Electronic supplementary materials *Mendeleev Commun.*, 2023, **33**, 491–493

Visible light-induced thiocyanation of *gem*-difluorinated phosphonium salts

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Content

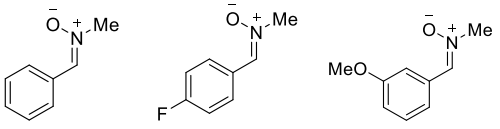
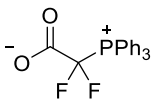
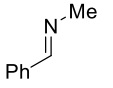
General methods

All reactions were performed under an argon atmosphere. *N,N*-Dimethylformamide (DMF) and dimethyl sulfoxide (DMSO) were distilled from CaH_2 under vacuum and stored over MS 4Å under an argon atmosphere. Dichloromethane (DCM) was distilled from CaH_2 and stored over MS 3Å. Acetonitrile (MeCN) was distilled successively from P_2O_5 and CaH_2 and stored over MS 3Å. Column chromatography was carried out employing silica gel (230-400 mesh). Precoated silica gel plates F-254 were used for thin-layer analytical chromatography visualizing with UV and/or acidic aq. $KMnO_4$ solution. High resolution mass spectra (HRMS) were measured using electrospray ionization (ESI) and time-of-flight (TOF) mass analyzer. The measurements were done in a positive ion mode (interface capillary voltage – 4500 V) or in a negative ion mode (3200 V); mass range from m/z 50 to m/z 3000. For irradiation, Hontiey 100 W/455 nm LED chip (blue light) and Hontiey 1 pc 100W LED High Power UV 400 nm LED chip (400 nm light) were used. The LED chip was connected to a power supply operated at 30V, 2A, which corresponds to 60W, unless otherwise noted. During irradiation, the reaction vessel was placed in a glass jacket for cooling (Huber minichiller 300 was used, water temperature *ca*. 5 °C). The distance between the reaction vessel and the LED chip was about 1 cm (the reaction set-up was assembled as previously described[S1]).

Starting materials

NH_4SCN was recrystallized from dry methanol and stored in a glovebox.

The following compounds were obtained according to literature procedures:

Compounds	Ref.
	S2
 (PDFA)	S3
	S4

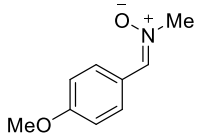
[S1] M. D. Kosobokov, M. O Zubkov, V. V. Levin, V. A. Kokorekin and A. D. Dilman, *Chem. Commun.*, 2020, **56**, 9453.
[S2] T.-Z. Li, S.-J. Liu, Y.-W. Sun, S. Deng, W. Tan, Y. Jiao, Y.-C. Zhang and F. Shi, *Angew. Chem., Int. Ed.,* 2021, **60**, 2355.
[S3] J. Zheng, J. Cai, J.-H. Lin, Y. Guo and J.-C. Xiao, *Chem. Commun.,* 2013, **49**, 7513.
[S4] A. Baldridge, J. Kowalik and L. M. Tolbert, *Synthesis,* 2010, **14**, 2424.

Synthesis of nitrones 1b,c,f. Aldehyde (14.3 mmol) and triethylamine (2.8 mL, 20.0 mmol) were successively added to a suspension of $MgSO_4$ (5.85 g, 48.6 mmol) in DCM (40 mL). The solution was cooled to 0 °C (ice bath), *N*-methylhydroxylamine hydrochloride (835 mg, 10 mmol) was added, the cooling bath was removed, and the mixture was stirred for 48 h at room temperature. The mixture was quenched with water (30 mL) and extracted with DCM (3×40 mL). The combined organic phases were filtered through Na_2SO_4, concentrated under vacuum and the residue was purified by column chromatography on silica gel.

1-(2-Fluorophenyl)-*N*-methylmethanimine oxide (1b)[S5]

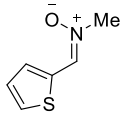
Yield 939 mg (61 %). Colorless crystals. Mp 56 – 57 °C. R_f 0.27 (EtOAc/MeOH, 15/1).
^{1}H NMR (300 MHz, $CDCl_3$), δ: 9.15 (td, 1H, *J* = 7.7, 1.9 Hz), 7.59 (s, 1H), 7.34 – 6.89 (m, 3H), 3.82 (s, 3H).
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$), δ: 159.8 (d, *J* = 252.8 Hz), 131.6 (d, *J* = 8.8 Hz), 128.5 (d, *J* = 1.3 Hz), 127.3 (d, *J* = 9.1 Hz), 124.3 (d, *J* = 3.6 Hz), 119.0 (d, *J* = 9.0 Hz), 114.6 (d, *J* = 21.3 Hz), 54.9.
^{19}F NMR (282 MHz, $CDCl_3$), δ: -117.8 (ddd, *J* = 11.1, 7.5, 5.5 Hz).

1-(4-Methoxyphenyl)-*N*-methylmethanimine oxide (1c) [S6]



Yield 1.26 g (76 %). Colorless crystals. Mp 75 – 76 °C. R_f 0.25 (EtOAc/MeOH, 8/1).
^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.18 (dm, 2H, *J* = 8.9 Hz), 7.26 (s, 1H), 6.90 (dm, 2H, *J* = 8.9 Hz), 3.81 (s, 3H), 3.80 (s, 3H).
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$), δ: 161.1, 134.8, 130.4, 123.6, 113.9, 55.4, 54.0.

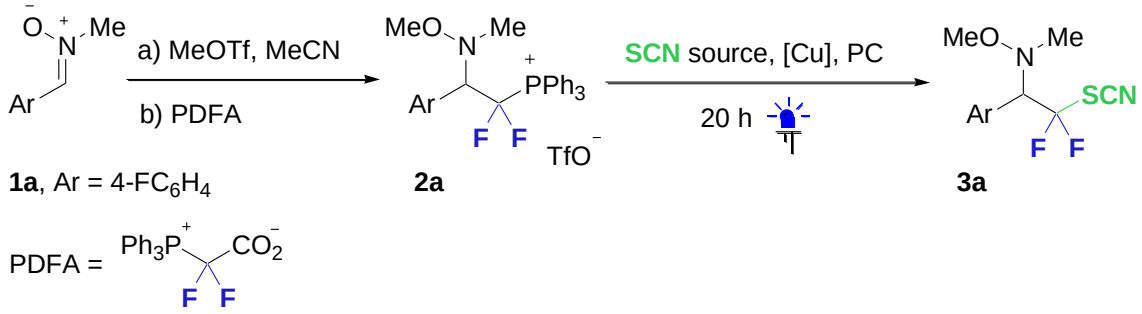
***N*-Methyl-1-(thiophen-2-yl)methanimine oxide (1f).**[S7]



Yield 566 mg (40 %). Colorless crystals. Mp 123 – 124 °C. R_f 0.25 (EtOAc/MeOH, 15/1).
^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.80 (d, *J* = 0.3 Hz, 1H), 7.39 – 7.28 (m, 2H), 7.03 (dd, *J* = 5.1, 3.9 Hz, 1H), 3.73 (s, 3H).
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$), δ: 132.2, 130.7, 129.2, 128.7, 126.3, 51.5.

[S5] S. Caddick and H. D. Bush, *Org. Lett.*, 2003, **5**, 2489.
[S6] J. Lasri, N. E. Eltayeb, M. Haukka and Y. Alghamdi, *J. Mol. Struct.*, 2017, **1128**, 70.
[S7] S. Colonna, V. Pironti, G. Carrea, P. Pasta and F. Zambianchi, *Tetrahedron*, 2004, **60**, 569.

Optimization studies



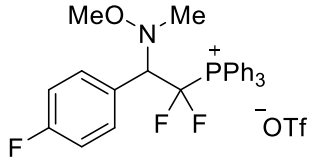
Entry	SCN source	Light, *T*	[Cu]	PC	Yield of **3a**, %[a]
1	NH_4SCN, 2 eq	450 nm, 60 W, rt	CuSCN, 0.25 eq	-	31
2	NH_4SCN, 2 eq	450 nm, 60 W, 5 °C	CuSCN, 2.0 eq	-	31
3	NH_4SCN, 2 eq	400 nm, 60 W, 5 °C	CuSCN, 1.0 eq	-	35
4	NH_4SCN, 2 eq	450 nm, 60 W, rt	CuSCN, 1.0 eq	-	60
5	NH_4SCN, 2 eq	450 nm, 60 W, 5 °C	CuSCN, 1.0 eq	-	63
6	NH_4SCN, 1.3 eq	450 nm, 60 W, 5 °C	CuSCN, 1.0 eq	-	63
7	**NH_4SCN, 1.3 eq**	**450 nm, 60 W, 5 °C**	**CuSCN, 1.0 eq**	**$Ir(ppy)_3$**	**70**
8[b]	**NH_4SCN, 1.3 eq**	**450 nm, 60 W, 5 °C**	**CuSCN, 1.0 eq**	**$Ir(ppy)_3$**	**60 (56[c])**
9	NH_4SCN, 1.3 eq	450 nm, 130 W, 5 °C	CuSCN, 1.0 eq	$Ir(ppy)_3$	48
10	NH_4SCN, 1.3 eq	450 nm, 15 W, 5 °C	CuSCN, 1.0 eq	$Ir(ppy)_3$	39
11	NH_4SCN, 1.3 eq	450 nm, 60 W, 5 °C	CuSCN, 0.25 eq	$Ir(ppy)_3$	28
12[d]	NH_4SCN, 1.3 eq	450 nm, 60 W, 5 °C	CuSCN, 0.25 eq	$Ir(ppy)_3$	18
13	TBASCN, 1.3 eq	450 nm, 60 W, 5 °C	CuSCN, 1.0 eq	$Ir(ppy)_3$	48
14	KSCN, 1.3 eq	450 nm, 60 W, 5 °C	CuSCN, 1.0 eq	$Ir(ppy)_3$	53
15	TMSNCS, 1.3 eq	450 nm, 60 W, 5 °C	CuSCN, 1.0 eq	$Ir(ppy)_3$	<5
16	NH_4SCN, 1.3 eq	450 nm, 60 W, 5 °C	$Cu(MeCN)_4BF_4$, 1.0 eq	$Ir(ppy)_3$	52
17	NH_4SCN, 1.3 eq	450 nm, 60 W, rt	CuSCN, 1.0 eq	$Ir(ppy)_3$	59
18	NH_4SCN, 1.3 eq	450 nm, 60 W, rt	CuSCN, 1.0 eq	$[Ir(dtbbpy)(ppy)_2]PF_6$	58
19	NH_4SCN, 1.3 eq	450 nm, 60 W, rt	CuSCN, 1.0 eq	$[Ir\{dF(CF_3)_2ppy\}_2(dtbbpy)]PF_6$	58
20	NH_4SCN, 1.3 eq	450 nm, 60 W, rt	CuSCN, 1.0 eq	4CzIPN	45
21[e]	NH_4SCN, 1.3 eq	450 nm, 60 W, 5 °C	CuSCN, 1.0 eq	$Ir(ppy)_3$	40
24[f]	NH_4SCN, 1.3 eq	450 nm, 60 W, 5 °C	CuSCN, 1.0 eq	$Ir(ppy)_3$	27
25[g]	NH_4SCN, 2 eq	450 nm, 60 W, rt	-	-	<1

[a] Determined by ^{19}F NMR with internal standard ($PhCF_3$).
[b] Performed on 2 mmol scale, isolated yield in parentheses.
[c] Isolated yield.
[d] 25% of phenanthroline was added.
[e] Photoreaction was performed in DMF.
[f] Photoreaction was performed in DMSO.
[g] Full conversion of phosphonium salt **2a** was observed.

Synthesis of thiocyanates 3 (General procedure).

Methyl triflate (234 µL, 2.1 mmol) was added dropwise to a solution of nitrone (2.0 mmol) in acetonitrile (5 mL) at 0 °C (ice bath). The resulting solution was stirred for 15 min, then the cooling bath was removed, and the stirring was continued for additional 15 min at room temperature. Then, PDFA (938 mg, 2.6 mmol) was added, and the mixture was stirred at 52 °C (oil bath) for 2 h until the complete dissolution of PDFA. The reaction mixture was cooled to room temperature and NH_4SCN (dry, see Starting Materials for details, 198 mg, 2.6 mmol), CuSCN (242 mg, 2 mmol) and $Ir(ppy)_3$ (0.005 mmol, 3.2 mg) were successively added. The mixture was irradiated using 455 nm LED, during irradiation the reaction temperature was maintained at 5 °C (see General Methods for details). For the work-up, water (5 mL) was added, and the mixture was extracted with ethyl acetate (4×5 mL). In case of substrate **3e**, a centrifuge was used for more efficient layer separation (3000 RPM, 2 min). The combined organic phases were filtered through Na_2SO_4, concentrated under vacuum and the residue was purified by column chromatography on silica gel. The combined fractions were concentrated under vacuum and additionally purified by high-vacuum short-path distillation using Hickman distillation head.

[1,1-Difluoro-2-(4-fluorophenyl)-2-(*N*-methoxy-*N*-methylamino)ethyl]triphenylphosphonium trifluoromethanesulfonate (2a).



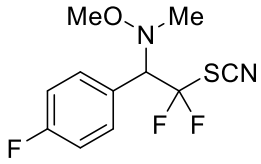
Methyl triflate (58 µL, 0.525 mmol) was added dropwise to a solution of nitrone **1a** (76 mg, 0.5 mmol) in DCM (1.0 mL) at 0 °C (ice bath). The resulting solution was stirred for 15 min at 0 °C, the cooling bath was removed, and the stirring was continued for additional 15 min at room temperature. Then, DCM was evaporated under vacuum, the flask was filled with argon, and the residue was dissolved in DMSO-d_6 (0.7 mL). Reagent PDFA (196 mg, 0.55 mmol) was added, and the mixture was stirred at 52 °C (oil bath) for 2 h until complete dissolution of PDFA. The crude reaction mixture was transferred into an NMR tube and analyzed by ^1H, ^{19}F and ^{31}P NMR spectroscopy. Integrals in the aromatic region of ^1H NMR spectrum are not representative due to excess of the phosphonium reagent.

^1H NMR (300 MHz, $(CD_3)_2SO$), δ: 8.10 – 7.81 (m), 7.70 – 7.59 (m, 2H), 7.28 – 7.13 (m, 2H), 4.92 (dd, 1H, *J* = 28.1, 5.9 Hz), 2.88 (s, 3H), 2.22 (s, 3H).

^{19}F NMR (282 MHz, $(CD_3)_2SO$), δ: -77.7, -86.0 (dd, *J* = 296.1, 93.6 Hz), -100.7 (ddd, *J* = 296.1, 97.4, 28.3 Hz), -111.9 – -112.1 (m).

