Three-Component Minisci Reaction Involving Trifluoromethyl Radical Promoted by TBHP

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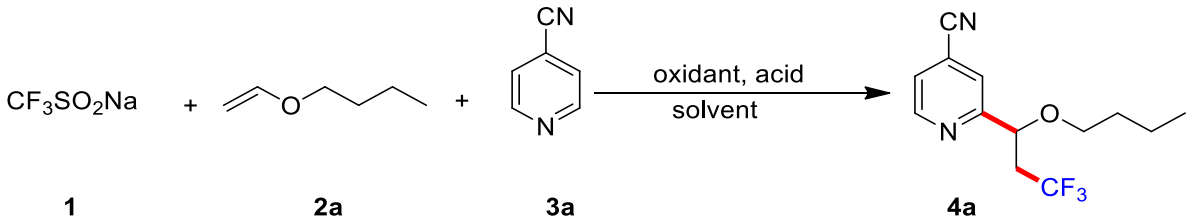
1. General information

Analytical grade solvents and commercially available reagents were purchased from Energy chemical company, J&K Scientific Ltd, Alfa Aesa chemical company and used directly without further purification unless otherwise stated. Yields refered to products isolated after purification by column chromatography, unless otherwise stated. Column chromatography was performed using silica gel (mesh 300-400). ^{1}H NMR spectra were recorded at 400 MHz or 600 MHz. ^{13}C NMR spectra were recorded at 151 MHz. ^{19}F NMR spectra were recorded at 376 MHz. ^{1}H and ^{13}C NMR chemical shifts are reported in parts per million and referenced to residual $CHCl_3$ signals in $CDCl_3$ (^{1}H: δ 7.26; ^{13}C: δ 77.00), or $CFCl_3$ (^{19}F: δ 0.0) and TMS as internal standard. Coupling constants (*J*) are reported in hertz. High-resolution mass data were recorded on a high-resolution mass spectrometer in the ESI mode on an orbitrap ID-X HRMS. XRD data was collected on a Bruker SMART APEX CCD diffractometer equipped with a graphite-monochromated Mo-Kα (λ = 0.71073 Å) radiation source.

2. Optimization of the reaction conditions

Table S1 Optimization of the three-component Minisci reaction conditions [a, b]



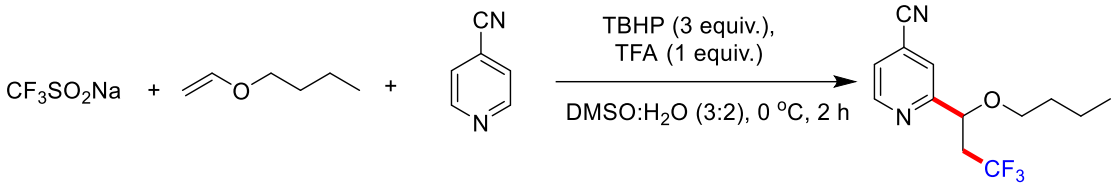
1 **2a** **3a** **4a**

Entry	Oxidant (equiv.)	Acid (equiv.)	Temp. (°C)	Time (h)	Solvent	Yield (%)[b]
1	TBHP (5)	TFA (2)	80	24	DMSO	11
2	DTBP (5)	TFA (2)	80	24	DMSO	n.d.
3	$Na_2S_2O_8$ (5)	TFA (2)	80	24	DMSO	n.d.
4	$K_2S_2O_8$ (5)	TFA (2)	80	24	DMSO	n.d.
5	$(NH_4)_2S_2O_8$ (5)	TFA (2)	80	24	DMSO	n.d.
6	Selectfluor (5)	TFA (2)	80	24	DMSO	n.d.
7	H_2O_2 (5)	TFA (2)	80	24	DMSO	n.d.
8	TBHP (5)	TFA (2)	30	24	DMSO	37
9	TBHP (5)	TFA (2)	30	24	DCM	n.d.
10	TBHP (5)	TFA (2)	30	24	CH_3CN	7
11	TBHP (5)	TFA (2)	30	24	THF	n.d.
12	TBHP (5)	TFA (2)	30	24	DCE	n.d.
13	TBHP (5)	TFA (2)	30	24	DMF	n.d.
14	TBHP (5)	TFA (2)	30	24	EA	n.d.
15	TBHP (5)	TFA (2)	30	24	Et_2O	n.d.
16	TBHP (5)	TFA (2)	30	24	MeOH	n.d.
17	TBHP (5)	TFA (2)	30	24	Cyclohexane	n.d.
18	TBHP (5)	TFA (2)	30	24	1,4-Dioxane	n.d.
19	TBHP (5)	TFA (2)	30	24	1-Propanol	n.d.
20	TBHP (5)	TFA (2)	30	24	^{i}PrOH	n.d.
21	TBHP (5)	TFA (2)	30	24	HFIP	n.d.
22	TBHP (5)	TFA (2)	30	24	NMP	n.d.
23	TBHP (5)	TFA (2)	30	24	PhMe	n.d.
24	TBHP (5)	TFA (2)	30	24	H_2O	12
25	TBHP (5)	TFA (2)	30	24	H_2O+1 eq TBAF	30
26	TBHP (5)	TFA (2)	30	24	H_2O+1 eq TBAB	18
27	TBHP (5)	TFA (2)	30	24	H_2O+1 eq TBAI	7

28	TBHP (5)	TFA (2)	30	24	H_2O+1 eq SDS	6
29	TBHP (5)	-	30	24	DMSO	n.d.
30	-	TFA (2)	30	24	DMSO	n.d.
31	TBHP (5)	TFA (3)	30	24	DMSO	30
32	TBHP (5)	TFA (1)	30	24	DMSO	38
33	TBHP (5)	MsOH (1)	30	24	DMSO	14
34	TBHP (5)	TfOH (1)	30	24	DMSO	13
35	TBHP (5)	Ph-SO_3H(1)	30	24	DMSO	7
36	TBHP (5)	TsOH (1)	30	24	DMSO	8
37	TBHP (5)	H_2SO_4(1)	30	24	DMSO	25
38	TBHP (5)	HCl (1)	30	24	DMSO	28
39	TBHP (5)	TFA (1)	30	2	DMSO	37
40	TBHP (3)	TFA (1)	30	2	DMSO	38
41	TBHP (2)	TFA (1)	30	2	DMSO	30
42	TBHP (3)	TFA (1)	30	2	DMSO-H_2O (4:1)	42
43	TBHP (3)	TFA (1)	30	2	DMSO-H_2O (3:2)	57
44	TBHP (3)	TFA (1)	30	2	DMSO-H_2O (2:3)	15
45	TBHP (3)	TFA (1)	30	2	DMSO-H_2O (1:4)	12
46	TBHP (3)	TFA (1)	0	2	DMSO-H_2O (3:2)	86
47	TBHP (3)	TFA (1)	-10	2	DMSO-H_2O (3:2)	18
48	TBHP (3)	TFA (1)	0	0.5	DMSO-H_2O (3:2)	36
49	TBHP (3)	TFA (1)	0	1	DMSO-H_2O (3:2)	66
50	TBHP (3)	TFA (1)	0	4	DMSO-H_2O (3:2)	84
51	TBHP (3)	TFA (1)	0	6	DMSO-H_2O (3:2)	88
52	TBHP (3)	TFA (1)	0	12	DMSO-H_2O (3:2)	85

[a]Reaction conditions: **3a** (0.20 mmol), CF_3SO_2Na (0.60 mmol), **2a** (1.0 mmol), oxidant (0.60 mmol), acid (0.20 mmol), solvent (2.0 mL), 0 °C, 2 h, under air atmosphere. n.d. = not detected. [b]Yields were determined by ^1H NMR.

3. General procedure of three-component Minisci reaction

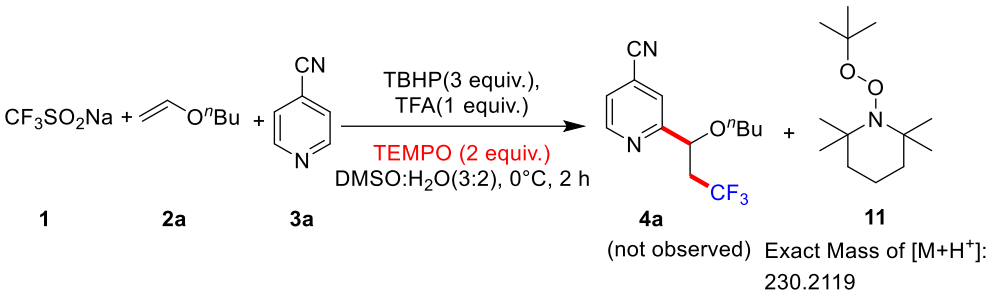


1 **2a** **3a** **4a**

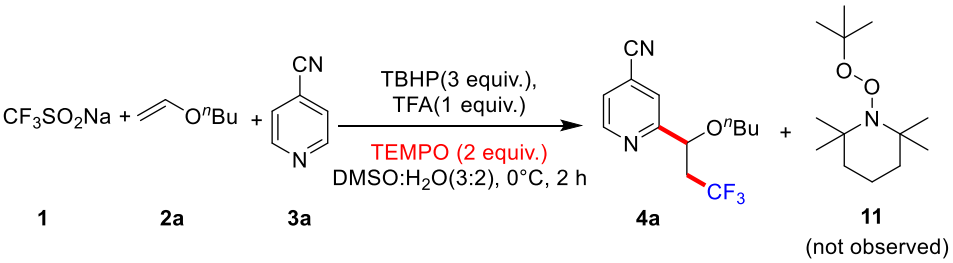
Procedure A: To a solution of the pyridine substrate (20.8 mg, 0.2 mmol, 1.0 equiv.) in 2 mL DMSO-H_2O (3:2), was added TFA (15 μL, 0.2 mmol, 1.0 equiv.) and the mixture was stirred at room temperature for 5 minutes. Then CF_3SO_2Na (94.8 mg, 0.6 mmol, 3.0 equiv.), *n*-butyl vinyl ether (129 μL, 1.0 mmol, 5.0 equiv.), TBHP (70% in H_2O, 82 μL, 0.6 mmol, 3.0 equiv.) were added. The reaction tuber was sealed and the system was stirred at room temperature for 1 minute. The tube was then immediately put into an ice bath and stirring was kept for 2 hours at 0 °C. The mixture was cooled to room temperature, diluted with 10 mL H_2O, neutralized with $NaHCO_3$. After extraction with EtOAc, the combined organic layers were dried over Na_2SO_4 and solvents were evaporated under reduced pressure. Purification by column chromatography on silica gel with hexane/ethyl acetate (8:1) as the eluent afforded the product 2-(1-butoxy-3,3,3-trifluoropropyl)isonicotinonitrile **(4a)**.

Procedure B: To a solution of the pyridine substrate (20.8 mg, 0.2 mmol, 1.0 equiv.) in 2 mL DMSO, was added TFA (15 μL, 0.2 mmol, 1.0 equiv.) and the mixture was stirred at room temperature for 5 minutes. Then CF_3SO_2Na (94.8 mg, 0.6 mmol, 3.0 equiv.), *n*-butyl vinyl ether (129 μL, 1.0 mmol, 5.0 equiv.), TBHP (70% in H_2O, 82 μL, 0.6 mmol, 3.0 equiv.) were added. The reaction tuber was sealed and the system was stirred at room temperature for 1 minute. The tube was then immediately put into an ice bath and stirring was kept for 2 hours at room temperature. The mixture was diluted with 10 mL H_2O, neutralized with $NaHCO_3$. After extraction with EtOAc, the combined organic layers were dried over Na_2SO_4 and solvents were evaporated under reduced pressure. Purification by column chromatography on silica gel with hexane/ethyl acetate (10:1) as the eluent afforded the product 2-(1-butoxy-3,3,3-trifluoropropyl)pyridin-4-yl)(phenyl)methanone (**4c**).

4. Mechanistic investigation



To a solution of the pyridine substrate (20.8 mg, 0.2 mmol, 1.0 equiv.) in 2 mL DMSO-H_2O (3:2), was added TFA (15 μL, 0.2 mmol, 1.0 equiv.) and stirring was kept at room temperature for 5 minutes. Then CF_3SO_2Na (94.8 mg, 0.6 mmol, 3.0 equiv.), *n*-butyl vinyl ether (129 μL, 1.0 mmol, 5.0 equiv.), TBHP (70% in H_2O, 82 μL, 0.6 mmol, 3.0 equiv.) and TEMPO (62.5 mg, 0.4 mmol, 2.0 equiv.) were added. The tube was sealed with and the reaction was stirred at room temperature for 1 minute. Then the tube was put in to an ice bath immediately and the system was stirred at 0°C for 2 hours. The mixture was detected by HRMS.



To a solution of the pyridine substrate (20.8 mg, 0.2 mmol, 1.0 equiv.) in 2 mL DMSO-H_2O (3:2), was added TFA (15 μL, 0.2 mmol, 1.0 equiv.) and stirring was kept at room temperature for 5 minutes. Then CF_3SO_2Na (94.8 mg, 0.6 mmol, 3.0 equiv.), *n*-butyl vinyl ether (129 μL, 1.0 mmol, 5.0 equiv.), TBHP (70% in H_2O, 82 μL, 0.6 mmol, 3.0 equiv.) and TEMPO (62.5 mg, 0.4 mmol, 2.0 equiv.) were added. The tube was sealed with and the reaction was stirred at room temperature for 1 minute. Then the tube was put in to an ice bath immediately and the system was stirred at 0°C for 0.5 hours, TEMPO (62.5 mg, 0.4 mmol, 2.0 equiv.) were added and stirred for 1.5h. The mixture was detected by HRMS.

5. X-ray diffraction for 5j

The X-ray crystallographic molecular structure of compound **5j** is depicted in Figure S1. The crystal was obtained through a slow evaporation and crystallization process in ethyl acetate at ambient temperature.

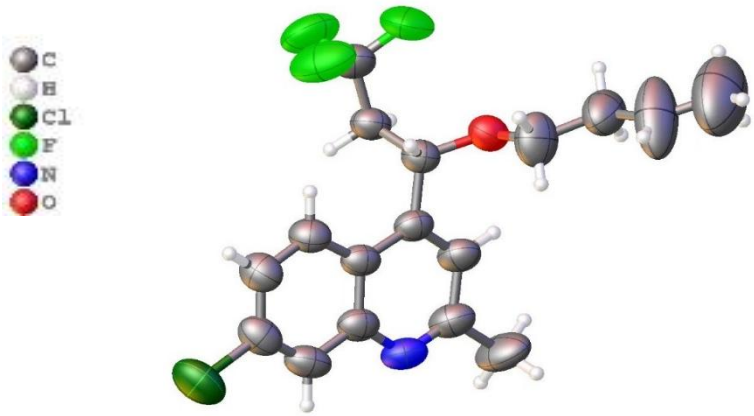


Figure S1. X-ray crystal diffraction molecular structure of product **5j** (ccdc 2413111)

Table S2 Crystallography data and structure refinement for **5j**

Compound	**5j**
Formula	$C_{17}H_{19}ClF_3NO$
M (g·mol^{-1})	345.78
Crystal system	Monoclinic
Space group	*P*21/c
a (Å)	a = 8.563(2)
b (Å)	b = 17.298(3)
c (Å)	c = 11.840(2)
V (Å3)	1752.6(6)
Z	4
D_{calcd} (g·cm^{-3})	1.310
F(000)	720
μ (mm^{-1})	0.249
T(K)	293
Θ range	2.355−24.992
Refl. collected/unique	53127/3015 [R_{int} = 0.0921]
Completeness to theta	24.992, 98.1%
R_1 [$I > 2\sigma(I)$]	0.0587
wR_2 (all data)	0.1943
Goodness of fit	1.095
Max/min Δρ (e Å^{-3})	0.276 and -0.201

Table S3 Bond lengths for **5j**

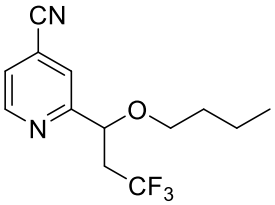
Cl(1)-C(00G)	1.758(3)	C(00F)-C(00G)	1.381(4)
F(003)-C(00I)	1.321(4)	C(00F)-C(008)	1.434(4)
F(004)-C(00I)	1.344(4)	C(00F)-H(00F)	0.9300
F(005)-C(00I)	1.341(4)	C(00G)-C(00H)	1.356(4)
O(002)-C(00J)	1.434(4)	C(00H)-H(00H)	0.9300
O(002)-C(00B)	1.472(3)	C(00J)-C(00K)	1.502(5)
N(006)-C(00E)	1.326(4)	C(00J)-H(00G)	0.9700
N(006)-C(008)	1.380(4)	C(00J)-H(00I)	0.9700
C(00A)-C(009)	1.374(4)	C(00K)-C(00M)	1.554(6)
C(00A)-C(00E)	1.388(4)	C(00K)-H(00J)	0.9700
C(00A)-H(00A)	0.9300	C(00K)-H(00K)	0.9700
C(00B)-C(009)	1.474(3)	C(00L)-H(00L)	0.9600
C(00B)-C(00C)	1.513(4)	C(00L)-H(00M)	0.9600
C(00B)-H(00B)	0.9800	C(00L)-H(00N)	0.9600
C(00C)-C(00I)	1.434(4)	C(00M)-C(00N)	1.370(7)
C(00C)-H(00C)	0.9700	C(00M)-H(00O)	0.9700
C(00C)-H(00D)	0.9700	C(00M)-H(00P)	0.9700
C(00D)-C(00H)	1.389(4)	C(00N)-H(00Q)	0.9600
C(00D)-C(007)	1.436(4)	C(00N)-H(00R)	0.9600
C(00D)-H(00E)	0.9300	C(00N)-H(00S)	0.9600
C(00E)-C(00L)	1.534(4)	C(007)-C(008)	1.377(3)
C(007)-C(009)	1.446(3)	O(002)-C(00J)-C(00K)	112.8(3)

Table S4 Bond angles for **5j**

C(00J)-O(002)-C(00B)	114.5(2)	O(002)-C(00J)-C(00K)	112.8(3)
C(00E)-N(006)-C(008)	121.1(2)	C(00K)-C(00J)-H(00G)	109.0
C(009)-C(00A)-C(00E)	117.6(3)	O(002)-C(00J)-H(00I)	109.0
C(009)-C(00A)-H(00A)	121.2	C(00K)-C(00J)-H(00I)	109.0
C(00E)-C(00A)-H(00A)	121.2	H(00G)-C(00J)-H(00I)	107.8
O(002)-C(00B)-C(009)	112.5(2)	C(00J)-C(00K)-C(00M)	114.0(4)
O(002)-C(00B)-C(00C)	108.7(2)	C(00J)-C(00K)-H(00J)	108.8
C(009)-C(00B)-C(00C)	108.0(2)	C(00M)-C(00K)-H(00J)	108.8
O(002)-C(00B)-H(00B)	109.2	C(00J)-C(00K)-H(00K)	108.8
C(009)-C(00B)-H(00B)	109.2	C(00M)-C(00K)-H(00K)	108.8
C(00C)-C(00B)-H(00B)	109.2	H(00J)-C(00K)-H(00K)	107.6
C(00I)-C(00C)-C(00B)	112.0(2)	C(00E)-C(00L)-H(00L)	109.5

C(00I)-C(00C)-H(00C)	109.2	C(00E)-C(00L)-H(00M)	109.5
C(00B)-C(00C)-H(00C)	109.2	H(00L)-C(00L)-H(00M)	109.5
C(00I)-C(00C)-H(00D)	109.2	C(00E)-C(00L)-H(00N)	109.5
C(00B)-C(00C)-H(00D)	109.2	H(00L)-C(00L)-H(00N)	109.5
H(00C)-C(00C)-H(00D)	107.9	H(00M)-C(00L)-H(00N)	109.5
C(00H)-C(00D)-C(007)	124.5(2)	C(00N)-C(00M)-C(00K)	122.2(6)
C(00H)-C(00D)-H(00E)	117.7	C(00N)-C(00M)-H(00O)	106.8
C(007)-C(00D)-H(00E)	117.7	C(00K)-C(00M)-H(00O)	106.8
N(006)-C(00E)-C(00A)	122.3(3)	C(00N)-C(00M)-H(00P)	106.8
N(006)-C(00E)-C(00L)	121.2(3)	C(00K)-C(00M)-H(00P)	106.8
C(00A)-C(00E)-C(00L)	116.5(3)	H(00O)-C(00M)-H(00P)	106.6
C(00G)-C(00F)-C(008)	123.4(3)	C(00M)-C(00N)-H(00Q)	109.5
C(00G)-C(00F)-H(00F)	118.3	C(00M)-C(00N)-H(00R)	109.5
C(008)-C(00F)-H(00F)	118.3	H(00Q)-C(00N)-H(00R)	109.5
C(00H)-C(00G)-C(00F)	118.9(3)	C(00M)-C(00N)-H(00S)	109.5
C(00H)-C(00G)-Cl(1)	118.2(3)	H(00Q)-C(00N)-H(00S)	109.5
C(00F)-C(00G)-Cl(1)	122.9(2)	H(00R)-C(00N)-H(00S)	109.5
C(00G)-C(00H)-C(00D)	118.7(3)	C(008)-C(007)-C(00D)	115.9(3)
C(00G)-C(00H)-H(00H)	120.7	C(008)-C(007)-C(009)	116.5(3)
C(00D)-C(00H)-H(00H)	120.7	C(00D)-C(007)-C(009)	127.6(2)
F(003)-C(00I)-F(005)	107.5(2)	C(007)-C(008)-N(006)	121.0(3)
F(003)-C(00I)-F(004)	104.4(3)	C(007)-C(008)-C(00F)	118.6(3)
F(005)-C(00I)-F(004)	107.2(3)	N(006)-C(008)-C(00F)	120.4(2)
F(003)-C(00I)-C(00C)	111.5(3)	C(00A)-C(009)-C(007)	121.5(2)
F(005)-C(00I)-C(00C)	112.3(3)	C(00A)-C(009)-C(00B)	117.9(2)
F(004)-C(00I)-C(00C)	113.4(3)	C(007)-C(009)-C(00B)	120.6(2)

6. Characterization data of products



2-(1-butoxy-3,3,3-trifluoropropyl)isonicotinonitrile (4a)

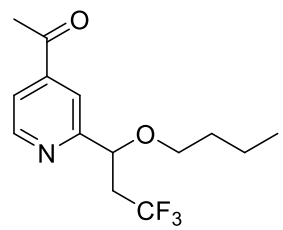
Following the typical experimental procedure A on 0.2 mmol scale. Compound **4a** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 5:1, v/v). 57.7 mg, 81% yield, yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.76 (d, J = 5.0 Hz, 1H), 7.70 (s, 1H), 7.46 (dd, J = 5.0, 0.9 Hz, 1H), 4.73 (dd, J = 8.6, 3.7 Hz, 1H), 3.51 – 3.43 (m, 2H), 2.71 – 2.61 (m, 1H), 2.60 – 2.52 (m, 1H), 1.67 – 1.55 (m, 2H), 1.44 – 1.36 (m, 2H), 0.92 (t, J = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 162.3, 150.4, 125.6 (q, J = 277.4 Hz), 124.3, 122.1, 121.4, 116.4, 70.4, 40.0 (q, J = 28.2 Hz), 31.7, 19.1, 13.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.2 (t, J = 10.3 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{13}H_{16}F_3N_2O^+$ 273.1210, Found 273.1209.



1-(2-(1-butoxy-3,3,3-trifluoropropyl)pyridin-4-yl)ethan-1-one (4b)

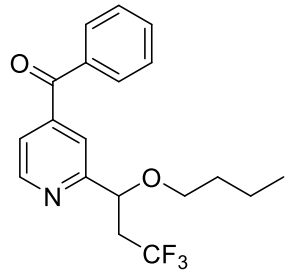
Following the typical experimental procedure A on 0.2 mmol scale. Compound **4b** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 5:1, v/v). 42 mg, 74% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, J = 5.0 Hz, 1H), 7.87 (s, 1H), 7.65 (dd, J = 5.0, 1.6 Hz, 1H), 4.76 (dd, J = 8.3, 4.3 Hz, 1H), 3.49 – 3.39 (m, 2H), 2.63 (s, 3H), 2.71 – 2.51 (m, 2H), 1.66 – 1.51 (m, 2H), 1.47 – 1.31 (m, 2H), 0.89 (t, J = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 197.1, 161.9, 150.6, 143.9, 125.8 (q, J = 277.4 Hz), 120.5, 118.1, 77.1 (q, J = 3.0 Hz), 70.0, 40.3 (q, J = 28.0 Hz), 31.7, 26.7, 19.2, 13.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.3 (t, J = 10.5 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{14}H_{19}F_3NO_2^+$ 290.1362, Found 290.1362.



(2-(1-butoxy-3,3,3-trifluoropropyl)pyridin-4-yl)(phenyl)methanone (4c)

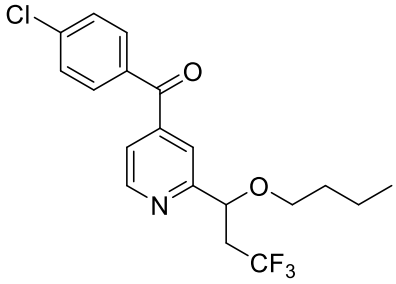
Following the typical experimental procedure B on 0.2 mmol scale. Compound **4c** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 5:1, v/v). 30 mg, 42% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, J = 4.9 Hz, 1H), 7.82 (d, J = 1.1 Hz, 1H), 7.80 (d, J = 1.3 Hz, 1H),7.73 (s, 1H), 7.69 – 7.63 (m, 1H), 7.55 – 7.49 (m, 3H), 4.78 (dd, J = 8.6, 3.9 Hz, 1H), 3.47 (t, J = 6.5 Hz, 2H), 2.78 – 2.53 (m, 2H), 1.62 – 1.51 (m, 2H), 1.43 – 1.31 (m, 2H), 0.88 (t, J = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 195.0, 161.2, 150.0, 145.6, 135.8, 133.6, 130.1, 128.7, 125.8 (q, J = 277.4 Hz), 122.2, 119.8, 77.1 (q, J = 3.1 Hz), 70.1, 40.3 (q, J = 27.9 Hz), 31.7, 19.2, 13.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.3 (t, J = 10.5 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{19}H_{20}F_3NO_2^+$ 352.1519, Found 352.1518.



(2-(1-butoxy-3,3,3-trifluoropropyl)pyridin-4-yl)(4-chlorophenyl)methanone (4d)

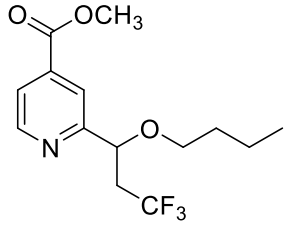
Following the typical experimental procedure B on 0.2 mmol scale. Compound **4d** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 8:1, v/v). 28 mg, 37% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, J = 4.9 Hz, 1H), 7.76 (d, J = 8.5 Hz, 2H), 7.70 (s, 1H), 7.55 – 7.45 (m, 3H), 4.78 (dd, J = 8.5, 3.9 Hz, 1H), 3.54 – 3.39 (m, 2H), 2.79 – 2.49 (m, 2H), 1.66 – 1.48 (m, 2H), 1.46 – 1.29 (m, 2H), 0.88 (t, J = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 193.8, 161.4, 150.1, 145.1, 140.3, 134.1, 131.4, 129.1, 125.8 (q, J = 277.4 Hz), 121.9, 119.6, 77.1 (q, J = 3.0 Hz), 70.1, 40.3 (q, J = 28.0 Hz), 31.7, 19.2, 13.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.2 (t, J = 10.5 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{19}H_{20}ClF_3NO_2^+$ 386.1130, Found 386.1129.



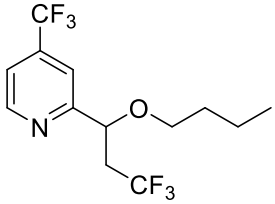
methyl 2-(1-butoxy-3,3,3-trifluoropropyl)isonicotinate (4e)[1]

Following the typical experimental procedure A on 0.2 mmol scale. Compound **4e** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 8:1, v/v). 47 mg, 77% yield, colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, J = 5.0 Hz, 1H), 8.00 (s, 1H), 7.78 (dd, J = 5.0, 1.4 Hz, 1H), 4.75 (dd, J = 7.6, 5.0 Hz, 1H), 3.97 (s, 3H), 3.43 (t, J = 6.5 Hz, 2H), 2.72 – 2.54 (m, 2H), 1.65 – 1.51 (m, 2H), 1.46 – 1.33 (m, 2H), 0.90 (t, J = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 165.5, 161.5, 150.3, 138.5, 125.8 (q, J = 277.3 Hz), 122.2, 119.9, 70.0, 52.8, 40.3 (q, J = 28.0 Hz), 31.7, 19.2, 13.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.5 (t, J = 10.4 Hz, 3F).



2-(1-butoxy-3,3,3-trifluoropropyl)-4-(trifluoromethyl)pyridine (4f)

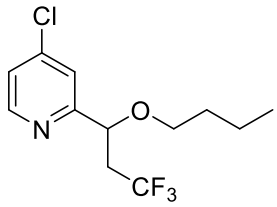
Following the typical experimental procedure A on 0.2 mmol scale. Compound **4f** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 8:1, v/v). 54 mg, 85% yield, colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, J = 5.0 Hz, 1H), 7.70 (s, 1H), 7.46 (d, J = 4.9 Hz, 1H), 4.77 (dd, J = 8.7, 3.8 Hz, 1H), 3.52 – 3.41 (m, 2H), 2.73 – 2.50 (m, 2H), 1.60 (tt, J = 12.8, 6.6 Hz, 2H), 1.46 – 1.35 (m, 2H), 0.91 (t, J = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 162.3, 150.5, 139.4 (q, J = 34.2 Hz), 125.7 (q, J = 277.3 Hz), 122.7 (q, J = 273.2 Hz), 118.5 (q, J = 3.5 Hz), 116.1 (q, J = 3.7 Hz), 70.2, 40.3 (qt, J = 27.9, 3.5 Hz), 31.7, 19.1, 13.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.5 (t, J = 10.5 Hz, 3F), -64.9 (s, 3F)

HRMS (ESI): $[M+H]^+$ calcd for $C_{13}H_{16}F_6NO^+$ 316.1131, Found 316.1133.



2-(1-butoxy-3,3,3-trifluoropropyl)-4-chloropyridine (4g)

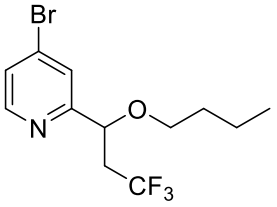
Following the typical experimental procedure A on 0.2 mmol scale. Compound **4g** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 5:1, v/v). 37 mg, 65% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, J = 5.3 Hz, 1H), 7.47 (d, J = 1.8 Hz, 1H), 7.24 (dd, J = 5.3, 2.0 Hz, 1H), 4.67 (dd, J = 8.7, 3.8 Hz, 1H), 3.52 – 3.36 (m, 2H), 2.70 – 2.44 (m, 2H), 1.67 – 1.51 (m, 2H), 1.46 – 1.33 (m, 2H), 0.91 (t, J = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 162.1, 150.3, 145.2, 125.7 (q, J = 277.4 Hz), 123.2, 120.9, 76.9 (q, J = 3.0 Hz), 70.1, 40.3 (q, J = 28.1 Hz), 31.7, 19.1, 13.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.4 (t, J = 10.4 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{12}H_{16}ClF_3NO^+$ 282.0867, Found 282.0866.



4-bromo-2-(1-butoxy-3,3,3-trifluoropropyl)pyridine (4h)

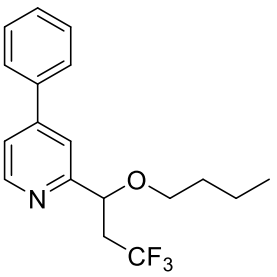
Following the typical experimental procedure A on 0.2 mmol scale. Compound **4h** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 8:1, v/v). 41 mg, 63% yield, yellow oil liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, J = 5.2 Hz, 1H), 7.63 (s, 1H), 7.40 (dd, J = 5.1, 1.3 Hz, 1H), 4.66 (dd, J = 8.6, 3.8 Hz, 1H), 3.49 – 3.39 (m, 2H), 2.70 – 2.45 (m, 2H), 1.66 – 1.52 (m, 2H), 1.46 – 1.33 (m, 2H), 0.91 (t, J = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 161.9, 150.2, 133.9, 126.3, 125.7 (q, J = 277.4 Hz), 123.9, 76.8 (q, J = 3.0 Hz), 70.1, 40.3 (q, J = 28.1 Hz), 31.7, 19.1, 13.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.38 (t, J = 10.4 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{12}H_{16}BrF_3NO^+$ 326.0362, Found 326.0361.



2-(1-butoxy-3,3,3-trifluoropropyl)-4-phenylpyridine (4i)

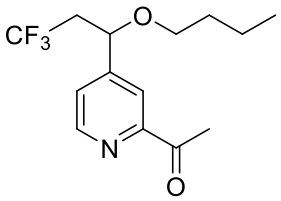
Following the typical experimental procedure A on 0.2 mmol scale. Compound **4i** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 10:1, v/v). 40 mg, 62% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, *J* = 5.1 Hz, 1H), 7.70 – 7.63 (m, 3H), 7.54 – 7.43 (m, 4H), 4.76 (dd, *J* = 8.6, 3.9 Hz, 1H), 3.57 – 3.41 (m, 2H), 2.79 – 2.52 (m, 2H), 1.70 – 1.52 (m, 2H), 1.49 – 1.35 (m, 2H), 0.91 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 160.8, 149.9, 149.4, 138.0, 129.2, 129.1, 127.0, 125.9 (q, *J* = 277.4 Hz), 120.8, 118.2, 77.3 (q, *J* = 3.0 Hz), 69.8, 40.6 (q, *J* = 27.8 Hz), 31.8, 19.2, 13.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.4 (t, *J* = 10.5 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{18}H_{21}F_3NO^+$ 324.1570, Found 324.1569.



1-(4-(1-butoxy-3,3,3-trifluoropropyl)pyridin-2-yl)ethan-1-one (4j)

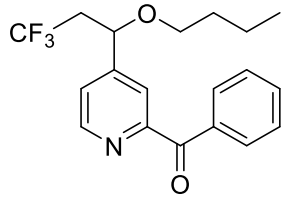
Following the typical experimental procedure A on 0.2 mmol scale. Compound **4j** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 5:1, v/v). 42 mg, 73% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, *J* = 4.9 Hz, 1H), 7.99 (s, 1H), 7.46 (d, *J* = 4.6 Hz, 1H), 4.60 (dd, *J* = 8.5, 4.1 Hz, 1H), 3.36 – 3.25 (m, 2H), 2.73 (s, 3H), 2.69 – 2.54 (m, 1H), 2.43 – 2.25 (m, 1H), 1.59 – 1.46 (m, 2H), 1.42 – 1.30 (m, 2H), 0.88 (t, *J* = 7.3 Hz, 3H)

^{13}C NMR (151 MHz, $CDCl_3$) δ 199.8, 154.1, 151.1, 149.6, 125.3 (q, *J* = 277.4 Hz), 124.5, 119.4, 75.0 (q, *J* = 3.1 Hz), 69.7, 41.7 (q, *J* = 28.1 Hz), 31.6, 25.8, 19.1, 13.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.4 (t, *J* = 10.3 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{13}H_{19}F_3NO_2^+$ 290.1363, Found 290.1362.



(4-(1-butoxy-3,3,3-trifluoropropyl)pyridin-2-yl)(phenyl)methanone (4k)

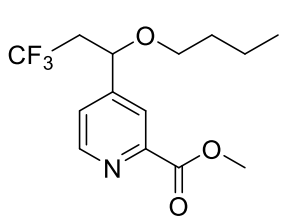
Following the typical experimental procedure B on 0.2 mmol scale. Compound **4k** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 8:1, v/v). 25 mg, 36% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 7.6 Hz, 2H), 7.95 (d, *J* = 4.3 Hz, 2H), 7.67 (p, *J* = 3.8 Hz, 1H), 7.61 (t, *J* = 7.3 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 2H), 4.75 (dd, *J* = 8.2, 4.4 Hz, 1H), 3.46 (t, *J* = 6.4 Hz, 2H), 2.78 – 2.52 (m, 2H), 1.68 – 1.53 (m, 2H), 1.47 – 1.35 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 193.4, 159.3, 154.8, 138.0, 136.0, 133.0, 131.1, 128.0, 125.8 (q *J* = 277.4 Hz), 123.7, 122.1, 69.9, 40.0 (q, *J* = 27.8 Hz), 31.8, 19.2, 13.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.0 (t, *J* = 10.5 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{19}H_{21}F_3NO_2^+$ 352.1519, Found 352.1519.



methyl 4-(1-butoxy-3,3,3-trifluoropropyl)picolinate (4l)

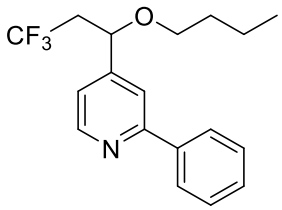
Following the typical experimental procedure A on 0.2 mmol scale. Compound **4l** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 2:1, v/v). 49 mg, 80% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, J = 4.9 Hz, 1H), 8.09 (s, 1H), 7.47 (dd, J = 4.9, 1.4 Hz, 1H), 4.61 (dd, J = 8.4, 4.2 Hz, 1H), 4.02 (s, 3H), 3.41 – 3.24 (m, 2H), 2.71 – 2.54 (m, 1H), 2.43 – 2.27 (m, 1H), 1.61 – 1.49 (m, 2H), 1.43 – 1.30 (m, 2H), 0.88 (t, J = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 165.4, 151.4, 150.3, 148.5, 125.2 (q, J = 277.4 Hz), 124.4, 122.8, 74.9 (q, J = 3.0 Hz), 69.7, 53.0, 41.7 (q, J = 28.1 Hz), 31.5, 19.0, 13.6.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.4 (t, J = 10.3 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{14}H_{19}F_3NO_3^+$ 306.1312, Found 306.1311.



4-(1-butoxy-3,3,3-trifluoropropyl)-2-phenylpyridine (4m)

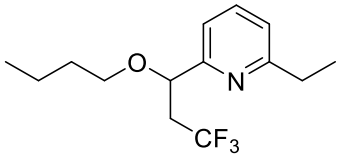
Following the typical experimental procedure A on 0.2 mmol scale. Compound **4m** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 10:1, v/v). 41 mg, 63% yield, colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (d, J = 5.0 Hz, 1H), 8.03 – 7.98 (m, 2H), 7.70 (s, 1H), 7.53 – 7.41 (m, 3H), 7.21 (dd, J = 4.9, 1.2 Hz, 1H), 4.61 (dd, J = 8.7, 3.9 Hz, 1H), 3.47 – 3.29 (m, 2H), 2.74 – 2.59 (m, 1H), 2.49 – 2.31 (m, 1H), 1.63 – 1.52 (m, 2H), 1.46 – 1.32 (m, 2H), 0.90 (t, J = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 158.1, 150.7, 150.1, 138.9, 129.3, 128.8, 127.0, 125.4 (q, J = 277.4 Hz), 119.7, 118.0, 75.3 (q, J = 3.0 Hz), 69.6, 42.0 (q, J = 28.0 Hz), 31.7, 19.2, 13.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.4 (t, J = 10.3 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{18}H_{21}F_3NO^+$ 324.1570, Found 324.1569.



2-(1-butoxy-3,3,3-trifluoropropyl)-6-ethylpyridine (4n)

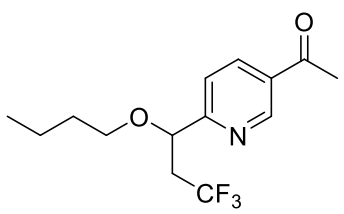
Following the typical experimental procedure A on 0.2 mmol scale. Compound **4n** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 10:1, v/v). 18 mg, 32% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (t, J = 7.7 Hz, 1H), 7.27 (d, J = 7.8 Hz, 1H), 7.10 (d, J = 7.7 Hz, 1H), 4.70 (dd, J = 9.2, 3.3 Hz, 1H), 3.53 – 3.39 (m, 2H), 2.83 (q, J = 7.6 Hz, 2H), 2.75 – 2.47 (m, 2H), 1.65 – 1.53 (m, 2H), 1.47 – 1.35 (m, 2H), 1.31 (t, J = 7.6 Hz, 3H), 0.92 (t, J = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 163.4, 159.5, 137.2, 126.0 (q, J = 277.5 Hz), 121.0, 117.4, 77.4 (q, J = 1.7 Hz), 69.7, 40.5 (q, J = 27.7 Hz), 31.8, 31.2, 19.2, 13.9, 13.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.4 (t, J = 10.6 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{14}H_{21}F_3NO^+$276.1570, Found 276.1569.



1-(6-(1-butoxy-3,3,3-trifluoropropyl)pyridin-3-yl)ethan-1-one (4o)

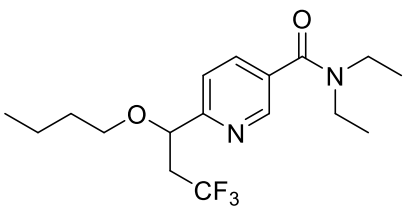
Following the typical experimental procedure A on 0.2 mmol scale. Compound **4o** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 5:1, v/v). 48 mg, 83% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (d, *J* = 1.7 Hz, 1H), 8.27 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.58 (d, *J* = 8.2 Hz, 1H), 4.75 (dd, *J* = 8.5, 3.9 Hz, 1H), 3.49 – 3.39 (m, 2H), 2.64 (s, 3H), 2.72 – 2.47 (m, 2H), 1.65 – 1.50 (m, 2H), 1.44 – 1.33 (m, 2H), 0.90 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 196.3, 164.7, 149.7, 136.6, 131.6, 125.7 (q, *J* = 277.4 Hz), 120.3, 77.1 (q, *J* = 3.0 Hz), 70.1, 40.1 (q, *J* = 28.1 Hz), 31.7, 26.7, 19.2, 13.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.3 (t, *J* = 10.4 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{14}H_{19}F_3NO^+$ 290.1363, Found 290.1362.



6-(1-butoxy-3,3,3-trifluoropropyl)-*N*,*N*-diethylnicotinamide (4p)

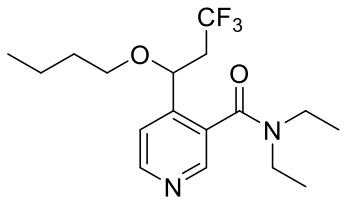
Following the typical experimental procedure A at room temperature on 0.2 mmol scale. Compound **4p** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 3:1, v/v). 33 mg, 48% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, *J* = 1.3 Hz, 1H), 7.74 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 4.68 (dd, *J* = 8.5, 3.9 Hz, 1H), 3.54 (q, *J* = 6.3 Hz, 2H), 3.40 (t, *J* = 6.4 Hz, 2H), 3.25 (q, *J* = 7.8 Hz, 2H), 2.68 – 2.46 (m, 2H), 1.60 – 1.49 (m, 2H), 1.42 – 1.30 (m, 2H), 1.28 – 1.19 (m, 3H), 1.18 – 1.09 (m, 3H), 0.87 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 168.3, 161.0, 146.9, 135.3, 132.1, 125.8 (q, *J* = 277.4 Hz), 120.1, 69.9, 43.4, 40.3 (q, *J* = 27.9 Hz), 39.5, 31.7, 19.1, 14.2, 13.7, 12.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.5 (t, *J* = 10.5 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{17}H_{26}F_3N_2O_2^+$ 347.1941, Found 347.1945.



4-(1-butoxy-3,3,3-trifluoropropyl)-N,N-diethylnicotinamide (4p')

Following the typical experimental procedure A at room temperature on 0.2 mmol scale. Compound **4p'** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 2:1, v/v). 15 mg, 22% yield, yellow oil liquid.

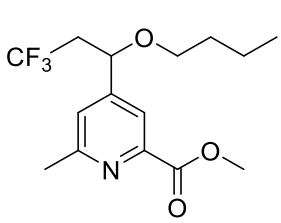
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, *J* = 5.1 Hz, 1H), 8.47 (s, 1H), 7.50 (d, *J* = 5.1 Hz, 1H), 4.63 (s, 1H), 3.66 – 3.42 (m, 2H), 3.37 – 3.26 (m, 2H), 3.16 (tq, *J* = 14.9, 7.5 Hz, 2H), 2.50 (s, 2H), 1.59

– 1.46 (m, 2H), 1.42 – 1.30 (m, 2H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.14 (t, *J* = 7.1 Hz, 3H), 0.88 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 166.9, 150.6, 147.4, 146.4, 131.4, 125.5 (q, *J* = 277.6 Hz), 121.0, 72.5, 69.8, 43.0, 41.1 (q, *J* = 28.1 Hz), 39.2, 31.7, 19.2, 14.2, 13.8, 12.5.

^{19}F NMR (376 MHz, CDCl$_3$) δ -63.6 (t, *J* = 10.4 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{17}H_{26}F_3N_2O_2^+$ 347.1941, Found 347.1945.



methyl 4-(1-butoxy-3,3,3-trifluoropropyl)-6-methylpicolinate (4q)

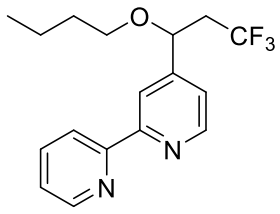
Following the typical experimental procedure A on 0.2 mmol scale. Compound **4q** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 5:1, v/v). 50 mg, 78% yield, yellow oil.

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.91 (s, 1H), 7.31 (s, 1H), 4.57 (dd, *J* = 8.5, 4.1 Hz, 1H), 4.01 (s, 3H), 3.31 (t, *J* = 6.4 Hz, 2H), 2.68 (s, 3H), 2.65 – 2.53 (m, 1H), 2.42 – 2.24 (m, 1H), 1.61 – 1.49 (m, 2H), 1.43 – 1.31 (m, 2H), 0.89 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 165.7, 159.8, 151.5, 148.2, 125.3 (q, *J* = 277.4 Hz), 124.3, 120.2, 74.9 (q, *J* = 3.2 Hz), 69.7, 53.0, 41.7 (q, *J* = 28.1 Hz), 31.6, 24.7, 19.1, 13.7.

^{19}F NMR (376 MHz, CDCl$_3$) δ -63.4 (t, *J* = 10.3 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{15}H_{21}F_3NO_3^+$ 320.1469, Found 320.1467.



4-(1-butoxy-3,3,3-trifluoropropyl)-2,2'-bipyridine (4r)

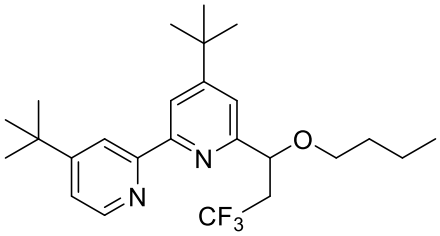
Following the typical experimental procedure B on 0.2 mmol scale. Compound **4r** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 2:1, v/v). 29 mg, 45% yield, yellow oil liquid.

^{1}H NMR (600 MHz, CDCl$_3$) δ 8.72 (d, *J* = 4.7 Hz, 2H), 8.41 (d, *J* = 7.9 Hz, 1H), 8.34 (s, 1H), 7.89 (t, *J* = 7.7 Hz, 1H), 7.43 – 7.35 (m, 2H), 4.67 (dd, *J* = 8.8, 3.8 Hz, 1H), 3.41 – 3.33 (m, 2H), 2.72 – 2.61 (m, 1H), 2.47 – 2.36 (m, 1H), 1.61 – 1.52 (m, 2H), 1.41 – 1.34 (m, 2H), 0.89 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 155.5, 154.5, 151.8, 149.7, 149.1, 137.8, 125.4 (q, *J* = 277.5 Hz), 124.5, 121.6, 121.5, 119.0, 75.3 (q, *J* = 3.1 Hz), 69.7, 41.7 (q, *J* = 28.1 Hz), 31.6, 19.1, 13.8.

^{19}F NMR (376 MHz, CDCl$_3$) δ -63.5 (t, *J* = 10.4 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{17}H_{20}F_3N_2O^+$ 325.1523, Found 325.1522.



6-(1-butoxy-3,3,3-trifluoropropyl)-4,4'-di-tert-butyl-2,2'-bipyridine (4s)

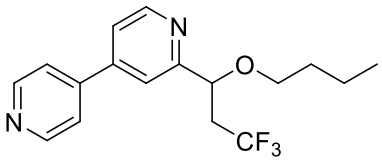
Following the typical experimental procedure B on 0.2 mmol scale. Compound **4s** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 15:1, v/v). 24 mg, 28% yield, yellow oil liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (d, J = 5.3 Hz, 1H), 8.40 (d, J = 1.4 Hz, 1H), 8.31 (d, J = 1.2 Hz, 1H), 7.49 (d, J = 1.6 Hz, 1H), 7.31 (dd, J = 5.2, 1.8 Hz, 1H), 4.82 (dd, J = 9.4, 3.1 Hz, 1H), 3.50 (t, J = 6.4 Hz, 2H), 2.82 – 2.68 (m, 1H), 2.68 – 2.54 (m, 1H), 1.67 – 1.58 (m, 2H), 1.45 – 1.42 (m, 2H), 1.39 (s, 18H), 0.92 (t, J = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 162.1, 159.5, 156.2, 148.9, 126.2 (q, J = 277.4 Hz), 121.4, 120.8, 118.9, 118.4, 117.4, 117.0, 77.5 (q, J = 3.0 Hz), 69.7, 40.6 (q, J = 27.7 Hz), 35.2, 35.0, 31.9, 30.7, 30.6, 19.3, 13.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.3 (t, J = 10.6 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{25}H_{36}F_3N_2O^+$ 437.2775, Found 437.2773.



2-(1-butoxy-3,3,3-trifluoropropyl)-4,4'-bipyridine (4t)

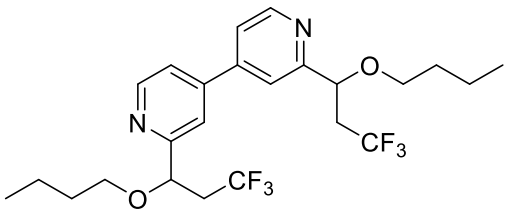
Following the typical experimental procedure A in 2mL DMSO-H_2O (2:1) on 0.2 mmol scale. Compound **4t** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 2:1, v/v). 34 mg, 53% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, J = 6.0 Hz, 2H), 8.69 (d, J = 5.1 Hz, 1H), 7.70 (s, 1H), 7.55 (dd, J = 4.5, 1.5 Hz, 2H), 7.47 (dd, J = 5.1, 1.7 Hz, 1H), 4.77 (dd, J = 8.7, 3.8 Hz, 1H), 3.51 – 3.45 (m, 2H), 2.76 – 2.52 (m, 2H), 1.66 – 1.54 (m, 2H), 1.46 – 1.35 (m, 2H), 0.90 (t, J = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 161.5, 150.6, 150.3, 146.6, 145.4, 125.8 (q, J = 277.4 Hz), 121.4, 120.6, 118.0, 77.17 (q, J = 3.1 Hz), 70.0, 40.4 (q, J = 27.9 Hz), 31.7, 19.1, 13.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.4 (t, J = 10.5 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{17}H_{20}F_3N_2O^+$ 325.1523, Found 325.1525.



2,2'-bis(1-butoxy-3,3,3-trifluoropropyl)-4,4'-bipyridine (4t')

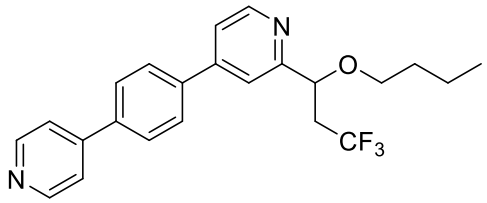
Following the typical experimental procedure A in 2mL DMSO-H_2O (2:1) on 0.2 mmol scale. Compound **4t'** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 5:1, v/v). 23 mg, 23% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, J = 5.1 Hz, 2H), 7.72 (dd, J = 3.5, 1.2 Hz, 2H), 7.51 – 7.45 (m, 2H), 4.78 (dd, J = 8.7, 3.8 Hz, 2H), 3.49 (t, J = 6.4 Hz, 4H), 2.77 – 2.54 (m, 4H), 1.67 – 1.54 (m, 4H), 1.48 – 1.34 (m, 4H), 0.91 (t, J = 7.4 Hz, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 161.6, 150.4, 146.63, 146.57, 125.8 (q, J = 277.5 Hz), 120.7, 120.6, 118.02, 118.05, 77.2, 70.0, 40.4 (q, J = 27.9 Hz), 31.8, 19.2, 13.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.4 (t, J = 10.9 Hz, 6F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{24}H_{31}F_6N_2O_2^+$ 493.2285, Found 493.2289.



2-(1-butoxy-3,3,3-trifluoropropyl)-4-(4-(pyridin-4-yl)phenyl)pyridine (4u)

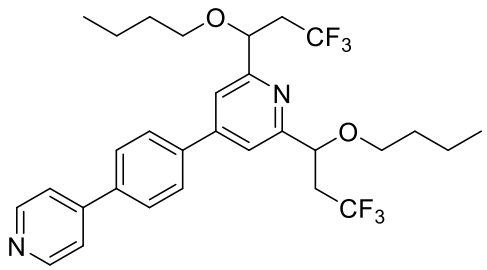
Following the typical experimental procedure A in 2mL DMSO-H_2O (2:1) on 0.2 mmol scale. Compound **4u** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 1:1, v/v). 21 mg, 26% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, J = 5.5 Hz, 2H), 8.66 (d, J = 5.1 Hz, 1H), 7.79 (s, 4H), 7.73 (d, J = 0.9 Hz, 1H), 7.57 (dd, J = 4.7, 1.4 Hz, 2H), 7.50 (dd, J = 5.1, 1.7 Hz, 1H), 4.78 (dd, J = 8.7, 3.9 Hz, 1H), 3.59 – 3.42 (m, 2H), 2.75 – 2.57 (m, 2H), 1.67 – 1.56 (m, 2H), 1.48 – 1.35 (m, 2H), 0.91 (t, J = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 161.1, 150.2, 150.1, 148.5, 147.6, 138.9, 138.8, 127.8, 125.9 (q, J = 277.8 Hz), 121.6, 120.7, 118.1, 77.3 (q, J = 3.1 Hz), 69.9, 40.5 (q, J = 27.8 Hz), 31.8, 19.2, 13.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.4 (t, J = 10.4 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{23}H_{24}F_3N_2O^+$ 401.1836, Found 401.1838.



2,6-bis(1-butoxy-3,3,3-trifluoropropyl)-4-(4-(pyridin-4-yl)phenyl)pyridine (4u')

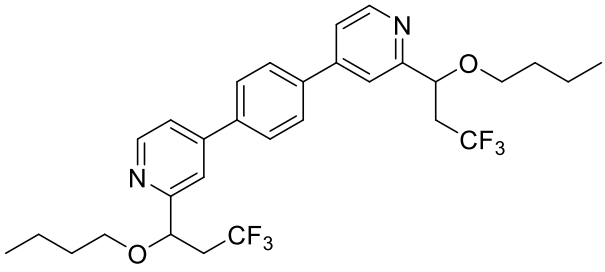
Following the typical experimental procedure A in 2mL DMSO-H_2O (2:1) on 0.2 mmol scale. Compound **4u'** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 2:1, v/v). 25 mg, 22% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (s, 2H), 7.80 (s, 4H), 7.65 (d, J = 3.7 Hz, 2H), 7.59 (d, J = 5.4 Hz, 2H), 4.84 – 4.68 (m, 2H), 3.60 – 3.44 (m, 4H), 2.79 – 2.52 (m, 4H), 1.67 – 1.57 (m, 4H), 1.48 – 1.37 (m, 4H), 0.92 (dt, J = 7.3, 2.0 Hz, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 161.0, 160.9, 150.2, 149.35, 149.41, 147.5, 139.0, 138.8, 127.84, 127.82, 127.7, 125.9 (q, J = 277.8 Hz), 125.0 (q, J = 277.8 Hz), 121.6, 117.3, 117.2, 70.00, 69.97, 40.4 (q, J = 27.9 Hz), 40.3 (q, J = 27.8 Hz), 31.84, 31.82, 19.24, 19.21, 13.82, 13.81.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.2 (t, J = 10.5 Hz, 6F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{30}H_{35}F_6N_2O_2^+$ 569.2598, Found 569.2603.



1,4-bis(2-(1-butoxy-3,3,3-trifluoropropyl)pyridin-4-yl)benzene (4u'')

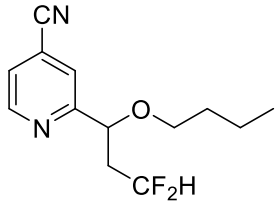
Following the typical experimental procedure A in 2mL DMSO-H_2O (2:1) on 0.2 mmol scale. Compound **4u''** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 2:1, v/v). 23 mg, 20% yield, white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, J = 5.1 Hz, 2H), 7.80 (s, 4H), 7.73 (s, 2H), 7.50 (dd, J = 5.1, 1.6 Hz, 2H), 4.78 (dd, J = 8.7, 3.8 Hz, 2H), 3.57 – 3.43 (m, 4H), 2.79 – 2.54 (m, 4H), 1.68 – 1.56 (m, 4H), 1.50 – 1.36 (m, 4H), 0.92 (t, J = 7.4 Hz, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 161.1, 150.1, 148.4, 138.9, 127.8, 125.9 (q, J = 277.5 Hz), 120.7, 118.1, 77.3 (q, J = 3.1 Hz), 70.0, 40.5 (q, J = 27.9 Hz), 31.8, 19.2, 13.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.4 (t, J = 10.5 Hz, 6F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{30}H_{35}F_6N_2O_2^+$ 569.2598, Found 569.2602.



2-(1-butoxy-3,3-difluoropropyl)isonicotinonitrile

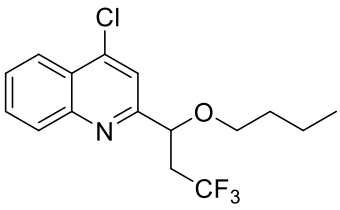
Following the typical experimental procedure A on 0.2 mmol scale. Compound **4v** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 8:1, v/v). 34 mg, 68% yield, yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.75 (dd, J = 5.1, 0.6 Hz, 1H), 7.67 (s, 1H), 7.45 (dd, J = 5.0, 1.4 Hz, 1H), 6.05 (tdd, J = 56.9, 6.0, 3.8 Hz, 1H), 4.63 (dd, J = 8.5, 4.9 Hz, 1H), 3.48 – 3.36 (m, 2H), 2.33 – 2.21 (m, 2H), 1.64 – 1.55 (m, 2H), 1.44 – 1.34 (m, 2H), 0.92 (t, J = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 163.0, 150.4, 124.2, 121.9, 121.4, 116.5, 115.4 (t, J = 238.9 Hz), 77.6 (dd, J = 8.5, 4.7 Hz), 70.1, 40.8 (t, J = 21.9 Hz), 31.7, 19.2, 13.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -117.3 – 117.8 (m, 2F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{13}H_{17}F_2N_2O^+$ 225.1304, Found 225.1309.



2-(1-butoxy-3,3,3-trifluoropropyl)-4-chloroquinoline (5a)

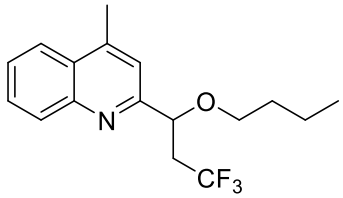
Following the typical experimental procedure A on 0.2 mmol scale. Compound **5a** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 10:1, v/v). 60 mg, 90% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, J = 8.4 Hz, 1H), 8.09 (d, J = 8.5 Hz, 1H), 7.79 (t, J = 7.7 Hz, 1H), 7.70 (s, 1H), 7.66 (t, J = 7.6 Hz, 1H), 4.87 (dd, J = 7.5, 5.2 Hz, 1H), 3.47 (t, J = 6.4 Hz, 2H), 2.75 – 2.57 (m, 2H), 1.68 – 1.54 (m, 2H), 1.47 – 1.33 (m, 2H), 0.91 (t, J = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 160.9, 148.4, 143.9, 130.7, 129.5, 127.6, 125.9, 125.8 (q, J = 277.5 Hz), 124.1, 118.1, 77.5 (q, J = 2.8 Hz), 70.0, 40.2 (q, J = 28.1 Hz), 31.7, 19.1, 13.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.1 (t, J = 10.4 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{16}H_{18}ClF_3NO^+$ 332.1024, Found 332.1023.



2-(1-butoxy-3,3,3-trifluoropropyl)-4-methylquinoline (5b)

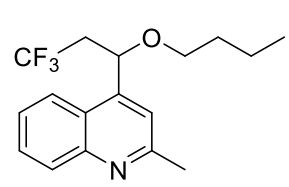
Following the typical experimental procedure A on 0.2 mmol scale, compound **5b** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 15:1, v/v). 47 mg, 76% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.5 Hz, 1H), 8.00 (d, J = 8.4 Hz, 1H), 7.75 – 7.69 (m, 1H), 7.61 – 7.54 (m, 1H), 7.43 (s, 1H), 4.85 (dd, J = 7.9, 5.0 Hz, 1H), 3.44 (t, J = 6.5 Hz, 2H), 2.74 (s, 3H), 2.71 – 2.57 (m, 2H), 1.69 – 1.51 (m, 2H), 1.45 – 1.33 (m, 2H), 0.90 (t, J = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 160.4, 147.4, 145.6, 129.7, 129.4, 127.7, 126.4, 125.9 (q, J = 277.6 Hz), 123.7, 118.5, 77.9 (q, J = 3.1 Hz), 69.7, 40.4 (q, J = 28.0 Hz), 31.8, 19.2, 19.0, 13.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.1 (t, J = 10.5 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{17}H_{21}F_3NO^+$ 312.1570, Found 312.1509.



4-(1-butoxy-3,3,3-trifluoropropyl)-2-methylquinoline (5c)

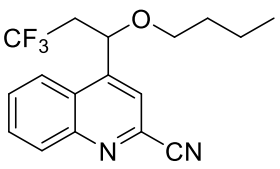
Following the typical experimental procedure A in 2mL DMSO-H_2O (2:1) on 0.2 mmol scale. Compound **5c** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 5:1, v/v). 46 mg, 74% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.4 Hz, 1H), 7.99 (d, J = 8.4 Hz, 1H), 7.71 (t, J = 7.6 Hz, 1H), 7.54 (t, J = 7.6 Hz, 1H), 7.41 (s, 1H), 5.24 (dd, J = 9.1, 2.1 Hz, 1H), 3.51 – 3.31 (m, 2H), 2.76 (s, 3H), 2.73 – 2.60 (m, 1H), 2.57 – 2.41 (m, 1H), 1.66 – 1.54 (m, 2H), 1.46 – 1.34 (m, 2H), 0.90 (t, J = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 159.0, 148.3, 145.9, 129.8, 129.4, 126.2, 125.7 (q, J = 277.7 Hz), 123.7, 122.2, 119.1, 73.0, 69.8, 41.4 (q, J = 27.9 Hz), 31.8, 25.4, 19.2, 13.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -64.0 (t, J = 10.4 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{17}H_{21}F_3NO^+$ 312.1570, Found 312.1569.



4-(1-butoxy-3,3,3-trifluoropropyl)quinoline-2-carbonitrile (5d)

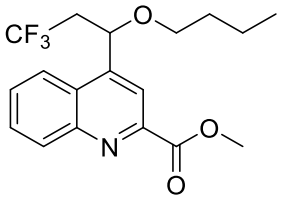
Following the typical experimental procedure A on 0.2 mmol scale. Compound **5d** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 10:1, v/v). 21 mg, 32% yield, White solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, J = 8.6 Hz, 1H), 8.07 (d, J = 8.5 Hz, 1H), 7.92 – 7.86 (m, 1H), 7.85 (s, 1H), 7.81 – 7.75 (m, 1H), 5.31 (dd, J = 9.1, 2.6 Hz, 1H), 3.42 (t, J = 6.6 Hz, 2H), 2.77 – 2.61 (m, 1H), 2.57 – 2.42 (m, 1H), 1.66 – 1.56 (m, 2H), 1.48 – 1.36 (m, 2H), 0.92 (t, J = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 148.51, 148.46, 133.9, 131.4, 131.1, 130.0, 126.0, 125.4 (q, J = 277.7 Hz), 122.4, 120.5, 117.4, 72.5 (q, J = 2.5 Hz), 70.4, 41.3 (q, J = 28.3 Hz), 31.7, 19.2, 13.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.9 (t, J = 10.2 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{17}H_{18}F_3N_2O^+$ 323.1366, Found 23.1365.



methyl 4-(1-butoxy-3,3,3-trifluoropropyl)quinoline-2-carboxylate (5e)

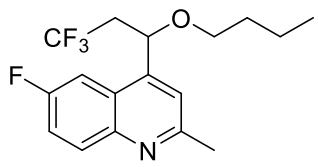
Following the typical experimental procedure A on 0.2 mmol scale. Compound **5e** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 5:1, v/v). 52 mg, 73% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, J = 8.5 Hz, 1H), 8.32 (s, 1H), 8.13 (d, J = 8.4 Hz, 1H), 7.82 (t, J = 7.6 Hz, 1H), 7.72 (t, J = 7.6 Hz, 1H), 5.31 (dd, J = 9.0, 2.1 Hz, 1H), 4.09 (s, 3H), 3.40 (t, J = 6.4 Hz, 2H), 2.85 – 2.66 (m, 1H), 2.59 – 2.42 (m, 1H), 1.67 – 1.52 (m, 2H), 1.46 – 1.34 (m, 2H), 0.89 (t, J = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 165.7, 148.0, 147.9, 147.6, 131.9, 130.2, 129.2, 126.1, 125.6 (q, J = 277.6 Hz), 122.4, 118.5, 73.1, 69.9, 53.3, 41.3 (q, J = 28.1 Hz), 31.7, 19.1, 13.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.9 (t, J = 10.3 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{18}H_{21}F_3NO_3^+$ 356.1469, Found 356.1467.



4-(1-butoxy-3,3,3-trifluoropropyl)-6-fluoro-2-methylquinoline (5f)

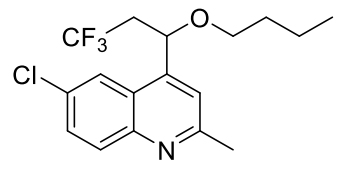
Following the typical experimental procedure A on 0.2 mmol scale. Compound **5f** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 5:1, v/v). 59 mg, 92% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (dd, J = 9.2, 5.6 Hz, 1H), 7.66 (dd, J = 10.1, 2.7 Hz, 1H), 7.46 (ddd, J = 9.2, 7.2, 2.7 Hz, 1H), 7.39 (s, 1H), 5.08 (dd, J = 9.0, 3.0 Hz, 1H), 3.37 (t, J = 6.4 Hz, 2H), 2.73 (s, 3H), 2.78 – 2.63 (m, 1H), 2.53 – 2.40 (m, 1H), 1.63 – 1.54 (m, 2H), 1.45 – 1.32 (m, 2H), , 0.89 (t, J = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 160.1 (d, J = 247.6 Hz), 158.2 (d, J = 2.6 Hz), 145.5, 145.3 (d, J = 5.6 Hz), 132.1 (d, J = 9.2 Hz), 125.6 (q, J = 277.5 Hz), 124.3 (d, J = 9.5 Hz), 120.2, 119.4 (d, J = 25.5 Hz), 106.4 (d, J = 23.1 Hz), 73.5, 69.7, 41.1 (q, J = 28.0 Hz), 31.7, 25.2, 18.9, 13.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -64.0 (t, J = 10.4 Hz, 3F), -112.3 (dd, J = 14.7, 8.9 Hz 1F)

HRMS (ESI): $[M+H]^+$ calcd for $C_{17}H_{20}F_4NO^+$ 330.1476, Found 330.1474.



4-(1-butoxy-3,3,3-trifluoropropyl)-6-chloro-2-methylquinoline (5g)

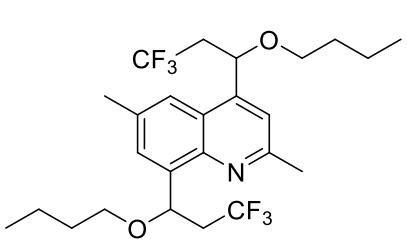
Following the typical experimental procedure A on 0.2 mmol scale. Compound **5g** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 2:1, v/v). 61 mg, 88% yield, yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 – 7.96 (m, 2H), 7.64 (dd, *J* = 8.9, 2.1 Hz, 1H), 7.40 (s, 1H), 5.12 (dd, *J* = 9.1, 2.6 Hz, 1H), 3.37 (t, *J* = 6.3 Hz, 2H), 2.74 (s, 3H), 2.72 – 2.62 (m, 1H), 2.56 – 2.38 (m, 1H), 1.63 – 1.54 (m, 2H), 1.45 – 1.34 (m, 2H), 0.89 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 159.3, 146.8, 145.1, 132.1, 131.3, 130.3, 125.6 (q, *J* = 277.6 Hz), 124.4, 121.6, 120.3, 73.4, 69. 8, 41.3 (q, *J* = 28.0 Hz), 31.7, 25.3, 19.2, 13.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.9 (t, *J* = 10.3 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{17}H_{20}ClF_3NO^+$ 346.1181, Found 346.1180.



