

**A Protocol for the *ortho*-Deuteration of Acidic Aromatic
Compounds in D₂O Catalyzed by Cationic Rh^{III}**

Alyssa L. Garreau, Hanyang Zhou, Michael C. Young*

Department of Chemistry and Biochemistry, School of Green Chemistry and Engineering, The University of Toledo,
Toledo, OH, 43606 United States.

Supporting Information

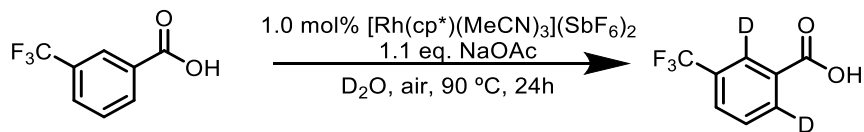
Table of Contents

1. General Information	S-2
2. Optimization of Deuteration Reactions	S-3
3. Procedure and Characterization for Deuteration Reactions	S-4
4. Procedure and Characterization for Reaction on Aspirin.....	S-15
5. Procedure and Characterization for Scale-Up Reactions	S-17
6. Co-Solvent Studies	S-18
7. ¹ H and ¹³ C of Deuterated Compounds.....	S-21
8. Select ² H of Deuterated Compounds.....	S-69
9. References	S-76

1. General Information

^1H spectra were recorded on either a Varian Inova 400 MHz NMR spectrometer or a Bruker Avance 600 MHz NMR spectrometer, and were processed using MestReNova by Mestrelab Research S.L. Proton (^1H) chemical shifts are reported in parts per million (δ) with respect to tetramethylsilane (TMS, $\delta=0$), and referenced internally with respect to the protio solvent impurity or TMS if the solvent peak is obscured.¹ Deuterium (^2H) NMR were obtained in 1% $\text{CDCl}_3/\text{CHCl}_3$. The average yields and levels of deuteration are shown, while the NMR spectra of the highest level of deuteration are provided – the transcriptions have been taken from these NMR spectra. HRMS data were recorded on an Agilent 6540 Accurate-Mass Q-TOF LC/MS, and processed using Mass Hunter Qualitative Analysis Software (B.05.00) at the Environmental Analysis Service Center, University of Cincinnati. LRMS data was recorded on an Agilent 5975C Inert XL MSD with Triple-Axis Detector, and processed using 5975C MSD Data Analysis software. Deuterated solvents were obtained from Cambridge Isotope Laboratories, Inc., Andover, MA, and used without further purification. Cationic rhodium catalyst $[\text{Rh}(\text{cp}^*)(\text{MeCN})_3](\text{SbF}_6)_2$ was obtained from Strem Chemicals, Newburyport, MA. All other materials were obtained from Sigma-Aldrich Chemical Company, St. Louis, MO, Combi-Blocks, San Diego, CA, Oakwood Chemical, Estill, SC, Alfa Aesar, Ward Hill, MA, Acros Organic, Geel, Belgium, or TCI, Tokyo, Japan, and were used as received. Substrates with only low levels of hydrogen/deuterium exchange (HDE) only have ^1H NMR provided as they are essentially unchanged from the commercially-available starting materials.

2. Optimization of Deuteration Reactions

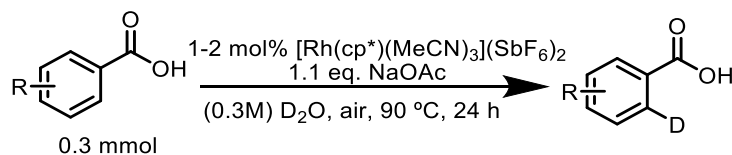


1	None	98 / 92
2	[Rh(cp*)(MeCN) ₃](SbF ₆) ₂ as catalyst (0.25 mol%)	97 / 67
3	RhCl ₃ ·3H ₂ O as catalyst (1 mol%)	4 / 6
4	[Rh(cp*)Cl ₂] ₂ as catalyst (1 mol%)	98 / 73
5	[Ir(cp*)Cl ₂] ₂ as catalyst (1 mol%)	98 / 81
6	[Ru(cp*)(cod)Cl] as catalyst (1 mol%)	< 4 / < 4
7	[Ru(PPh ₃) ₂ Cl ₂] as catalyst (1 mol%)	< 4 / < 4
8	Pd(OAc) ₂ as catalyst (1 mol%)	< 4 / < 4
9	No catalyst	< 4 / < 4
10	NaHCO ₃ as base (1.2 equiv.)	65 / 17
11	Cs ₂ CO ₃ as base (1.2 equiv.)	35 / 9
12	Na ₂ CO ₃ as base (1.2 equiv.)	65 / 17
13	6 h reaction time	97 / 50
14	12 h reaction time	98 / 88
15	80 °C reaction temperature	98 / 90
16	70 °C reaction temperature	95 / 61
17	100 °C and 0.25 mol% Rh ^{III} catalyst loading	93 / 42
18	70 °C and 48 h reaction time	98 / 69
19	70 °C, 48 h, and 0.25 mol% Rh ^{III} catalyst loading	91 / 39

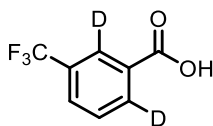
To a 2 dram vial with a PTFE-lined cap and stir bar was added 3-(trifluoromethyl)benzoic acid (50.0 mg, 0.26 mmol), transition metal catalyst (0.25 – 1 mol%), base (1.1 – 1.2 eq.), and D₂O (1.0 mL, 55 mmol), followed by immediately capping. The reactions were then transferred to a pre-heated pie block (70 – 90 °C), and heated with stirring (6 – 48 h). After completion, the reactions were diluted with 1.2 M HCl (3 mL) and dichloromethane (3 mL), followed by stirring for 15 min. The mixture was then poured into additional 1.2 M HCl (15 mL), followed by extracting with dichloromethane (3 x 10 mL). The combined organic phase was dried over Na₂SO₄, then evaporated *in vacuo*, and the level of deuteration quantified by ¹H NMR, using the protons at C⁴ and C⁵ as internal standards.

