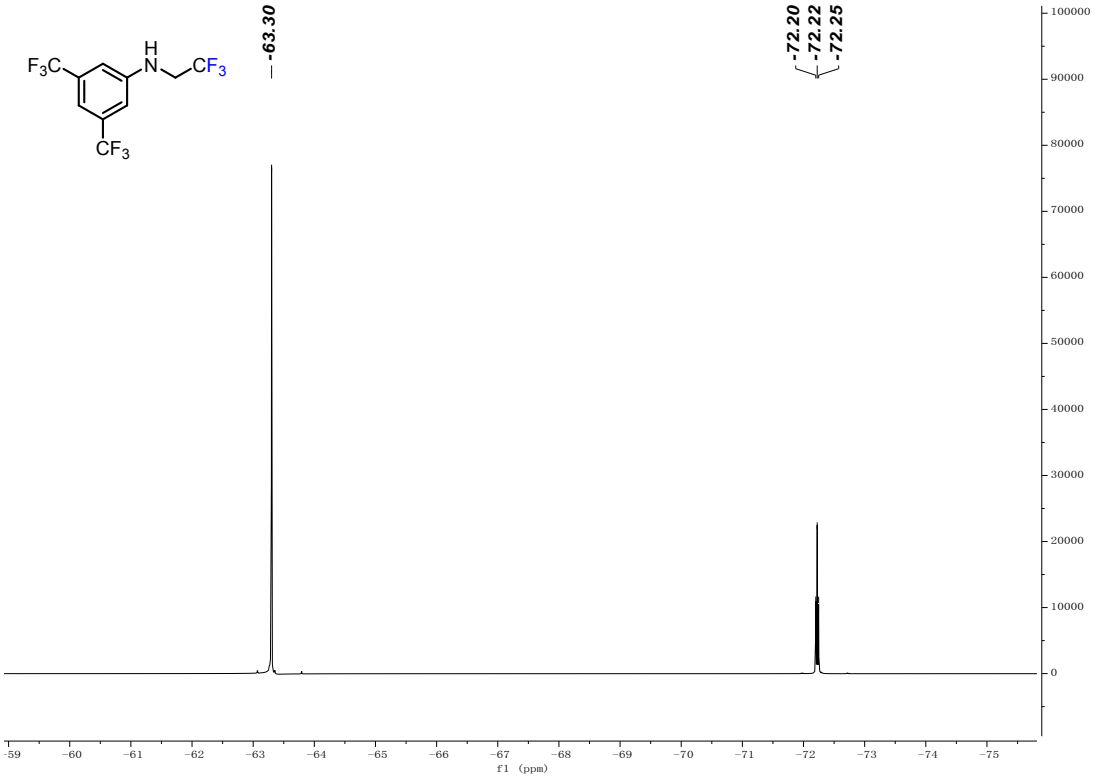
^{1}H NMR ($CDCl_3$, 400 MHz) of **3l**



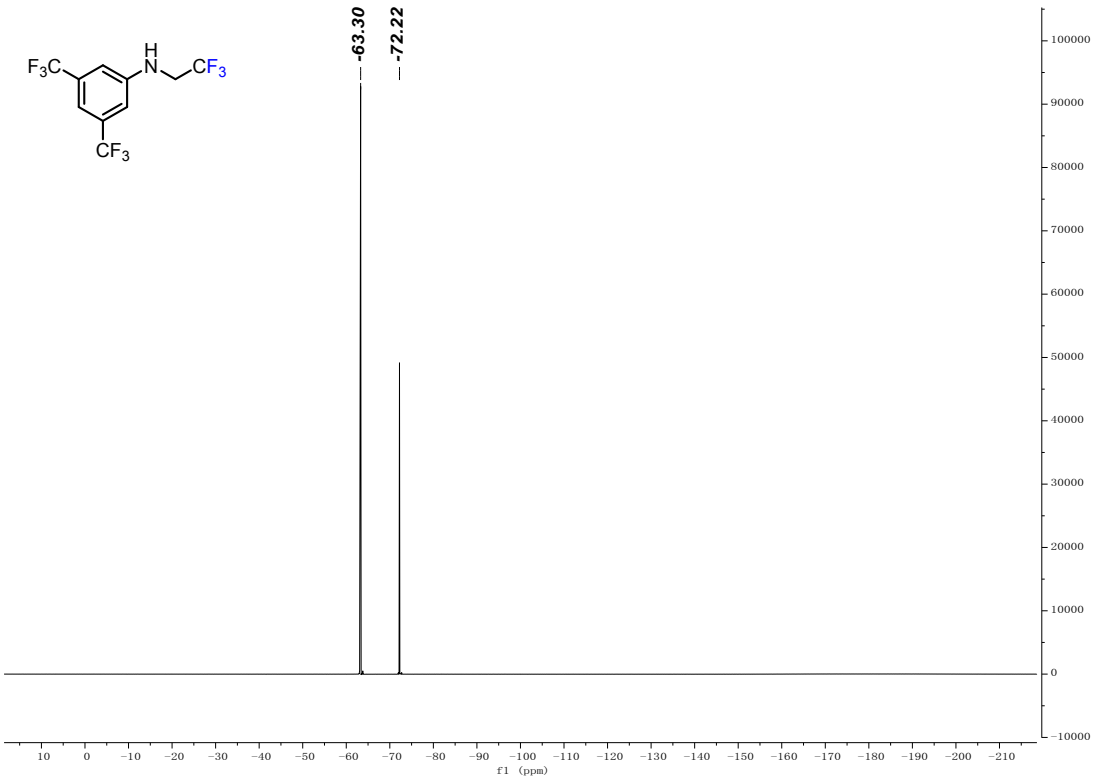
^{13}C NMR ($CDCl_3$, 400 MHz) of **3l**



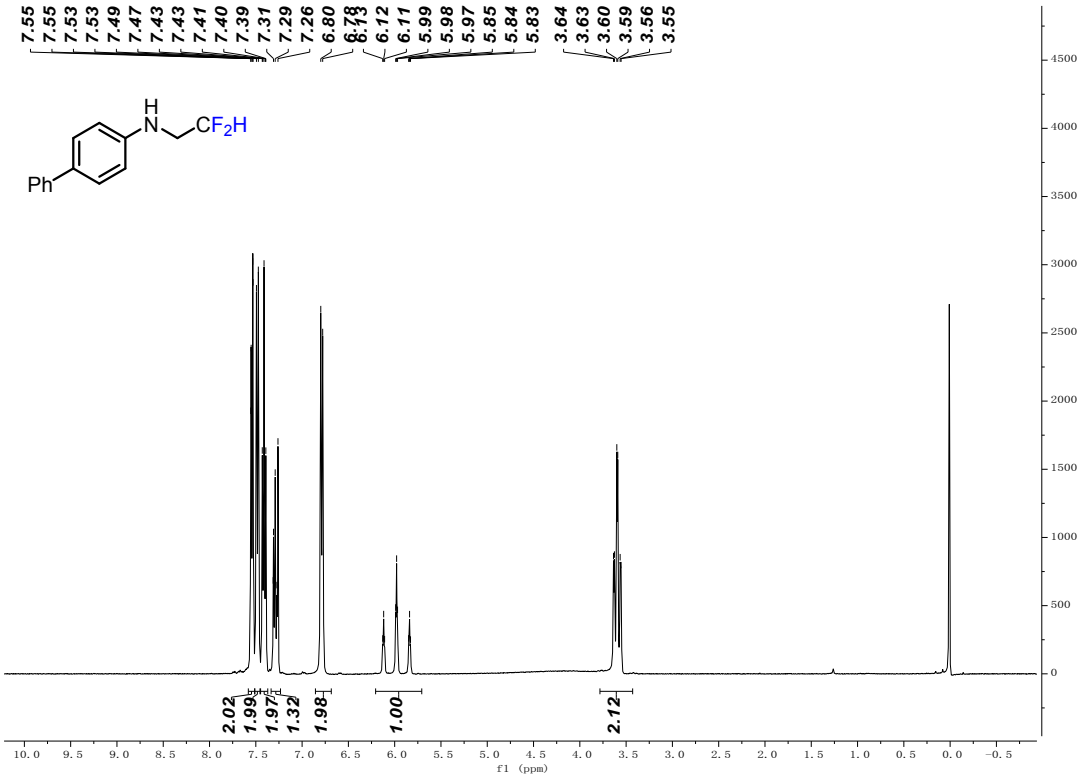
^{19}F NMR ($CDCl_3$, 376 MHz) of **3l**



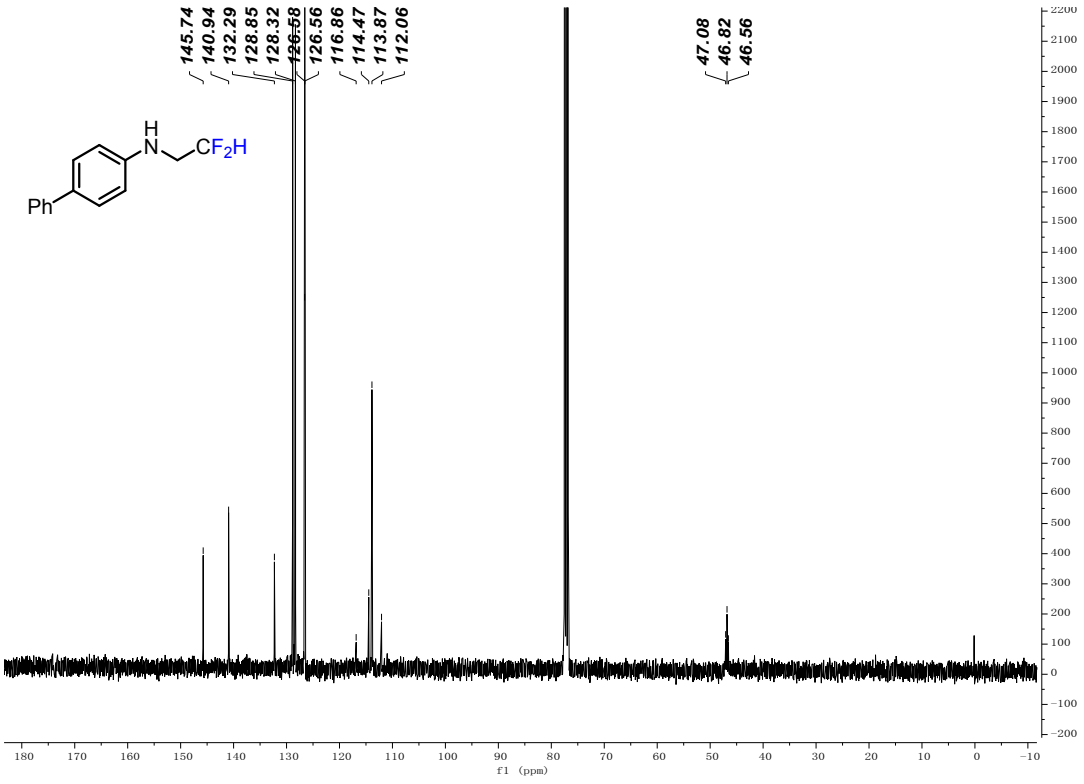
^{19}F {^{1}H} NMR ($CDCl_3$, 376 MHz) of **3l**



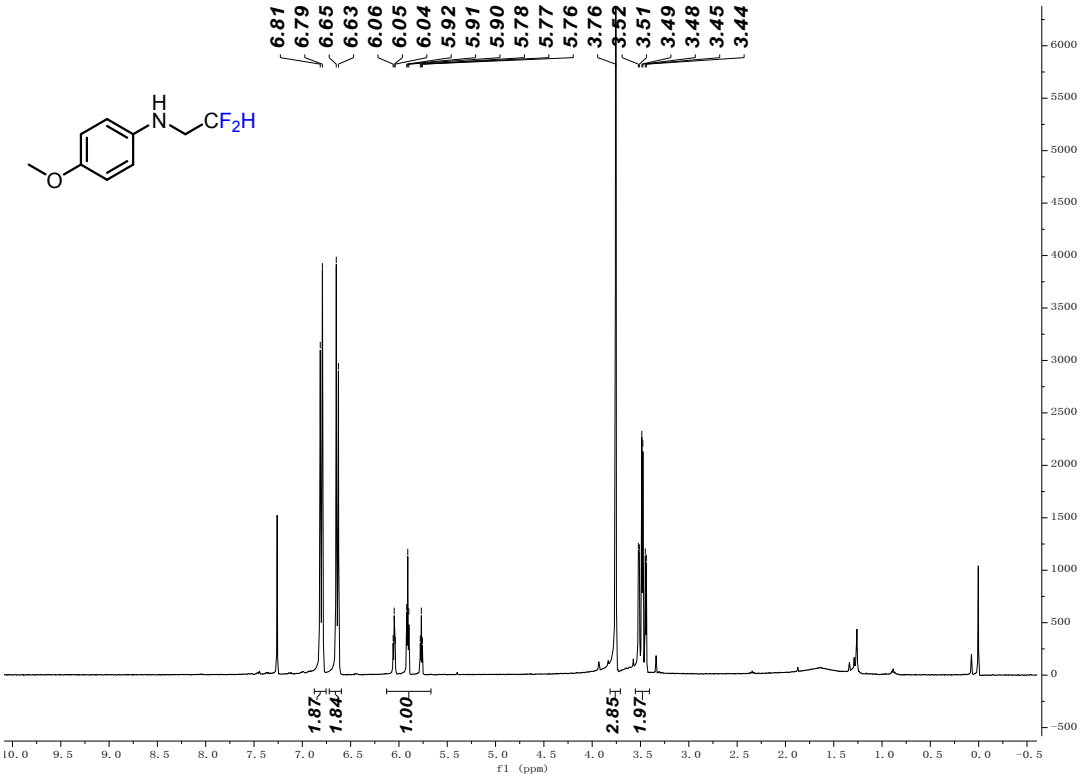
^{1}H NMR ($CDCl_3$, 400 MHz) of **7a**



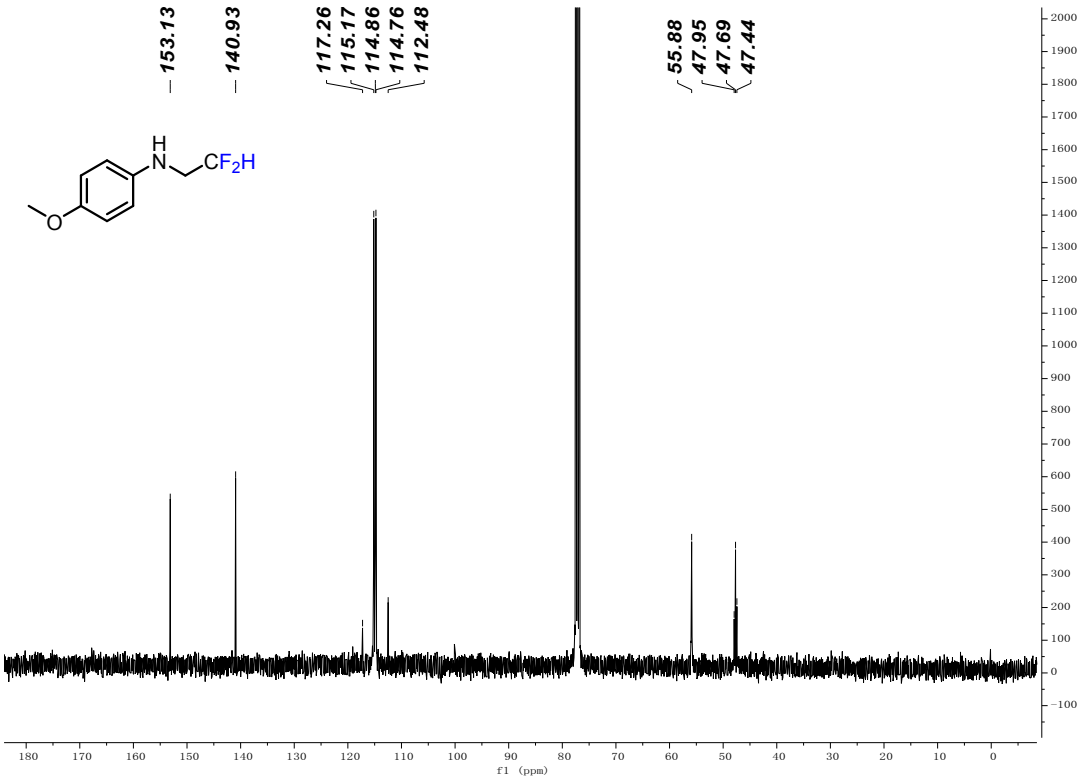
^{13}C NMR ($CDCl_3$, 400 MHz) of **7a**



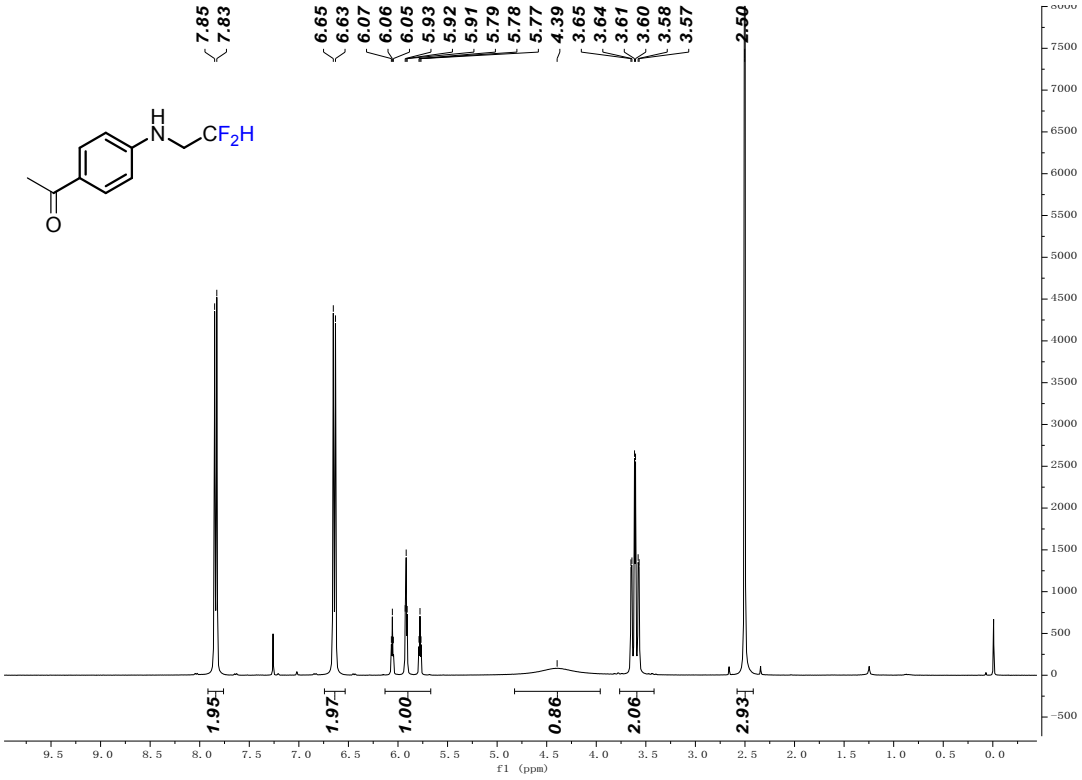
^{1}H NMR ($CDCl_3$, 400 MHz) of **7b**



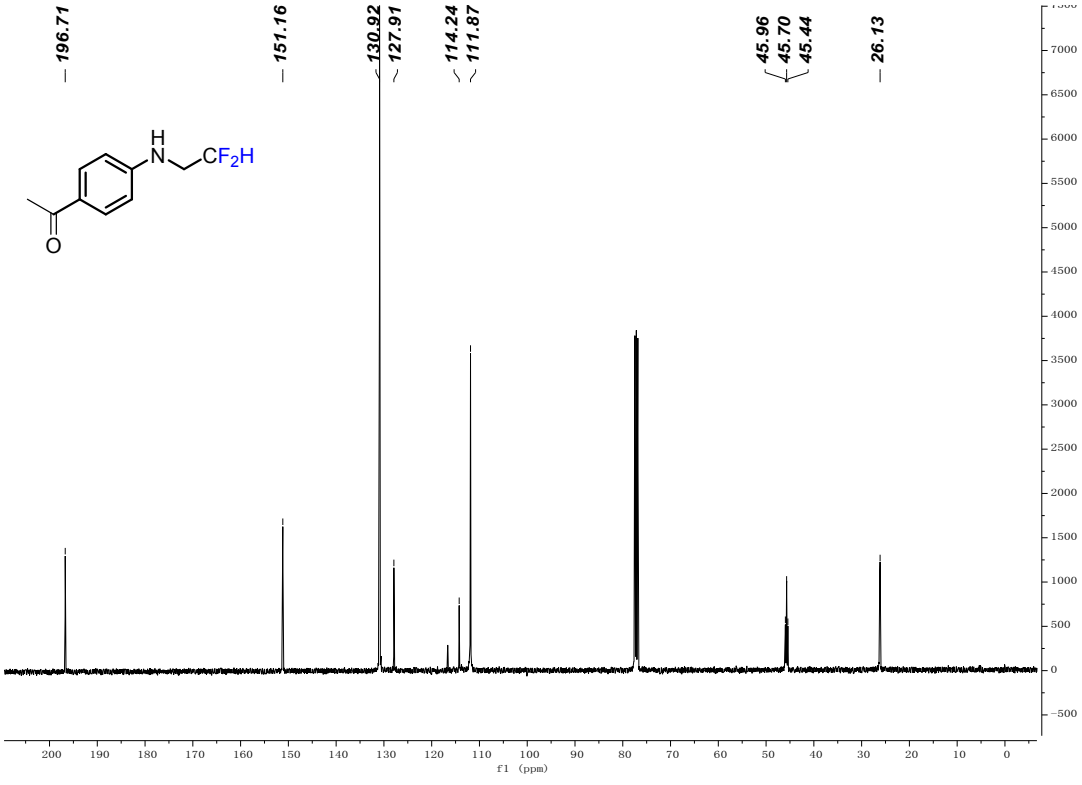
^{13}C NMR ($CDCl_3$, 400 MHz) of **7b**



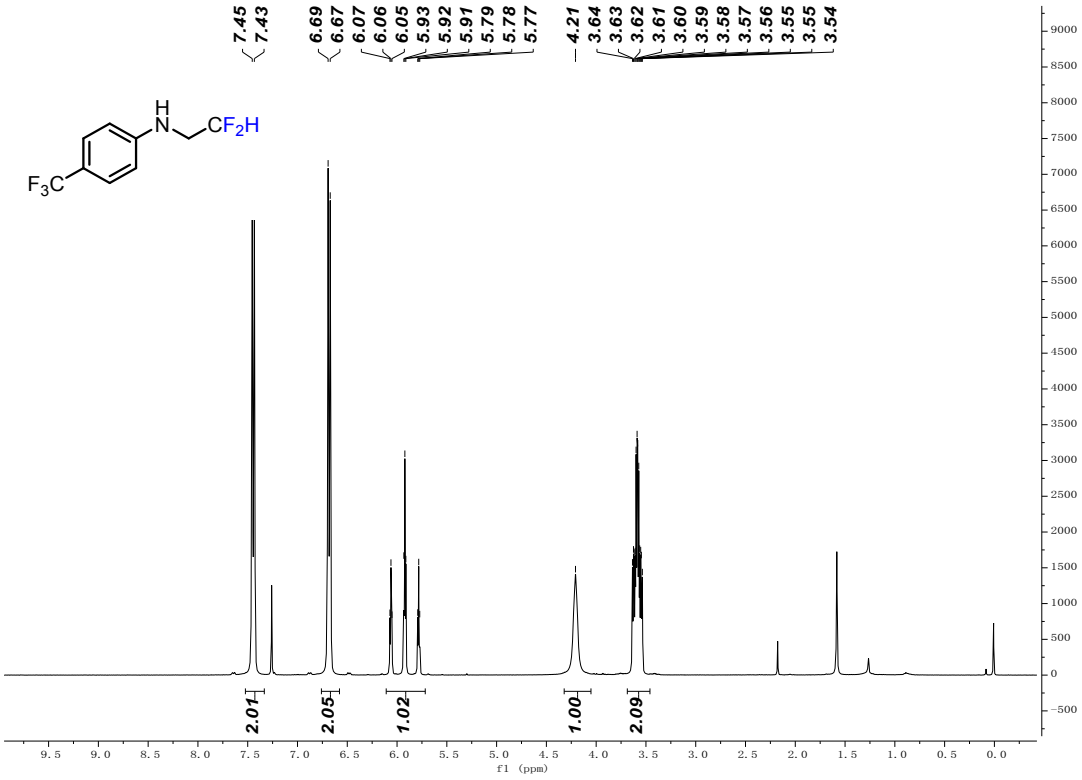
^{1}H NMR ($CDCl_3$, 400 MHz) of **7c**



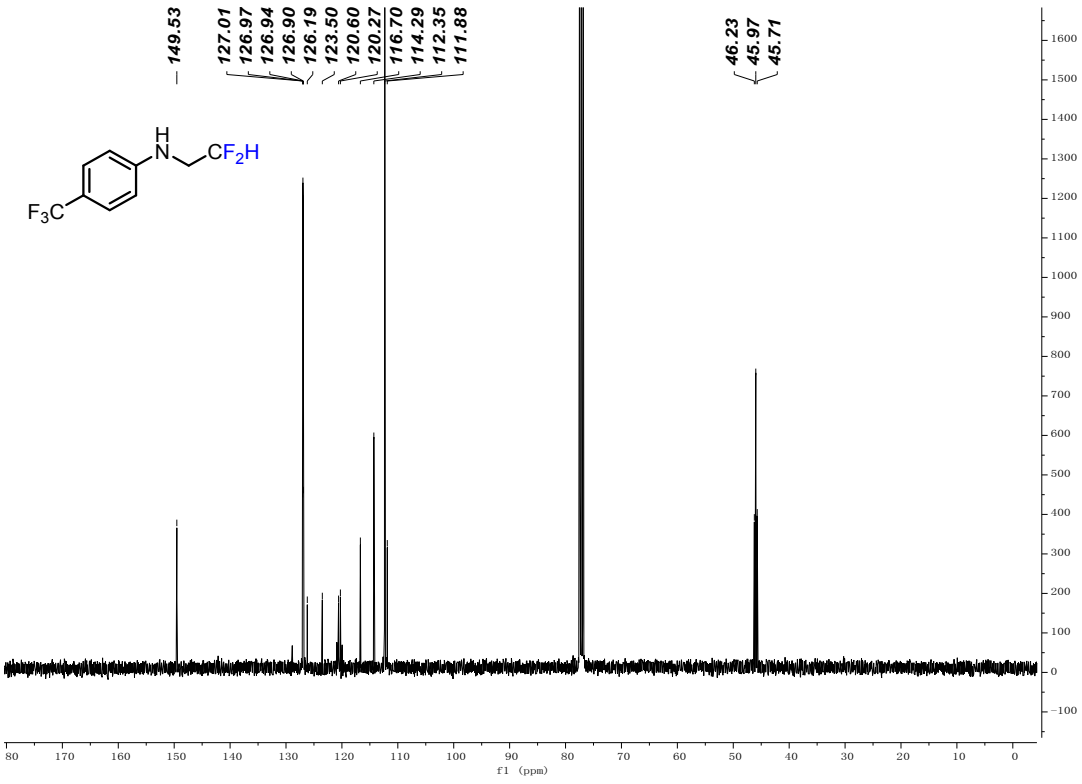
^{13}C NMR ($CDCl_3$, 400 MHz) of **7c**



