

Supporting Information for

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

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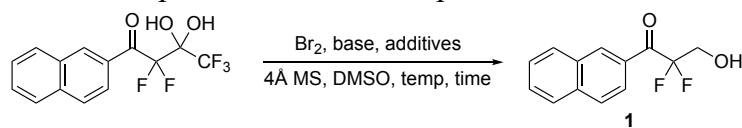
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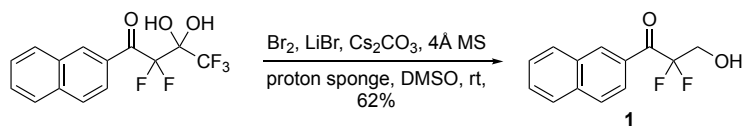
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I. Experimental and Characterization Data

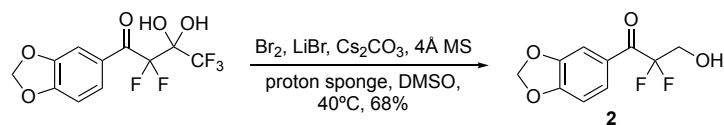
General Procedures. Experiments requiring anhydrous conditions were performed under argon atmosphere and organic solvents were dried over molecular sieves. All solvents and reagents were purchased from commercial sources unless otherwise noted. Starting materials for compounds **1–6** and **10–14** were prepared according to our laboratory's published methods.^{1–4} Thin-layer chromatography was conducted using MilliporeSigma TLC silica gel 60 F₂₅₄ 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 ¹H and ¹³C NMR spectra whereas trifluorotoluene was used as an added internal standard for ¹⁹F 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**

Entry	Base	Additive	Temp	Time	Yield (¹⁹ F NMR)
1	Li ₂ CO ₃	-	rt	12 h	0%
2	Na ₂ CO ₃	-	50 °C	12 h	30%
3	K ₂ CO ₃	-	rt	12 h	33%
4	Cs ₂ CO ₃	LiBr	rt	12 h	61%
5	Cs ₂ CO ₃	LiBr, proton sponge	rt	20 h	73%
6	K ₂ CO ₃	LiBr, proton sponge	rt	20 h	61%
7	Na ₂ CO ₃	LiBr, proton sponge	rt	20 h	52%
8	Cs ₂ CO ₃	LiBr, proton sponge	rt	12 h	78%
9	Cs ₂ CO ₃	LiBr, <i>i</i> -Pr ₂ NEt	rt	12 h	64%

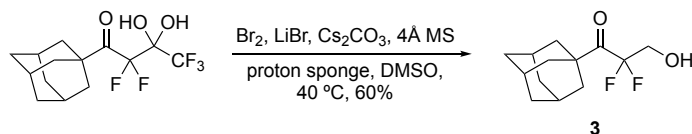


2,2-Difluoro-3-hydroxy-1-(naphthalen-2-yl)propan-1-one (1). A mixture of activated 4Å molecular sieves (100 mg), Cs₂CO₃ (106 mg, 0.325 mmol), LiBr (14 mg, 0.16 mmol), and proton sponge (14 mg, 0.07 mmol) in DMSO (1.0 mL) was cooled to 10 °C and treated with the dropwise addition of bromine (15 μL, 0.29 mmol). After 15 min, a solution of the *gem*-diol² (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 NH₄Cl (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 Na₂SO₄, and concentrated under reduced pressure. Preparative TLC (3% EtOAc in CHCl₃) afforded the title compound **1** as a pale yellow solid (4.5 mg, 62%): mp 42–44 °C; ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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); ¹⁹F NMR (376 MHz, CDCl₃) 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 C₁₃H₉F₂O₂ [M-H]⁻ 235.0571, found 235.0563.

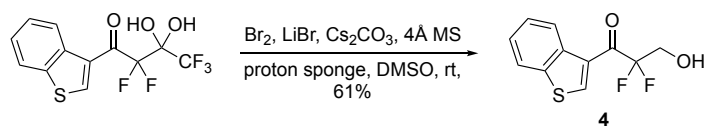


1-(Benzo[1,3]dioxol-5-yl)-2,2-difluoro-3-hydroxypropan-1-one (2). A mixture of activated 4Å molecular sieves (150 mg), Cs₂CO₃ (135 mg, 0.414 mmol), LiBr (17 mg, 0.20 mmol), and proton sponge (17 mg, 0.079 mmol) in DMSO (1.5 mL) was cooled to 10 °C and treated with the dropwise addition of bromine (20 μL, 0.39 mmol). After 15 min, a solution of the *gem*-diol² (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 °C. Next, the reaction mixture was cooled to rt, treated with saturated aqueous NH₄Cl (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 Na₂SO₄, and concentrated under reduced pressure. Preparative TLC (10% EtOAc in CHCl₃) afforded the title compound **2** as a yellow oil (6 mg, 68%): ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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); ¹⁹F NMR (471 MHz, CDCl₃) 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 C₁₀H₇F₂O₄ [M-H]⁻ 229.0312, found 229.0292.

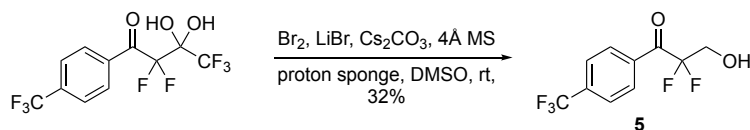


1-(Adamantan-1-yl)-2,2-difluoro-3-hydroxypropan-1-one (3). A mixture of activated 4Å molecular sieves (200 mg), Cs₂CO₃ (210 mg, 0.645 mmol), LiBr (25 mg, 0.29 mmol), and proton sponge (25 mg, 0.12 mmol) in DMSO (2 mL) was cooled to 10 °C and treated with the dropwise addition of bromine (30 μL, 0.58 mmol). After 15 min, a solution of the *gem*-diol² (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 °C. Next, the reaction mixture was cooled to rt, treated with saturated aqueous NH₄Cl (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 Na₂SO₄, and concentrated under reduced pressure. Preparative TLC (1% Et₂O in CH₂Cl₂) afforded the title compound **3** as a yellow oil (9 mg, 60%): ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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); ¹⁹F NMR (471 MHz, CDCl₃) 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 C₁₃H₁₇F₂O₂ [M-H]⁻ 243.1197, found 243.1193.

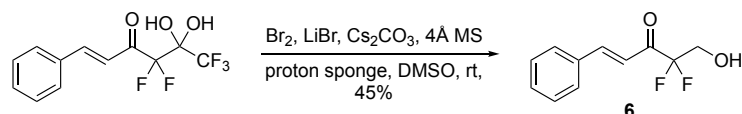


1-(Benzothiophen-3-yl)-2,2-difluoro-3-hydroxypropan-1-one (4). A mixture of activated 4Å molecular sieves (200 mg), Cs₂CO₃ (220 mg, 0.675 mmol), LiBr (27 mg, 0.31 mmol), and proton sponge (27 mg, 0.13 mmol) in DMSO (2 mL) was cooled to 10 °C and treated with the dropwise addition of bromine (32 μL, 0.62 mmol). After 15 min, a solution of the *gem*-diol³ (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 NH₄Cl (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 Na₂SO₄, and concentrated under reduced pressure. Preparative TLC (20% acetone in hexanes) afforded the title compound **4** as a brown oil (9 mg, 61%): ¹H 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,

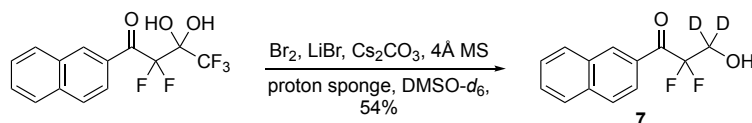
7.1, 1.3 Hz, 1H), 5.85 (t, $J = 6.3$ Hz, 2H), 4.05 (td, $J = 14.2, 6.3$ Hz 1H); ^{13}C NMR (125 MHz, DMSO- d_6) δ 184.3 (t, $J_{\text{CF}} = 27.9$ Hz, 1C), 144.4 (t, $J_{\text{CF}} = 8.2$ Hz, 1C), 138.8, 136.6, 128.3, 126.4, 125.9, 124.3, 123.1, 117.6 (t, $J_{\text{CF}} = 257.0$ Hz, 1C), 61.9 (t, $J_{\text{CF}} = 28.2$ Hz, 1C); ^{19}F NMR (471 MHz, CDCl_3) δ -107.9 (t, $J_{\text{HF}} = 12.9$ Hz, 2F); IR (film) ν_{max} 3423, 3119, 2929, 1677, 1490, 1460, 1174 cm^{-1} ; HRMS (ESI-TOF) m/z calcd for $\text{C}_{11}\text{H}_7\text{F}_2\text{O}_2\text{S}$ $[\text{M}-\text{H}]^-$ 241.0135, found 241.0110.



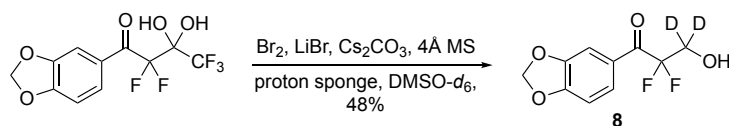
2,2-Difluoro-3-hydroxy-1-(4-(trifluoromethyl)phenyl)propan-1-one (5). A mixture of activated 4Å molecular sieves (300 mg), Cs_2CO_3 (290 mg, 0.89 mmol), LiBr (38 mg, 0.44 mmol), and proton sponge (38 mg, 0.18 mmol) in DMSO (3 mL) was cooled to 10 °C and treated with the dropwise addition of bromine (38 μL , 0.74 mmol). After 15 min, a solution of the *gem*-diol⁴ (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%): ^1H 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, $J_{\text{CF}} = 28.8$ Hz, 1C), 135.7, 133.5 (q, $J_{\text{CF}} = 32.2$ Hz, 1C), 130.4 (t, $J_{\text{CF}} = 3.2$ Hz, 2C), 126.0 (q, $J_{\text{CF}} = 3.9$ Hz, 2C), 123.6 (q, $J_{\text{CF}} = 272.9$ Hz, 1C), 117.6 (t, $J_{\text{CF}} = 254.3$ Hz, 1C), 61.6 (t, $J_{\text{CF}} = 28.2$ Hz, 1C); ^{19}F NMR (471 MHz, CDCl_3) δ -63.5 (s, 3F), -109.3 (t, $J_{\text{HF}} = 12.8$ Hz, 2F); IR (film) ν_{max} 3362, 2867, 1709, 1413, 1329, 1174 cm^{-1} ; HRMS (ESI-TOF) m/z calcd for $\text{C}_{10}\text{H}_6\text{F}_5\text{O}_2$ $[\text{M}-\text{H}]^-$ 253.0288, found 253.0287.



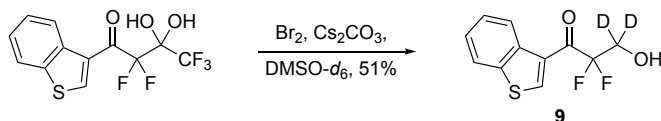
(E)-4,4-Difluoro-5-hydroxy-1-phenylpent-1-en-3-one (6). A mixture of activated 4Å molecular sieves (150 mg), Cs_2CO_3 (153 mg, 0.47 mmol), LiBr (20 mg, 0.23 mmol), and proton sponge (20 mg, 0.09 mmol) in DMSO (1.5 mL) was cooled to 10 °C and treated with the dropwise addition of bromine (15 μL , 0.29 mmol). After 15 min, a solution of the *gem*-diol³ (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%): ^1H 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, $J_{\text{CF}} = 30.0$ Hz, 1C), 148.5 (t, $J_{\text{CF}} = 1.4$ Hz, 1C), 134.0, 132.0, 129.3 (2C), 129.2 (2C) 118.1, 115.3 (t, $J_{\text{CF}} = 254.9$ Hz, 1C), 62.4 (t, $J_{\text{CF}} = 29.1$ Hz, 1C); ^{19}F NMR (471 MHz, CDCl_3) δ -116.8 (t, $J_{\text{HF}} = 12.6$ Hz, 2F); IR (film) ν_{max} 3388, 2958, 2926, 1701, 1610, 1451, 1329, 1181 cm^{-1} ; HRMS (ESI-TOF) m/z calcd for $\text{C}_{11}\text{H}_9\text{F}_2\text{O}_2$ $[\text{M}-\text{H}]^-$ 211.0571, found 211.0580.



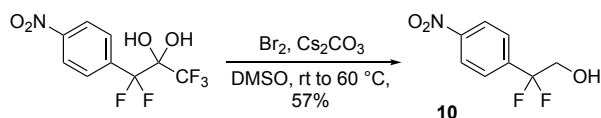
3,3-Dideutero-2,2-difluoro-3-hydroxy-1-(naphthalen-2-yl)propan-1-one (7). A mixture of activated 4Å molecular sieves (200 mg), LiBr (27 mg, 0.31 mmol), proton sponge (27 mg, 0.13 mmol), Cs₂CO₃ (242 mg, 0.743 mmol) in DMSO-*d*₆ (1.6 mL) was cooled to 10 °C and treated with the dropwise addition of bromine (32 μL, 0.62 mmol). After 15 min, a solution of the *gem*-diol² (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 NH₄Cl (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 Na₂SO₄, and concentrated under reduced pressure. Preparative TLC (5% EtOAc in CHCl₃) afforded the title compound **7** as a colorless solid (8 mg, 54%): mp 43–44 °C; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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); ¹⁹F NMR (471 MHz, CDCl₃) 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 C₁₃H₇D₂F₂O₂ [M-H]⁻ 237.0696, found 237.0710.



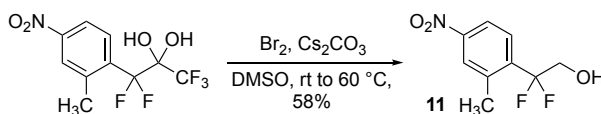
3,3-Dideutero-1-(benzo[1,3]dioxol-5-yl)-2,2-difluoro-3-hydroxypropan-1-one (8). A mixture of activated 4Å molecular sieves (150 mg), LiBr (19 mg, 0.22 mmol), proton sponge (19 mg, 0.18 mmol), Cs₂CO₃ (160 mg, 0.492 mmol) in DMSO-*d*₆ (1.7 mL) was cooled to 10 °C and treated with the dropwise addition of bromine (32 μL, 0.62 mmol). After 15 min, a solution of the *gem*-diol² (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 NH₄Cl (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 Na₂SO₄, and concentrated under reduced pressure. Preparative TLC (30% acetone in hexanes) afforded the title compound **8** as a yellow oil (5 mg, 48%): ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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); ¹⁹F NMR (471 MHz, CDCl₃) δ -108.2 (s, 2F); IR (film) ν_{max} 3420, 2916, 1681, 1605, 1446, 1247 cm⁻¹; HRMS (ESI-TOF) *m/z* calcd for C₁₀H₆D₂F₂O₄ (M+H)⁺ 233.0594, found 233.0595.



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), Cs₂CO₃ (285 mg, 0.875 mmol) in DMSO-*d*₆ (3 mL) was cooled to 10 °C and treated with the dropwise addition of bromine (40 μL, 0.78 mmol). After 15 min, a solution of the *gem*-diol³ (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 NH₄Cl (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 Na₂SO₄, and concentrated under reduced pressure. Preparative TLC (5% EtOAc in hexanes) afforded the title compound **9** as a brown oil (10 mg, 51%): ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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); ¹⁹F NMR (471 MHz, CDCl₃) 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 C₁₁H₅D₂F₂O₂S (M-H)⁻, 243.0260, found 243.0254.

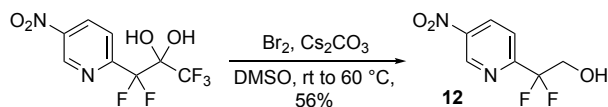


2,2-Difluoro-2-(4-nitrophenyl)ethan-1-ol (10). A mixture of activated 4Å molecular sieves (130 mg) and Cs₂CO₃ (115 mg, 0.350 mmol) in DMSO (1.2 mL) was cooled to 10 °C and treated with the dropwise addition of bromine (17 μL, 0.33 mmol). After 15 min, a solution of the *gem*-diol¹ (10 mg, 0.035 mmol) 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 NH₄Cl (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 Na₂SO₄, and concentrated under reduced pressure. Preparative TLC (3% EtOAc in CHCl₃) afforded the title compound **10** as a colorless solid (4 mg, 57%): mp 86–89 °C; ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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); ¹⁹F NMR (376 MHz, CDCl₃) 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 C₈H₇F₂NO₃ [M]⁺ 203.0394, found, 203.0392.

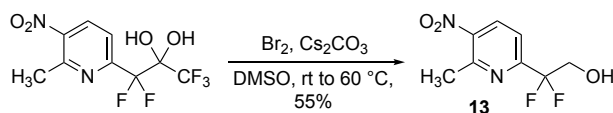


2,2-Difluoro-2-(2-methyl-4-nitrophenyl)ethan-1-ol (11). A mixture of activated 4Å molecular sieves (170 mg) and Cs₂CO₃ (130 mg, 0.40 mmol) in DMSO (1.5 mL) was cooled to 10 °C and treated with the dropwise addition of bromine (20 μL, 0.39 mmol). After 15 min, a solution of the *gem*-diol¹ (12 mg, 0.04 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 NH₄Cl (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 Na₂SO₄, and concentrated under reduced pressure. Preparative

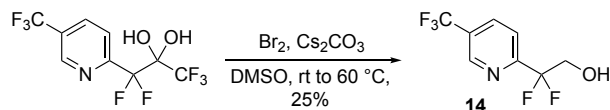
TLC (3% EtOAc in CHCl₃) afforded the title compound **11** as a colorless solid (5 mg, 58%): mp 106–107 °C; ¹H NMR (500 MHz, CDCl₃) δ 8.09 (s, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 7.69 (d, *J* = 8.2 Hz, 1H), 4.06 (t, *J* = 13.3 Hz, 2H), 2.59 (s, 3H), 1.96 (br s, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 148.7, 138.8 (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); ¹⁹F NMR (471 MHz, CDCl₃) 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 C₉H₈F₂NO₃ [M–H]⁻ 216.0472, found 216.0473.



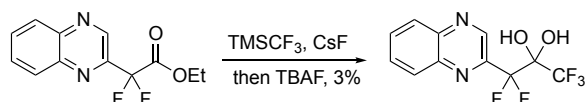
2,2-Difluoro-2-(5-nitropyridin-2-yl)ethan-1-ol (12). A mixture of activated 4Å molecular sieves (100 mg) and Cs₂CO₃ (110 mg, 0.338 mmol) in DMSO (1.2 mL) was cooled to 10 °C and treated with the dropwise addition of bromine (15 μL, 0.29 mmol). After 15 min, a solution of the *gem*-diol¹ (10 mg, 0.033 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 NH₄Cl (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 Na₂SO₄, and concentrated under reduced pressure. Preparative TLC (10% EtOAc in CHCl₃) afforded the title compound **12** as a colorless oil (4 mg, 56%): ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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). ¹⁹F NMR (471 MHz, CDCl₃) 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 C₇H₇F₂N₂O₃ [M+H]⁺ 205.0425, found 205.0424.



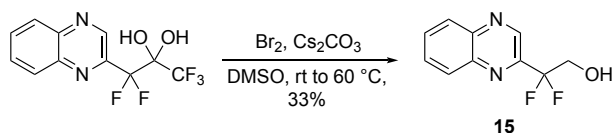
2,2-Difluoro-2-(6-methyl-5-nitropyridin-2-yl)ethan-1-ol (13). A mixture of activated 4Å molecular sieves (100 mg) and Cs₂CO₃ (110 mg, 0.338 mmol) in DMSO (1.0 mL) was cooled to 10 °C and treated with the dropwise addition of bromine (15 μL, 0.29 mmol). After 15 min, a solution of the *gem*-diol¹ (10 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 NH₄Cl (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 Na₂SO₄, and concentrated under reduced pressure. Preparative TLC (10% EtOAc in CHCl₃) afforded the title compound **13** as a colorless solid (4 mg, 55%): mp 73–75 °C; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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; ¹⁹F NMR (376 MHz, CDCl₃) 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 C₈H₇F₂N₂O₃ [M–H]⁻ 217.0425, found 217.0415.



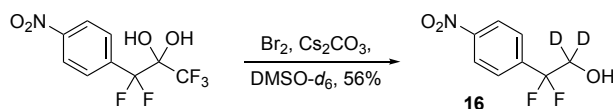
2,2-Difluoro-2-(5-(trifluoromethyl)pyridin-2-yl)ethan-1-ol (14). A mixture of activated 4Å molecular sieves (200 mg) and Cs_2CO_3 (208 mg, 0.638 mmol) in DMSO (2.0 mL) was cooled to 10 °C and treated with the dropwise addition of bromine (30 μL , 0.59 mmol). After 15 min, a solution of the *gem*-diol¹ (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 \times 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%): ^1H 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, $J_{\text{CF}} = 29.6$ Hz, 1C), 146.2 (q, $J_{\text{CF}} = 3.9$ Hz, 1C), 135.1 (q, $J_{\text{CF}} = 3.7$ Hz, 1C), 128.2 (q, $J_{\text{CF}} = 33.7$ Hz, 1C), 122.9 (q, $J_{\text{CF}} = 272.5$ Hz, 1C), 121.3 (t, $J_{\text{CF}} = 3.3$ Hz, 1C), 117.9 (t, $J_{\text{CF}} = 244.0$ Hz, 1C), 64.1 (t, $J_{\text{CF}} = 30.8$ Hz, 1C); ^{19}F NMR (471 MHz, CDCl_3) δ -62.7 (s, 3F), -106.9 (t, $J_{\text{HF}} = 12.6$ Hz, 2F); IR (film) ν_{max} 3339, 2930, 2854, 1735, 1689, 1556, 1350, 1463, 1325 cm^{-1} ; HRMS (ESI-TOF) m/z calcd for $\text{C}_8\text{H}_7\text{F}_5\text{NO}$ $[\text{M}+\text{H}]^+$ 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-quinoxalinyloxy)acetate⁵ (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 \times 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 \times 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%): ^1H 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, $J_{\text{CF}} = 29.1$ Hz, 1C), 143.6, 141.8 (t, $J_{\text{CF}} = 5.1$ Hz, 1C), 139.0, 132.5, 132.1, 129.7, 128.9, 121.3 (q, $J_{\text{CF}} = 288.3$ Hz, 1C), 113.1 (t, $J_{\text{CF}} = 256.0$ Hz, 1C), 93.6 (ddt, $J_{\text{CF}} = 32.6, 28.2, 4.8$ Hz, 1C); ^{19}F NMR (376 MHz, CDCl_3) δ -80.73 (t, $J_{\text{FF}} = 10.9$ Hz, 3F), -111.80 (q, $J_{\text{FF}} = 11.2$ Hz, 2F); IR (film) ν_{max} cm^{-1} 3067.6, 1267.3, 1161.1, 1073.5; HRMS (ESI-TOF) m/z calcd for $\text{C}_{11}\text{H}_6\text{F}_5\text{N}_2\text{O}_2$ $(\text{M}-\text{H})^-$ 293.0349, found 293.0343.



2,2-Difluoro-2-(quinoxalin-2-yl)ethan-1-ol (15). A mixture of activated 4Å molecular sieves (600 mg) and Cs₂CO₃ (692 mg, 2.13 mmol) in DMSO (8.0 mL) was cooled to 10 °C 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 NH₄Cl (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 Na₂SO₄, and concentrated under reduced pressure. Preparative TLC (10% *i*-PrOH, 40% CH₂Cl₂, 50% hexanes) afforded the title compound **15** as a yellow solid (11 mg, 31%): mp 99–100 °C; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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); ¹⁹F NMR (376 MHz, CDCl₃) 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 C₁₀H₉F₂N₂O [M+H]⁺ 211.0683, found 211.0679.

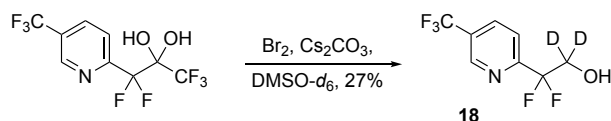


1,1-Dideutero-2,2-difluoro-2-(4-nitrophenyl)ethan-1-ol (16). A mixture of activated 4Å molecular sieves (100 mg) and Cs₂CO₃ (115 mg, 0.350 mmol) in DMSO-*d*₆ (1.2 mL) was cooled to 10 °C and treated with the dropwise addition of bromine (17 μL, 0.33 mmol). After 15 min, a solution of the *gem*-diol¹ (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 NH₄Cl (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 Na₂SO₄, and concentrated under reduced pressure. Preparative TLC (5% EtOAc in CHCl₃) afforded the title compound **16** as a colorless solid (4 mg, 56%): mp 86–89 °C; ¹H NMR (500 MHz, CDCl₃) δ 8.31 (d, *J* = 8.9 Hz, 2H), 7.73 (d, *J* = 8.9 Hz, 2H), 2.17 (br s, 1H); ¹³C NMR (125 MHz, CDCl₃) 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); ¹⁹F NMR (471 MHz, CDCl₃) δ –107.3; IR (film) ν_{max} 3409, 3088, 2868, 1611, 1529, 1352, 1284, 1113 cm⁻¹; HRMS (ESI–TOF) *m/z* calcd for C₈H₄D₂F₂NO₃ [M–H]⁻ 204.0441, found 204.0418.

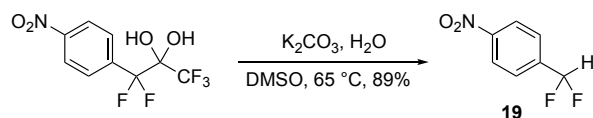


1,1-Dideutero-2,2-difluoro-2-(2-methyl-4-nitrophenyl)ethan-1-ol (17). A mixture of activated 4Å molecular sieves (200 mg) and Cs₂CO₃ (170 mg, 0.522 mmol) in DMSO-*d*₆ (2 mL) was cooled to 10 °C and treated with the dropwise addition of bromine (25 μL, 0.49 mmol). After 15 min, a solution of the *gem*-diol¹ (15 mg, 0.05 mmol) in DMSO-*d*₆ (0.5 mL) was added to the reaction

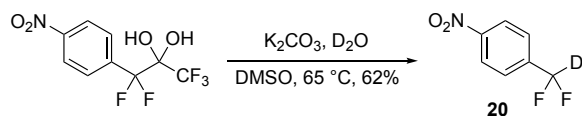
mixture across 1 h via syringe pump. The reaction mixture was then stirred for 24 h at 65 °C. Next, the reaction mixture was cooled to rt, treated with saturated aqueous NH₄Cl (5 mL), diluted EtOAc (50 mL), and stirred for 1 h. The resultant mixture was filtered through Celite, and the organics were washed with brine (3 × 5 mL), dried over Na₂SO₄, and concentrated under reduced pressure. Preparative TLC (5% EtOAc in CHCl₃) afforded the title compound **17** as a colorless solid (7 mg, 64%): mp 107–108 °C; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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); ¹⁹F NMR (471 MHz, CDCl₃) δ –104.3 (s, 2F); IR (film) ν_{max} 3521, 3096, 2946, 1520, 1351 cm⁻¹; HRMS (ESI–TOF) *m/z* calcd for C₉H₆F₂D₂NO₃ [M–H]⁻ 218.0598, found 218.0605.



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 Cs₂CO₃ (208 mg, 0.638 mmol) in DMSO-*d*₆ (2 mL) was cooled to 10 °C and treated with the dropwise addition of bromine (25 μL, 0.48 mmol). After 15 min, a solution of the *gem*-diol¹ (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 NH₄Cl (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 Na₂SO₄, and concentrated under reduced pressure. Preparative TLC (4% Et₂O in CHCl₃) afforded the title compound **18** as a colorless oil (3 mg, 27%): ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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); ¹⁹F NMR (471 MHz, CDCl₃) 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 C₈H₅D₂F₅NO (M+H)⁺ 230.0573, found 230.0572.



1-(Difluoromethyl)-4-nitrobenzene (19).⁶ A solution of the *gem*-diol¹ (100 mg, 0.348 mmol) in DMSO (2.0 mL) was treated with H₂O (19 μL) and K₂CO₃ (194 mg, 1.40 mmol). The reaction mixture was stirred at 65 °C for 3 h. Next, the reaction mixture was cooled to rt, treated with saturated aqueous NH₄Cl (2 mL), and extracted with CH₂Cl₂ (5 × 5 mL). The organics were dried over Na₂SO₄ and concentrated under reduced pressure. SiO₂ flash column chromatography (8:2 hexanes/EtOAc) afforded the title compound **19** as a colorless oil (54 mg, 89%): ¹H NMR (300 MHz, CDCl₃) 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); ¹⁹F NMR (282 MHz, CDCl₃) 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*-diol¹ (100 mg, 0.348 mmol) in DMSO (2.0 mL) was treated with D₂O (19 μ L) and K₂CO₃ (194 mg, 1.40 mmol). The reaction mixture was stirred at 65 °C for 30 min. Next, the reaction mixture was cooled to rt, treated with saturated aqueous NH₄Cl (2 mL), and extracted with CH₂Cl₂ (5 \times 5 mL). The organics were dried over Na₂SO₄ and concentrated under reduced pressure. SiO₂ flash column chromatography (8:2 hexanes/EtOAc) afforded the title compound **20** as a colorless oil (38 mg, 62%): ¹H NMR (300 MHz, CDCl₃) δ 8.33 (d, *J* = 9.0 Hz, 2H), 7.72 (d, *J* = 9.0 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) 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); ¹⁹F NMR (282 MHz, CDCl₃) 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 C₇H₄DF₂NO₂ [M]⁺, 174.0351; found, 174.0353.

II. Computations

Geometry optimization and frequency calculations were performed with the Gaussian 09⁸ software package using hybrid density functional theory⁹ with the M06-2X¹⁰ 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
Br [⊖]	-2574.376153	-2574.357617
	-3126.697791	-3126.656971

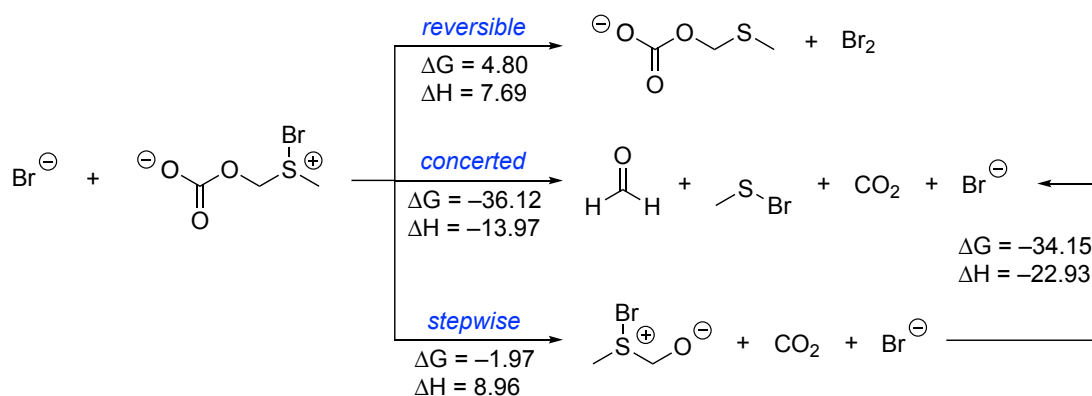


Figure S1. Free energies (G) and enthalpies (H) of the three investigated processes (in kcal/mol at 298.15K).