3. Procedure and Characterization for Deuteration Reactions

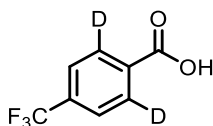
a. Aromatic and Heteroaromatic Carboxylic Acids



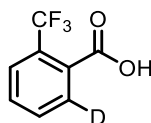
General Procedure: In duplicate, to a 2 dram vial with a PTFE-lined cap and stir bar was added acid (0.300 mmol), Tris(acetonitrile)pentamethylcyclopentadienylrhodium(III) hexafluoroantimonate (2.5 mg, 3.0 μ mol), sodium acetate (27.1 mg, 0.33 mmol), and D₂O (1.0 mL, 55 mmol), followed by immediately capping. The reactions were then transferred to a pre-heated pie block (90 °C), and heated with stirring (24 h). Notably, solid occasionally collected on the sides of the vial above the solvent line, requiring manual dislodgement by shaking. When necessary, this action was performed at least twice over the 24 h period. Unless stated otherwise, after completion the reactions were diluted with 1.2 M HCl (3 mL) and dichloromethane (3 mL), followed by stirring for 15 min. The mixture was then poured into additional 1.2 M HCl (15 mL), followed by extracting with dichloromethane (3 x 10 mL). The combined organic phase was dried over Na₂SO₄, then evaporated *in vacuo*, and the level of deuteration quantified by ¹H NMR, using unexchanged positions to quantify deuteration when possible, or by addition of standards when not. The mass recovery (yield) as well as the % deuteration is reported as an average of all runs.



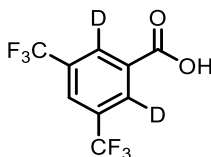
3-(Trifluoromethyl)benzoic-2,6-*d*₂ Acid (1a): 3-(Trifluoromethyl)benzoic Acid (57.0 mg, 0.300 mmol) was used,² giving the deuterated product as a faint pink solid (53.6 mg, 93%), showing 92% deuteration at C²/C⁶ and 98% deuteration at C⁶. ¹H NMR (400 MHz, CDCl₃) δ 8.40 (s, 0.08 H), 8.31 (d, J = 7.8 Hz, 0.02 H), 7.89 (d, J = 7.8 Hz, 1 H), 7.65 (d, J = 7.8 Hz, 1 H).



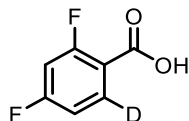
4-(Trifluoromethyl)benzoic-2,6-*d*₂ Acid (1b): 4-(Trifluoromethyl)benzoic Acid (57.0 mg, 0.300 mmol) was used, giving the deuterated product as a faint red solid (49.3 mg, 86%), showing 55% deuteration at C²/C⁶. When the reaction was performed with 2 mol% Rh, the deuteration was 74% at C²/C⁶. ¹H NMR (400 MHz, CDCl₃) δ 8.22 (d, J = 8.5 Hz, 0.89 H), 7.79 – 7.74 (m, 2 H). ¹³C NMR (151 MHz, CD₃OD) δ 168.7, 135.5, 135.1 (q, J = 32.3 Hz), 131.3, 131.0 (t, J = 25.4 Hz), 127.9, 126.5 (q, J = 3.5 Hz), 126.4 (q, J = 3.8 Hz), 125.2 (q, J = 271.8 Hz). HRMS (ESI, Negative Mode) for C₈H₂D₂F₃O₂ [M-H]⁻ calc. 191.0294, exp. 191.0288.



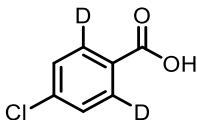
2-(Trifluoromethyl)benzoic-6-*d* Acid (1c): 2-(Trifluoromethyl)benzoic Acid (57.0 mg, 0.300 mmol) was used, giving the deuterated product as a faint red solid (46.8 mg, 82%), showing 28% deuteration at C⁶. When the reaction was performed with 2 mol% Rh, the deuteration was 84%. ¹H NMR (400 MHz, CDCl₃) δ 8.01 – 7.95 (m, 0.72 H), 7.82 (dd, *J* = 5.2, 3.8 Hz, 1 H), 7.71 – 7.63 (m, 2 H). ¹³C NMR (151 MHz, CD₃OD) δ 170.1, 133.6, 133.5, 133.2, 133.1, 132.2, 131.1, 130.8 (t, *J* = 25.2 Hz), 129.3 (q, *J* = 32.3 Hz), 127.6 (q, *J* = 5.4 Hz), 125.0 (q, *J* = 272.6 Hz). HRMS (ESI, Negative Mode) for C₈H₃DF₃O₂ [M-H]⁻ calc. 190.0232, exp. 190.225.



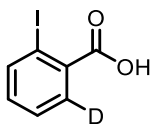
3,5-Bis(trifluoromethyl)benzoic-2,6-*d*2 Acid (1d): 3,5-Bis(trifluoromethyl)benzoic Acid (77.4 mg, 0.300 mmol) was used, giving the deuterated product as an orange solid (73.0 mg, 94%), showing 36% deuteration at C⁶. When the reaction was performed with 2 mol% Rh, the deuteration was 74%. ¹H NMR (400 MHz, CDCl₃) δ 8.57 (s, 1.29 H), 8.14 (s, 2 H). ¹³C NMR (151 MHz, CDCl₃) δ 169.5 (m), 132.6 (q, *J* = 34.2 Hz), 132.5 (q, *J* = 34.2 Hz), 131.6 (m), 130.5, 130.1 (t, *J* = 23.1 Hz), 127.4 (sept, *J* = 3.4 Hz), 122.9 (q, *J* = 272.9 Hz). HRMS (ESI, Negative Mode) for C₉D₂F₆O₂ [M-H]⁻ calc. 259.0168, exp. 259.0164.



2,4-Difluorobenzoic-6-*d* Acid (1e): 2,4-Difluorobenzoic Acid (47.4 mg, 0.300 mmol) was used, giving the deuterated product as a yellow-orange solid (35.8 mg, 75%), showing 99% deuteration at C⁶. ¹H NMR (400 MHz, CDCl₃) δ 8.10 – 8.05 (m, 0.01 H), 6.98 (d, *J* = 7.6 Hz, 1 H), 6.92 (ddd, *J* = 11.0, 8.8, 2.4 Hz, 1 H). ¹³C NMR (151 MHz, CD₃OD) δ 167.15 (dd, *J* = 254.2, 12.0 Hz), 166.4 (d, *J* = 2.6 Hz), 164.4 (dd, *J* = 261.7, 12.8 Hz), 135.13 (ddt, 25.4, 10.9, 1.4 Hz), 116.9 (dd, *J* = 9.7, 2.9 Hz), 112.5 (dd, *J* = 21.8, 3.8 Hz), 106.0 (t, *J* = 26.1 Hz). HRMS (ESI, Negative Mode) for C₇H₂DF₂O₂ [M-H]⁻ calc. 158.0169, exp. 158.0163.

