Supporting Information for

Generation of Formaldehyde and Formaldehyde-d_2 for Hydroxymethylations and Hydroxydeuteromethylations of Difluoroenolates and Difluorobenzyl Carbanions

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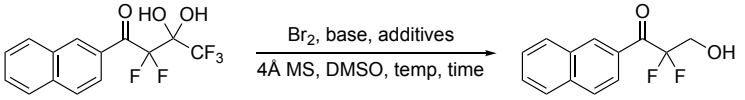
I. Experimental and Characterization Data

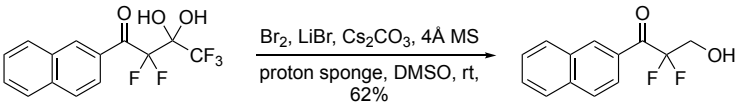
General Procedures. Experiments requiring anhydrous conditions were performed under argon atmosphere and organic solvents were dried over molecular sieves. All solvents and reagents were purchased from commercial sources unless otherwise noted. Starting materials for compounds **1**–**6** and **10**–**14** were prepared according to our laboratory's published methods.[1–4] Thin-layer chromatography was conducted using MilliporeSigma TLC silica gel 60 F_{254} plates. Preparative thin-layer chromatography was performed using Sorbent Technologies silica G prep TLC plates with UV254. Flash chromatography was conducted using SiliCycle Siliaflash silica gel P60 (40–63 μm) 60Å. Melting points were taken on an OptiMelt apparatus from Stanford Research Systems and are not corrected. NMR spectra were recorded on a Bruker ARX 300 MHz, a Bruker Topspin Avance III HD 500 MHz spectrometer equipped with prodigy cryoprobe, or a Bruker Avance III HD 400 MHz spectrometer. The residual solvent peaks were used as an internal standard for ^{1}H and ^{13}C NMR spectra whereas trifluorotoluene was used as an added internal standard for ^{19}F NMR spectra. Mass spectrometry was acquired by the Department of Chemistry at the University of Mississippi using SYNAPT HD Mass Spectrometer from Waters. Infrared spectra were recorded on Agilent Technologies Cary 630 FTIR.

Table S1. Optimization of the Preparation of Difluoroethanol **1**



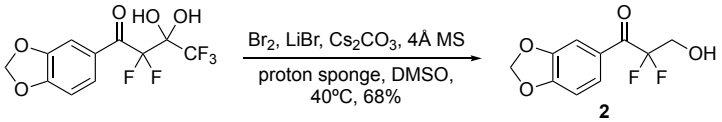
1

Entry	Base	Additive	Temp	Time	Yield (^{19}F NMR)
1	Li_2CO_3	-	rt	12 h	0%
2	Na_2CO_3	-	50 °C	12 h	30%
3	K_2CO_3	-	rt	12 h	33%
4	Cs_2CO_3	LiBr	rt	12 h	61%
5	Cs_2CO_3	LiBr, proton sponge	rt	20 h	73%
6	K_2CO_3	LiBr, proton sponge	rt	20 h	61%
7	Na_2CO_3	LiBr, proton sponge	rt	20 h	52%
8	Cs_2CO_3	LiBr, proton sponge	rt	12 h	78%
9	Cs_2CO_3	LiBr, *i*-Pr_2NEt	rt	12 h	64%



1

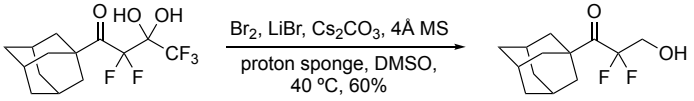
2,2-Difluoro-3-hydroxy-1-(naphthalen-2-yl)propan-1-one (1). A mixture of activated 4Å molecular sieves (100 mg), Cs_2CO_3 (106 mg, 0.325 mmol), LiBr (14 mg, 0.16 mmol), and proton sponge (14 mg, 0.07 mmol) in DMSO (1.0 mL) was cooled to 10 ºC and treated with the dropwise addition of bromine (15 µL, 0.29 mmol). After 15 min, a solution of the *gem*-diol[2] (10 mg, 0.031 mmol) in DMSO (0.3 mL) was added to the reaction mixture across 1 h via syringe pump. The reaction mixture was then stirred for 12 h at rt. Next, the reaction mixture was treated with saturated aqueous NH_4Cl (2 mL), diluted EtOAc (50 mL), and stirred for 1 h. The resultant mixture was filtered through Celite, and the organics were washed with brine (3 × 5 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Preparative TLC (3% EtOAc in $CHCl_3$) afforded the title compound **1** as a pale yellow solid (4.5 mg, 62%): mp 42–44 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.75 (s, 1H), 8.10 (d, J = 8.5 Hz, 1H), 8.02 (d, J = 8.1 Hz, 1H), 7.93 (d, J = 8.7 Hz, 1H), 7.90 (d, J = 8.1 Hz, 1H), 7.66 (ddd, J = 8.3, 7.0, 1.5 Hz, 1H), 7.59 (ddd, J = 8.0, 7.0, 1.0 Hz, 1H), 4.22 (td, J = 12.9, 7.5 Hz, 2H), 2.39 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.6 (t, J_{CF} = 30.8 Hz, 1C), 136.2, 133.3 (t, J_{CF} = 4.5 Hz, 1C), 132.2, 130.2, 129.6, 128.8 (t, J_{CF} = 3.1 Hz, 1C), 128.7, 127.8, 127.1, 124.5, 116.2 (t, J_{CF} = 257.0 Hz, 1C), 62.8 (t, J_{CF} = 28.8 Hz, 1C); ^{19}F NMR (376 MHz, $CDCl_3$) δ –109.1 (t, J_{HF} = 12.8 Hz, 2F); IR (film) ν_{max} 3390, 3062, 2924, 2853, 1692, 1626, 1597, 1467 cm^{-1}; HRMS (ESI–TOF) *m/z* calcd for $C_{13}H_9F_2O_2$ $[M–H]^-$ 235.0571, found 235.0563.



2

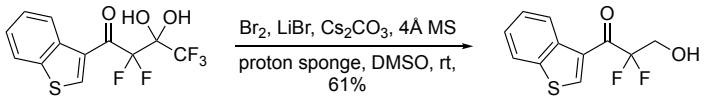
1-(Benzo[1,3]dioxol-5-yl)-2,2-difluoro-3-hydroxypropan-1-one (2). A mixture of activated 4Å molecular sieves (150 mg), Cs_2CO_3 (135 mg, 0.414 mmol), LiBr (17 mg, 0.20 mmol), and proton sponge (17 mg, 0.079 mmol) in DMSO (1.5 mL) was cooled to 10 ºC and treated with the dropwise addition of bromine (20 µL, 0.39 mmol). After 15 min, a solution of the *gem*-diol[2] (12 mg, 0.038 mmol) in DMSO (1.0 mL) was added to the reaction mixture across 1 h via syringe pump. The

reaction mixture was then stirred for 20 h at 40 ºC. Next, the reaction mixture was cooled to rt, treated with saturated aqueous NH_4Cl (3 mL), diluted EtOAc (50 mL), and stirred for 1 h. The resultant mixture was filtered through Celite, and the organics were washed with brine (3 × 5 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Preparative TLC (10% EtOAc in $CHCl_3$) afforded the title compound **2** as a yellow oil (6 mg, 68%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (dd, J = 8.4, 1.5 Hz, 1H), 7.54 (s, 1H), 6.90 (d, J = 8.3 Hz, 1H), 6.08 (s, 2H), 4.12 (t, J = 12.9 Hz, 2H), 2.49 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.6 (t, J_{CF} = 27.7 Hz, 1C), 152.8, 148.0, 127.0 (t, J_{CF} = 4.1 Hz, 1C), 126.5 (t, J_{CF} = 1.4 Hz, 1C), 117.8 (t, J_{CF} = 253.9 Hz, 1C), 108.6 (t, J_{CF} = 2.7 Hz, 1C), 108.4, 102.5, 61.8 (t, J_{CF} = 27.9 Hz, 1C); ^{19}F NMR (471 MHz, $CDCl_3$) δ –108.0 (t, J_{HF} = 13.0 Hz, 2F); IR (film) ν_{max} 3463, 2916, 1685, 1606, 1491, 1448, 1359, 1255 cm^{-1}; HRMS (ESI–TOF) *m/z* calcd for $C_{10}H_7F_2O_4$ $[M–H]^-$ 229.0312, found 229.0292.



3

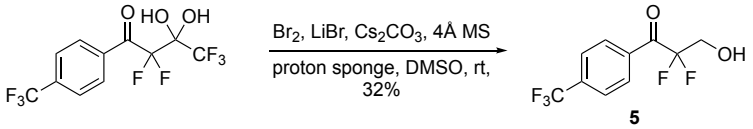
1-(Adamantan-1-yl)-2,2-difluoro-3-hydroxypropan-1-one (3). A mixture of activated 4Å molecular sieves (200 mg), Cs_2CO_3 (210 mg, 0.645 mmol), LiBr (25 mg, 0.29 mmol), and proton sponge (25 mg, 0.12 mmol) in DMSO (2 mL) was cooled to 10 ºC and treated with the dropwise addition of bromine (30 μL, 0.58 mmol). After 15 min, a solution of the *gem*-diol[2] (20 mg, 0.06 mmol) in DMSO (0.3 mL) was added to the reaction mixture across 30 min via syringe pump. The reaction mixture was then stirred for 12 h at 40 ºC. Next, the reaction mixture was cooled to rt, treated with saturated aqueous NH_4Cl (4 mL), diluted EtOAc (50 mL), and stirred for 1 h. The resultant mixture was filtered through Celite, and the organics were washed with brine (3 × 5 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Preparative TLC (1% Et_2O in CH_2Cl_2) afforded the title compound **3** as a yellow oil (9 mg, 60%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.94 (t, J = 12.9 Hz, 2H), 2.08 (br s, 3H), 1.99 (br s, 6H), 1.75 (dd, J = 20.5, 12.5 Hz, 6H), 1.61 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.7 (t, J_{CF} = 27.7 Hz, 1C), 116.9 (t, J_{CF} = 258.7 Hz, 1C), 62.8 (t, J_{CF} = 29.2 Hz, 1C), 46.3 (t, J_{CF} = 2.6 Hz, 1C), 37.2 (3C), 36.3 (3C), 27.8 (3C); ^{19}F NMR (471 MHz, $CDCl_3$) δ –111.3 (t, J_{HF} = 13.0 Hz, 2F); IR (film) ν_{max} 3408, 2906, 2853, 1715, 1454 cm^{-1}; HRMS (ESI–TOF) *m/z* calcd for $C_{13}H_{17}F_2O_2$ $[M–H]^-$ 243.1197, found 243.1193.



4

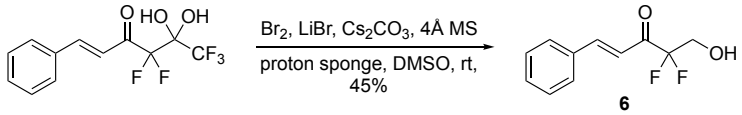
1-(Benzothiophen-3-yl)-2,2-difluoro-3-hydroxypropan-1-one (4). A mixture of activated 4Å molecular sieves (200 mg), Cs_2CO_3 (220 mg, 0.675 mmol), LiBr (27 mg, 0.31 mmol), and proton sponge (27 mg, 0.13 mmol) in DMSO (2 mL) was cooled to 10 ºC and treated with the dropwise addition of bromine (32 μL, 0.62 mmol). After 15 min, a solution of the *gem*-diol[3] (20 mg, 0.061 mmol) in DMSO (1.0 mL) was added to the reaction mixture across 30 min via syringe pump. The reaction mixture was then stirred for 20 h at rt. Next, the reaction mixture was treated with saturated aqueous NH_4Cl (4 mL), diluted EtOAc (50 mL), and stirred for 1 h. The resultant mixture was filtered through Celite, and the organics were washed with brine (3 × 5 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Preparative TLC (20% acetone in hexanes) afforded the title compound **4** as a brown oil (9 mg, 61%): ^{1}H NMR (500 MHz, DMSO–d_6) δ 9.08 (s, 1H), 8.59 (d, J = 8.1 Hz, 1H), 8.16 (d, J = 8.0 Hz, 1H), 7.58 (t, J = 7.7 Hz, 1H), 7.52 (t, J = 7.0,

7.1, 1.3 Hz, 1H), 5.85 (t, J = 6.3 Hz, 2H), 4.05 (td, J = 14.2, 6.3 Hz 1H); ^{13}C NMR (125 MHz, DMSO–d_6) δ 184.3 (t, J_{CF} = 27.9 Hz, 1C), 144.4 (t, J_{CF} = 8.2 Hz, 1C), 138.8, 136.6, 128.3, 126.4, 125.9, 124.3, 123.1, 117.6 (t, J_{CF} = 257.0 Hz, 1C), 61.9 (t, J_{CF} = 28.2 Hz, 1C); ^{19}F NMR (471 MHz, $CDCl_3$) δ –107.9 (t, J_{HF} = 12.9 Hz, 2F); IR (film) ν_{max} 3423, 3119, 2929, 1677, 1490, 1460, 1174 cm^{-1}; HRMS (ESI–TOF) *m/z* calcd for $C_{11}H_7F_2O_2S$ [M–H]$^-$ 241.0135, found 241.0110.



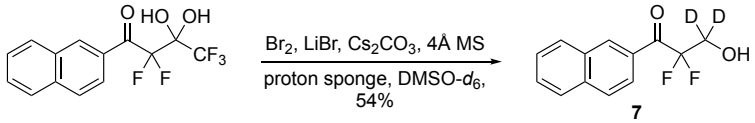
5

2,2-Difluoro-3-hydroxy-1-(4-(trifluoromethyl)phenyl)propan-1-one (5). A mixture of activated 4Å molecular sieves (300 mg), Cs_2CO_3 (290 mg, 0.89 mmol), LiBr (38 mg, 0.44 mmol), and proton sponge (38 mg, 0.18 mmol) in DMSO (3 mL) was cooled to 10 ºC and treated with the dropwise addition of bromine (38 µL, 0.74 mmol). After 15 min, a solution of the *gem*-diol[4] (25 mg, 0.074 mmol) in DMSO (1.0 mL) was added to the reaction mixture across 1 h via syringe pump. The reaction mixture was then stirred for 12 h at rt. Next, the reaction mixture was treated with saturated aqueous NH_4Cl (6 mL), diluted EtOAc (50 mL), and stirred for 1 h. The resultant mixture was filtered through Celite, and the organics were washed with brine (3 × 5 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Preparative TLC (6% EtOAc in $CHCl_3$) afforded the title compound **5** as a yellow oil (6 mg, 32%): ^{1}H NMR (500 MHz, DMSO–d_6) δ 8.20 (d, J = 8.1 Hz, 2H), 7.99 (d, J = 8.7 Hz, 2H), 5.94 (s, 1H), 4.04 (t, J = 13.9, 3.1 Hz, 2H),; ^{13}C NMR (125 MHz, DMSO–d_6) δ 189.9 (t, J_{CF} = 28.8 Hz, 1C), 135.7, 133.5 (q, J_{CF} = 32.2 Hz, 1C), 130.4 (t, J_{CF} = 3.2 Hz, 2C), 126.0 (q, J_{CF} = 3.9 Hz, 2C), 123.6 (q, J_{CF} = 272.9 Hz, 1C), 117.6 (t, J_{CF} = 254.3 Hz, 1C), 61.6 (t, J_{CF} = 28.2 Hz, 1C); ^{19}F NMR (471 MHz, $CDCl_3$) δ –63.5 (s, 3F), –109.3 (t, J_{HF} = 12.8 Hz, 2F); IR (film) ν_{max} 3362, 2867, 1709, 1413, 1329, 1174 cm^{-1}; HRMS (ESI–TOF) *m/z* calcd for $C_{10}H_6F_5O_2$ [M–H]$^-$ 253.0288, found 253.0287.



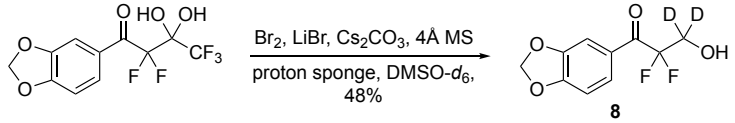
6

(*E*)-4,4-Difluoro-5-hydroxy-1-phenylpent-1-en-3-one (6). A mixture of activated 4Å molecular sieves (150 mg), Cs_2CO_3 (153 mg, 0.47 mmol), LiBr (20 mg, 0.23 mmol), and proton sponge (20 mg, 0.09 mmol) in DMSO (1.5 mL) was cooled to 10 ºC and treated with the dropwise addition of bromine (15 µL, 0.29 mmol). After 15 min, a solution of the *gem*-diol[3] (14 mg, 0.047 mmol) in DMSO (0.5 mL) was added to the reaction mixture across 1 h via syringe pump. The reaction mixture was then stirred for 12 h at rt. Next, the reaction mixture was treated with saturated aqueous NH_4Cl (3 mL), diluted EtOAc (25 mL), and stirred for 1 h. The resultant mixture was filtered through Celite, and the organics were washed with brine (3 × 5 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Preparative TLC (6% EtOAc in $CHCl_3$) afforded the title compound **6** as a yellow oil (4.5 mg, 45%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, J = 15.9 Hz, 1H), 7.64 (dd, J = 7.6, 1.7 Hz, 2H), 7.46 (m, 3H), 7.17 (dt, J = 16.0, 1.3 Hz, 1H), 4.08 (td, J = 12.9, 7,3 Hz, 2H), 2.17 (t, J = 7.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.3 (t, J_{CF} = 30.0 Hz, 1C), 148.5 (t, J_{CF} = 1.4 Hz, 1C), 134.0, 132.0, 129.3 (2C), 129.2 (2C) 118.1, 115.3 (t, J_{CF} = 254.9 Hz, 1C), 62.4 (t, J_{CF} = 29.1 Hz, 1C); ^{19}F NMR (471 MHz, $CDCl_3$) δ –116.8 (t, J_{HF} = 12.6 Hz, 2F); IR (film) ν_{max} 3388, 2958, 2926, 1701, 1610, 1451, 1329, 1181 cm^{-1}; HRMS (ESI–TOF) *m/z* calcd for $C_{11}H_9F_2O_2$ [M–H]$^-$ 211.0571, found 211.0580.



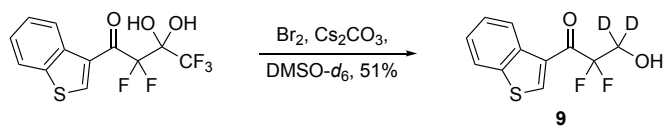
7

3,3-Dideutero-2,2-difluoro-3-hydroxy-1-(naphthalen-2-yl)propan-1-one (7). A mixture of activated 4Å molecular sieves (200 mg), LiBr (27 mg, 0.31 mmol), proton sponge (27 mg, 0.13 mmol), Cs_2CO_3 (242 mg, 0.743 mmol) in DMSO-d_6 (1.6 mL) was cooled to 10 ºC and treated with the dropwise addition of bromine (32 µL, 0.62 mmol). After 15 min, a solution of the *gem*-diol[2] (20 mg, 0.062 mmol) in DMSO-d_6 (0.5 mL) was added to the reaction mixture across 1 h via syringe pump. The reaction mixture was then stirred for 12 h at rt. Next, the reaction mixture was cooled to rt, treated with saturated aqueous NH_4Cl (5 mL), diluted EtOAc (50 mL), and stirred for 1 h. The resultant mixture was filtered through Celite, and the organics were washed with brine (3 × 5 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Preparative TLC (5% EtOAc in $CHCl_3$) afforded the title compound **7** as a colorless solid (8 mg, 54%): mp 43–44 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (s, 1H), 8.10 (d, J = 8.5 Hz, 1H), 8.01 (d, J = 8.1 Hz, 1H), 7.93 (d, J = 8.7 Hz, 1H), 7.89 (d, J = 8.1 Hz, 1H), 7.66 (td, J = 7.8, 1,1 Hz, 1H), 7.59 (td, J = 7.5, 1.2 Hz, 1H), 2.40 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.6 (t, J_{CF} = 30.5 Hz, 1C), 136.2, 133.3 (t, J_{CF} = 4.5 Hz, 1C), 132.2, 130.2, 129.6, 128.9 (t, J_{CF} = 3.0 Hz, 1C), 128.7, 127.8, 127.2, 124.5, 116.2 (t, J_{CF} = 257.0 Hz, 1C), 62.8 (m, 1C); ^{19}F NMR (471 MHz, $CDCl_3$) δ –108.4 (s, 2F); IR (film) ν_{max} 3439, 3062, 2958, 2928, 2864, 1689, 1627, 1467, 1296, 1371 cm^{-1}; HRMS (ESI–TOF) *m/z* calcd for $C_{13}H_7D_2F_2O_2$ $[M–H]^-$ 237.0696, found 237.0710.



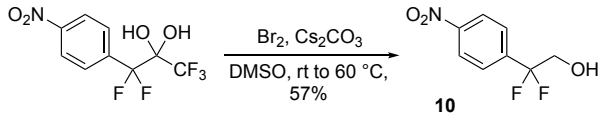
8

3,3-Dideutero-1-(benzo[1,3]dioxol-5-yl)-2,2-difluoro-3-hydroxypropan-1-one (8). A mixture of activated 4Å molecular sieves (150 mg), LiBr (19 mg, 0.22 mmol), proton sponge (19 mg, 0.18 mmol), Cs_2CO_3 (160 mg, 0.492 mmol) in DMSO-d_6 (1.7 mL) was cooled to 10 ºC and treated with the dropwise addition of bromine (32 µL, 0.62 mmol). After 15 min, a solution of the *gem*-diol[2] (14 mg, 0.044 mmol) in DMSO-d_6 (1.0 mL) was added to the reaction mixture across 1 h via syringe pump. The reaction mixture was then stirred for 24 h at 40 °C. Next, the reaction mixture was cooled to rt, treated with saturated aqueous NH_4Cl (5 mL), diluted EtOAc (50 mL), and stirred for 1 h. The resultant mixture was filtered through Celite, and the organics were washed with brine (3 × 5 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Preparative TLC (30% acetone in hexanes) afforded the title compound **8** as a yellow oil (5 mg, 48%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, J = 10.1 Hz, 1H), 7.55 (s, 1H), 6.90 (d, J = 8.4 Hz, 1H), 6.08 (s, 2H), 2.44 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.7 (t, J_{CF} = 30.4 Hz, 1C), 153.4, 148.2, 127.7 (t, J_{CF} = 4.3 Hz, 1C), 126.1 (t, J_{CF} = 3.2 Hz, 1C), 116.0 (t, J_{CF} = 257.0 Hz, 1C), 109.5 (t, J_{CF} = 2.7 Hz, 1C), 108.3, 102.2, 62.7 (m, 1C); ^{19}F NMR (471 MHz, $CDCl_3$) δ –108.2 (s, 2F); IR (film) ν_{max} 3420, 2916, 1681, 1605, 1446, 1247 cm^{-1}; HRMS (ESI–TOF) *m/z* calcd for $C_{10}H_6D_2F_2O_4$ $(M+H)^+$ 233.0594, found 233.0595.

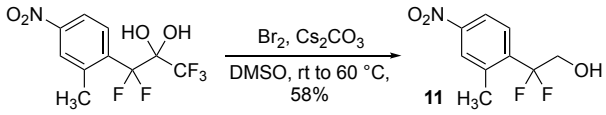


9

3,3-Dideutero-1-(benzothiophen-3-yl)-2,2-difluoro-3-hydroxypropan-1-one (9). A mixture of activated 4Å molecular sieves (250 mg), LiBr (35 mg, 0.40 mmol), proton sponge (35 mg, 0.16 mmol), Cs_2CO_3 (285 mg, 0.875 mmol) in DMSO-d_6 (3 mL) was cooled to 10 ºC and treated with the dropwise addition of bromine (40 µL, 0.78 mmol). After 15 min, a solution of the *gem*-diol[3] (26 mg, 0.080 mmol) in DMSO-d_6 (1.0 mL) was added to the reaction mixture across 1 h via syringe pump. The reaction mixture was then stirred for 24 h at 40 °C. Next, the reaction mixture was cooled to rt, treated with saturated aqueous NH_4Cl (5 mL), diluted EtOAc (50 mL), and stirred for 1 h. The resultant mixture was filtered through Celite, and the organics were washed with brine (3 × 5 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Preparative TLC (5% EtOAc in hexanes) afforded the title compound **9** as a brown oil (10 mg, 51%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.80 (t, J = 1.8 Hz, 1H), 8.72 (d, J = 8.9 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.54 (t, J = 7.7 Hz, 1H), 7.47 (t, J = 7.6 Hz, 1H), 2.33 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 184.3 (t, J_{CF} = 30.1 Hz, 1C), 142.7 (t, J_{CF} = 8.4 Hz, 1C), 139.0, 136.9, 128.5 (t, J_{CF} = 3.0 Hz, 1C), 126.4, 126.0, 125.1, 122.3, 116.0 (t, J_{CF} = 257.0 Hz, 1C), 62.1 (m, 1C); ^{19}F NMR (471 MHz, $CDCl_3$) δ –108.0 (s, 2F); IR (film) ν_{max} 3405, 3119, 3063, 1673, 1490, 1219, 1100 cm^{-1}; HRMS (ESI–TOF) *m/z* calcd for $C_{11}H_5D_2F_2O_2S$ $(M–H)^-$, 243.0260, found 243.0254.

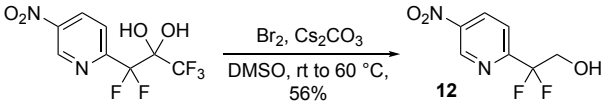


2,2-Difluoro-2-(4-nitrophenyl)ethan-1-ol (10). A mixture of activated 4Å molecular sieves (130 mg) and Cs_2CO_3 (115 mg, 0.350 mmol) in DMSO (1.2 mL) was cooled to 10 ºC and treated with the dropwise addition of bromine (17 µL, 0.33 mmol). After 15 min, a solution of the *gem*-diol[1] (10 mg, 0.035 mmol) in DMSO (0.3 mL) was added to the reaction mixture across 1 h via syringe pump. The reaction mixture was then stirred for 18 h at 60 °C. Next, the reaction mixture was cooled to rt, treated with saturated aqueous NH_4Cl (2 mL), diluted EtOAc (50 mL), and stirred for 1 h. The resultant mixture was filtered through Celite, and the organics were washed with brine (3 × 5 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Preparative TLC (3% EtOAc in $CHCl_3$) afforded the title compound **10** as a colorless solid (4 mg, 57%): mp 86–89 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, J = 8.4 Hz, 2H), 7.74 (d, J = 8.6 Hz, 2H), 4.02 (t, J = 12.7 Hz, 2H), 1.84 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.4, 140.7 (t, J_{CF} = 26.1 Hz, 1C), 127.0 (t, J_{CF} = 6.1 Hz, 2C), 123.7 (2C), 119.6 (t, J_{CF} = 253.1 Hz, 1C), 65.6 (t, J_{CF} = 32.9 Hz, 1C); ^{19}F NMR (376 MHz, $CDCl_3$) δ –107.1 (t, J_{HF} = 12.8 Hz, 2F); IR (film) ν_{max} 3519, 1519, 1352, 1314 cm^{-1}; HRMS (EI–BE) *m/z* calcd for $C_8H_7F_2NO_3$ $[M]^+$ 203.0394, found, 203.0392.

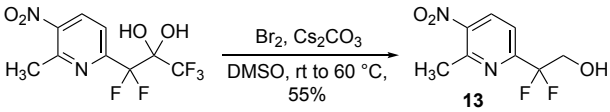


2,2-Difluoro-2-(2-methyl-4-nitrophenyl)ethan-1-ol (11). A mixture of activated 4Å molecular sieves (170 mg) and Cs_2CO_3 (130 mg, 0.40 mmol) in DMSO (1.5 mL) was cooled to 10 ºC and treated with the dropwise addition of bromine (20 µL, 0.39 mmol). After 15 min, a solution of the *gem*-diol[1] (12 mg, 0.04 mmol) in DMSO (0.5 mL) was added to the reaction mixture across 1 h via syringe pump. The reaction mixture was then stirred for 24 h at 65 °C. Next, the reaction mixture was cooled to rt, treated with saturated aqueous NH_4Cl (3 mL), diluted EtOAc (50 mL), and stirred for 1 h. The resultant mixture was filtered through Celite, and the organics were washed with brine (3 × 5 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Preparative

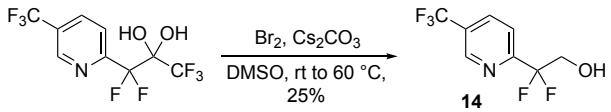
TLC (3% EtOAc in $CHCl_3$) afforded the title compound **11** as a colorless solid (5 mg, 58%): mp 106–107 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (s, 1H), 8.08 (d, J = 8.5 Hz, 1H), 7.69 (d, J = 8.2 Hz, 1H), 4.06 (t, J = 13.3 Hz, 2H), 2.59 (s, 3H), 1.96 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.7, 138.8 (t, J_{CF} = 2.3 Hz, 1C) 138.5 (t, J_{CF} = 24.4 Hz, 1C), 128.4 (t, J_{CF} = 8.7 Hz, 1C), 126.6, 120.8 (t, J_{CF} = 246.1 Hz, 1C), 120.8, 64.9 (t, J_{CF} = 31.7 Hz, 1C), 20.5 (t, J_{CF} = 4.0 Hz, 1C); ^{19}F NMR (471 MHz, $CDCl_3$) δ –105.0 (t, J_{HF} = 13.4 Hz, 2F); IR (film) ν_{max} 3521, 3096, 2946, 1520, 1351 cm^{-1}; HRMS (ESI–TOF) *m/z* calcd for $C_9H_8F_2NO_3$ [M–H]$^-$ 216.0472, found 216.0473.



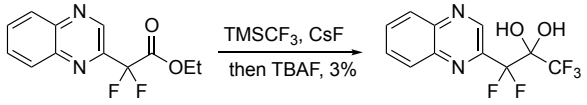
2,2-Difluoro-2-(5-nitropyridin-2-yl)ethan-1-ol (12). A mixture of activated 4Å molecular sieves (100 mg) and Cs_2CO_3 (110 mg, 0.338 mmol) in DMSO (1.2 mL) was cooled to 10 ºC and treated with the dropwise addition of bromine (15 µL, 0.29 mmol). After 15 min, a solution of the *gem*-diol[1] (10 mg, 0.033 mmol) in DMSO (0.5 mL) was added to the reaction mixture across 1 h via syringe pump. The reaction mixture was then stirred for 24 h at 60 °C. Next, the reaction mixture was cooled to rt, treated with saturated aqueous NH_4Cl (2 mL), diluted EtOAc (50 mL), and stirred for 1 h. The resultant mixture was filtered through Celite, and the organics were washed with brine (3 × 5 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Preparative TLC (10% EtOAc in $CHCl_3$) afforded the title compound **12** as a colorless oil (4 mg, 56%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.45 (s, 1H), 8.65 (dd, J = 8.6, 2.6 Hz, 1H), 7.95 (d, J = 8.6 Hz, 1H), 4.28 (t, J = 12.5 Hz, 2H), 2.70 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.5 (t, J_{CF} = 30.1 Hz, 1C), 144.8, 144.6, 132.7, 121.8 (t, J_{CF} = 3.6 Hz, 1C), 117.7 (t, J_{CF} = 244.6 Hz, 1C), 63.7 (t, J_{CF} = 30.7 Hz, 1C).^{19}F NMR (471 MHz, $CDCl_3$) δ –107.1 (t, J_{HF} = 12.5 Hz, 2F); IR (film) ν_{max} 3585, 3109, 2936, 1607, 1530, 1358, 1320 cm^{-1}; HRMS (ESI–TOF) *m/z* calcd for $C_7H_7F_2N_2O_3$ [M+H]$^+$ 205.0425, found 205.0424.



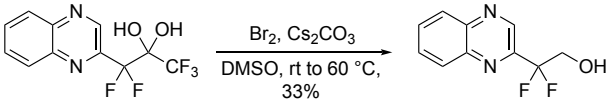
2,2-Difluoro-2-(6-methyl-5-nitropyridin-2-yl)ethan-1-ol (13). A mixture of activated 4Å molecular sieves (100 mg) and Cs_2CO_3 (110 mg, 0.338 mmol) in DMSO (1.0 mL) was cooled to 10 ºC and treated with the dropwise addition of bromine (15 µL, 0.29 mmol). After 15 min, a solution of the *gem*-diol[1] (10 mg, 0.033 mmol) in DMSO (0.4 mL) was added to the reaction mixture across 1 h via syringe pump. The reaction mixture was then stirred for 24 h at 60 °C. Next, the reaction mixture was cooled to rt, treated with saturated aqueous NH_4Cl (2 mL), diluted EtOAc (50 mL), and stirred for 1 h. The resultant mixture was filtered through Celite, and the organics were washed with brine (3 × 5 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Preparative TLC (10% EtOAc in $CHCl_3$) afforded the title compound **13** as a colorless solid (4 mg, 55%): mp 73–75 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, J = 8.4 Hz, 1H), 7.78 (d, J = 8.6 Hz, 1H), 4.27 (td, J = 12.3, 6.2 Hz, 3H), 2.90 (s, 3H), 2.74 (t, J = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.3 (t, J_{CF} = 30.1 Hz, 1C), 153.6, 146.3, 134.0, 119.6 (t, J_{CF} = 3.6 Hz, 1C) 117.5 (t, J_{CF} = 244.9 Hz, 1C), 63.8 (t, J_{CF} = 30.6 Hz, 1C), 23.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ –108.2 (t, J_{HF} = 12.6 Hz, 2F); IR (film) ν_{max} 3400, 3094, 2934, 1602, 1582, 1530, 1350, 1332 cm^{-1}; HRMS (ESI–TOF) *m/z* calcd for $C_8H_7F_2N_2O_3$ [M–H]$^-$ 217.0425, found 217.0415.



2,2-Difluoro-2-(5-(trifluoromethyl)pyridin-2-yl)ethan-1-ol (14). A mixture of activated 4Å molecular sieves (200 mg) and Cs_2CO_3 (208 mg, 0.638 mmol) in DMSO (2.0 mL) was cooled to 10 ºC and treated with the dropwise addition of bromine (30 µL, 0.59 mmol). After 15 min, a solution of the *gem*-diol[1] (18 mg, 0.058 mmol) in DMSO (0.5 mL) was added to the reaction mixture across 1 h via syringe pump. The reaction mixture was then stirred for 24 h at 60 °C. Next, the reaction mixture was cooled to rt, treated with saturated aqueous NH_4Cl (4 mL), diluted EtOAc (50 mL), and stirred for 1 h. The resultant mixture was filtered through Celite, and the organics were washed with brine (3 × 10 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Preparative TLC (25% acetone in hexanes) afforded the title compound **14** as a colorless oil (4 mg, 25%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.91 (s, 1H), 8.13 (dd, J = 8.2 Hz, 1H), 7.88 (d, J = 8.2 Hz, 1H), 4.27 (t, J = 12.5 Hz, 2H), 2.83 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.1 (t, J_{CF} = 29.6 Hz, 1C), 146.2 (q, J_{CF} = 3.9 Hz, 1C), 135.1 (q, J_{CF} = 3.7 Hz, 1C), 128.2 (q, J_{CF} = 33.7 Hz, 1C), 122.9 (q, J_{CF} = 272.5 Hz, 1C), 121.3 (t, J_{CF} = 3.3 Hz, 1C), 117.9 (t, J_{CF} = 244.0 Hz, 1C), 64.1 (t, J_{CF} = 30.8 Hz, 1C); ^{19}F NMR (471 MHz, $CDCl_3$) δ –62.7 (s, 3F), –106.9 (t, J_{HF} = 12.6 Hz, 2F); IR (film) ν_{max} 3339, 2930, 2854, 1735, 1689, 1556, 1350, 1463, 1325 cm^{-1}; HRMS (ESI–TOF) *m/z* calcd for $C_8H_7F_5NO$ $[M+H]^+$ 228.0448, found 228.0457.

