Supporting Information

Copper-Mediated Trifluoromethylation of Aryl-,Heteroaryl-, and Vinyltrifluoroborates with Langlois' Reagent

By
Srinivas Reddy Dubbaka*, Manohar Salla, Raghu Bolisetti, and Shashidhar Nizalapur

Department of Medicinal Chemistry, Albany Molecular Research Singapore Research Centre, Pte. Ltd., 61 Science Park Road, #05-01, Galen, Science Park II, Singapore-117525

TABLE OF CONTENTS

EXPERIMENTAL

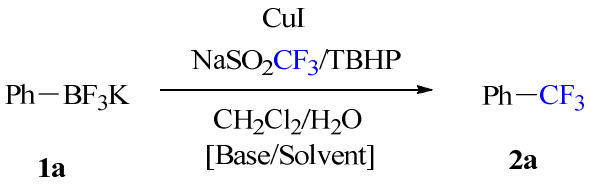
General information: ^{1}H NMR Spectra, ^{19}F NMR and ^{13}C NMR were recorded on Bruker 400 MHz or 300 MHz in the solvents indicated; chemical shifts are reported in units (ppm) by assigning $CDCl_3$ resonance in the ^{1}H spectrum as 7.26 ppm and $CDCl_3$ resonance in the ^{13}C spectrum as 77.0 ppm. ^{19}F NMR chemical shifts were determined relative to $CFCl_3$ as internal standard and are measured proton decoupled. All coupling constants (*J* values) were reported in Hertz (Hz). GC-MS spectra were measured on Shimadzu. Column chromatography was performed on silica gel 200-300 mesh on Combiflash. If not specially mentioned, all the solvents and reagents were used as purchased and without further purification.

Reagents' commercial sources: Reactants (boronic acids or trifluoroborates) were purchased from Combi-Blocks, Tokyo chemical industry (TCI) Japan, Frontier Scientific and Aldrich and used without purification. Commercial sources for other relevant reagents are shown below.

Chemical name	Commercial source	CAS no	Product no
Copper (I) chloride	Aldrich	7758-89-6	61168
$NaSO_2CF_3$ (Langlois Reagent)	Tokyo chemical industry (TCI)	2926-29-6	T2033
tert-Butyl Hydroperoxide (TBHP) (70% in Water)	Tokyo chemical industry (TCI)	75-91-2	B3153

Experimental Details:

Base and solvent screen for Cu-Mediated for Trifluoromethylation of phenyltrifluoroborate ($PhBF_3K$, 1a) with $NaSO_2CF_3$/TBHP.



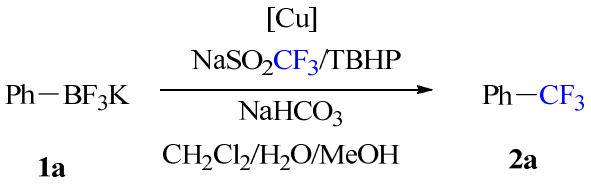
A mixture of the $PhBF_3K$ (27.6 mg, 0.15 mmol, 1.0 equiv), CuI (28.6 mg, 0.15 mmol, 1.0 equiv), $NaSO_2CF_3$ (70.2 mg, 0.45 mmol, 3.0 equiv), Base (0.15 mmol, 3.0 equiv) in CH_2Cl_2 (0.7 mL), and H_2O (0.5 mL) was cooled to 0 ℃, and TBHP (70% solution in water) (104 µL, 5.0 equiv, 0.75 mmol) was added under vigorous stirring. Stirring was continued for overnight at room temperature. To this, 4-fluorobenzonitrile (0.15 mmol) was added as reference to the reaction mixture, stirred for 5 min, an aliquot of the organic phase was withdrawn for the ^{19}F NMR measurement in $CDCl_3$. The yields of **2a** as a function of bases and solvents are listed in **Table S1.**

Table S1. Base and solvent screen for Cu-Mediated for Trifluoromethylation of phenyltrifluoroborate (**1a**) with $NaSO_2CF_3$/TBHP.

Entry	Bases	%Yield
1	Et_3N	traces
2	Na_2CO_3	15
3[c]	Cs_2CO_3	20
4	$NaHCO_3$	50
5	NaOAc	28
6	K_3PO_4	31
7	$NaHCO_3$	5[a]
8	$NaHCO_3$/MeOH (0.7 mL)	51
9	$NaHCO_3$/1,4-Dioxane (0.7 mL)	45
10	$NaHCO_3$/1,2-dimethoxyethane (0.7 mL)	45

[a] reaction carried out without H_2O and TBHP (5.5 M in decane)

Copper salt screen for Cu-Mediated for Trifluoromethylation of $PhBF_3K$ (1a) with $NaSO_2CF_3$/TBHP.



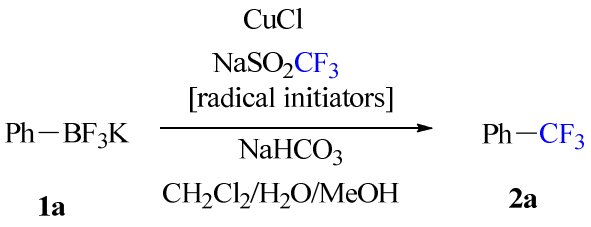
A mixture of the $PhBF_3K$ (27.6 mg, 0.15 mmol, 1.0 equiv), Cu salt (0.15 mmol, 1.0 equiv), $NaSO_2CF_3$ (70.2 mg, 0.45 mmol, 3.0 equiv), $NaHCO_3$ (12.6 mg, 0.15 mmol, 3.0 equiv) in CH_2Cl_2 (0.7 mL), MeOH (0.7 mL), and H_2O (0.5 mL) was cooled to 0 ℃, and TBHP (70% solution in water) (104 µL, 5.0 equiv, 0.75 mmol) was added under vigorous stirring. Stirring was continued for overnight at room temperature. To this, 4-fluorobenzonitrile (0.15 mmol) was added as reference to the reaction mixture, stirred for 5 min, an aliquot of the organic phase was withdrawn for the ^{19}F NMR measurement in $CDCl_3$. The yields of **2a** as a function of copper salts are listed in **Table S2.**

Table S2. Copper salt screen for Cu-Mediated for Trifluoromethylation of phenyltrifluoroborate (**1a**) with $NaSO_2CF_3$/TBHP.

Entry	Cu Salts	%Yield
1	Cu(I) acetate	10
2	Cu(II) acetate	traces
3	$Cu(OCOCF_3)$	40
4	$Cu(OCOCF_3)_2$	20
5[a]	$Cu(OSO_2CF_3)$	50
6	$Cu(OSO_2CF_3)_2$	20
7	$(CH_3CN)_4CuPF_6$	traces
8	CuBr	10
9[b]	CuTc	50
10	CuCl	80
11	CuCl/1,10-Phen	(8)[c](15)[d]
12	catalytic	(8)[e]

[a]Used as benzene complex. [d]Copper(I)-thiophene-2-carboxylate; [c]20% CuCl; [d]20% CuCl and 20% 1,10-phenanthroline. [e]**1a** (1.0 equiv., 0.15 mmol), $Cu(OAc)_2$ (0.2 equiv.), imidazole (0.2 equiv.), 2,4,6-collidine (2.0 equiv.), NH_4Cl (2.5 equiv.), $NaSO_2CF_3$ (7.0 equiv.), TBHP (70% in H_2O, 16.0 equiv.), CH_2Cl_2/H_2O, air, rt, 15 h.

Radical initiators screen for Cu-Mediated for Trifluoromethylation of $PhBF_3K$ (1a) with $NaSO_2CF_3$.



A mixture of the $PhBF_3K$ (27.6 mg, 0.15 mmol, 1.0 equiv), CuCl (14.8 mg, 0.15 mmol, 1.0 equiv), $NaSO_2CF_3$ (70.2 mg, 0.45 mmol, 3.0 equiv), $NaHCO_3$ (12.6 mg, 0.15 mmol, 3.0 equiv) in CH_2Cl_2 (0.7 mL), MeOH (0.7 mL), and H_2O (0.5 mL) was cooled to 0 ℃, and radical initiators (5.0 equiv, 0.75 mmol) was added under vigorous stirring. Stirring was continued for overnight at room temperature. To this, 4-fluorobenzonitrile (0.15 mmol) was added as reference to the reaction mixture, stirred for 5 min, an aliquot of the organic phase was withdrawn for the ^{19}F NMR measurement in $CDCl_3$. The yields of **2a** as a function of radical initiators are listed in **Table S3.**

Table S3. Radical initiators screen for Cu-Mediated for Trifluoromethylation of phenyltrifluoroborate (**1a**) with $NaSO_2CF_3$.

Entry	Radical initiators	%Yield
1	H_2O_2	0
2	NaOCl	traces
3	O_2	8
4	DDQ	0
5	$PhI(OAc)_2$	traces
6	BzOOBz	20

General procedure for the Synthesis of Aryl-CF_3 compounds: (Table 2).

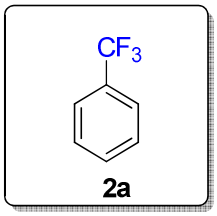
A mixture of the trifluoroborate (0.25 mmol, 1.0 equiv), CuCl (24.8 mg, 0.25 mmol, 1.0 equiv), $NaSO_2CF_3$ (117 mg, 0.75 mmol, 3.0 equiv), $NaHCO_3$ (21.0 mg, 0.25 mmol, 3.0 equiv) in CH_2Cl_2 (1.5 mL), MeOH (1.5 mL), and H_2O (1.2 mL) was cooled to 0 °C, and TBHP (70% solution in water) (172 µL, 5.0 equiv, 1.25 mmol, (86 µL, 2.5 equiv, 0.625 mmol for **2i**, and 138 µL, 4.0 equiv, 1.0 mmol for **2j**)) was added under vigorous stirring. Stirring was continued for 6 –12h at room temperature.

For the compounds reported as isolated yields (**2b**, **2n**, and **2r**), the organic phase was separated, the aqueous phase was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic phases were dried over anhydrous Na_2SO_4, the solvent was removed at 1 atm and the residue was purified by column chromatography on Combiflash with hexanes to afford the desired compounds.

The volatile products were not isolated and their yields were determined only by ^{19}F NMR of the reaction mixture. For the compounds reported with ^{19}F NMR yields, 4-fluorobenzonitrile (0.25 mmol) was added as reference to the reaction mixture, stirred for 5 min, an aliquot of the organic phase was withdrawn for the ^{19}F NMR measurement in $CDCl_3$.

Spectral data of Aryl-CF_3 compounds (Table 2):

1-(Trifluoromethyl)benzene (**2a**):

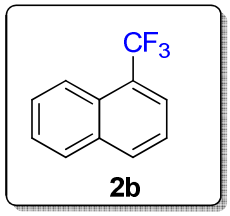


2a

The yield (80%) of **2a** was determined by ^{19}F NMR. The ^{19}F NMR spectral data for **2a** matched that of an authentic sample (Aldrich, s, –62.3 ppm).

^{19}F NMR ($CDCl_3$, 376 M Hz): δ –62.75 (s, 3F); GC–MS *m/z*, 146 (M^+).

1-(Trifluoromethyl)naphthalene (2b):[1]



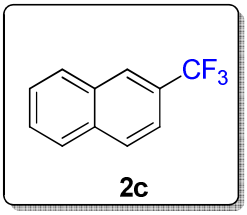
2b

Compound **2b** was isolated in 60% yield (49 mg) and 82% yield was determined by ^{19}F NMR.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.18 (d, *J* = 8.6 Hz, 1H), 8.0 (d, *J* = 8.2 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 1H); 7.86 (d, *J* = 7.3 Hz, 1H), 7.55-7.65 (m, 2H), 7.50 (t, *J* = 7.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 133.9 (s, 1C), 132.7 (s, 1C), 129.0 (s, 1C), 128.7 (s, 1C), 127.6 (s, 1C), 127.4 (q, *J* = 269.8 Hz, 1C), 126.6 (s, 1C), 124.6 (q, *J* = 6.2 Hz, 1C), 124.2 (*J* = 2.2 Hz, 1C), 124.1 (s, 1C), 123.3 (s, 1C).

^{19}F NMR ($CDCl_3$, 282 M Hz): δ –60.43 (s, 3F); GC–MS *m/z*, 196 (M^+).

2-(Trifluoromethyl)naphthalene (2c):[2]

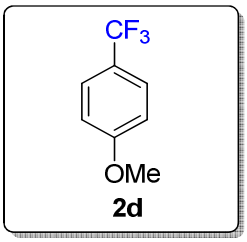


2c

The yield (59%) of **2c** was determined by ^{19}F NMR.

^{19}F NMR ($CDCl_3$, 282 M Hz): δ –62.86 (s, 3F); GC–MS *m/z*, 196 (M^+).

1-Methoxy-4-(trifluoromethyl)benzene (2d):[3]

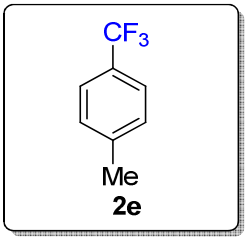


2d

The yield (74%) of **2d** was determined by ^{19}F NMR.

^{19}F NMR ($CDCl_3$, 282 M Hz): δ –62.20 (s, 3F); GC–MS *m/z*, 176 (M^+).

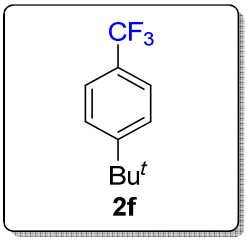
1-Methyl-4-(trifluoromethyl)benzene (2e):[4]



2e

The yield (79%) of **2e** was determined by ^{19}F NMR.
^{19}F NMR ($CDCl_3$, 282 M Hz): δ –62.98 (s, 3F); GC–MS *m/z*, 160 (M^+).

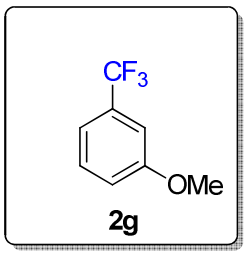
1-(*Tert*-Butyl)-4-(trifluoromethyl)benzene (2f):[2,4]



2f

The yield (77%) of **2f** was determined by ^{19}F NMR.
^{19}F NMR ($CDCl_3$, 282 M Hz): δ –62.98 (s, 3F); GC–MS *m/z*, 202 (M^+).

1-Methoxy-3-(trifluoromethyl)benzene (2g):[3,4]

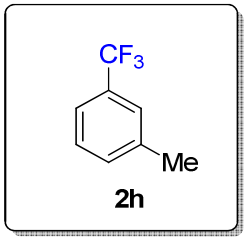


2g

Compound **2g** was isolated in 56% yield (25.0 mg) and 60% yield was determined by ^{19}F NMR.

^1H NMR ($CDCl_3$, 400 MHz): δ 7.39 (d, J = 8.0 Hz, 1H), 7.21 (dt, J = 7.6 Hz, J = 0.9 Hz, 1H), 7.12 (br.s, 1H); 7.07 (dd, J = 8.0 Hz, J = 0.9 Hz, 1H); ^{19}F NMR ($CDCl_3$, 282 M Hz): δ –63.34 (s, 3F); GC–MS *m/z*, 176 (M^+).

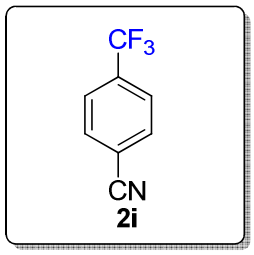
1-Methyl-3-(trifluoromethyl)benzene (2h): [3,4]



2h

The yield (51%) of **2h** was determined by ^{19}F NMR.
^{19}F NMR ($CDCl_3$, 282 M Hz): δ –63.25 (s, 3 F); GC–MS *m/z*, 160 (M^+).

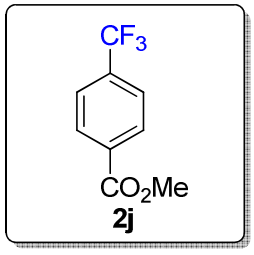
4-(trifluoromethyl)benzonitril (2i):[5]



2i

The yield (40%) of **2i** was determined by ^{19}F NMR.
^{19}F NMR ($CDCl_3$, 282 M Hz): δ –64.17 (s, 3F); GC–MS *m/z*, 171 (M^+).

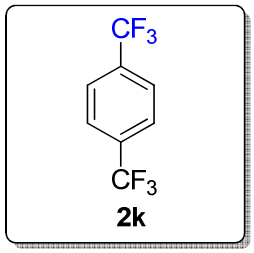
Methyl 4-(trifluoromethyl)benzoate (2j):[5]



2j

The yield (41%) of **2j** was determined by ^{19}F NMR.
^{19}F NMR ($CDCl_3$, 282 M Hz): δ –63.79 (s, 3F); GC–MS *m/z*, 204 (M^+).

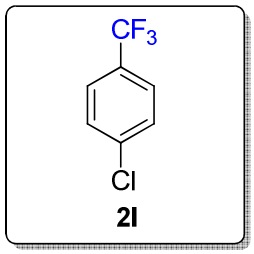
1,4-Bis(trifluoromethyl)benzene (2k):[5]



2k

Traces product of **2k** was determined by GC-MS.

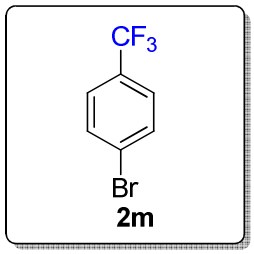
1-Chloro-4-(trifluoromethyl)benzene (2l):[5]



2l

The yield (45%) of **2l** was determined by ^{19}F NMR.
^{19}F NMR ($CDCl_3$, 282 M Hz): δ –63.18 (s, 3F); GC–MS *m/z*, 180 (M^+).

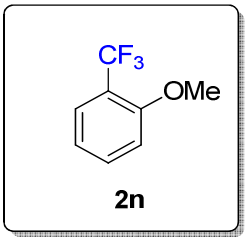
1-Bromo-4-(trifluoromethyl)benzene (2m):[5]



2m

The yield (57%) of **2m** was determined by ^{19}F NMR.
^{19}F NMR ($CDCl_3$, 282 M Hz): δ –63.48 (s, 3F); GC–MS *m/z*, 224 (M^+).

1-Methoxy-2-(trifluoromethyl)benzene (2n):[5]



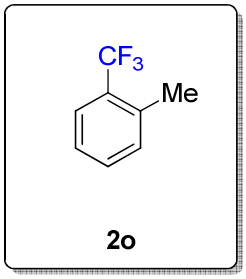
2n

Compound **2n** was isolated in 65% yield (29 mg) and 89% yield was determined by ^{19}F NMR.

^1H NMR ($CDCl_3$, 400 MHz): δ 7.56 (d, 1H, *J* = 7.8 Hz), 7.49 (t, 1H, *J* = 7.8 Hz), 7.05-6.95 (m, 3H), 3.90 (s, 3H); $^{13}CNMR$ ($CDCl_3$, 100 MHz): δ 157.5 (s, 1C), δ

133.2 (s, 1C), 127.1 (q, J = 5.2 Hz, 1C), 123.5 (q, J = 277.1 Hz, 1C), 120.0 (s,1C), 118.7 (q, J = 30.1 Hz, 1C), 111.9 (s,1C), 55.9 (s,1C); ^{19}F NMR ($CDCl_3$, 282 MHz): δ –63.05 (s, 3F); GC–MS *m/z*, 176 (M^+).

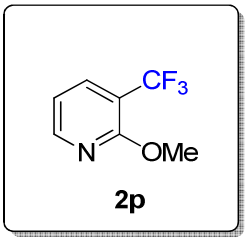
1-Methyl-2-(trifluoromethyl)benzene (2o):[5]



2o

The yield (55%) of **2o** was determined by ^{19}F NMR.
^{19}F NMR ($CDCl_3$, 282 M Hz): δ –63.21 (s, 3 F); GC–MS *m/z*, 160 (M^+).

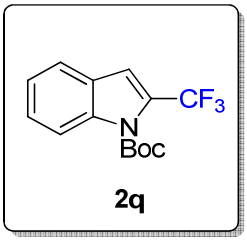
2-Methoxy-3-(trifluoromethyl)pyridine (2p):[2]



2p

The yield (85%) of **2p** was determined by ^{19}F NMR.
^{19}F NMR ($CDCl_3$, 282 M Hz): δ –64.47 (s, 3F); GC–MS *m/z*, 177 (M^+).

***Tert*-Butyl-2-(trifluoromethyl)-1*H*-indole-1-carboxylate (2q):**[2]

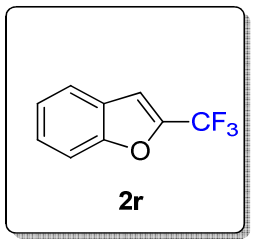


2q

Compound **2r** was isolated in 53% yield (37.8 mg) and 55% yield was determined by ^{19}F NMR.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.29 (dd, J = 8.4 Hz, J = 0.8 Hz 1H), 7.62 (d, J = 7.8 Hz, 1H), 7.45 (td, J = 7.8 Hz, J = 1.2 Hz, 1H), 7.29 (td, J =7.1 Hz, J = 1.1 Hz, 1H); 7.14 (br.s), 1.67 (s, 3H); ^{19}F NMR ($CDCl_3$, 376 M Hz): δ –58.29 (s, 3F); GC–MS *m/z*, 185 (M–Boc).

2-(Trifluoromethyl)benzofuran (2r):[2]



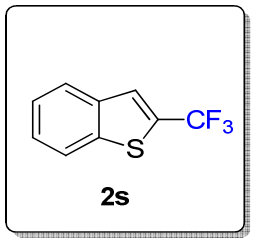
2r

Compound **2r** was isolated in 75% yield (34.8 mg) and 91% yield was determined by ^{19}F NMR.

^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.66 (d, *J* = 8.05 Hz, 1H), 7.56 (dq, *J* = 8.4 Hz, *J* = 0.9 Hz, 1H), 7.44 (td, *J* =8.4 Hz, *J* = 1.2 Hz, 1H); 7.32 (td, *J* = 8.4 Hz, *J* = 0.9 Hz 1H), 7.17-7.13 (m, 1H); ^{13}CNMR ($CDCl_3$, 100 MHz): δ 155.2 (s,1C), δ 143.5 (q, *J* = 48.5 Hz, 1C), 126.9 (s,1C), 126.9 (s,1C), 126.0 (s,1C), 124.2 (s,1C), 122.5 (s,1C), 119.4 (q, *J* = 268.2 Hz, 1C), 112.1 (s,1C), 108.1 (q, *J* = 2.9 Hz, 1C).

^{19}F NMR ($CDCl_3$, 282 MHz): δ –66.09 (s, 3 F); GC–MS *m/z*, 186 (M^+).

2-(Trifluoromethyl)benzo[b]thiophene (2s):[2]



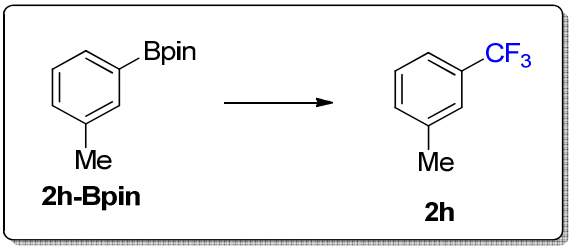
2s

Compound **2r** was isolated in 52% yield (26.2 mg) and 54% yield was determined by ^{19}F NMR.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.89-7.85 (m, 2H), 7.70 (s, 1H), 7.47-7.43 (m, 2H).

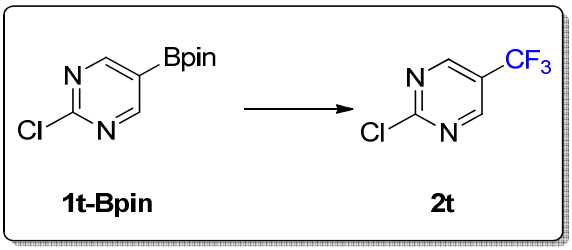
^{19}F NMR ($CDCl_3$, 282 MHz): δ –57.04 (s, 3F); GC–MS *m/z*, 202 (M^+).

1-Methyl-3-(trifluoromethyl)benzene (2h) from **2h-Bpin:**[3,4]



The yield (28%) of **2h** was determined by ^{19}F NMR.
^{19}F NMR ($CDCl_3$, 282 MHz): δ –63.27 (s, 3 F); GC–MS *m/z*, 160 (M^+).

2-Chloro-5-(trifluoromethyl)pyrimidine (2t) from **1t-Bpin:** [3,4]

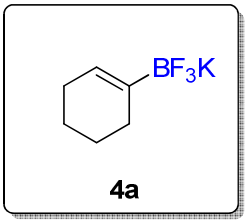


The yield (30%) of **2t** was determined by ^{19}F NMR.
^{19}F NMR ($CDCl_3$, 282 MHz): δ –62.80 (s, 3F); GC–MS *m/z*, 182 (M^+).

General Procedure for the Synthesis of Potassium Alkenyltrifluoroborats: Synthesis of compounds **3a-d** (Scheme 2).

To a solution of the boronic acid (1.4 mmol, 1.0 equiv) in MeOH (1.0 mL) was added 4.5 M aq. KHF_2 (933 µL, 4.2 mmol, 3.0 equiv) at 0 °C, the resulting mixture was stirred at the same temperature for 1 h. Solvent was removed by distillation; residue was dissolved in hot acetone (20 mL) and filtered. The filtrate was concentrated and dissolved in minimum amount of acetone, precipitated by adding MTBE. The precipitate was collected by filtration to get products as white solids.[6]

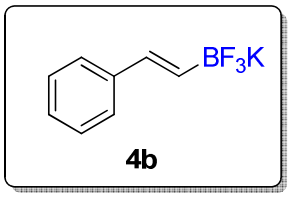
Cyclohex-1-en-1-yltrifluoroborate (4a). The title compound was isolated as a colourless solid in 84% yield (220 mg). The physical data matched with the literature data.[6]



^1H NMR (CD_3OD, 300 MHz): δ ppm 5.75 (s, 1H), 2.0-3.39 (m, 4H), 1.57-1.52 (m,

4H); ^{13}C NMR (CD_3OD, 100 MHz): δ ppm 126.5 (q, *J* = 3.5 Hz, 1C), 126.22 (s, 1C), 27.52 (s, 1C), 27.09 (s, 1C), 24.61 (s, 1C), 24.41 (s,1C); ^{19}F NMR (CD_3OD, 282 MHz): δ ppm –147.9.

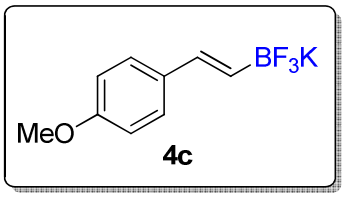
Potassium trans-styryltrifluoroborate (4b). The title compound was isolated as a colourless solid in 81% yield (240 mg). The physical data matched with the literature data.[6]



4b

^{1}H NMR (CD_3OD, 300 MHz): δ ppm 7.46–7.34 (m, 5H), 6.67 (d, *J* = 18.0 Hz, 1H), 6.27-6.19 (m, 1H); ^{19}F NMR (CD_3OD, 282 MHz): δ ppm –143.5.

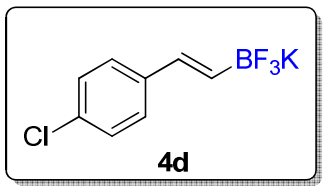
Potassium 4-methoxy trans-styryltrifluoroborate (4c). The title compound was obtained as a colorless solid in 73% yield (245 mg). physical data matched with the literature data.[6]



4c

^{1}H NMR (DMSO-d_6, 300 MHz): δ ppm 7.22 (d, *J* = 8.4 Hz, 2H), 6.81 (d, *J* = 8.4 Hz, 2H), 6.39 (d, *J* = 18.0 Hz, 1H), 6.01-5.92 (m, 1H); ^{19}F NMR (DMSO-d_6, 282 M Hz): δ ppm –138.0.

Potassium 4-chloro trans-styryltrifluoroborate (4d). The title compound was obtained as a colorless solid in 62% yield (215 mg). physical data matched with the literature data.[6]



4d

^{1}H NMR (DMSO-d_6, 300 MHz): δ ppm 7.34–7.25 (m, 4H), 6.44 (d, *J* = 18.3 Hz, 1H), 6.21-5.93 (m, 1H); ^{19}F NMR (DMSO-d_6, 282 M Hz): δ ppm –138.53.

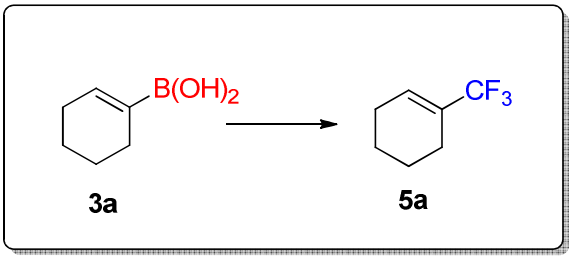
General procedure for the Synthesis of Alkenyl-CF_3 compounds: Synthesis of compounds **5a** to **5d** (Scheme 2).

A mixture of boronic acids or trifluoroborates (0.25 mmol, 1.0 equiv), CuCl (24.8 mg, 0.25 mmol, 1.0 equiv), $NaSO_2CF_3$ (117 mg, 0.75 mmol, 3.0 equiv), $NaHCO_3$ (21.0 mg, 0.25 mmol, 3.0 equiv) in CH_2Cl_2 (1.5 mL), MeOH (1.5 mL), and H_2O (1.2 mL) was cooled to 0 ℃, and TBHP (70% solution in water) (172 µL, 5.0 equiv, 1.25 mmol) was added under vigorous stirring. Stirring was continued for 6 –12h at room temperature.

For the compounds reported as isolated yields, the organic phase was separated, the aqueous phase was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic phases were dried over anhydrous Na_2SO_4, the solvent was removed at 1 atm and the residue was purified by column chromatography on Combiflash with hexanes to afford the desired compounds.

The volatile products were not isolated and their yields were determined only by ^{19}F NMR of the reaction mixture. For the compounds reported with ^{19}F NMR yields, 4-fluorobenzonitrile (0.25 mmol) was added as reference to the reaction mixture, stirred for 5 min, an aliquot of the organic phase was withdrawn for the ^{19}F NMR measurement in $CDCl_3$.

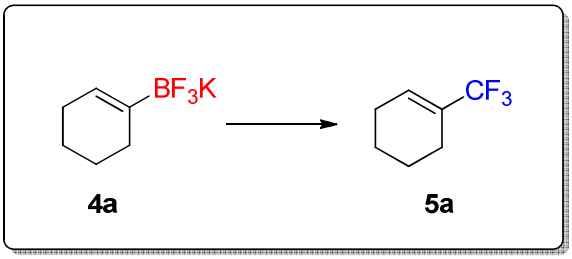
1-(Trifluoromethyl)cyclohex-1-ene (5a)[10] from **3a:**



According to the general procedure; compound **5a** was formed in 64% yield by ^{19}F NMR.

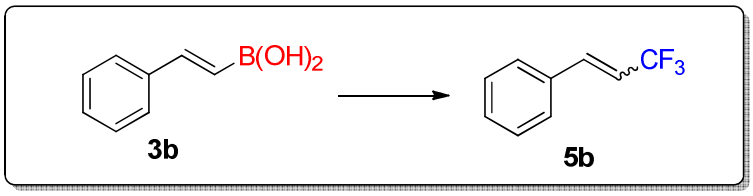
^{19}F NMR ($CDCl_3$, 282 MHz): δ –70.30 (s, 3F); GC–MS *m/z*, 150 (M^+).

1-(Trifluoromethyl)cyclohex-1-ene (5a) [7] from **4a:**



According to the general procedure; compound **5a** was formed in 60% yield by ^{19}F NMR.
^{19}F NMR ($CDCl_3$, 282 MHz): δ –70.30 (s, 3F); GC–MS *m/z*, 150 (M^+).

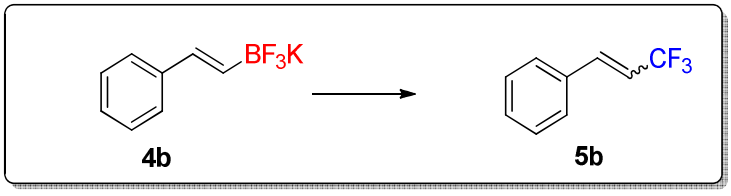
(*E*)-(3,3,3-Trifluoro-1-en-1-yl)benzene (5b)[8] from **3b:**



According to the general procedure compound **5b** was obtained in 80% (35 mg) yield and 92% yield was determined by ^{19}F NMR. A ratio of E/Z = 25:1 was determined by ^{1}H NMR

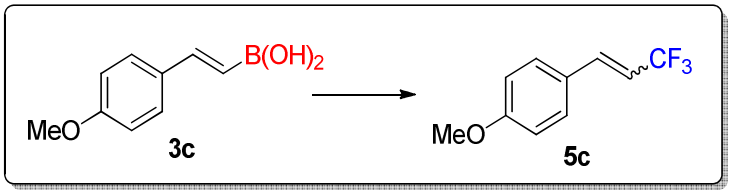
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.46-7.42 (m, 2H, mixed signal of *E* and *Z* isomers), 7.40-7.34 (m, 3H, mixed signal of *E* and *Z* isomers), 7.14 (dq, *J* = 16.2, 2.2 Hz, 1H, *E*-isomer), 6.91 (d, *J* = 12.7 Hz, *Z*-isomer), 6.19 (dq, *J* = 16.4, 7.3 Hz, 1H, *E*-isomer), 5.76 (d, *J* = 12.7, 9.2 Hz, *Z*-isomer); ^{19}F NMR ($CDCl_3$, 282 MHz): δ –64.05 (s, 3F, *E*-isomer); GC–MS *m/z*, 172 (M^+).

(*E*)-(3,3,3-Trifluoro-1-en-1-yl)benzene (5b) from **4b:**



According to the general procedure; compound **5b** was formed in 98% yield by ^{19}F NMR. A ratio of E/Z = 20:1 was determined by ^{1}H NMR.
^{19}F NMR ($CDCl_3$, 282 MHz). δ –64.03 (s, 3F, *E*-isomer); GC–MS *m/z*, 172 (M^+).

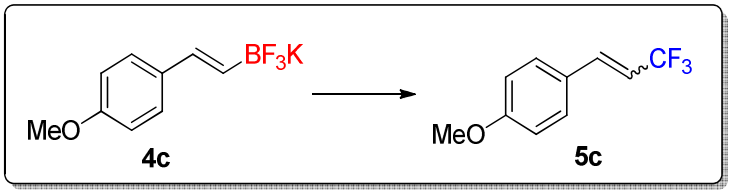
(*E*)-1-methoxy-4-(3,3,3-Trifluoro-1-en-1-yl)benzene (**5c**)[9] from **3c:**



According to the general procedure compound **5c** was isolated in 85% yield (43mg) and 93% yield was determined by ^{19}F NMR. A ratio of E/Z = 16:1 was determined by ^{1}H NMR

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.39 (d, *J* = 8.8 Hz, 2H, mixed signals of *E* and *Z* isomers), 7.08 (dq, *J* = 16.2, 2.3 Hz, 1H, *E*-isomer), 6.90 (d, *J* = 8.8 Hz, 2H, mixed signals of *E* and *Z* isomers), 6.81 (d, *J* = 12.8 Hz, *Z*-isomer), 6.05 (dq, *J* = 16.2, 6.6 Hz, 1H, *E*-isomer), 5.62 (dq, *J* = 12.8, 9.4 Hz, *Z*-isomer), 3.82 (s, 3H, mixed signals of *E* and *Z* isomers); ^{19}F NMR ($CDCl_3$, 282 MHz): δ –63.49 (s, 3 F, *E*-isomer); GC–MS *m/z*, 202 (M^+).

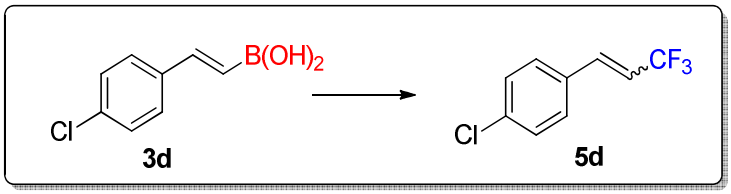
(*E*)-1-methoxy-4-(3,3,3-Trifluoro-1-en-1-yl)benzene (**5c**)[9] from **3c:**



According to the general procedure; compound **5c** was formed in 94% yield by ^{19}F NMR. A ratio of E/Z = 13:1 was determined by ^{1}H NMR.

^{19}F NMR ($CDCl_3$, 282 MHz): δ –63.36 (s, 3F, *E*-isomer); GC–MS *m/z*, 202 (M^+).

(*E*)-1-chloro-4-(3,3,3-Trifluoro-1-en-1-yl)benzene (**5d**)[9] from **3d:**

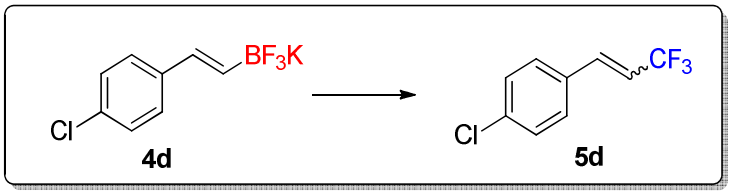


According to the general procedure compound **5d** was isolated in 62% yield

(32mg) and 86% yield was determined by ^{19}F NMR. A ratio of E/Z = 12:1 was determined by ^{1}H NMR.

^{1}H NMR (DMSO d_6, 300 MHz): δ 7.37–7.32 (m, 4H, mixed signals of *E* and *Z* isomers), 7.09 (dq, *J* = 16.2, 2.2 Hz, 1H, *E*-isomer), 6.86 (d, *J* = 12.4 Hz, *E*-isomer), 6.17 (dq, *J* = 16.2, 6.6 Hz, 1H, *E*-isomer), 5.78 (dq, *J* = 12.4, 9.0 Hz, *Z*-isomer); ^{19}F NMR ($CDCl_3$, 282 M Hz): δ –64.08 (s, 3F, *E*-isomer); GC–MS *m/z*, 206 (M^+).

(*E*)-1-chloro-4-(3,3,3-Trifluoro-1-en-1-yl)benzene (**5d**)[9] from **4d:**



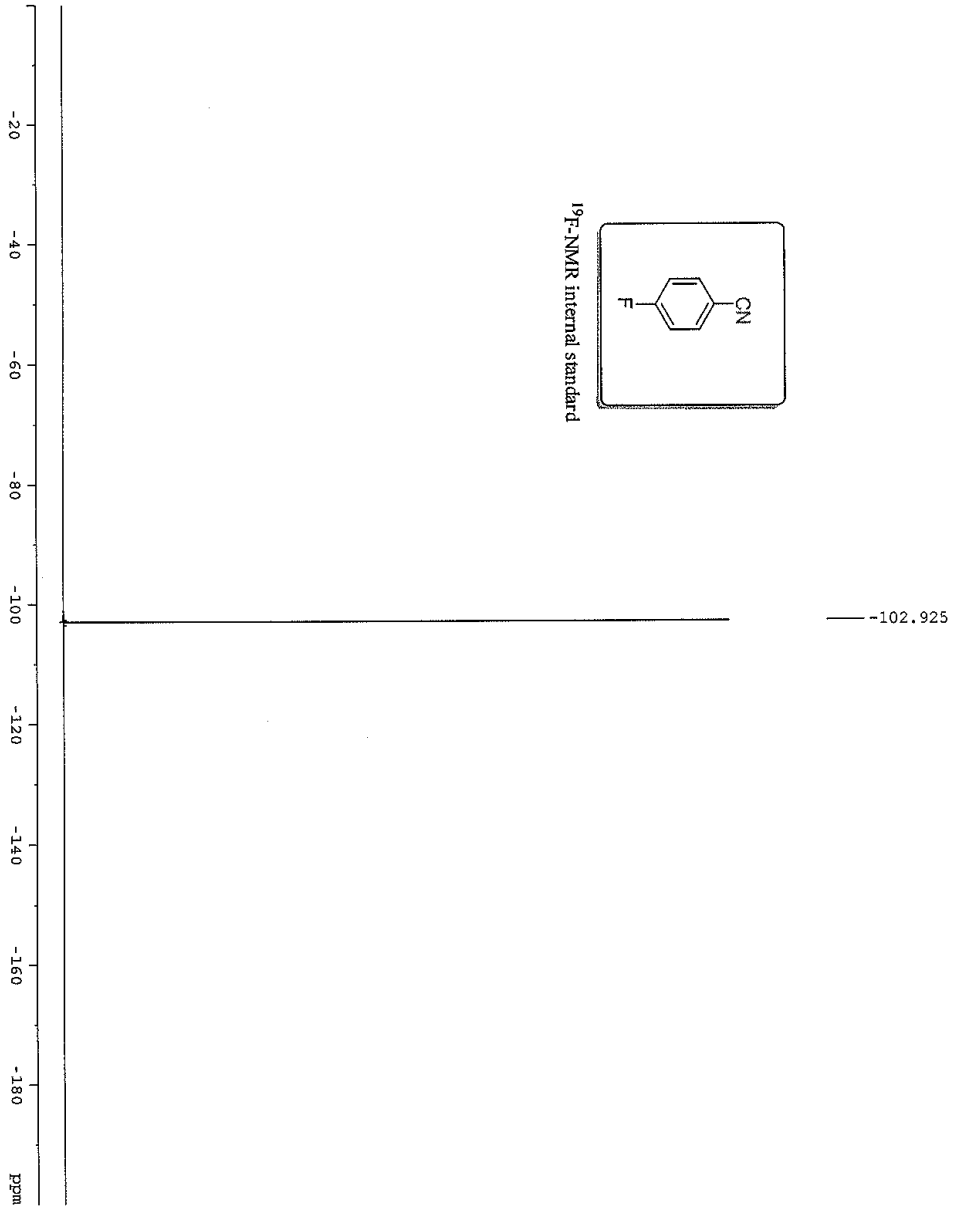
According to the general procedure compound **5d** was formed in 74% yield by ^{19}F NMR. A ratio of E/Z = 3:1 was determined by ^{1}H NMR.

^{19}F NMR ($CDCl_3$, 282 M Hz): δ –63.98 (s, 3F, *E*-isomer); GC–MS *m/z*, 206 (M^+).

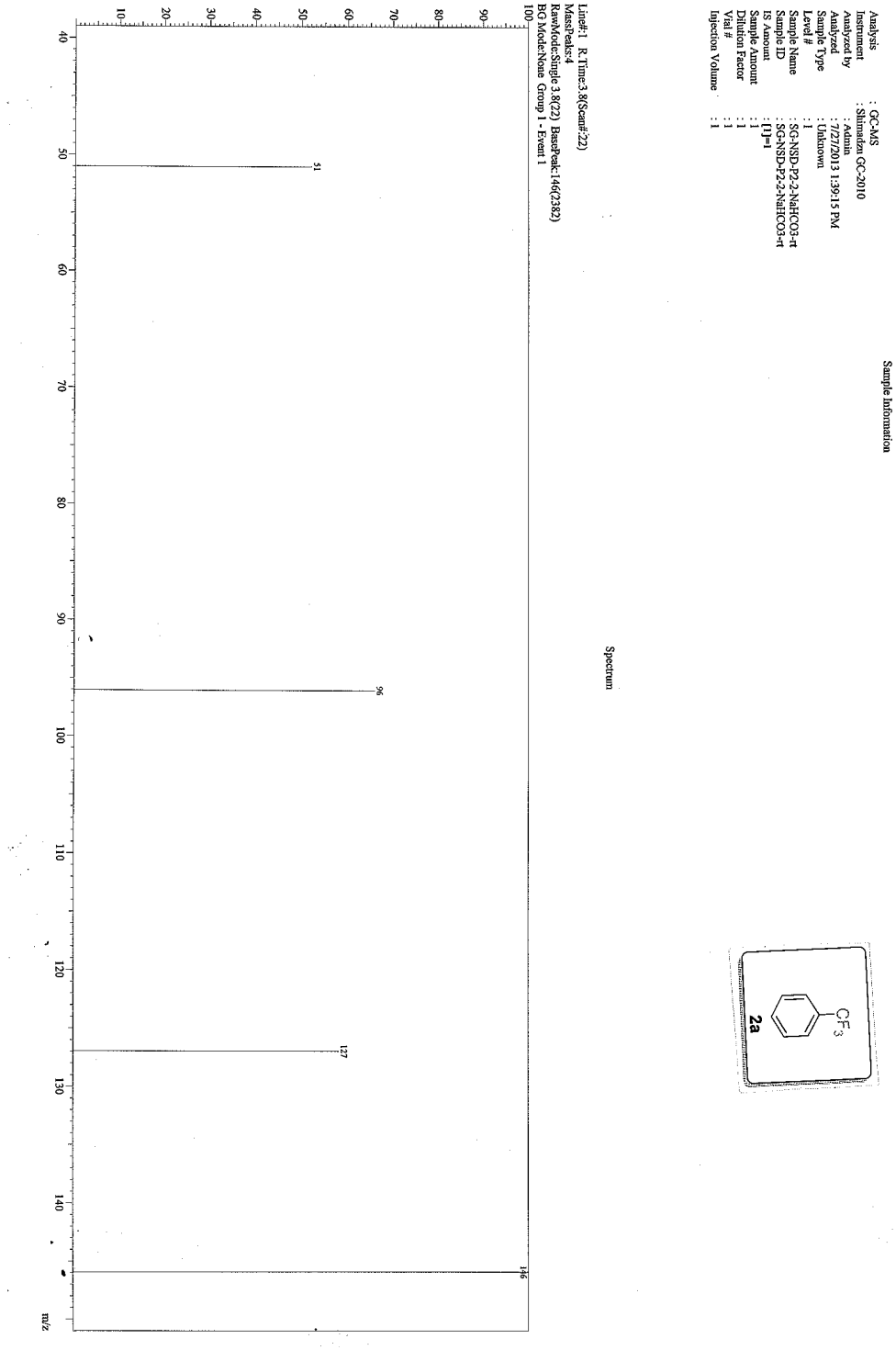
References

1. Xu, J.; Luo, D.-F.; Xiao, B.; Liu, Z.-J.; Gong, T.-J.; Fu, Y.; Liu, L. *Chem. Commun*. **2011**, 4300.
2. Liu, T.; Shen, Q. *Org. Lett.* **2011**,13, 2342; Chu, L.; Qing, F.-L. *Org. Lett.* **2010**, *12,* 5060
3. (a) Khan, B. A.; Buba, A. E.; Gooßen, L. J. *Chem. — Eur. J*. **2011**, 17, 2689. (b) Novàk, P.; Lishchynskyi, A.; Grushin, V. V. *Angew. Chem., Int. Ed.* **2012**, *51*, 7767.
4. Huang, Y; Fang, X.; Li, H.; H, W.; Huang, K.-W.; Yuan, Y.; Weng, Z. *Tetrahedron Lett.* **2012**, *68*, 9949.
5. (a) Ye, Y.; Künzi, S. A.; Sanford, M. S. *Org. Lett.* **2012**, *14*, 4979. (b) Ye, Y.; Sanford, M. S. *J. Am. Chem. Soc.* **2012**, *134*, 9034.
6. (a) Brak, K.; Ellman, J. A. *J. Am. Chem. Soc.* **1999**, *131*, 3850 and references therein. (b) Molander, G. A.; Petrillo, D. E. *J. Am. Chem. Soc.* **2006**, *128*, 9634. (c) Vedejs, E.; Fields, S. C.; Hayashi, R.; Hithccock, S. R.; Powell, D. R.; Schrimpf, M. R. *J. Am. Chem. Soc.* **1999**, 121, 2460
7. Cho, E. J.; Buchwald, S. L. *Org. Lett.* **2011**, 13, 6552.
8. Prakash, G. K. S.; Krishnan, H. S.; Jog, P. V.; Lyer, A. P.; Olah, G. A. *Org. Lett.* **2012**, 14, 1146.
9. (a) Liu, T.; Shen, Q. *Org. Lett.* **2011**, 13, 2342; (b) Hanamoto, T.; Morita, N.; Shindo, K. *Eur.J. Org. Chem.* **2003**, *21*, 4279.