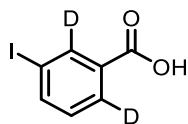


4-Chlorobenzoic-2,6-*d*2 Acid (1f): 4-Chlorobenzoic Acid (47.0 mg, 0.300 mmol) was used, giving the deuterated product as a white solid (14.6 mg, 31%), showing 86% deuteration at C^{2/6}. ¹H NMR (400 MHz, CDCl₃) δ 8.04 (d, *J* = 8.9 Hz, 0.28 H), 7.46 (s, 2 H). ¹³C NMR (151 MHz, CD₃OD) δ 169.2, 140.3, 132.3, 132.0 (t, *J* = 25.2 Hz), 129.7, 129.6. HRMS (ESI, Negative Mode) for C₇H₂D₂ClO₂ [M-H]⁻ calc. 157.0031, exp. 157.0024.

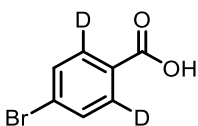


2-Iodobenzoic-6-*d* Acid (1g): 2-Iodobenzoic Acid (74.4 mg, 0.300 mmol) was used, giving the deuterated product as a faint red solid (69.4 mg, 93%), showing 52% deuteration at C⁶. ¹H NMR (400 MHz, CDCl₃) δ 8.07 (d, *J* = 7.9 Hz,

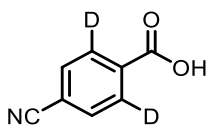
1 H), 8.02 (dd, $J = 7.8, 1.6$ Hz, 0.46 H), 7.45 (dt, $J = 6.6, 3.4$ Hz, 1 H), 7.21 (t, $J = 7.7$ Hz, 1 H). ^{13}C NMR (100 MHz, CD_3OD) δ 170.1, 142.3, 133.4, 131.6, 129.0, 128.9, 94.2. HRMS (ESI, Negative Mode) for $\text{C}_7\text{H}_3\text{DIO}_2$ $[\text{M-H}]^-$ calc. 247.9324, exp. 247.9313.



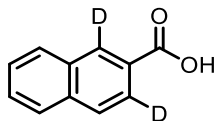
3-Iodobenzoic-2,6- d_2 acid (1h): 3-Iodobenzoic Acid (74.4 mg, 0.300 mmol) was used, giving the deuterated product as a faint red solid (68.2 mg, 91%), showing 99% deuteration at C^2 and C^6 . ^1H NMR (400 MHz, CDCl_3) δ 8.45 (d, $J = 2.0$ Hz, 0.01 H), 8.07 (d, $J = 7.8$ Hz, 0.01 H), 7.95 (d, $J = 7.9$ Hz, 1 H), 7.23 (d, $J = 7.9$ Hz, 1 H). ^{13}C NMR (151 MHz, CDCl_3) δ 170.2, 142.8, 138.9 (t, $J = 26.1$ Hz), 131.0, 130.2, 129.2 (t, $J = 25.3$ Hz), 93.8. HRMS (ESI, Negative Mode) for $\text{C}_7\text{H}_2\text{D}_2\text{IO}_2$ $[\text{M-H}]^-$ calc. 248.9387, exp. 248.9380.



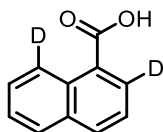
4-Bromobenzoic-2,6- d_2 Acid (1i): 4-Bromobenzoic Acid (60.3 mg, 0.300 mmol) was used, giving the deuterated product as a pale white solid (24.3 mg, 40%), showing 77% deuteration at $\text{C}^{2,6}$. ^1H NMR (400 MHz, CDCl_3) δ 7.96 (d, $J = 8.7$ Hz, 0.29 H), 7.63 (s, 2 H). ^{13}C NMR (151 MHz, CD_3OD) δ 168.8, 132.8, 132.7, 132.5, 132.2 (t, $J = 25.3$ Hz), 128.7. HRMS (ESI, Negative Mode) for $\text{C}_7\text{H}_2\text{D}_2\text{BrO}_2$ $[\text{M-H}]^-$ calc. 200.9526, exp. 200.9517.



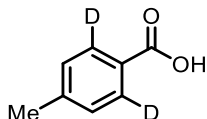
4-Cyanobenzoic-2,6- d_2 Acid (1j): 4-Cyanobenzoic Acid (44.1 mg, 0.300 mmol) was used, giving the deuterated product as a pale white solid (24.2 mg, 54%), showing 97% deuteration at $\text{C}^{2,6}$. ^1H NMR (400 MHz, CDCl_3) δ 8.22 (d, $J = 8.5$ Hz, 0.03 H), 7.80 (s, 2 H). ^{13}C NMR (151 MHz, CDCl_3) δ 169.3, 133.0, 132.4, 130.5 (t, $J = 25.9$ Hz), 118.0, 117.4. HRMS (ESI, Negative Mode) for $\text{C}_8\text{H}_2\text{D}_2\text{NO}_2$ $[\text{M-H}]^-$ calc. 148.0373, exp. 148.0369.



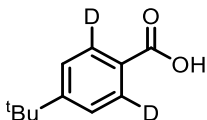
2-Naphthoic-1,3- d_2 Acid (1k): 2-Naphthoic Acid (51.7 mg, 0.300 mmol) was used, giving the deuterated product as a faint red solid (47.5 mg, 91%), showing 96% deuteration at C^1 and 96% deuteration at C^3 . ^1H NMR (400 MHz, CDCl_3) δ 8.73 (s, 0.04 H), 8.13 (d, $J = 8.7$ Hz, 0.04 H), 7.92 (d, $J = 10.8$ Hz, 1 H), 7.68 – 7.55 (m, 2 H). ^{13}C NMR (151 MHz, CDCl_3) δ 171.5, 136.1, 132.5, 132.0 (t, $J = 25.0$ Hz), 129.6, 128.8, 128.4, 128.0, 126.9, 126.4, 125.3 (t, $J = 24.9$ Hz). HRMS (ESI, Negative Mode) for $\text{C}_{11}\text{H}_5\text{D}_2\text{O}_2$ $[\text{M-H}]^-$ calc. 173.0577, exp. 173.0575.