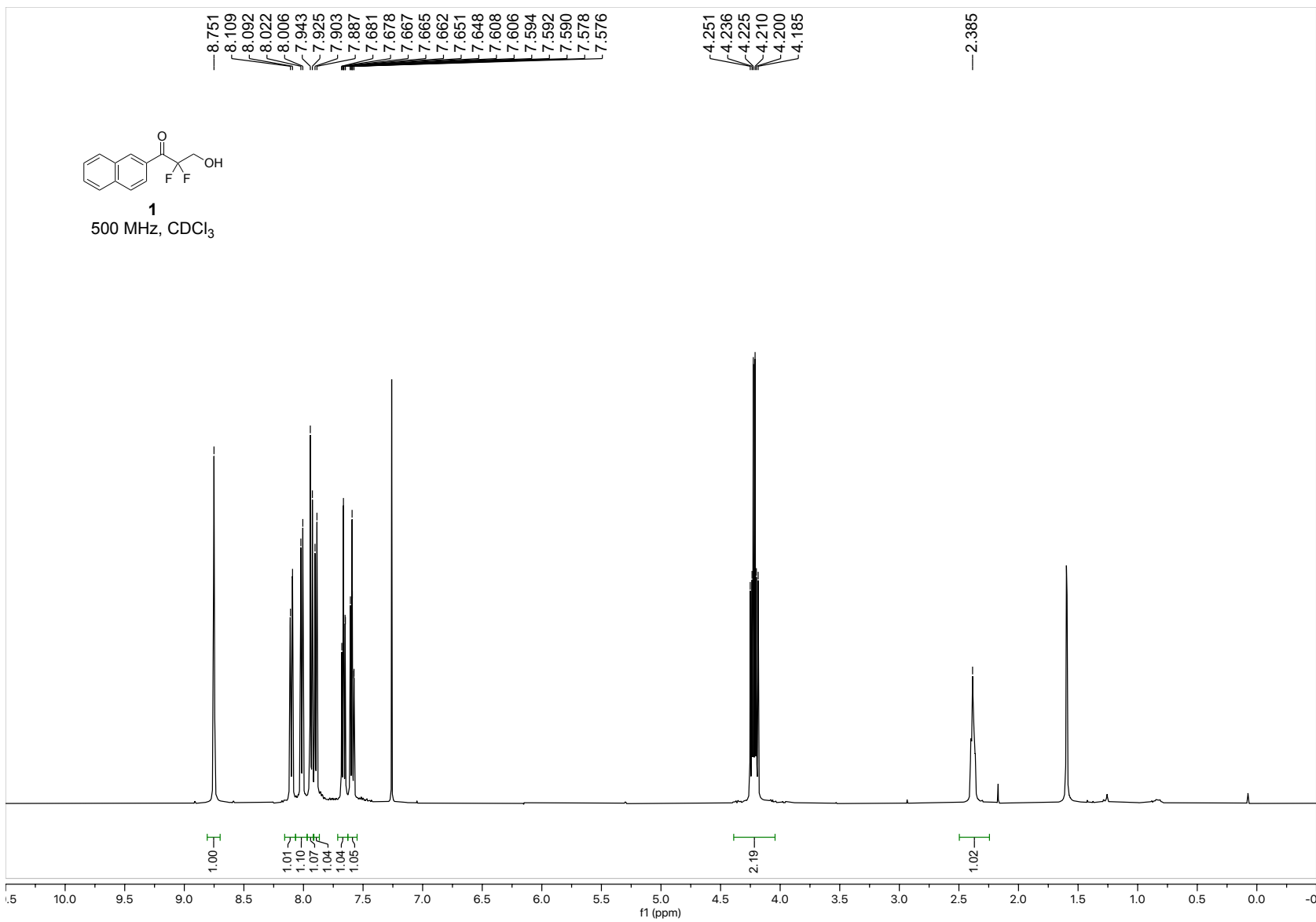
III. References

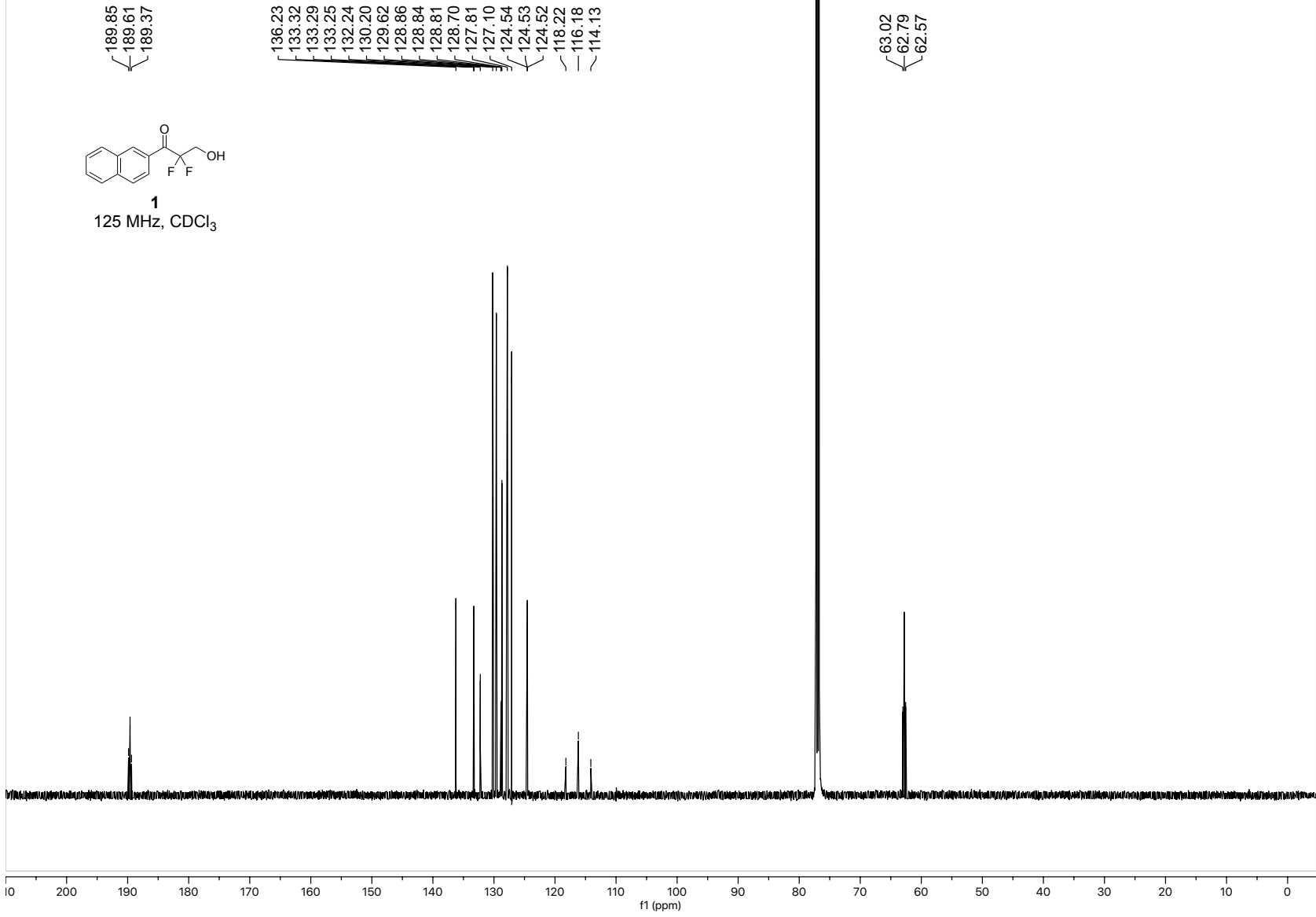
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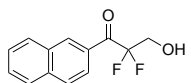
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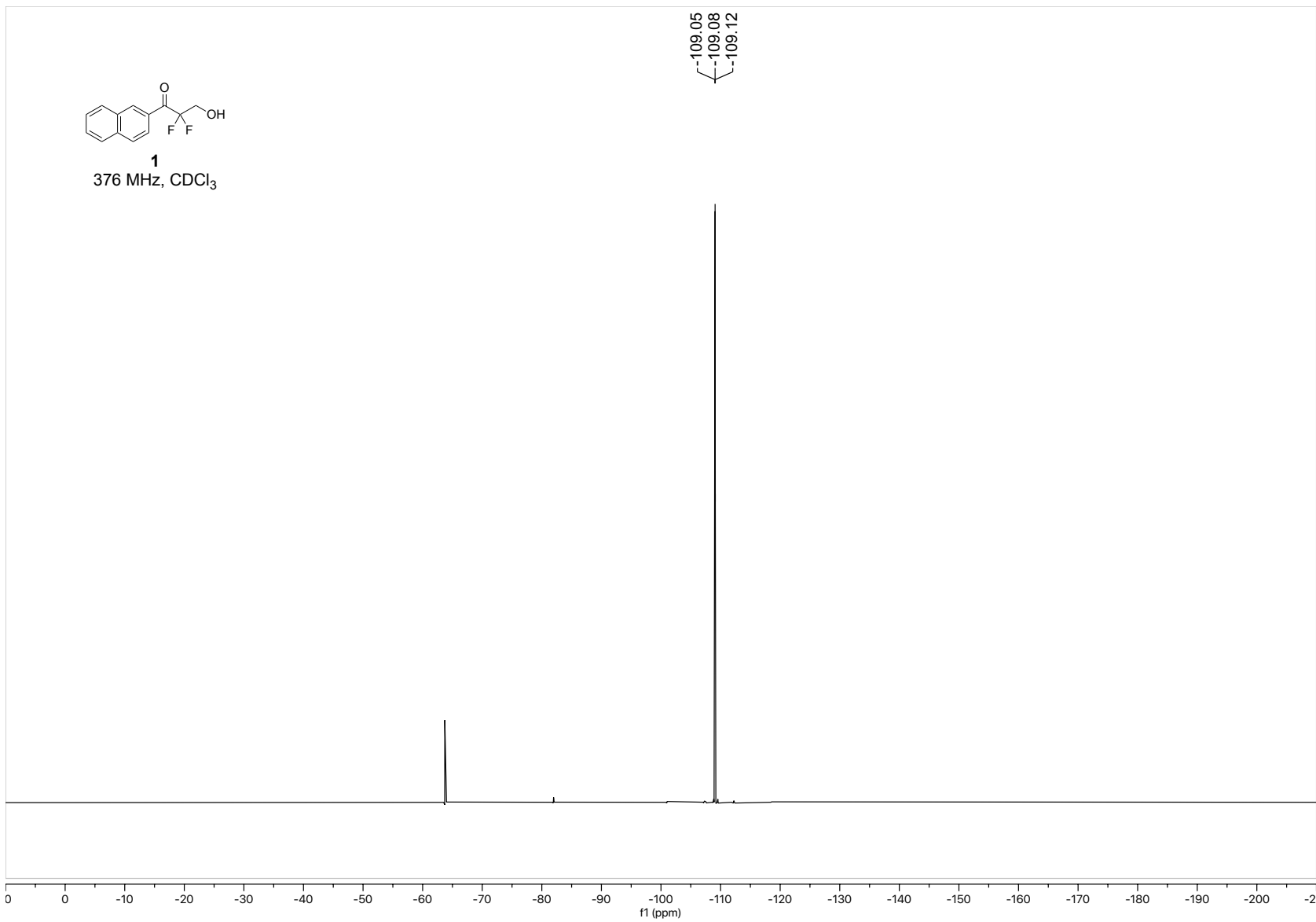


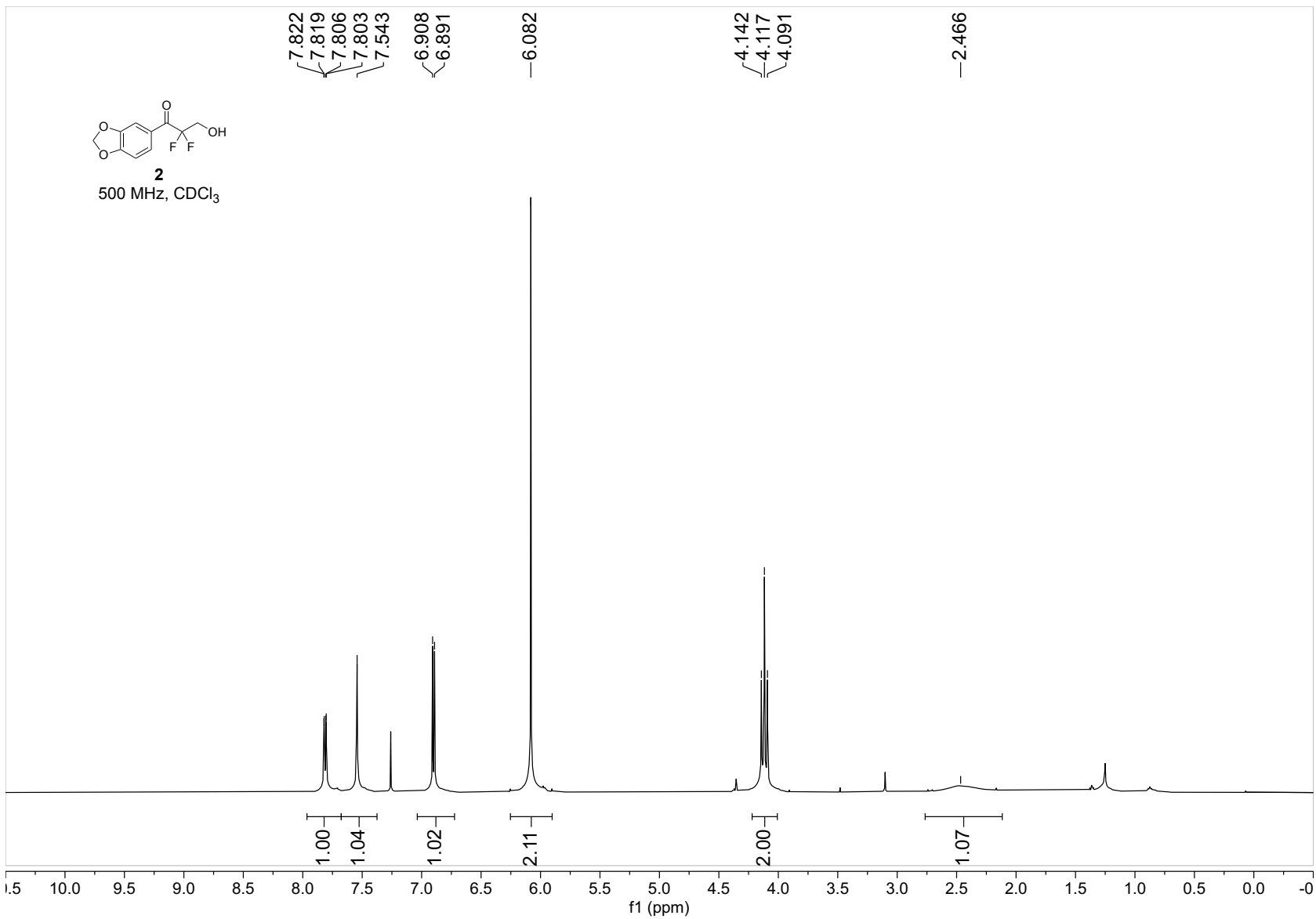


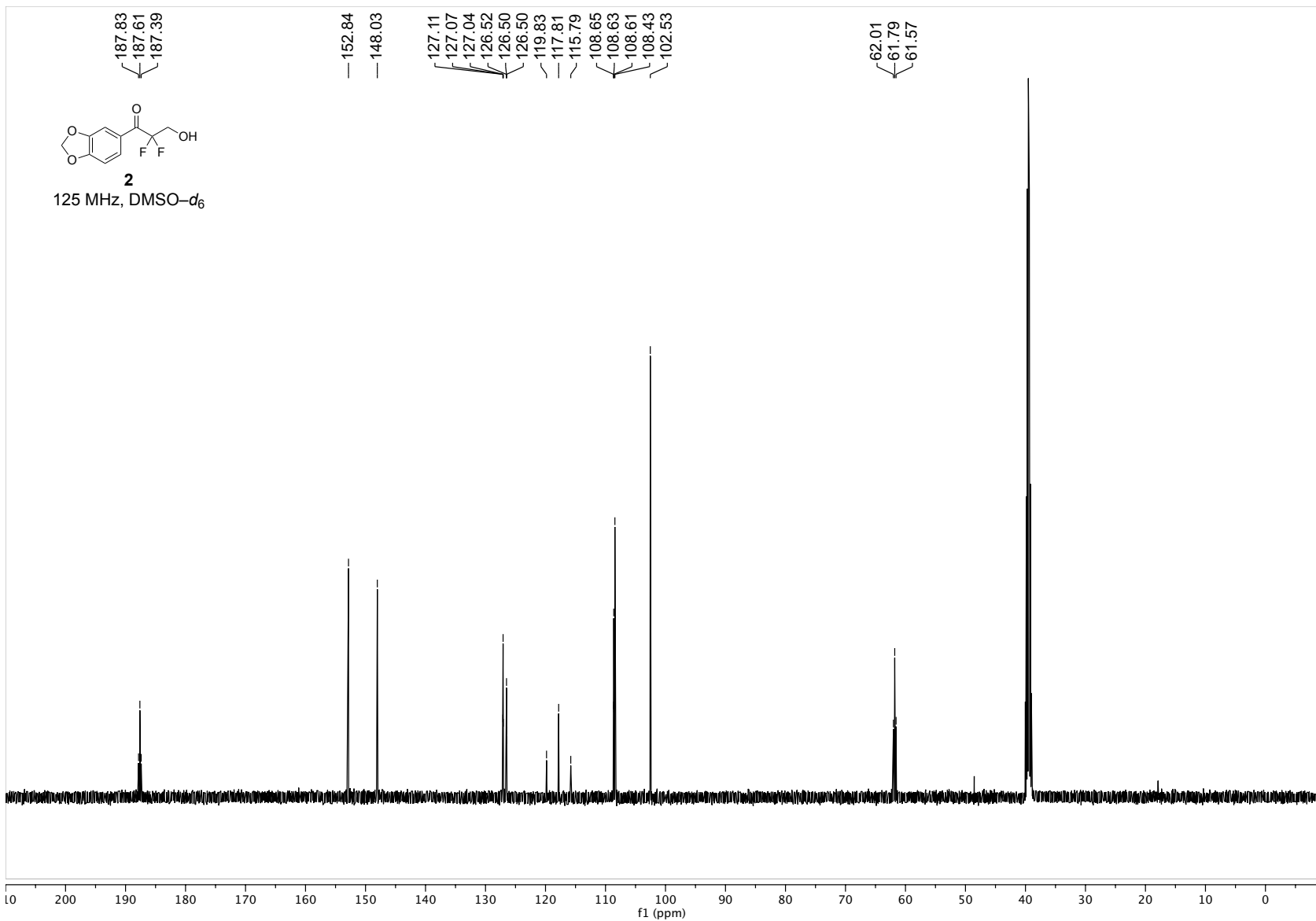


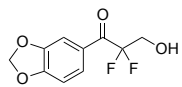
1
376 MHz, CDCl₃

-109.05
-109.08
-109.12



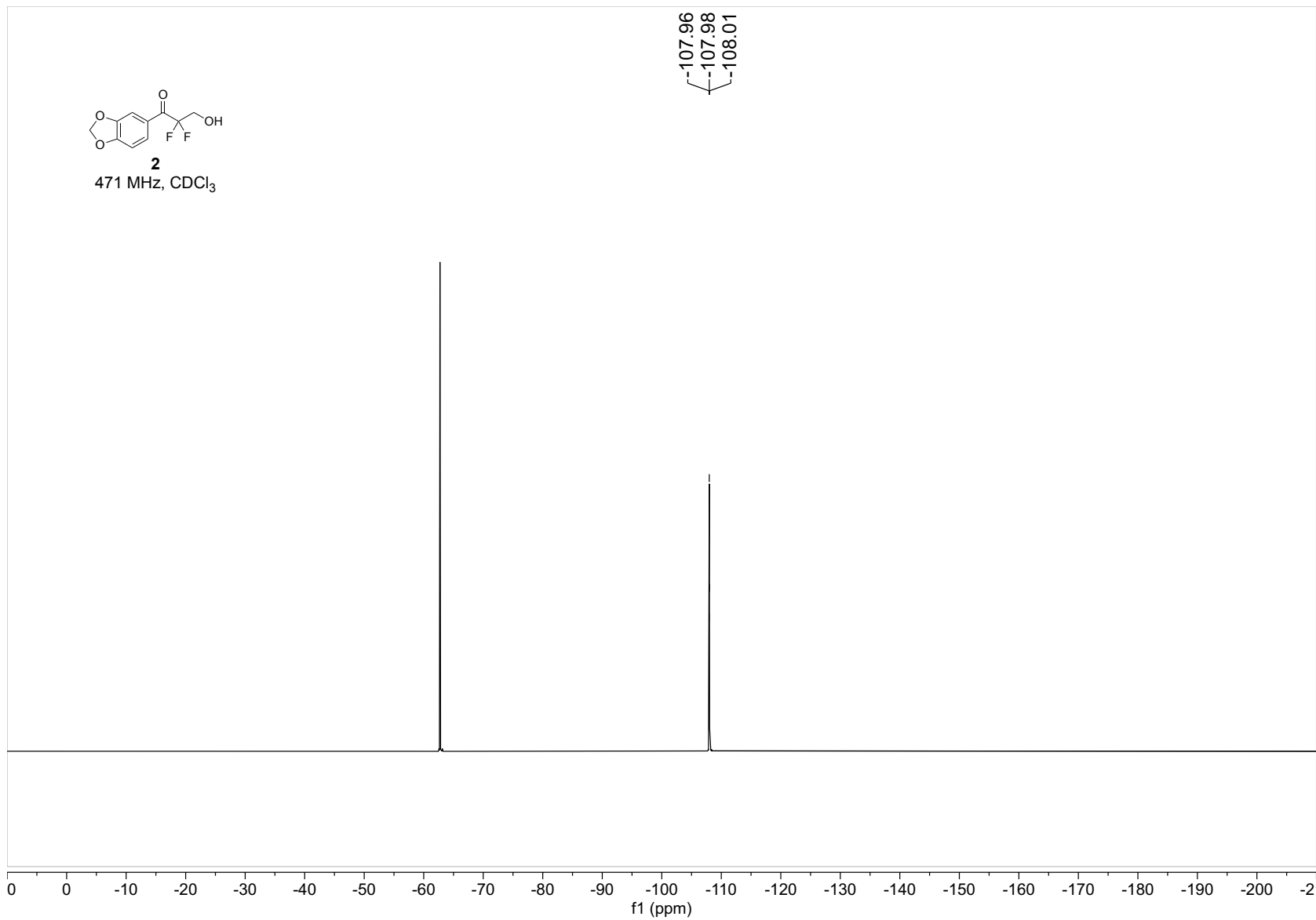


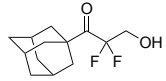




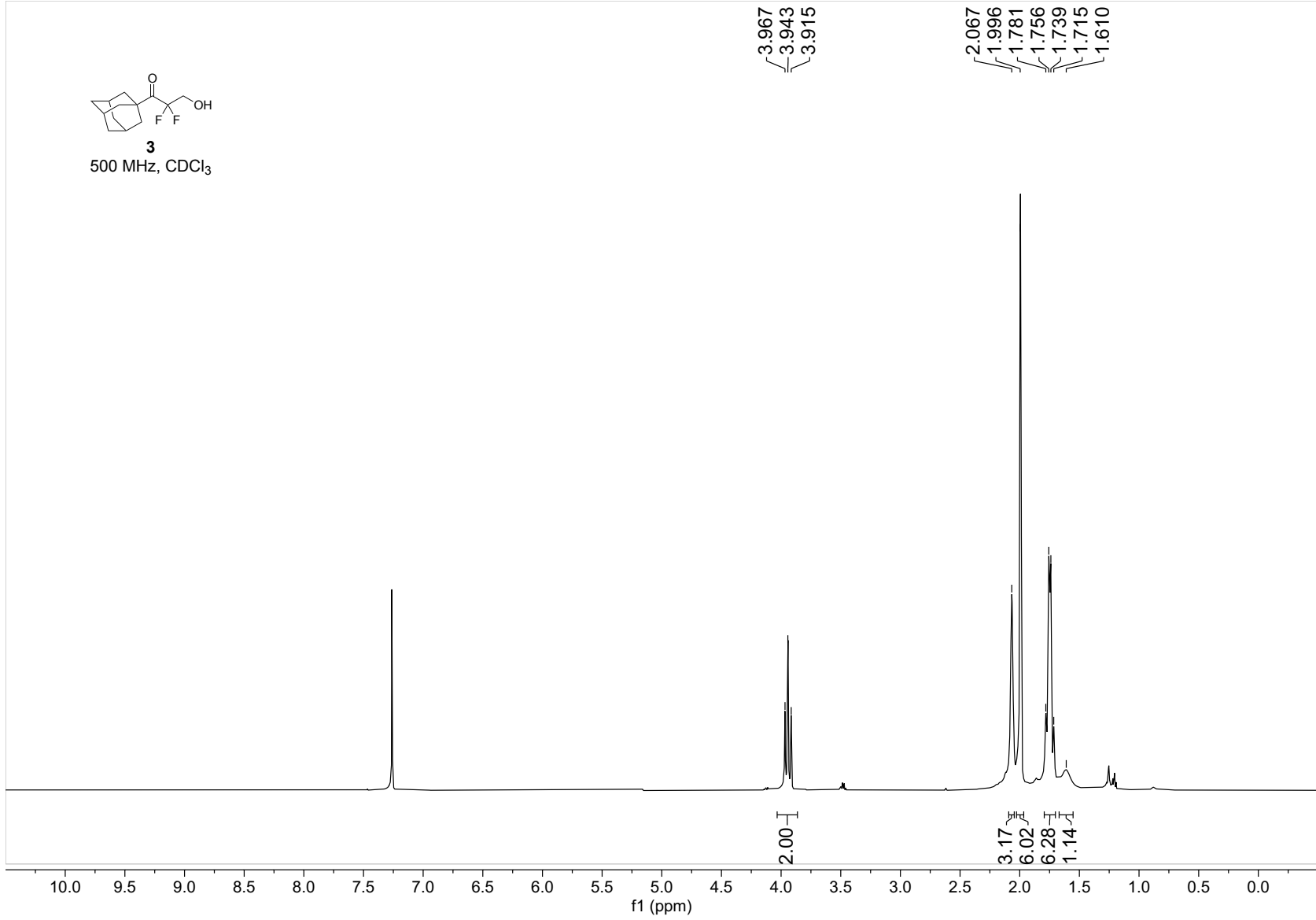
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471 MHz, CDCl₃