^{31}P NMR (122 MHz, $(CD_3)_2SO$), δ: 28.7 (t, *J* = 96.4 Hz).

_N_-[2,2-Difluoro-1-(4-fluorophenyl)-2-thiocyanatoethyl]-_N,O_-dimethylhydroxylamine (3a).



Yield 309 mg (56%). Pale yellow oil. Bp 125 – 135 °C (bath temperature)/1 mbar. R_f 0.25 (Hexane/EtOAc, 5/1).

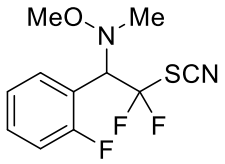
^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.41 (ddm, 2H, *J* = 8.9, 5.4 Hz), 7.13 – 7.03 (m, 2H), 4.11 (dd, 1H, *J* = 17.9, 4.7 Hz), 3.60 (s, 3H), 2.45 (s, 3H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$), δ: 163.6 (d, *J* = 249.6 Hz), 132.8 (dd, *J* = 8.5, 1.6 Hz), 129,0 (dd, *J* = 296.4, 288.6 Hz), 115.7 (d, *J* = 21.5 Hz), 107.3 (d, *J* = 5.3 Hz), 76.0 (dd, *J* = 25.3, 20.0 Hz), 59.6, 42.1 (t, *J* = 1.6 Hz).

^{19}F NMR (282 MHz, $CDCl_3$), δ: -64.7 (d, 1F, *J* = 190.0 Hz), -72.8 (dd, 1F, *J* = 190.0, 17.9 Hz), -111.1 – -111.2 (m, 1F).

HRMS (ESI): calcd for $C_{11}H_{12}F_3N_2OS$ (M+H) 277.0617, found 277.0611.

_N_-[2,2-Difluoro-1-(2-fluorophenyl)-2-thiocyanatoethyl]-_N,O_-dimethylhydroxylamine (3b)



Yield 285 mg (52%). Pale yellow oil. Bp 120 – 130 °C (bath temperature)/1 mbar. R_f 0.27 (Hexane/EtOAc, 10/1).

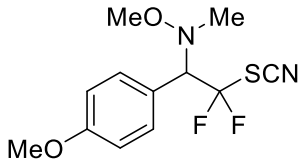
^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.75 – 7.63 (m, 1H), 7.47 – 7.34 (m, 1H), 7.22 – 7.07 (m, 2H), 4.68 (ddd, 1H, *J* = 18.7, 4.9, 0.5 Hz), 3.61 (s, 3H), 2.51 (s, 3H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$), δ: 161.8 (d, *J* = 248.2 Hz), 132.3 (d, *J* = 4.2 Hz), 131.6 (d, *J* = 8.8 Hz), 129.4 (dd, *J* = 303.7, 290.3 Hz), 124.4 (d, *J* = 3.7 Hz), 116.7 (d, *J* = 12.4 Hz), 115.5 (d, *J* = 23.2 Hz), 107.1 (d, *J* = 5.1 Hz), 66.9 (ddd, *J* = 26.0, 20.4, 4.0 Hz), 59.7, 42.2 (t, *J* = 1.6 Hz).

^{19}F NMR (282 MHz, $CDCl_3$), δ: -65.6 (d, 1F, *J* = 188.5 Hz), -72.4 (dd, 1F, *J* = 188.5, 18.7 Hz), -116.8 – -117.0 (m, 1F).

HRMS (ESI): calcd for $C_{11}H_{12}F_3N_2OS$ (M+H) 277.0617, found 277.0624.

***N*-[2,2-Difluoro-1-(4-methoxyphenyl)-2-thiocyanatoethyl]-*N,O*-dimethylhydroxylamine (3c).**



Yield 275 mg (48%). Pale yellow oil. Bp 160 – 170 °C (bath temperature)/1 mbar. R_f 0.25 (Hexane/EtOAc, 8/1).

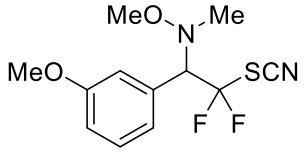
^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.33 (dm, 2H, *J* = 8.9, 0.9 Hz), 6.90 (dm, 2H, *J* = 8.9 Hz), 4.06 (dd, 1H, *J* = 17.7, 5.1 Hz), 3.80 (s, 3H), 3.60 (s, 3H), 2.45 (s, 3H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$), δ: 160.7, 132.1 (d, *J* = 1.1 Hz), 129.3 (dd, *J* = 302.7, 290.5 Hz) 121.8, 114.1, 107.6 (d, *J* = 5.0 Hz), 76.3 (dd, *J* = 24.9, 19.8 Hz), 59.5, 55.3, 42.1 (t, *J* = 1.6 Hz).

^{19}F NMR (282 MHz, $CDCl_3$), δ: -64.67 (d, *J* = 188.1 Hz), -72.14 (dd, *J* = 188.1, 17.7 Hz).

HRMS (ESI): calcd for $C_{12}H_{15}F_2N_2O_2S$ (M+H) 289.0817, found 289.0814.

***N*-[2,2-Difluoro-1-(3-methoxyphenyl)-2-thiocyanatoethyl]-*N,O*-dimethylhydroxylamine (3d)**



Yield 295 mg (51%). Pale yellow oil. Bp 160 – 170 °C (bath temperature)/1 mbar. R_f 0.27 (Hexane/EtOAc, 8/1).

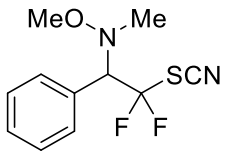
^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.34 – 7.21 (m, 1H), 7.01 – 6.90 (m, 3H), 4.09 (dd, 1H, *J* = 17.2, 4.9 Hz), 3.79 (s, 3H), 3.60 (s, 3H), 2.46 (s, 3H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$), δ: 159.6, 131.5, 129.6, 129.0 (dd, *J* = 302.7, 291.3 Hz), 123.1, 116.5, 115.0, 107.4 (d, *J* = 5.2 Hz), 76.8 (dd, *J* = 27.1, 20.1 Hz), 59.5, 55.3, 42.2.

^{19}F NMR (282 MHz, $CDCl_3$), δ: -64.5 (d, *J* = 188.8 Hz), -71.9 (dd, *J* = 188.8, 17.2 Hz).

HRMS (ESI): calcd for $C_{12}H_{15}F_2N_2O_2S$ (M+H) 289.0817, found 289.0827.

***N*-(2,2-Difluoro-1-phenyl-2-thiocyanatoethyl)-*N,O*-dimethylhydroxylamine (3e).**



Yield 237 mg (46%). Pale yellow oil. Bp 130 – 140 °C (bath temperature)/1 mbar. R_f 0.23 (Hexane/EtOAc, 5/1).

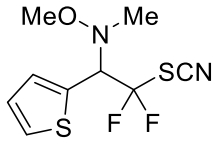
^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.46 – 7.34 (m, 5H), 4.12 (dd, 1H, *J* = 17.7, 4.9 Hz), 3.62 (s, 3H), 2.46 (s, 3H).

$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$), δ: 130.8 (d, *J* = 2.1 Hz), 130.1, 129.8, 129.1 (dd, *J* = 302.9, 290.8 Hz), 128.7, 107.5 (d, *J* = 5.2 Hz), 77.1 (dd, *J* = 17.7, 4.8 Hz), 59.6, 42.3 (t, *J* = 1.5 Hz).

^{19}F NMR (282 MHz, $CDCl_3$), δ: -64.4 (d, *J* = 189.4 Hz), -72.0 (dd, *J* = 189.4, 17.7 Hz).

HRMS (ESI): calcd for $C_{11}H_{13}F_2N_2OS$ (M+H) 259.0711, found 259.0711.

_N_-(2,2-Difluoro-2-thiocyanato-1-(thiophen-2-yl)ethyl)-_N,O_-dimethylhydroxylamine (3f).



Yield 186 mg (35%). Pale yellow oil. Bp 140 – 150 °C (bath temperature)/1 mbar. R_f 0.15 (Hexane/EtOAc, 10/1).

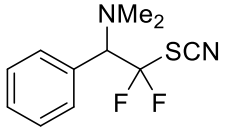
^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.45 (dm, 1H, *J* = 5.1 Hz), 7.17 (dd, 1H, *J* = 3.6, 0.3 Hz), 7.06 (dd, 1H, *J* = 5.1, 3.6 Hz), 4.52 (dd, 1H, *J* = 17.8, 5.8 Hz), 3.63 (s, 3H), 2.53 (s, 3H).

$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$), δ: 131.8, 129.3 (dd, *J* = 303.0, 291.8 Hz), 129.2, 127.7, 126.4, 107.2 (d, *J* = 4.5 Hz), 71.6 (dd, *J* = 25.5, 20.8 Hz), 59.8, 41.7 (t, *J* = 1.9 Hz).

^{19}F NMR (282 MHz, $CDCl_3$), δ: -65.7 (dd, *J* = 185.2, 5.7 Hz), -72.2 (dd, *J* = 185.2, 17.8 Hz).

HRMS (ESI): calcd for $C_9H_{11}F_2N_2OS_2$ (M+H) 265.0275, found 265.0281.

2,2-Difluoro-_N,N_-dimethyl-1-phenyl-2-thiocyanatoethan-1-amine (5).



Methyl triflate (234 µL, 2.1 mmol) was added dropwise to a solution of benzaldehyde *N*-methylimine (2.0 mmol) in acetonitrile (5 mL) at 0 °C (ice bath). The resulting solution was stirred for 15 min, then the bath was removed while the stirring was continued for additional 15 min at rt. Then PDFA (938 mg, 2.6 mmol) was added, and the mixture was stirred at 52 °C (oil bath) for 2 h until complete dissolution of PDFA. The reaction mixture was cooled to rt and NH_4SCN (dry, see Starting Materials for details, 304 mg, 4 mmol), CuSCN (61 mg, 0.5 mmol) were successively added. The mixture was irradiated using 400 nm LED, during irradiation the reaction temperature was maintained at 5 °C (see General Methods for details). For the work-up, water (5 mL) was added, and the mixture was extracted with ethyl acetate (4×5 mL). The combined organic phases were filtered through Na_2SO_4,

concentrated under vacuum and the residue was purified by column chromatography on silica gel. The combined fractions were concentrated under vacuum and additionally purified by high-vacuum short-path distillation using Hickman distillation head.

Yield 182 mg (38%). Yellow oil. Bp 130 – 140 °C (bath temperature)/1 mbar. R_f 0.27 (Hexane/EtOAc, 15/1).

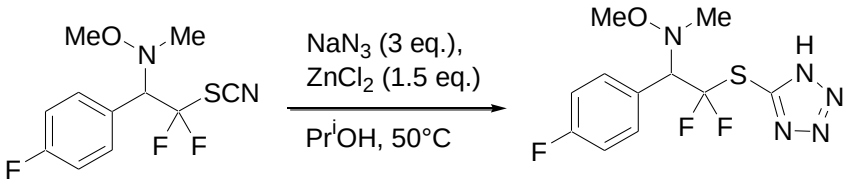
^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.45 – 7.38 (m, 3H), 7.37 – 7.30 (m, 2H), 4.07 (dd, 1H, *J* = 20.7, 7.5 Hz), 2.31 (s, 6H).

$^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$), δ: 134.2 (dd, *J* = 303.7, 296.6 Hz), 130.6 (d, *J* = 3.6 Hz), 129.4, 128.6, 128.3 (d, *J* = 2.2 Hz), 108.9 (d, *J* = 3.5 Hz), 73.5 (dd, *J* = 26.0, 19.1 Hz), 42.4 (d, *J* = 1.6 Hz).

^{19}F NMR (282 MHz, $CDCl_3$), δ: -64.0 (dd, *J* = 183.9, 7.6 Hz), -69.0 (dd, *J* = 183.9, 20.7 Hz).

HRMS (ESI): calcd for $C_{11}H_{13}F_2N_2S$ (M+H) 243.0762, found 243.0760.

_N_-(2,2-Difluoro-1-(4-fluorophenyl)-2-(1_H_-tetrazol-5-ylthio)ethyl)-_N,O_-dimethylhydroxylamine (7).



Sodium azide (147 mg, 2.26 mmol) and zinc chloride (154 mg, 1.13 mmol) were successively added to a solution of compound **3a** (208 mg, 0.75 mmol) in propan-2-ol (4 mL) at room temperature. Then the mixture was heated at 50 °C (oil bath) for 24 h. For the work-up, water (5 mL) was added, and the mixture was extracted with ethyl acetate (3×5 mL). The combined organic phases were filtered through Na_2SO_4, concentrated under vacuum, and the residue was purified by column chromatography on silica gel.

Yield 147 mg (46%). Pale yellow oil. R_f 0.26 (DCM/MeOH, 5/1).

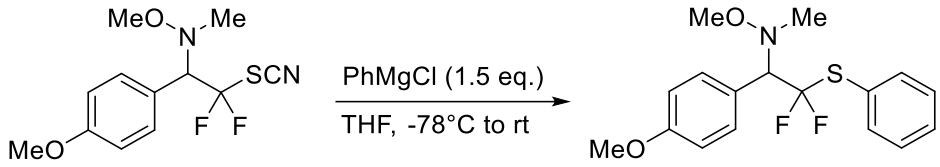
^{1}H NMR (300 MHz, $CDCl_3$), δ: 12.37 – 12.19 (m, 2H), 12.03 – 11.86 (m, 2H), 9.24 (dd, 1H, *J* = 17.1, 8.2 Hz), 8.29 (s, 3H), 7.15 (s, 3H)

$^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$), δ: 162.4 (d, *J* = 245.4 Hz), 149.3 – 149.0 (m), 133.5 (d, *J* = 8.2 Hz), 128.2 (dd, *J* = 294.8, 281.1 Hz), 127.5 (d, *J* = 2.7 Hz), 114.8 (d, *J* = 21.3 Hz), 73.5 (dd, *J* = 25.6, 22.1 Hz), 59.1, 41.9

^{19}F NMR (282 MHz, $CDCl_3$), δ: -66.6 (d, 1F, *J* = 201.5 Hz), -69.7 (dd, 1F, *J* = 201.5, 14.5 Hz), -108.46 – -108.61 (m, 1F).

HRMS (ESI): calcd for $C_{11}H_{13}F_3N_5OS$ (M+H) 320.0787, found 320.0776.

