Supporting Information

Regioselective installation of fluorosulfate (-OSO_2F) functionality into aromatic C(sp^2)–H bonds for the construction of *para*-amino-arylfluorosulfates

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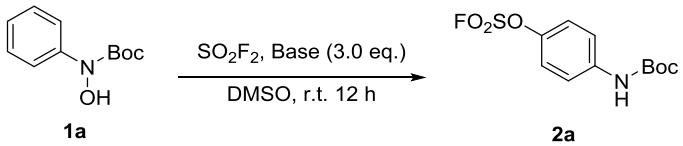
1. General information

All reactions were carried out under an air atmosphere. Unless otherwise specified, NMR spectra were recorded in $CDCl_3$ on a 500 MHz (for ^{1}H), 471 MHz (for ^{19}F), 126 MHz (for ^{13}C) spectrometer. All chemical shifts were reported in ppm relative to TMS (^{1}H NMR, 0 ppm) as internal standards. The HPLC experiments were carried out on a Waters e2695 instrument (column: J&K, RP-C18, 5 μm, 4.6 × 150 mm), and the yields of the products were determined by using the corresponding pure compounds as the external standards. The coupling constants were reported in Hertz (Hz). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Melting points were measured and uncorrected. MS experiments were performed on a TOF-Q ESI or CI/EI instrument. All reagents used in the reactions were all purchased from commercial sources and used without further purification.

2. Optimization of the reaction conditions

Table 1 Screening of the Reaction Condition[a]

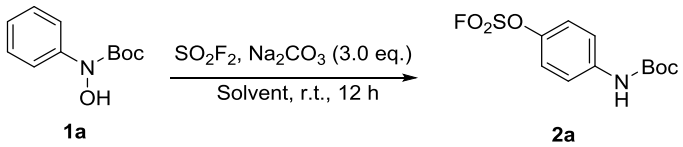


1a **2a**

Entry	Base	Yield (**2a**, %)[b]
1	Et_3N	43
2	DBU	14
3	DABCO	43
4	Pyridine	< 2
5	TMEDA	56
6	DIPEA	48
7	K_2CO_3	36
8	**Na_2CO_3**	**54**
9	NaOAc	18
10	Na_3PO_4	30
11	Na_3PO_4•$12H_2O$	50

[a]General conditions: *tert*-butyl hydroxy(phenyl)carbamate (**1a**, 0.2 mmol), Base (3.0 eq.) and DMSO (0.1 M, 2 mL) were added into a 20 mL tube equipped with a stirring bar. Then SO_2F_2 gas was introduced into the solution by slow bubbling through a SO_2F_2 balloon before allowed to stir at room temperature for 12 h. [b]Yields were determined by HPLC using the pure 4-((*tert*-butoxycarbonyl)amino)phenyl sulfurofluoridate (**2a**, 0.2 mmol) as the external standard (t_R = 4.727 min, λ_{max} = 239.3 nm, MeOH/H_2O = 80 : 20 (v / v)).

Table 2 Screening of the Solvent[a]



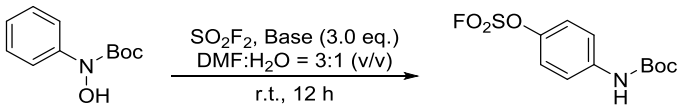
1a **2a**

Entry	Solvent	Yield (**2a**, %)[b]
1	DCM	37
2	Toluene	19
3	*m*-Xylene	15

4	MeCN	41
5	**DMF**	**62**
6	DMSO	54

[a]General conditions: *tert*-butyl hydroxy(phenyl)carbamate (**1a**, 0.2 mmol), Na_2CO_3 (3.0 eq.) and solvent (0.1 M, 2 mL) were added into a 20 mL tube equipped with a stirring bar. Then SO_2F_2 gas was introduced into the solution by slow bubbling through a SO_2F_2 balloon before allowed to stir at room temperature for 12 h. [b]Yields were determined by HPLC using the pure 4-((*tert*-butoxycarbonyl)amino)phenyl sulfurofluoridate (**2a**, 0.2 mmol) as the external standard (t_R = 4.727 min, λ_{max} = 239.3 nm, MeOH/H_2O = 80 : 20 (v / v)).

Table 3 Screening of the Reaction Condition[a]

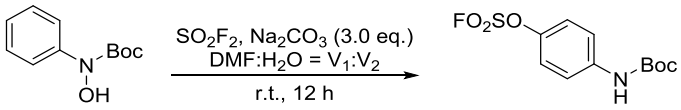


1a **2a**

Entry	Base	Yield (**2a**, %)[b]
1	**Na_2CO_3**	**82**
2	K_2CO_3	74
3	Cs_2CO_3	75
4	Na_3PO_4•$12H_2O$	79
5	K_3PO_4	68

[a]General conditions: *tert*-butyl hydroxy(phenyl)carbamate (**1a**, 0.2 mmol), Base (3.0 eq.) and co-solvent (2 mL, DMF:H_2O =3:1 (v/v)) were added into a 20 mL tube equipped with a stirring bar. Then SO_2F_2 gas was introduced into the solution by slow bubbling through a SO_2F_2 balloon before allowed to stir at room temperature for 12 h. [b]Yields were determined by HPLC using the pure 4-((*tert*-butoxycarbonyl)amino)phenyl sulfurofluoridate (**2a**, 0.2 mmol) as the external standard (t_R = 4.727 min, λ_{max} = 239.3 nm, MeOH/H_2O = 80 : 20 (v / v)).

Table 4 Screening of the volume ration of DMF and H_2O[a]



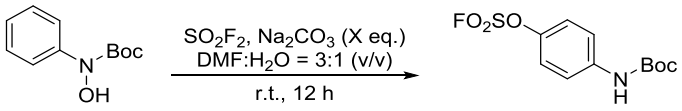
1a **2a**

Entry	DMF:H_2O = V_1:V_2	Yield (**2a**, %)[b]
1	1:9	57
2	1:3	63

3	1:1	74
4	**3:1**	**82**
5	9:1	80
6	10:0	62

[a]General conditions: *tert*-butyl hydroxy(phenyl)carbamate (**1a**, 0.2 mmol), Na_2CO_3 (3.0 eq.) and co-solvent (2 mL, DMF:H_2O = (V_1:V_2)) were added into a 20 mL tube equipped with a stirring bar. Then SO_2F_2 gas was introduced into the solution by slow bubbling through a SO_2F_2 balloon before allowed to stir at room temperature for 12 h. [b]Yields were determined by HPLC using the pure 4-((*tert*-butoxycarbonyl)amino)phenyl sulfurofluoridate (**2a**, 0.2 mmol) as the external standard (t_R = 4.727 min, λ_{max} = 239.3 nm, MeOH/H_2O = 80 : 20 (v / v)).

Table 5 Screening of the Na_2CO_3 loading[a]

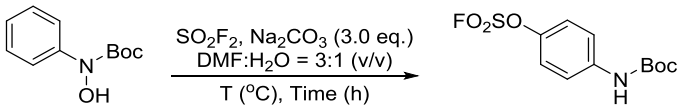


1a **2a**

Entry	Na_2CO_3 (X eq.)	Yield (**2a**, %)[b]
1	1.0	**7**
2	1.5	16
3	2.0	33
4	**3.0**	**82**
5	5.0	84

[a]General conditions: *tert*-butyl hydroxy(phenyl)carbamate (**1a**, 0.2 mmol), Na_2CO_3 (X eq.) and co-solvent (2 mL, DMF:H_2O =3:1 (v/v)) were added into a 20 mL tube equipped with a stirring bar. Then SO_2F_2 gas was introduced into the solution by slow bubbling through a SO_2F_2 balloon before allowed to stir at room temperature for 12 h. [b]Yields were determined by HPLC using the pure 4-((*tert*-butoxycarbonyl)amino)phenyl sulfurofluoridate (**2a**, 0.2 mmol) as the external standard (t_R = 4.727 min, λ_{max} = 239.3 nm, MeOH/H_2O = 80 : 20 (v / v)).

Table 6 Screening of the Reaction Condition[a]



1a **2a**

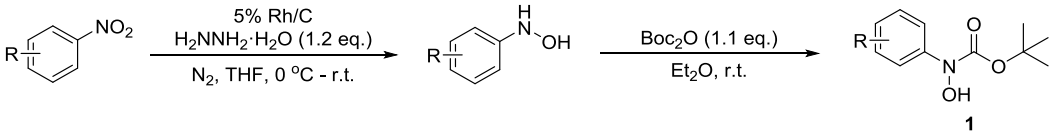
Entry	T (^oC)	Time (h)	Yield (**2a**, %)[b]
1	r.t.	12	82

2	50	12	83
3	70	12	71
4	r.t.	5	80
6	**r.t.**	**3**	**82**
7	r.t.	2	74

[a]General conditions: *tert*-butyl hydroxy(phenyl)carbamate (**1a**, 0.2 mmol), Na_2CO_3 (3.0 eq.) and co-solvent (2 mL, DMF:H_2O = (V_1:V_2)) were added into a 20 mL tube equipped with a stirring bar. Then SO_2F_2 gas was introduced into the solution by slow bubbling through a SO_2F_2 balloon before allowed to stir at the corresponding temperature. [b]Yields were determined by HPLC using the pure 4-((*tert*-butoxycarbonyl)amino)phenyl sulfurofluoridate (**2a**, 0.2 mmol) as the external standard (t_R = 4.727 min, λ_{max} = 239.3 nm, MeOH/H_2O = 80 : 20 (v / v)).

3. General procedures for synthesis of protected *N*-aryl-*N*-hydroxylamine

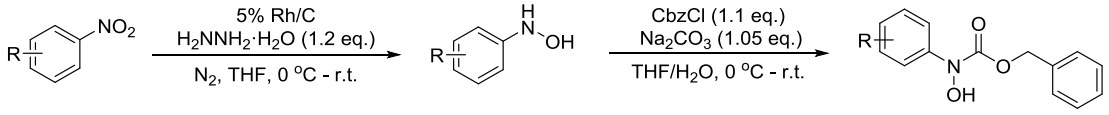
3.1 Procedure for the synthesis of Boc-protected *N*-aryl-*N*-hydroxylamines[1]



1

A suspension of aryl nitro compound (10 mmol, 1.0 eq.) and 5% Rh/C (62 mg, 0.30 mol% Rh) in THF (30 mL, 0.33 M) was cooled to 0 °C under Argon atmosphere. Then Hydrazine monohydrate (600 mg, 12 mmol, 1.2 eq.) was added to the suspension dropwise and the reaction mixture was stirred at 0 °C for 1 h followed by slowly warming up to room temperature. The reaction was monitored *via* TLC until the disappearance of the aryl nitro compound and the appearance of the hydroxylamine intermediate. The reaction was filtered through a short pad of celite and concentrated *in vacuo*. The residue was used for the next step without further purification. Then to a solution of crude *N*-aryl-*N*-hydroxylamine (10 mmol) in anhydrous Et_2O (30 mL) was added Boc_2O (2.4 g, 11 mmol) dissolved in dry Et_2O (20 mL) dropwise at room temperature, and the stirring was kept for 12 h. The solvent was evaporated in vacuum and the residue was purified through silica gel flash chromatography to give the desired product *tert*-butyl hydroxy(aryl)carbamate **1**.

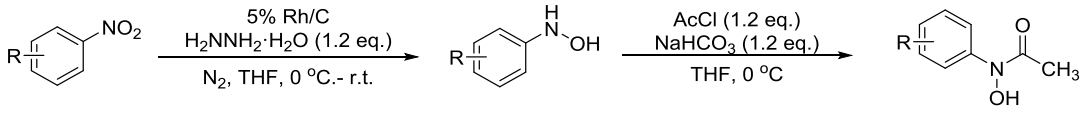
3.2 Procedure for the synthesis of Cbz-protected *N*-aryl-*N*-hydroxylamines[2, 3]



3

The crude *N*-aryl-*N*-hydroxylamine was synthesized according to the above mentioned procedure. Subsequently, the solution of crude *N*-aryl-*N*-hydroxylamine dissolved in THF (12 mL) and H_2O (1.0 mL) at 0 ^oC was added the benzyl chloroformate (1.88 g, 11 mmol, 1.1 eq.) and Na_2CO_3 (1.11 g, 10.5 mmol, dissolved in 4 mL H_2O) over 7 min simultaneously before the removal of ice bath. When the reaction reached its completion, the mixture was diluted with Et_2O (10 mL) and washed with 0.5 M H_3PO_4 (10 mL). Aqueous phase was extracted with EtOAc (15 mL ×3) and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated to dryness. The residue was purified through silica gel chromatography using a mixture of ethyl acetate and petroleum ether as eluent to afford the desired Cbz-protected *N*-aryl-*N*-hydroxylamine **3.**

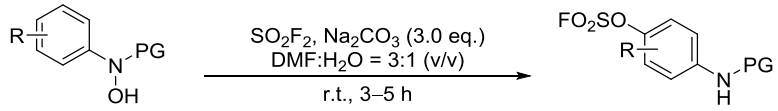
3.3 Procedure for the synthesis of Ac-protected *N*-aryl-*N*-hydroxylamines[2]



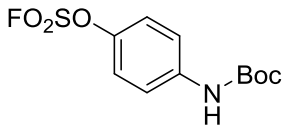
7

The crude *N*-aryl-*N*-hydroxylamine was synthesized according to the above mentioned procedure. Then to a stirred suspension of crude *N*-aryl-*N*-hydroxylamine (10 mmol) and $NaHCO_3$ (12 mmol, 1.0 g) in THF (30 mL) at 0 ^oC was slowly added a solution of AcCl (12 mmol, 0.95 g) in THF (20 mL) dropwise. After the addition was complete, the reaction mixture was filtered through a short pad of celite and the celite was washed with EtOAc. The combine organic layers was concentrated in vacuum and the residue was further purified through silica gel chromatography using a mixture of ethyl acetate and petroleum ether as eluent to afford the desired Ac-protected *N*-aryl-*N*-hydroxylamine **7**.

4. General procedure for the rearrangement

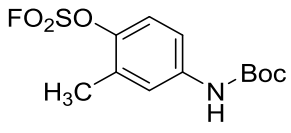


To an oven-dried 30 mL reaction tube equipped with a stirring bar was added protected *N*-aryl-*N*-hydroxylamine (1.0 mmol, 1.0 eq.), Na_2CO_3 (318 mg, 3 mmol, 3.0 eq.) and co-solvent (10 mL, 0.1 M, DMF : H_2O = 3:1 (v/v)). Then the reaction tube was fitted with a plastic stopper and SO_2F_2 was introduced into the stirring mixture by slow bubbling from a SO_2F_2 balloon at room temperature for 3-5 h (monitored by TLC). When the reaction reached its completion, the reaction mixture was diluted with water and aqueous phase was extracted with EtOAc (10 mL ×3) and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated to dryness. The residue was purified through silica gel chromatography using a mixture of ethyl acetate and petroleum ether as eluent to afford the desired rearrangement product.



2a

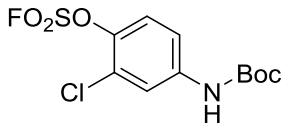
4-((*tert*-butoxycarbonyl)amino)phenyl sulfurofluoridate (**2a**). White soild, 224 mg, 77% yield. M.p. 123-124 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, J = 8.8 Hz, 2H), 7.26 (d, J = 8.8 Hz, 2H), 6.65 (br s, 1H), 1.53 (s, 9H). ^{19}F (471 MHz, $CDCl_3$) +36.9 (s, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.6, 145.1, 138.9, 121.7, 119.8, 81.4, 28.4. ESI-MS HRMS calculated for $C_{11}H_{14}FNNaO_5S$ $[M+Na]^+$ 314.0469, found: 314.0462.



2b

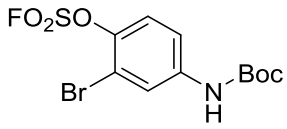
4-((*tert*-butoxycarbonyl)amino)-2-methylphenyl sulfurofluoridate (**2b**). Light yellow solid, 244 mg, 80% yield. M.p. 89-91 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (s, 1H), 7.23-7.19 (m, 2H), 6.55 (br s, 1H), 2.35 (s, 3H), 1.52 (s, 9H). ^{19}F (471 MHz, $CDCl_3$)

+38.4 (s, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.6, 144.2, 138.6, 131.5, 121.6, 121.4, 117.2, 81.3, 28.4, 16.3. ESI-MS HRMS calculated for $C_{12}H_{16}FNNaO_5S$ $[M+Na]^+$ 328.0625, found: 328.0620.



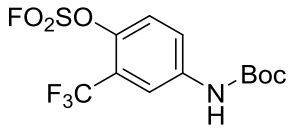
2c

4-((*tert*-butoxycarbonyl)amino)-2-chlorophenyl sulfurofluoridate (**2c**). White solid, 202 mg, 62% yield. M.p. 97-99 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.33 (d, J = 9.0 Hz, 1H), 7.26-7.24 (m, 1H), 6.66 (br s, 1H), 1.52 (s, 9H). ^{19}F (471 MHz, $CDCl_3$) +40.3 (s, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.2, 140.9, 139.6, 127.6, 123.1, 120.4, 117.5, 81.9, 28.3. ESI-MS HRMS calculated for $C_{11}H_{13}ClFNNaO_5S$ $[M+Na]^+$ 348.0079, found: 348.0076.



2d

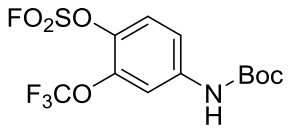
2-bromo-4-((*tert*-butoxycarbonyl)amino)phenyl sulfurofluoridate (**2d**). White solid, 260 mg, 70% yield. M.p. 120-122 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.34-7.30 (m, 2H), 6.65 (br s, 1H), 1.54 (s, 9H). ^{19}F (471 MHz, $CDCl_3$) +40.8 (s, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.2, 142.3, 139.7, 123.4, 122.8, 118.3, 116.0, 81.9, 28.3. ESI-MS HRMS calculated for $C_{11}H_{13}BrFNNaO_5S$ $[M+Na]^+$ 391.9574, found: 391.9565.



2e

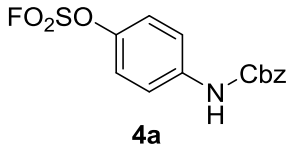
4-((*tert*-butoxycarbonyl)amino)-2-(trifluoromethyl)phenyl sulfurofluoridate (**2e**). Light yellow oil, 201 mg, 56% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (s, 1H),

7.63 (d, *J* = 8.5 Hz, 1H), 7.42 (d, *J* = 9.1 Hz, 1H), 7.17 (br s, 1H), 1.52 (s, 9H). ^{19}F (471 MHz, $CDCl_3$) +41.6 (s, 1F), -61.1 (s, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.6, 141.3, 139.2, 123.5 (q, *J* = 32.7 Hz), 122.8, 122.6, 122.0 (q, *J* = 273.3 Hz), 117.3, (d, *J* = 4.6 Hz), 82.1, 28.2. ESI-MS HRMS calculated for $C_{12}H_{13}F_4NNaO_5S$+ $[M+Na]^+$ 382.0343, found: 382.0338.



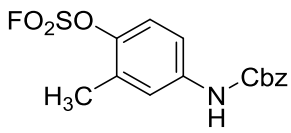
2f

4-((*tert*-butoxycarbonyl)amino)-2-(trifluoromethoxy)phenyl sulfurofluoridate (**2f**). Light yellow oil, 229 mg, 61% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.35 (d, *J* = 9.1 Hz, 1H), 7.27 (d, *J* = 6.7 Hz, 1H), 6.91 (br s, 1H), 1.52 (s, 9H). ^{19}F (471 MHz, $CDCl_3$) +39.6 (s, 1F), -57.9 (s, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.2, 141.0 (d, *J* = 1.8 Hz), 140.0, 136.0, 123.5, 120.4 (q, *J* = 261.6 Hz), 116.9, 112.3, 82.1, 28.3. ESI-MS HRMS calculated for $C_{12}H_{13}F_4NNaO_6S$ $[M+Na]^+$ 398.0292, found: 398.0285.



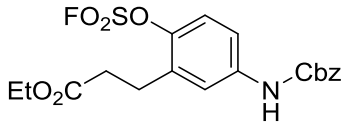
4a

4-(((benzyloxy)carbonyl)amino)phenyl sulfurofluoridate (**4a**). White solid, 254 mg, 78% yield. M.p. 90-91 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.5 Hz, 2H), 7.40-7.36 (m, 5H), 7.27 (d, *J* = 8.7 Hz, 2H), 6.90 (br s, 1H), 5.22 (s, 2H). ^{19}F (471 MHz, $CDCl_3$) +37.0 (s, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.2, 145.5, 138.3, 135.8, 128.8, 128.7, 128.5, 121.8, 120.0, 67.6. ESI-MS HRMS calculated for $C_{14}H_{12}FNNaO_5S$ $[M+Na]^+$ 348.0312, found: 348.0310.



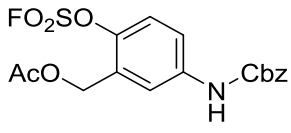
4b

4-(((benzyloxy)carbonyl)amino)-2-methylphenyl sulfurofluoridate (**4b**). White solid, 217 mg, 64% yield. M.p. 84-86°C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.35 (m, 6H), 7.28-7.22 (m, 2H), 6.80 (br s, 1H), 5.21 (s, 2H), 2.35 (s, 3H). ^{19}F (471 MHz, $CDCl_3$) +38.5 (s, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.2, 144.6, 138.0, 135.8, 131.7, 128.8, 128.7, 128.5, 121.8, 121.6, 117.5, 67.5, 16.3. ESI-MS HRMS calculated for $C_{15}H_{14}FNNaO_5S$ $[M+Na]^+$ 362.0469, found: 362.0461.



4c

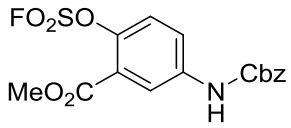
Ethyl 3-(5-(((benzyloxy)carbonyl)amino)-2-((fluorosulfonyl)oxy)phenyl)propanoate (**4c**). Yellow oil, 387 mg, 91% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (s, 1H), 7.38-7.33 (m, 6H), 7.24 (d, J = 9.0 Hz, 1H), 7.21 (br s, 1H), 5.19 (s, 2H), 4.13 (q, J = 7.2 Hz, 2H), 3.00 (t, J = 7.8 Hz, 2H), 2.63 (t, J = 7.8 Hz, 2H), 1.23 (t, J = 7.1 Hz, 3H). ^{19}F (471 MHz, $CDCl_3$) +39.0 (s, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.4, 153.3, 144.0, 138.4, 135.8, 133.7, 128.7, 128.5, 128.4, 121.6, 120.5, 118.0, 67.3, 60.9, 34.0, 25.0, 14.1. ESI-MS HRMS calculated for $C_{19}H_{20}FNNaO_7S$ $[M+Na]^+$ 448.0837, found: 448.0834.



4d

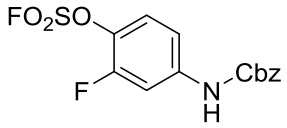
5-(((benzyloxy)carbonyl)amino)-2-((fluorosulfonyl)oxy)benzyl acetate (**4d**). Light yellow oil, 290 mg, 73% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (s, 1H), 7.49 (d, J = 8.6 Hz, 1H), 7.38-7.33 (m, 5H), 7.30-7.29 (m, 2H), 5.20 (s, 2H), 5.15 (s, 2H), 2.09

(s, 3H). ^{19}F (471 MHz, $CDCl_3$) +39.8 (s, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.7, 153.2, 143.7, 138.4, 135.7, 129.5, 128.8, 128.7, 128.5, 122.0, 120.5, 119.7, 67.5, 60.7, 20.8. ESI-MS HRMS calculated for $C_{17}H_{16}FNNaO_7S$ $[M+Na]^+$ 420.0524, found: 420.0515.



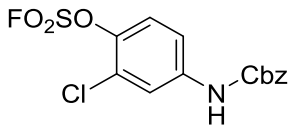
4e

Methyl 5-(((benzyloxy)carbonyl)amino)-2-((fluorosulfonyl)oxy)benzoate (**4e**). White solid, 245 mg, 64% yield. M.p. 124-125 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.90 (d, J = 7.5 Hz, 1H), 7.39-7.33 (m, 6H), 7.24 (br s, 1H), 5.22 (s, 2H), 3.91 (s, 3H). ^{19}F (471 MHz, $CDCl_3$) +41.0 (s, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.9, 153.2, 143.6, 138.7, 135.6, 128.84, 128.77, 128.6, 124.3, 123.6, 123.5, 122.2, 67.7, 53.1. ESI-MS HRMS calculated for $C_{16}H_{14}FNNaO_7S$ $[M+Na]^+$ 406.0367, found: 406.0366.



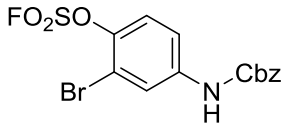
4f

4-(((benzyloxy)carbonyl)amino)-2-fluorophenyl sulfurofluoridate (**4f**). Off-white solid, 199 mg, 58% yield. M.p. 83-85^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, J = 11.6 Hz, 1H), 7.40-7.35 (m, 5H), 7.31 (t, J = 8.5 Hz, 1H), 7.08 (d, J = 9.0 Hz, 1H), 6.96 (br s, 1H), 5.22 (s, 2H). ^{19}F (471 MHz, $CDCl_3$) +38.5 (s, 1F), -125.9 - -126.0 (m, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.9 (d, J = 252.5 Hz), 153.0, 139.6 (d, J = 10.0 Hz), 135.5, 132.4 (d, J = 13.6 Hz), 128.9, 128.8, 128.6, 123.6, 114.2, 107.9 (d, J = 23.6 Hz), 67.8. ESI-MS HRMS calculated for $C_{14}H_{11}F_2NNaO_5S$ $[M+Na]^+$ 366.0218, found: 366.0208.



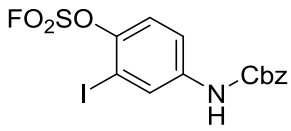
4g

4-(((benzyloxy)carbonyl)amino)-2-chlorophenyl sulfurofluoridate (**4g**). Off-white gum, 213 mg, 59% yield. M.p. 66-68 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.40-7.31 (m, 7H), 7.03 (br s, 1H), 5.21 (s, 2H). ^{19}F (471 MHz, $CDCl_3$) +40.4 (s, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.0, 141.3, 139.0, 135.6, 128.9, 128.8, 128.6, 127.7, 123.2, 120.7, 117.8, 67.8. ESI-MS HRMS calculated for $C_{14}H_{11}ClFNNaO_5S$ $[M+Na]^+$ 381.9923, found: 381.9913.



4h

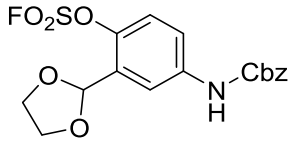
4-(((benzyloxy)carbonyl)amino)-2-bromophenyl sulfurofluoridate (**4h**). Off-white solid, 259 mg, 64% yield. M.p. 97-99 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.40-7.33 (m, 7H), 7.07 (br s, 1H), 5.21 (s, 2H). ^{19}F (471 MHz, $CDCl_3$) +40.7 (s, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.1, 142.6, 139.2, 135.6, 128.84, 128.76, 128.5, 123.7, 122.9, 118.6, 116.1, 67.7. ESI-MS HRMS calculated for $C_{14}H_{11}BrFNNaO_5S$ $[M+Na]^+$ 425.9418, found: 425.9416.



4i

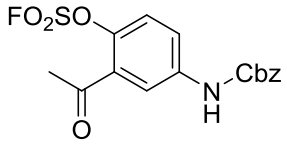
4-(((benzyloxy)carbonyl)amino)-2-iodophenyl sulfurofluoridate (**4i**). Light yellow solid, 270 mg, 60% yield. M.p. 118-119 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.45 (d, J = 8.7 Hz, 1H), 7.40-7.36 (m, 5H), 7.31 (d, J = 9.0 Hz, 1H), 6.81 (br s, 1H), 5.22 (s, 2H). ^{19}F (471 MHz, $CDCl_3$) +41.6 (s, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.0, 146.0, 138.9, 135.6, 129.7, 128.9, 128.8, 128.5, 121.9, 119.7, 88.9, 67.8.

ESI-MS HRMS calculated for $C_{14}H_{11}FINNaO_5S$ $[M+Na]^+$ 473.9279, found: 473.9267.



4j

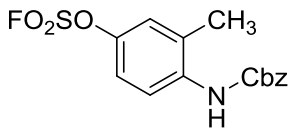
4-(((benzyloxy)carbonyl)amino)-2-(1,3-dioxolan-2-yl)phenyl sulfurofluoridate (**4j)**. Yellow solid, 374 mg, 94% yield. M.p. 70-72 ^oC. ^1H NMR (500 MHz, $CDCl_3$) δ 7.62 (s, 1H), 7.52 (d, J = 8.1 Hz, 1H), 7.39-7.35 (m, 5H), 7.28 (d, J = 9.0 Hz, 1H), 7.05 (br s, 1H), 6.01 (s, 1H), 5.20 (s, 2H), 4.11-4.07 (m, 2H), 4.06-4.01 (m, 2H). ^{19}F (471 MHz, $CDCl_3$) +41.2 (s, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.2, 143.7, 138.1, 135.7, 131.3, 128.7, 128.6, 128.3, 121.8, 120.3, 118.3, 99.2, 67.4, 65.5. ESI-MS HRMS calculated for $C_{17}H_{16}FNNaO_7S$ $[M+Na]^+$ 420.0524, found: 420.0511.



4k

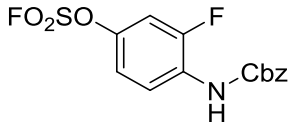
2-acetyl-4-(((benzyloxy)carbonyl)amino)phenyl sulfurofluoridate (**4k**). Light yellow gum, 289 mg, 79% yield. M.p. 59-61 ^oC. ^1H NMR (500 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.69 (d, J = 8.1 Hz, 1H), 7.52 (br s, 1H), 7.37-7.34 (m, 5H), 7.31 (d, J = 9.0 Hz, 1H), 5.21 (s, 2H), 2.59 (s, 3H). ^{19}F (471 MHz, $CDCl_3$) +40.7 (s, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.5, 153.4, 142.4, 138.8, 135.6, 131.8, 128.7, 128.6, 128.4, 123.0, 120.4, 67.5, 29.7. ESI-MS HRMS calculated for $C_{16}H_{14}FNNaO_6S$ $[M+Na]^+$ 390.0418, found: 390.0409.

In the ^{13}C NMR spectrum of **4k**, theoretically, there should be fourteen peaks. Due to the compact overlaying, it is difficult to specify the overlaying peaks.



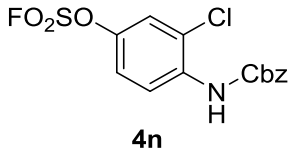
4l

4-(((benzyloxy)carbonyl)amino)-3-methylphenyl sulfurofluoridate (**4l**). White solid, 268 mg, 79% yield. M.p. 98-100 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, J = 6.3 Hz, 1H), 7.43-7.37 (m, 5H), 7.19 (d, J = 9.0 Hz, 1H), 7.15 (s, 1H), 6.56 (s, 1H), 5.23 (s, 2H), 2.27 (s, 3H). ^{19}F (471 MHz, $CDCl_3$) +37.1 (s, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.4, 145.7, 136.4, 135.8, 129.5, 128.8, 128.7, 128.6, 122.7, 121.9, 119.4, 67.6, 17.9. ESI-MS HRMS calculated for $C_{15}H_{14}FNNaO_5S$ $[M+Na]^+$ 362.0469, found: 362.0461.



4m

4-(((benzyloxy)carbonyl)amino)-3-fluorophenyl sulfurofluoridate (**4m**). White solid, 196 mg, 57% yield. M.p. 82-84 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (t, J = 7.1 Hz, 1H), 7.43-7.36 (m, 5H), 7.17-7.13 (m, 2H), 6.98 (br s, 1H), 5.24 (s, 2H). ^{19}F (471 MHz, $CDCl_3$) +37.4 (s, 1F), -127.1 (s, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.9, 151.4 (d, J = 248.0 Hz), 144.1 (d, J = 10.0 Hz), 135.5, 128.9, 128.8, 128.6, 127.4 (d, J = 10.0 Hz), 120.7, 117.5 (d, J = 3.7 Hz), 109.1 (d, J = 23.6 Hz), 67.9. ESI-MS HRMS calculated for $C_{14}H_{11}F_2NNaO_5S$ $[M+Na]^+$ 366.0218, found: 366.0208.

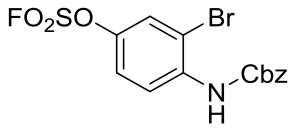


4n

4-(((benzyloxy)carbonyl)amino)-3-chlorophenyl sulfurofluoridate (**4n**). Light yellow solid, 245 mg, 68% yield. M.p. 53-55 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.37 (d, J = 9.1 Hz, 1H), 7.44-7.36 (m, 6H), 7.30-7.27 (m, 2H), 5.24 (s, 2H). ^{19}F (471 MHz, $CDCl_3$) +37.6 (s, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.9, 144.4, 135.52, 135.47, 128.9, 128.8, 128.7, 122.6, 122.1, 120.6, 67.9. ESI-MS HRMS calculated for

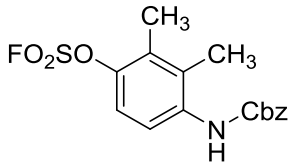
$C_{14}H_{11}ClFNNaO_5S$ $[M+Na]^+$ 381.9923, found: 381.9913.

In the ^{13}C NMR spectrum of **4n**, theoretically, there should be twelve peaks. Due to the compact overlaying, it is difficult to specify the overlaying peaks.



4o

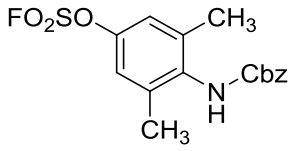
4-(((benzyloxy)carbonyl)amino)-3-bromophenyl sulfurofluoridate (**4o**). Light yellow solid, 344 mg, 85% yield. M.p. 77-79 ^oC. ^1H NMR (500 MHz, $CDCl_3$) δ 8.35 (d, J = 9.1 Hz, 1H), 7.55 (d, J = 1.9 Hz, 1H), 7.44-7.37 (m, 5H), 7.33 (d, J = 9.3 Hz, 1H), 7.27 (br s, 1H), 5.25 (s, 2H). ^{19}F (471 MHz, $CDCl_3$) +37.6 (s, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.9, 144.5, 136.7, 135.5, 128.9, 128.8, 128.7, 125.1, 121.2, 120.7, 112.4, 67.9. ESI-MS HRMS calculated for $C_{14}H_{11}BrFNNaO_5S$ $[M+Na]^+$ 425.9418, found: 425.9406.



4p

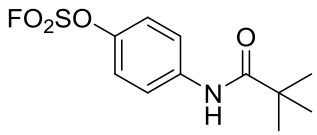
4-(((benzyloxy)carbonyl)amino)-2,3-dimethylphenyl sulfurofluoridate (**4p**). White solid, 257 mg, 73% yield. M.p. 119-120 ^oC. ^1H NMR (500 MHz, $CDCl_3$) δ 7.68-7.67 (m, 1H), 7.39-7.33 (m, 5H), 7.17 (d, J = 9.0 Hz, 1H), 6.78 (br s, 1H), 5.19 (s, 2H), 2.28 (s, 3H), 2.19 (s, 3H). ^{19}F (471 MHz, $CDCl_3$) +38.6 (s, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.9, 145.7, 135.9, 135.8, 130.0, 128.8, 128.7, 128.6, 121.0, 119.0, 67.6, 14.2, 13.5. ESI-MS HRMS calculated for $C_{16}H_{16}FNNaO_5S$ $[M+Na]^+$ 376.0625, found: 376.0615.

In the ^{13}C NMR spectrum of **4p**, theoretically, there should be fourteen peaks. Due to the compact overlaying, it is difficult to specify the overlaying peaks.



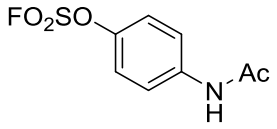
4q

4-(((benzyloxy)carbonyl)amino)-3,5-dimethylphenyl sulfurofluoridate (**4q**). Off-white solid, 251 mg, 71% yield. M.p. 133-134 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.36 (m, 5H), 7.06 (s, 2H), 6.30 (br s, 1H), 5.20 (s, 2H), 2.27 (s, 6H). ^{19}F (471 MHz, $CDCl_3$) +37.6 (s, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.1, 148.3, 138.9, 136.1, 134.1, 128.8, 128.5, 128.4, 120.3, 67.6, 18.7. ESI-MS HRMS calculated for $C_{16}H_{16}FNNaO_5S$ $[M+Na]^+$ 376.0625, found: 376.0615.



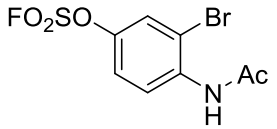
6

4-pivalamidophenyl sulfurofluoridate (**6**). Gray soild, 165 mg, 60% yield. M.p. 110-112 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, J = 9.0 Hz, 2H), 7.44 (br s, 1H), 7.29 (d, J = 8.5 Hz, 2H), 1.32 (s, 9H). ^{19}F (471 MHz, $CDCl_3$) +37.1 (s, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.0, 145.8, 138.5, 121.6, 121.5, 39.8, 27.6. ESI-MS HRMS calculated for $C_{11}H_{14}FNNaO_4S$ $[M+Na]^+$ 298.0520, found: 298.0520.



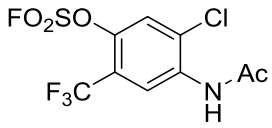
8a

4-acetamidophenyl sulfurofluoridate (**8a**).[4] White soild, 168 mg, 72% yield. M.p. 142-144 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (br s, 1H), 7.63 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 8.3 Hz, 2H), 2.18 (s, 3H). ^{19}F (471 MHz, $CDCl_3$) +37.2 (s, 1F).



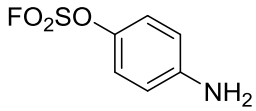
8b

4-acetamido-3-bromophenyl sulfurofluoridate (**8b**). Off-white solid, 218 mg, 70% yield. M.p. 133-134 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 (d, J = 9.0 Hz, 1H), 7.64 (br s, 1H), 7.56 (d, J = 2.4 Hz, 1H), 7.33 (dd, J_1 = 9.3 Hz, J_2 = 2.3 Hz, 1H), 2.27 (s, 3H). ^{19}F (471 MHz, $CDCl_3$) +37.8 (s, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.5, 145.0, 136.5, 125.0, 122.5, 121.1, 113.1, 25.0. ESI-MS HRMS calculated for $C_8H_7BrFNNaO_4S$ $[M+Na]^+$ 333.9155, found: 333.9149.



8c

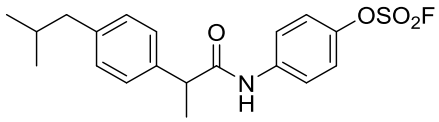
4-acetamido-5-chloro-2-(trifluoromethyl)phenyl sulfurofluoridate (**8c**). Brownish red solid, 181 mg, 54% yield. M.p. 122-124 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.96 (s, 1H), 7.70 (br s, 1H), 7.61 (s, 1H), 2.30 (s, 3H). ^{19}F (471 MHz, $CDCl_3$) +41.9 (s, 1F), -60.89 - -60.91 (m, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.6, 141.3, 135.5, 126.3, 123.1, 122.7 (d, J = 33.6 Hz), 121.6 (q, J = 273.4 Hz), 120.0 (q, J = 5.5 Hz), 25.0. ESI-MS HRMS calculated for $C_9H_6ClF_4NNaO_4S$ $[M+Na]^+$ 357.9534, found: 357.9526.



9

4-aminophenyl sulfurofluoridate (**9**).[5] A reaction tube (20 mL) equipped with a stir bar was charged with rearrangement product **2a** (0.5 mmol, 146 mg) to which DCM (2 mL) and trifluoroacetic acid (2 mL) were added sequentially *via* syringe and the solution was allowed to stir at room temperature for 12 h. Then the resulting mixture was diluted with DCM, washed $NaHCO_3$ (aq.) and the aqueous phase was extracted with DCM (10 mL ×3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated to dryness. The residue was purified through silica gel chromatography using a mixture of ethyl acetate and petroleum ether = 1:3 (v/v) as eluent to afford the desired product **9** (92 mg, 96% yield) as a

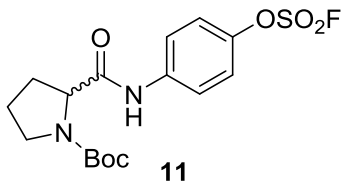
brown solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10 (d, J = 8.9 Hz, 2H), 6.66 (d, J = 9.0 Hz, 2H), 3.82 (br s, 2H). ^{19}F (471 MHz, $CDCl_3$) +36.0 (s, 1F).



10

4-(2-(4-isobutylphenyl)propanamido)phenyl sulfurofluoridate (**10**). The Ibuprofen amide **10** was synthesized from the coupling of Ibuprofen and aniline **9** according to a reported procedure.[6] Ibuprofen (1.0 mmol, 1.0 equiv), aniline (**9**, 2.0 mmol, 2.0 equiv), DIPEA (3.0 mmol, 3.0 equiv) and MeCN (reaction mixture was diluted to 0.3 M) were added to an oven-dried 25 mL reaction flask equipped with a stirring bar and covered with a rubber stopper. Then SO_2F_2 was introduced into the solution by slowly bubbling from a balloon and the mixture was allowed to react at room temperature for 5 h. Once the reaction reached its completion, the mixture was diluted with DCM and washed with 1 M aqueous HCl solution to remove the excess amine **9**. Then the aqueous phrase extracted with DCM (3× 20 mL) and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under the reduced pressure. The residue was purified by column chromatography on silica gel using petroleum ether / ethyl acetate = 5 : 1 (v /v) as eluent to give Ibuprofen amide **10** in 80% yield.

White gum, 302 mg, 80% yield. M.p. 69-71 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, J = 9.1 Hz, 2H), 7.34 (br s, 1H), 7.24 (d, J = 8.0 Hz, 2H), 7.21 (d, J = 9.0 Hz, 2H), 7.15 (d, J = 7.9 Hz, 2H), 3.70 (q, J = 7.1 Hz, 1H), 2.47 (d, J = 7.2 Hz, 2H), 1.90-1.82 (m, 1H), 1.58 (d, J = 7.1 Hz, 3H), 0.90 (d, J = 6.6 Hz, 6H). ^{19}F (471 MHz, $CDCl_3$) +37.1 (s, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.0, 145.8, 141.5, 138.4, 137.7, 130.1, 127.5, 121.5, 121.1, 47.8, 45.1, 30.3, 22.5, 18.5. ESI-MS HRMS calculated for $C_{19}H_{22}FNNaO_4S$ $[M+Na]^+$ 402.1146, found: 402.1150.

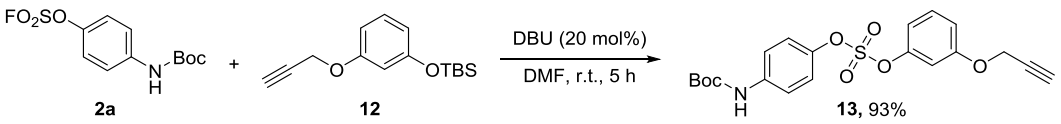


11

tert-butyl 2-((4-((fluorosulfonyl)oxy)phenyl)carbamoyl)pyrrolidine-1-carboxylate (**11**). The *N*-Boc-proline amide **11** was synthesized from the coupling of *N*-Boc-proline and aniline **9** according to a reported procedure.[6] *N*-Boc-proline (1.0 mmol, 1.0 equiv), aniline (**9**, 2.0 mmol, 2.0 equiv), DIPEA (3.0 mmol, 3.0 equiv) and MeCN (reaction mixture was diluted to 0.3 M) were added to an oven-dried 25 mL reaction flask equipped with a stirring bar and covered with a rubber stopper. Then SO_2F_2 was introduced into the solution by slowly bubbling from a balloon and the mixture was allowed to react at room temperature for 5 h. Once the reaction reached its completion, the mixture was diluted with DCM and washed with 1 M aqueous HCl solution to remove the excess amine **9**. Then the aqueous phrase extracted with DCM (3× 20 mL) and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under the reduced pressure. The residue was purified by column chromatography on silica gel using petroleum ether / ethyl acetate = 3 : 1 (v /v) as eluent to give *N*-Boc-proline amide **11** in 89% yield.

White solid, 346 mg, 89% yield. M.p. 140-142 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.92 (br s, 1H), 7.54-7.53 (m, 2H), 7.12-7.10 (m, 2H), 4.51 (s, 1H), 3.53-3.50 (m, 1H), 3.40 (s, 1H), 2.33 (s, 1H), 2.03-1.91 (m, 3H), 1.50 (s, 9H). ^{19}F (471 MHz, $CDCl_3$) +36.9 (s, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.7, 156.5, 145.4, 139.0, 121.3, 120.7, 81.2, 60.6, 47.4, 28.5, 28.1, 24.7. ESI-MS HRMS calculated for $C_{16}H_{21}FN_2NaO_6S$ $[M+Na]^+$ 411.0997, found: 411.0990.

5. SuFEx click reaction of 2a



2a **12** **13,** 93%

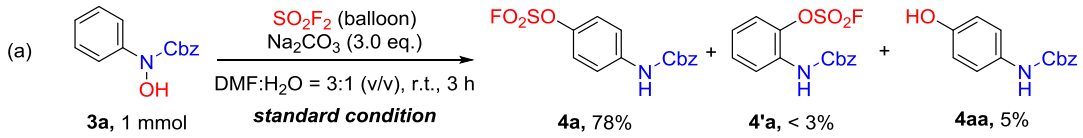
To an oven- dried reaction tube (10 mL) were charged with rearrangement product **2a** (0.5 mmol), *tert*-butyldimethyl(3-(prop-2-yn-1-yloxy)phenoxy)silane (**12**, 0.5 mmol,

131 mg, 1.0 equiv.), catalytic amount of DBU (20 mol%, 0.1 mmol, 16 mg) and DMF (2.5 mL, 0.2 M), and the resulting mixture was allowed to stir at room temperature for 5 h. Then the solution was diluted with DCM and washed with water. The aqueous phrase extracted with DCM (3× 10 mL) and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under the reduced pressure. The residue was purified by column chromatography on silica gel using petroleum ether / ethyl acetate = 5 : 1 (v /v) as eluent to give 4-((*tert*-butoxycarbonyl)amino)phenyl (3-(prop-2-yn-1-yloxy)phenyl) sulfate **13** in 93% yield.