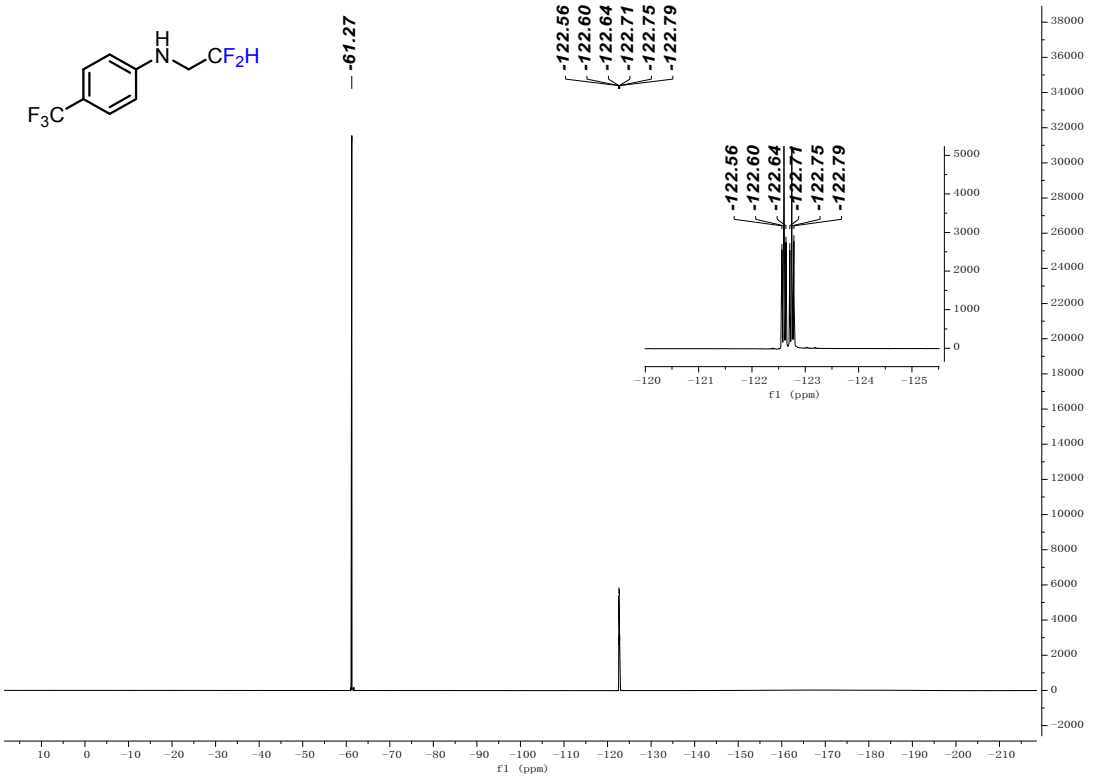
^{1}H NMR ($CDCl_3$, 400 MHz) of **7d**



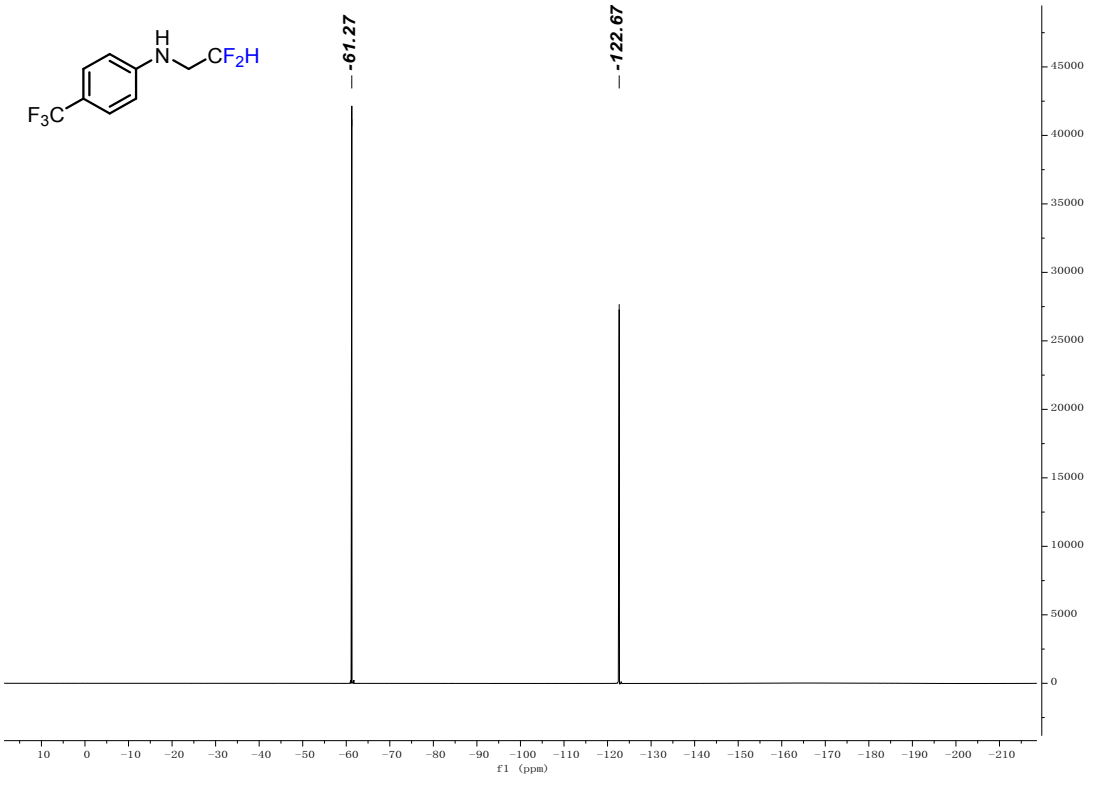
^{13}C NMR ($CDCl_3$, 400 MHz) of **7d**



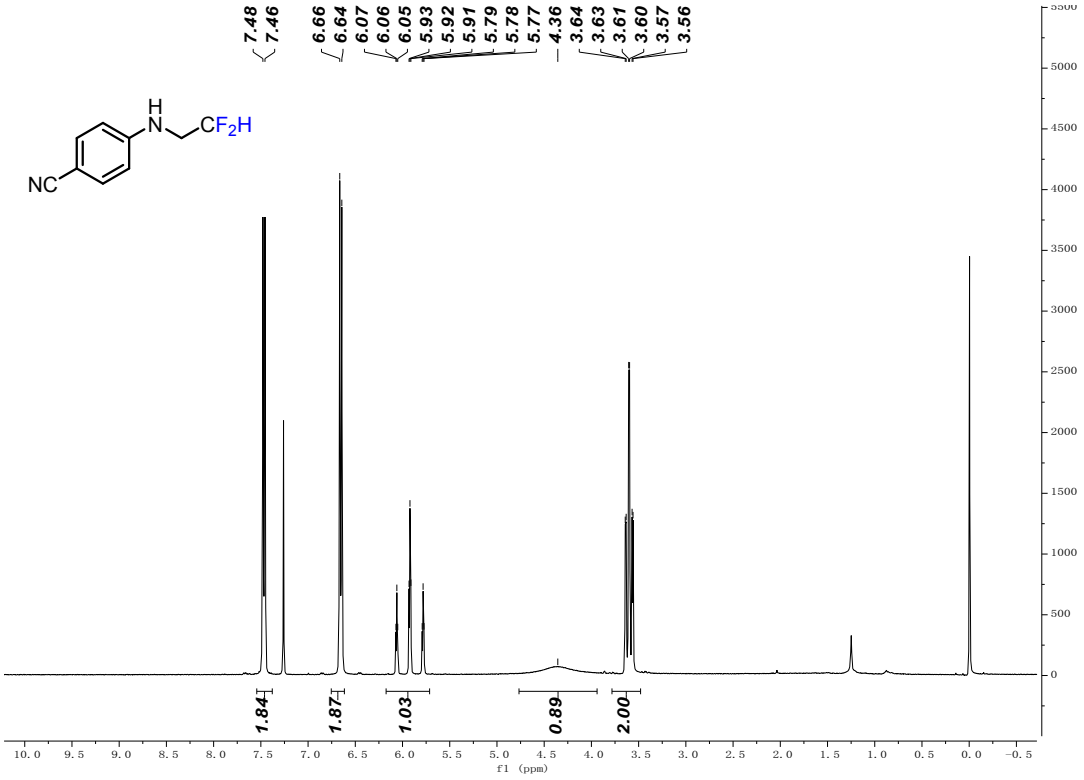
^{19}F NMR ($CDCl_3$, 376 MHz) of **7d**



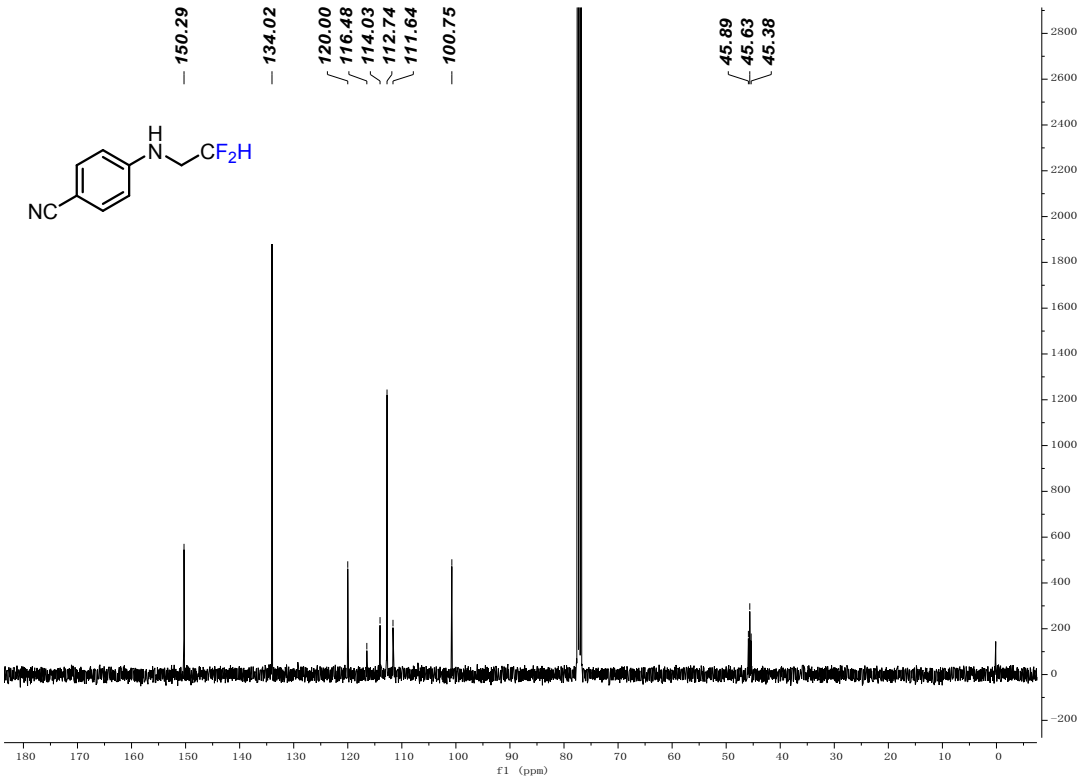
^{19}F {^{1}H} NMR ($CDCl_3$, 376 MHz) of **7d**



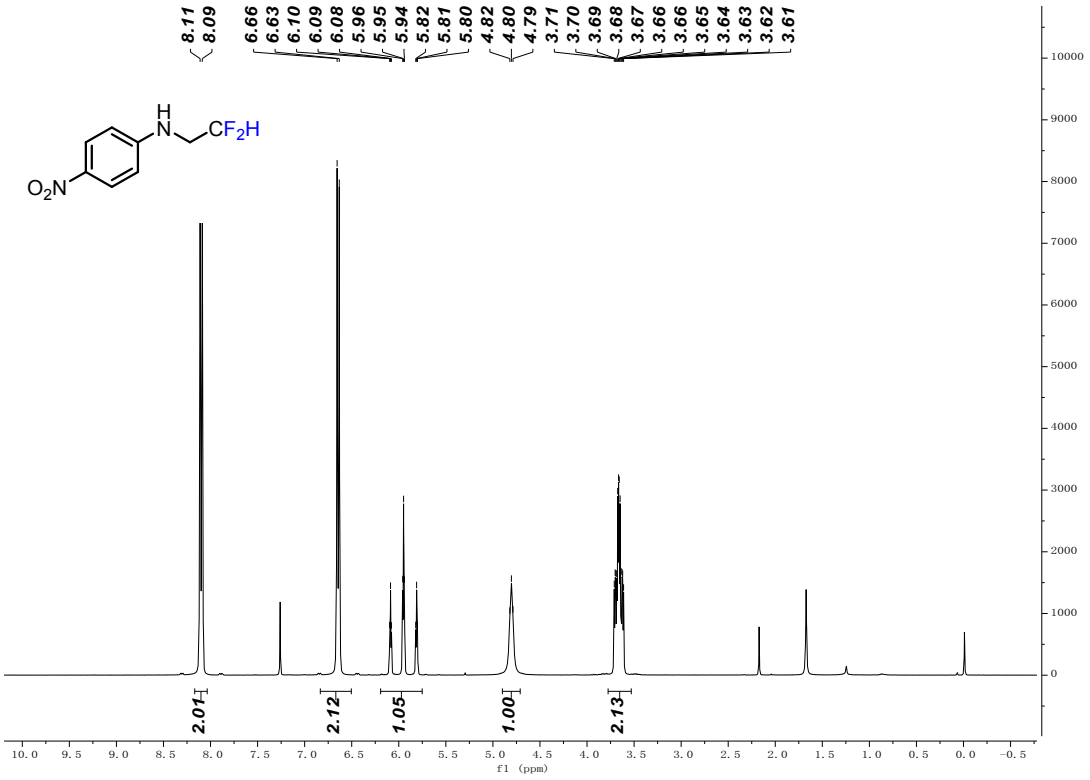
^{1}H NMR ($CDCl_3$, 400 MHz) of **7e**



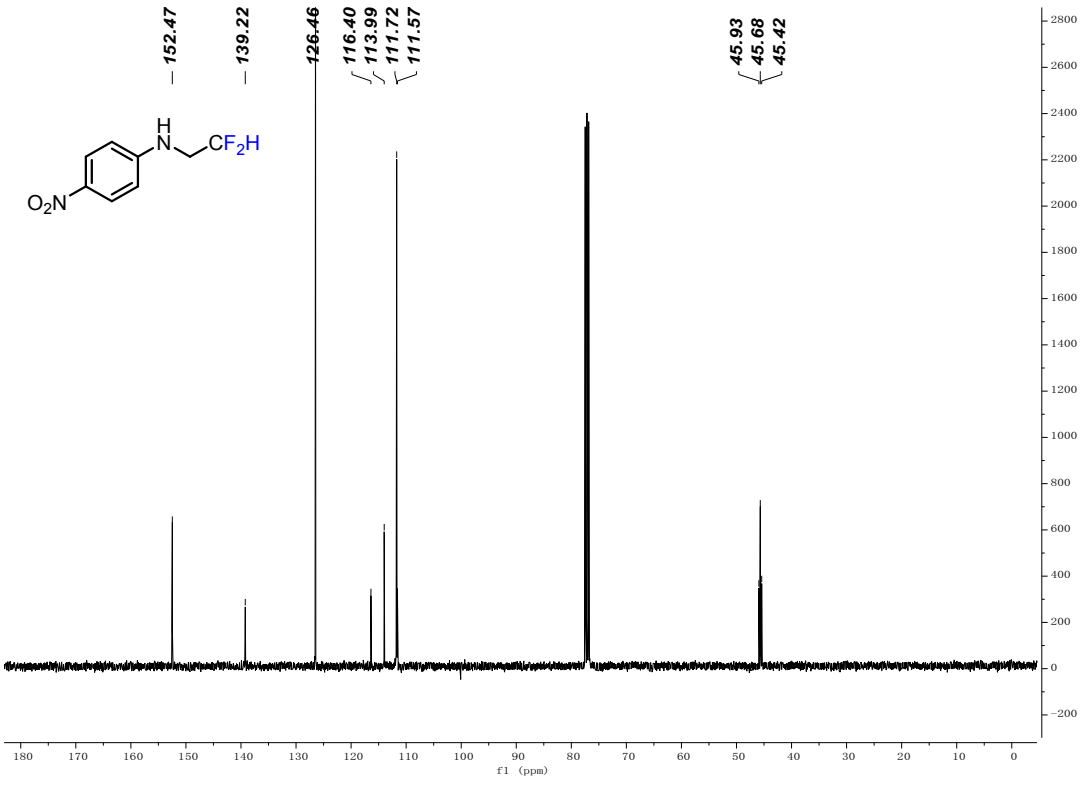
^{13}C NMR ($CDCl_3$, 400 MHz) of **7e**



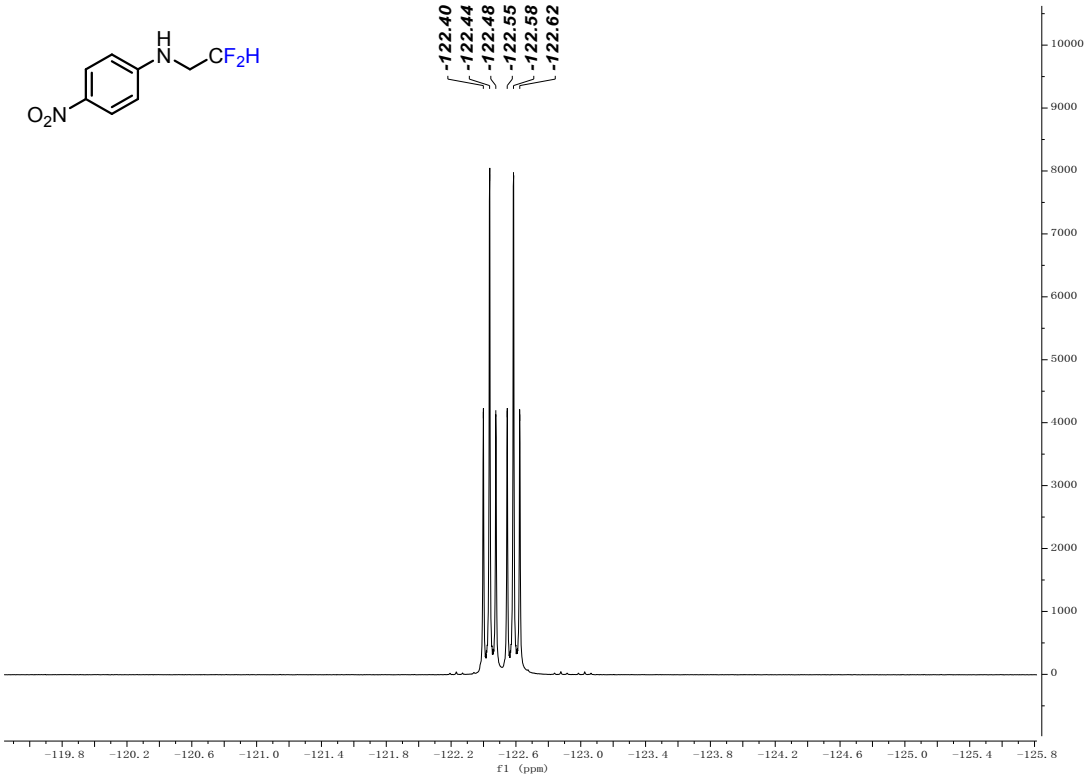
^{1}H NMR ($CDCl_3$, 400 MHz) of **7f**



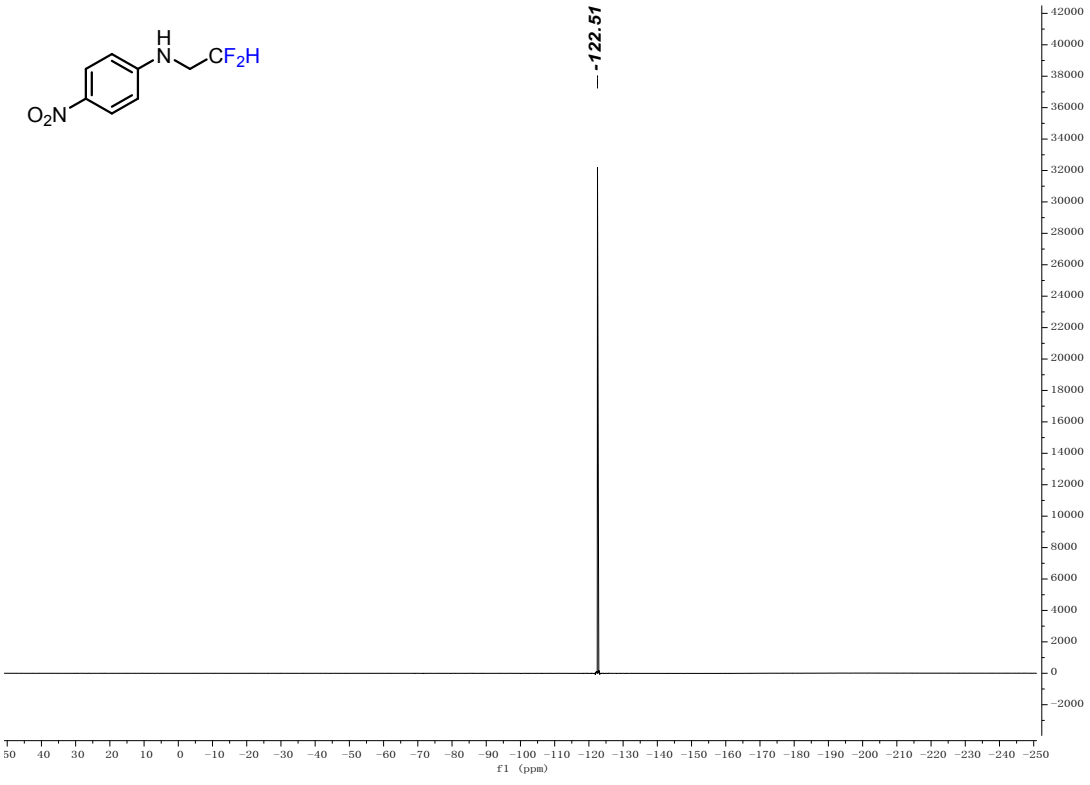
^{13}C NMR ($CDCl_3$, 400 MHz) of **7f**



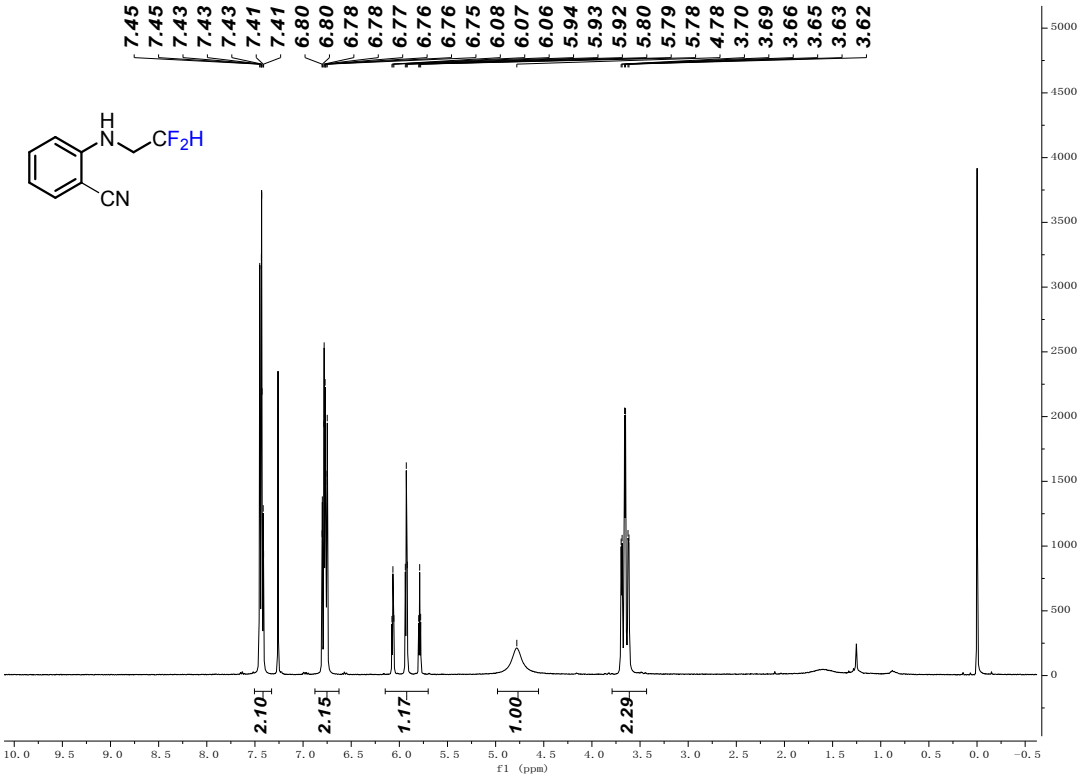
^{19}F NMR ($CDCl_3$, 376 MHz) of **7f**



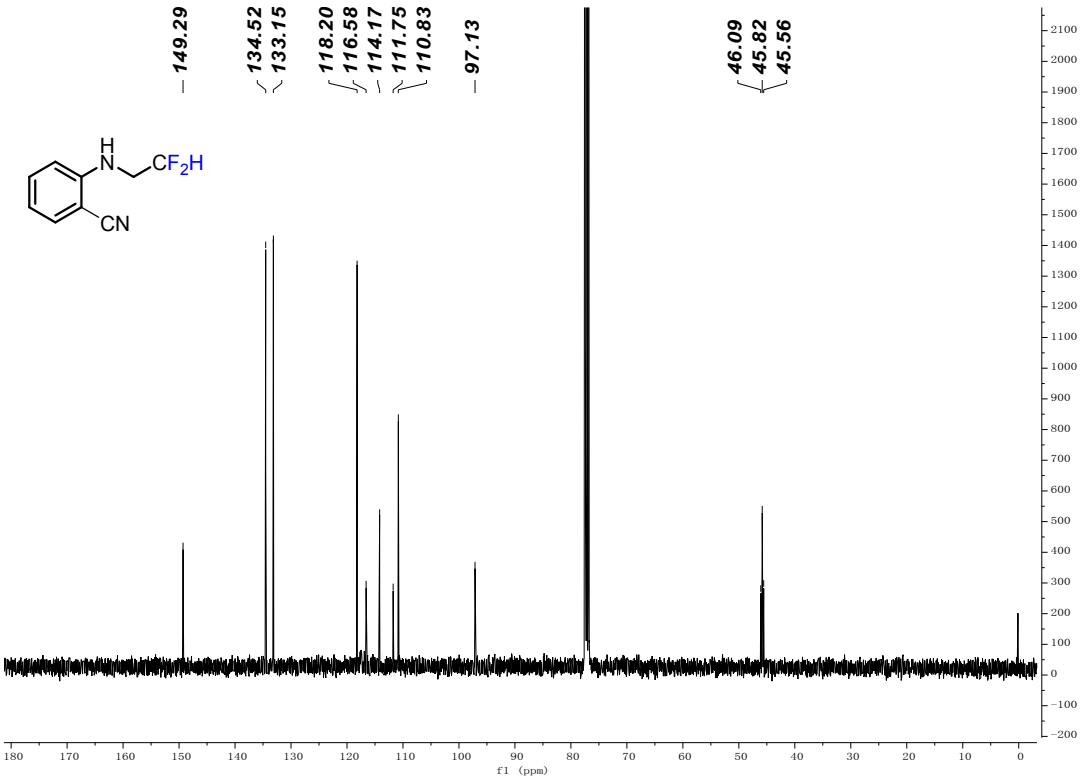
^{19}F {^{1}H} NMR ($CDCl_3$, 376 MHz) of **7f**