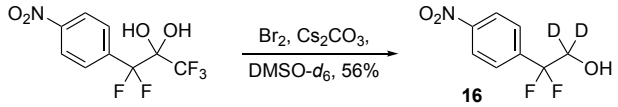


1,1,1,3,3-Pentafluoro-3-(quinoxalin-2-yl)propane-2,2-diol. A solution of ethyl 2,2-difluoro-2-(2-quinoxalinyl)acetate[5] (603 mg, 2.39 mmol) in CH_3CN (6 mL) was treated with trimethyl(trifluoromethyl)silane (0.71 mL, 4.8 mmol). The mixture was stirred for 20 min at rt and then cooled to −30 °C. Next, a mixture of cesium fluoride (182 mg, 1.20 mmol) in CH_3CN (12 mL) was added, and the resultant mixture was stirred for 18 h at rt. The reaction mixture was quenched with saturated aqueous NH_4Cl (20 mL) at −20 °C and stirred for 1 h. The mixture was filtered through Celite and extracted with CH_2Cl_2 (20 mL × 3). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude reaction mixture was treated with TBAF (3 mL, 1.0 M in THF) in CH_2Cl_2 (6 mL) and stirred at rt for 20 h. Then, the mixture was quenched with saturated aqueous NH_4Cl (10 mL) and filtered through Celite. Next, the mixture was extracted with CH_2Cl_2 (10 mL × 3), filtered, and concentrated under reduced pressure. Preparative TLC (10% isopropanol/40% dichloromethane/50% hexanes, then 7% isopropanol/13% dichloromethane/80% hexanes) afforded 1,1,1,3,3-pentafluoro-3-(quinoxalin-2-yl)propane-2,2-diol as a yellow oil (20 mg, 3%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.37 (s, 1H), 8.25 (dd, J = 8.2, 1.8 Hz, 1H), 8.12 (dd, J = 8.1, 1.8 Hz, 1H), 7.99−7.89 (m, 2H), 5.92 (s, 2H); ^{13}C NMR (125 MHz, ($CDCl_3$) δ 146.7 (t, J_{CF} = 29.1 Hz, 1C), 143.6, 141.8 (t, J_{CF} = 5.1 Hz, 1C), 139.0, 132.5, 132.1, 129.7, 128.9, 121.3 (q, J_{CF} = 288.3 Hz, 1C), 113.1 (t, J_{CF} = 256.0 Hz, 1C), 93.6 (ddt, J_{CF} = 32.6, 28.2, 4.8 Hz, 1C); ^{19}F NMR (376 MHz, ($CDCl_3$) δ −80.73 (t, J_{FF} = 10.9 Hz, 3F), −111.80 (q, J_{FF} = 11.2 Hz, 2F); IR (film) ν_{max} cm^{-1} 3067.6, 1267.3, 1161.1, 1073.5; HRMS (ESI–TOF) *m/z* calcd for $C_{11}H_6F_5N_2O_2$ $(M-H)^-$ 293.0349, found 293.0343.



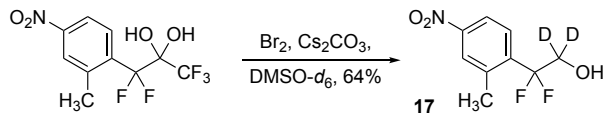
15

2,2-Difluoro-2-(quinoxalin-2-yl)ethan-1-ol (15). A mixture of activated 4Å molecular sieves (600 mg) and Cs_2CO_3 (692 mg, 2.13 mmol) in DMSO (8.0 mL) was cooled to 10 ºC and treated with the dropwise addition of bromine (90 µL, 1.8 mmol). After 15 min, a solution of the 1,1,1,3,3-pentafluoro-3-(quinoxalin-2-yl)propane-2,2-diol (50 mg, 0.17 mmol) in DMSO (1.0 mL) was added to the reaction mixture across 1 h via syringe pump. The reaction mixture was then stirred for 24 h at 60 °C. Next, the reaction mixture was cooled to rt, treated with saturated aqueous NH_4Cl (15 mL), diluted EtOAc (50 mL), and stirred for 1 h. The resultant mixture was filtered through Celite, and the organics were washed with brine (4 × 25 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Preparative TLC (10% *i*-PrOH, 40% CH_2Cl_2, 50% hexanes) afforded the title compound **15** as a yellow solid (11 mg, 31%): mp 99–100 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.25 (s, 1H), 8.20 (dd, J = 7.2, 2.3 Hz, 1H), 8.13 (dd, J = 8.0, 1.8 Hz, 1H), 7.91–7.83 (m, 2H), 4.41 (t, J = 12.4 Hz, 2H), 2.75 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.2 (t, J_{CF} = 30.1 Hz, 1C), 143.3, 142.5, 140.6, 131.8, 131.3, 129.7, 129.7, 118.3 (t, J_{CF} = 243.6 Hz, 1C), 64.1 (t, J_{CF} = 30.5 Hz, 1C); ^{19}F NMR (376 MHz, $CDCl_3$) δ –106.11 (t, J_{HF} = 12.5 Hz, 2F); IR (film) ν_{max} 3259, 3060, 2967, 2924, 2853, 1498, 1256, 1088 cm^{-1}; HRMS (ESI–TOF) *m/z* calcd for $C_{10}H_9F_2N_2O$ $[M+H]^+$ 211.0683, found 211.0679.



16

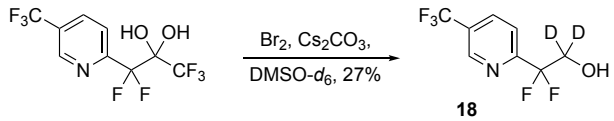
1,1,-Dideutero-2,2-difluoro-2-(4-nitrophenyl)ethan-1-ol (16). A mixture of activated 4Å molecular sieves (100 mg) and Cs_2CO_3 (115 mg, 0.350 mmol) in DMSO-d_6 (1.2 mL) was cooled to 10 ºC and treated with the dropwise addition of bromine (17 µL, 0.33 mmol). After 15 min, a solution of the *gem*-diol[1] (10 mg, 0.035 mmol) in DMSO-d_6 (0.3 mL) was added to the reaction mixture across 1 h via syringe pump. The reaction mixture was then stirred for 24 h at 65 °C. Next, the reaction mixture was cooled to rt, treated with saturated aqueous NH_4Cl (2 mL), diluted EtOAc (50 mL), and stirred for 1 h. The resultant mixture was filtered through Celite, and the organics were washed with brine (3 × 5 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Preparative TLC (5% EtOAc in $CHCl_3$) afforded the title compound **16** as a colorless solid (4 mg, 56%): mp 86–89 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, J = 8.9 Hz, 2H), 7.73 (d, J = 8.9 Hz, 2H), 2.17 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.1, 140.7 (t, J_{CF} = 26.1 Hz, 1C), 127.0 (t, J_{CF} = 6.1 Hz, 2C), 123.7 (2C), 119.6 (t, J_{CF} = 244.8 Hz, 1C), 64.9 (m, 1C); ^{19}F NMR (471 MHz, $CDCl_3$) δ –107.3; IR (film) ν_{max} 3409, 3088, 2868, 1611, 1529, 1352, 1284, 1113 cm^{-1}; HRMS (ESI–TOF) *m/z* calcd for $C_8H_4D_2F_2NO_3$ $[M–H]^–$ 204.0441, found 204.0418.



17

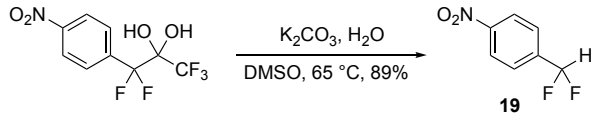
1,1-Dideutero-2,2-difluoro-2-(2-methyl-4-nitrophenyl)ethan-1-ol (17). A mixture of activated 4Å molecular sieves (200 mg) and Cs_2CO_3 (170 mg, 0.522 mmol) in DMSO-d_6 (2 mL) was cooled to 10 ºC and treated with the dropwise addition of bromine (25 µL, 0.49 mmol). After 15 min, a solution of the *gem*-diol[1] (15 mg, 0.05 mmol) in DMSO-d_6 (0.5 mL) was added to the reaction

mixture across 1 h via syringe pump. The reaction mixture was then stirred for 24 h at 65 °C. Next, the reaction mixture was cooled to rt, treated with saturated aqueous NH_4Cl (5 mL), diluted EtOAc (50 mL), and stirred for 1 h. The resultant mixture was filtered through Celite, and the organics were washed with brine (3 × 5 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Preparative TLC (5% EtOAc in $CHCl_3$) afforded the title compound **17** as a colorless solid (7 mg, 64%): mp 107–108 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 8.09 (d, J = 8.3 Hz, 1H), 7.69 (d, J = 8.4 Hz, 1H), 2.59 (t, J = 2.4 Hz, 3H), 2.05 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.9, 138.8 (t, J = 2.3 Hz), 138.7 (t, J_{CF} = 24.4 Hz, 1C), 128.5 (t, J_{CF} = 8.6 Hz, 1C), 126.8, 120.9 (t, J_{CF} = 245.9 Hz, 1C).120.9, 64.5 (m, 1C), 20.6 (t, J_{CF} = 4.1 Hz, 1C); ^{19}F NMR (471 MHz, $CDCl_3$) δ –104.3 (s, 2F); IR (film) ν_{max} 3521, 3096, 2946, 1520, 1351 cm^{-1}; HRMS (ESI–TOF) *m/z* calcd for $C_9H_6F_2D_2NO_3$ $[M–H]^-$ 218.0598, found 218.0605.



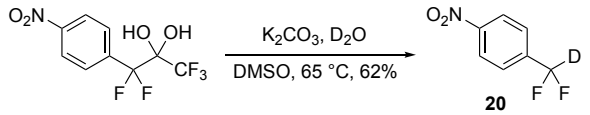
18

1,1-Dideutero-2,2-difluoro-2-(5-(trifluoromethyl)pyridin-2-yl)ethan-1-ol (18). A mixture of activated 4Å molecular sieves (150 mg) and Cs_2CO_3 (208 mg, 0.638 mmol) in DMSO-d_6 (2 mL) was cooled to 10 ºC and treated with the dropwise addition of bromine (25 µL, 0.48 mmol). After 15 min, a solution of the *gem*-diol[1] (15 mg, 0.05 mmol) in DMSO-d_6 (0.5 mL) was added to the reaction mixture across 1 h via syringe pump. The reaction mixture was then stirred for 24 h at 65 °C. Next, the reaction mixture was cooled to rt, treated with saturated aqueous NH_4Cl (5 mL), diluted EtOAc (50 mL), and stirred for 1 h. The resultant mixture was filtered through Celite, and the organics were washed with brine (3 × 5 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Preparative TLC (4% Et_2O in $CHCl_3$) afforded the title compound **18** as a colorless oil (3 mg, 27%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.91 (d, J = 2.5 Hz, 1H), 8.12 (d, J = 8.2 Hz, 1H), 7.88 (d, J = 8.2 Hz, 1H), 2.76 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.9 (t, J_{CF} = 30.2 Hz, 1C), 146.1 (q, J = 4.1 Hz, 1C), 135.0 (q, J = 3.6 Hz, 1C), 128.3 (q, J_{CF} = 33.5 Hz, 1C), 122.9 (q, J_{CF} = 272.9 Hz, 1C), 121.1 (t, J_{CF} = 3.4 Hz), 117.8 (t, J_{CF} = 243.9 Hz, 1C), 63.3 (m, 1C); ^{19}F NMR (471 MHz, $CDCl_3$) δ –62.8 (s, 3F), –107.1 (s, 2F); IR (film) ν_{max} 3343, 2918, 2850, 1724, 1609, 1398, 1332, 1143 cm^{-1}; HRMS (ESI–TOF) *m/z* calcd for $C_8H_5D_2F_5NO$ $(M+H)^+$ 230.0573, found 230.0572.



19

1-(Difluoromethyl)-4-nitrobenzene (19).[6] A solution of the *gem*-diol[1] (100 mg, 0.348 mmol) in DMSO (2.0 mL) was treated with H_2O (19 µL) and K_2CO_3 (194 mg, 1.40 mmol). The reaction mixture was stirred at 65 ºC for 3 h. Next, the reaction mixture was cooled to rt, treated with saturated aqueous NH_4Cl (2 mL), and extracted with CH_2Cl_2 (5 × 5 mL). The organics were dried over Na_2SO_4 and concentrated under reduced pressure. SiO_2 flash column chromatography (8:2 hexanes/EtOAc) afforded the title compound **19** as a colorless oil (54 mg, 89%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.33 (d, J = 8.9 Hz, 2H), 7.72 (d, J = 8.6 Hz, 2H), 6.65 (t, J = 55.7 Hz, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ –114.0 (d, J_{HF} = 55.7 Hz, 2F). All spectral and characterization data matched the reported data.[7]

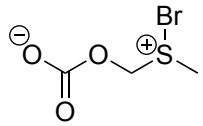
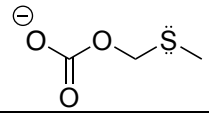


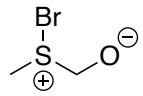
1-(Deutrodifluoromethyl)-4-nitrobenzene (20).[6] A solution of the *gem*-diol[1] (100 mg, 0.348 mmol) in DMSO (2.0 mL) was treated with D_2O (19 μL) and K_2CO_3 (194 mg, 1.40 mmol). The reaction mixture was stirred at 65 ºC for 30 min. Next, the reaction mixture was cooled to rt, treated with saturated aqueous NH_4Cl (2 mL), and extracted with CH_2Cl_2 (5 × 5 mL). The organics were dried over Na_2SO_4 and concentrated under reduced pressure. SiO_2 flash column chromatography (8:2 hexanes/EtOAc) afforded the title compound **20** as a colorless oil (38 mg, 62%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.33 (d, J = 9.0 Hz, 2H), 7.72 (d, J = 9.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.3, 140.1 (t, J_{CF} = 22.7 Hz, 1C), 126.8 (t, J_{CF} = 5.9 Hz, 2C), 124.0 (2C), 112.8 (tt, J_{CF} = 238.8, 28.4 Hz, 1C); ^{19}F NMR (282 MHz, $CDCl_3$) δ –114.5 (t, J_{DF} = 8.5 Hz, 2F); IR (film) ν_{max} 1529, 1351, 1277 cm^{-1}; HRMS (CI–Q) *m/z* calcd. for $C_7H_4DF_2NO_2$ $[M]^+$, 174.0351; found, 174.0353.

II. Computations

Geometry optimization and frequency calculations were performed with the Gaussian 09[8] software package using hybrid density functional theory[9] with the M06-2X[10] level of theory and 6-311++G(3df, 3pd) basis set. Integral calculations utilized an UltraFine grid. and Cartesian coordinates were utilized in. all cases, except that a Z-matrix was used for (bromo(methyl)sulfonio)methanolate. Calculations included DMSO solvent effects using the Polarizable Continuum Model (PCM) with the integral equation formalism variant (IEFPCM). No imaginary frequencies were observed for the obtained minima. Free energies (G) and enthalpies (H) are reported in atomic units at 298.15 K (Table S1) and include the zero-point energy. The concerted fragmentation process has the lowest energies compared to both the reversible and the stepwise fragmentation processes (Figure S1).

Table S2. Free energies (G) and enthalpies (H) of intermediates and products in the proposed mechanism.

Compound	**G (au)**	**H (au)**
	–3315.295323	–3315.247698
	–741.305751	–741.262752
Br_2	–5148.358075	–5148.330310

	–114.494958	–114.470157
CO_2	–188.600670	–188.576452
	–3012.257250	–3012.223359
	–2574.376153	–2574.357617
	–3126.697791	–3126.656971

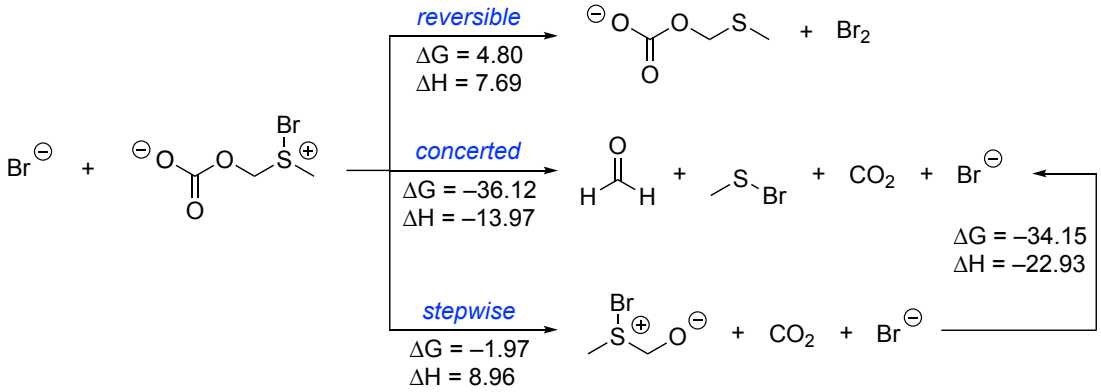


Figure S1. Free energies (G) and enthalpies (H) of the three investigated processes (in kcal/mol at 298.15K).

