Gold Redox Catalysis for Cyclization/Arylation of Allylic Oximes: Synthesis of Isoxazoline Derivatives

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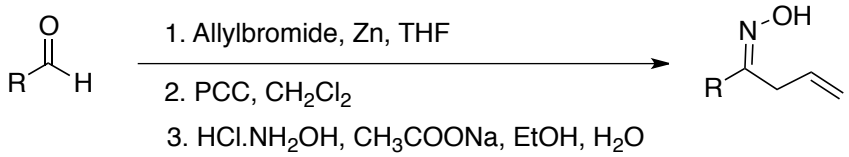
I. General Methods and Materials

All commercial reagents and solvents were obtained from the commercial provider and used without further purification. Analytical thin layer chromatography was performed with pre-coated, glass-baked plates (250μ) and visualized by fluorescence or charring with potassium permanganate stain. Flash column chromatography was performed on 230 - 430 mesh silica gel. ^{1}H NMR, ^{13}C NMR, and ^{19}F NMR spectra were recorded on Agilent 400 MHz. Chemical shifts were reported relative to internal tetramethylsilane (δ 0.00 ppm) or $CDCl_3$ (δ 7.26 ppm) for ^{1}H, $CDCl_3$ (δ 77.0 ppm) for ^{13}C. Data are presented as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t =triplet, dd = doublet of doublets, m = multiplet, br = broad), coupling constant J (Hz) and integration. HRMS were recorded on Agilent 6540 LC/QTOF spectrometer.

1.1 General Procedure for the synthesis of Allyl-oximes 1a- 1n

They were synthesized according to literature procedure[1, 2].



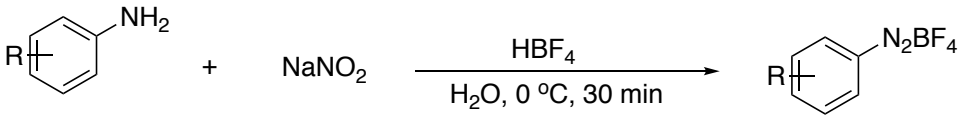
Zinc dust (229 mg, 3.50 mmol) was slowly added to a solution of allylbromide (423 mg, 3.50 mmol) in anhydrous THF (2 mL). The aldehyde (1.00 mmol) was dissolved in anhydrous THF (2 mL) and was added to the stirring solution. The resulting suspension was stirred (sonication was used for a much faster reaction) overnight at room temperature. The reaction was quenched with NH_4Cl (aq.) carefully at 0°C, filtered and extracted with ethyl acetate (3 x 10 mL). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, filtered and concentrated in vacuo.

The crude homoallylic alcohol product was dissolved in dichloromethane (5 mL) and the solution was stirred at 0 °C. Pyridinium chlorochromate (1.75 mL, 3.50 mmol) was added slowly. The resulting suspension was stirred for 1 h at room temperature. The reaction was diluted with H_2O (5 mL) and extracted with ethyl acetate (2 x 10 mL). The combined organic layers were washed with brine (1 x 10 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The crude mixture was used in the next step without further purification.

A flask was charged with a solution of hydroxylamine hydrochloride (347 mg, 5.00 mmol) in ethanol (3 mL). Sodium acetate (595 mg, 7.00 mmol) was dissolved in water (3 mL) and the solution was added to the flask. The crude ketone was dissolved in ethanol (3 mL) and added to the solution. The resulting suspension was stirred until the reaction was shown to be complete by TLC (about 6 hrs). The reaction was concentrated in vacuo and extracted with ethyl acetate (3 x 15 mL). The organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by column chromatography eluting with hexane: acetate (90:10).

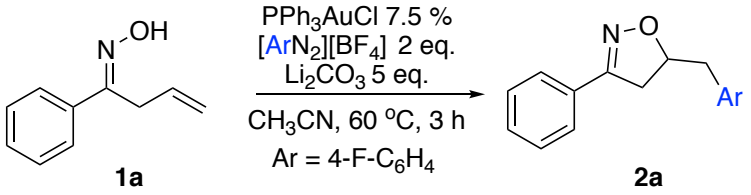
1.2 Procedures for the Synthesis of arenediazonium tetrafluoroborates

All diazonium salts were prepared according to literature procedure[3].



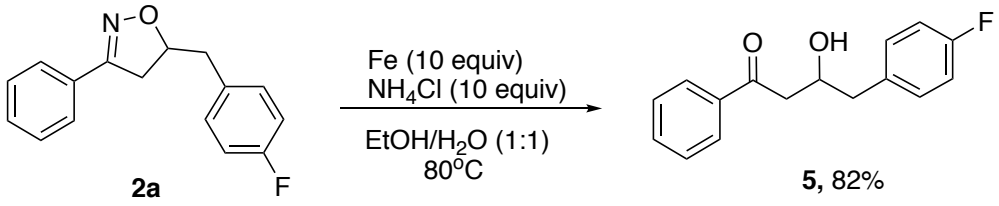
In a 25 mL round-bottom flask, the aniline (5.0 mmol) was dissolved in a mixture of H_2O (1 mL) and an aqueous solution of HBF_4 (50%, 1.9 mL). The mixture was cooled at 0 °C with an ice bath and an solution of $NaNO_2$ (0.68 g, in 1 mL H_2O) was added dropwise. The reaction was stirred at 0 °C for 30 min. The arenediazonium tetrafluoroborate was removed by filtration, washed successively with a small amount ice water, alcohol, and diethyl ether. The arenediazonium tetrafluoroborate was dried in vacuo (10-3 mbar) for 10 minutes and was then directly used without further purification.

1.3 General Procedure for Gold Catalyzed Cyclization/Arylation of Allylic Oximes



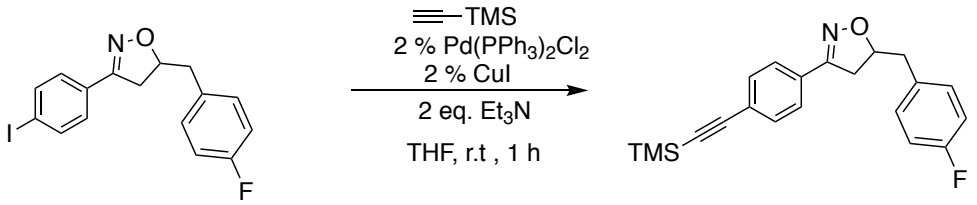
In a 5 ml vial, to a solution of oxime **1a** (0.33 mmol) in 0.83 ml acetonitrile (0.4 M), gold catalyst (12 mg, 7.5%), diazonium salt (0.66 mmol) and lithium carbonate (122 mg, 5 mmol) was added respectively. The resulting mixture was stirred at 60 °C for 3 hours. After that, the reaction mixture was directly loaded on column chromatography on silica gel for purification by hexane/ethyl acetate (20:1) as solvent to isolate the desired product.

1.4 Procedure for Isoxazoline Ring Opening



Fe powder (112 mg, 2 mmol, 10 equiv) was added to isoxazoline **2a** (51 mg, 0.2mmol) and NH_4Cl (107 mg, 2 mmol, 10 equiv) in ethanol and water (1:1, 10mL). The mixture was stirred at 80 °C. After the reaction was completed by TLC monitoring, the reaction mixture was cooled to room temperature, diluted with ethyl acetate, and filtered. The filtrate was washed with brine and the organic layer was separated, dried over Na_2SO_4, and evaporated in vacuo. The residue was then purified by flash chromatography on silica gel to give product 5 in 82% yield.

1.5 Procedure for Palladium-catalyzed cross-coupling of Isoxazoline.

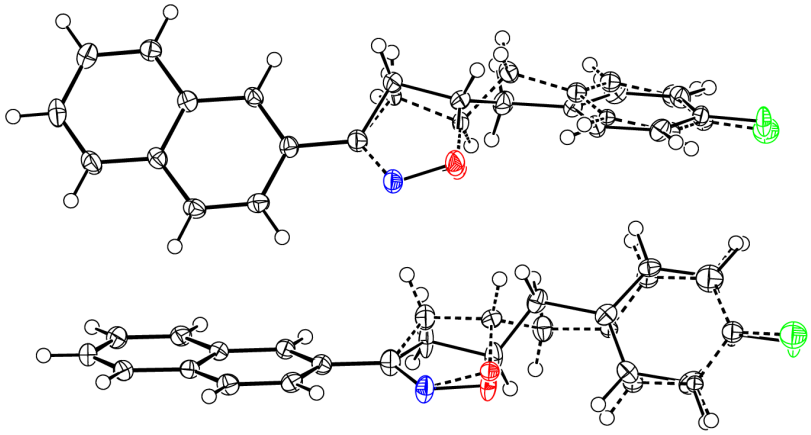


A vial was charged with $Pd(PPh_3)_2Cl_2$ (5.47 mg, 0.0078 mmol, 0.03 equiv) and copper iodide (2.95 mg, 0.0156 mmol, 0.06 equiv). To this were added THF (1.5 mL) and triethylamine (0.145 mL, 1.04 mmol, 4 equiv) via syringe.5-(4-fluorobenzyl)-3-(4-iodophenyl)-4,5-dihydroisoxazole (6) (100 mg, 0.26 mmol, 1 equiv) was then introduced, and the resulting solution was carefully sparged with nitrogen for 10 min. Ethynyltrimethylsilane (0.072 mL, 0.52 mmol, 2 equiv) was then added via syringe, and the resulting brown-black solution was stirred for 45 min. The mixture was partitioned between water and EtOAc and the organic layer collected and then dried over anhydrous MgSO4, filtered, and concentrated. The product was purified by column chromatography on silica gel eluting with hexanes then 5% EtOAc in hexanes to afford compound 8, 91% as white solid.

1. Kong, W.; Guo, Q.; Xu, Z.; Wang, G.; Jiang, X.; Wang, R. *Org. Lett.* **2015,** *17*, 3686-3689.
2. Triandafillidi, I.; Kokotos, C. G. *Org. Lett.* **2017,** *19*, 106
3. Wu, J.; Gu, Y.; Leng, X.; Shen, Q. *Angew. Chem. Int. Ed.* **2015,** *54*, 7648

X-Ray Crystallographic Data

The X-ray diffraction data were measured on Bruker D8 Venture PHOTON 100 CMOS diffractometer equipped with a Cu K_α INCOATEC ImuS micro-focus source (λ = 1.54178 Å). Indexing was performed using Apex3 [1]. Data integration and reduction were performed using Saint [2]. Absorption correction was performed by multi-scan method implemented in SADABS [3]. Space group was determined using XPREP implemented in APEX3 [1]. Structure was solved using SHELXT [4] and refined using SHELXL-2018 [5-7] (full-matrix least-squares on F^2) within OLEX2 interface program [8]. All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were placed in geometrically calculated positions and were included in the refinement process using riding model with isotropic thermal parameters**.** Crystal data and refinement conditions are shown in Table 1. The crystal is a racemic mixture that crystallized in non-centrosymmetric space group. Opposite enantiomers occupy positions across pseudo-inversion center and also share the same site. This leads to observed disorder. Occupancy of disordered parts was refined using free variables (FVAR) in Shelxl and disordered parts of molecules were refined using restraints. Although the average structure could be solved in P21/m centrosymmetric space group, the resulting R-factor is very high (40%) and high residual peaks are observed. Careful analysis of packing indicates the mirror plane is not present in the structure.



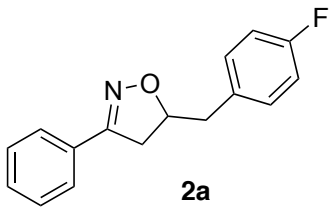
X-Ray Diffraction Analysis of Compound 2i(CCDC 1882657)

Table 1 Crystal data and structure refinement for AAJ_2055.	
Identification code	AAJ_2055
Empirical formula	$C_{20}H_{16}FNO$
Formula weight	305.34
Temperature/K	100
Crystal system	monoclinic
Space group	$P2_1$
a/Å	5.84790(10)
b/Å	14.8989(4)
c/Å	17.0994(4)
α/°	90
β/°	95.9410(10)
γ/°	90
Volume/Å^3	1481.82(6)
Z	4
ρ_{calc}g/cm^3	1.369
μ/mm^{-1}	0.751
F(000)	640.0
Crystal size/mm^3	0.429 × 0.408 × 0.196
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	5.196 to 144.722
Index ranges	$-6 \le h \le 7$, $-18 \le k \le 18$, $-21 \le l \le 21$
Reflections collected	21984
Independent reflections	5786 [R_{int} = 0.0334, R_{sigma} = 0.0316]
Data/restraints/parameters	5786/1090/542
Goodness-of-fit on F^2	1.026
Final R indexes [I>=2σ (I)]	R_1 = 0.0348, wR_2 = 0.0878
Final R indexes [all data]	R_1 = 0.0361, wR_2 = 0.0888
Largest diff. peak/hole / e Å^{-3}	0.17/-0.22

Flack parameter	0.20(7)

[1] Bruker (2017). *APEX3* (Version 2015.9). Bruker AXS Inc., Madison, Wisconsin, USA.
[2] Bruker (2017) SAINT V8.35A. Data Reduction Software.
[3] Sheldrick, G. M. (1996). *SADABS. Program for Empirical Absorption Correction.* University of Gottingen, Germany.
[4] Sheldrick, G. M. (2015) "SHELXT - Integrated space-group and crystal structure determination" Acta Cryst. A71, 3-8
[5] Sheldrick, G.M. (1990) Acta Cryst. A46, 467-473
[6] Sheldrick, G. M. (2008) Acta Cryst. A64, 112-122.
[7] G.M. Sheldrick (2015) "Crystal structure refinement with SHELXL", Acta Cryst., C71, 3-8
[8] Dolomanov, O.V.; Bourhis, L.J.; Gildea, R.J.; Howard, J.A.K.; Puschmann, H., OLEX2: A complete structure solution, refinement and analysis program (2009). J. Appl. Cryst., 42, 339-341.

II. Compounds Characterization



2a

Chemical name: 5-(4-fluorobenzyl)-3-phenyl-4,5-dihydroisoxazole

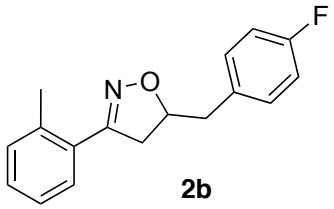
2a was prepared following the General Procedure 1.3 and purified by flash chromatography (Hexane: EA = 20:1) as light-yellow solid, 63 mg, 74% yield.

^{1}H NMR (400MHz, $CDCl_3$): δ 7.62 (dd, 2H), 7.38 (dd, 3H), 7.22 (t, 2H), 7.01 (t, 2H), 4.94 (m, 1H), 3.31(m, 1H), 3.05 (dd, 2H), 2.86 (dd, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 161.8 (d, J = 245.4 Hz), 156.4, 132.6 (d, J = 3.0 Hz), 130.8 (d, J = 8.1 Hz), 130.0, 129.6, 128.7, 126.6, 115.4 (d, J = 21.2 Hz), 81.6, 40.2, 38.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ -116.3

HRMS exact mass calcd for $[M+H]^+$ $C_{16}H_{15}FNO^+$ requires 256.1132, found 256.1131.



2b

Chemical name: 5-(4-fluorobenzyl)-3-(o-tolyl)-4,5-dihydroisoxazole

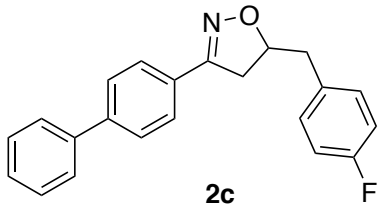
It was prepared following the General Procedure 1.3 and purified by flash chromatography (Hexane: EA = 20:1) as brown solid, 52 mg, 58% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.21 (m, 6H), 6.99 (t, J = 8.6 Hz, 2H), 4.94 – 4.89 (m, 1H), 3.38 (dd, J = 16.5, 10.2 Hz, 1H), 3.13 – 2.97 (m, 2H), 2.90 (dd, J = 14.1, 6.2 Hz, 1H), 2.51 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.8 (d, J = 244.4 Hz), 157.3, 137.9, 132.6, 131.5, 130.9 (d, J = 7.1 Hz), 129.3, 128.7, 125.7, 115.4 (d, J = 21.2 Hz), 80.5, 41.9, 40.0, 22.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -116.4

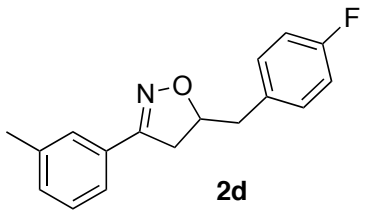
HRMS exact mass calcd for $[M+H]^+$ $C_{17}H_{17}FNO^+$ requires 270.1289, found 270.1286



2c

Chemical name: 3-([1,1'-biphenyl]-4-yl)-5-(4-fluorobenzyl)-4,5-dihydroisoxazole
It was prepared following the General Procedure 1.3 and purified by flash chromatography (Hexane: EA = 20:1) as brown solid, 85 mg,78 % yield.

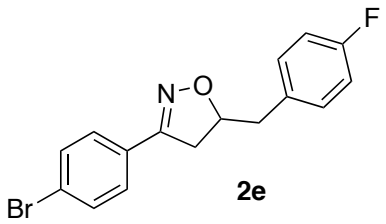
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.2 Hz, 2H), 7.63 – 7.53 (m, 4H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.36 (t, *J* = 7.2 Hz, 1H), 7.23 (dd, *J* = 8.5, 4.7 Hz, 2H), 7.00 (t, *J* = 8.6 Hz, 2H), 5.02 – 4.94 (m, 1H), 3.42 – 3.34 (dd, *J* = 16.5, 10.3 Hz, 1H), 3.11 – 3.03 (m, 2H), 2.90 (dd, *J* = 14.0, 6.5 Hz, 1H**).**
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.8 (d, *J* = 246.4 Hz), 156.2, 142.8, 140.1, 132.6, 130.9 (d, *J* = 8.1 Hz), 128.9, 128.4, 127.8, 127.6, 127.3, 127.0 (d, *J* = 3.0 Hz), 115.4 (d, *J* = 21.2 Hz), 81.7, 40.2, 39.4.
^{19}F NMR (376 MHz, $CDCl_3$) δ -116.2
HRMS exact mass calcd for $[M+H]^+$ $C_{22}H_{19}FNO^+$ requires m/z 332.1445, found m/z 332.1448



2d

Chemical name: 5-(4-fluorobenzyl)-3-(m-tolyl)-4,5-dihydroisoxazole
It was prepared following the General Procedure 1.3 and purified by flash chromatography (Hexane: EA = 20:1) as light-yellow solid, 54.7 mg, 61% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (s, 1H), 7.40 (d, *J* = 7.5 Hz, 1H), 7.30 – 7.14 (m, 4H), 6.99 (t, *J* = 8.5 Hz, 2H), 5.02 – 4.79 (m, 1H), 3.31 (dd, *J* = 16.5, 10.3 Hz, 1H), 3.04 (ddd, *J* = 24.3, 15.3, 7.0 Hz, 1H), 2.87 (dd, *J* = 14.0, 6.5 Hz, 1H), 2.35 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.8 (d, *J* = 246.4 Hz), 156.5, 138.4, 132.6 (d, *J* = 3.0 Hz), 130.9, 130.8 (d, *J* = 7.1 Hz), 129.4, 128.5, 127.2, 123.8, 115.4 (d, *J* = 21.2 Hz), 81.6, 40.2, 39.4, 21.3.
^{19}F NMR (376 MHz, $CDCl_3$) δ -116.3
HRMS exact mass calcd for $[M+H]^+$ $C_{17}H_{17}FNO^+$ requires m/z 270.1289, found m/z 270.1289

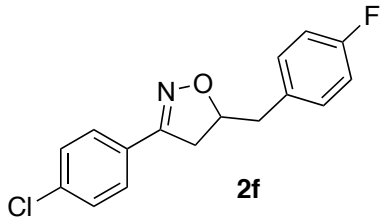


2e

Chemical name: 3-(4-bromophenyl)-5-(4-fluorobenzyl)-4,5-dihydroisoxazole

It was prepared following the General Procedure 1.3 and purified by flash chromatography (Hexane: EA = 20:1) as brown solid, 80 mg, 72% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 6.5, 3.0 Hz, 2H), 7.47 – 7.33 (m, 2H), 7.24 (dd, *J* = 9.1, 6.3 Hz, 2H), 7.00 (t, *J* = 8.6 Hz, 2H), 4.96 (dq, *J* = 10.2, 6.6 Hz, 1H), 3.34 (dd, *J* = 16.6, 10.3 Hz, 1H), 3.06 (ddd, *J* = 24.3, 15.3, 7.1 Hz, 1H), 2.90 (dd, *J* = 14.1, 6.5 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.8 (d, *J* = 245.4 Hz), 155.6, 132.4 (d, *J* = 3.0 Hz), 131.9, 130.8 (d, *J* = 8.1 Hz), 128.5, 128.0, 124.3, 115.4 (d, *J* = 21.2 Hz), 81.9, 40.1, 39.1.
^{19}F NMR (376 MHz, $CDCl_3$) δ -116.1
HRMS exact mass calcd forb$[M+H]^+$ $C_{16}H_{14}BrFNO^+$ requires m/z 334.0237, found m/z 334.0234

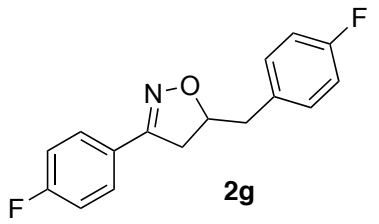


2f

Chemical name: 3-(4-chlorophenyl)-5-(4-fluorobenzyl)-4,5-dihydroisoxazole

It was prepared following the General Procedure 1.3 and purified by flash chromatography (Hexane: EA = 20:1) as white solid, 68.4 mg, 71% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.5 Hz, 2H), 7.34 (d, *J* = 8.5 Hz, 2H), 7.26 – 7.15 (m, 2H), 6.98 (t, *J* = 8.6 Hz, 2H), 5.13 – 4.80 (m, 1H), 3.29 (dd, *J* = 16.5, 10.3 Hz, 1H), 3.06 (dt, *J* = 18.1, 9.1 Hz, 1H), 2.97 (dd, *J* = 16.5, 7.9 Hz, 1H), 2.88 (dd, *J* = 14.1, 6.4 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.8 (d, *J* = 245.4 Hz), 155.5, 135.9, 132.4 (d, *J* = 3.0 Hz), 130.8 (d, *J* = 8.1 Hz), 128.9, 128.1, 127.8, 115.4 (d, *J* = 21.2 Hz), 81.9, 40.1, 39.2.
^{19}F NMR (376 MHz, $CDCl_3$) δ -116.2
HRMS exact mass calcd for $[M+H]^+$ $C_{16}H_{14}ClFNO^+$ requires m/z 290.0742, found m/z 290.0744

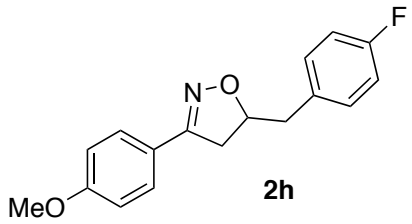


2g

Chemical name: 3-(4-florophenyl)-5-(4-fluorobenzyl)-4,5-dihydroisoxazole

It was prepared following the General Procedure 1.3 and purified by flash chromatography (Hexane: EA = 20:1) as white solid, 57.3mg, 63% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.57 (m, 2H), 7.22 (m, 2H), 7.21 – 7.03 (m, 4H), 4.94 (ddt, *J* = 10.3, 7.9, 6.4 Hz, 1H), 3.29 (dd, *J* = 16.5, 10.3 Hz, 1H), 3.14 – 2.92 (m, 2H), 2.87 (dd, *J* = 14.1, 6.5 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 163.7 (d, *J* = 252.5 Hz), 161.8 (d, *J* = 245.4 Hz), 155.4, 132.5, 130.8, 128.4, 125.8 (d, *J* = 2.0 Hz), 115.7 (d, *J* = 21.2 Hz), 115.5 (d, *J* = 21.2 Hz), 81.7, 40.1, 39.4.
^{19}F NMR (376 MHz, $CDCl_3$) δ -110.0, -116.2.
HRMS exact mass calcd for $[M+H]^+$ $C_{16}H_{14}F_2NO^+$ requires m/z 274.1038, found m/z 274.1034.

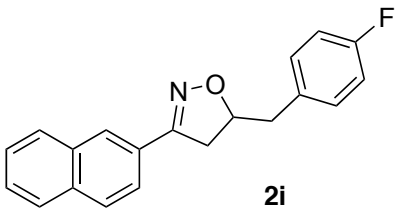


2h

Chemical name: 5-(4-fluorobenzyl)-3-(4-methoxyphenyl)-4,5-dihydroisoxazole

It was prepared following the General Procedure 1.3 and purified by flash chromatography (Hexane: EA = 20:1) as white solid, 53 mg, 56% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, 2H), 7.23 (t, 2H), 7.01 (m, 2H), 6.90 (m, 2H), 4.92 (t, *J* = 8.2 Hz, 1H), 3.81 (s, 3H), 3.31 (dd, *J* = 16.2, 10.9 Hz, 1H), 3.12 – 2.95 (m, 2H), 2.88 (dd, *J* = 14.5, 5.9 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.8 (d, *J* = 245.4 Hz), 161.0, 156.0, 132.7 (d, *J* = 3.0 Hz), 130.9, 128.1 (d, *J* = 10.0 Hz), 122.1, 115.4 (d, *J* = 21.2 Hz), 114.1, 81.4 (d, *J* = 15.0 Hz). 55.3, 40.2, 39.6
^{19}F NMR (376 MHz, $CDCl_3$) δ -116.3
HRMS exact mass calcd for $[M+H]^+$ $C_{17}H_{17}FNO_2^+$ requires m/z 286.1238, found m/z 286.1236.

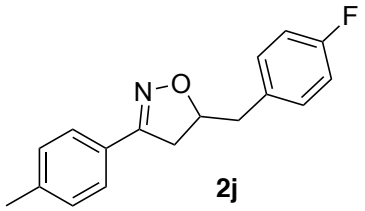


2i

Chemical name: 5-(4-fluorobenzyl)-3-(naphthalen-2-yl)-4,5-dihydroisoxazole

It was prepared following the General Procedure 1.3 and purified by flash chromatography (Hexane: EA = 20:1) as white solid, 77 mg, 76% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.77 (m, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.32 – 7.16 (m, 3H), 7.00 (t, *J* = 8.7 Hz, 3H), 4.45 (ddd, *J* = 10.5, 8.9, 3.3 Hz, 1H), 3.11 (qd, *J* = 17.6, 5.8 Hz, 2H), 2.98 – 2.85 (m, 1H), 2.83 (dd, *J* = 13.8, 6.0 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.8 (d, *J* = 246.4 Hz), 156.6, 134.0, 132.9, 132.6 (d, *J* = 2.0 Hz), 130.9 (d, *J* = 8.1 Hz), 128.5, 128.3, 127.9, 127.2, 127.1, 126.8, 126.7, 123.5, 115.4 (d, *J* = 21.2 Hz), 81.9, 40.2, 39.3.
^{19}F NMR (376 MHz, $CDCl_3$) δ -116.7
HRMS exact mass calcd for [M+H]$^+$ $C_{20}H_{17}FNO^+$ requires m/z 306.1289, found m/z 306.1295

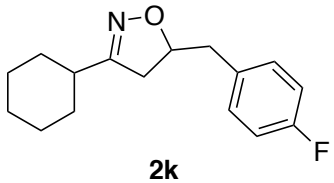


2j

Chemical name: 5-(4-fluorobenzyl)-5-methyl-3-phenyl-4,5-dihydroisoxazole

It was prepared following the General Procedure 1.3 and purified by flash chromatography (Hexane: EA = 20:1) as yellow solid, 60 mg, 67% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 31.4, 12.0 Hz, 2H), 7.24 – 7.17 (m, 4H), 6.99 (m, 2H), 4.92 (m, 1H), 3.31 (dd, *J* = 16.6, 10.3 Hz, 1H), 3.13 – 2.93 (m, 2H), 2.87 (dd, *J* = 14.0, 6.5 Hz, 1H), 2.36 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.8 (d, *J* = 246.4 Hz), 156.4, 140.3, 132.6, 130.8 (d, *J* = 3.0 Hz), 129.3, 126.5, 125.6, 115.4 (d, *J* = 21.2 Hz), 81.5, 40.2, 39.5, 21.5.
^{19}F NMR (376 MHz, $CDCl_3$) δ -116.4
HRMS exact mass calcd for $[M+H]^+$ $C_{17}H_{17}FNO^+$ requires m/z 270.1289, found m/z 270.1288.

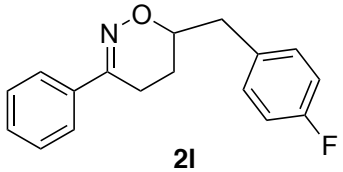


2k

It was prepared following the General Procedure 1.3 and purified by flash chromatography (Hexane: EA = 20:1) as white solid, 26.1 mg, 30% yield.

Chemical name: 3-cyclohexyl-5-(4-fluorobenzyl)-4,5-dihydroisoxazole

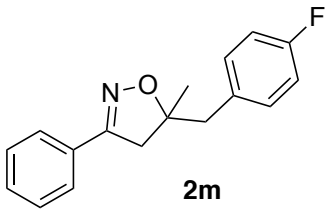
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (dd, *J* = 8.4, 5.4 Hz, 2H), 6.98 (t, *J* = 8.7 Hz, 2H), 4.73 (dd, *J* = 10.1, 6.7 Hz, 1H), 2.91 – 2.79 (dd, *J* = 15.0, 5.8 Hz, 3H), 2.78 (m, 1H), 2.34 (dd, *J* = 16.8, 7.2 Hz, 1H), 1.83 – 1.58 (m, 5H), 1.28 – 1.17 (m, 5H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.8 (d, *J* = 245.4 Hz), 162.6, 132.8 (d, *J* = 3.0 Hz), 130.7 (d, *J* = 7.1 Hz), 115.2 (d, *J* = 21.2 Hz), 79.9, 79.8, 40.0, 39.5, 37.2, 30.3, 25.8, 25.7.
^{19}F NMR (376 MHz, $CDCl_3$) δ -116.6
HRMS exact mass calcd for $[M+H]^+$ $C_{16}H_{21}FNO^+$ requires m/z 262.1602, found m/z 262.1598.



2l

Chemical name: 6-(4-fluorobenzyl)-3-phenyl-5,6-dihydro-4H-1,2-oxazine
It was prepared following the General Procedure 1.3 and purified by flash chromatography (Hexane: EA = 20:1) as white solid, 62 mg, 69% yield.

