Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information
For

Combinatorial Nickel-Catalyzed Directly Difluoromethylation of Aryl Boronic Acids

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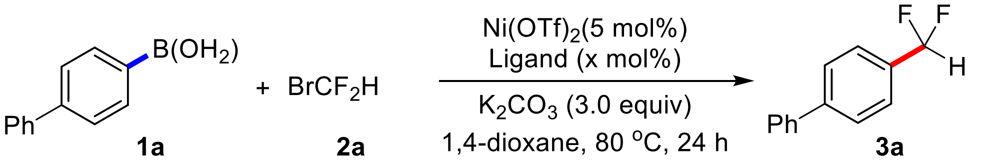
General Information:

NMR spectra were recorded on Bruker-400 (400 MHz for ^{1}H; 101 MHz for ^{13}C and 376 MHz for ^{19}F {^{1}H, ^{13}C decoupled}) instruments internally referenced to $SiMe_4$ signal. High resolution mass spectra were recorded on P-SIMS-Gly of Bruker Daltonics Inc. using ESI-TOF (electrospray ionization-time of flight) or Micromass GCT using EI (electron impact). Infrared spectra were recorded on a Thermo Scientific Nicolet iS10 as either neat films or solids. 1,4-Dioxane was distilled from sodium immediately and degassed before use. $Ni(OTf)_2$, $P(4\text{-}OMePh)_3$ were obtained from Boka chemical and used as received. Bpy, phen were obtained from Energy and used as received. Dtbpy was obtained from Macklin and used as received. PCy_3 was obtained from J&K and used as received. PPh_3 and K_2CO_3 were purchased from Sinopharm and used as received. $BrCF_2H$ was obtained from Shanghai Qinba Chemical.

Tables of the Optimization of Reaction Conditions

Table S1. Ligands Screening[a]



Entry	ligand (x mol%)	Yield (%)[b]
1	No	0
2	phen (5)	12
3	bpy (5)	7
4	dtbpy (5)	21
5	dmbpy (5)	16
6	dombpy (5)	10
7	pyridine (10)	3
8	L1 (5)	9
9	L2 (5)	13
10	L3 (5)	7
11	L4 (5)	3
12	PPh_3 (10)	trace
13	PCy_3 (10)	0
14	dppp(5)	trace
15	dppe (5)	trace
16	bpy (5)/PPh_3 (10)	32
17	dtbpy(5)/PPh_3(10)	62(72)
18	dtbpy(5)/dpph(5)	59
19	dtbpy(5)/dppe(5)	21
20	dtbpy(5)/dppb(5)	53
21	dtbpy(5)/P*t*-Bu_3(10)	42
22	bpy(5)/P(4-OMePh)$_3$(10)	45
23	phen(5)/PCy_3(10)	44

[a] Unless otherwise noted, the reaction conditions were as follows: **1a** (2.0 equiv), **2** (0.2 mmol, 1.0 equiv), $Ni(OTf)_2$ (5 mol%), ligands, K_2CO_3 (3.0 equiv), 1,4-dioxane (2.0 mL), 80 °C, 24 h, N_2, 25 mL tube. [b] Yields determined by ^{19}F NMR using $PhOCF_3$ as an internal standard; numbers in parentheses were isolated yields

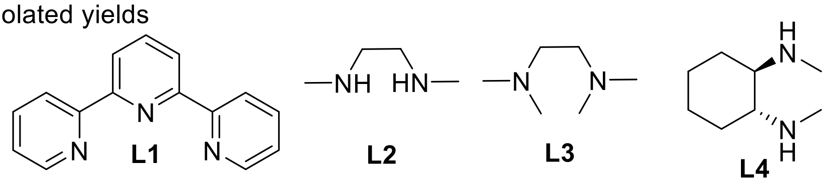
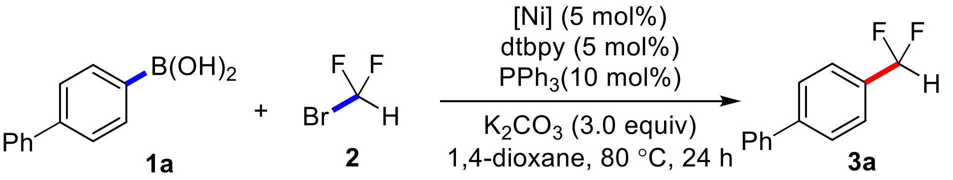


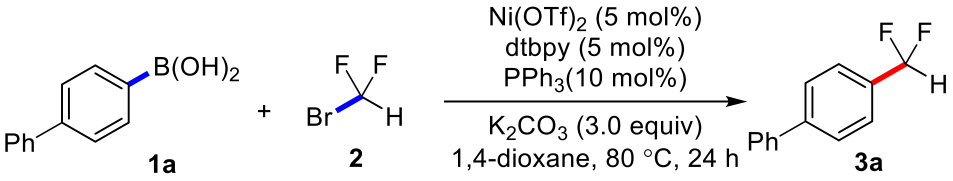
Table S2. Ni-Source Screening[a]



Entry	[Ni]	Yield (%)[b]	Entry	[Ni]	Yield (%)[b]
1	No	0	8	$NiCl_2$(dppe)	36
2	$NiBr_2$	47	9	$NiCl_2$(dppf)	10
3	NiI_2	26	**10**	**$Ni(OTf)_2$**	**82 (94)**[c]
4	$NiCl_2$	0	11	$Ni(NO_3)_2$•$6H_2O$	17
5	$Ni(acac)_2$	0	12	$NiCl_2$(dme)	6
6	$NiCl_2(PPh_3)_2$	trace	13	$Ni(OAc)_2$	11
7	$NiCl_2$(dppp)	50			

[a] Unless otherwise noted, the reaction conditions were as follows: **1a** (2.0 equiv), **2** (0.2 mmol, 1.0 equiv), [Ni] (5 mol%), bpy (5 mol%), P(4-OMePh)$_3$ (10 mol%), K_2CO_3 (3.0 equiv), 1,4-dioxane (2.0 mL), 80 °C, 24 h, N_2. [b] Yields determined by ^{19}FNMR using $PhOCF_3$ as an internal standard; numbers in parentheses were isolated yields. [c] Reaction was performed in 5 mL sealed tube

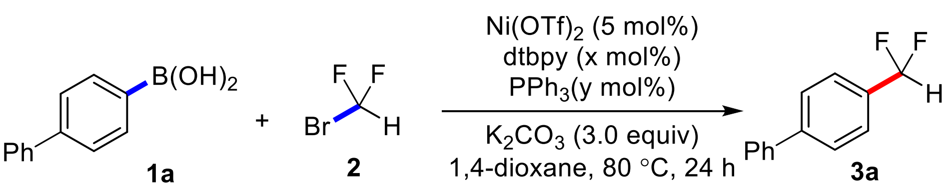
Table S3 Solvent Screening[a]



entry	solvent	yield (%)[b]
1	THF	47
2	DMF	21
3	DCM	0
4	$CHCl_3$	12
5	CH_3CN	3
6	Toluene	0
7	EA	6

[a] Unless otherwise noted, the reaction conditions were as follows: **1a** (2.0 equiv), **2** (0.2 mmol, 1.0 equiv), $NiOTf_2$ (5 mol%), dtbpy (5 mol%), PPh_3 (10 mol%), K_2CO_3 (3.0 equiv), solvent (2.0 mL), 80 °C, 24 h, N_2, 5 mL sealed tube. [b] Yields determined by ^{19}FNMR using $PhOCF_3$ as an internal standard.

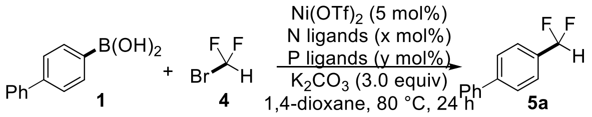
Table S4 Optimization the amount of ligands[a]



entry	x	y	yield (%)[b]
1	5	0	22
2	10	0	19
3	15	0	26
4	0	5	0
5	0	10	0
6	0	20	0
7	5	5	70
8	5	15	86 (94)
9	10	10	81

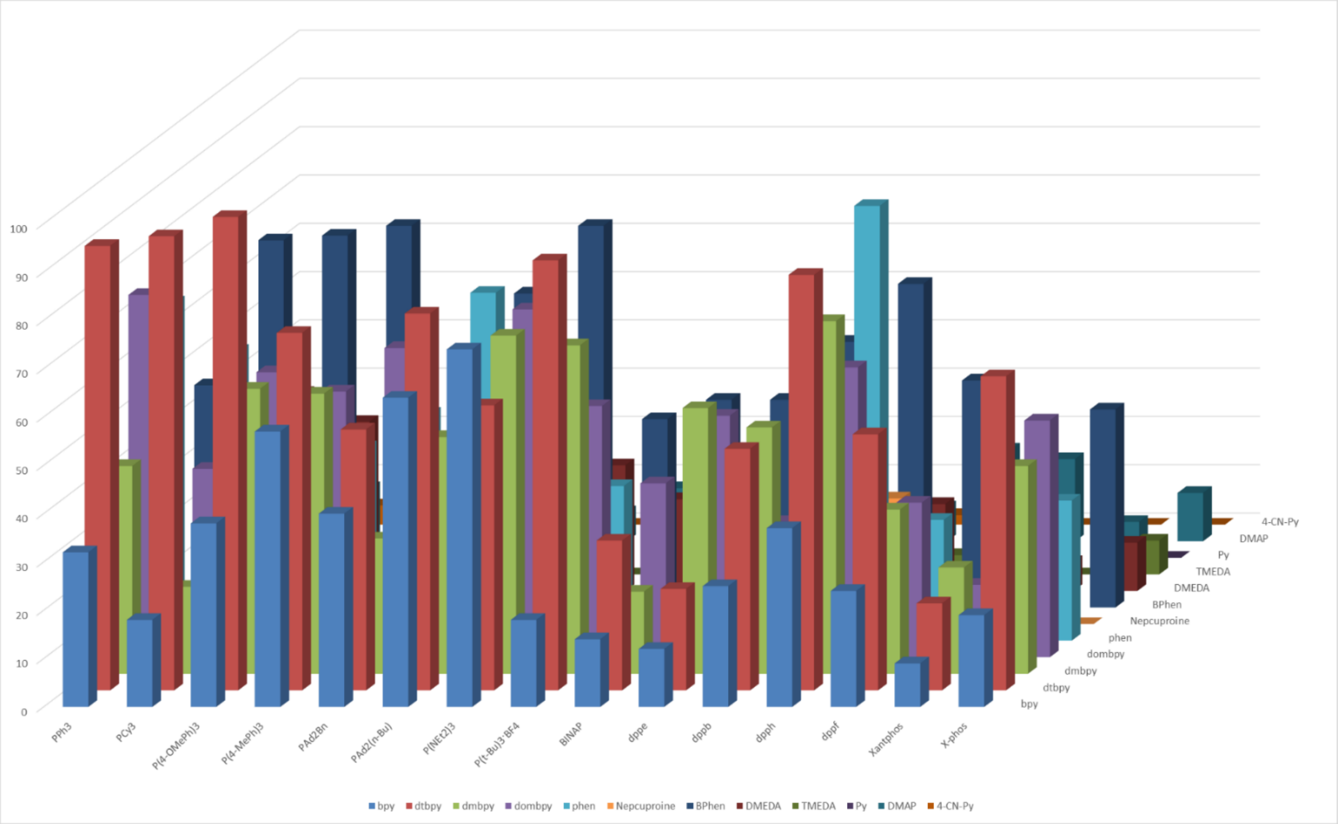
[a] Unless otherwise noted, the reaction conditions were as follows: **1a** (2.0 equiv), **2** (0.2 mmol, 1.0 equiv), $Ni(OTf)_2$ (5 mol%), bpy (x mol%), PPh_3 (y mol%), K_2CO_3 (3.0 equiv), 1,4-dioxane (2 mL), 80 ^{o}C, 24 h, N_2, 5 mL sealed tube. [b] Yields determined by ^{19}FNMR using $PhOCF_3$ as an internal standard; numbers in parentheses were isolated yields..

Table S5 Optimization of N, P ligands combination[a, b]



N, P ligand(mol%)	bpy(5)	dtbpy(5)	dmbpy(5)	dombpy(5)	phen(5)	Neocuproine(5)	Bphen(5)	DMEDA(5)	TMEDA(5)	Py(10)	DMAP(10)	4-CN-Py(10)
PPh_3(10)	32	**82(94)**	43	75	70	0	46	17	1	0	8	3
PCy_3(10)	18	**83(94)**	18	39	60	0	76	41	2	0	11	4
$P(4\text{-}OMePh)_3$(10)	38	**88(98)**	59	59	29	2	77	35	0	0	12	3
$P(4\text{-}MePh)_3$(10)	57	74	58	55	40	0	79	26	0	0	14	1
PAd_2Bn(10)	40	54	28	64	47	0	44	18	3	1	7	0
PAd_2(*n*-Bu)(10)	64	78	49	47	72	3	65	21	0	2	6	0
$P(NEt_2)_3$(10)	74	59	70	72	61	1	79	26	0	0	11	0
$P(t\text{-}Bu)_3{\bullet}BF_4$(10)	18	**82(89)**	68	52	32	0	39	19	0	0	10	2
BINAP	14	31	17	36	6	0	43	9	0	0	18	0
dppe(5)	12	21	55	50	31	10	43	1	0	0	7	0
dppb(5)	25	50	51	28	24	9	55	8	2	2	7	2
dpph(5)	37	**86(90)**	73	60	**90(95)**	26	67	18	4	3	19	6
dppf(5)	24	53	34	32	25	1	47	4	1	0	17	0
Xantphos(5)	9	18	22	15	9	0	18	6	3	0	4	0
X-phos(10)	19	65	43	49	29	0	41	10	7	0	10	0

Unless otherwise noted, the reaction conditions were as follows: **1** (2.0 equiv), **4** (1.0 equiv), $Ni(OTf)_2$ (5 mol%), N ligand (x mol%), P ligand (y mol%), K_2CO_3 (3.0 equiv), 1,4-dioxane (2 mL), 80 ^{o}C, 24 h, N_2, 5 mL sealed tube. Yields determined by ^{19}FNMR using $PhOCF_3$ as an internal standard; numbers in parentheses were isolated yields.


100
90
80
70
60
50
40
30
20
10
0
PPh3
PCy3
P(4-OMePh)3
P(4-MePh)3
PAd2Bn
PAd2(n-Bu)
P(NEt2)3
P(t-Bu)3·BF4
BINAP
dppe
dppb
dpph
dppf
Xantphos
X-phos
4-CN-Py
DMAP
Py
TMEDA
DMEDA
BPhen
Nepcuproine
phen
dombpy
dmbpy
dtbpy
bpy
■ bpy ■ dtbpy ■ dmbpy ■ dombpy ■ phen ■ Nepcuproine ■ BPhen ■ DMEDA ■ TMEDA ■ Py ■ DMAP ■ 4-CN-Py

Preparation of Aryl boronic acids

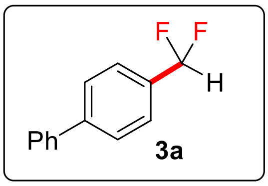
Boronic acids **1n**[1], **1x**[2] and **6**[3] were synthesized via known methods. Compound **4**[4] was synthesized via known method.

Preparation of $BrCF_2H$ Stock Solution[5]

Dry 1, 4-dioxane (~23 mL) was added to a Schlenk graduated cylinder under nitrogen. The vessel and solvent were weighed. Next, $BrCF_2H$ was bubbled through the 1,4-dioxane solution using a long needle until the total volume of the solution reached approximately 25 mL. The vessel was sealed weighed again. The concentration of the $BrCF_2H$ stock solution was calculated based on the mass of $BrCF_2H$ added and the total volume of the solution (~1.0 mol/L).

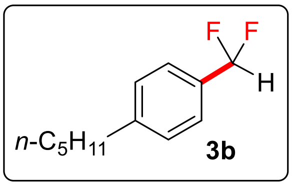
General Procedure for Nickel-Catalyzed Cross-Coupling between Aryl boronic Acids and Difluorobromomethane

$Ni(OTf)_2$ (5 mol %, 0.01 mmol, 3.6 mg), N ligand (5 mol%, 0.01 mmol), P ligand (5 mol%, 0.01 mmol for biphosphine ligands, or 10 mol%, 0.02 mmol for monophosphine ligands), phenylboronic acid **1** (2.0 equiv, 0.4 mmol) and K_2CO_3 (3.0 equiv, 0.6 mmol, 82.8 mg) were combined in a 5 mL oven-dried sealing tube. The vessel was evacuated and backfilled with N_2 (repeated for 3 times), and **2** (1.0 equiv, 0.2 mmol), 1, 4-dioxane (2.0 mL) were then added via syringe. The tube was sealed with a Teflon lined cap and heated in a preheated oil bath at 80 ˚C for 24 h. The reaction mixture was then cooled to room temperature, diluted with EtOAc and filtered through a pad of celite. The filtrate was concentrated under vacuum and purified by flash column chromatography (PE) to give **3** as colorless solid or oil.



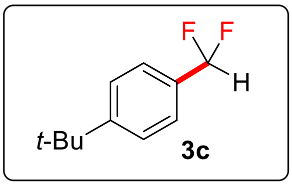
3a

4-(difluoromethyl)-1,1'-biphenyl (3a): dtbpy (5 mol%), PPh_3 (10 mol%) were used as ligands, the reaction was run for 24 h. The product **3a** was purified with silica gel chromatography (PE) as a colorless solid (92% yield). This compound is known.[6] ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 8.0 Hz, 2H), 7.57 (t, J = 7.6 Hz, 4H), 7.45 (t, J = 7.4 Hz, 2H), 7.37 (t, J = 7.3 Hz, 1H), 6.67 (t, J = 56.5 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.23 (d, J = 56.5 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.80 (t, J = 1.8 Hz), 140.28 (s), 133.31 (t, J = 22.5 Hz), 129.05 (s), 128.03 (s), 127.55 (s), 127.37 (s), 126.16 (t, J = 6.0 Hz), 114.89 (t, J = 238.4 Hz).



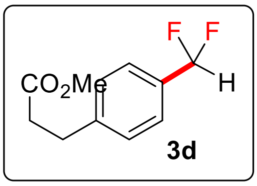
3b

1-(difluoromethyl)-4-pentylbenzene (3b): dtbpy (5 mol%), PPh_3 (10 mol%) were used as ligands, the reaction was run for 24 h. **Note**: The product **3b** was isolated with silica gel chromatography (PE) to give a unseparated mixture with homo-coupling biarene as a colorless oil, the yield (85% yield) was determined by the ratio of the mixture via ^1H NMR analysis (10:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, J = 7.7 Hz, 2H), 7.26 (d, J = 8.1 Hz, 2H), 6.62 (t, J = 56.7 Hz, 1H), 2.63 (t, *J* = 7.7 Hz, 2H), 1.68 – 1.58 (m, 2H), 1.42 -1.28 (m, 4H), 0.89 (t, J = 6.3 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -109.67 (d, J = 56.9 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.02 (t, J = 1.8 Hz), 131.89 (t, J = 22.0 Hz), 128.83 (s), 125.63 (t, J = 6.0 Hz), 115.11 (t, J = 238.1 Hz), 35.92 (s), 31.56 (s), 31.14 (s), 22.66 (s), 14.15 (s). HRMS EI (m/z): $[M]^+$ calcd. for $C_{12}H_{16}F_2$: 198.1220 found: 198.1223.

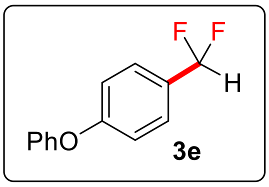


3c

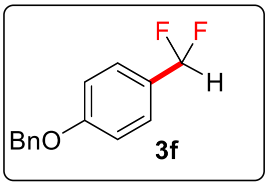
1-(tert-butyl)-4-(difluoromethyl)benzene (3c): dtbpy (5 mol%), PPh_3 (10 mol%) were used as ligands, the reaction was run for 24 h. **Note**: The product **3c** was isolated with silica gel chromatography (PE) to give a unseparated mixture with homo-coupling biarene as a colorless oil, the yield (89% yield) was determined by the ratio of the mixture via ^{1}H NMR analysis (9:1). This compound is known.[6] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.6 Hz, 2H), 7.44 (d, J = 8.6 Hz, 2H), 6.63 (t, J = 56.6 Hz, 1H), 1.34 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -109.85 (d, *J* = 56.8 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.14 (t, J = 2.0 Hz), 131.67 (t, J = 23.5 Hz), 125.76 (s), 125.45 (t, J = 6.0 Hz), 115.04 (t, J = 238.5 Hz), 35.00 (s), 31.36 (s).


3d

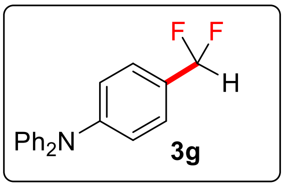
Methyl 3-(4-(difluoromethyl)phenyl)propanoate (3d): dtbpy (5 mol%), PCy_3 (10 mol%) were used as ligands, the reaction was run for 24 h. The product **3d** was purified with silica gel chromatography (PE/EA = 20:1) as a colorless oil (76% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, J = 6.0 Hz, 2H), 7.29 (d, J = 5.8 Hz, 2H), 6.62 (t, J = 56.6 Hz, 1H), 3.67 (s, 3H), 2.99 (t, J = 7.1 Hz, 2H), 2.65 (t, J = 7.6 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.08 (d, J = 58.5 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.16 (s), 143.51 (s), 132.59 (t, J = 22.6 Hz), 128.75 (s), 125.90 (t, J = 6.0 Hz), 114.87 (t, J = 238.2 Hz), 51.83 (s), 35.46 (s), 30.80 (s). IR (neat, cm^{-1}) 3011, 2940, 1734, 1595, 1519, 1497, 1479, 1450, 1382, 1356, 1334, 1313, 1245, 1223, 1210, 1177, 1160, 1147, 1120, 1107, 1060, 1018, 924, 841, 749, 698, 668, 639. HRMS EI (m/z): [M]$^+$ calcd. for $C_{11}H_{12}OF_2$: 214.0805 found: 214.0806.


3e

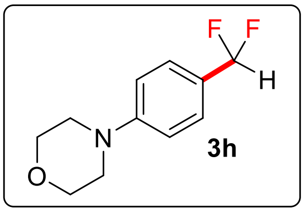
1-(difluoromethyl)-4-phenoxybenzene (3e): dtbpy (5 mol%), PPh_3 (10 mol%) were used as ligands, the reaction was run for 24 h. The product **3e** was purified with silica gel chromatography (PE) as a colorless solid (69% yield). This compound is known.[7] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 7.8 Hz, 2H), 7.37 (t, J = 7.1 Hz, 2H), 7.16 (t, J = 6.9 Hz, 1H), 7.04 (d, J = 7.6 Hz, 4H), 6.62 (t, J = 56.6 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -108.94 (d, J = 56.6 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.73 (s), 156.30 (s), 130.11 (s), 129.01 (t, J = 22.8 Hz), 127.46 (t, J = 5.9 Hz), 124.26 (s), 119.77 (s), 118.38 (s), 114.74 (t, J = 238.0 Hz).


3f

1-(benzyloxy)-4-(difluoromethyl)benzene (3f): dtbpy (5 mol%), PPh_3 (10 mol%) were used as ligands, the reaction was run for 24 h. The product **3f** was purified with silica gel chromatography (PE) as a colorless solid (65% yield). This compound is known.[6] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (dd, J = 8.4, 4.8 Hz, 4H), 7.32 – 7.24 (m, 3H), 6.94 (d, J = 8.8 Hz, 2H), 6.51 (t, J = 56.7 Hz, 1H), 5.01 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -108.32 (d, J = 56.8 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.68 (s), 136.62 (s), 128.80 (s), 128.28 (s), 127.58 (s), 127.28 (t, J = 5.9 Hz), 127.17 (t, J = 22.7 Hz), 115.08 (s), 114.99 (t, J = 237.5 Hz), 70.24 (s).

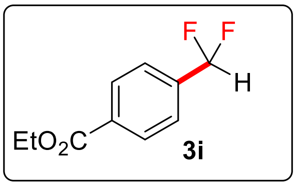

3g

4-(difluoromethyl)-N,N-diphenylaniline (3g): dtbpy (5 mol%), PPh_3 (10 mol%) were used as ligands, the reaction was run for 24 h. ^{19}F NMR yield: 69% (using $PhOCF_3$ as internal standard). **Note:** Compound **3g** is unstable upon purification with silica gel chromatography. HRMS ESI (m/z): [M+H]$^+$ calced. for $C_{19}H_{16}F_2N$: 296.1245 found: 296.1249.

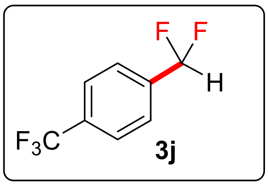

3h

4-(4-(difluoromethyl)phenyl)morpholine (3h): dtbpy (5 mol%), PPh_3 (10 mol%) were used as ligands, the reaction was run for 24 h. The product **3h** was purified with silica gel chromatography (PE/EA = 5:1) as a colorless solid (78% yield). This compound is known.[7] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 8.3 Hz, 2H), 6.93 (d, J = 8.4 Hz, 2H), 6.58 (t, J = 56.9 Hz, 1H), 3.90 – 3.82 (m, 2H), 3.24 – 3.18 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -108.05 (d, J = 56.9 Hz). ^{13}C NMR (101 MHz,

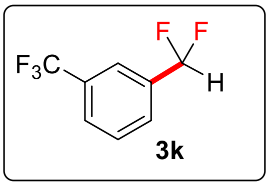
$CDCl_3$) δ 153.00 (s), 126.87 (t, J = 5.9 Hz), 125.39 (t, J = 22.8 Hz), 115.23 (t, J = 236.9 Hz), 114.94 (s), 66.85 (s), 48.65 (s).


3i

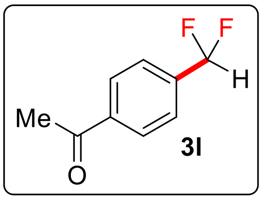
Ethyl 4-(difluoromethyl)benzoate (3i): dtbpy (5 mol%), PCy_3 (10 mol%) were used as ligands, the reaction was run for 24 h. The product **3i** was purified with silica gel chromatography (PE/EA = 10:1) as a colorless oil (86% yield). This compound is known.[8] ^1H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 8.1 Hz, 2H), 7.58 (d, J = 8.1 Hz, 2H), 6.69 (t, J = 56.1 Hz, 1H), 4.40 (q, J = 7.1 Hz, 2H), 1.41 (t, J = 7.1 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.16 (d, J = 56.1 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.91 (s), 138.47 (t, J = 22.4 Hz), 132.80 (t, J = 1.8 Hz), 130.04 (s), 125.72 (t, J = 6.0 Hz), 114.17 (t, J = 239.7 Hz), 61.49 (s), 14.40 (s).


3j

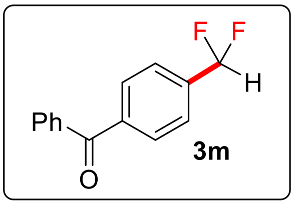
1-(difluoromethyl)-4-(trifluoromethyl)benzene (3j): dtbpy (5 mol%), PCy_3 (10 mol%) were used as ligands, the reaction was run for 24 h. This compound is known.[8] Due to the low boiling point of the product, the yield (52%) was determined by ^{19}F NMR using $PhOCF_3$ as an internal standard. This compound is known[8]. The product was characterized by ^{19}F NMR and GC-MS analysis.


3k

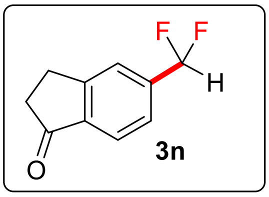
1-(difluoromethyl)-3-(trifluoromethyl)benzene (3k): dtbpy (5 mol%), PCy_3 (10 mol%) were used as ligands, the reaction was run for 24 h. This compound is known.[7] Due to the low boiling point of the product, the yield (62%) was determined by ^{19}F NMR using $PhOCF_3$ as an internal standard. This compound is known[7]. The product was characterized by ^{19}F NMR and GC-MS analysis.


3l

1-(4-(difluoromethyl)phenyl)ethan-1-one (3l): dtbpy (5 mol%), PCy_3 (10 mol%) were used as ligands, the reaction was run for 48 h. Due to the low boiling point of the product, the yield (67%) was determined by ^{19}F NMR using $PhOCF_3$ as an internal standard and the product **3l** was purified with silica gel chromatography (PE/EA = 10:1) as a colorless oil (49% yield). This compound is known.[7] ^1H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.0 Hz, 2H), 7.81 (d, J = 7.7 Hz, 2H), 7.64 (d, J = 8.2 Hz, 2H), 7.61 (d, J = 8.0 Hz, 1H), 7.50 (t, J = 7.7 Hz, 2H), 6.73 (t, J = 56.1 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.29 (d, J = 56.1 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.53 (s), 138.99 (t, J = 1.7 Hz), 138.64 (t, J = 22.5 Hz), 128.78 (s), 126.04 (t, J = 6.0 Hz), 114.08 (t, J = 239.8 Hz), 26.92 (s).

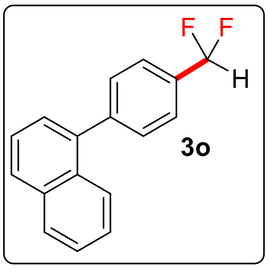

3m

(4-(difluoromethyl)phenyl)(phenyl)methanone (3m): dtbpy (5 mol%), PCy_3 (10 mol%) were used as ligands, the reaction was run for 48 h. The product **3m** was purified with silica gel chromatography (PE/EA = 10:1) as a colorless solid (80% yield). This compound is known.[9] ^1H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.0 Hz, 2H), 7.81 (d, J = 7.7 Hz, 2H), 7.66 – 7.62 (m, 2H), 7.60 (s, 1H), 7.50 (t, J = 7.7 Hz, 2H), 6.73 (t, J = 56.1 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.00 (d, J = 56.1 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.07 (s), 139.85 (t, J = 1.8 Hz), 137.93 (t, J = 22.4 Hz), 137.14 (s), 133.03 (s), 130.37 (s), 130.23 (s), 128.59 (s), 125.72 (t, J = 6.0 Hz), 114.18 (t, J = 239.7 Hz).



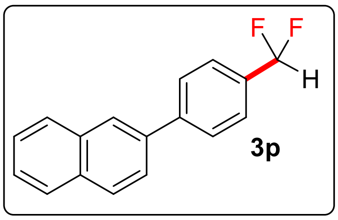
3n

5-(difluoromethyl)-2,3-dihydro-1H-inden-1-one (3n): dtbpy (5 mol%), PCy_3 (10 mol%) were used as ligands, the reaction was run for 24 h. The product **3n** was purified with silica gel chromatography (PE/EA = 8:1) as a colorless solid (51% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 7.9 Hz, 1H), 7.65 (s, 1H), 7.51 (d, J = 7.9 Hz, 1H), 6.71 (t, J = 56.1 Hz, 1H), 3.23 – 3.18 (m, 2H), 2.79 – 2.73 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -111.82 (d, J = 56.1 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.35 (s), 155.46 (s), 140.24 (t, J = 22.0 Hz), 139.05 (t, J = 1.6 Hz), 124.98 (t, J = 5.9 Hz), 124.35 (s), 124.15 (t, J = 6.2 Hz), 114.18 (t, J = 240.2 Hz), 36.53 (s), 25.96 (s). IR (neat, cm^{-1}) 3006, 2939, 2359, 1705, 1615, 1486, 1450, 1431, 1406, 1383, 1322, 1297, 1274, 1192, 1142, 1062, 1020, 965, 934, 898, 843, 778, 760, 710, 685. HRMS EI (m/z): $[M]^+$ calcd. for $C_{10}H_8OF_2$: 182.0543 found: 182.0535.



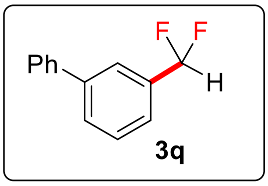
3o

1-(4-(difluoromethyl)phenyl)naphthalene (3o): dtbpy (5 mol%), $P(4\text{-}OMePh)_3$ (10 mol%) were used as ligands, the reaction was run for 24 h. The product **3o** was purified with silica gel chromatography (PE/EA = 50:1) as a colorless solid. (74% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (dd, J = 12.0, 8.2 Hz, 2H), 7.83 (d, J = 8.4 Hz, 1H), 7.64 (d, J = 8.0 Hz, 2H), 7.58 (d, J = 8.1 Hz, 2H), 7.55-7.52 (m, 1H), 7.51-7.48 (m, 1H), 7.47-7.39 (m, 2H), 6.75 (t, J = 56.5 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.21 (d, J = 56.6 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.51 (t, J = 2.0 Hz), 139.28 (s), 133.90 (s), 133.41 (t, J = 22.4 Hz), 131.49 (s), 130.52 (s), 128.52 (s), 128.29 (s), 127.12 (s), 126.45 (s), 126.09 (s), 125.79 (s), 125.69 (t, J = 6.0 Hz), 125.49 (s), 114.94 (t, J = 238.6 Hz). IR (neat, cm^{-1}) 3043, 2939, 2360, 1927, 1615, 1505, 1493, 1460, 1396, 1377, 1218, 1181, 1143, 1070, 1017, 964, 840, 798, 791, 775, 718, 734, 697, 626. HRMS EI (m/z): $[M]^+$ calcd. for $C_{17}H_{12}F_2$: 254.0907 found: 254.0911



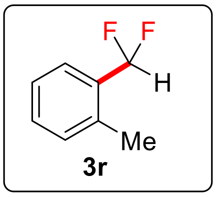
3p

2-(4-(difluoromethyl)phenyl)naphthalene (3p): dtbpy (5 mol%), PPh_3 (10 mol%) were used as ligands, the reaction was run for 24 h. The product **3p** was purified with silica gel chromatography (PE) as a colorless solid (55% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.95 – 7.85 (m, 3H), 7.78 (d, J = 8.0 Hz, 2H), 7.72 (dd, J = 8.5, 1.6 Hz, 1H), 7.61 (d, J = 8.0 Hz, 2H), 7.55 – 7.46 (m, 2H), 6.71 (t, J = 56.5 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.28 (d, J = 56.5 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.72 (t, J = 2.0 Hz), 137.58 (s), 133.71 (s), 133.37 (t, J = 22.5 Hz), 132.98 (s), 128.79 (s), 128.41 (s), 127.81 (s), 126.64 (s), 126.45 (s), 126.31 (s), 126.25 (t, J = 6.1 Hz), 125.44 (s), 114.89 (t, J = 238.5 Hz). IR (neat, cm^{-1}) 3395, 2964, 2927, 2358, 1504, 1443, 1373, 1361, 1233, 1192, 1155, 1086, 1047, 880, 795, 768, 694, 677, 651, 637. HRMS EI (m/z): $[M]^+$ calcd. for $C_{17}H_{12}F_2$: 254.0907 found: 254.0905.



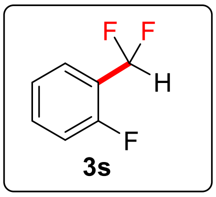
3q

3-(difluoromethyl)-1,1'-biphenyl (3q): phen (5 mol%), dpph (5 mol%) were used as ligands, the reaction was run for 24 h. The product **3q** was purified with silica gel chromatography (PE) as a colorless oil (65% yield). This compound is known.[7] ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.69 (d, J = 7.5 Hz, 1H), 7.62 – 7.57 (m, 2H), 7.56- 7.42 (m, 4H), 7.38 (t, J = 7.3 Hz, 1H), 6.70 (t, J = 56.5 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.56 (d, J = 56.5 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.99 (s), 140.32 (s), 135.04 (t, J = 22.3 Hz), 129.58 (t, J = 1.9 Hz), 129.32 (s), 129.06 (s), 127.94 (s), 127.32 (s), 124.46 (td, J = 6.0, 4.6 Hz), 114.90 (t, J = 239.0 Hz).



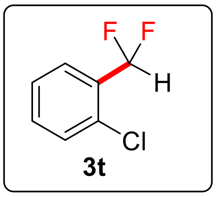
3r

1-(difluoromethyl)-2-methylbenzene (3r): dtbpy (5 mol%), dpph (5 mol%) were used as ligands, the reaction was run for 48 h. This compound is known.[10] Due to the low boiling point of the product, the yield (76%) was determined by ^{19}F NMR using PhOCF$_3$ as an internal standard. This compound is known. The product was characterized by ^{19}F NMR and GC-MS analysis.



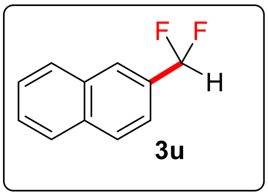
3s

1-(difluoromethyl)-2-fluorobenzene (3s): dtbpy (5 mol%), dpph (5 mol%) were used as ligands, the reaction was run for 48 h. This compound is known.[11] Due to the low boiling point of the product, the yield (67%) was determined by ^{19}F NMR using PhOCF$_3$ as an internal standard. This compound is known. The product was characterized by ^{19}F NM R and GC-MS analysis.



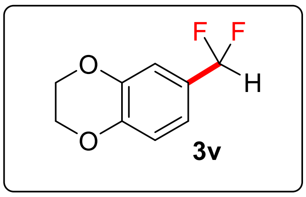
3t

1-chloro-2-(difluoromethyl)benzene (3t): dtbpy (5 mol%), dpph (5 mol%) were used as ligands, the reaction was run for 48 h. This compound is known.[12] Due to the low boiling point of the product, the yield (62%) was determined by ^{19}F NMR using PhOCF$_3$ as an internal standard. This compound is known. The product was characterized by ^{19}F NMR and GC-MS analysis.



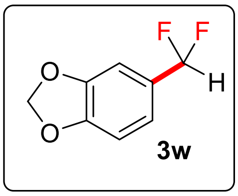
3u

2-(difluoromethyl)naphthalene (3u): dtbpy (5 mol%), PPh$_3$ (10 mol%) were used as ligands, the reaction was run for 24 h. The product **3u** was purified with silica gel chromatography (PE/EA = 30:1) as a colorless solid (51% yield). This compound is known.[7] ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.97 (s, 1H), 7.95 – 7.86 (m, 3H), 7.62 – 7.52 (m, 3H), 6.80 (t, J = 56.4 Hz, 1H). ^{19}F NMR (376 MHz, CDCl$_3$) δ -109.82 (d, J = 56.4 Hz). ^{13}C NMR (101 MHz, CDCl$_3$) δ 134.44 (s), 132.68 (s), 131.74 (t, J = 22.5 Hz), 129.03 (s), 128.66 (s), 128.02 (s), 127.54 (s), 126.95 (s), 126.03 (t, J = 7.1 Hz), 122.16 (t, J = 4.7 Hz), 115.18 (t, J = 238.9 Hz).