III. References

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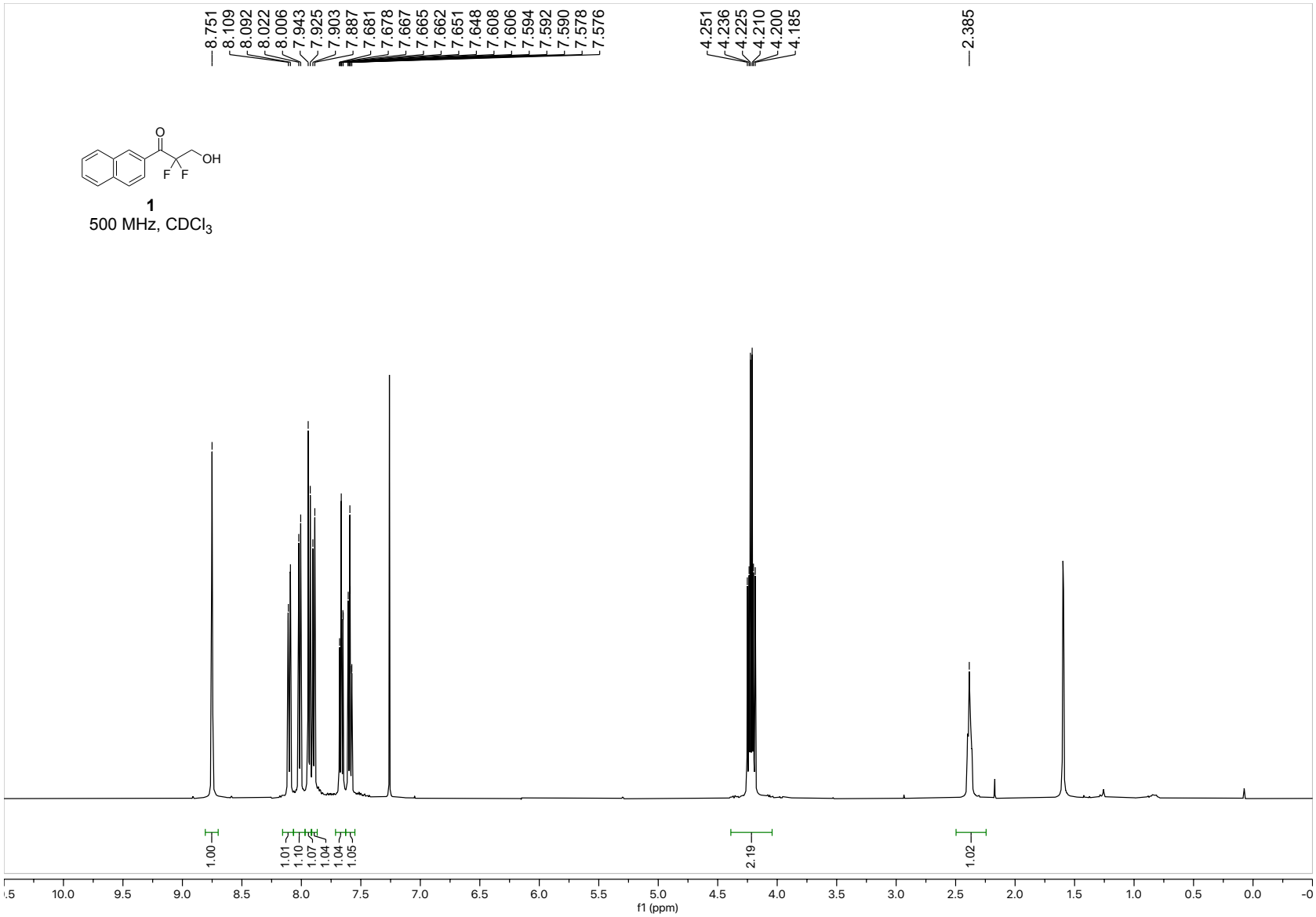
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7.662
7.651
7.648
7.608
7.606
7.594
7.592
7.590
7.578
7.576
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4.236
4.225
4.210
4.200
4.185
2.385
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OH
F F
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1.07
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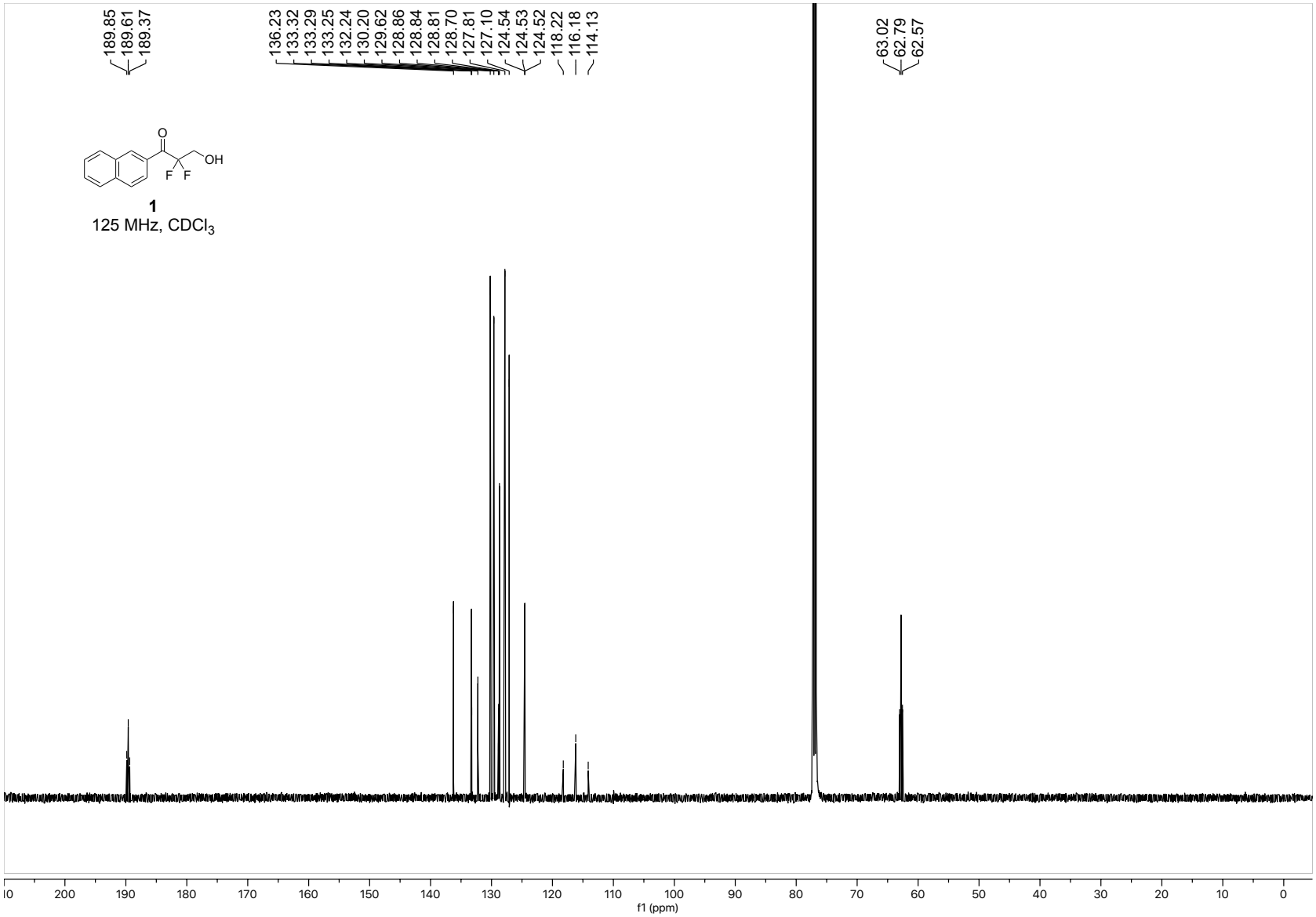
1.05
2.19
1.02
f1 (ppm)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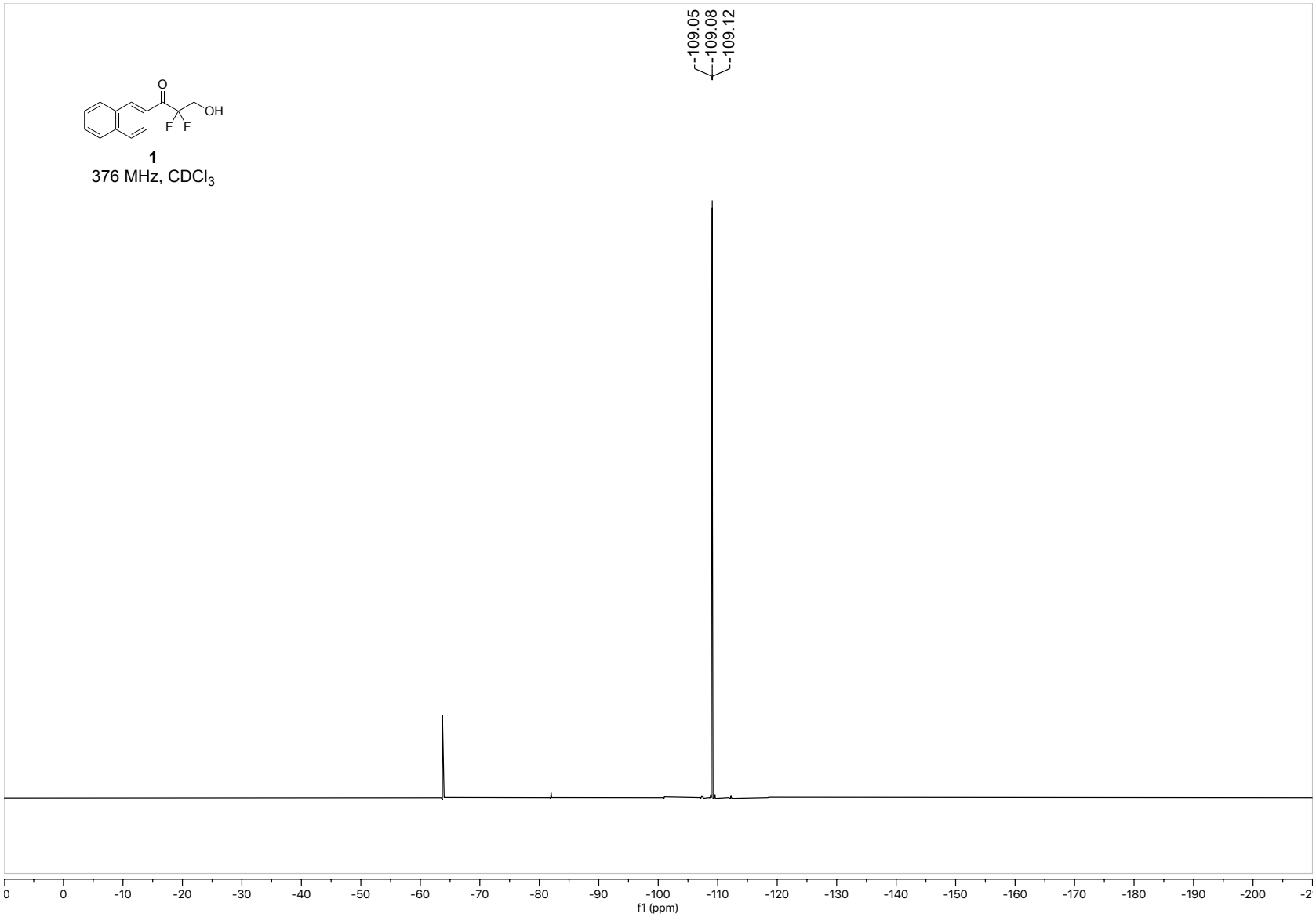
f1 (ppm)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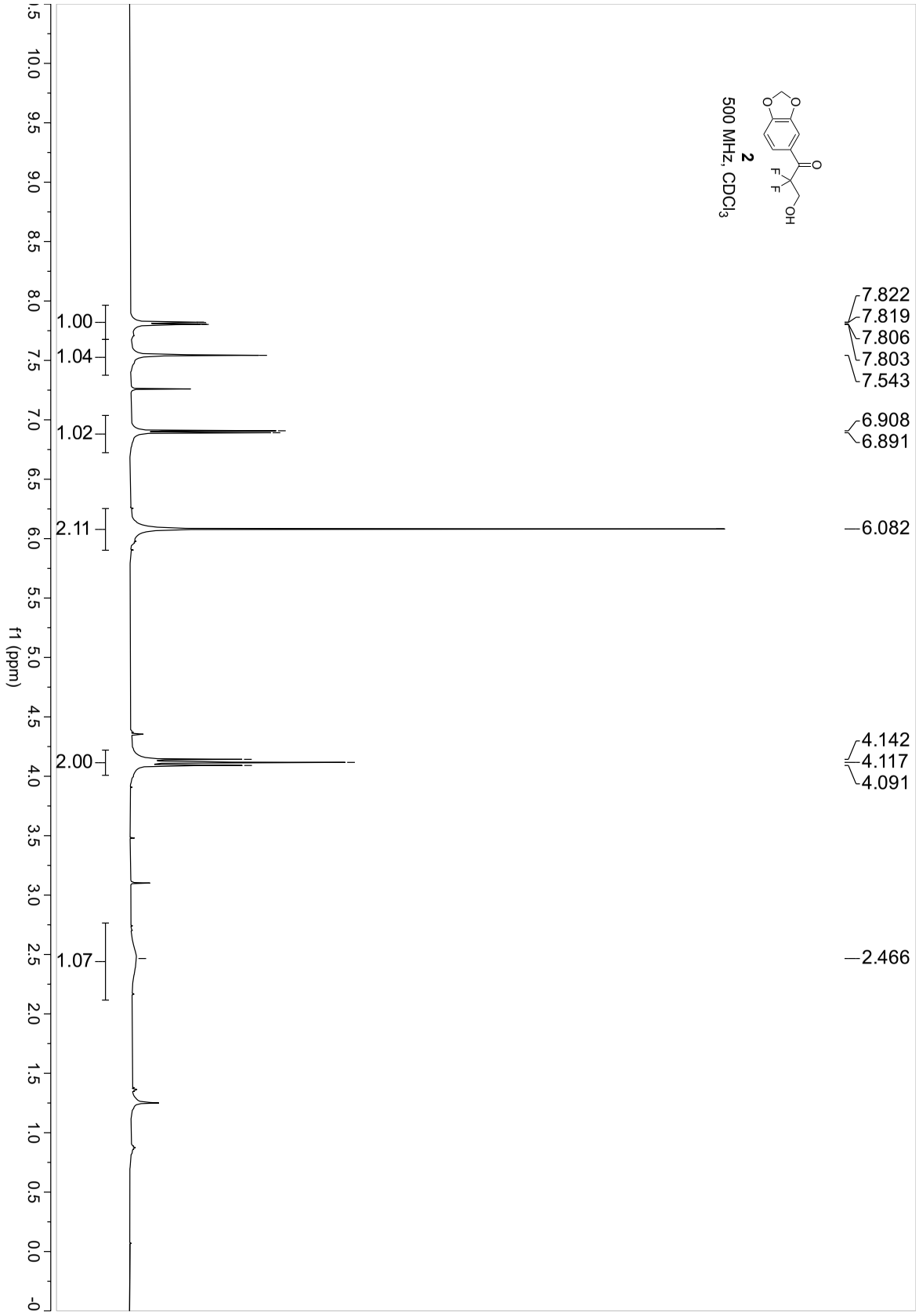
f1 (ppm)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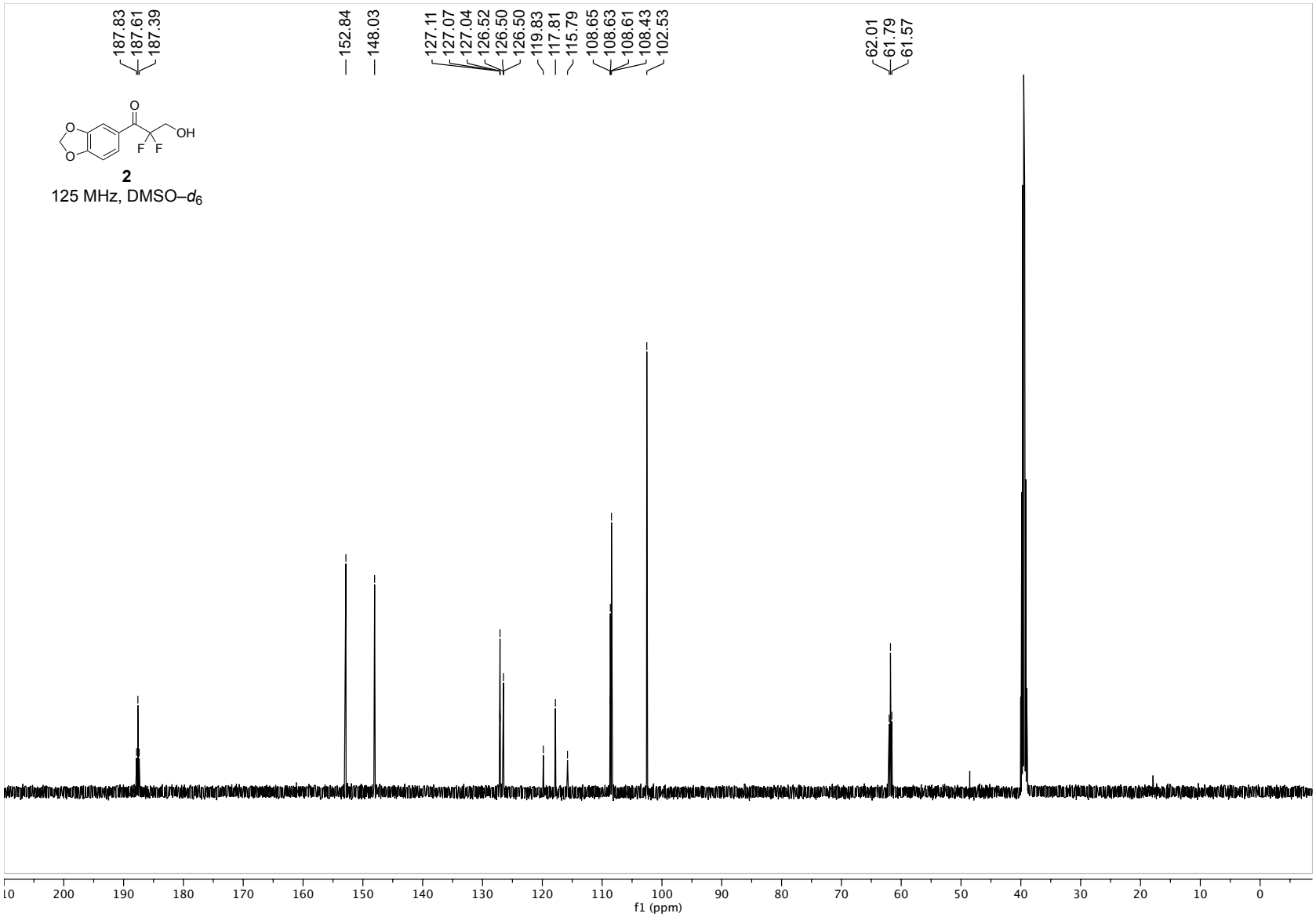
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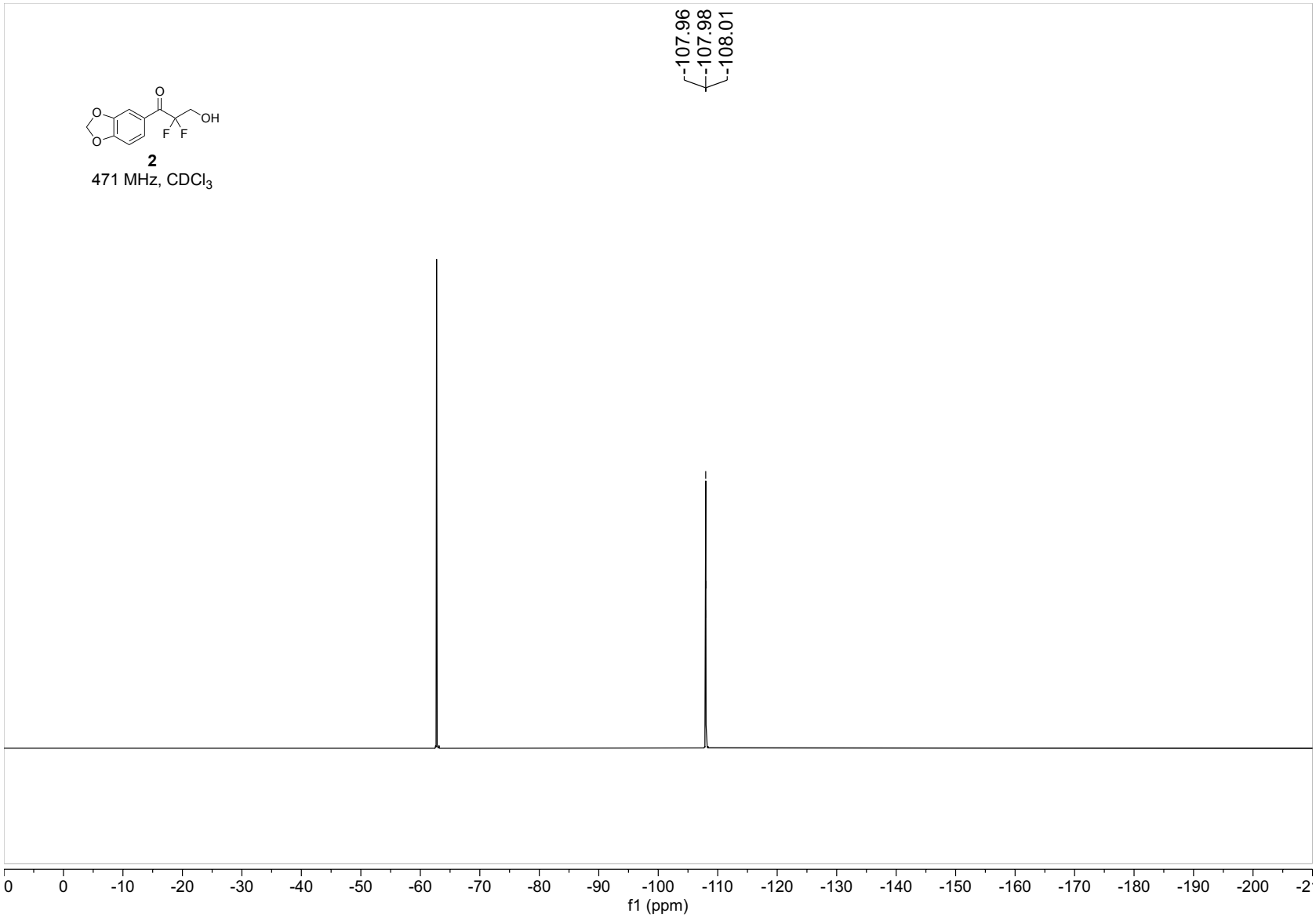
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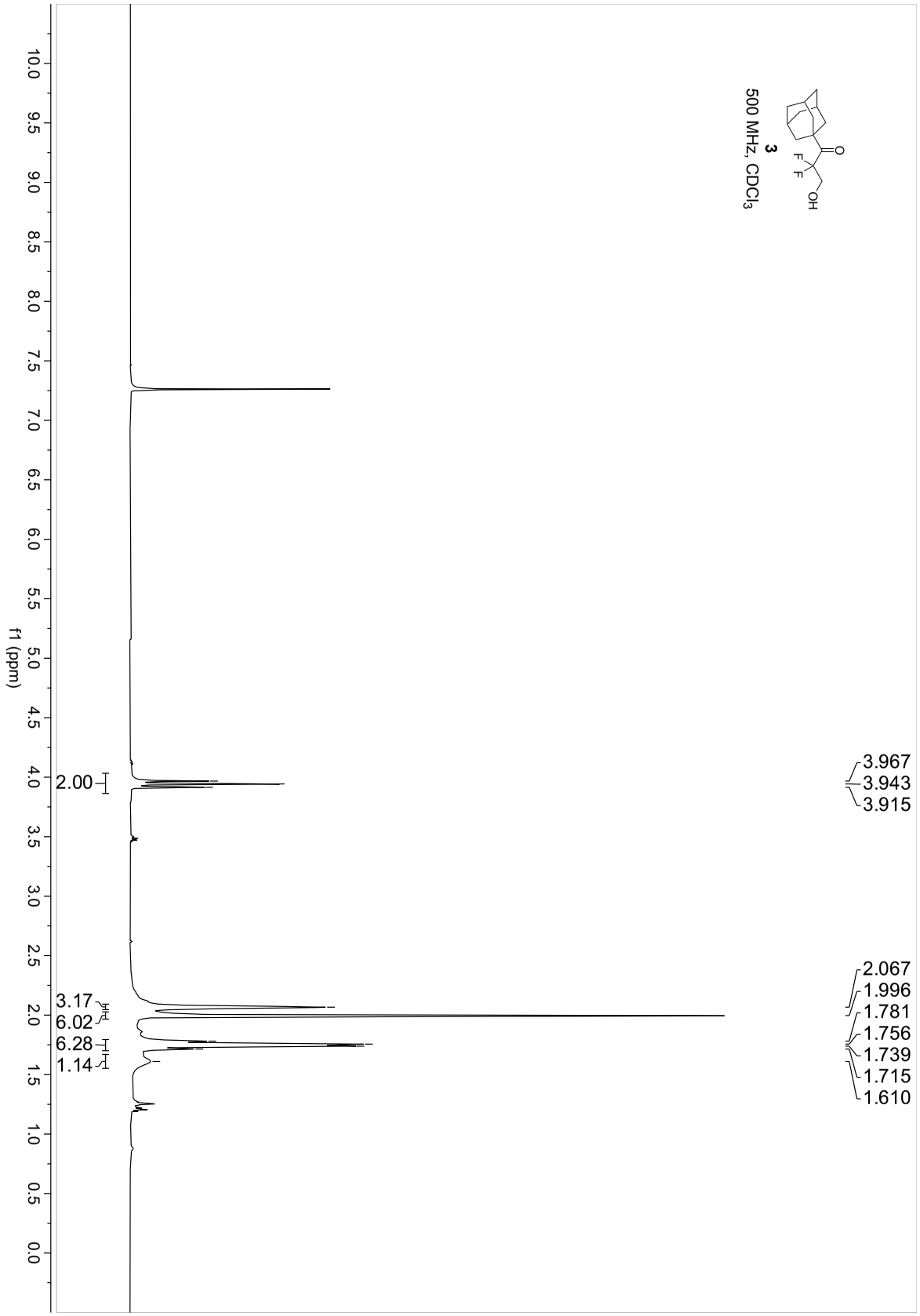
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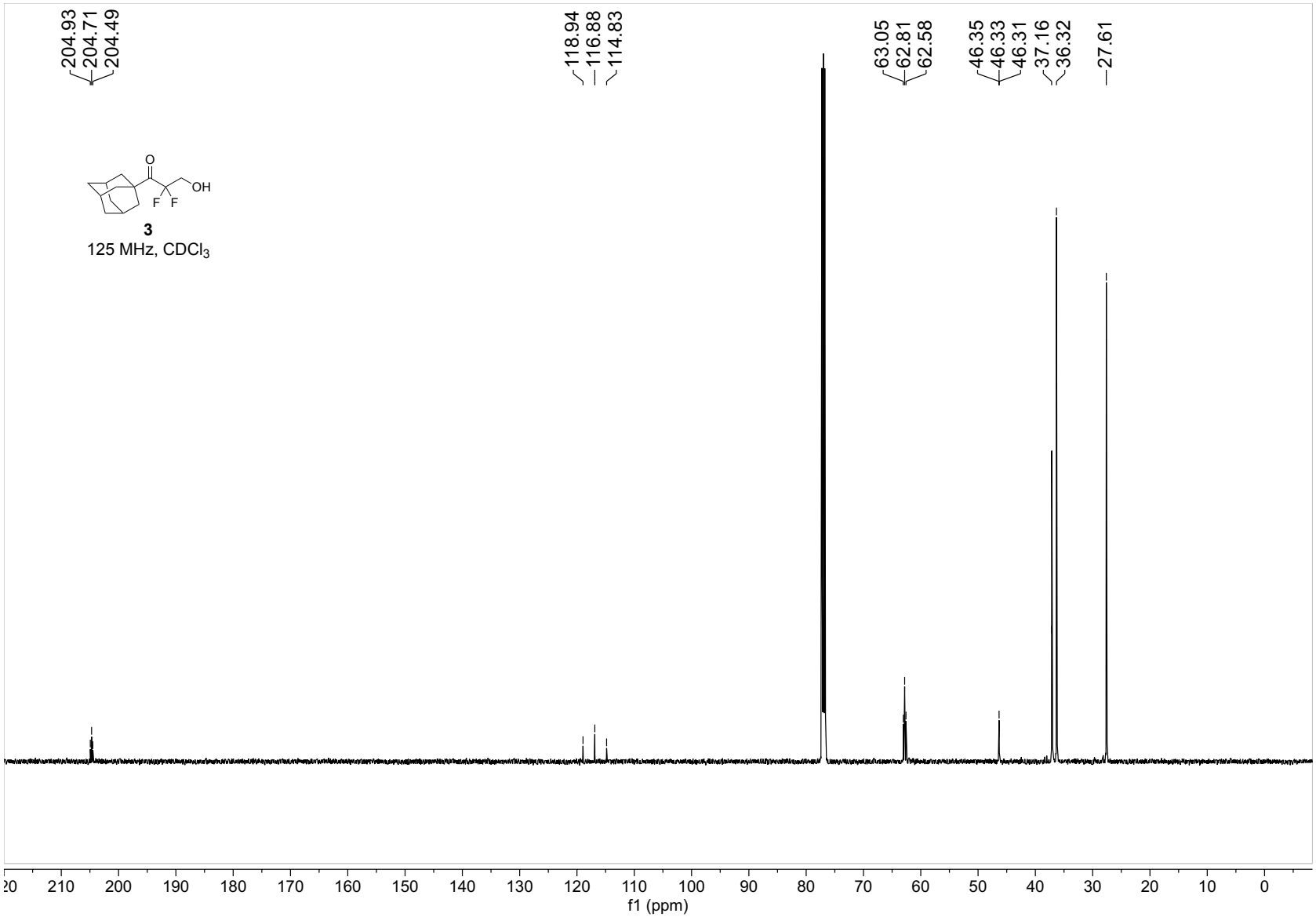
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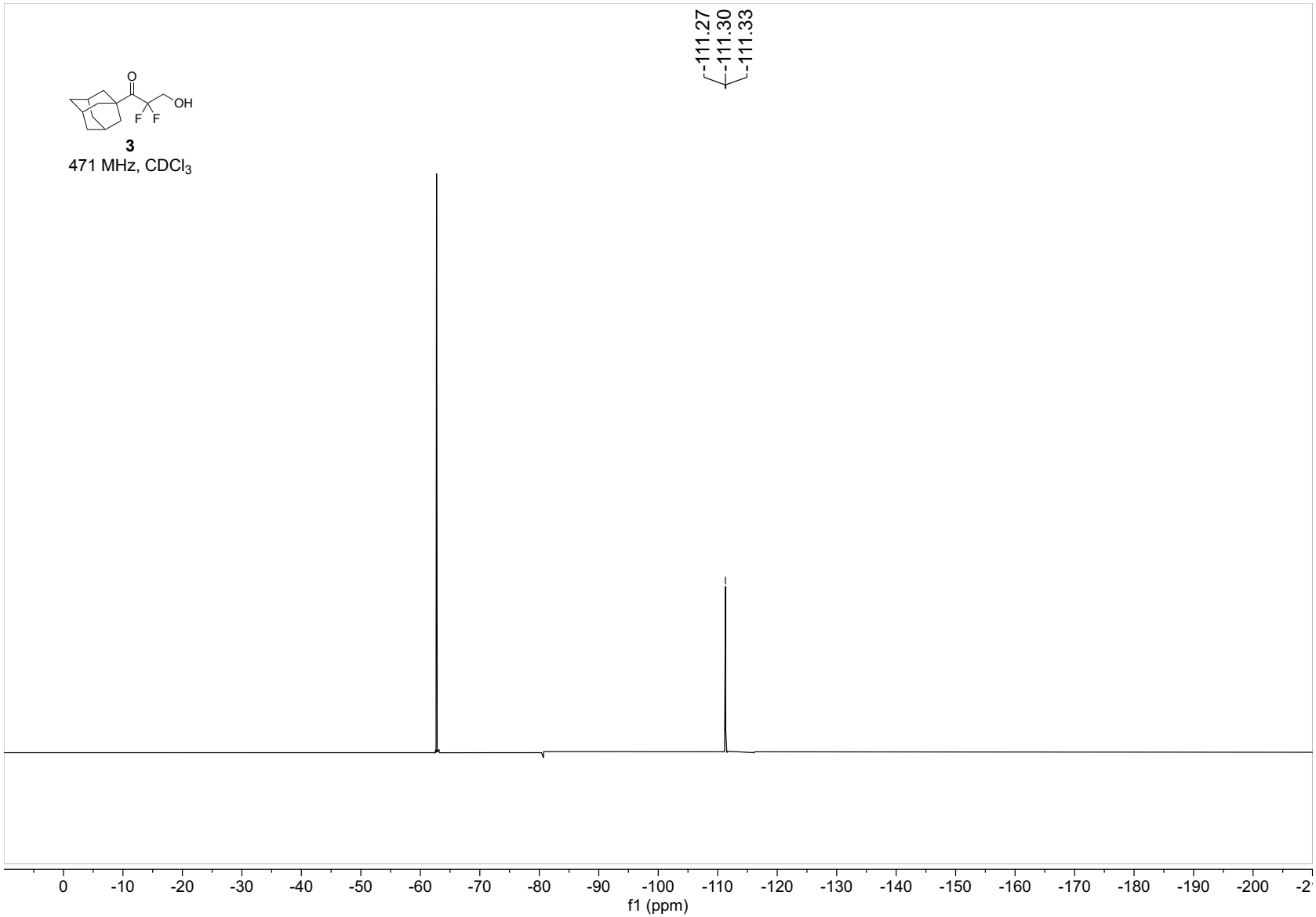
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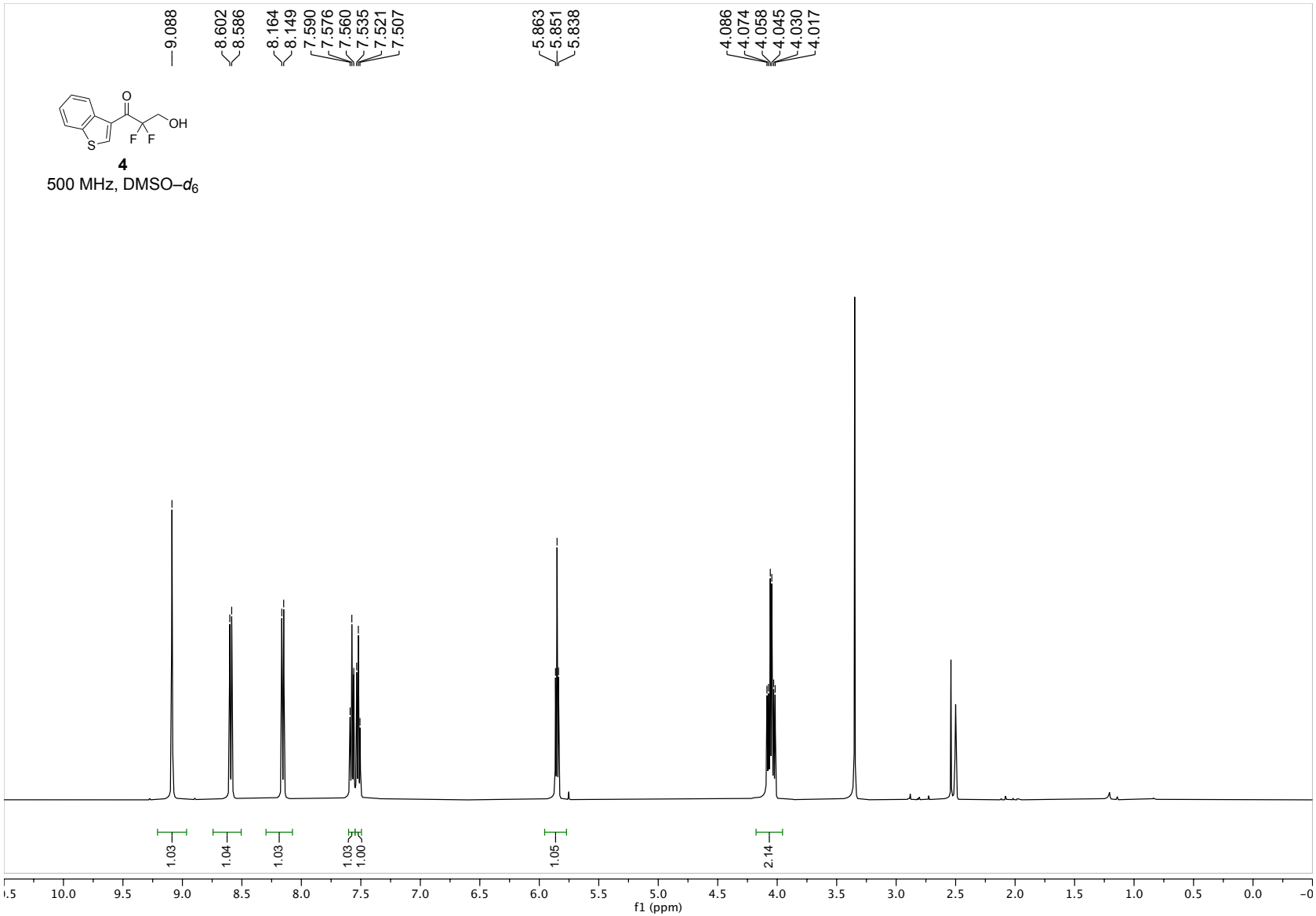
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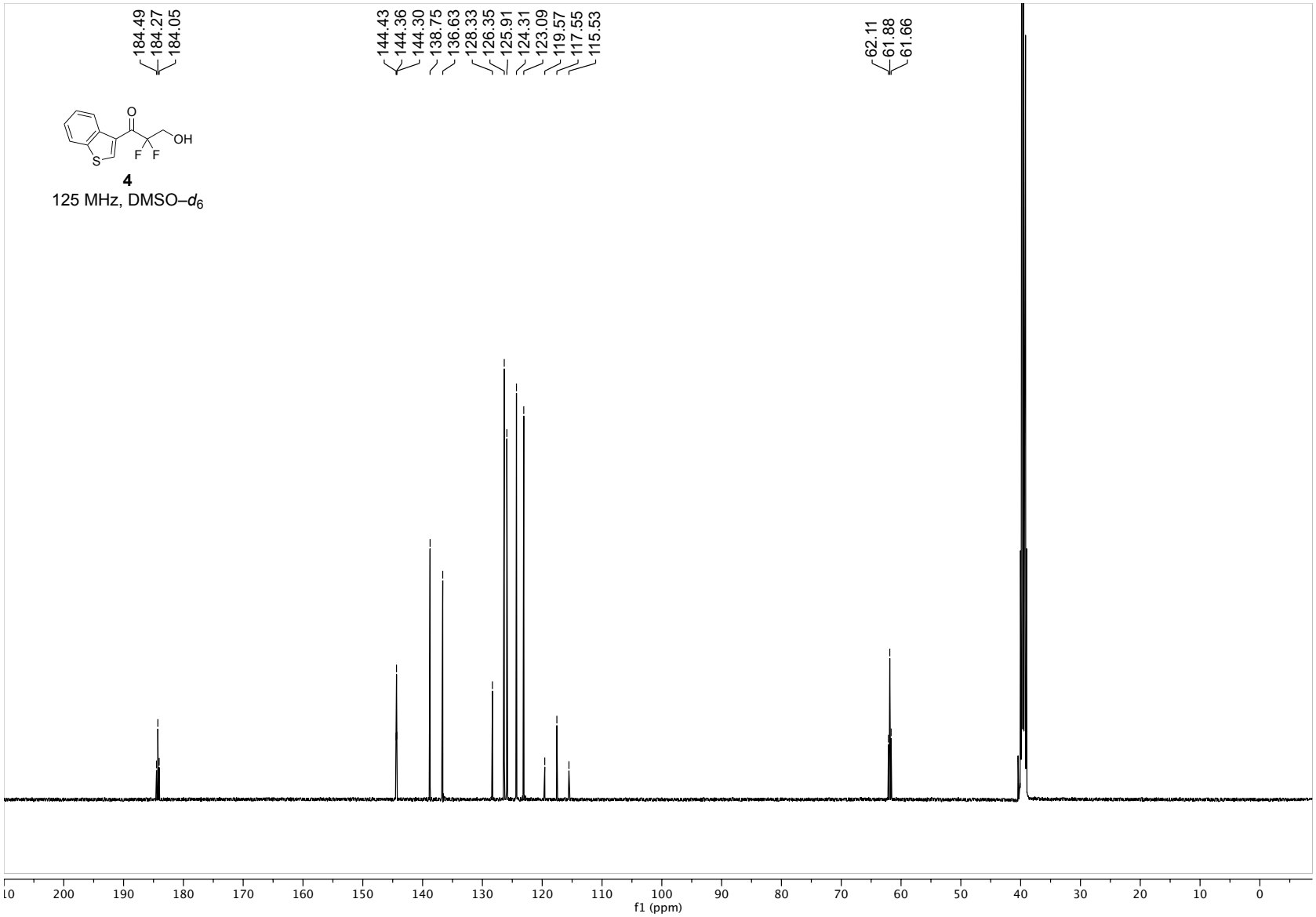
f1 (ppm)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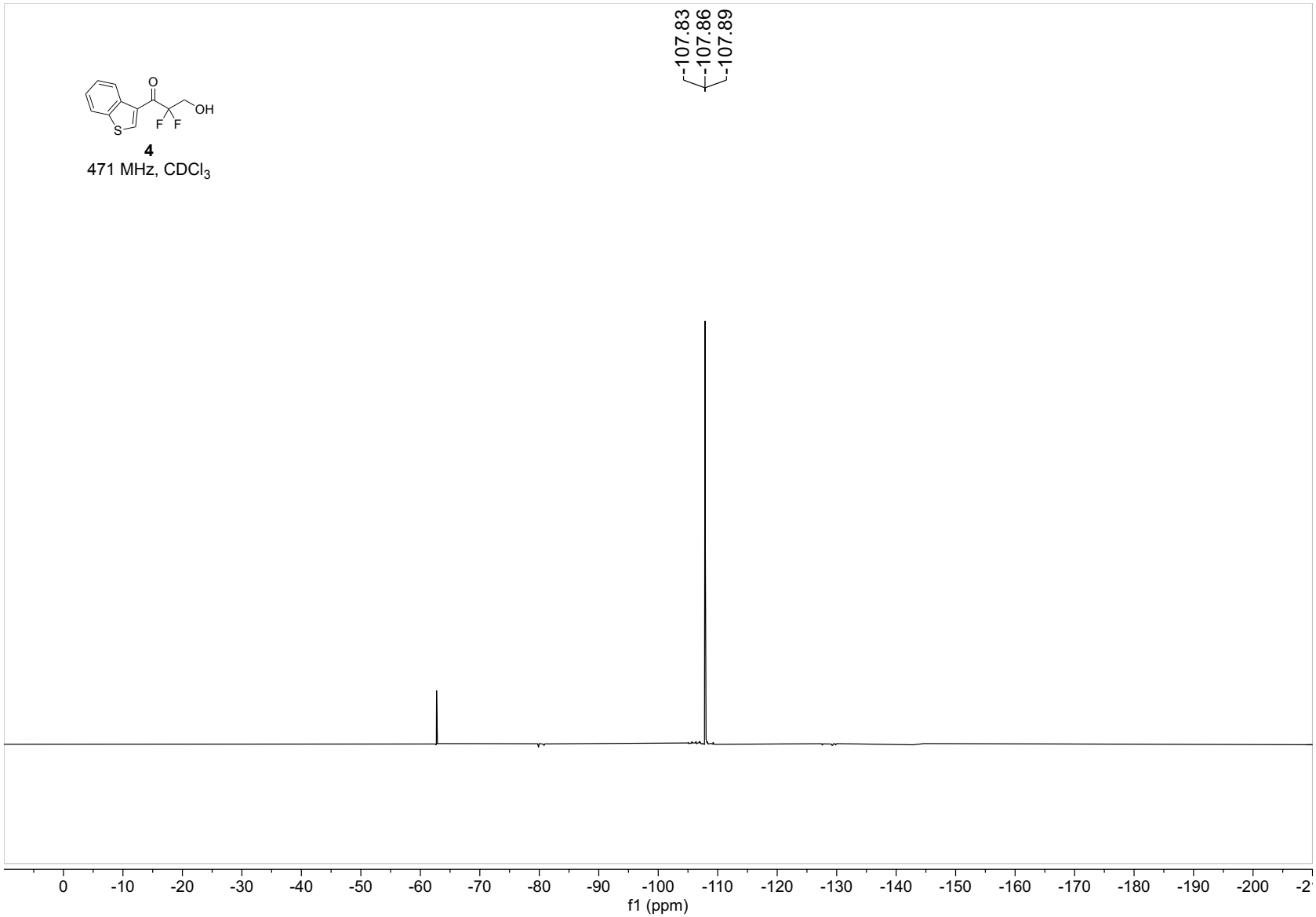
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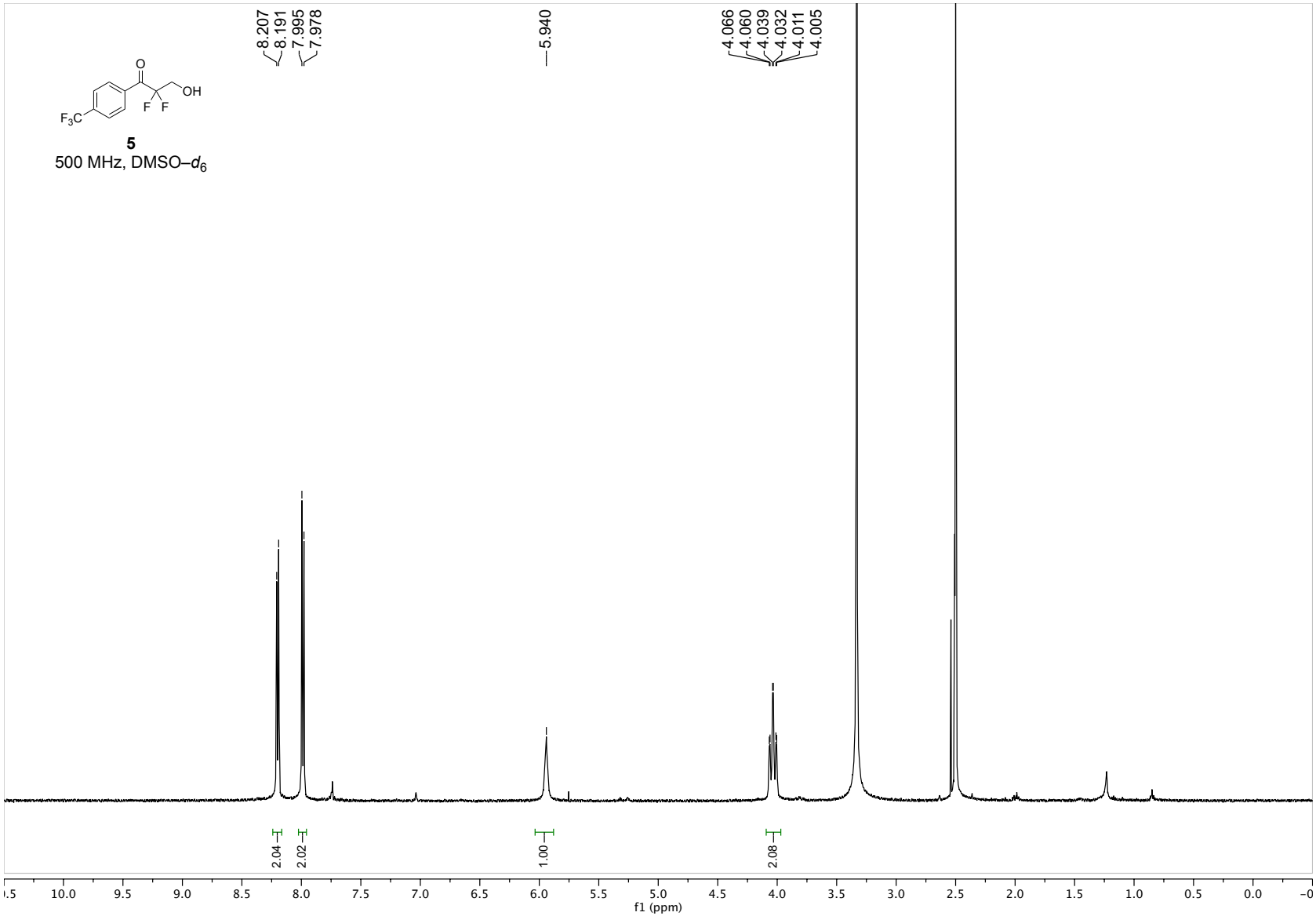
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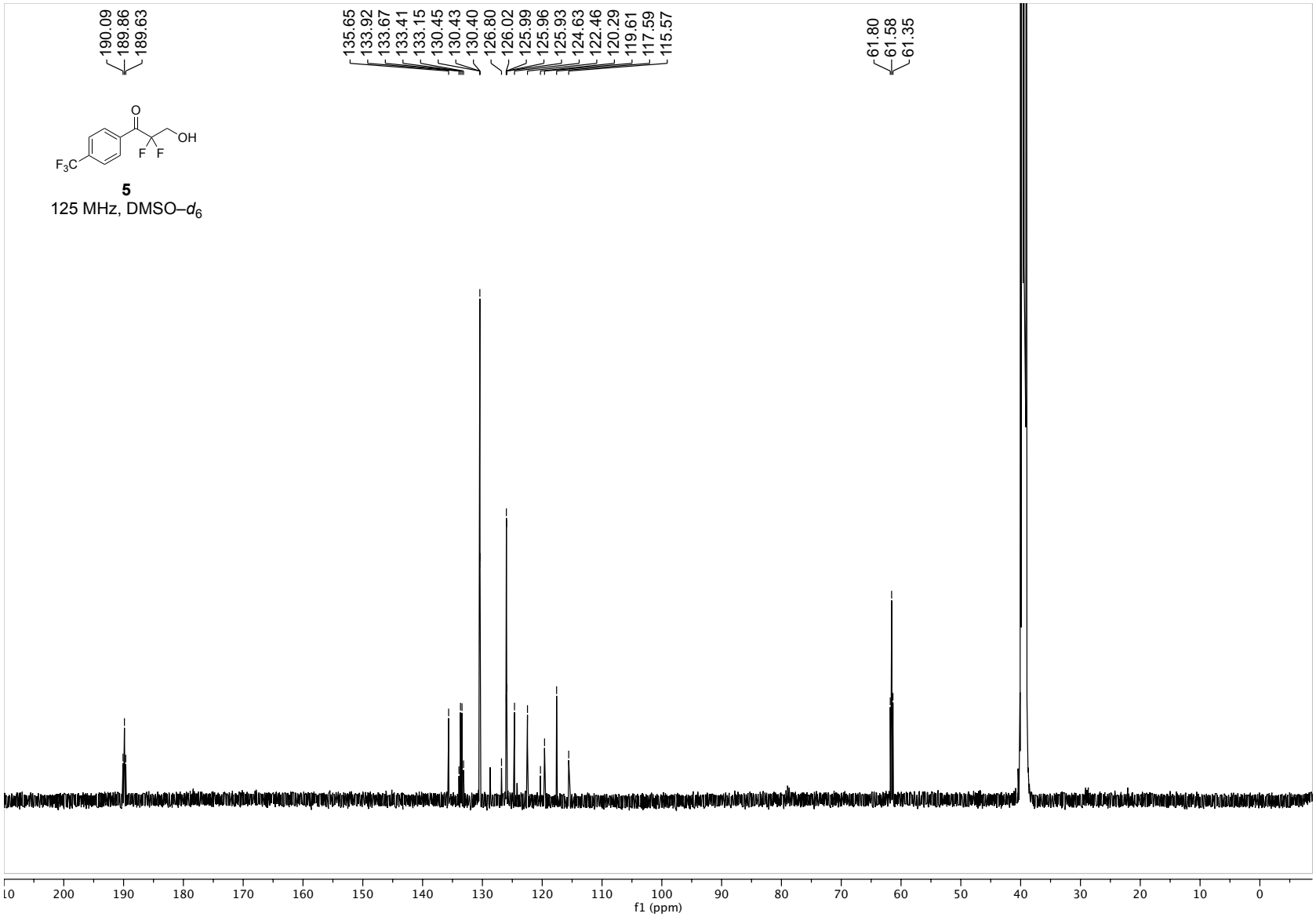
f1 (ppm)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F3C
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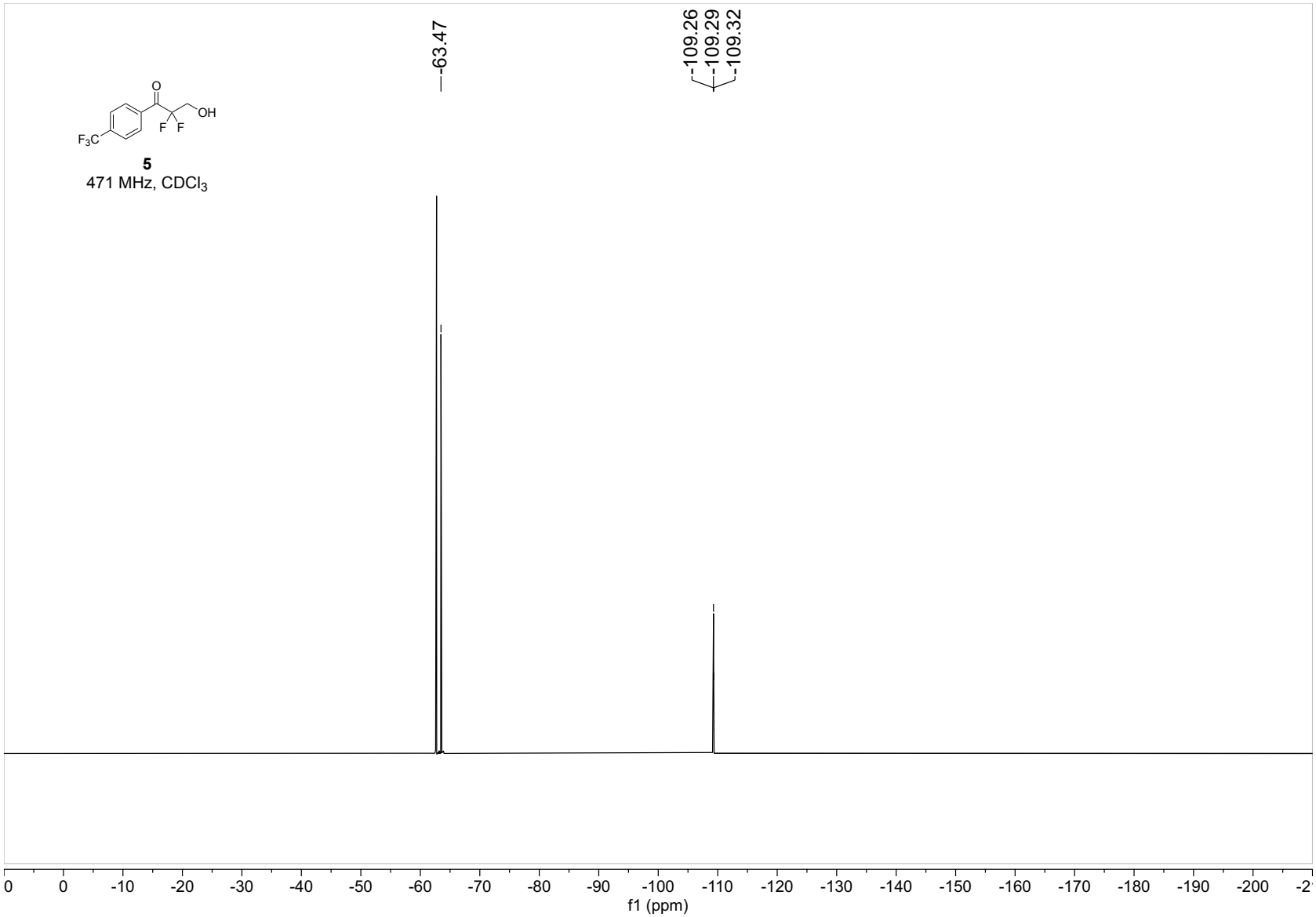
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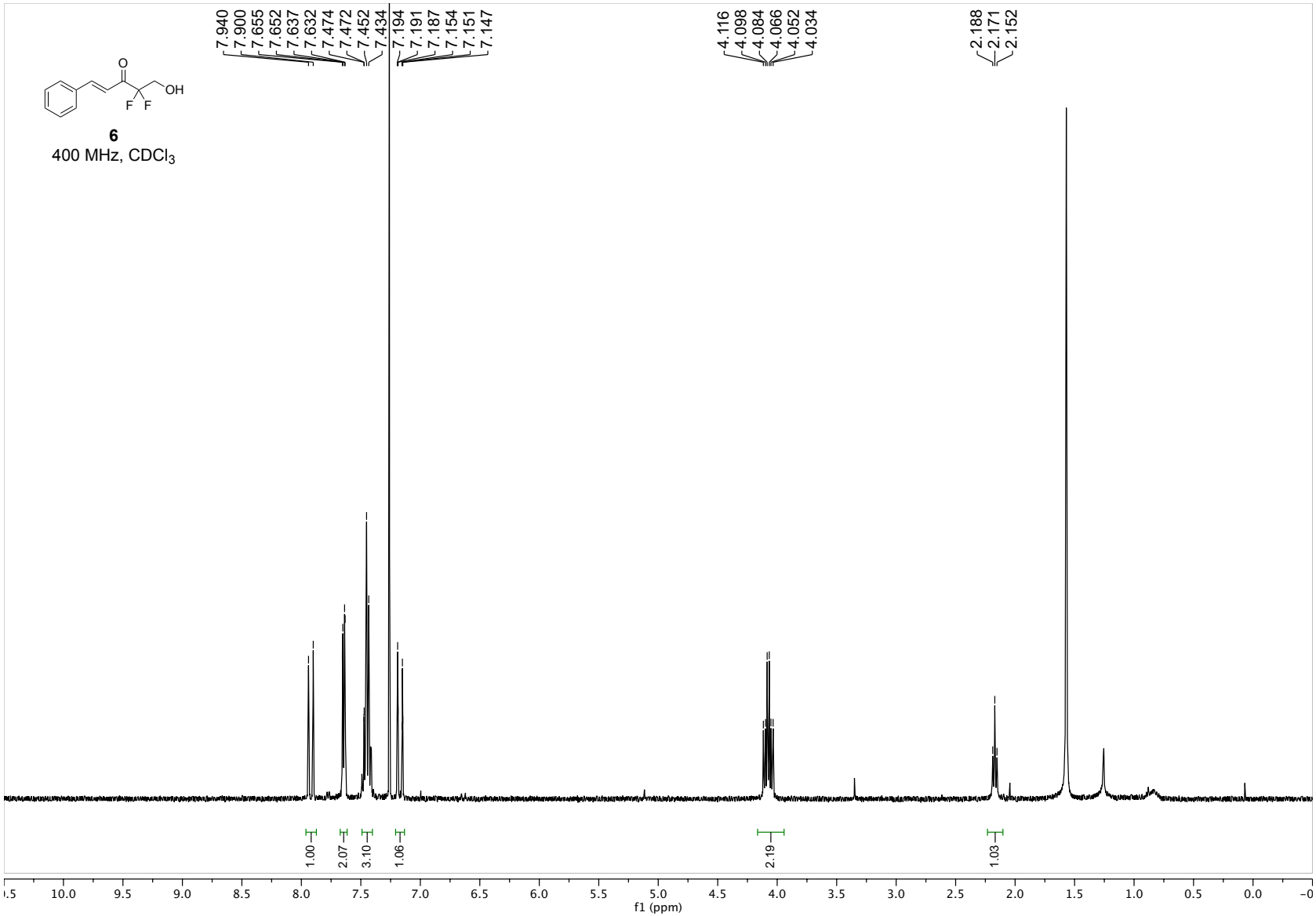
f1 (ppm)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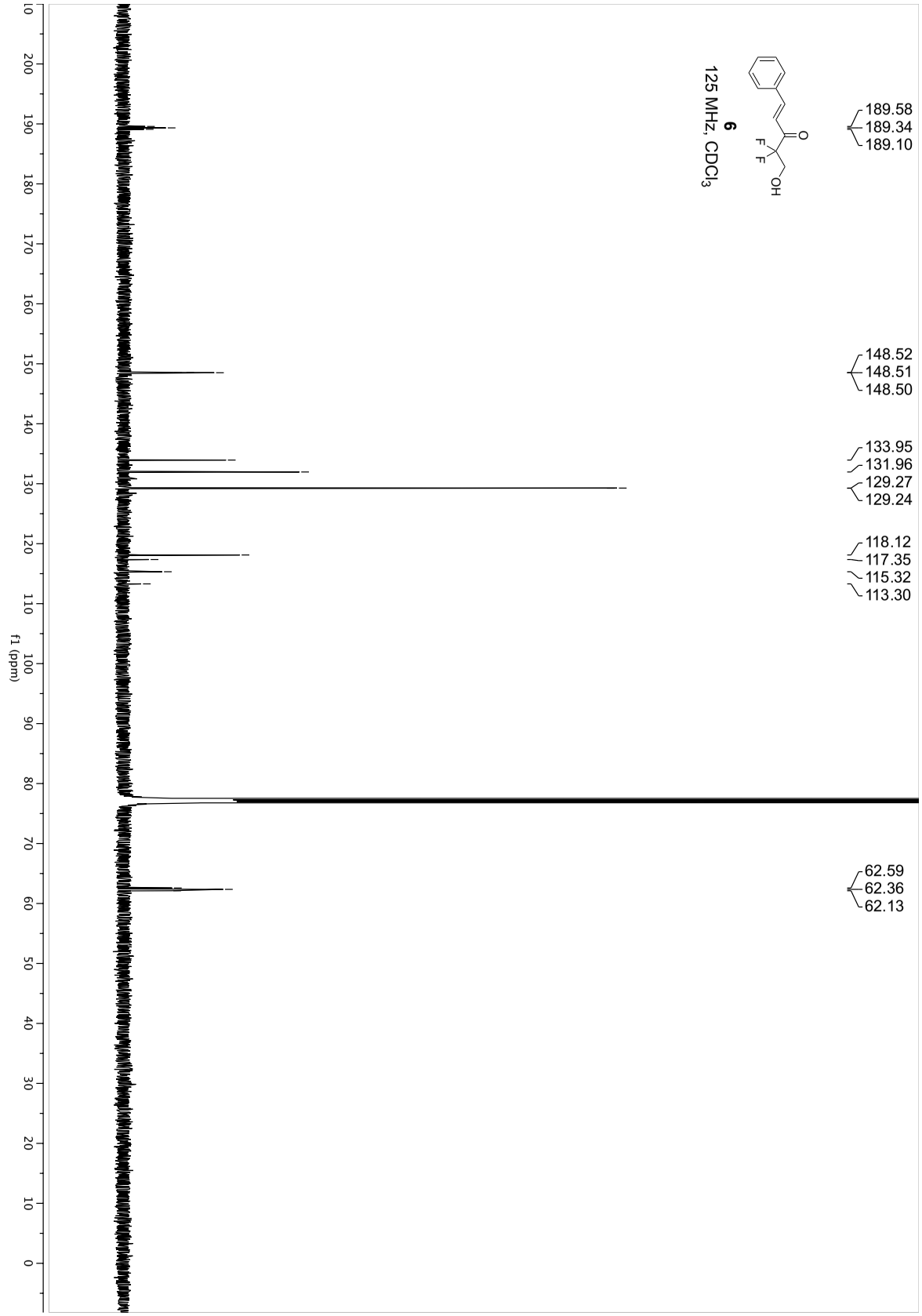
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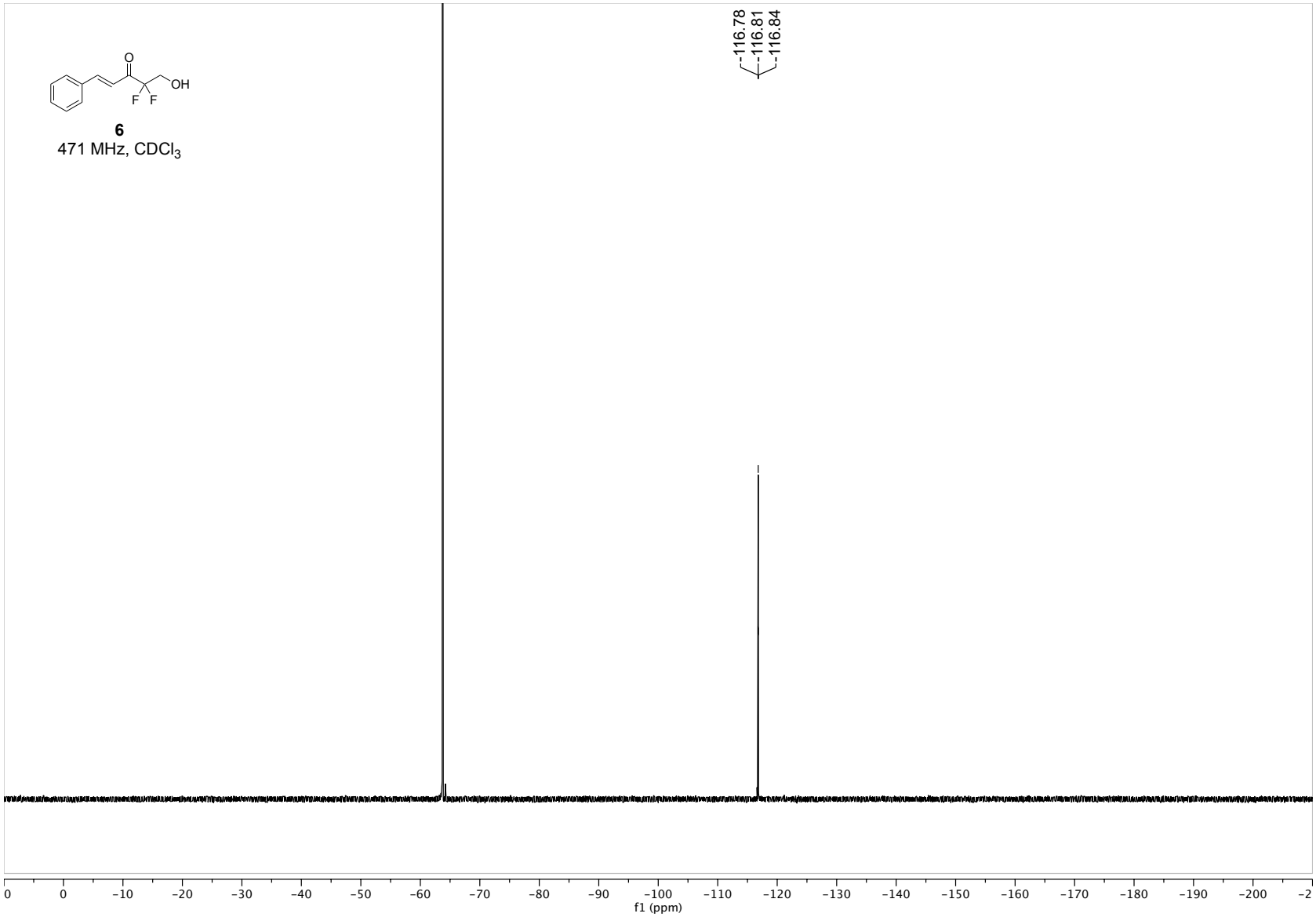
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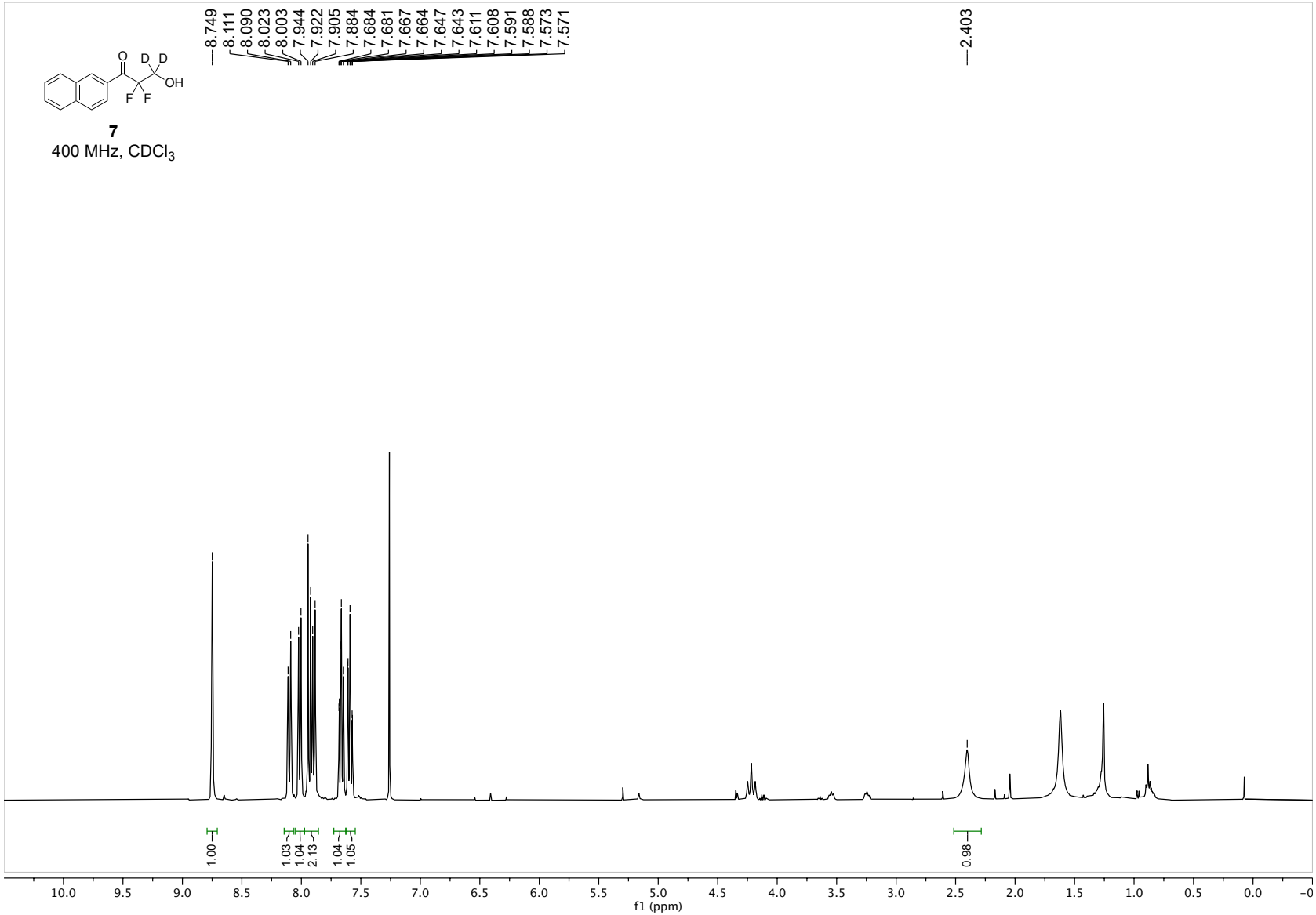
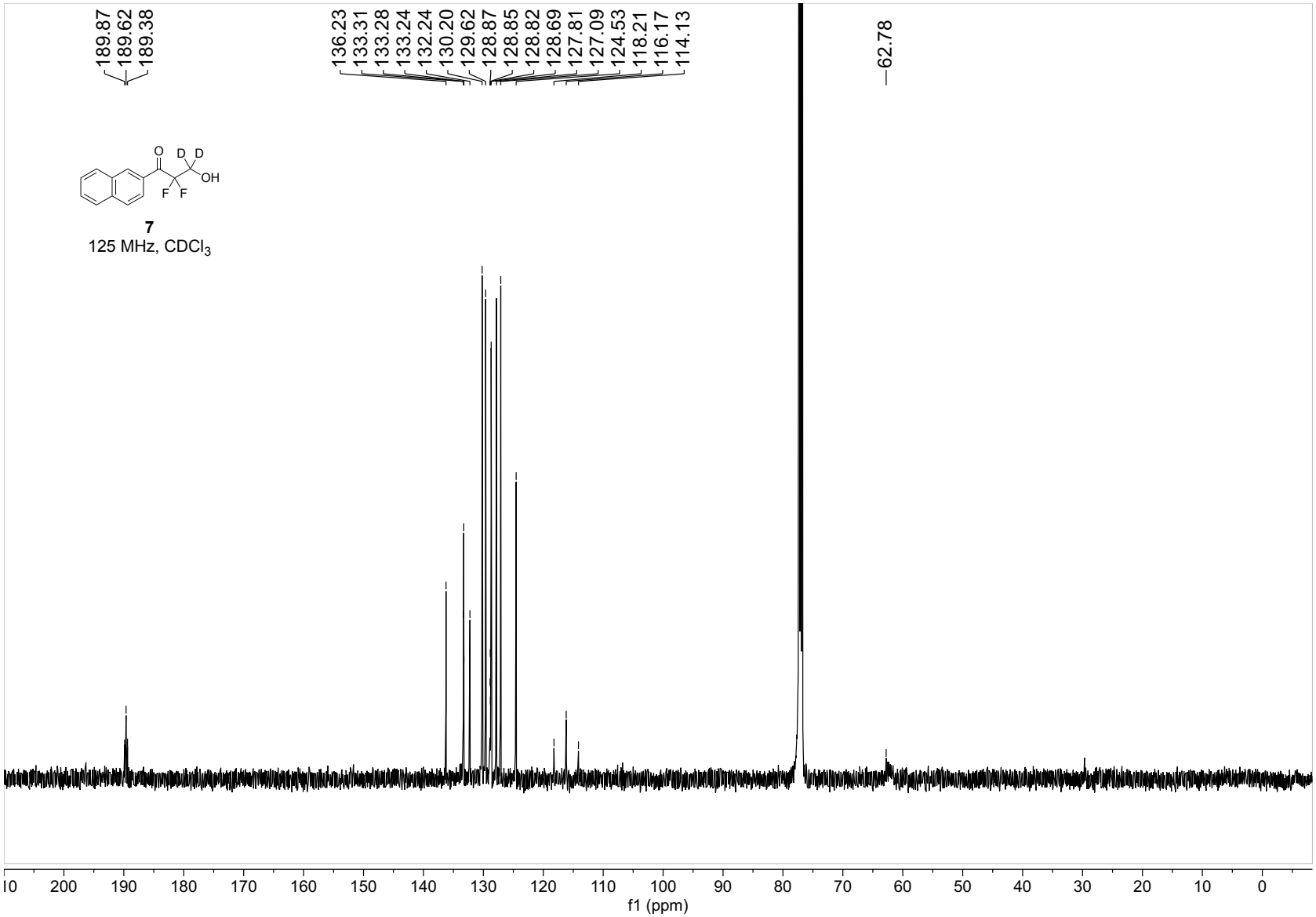
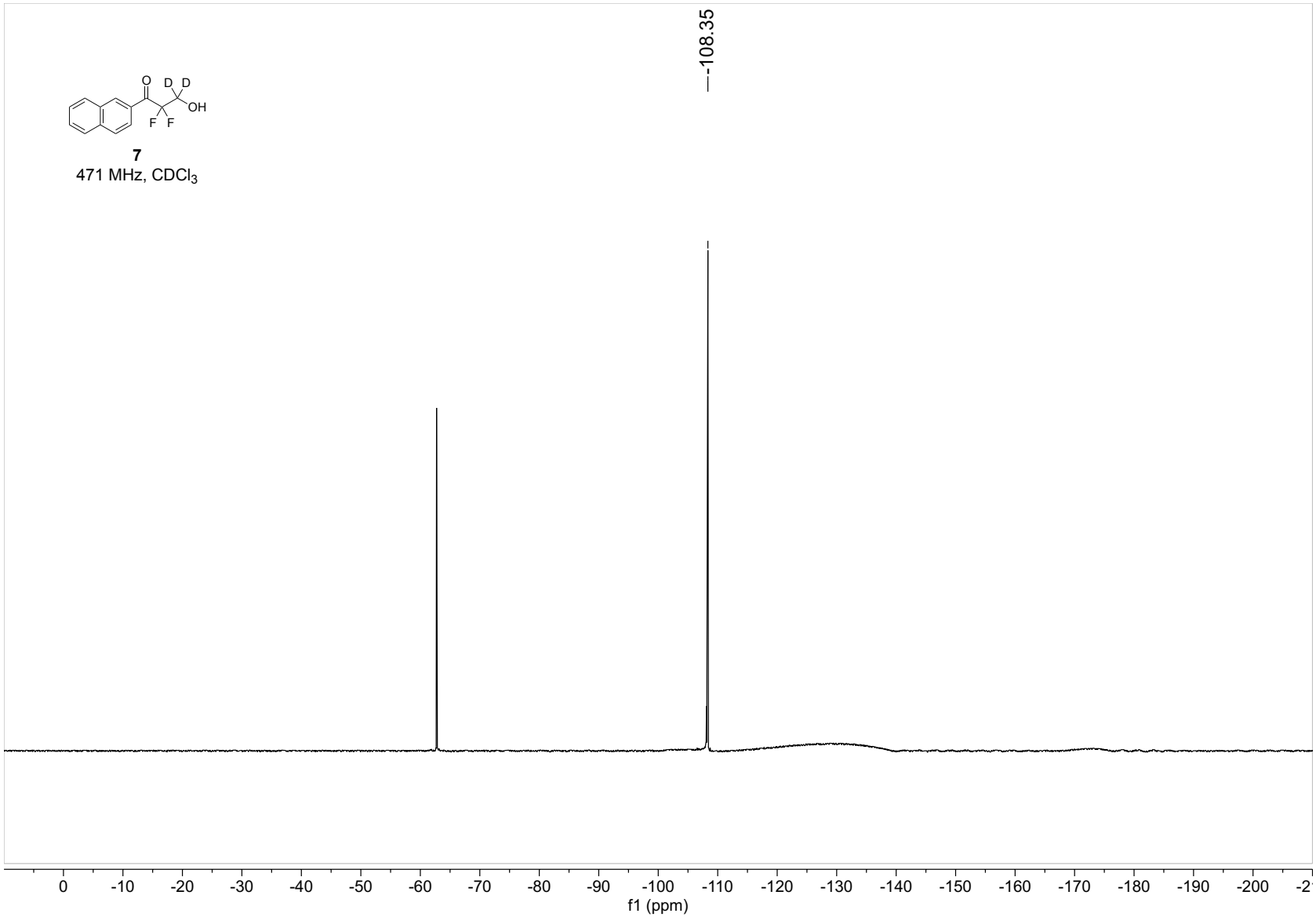
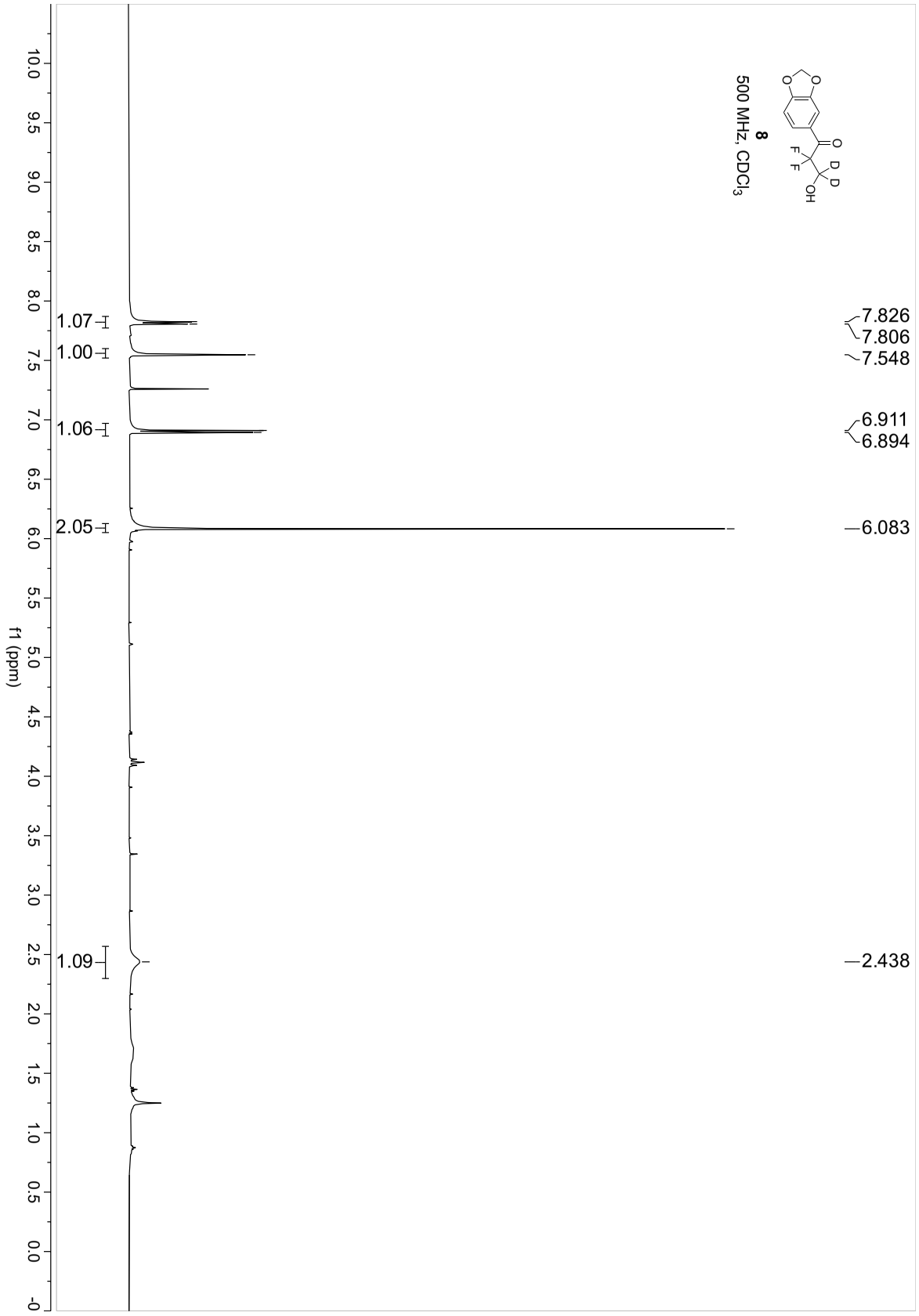
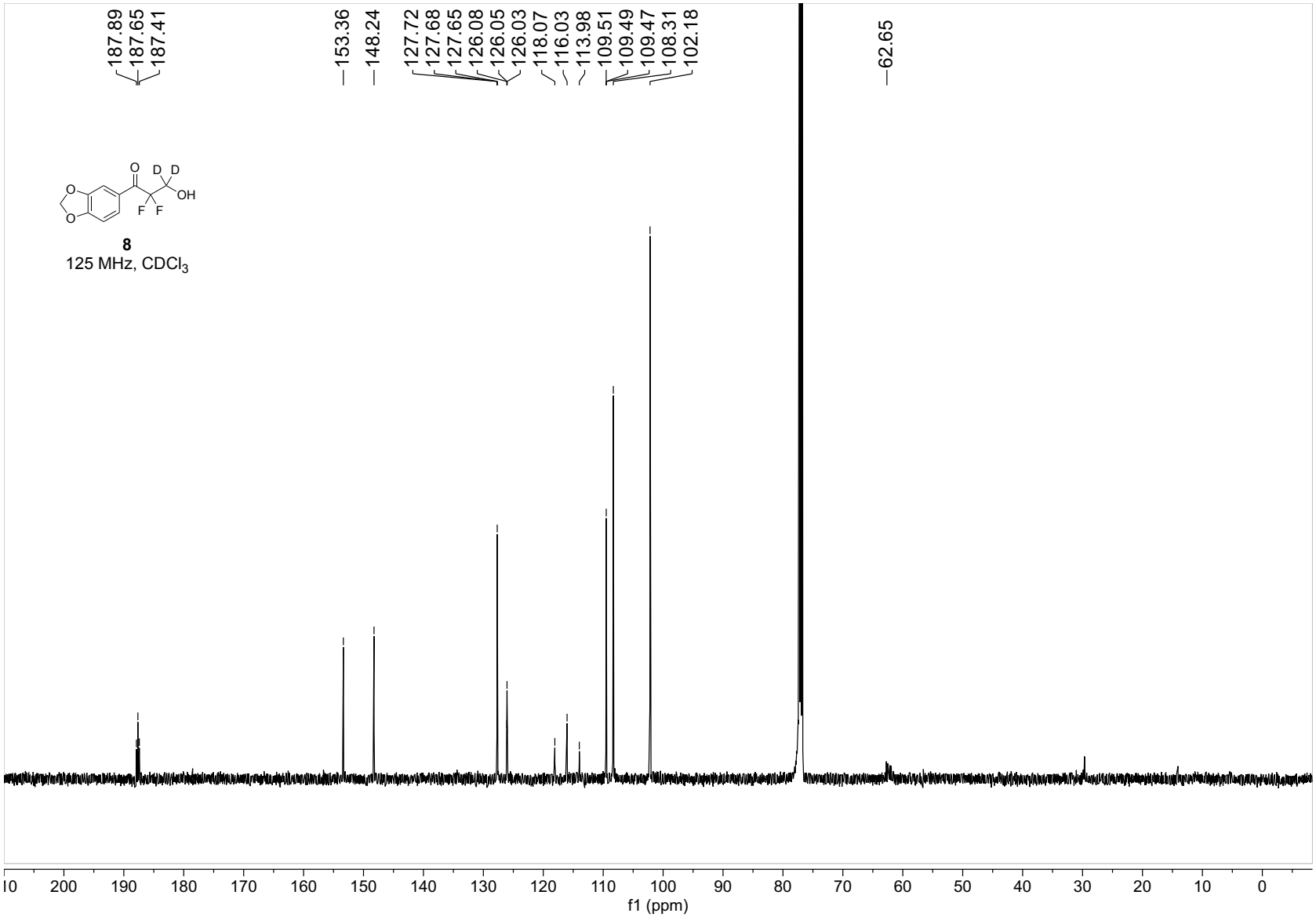
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-2
f1 (ppm)