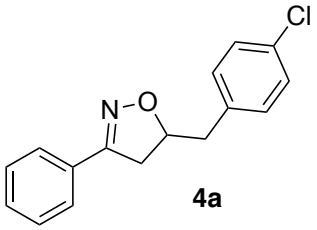
^{1}H NMR (400MHz, $CDCl_3$): δ 7.66 (dd, 2H), 7.36 (t, 3H), 7.22 (t, 2H), 6.98 (t, 2H), 3.94 (m, 1H), 3.05 (m, 1H), 2.84 (dd, 1H), 2.60 (m, 2H), 2.01(m, 1H) 1.75 m, 1H).
^{13}C NMR (400 MHz, $CDCl_3$): δ 161.7 (d, *J* = 245.4 Hz), 156.6, 135.7, 132.8 (d, *J* = 3.0 Hz), 131.0 (d, *J* = 8.1 Hz), 129.5, 128.4, 125.3, 115.2 (d, *J* = 21.2 Hz), 75.7, 39.6, 23.8, 21.9
^{19}F NMR (400 MHz, $CDCl_3$): δ -116.7
HRMS exact mass calcd for $[M+H]^+$ $C_{17}H_{17}FNO^+$ requires m/z 270.1289, found m/z 270.1288



2m

Chemical name: 5-(4-fluorobenzyl)-5-methyl-3-phenyl-4,5-dihydroisoxazole
It was prepared following the General Procedure 1.3 and purified by flash chromatography (Hexane: EA = 20:1) as yellow solid, 55 mg, 61% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.48 (m, 2H), 7.40 – 7.30 (m, 3H), 7.26 – 7.16 (m, 3H), 7.02 – 6.81 (m, 2H), 3.14 (d, J = 16.5 Hz, 1H), 3.00 – 2.89 (m, 3H), 1.40 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9 (d, *J* = 245.4 Hz), 156.4, 132.3 (d, *J* = 2.0 Hz), 131.8 (d, *J* = 8.1 Hz), 129.8, 128.6, 126.4, 115.0 (d, *J* = 21.2 Hz), 87.1, 44.8, 44.5, 36.6, 25.8.
^{19}F NMR (376 MHz, $CDCl_3$) δ -116.40
HRMS exact mass calcd for $[M+H]^+$ $C_{17}H_{17}FNO^+$ requires m/z 270.1289, found m/z 270.1289.



4a

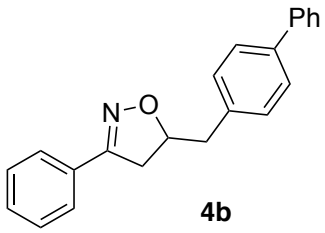
Chemical name: 5-(4-chlorobenzyl)-3-phenyl-4,5-dihydroisoxazole

It was prepared following the General Procedure 1.3 and purified by flash chromatography (Hexane: EA = 20:1) as white solid, 75.6 mg, 72% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (m, 2H), 7.37 (dd, *J* = 5.2, 2.0 Hz, 3H), 7.31 – 7.17 (m, 5H), 4.93 (ddt, *J* = 10.3, 7.8, 6.5 Hz, 1H), 3.32 (dd, *J* = 16.6, 10.3 Hz, 1H), 3.17 – 2.94 (m, 2H), 2.85 (dd, *J* = 14.0, 6.5 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.5, 140.8, 139.7, 136.0, 130.0, 129.8, 128.7, 127.4, 126.7, 81.8, 40.7, 39.5

HRMS exact mass calcd for [M+H]$^+$ $C_{16}H_{15}ClNO^+$ requires m/z 272.0837, found m/z 272.0838.



4b

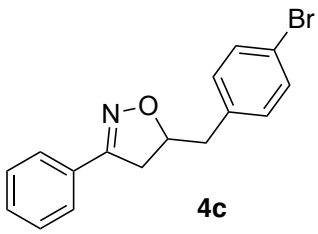
Chemical name: 5-([1,1'-biphenyl]-4-ylmethyl)-3-phenyl-4,5-dihydroisoxazole

It was prepared following the General Procedure 1.3 and purified by flash chromatography (Hexane: EA = 20:1) as white solid, 71 mg, 79% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 6.7, 3.0 Hz, 2H), 7.55 (dd, *J* = 9.9, 7.7 Hz, 4H), 7.48 – 7.27 (m, 8H), 5.02 (dq, *J* = 10.1, 7.0 Hz, 1H), 3.35 (dd, *J* = 16.5, 10.2 Hz, 1H), 3.24 – 3.17 (m, 1H), 3.08 (m, 1H), 2.93 (dd, *J* = 13.9, 7.1 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.4, 135.4, 132.7, 130.7, 130.1, 129.5, 128.7, 128.7, 126.6, 81.4, 40.3, 39.4

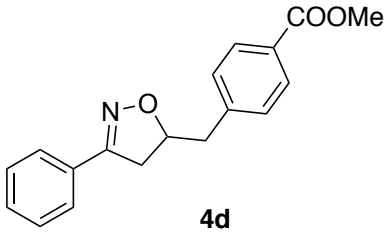
HRMS exact mass calcd for $[M+H]^+$ $C_{22}H_{20}NO^+$ requires m/z 314.1539, found m/z 314.1539.



4c

Chemical name: 5-(4-bromobenzyl)-3-phenyl-4,5-dihydroisoxazole

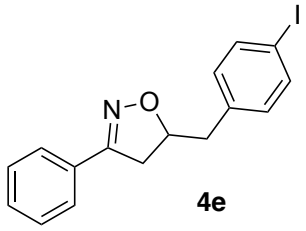
It was prepared following the General Procedure 1.3 and purified by flash chromatography (Hexane: EA = 20:1) as brown solid, 75.6 mg, 72% yield.
^{1}H NMR (400 MHz, $CDCl_3$) 7.63 (m, 2H), 7.45-7.39 (dd, *J* = 19.4, 6.5 Hz, 5H), 7.15 (d, *J* = 8.1 Hz, 2H), 4.96 (dq, *J* = 14.1, 6.9 Hz, 1H), 3.35 (dd, *J* = 16.5, 10.3 Hz, 1H), 3.22 – 2.94 (m, 2H), 2.87 (dd, *J* = 14.0, 6.4 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 156.4, 135.9, 131.7, 131.1, 130.1, 129.5, 128.7, 126.6, 120.7, 81.4, 40.4, 39.4.
HRMS exact mass calcd for $[M+H]^+$ $C_{16}H_{15}BrNO^+$ requires m/z 316.0332 found m/z 316.0332.



4d

Chemical name: methyl 4-((3-phenyl-4,5-dihydroisoxazol-5-yl) methyl) benzoate
It was prepared following the General Procedure 1.3 and purified by flash chromatography (Hexane: EA = 20:1) as white solid, 67.9 mg, 69% yield.

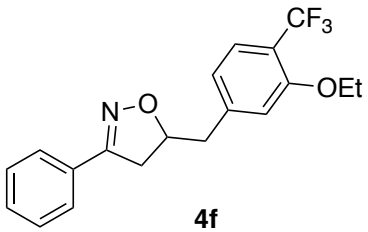
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.0 Hz, 2H), 7.60 (dd, *J* = 6.8, 2.9 Hz, 2H), 7.43 – 7.31 (m, 5H), 5.01 (dq, *J* = 10.3, 6.9 Hz, 1H), 3.88 (s, 1H), 3.34 (dd, *J* = 16.6, 10.3 Hz, 1H), 3.17 – 3.13 (m, 1H), 3.04 - 2.92 (dd, *J* = 14.0, 6.4 Hz, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.9, 156.5, 142.3, 130.1, 129.9, 129.4, 129.3, 128.9, 128.7, 126.6, 81.2, 52.1, 41.0, 39.5.
HRMS exact mass calcd for $[M+H]^+$ $C_{18}H_{18}NO_3^+$ requires m/z 296.1281, found m/z 296.1284



4e

Chemical name: 5-(4-iodobenzyl)-3-phenyl-4,5-dihydroisoxazole
It was prepared following the General Procedure 1.3 and purified by flash chromatography (Hexane: EA = 20:1) as brown solid, 65 mg, 53% yield.

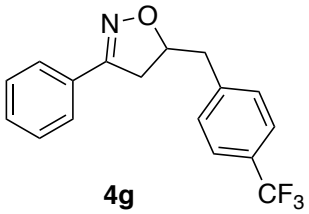
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 7.8 Hz, 4H), 7.38 (s, 3H), 7.01 (d, J = 7.7 Hz, 2H), 5.03 – 4.84 (m, 1H), 3.33 (dd, J = 16.5, 10.3 Hz, 1H), 3.14 – 2.92 (m, 2H), 2.84 (dd, J = 14.0, 6.4 Hz, 1H).
13C NMR (101 MHz, $CDCl_3$) δ 156.4, 137.6, 136.6, 131.4, 130.1, 129.5, 128.7, 126.6, 92.2, 81.4, 40.5, 39.4.
HRMS exact mass calcd for $[M+H]^+$ $C_{16}H_{15}INO^+$ requires m/z 364.0193, found m/z 364.0196



4f

Name: Ethyl4-((3-phenyl-4,5-dihydroisoxazol-5-yl) methyl)-2-(trifluoromethyl)benzoate.
It was prepared following the General Procedure 1.3 and purified by flash chromatography (Hexane: EA = 20:1) as white solid, 82.6 mg, 71% yield.

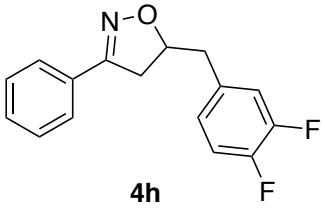
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 6.7, 3.0 Hz, 2H), 7.50 – 7.33 (m, 5H), 6.92 (d, *J* = 8.5 Hz, 1H), 4.94 (dt, *J* = 8.4, 6.1 Hz, 1H), 4.10 (q, 2H), 3.36 (dd, *J* = 16.5, 10.2 Hz, 1H), 3.16 – 2.97 (m, 2H), 2.86 (dd, *J* = 14.2, 6.1 Hz, 1H), 1.41 (t, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 156.5, 155.8, 134.1, 130.1, 129.5, 128.7, 128.5, 127.8 (q, *J* = 5.0 Hz), 126.6, 123.6 (q, *J* = 272.7 Hz), 119.0 (q, *J* = 30.3 Hz), 113.3, 81.6, 64.6, 40.0, 39.4, 14.6.
^{19}F NMR (376 MHz, $CDCl_3$) δ -62.4.
HRMS exact mass calcd for $[M+H]^+$ $C_{19}H_{19}F_3NO_2^+$ requires m/z 350.1362, found m/z 350.1363



4g

Chemical name: 3-phenyl-5-(4-(trifluoromethyl) benzyl)-4,5-dihydroisoxazole
It was prepared following the General Procedure 1.3 and purified by flash chromatography (Hexane: EA = 20:1) as yellow solid, 71mg, 70% yield.

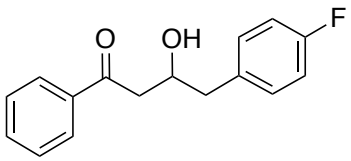
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.57 (m, 4H), 7.40 (dd, *J* = 4.5, 2.8 Hz, 5H), 4.99 (dq, *J* = 10.0, 6.9 Hz, 1H), 3.38 (dd, *J* = 16.5, 10.3 Hz, 1H), 3.17 (dd, *J* = 14.0, 6.8 Hz, 1H), 3.07 – 2.84 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 156.5, 141.1, 130.1, 129.7, 129.4 (q, *J* = 32.3 Hz), 128.7, 126.6, 125.5 (q, *J* = 3.0 Hz), 121.5 (q, *J* = 272.7 Hz), 81.2, 40.8, 39.6.
^{19}F NMR (376 MHz, $CDCl_3$) δ -62.5
HRMS exact mass calcd for $[M+H]^+$ $C_{17}H_{15}F_3NO^+$ requires m/z 306.1100 found m/z 306.1113



4h

Chemical name: 5-(3,4-difluorobenzyl)-3-phenyl-4,5-dihydroisoxazole
It was prepared following the General Procedure 1.3 and purified by flash chromatography (Hexane: EA = 20:1) as brown solid, 56 mg, 62% yield.

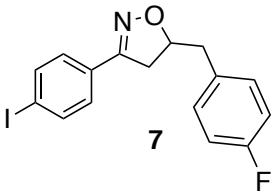
^{1}H NMR (400 MHz, $CDCl_3$) 7.64 (dd, J = 6.2, 2.7 Hz, 2H), 7.40 (m, 3H), 7.18 – 7.03 (m, 2H), 7.03 – 6.91 (m, 1H), 4.95 (dq, J = 10.2, 6.9 Hz, 1H), 3.38 (dd, J = 16.6, 10.3 Hz, 1H), 3.10 – 2.97 (m, 2H), 2.89 (dd, J = 14.2, 5.9 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 156.4, 151.0 (dd, J = 304.6, 48.9 Hz), 148.5 (dd, J = 300.8, 48.9 Hz), 133.9 (dd, J = 18.8, 18.8 Hz), 130.1, 129.4, 128.9, 126.6, 125.3 (dd, J = 18.8, 18.8 Hz), 118.2 (d, J = 63.9 Hz), 117.2 (d, J = 63.9 Hz), 81.2, 40.1, 39.4
^{19}F NMR (376 MHz, $CDCl_3$) δ -137.7, -140.8 (m, $J^3_{F\text{-}F}$ = 18.8 Hz)
HRMS exact mass calcd for $[M+H]^+$ $C_{16}H_{14}F_2NO^+$ requires m/z 274.1038, found 274.1045



5a

Chemical name: 4-(4-fluorophenyl)-3-hydroxy-1-phenylbutan-1-one
It was prepared following the General Procedure 1.4 and purified by flash chromatography (Hexane: EA = 20:1) as white solid, 42 mg, 82% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.9 (d, J = 7.7 Hz, 2H), 7.59 (dt, J = 48.2, 7.5 Hz, 1H), 7.56 – 7.46 (m, 2H), 7.44 – 7.26 (m, 2H), 7.22 - 6.98 (t, J = 8.5 Hz, 2H), 4.45 (t, J = 7.7 Hz, 1H), 3.18– 3.03 (m, 2 H), 2.95 – 2.80 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 200.4, 161.7 (d, J = 245.4 Hz), 136.6, 133.7 (d, J = 3.0 Hz), 133.6, 130.8 (d, J = 8.1 Hz), 128.7, 128.0, 115.3 (d, J = 21.2 Hz), 68.8, 44.0, 42.0
^{19}F NMR (376 MHz, $CDCl_3$) δ -116.7
HRMS exact mass calcd for $[M+H]^+$ $C_{16}H_{16}FO_2^+$ requires m/z 259.1129, found 259.1128

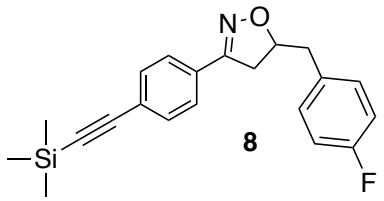


7

It was prepared following the General Procedure 1.4 and purified by flash chromatography (Hexane: EA = 20:1) as off-white solid, 42 mg, 71% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (m, 2H), 7.35 (m, 2H), 7.22 (dt, J = 16.9, 9.4 Hz, 2H), 7.0 (m, 2H), 4.99 – 4.93 (m, 1H), 3.33 – 3.16 (m, 1H), 3.08 (dt, J = 15.1, 7.5 Hz, 1H), 2.99 – 2.82 (ddd, J = 20.5, 15.3, 7.1 Hz, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.8 (d, J = 246.4 Hz), 155.7, 137.8, 132.4 (d, J = 2.0 Hz), 130.8 (d, J = 8.1 Hz), 129.0, 128.1, 115.4 (d, J = 21.2 Hz), 96.2, 82.0, 40.1, 39.0

^{19}F NMR (376 MHz, $CDCl_3$) δ -116.3
HRMS exact mass calcd for M+H]$^+$ $C_{16}H_{14}FINO^+$ requires m/z 382.0099, found m/z 382.0106



8

It was prepared following the General Procedure 1.4 and purified by flash chromatography (Hexane: EA = 20:1) as off-white solid, 91% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (dd, 2H), 7.46 (m, 2H), 7.24 (m, 2H), 7.00 (m, 2H), 4.96 (m, 1H), 3.34 – 3.28 (m, 1H), 3.08 (dd, 1H), 2.98 (dd, 1H), 2.88 (dd, 1H), 0.25 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9 (d, J = 246.4 Hz), 155.9, 132.4, 132.2, 130.8 (d, J = 7.1 Hz), 129.4, 126.3, 124.7, 115.4 (d, J = 21.2 Hz), 104.4, 96.4, 81.9 (d, J = 10.0 Hz), 40.2, 39.1, -0.1
^{19}F NMR (376 MHz, $CDCl_3$) δ -116.2
HRMS exact mass calcd for $C_{21}H_{23}FNOSi^+$ requires m/z 352.1527, found m/z 352.1538

III. NMR Spectra Data


7.63
7.63
7.62
7.61
7.39
7.38
7.37
7.37
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7.24
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7.23
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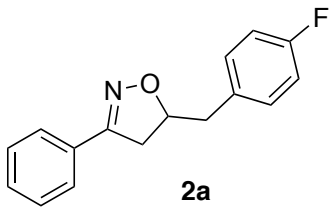
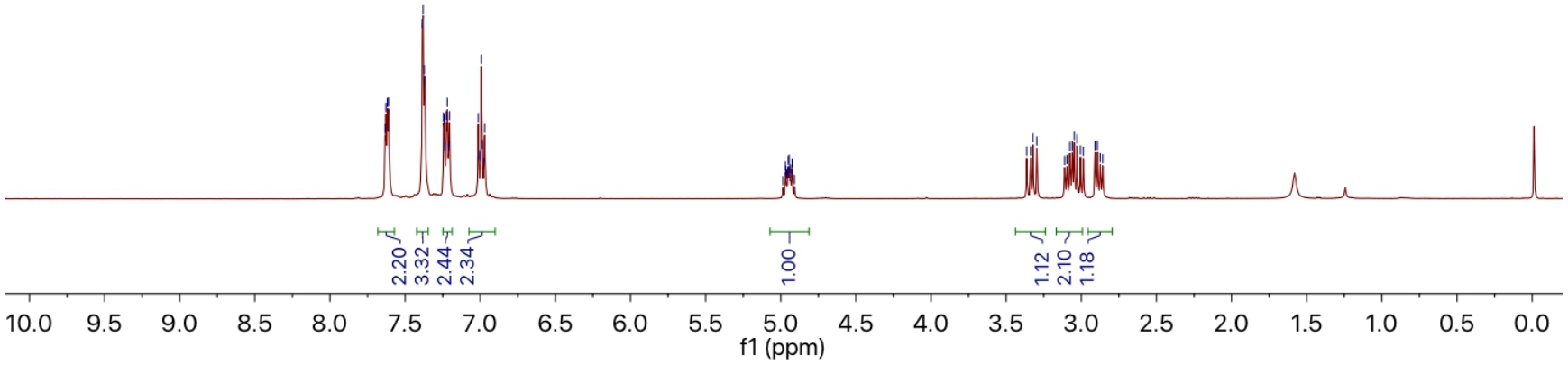
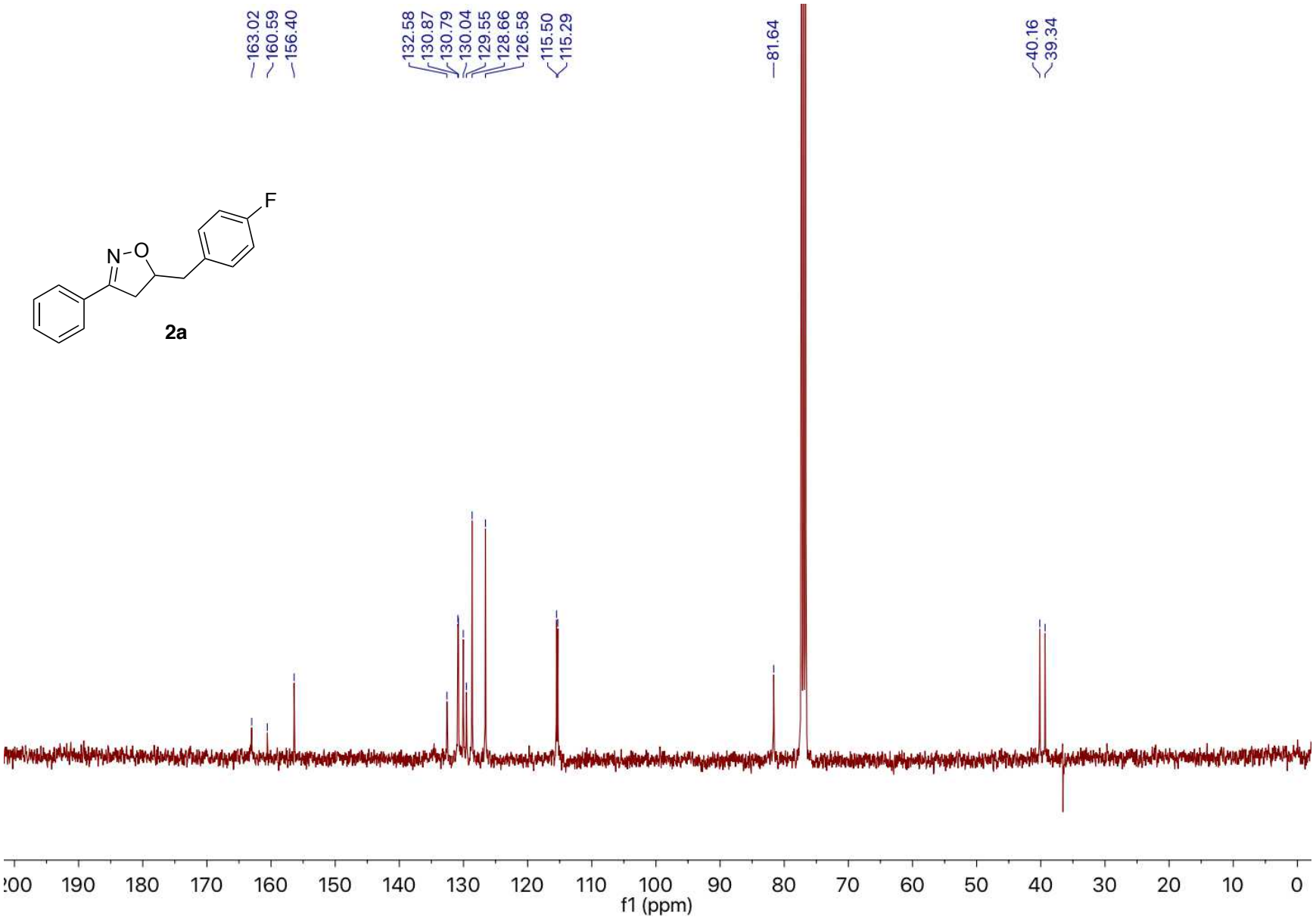
2.99
2.91
2.89
2.87
2.86


F
N
O

2a


2.20
3.32
2.44
2.34
1.00
1.12
2.10
1.18
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
f1 (ppm)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160.59
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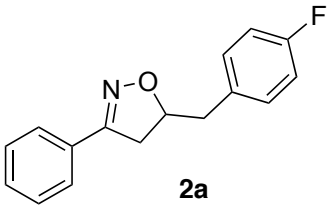
132.58
130.87
130.79
130.04
129.55
128.66
126.58
115.50
115.29
81.64
40.16
39.34
F
N
O
2a
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


F
N
O

2a

-116.30
10
0
-10
-20
-30
-40
-50
-60
-70
-80
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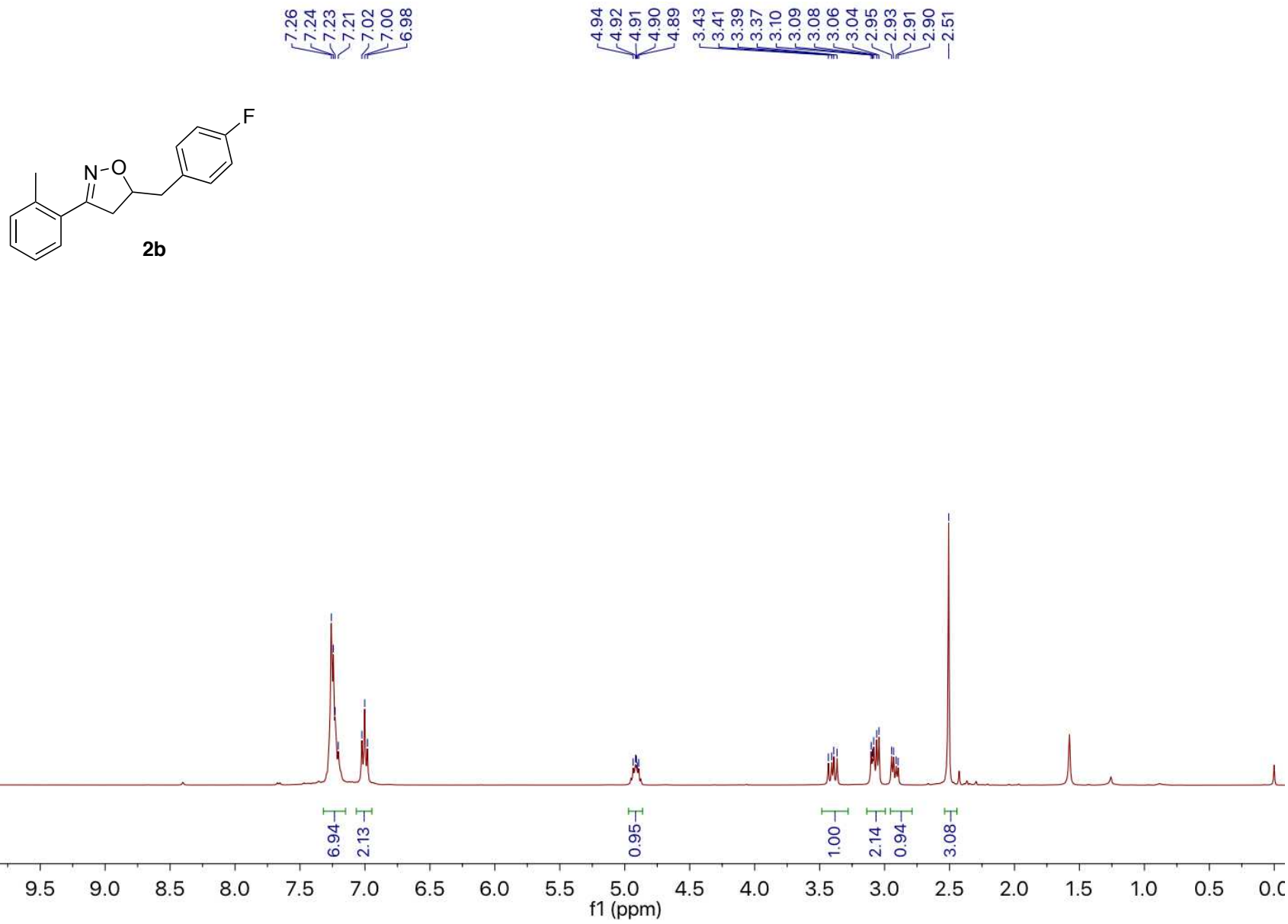
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)


7.26
7.24
7.23
7.21
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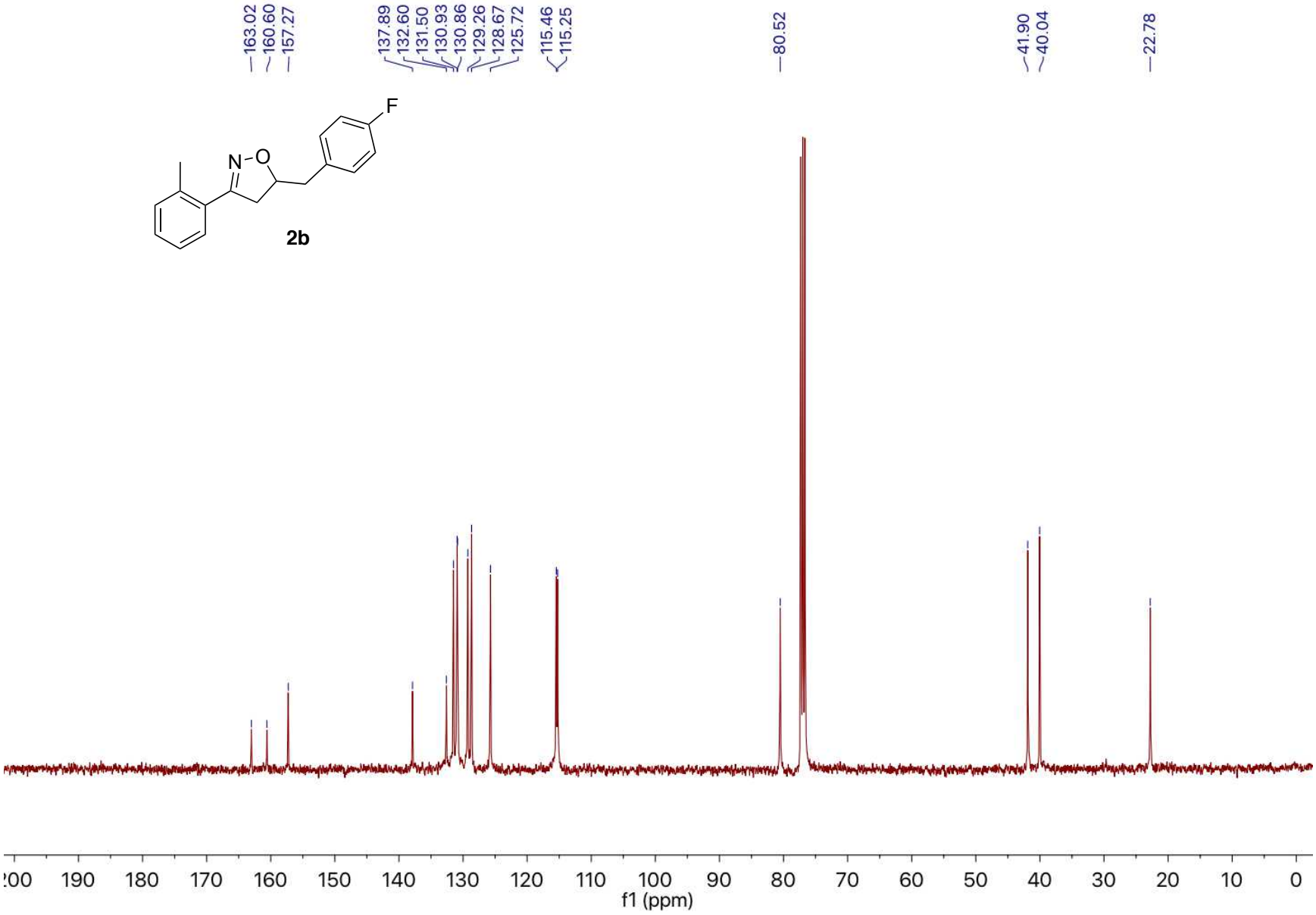
7.00
6.98
4.94
4.92
4.91
4.90
4.89
3.43
3.41
3.39
3.37
3.10
3.09
3.08
3.06
3.04
2.95
2.93
2.91
2.90
2.51
F
N
O
2b
6.94
2.13
0.95
1.00
2.14
0.94
3.08
f1 (ppm)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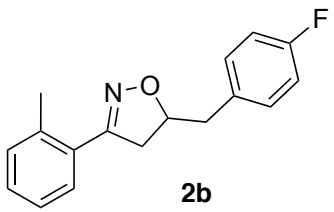
160.60
157.27
137.89
132.60
131.50
130.93
130.86
129.26
128.67
125.72
115.46
115.25
80.52
41.90
40.04
22.78
F
N
O
2b
f1 (ppm)