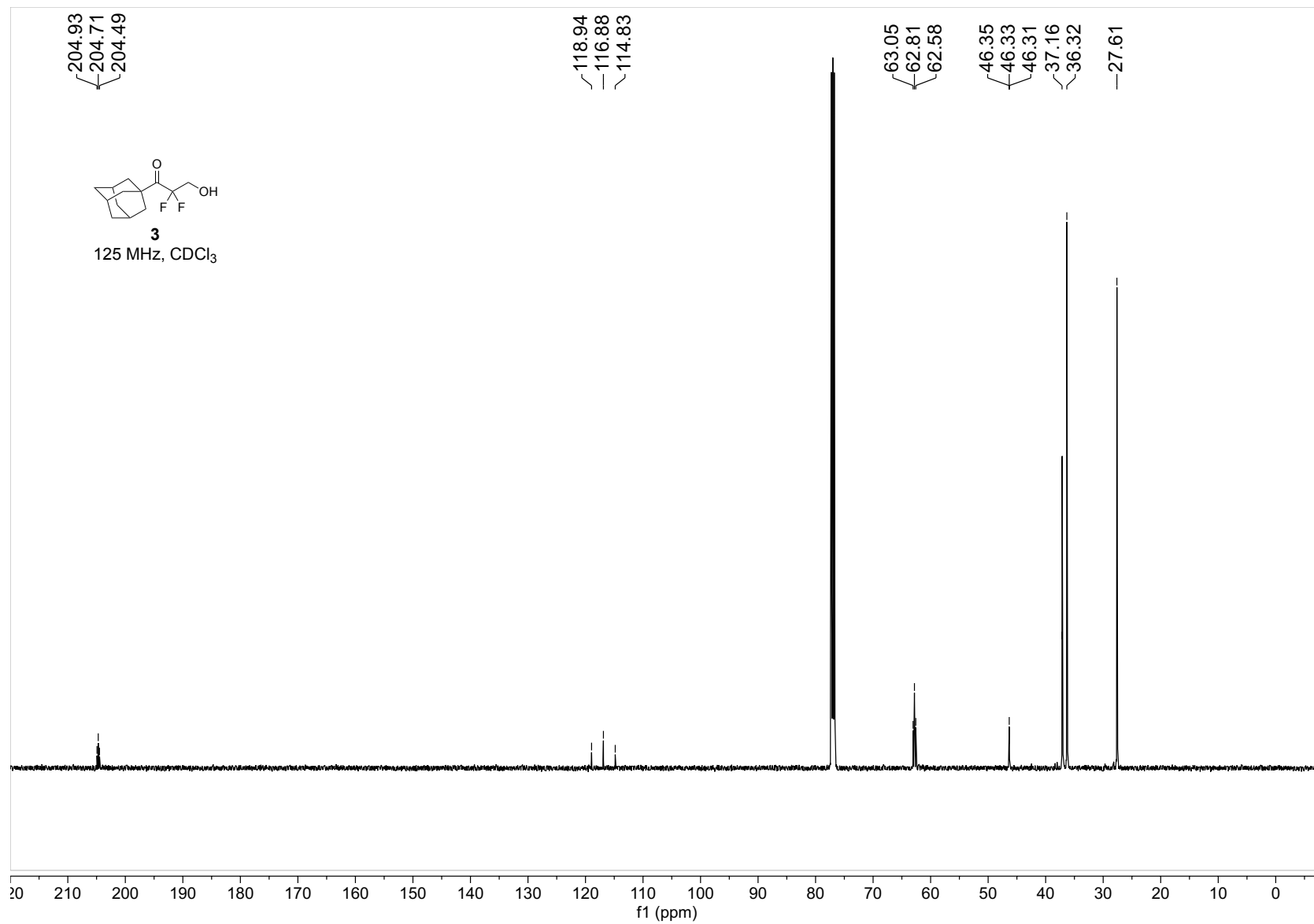
107.96
107.98
108.01

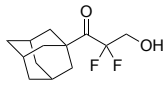




3
500 MHz, CDCl₃



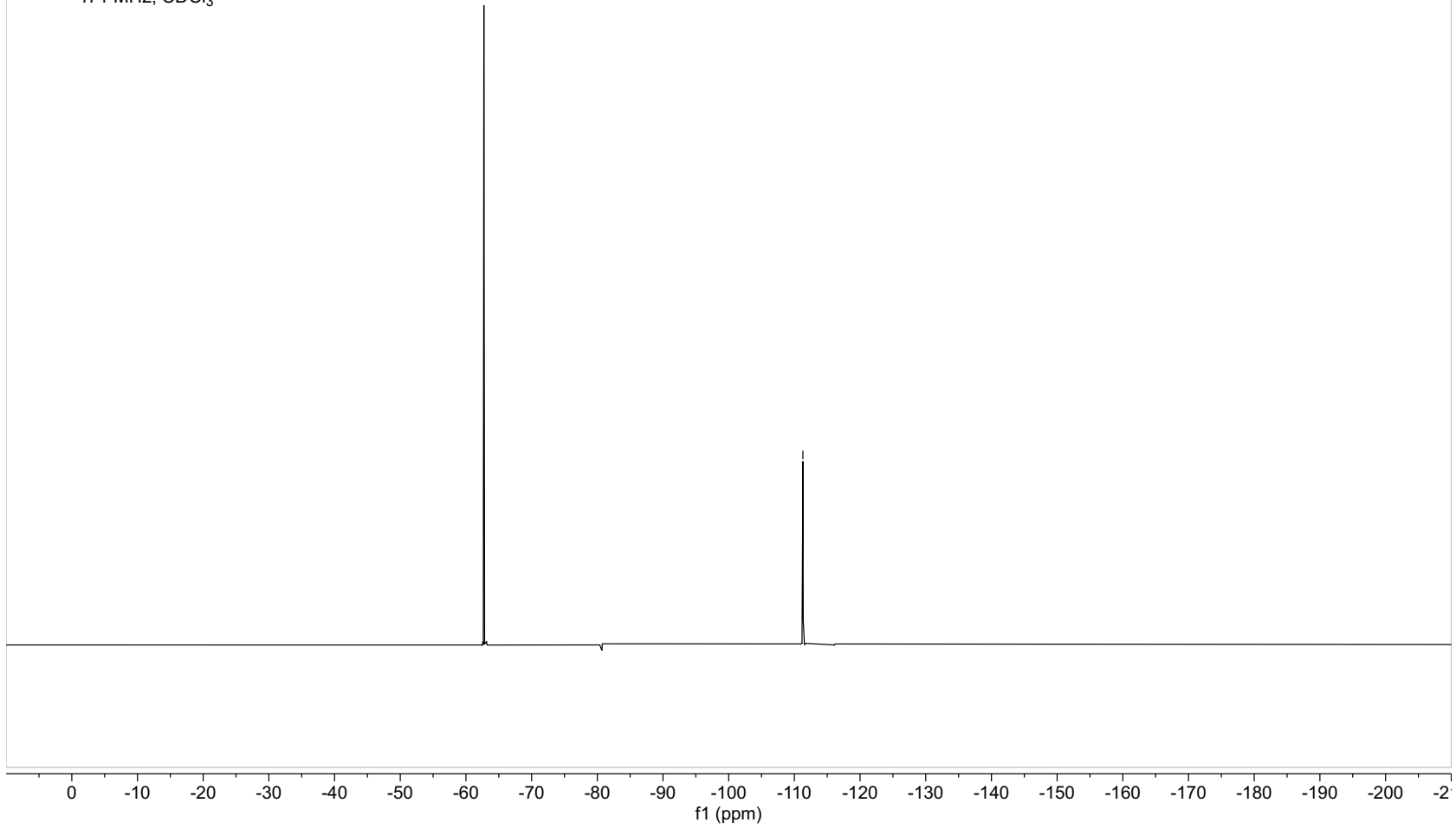


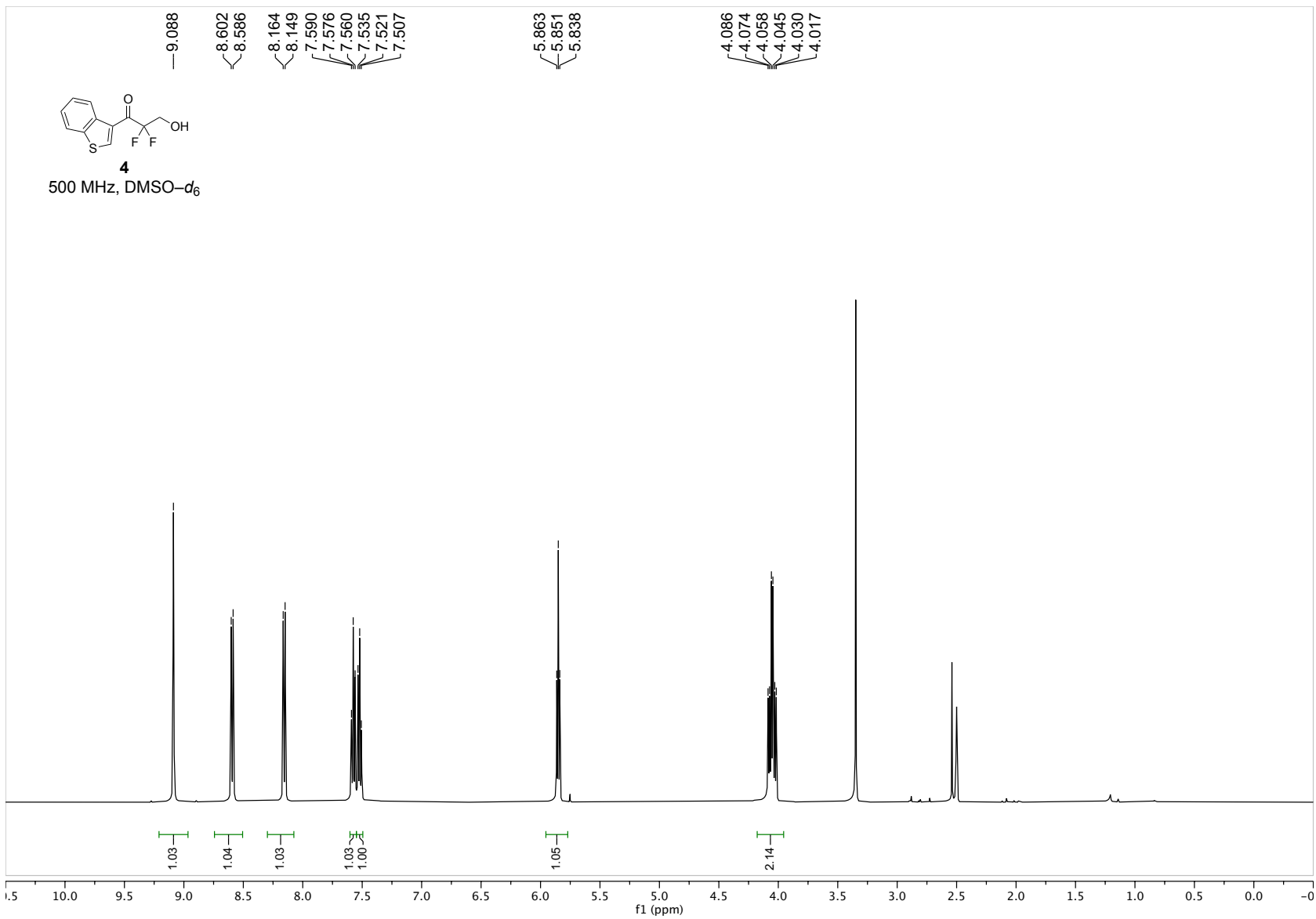


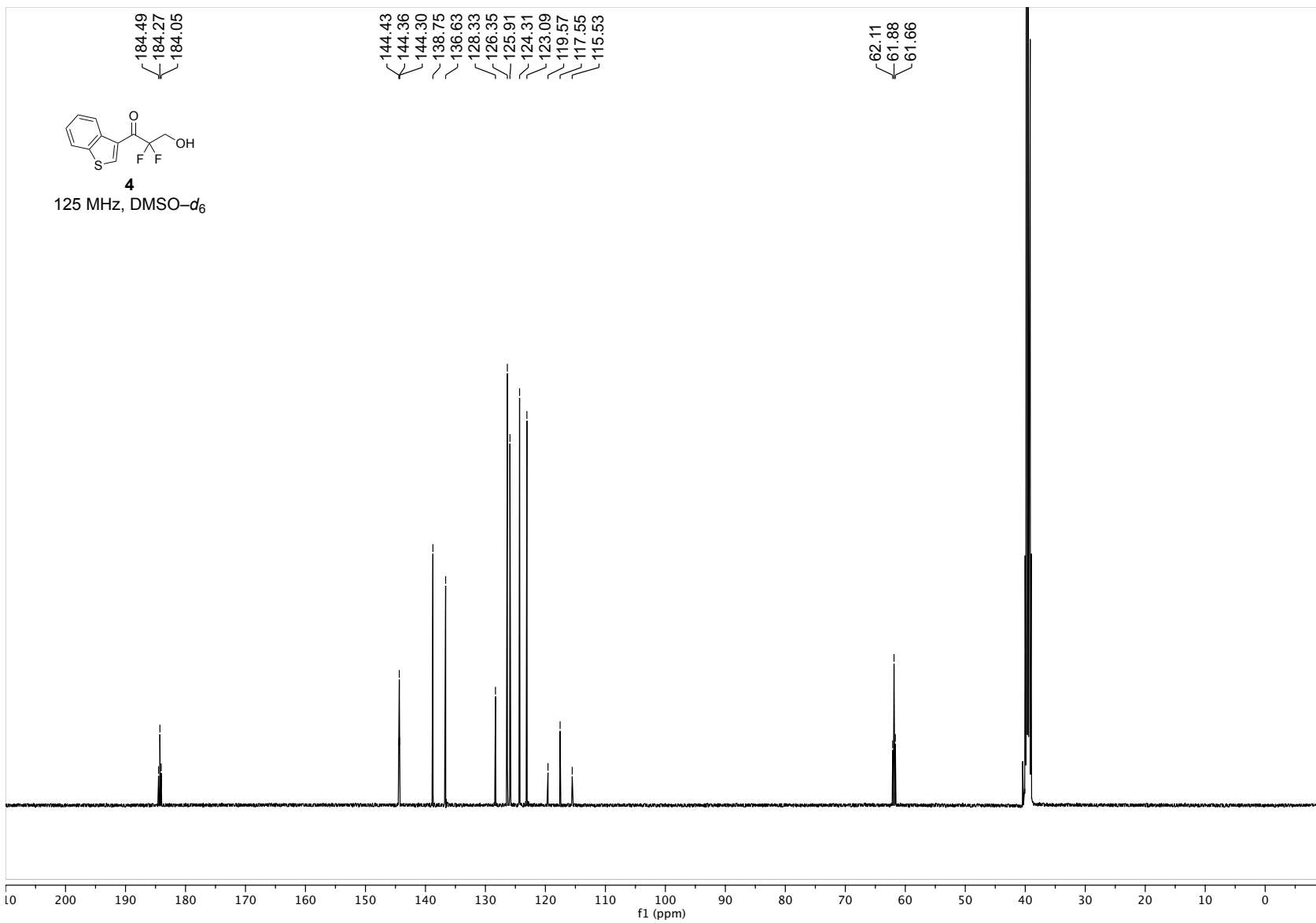
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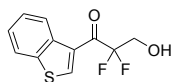
471 MHz, CDCl₃

-111.27
-111.30
-111.33





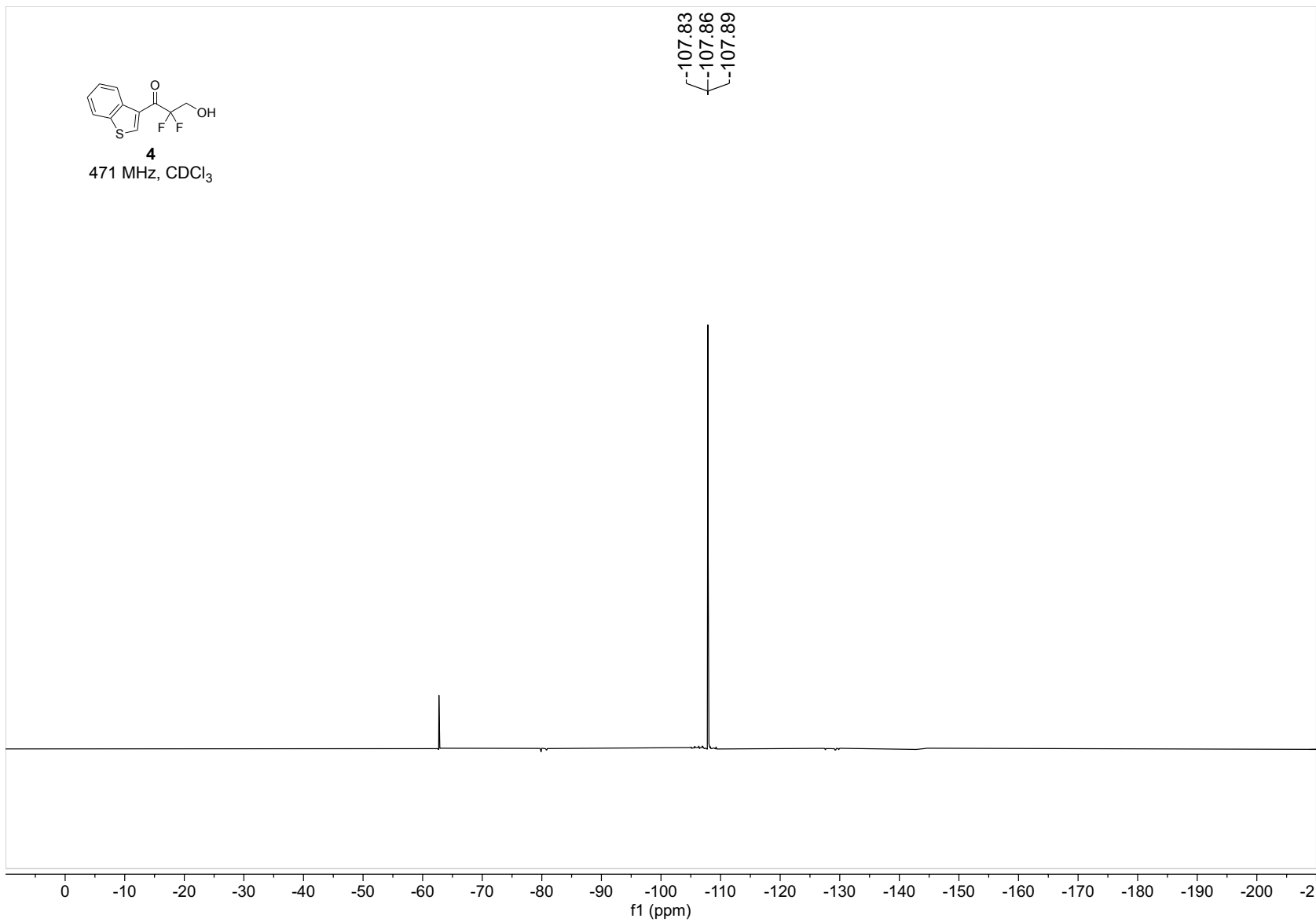


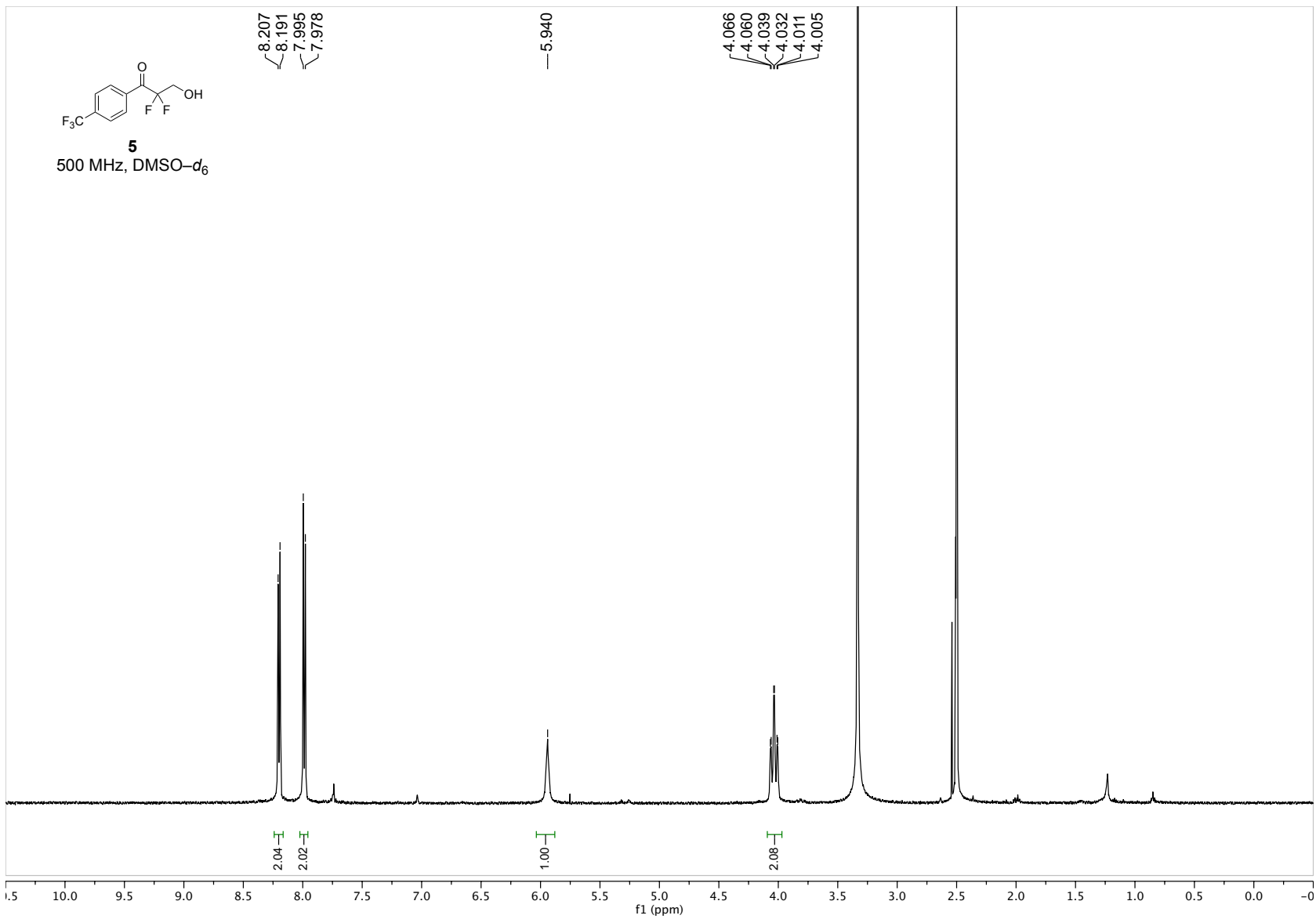


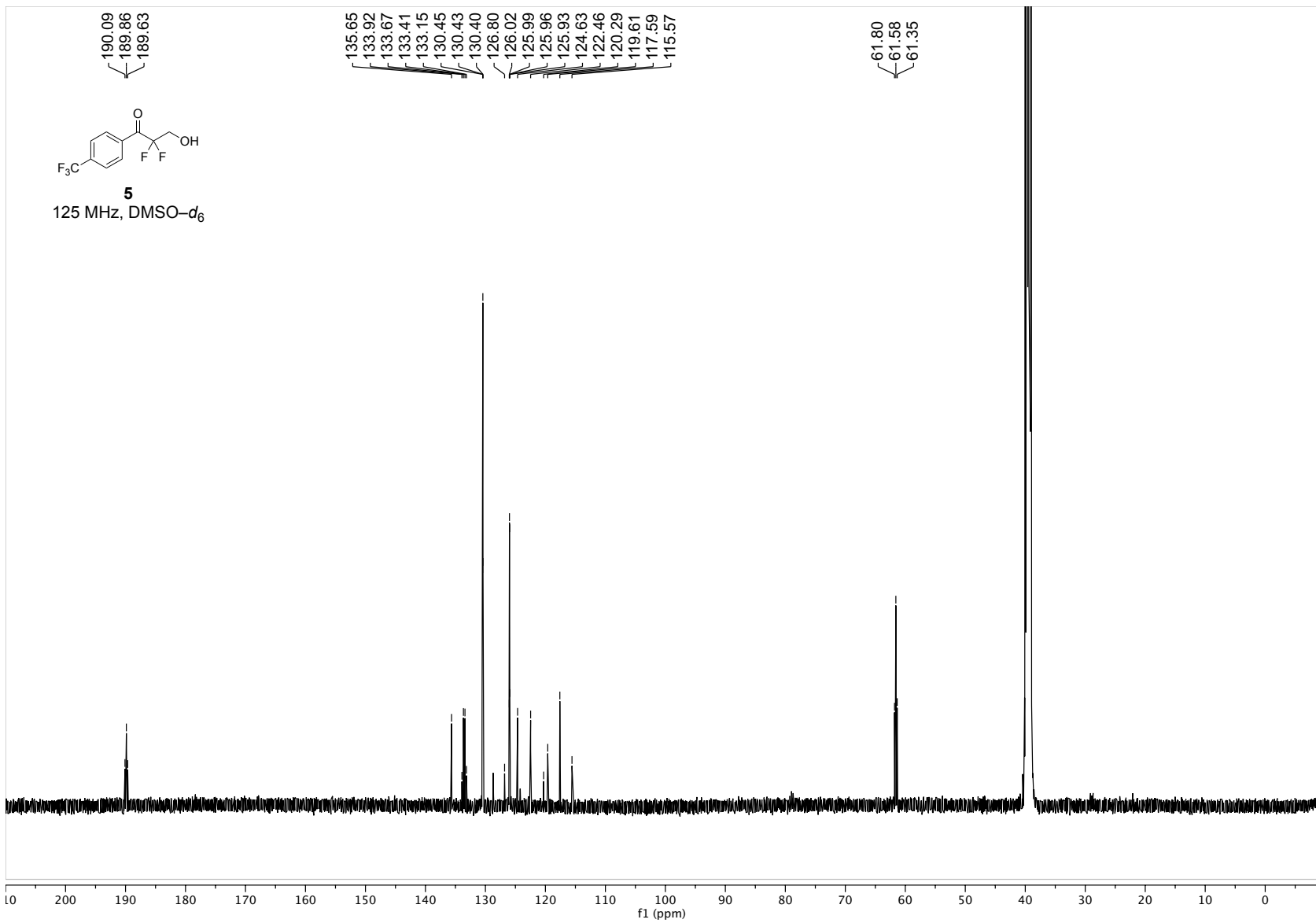
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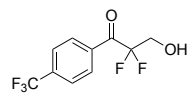
471 MHz, CDCl₃