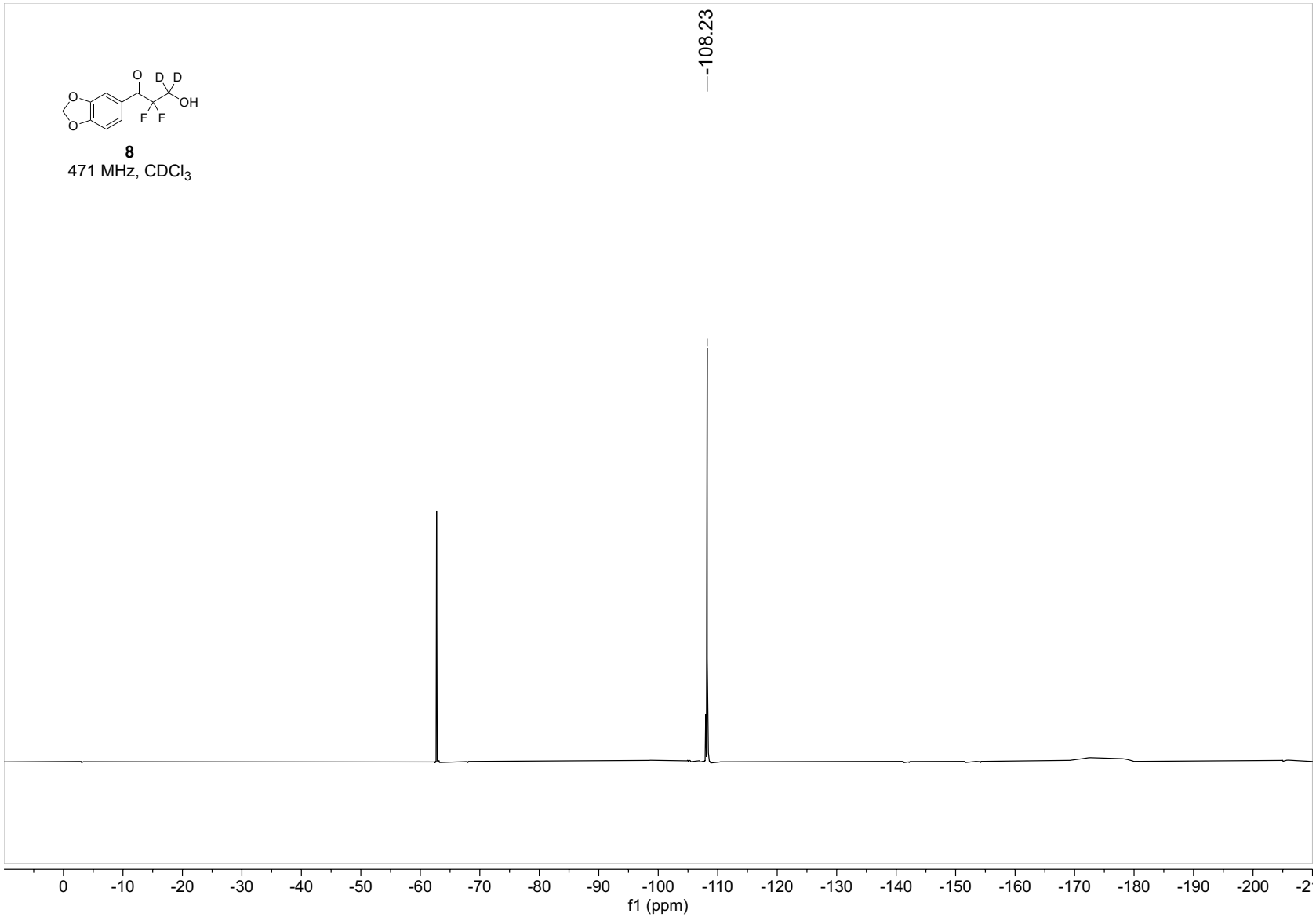

8.749
8.111
8.090
8.023
8.003
7.944
7.922
7.905
7.884
7.684
7.681
7.667
7.664
7.647
7.643
7.611
7.608
7.591
7.588
7.573
7.571
2.403
O
D
D
OH
F
F
7
400 MHz, CDCl3
1.00
1.03
1.04
2.13
1.04
1.05
0.98
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0
f1 (ppm)

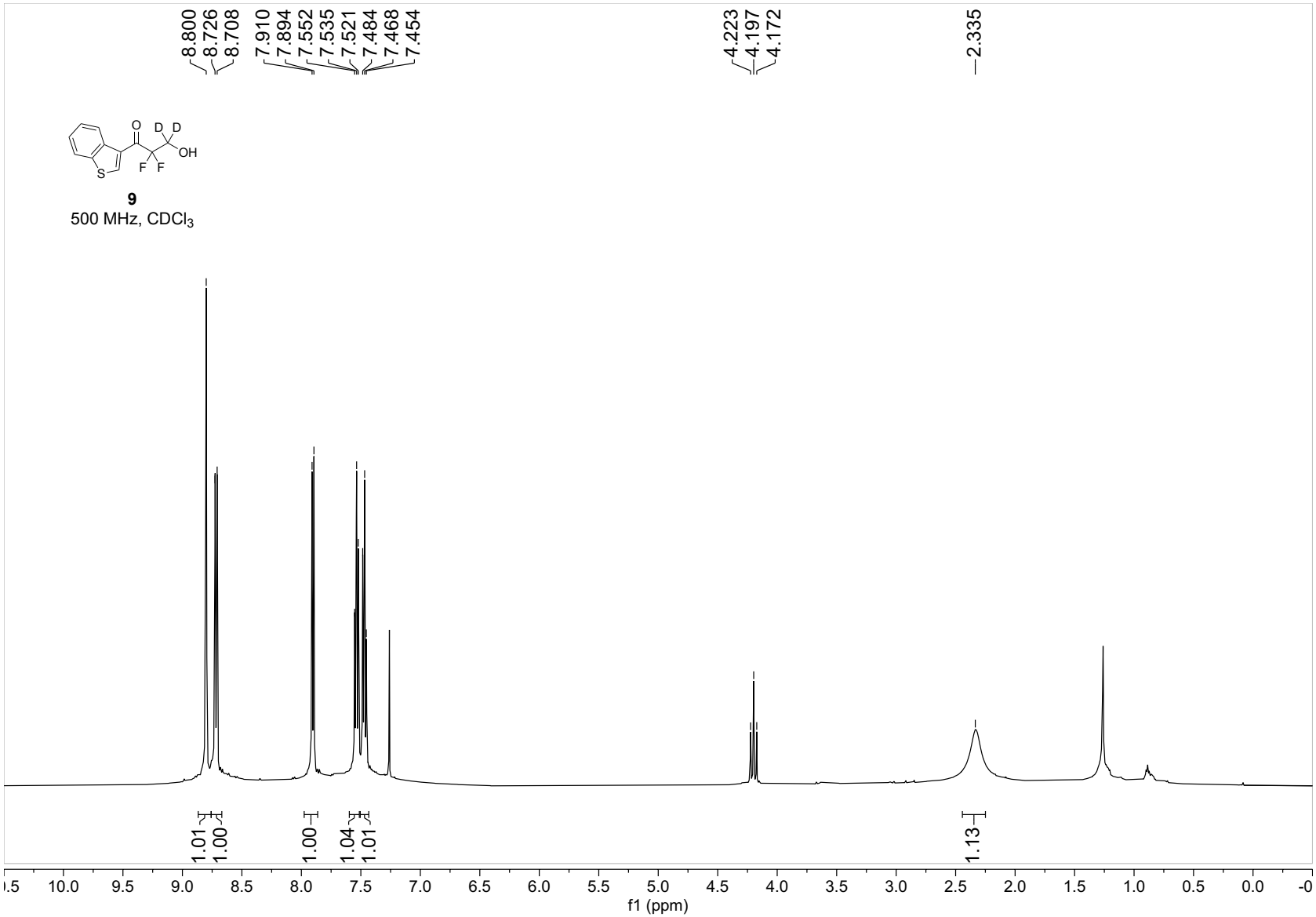

189.87
189.62
189.38
136.23
133.31
133.28
133.24
132.24
130.20
129.62
128.87
128.85
128.82
128.69
127.81
127.09
124.53
118.21
116.17
114.13
62.78
O
D D
OH
F F
7
125 MHz, CDCl3
f1 (ppm)