***N*-[2,2-Difluoro-1-(4-methoxyphenyl)-2-(phenylthio)ethyl]-*N,O*-dimethylhydroxylamine (8).**



A solution of PhMgCl in THF (1.86 M, 715 µL, 1.33 mmol) was added dropwise to a solution of thiocyanate **3c** (256 mg, 0.89 mmol) in THF (5 mL) at -78 °C (acetone bath). The temperature was slowly raised to 5 °C during 3 h. The completion of the reaction was checked by GC and then the mixture was quenched by addition of methanol (1 mL). For the work-up, water (5 mL) was added, and the mixture was extracted with DCM (3×5 mL). The combined organic phases were filtered through Na_2SO_4, concentrated under vacuum and the residue was purified by column chromatography on silica gel.

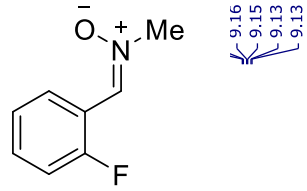
Yield 188 mg (63%). Colorless crystals. R_f 0.20 (Hexane/EtOAc, 20/1). Mp 81 – 82 °C.

^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.63 (dm, 2H, *J* = 8.5 Hz), 7.49 – 7.29 (m, 5H), 6.92 (dm, 2H, *J* = 8.5 Hz), 4.14 (dd, *J* = 12.0, 10.0 Hz, 1H), 3.82 (s, 3H), 3.69 (s, 3H), 2.52 (s, 3H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$), δ: 160.0, 136.5, 132.3, 129.6, 129.5 (dd, *J* = 281.0, 268.9 Hz), 128.9, 127.4 (t, *J* = 2.0 Hz), 124.4, 113.6, 76.3 (dd, *J* = 24.7, 22.5 Hz), 59.7, 55.2, 42.8 (t, *J* = 1.5 Hz).

^{19}F NMR (282 MHz, $CDCl_3$), δ: -73.4 (d, *J* = 206.0 Hz), -75.8 (dd, *J* = 206.0, 12.0 Hz)

HRMS (ESI): calcd for $C_{17}H_{20}F_2NO_2S$ (M+H) 340.1177, found 340.1170.