107.83
107.86
107.89



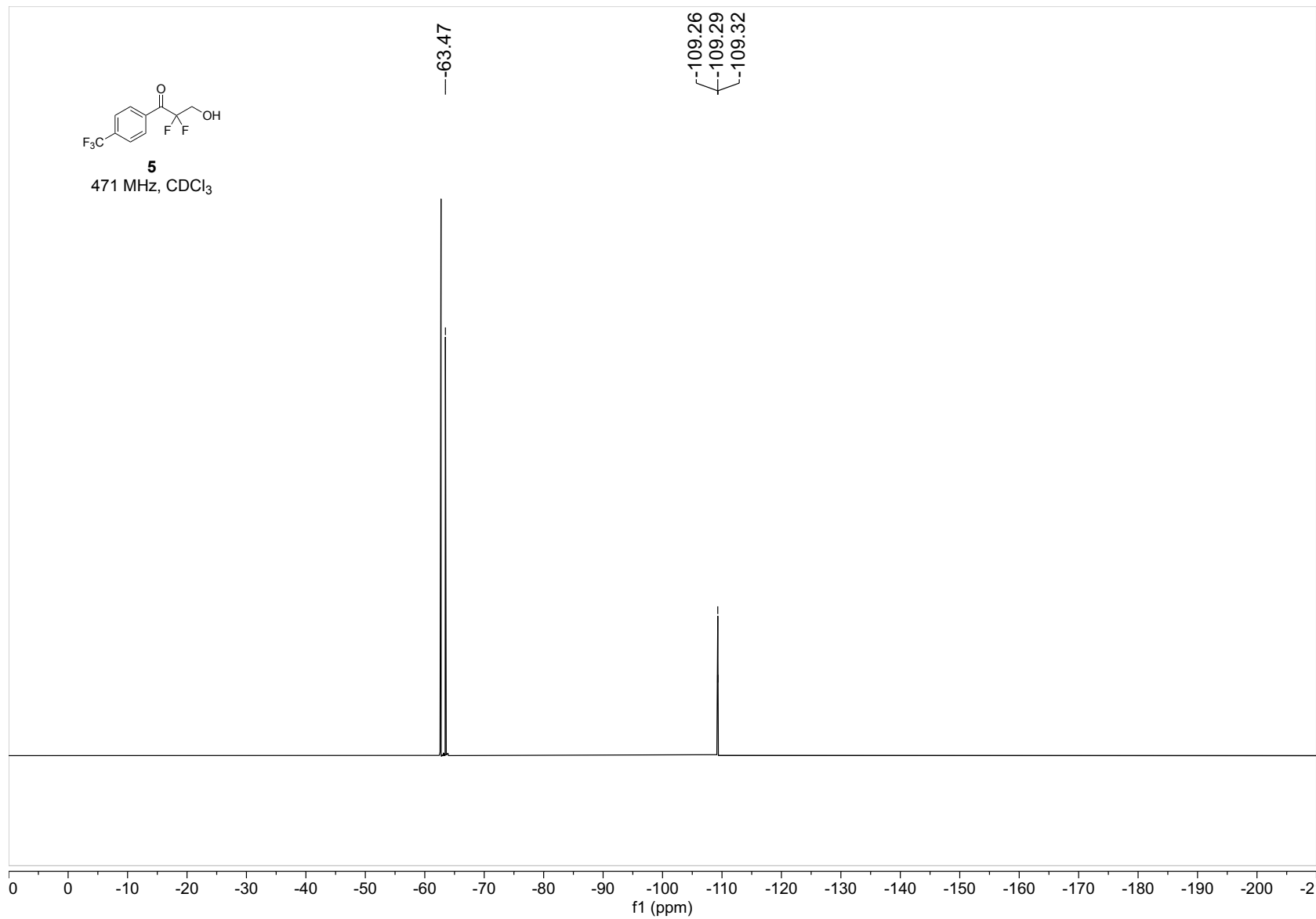


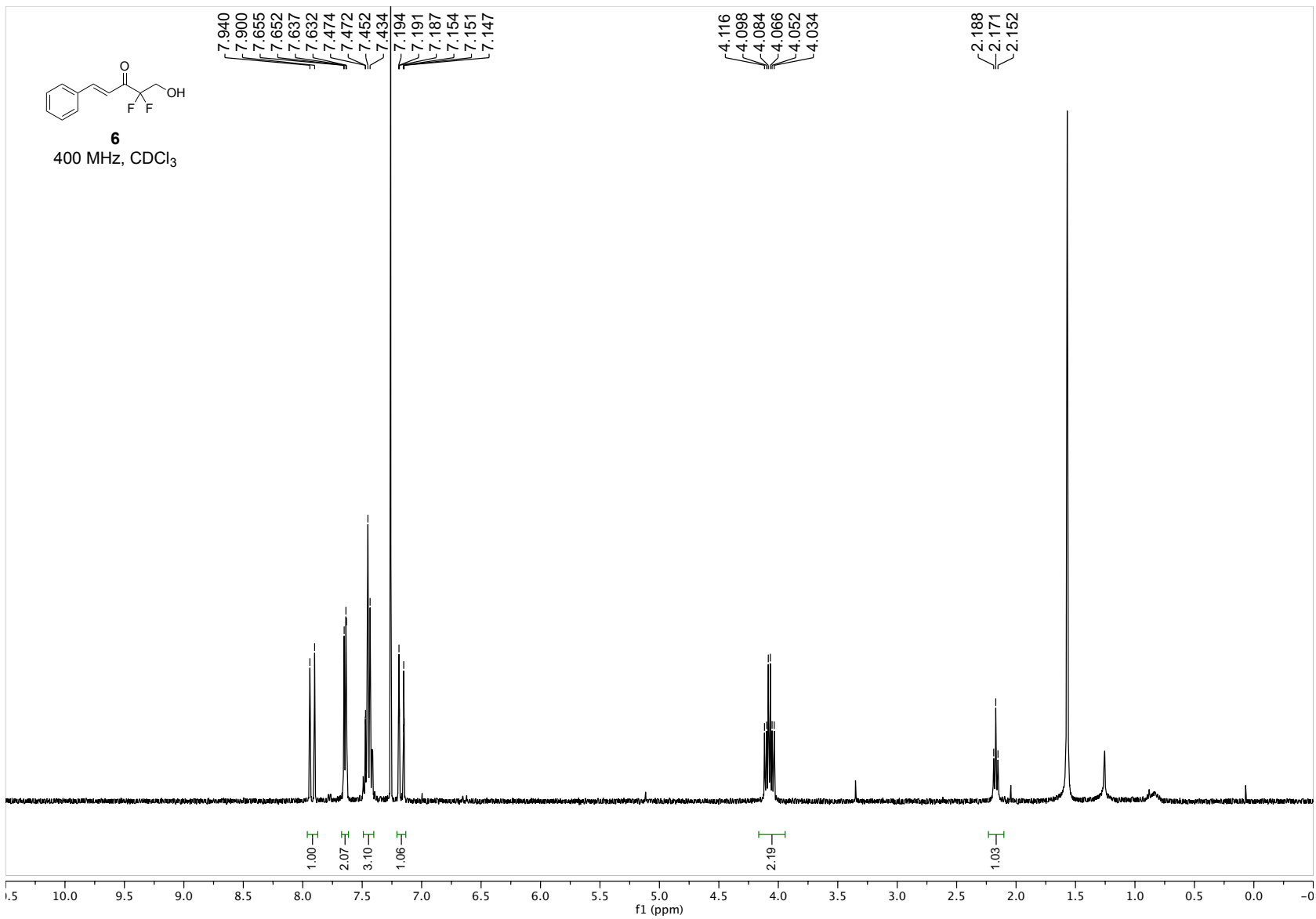


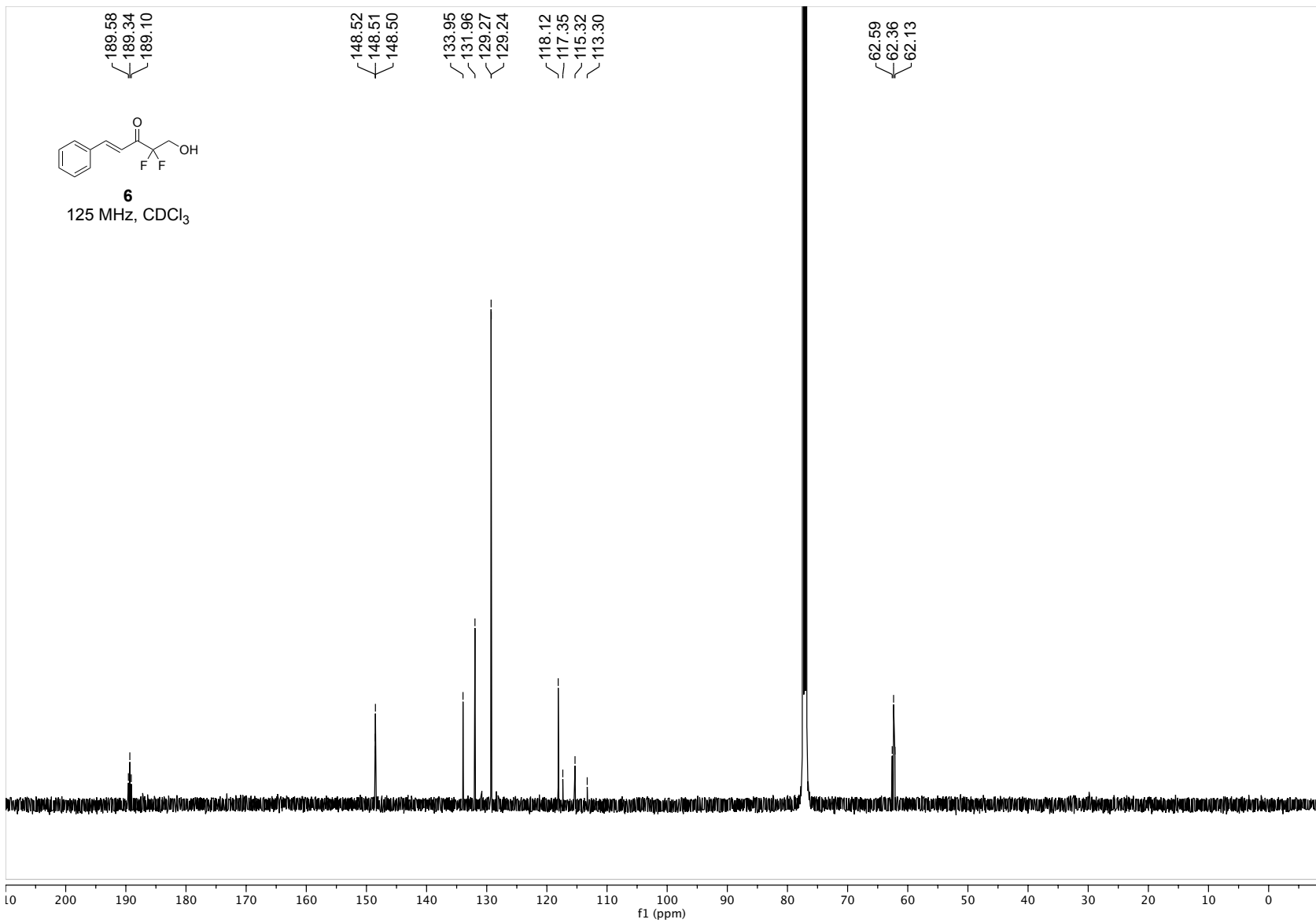


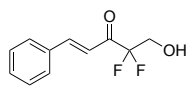
5

471 MHz, CDCl₃

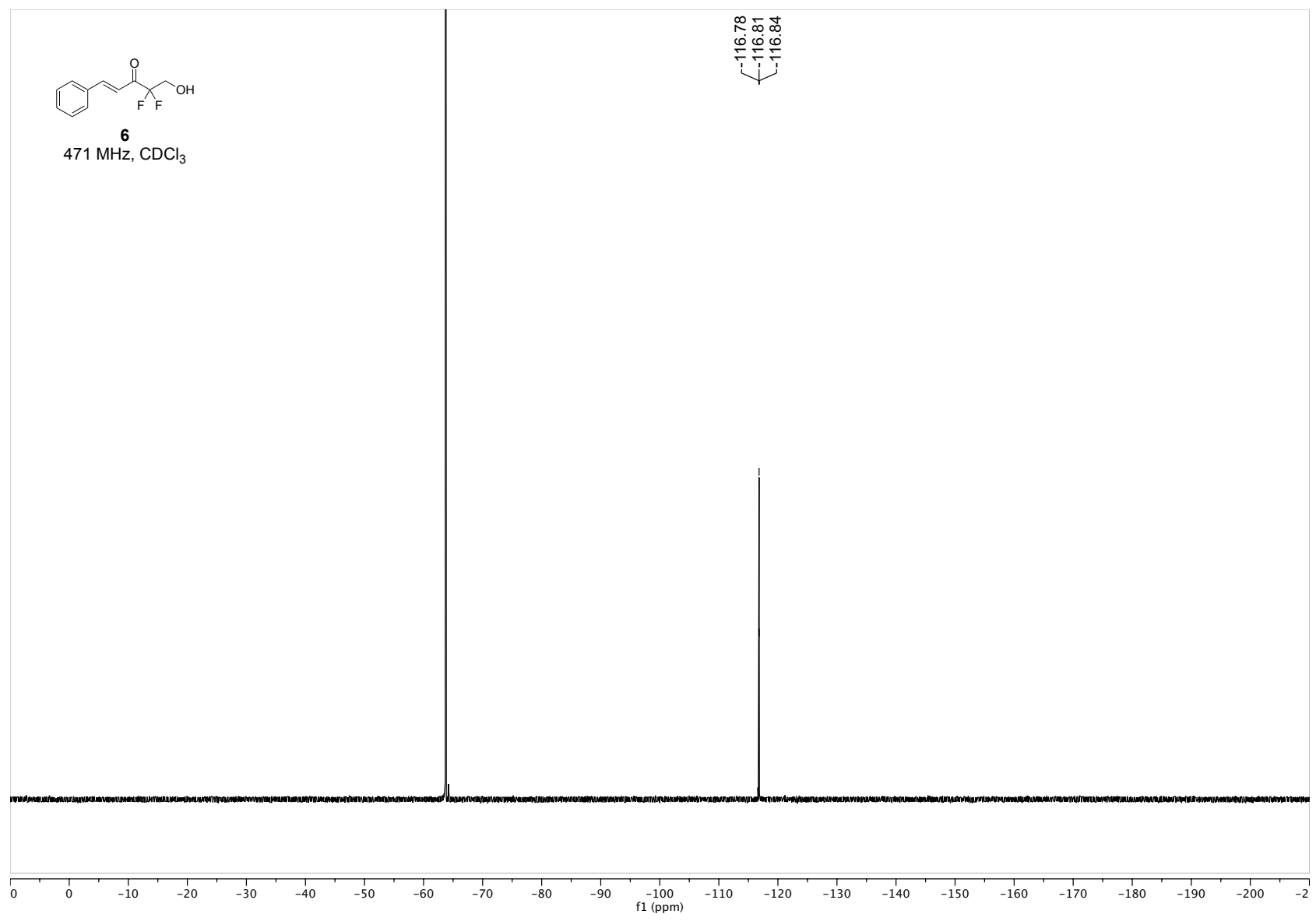


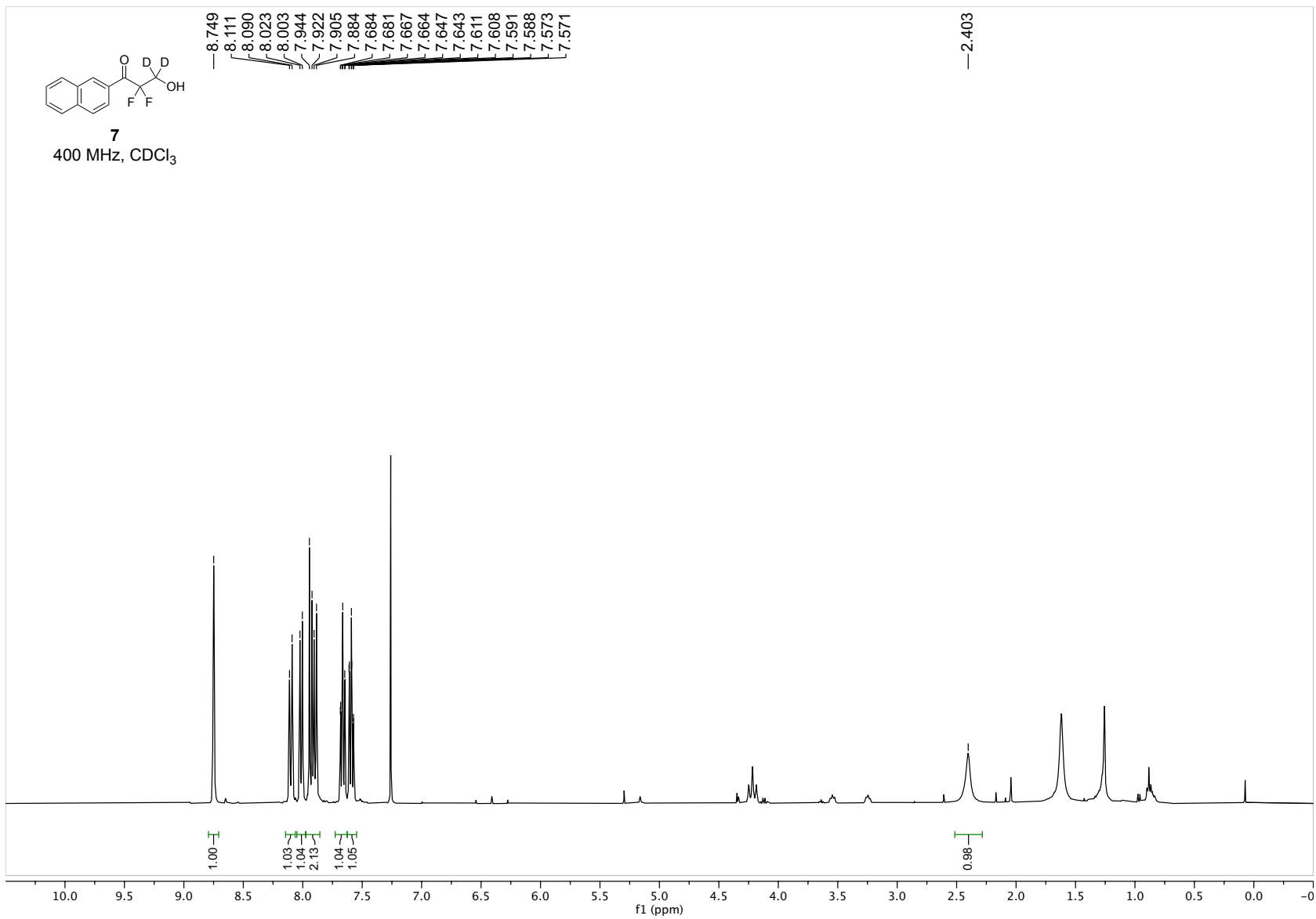


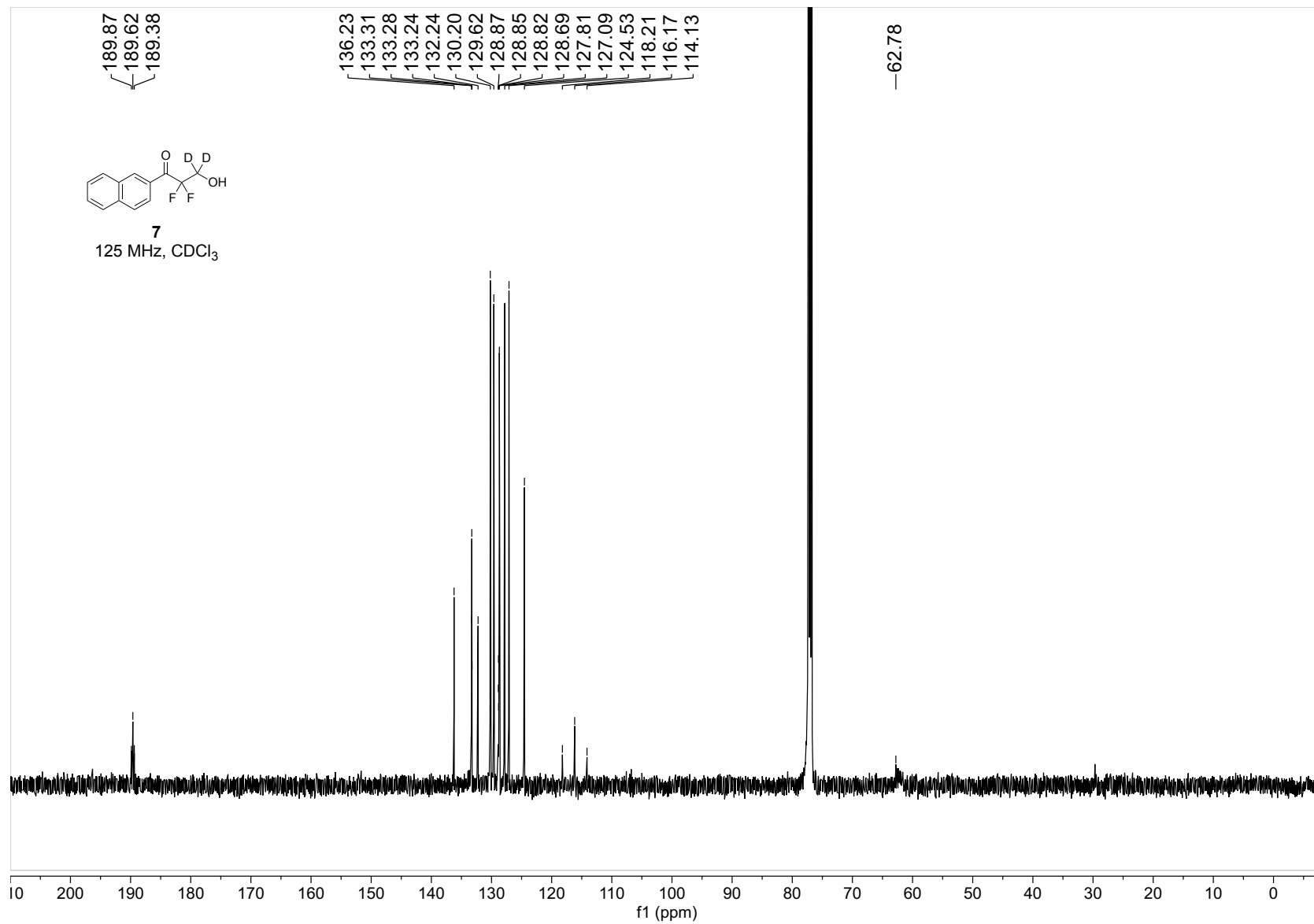


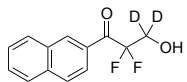


6
471 MHz, CDCl₃

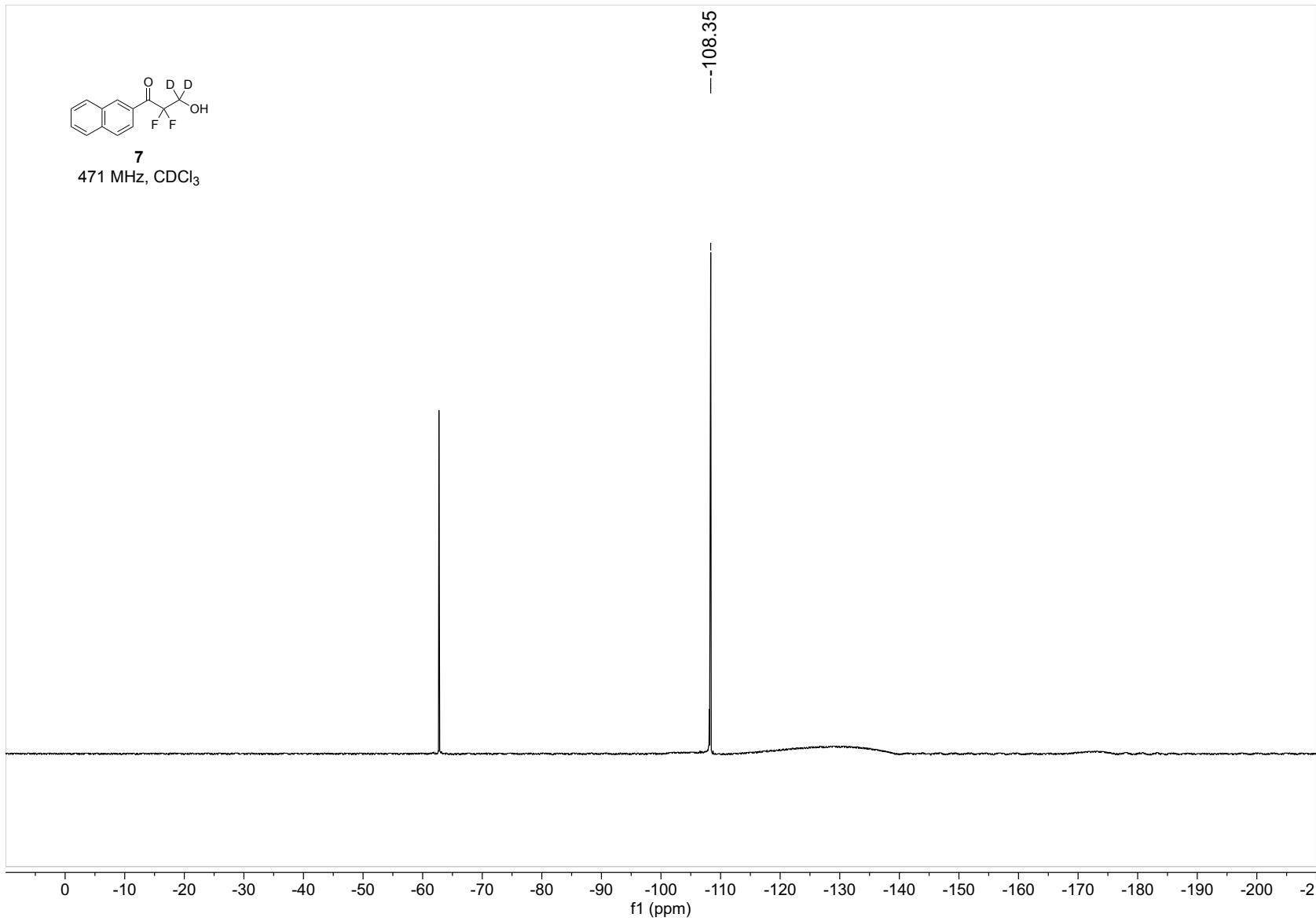


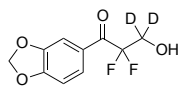




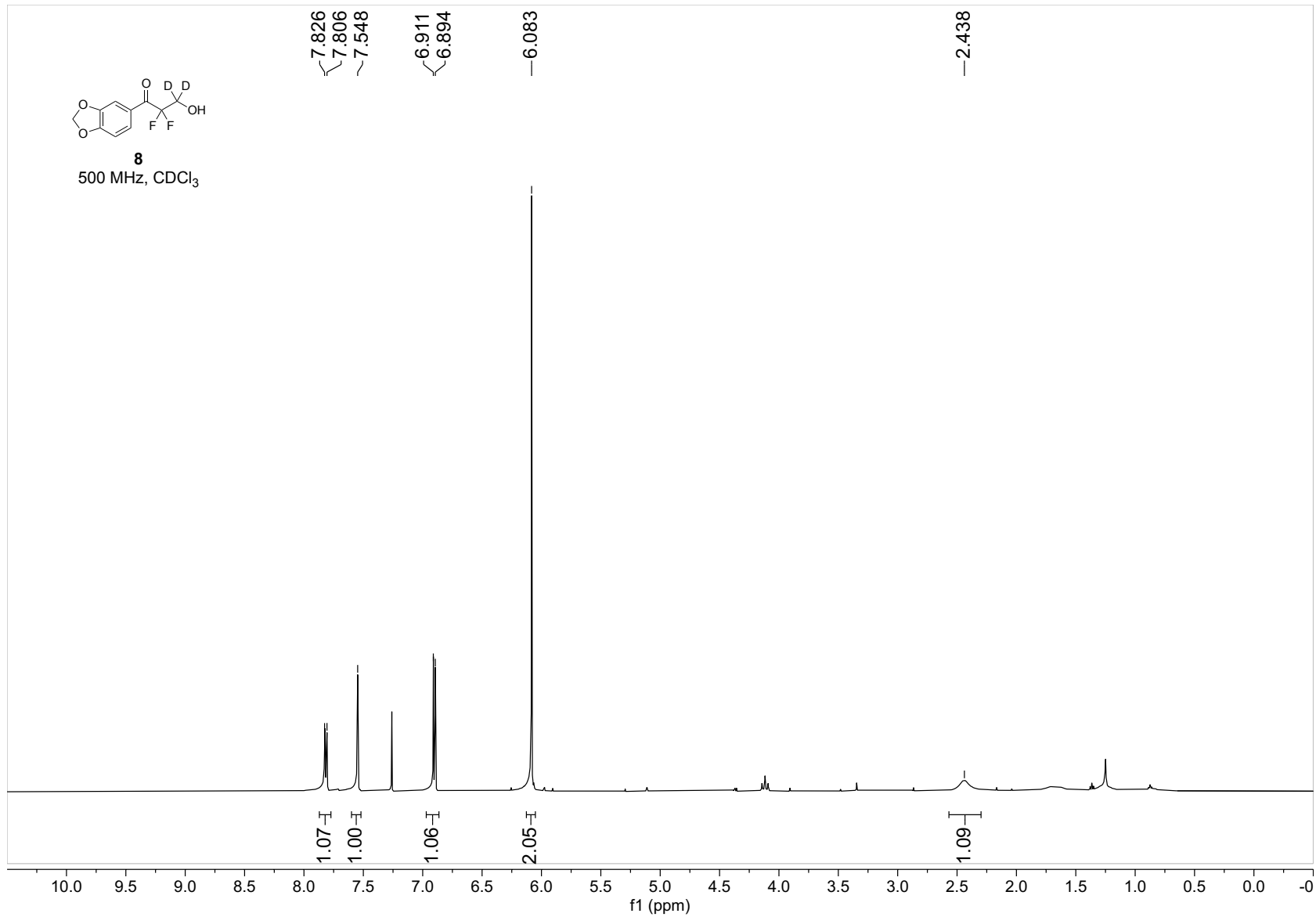


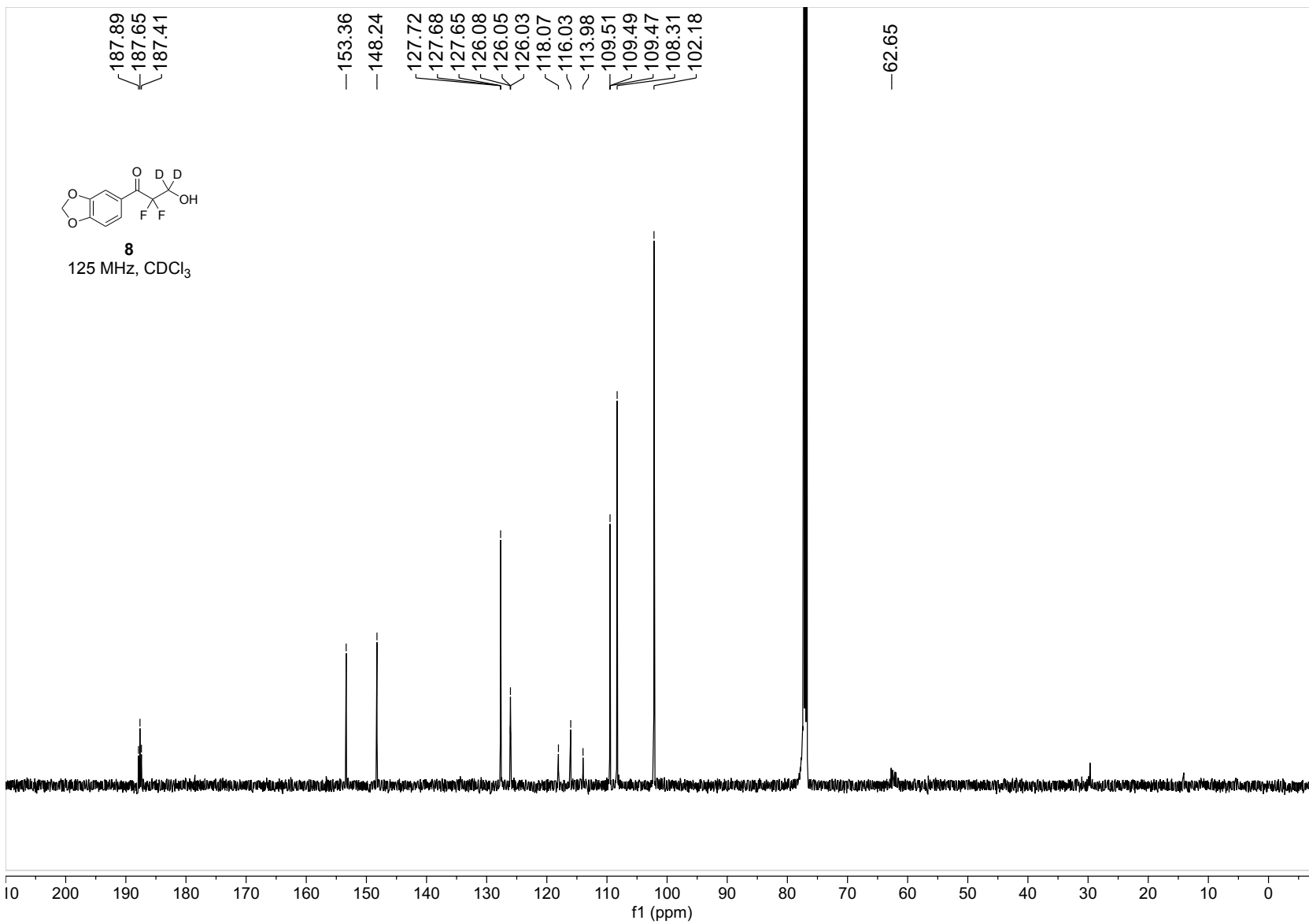
7
471 MHz, CDCl₃

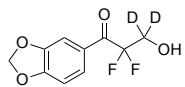




8
500 MHz, CDCl₃

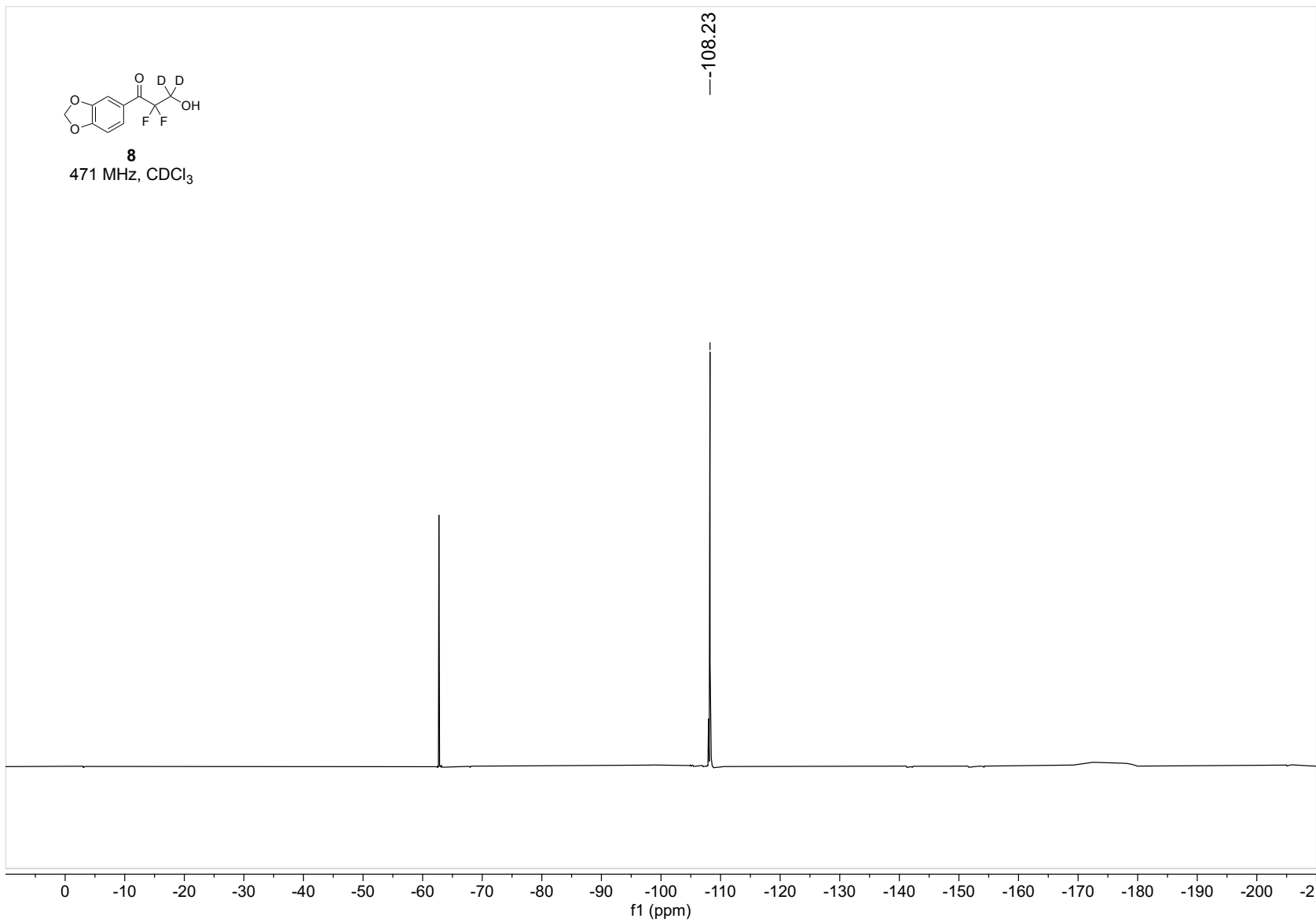


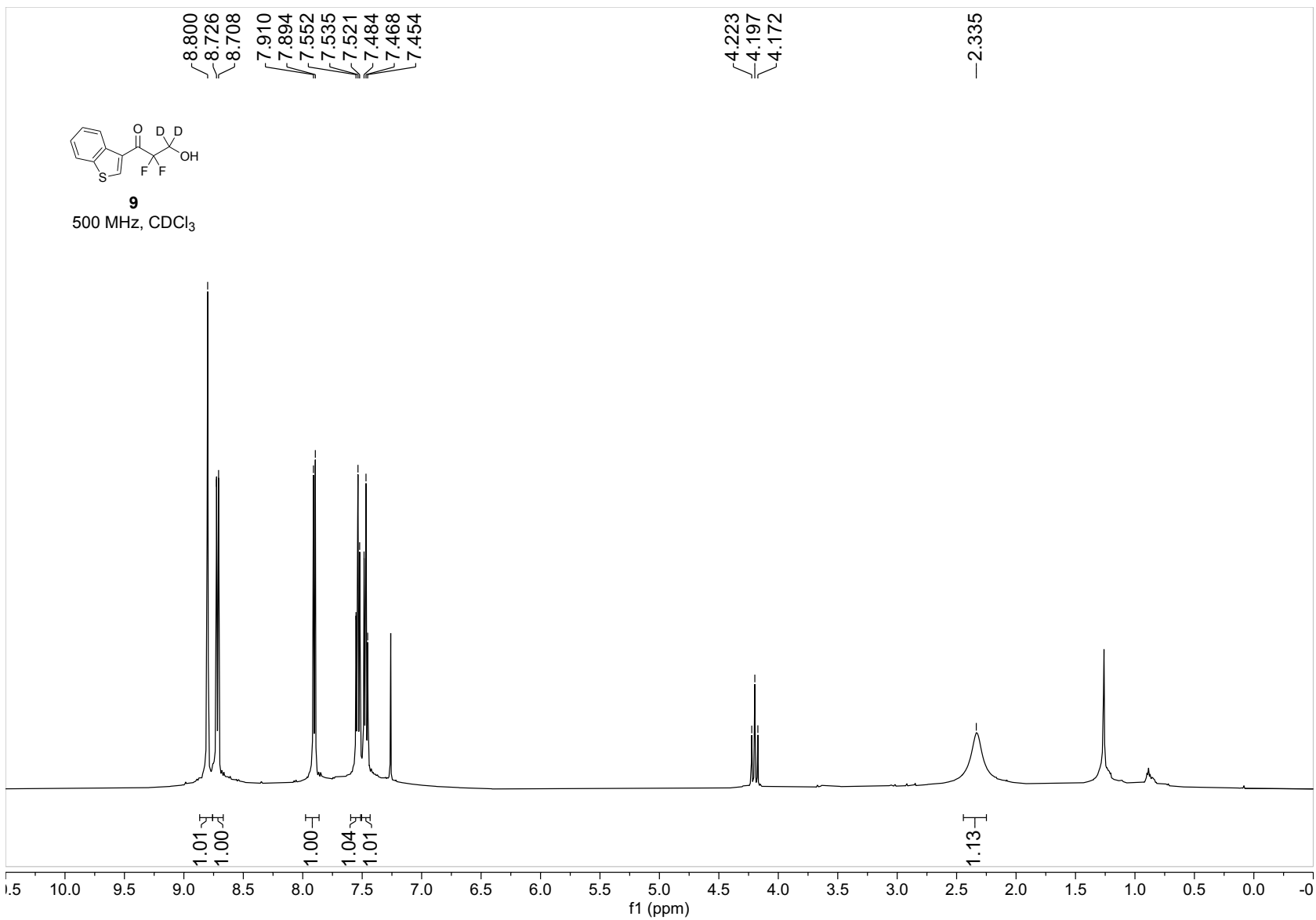


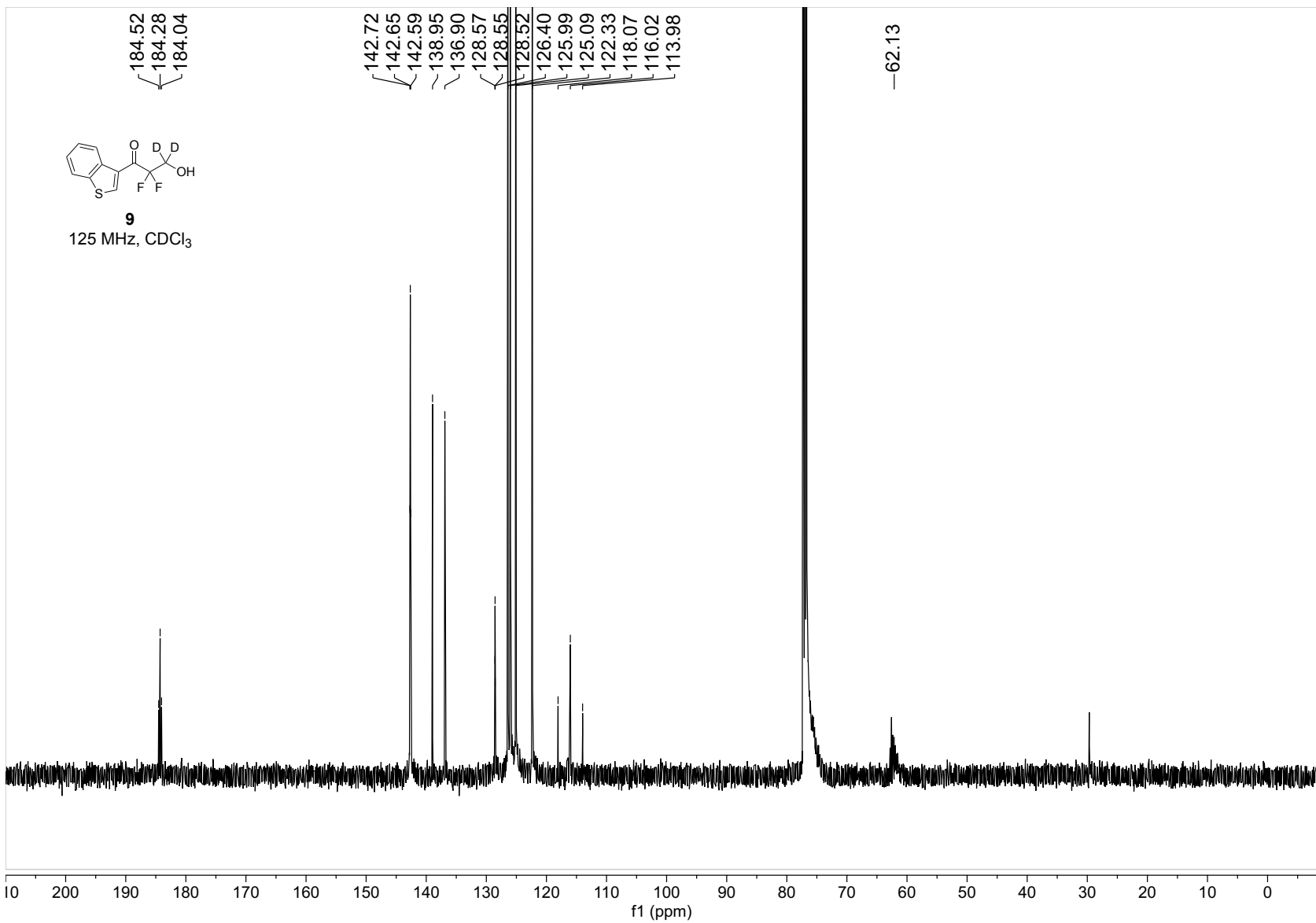


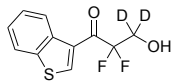
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471 MHz, CDCl₃