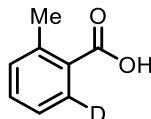
1-Naphthoic-2,8-*d*₂ Acid (1l): 1-Naphthoic Acid (51.7 mg, 0.300 mmol) was used, giving the deuterated product as a faint red solid (49.1 mg, 94%), showing 89% deuteration at C² and 83% deuteration at C⁸. ¹H NMR (400 MHz, CDCl₃) δ 9.09 (d, *J* = 8.6 Hz, 0.17 H), 8.42(d, *J* = 7.3 Hz, 0.11 H), 8.11 (d, *J* = 8.2 Hz, 1 H), 7.93 (dd, *J* = 8.2, 1.3 Hz, 1 H), 7.67 (d, *J* = 5.6 Hz, 1 H), 7.61 – 7.52 (m, 2 H). ¹³C NMR (151 MHz, CD₃OD) δ 171.0, 135.4, 134.3, 132.7, 132.6, 131.3, 131.0 (t, *J* = 24.9 Hz), 129.6, 128.7, 128.5, 128.4, 127.2, 126.9, 126.6 (t, *J* = 25.0 Hz), 125.6, 125.5. HRMS (ESI, Negative Mode) for C₁₁H₅D₂O₂ [M-H]⁻ calc. 173.0577, exp. 173.0573.



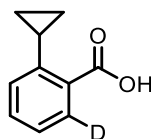
4-Methylbenzoic-2,6-*d*₂ Acid (1m): 4-Methylbenzoic Acid (40.9 mg, 0.300 mmol) was used, giving the deuterated product as a pink solid (40.2 mg, 97%), showing 96% deuteration at C² and C⁶. ¹H NMR (400 MHz, CDCl₃) δ 8.00 (d, *J* = 8.4 Hz, 0.04 H), 7.27 (s, 2 H), 2.44 (s, 3 H). ¹³C NMR (151 MHz, CDCl₃) δ 171.9, 144.8, 130.1 (t, *J* = 25.2 Hz), 129.2, 126.5, 21.9. HRMS (ESI, Negative Mode) for C₈H₅D₂O₂ [M-H]⁻ calc. 137.0577, exp. 137.0574.



4-(*Tert*-butyl)benzoic-2,6-*d*₂ Acid (1n): 4-(*Tert*-butyl)benzoic Acid (53.5mg, 0.300 mmol) was used, giving the deuterated product as a faint red solid (50.2 mg, 93%), showing 87% deuteration at C^{2/6}. ¹H NMR (400 MHz, CDCl₃) δ 8.04 (d, *J* = 8.8 Hz, 0.10H), 7.51 (s, 2 H), 1.35 (s, 9 H). ¹³C NMR (151 MHz, CDCl₃) δ 172.5, 157.7, 130.0 (t, *J* = 24.2 Hz), 126.5, 125.6, 125.5, 35.3, 31.2. HRMS (ESI, Negative Mode) for C₁₁H₁₁D₂O₂ [M-H]⁻ calc. 179.1047, exp. 179.1048.

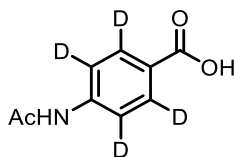


2-Methylbenzoic-6-*d* Acid (1o): 2-Methylbenzoic Acid (40.9 mg, 0.300 mmol) was used, giving the deuterated product as a faint red solid (37.0 mg, 90%), showing 99% deuteration at C⁶. ¹H NMR (400 MHz, CDCl₃) δ 8.09 – 8.03 (m, 0.01 H), 7.46 (t, *J* = 7.5 Hz, 1 H), 7.29 (d, *J* = 7.5 Hz, 2 H), 2.67 (s, 3 H). ¹³C NMR (151 MHz, CDCl₃) δ 173.7, 141.5, 133.1, 132.1, 131.5 (t, *J* = 24.7 Hz), 128.4, 125.9, 22.3. HRMS (ESI, Negative Mode) for C₈H₆DO₂ [M-H]⁻ calc. 136.0514, exp. 136.0512.

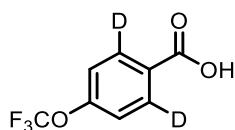


2-Cyclopropylbenzoic-6-*d* Acid (1p): 2-Cyclopropylbenzoic Acid (48.7 mg, 0.300 mmol) was used, giving the deuterated product as a faint pink solid (45.5 mg, 93%), showing 99% deuteration C⁶. ¹H NMR (400 MHz, CDCl₃) δ 8.00 (d, *J* = 7.8 Hz, 0.01 H), 7.46 (t, *J* = 7.6 Hz, 1 H), 7.25 (t, *J* = 5.9 Hz, 1 H), 7.05 (d, *J* = 7.9 Hz, 1 H), 2.86 – 2.79 (m, 1 H), 1.13 – 1.01 (m, 2 H), 0.83 – 0.70 (m, 2 H). ¹³C NMR (151 MHz, CDCl₃) δ 174.3, 146.1, 133.0, 131.0 (t, *J* =

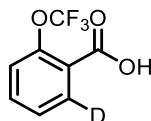
24.7 Hz), 129.8, 125.8, 125.4, 125.3, 13.7, 9.2. HRMS (ESI, Negative Mode) for $C_{10}H_8DO_2$ $[M-H]^-$ calc. 162.0671, exp. 162.0666.



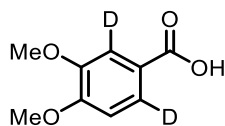
4-Acetamidobenzoic-2,3,5,6-*d*₄ Acid (1q): 4-Acetamidobenzoic Acid (53.8 mg, 0.300 mmol) was used, giving the deuterated product as a brown solid (39.2 mg, 72%), showing 92% deuteration at $C^{2/6}$ and 27% at $C^{3/5}$. 1H NMR (400 MHz, CD_3OD) δ 7.98 – 7.93 (m, 0.09 H), 7.67 (m, 1.33 H), 2.15 (s, 3 H). ^{13}C NMR (151 MHz, $DMSO-d_6$) δ 169.0, 167.1, 167.0, 146.5 (m), 143.5, 143.5, 130.8 (t, $J = 24.0$ Hz), 130.1 (t, $J = 20.4$ Hz), 124.7, 122.0 (m), 118.1, 116.9, 24.2. HRMS (ESI, Negative Mode) for $C_9H_4D_4NO_3$ $[M-H]^-$ calc. 182.0761, exp. 182.0752.



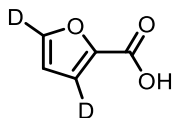
4-(Trifluoromethoxy)benzoic-2,6-*d*₂ Acid (1r): 4-(Trifluoromethoxy)benzoic Acid (61.8 mg, 0.300 mmol) was used, giving the deuterated product as a faint yellow solid (54.3 mg, 87%), showing 94% deuteration at $C^{2/6}$. 1H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, $J = 9.1$ Hz, 0.12 H), 7.31 (s, 2 H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.3, 153.5, 132.5, 132.2 (t, $J = 25.4$ Hz), 127.6, 120.5 (q, $J = 258.8$ Hz), 120.4, 120.3. HRMS (ESI, Negative Mode) for $C_8H_2D_2F_3O_3$ $[M-H]^-$ calc. 207.0244, exp. 207.0242.