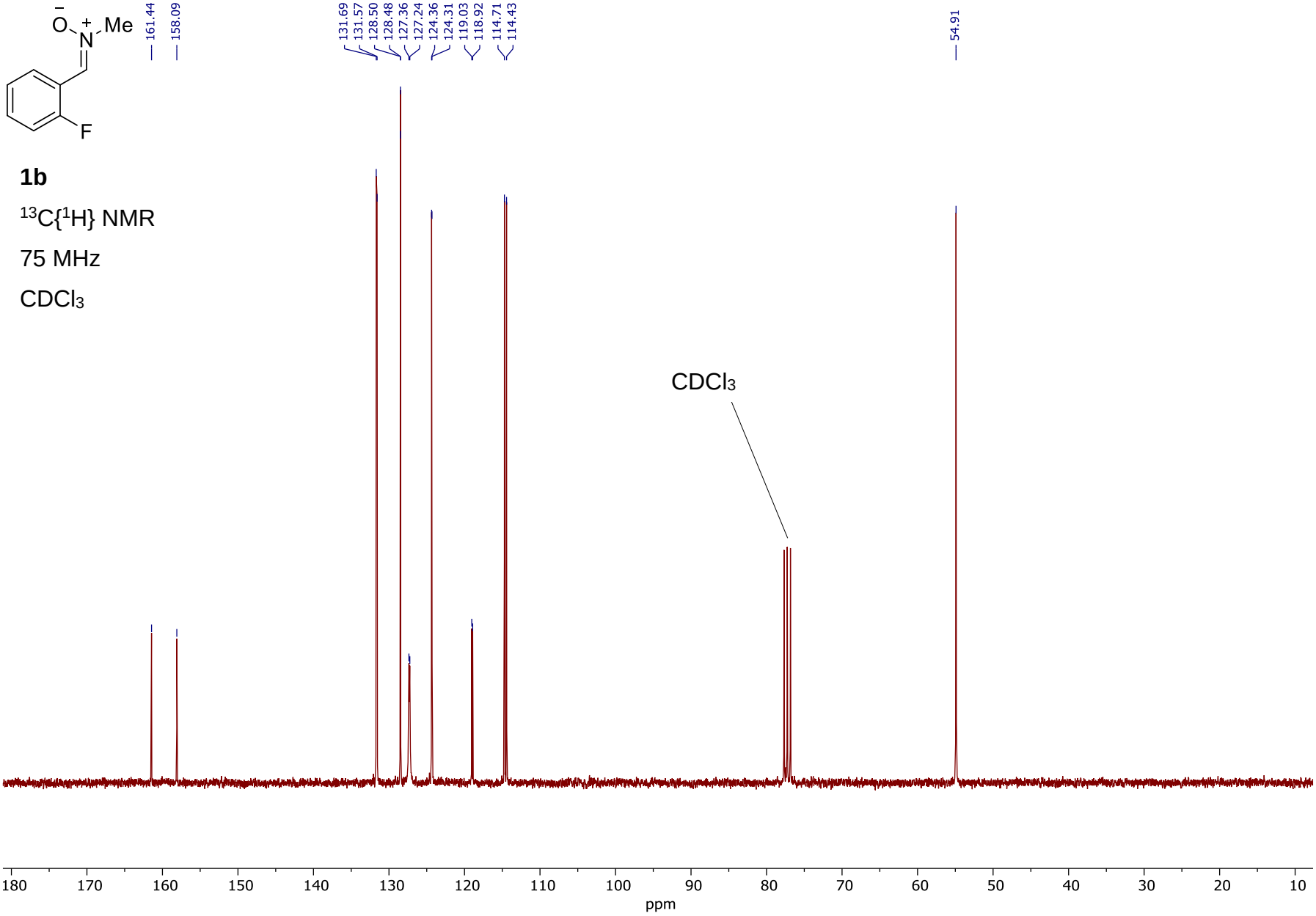


1b

^{1}H NMR

300 MHz

$CDCl_3$

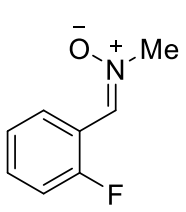


1b

$^{13}C\{^{1}H\}$ NMR

75 MHz

$CDCl_3$

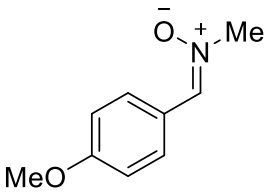


1b

^{19}F NMR

282 MHz

$CDCl_3$

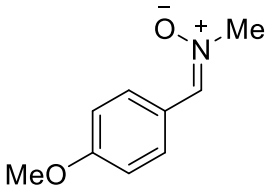


1c

^{1}H NMR

300 MHz

$CDCl_3$

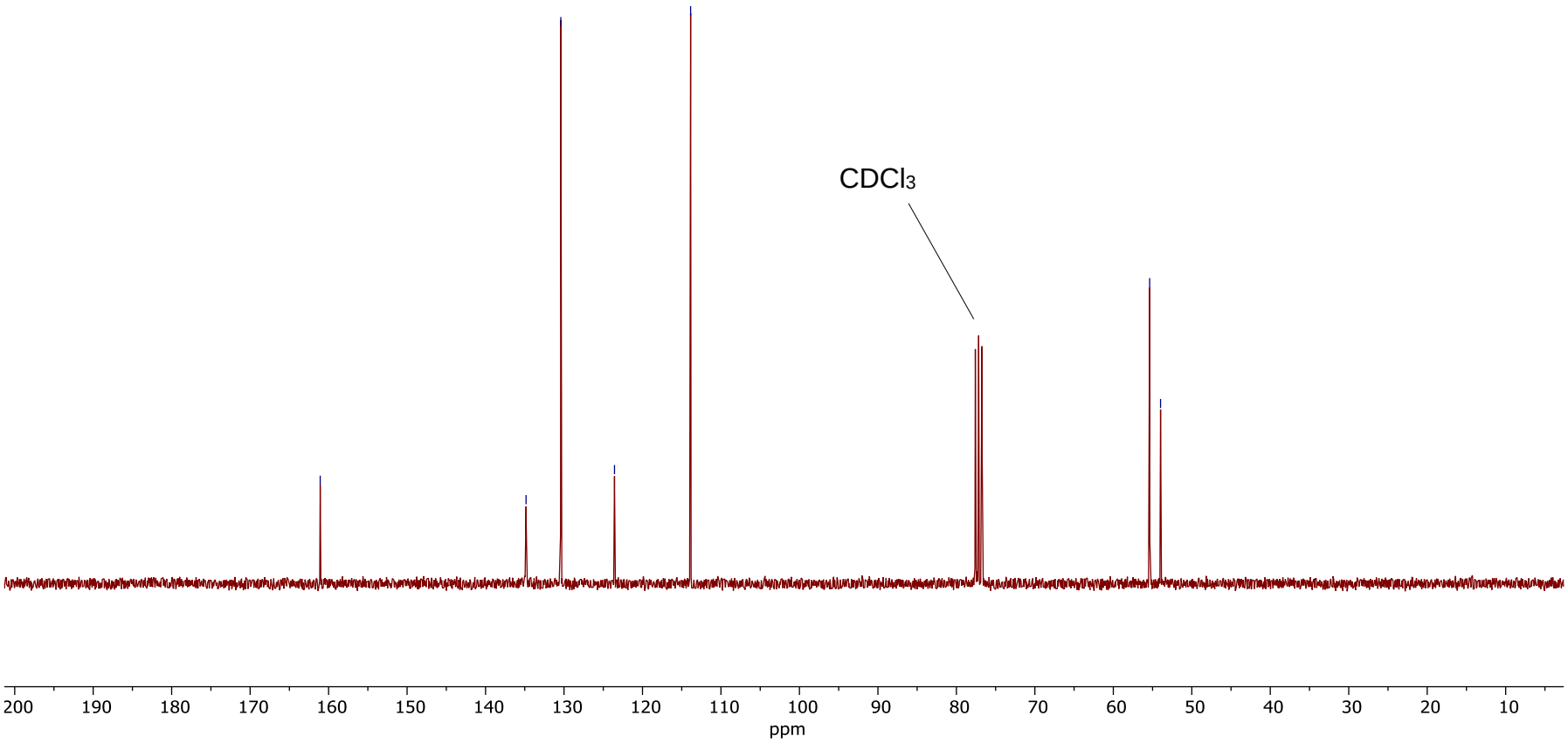


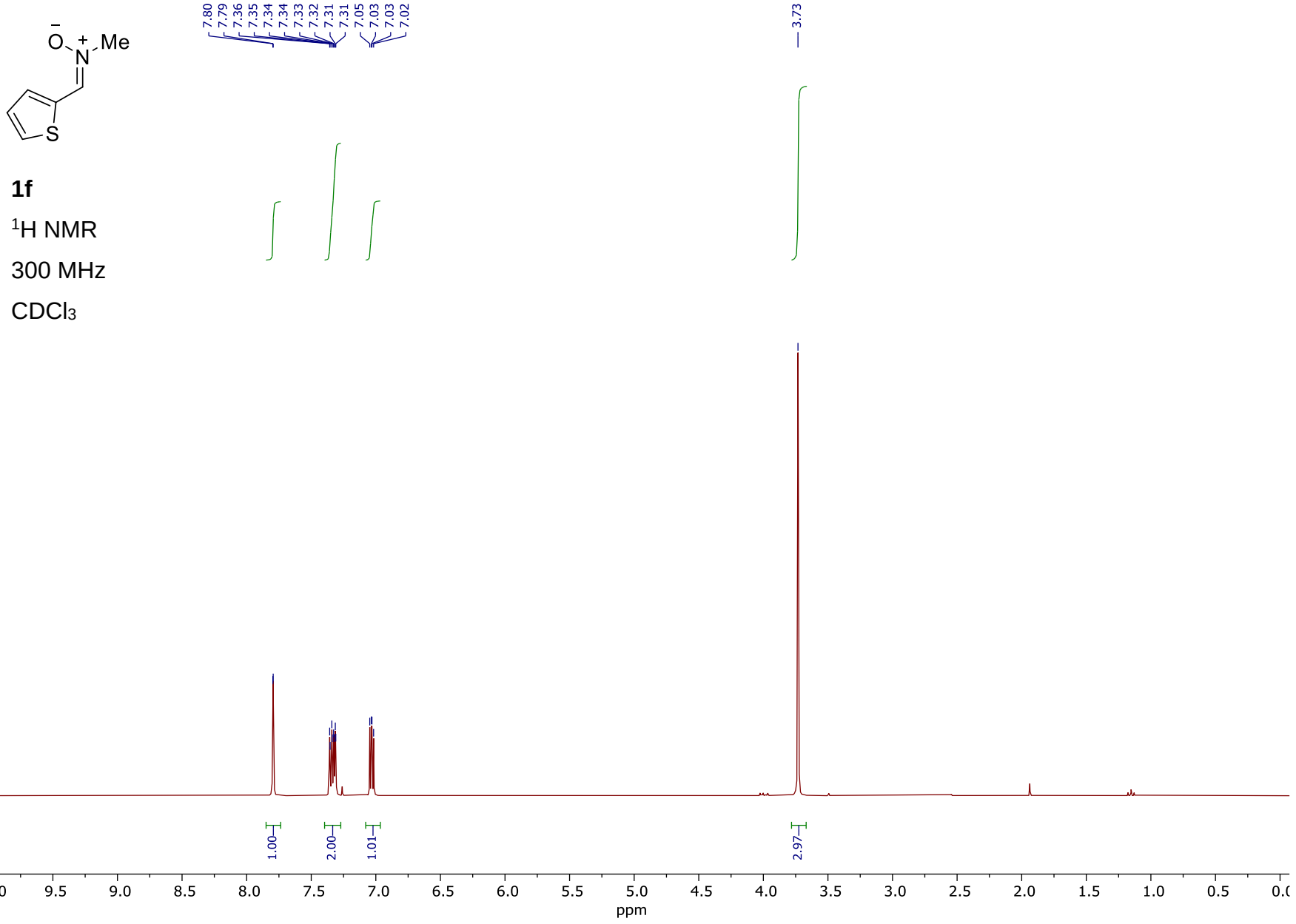
1c

$^{13}C\{^{1}H\}$ NMR

75 MHz

$CDCl_3$



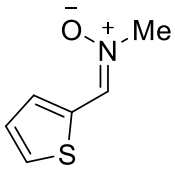


1f

^{1}H NMR

300 MHz

$CDCl_3$

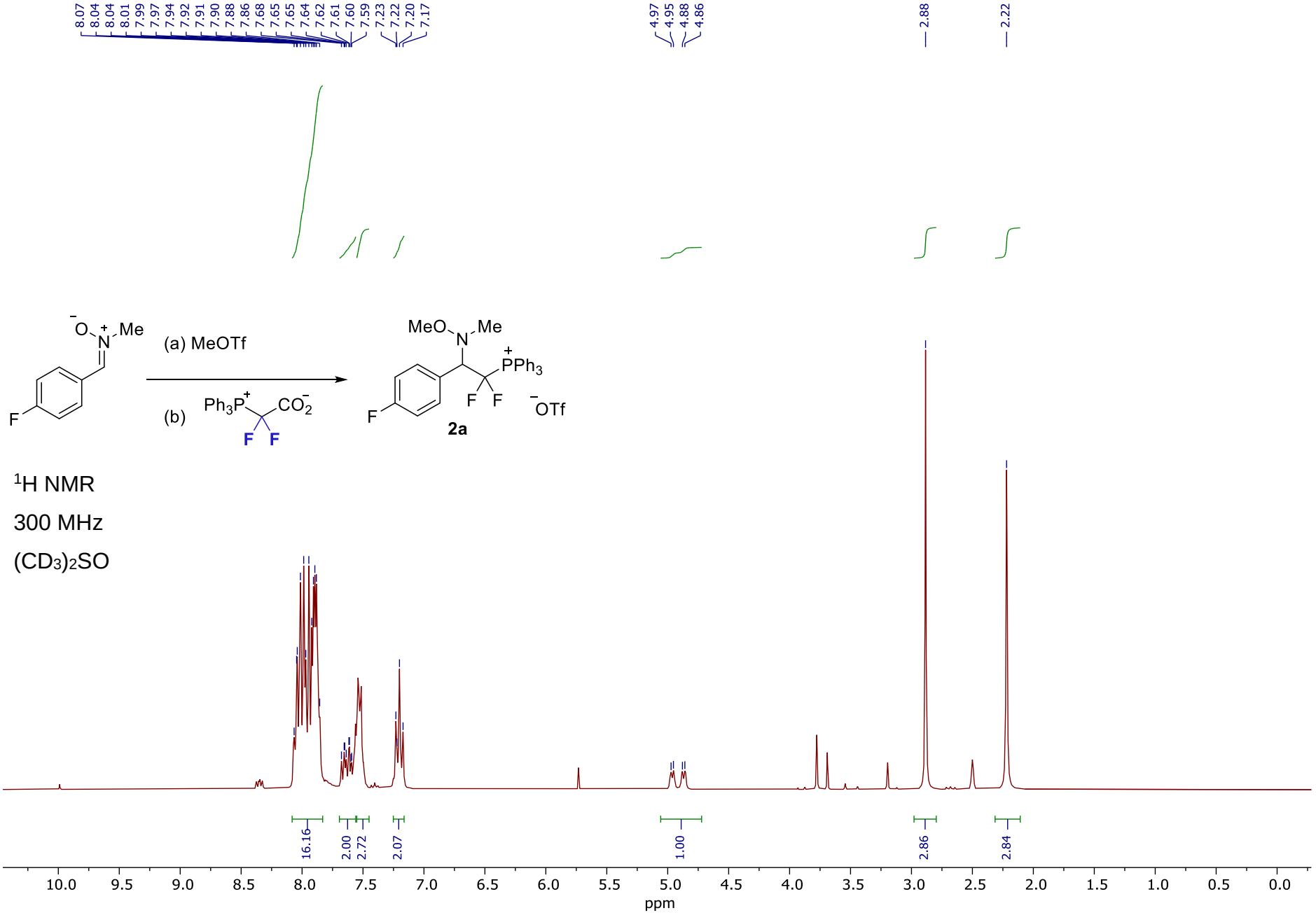


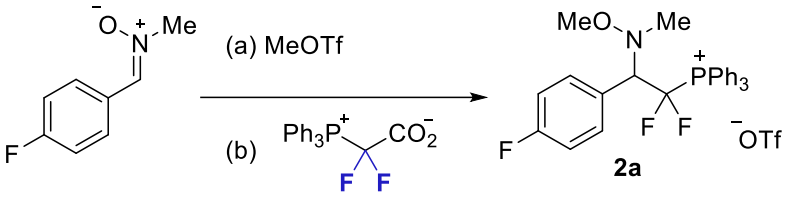
1f

$^{13}C\{^{1}H\}$ NMR

75 MHz

$CDCl_3$

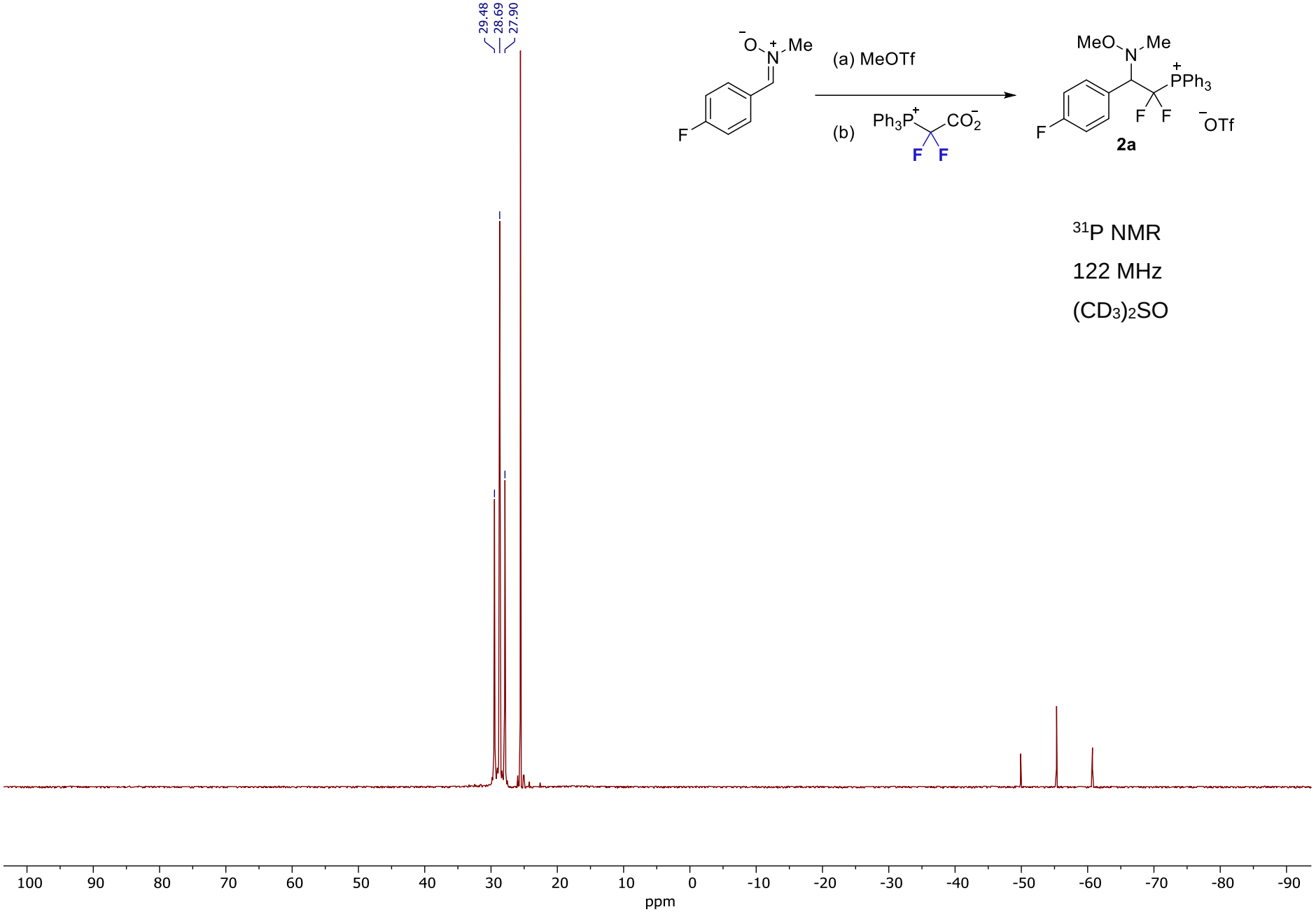

8.07
8.04
8.04
8.01
7.99
7.97
7.94
7.92
7.91
7.90
7.88
7.86
7.68
7.65
7.65
7.64
7.62
7.61
7.60
7.59
7.23
7.22
7.20
7.17
4.97
4.95
4.88
4.86
2.88
2.22
(a) MeOTf
(b)
2a
1H NMR
300 MHz
(CD3)2SO
16.16
2.00
2.72
2.07
1.00
2.86
2.84
ppm

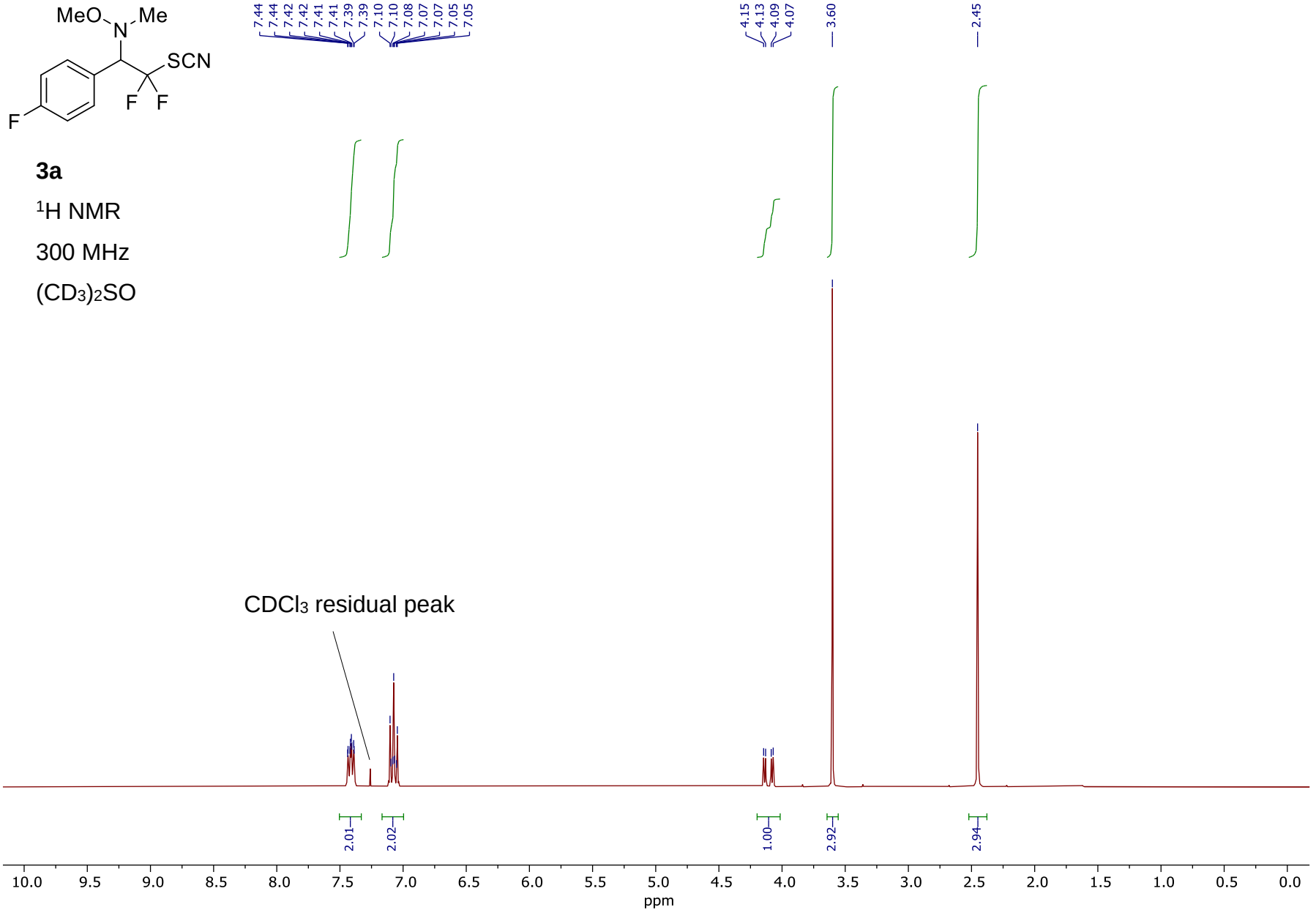


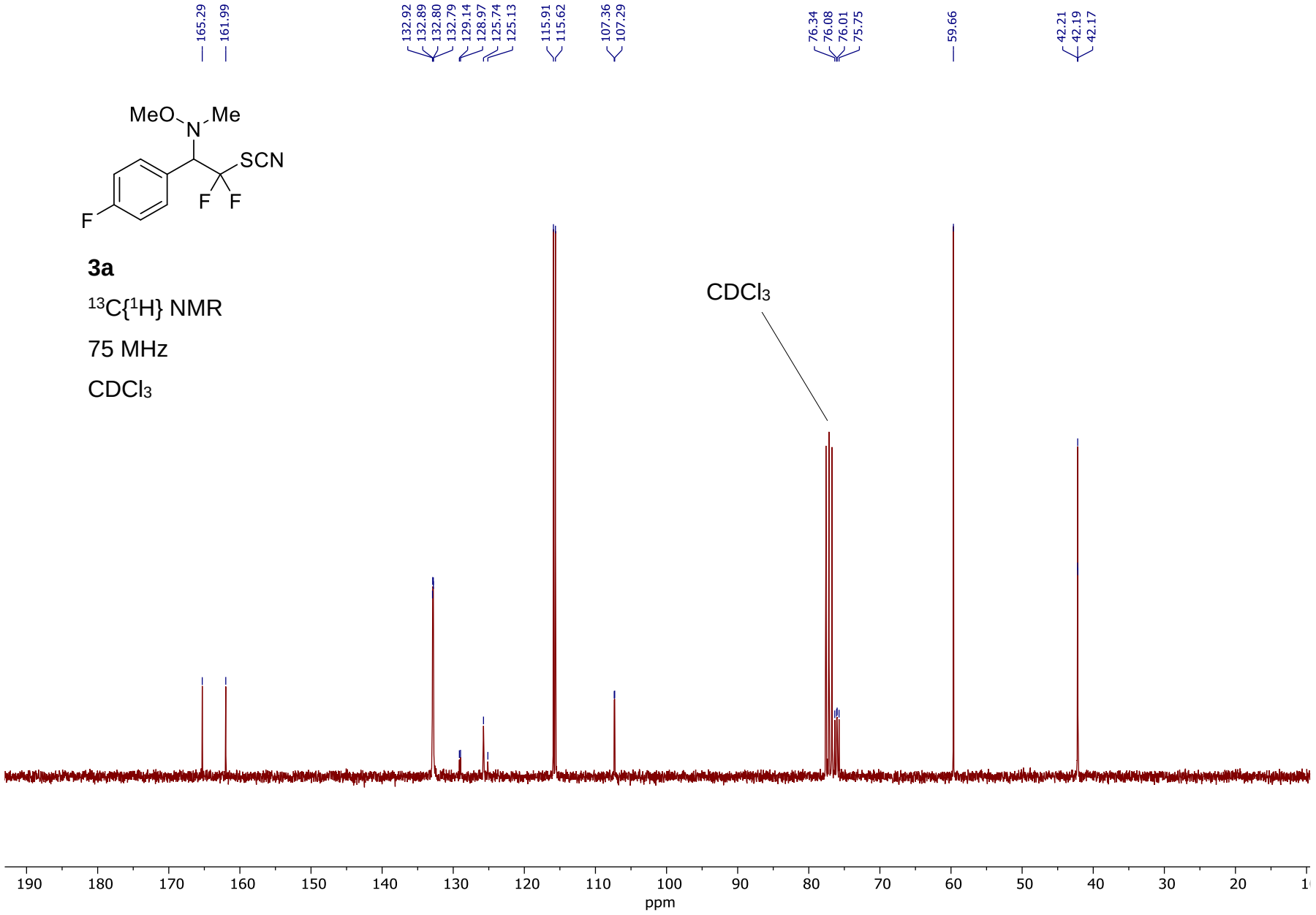
^{19}F NMR

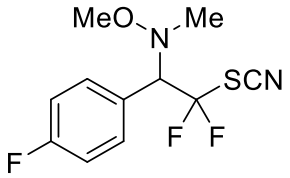
282 MHz

$(CD_3)_2SO$


29.48
28.69
27.90
(a) MeOTf
(b)
2a
31P NMR
122 MHz
(CD3)2SO
ppm


MeO
N
Me
SCN
F
F
F
3a
1H NMR
300 MHz
(CD3)2SO
7.44
7.44
7.42
7.42
7.41
7.41
7.39
7.39
7.10
7.10
7.08
7.07
7.07
7.05
7.05
4.15
4.13
4.09
4.07
3.60
2.45
CDCl3 residual peak
2.01
2.02
1.00
2.92
2.94
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
ppm