4,8-bis(1-butoxy-3,3,3-trifluoropropyl)-2,6-dimethylquinoline (5h)

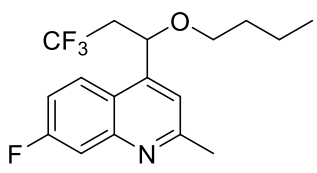
Following the typical experimental procedure B on 0.2 mmol scale. compound **5h** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 8:1, v/v). 27mg, 28% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.75 (s, 1H), 7.38 (s, 1H), 5.21 (d, *J* = 9.1 Hz, 1H), 4.92 (dd, *J* = 8.7, 2.9 Hz, 1H), 3.45 – 3.36 (m, 3H), 3.33 – 3.25 (m, 1H), 2.76 (s, 3H), 2.71 – 2.59 (m, 2H), 2.54 (s, 3H), 2.50 – 2.27 (m, 2H), 1.65 – 1.50 (m, 4H), 1.46 – 1.32 (m, 4H), 0.94 – 0.86 (m, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 158.7, 147.2, 145.3, 141.6, 133.7, 126.9, 125.79 (q, *J* = 277.6 Hz), 125.75 (q, *J* = 277.7 Hz), 123.4 (d, *J* = 3.0 Hz), 123.3, 119.3 (d, *J* = 6.3 Hz), 73.2, 72.9, 69.8 (d, *J* = 3.7 Hz), 69.2, 41.36 (q, *J* = 55.1, 27.6 Hz), 41.34 (q, *J* = 55.8, 28.0 Hz), 31.77 (d, *J* = 4.9 Hz), 29.7, 25.3, 19.6, 19.2 (d, *J* = 6.2 Hz), 13.8 (d, *J* = 14.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -64.0 (dt, *J* = 10.4, 7.4 Hz, 6F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{25}H_{34}F_6NO_2^+$ 494.2488, Found 494.2486.



4-(1-butoxy-3,3,3-trifluoropropyl)-7-fluoro-2-methylquinoline (5i)

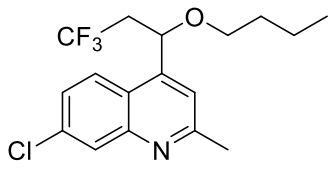
Following the typical experimental procedure A on 0.2 mmol scale. Compound **5i** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 5:1, v/v). 57 mg, 87% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (dd, *J* = 9.2, 6.0 Hz, 1H), 7.70 (dd, *J* = 10.1, 2.4 Hz, 1H), 7.36 – 7.28 (m, 2H), 5.16 (dd, *J* = 9.0, 2.4 Hz, 1H), 3.38 (t, *J* = 6.4 Hz, 2H), 2.74 (s, 3H), 2.72 – 2.63 (m, 1H), 2.54 – 2.39 (m, 1H), 1.64 – 1.52 (m, 2H), 1.45 – 1.33 (m, 2H), 0.89 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 162.9 (d, *J* = 250.4 Hz), 160.4, 149.7 (d, *J* = 12.2 Hz), 146.0, 125.6 (q, *J* = 277.6 Hz), 124.6 (d, *J* = 9.8 Hz), 120.8, 118.8, 116.4 (d, *J* = 34.4 Hz), 113.4 (d, *J* = 20.0 Hz), 73.4, 69.8, 41.4 (q, *J* = 28.0 Hz), 31.7, 25.4, 19.2, 13.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.0 (t, *J* = 10.3 Hz, 3F), -109.65 (s, 1F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{17}H_{20}F_4NO^+$ 330.1476, Found 330.1474.



4-(1-butoxy-3,3,3-trifluoropropyl)-7-chloro-2-methylquinoline (5j)

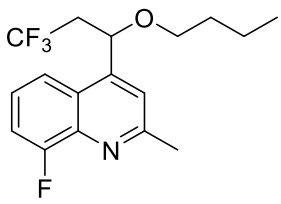
Following the typical experimental procedure A on 0.2 mmol scale, compound **5j** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 10:1, v/v). 59 mg, 86% yield, yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 1.7 Hz, 1H), 7.98 (d, *J* = 9.0 Hz, 1H), 7.48 (dd, *J* = 9.0, 1.8 Hz, 1H), 7.37 (s, 1H), 5.15 (dd, *J* = 8.9, 2.3 Hz, 1H), 3.38 (t, *J* = 6.4 Hz, 2H), 2.74 (s, 3H), 2.73 – 2.63 (m, 1H), 2.54 – 2.38 (m, 1H), 1.64 – 1.53 (m, 2H), 1.45 – 1.33 (m, 2H), 0.89 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 160.3, 149.0, 145. 9, 135.3, 128.8, 127.1, 125.6 (q, *J* = 277.6 Hz), 123.8, 122.2, 119.6, 73.4, 69.8, 41.3 (q, *J* = 28.0 Hz), 31.7, 25.4, 19.2, 13.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.98 (t, *J* = 10.3 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{17}H_{20}ClF_3NO^+$ 346.1181, Found 346.1179.



4-(1-butoxy-3,3,3-trifluoropropyl)-8-fluoro-2-methylquinoline (5k)

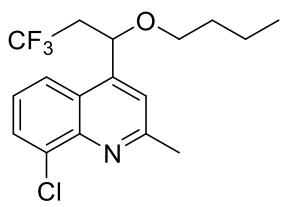
Following the typical experimental procedure A on 0.2 mmol scale. Compound **5k** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 5:1, v/v). 61 mg, 92% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.3 Hz, 1H), 7.53 – 7.35 (m, 3H), 5.19 (dd, *J* = 9.1, 2.5 Hz, 1H), 3.45 – 3.33 (m, 2H), 2.80 (s, 3H), 2.75 – 2.59 (m, 1H), 2.56 – 2.40 (m, 1H), 1.63 – 1.55 (m, 2H), 1.46 – 1.33 (m, 2H), 0.90 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 159.6, 158.2 (d, *J* = 256.1 Hz), 145.9 (d, *J* = 2.1 Hz), 138.7 (d, *J* = 10.8 Hz), 125.9 (d, *J* = 8.3 Hz), 125.6 (q, *J* = 277.6 Hz), 125.5 (d, *J* = 1.7 Hz), 120.2, 118.0 (d, *J* = 4.7 Hz), 113.6 (d, *J* = 19.3 Hz), 73.1, 69.9, 41.3 (q, *J* = 28.0 Hz), 31.7, 25.6, 19.1, 13.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -64.0 (t, *J* = 10.3 Hz, 3F), -123.3 (dd, *J* = 9.5, 4.7 Hz, 1F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{17}H_{20}F_4NO^+$ 330.1476, Found 330.1474.



4-(1-butoxy-3,3,3-trifluoropropyl)-8-chloro-2-methylquinoline (5l)

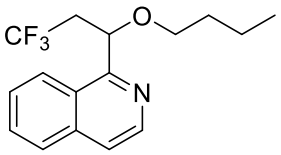
Following the typical experimental procedure A on 0.2 mmol scale. Compound **5l** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 10:1, v/v). 63 mg, 91% yield, yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.4 Hz, 1H), 7.80 (d, J = 7.5 Hz, 1H), 7.47 (s, 1H), 7.43 (t, J = 8.0 Hz, 1H), 5.20 (dd, J = 9.1, 1.7 Hz, 1H), 3.38 (t, J = 6.3 Hz, 2H), 2.81 (s, 3H), 2.75 – 2.60 (m, 1H), 2.54 – 2.39 (m, 1H), 1.64 – 1.53 (m, 2H), 1.45 – 1.32 (m, 2H), 0.88 (t, J = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 160.0, 146.2, 144.6, 134.0, 129.5, 125.9, 125.6 (q, J = 277.6 Hz), 125.1, 121.3, 120.1, 73.1, 69.8, 41.3 (q, J = 28.0 Hz), 31.7, 25.7, 19.1, 13.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -64.0 (t, J = 10.3 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{17}H_{20}ClF_3NO^+$ 346.1181, Found 346.1180.



1-(1-butoxy-3,3,3-trifluoropropyl)isoquinoline (5m)

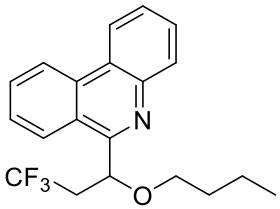
Following the typical experimental procedure A in 2mL DMSO-H_2O (2:1) on 0.2 mmol scale. Compound **5m** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 5:1, v/v). 43 mg, 72% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, J = 8.5 Hz, 1H), 8.50 (d, J = 5.7 Hz, 1H), 7.87 (d, J = 8.2 Hz, 1H), 7.75 – 7.67 (m, 1H), 7.66 – 7.57 (m, 2H), 5.41 (dd, J = 8.5, 4.4 Hz, 1H), 3.41 – 3.32 (m, 2H), 3.13 – 2.95 (m, 1H), 2.83 – 2.66 (m, 1H), 1.60 – 1.43 (m, 2H), 1.36 – 1.23 (m, 2H), 0.81 (t, J = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 158.2, 141.6, 136.8, 130.1, 127.6, 127.5, 126.3, 126.0 (q, J = 277.2 Hz), 124.7, 121.2, 76.9 (q, J = 2.8 Hz), 68.8, 39.1 (q, J = 27.9 Hz), 31.7, 19.1, 13.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.6 (t, J = 10.6, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{16}H_{19}F_3NO^+$ 298.1413, Found 298.1413.



6-(1-butoxy-3,3,3-trifluoropropyl)phenanthridine (5n)

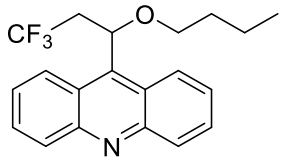
Following the typical experimental procedure B for 12 hours on 0.2 mmol scale. Compound **5n** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 5:1, v/v). 47 mg, 68% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, J = 8.3 Hz, 1H), 8.68 (d, J = 8.3 Hz, 1H), 8.58 (d, J = 8.1 Hz, 1H), 8.21 (dd, J = 8.1, 0.9 Hz, 1H), 7.92 – 7.83 (m, 1H), 7.80 – 7.66 (m, 3H), 5.51 (dd, J = 8.9, 4.0 Hz, 1H), 3.54 – 3.39 (m, 2H), 3.24 – 3.05 (m, 1H), 2.96 – 2.79 (m, 1H), 1.63 – 1.47 (m, 2H), 1.39 – 1.26 (m, 2H), 0.83 (t, J = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 158.0, 143.0, 133.5, 130.7, 130.3, 128.8, 127.4, 126.2 (q, J = 277.3 Hz), 126.0, 124.12, 124.11, 122.6, 121.9, 77.8 (q, J = 3.0 Hz), 68.6, 38.6 (q, J = 28.0 Hz), 31.8, 19.1, 13.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.4 (dt, J = 10.8, 2.1 Hz, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{20}H_{21}F_3NO^+$ 348.1570, Found 348.1568.



9-(1-butoxy-3,3,3-trifluoropropyl)acridine (5o)

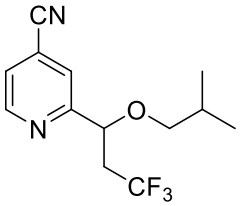
Following the typical experimental procedure B for 12 hours on 0.2 mmol scale. Compound **5o** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 5:1, v/v). 44 mg, 63% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (d, J = 8.3 Hz, 1H), 8.27 (d, J = 8.4 Hz, 3H), 7.80 (t, J = 7.5 Hz, 2H), 7.67 – 7.53 (m, 2H), 6.13 (dd, J = 8.8, 3.7 Hz, 1H), 3.44 – 3.36 (m, 1H), 3.34 – 3.19 (m, 2H), 2.73 – 2.58 (m, 1H), 1.56 – 1.47 (m, 2H), 1.39 – 1.23 (m, 2H), 0.81 (t, J = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 149.0, 148.4, 141.6, 130.8, 130.6, 130.0, 129.8, 126.8, 126.0, 125.8 (q, J = 277.6 Hz), 125.7, 124.5, 124.0, 122.0, 71.6 (q, J = 3.1 Hz), 69.6, 40.8 (q, J = 28.1 Hz), 31.7, 19.1, 13.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -64.0 (t, J = 10.4, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{20}H_{21}F_3NO^+$ 348.1570, Found 348.1569.



2-(3,3,3-trifluoro-1-isobutoxypropyl)isonicotinonitrile (6a)

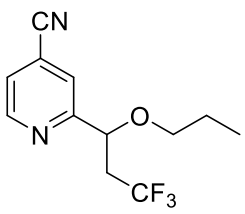
Following the typical experimental procedure A on 0.2 mmol scale. Compound **6a** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 5:1, v/v). 37 mg, 68% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, J = 5.0 Hz, 1H), 7.70 (s, 1H), 7.46 (dd, J = 4.9, 1.4 Hz, 1H), 4.72 (dd, J = 8.5, 3.8 Hz, 1H), 3.27 – 3.18 (m, 2H), 2.72 – 2.48 (m, 2H), 2.00 – 1.84 (m, 1H), 0.94 (t, J = 6.9 Hz, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 162.3, 150.4, 125.6 (q, J = 277.4 Hz), 124.3, 122.1, 121.4, 116.4, 77.3, 77.0 (q, J = 3.0 Hz), 40.0 (q, J = 28.2 Hz), 28.6, 19.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.2 (t, J = 10.3, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{13}H_{16}F_3N_2O^+$ 273.1210, Found 273.1208.



2-(3,3,3-trifluoro-1-propoxypropyl)isonicotinonitrile (6b)

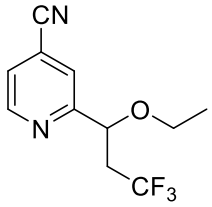
Following the typical experimental procedure on A 0.2 mmol scale. Compound **6b** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 5:1, v/v). 38 mg, 73% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, J = 4.9 Hz, 1H), 7.71 (s, 1H), 7.46 (dd, J = 5.0, 1.4 Hz, 1H), 4.74 (dd, J = 8.5, 3.8 Hz, 1H), 3.43 (t, J = 6.7 Hz, 2H), 2.81 – 2.47 (m, 2H), 1.72 – 1.59 (m, 2H), 0.95 (t, J = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 162.3, 150.4, 125.6 (q, J = 277.4 Hz), 124.3, 122.1, 121.4, 116.4, 76.8 (q, J = 3.1 Hz), 72.3, 40.0 (q, J = 28.2 Hz), 22.9, 10.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.3 (t, J = 10.4, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{12}H_{14}F_3N_2O^+$ 259.1053, Found 259.1052.



2-(1-ethoxy-3,3,3-trifluoropropyl)isonicotinonitrile (6c)

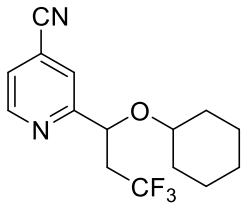
Following the typical experimental procedure A on 0.2 mmol scale. Compound **6c** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 5:1, v/v). 35 mg, 72% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, J = 4.9 Hz, 1H), 7.72 (s, 1H), 7.47 (dd, J = 4.9, 1.3 Hz, 1H), 4.75 (dd, J = 8.5, 3.8 Hz, 1H), 3.61 – 3.48 (m, 2H), 2.76 – 2.49 (m, 2H), 1.26 (t, J = 7.0 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 162.3, 150.4, 125.6 (q, J = 277.4 Hz), 124.3, 122.1, 121.4, 116.4, 76.6 (q, J = 3.0 Hz), 66.0, 40.1 (q, J = 28.1 Hz), 15.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.3 (t, J = 10.4, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{11}H_{12}F_3N_2O^+$ 245.0897, Found 245.0895.



2-(1-(cyclohexyloxy)-3,3,3-trifluoropropyl)isonicotinonitrile (6d)

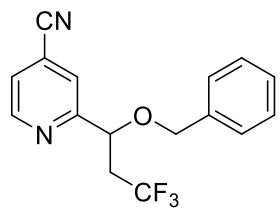
Following the typical experimental procedure A on 0.2 mmol scale. Compound **6d** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 10:1, v/v). 48 mg, 81% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, J = 4.9 Hz, 1H), 7.77 (s, 1H), 7.45 (dd, J = 4.9, 1.3 Hz, 1H), 4.92 (dd, J = 8.9, 3.4 Hz, 1H), 3.33 – 3.23 (m, 1H), 2.68 – 2.44 (m, 2H), 1.97 (d, J = 11.4 Hz, 1H), 1.82 – 1.65 (m, 3H), 1.57 – 1.46 (m, 1H), 1.45 – 1.27 (m, 2H), 1.26 – 1.16 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 163.4, 150.2, 125.6 (q, J = 277.6 Hz), 124.2, 122.2, 121.3, 116.4, 77.7, 74.0 (q, J = 2.9 Hz), 40.6 (q, J = 27.9 Hz), 33.1, 31.5, 25.5, 24.0, 23.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.1 (t, J = 10.3, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{15}H_{18}F_3N_2O^+$ 299.1366, Found 299.1365.



2-(1-(benzyloxy)-3,3,3-trifluoropropyl)isonicotinonitrile (6e)

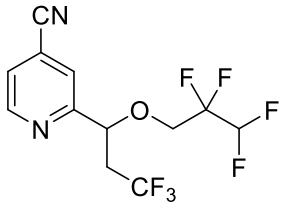
Following the typical experimental procedure A on 0.2 mmol scale. Compound **6e** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 5:1, v/v). 50 mg, 82% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (dd, J = 5.0, 0.6 Hz, 1H), 7.70 (s, 1H), 7.47 (dd, J = 5.0, 1.4 Hz, 1H), 7.40 – 7.29 (m, 5H), 4.89 (dd, J = 7.0, 5.3 Hz, 1H), 4.55 (s, 2H), 2.75 – 2.62 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 161.6, 150.4, 136.6, 128.5, 128.2, 128.0, 125.6 (q, J = 277.4 Hz), 124.4, 122.4, 121.4, 116.3, 76.2 (q, J = 2.9 Hz), 72.4, 40.0 (q, J = 28.3 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.0 (t, J = 10.3, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{16}H_{14}F_3N_2O^+$ 307.1053, Found 307.1053.



2-(3,3,3-trifluoro-1-(2,2,3,3-tetrafluoropropoxy)propyl)isonicotinonitrile (6f)

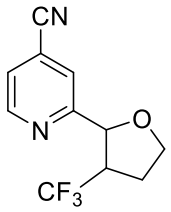
Following the typical experimental procedure A on 0.2 mmol scale. Compound **6f** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 5:1, v/v). 32 mg, 48% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, J = 4.9 Hz, 1H), 7.68 (s, 1H), 7.54 (dd, J = 4.9, 1.3 Hz, 1H), 5.97 (tt, J = 53.2, 5.0 Hz, 1H), 4.90 (dd, J = 8.1, 4.3 Hz, 1H), 3.95 – 3.80 (m, 2H), 2.77 – 2.61 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 159.7, 150.8, 125.2 (q, J = 277.3 Hz), 125.1, 122.1, 121.9, 116.0, 114.5 (tt, J = 250.1, 27.2 Hz), 109.0 (tt, J = 249.7, 34.7 Hz), 78.4 (q, J = 2.9 Hz), 67.0 (t, J = 28.9 Hz), 40.0 (q, J = 28.8 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.6 (t, J = 10.1, 3F), -123.85 – 126.19 (m, 2F), -137.89 –140.55 (m ,2F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{12}H_{10}F_7N_2O^+$ 331.0676, Found 331.0678.



2-(3-(trifluoromethyl)tetrahydrofuran-2-yl)isonicotinonitrile (6g)

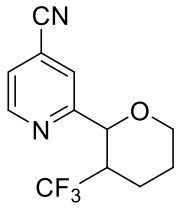
Following the typical experimental procedure B in 2mL DMSO-H_2O (3:2) on 0.2 mmol scale. Compound **6g** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 5:1, v/v). 21 mg, 43% yield, yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.78 (d, J = 4.9 Hz, 1H), 7.71 (s, 1H), 7.46 (dd, J = 4.9, 1.2 Hz, 1H), 5.16 (d, J = 4.6 Hz, 1H), 4.09 (t, J = 6.9 Hz, 2H), 3.48 – 3.38 (m, 1H), 2.25 – 2.20 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 161.4, 150.4, 128.0 (q, J = 277.9 Hz), 124.3, 122.9, 121.2, 116.3, 80.1 (q, J = 4.7, 2.2 Hz), 68.6, 48.5 (q, J = 27.5 Hz), 26.6 (q, J = 2.5 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -69.7 (d, J = 9.6, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{11}H_{10}F_3N_2O^+$ 243.0740, Found 243.0738.



2-(3-(trifluoromethyl)tetrahydro-2H-pyran-2-yl)isonicotinonitrile (6h)

Following the typical experimental procedure A at 60 °C on 0.2 mmol scale. Compound **6h** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 5:1, v/v). 19 mg, 38% yield, yellow oil liquid.

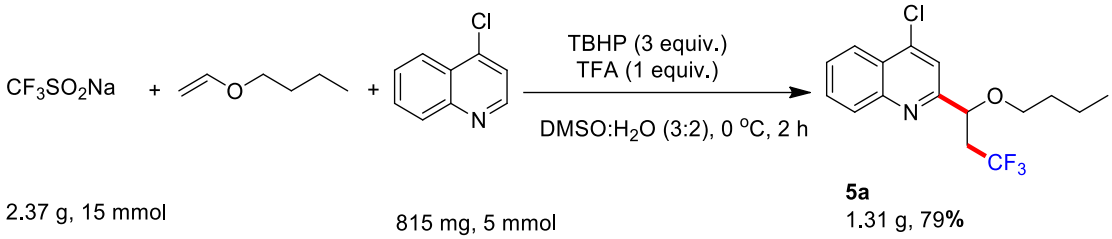
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, J = 4.9 Hz, 1H), 7.58 (s, 1H), 7.48 (dd, J = 5.0, 1.4 Hz, 1H), 4.54 (d, J = 9.5 Hz, 1H), 4.14 – 4.07 (m, 1H), 3.60 (dt, J = 11.3, 3.6 Hz, 1H), 2.89 – 2.74 (m, 1H), 2.27 – 2.19 (m, 1H), 1.90 – 1.72 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 160.0, 150.4, 125.9 (q, J = 279.8 Hz), 124.8, 124.3, 121.1, 116.2, 79.2 (q, J = 1.6 Hz), 68.2, 44.2 (q, J = 24.9 Hz), 23.9, 22.7 (q, J = 2.7 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -69.7 (d, J = 8.3, 3F).

HRMS (ESI): $[M+H]^+$ calcd for $C_{12}H_{12}F_3N_2O^+$ 257.0897, Found 257.0895.

7. Scale-up experiment



2.37 g, 15 mmol

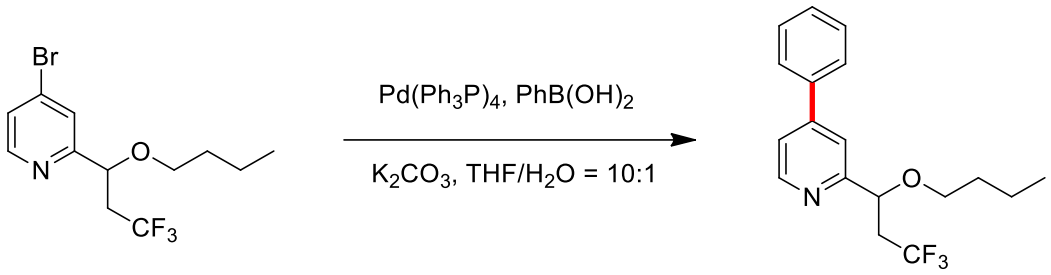
815 mg, 5 mmol

5a
1.31 g, 79%

To a solution of the quinoline substrate (0.82 g, 5 mmol, 1.0 equiv.) in 50 mL DMSO-H_2O (3:2) was added TFA (383μL, 5mmol, 1.0 equiv.) and stirrling was kept at room temperature for 5 minutes. Subsequently, CF_3SO_2Na (2.37 g, 15 mmol, 3.0 equiv.), *n*-butyl vinyl ether (3.24 mL, 25 mmol, 5.0 equiv.) and TBHP (2.06 mL, 15 mmol, 3.0 equiv.) were added. The tube was sealed with and the reaction was stirred at room temperature for 1 minute. The system was immediately put in an ice bath and stirred at 0 ℃ for 2 hours. The mixture was cooled to room temperature, diluted with 80ml H_2O and neutralized with $NaHCO_3$. After extraction with EA three times, the combined organic layers were washed with brine and dried over Na_2SO_4. The crude mixture was purified by silica gel column chromatography using hexane / ethyl acetate (8:1) as the eluent, affording the product as a yellow oil (1.21 g, 79%).

8. Transformation of product

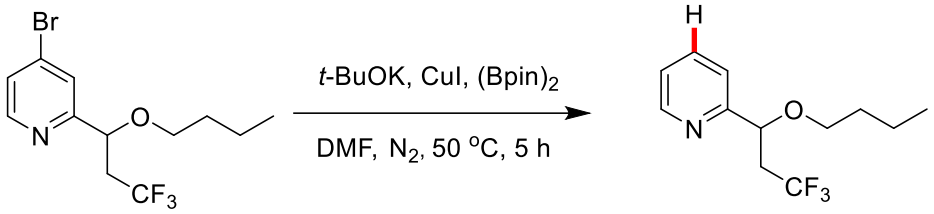
8.1. Suzuki coupling reaction



4h **4i**, 76%

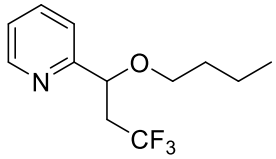
Compound **4h** (65.0 mg, 0.2 mmol, 1.0 equiv.), phenylboronic acid (60.8 mg, 0.4 mmol, 2.0 equiv.), K_2CO_3 (82.9 mg, 0.6 mmol, 3.0 equiv.), $Pd(Ph_3P)_4$ (23.1 mg, 0.02 mmol, 0.1 equiv.), were successively added to a 15 mL Schlenk tube, followed by the addition of THF (2.0 mL) and H_2O (0.2 mL) under nitrogen atmosphere. The mixture was heated to 70 ℃ for and stirred for 6 h. After cooling to room temperature, the solvent was removed by distillation under reduced pressure. The product was purified by silica gel column chromatography using hexane / ethyl acetate (30:1) as the eluent to give the product as a yellow oil (49.1 mg, 76%).

8.2. Dehalogenation reaction



4h **7**, 52%

Under nitrogen atmosphere Compound **4h** (65.0 mg, 0.2 mmol, 1.0 equiv.), DMF (2 mL), *t*-BuOK (67.2 mg, 0.6 mmol, 3.0 equiv.), CuI (17.2 mg, 0.09 mmol, 0.45 equiv.), $(Bpin)_2$ (152.3mg, 0.6mol, 3.0 equiv.), were successively added to a 15 mL Schlenk tube under nitrogen atmosphere. The mixture was heated to at 80 ℃ for 5h. After cooling to room temperature, the solvent was removed by distillation under reduced pressure. The crude mixture was purified by silica gel column chromatography using hexane / ethyl acetate (15:1) as the eluent to give the product as a yellow oil (26.2 mg, 53%).



2-(1-butoxy-3,3,3-trifluoropropyl)pyridine (7)

Compound 7 was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 8:1, v/v). 26 mg, 53% yield, yellow oil liquid. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.58 (d, J = 4.6 Hz, 1H), 7.73 (td, J = 7.7, 1.5 Hz, 1H), 7.45 (d, J = 7.9 Hz, 1H), 7.23 (dd, J = 7.0, 5.2 Hz, 1H), 4.69 (dd, J = 8.5, 4.1 Hz, 1H),

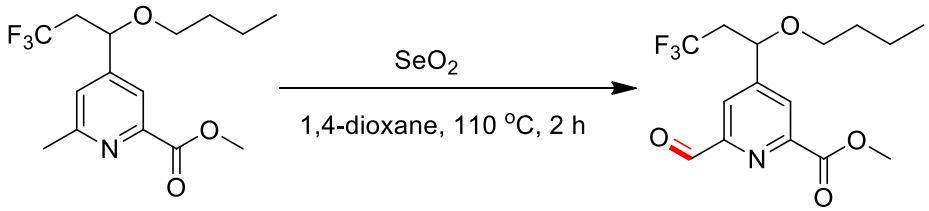
3.47 – 3.37 (m, 2H), 2.68 – 2.51 (m, 2H), 1.65 – 1.51 (m, 2H), 1.44 – 1.32 (m, 2H), 0.89 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 160.2, 149.4, 137.0, 125.9 (q, *J* = 277.4 Hz), 122.9, 120.4, 77.3 (q, *J* = 3.0 Hz), 69.7, 40.5 (q, *J* = 27.8 Hz), 31.8, 19.2, 13.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ 63.5 (t, *J* = 10.6 Hz, 3F).

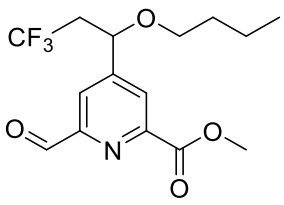
HRMS (ESI): $[M+H]^+$ calcd for $C_{12}H_{17}F_3NO^+$ 248.1257, Found 248.1260.

8.3. Oxidation by SeO_2



4q **8**, 78%

To a solution of **4q** (63.8 mg, 0.2 mmol, 1.0 equiv.) in 1,4-dioxane (2 mL), was added SeO_2 (22mg, 0.4 mmol, 2.0 equiv.). The reaction vial was then sealed and heated at 110 °C for 2 hours. The reaction was then cooled to room temperature, filtered through celite, and extraced with EtOAc. The filtrate was dried over Na_2SO_4 and then concentrated in vacuo. The crude product was purified by column chromatography using petroleum ether/ethyl acetate (15:1) as eluent, giving the product as a white solid (52.1 mg, 78%).



methyl 4-(1-butoxy-3,3,3-trifluoropropyl)-6-formylpicolinate (8)

Compound **8** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 2:1, v/v). 52 mg, 78% yield, white solid.

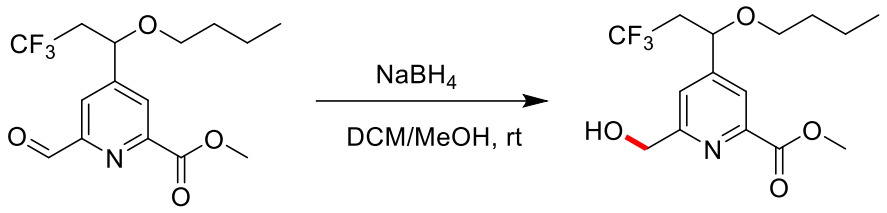
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.19 (s, 1H), 8.31 (d, *J* = 1.3 Hz, 1H), 8.10 (d, *J* = 1.3 Hz, 1H), 4.70 (dd, *J* = 8.2, 4.4 Hz, 1H), 4.07 (s, 3H), 3.39 – 3.27 (m, 2H), 2.73 – 2.59 (m, 1H), 2.45 – 2.31 (m, 1H), 1.60 – 1.51 (m, 2H), 1.42 – 1.31 (m, 2H), 0.88 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 192.3, 164.6, 153.4, 153.3, 149.2, 126.6, 125.1 (q, *J* = 277.4 Hz), 121.9, 74.8 (q, *J* = 3.1 Hz), 70.0, 53.4, 41.6 (q, *J* = 28.3 Hz), 31.5, 19.0, 13.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ 63.4 (t, *J* = 10.2 Hz, 3F).

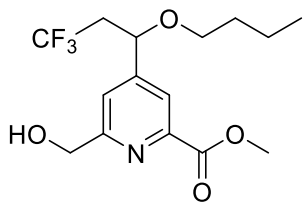
HRMS (ESI): $[M+H]^+$ calcd for $C_{15}H_{19}F_3NO_4^+$ 334.1261, Found 334.1266.

8.4. Reduction



8 **9**, 63%

To a reaction tube containing **8** (66.7 mg, 0.2 mmol, 1.0 equiv.) and 2 mL DCM-MeOH (4:1) was added sodium borohydride (7.62 mg, 0.20 mmol, 1.0 equiv.) at room temperature. The reaction was stirred until no starting material remained by TLC. The reaction was quenched by the addition of citric acid monohydrate (41.90 mg, 0.20 mmol, 1.0 equiv.). After stirring for an additional 10 minutes, the mixture was basified by the addition of saturated aqueous $NaHCO_3$. The organic layers were separated and the aqueous phase was extracted with CH_2Cl_2. The combined organic phase was dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by column chromatography (hexane/ethyl acetate = 1:2), affording the product as a yellow oil (32.2 mg, 63% yield).



methyl 4-(1-butoxy-3,3,3-trifluoropropyl)-6-(hydroxymethyl)picolinate (9)

Compound **9** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 1:2, v/v). 22 mg, 63% yield, yellow oil.

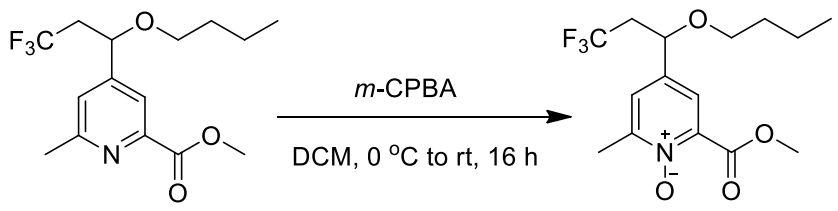
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.53 (s, 1H), 4.88 (s, 2H), 4.62 (dd, J = 8.5, 4.1 Hz, 1H), 4.00 (s, 3H), 3.32 (t, J = 6.4 Hz, 2H), 2.71 – 2.55 (m, 1H), 2.44 – 2.28 (m, 1H), 1.61 – 1.49 (m, 2H), 1.43 – 1.29 (m, 2H), 0.89 (t, J = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 165.3, 161.1, 152.2, 147.8, 125.2 (q, J = 277.4 Hz), 121.6, 121.5, 75.0 (q, J = 3.1 Hz), 69.8, 64.6, 53.0, 41.7 (q, J = 28.1 Hz), 31.6, 19.1, 13.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ 63.5 (t, J = 10.3 Hz, 3F).

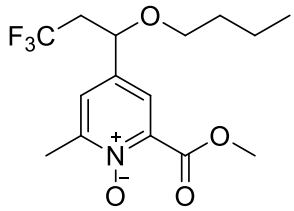
HRMS (ESI): $[M+H]^+$ calcd for $C_{15}H_{21}F_3NO_4^+$ 336.1418, Found 336.1414.

8.5. Oxidation by *m*-CPBA



4q **10**, 86%

To a solution of **4q** (63.8 mg, 0.2 mmol, 1.0 equiv.) in DCM (2 mL) was added *m*-CPBA (51.8 mg, 0.3 mmol, 1.5 equiv.) in batches at 0 °C. After stirring for 16 h at room temperature, sodium bicarbonate solution was added. The aqueous layer was extracted with DCM and the combined organic phase was dried with Na_2SO_4. After removal of the solvent under reduced pressure, the crude product was subjected to column chromatography, affording the product as a yellow oil (57.6 mg, 86%).



4-(1-butoxy-3,3,3-trifluoropropyl)-2-(methoxycarbonyl)-6-methylpyridine 1-oxide (10)

Compound **10** was obtained by silica gel column chromatography (eluent: petroleum ether/EtOAc = 1:2, v/v). 58 mg, 87% yield, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 1.8 Hz, 1H), 7.30 (d, J = 1.9 Hz, 1H), 4.49 (dd, J = 8.0, 4.6 Hz, 1H), 3.99 (s, 3H), 3.36 – 3.27 (m, 2H), 2.66 – 2.56 (m, 1H), 2.52 (s, 3H), 2.41 – 2.25 (m, 1H), 1.57 – 1.49 (m, 2H), 1.41 – 1.29 (m, 2H), 0.88 (t, J = 7.3 Hz, 3H)

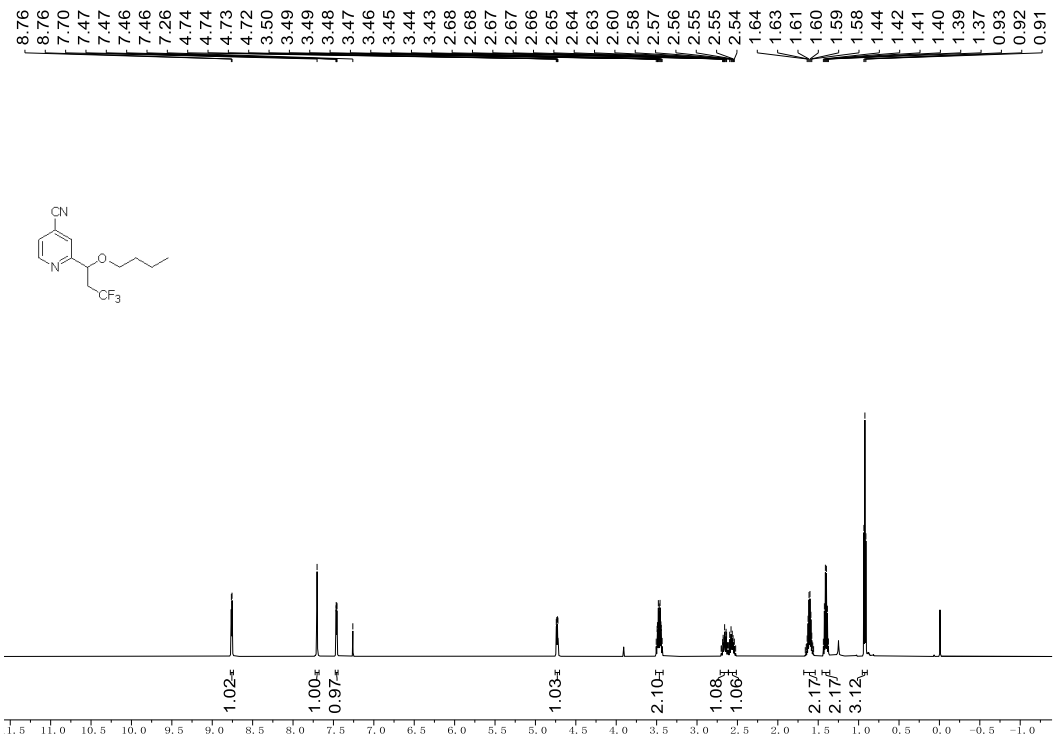
^{3}C NMR (151 MHz, $CDCl_3$) δ 162.4, 150.8, 141.9, 137.9, 125.2, 125.1 (q, J = 277.4 Hz), 121.7, 74.2 (q, J = 3.0 Hz), 69.7, 53.3, 41.5 (q, J = 28.0 Hz), 31.5, 19.0, 17.9, 13.6.

^{19}F NMR (376 MHz, $CDCl_3$) δ 63.4 (t, J = 10.3 Hz, 3F).

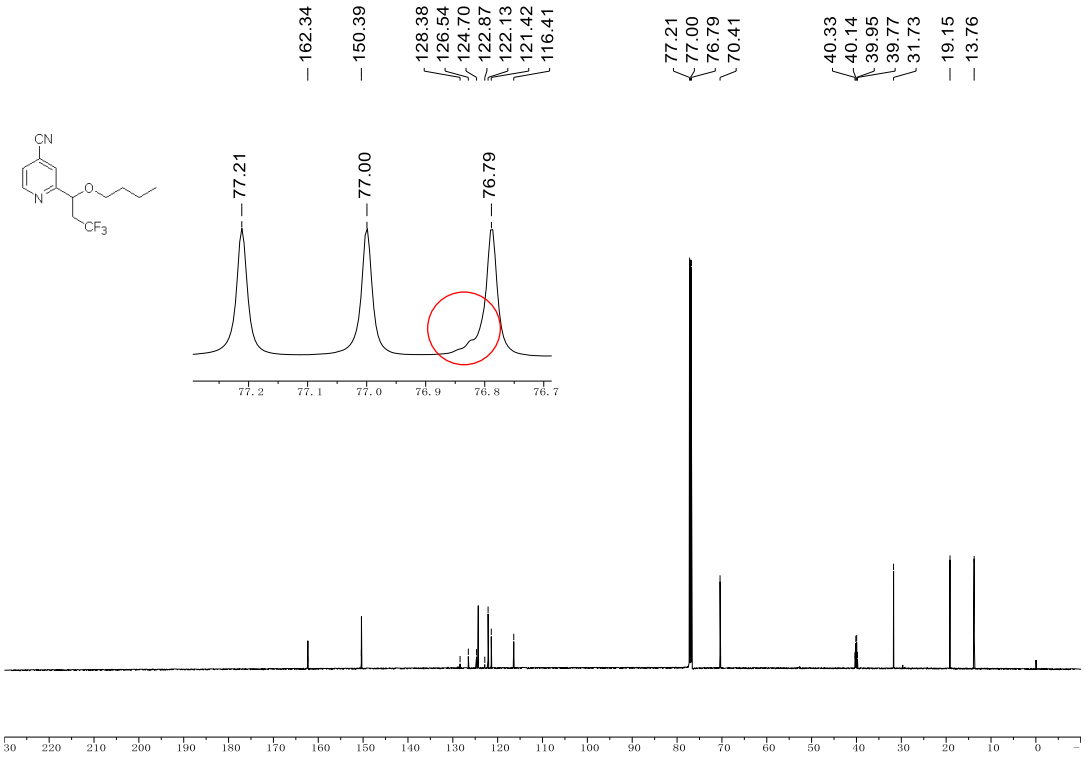
HRMS (ESI): $[M+H]^+$ calcd for $C_{15}H_{21}F_3NO_4^+$ 336.1418, Found 336.1419.

9. Copies of ^{1}H, ^{13}C and ^{19}F NMR spectra

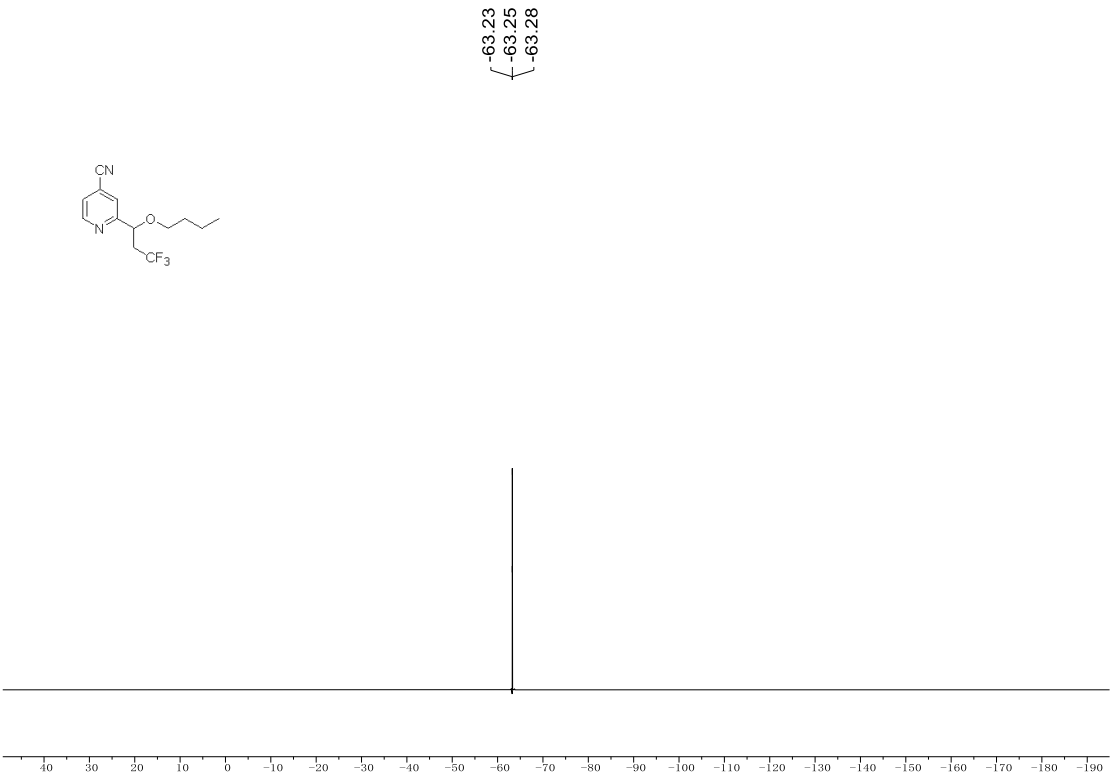
^{1}H NMR spectrum of compound **4a** in $CDCl_3$ (600 MHz)



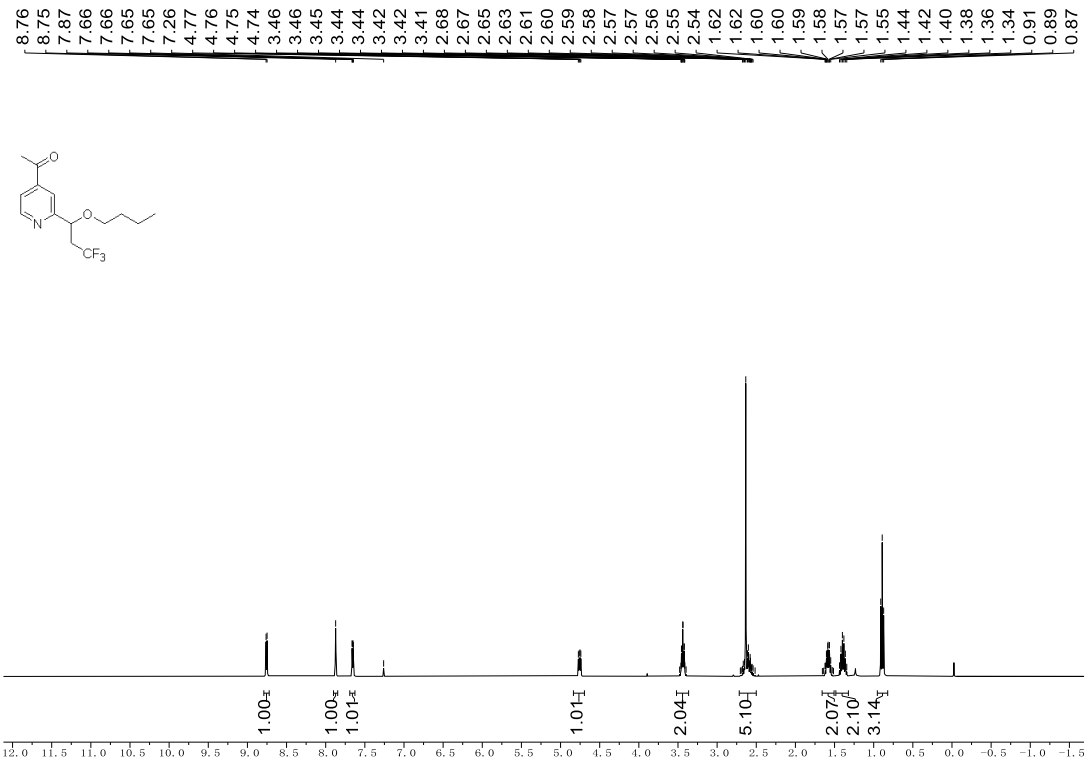
^{13}C NMR spectrum of compound compound **4a** in $CDCl_3$ (151 MHz)



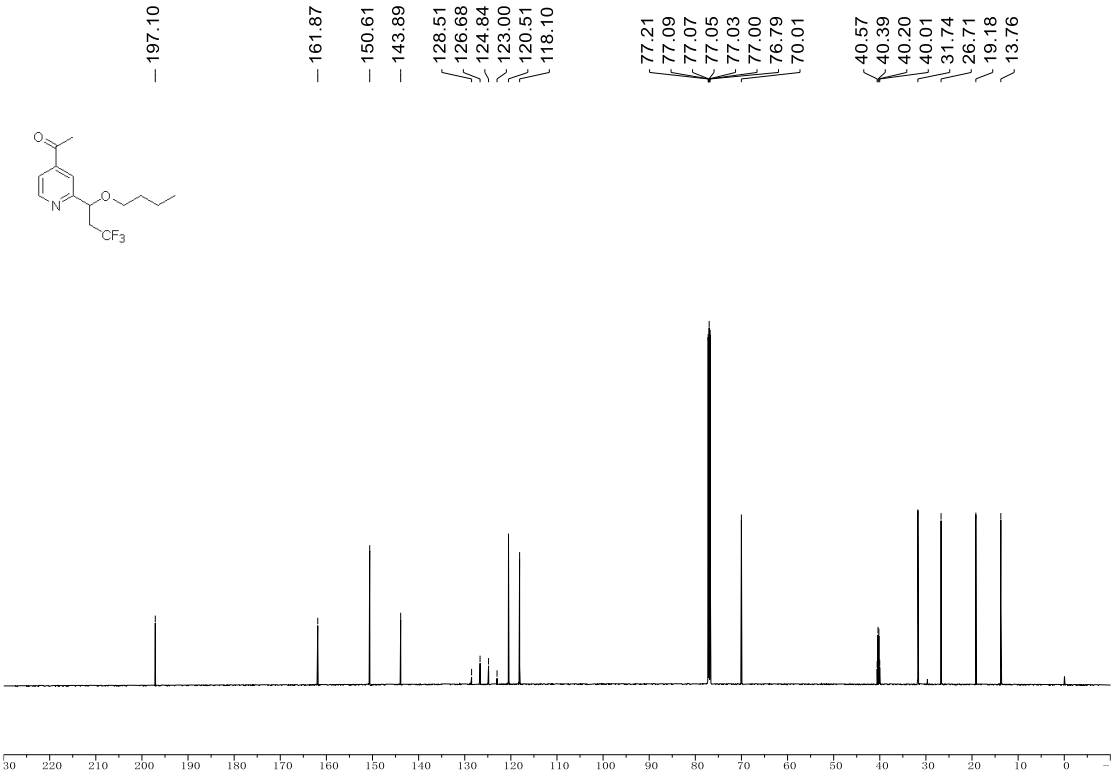
^{19}F NHR spectrum of compound **4a** in $CDCl_3$ (376 MHz)



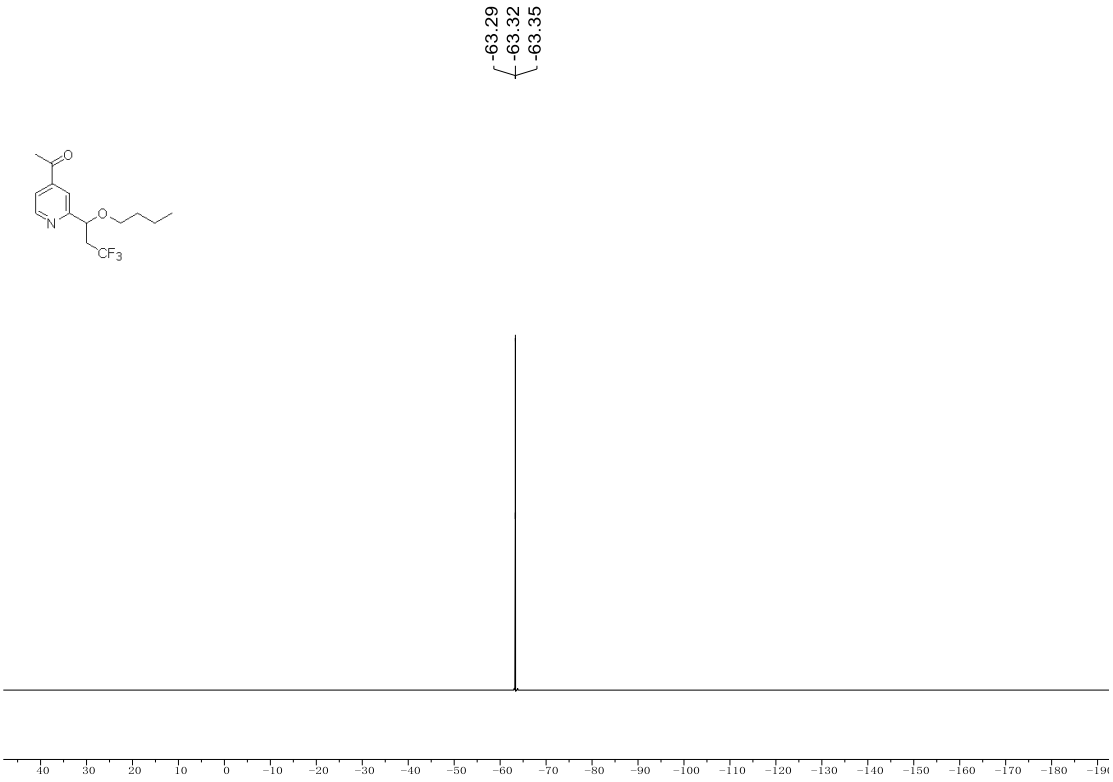
^{1}H NMR spectrum of compound **4b** in $CDCl_3$ (400 MHz)



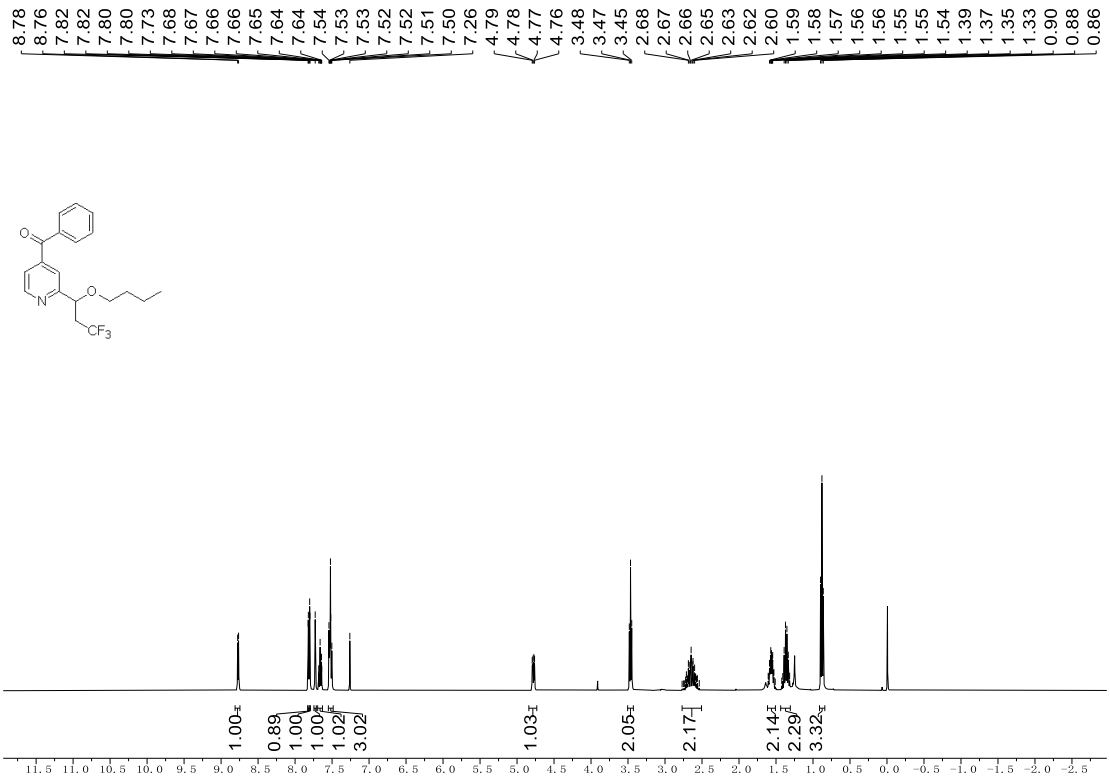
^{13}C NMR spectrum of compound **4b** in $CDCl_3$ (151 MHz)



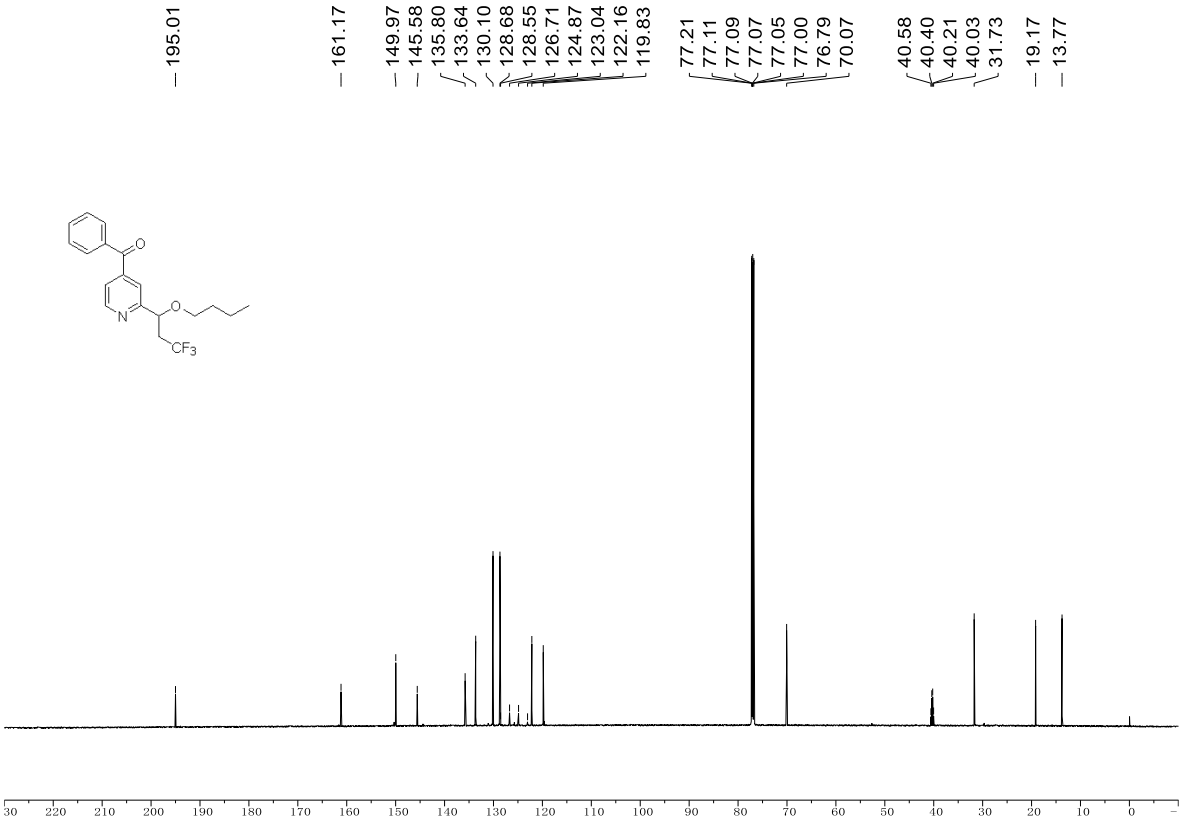
^{19}F NHR spectrum of compound **4b** in $CDCl_3$ (376 MHz)



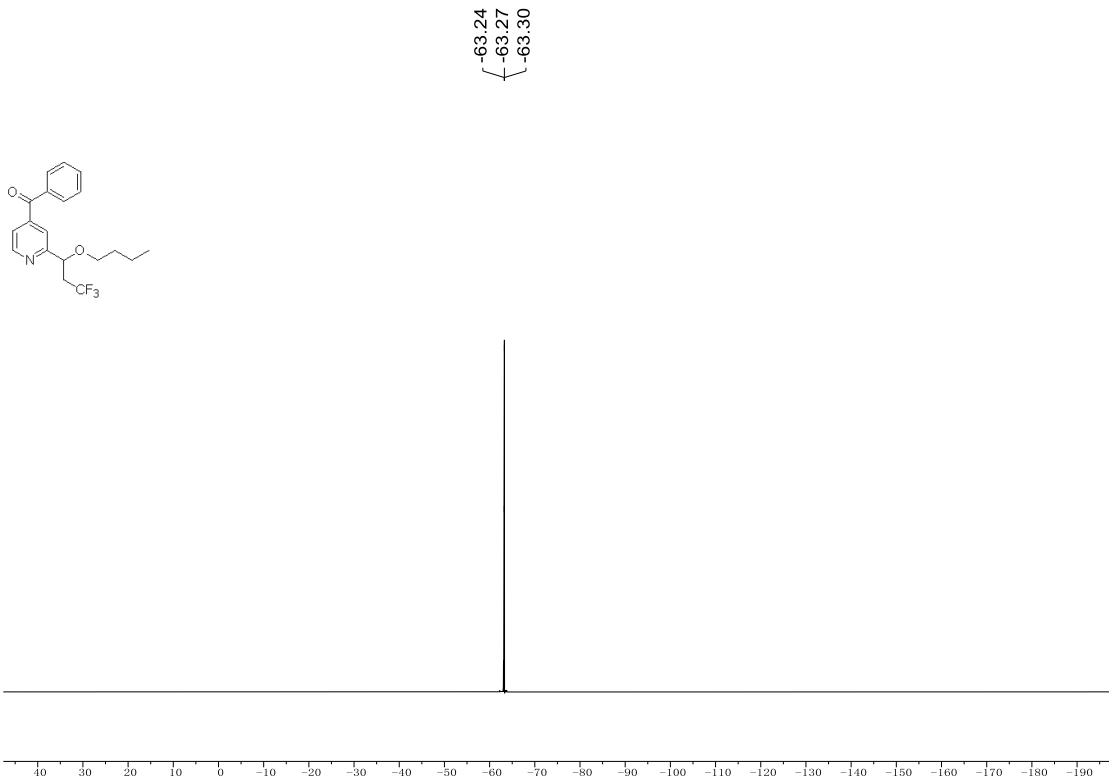
^{1}H NMR spectrum of compound **4c** in $CDCl_3$ (400 MHz)



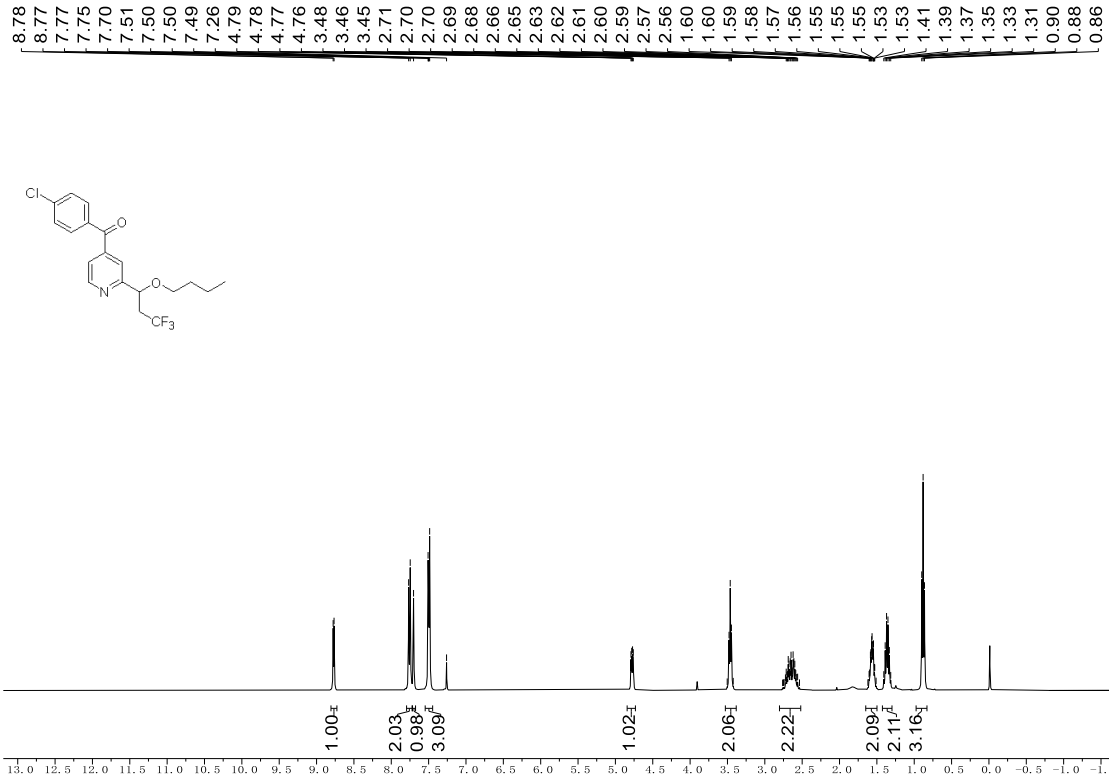
^{13}C NMR spectrum of compound **4c** in $CDCl_3$ (151 MHz)



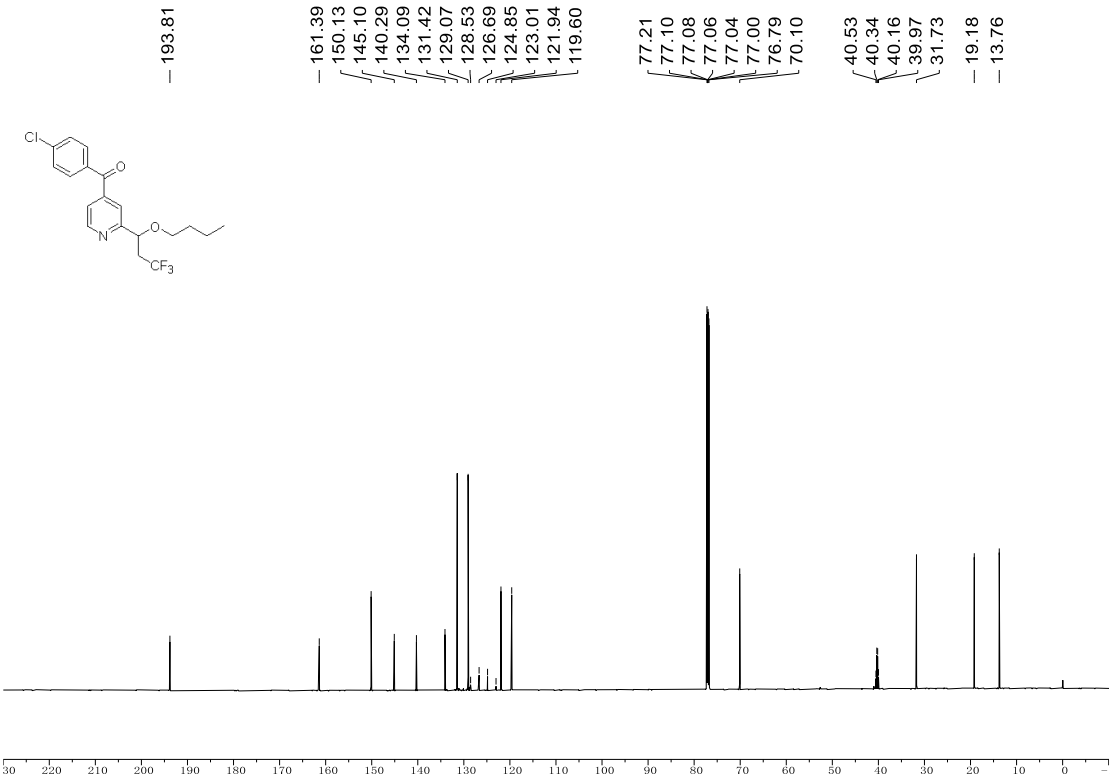
^{19}F NHR spectrum of compound **4c** in $CDCl_3$ (376 MHz)



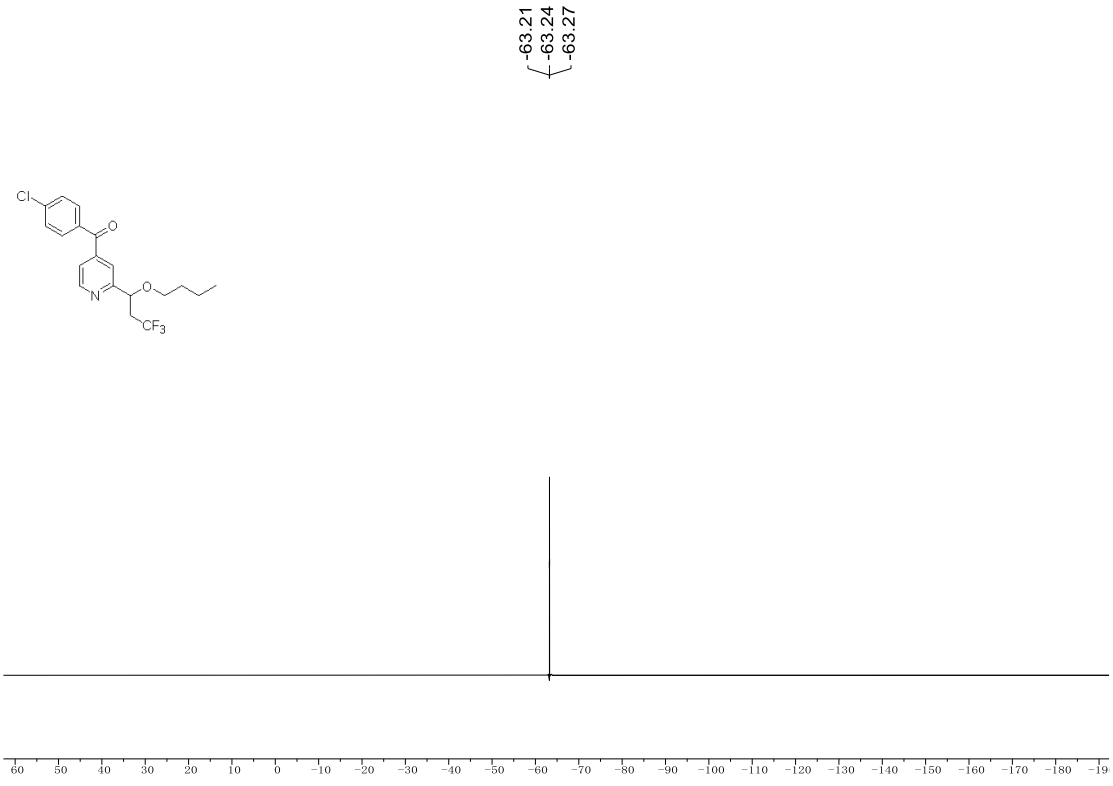
^{1}H NMR spectrum of compound **4d** in $CDCl_3$ (400 MHz)