Colorless oil, 195 mg, 93% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, J =8.9 Hz, 2H), 7.34 (t, J = 8.2 Hz, 1H), 7.24 (d, J = 9.2 Hz, 2H), 6.98-6.95 (m, 3H), 6.61 (br s, 1H), 4.69 (d, J = 2.3 Hz, 2H), 2.55 (t, J = 2.3 Hz, 1H), 1.52 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.7, 152.7, 151.2, 145.6, 138.0, 130.6, 121.9, 119.6, 114.4, 114.0, 108.3, 81.2, 77.8, 76.4, 56.3, 28.4. ESI-MS HRMS calculated for $C_{20}H_{21}NNaO_7S$ $[M+Na]^+$ 442.0931 found: 442.0937.

6. Mechanism Studies.

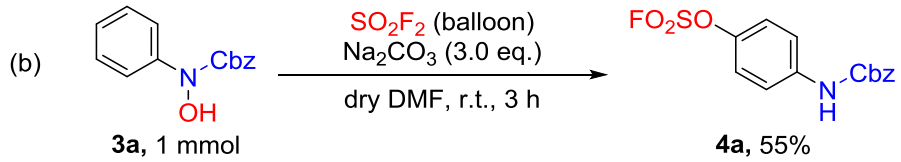
Experiment (a):



To an oven-dried 30 mL reaction tube equipped with a stirring bar was added Cbz-protected *N*-aryl-*N*-hydroxylamine (**3a**, 1.0 mmol, 1.0 eq.), Na_2CO_3 (318 mg, 3 mmol, 3.0 eq.) and co-solvent (10 mL, 0.1 M, DMF : H_2O = 3:1 (v/v)). Then the reaction tube was fitted with a plastic stopper and SO_2F_2 was introduced into the stirring mixture by slow bubbling from a SO_2F_2 balloon at room temperature for 3 h (monitored by TLC). When the reaction reached its completion, the reaction mixture was diluted with water, acidized with 1 M HCl, and aqueous phase was extracted with EtOAc (10 mL ×3) and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated to dryness. The residue was purified

through silica gel chromatography using a mixture of ethyl acetate and petroleum ether as eluent to afford the final products.

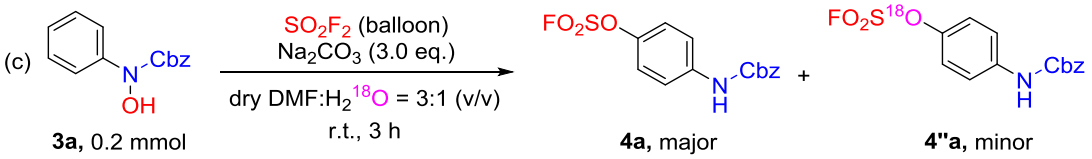
Experiment (b):



3a, 1 mmol **4a,** 55%

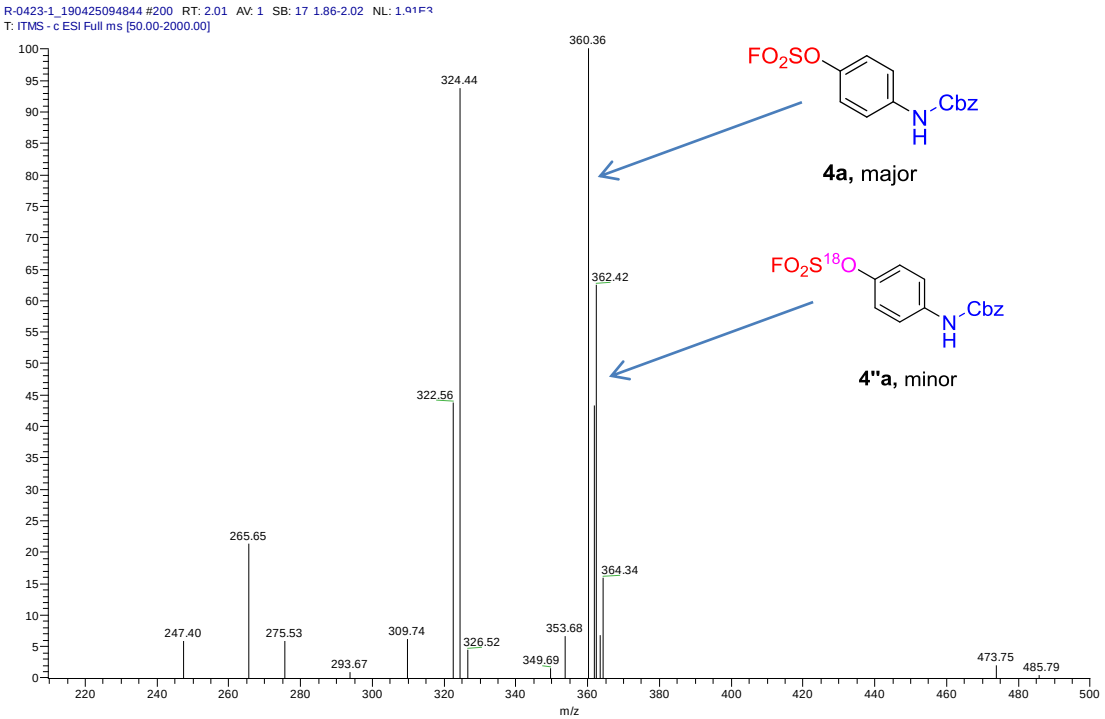
Following the procedure of **Experiment (a)** and dry DMF (10 mL, 0.1 M) was used as sole solvent. The final product **4a** was isolated in 55% yield through silica gel chromatography using a mixture of ethyl acetate and petroleum ether as eluent.

Experiment (c):



3a, 0.2 mmol **4a,** major **4"a,** minor

Following the procedure of **Experiment (a)** in 0.2 mmol scale and co-solvent (2 mL, 0.1 M, dry DMF : $H_2{}^{18}O$ = 3:1 (v/v)) was used. When the reaction reached its completion, the reaction mixture was evaporated under vacuum to remove excess $H_2{}^{18}O$ and the residue was purified by prepared TLC to get the mixture of final products **4a** and **4”a**. ESI-Ms analysis clearly assigned the unlabeled product **4a** in majority while the ^{18}O labeled product **4”a** in minority (^{18}O-**4”a**, M+Cl^- at 362.02)


R-0423-1_190425094844 #200 RT: 2.01 AV: 1 SB: 17 1.86-2.02 NL: 1.91E3
T: ITMS - c ESI Full ms [50.00-2000.00]
360.36
324.44
362.42
322.56
265.65
364.34
247.40
275.53
309.74
353.68
326.52
293.67
349.69
473.75
485.79
m/z
FO2SO
Cbz
N
H
4a, major
FO2S18O
Cbz
N
H
4"a, minor

7. Reference:

[1] Y. Wang, L. Liu and L. Zhang, *Chem. Sci.*, 2013, **4**, 739-746.

[2] K. N. Hojczyk, P. Feng, C. Zhan and M.-Y. Ngai, *Angew. Chem., Int. Ed.*, 2014, **53**, 14559–14563.

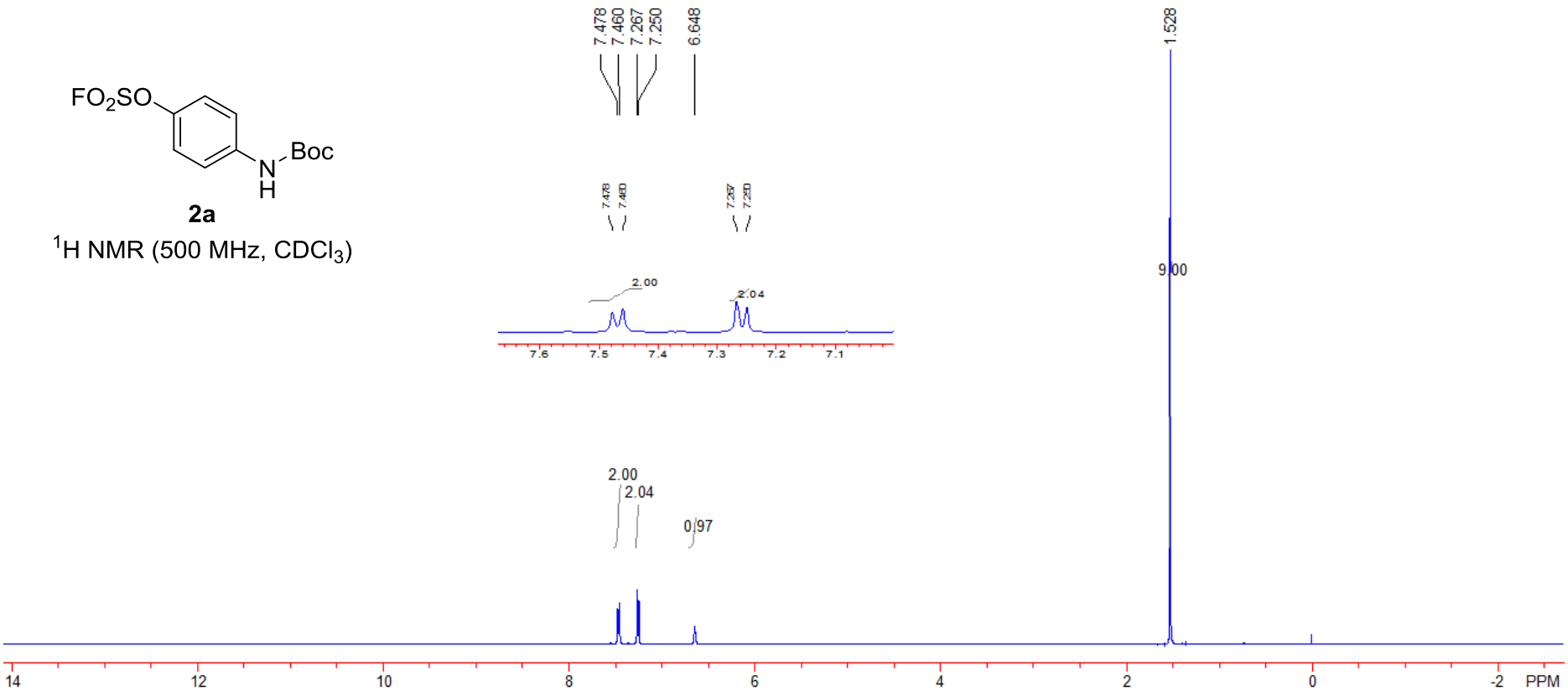
[3] A. Pohjakallio and P. M. Pihko, *Chem. Eur. J.*, 2009, **15**, 3960–3964.

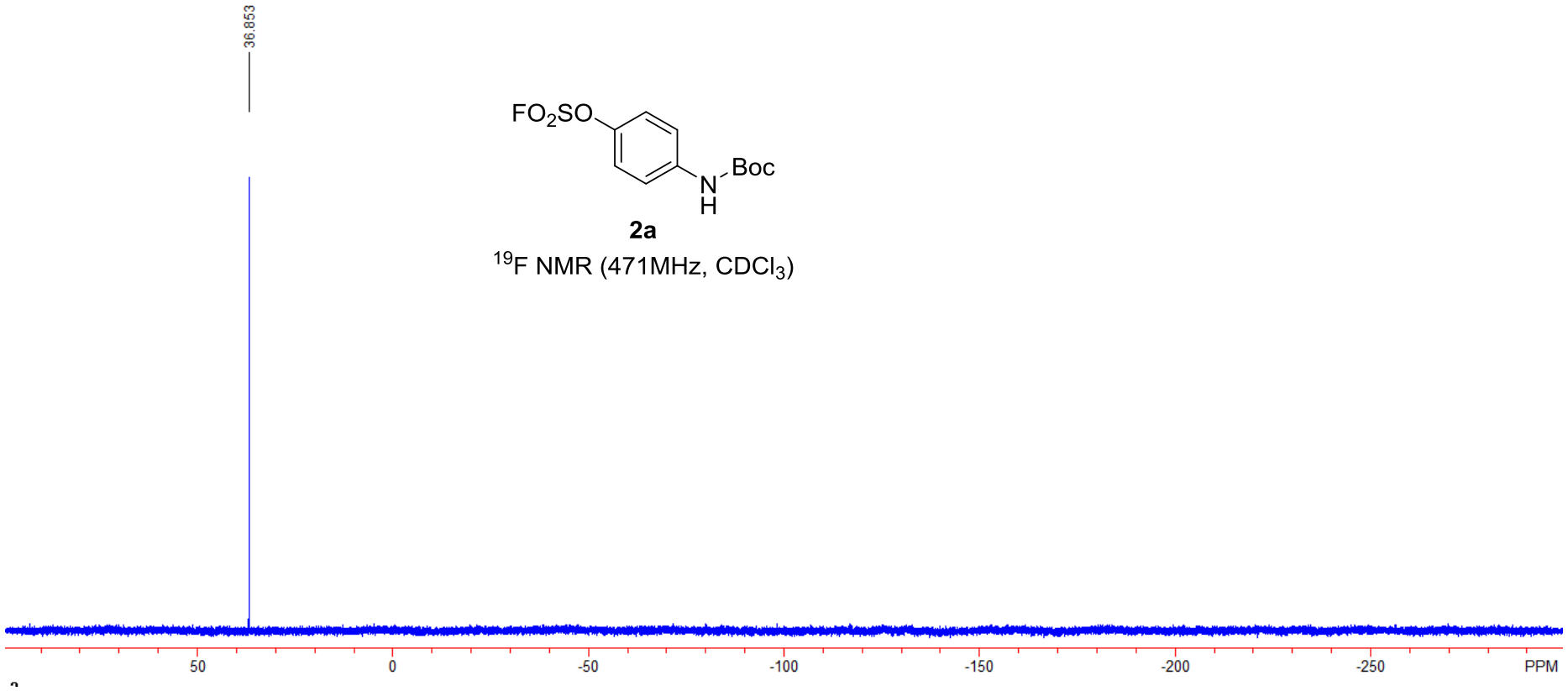
[4] T. Guo, G. Meng, X. Zhan, Q. Yang, T. Ma, L. Xu, K. B. Sharpless and J. Dong, *Angew. Chem. Int. Ed.*, 2018, **57,** 2605–2610.

[5] J. Dong, L. Krasnova, M. G. Finn and K. B. Sharpless, *Angew. Chem., Int. Ed.*, 2014, **53**, 9430.

[6] S.-M. Wang, C. Zhao, X. Zhang and H.-L. Qin, *Org. Biomol. Chem.*, 2019, **17**, 4087.

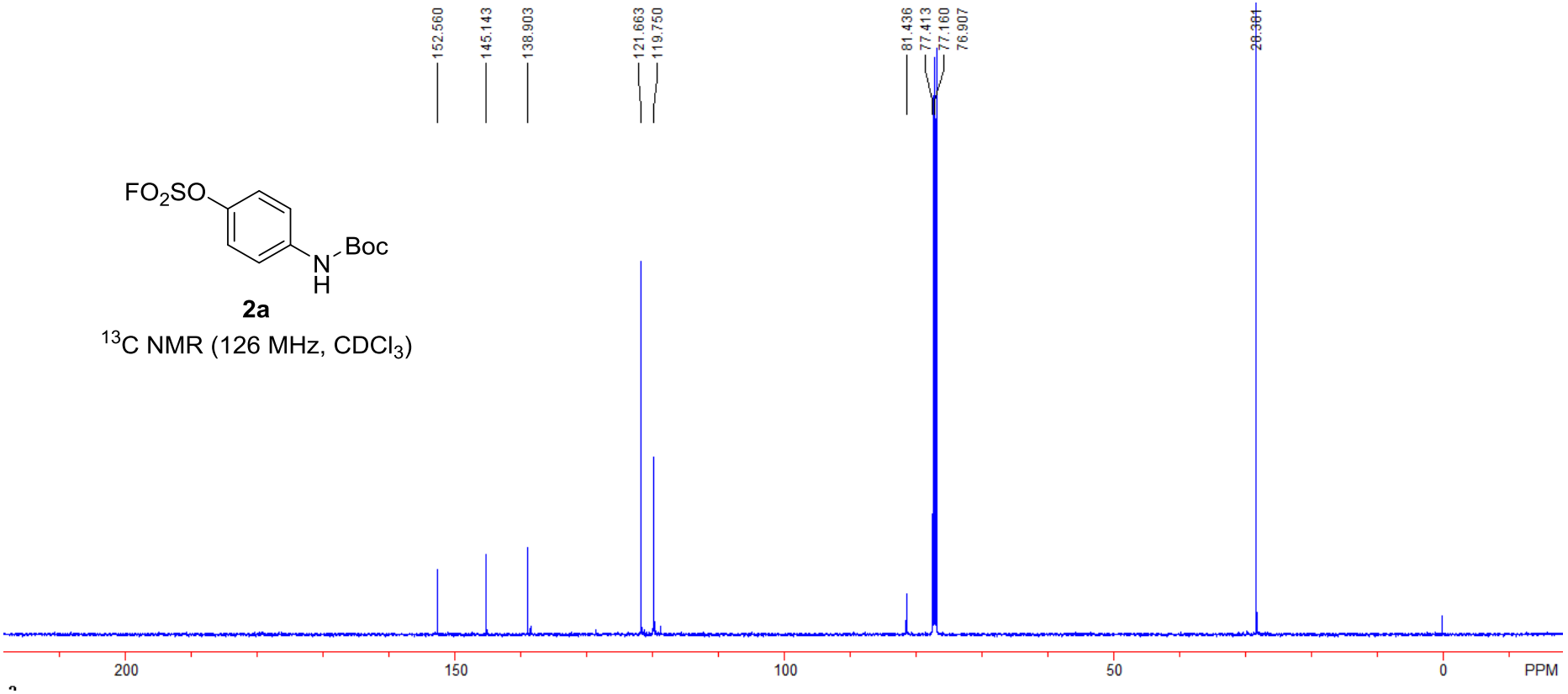
8. NMR spectra





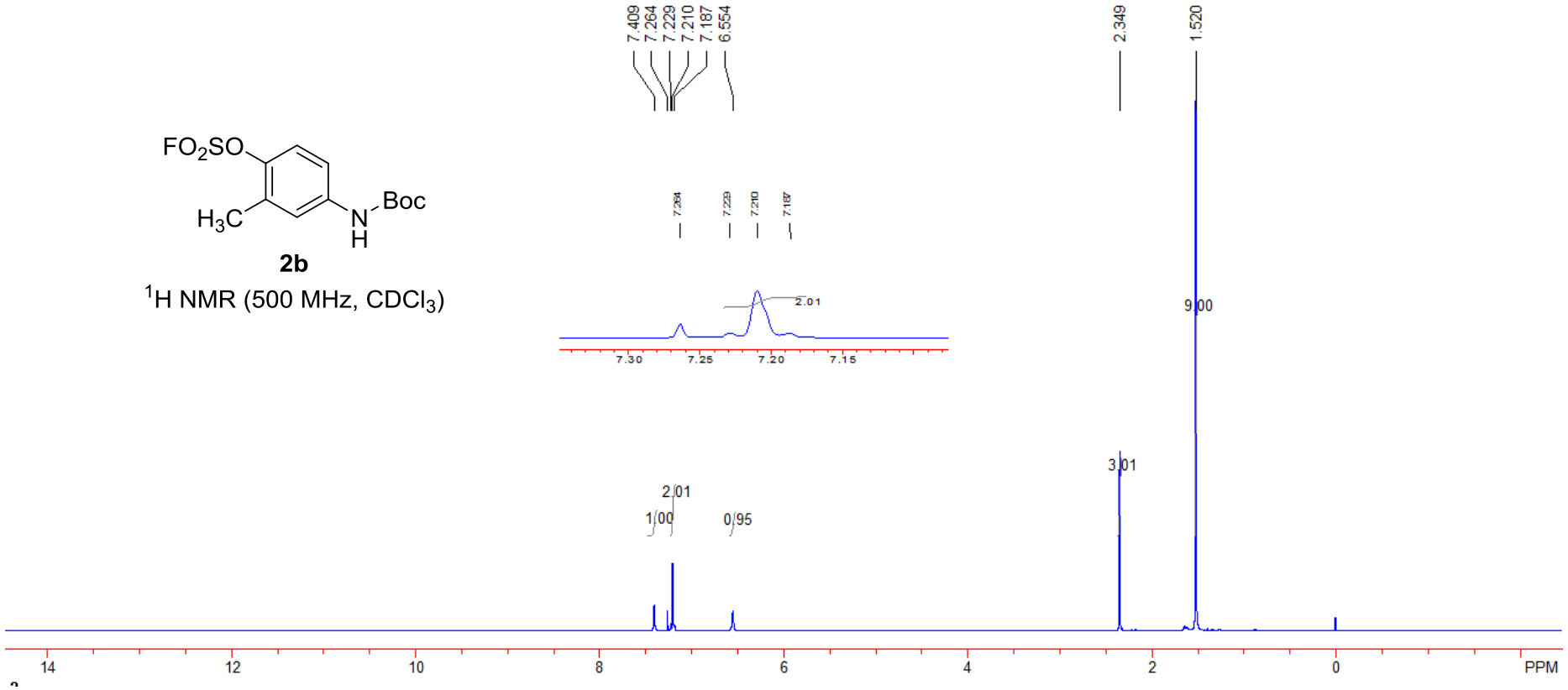
2a

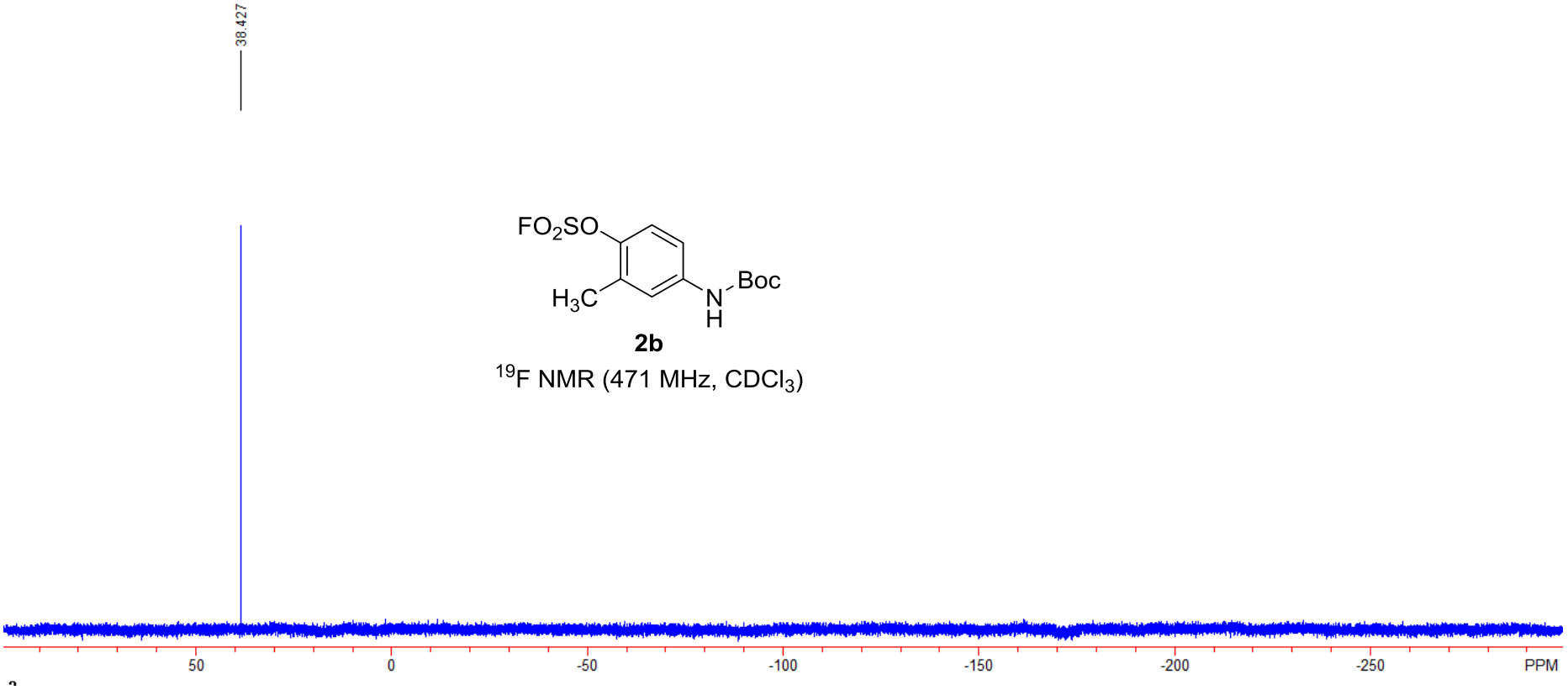
^{19}F NMR (471MHz, $CDCl_3$)



2a

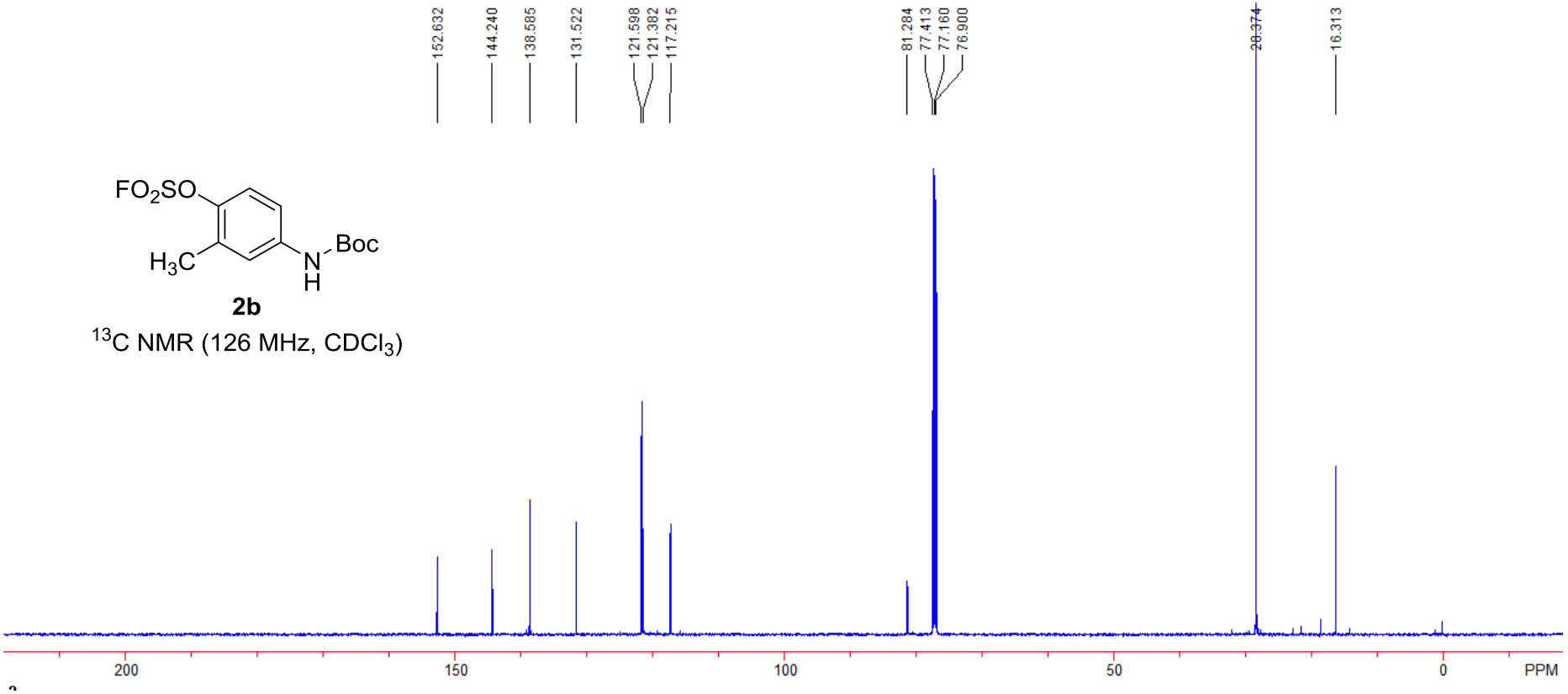
^{13}C NMR (126 MHz, $CDCl_3$)

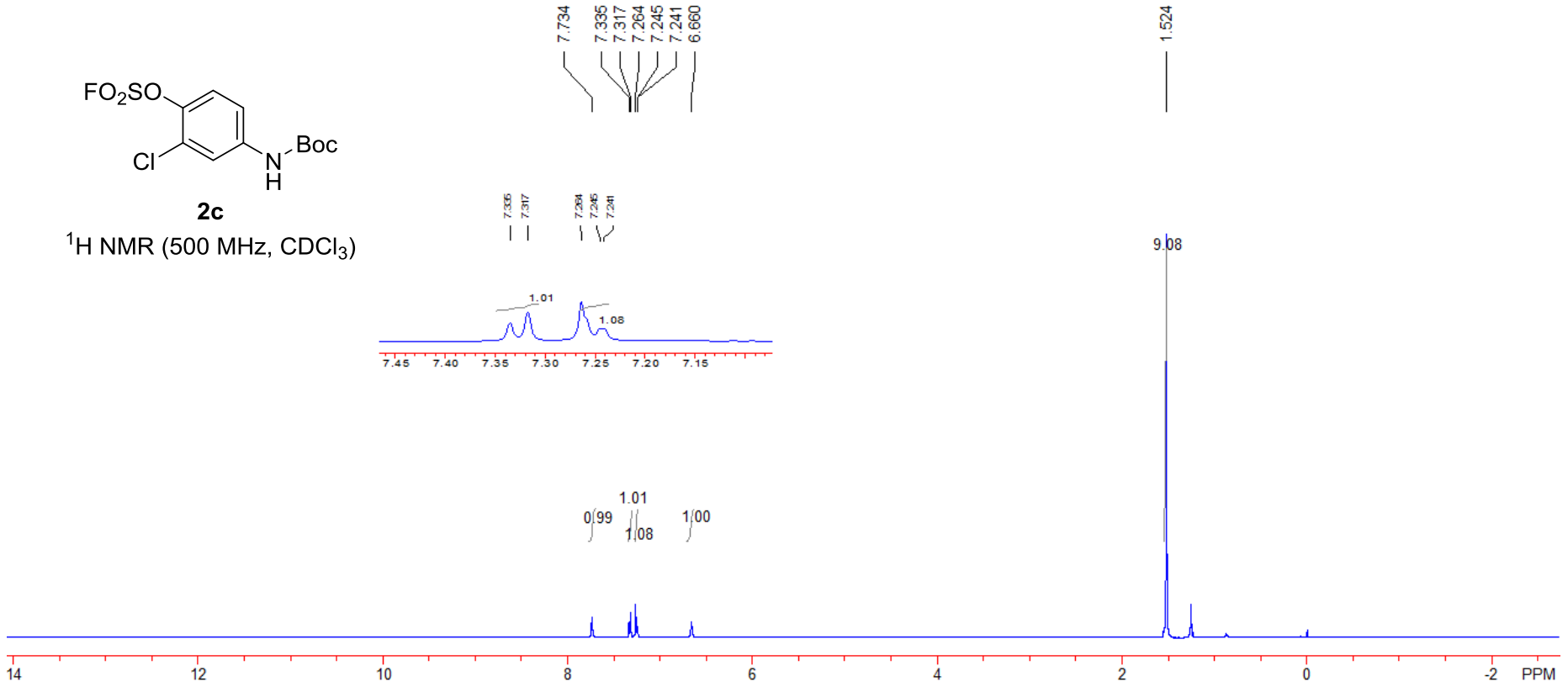

FO2SO
H3C
N
H
Boc
2b
1H NMR (500 MHz, CDCl3)
7.409
7.264
7.229
7.210
7.187
6.554
2.349
1.520
2.01
9.00
3.01
2.01
1.00
0.95
14
12
10
8
6
4
2
0
PPM

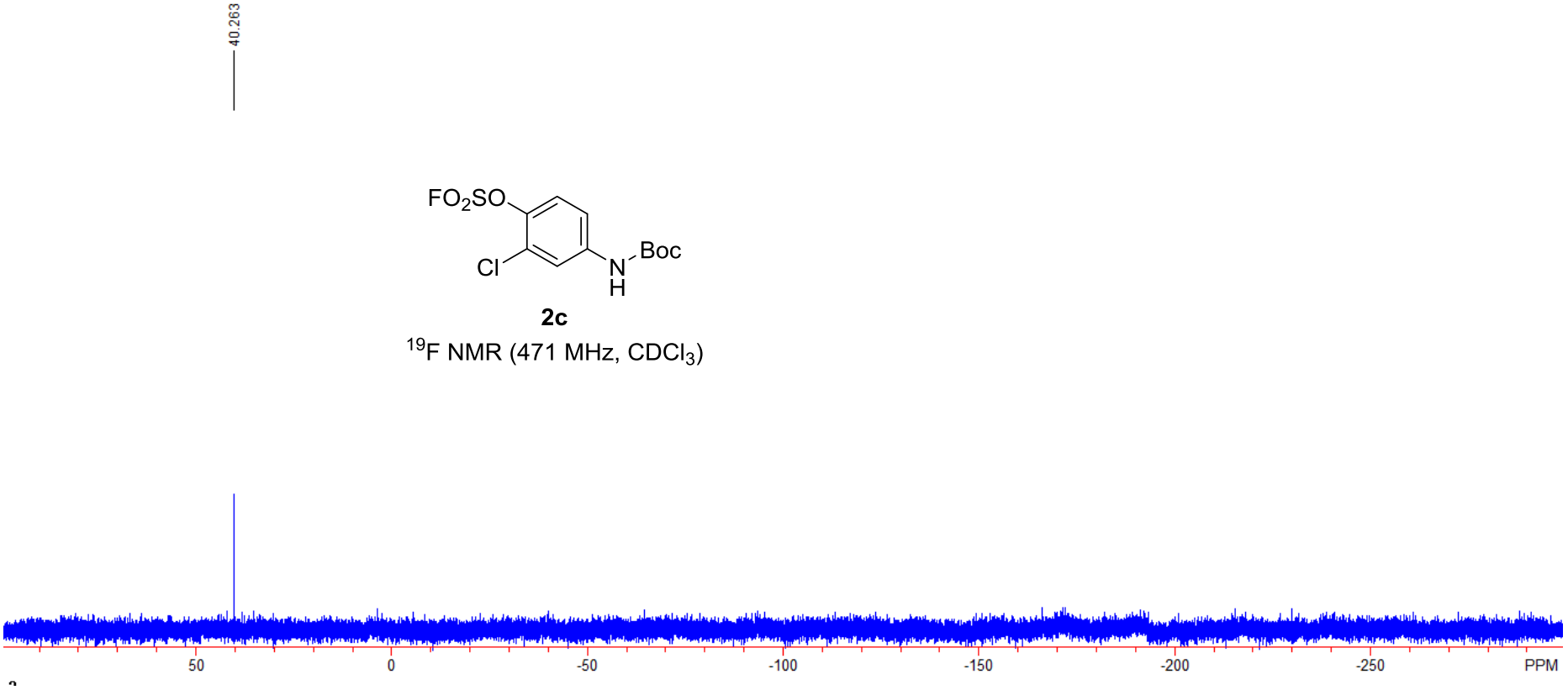


2b

^{19}F NMR (471 MHz, $CDCl_3$)

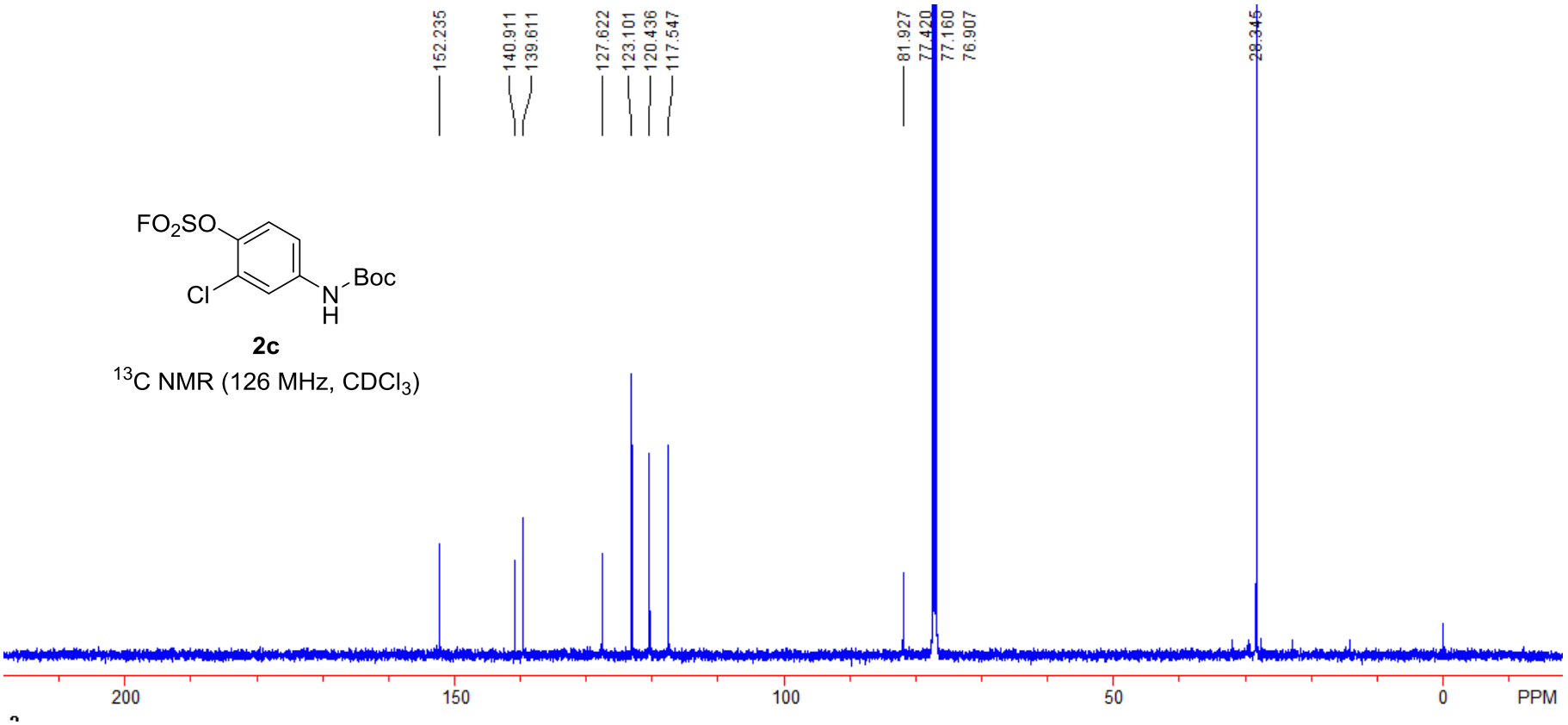

152.632
144.240
138.585
131.522
121.598
121.382
117.215
81.284
77.413
77.160
76.900
28.374
16.313
FO2SO
H3C
N
H
Boc
2b
13C NMR (126 MHz, CDCl3)
200
150
100
50
0
PPM


FO2SO
Cl
N
H
Boc
2c
1H NMR (500 MHz, CDCl3)
7.734
7.335
7.317
7.264
7.245
7.241
6.660
1.524
9.08
1.01
1.08
0.99
1.01
1.08
1.00
14
12
10
8
6
4
2
0
-2
PPM



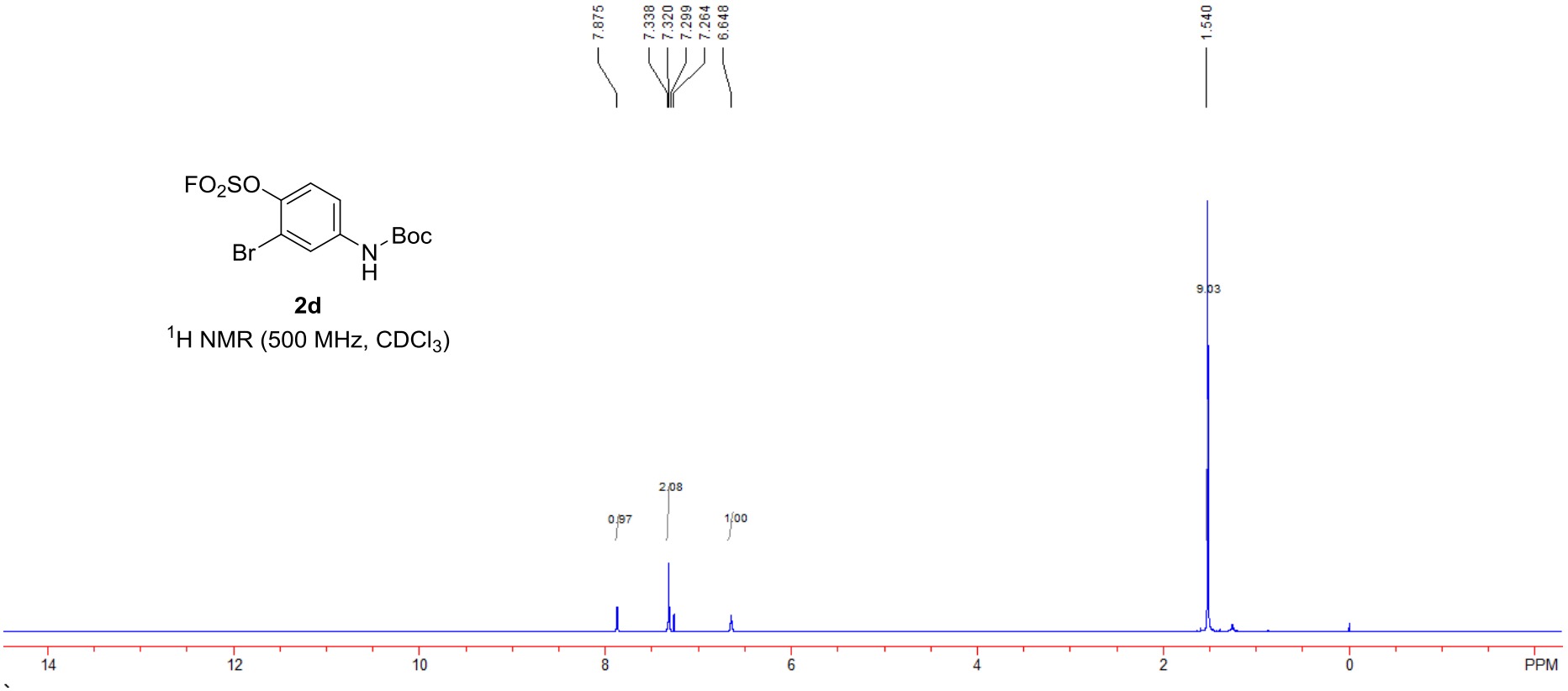
2c

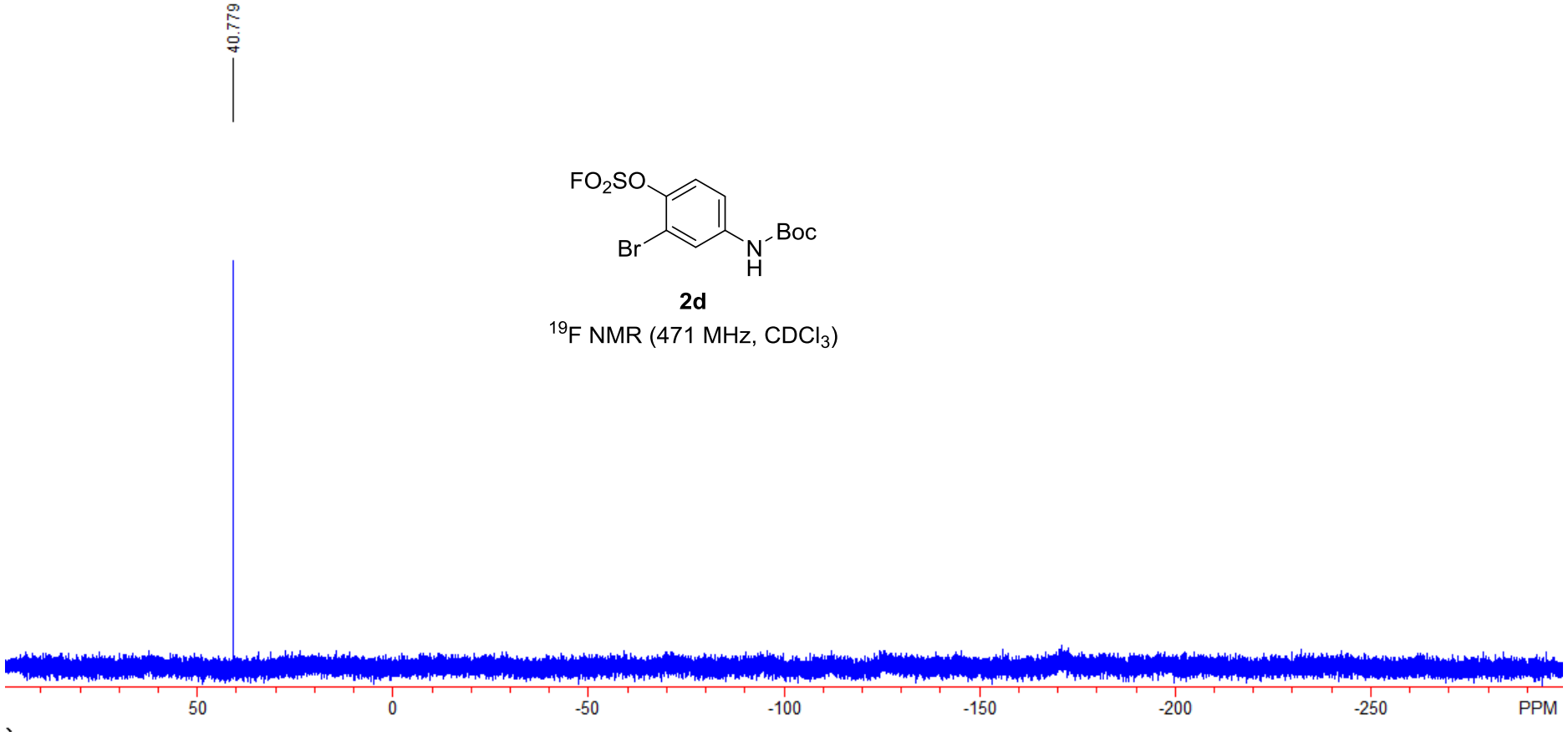
^{19}F NMR (471 MHz, $CDCl_3$)