165.29
161.99
132.92
132.89
132.80
132.79
129.14
128.97
125.74
125.13
115.91
115.62
107.36
107.29
76.34
76.08
76.01
75.75
59.66
42.21
42.19
42.17
MeO
N
Me
SCN
F
F
F
3a
13C{1H} NMR
75 MHz
CDCl3
CDCl3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

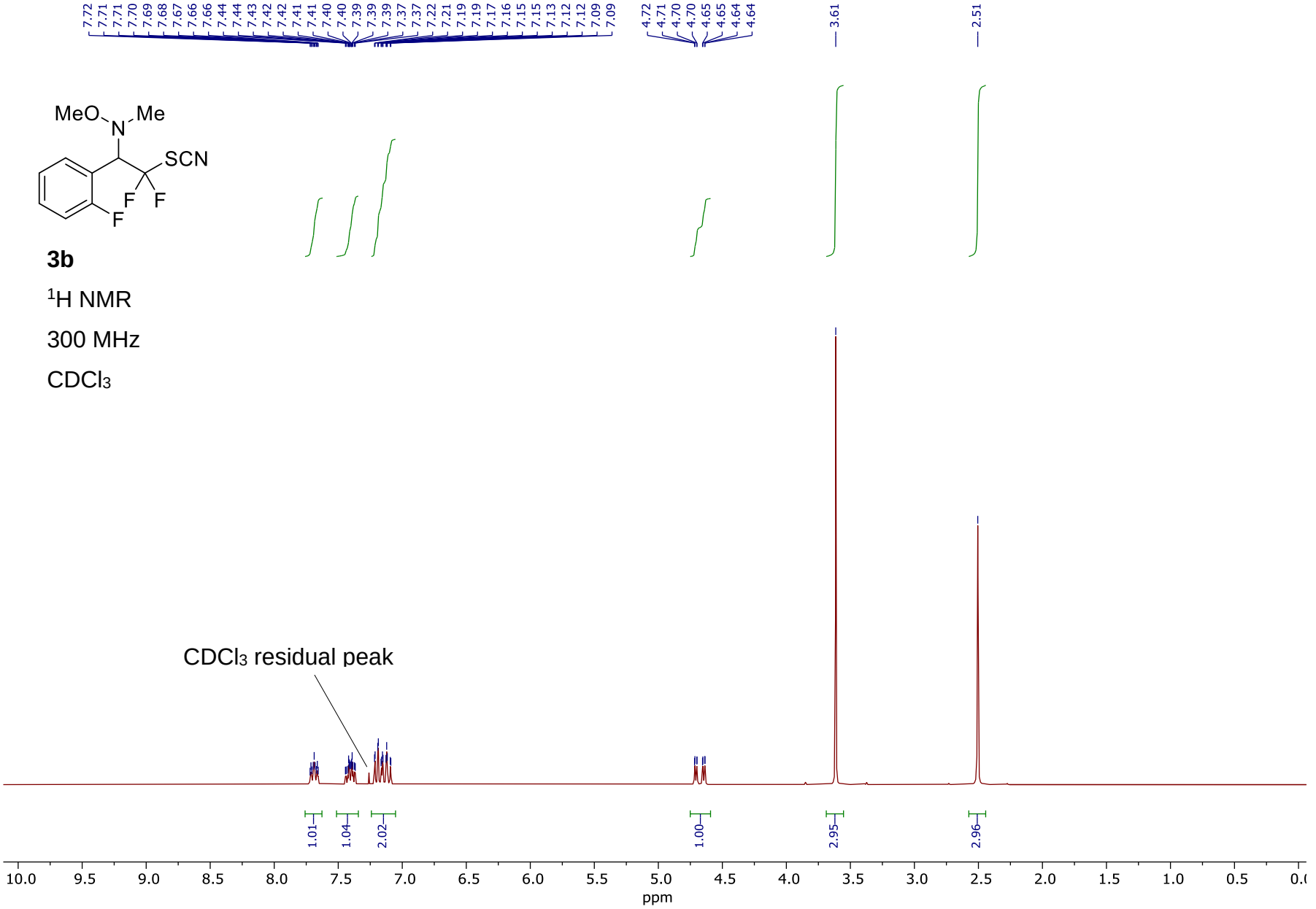


3a

^{19}F NMR

282 MHz

$CDCl_3$


7.72
7.71
7.71
7.70
7.69
7.68
7.67
7.66
7.66
7.44
7.44
7.43
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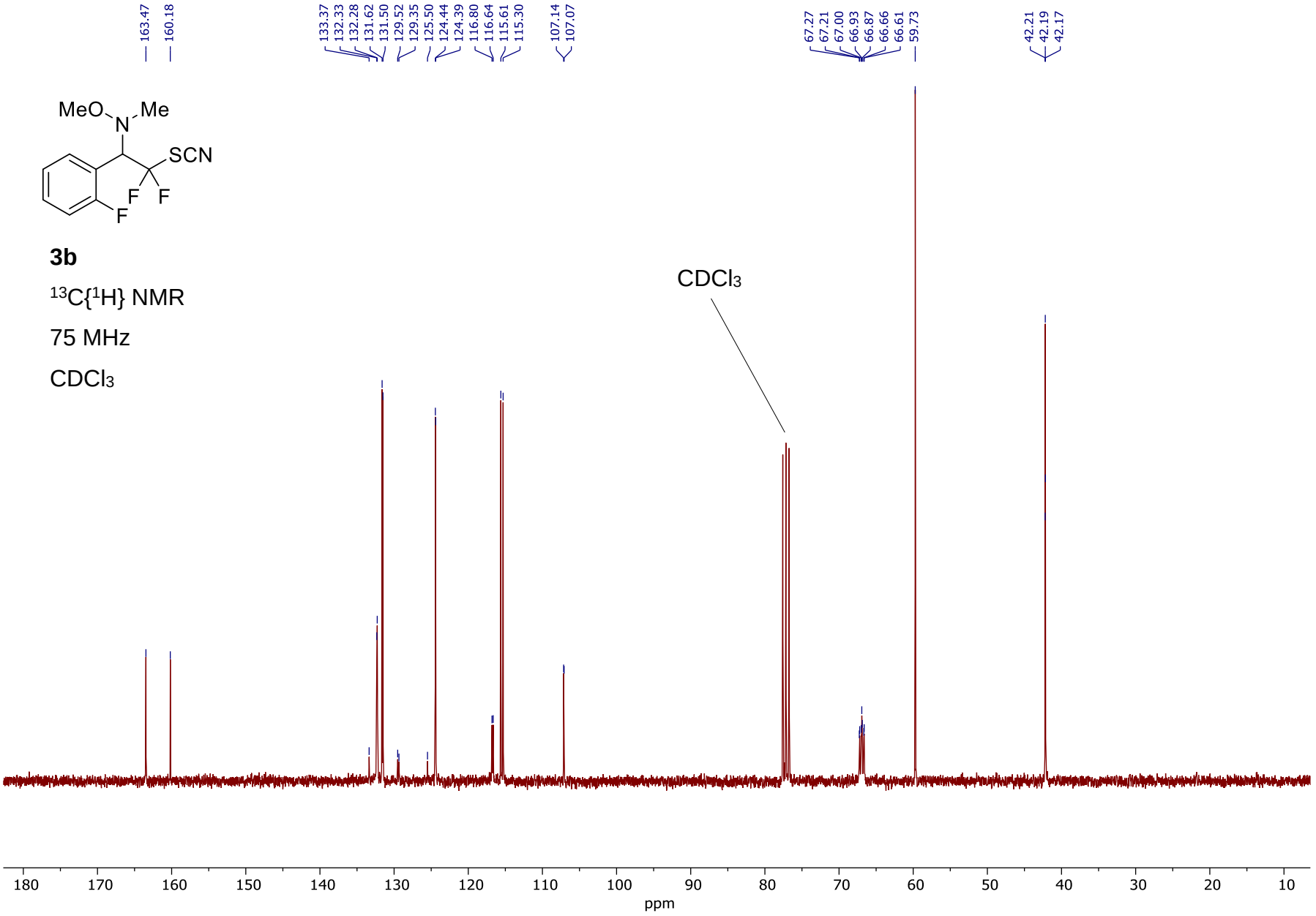
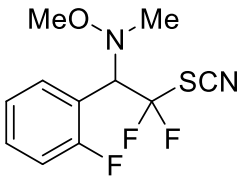
7.42
7.41
7.41
7.40
7.40
7.39
7.39
7.39
7.37
7.37
7.22
7.21
7.19
7.19
7.17
7.16
7.15
7.15
7.13
7.12
7.12
7.09
7.09
4.72
4.71
4.70
4.70
4.65
4.65
4.64
4.64
3.61
2.51
MeO
N
Me
SCN
F
F
F
3b
1H NMR
300 MHz
CDCl3
CDCl3 residual peak
1.01
1.04
2.02
1.00
2.95
2.96
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


163.47
160.18
133.37
132.33
132.28
131.62
131.50
129.52
129.35
125.50
124.44
124.39
116.80
116.64
115.61
115.30
107.14
107.07
67.27
67.21
67.00
66.93
66.87
66.66
66.61
59.73
42.21
42.19
42.17
MeO
N
Me
SCN
F
F
F
3b
13C{1H} NMR
75 MHz
CDCl3
CDCl3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