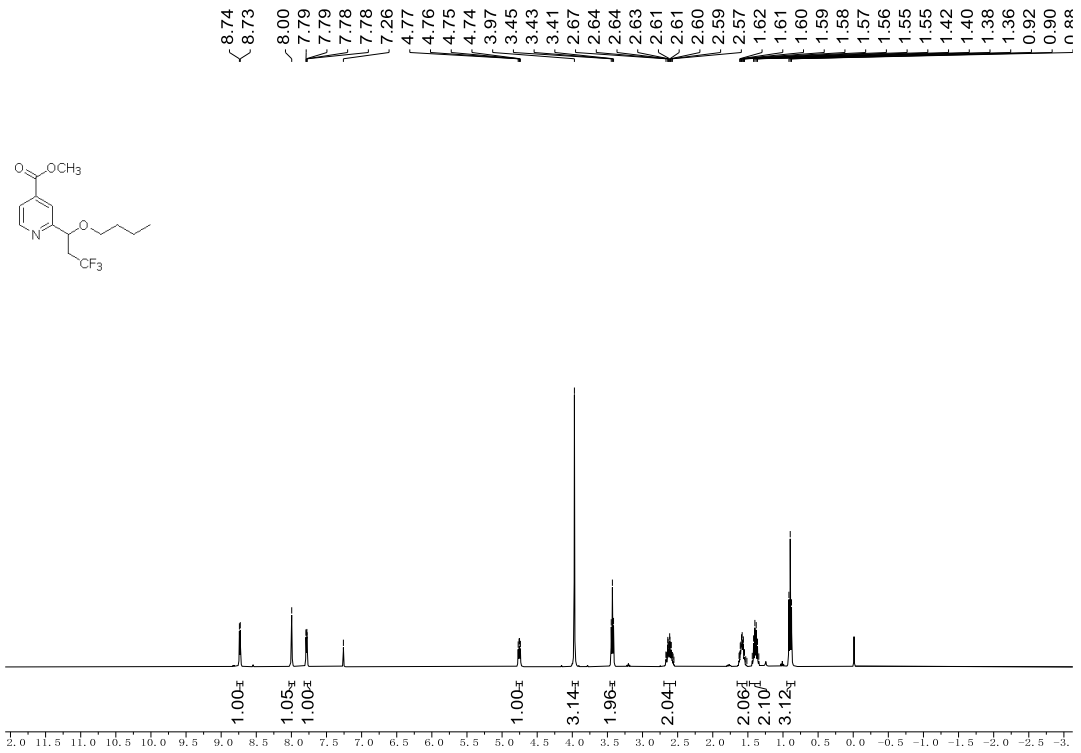
^{13}C NMR spectrum of compound **4d** in $CDCl_3$ (151 MHz)



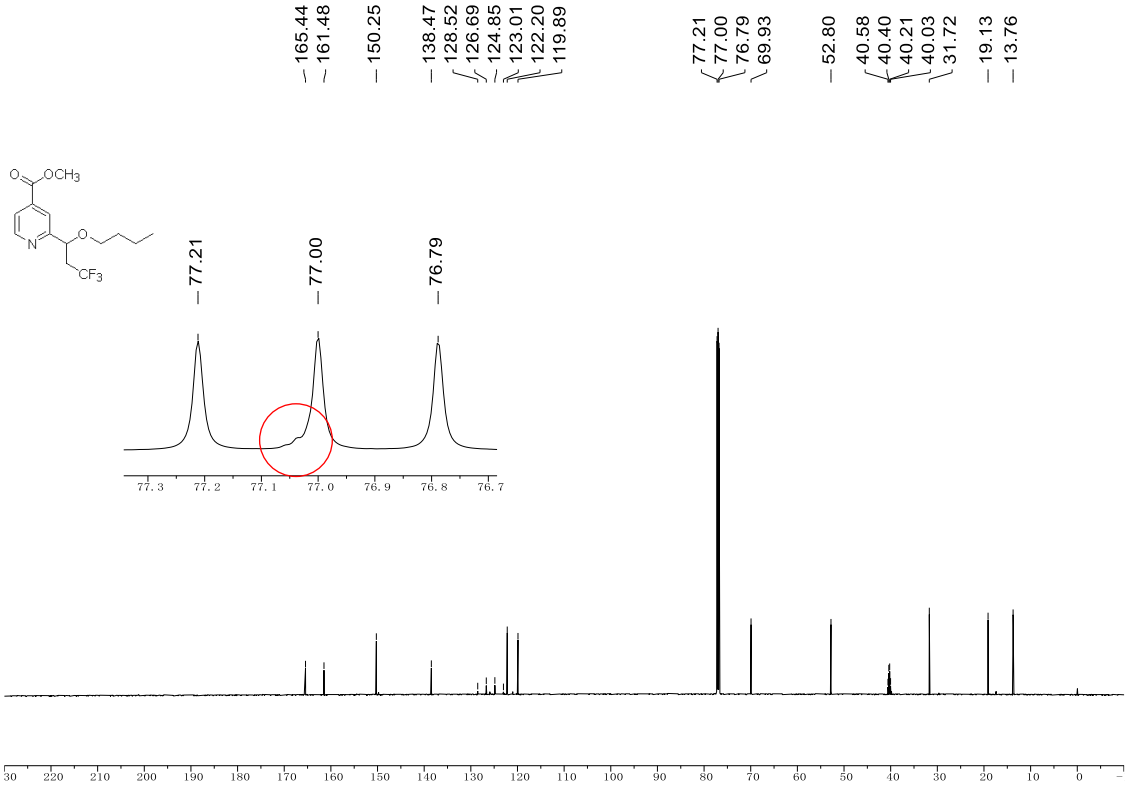
^{19}F NHR spectrum of compound **4d** in $CDCl_3$ (376 MHz)



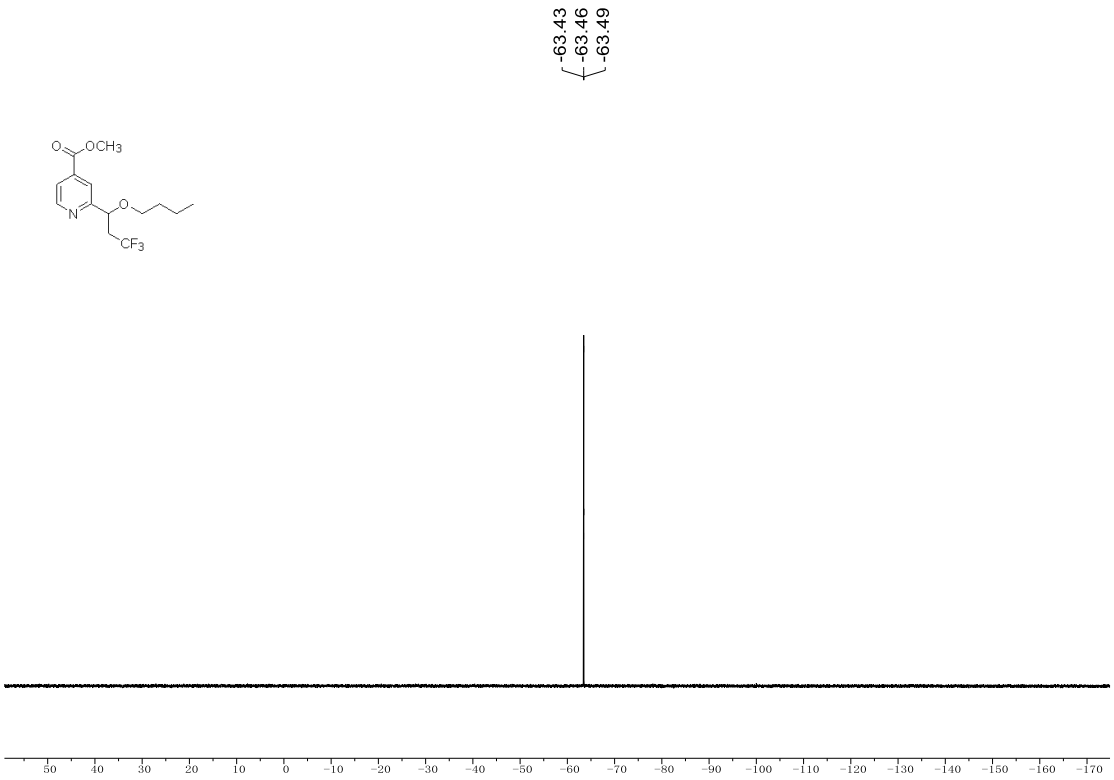
^{1}H NMR spectrum of compound **4e** in $CDCl_3$ (400 MHz)



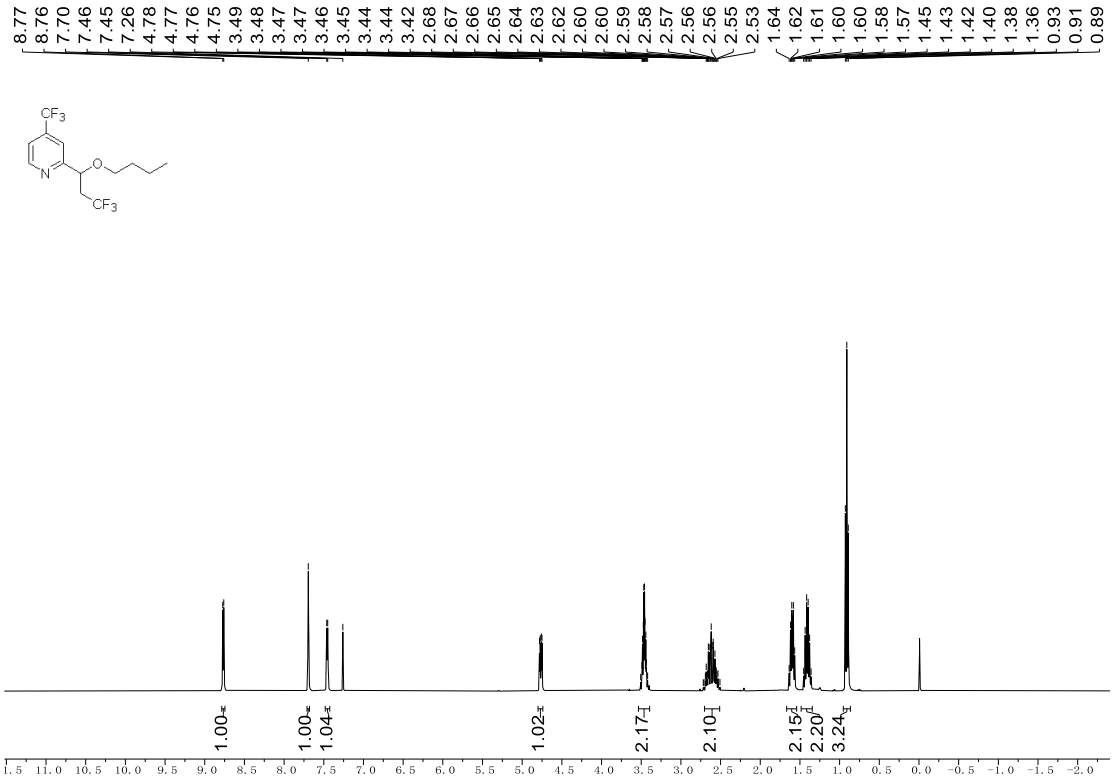
^{13}C NMR spectrum of compound **4e** in $CDCl_3$ (151 MHz)



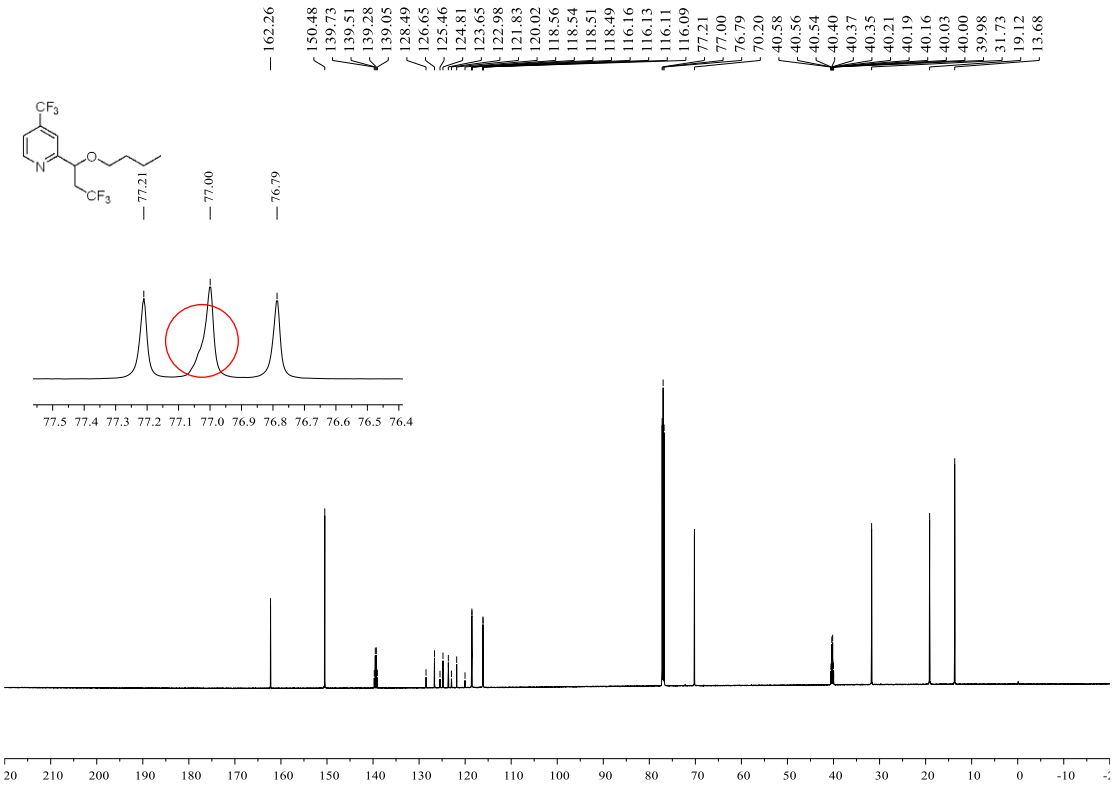
^{19}F NHR spectrum of compound **4e** in $CDCl_3$ (376 MHz)



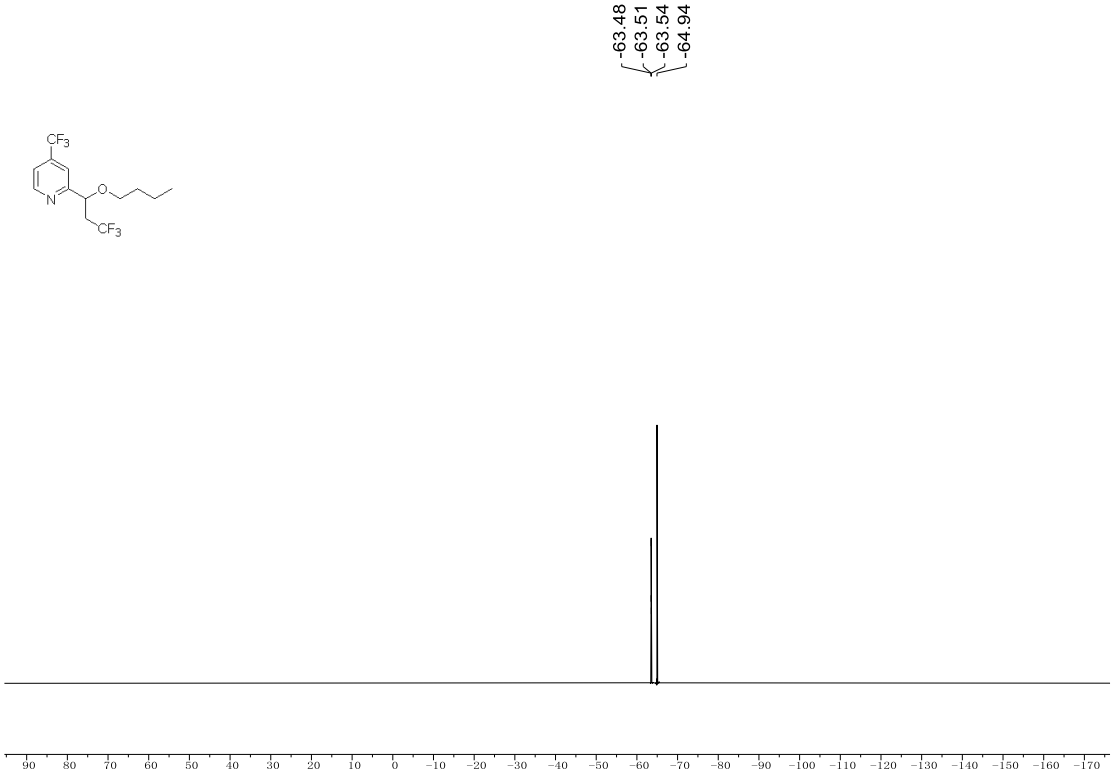
^{1}H NMR spectrum of compound **4f** in $CDCl_3$ (400 MHz)



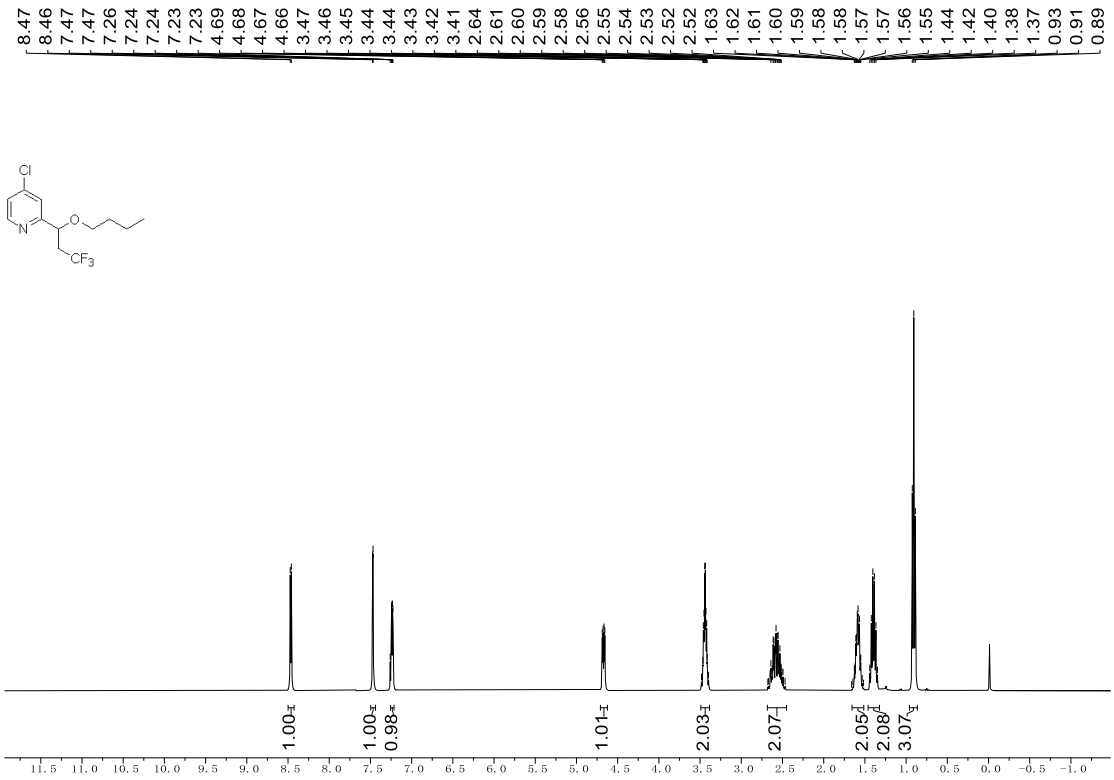
^{13}C NMR spectrum of compound **4f** in $CDCl_3$ (151 MHz)



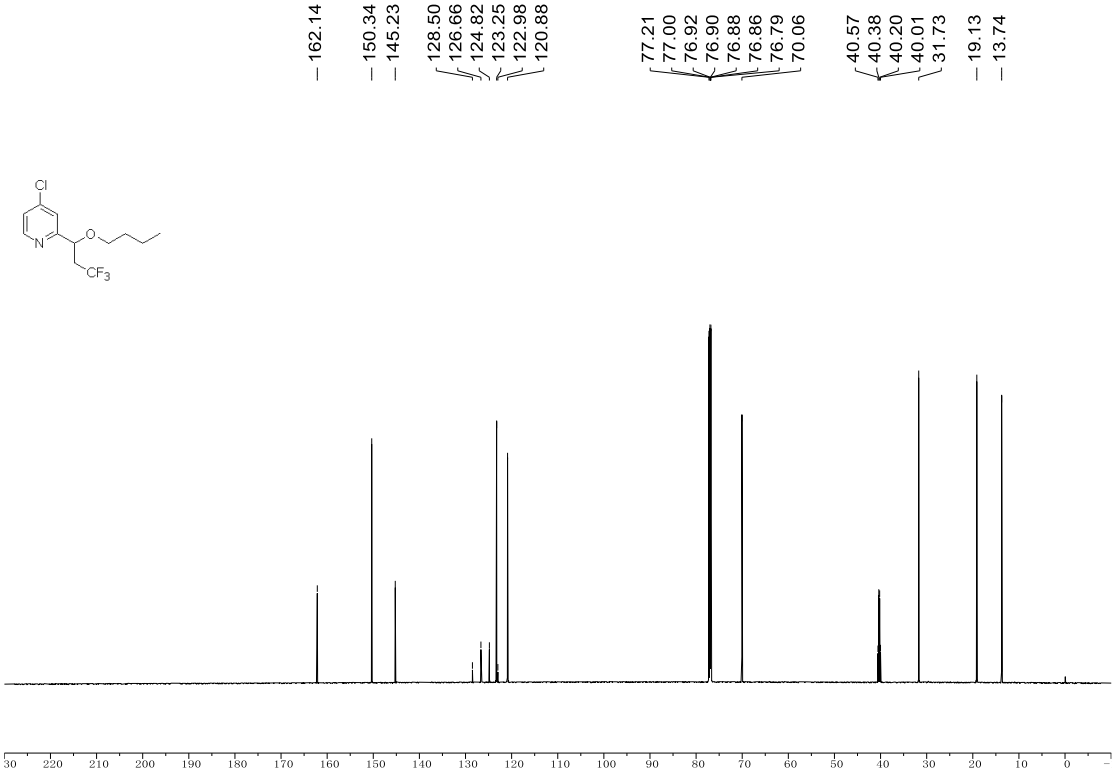
^{19}F NHR spectrum of compound **4f** in $CDCl_3$ (376 MHz)



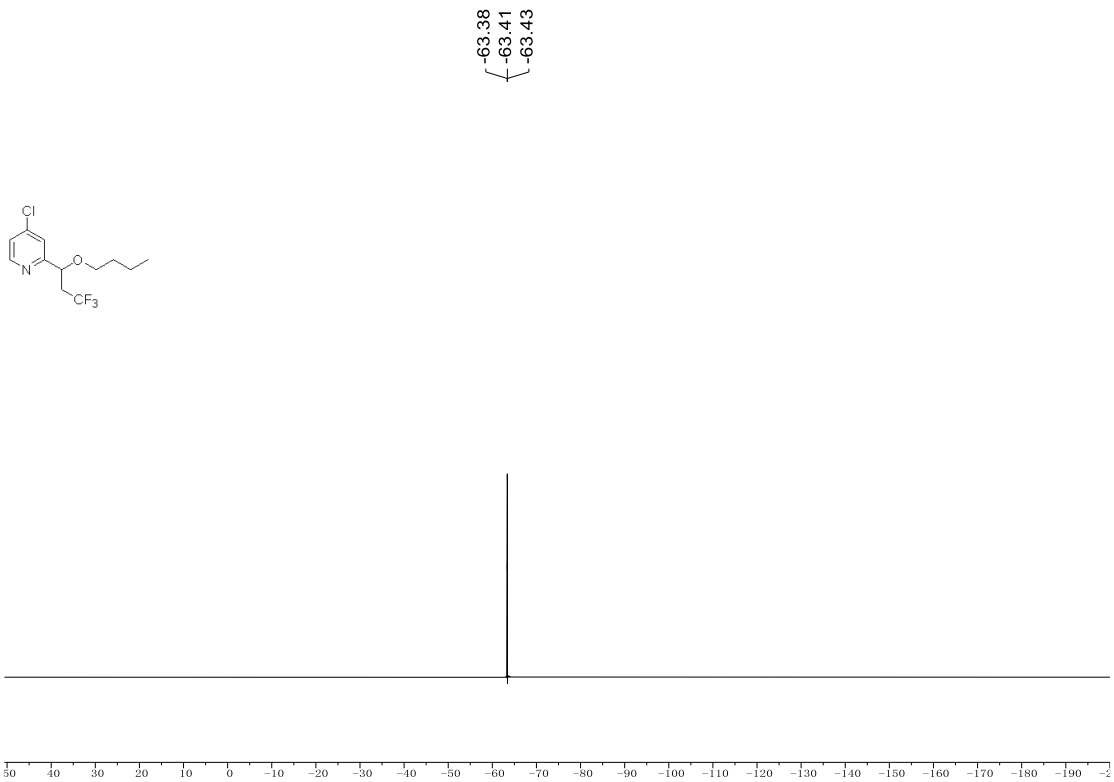
^{1}H NMR spectrum of compound **4g** in $CDCl_3$ (400 MHz)



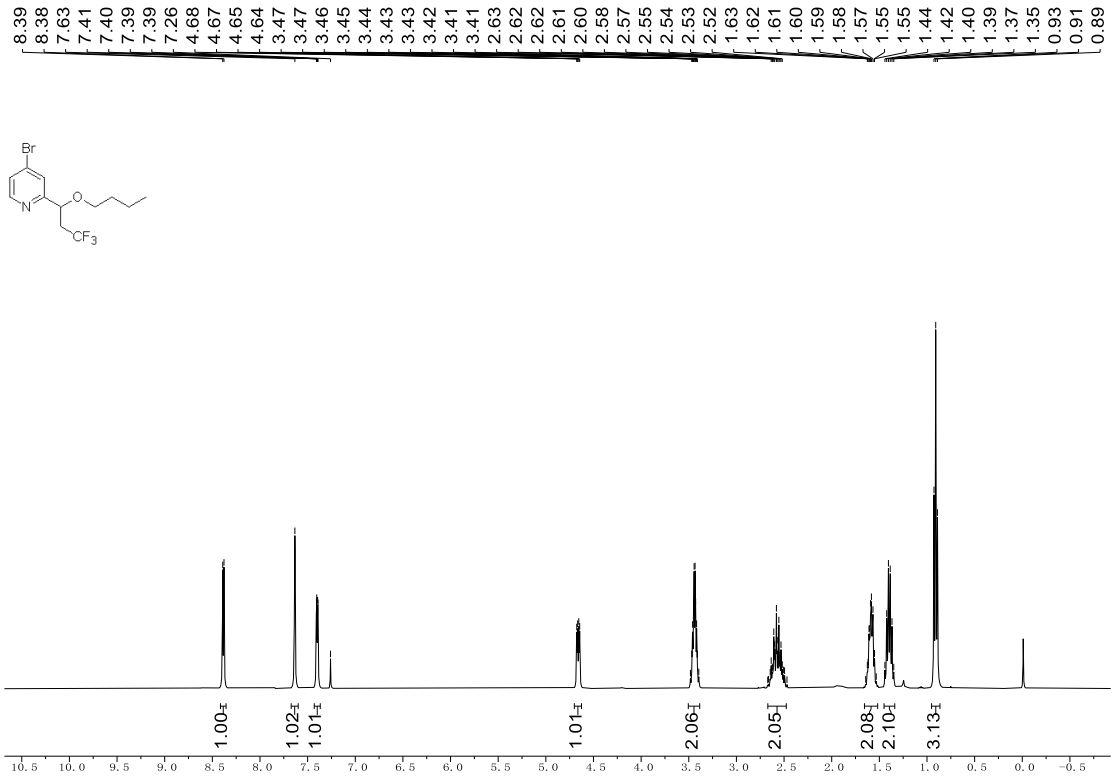
^{13}C NMR spectrum of compound **4g** in $CDCl_3$ (151 MHz)



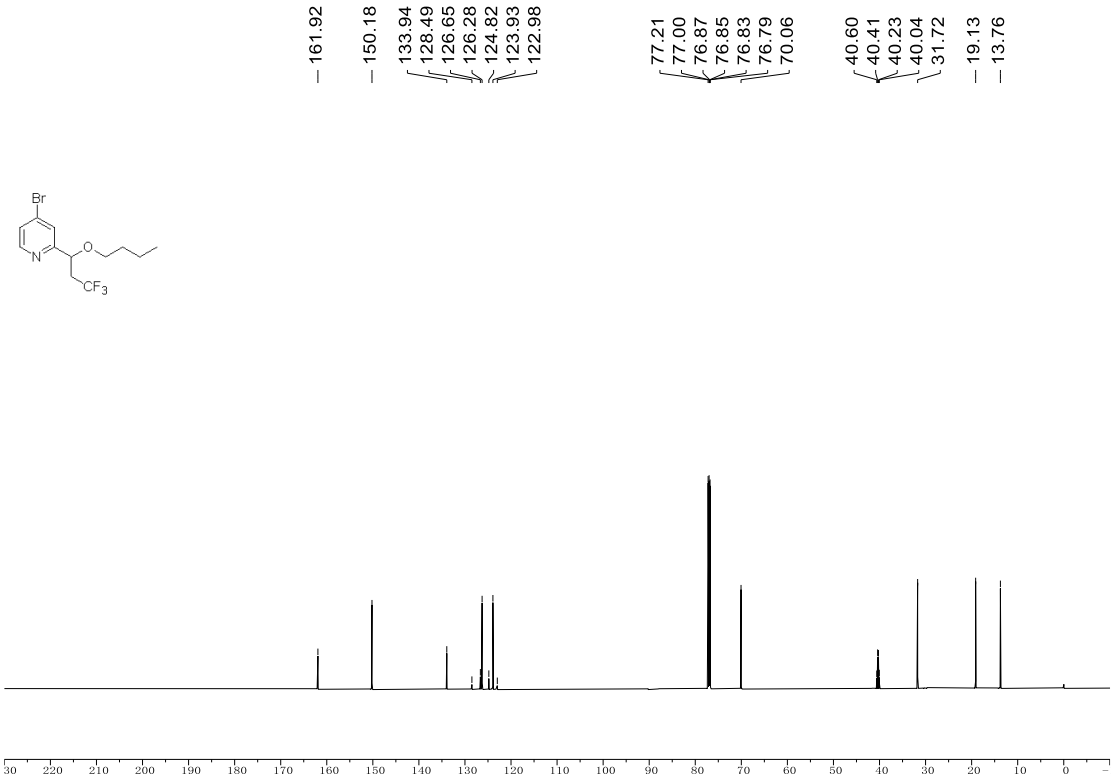
^{19}F NHR spectrum of compound **4g** in $CDCl_3$ (376 MHz)



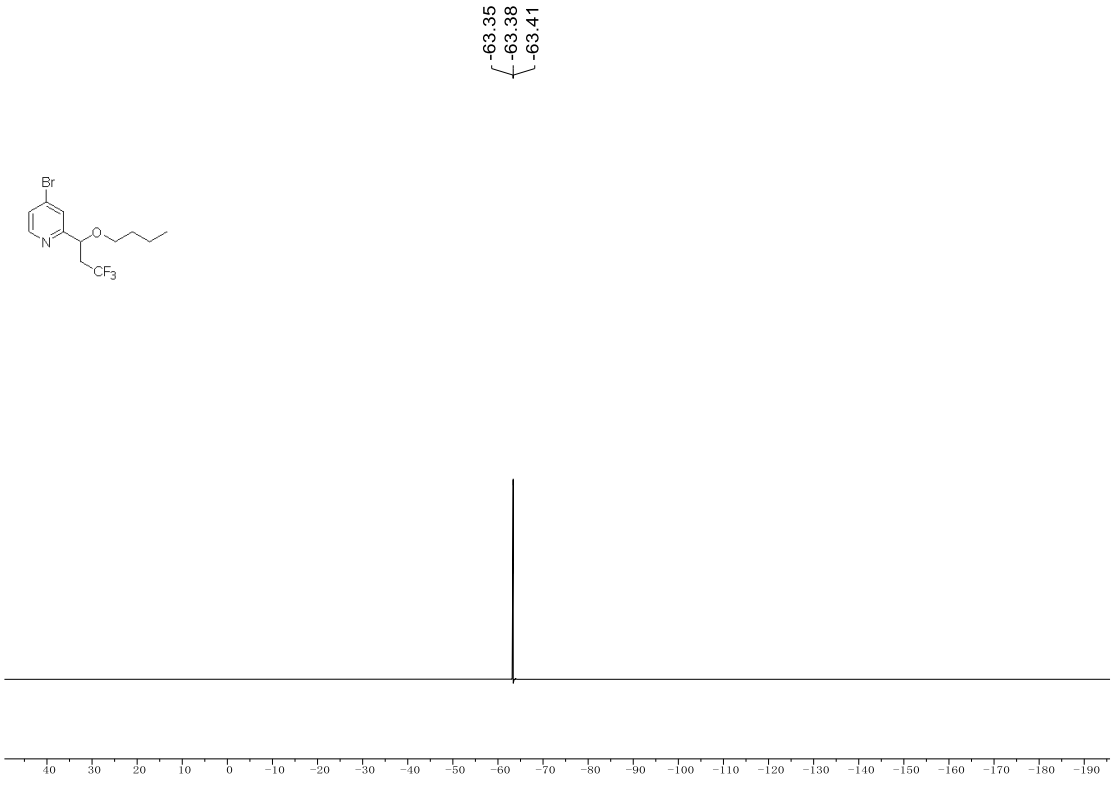
^{1}H NMR spectrum of compound **4h** in $CDCl_3$ (400 MHz)



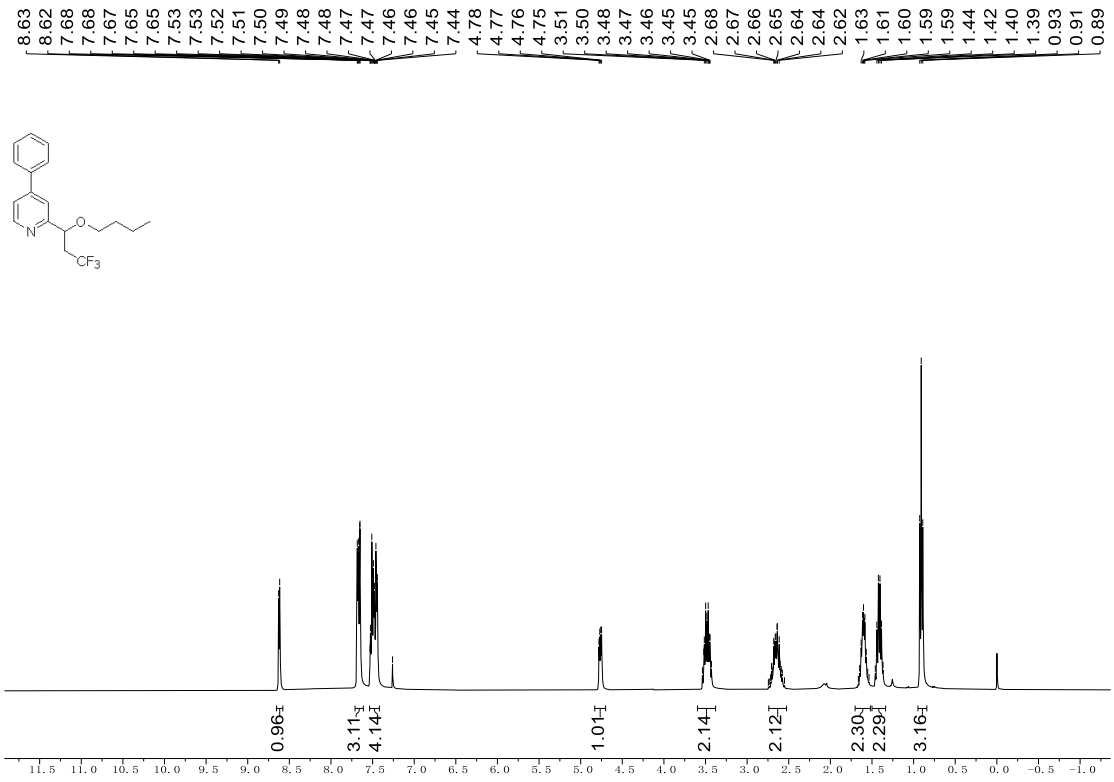
^{13}C NMR spectrum of compound **4h** in $CDCl_3$ (151 MHz)



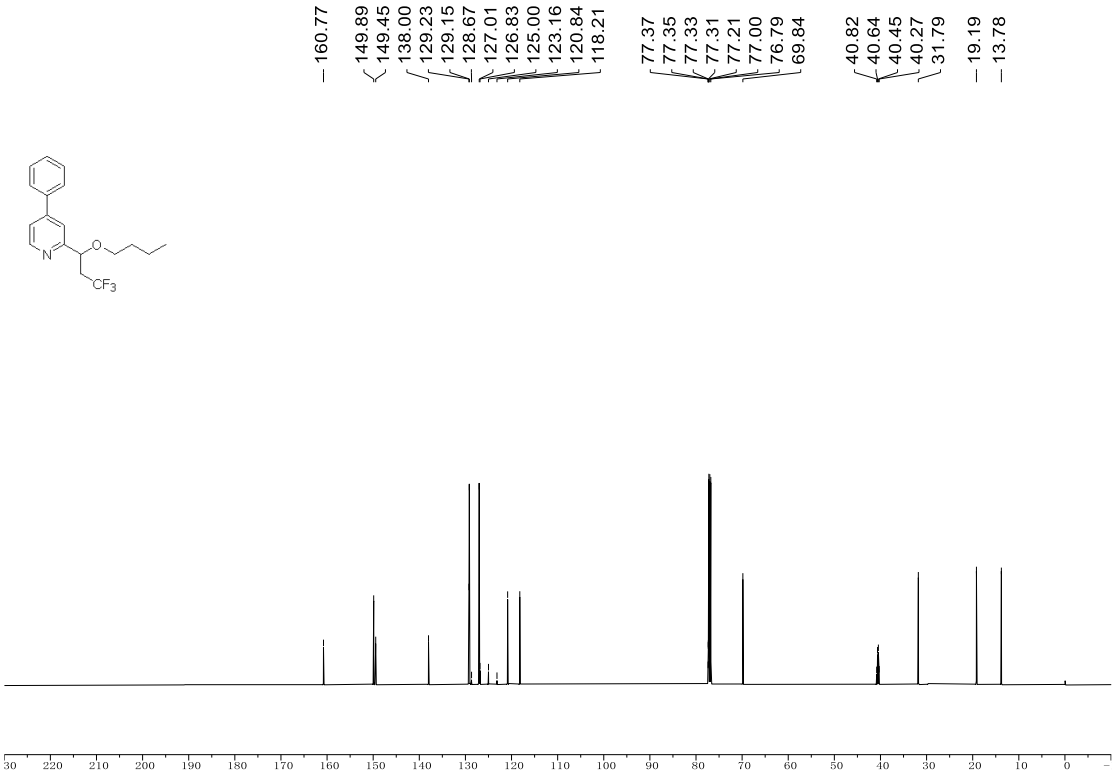
^{19}F NHR spectrum of compound **4h** in $CDCl_3$ (376 MHz)



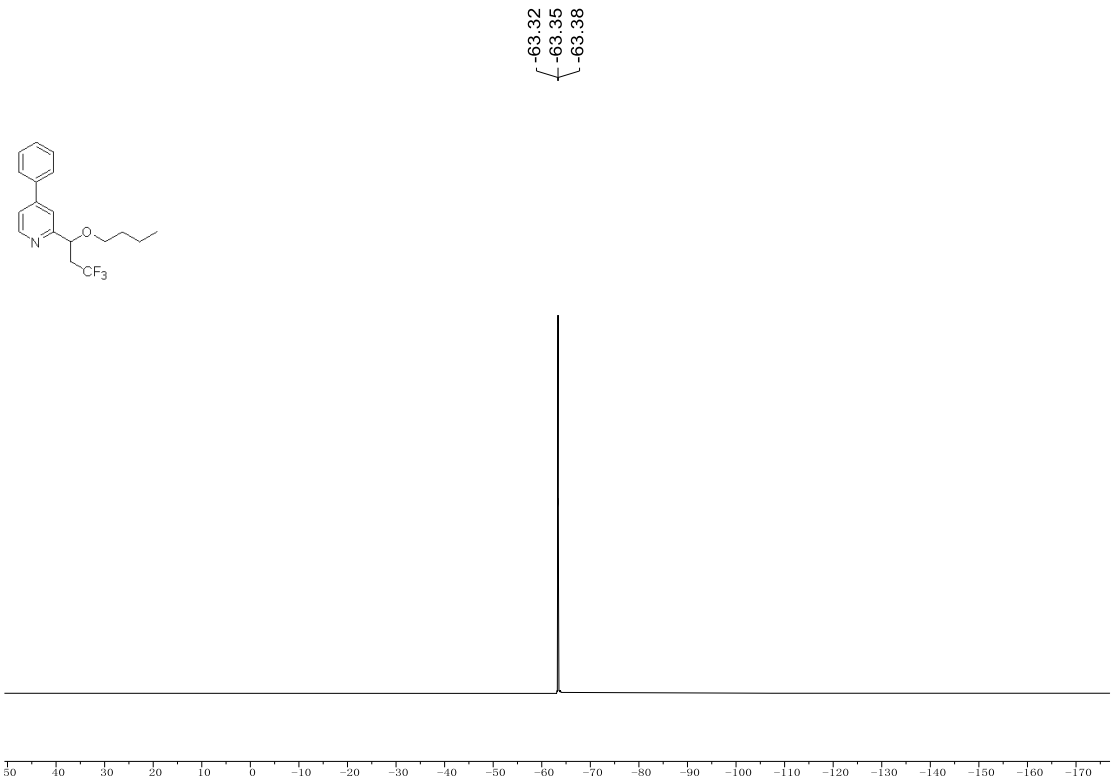
^{1}H NMR spectrum of compound **4i** in $CDCl_3$ (400 MHz)



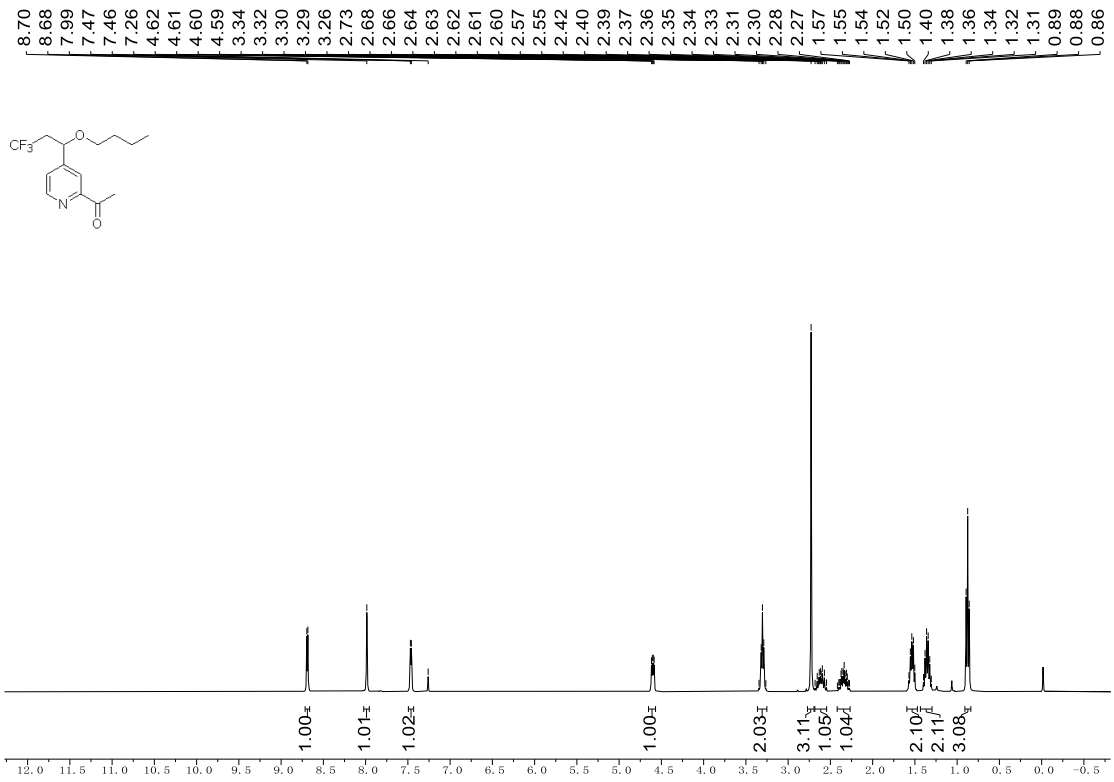
^{13}C NMR spectrum of compound **4i** in $CDCl_3$ (151 MHz)



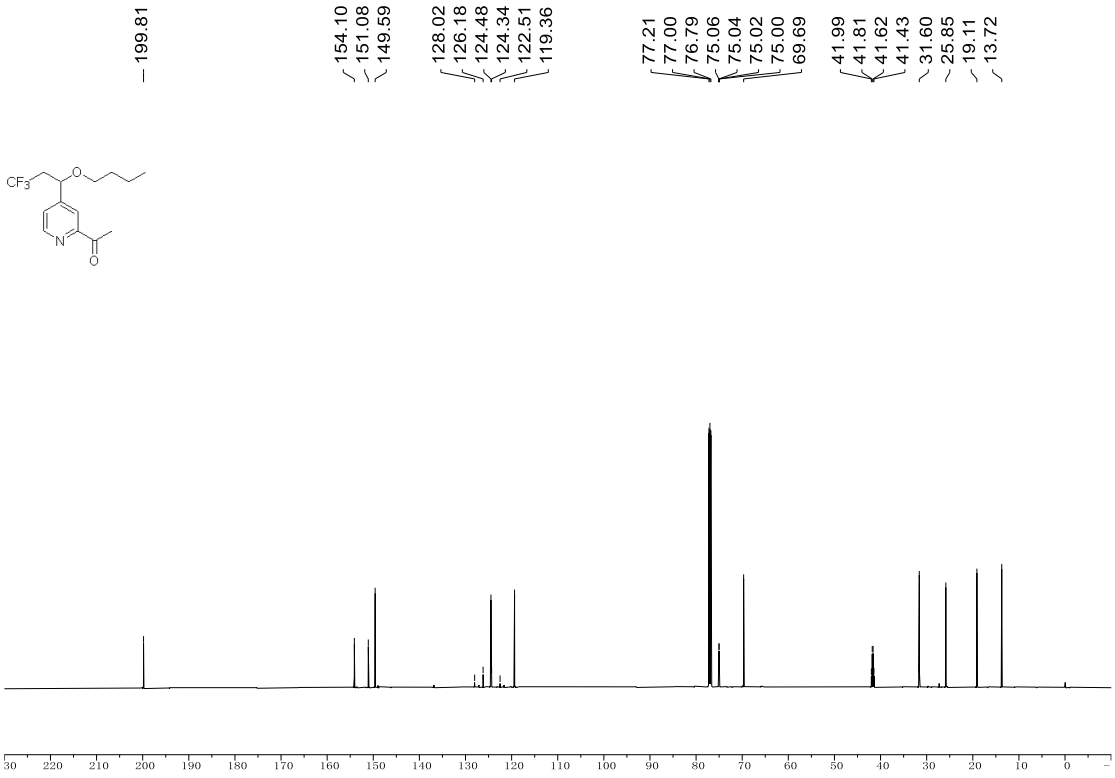
^{19}F NHR spectrum of compound **4i** in $CDCl_3$ (376 MHz)



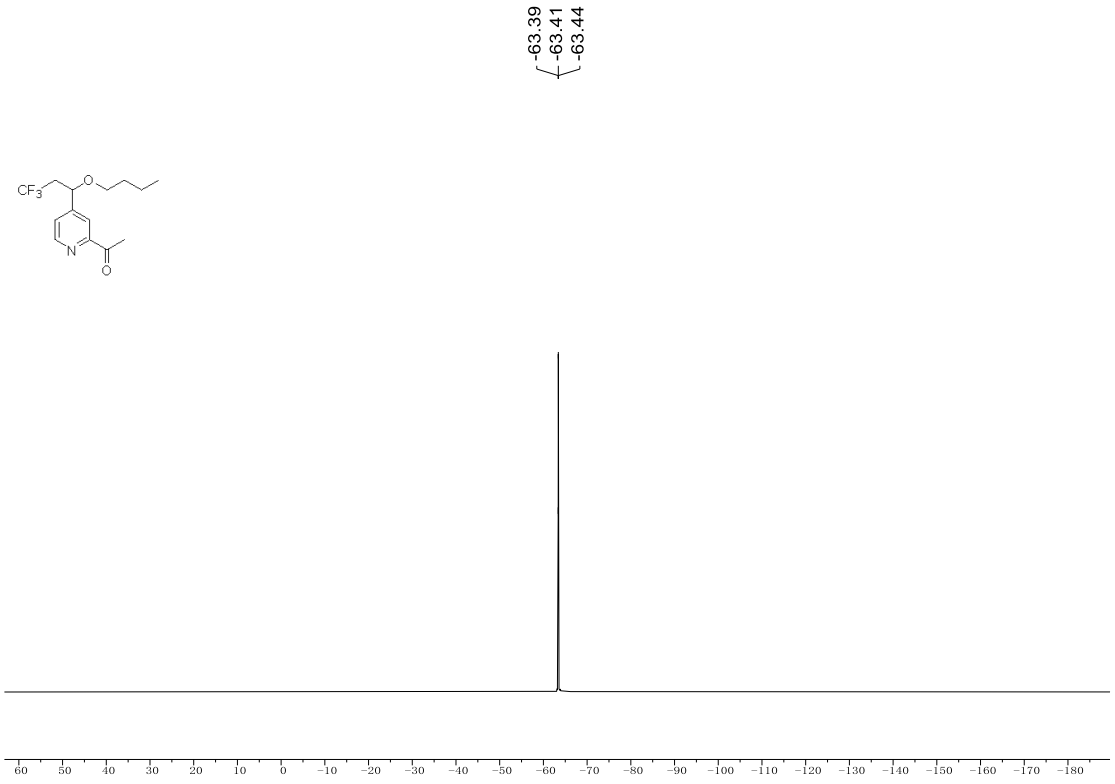
^{1}H NMR spectrum of compound **4j** in $CDCl_3$ (400 MHz)



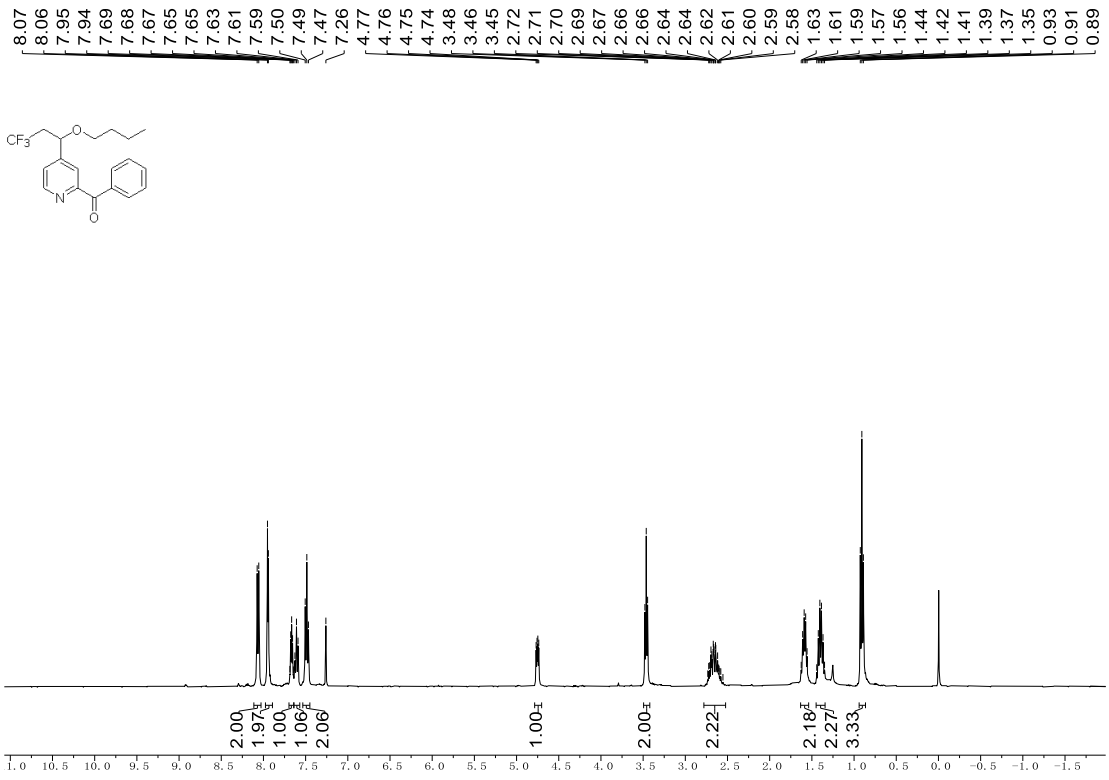
^{13}C NMR spectrum of compound **4j** in $CDCl_3$ (151 MHz)



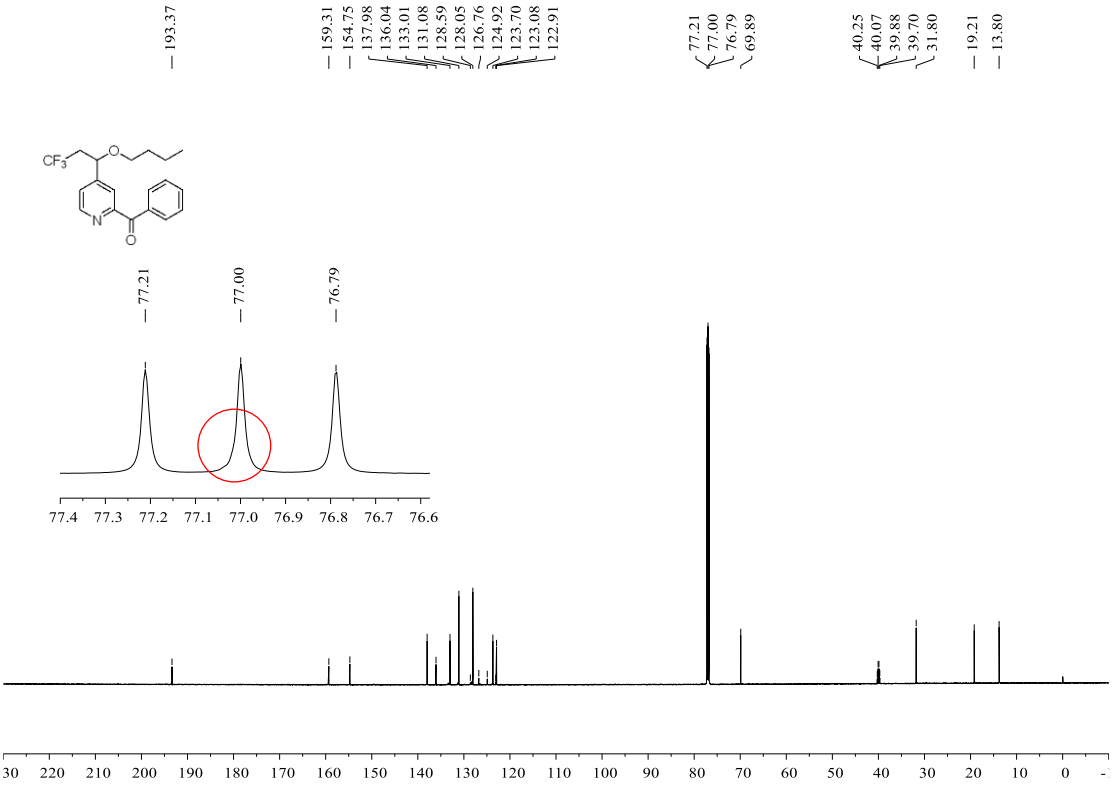
^{19}F NHR spectrum of compound **4j** in $CDCl_3$ (376 MHz)



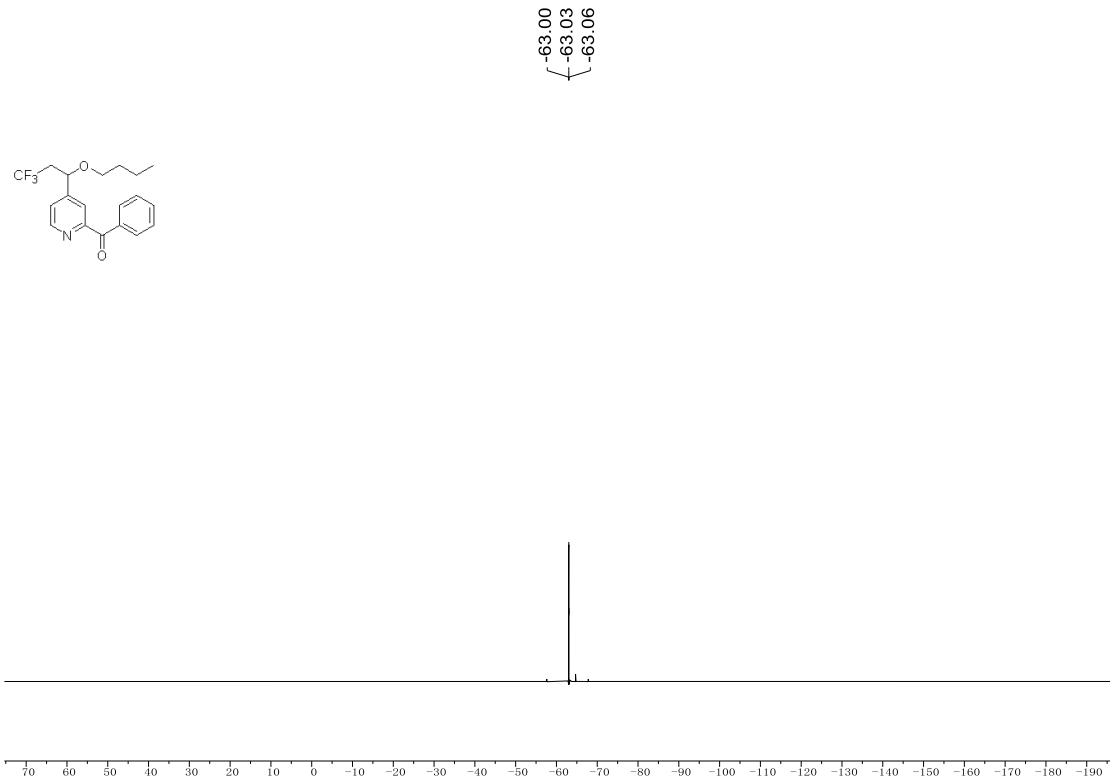
^{1}H NMR spectrum of compound **4k** in $CDCl_3$ (400 MHz)



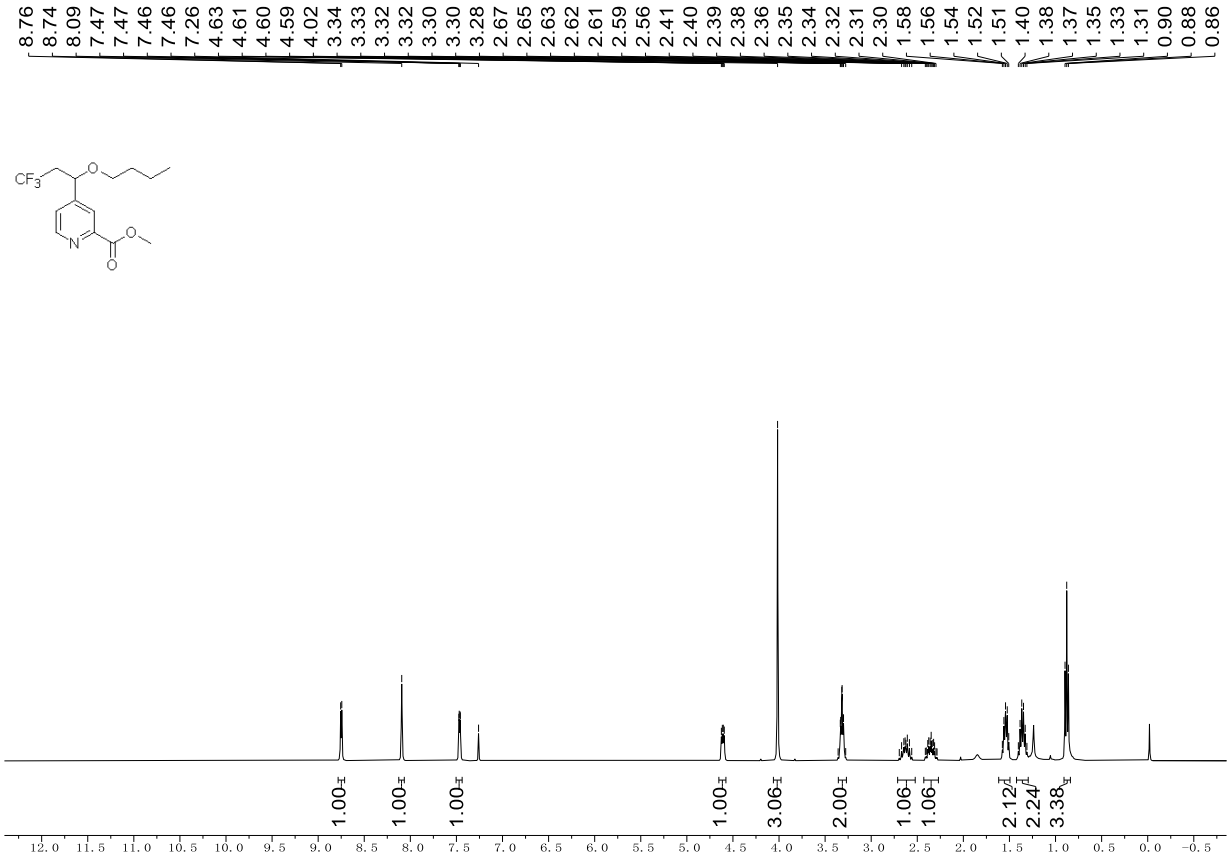
^{13}C NMR spectrum of compound **4k** in $CDCl_3$ (151 MHz)



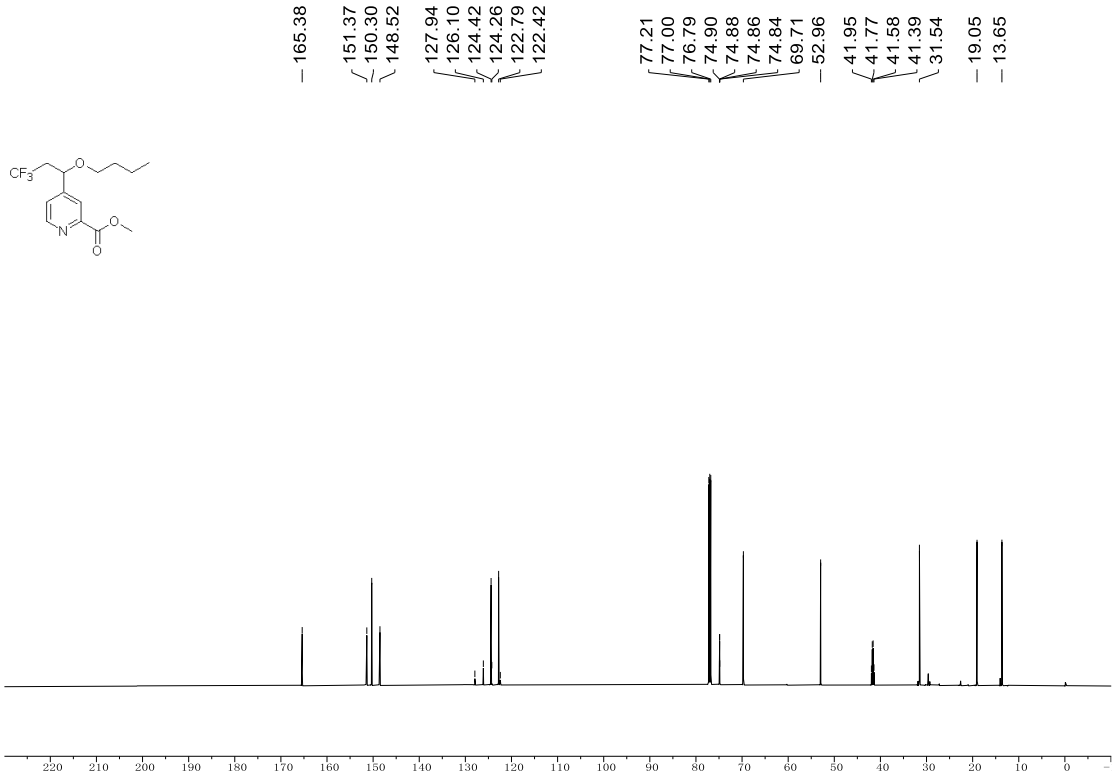
^{19}F NHR spectrum of compound **4k** in $CDCl_3$ (376 MHz)



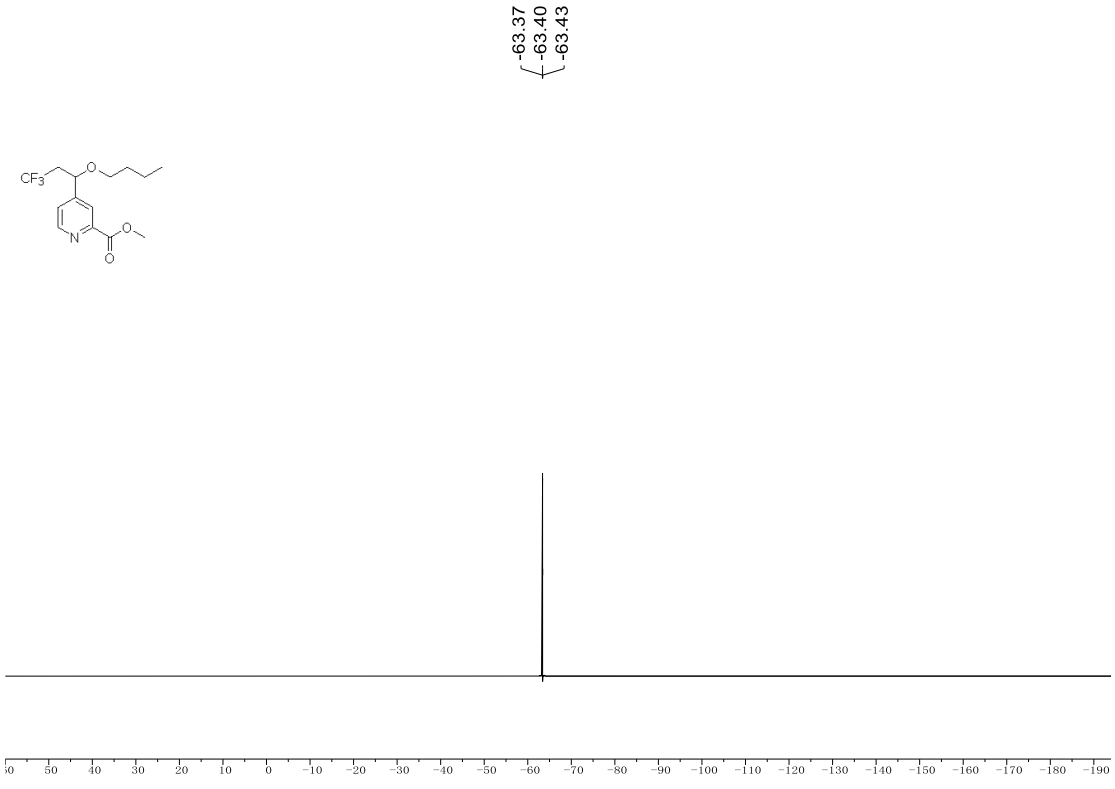
^{1}H NMR spectrum of compound **4l** in $CDCl_3$ (400 MHz)



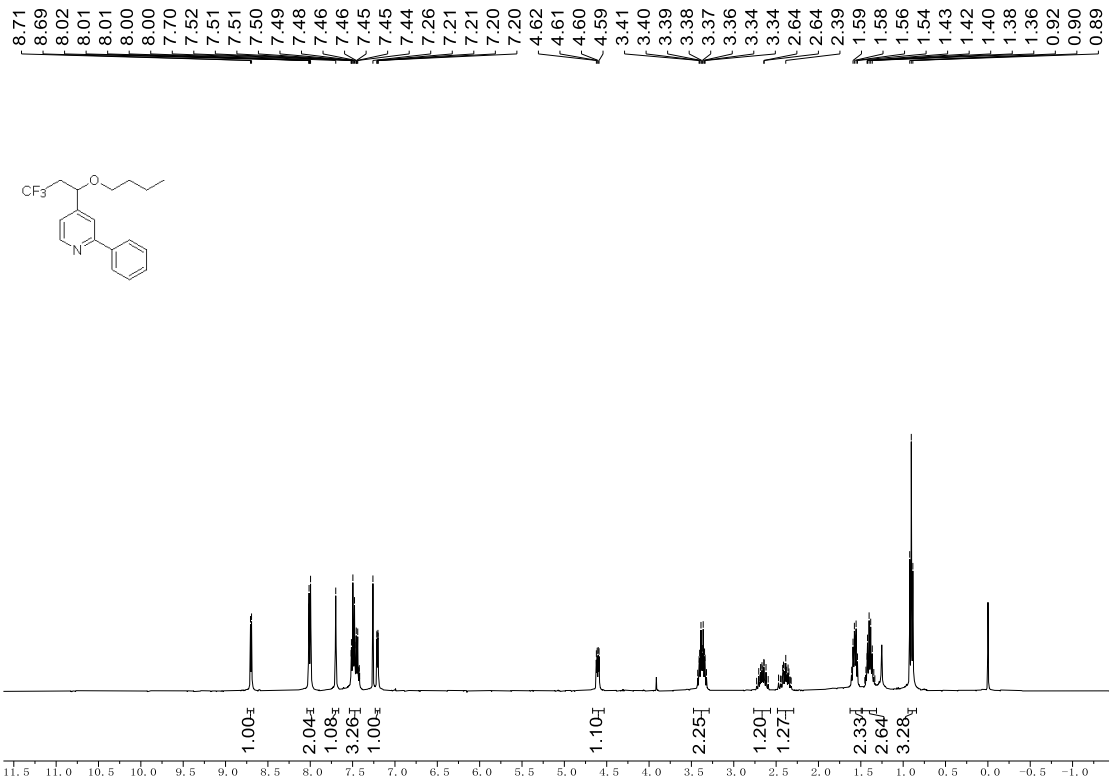
^{13}C NMR spectrum of compound **4l** in $CDCl_3$ (151 MHz)