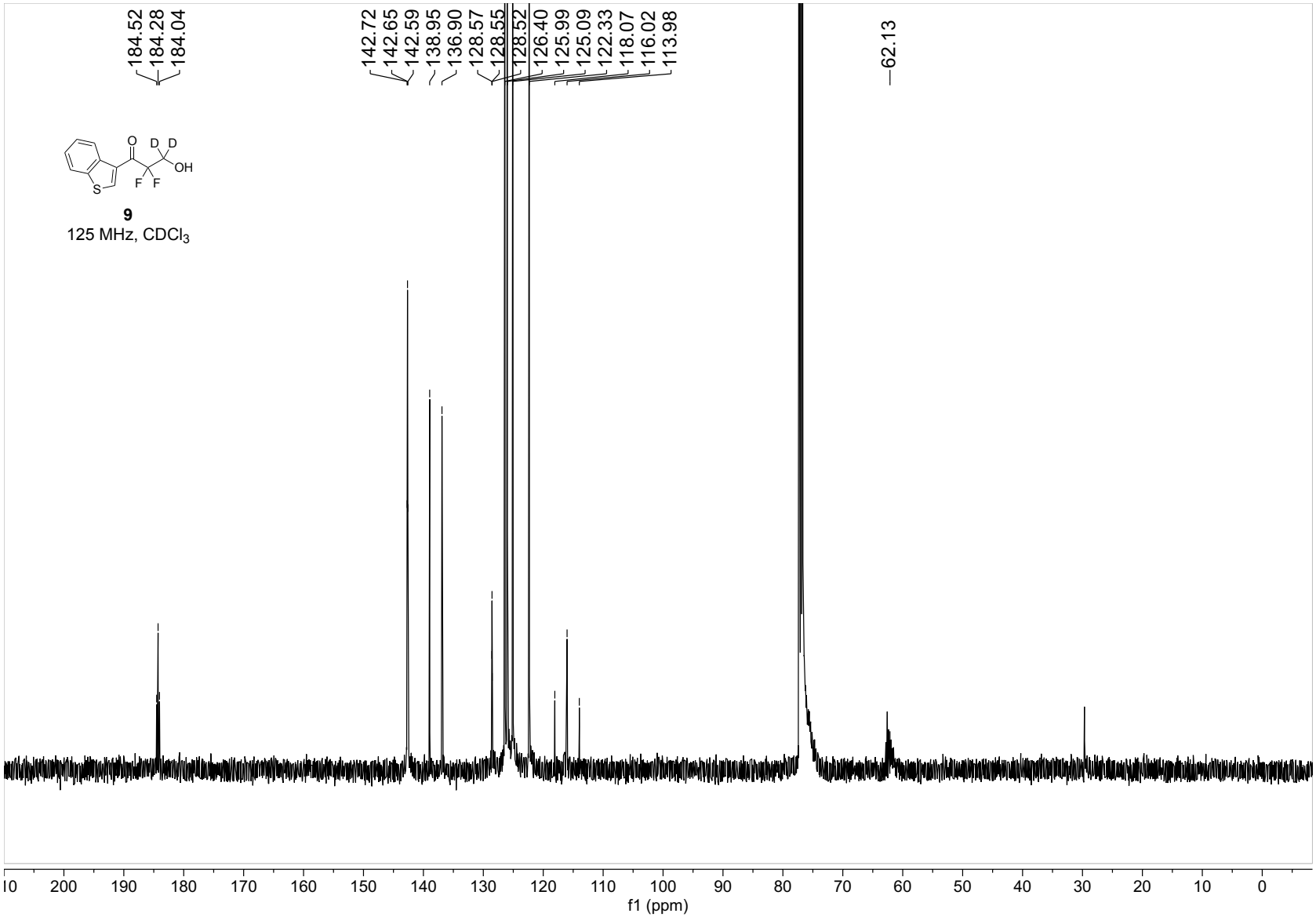

-108.35
O
D D
OH
F F
7
471 MHz, CDCl3
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

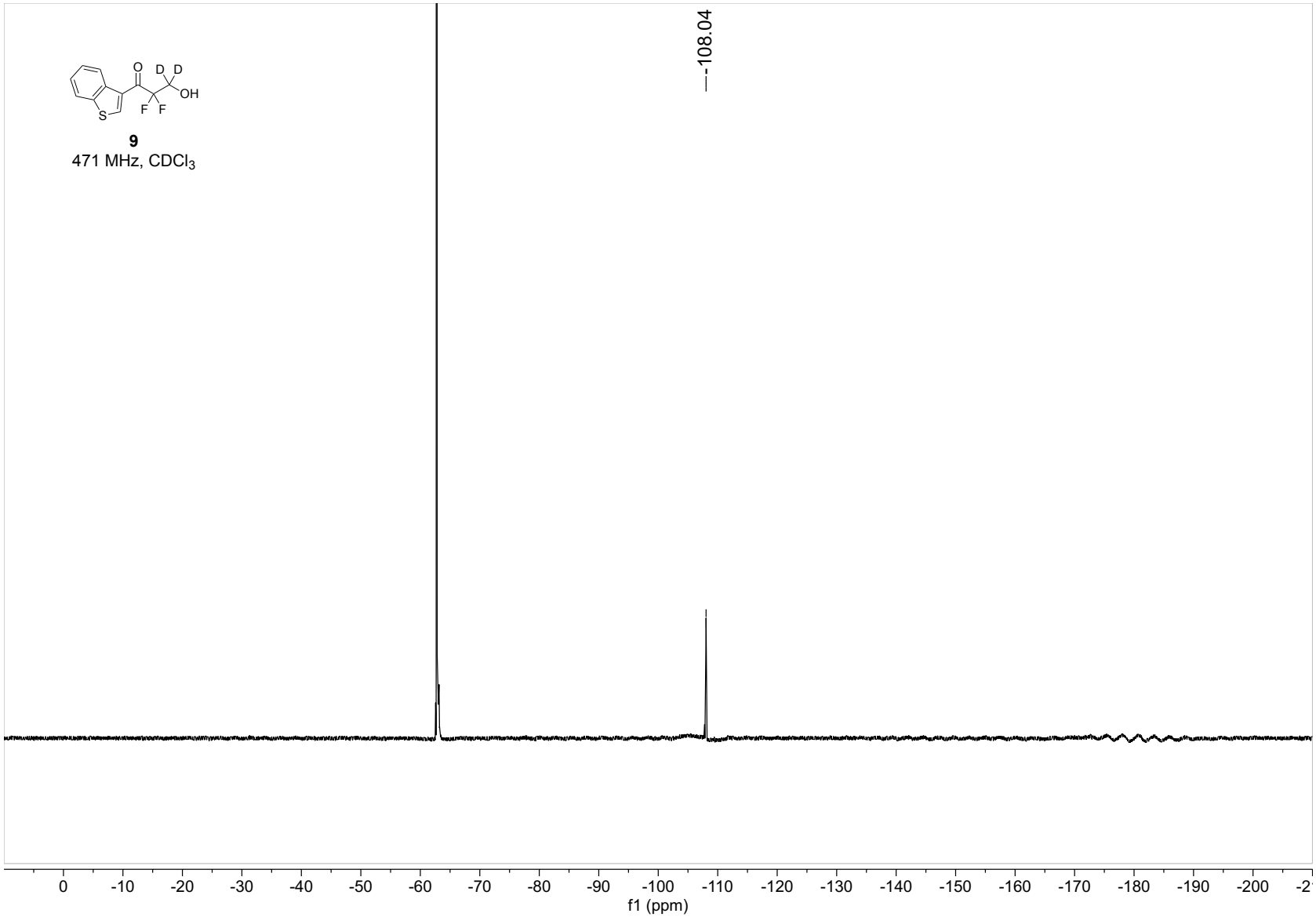

8
500 MHz, CDCl3
1.07
1.00
1.06
2.05
1.09
7.826
7.806
7.548
6.911
6.894
6.083
2.438
f1 (ppm)

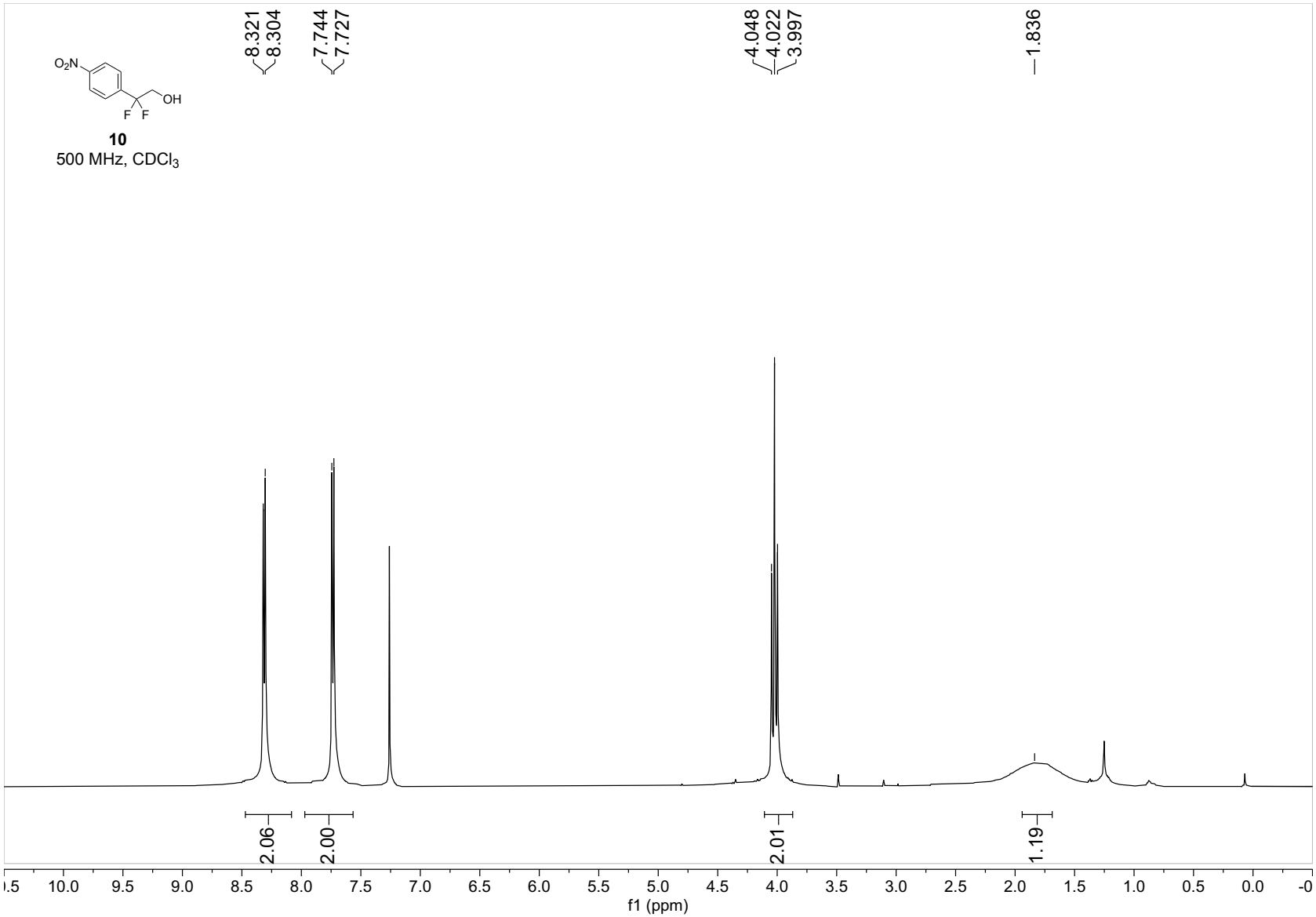

187.89
187.65
187.41
153.36
148.24
127.72
127.68
127.65
126.08
126.05
126.03
118.07
116.03
113.98
109.51
109.49
109.47
108.31
102.18
62.65
O
D D
OH
F F
O
O
8
125 MHz, CDCl3
f1 (ppm)

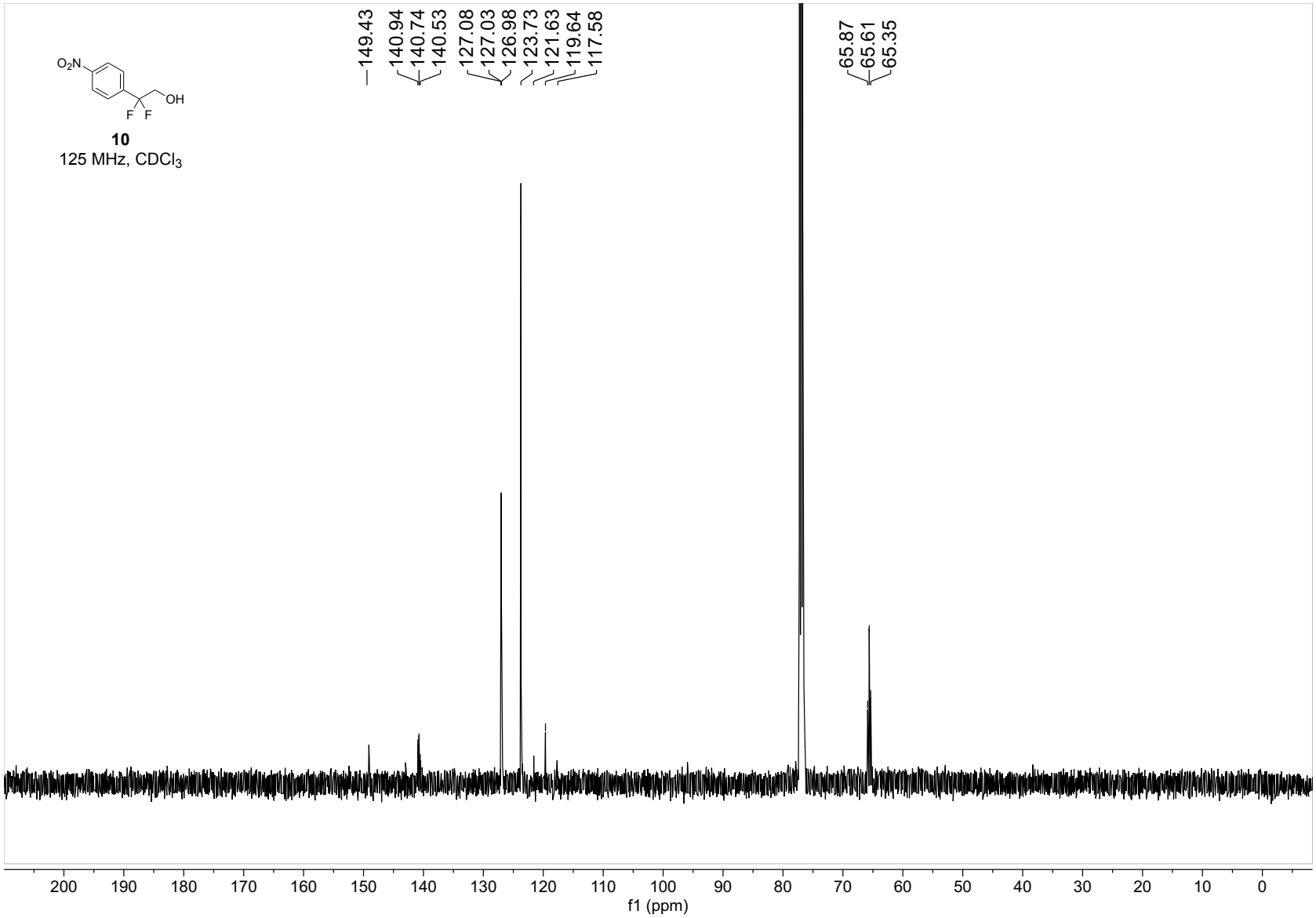

-108.23
O
D D
OH
O
O
F F
8
471 MHz, CDCl3
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

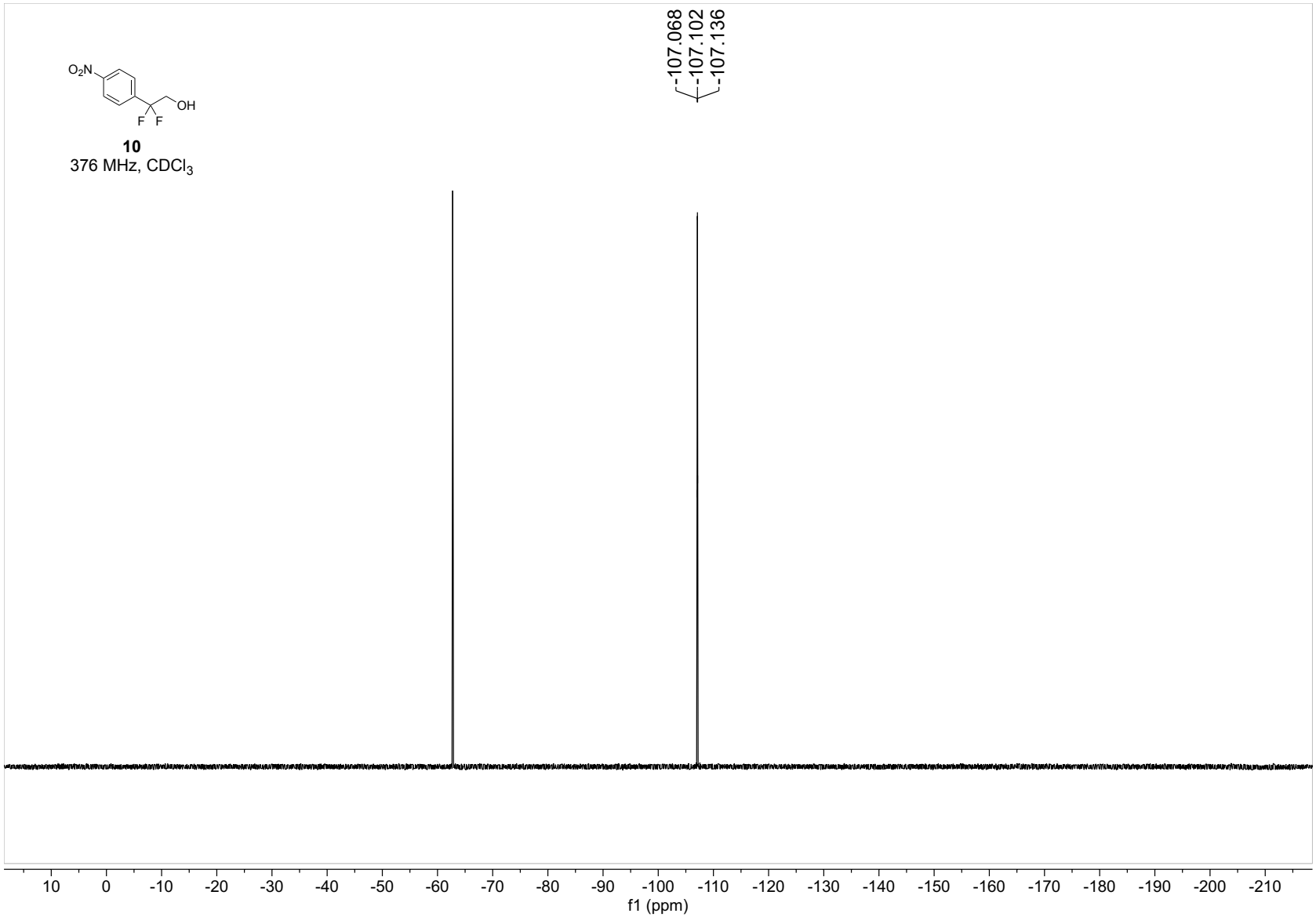

8.800
8.726
8.708
7.910
7.894
7.552
7.535
7.521
7.484
7.468
7.454
4.223
4.197
4.172
2.335
O
D D
OH
F F
S
9
500 MHz, CDCl3
1.01
1.00
1.00
1.04
1.01
1.13
f1 (ppm)

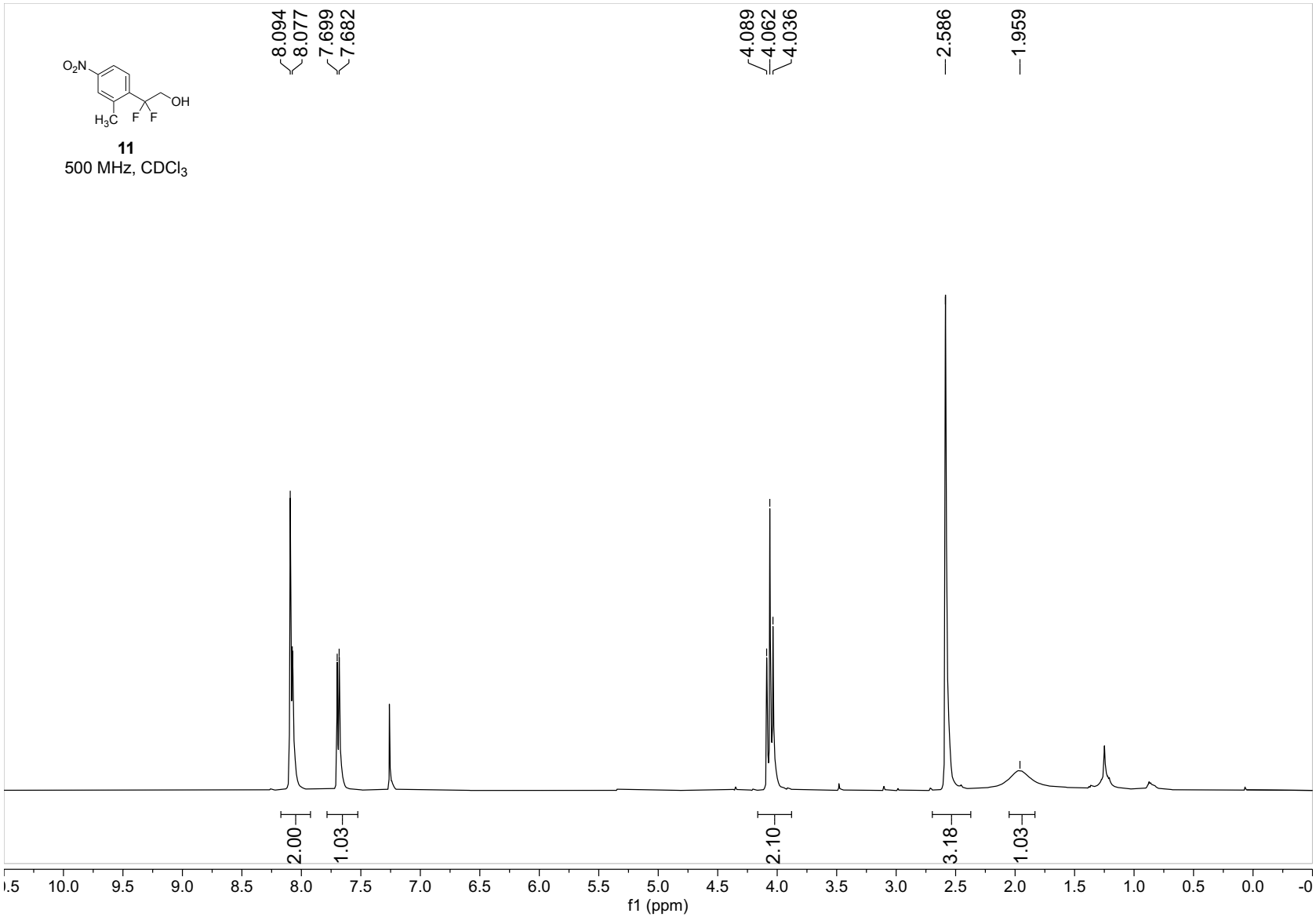

184.52
184.28
184.04
142.72
142.65
142.59
138.95
136.90
128.57
128.55
128.52
126.40
125.99
125.09
122.33
118.07
116.02
113.98
62.13
O
D
D
OH
F
F
S
9
125 MHz, CDCl3
f1 (ppm)

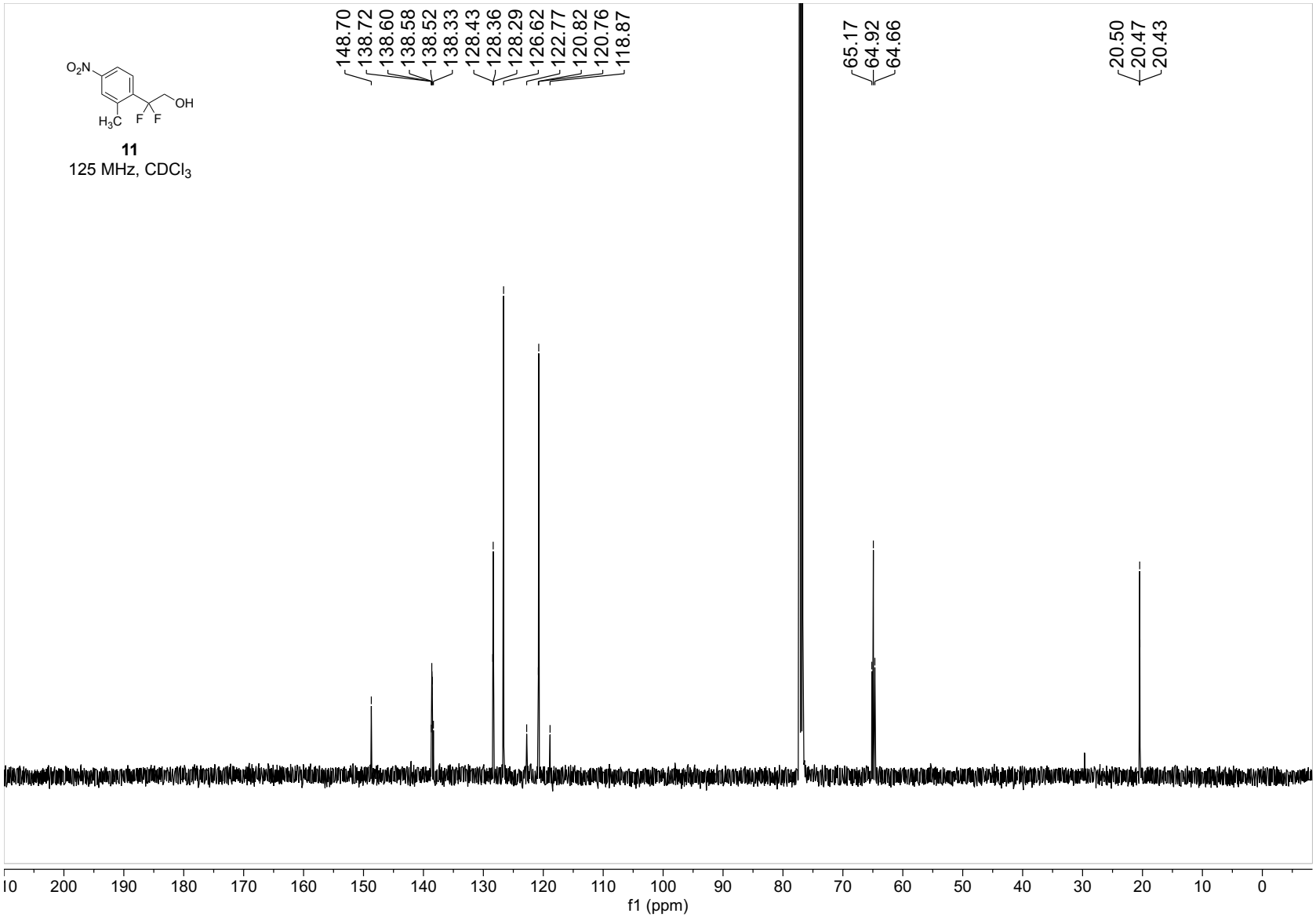

O
D D
OH
F F
S
9
471 MHz, CDCl3
-108.04
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

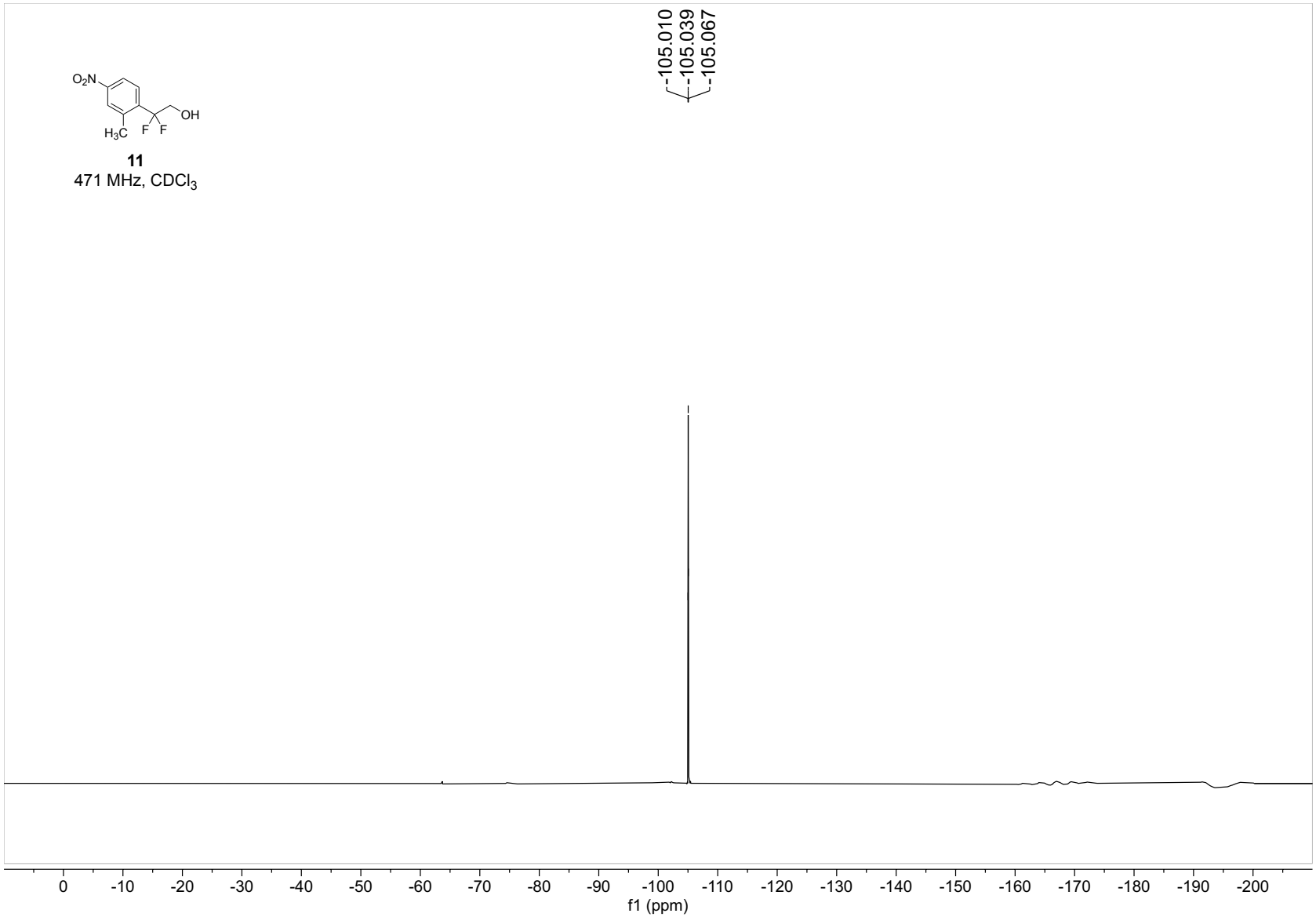

8.321
8.304
7.744
7.727
4.048
4.022
3.997
1.836
O2N
OH
F F
10
500 MHz, CDCl3
2.06
2.00
2.01
1.19
f1 (ppm)

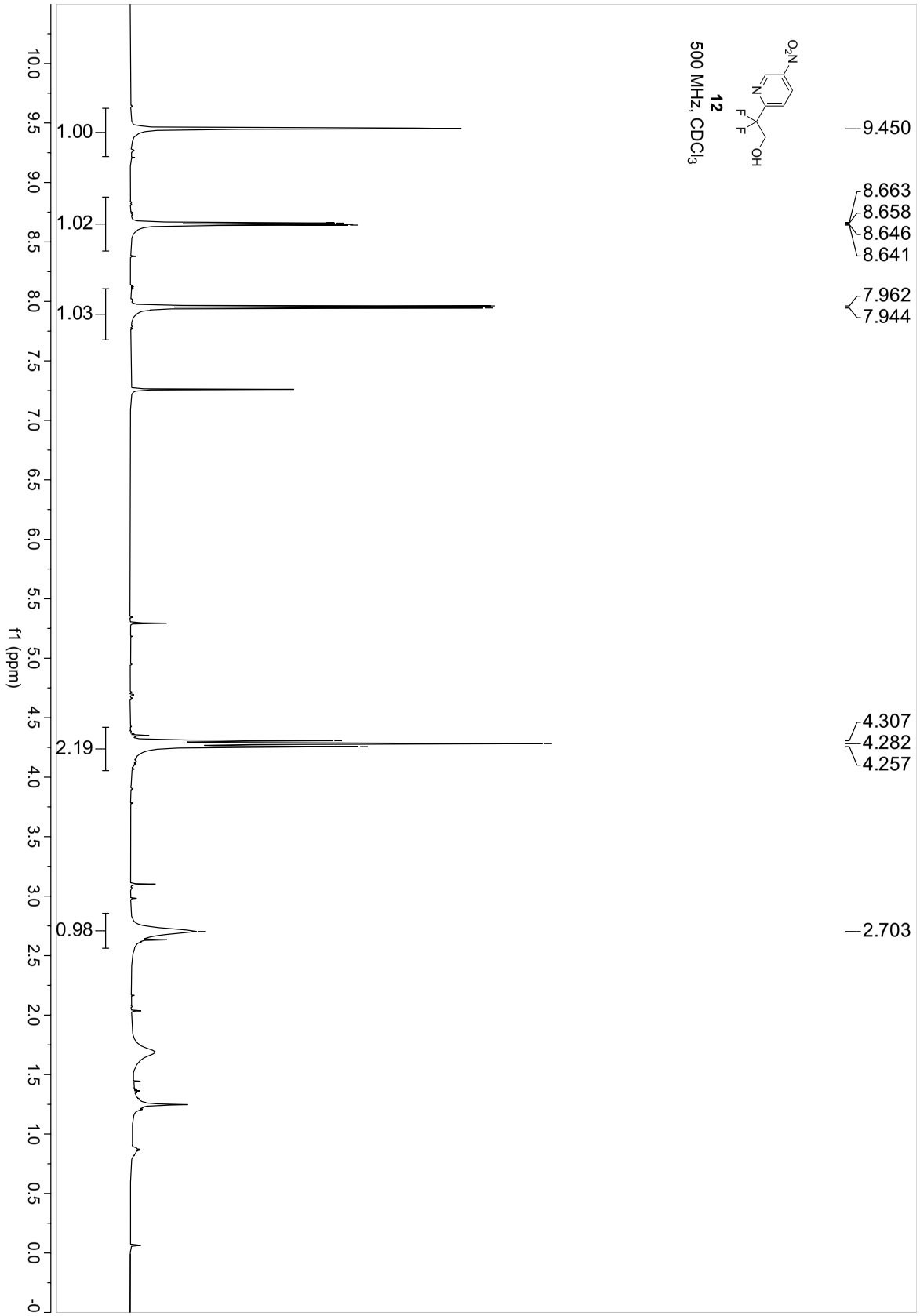

149.43
140.94
140.74
140.53
127.08
127.03
126.98
123.73
121.63
119.64
117.58
65.87
65.61
65.35
O2N
OH
F F
10
125 MHz, CDCl3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