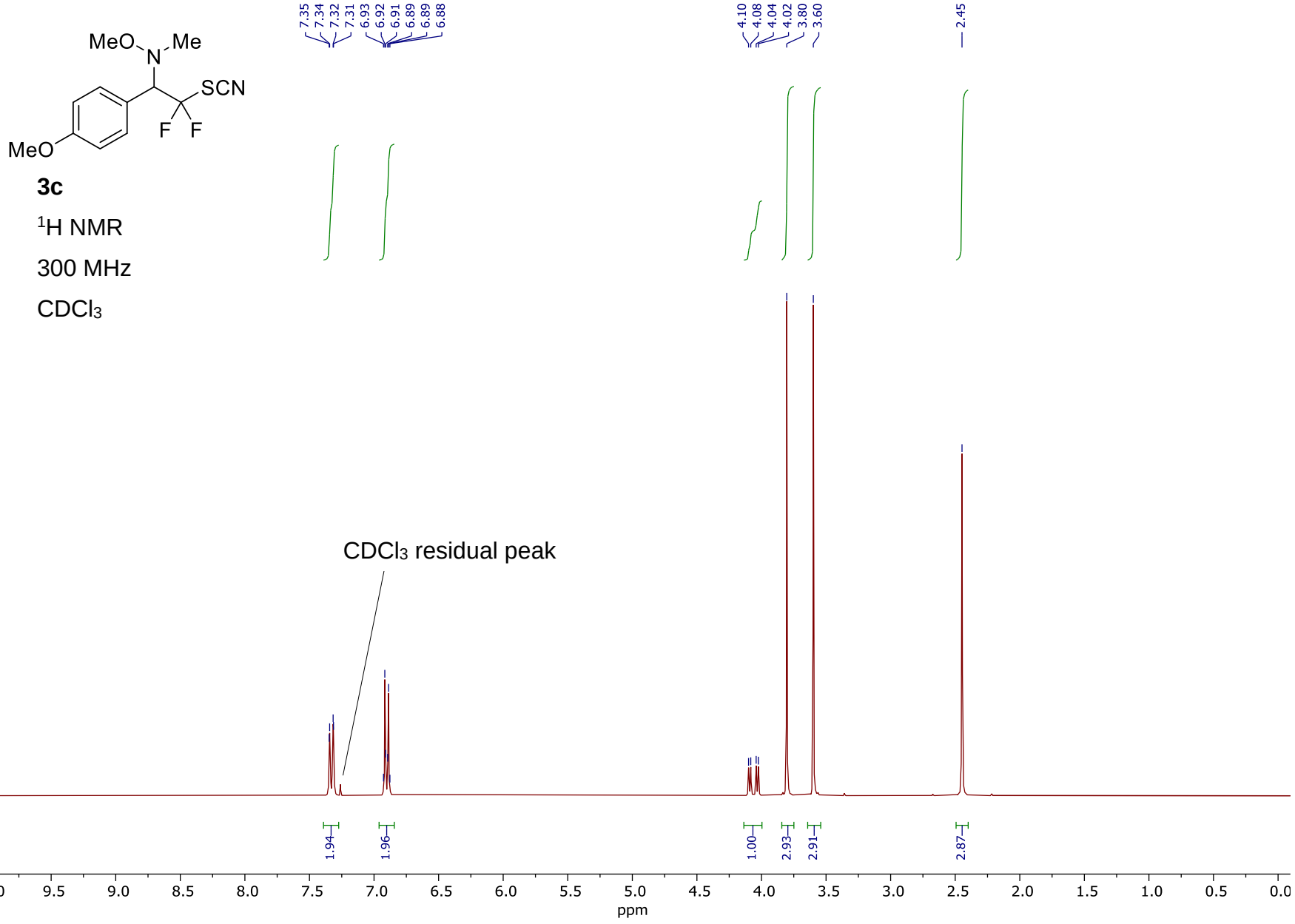


3b

^{19}F NMR

282 MHz

$CDCl_3$


MeO
N
Me
SCN
F
F
MeO
3c
1H NMR
300 MHz
CDCl3
7.35
7.34
7.32
7.31
6.93
6.92
6.91
6.89
6.89
6.88
4.10
4.08
4.04
4.02
3.80
3.60
2.45
CDCl3 residual peak
1.94
1.96
1.00
2.93
2.91
2.87
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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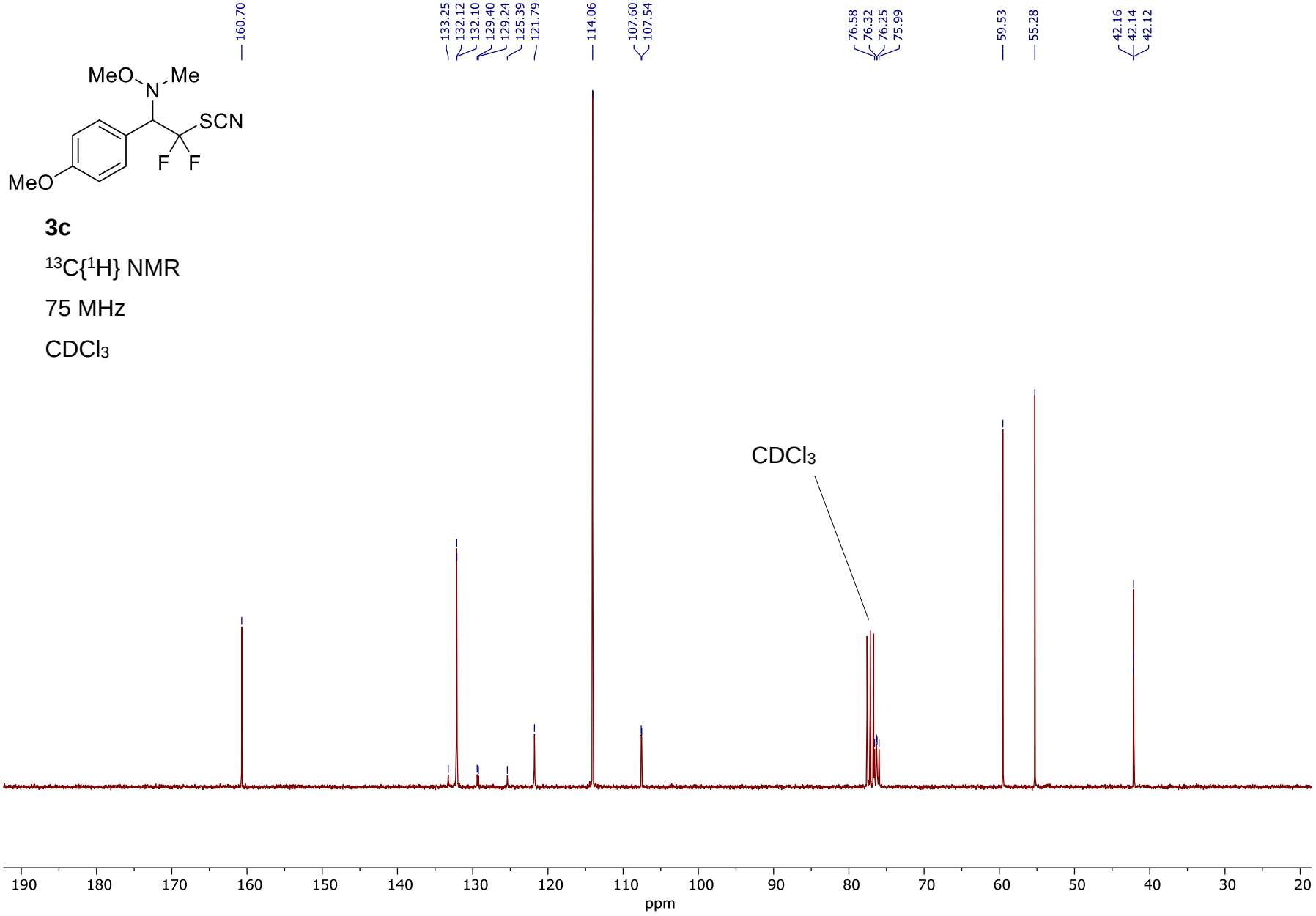
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

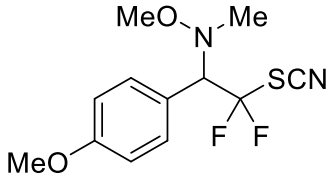


3c

$^{13}C\{^{1}H\}$ NMR

75 MHz

$CDCl_3$

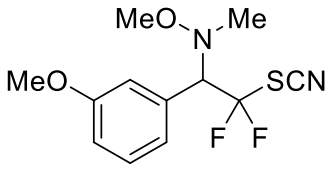


3c

^{19}F NMR

282 MHz

$CDCl_3$

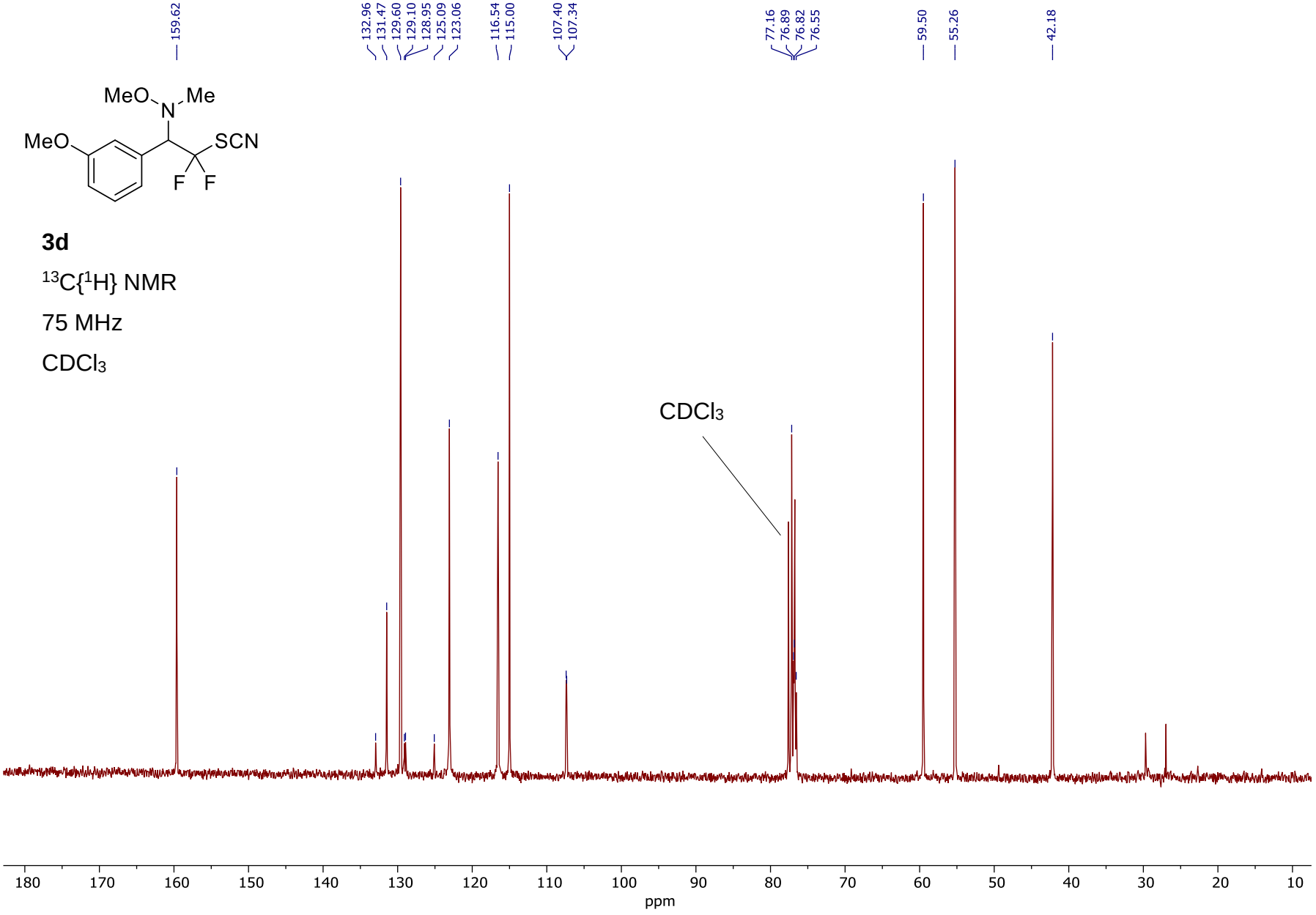


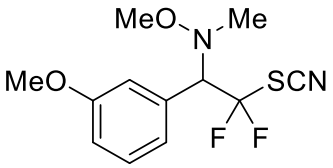
3d

^{1}H NMR

300 MHz

$CDCl_3$


159.62
132.96
131.47
129.60
129.10
128.95
125.09
123.06
116.54
115.00
107.40
107.34
77.16
76.89
76.82
76.55
59.50
55.26
42.18
MeO
N
Me
MeO
SCN
F
F
3d
13C{1H} NMR
75 MHz
CDCl3
CDCl3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

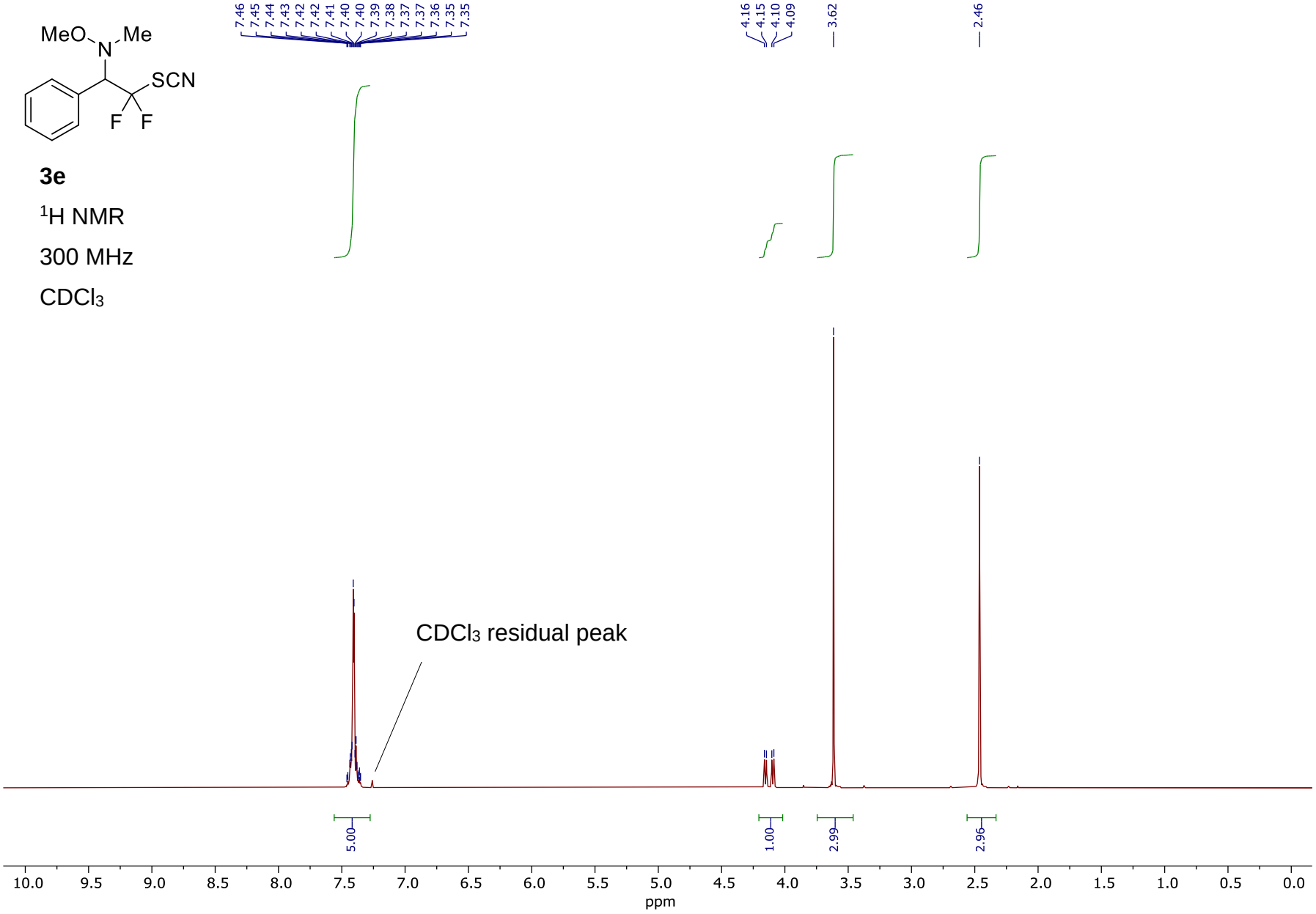


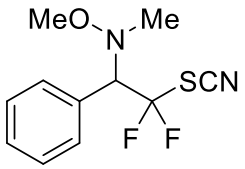
3d

^{19}F NMR

282 MHz

$CDCl_3$


MeO
N
Me
SCN
F
F
3e
1H NMR
300 MHz
CDCl3
7.46
7.45
7.44
7.43
7.42
7.42
7.41
7.40
7.40
7.39
7.38
7.37
7.37
7.36
7.35
7.35
4.16
4.15
4.10
4.09
3.62
2.46
CDCl3 residual peak
5.00
1.00
2.99
2.96
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
ppm