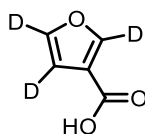
2-(Trifluoromethoxy)benzoic-6-*d* acid (1s): 2-(Trifluoromethoxy)benzoic Acid (61.8 mg, 0.300 mmol) was used, giving the deuterated product as a light orange solid (53.4 mg, 86%), showing 99% deuteration at C^6 . 1H NMR (400 MHz, $CDCl_3$) δ 8.11 (dd, $J = 7.8, 1.7$ Hz, 0.01 H), 7.64 (t, $J = 7.9$ Hz, 1 H), 7.43 (d, $J = 7.2$ Hz, 1 H), 7.38 (dt, $J = 8.2, 1.2$ Hz, 1 H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.4, 148.6, 134.8, 133.0, 132.7 (t, $J = 25.3$ Hz), 127.2, 127.1, 123.8, 123.7, 123.0, 122.9, 120.5 (q, $J = 258.3$ Hz). HRMS (ESI, Negative Mode) for $C_8H_3DF_3O_3$ $[M-H]^-$ calc. 206.0181, exp. 206.0175.



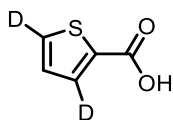
3,4-Dimethoxybenzoic-2,6-*d*₂ Acid (1t): 3,4-Dimethoxybenzoic Acid (54.7 mg, 0.300 mmol) was used, giving the deuterated product as a tan solid (45.0 mg, 81%), showing 95% deuteration at C^2 and 94% deuteration at C^6 . 1H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, $J = 8.4$ Hz, 0.05 H), 7.60 (s, 0.06 H), 6.92 (s, 1 H), 3.96 (s, 3 H), 3.95 (s, 3 H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.2, 153.8, 148.8, 148.7, 124.7, 124.5 (t, $J = 25.0$ Hz), 121.7, 112.4, 112.1 (t, $J = 24.3$ Hz), 110.4, 110.3, 56.2, 56.1. HRMS (ESI, Negative Mode) for $C_9H_7D_2O_4$ $[M-H]^-$ calc. 183.0632, exp. 183.0628.



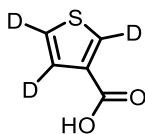
Furan-2-carboxylic-3,5-*d*₂ Acid (1u): Furan-2-carboxylic Acid (33.6 mg, 0.300 mmol) was used, giving the deuterated product as a tan solid (20.6 mg, 61%) after a modified work-up (mixture was diluted with 15 mL of saturated NH₄Cl_(aq) instead of 1.2M HCl), showing 99% deuteration at C³ and 53% deuteration at C⁵. ¹H NMR (400 MHz, CDCl₃) δ 7.65 (d, *J* = 1.7 Hz, 0.47 H), 7.34 (d, *J* = 3.4 Hz, 0.01 H), 6.57 (d, *J* = 2.6 Hz, 1 H). ¹³C NMR (151 MHz, CDCl₃) δ 163.9, 147.6, 147.4 (t, *J* = 31.2 Hz), 143.9, 143.8, 120.1 (t, *J* = 27.4 Hz), 112.3, 112.1. HRMS (ESI, Negative Mode) for C₅HD₂O₃ [M-H]⁻ calc. 113.0213, exp. 113.0211.



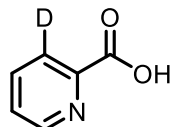
Furan-3-carboxylic-2,4,5-*d*₃ Acid (1v): Furan-3-carboxylic Acid (33.6 mg, 0.300 mmol) was used, giving the deuterated product as an offwhite solid (12.4 mg, 36%) after a modified work-up (mixture was diluted with 15 mL of saturated NH₄Cl_(aq) instead of 1.2M HCl), showing 99% deuteration at C² and C⁴, and 24% deuteration at C⁵. ¹H NMR (400 MHz, CDCl₃) δ 8.12 (d, *J* = 1.6 Hz, 0.01 H), 7.46 (s, 0.76 H), 6.78 (d, *J* = 1.9 Hz, 0.01 H). ¹³C NMR (151 MHz, CDCl₃) δ 168.7, 149.0 (t, *J* = 31.7 Hz), 144.1, 143.8 (t, *J* = 31.3 Hz), 118.6, 109.9 (t, *J* = 27.5 Hz), 109.5. HRMS (ESI, Negative Mode) for C₅D₃O₃ [M-H]⁻ calc. 114.0276, exp. 114.0273.



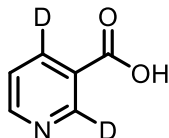
Thiophene-2-carboxylic-3,5-*d*₂ Acid (1w): Thiophene-2-carboxylic Acid (38.4 mg, 0.300 mmol) was used, giving the deuterated product as a tan solid (28.3 mg, 73%), showing 98% deuteration at C³ and 8% deuteration at C⁵. ¹H NMR (400 MHz, CDCl₃) δ 7.92 – 7.87 (m, 0.02 H), 7.66 (d, *J* = 5.0 Hz, 0.92 H), 7.15 (d, *J* = 4.9 Hz, 1 H). ¹³C NMR (151 MHz, CDCl₃) δ 168.0, 135.0 (t, *J* = 26.2 Hz), 134.2, 132.9, 128.1, 128.0. HRMS (ESI, Negative Mode) for C₅H₂DO₂S [M-H]⁻ calc. 127.9922, exp. 127.9919.



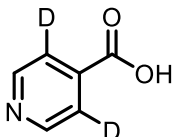
Thiophene-3-carboxylic-2,4,5-*d*₃ Acid (1x): Thiophene-3-carboxylic Acid (38.4 mg, 0.300 mmol) was used, giving the deuterated product as a tan solid (30.9 mg, 79%), showing 99% deuteration at C², 98% deuteration at C⁴, and 10% deuteration at C⁵. ¹H NMR (400 MHz, CDCl₃) δ 8.25 (d, *J* = 3.1 Hz, 0.01 H), 7.58 (d, *J* = 5.0 Hz, 0.02 H), 7.34 (s, 0.90 H). ¹³C NMR (151 MHz, CDCl₃) δ 168.3, 134.6 (t, *J* = 29.1 Hz), 132.8, 128.1 (t, *J* = 26.4 Hz), 126.3. HRMS (ESI, Negative Mode) for C₅HD₂O₂S [M-H]⁻ calc. 128.9985, exp. 128.9982.