2c

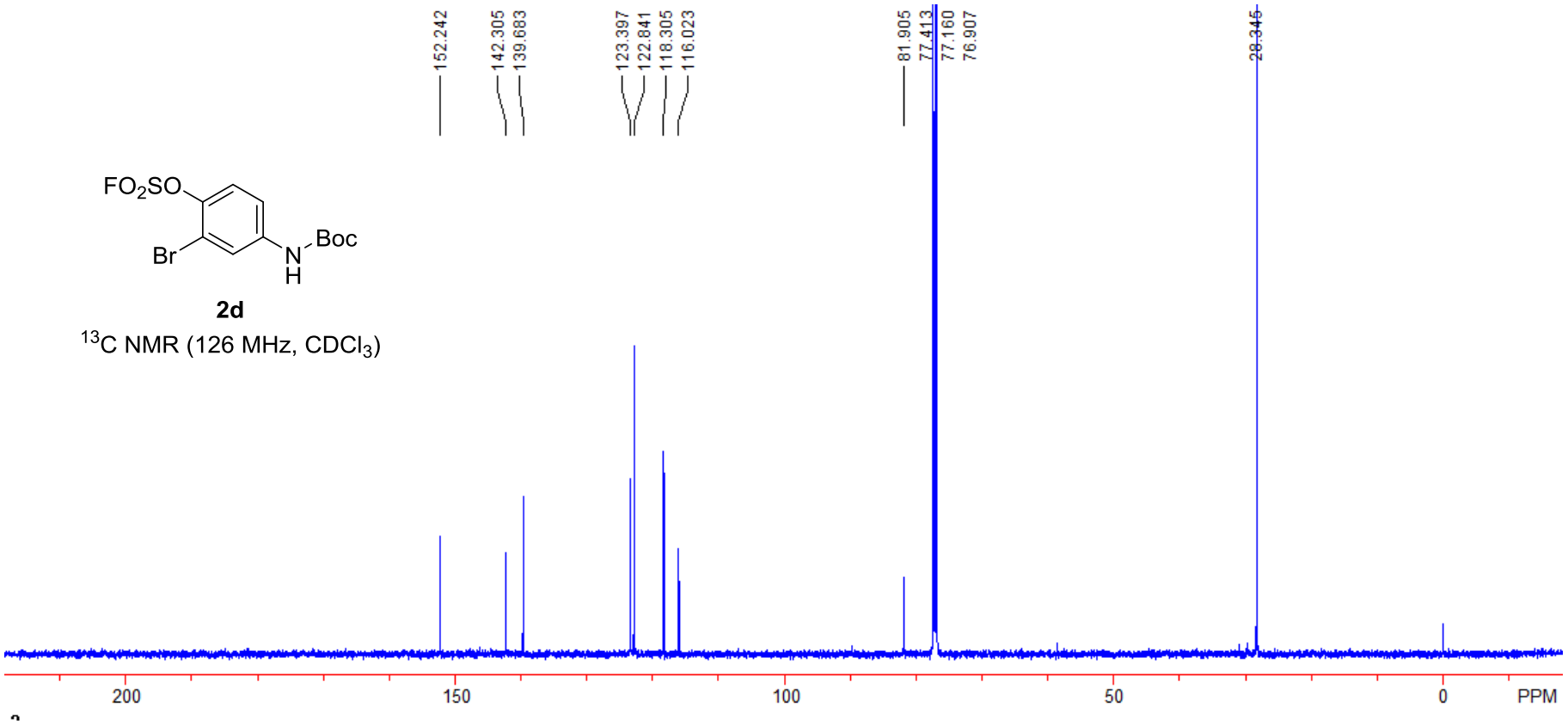
^{13}C NMR (126 MHz, $CDCl_3$)


7.875
7.338
7.320
7.299
7.264
6.648
1.540
FO2SO
Br
N
H
Boc
2d
1H NMR (500 MHz, CDCl3)
9.03
2.08
0.97
1.00
14
12
10
8
6
4
2
0
PPM



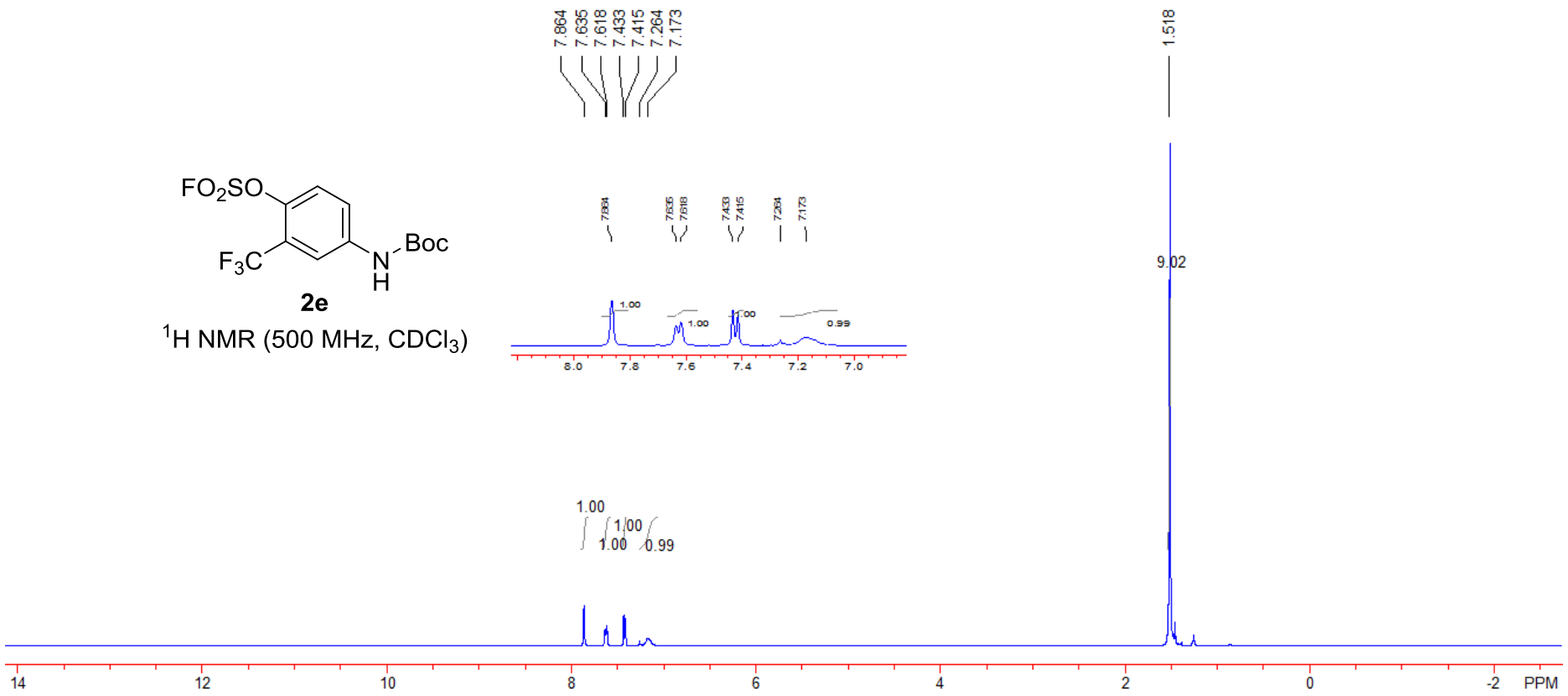
2d

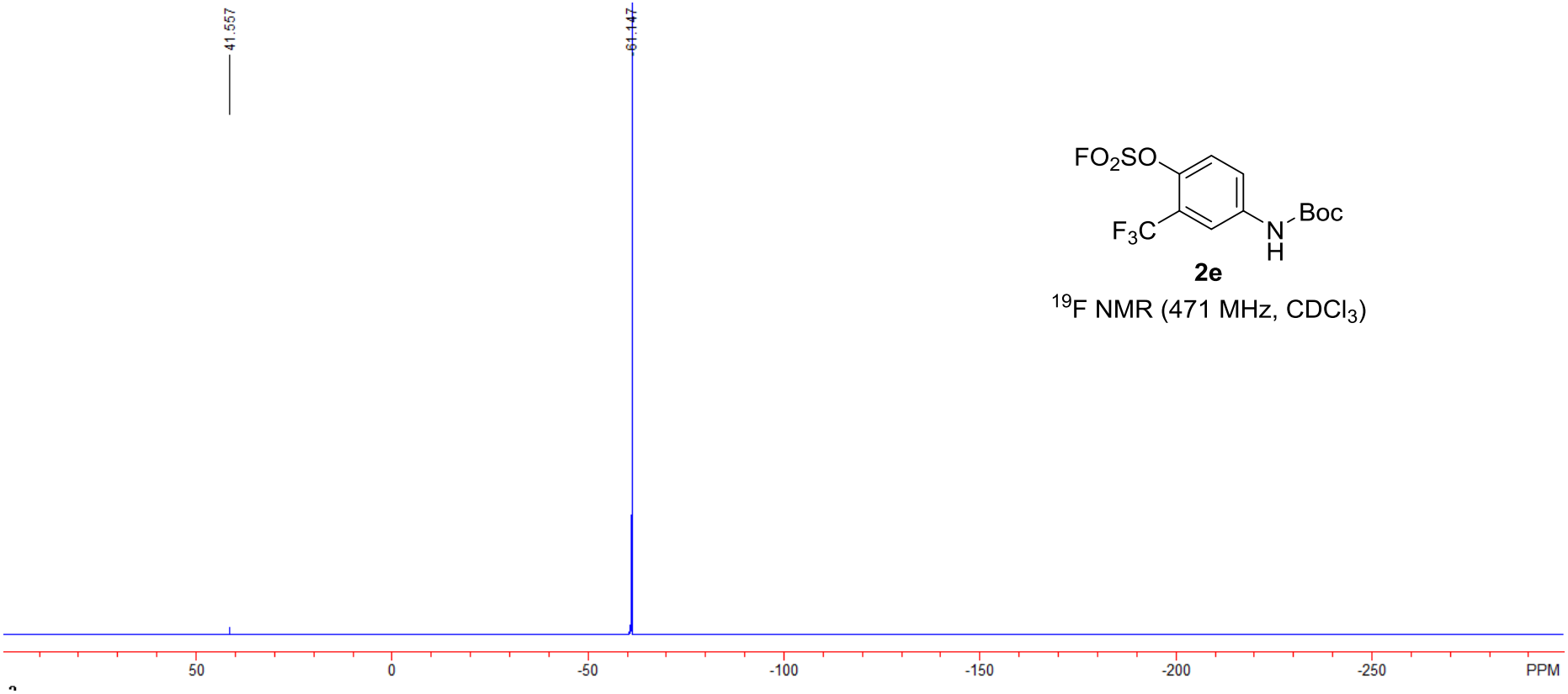
^{19}F NMR (471 MHz, $CDCl_3$)



2d

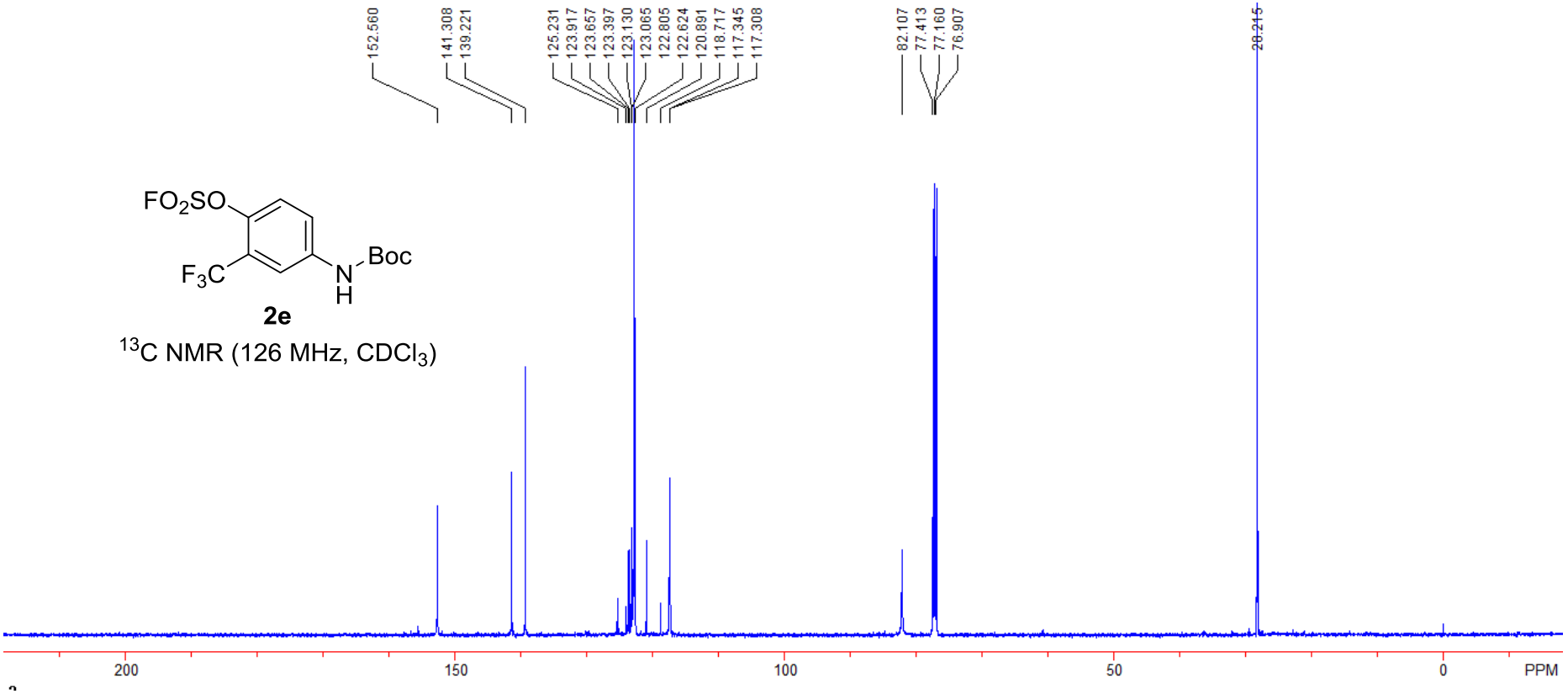
^{13}C NMR (126 MHz, $CDCl_3$)

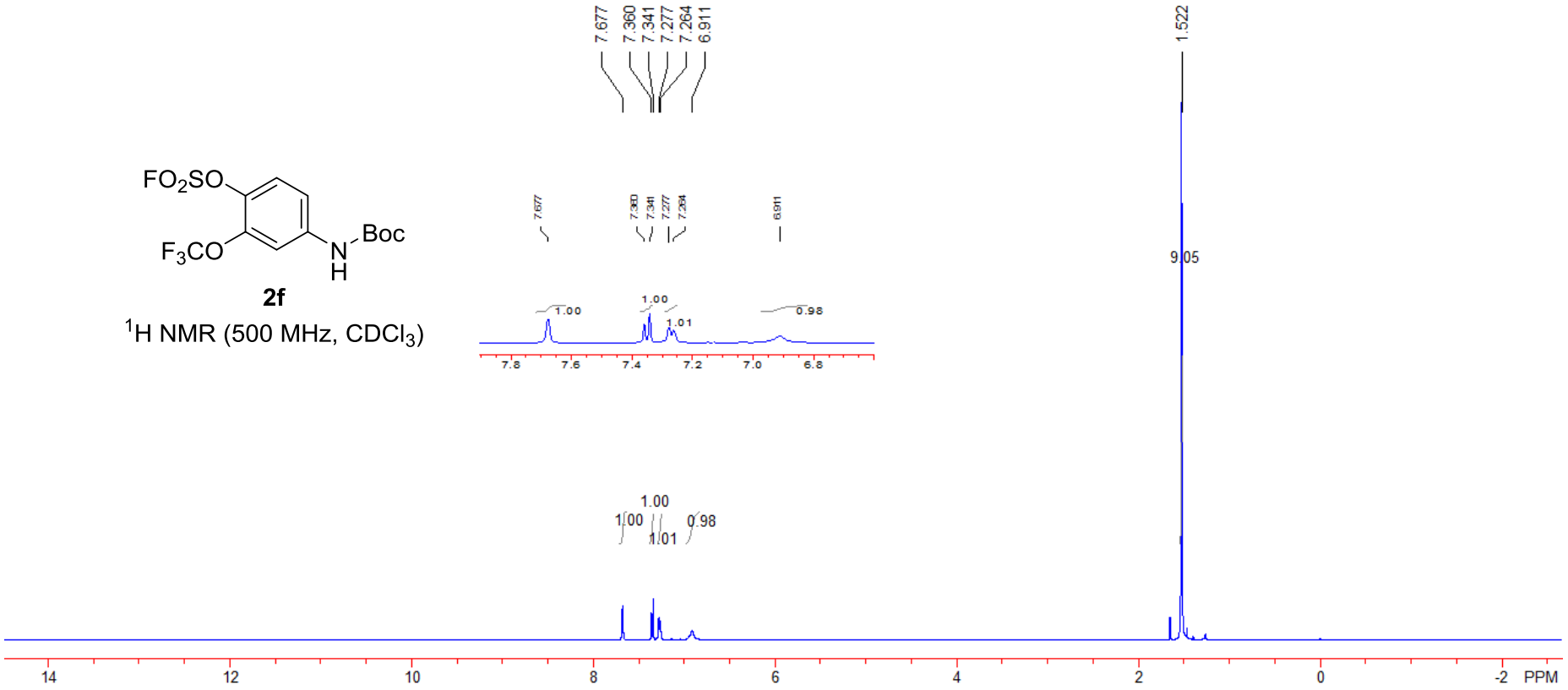

FO2SO
F3C
N
H
Boc
2e
1H NMR (500 MHz, CDCl3)
7.864
7.635
7.618
7.433
7.415
7.264
7.173
1.518
9.02
1.00
1.00
1.00
0.99
14
12
10
8
6
4
2
0
-2
PPM

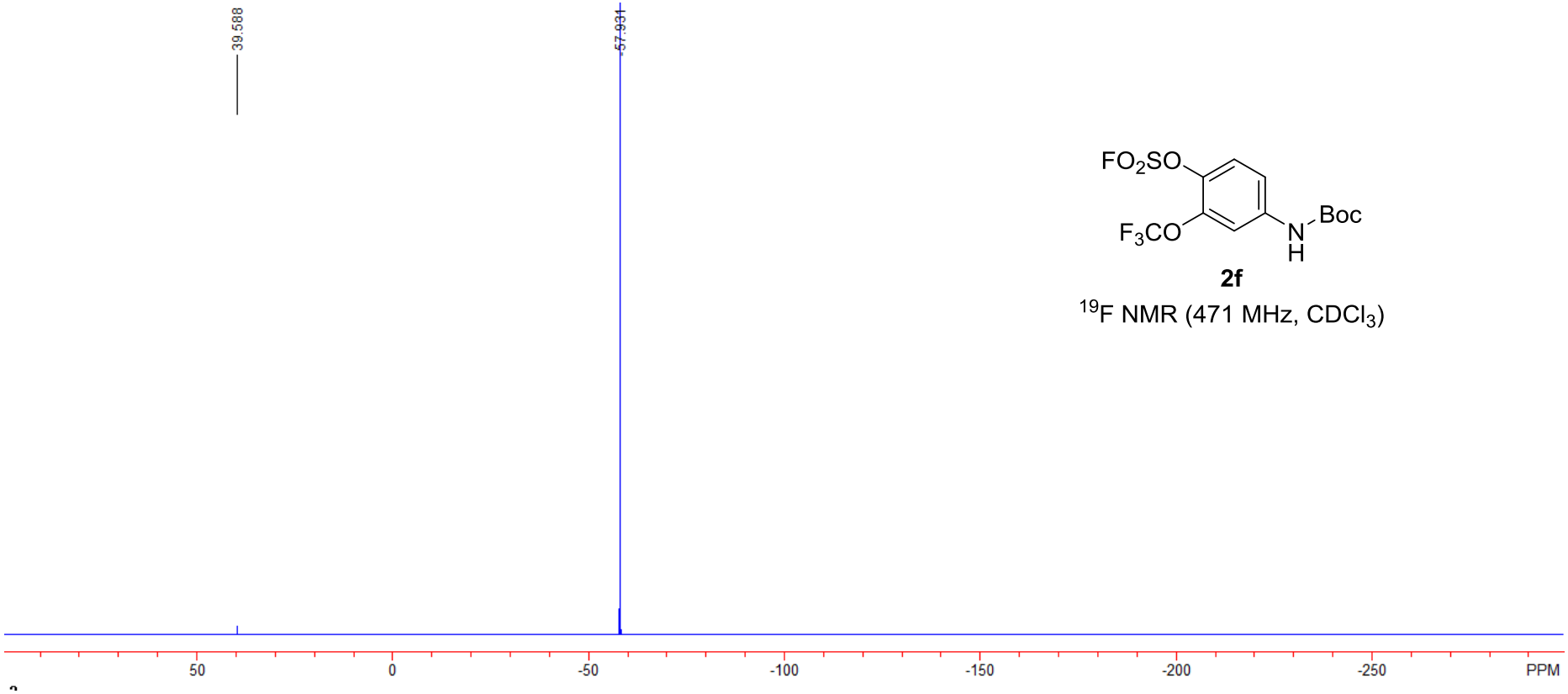


2e

^{19}F NMR (471 MHz, $CDCl_3$)

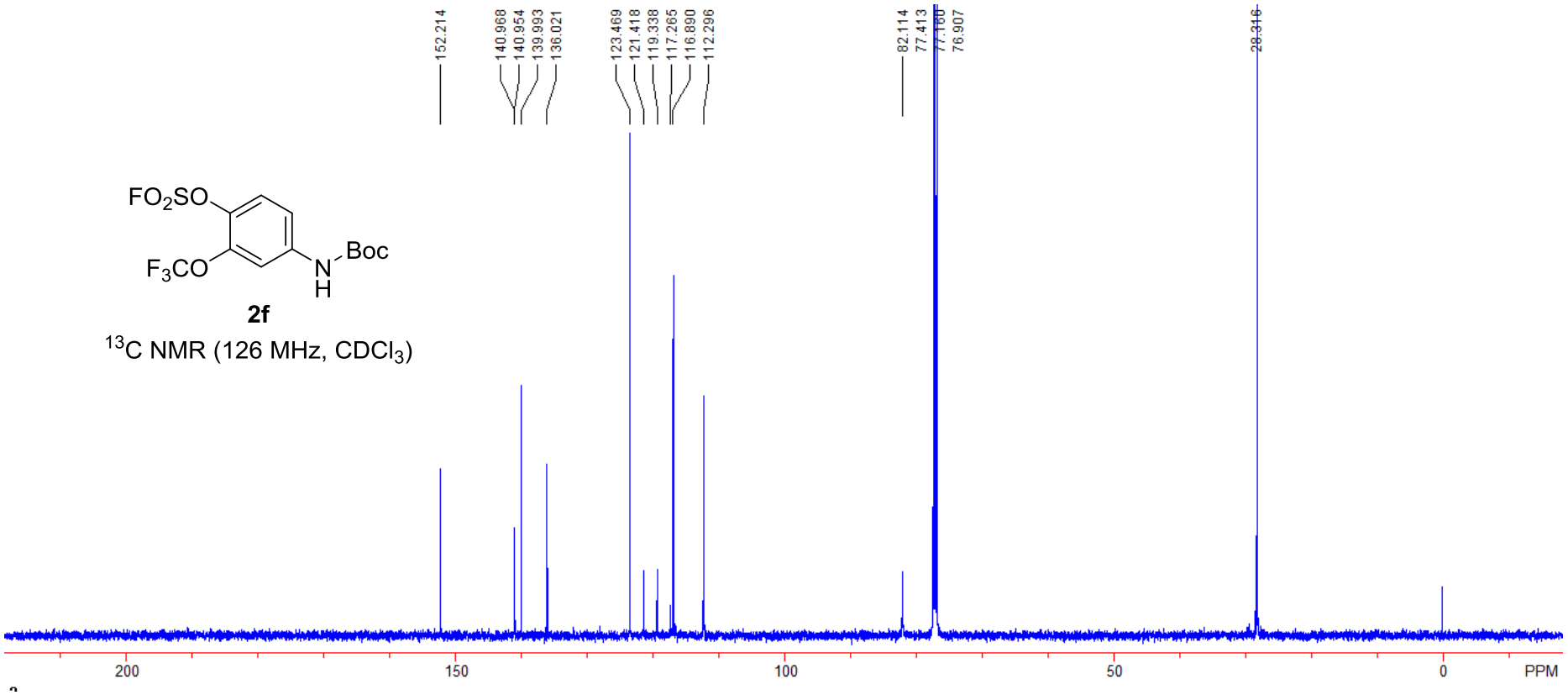

152.560
141.308
139.221
125.231
123.917
123.657
123.397
123.130
123.065
122.805
122.624
120.891
118.717
117.345
117.308
82.107
77.413
77.160
76.907
28.215
FO2SO
F3C
N
H
Boc
2e
13C NMR (126 MHz, CDCl3)
200
150
100
50
0
PPM

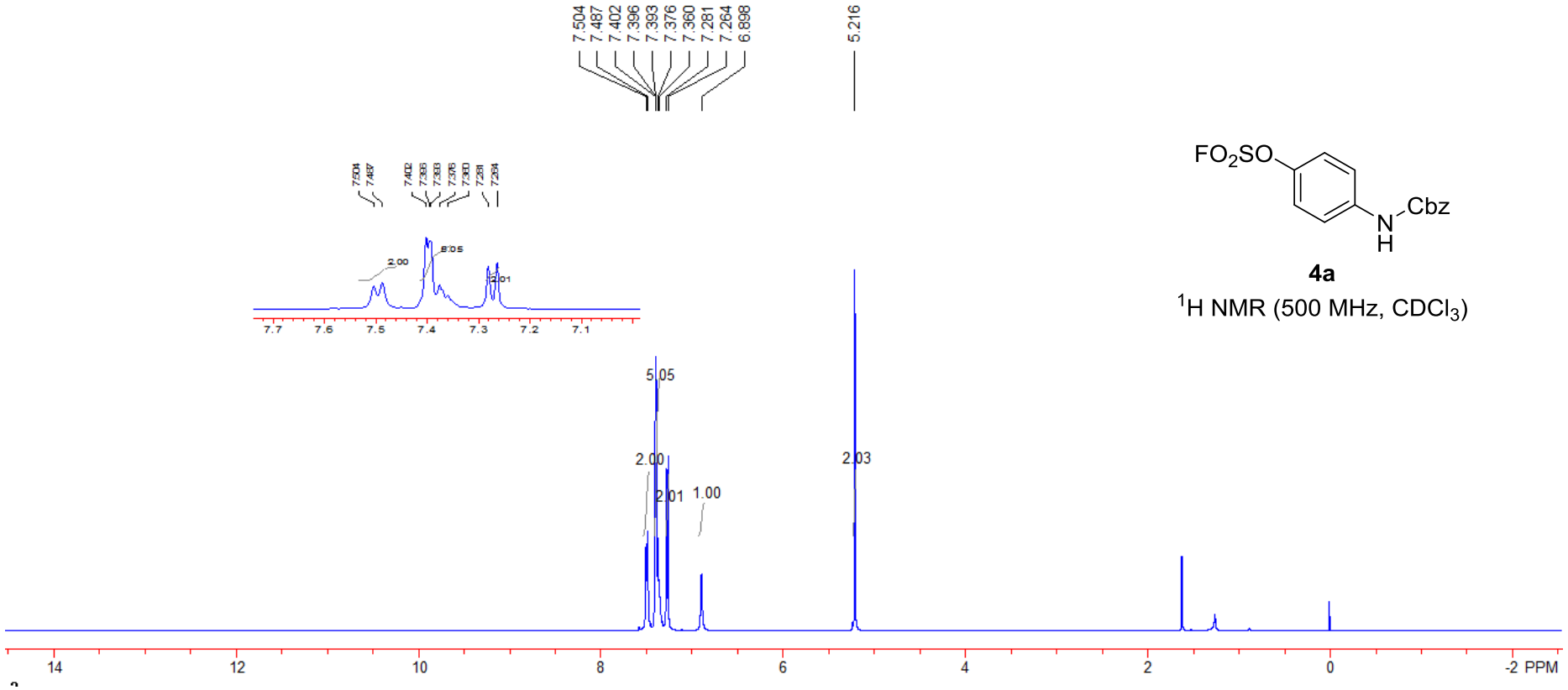

FO2SO
F3CO
N
H
Boc
2f
1H NMR (500 MHz, CDCl3)
7.677
7.360
7.341
7.277
7.264
6.911
1.522
9.05
1.00
1.00
1.01
0.98
14
12
10
8
6
4
2
0
-2
PPM

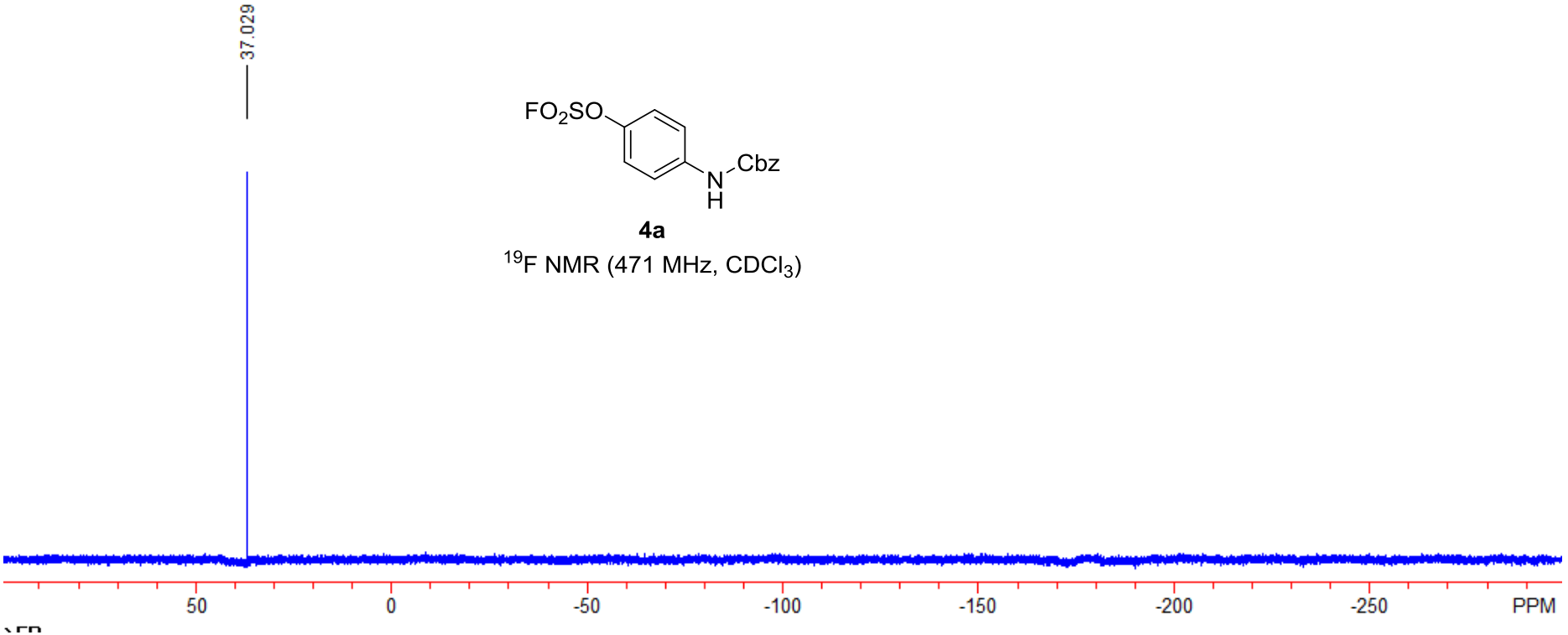


2f

^{19}F NMR (471 MHz, $CDCl_3$)

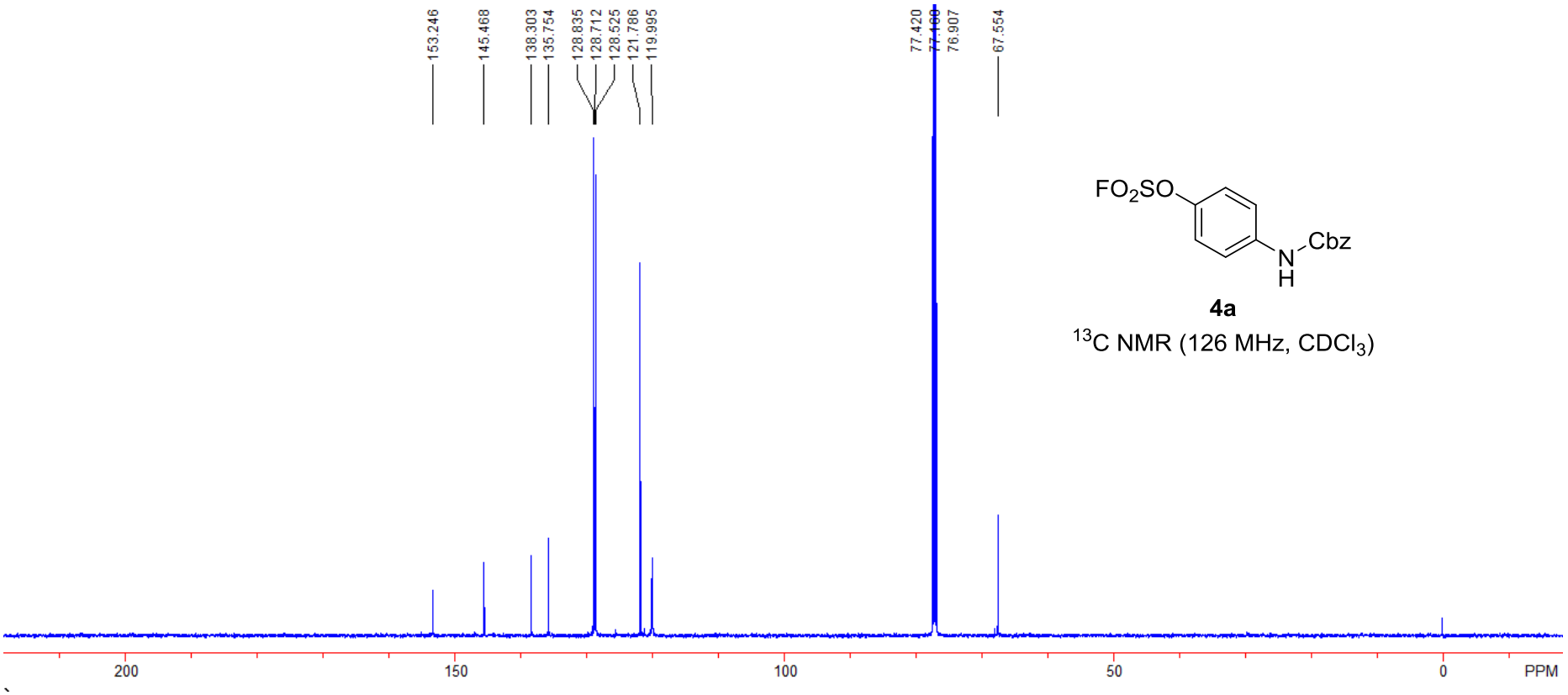

152.214
140.968
140.954
139.993
136.021
123.469
121.418
119.338
117.265
116.890
112.296
82.114
77.413
77.160
76.907
28.316
FO2SO
F3CO
N
H
Boc
2f
13C NMR (126 MHz, CDCl3)
200
150
100
50
0
PPM


7.504
7.487
7.402
7.396
7.393
7.376
7.360
7.281
7.264
6.898
5.216
FO2SO
Cbz
N
H
4a
1H NMR (500 MHz, CDCl3)
5.05
2.00
2.01
1.00
2.03
14
12
10
8
6
4
2
0
-2 PPM



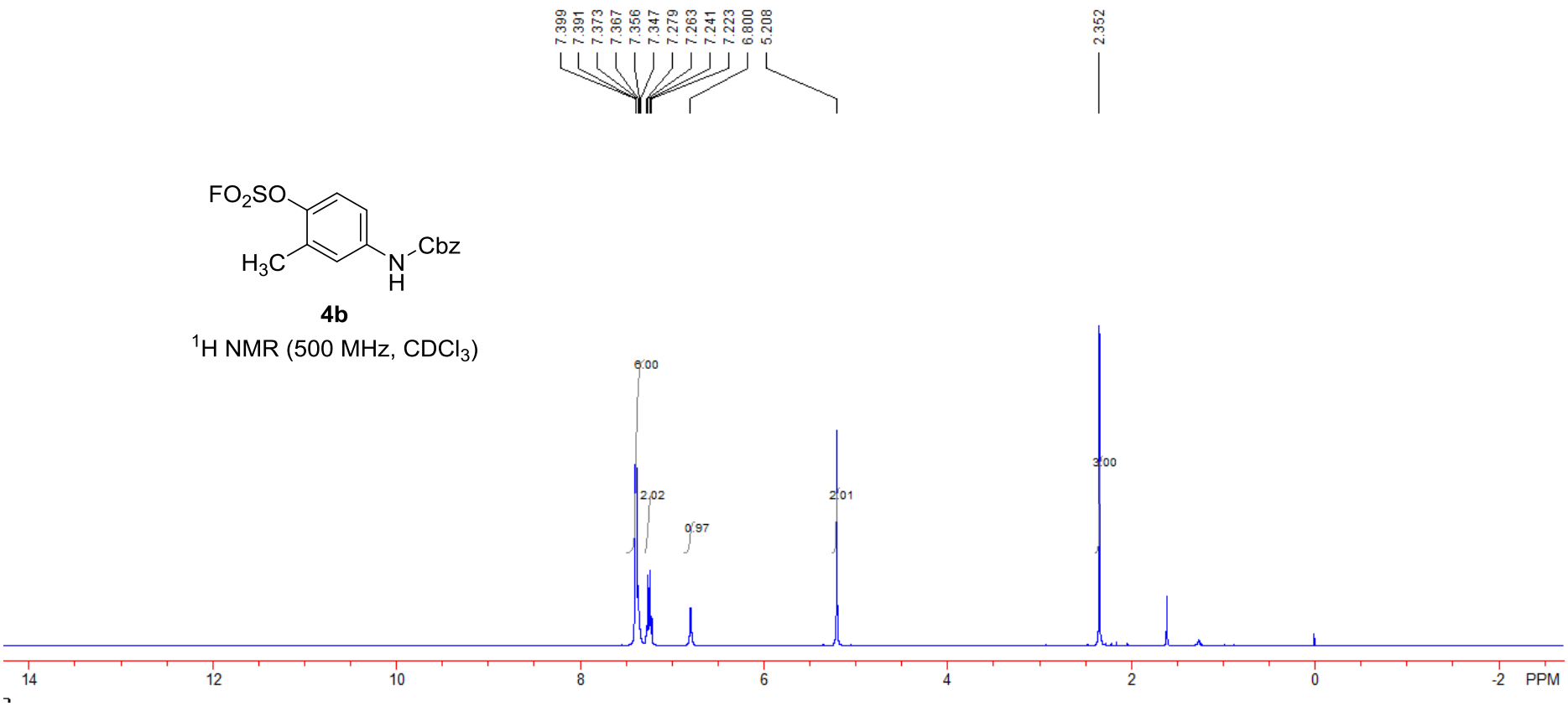
4a

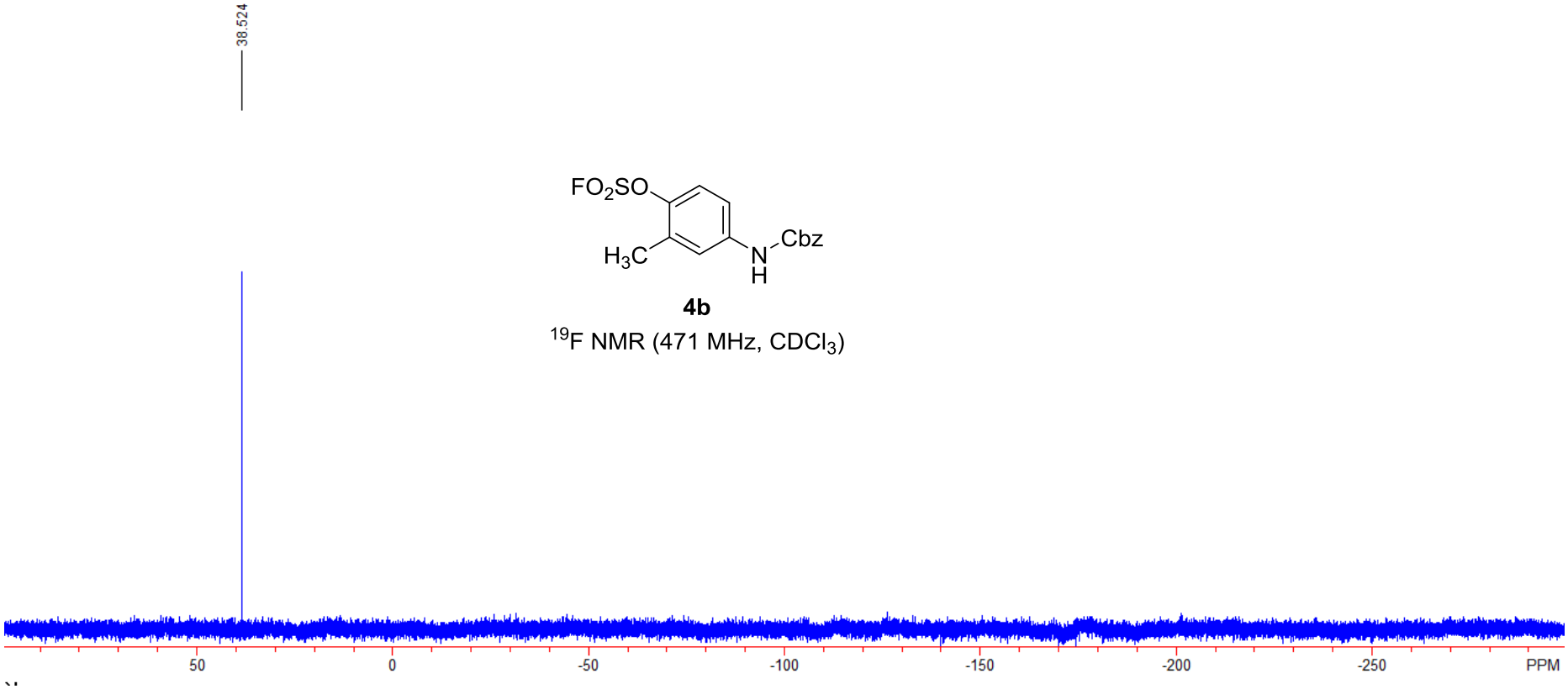
^{19}F NMR (471 MHz, $CDCl_3$)



4a

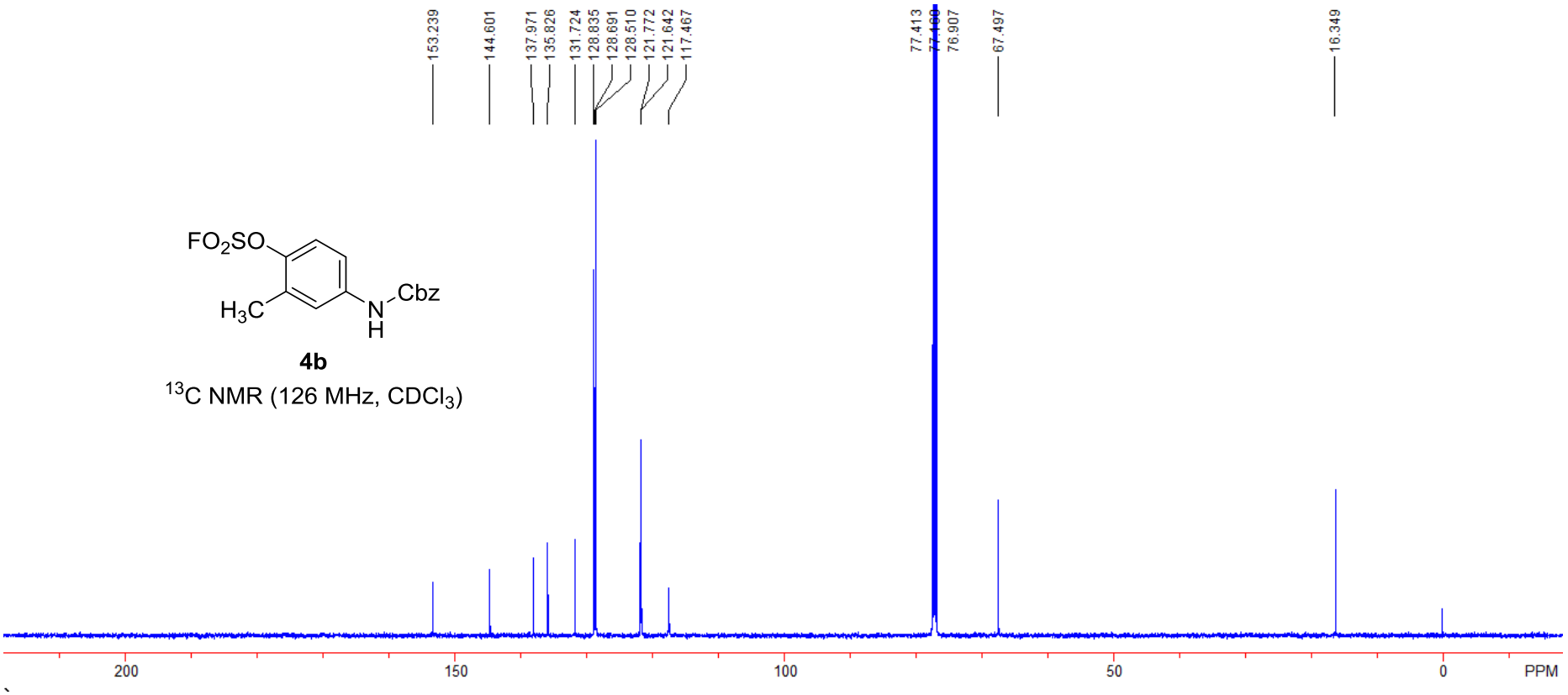
^{13}C NMR (126 MHz, $CDCl_3$)


7.399
7.391
7.373
7.367
7.356
7.347
7.279
7.263
7.241
7.223
6.800
5.208
2.352
FO2SO
H3C
N
H
Cbz
4b
1H NMR (500 MHz, CDCl3)
6.00
2.02
0.97
2.01
3.00
14
12
10
8
6
4
2
0
-2
PPM