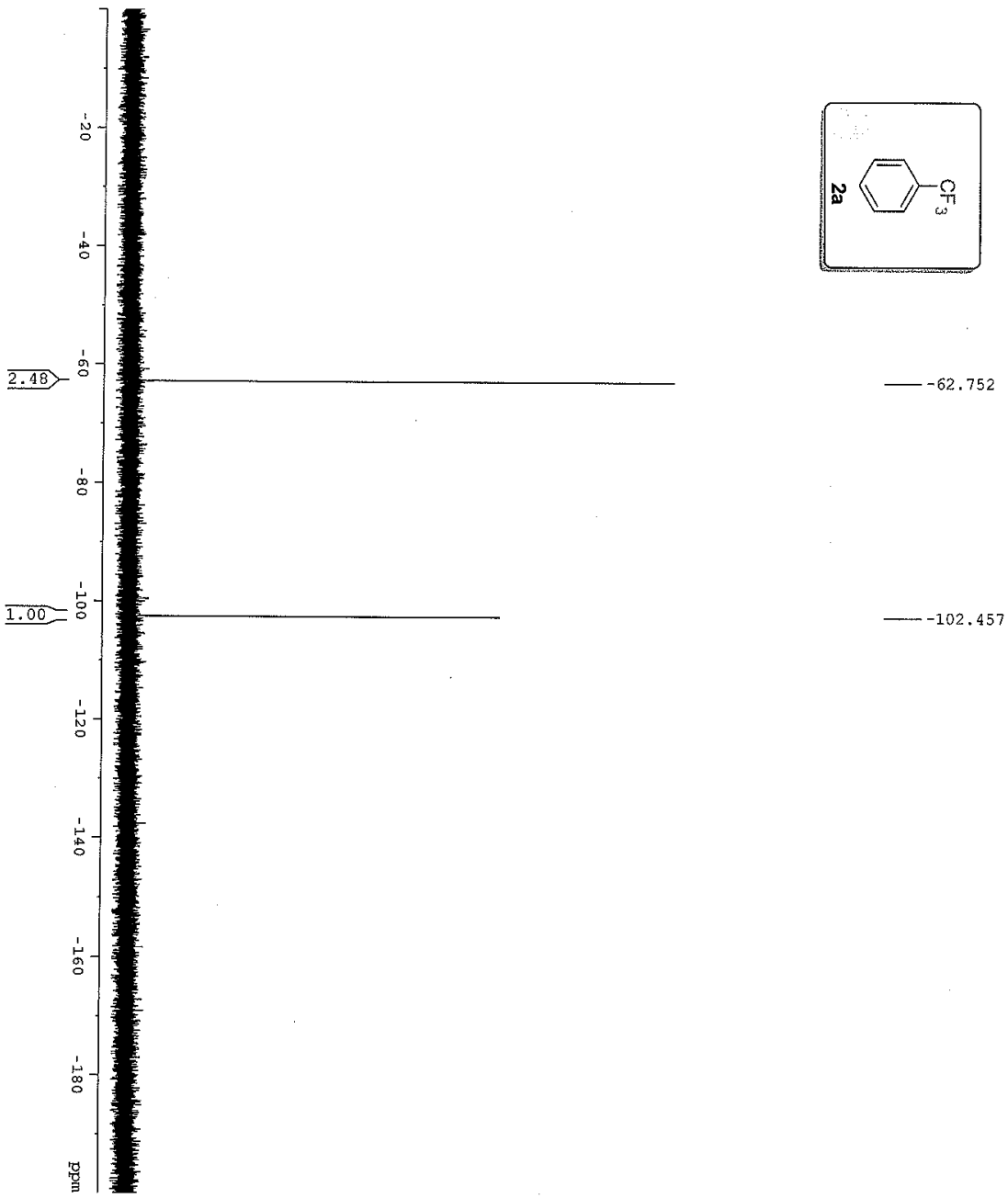
^{19}F NMR of 4-fluorobenzonitrile (internal standard) in $CDCl_3$



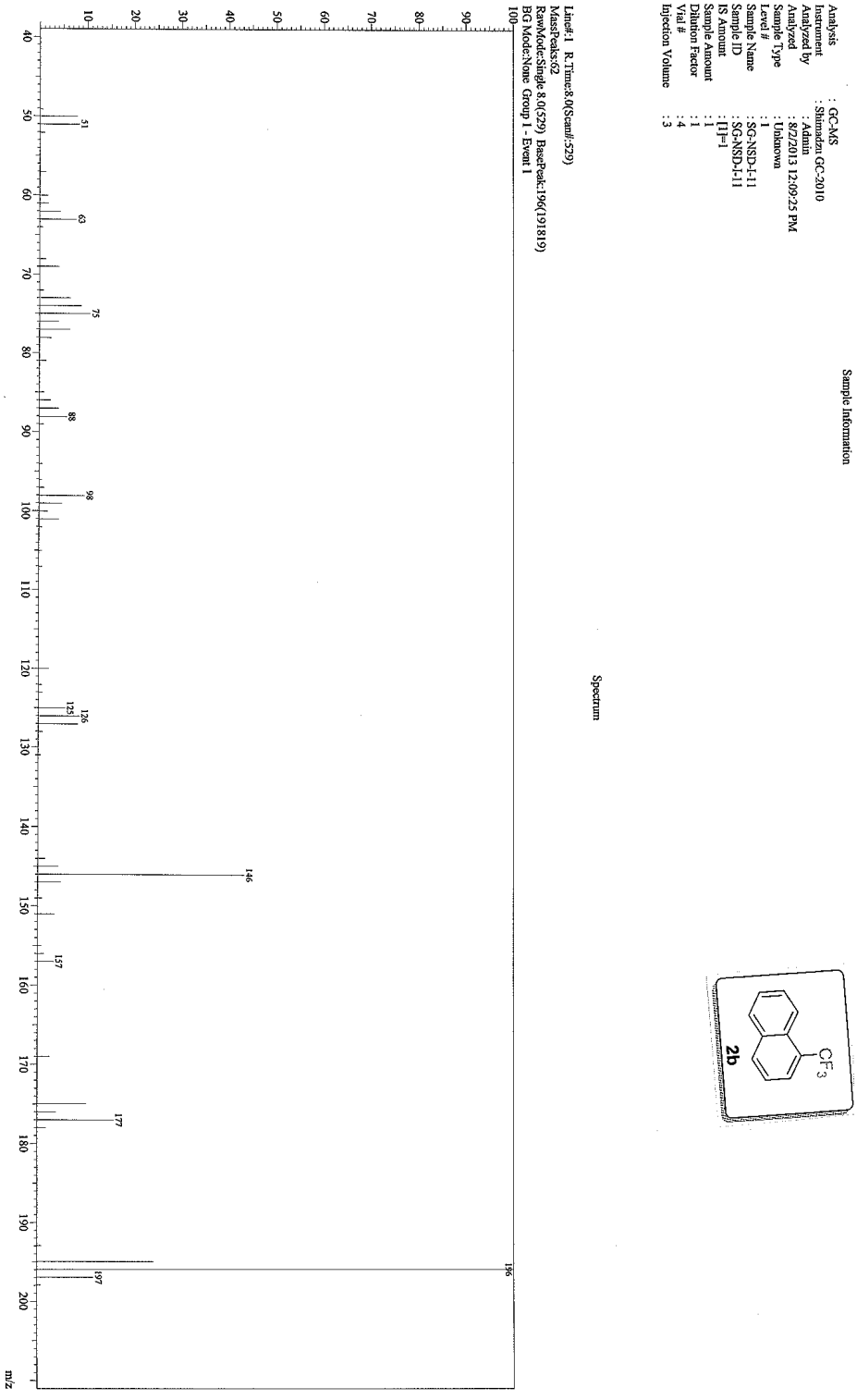
GC-MS of crude 2a



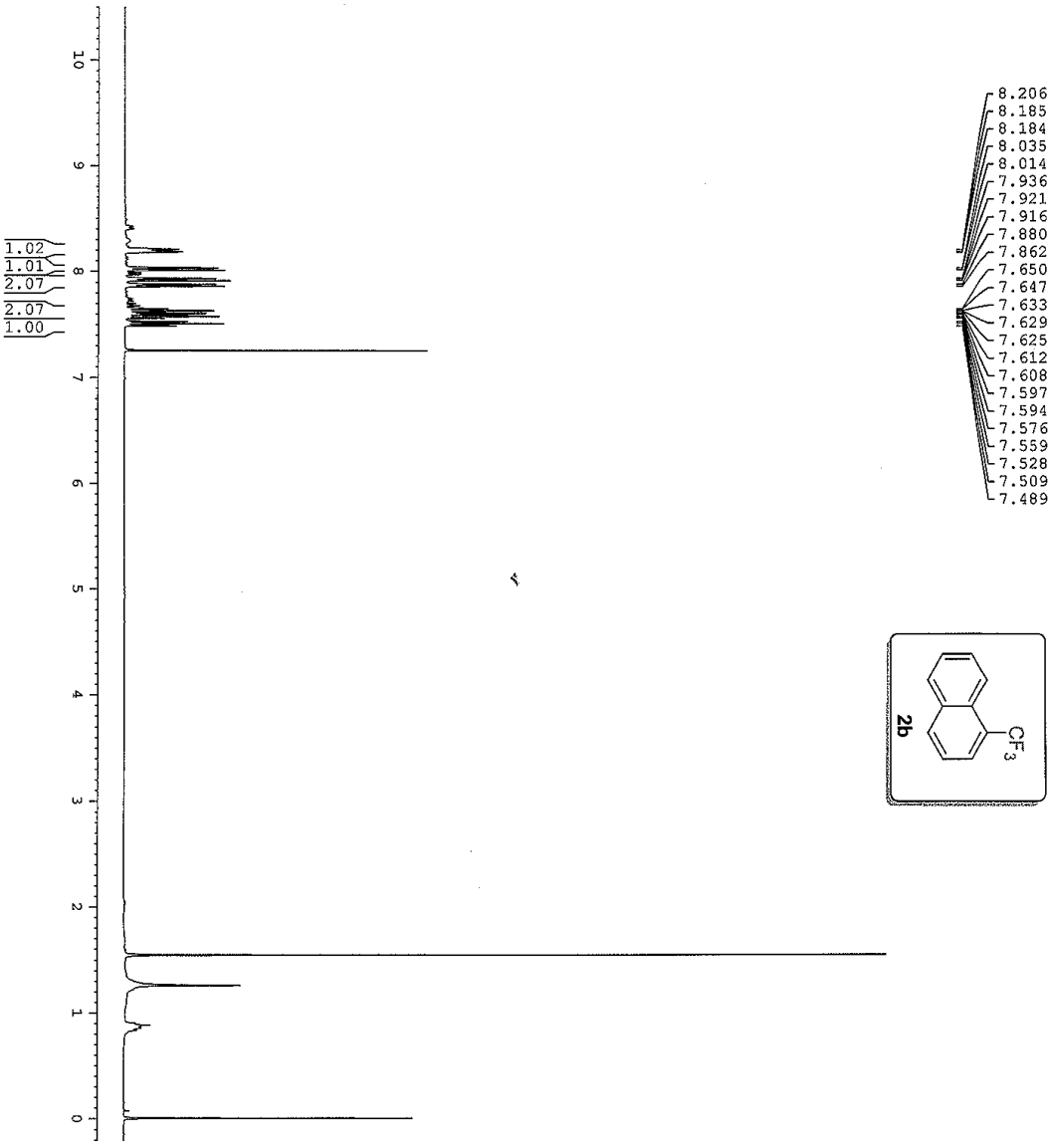
^{19}F NMR yield of compound 2a (2.48/(1×3)×100% = 82%) in $CDCl_3$



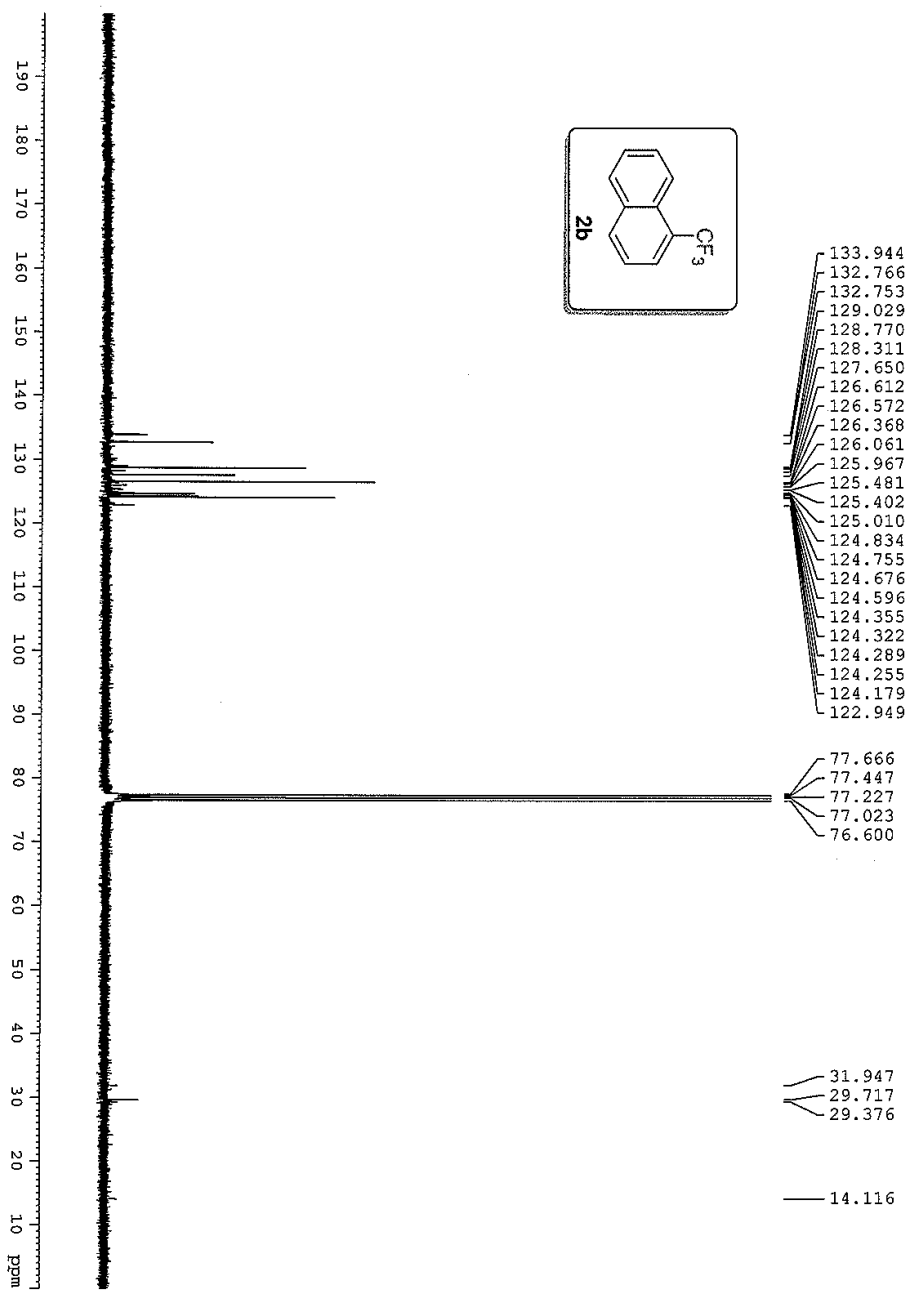
GC-MS of crude 2b



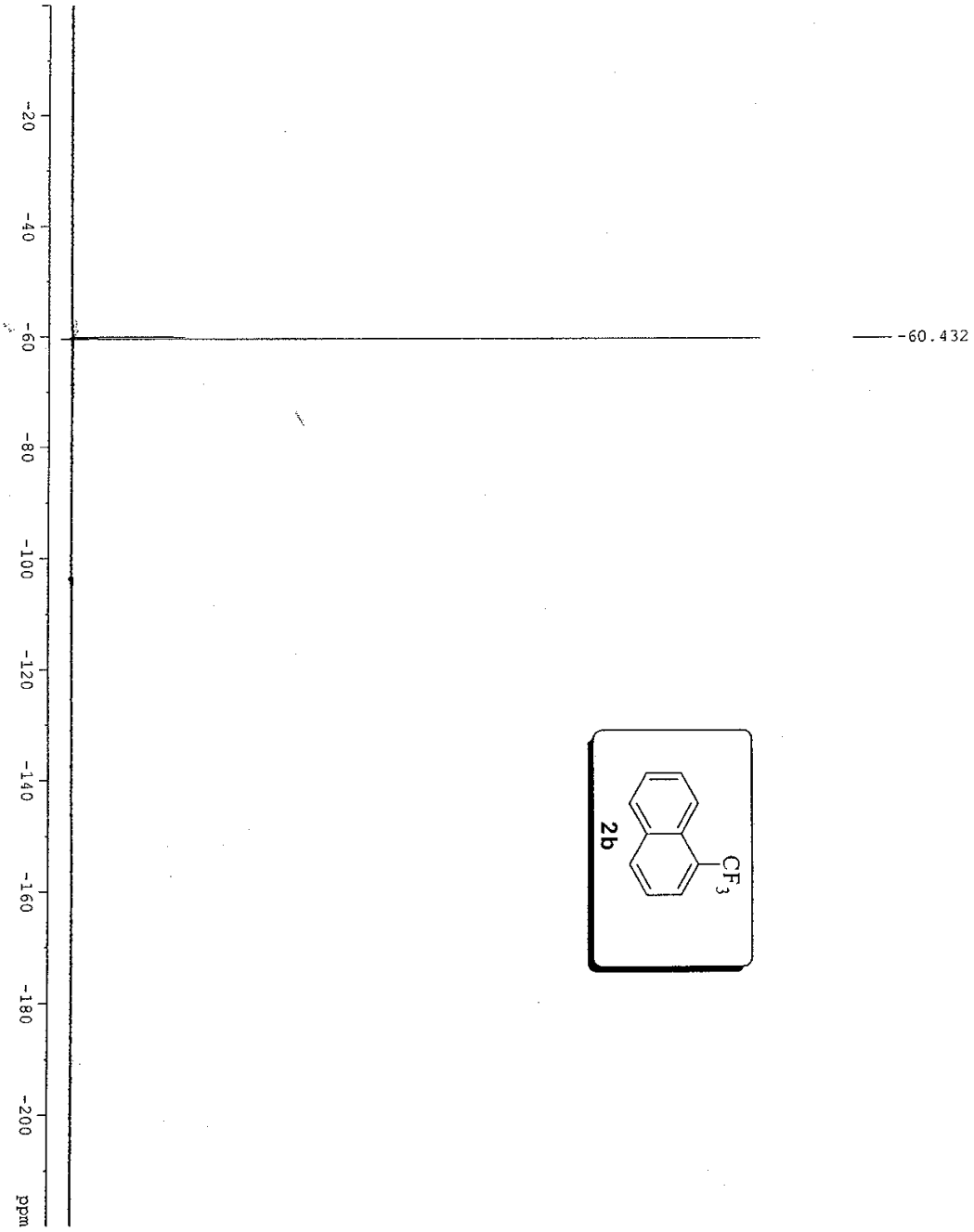
^{1}H NMR of compound 2b



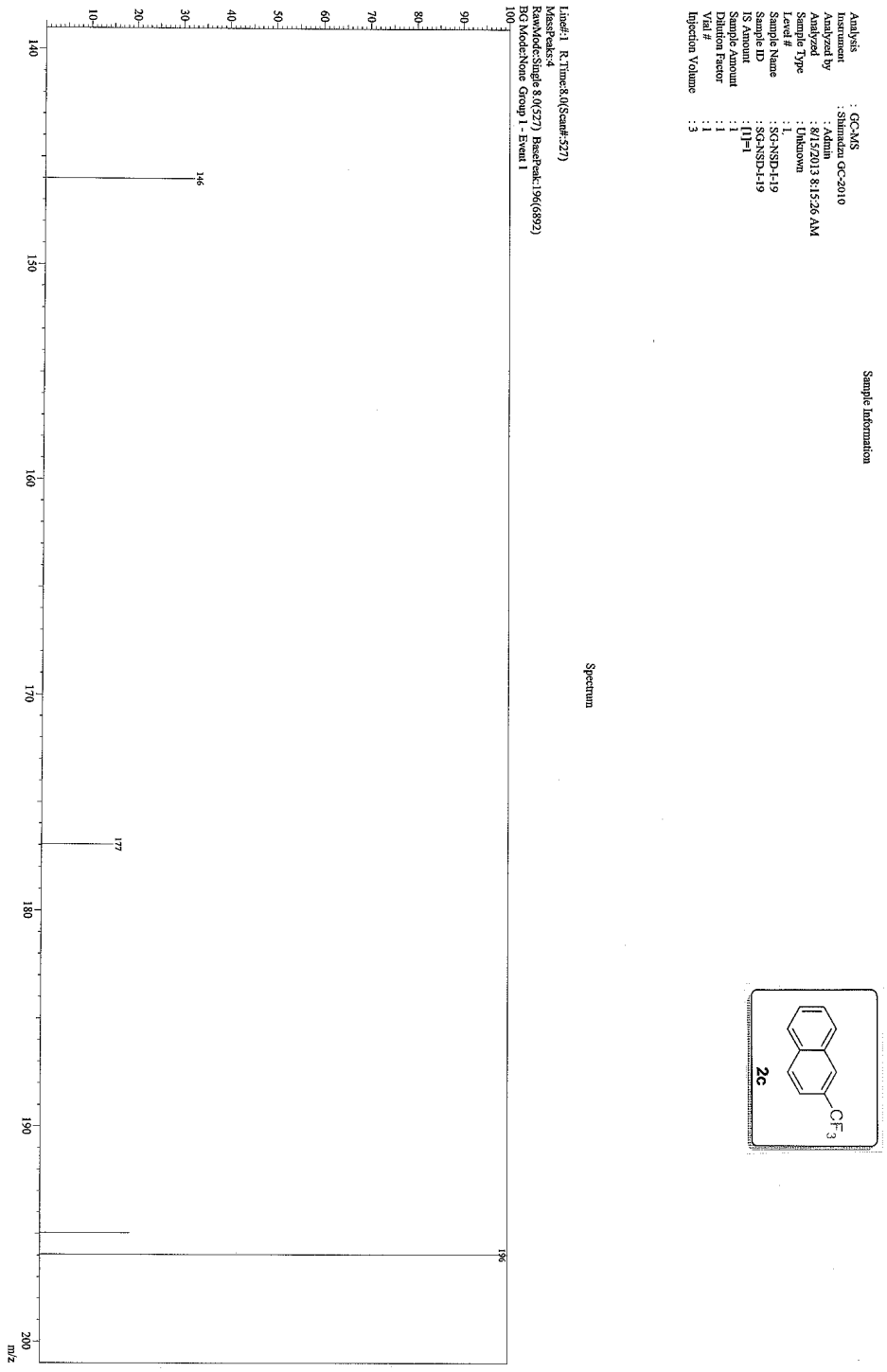
^{13}C NMR of compound 2b



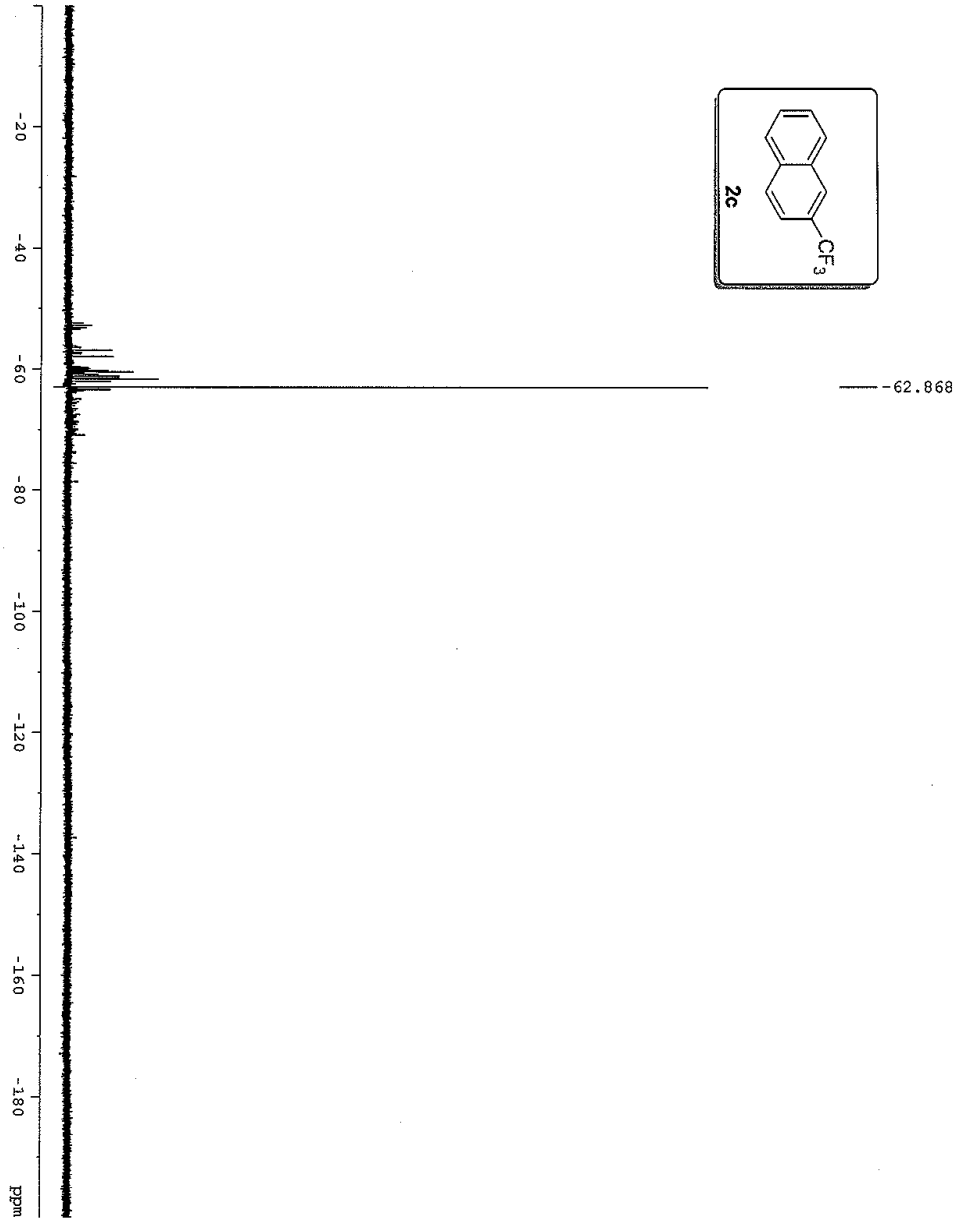
^{19}F NMR of isolated 2b in $CDCl_3$



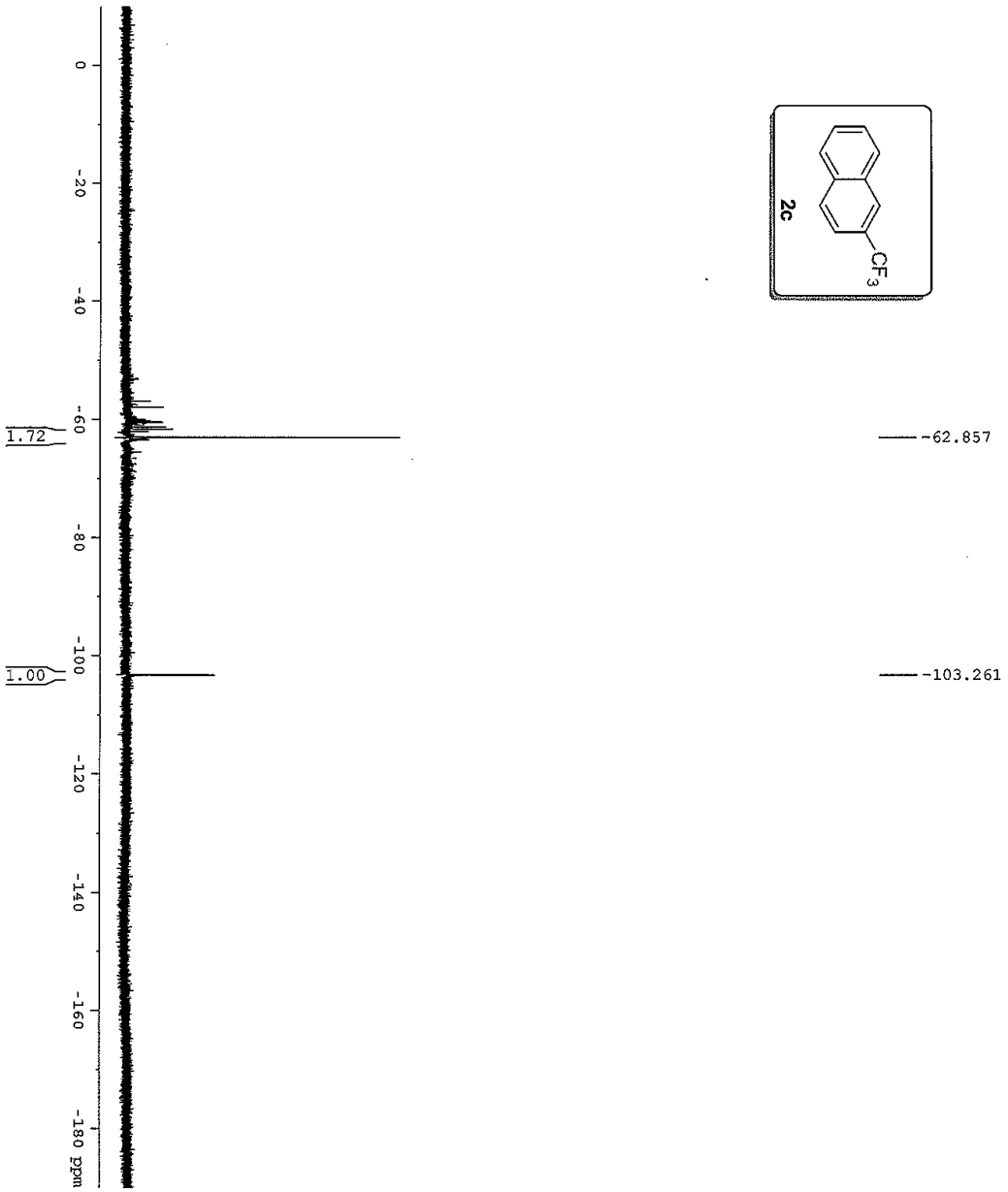
GC-MS of crude 2c



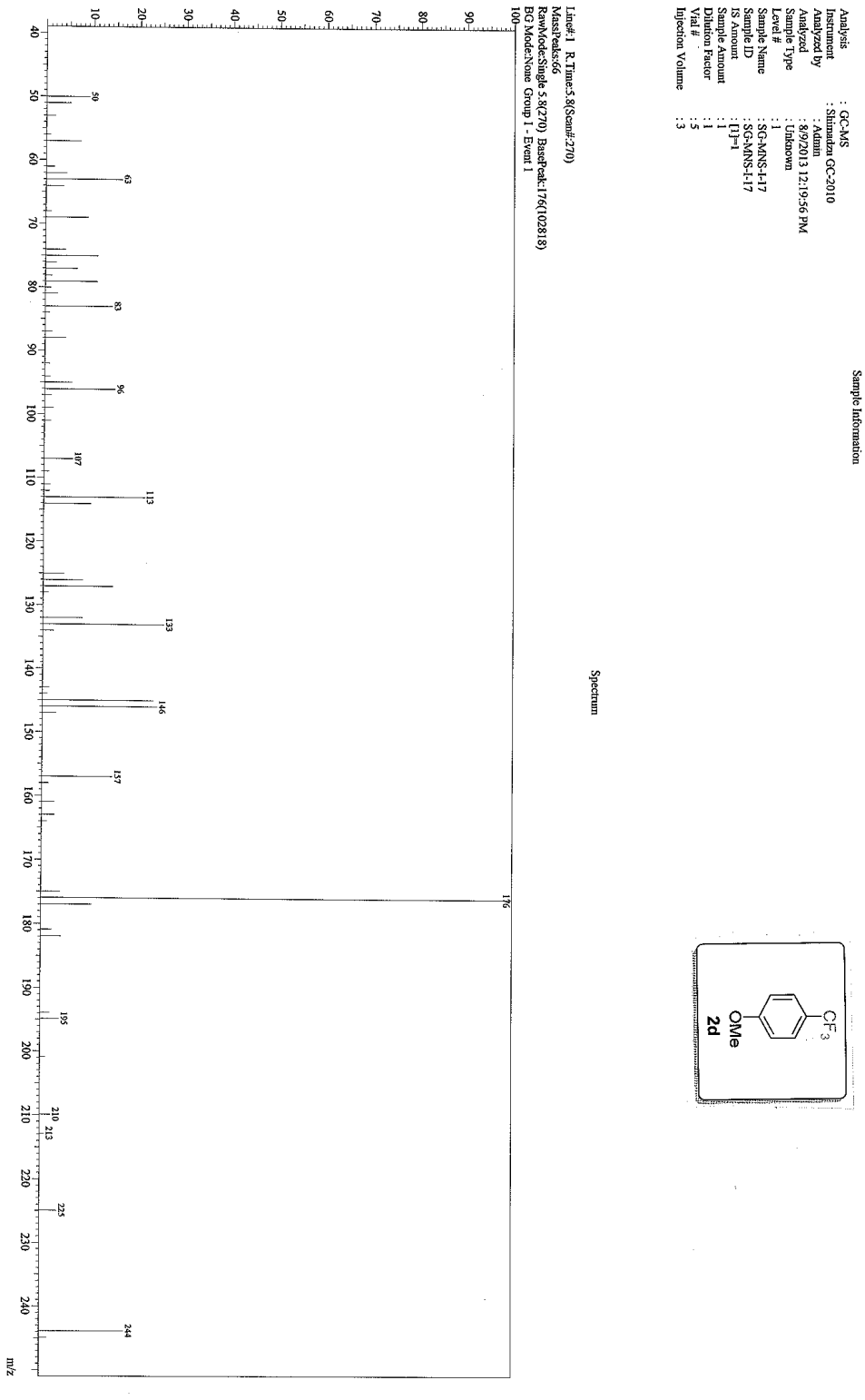
^{19}F NMR of crude 2c in $CDCl_3$



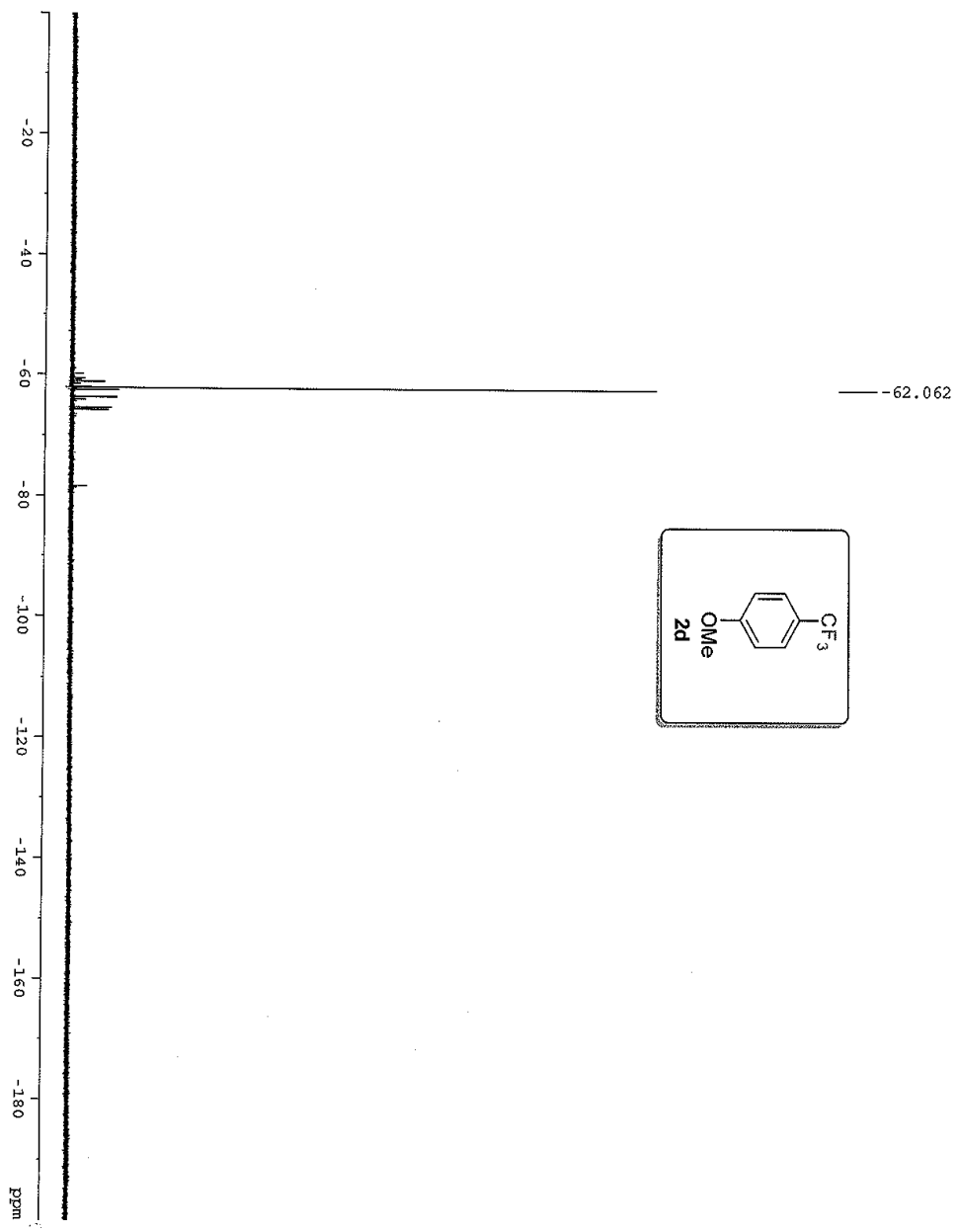
^{19}F NMR yield of compound 2c (1.72/(1×3)×100% = 57%) in $CDCl_3$



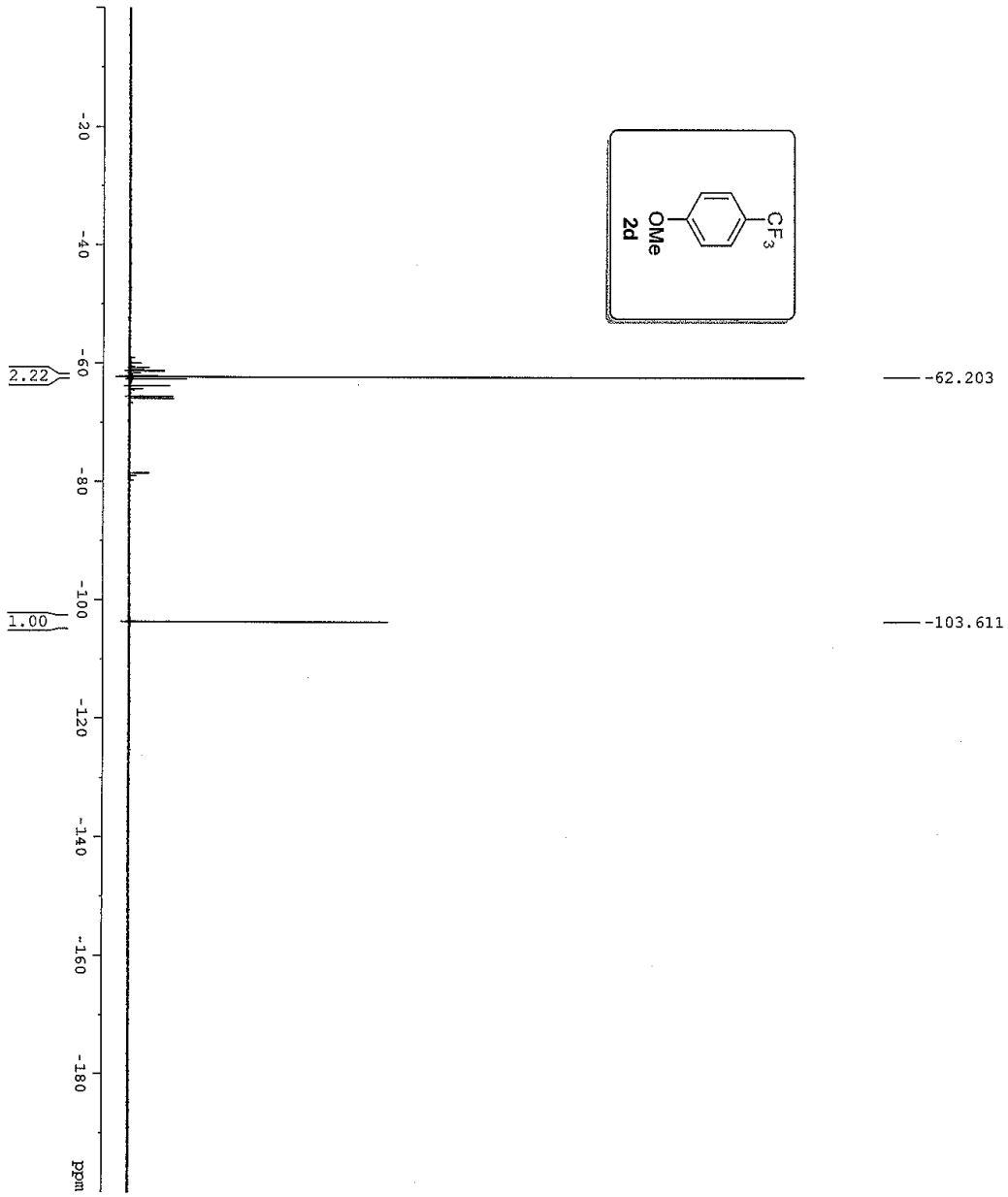
GC-MS of crude 2d



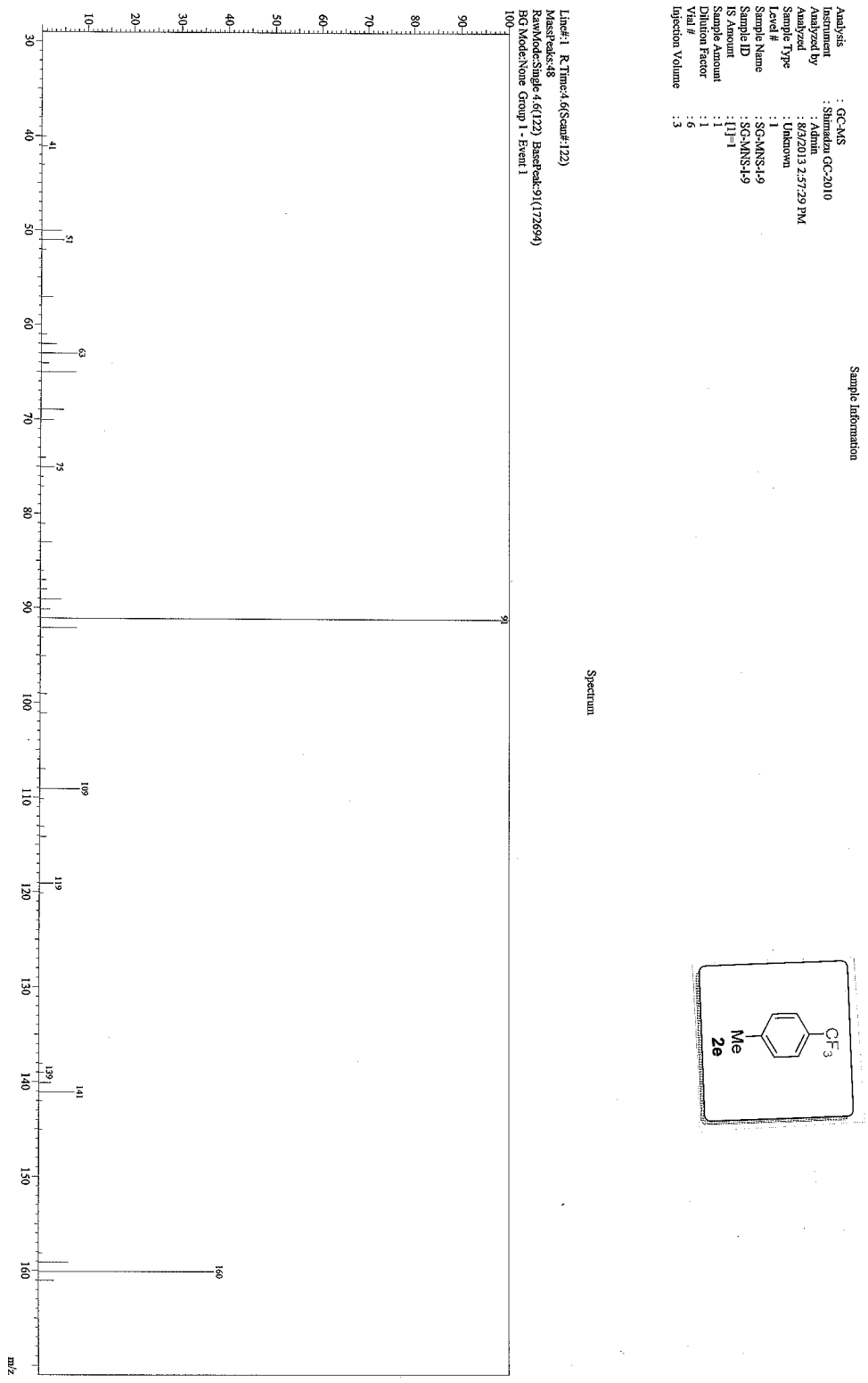
^{19}F NMR of crude 2d in $CDCl_3$



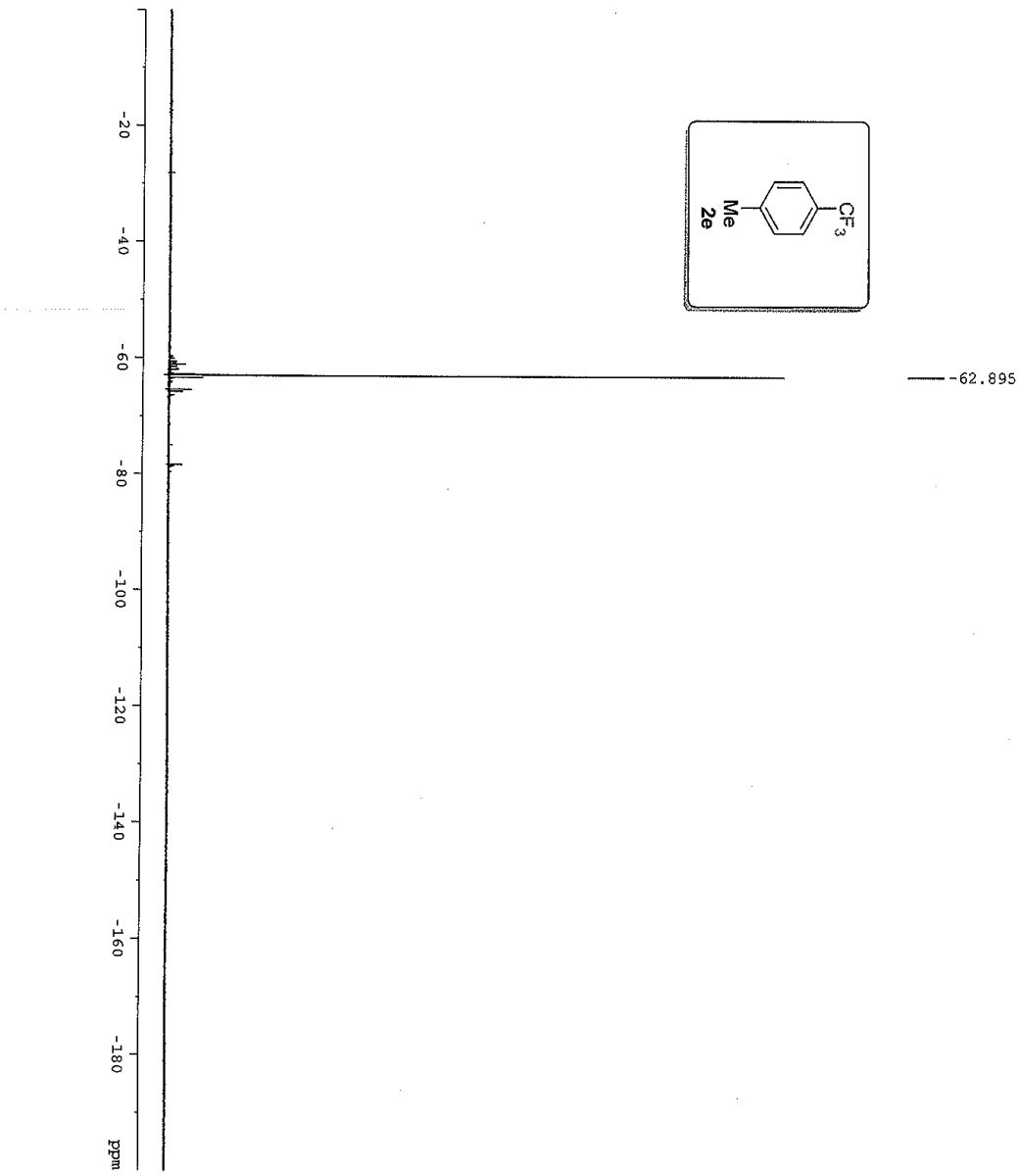
^{19}F NMR yield of compound 2d (2.22/(1×3)×100% = 74%) in $CDCl_3$



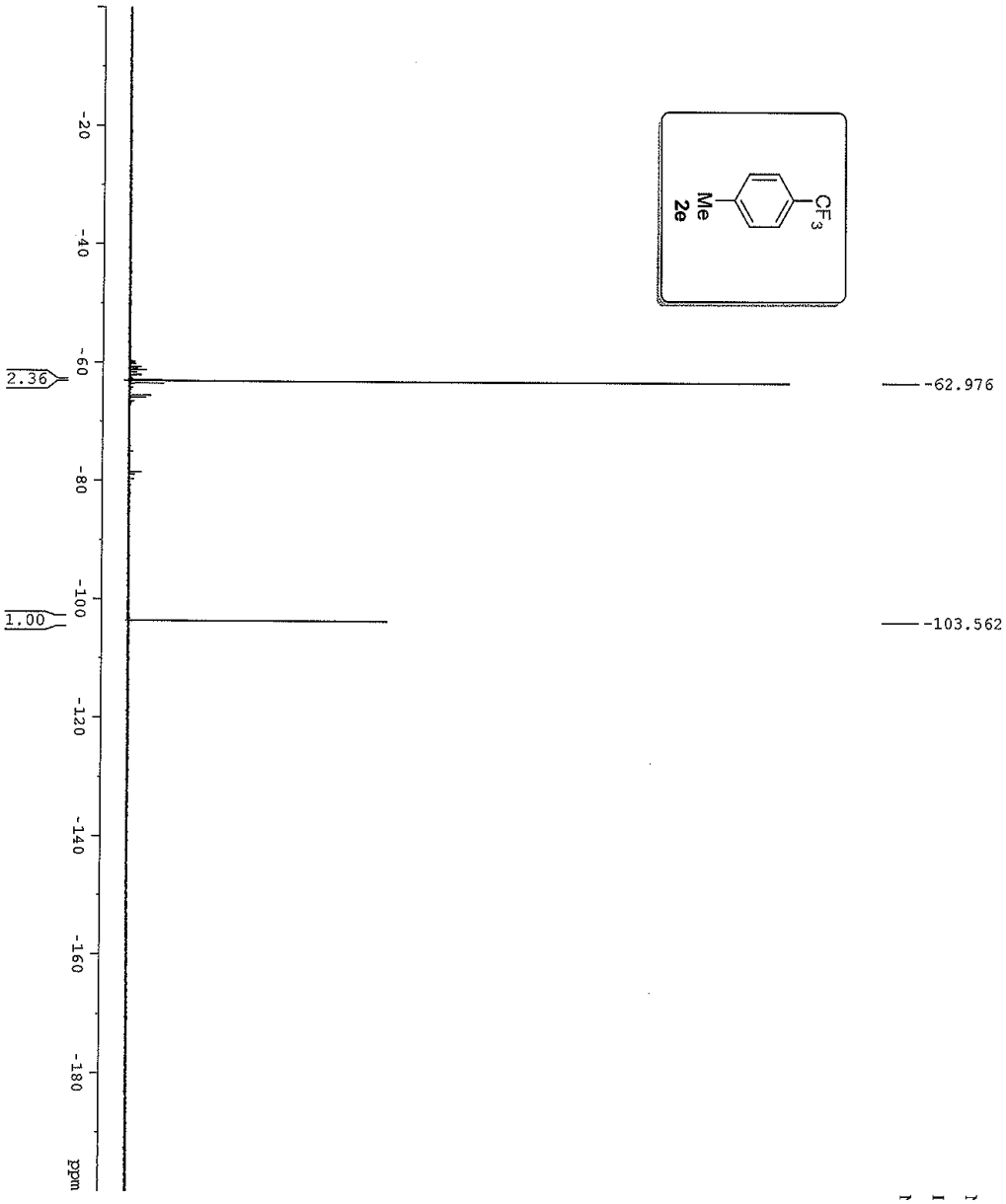
GC-MS of crude 2e



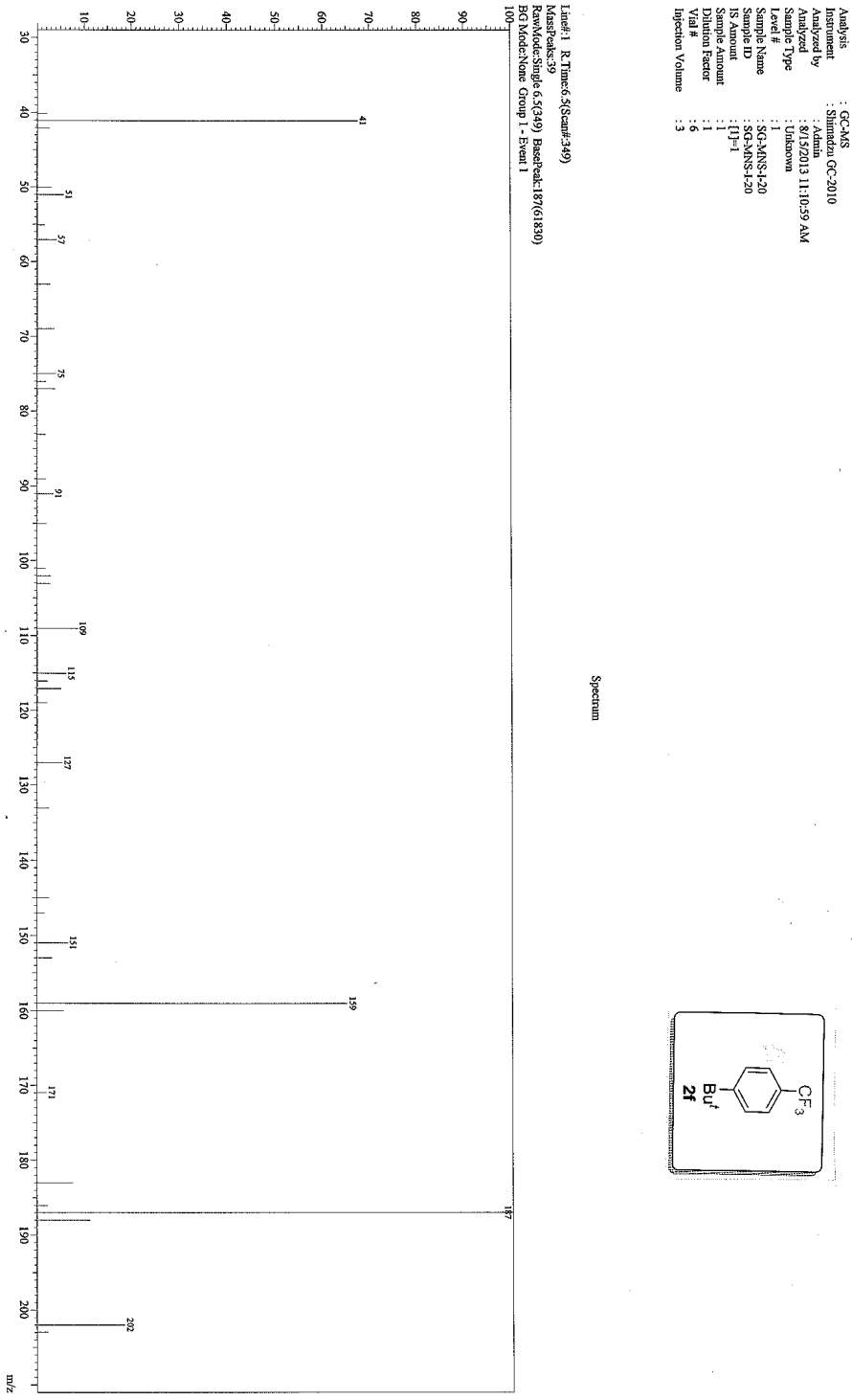
^{19}F NMR of crude 2e in $CDCl_3$



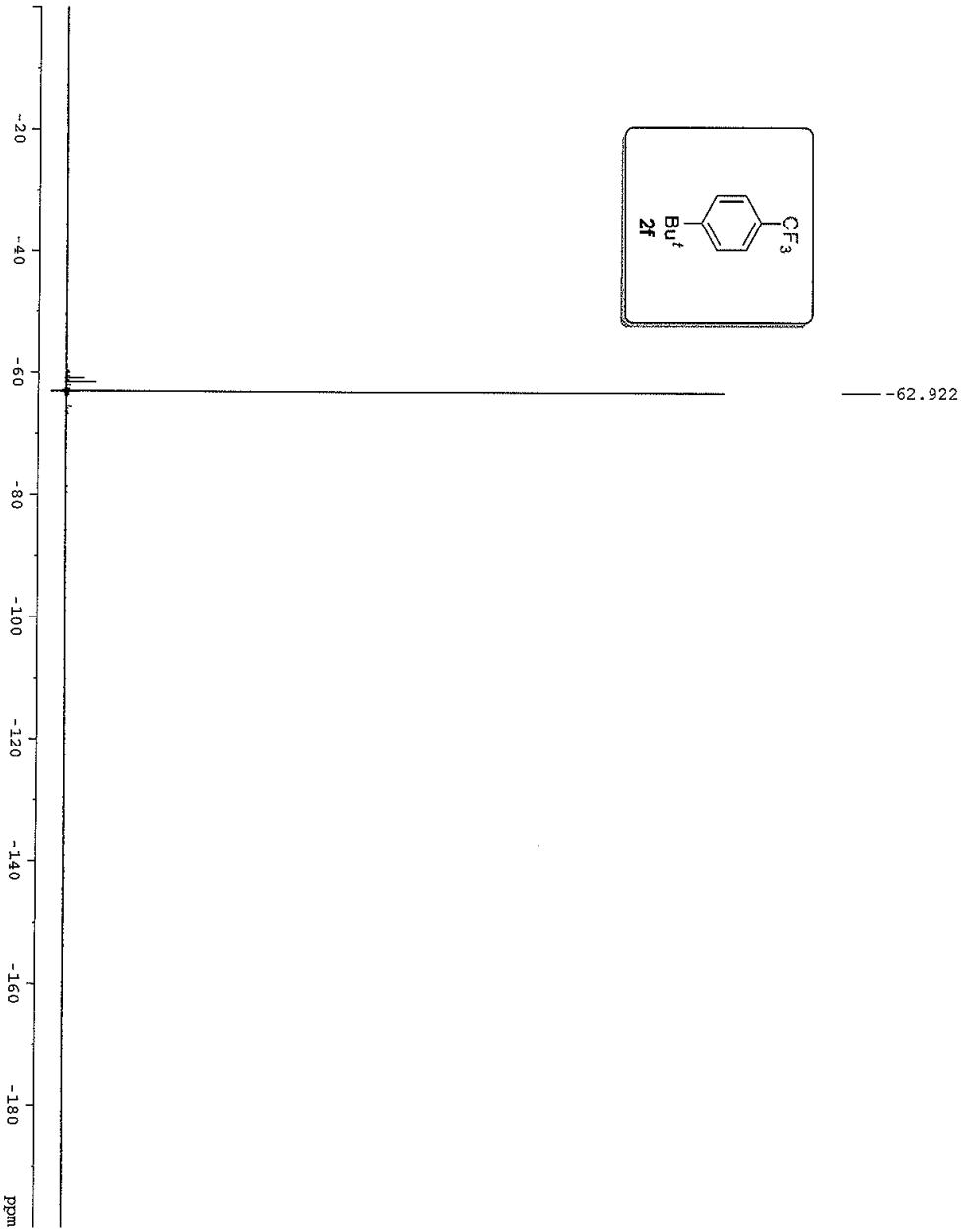
^{19}F NMR yield of compound 2e (2.36/(1×3)×100% = 79%) in $CDCl_3$