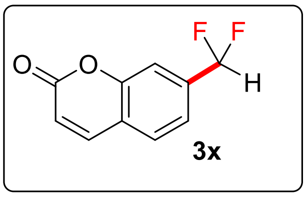
3v

6-(difluoromethyl)-2,3-dihydrobenzo[*b*][1,4]dioxine (3v): dtbpy (5 mol%), PCy$_3$ (10 mol%) were used as ligands, the reaction was run for 24 h. The product **3v** was purified with silica gel chromatography (PE) as a colorless oil (68% yield). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.03 (s, 1H), 6.98 (d, J = 8.7 Hz, 1H), 6.92 (d, J = 8.4 Hz, 1H), 6.54 (t, J = 56.7 Hz, 1H), 4.28 (s, 4H). ^{19}F NMR (376 MHz, CDCl$_3$) δ -108.63 (d, J = 56.7 Hz). ^{13}C NMR (101 MHz, CDCl$_3$) δ 145.65 (t, J = 1.8 Hz), 143.75 (s), 127.82 (t, J = 22.8 Hz), 118.93 (t, J = 6.2 Hz), 117.69 (s), 115.01 (t, J = 6.1 Hz), 114.66 (t, J = 238.0 Hz), 64.55 (s), 64.40 (s). IR (neat, cm^{-1}) 3424, 3010, 2919, 2850, 2359, 1592, 1494, 1450, 1391, 1353, 1334, 1246, 1226, 1210, 1178, 1160, 1145, 1062, 1029, 924, 838, 805, 748, 720, 697, 667, 615, 639. HRMS EI (m/z): [M]$^+$ calcd. for C$_9$H$_8$O$_2$F$_2$: 186.0492 found: 186.0500.



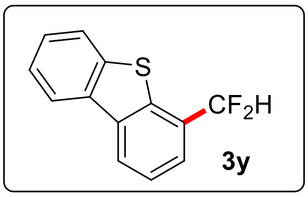
3w

5-(difluoromethyl)benzo[*d*][1,3]dioxole (3w): dtbpy (5 mol%), PCy$_3$ (10 mol%) were used as ligands, the reaction was run for 24 h. The product **3w** was purified with silica gel chromatography (PE) as a colorless oil (62% yield). This compound is known.[7] ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.98 (d, J = 7.8 Hz, 1H), 6.85 (d, J = 7.7 Hz, 1H), 6.54 (t, J = 56.6 Hz, 1H), 6.02 (s, 1H). ^{19}F NMR (376 MHz, CDCl$_3$) δ -107.89 (d, J = 56.6 Hz). ^{13}C NMR (101 MHz, CDCl$_3$) δ 149.69 (t, J = 2.0 Hz), 148.18 (s), 128.43 (t, J = 22.7 Hz), 120.28 (t, J = 7.2 Hz), 114.76 (t, J = 238.1 Hz), 108.36 (s), 105.92 (t, J = 5.5 Hz), 101.71 (s).



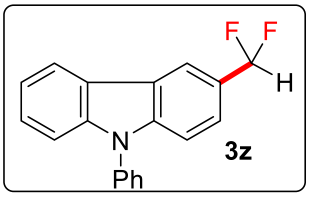
3x

7-(difluoromethyl)-2H-chromen-2-one (3x): dtbpy (5 mol%), dpph (5 mol%) were used as ligands, the reaction was run for 24 h. The product **3x** was purified with silica gel chromatography (PE/EA = 20:1) as a colorless oil (53% yield). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.75 (d, J = 9.6 Hz, 1H), 7.60 (d, J = 7.9 Hz, 1H), 7.47 (s, 1H), 7.44 (d, J = 8.0 Hz, 1H), 6.72 (t, J = 56.0 Hz, 1H), 6.52 (d, J = 9.6 Hz, 1H). ^{19}F NMR (376 MHz, CDCl$_3$) δ -112.06 (d, J = 56.0 Hz). ^{13}C NMR (101 MHz, CDCl$_3$) δ 160.16 (s), 154.02 (s), 142.72 (s), 137.86 (t, J = 20.1 Hz), 128.63 (s), 121.50 (t, J = 5.9 Hz), 120.61 (s), 118.38 (s), 114.59 (t, J = 6.6 Hz), 113.55 (t, J = 240.6 Hz). IR (neat, cm^{-1}) 3417, 3318, 2991, 2931, 2852, 2360, 1596, 1494, 1458, 1395, 1382, 1315, 1278, 1248, 1210, 1160, 1144, 1043, 991, 908, 924, 873, 850, 781, 749, 697, 668, 619. HRMS EI (m/z): [M]$^+$ calcd. for $C_{14}H_{12}F_2$: 218.0907 found: 218.0914.



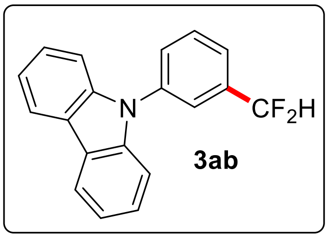
3y

4-(difluoromethyl)dibenzo[b,d]thiophene (3y): dtbpy (5 mol%), P(4-OMePh)$_3$ (10 mol%) were used as ligands, the reaction was run for 24 h. The product **3y** was purified with silica gel chromatography (PE) as a colorless solid (51% yield). This compound is known.[7] ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.24 (dd, J = 7.9, 1.0 Hz, 1H), 8.20 – 8.14 (m, 1H), 7.91 – 7.85 (m, 1H), 7.61 (dd, J = 7.4, 0.7 Hz, 1H), 7.53 (d, J = 7.7 Hz, 1H), 7.51 – 7.46 (m, 2H), 6.93 (t, J = 55.6 Hz, 1H). ^{19}F NMR (376 MHz, CDCl$_3$) δ -113.35 (d, J = 55.6 Hz). ^{13}C NMR (101 MHz, CDCl$_3$) δ 139.62 (s), 137.14 (s), 136.78 (t, J = 3.2 Hz), 134.77 (s), 128.67 (t, J = 22.9 Hz), 127.50 (s), 124.83 (s), 124.53 (s), 124.46 (t, J = 7.1 Hz), 123.89 (s), 122.85 (s), 121.83 (s), 114.60 (t, J = 239.6 Hz).



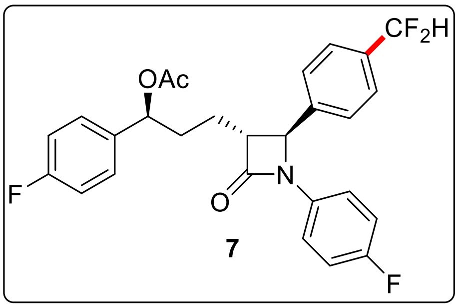
3z

3-(difluoromethyl)-9-phenyl-9H-carbazole (3z): dtbpy (5 mol%), dpph (5 mol%) were used as ligands, the reaction was run for 24 h. The product **3z** was purified with silica gel chromatography (PE/EA = 50:1) as a colorless solid (73 % yield). This compound is known.[7] ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.21 (d, J = 0.5 Hz, 1H), 8.12 – 8.04 (m, 1H), 7.56 – 7.49 (m, 2H), 7.48 – 7.43 (m, 3H), 7.43 – 7.39 (m, 1H), 7.37 – 7.30 (m, 3H), 7.24 (ddd, J = 8.0, 6.8, 1.4 Hz, 1H), 6.76 (t, J = 56.9 Hz, 1H). ^{19}F NMR (376 MHz, CDCl$_3$) δ -106.25 (d, J = 56.9 Hz). ^{13}C NMR (101 MHz, CDCl$_3$) δ 142.20 (s), 141.65 (s), 137.35 (s), 130.16 (s), 128.05 (s), 127.29 (s), 126.75 (s), 126.29 (t, J = 22.5 Hz), 123.38 (t, J = 6.1 Hz), 123.33 (s), 123.13 (s), 120.63 (s), 120.62 (s), 118.27 (t, J = 6.5 Hz), 115.88 (t, J = 234.7 Hz), 110.23 (s), 110.13 (s).



3ab

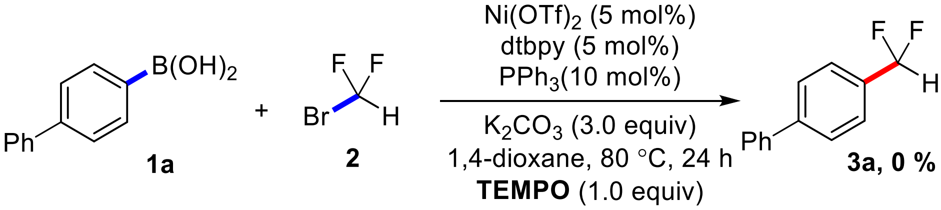
9-(3-(difluoromethyl)phenyl)-9H-carbazole(3ab): dtbpy (5 mol%), PCy$_3$ (10 mol%) were used as ligands, the reaction was run for 48 h. The product **3ab** was purified with silica gel chromatography (PE) as a colorless solid (81 % yield). ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.14 (d, J = 7.5 Hz, 2H), 7.73 (s, 1H), 7.69 (d, J = 5.0 Hz, 2H), 7.60 (t, J = 4.2 Hz, 1H), 7.45 – 7.35 (m, 4H), 7.35 – 7.26 (m, 2H), 6.73 (t, J = 56.2 Hz, 1H). ^{19}F NMR (376 MHz, CDCl$_3$) δ -111.02 (d, J = 56.3 Hz). ^{13}C NMR (101 MHz, CDCl$_3$) δ 140.73 (s), 138.45 (s), 136.50 (t, J = 22.7 Hz), 130.59 (s), 129.43 (t, J = 1.7 Hz), 126.27 (s), 124.62 (t, J = 6.0 Hz), 124.34 (t, J = 6.1 Hz), 123.67 (s), 114.22 (t, J = 239.7 Hz), 109.67 (s). IR (neat, cm^{-1}) 3042, 2939, 2359, 1594, 1496, 1478, 1457, 1448, 1389, 1366, 1334, 1313, 1245, 1226, 1210, 1178, 1160, 1146, 1120, 1058, 1019, 924, 907, 864, 794, 748, 720, 698, 668, 615. HRMS EI (m/z): [M]$^+$ calcd. for $C_{19}H_{13}NF_2$: 293.1016 found: 293.1013.



(S)-3-(2S,3R-2-(4-(difluoromethyl)phenyl)-1-(4-fluorophenyl)-4-oxoazetidin-3-yl)-1-(4-fluorophenyl)propyl acetate(7): dtbpy (5 mol%), PPh_3 (10 mol%) were used as ligands, the reaction was run for 24 h. The product **7** was purified with silica gel chromatography (PE/EA = 5:1) as a colorless solid (81% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 8.0 Hz, 2H), 7.41 (d, J = 8.0 Hz, 2H), 7.31 – 7.24 (m, 2H), 7.23 – 7.17 (m, 2H), 7.02 (t, J = 8.6 Hz, 2H), 6.93 (t, J = 8.6 Hz, 2H), 6.64 (t, J = 56.3 Hz, 1H), 5.70 (t, J = 6.7 Hz, 1H), 4.65 (d, J = 2.0 Hz, 1H), 3.07 (td, J = 7.7, 2.1 Hz, 1H), 2.09 – 1.99 (m, 5H), 1.94 – 1.83 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.89 (d, J = 56.6 Hz), -113.68 (ddd, J = 18.2, 9.0, 5.5 Hz), -117.56 (ddd, J = 13.5, 8.7, 4.8 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.33 (s), 166.60 (s), 162.57 (d, J = 246.8 Hz), 159.21 (d, J = 243.8 Hz), 140.45 (s), 135.74 (d, J = 3.2 Hz), 134.98 (t, J = 22.6 Hz), 133.68 (d, J = 2.7 Hz), 128.39 (s), 128.31 (s), 126.80 (t, J = 6.0 Hz), 126.27 (s), 118.40 (d, J = 7.9 Hz), 116.09 (d, J = 22.7 Hz), 115.68 (d, J = 21.6 Hz), 114.31 (t, J = 239.1 Hz), 74.91 (s), 60.84 (s), 60.33 (s), 33.72 (s), 25.04 (s), 21.30 (s). IR (neat, cm^{-1}) 3426, 3012, 2937, 2360, 1742, 1595, 1509, 1496, 1479, 1457, 1448, 1388, 1354, 1334, 1312, 1244, 1159, 1146, 1120, 1017, 924, 907, 834, 795, 748, 720, 697, 668, 639. HRMS ESI (m/z): $[M+Na]^+$ calcd. for $C_{27}H_{23}O_3NF_4Na$: 508.1512 found: 508.1516.

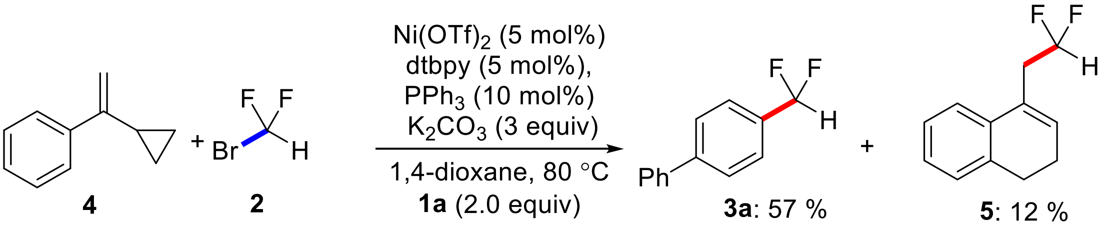
Mechanistic Studies:

1. Radical Trapping Experiment with TEMPO



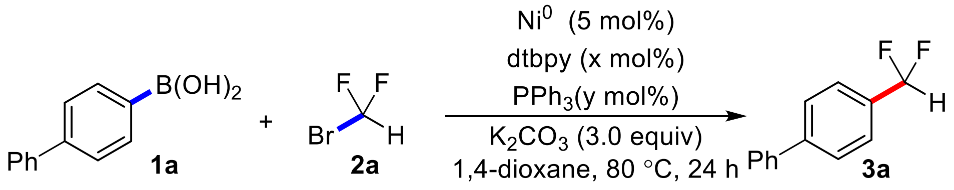
To a 5 mL sealed tube were added **1a** (2.0 equiv, 0.4 mmol), $Ni(OTf)_2$ (5 mol %, 0.01 mmol), dtbpy (5 mol %, 0.01 mmol) , PPh_3 (10 mol%, 0.02 mol) and K_2CO_3 (3.0 equiv, 0.6 mmol) under air. The vessel was evacuated and backfilled wit N_2 (3 times) and 1,4-dioxane (2.0 mL) were added via syringe, then **2** (1.0 equiv, 0.2 mmol) and TEMPO (1.0 equiv, 0.2 mmol) were added. The reaction mixture was heated in a preheated oil bath at 80 ˚C for 24 h, and was cooled to room temperature. No product **3a** was detected by crude ^{19}F NMR.

2. Radical Clock Experiment:



To a 5 mL sealed tube were added **1a** (2.0 equiv, 0.4 mmol), $Ni(OTf)_2$ (5 mol %, 0.01 mmol), dtbpy (5 mol %, 0.01 mmol) , PPh_3 (10 mol%, 0.02 mol) and K_2CO_3 (3.0 equiv, 0.6 mmol) under air. The vessel was evacuated and backfilled wit N_2 (3 times) and 1,4-dioxane (2.0 mL) was added via syringe, then **2a** (1.0 equiv, 0.2 mmol) and **4** (2.0 equiv, 0.4 mmol) were added. The tube was screw capped and put into a preheated oil bath at 80 ˚C for 24 h. After cooling to room temperature, the reaction mixture was diluted with EtOAc and filtered through a pad of celite. The filtrate was concentrated under vacuum and purified by flash column chromatography (PE) to give product **3a** in 57% yield and the yield of product **5** was determined by crude ^{19}F NMR. **Note**: The product **5** was isolated with silica gel chromatography (PE) to give a unseparated mixture with **3a** as a colorless solid, the yield (12% yield) was determined by the ratio of the mixture via ^{19}F NMR analysis ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.93 (dt, J = 56.8, 16.5 Hz). HRMS EI (m/z): $[M]^+$ calced. for $C_{12}H_{12}F_2$: 194.0907 found: 194.0914.

3. Procedure of Monofluoroalkylation with Ni^0 used as the catalyst



entry	Ni^0	x	y	yield (%)[b]
1	$Ni(cod)_2$	0	0	trace
2	$Ni(cod)_2$	5	0	4
3	$Ni(cod)_2$	0	10	0
4	$Ni(cod)_2$	5	10	84(90)

[a] Unless otherwise noted, the reaction conditions were as follows: **1a** (2.0 equiv), **2a** (0.2 mmol, 1.0 equiv), Ni^0 (5 mol%), bpy (x mol%), PPh_3 (y mol%), K_2CO_3 (3.0 equiv), 1,4-dioxane (2 mL), 80 °C, 24 h, N_2. 5 mL sealed tube. [b] Yields determined by ^{19}FNMR using $PhOCF_3$ as an internal standard; number in parenthese was isolated yields

References:

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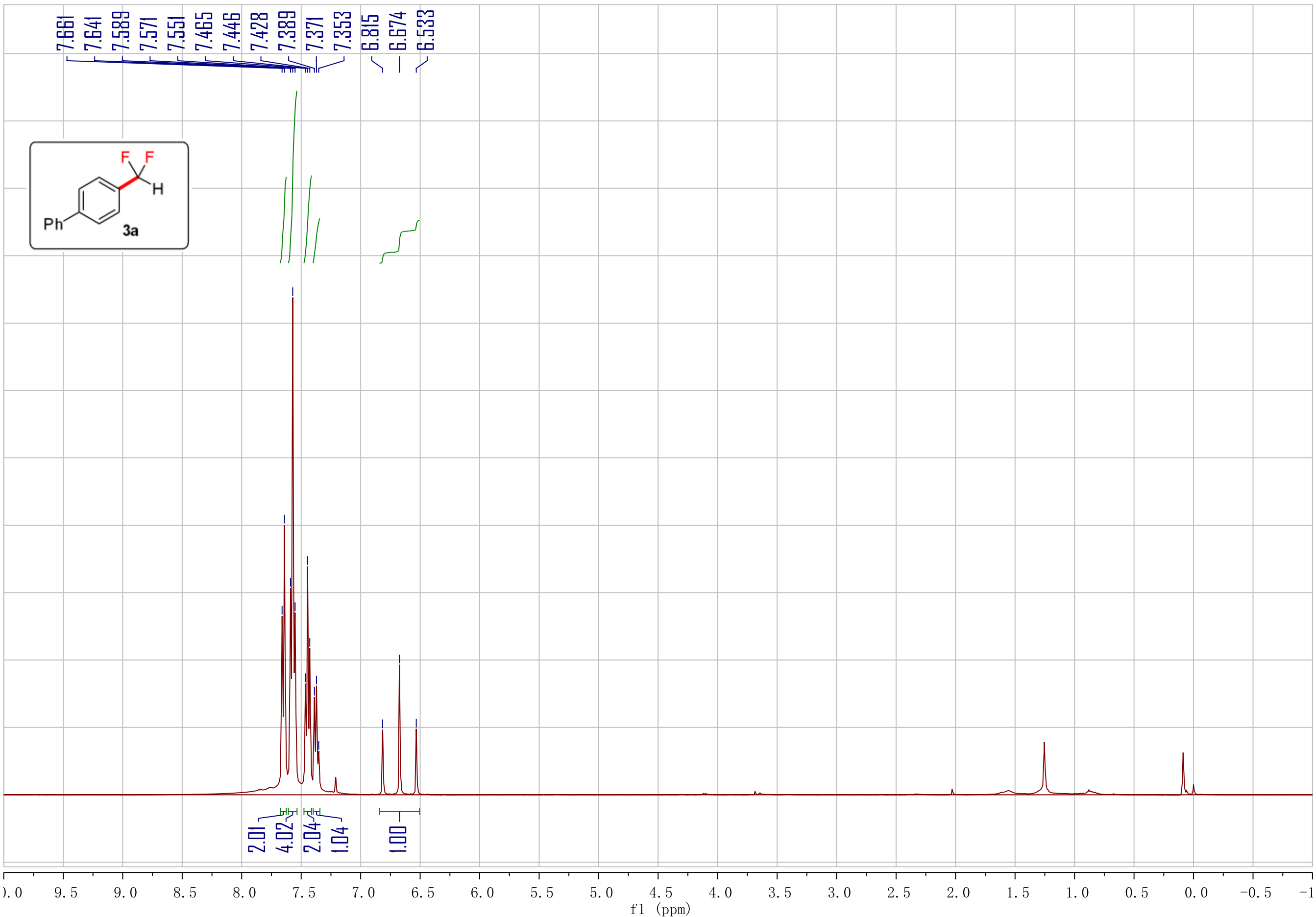
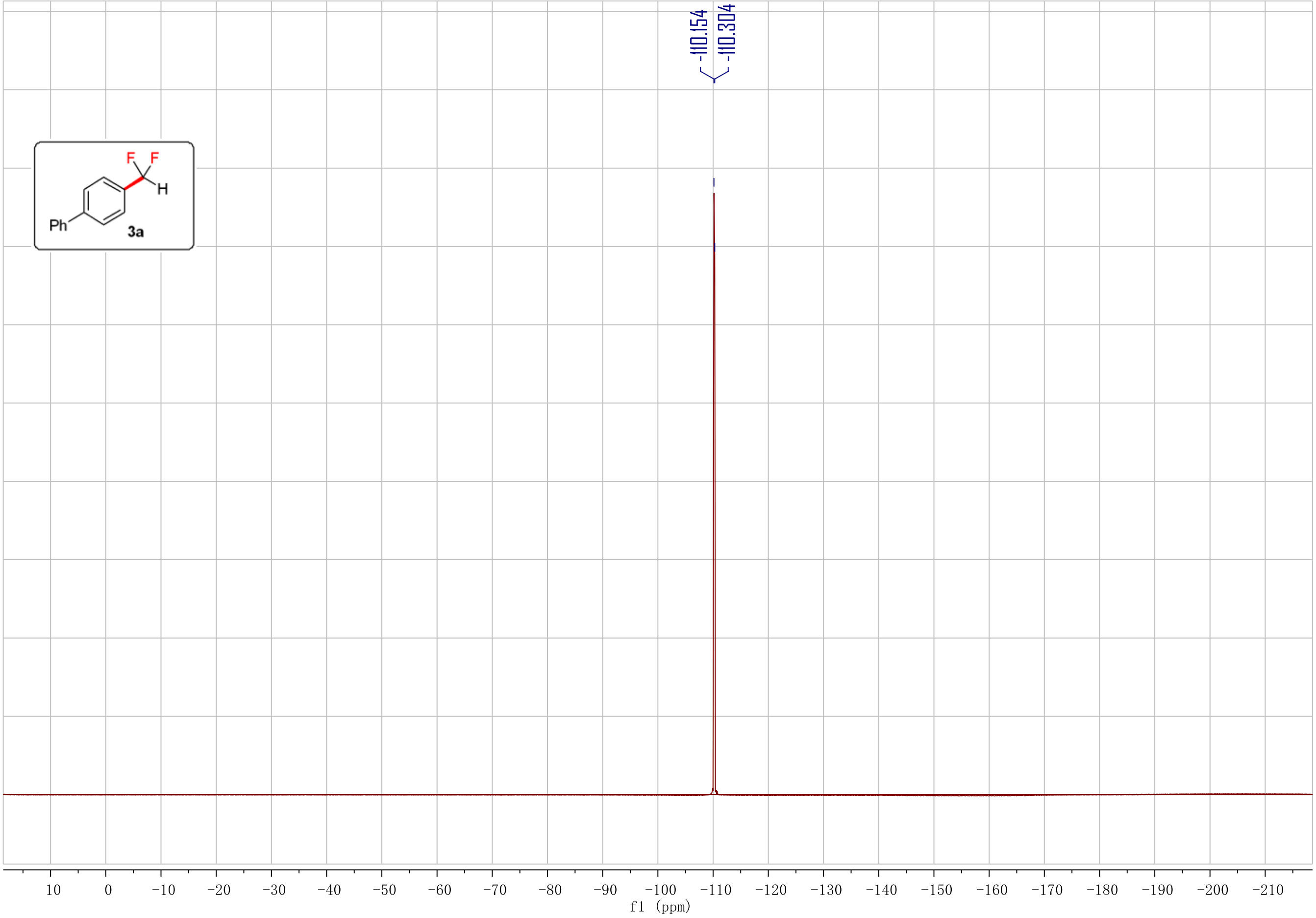
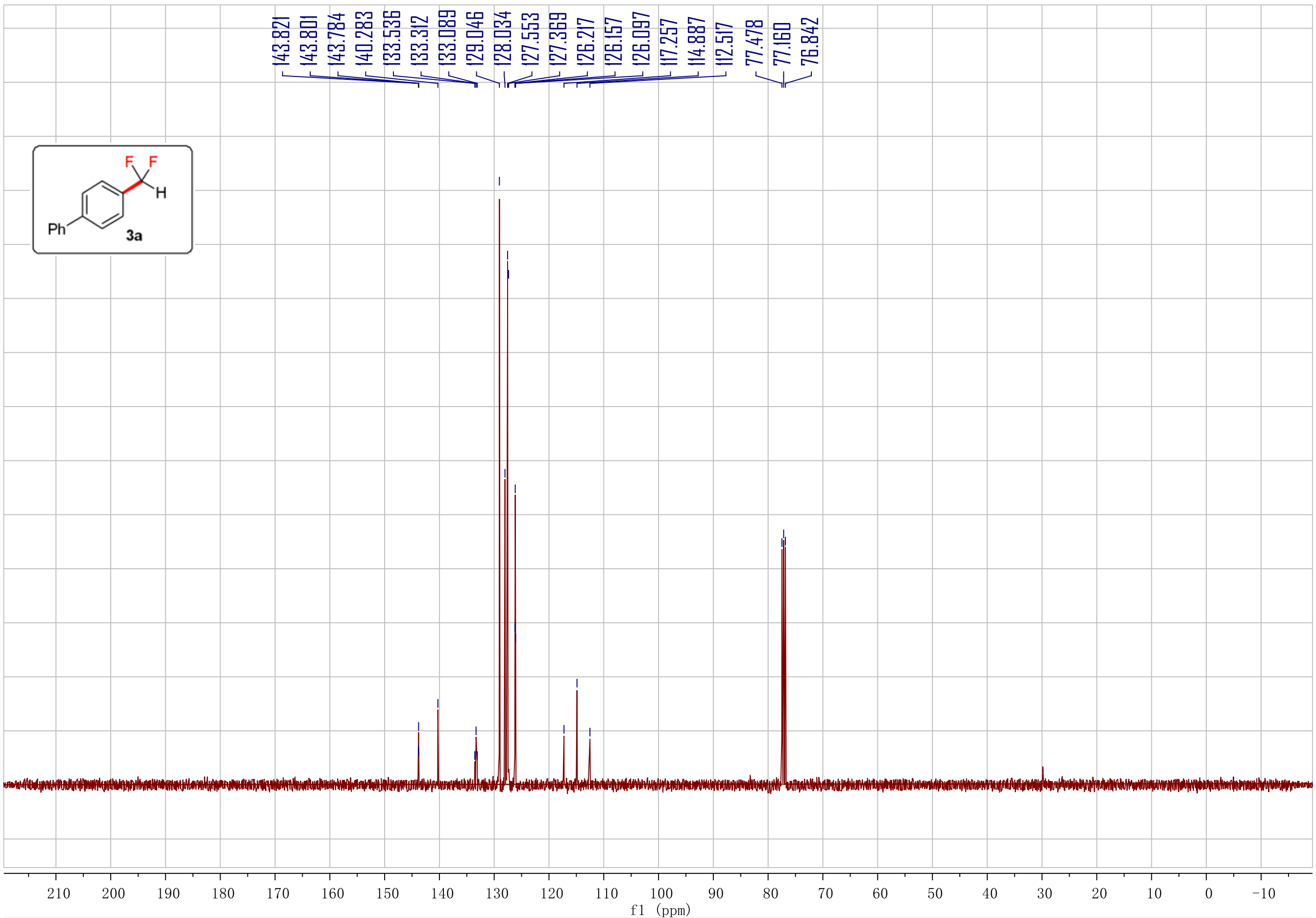
NMR Spectra of New Compounds (^{1}H NMR, ^{19}F NMR, ^{13}C NMR).