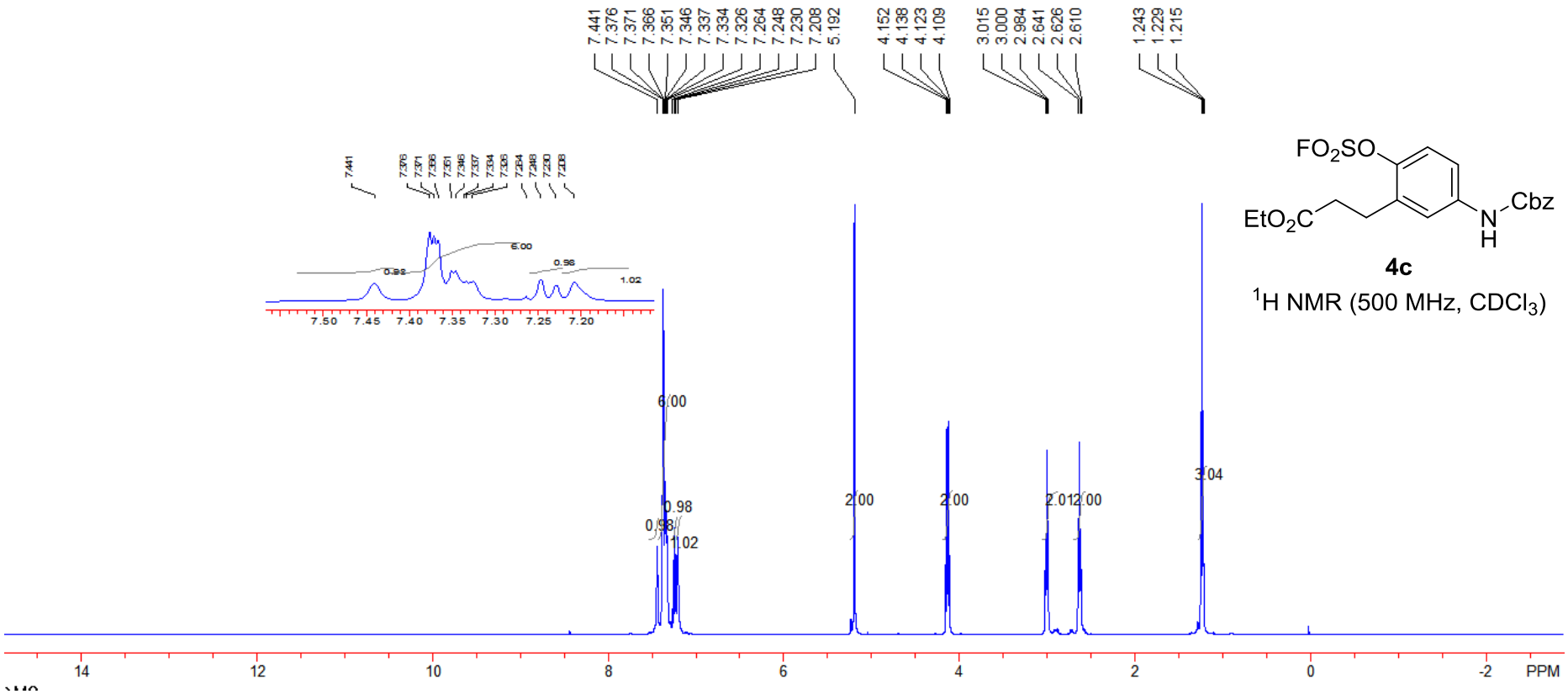
4b

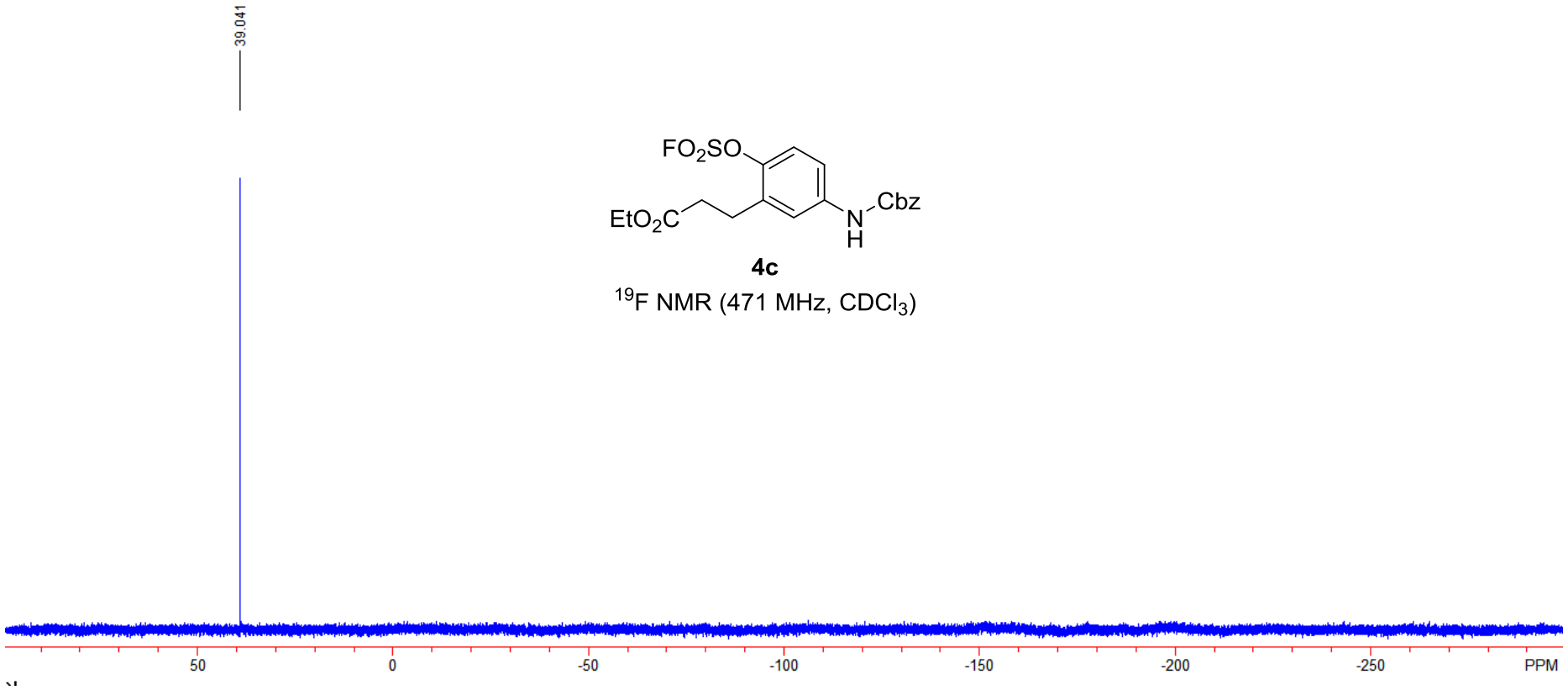
^{19}F NMR (471 MHz, $CDCl_3$)



4b

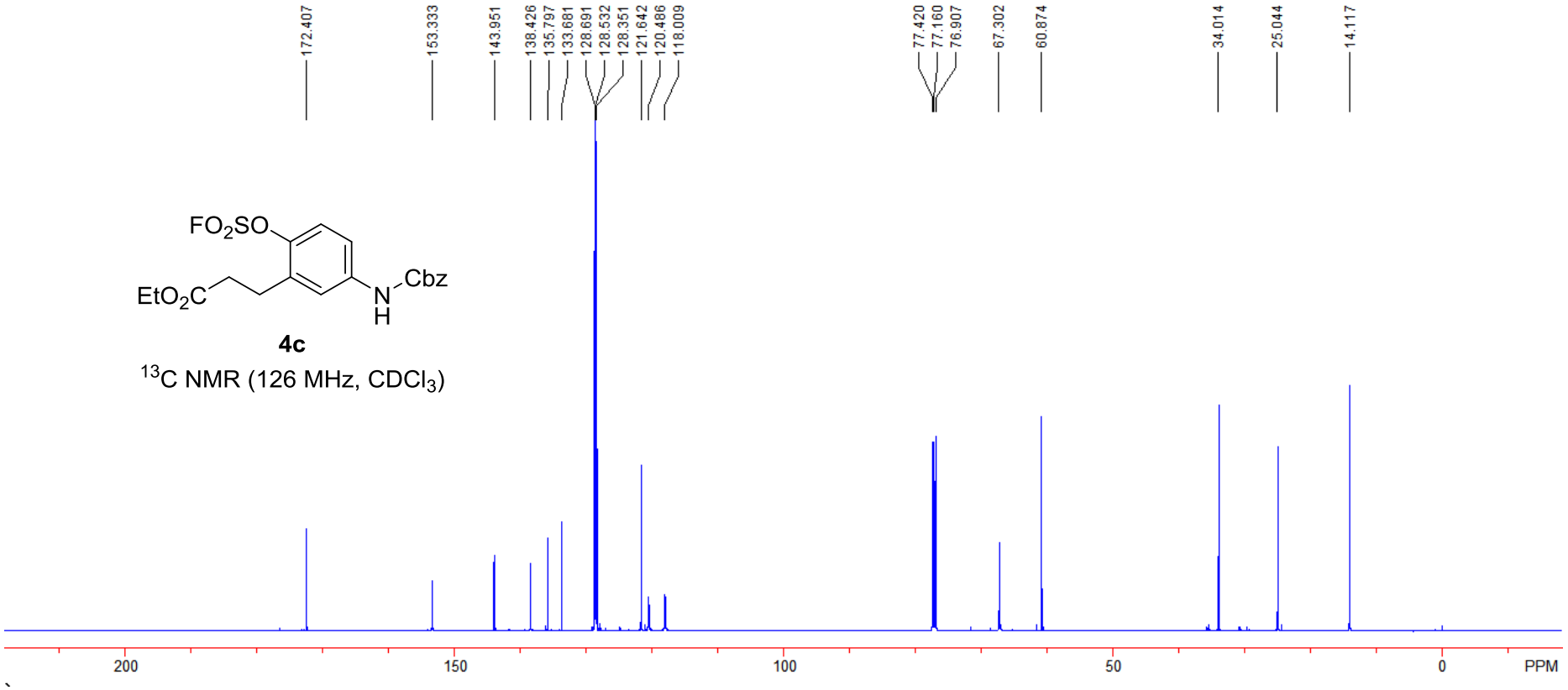
^{13}C NMR (126 MHz, $CDCl_3$)

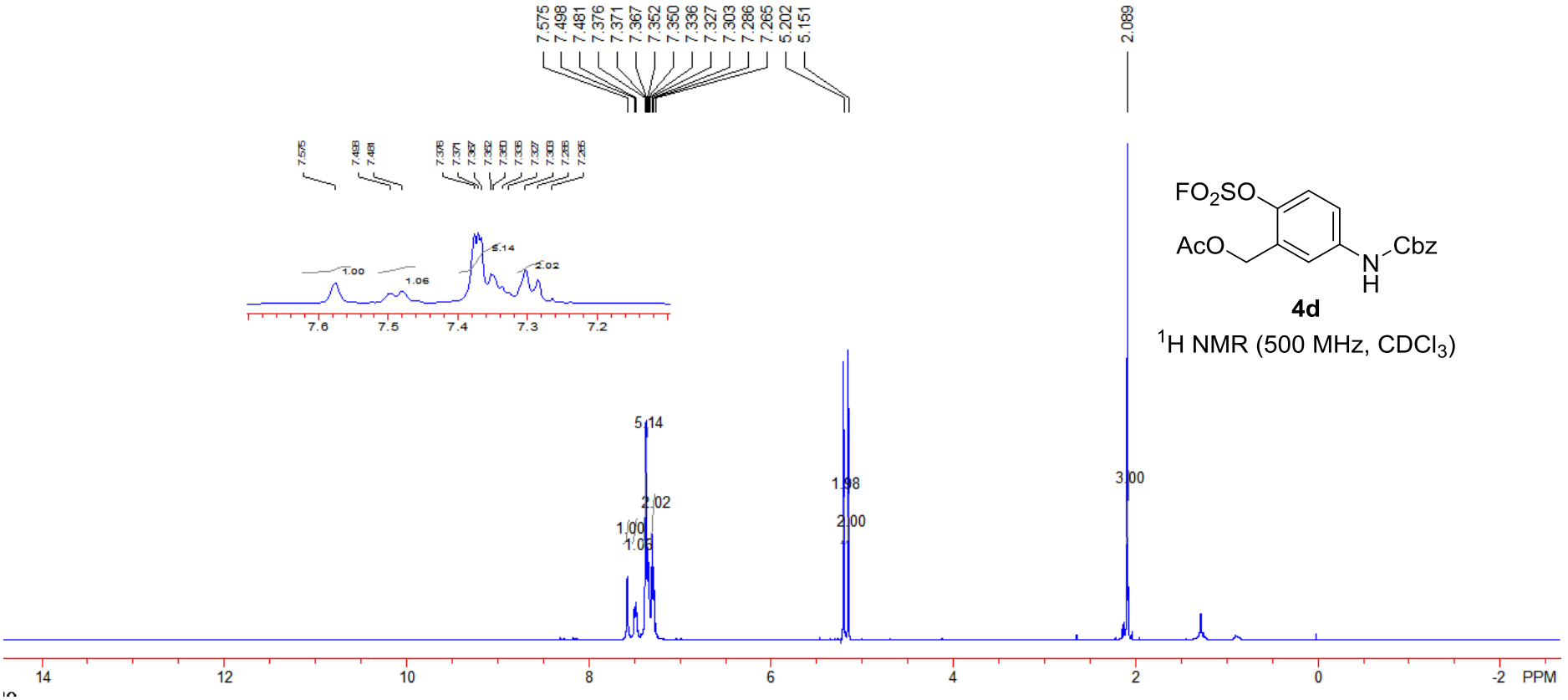

7.441
7.376
7.371
7.366
7.351
7.346
7.337
7.334
7.326
7.264
7.248
7.230
7.208
5.192
4.152
4.138
4.123
4.109
3.015
3.000
2.984
2.641
2.626
2.610
1.243
1.229
1.215
6.00
0.98
0.98
1.02
2.00
2.00
2.01
2.00
3.04
14
12
10
8
6
4
2
0
-2
PPM
FO2SO
EtO2C
N
H
Cbz
4c
1H NMR (500 MHz, CDCl3)

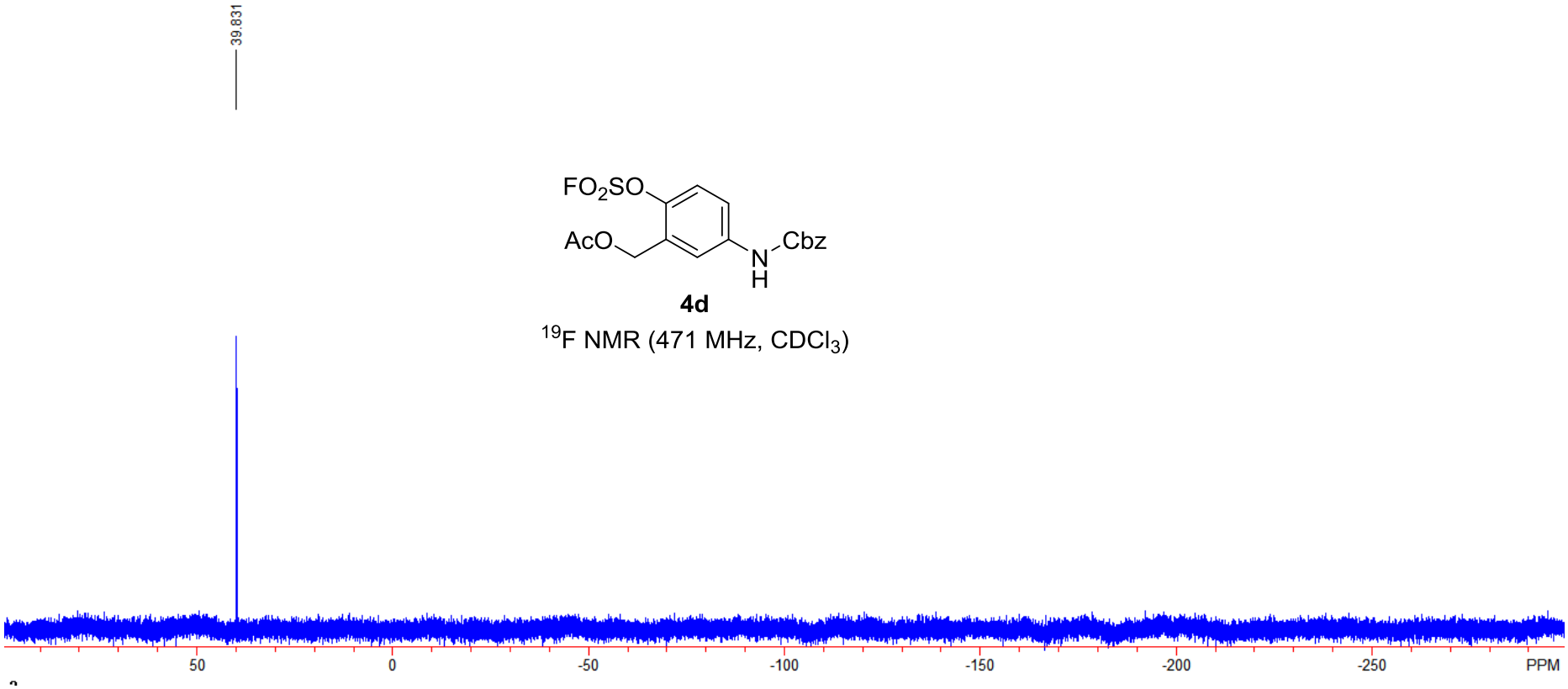


4c

^{19}F NMR (471 MHz, $CDCl_3$)

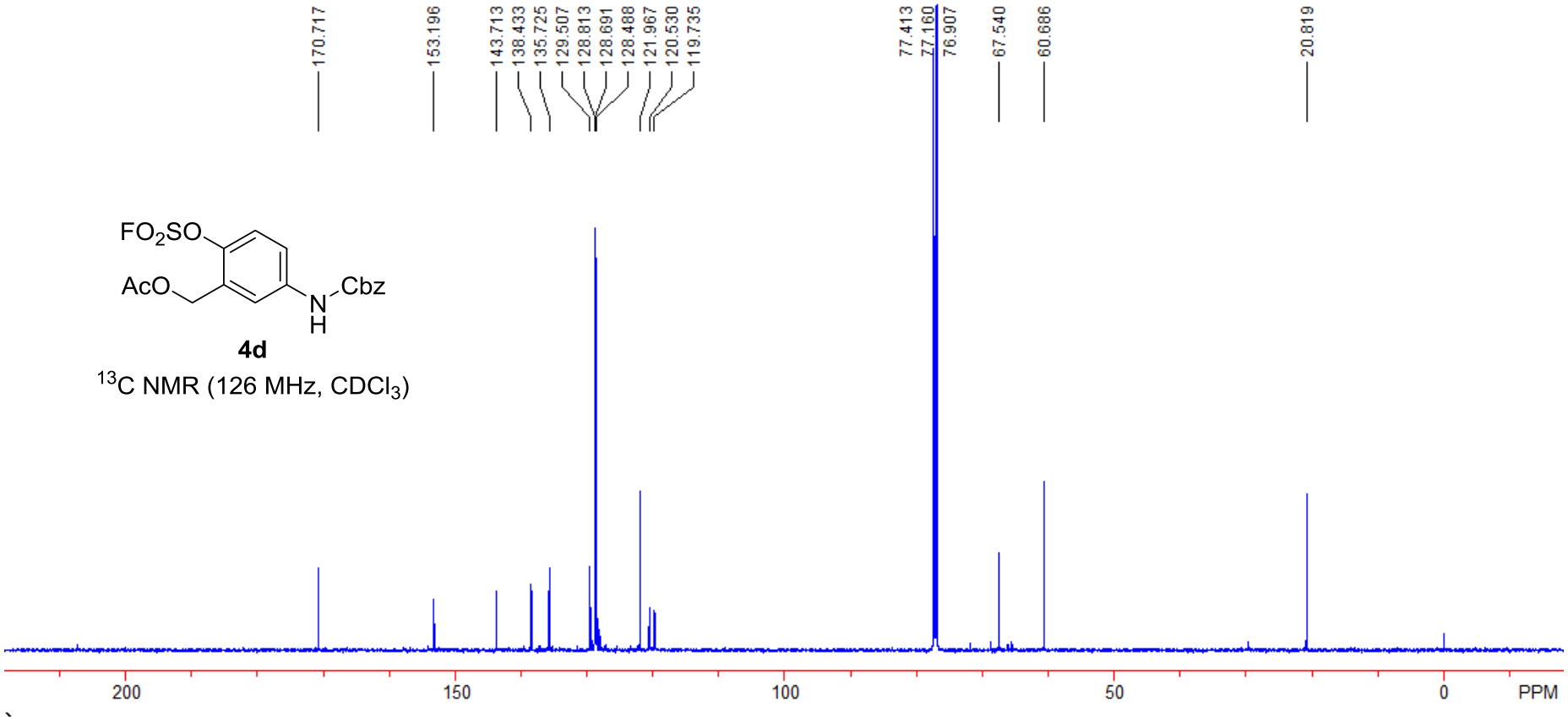

172.407
153.333
143.951
138.426
135.797
133.681
128.691
128.532
128.351
121.642
120.486
118.009
77.420
77.160
76.907
67.302
60.874
34.014
25.044
14.117
FO2SO
EtO2C
N
H
Cbz
4c
13C NMR (126 MHz, CDCl3)
200
150
100
50
0
PPM


7.575
7.498
7.481
7.376
7.371
7.367
7.352
7.350
7.336
7.327
7.303
7.286
7.265
5.202
5.151
2.089
5.14
2.02
1.00
1.06
1.98
2.00
3.00
14
12
10
8
6
4
2
0
-2
PPM
7.6
7.5
7.4
7.3
7.2
FO2SO
AcO
N
H
Cbz
4d
1H NMR (500 MHz, CDCl3)



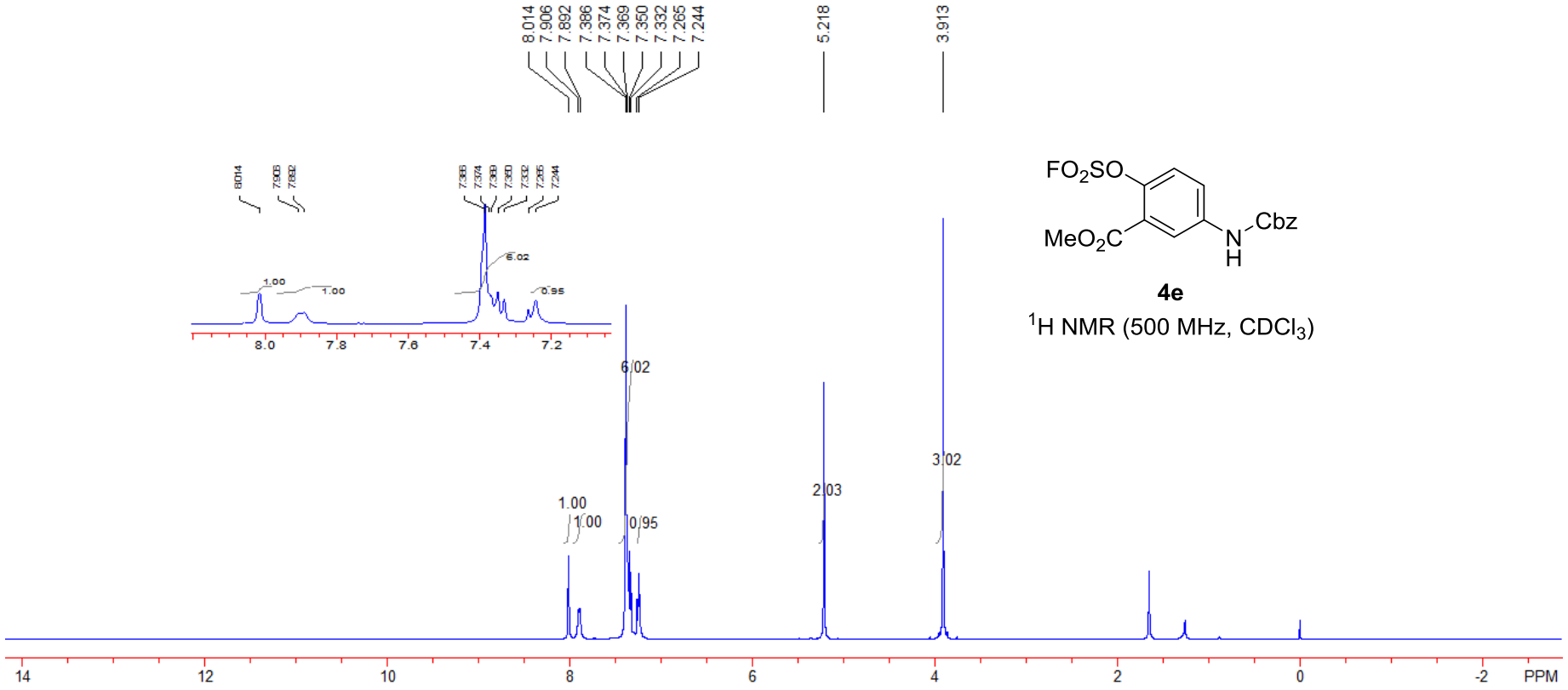
4d

^{19}F NMR (471 MHz, $CDCl_3$)



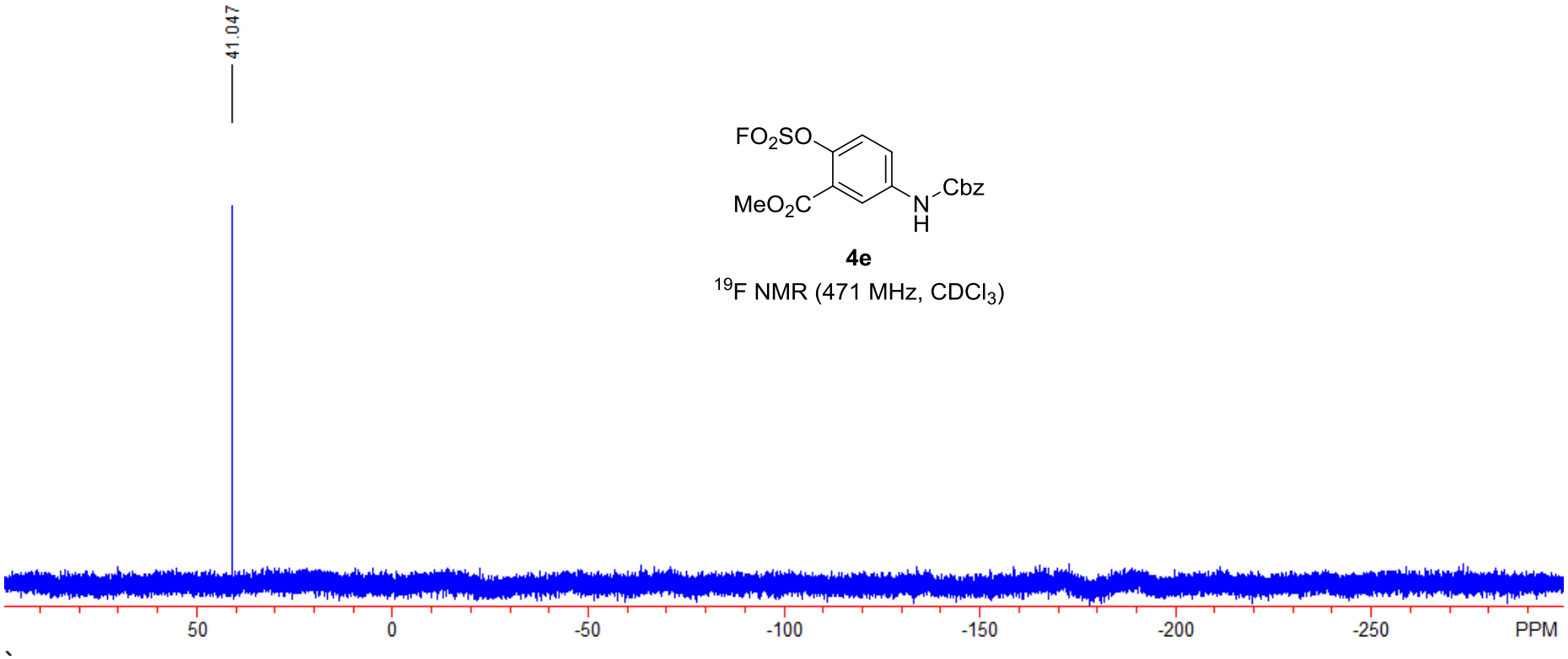
4d

^{13}C NMR (126 MHz, $CDCl_3$)



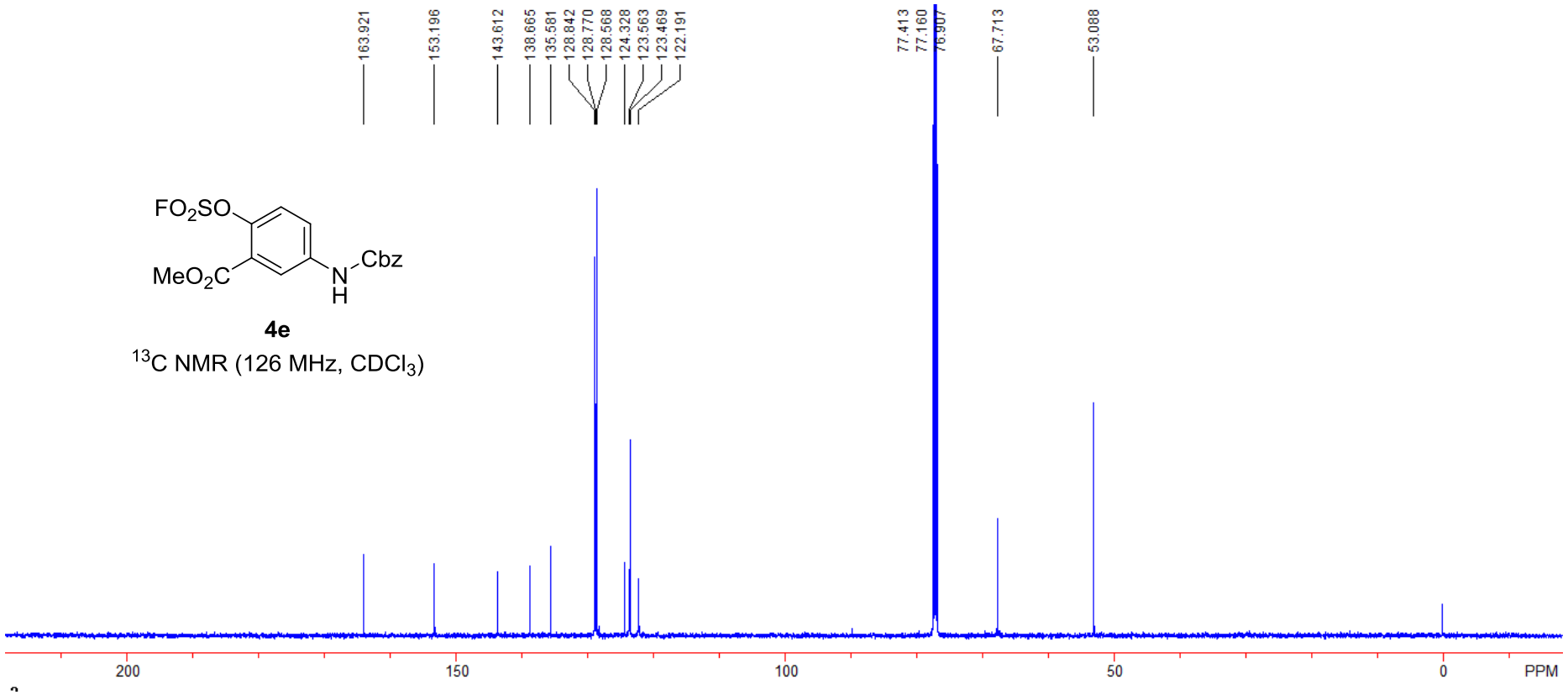
4e

^{1}H NMR (500 MHz, $CDCl_3$)



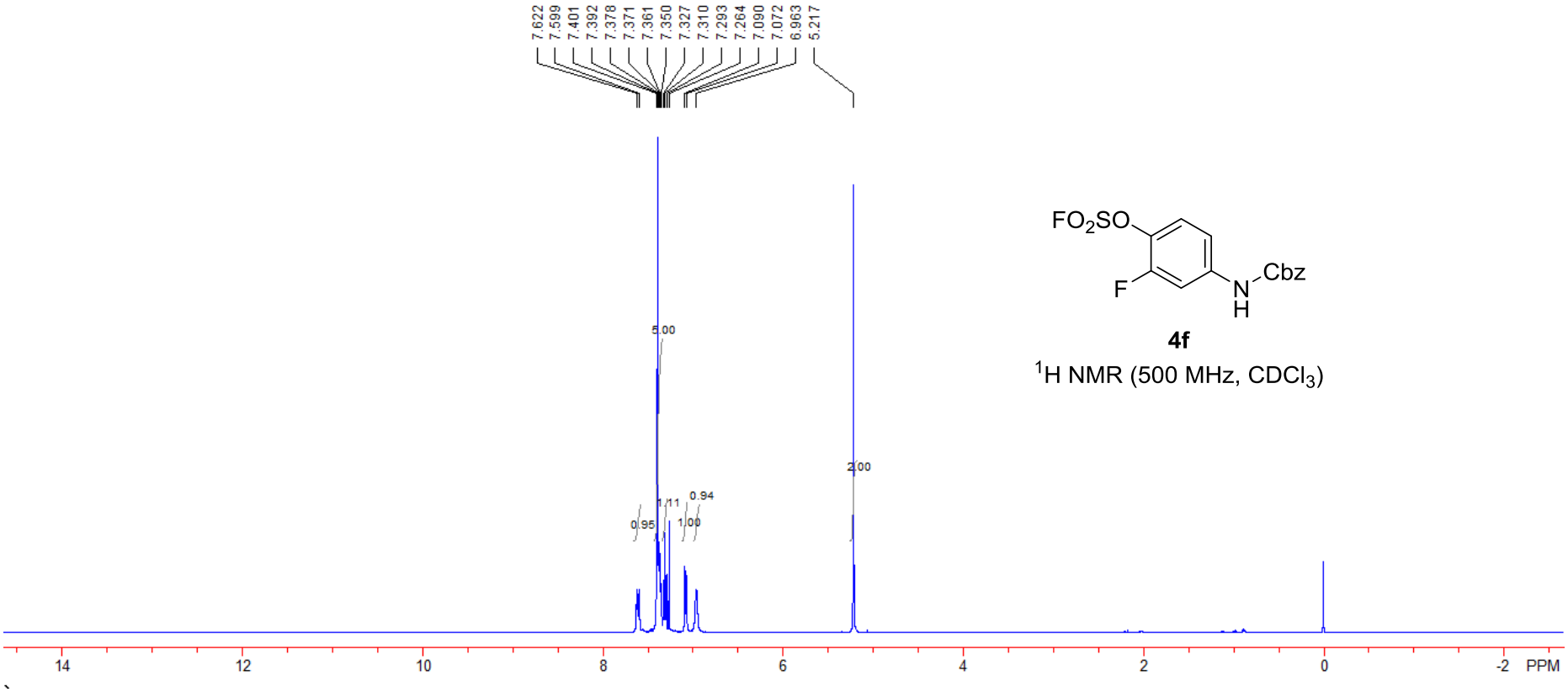
4e

^{19}F NMR (471 MHz, $CDCl_3$)



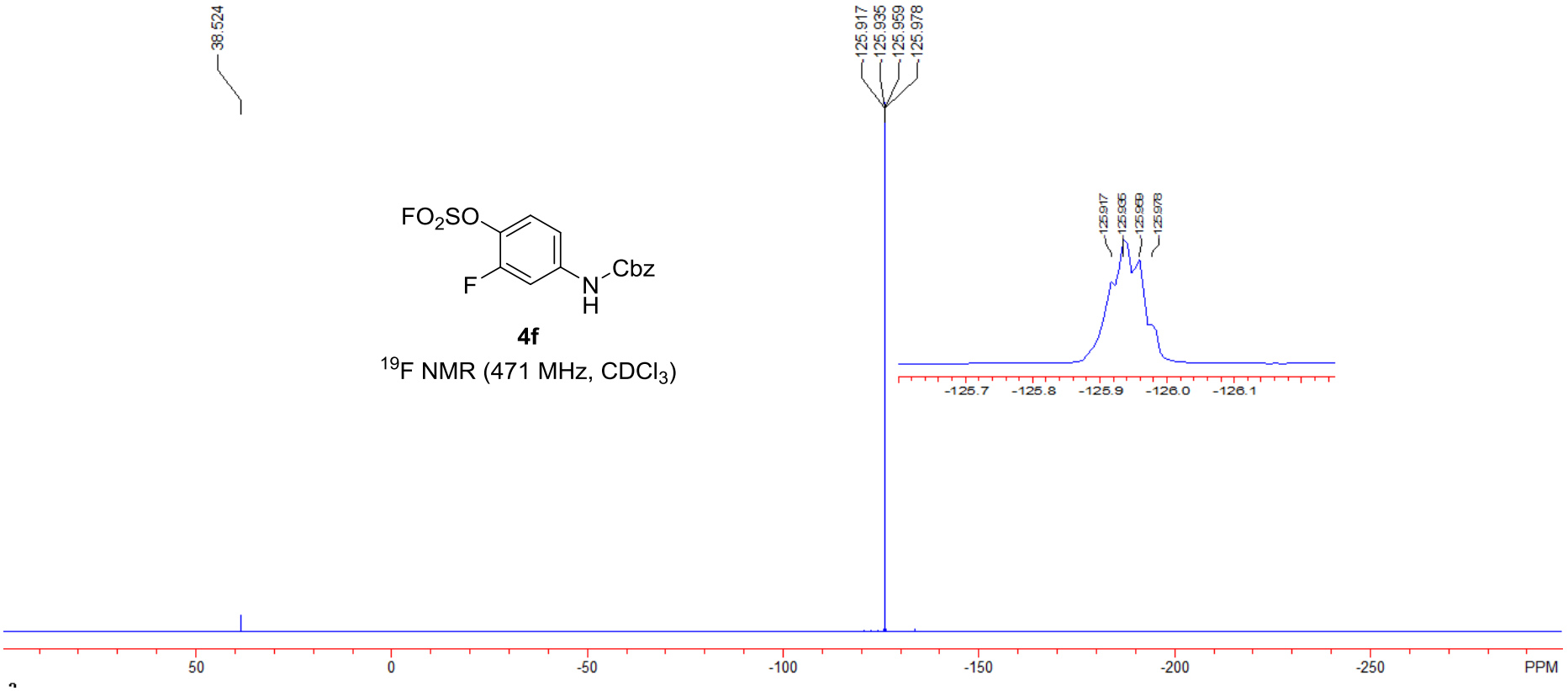
4e

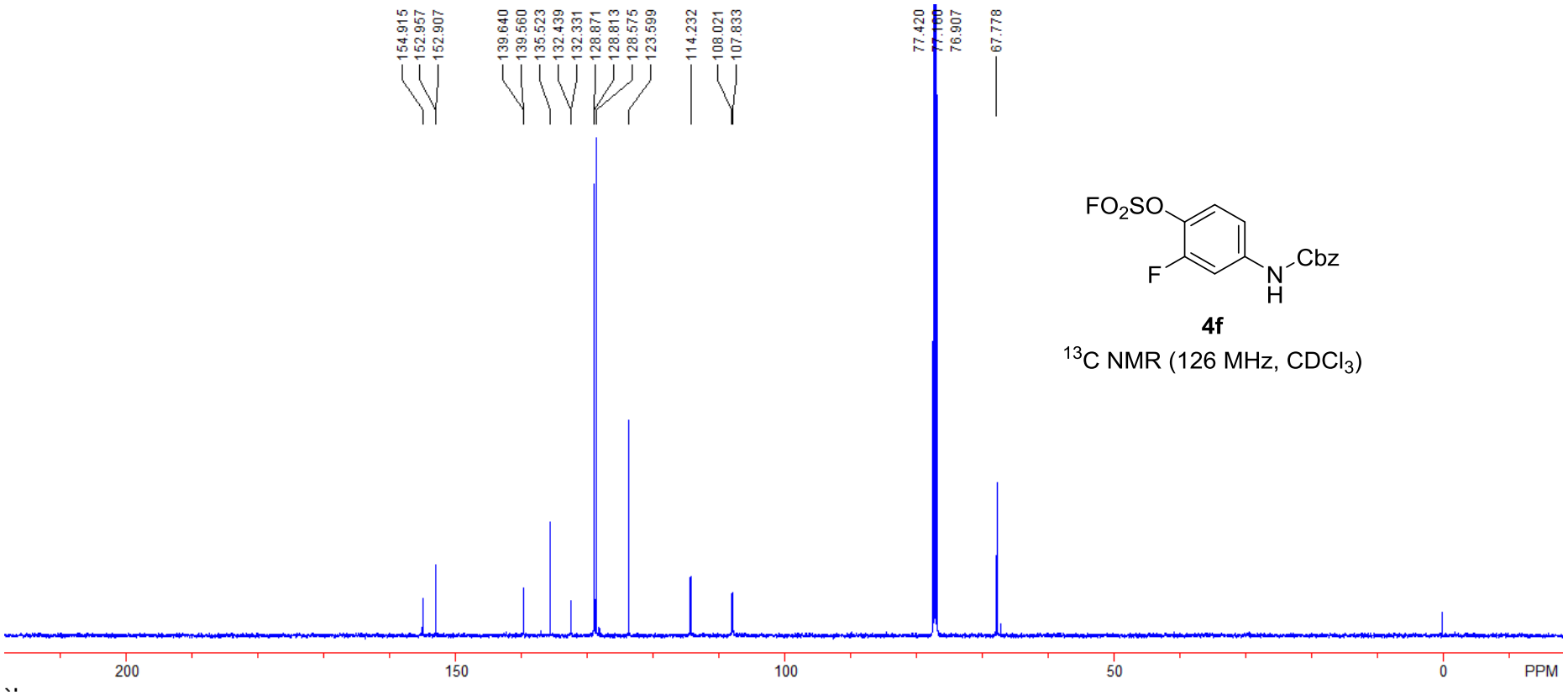
^{13}C NMR (126 MHz, $CDCl_3$)



4f

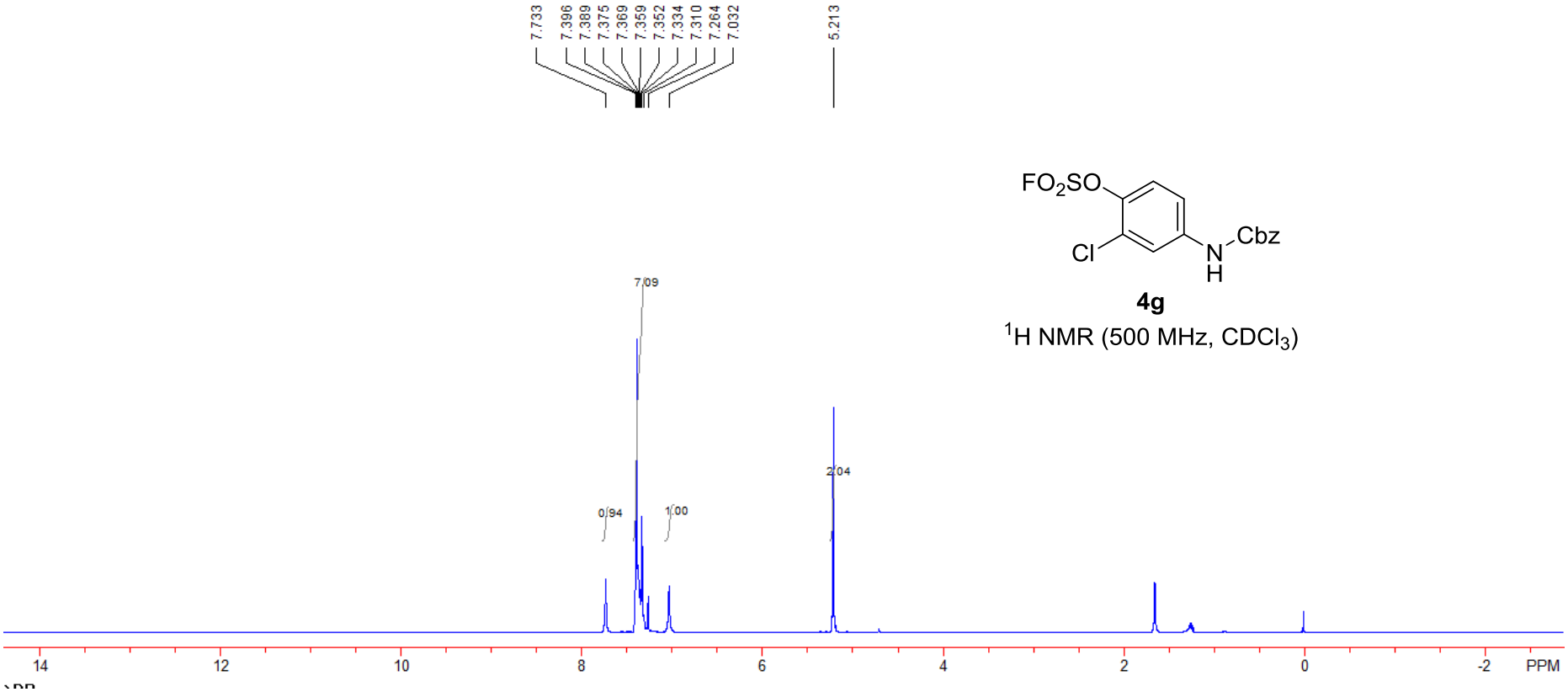
^{1}H NMR (500 MHz, $CDCl_3$)

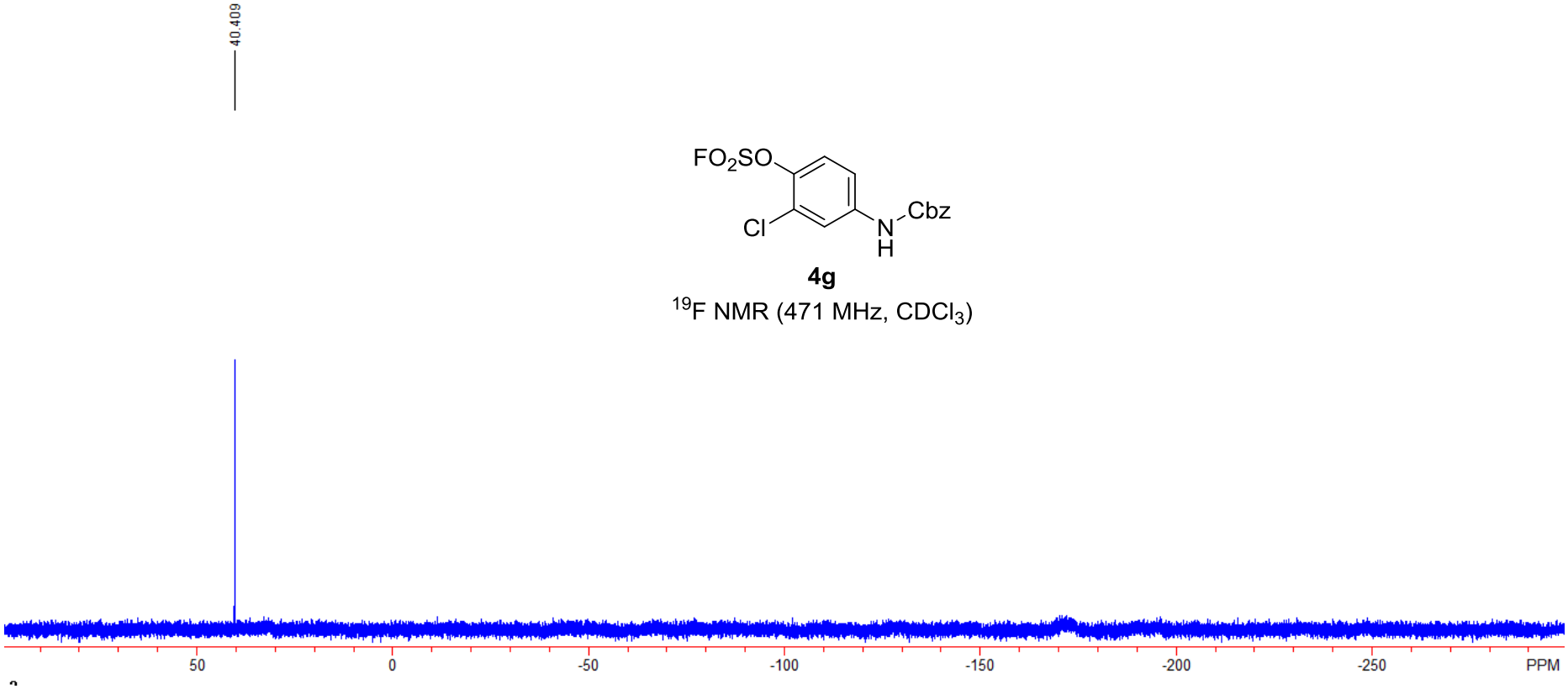

38.524
125.917
125.935
125.959
125.978
FO2SO
F
N
H
Cbz
4f
19F NMR (471 MHz, CDCl3)
125.917
125.936
125.958
125.978
-125.7
-125.8
-125.9
-126.0
-126.1
50
0
-50
-100
-150
-200
-250
PPM