F
N
O

2b

-116.38
10
0
-10
-20
-30
-40
-50
-60
-70
-80
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-110
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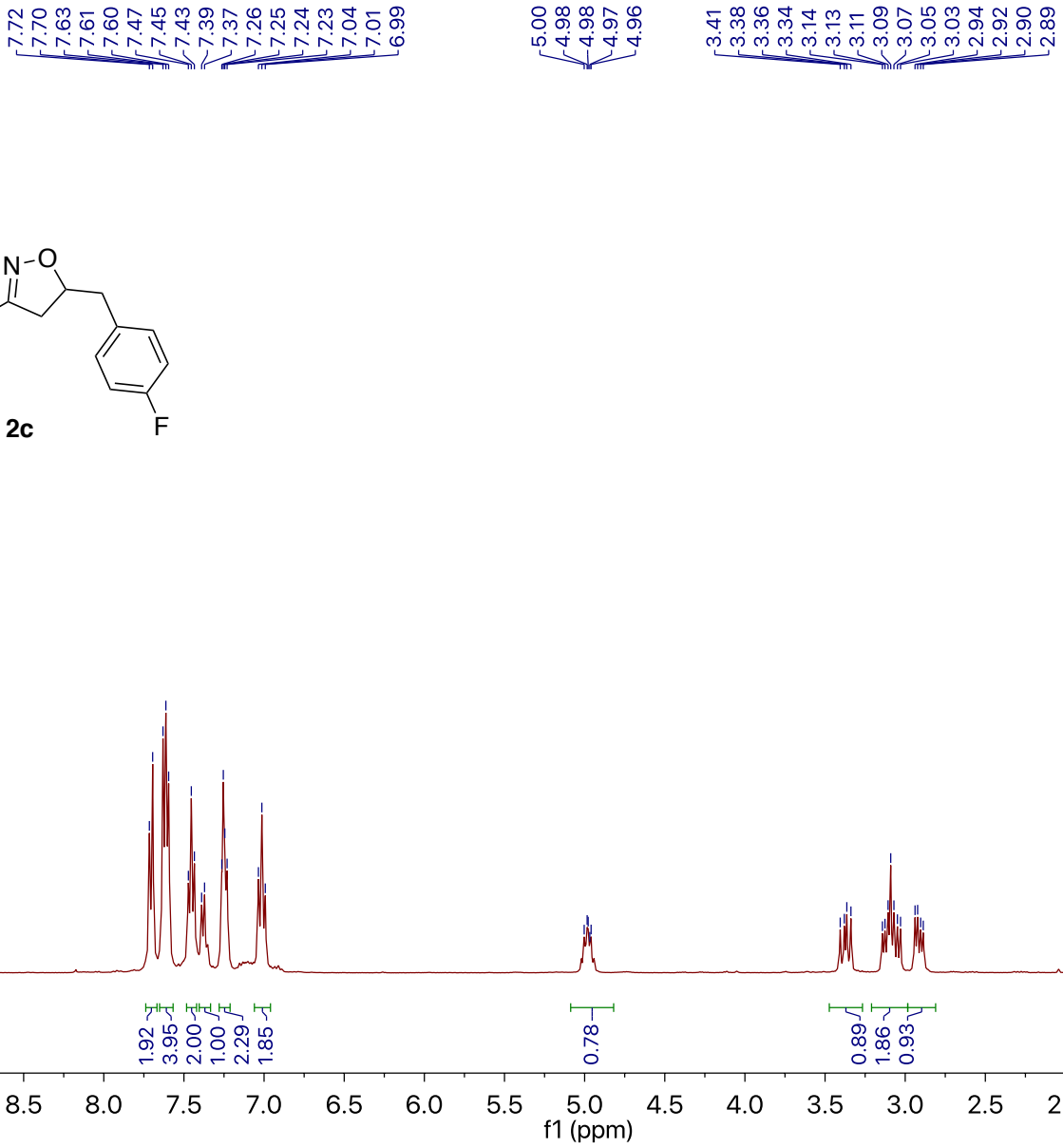
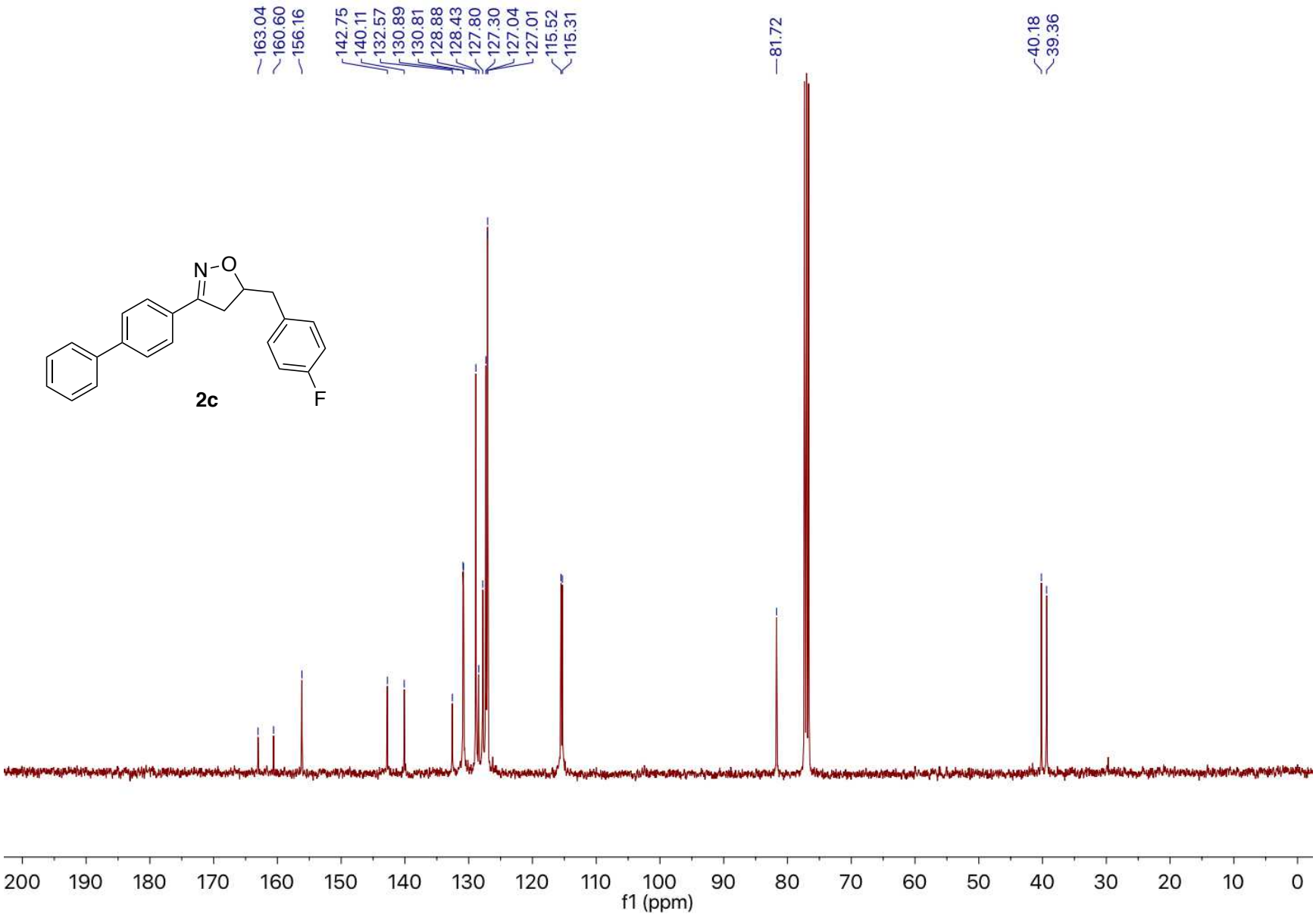
-140
-150
-160
-170
-180
-190
f1 (ppm)


7.72
7.70
7.63
7.61
7.60
7.47
7.45
7.43
7.39
7.37
7.26
7.25
7.24
7.23
7.04
7.01
6.99
5.00
4.98
4.98
4.97
4.96
3.41
3.38
3.36
3.34
3.14
3.13
3.11
3.09
3.07
3.05
3.03
2.94
2.92
2.90
2.89
N
O
F
2c
1.92
3.95
2.00
1.00
2.29
1.85
0.78
0.89
1.86
0.93
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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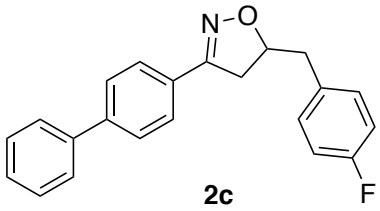
160.60
156.16
142.75
140.11
132.57
130.89
130.81
128.88
128.43
127.80
127.30
127.04
127.01
115.52
115.31
81.72
40.18
39.36
N
O
F
2c
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


N
O
F

2c

-116.23
10
0
-10
-20
-30
-40
-50
-60
-70
-80
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-120
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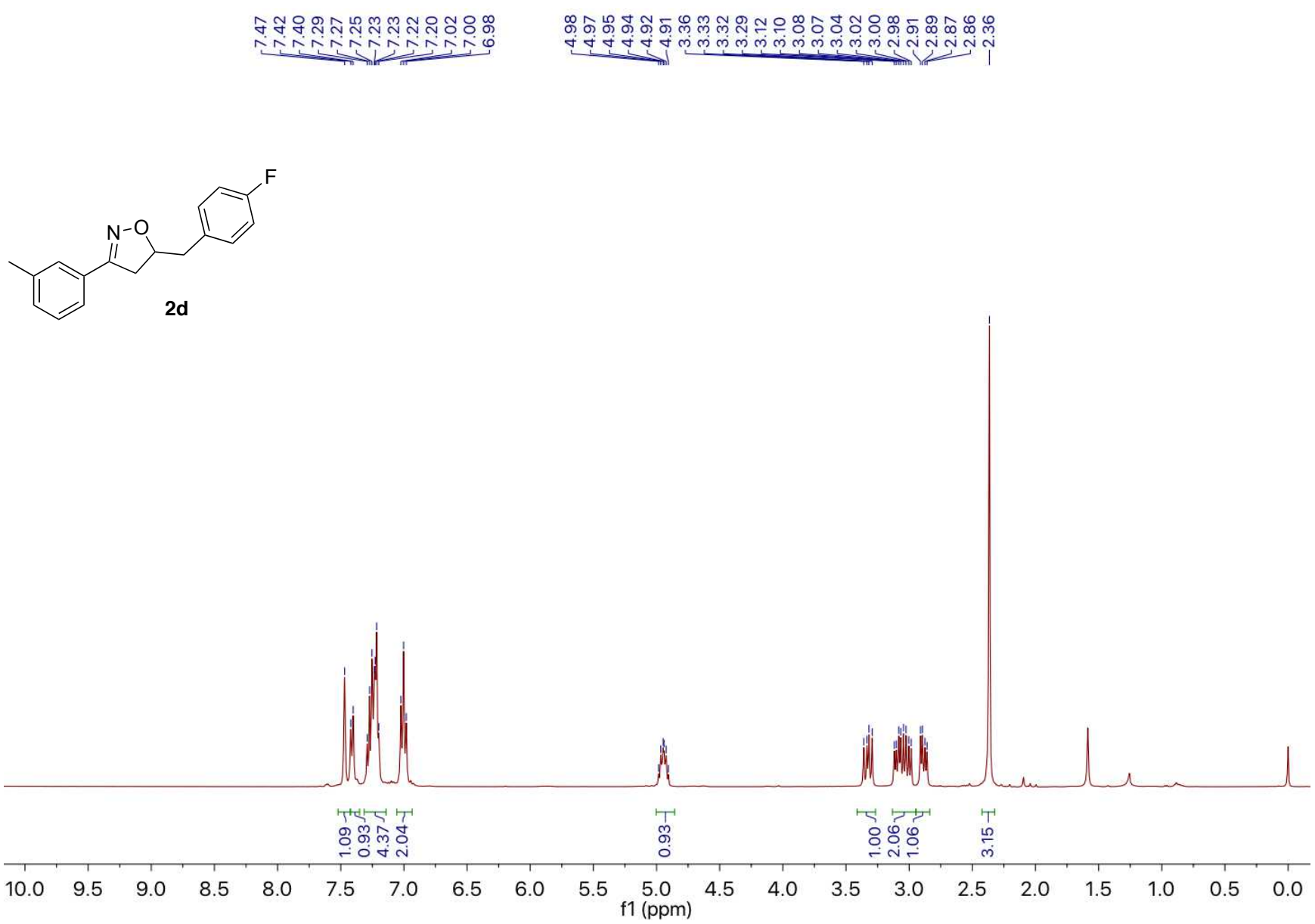
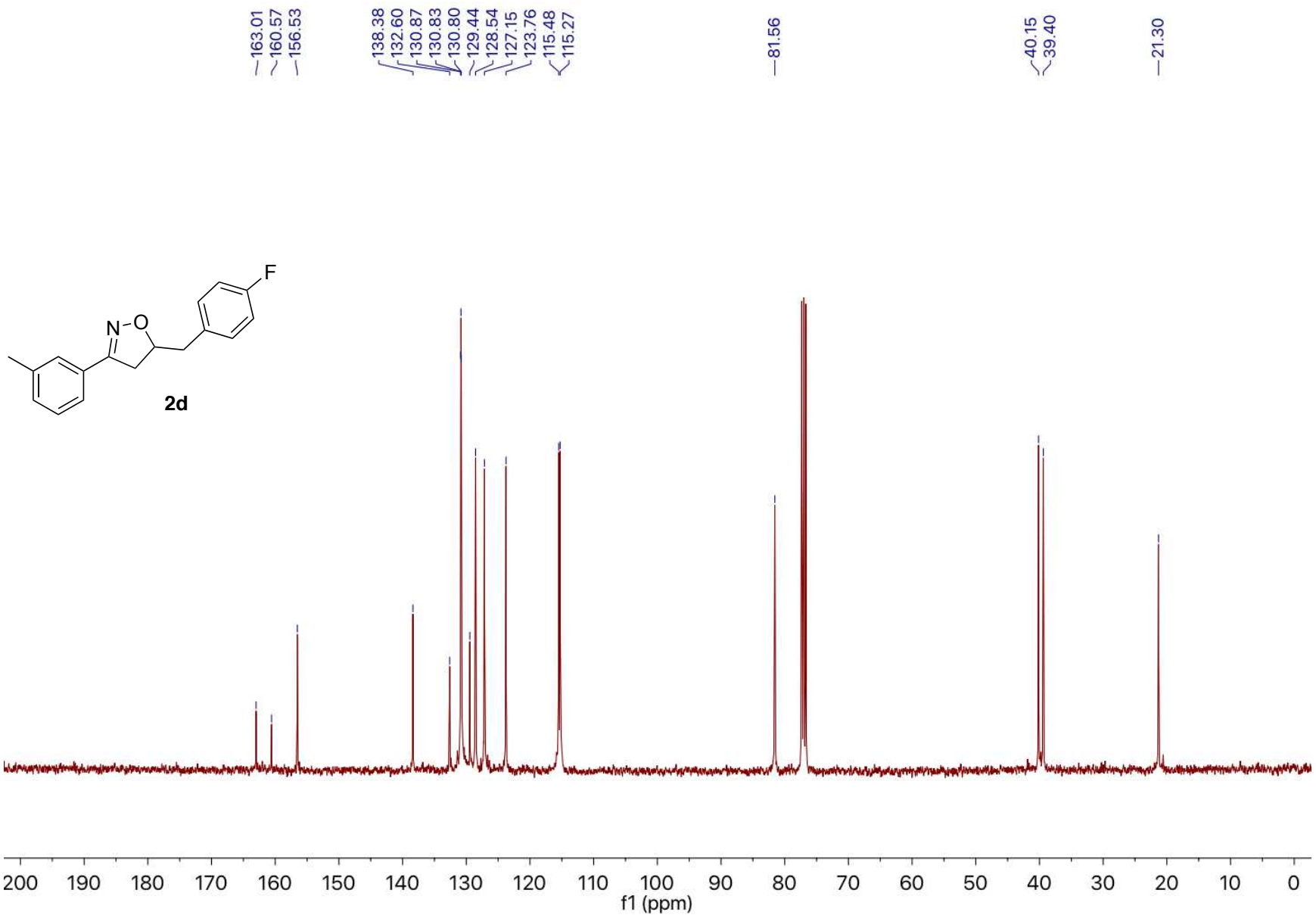
-140
-150
-160
-170
-180
-190
f1 (ppm)


7.47
7.42
7.40
7.29
7.27
7.25
7.23
7.23
7.22
7.20
7.02
7.00
6.98
4.98
4.97
4.95
4.94
4.92
4.91
3.36
3.33
3.32
3.29
3.12
3.10
3.08
3.07
3.04
3.02
3.00
2.98
2.91
2.89
2.87
2.86
2.36
F
N
O
2d
1.09
0.93
4.37
2.04
0.93
1.00
2.06
1.06
3.15
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
f1 (ppm)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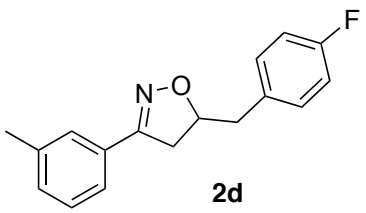
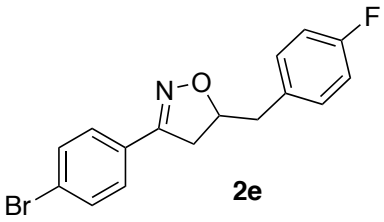
160.57
156.53
138.38
132.60
130.87
130.83
130.80
129.44
128.54
127.15
123.76
115.48
115.27
81.56
40.15
39.40
21.30
F
N
O
2d
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


F
N
O

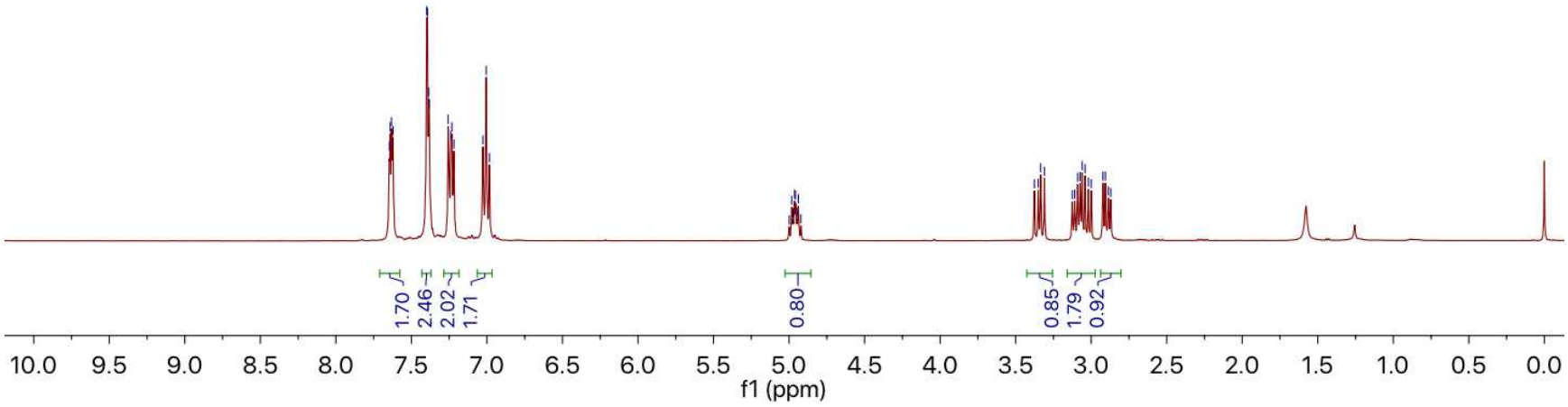
2d

-116.33
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)


7.65
7.64
7.63
7.62
7.40
7.39
7.39
7.38
7.26
7.24
7.23
7.22
7.03
7.00
6.98
5.00
4.98
4.97
4.96
4.96
4.95
4.94
4.92
3.38
3.35
3.33
3.31
3.12
3.11
3.09
3.07
3.06
3.04
3.02
3.00
2.92
2.91
2.89
2.87


F
N
O
Br

2e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2.46
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0.85
1.79
0.92
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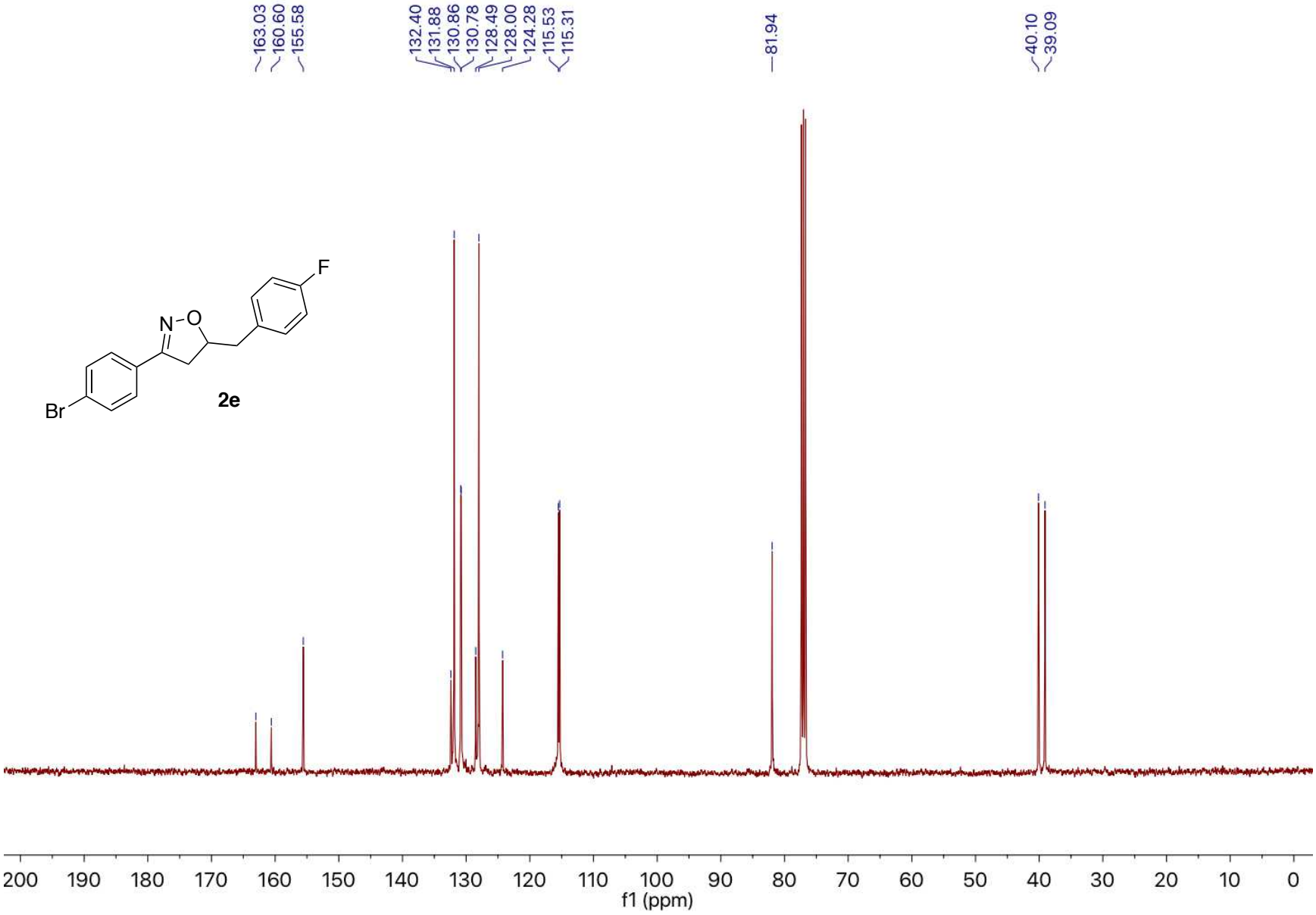
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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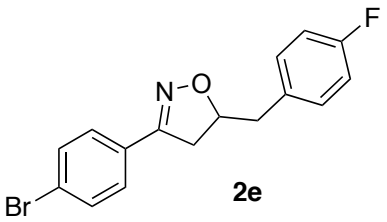
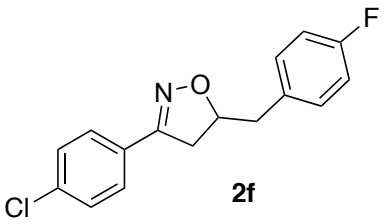
155.58
132.40
131.88
130.86
130.78
128.49
128.00
124.28
115.53
115.31
81.94
40.10
39.09
F
N
O
Br
2e
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


F
N
O
Br

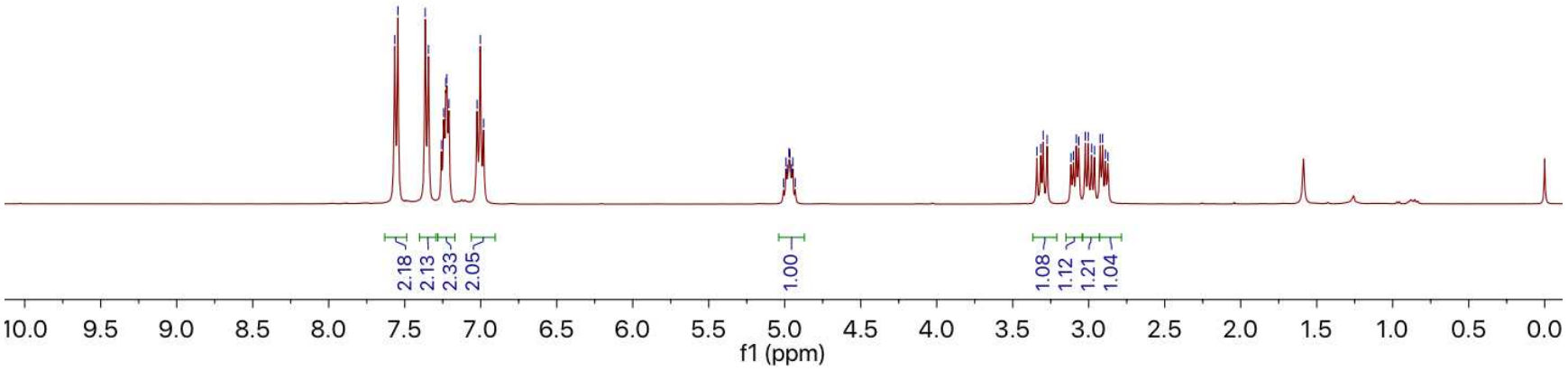
2e

-116.12
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)


7.57
7.54
7.37
7.34
7.26
7.24
7.23
7.22
7.21
7.02
7.00
6.98
5.01
4.99
4.98
4.97
4.97
4.96
4.95
4.93
3.34
3.31
3.30
3.27
3.12
3.10
3.08
3.07
3.02
3.00
2.98
2.96
2.92
2.91
2.89
2.87


F
N
O
Cl

2f


2.18
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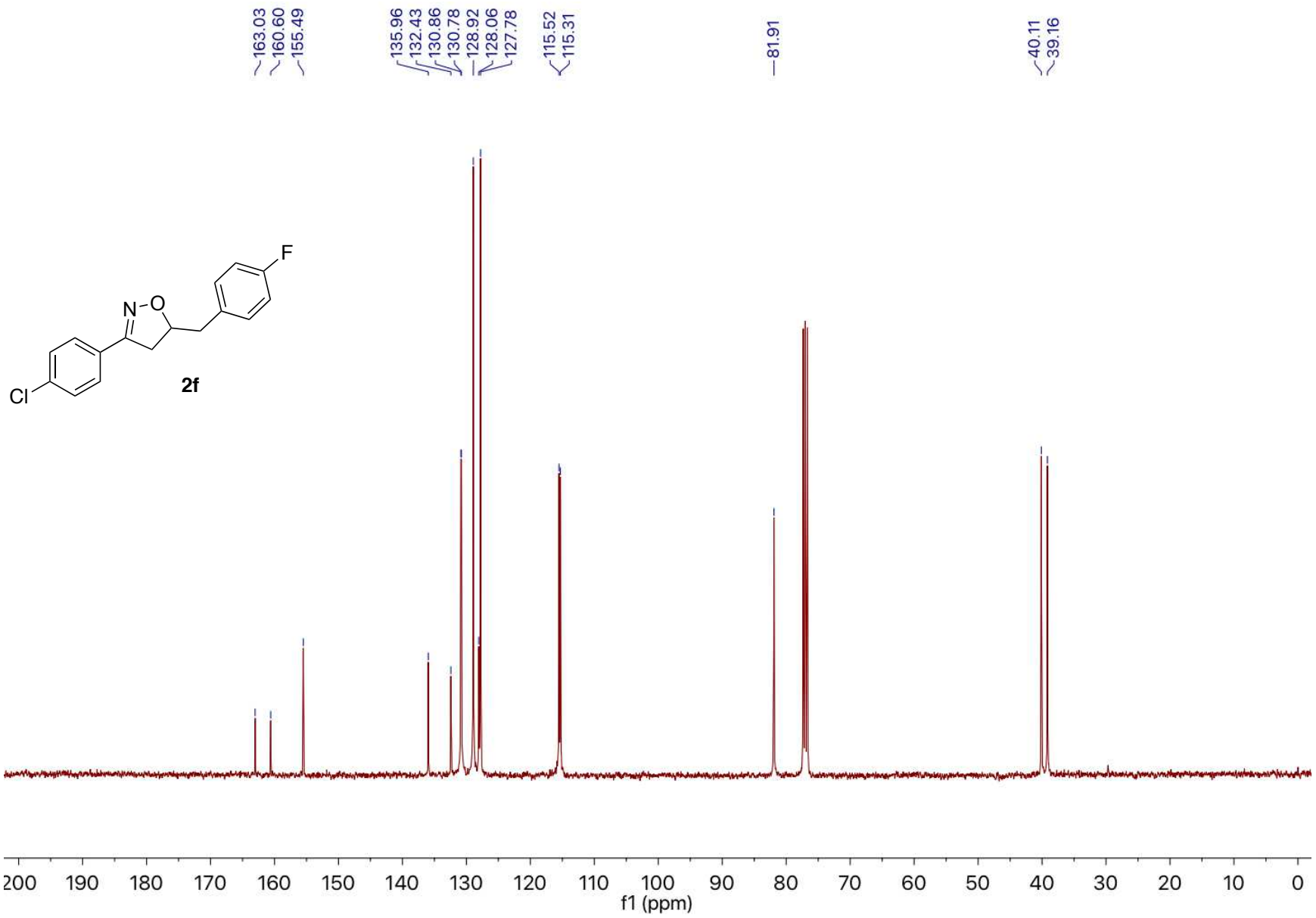
2.33
2.05
1.00
1.08
1.12
1.21
1.04
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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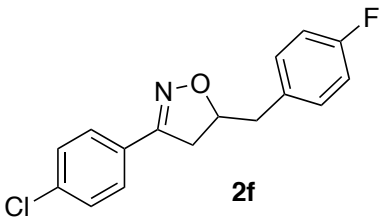
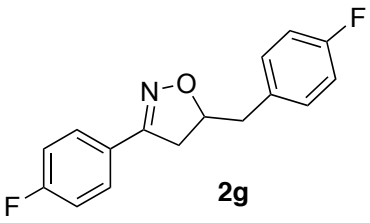
155.49
135.96
132.43
130.86
130.78
128.92
128.06
127.78
115.52
115.31
81.91
40.11
39.16
F
N
O
Cl
2f
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