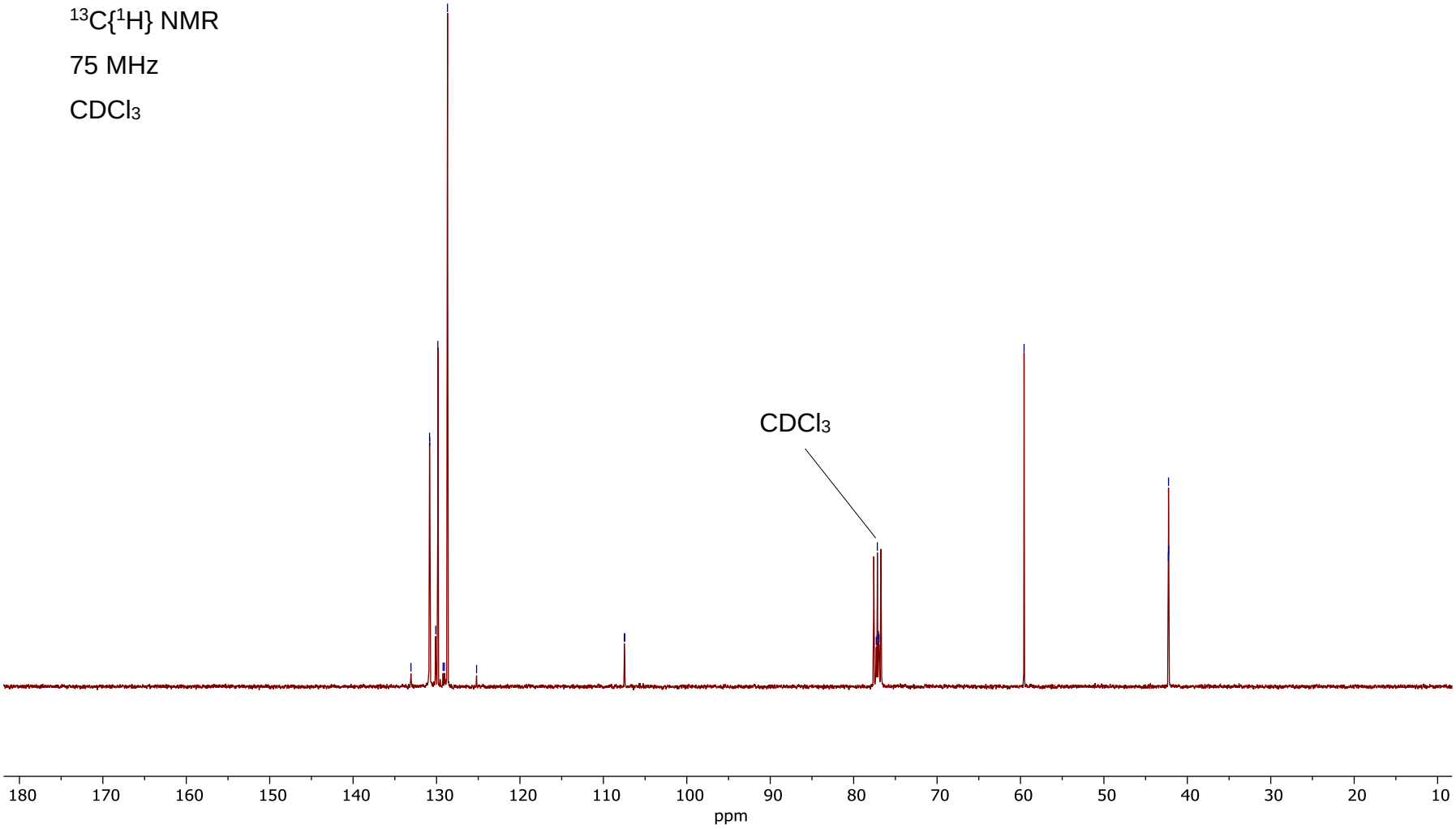


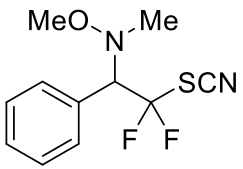
3e

$^{13}C\{^{1}H\}$ NMR

75 MHz

$CDCl_3$



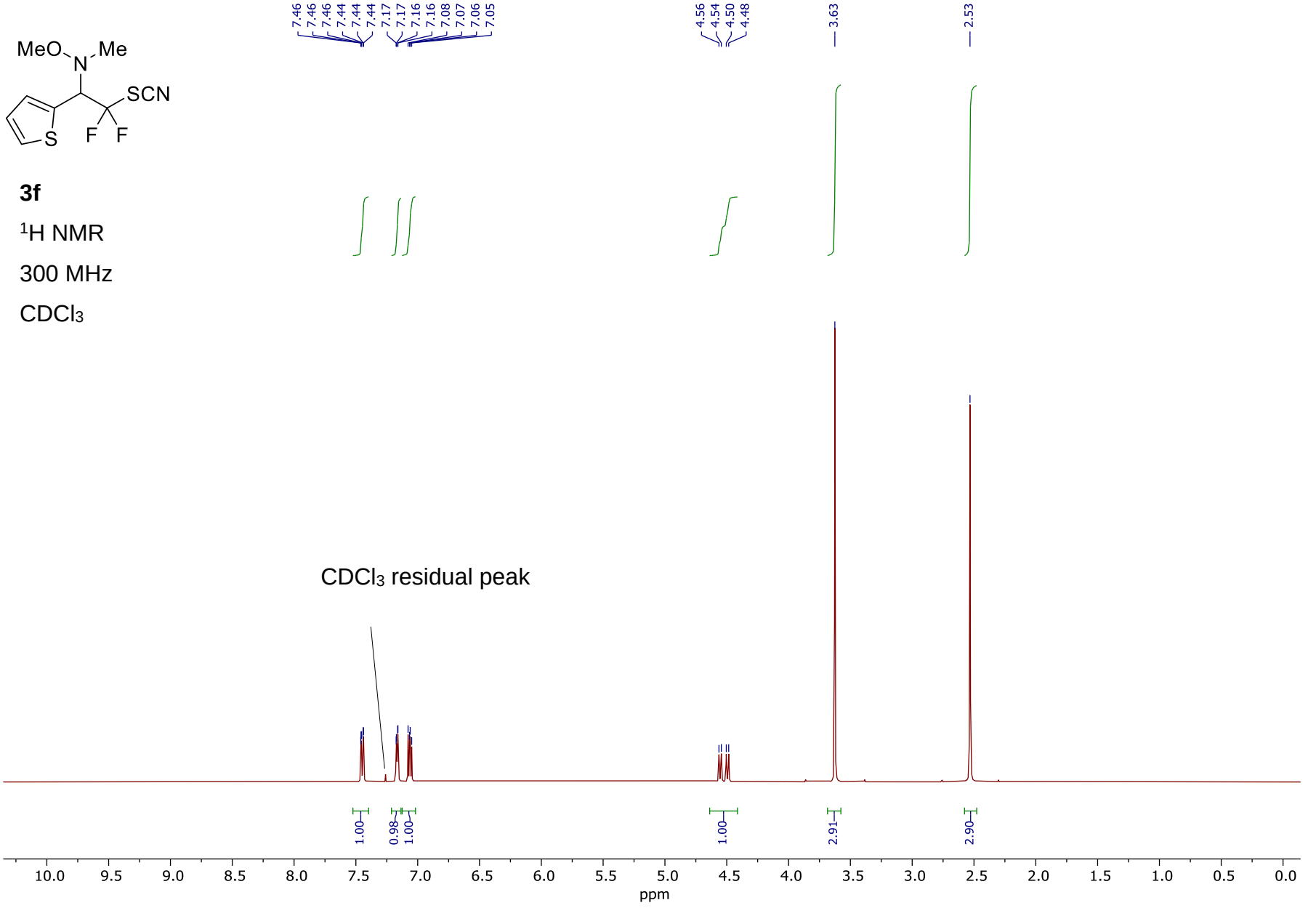


3e

^{19}F NMR

282 MHz

$CDCl_3$

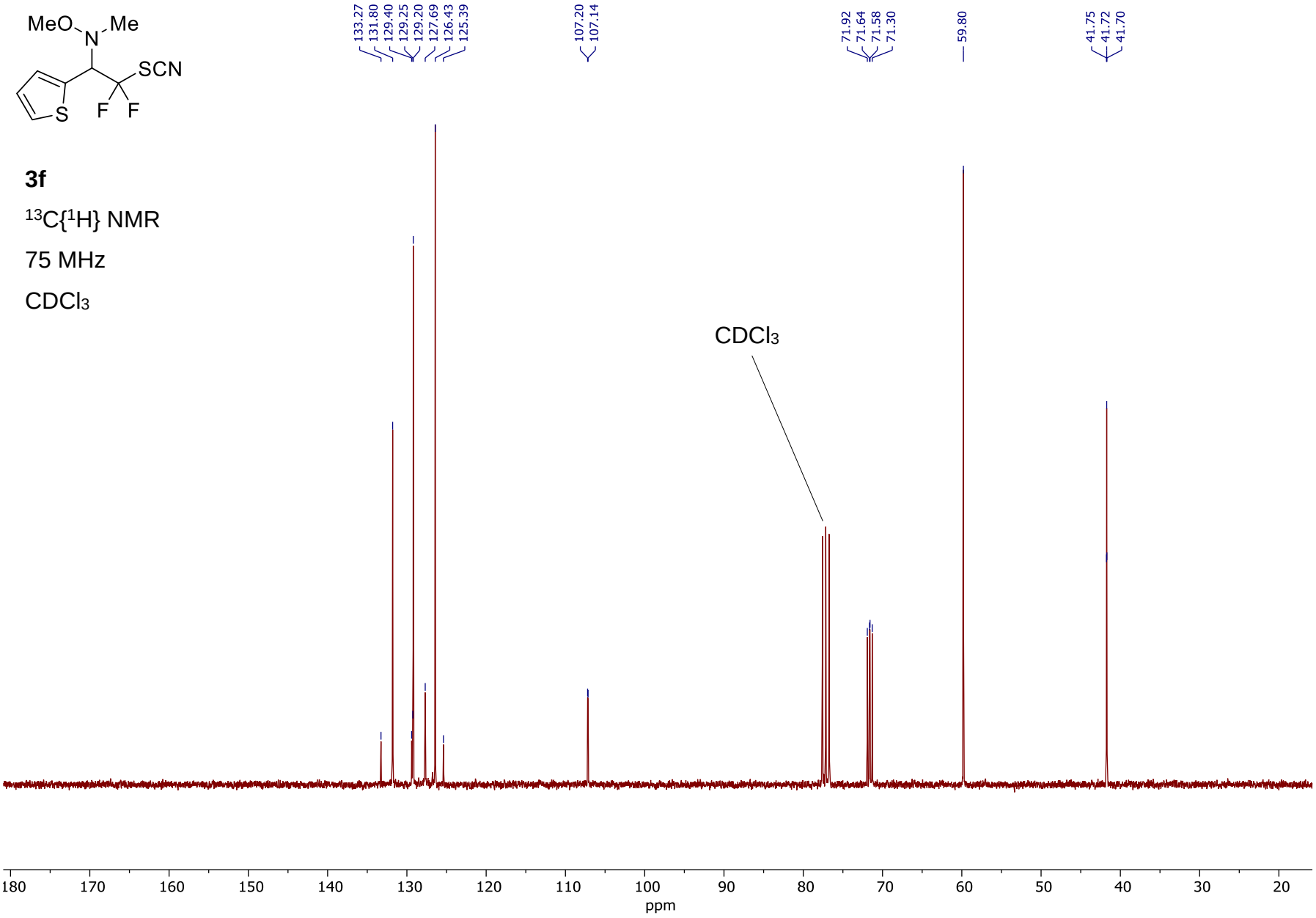


3f

^{1}H NMR

300 MHz

$CDCl_3$

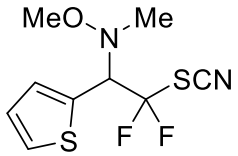


3f

$^{13}C\{^{1}H\}$ NMR

75 MHz

$CDCl_3$

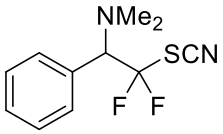


3f

^{19}F NMR

282 MHz

$CDCl_3$

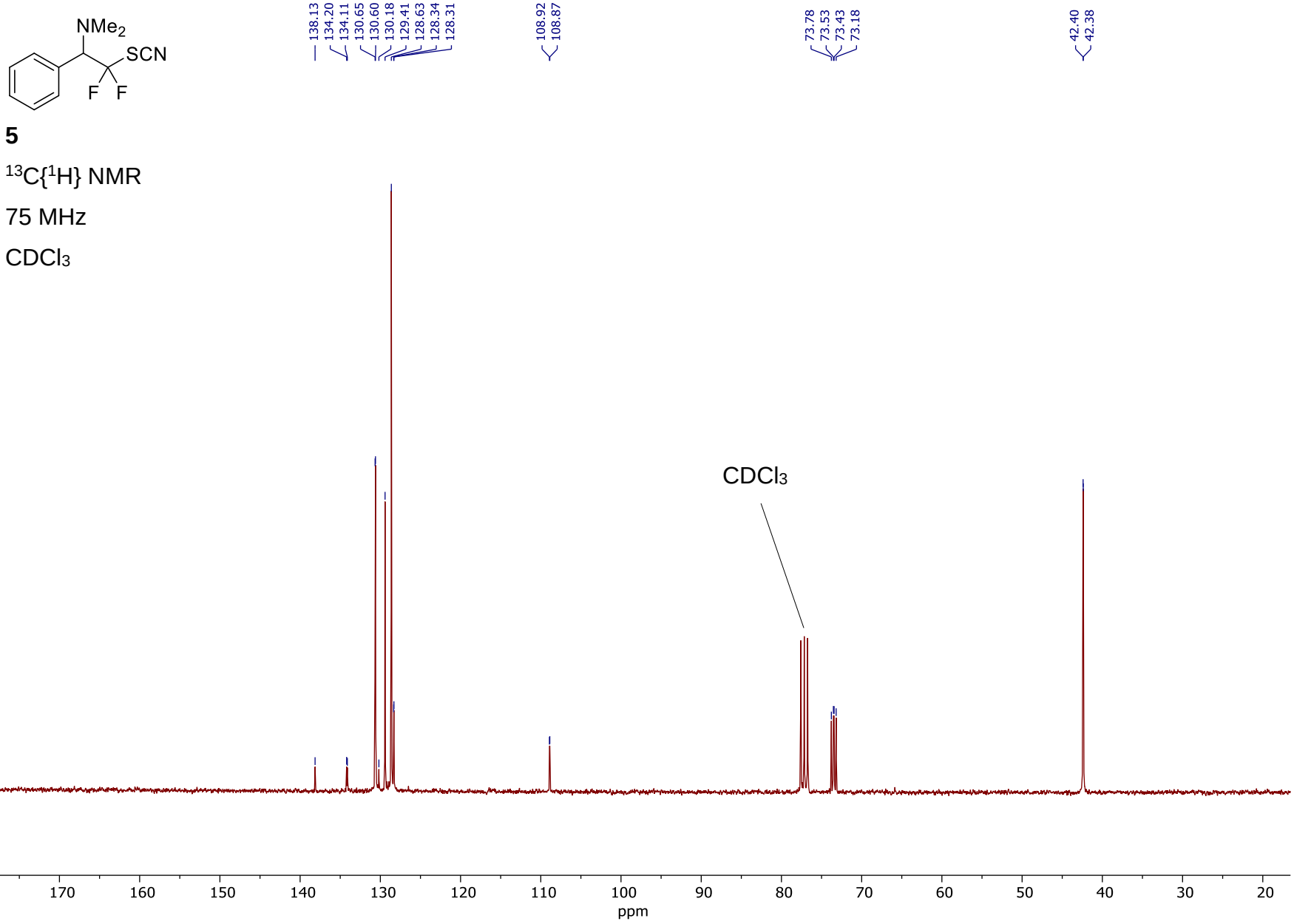


5

^{1}H NMR

300 MHz

$CDCl_3$

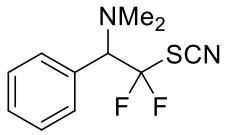


5

$^{13}C\{^{1}H\}$ NMR

75 MHz

$CDCl_3$

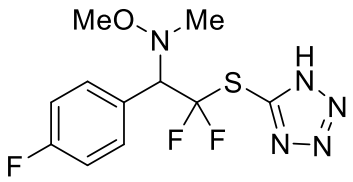


5

^{19}F NMR

282 MHz

$CDCl_3$

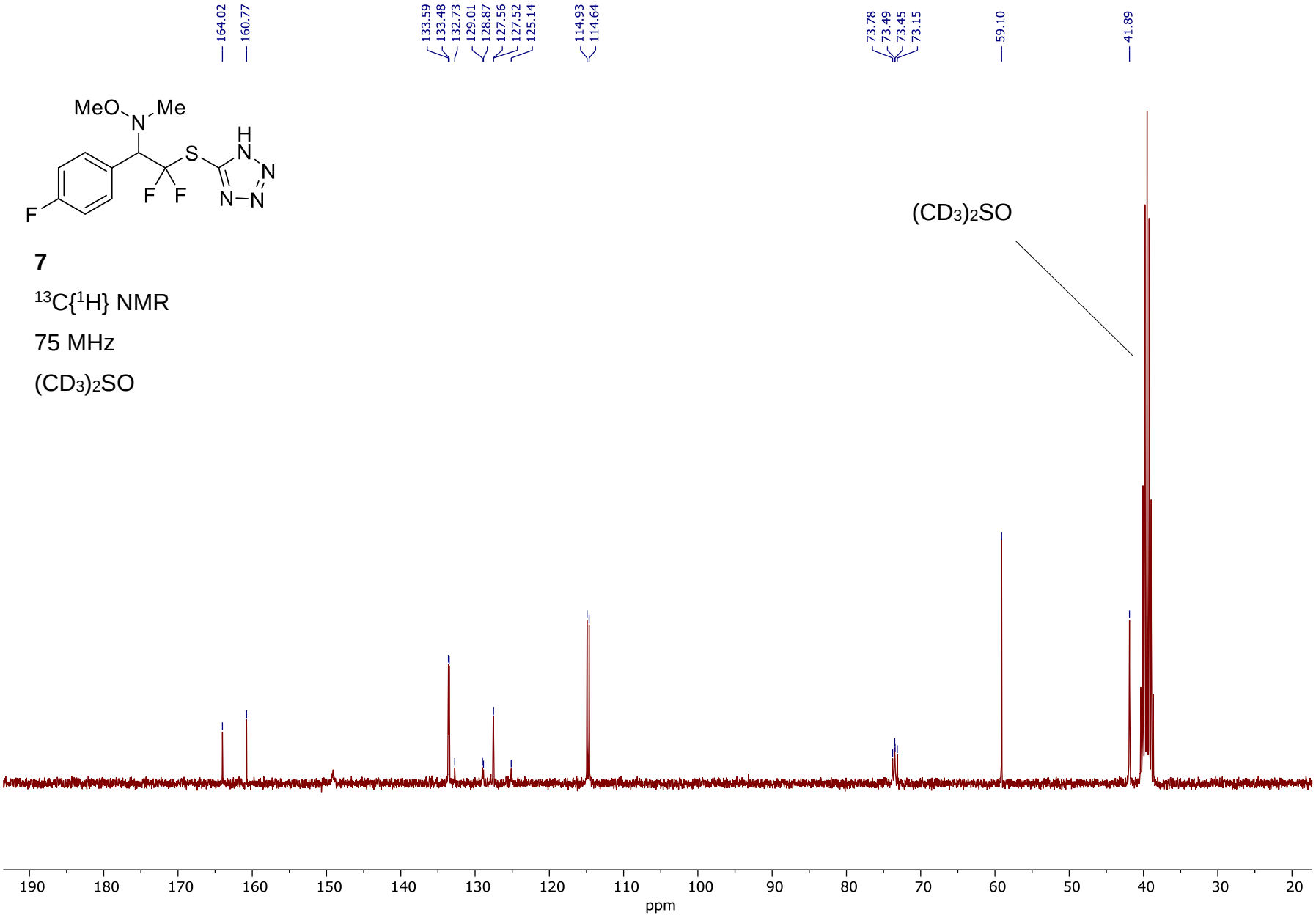


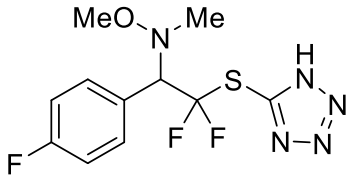
7

^{1}H NMR

300 MHz

$(CD_3)_2SO$


164.02
160.77
133.59
133.48
132.73
129.01
128.87
127.56
127.52
125.14
114.93