4f

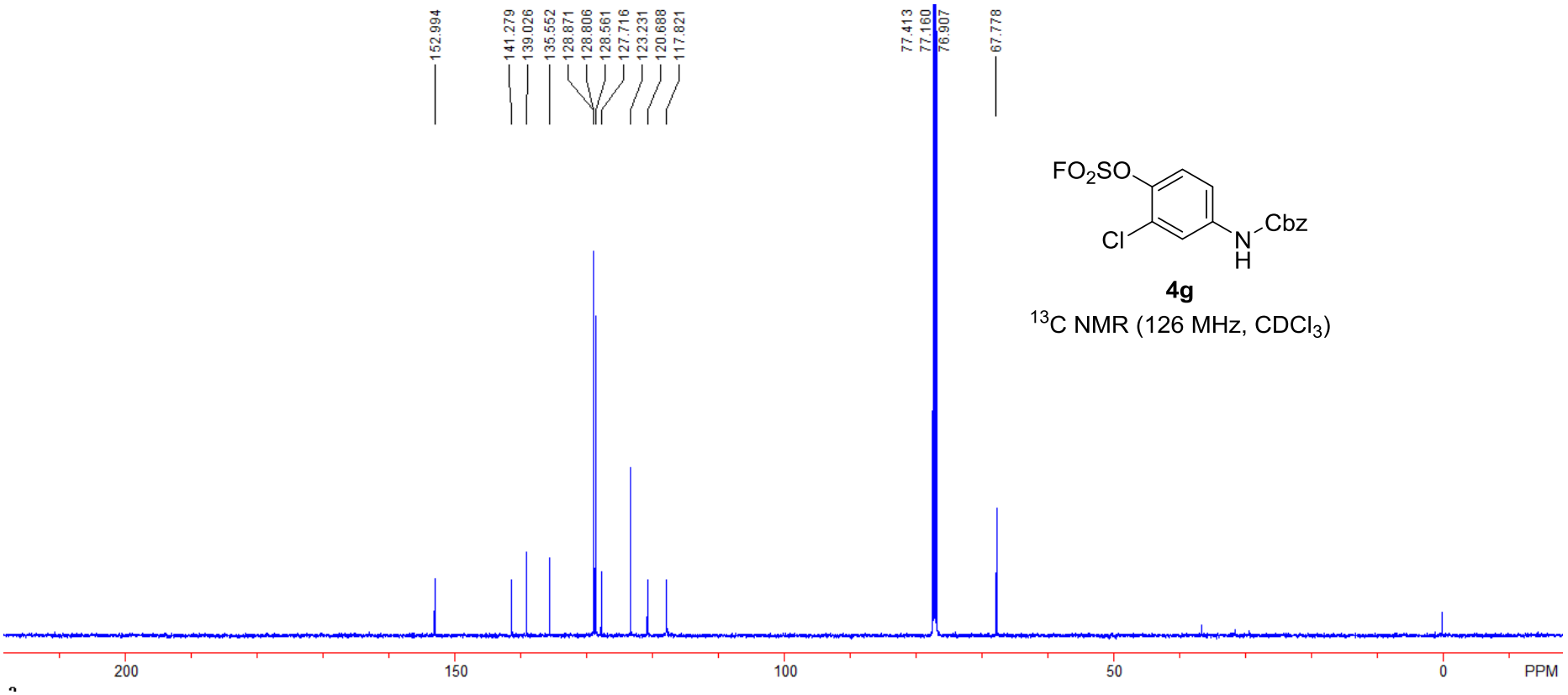
^{13}C NMR (126 MHz, $CDCl_3$)


7.733
7.396
7.389
7.375
7.369
7.359
7.352
7.334
7.310
7.264
7.032
5.213
FO2SO
Cl
N
H
Cbz
4g
1H NMR (500 MHz, CDCl3)
7.09
2.04
0.94
1.00
14
12
10
8
6
4
2
0
-2
PPM



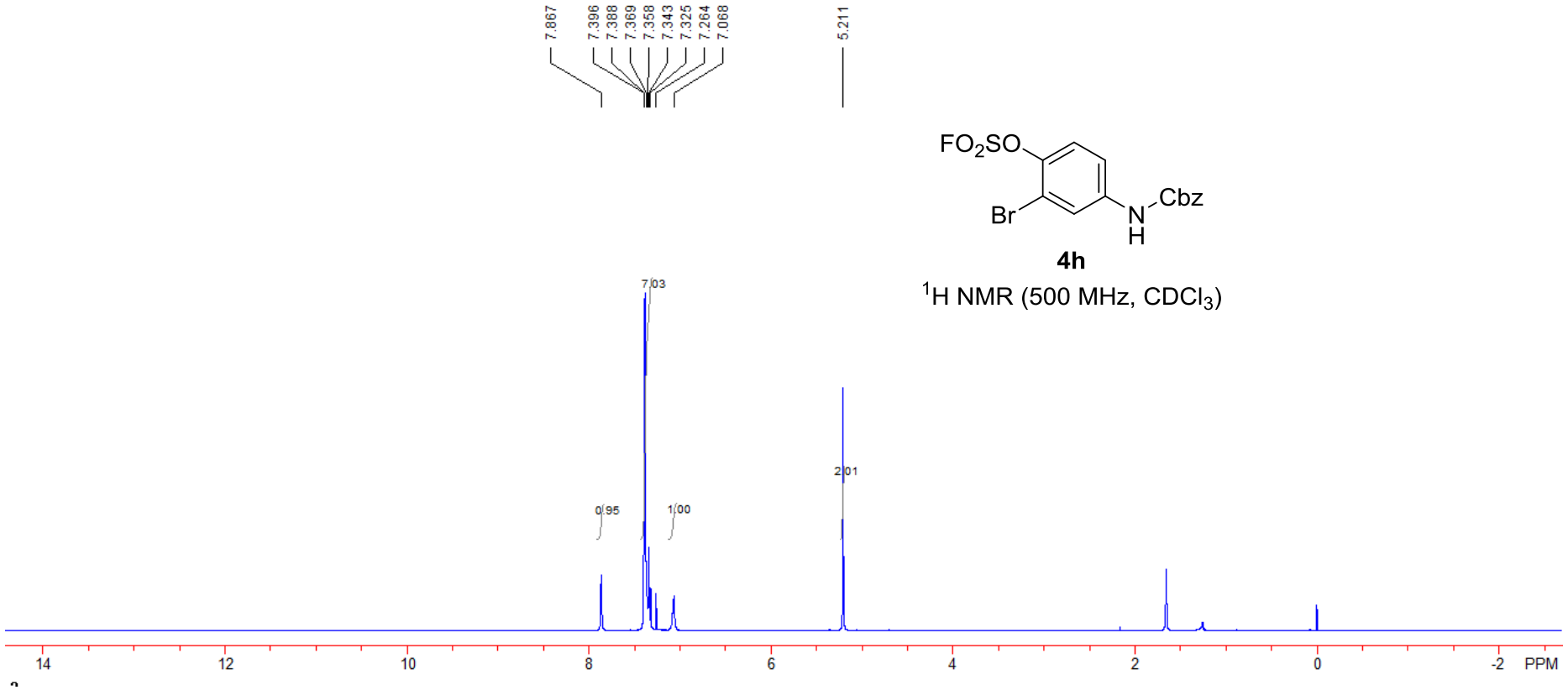
4g

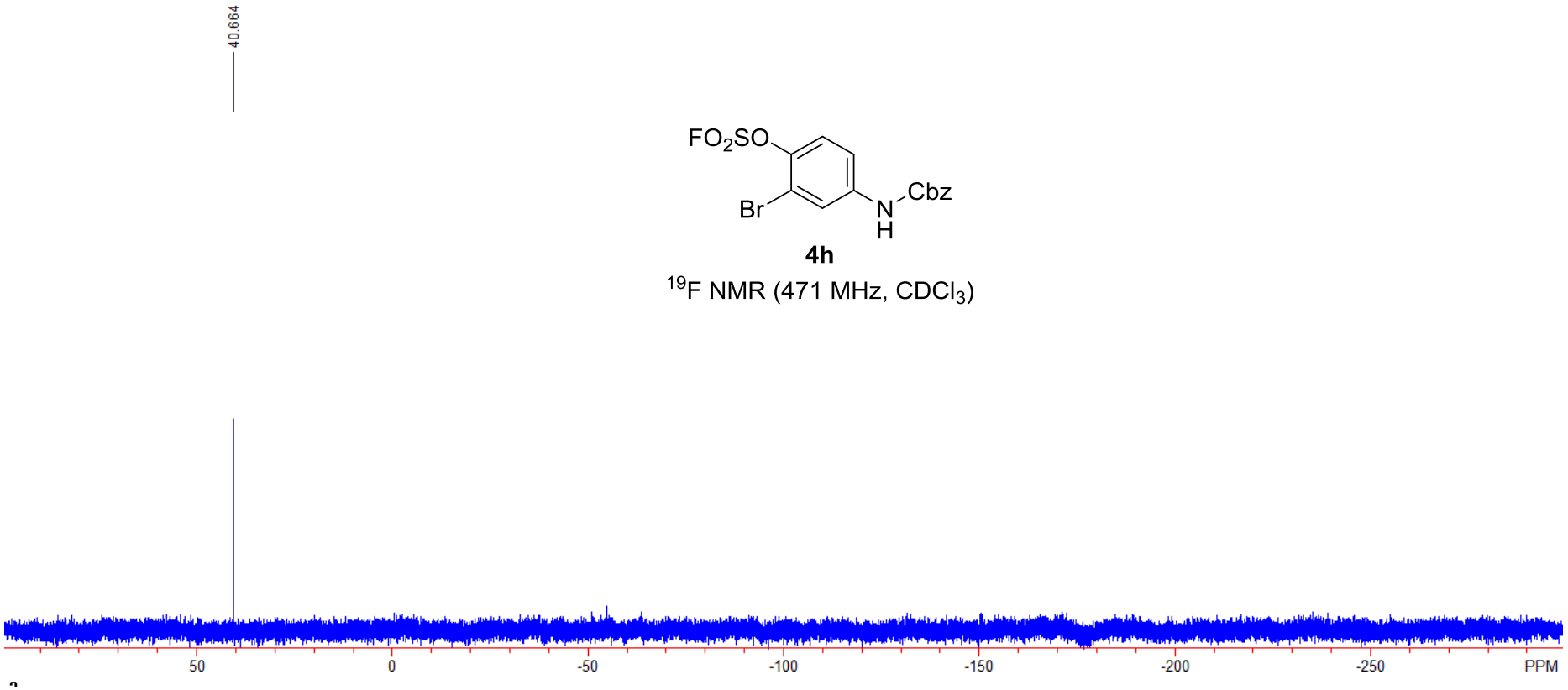
^{19}F NMR (471 MHz, $CDCl_3$)



4g

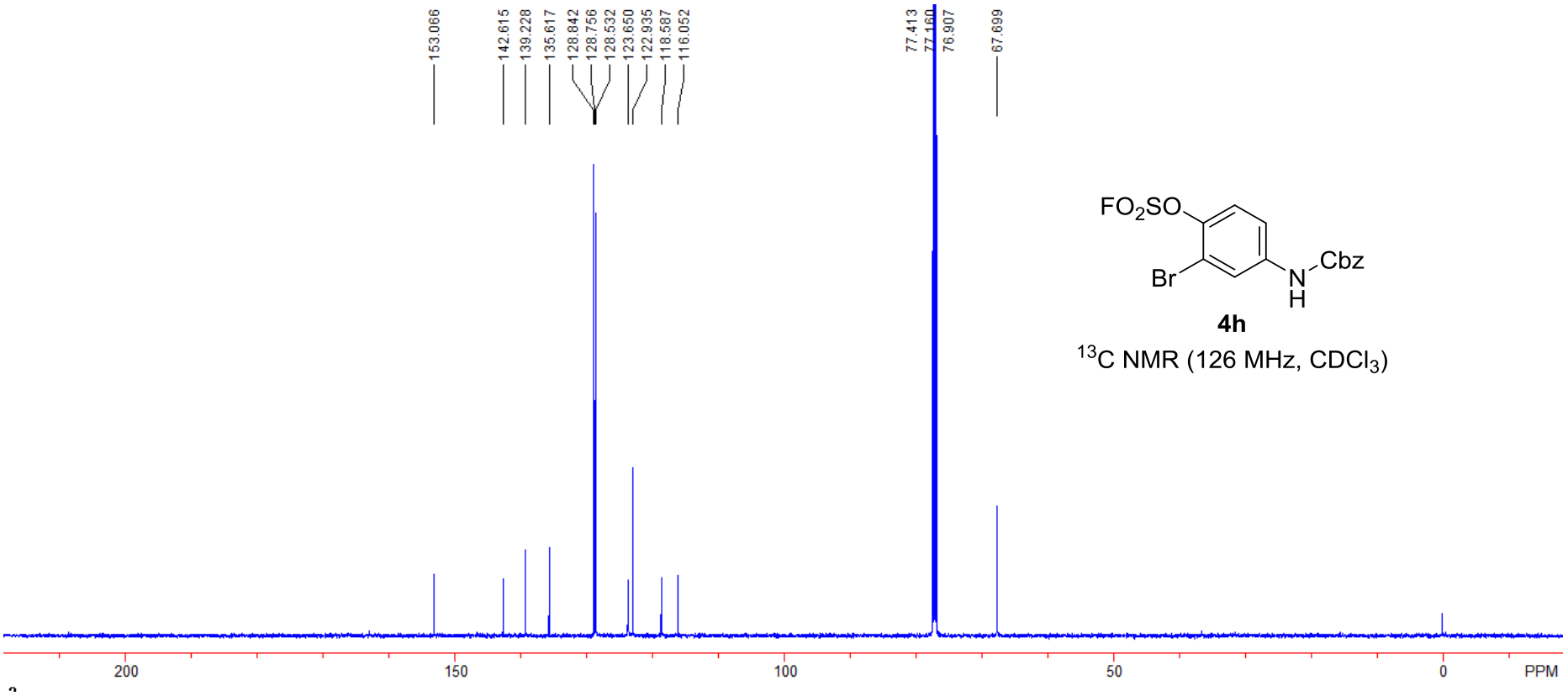
^{13}C NMR (126 MHz, $CDCl_3$)

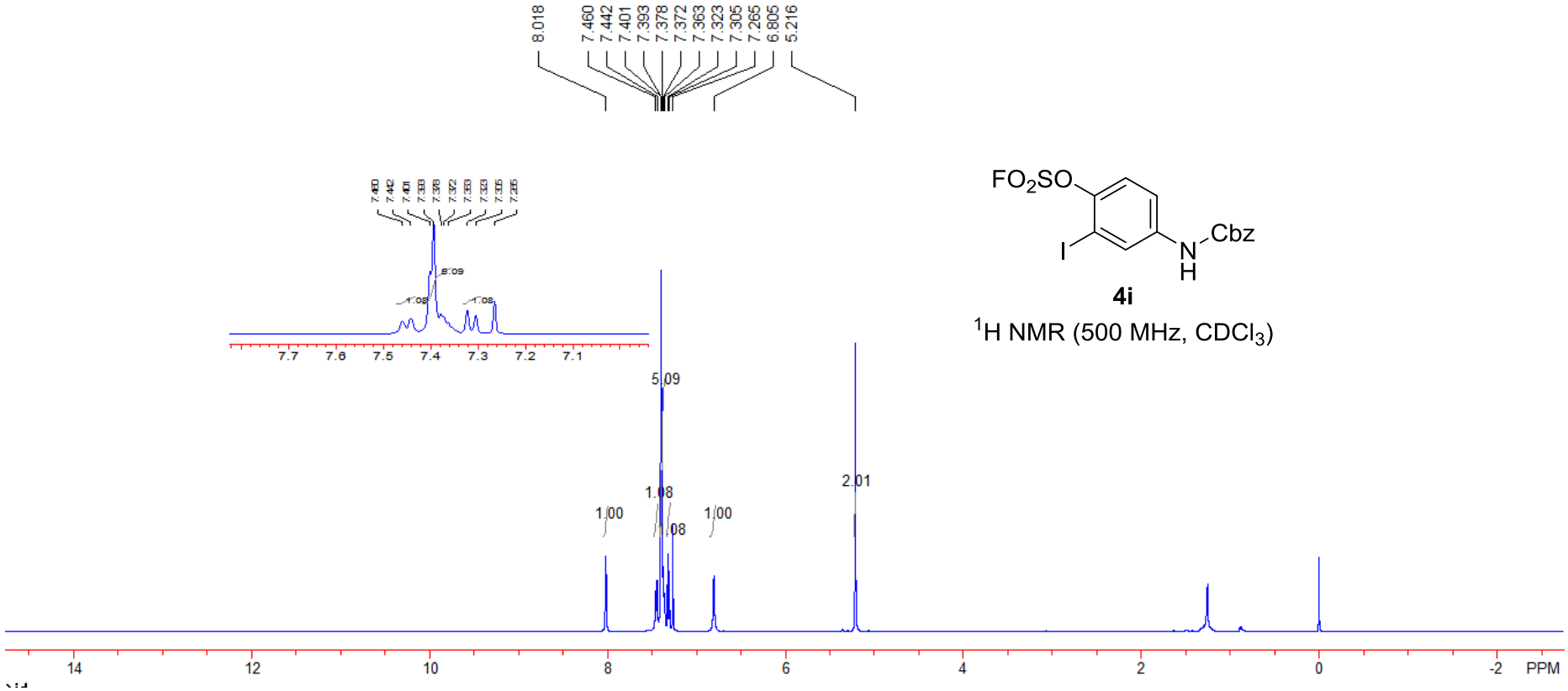

7.867
7.396
7.388
7.369
7.358
7.343
7.325
7.264
7.068
5.211
FO2SO
Br
N
H
Cbz
4h
1H NMR (500 MHz, CDCl3)
7.03
2.01
0.95
1.00
14
12
10
8
6
4
2
0
-2
PPM



4h

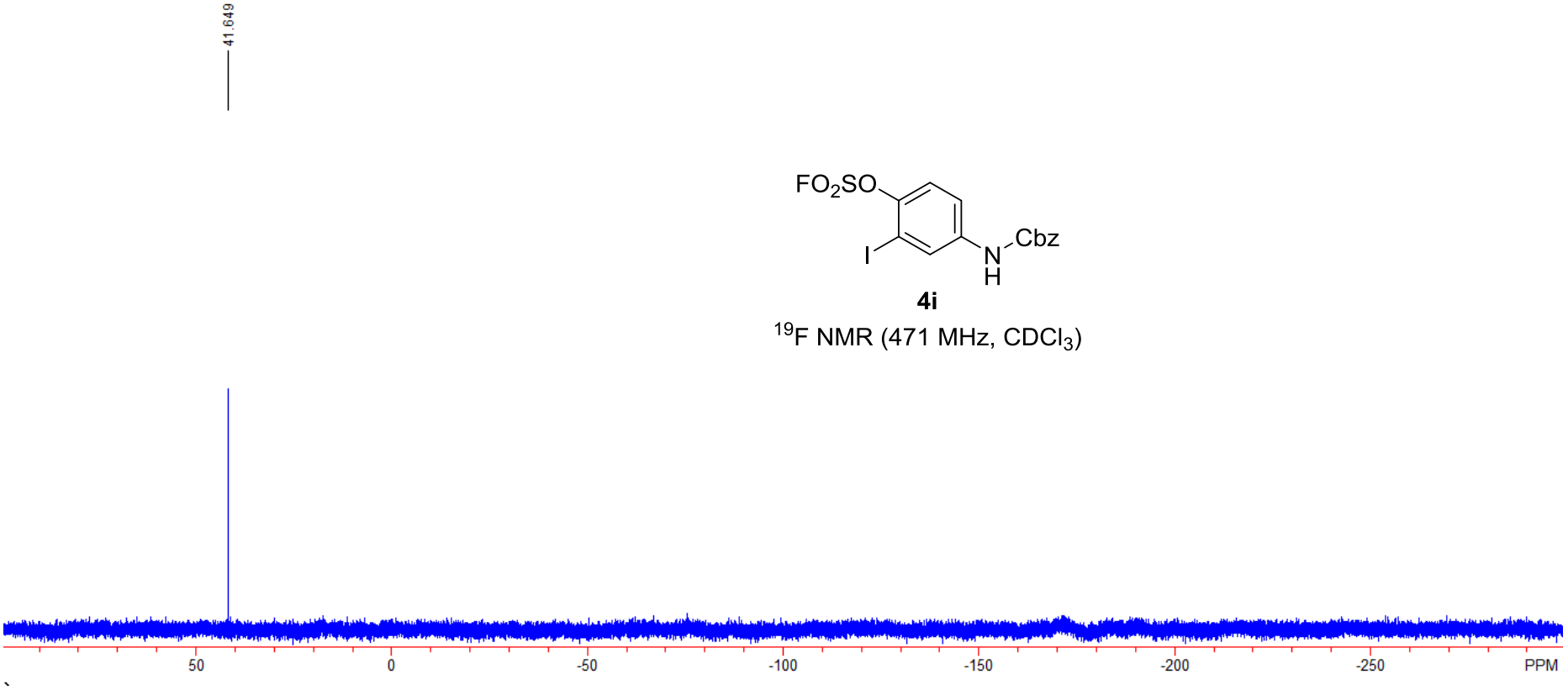
^{19}F NMR (471 MHz, $CDCl_3$)


153.066
142.615
139.228
135.617
128.842
128.756
128.532
123.650
122.935
118.587
116.052
77.413
77.160
76.907
67.699
200
150
100
50
0
PPM
FO2SO
Br
N
H
Cbz
4h
13C NMR (126 MHz, CDCl3)



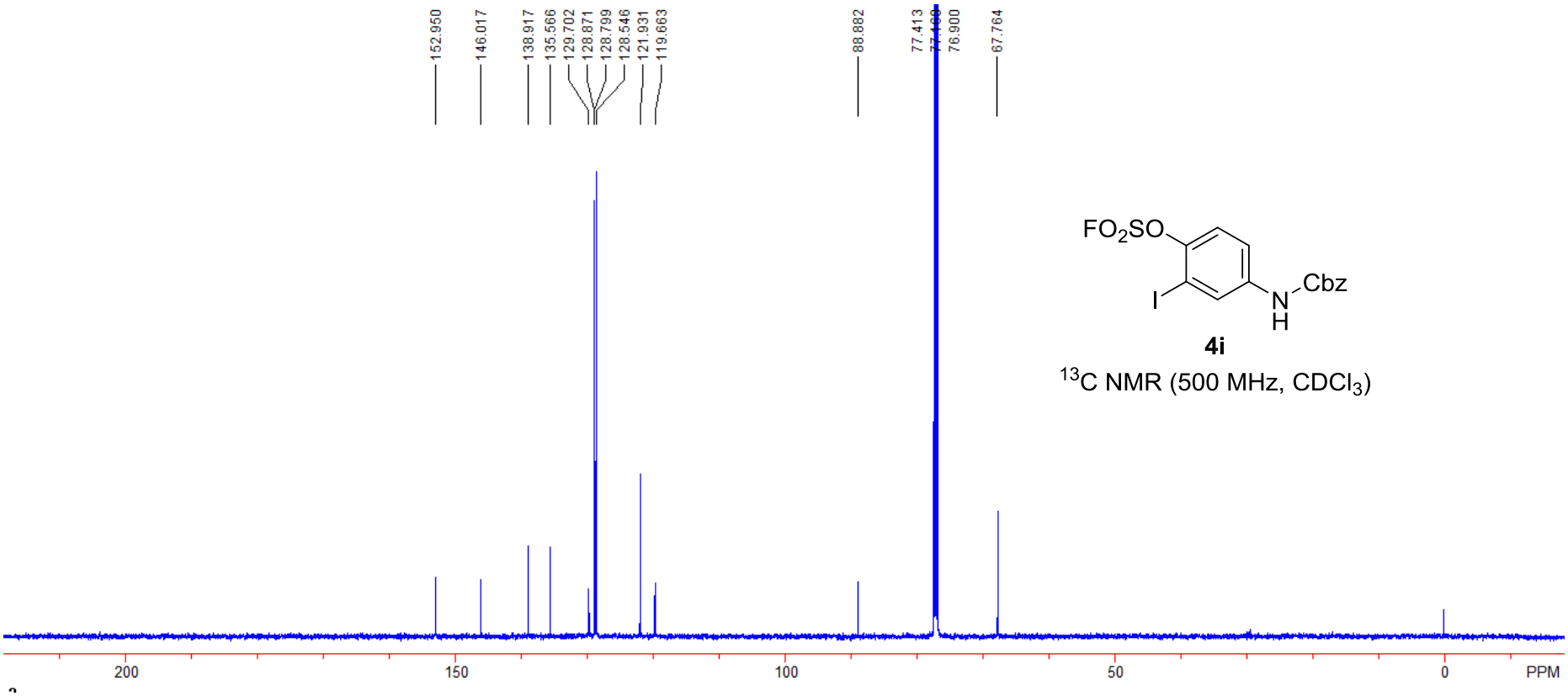
4i

^{1}H NMR (500 MHz, $CDCl_3$)



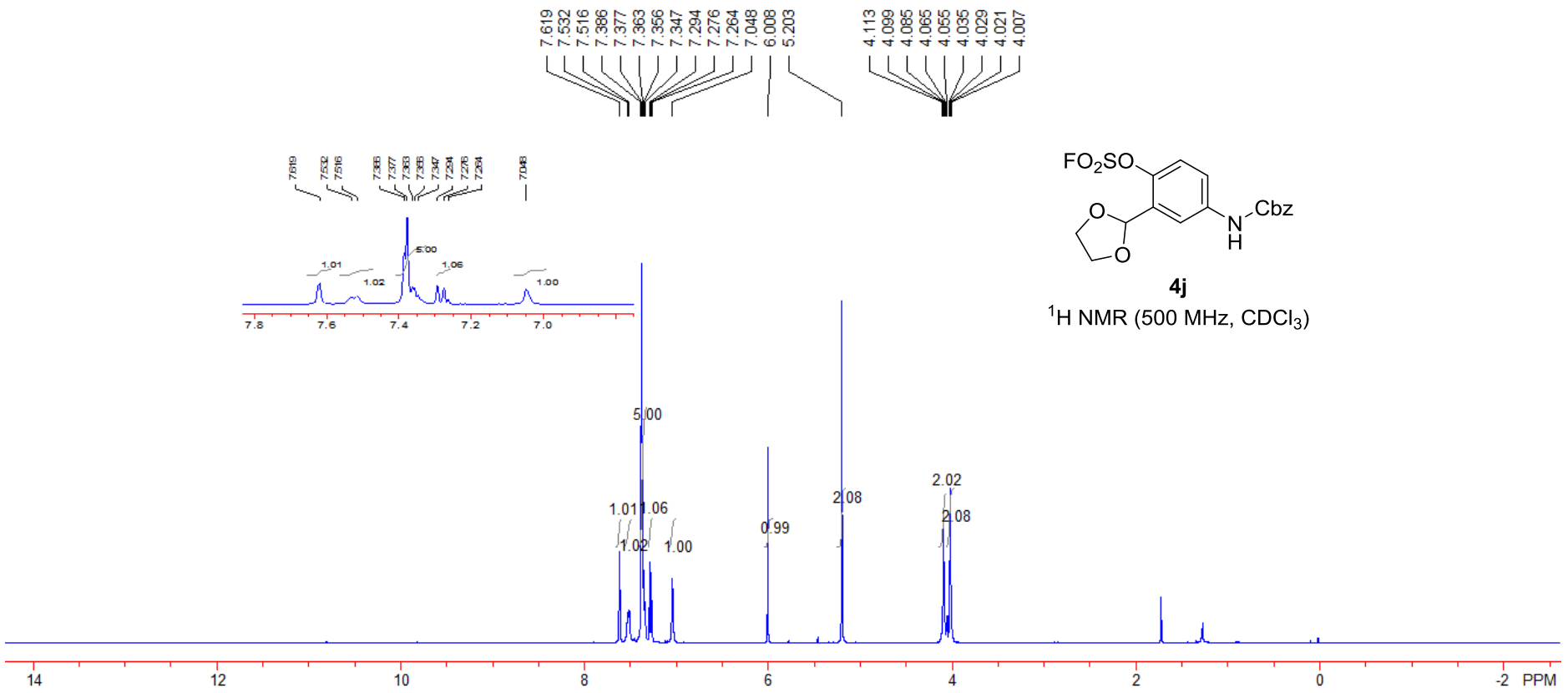
4i

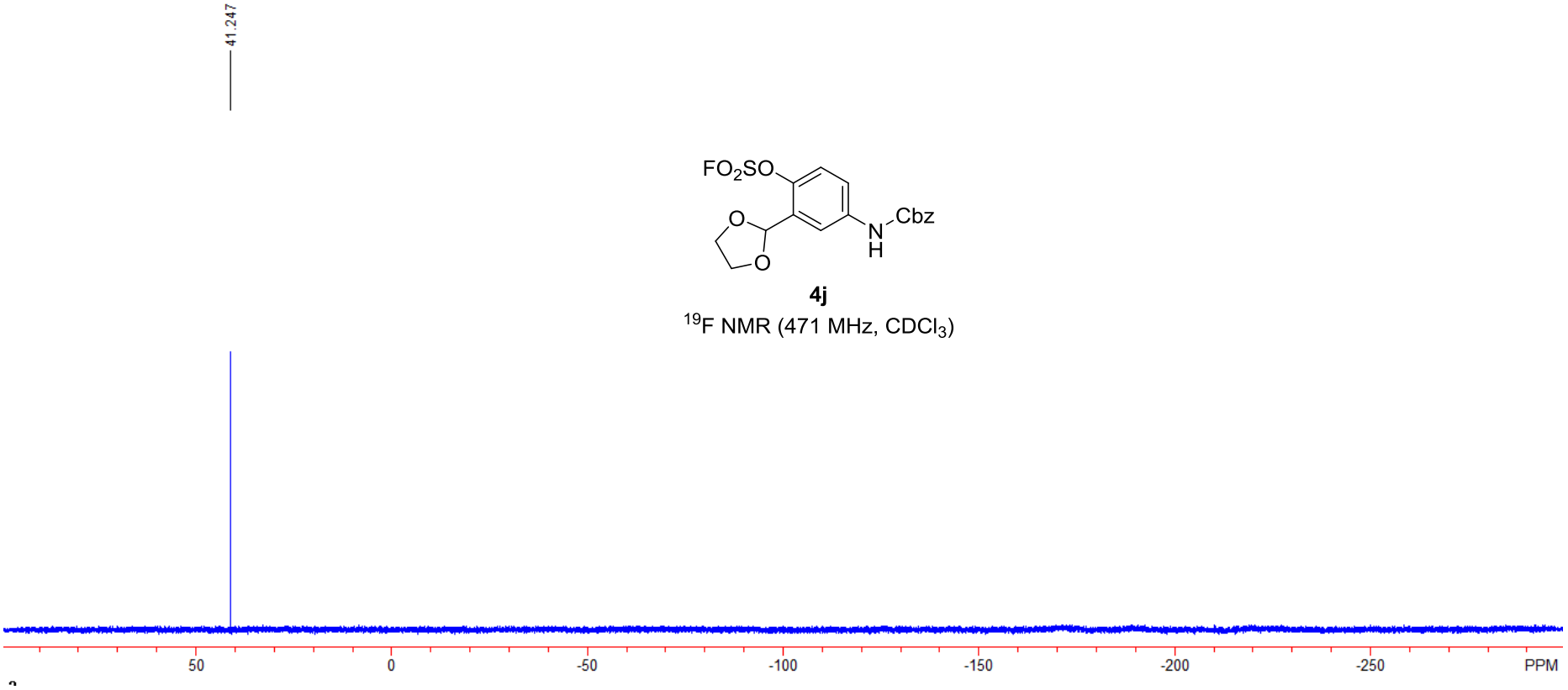
^{19}F NMR (471 MHz, $CDCl_3$)



4i

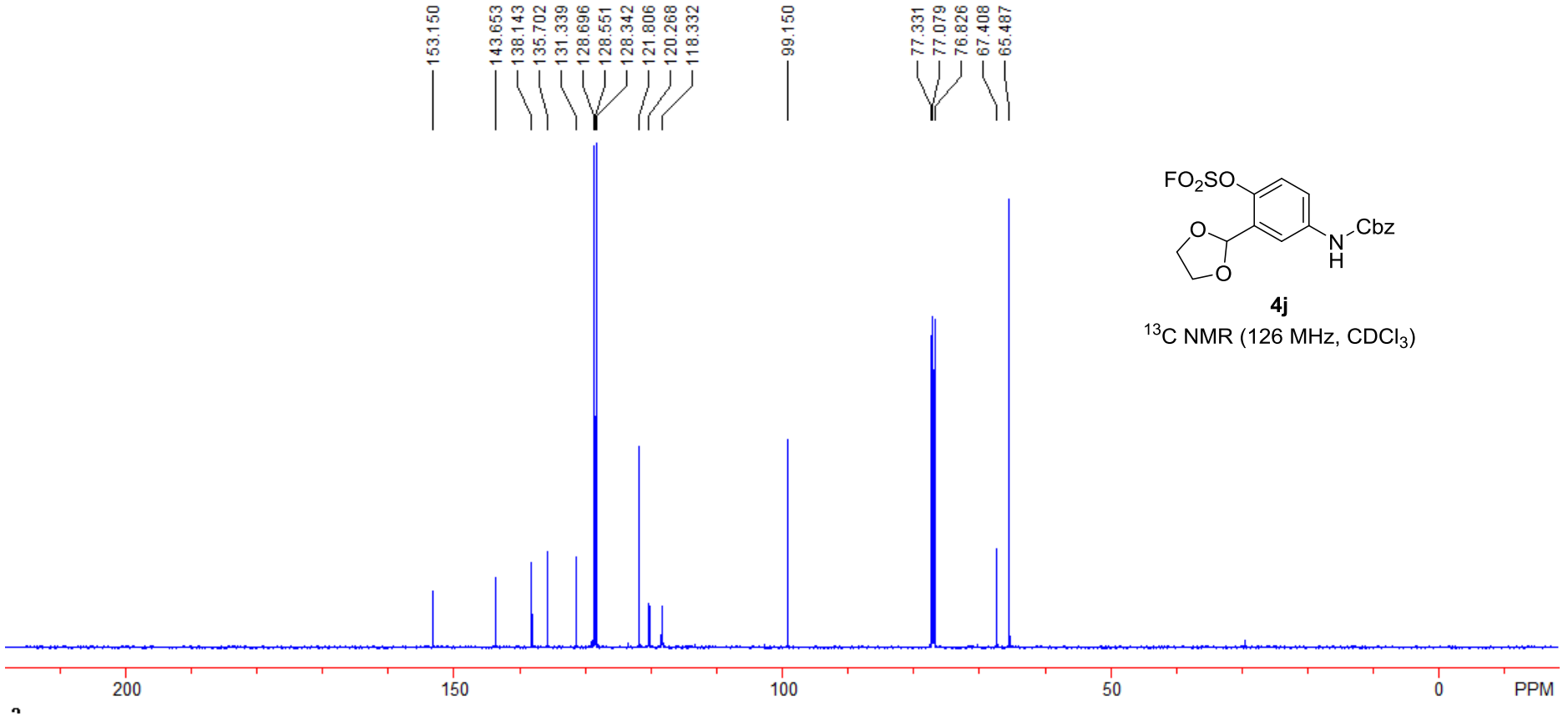
^{13}C NMR (500 MHz, $CDCl_3$)


7.619
7.532
7.516
7.386
7.377
7.363
7.356
7.347
7.294
7.276
7.264
7.048
6.008
5.203
4.113
4.099
4.085
4.065
4.055
4.035
4.029
4.021
4.007
FO2SO
O
O
N
H
Cbz
4j
1H NMR (500 MHz, CDCl3)
5.00
1.01
1.02
1.06
1.00
0.99
2.08
2.02
2.08
14
12
10
8
6
4
2
0
-2 PPM



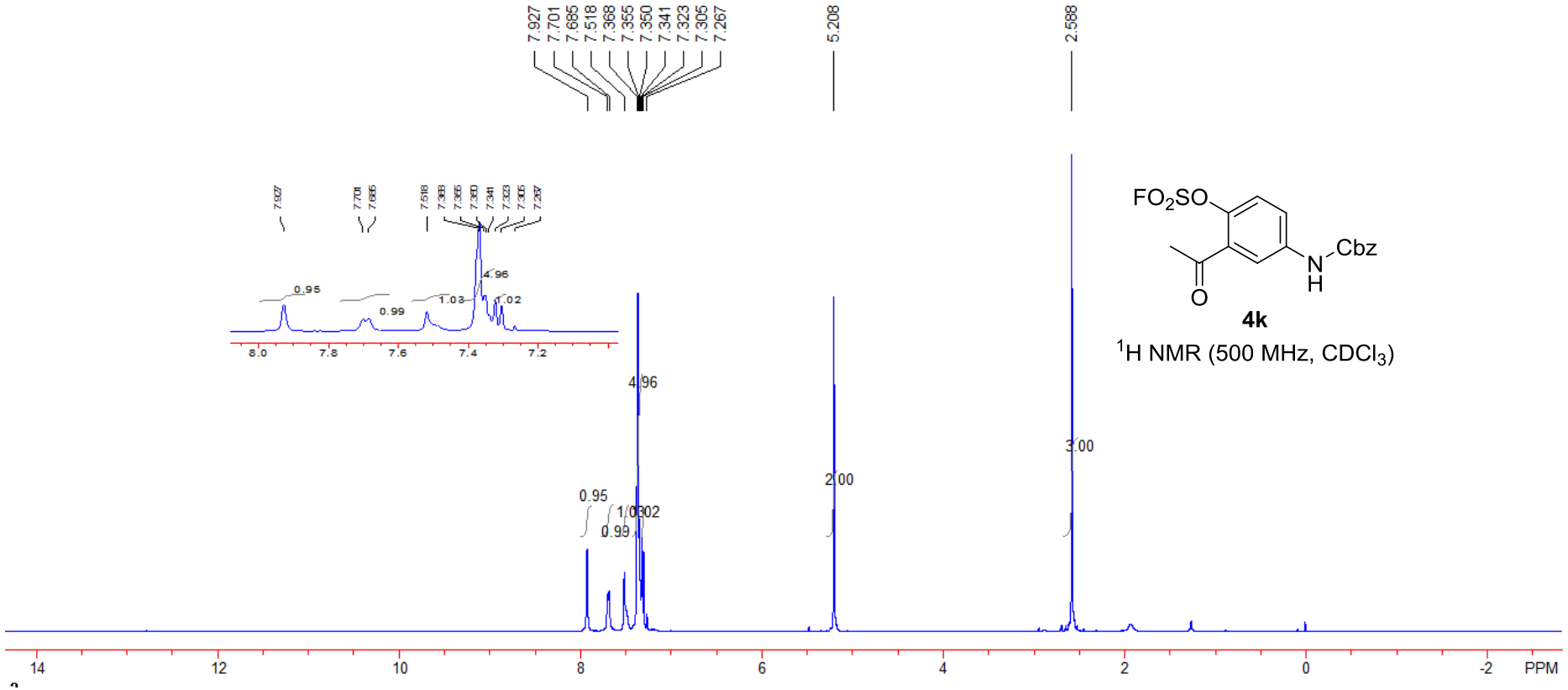
4j

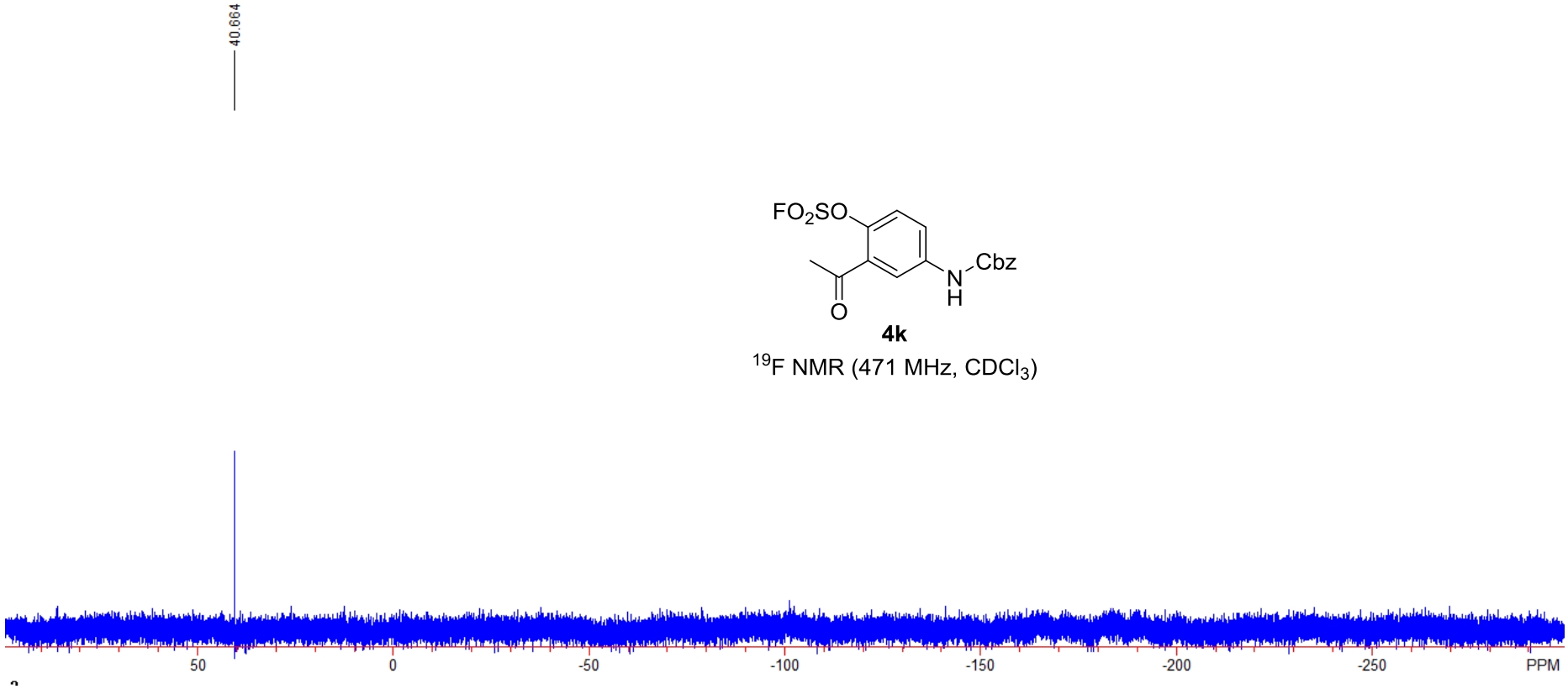
^{19}F NMR (471 MHz, $CDCl_3$)



4j

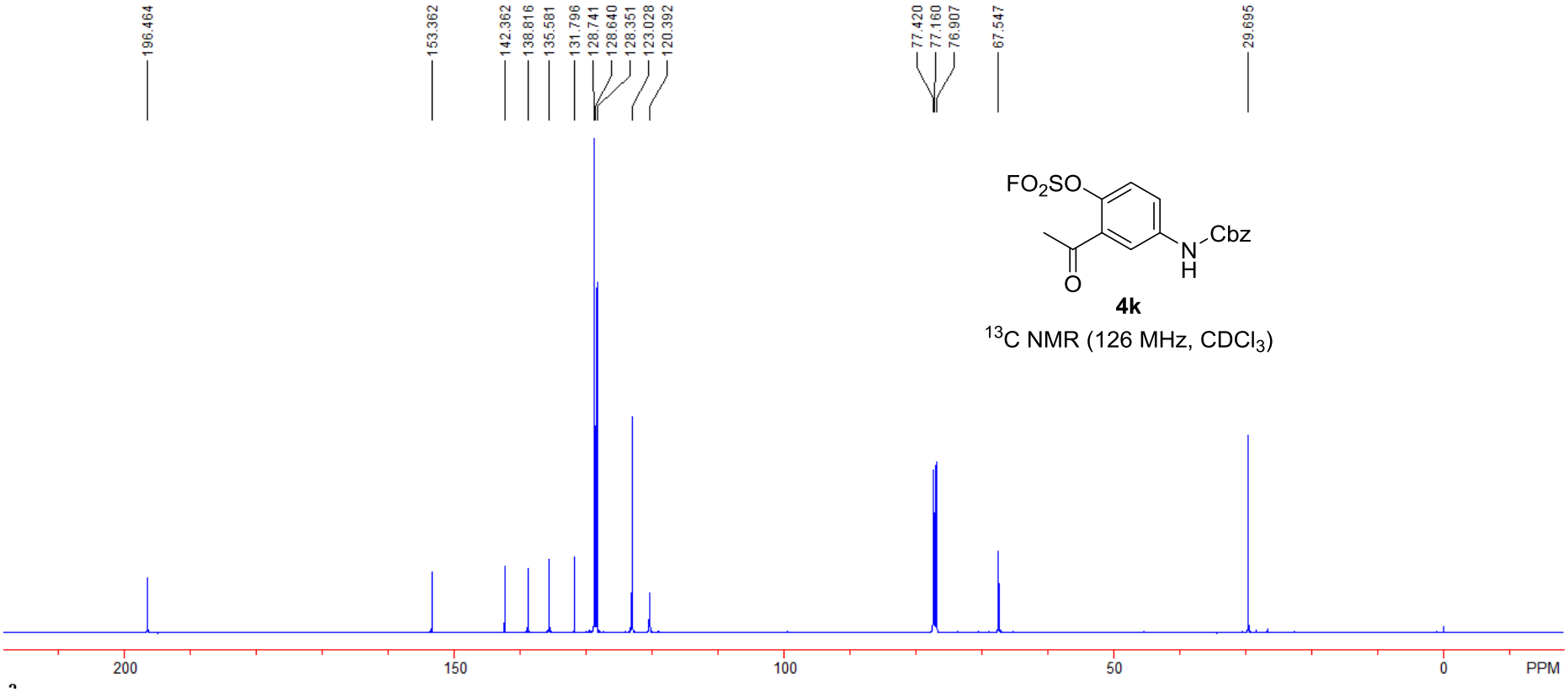
^{13}C NMR (126 MHz, $CDCl_3$)