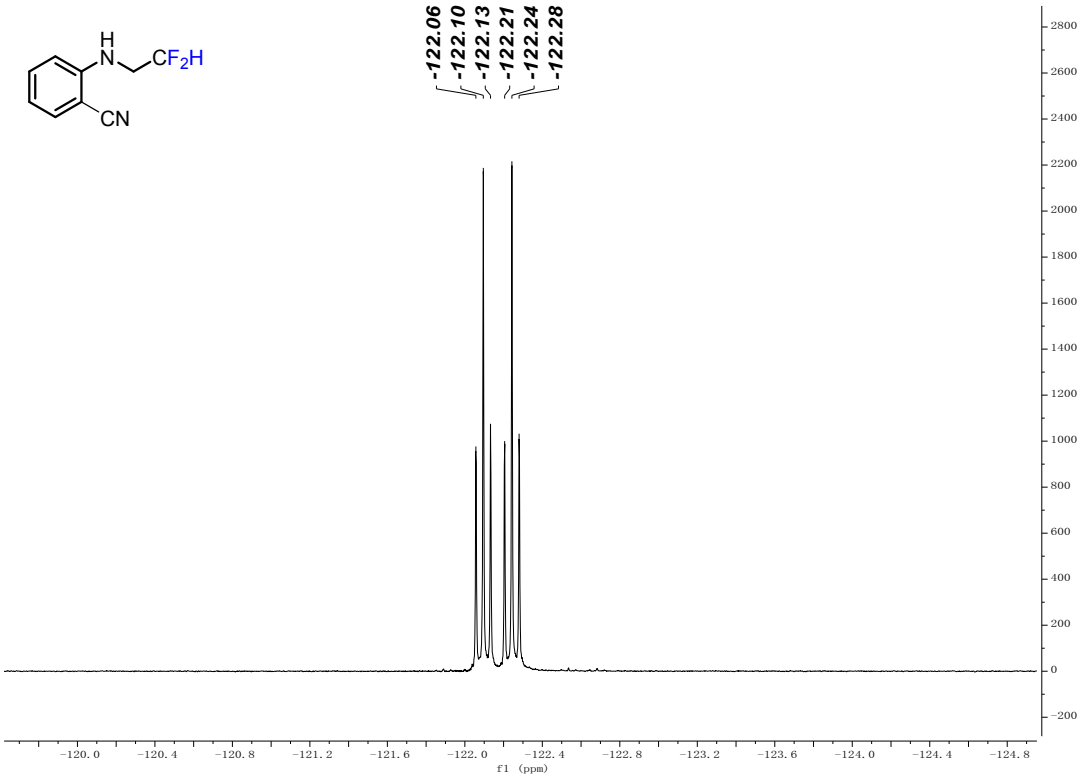
^{1}H NMR ($CDCl_3$, 400 MHz) of **7g**



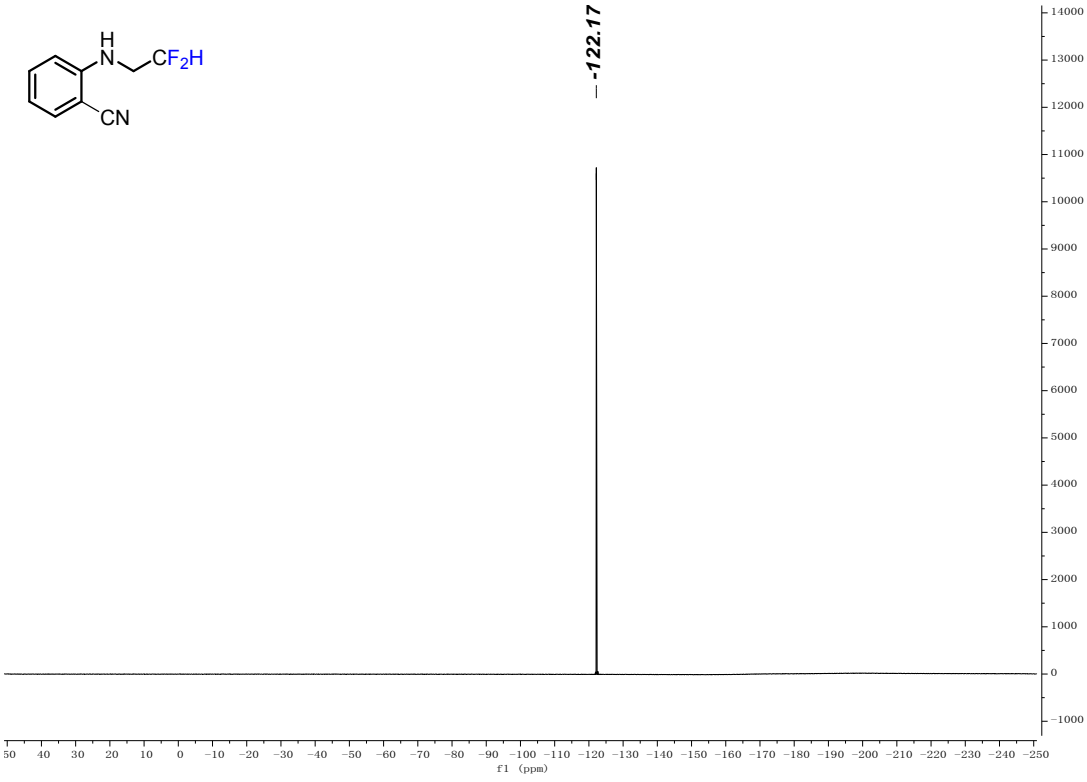
^{13}C NMR ($CDCl_3$, 400 MHz) of **7g**



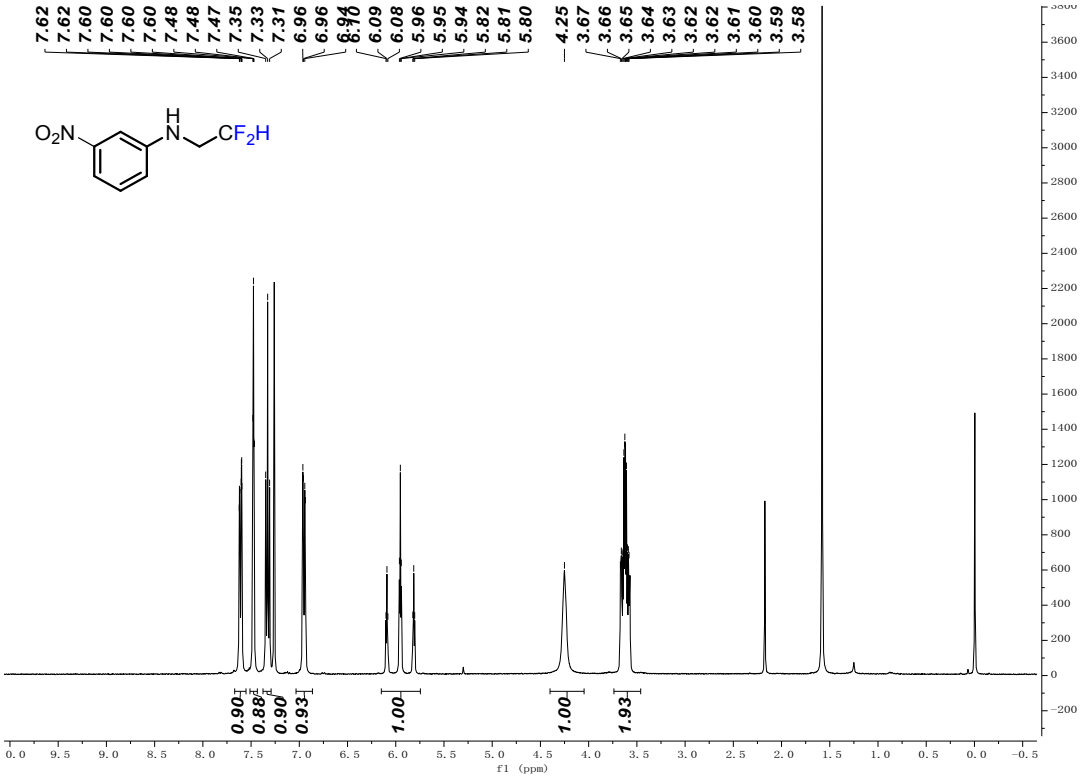
^{19}F NMR ($CDCl_3$, 376 MHz) of **7g**



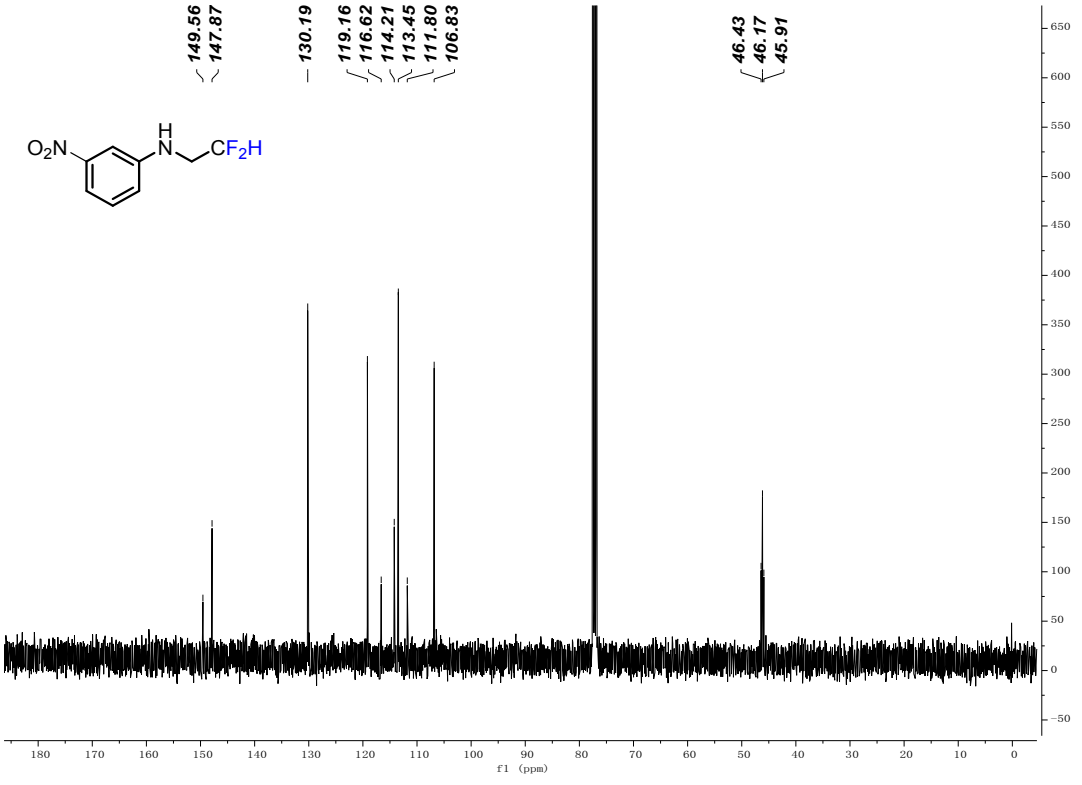
^{19}F {^{1}H} NMR ($CDCl_3$, 376 MHz) of **7g**



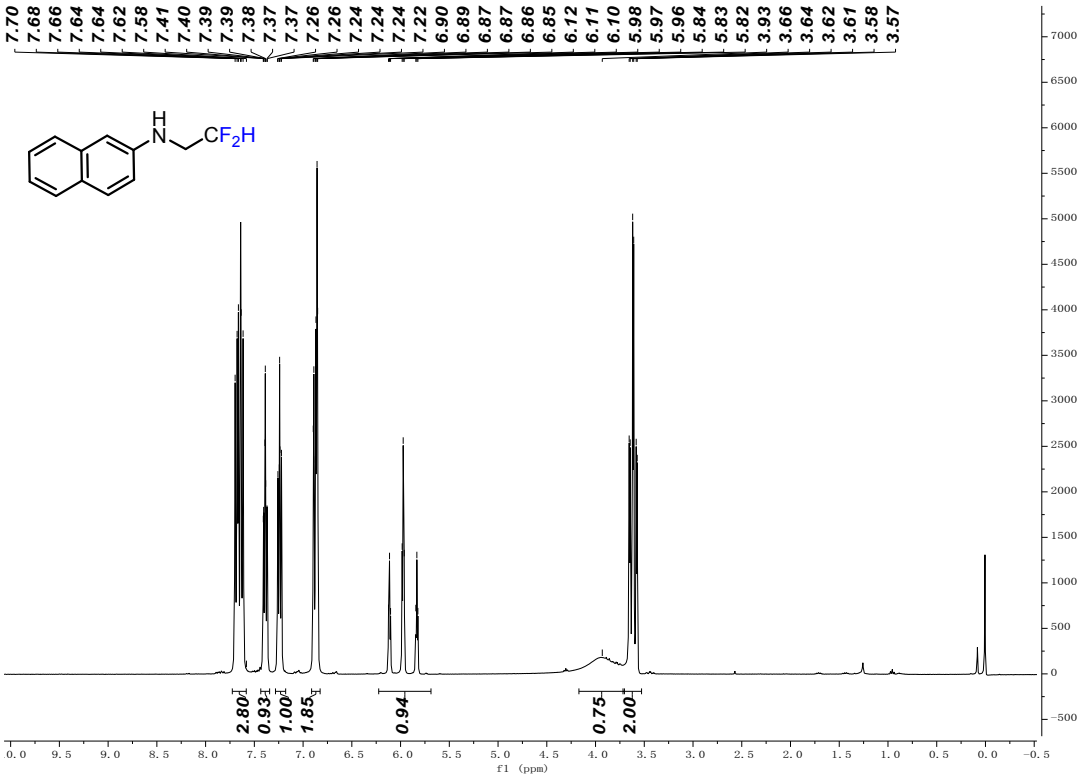
^{1}H NMR ($CDCl_3$, 400 MHz) of **7h**



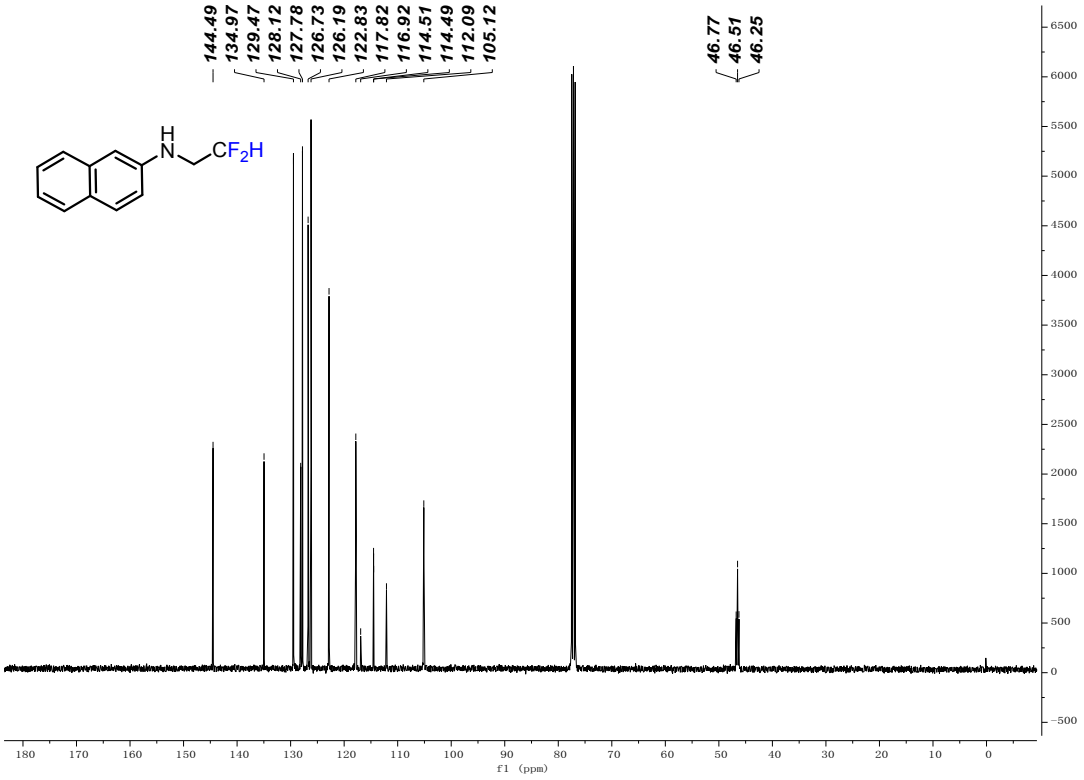
^{13}C NMR ($CDCl_3$, 400 MHz) of **7h**



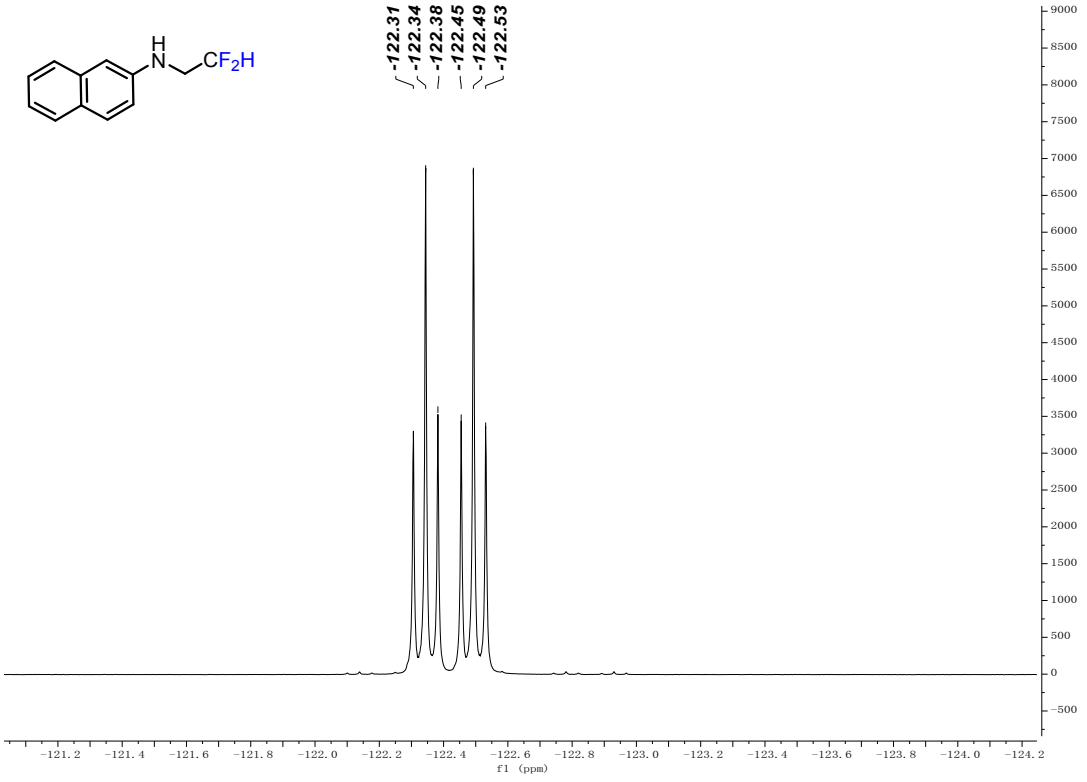
^{1}H NMR ($CDCl_3$, 400 MHz) of **7i**



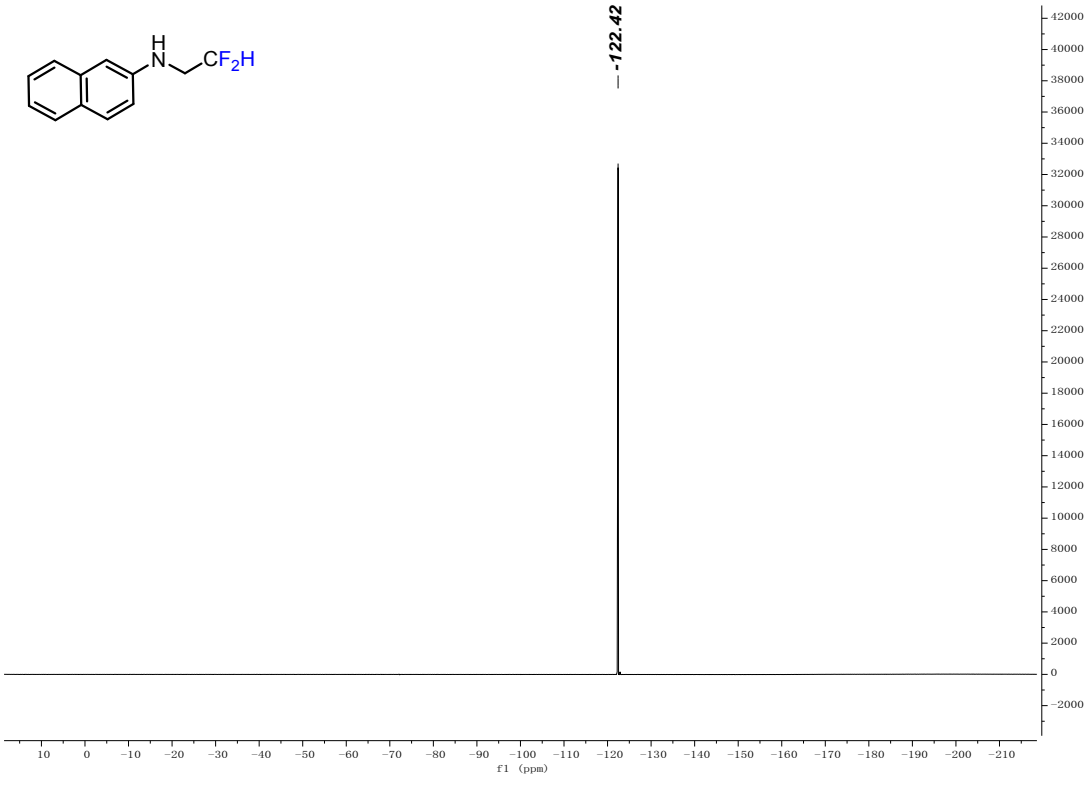
^{13}C NMR ($CDCl_3$, 400 MHz) of **7i**



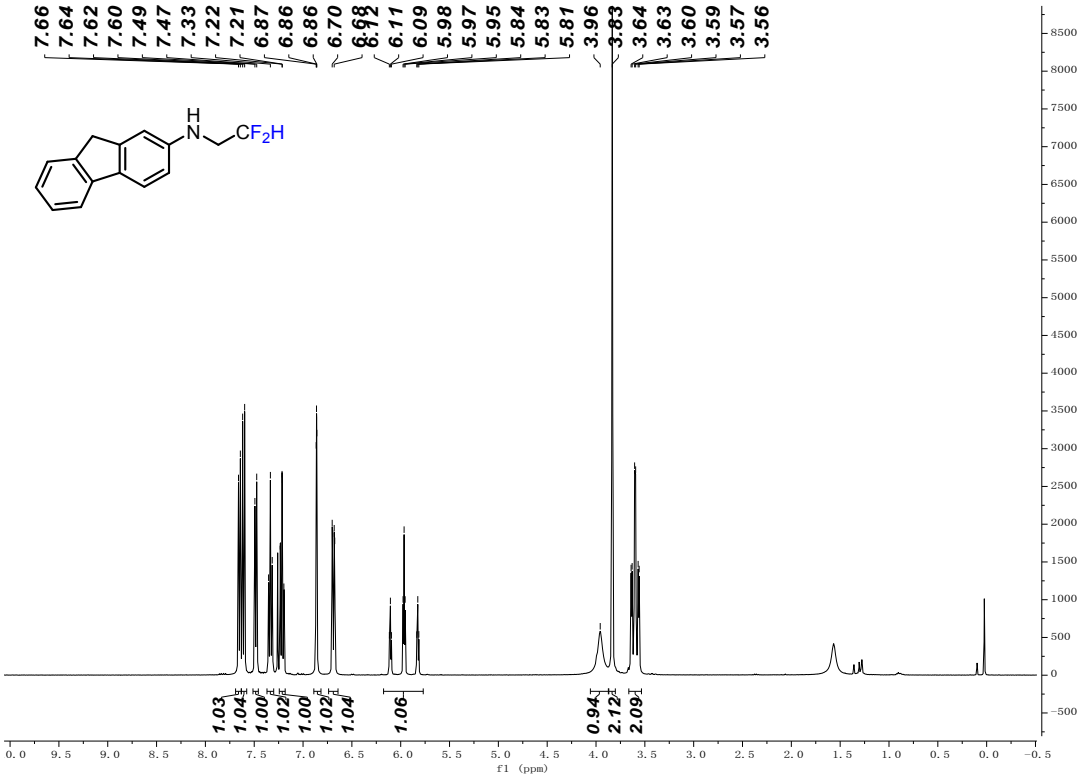
^{19}F NMR ($CDCl_3$, 376 MHz) of **7i**



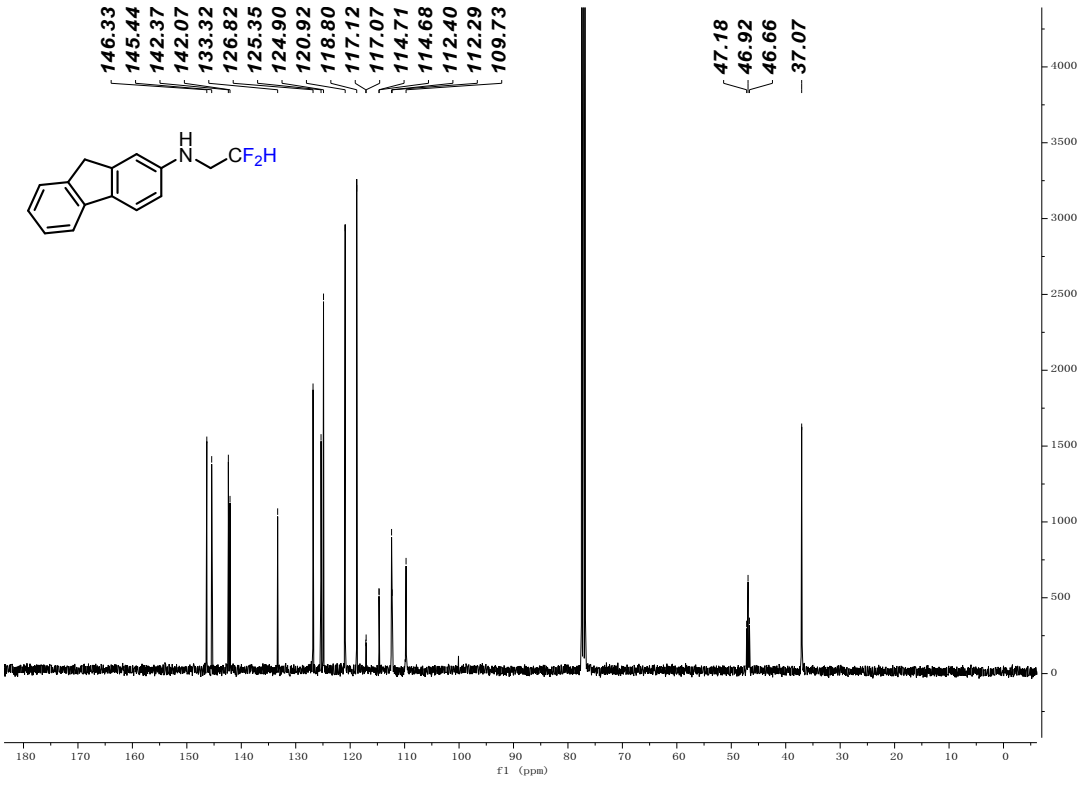
^{19}F {^{1}H} NMR ($CDCl_3$, 376 MHz) of **7i**