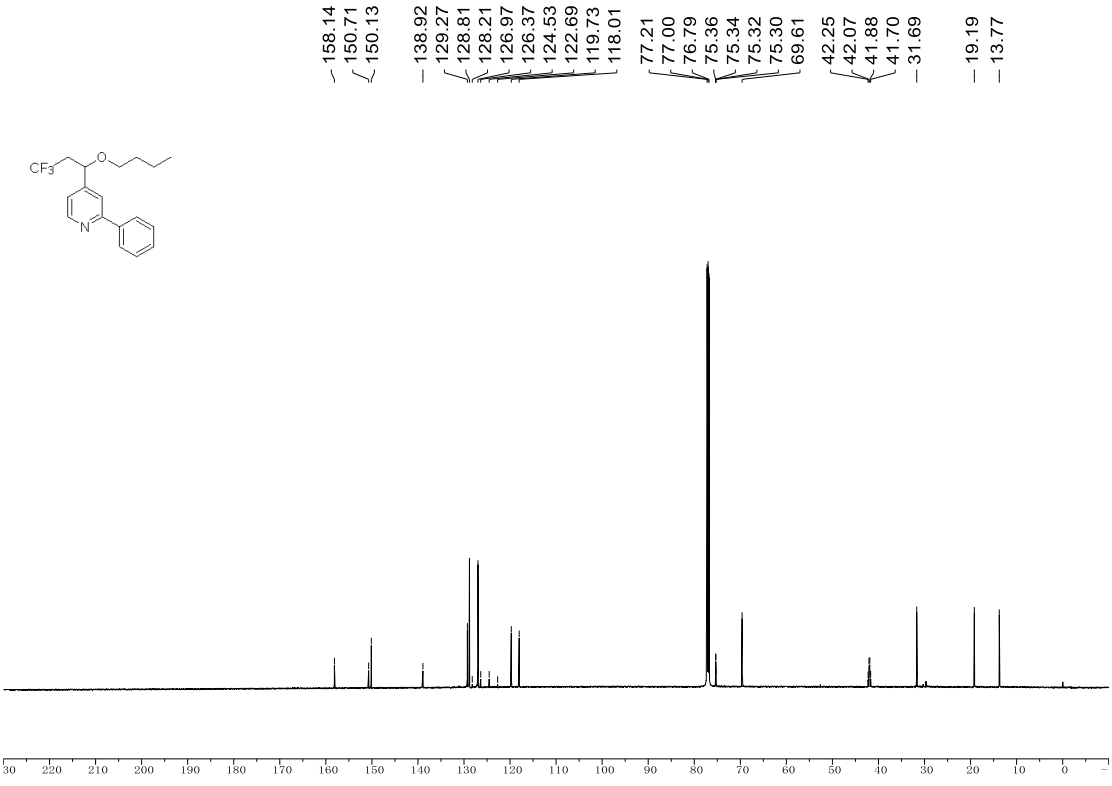
^{19}F NHR spectrum of compound **4l** in $CDCl_3$ (376 MHz)



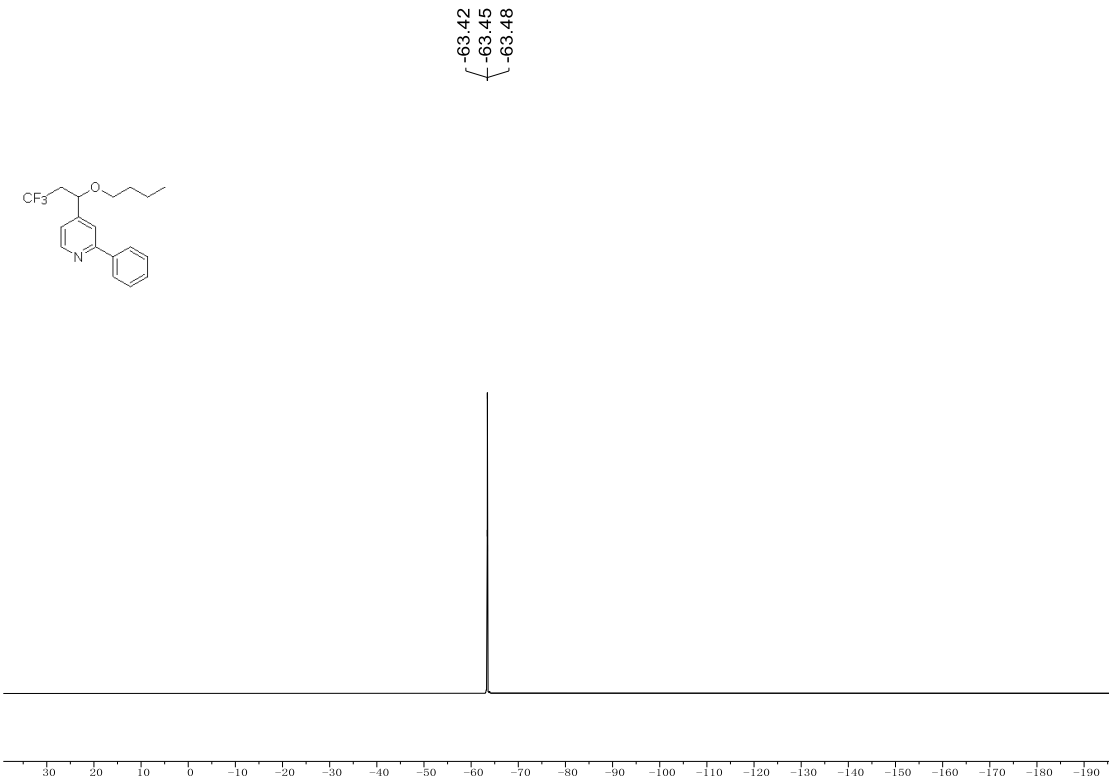
^{1}H NMR spectrum of compound **4m** in $CDCl_3$ (400 MHz)



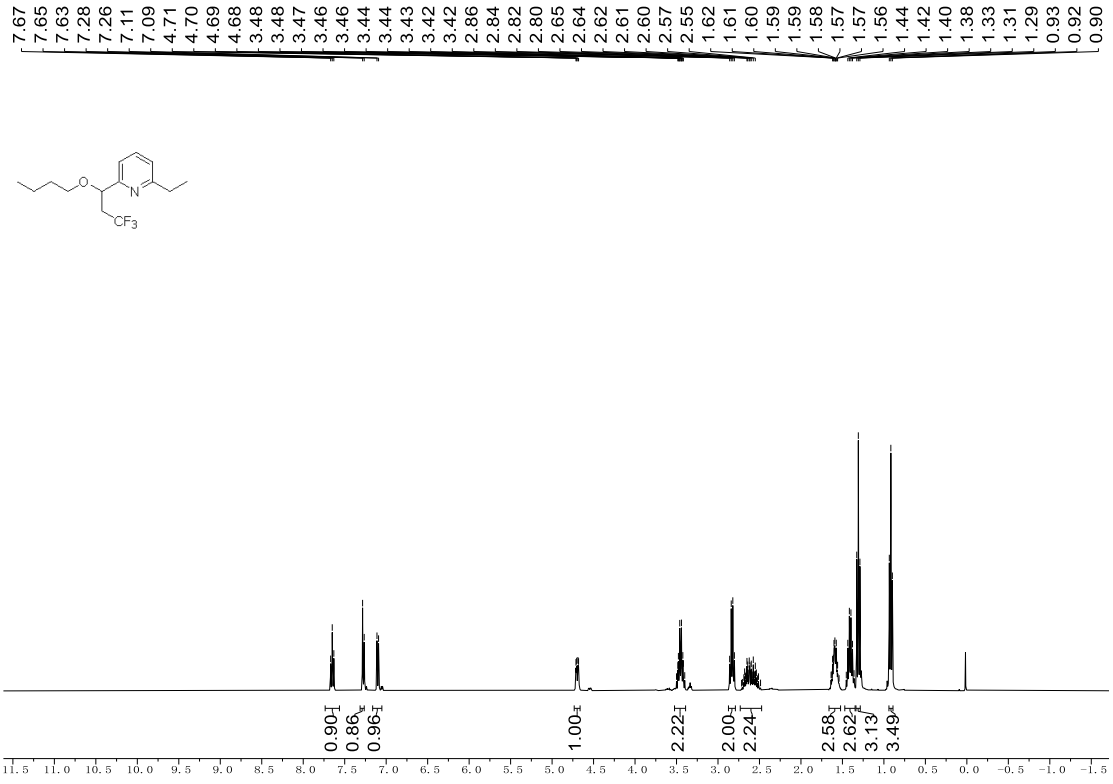
^{13}C NMR spectrum of compound **4m** in $CDCl_3$ (151 MHz)



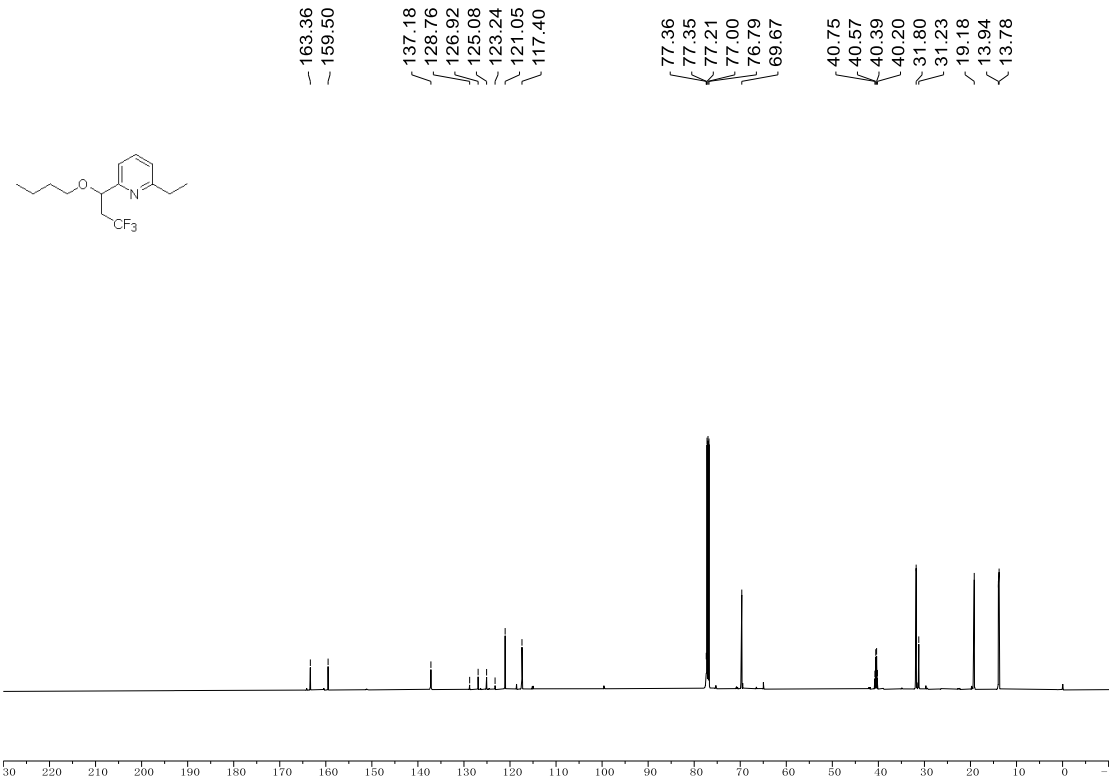
^{19}F NHR spectrum of compound **4m** in $CDCl_3$ (376 MHz)



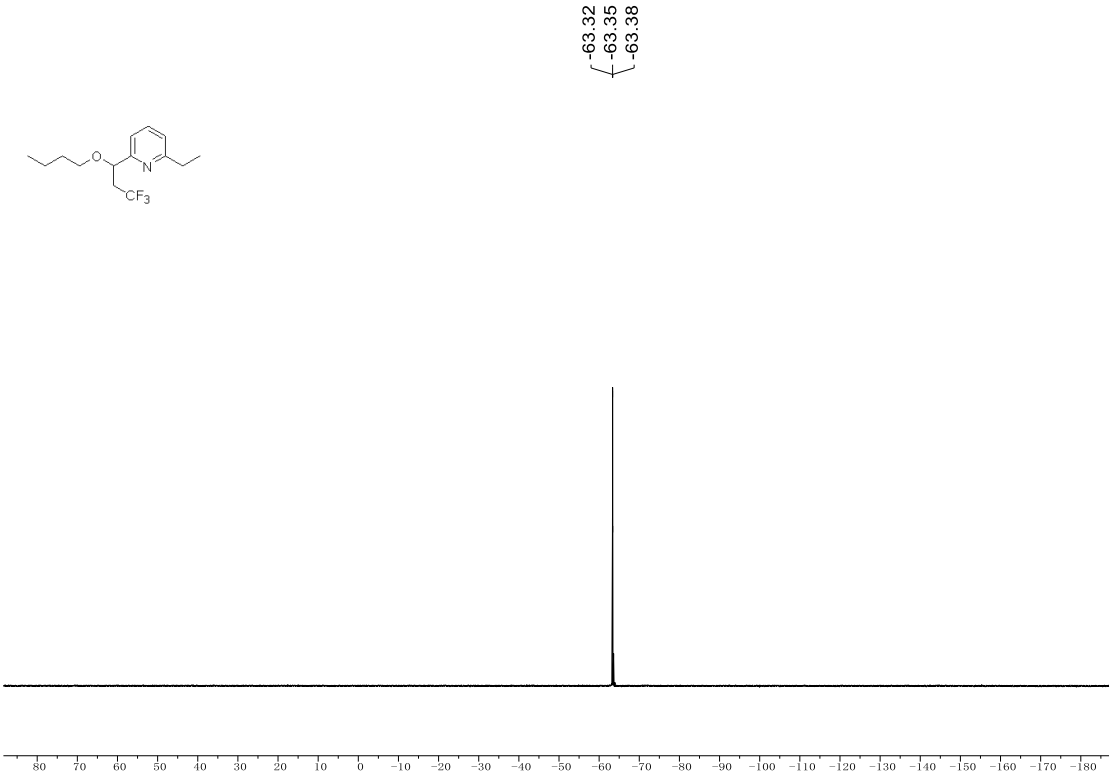
^{1}H NMR spectrum of compound **4n** in $CDCl_3$ (400 MHz)



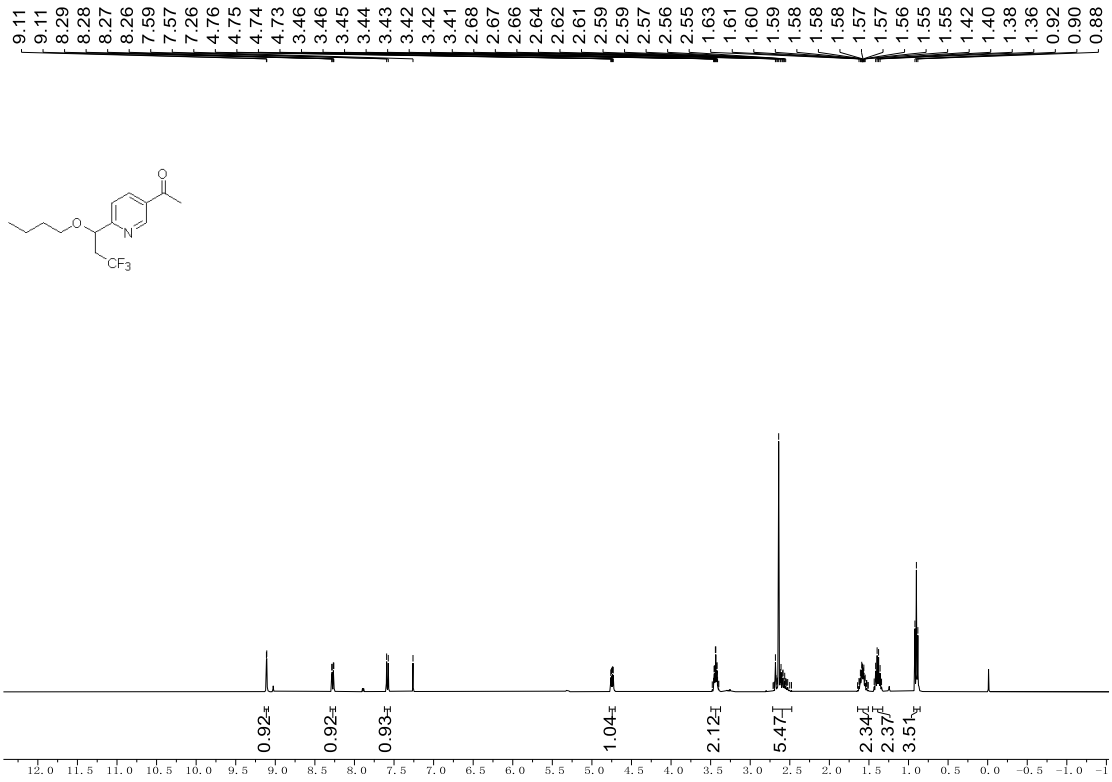
^{13}C NMR spectrum of compound **4n** in $CDCl_3$ (151 MHz)



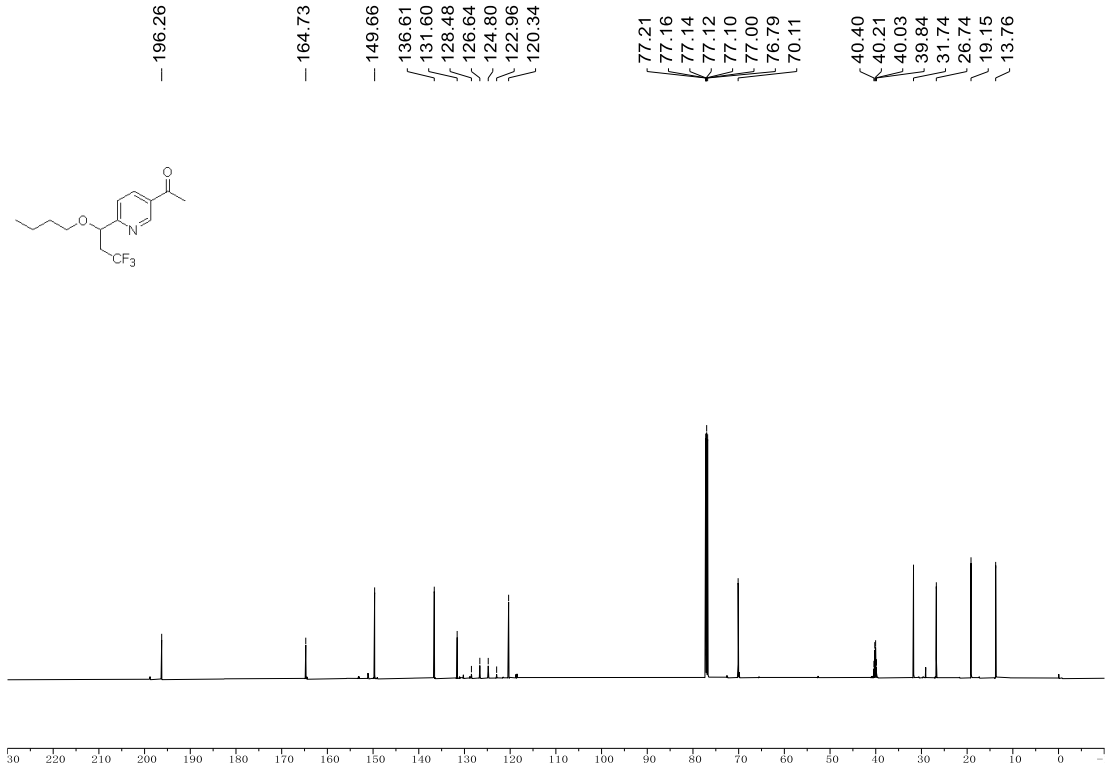
^{19}F NHR spectrum of compound **4n** in $CDCl_3$ (376 MHz)



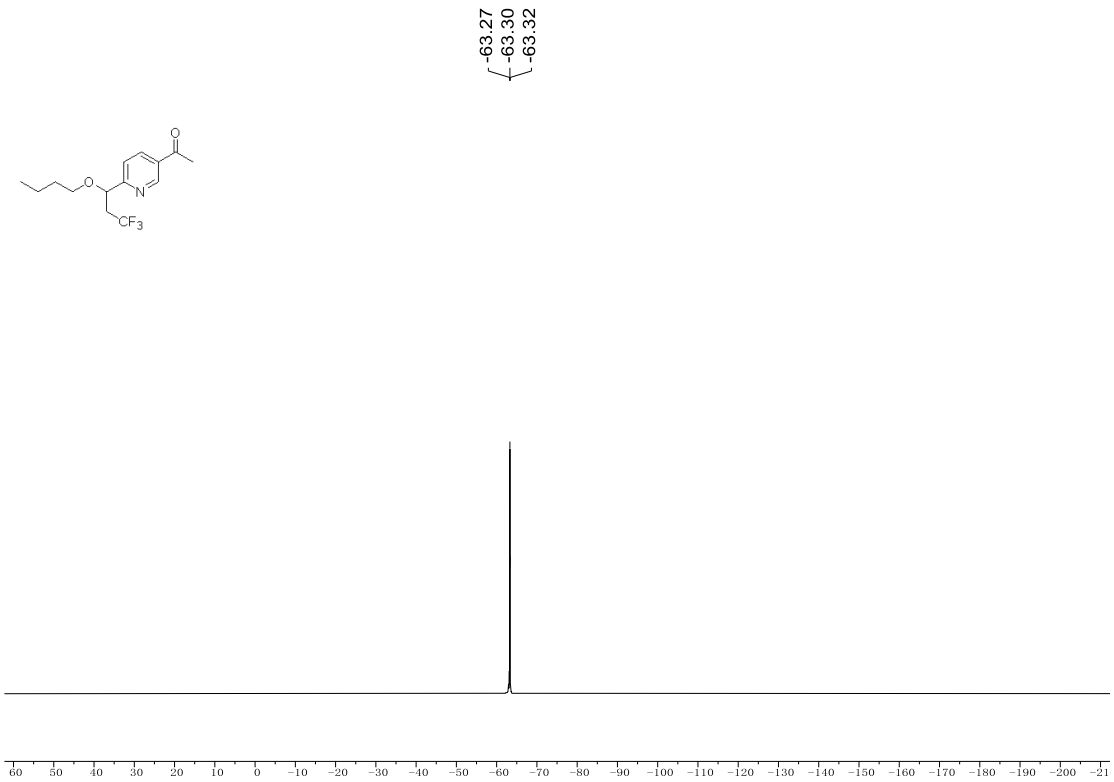
^{1}H NMR spectrum of compound **4o** in $CDCl_3$ (400 MHz)



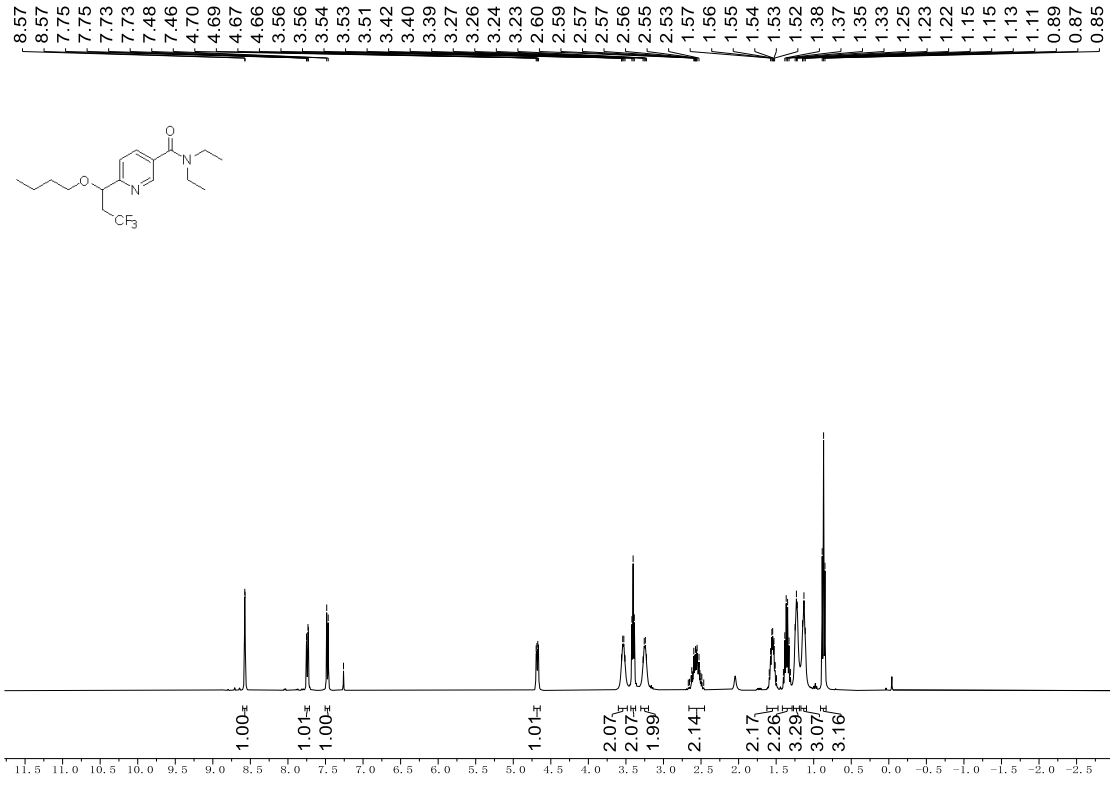
^{13}C NMR spectrum of compound **4o** in $CDCl_3$ (151 MHz)



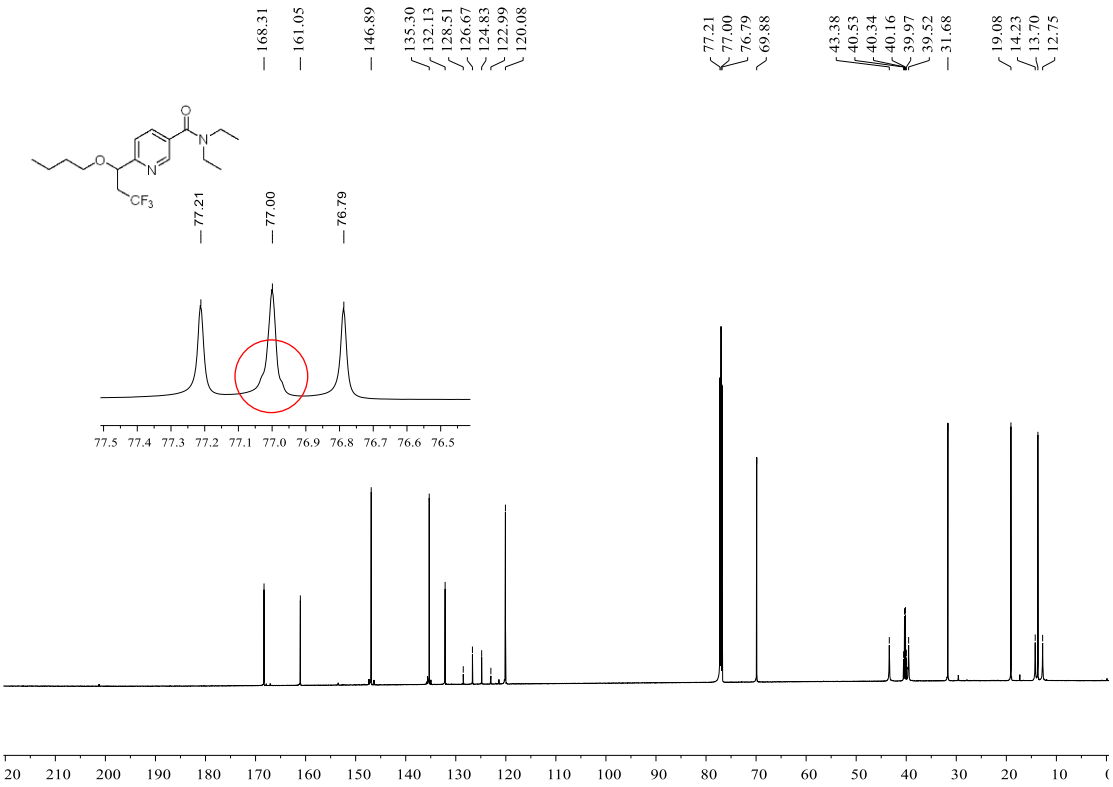
^{19}F NHR spectrum of compound **4o** in $CDCl_3$ (376 MHz)



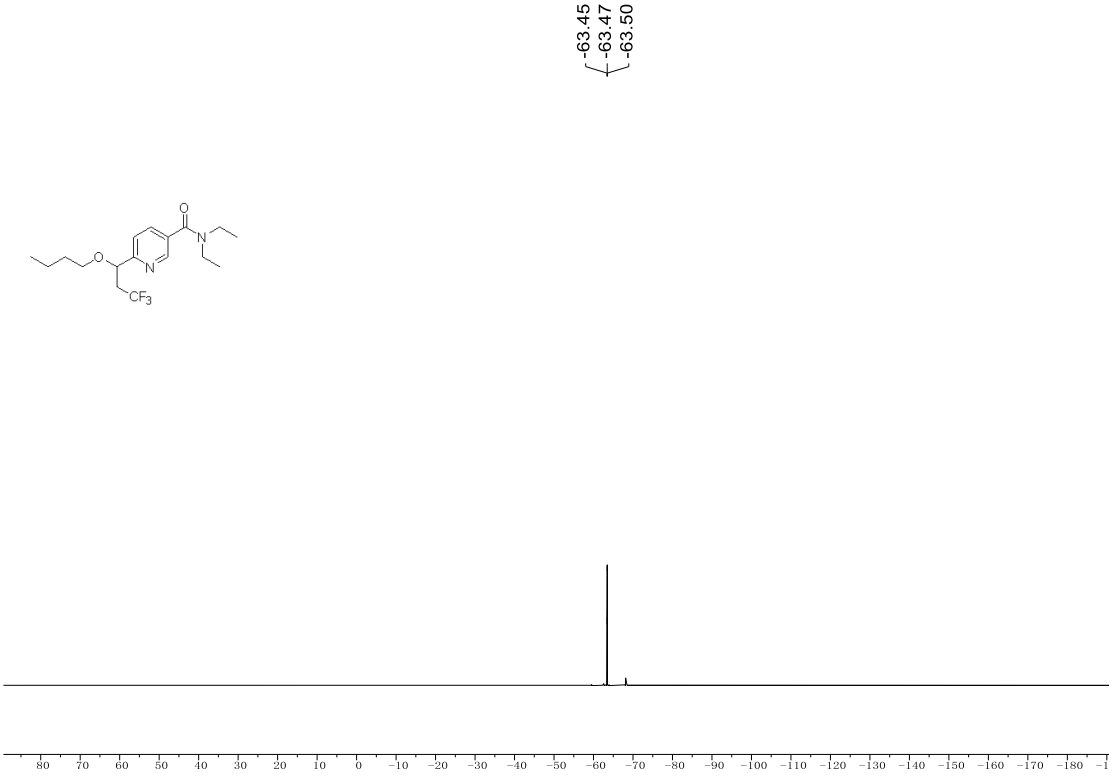
^{1}H NMR spectrum of compound **4p** in $CDCl_3$ (400 MHz)



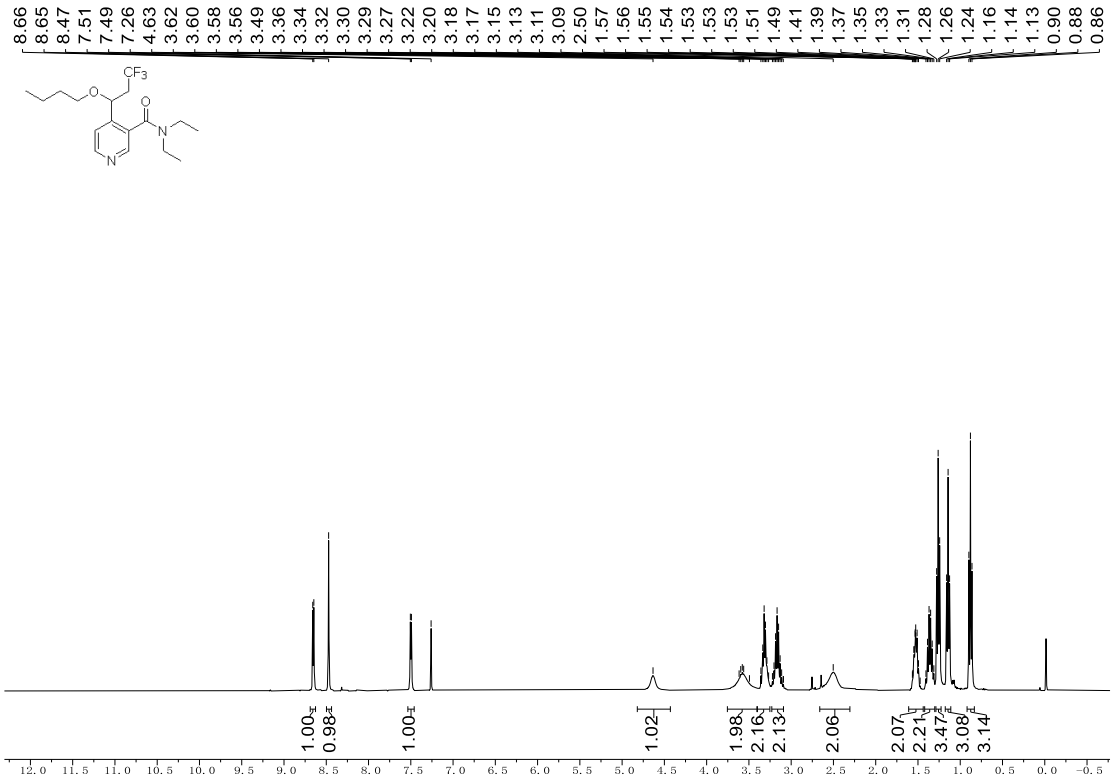
^{13}C NMR spectrum of compound **4p** in $CDCl_3$ (151 MHz)



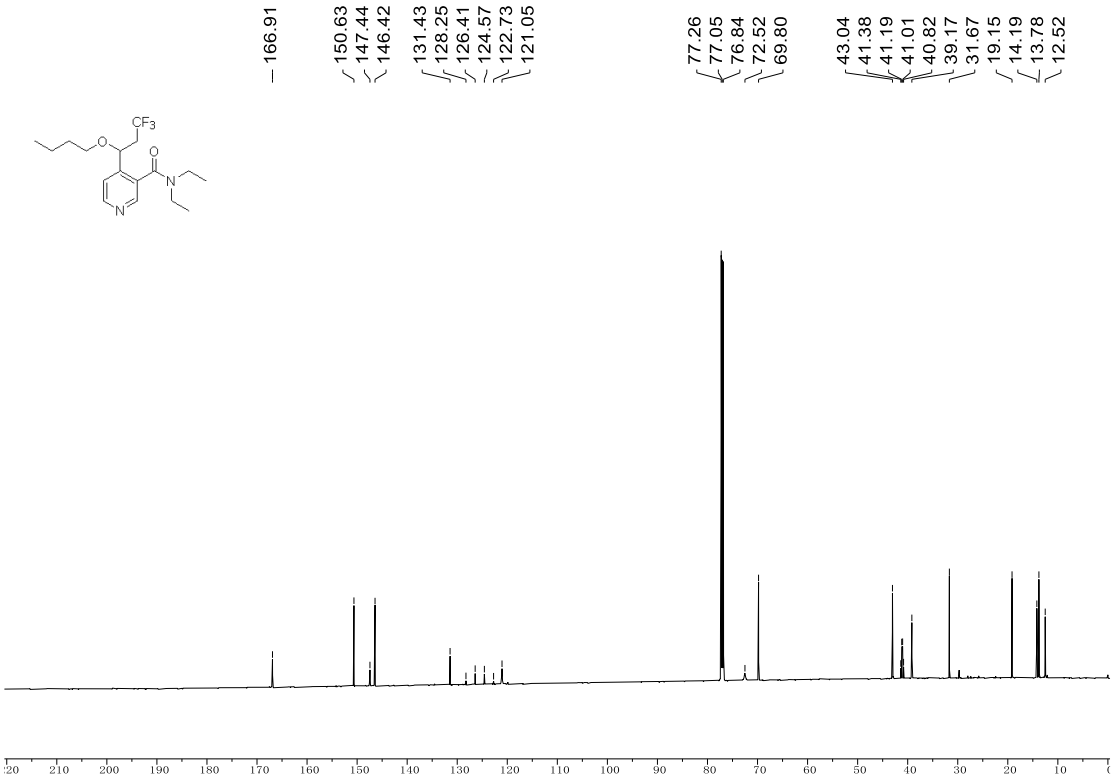
^{19}F NHR spectrum of compound **4p** in $CDCl_3$ (376 MHz)



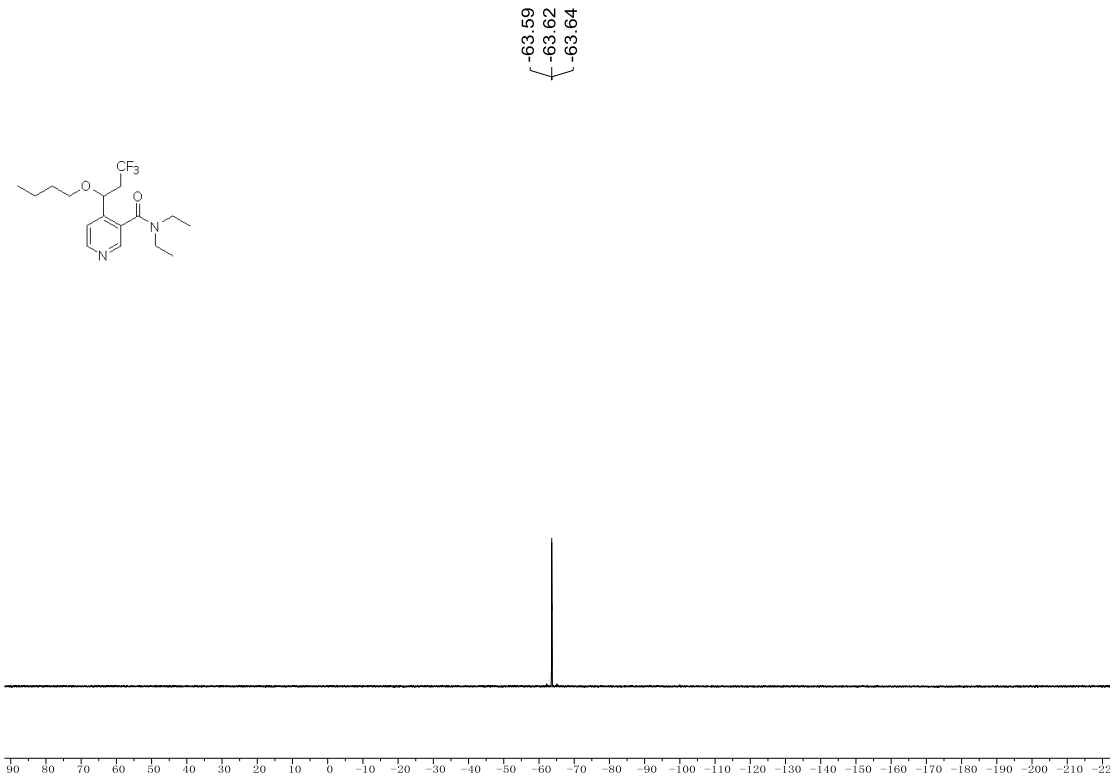
^{1}H NMR spectrum of compound **4p'** in $CDCl_3$ (400 MHz)



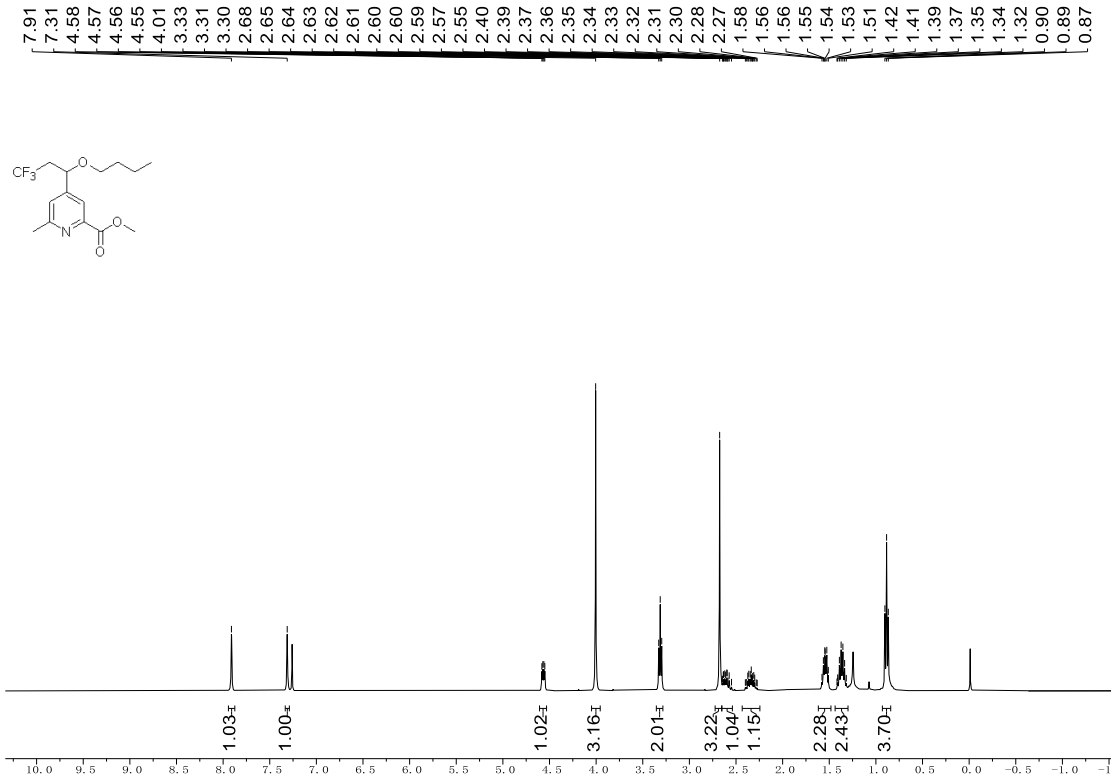
^{13}C NMR spectrum of compound **4p'** in $CDCl_3$ (151 MHz)



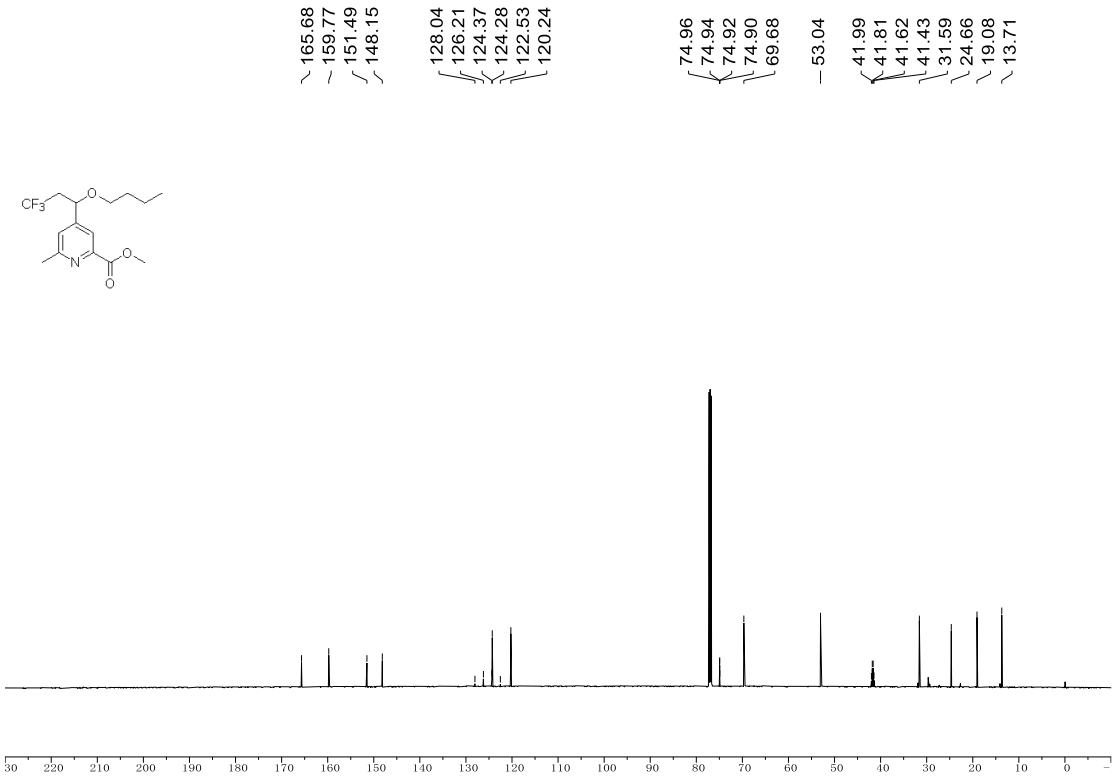
^{19}F NHR spectrum of compound **4p'** in $CDCl_3$ (376 MHz)



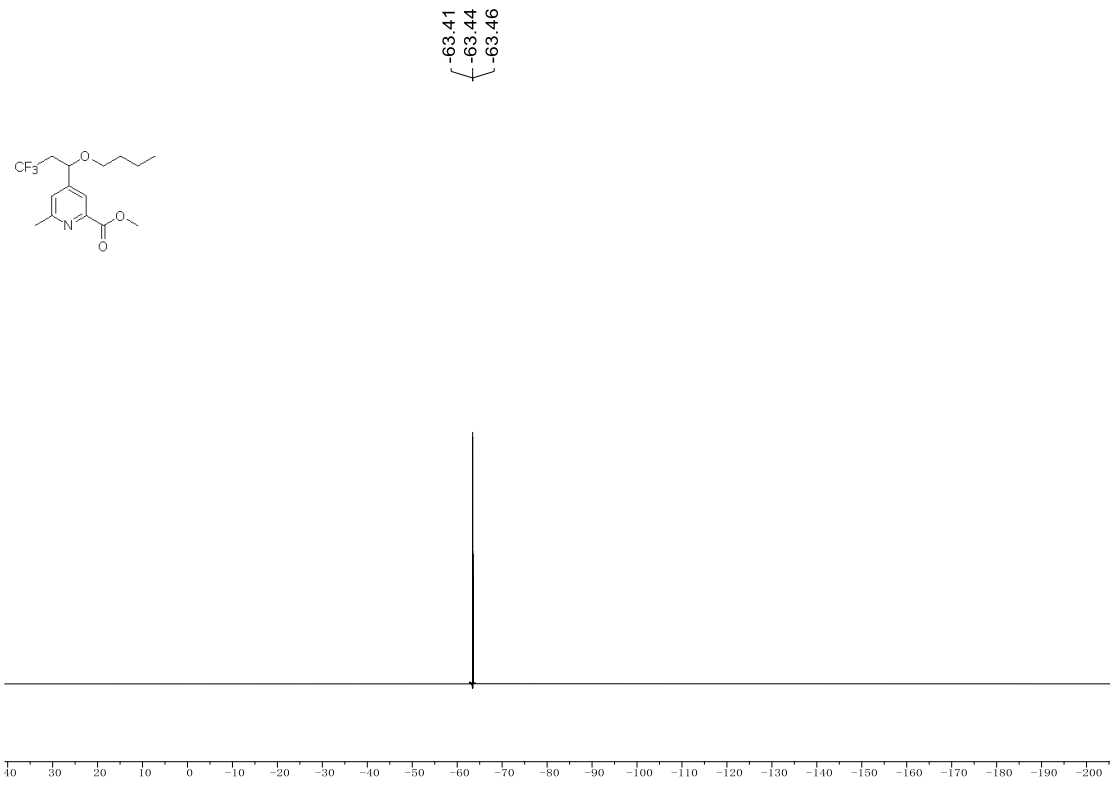
^{1}H NMR spectrum of compound **4q** in $CDCl_3$ (400 MHz)



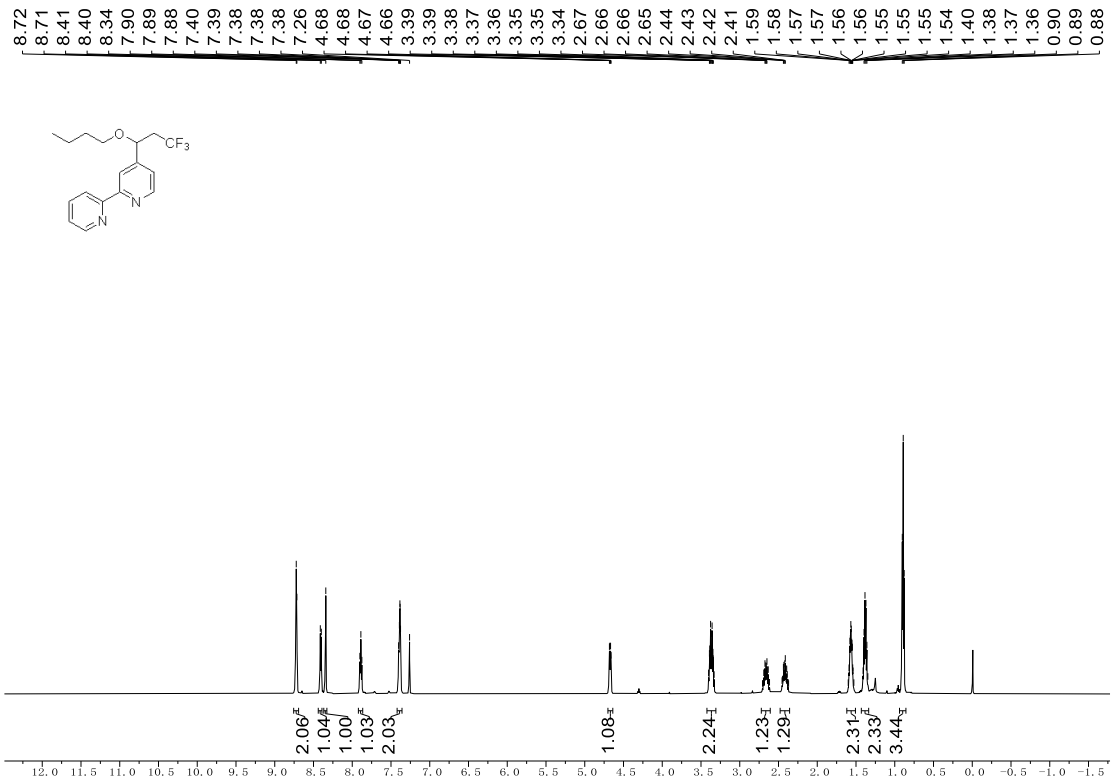
^{13}C NMR spectrum of compound **4q** in $CDCl_3$ (151 MHz)



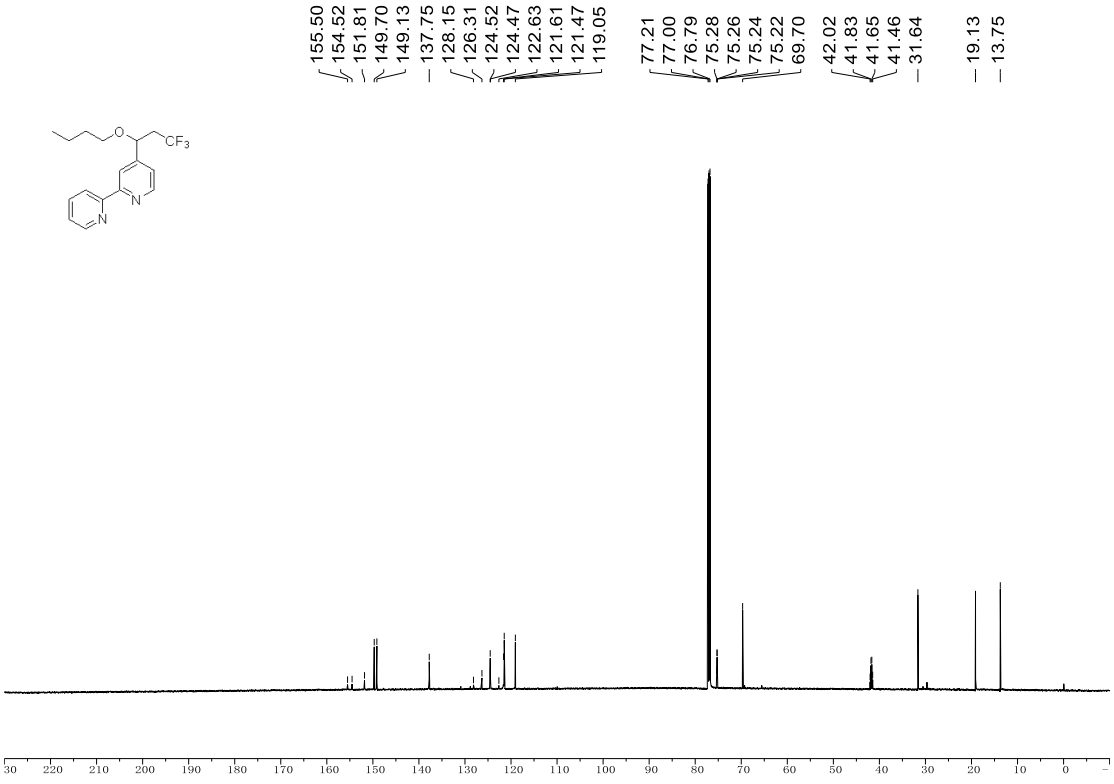
^{19}F NHR spectrum of compound **4q** in $CDCl_3$ (376 MHz)



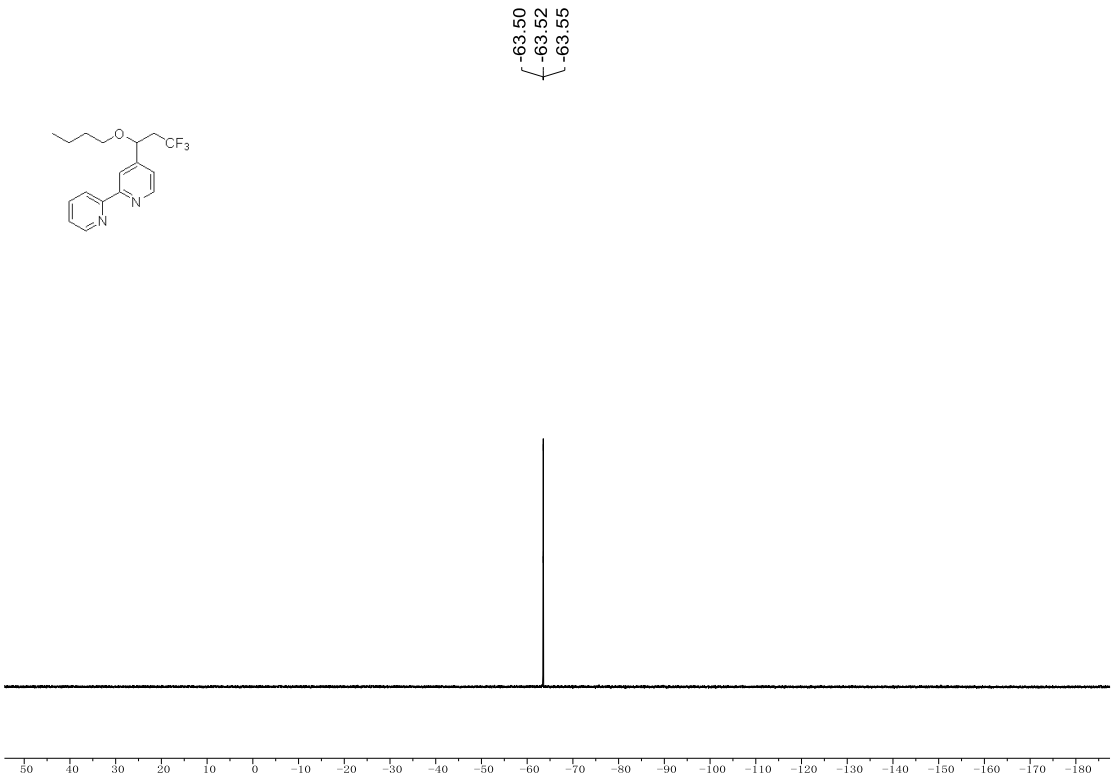
^{1}H NMR spectrum of compound **4r** in $CDCl_3$ (600 MHz)



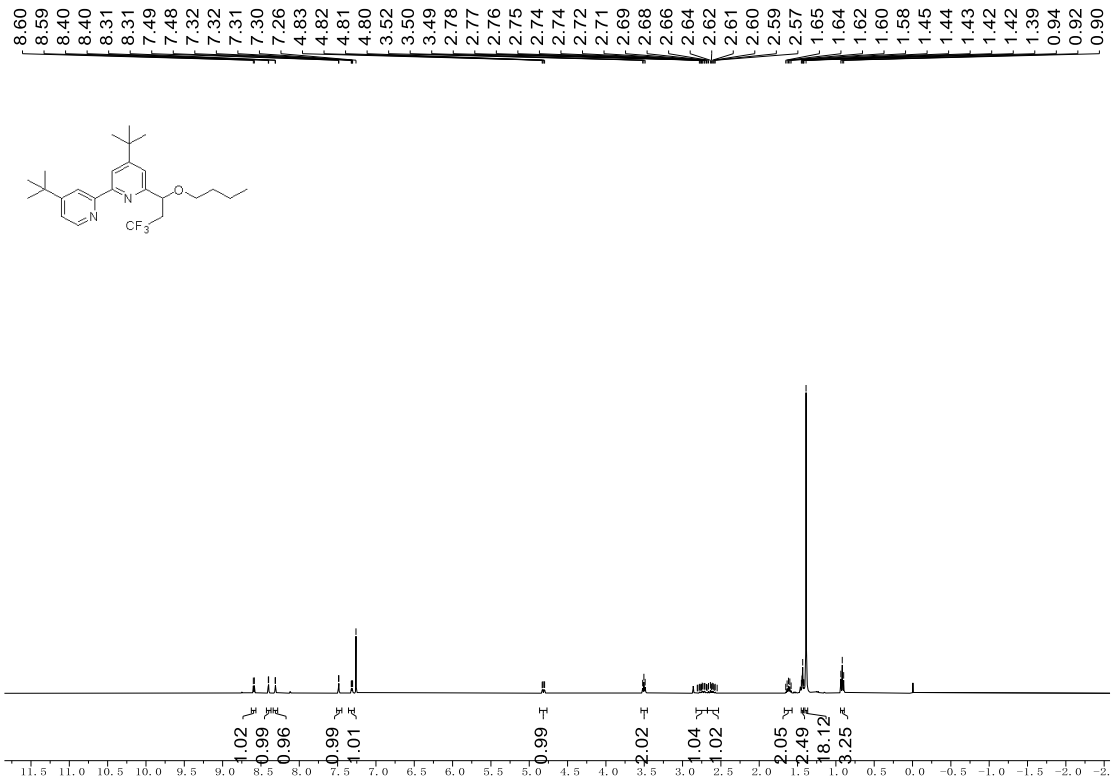
^{13}C NMR spectrum of compound **4r** in $CDCl_3$ (151 MHz)



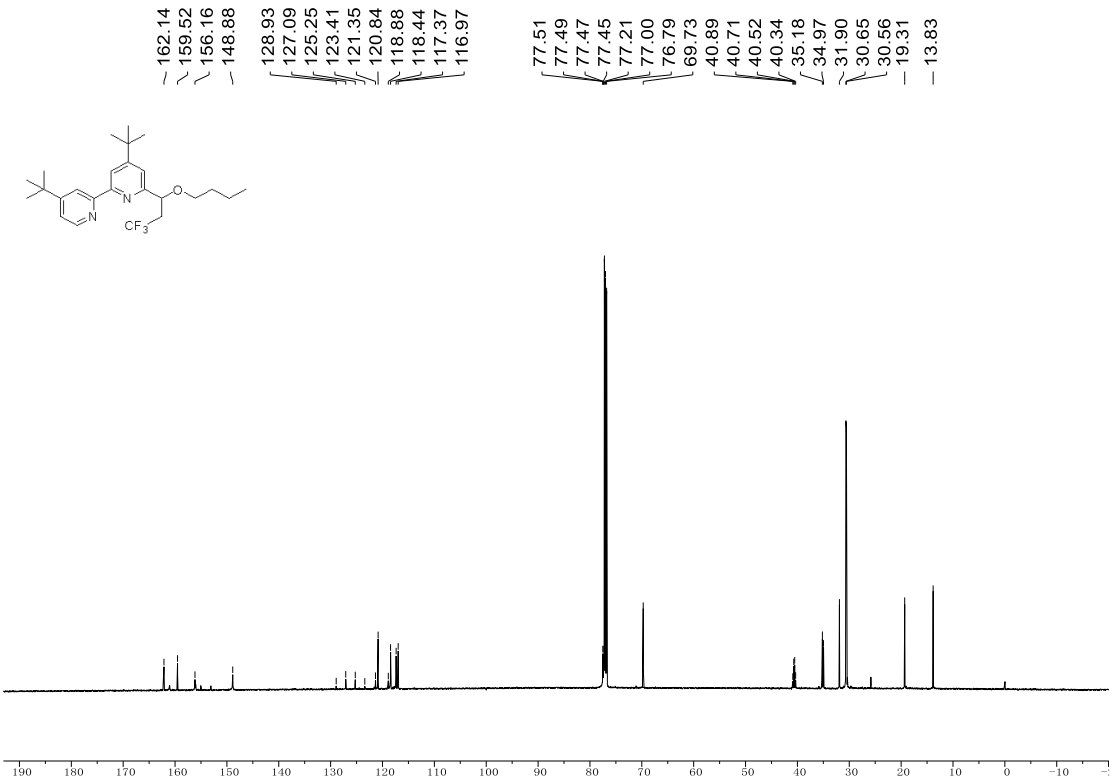
^{19}F NHR spectrum of compound **4r** in $CDCl_3$ (376 MHz)



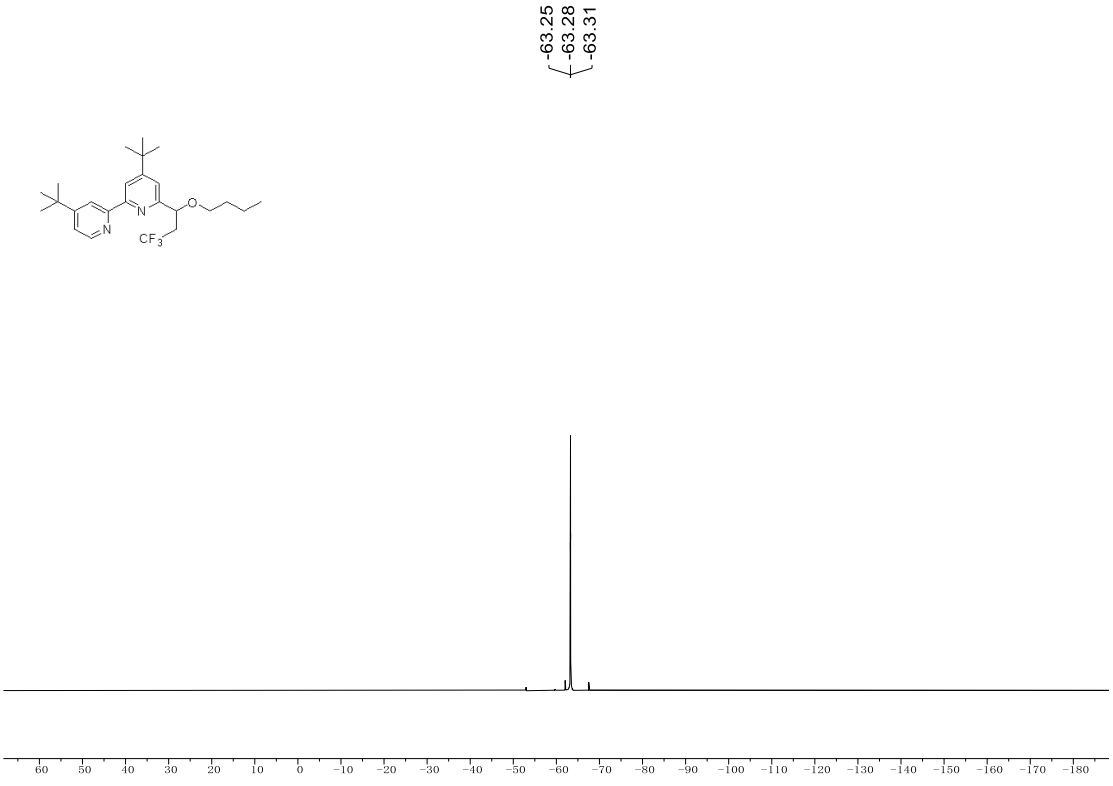
^{1}H NMR spectrum of compound **4s** in $CDCl_3$ (400 MHz)



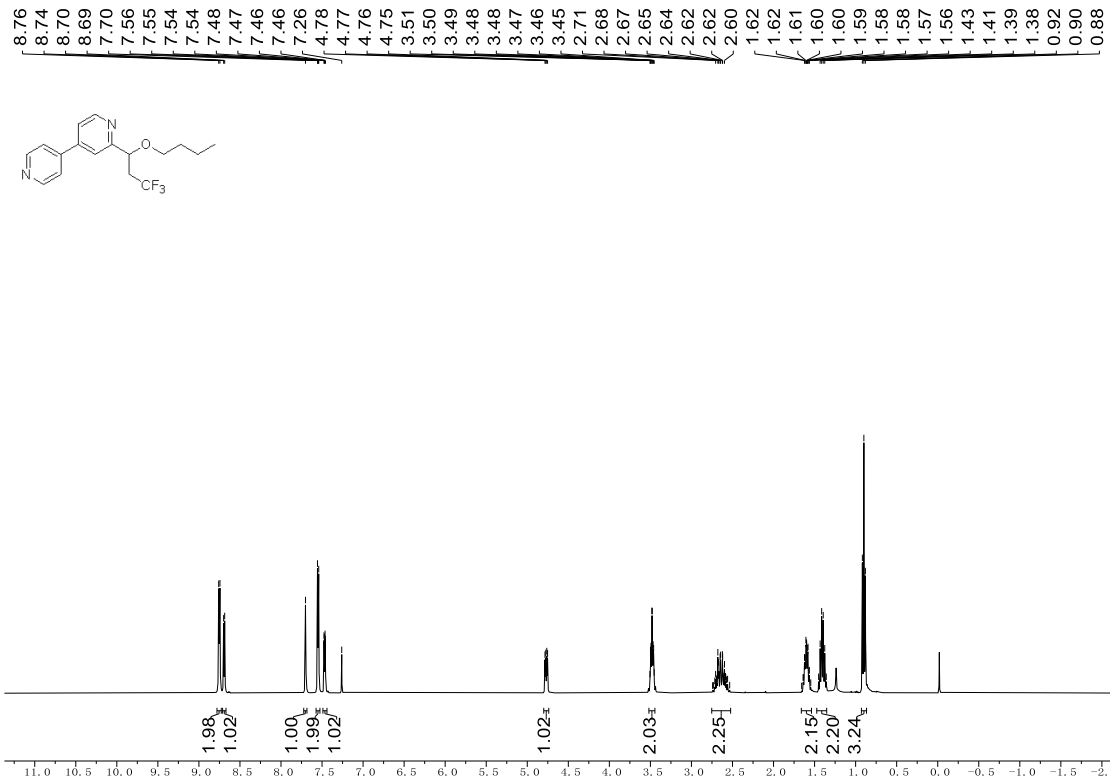
^{13}C NMR spectrum of compound **4s** in $CDCl_3$ (151 MHz)