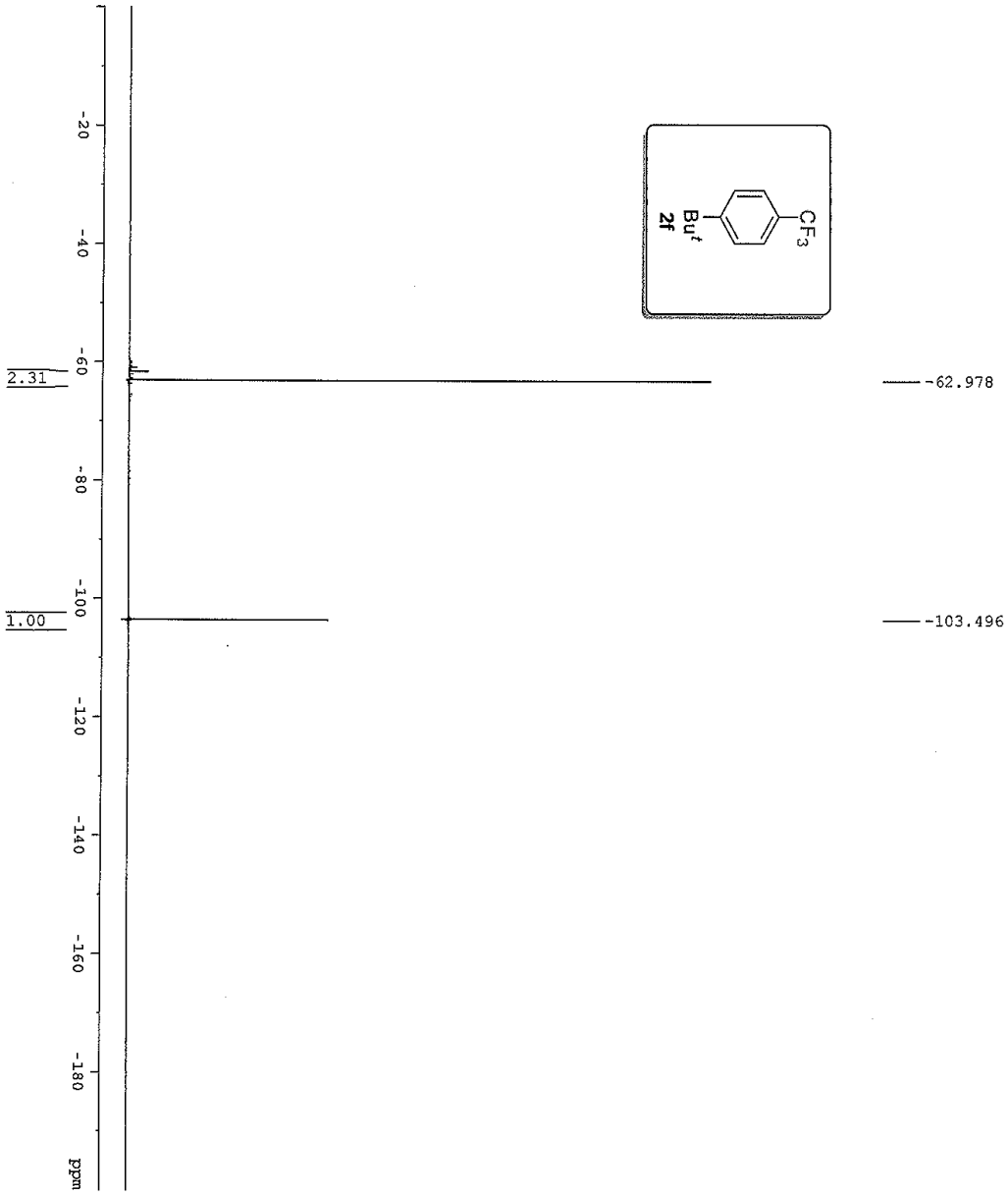
GC-MS of crude 2f



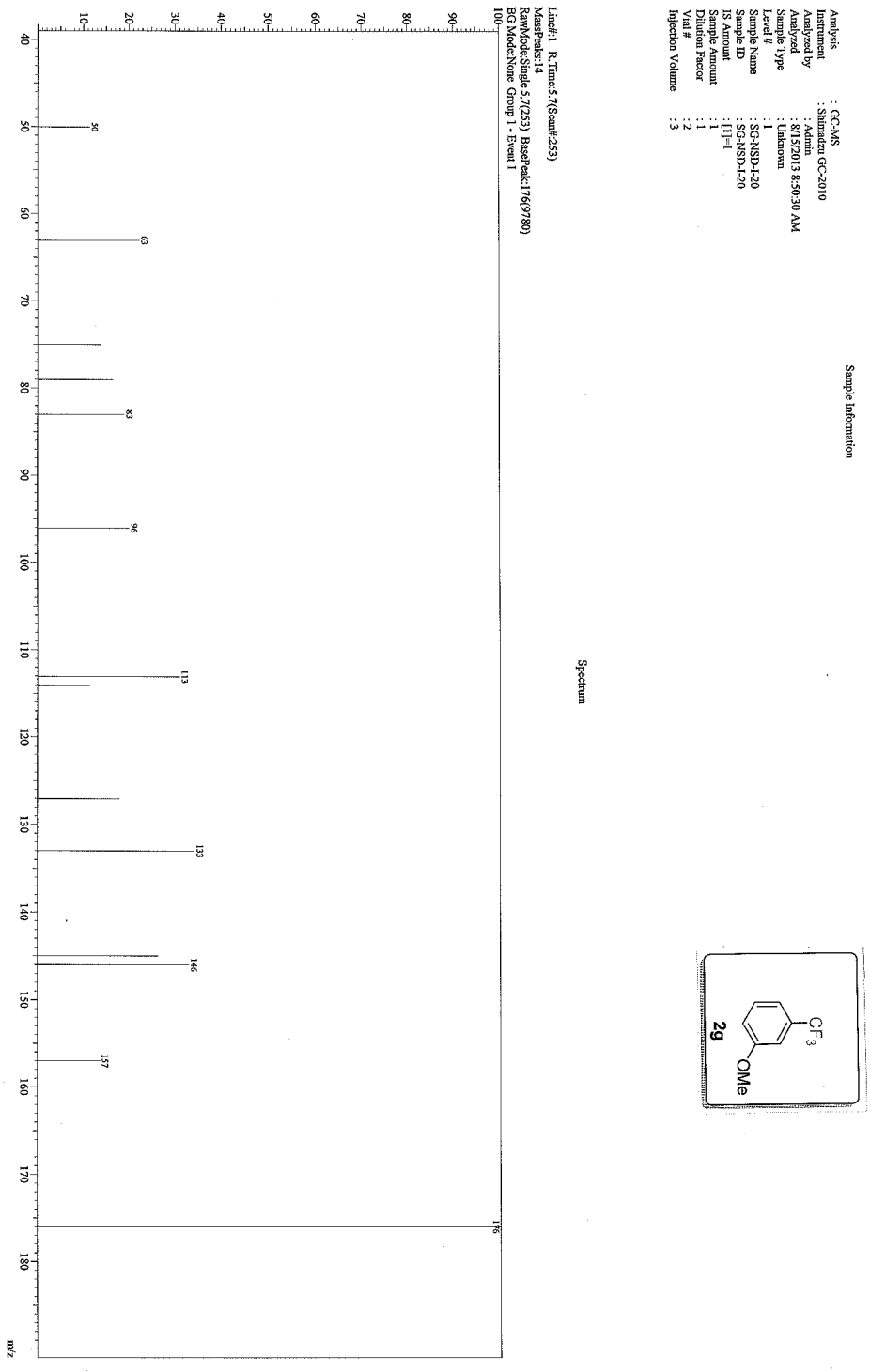
^{19}F NMR of crude 2f in $CDCl_3$



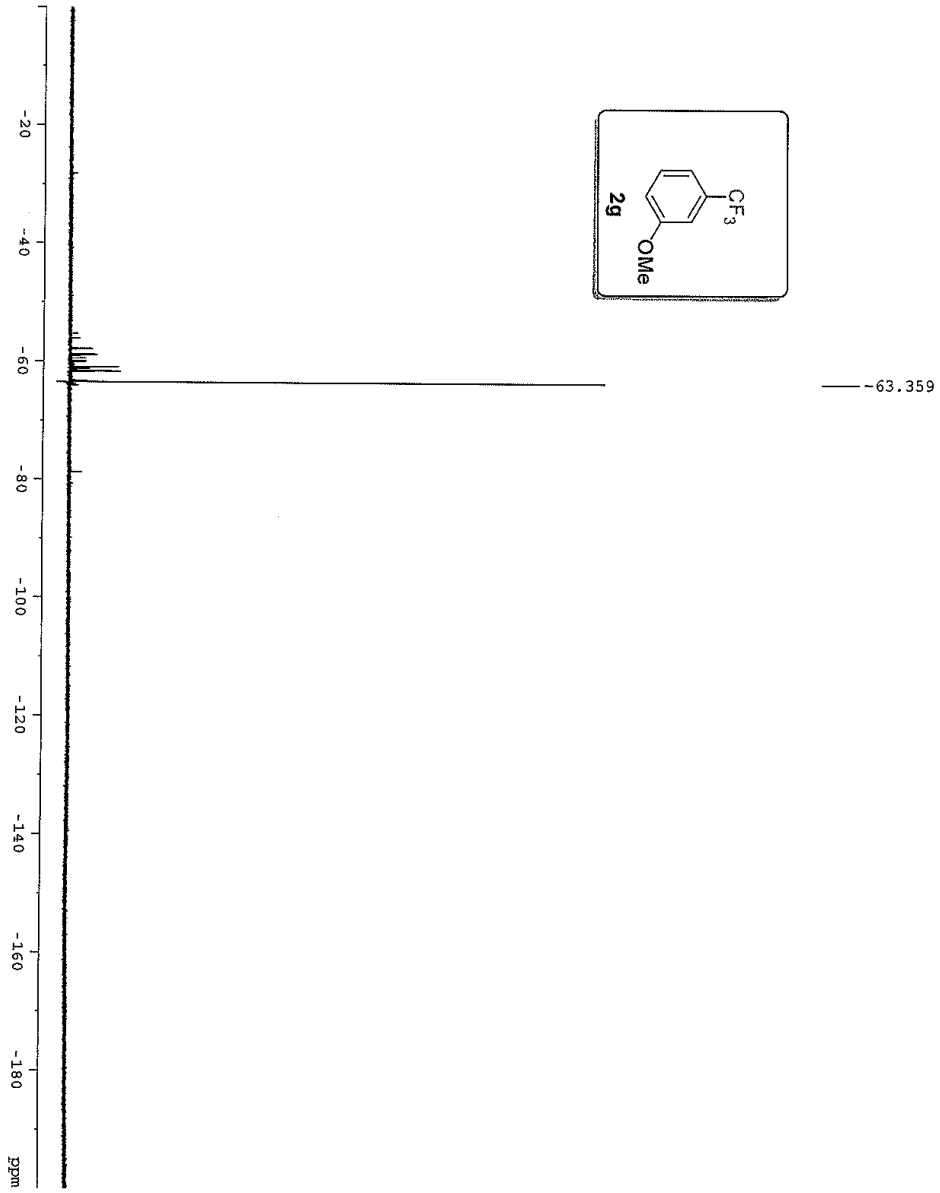
^{19}F NMR yield of compound 2f (2.31/(1×3)×100% = 77%) in $CDCl_3$



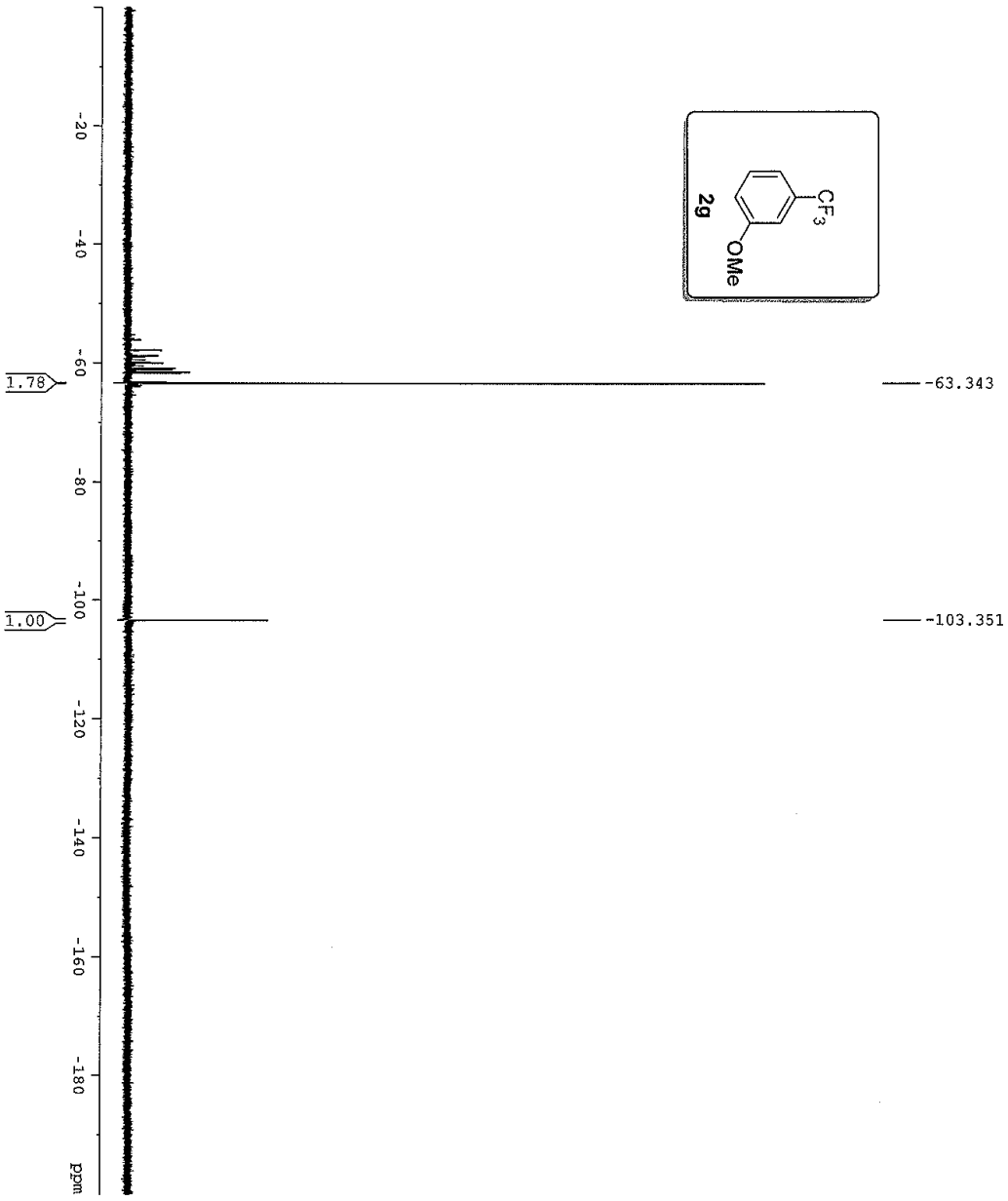
GC-MS of crude 2g



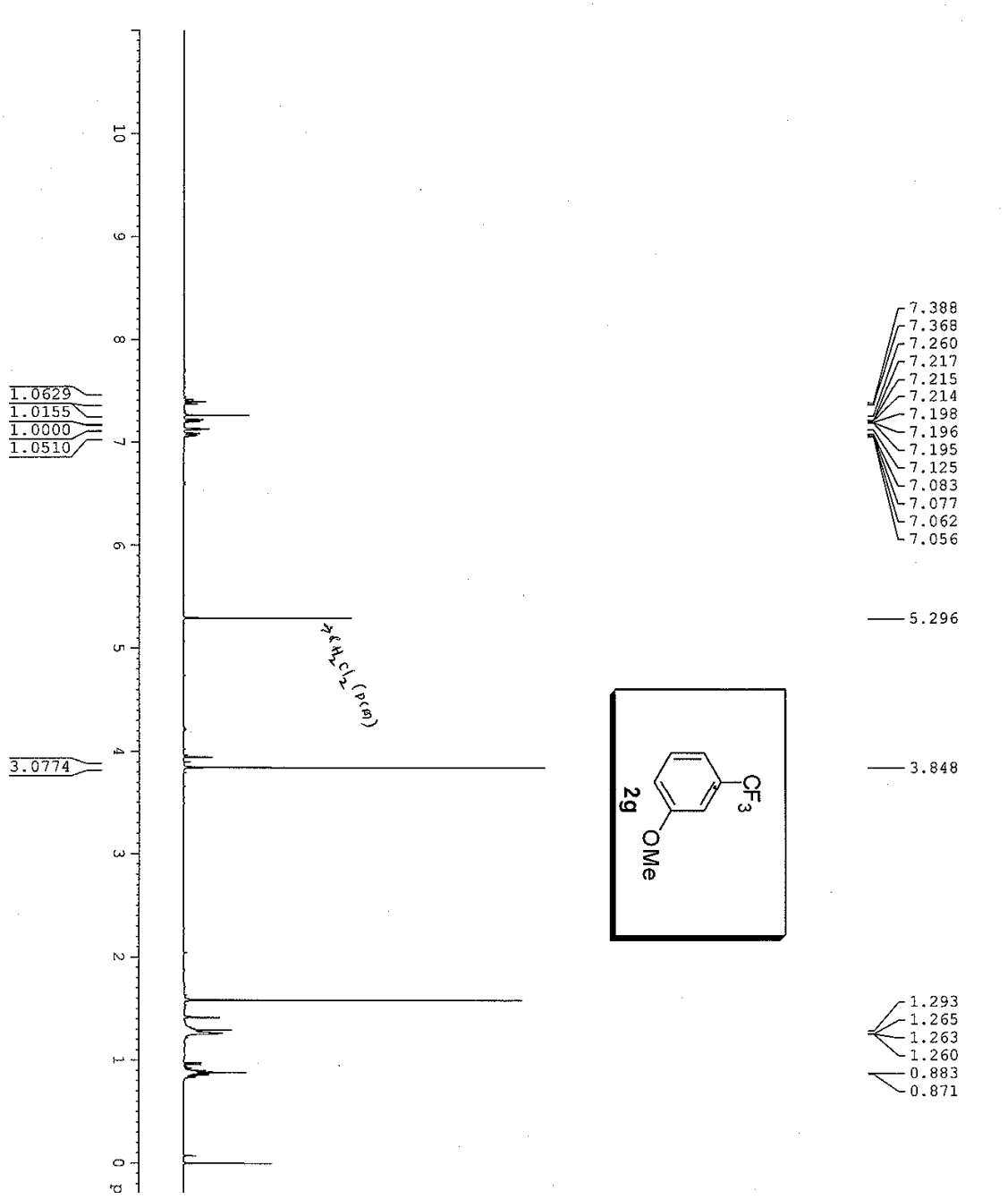
^{19}F NMR of crude 2g in $CDCl_3$



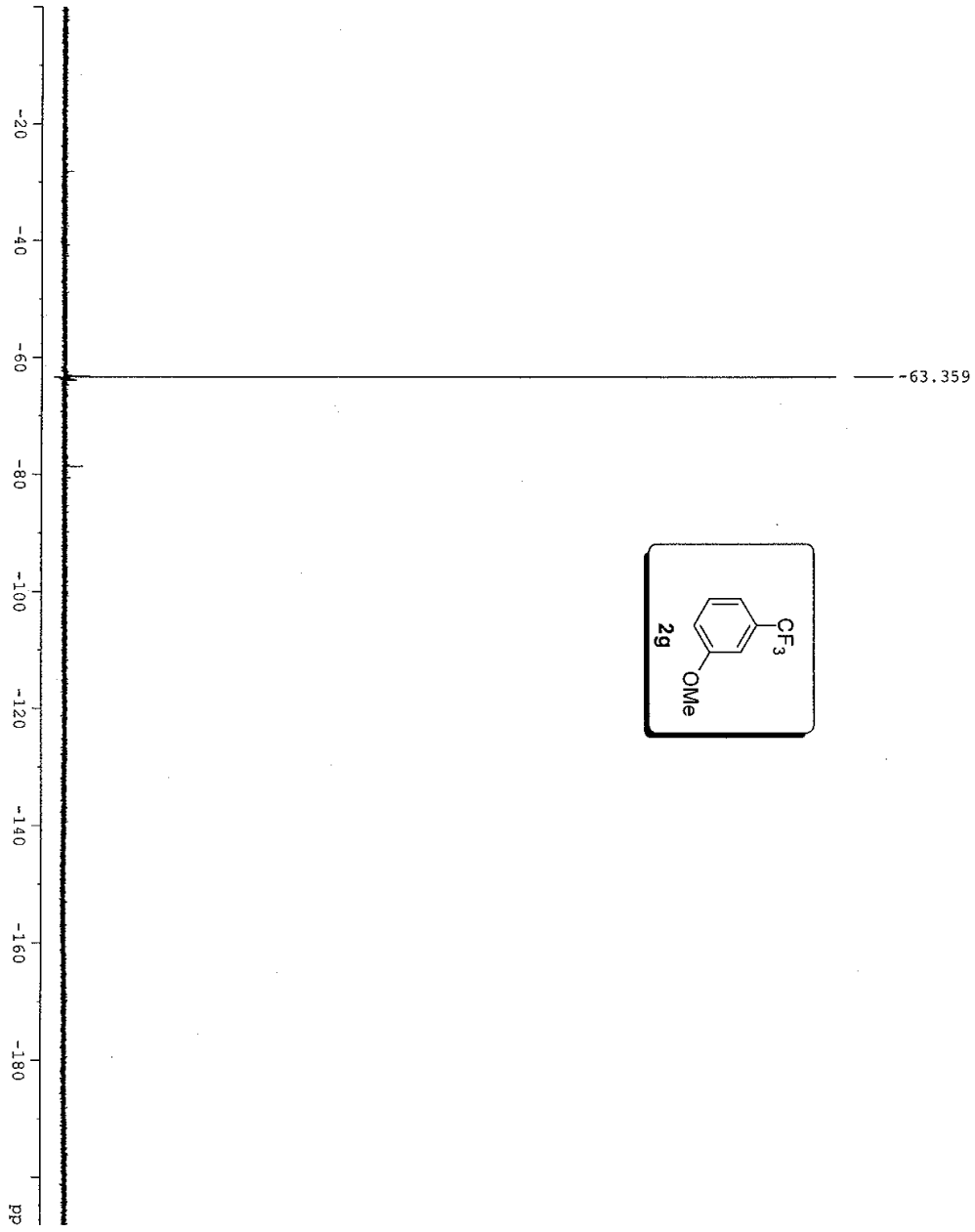
^{19}F NMR yield of compound 2g (1.78/(1×3)×100% = 60%) in $CDCl_3$



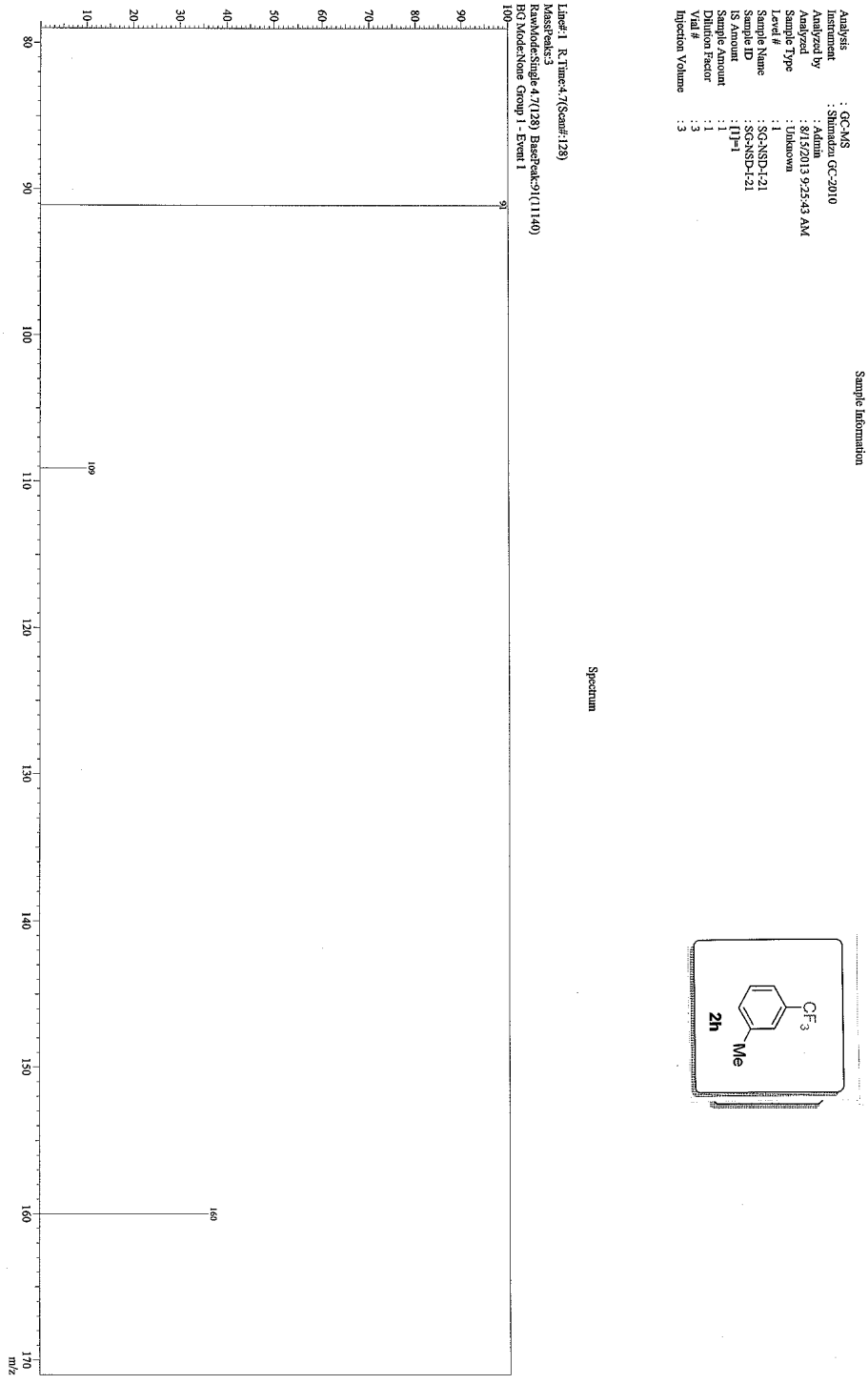
^{1}H NMR of compound 2g



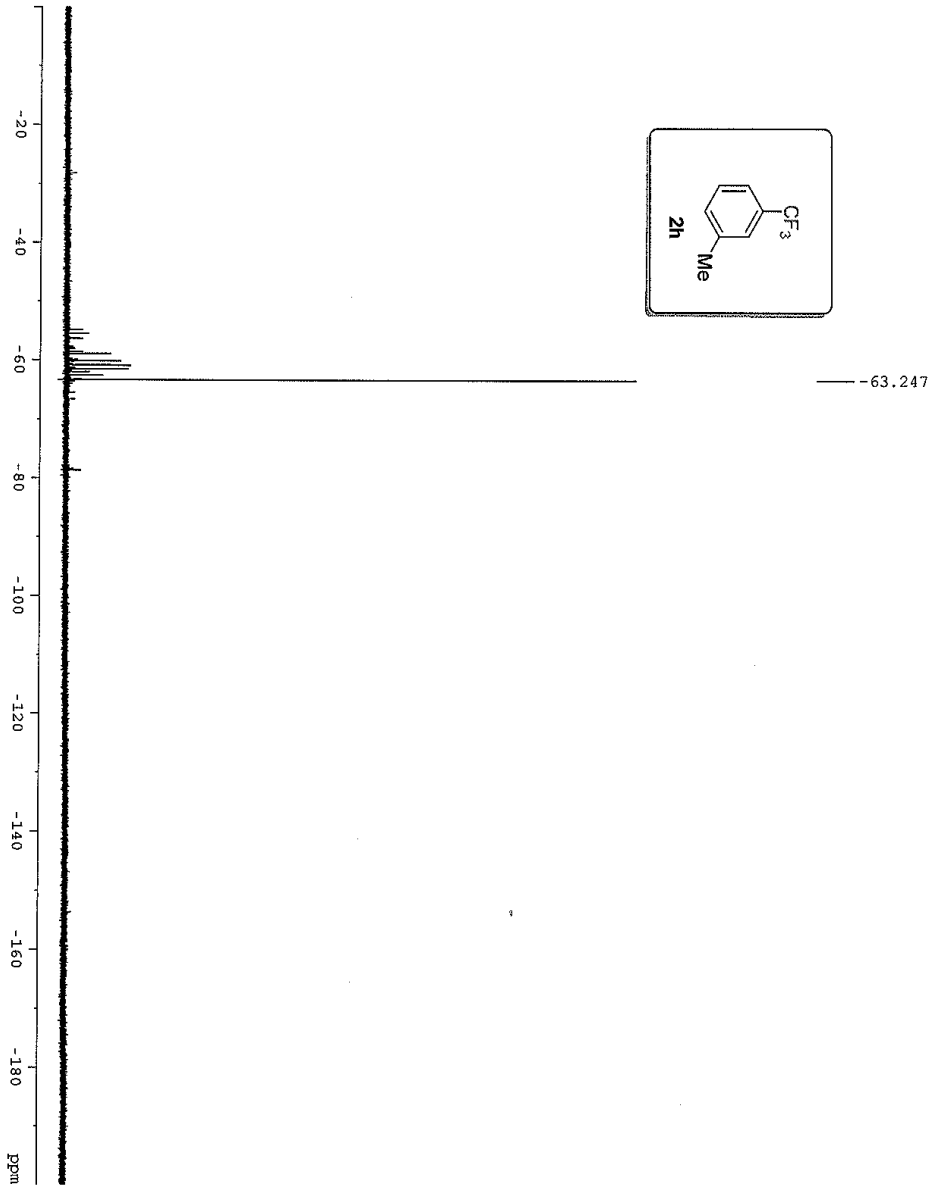
^{19}F NMR of isolated of 2g in $CDCl_3$



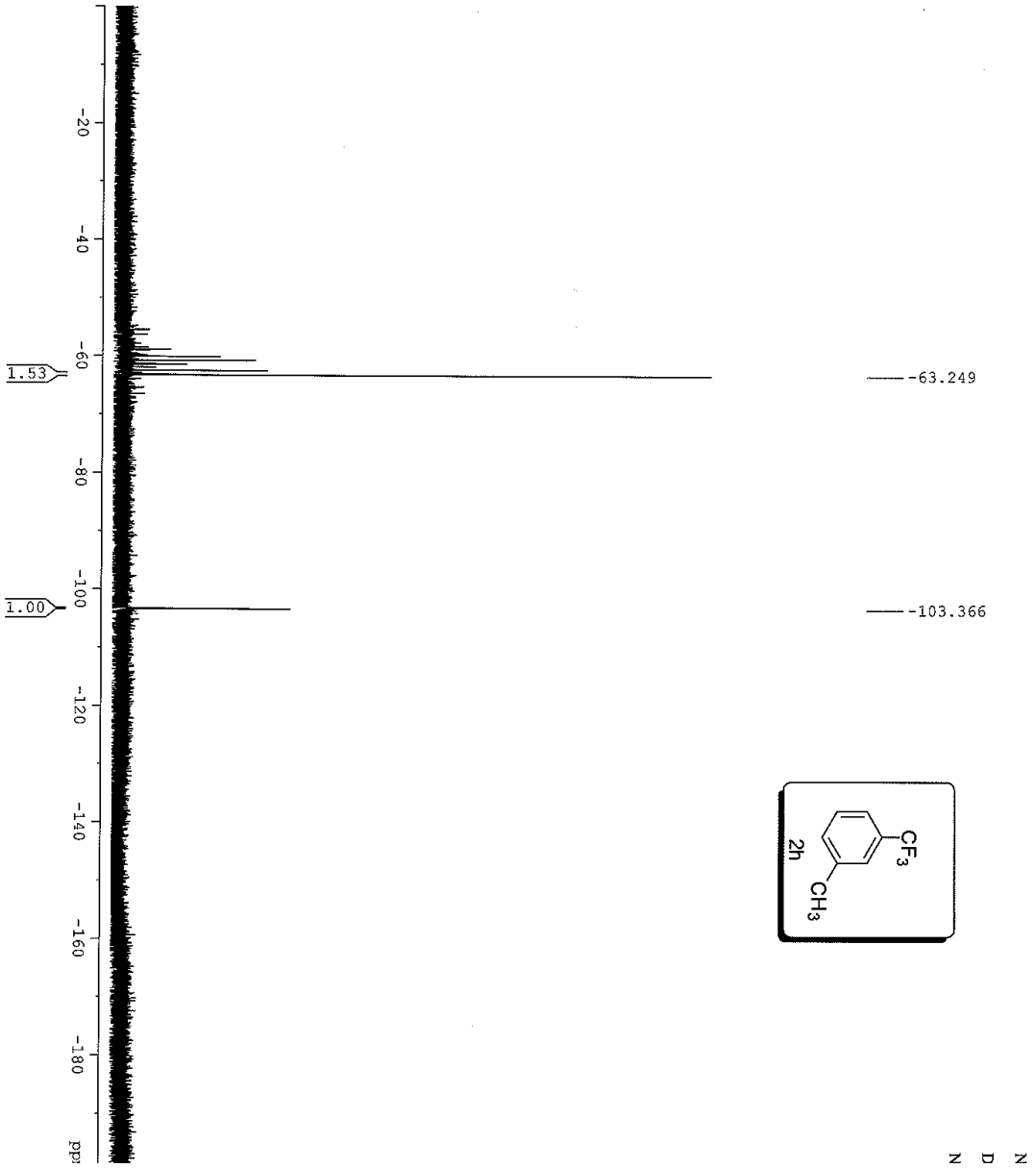
GC-MS of crude 2h



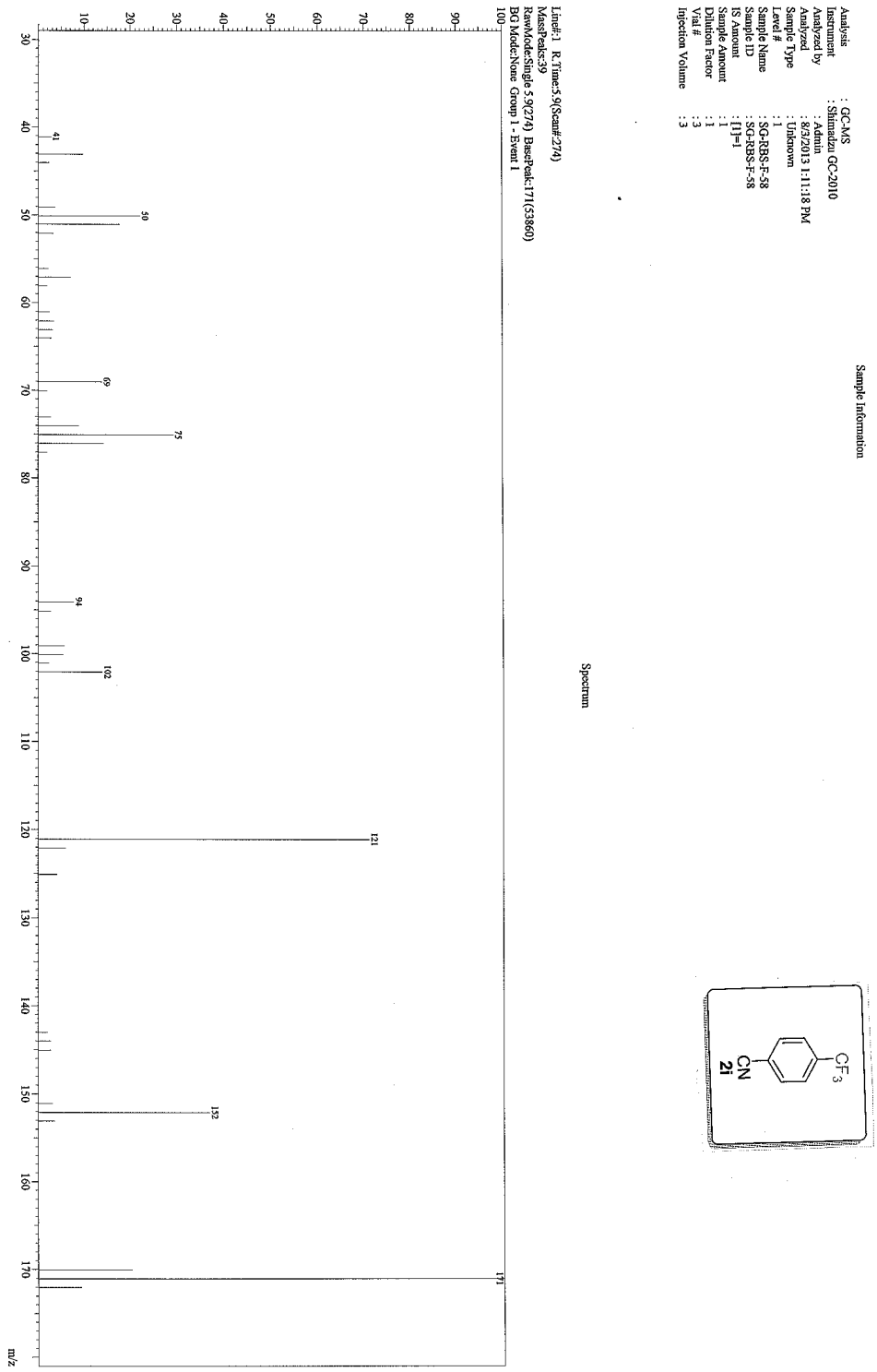
^{19}F NMR of crude 2h in $CDCl_3$



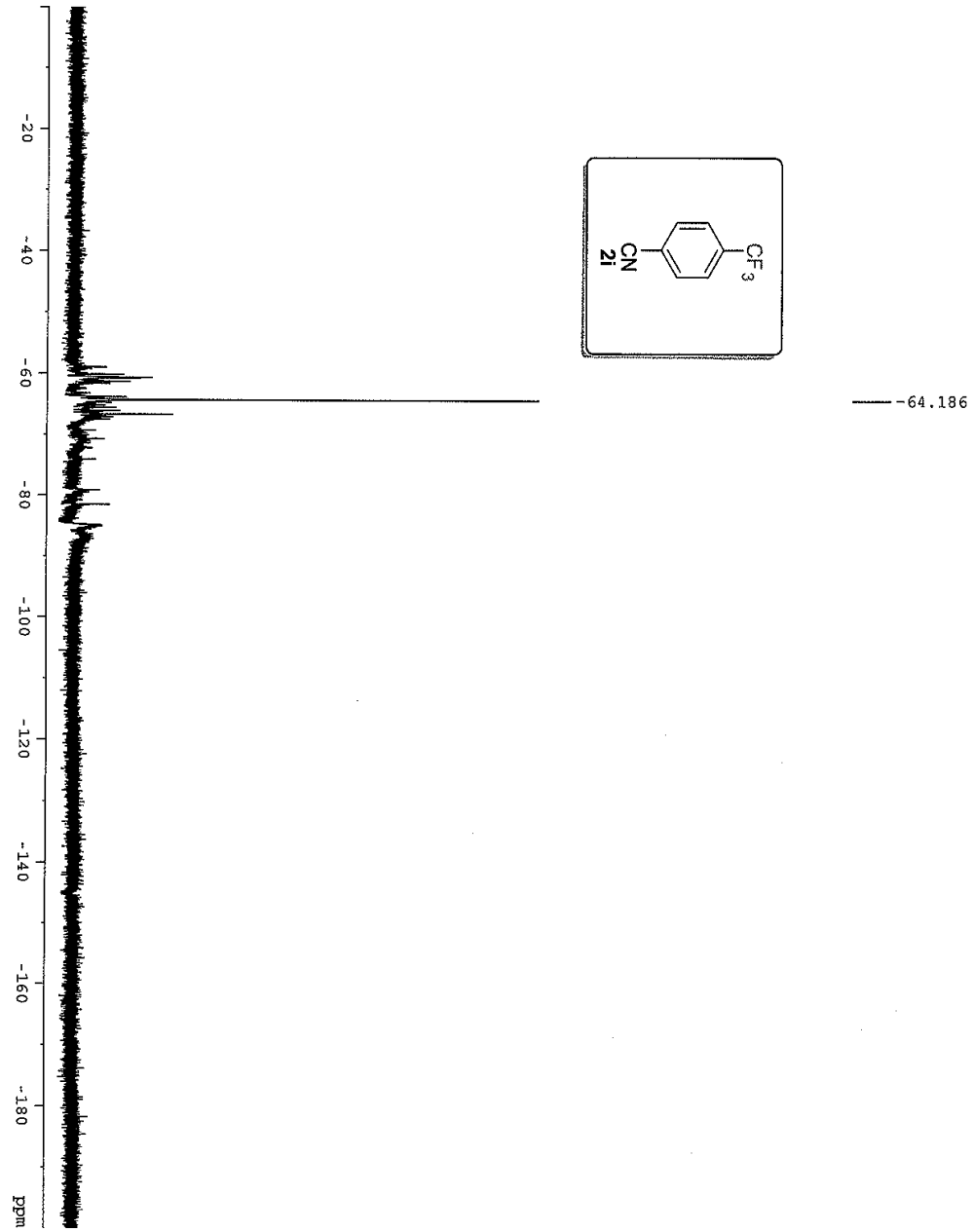
^{19}F NMR yield of compound 2h (1.53/(1×3)×100% = 51%) in $CDCl_3$



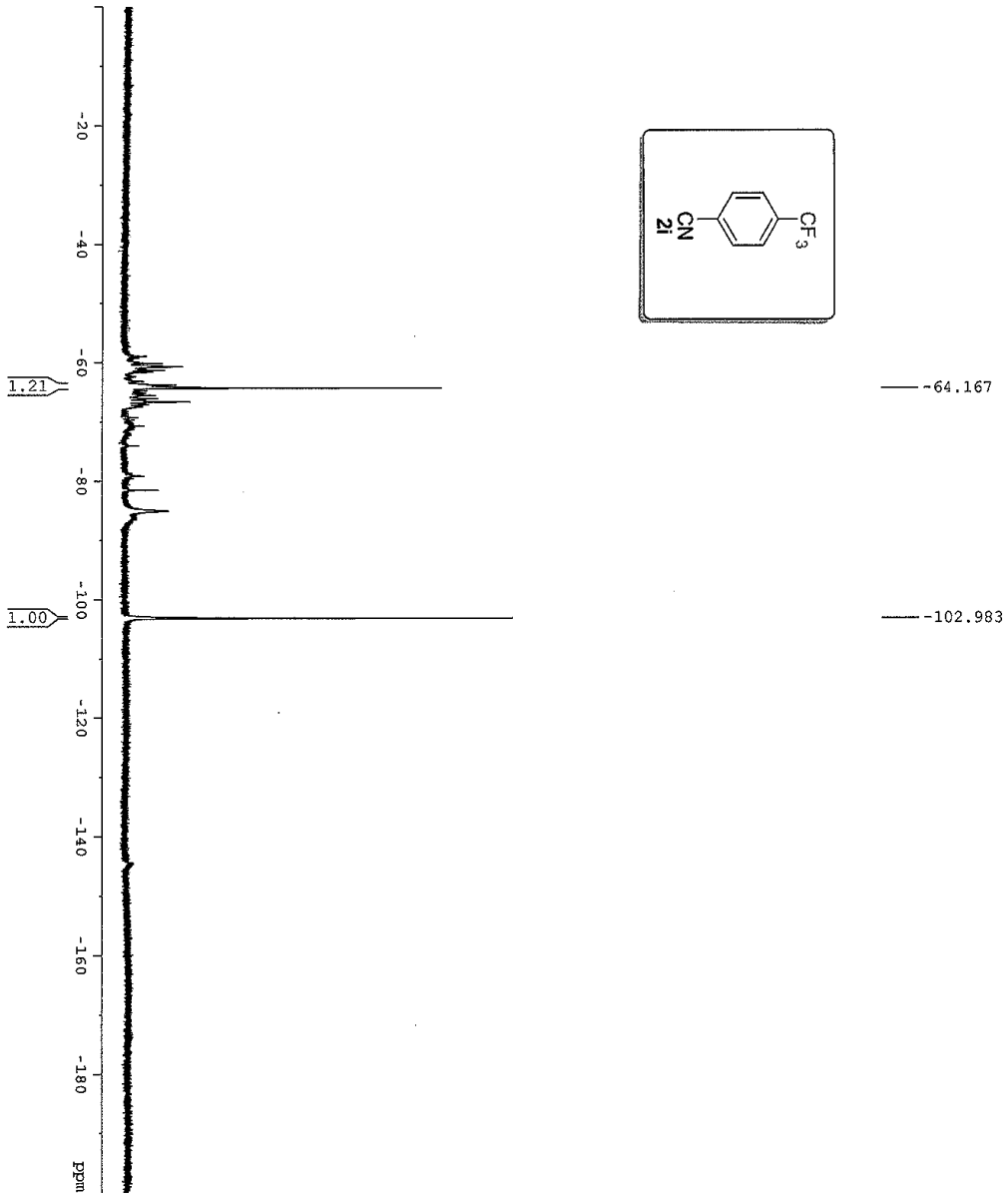
GC-MS of crude 2i



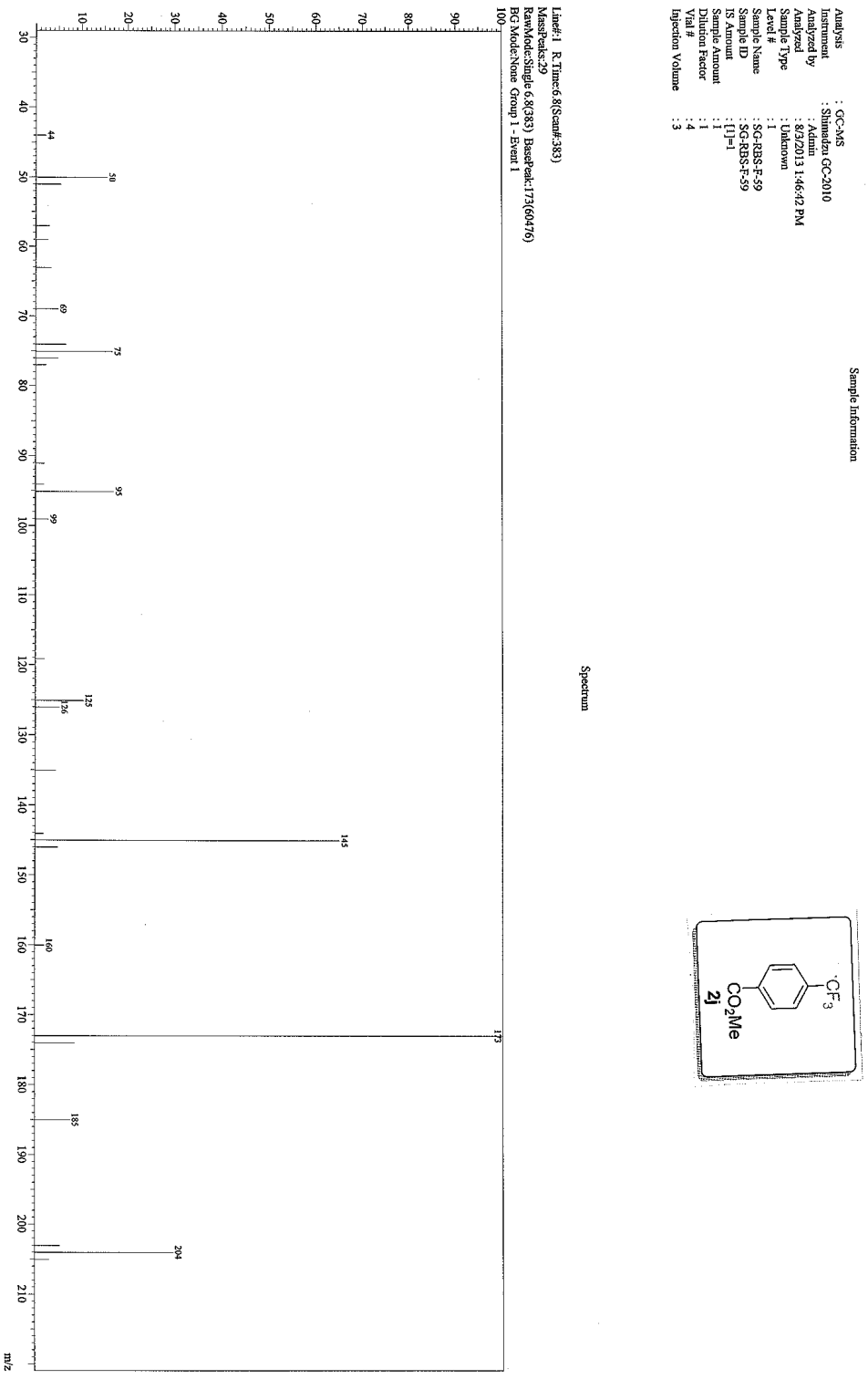
^{19}F NMR of crude 2i in $CDCl_3$



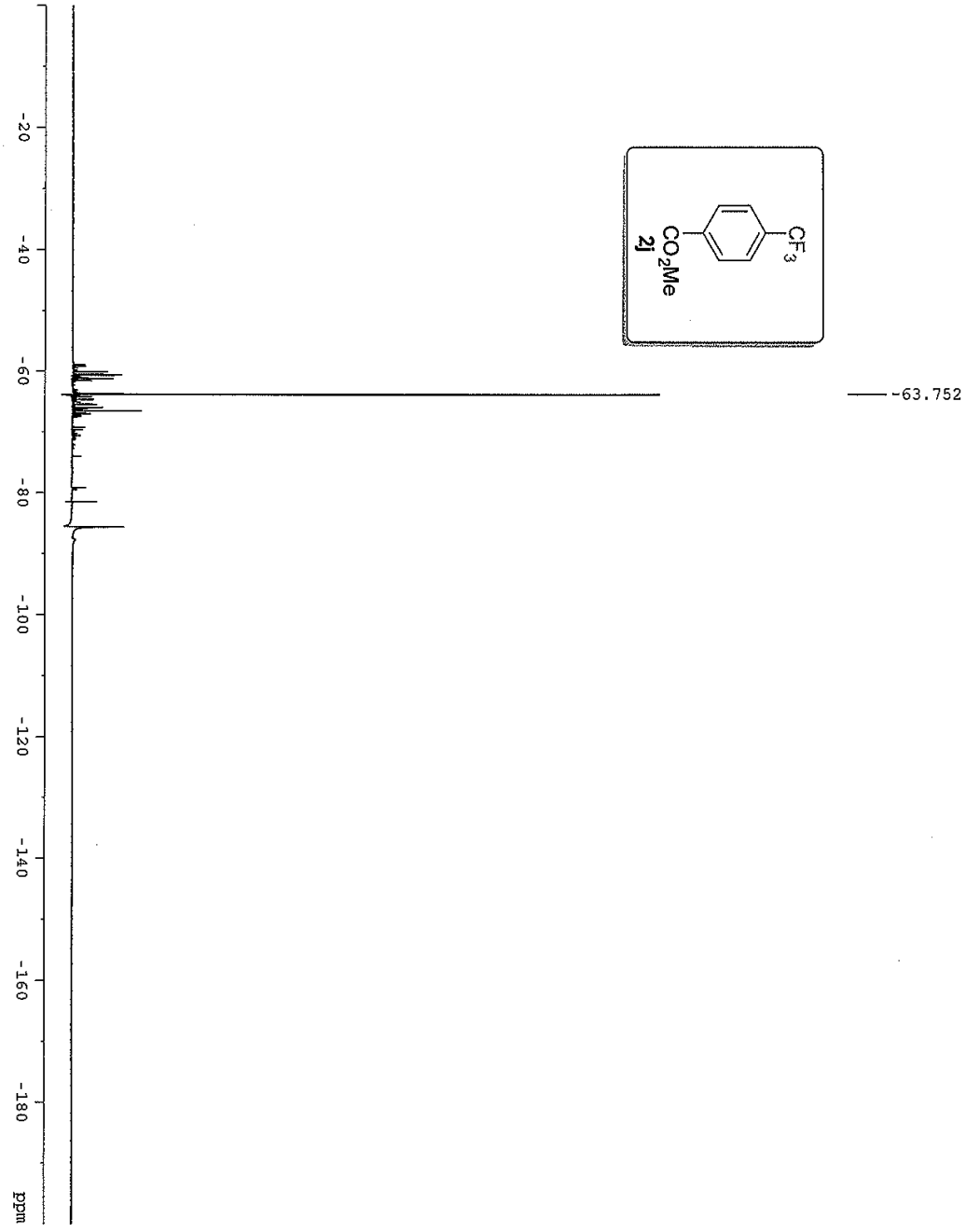
^{19}F NMR yield of compound 2i (1.21/(1×3)×100% = 40%) in $CDCl_3$



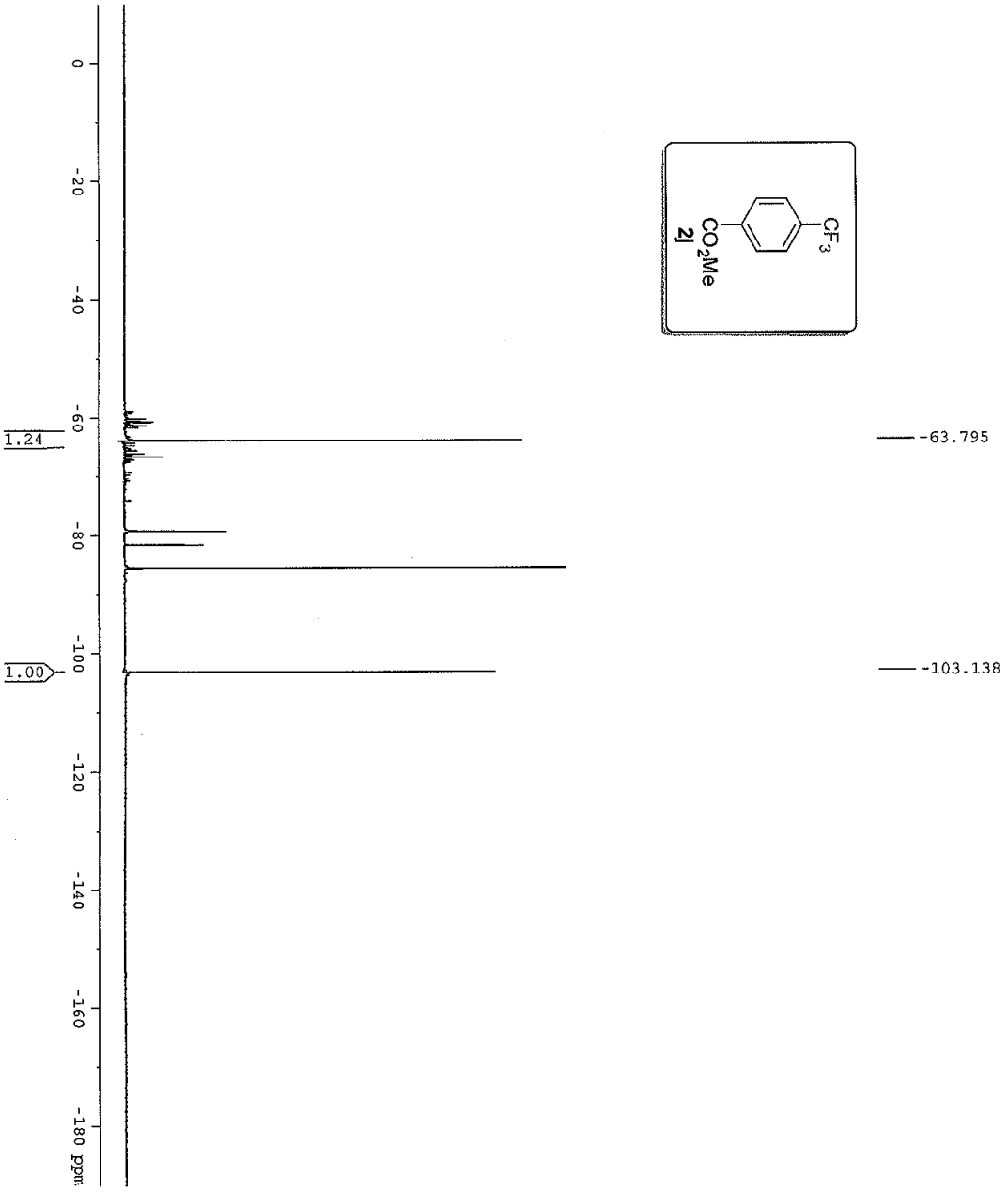
GC-MS of crude 2j



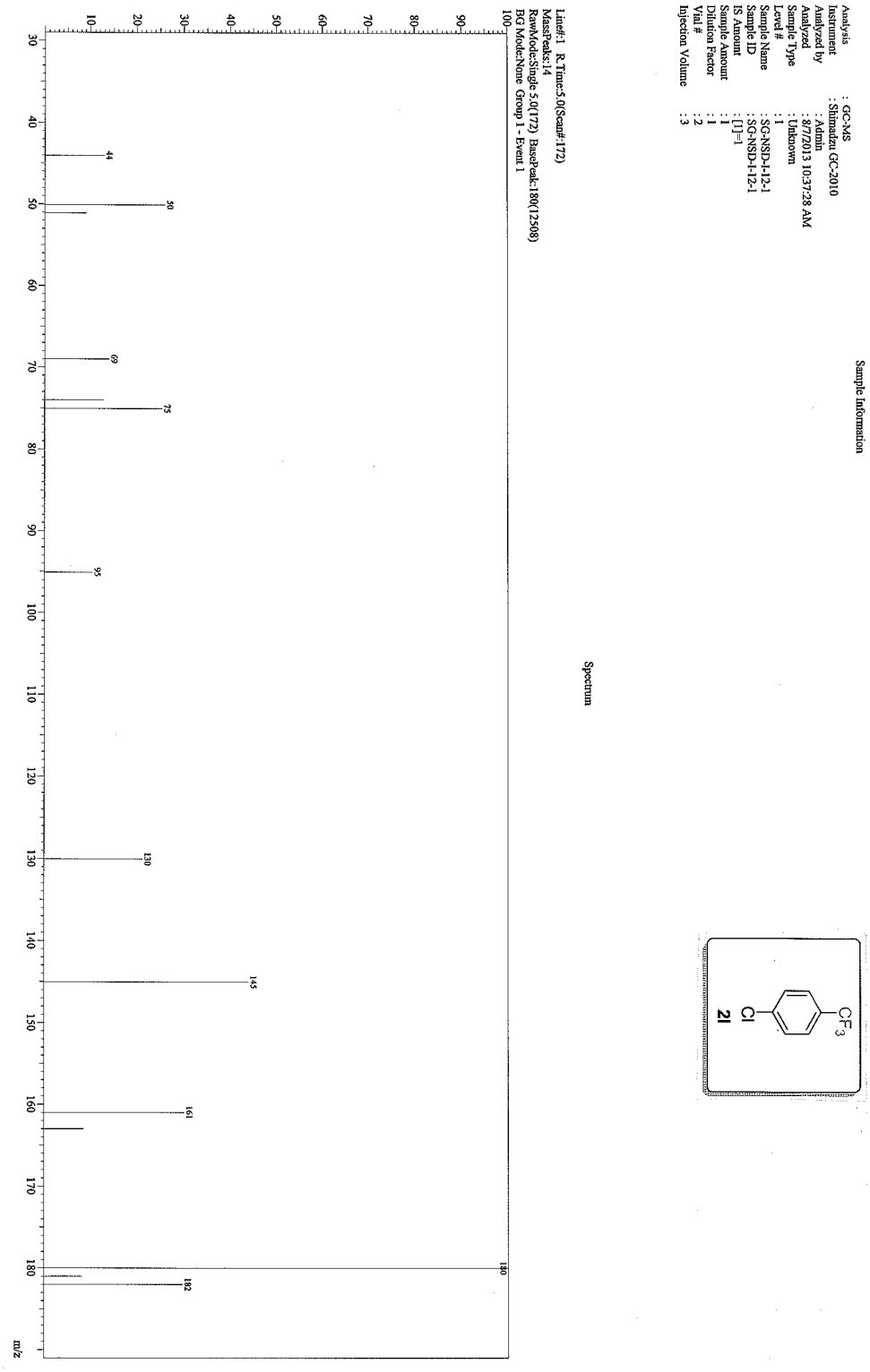
^{19}F NMR of crude 2j in $CDCl_3$



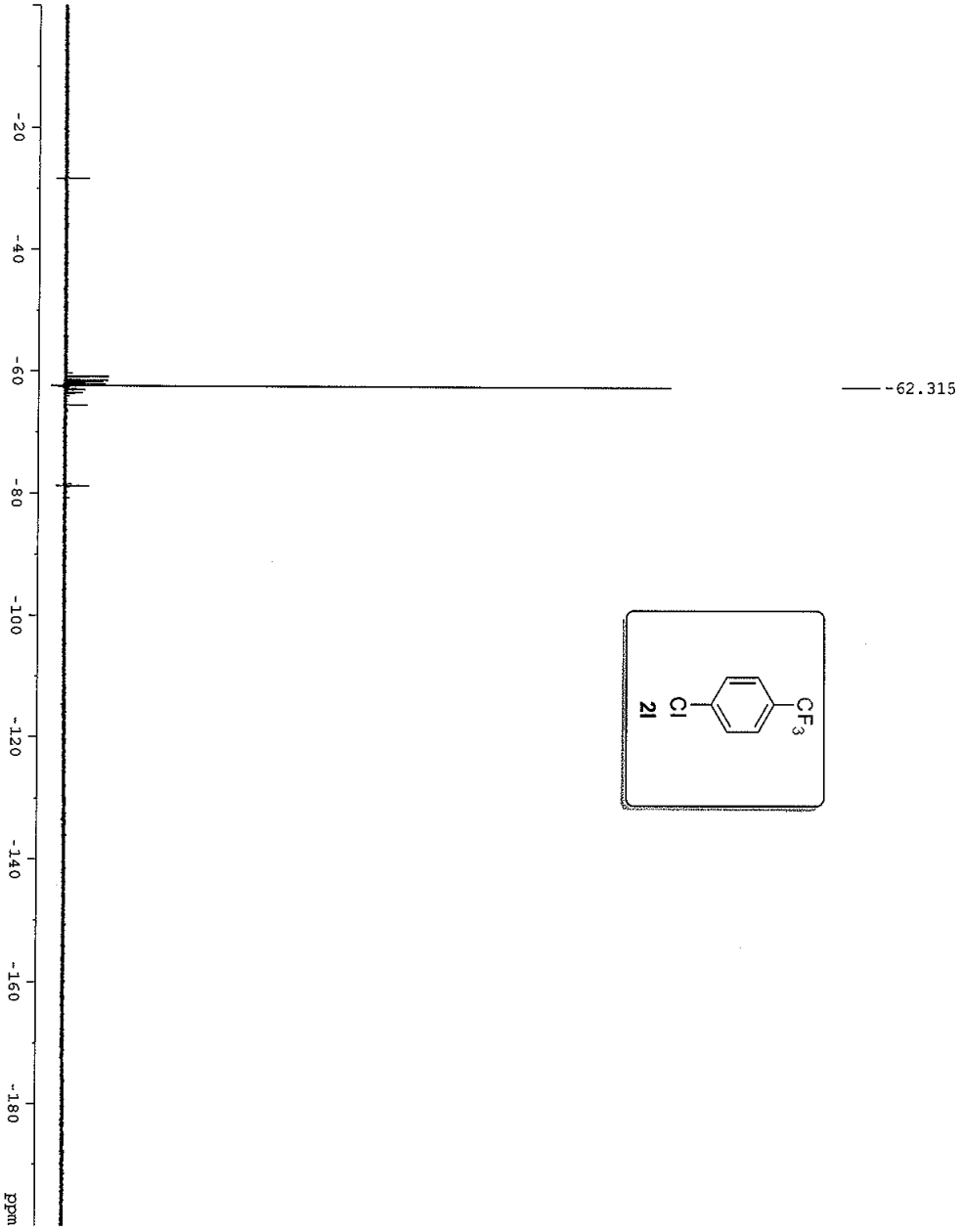
^{19}F NMR yield of compound 2j (1.24/(1×3)×100% = 41%) in $CDCl_3$