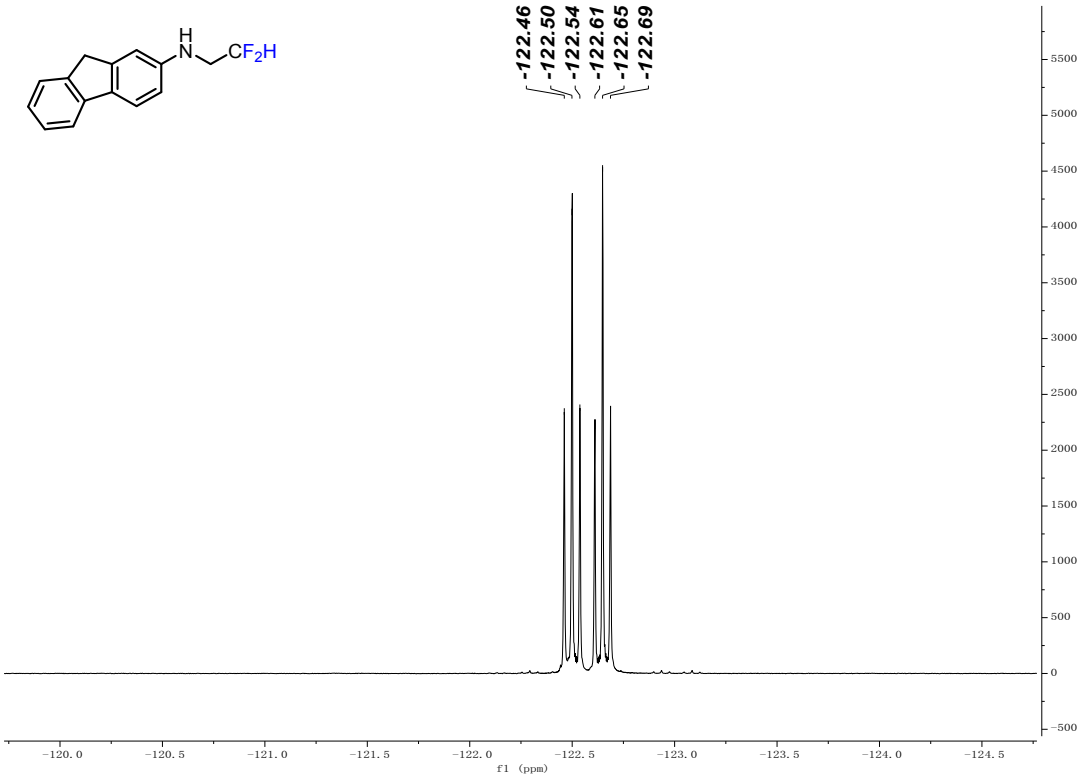
^{1}H NMR ($CDCl_3$, 400 MHz) of **7j**



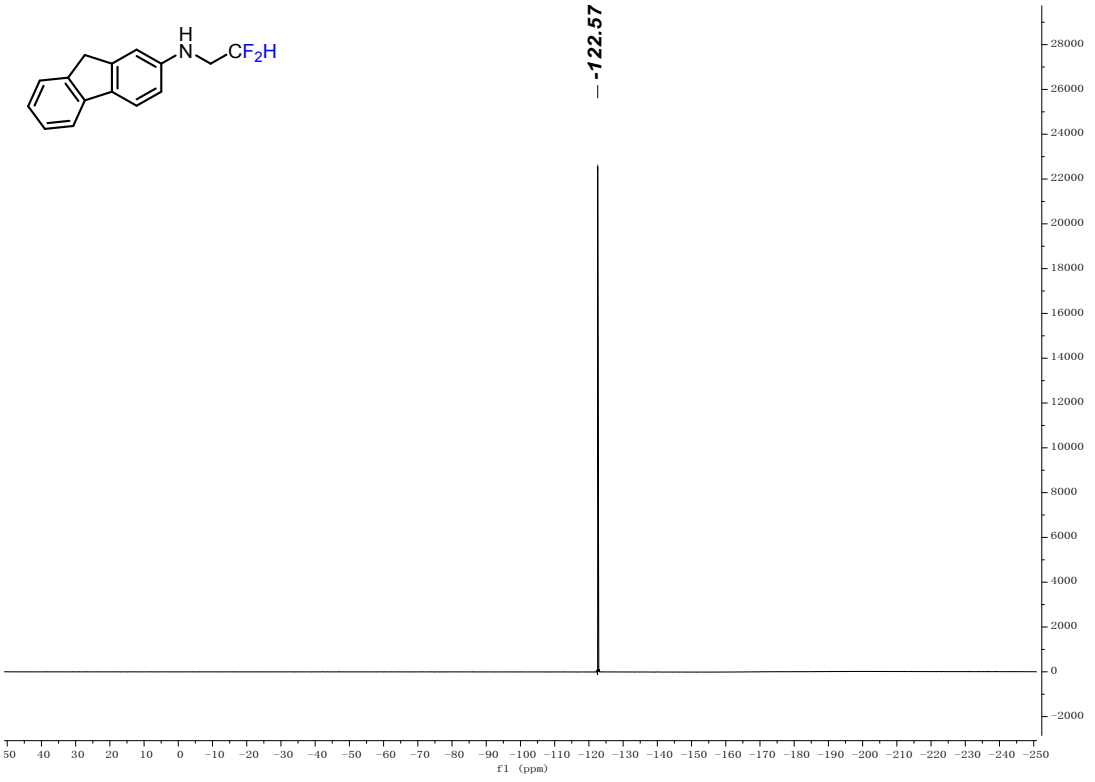
^{13}C NMR ($CDCl_3$, 400 MHz) of **7j**



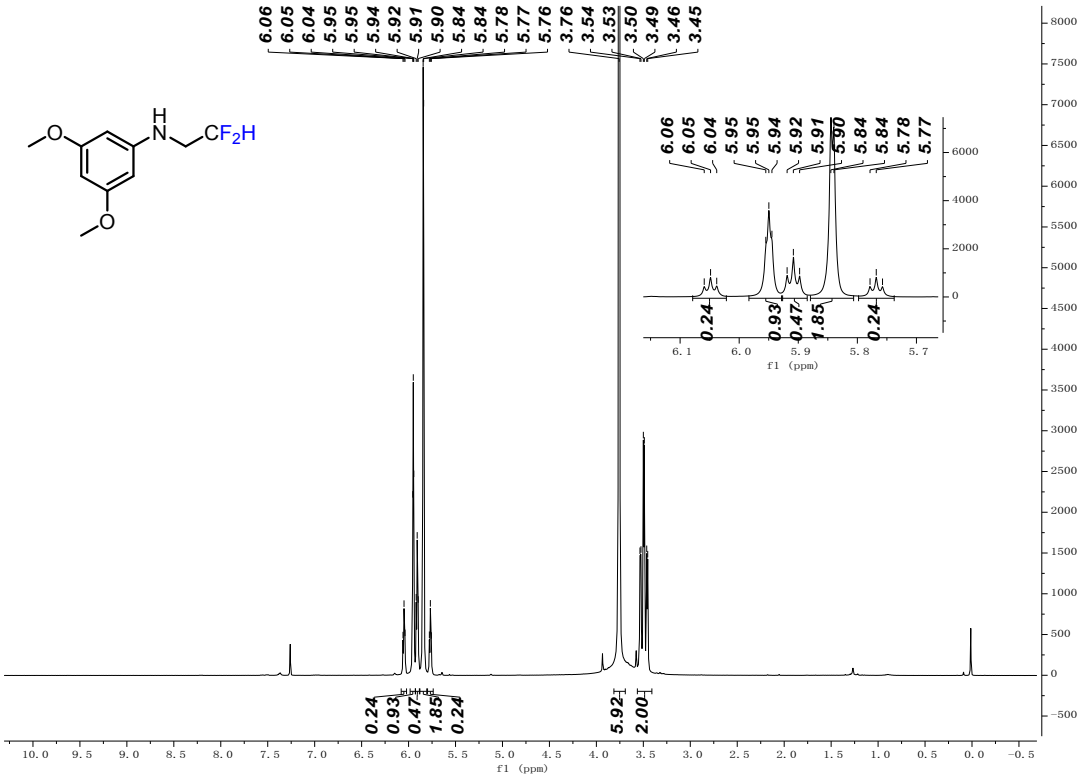
^{19}F NMR ($CDCl_3$, 376 MHz) of **7j**



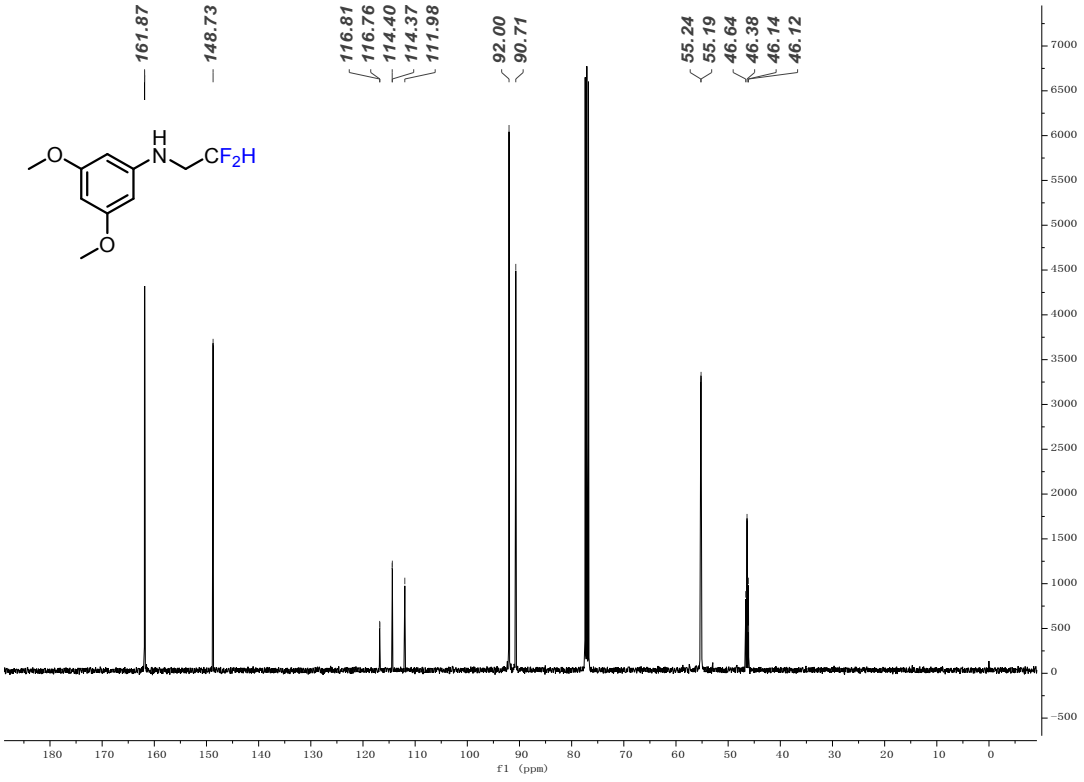
^{19}F {^{1}H} NMR ($CDCl_3$, 376 MHz) of **7j**



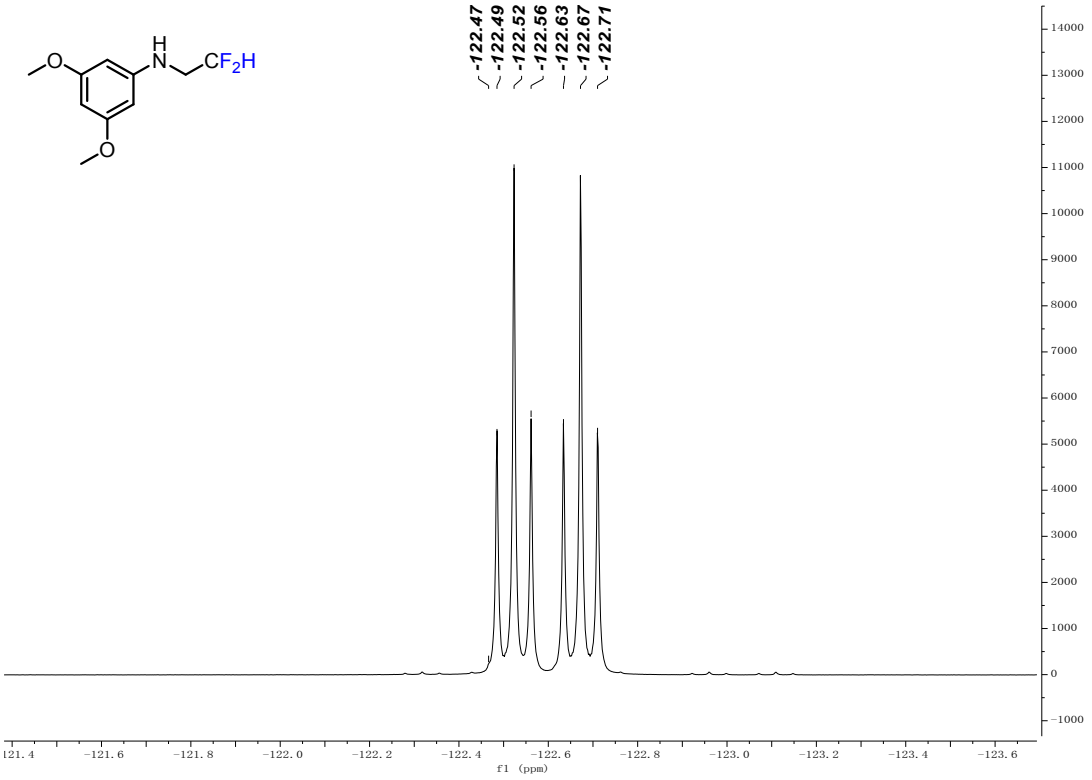
^{1}H NMR ($CDCl_3$, 400 MHz) of **7k**



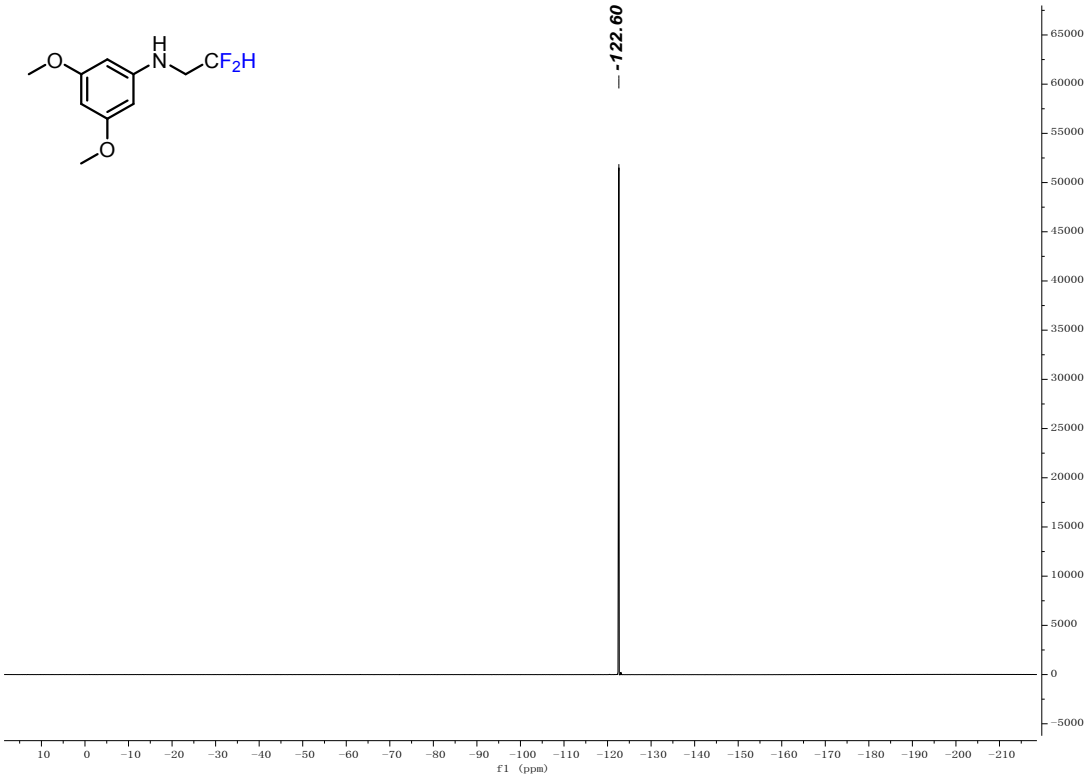
^{13}C NMR ($CDCl_3$, 400 MHz) of **7k**



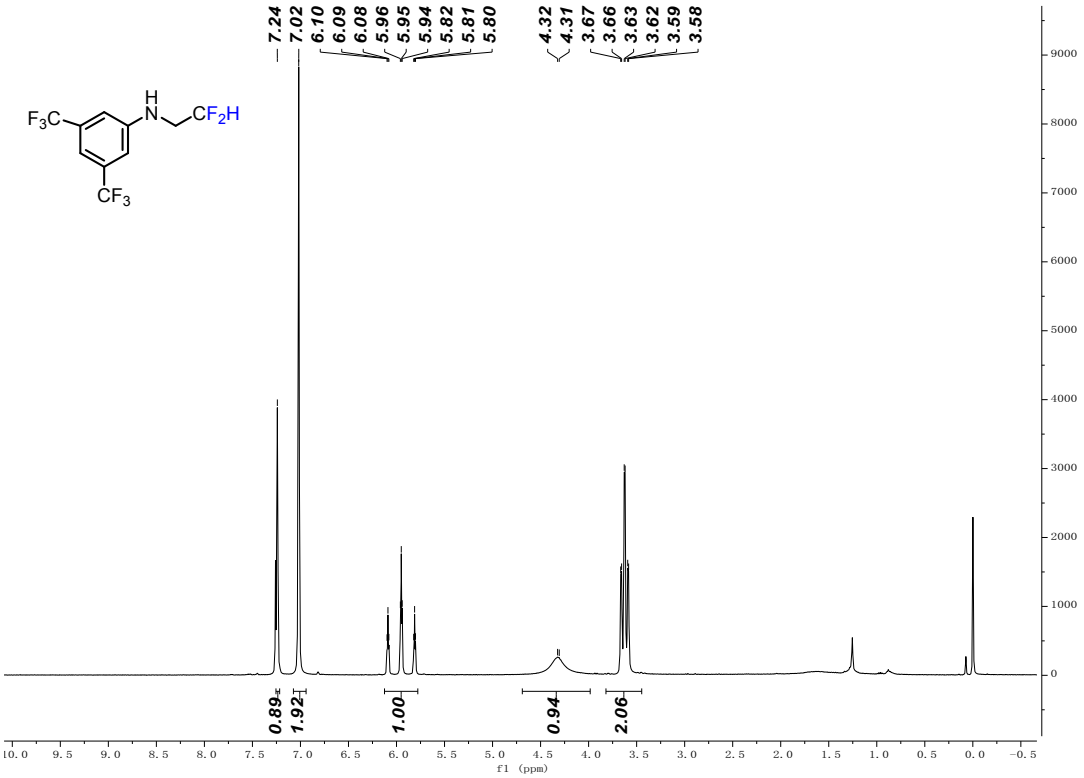
^{19}F NMR ($CDCl_3$, 376 MHz) of 7**k**



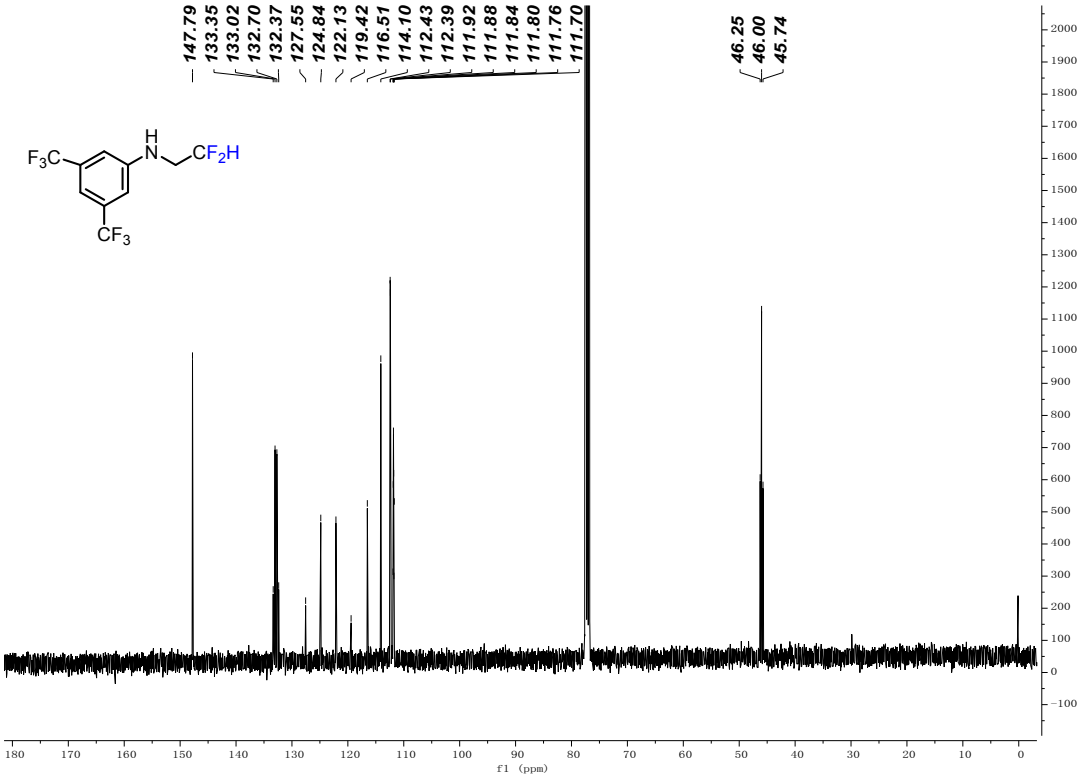
^{19}F {^{1}H} NMR ($CDCl_3$, 376 MHz) of **7k**



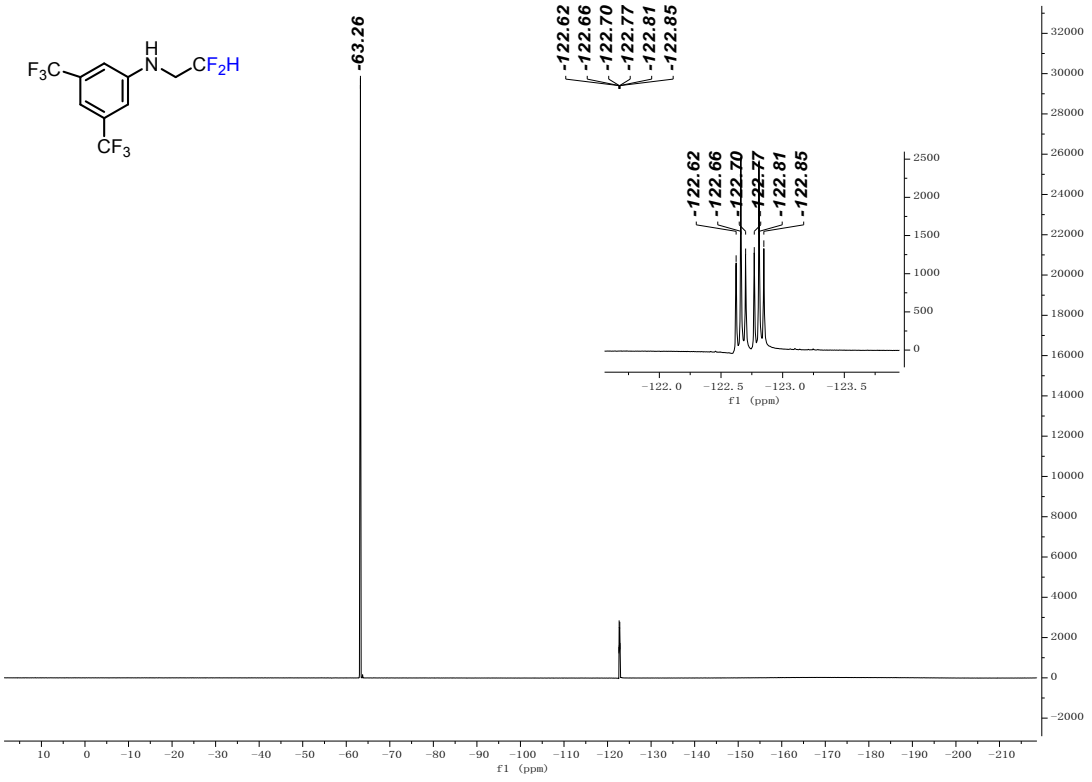
^{1}H NMR ($CDCl_3$, 400 MHz) of **7l**



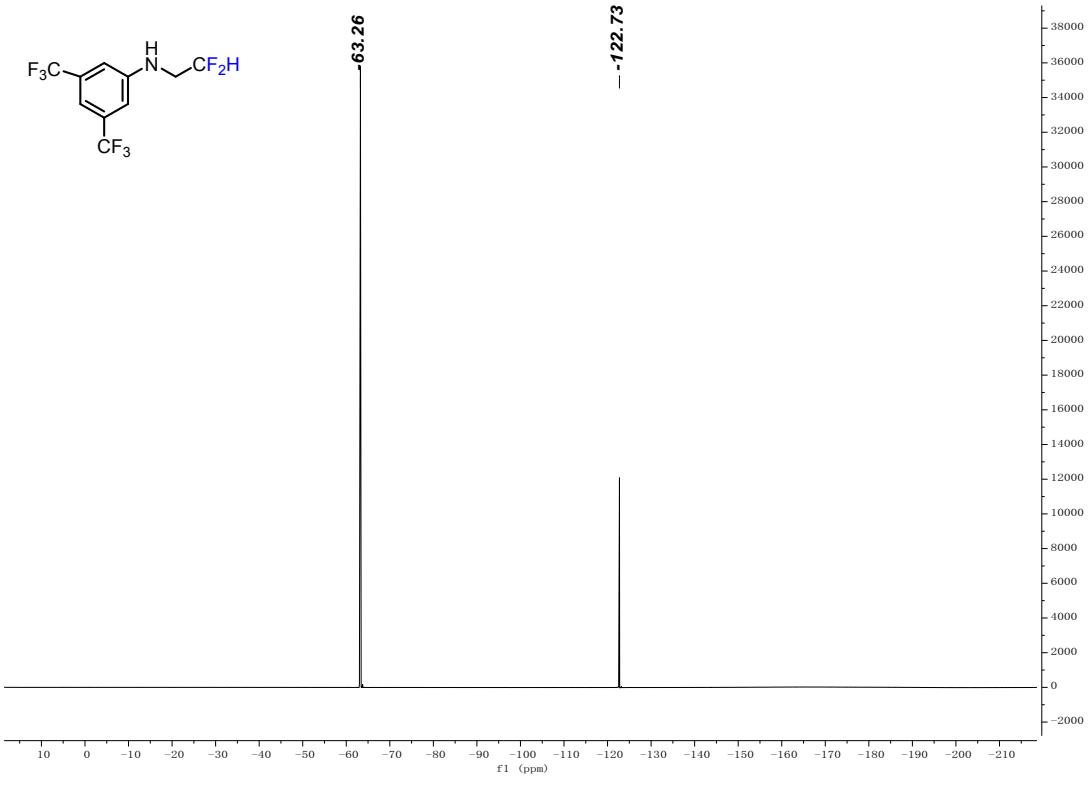
^{13}C NMR ($CDCl_3$, 400 MHz) of **7l**