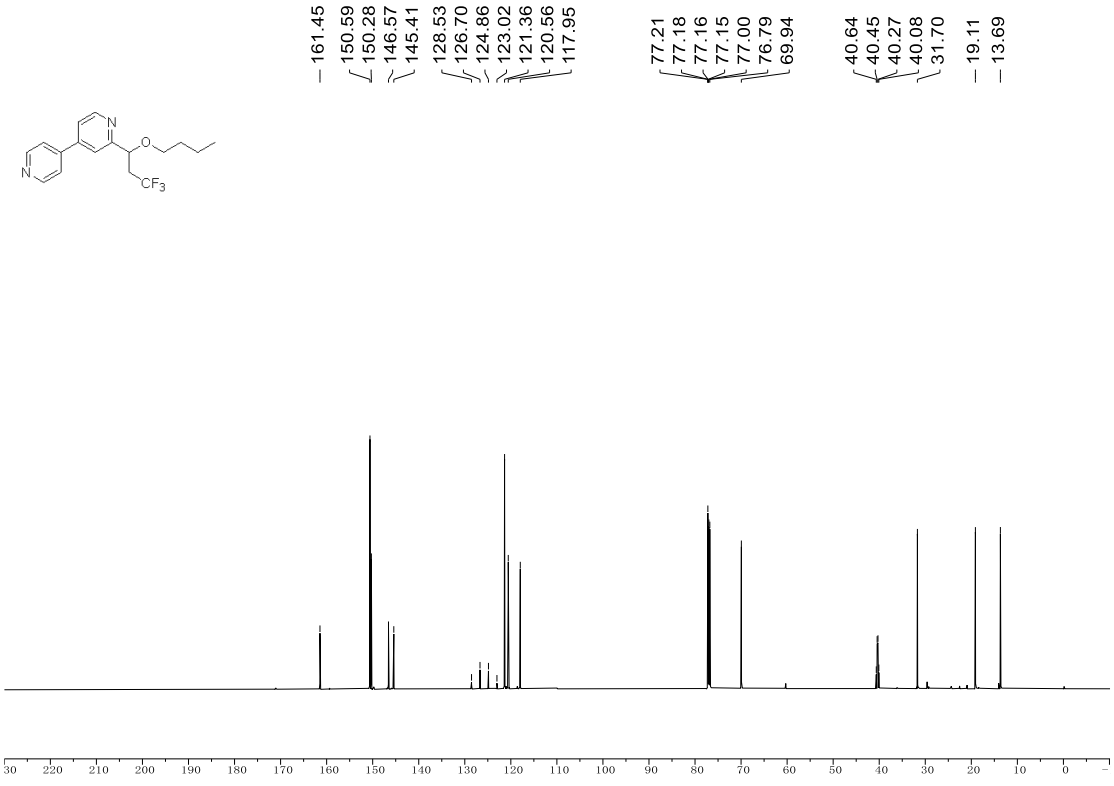
^{19}F NHR spectrum of compound **4s** in $CDCl_3$ (376 MHz)



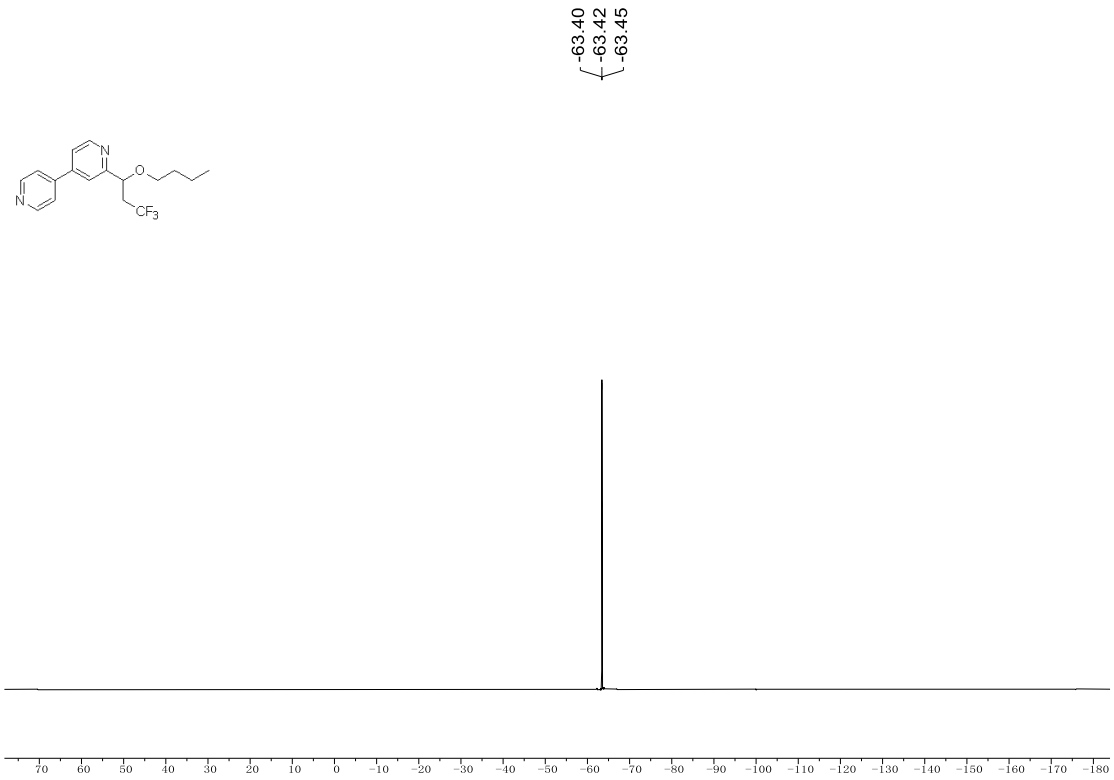
^{1}H NMR spectrum of compound **4t** in $CDCl_3$ (400 MHz)



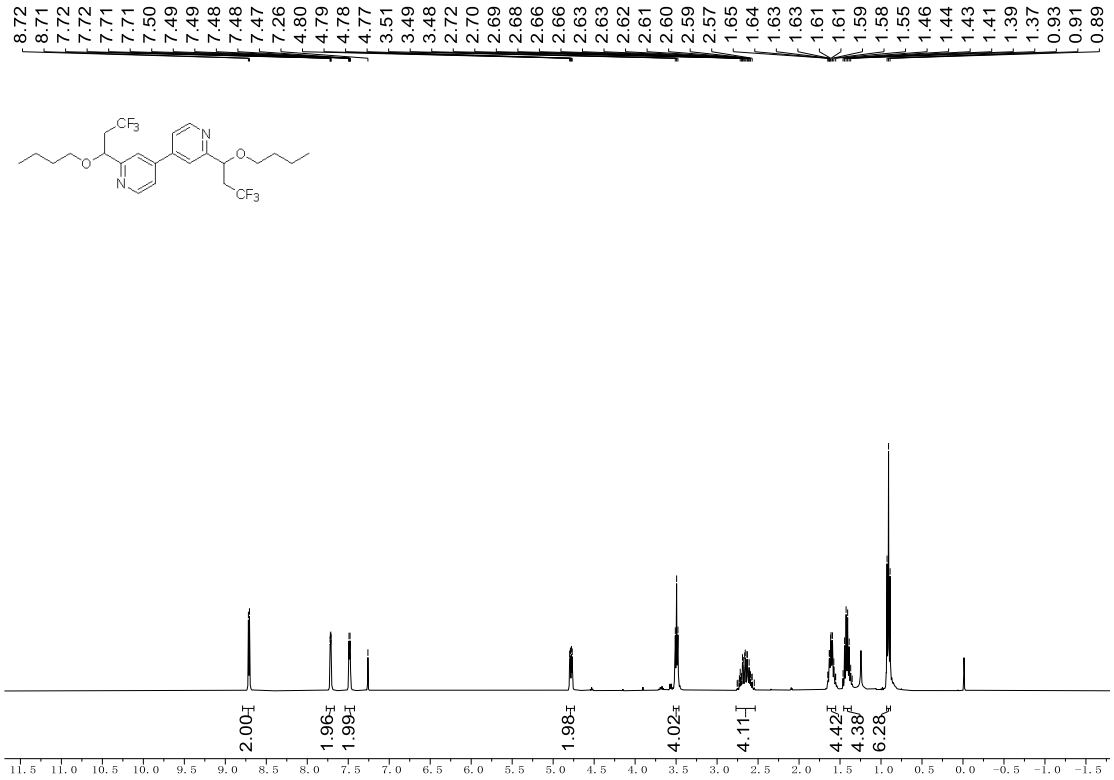
^{13}C NMR spectrum of compound **4t** in $CDCl_3$ (151 MHz)



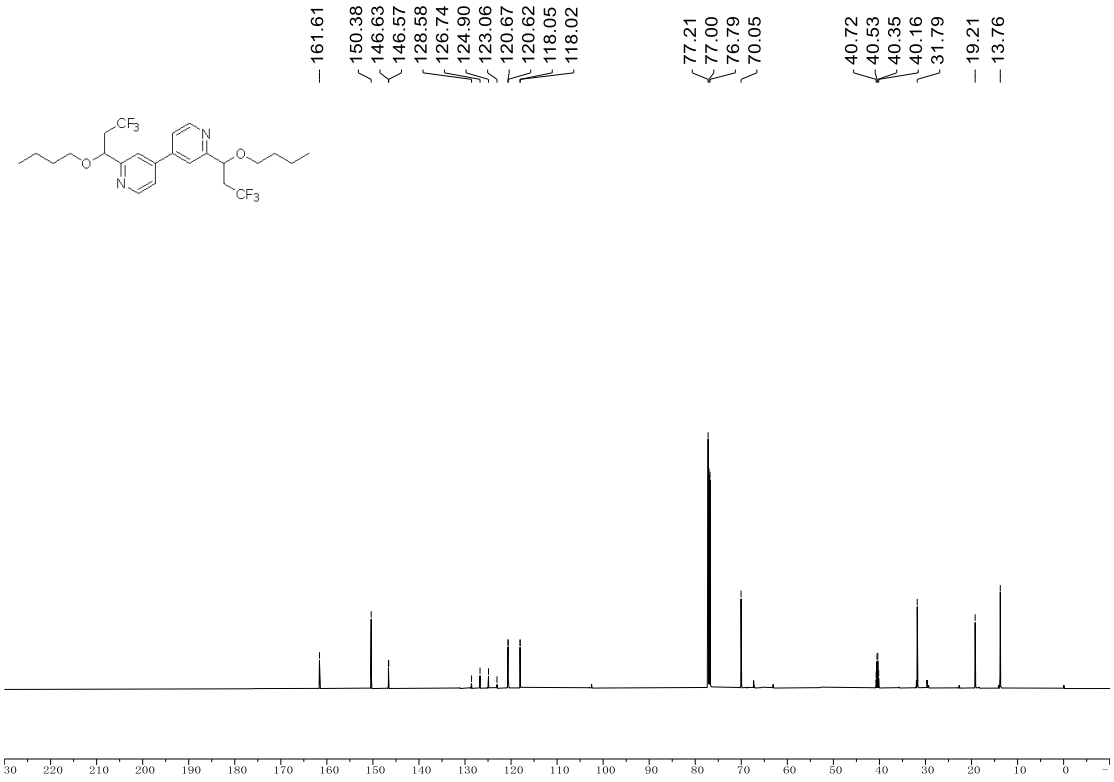
^{19}F NHR spectrum of compound **4t** in $CDCl_3$ (376 MHz)



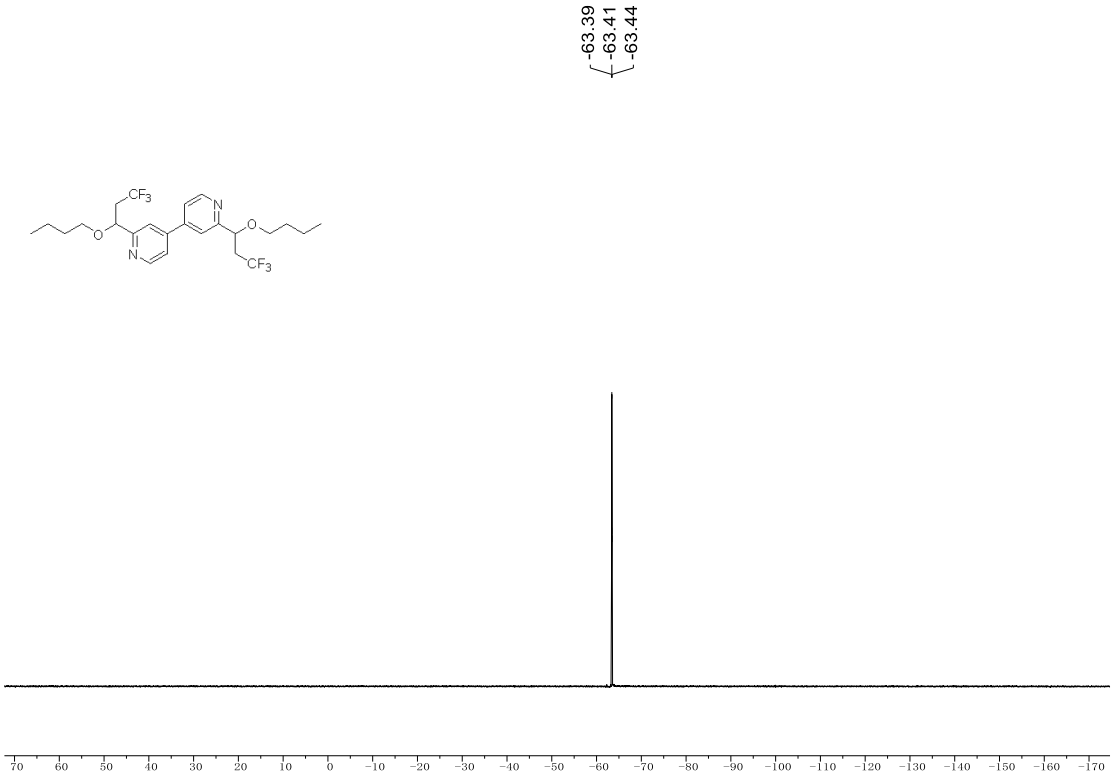
^{1}H NMR spectrum of compound **4t'** in $CDCl_3$ (400 MHz)



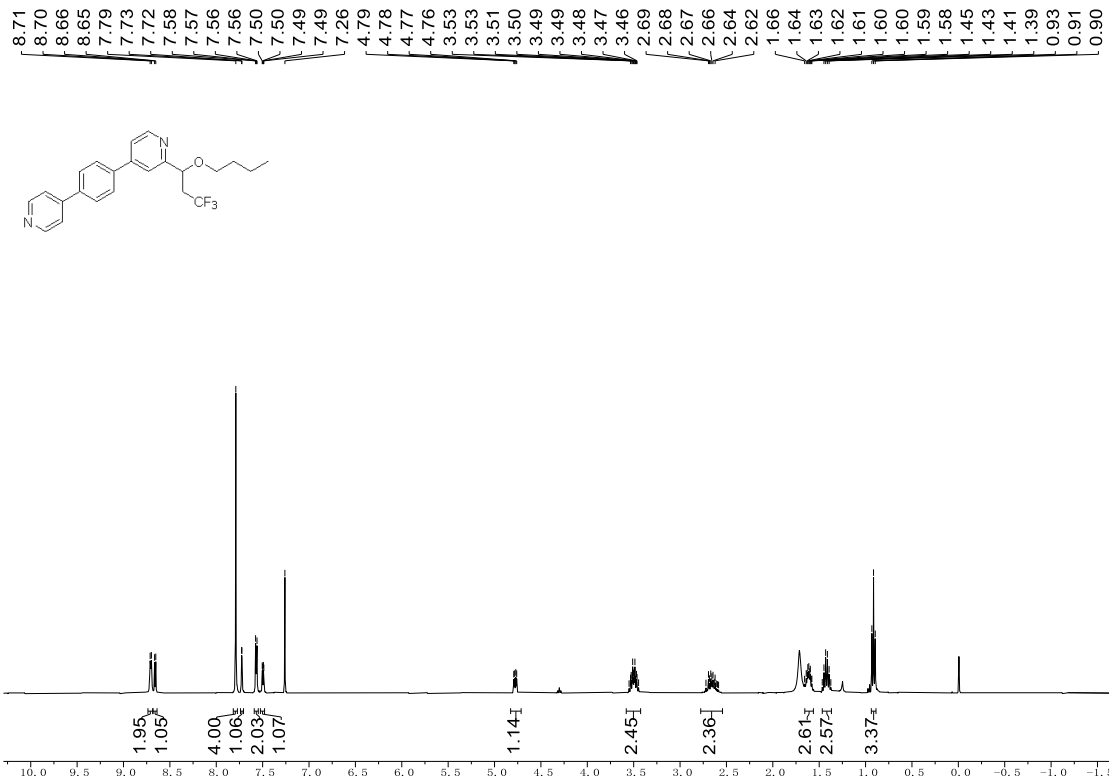
^{13}C NMR spectrum of compound **4t'** in $CDCl_3$ (151 MHz)



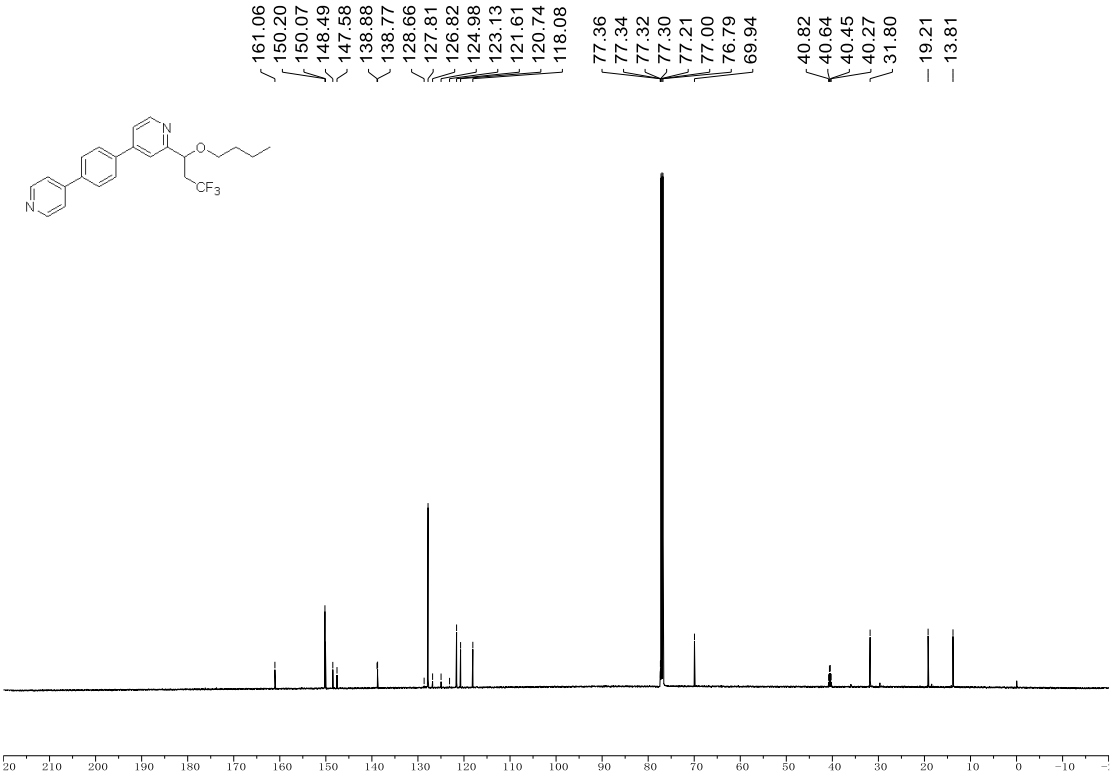
^{19}F NHR spectrum of compound **4t'** in $CDCl_3$ (376 MHz)



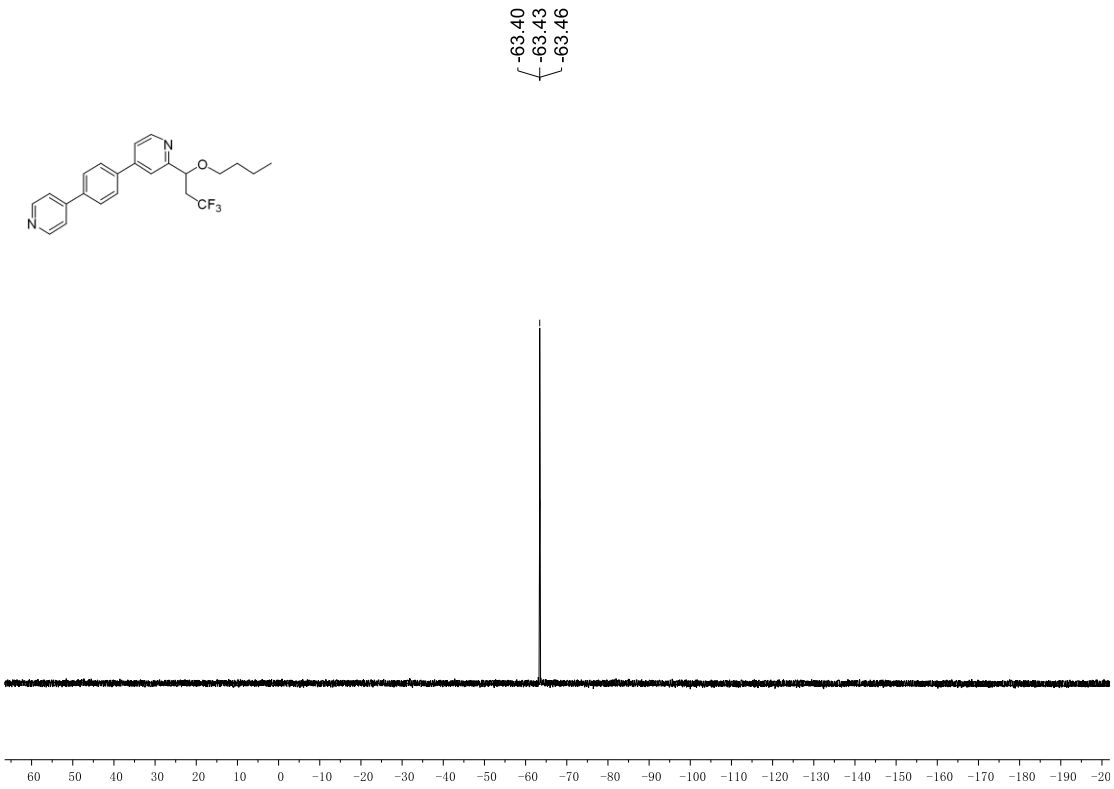
^{1}H NMR spectrum of compound **4u** in $CDCl_3$ (400 MHz)



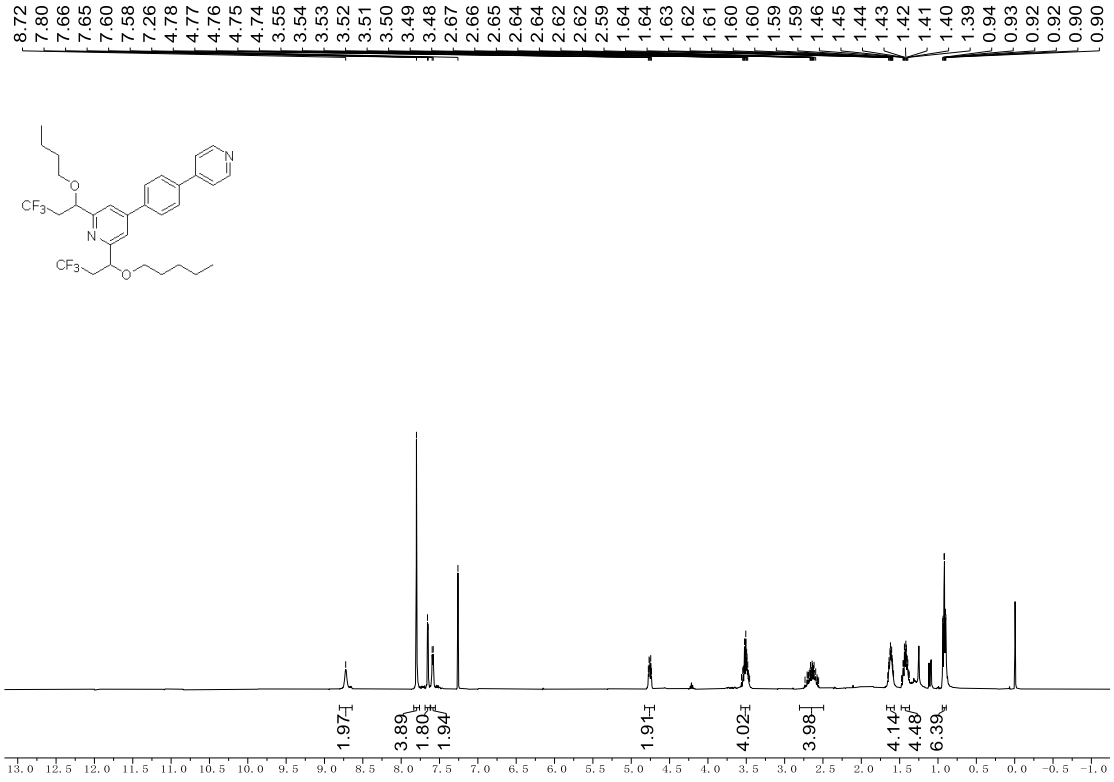
^{13}C NMR spectrum of compound **4u** in $CDCl_3$ (151 MHz)



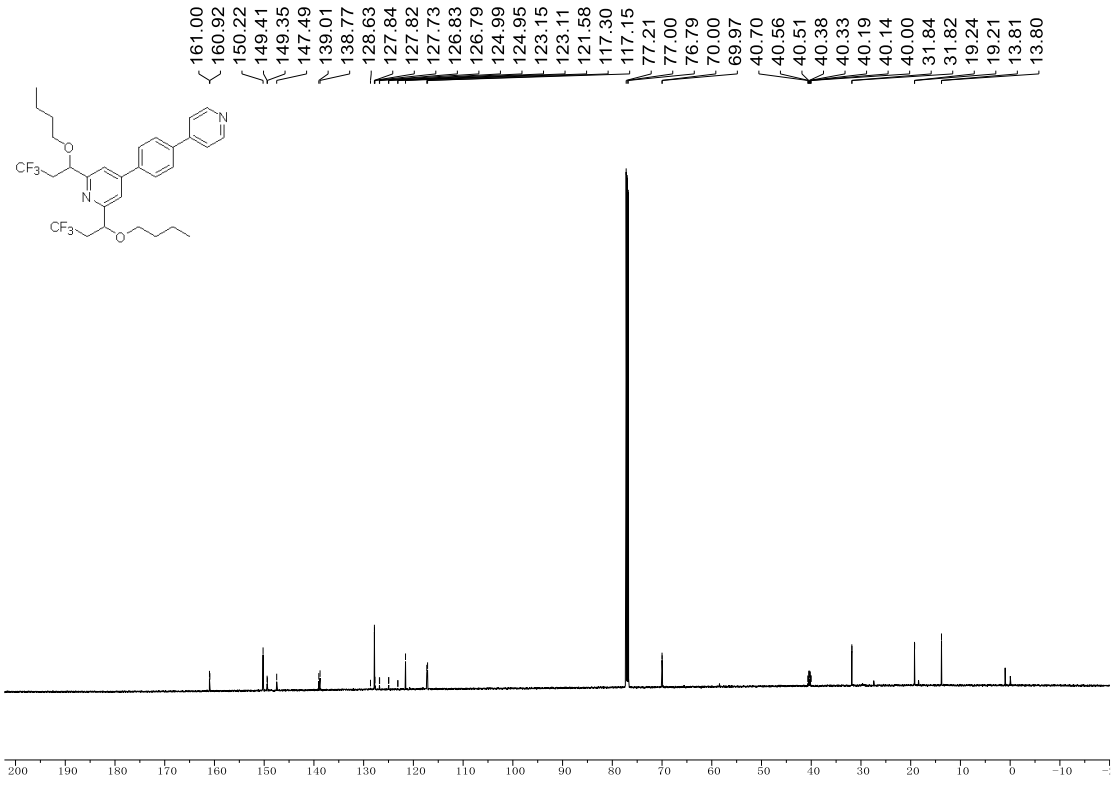
^{19}F NHR spectrum of compound **4u** in $CDCl_3$ (376 MHz)



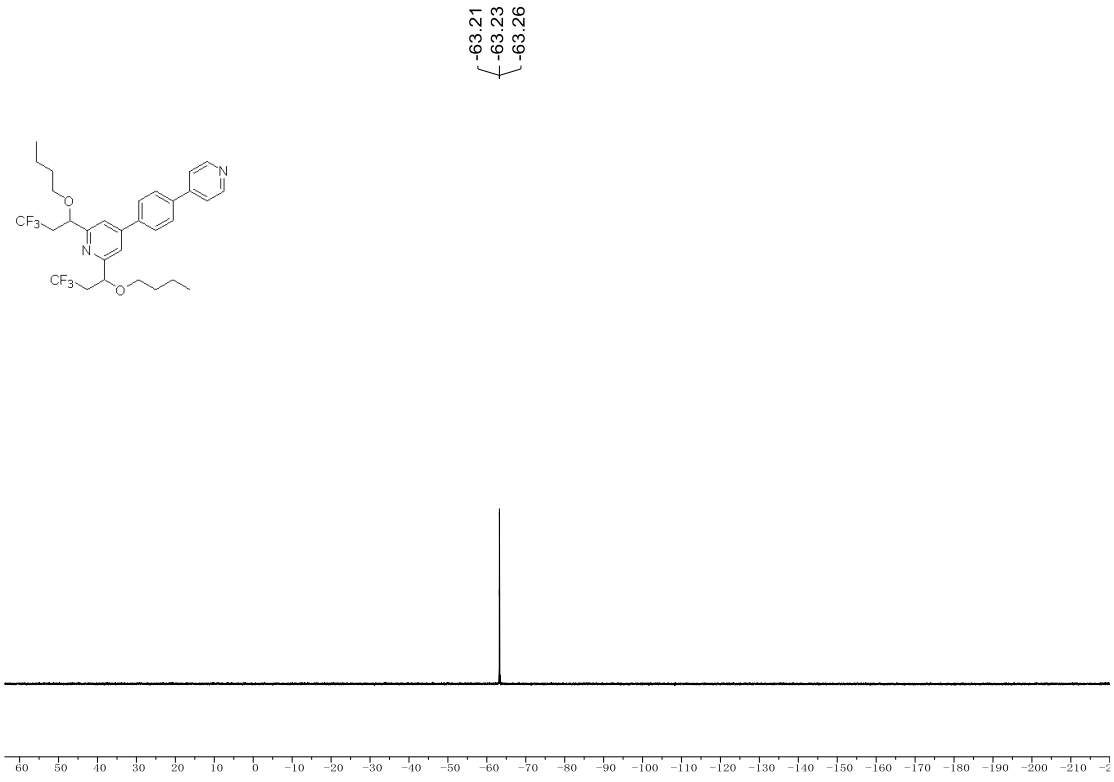
^{1}H NMR spectrum of compound **4u'** in $CDCl_3$ (400 MHz)



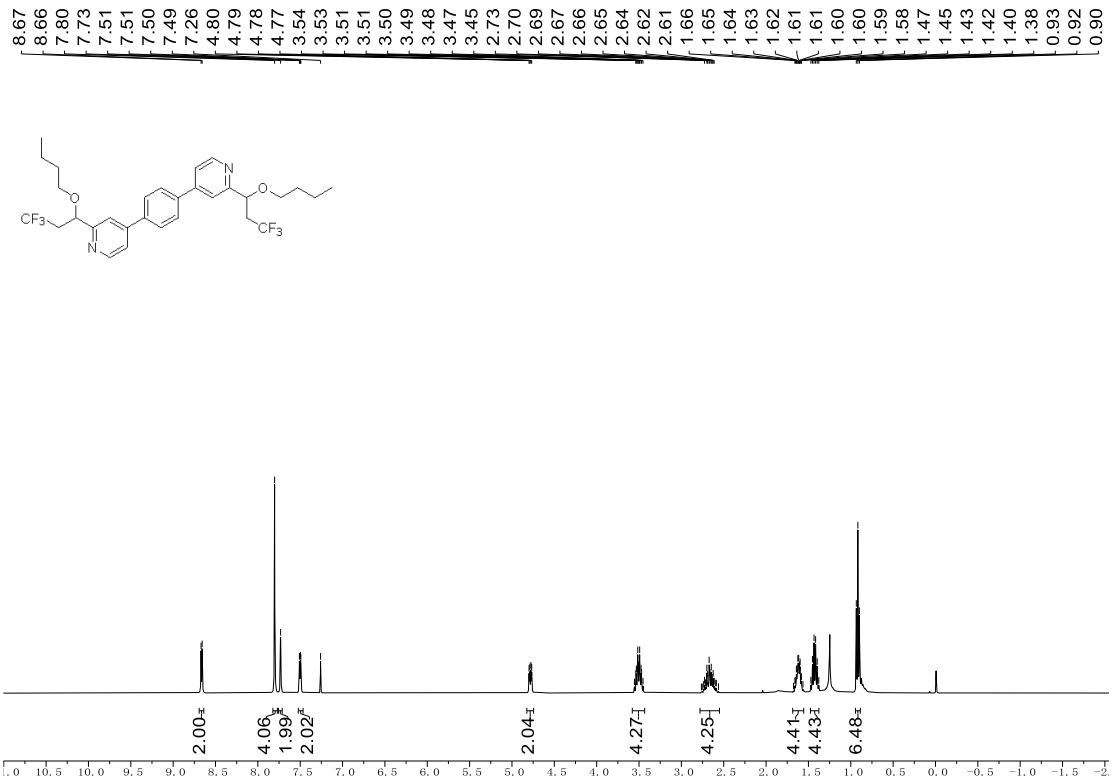
^{13}C NMR spectrum of compound **4u'** in $CDCl_3$ (151 MHz)



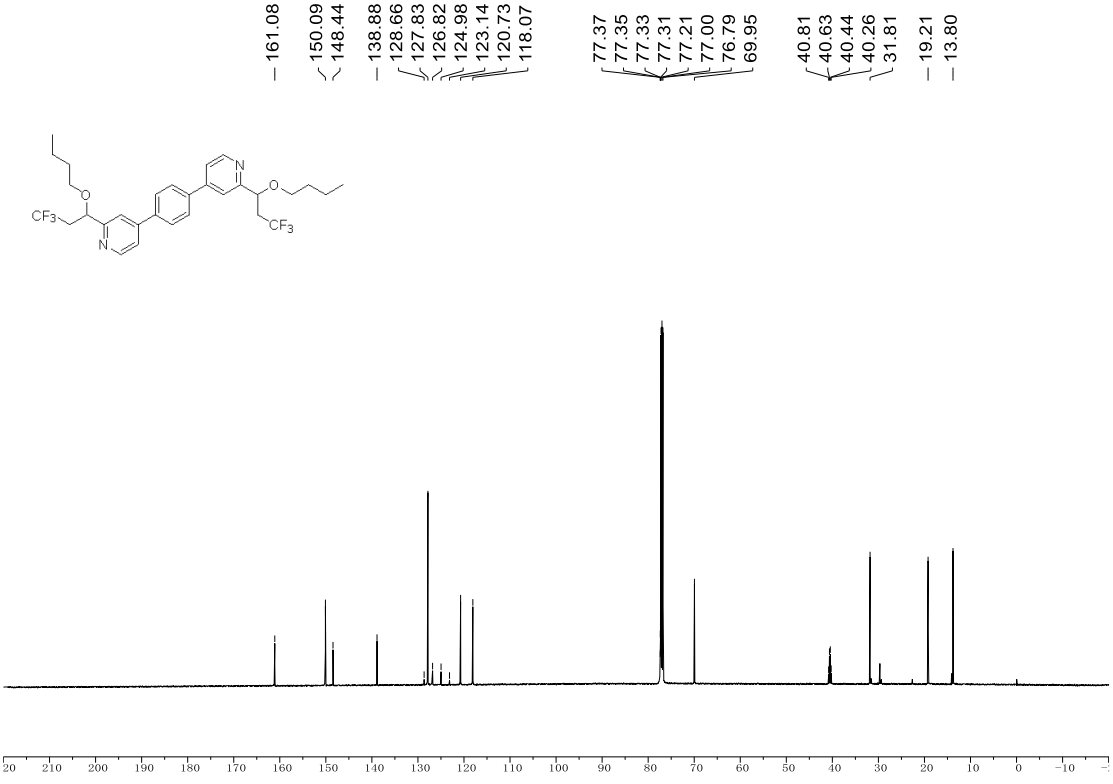
^{19}F NHR spectrum of compound **4u'** in $CDCl_3$ (376 MHz)



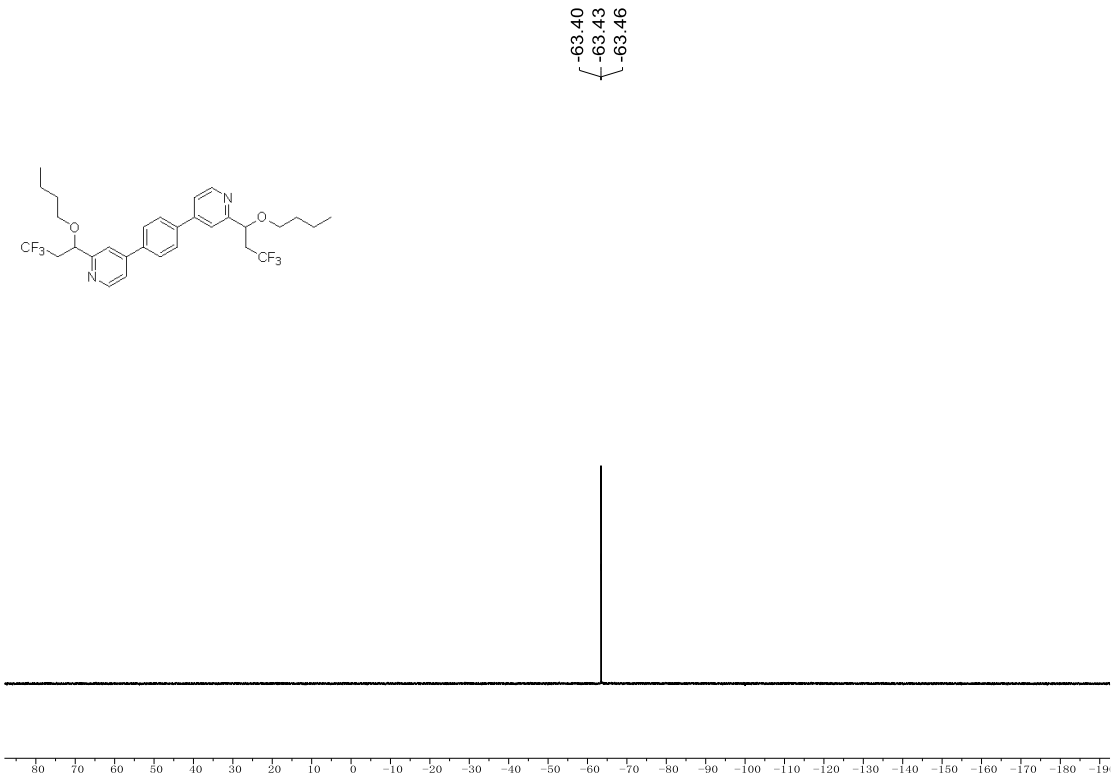
^{1}H NMR spectrum of compound **4u''** in $CDCl_3$ (400 MHz)



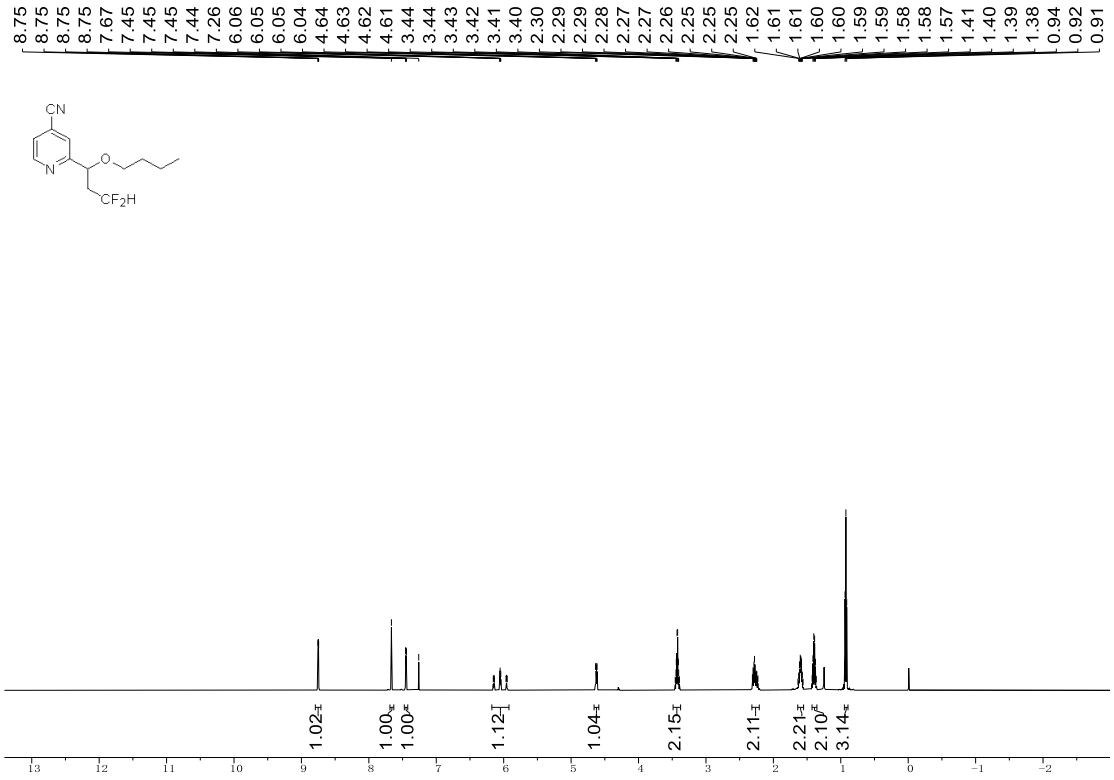
^{13}C NMR spectrum of compound **4u''** in $CDCl_3$ (151 MHz)



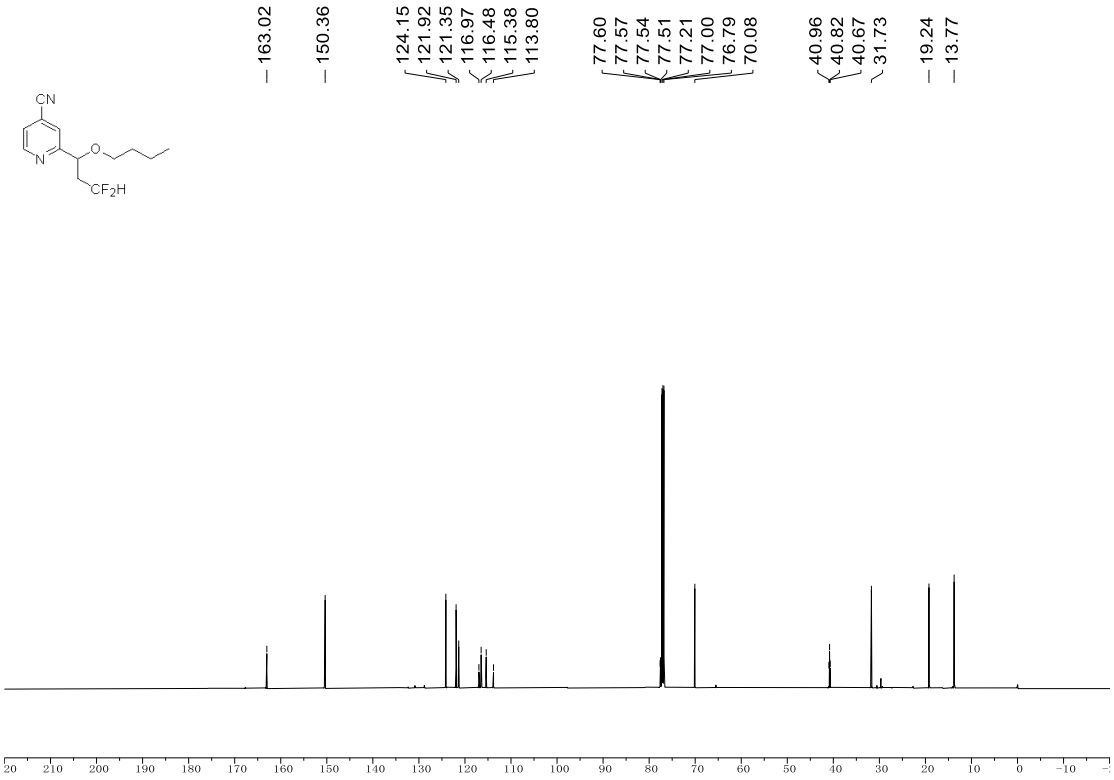
^{19}F NHR spectrum of compound **4u''** in $CDCl_3$ (376 MHz)



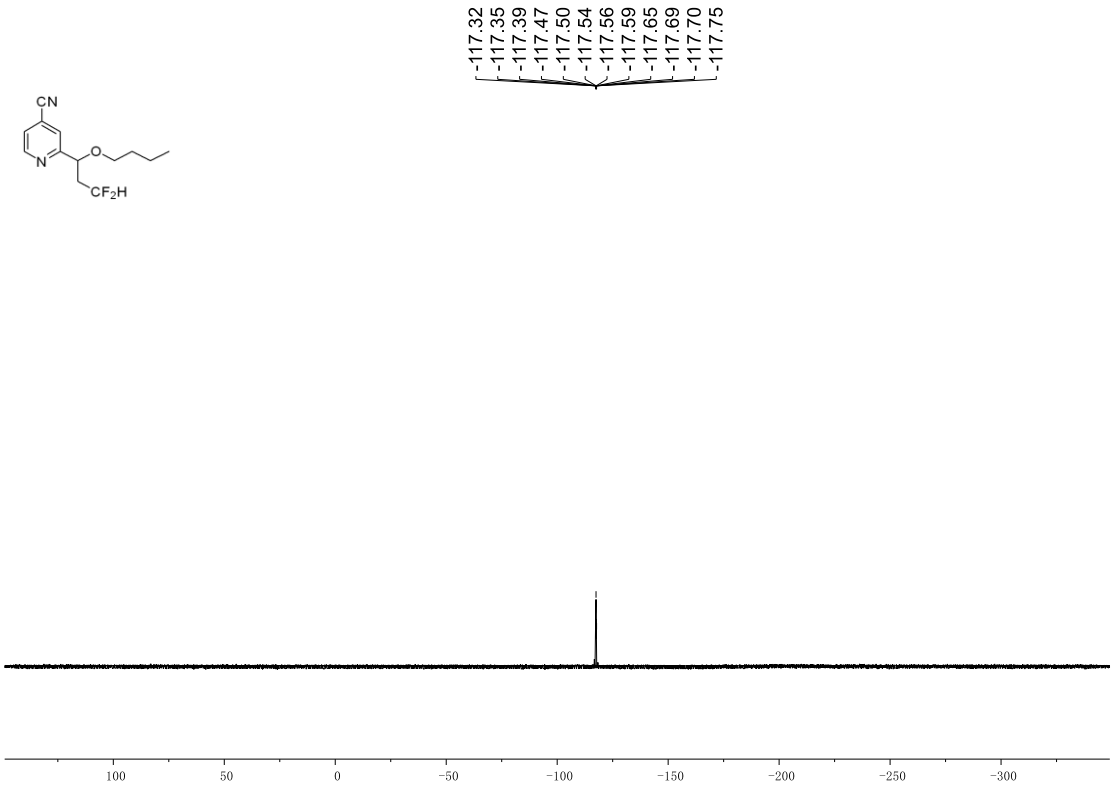
^{1}H NMR spectrum of compound **4V** in $CDCl_3$ (600 MHz)



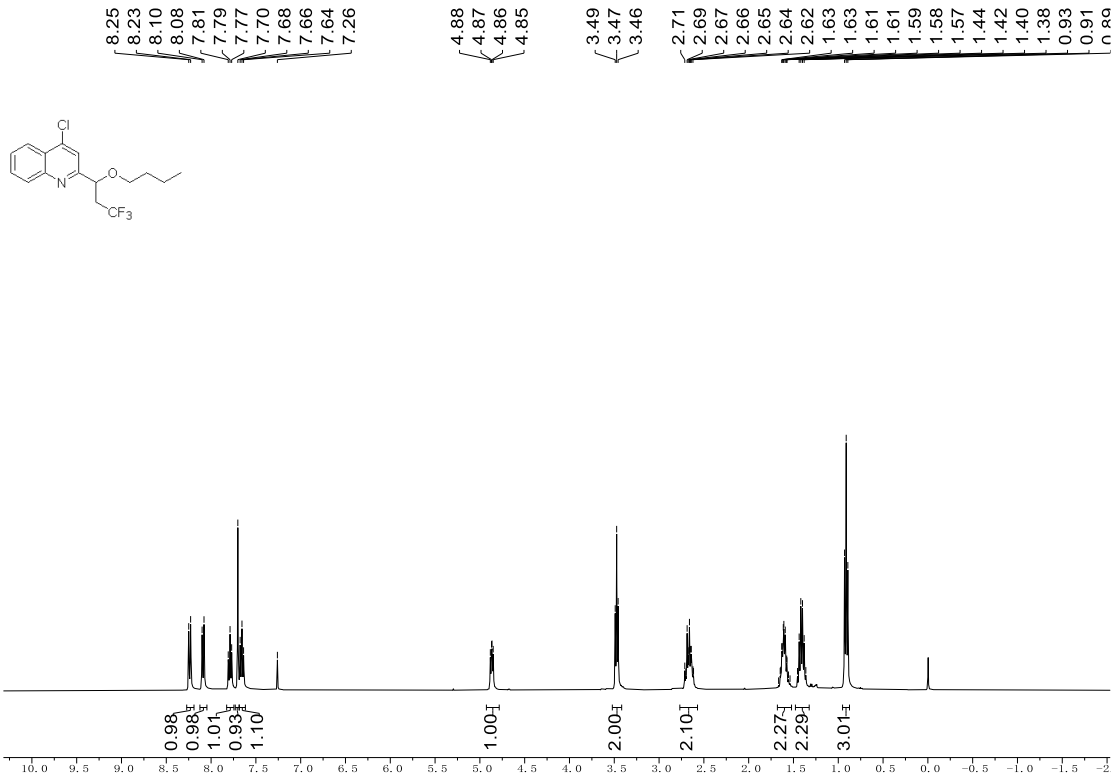
^{13}C NMR spectrum of compound **4V** in $CDCl_3$ (151 MHz)



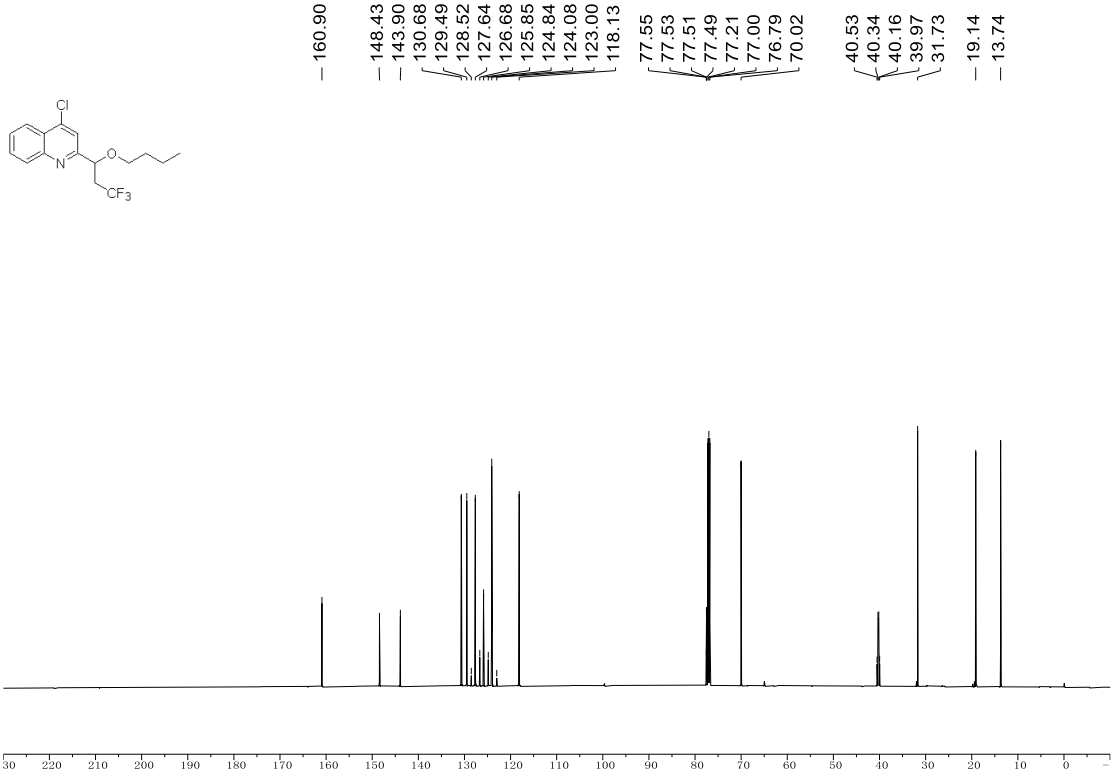
^{19}F NHR spectrum of compound **4v** in $CDCl_3$ (376 MHz)



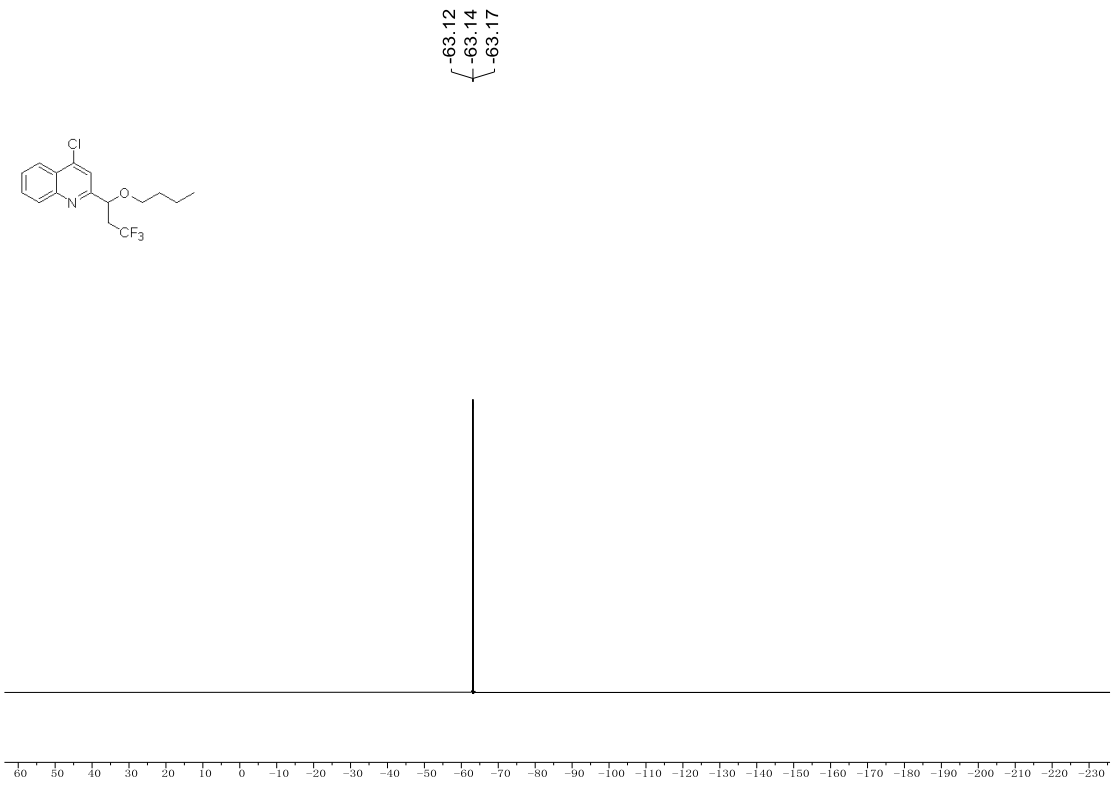
^{1}H NMR spectrum of compound **5a** in $CDCl_3$ (400 MHz)



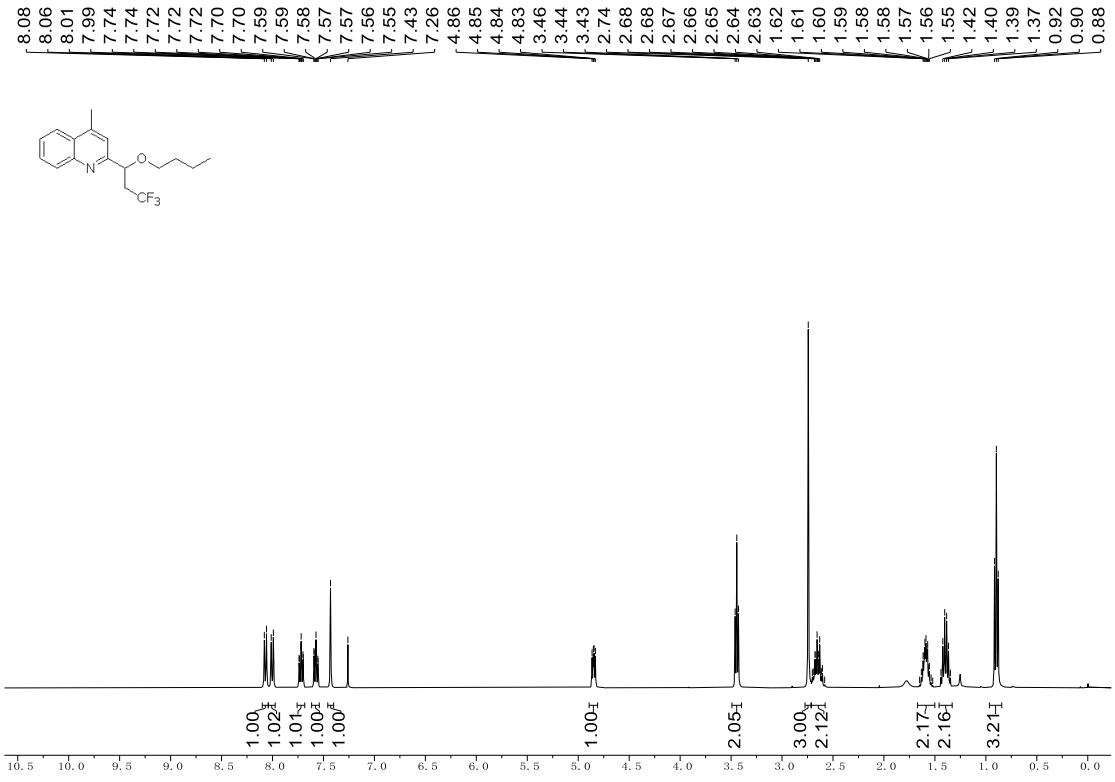
^{13}C NMR spectrum of compound **5a** in $CDCl_3$ (151 MHz)



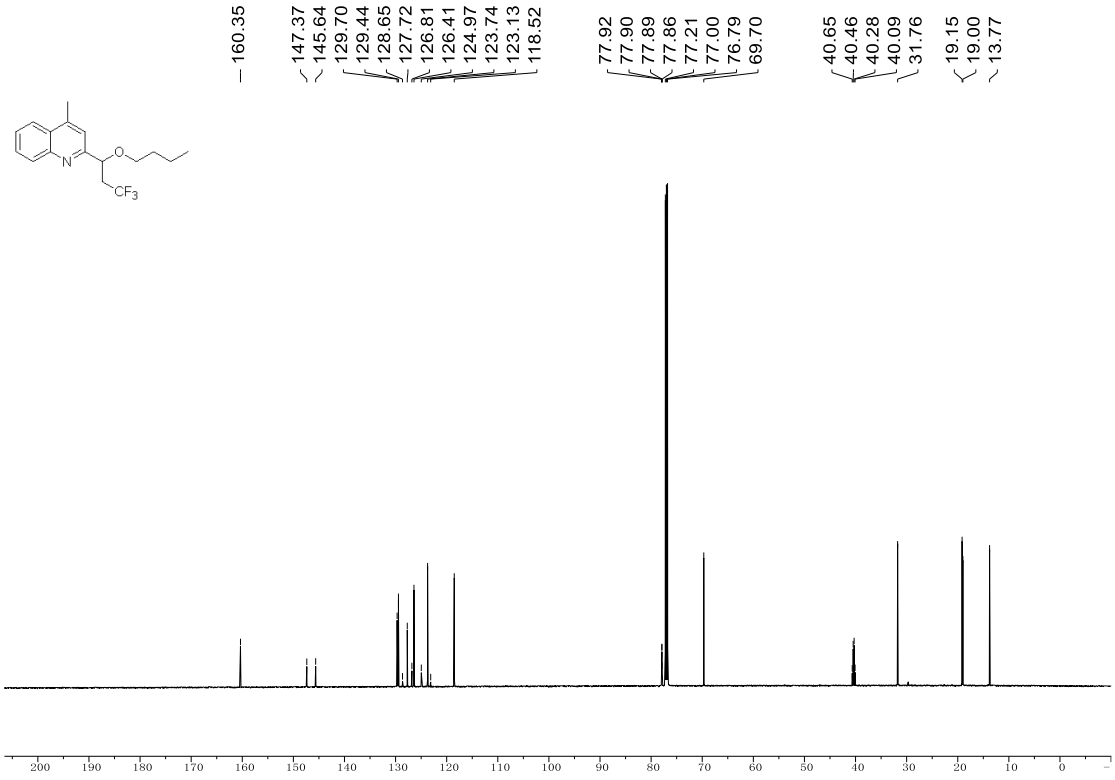
^{19}F NHR spectrum of compound **5a** in $CDCl_3$ (376 MHz)



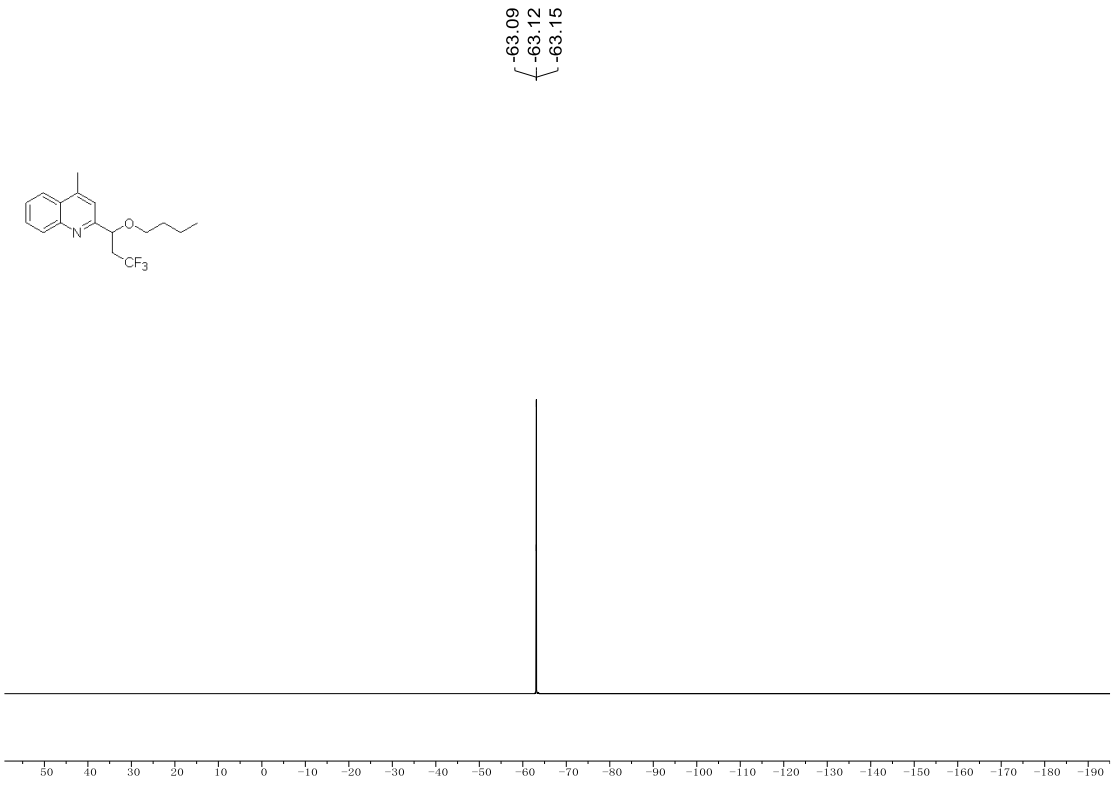
^{1}H NMR spectrum of compound **5b** in $CDCl_3$ (400 MHz)



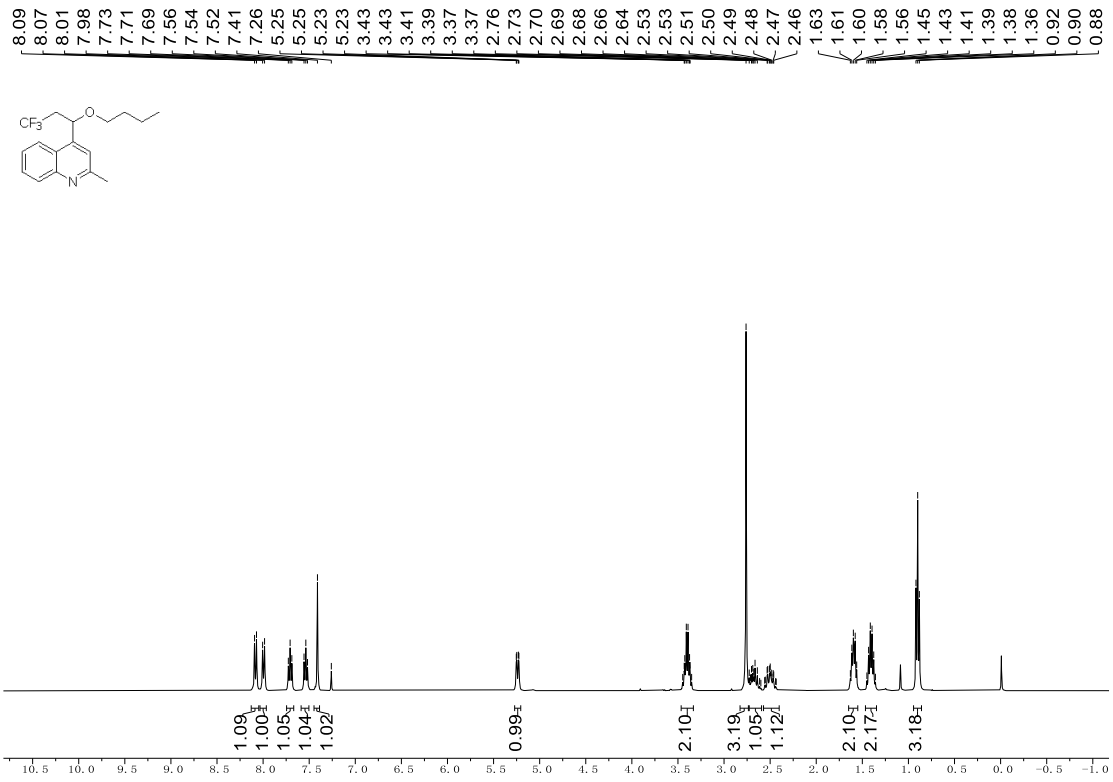
^{13}C NMR spectrum of compound **5b** in $CDCl_3$ (151 MHz)



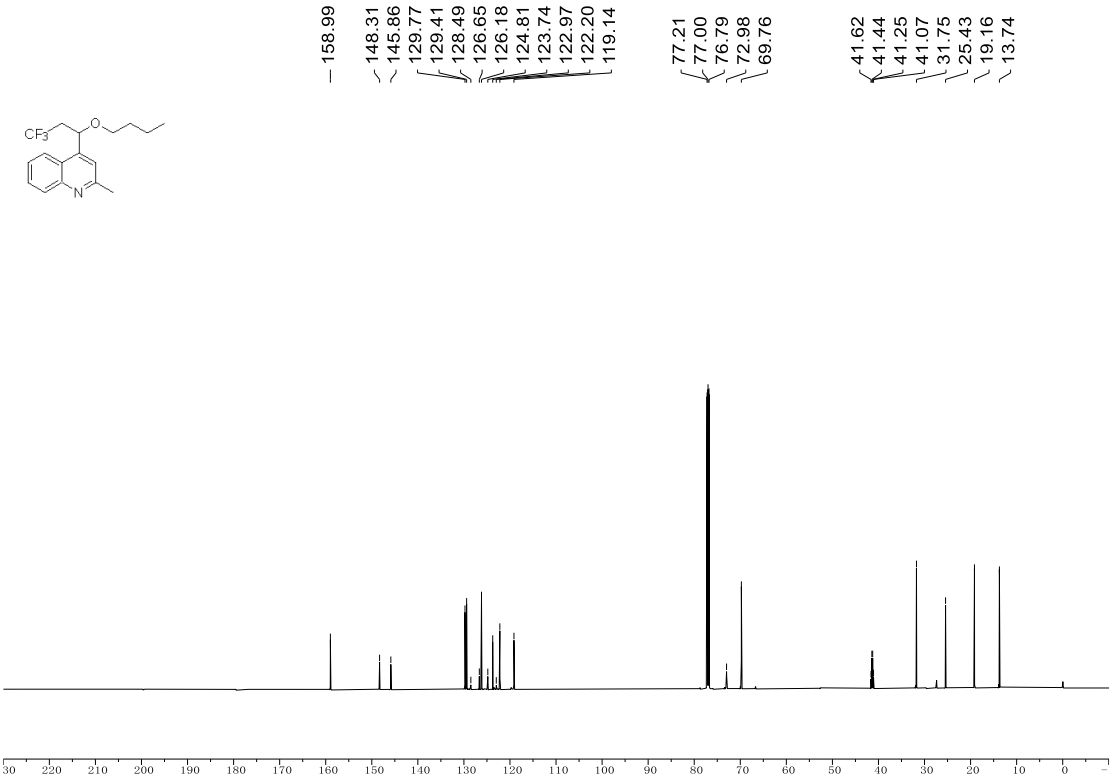
^{19}F NHR spectrum of compound **5b** in $CDCl_3$ (376 MHz)