7.927
7.701
7.685
7.518
7.368
7.355
7.350
7.341
7.323
7.305
7.267
5.208
2.588
4.96
2.00
3.00
0.95
1.02
0.99
FO2SO
Cbz
N
H
O
4k
1H NMR (500 MHz, CDCl3)
14
12
10
8
6
4
2
0
-2
PPM



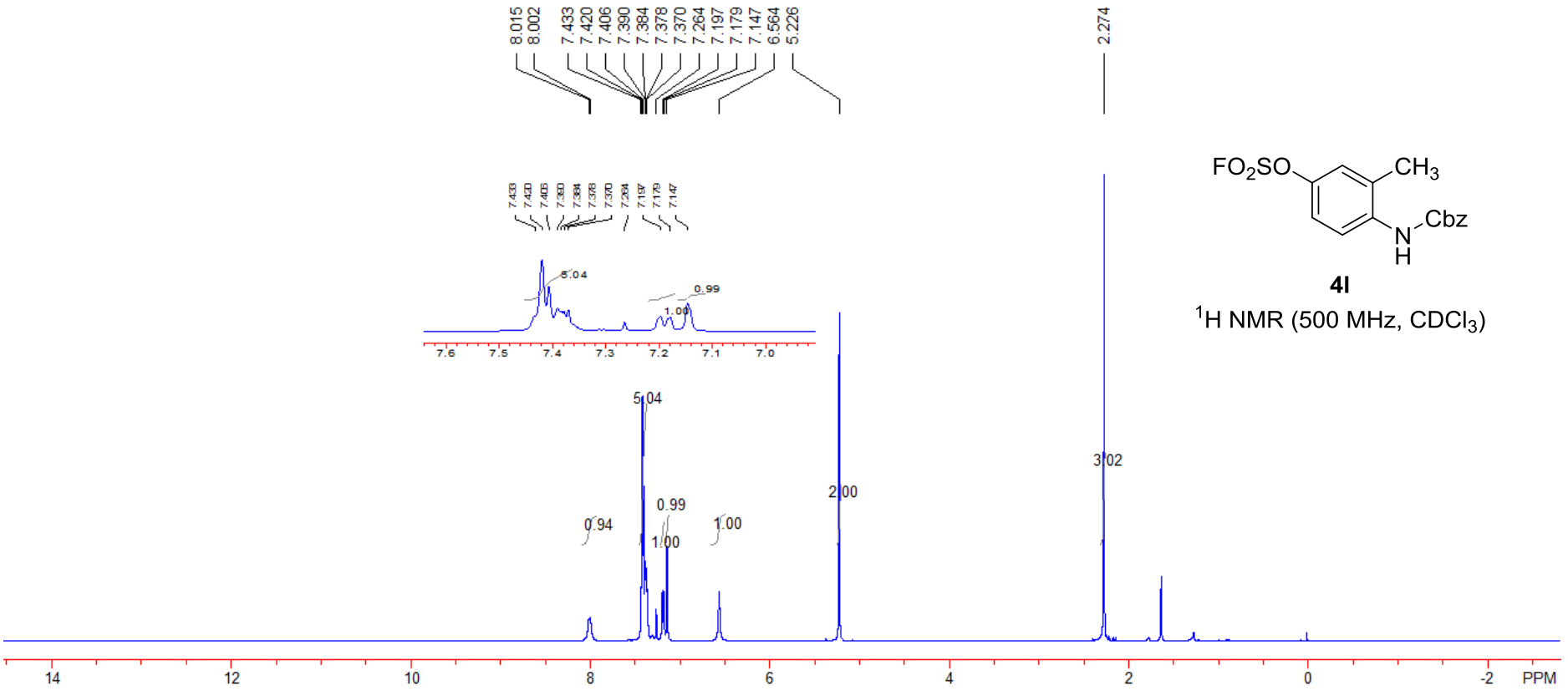
4k

^{19}F NMR (471 MHz, $CDCl_3$)



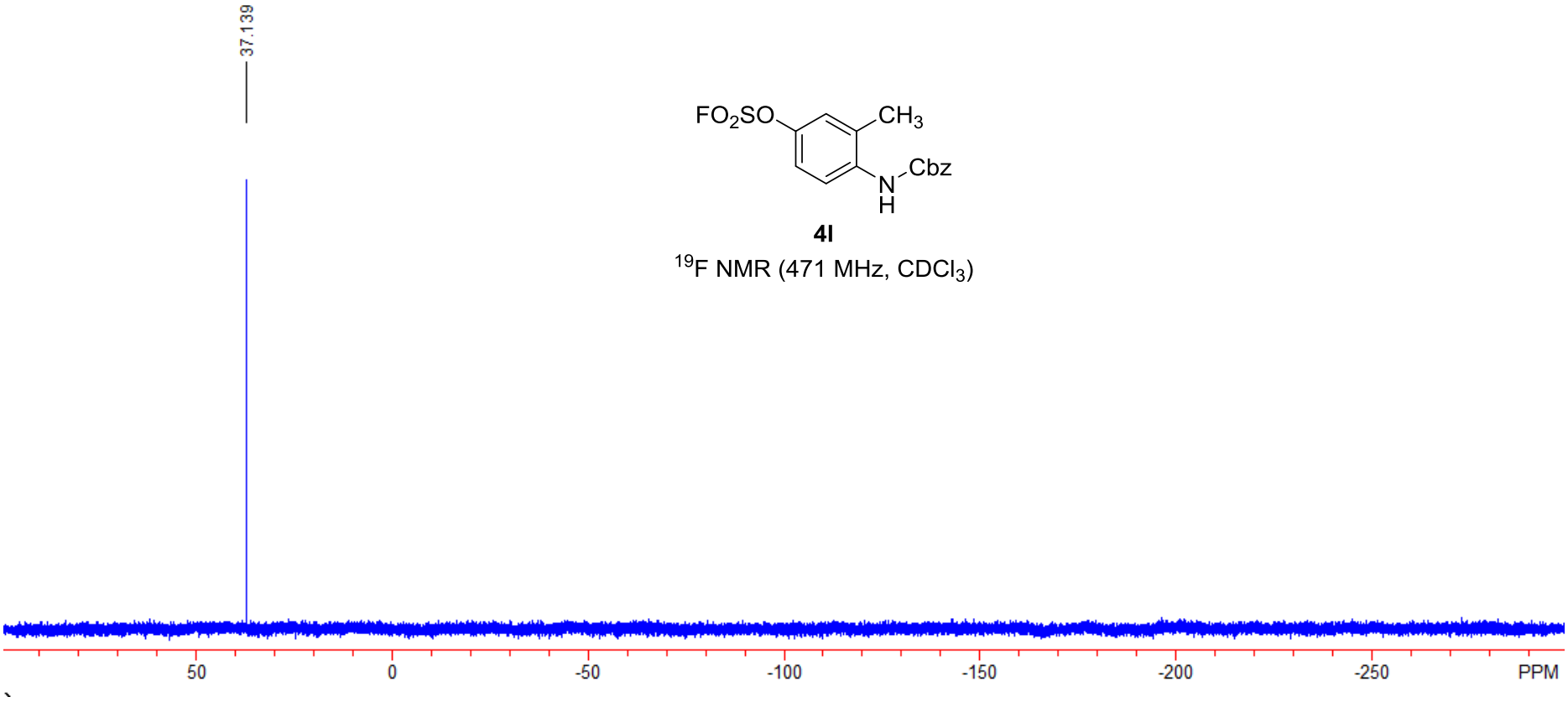
4k

^{13}C NMR (126 MHz, $CDCl_3$)



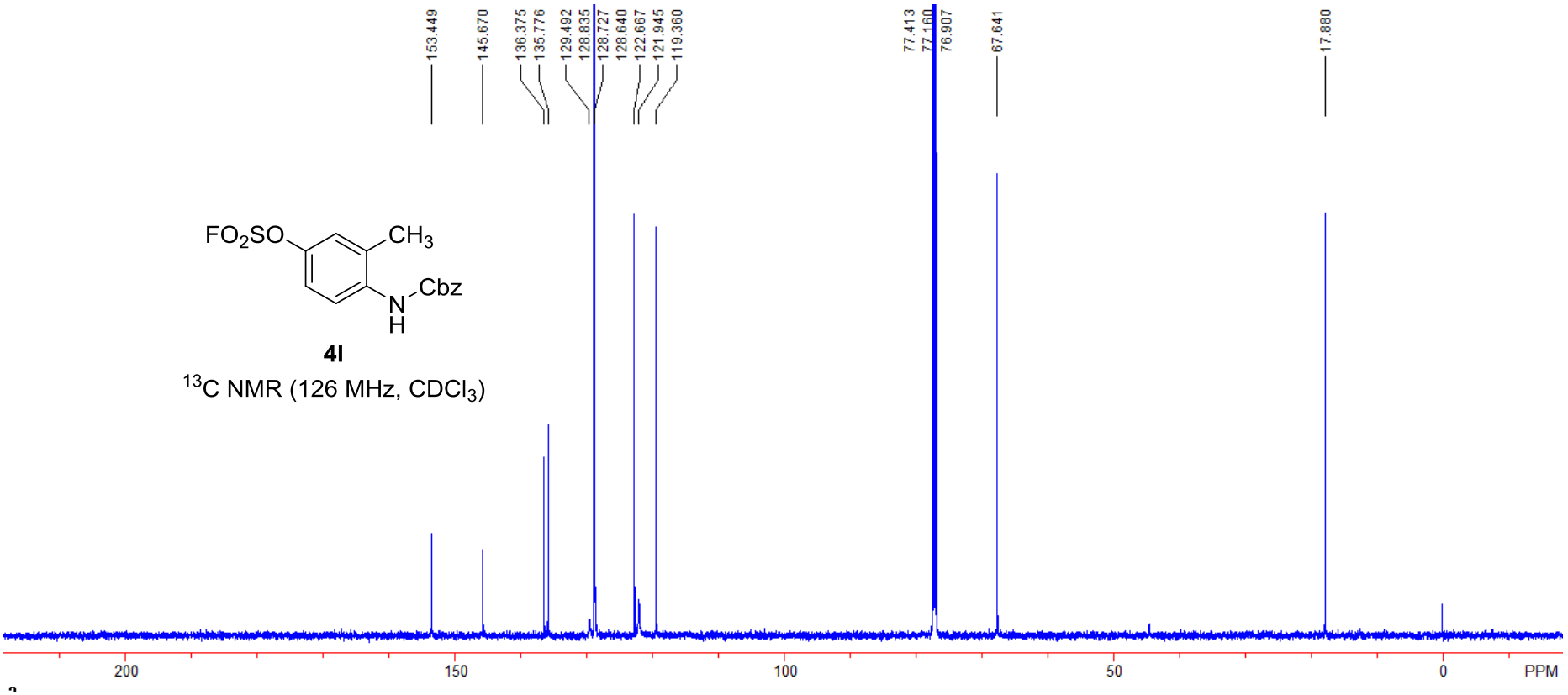
4l

^{1}H NMR (500 MHz, $CDCl_3$)



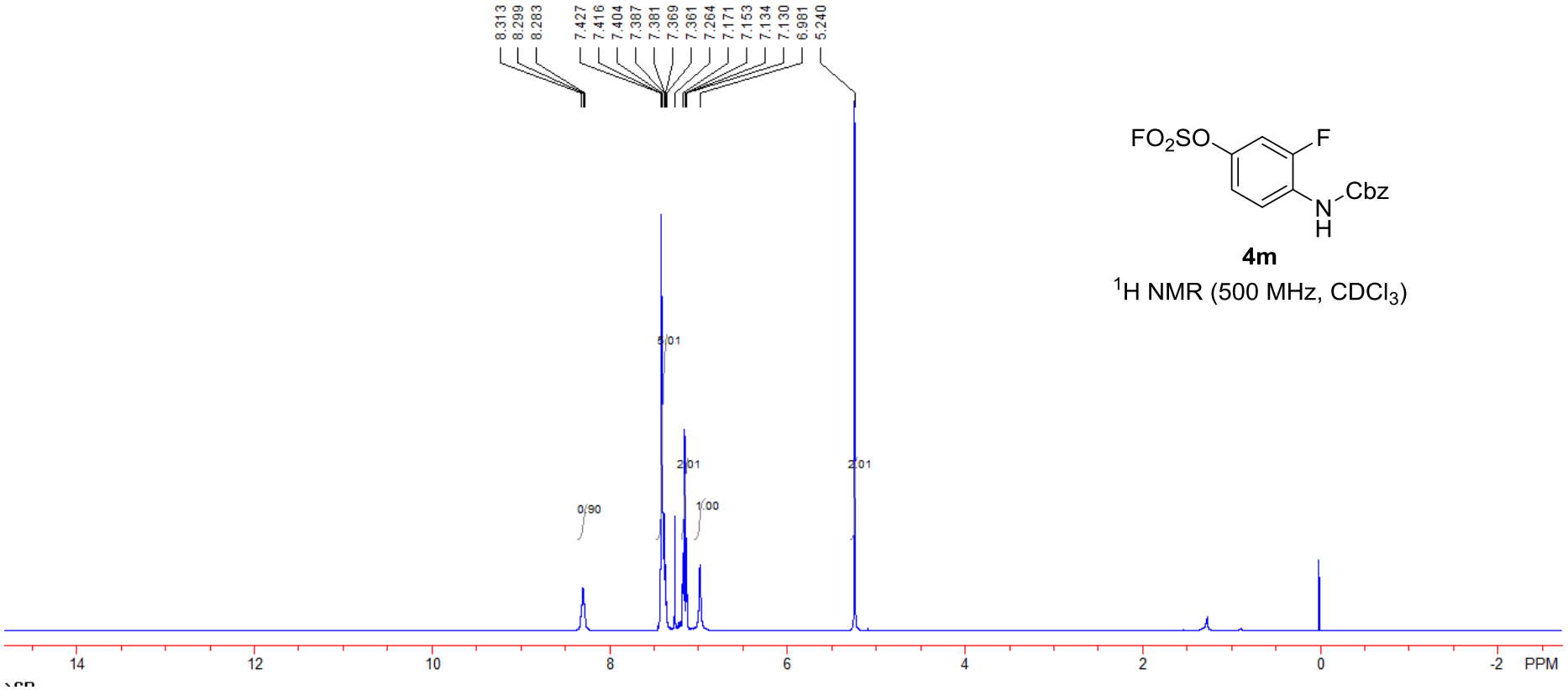
4l

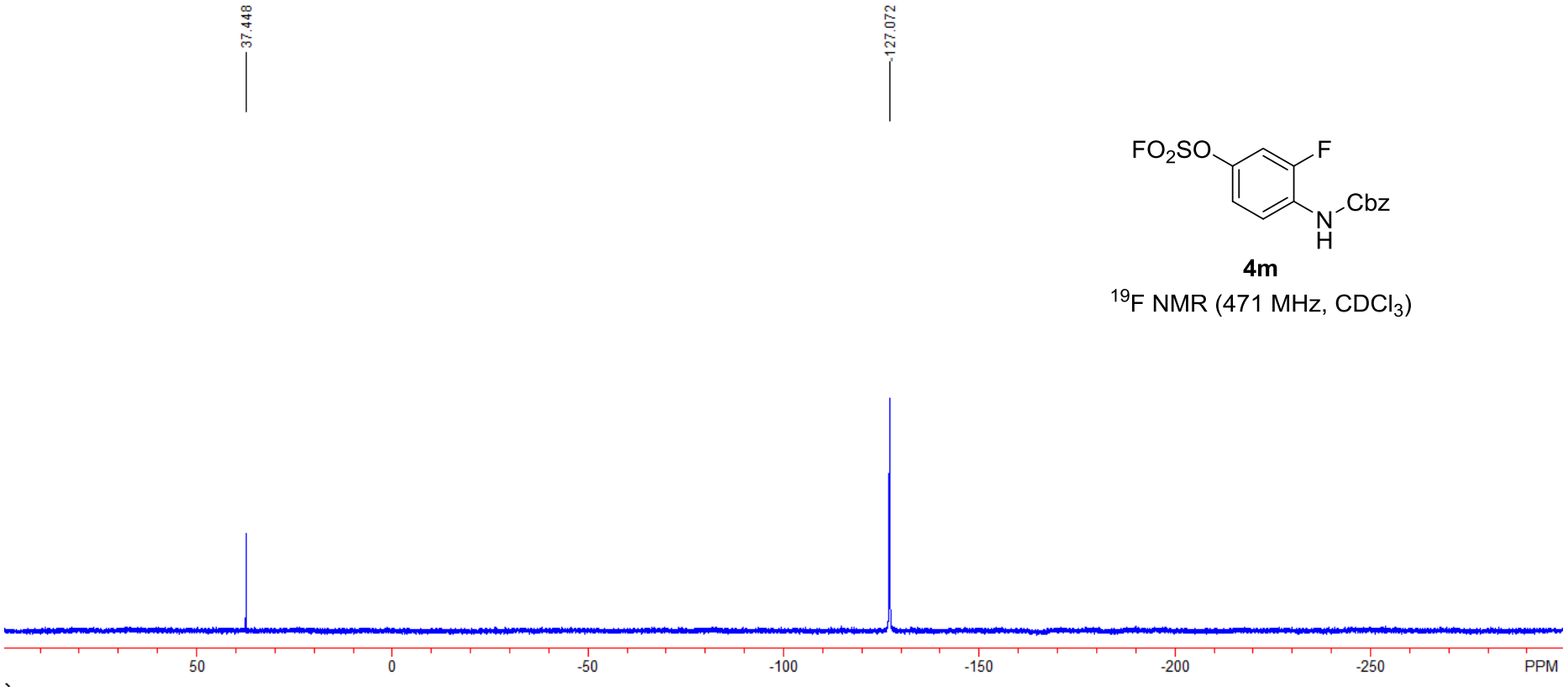
^{19}F NMR (471 MHz, $CDCl_3$)



4l

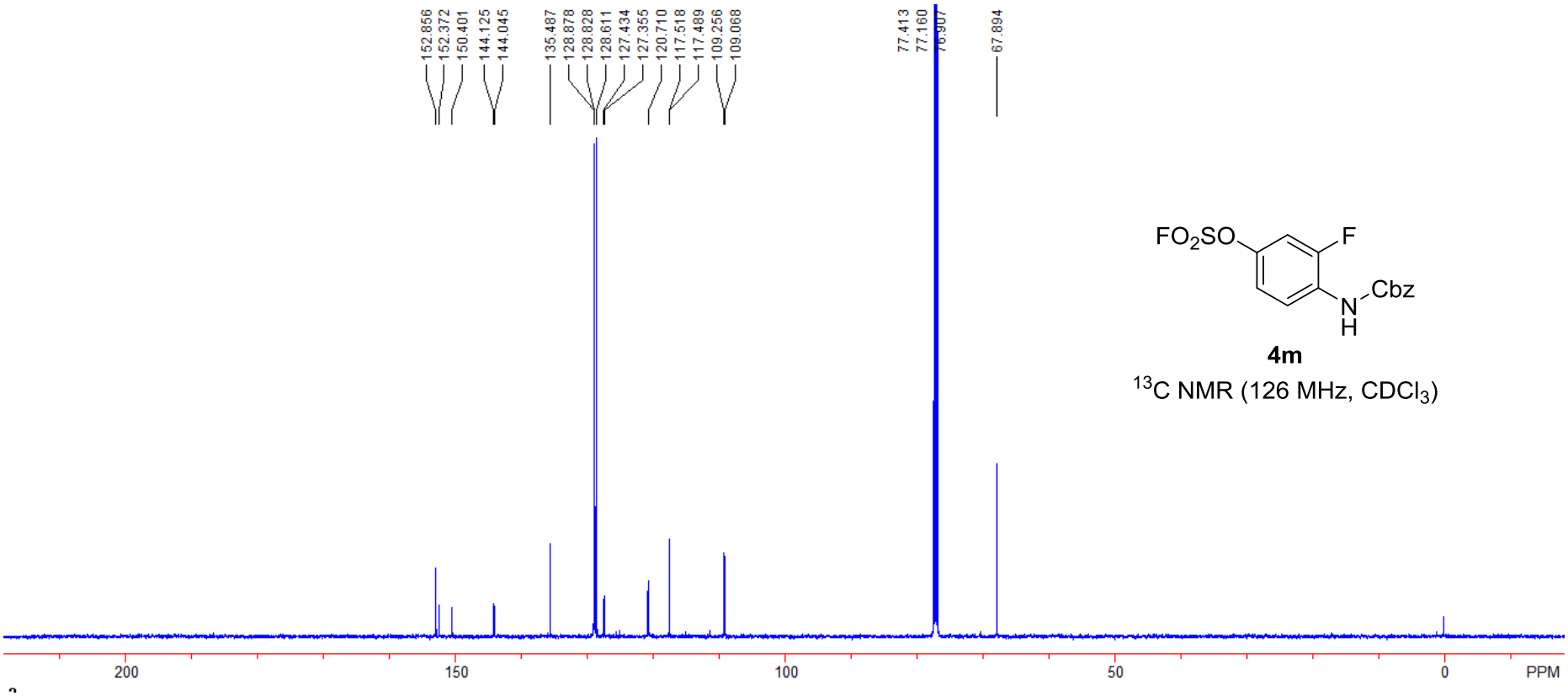
^{13}C NMR (126 MHz, $CDCl_3$)


8.313
8.299
8.283
7.427
7.416
7.404
7.387
7.381
7.369
7.361
7.264
7.171
7.153
7.134
7.130
6.981
5.240
5.01
2.01
2.01
0.90
1.00
14
12
10
8
6
4
2
0
-2
PPM
FO2SO
F
Cbz
N
H
4m
1H NMR (500 MHz, CDCl3)



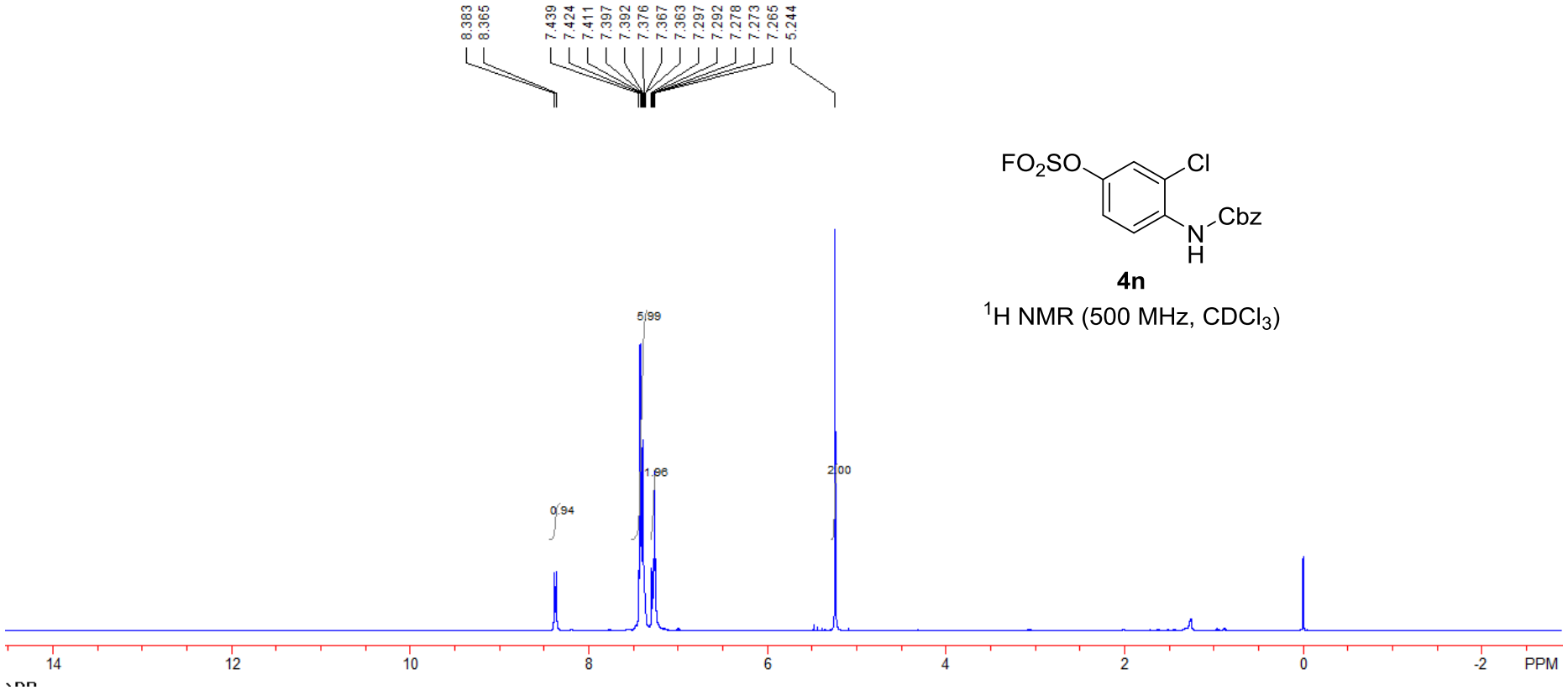
4m

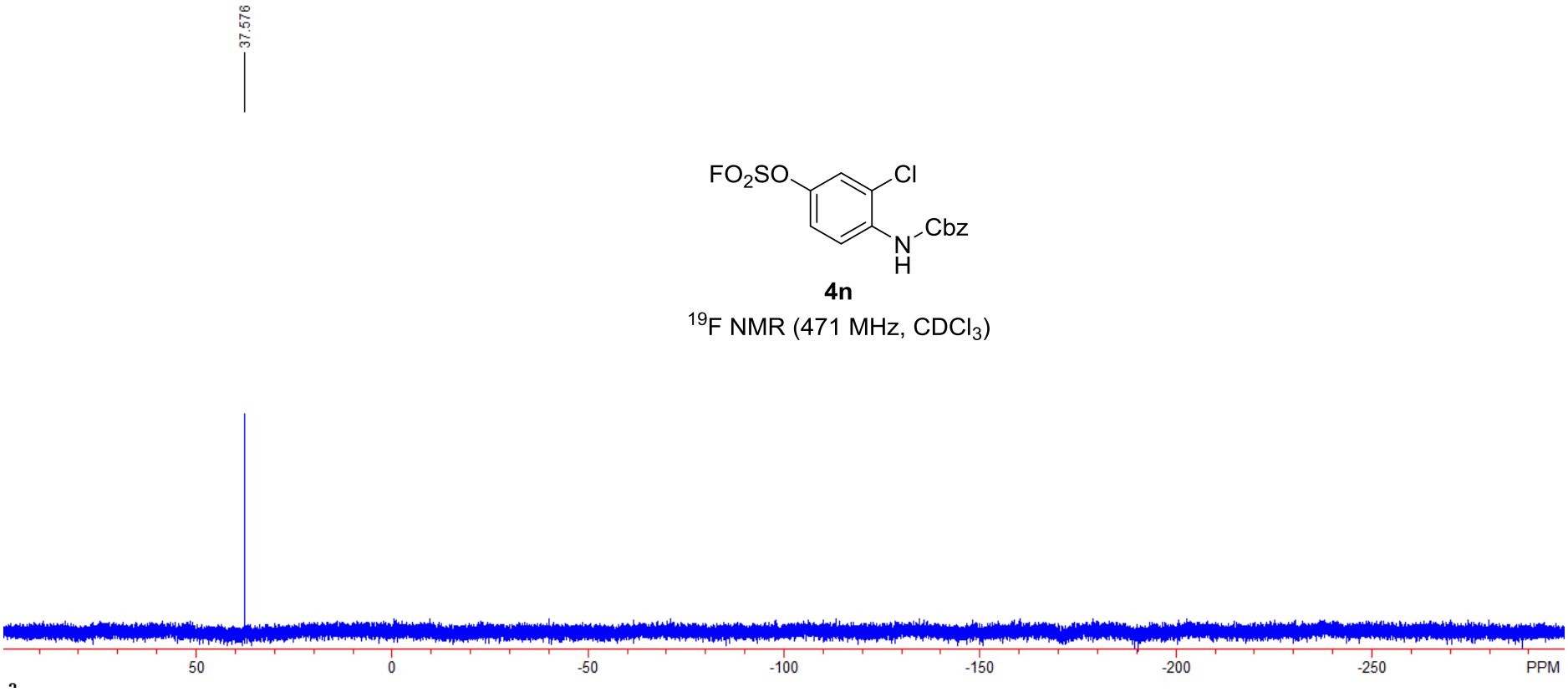
^{19}F NMR (471 MHz, $CDCl_3$)



4m

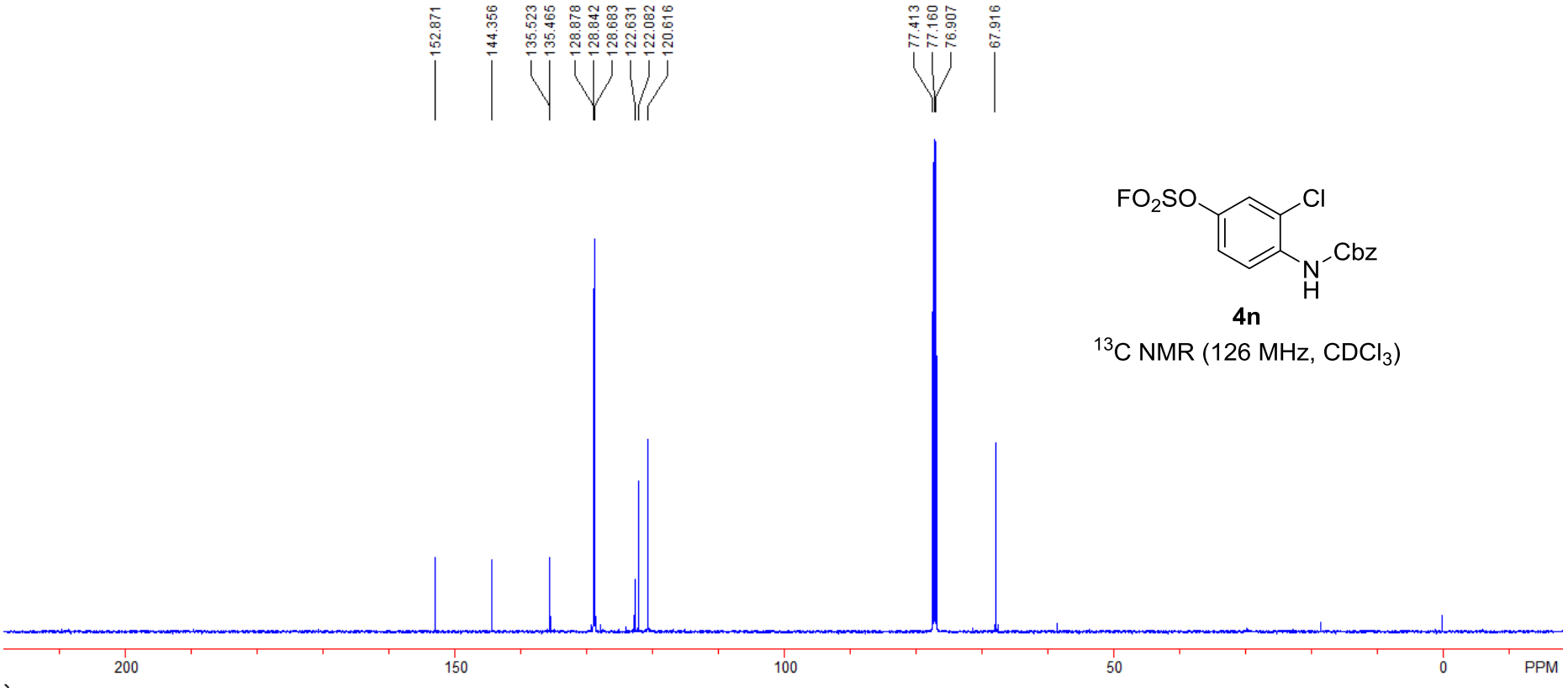
^{13}C NMR (126 MHz, $CDCl_3$)


8.383
8.365
7.439
7.424
7.411
7.397
7.392
7.376
7.367
7.363
7.297
7.292
7.278
7.273
7.265
5.244
FO2SO
Cl
N
H
Cbz
4n
1H NMR (500 MHz, CDCl3)
5.99
1.96
2.00
0.94
14
12
10
8
6
4
2
0
-2
PPM



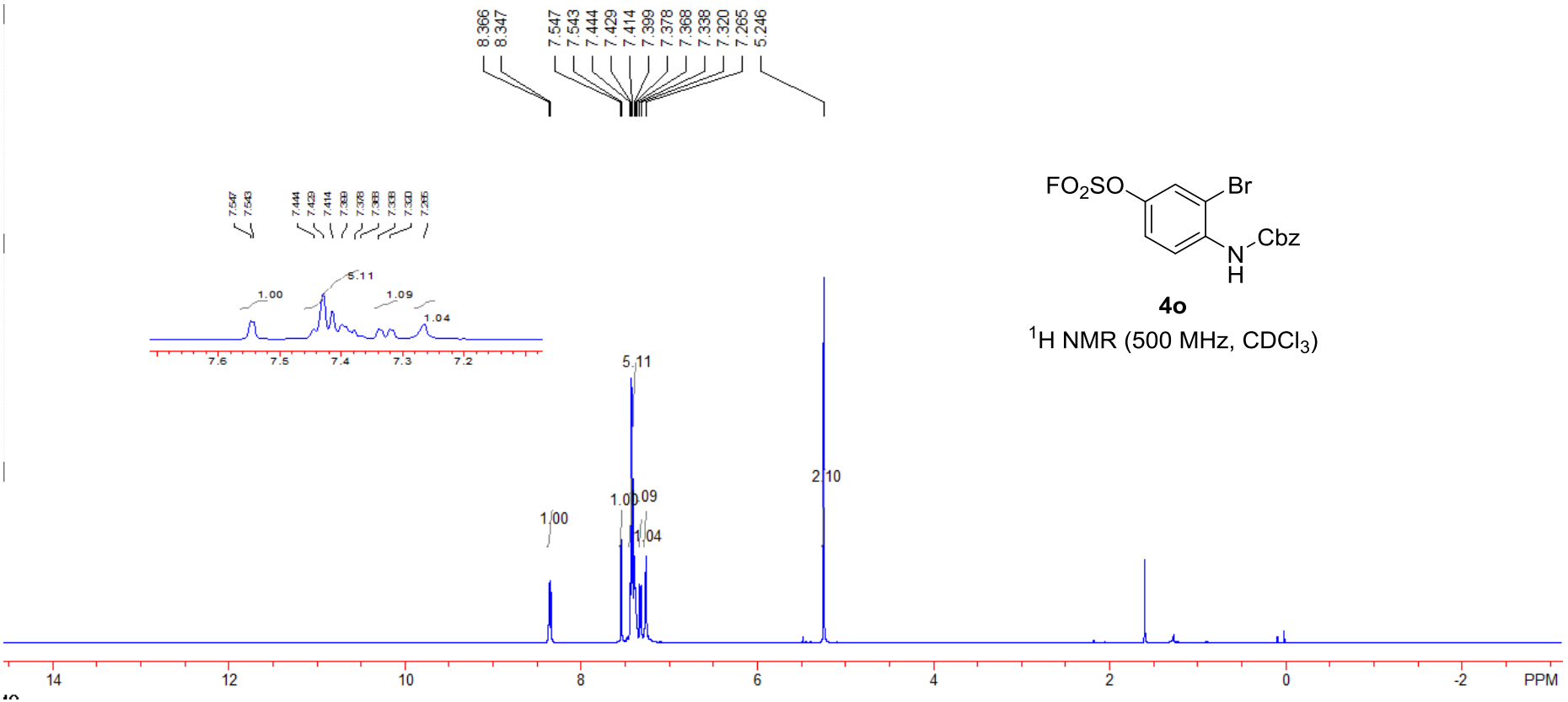
4n

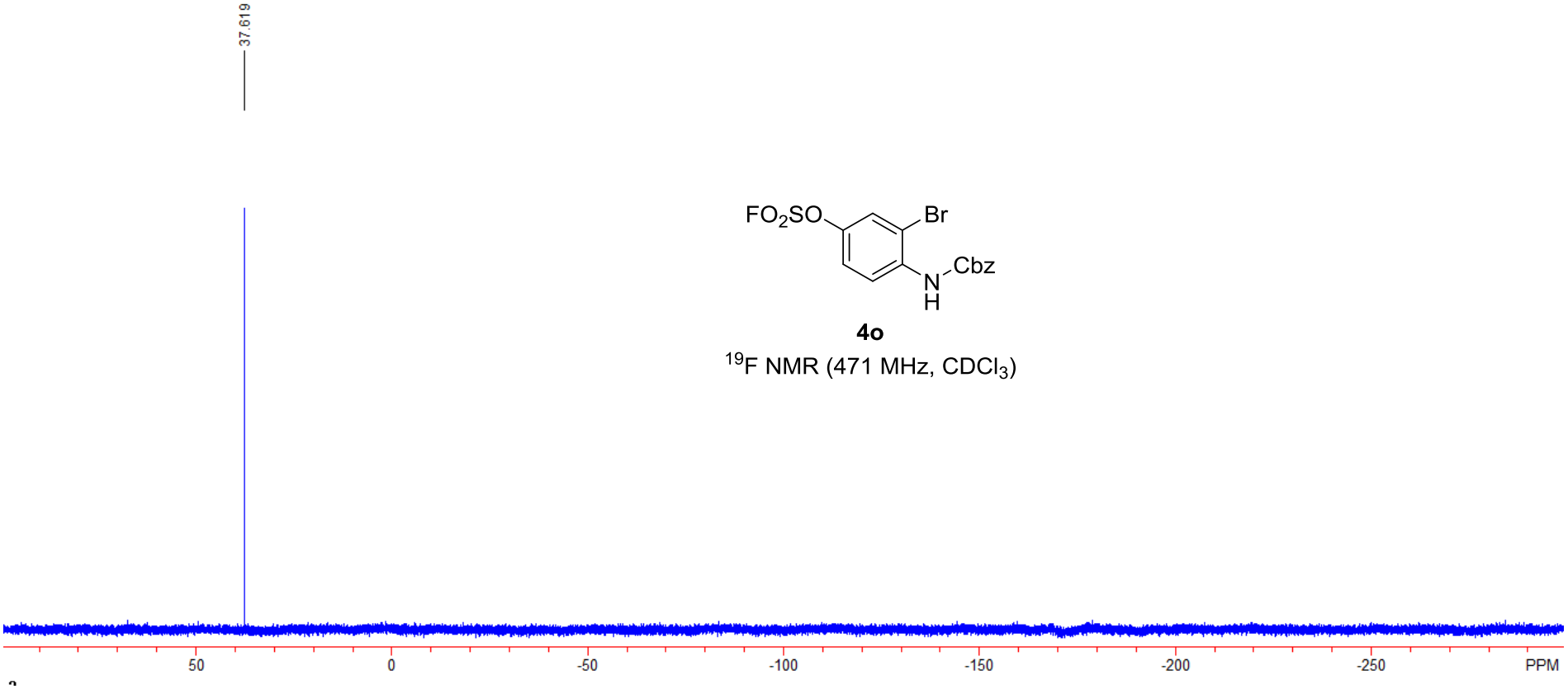
^{19}F NMR (471 MHz, $CDCl_3$)



4n

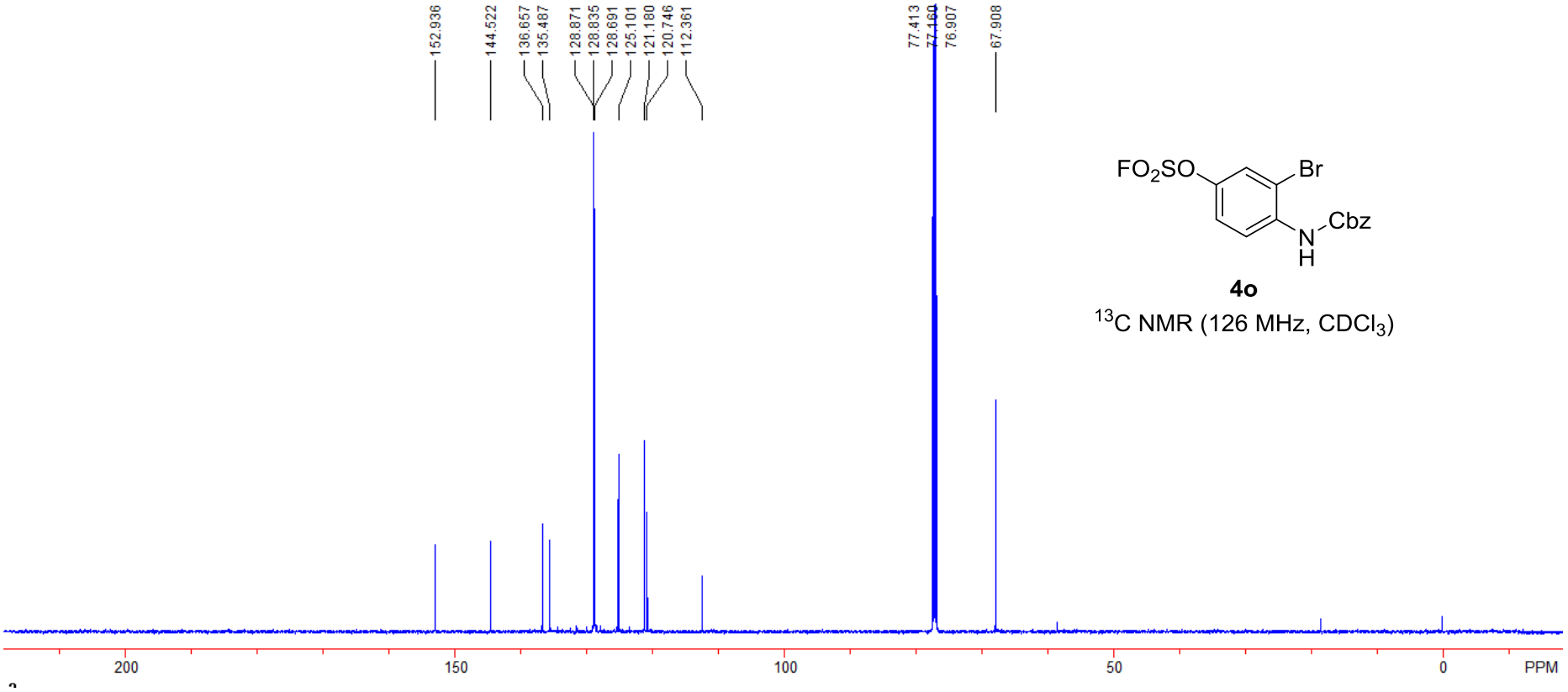
^{13}C NMR (126 MHz, $CDCl_3$)


8.366
8.347
7.547
7.543
7.444
7.429
7.414
7.399
7.378
7.368
7.338
7.320
7.265
5.246
1.00
5.11
1.09
1.04
7.6
7.5
7.4
7.3
7.2
FO2SO
Br
Cbz
N
H
4o
1H NMR (500 MHz, CDCl3)
2.10
14
12
10
8
6
4
2
0
-2
PPM