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133.312
133.089
129.046
128.034
127.553
127.369
126.217
126.157
126.097
117.257
114.887
112.517
77.478
77.160
76.842
Ph
F
F
H
3a
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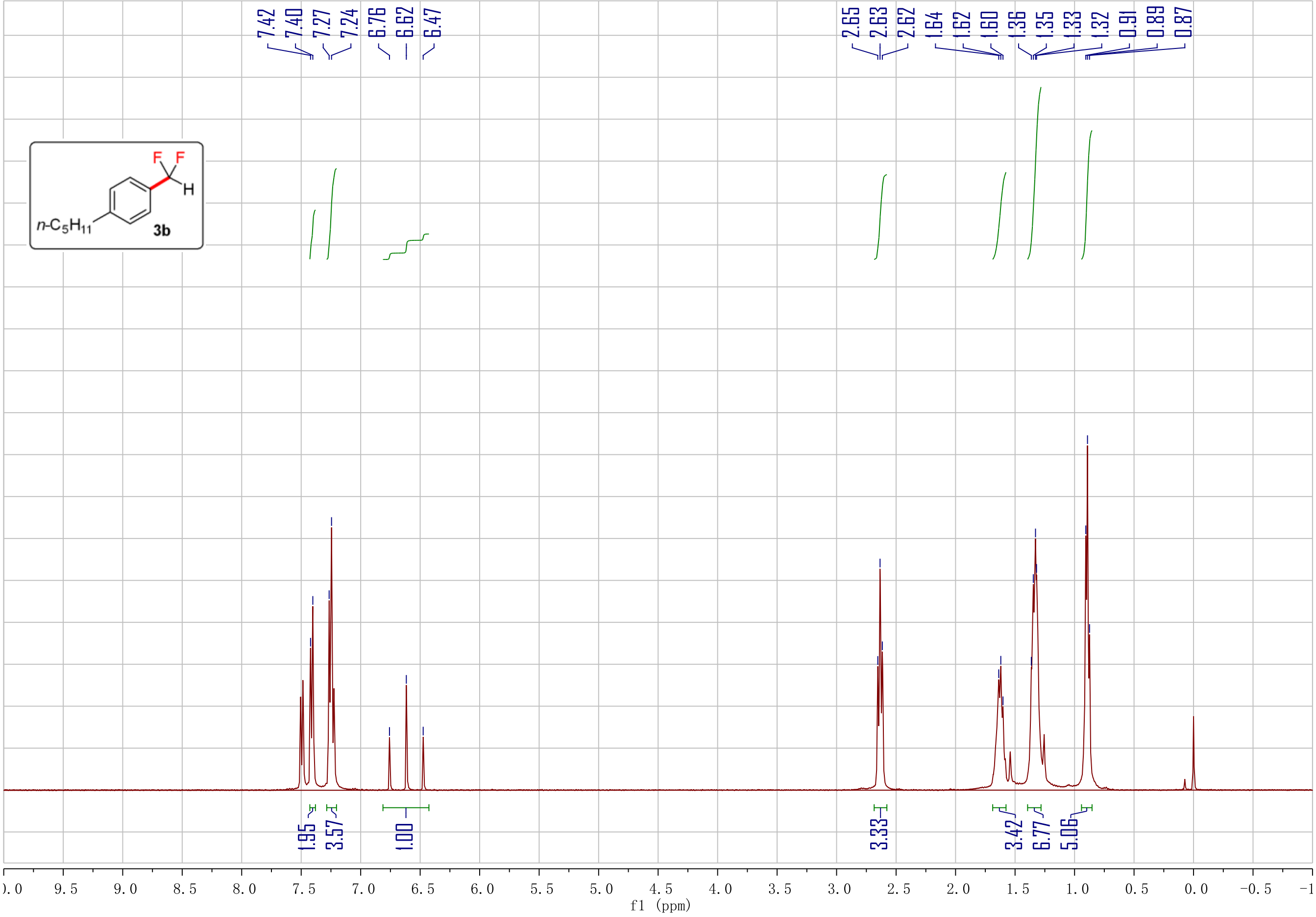
f1 (ppm)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7.27
7.24
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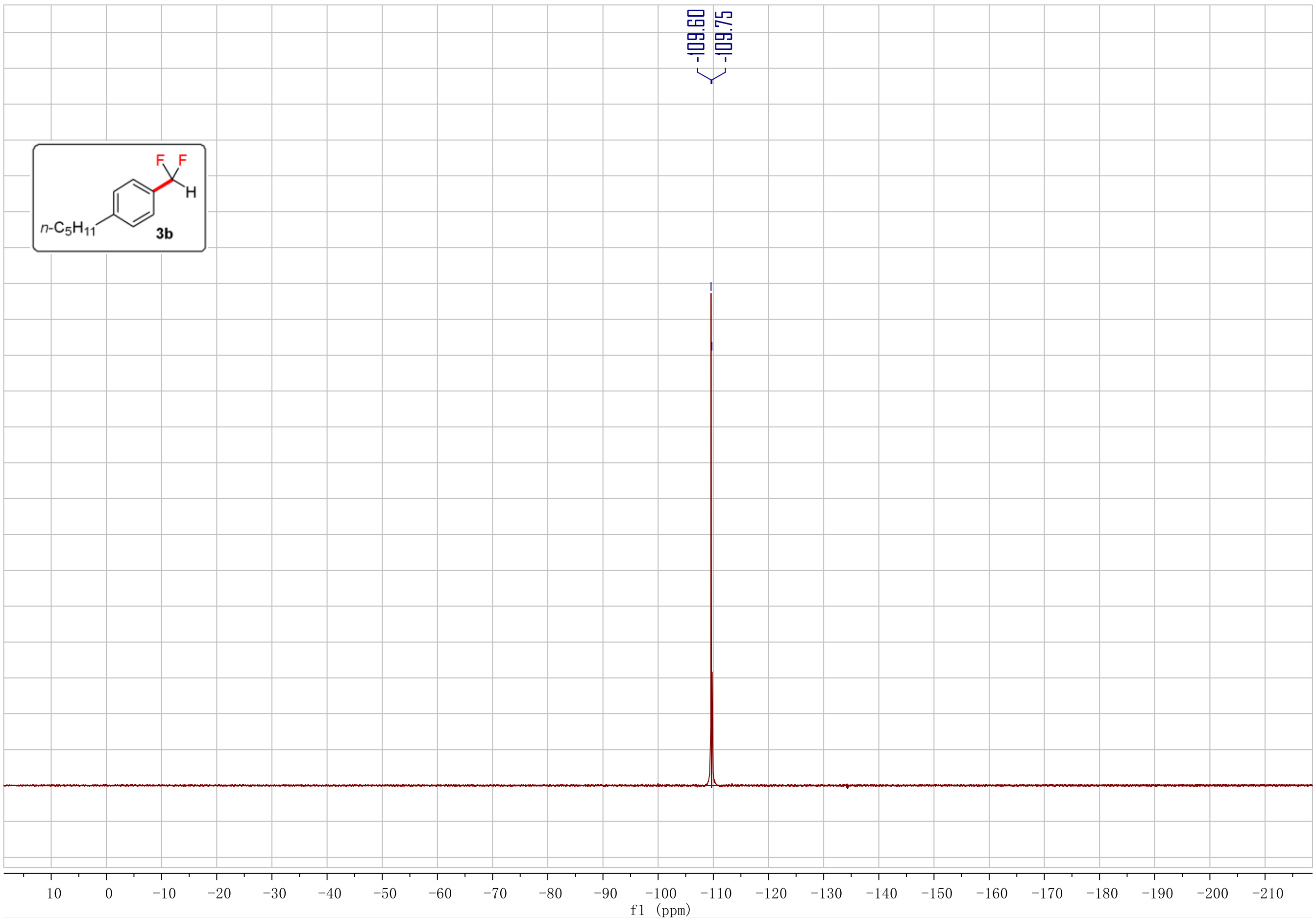
6.62
6.47
2.65
2.63
2.62
1.64
1.62
1.60
1.36
1.35
1.33
1.32
0.91
0.89
0.87
n-C5H11
F
F
H
3b
1.95
3.57
1.00
3.33
3.42
6.77
5.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)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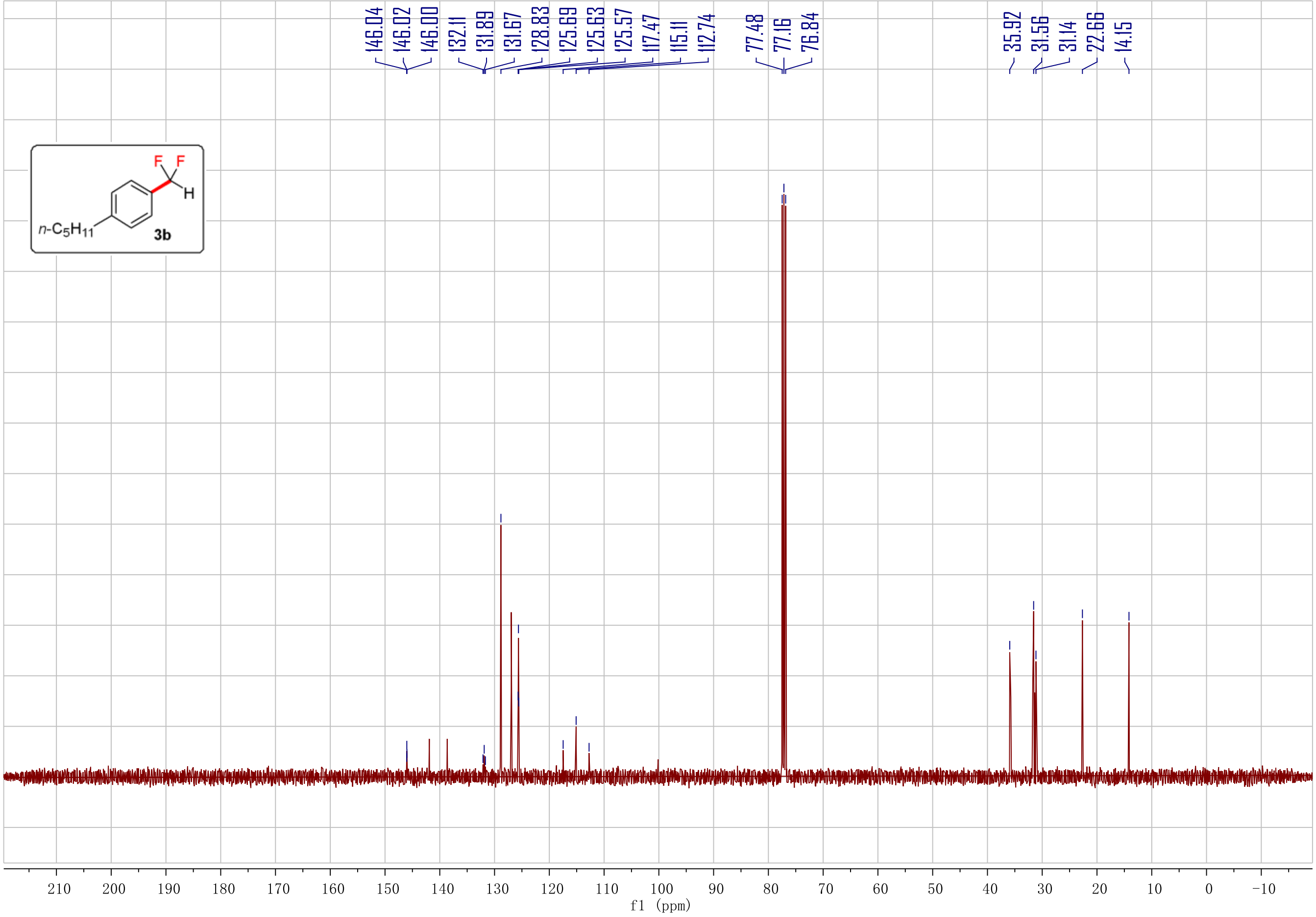
f1 (ppm)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76.84
35.92
31.56
31.14
22.66
14.15
F
F
H
n-C5H11
3b
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190
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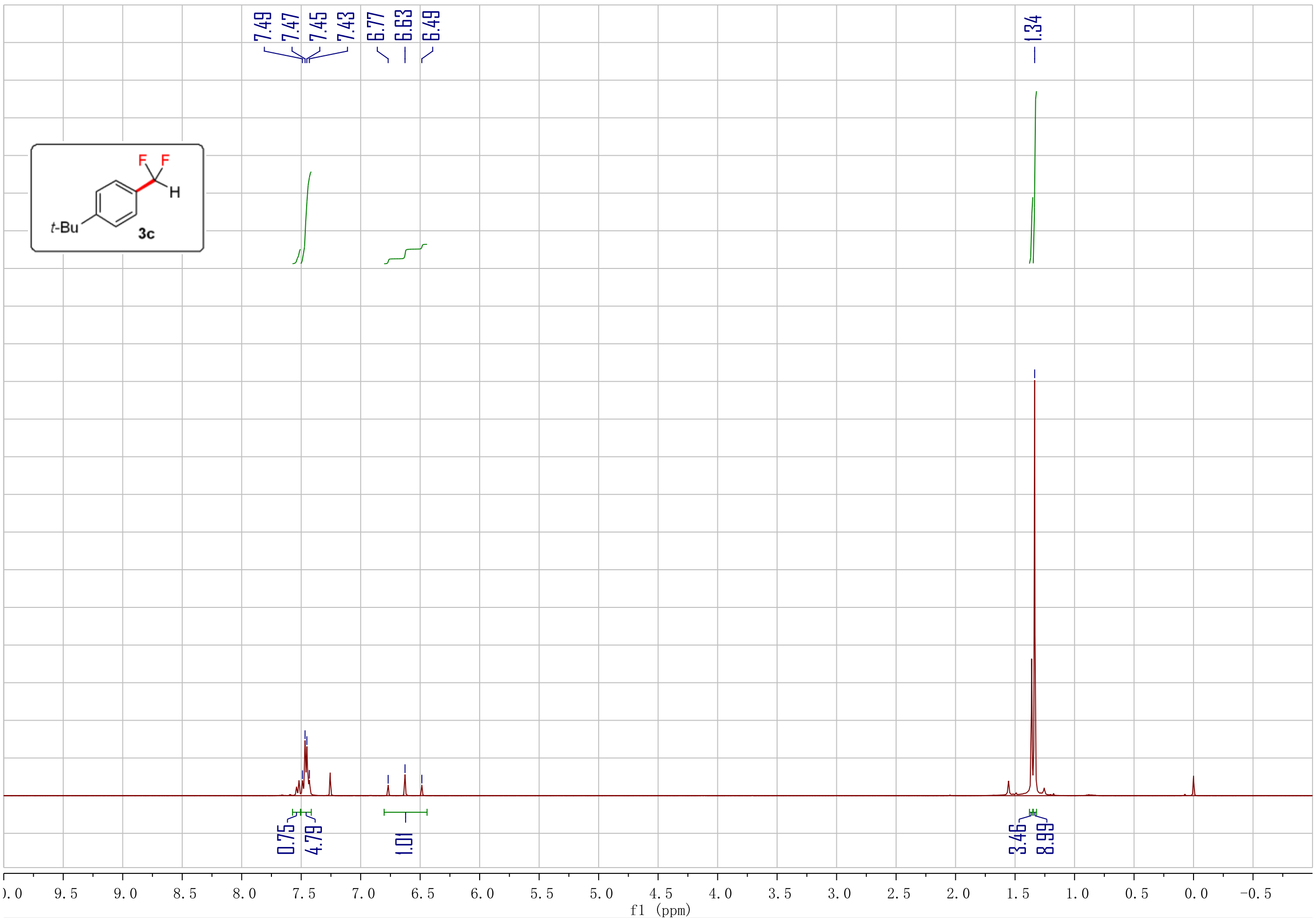
f1 (ppm)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1.01
3.46
8.99
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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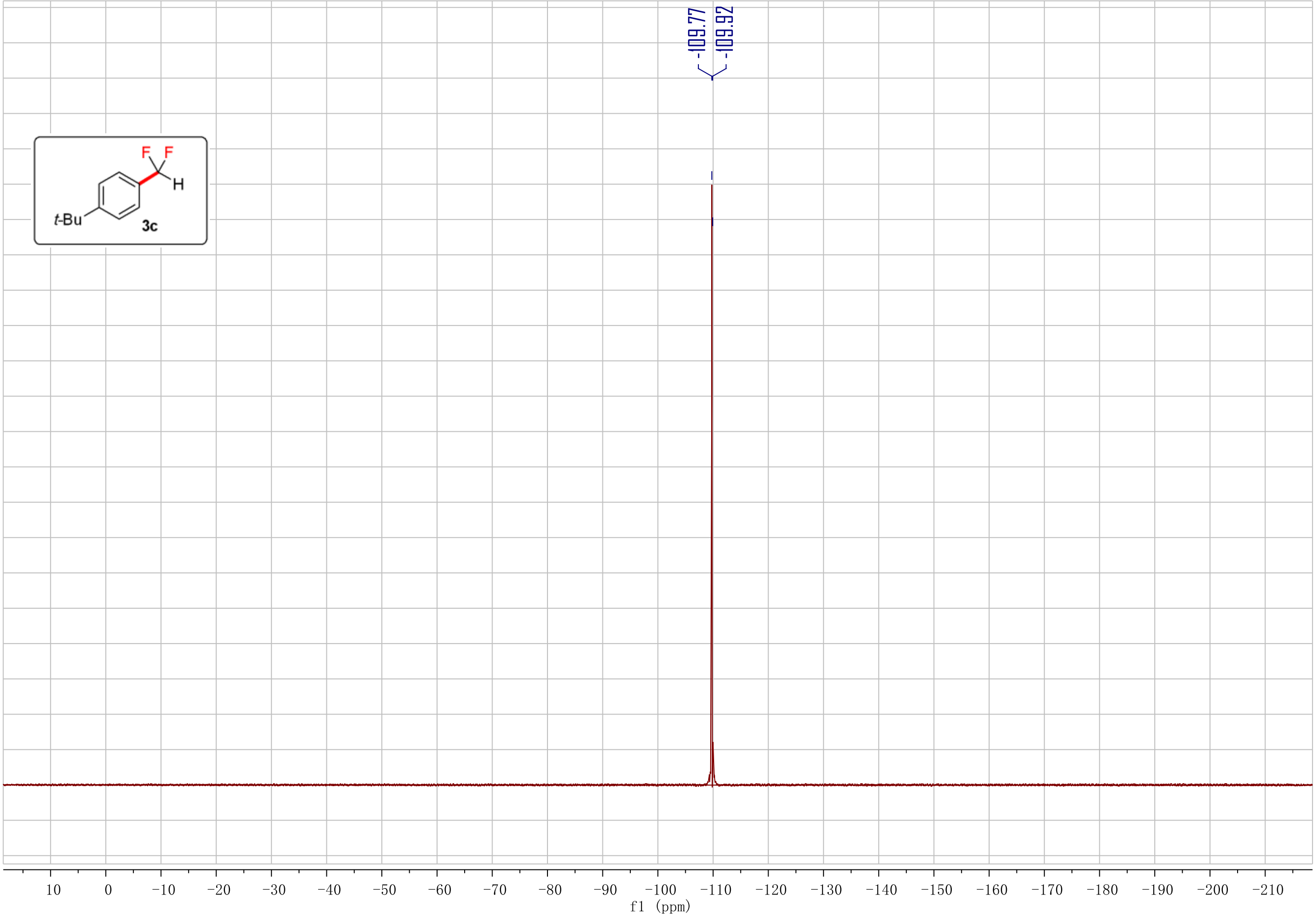
f1 (ppm)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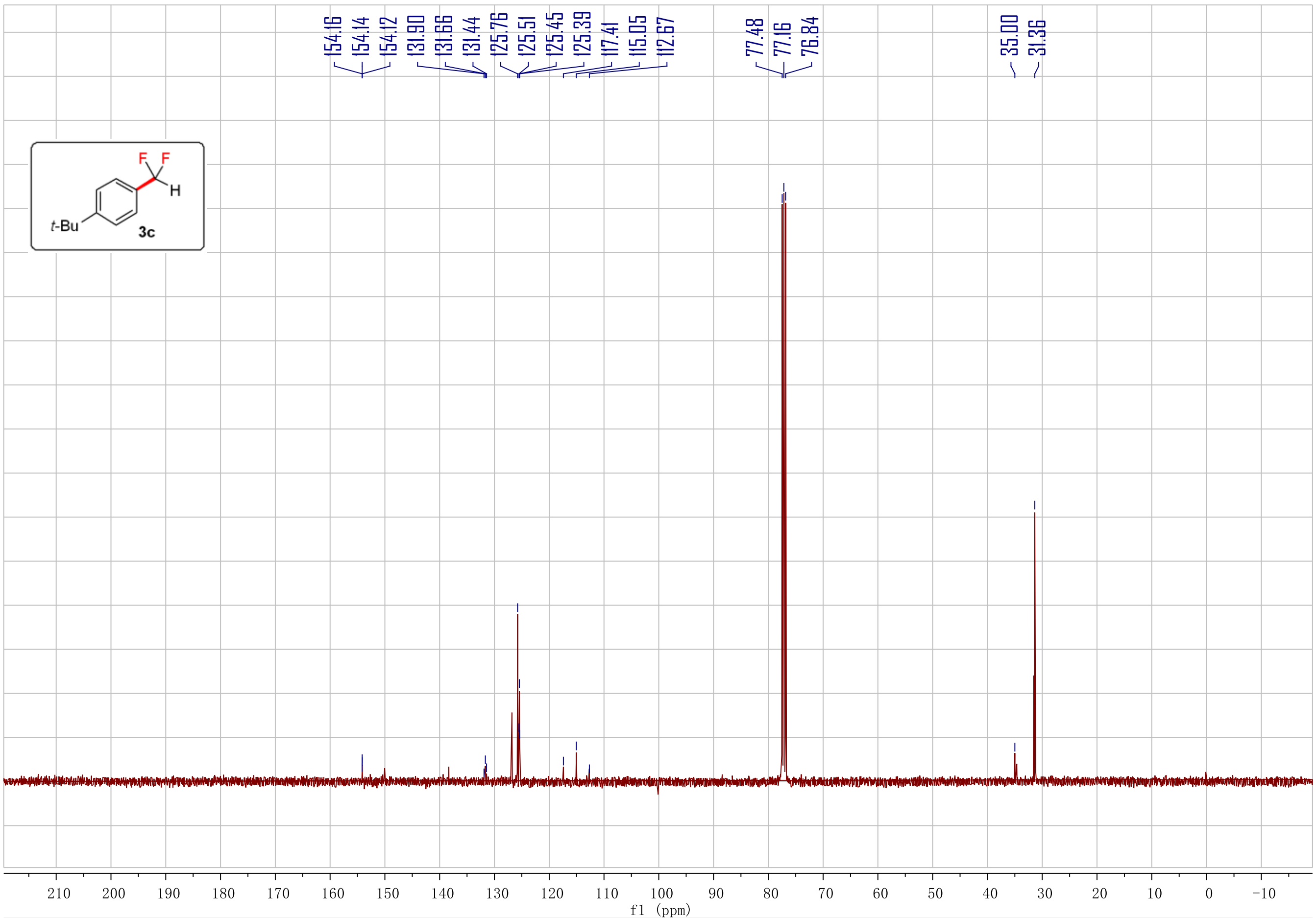
f1 (ppm)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125.39
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112.67
77.48
77.16
76.84
35.00
31.36
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F
H
t-Bu
3c
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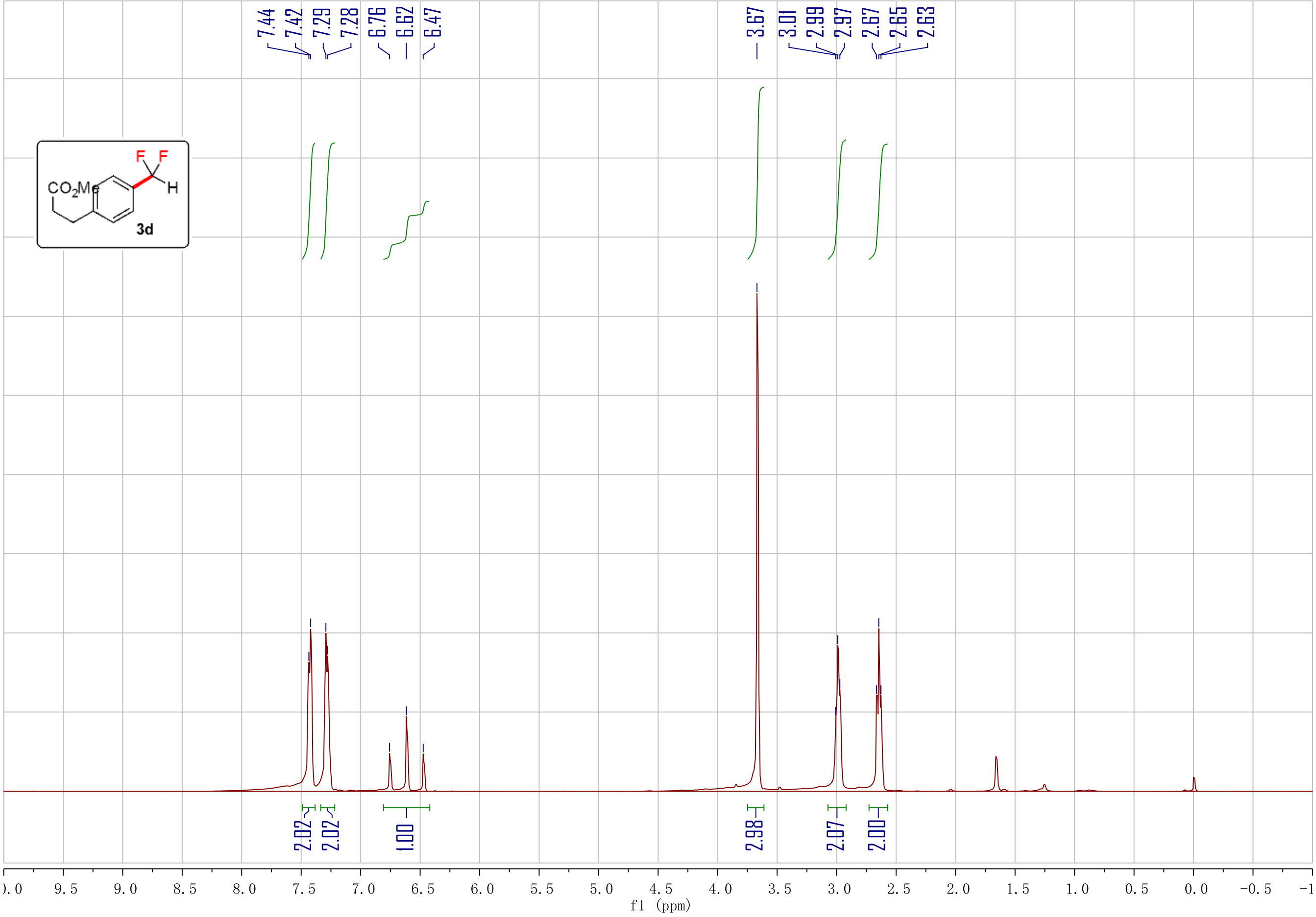
f1 (ppm)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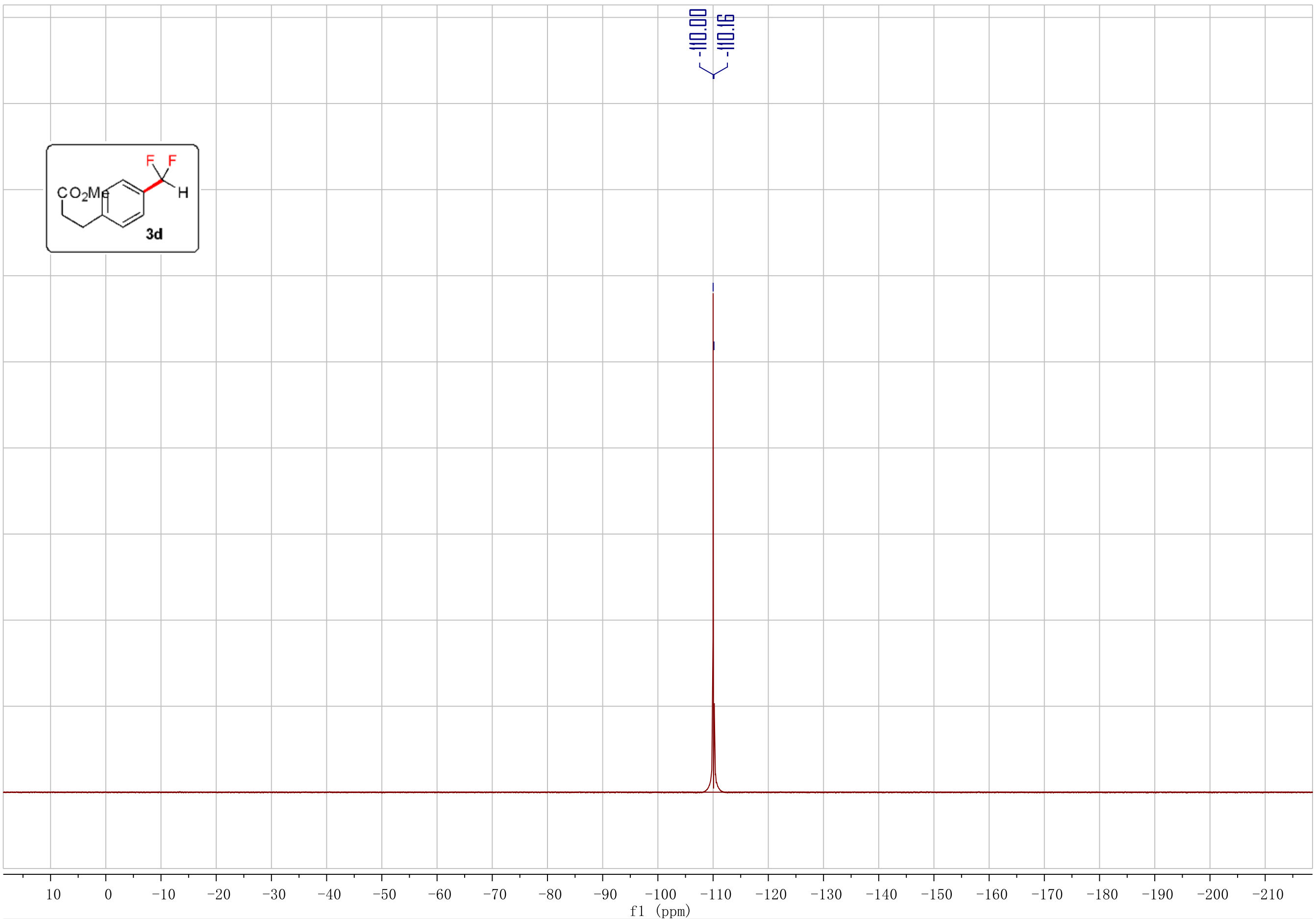
2.65
2.63
F
F
H
CO2Me
3d
2.02
2.02
1.00
2.98
2.07
2.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)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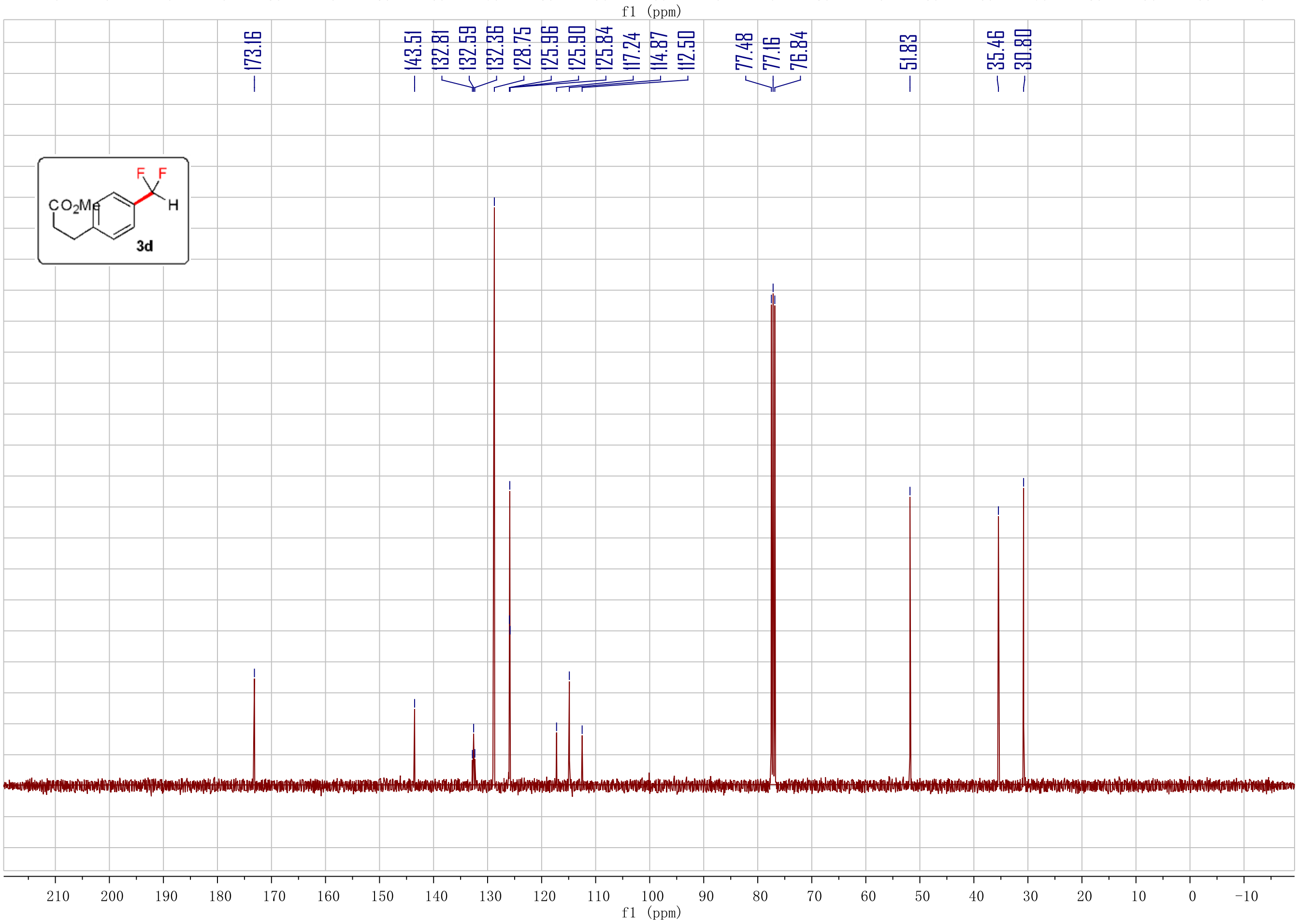
f1 (ppm)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77.48
77.16
76.84
51.83
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F
F
H
CO2Me
3d
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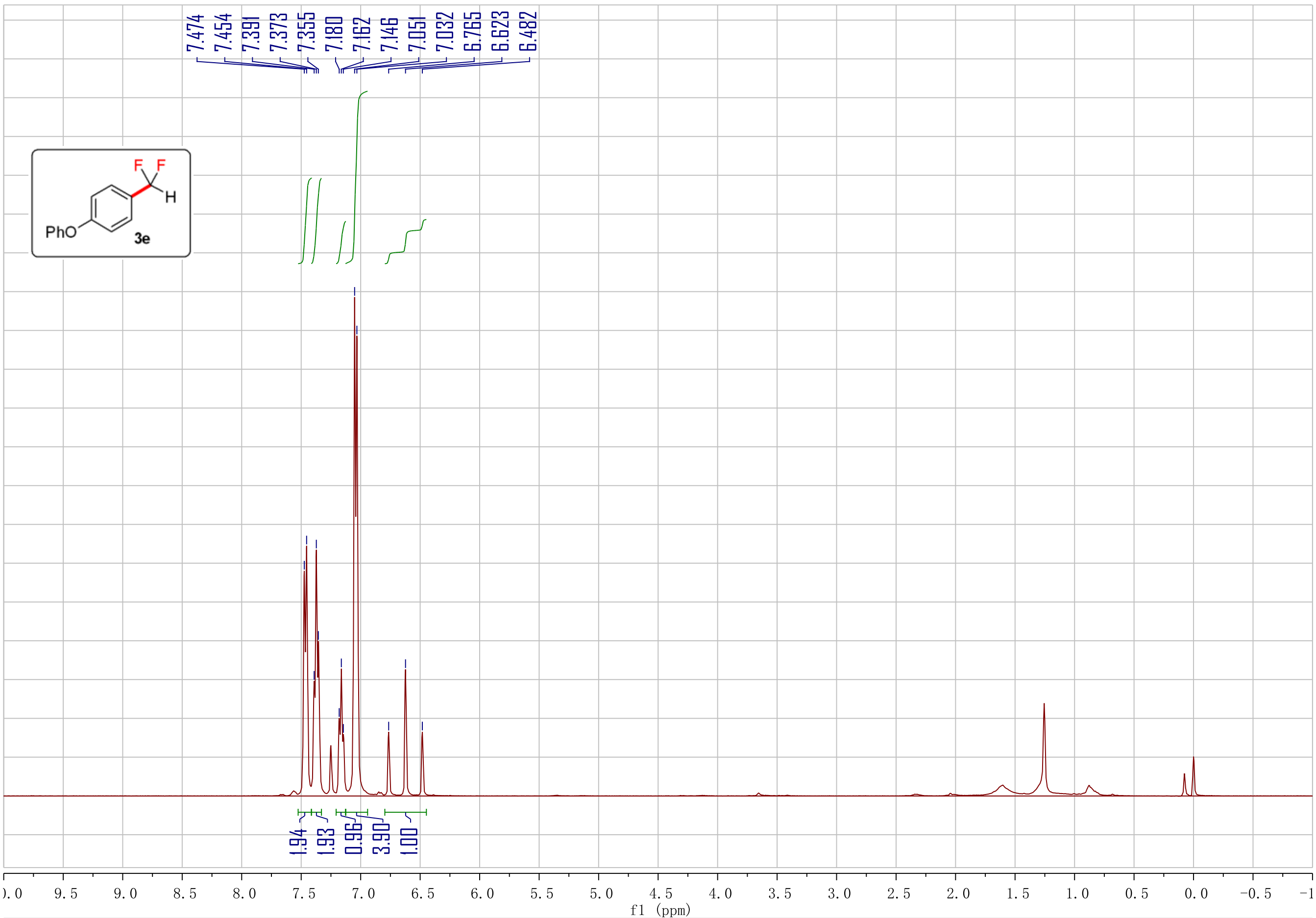
f1 (ppm)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F
H
PhO
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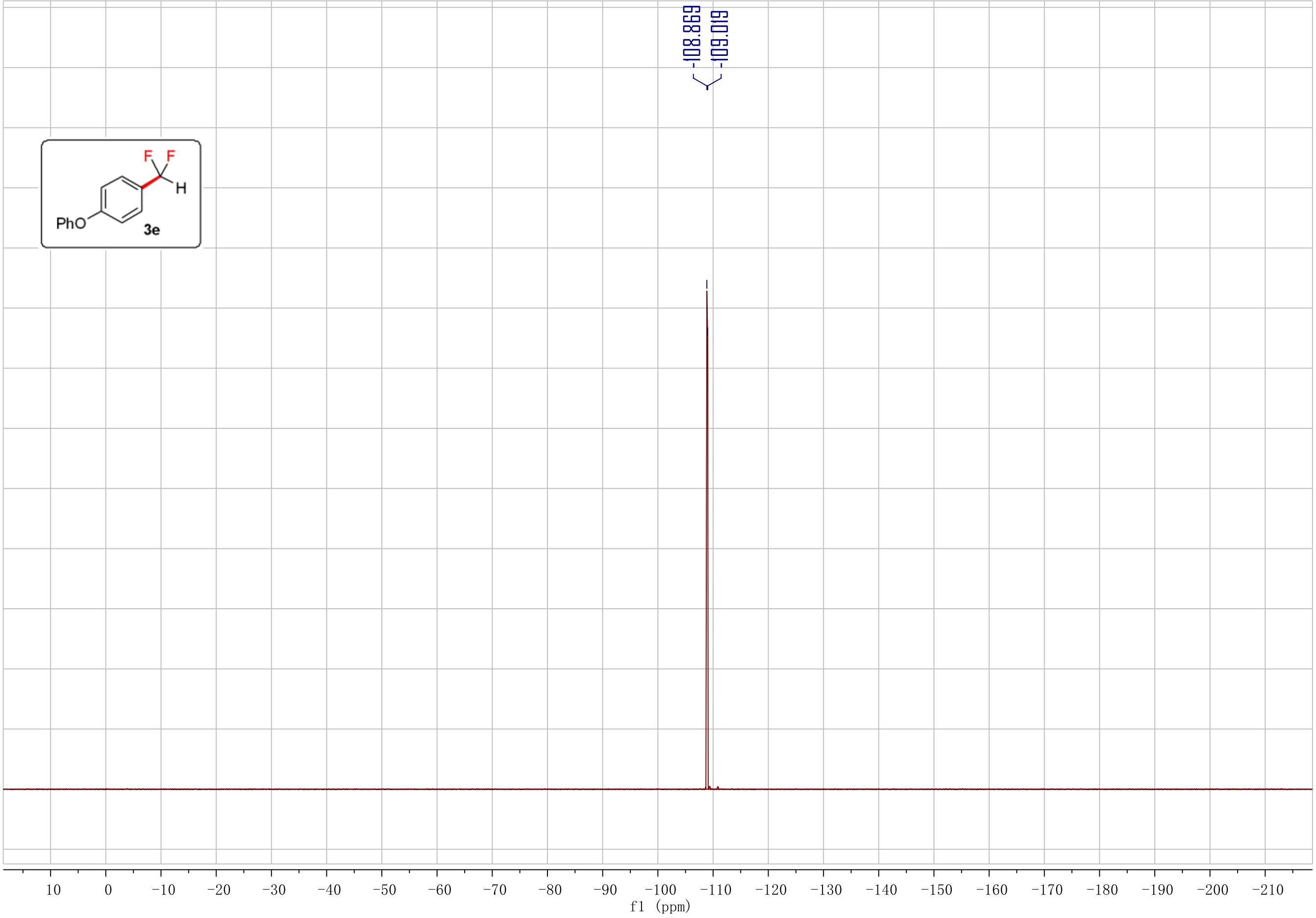
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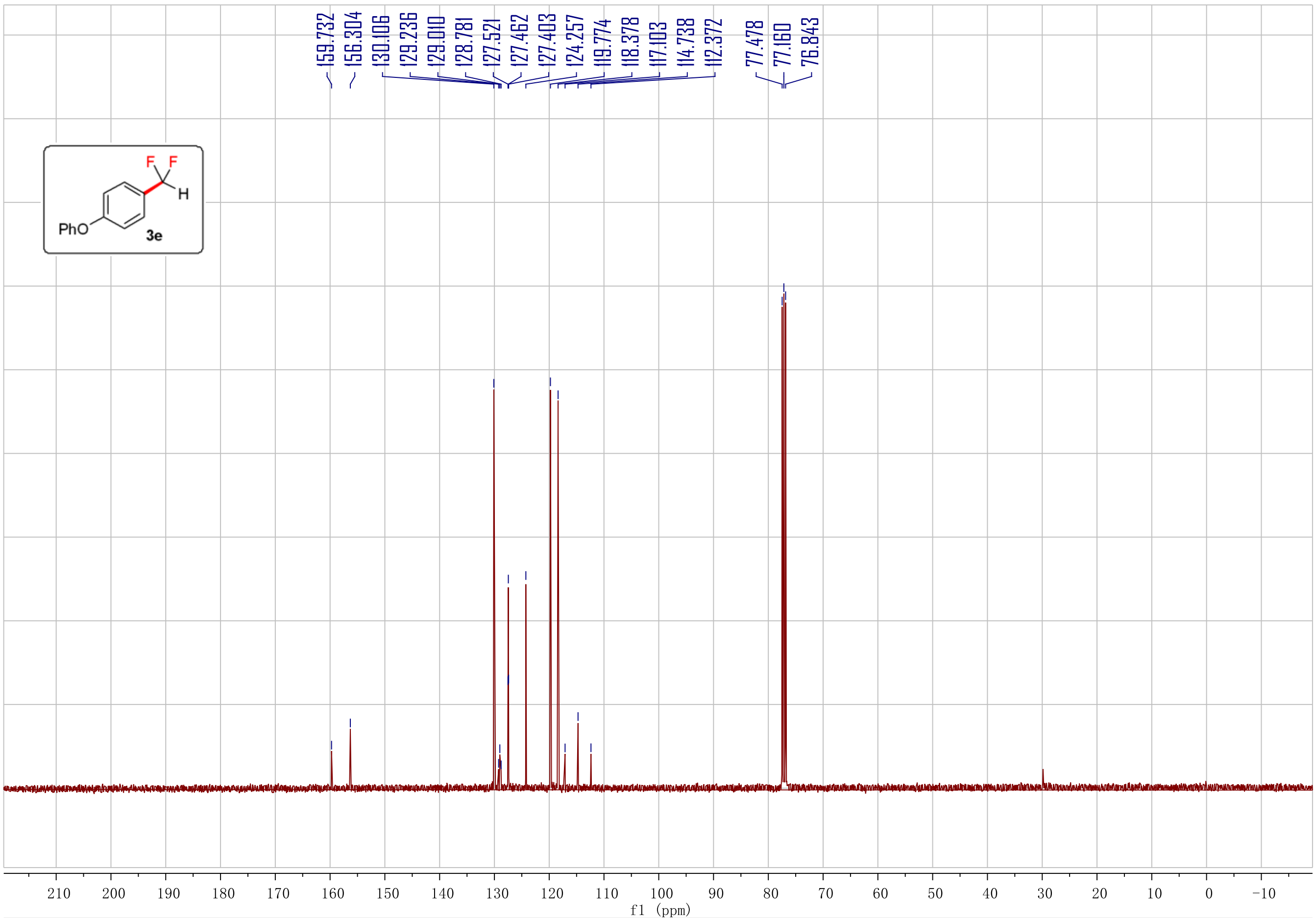
f1 (ppm)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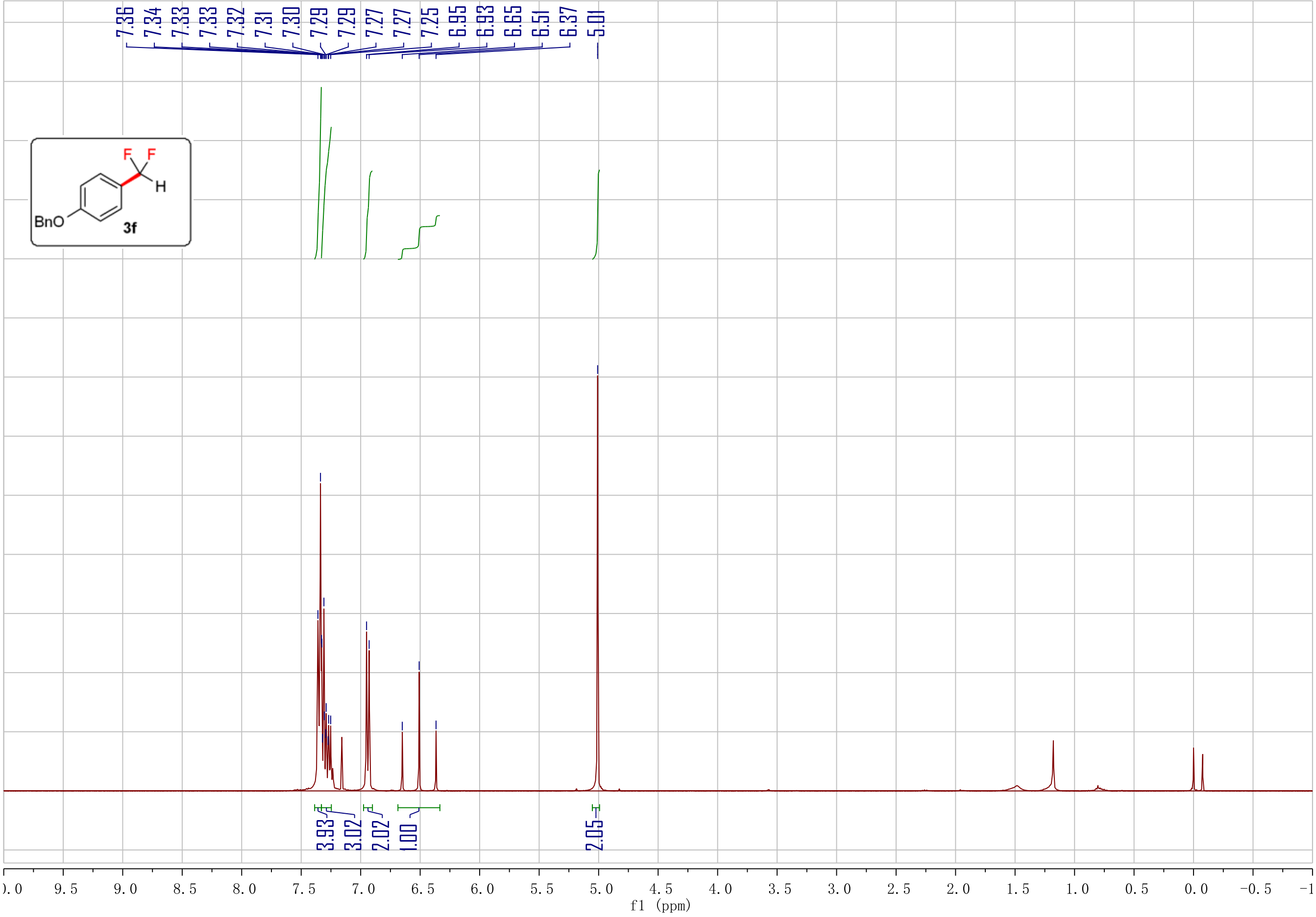
f1 (ppm)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6.93
6.65
6.51
6.37
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F
F
H
BnO
3f
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2.02
1.00
2.05
.0
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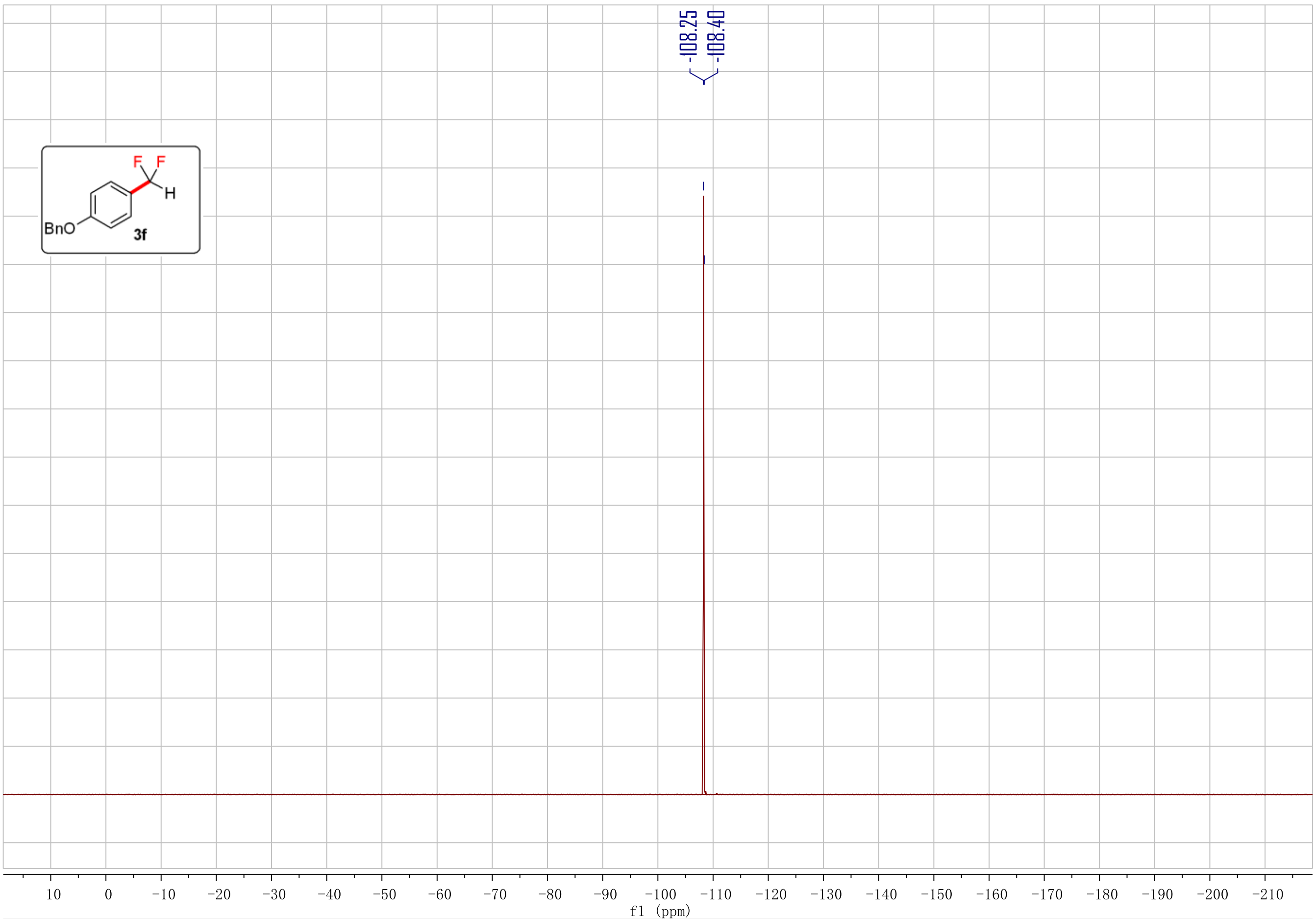
f1 (ppm)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F
H
BnO
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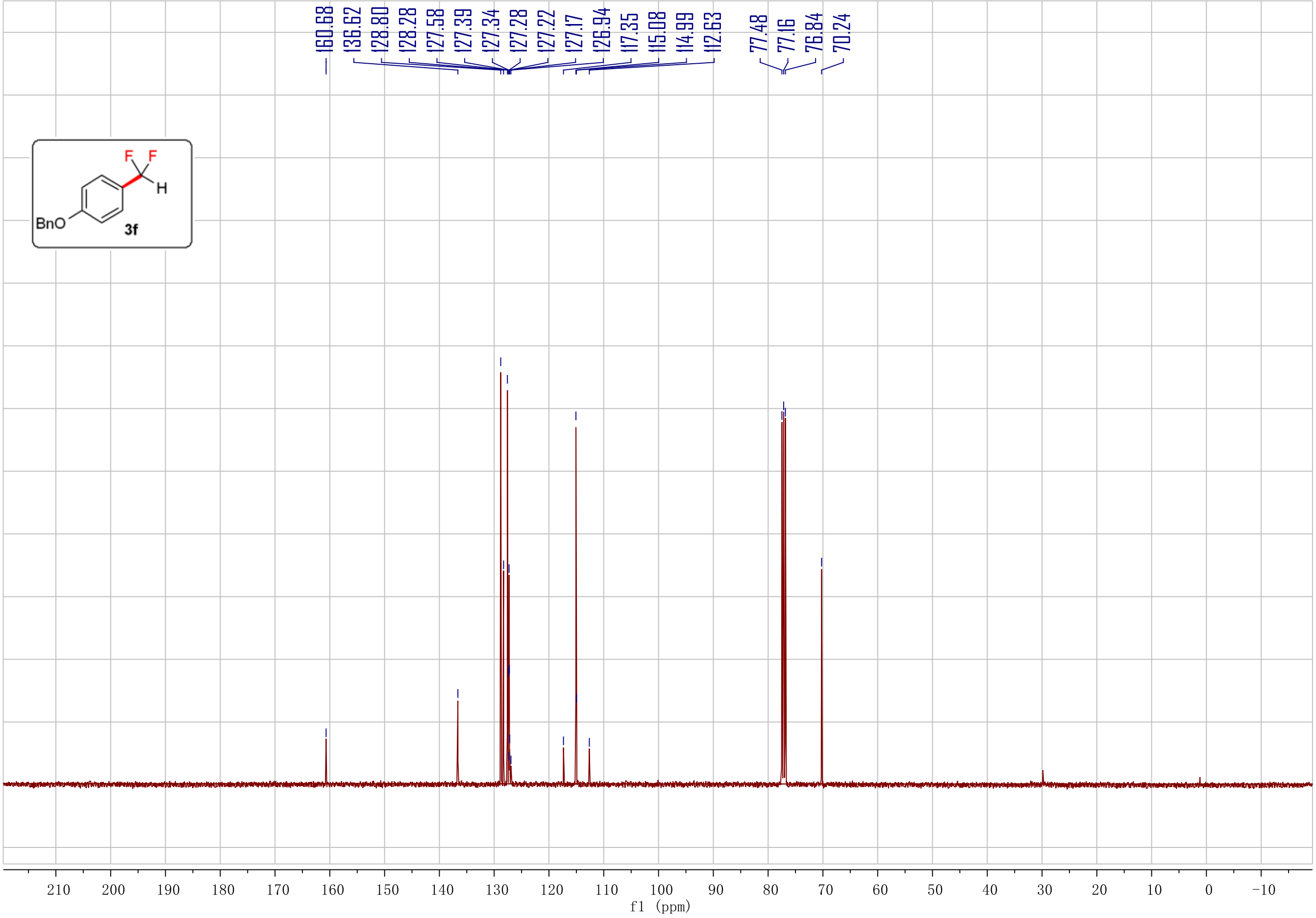
f1 (ppm)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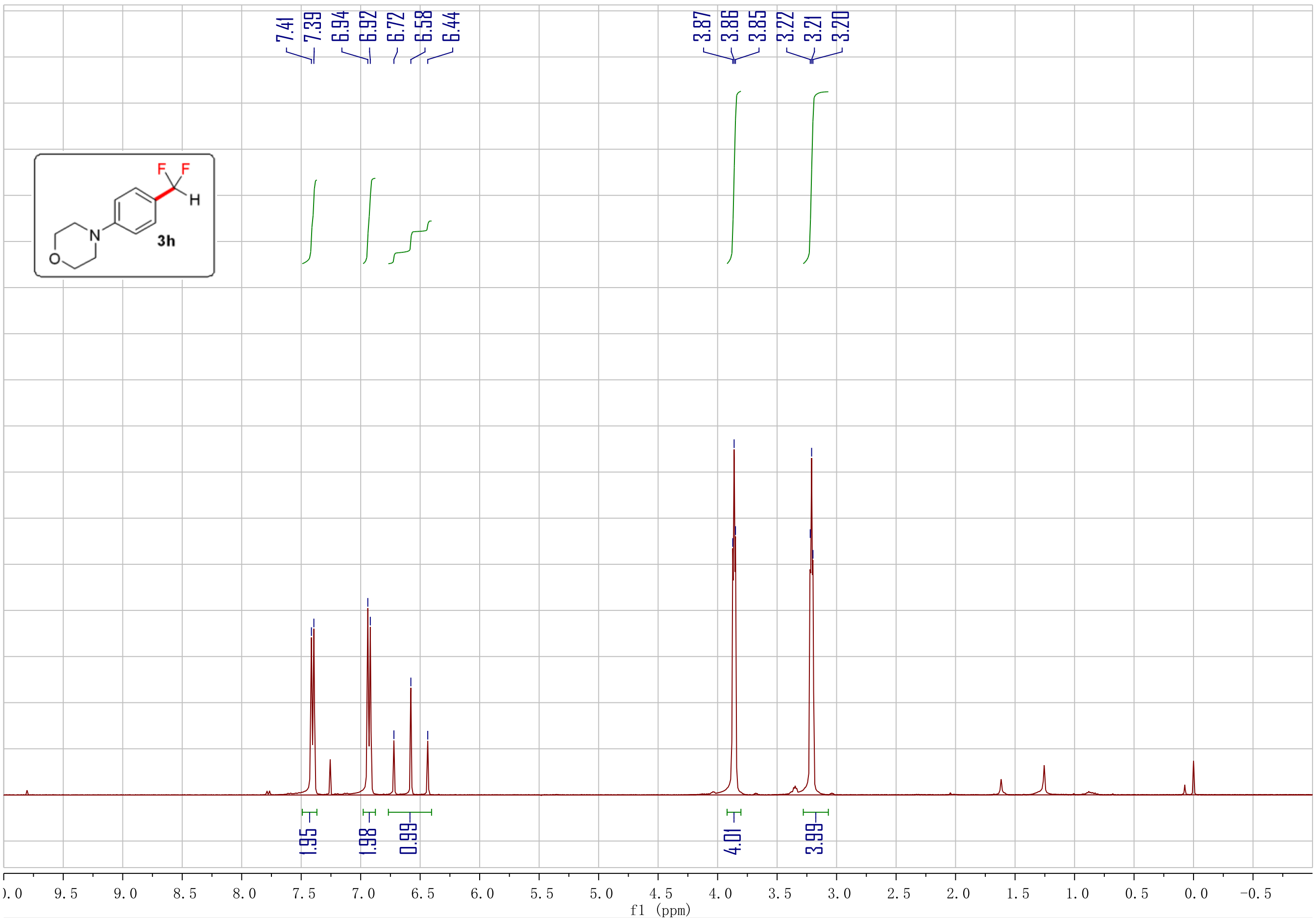
114.99
112.63
77.48
77.16
76.84
70.24
F
F
H
BnO
3f
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)