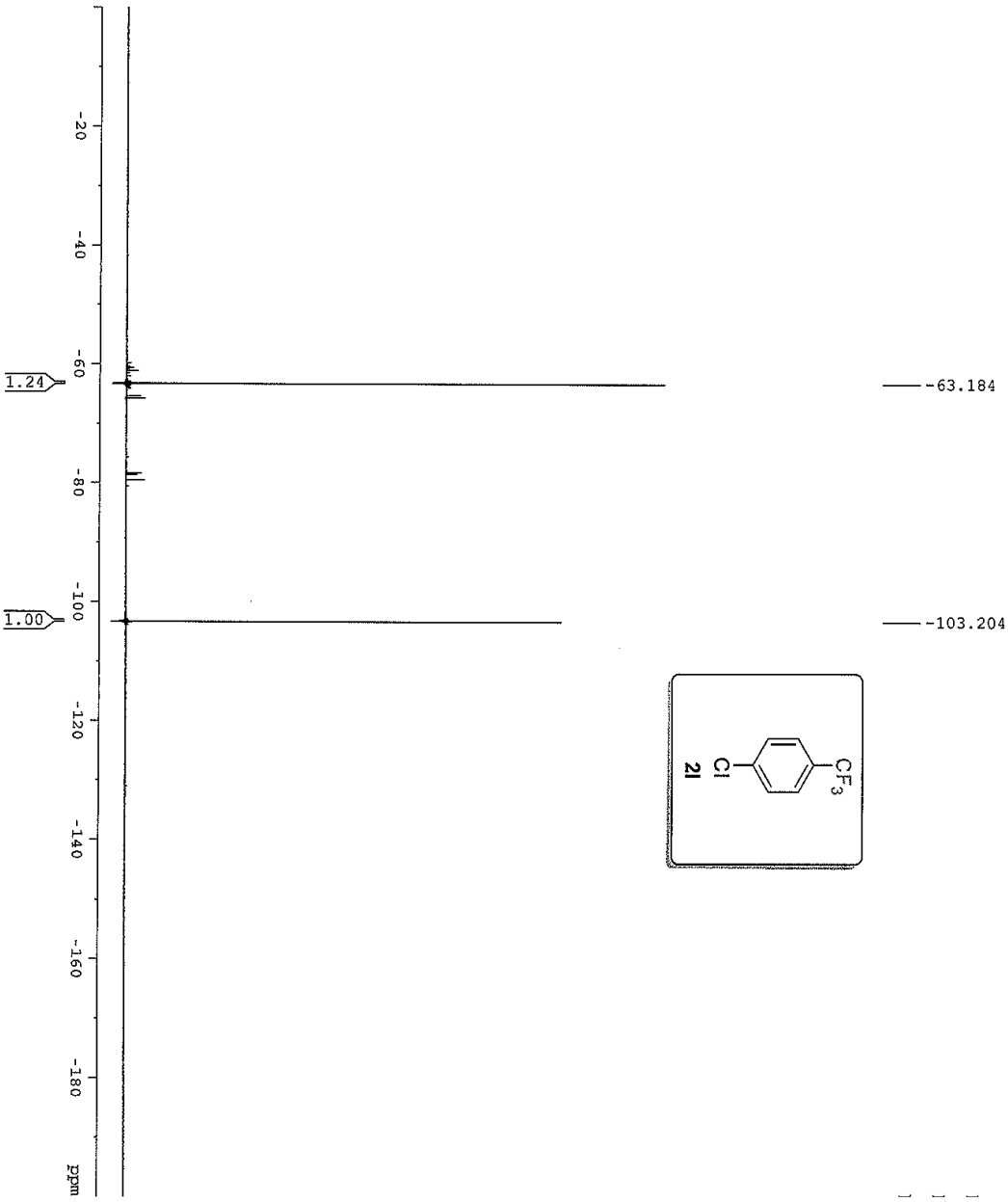
GC-MS of crude 2l



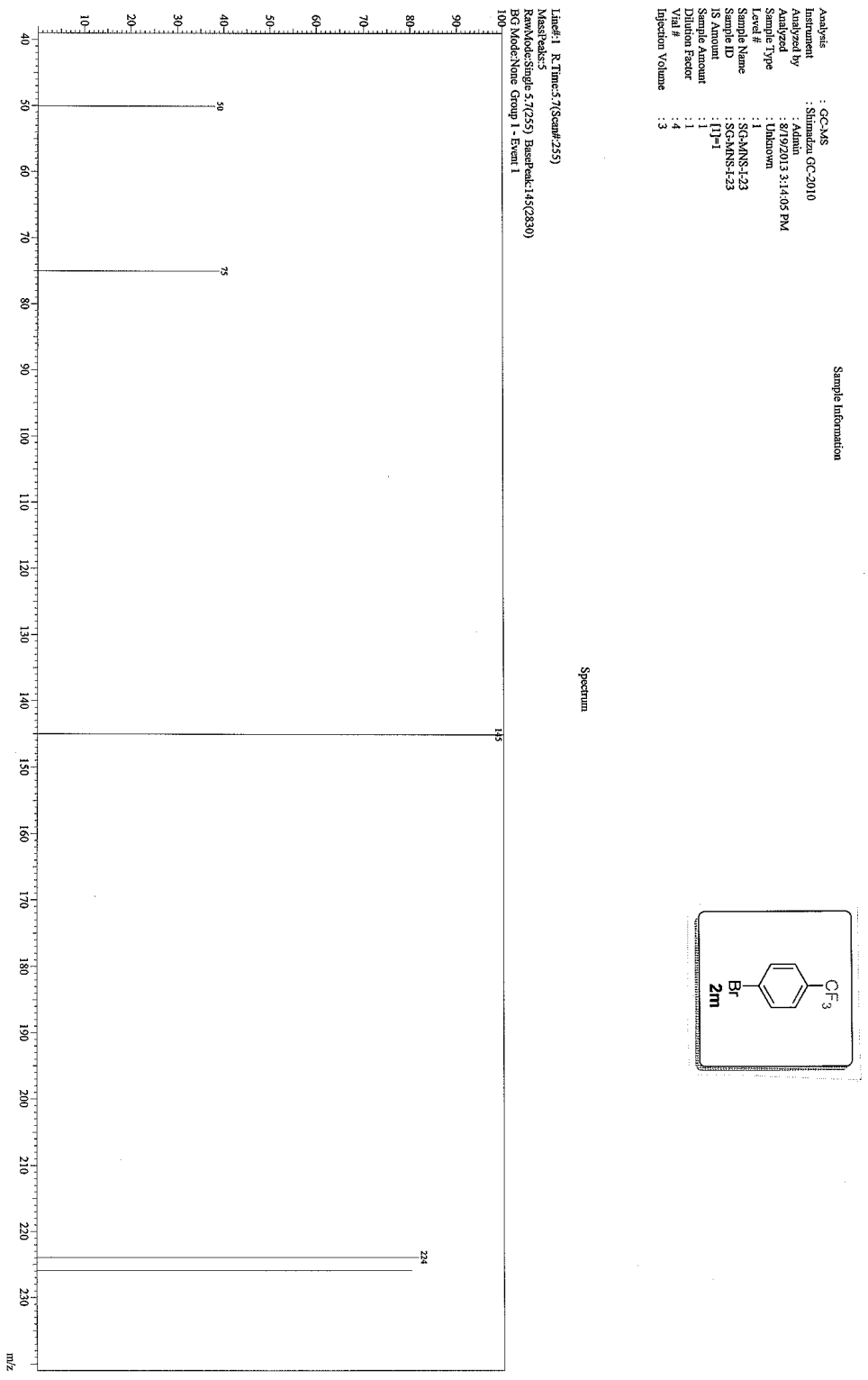
^{19}F NMR of crude 2l in $CDCl_3$



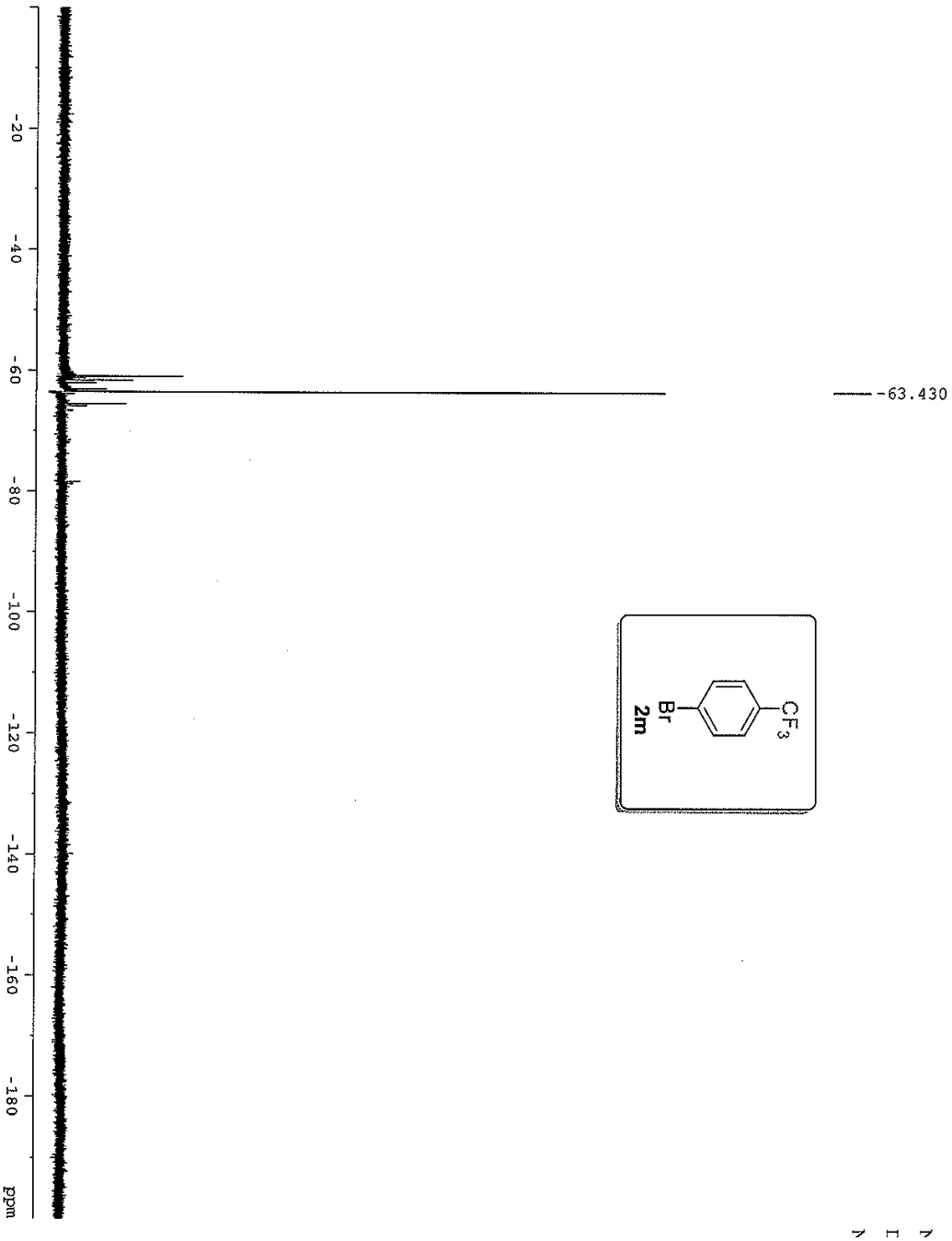
^{19}F NMR yield of compound 2l (1.24/(1×3)×100% = 41%) in $CDCl_3$



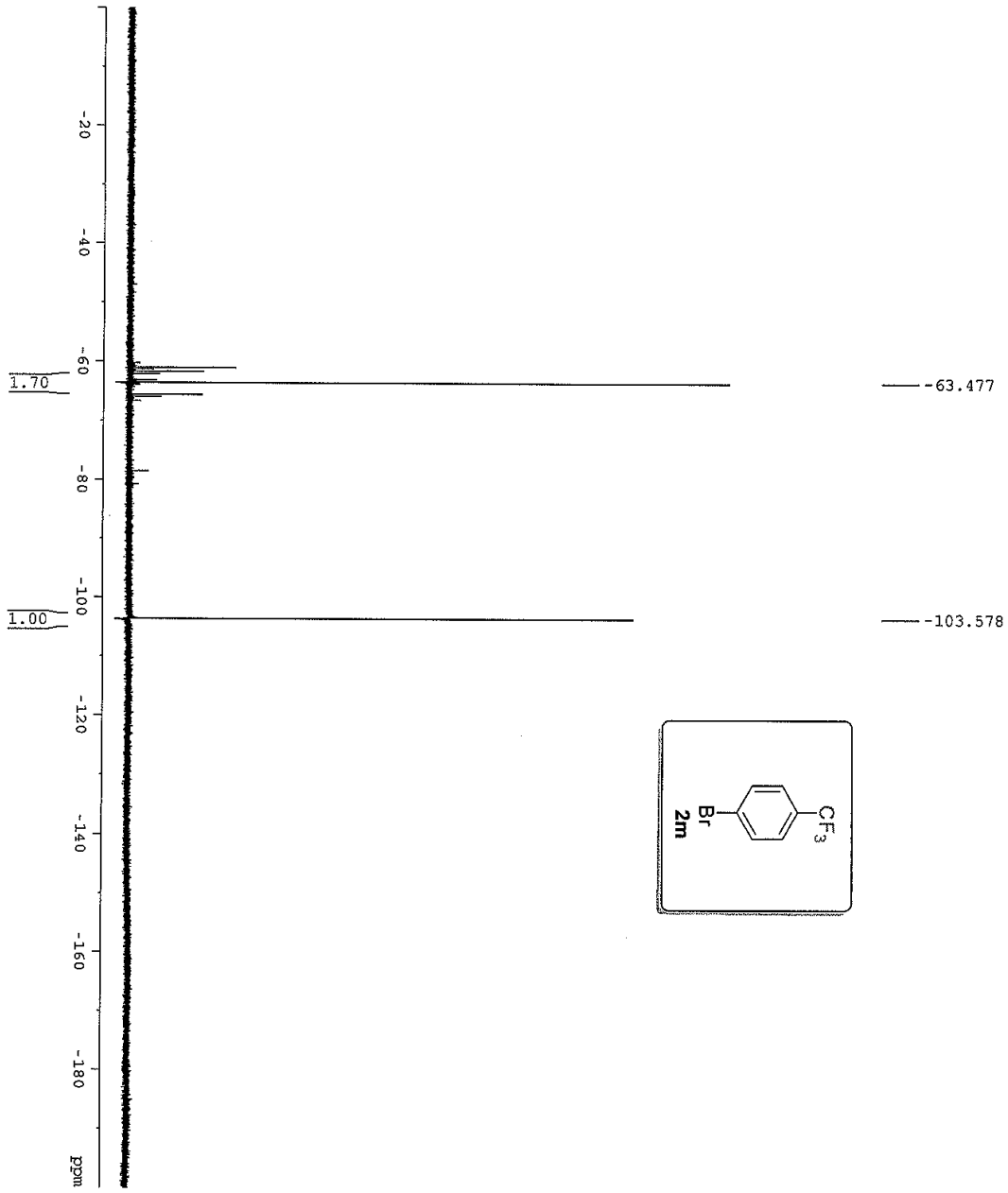
GC-MS of crude 2m



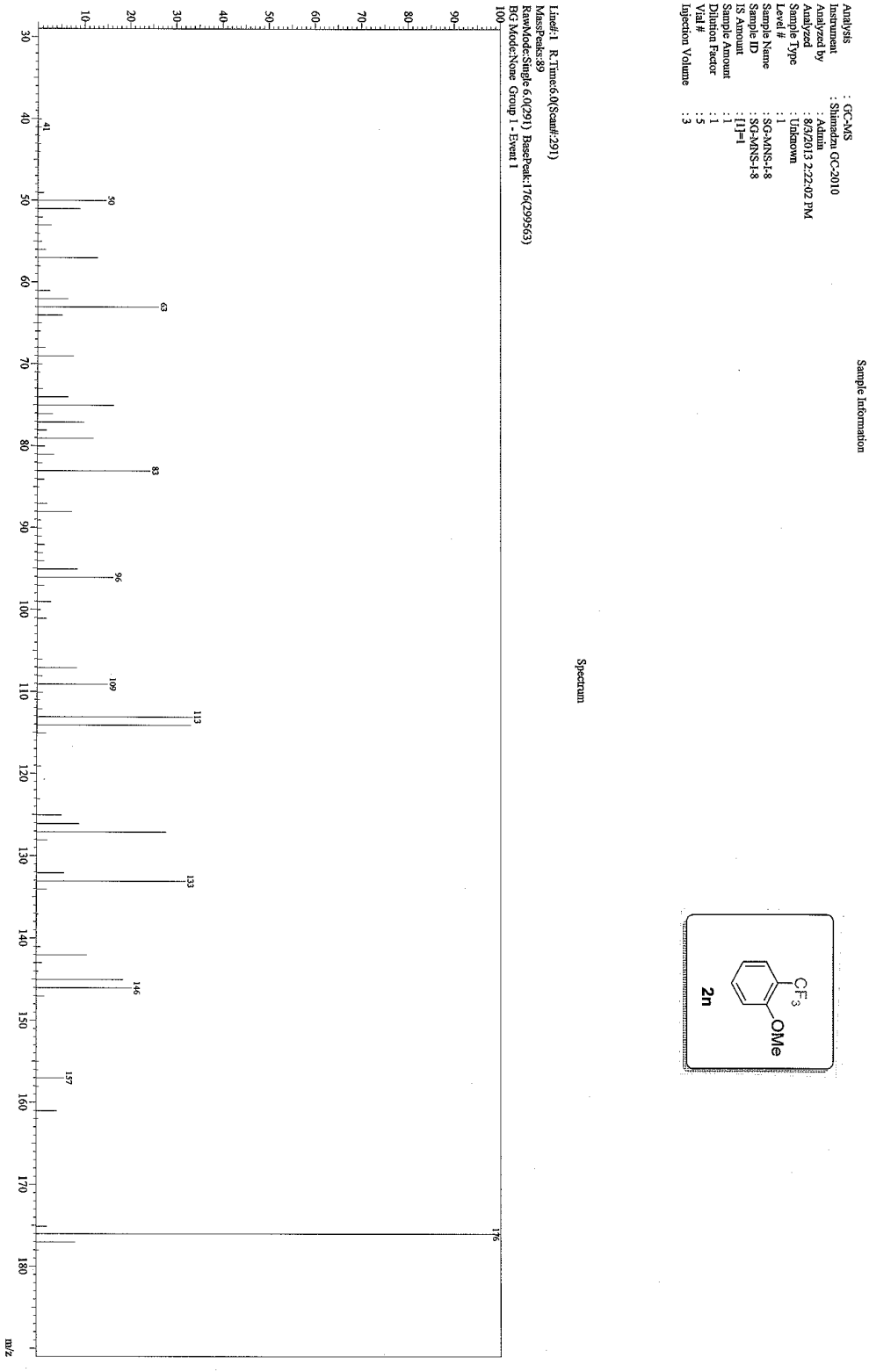
^{19}F NMR of crude 2m in $CDCl_3$



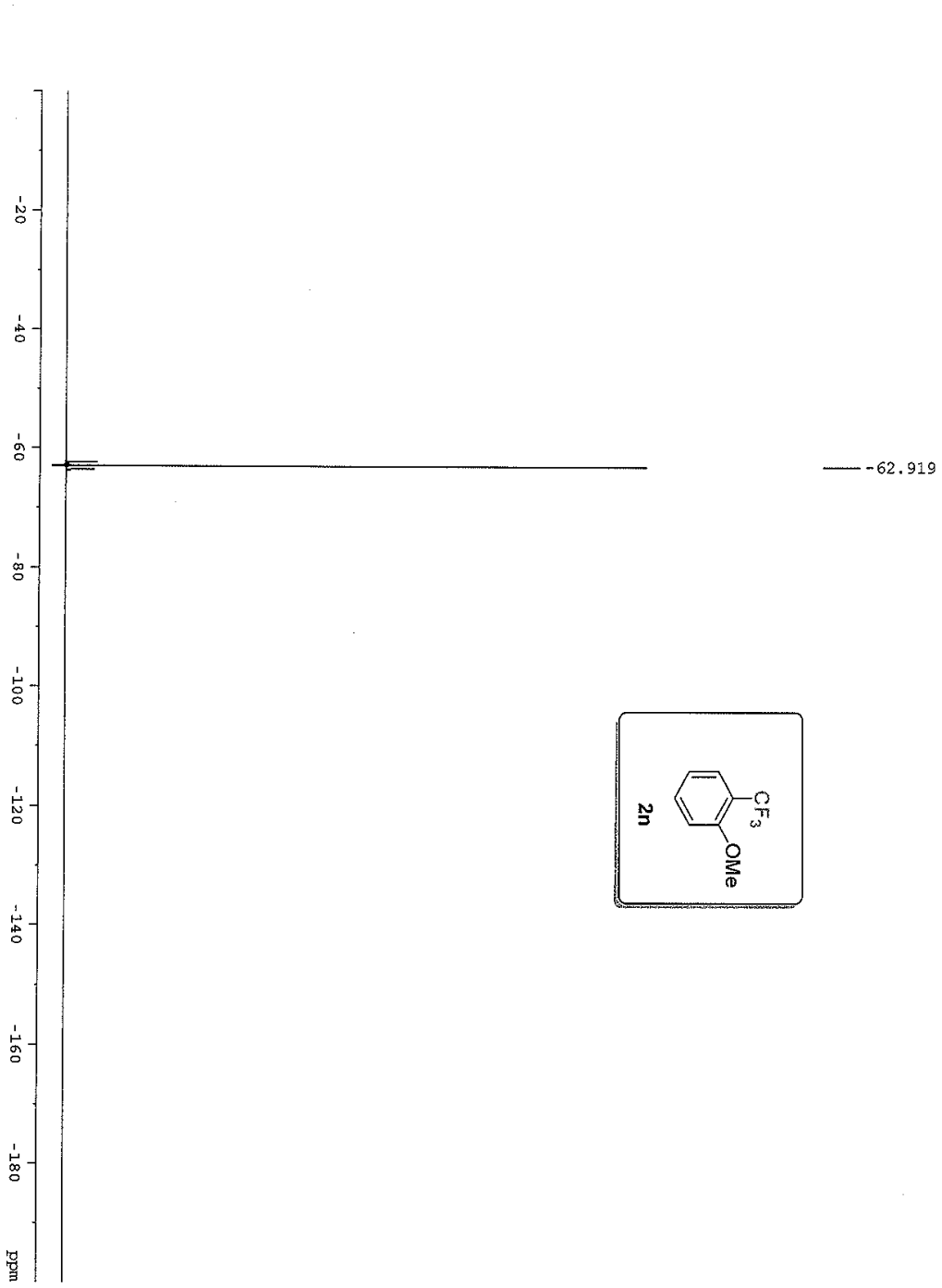
^{19}F NMR yield of compound 2m (1.70/(1×3)×100% = 57%) in $CDCl_3$



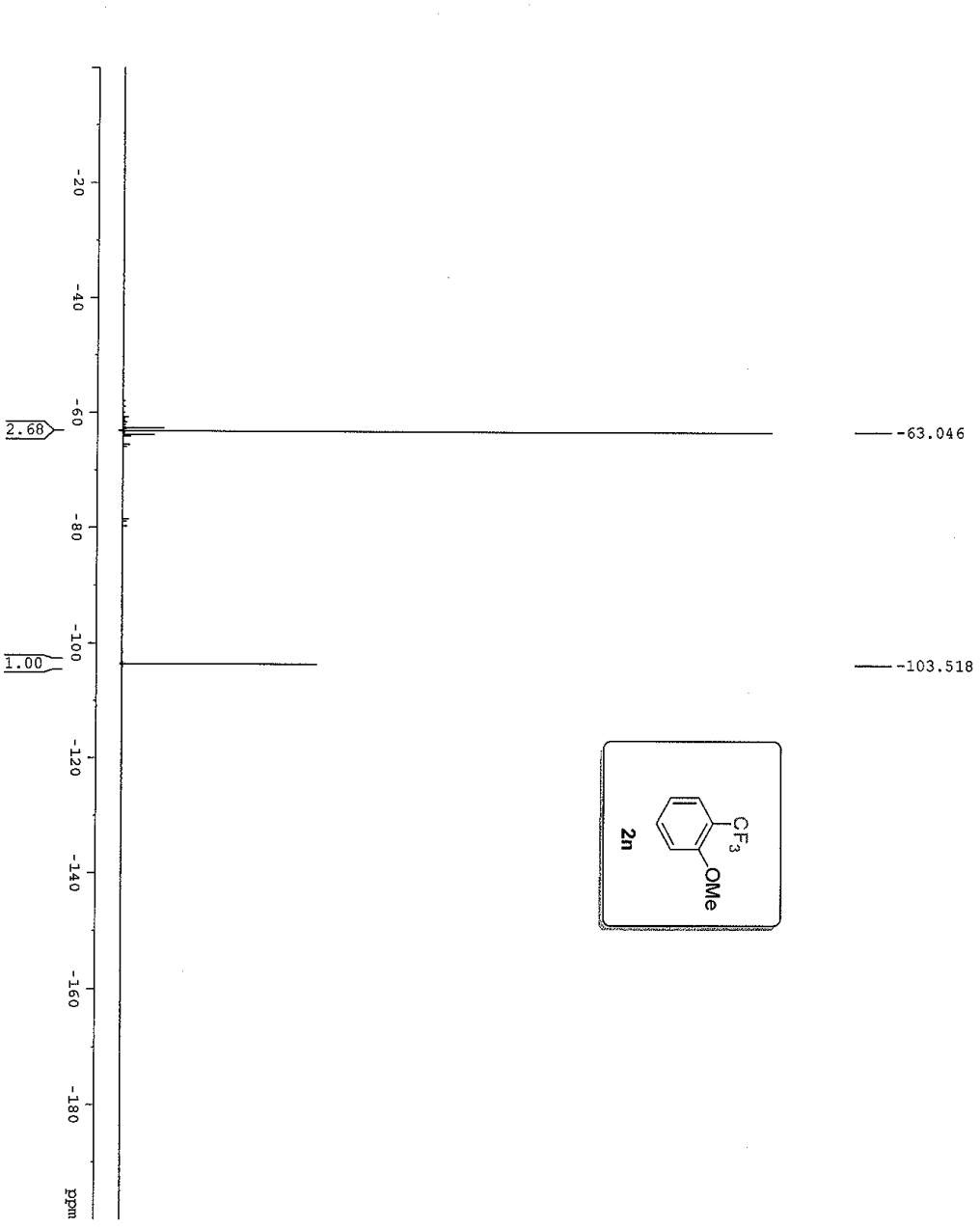
GC-MS of crude 2n



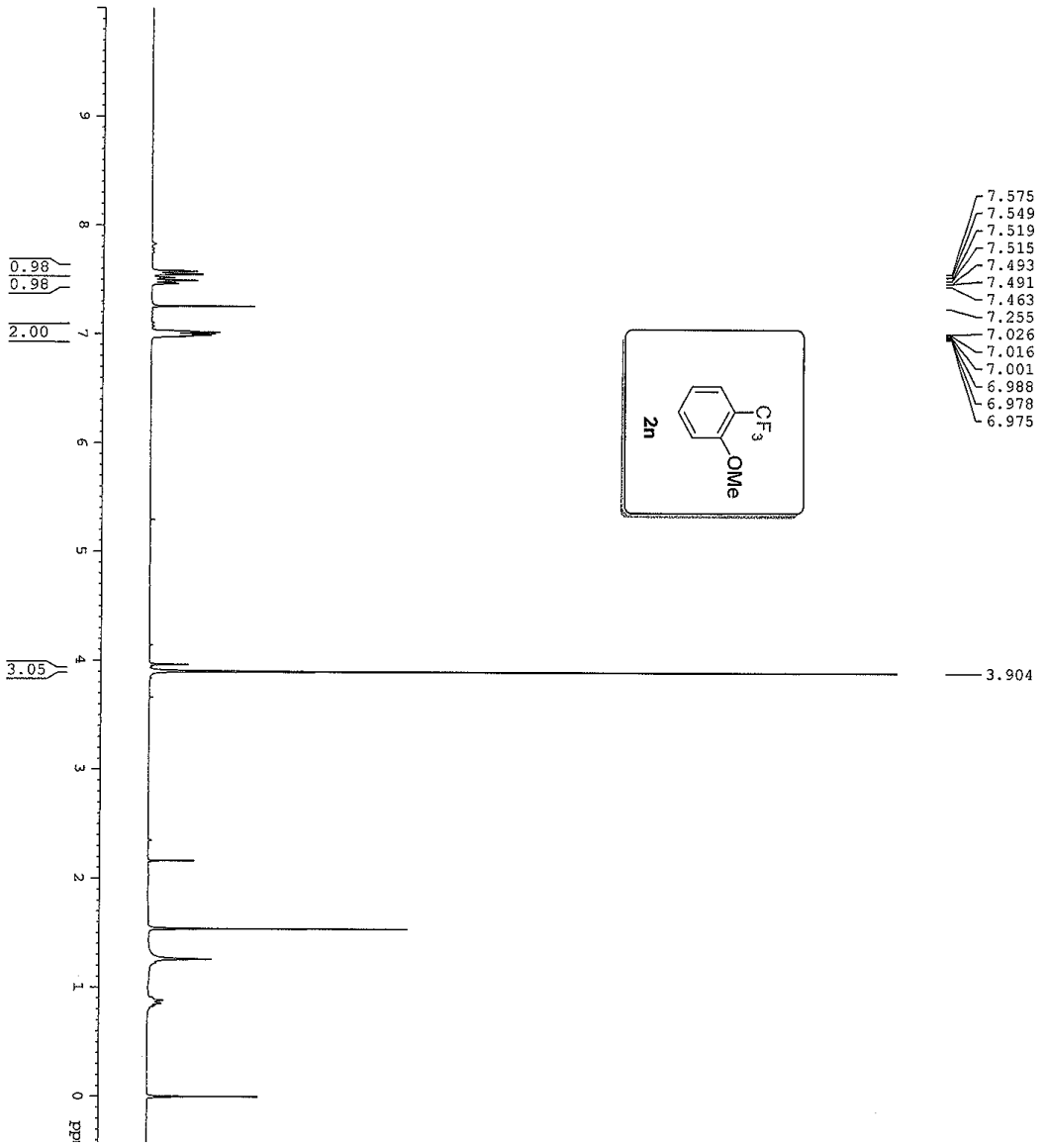
^{19}F NMR of crude 2n in $CDCl_3$



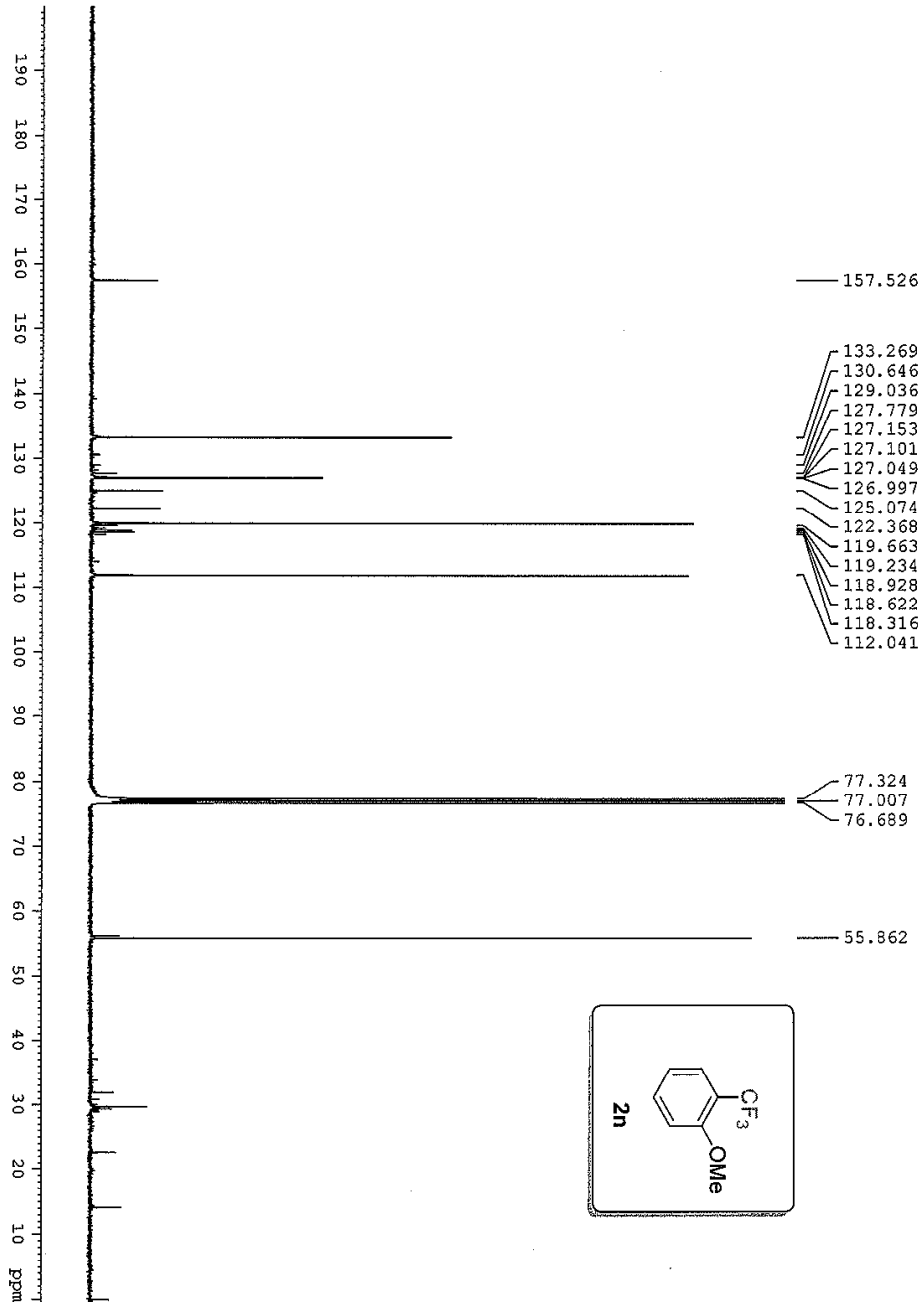
^{19}F NMR yield of compound 2n (2.68/(1×3)×100% = 89%) in $CDCl_3$



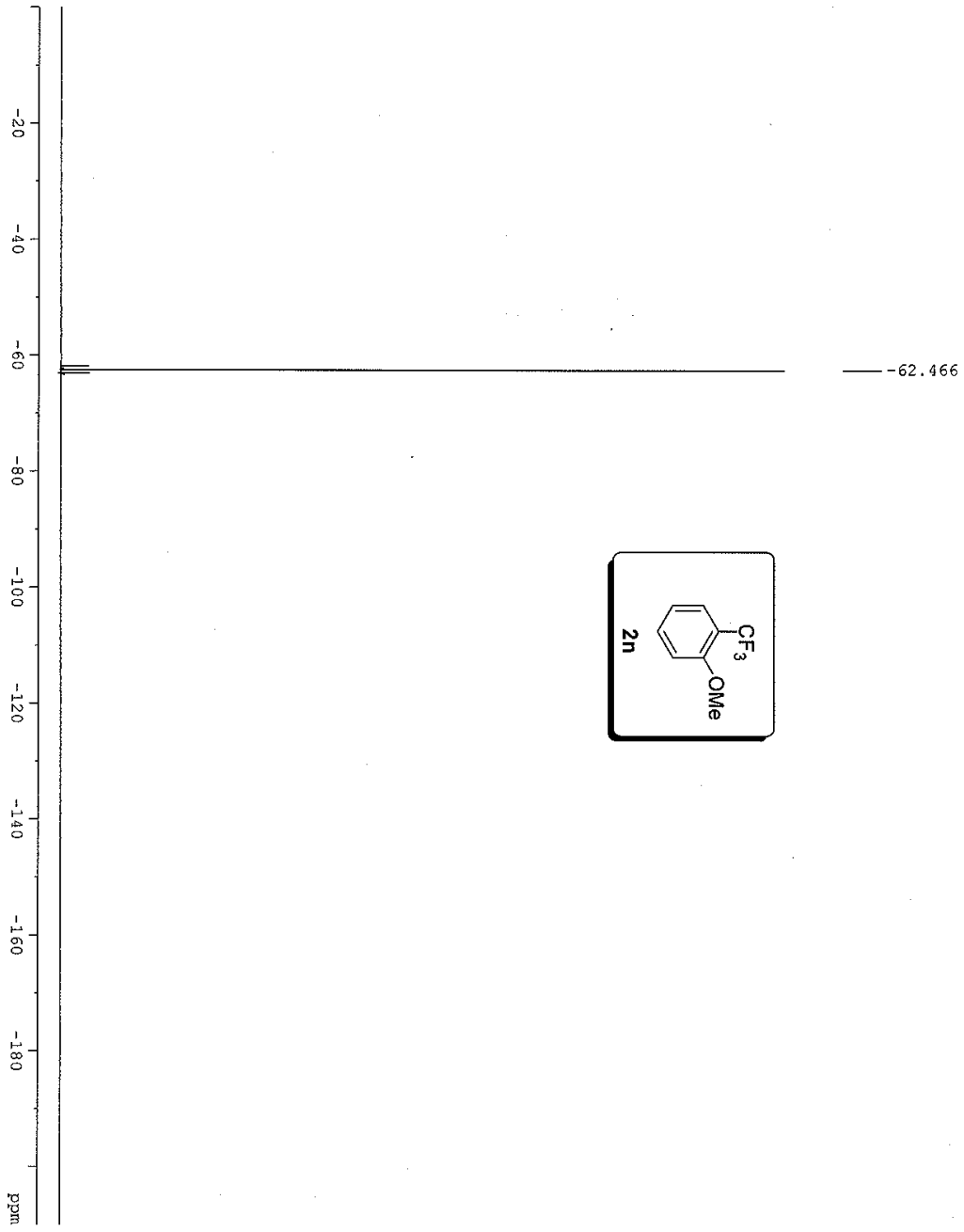
^{1}H NMR of 2n in $CDCl_3$



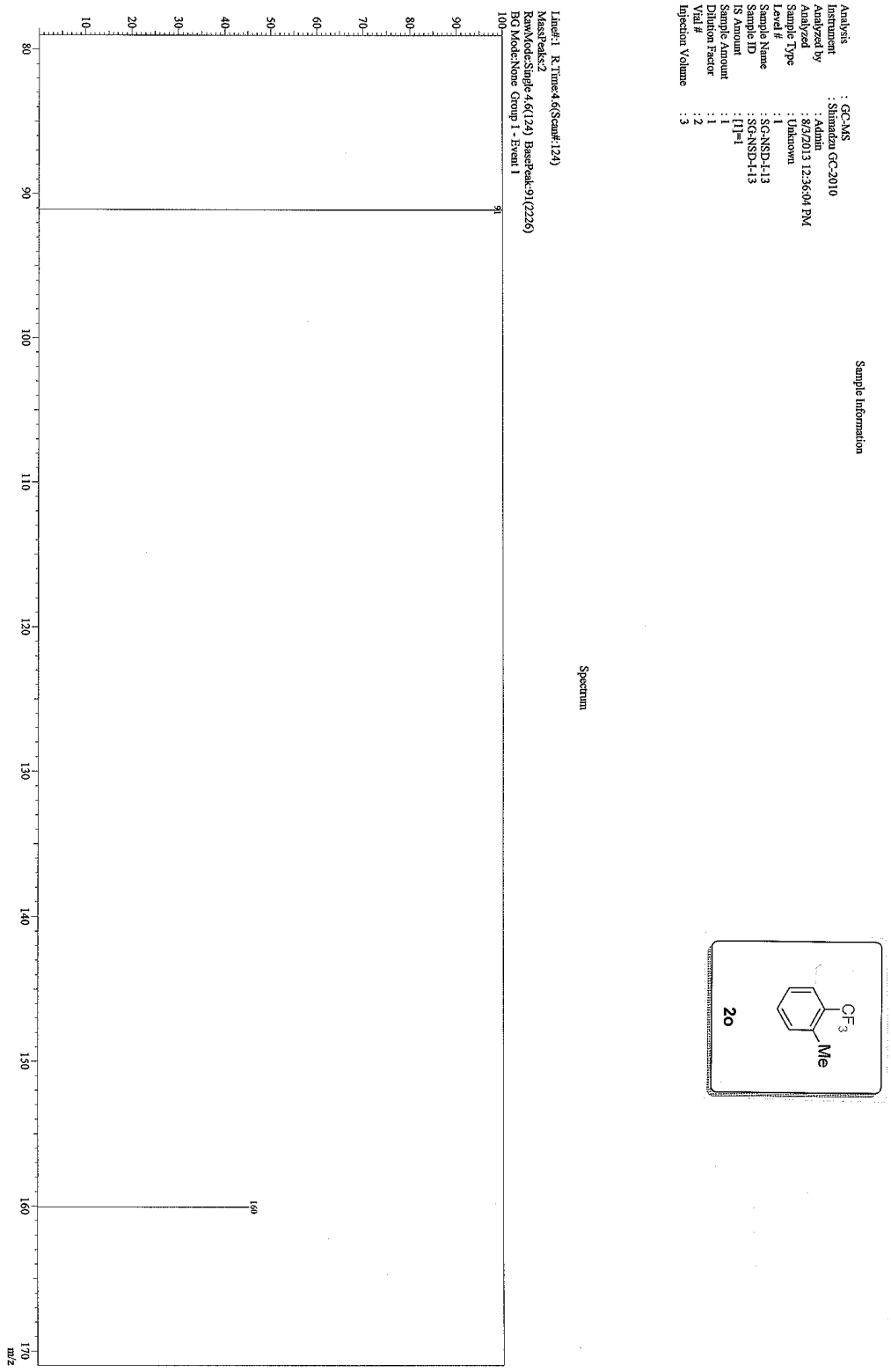
^{13}C NMR of 2n in $CDCl_3$



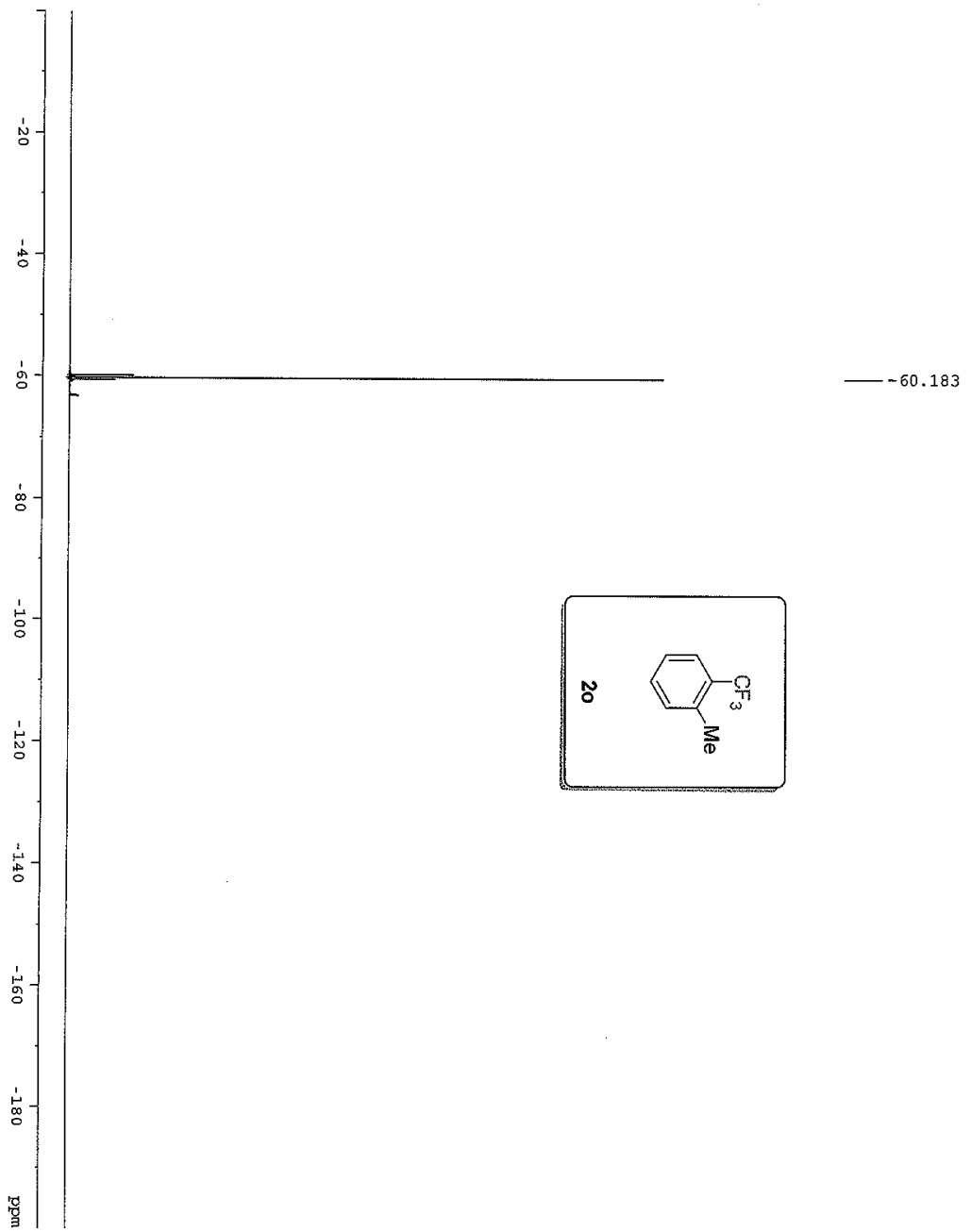
^{19}F NMR of isolated 2n in $CDCl_3$



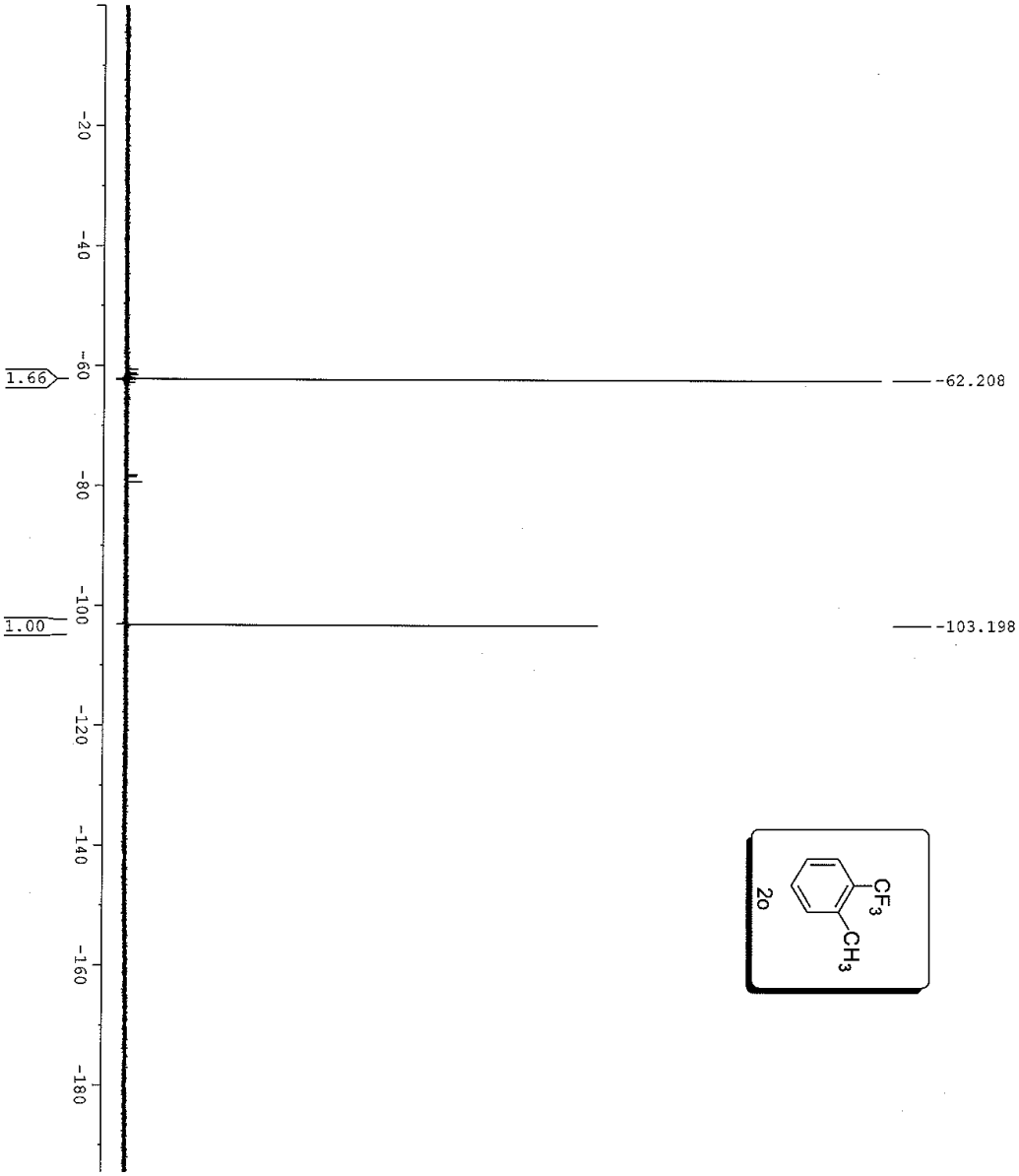
GC-MS of crude 2o



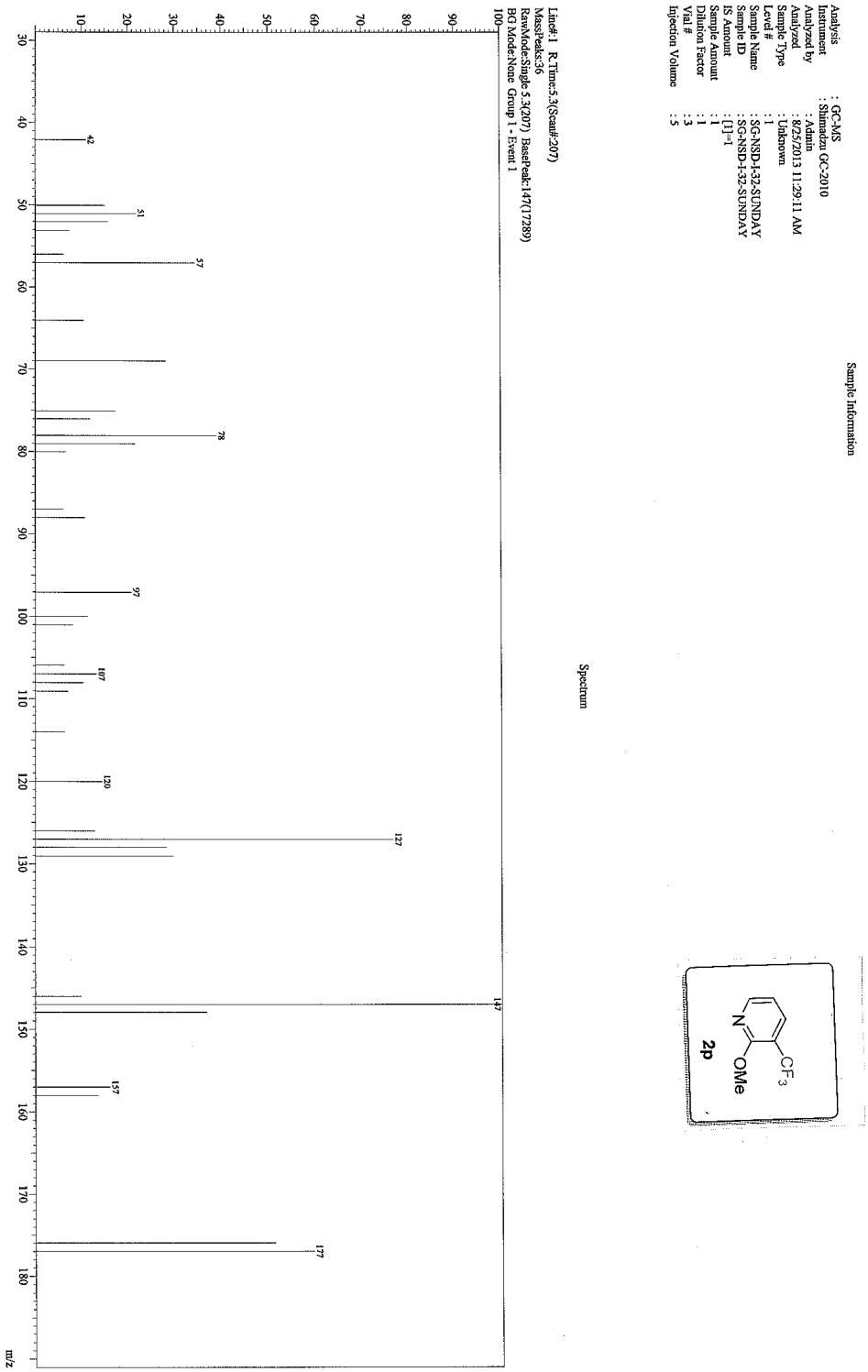
^{19}F NMR of crude 2o in $CDCl_3$



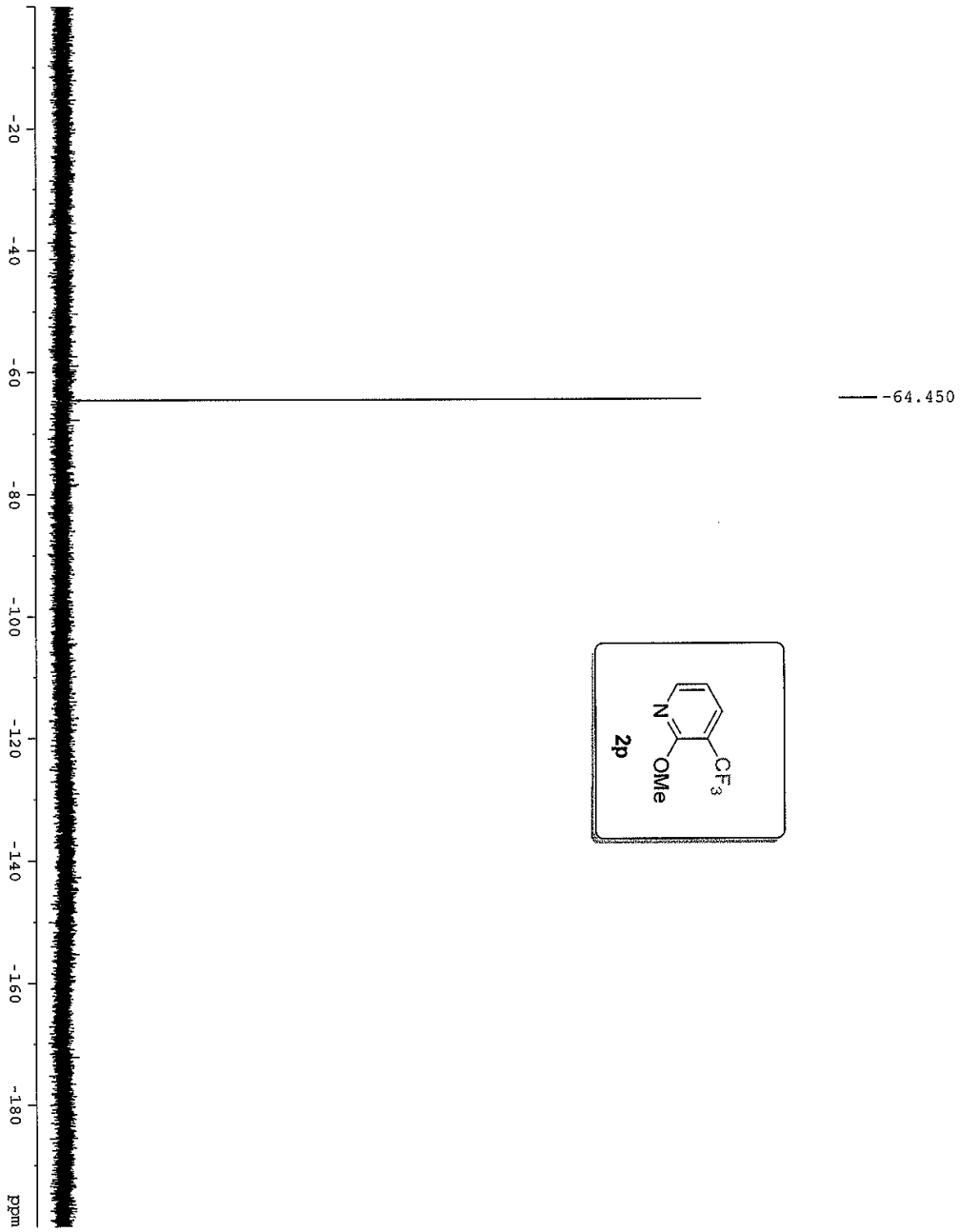
^{19}F NMR yield of compound 2o (1.66/(1×3)×100% = 55%) in $CDCl_3$