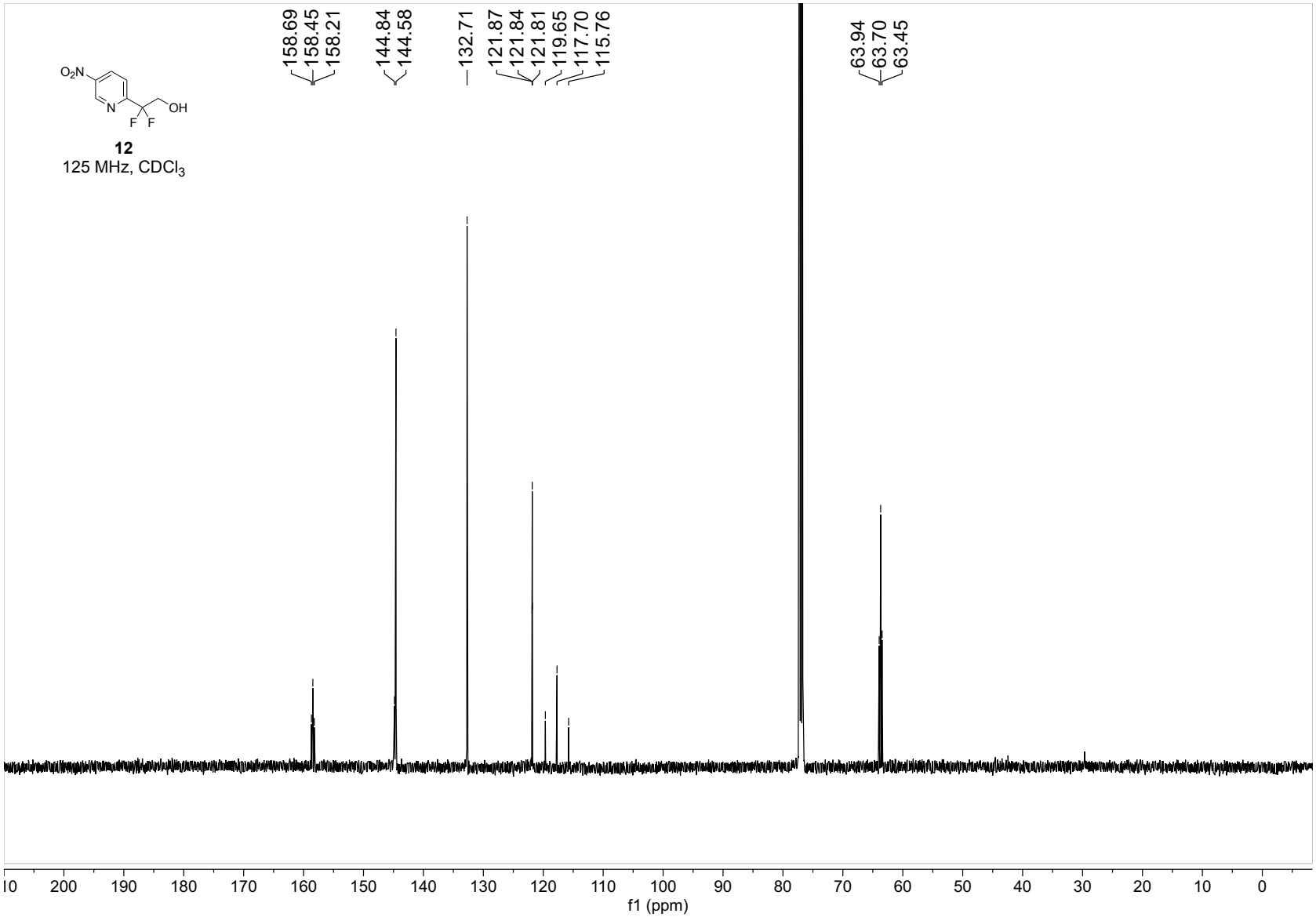

O2N
OH
F F
10
376 MHz, CDCl3
-107.068
-107.102
-107.136
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

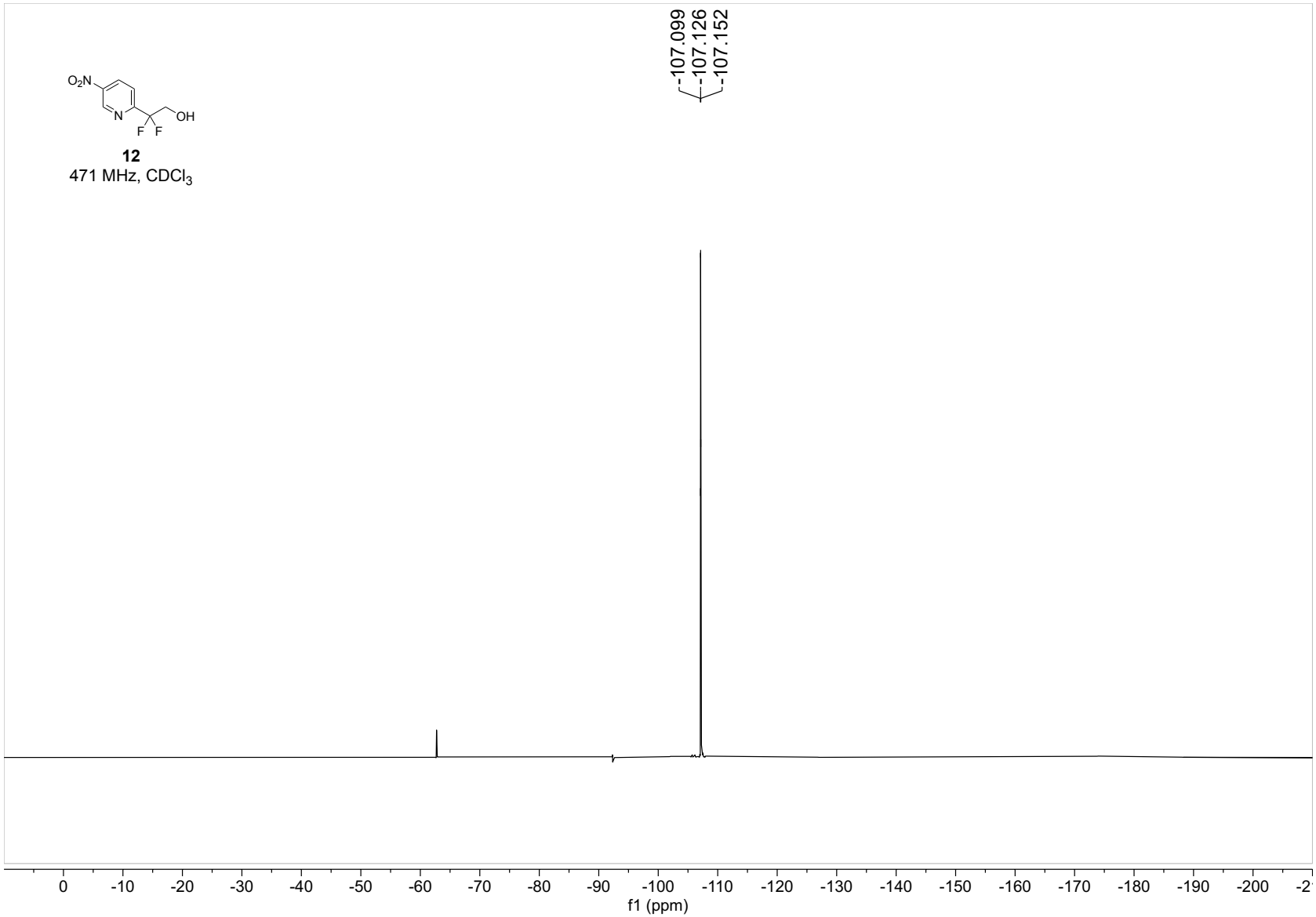

8.094
8.077
7.699
7.682
4.089
4.062
4.036
2.586
1.959
O2N
OH
H3C
F
F
11
500 MHz, CDCl3
2.00
1.03
2.10
3.18
1.03
f1 (ppm)

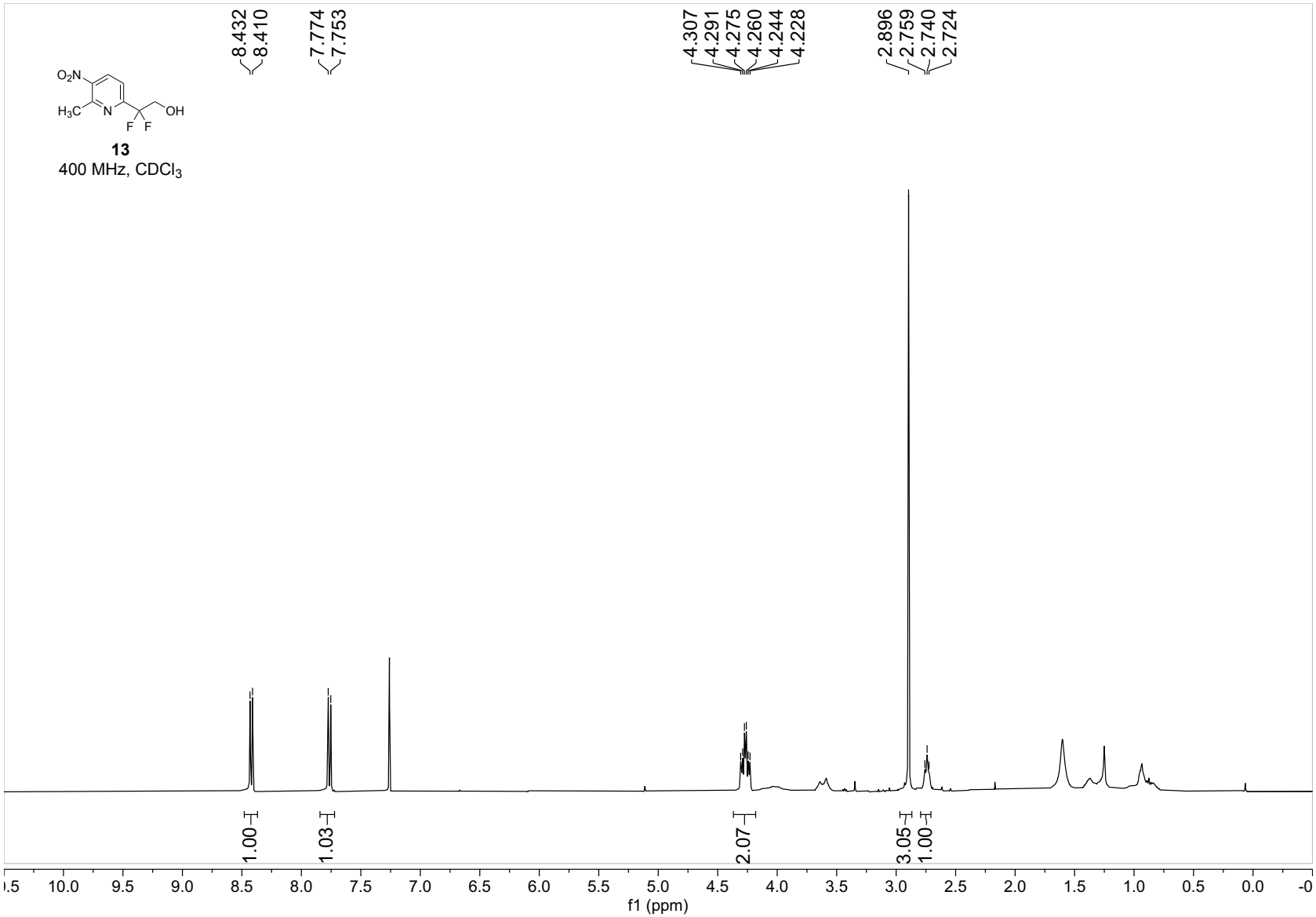

148.70
138.72
138.60
138.58
138.52
138.33
128.43
128.36
128.29
126.62
122.77
120.82
120.76
118.87
65.17
64.92
64.66
20.50
20.47
20.43
O2N
OH
H3C
F F
11
125 MHz, CDCl3
f1 (ppm)

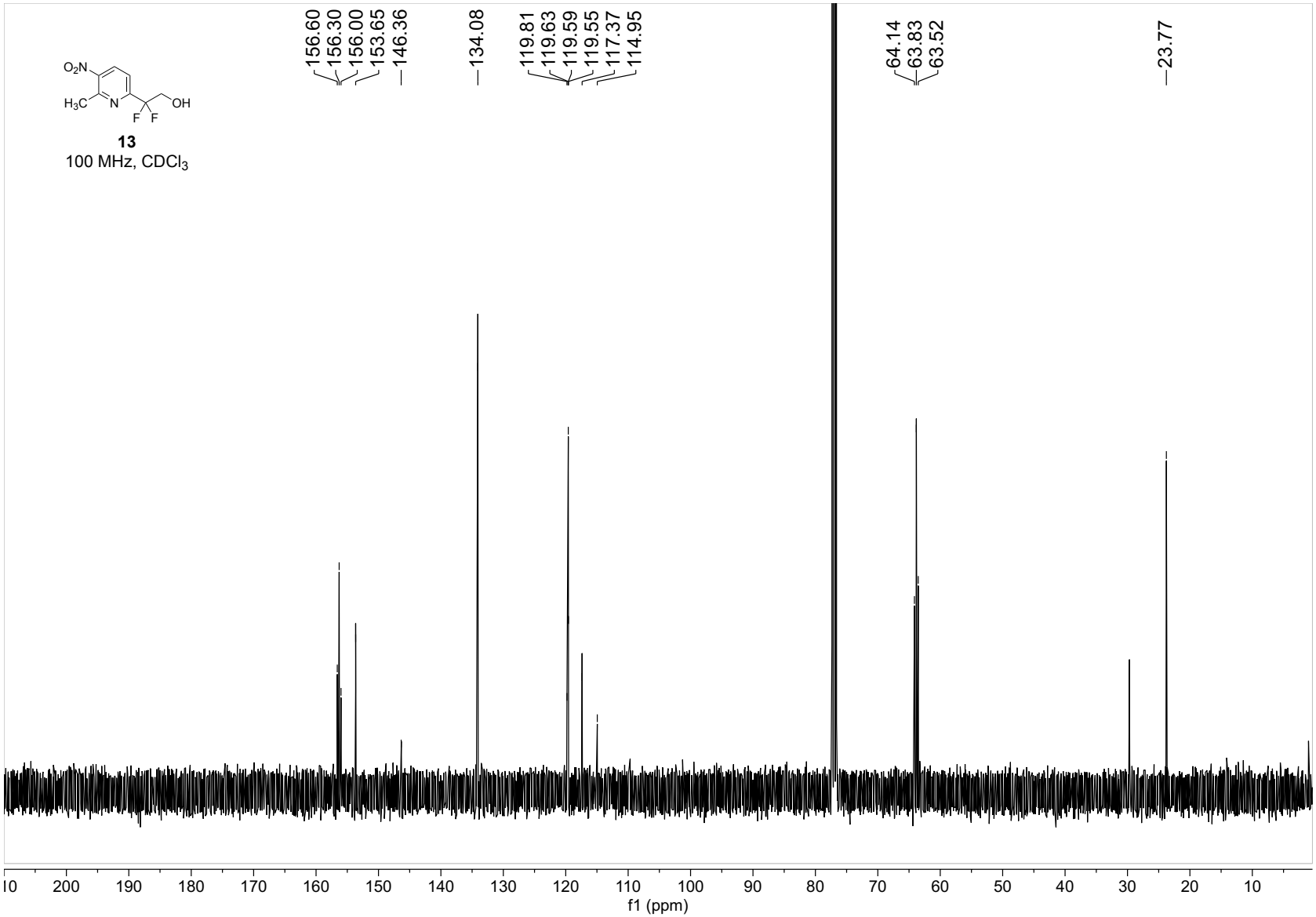

O2N
H3C
F F
OH
11
471 MHz, CDCl3
-105.010
-105.039
-105.067
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

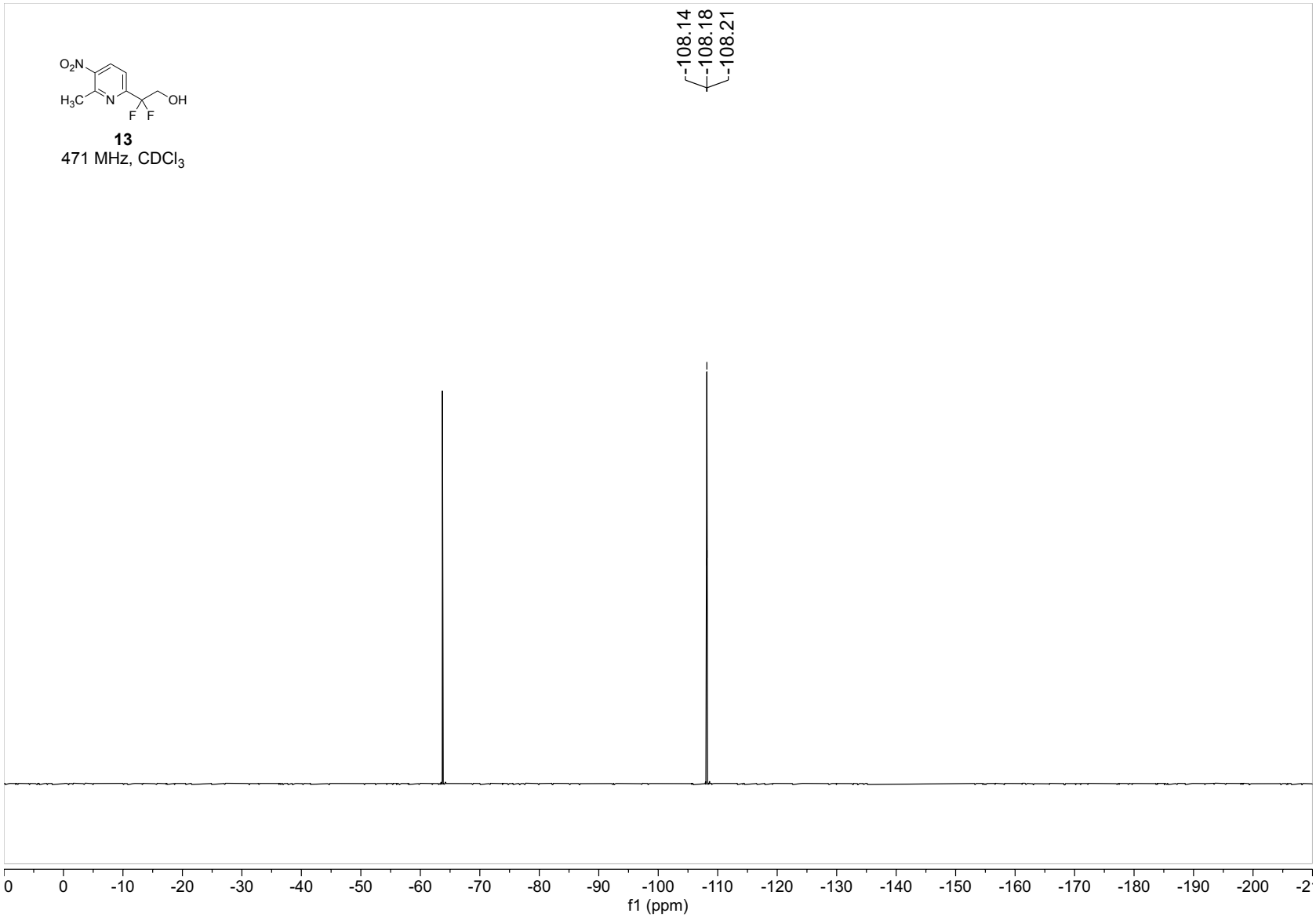

12
500 MHz, CDCl3
O2N
N
F F
OH
9.450
8.663
8.658
8.646
8.641
7.962
7.944
4.307
4.282
4.257
2.703
1.00
1.02
1.03
2.19
0.98
f1 (ppm)

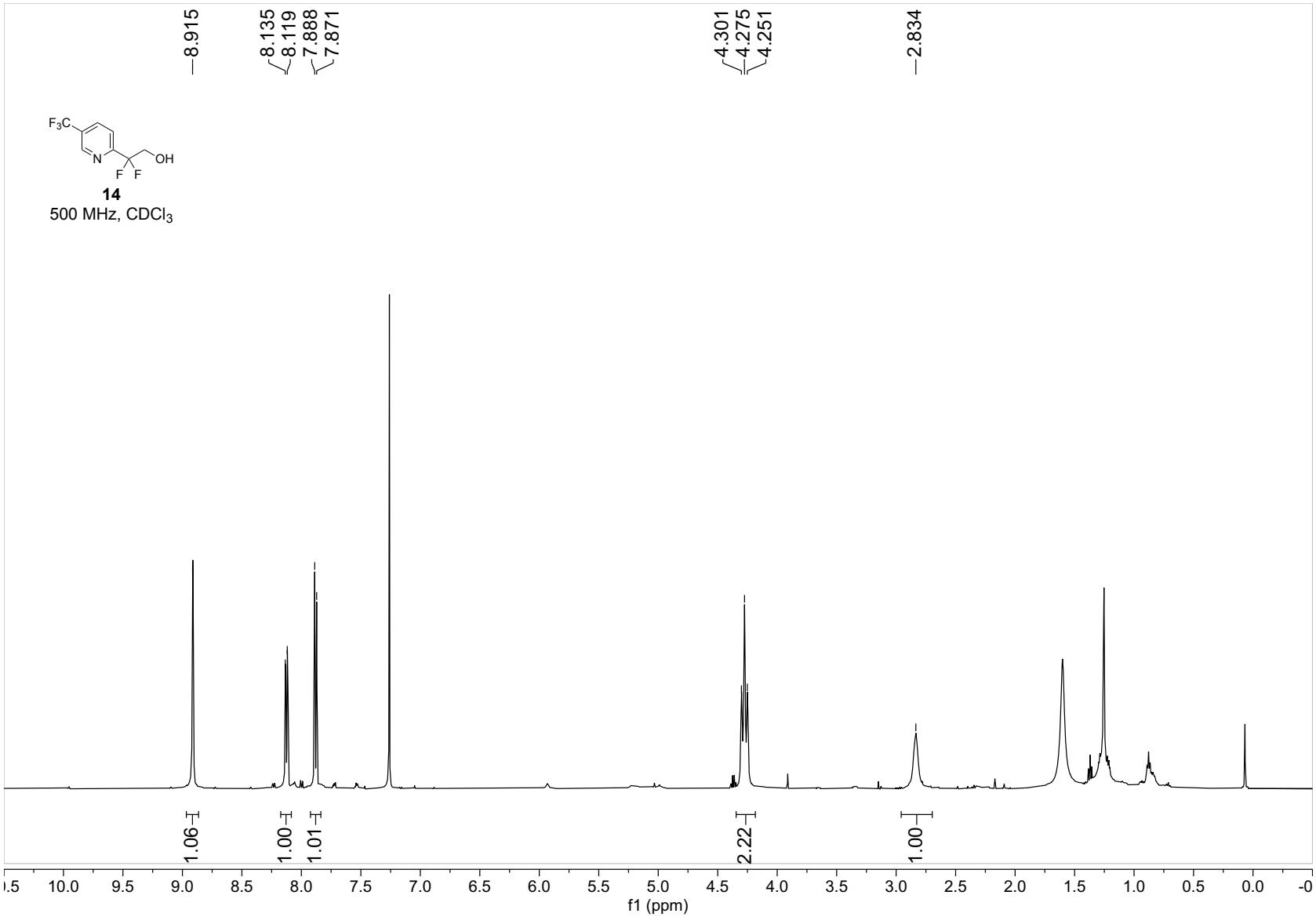

158.69
158.45
158.21
144.84
144.58
132.71
121.87
121.84
121.81
119.65
117.70
115.76
63.94
63.70
63.45
O2N
N
OH
F F
12
125 MHz, CDCl3
f1 (ppm)

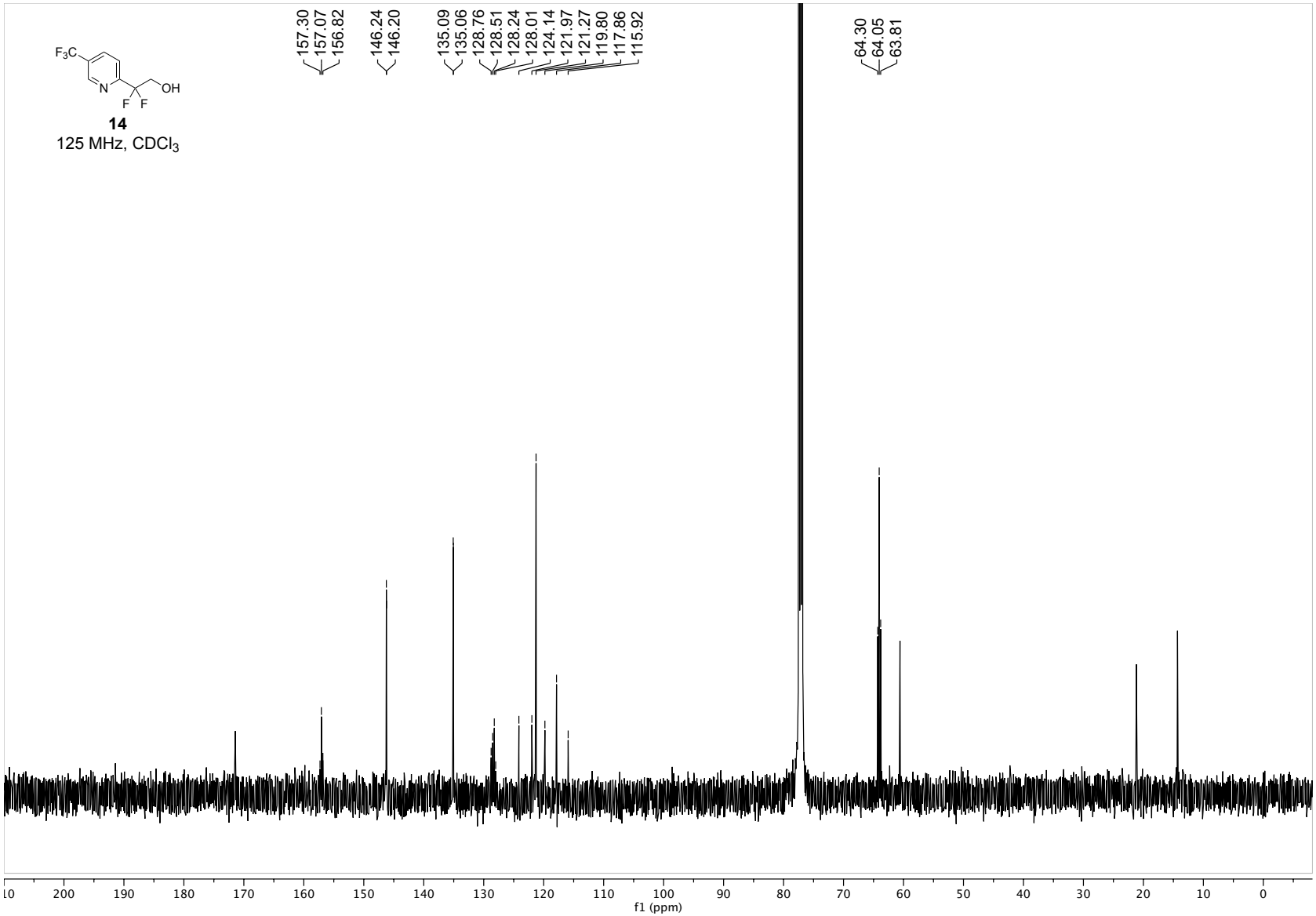

-107.099
-107.126
-107.152
O2N
N
OH
F F
12
471 MHz, CDCl3
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

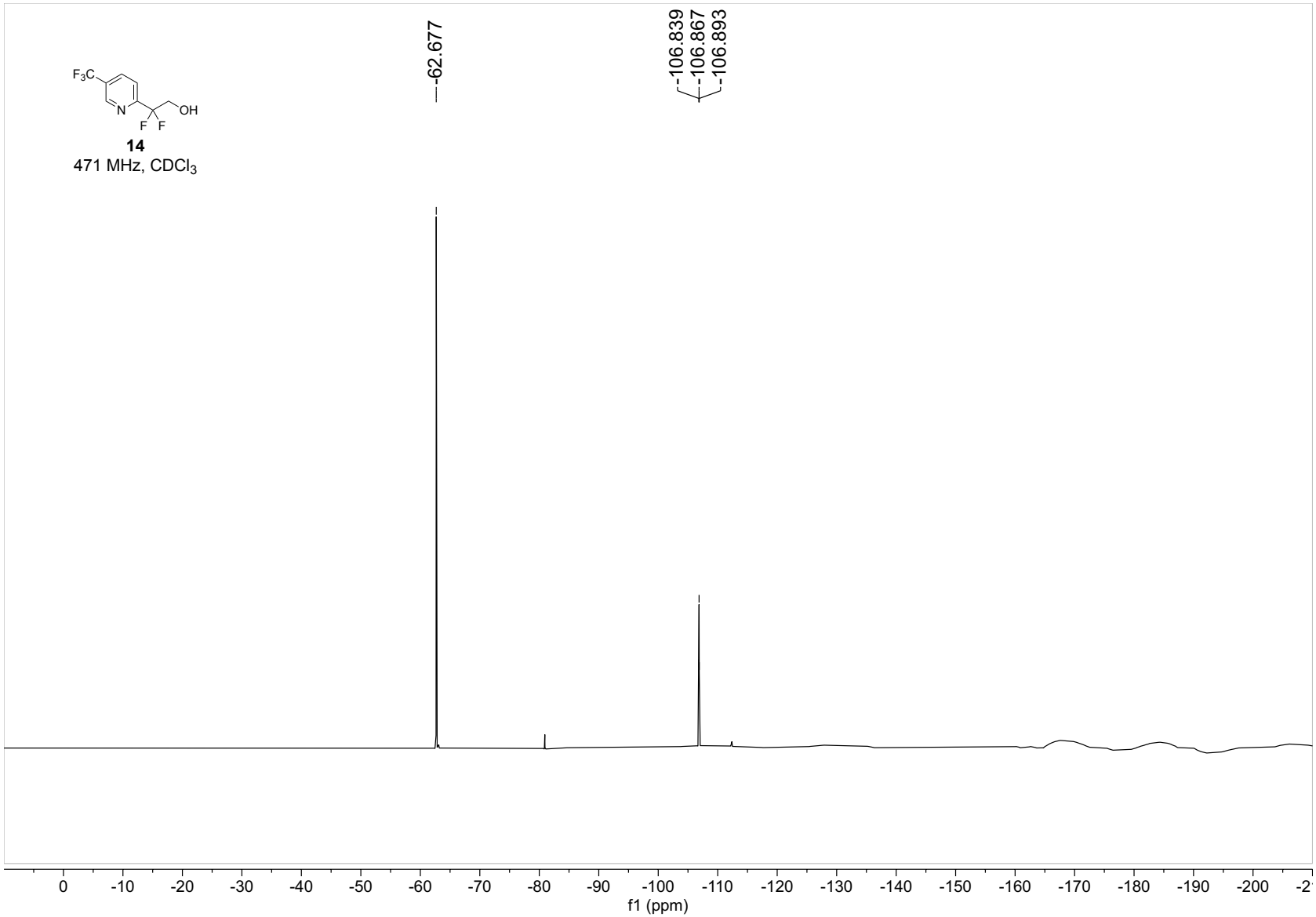

8.432
8.410
7.774
7.753
4.307
4.291
4.275
4.260
4.244
4.228
2.896
2.759
2.740
2.724
O2N
H3C
N
OH
F F
13
400 MHz, CDCl3
1.00
1.03
2.07
3.05
1.00
f1 (ppm)

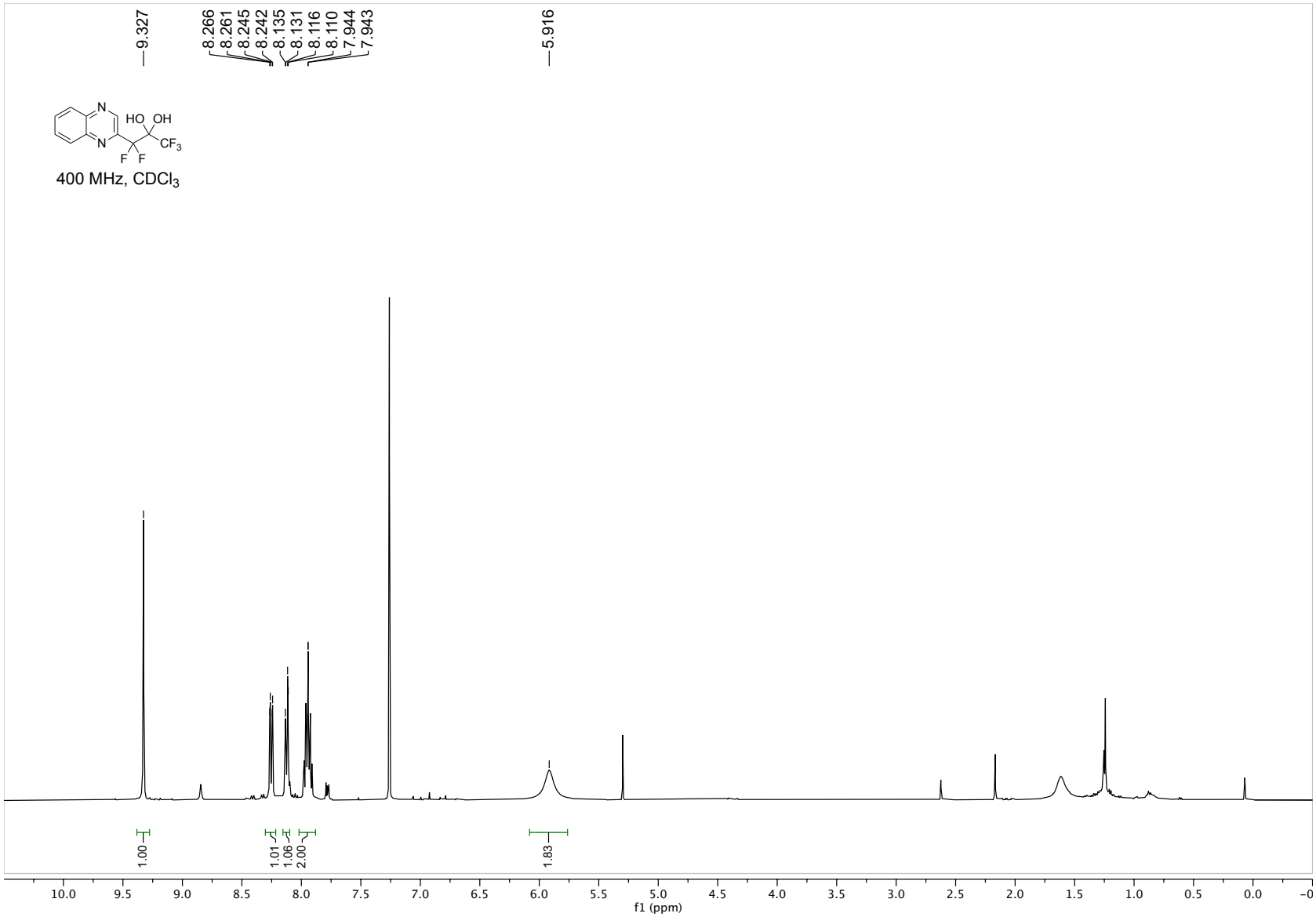

156.60
156.30
156.00
153.65
146.36
134.08
119.81
119.63
119.59
119.55
117.37
114.95
64.14
63.83
63.52
23.77
O2N
H3C
N
OH
F F
13
100 MHz, CDCl3
f1 (ppm)

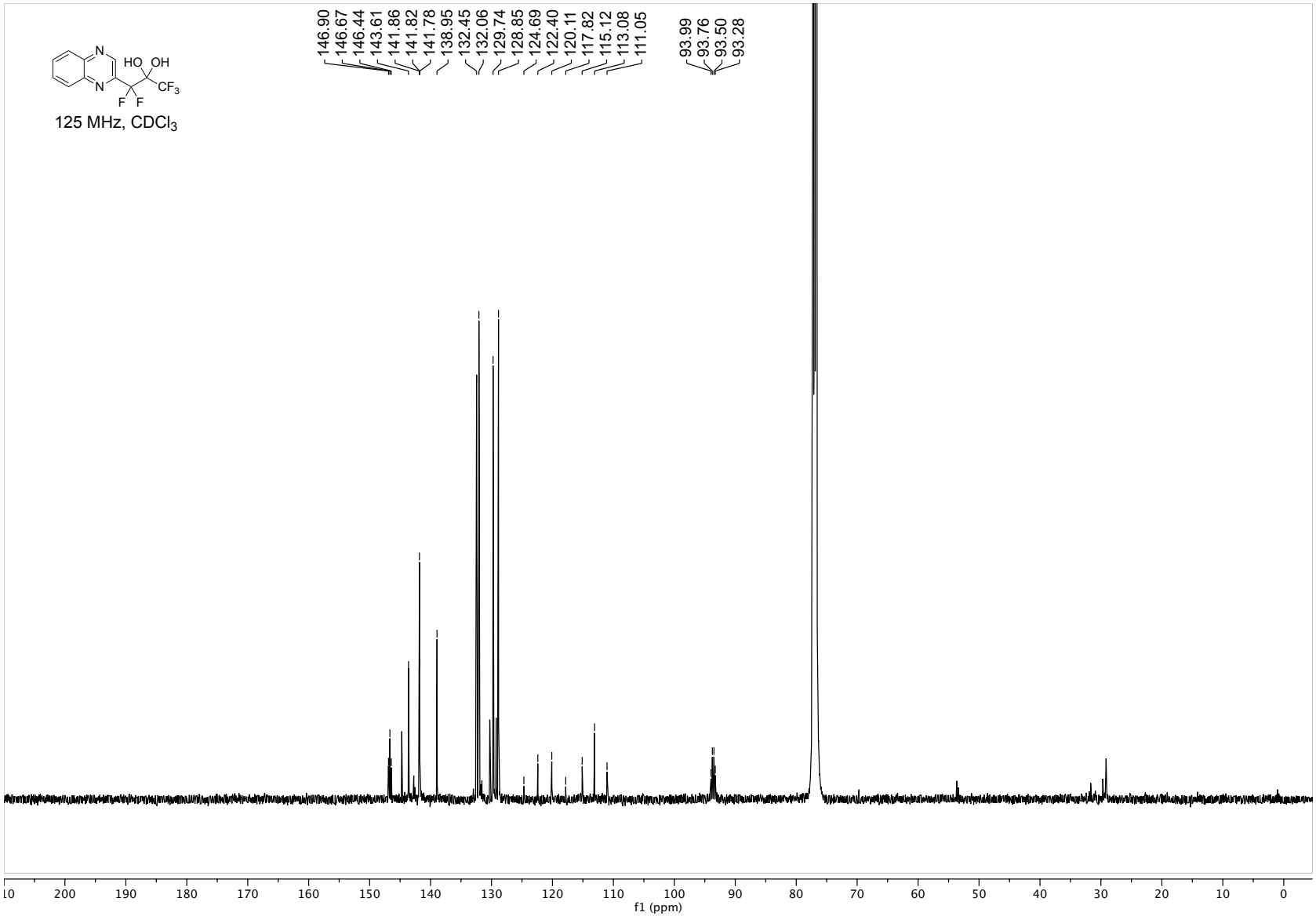

O2N
H3C
N
F F
OH
13
471 MHz, CDCl3
-108.14
-108.18
-108.21
0 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