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F
F
H
N
O
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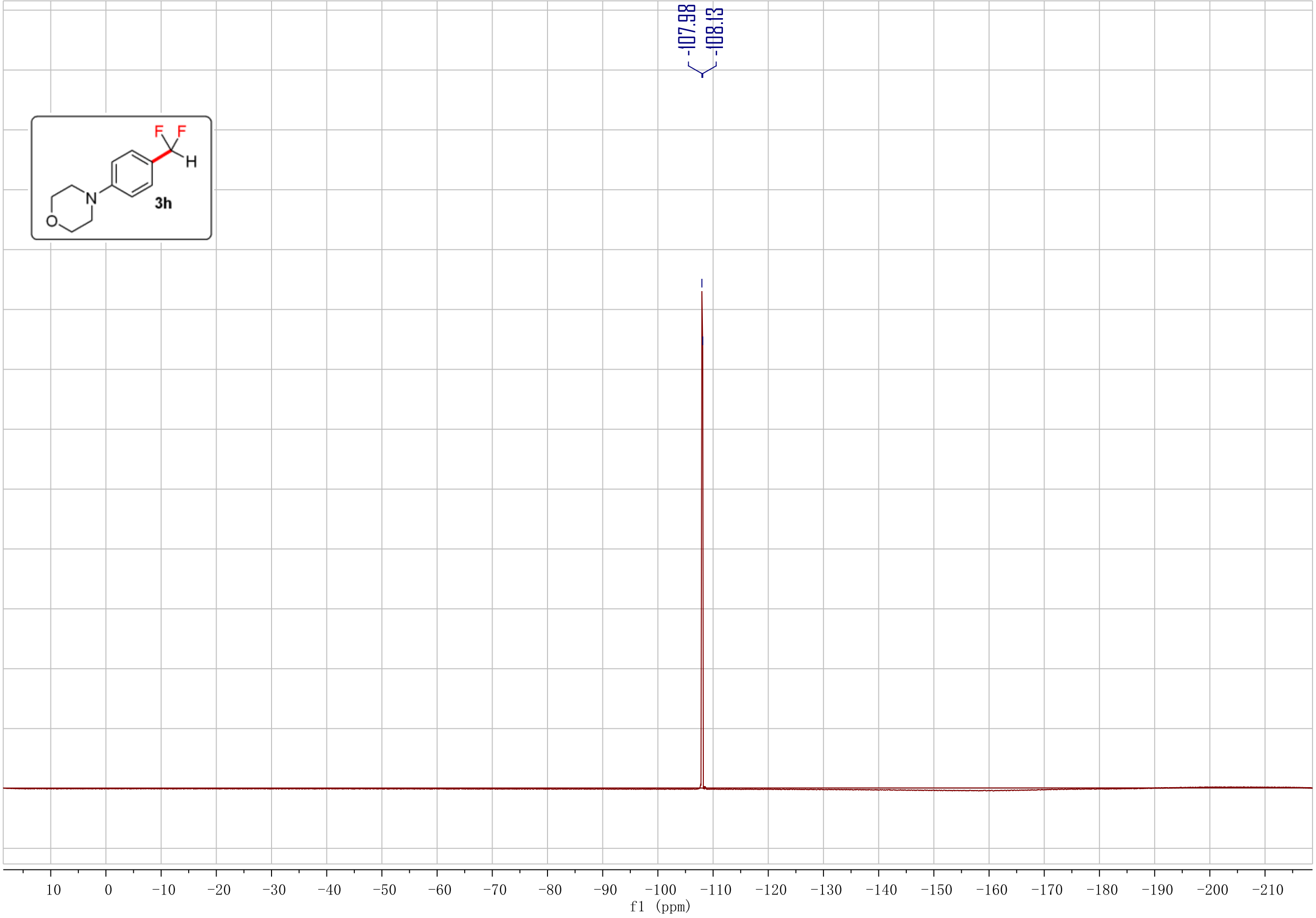

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F
H
N
O
3h
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−70
−80
−90
−100
−110
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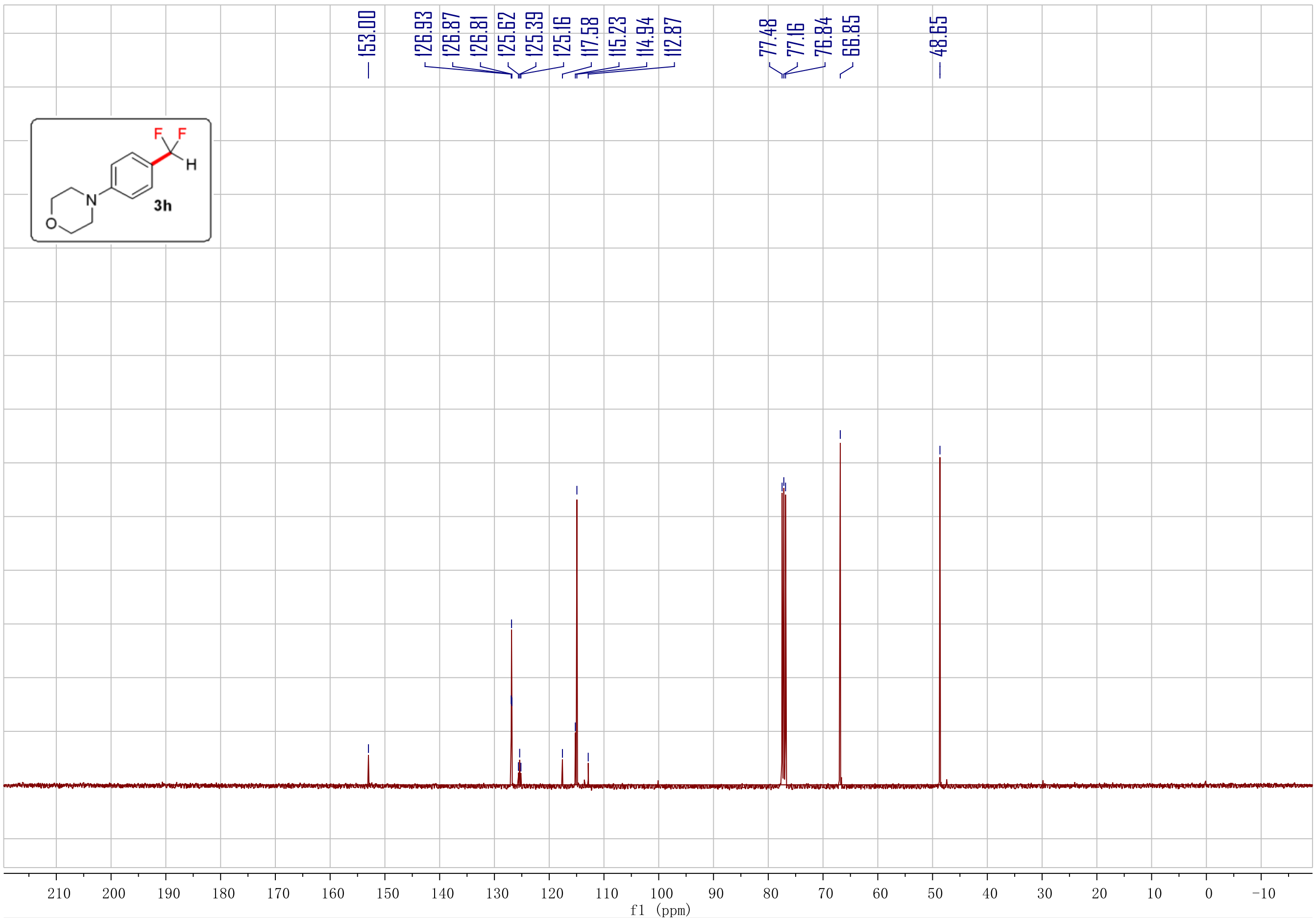
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)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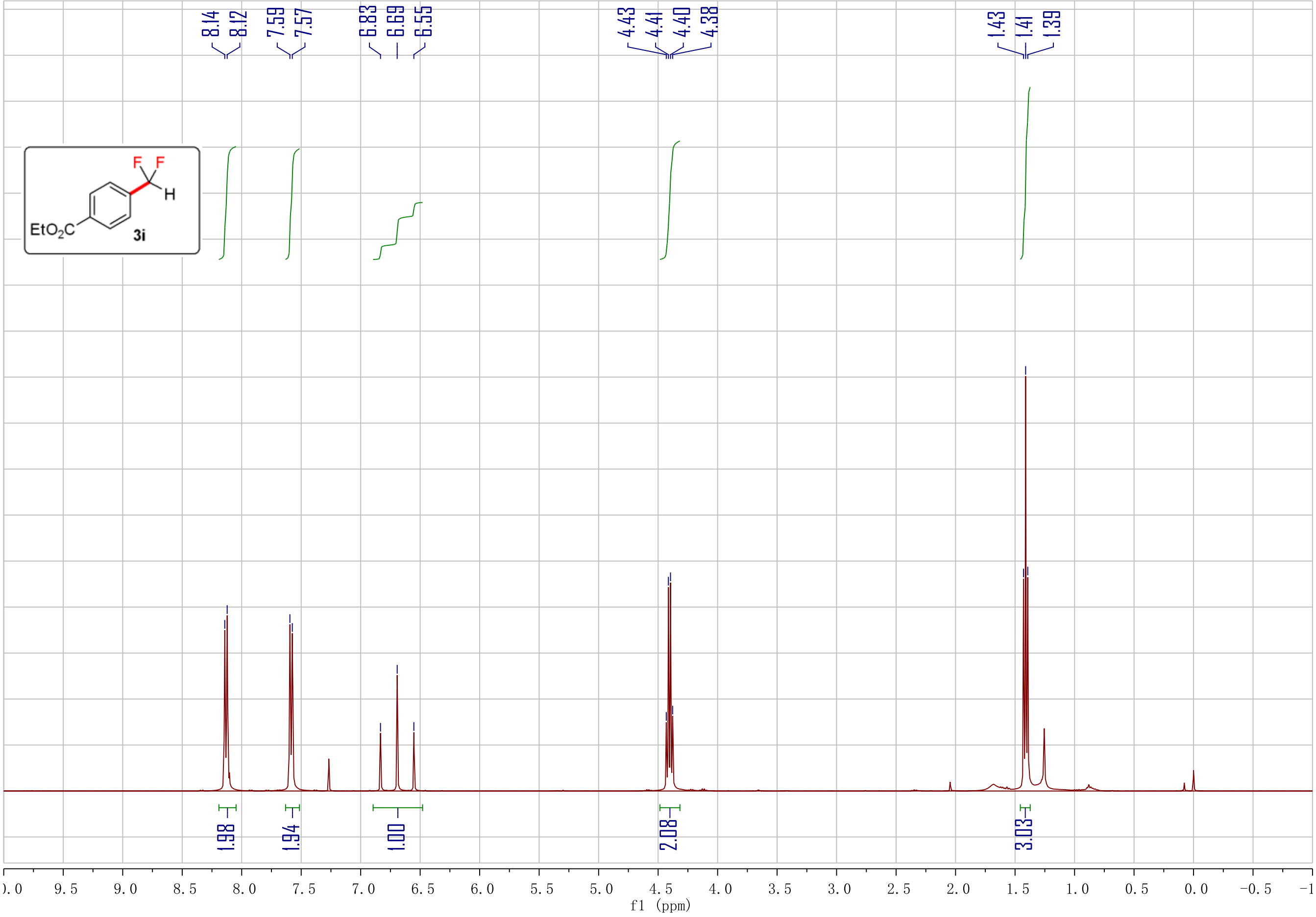
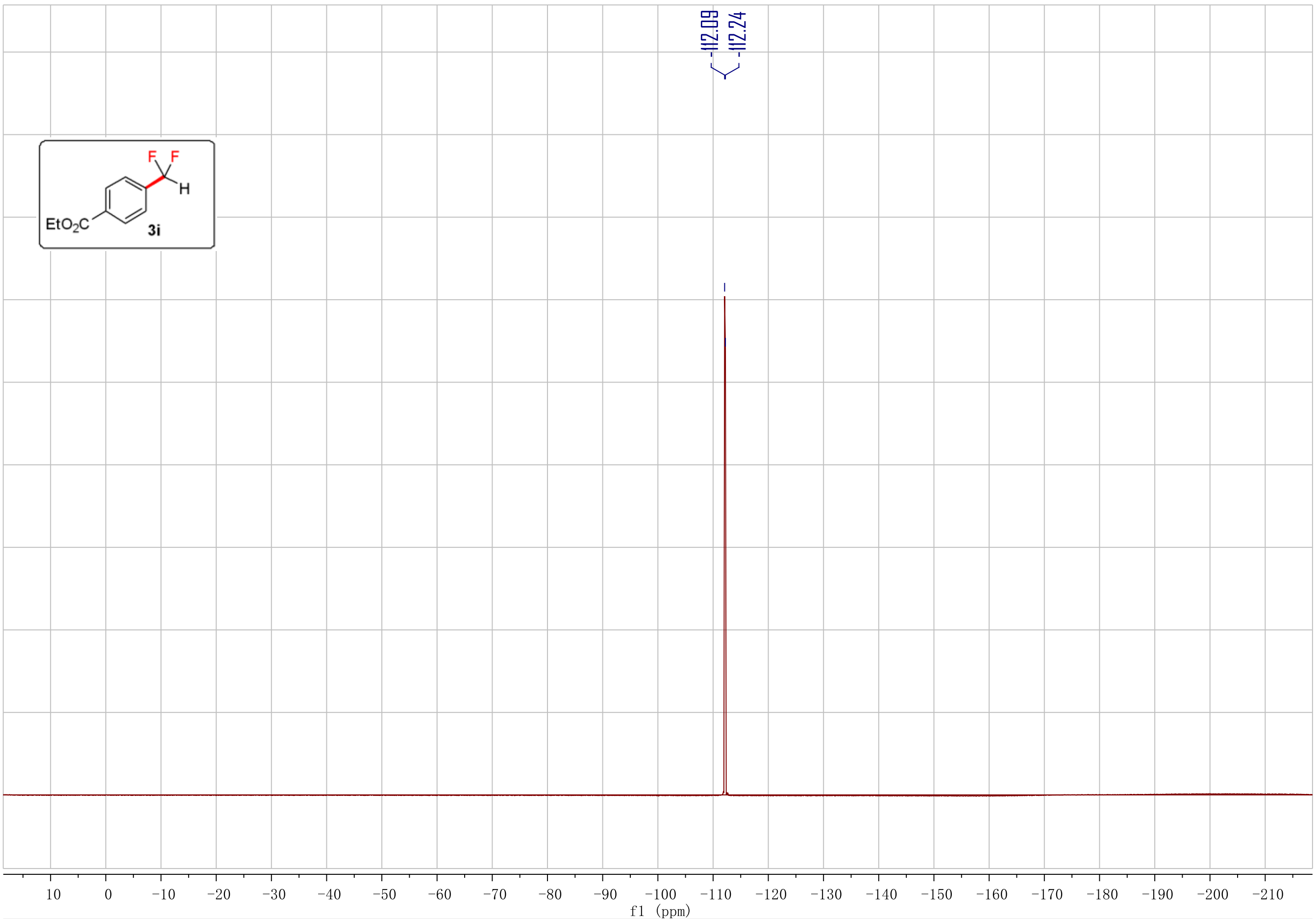
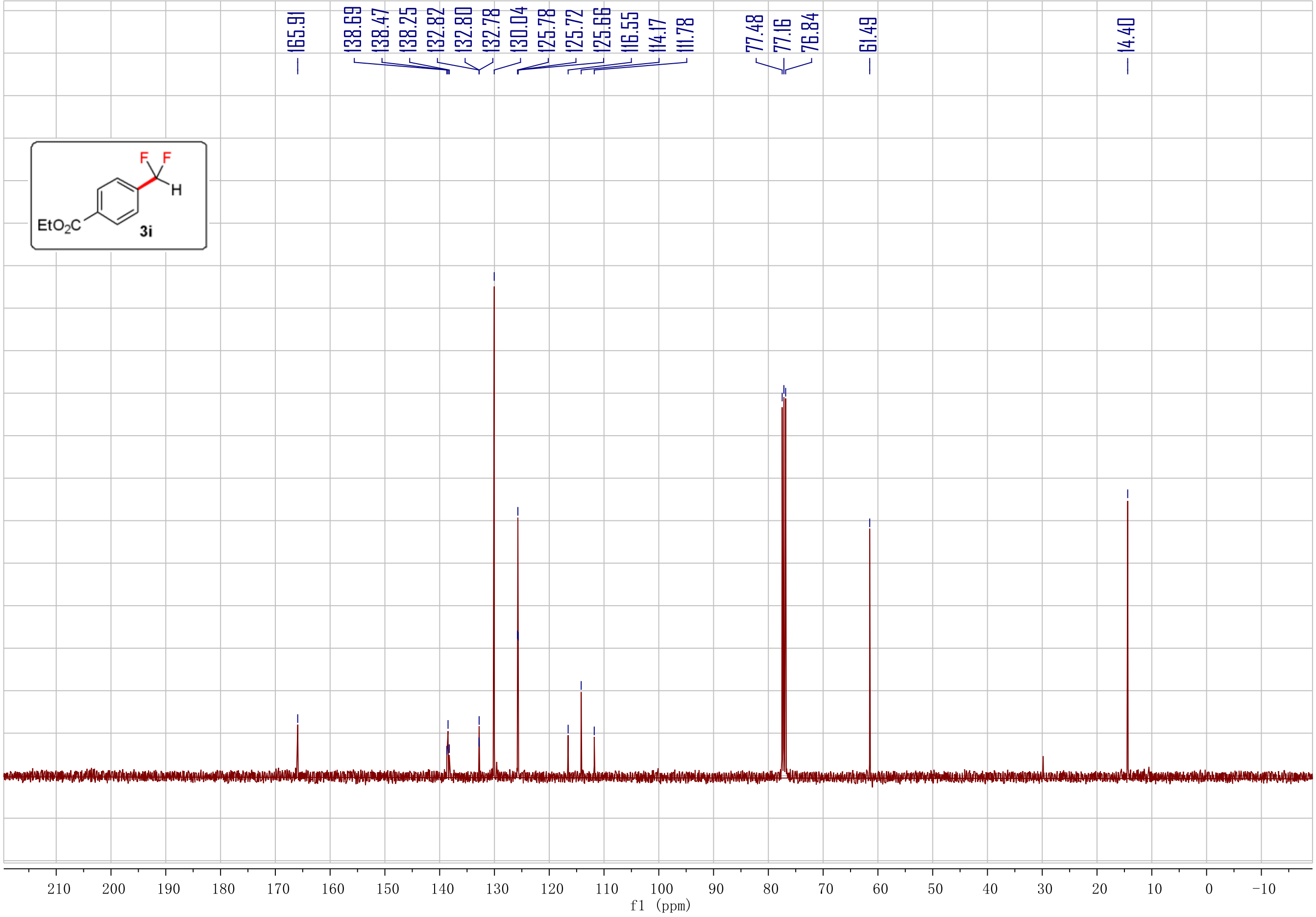
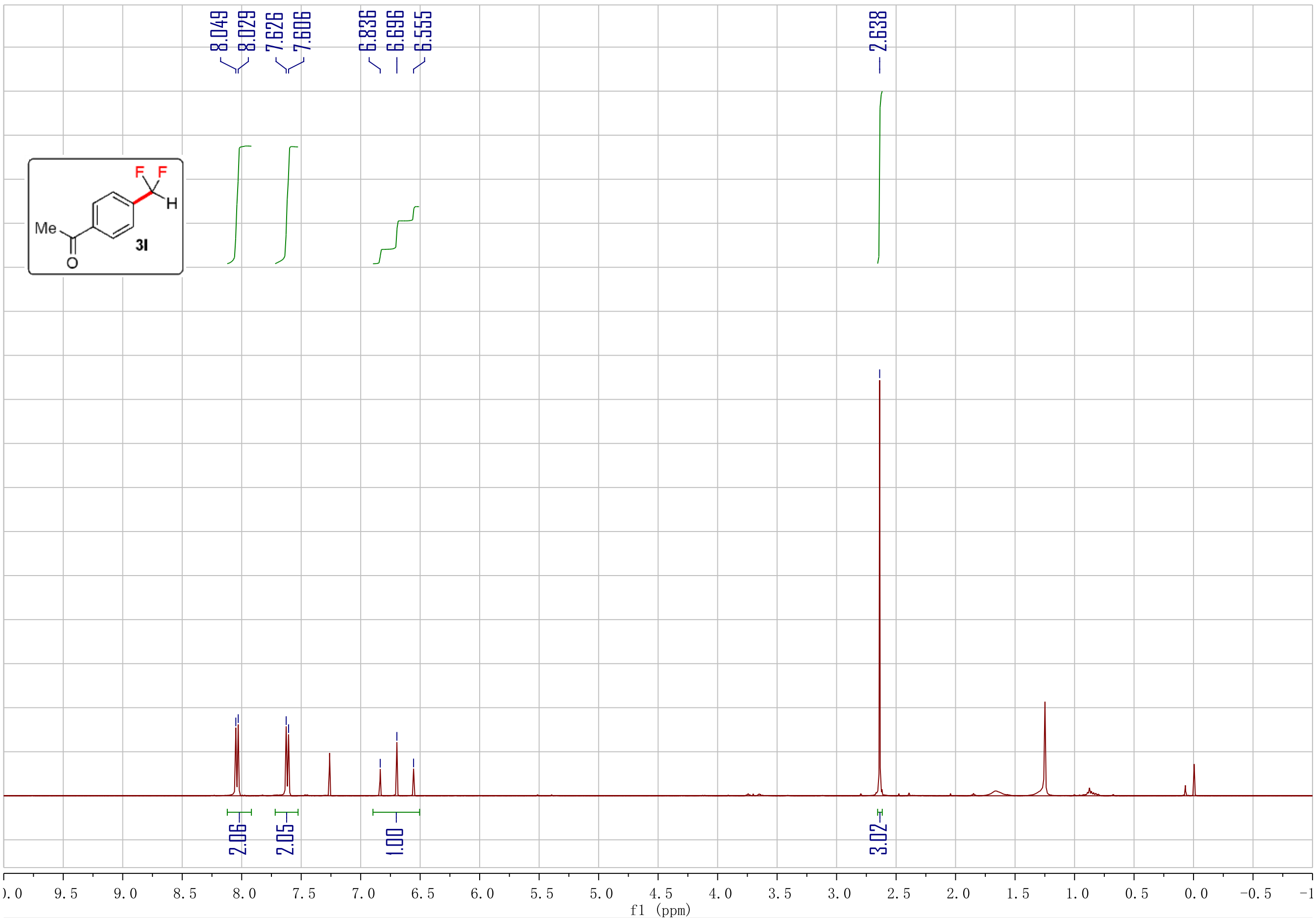
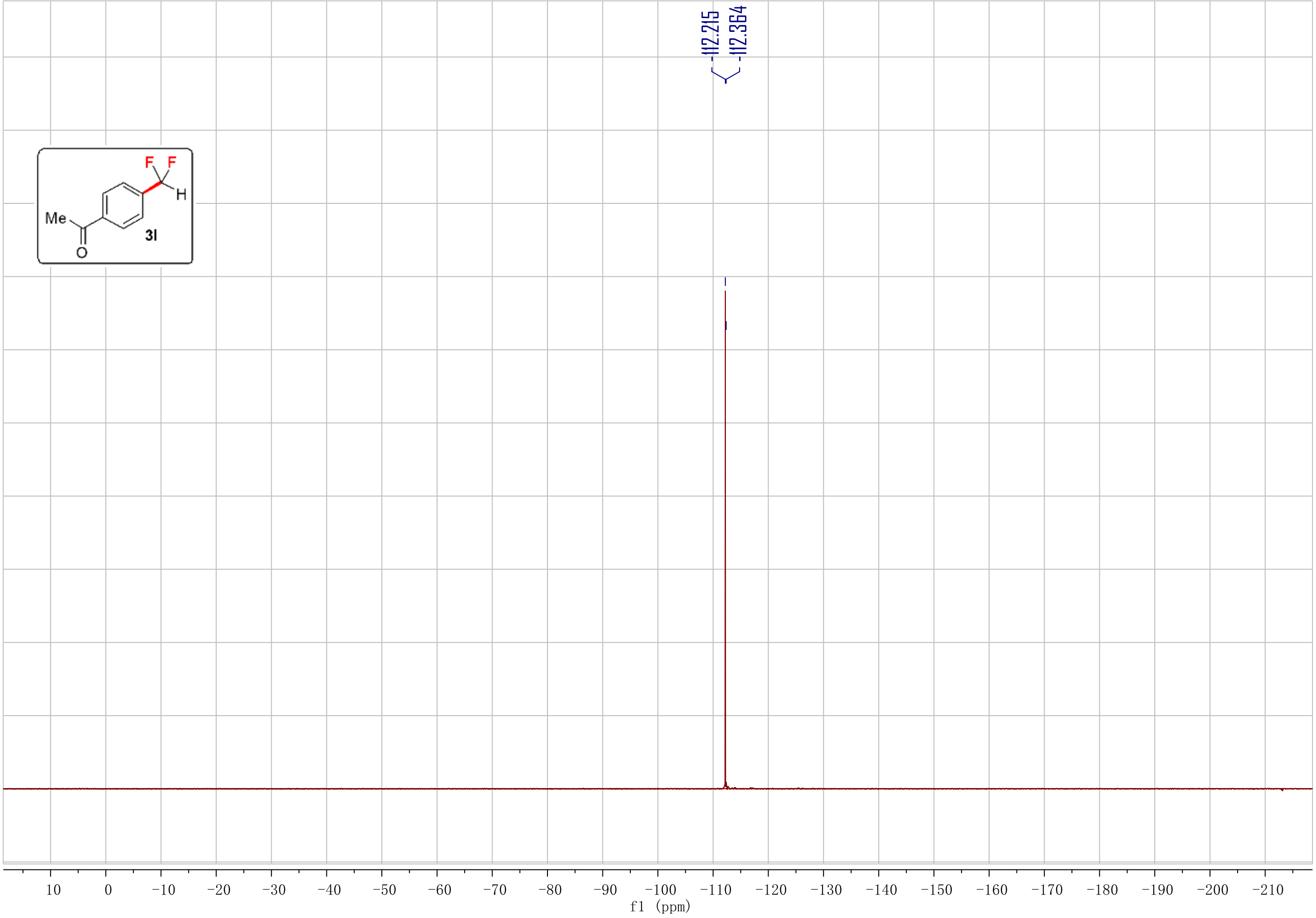
126.93
126.87
126.81
125.62
125.39
125.16
117.58
115.23
114.94
112.87
77.48
77.16
76.84
66.85
48.65
F
F
H
N
O
3h
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

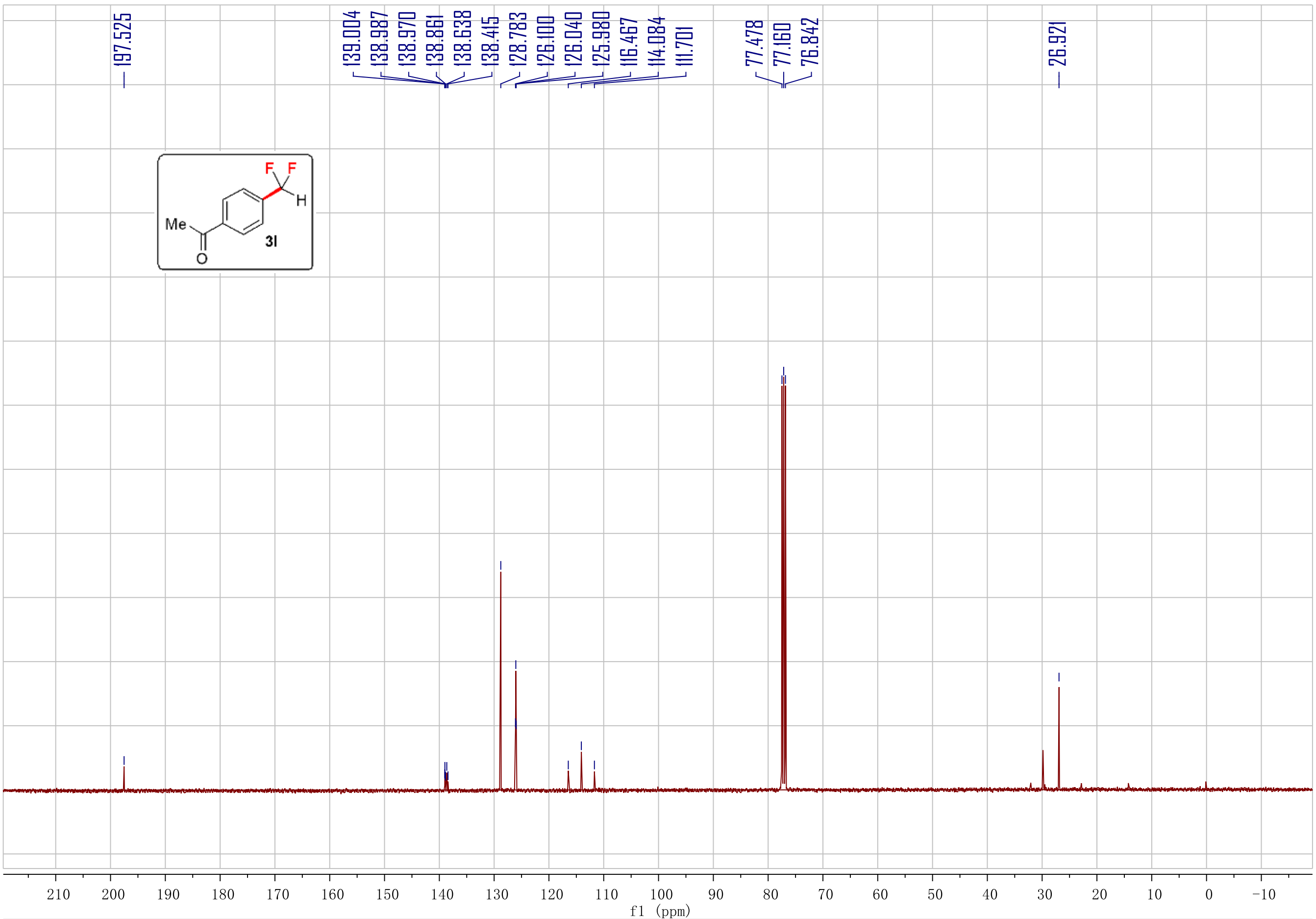

8.14
8.12
7.59
7.57
6.83
6.69
6.55
4.43
4.41
4.40
4.38
1.43
1.41
1.39
F
F
H
EtO_2C
3i
1.98
1.94
1.00
2.08
3.03
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