F
N
O
Cl

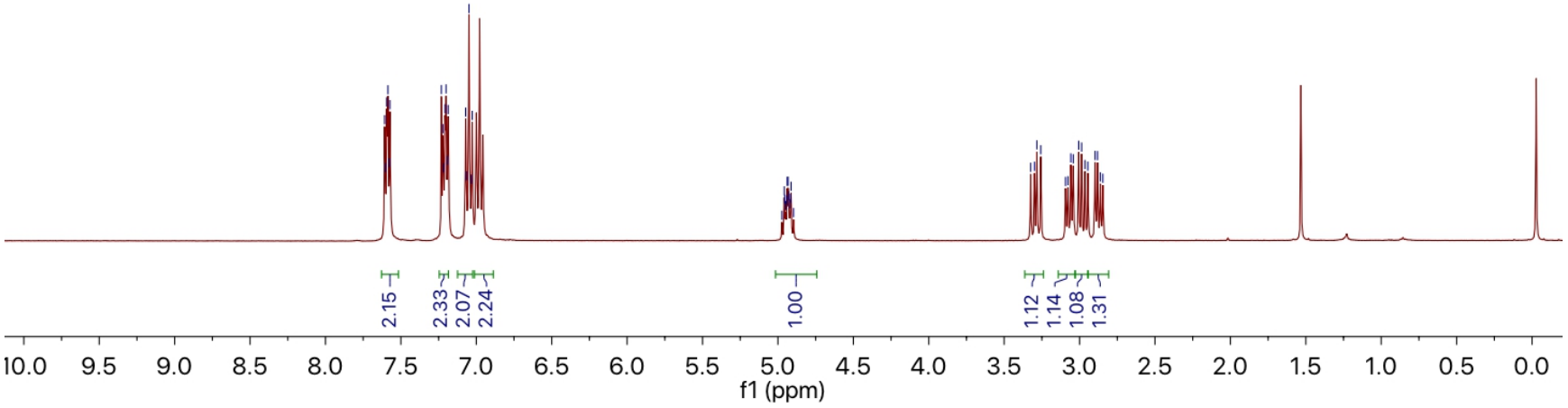
2f

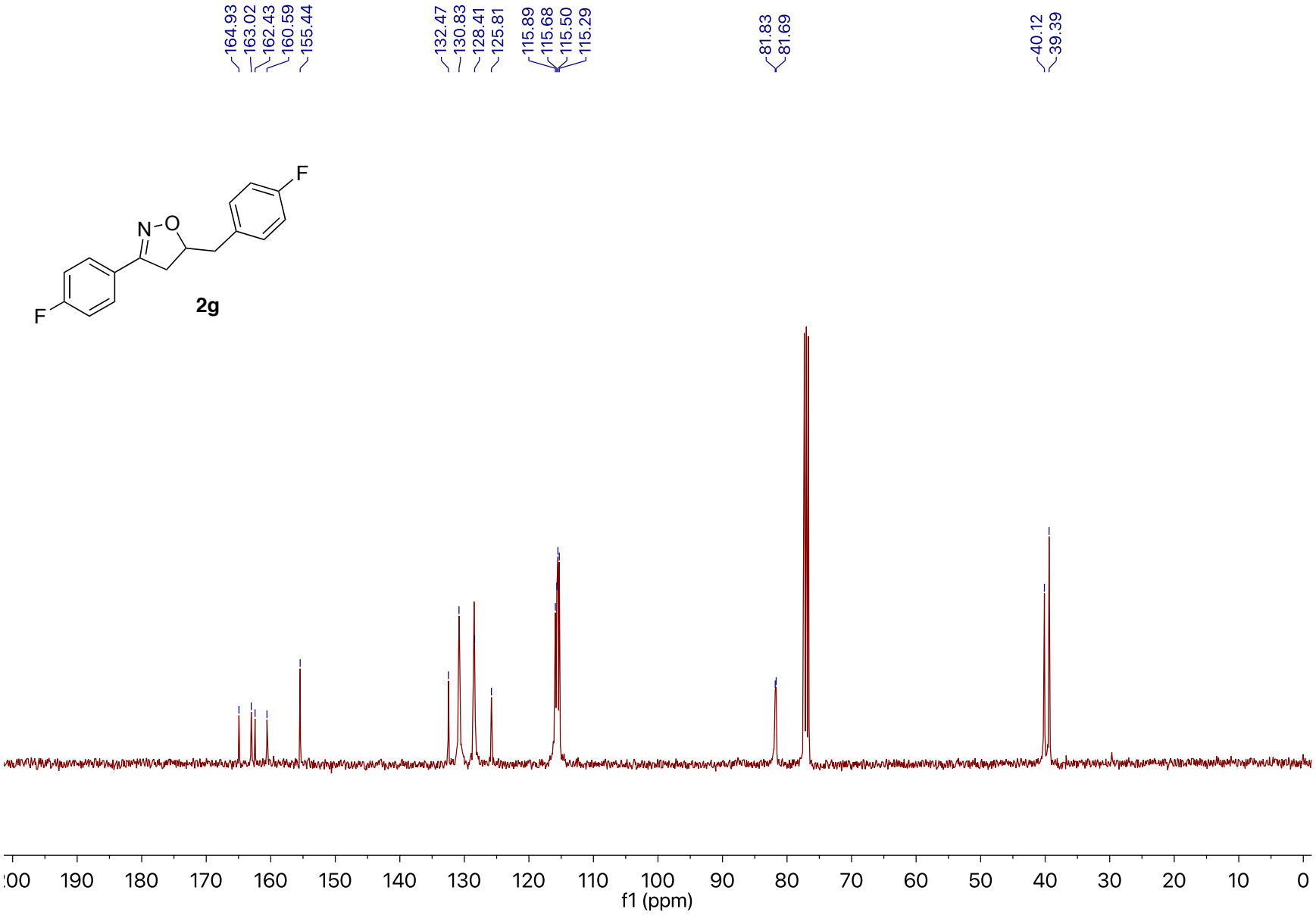
-116.15
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)


7.61
7.60
7.59
7.59
7.58
7.57
7.23
7.22
7.22
7.21
7.20
7.19
7.19
7.07
7.07
7.05
7.03
7.03
4.97
4.96
4.95
4.95
4.94
4.94
4.93
4.93
4.92
4.92
4.91
4.90
3.32
3.30
3.28
3.26
3.09
3.08
3.06
3.04
3.01
2.99
2.96
2.95
2.90
2.88
2.86
2.85


F
N
O
F

2g


2.15
2.33
2.07
2.24
1.00
1.12
1.14
1.08
1.31
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
f1 (ppm)


164.93
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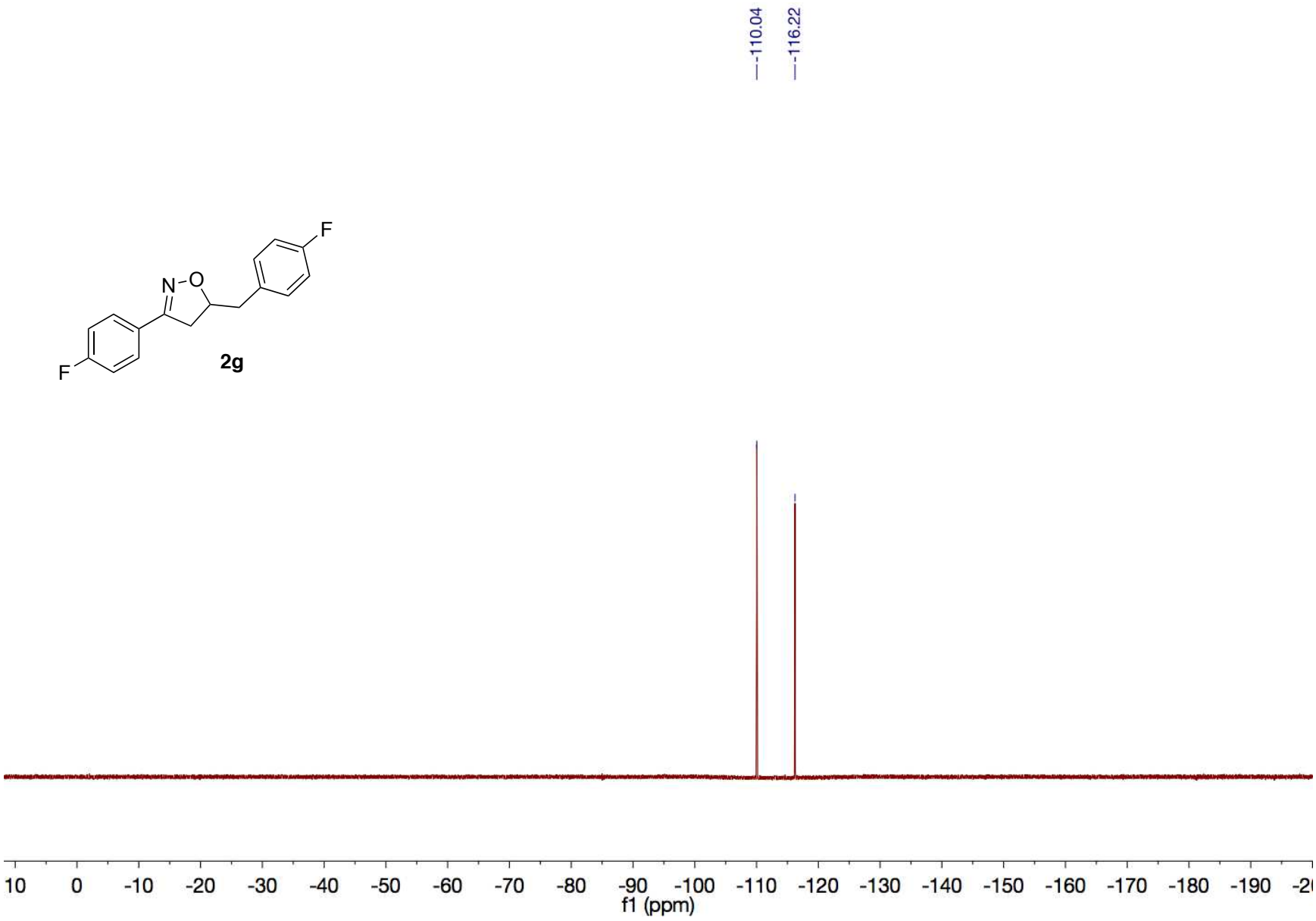
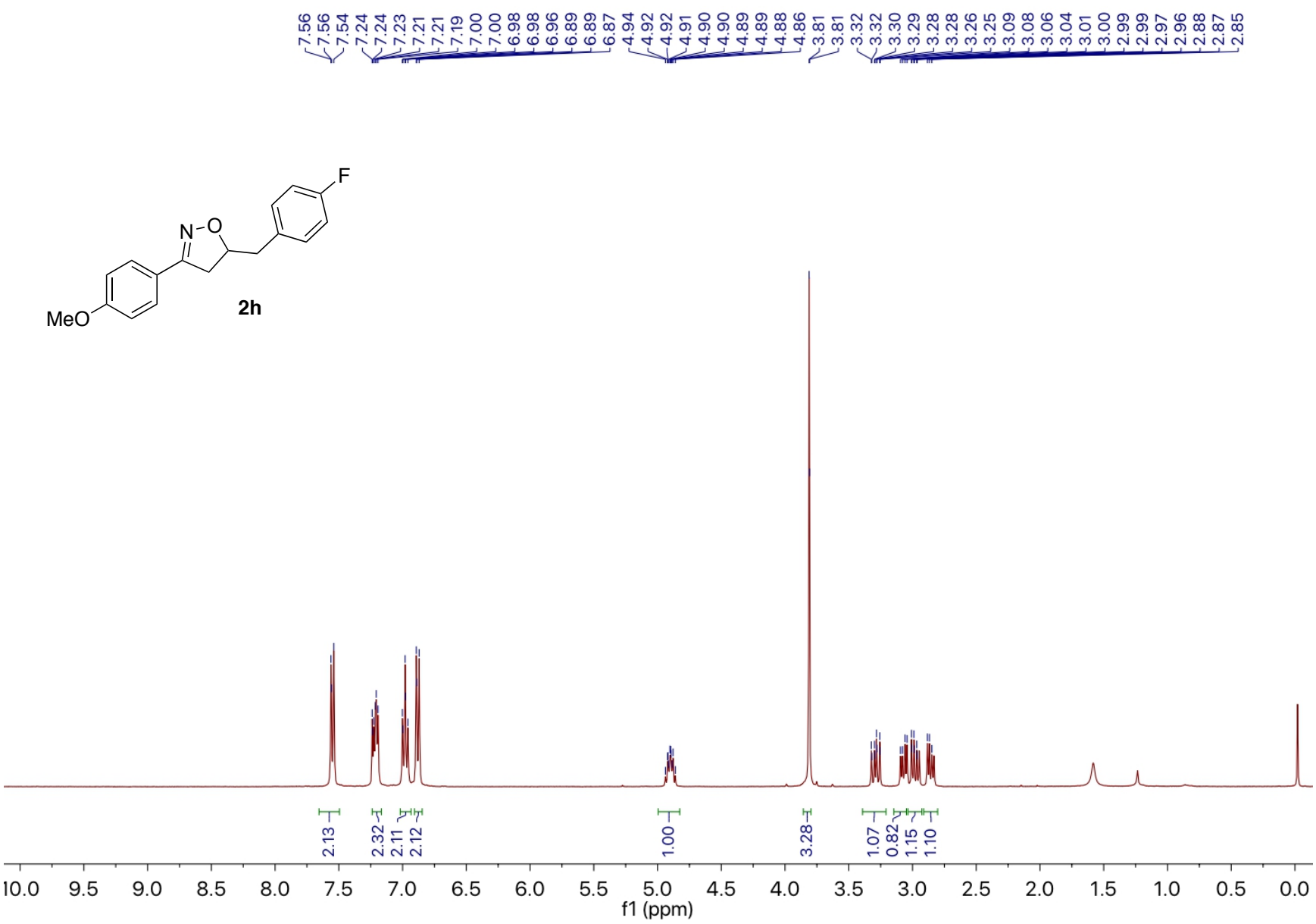
160.59
155.44
132.47
130.83
128.41
125.81
115.89
115.68
115.50
115.29
81.83
81.69
40.12
39.39
F
N
O
F
2g
f1 (ppm)


-110.04
-116.22
F
N
O
F
2g
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)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7.24
7.23
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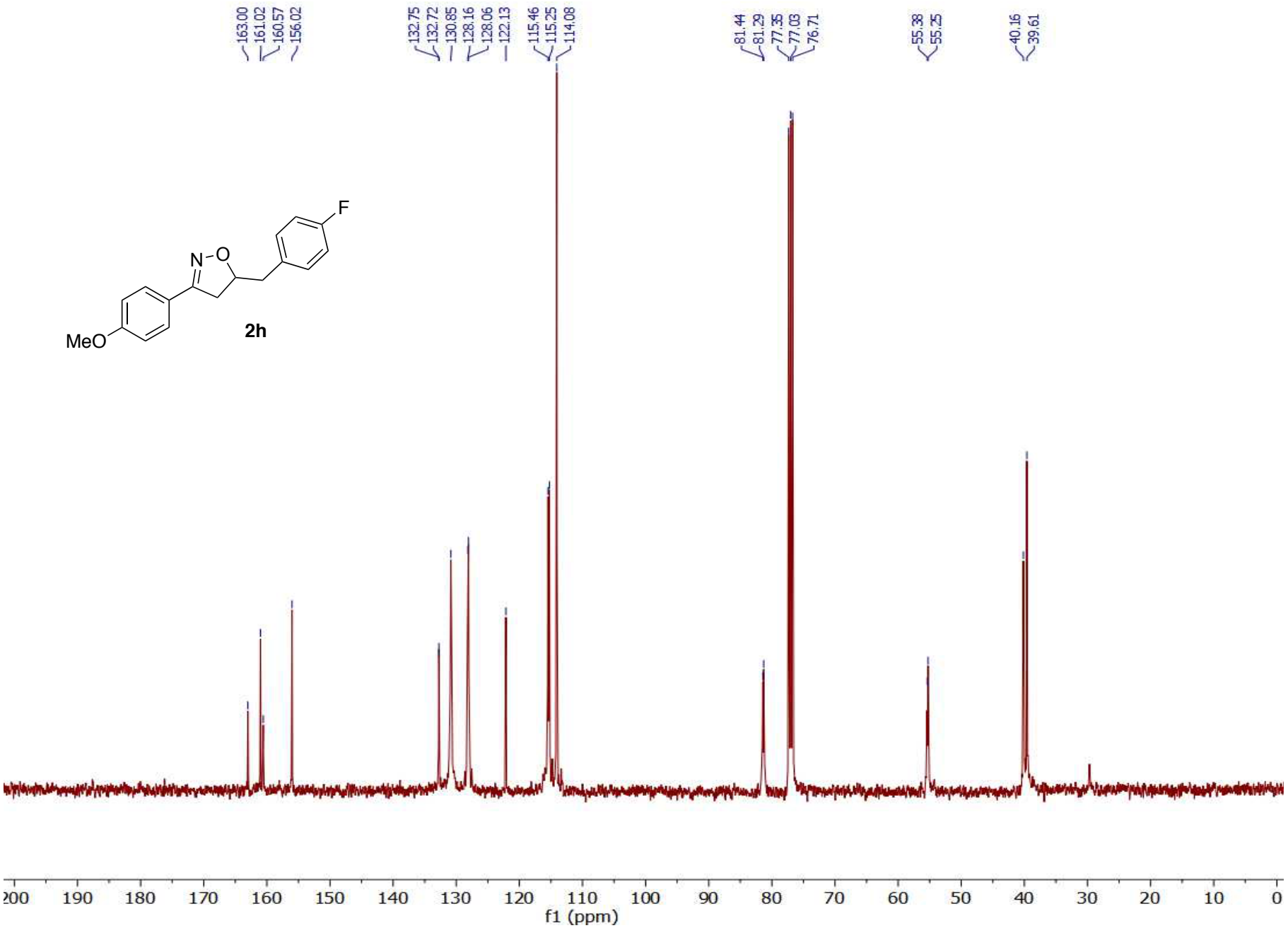
7.21
7.19
7.00
7.00
6.98
6.98
6.96
6.89
6.89
6.87
4.94
4.92
4.92
4.91
4.90
4.90
4.89
4.89
4.88
4.86
3.81
3.81
3.32
3.32
3.30
3.29
3.28
3.28
3.26
3.25
3.09
3.08
3.06
3.04
3.01
3.00
2.99
2.99
2.97
2.96
2.88
2.87
2.85
F
N
O
MeO
2h
2.13
2.32
2.11
2.12
1.00
3.28
1.07
0.82
1.15
1.10
10.0
9.5
9.0
8.5
8.0
7.5
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
f1 (ppm)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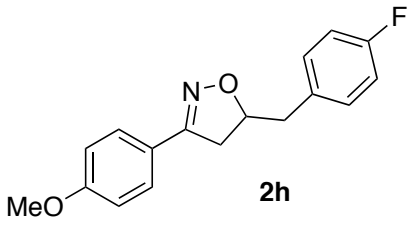
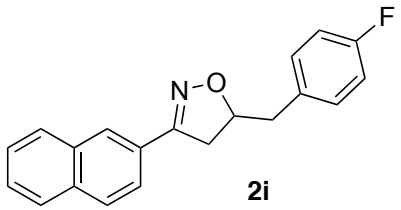
161.02
160.57
156.02
132.75
132.72
130.85
128.16
128.06
122.13
115.46
115.25
114.08
81.44
81.29
77.35
77.03
76.71
55.38
55.25
40.16
39.61
F
N
O
MeO
2h
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


F
N
O
MeO

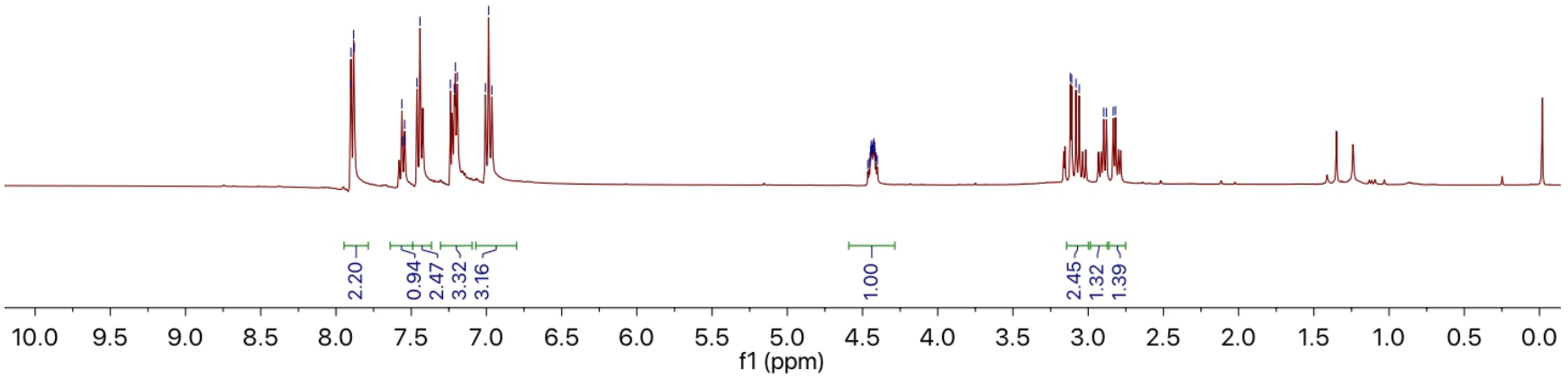
2h

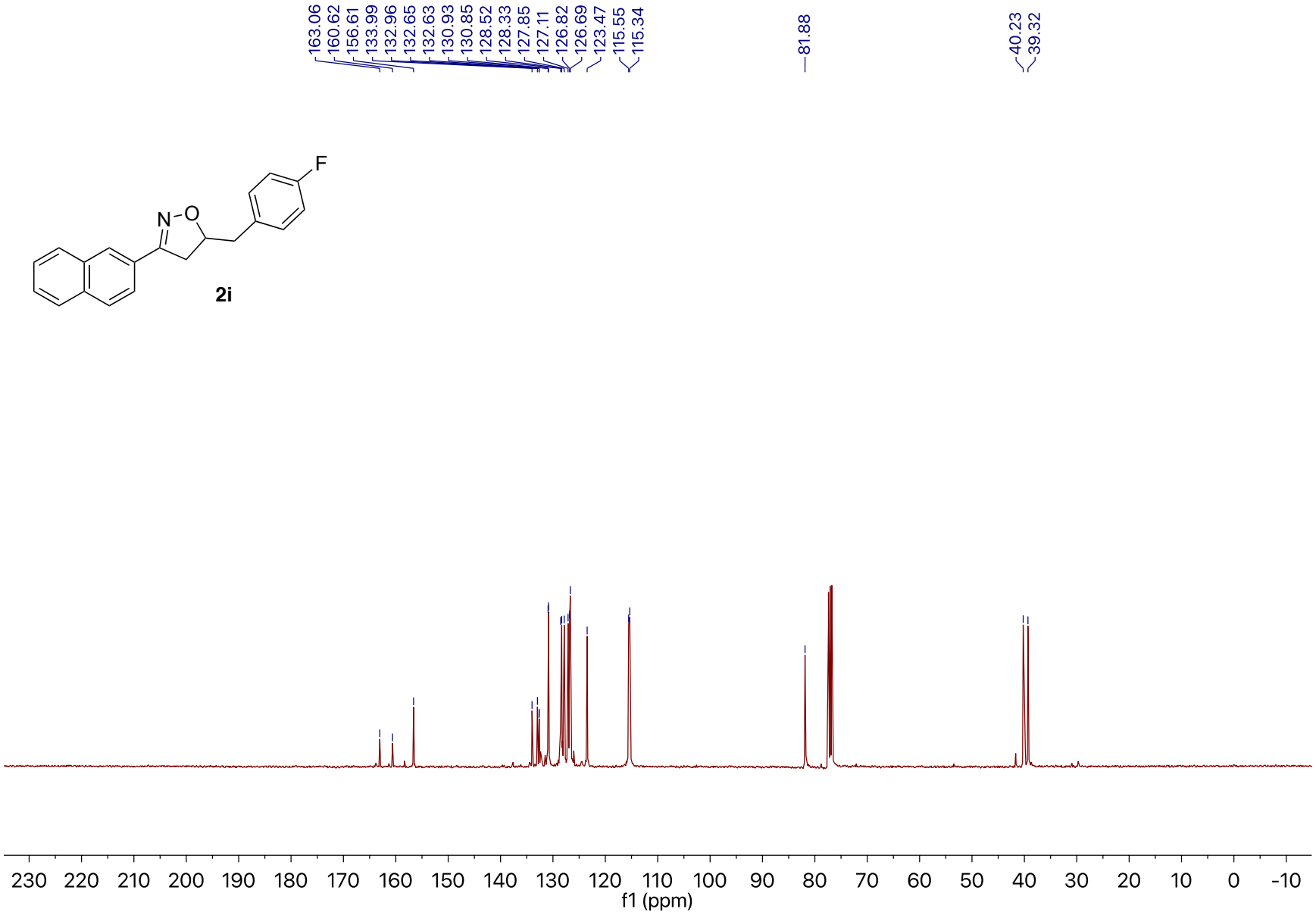
-116.31
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

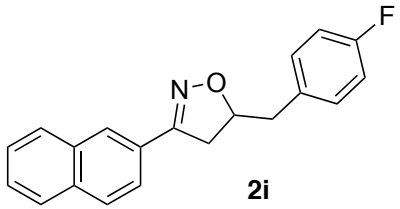

7.90
7.90
7.88
7.88
7.56
7.56
7.54
7.54
7.46
7.44
7.24
7.21
7.19
7.01
6.99
6.96
4.46
4.46
4.45
4.45
4.44
4.44
4.44
4.43
4.43
4.42
4.42
4.42
4.41
4.40
3.12
3.11
3.08
3.06
2.90
2.88
2.83
2.82


F
N
O

2i


2.20
0.94
2.47
3.32
3.16
1.00
2.45
1.32
1.39
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
f1 (ppm)


163.06
160.62
156.61
133.99
132.96
132.65
132.63
130.93
130.85
128.52
128.33
127.85
127.11
126.82
126.69
123.47
115.55
115.34
81.88
40.23
39.32
F
N
O
2i
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