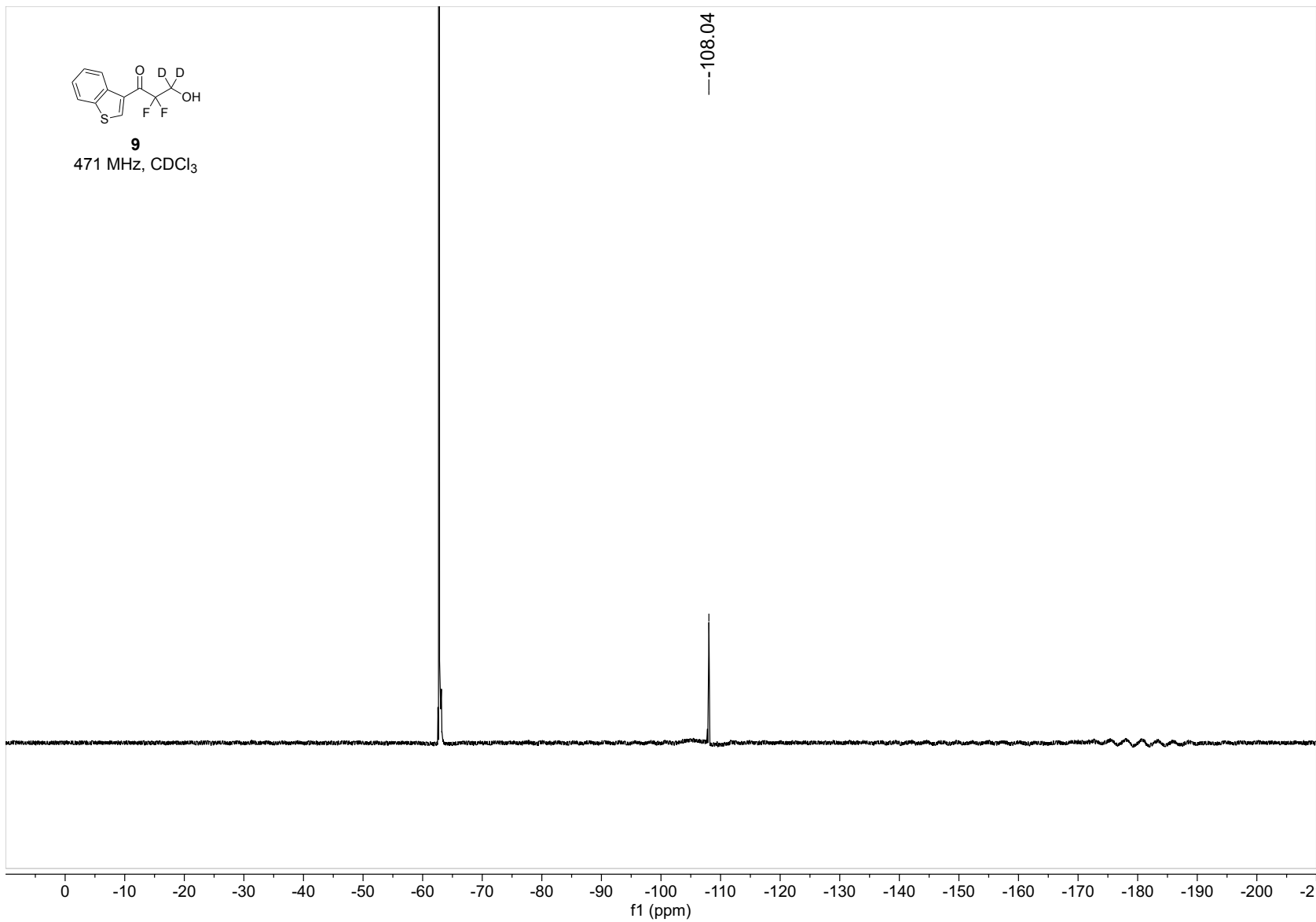


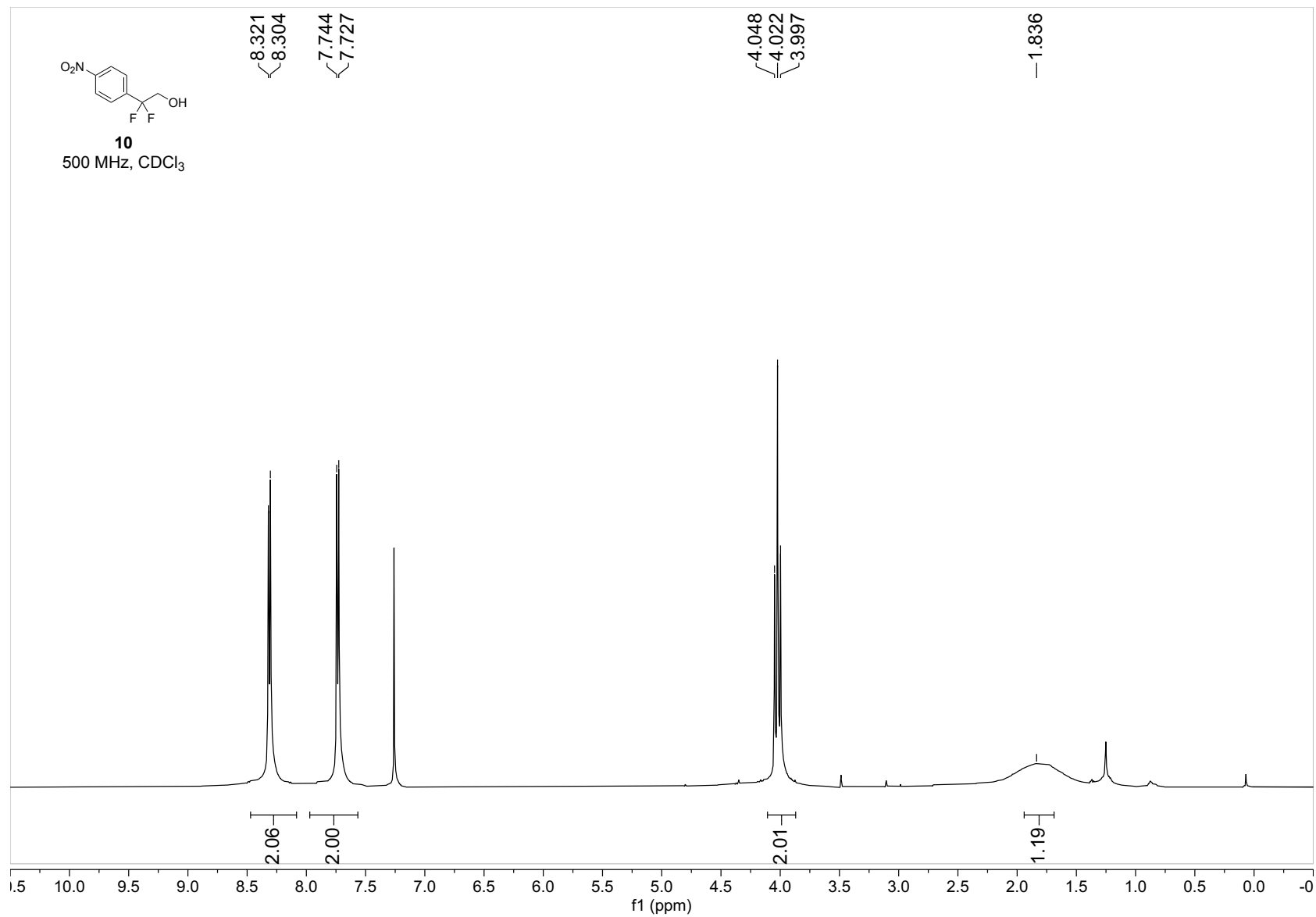


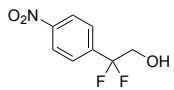




9
471 MHz, CDCl₃

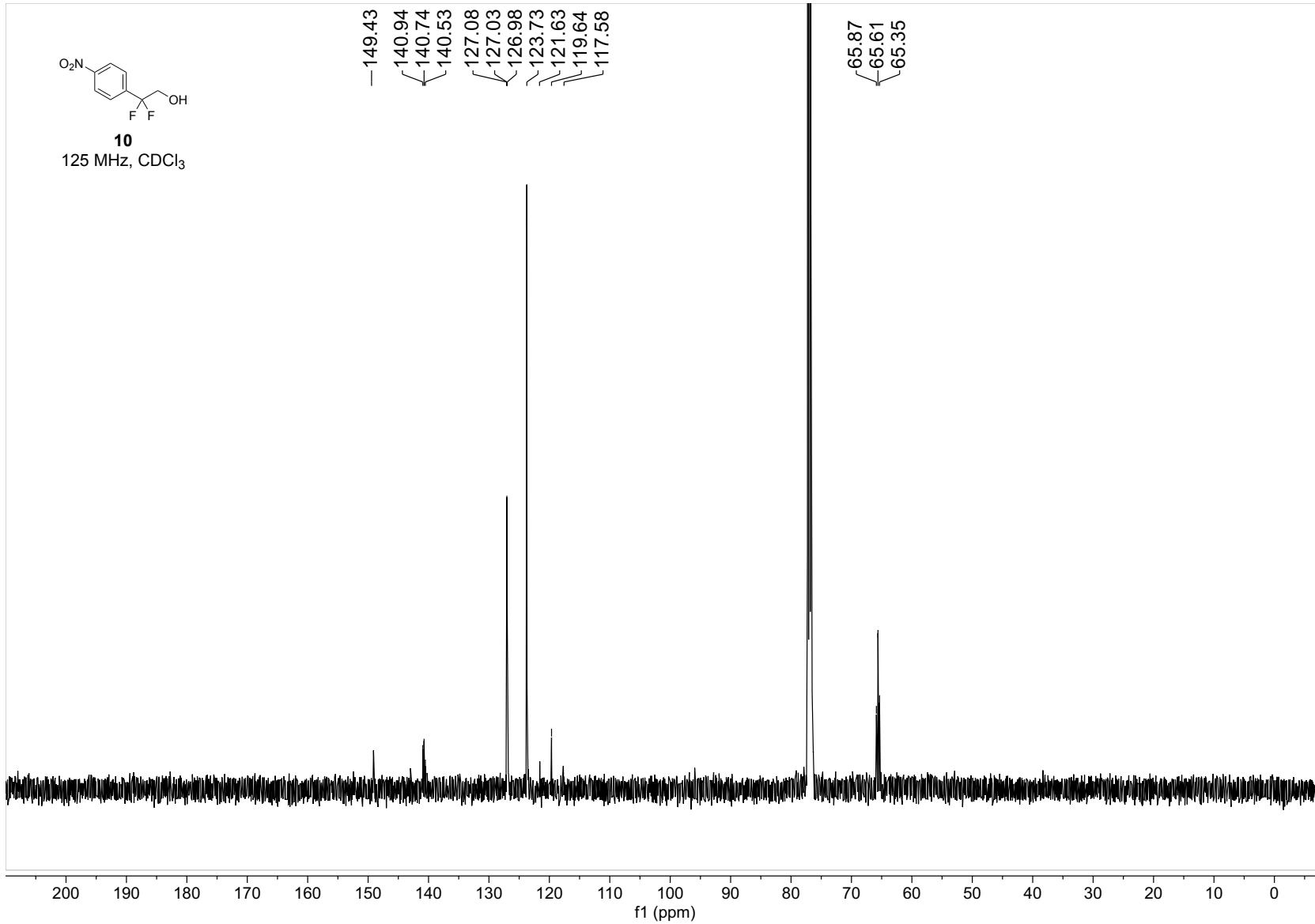


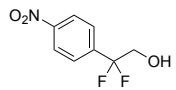




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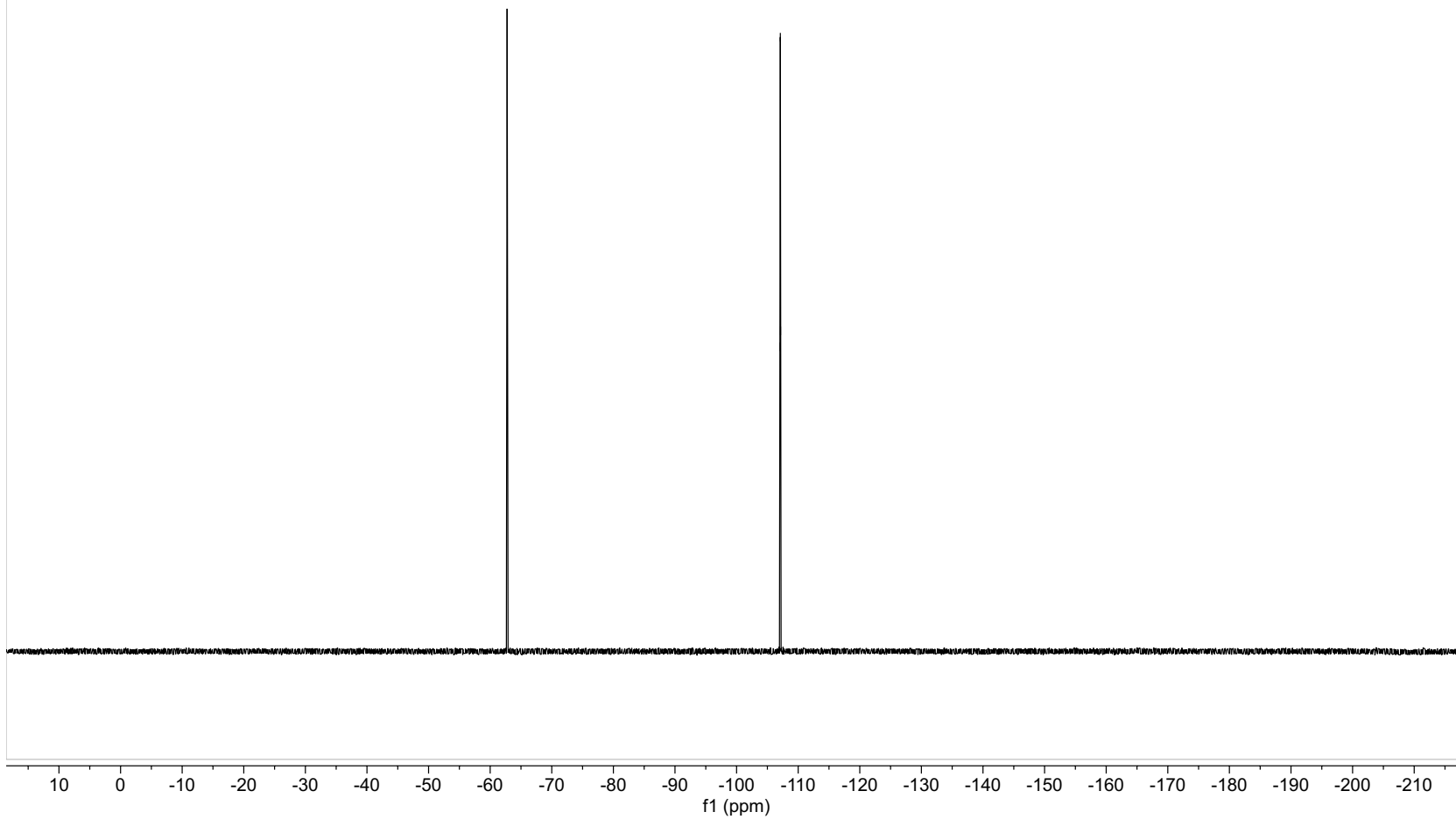
125 MHz, CDCl₃

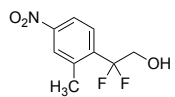




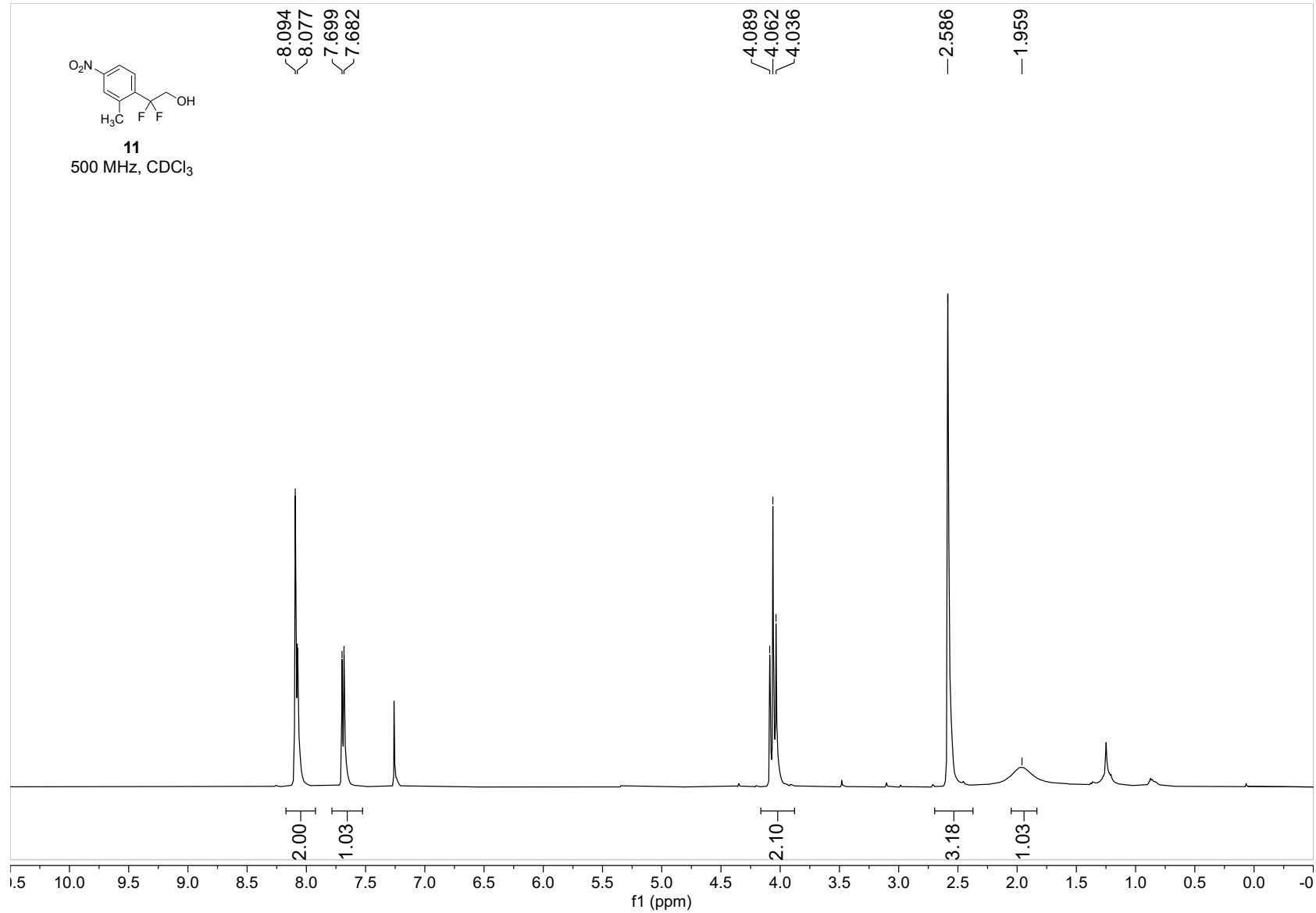
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376 MHz, CDCl₃

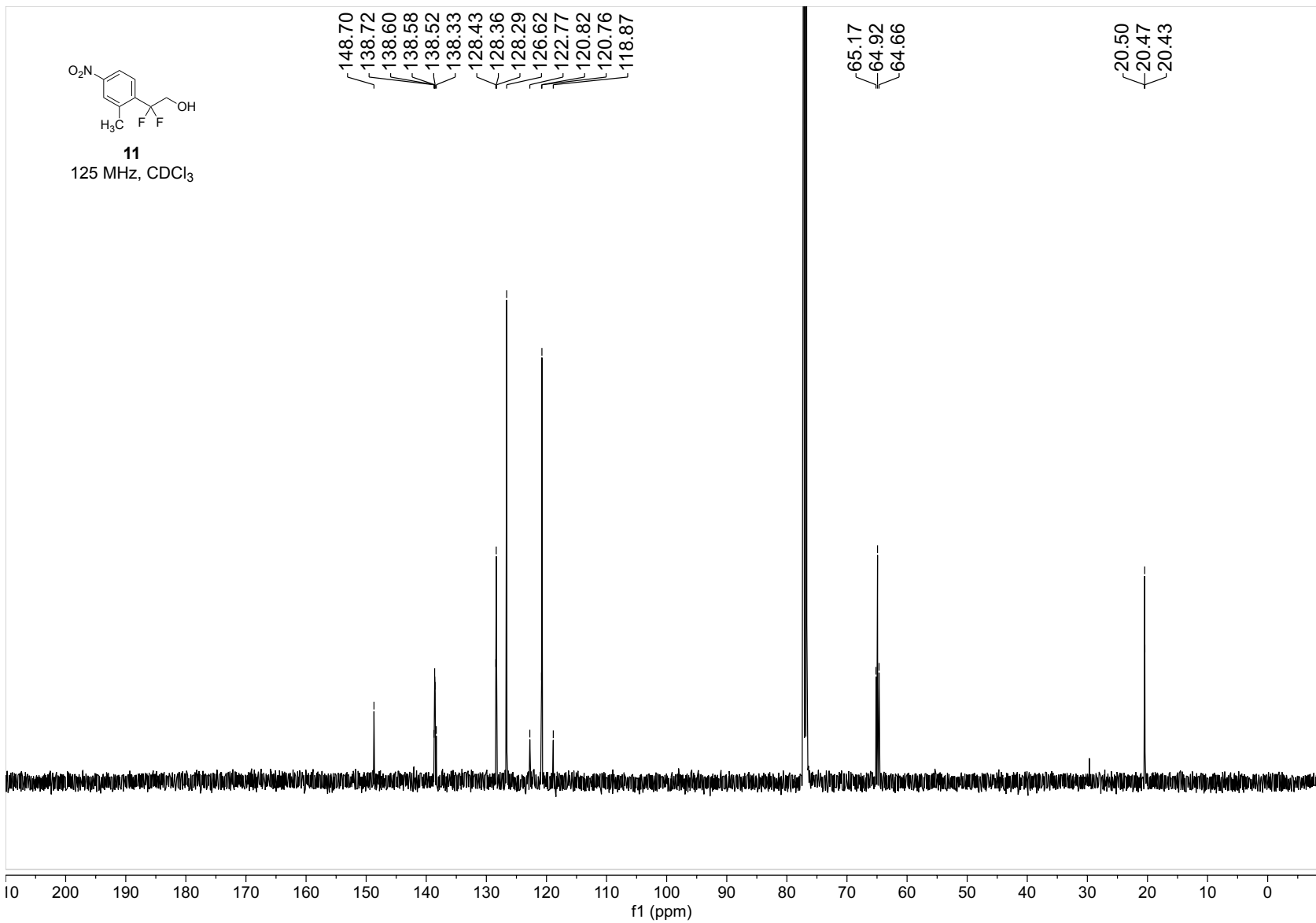
107.068
107.102
107.136

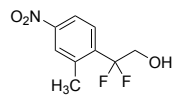




11
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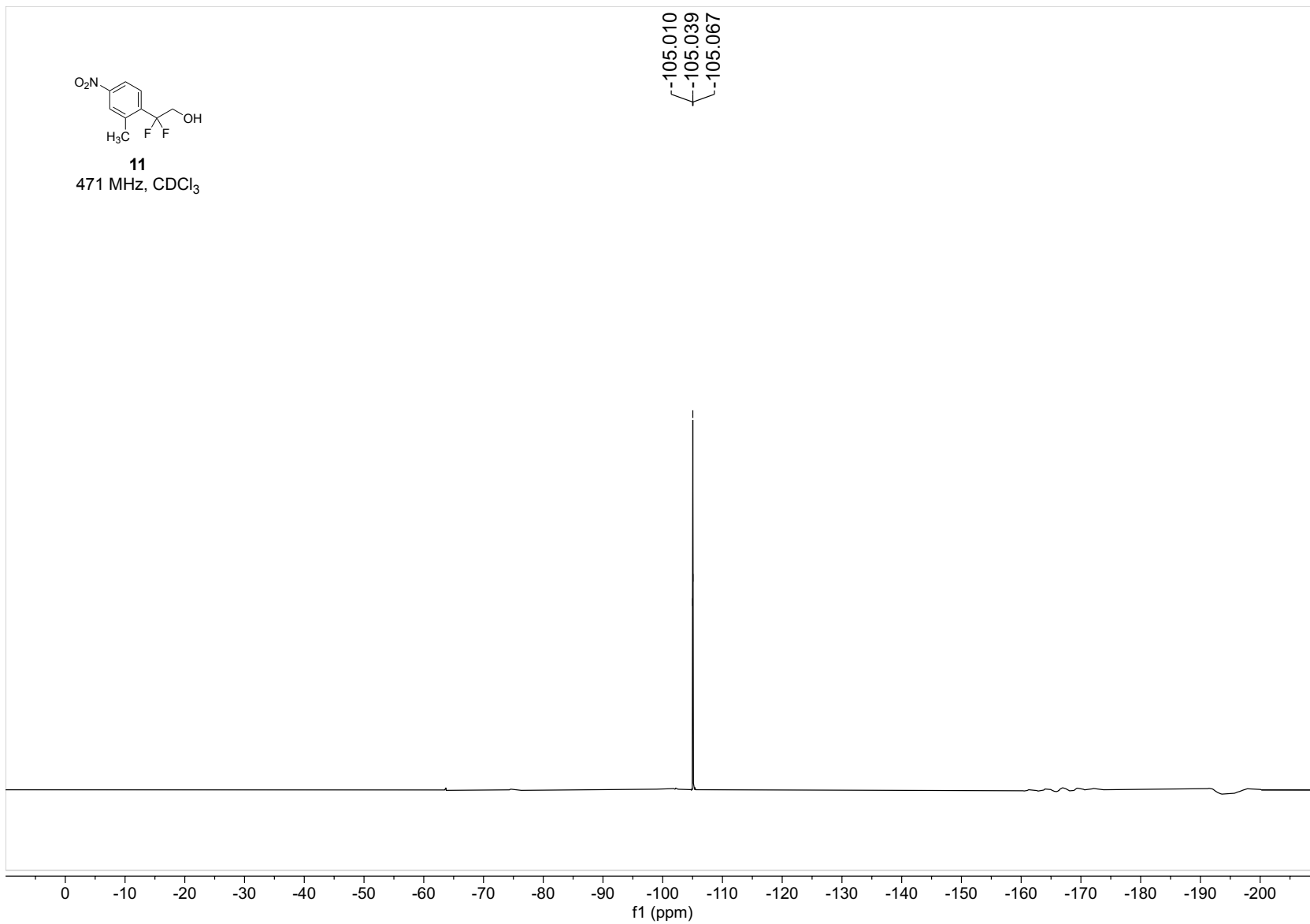


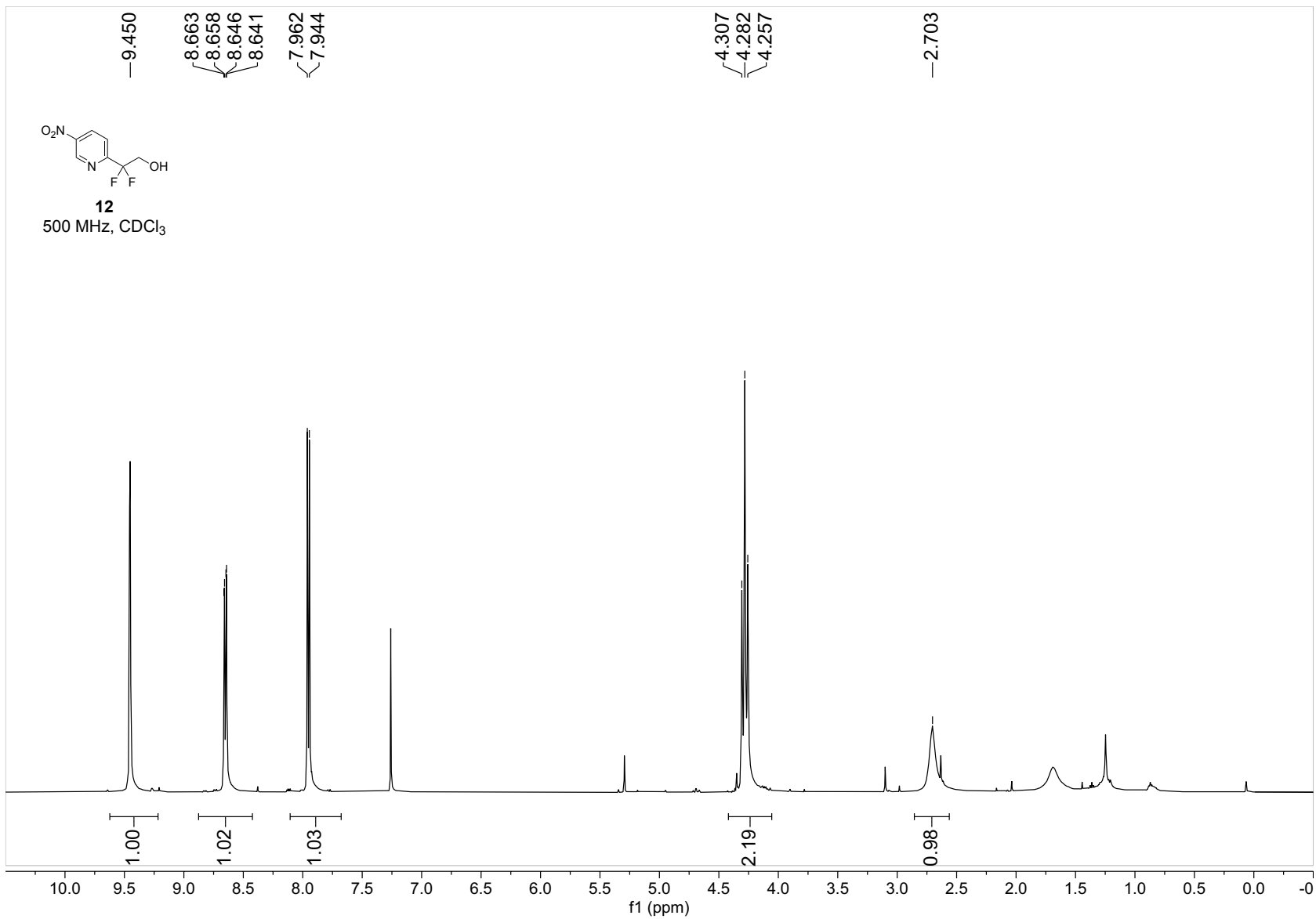


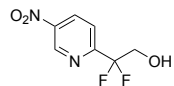


11
471 MHz, CDCl₃

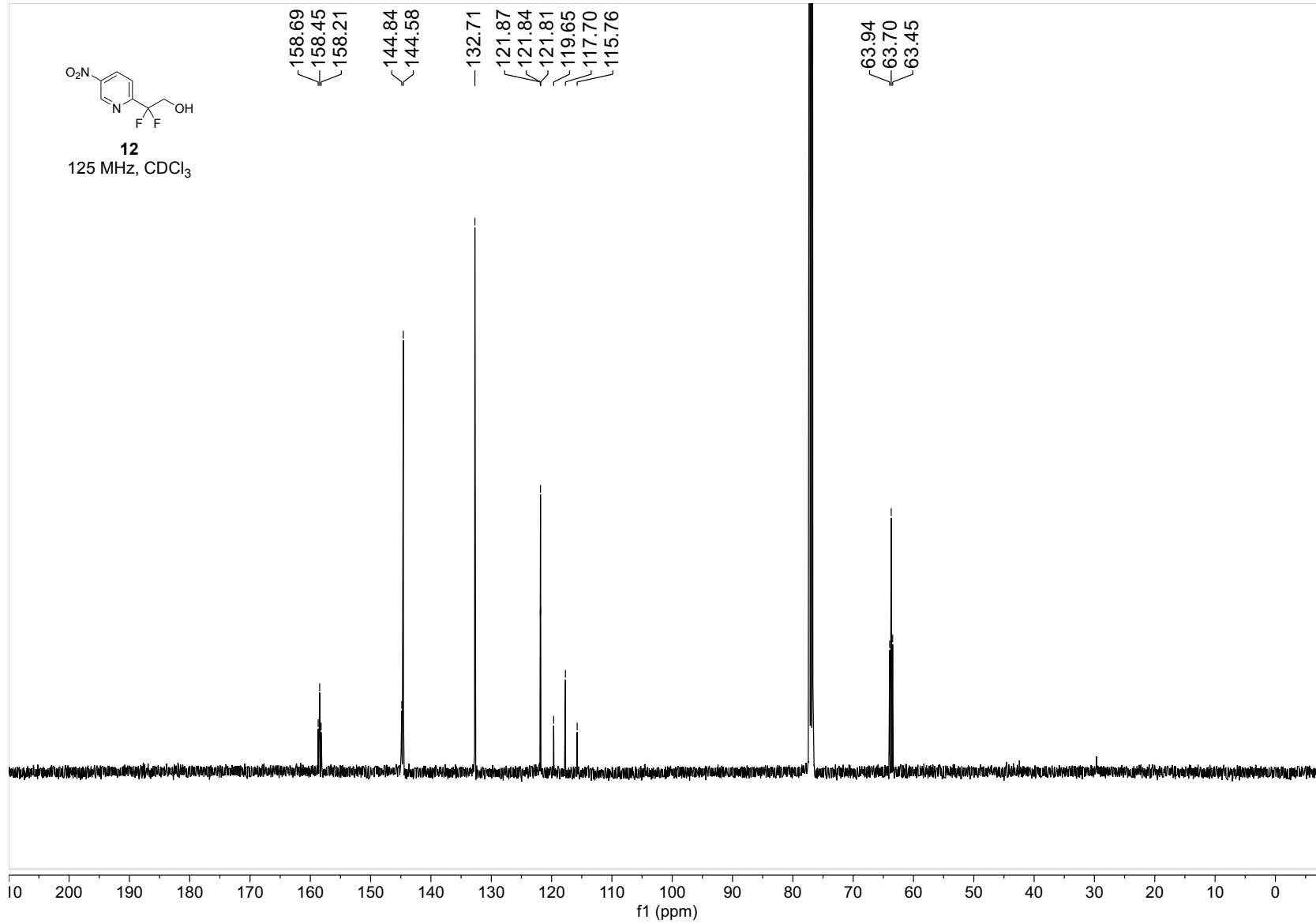
-105.010
-105.039
-105.067

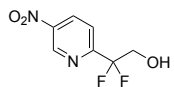






12
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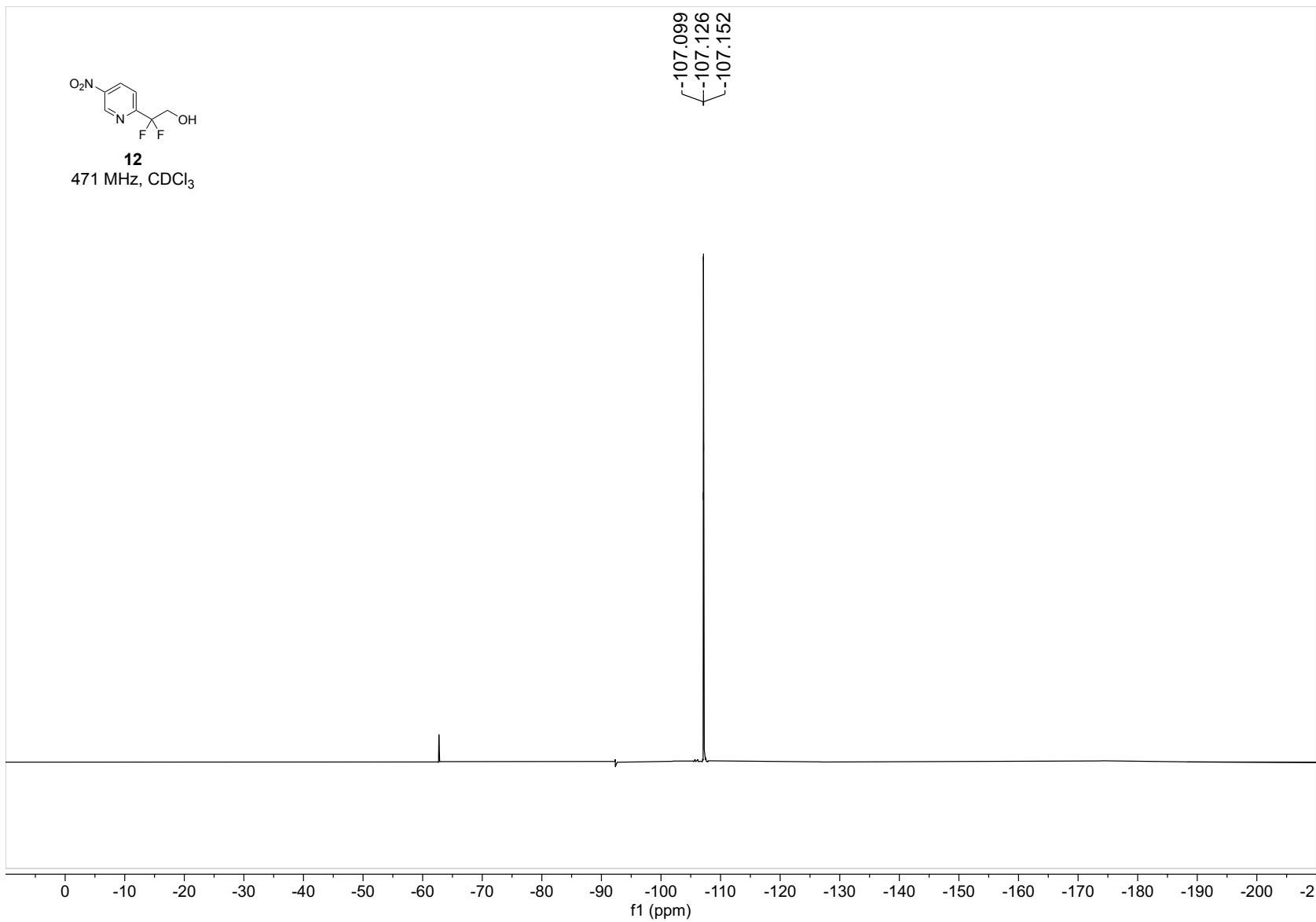