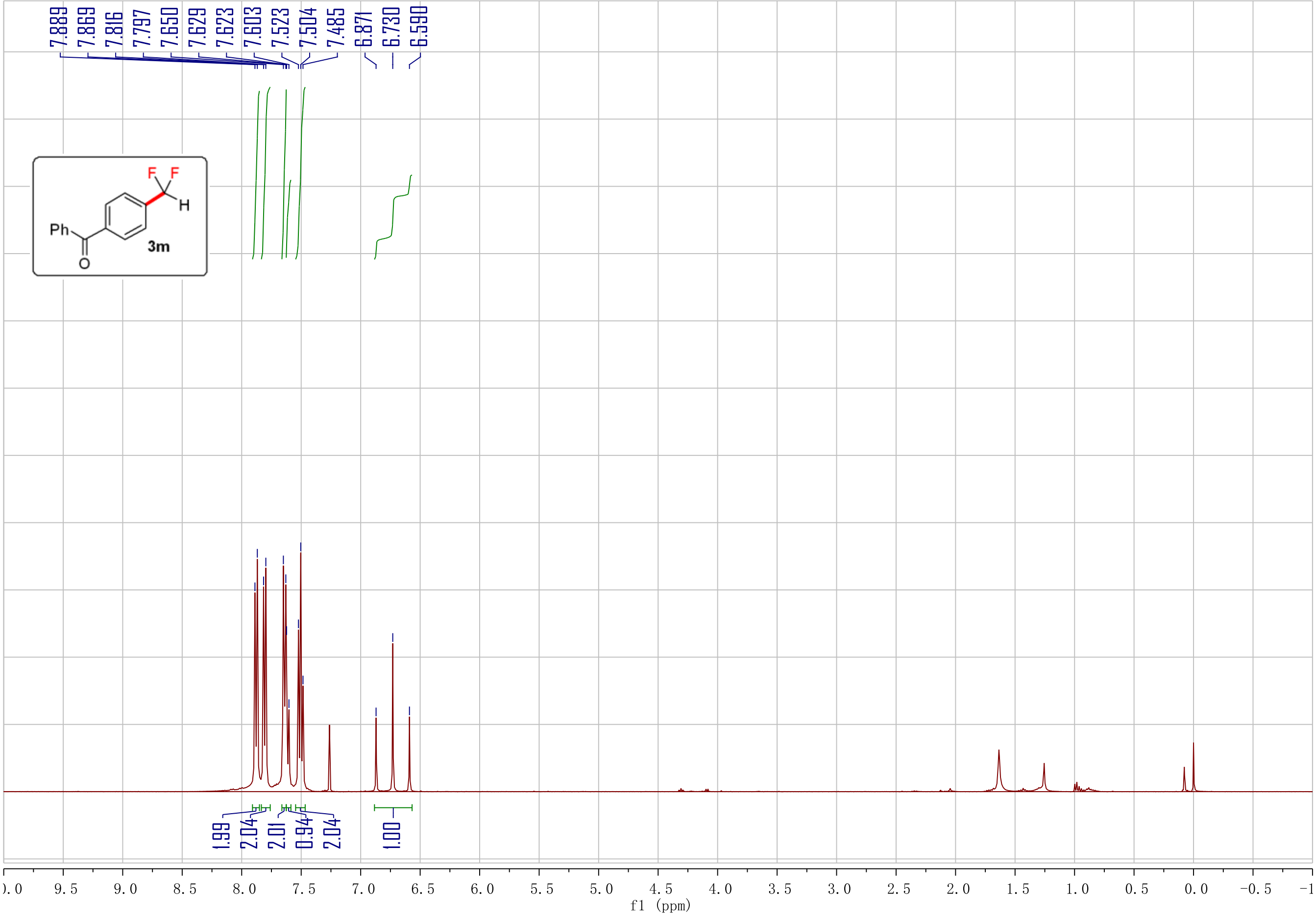

-112.09
-112.24
F
F
H
EtO2C
3i
10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)

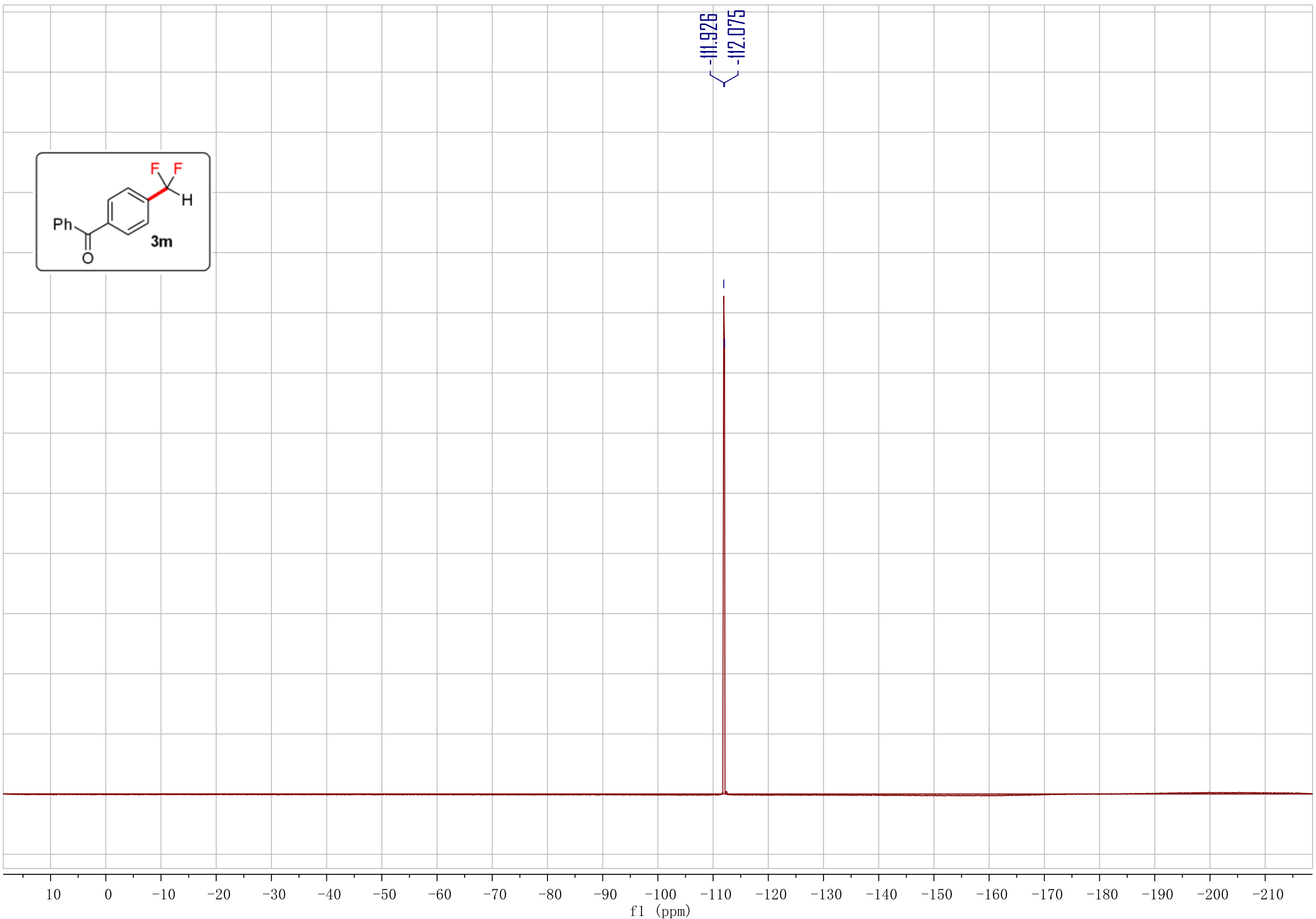

165.91
138.69
138.47
138.25
132.82
132.80
132.78
130.04
125.78
125.72
125.66
116.55
114.17
111.78
77.48
77.16
76.84
61.49
14.40
F
F
H
EtO2C
3i
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

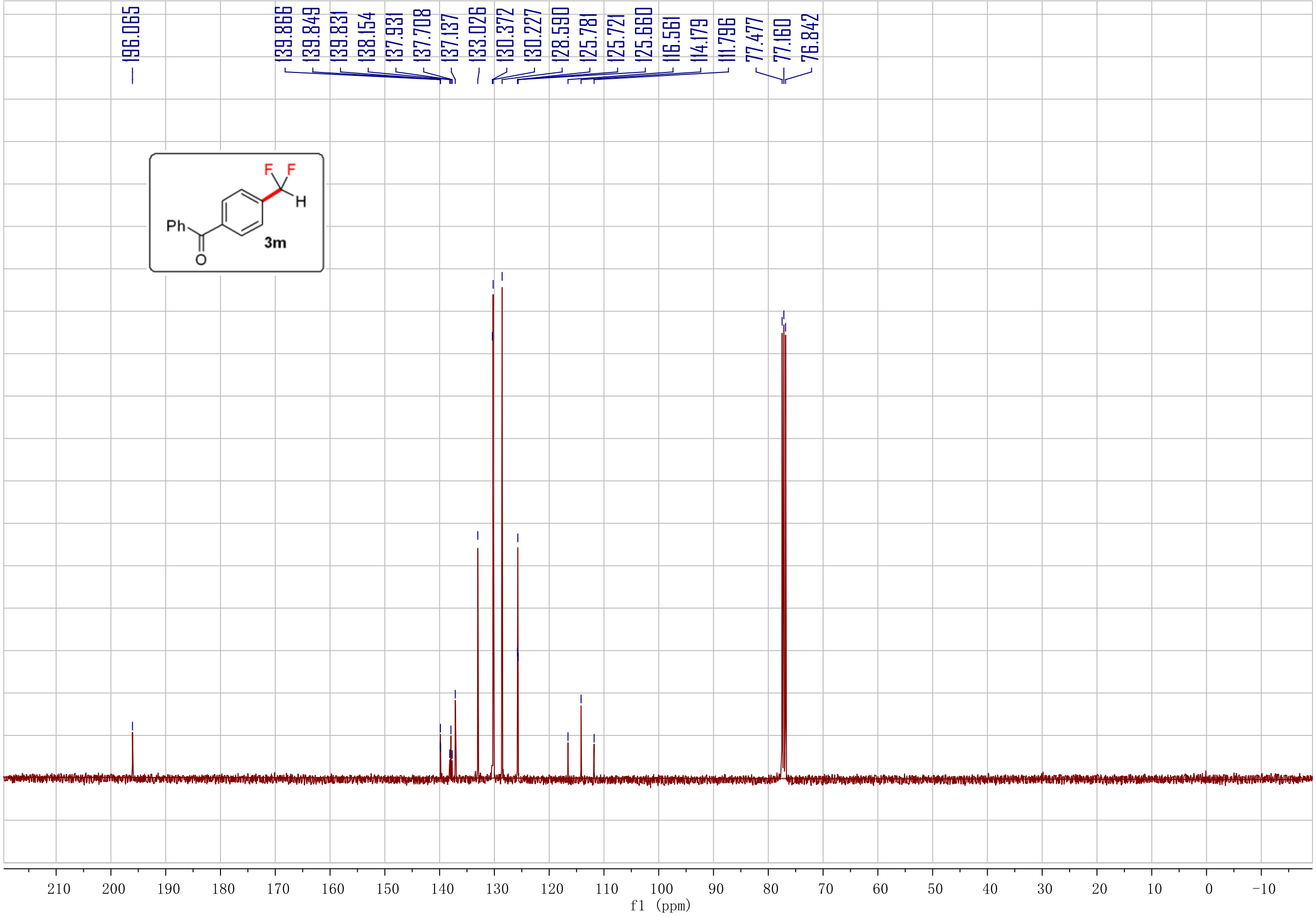

8.049
8.029
7.626
7.606
6.836
6.696
6.555
2.638
F
F
H
Me
O
3l
2.06
2.05
1.00
3.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

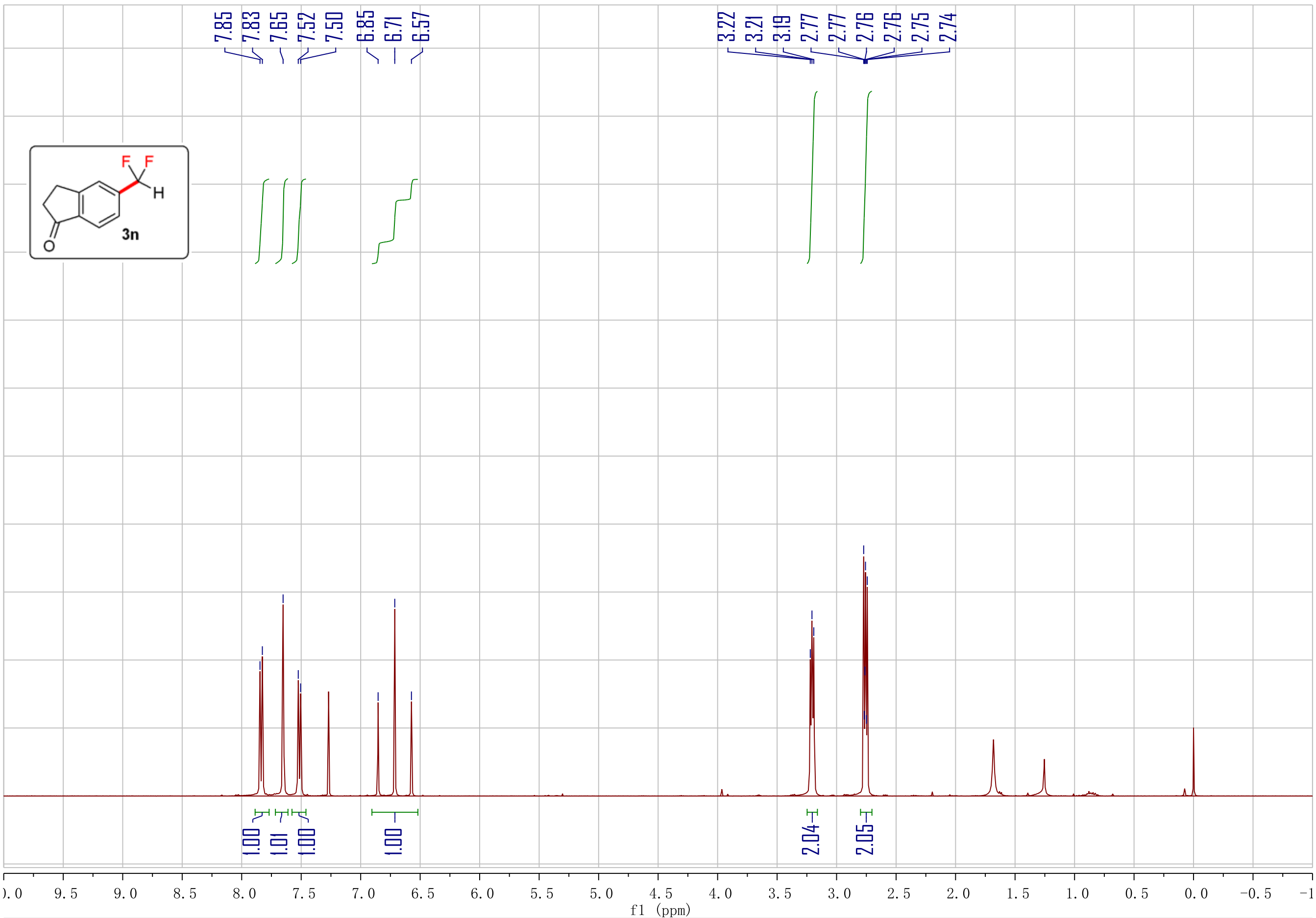

-112.215
-112.364
F
F
H
Me
O
3l
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

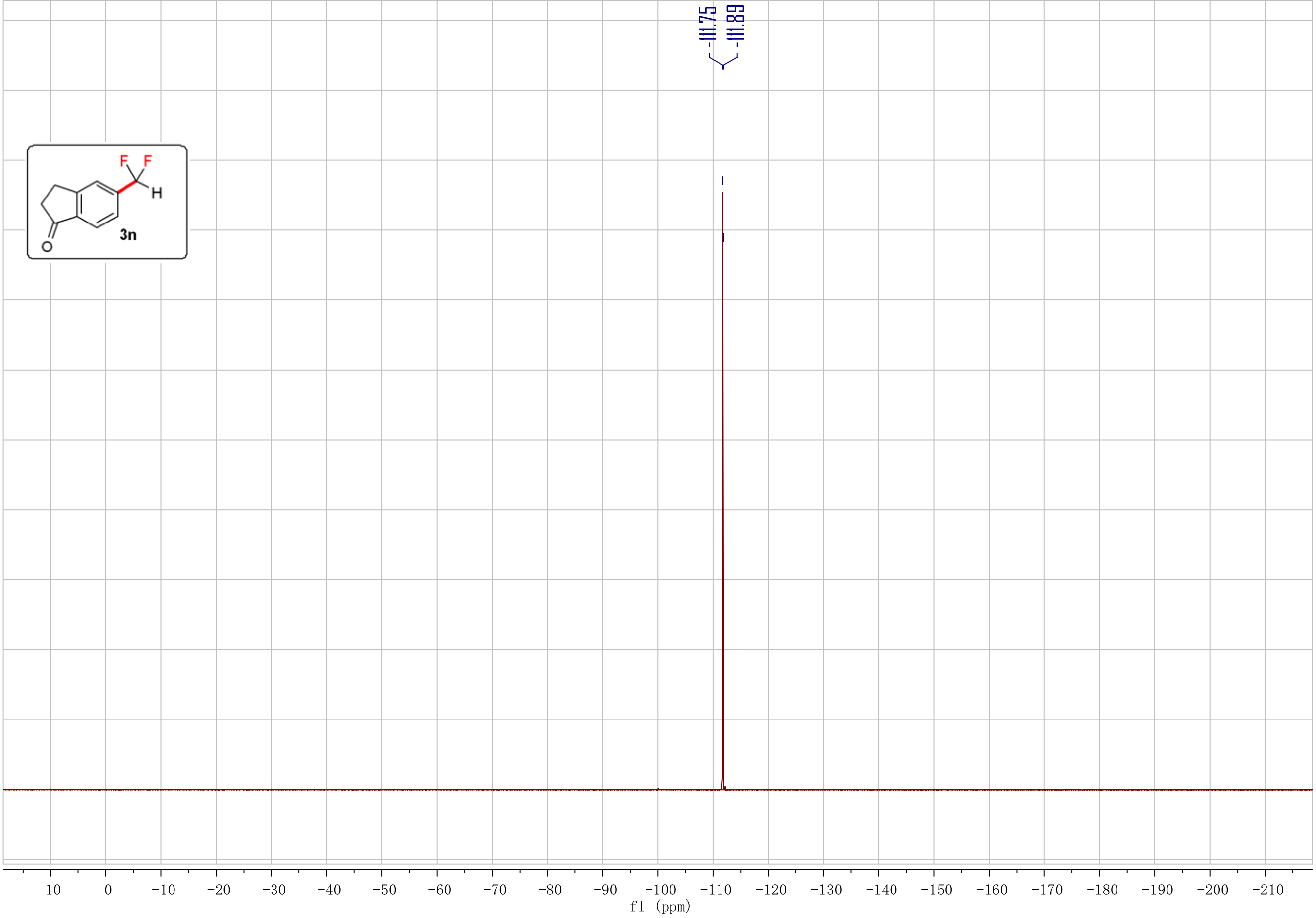

197.525
139.004
138.987
138.970
138.861
138.638
138.415
128.783
126.100
126.040
125.980
116.467
114.084
111.701
77.478
77.160
76.842
26.921
F
F
H
Me
O
3l
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

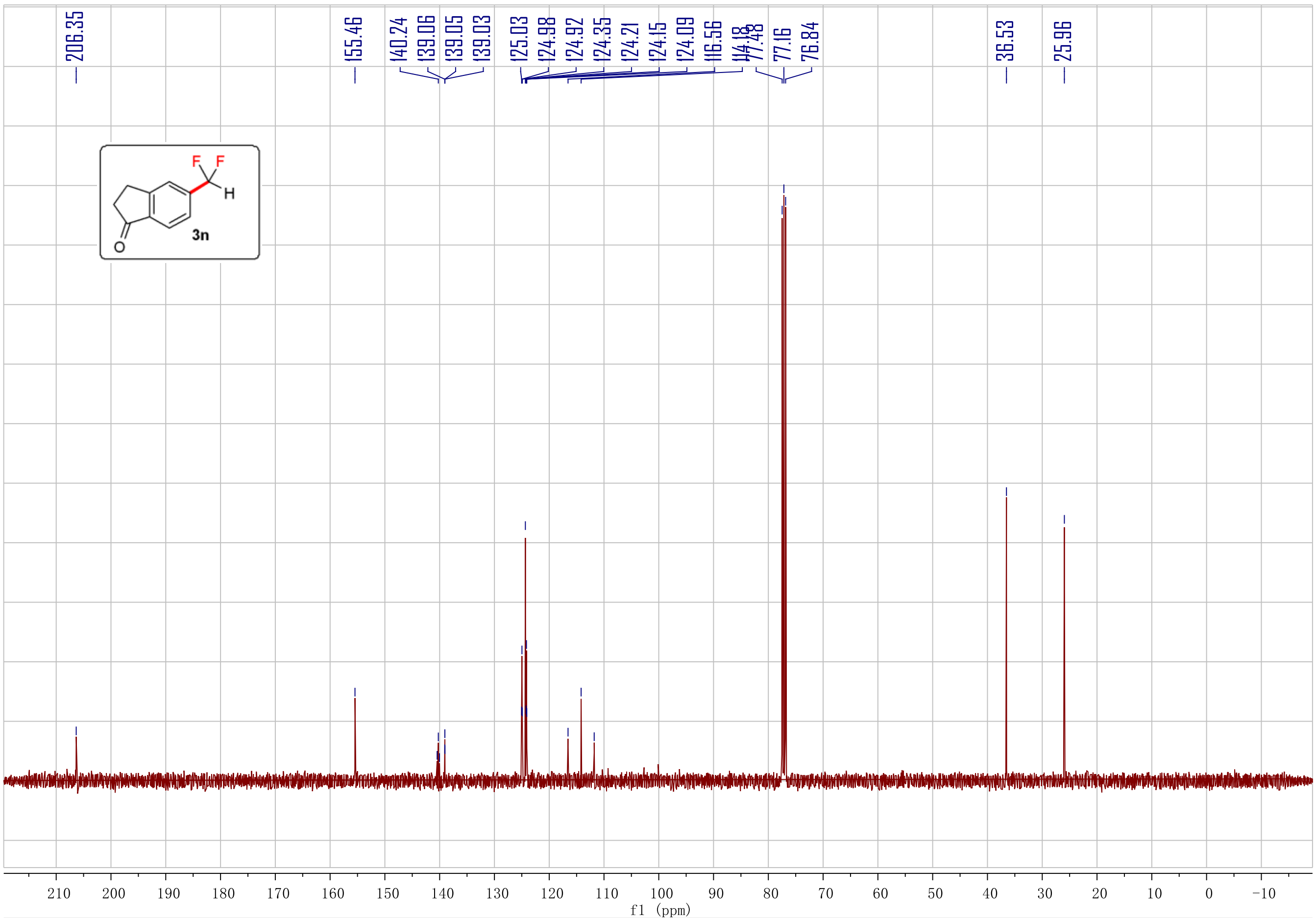

7.889
7.869
7.816
7.797
7.650
7.629
7.623
7.603
7.523
7.504
7.485
6.871
6.730
6.590
F
F
H
Ph
O
3m
1.99
2.04
2.01
0.94
2.04
1.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
f1 (ppm)

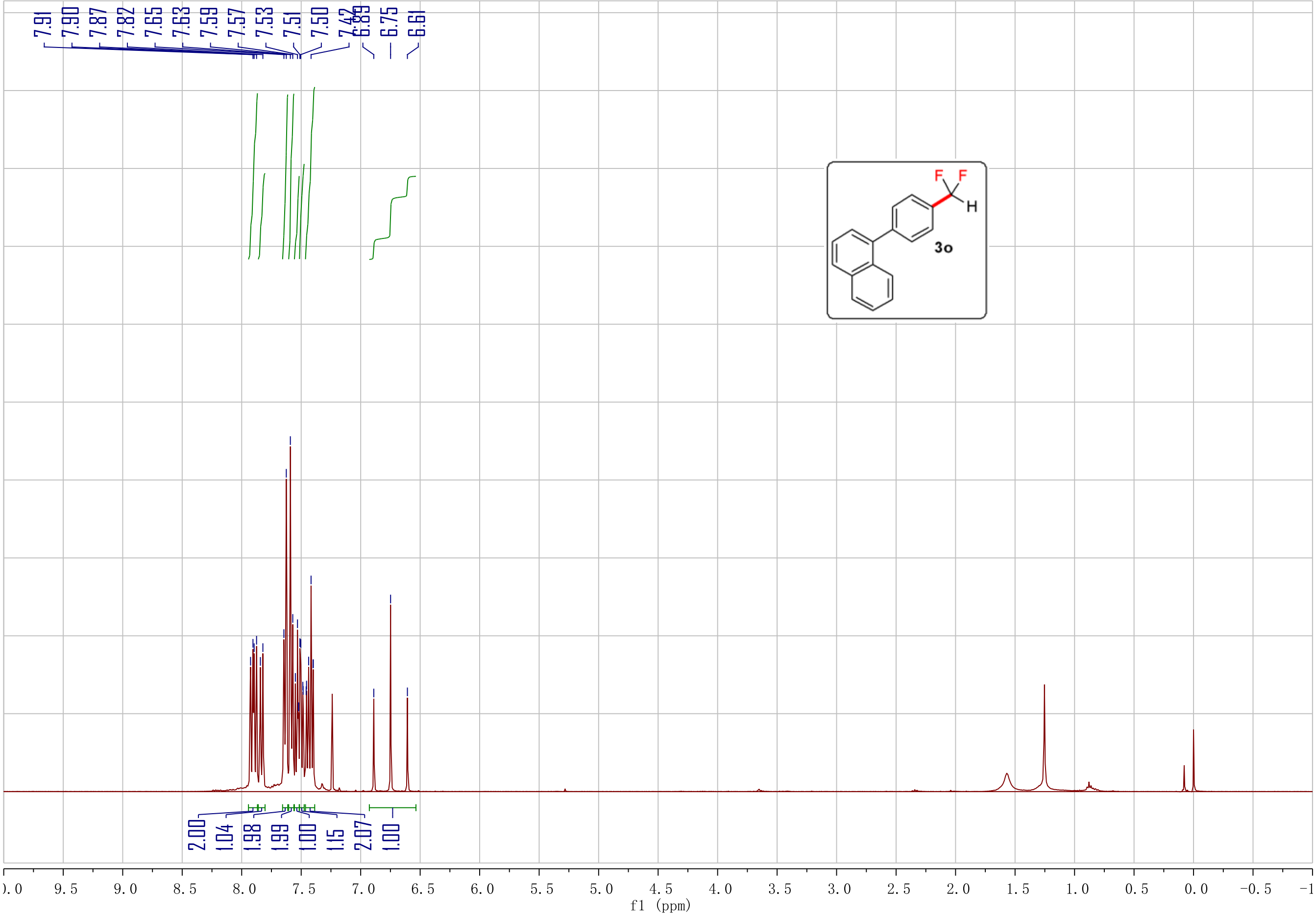

-111.926
-112.075
F
F
H
Ph
O
3m
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

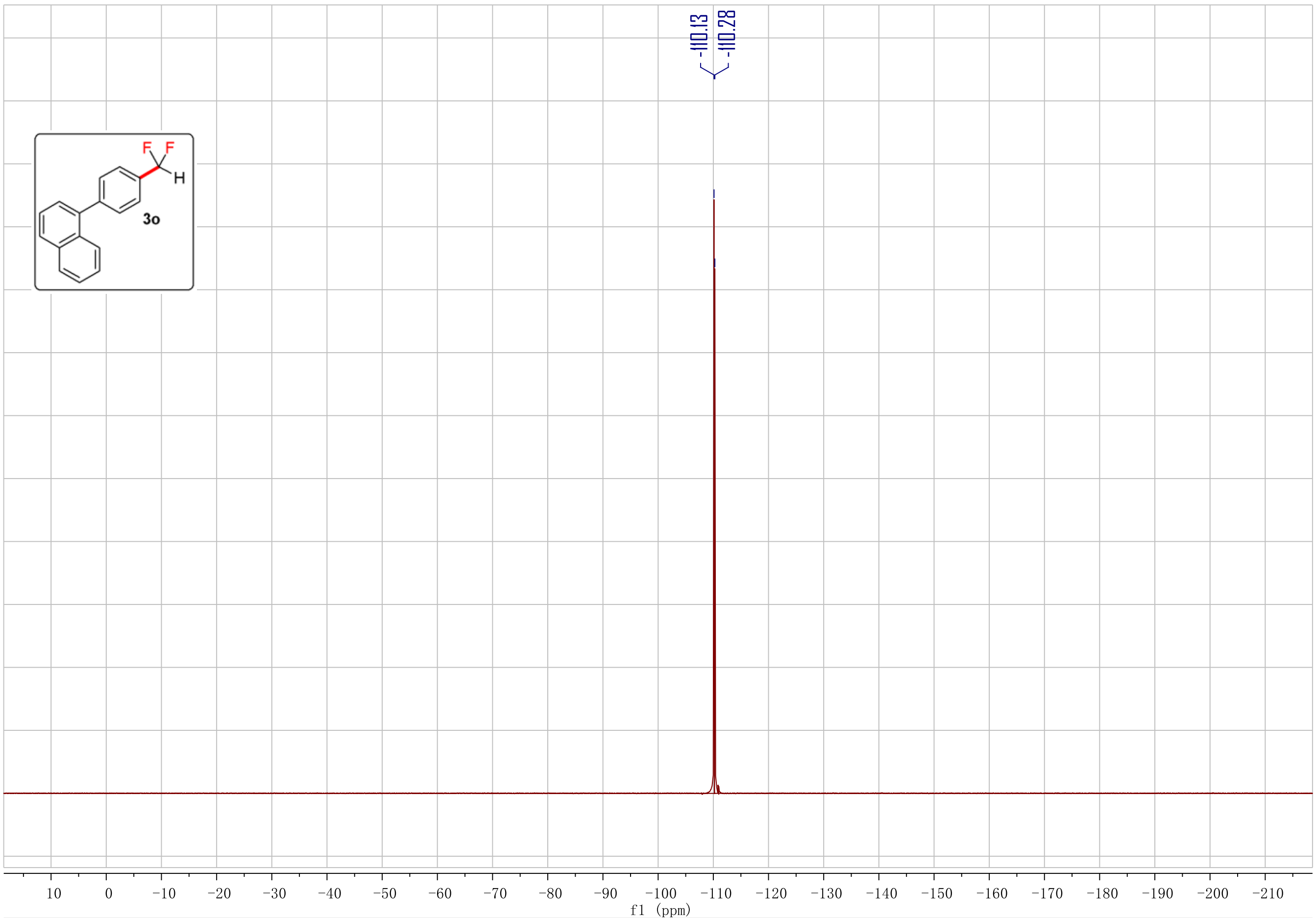

196.065
139.866
139.849
139.831
138.154
137.931
137.708
137.137
133.026
130.372
130.227
128.590
125.781
125.721
125.660
116.561
114.179
111.796
77.477
77.160
76.842
F
F
H
Ph
O
3m
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

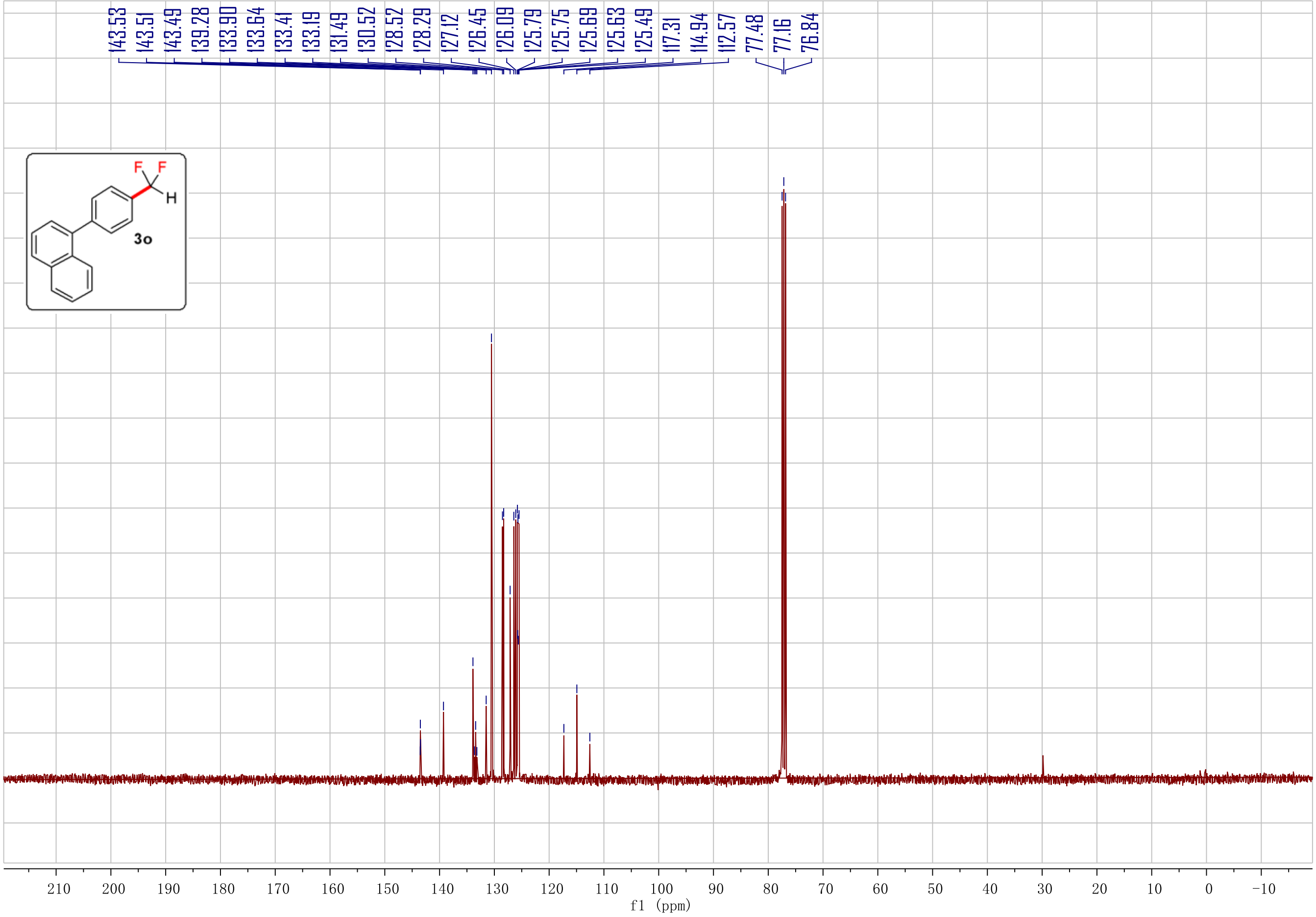

7.85
7.83
7.65
7.52
7.50
6.85
6.71
6.57
3.22
3.21
3.19
2.77
2.77
2.76
2.76
2.75
2.74
F
F
H
O
3n
1.00
1.01
1.00
1.00
2.04
2.05
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
f1 (ppm)

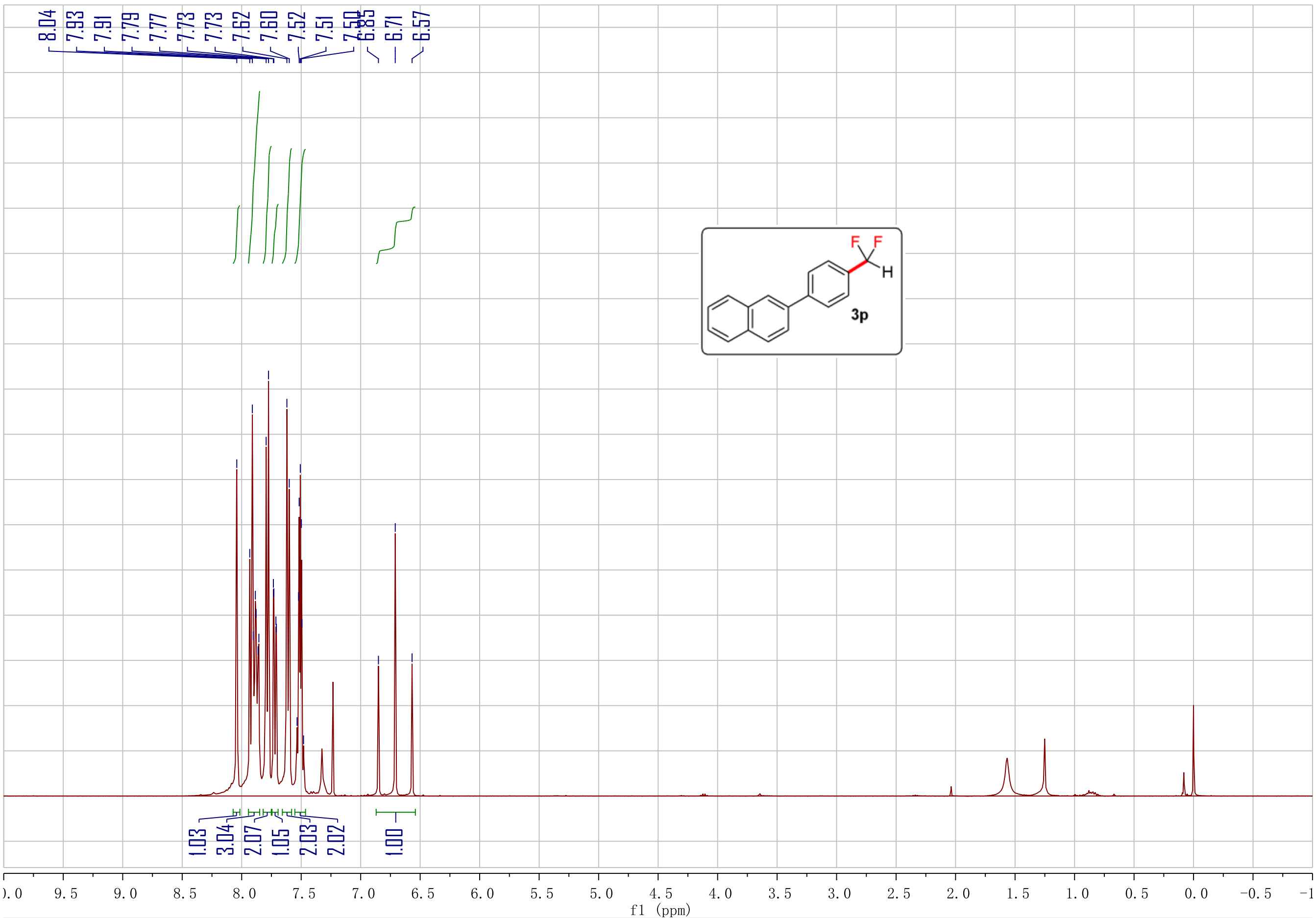

-111.75
-111.89
F
F
H
O
3n
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)