F
N
O

2i

-116.66
10
0
-10
-20
-30
-40
-50
-60
-70
-80
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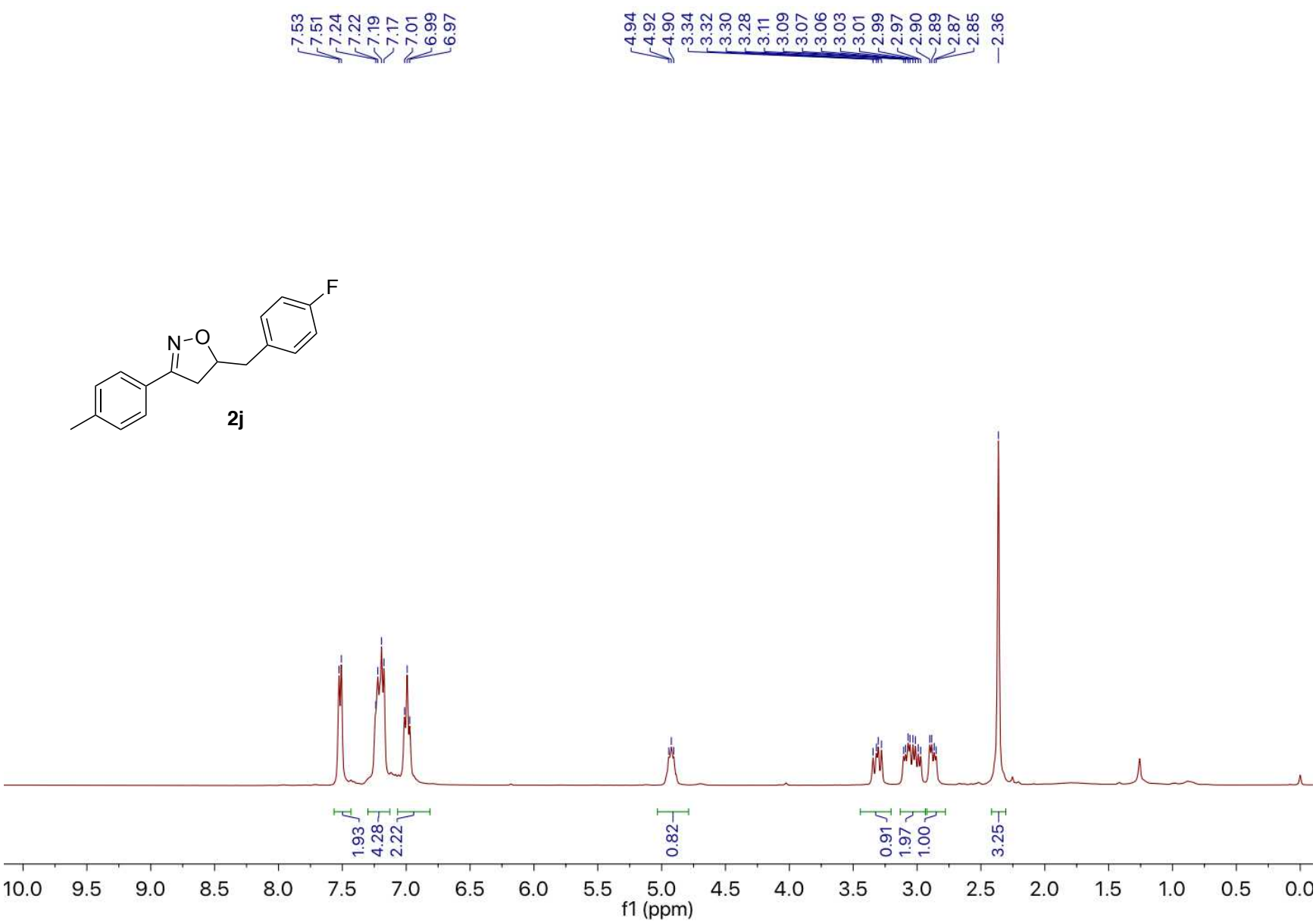
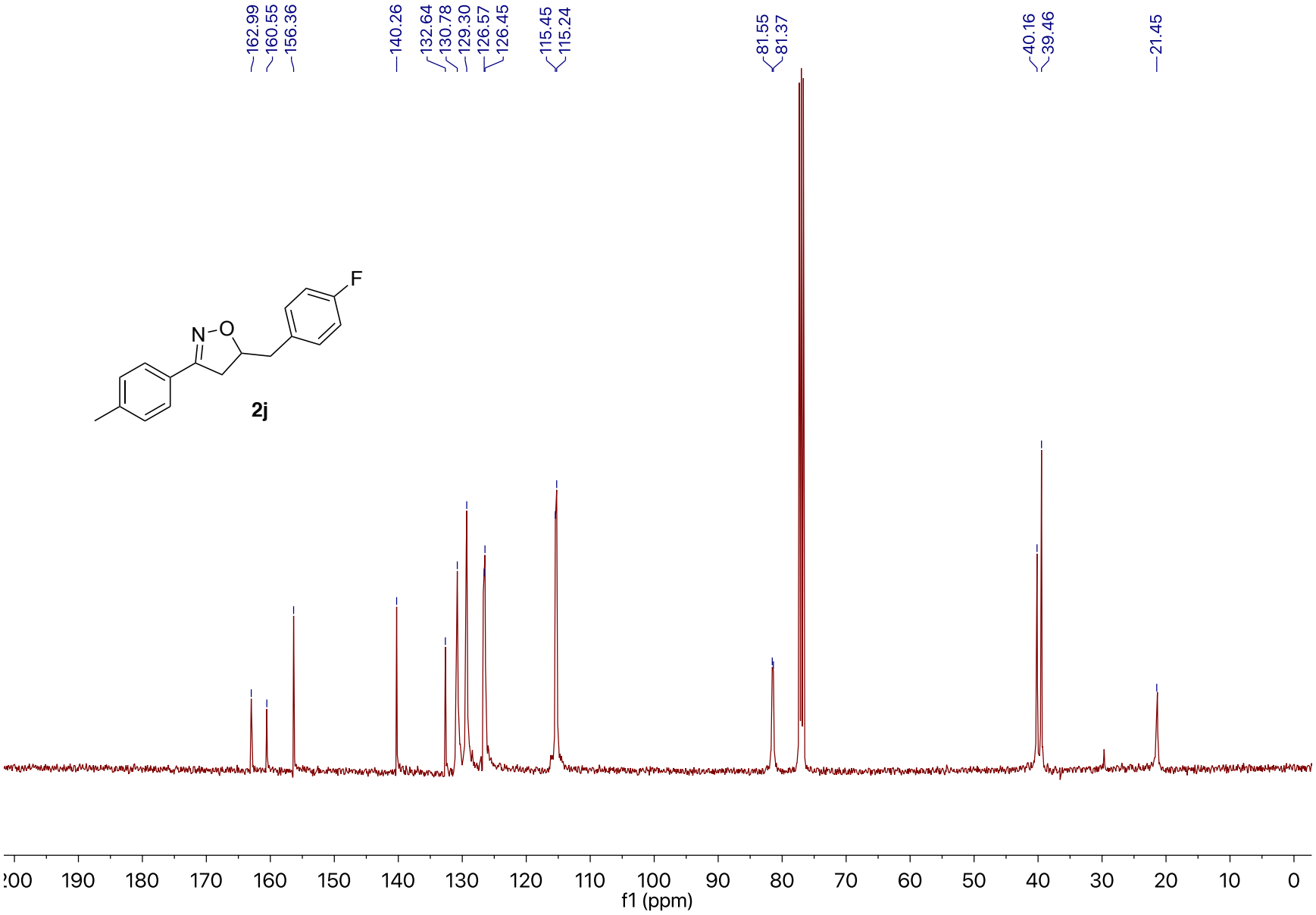
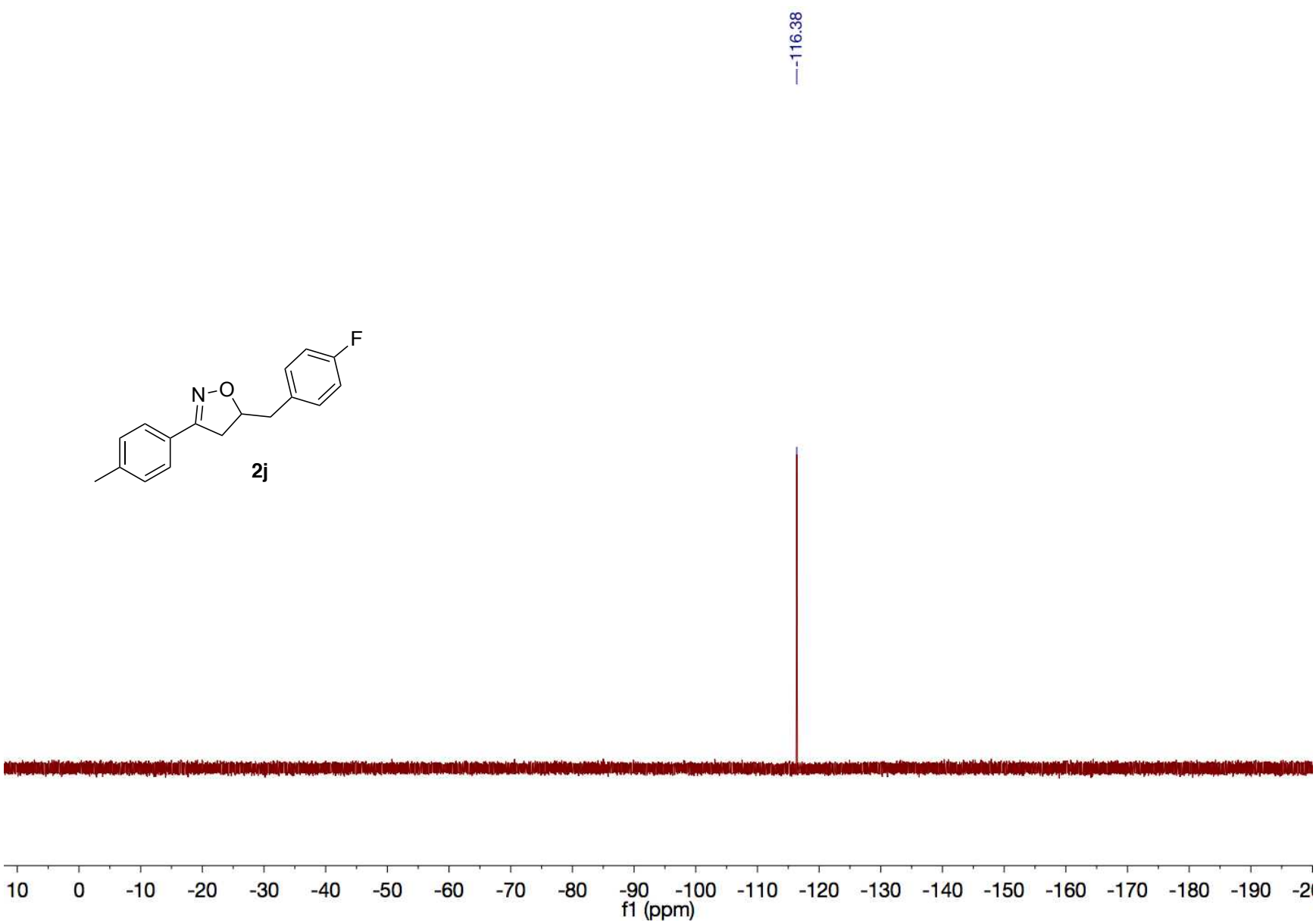
-150
-160
-170
-180
-190
f1 (ppm)


7.53
7.51
7.24
7.22
7.19
7.17
7.01
6.99
6.97
4.94
4.92
4.90
3.34
3.32
3.30
3.28
3.11
3.09
3.07
3.06
3.03
3.01
2.99
2.97
2.90
2.89
2.87
2.85
2.36
F
N
O
2j
1.93
4.28
2.22
0.82
0.91
1.97
1.00
3.25
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
f1 (ppm)


162.99
160.55
156.36
140.26
132.64
130.78
129.30
126.57
126.45
115.45
115.24
81.55
81.37
40.16
39.46
21.45
F
N
O
2j
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-116.38
F
N
O
2j
10
0
-10
-20
-30
-40
-50
-60
-70
-80
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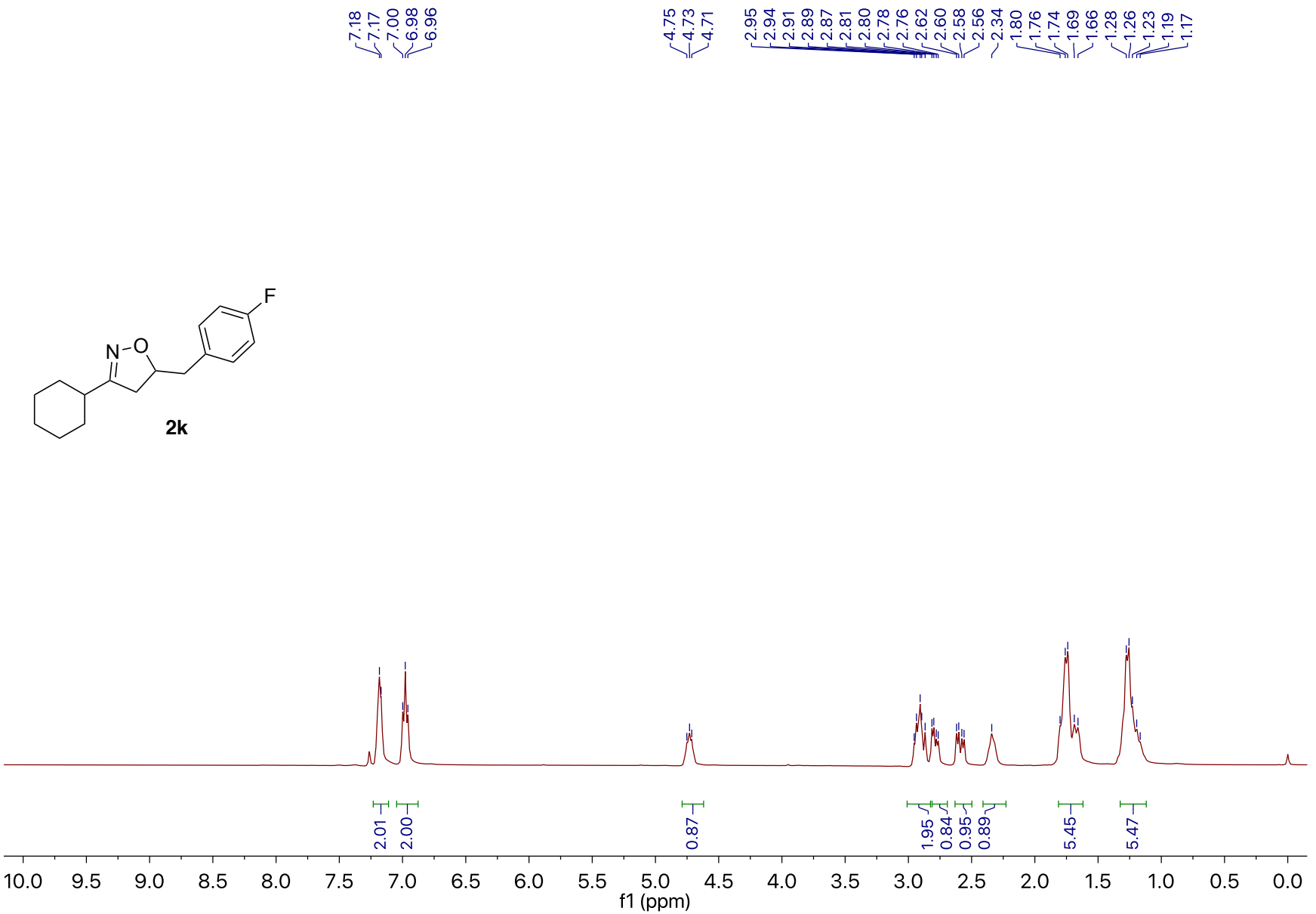
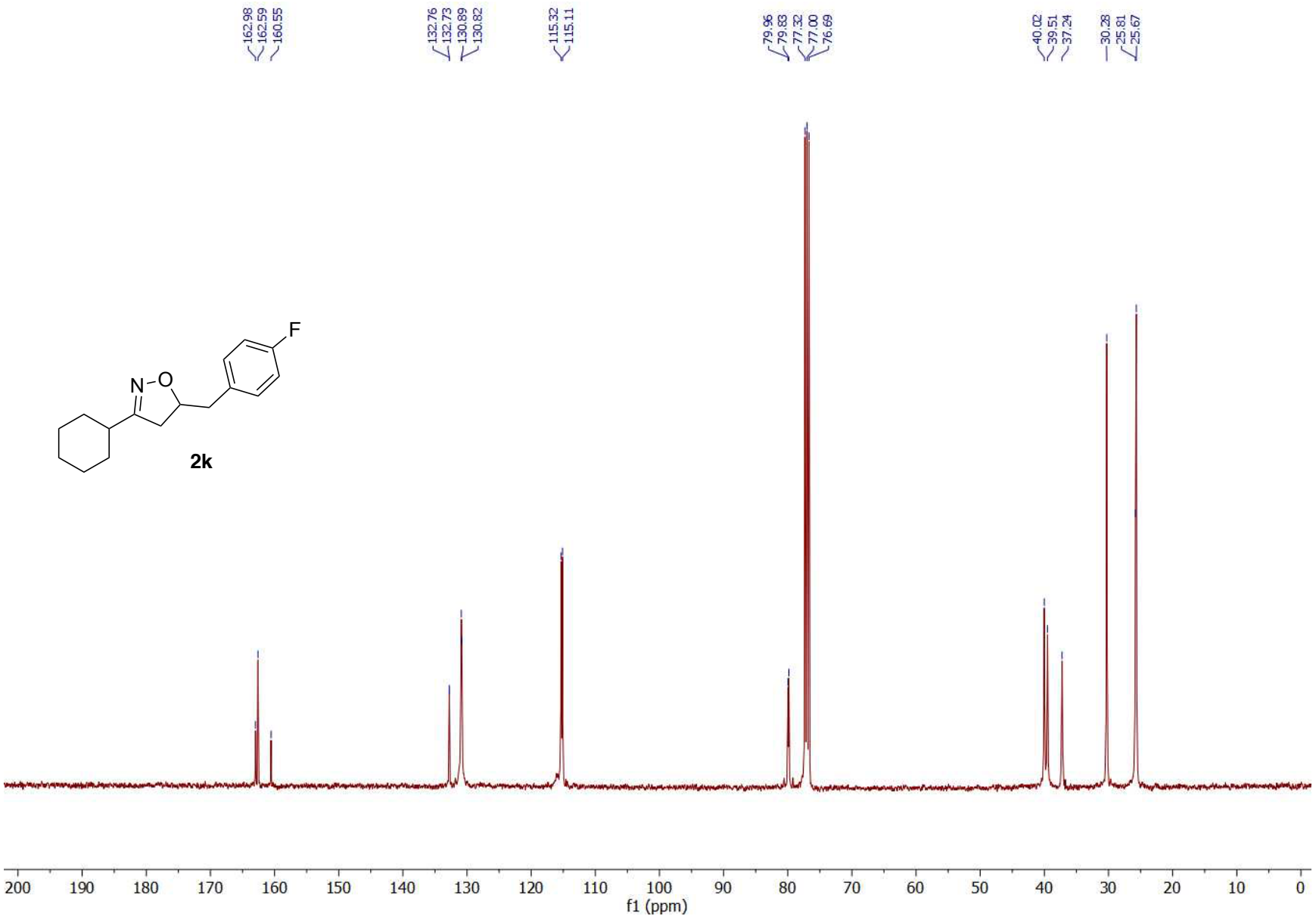
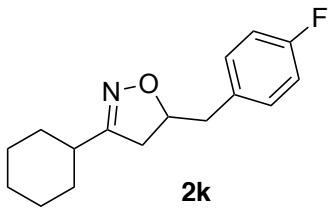
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

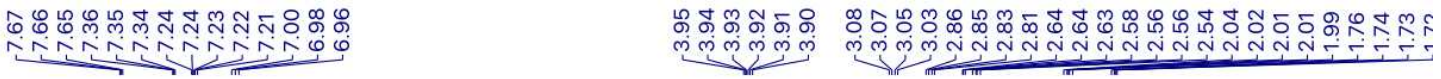

7.18
7.17
7.00
6.98
6.96
4.75
4.73
4.71
2.95
2.94
2.91
2.89
2.87
2.81
2.80
2.78
2.76
2.62
2.60
2.58
2.56
2.34
1.80
1.76
1.74
1.69
1.66
1.28
1.26
1.23
1.19
1.17
F
N
O
2k
2.01
2.00
0.87
1.95
0.84
0.95
0.89
5.45
5.47
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


162.98
162.59
160.55
132.76
132.73
130.89
130.82
115.32
115.11
79.96
79.83
77.32
77.00
76.69
40.02
39.51
37.24
30.28
25.81
25.67
F
N
O
2k
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


F
N
O

2k

-116.59
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)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7.66
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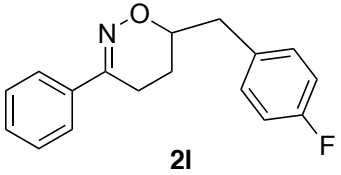
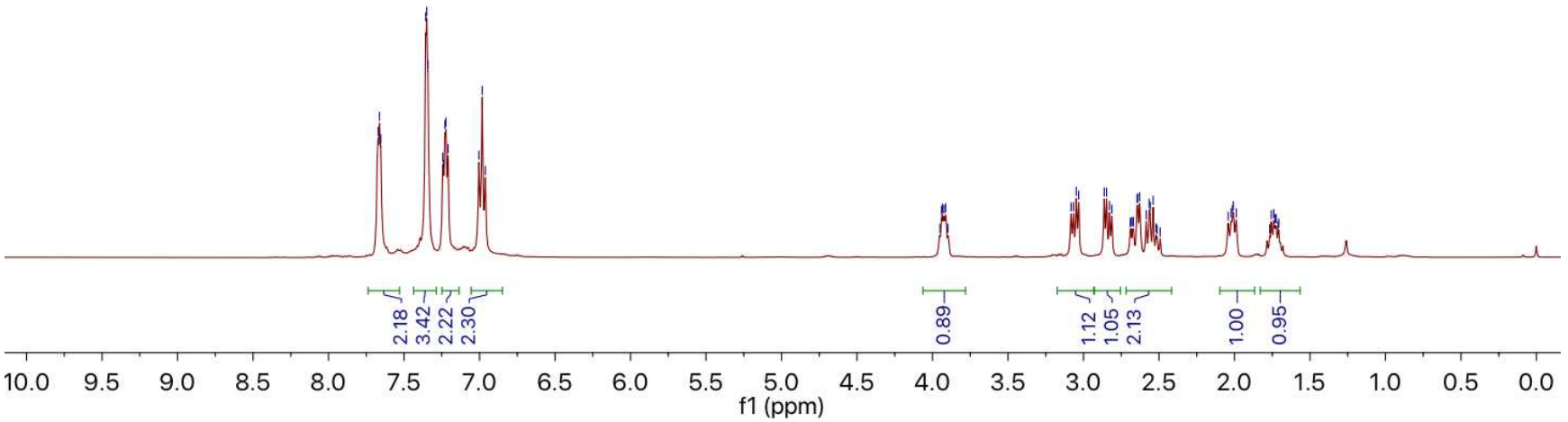
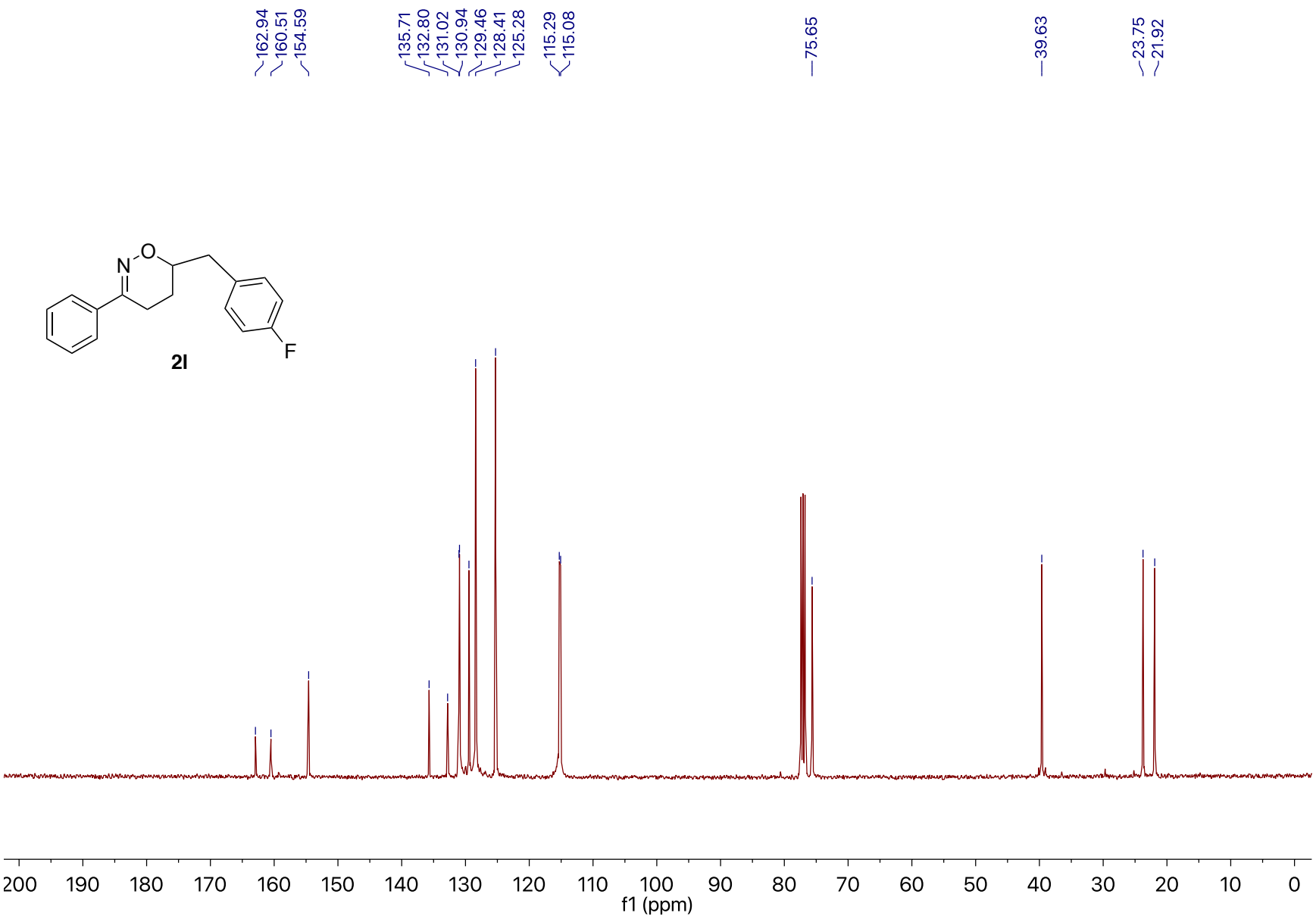
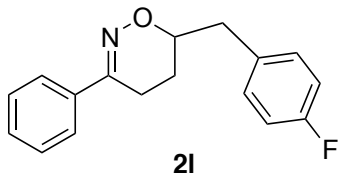
7.36
7.35
7.34
7.24
7.24
7.23
7.22
7.21
7.00
6.98
6.96
3.95
3.94
3.93
3.92
3.91
3.90
3.08
3.07
3.05
3.03
2.86
2.85
2.83
2.81
2.64
2.64
2.63
2.58
2.56
2.56
2.54
2.04
2.02
2.01
2.01
1.99
1.76
1.74
1.73


N
O
F

2l

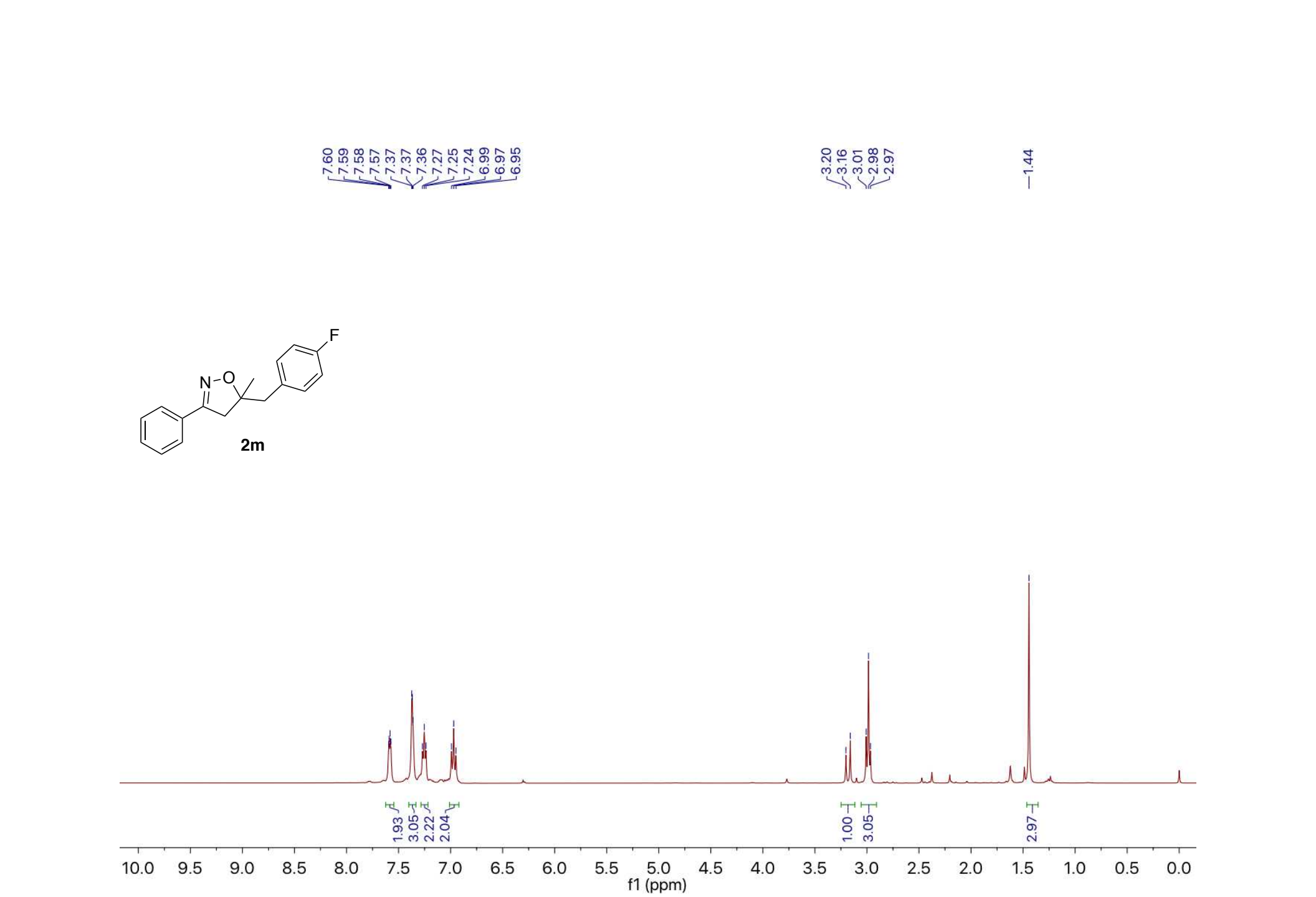

2.18
3.42
2.22
2.30
0.89
1.12
1.05
2.13
1.00
0.95
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


162.94
160.51
154.59
135.71
132.80
131.02
130.94
129.46
128.41
125.28
115.29
115.08
75.65
39.63
23.75
21.92
N
O
F
2l
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


N
O
F

2l

-116.71
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)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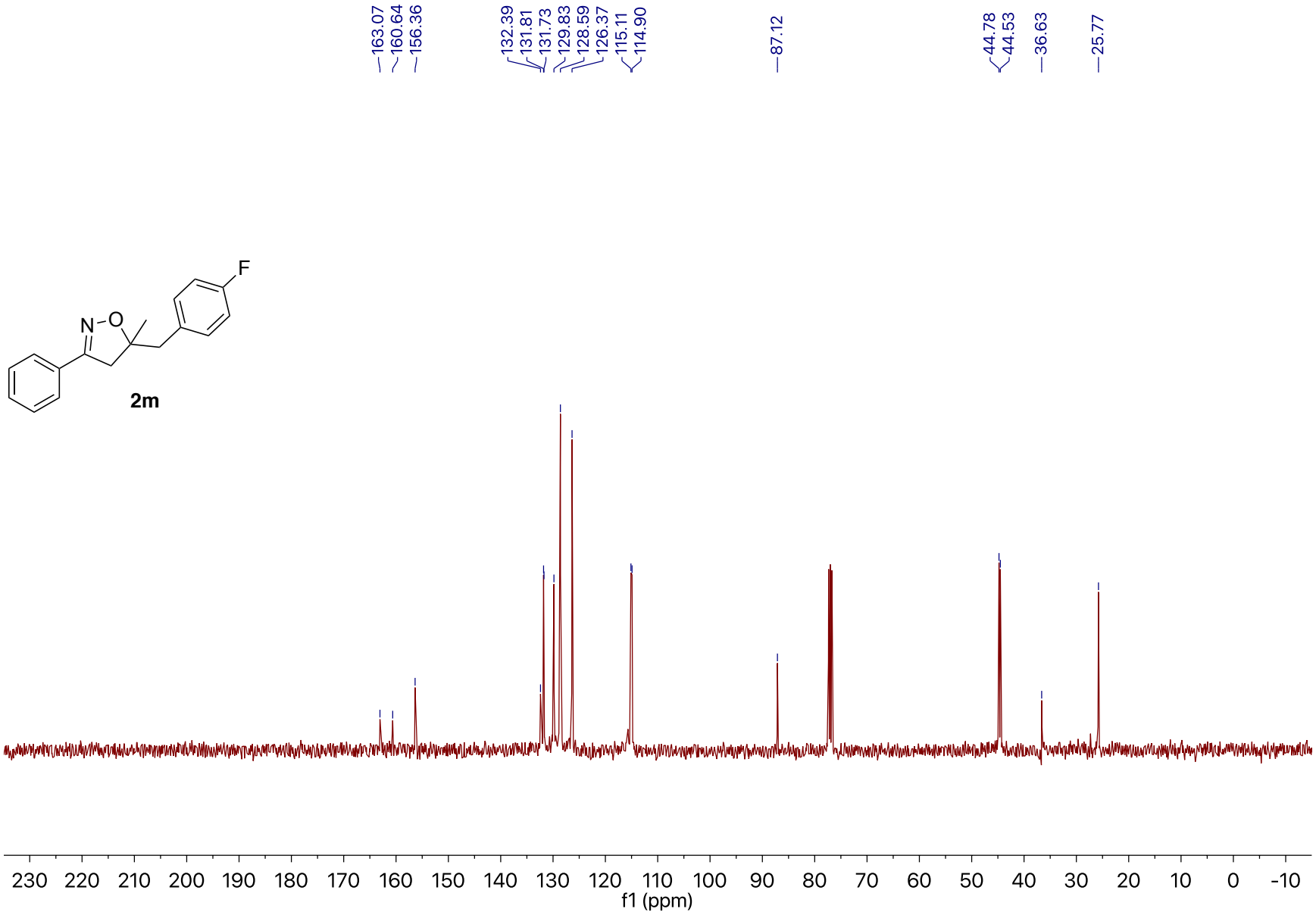
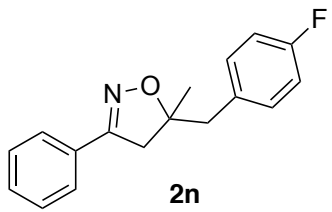
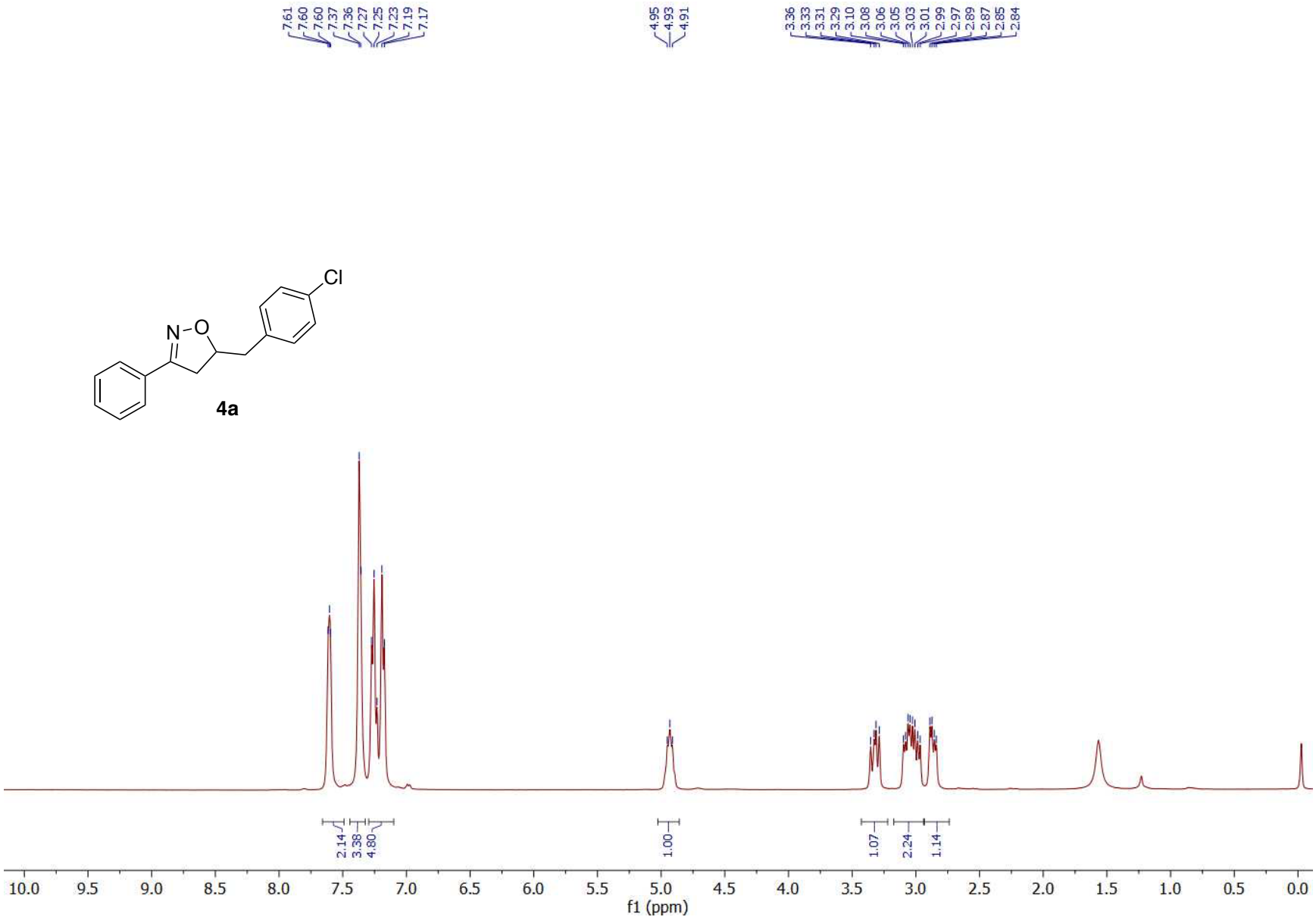
7.59
7.58
7.57
7.37
7.37
7.36
7.27
7.25
7.24
6.99
6.97
6.95
3.20
3.16
3.01
2.98
2.97
1.44
F
N
O
2m
1.93
3.05
2.22
2.04
1.00
3.05
2.97
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