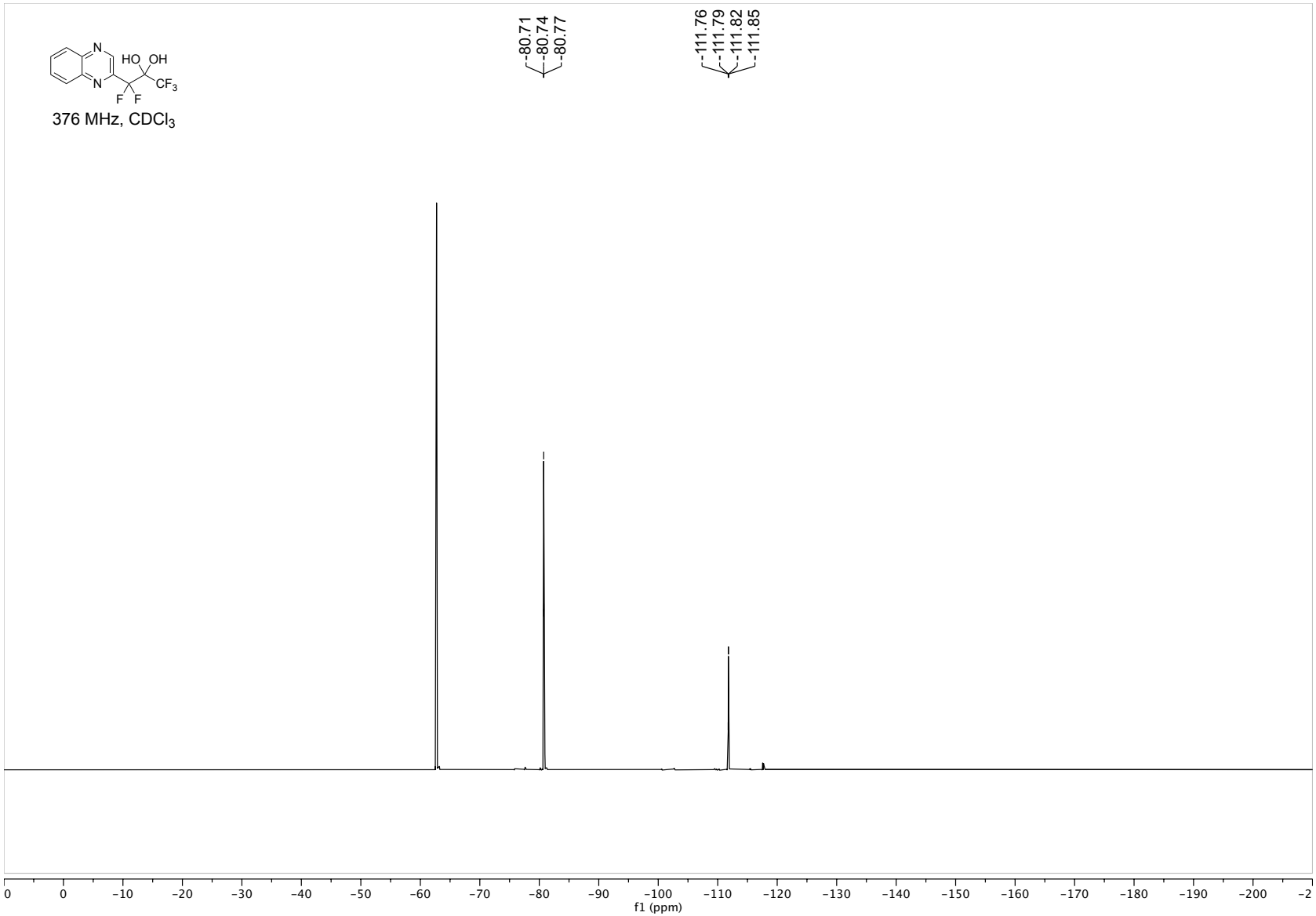

8.915
8.135
8.119
7.888
7.871
4.301
4.275
4.251
2.834
F3C
N
F F
OH
14
500 MHz, CDCl3
1.06
1.00
1.01
2.22
1.00
f1 (ppm)

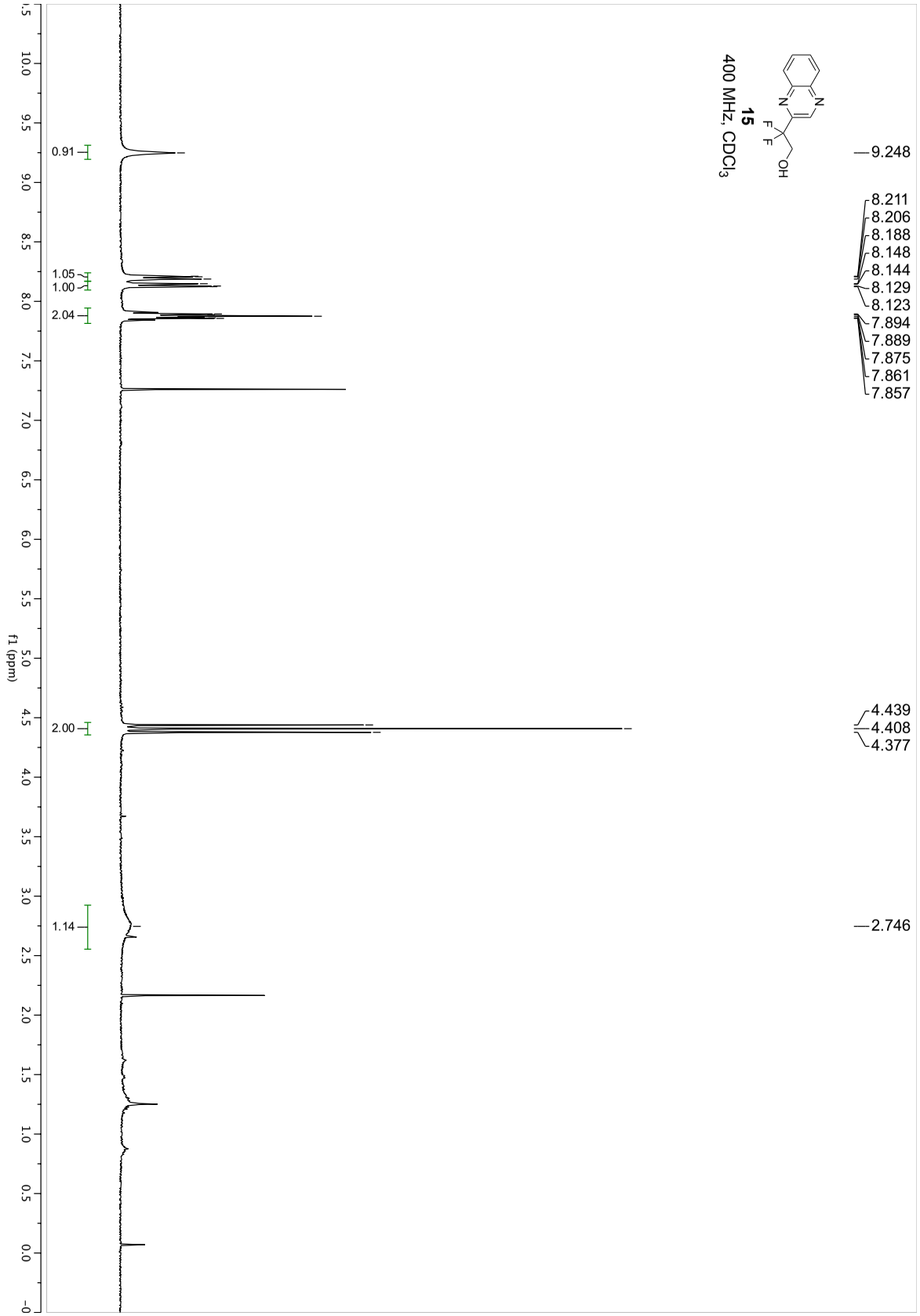

157.30
157.07
156.82
146.24
146.20
135.09
135.06
128.76
128.51
128.24
128.01
124.14
121.97
121.27
119.80
117.86
115.92
64.30
64.05
63.81
F3C
N
OH
F F
14
125 MHz, CDCl3
f1 (ppm)

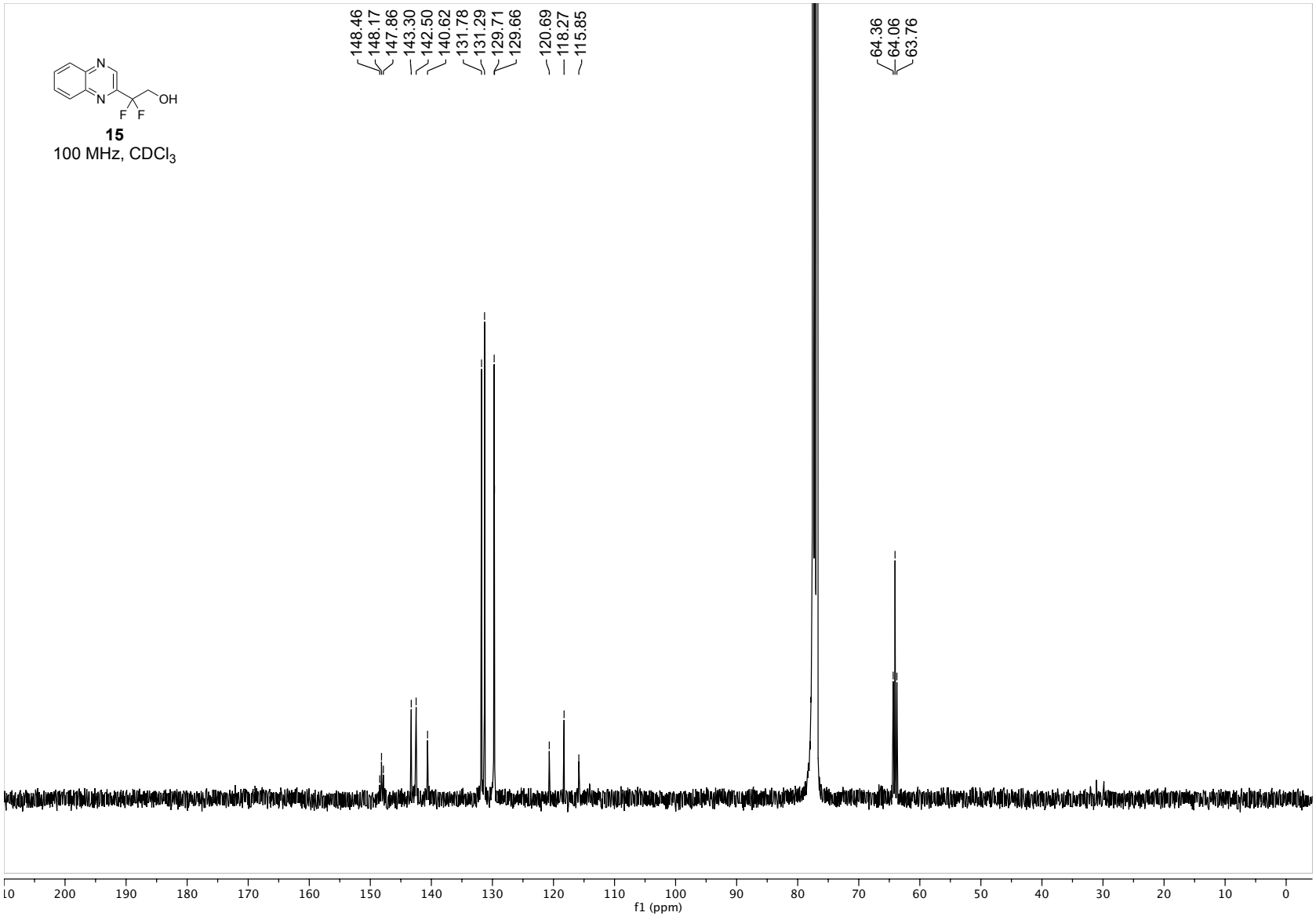

F3C
N
F F
OH
14
471 MHz, CDCl3
-62.677
-106.839
-106.867
-106.893
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

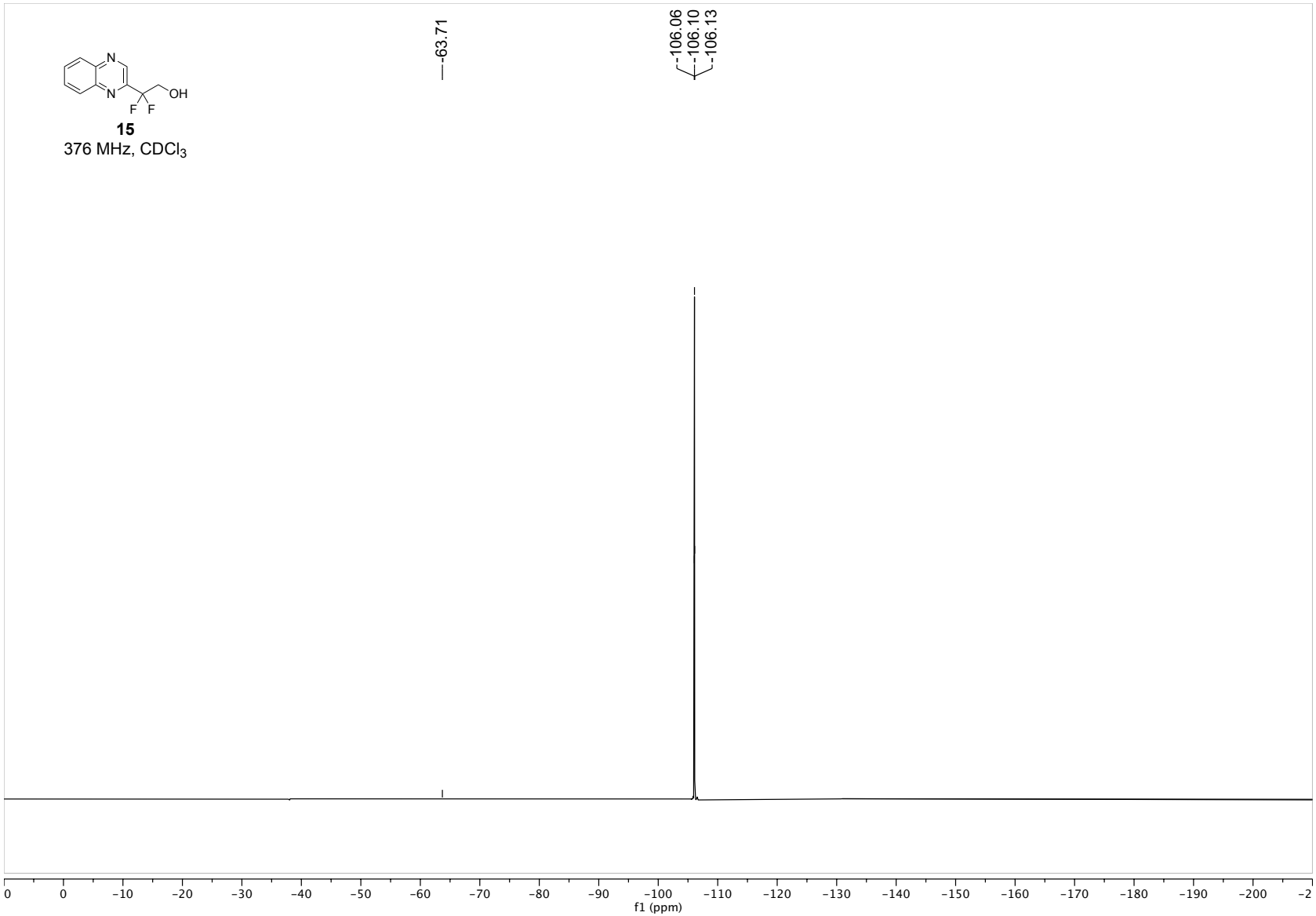

9.327
8.266
8.261
8.245
8.242
8.135
8.131
8.116
8.110
7.944
7.943
5.916
HO
OH
CF3
F
F
400 MHz, CDCl3
1.00
1.01
1.06
2.00
1.83
f1 (ppm)

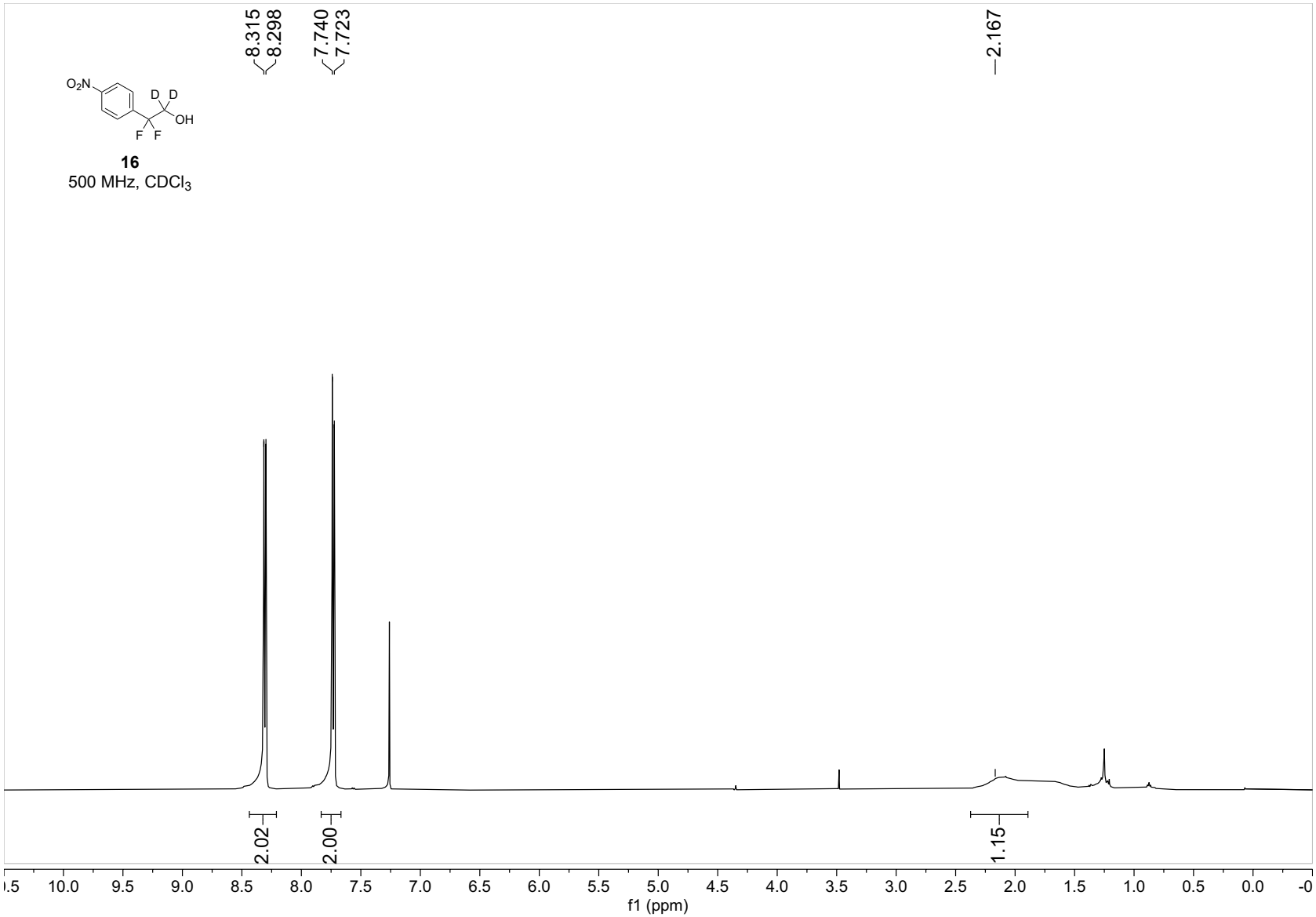

146.90
146.67
146.44
143.61
141.86
141.82
141.78
138.95
132.45
132.06
129.74
128.85
124.69
122.40
120.11
117.82
115.12
113.08
111.05
93.99
93.76
93.50
93.28
HO
OH
CF3
F
F
N
N
125 MHz, CDCl3
f1 (ppm)

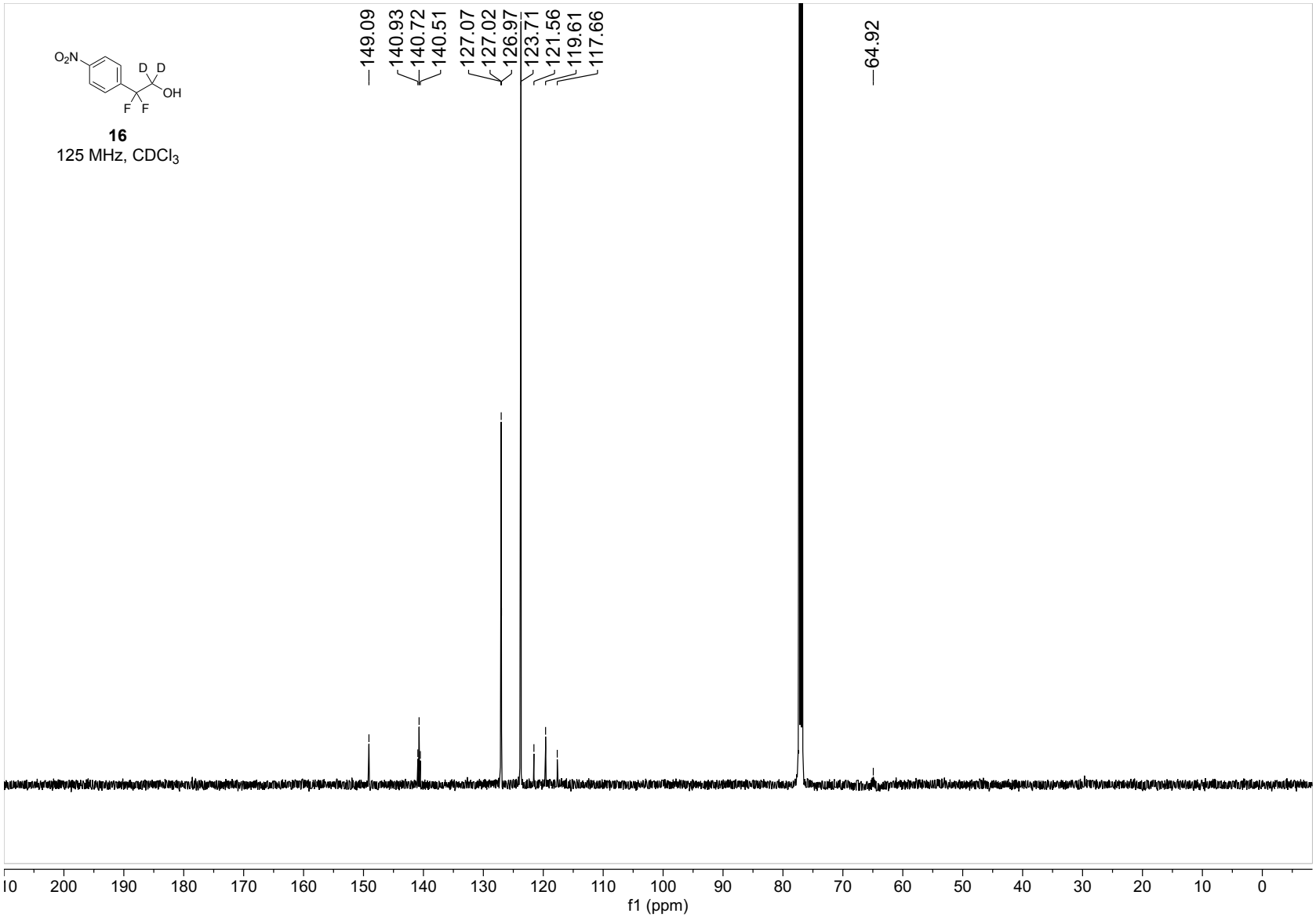

-80.71
-80.74
-80.77
-111.76
-111.79
-111.82
-111.85
HO
OH
CF3
F
F
376 MHz, CDCl3
0
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-2
f1 (ppm)

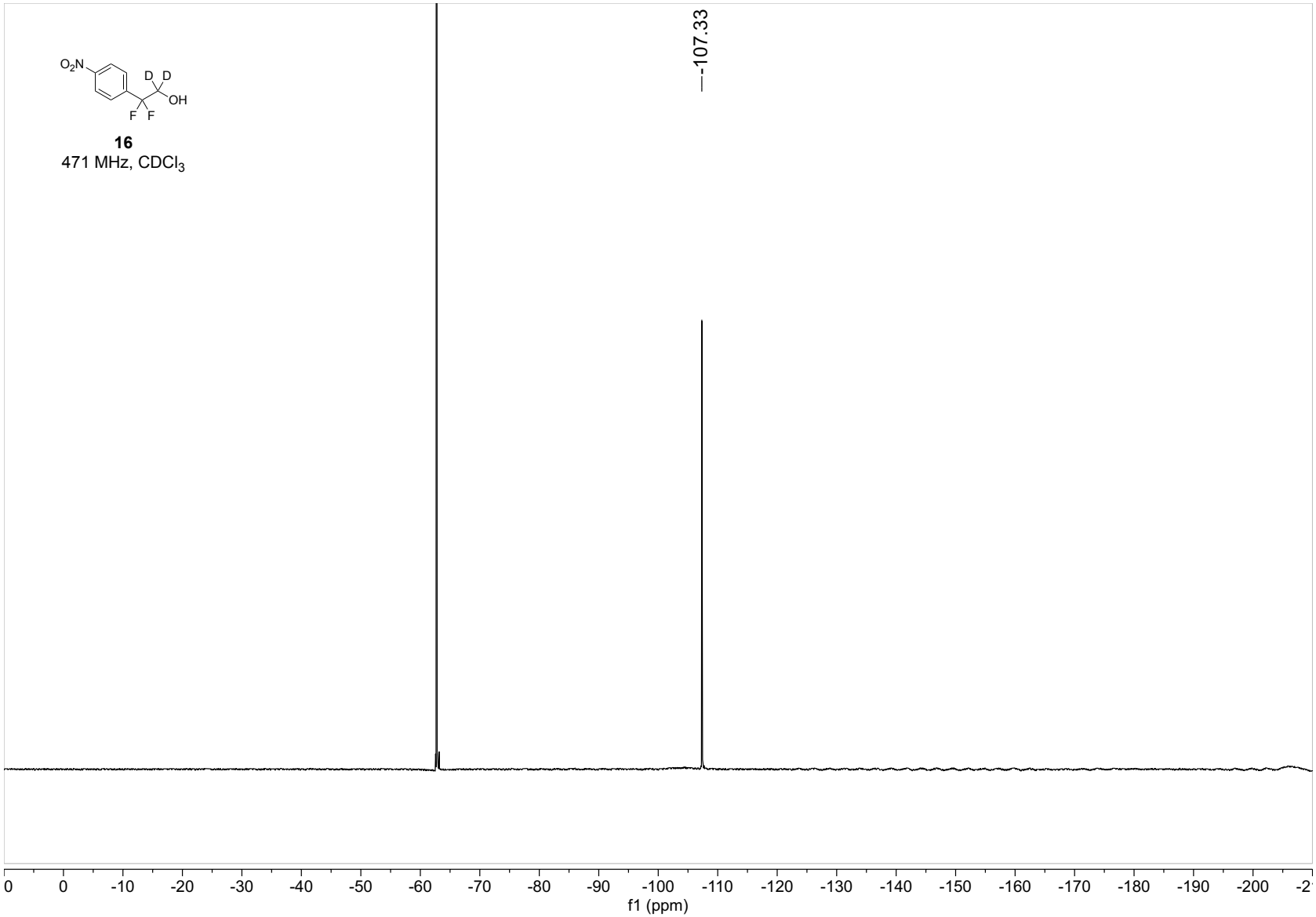

400 MHz, CDCl3
15
9.248
8.211
8.206
8.188
8.148
8.144
8.129
8.123
7.894
7.889
7.875
7.861
7.857
4.439
4.408
4.377
2.746
0.91
1.05
1.00
2.04
2.00
1.14
f1 (ppm)

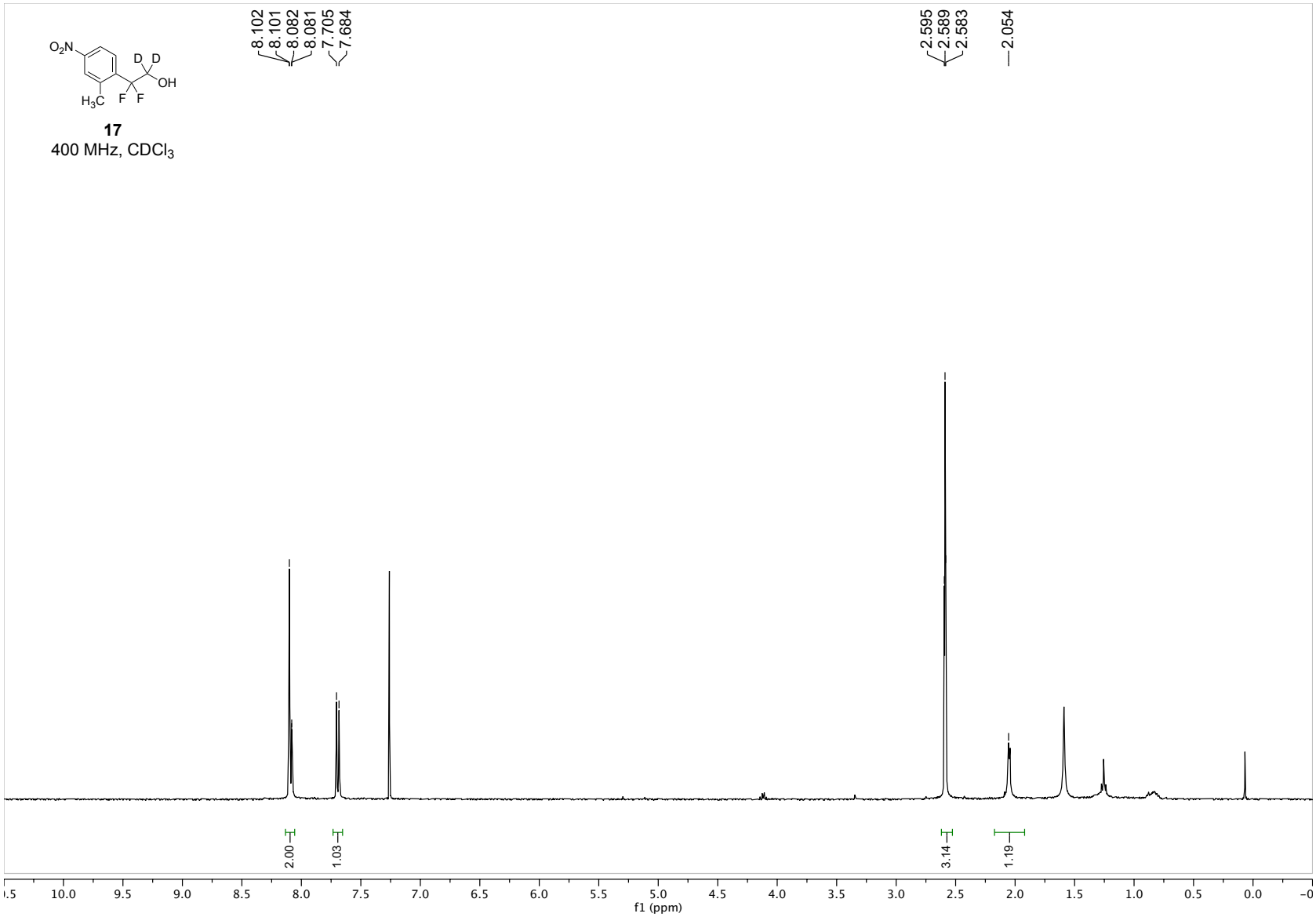

148.46
148.17
147.86
143.30
142.50
140.62
131.78
131.29
129.71
129.66
120.69
118.27
115.85
64.36
64.06
63.76
N
N
OH
F F
15
100 MHz, CDCl3
f1 (ppm)

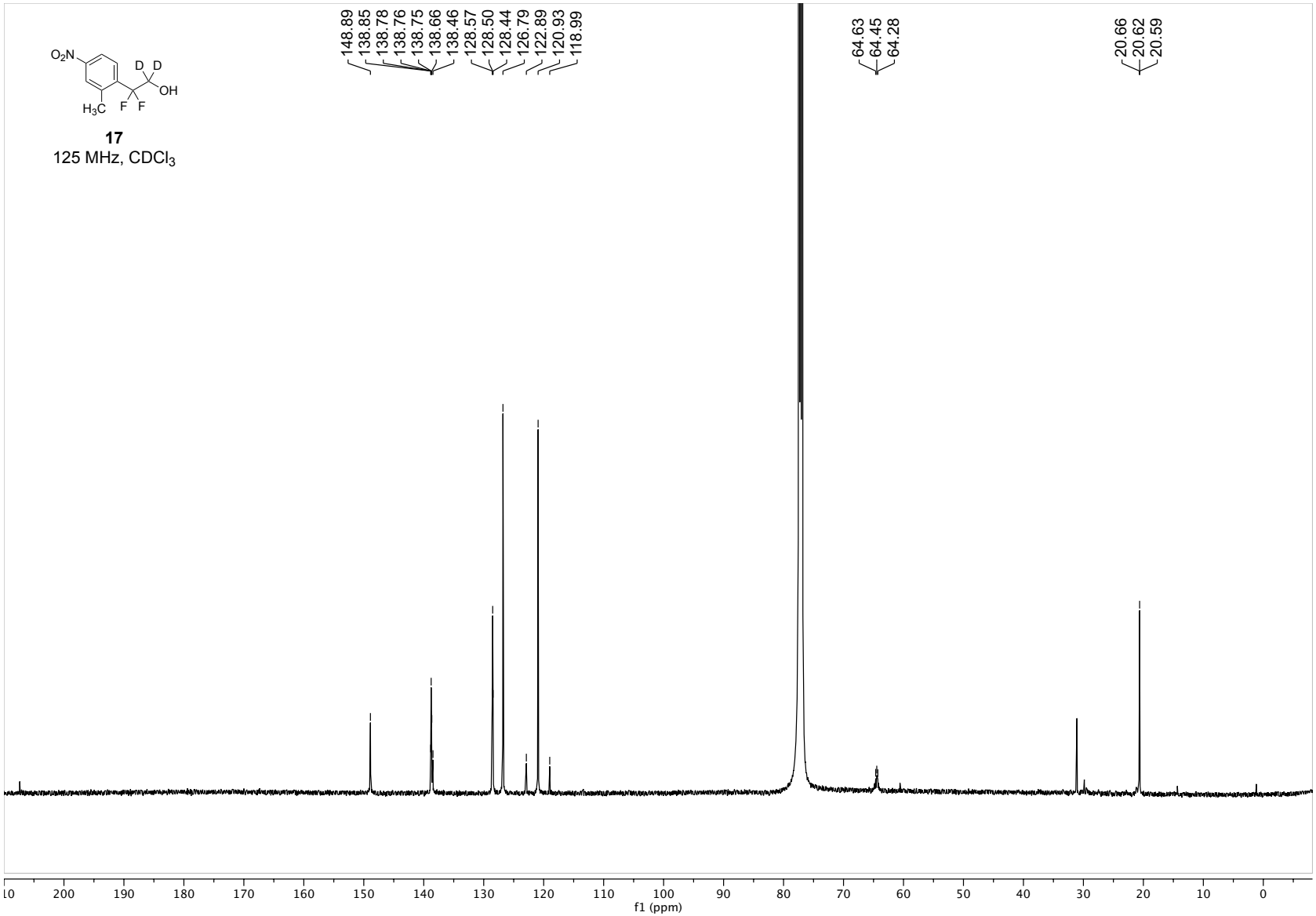

-63.71
-106.06
-106.10
-106.13
N
N
OH
F F
15
376 MHz, CDCl3
0
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-2
f1 (ppm)