206.35
155.46
140.24
139.06
139.05
139.03
125.03
124.98
124.92
124.35
124.21
124.15
124.09
116.56
114.18
77.48
77.16
76.84
36.53
25.96
F
F
H
O
3n
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

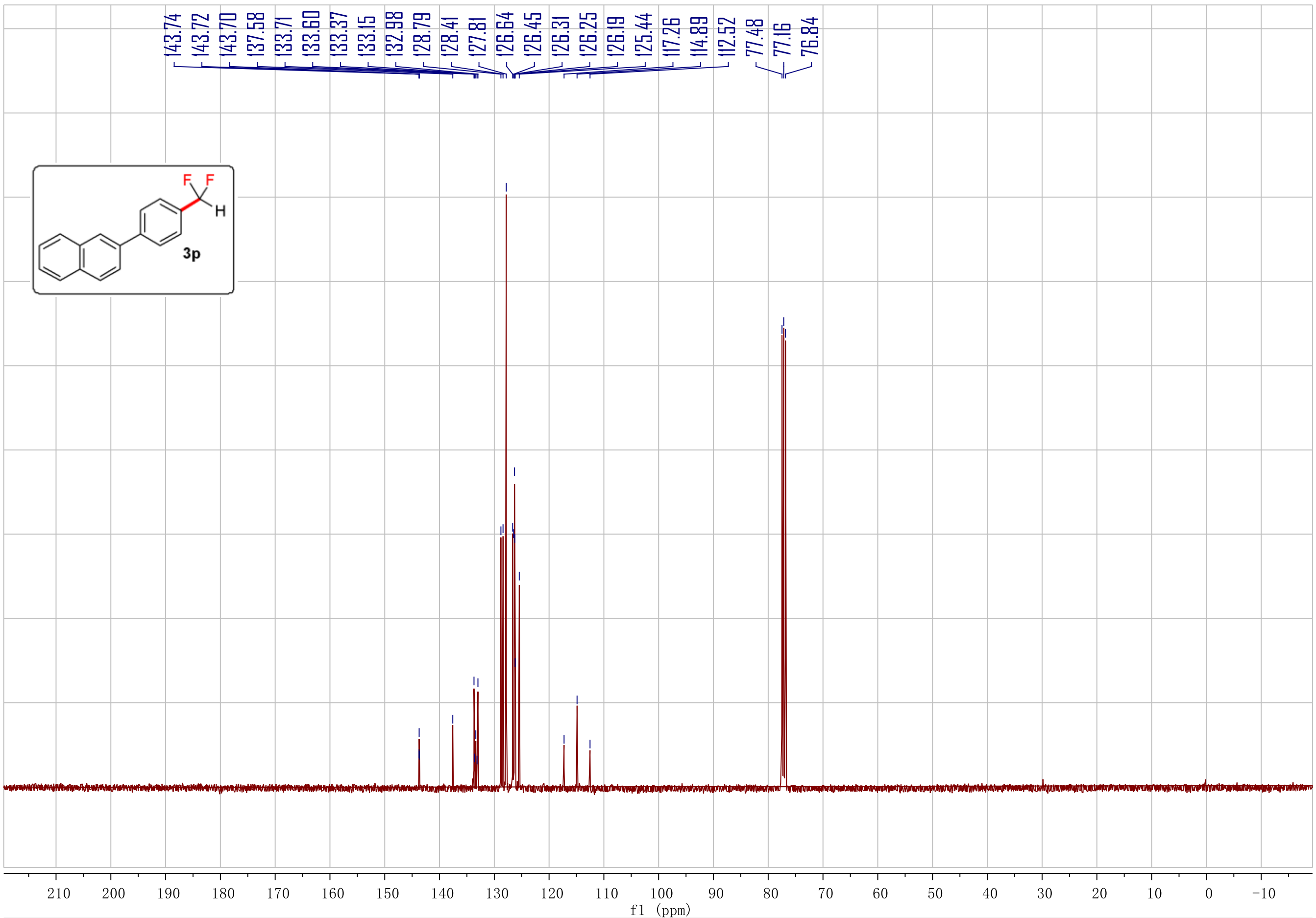

7.91
7.90
7.87
7.82
7.65
7.63
7.59
7.57
7.53
7.51
7.50
7.42
6.89
6.75
6.61
F
F
H
3o
2.00
1.04
1.98
1.99
1.00
1.15
2.07
1.00
.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

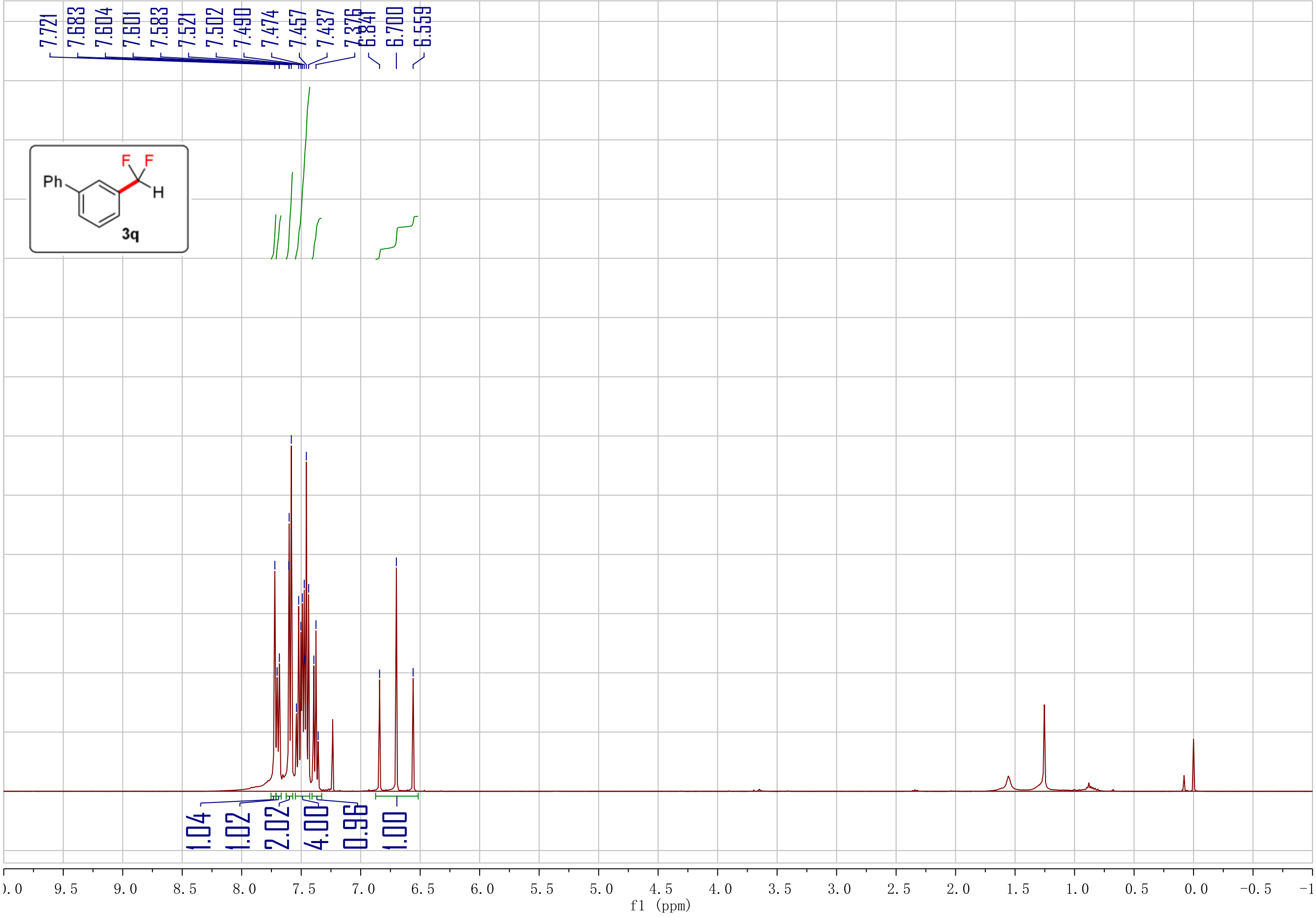

-110.13
-110.28
F
F
H
3o
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

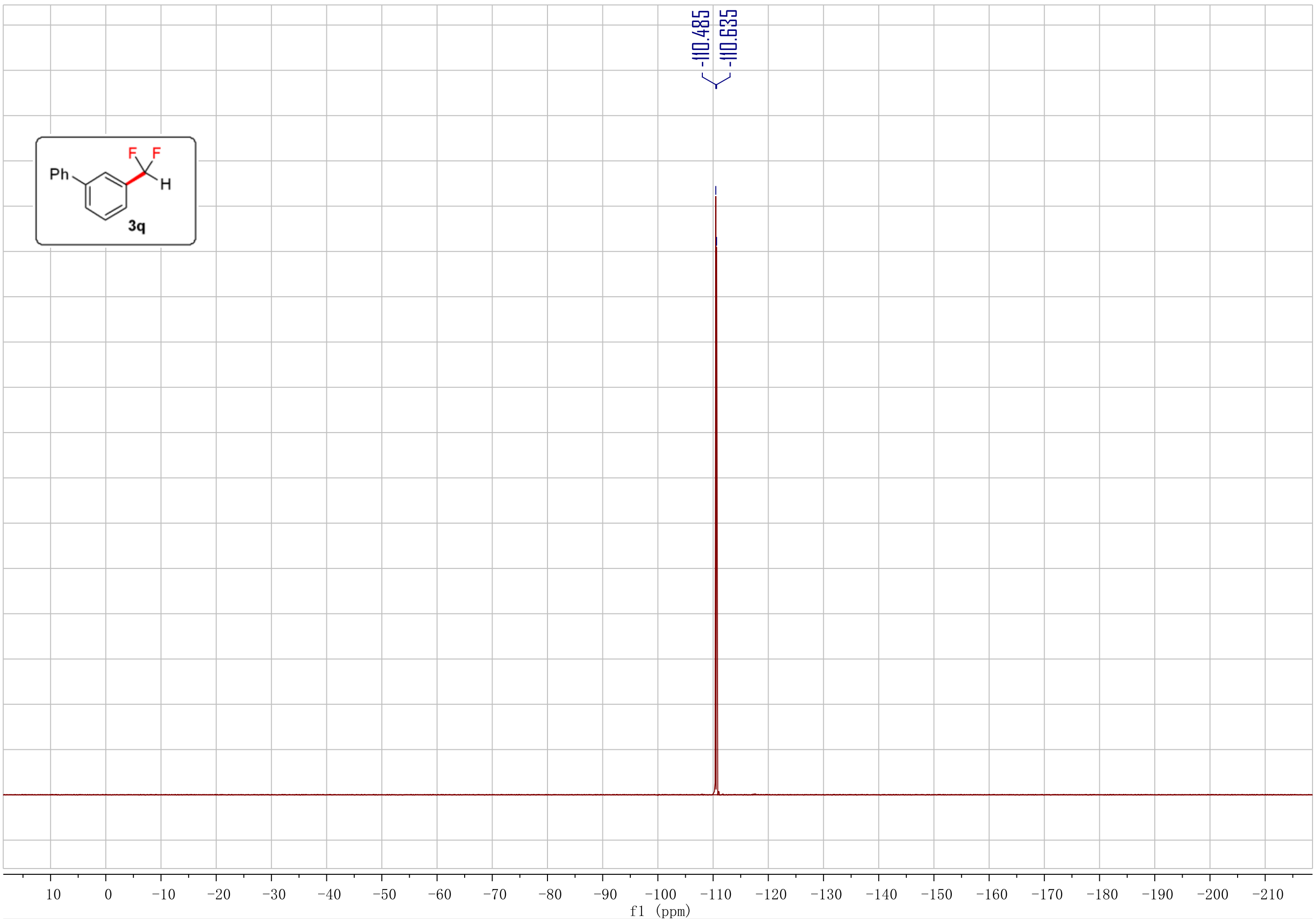

143.53
143.51
143.49
139.28
133.90
133.64
133.41
133.19
131.49
130.52
128.52
128.29
127.12
126.45
126.09
125.79
125.75
125.69
125.63
125.49
117.31
114.94
112.57
77.48
77.16
76.84
F
F
H
3o
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

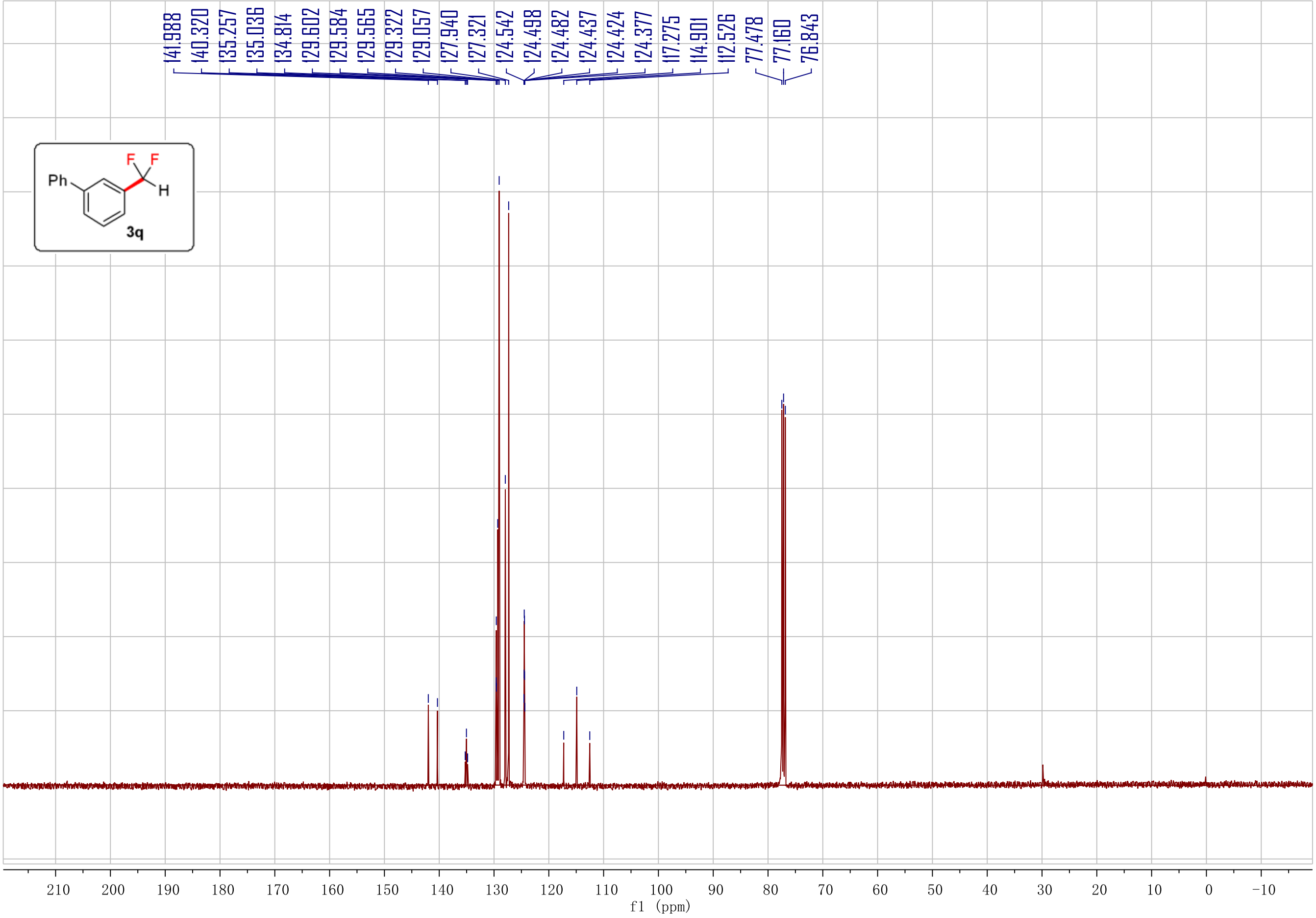

8.04
7.93
7.91
7.79
7.77
7.73
7.73
7.62
7.60
7.52
7.51
7.50
6.85
6.71
6.57
F
F
H
3p
1.03
3.04
2.07
1.05
2.03
2.02
1.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
f1 (ppm)

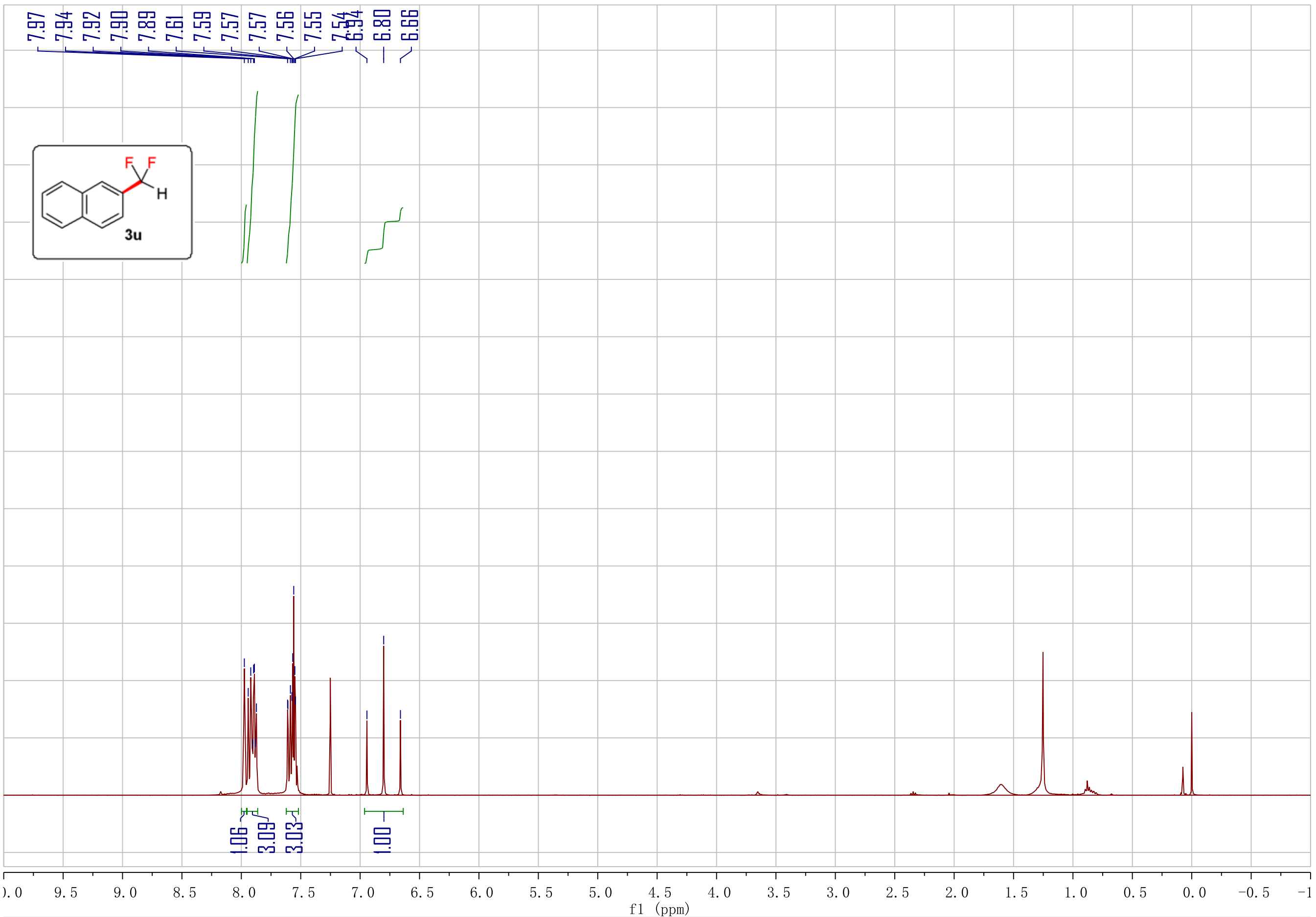

-110.20
-110.35
F
F
H
3p
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

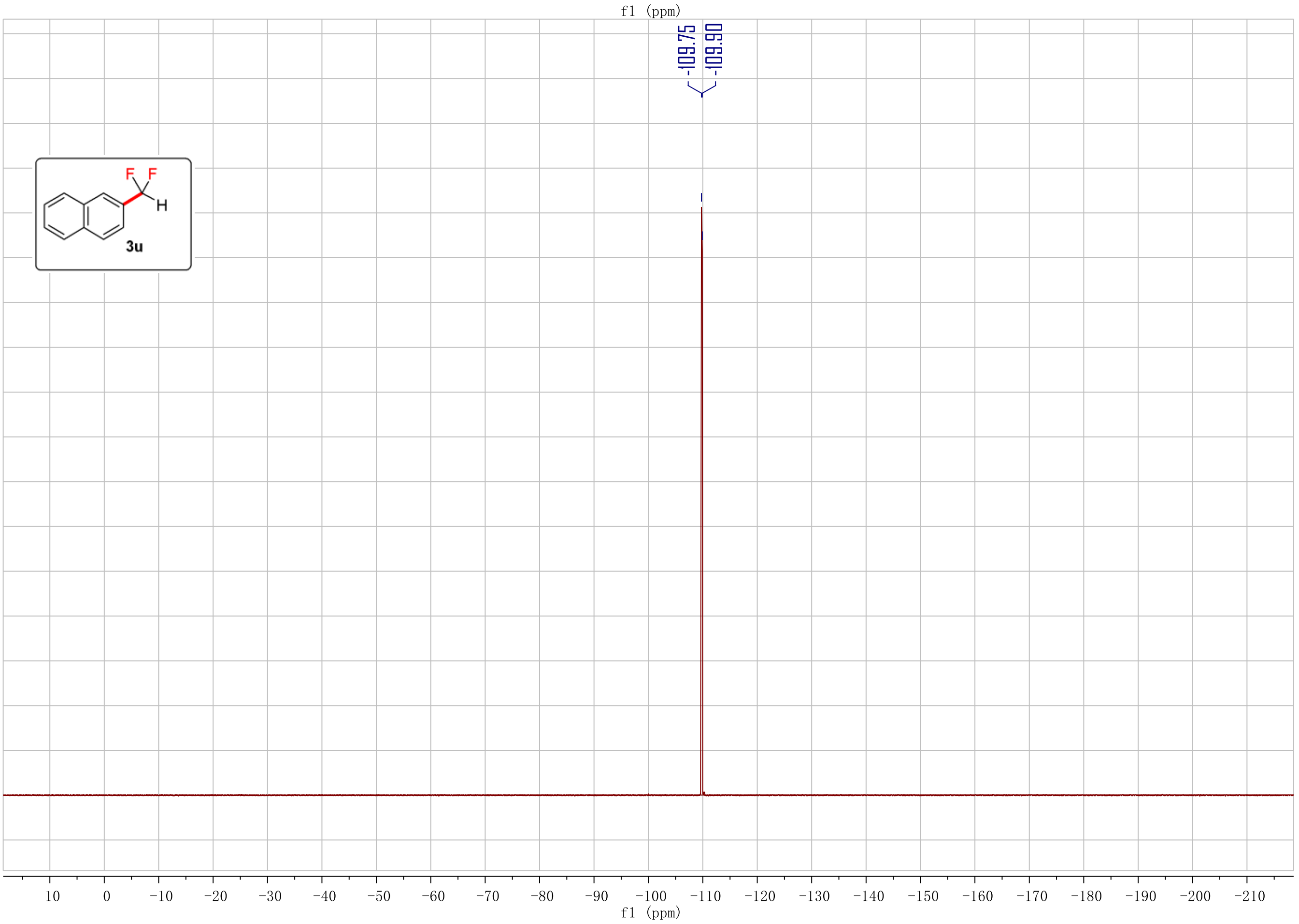

143.74
143.72
143.70
137.58
133.71
133.60
133.37
133.15
132.98
128.79
128.41
127.81
126.64
126.45
126.31
126.25
126.19
125.44
117.26
114.89
112.52
77.48
77.16
76.84
F
F
H
3p
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

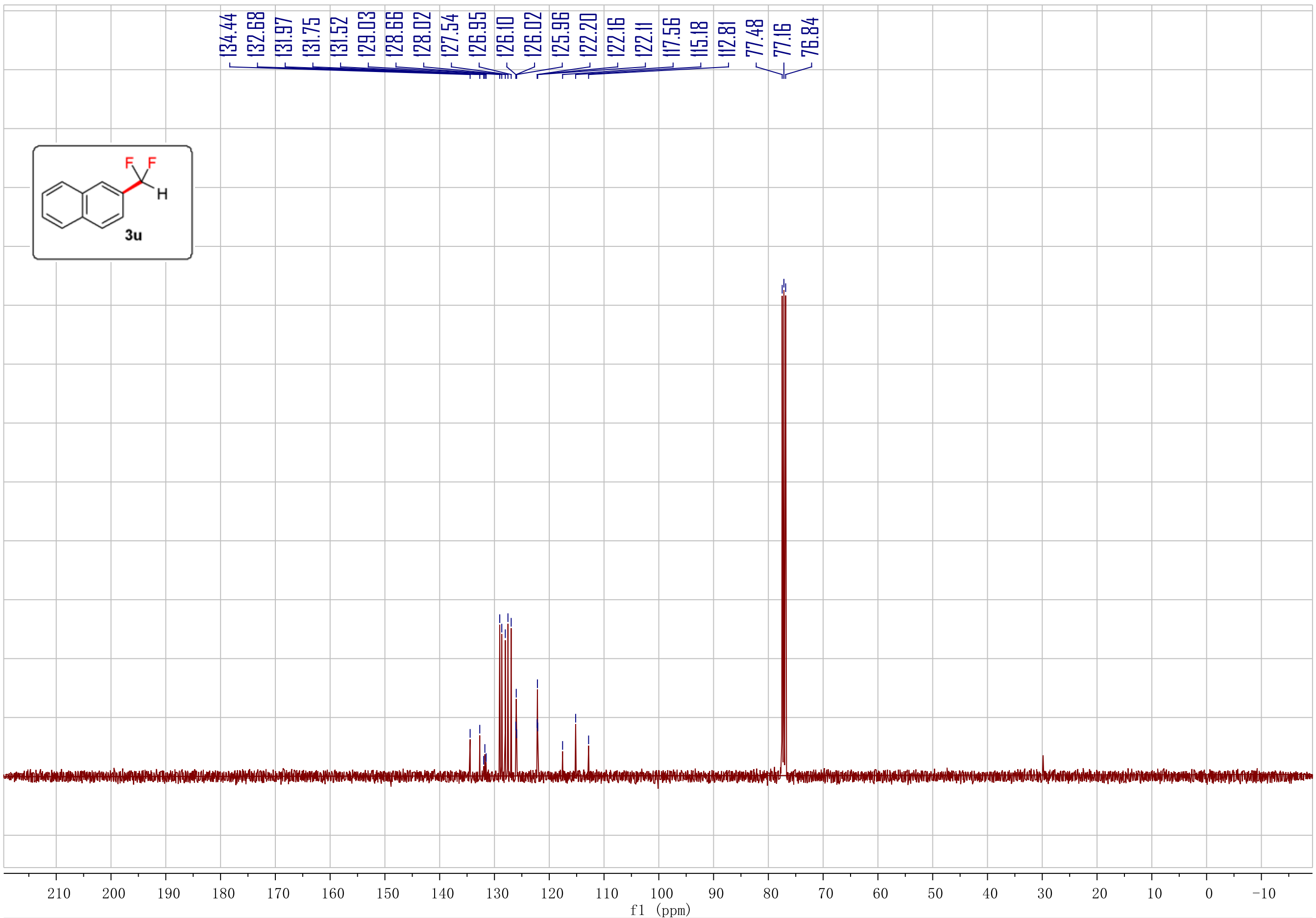

7.721
7.683
7.604
7.601
7.583
7.521
7.502
7.490
7.474
7.457
7.437
7.376
6.841
6.700
6.559
Ph
F
F
H
3q
1.04
1.02
2.02
4.00
0.96
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

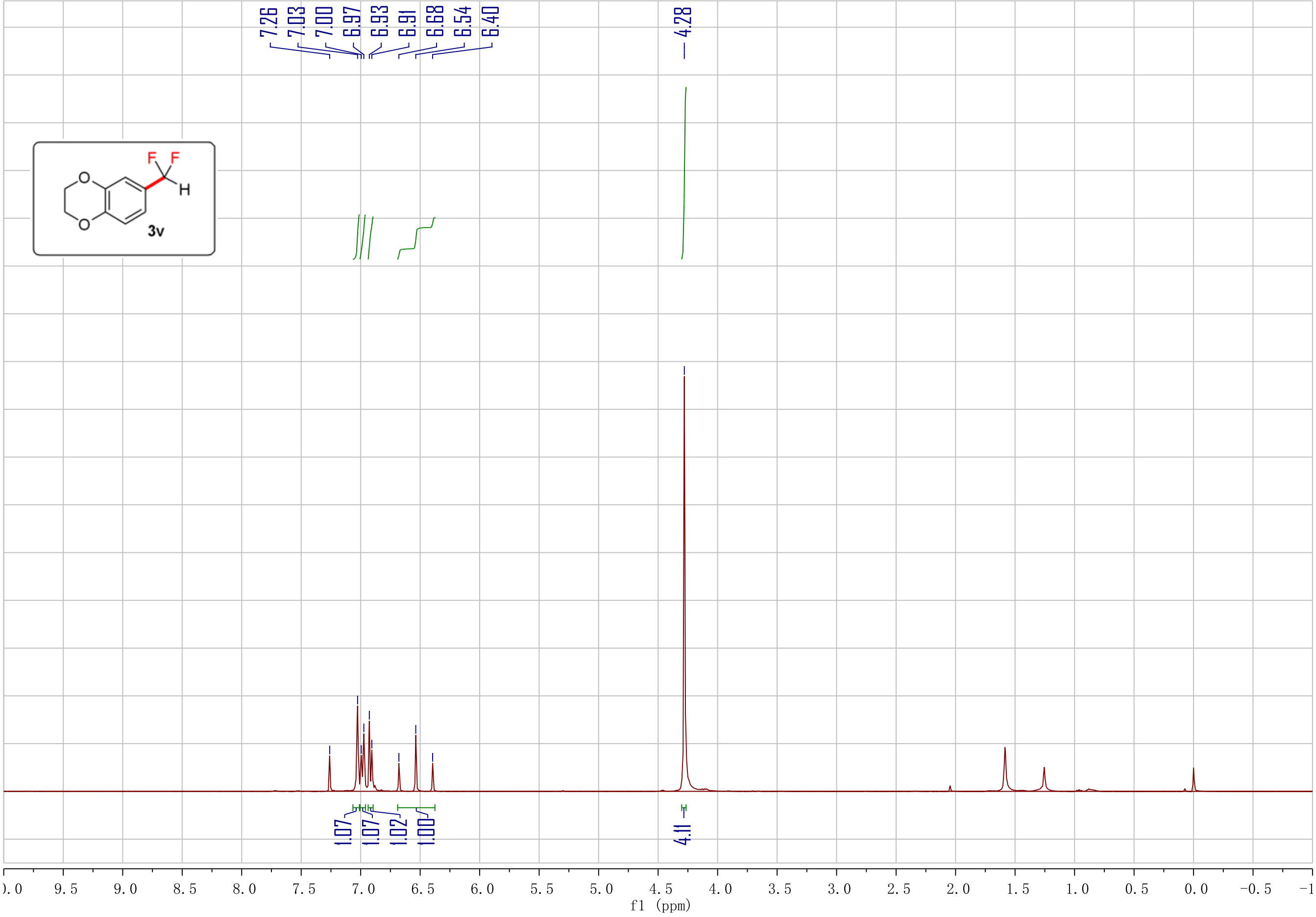

-110.485
-110.635
Ph
F
F
H
3q
10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)

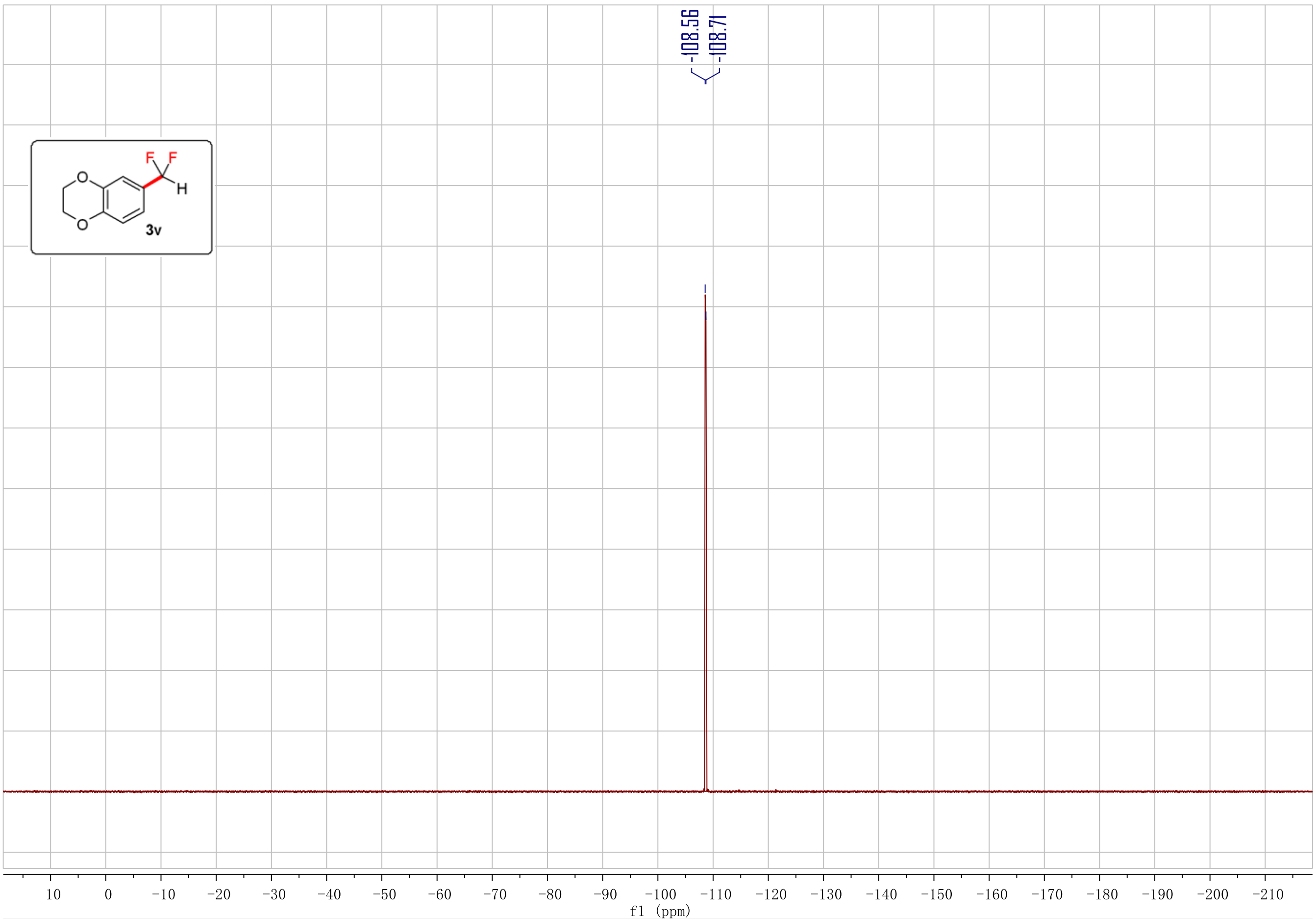

141.988
140.320
135.257
135.036
134.814
129.602
129.584
129.565
129.322
129.057
127.940
127.321
124.542
124.498
124.482
124.437
124.424
124.377
117.275
114.901
112.526
77.478
77.160
76.843
Ph
F
F
H
3q
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