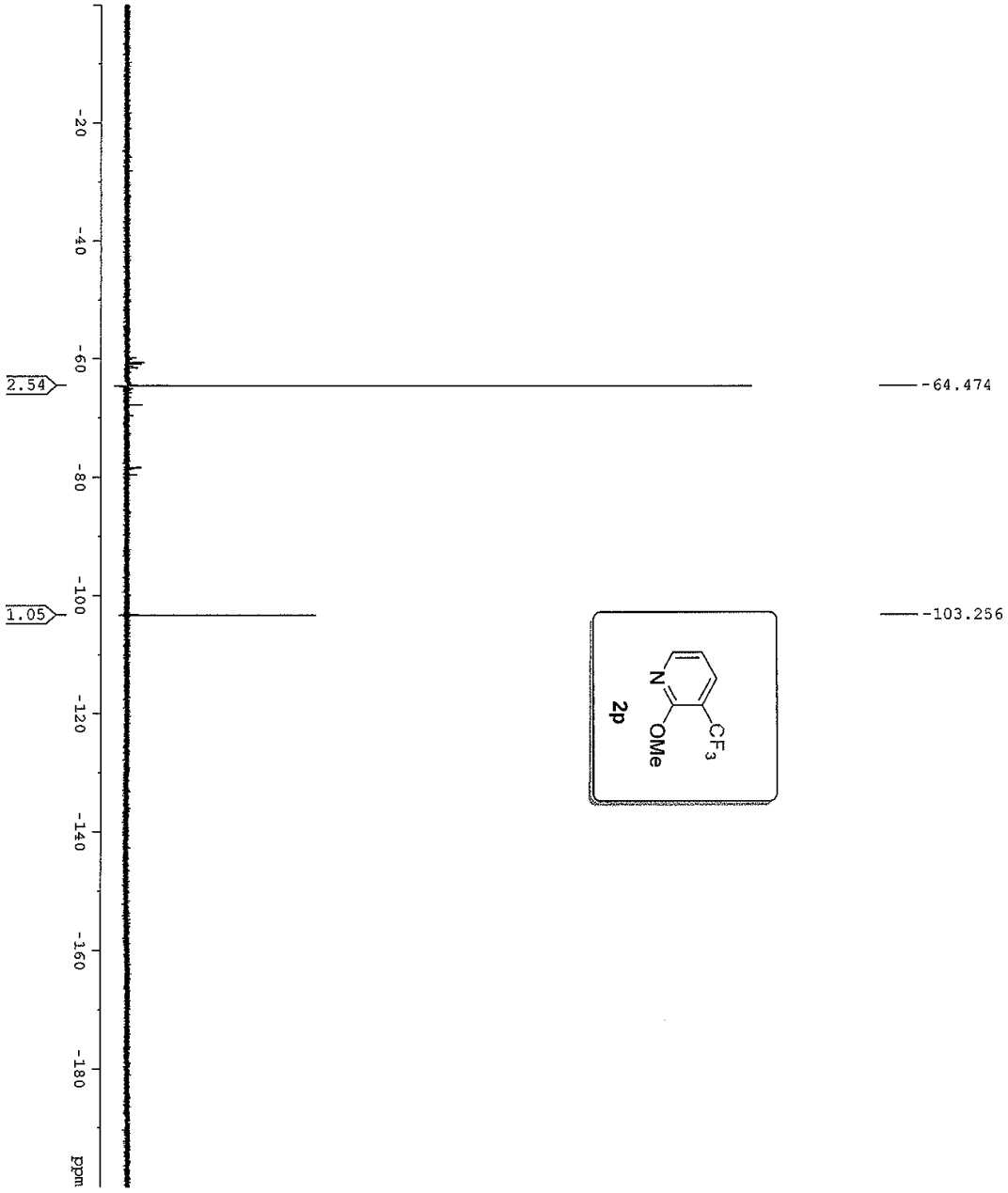
GC-MS of crude 2p



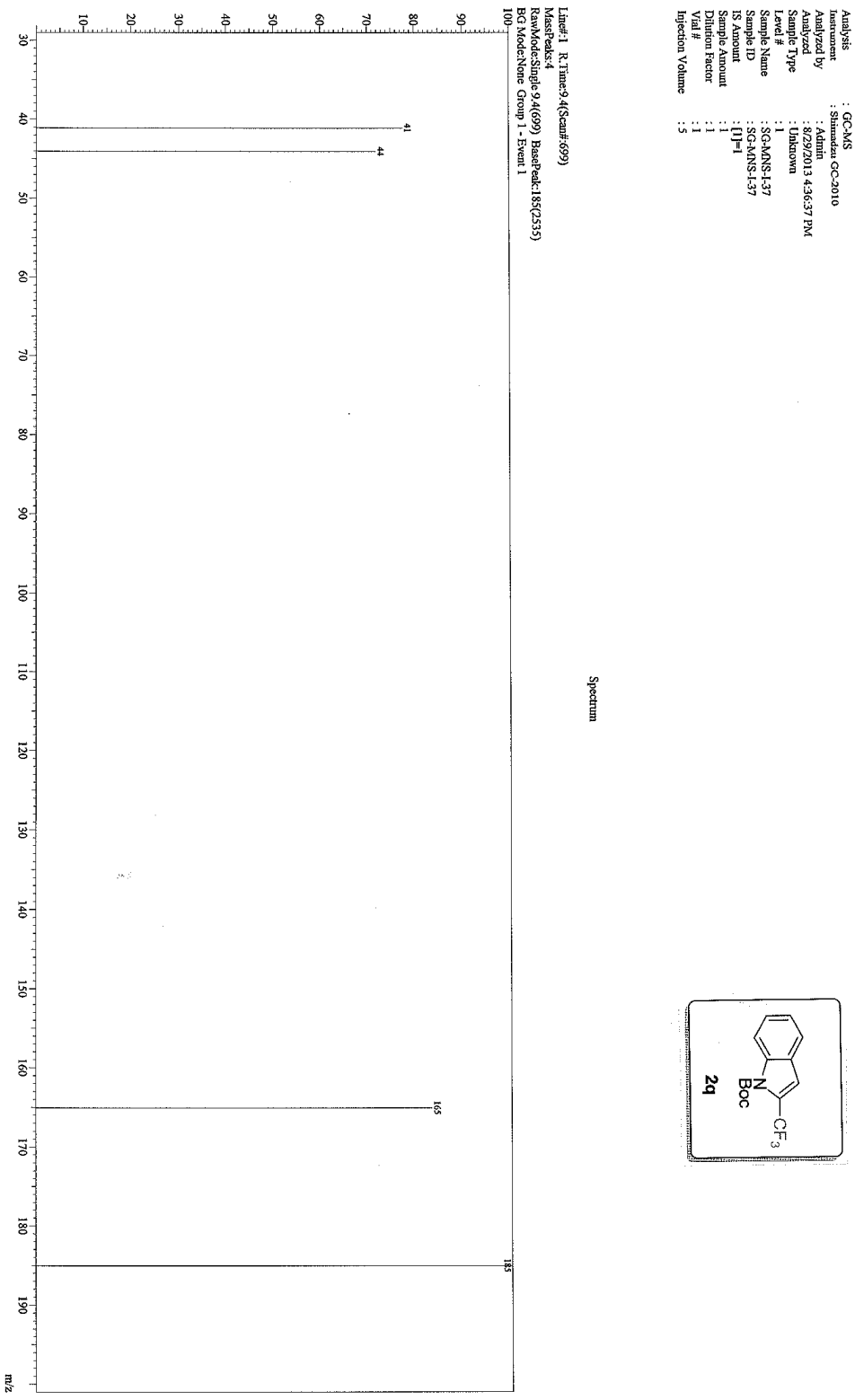
^{19}F NMR of crude 2p in $CDCl_3$



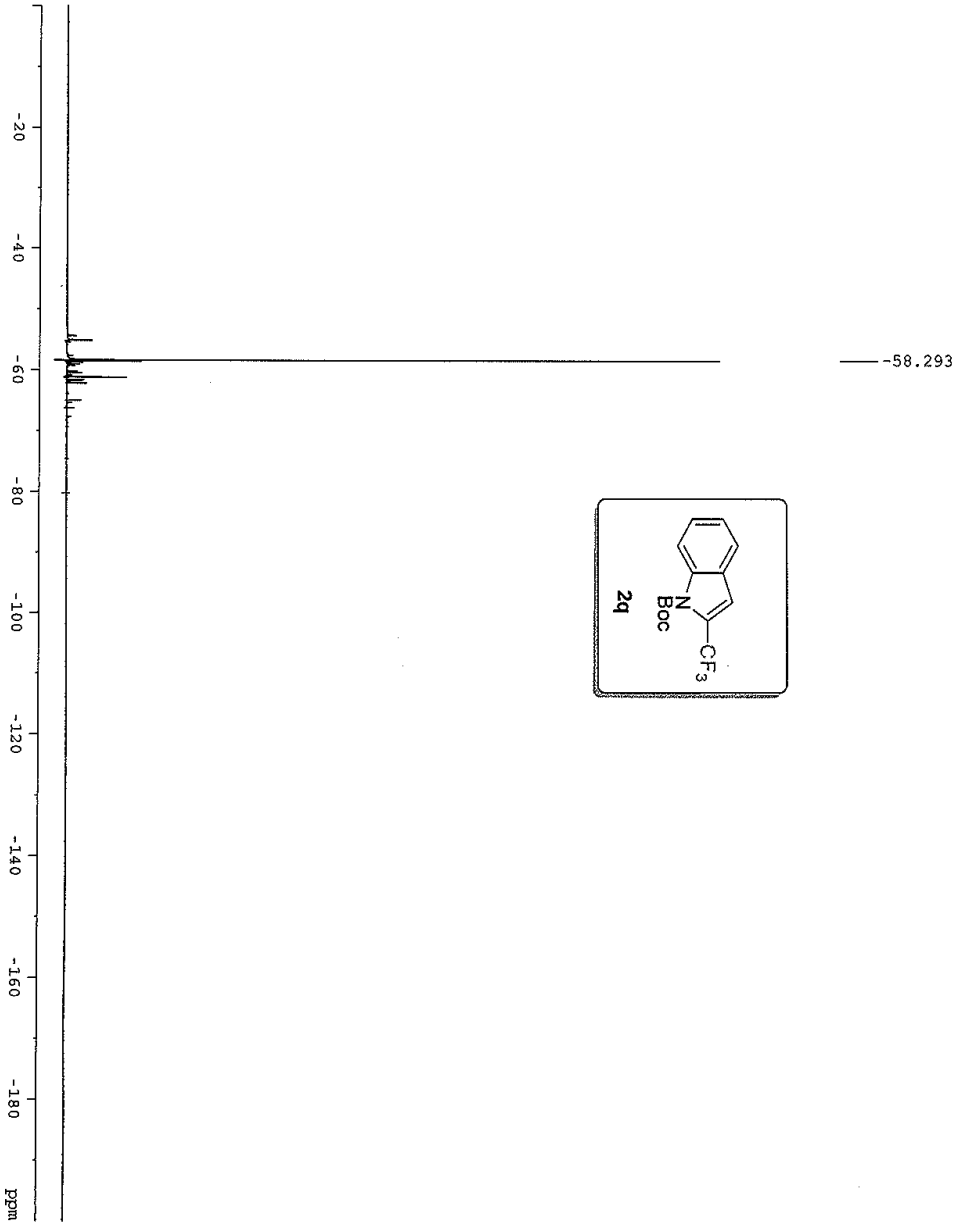
^{19}F NMR yield of compound 2p (2.54/(1×3)×100% = 85%) in $CDCl_3$



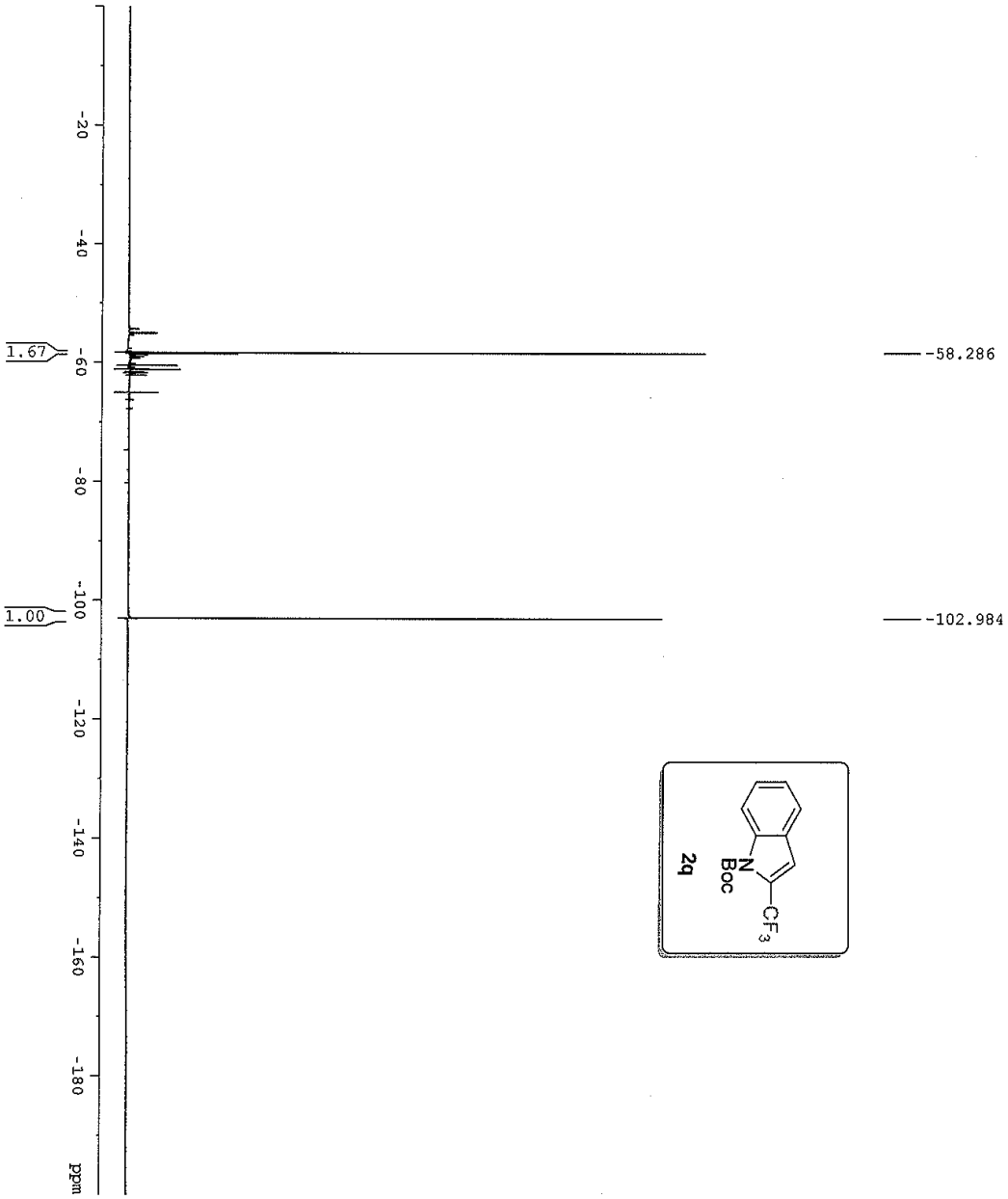
GC-MS of crude 2q



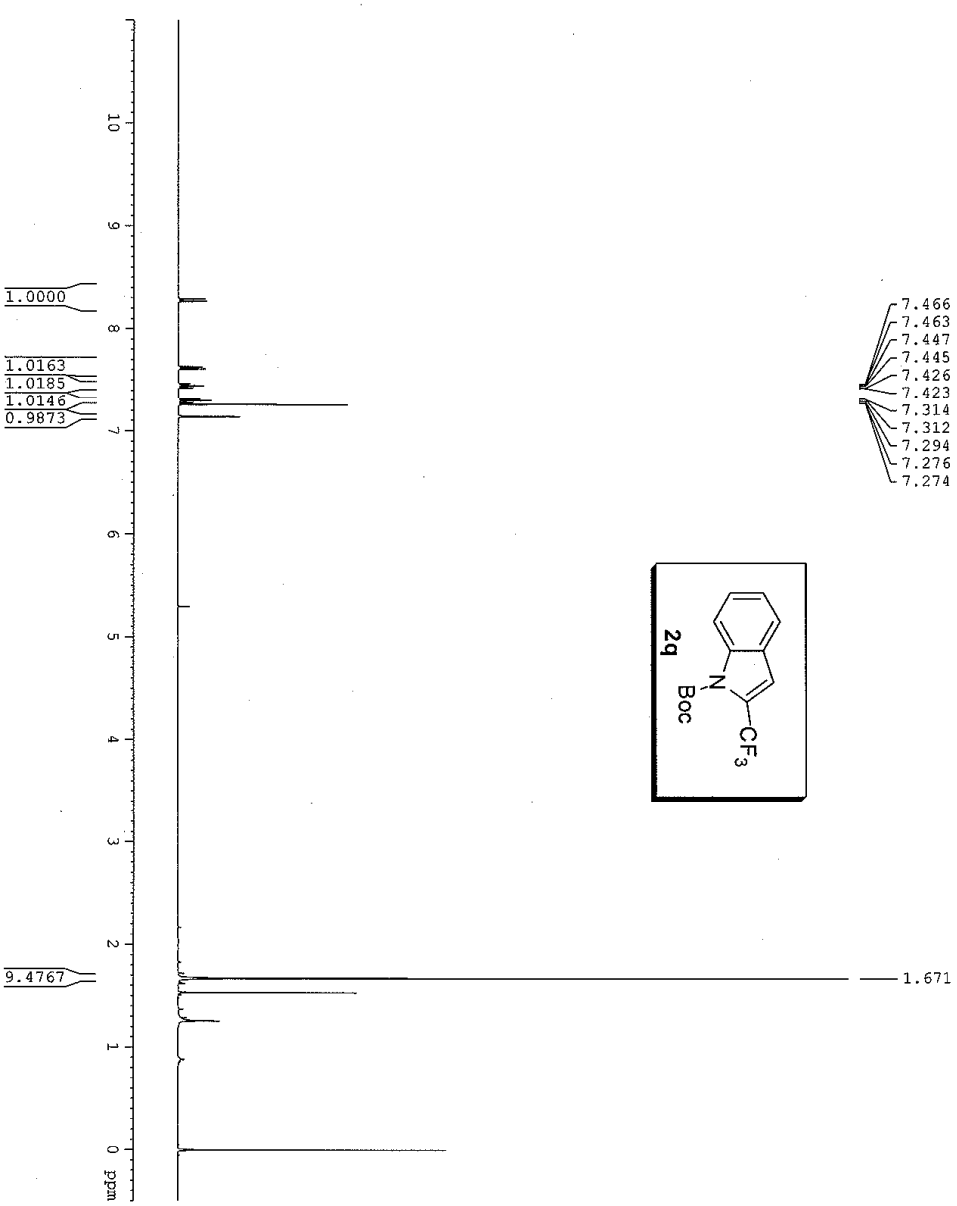
^{19}F NMR of crude 2q in $CDCl_3$



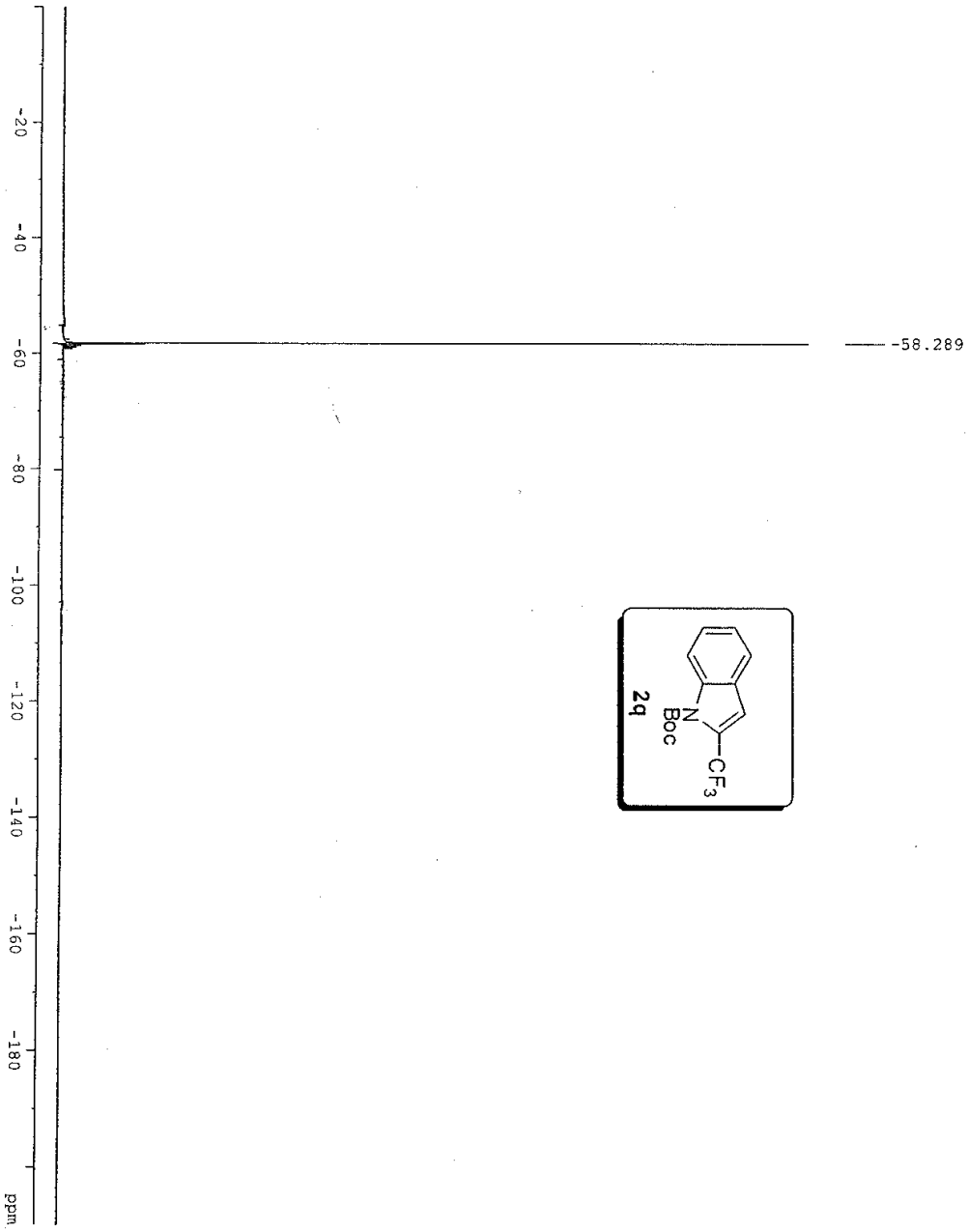
^{19}F NMR yield of compound 2q (1.67/(1×3)×100% = 55%) in $CDCl_3$



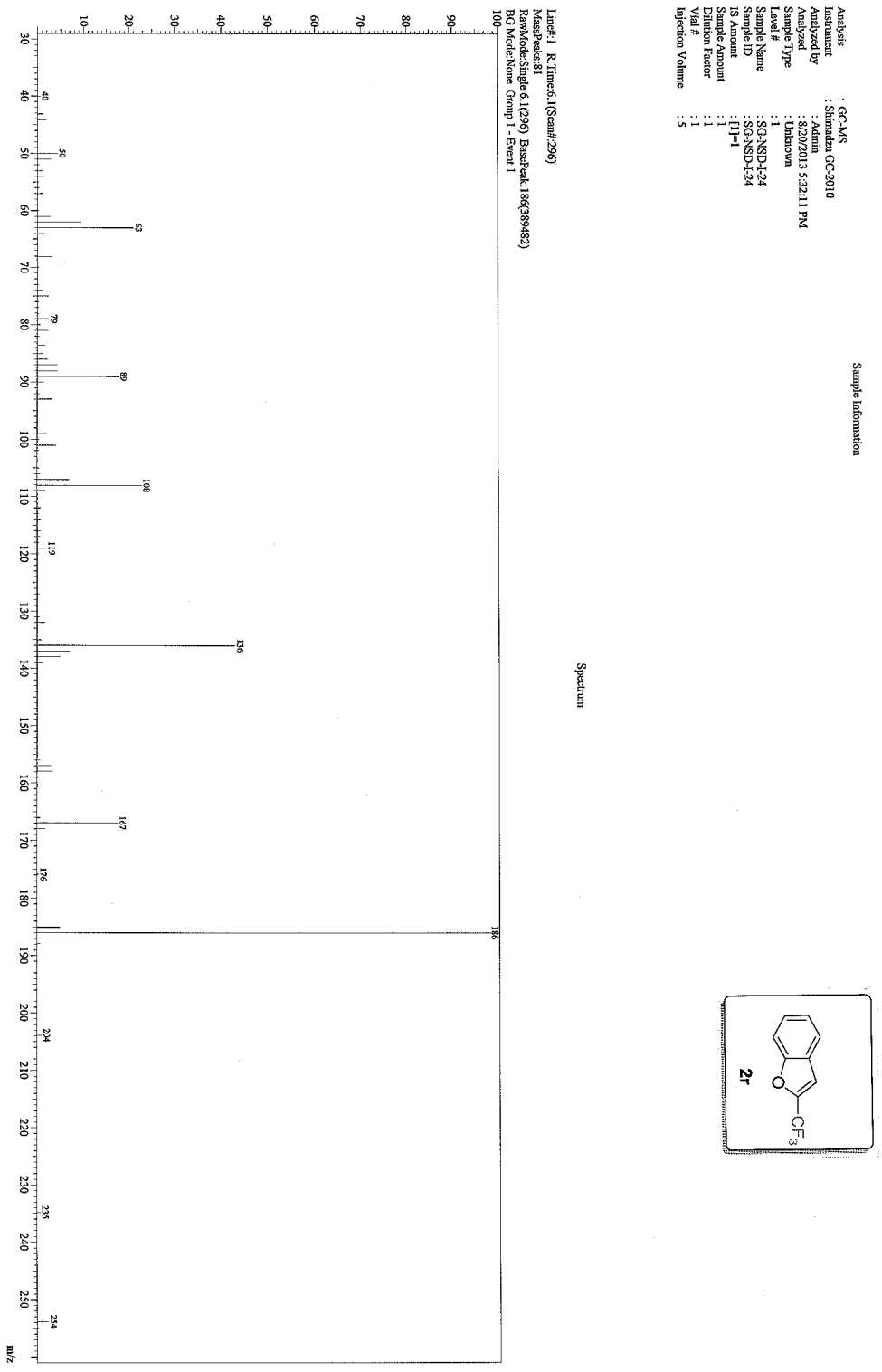
^{1}H NMR of compound 2q



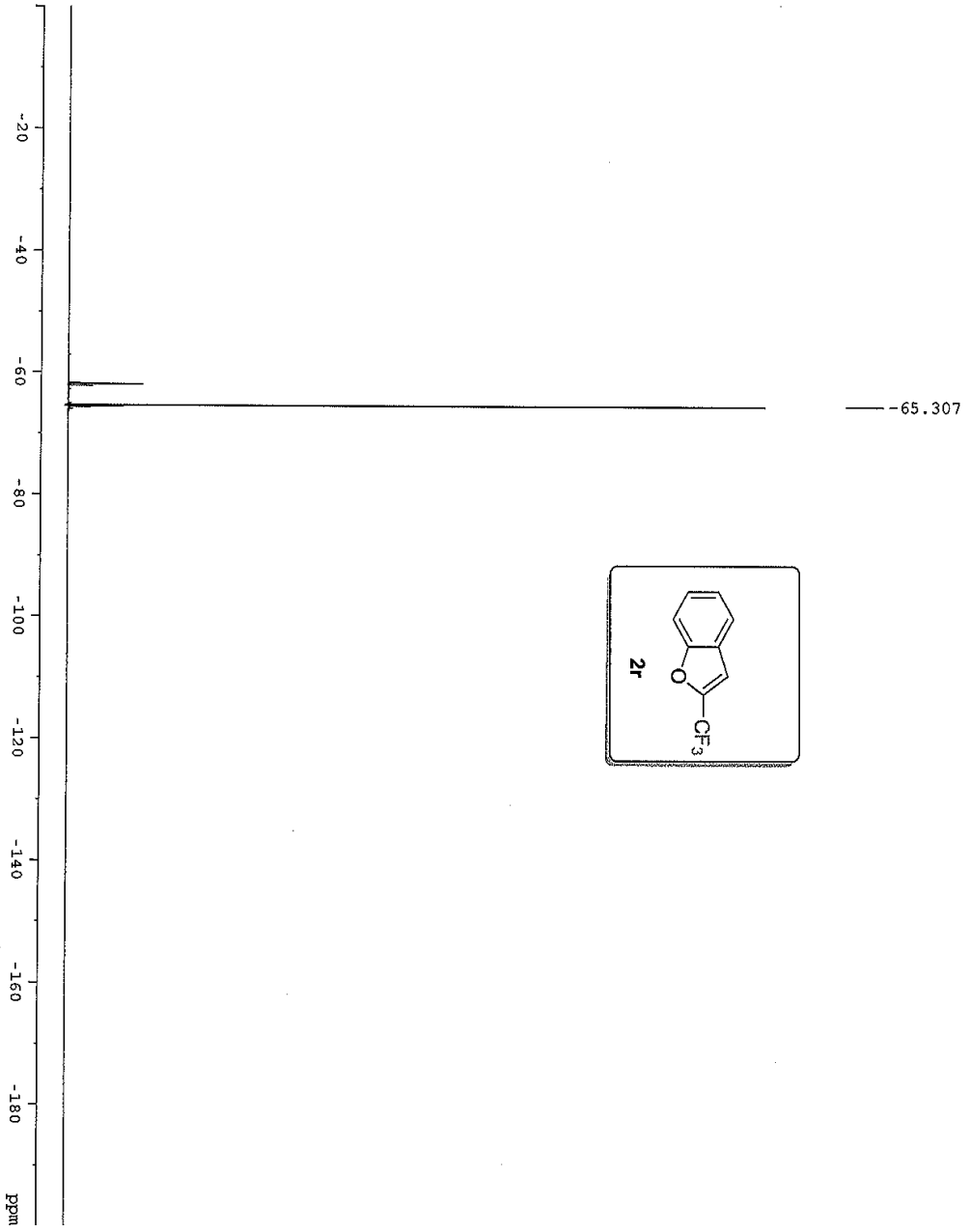
^{19}F NMR of isolated 2q in $CDCl_3$



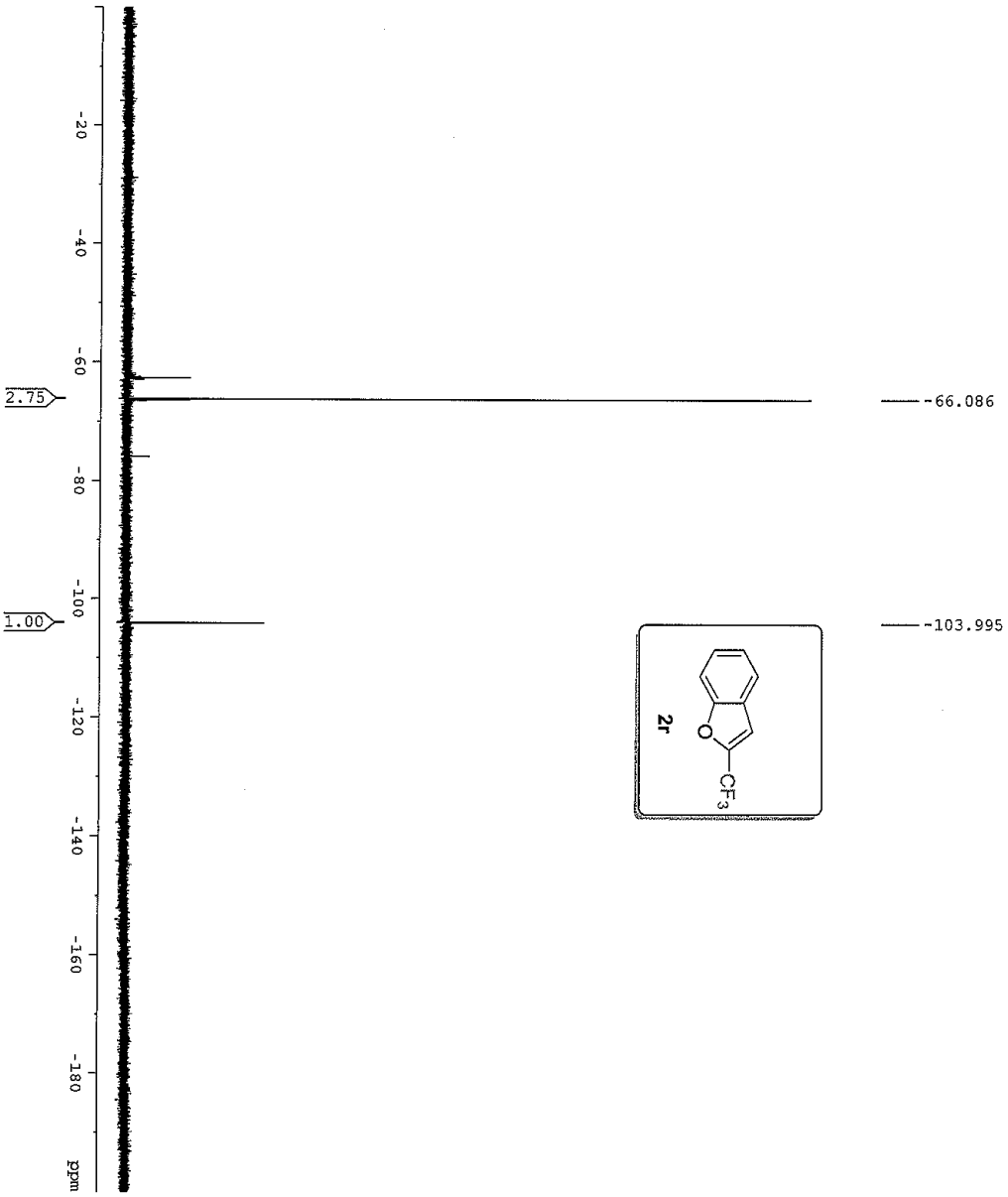
GC-MS of crude 2r



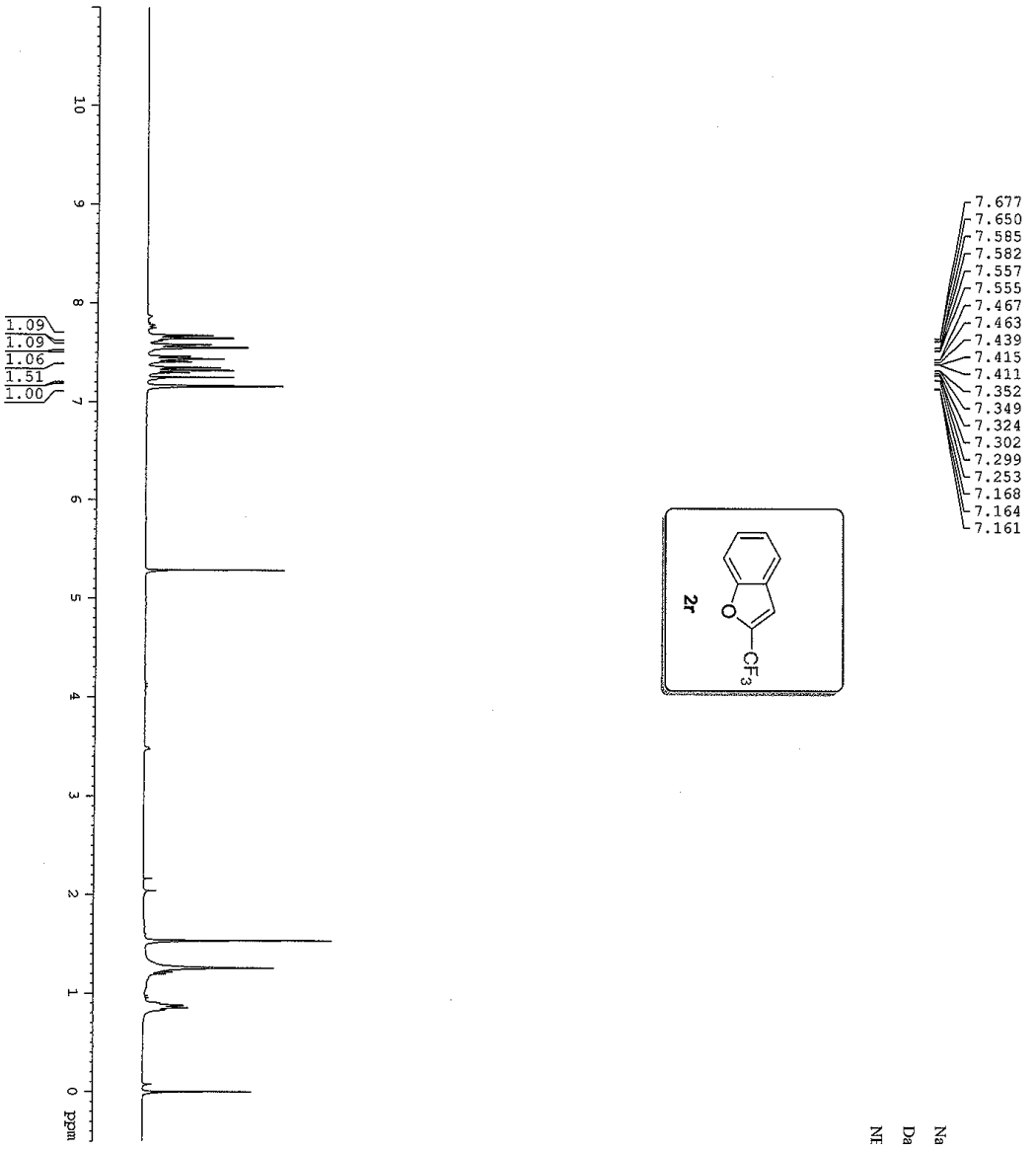
^{19}F NMR of crude 2r in $CDCl_3$



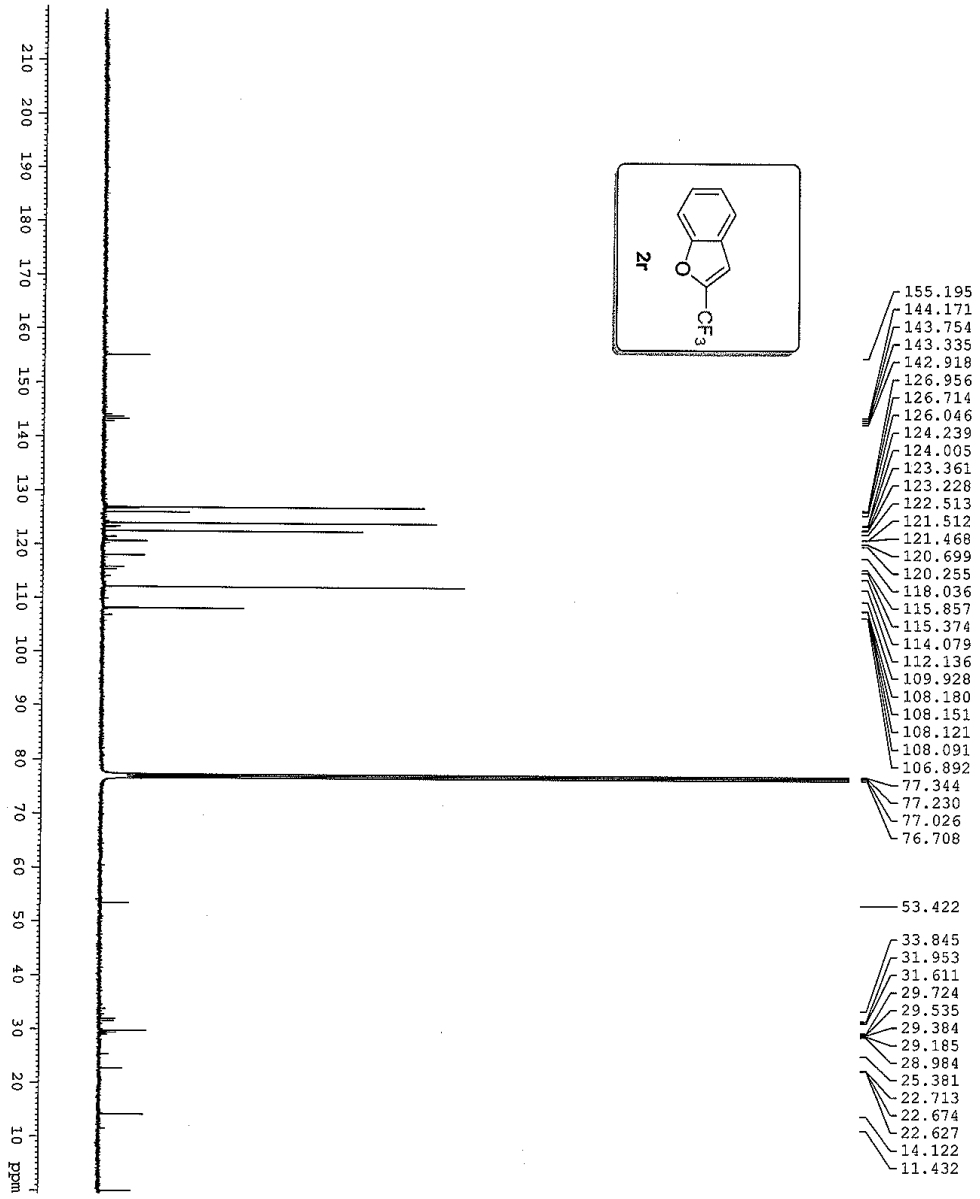
^{19}F NMR yield of compound 2r (2.75/(1×3)×100% = 91%) in $CDCl_3$