163.07
160.64
156.36
132.39
131.81
131.73
129.83
128.59
126.37
115.11
114.90
87.12
44.78
44.53
36.63
25.77
F
N
O
2m
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


F
N
O

2n

-116.40
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)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7.37
7.36
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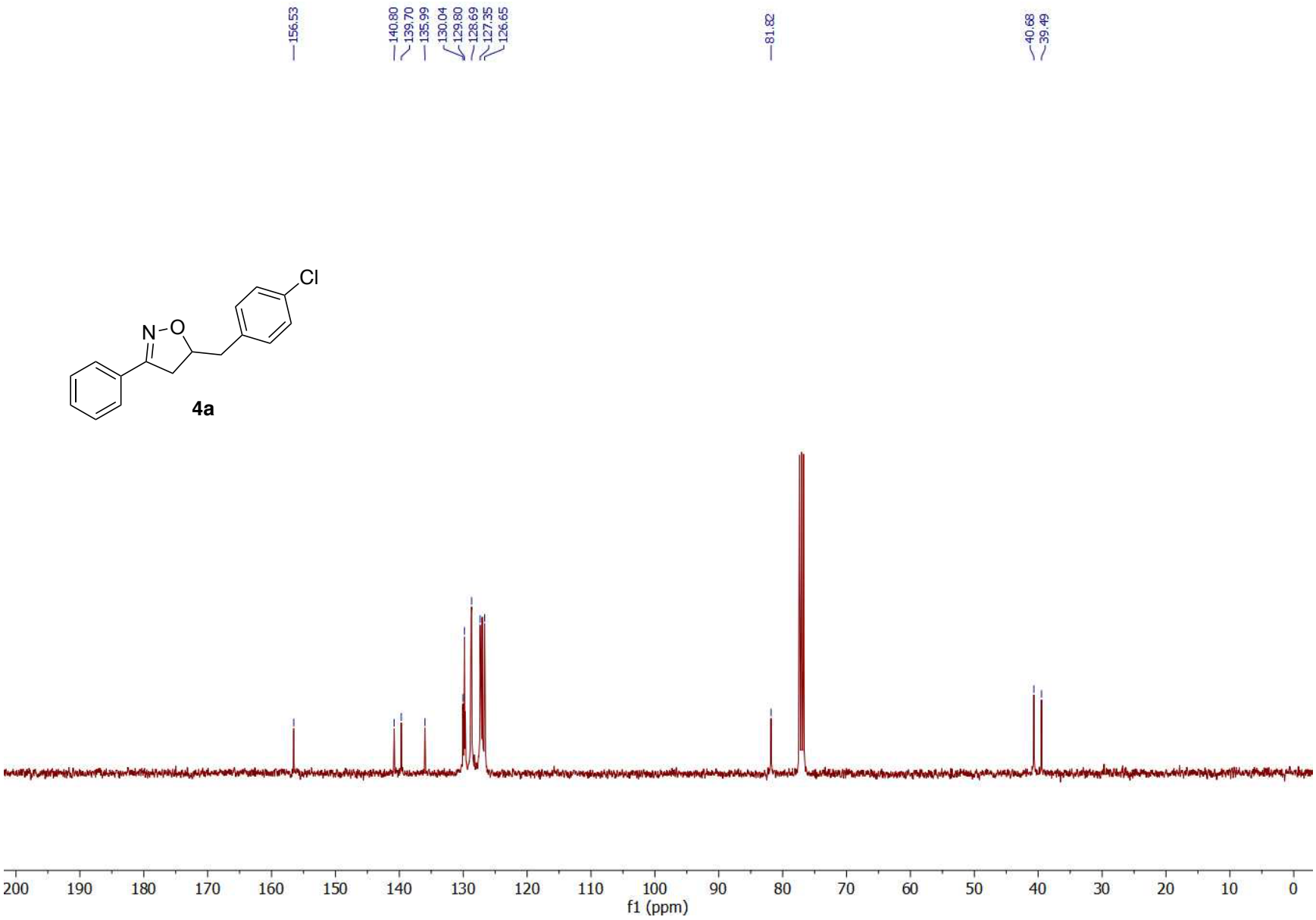
7.25
7.23
7.19
7.17
4.95
4.93
4.91
3.36
3.33
3.31
3.29
3.10
3.08
3.06
3.05
3.03
3.01
2.99
2.97
2.89
2.87
2.85
2.84
Cl
N
O
4a
2.14
3.38
4.80
1.00
1.07
2.24
1.14
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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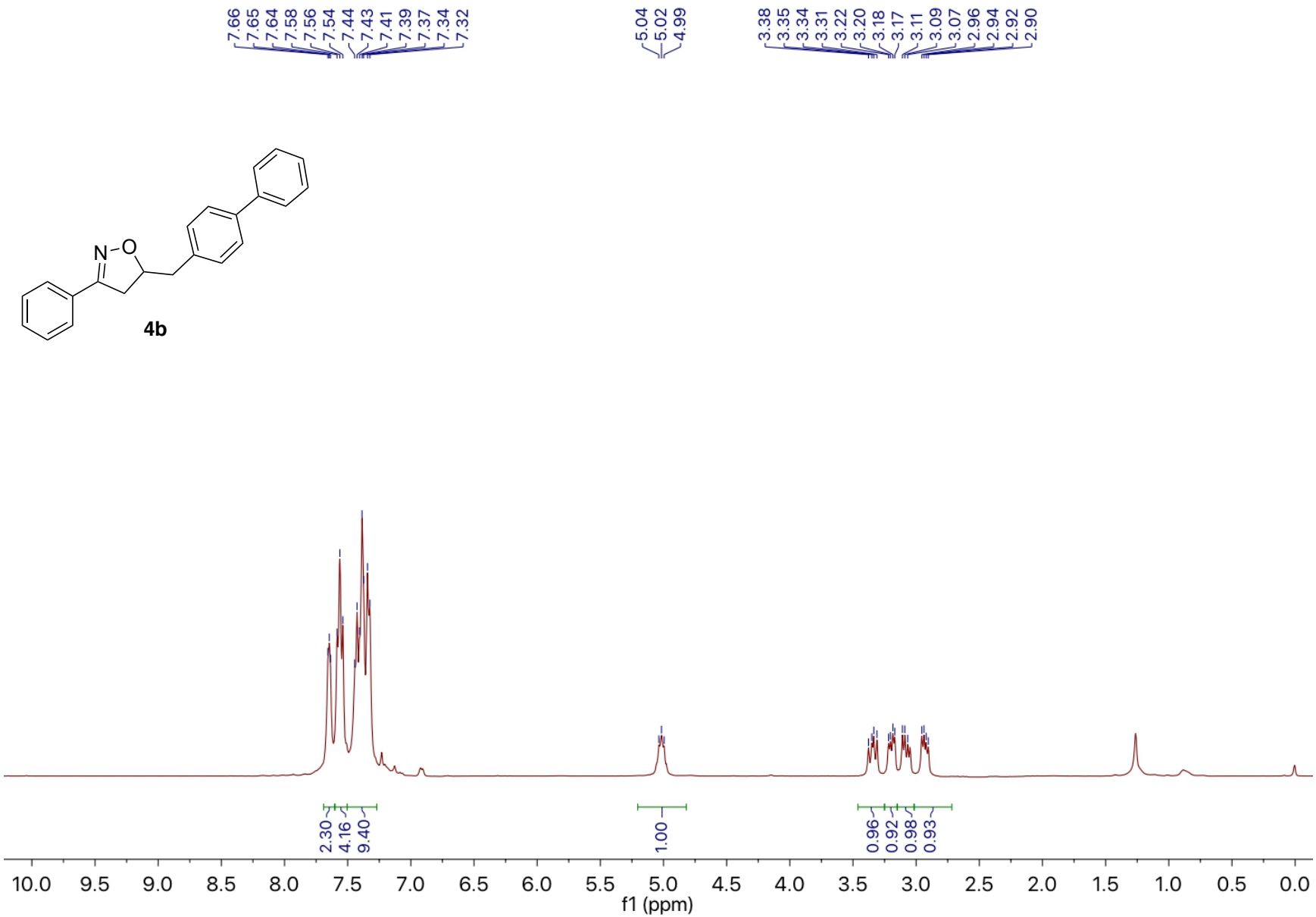
140.80
139.70
135.99
130.04
129.80
128.69
127.35
126.65
81.82
40.68
39.49
Cl
N
O
4a
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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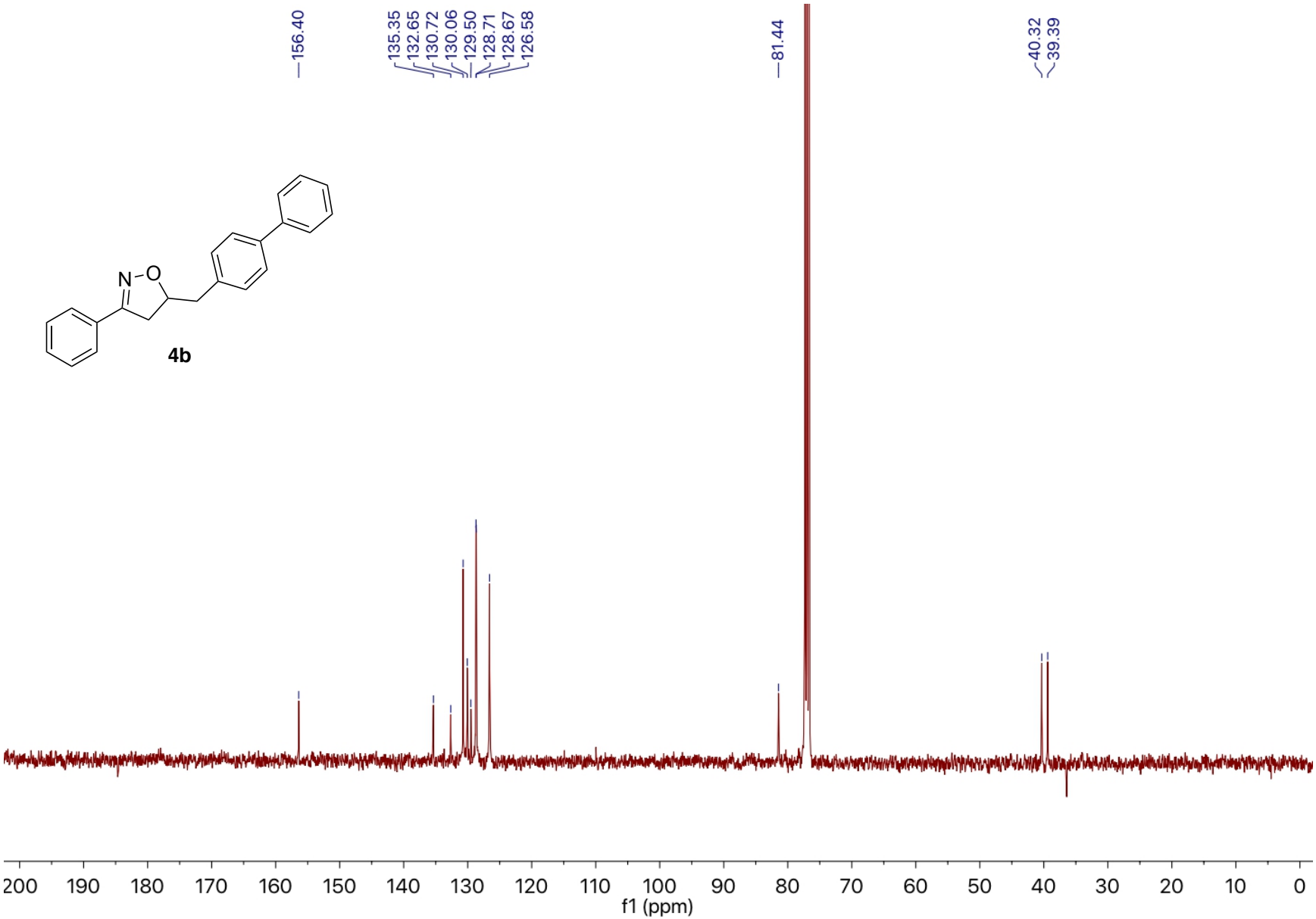
7.43
7.41
7.39
7.37
7.34
7.32
5.04
5.02
4.99
3.38
3.35
3.34
3.31
3.22
3.20
3.18
3.17
3.11
3.09
3.07
2.96
2.94
2.92
2.90
N
O
4b
2.30
4.16
9.40
1.00
0.96
0.92
0.98
0.93
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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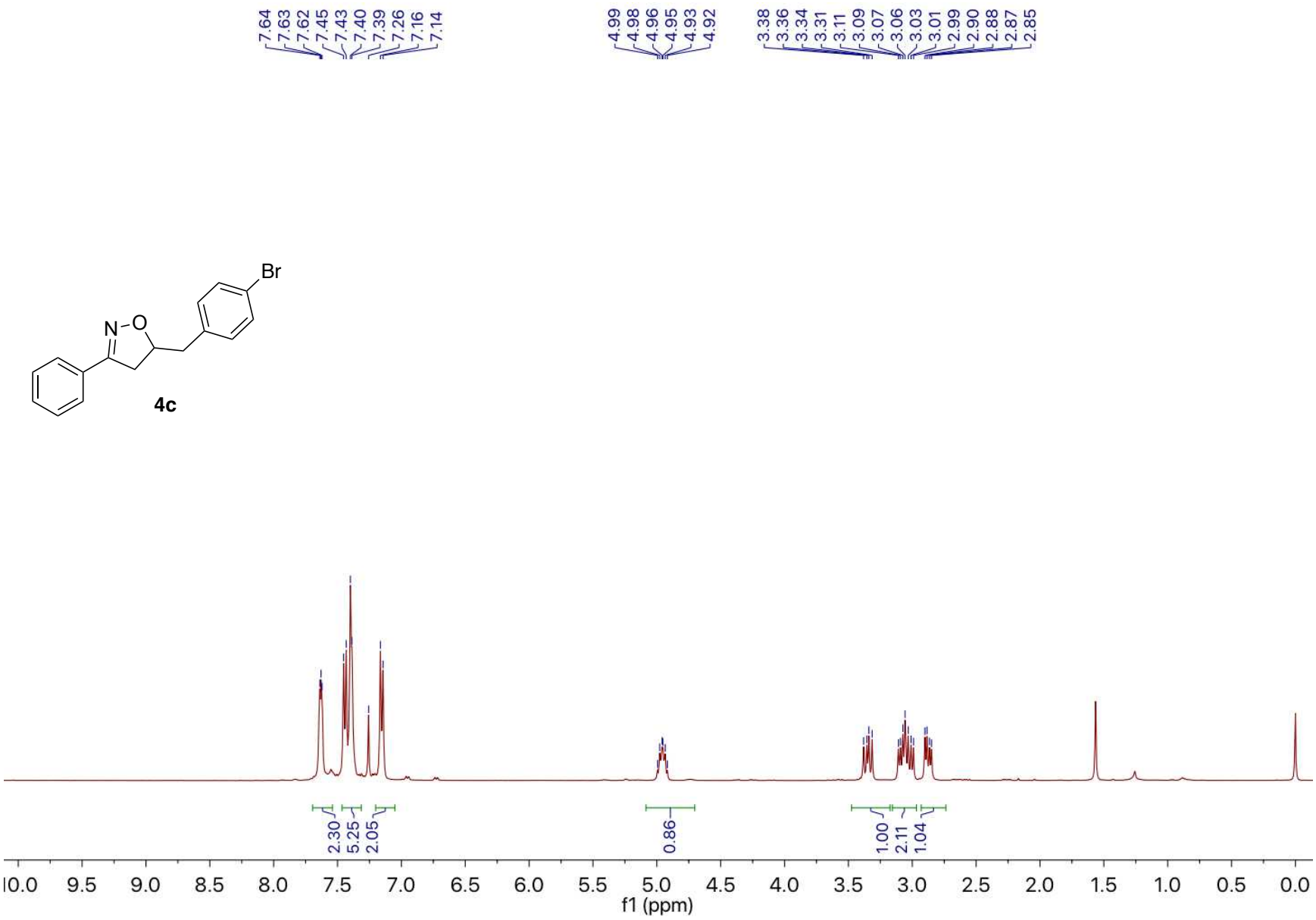
135.35
132.65
130.72
130.06
129.50
128.71
128.67
126.58
81.44
40.32
39.39
N
O
4b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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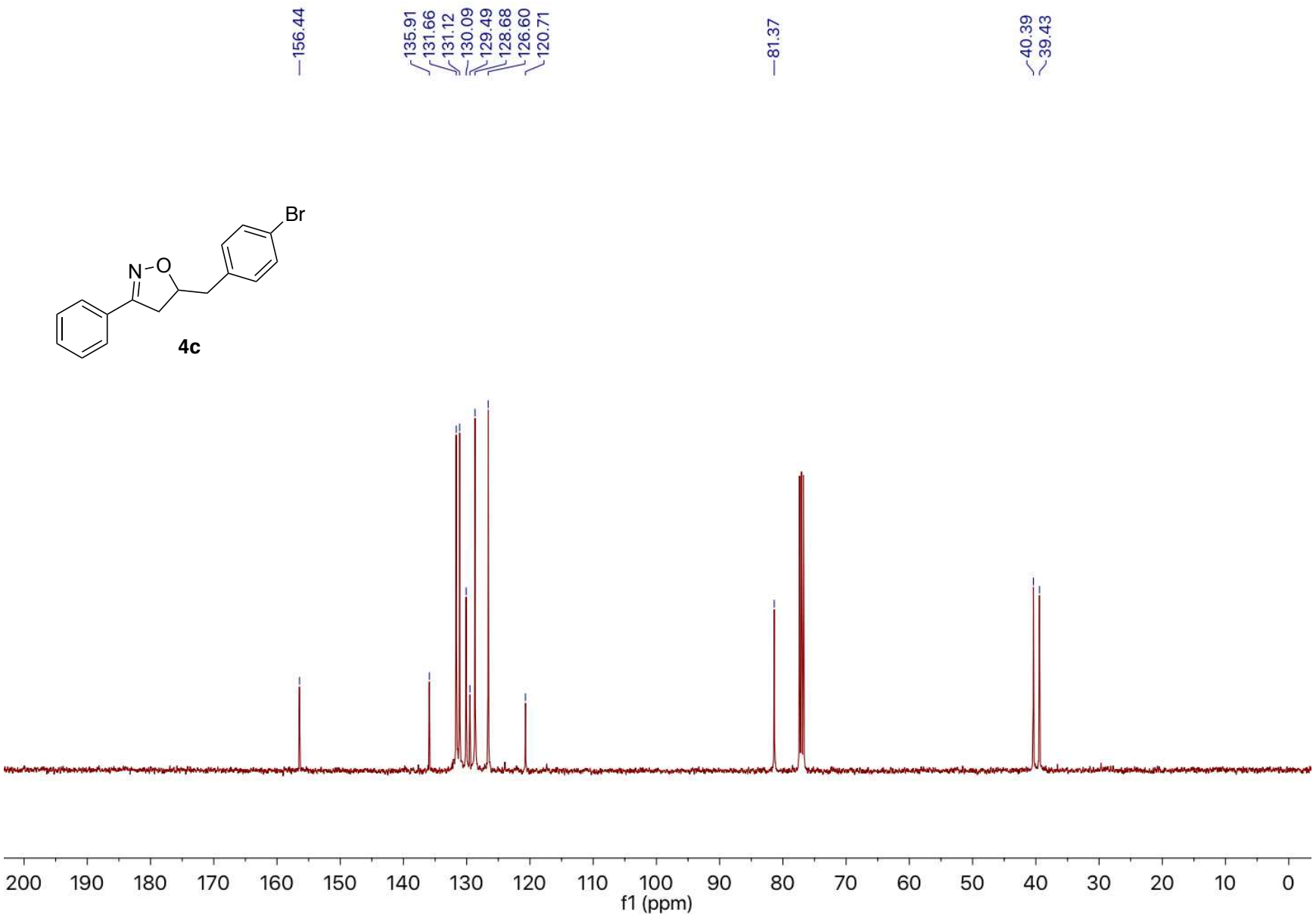
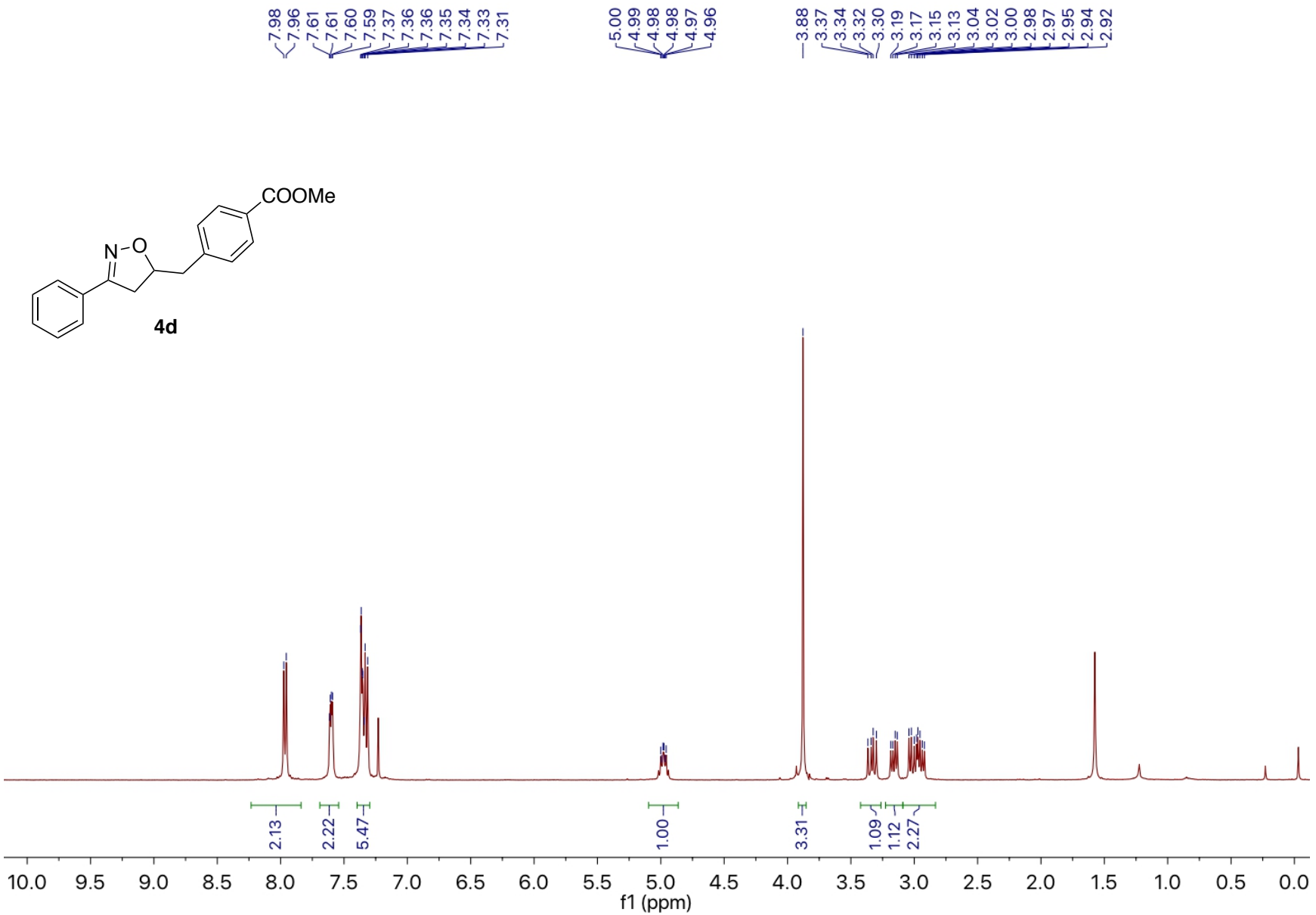
7.40
7.39
7.26
7.16
7.14
4.99
4.98
4.96
4.95
4.93
4.92
3.38
3.36
3.34
3.31
3.11
3.09
3.07
3.06
3.03
3.01
2.99
2.90
2.88
2.87
2.85
Br
N
O
4c
2.30
5.25
2.05
0.86
1.00
2.11
1.04
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


156.44
135.91
131.66
131.12
130.09
129.49
128.68
126.60
120.71
81.37
40.39
39.43
Br
N
O
4c
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.98
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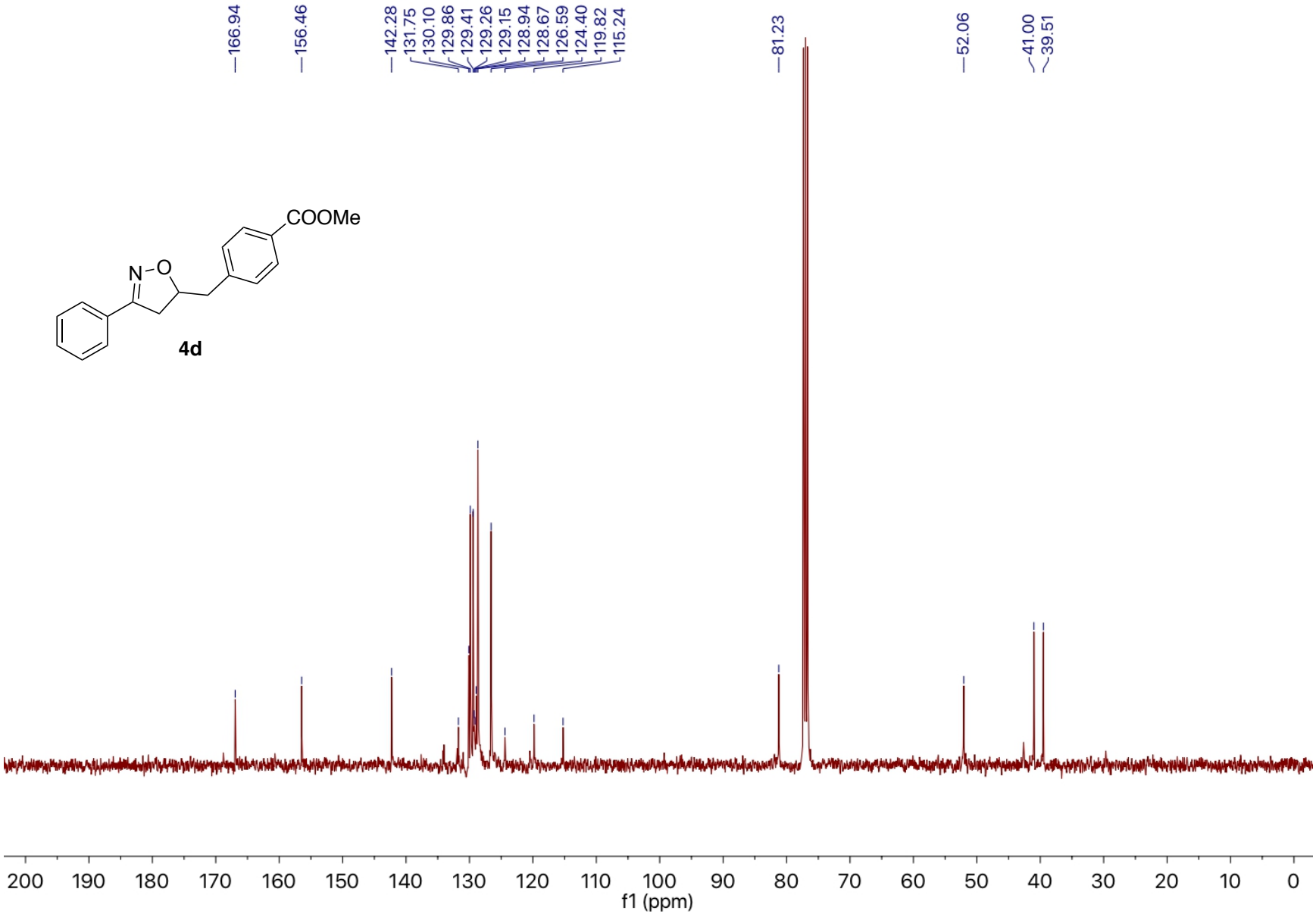
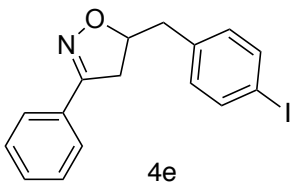
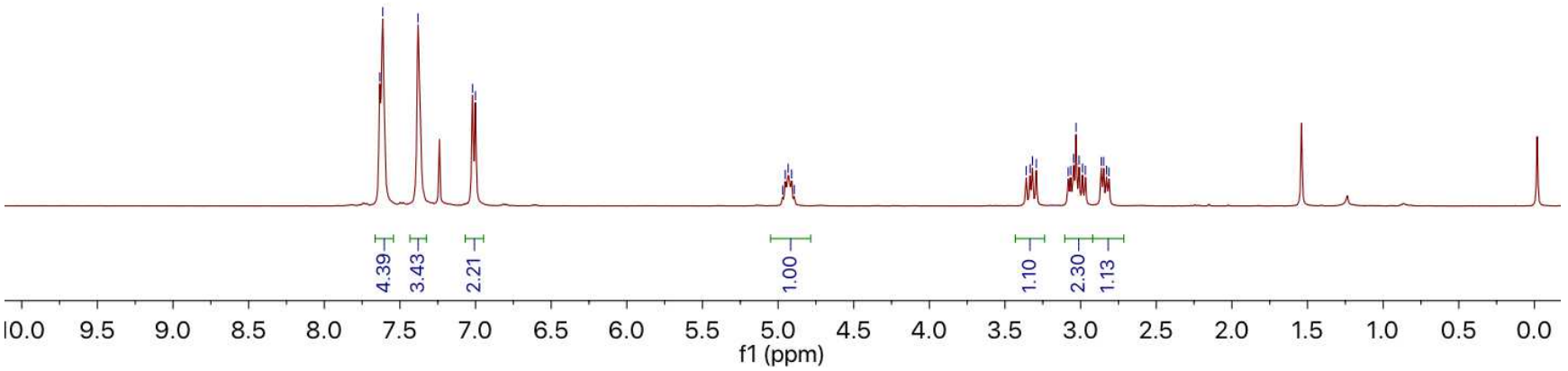
7.61
7.60
7.59
7.37
7.36
7.36
7.35
7.34
7.33
7.31
5.00
4.99
4.98
4.98
4.97
4.96
3.88
3.37
3.34
3.32
3.30
3.19
3.17
3.15
3.13
3.04
3.02
3.00
2.98
2.97
2.95
2.94
2.92
COOMe
N
O
4d
2.13
2.22
5.47
1.00
3.31
1.09
1.12
2.27
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