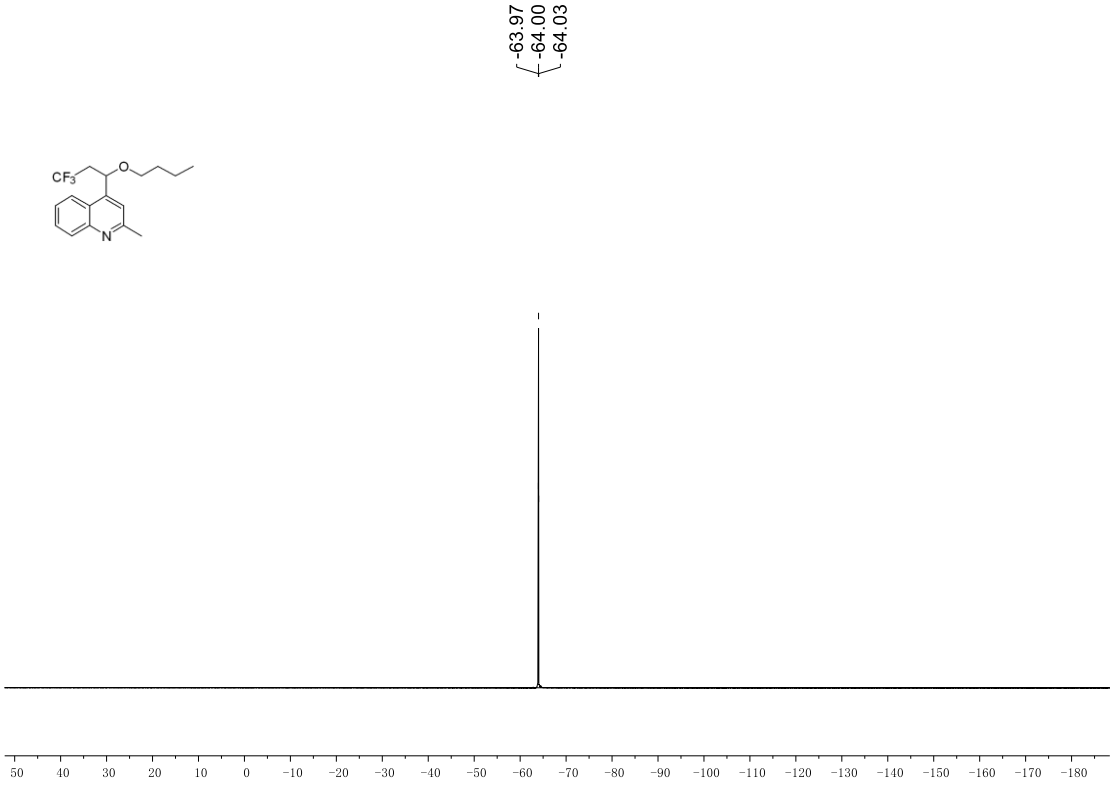
^{1}H NMR spectrum of compound **5c** in $CDCl_3$ (400 MHz)



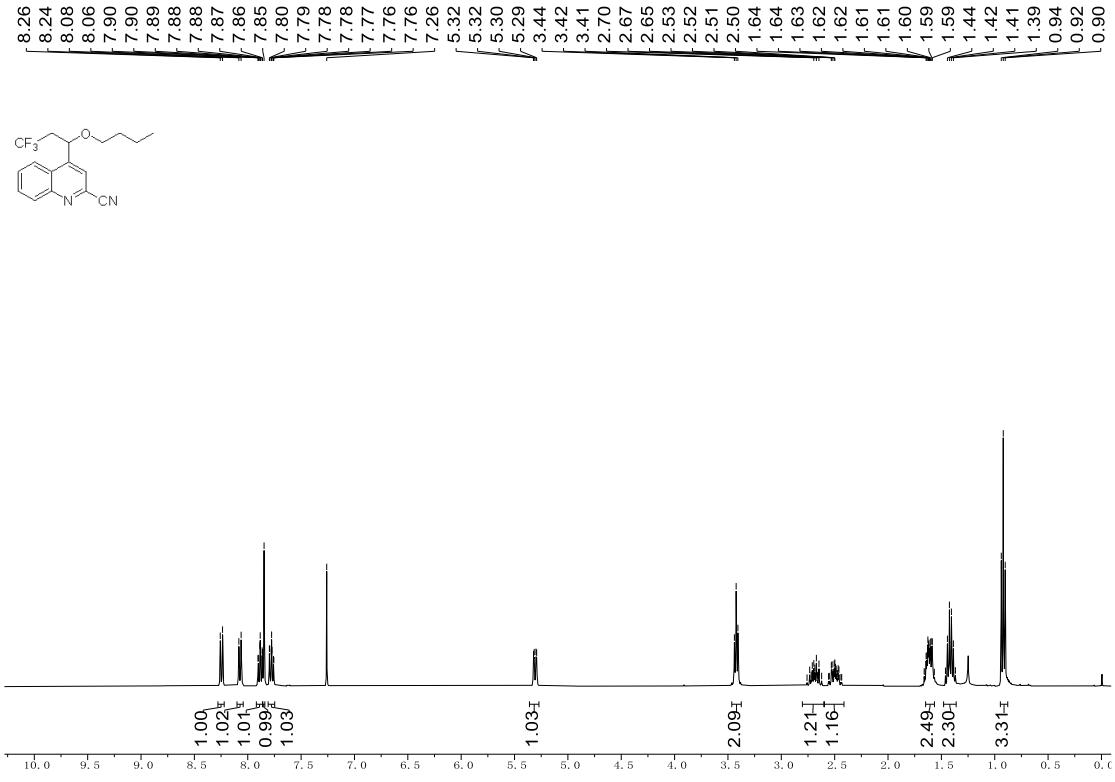
^{13}C NMR spectrum of compound **5c** in $CDCl_3$ (151 MHz)



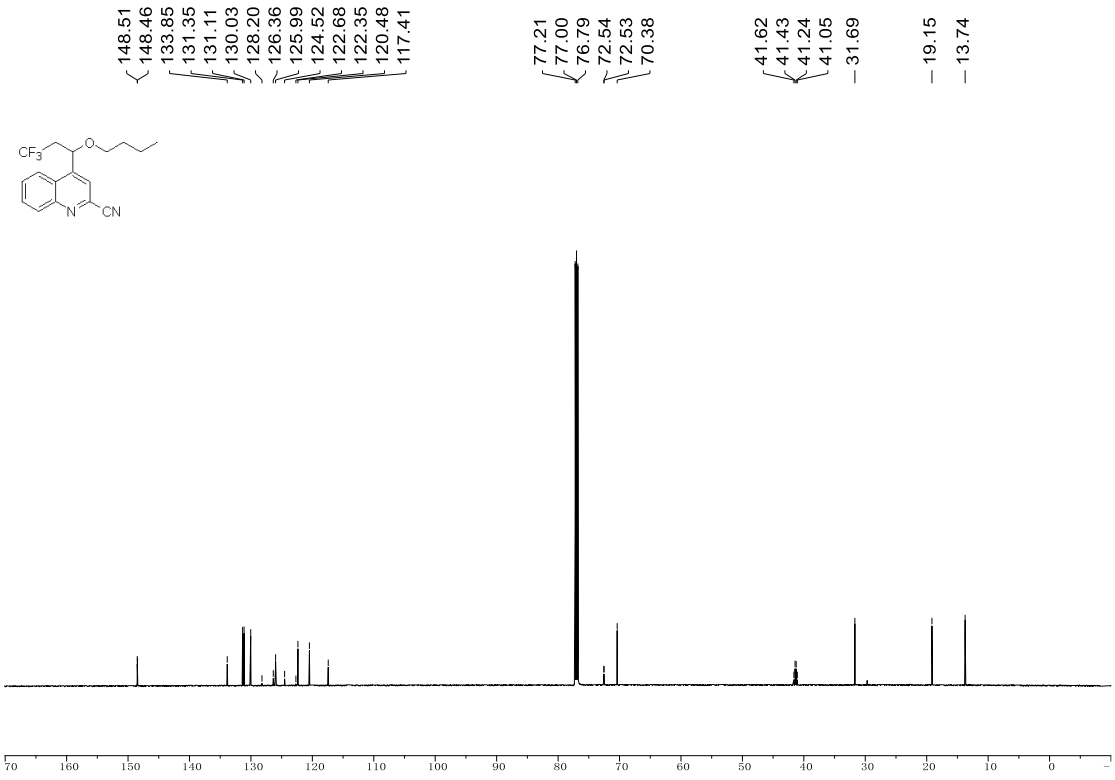
^{19}F NHR spectrum of compound **5c** in $CDCl_3$ (376 MHz)



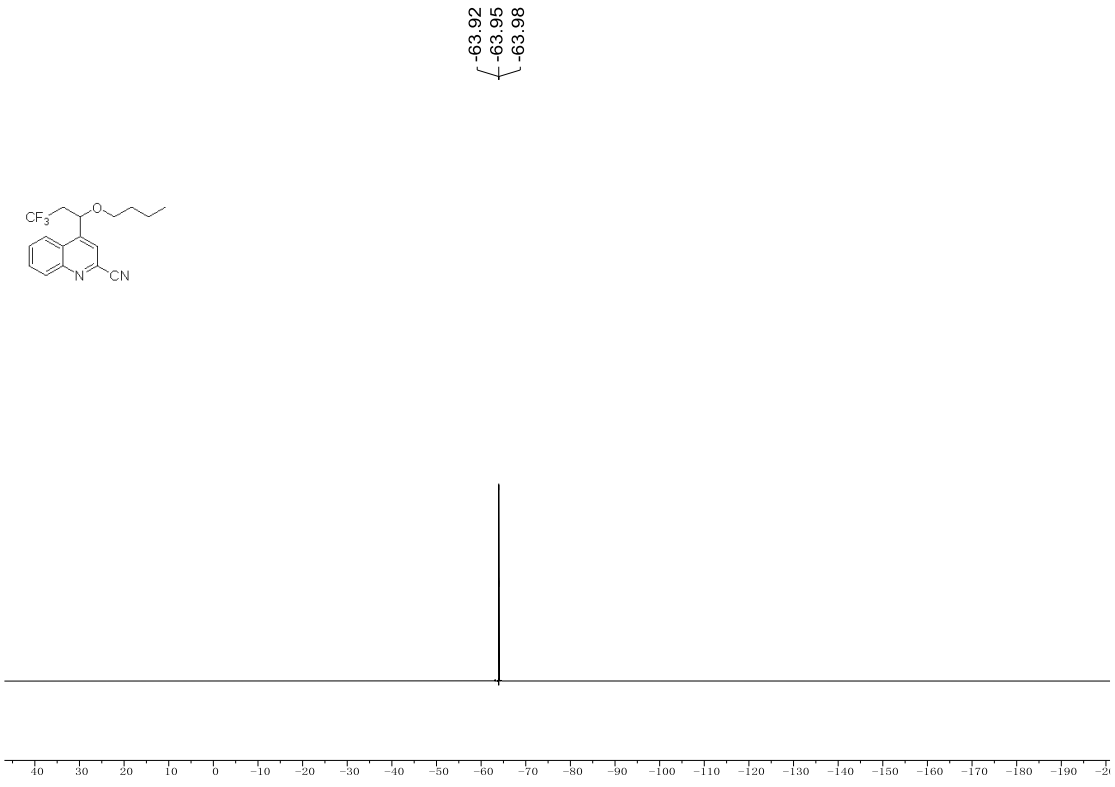
^{1}H NMR spectrum of compound **5d** in $CDCl_3$ (400 MHz)



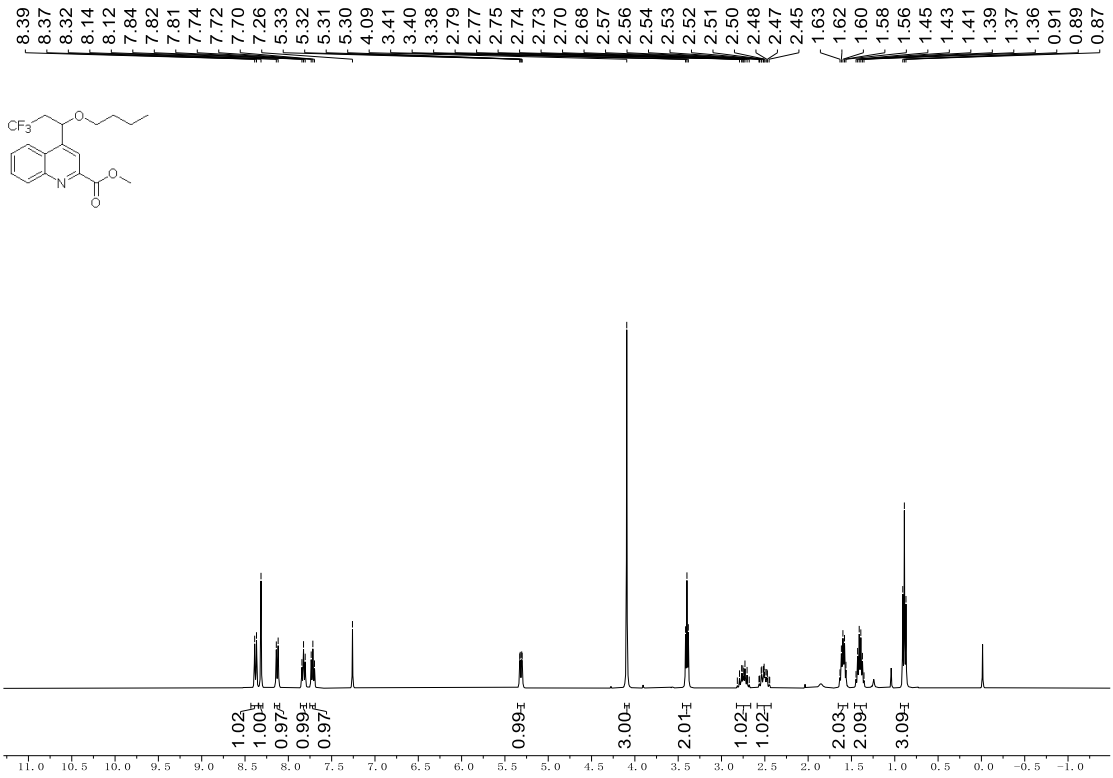
^{13}C NMR spectrum of compound **5d** in $CDCl_3$ (151 MHz)



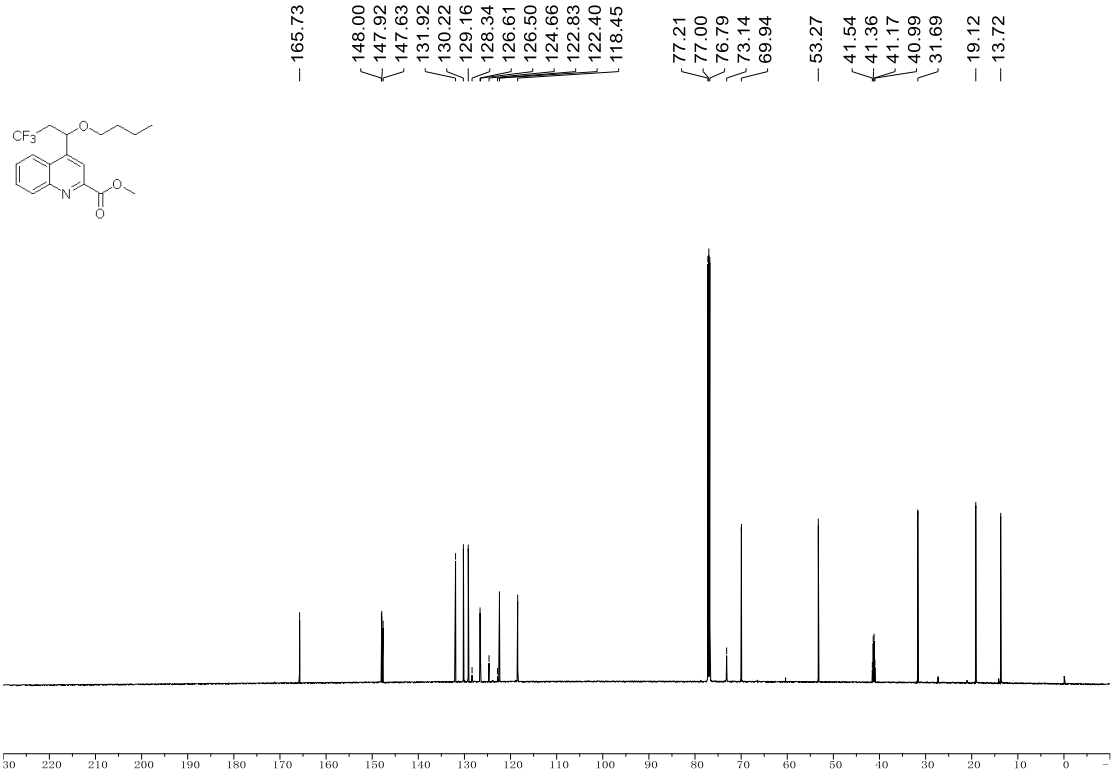
^{19}F NHR spectrum of compound **5d** in $CDCl_3$ (376 MHz)



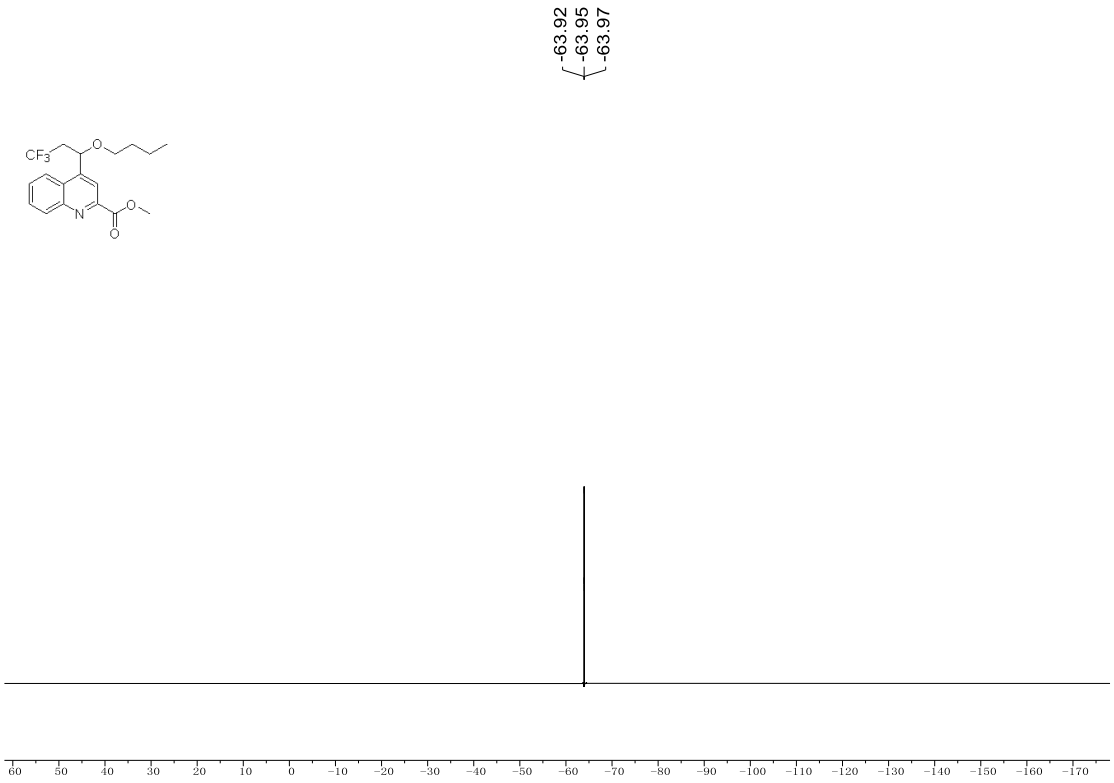
^{1}H NMR spectrum of compound **5e** in $CDCl_3$ (400 MHz)



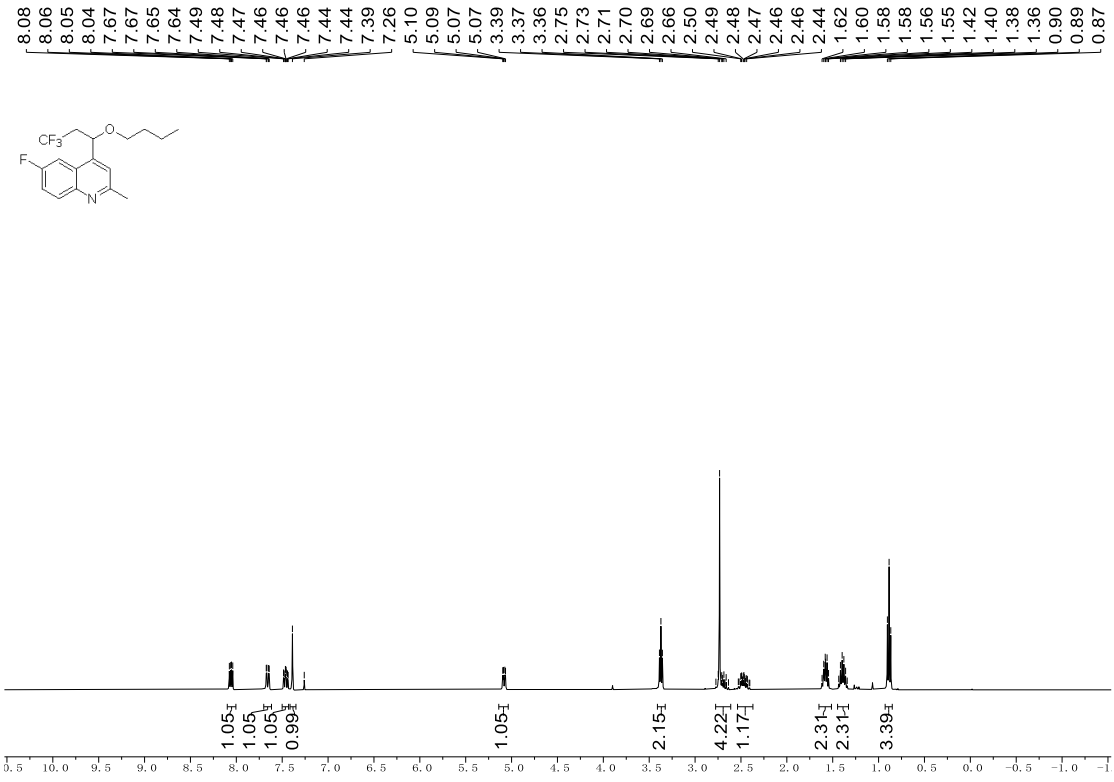
^{13}C NMR spectrum of compound **5e** in $CDCl_3$ (151 MHz)



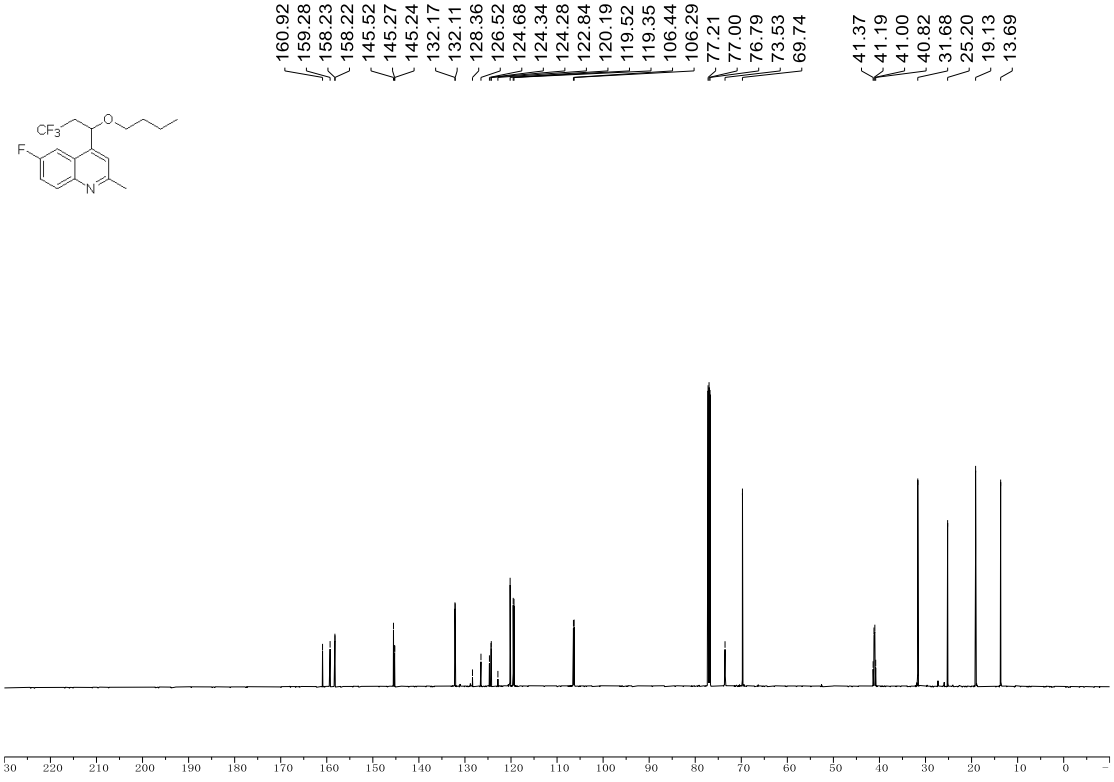
^{19}F NHR spectrum of compound **5e** in $CDCl_3$ (376 MHz)



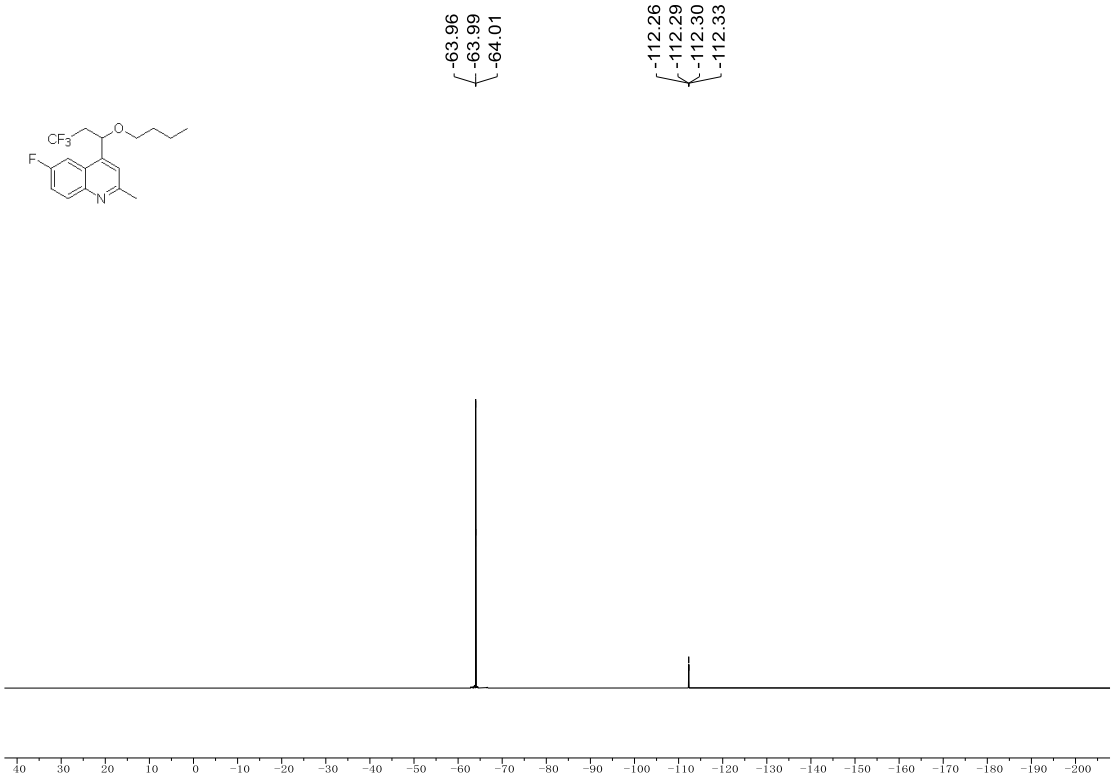
^{1}H NMR spectrum of compound **5f** in $CDCl_3$ (400 MHz)



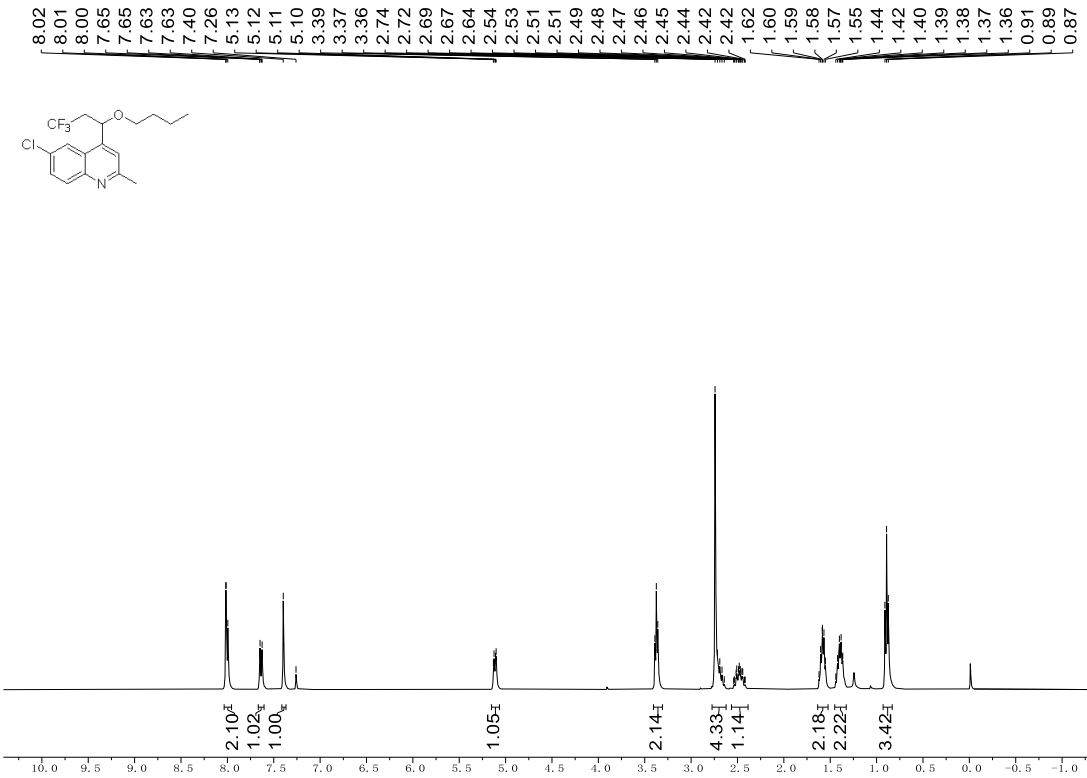
^{13}C NMR spectrum of compound **5f** in $CDCl_3$ (151 MHz)



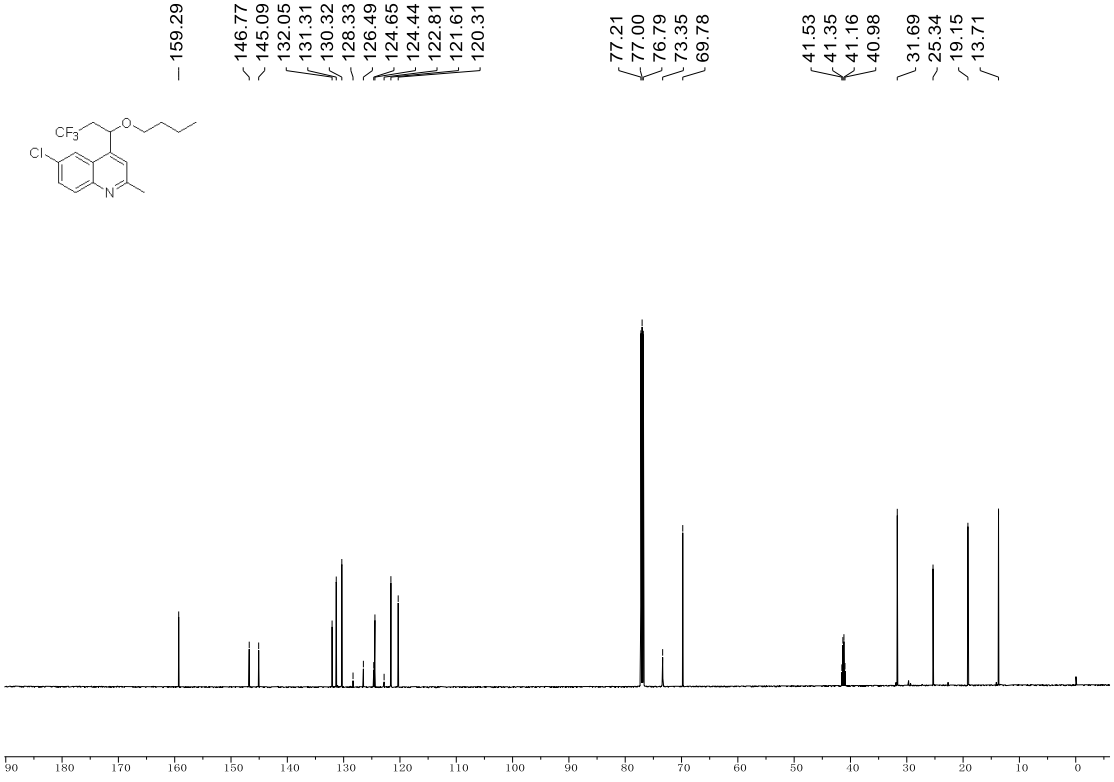
^{19}F NHR spectrum of compound **5f** in $CDCl_3$ (376 MHz)



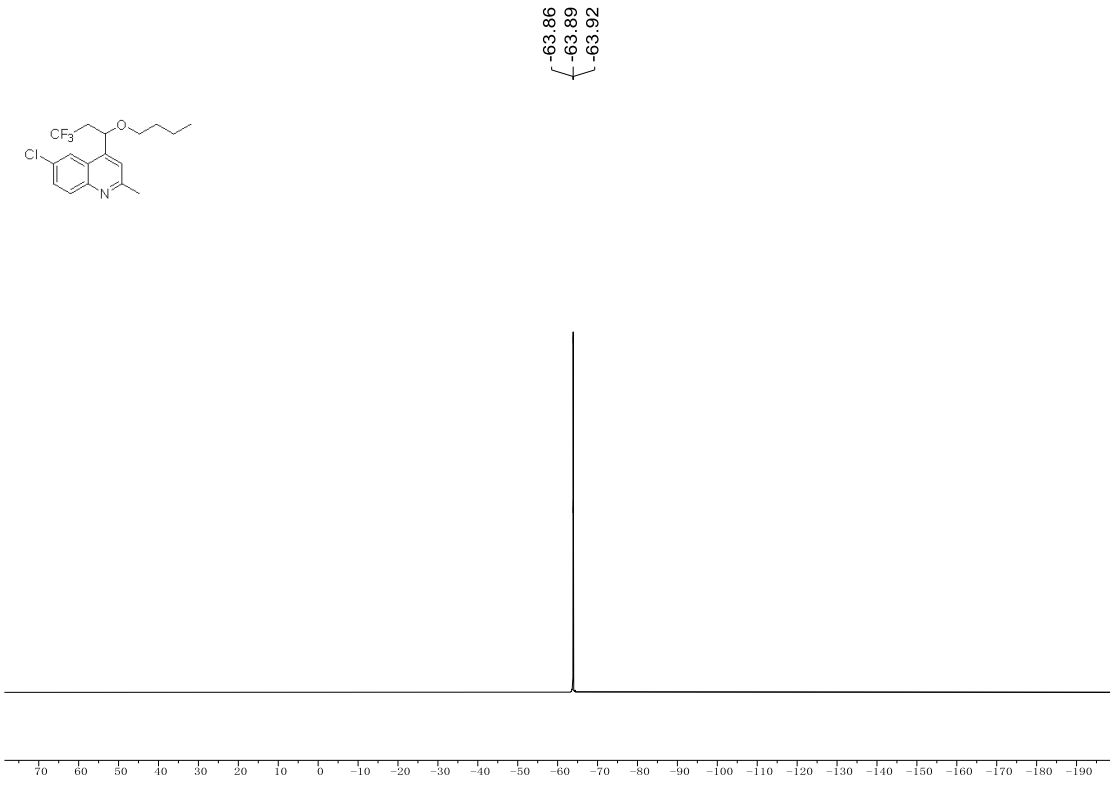
^{1}H NMR spectrum of compound **5g** in $CDCl_3$ (400 MHz)



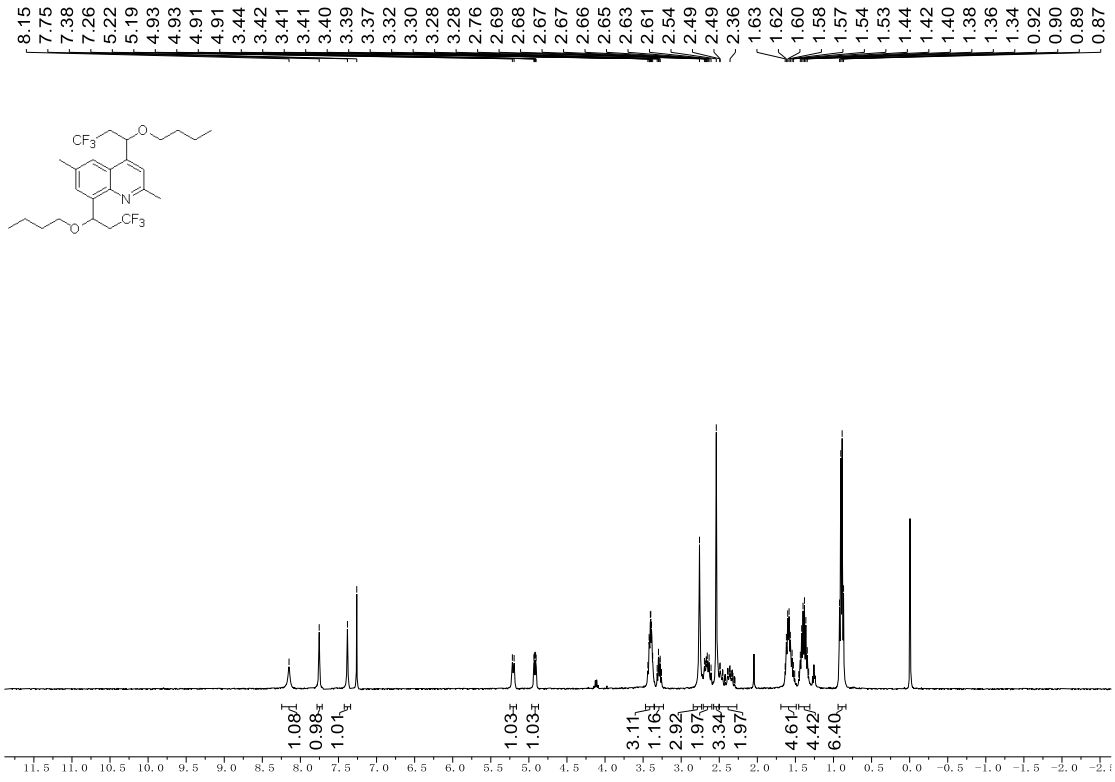
^{13}C NMR spectrum of compound **5g** in $CDCl_3$ (151 MHz)



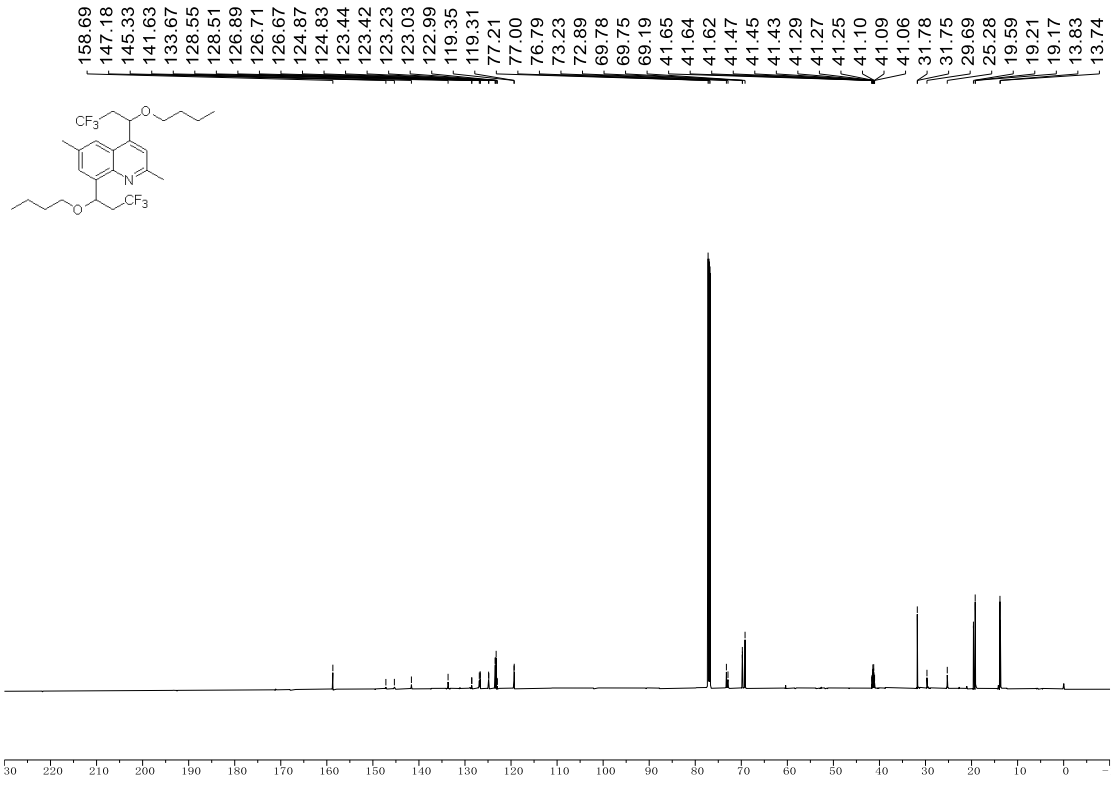
^{19}F NHR spectrum of compound **5g** in $CDCl_3$ (376 MHz)



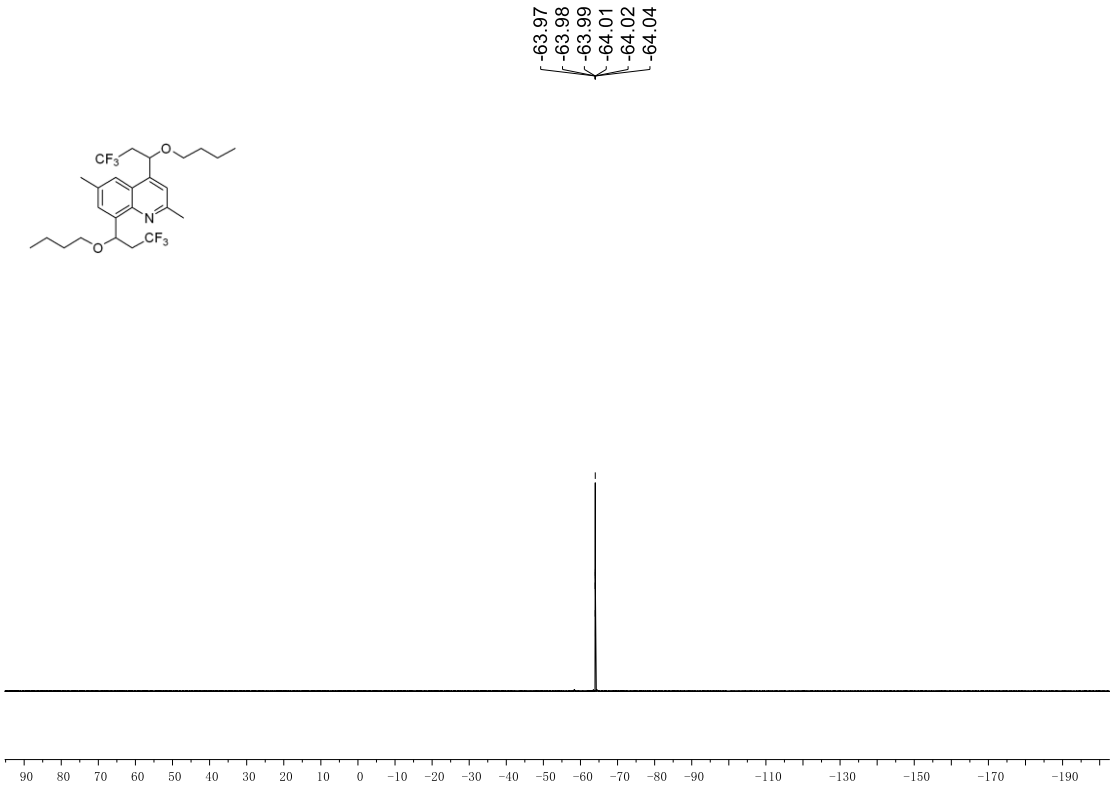
^{1}H NMR spectrum of compound **5h** in $CDCl_3$ (400 MHz)



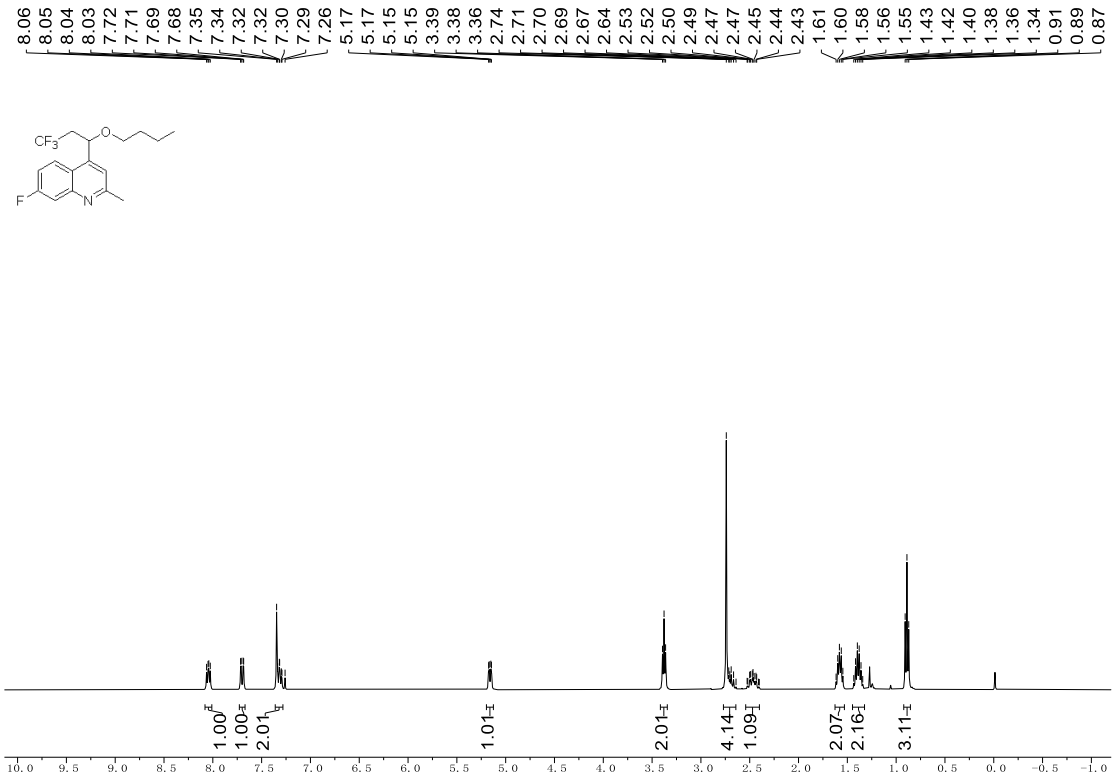
^{13}C NMR spectrum of compound **5h** in $CDCl_3$ (151 MHz)



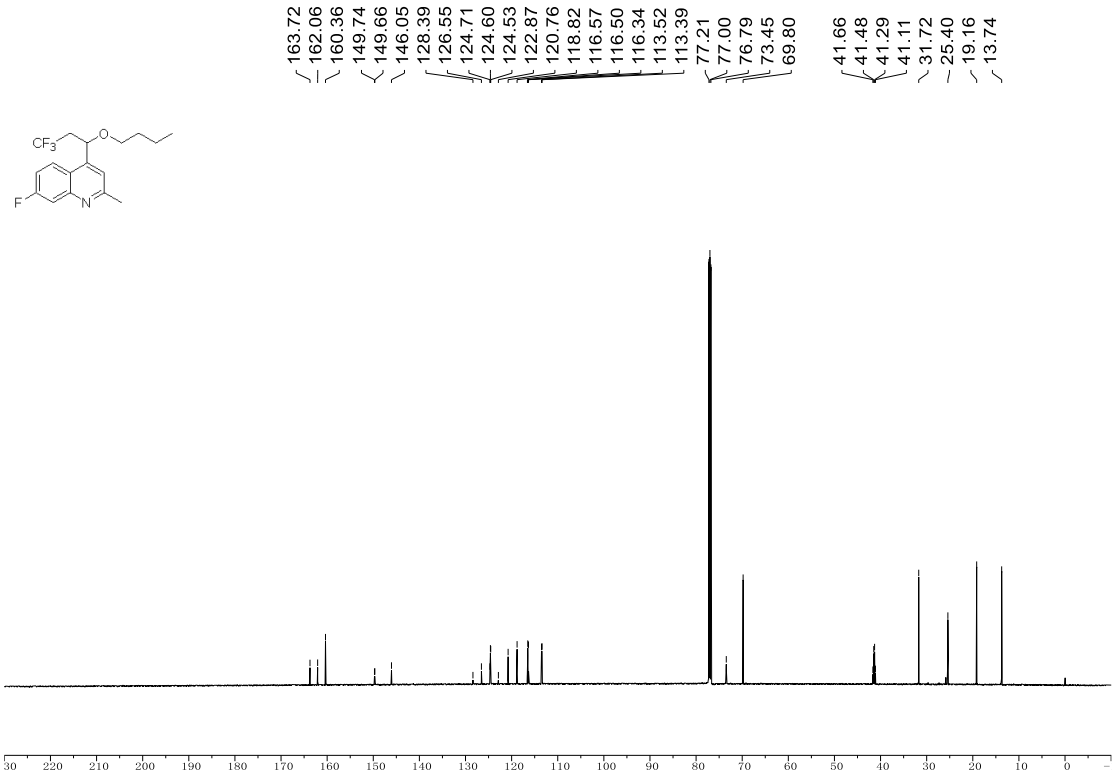
^{19}F NHR spectrum of compound **5h** in CDCl3 (376 MHz)



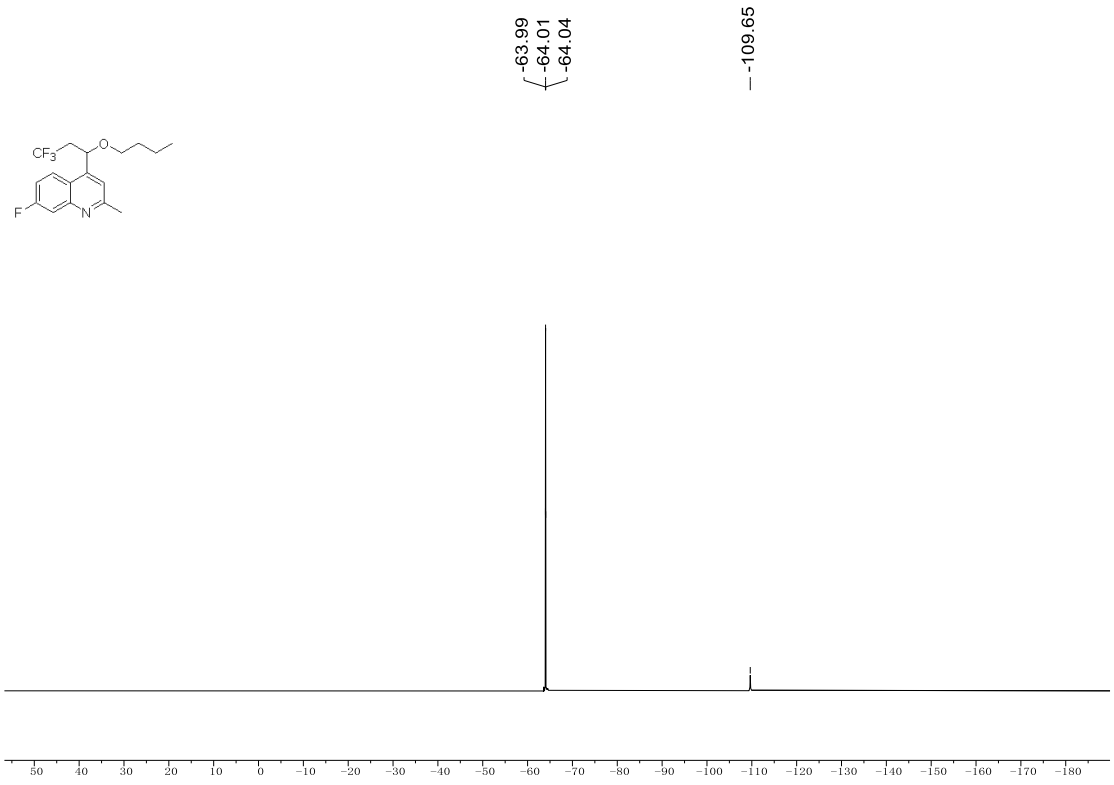
^{1}H NMR spectrum of compound **5i** in $CDCl_3$ (400 MHz)



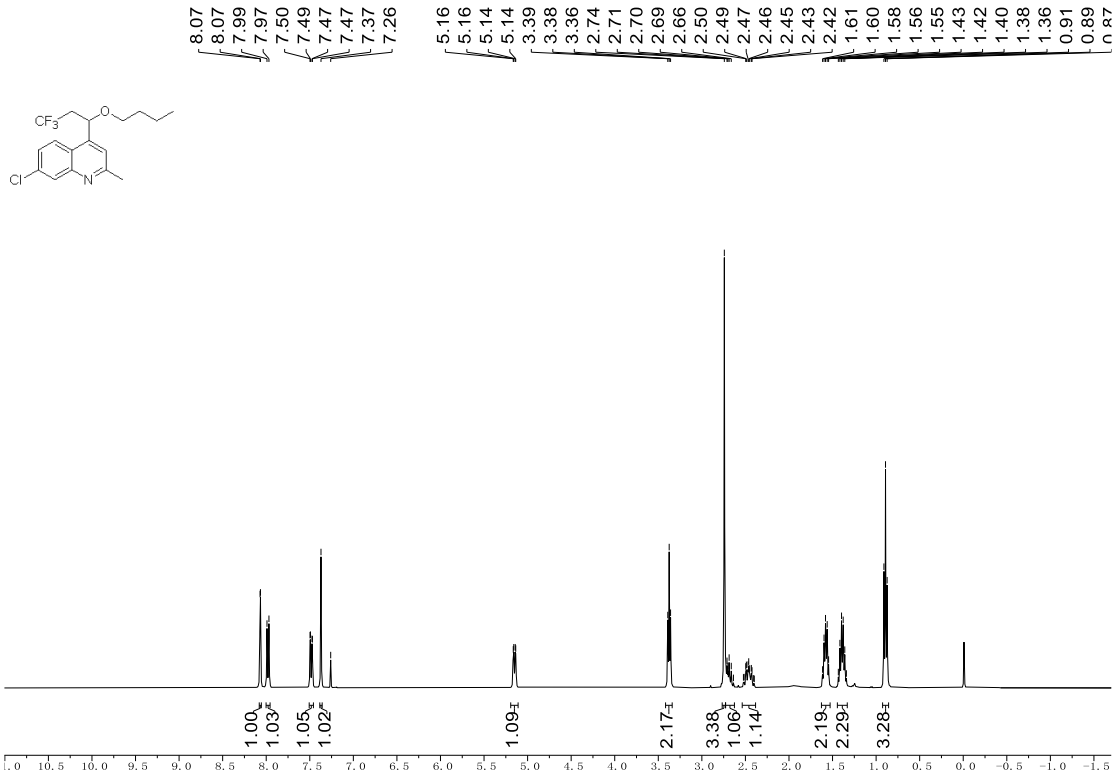
^{13}C NMR spectrum of compound **5i** in $CDCl_3$ (151 MHz)



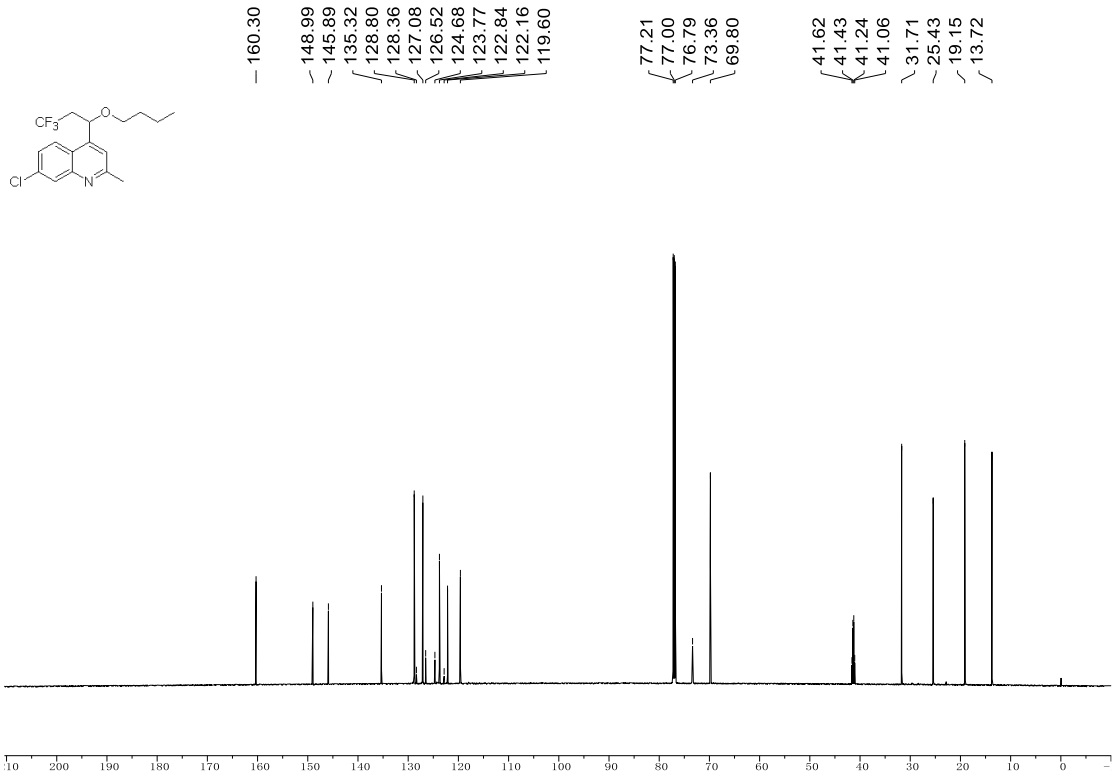
^{19}F NHR spectrum of compound **5i** in $CDCl_3$ (376 MHz)



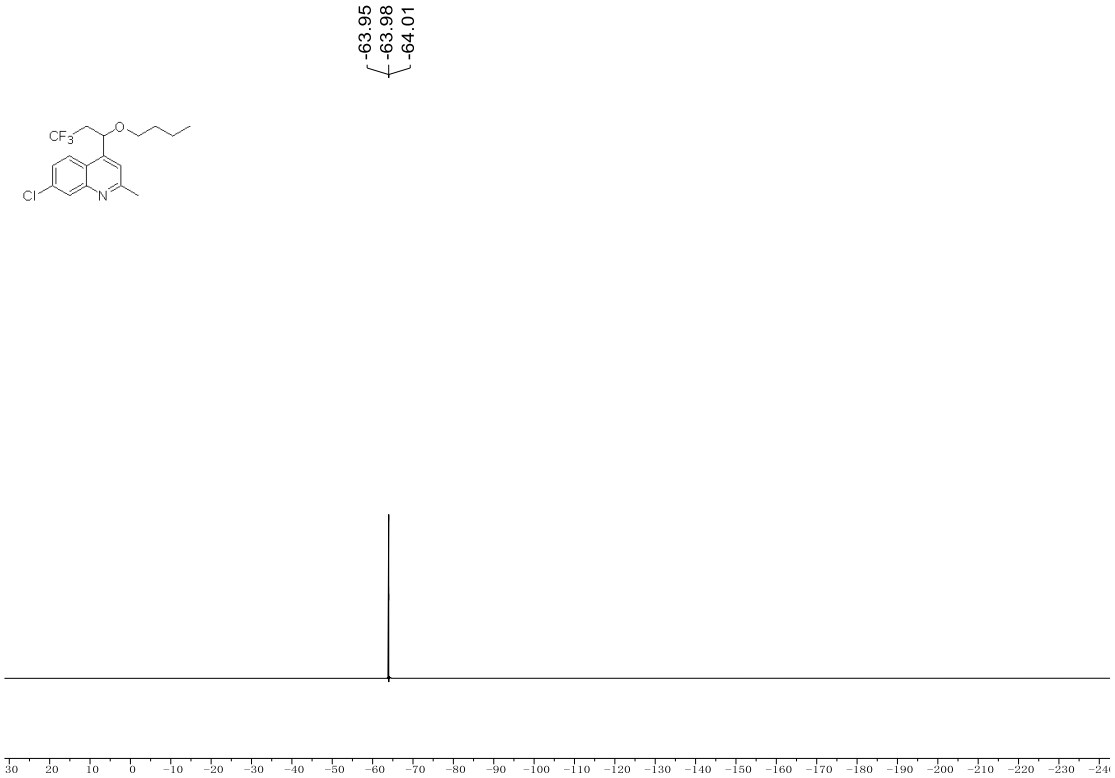
^{1}H NMR spectrum of compound **5j** in $CDCl_3$ (400 MHz)



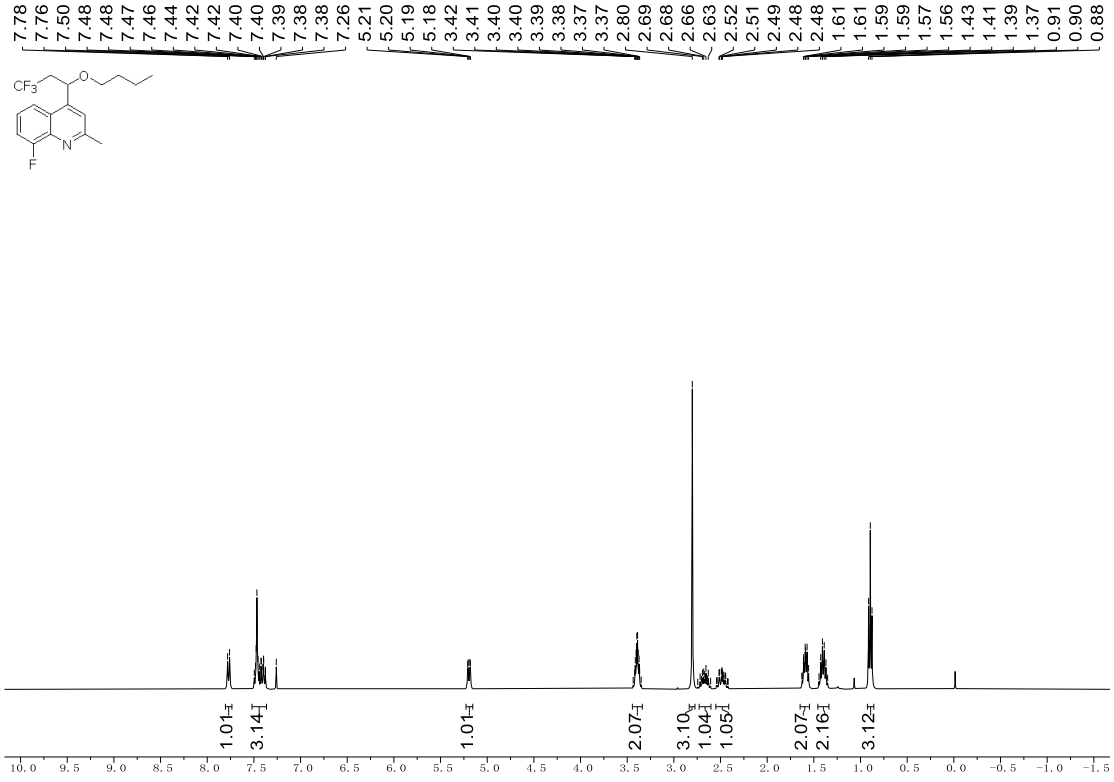
^{13}C NMR spectrum of compound **5j** in $CDCl_3$ (151 MHz)



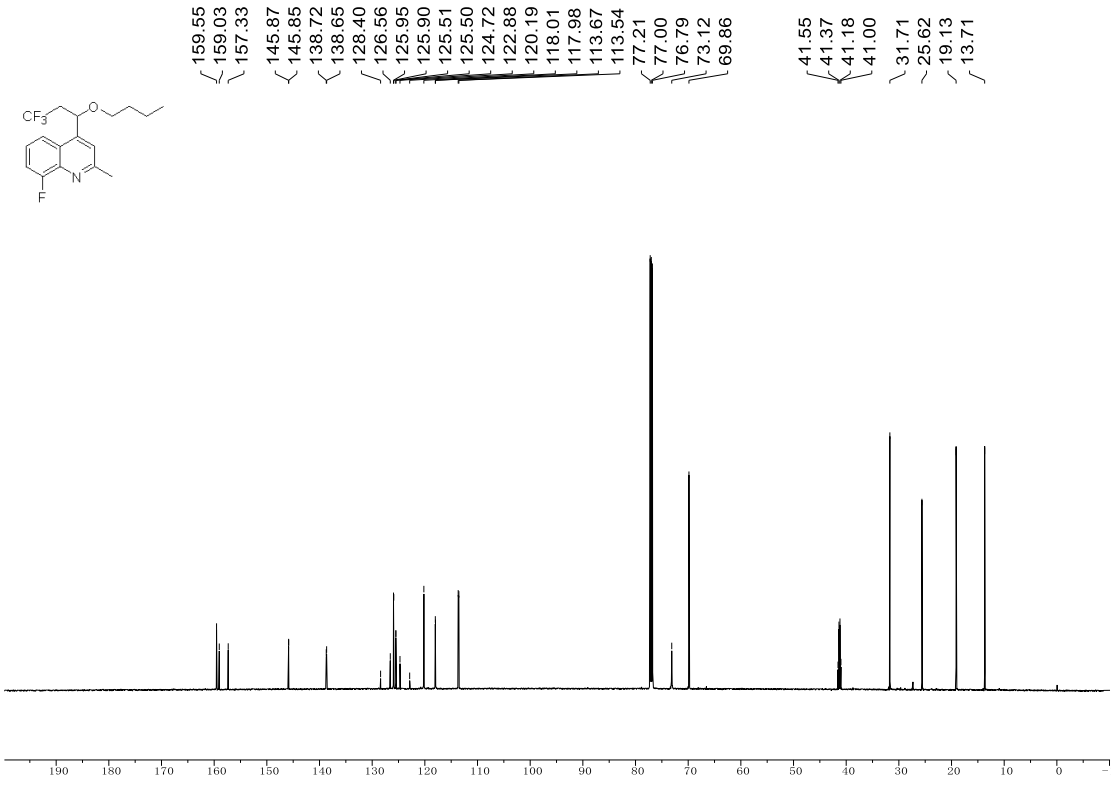
^{19}F NHR spectrum of compound **5j** in $CDCl_3$ (376 MHz)



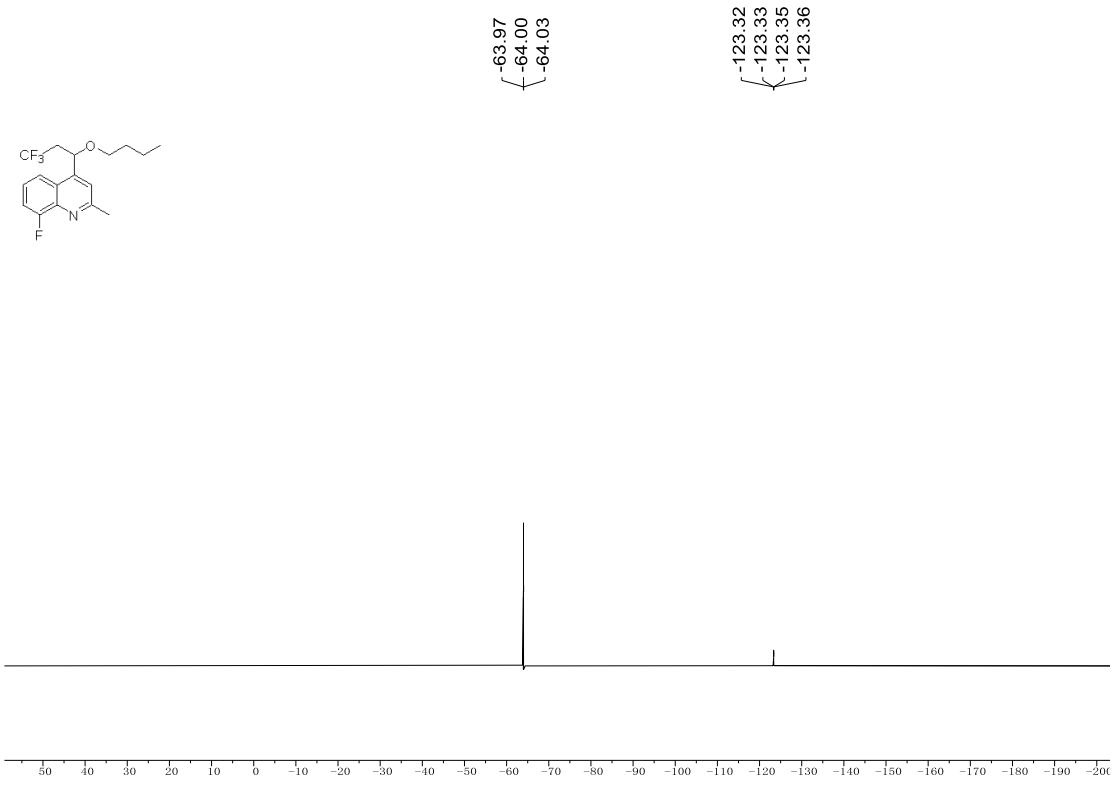
^{1}H NMR spectrum of compound **5k** in $CDCl_3$ (400 MHz)