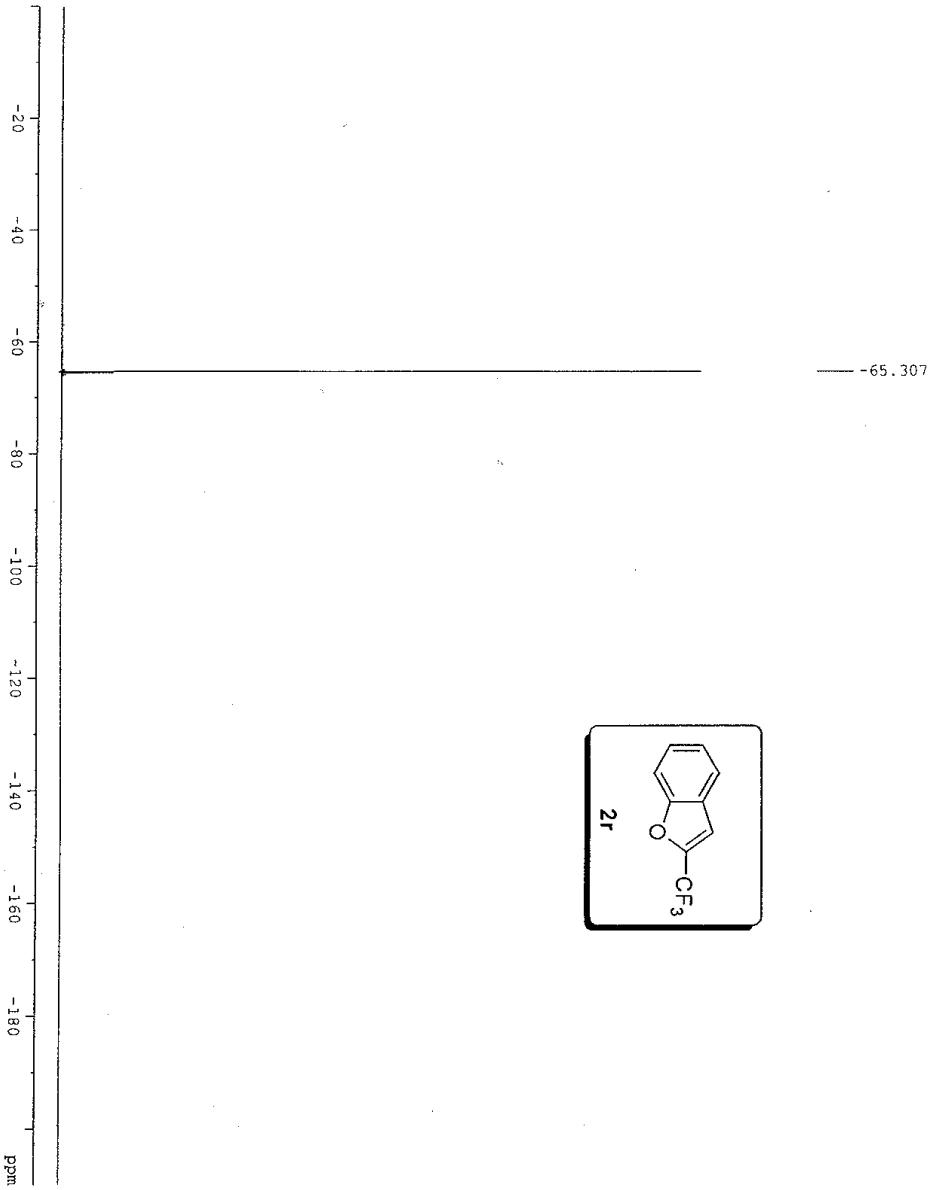
^{1}H NMR of 2r in $CDCl_3$



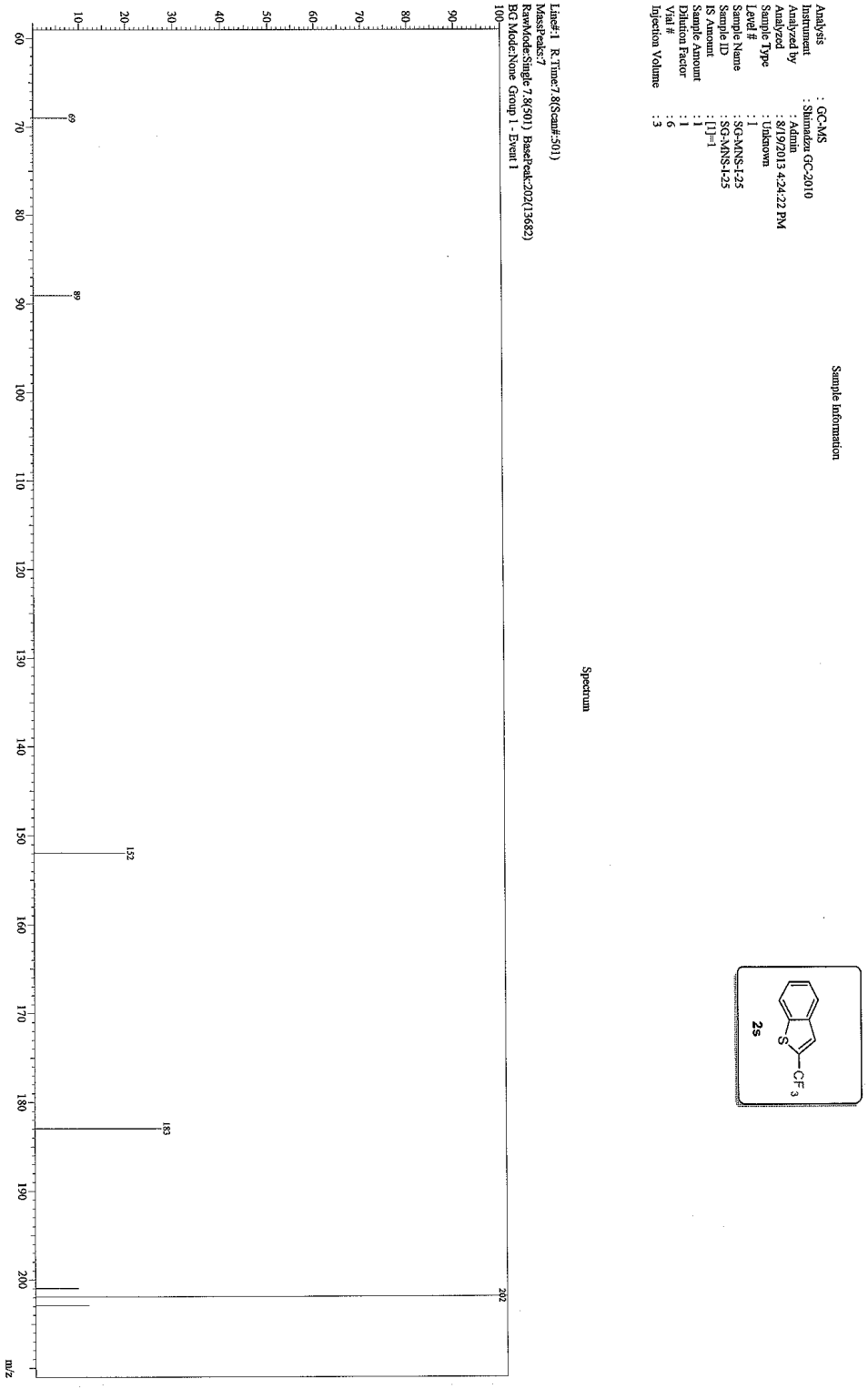
^{13}C NMR of 2r in $CDCl_3$



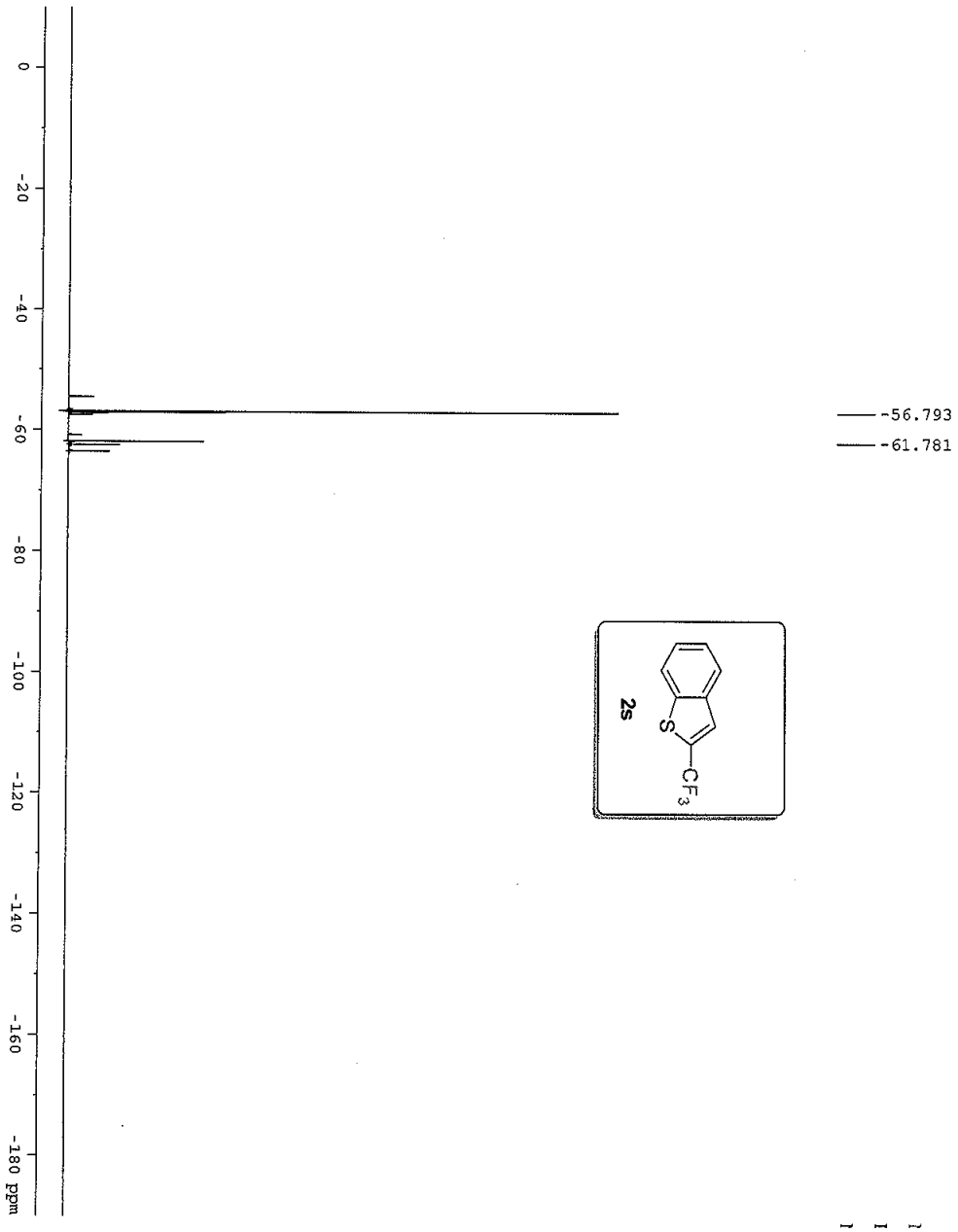
^{19}F NMR of isolated 2r in $CDCl_3$



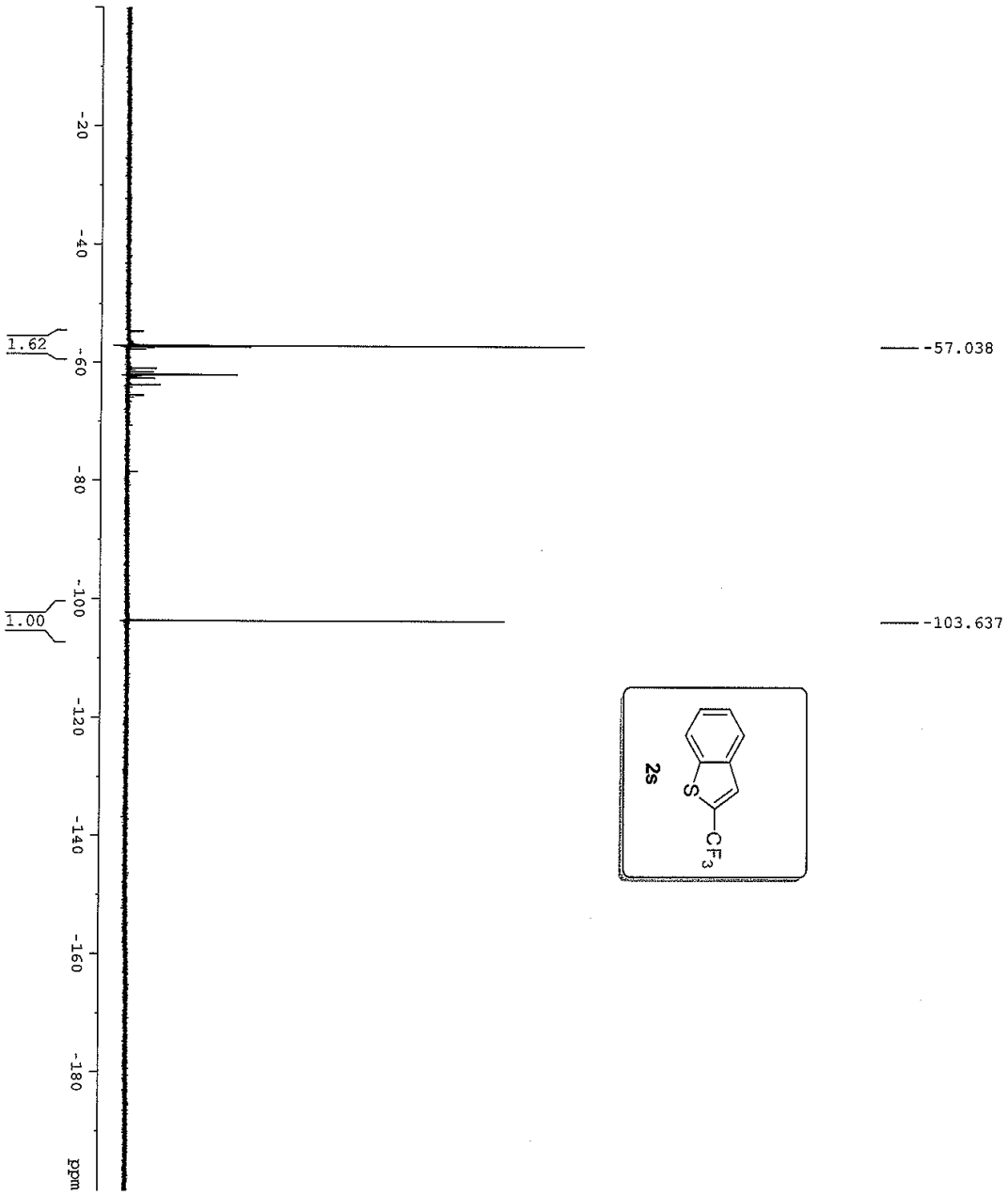
GC-MS of crude 2s



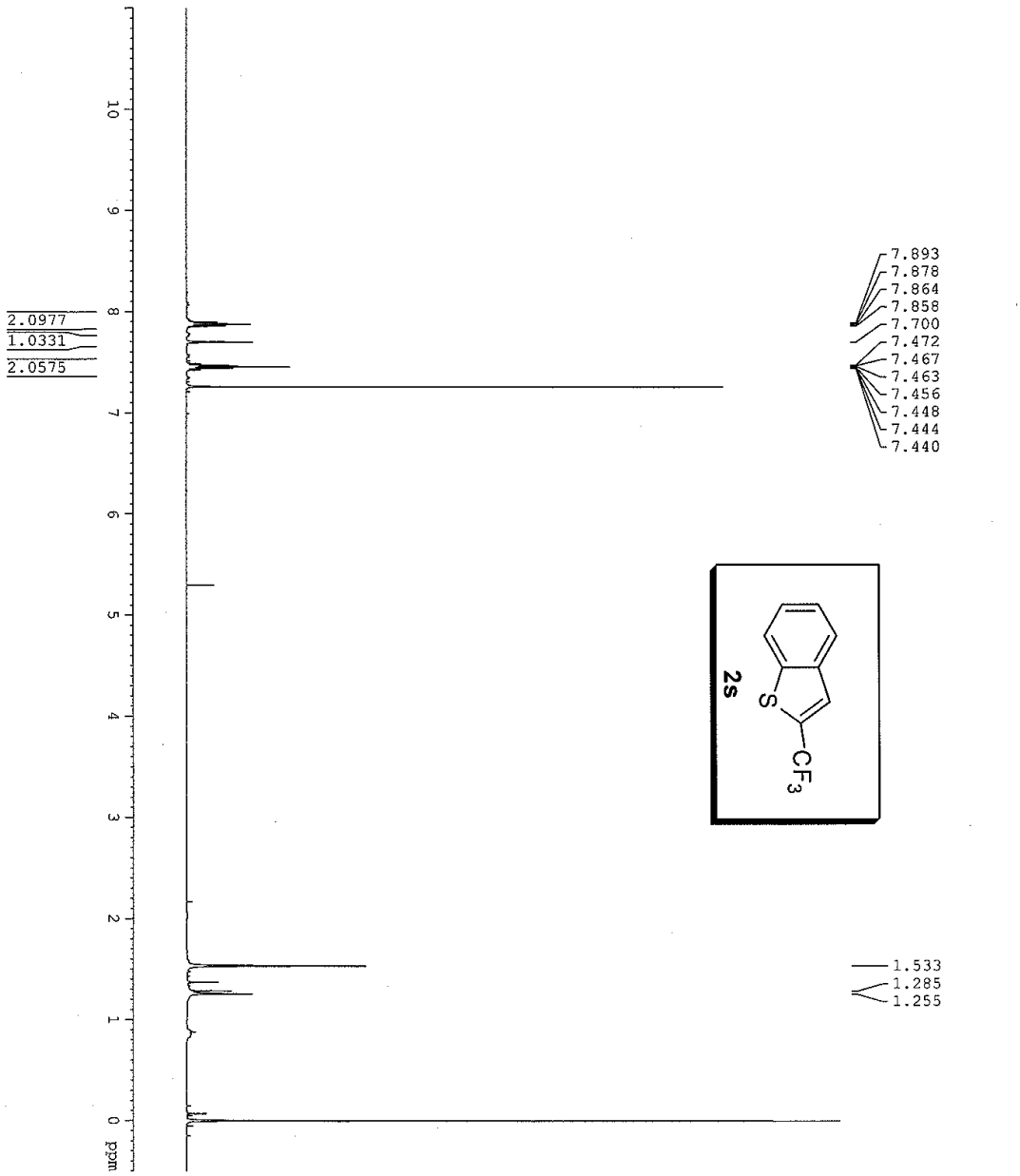
^{19}F NMR of crude 2s in $CDCl_3$



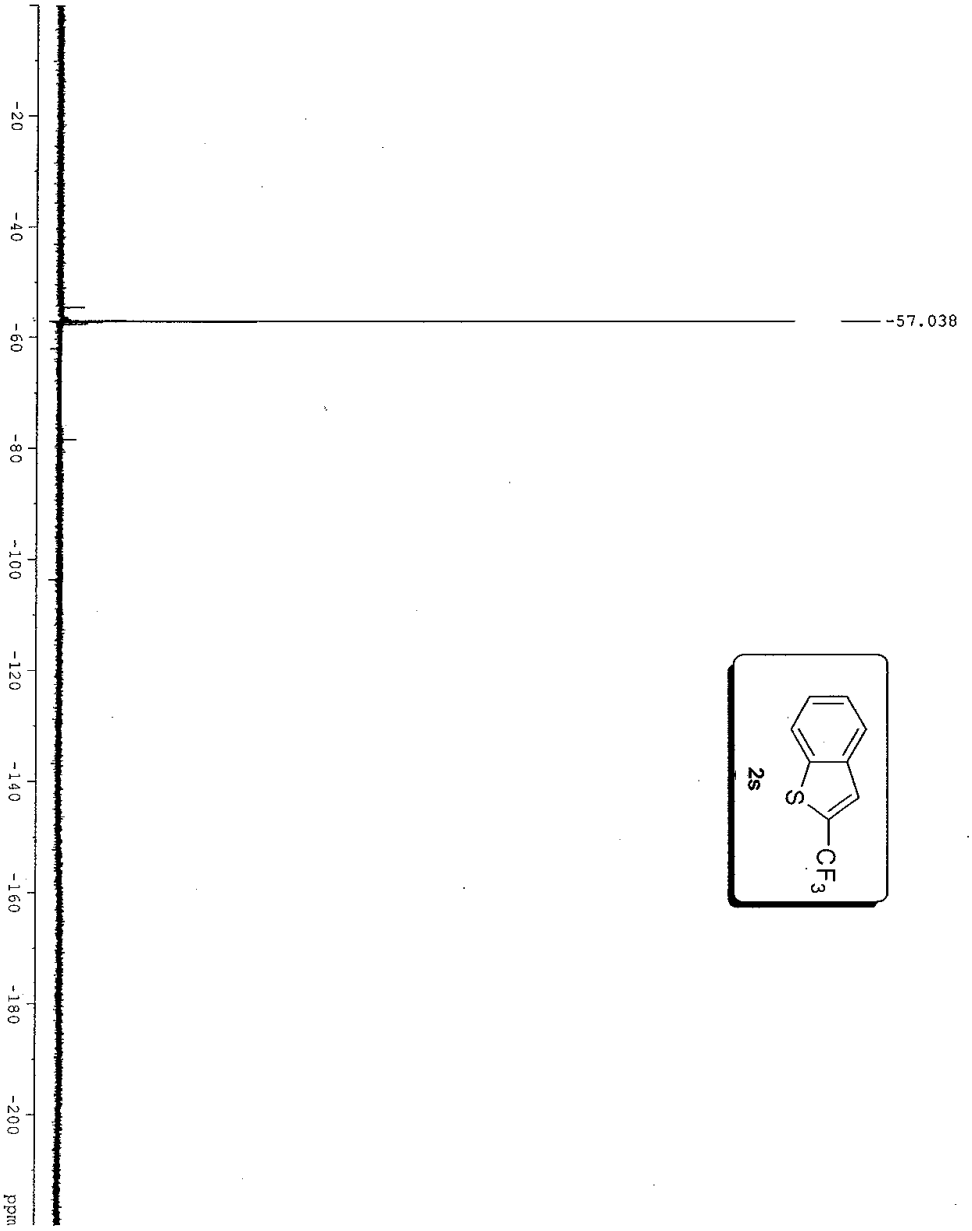
^{19}F NMR yield of compound 2s (1.62/(1×3)×100% = 54%) in $CDCl_3$



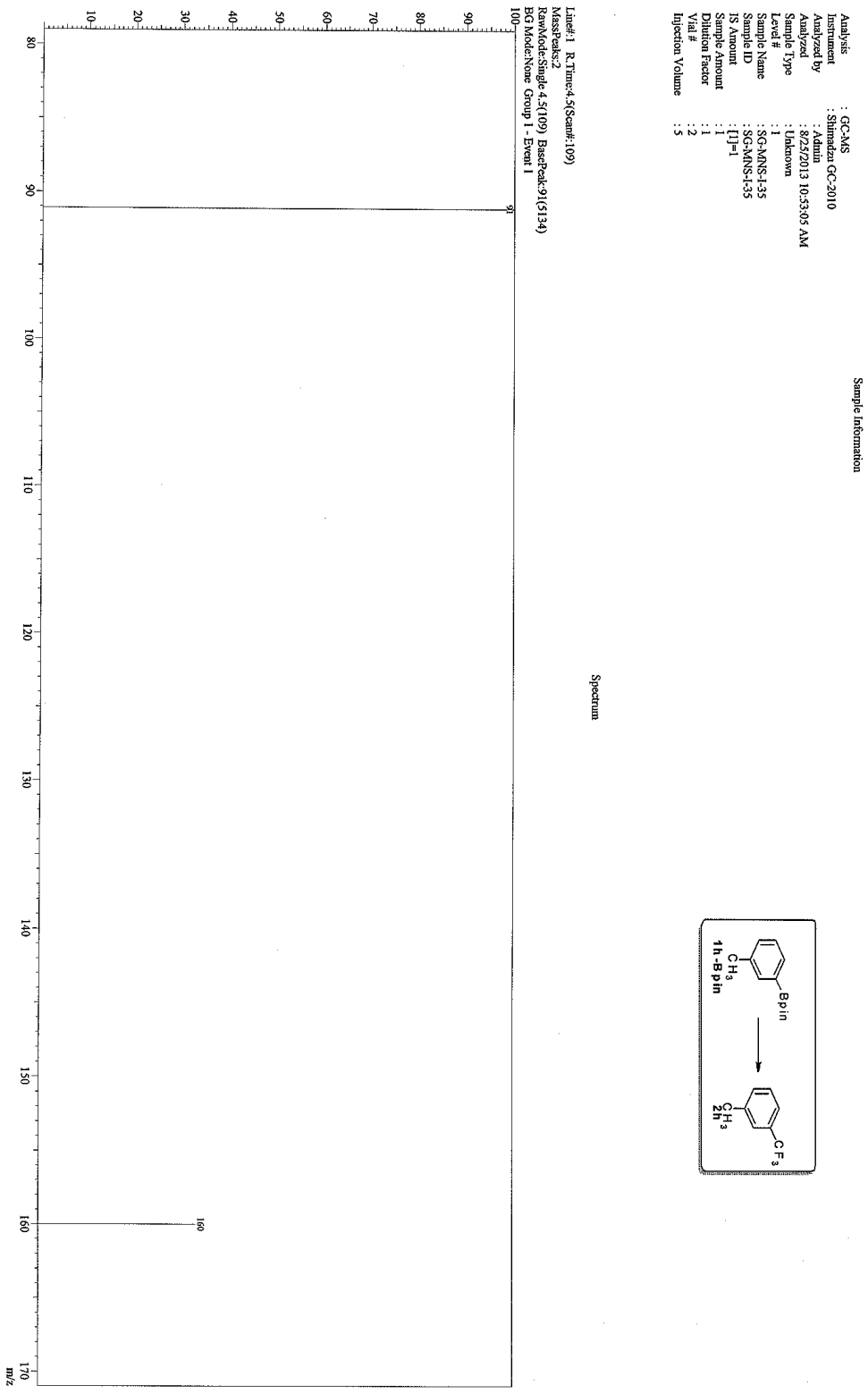
^{1}H NMR of compound 2s



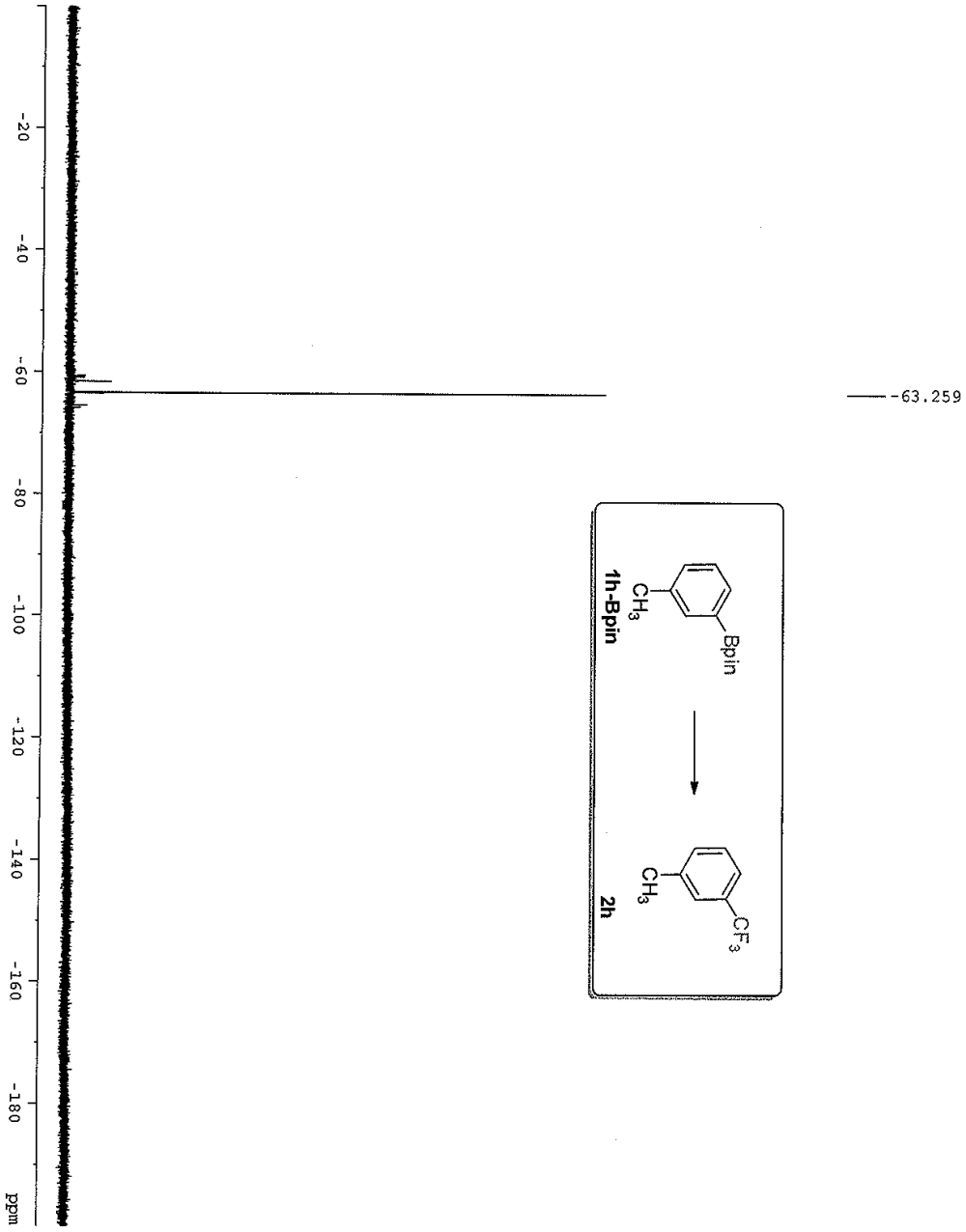
^{19}F NMR of isolated 2s in $CDCl_3$



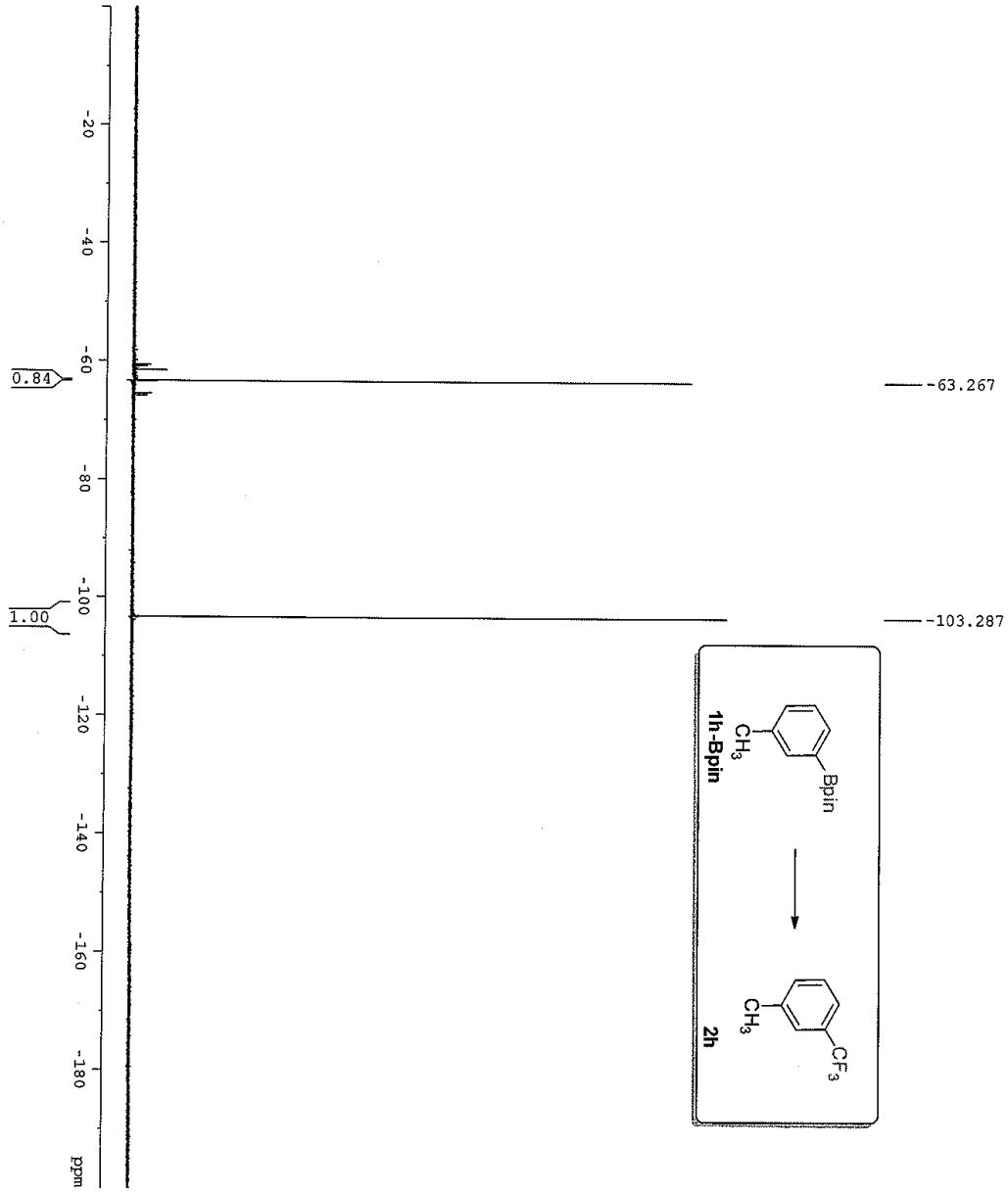
GC-MS of crude 2h



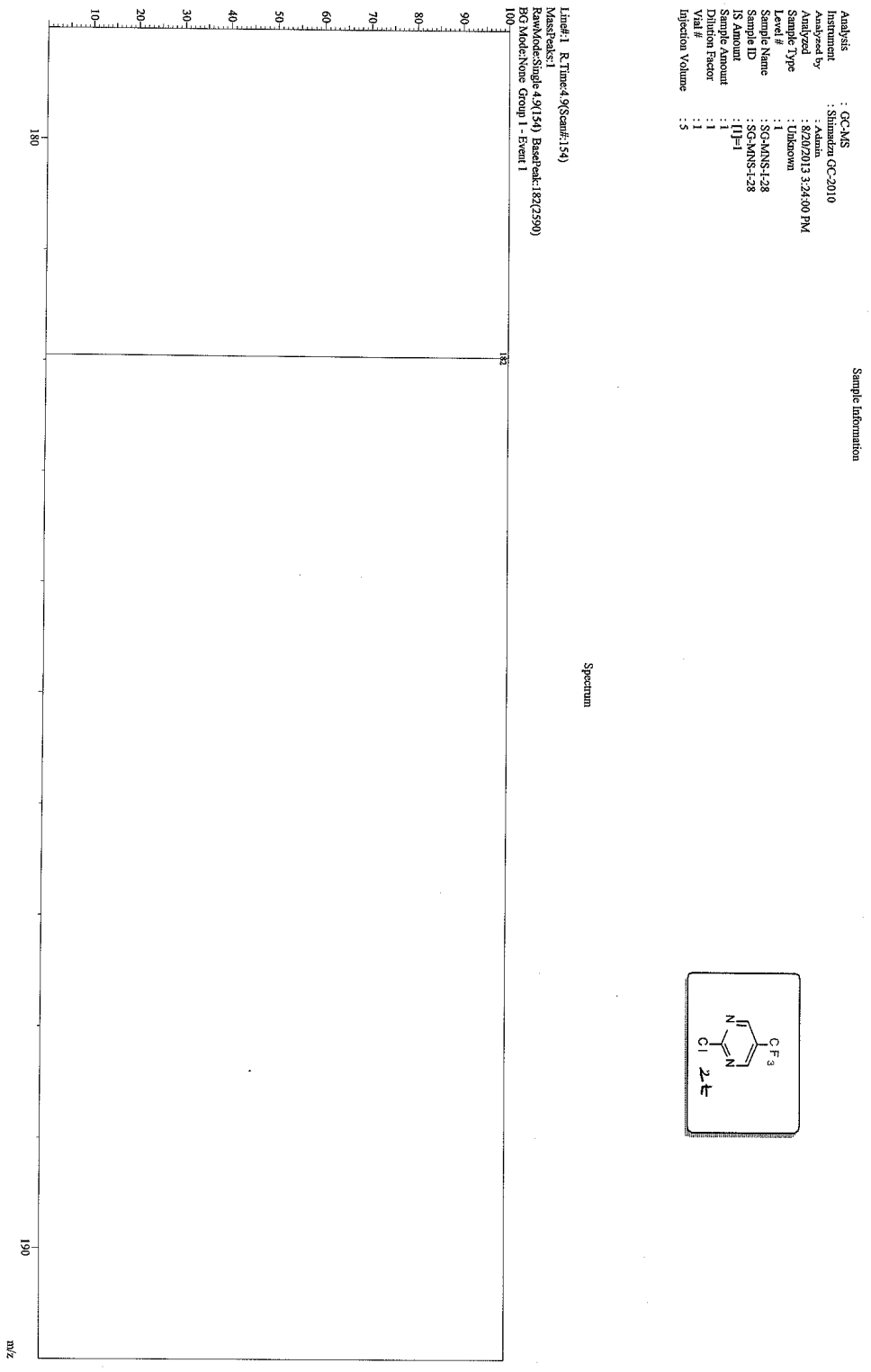
^{19}F NMR of crude 2h in $CDCl_3$



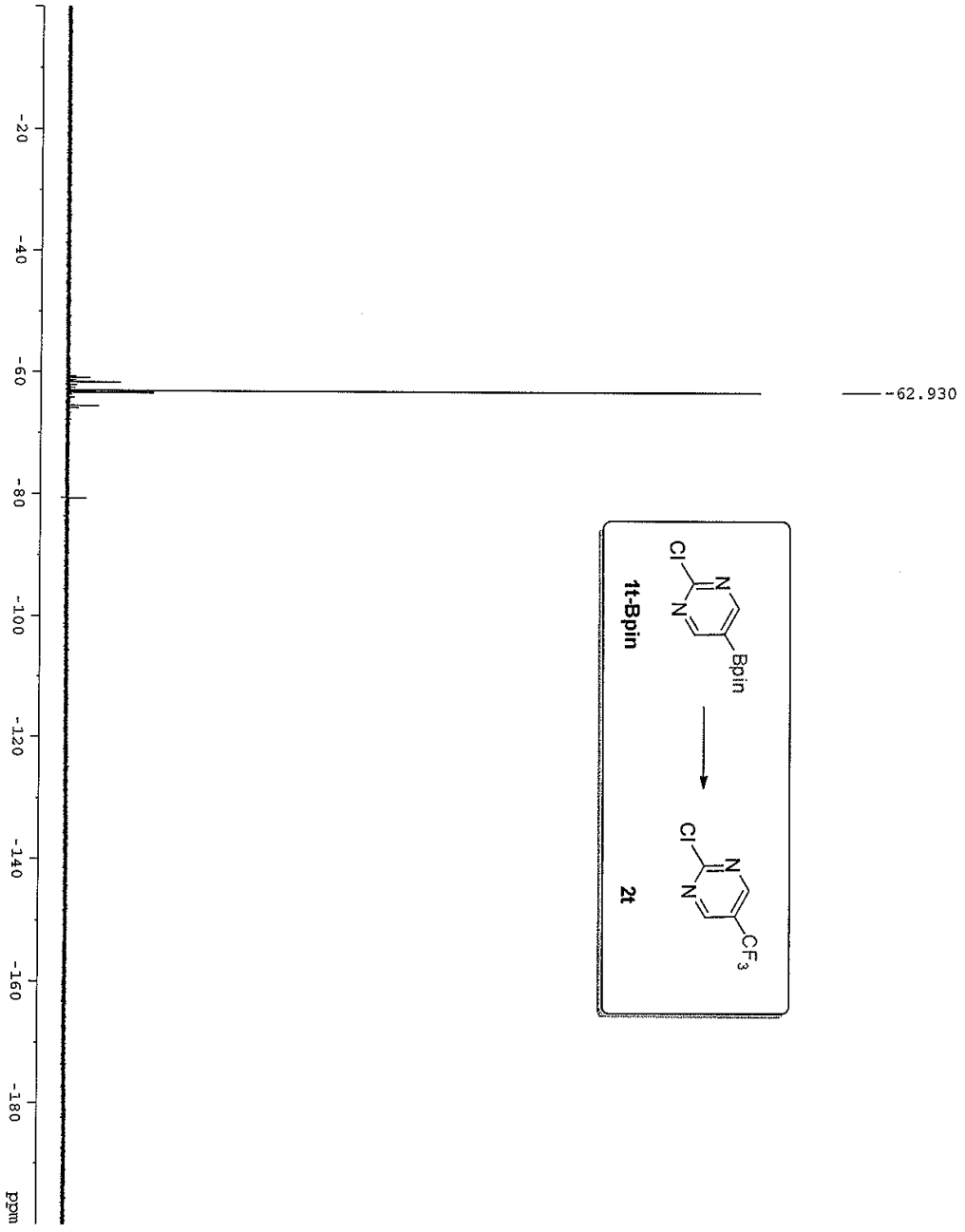
^{19}F NMR yield of compound 2h (0.84/(1×3)×100% = 28%) in $CDCl_3$



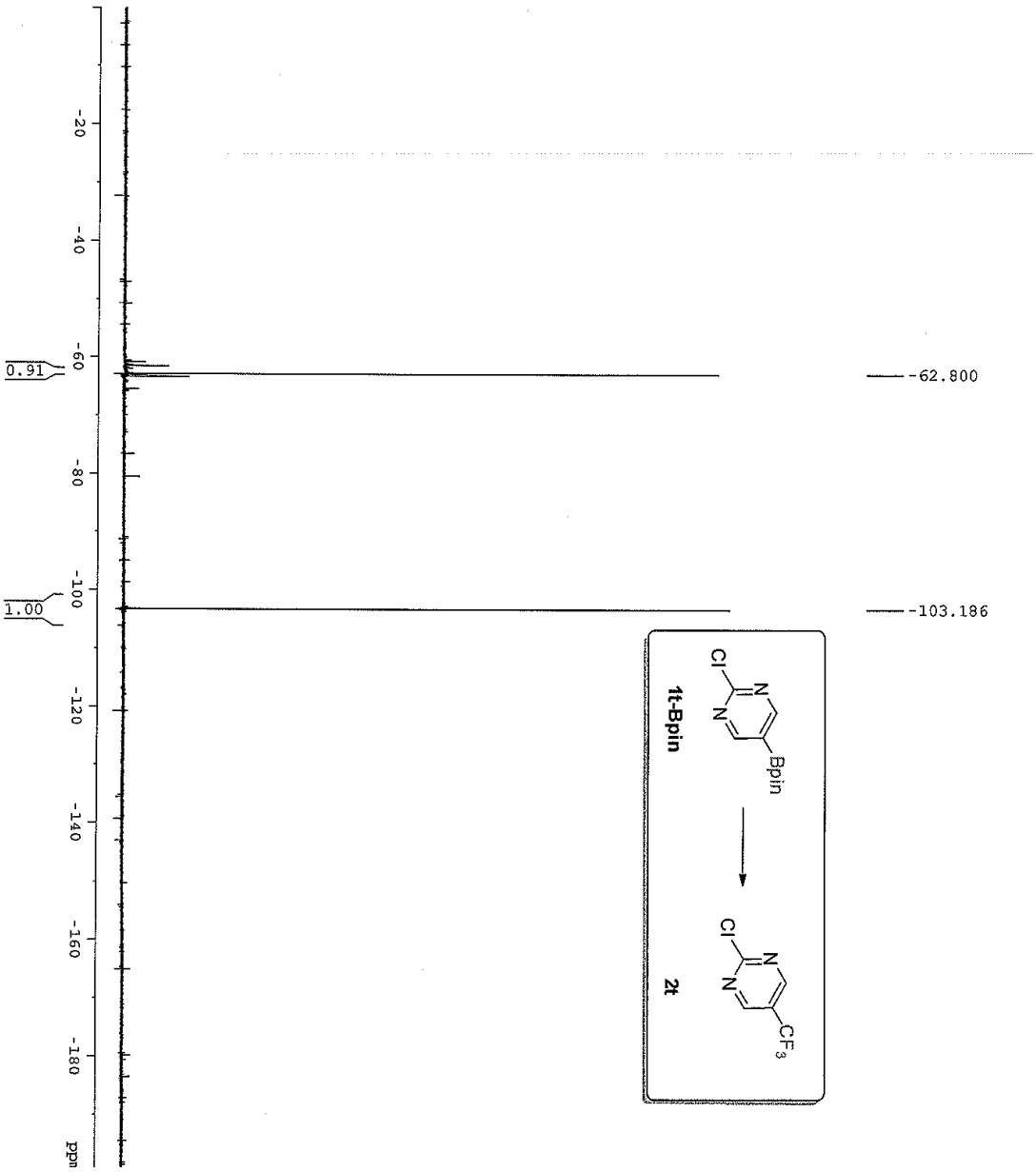
GC-MS of crude 2t



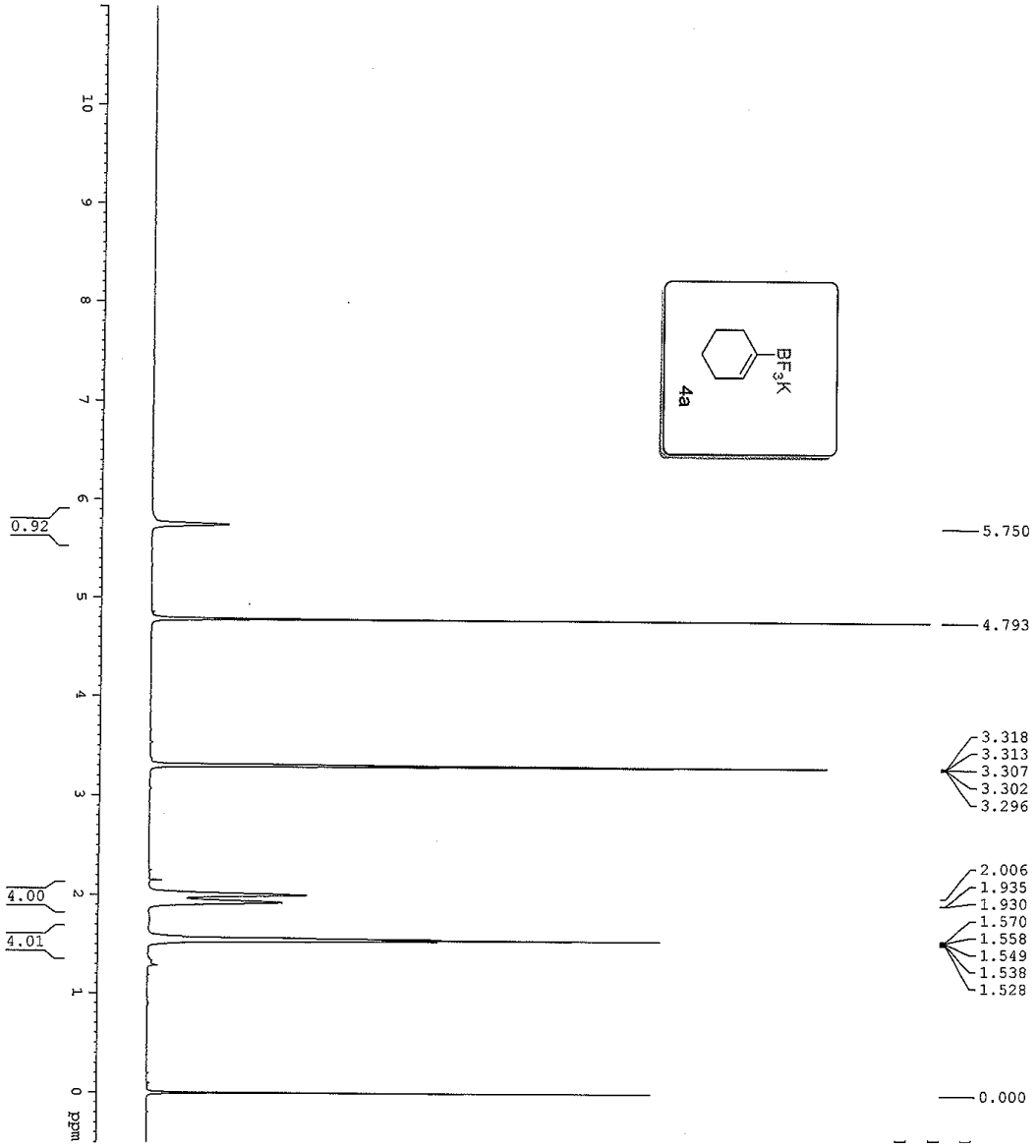
^{19}F NMR of crude 2t in $CDCl_3$



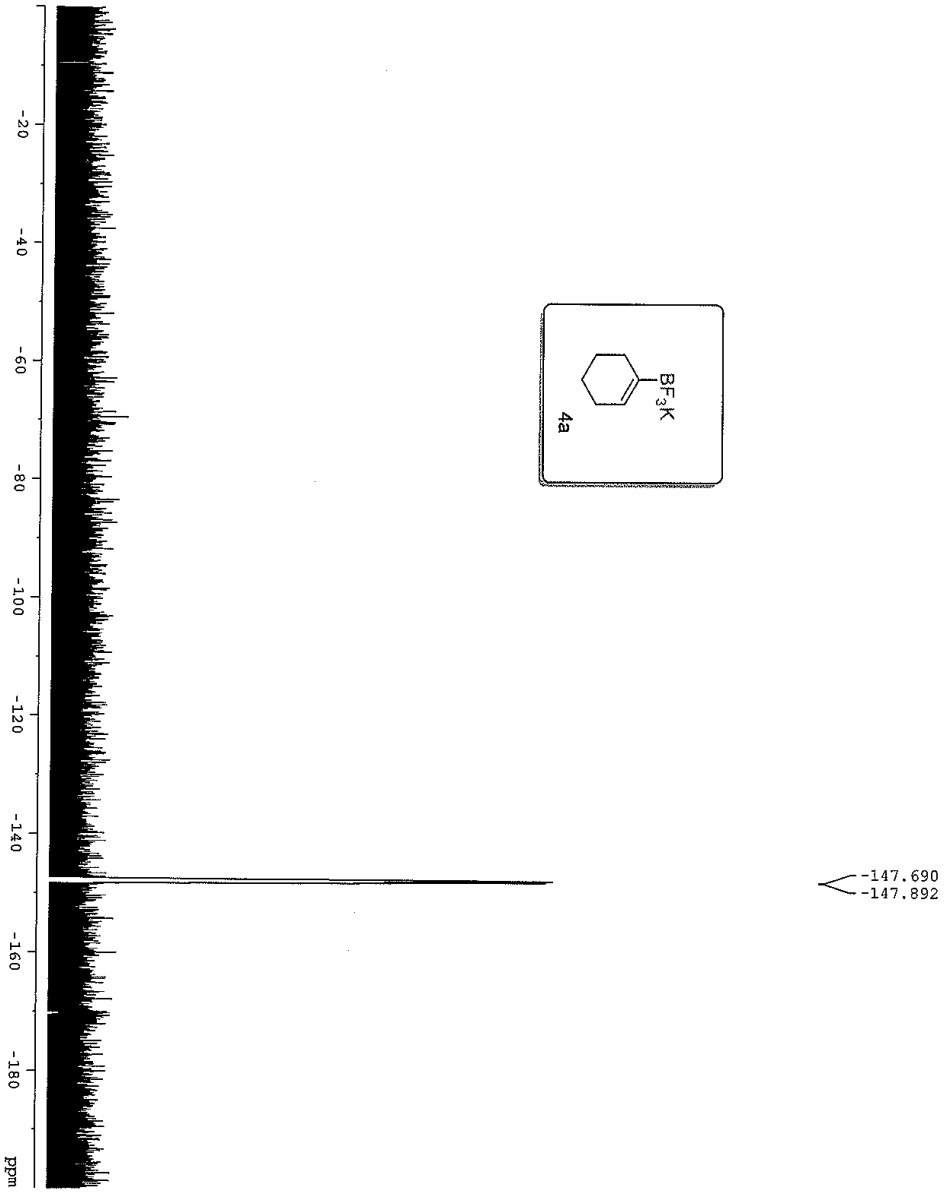
^{19}F NMR yield of compound 2t (0.91/(1×3)×100% = 30%) in $CDCl_3$