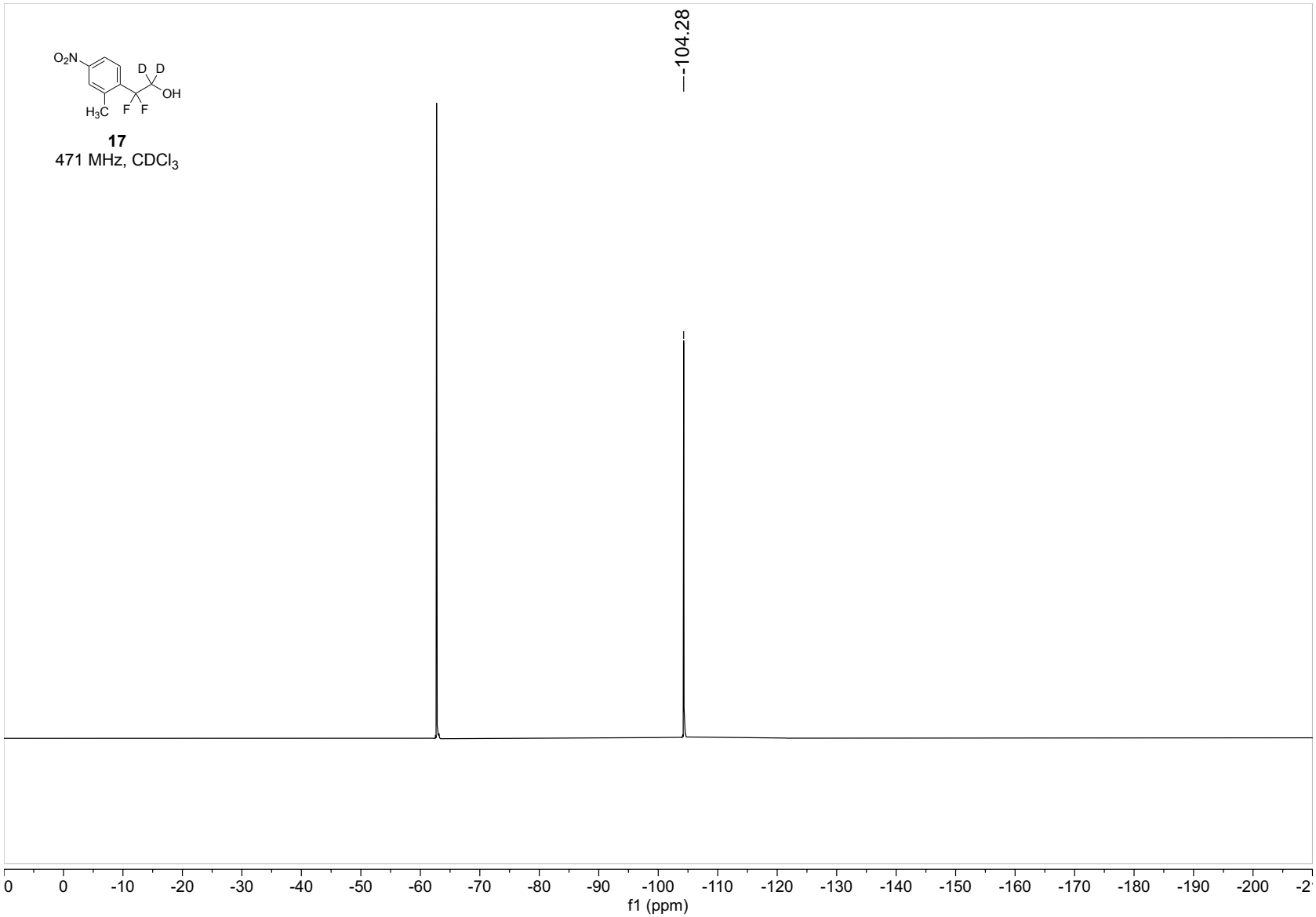

8.315
8.298
7.740
7.723
2.167
O2N
D D
OH
F F
16
500 MHz, CDCl3
2.02
2.00
1.15
f1 (ppm)

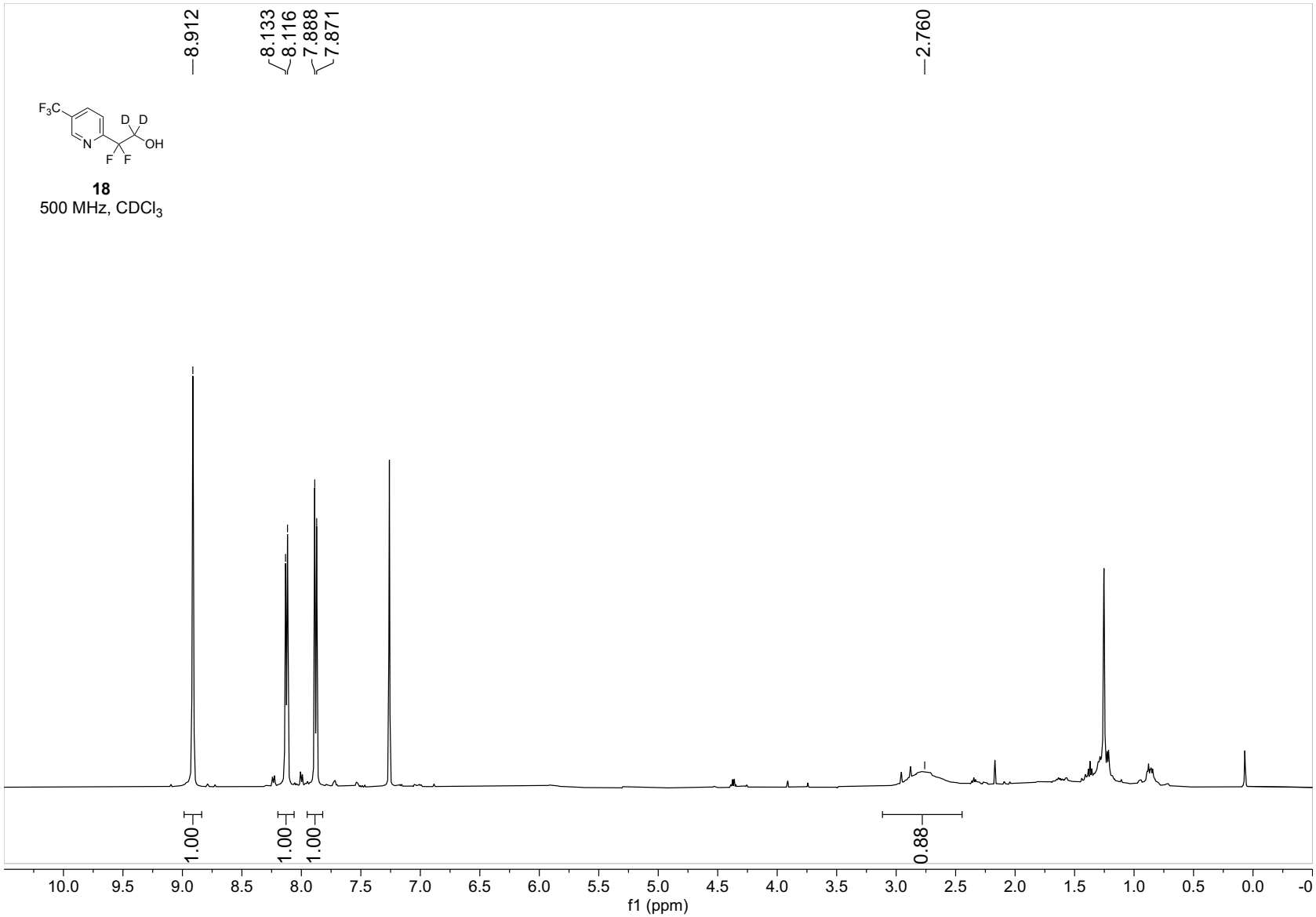

149.09
140.93
140.72
140.51
127.07
127.02
126.97
123.71
121.56
119.61
117.66
64.92
O2N
D D
OH
F F
16
125 MHz, CDCl3
f1 (ppm)

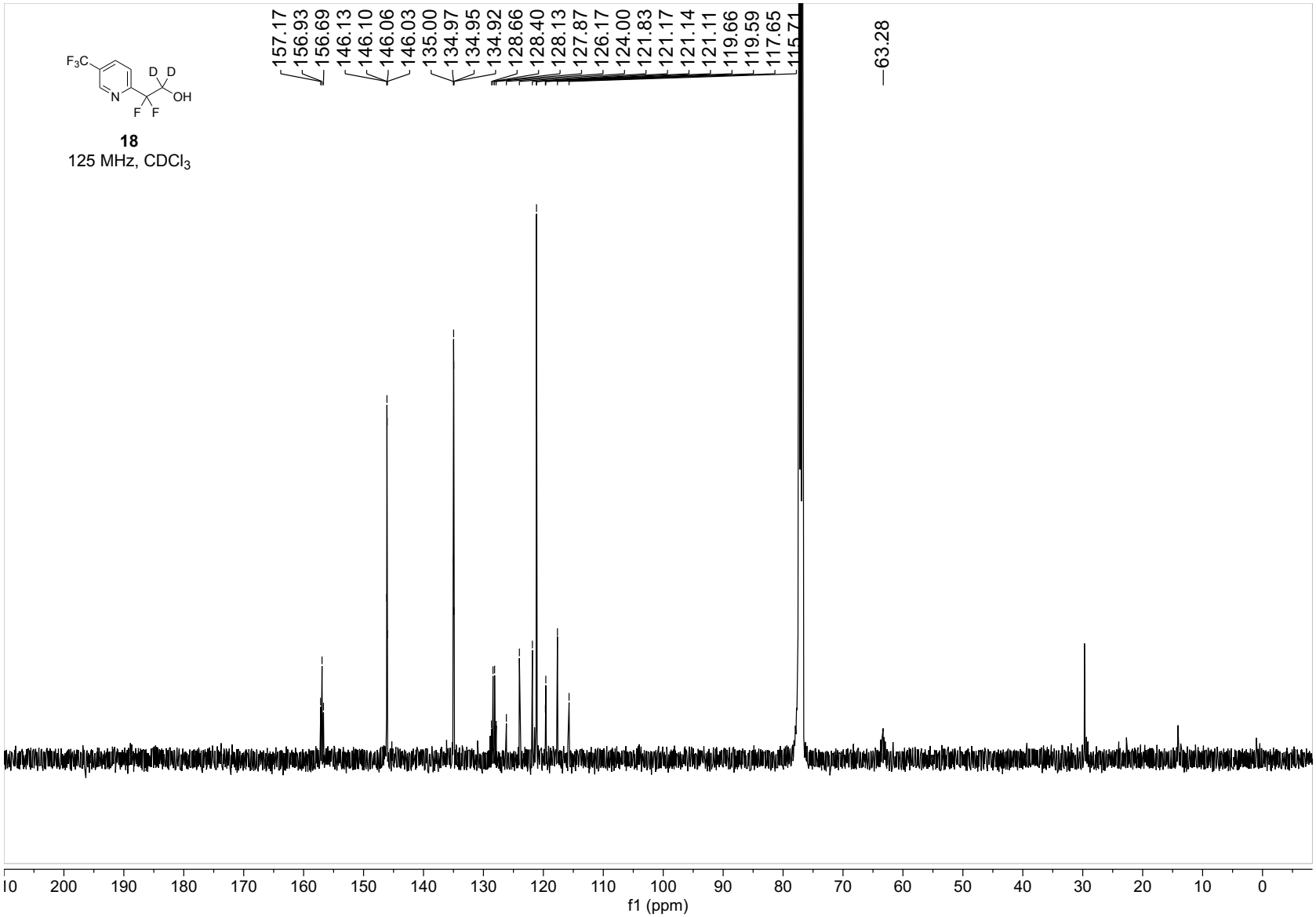

O2N
D D
OH
F F
16
471 MHz, CDCl3
-107.33
0 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

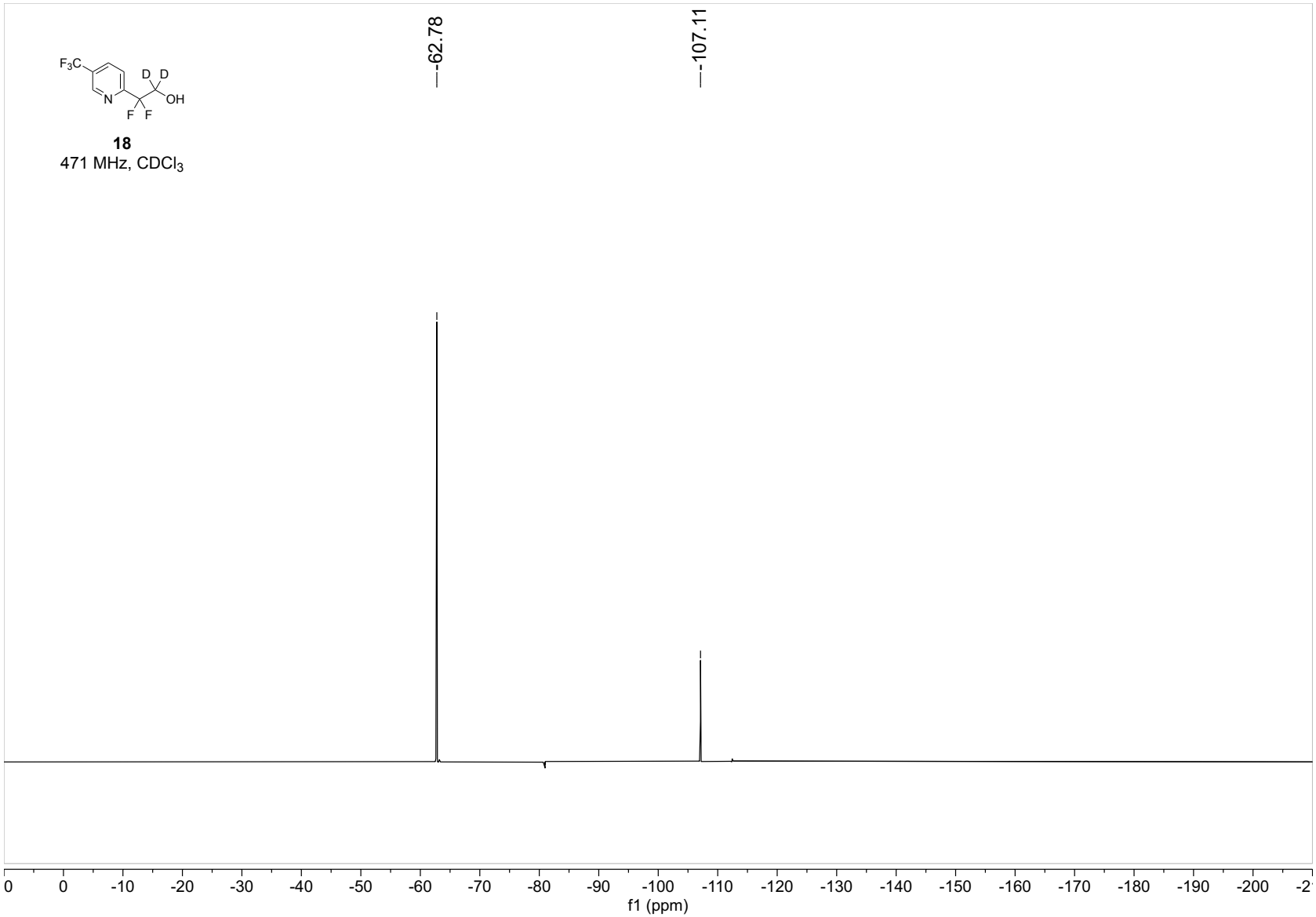

8.102
8.101
8.082
8.081
7.705
7.684
2.595
2.589
2.583
2.054
O2N
D D
OH
H3C
F F
17
400 MHz, CDCl3
2.00
1.03
3.14
1.19
f1 (ppm)


148.89
138.85
138.78
138.76
138.75
138.66
138.46
128.57
128.50
128.44
126.79
122.89
120.93
118.99
64.63
64.45
64.28
20.66
20.62
20.59
O2N
D D
OH
H3C F F
17
125 MHz, CDCl3
f1 (ppm)

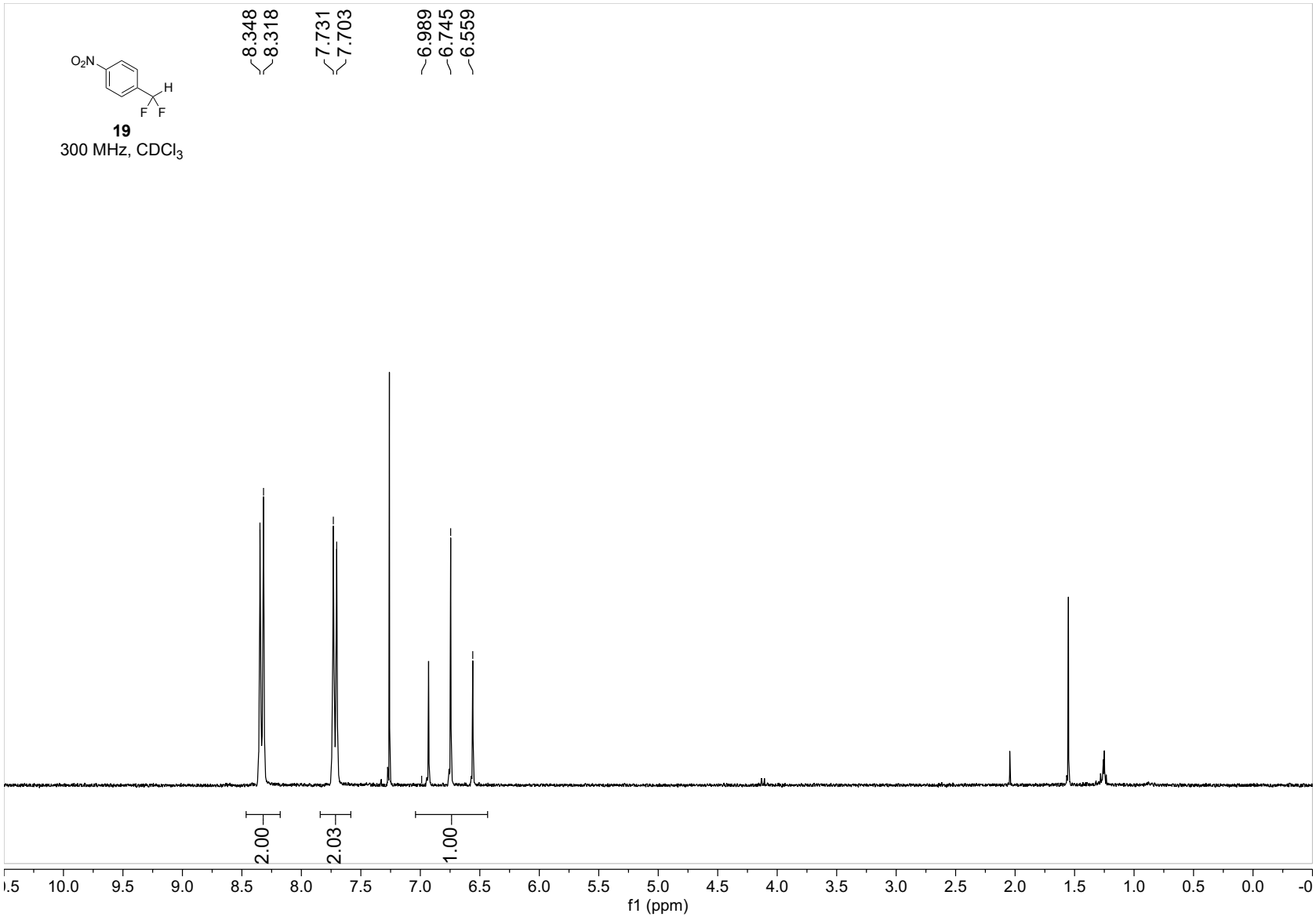

O2N
D D
OH
H3C F F
17
471 MHz, CDCl3
-104.28
0 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

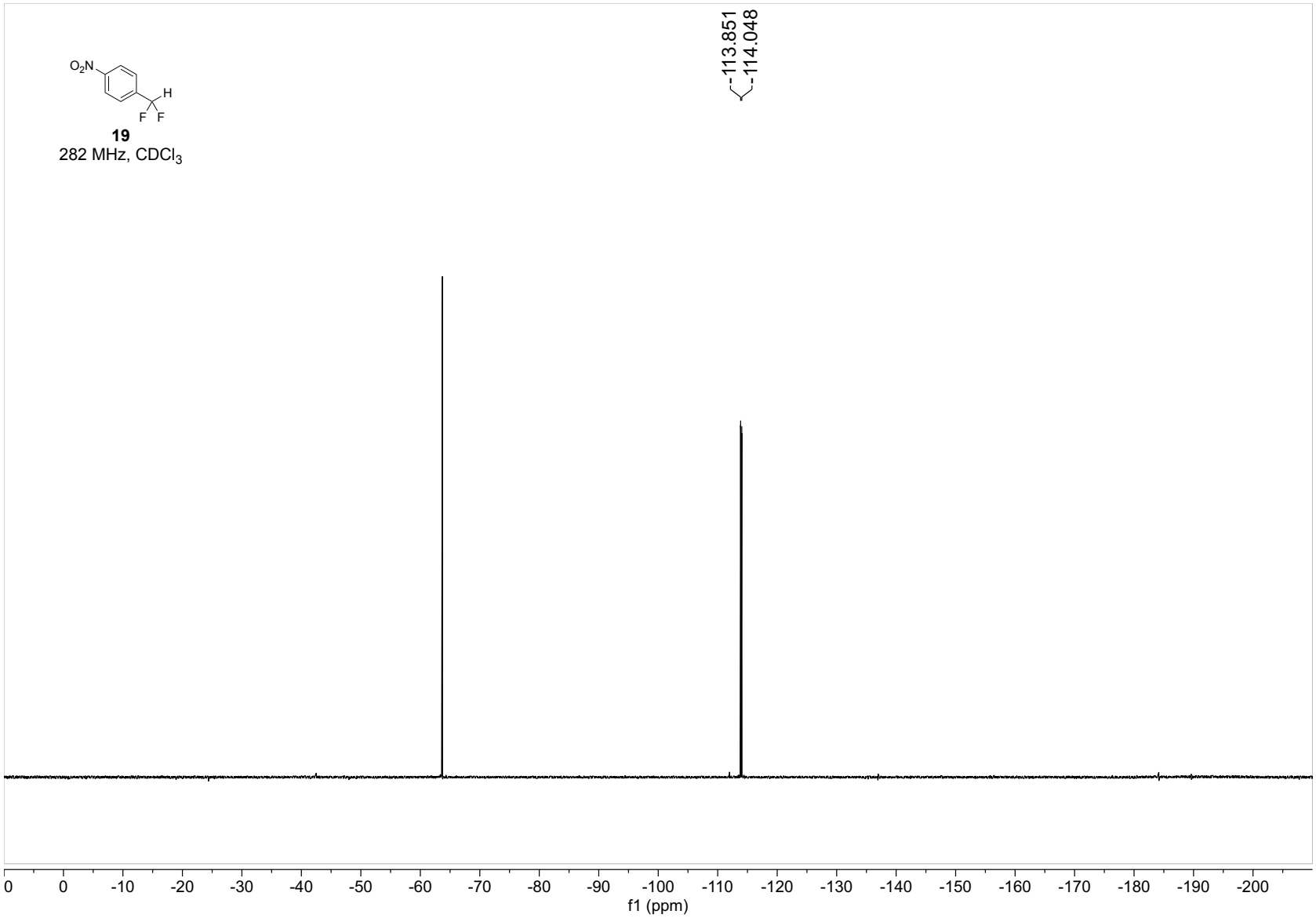

8.912
8.133
8.116
7.888
7.871
2.760
F3C
D D
N
OH
F F
18
500 MHz, CDCl3
1.00
1.00
1.00
0.88
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)

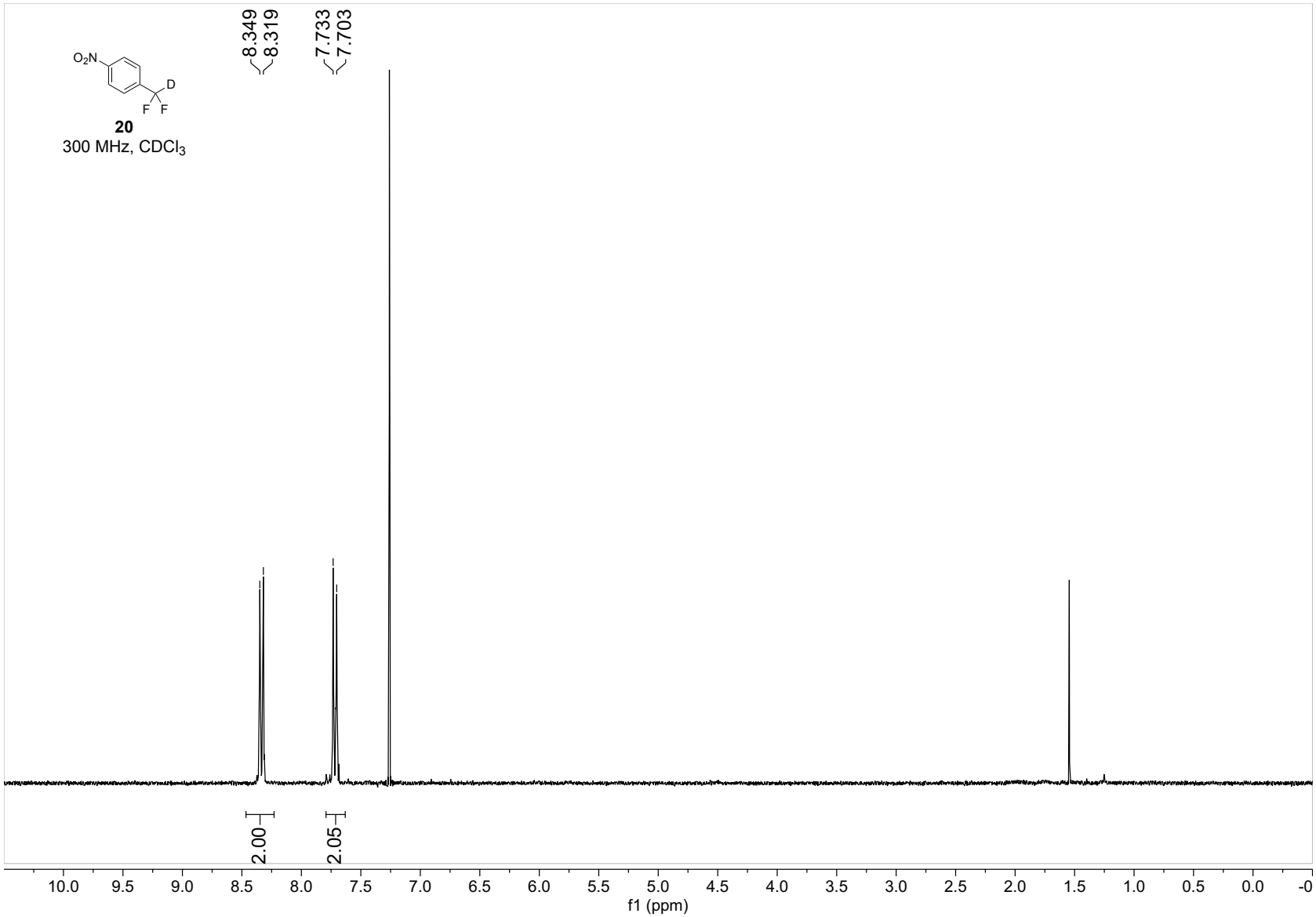

157.17
156.93
156.69
146.13
146.10
146.06
146.03
135.00
134.97
134.95
134.92
128.66
128.40
128.13
127.87
126.17
124.00
121.83
121.17
121.14
121.11
119.66
119.59
117.65
115.71
63.28
F3C
N
D D
OH
F F
18
125 MHz, CDCl3
f1 (ppm)

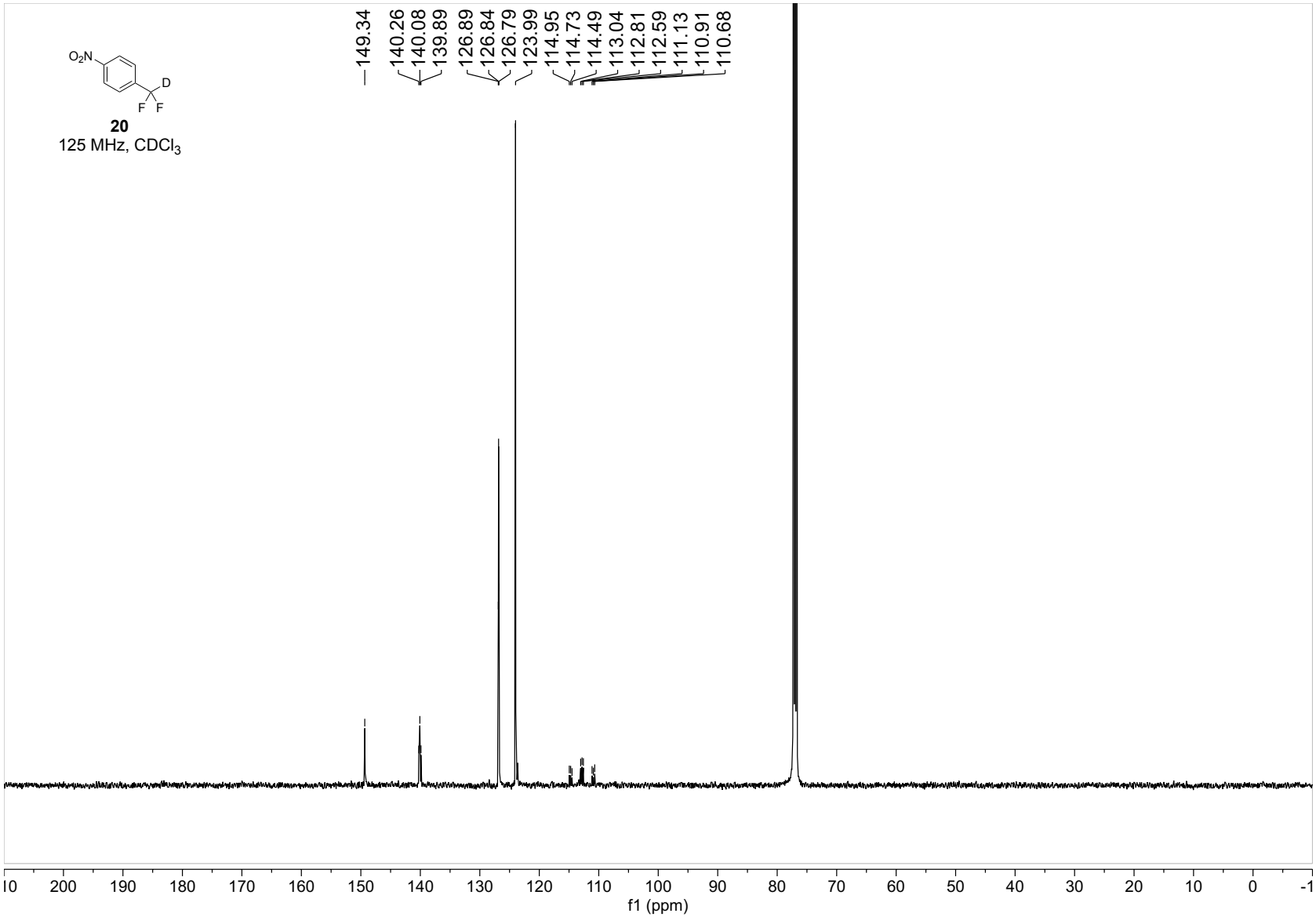


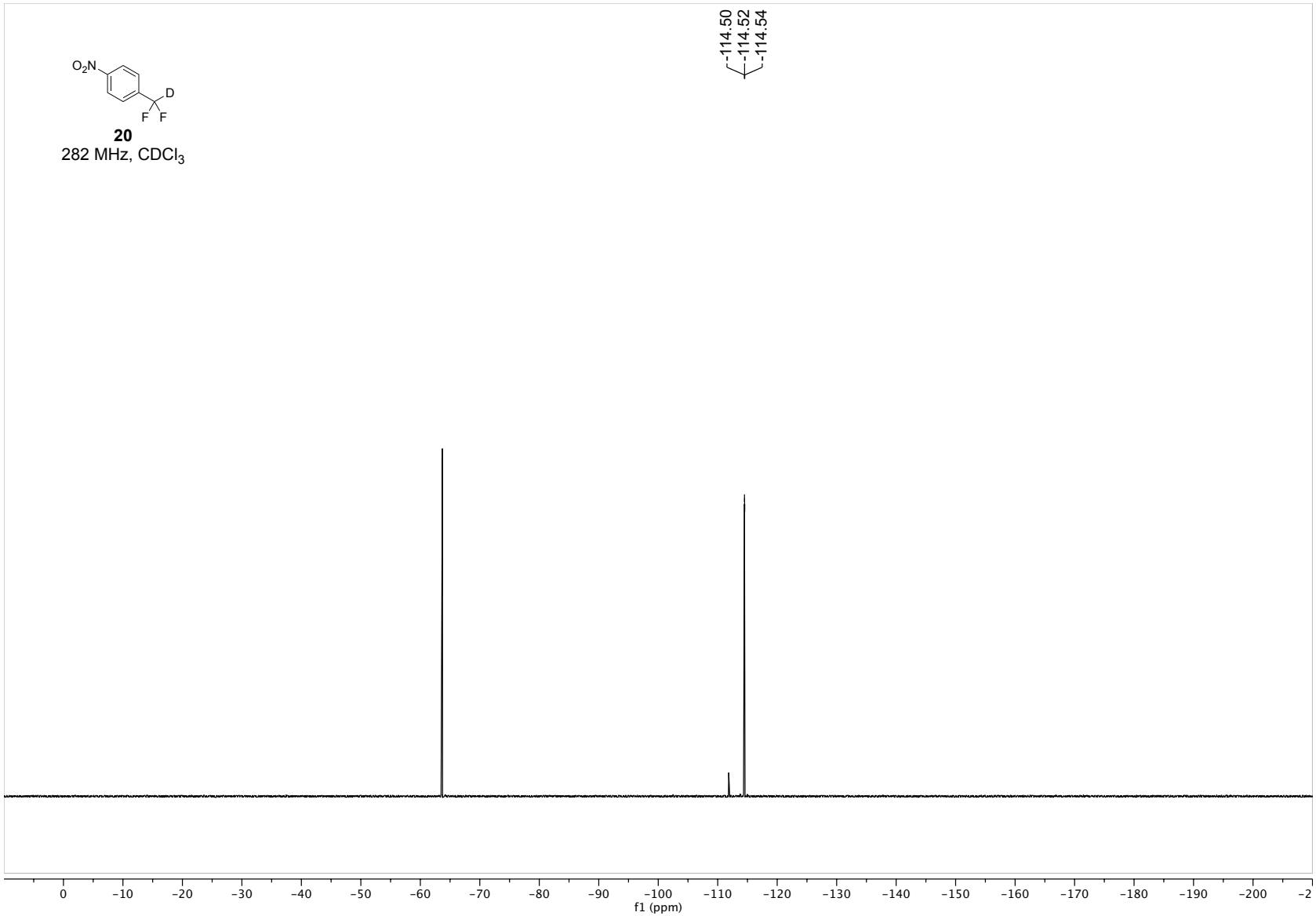
18
471 MHz, $CDCl_3$


8.348
8.318
7.731
7.703
6.989
6.745
6.559
O2N
H
F F
19
300 MHz, CDCl3
2.00
2.03
1.00
f1 (ppm)


O2N
H
F F
19
282 MHz, CDCl3
-113.851
-114.048
0 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)


8.349
8.319
7.733
7.703
O2N
D
F F
20
300 MHz, CDCl3
2.00
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 -0
f1 (ppm)


149.34
140.26
140.08
139.89
126.89
126.84
126.79
123.99
114.95
114.73
114.49
113.04
112.81
112.59
111.13
110.91
110.68
O2N
D
F F
20
125 MHz, CDCl3
f1 (ppm)


O2N
D
F F
20
282 MHz, CDCl3
-114.50
-114.52
-114.54
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-2
f1 (ppm)