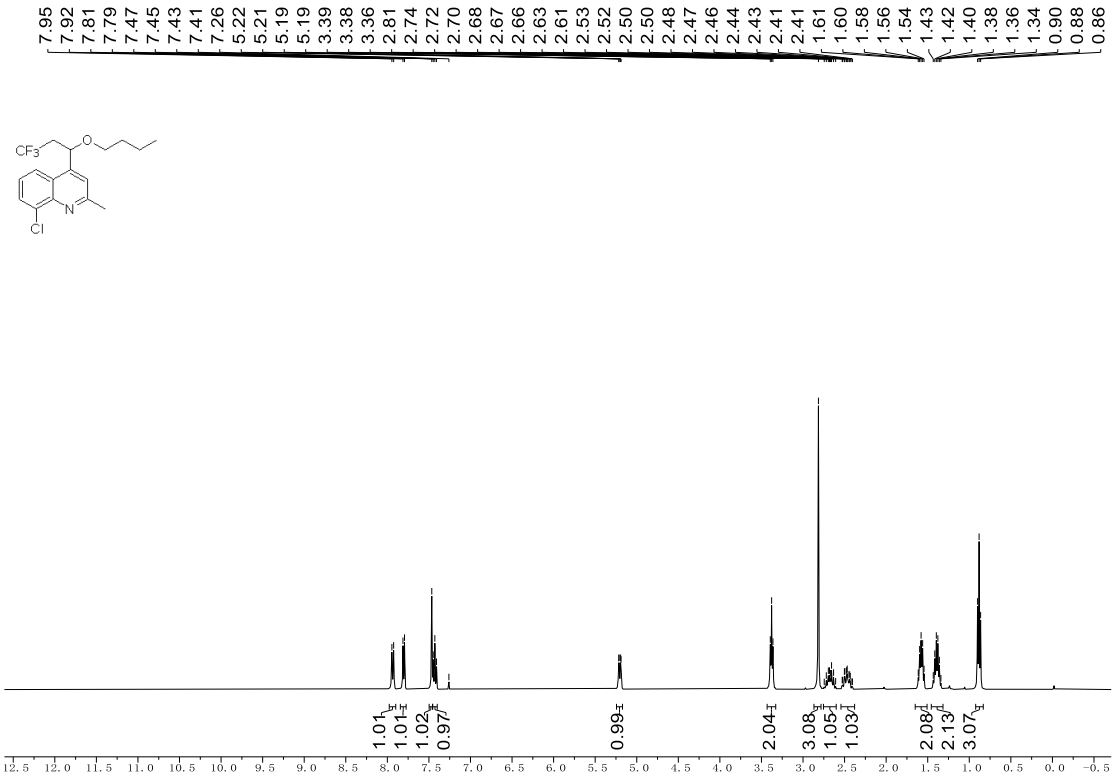
^{13}C NMR spectrum of compound **5k** in $CDCl_3$ (151 MHz)



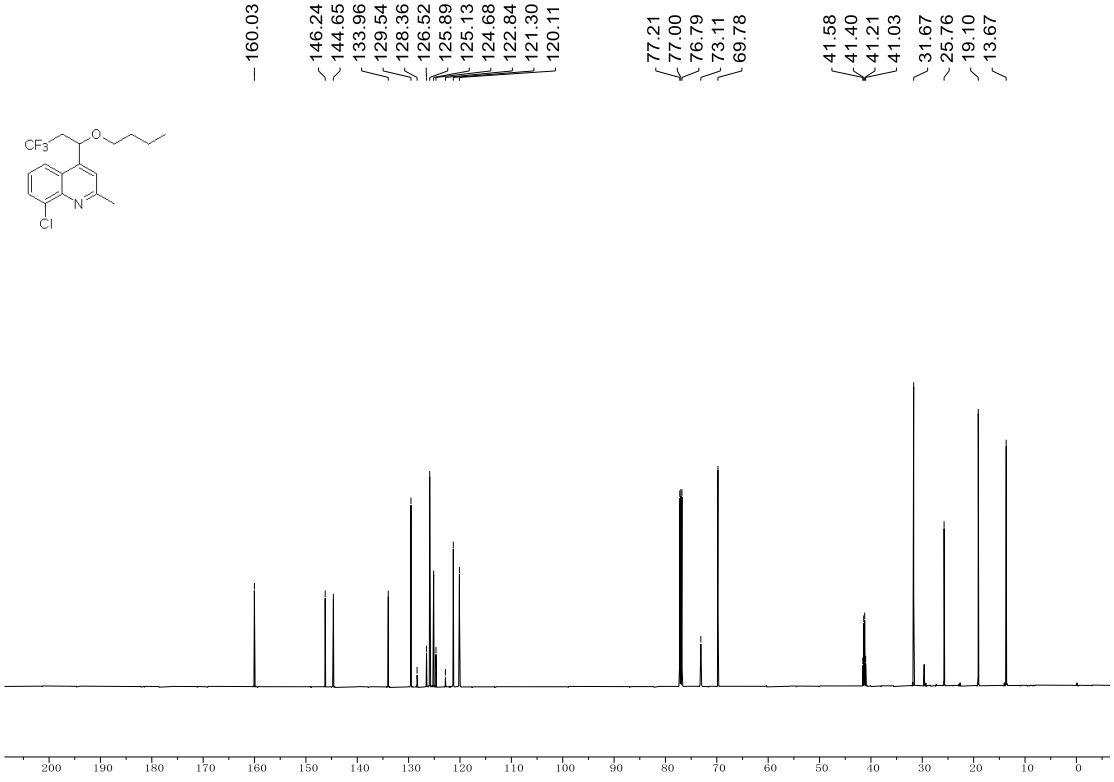
^{19}F NHR spectrum of compound **5k** in $CDCl_3$ (376 MHz)



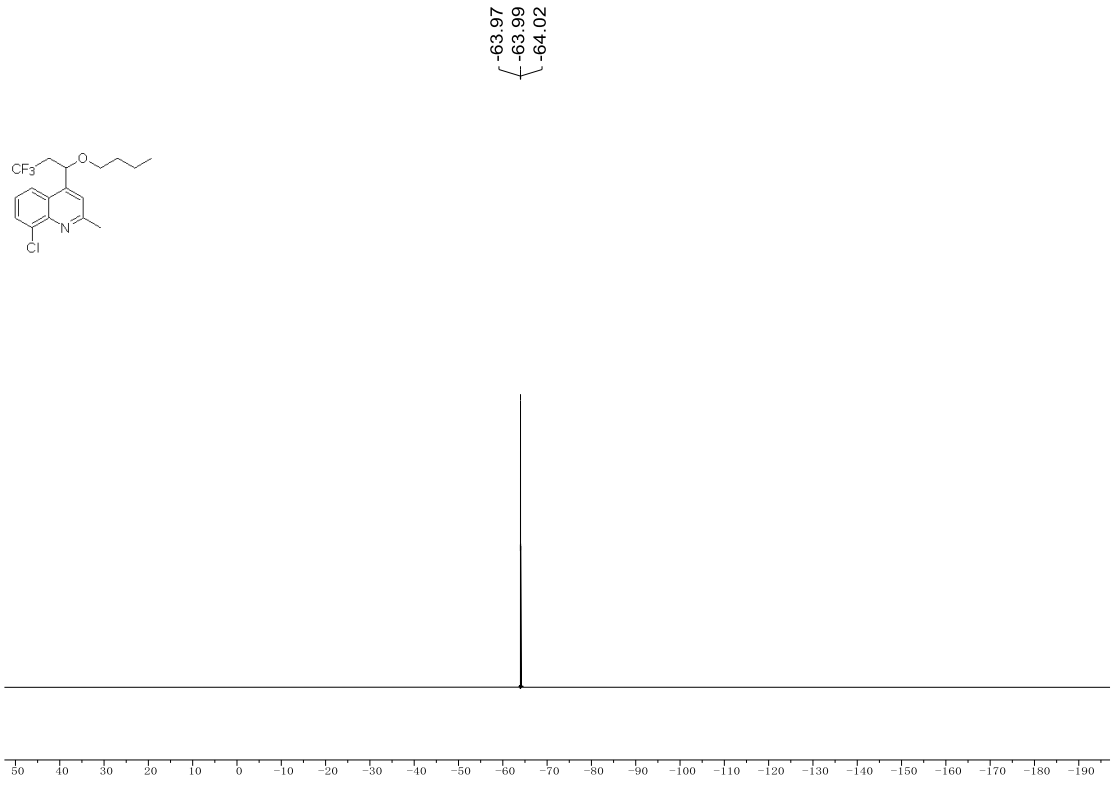
^{1}H NMR spectrum of compound **5l** in $CDCl_3$ (400 MHz)



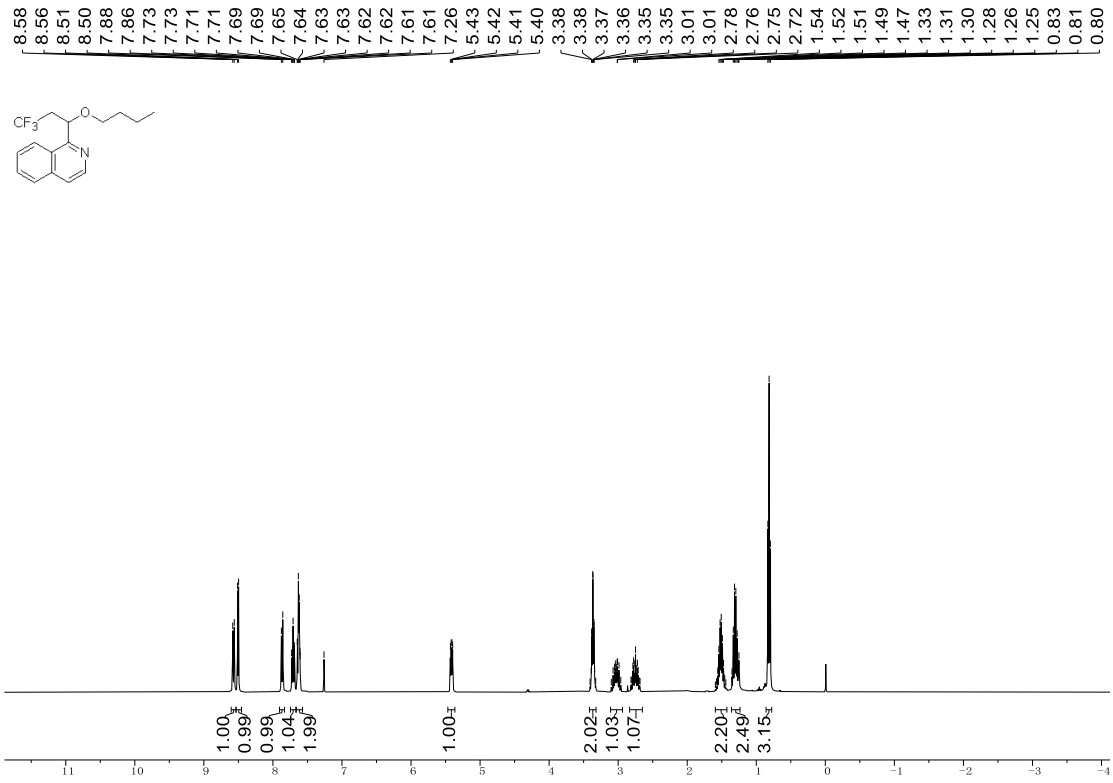
^{13}C NMR spectrum of compound **5l** in $CDCl_3$ (151 MHz)



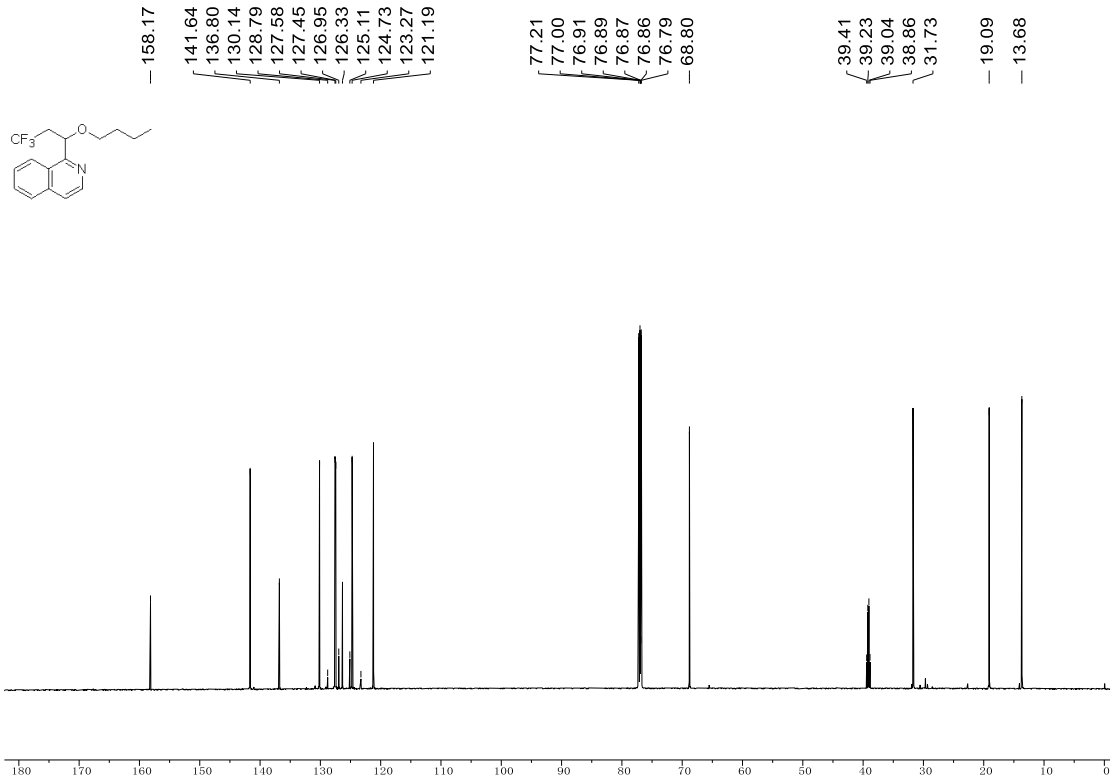
^{19}F NHR spectrum of compound **5l** in $CDCl_3$ (376 MHz)



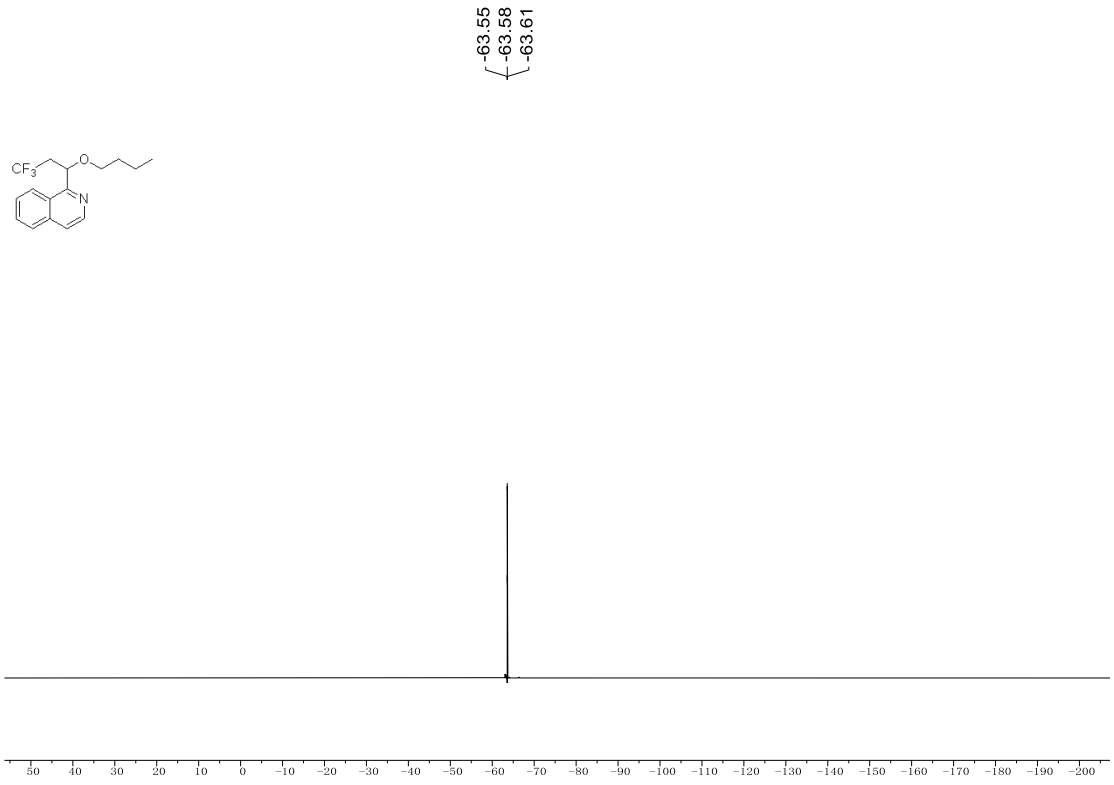
^{1}H NMR spectrum of compound **5m** in $CDCl_3$ (400 MHz)



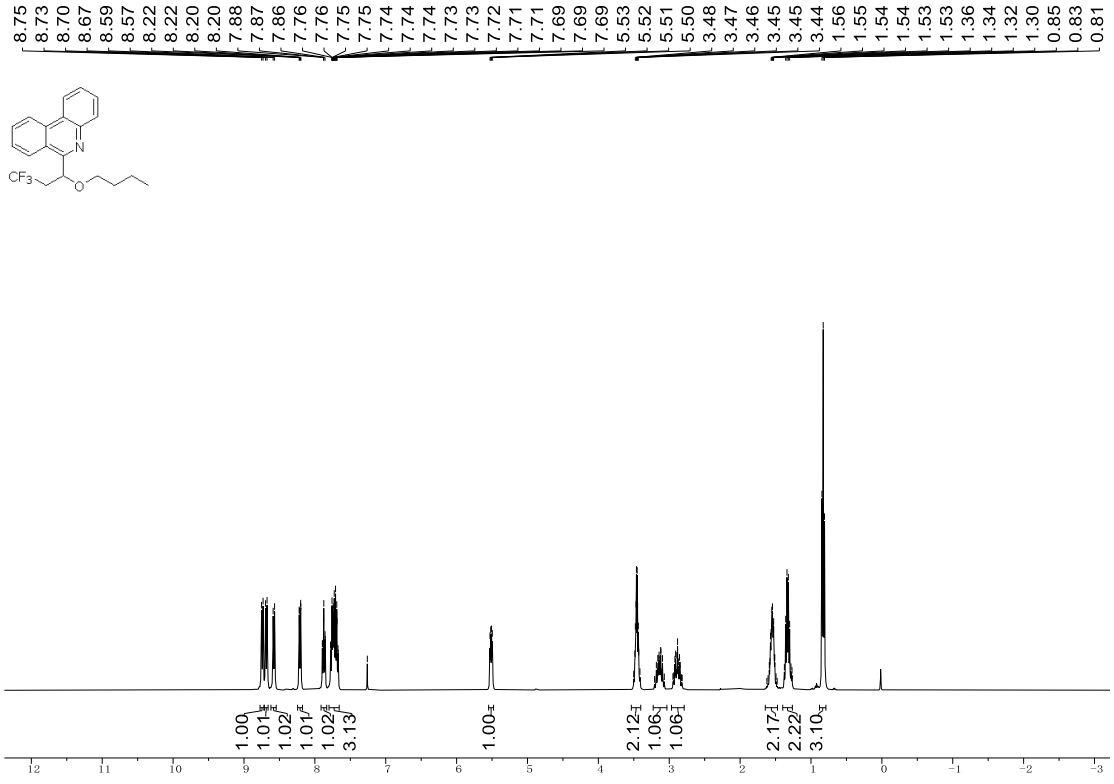
^{13}C NMR spectrum of compound **5m** in $CDCl_3$ (151 MHz)



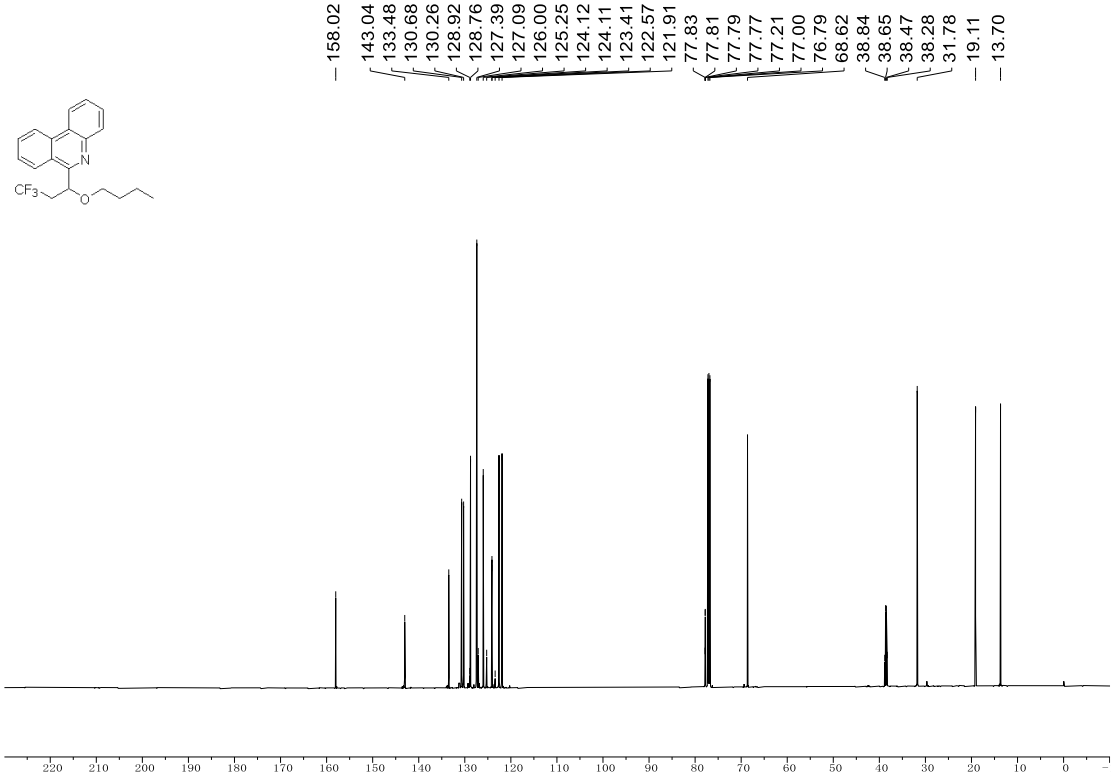
^{19}F NHR spectrum of compound **5m** in $CDCl_3$ (376 MHz)



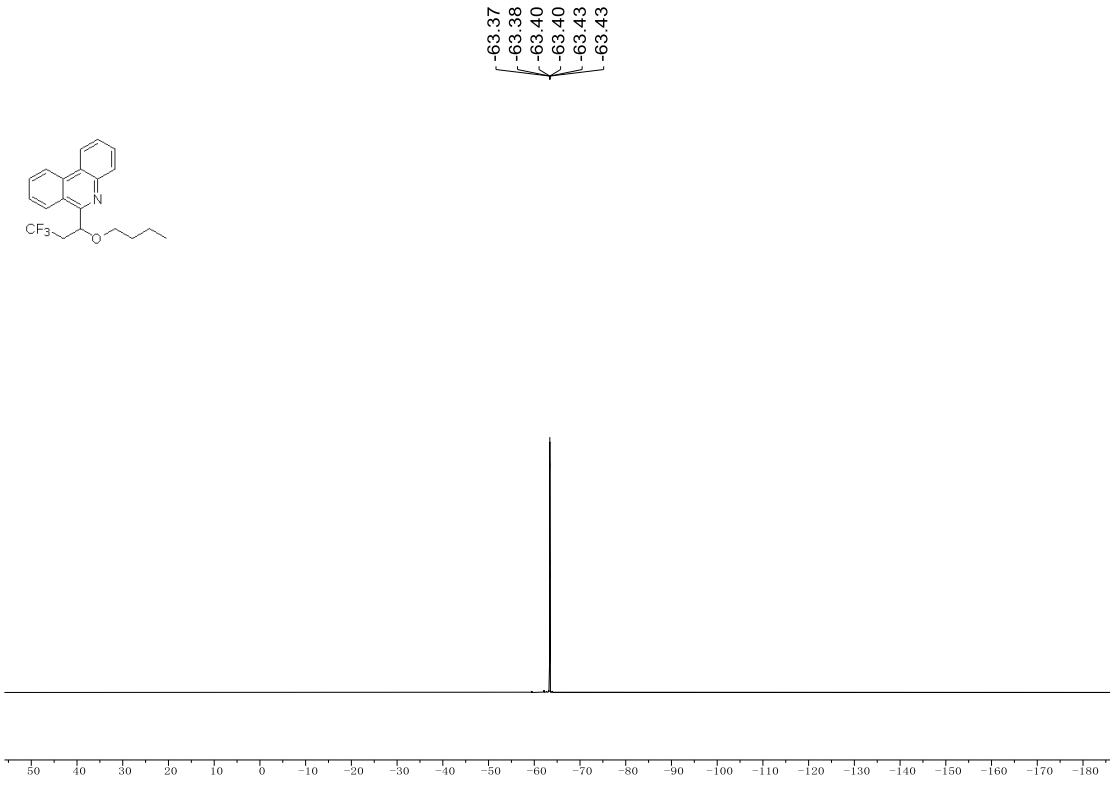
^{1}H NMR spectrum of compound **5n** in $CDCl_3$ (400 MHz)



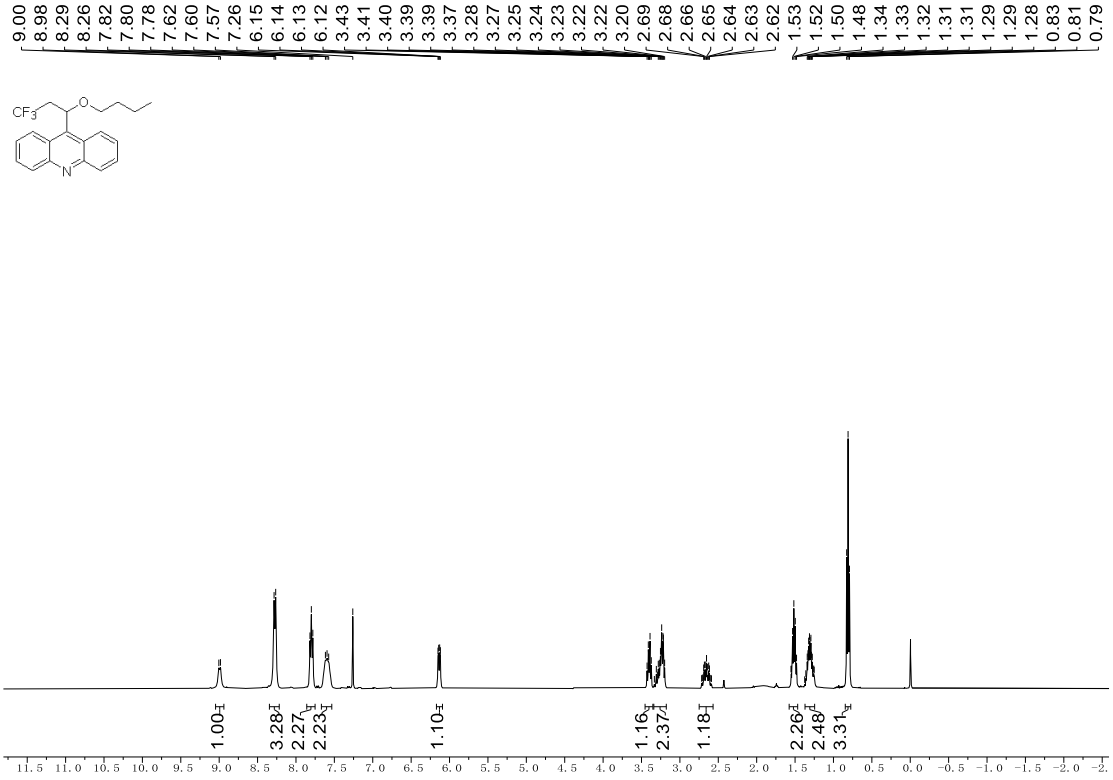
^{13}C NMR spectrum of compound **5n** in CDCl3 (151 MHz)



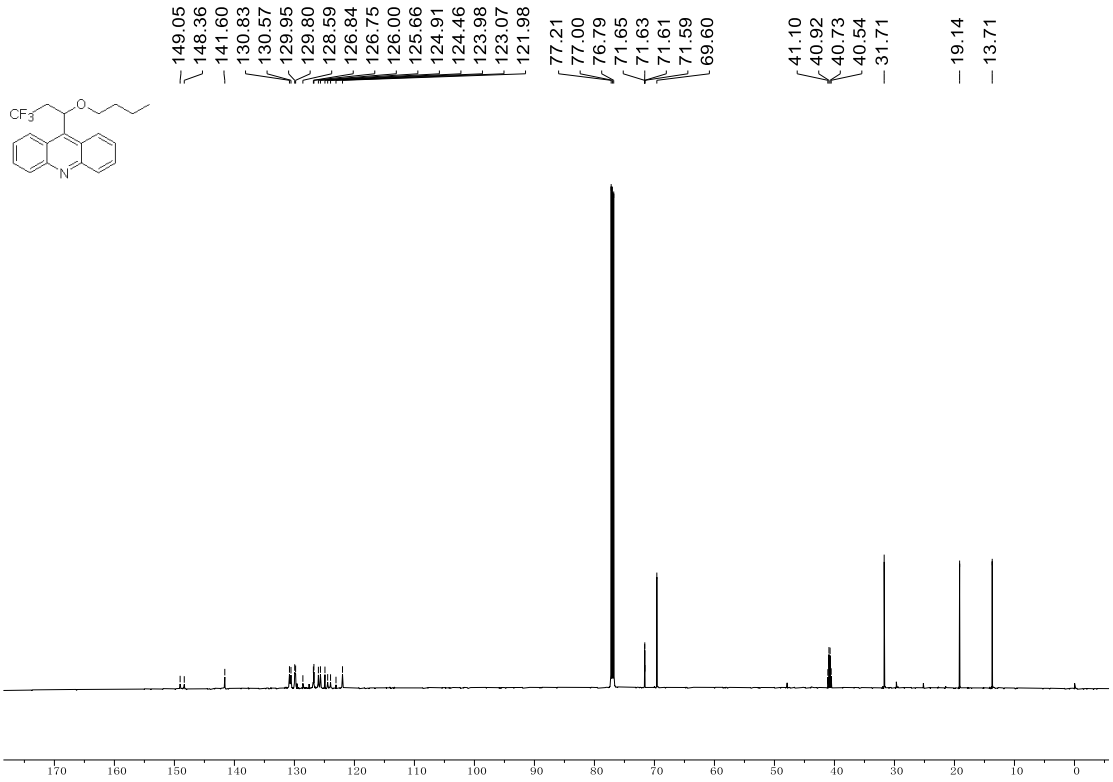
^{19}F NHR spectrum of compound **5n** in $CDCl_3$ (376 MHz)



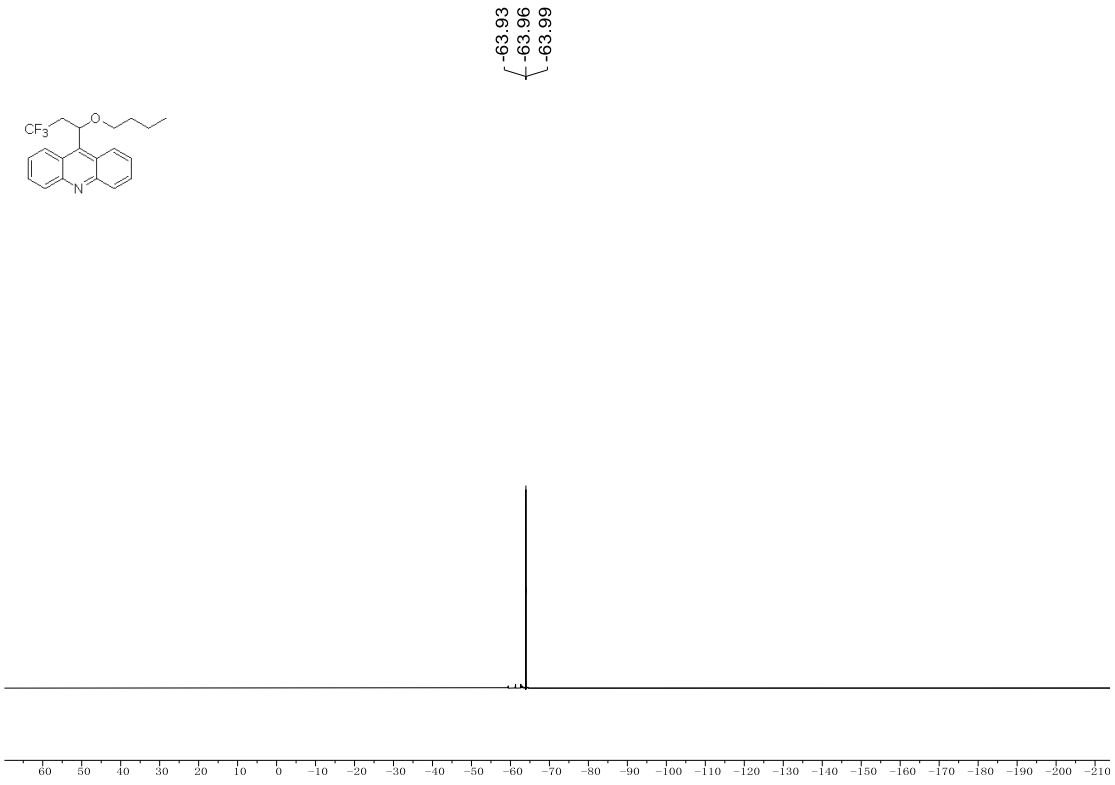
^{1}H NMR spectrum of compound **5o** in $CDCl_3$ (400 MHz)



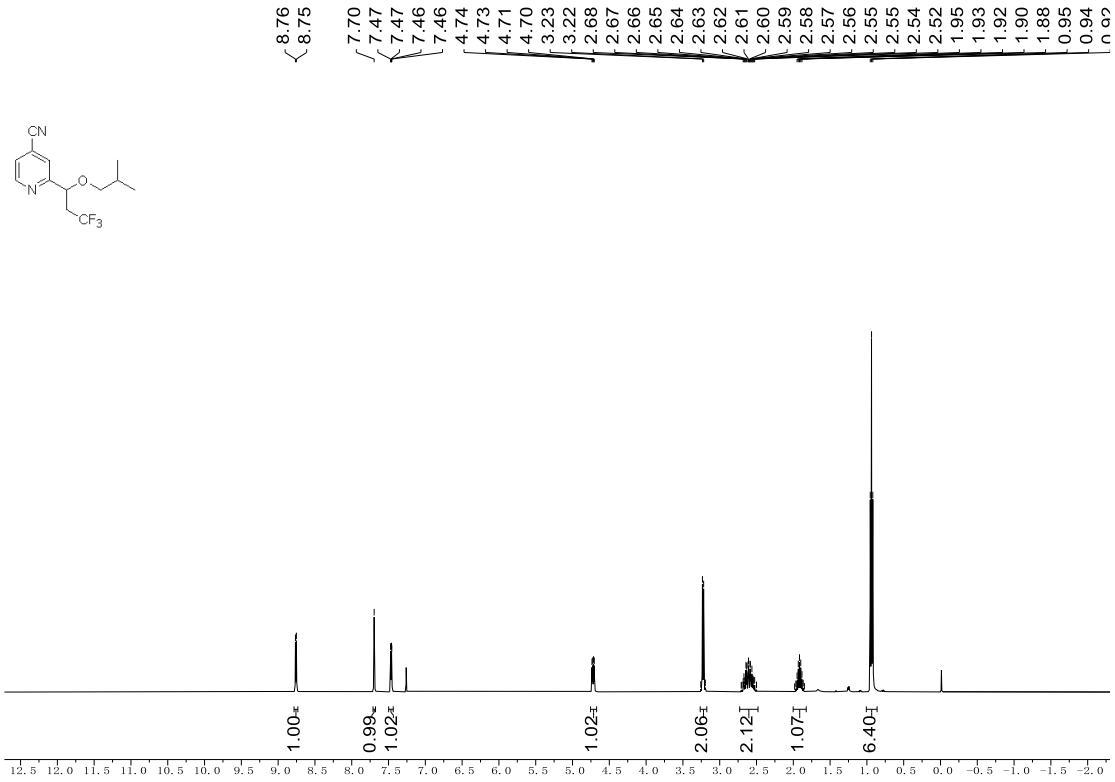
^{13}C NMR spectrum of compound **5o** in $CDCl_3$ (151 MHz)



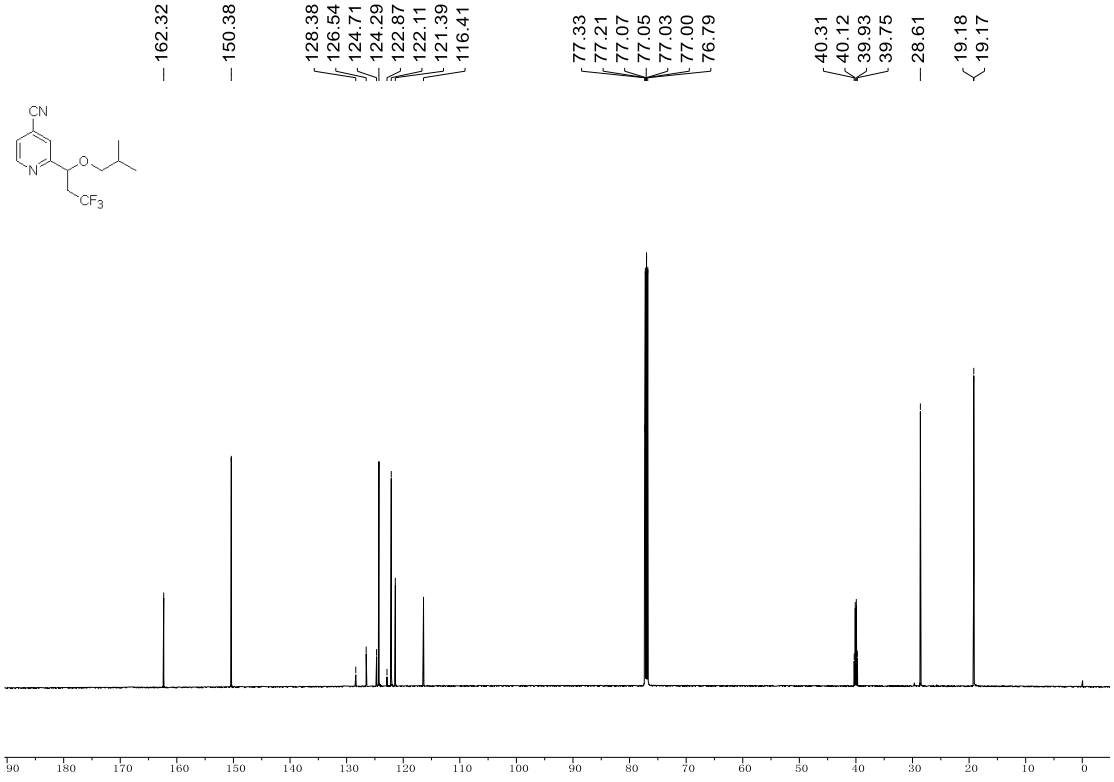
^{19}F NHR spectrum of compound **5o** in $CDCl_3$ (376 MHz)



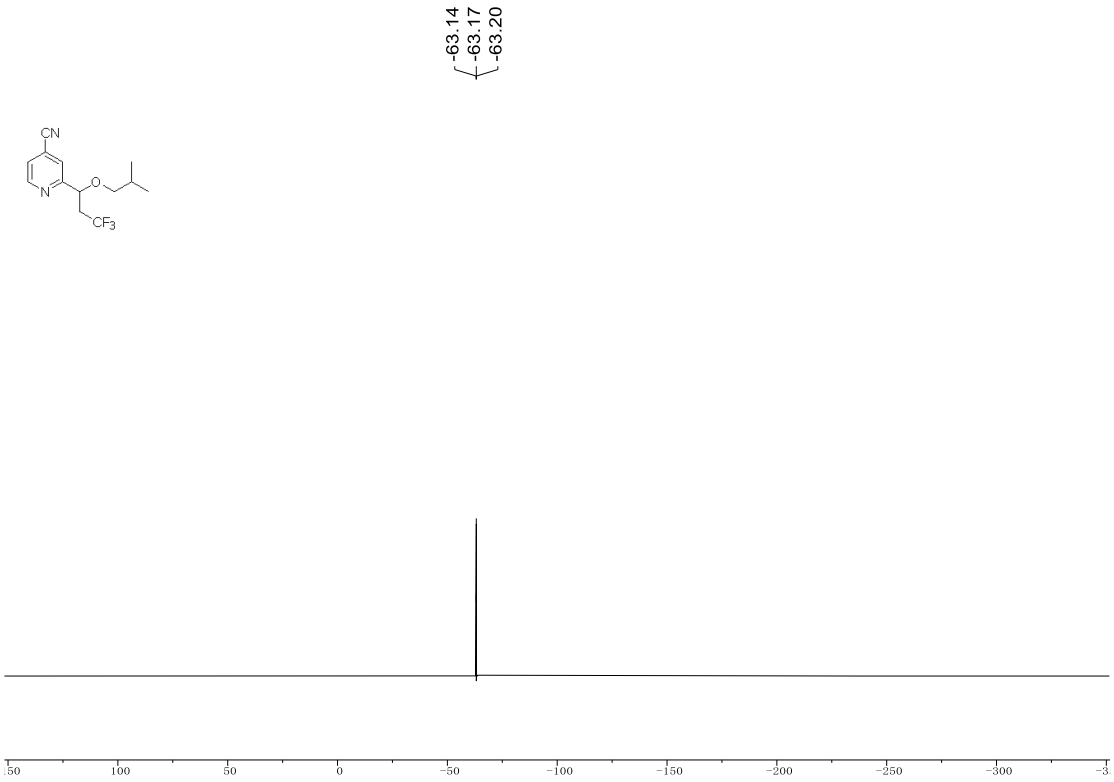
^{1}H NMR spectrum of compound **6a** in $CDCl_3$ (400 MHz)



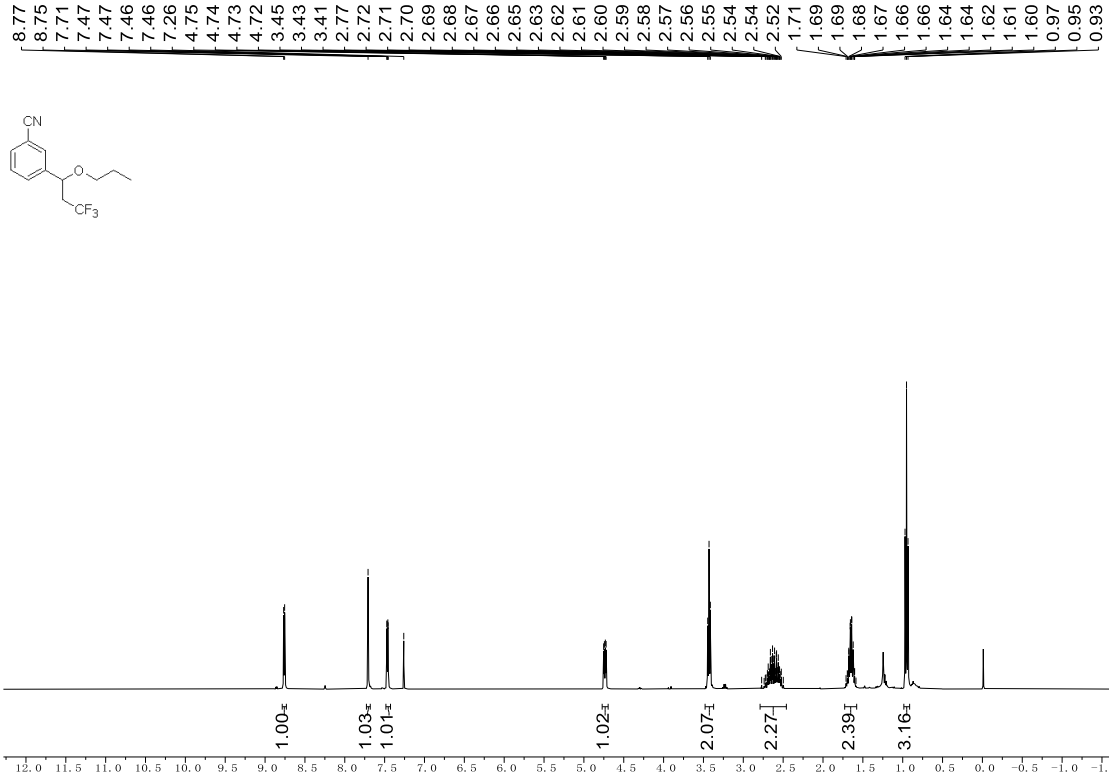
^{13}C NMR spectrum of compound **6a** in $CDCl_3$ (151 MHz)



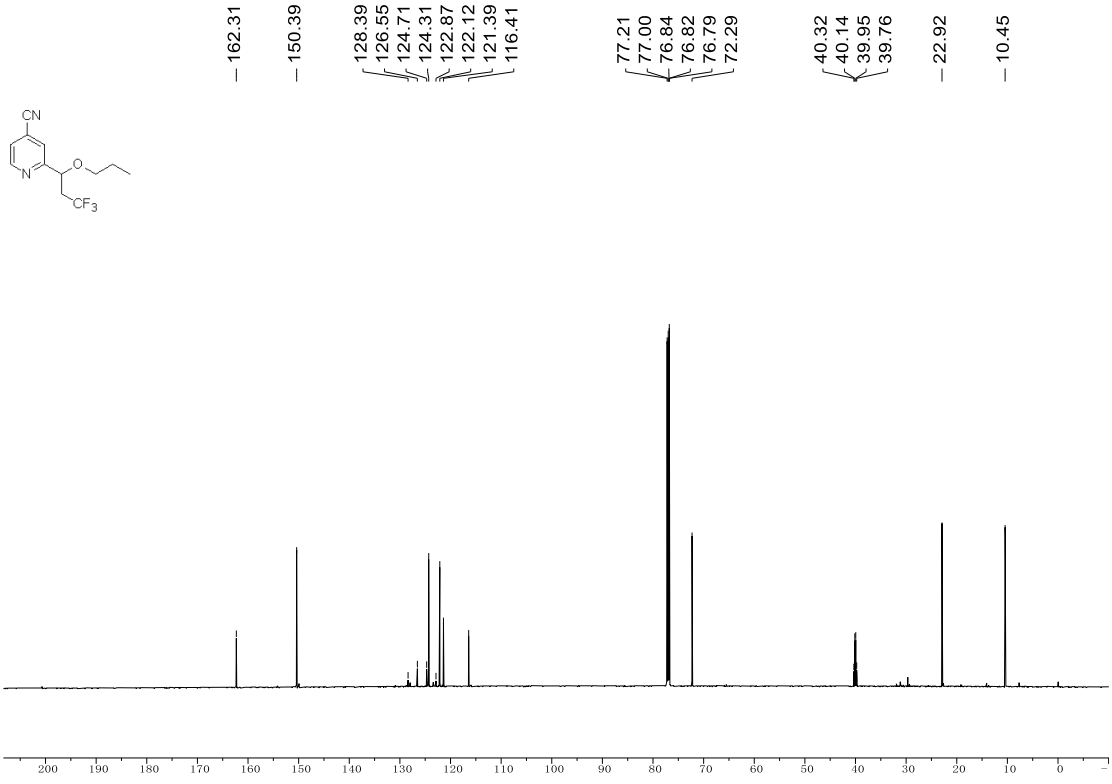
^{19}F NHR spectrum of compound **6a** in $CDCl_3$ (376 MHz)



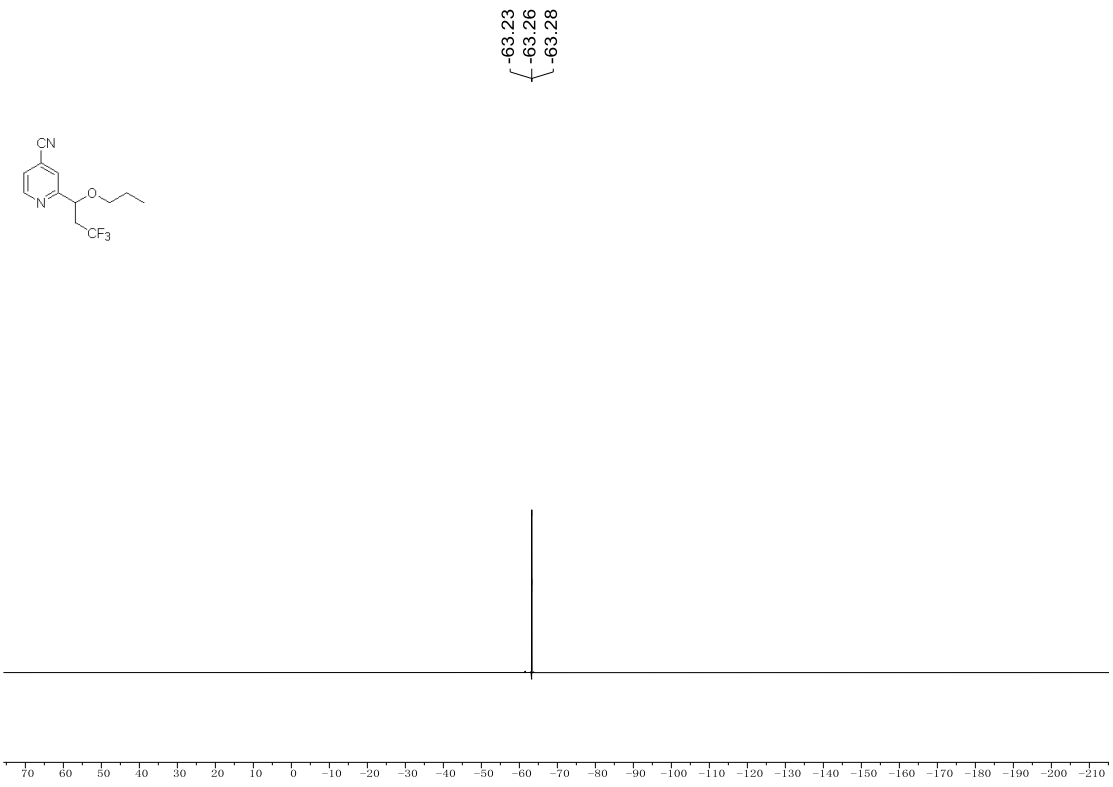
^{1}H NMR spectrum of compound **6b** in $CDCl_3$ (400 MHz)



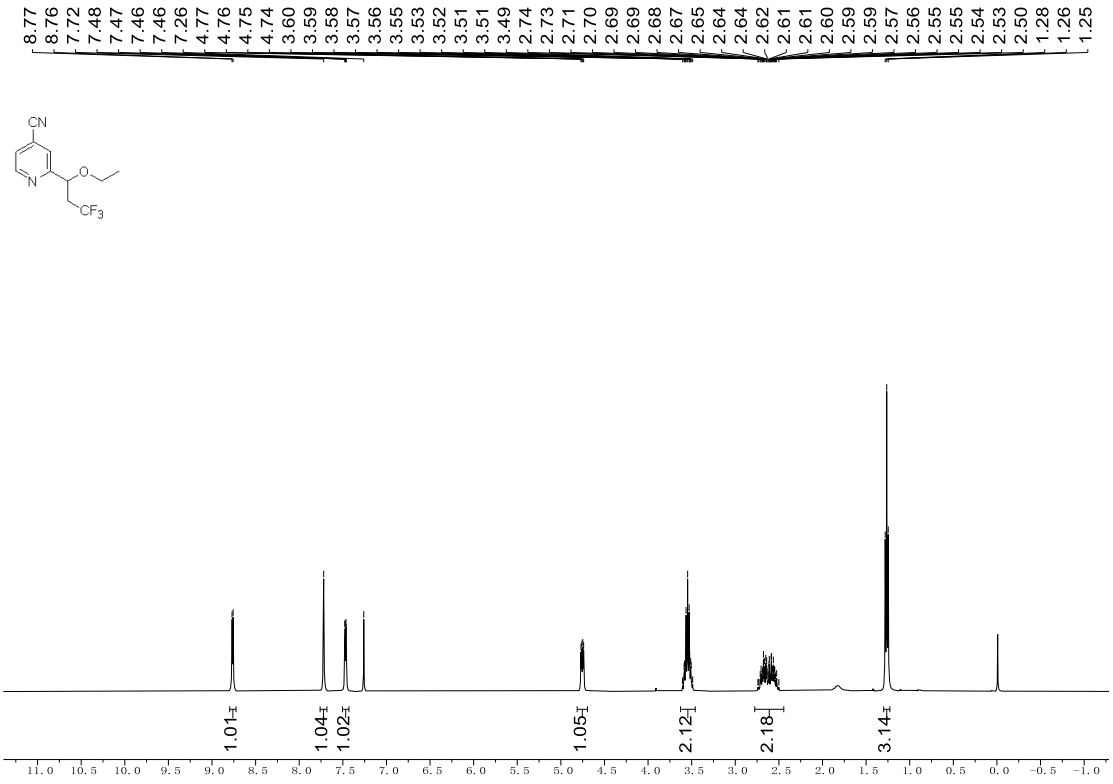
^{13}C NMR spectrum of compound **6b** in $CDCl_3$ (151 MHz)



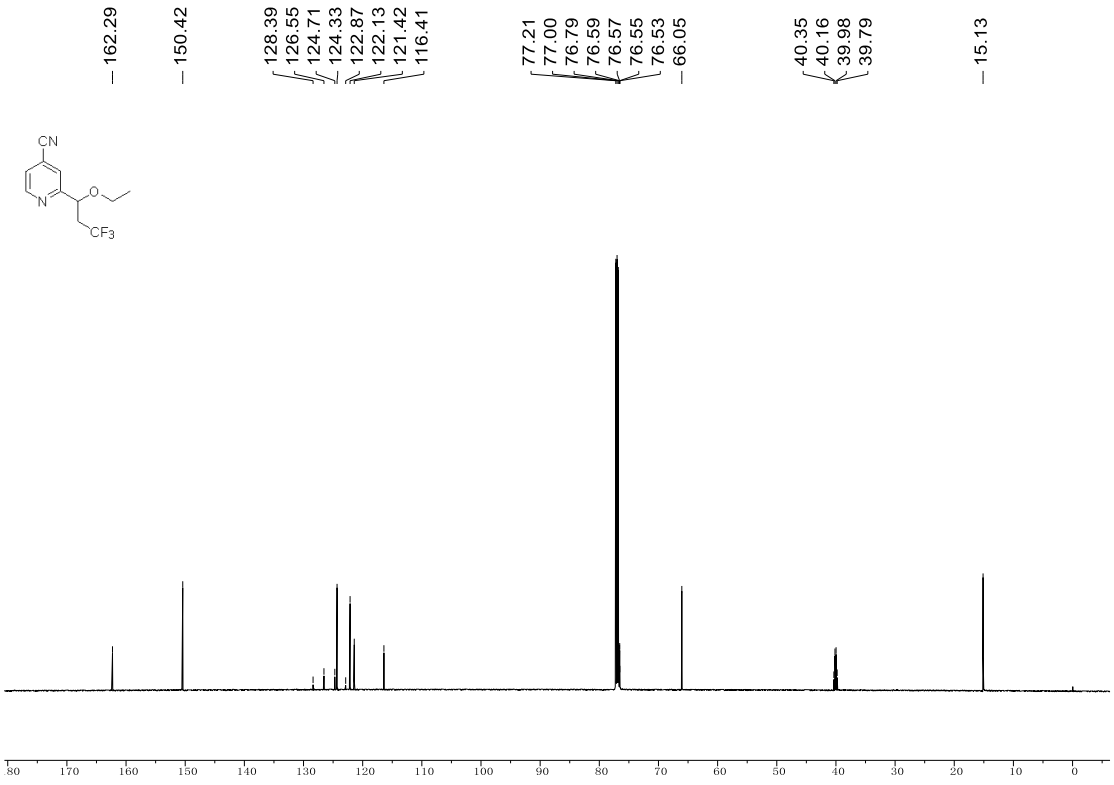
^{19}F NHR spectrum of compound **6b** in $CDCl_3$ (376 MHz)



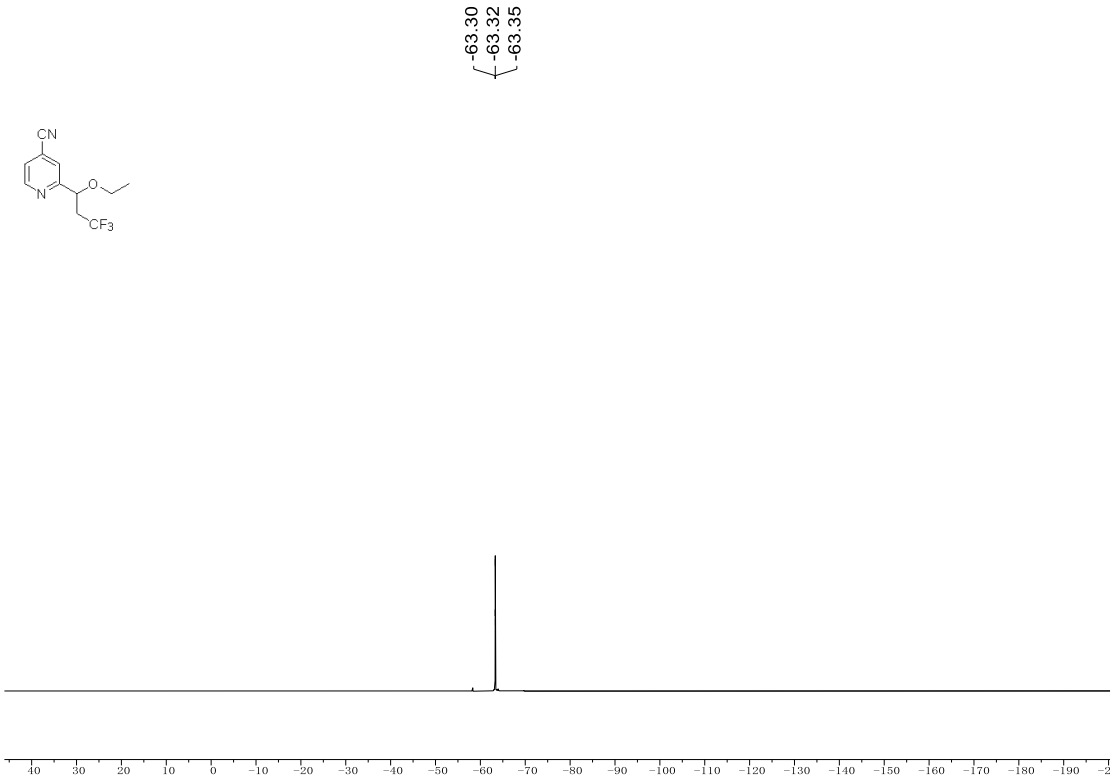
^{1}H NMR spectrum of compound **6c** in $CDCl_3$ (400 MHz)



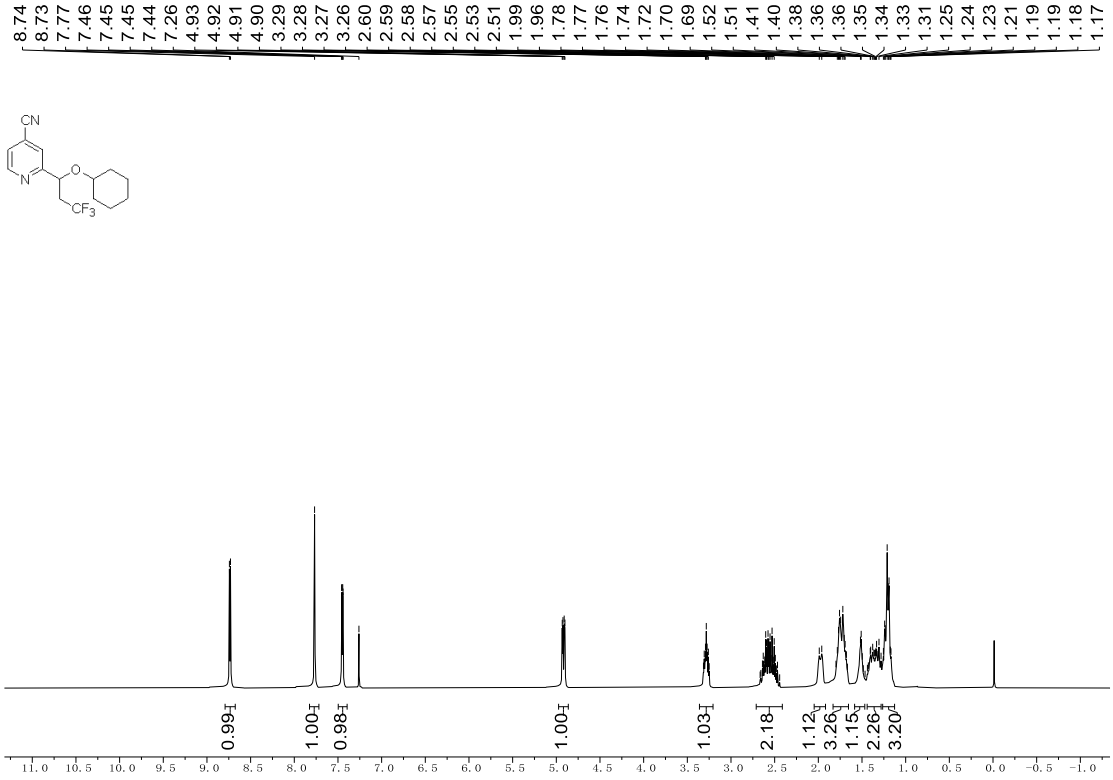
^{13}C NMR spectrum of compound **6c** in $CDCl_3$ (151 MHz)



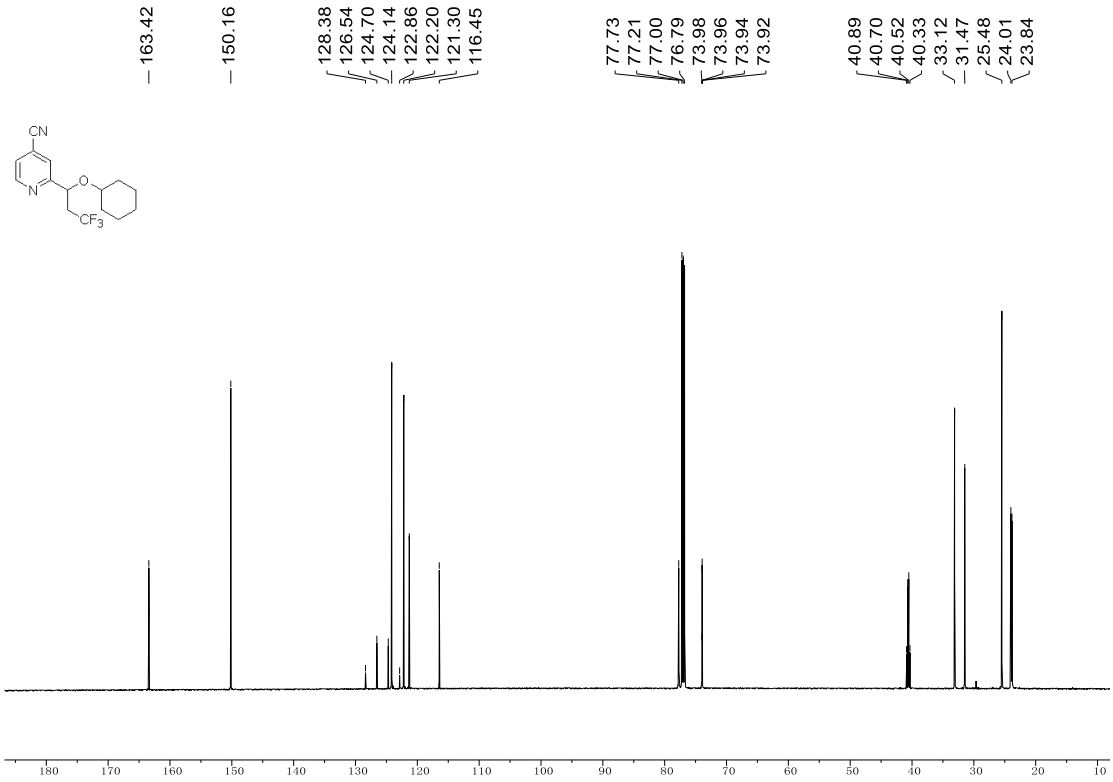
^{19}F NHR spectrum of compound **6c** in $CDCl_3$ (376 MHz)



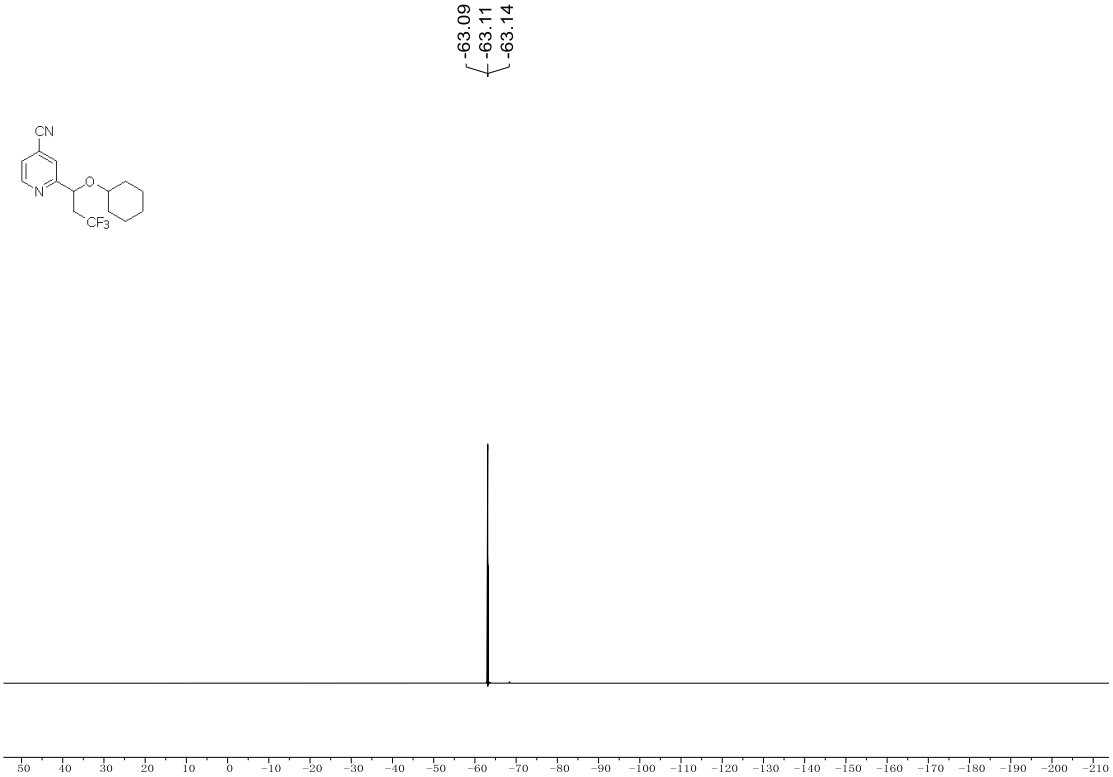
^{1}H NMR spectrum of compound **6d** in $CDCl_3$ (400 MHz)



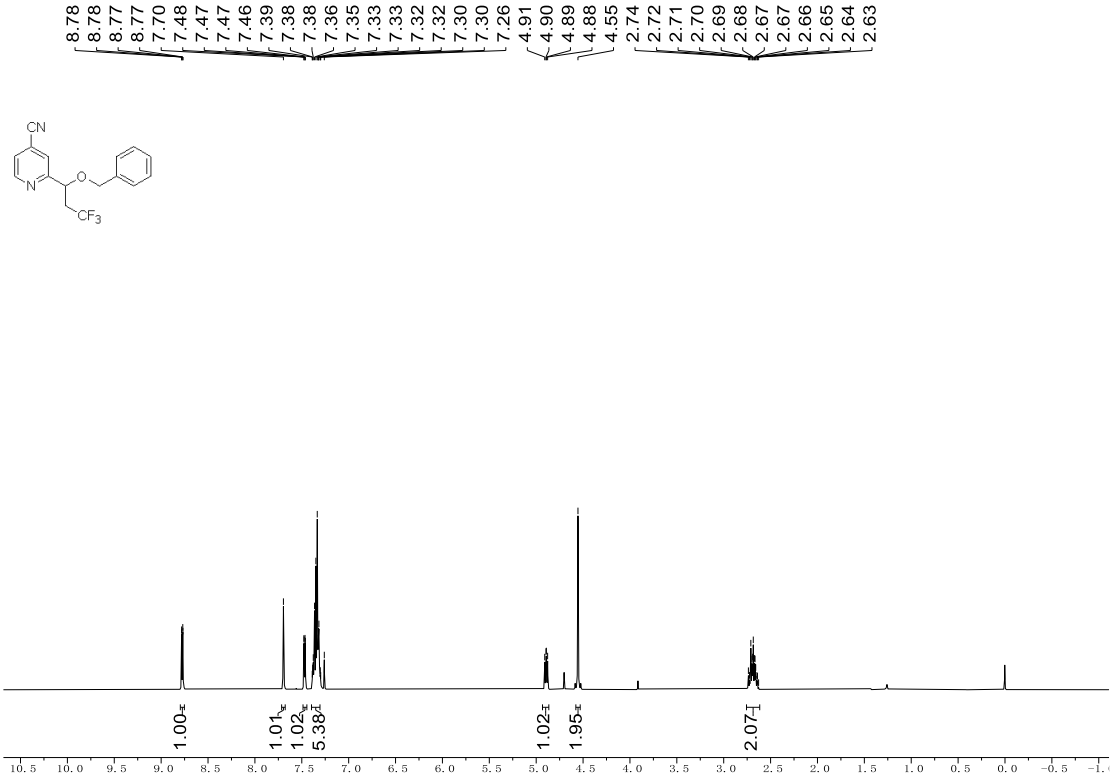
^{13}C NMR spectrum of compound **6d** in $CDCl_3$ (151 MHz)