Picolinic-3-*d* Acid (1z): Picolinic Acid (36.9 mg, 0.300 mmol) was used. Due to poor extraction efficiency, product was analyzed by ^1H NMR directly from the crude reaction mixture in D_2O , showing < 4% deuteration at C^3 , so essentially starting material. ^1H NMR (400 MHz, D_2O) δ 8.57 (s, 0.98H), 9.29 (s, 1H), 8.10 (d, $J = 6.8$ Hz, 1H), 7.80 (s, 1H).

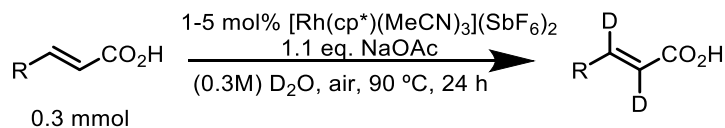


Nicotinic-2,4-*d*₂ Acid (1aa): Nicotinic Acid (36.9 mg, 0.300 mmol) was used. Due to poor extraction efficiency, product was analyzed by ^1H NMR directly from the crude reaction mixture in D_2O , showing < 4% deuteration at $\text{C}^{2/4}$, so essentially starting material. ^1H NMR (400 MHz, D_2O) δ 8.93 (br s, 1 H), 8.63 (br s, 1 H), 8.47 (d, $J = 6.6$ Hz, 1 H), 7.73 (br s, 1 H).

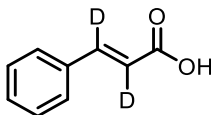


Isonicotinic-3,5-*d*₂ Acid (1ab): Isonicotinic Acid (36.9 mg, 0.300 mmol) was used. Due to poor extraction efficiency, product was analyzed by ^1H NMR directly from the crude reaction mixture in D_2O , showing < 4% deuteration at $\text{C}^{3/5}$, so essentially starting material. ^1H NMR (400 MHz, D_2O) δ 8.59 (d, $J = 4.8$ Hz, 2 H), 7.83 (d, $J = 5.5$ Hz, 2 H).

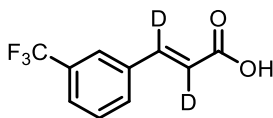
b. Vinylic Carboxylic Acids



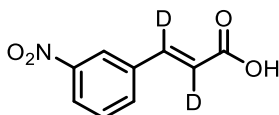
General Procedure: To a 2 dram vial with a PTFE-lined cap and stir bar was added acid (0.300 mmol), Tris(acetonitrile)pentamethylcyclopentadienylrhodium(III) hexafluoroantimonate (2.5 mg, 3.0 μmol), sodium acetate (27.1 mg, 0.33 mmol), and D_2O (1.0 mL, 55 mmol), followed by immediately capping. The reactions were then transferred to a pre-heated pie block (90 $^\circ\text{C}$) and heated with stirring (24 h). Notably, solid occasionally collected on the sides of the vial above the solvent line, requiring manual dislodgement by shaking. When necessary, this action was performed at least twice over the 24 h period. Unless stated otherwise, after completion the reactions were diluted with 1.2 M HCl (3 mL) and dichloromethane (3 mL), followed by stirring for 15 min. The mixture was then poured into additional 1.2 M HCl (15 mL), followed by extracting with dichloromethane (3 x 10 mL). The combined organic phase was dried over Na_2SO_4 , then evaporated *in vacuo*, and the level of deuteration quantified by ^1H NMR, using unexchanged positions to quantify deuteration when possible, or by addition of standards when not.



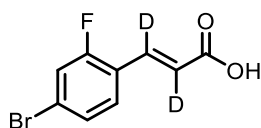
Cinnamic-2,3-*d*₂ Acid (2a): Cinnamic Acid (44.4 mg, 0.300 mmol) was used, giving the deuterated product as a faint orange solid (44.4 mg, 99%), showing 99% deuteration at C^β and 12% deuteration at C^α. ¹H NMR (400 MHz, CDCl₃) δ 7.81 (t, *J* = 16.0 Hz, 0.01 H), 7.57 (m, 2 H), 7.42 (m, 3 H), 6.46 (s, 0.88H). ¹³C NMR (151 MHz, CDCl₃) δ 172.8, 146.9 (t, *J* = 23.7 Hz), 134.1, 130.9, 129.1, 128.5, 117.4. HRMS (ESI, Negative Mode) for C₉H₆DO₂ [M-H]⁻ calc. 148.0514, exp. 148.0512.



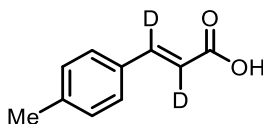
(*E*)-3-(3-(Trifluoromethyl)phenyl)acrylic-2,3-*d*₂ Acid (2b): 3-(Trifluoromethyl)cinnamic Acid (64.8 mg, 0.300 mmol) was used, giving the deuterated product as a yellow-orange solid (63.4 mg, 97%), showing 98% deuteration at C^β and 18% deuteration at C^α. ¹H NMR (400 MHz, CDCl₃) δ 7.80 (m, 1.02 H), 7.74 (d, *J* = 7.7 Hz, 1 H), 7.67 (d, *J* = 7.8 Hz, 1 H), 7.55 (t, *J* = 7.8 Hz, 1 H), 6.53 (s, 0.82 H). ¹³C NMR (151 MHz, CDCl₃) δ 172.0, 145.1 (t, *J* = 24.0 Hz), 134.8, 131.7 (q, *J* = 32.5 Hz), 131.4, 129.7, 127.3 (q, *J* = 3.3 Hz), 126.6, 125.1 (q, *J* = 3.4 Hz), 123.9 (q, *J* = 272.7 Hz), 119.3. HRMS (ESI, Negative Mode) for C₁₀H₅DF₃O₂ [M-H]⁻ calc. 216.0388, exp. 216.0387.



(*E*)-3-(3-Nitrophenyl)acrylic-2,3-*d*₂ Acid (2c): 3-Nitrocinnamic Acid (57.9 mg, 0.300 mmol) was used, giving the deuterated product as a white solid (46.3 mg, 80%), showing 22% deuteration at C^β and < 4% deuteration at C^α. ¹H NMR (400 MHz, CDCl₃) δ 8.42 (s, 1 H), 8.28 (d, *J* = 8.2 Hz, 1 H), 7.90 – 7.80 (m, 1.78 H), 7.62 (t, *J* = 8.0 Hz, 1 H), 6.63 – 6.55 (m, 1 H). See Section 6 for ¹³C data. HRMS (ESI, Negative Mode) for C₉H₆DNO₄ [M-H]⁻ calc. 193.0365, exp. 193.0358.