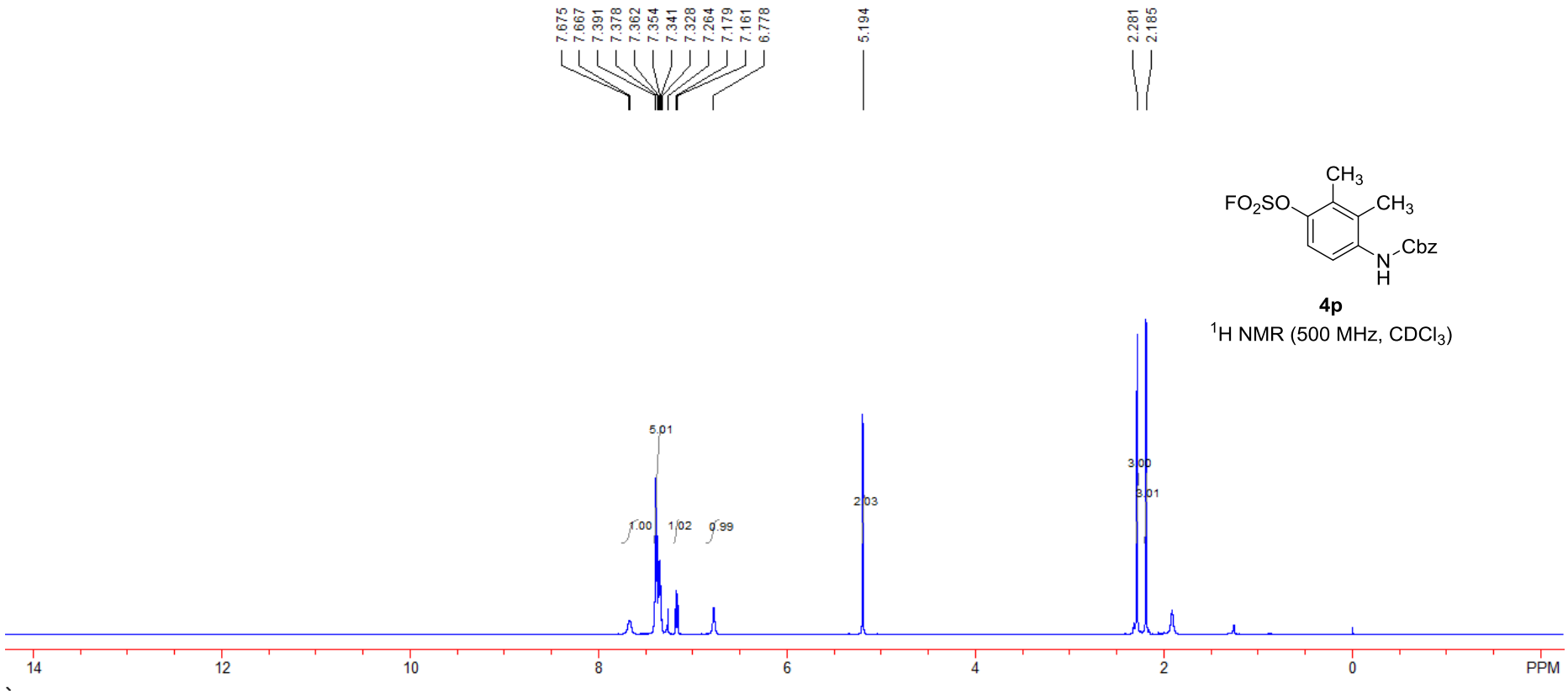
4o

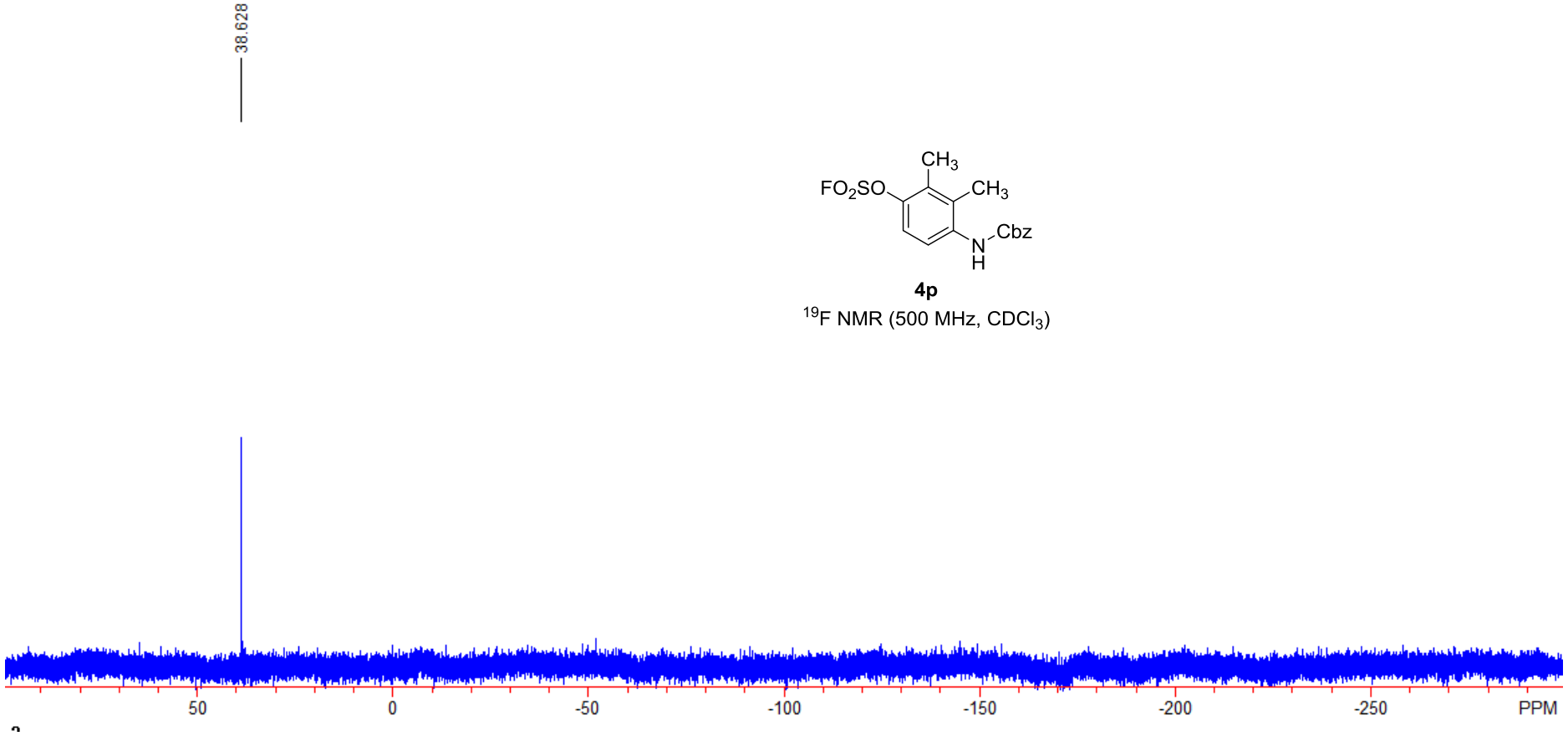
^{19}F NMR (471 MHz, $CDCl_3$)



4o

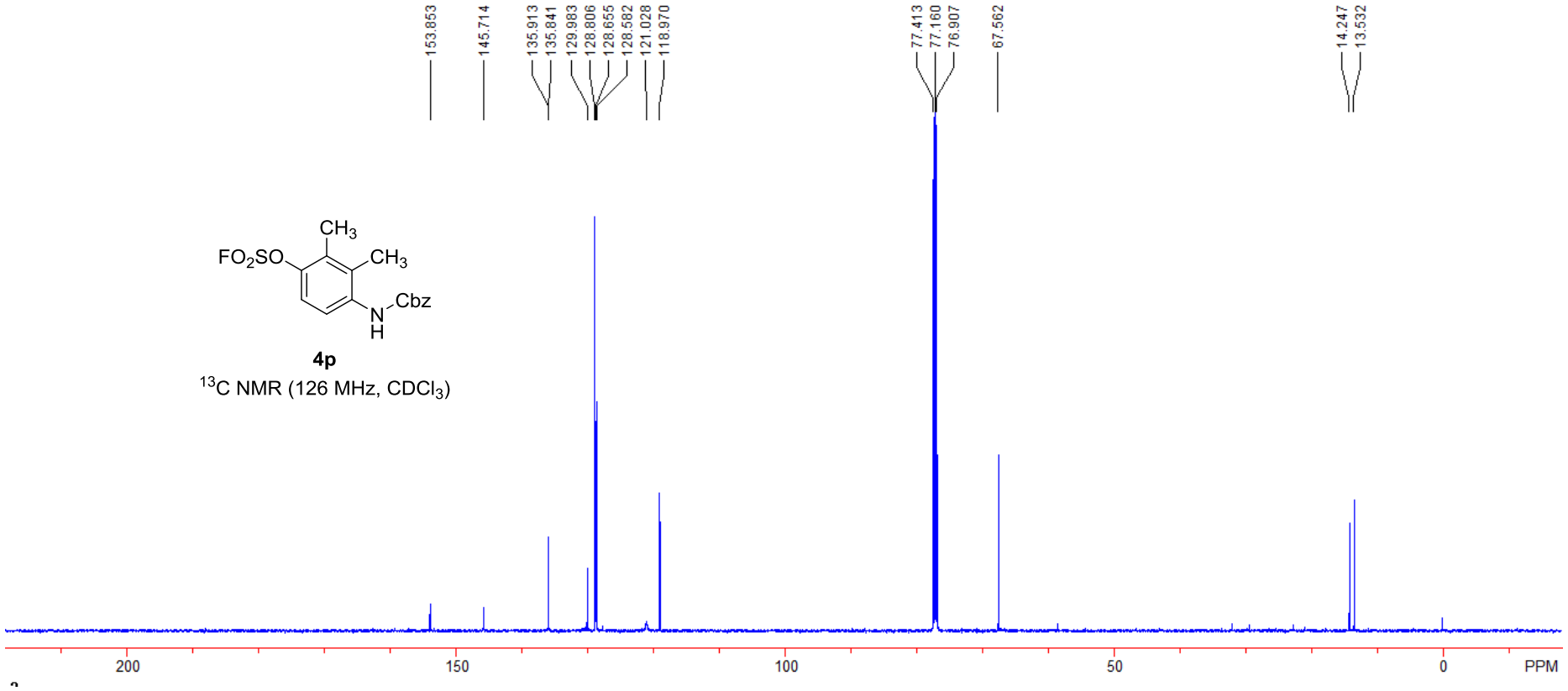
^{13}C NMR (126 MHz, $CDCl_3$)


7.675
7.667
7.391
7.378
7.362
7.354
7.341
7.328
7.264
7.179
7.161
6.778
5.194
2.281
2.185
CH3
FO2SO
CH3
N
H
Cbz
4p
1H NMR (500 MHz, CDCl3)
5.01
1.00
1.02
0.99
2.03
3.00
3.01
14
12
10
8
6
4
2
0
PPM



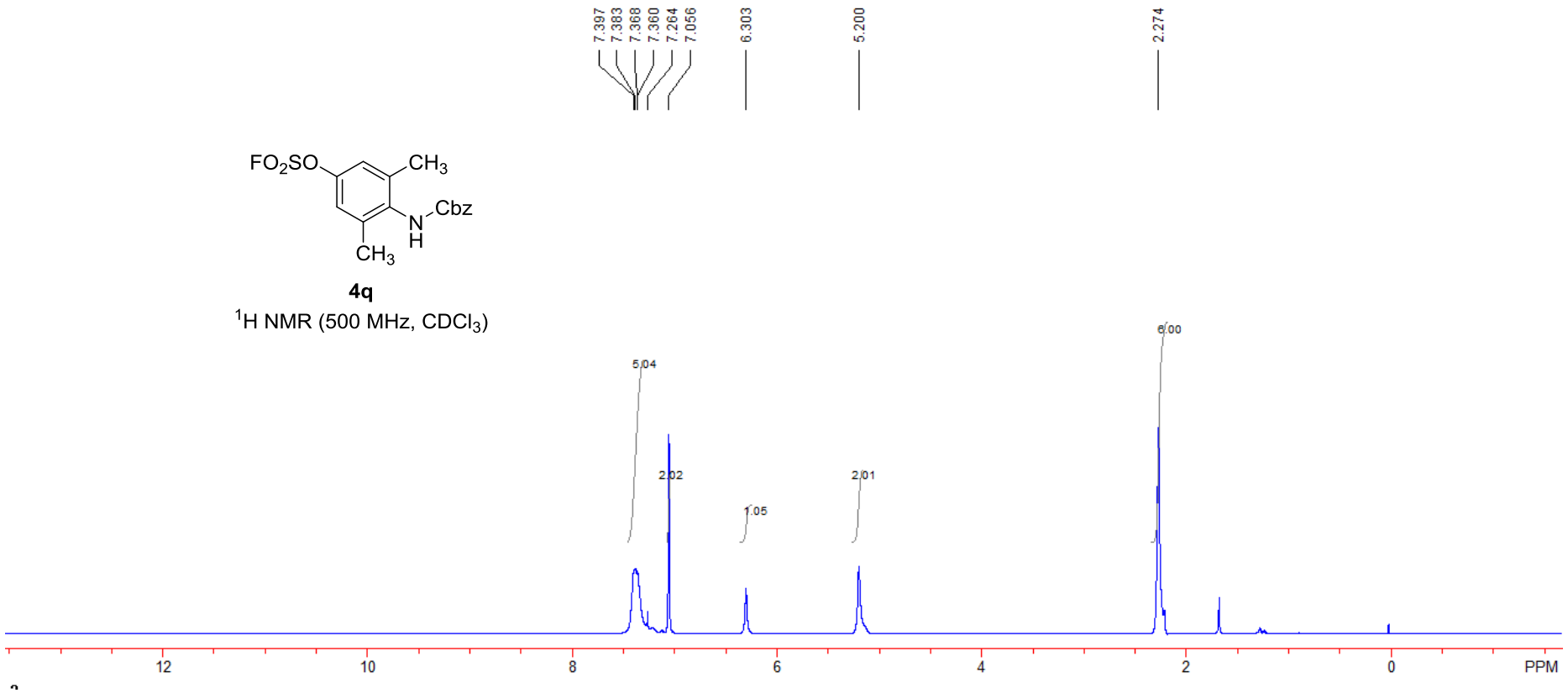
4p

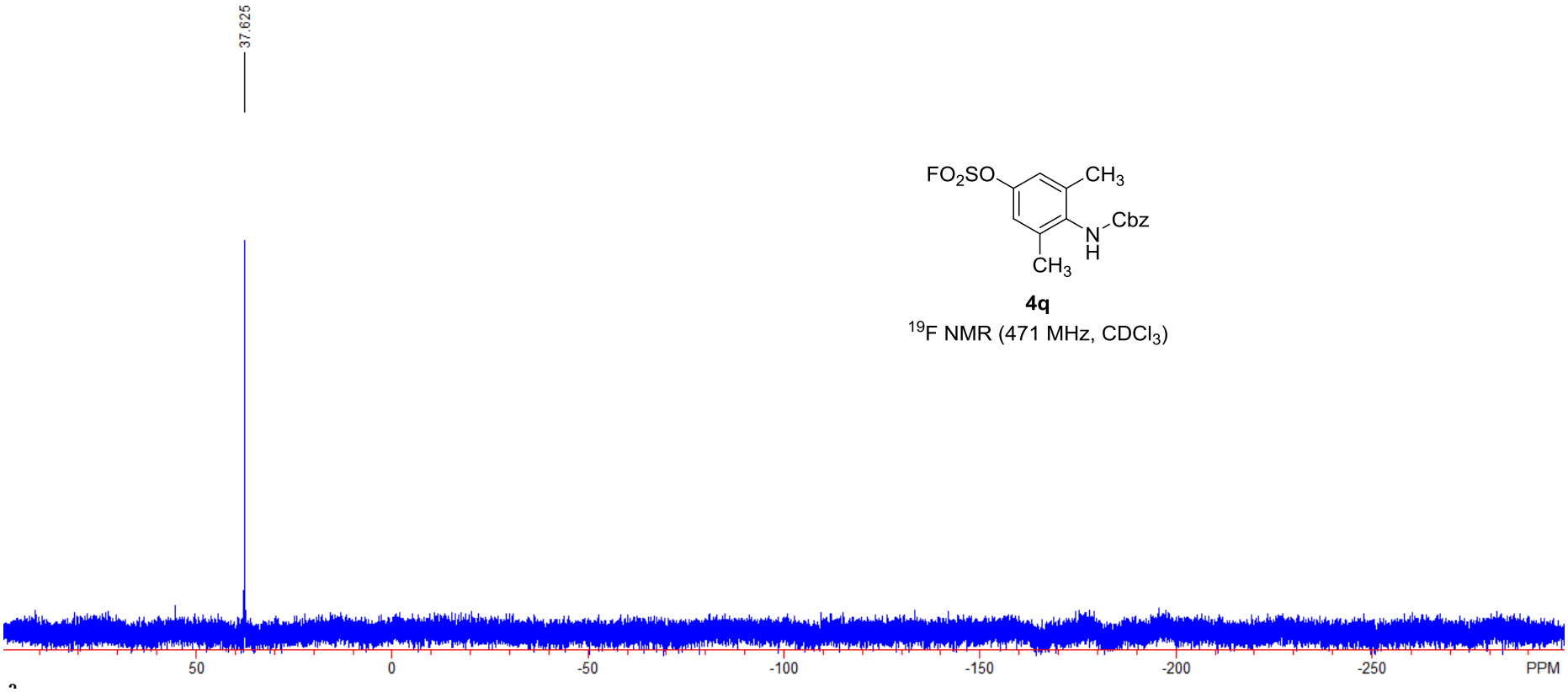
^{19}F NMR (500 MHz, $CDCl_3$)



4p

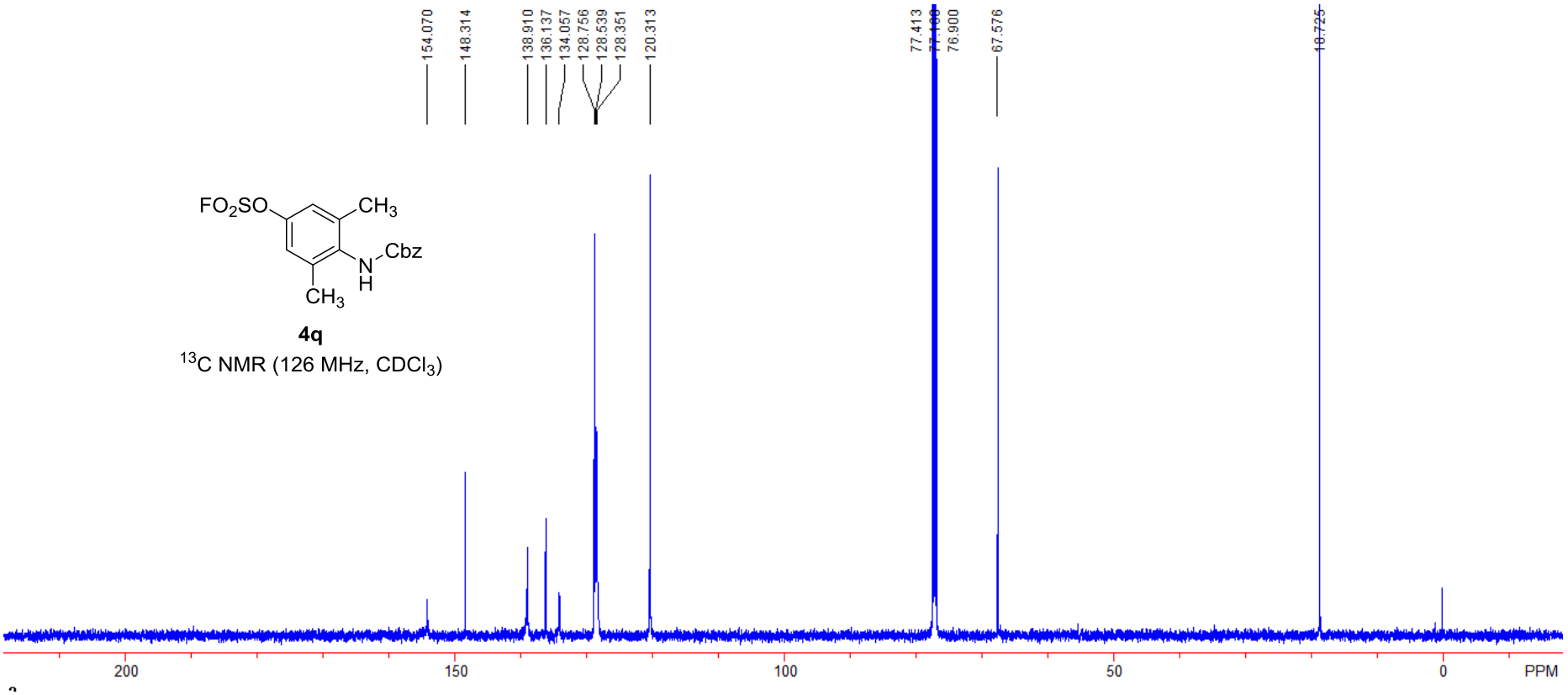
^{13}C NMR (126 MHz, $CDCl_3$)


7.397
7.383
7.368
7.360
7.264
7.056
6.303
5.200
2.274
FO2SO
CH3
Cbz
N
H
CH3
4q
1H NMR (500 MHz, CDCl3)
5.04
2.02
1.05
2.01
6.00
12
10
8
6
4
2
0
PPM



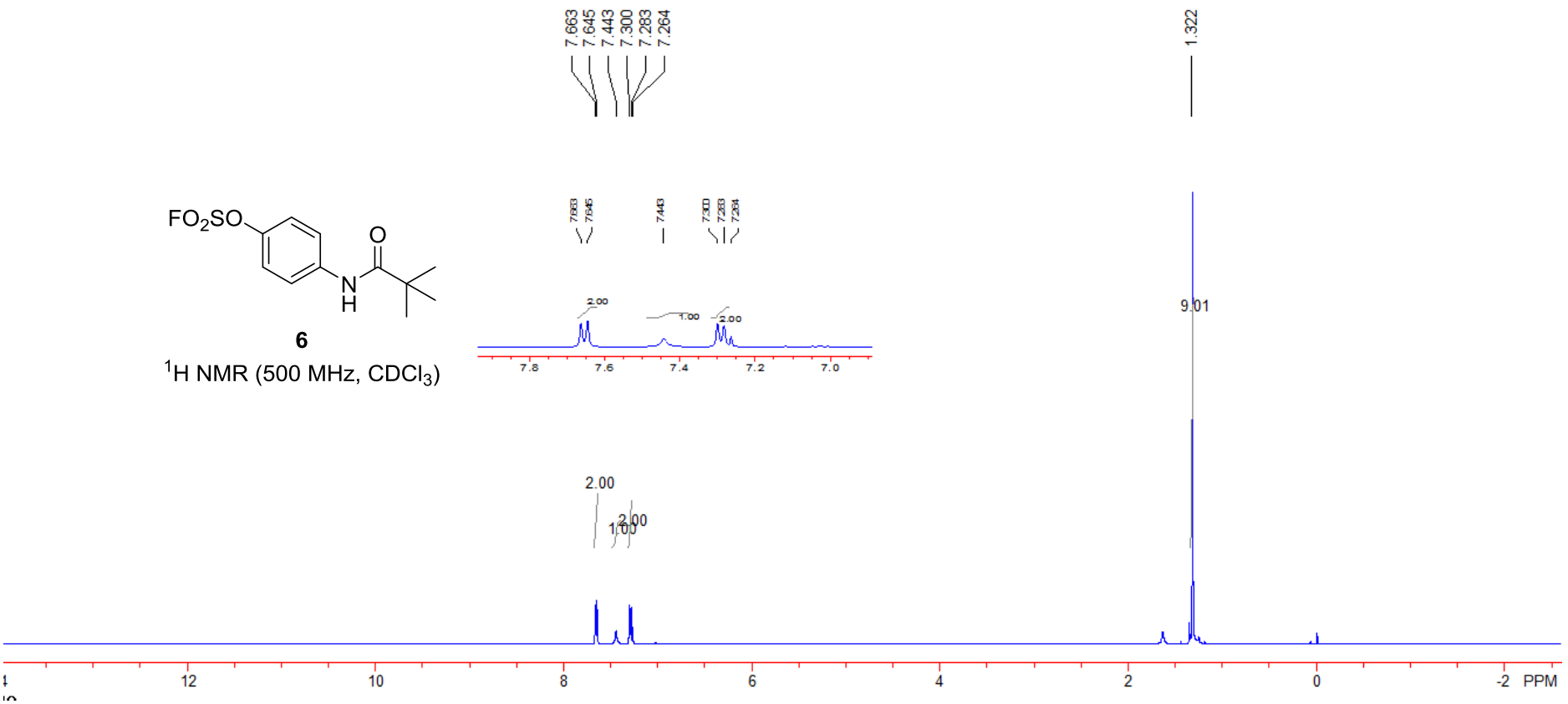
4q

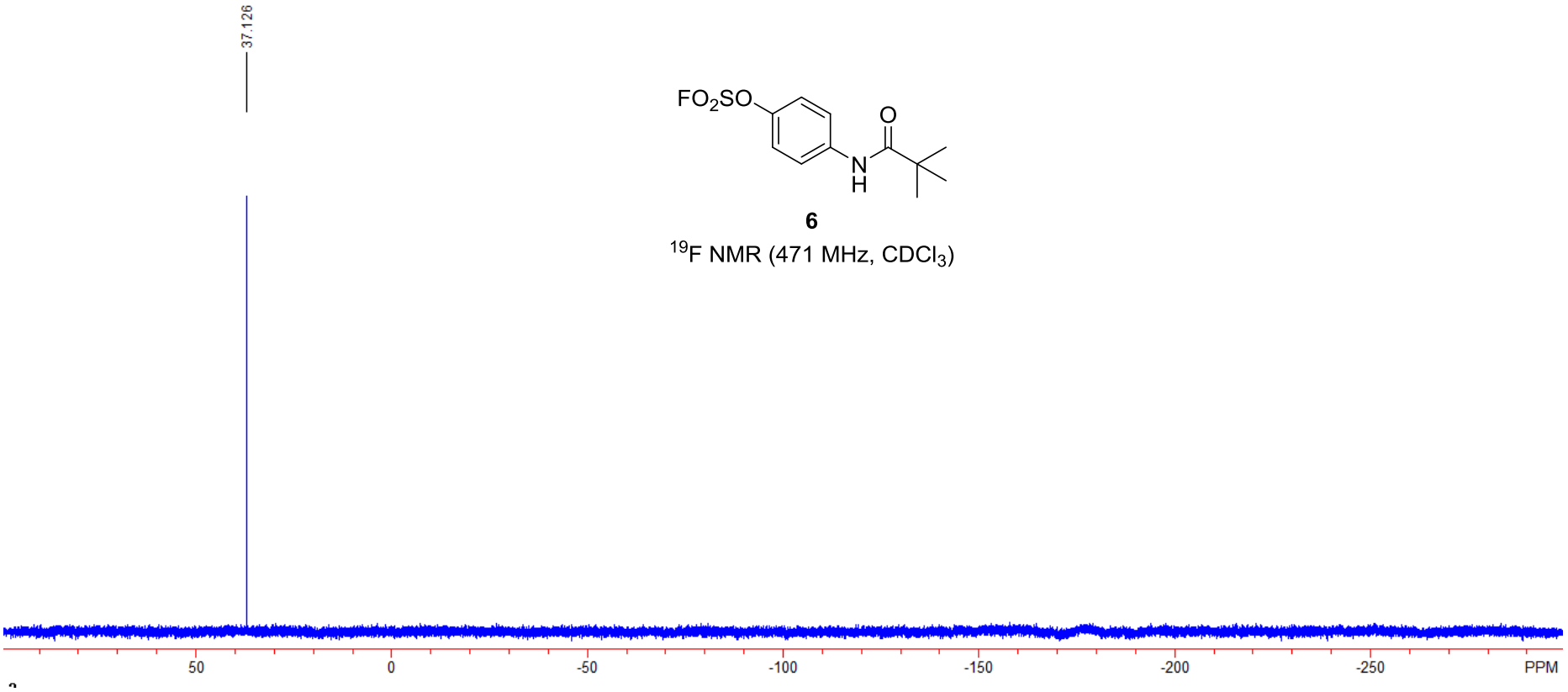
^{19}F NMR (471 MHz, $CDCl_3$)



4q

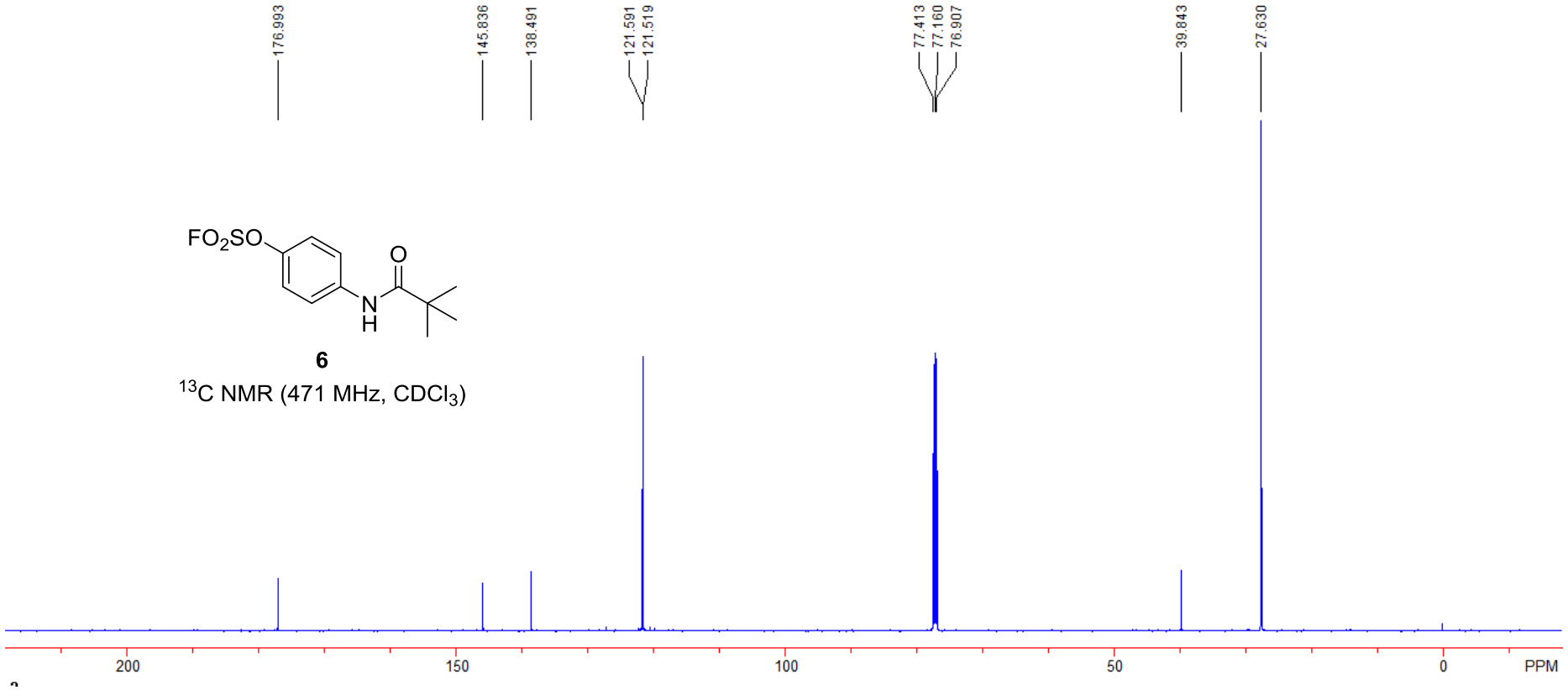
^{13}C NMR (126 MHz, $CDCl_3$)


FO2SO
O
N
H
6
1H NMR (500 MHz, CDCl3)
7.663
7.645
7.443
7.300
7.283
7.264
1.322
9.01
2.00
1.00
2.00
2.00
1.00
2.00
12
10
8
6
4
2
0
-2
PPM



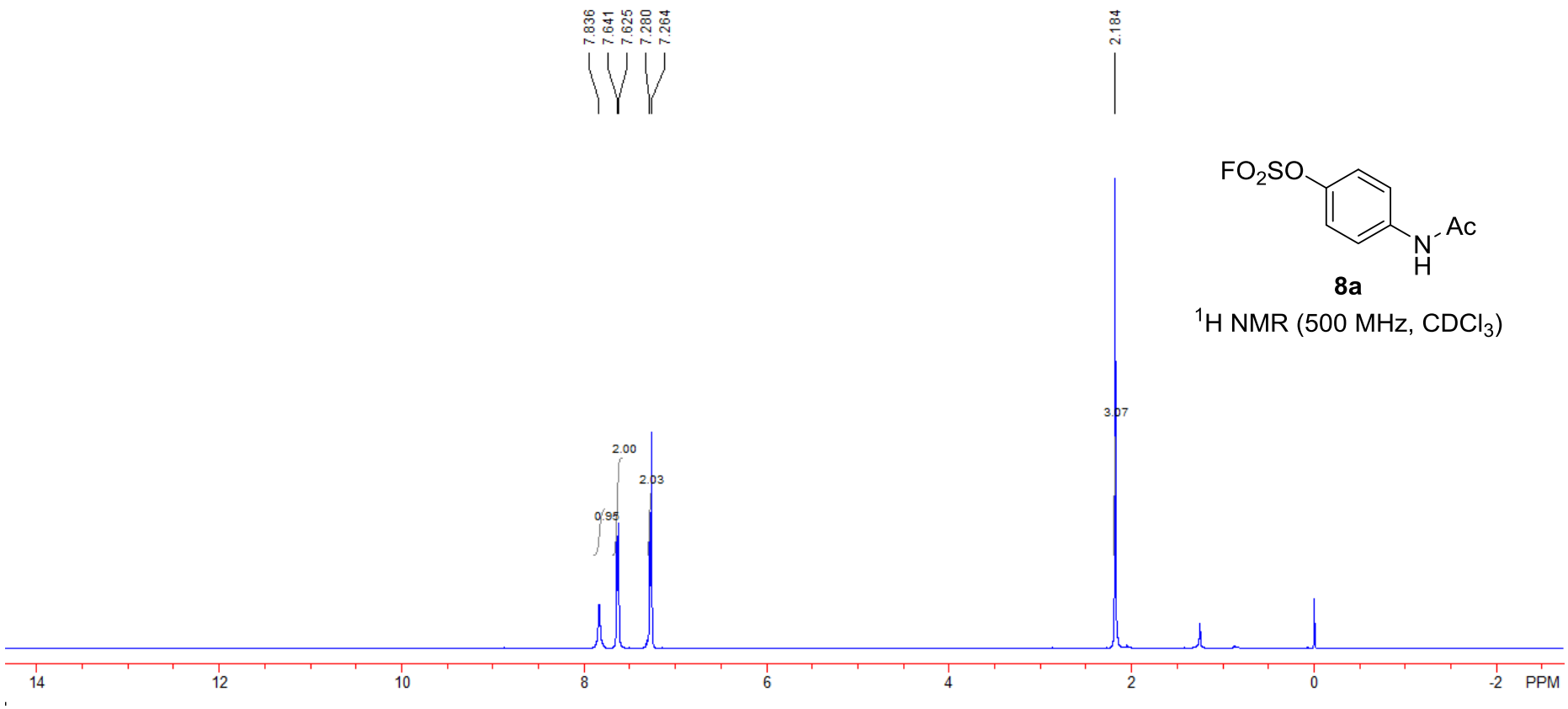
6

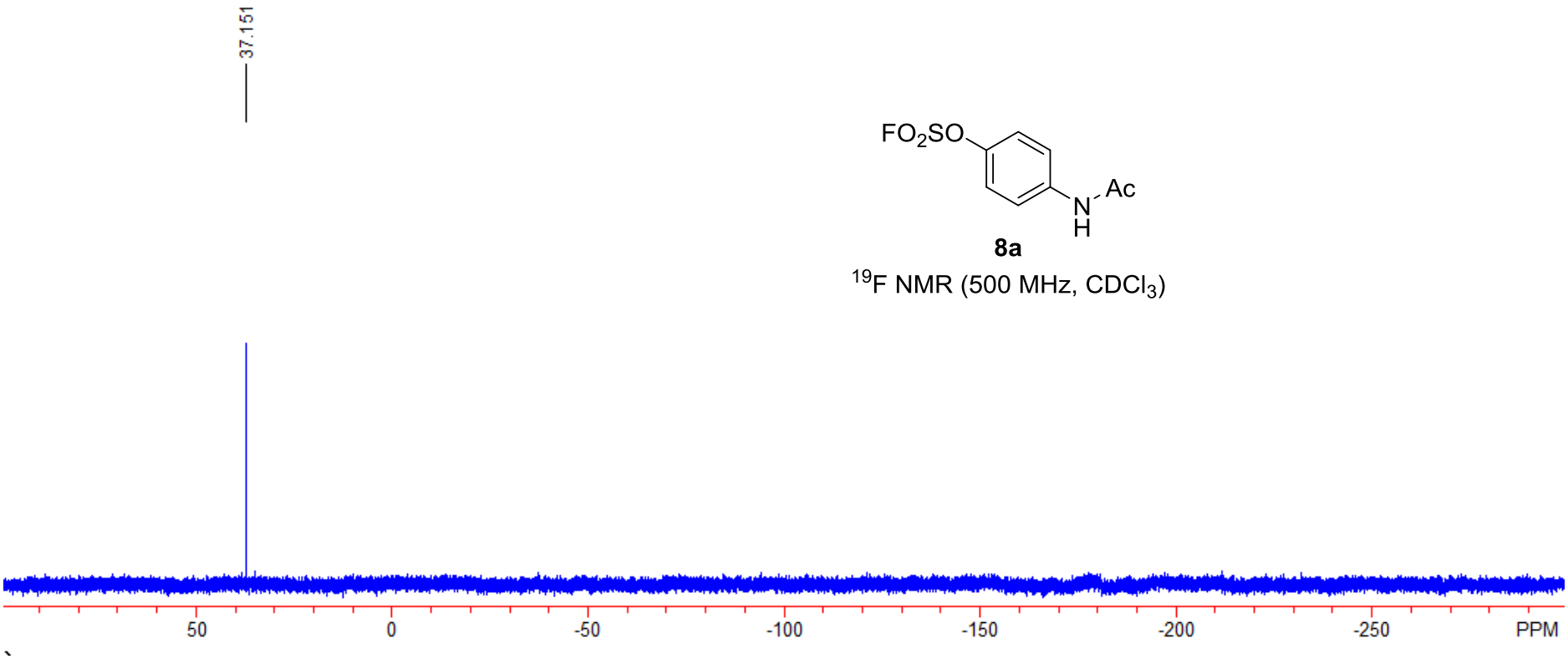
^{19}F NMR (471 MHz, $CDCl_3$)



6

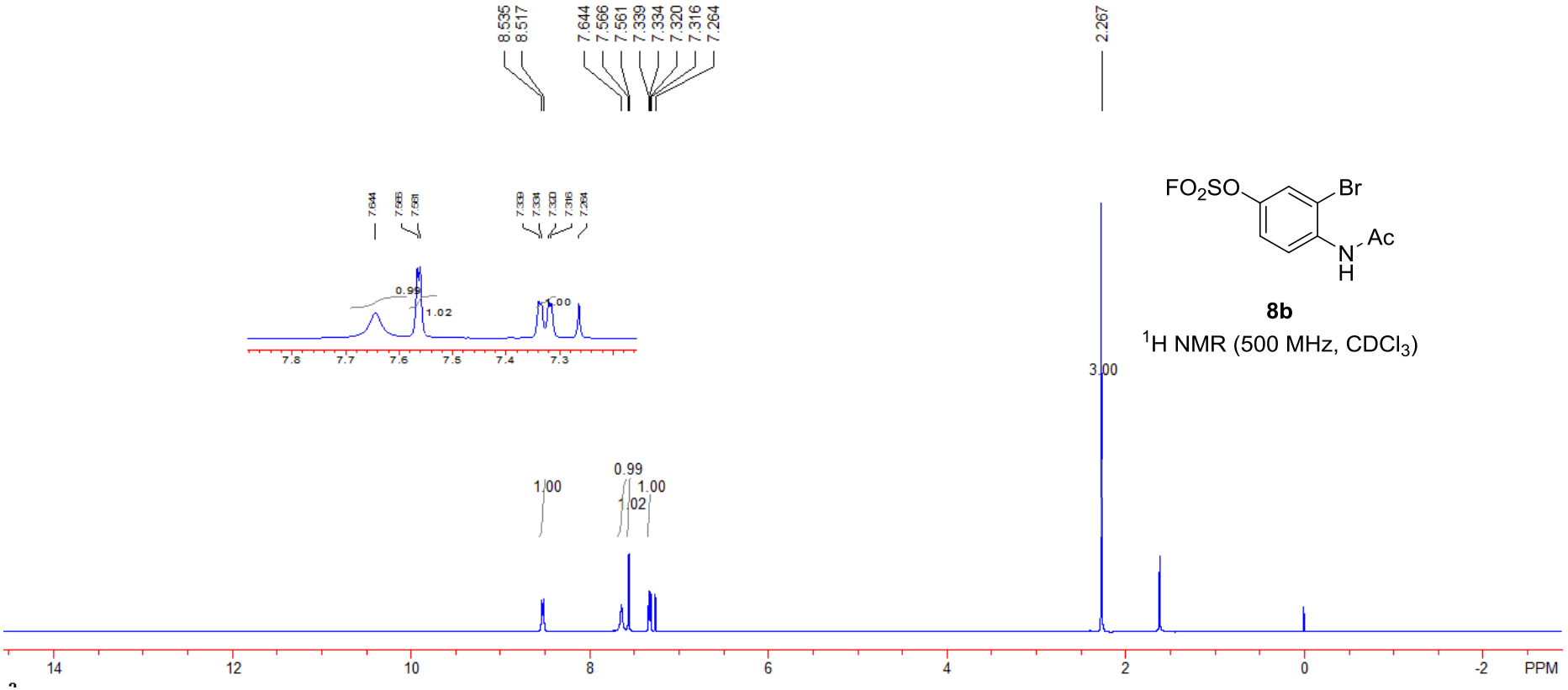
^{13}C NMR (471 MHz, $CDCl_3$)

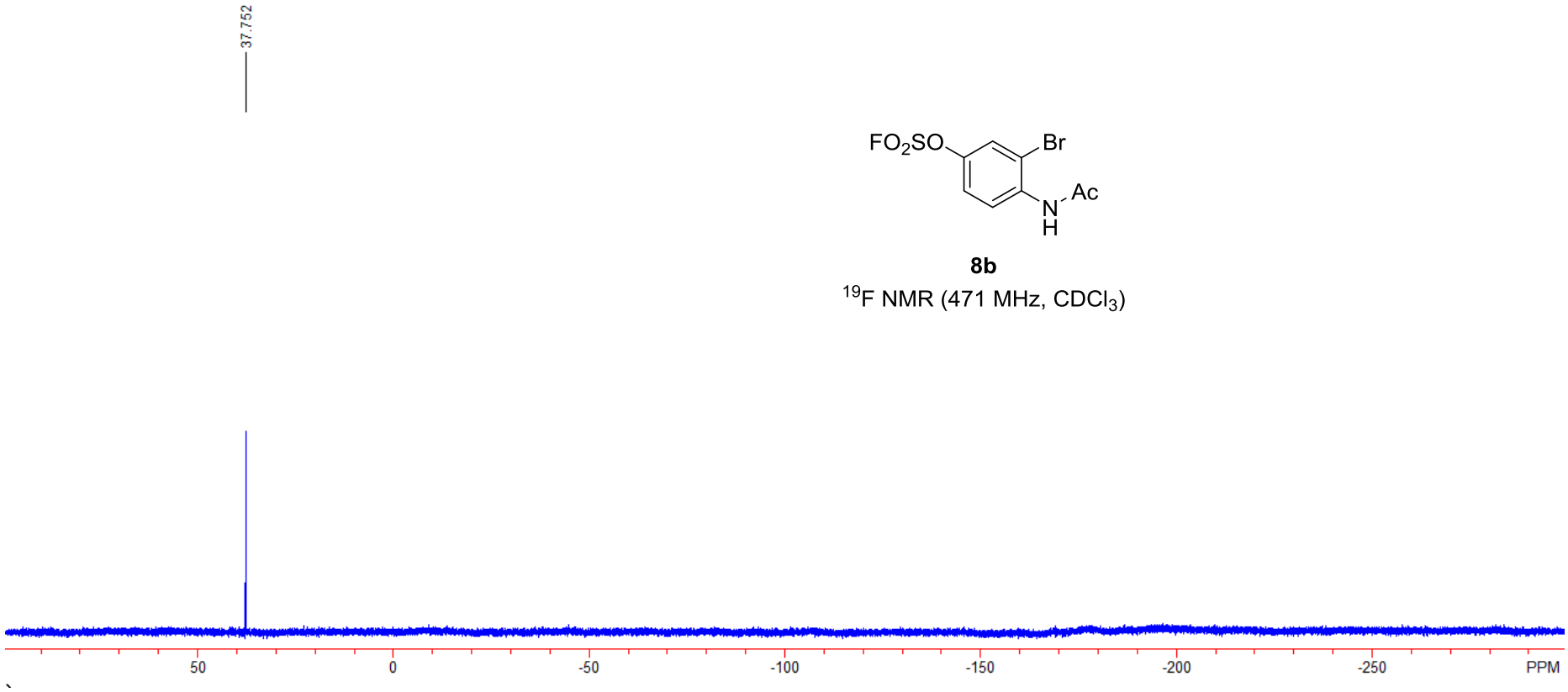

7.836
7.641
7.625
7.280
7.264
2.184
3.07
2.00
2.03
0.95
14
12
10
8
6
4
2
0
-2
PPM
FO2SO
Ac
N
H
8a
1H NMR (500 MHz, CDCl3)



8a

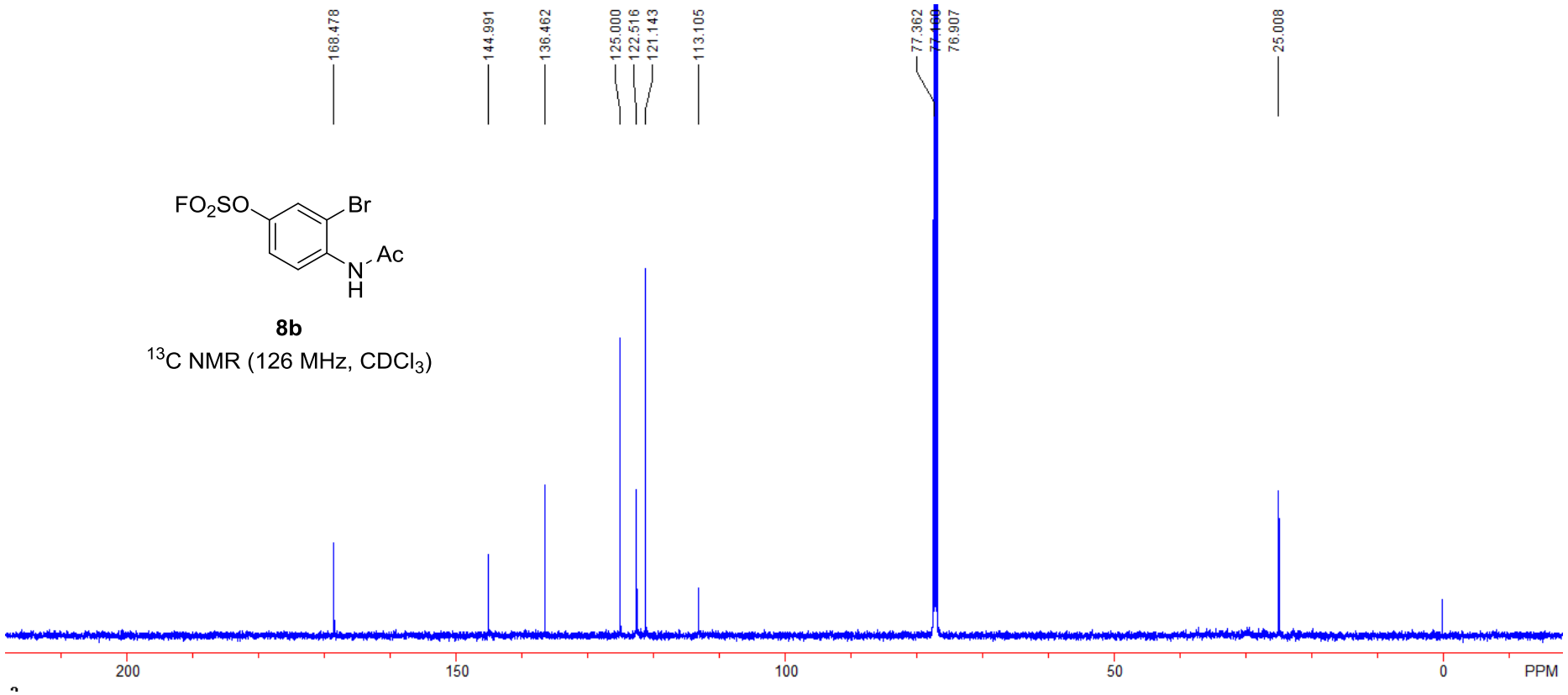
^{19}F NMR (500 MHz, $CDCl_3$)


8.535
8.517
7.644
7.566
7.561
7.339
7.334
7.320
7.316
7.264
2.267
FO2SO
Br
Ac
N
H
8b
1H NMR (500 MHz, CDCl3)
3.00
1.00
0.99
1.00
1.02
0.99
1.02
14
12
10
8
6
4
2
0
-2
PPM