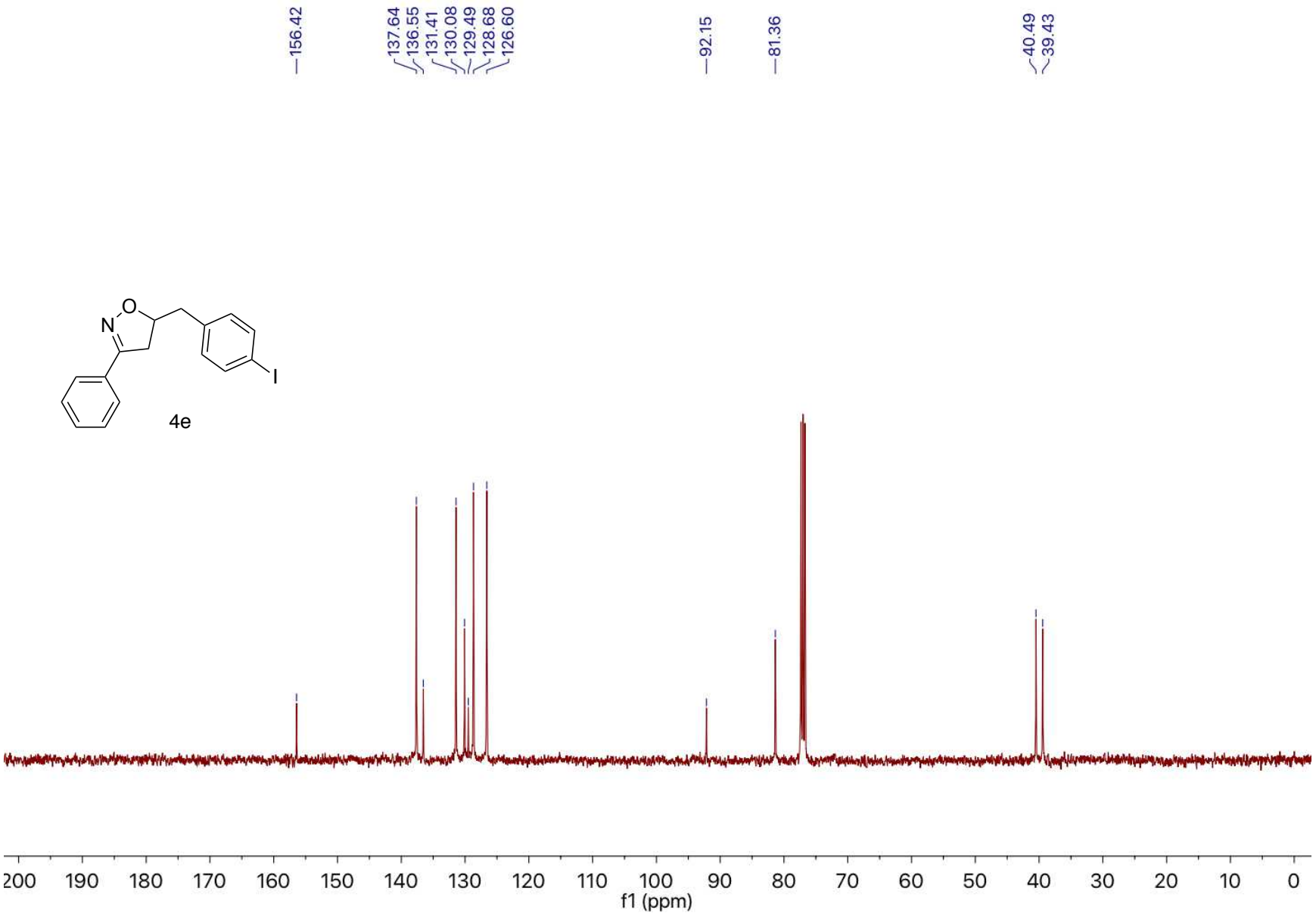

166.94
156.46
142.28
131.75
130.10
129.86
129.41
129.26
129.15
128.94
128.67
126.59
124.40
119.82
115.24
81.23
52.06
41.00
39.51
COOMe
N
O
4d
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.63
7.61
7.38
7.02
7.00
4.97
4.95
4.93
4.91
4.89
3.36
3.33
3.32
3.29
3.08
3.07
3.05
3.03
3.01
2.99
2.97
2.86
2.85
2.83
2.81


O
N
I

4e


4.39
3.43
2.21
1.00
1.10
2.30
1.13
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
f1 (ppm)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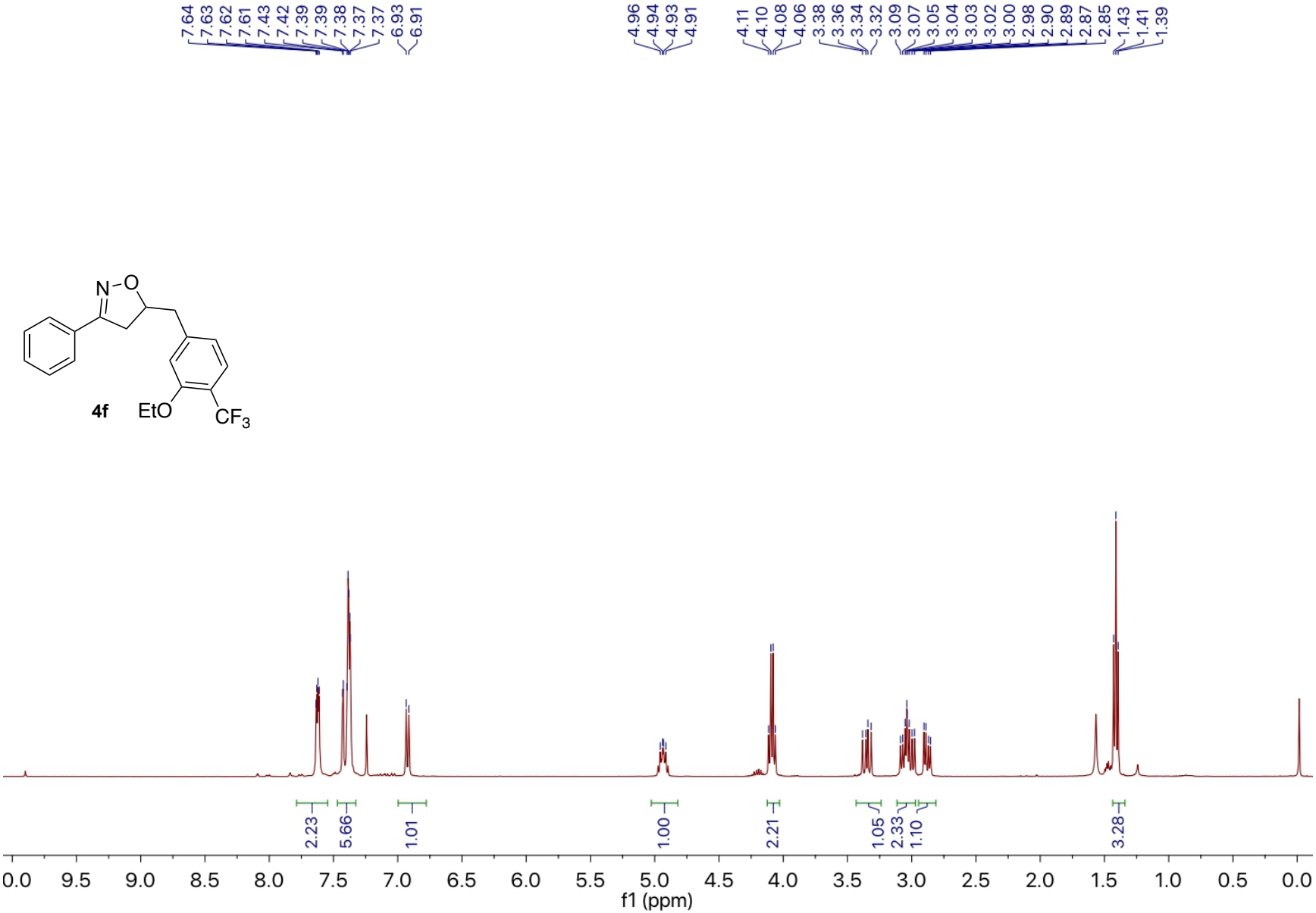
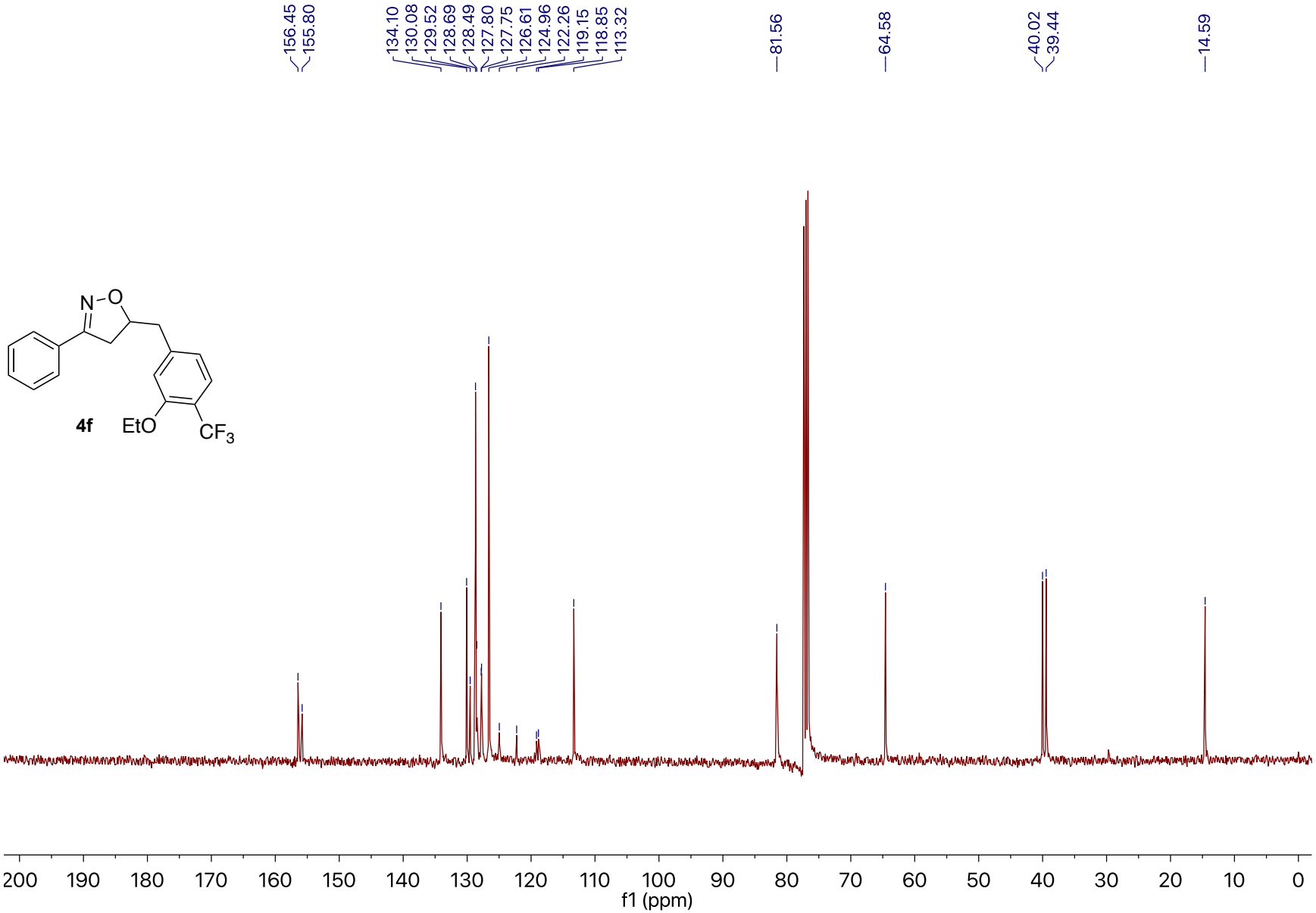
137.64
136.55
131.41
130.08
129.49
128.68
126.60
92.15
81.36
40.49
39.43
O
N
I
4e
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.64
7.63
7.62
7.61
7.43
7.42
7.39
7.39
7.38
7.37
7.37
6.93
6.91
4.96
4.94
4.93
4.91
4.11
4.10
4.08
4.06
3.38
3.36
3.34
3.32
3.09
3.07
3.05
3.04
3.03
3.02
3.00
2.98
2.90
2.89
2.87
2.85
1.43
1.41
1.39
N
O
4f
EtO
CF3
2.23
5.66
1.01
1.00
2.21
1.05
2.33
1.10
3.28
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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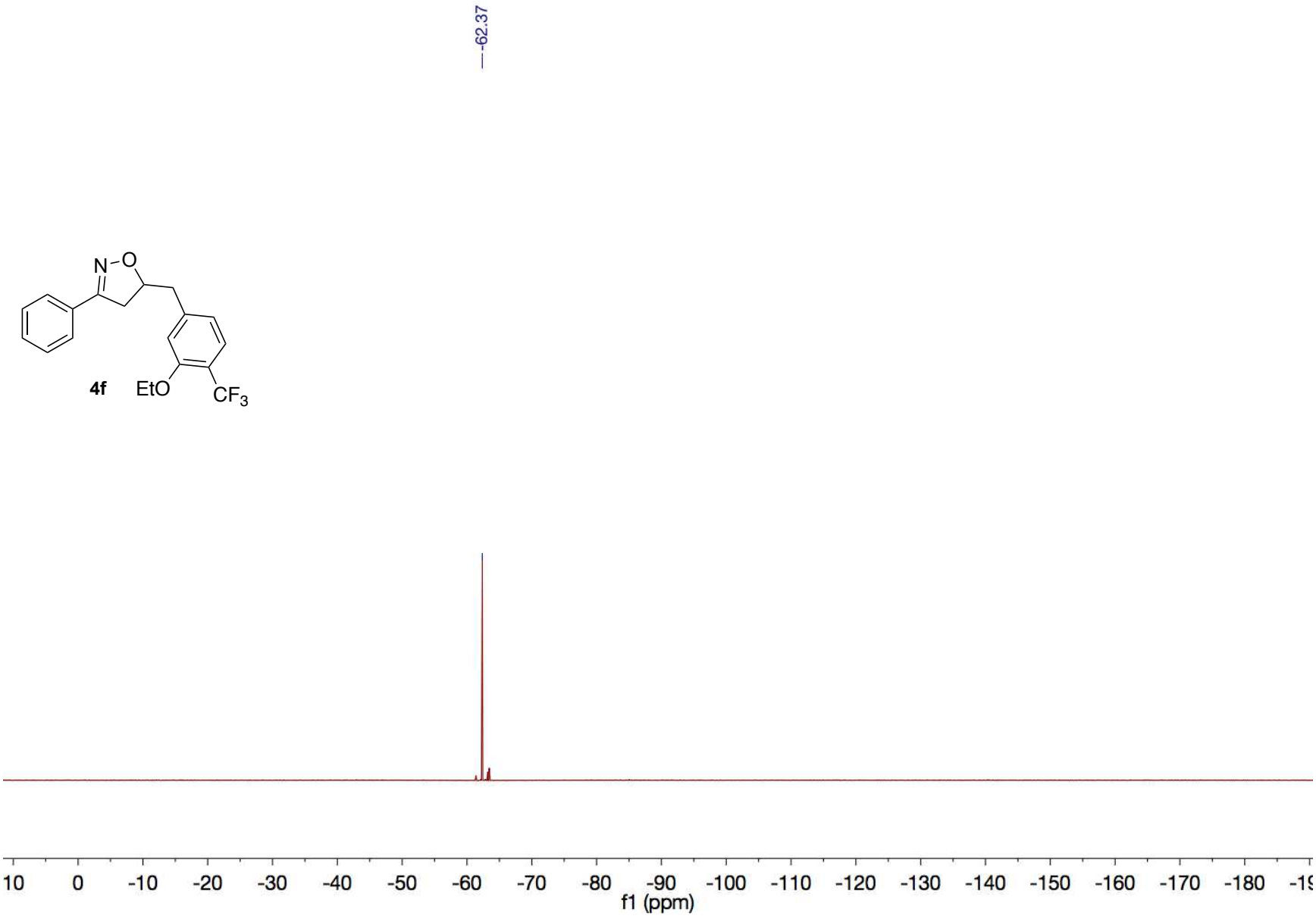
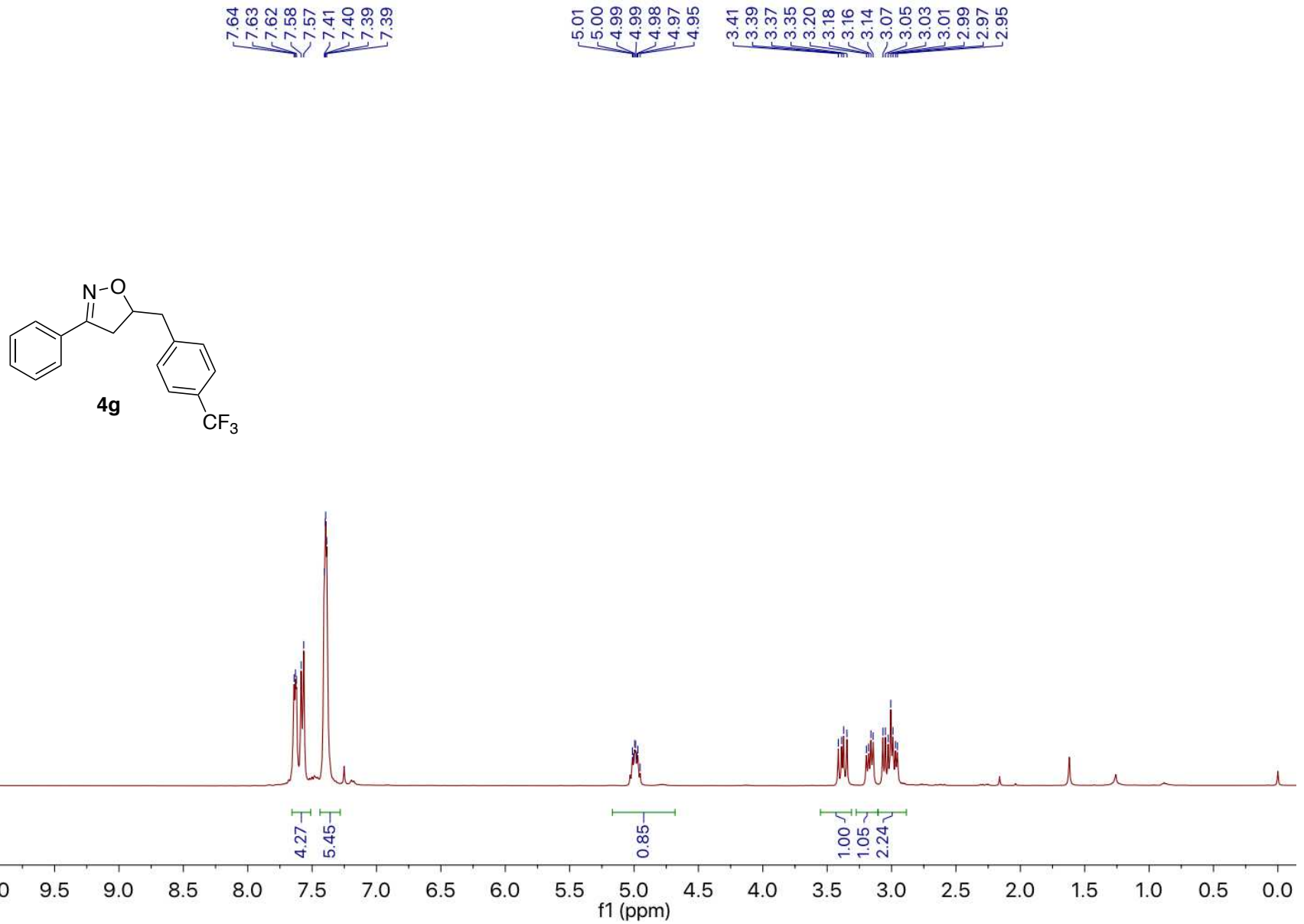
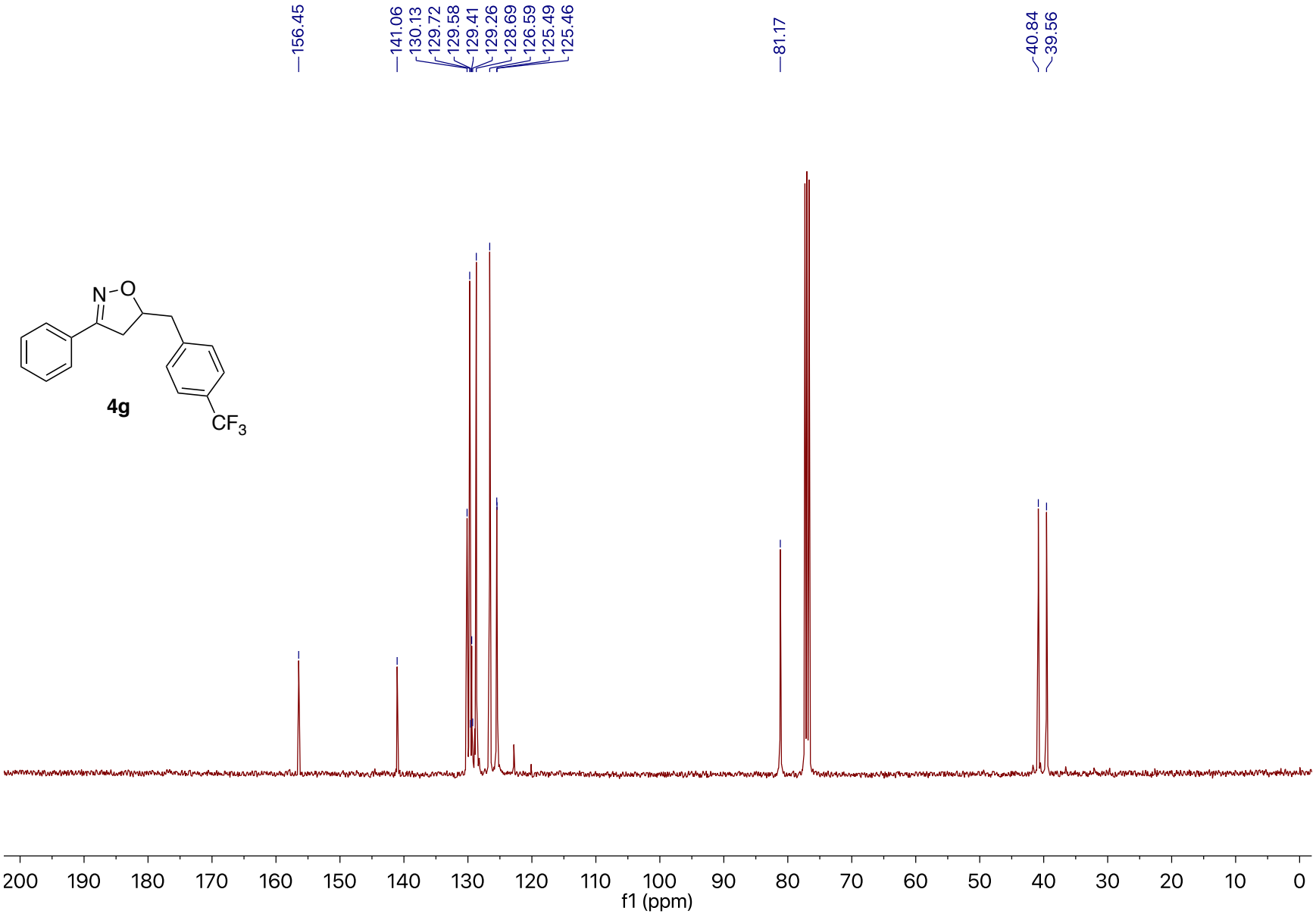
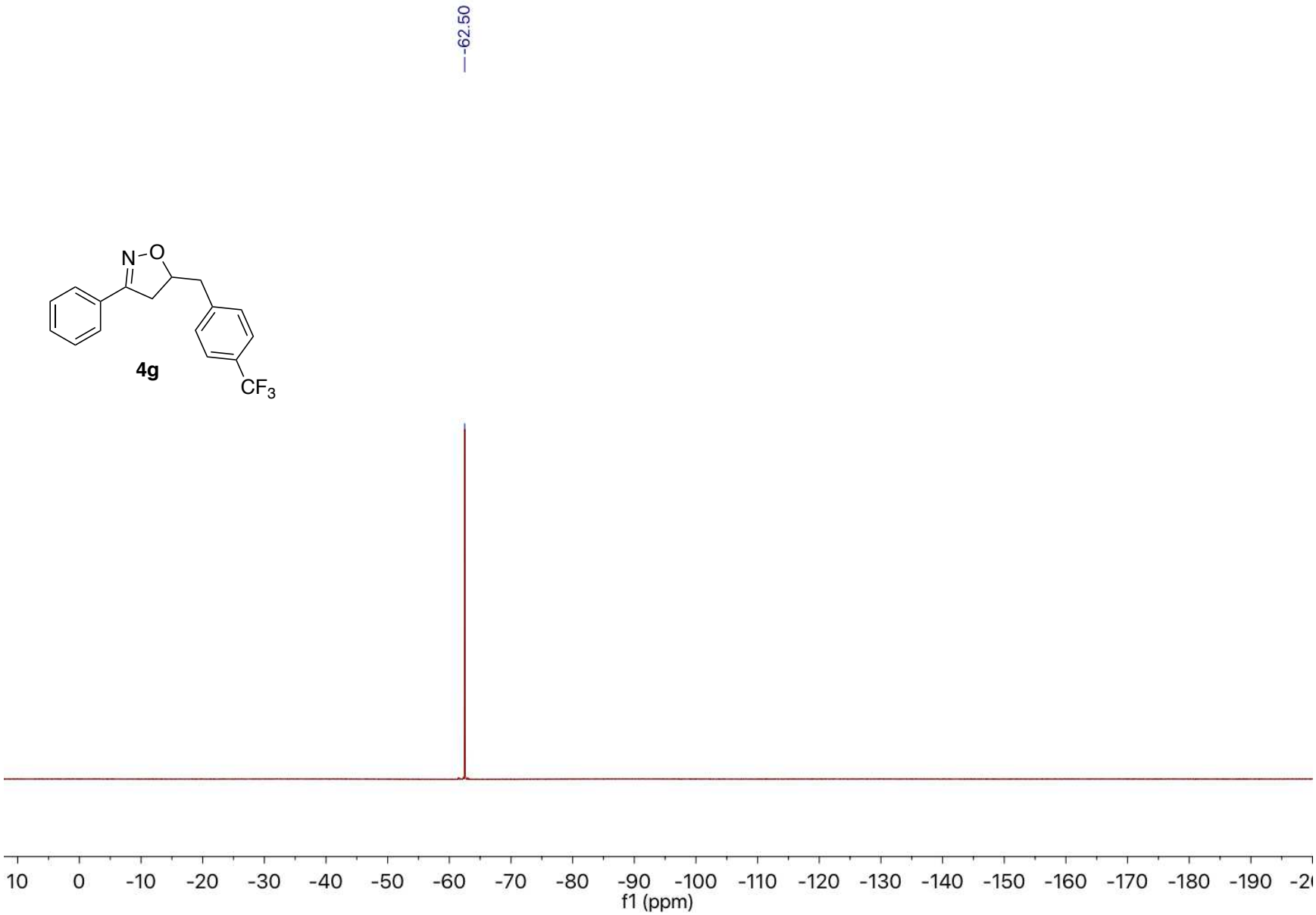
155.80
134.10
130.08
129.52
128.69
128.49
127.80
127.75
126.61
124.96
122.26
119.15
118.85
113.32
81.56
64.58
40.02
39.44
14.59
N
O
4f
EtO
CF3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

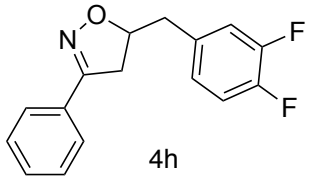

-62.37
N
O
4f
EtO
CF3
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
f1 (ppm)


7.64
7.63
7.62
7.58
7.57
7.41
7.40
7.39
7.39
5.01
5.00
4.99
4.99
4.98
4.97
4.95
3.41
3.39
3.37
3.35
3.20
3.18
3.16
3.14
3.07
3.05
3.03
3.01
2.99
2.97
2.95
N
O
CF3
4g
4.27
5.45
0.85
1.00
1.05
2.24
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
f1 (ppm)