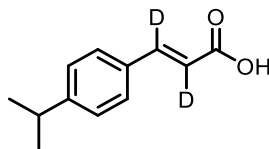


(*E*)-3-(4-Bromo-2-fluorophenyl)acrylic-2,3-*d*₂ Acid (2d): 4-Bromo-2-fluorocinnamic Acid (73.5 mg, 0.300 mmol) was used, giving the deuterated product as a faint pink solid (69.3 mg, 94%), showing 36% deuteration at C^β and < 4% deuteration at C^α. ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.69 (br s, 0.55 H), 7.82 (t, *J* = 8.3 Hz, 1 H), 7.68 (dd, *J* = 10.4, 1.8 Hz, 1 H), 7.58 (d, *J* = 16.2 Hz, 0.64 H), 7.48 (dd, *J* = 8.4, 1.7 Hz, 1 H), 6.63 (m, 1 H). See Section 6 for ¹³C data. HRMS (ESI, Negative Mode) for C₉H₄DBrFO₂ [M-H]⁻ calc. 243.9525, exp. 243.953.

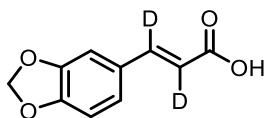


(*E*)-3-(*p*-Tolyl)acrylic-2,3-*d*₂ Acid (2e): 4-Methylcinnamic Acid (48.7 mg, 0.300 mmol) was used, giving the deuterated product as a tan solid (48.6 mg, 99%), showing 54% deuteration at C^β and < 4% deuteration at C^α. Attempts to perform the reaction using greater catalyst loadings did not give consistent levels of deuteration, though they were usually higher than 54% at C^β. ¹H NMR (400 MHz, CDCl₃) δ 7.78 (d, *J* = 16.0 Hz, 0.46 H), 7.46 (d, *J* = 8.1 Hz, 2 H),

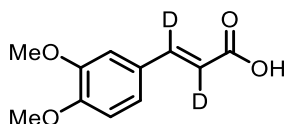
7.22 (d, $J = 8.0$ Hz, 2 H), 6.45 – 6.37 (m, 0.99 H), 2.39 (s, 3 H). See Section 6 for ^{13}C data. HRMS (ESI, Negative Mode) for $\text{C}_{10}\text{H}_8\text{DO}_2$ $[\text{M}-\text{H}]^-$ calc. 162.0671, exp. 162.0665.



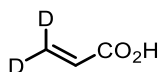
(E)-3-(4-Isopropylphenyl)acrylic-2,3- d_2 Acid (2f): 4-Isopropylcinnamic Acid (57.1 mg, 0.300 mmol) was used, giving the deuterated product as a light orange-yellow solid (50.1 mg, 87%), showing 70% deuteration at C^β and 11% deuteration at C^α . Increasing catalyst loading to 3 mol% led to 83% deuteration at C^β and 18% at C^α , while using 5 mol% catalyst gave 87% deuteration at C^β and 39% at C^α . ^1H NMR (400 MHz, CDCl_3) δ 7.79 (d, $J = 15.9$ Hz, 0.30 H), 7.49 (d, $J = 8.0$ Hz, 2 H), 7.27 (d, $J = 8.1$ Hz, 2 H), 6.42 (m, 0.89 H), 2.94 (sept, $J = 6.9$ Hz, 1 H), 1.26 (2, $J = 6.9$ Hz, 6 H). ^{13}C NMR (151 MHz, CDCl_3) δ 172.9, 152.3, 147.2, 146.9 (m), 131.8, 131.8, 128.7, 128.6, 128.5, 127.2, 125.2, 116.3, 34.3, 23.9. HRMS (ESI, Negative Mode) for $\text{C}_{12}\text{H}_{11}\text{D}_2\text{O}_2$ $[\text{M}-\text{H}]^-$ calc. 191.1047, exp. 191.1043.



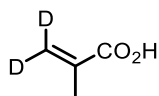
(E)-3-(Benzo[d][1,3]dioxol-5-yl)acrylic-2,3- d_2 Acid (2g): 3,4-Methylenedioxcinnamic Acid (57.7 mg, 0.300 mmol) was used, giving the deuterated product as a tan solid (51.0 mg, 88%), showing 25% deuteration at C^β and < 4% deuteration at C^α . ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 12.25 (br s, 0.79 H), 7.50 (d, $J = 15.9$ Hz, 0.75 H), 7.37 (d, $J = 1.4$ Hz, 1 H), 7.16 (d, $J = 8.1$, 1 H), 6.94 (d, $J = 8.0$ Hz, 1 H), 6.43 – 6.35 (m, 0.99 H), 6.07 (s, 2 H). See Section 6 for ^{13}C data. LRMS (EI) for $\text{C}_{10}\text{H}_5\text{DO}_4$ $[\text{M}]^{++}$ calc. 191.0, exp. 191.



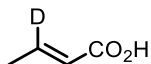
(E)-3-(3,4-Dimethoxyphenyl)acrylic-2,3- d_2 Acid (2h): 3,4-Dimethoxycinnamic Acid (62.5 mg, 0.300 mmol) was used, giving the deuterated product as an off-white solid (62.6 mg, 99%), showing 86% deuteration at C^β and 6% deuteration at C^α . ^1H NMR (400 MHz, CDCl_3) δ 7.74 (d, $J = 15.9$ Hz, 0.14 H), 7.14 (dd, $J = 8.2, 1.9$ Hz, 1 H), 7.08 (d, $J = 1.9$ Hz, 1 H), 6.88 (d, $J = 8.3$ Hz, 1 H), 6.37 – 6.29 (m, 0.94 H), 3.93 (s, 6 H). ^{13}C NMR (151 MHz, CDCl_3) δ 172.8, 151.6, 149.3, 147.1, 146.8 (t, $J = 23.5$ Hz), 127.1, 123.3, 115.0, 114.9, 111.1, 109.8, 56.1, 56.0. HRMS (ESI, Negative Mode) for $\text{C}_{11}\text{H}_{10}\text{DO}_4$ $[\text{M}-\text{H}]^-$ calc. 208.0726, exp. 208.0724.



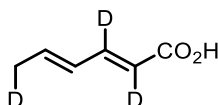
Acrylic-3,3- d_2 Acid (2i): Acrylic Acid (21.3 mg, 0.300 mmol) was used. Due to poor extraction efficiency, product was analyzed by ^1H NMR directly from the crude reaction mixture in D_2O , but was observed to have oligomerized, and thus the level of deuteration could not be ascertained.