114.64
73.78
73.49
73.45
73.15
59.10
41.89
MeO
N
Me
S
H
N
N
N
N
F
F
F
(CD3)2SO
7
13C{1H} NMR
75 MHz
(CD3)2SO
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

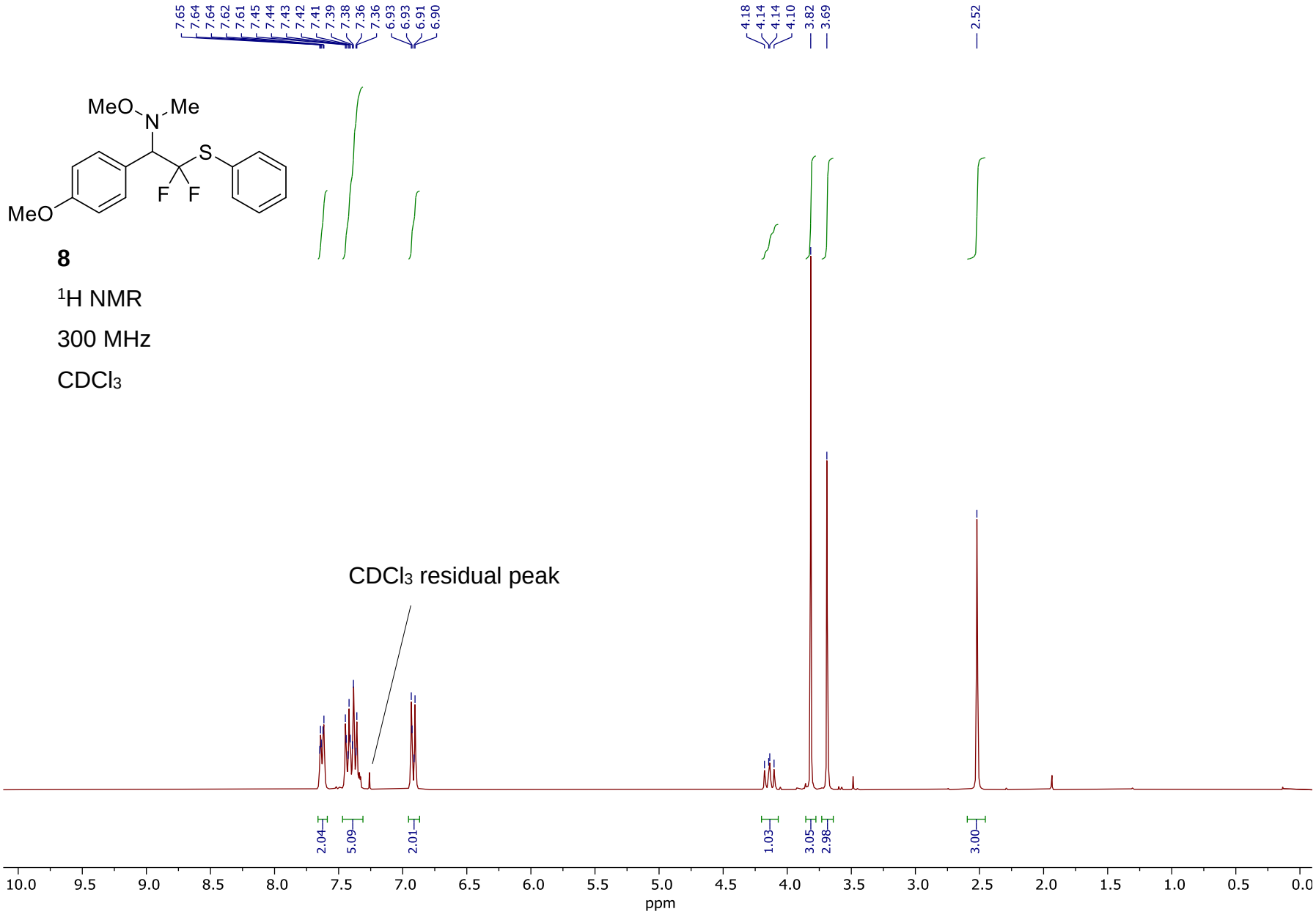


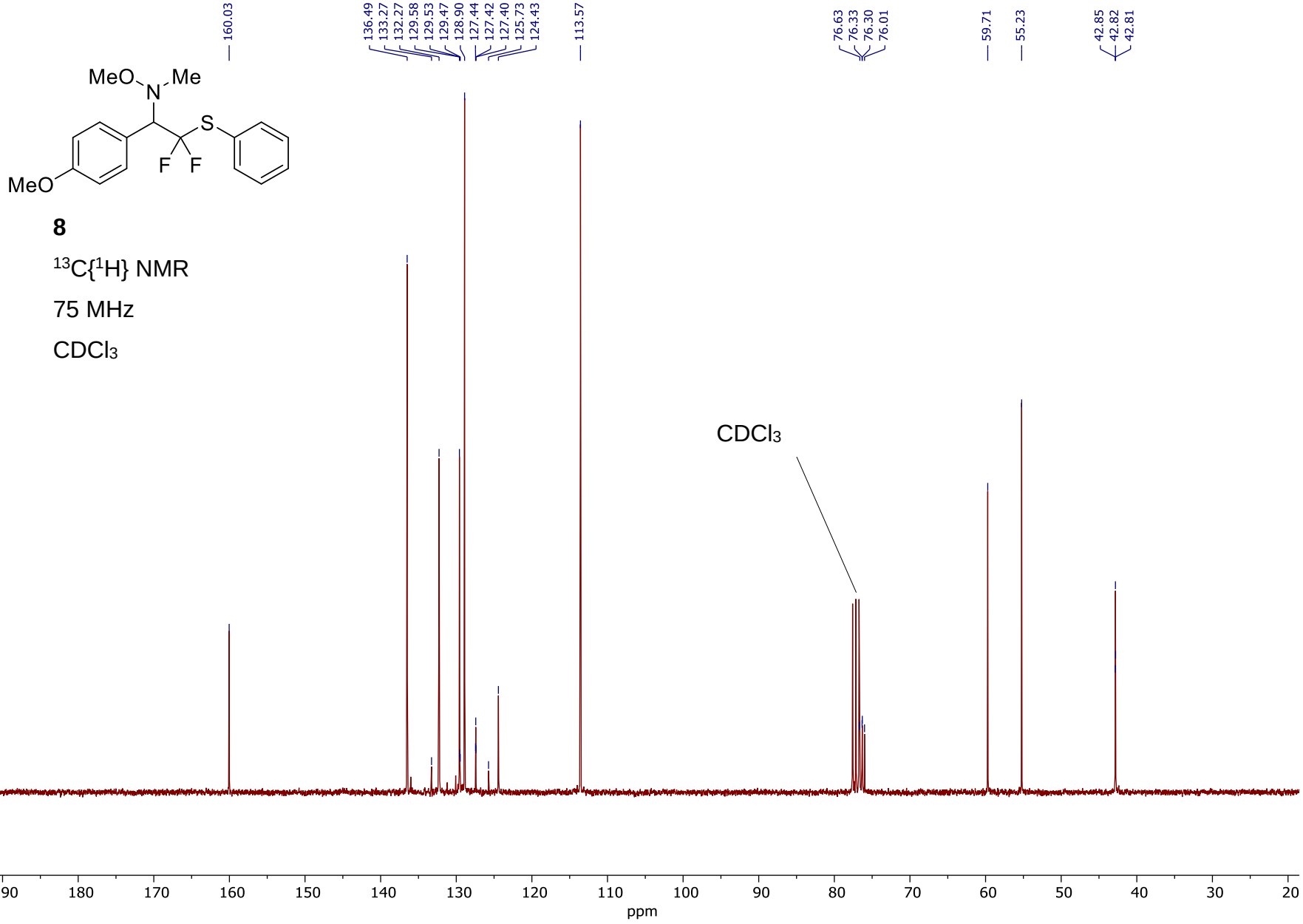
7

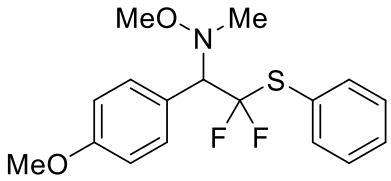
^{19}F NMR

282 MHz

$(CD_3)_2SO$


7.65
7.64
7.64
7.62
7.61
7.45
7.44
7.43
7.42
7.41
7.39
7.38
7.36
7.36
6.93
6.91
6.90
4.18
4.14
4.14
4.10
3.82
3.69
2.52
MeO
N
Me
S
F
F
MeO
8
1H NMR
300 MHz
CDCl3
CDCl3 residual peak
2.04
5.09
2.01
1.03
3.05
2.98
3.00
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
ppm


MeO
N
Me
S
F
F
MeO
8
13C{1H} NMR
75 MHz
CDCl3
160.03
136.49
133.27
132.27
129.58
129.53
129.47
128.90
127.44
127.42
127.40
125.73
124.43
113.57
76.63
76.33
76.30
76.01
59.71
55.23
42.85
42.82
42.81
CDCl3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm



8

^{19}F NMR

282 MHz

$CDCl_3$