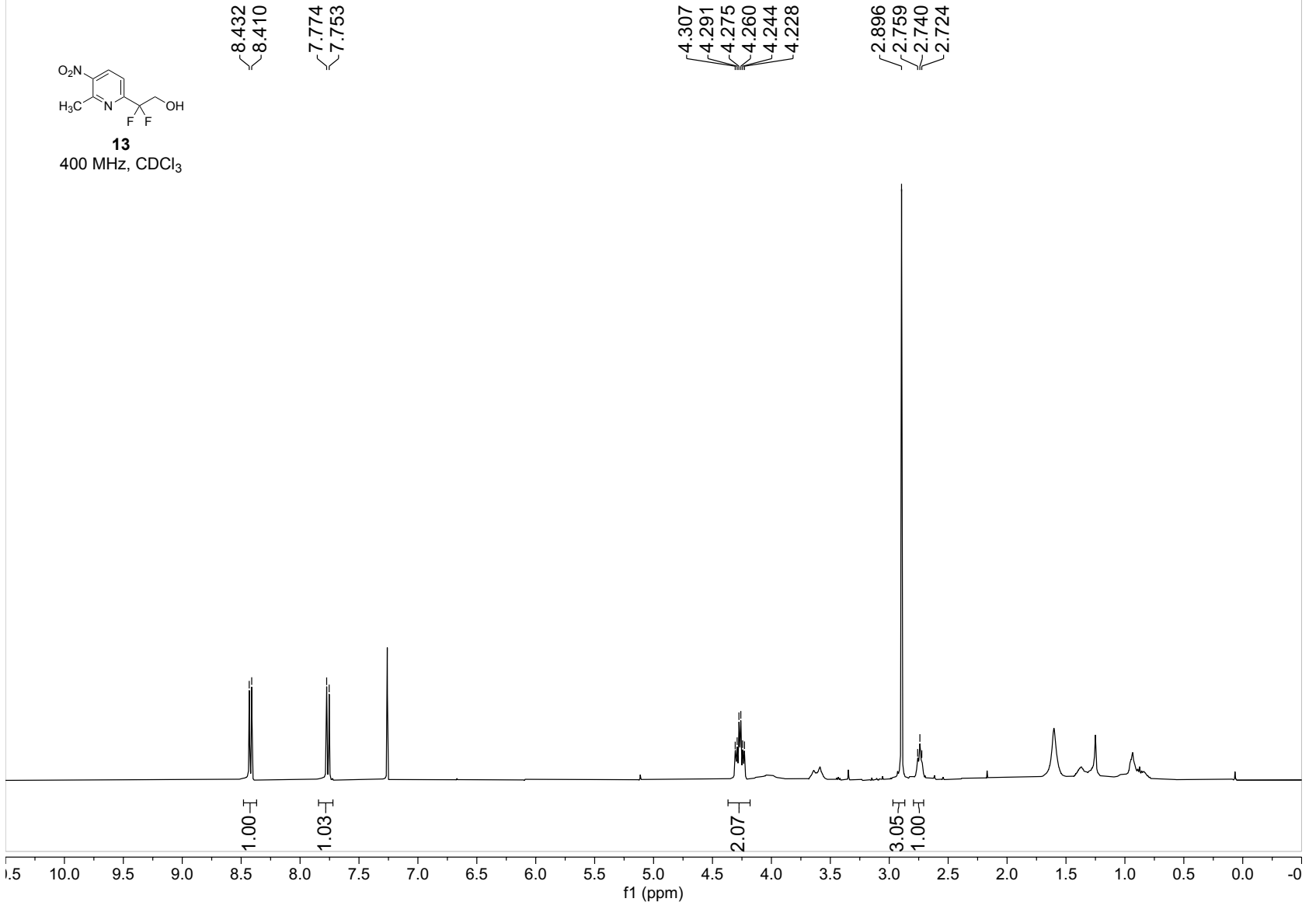


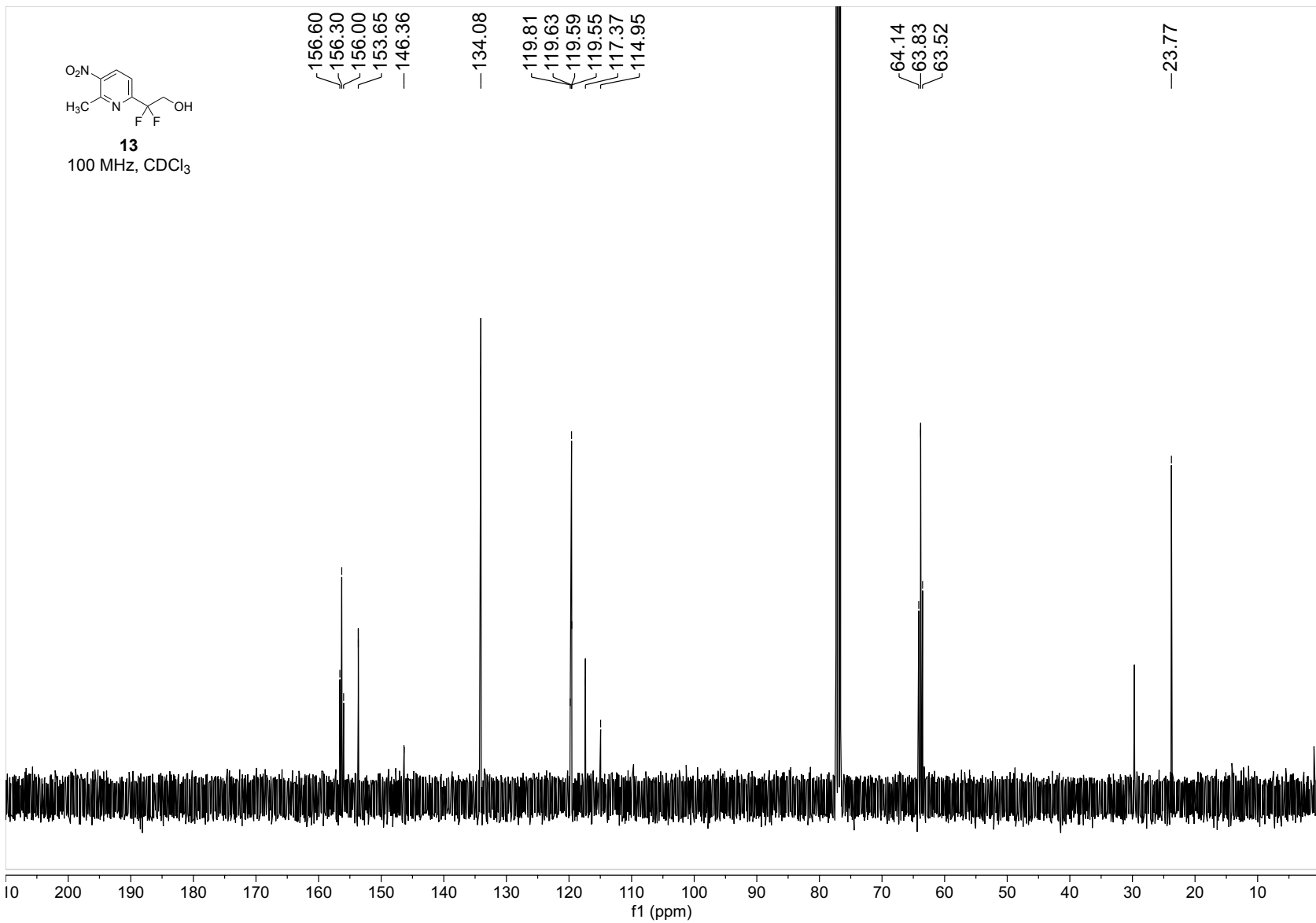
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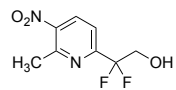
471 MHz, CDCl₃

-107.099
-107.126
-107.152



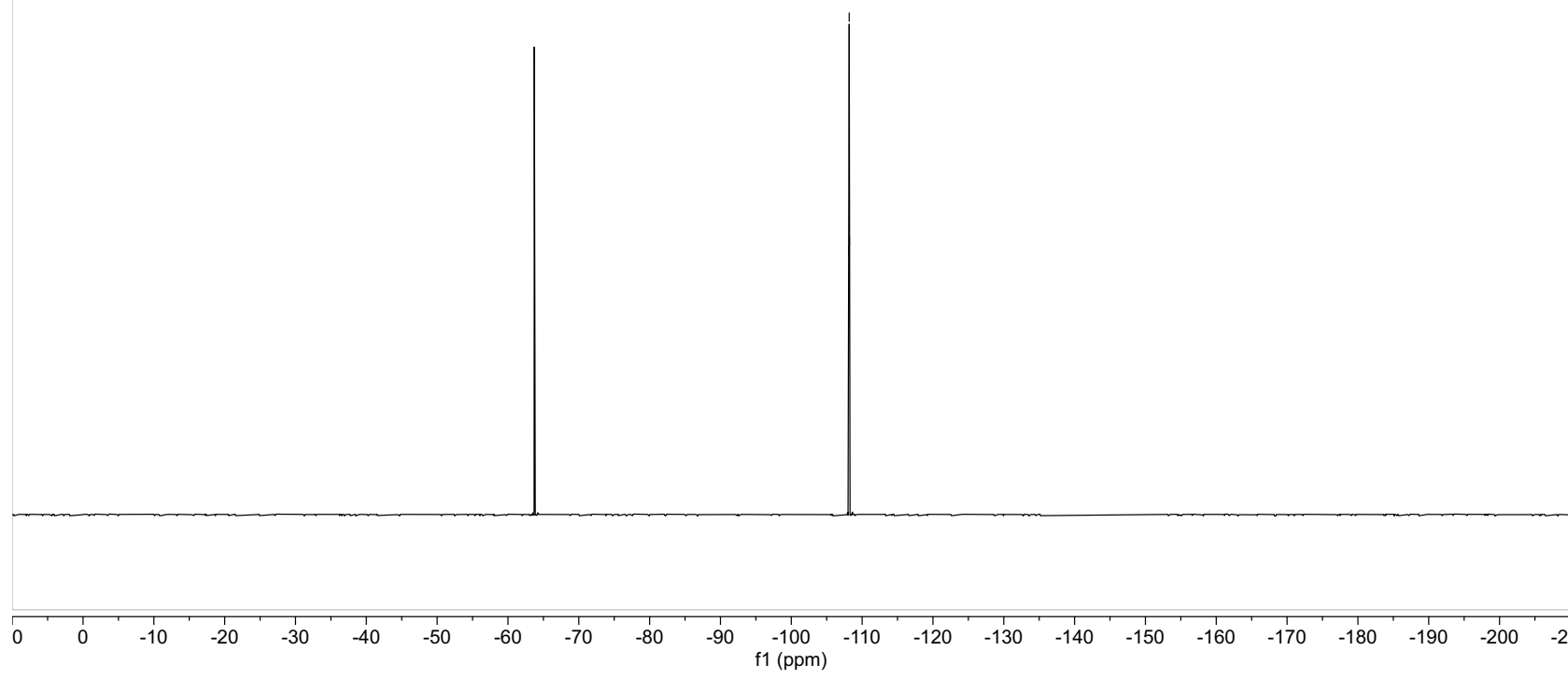


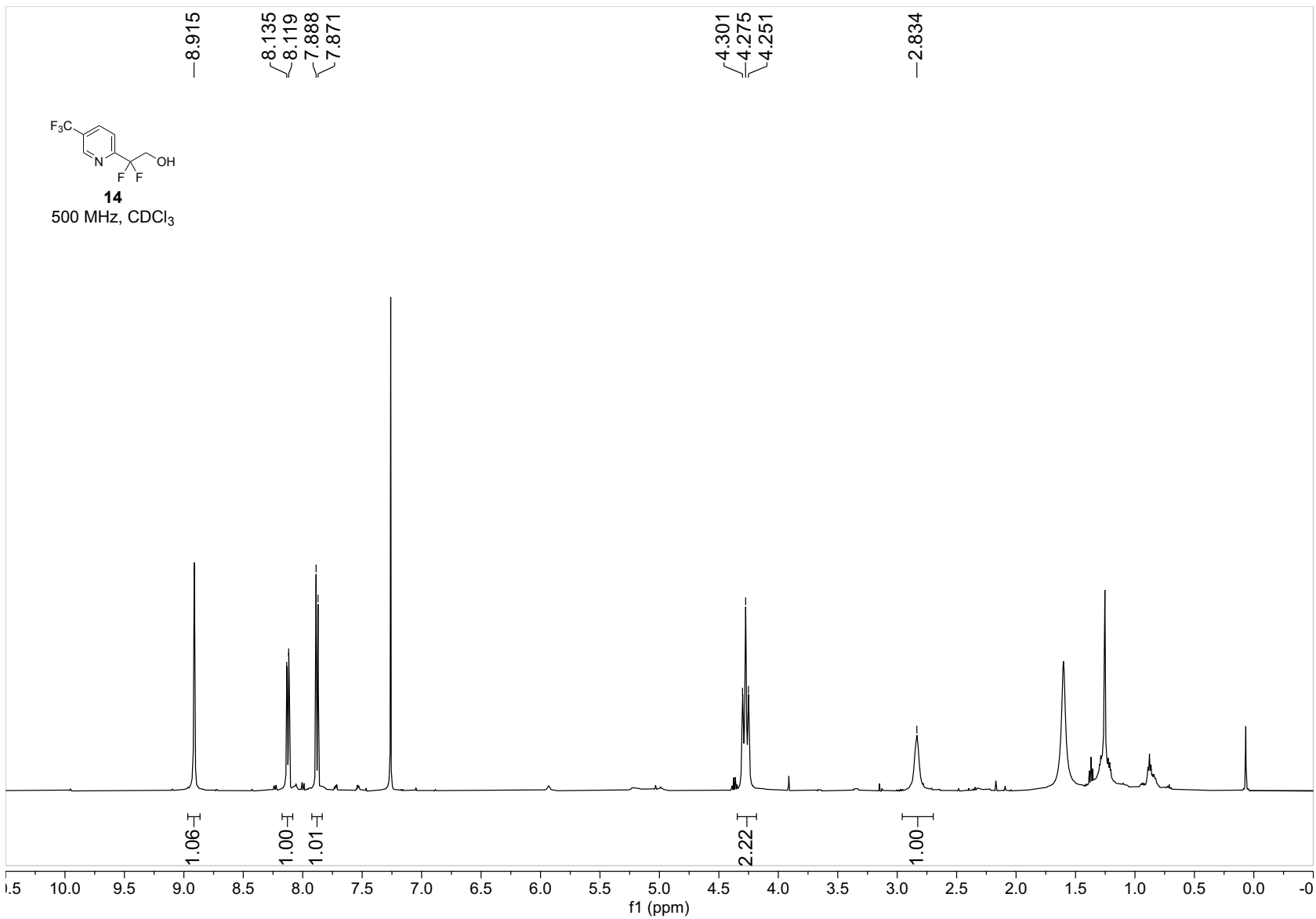


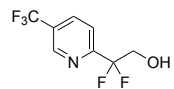


13
471 MHz, CDCl₃

108.14
108.18
108.21

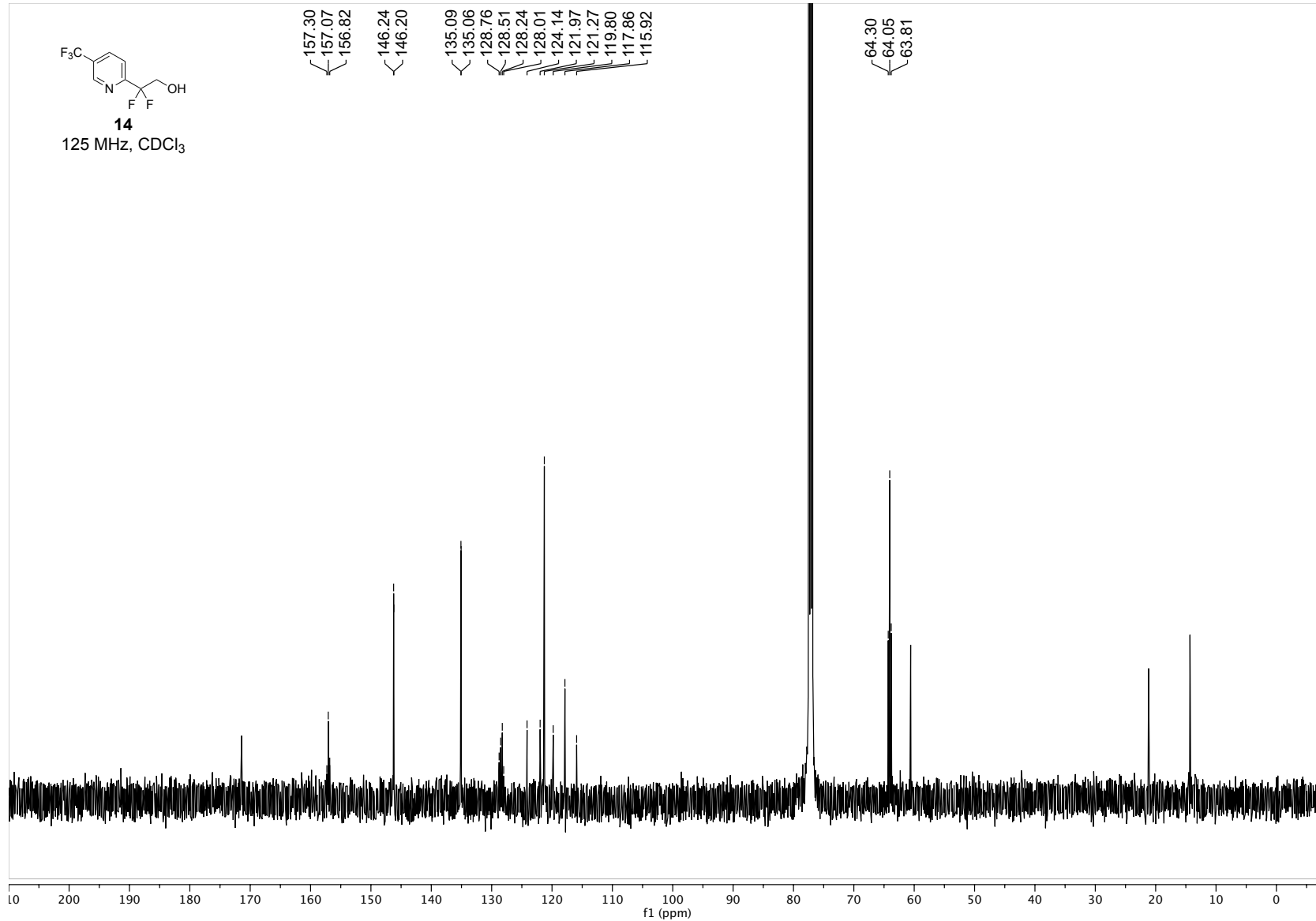


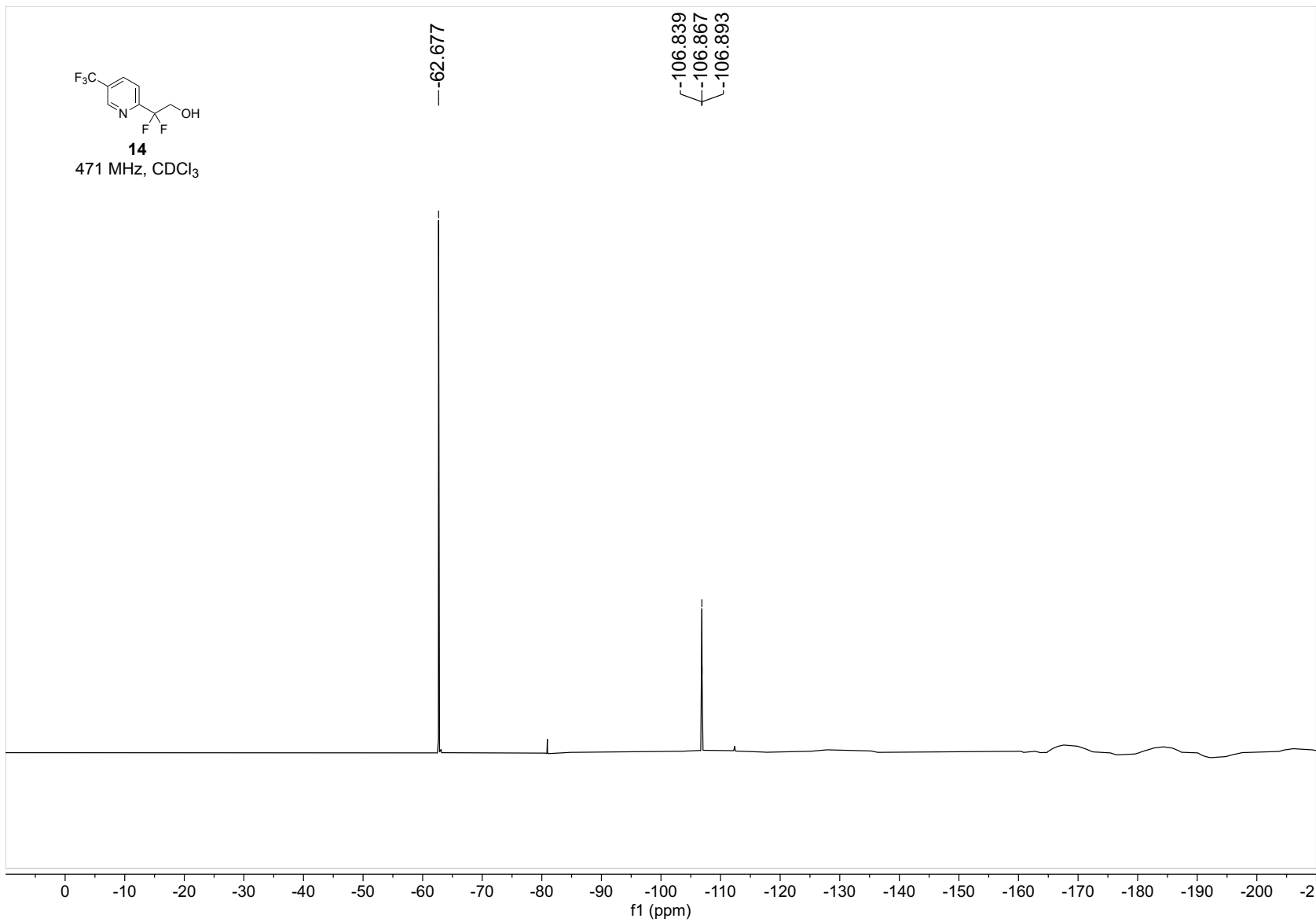
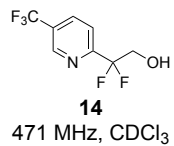