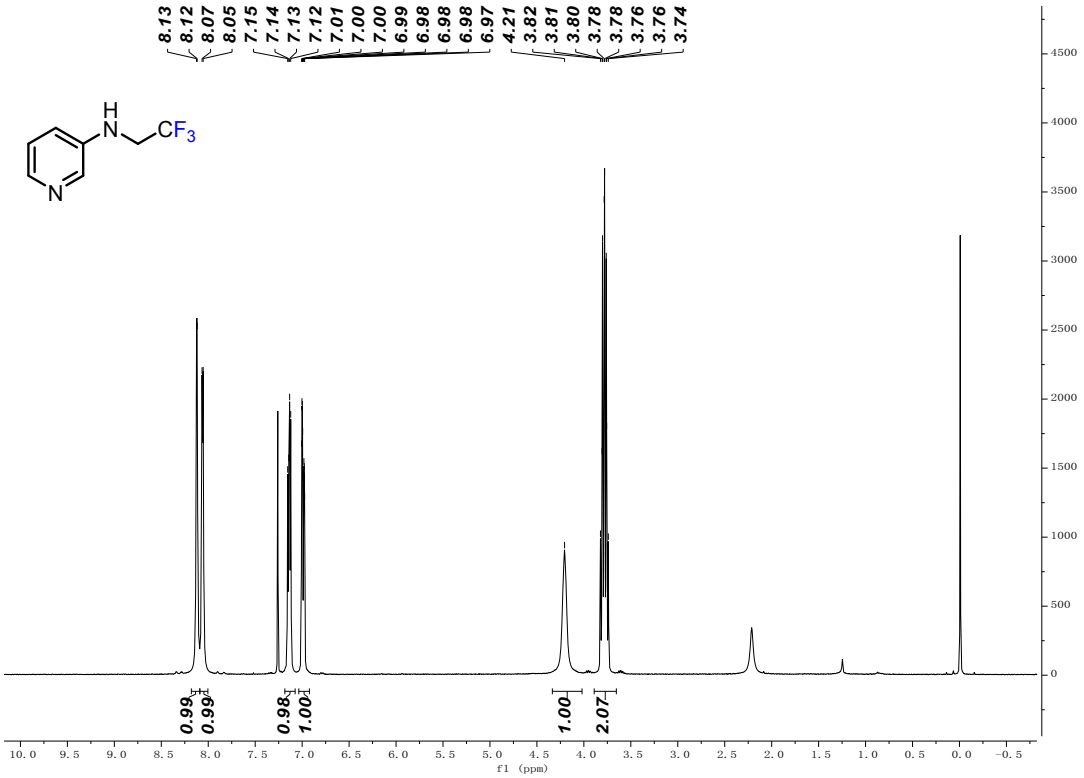
^{19}F NMR ($CDCl_3$, 376 MHz) of **7l**



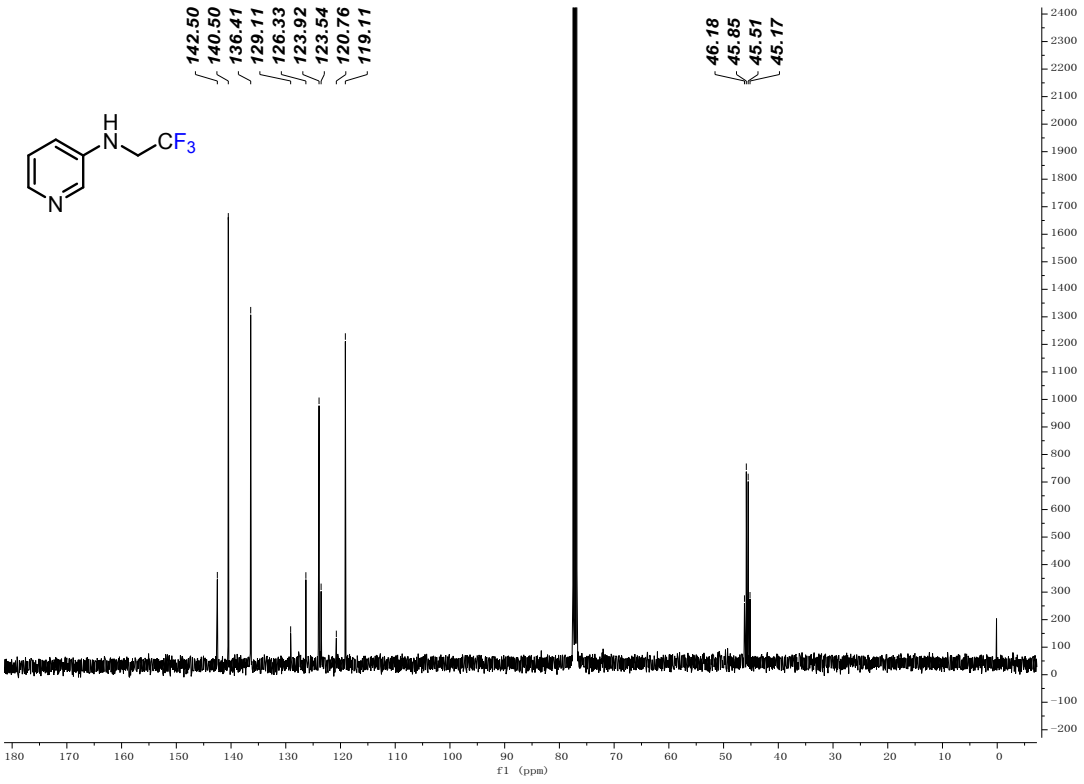
^{19}F {^{1}H} NMR ($CDCl_3$, 376 MHz) of **7l**



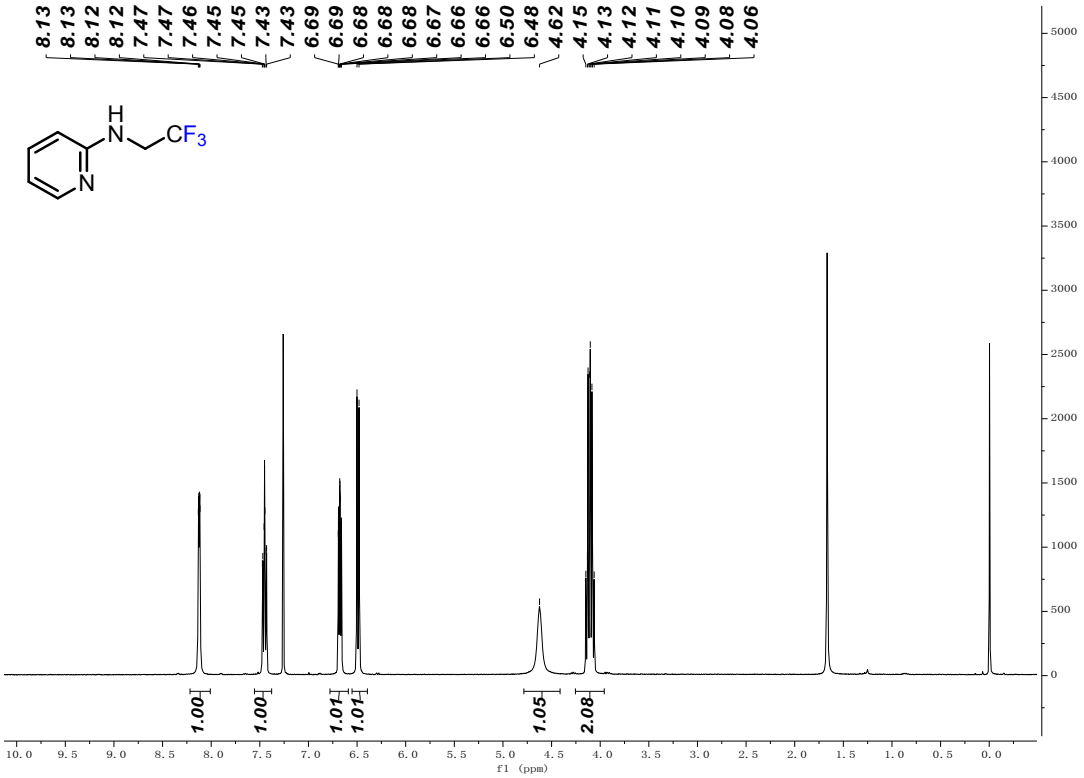
^{1}H NMR ($CDCl_3$, 400 MHz) of **9a**



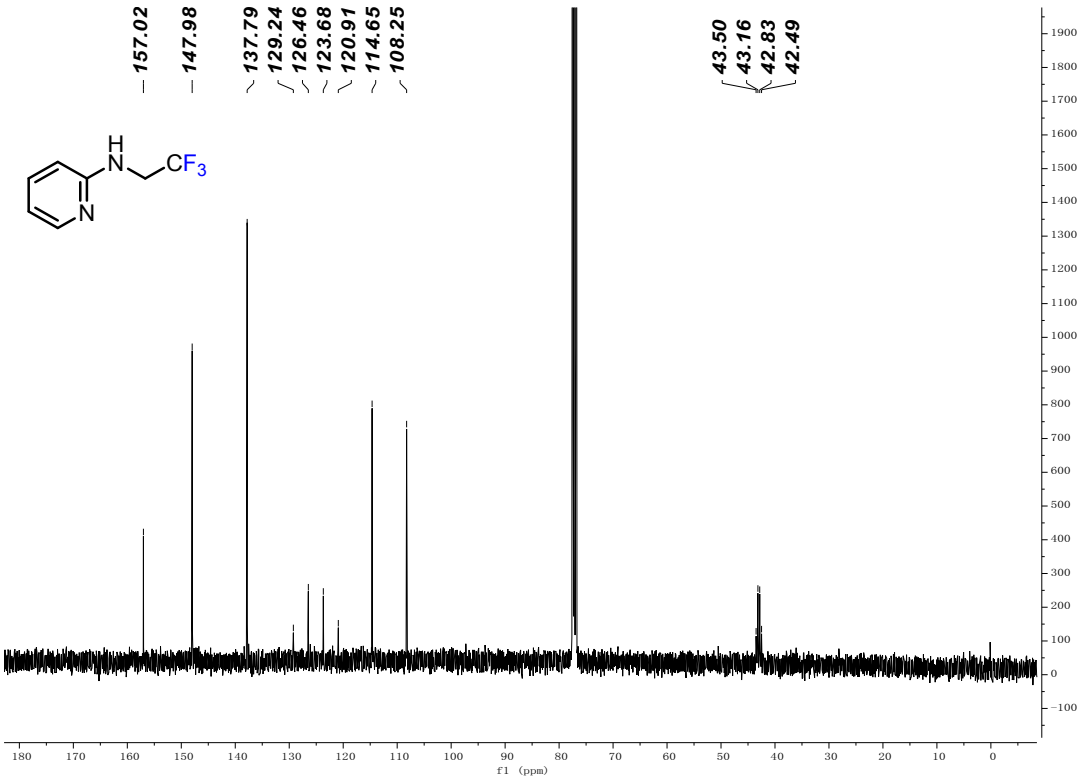
^{13}C NMR ($CDCl_3$, 400 MHz) of **9a**



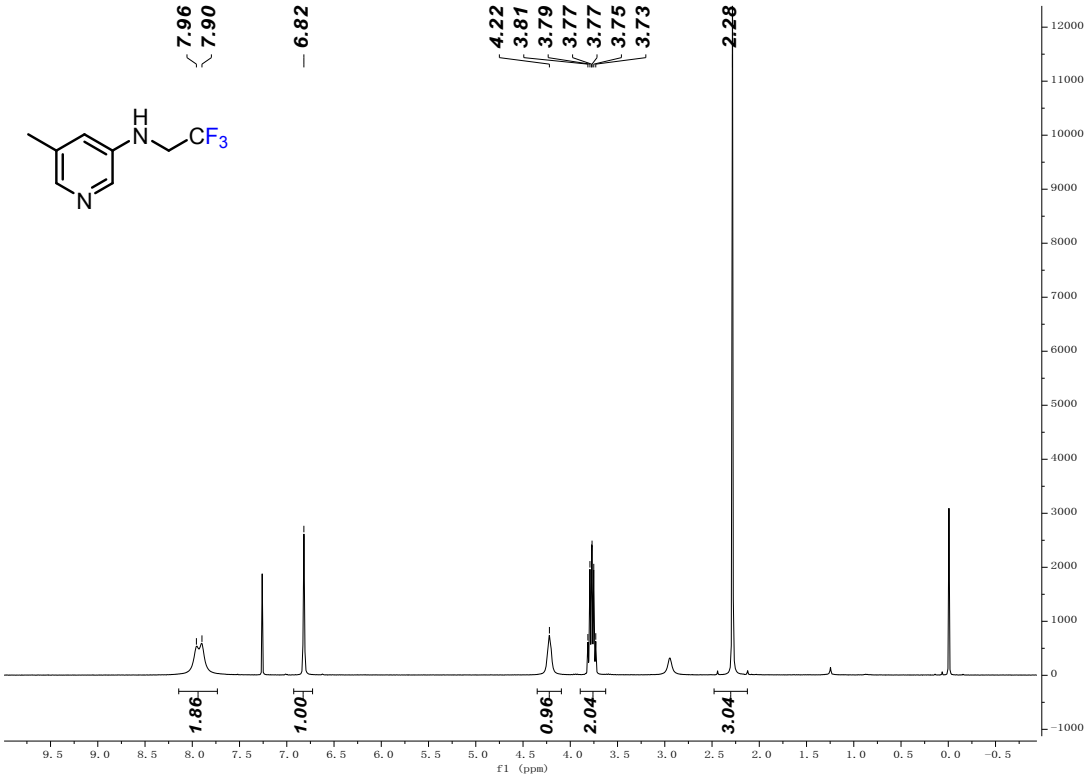
^{1}H NMR ($CDCl_3$, 400 MHz) of **9b**



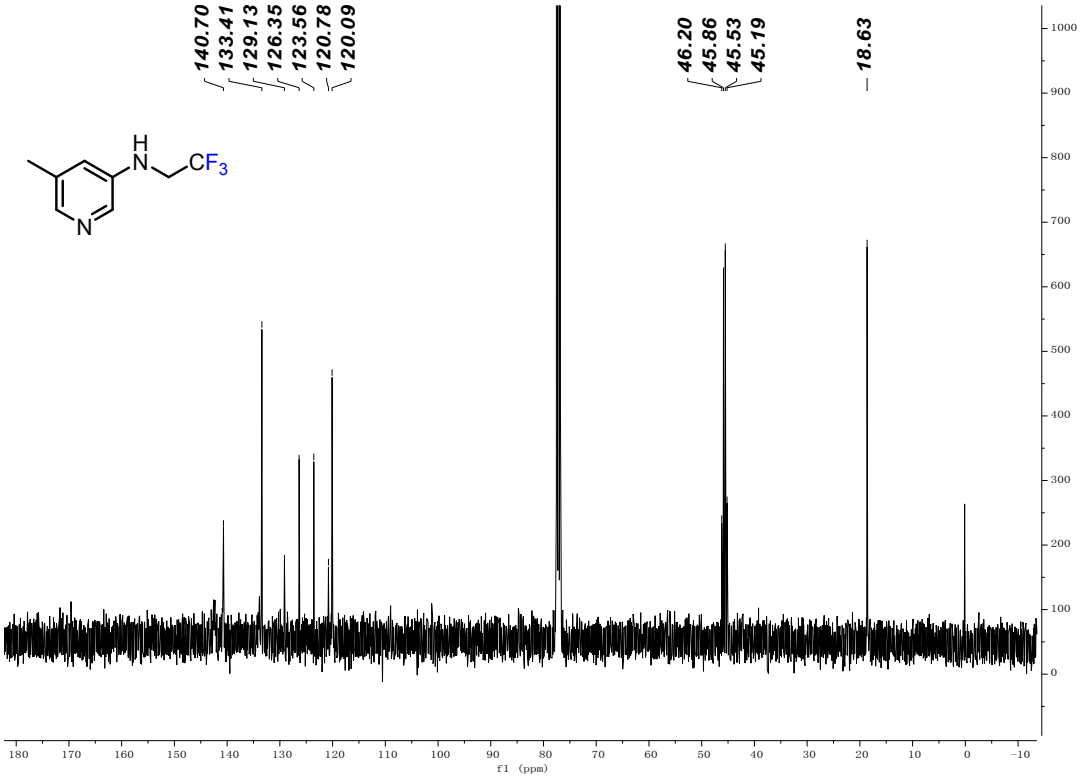
^{13}C NMR ($CDCl_3$, 400 MHz) of **9b**



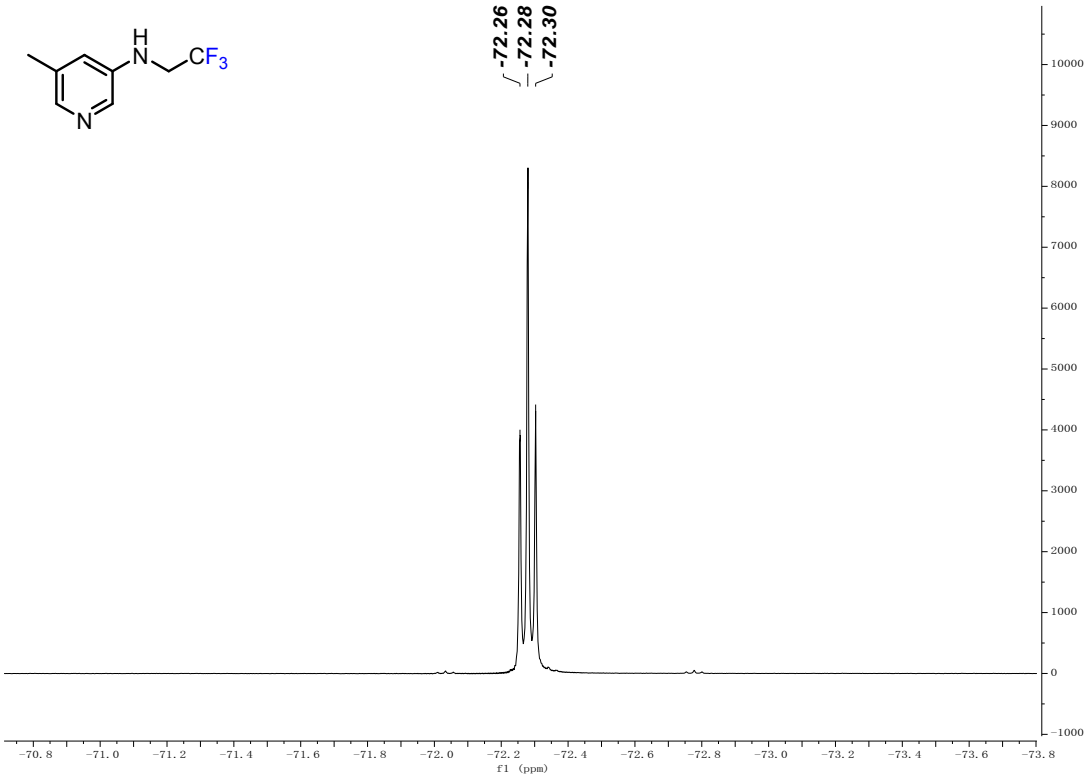
^{1}H NMR ($CDCl_3$, 400 MHz) of **9c**



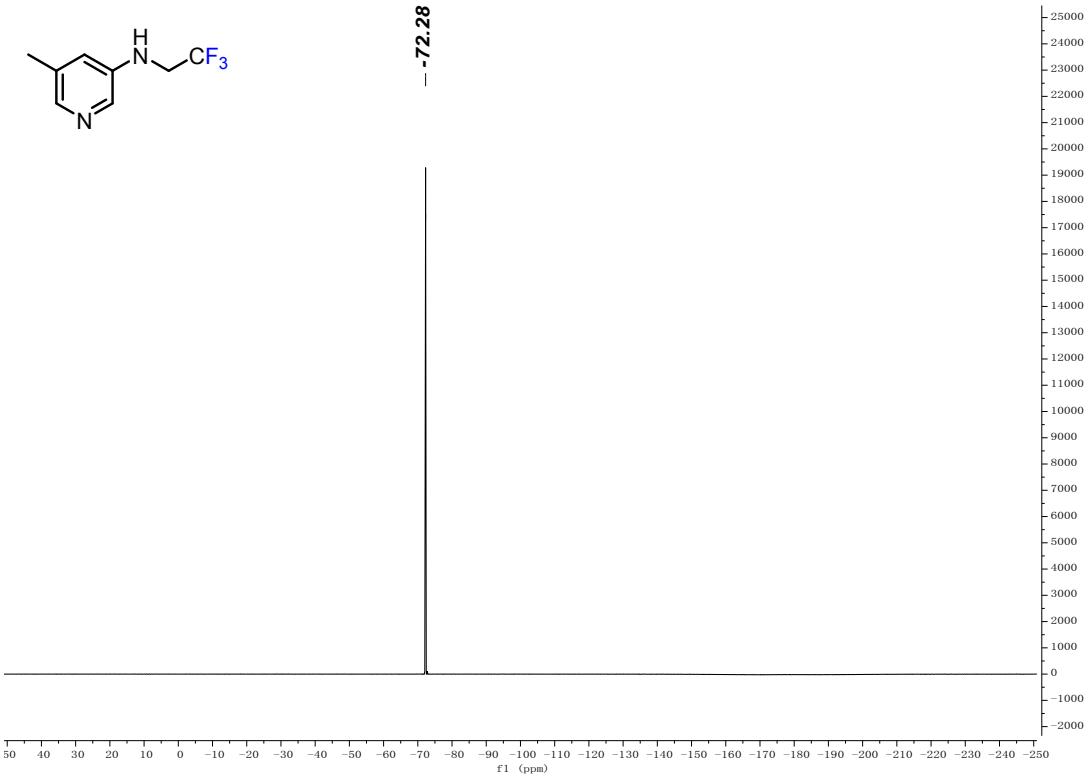
^{13}C NMR ($CDCl_3$, 400 MHz) of **9c**



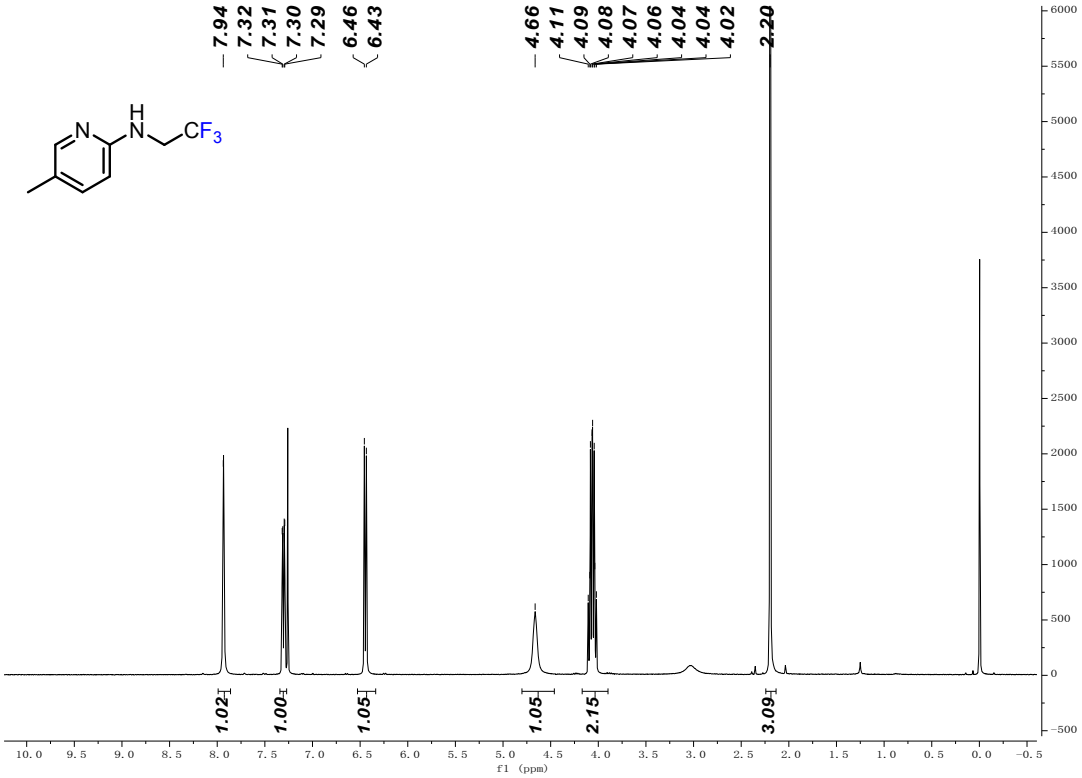
^{19}F NMR ($CDCl_3$, 376 MHz) of **9c**



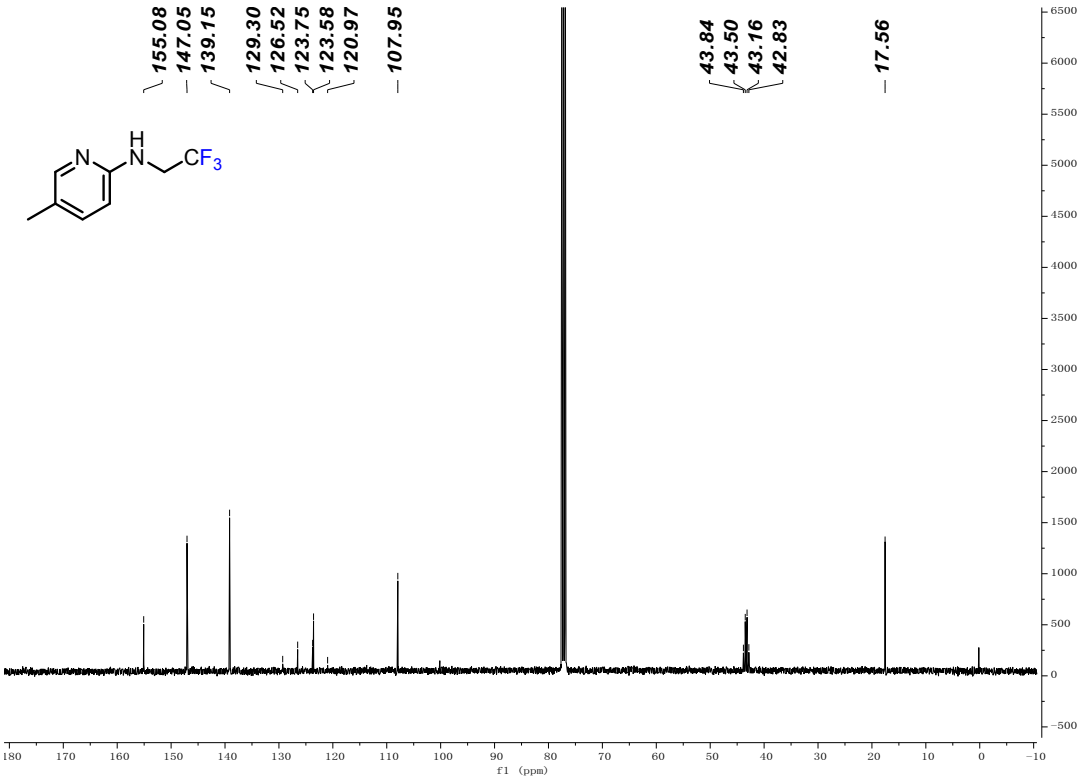
^{19}F {^{1}H} NMR ($CDCl_3$, 376 MHz) of **9c**