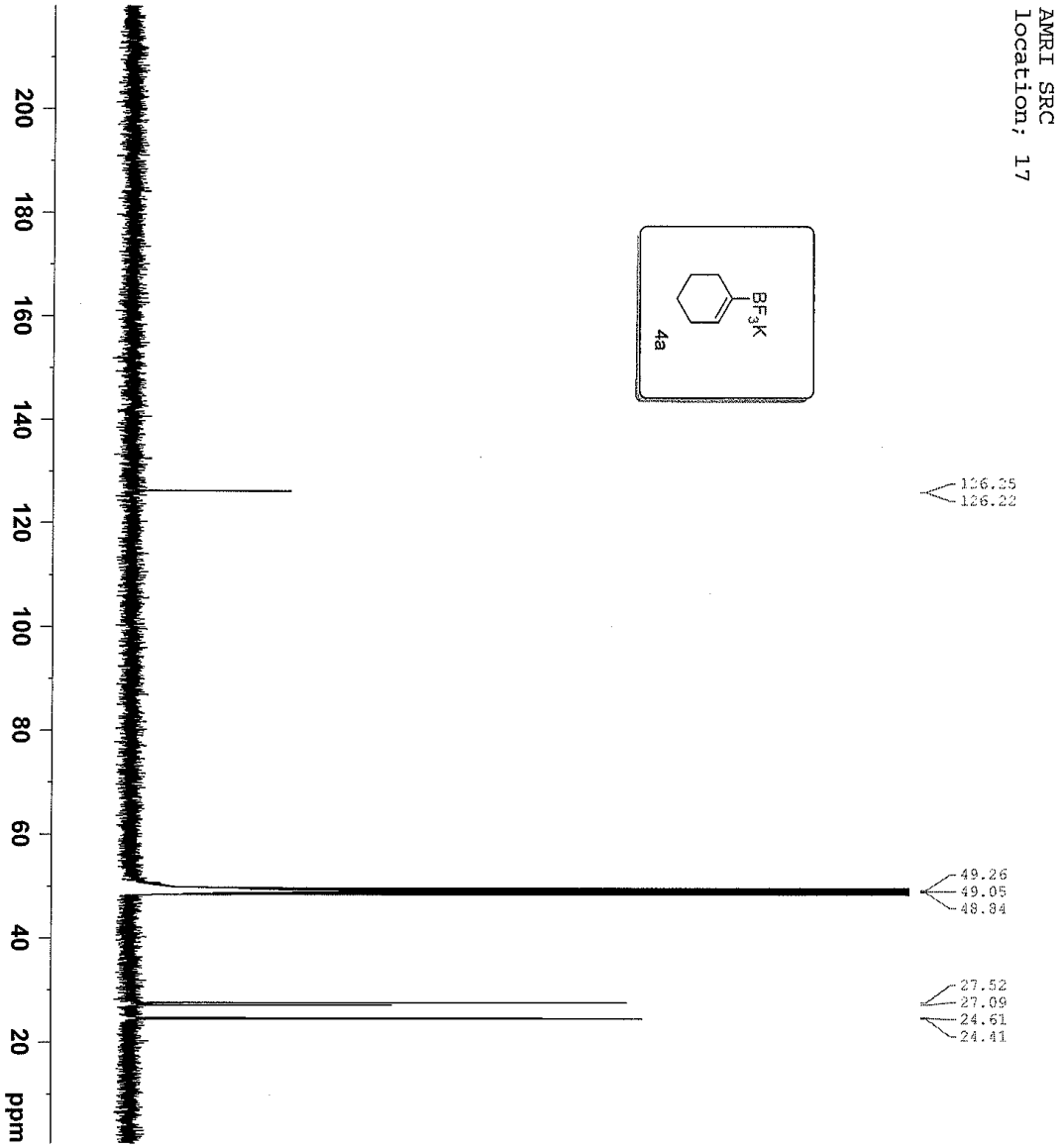
^{1}H NMR of 4a in CD_3OD



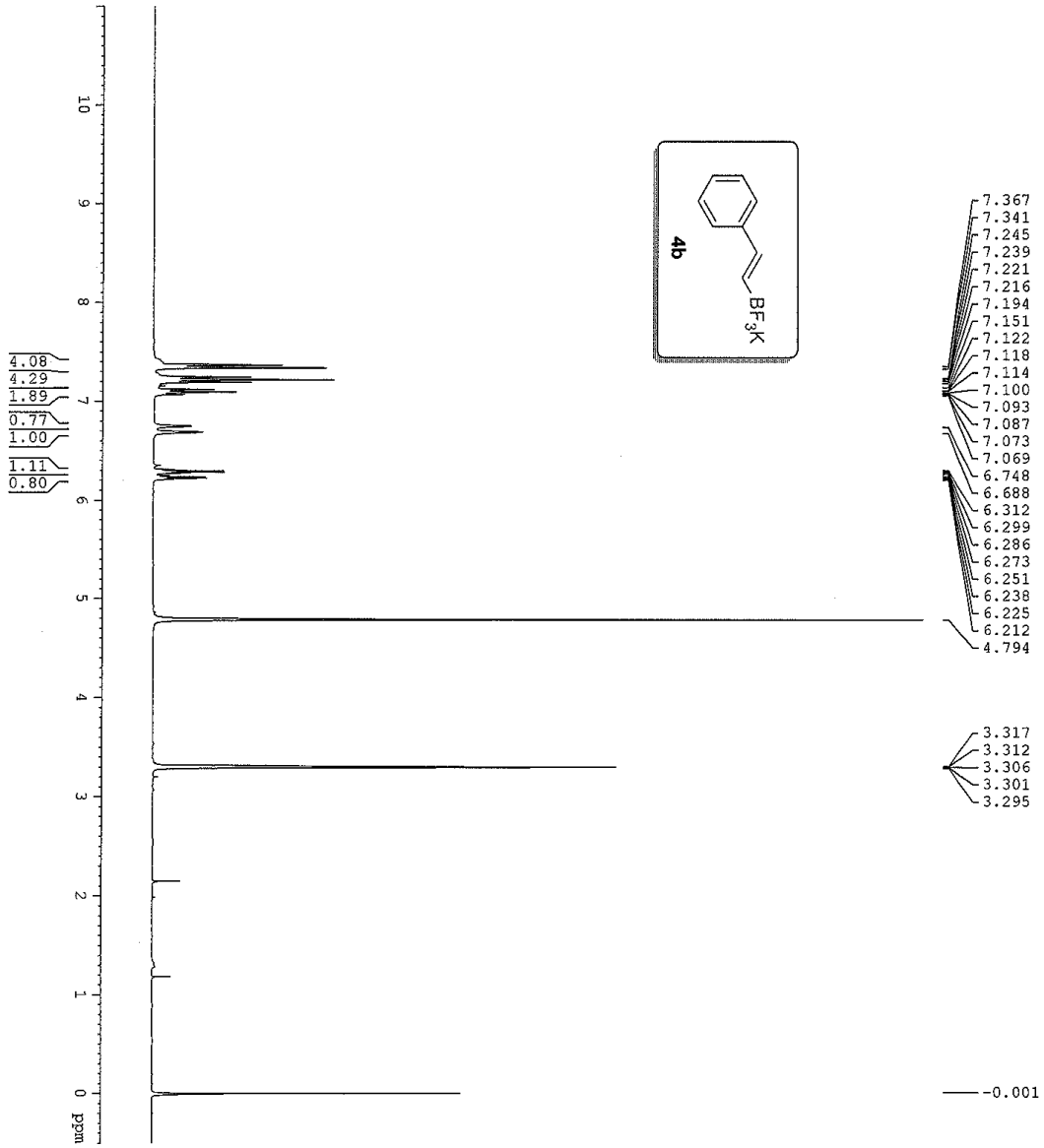
^{19}F NMR of 4a in CD_3OD



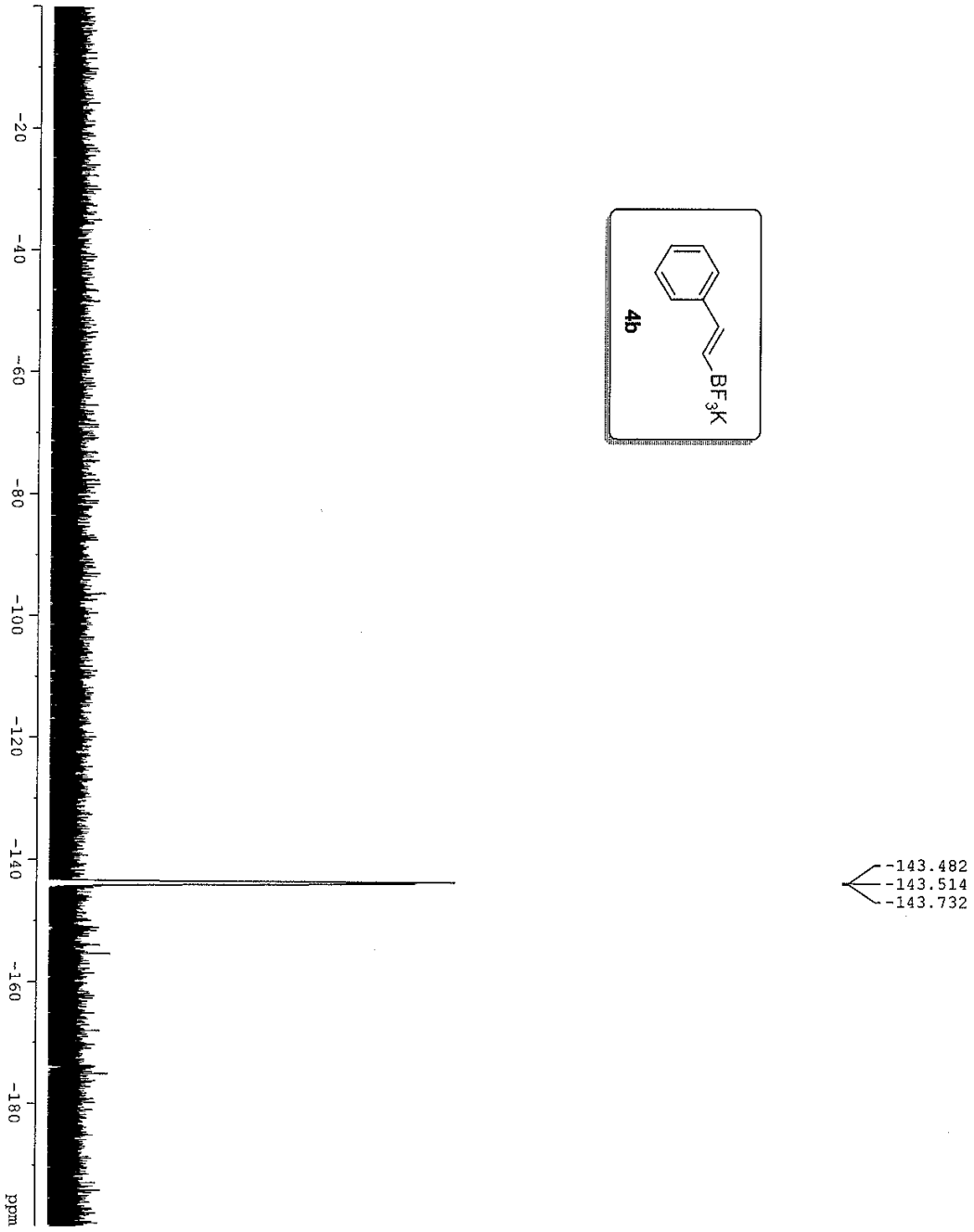
^{13}C NMR of 4a in CD_3OD



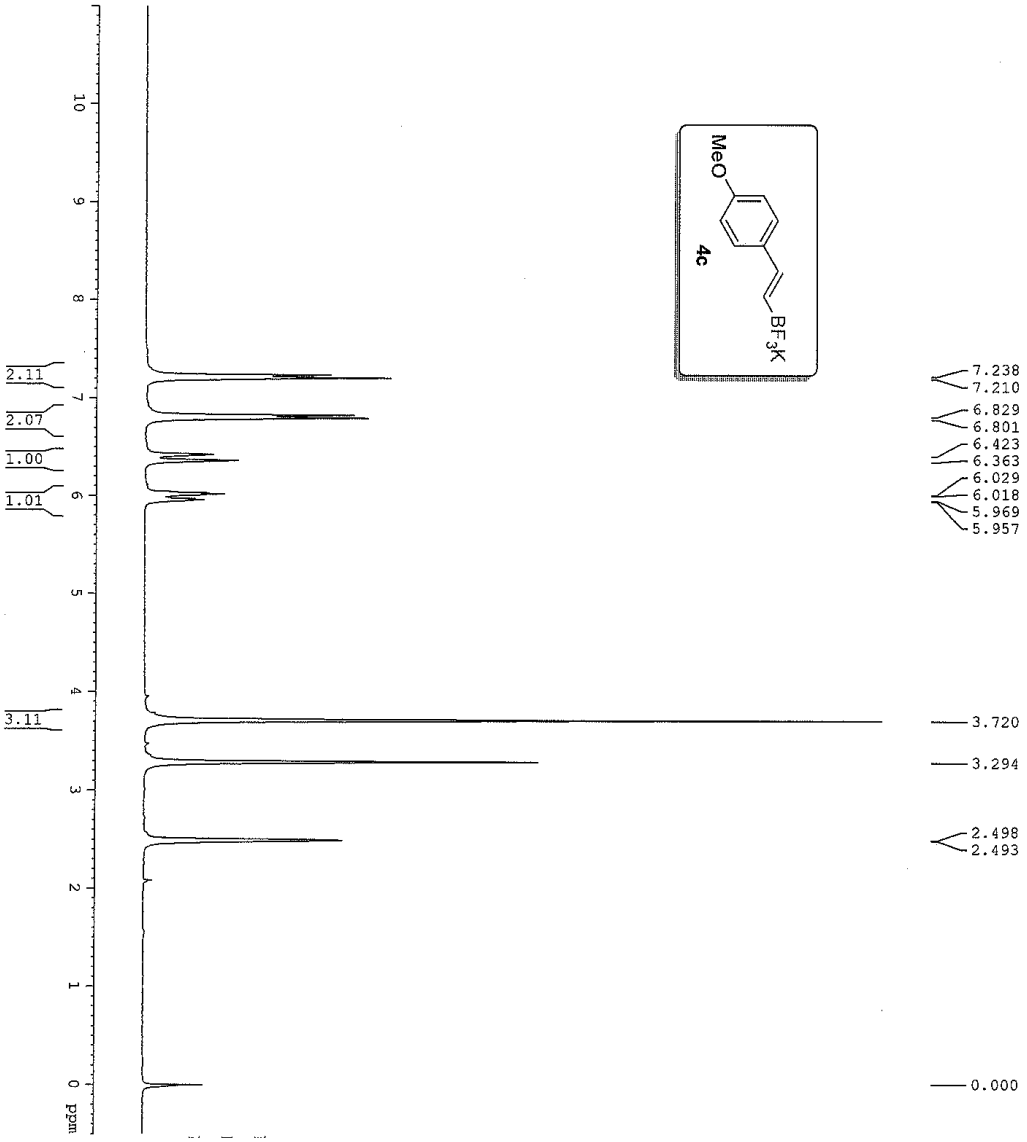
^{1}H NMR of 4b in CD_3OD



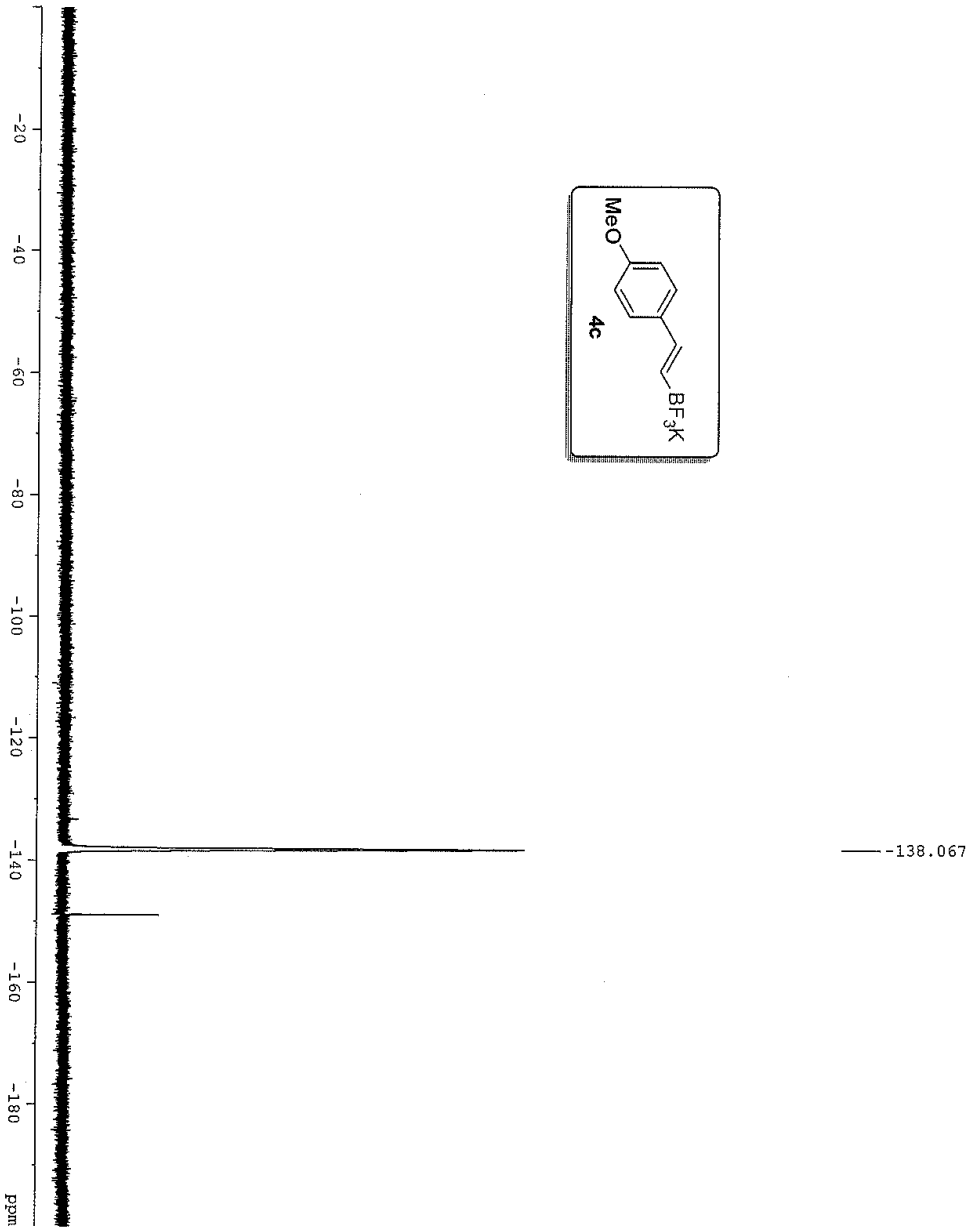
^{13}F NMR of 4b in CD_3OD



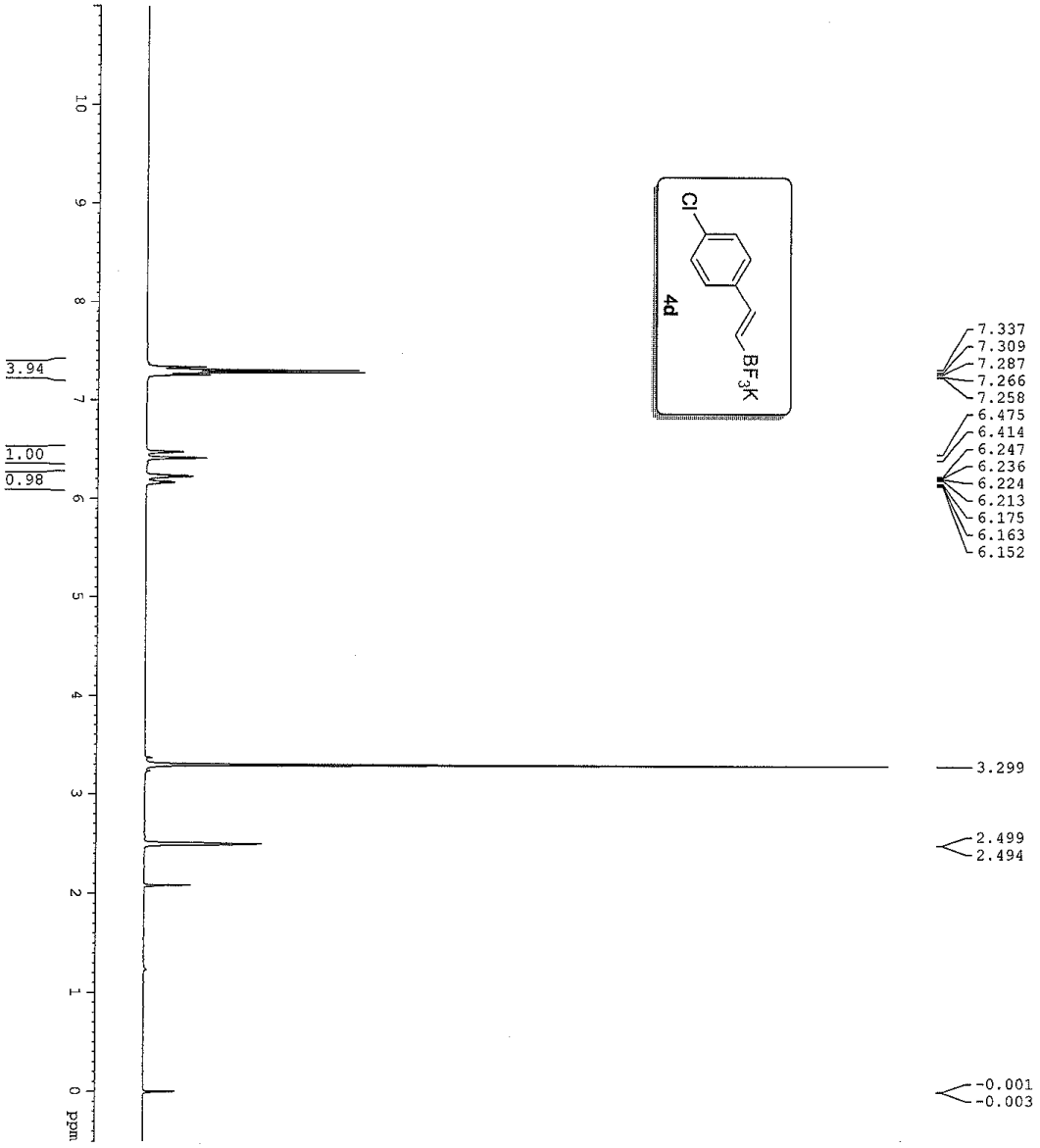
^{1}H NMR of 4c in DMSO-d_6



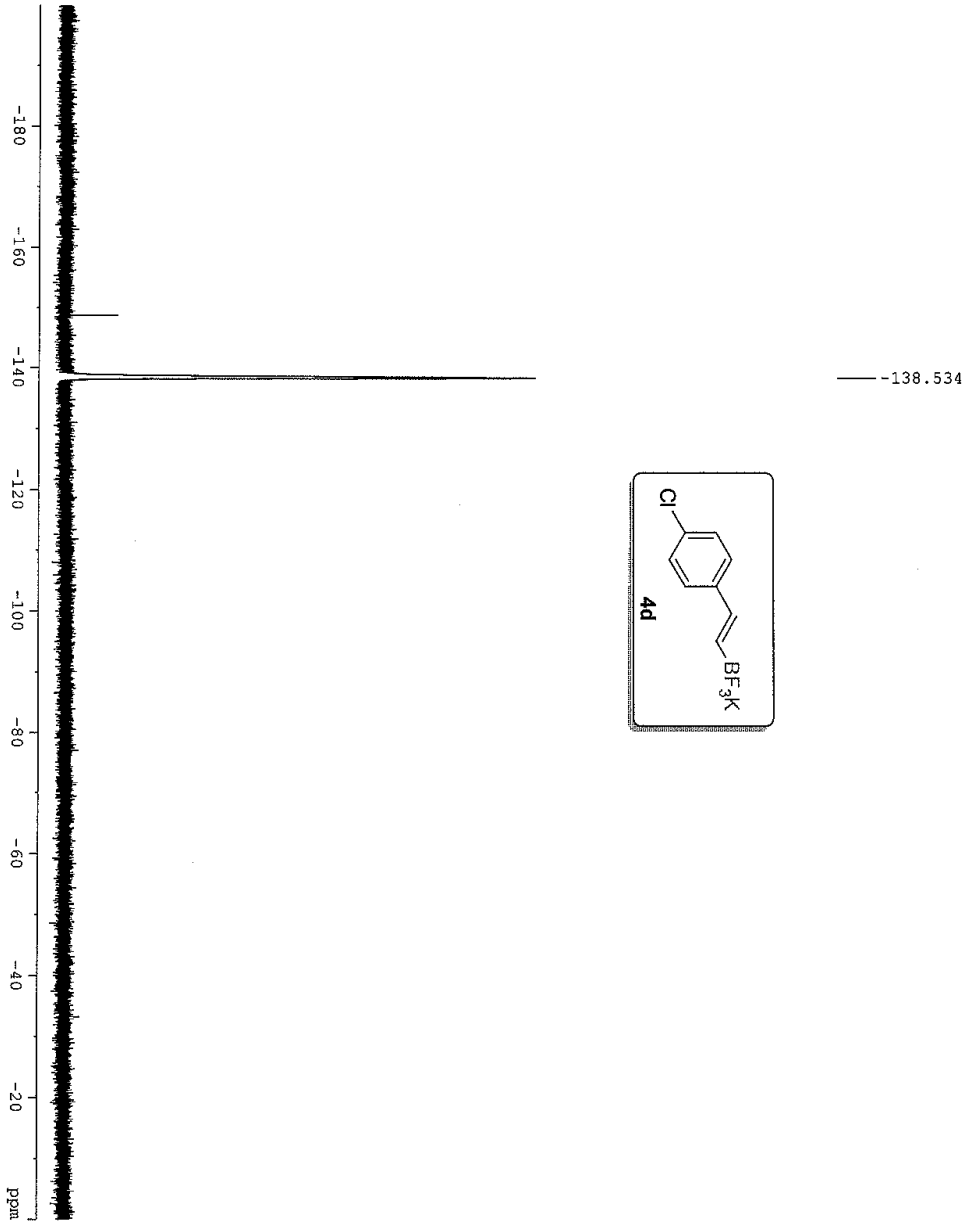
^{19}F NMR of 4c in DMSO-d_6



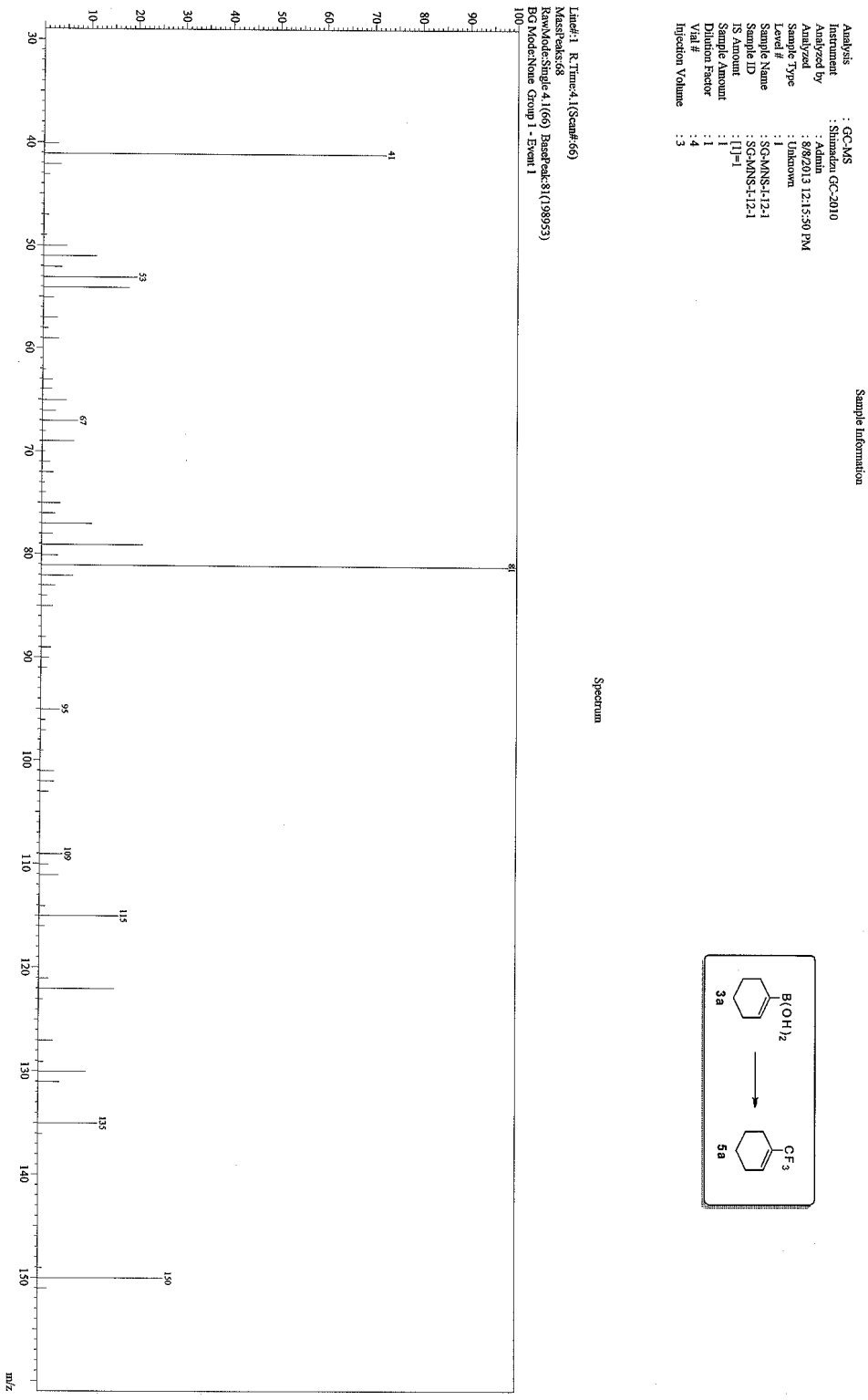
^{1}H NMR of 4d in DMSO-d_6



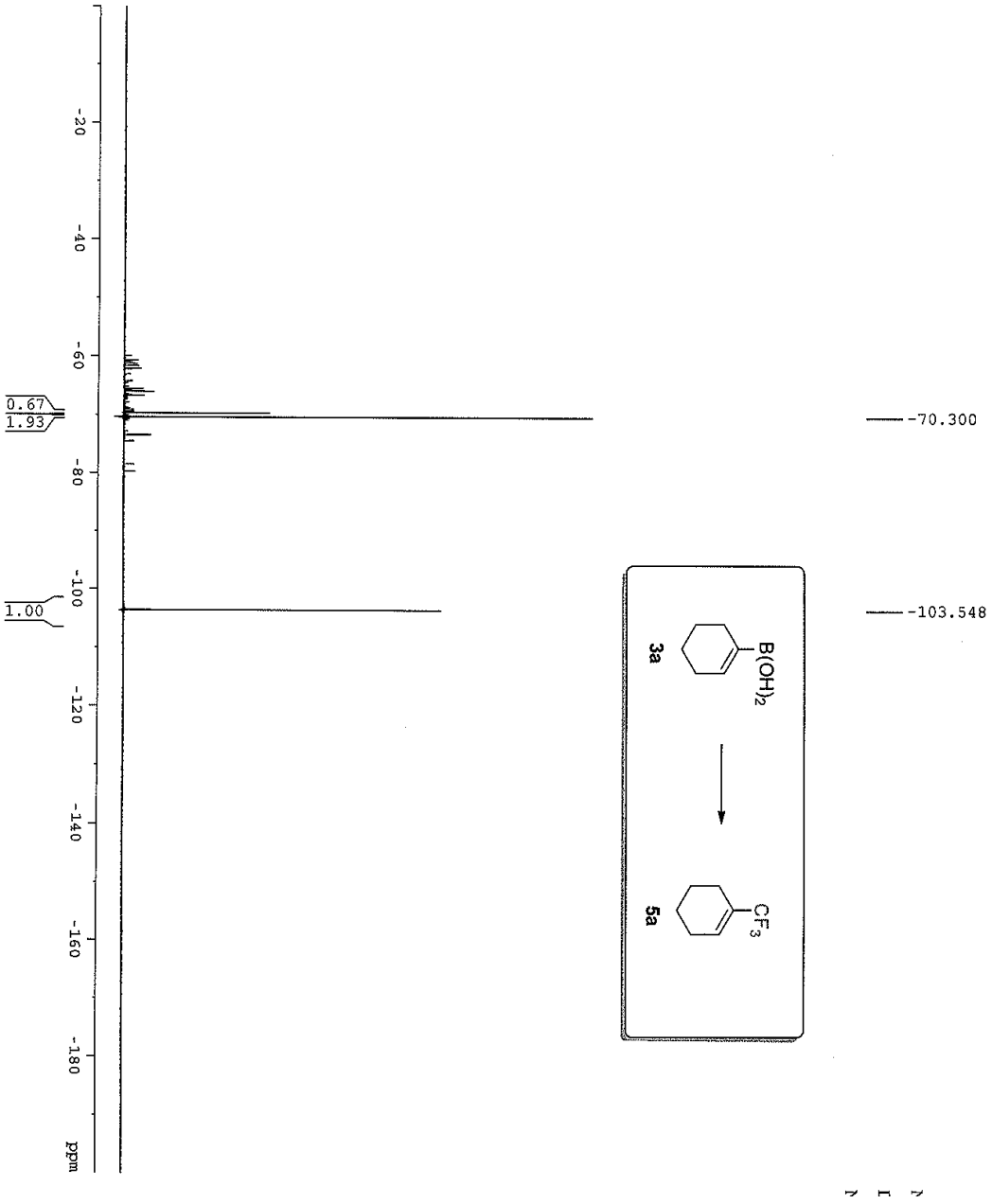
^{19}F NMR of 4d in DMSO-d_6



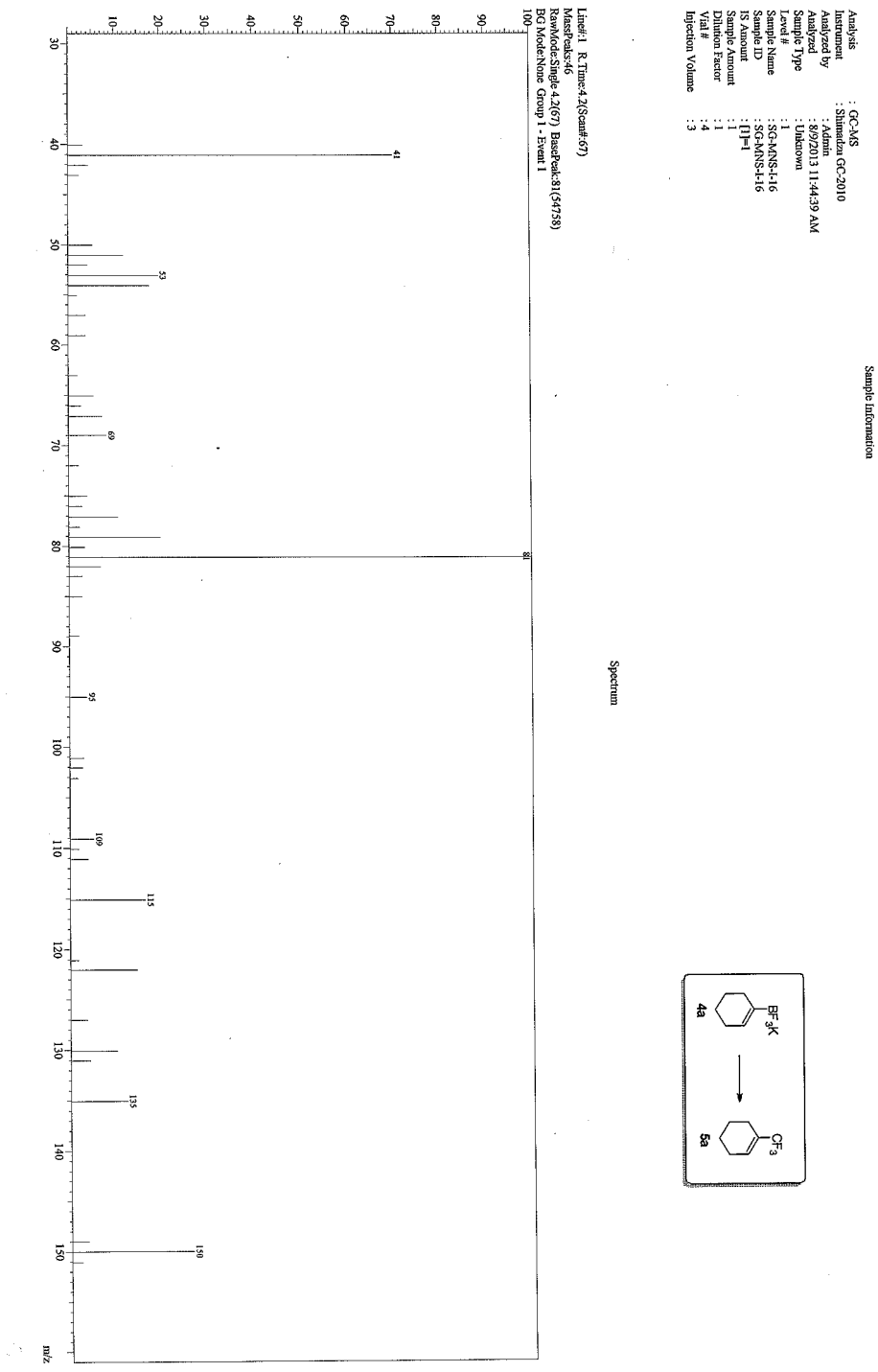
GC-MS of crude 5a



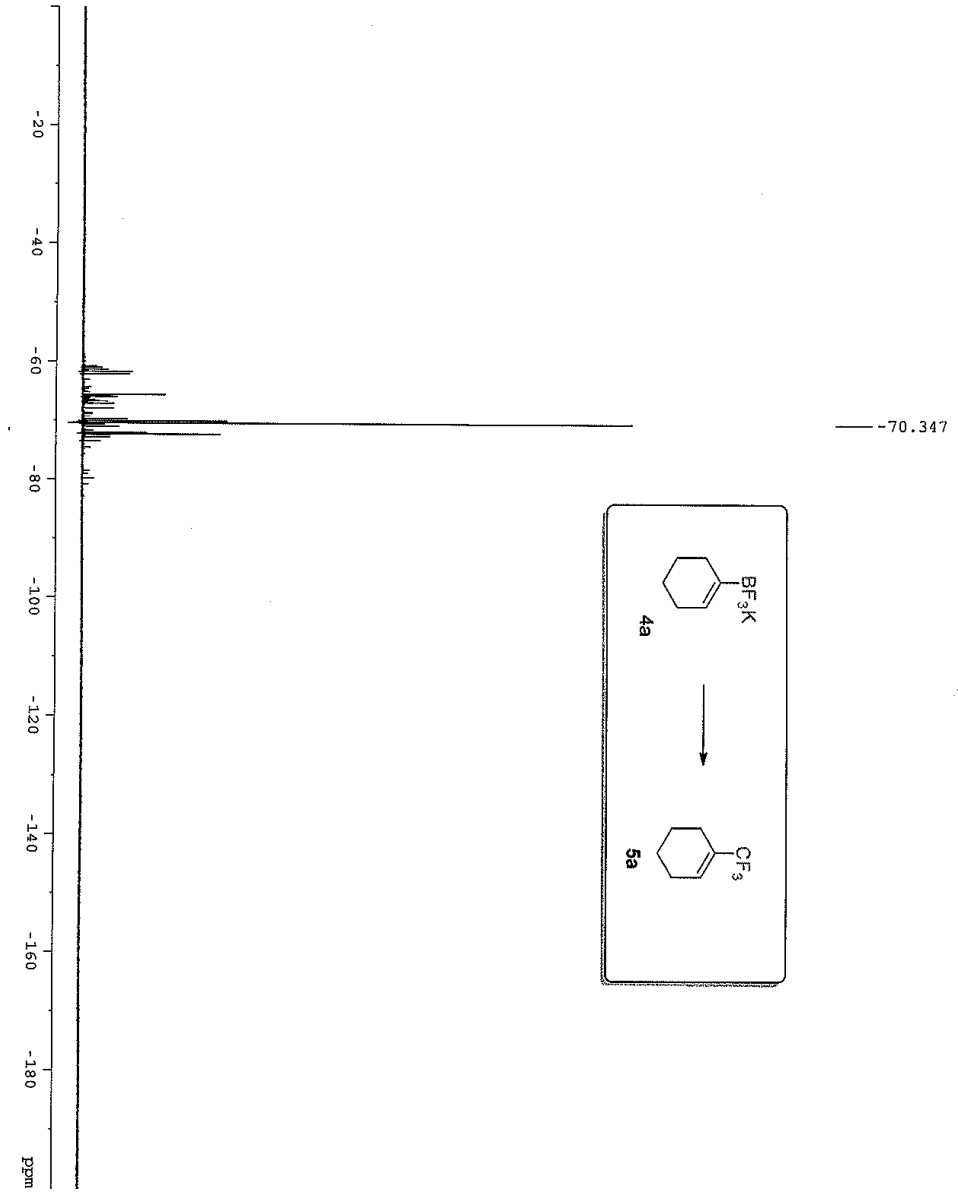
^{19}F NMR yield of compound 5a (1.93/(1×3)×100% = 64%) in $CDCl_3$



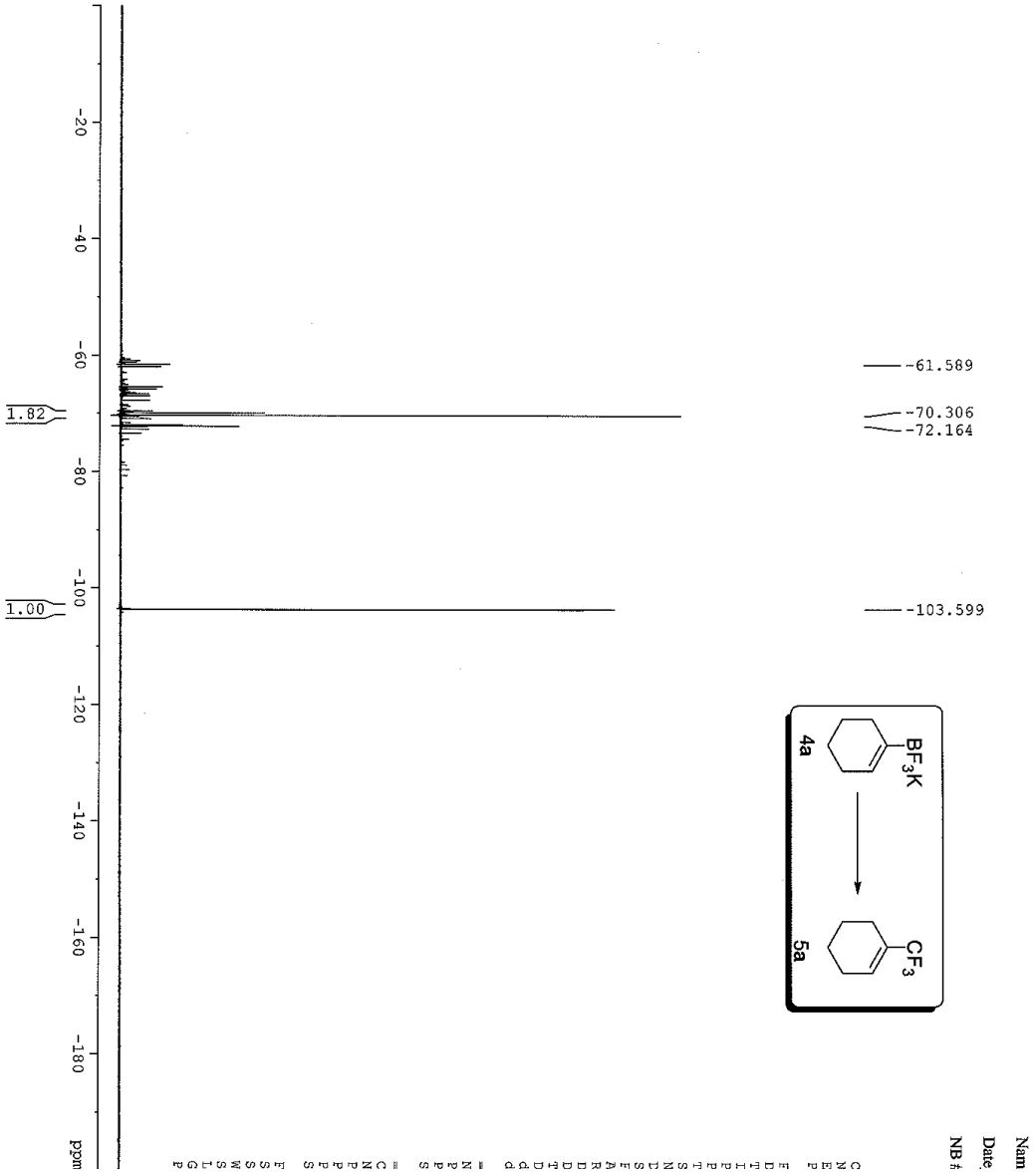
GC-MS of crude 5a



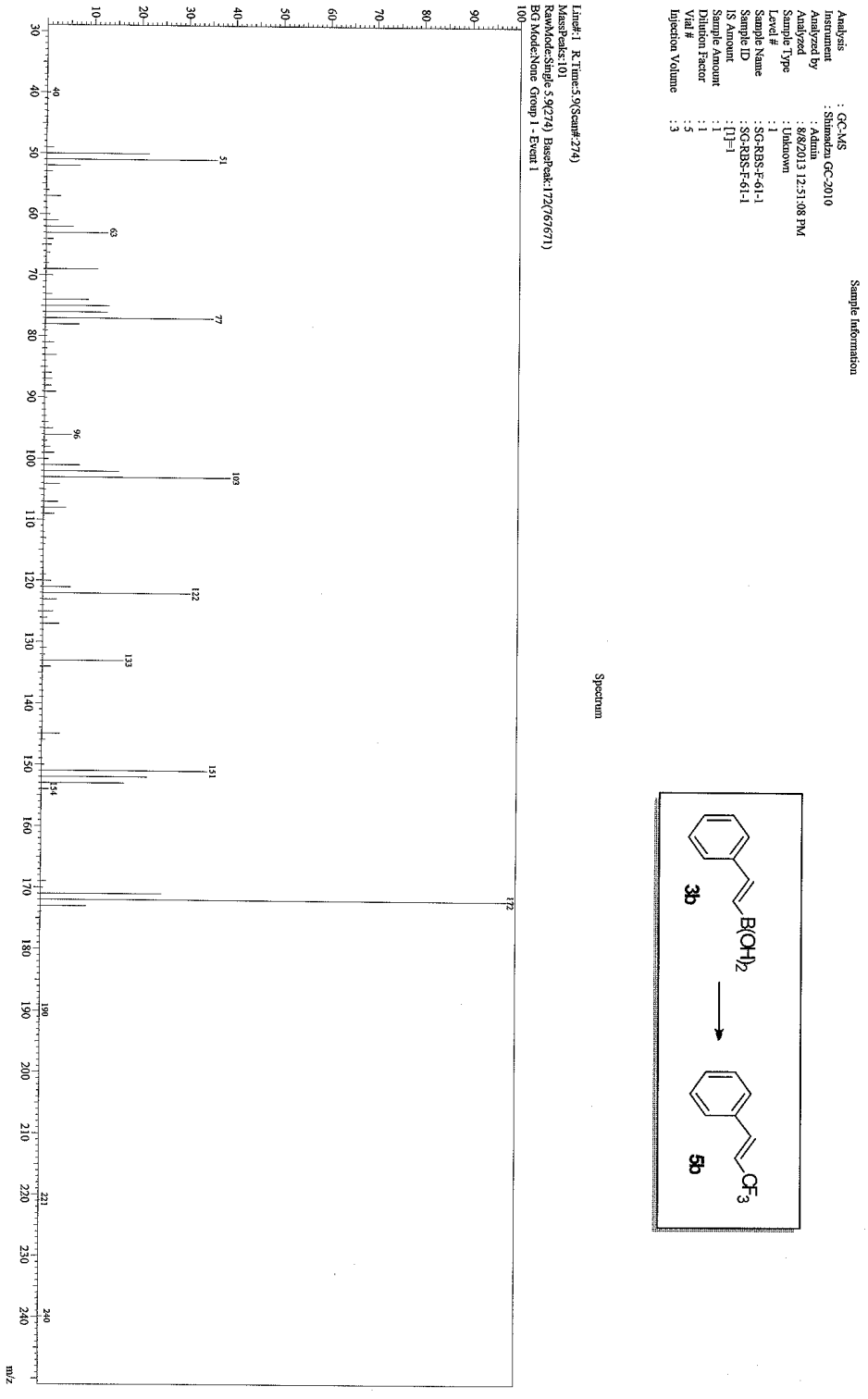
^{19}F NMR of crude 5a in $CDCl_3$



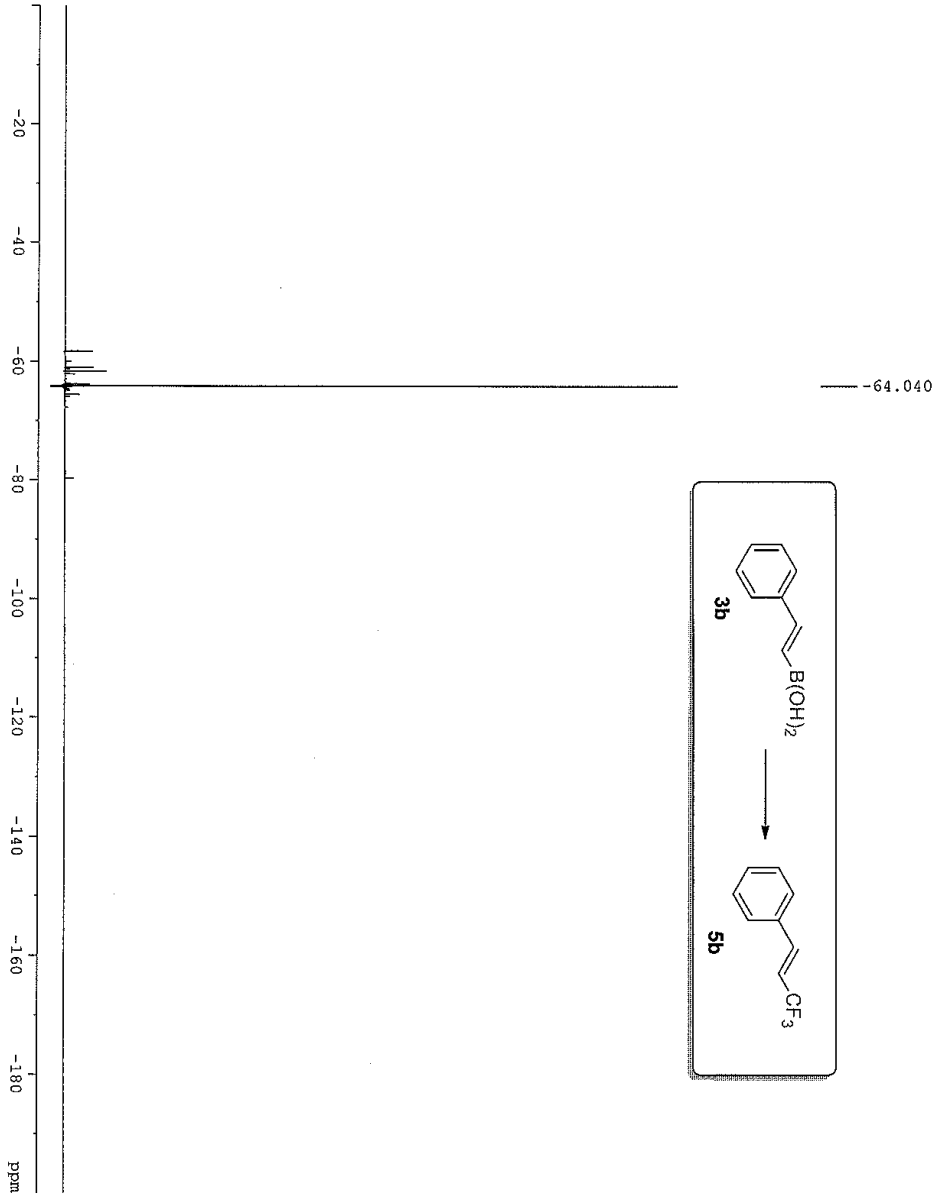
^{19}F NMR yield of compound 2h (1.82/(1×3)×100% = 60%) in $CDCl_3$



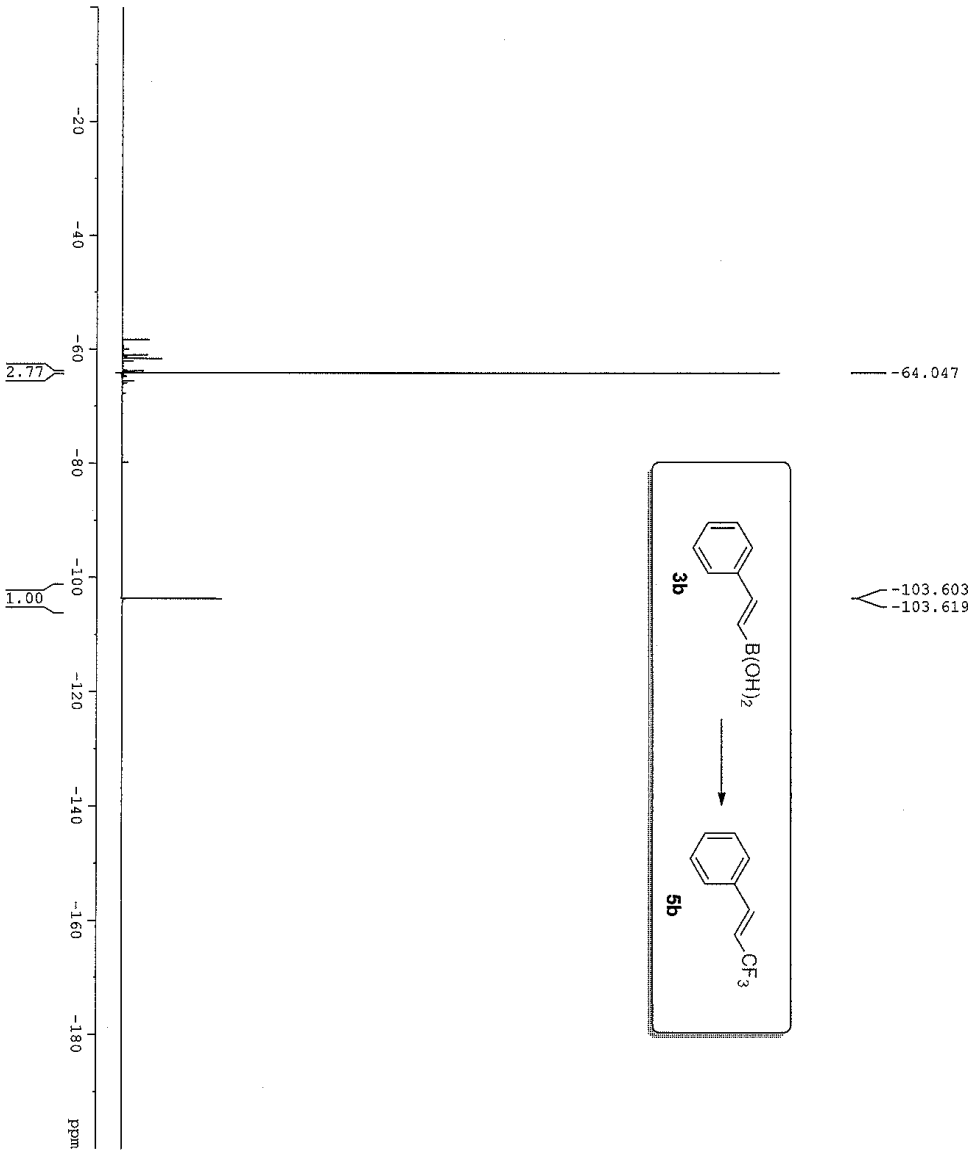
GC-MS of crude 5b



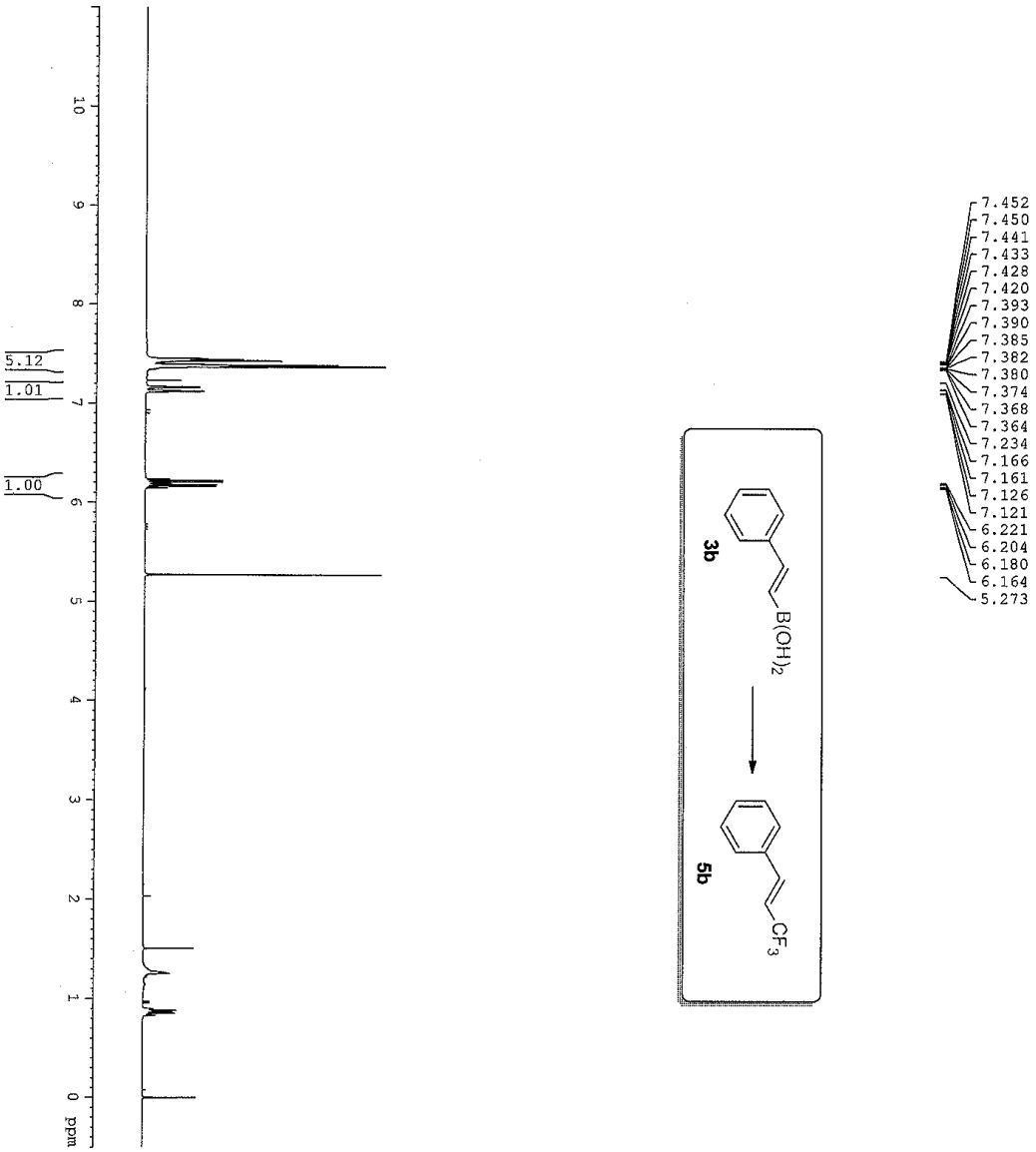
^{19}F NMR of crude 5b in $CDCl_3$



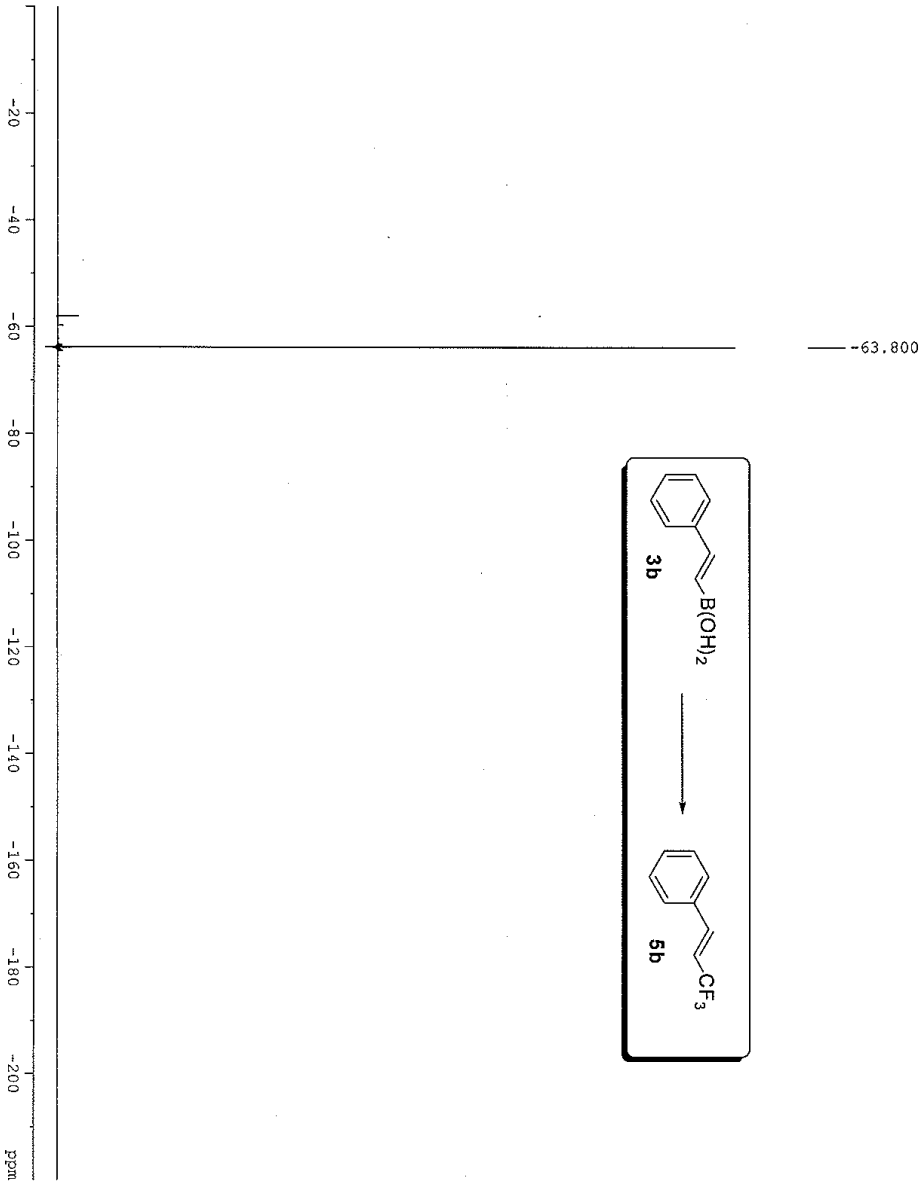
^{19}F NMR yield of compound 5b (2.77/(1×3)×100% = 92%) in $CDCl_3$