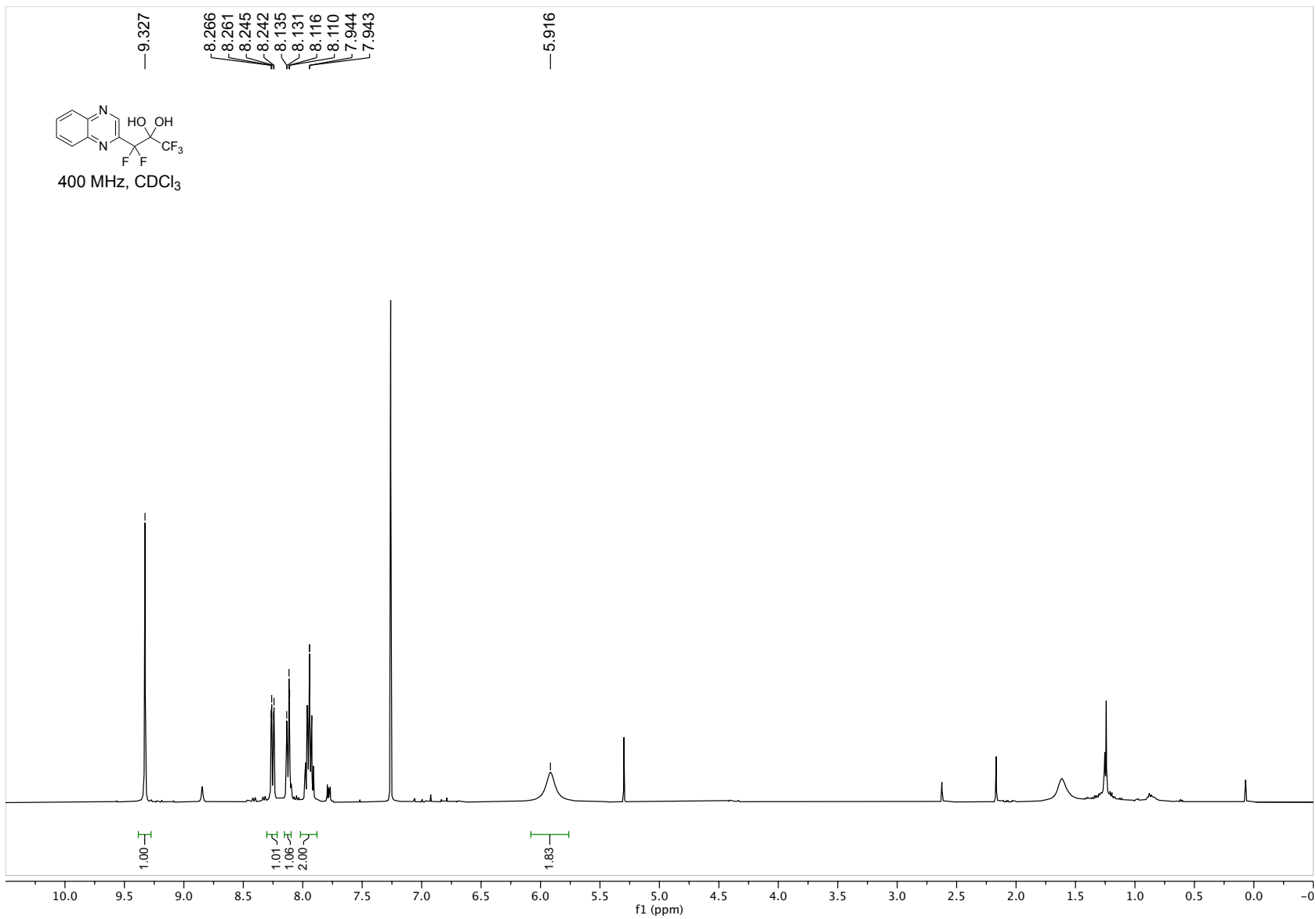


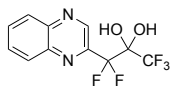
14

125 MHz, CDCl₃

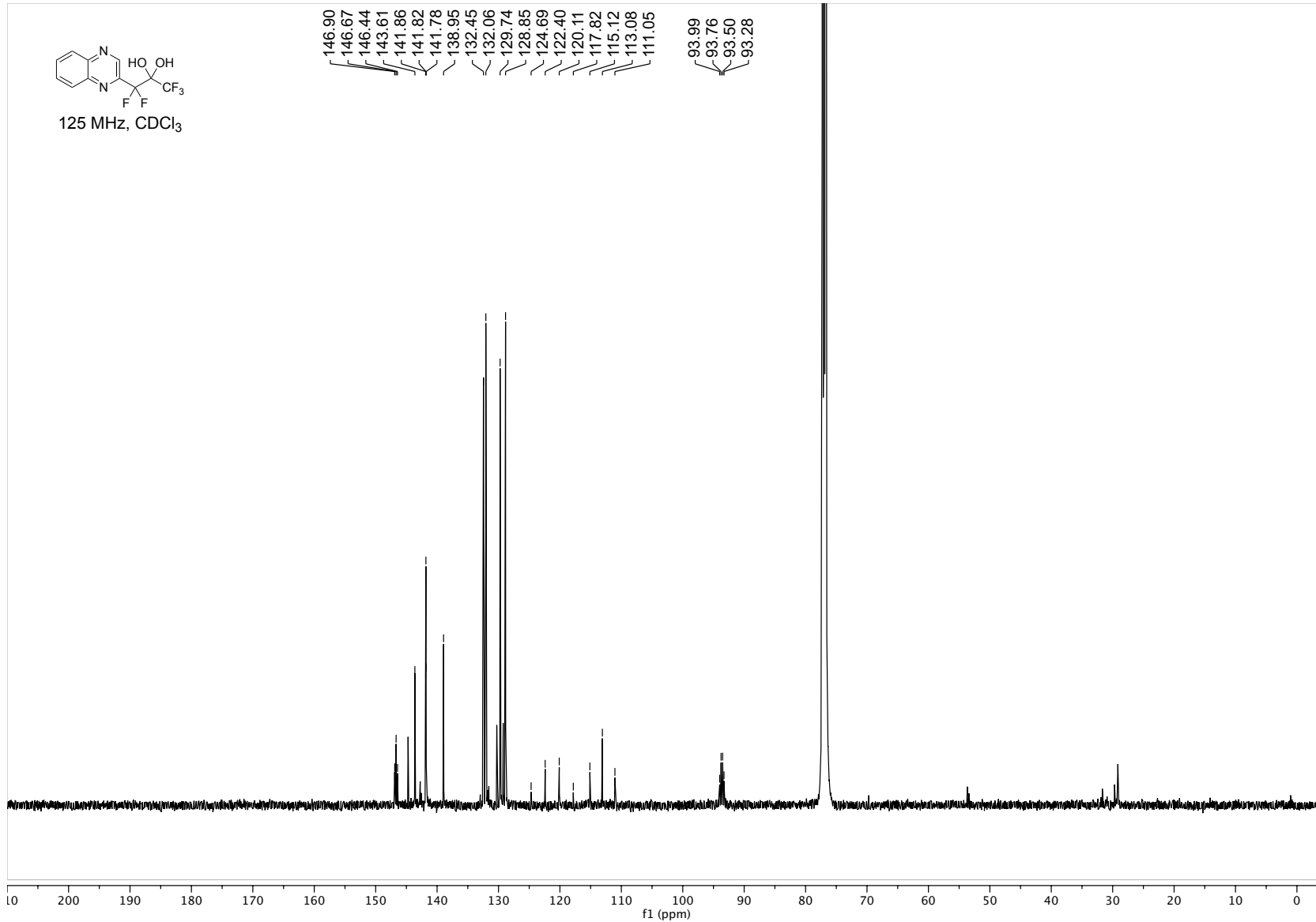


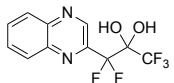






125 MHz, CDCl₃

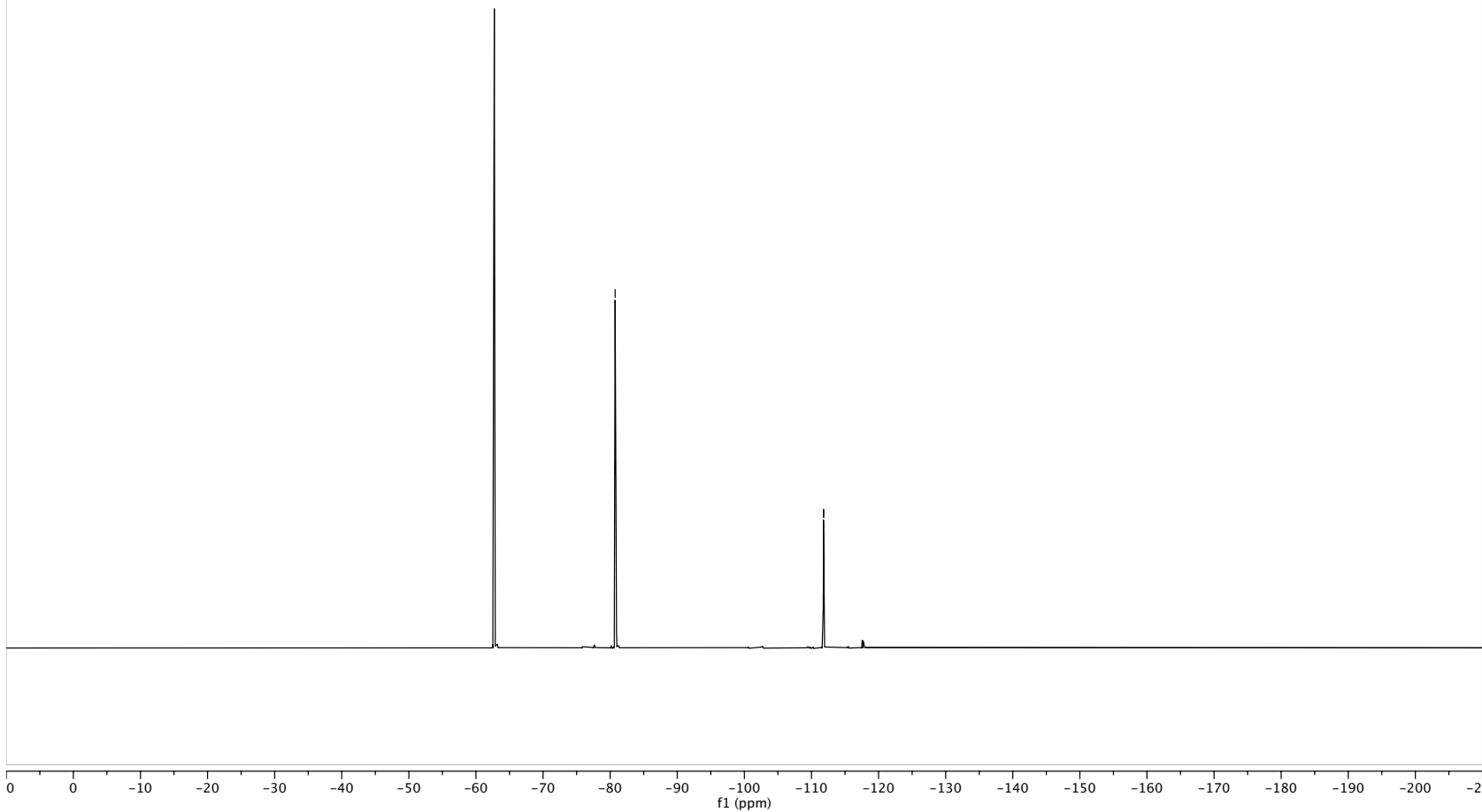


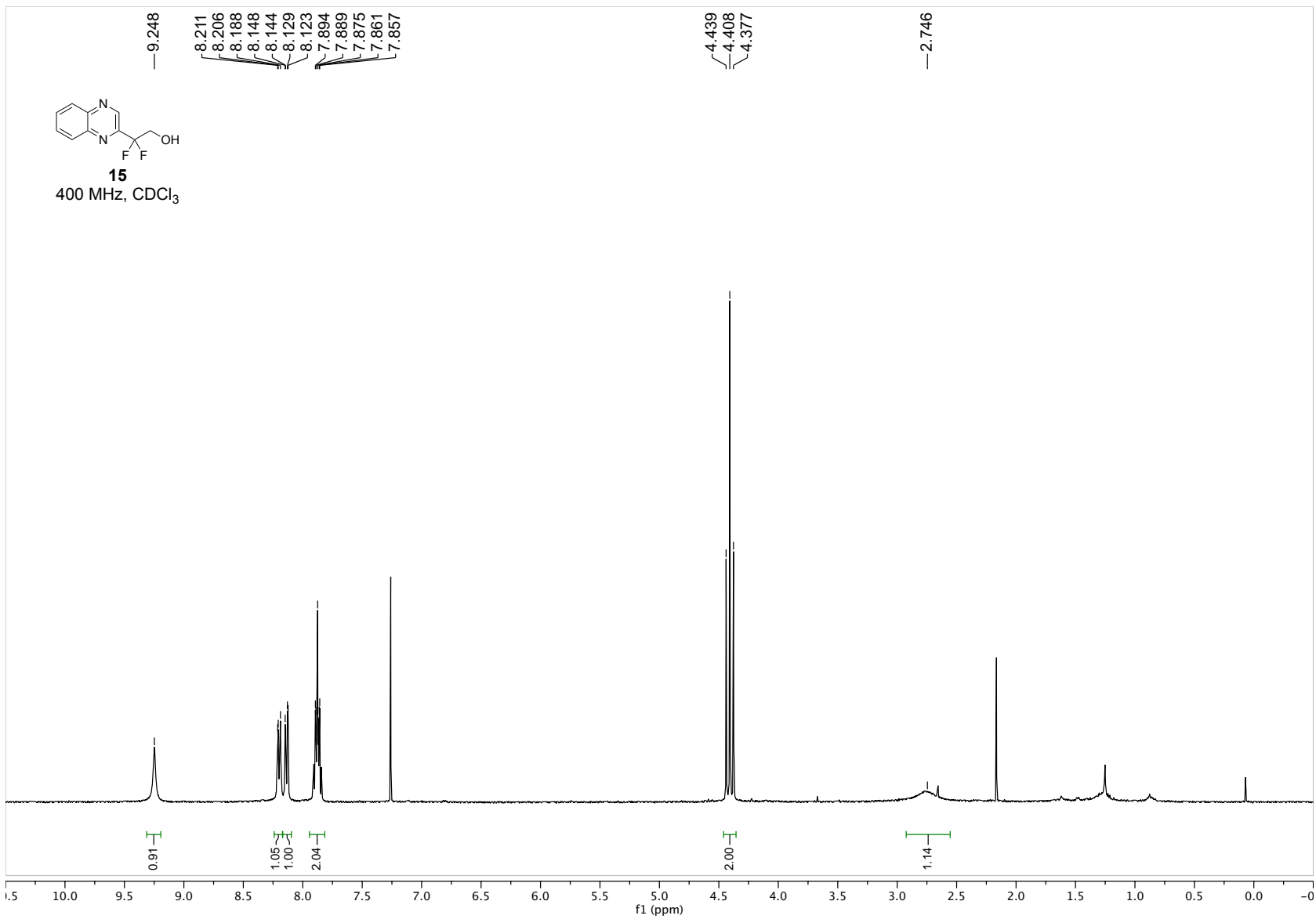


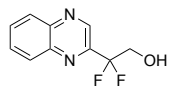
376 MHz, CDCl₃

-80.71
-80.74
-80.77

-111.76
-111.79
-111.82
-111.85

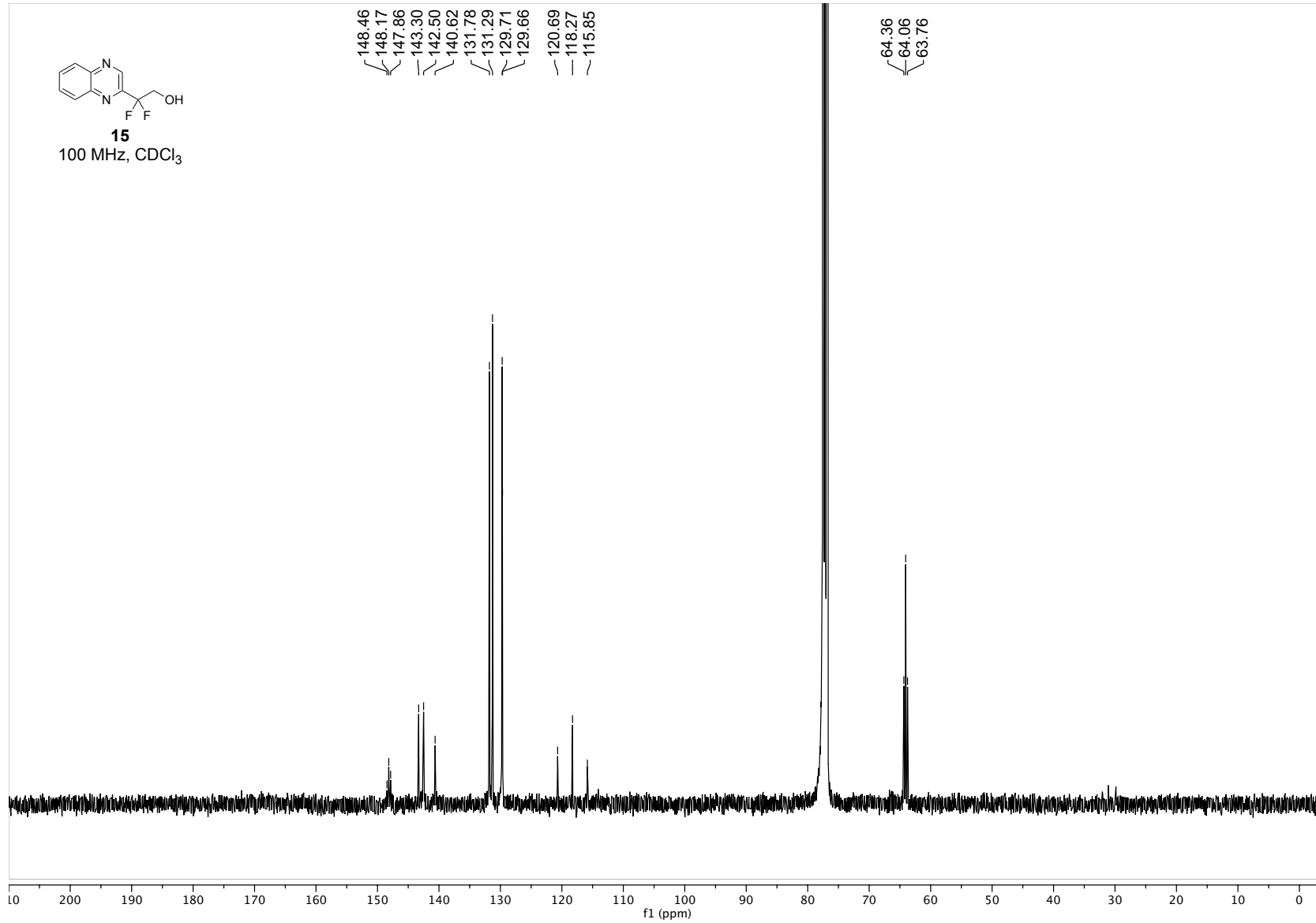


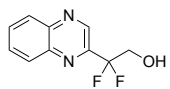




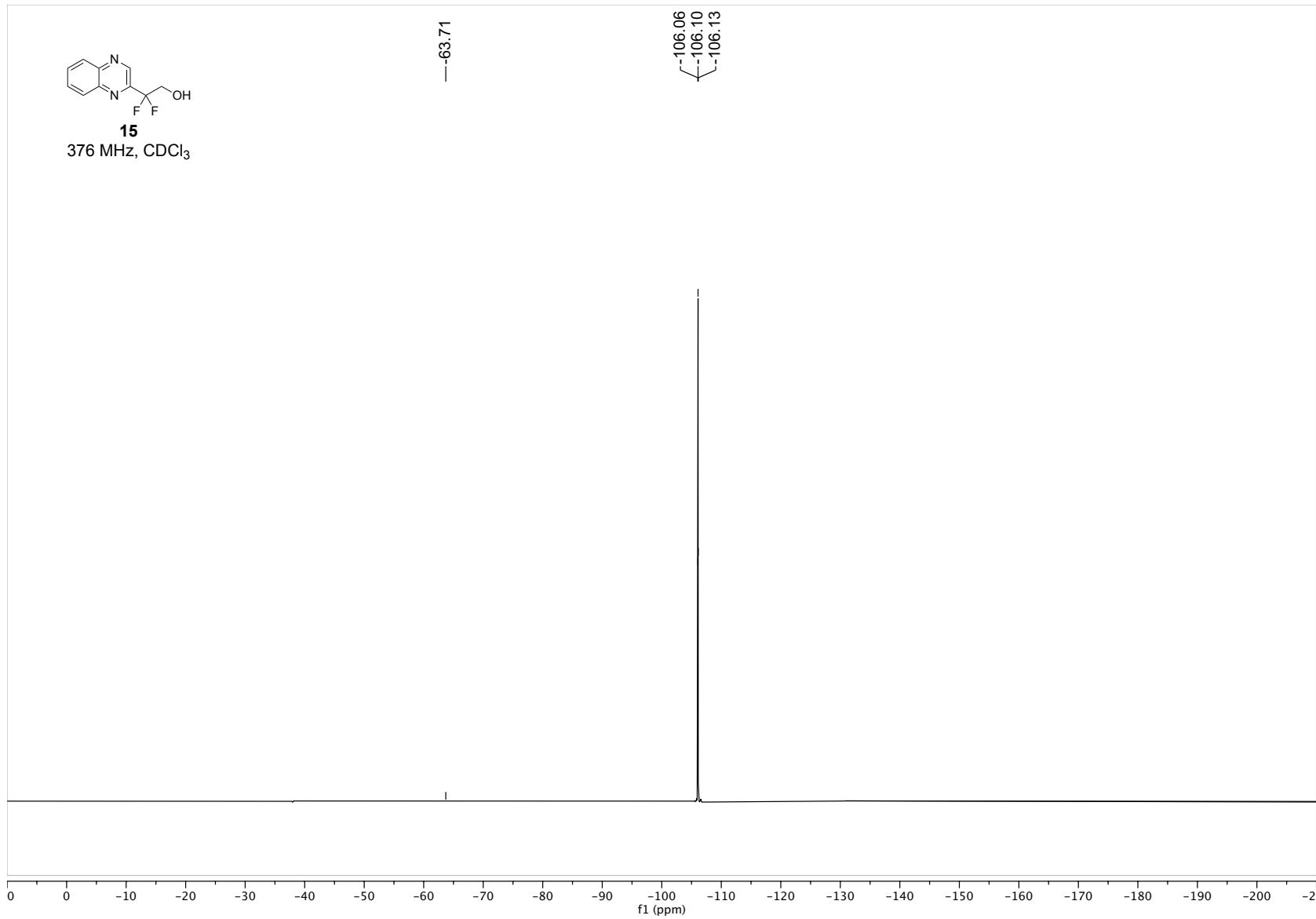
15

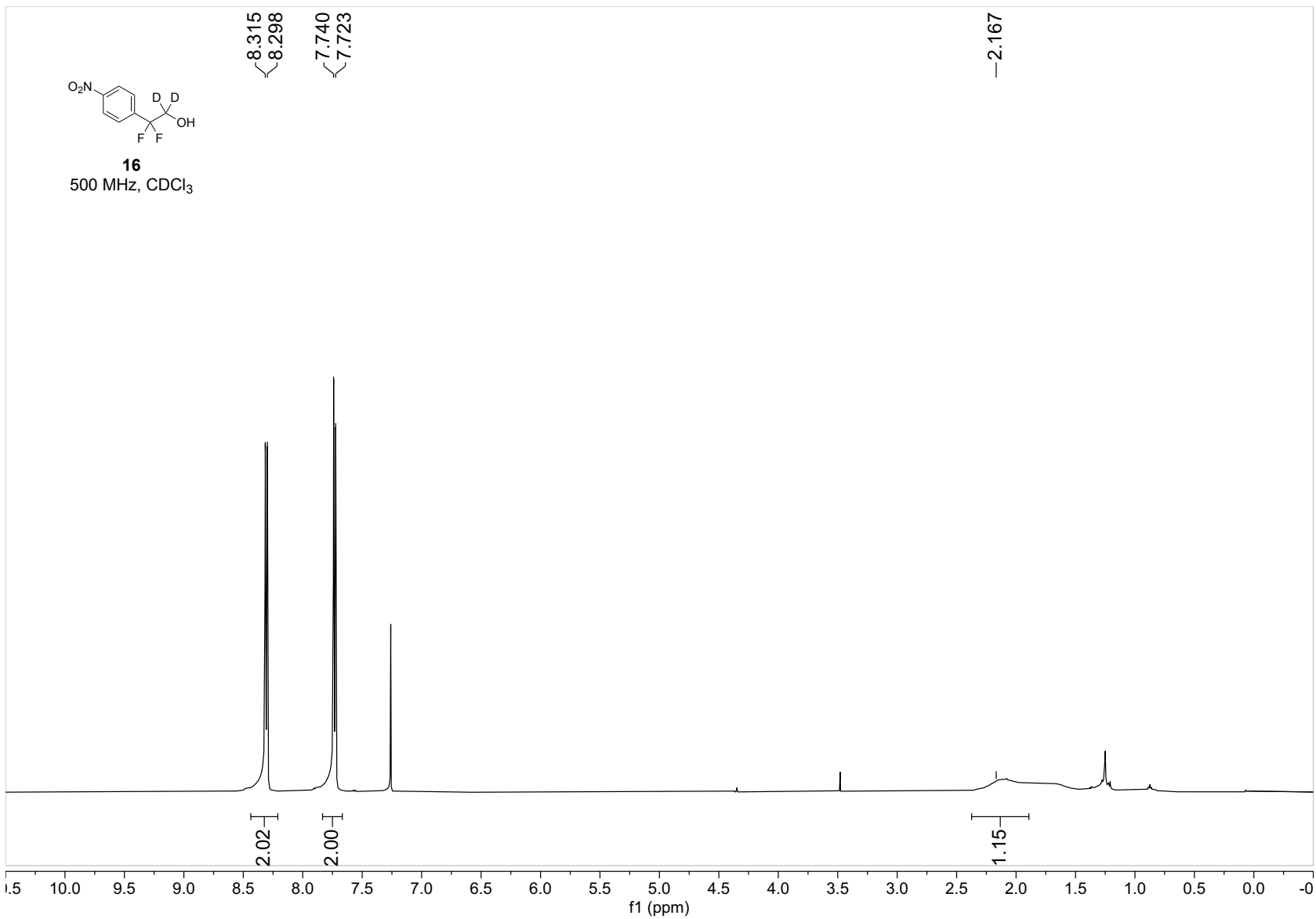
100 MHz, CDCl₃

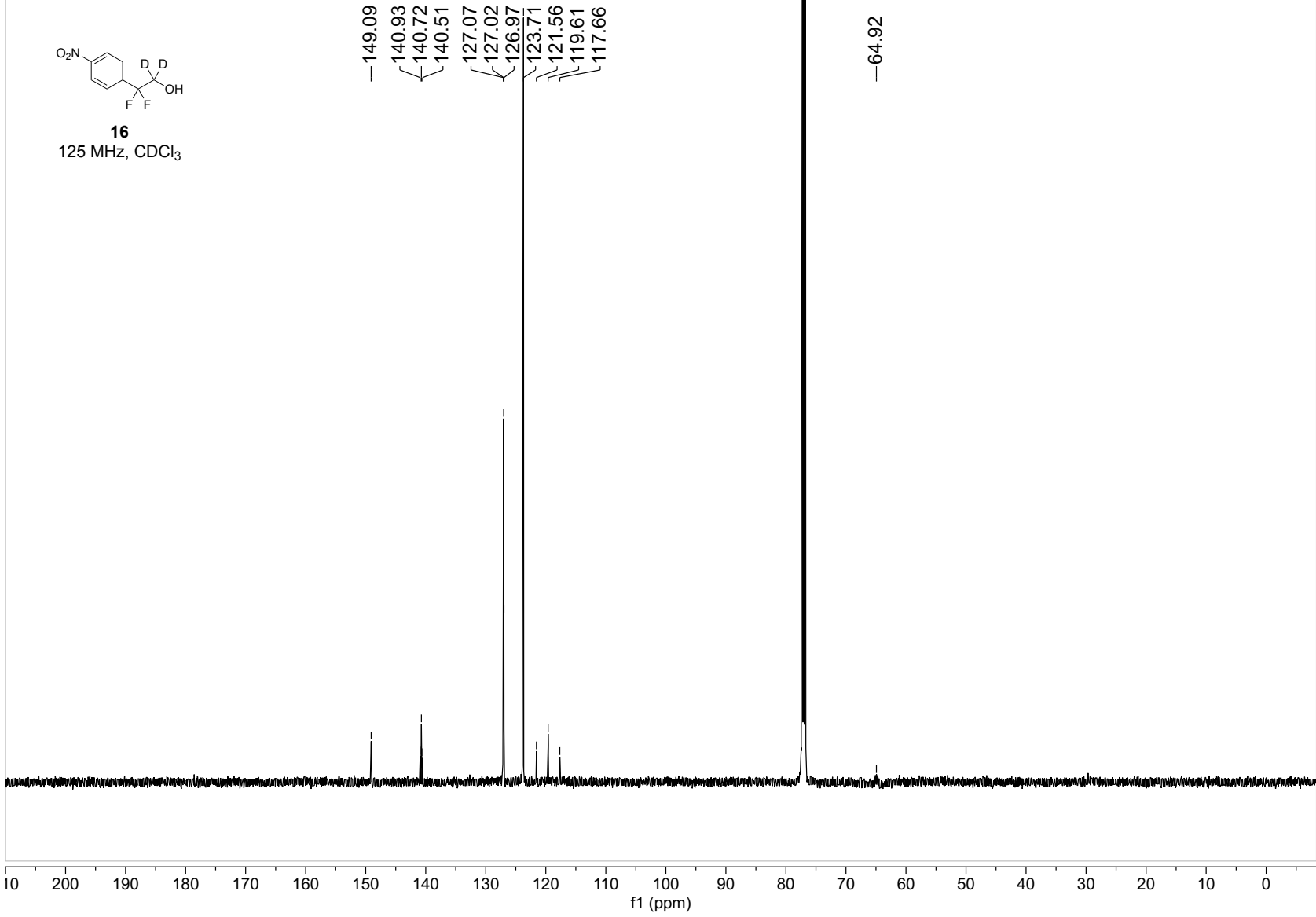


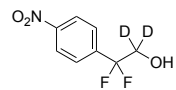


15
376 MHz, CDCl₃

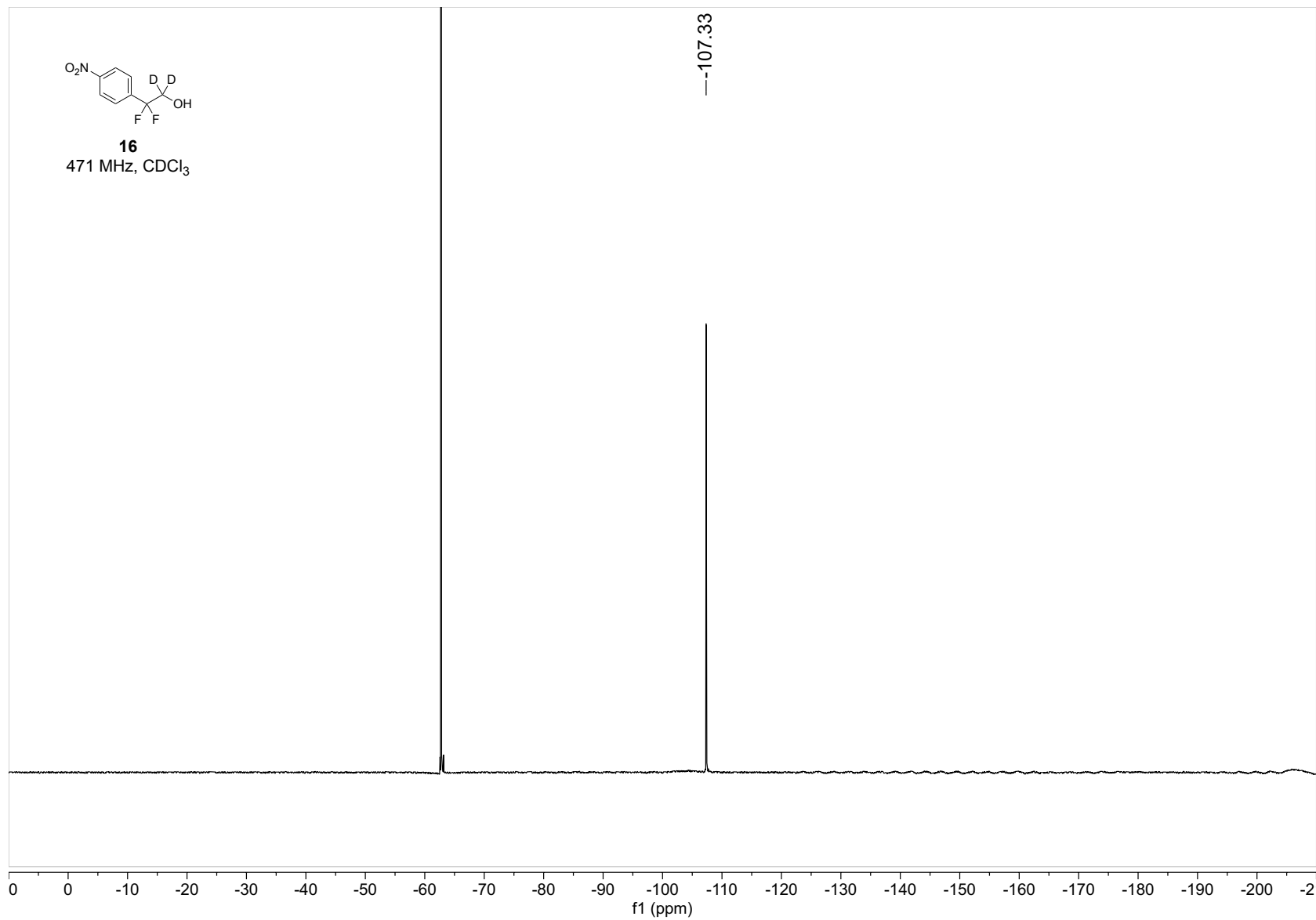