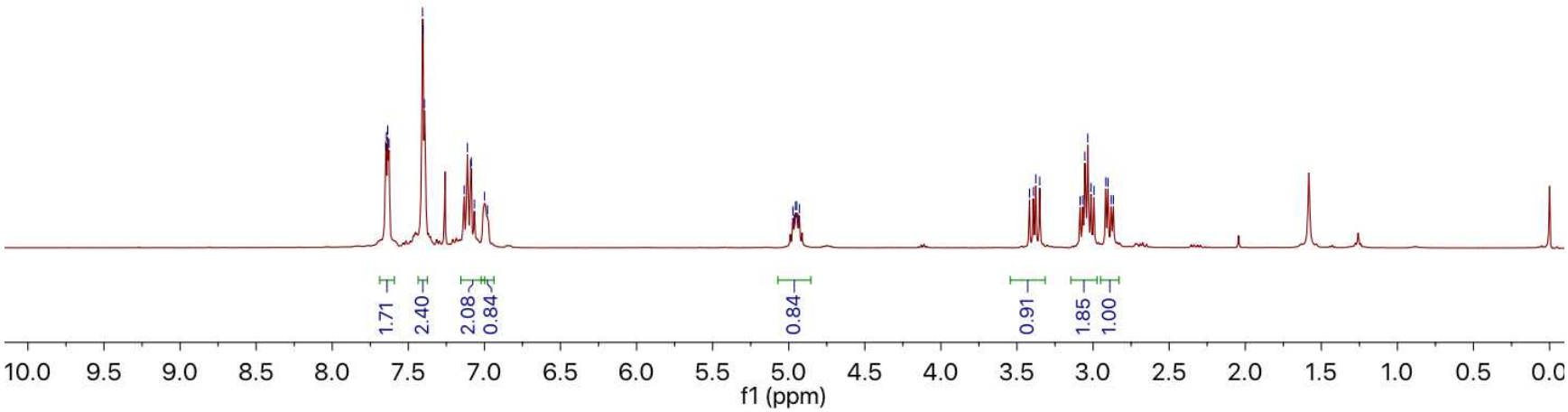

156.45
141.06
130.13
129.72
129.58
129.41
129.26
128.69
126.59
125.49
125.46
81.17
40.84
39.56
N
O
4g
CF3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

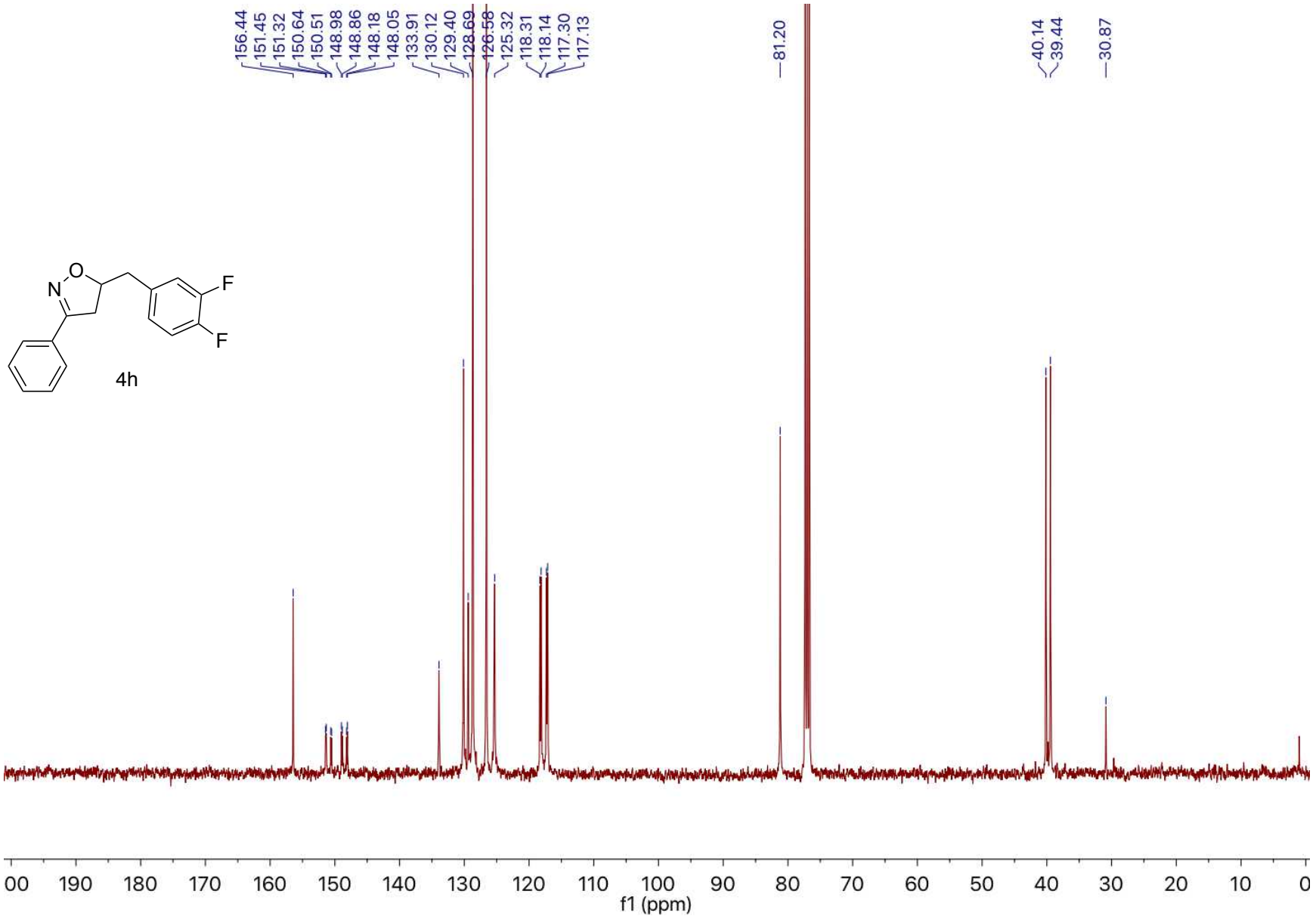

-62.50
N
O
4g
CF3
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)


7.65
7.64
7.64
7.63
7.41
7.40
7.39
7.13
7.11
7.09
7.09
7.07
7.00
6.98
4.97
4.96
4.96
4.95
4.94
4.93
3.42
3.39
3.38
3.35
3.09
3.07
3.05
3.03
3.01
2.99
2.92
2.90
2.88
2.87


O
N
F
F

4h


1.71
2.40
2.08
0.84
0.84
0.91
1.85
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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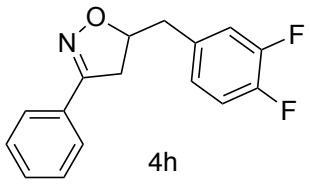
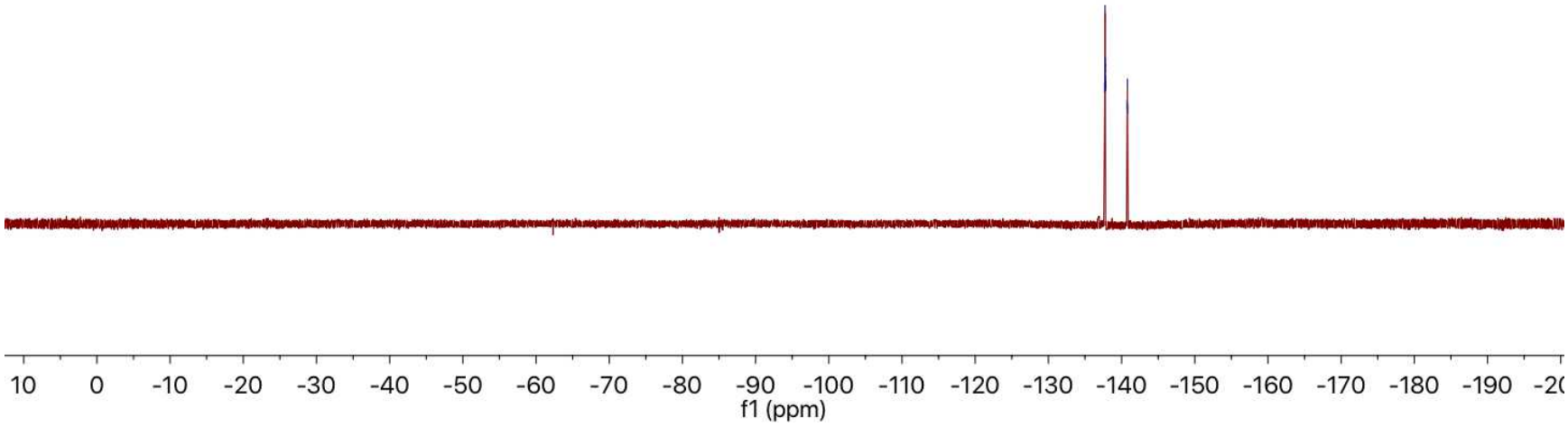
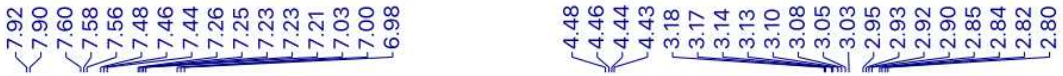
151.45
151.32
150.64
150.51
148.98
148.86
148.18
148.05
133.91
130.12
129.40
128.69
126.58
125.32
118.31
118.14
117.30
117.13
81.20
40.14
39.44
30.87
N
O
F
F
4h
f1 (ppm)

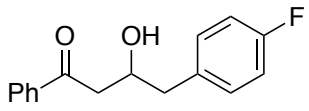

O
N
F
F

4h

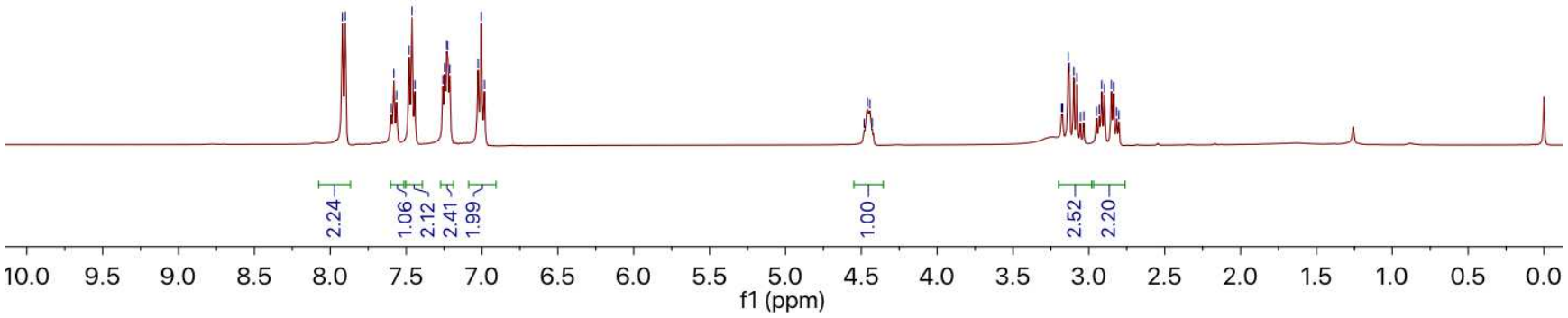

137.69
137.71
137.72
137.72
137.74
137.75
137.77
137.77
137.78
137.80
140.77
140.80
140.82

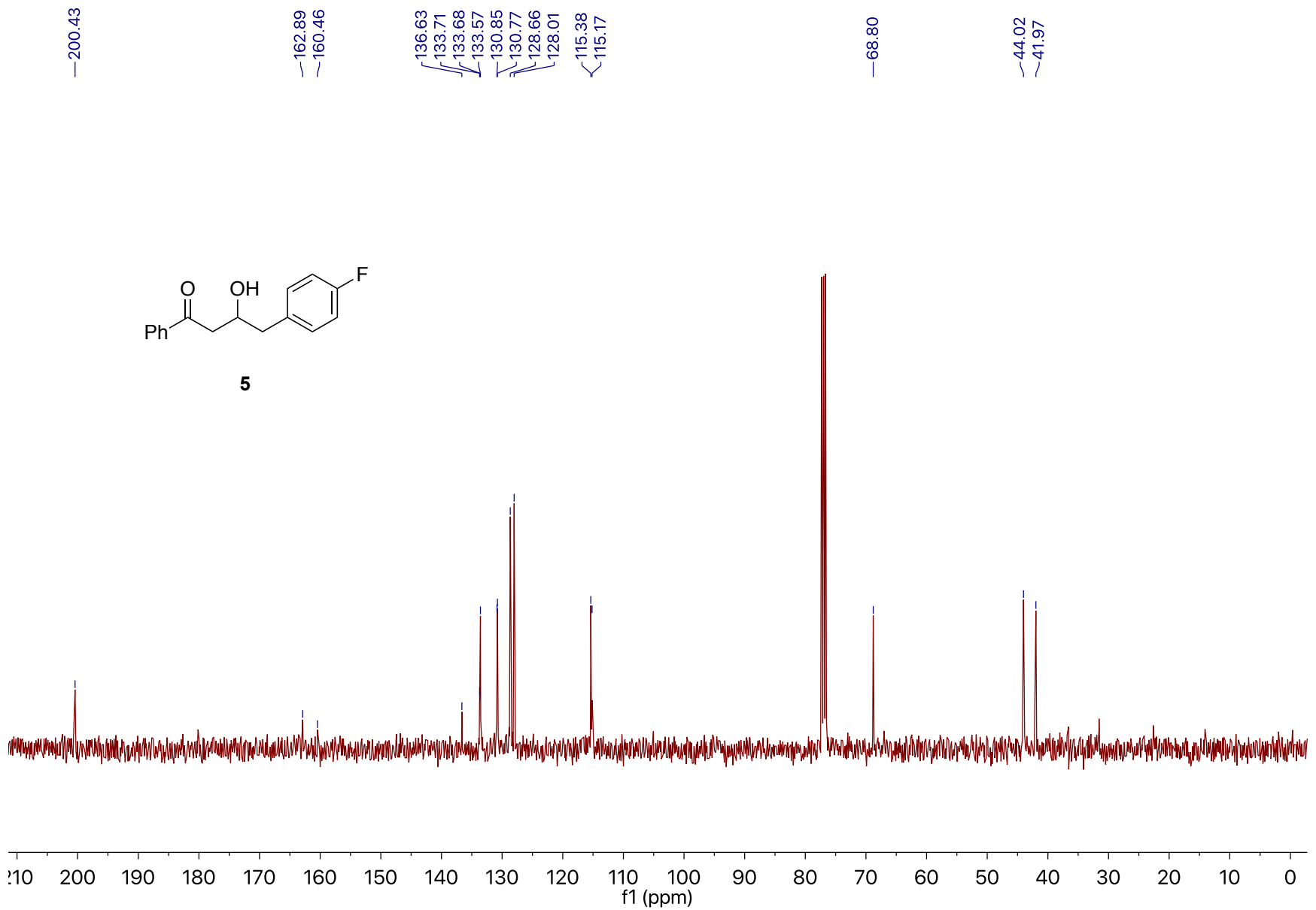

10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

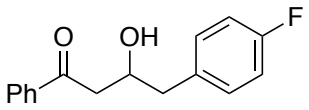

7.92
7.90
7.60
7.58
7.56
7.48
7.46
7.44
7.26
7.25
7.23
7.23
7.21
7.03
7.00
6.98
4.48
4.46
4.44
4.43
3.18
3.17
3.14
3.13
3.10
3.08
3.05
3.03
2.95
2.93
2.92
2.90
2.85
2.84
2.82
2.80


O
OH
F
Ph

5

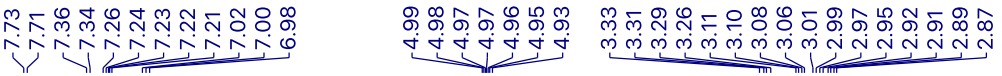

2.24
1.06
2.12
2.41
1.99
1.00
2.52
2.20
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


200.43
162.89
160.46
136.63
133.71
133.68
133.57
130.85
130.77
128.66
128.01
115.38
115.17
68.80
44.02
41.97
O
OH
Ph
F
5
f1 (ppm)


O
OH
Ph
F

5

-116.66
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)


7.73
7.71
7.36
7.34
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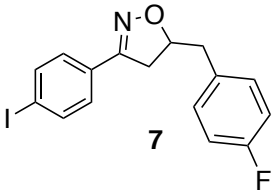
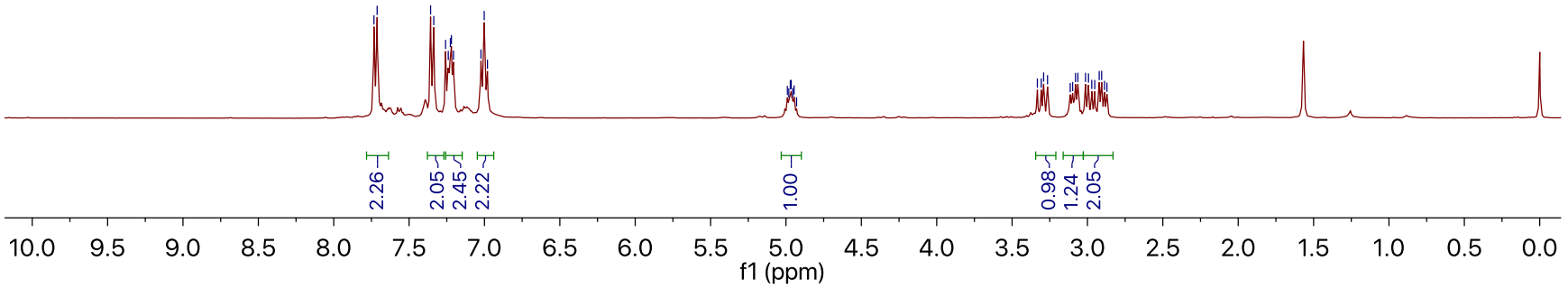
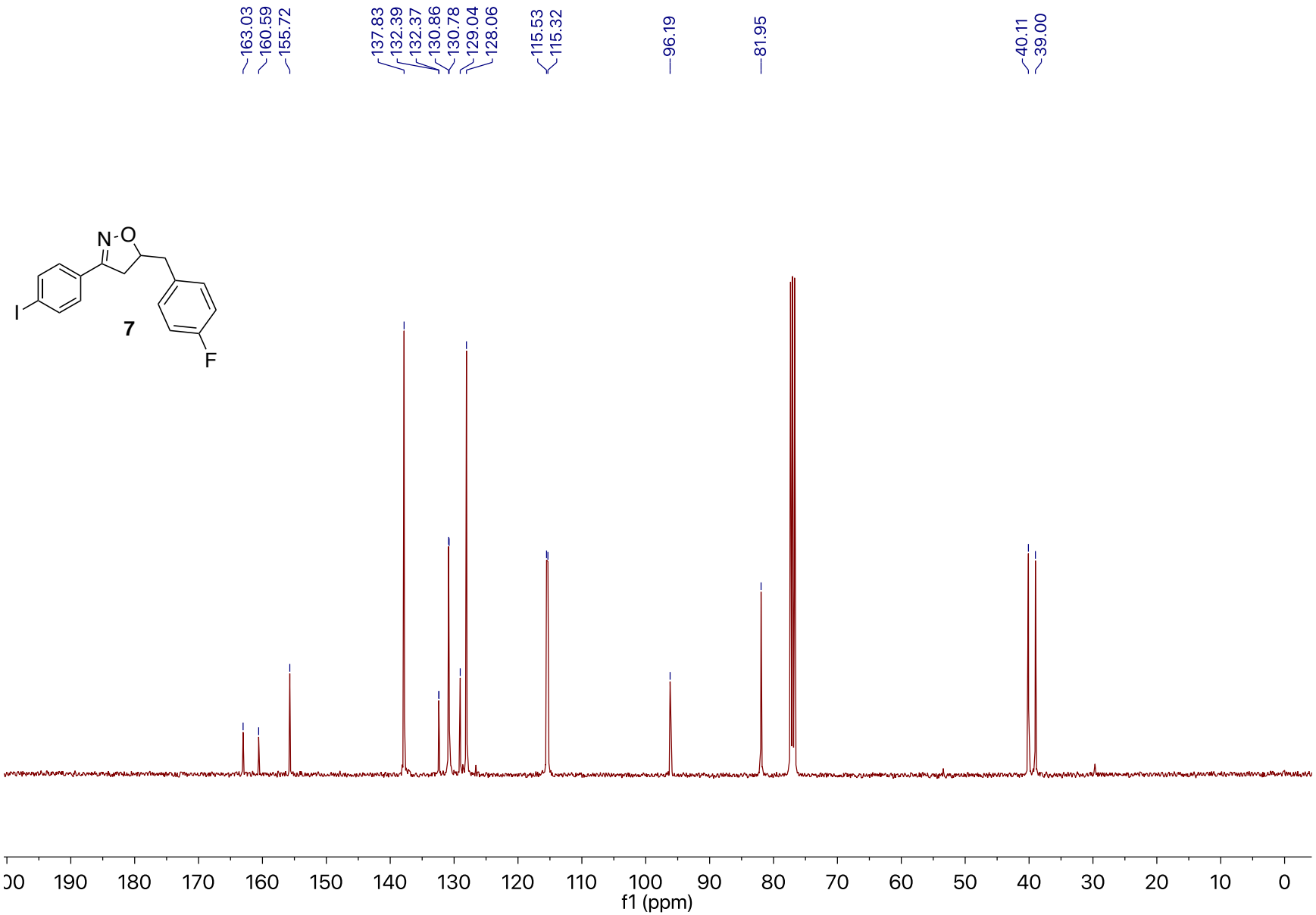
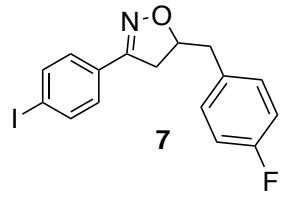
7.24
7.23
7.22
7.21
7.02
7.00
6.98
4.99
4.98
4.97
4.97
4.96
4.95
4.93
3.33
3.31
3.29
3.26
3.11
3.10
3.08
3.06
3.01
2.99
2.97
2.95
2.92
2.91
2.89
2.87


N
O
I
F

7


2.26
2.05
2.45
2.22
1.00
0.98
1.24
2.05
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
f1 (ppm)


163.03
160.59
155.72
137.83
132.39
132.37
130.86
130.78
129.04
128.06
115.53
115.32
96.19
81.95
40.11
39.00
N
O
I
F
7
f1 (ppm)


N
O
I
F

7

-116.20
0
-10
-20
-30
-40
-50
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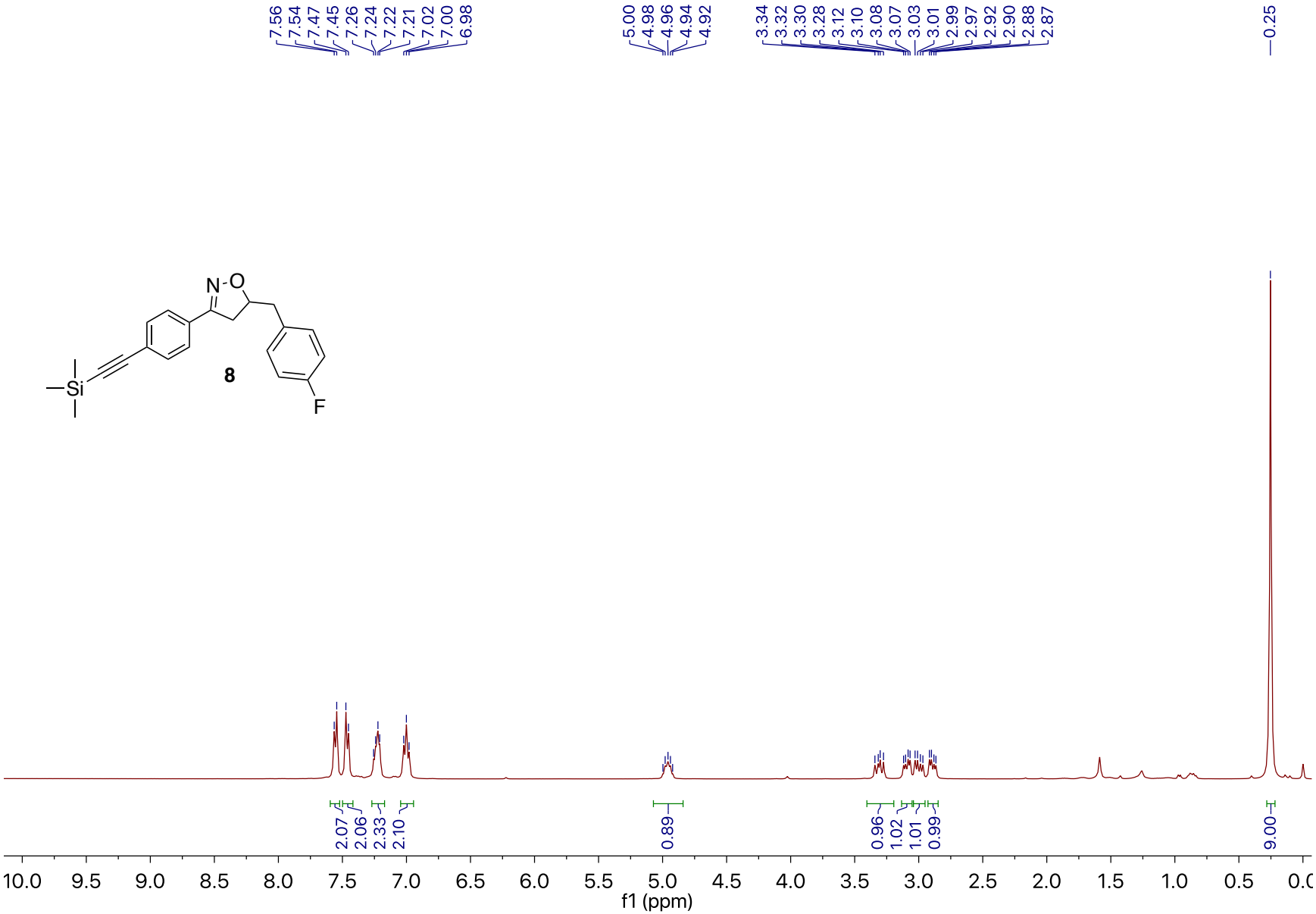
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190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7.54
7.47
7.45
7.26
7.24
7.22
7.21
7.02
7.00
6.98
5.00
4.98
4.96
4.94
4.92
3.34
3.32
3.30
3.28
3.12
3.10
3.08
3.07
3.03
3.01
2.99
2.97
2.92
2.90
2.88
2.87
0.25
N
O
Si
F
8
2.07
2.06
2.33
2.10
0.89
0.96
1.02
1.01
0.99
9.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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5.0
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4.0
3.5
3.0
2.5
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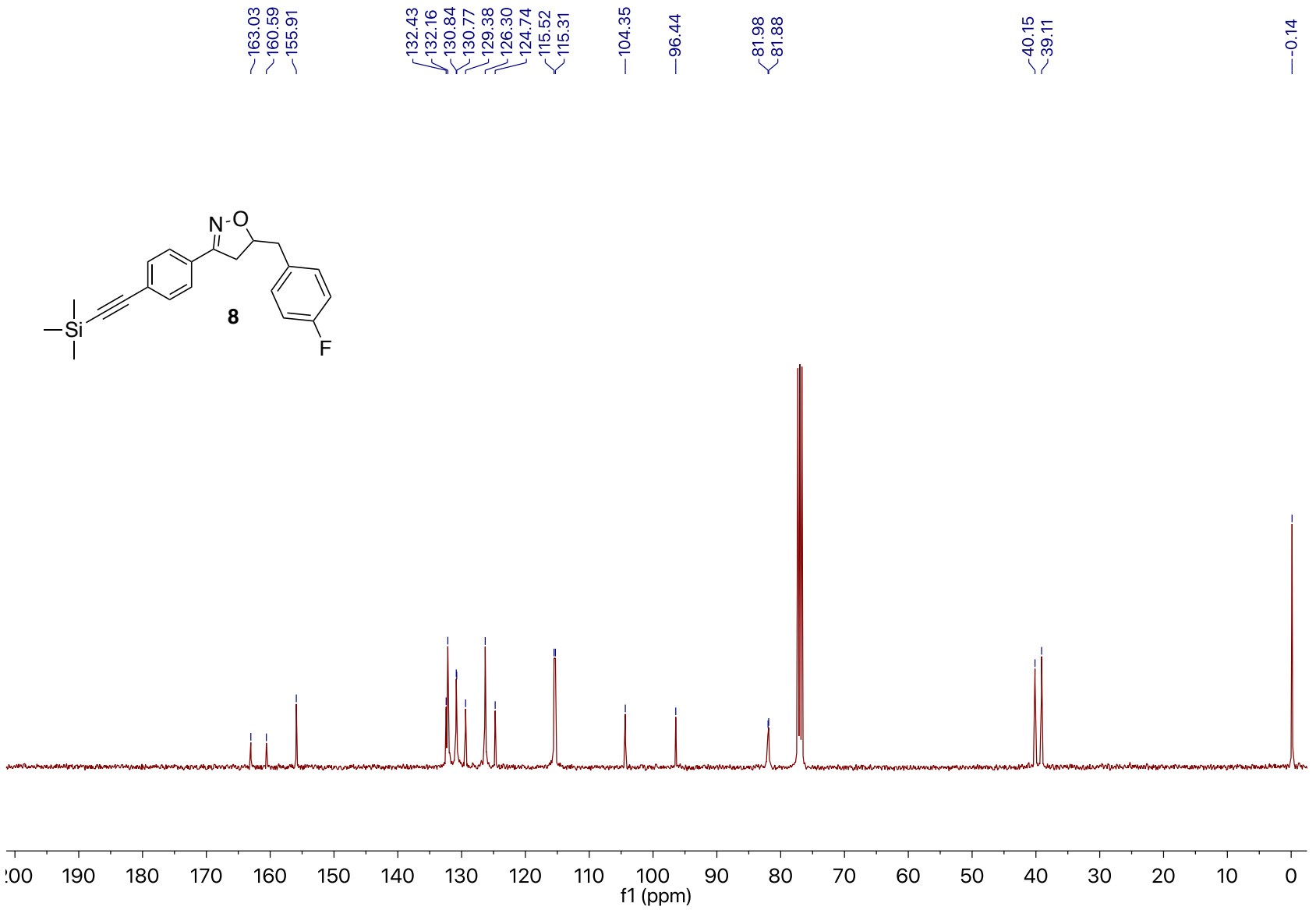
1.5
1.0
0.5
f1 (ppm)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160.59
155.91
132.43
132.16
130.84
130.77
129.38
126.30
124.74
115.52
115.31
104.35
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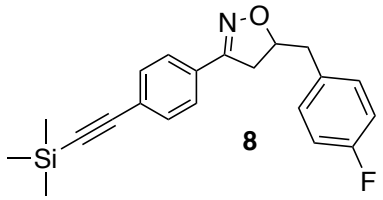
81.98
81.88
40.15
39.11
-0.14
N
O
Si
F
8
f1 (ppm)


N
O
Si
F

8

-116.20
0
-10
-20
-30
-40
-50
-60
-70
-80
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-100
-110
-120
-130
-140
-150
-160
-170
-180
-190