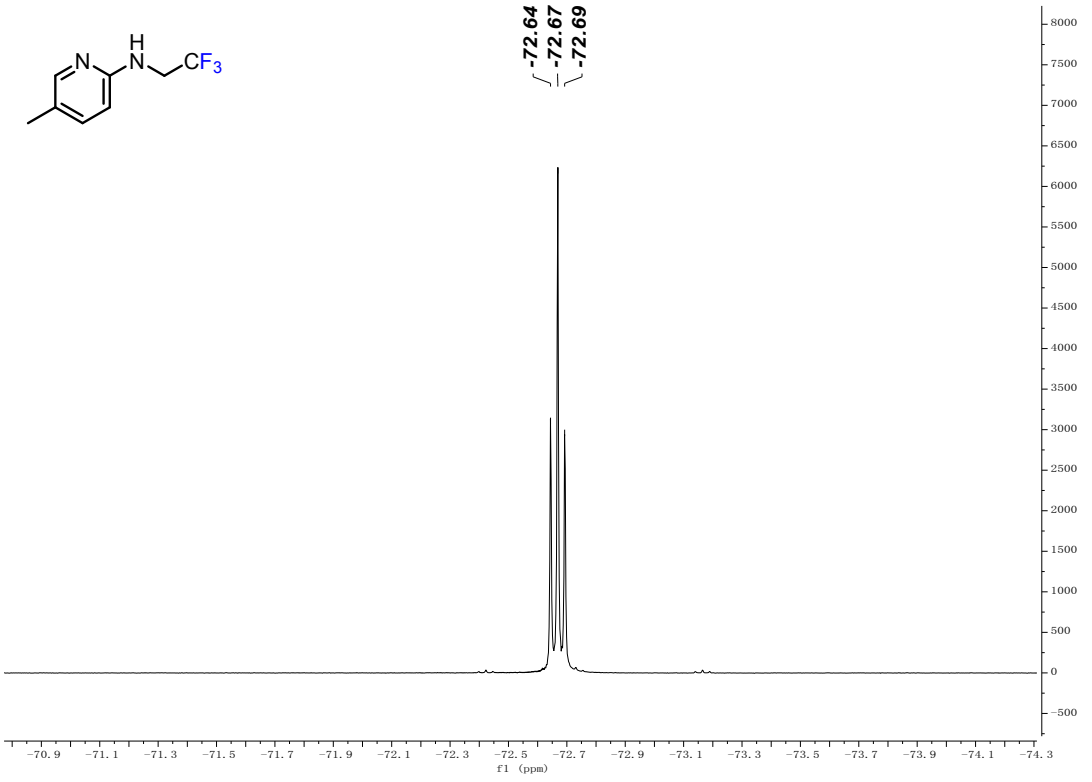
^{1}H NMR ($CDCl_3$, 400 MHz) of **9d**



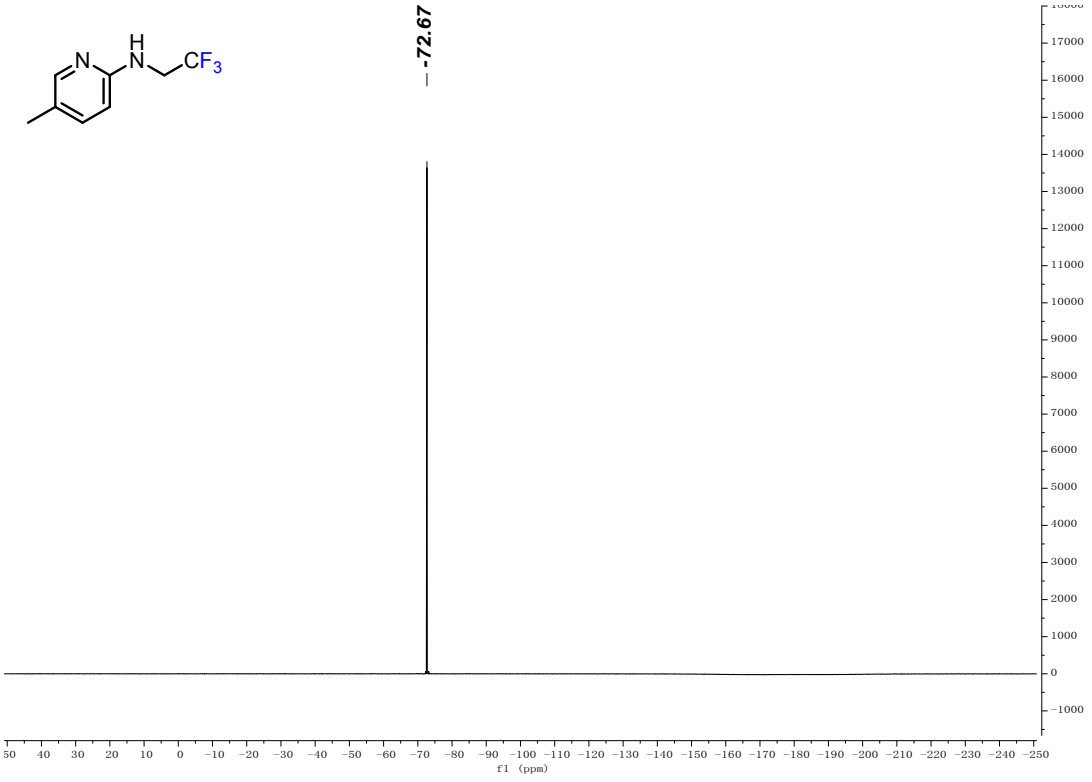
^{13}C NMR ($CDCl_3$, 400 MHz) of **9d**



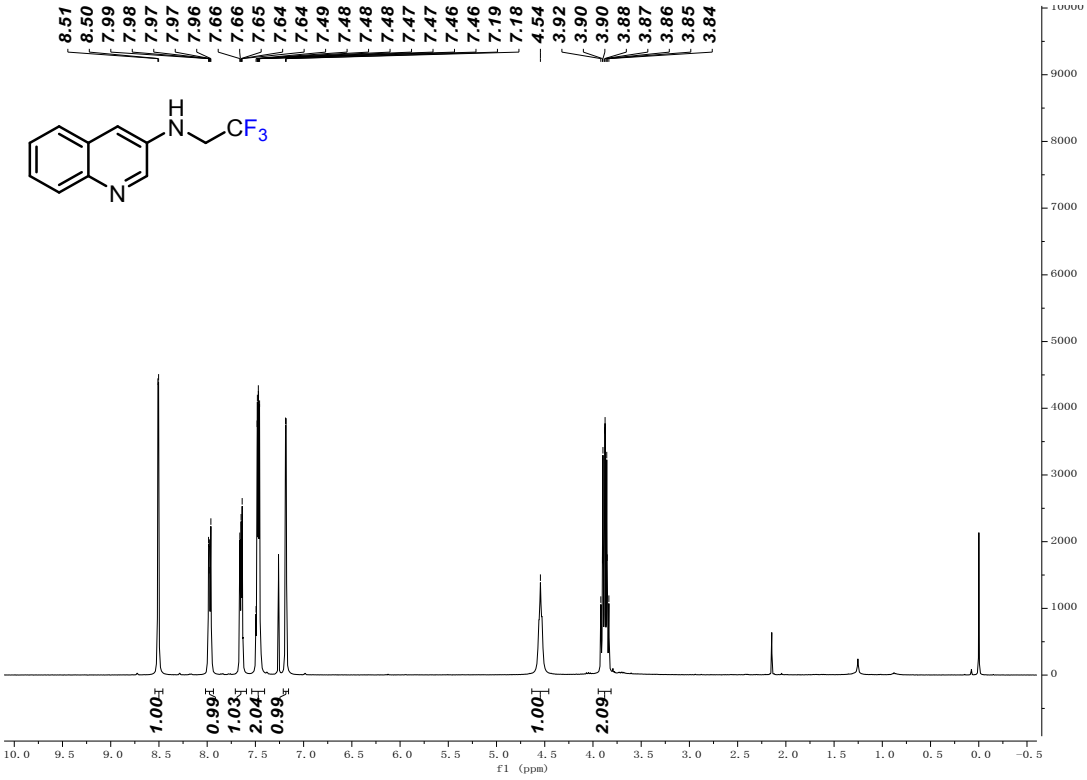
^{19}F NMR ($CDCl_3$, 376 MHz) of **9d**



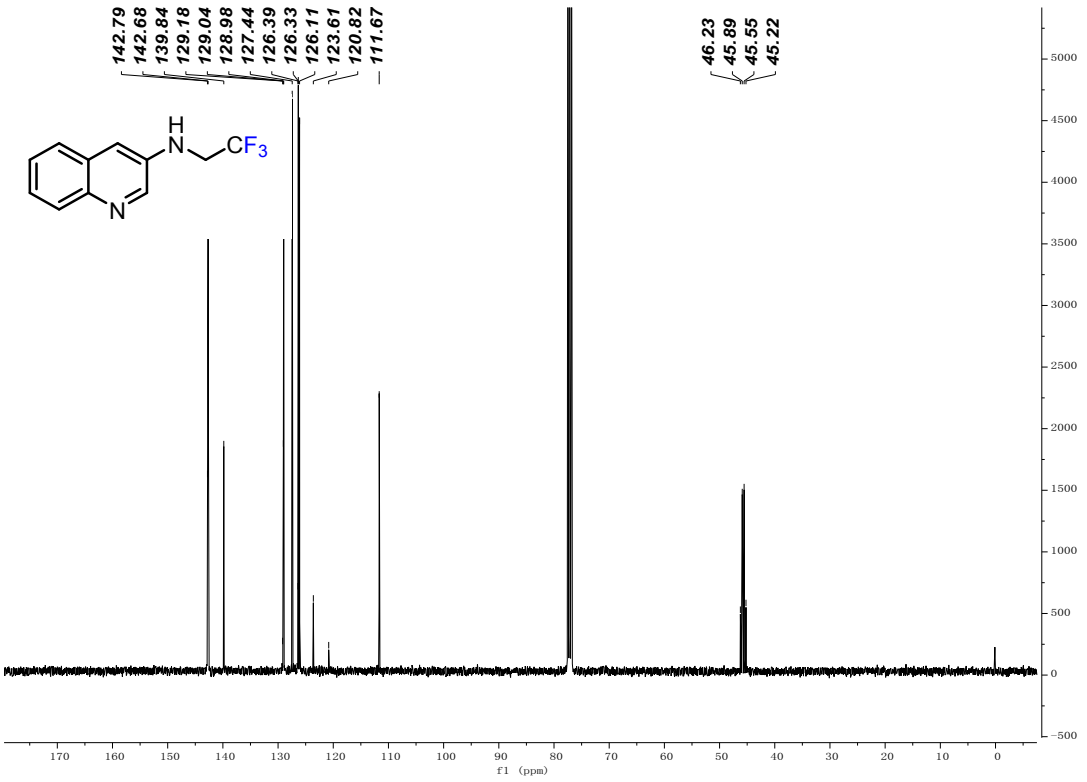
^{19}F {^{1}H} NMR ($CDCl_3$, 376 MHz) of **9d**



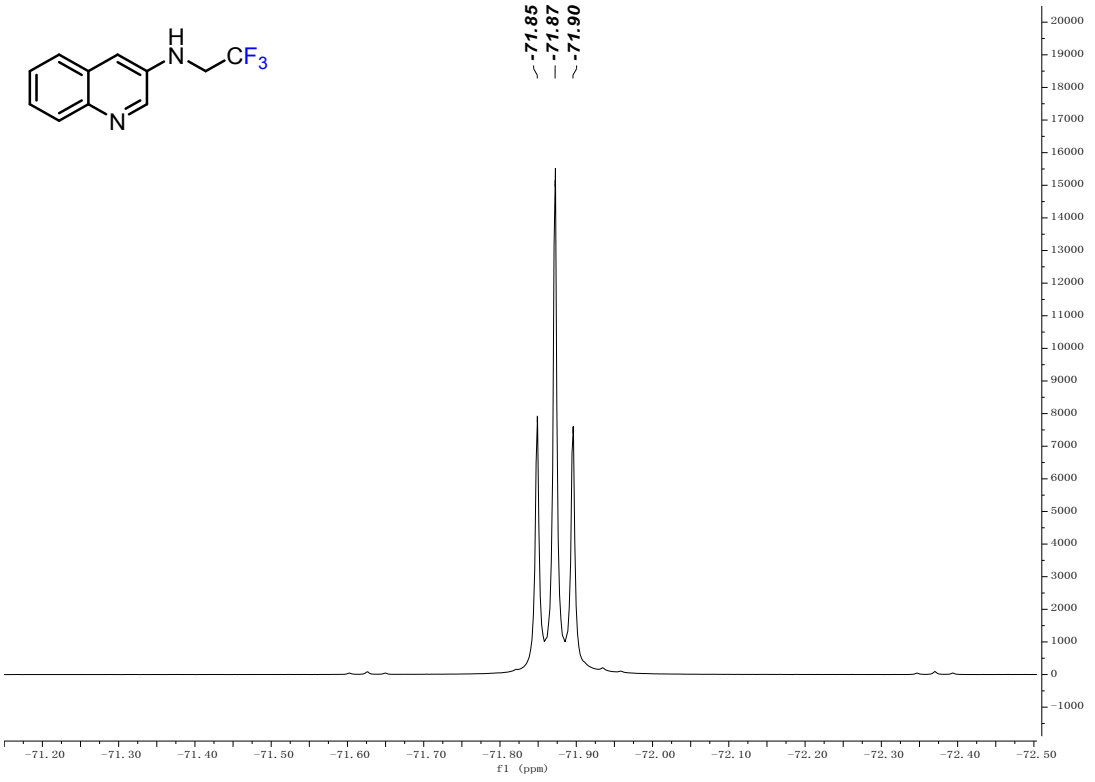
^{1}H NMR ($CDCl_3$, 400 MHz) of **9e**



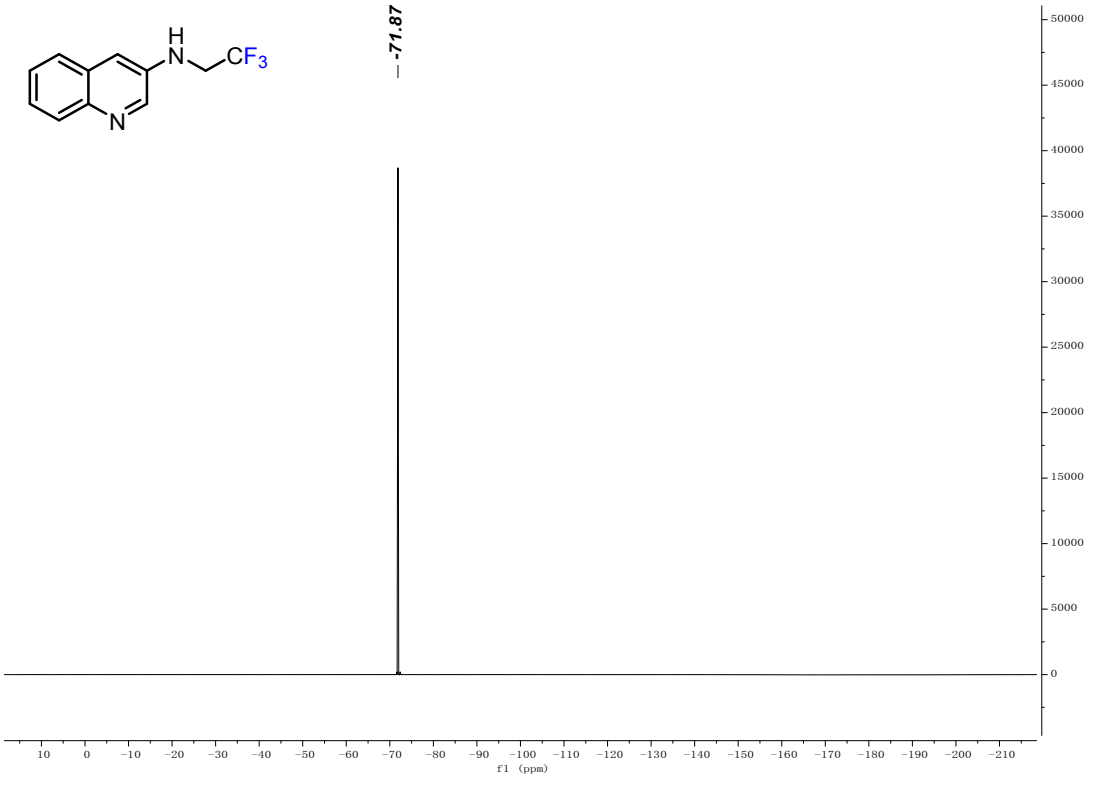
^{13}C NMR ($CDCl_3$, 400 MHz) of **9e**



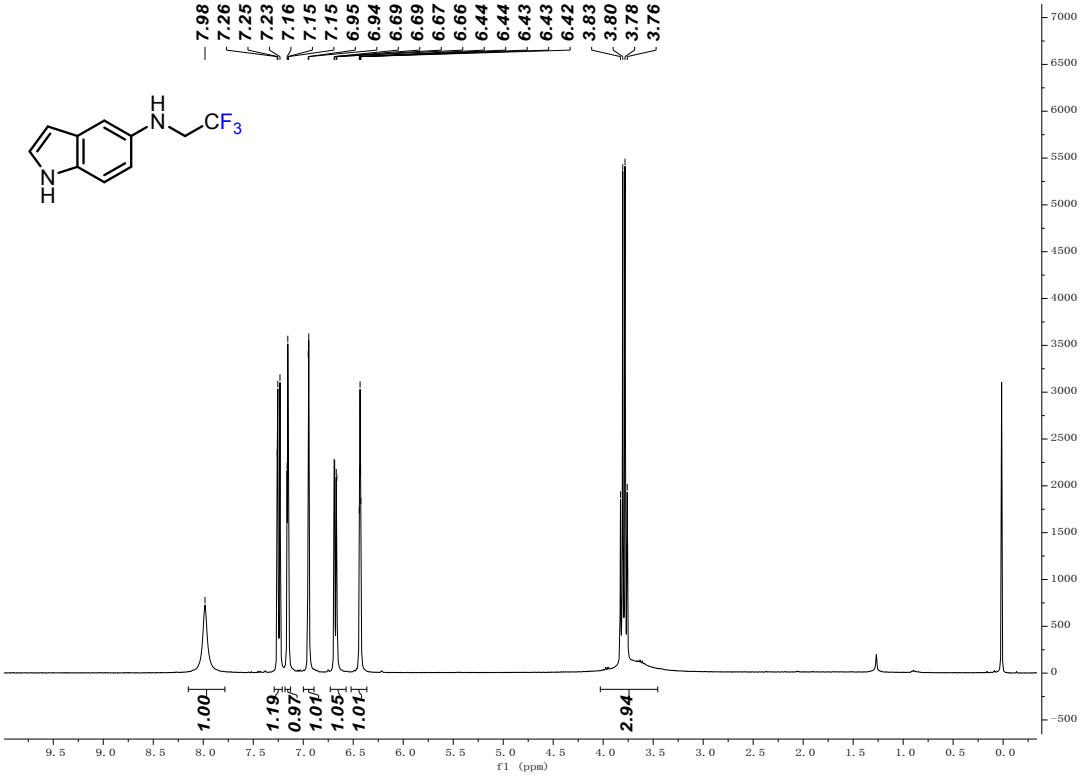
^{19}F NMR ($CDCl_3$, 376 MHz) of **9e**



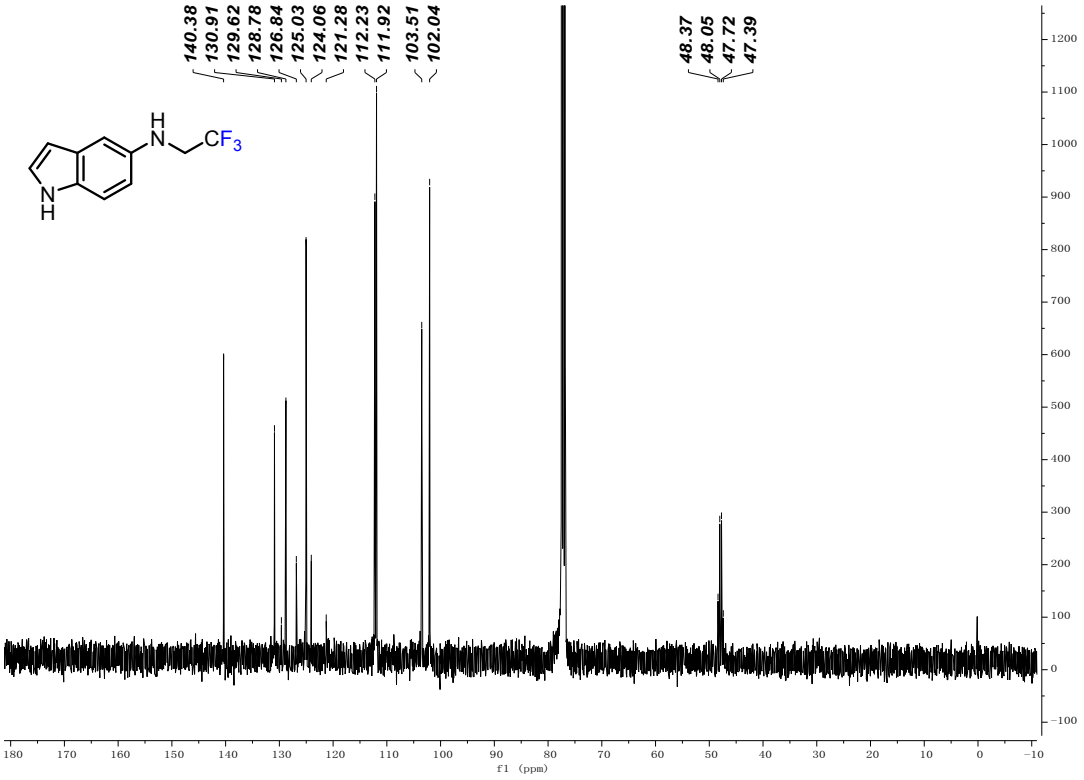
^{19}F {^{1}H} NMR ($CDCl_3$, 376 MHz) of **9e**



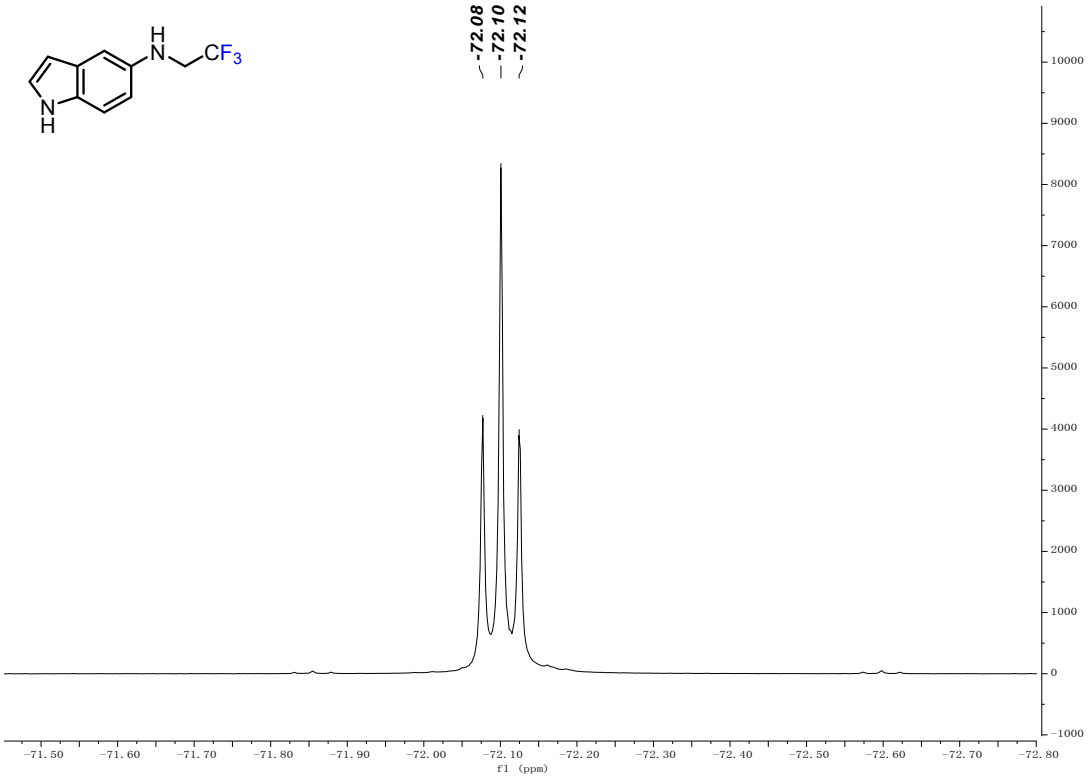
^{1}H NMR ($CDCl_3$, 400 MHz) of **9f**



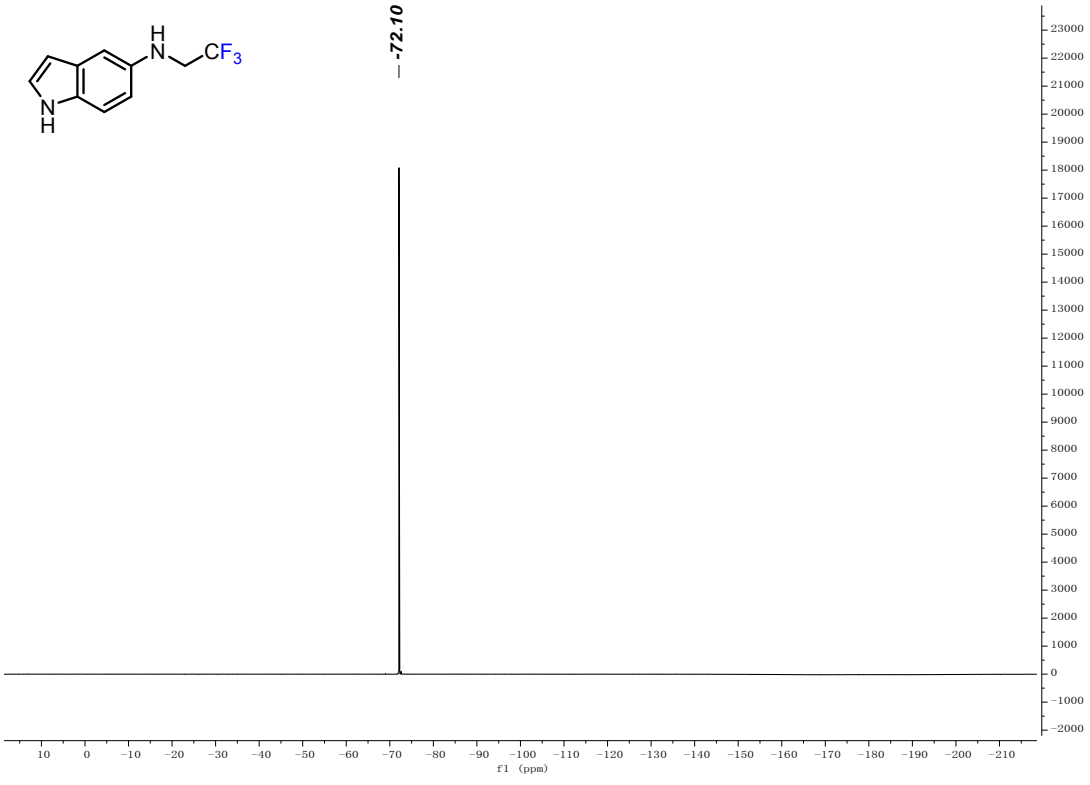
^{13}C NMR ($CDCl_3$, 400 MHz) of **9f**



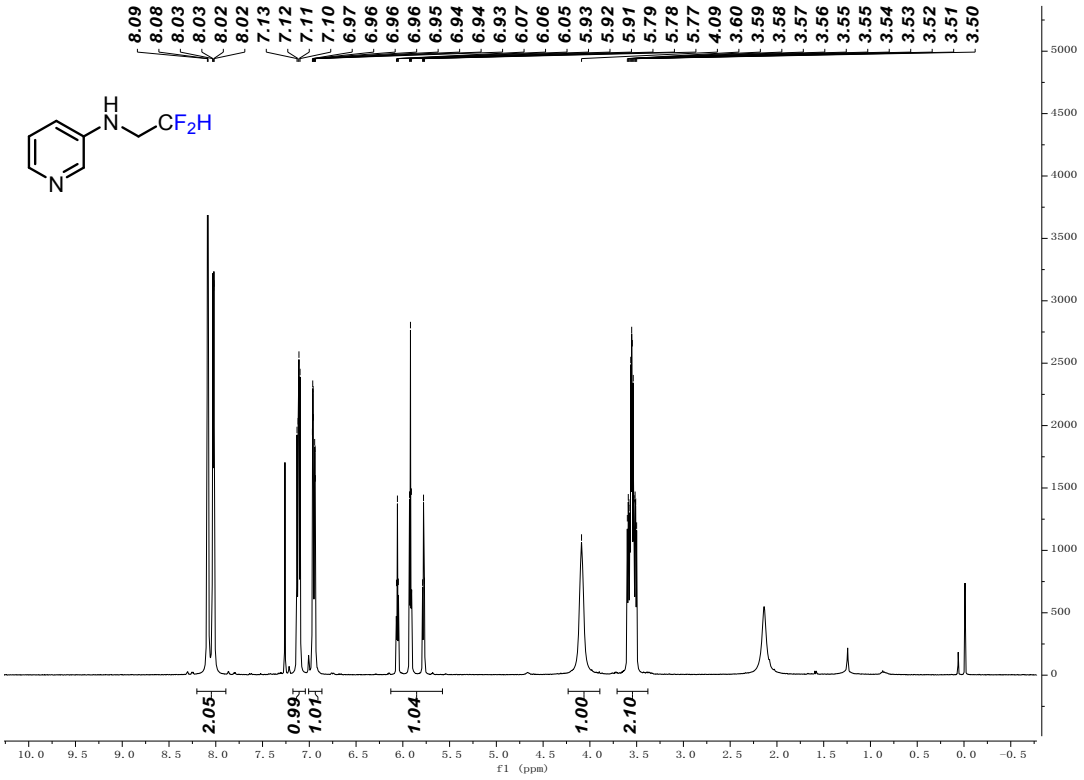
^{19}F NMR ($CDCl_3$, 376 MHz) of **9f**