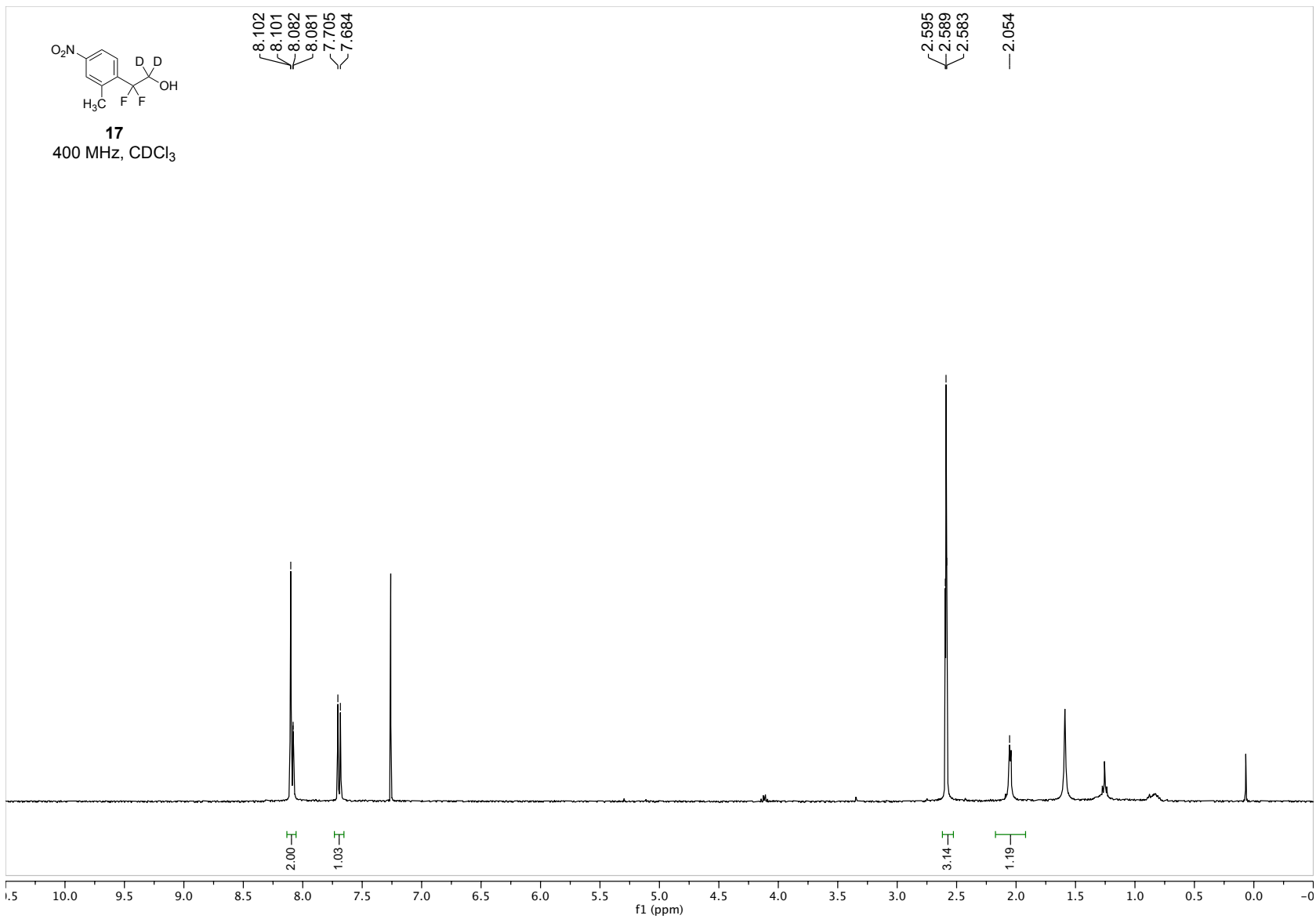


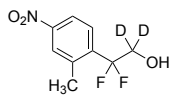




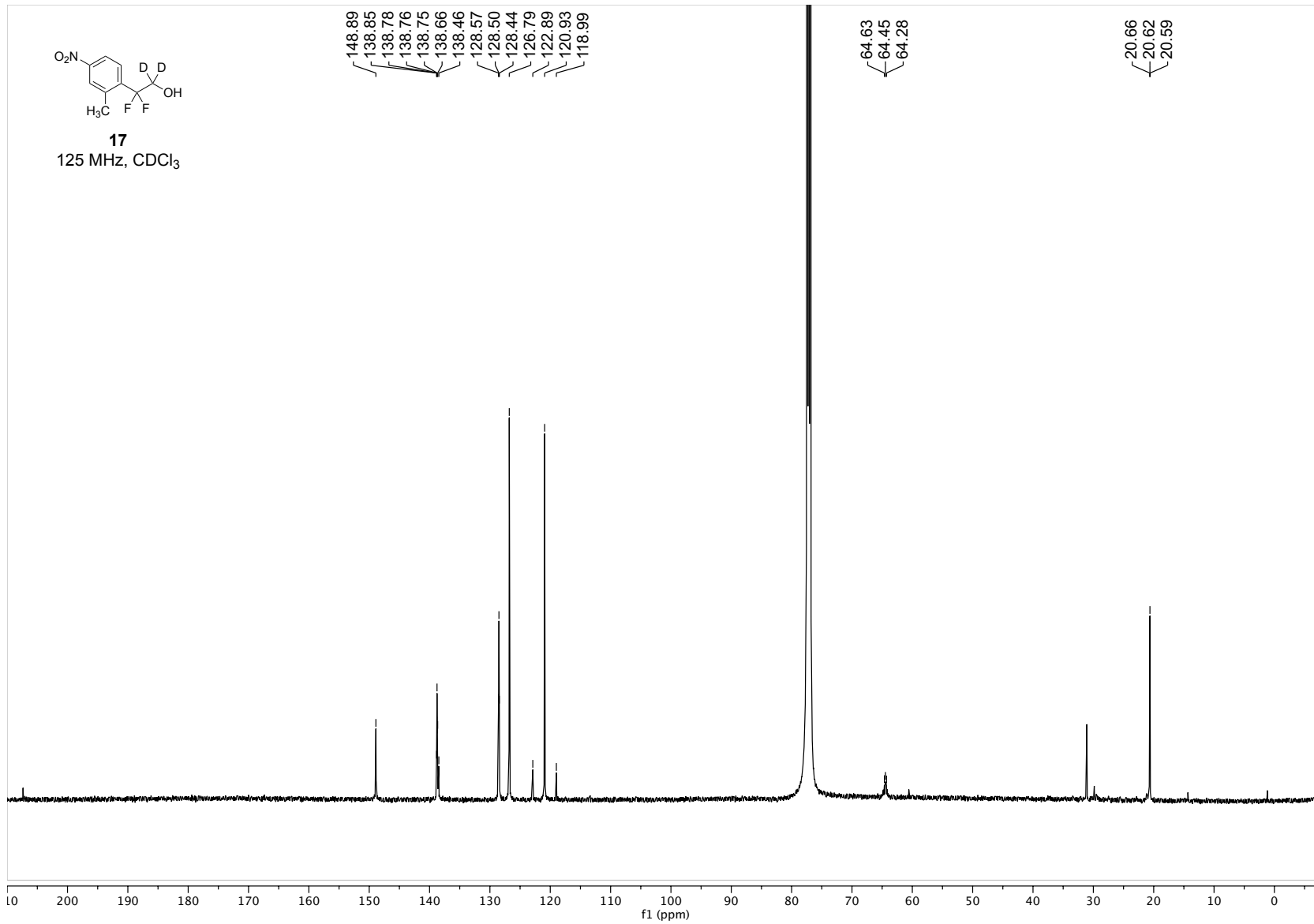
16
471 MHz, CDCl₃

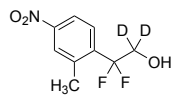




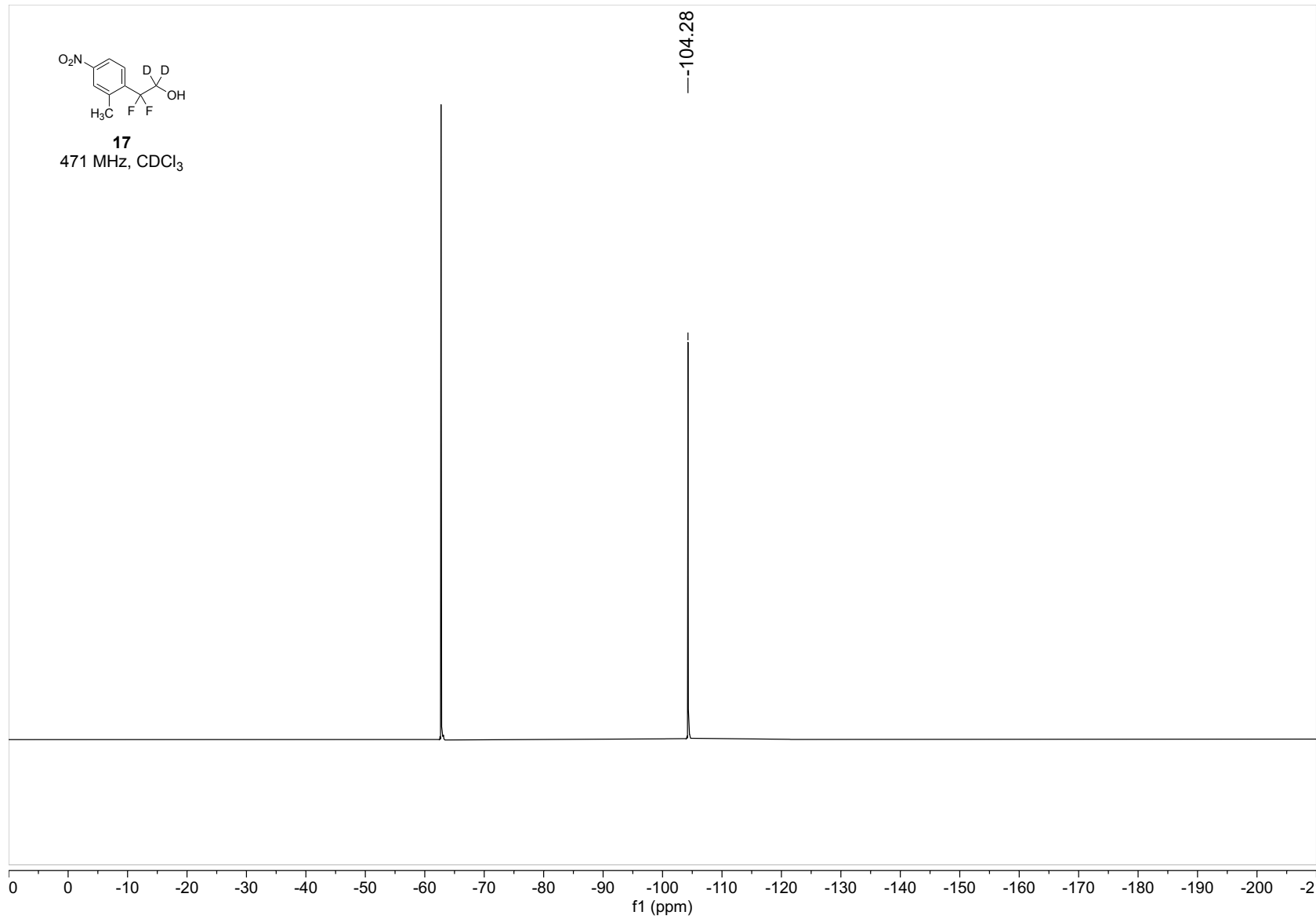


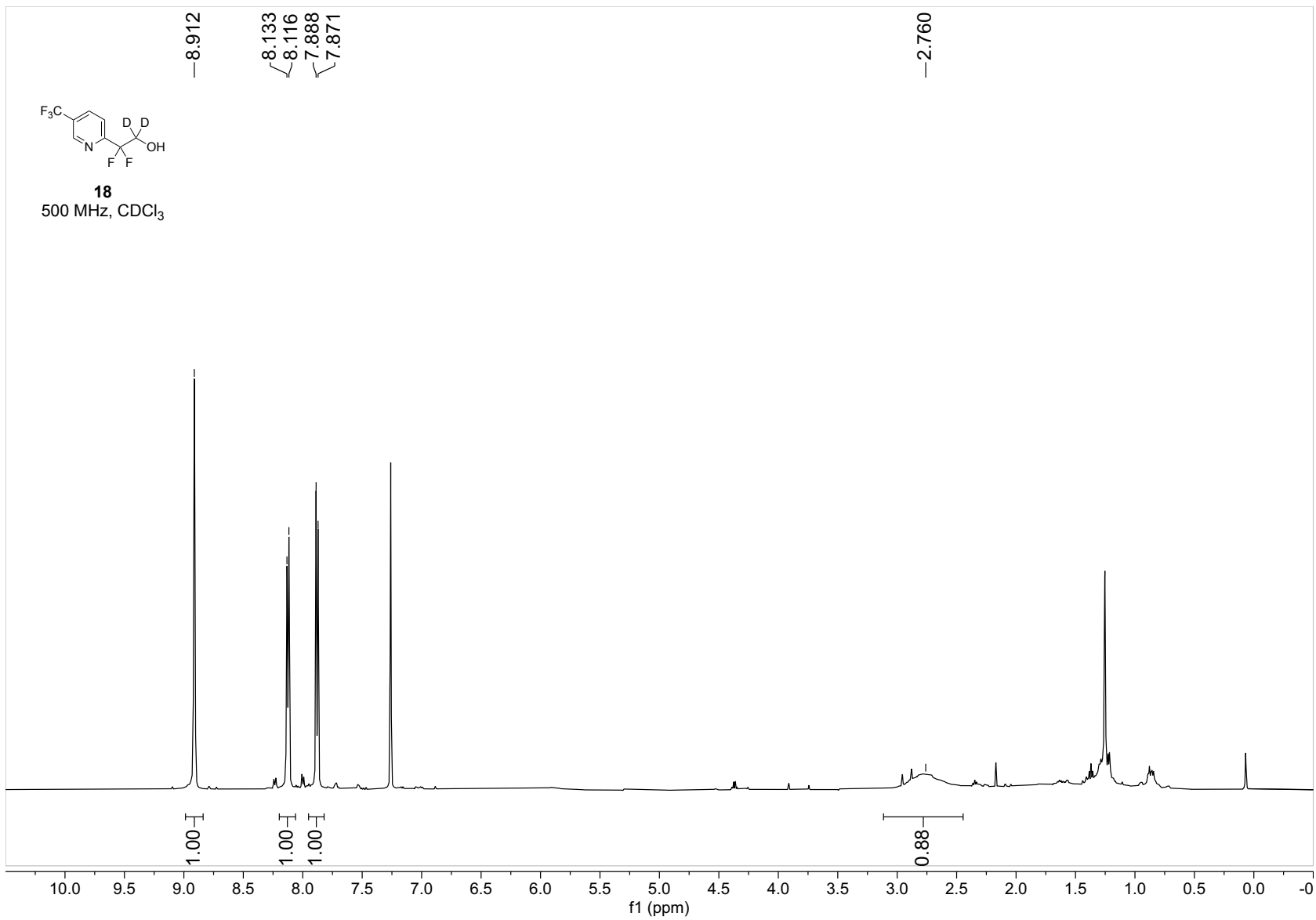
17
125 MHz, CDCl₃

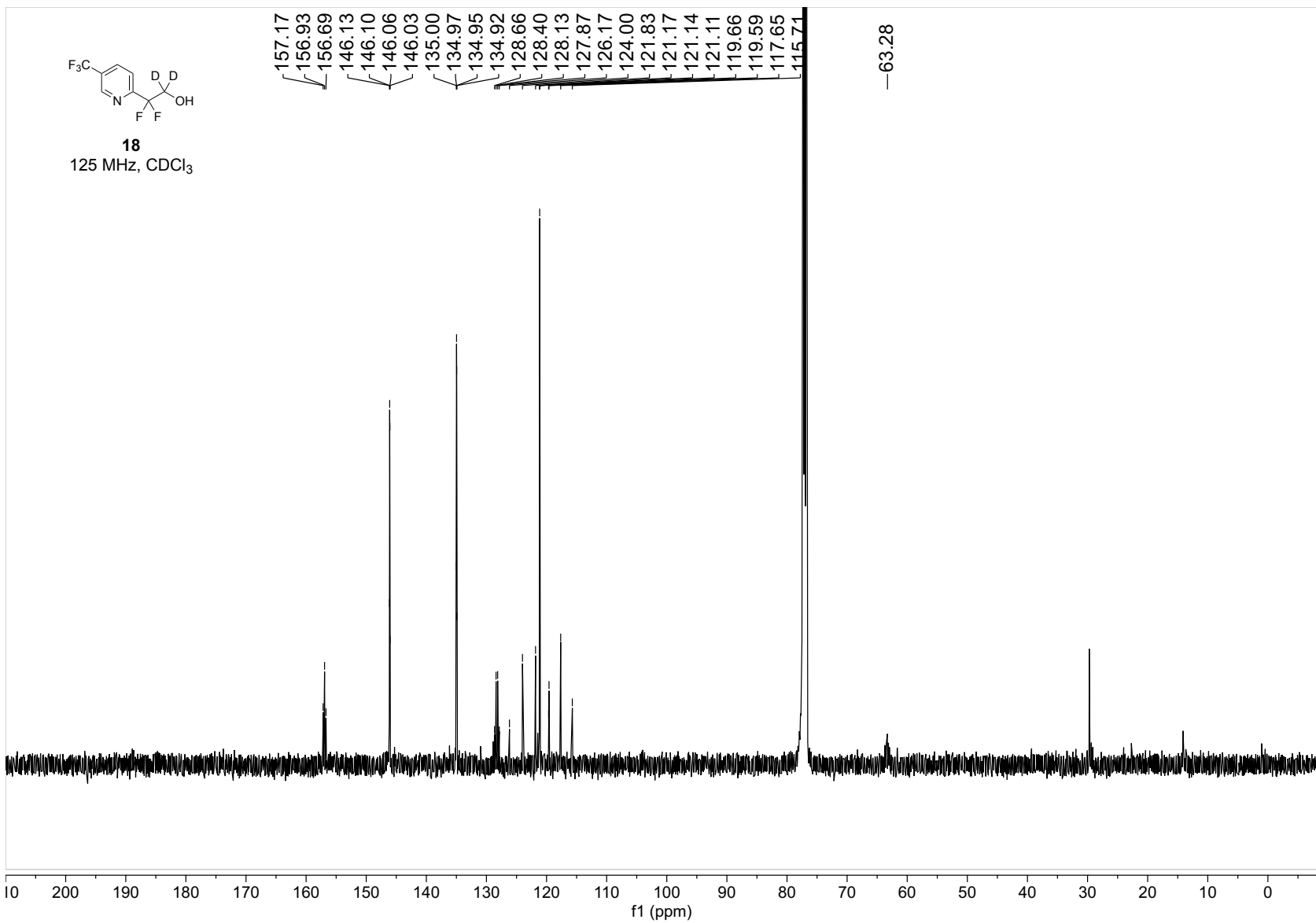


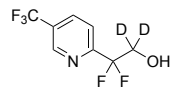


17
471 MHz, CDCl₃

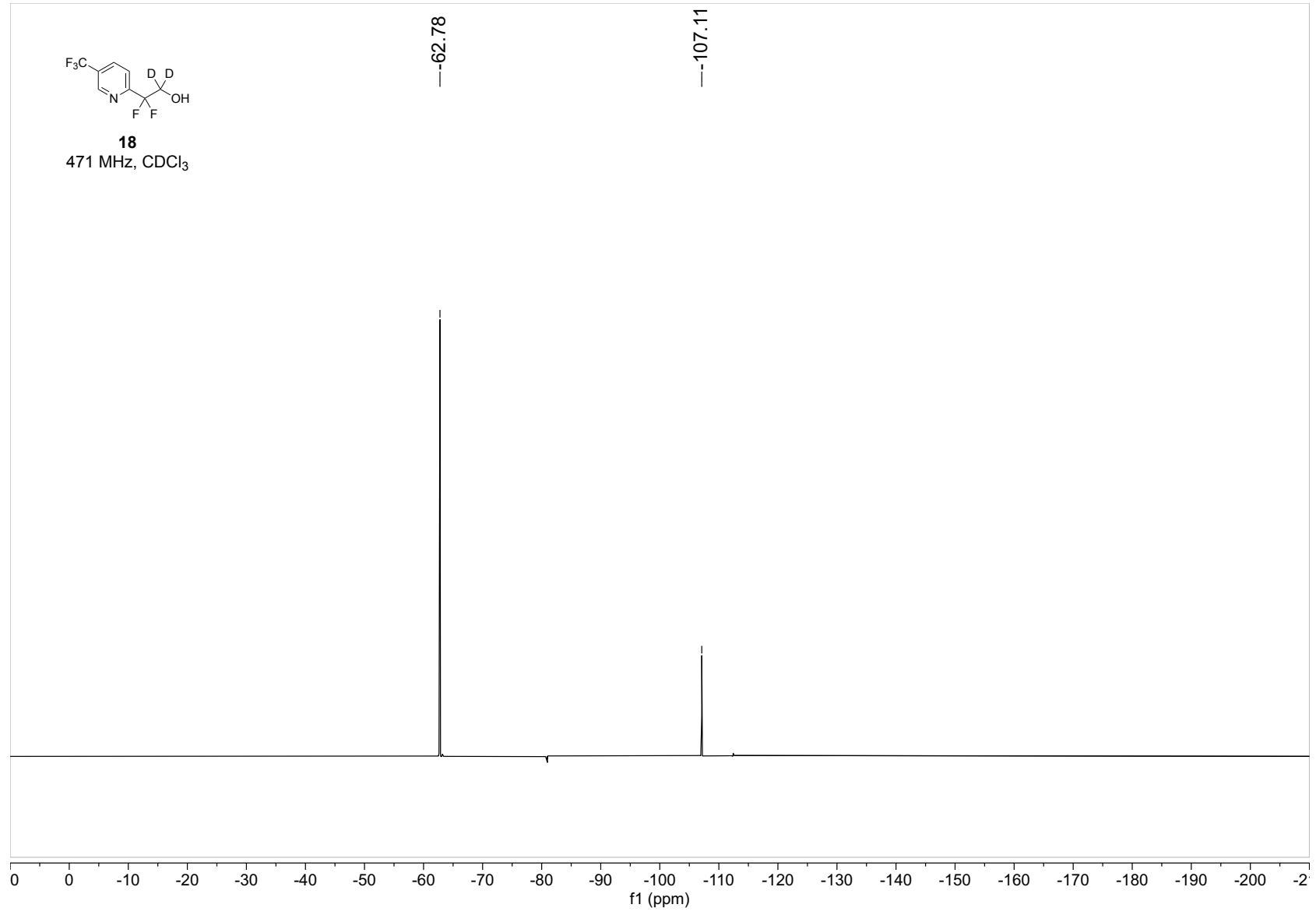


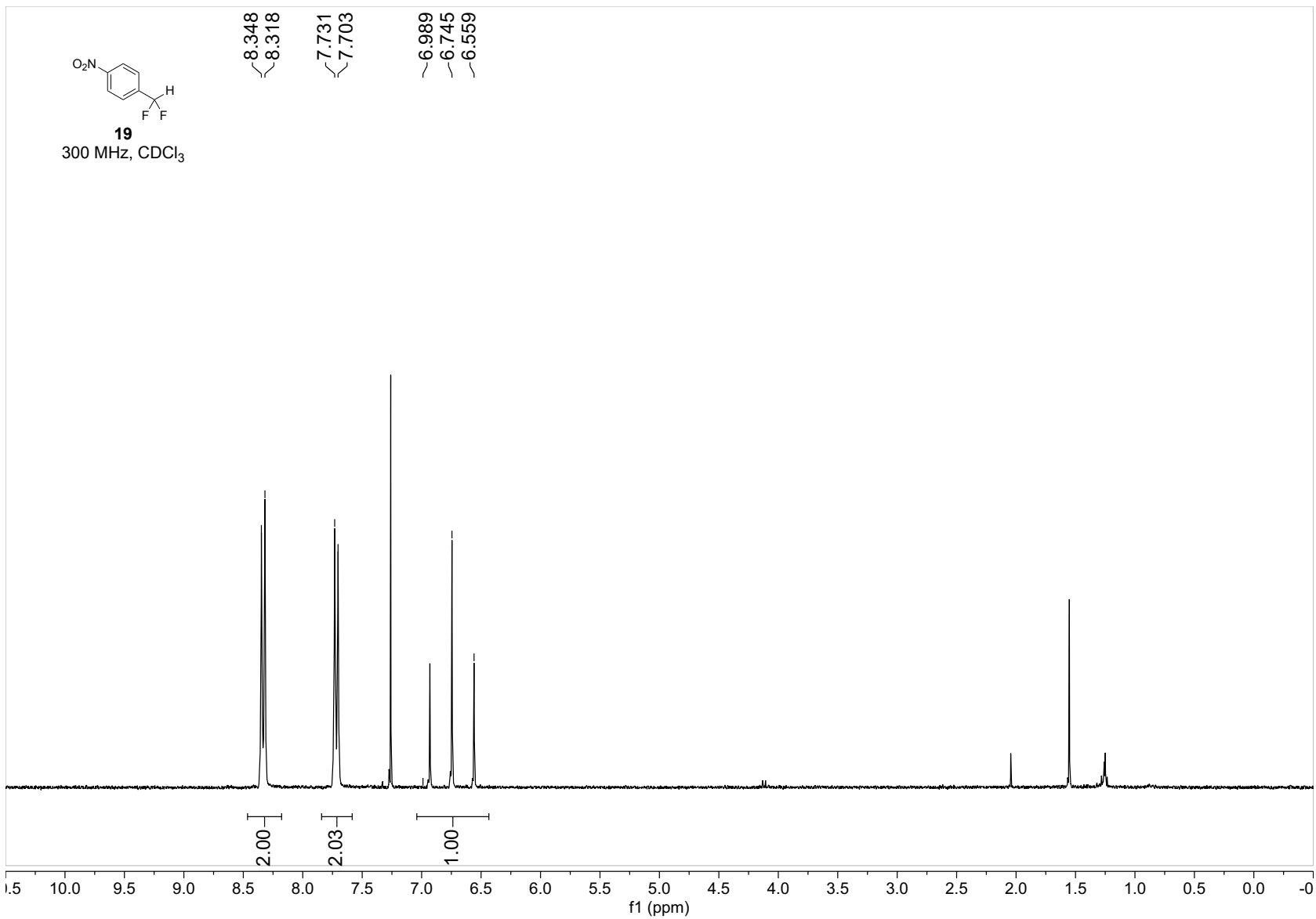


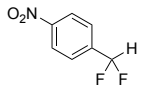




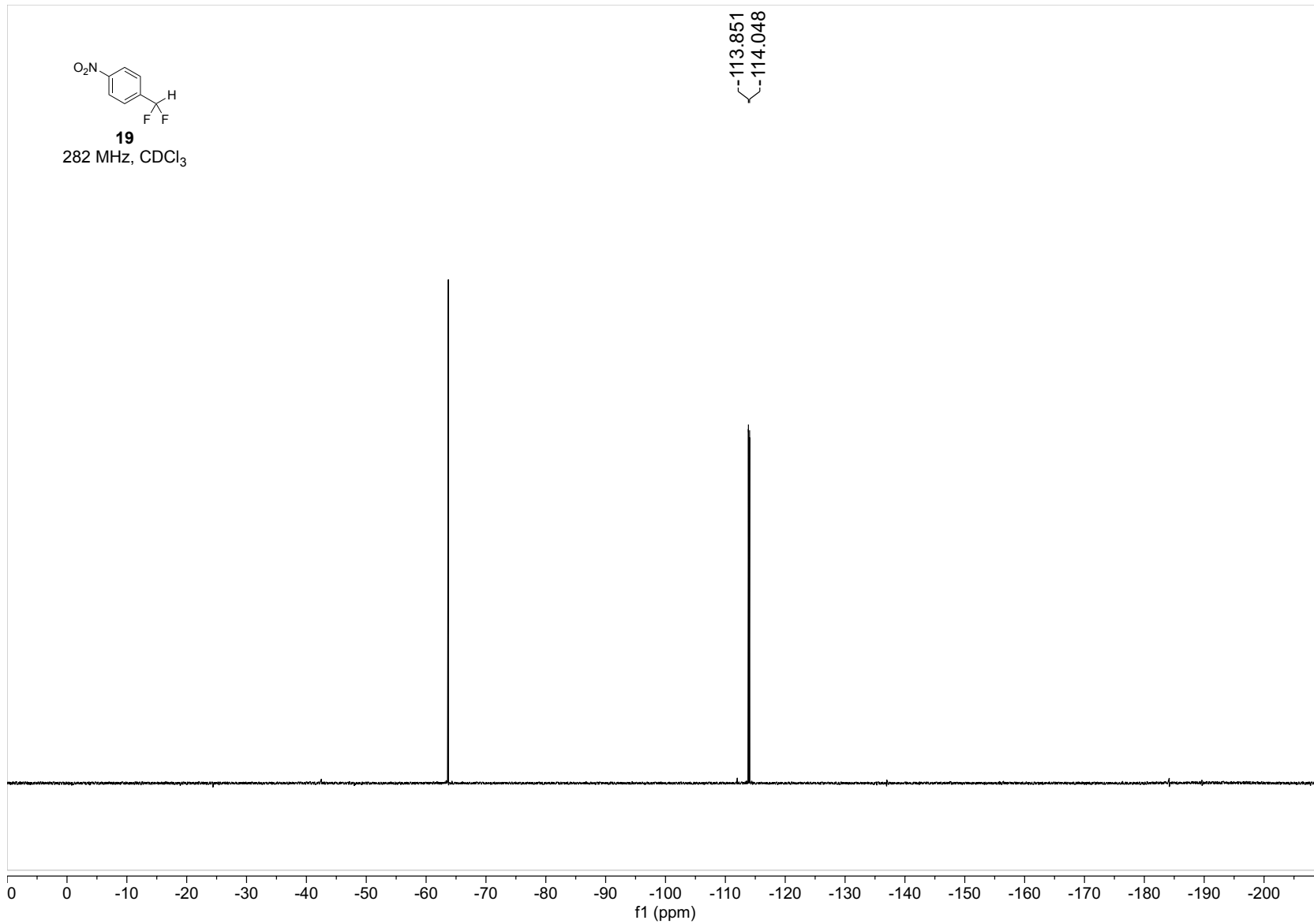
18
471 MHz, CDCl₃

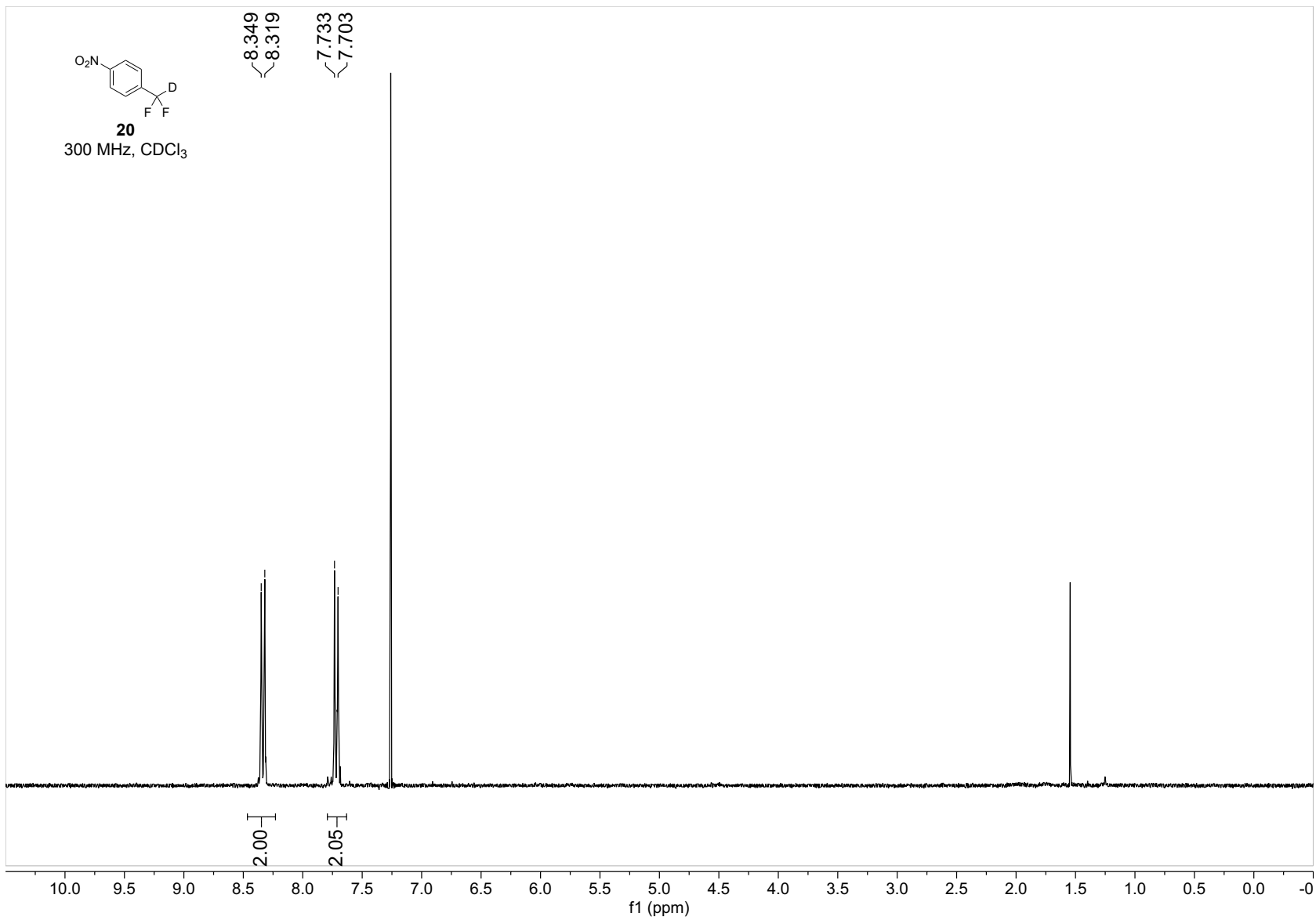


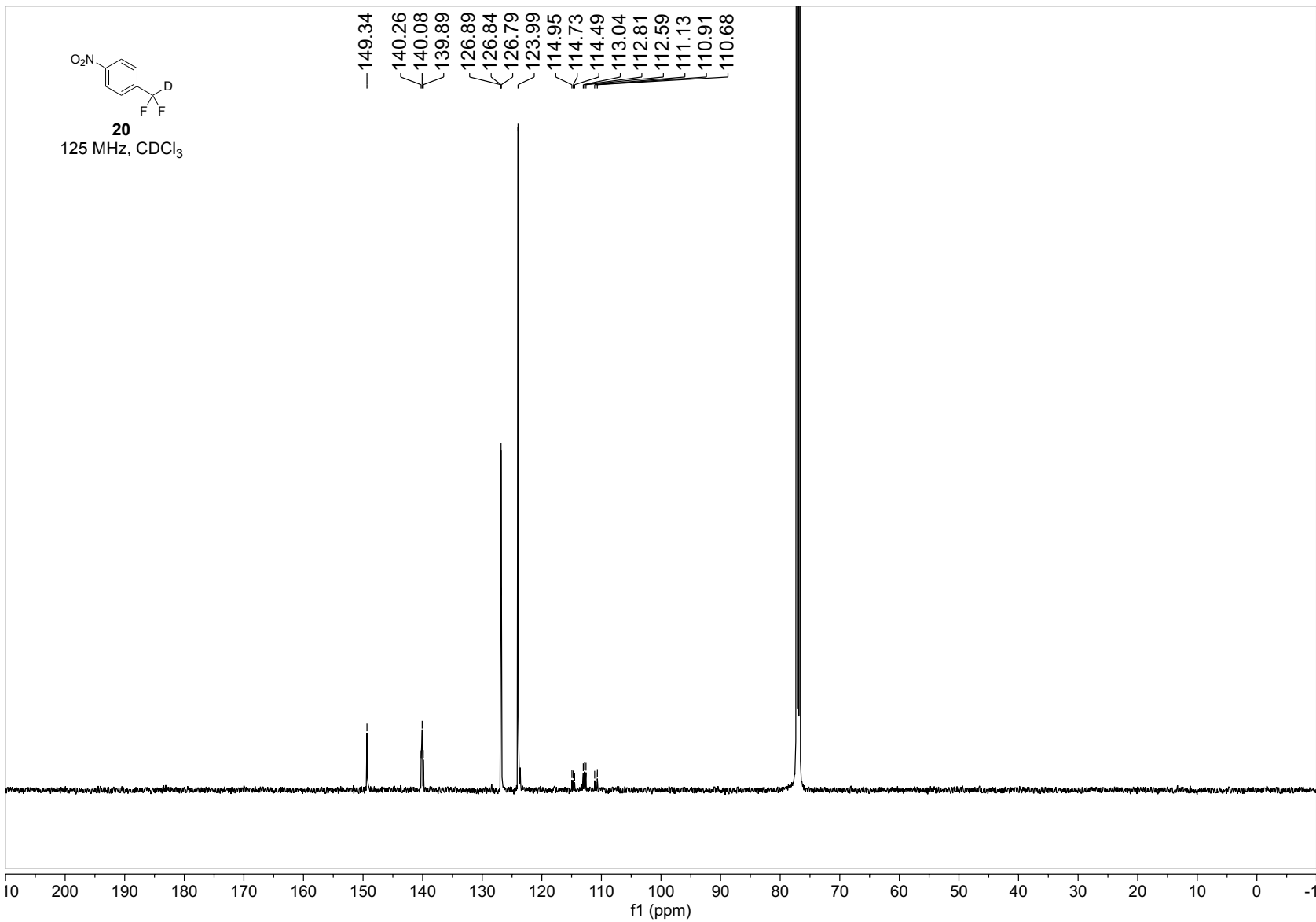


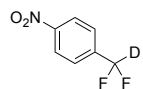


19
282 MHz, CDCl₃









20
282 MHz, CDCl₃