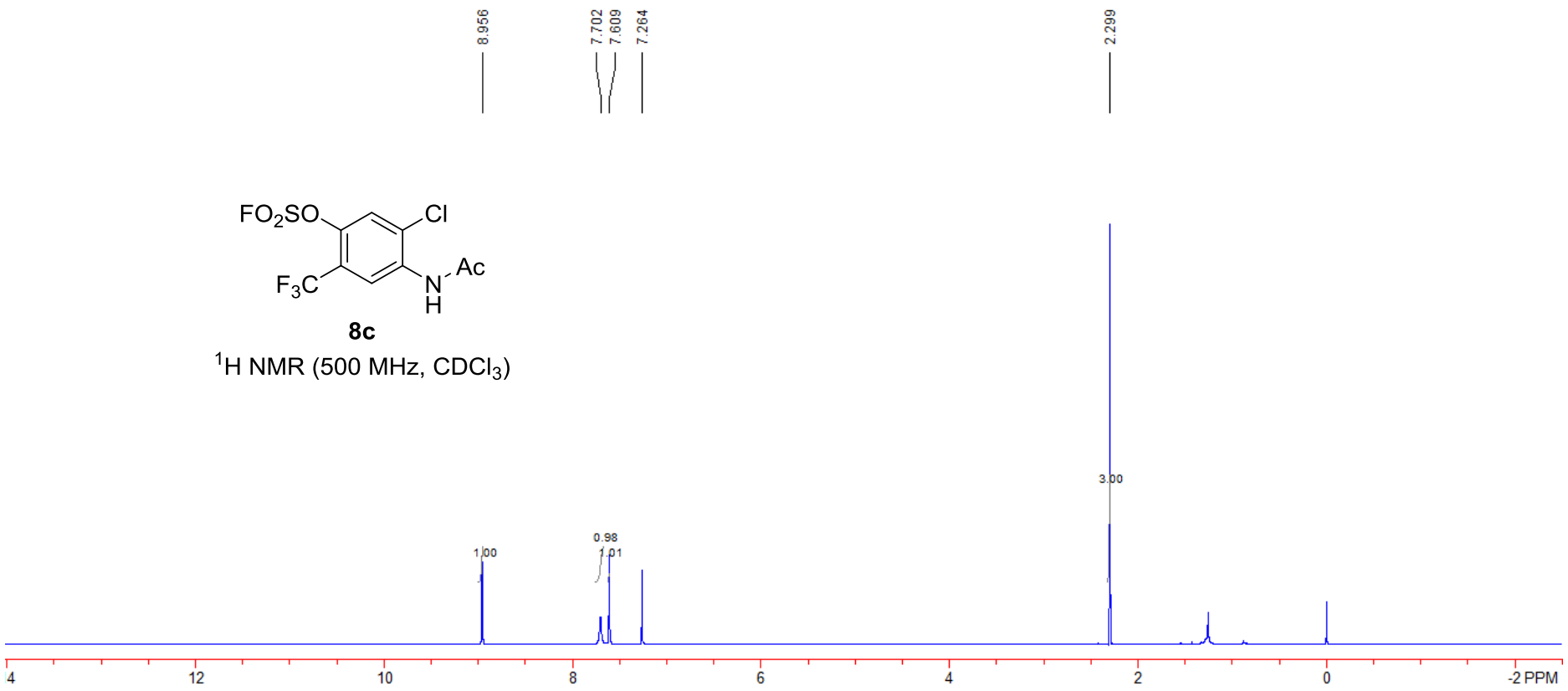
8b

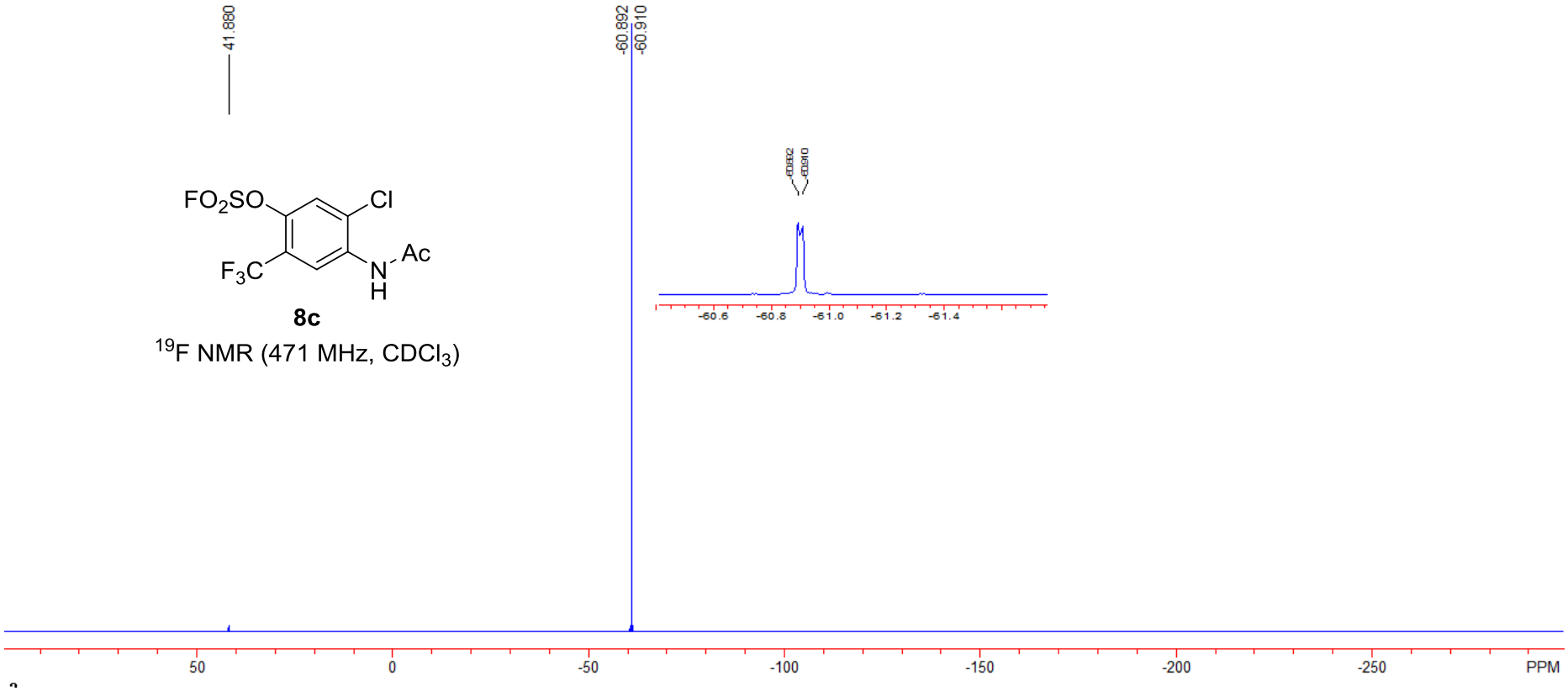
^{19}F NMR (471 MHz, $CDCl_3$)



8b

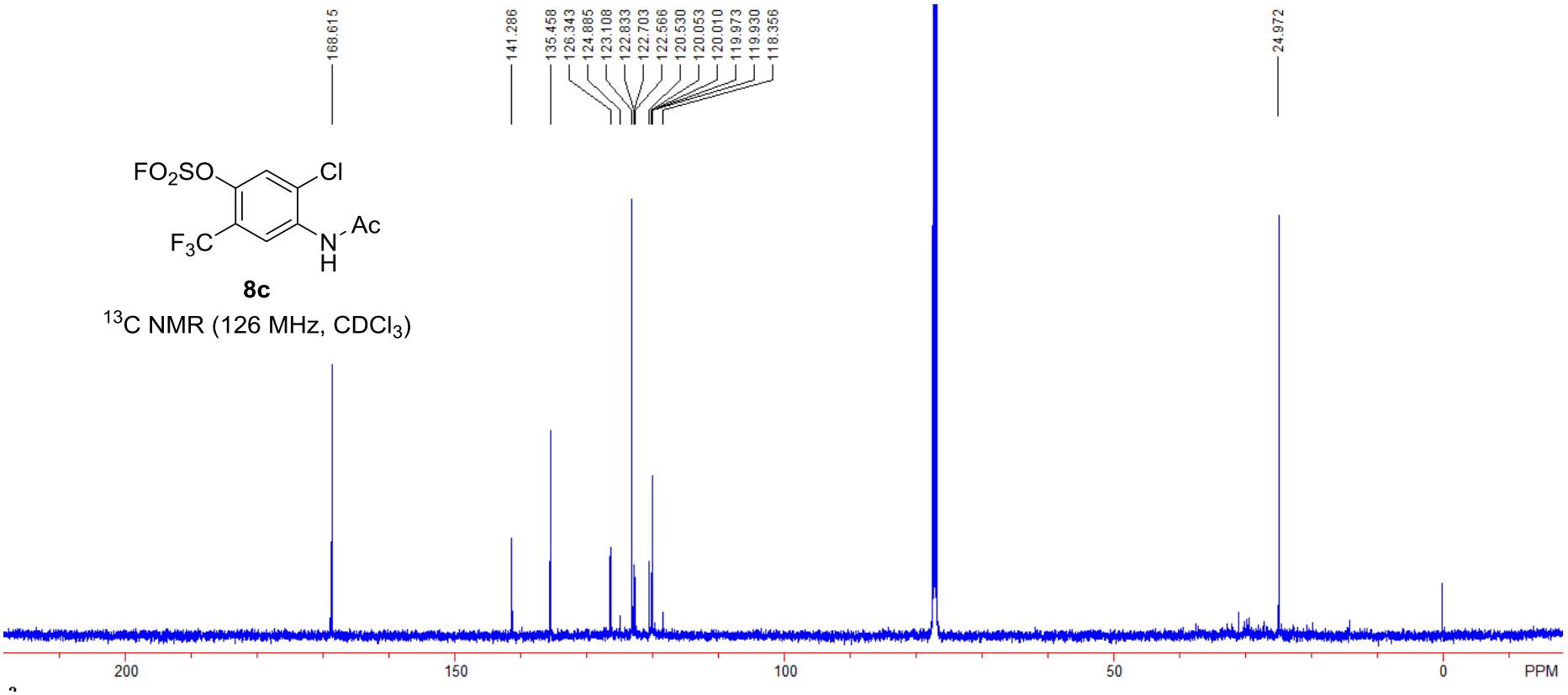
^{13}C NMR (126 MHz, $CDCl_3$)

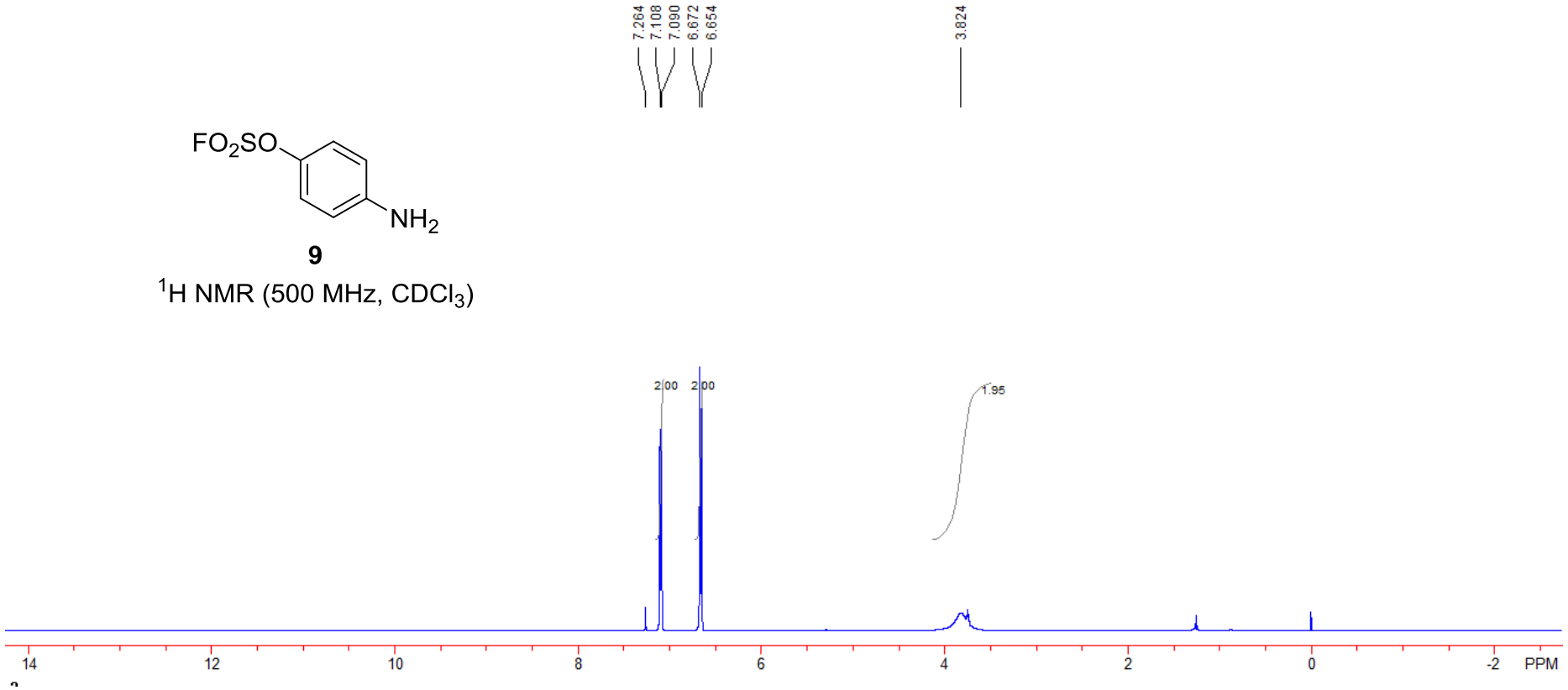

8.956
7.702
7.609
7.264
2.299
FO2SO
Cl
F3C
N
H
Ac
8c
1H NMR (500 MHz, CDCl3)
1.00
0.98
1.01
3.00
4
12
10
8
6
4
2
0
-2 PPM

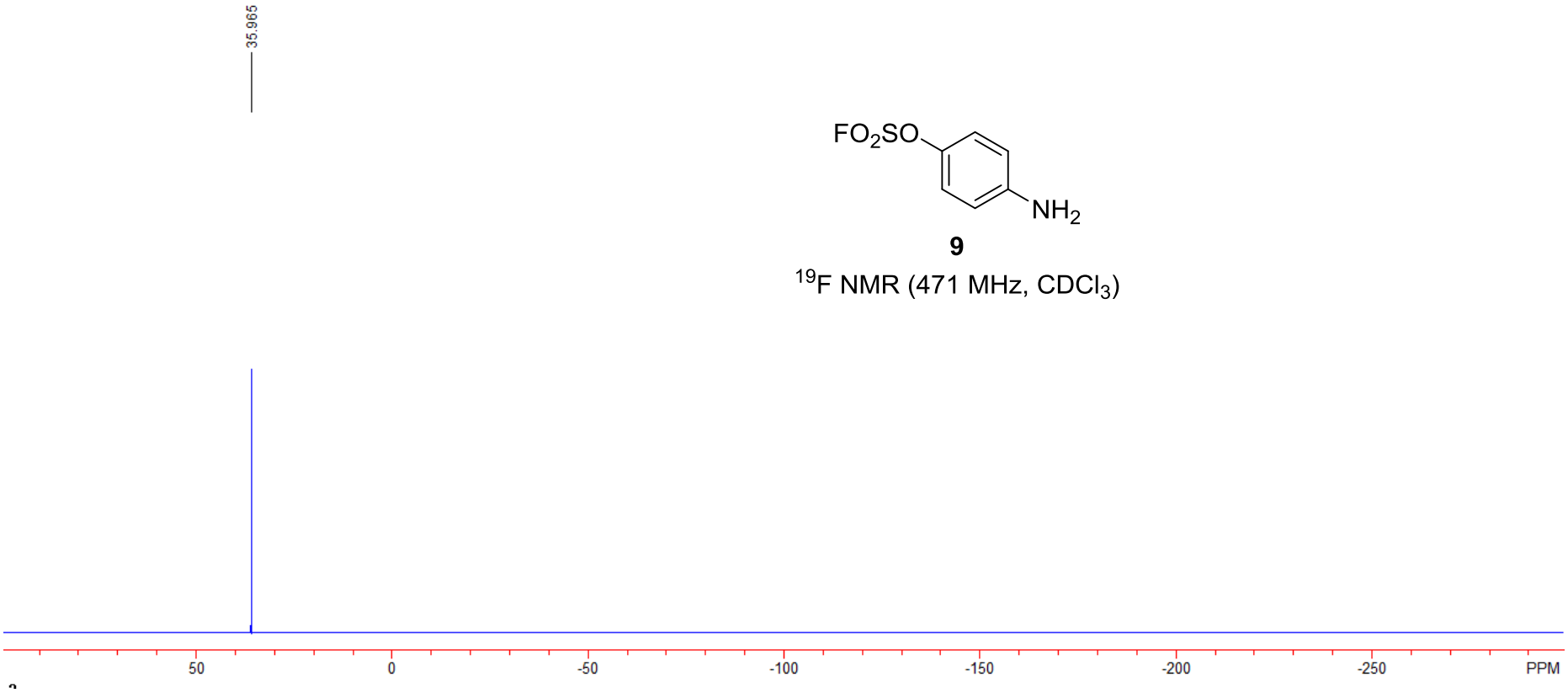


8c

^{19}F NMR (471 MHz, $CDCl_3$)

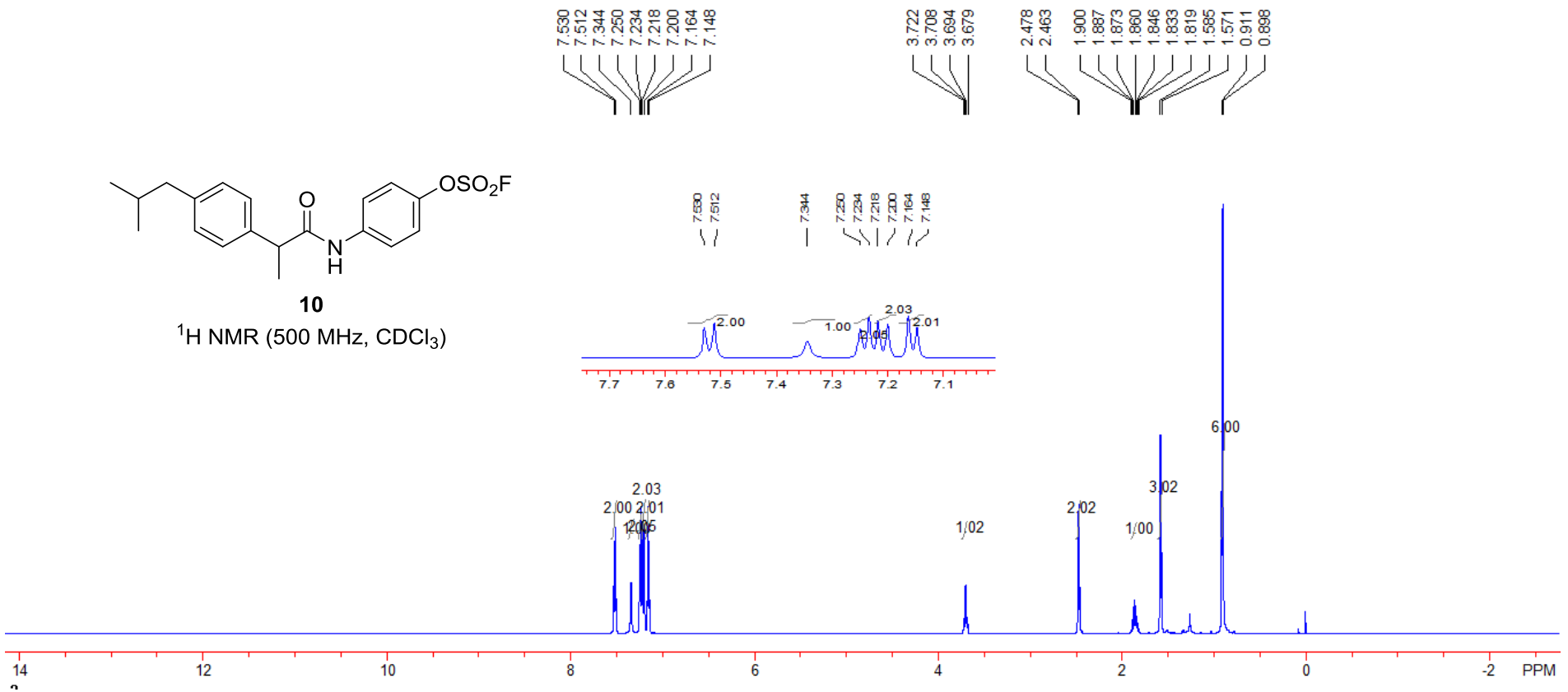

168.615
141.286
135.458
126.343
124.885
123.108
122.833
122.703
122.566
120.530
120.053
120.010
119.973
119.930
118.356
24.972
FO2SO
Cl
F3C
N
H
Ac
8c
13C NMR (126 MHz, CDCl3)
200
150
100
50
0
PPM

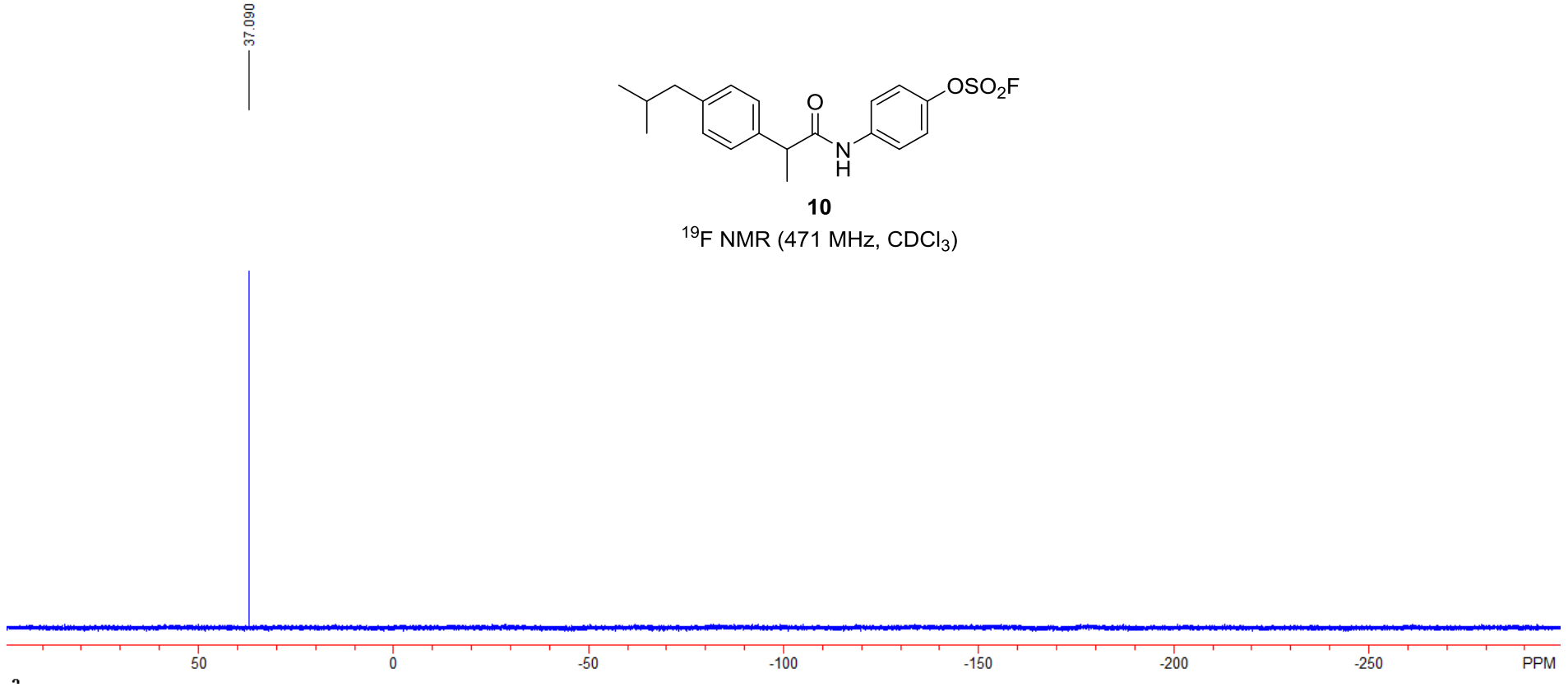

7.264
7.108
7.090
6.672
6.654
3.824
FO2SO
NH2
9
1H NMR (500 MHz, CDCl3)
2.00
2.00
1.95
14
12
10
8
6
4
2
0
-2
PPM



9

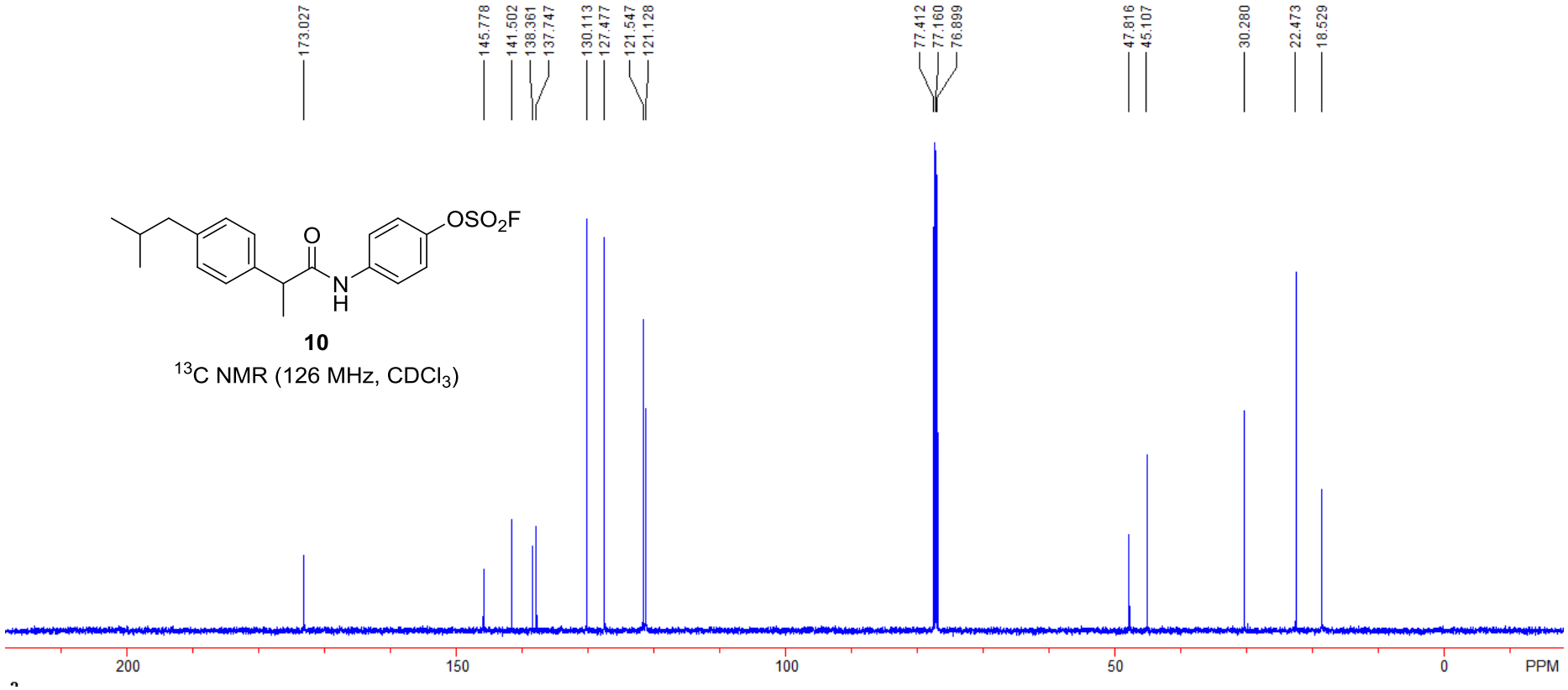
^{19}F NMR (471 MHz, $CDCl_3$)


7.530
7.512
7.344
7.250
7.234
7.218
7.200
7.164
7.148
3.722
3.708
3.694
3.679
2.478
2.463
1.900
1.887
1.873
1.860
1.846
1.833
1.819
1.585
1.571
0.911
0.898
OSO2F
O
N
H
10
1H NMR (500 MHz, CDCl3)
2.00
1.00
2.03
2.01
7.7
7.6
7.5
7.4
7.3
7.2
7.1
2.03
2.00
2.01
1.02
2.02
1.00
3.02
6.00
14
12
10
8
6
4
2
0
-2
PPM



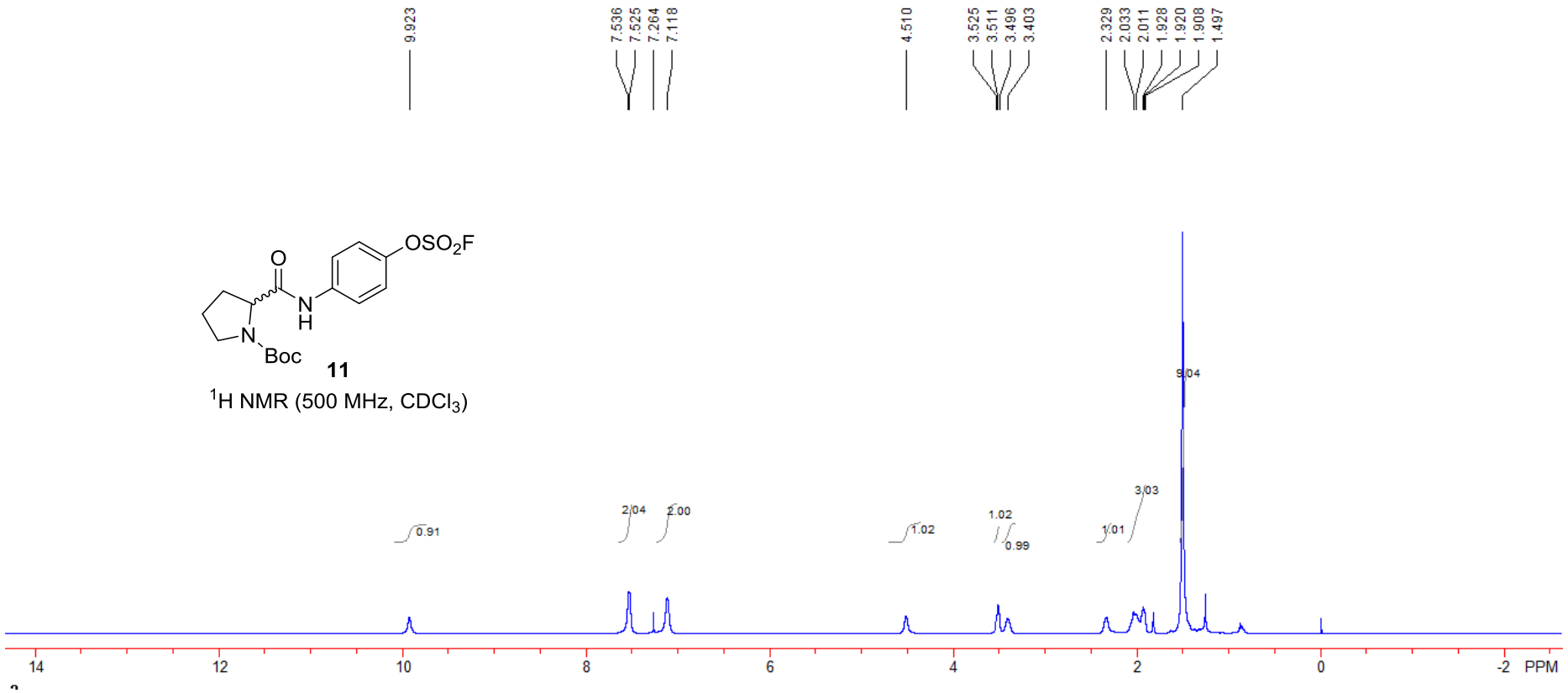
10

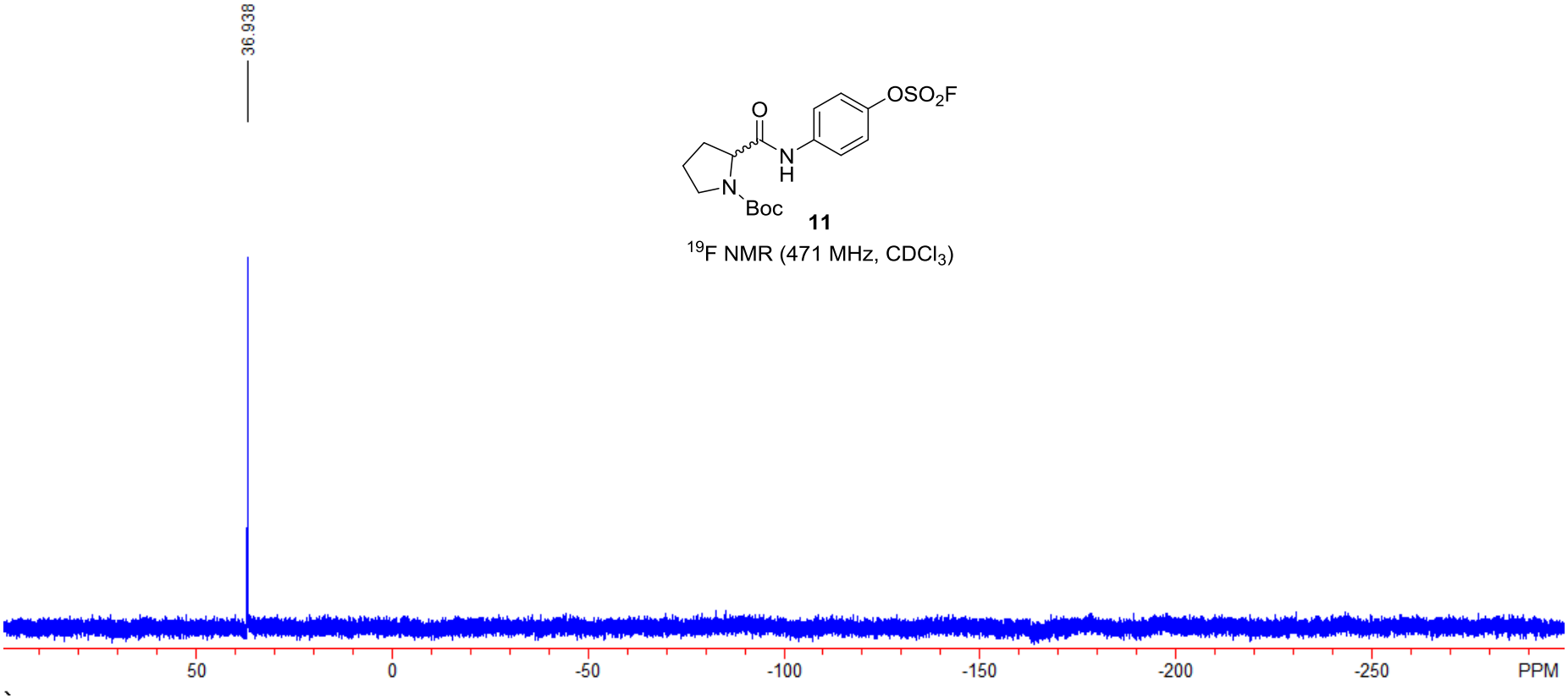
^{19}F NMR (471 MHz, $CDCl_3$)



10

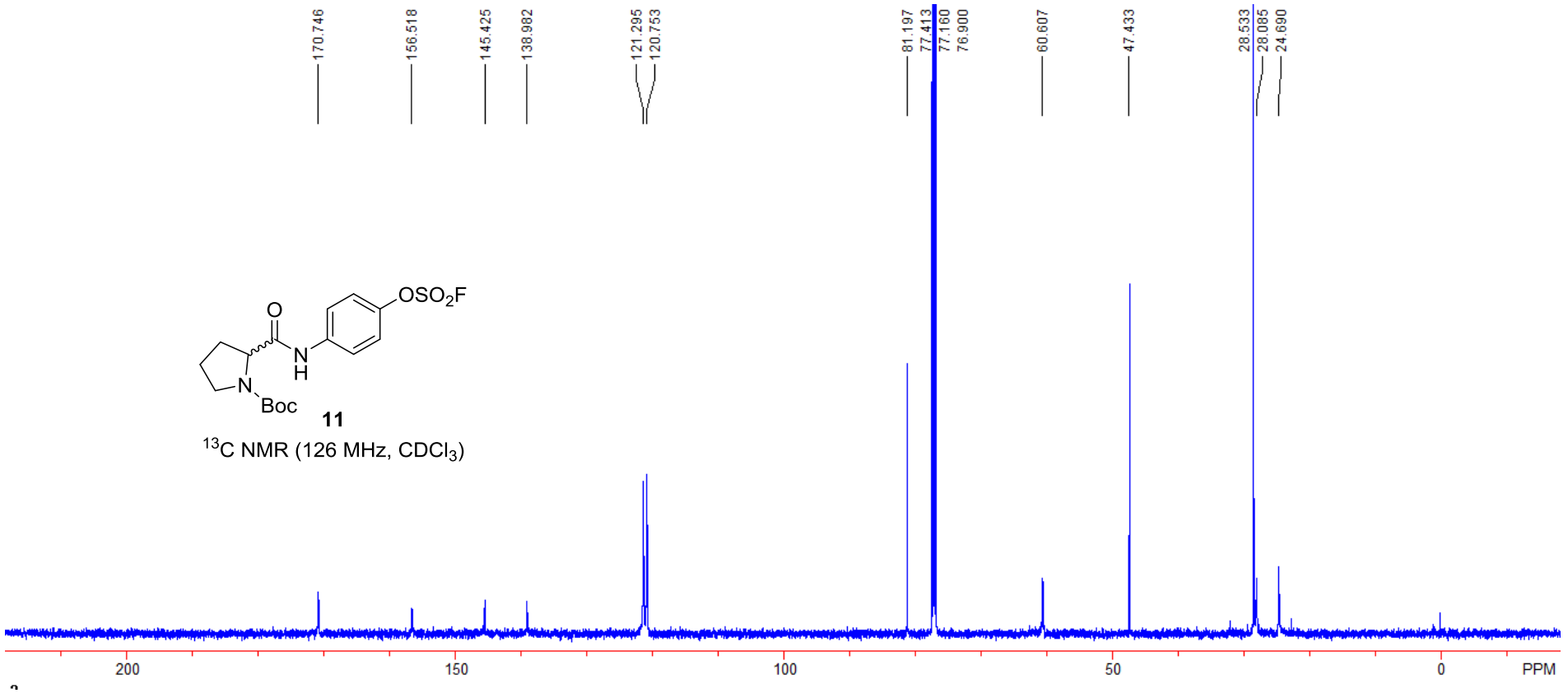
^{13}C NMR (126 MHz, $CDCl_3$)


9.923
7.536
7.525
7.264
7.118
4.510
3.525
3.511
3.496
3.403
2.329
2.033
2.011
1.928
1.920
1.908
1.497
OSO2F
O
N
H
N
Boc
11
1H NMR (500 MHz, CDCl3)
0.91
2.04
2.00
1.02
1.02
0.99
1.01
3.03
9.04
14
12
10
8
6
4
2
0
-2
PPM



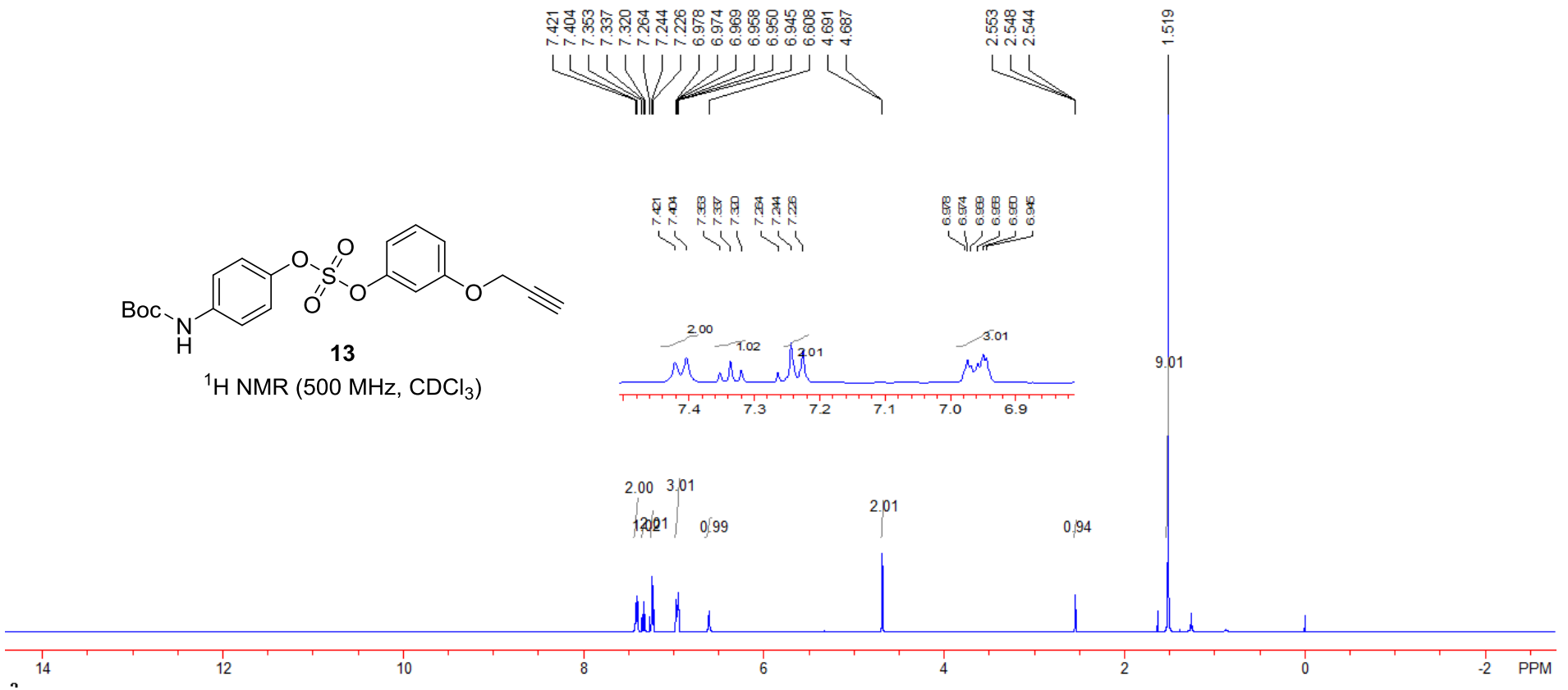
11

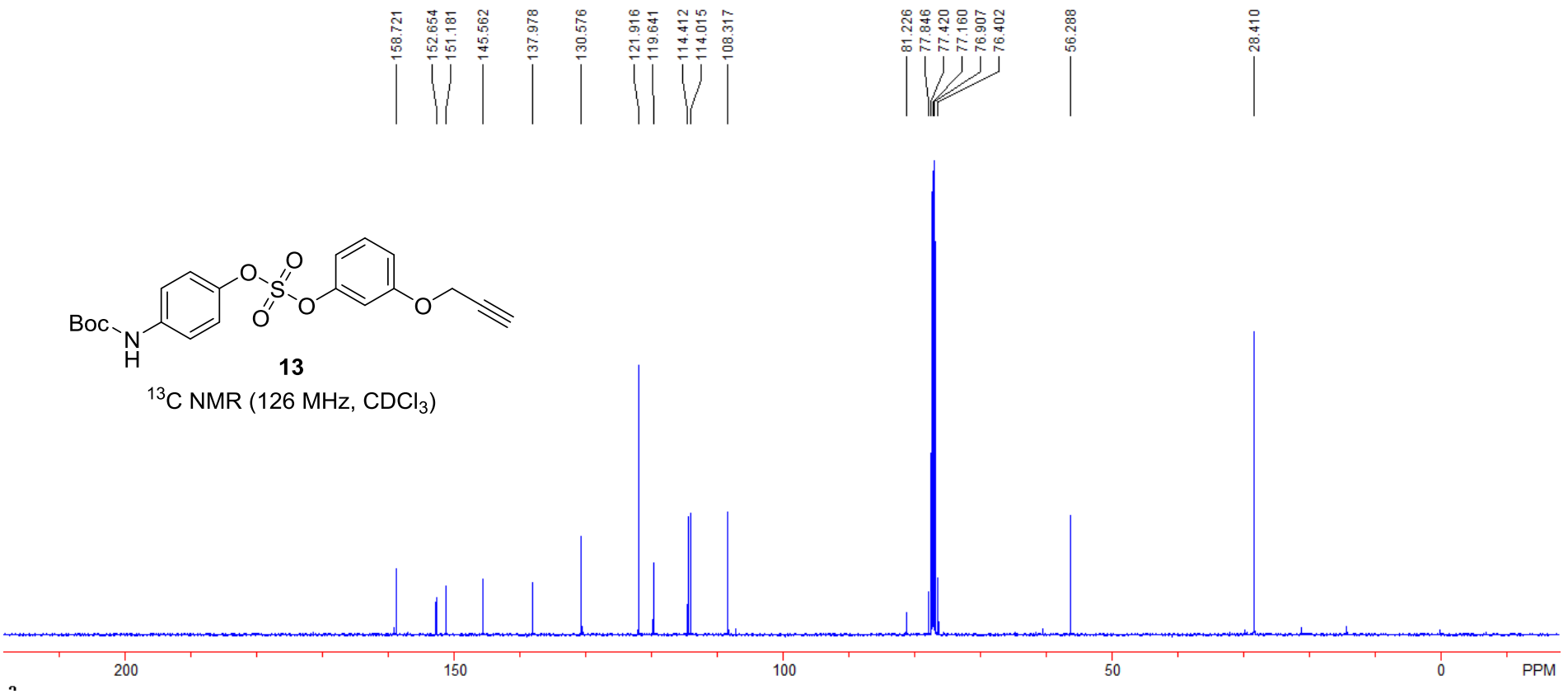
^{19}F NMR (471 MHz, $CDCl_3$)



11

^{13}C NMR (126 MHz, $CDCl_3$)


Boc
N
H
O
O
S
O
O
O
O
13
1H NMR (500 MHz, CDCl3)
7.421
7.404
7.353
7.337
7.320
7.264
7.244
7.226
6.978
6.974
6.969
6.958
6.950
6.945
6.608
4.691
4.687
2.553
2.548
2.544
1.519
2.00
1.02
3.01
3.01
9.01
2.00
3.01
2.01
0.99
0.94
14
12
10
8
6
4
2
0
-2
PPM



13

^{13}C NMR (126 MHz, $CDCl_3$)