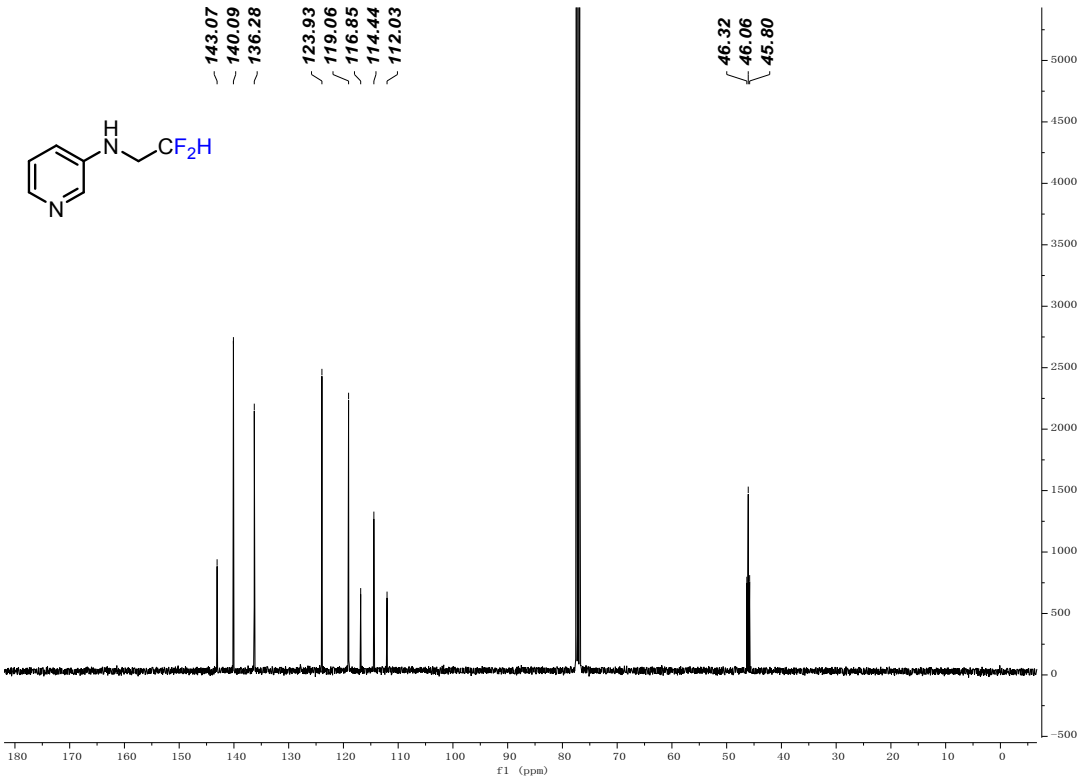
^{19}F {^{1}H} NMR ($CDCl_3$, 376 MHz) of **9f**



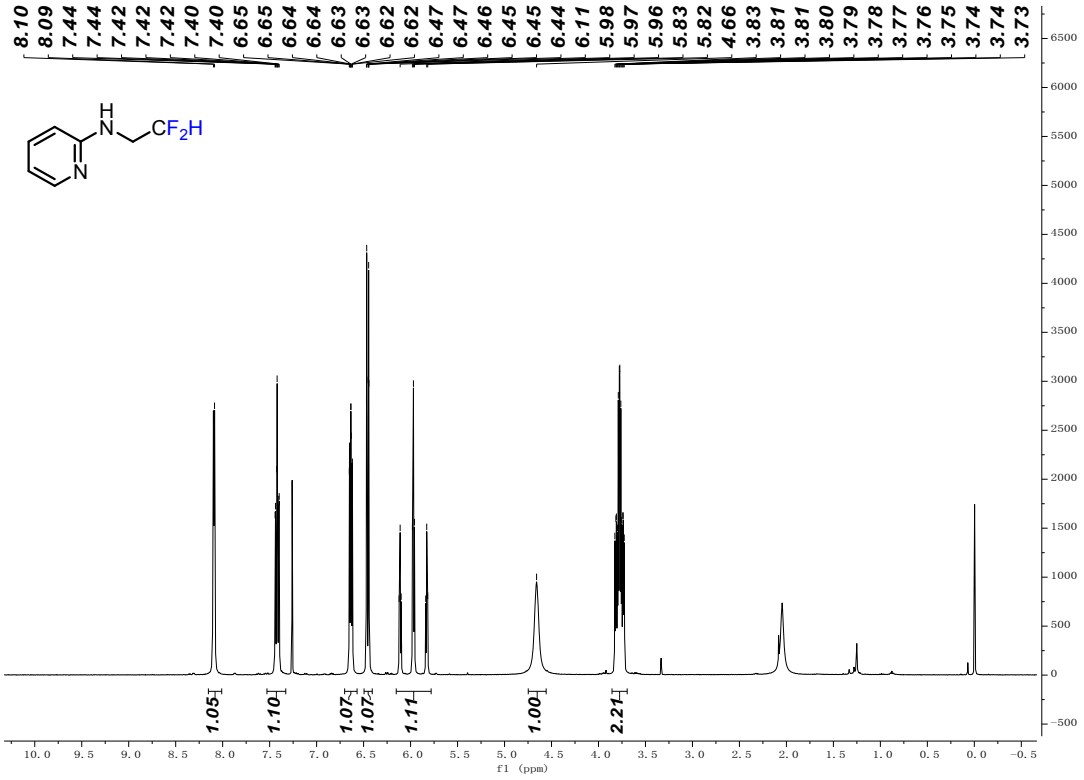
^{1}H NMR ($CDCl_3$, 400 MHz) of **10a**



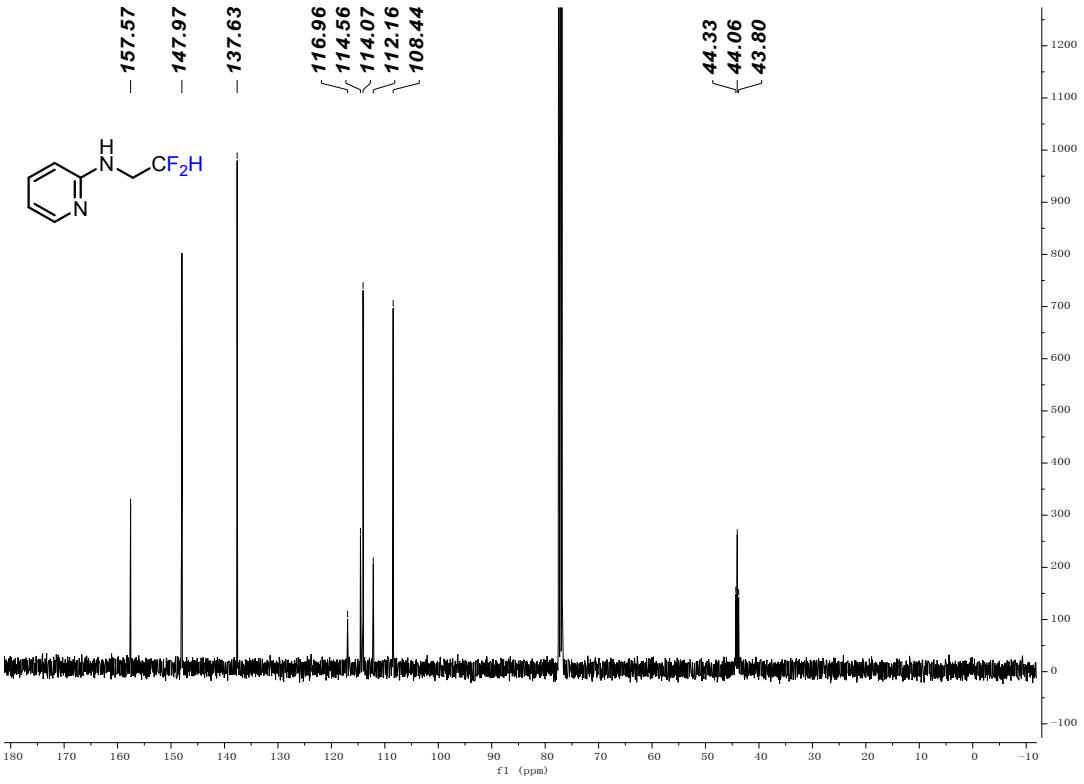
^{13}C NMR ($CDCl_3$, 400 MHz) of **10a**



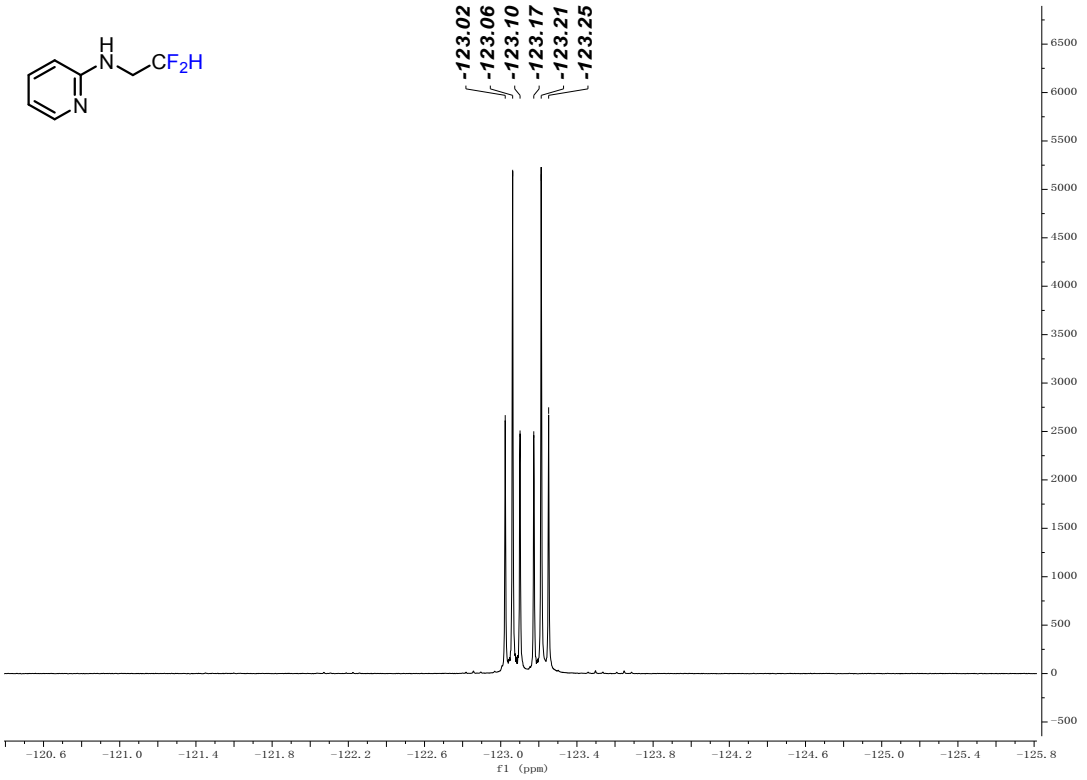
^{1}H NMR ($CDCl_3$, 400 MHz) of **10b**



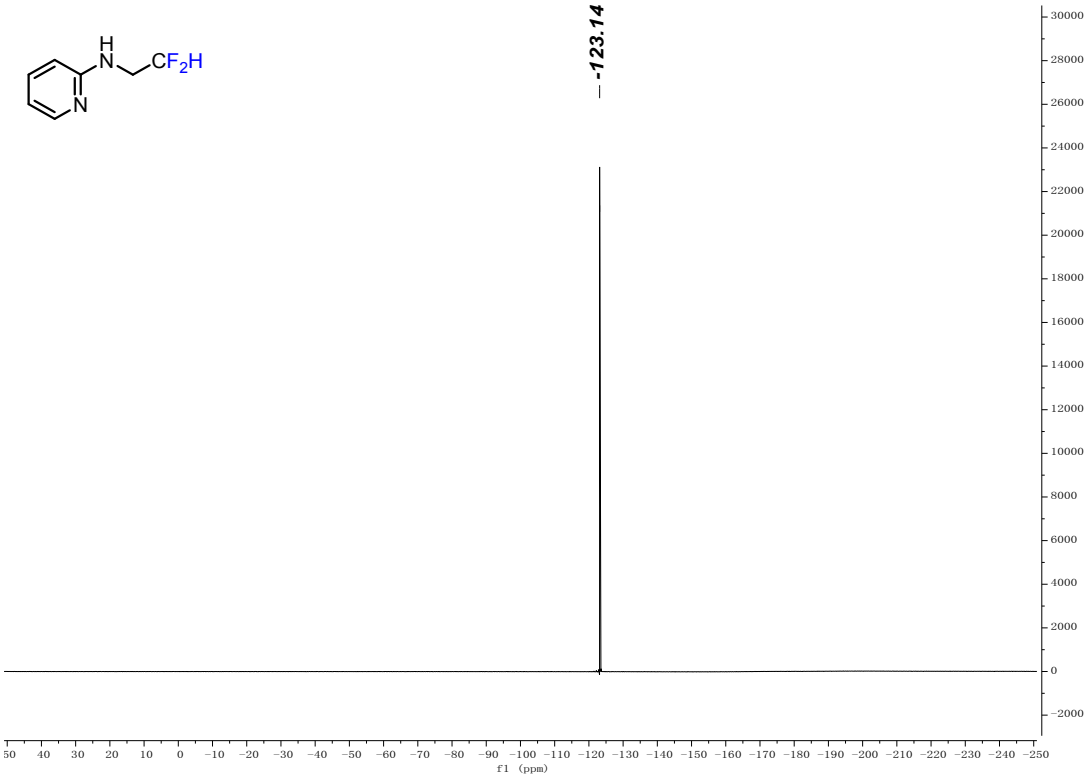
^{13}C NMR ($CDCl_3$, 400 MHz) of **10b**



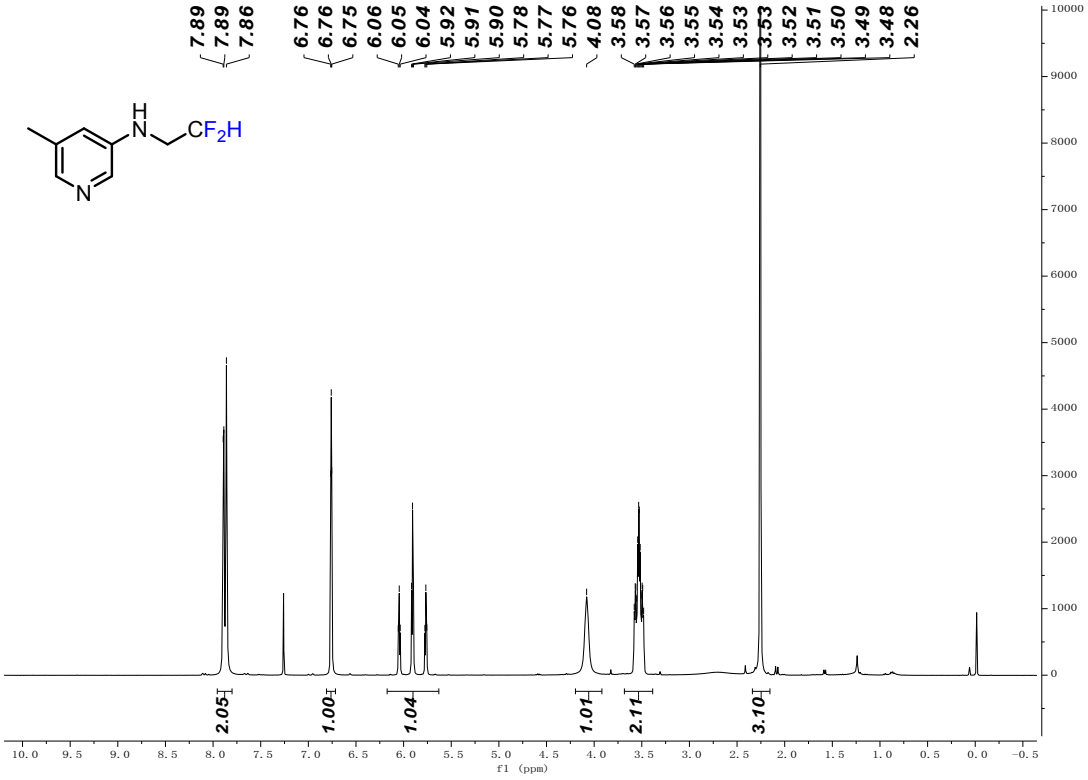
^{19}F NMR ($CDCl_3$, 376 MHz) of **10b**



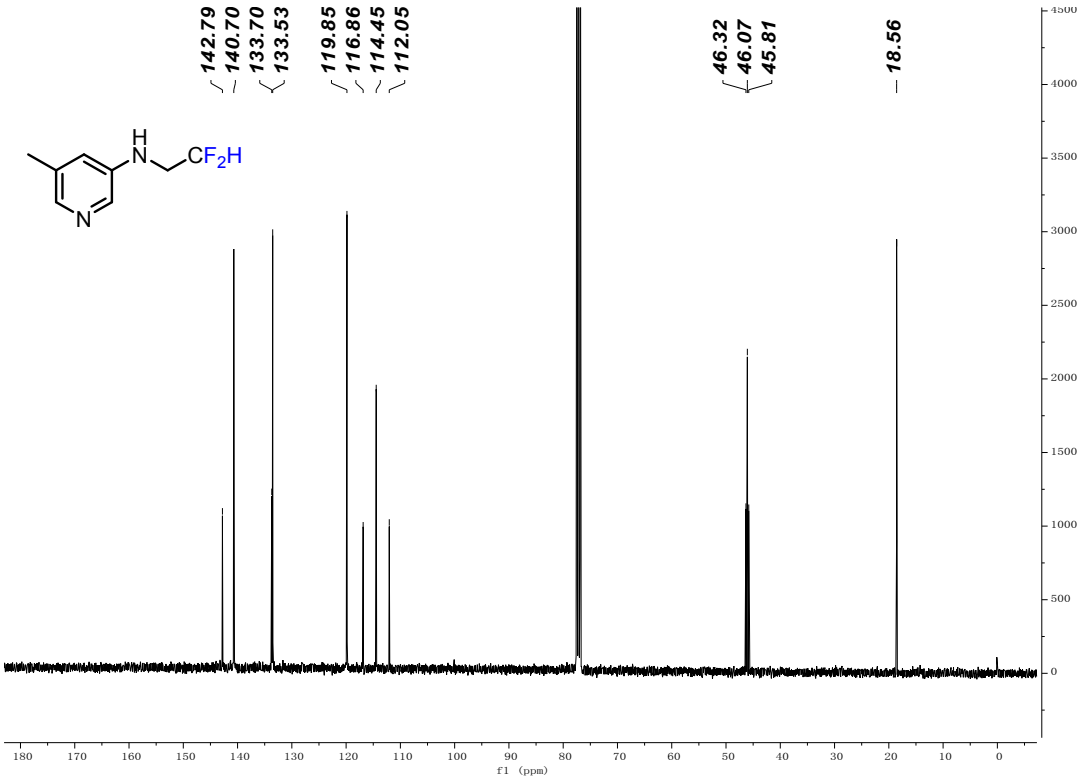
^{19}F {^{1}H} NMR ($CDCl_3$, 376 MHz) of **10b**



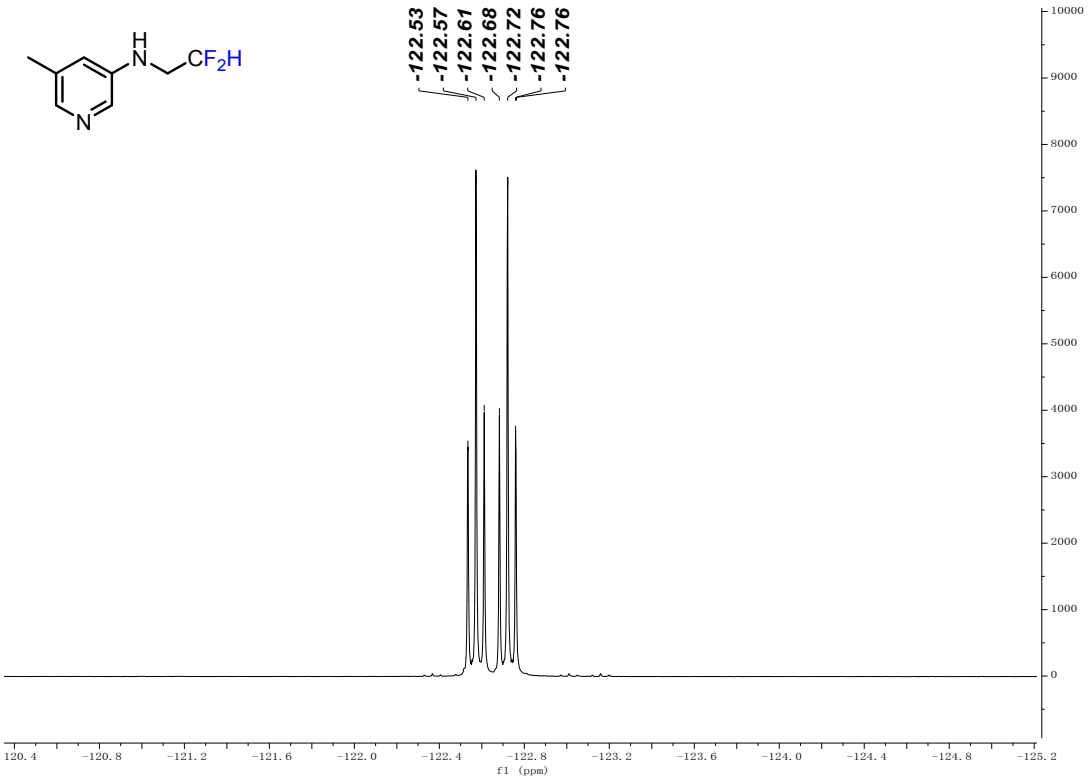
^{1}H NMR ($CDCl_3$, 400 MHz) of **10c**



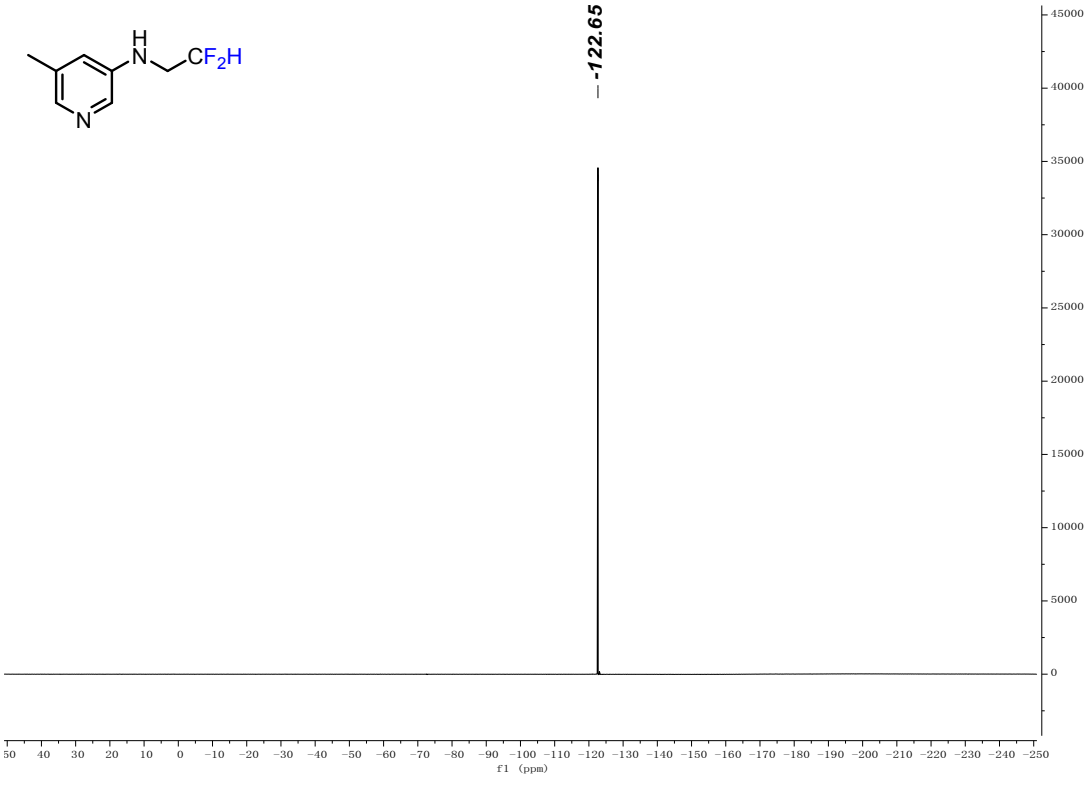
^{13}C NMR ($CDCl_3$, 400 MHz) of **10c**



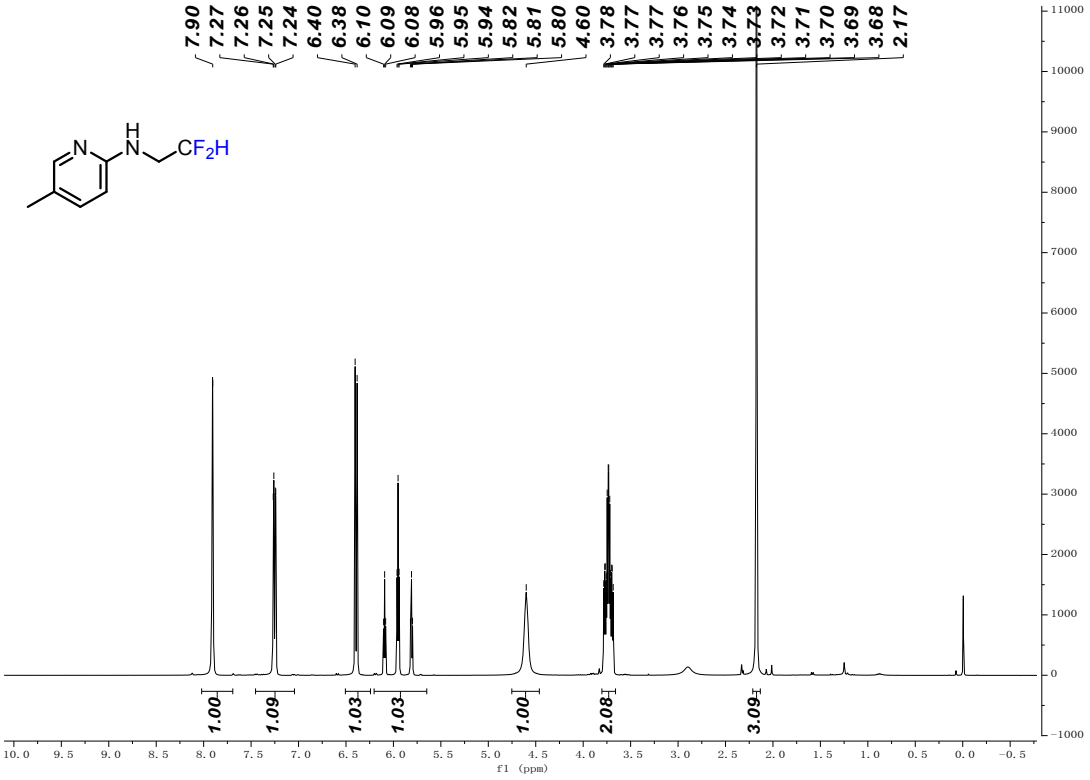
^{19}F NMR ($CDCl_3$, 376 MHz) of **10c**