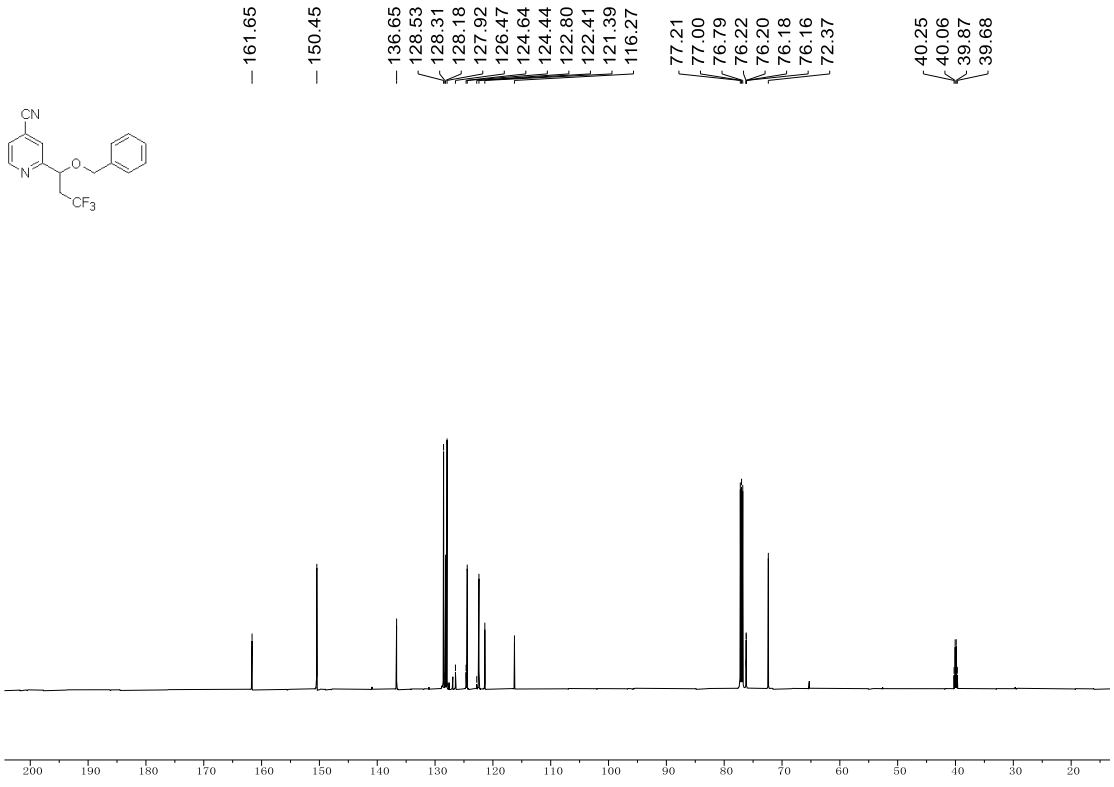
^{19}F NHR spectrum of compound **6d** in $CDCl_3$ (376 MHz)



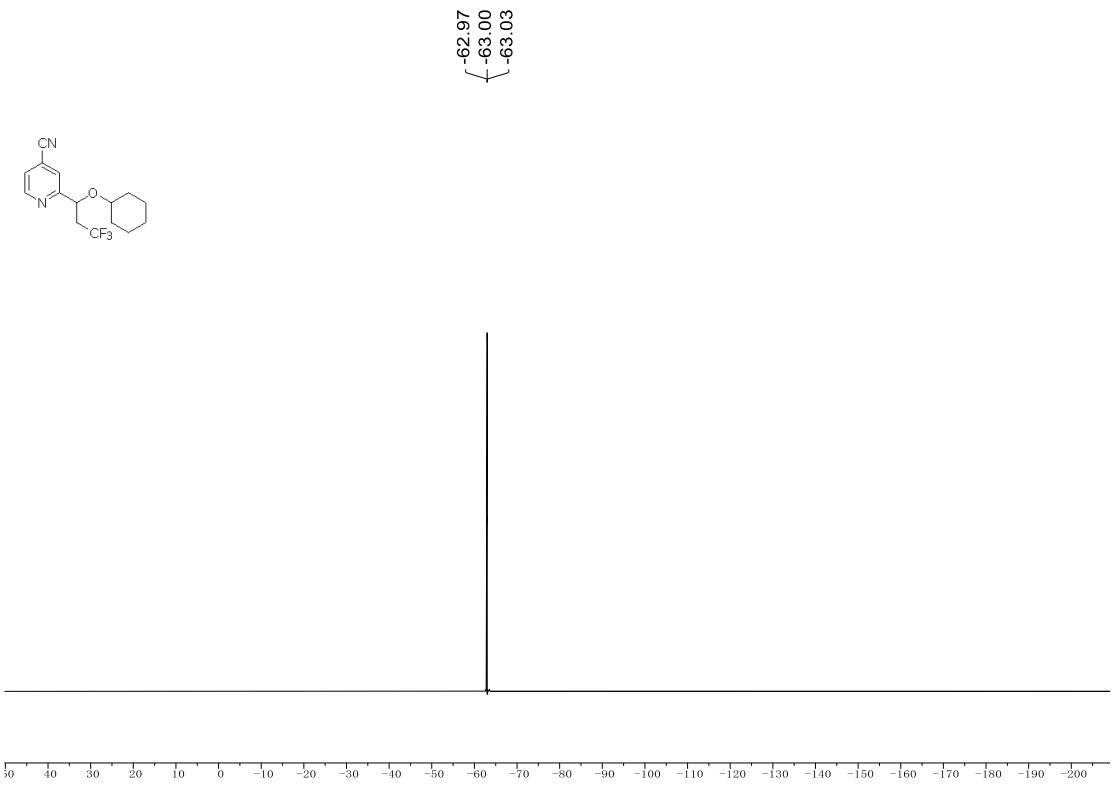
^{1}H NMR spectrum of compound **6e** in $CDCl_3$ (400 MHz)



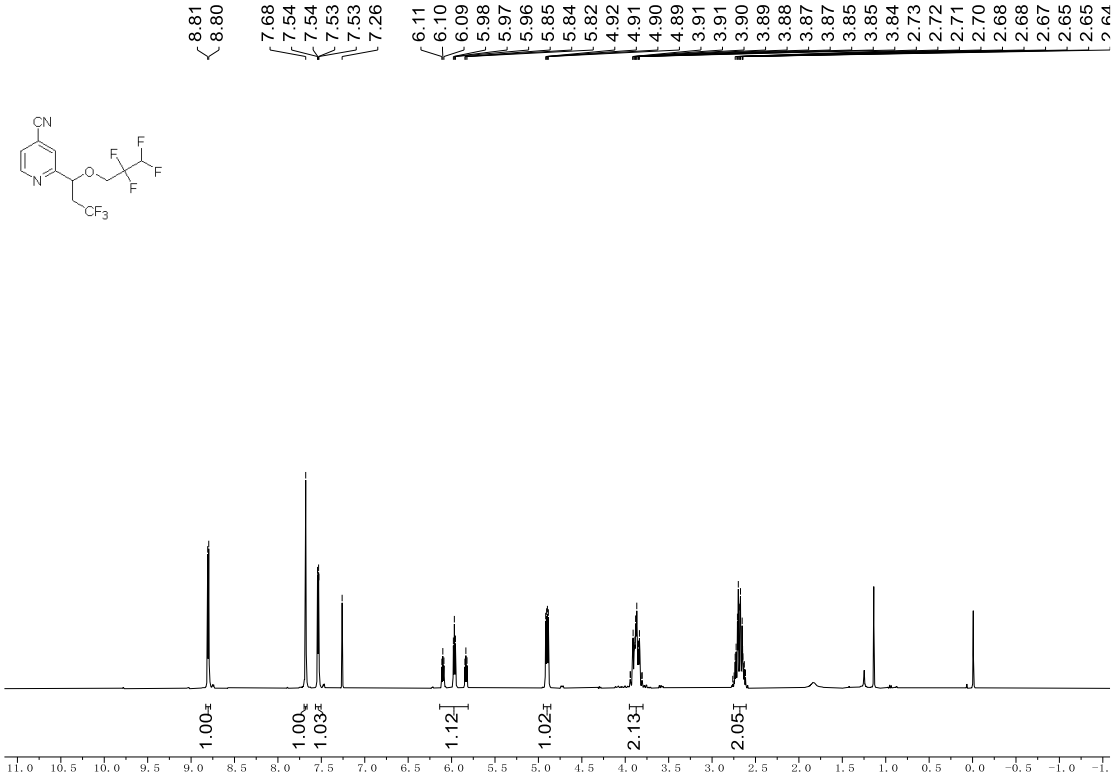
^{13}C NMR spectrum of compound **6e** in $CDCl_3$ (151 MHz)



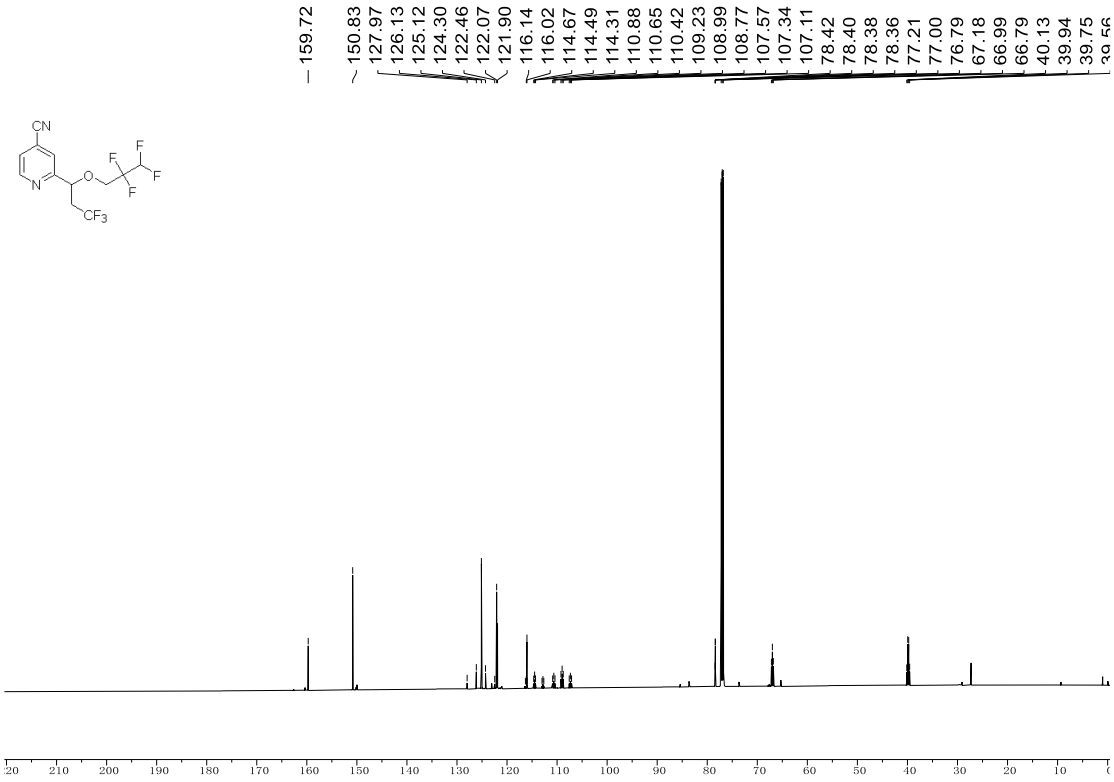
^{19}F NHR spectrum of compound **6e** in $CDCl_3$ (376 MHz)



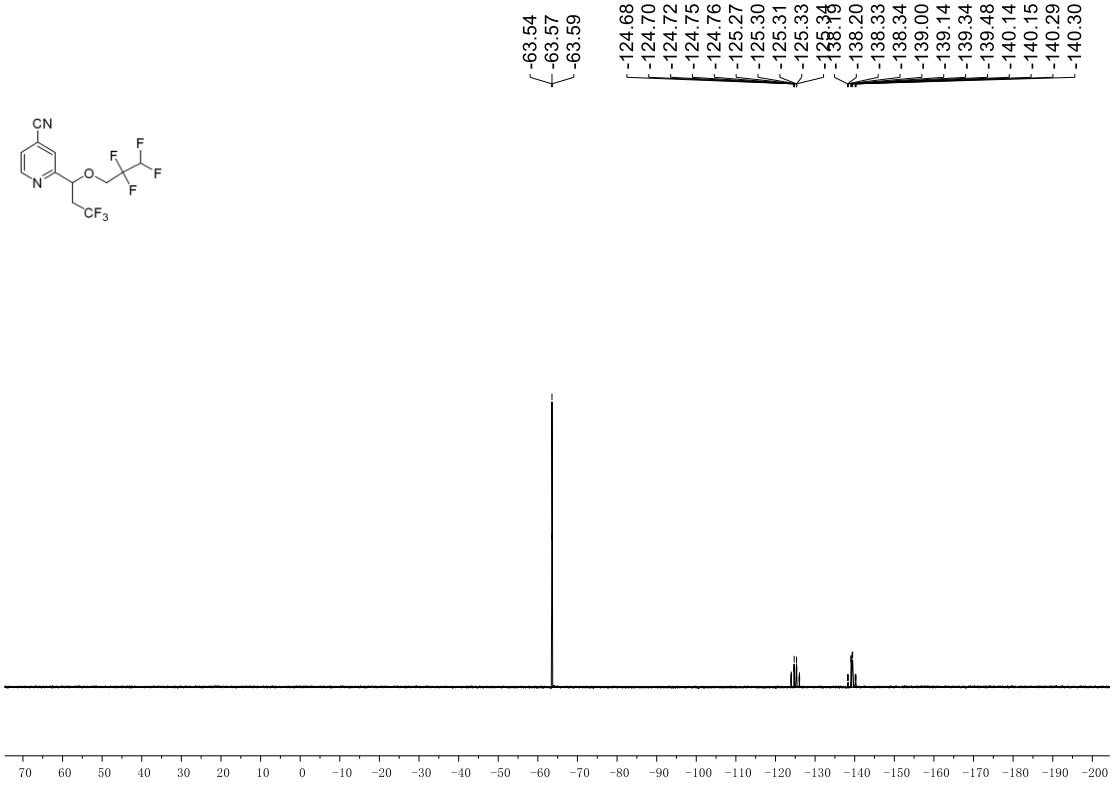
^{1}H NMR spectrum of compound **6f** in $CDCl_3$ (400 MHz)



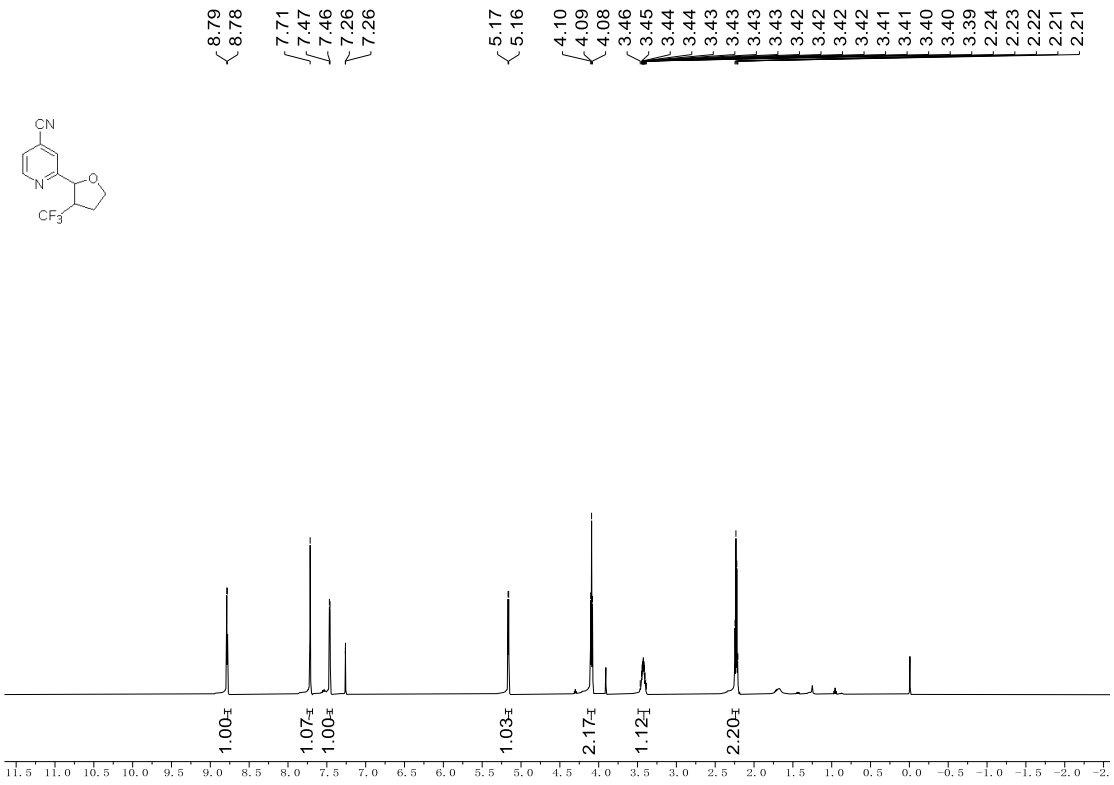
^{13}C NMR spectrum of compound **6f** in $CDCl_3$ (151 MHz)



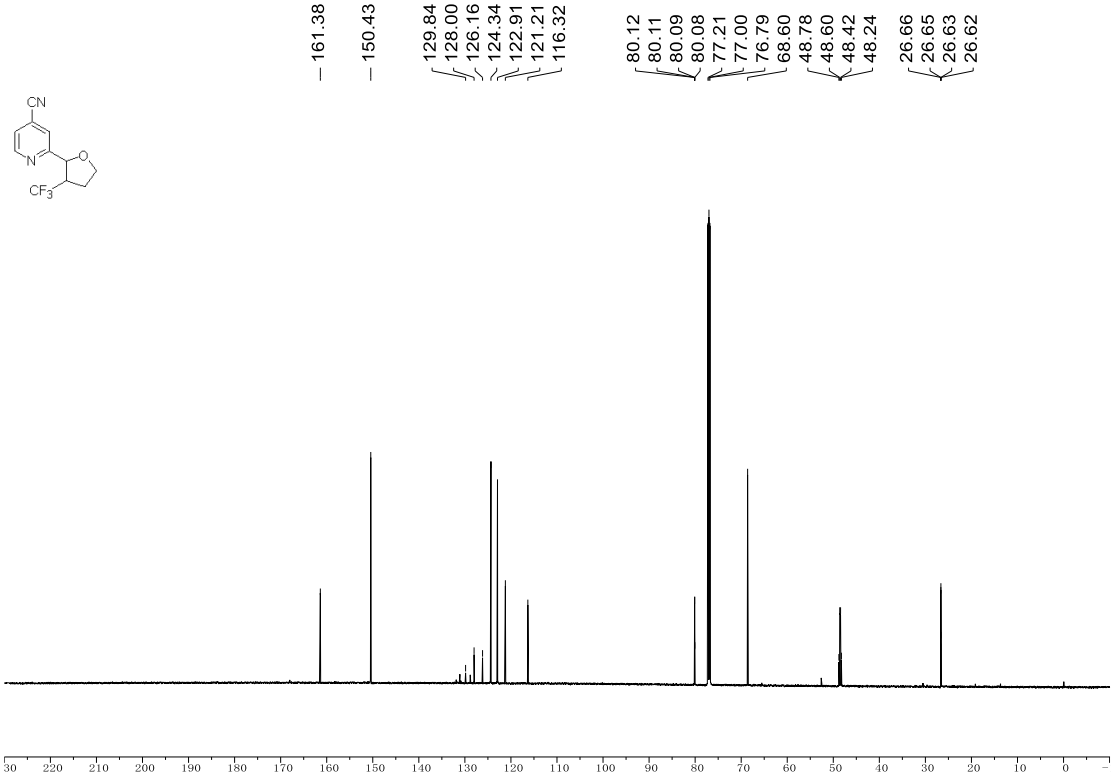
^{19}F NHR spectrum of compound **6f** in $CDCl_3$ (376 MHz)



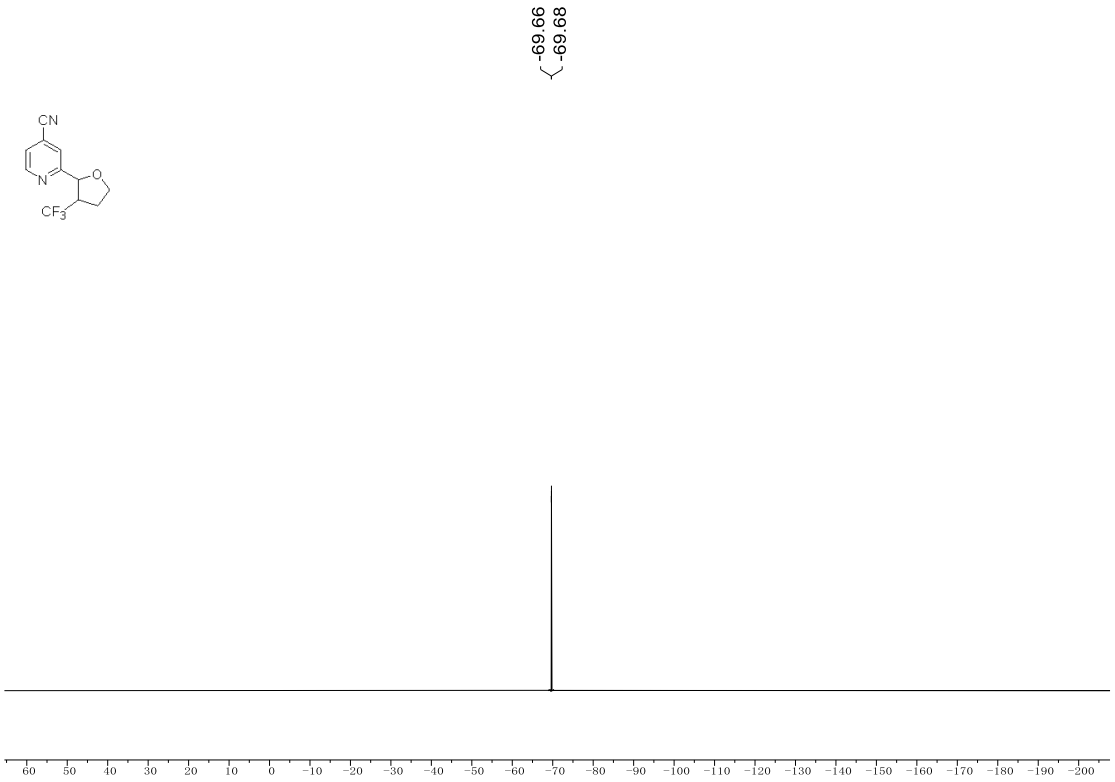
^{1}H NMR spectrum of compound **6g** in $CDCl_3$ (600 MHz)



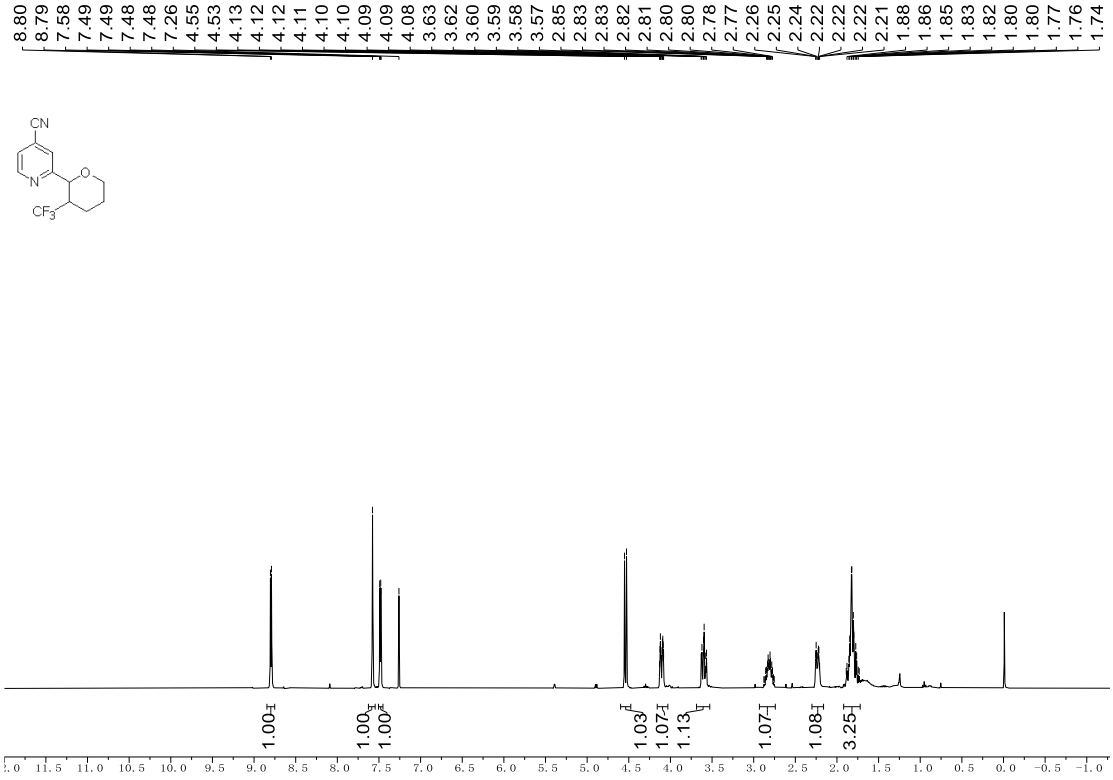
^{13}C NMR spectrum of compound **6g** in $CDCl_3$ (151 MHz)



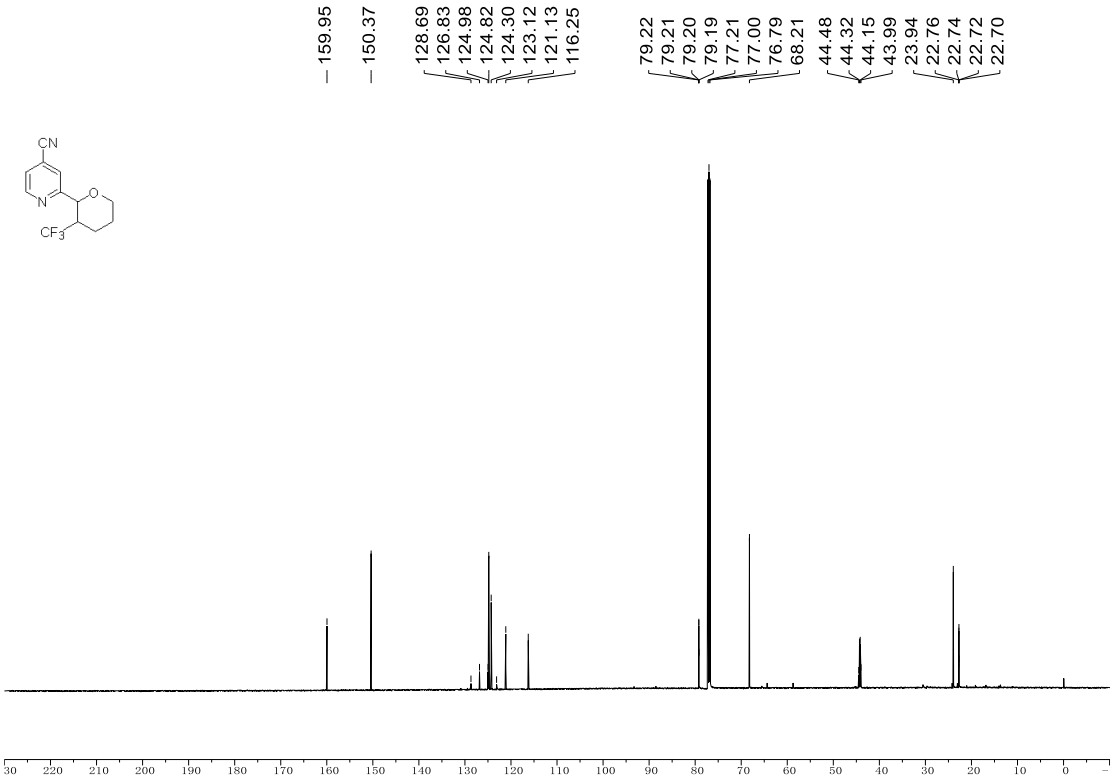
^{19}F NHR spectrum of compound **6g** in $CDCl_3$ (376 MHz)



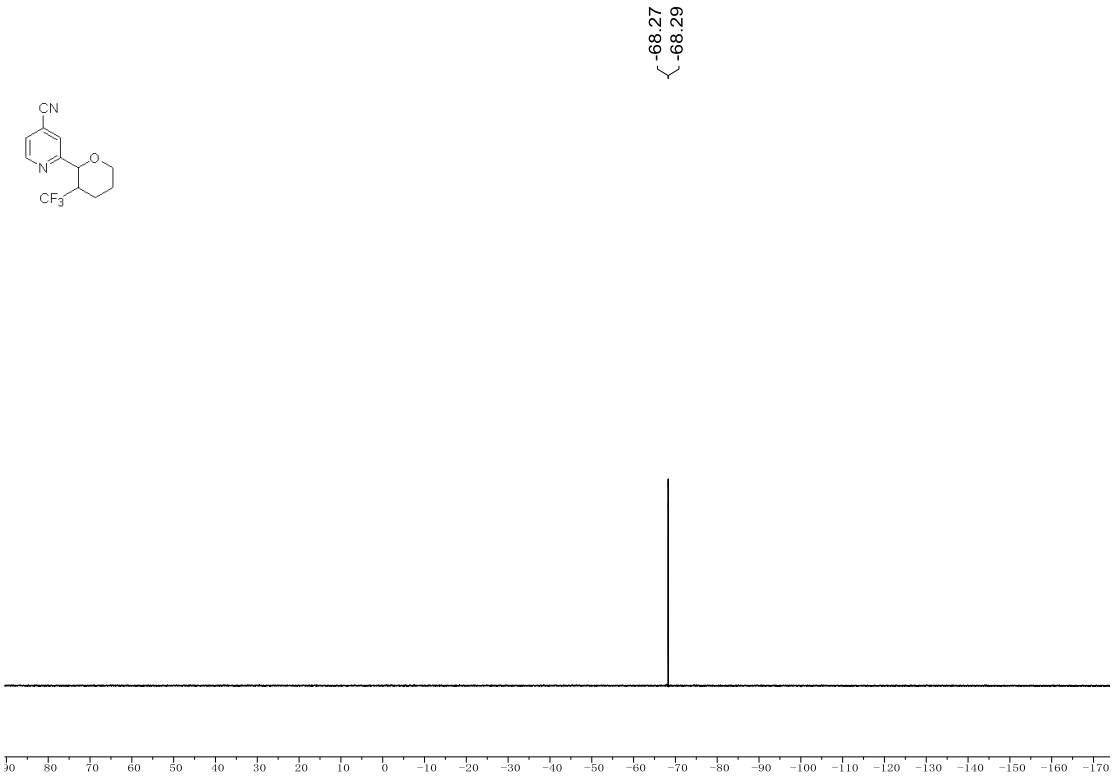
^{1}H NMR spectrum of compound **6h** in $CDCl_3$ (400 MHz)



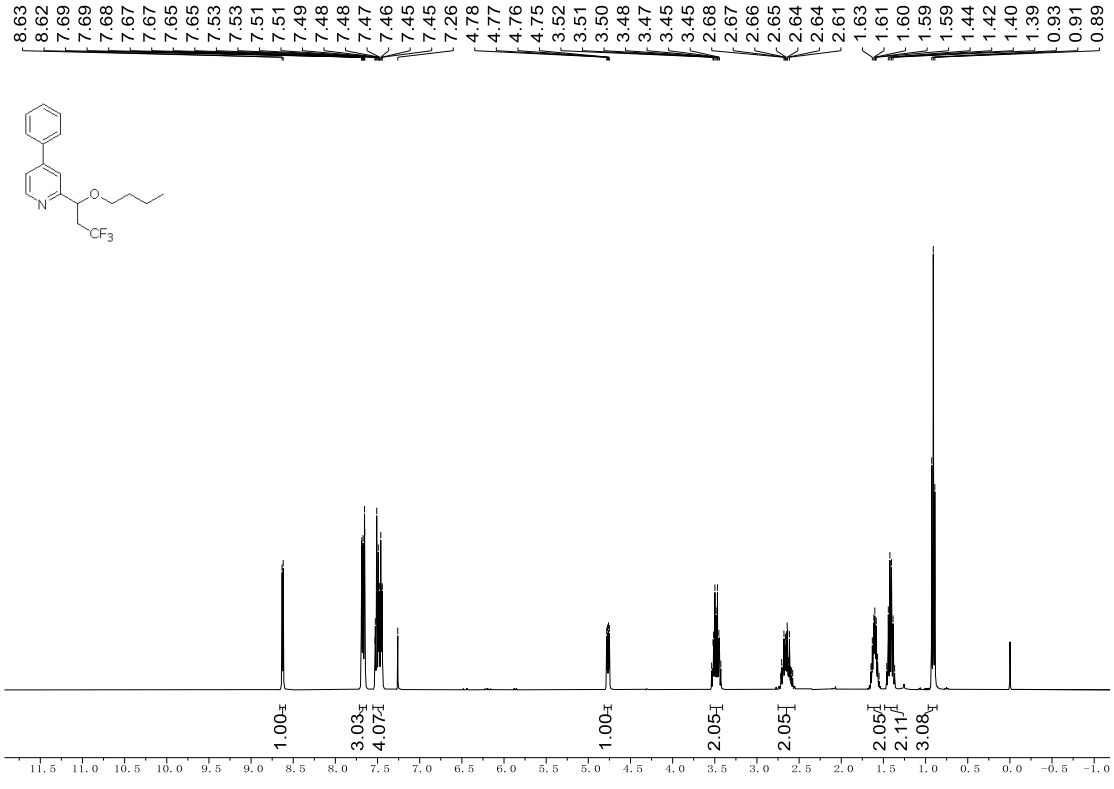
^{13}C NMR spectrum of compound **6h** in $CDCl_3$ (151 MHz)



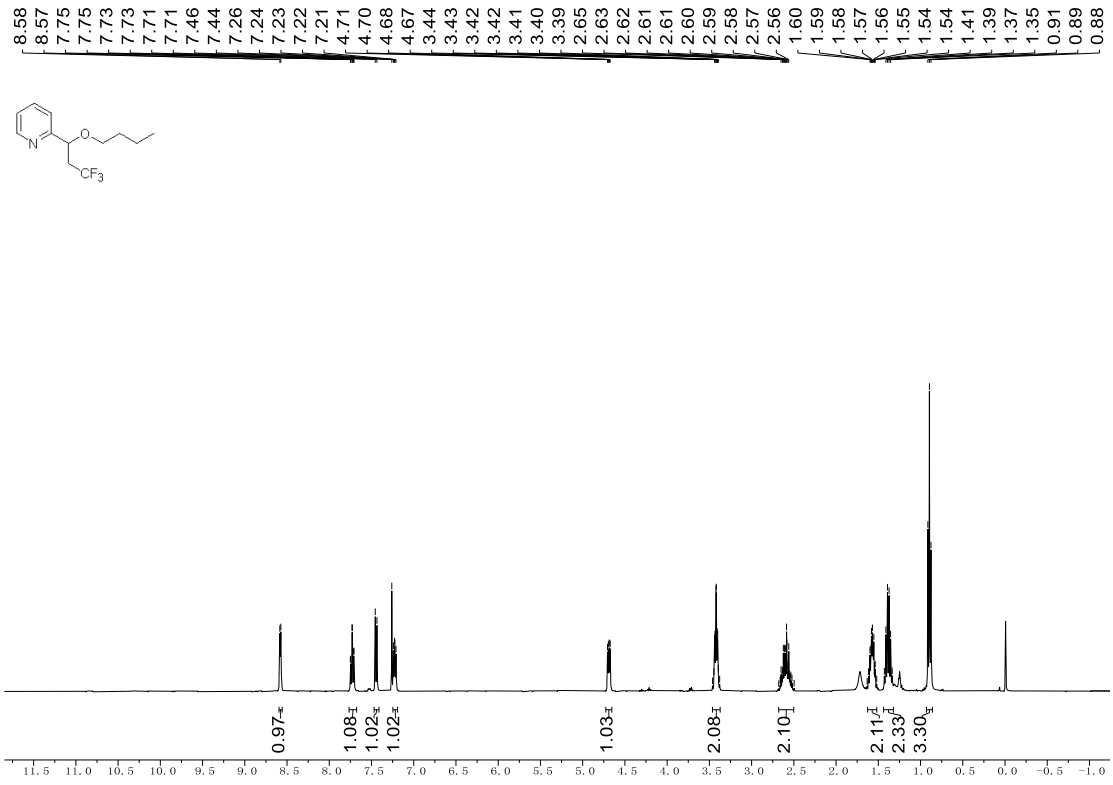
^{19}F NHR spectrum of compound **6h** in $CDCl_3$ (376 MHz)



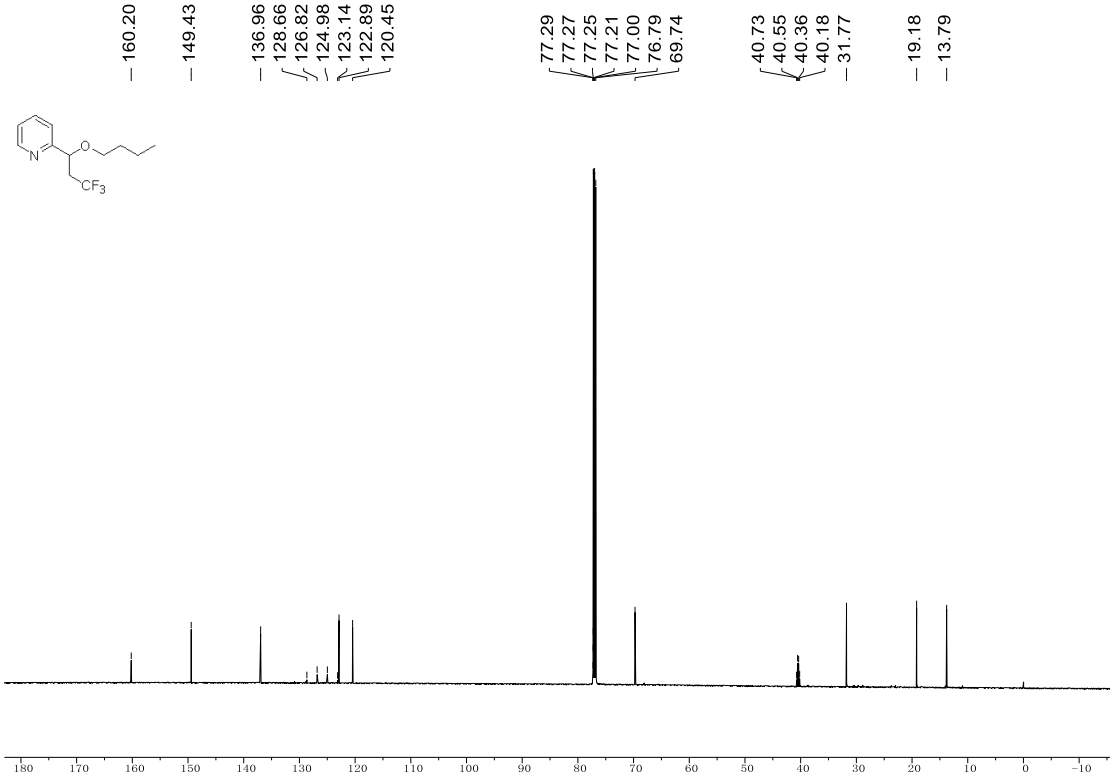
^{1}H NMR spectrum of compound **4i** in $CDCl_3$ (400 MHz)



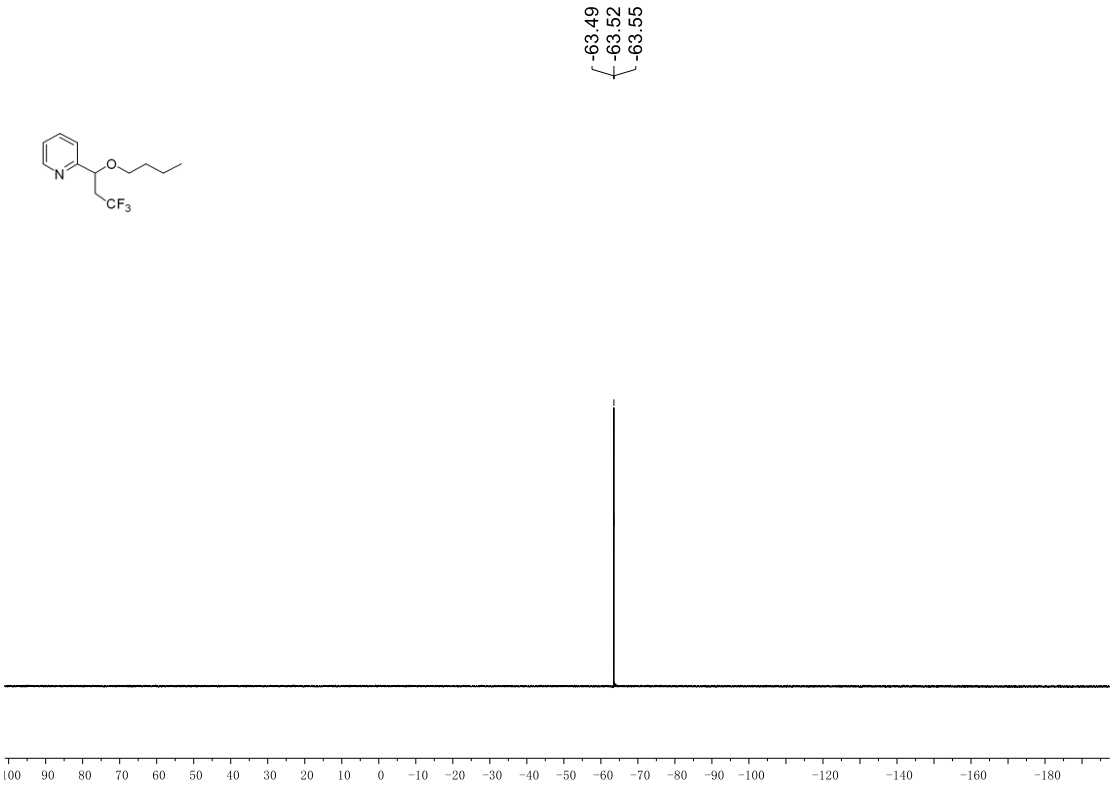
^{1}H NMR spectrum of compound **7** in $CDCl_3$ (400 MHz)



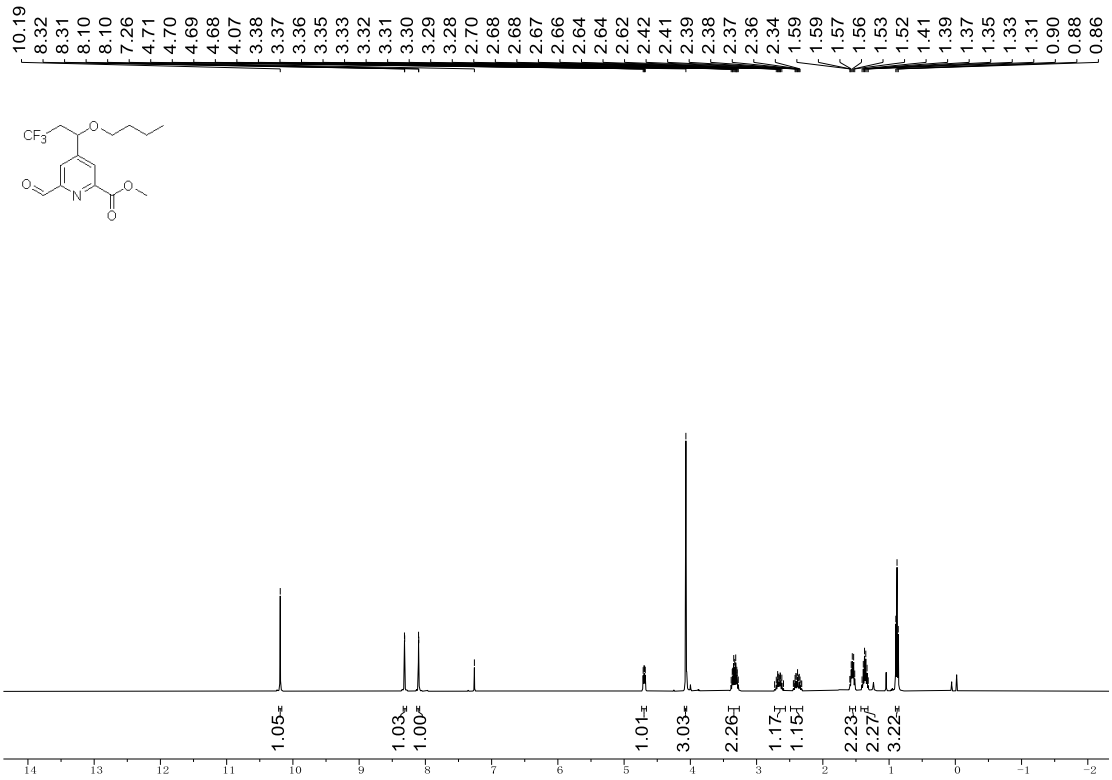
^{13}C NMR spectrum of compound **7** in $CDCl_3$ (151 MHz)



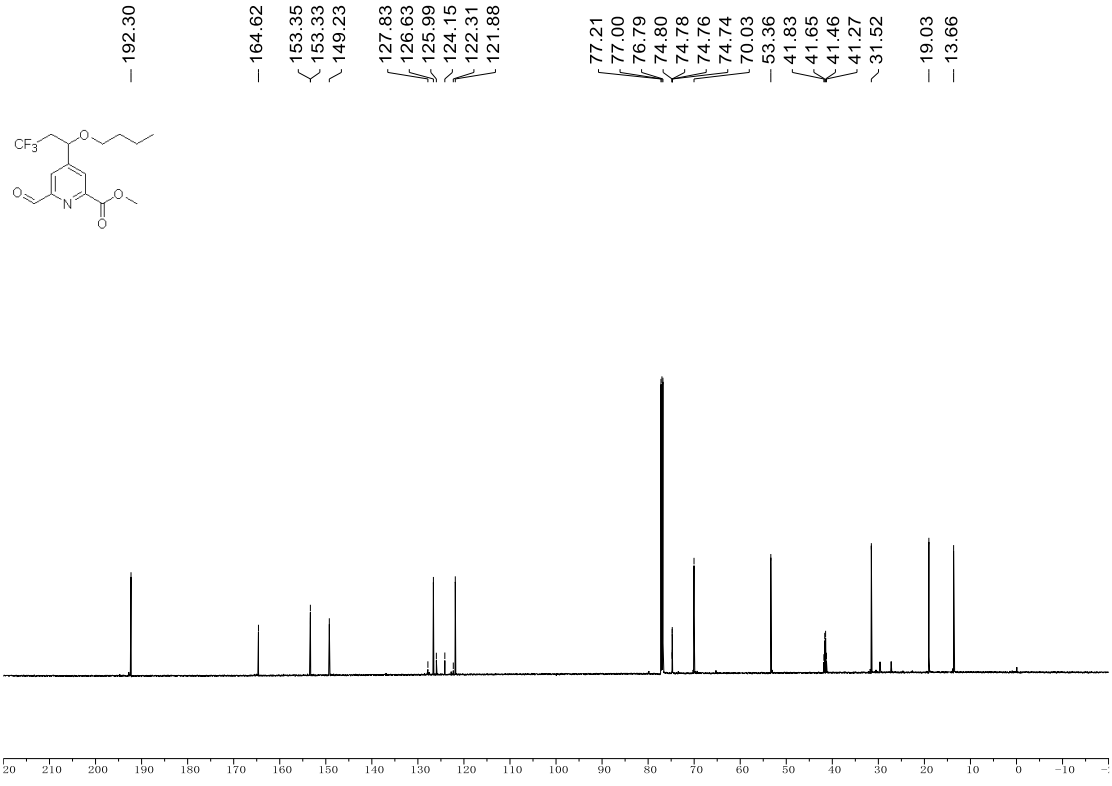
^{19}F NHR spectrum of compound **7** in $CDCl_3$ (376 MHz)



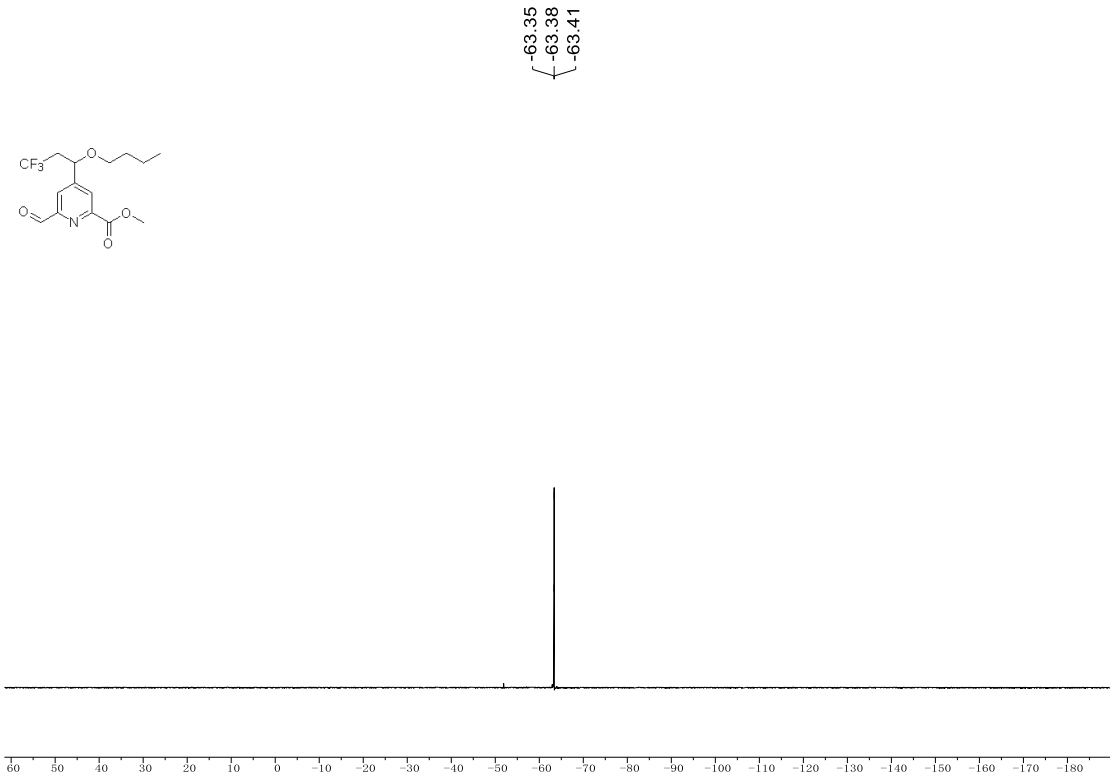
^{1}H NMR spectrum of compound **8** in $CDCl_3$ (400 MHz)



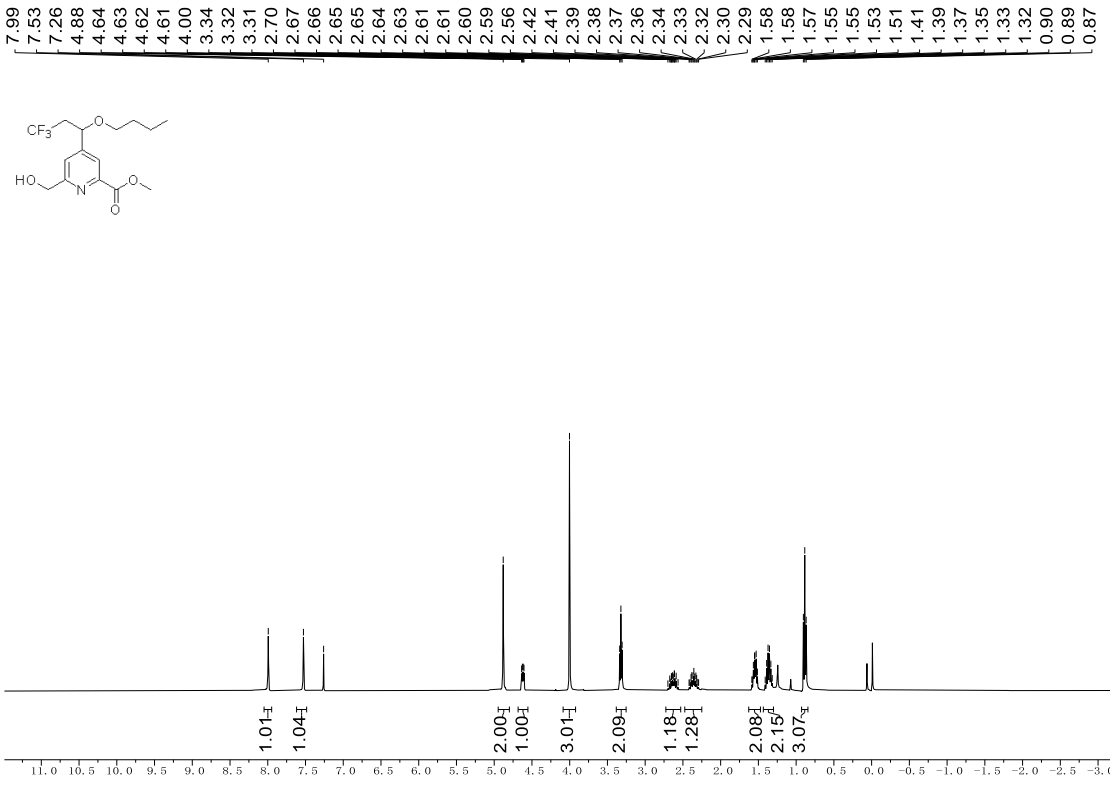
^{13}C NMR spectrum of compound **8** in $CDCl_3$ (151 MHz)



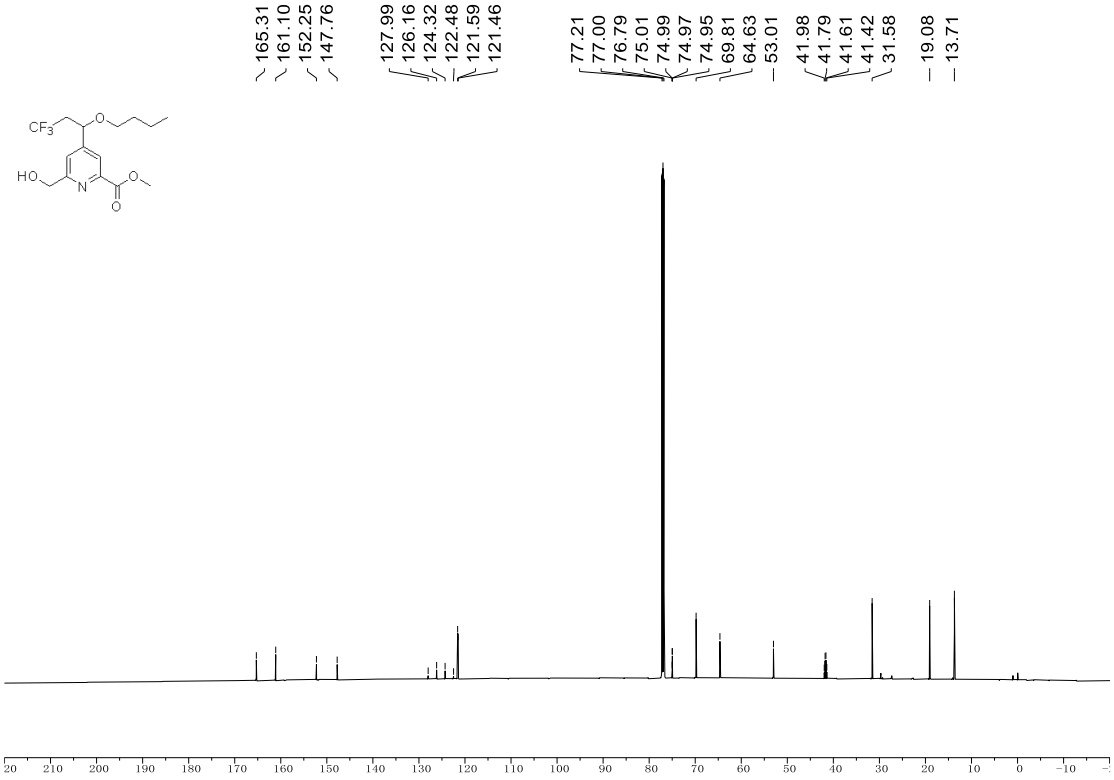
^{19}F NHR spectrum of compound **8** in $CDCl_3$ (376 MHz)



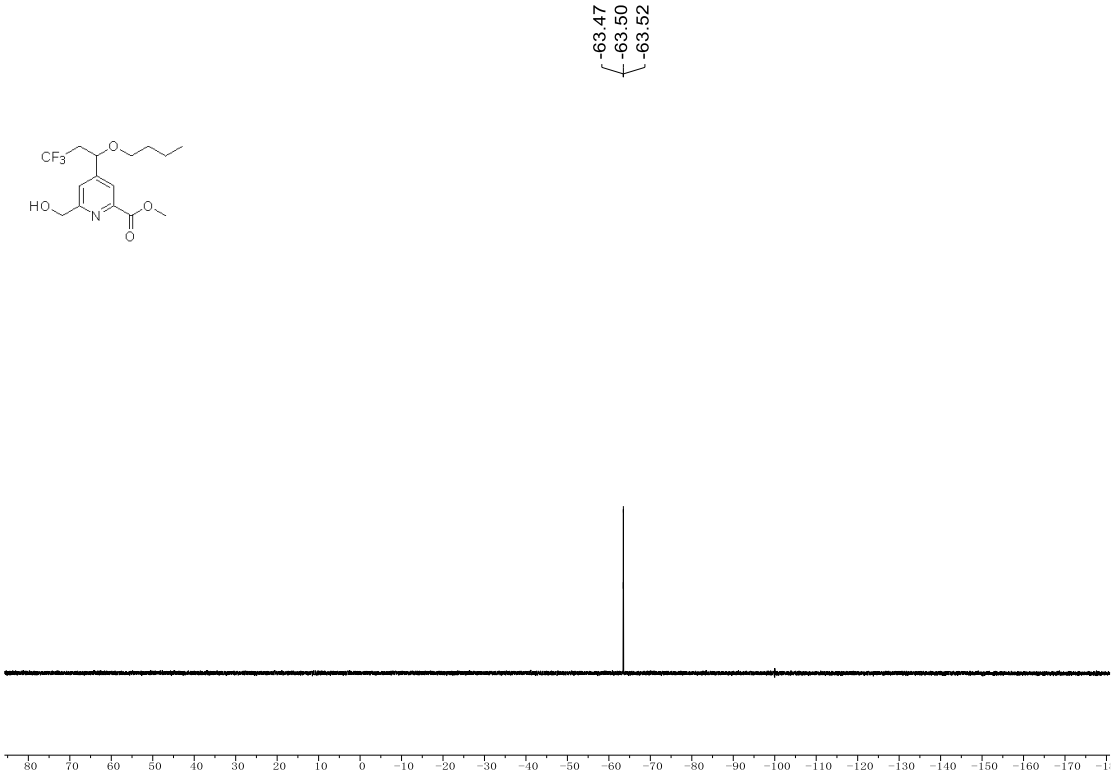
^{1}H NMR spectrum of compound **9** in $CDCl_3$ (400 MHz)



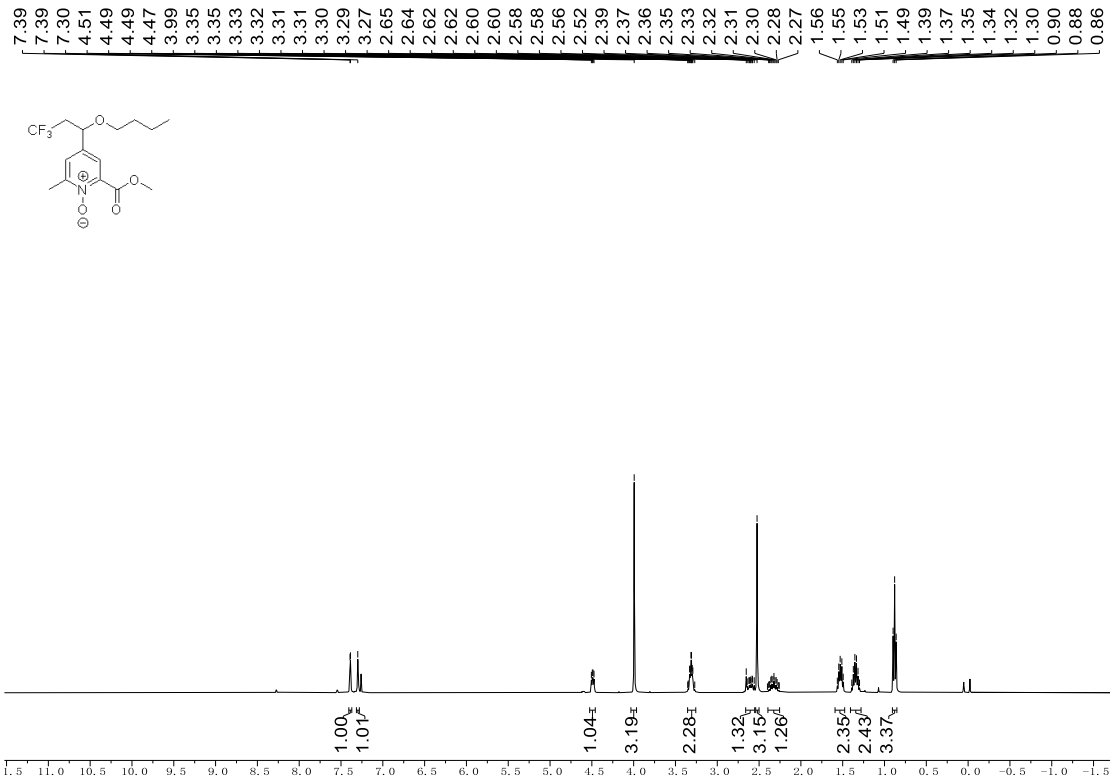
^{13}C NMR spectrum of compound **9** in $CDCl_3$ (151 MHz)



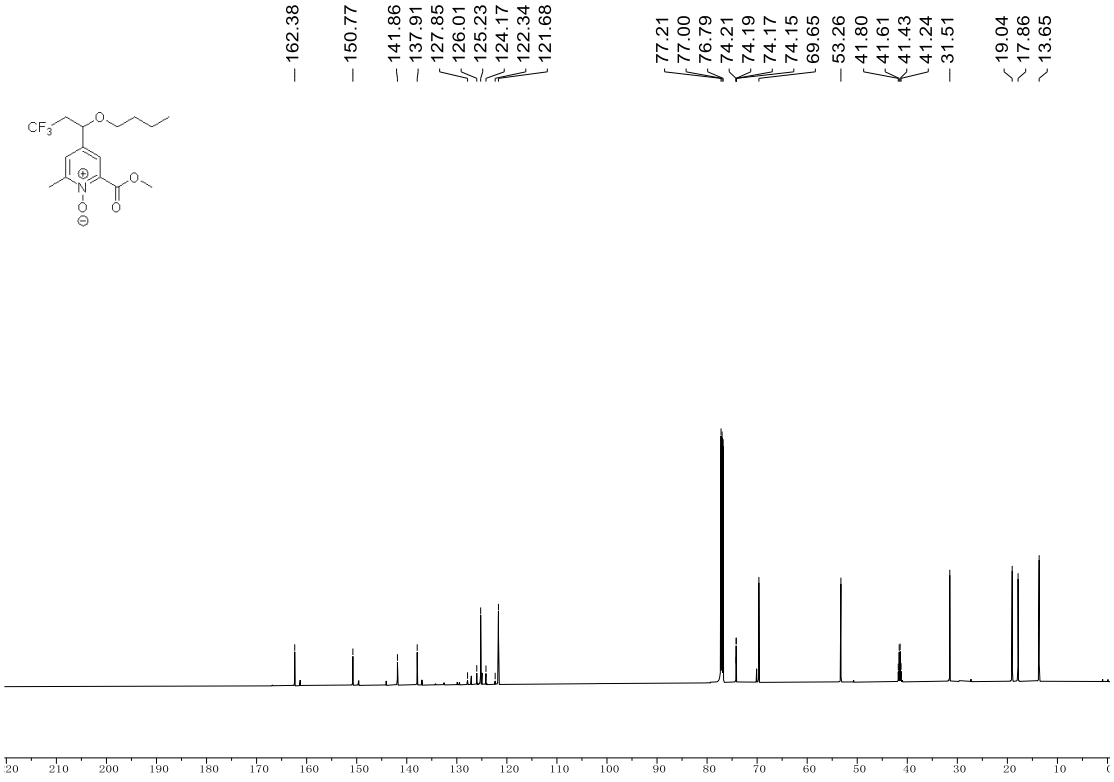
^{19}F NHR spectrum of compound **9** in $CDCl_3$ (376 MHz)



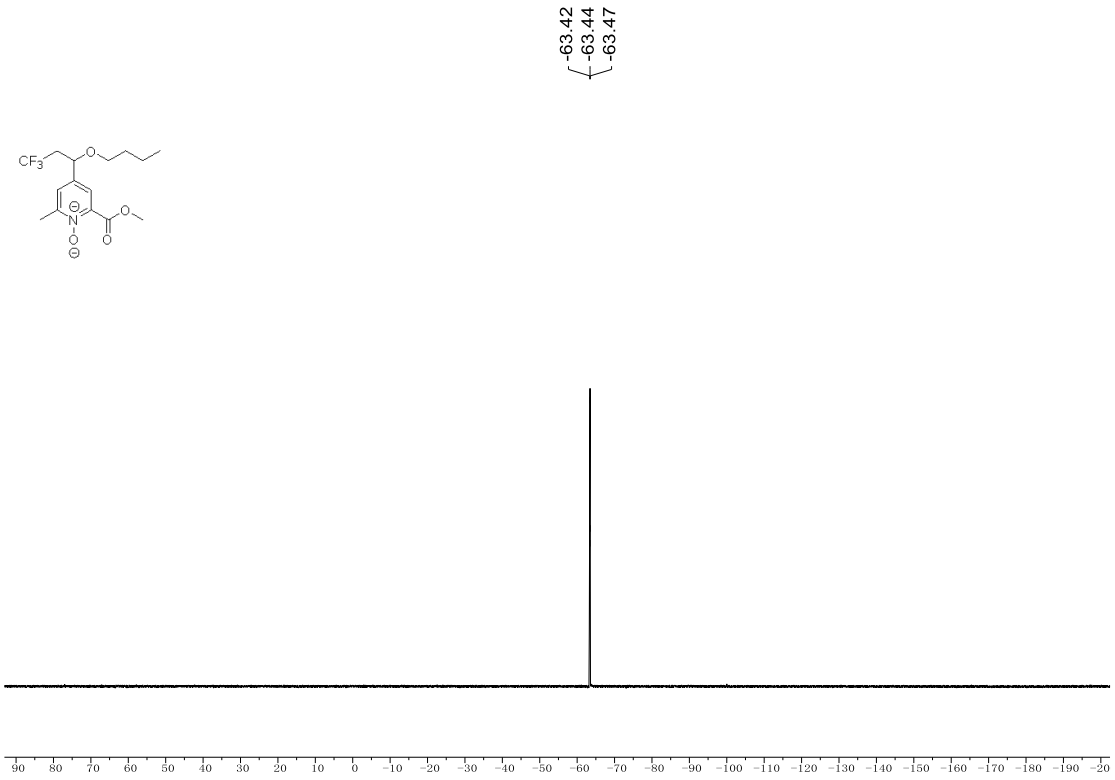
^{1}H NMR spectrum of compound **10** in $CDCl_3$ (400 MHz)



^{13}C NMR spectrum of compound **10** in $CDCl_3$ (151 MHz)



^{19}F NHR spectrum of compound **10** in $CDCl_3$ (376 MHz)



10. References

1. Y. T. He, D. Kang, I. Kim and S. Hong, Metal-free photocatalytic trifluoromethylative pyridylation of unactivated alkenes, *Green Chem*., 2018, **20**, 5209-5214.