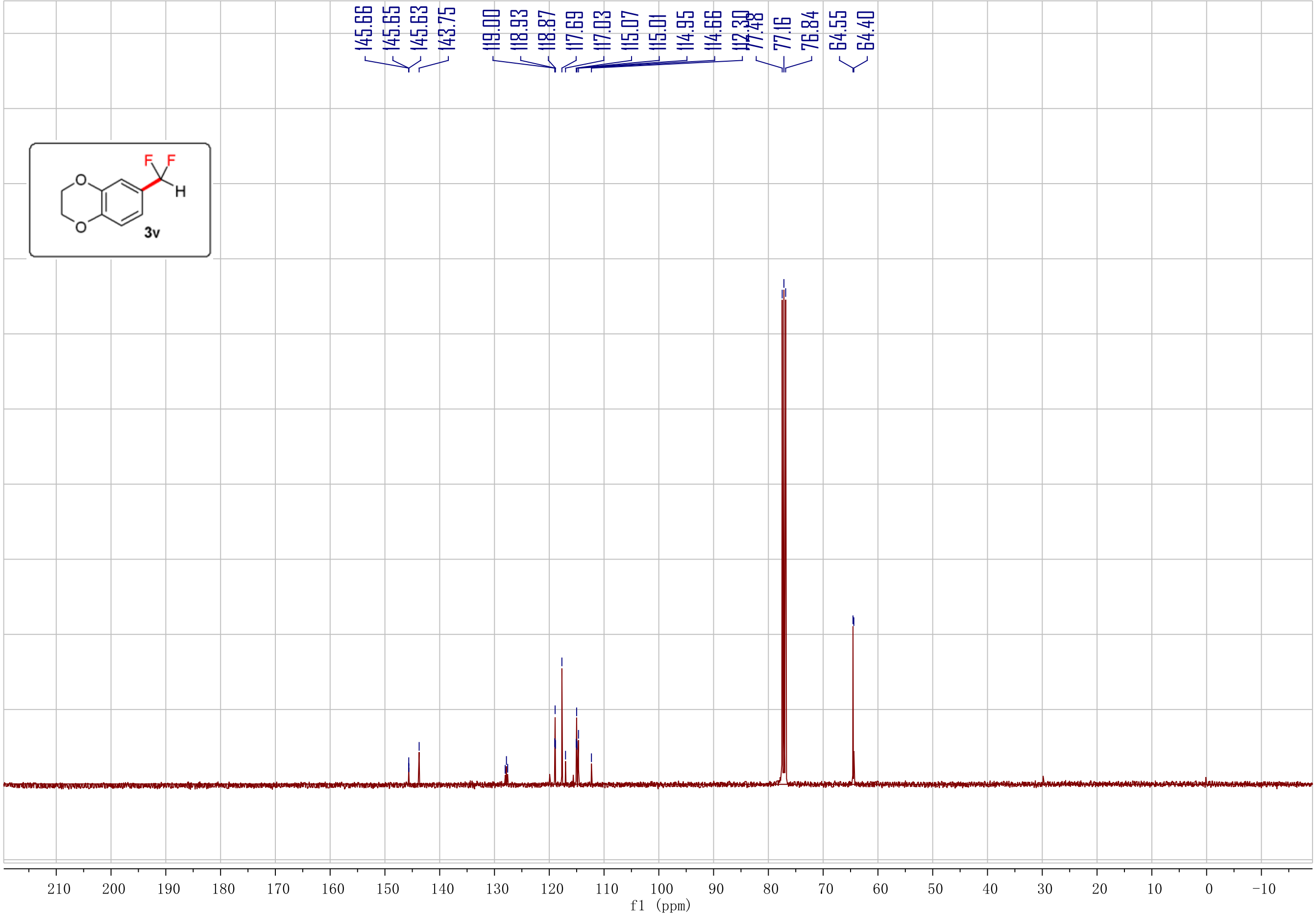

7.97
7.94
7.92
7.90
7.89
7.61
7.59
7.57
7.57
7.56
7.55
7.54
6.94
6.80
6.66
F
F
H
3u
1.06
3.09
3.03
1.00
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

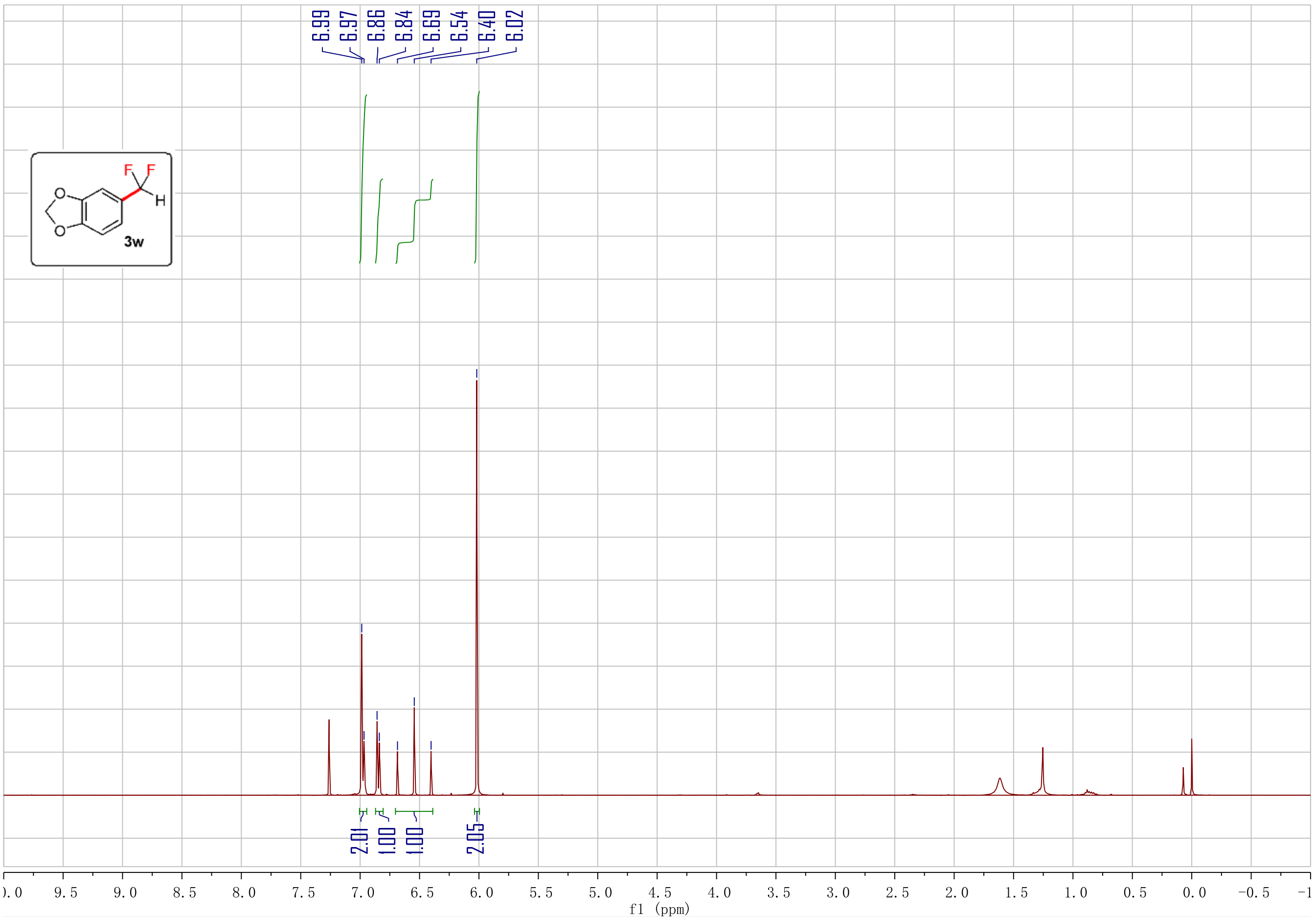

-109.75
-109.90
F
F
H
3u
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

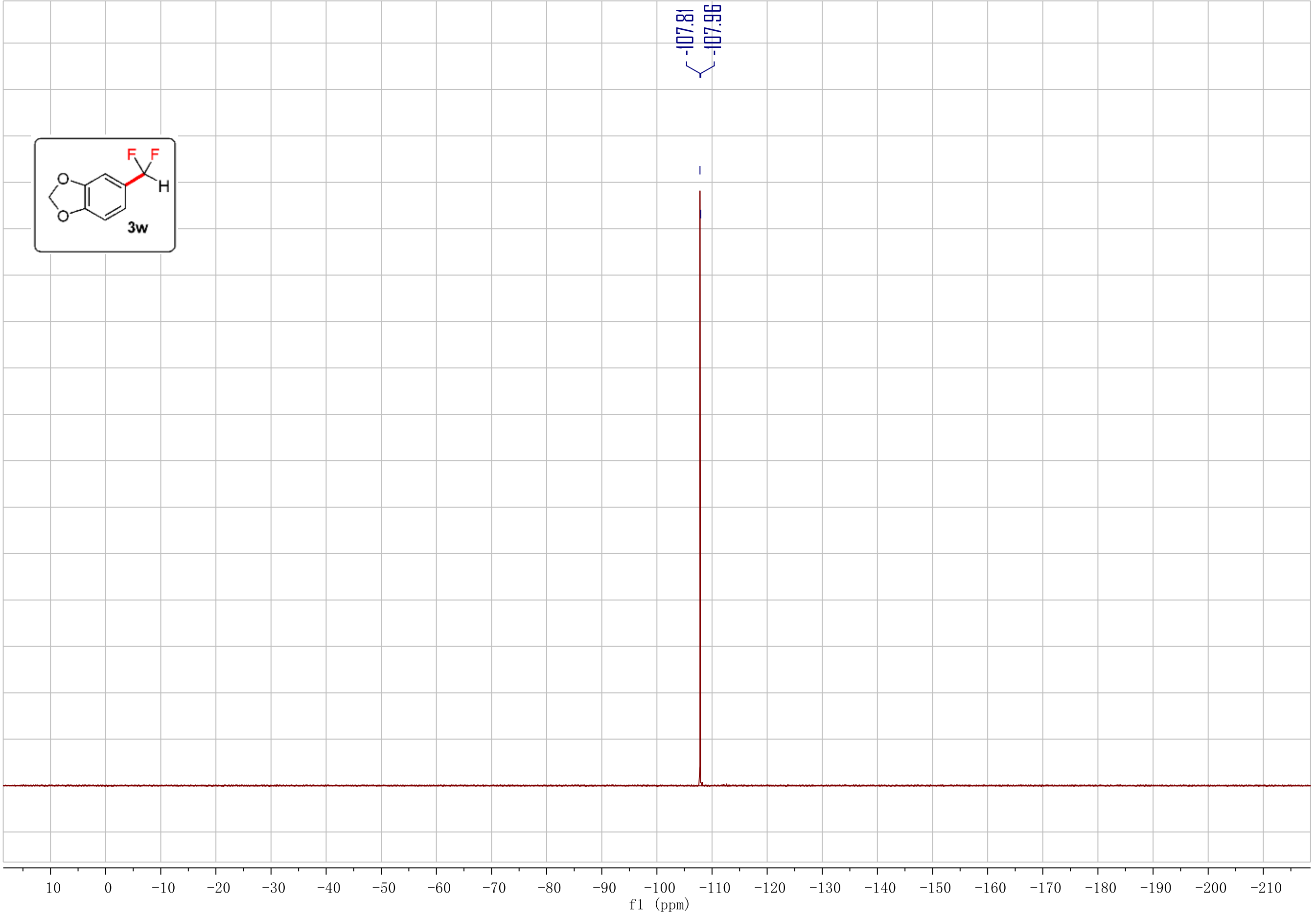

134.44
132.68
131.97
131.75
131.52
129.03
128.66
128.02
127.54
126.95
126.10
126.02
125.96
122.20
122.16
122.11
117.56
115.18
112.81
77.48
77.16
76.84
F
F
H
3u
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

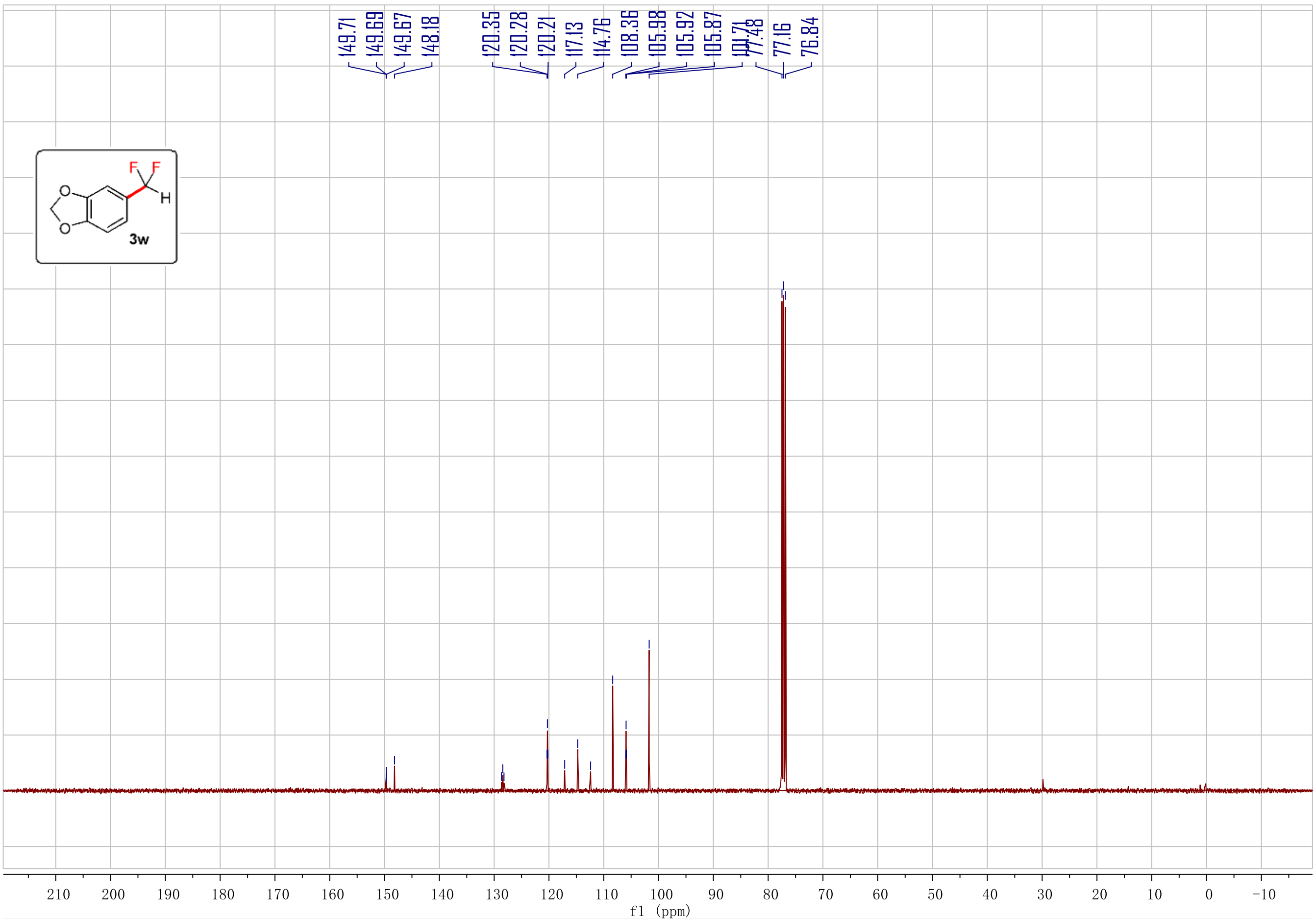

7.26
7.03
7.00
6.97
6.93
6.91
6.68
6.54
6.40
4.28
O
O
F
F
H
3v
1.07
1.07
1.02
1.00
4.11
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

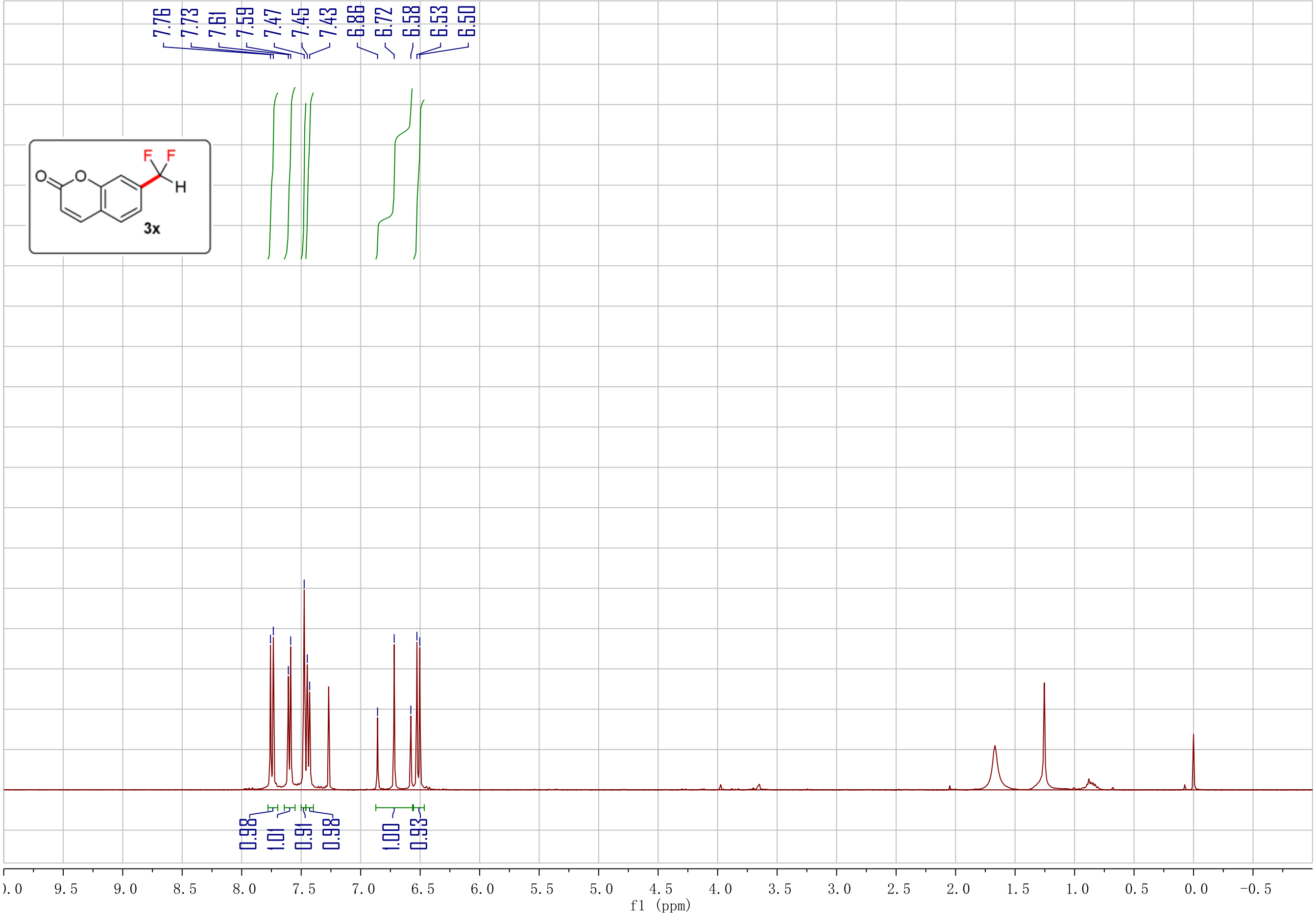

-108.56
-108.71
F
F
H
O
O
3v
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

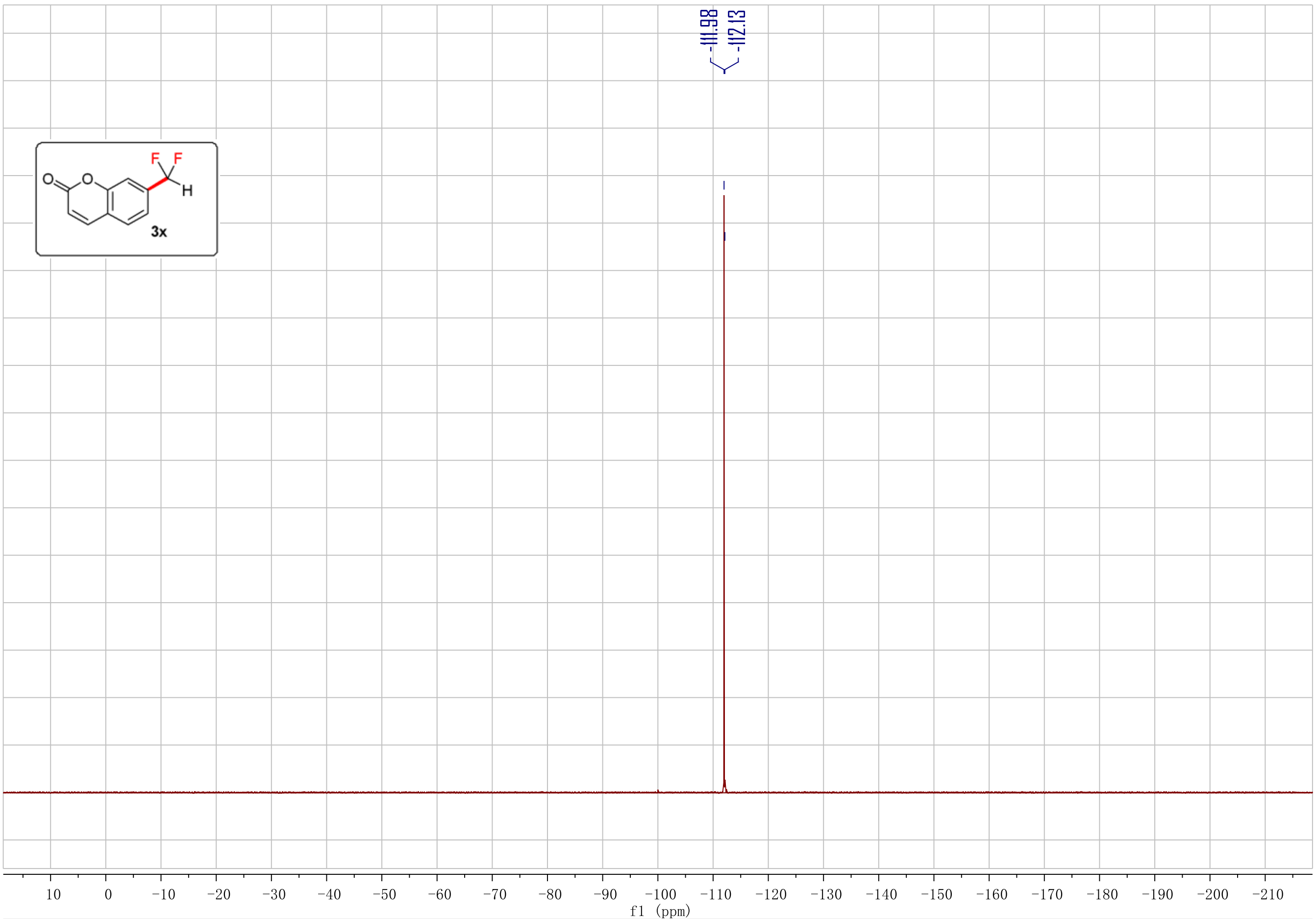

145.66
145.65
145.63
143.75
119.00
118.93
118.87
117.69
117.03
115.07
115.01
114.95
114.66
112.30
77.48
77.16
76.84
64.55
64.40
F
F
H
O
O
3v
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

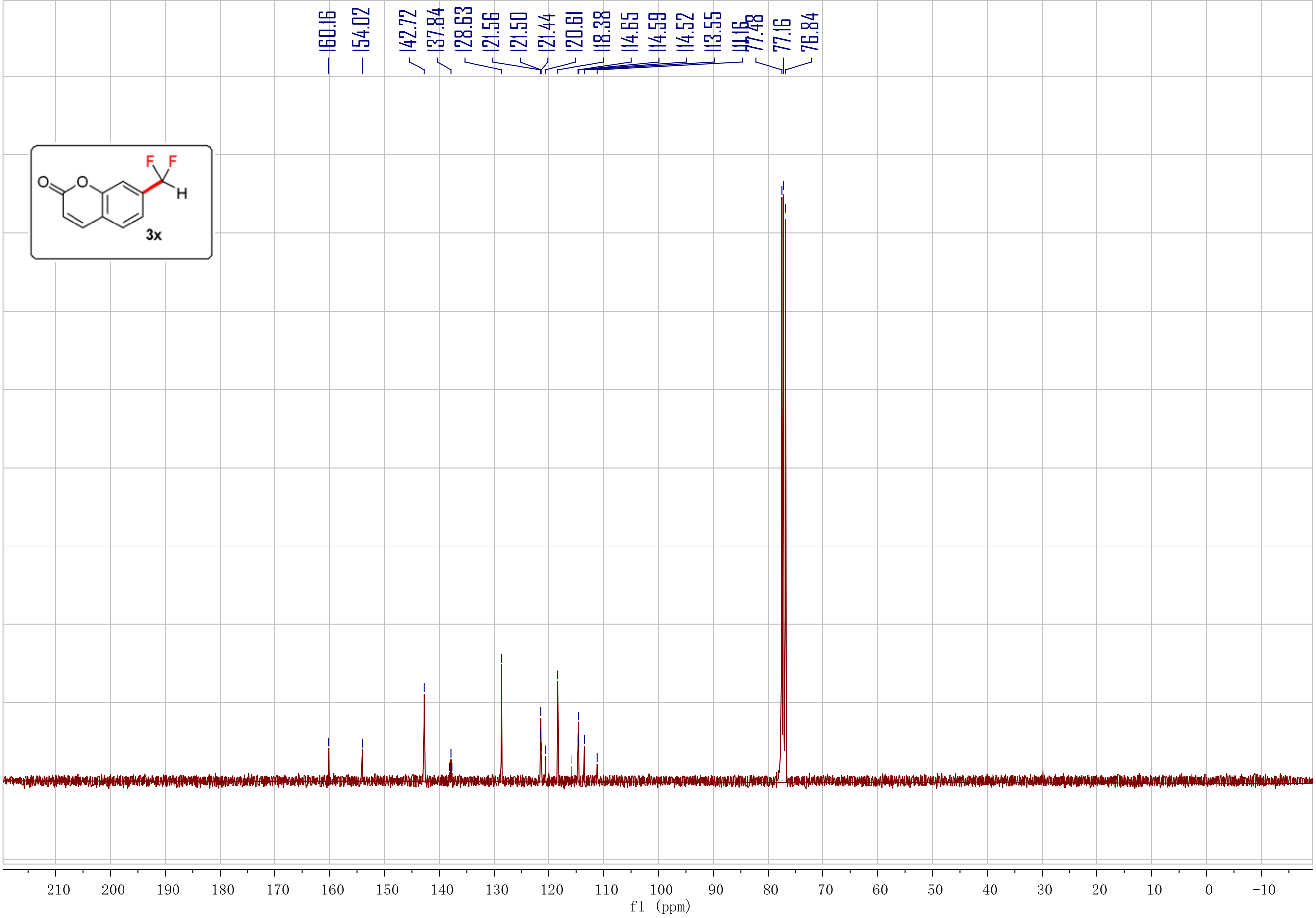

6.99
6.97
6.86
6.84
6.69
6.54
6.40
6.02
2.01
1.00
1.00
2.05
F
F
H
O
O
3w
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
f1 (ppm)

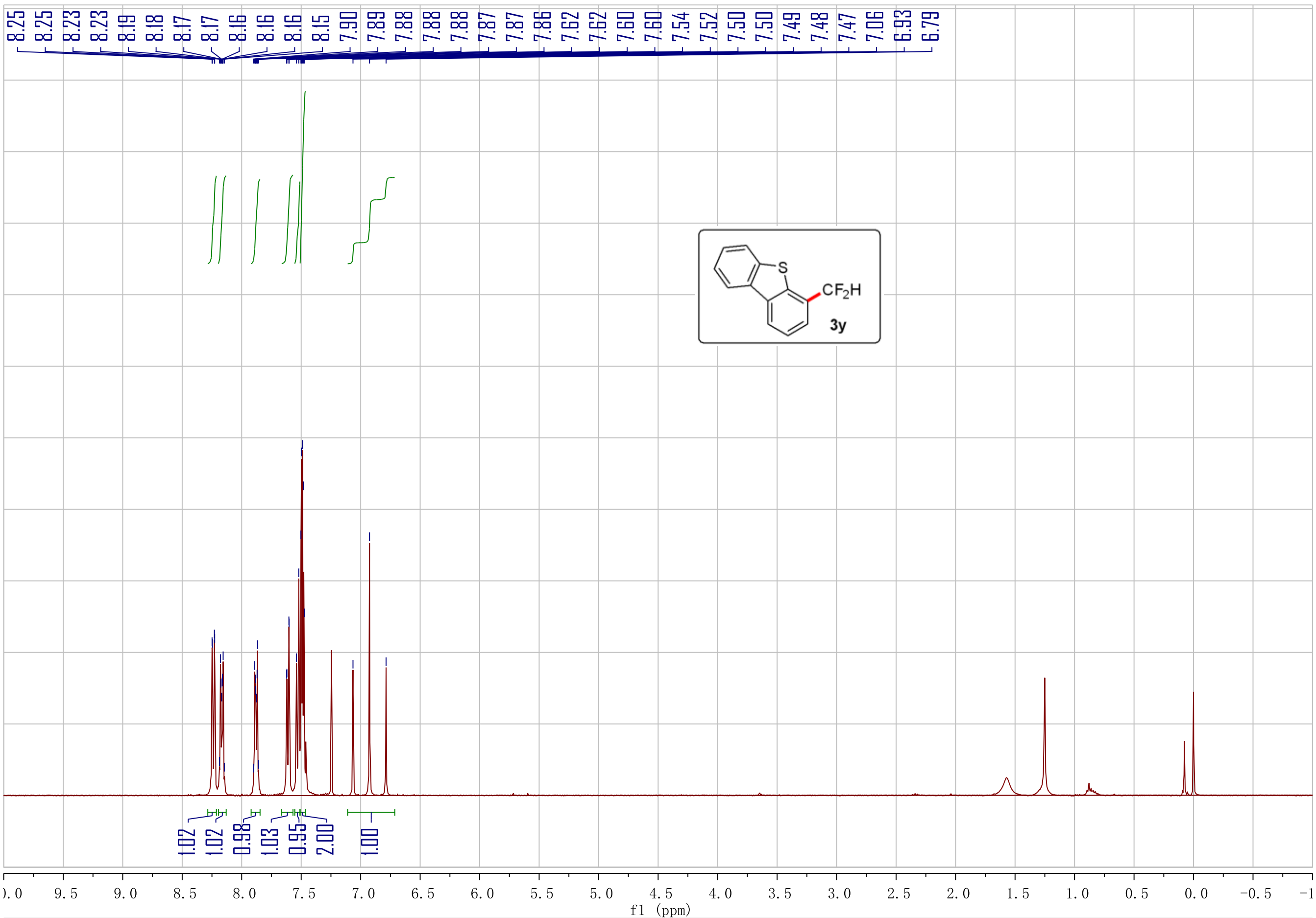

-107.81
-107.96
F
F
H
O
O
3w
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

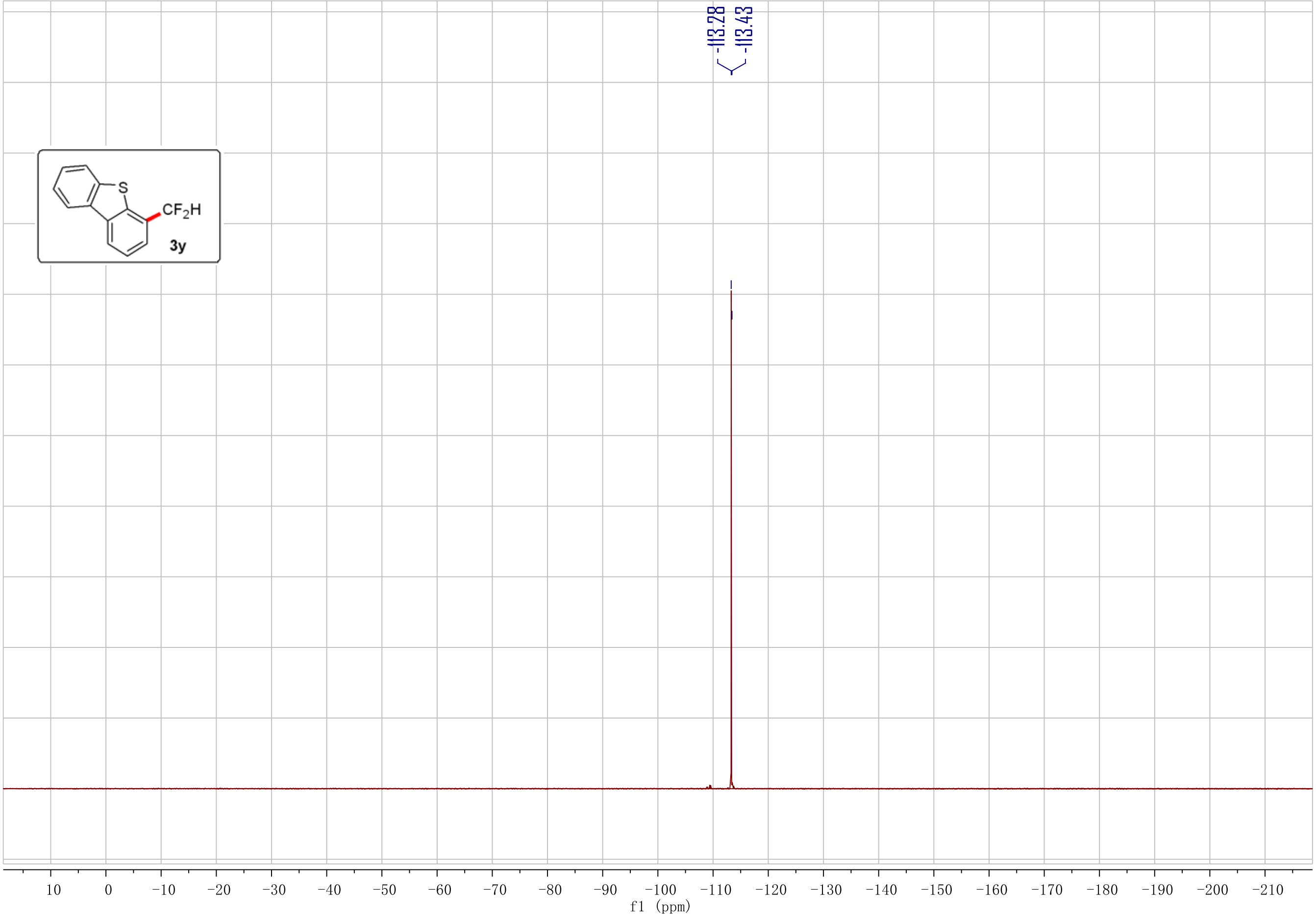

149.71
149.69
149.67
148.18
120.35
120.28
120.21
117.13
114.76
108.36
105.98
105.92
105.87
101.71
77.48
77.16
76.84
F
F
H
O
O
3w
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

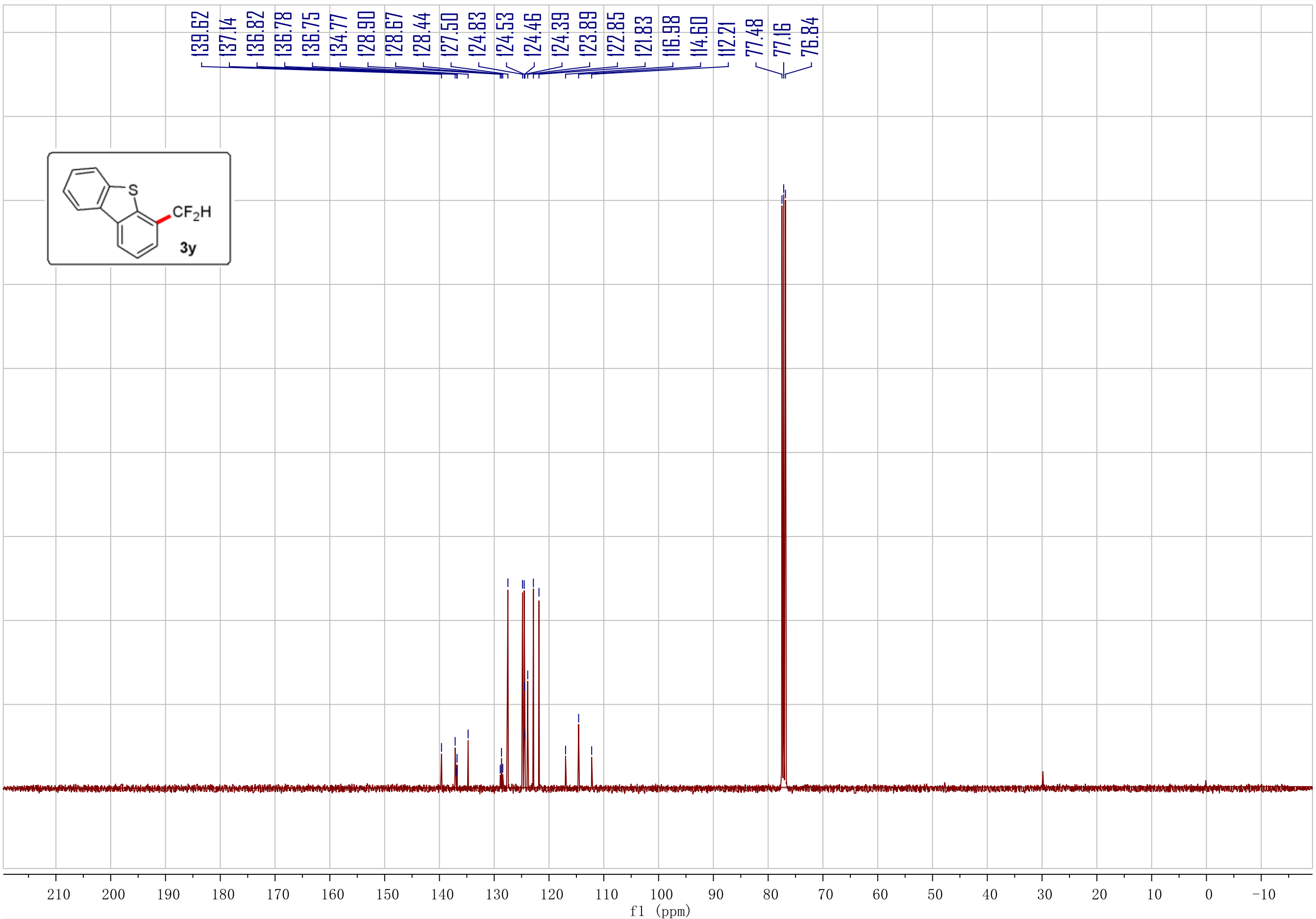

7.76
7.73
7.61
7.59
7.47
7.45
7.43
6.86
6.72
6.58
6.53
6.50
O
O
F
F
H
3x
0.98
1.01
0.91
0.98
1.00
0.93
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
f1 (ppm)

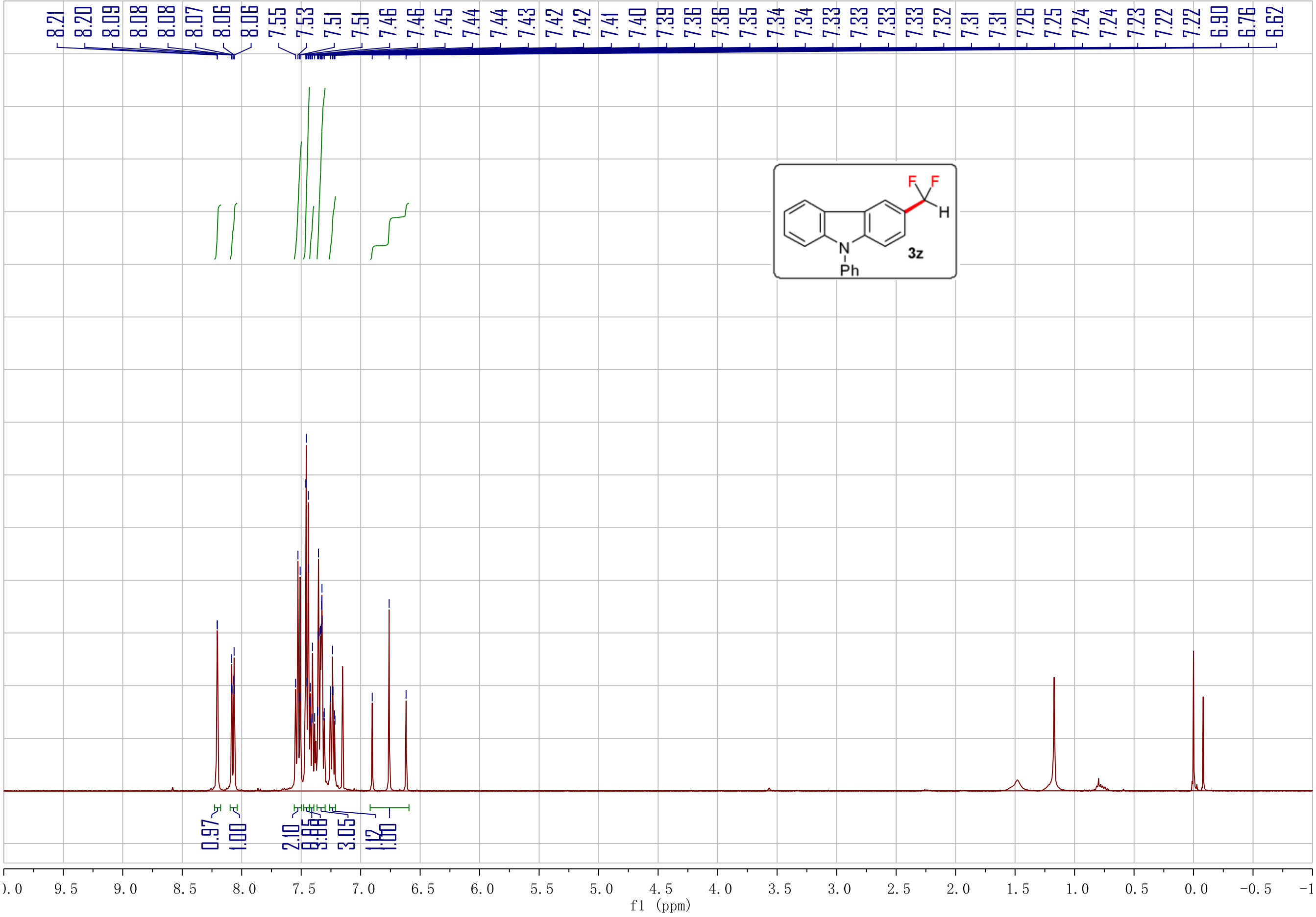

-111.98
-112.13
3x
F
F
H
O
O
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