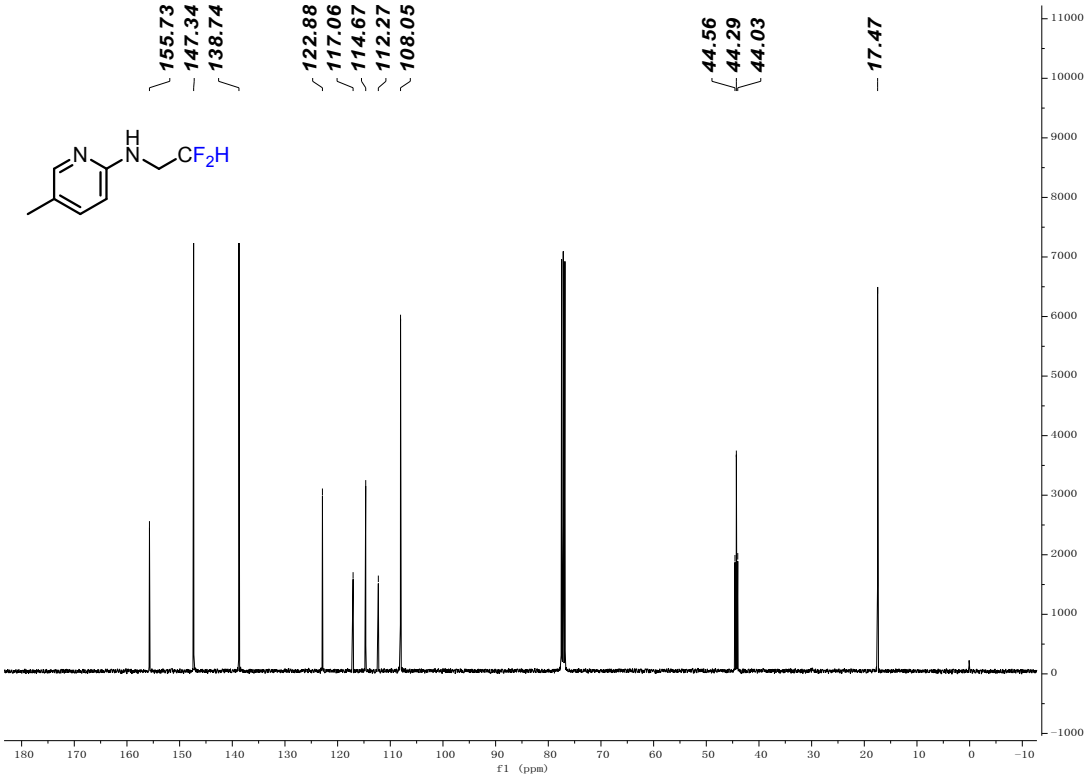
^{19}F {^{1}H} NMR ($CDCl_3$, 376 MHz) of **10c**



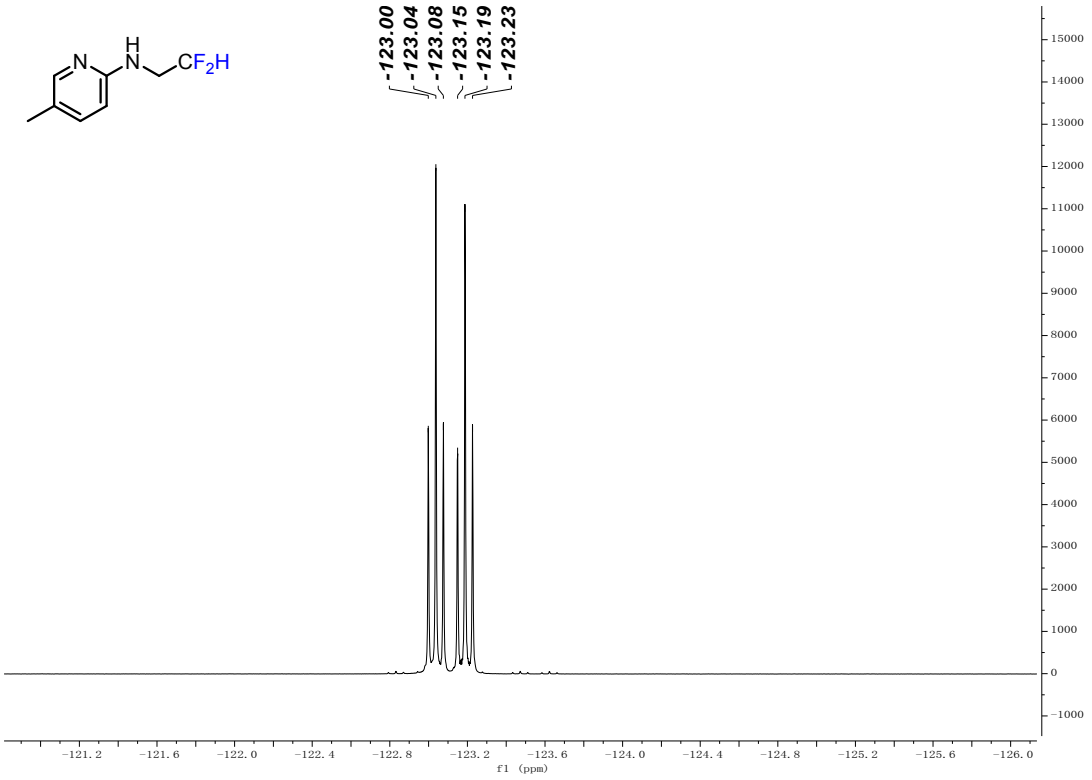
^{1}H NMR ($CDCl_3$, 400 MHz) of **10d**



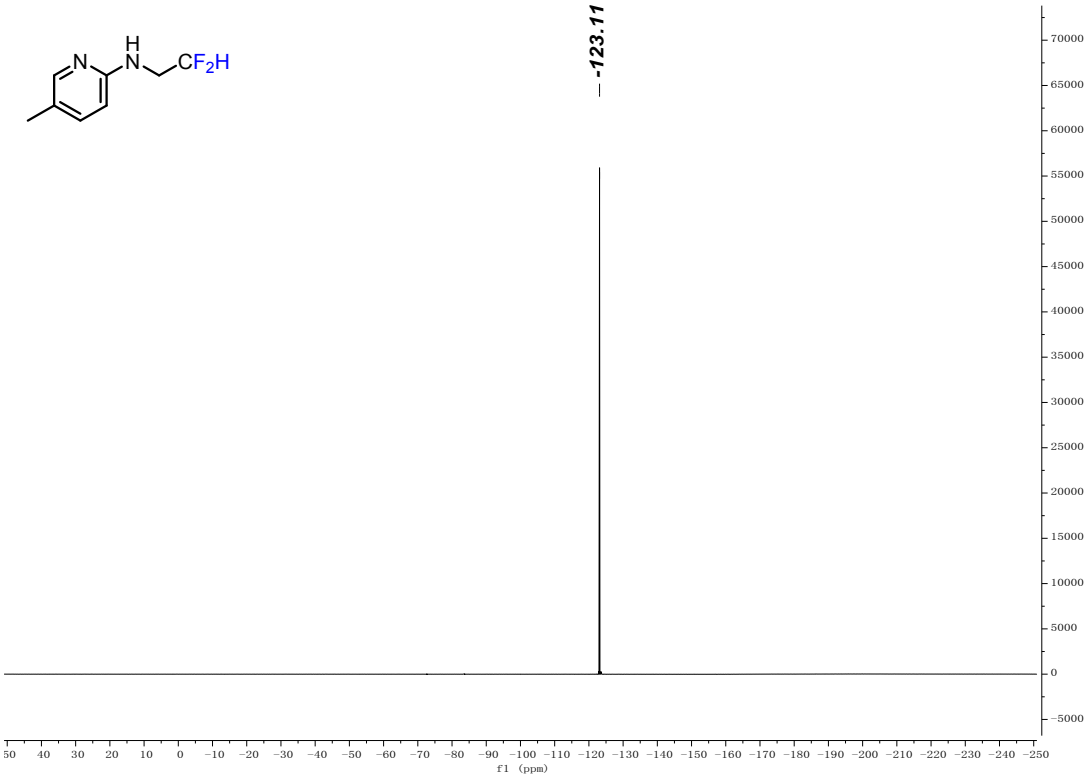
^{13}C NMR ($CDCl_3$, 400 MHz) of **10d**



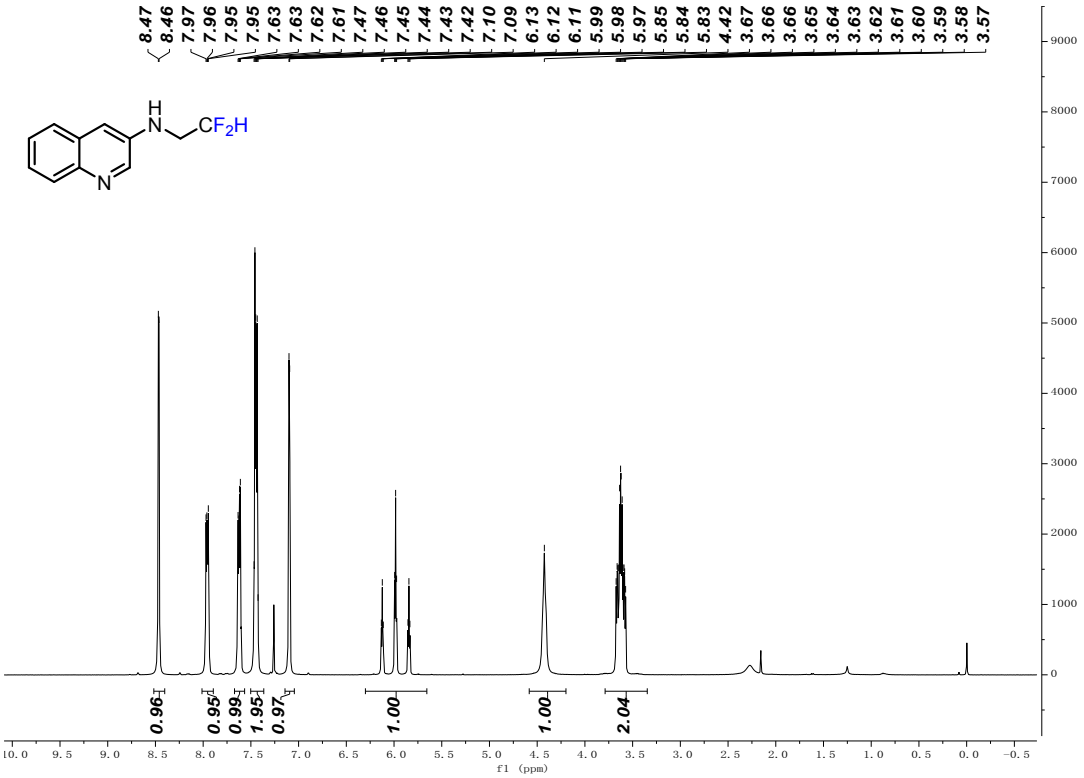
^{19}F NMR ($CDCl_3$, 376 MHz) of **10d**



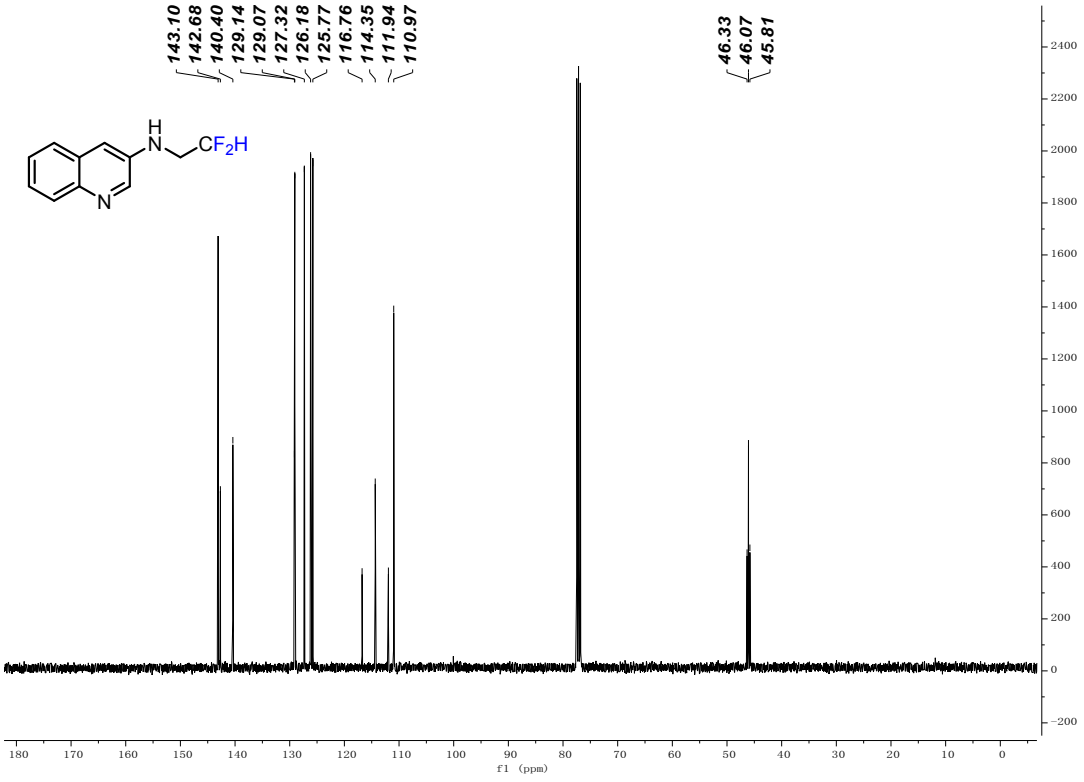
^{19}F {^{1}H} NMR ($CDCl_3$, 376 MHz) of **10d**



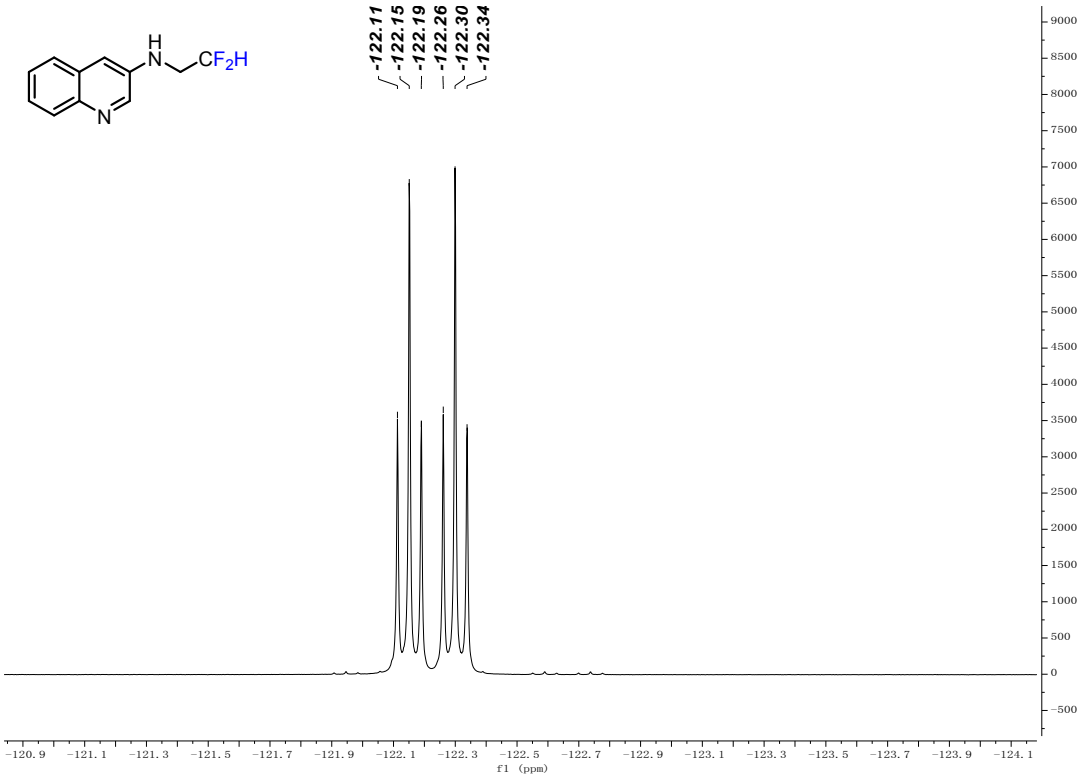
^{1}H NMR ($CDCl_3$, 400 MHz) of **10e**



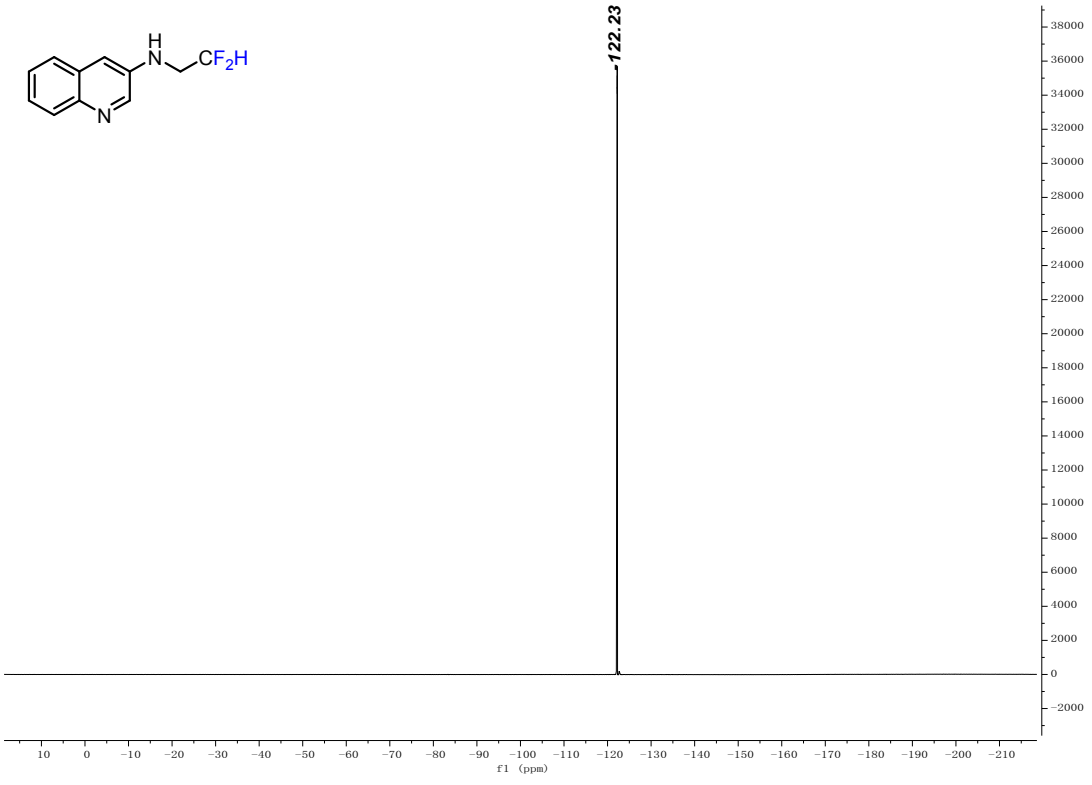
^{13}C NMR ($CDCl_3$, 400 MHz) of **10e**



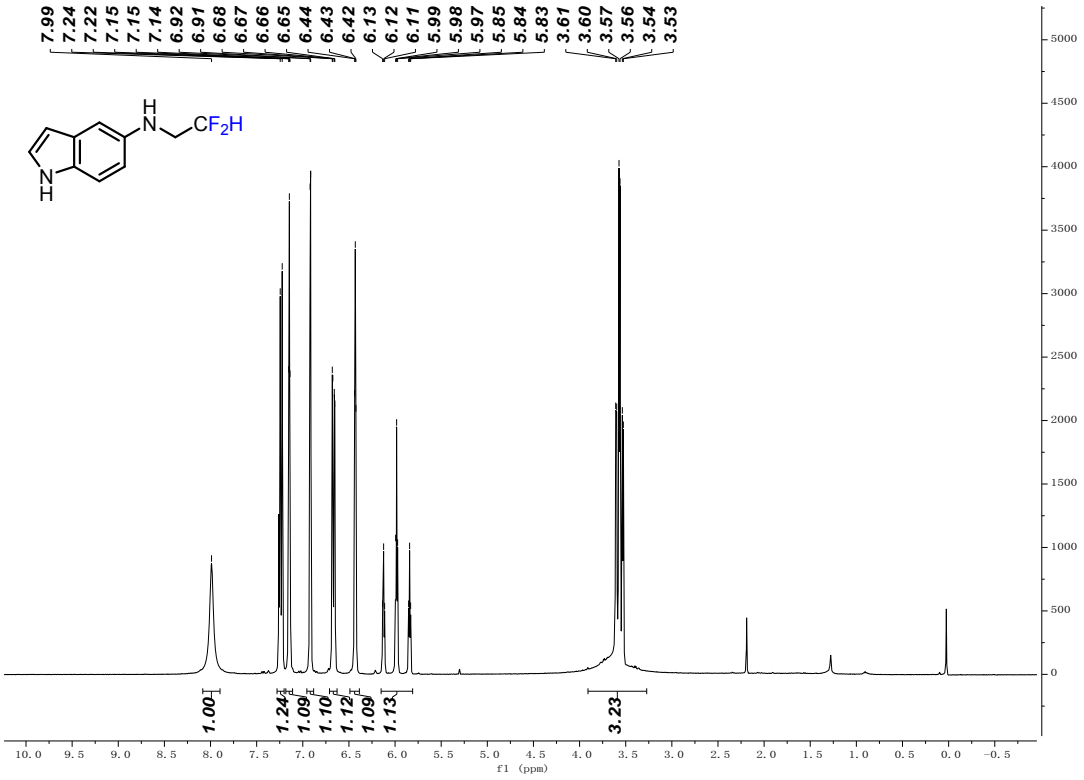
^{19}F NMR ($CDCl_3$, 376 MHz) of **10e**



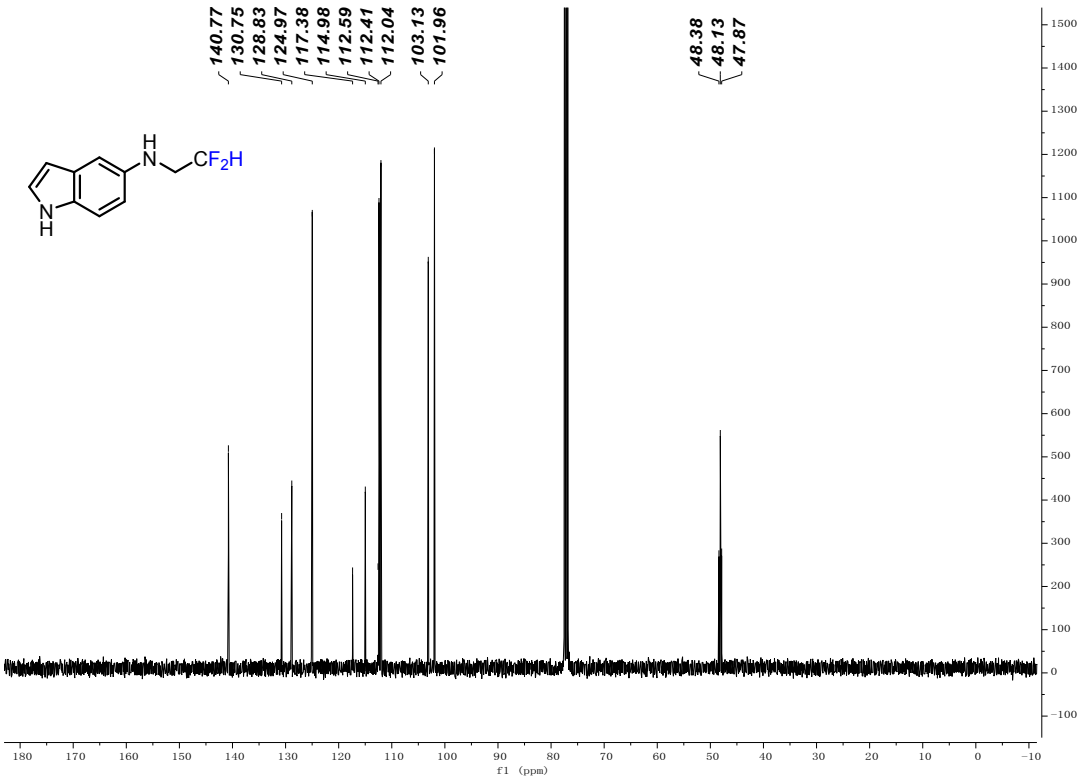
^{19}F {^{1}H} NMR ($CDCl_3$, 376 MHz) of **10e**



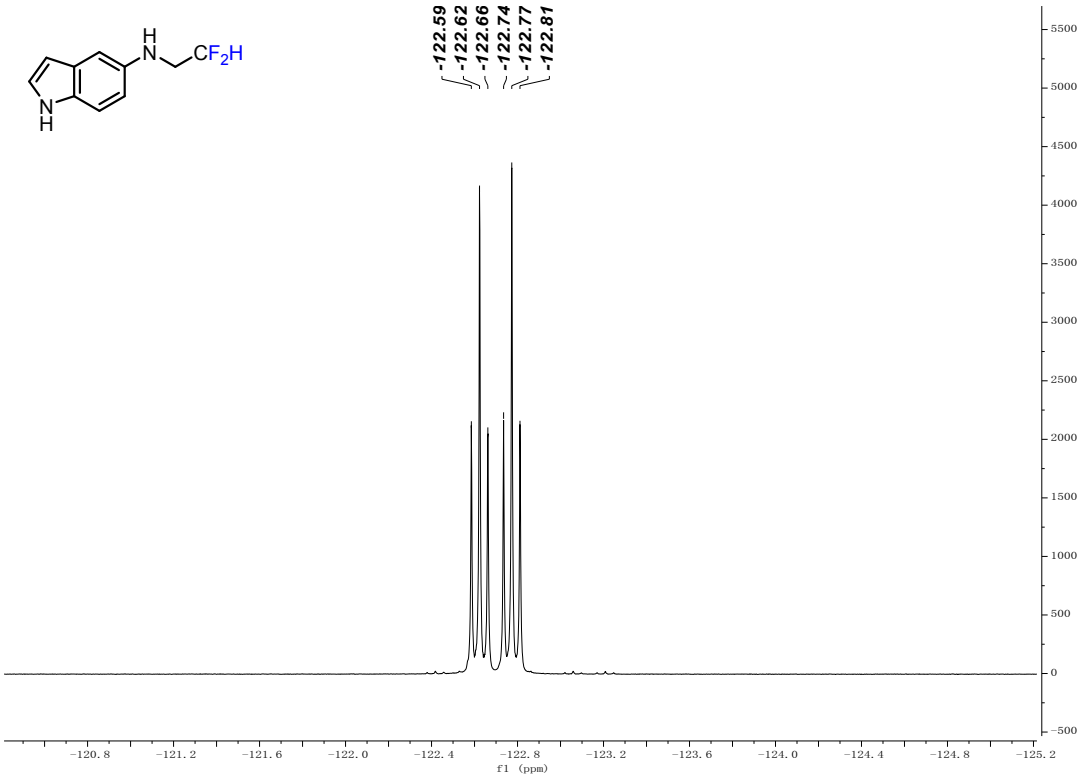
^{1}H NMR ($CDCl_3$, 400 MHz) of **10f**



^{13}C NMR ($CDCl_3$, 400 MHz) of **10f**



^{19}F NMR ($CDCl_3$, 376 MHz) of **10f**



^{19}F {^{1}H} NMR ($CDCl_3$, 376 MHz) of **10f**