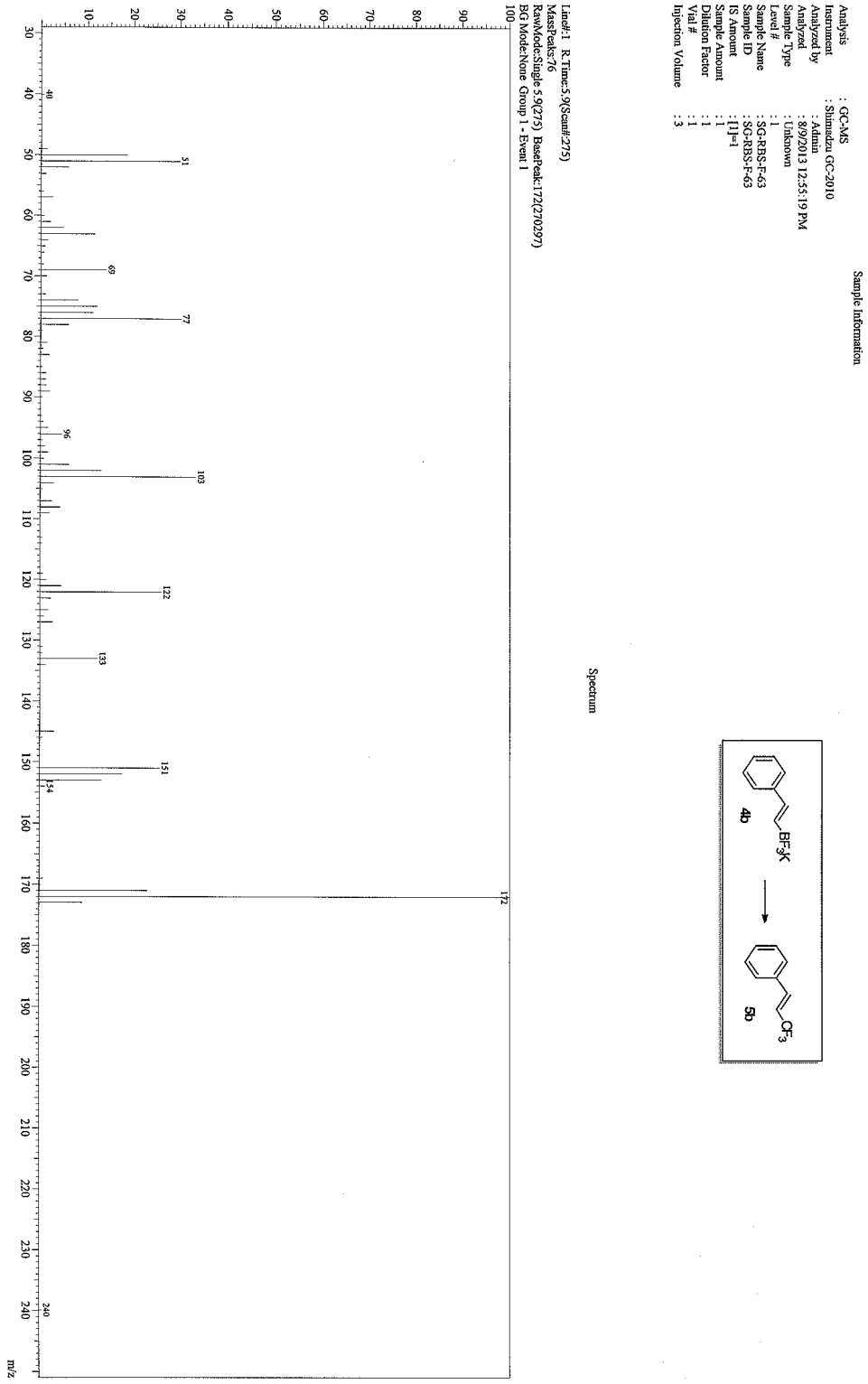
^{1}H NMR of 5b in $CDCl_3$



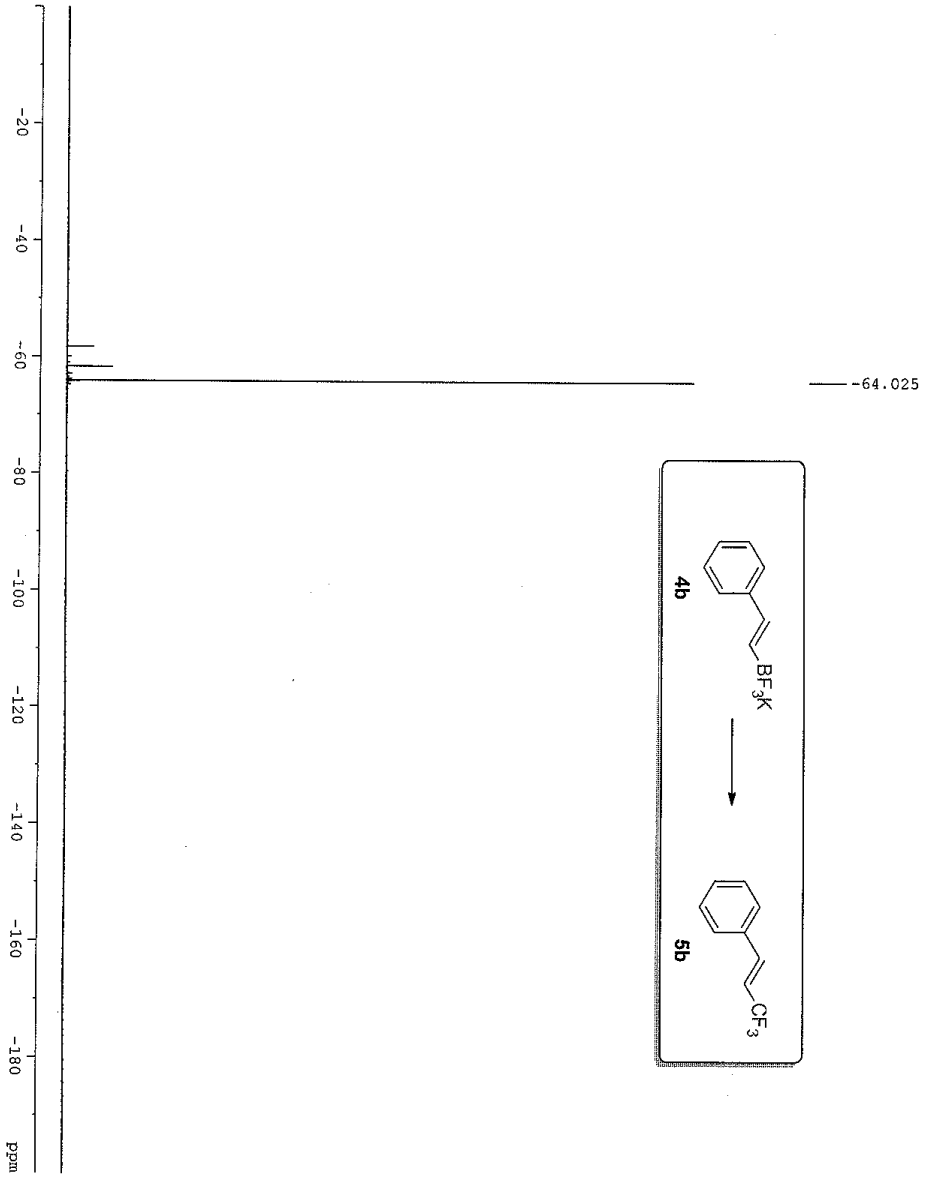
^{19}F NMR of isolated 5b in $CDCl_3$



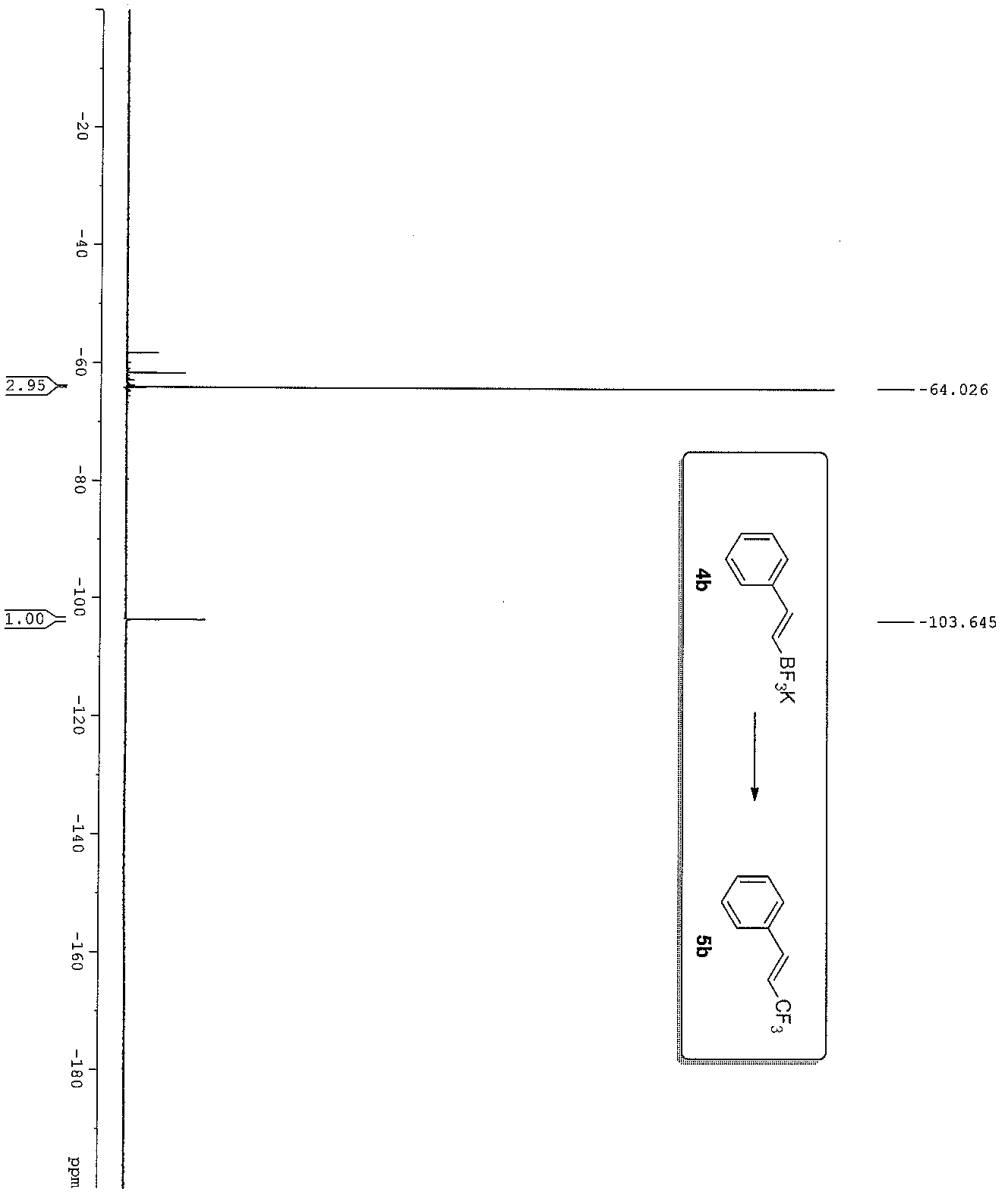
GC-MS of crude 5b



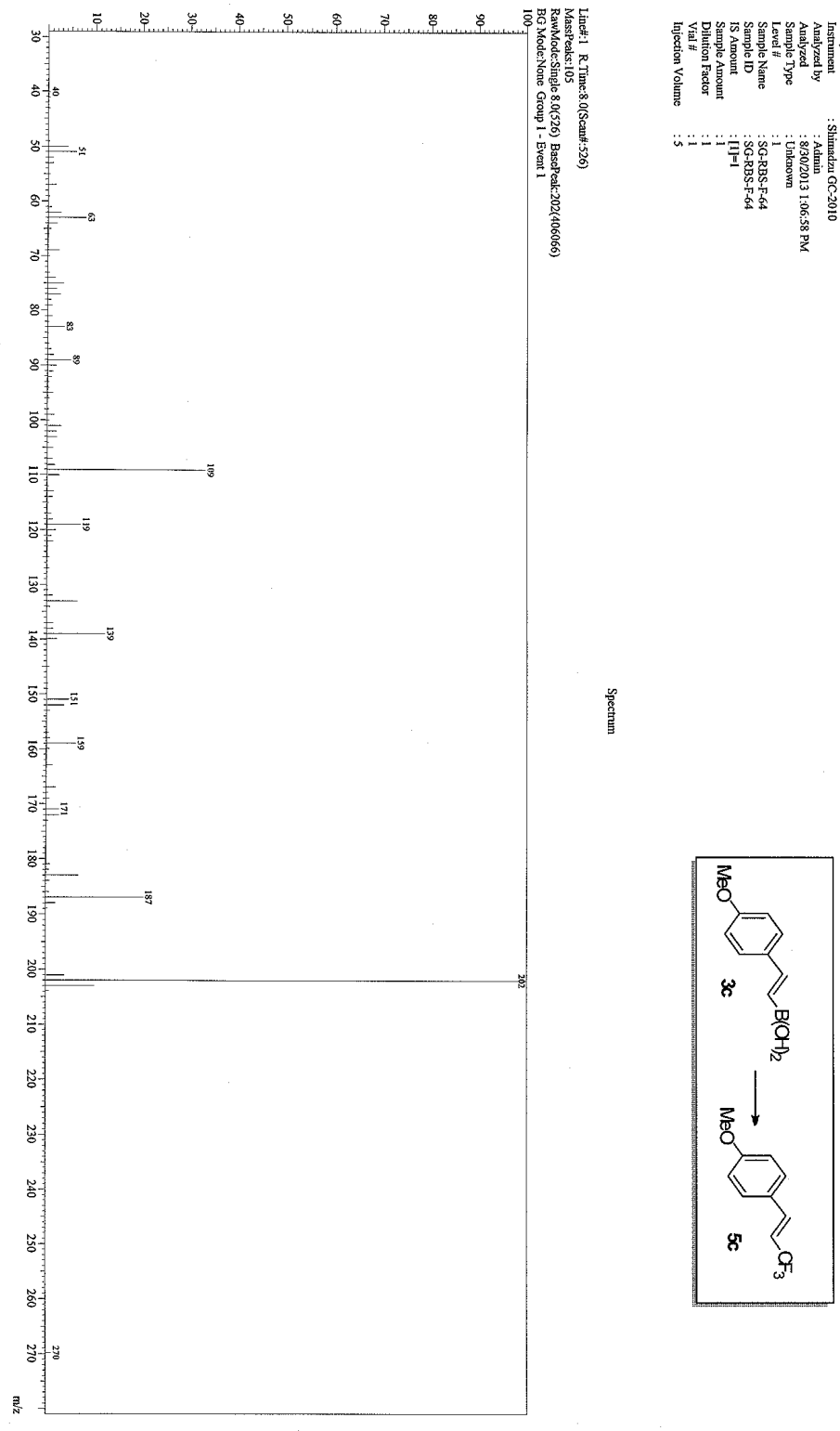
^{19}F NMR of crude 5b in $CDCl_3$



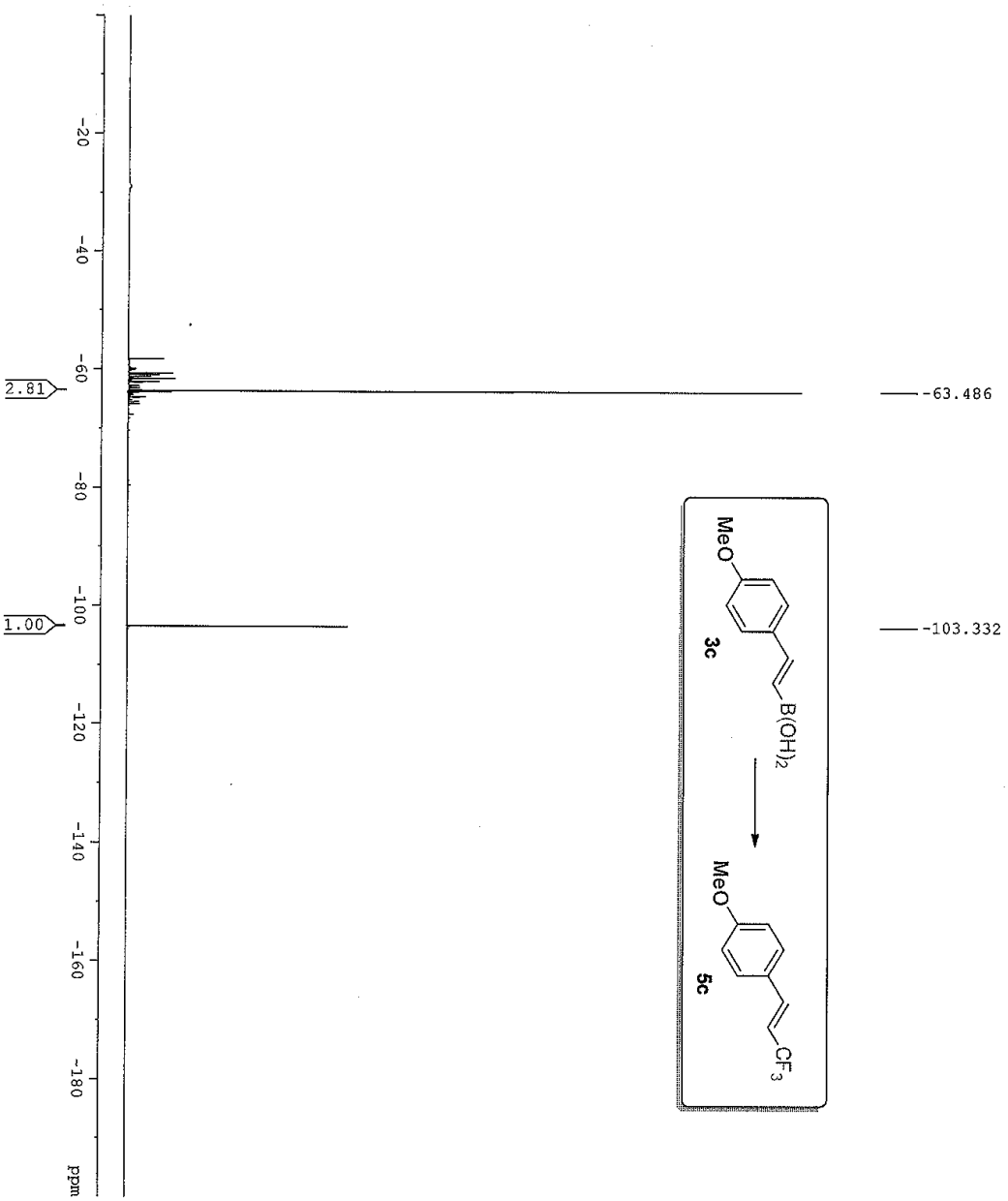
^{19}F NMR yield of compound 5b (2.95/(1×3)×100% = 98%) in $CDCl_3$



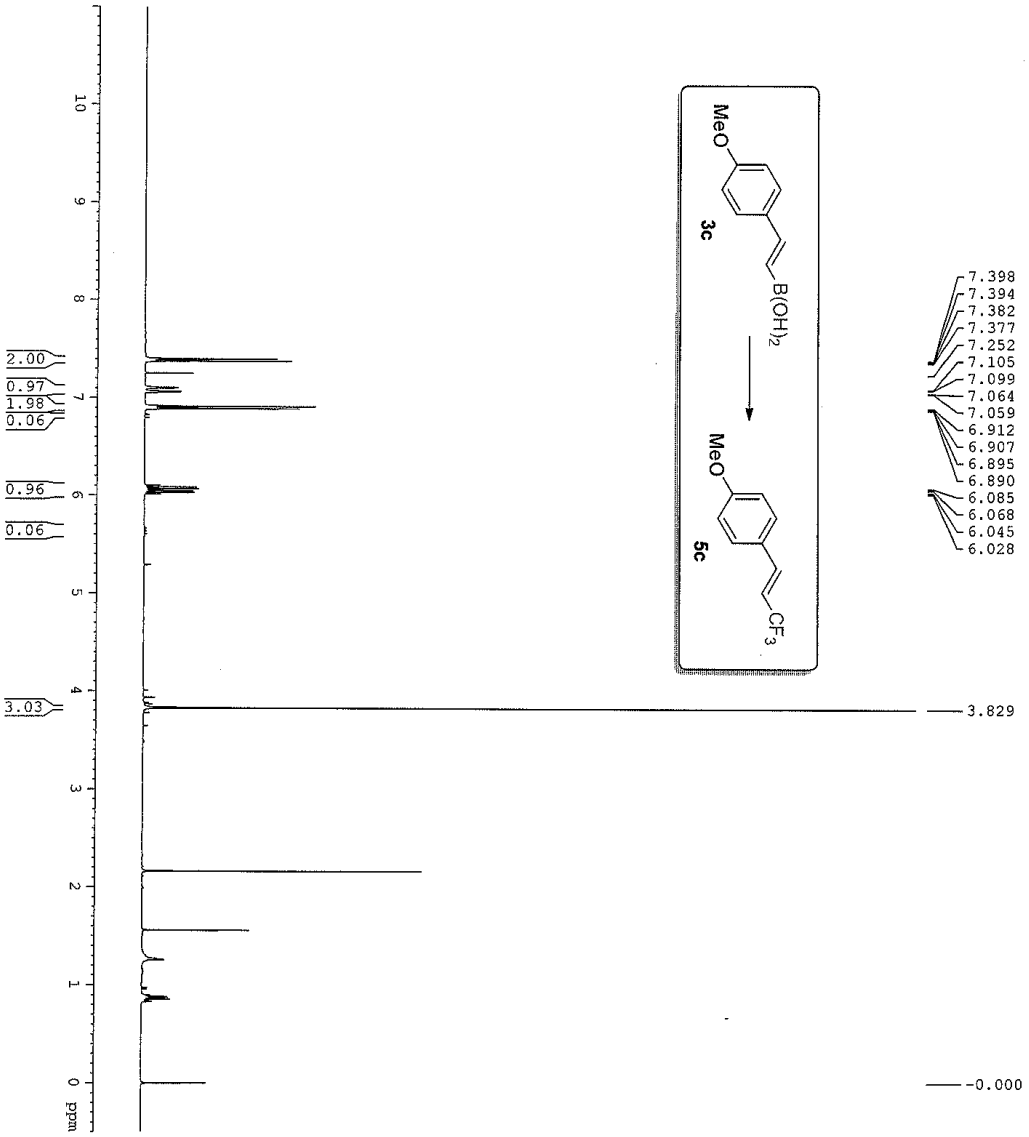
GC-MS of crude 5c



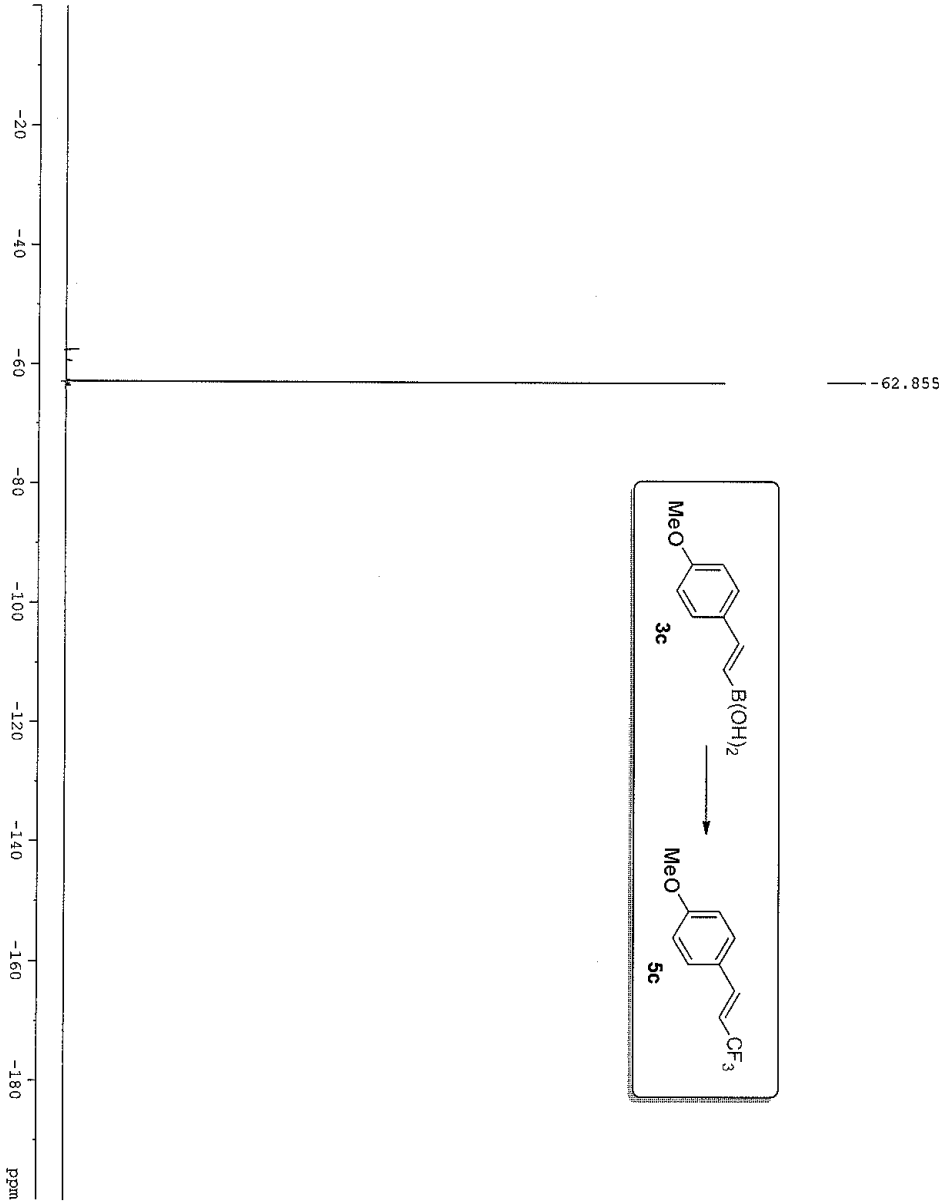
^{19}F NMR yield of compound 5c (2.81/(1×3)×100% = 93%) in $CDCl_3$



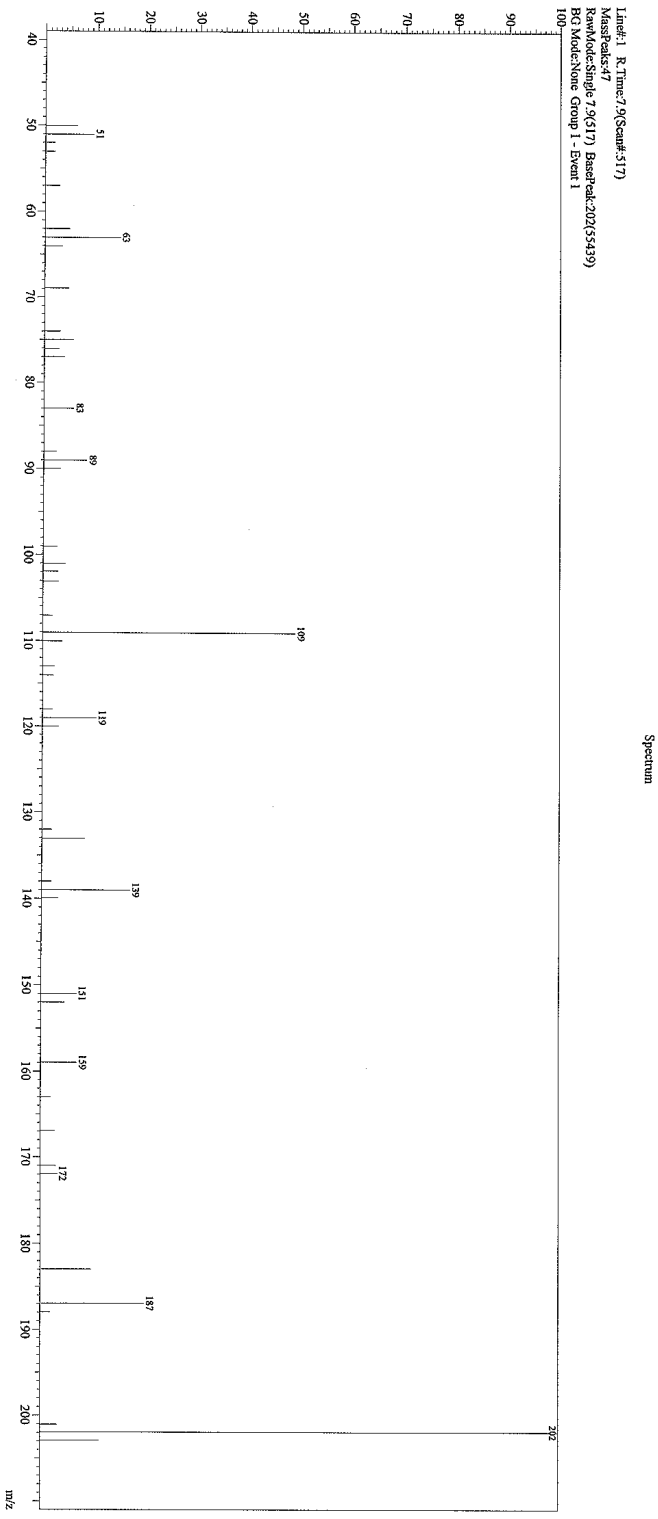
^{1}H NMR of 5c in $CDCl_3$

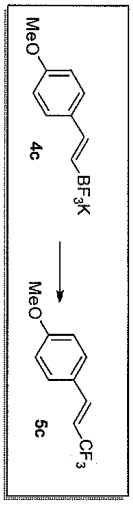


^{19}F NMR of isolated 5c in $CDCl_3$

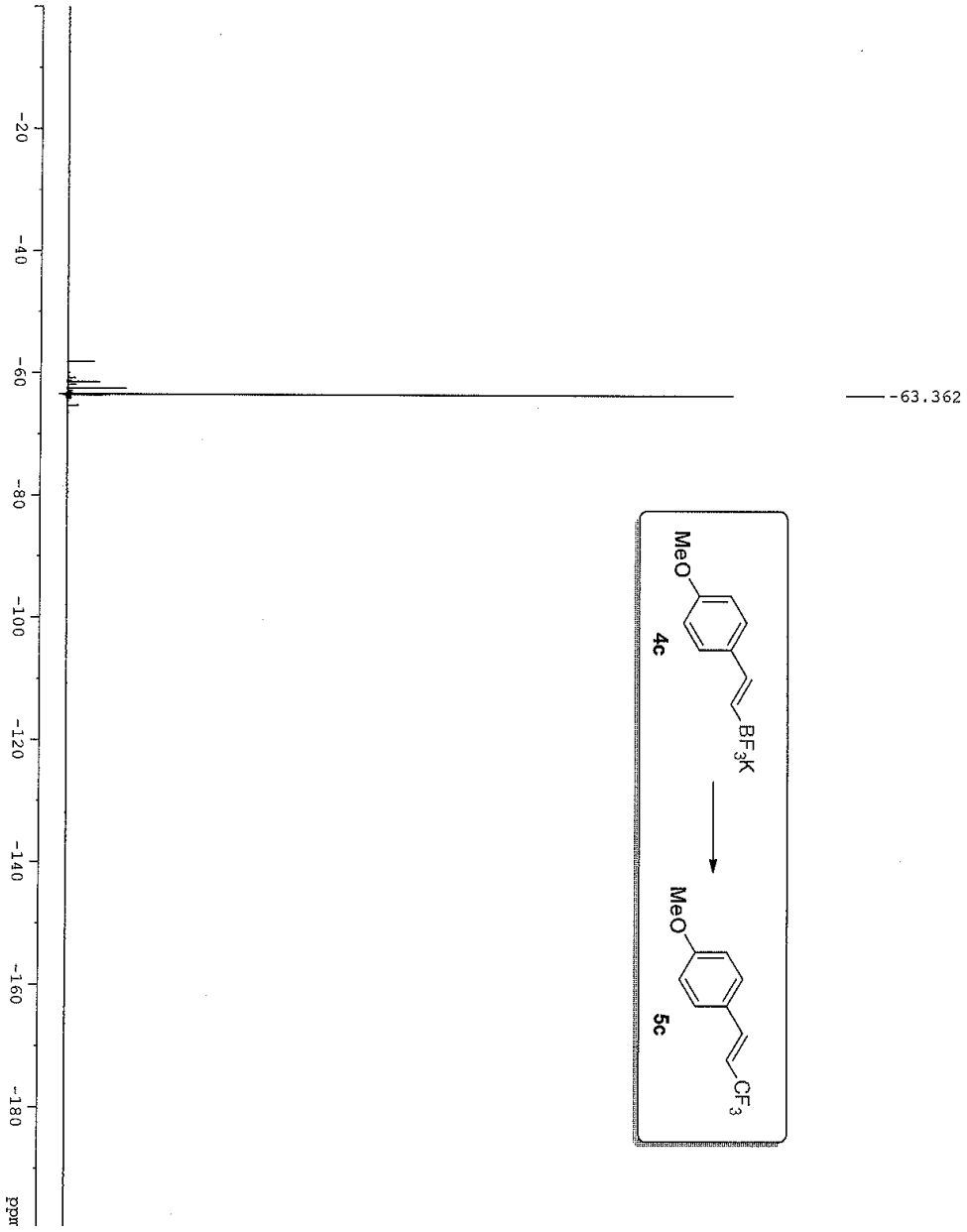


GC-MS of crude 5c

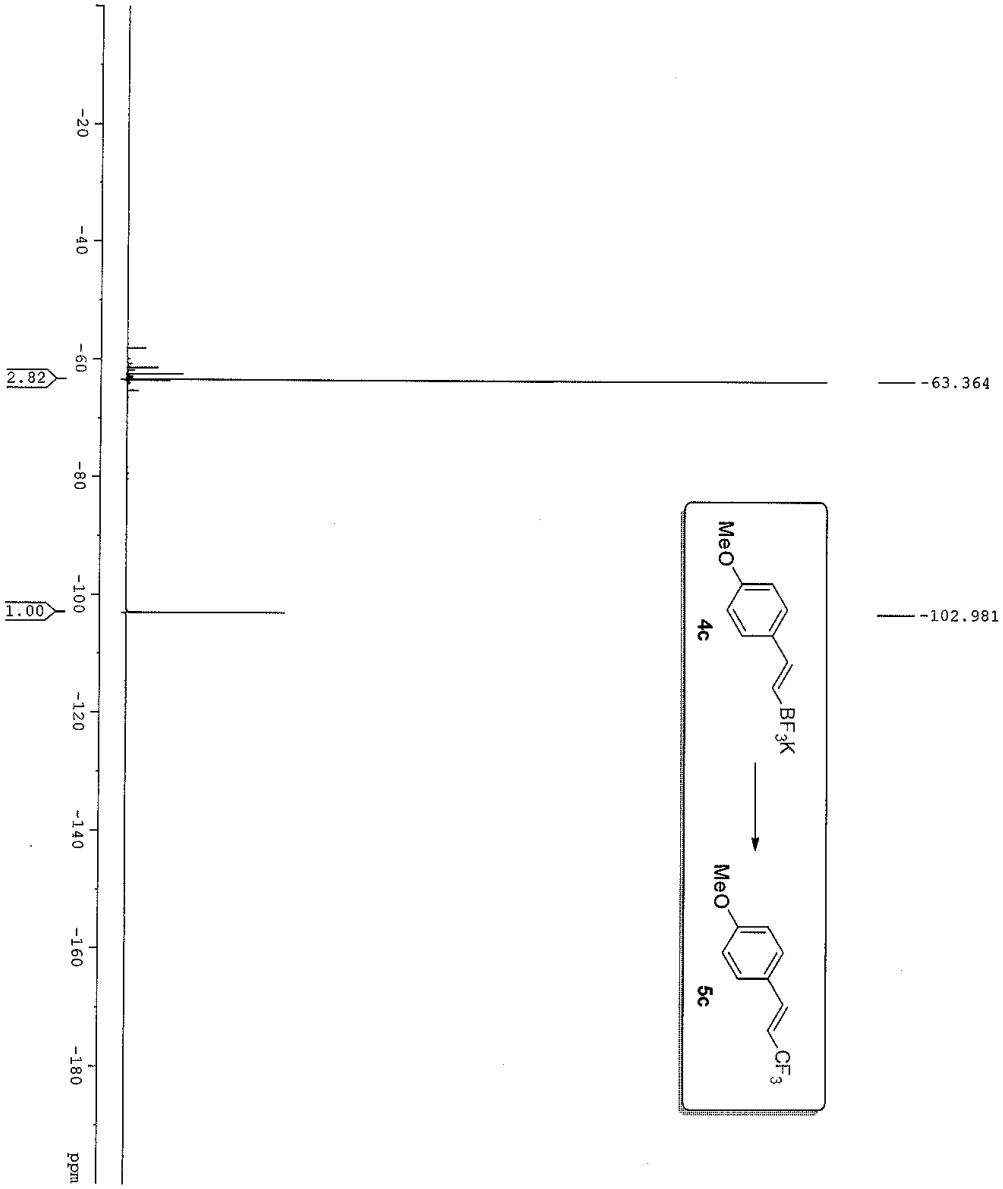




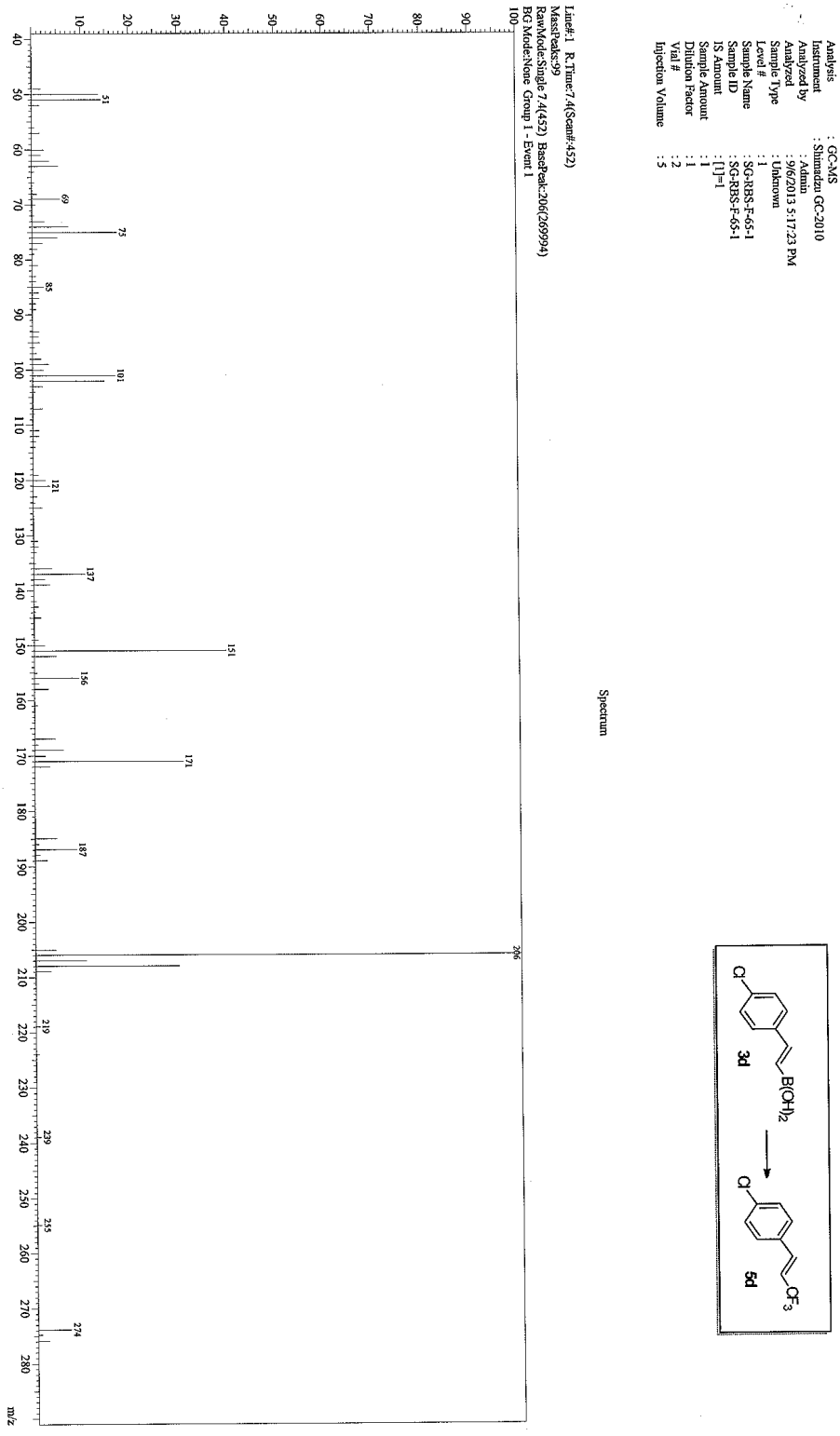
^{19}F NMR of crude 5c in $CDCl_3$



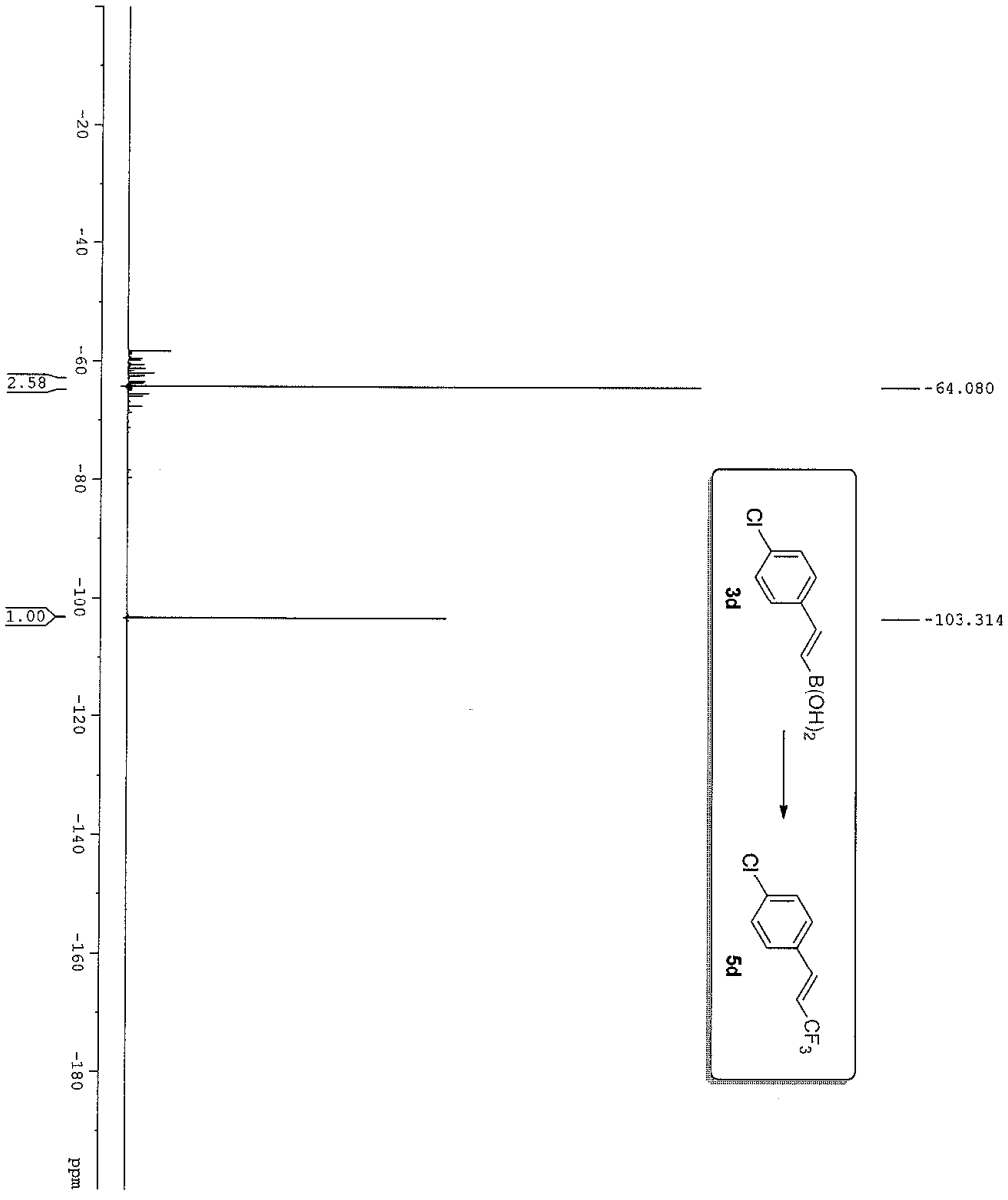
^{19}F NMR yield of compound 5c (2.82/(1×3)×100% = 94%) in $CDCl_3$



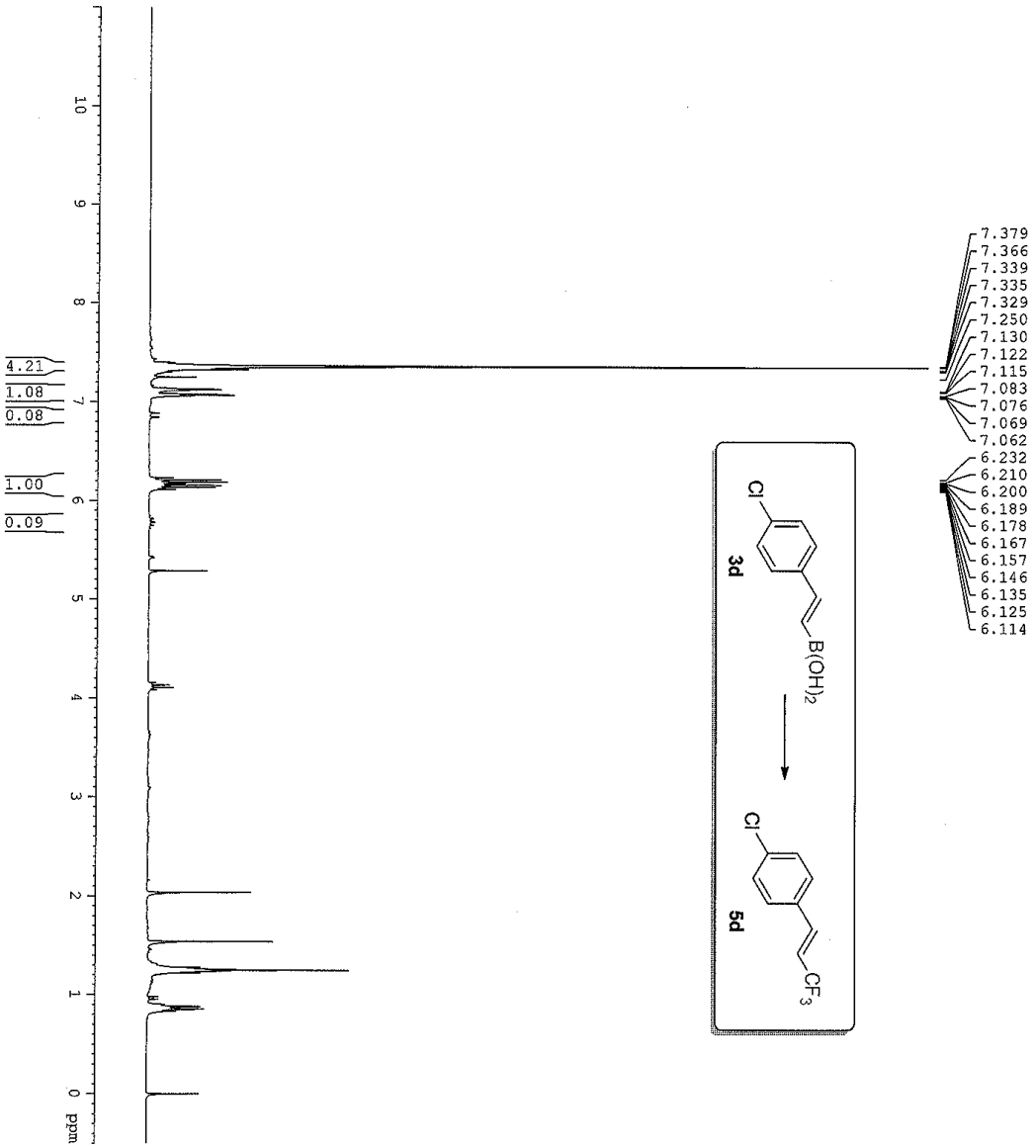
GC-MS of crude 5d



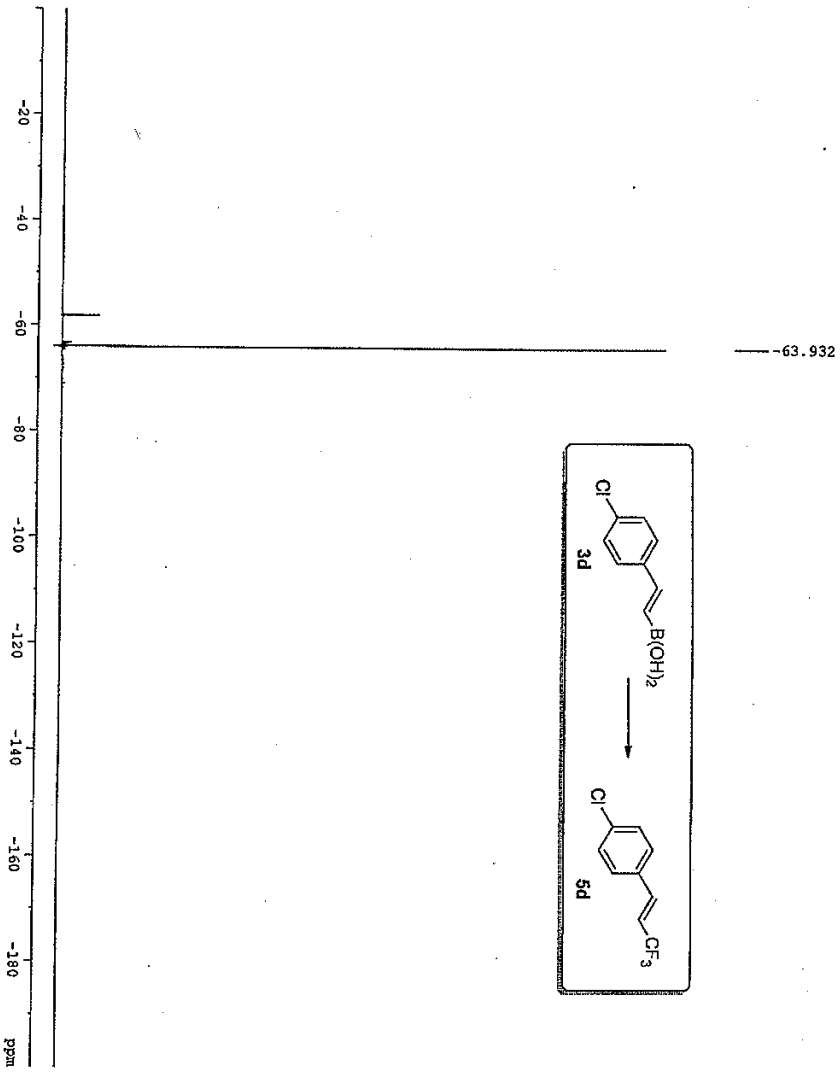
^{19}F NMR yield of compound 5d (2.58/(1×3)×100% = 86%) in $CDCl_3$



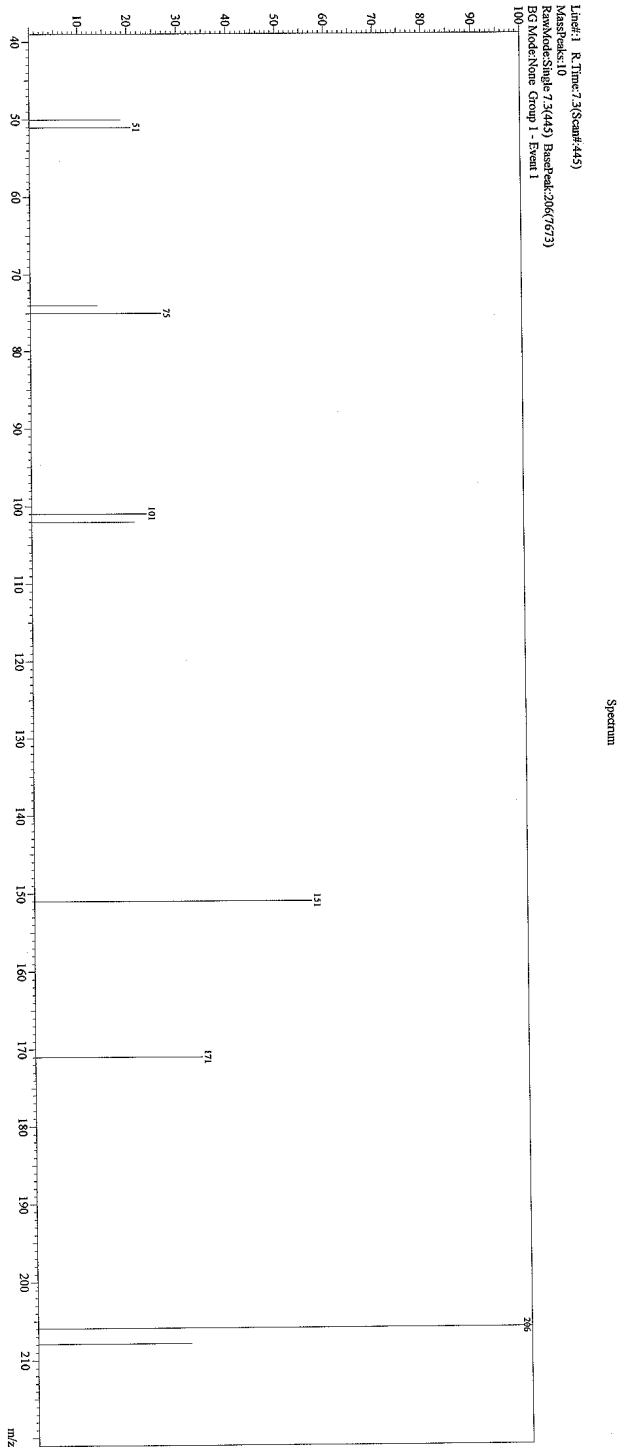
^{1}H NMR of 5c in $CDCl_3$



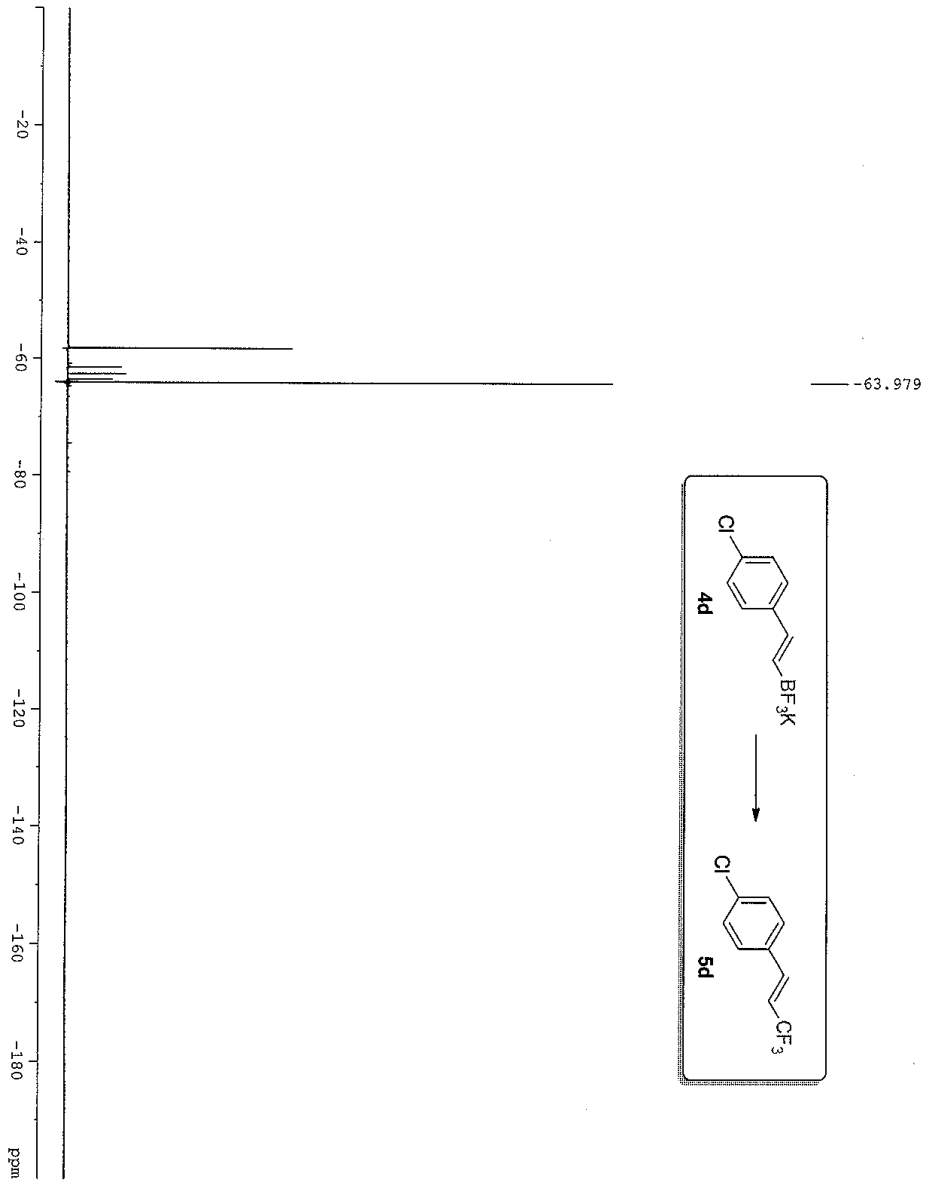
^{19}F NMR of isolated 5d in $CDCl_3$



GC-MS of crude 5d



^{19}F NMR of crude 5d in $CDCl_3$



^{19}F NMR yield of compound 5d (2.22/(1×3)×100% = 74%) in $CDCl_3$