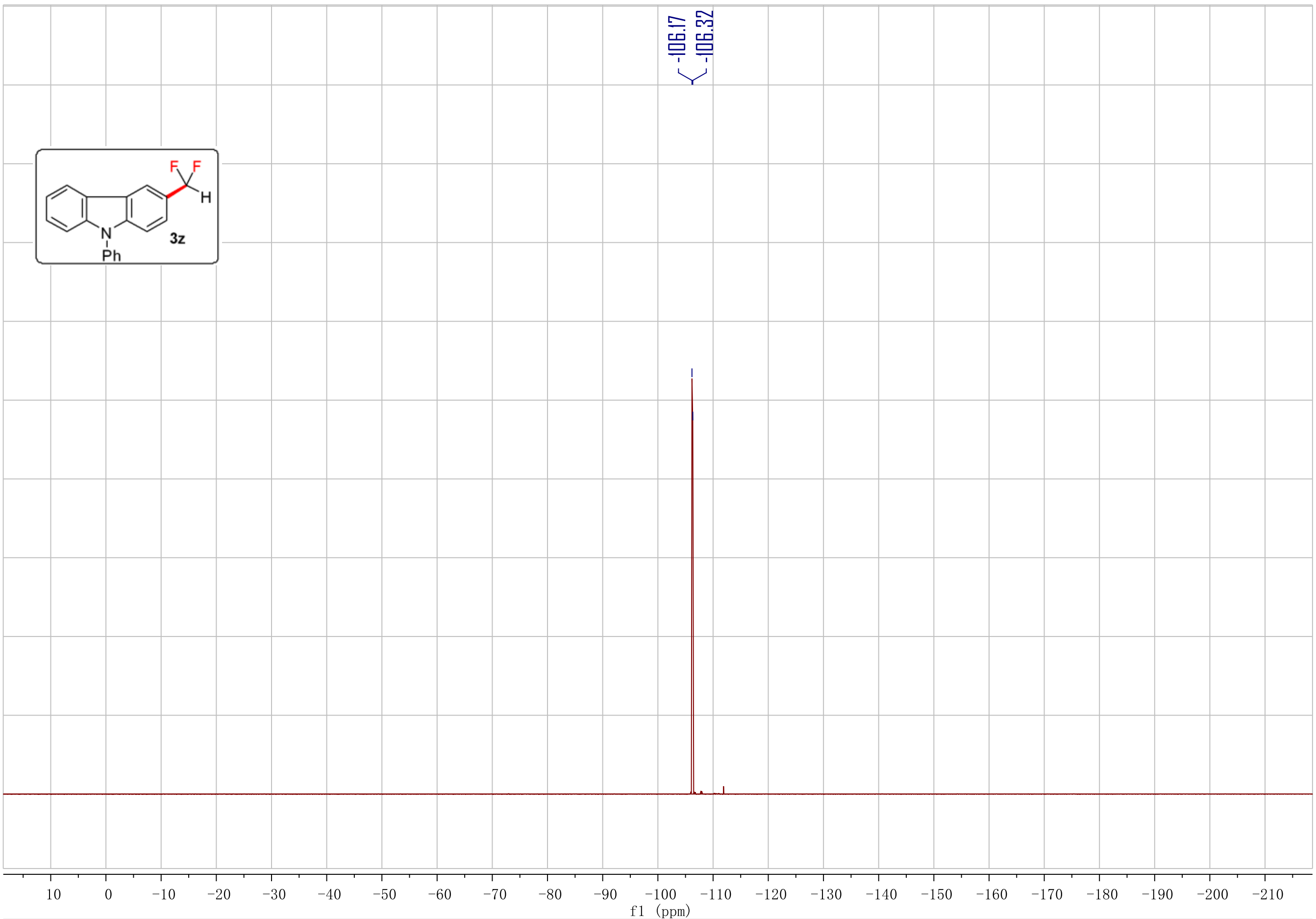

160.16
154.02
142.72
137.84
128.63
121.56
121.50
121.44
120.61
118.38
114.65
114.59
114.52
113.55
111.16
77.48
77.16
76.84
3x
F
F
H
O
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

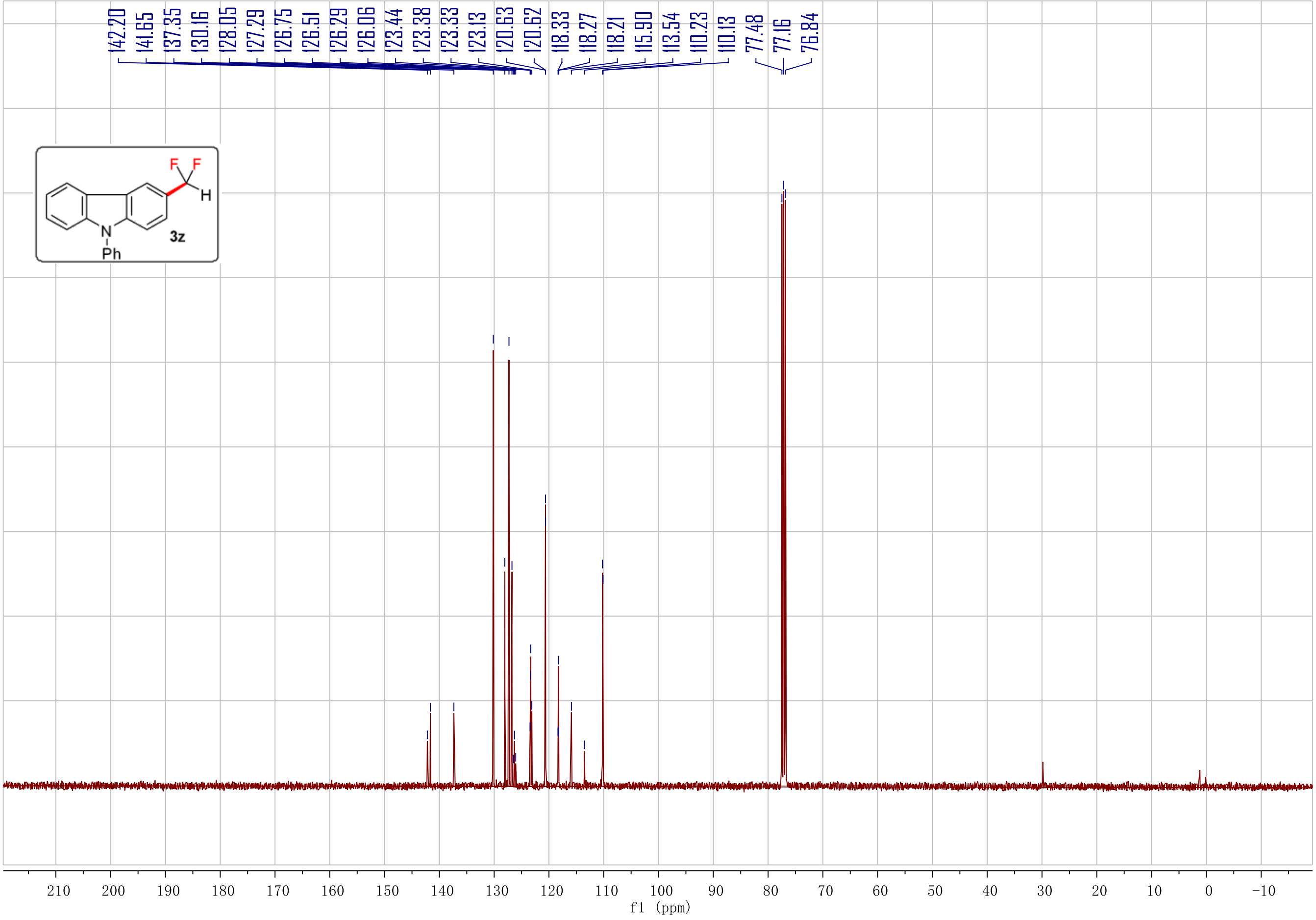

8.25
8.25
8.23
8.23
8.19
8.18
8.17
8.17
8.16
8.16
8.16
8.15
7.90
7.89
7.88
7.88
7.88
7.87
7.87
7.86
7.62
7.62
7.60
7.60
7.54
7.52
7.50
7.50
7.49
7.48
7.47
7.06
6.93
6.79
S
CF_2H
3y
1.02
1.02
0.98
1.03
0.95
2.00
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

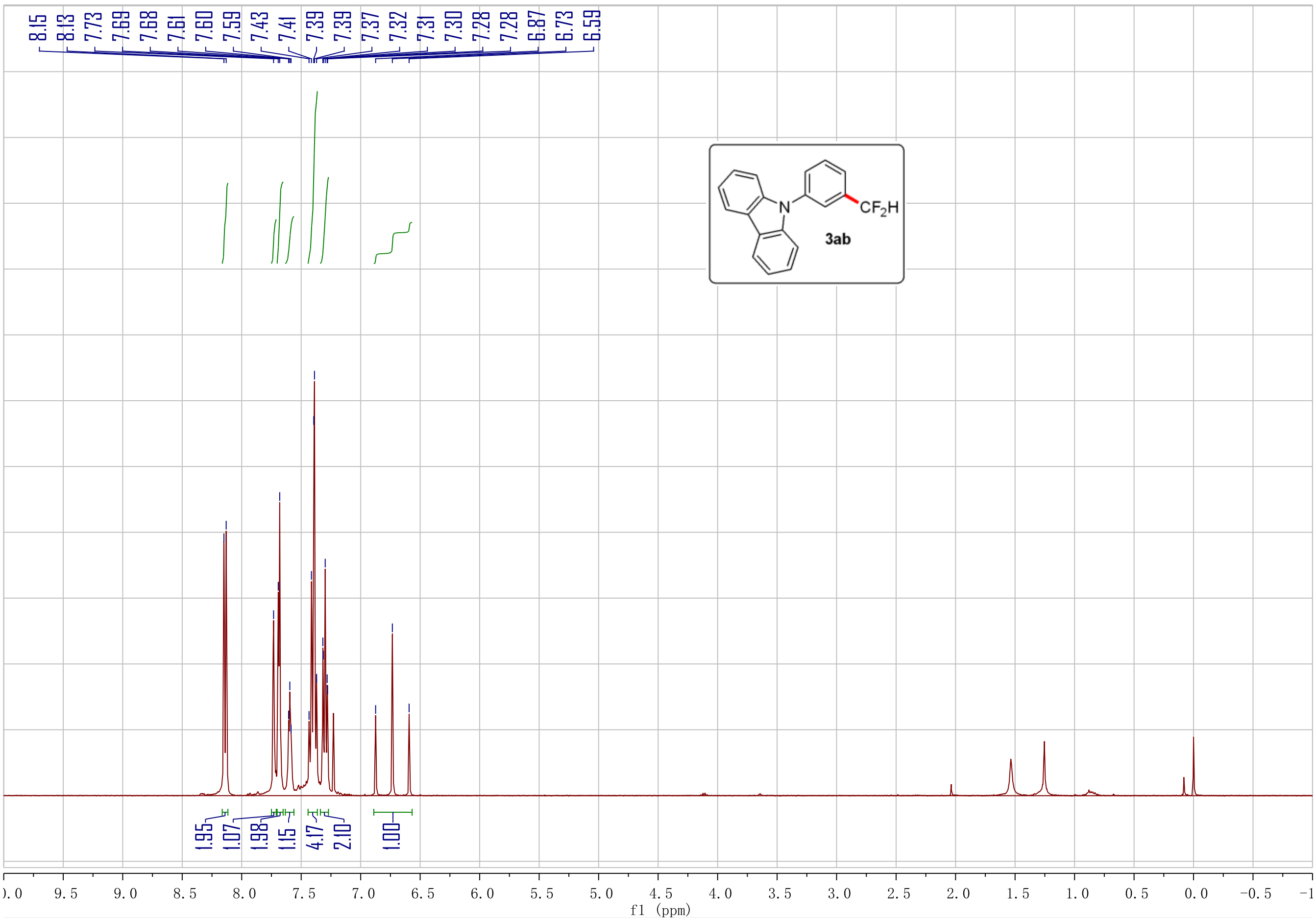

-113.28
-113.43
S
CF_2H
3y
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

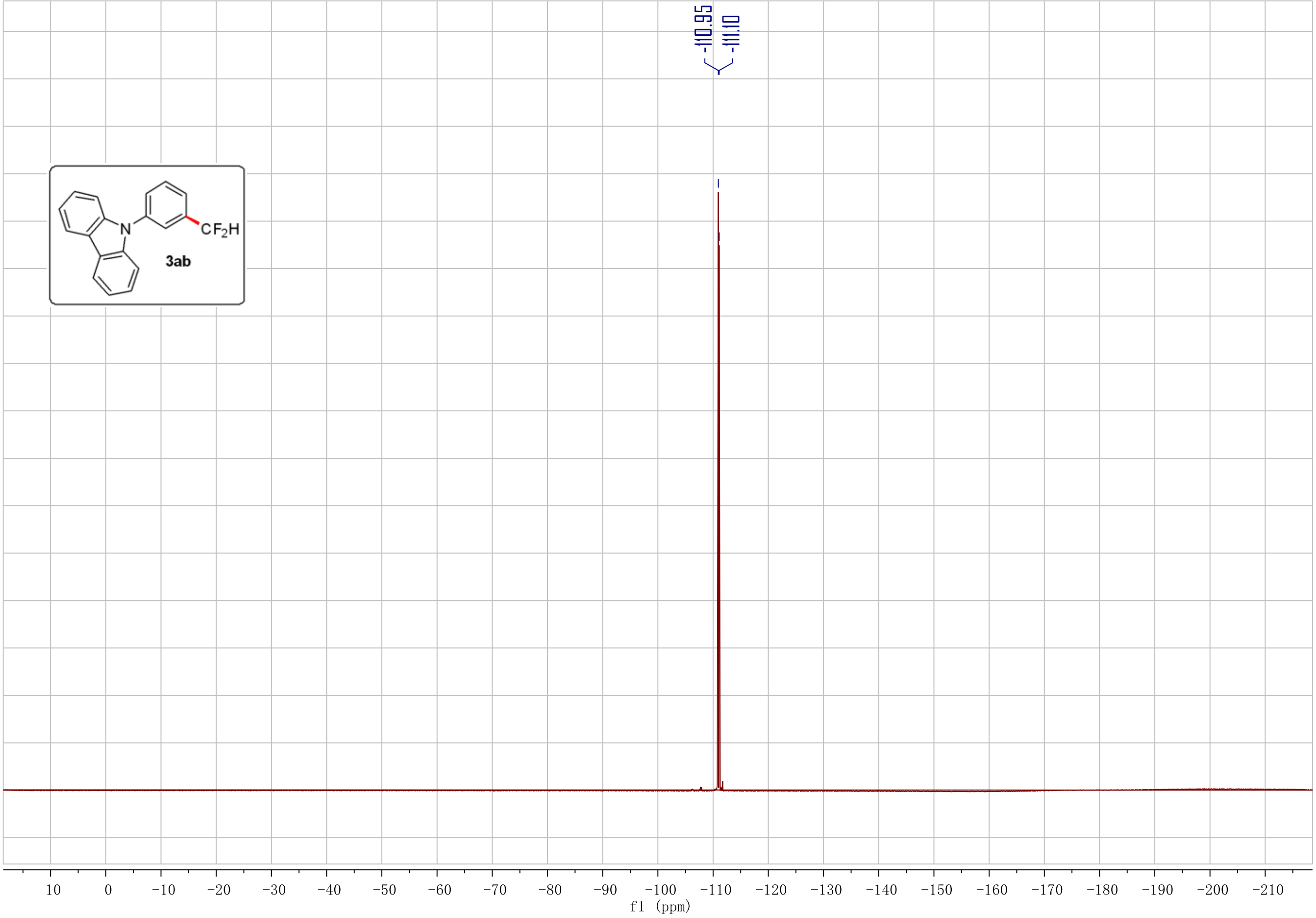

139.62
137.14
136.82
136.78
136.75
134.77
128.90
128.67
128.44
127.50
124.83
124.53
124.46
124.39
123.89
122.85
121.83
116.98
114.60
112.21
77.48
77.16
76.84
S
CF2H
3y
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

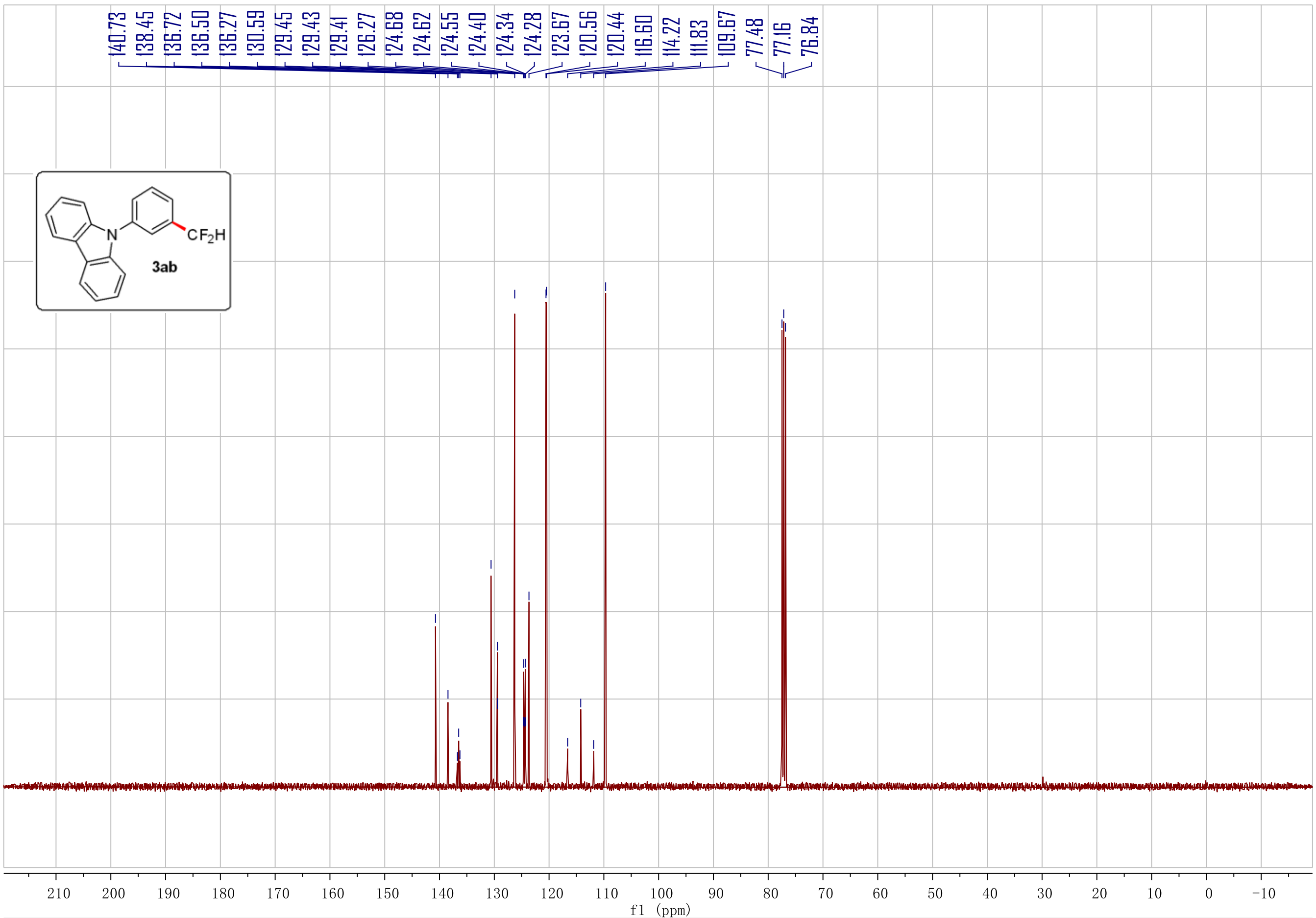

8.21
8.20
8.09
8.08
8.08
8.07
8.06
8.06
7.55
7.53
7.51
7.51
7.46
7.46
7.45
7.44
7.44
7.43
7.42
7.42
7.41
7.40
7.39
7.36
7.36
7.35
7.34
7.34
7.33
7.33
7.33
7.33
7.32
7.31
7.31
7.26
7.25
7.24
7.24
7.23
7.22
7.22
6.90
6.76
6.62
F
F
H
N
Ph
3z
0.97
1.00
2.10
0.95
3.98
3.05
1.12
1.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

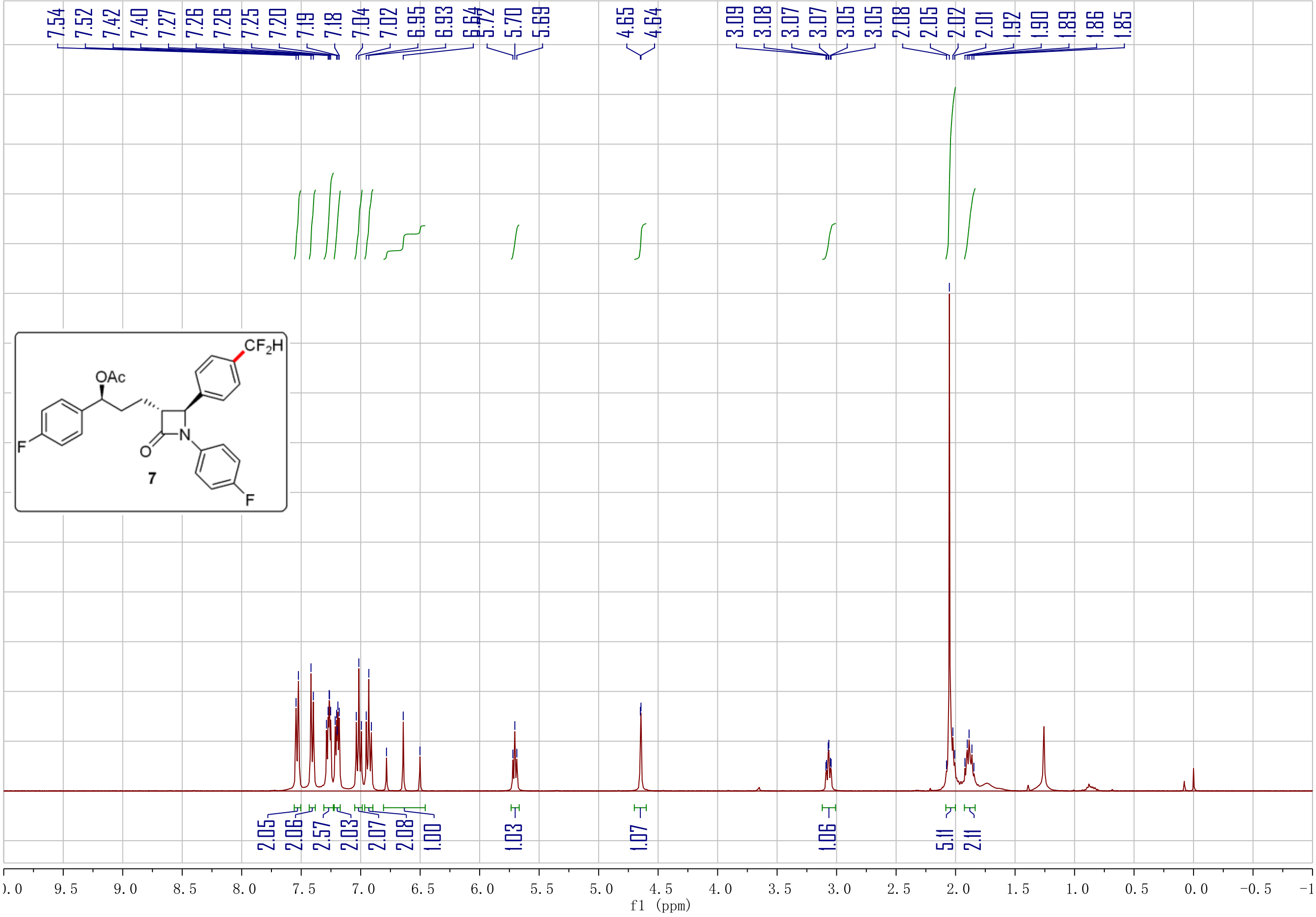

-106.17
-106.32
F
F
H
N
Ph
3z
10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)

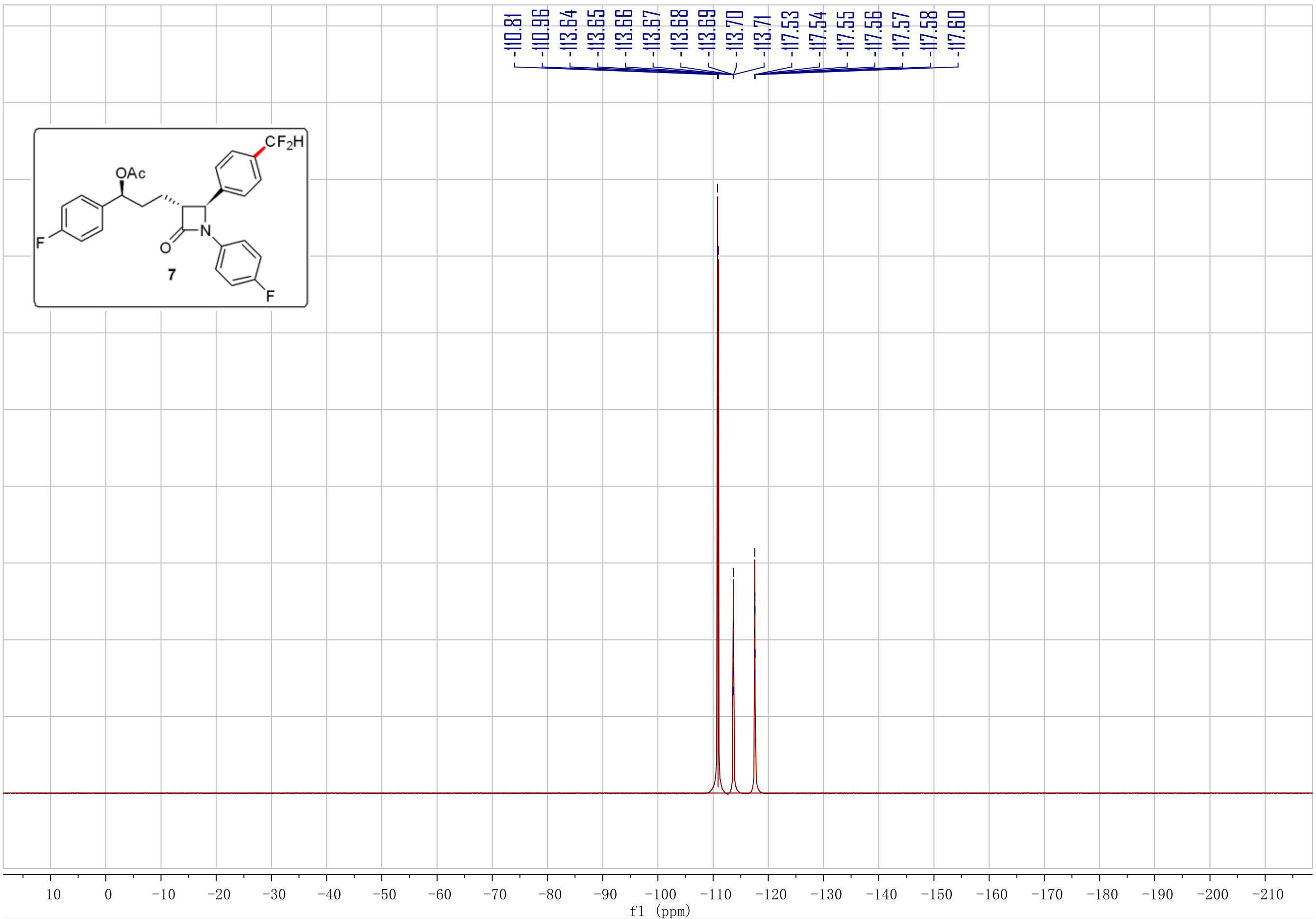

142.20
141.65
137.35
130.16
128.05
127.29
126.75
126.51
126.29
126.06
123.44
123.38
123.33
123.13
120.63
120.62
118.33
118.27
118.21
115.90
113.54
110.23
110.13
77.48
77.16
76.84
F
F
H
N
Ph
3z
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

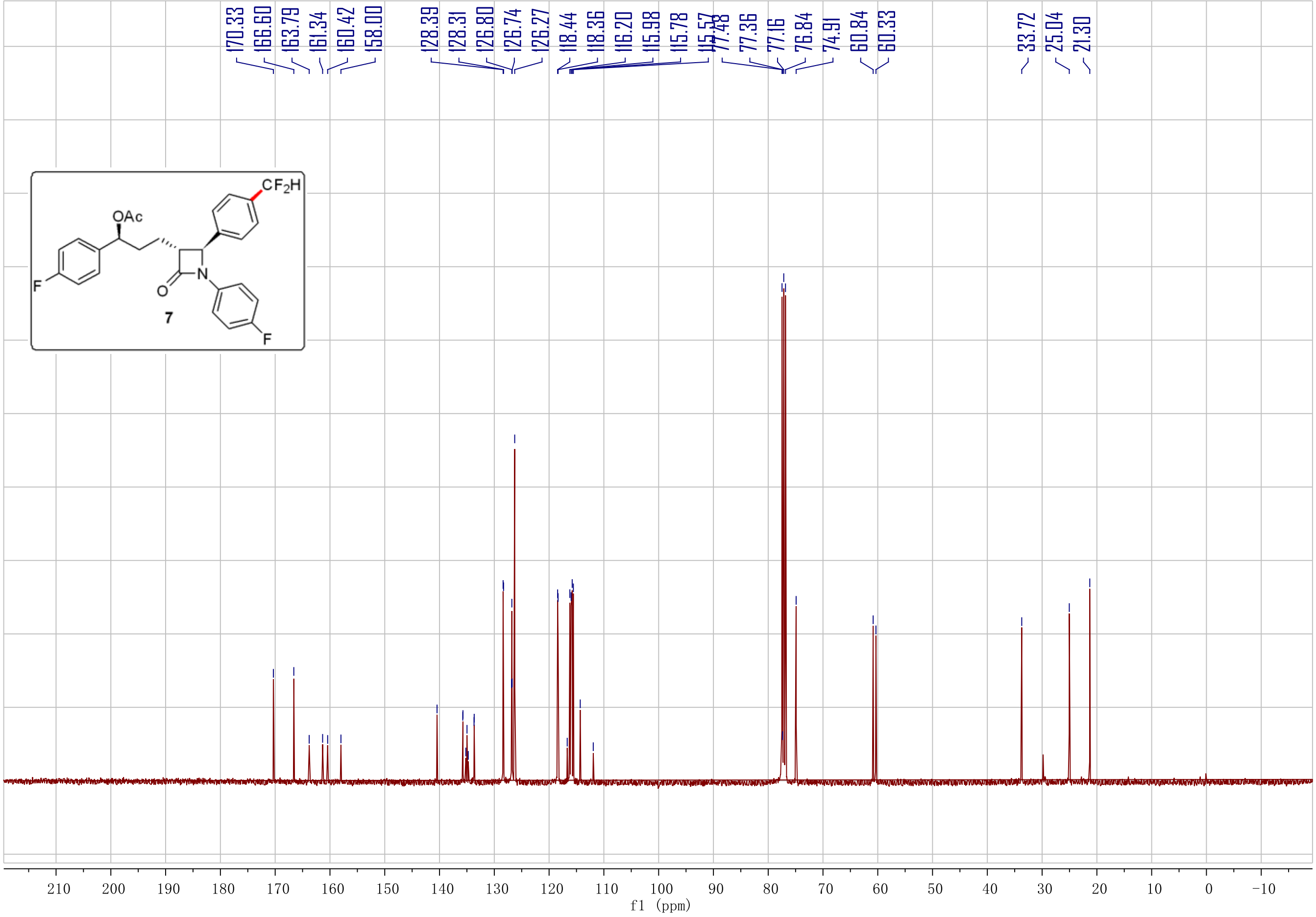

8.15
8.13
7.73
7.69
7.68
7.61
7.60
7.59
7.43
7.41
7.39
7.39
7.37
7.32
7.31
7.30
7.28
7.28
6.87
6.73
6.59
N
CF2H
3ab
1.95
1.07
1.98
1.15
4.17
2.10
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

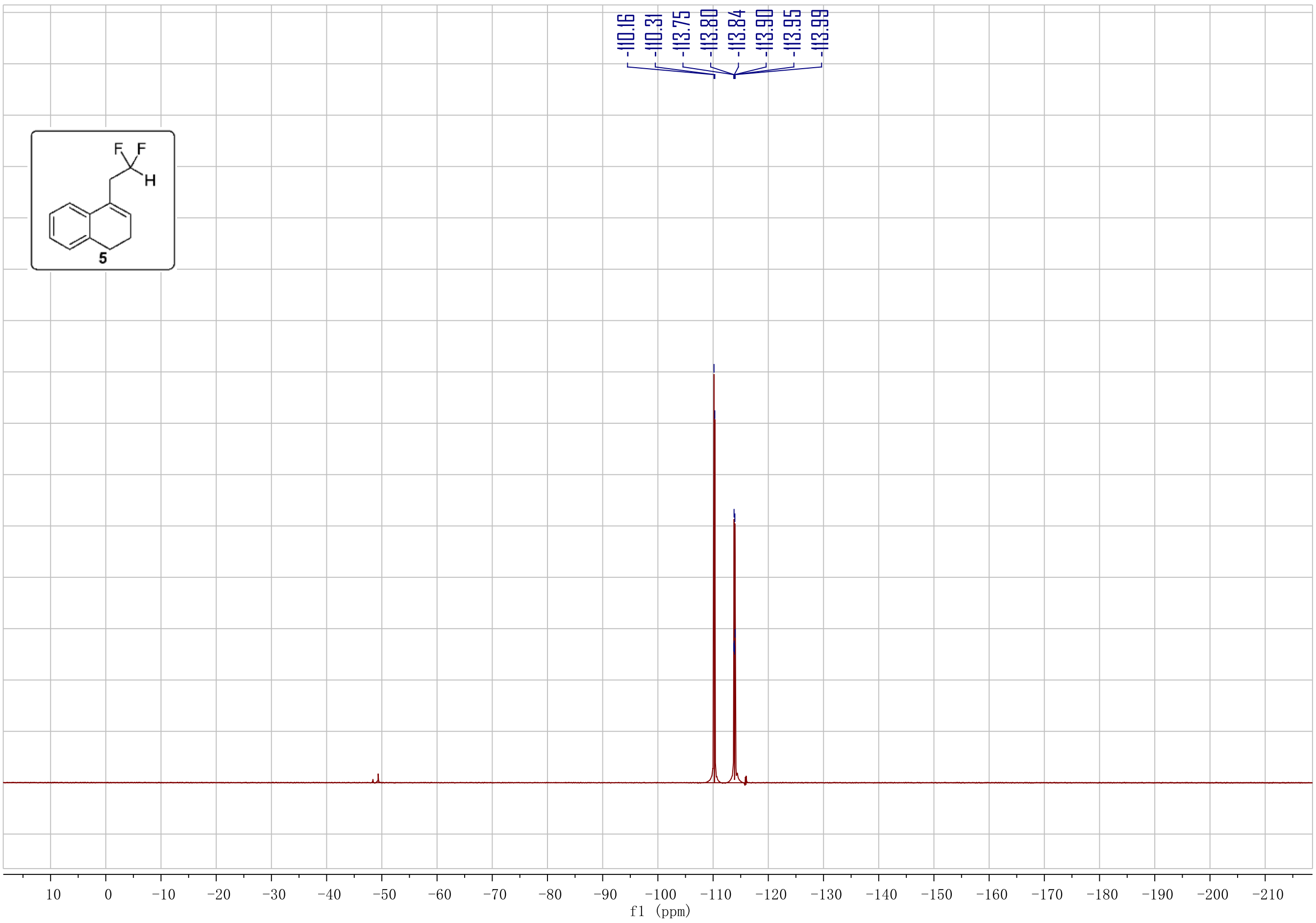

-110.95
-111.10
N
CF2H
3ab
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)


140.73
138.45
136.72
136.50
136.27
130.59
129.45
129.43
129.41
126.27
124.68
124.62
124.55
124.40
124.34
124.28
123.67
120.56
120.44
116.60
114.22
111.83
109.67
77.48
77.16
76.84
N
CF2H
3ab
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.54
7.52
7.42
7.40
7.27
7.26
7.26
7.25
7.20
7.19
7.18
7.04
7.02
6.95
6.93
6.64
5.72
5.70
5.69
4.65
4.64
3.09
3.08
3.07
3.07
3.05
3.05
2.08
2.05
2.02
2.01
1.92
1.90
1.89
1.86
1.85
CF2H
OAc
F
O
N
F
7
2.05
2.06
2.57
2.03
2.07
2.08
1.00
1.03
1.07
1.06
5.11
2.11
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


-110.81
-110.96
-113.64
-113.65
-113.66
-113.67
-113.68
-113.69
-113.70
-113.71
-117.53
-117.54
-117.55
-117.56
-117.57
-117.58
-117.60
OAc
CF2H
F
O
N
F
7
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)


170.33
166.60
163.79
161.34
160.42
158.00
128.39
128.31
126.80
126.74
126.27
118.44
118.36
116.20
115.98
115.78
115.57
77.48
77.36
77.16
76.84
74.91
60.84
60.33
33.72
25.04
21.30
OAc
CF2H
F
O
N
F
7
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


-110.16
-110.31
-113.75
-113.80
-113.84
-113.90
-113.95
-113.99
F
F
H
5
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)