2-Methylacrylic-3,3-*d*2 Acid (2j): Methylacrylic Acid (25.8 mg, 0.300 mmol) was used. Due to poor extraction efficiency, product was analyzed by ¹H NMR directly from the crude reaction mixture in D₂O, showing 21% deuteration at C^{β-E} and 31% deuteration at C^{β-Z}. ¹H NMR (400 MHz, D₂O) δ 5.66 – 5.62 (m, 0.69 H), 5.33 – 5.26 (m, 0.79 H), 1.68 (d, *J* = 1.1 Hz, 3 H).

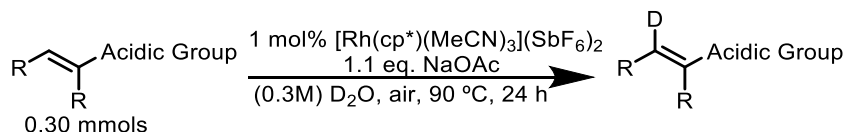


(E)-But-2-enoic-3-*d* Acid (2k): (E)-But-2-enoic Acid (10% Water by weight, 28.7 mg, 0.300 mmol) was used. Due to poor extraction efficiency, product was analyzed by ¹H NMR directly from the crude reaction mixture in D₂O, showing 7% deuteration at C^β and 5% deuteration at C^α. ¹H NMR (400 MHz, D₂O) δ 6.80 (dq, *J* = 15.5, 6.9 Hz, 0.95 H), 5.80 (dq, *J* = 15.5, 1.6 Hz, 0.97 H), 1.79 (dd, *J* = 6.9, 1.7 Hz, 3 H).

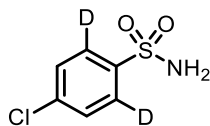


(2E,4E)-Hexa-2,4-dienoic-2,3-*d*2 Acid (2l): (2E,4E)-Hexa-2,4-dienoic Acid (33.6 mg, 0.300 mmol) was used, giving the deuterated product as a tan solid (24.3 mg, 65%), showing 9% deuteration at C^β, < 4% deuteration at C^α, and 7% deuteration at C^ε. ¹H NMR (400 MHz, CDCl₃) δ 7.39 – 7.28 (m, 0.91 H), 6.27 – 6.12 (m, 2 H), 5.77 (d, *J* = 15.4 Hz, 0.98 H), 1.98 – 1.77 (m, 2.80 H).

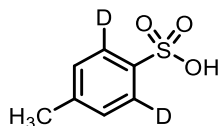
c). Other Acidic Substrates



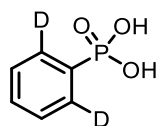
General Procedure: To a 2 dram vial with a PTFE-lined cap and stir bar was added acid (0.300 mmol), Tris(acetonitrile)pentamethylcyclopentadienylrhodium(III) hexafluoroantimonate (2.5 mg, 3.0 μmol), sodium acetate (27.1 mg, 0.33 mmol), and D₂O (1.0 mL, 55 mmol), followed by immediately capping. The reactions were then transferred to a pre-heated pie block (90 °C) and heated with stirring (24 h). Notably, solid occasionally collected on the sides of the vial above the solvent line, requiring manual dislodgement by shaking. When necessary, this action was performed at least twice over the 24 h period. Unless stated otherwise, after completion the reactions were diluted with 1.2 M HCl (3 mL) and dichloromethane (3 mL), followed by stirring for 15 min. The mixture was then poured into additional 1.2 M HCl (15 mL), followed by extracting with dichloromethane (3 x 10 mL). The combined organic phase was dried over Na₂SO₄, then evaporated *in vacuo*, and the level of deuteration quantified by ¹H NMR, using unexchanged positions to quantify deuteration when possible, or by addition of standards when not.



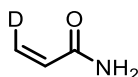
4-Chlorobenzene-2,6-*d*₂-sulfonamide (3a): 4-chlorobenzenesulfonamide (57.5 mg, 0.300 mmol) was used, giving the mostly undeuterated product as a light yellow solid (46.0 mg, 80%), showing < 4% deuteration at C^{2/6}. ¹H NMR (400 MHz, CDCl₃) δ 7.87 (d, *J* = 8.5 Hz, 1.99 H), 7.50 (d, *J* = 8.4 Hz, 2 H), 4.92 (br s, 1.86 H).



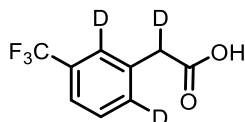
4-Methylbenzene-2,6-*d*₂-sulfonic Acid (3b): 4-Methylbenzenesulfonic Acid Monohydrate (57.1 mg, 0.300 mmol) was used. Due to poor extraction efficiency, product was analyzed by ¹H NMR directly from the crude reaction mixture in D₂O, showing < 4% deuteration at C^{2/6}. ¹H NMR (400 MHz, D₂O) δ 7.64 (d, *J* = 8.2 Hz, 1.94 H), 7.29 (d, *J* = 8.1 Hz, 2 H), 2.32 (s, 3 H).



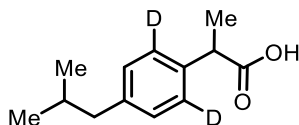
(Phenyl-2,6-*d*₂)phosphonic Acid (3c): Phenylphosphonic Acid (47.4 mg, 0.300 mmol) was used. Due to poor extraction efficiency, product was analyzed by ¹H NMR directly from the crude reaction mixture in D₂O, showing 8% deuteration at C^{2/6}. ¹H NMR (400 MHz, D₂O) δ 7.71 – 7.62 (m, 1.84 H), 7.48 – 7.37 (m, 3 H).



(*Z*)-Acrylamide-3-*d* (3d): Acrylamide (21.3 mg, 0.300 mmol) was used. Due to poor extraction efficiency, product was analyzed by ¹H NMR directly from the crude reaction mixture in D₂O, showing < 4% deuteration at C^β. ¹H NMR (400 MHz, D₂O) δ 6.29 – 6.12 (m, 1.99 H), 5.77 (dd, *J* = 9.7, 1.6 Hz, 1 H).

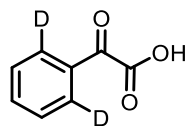


2-(3-(Trifluoromethyl)phenyl-2,6-*d*₂)acetic-2-*d* Acid (3e): 2-(3-(Trifluoromethyl)phenyl)acetic Acid (61.2 mg, 0.300 mmol) was used, giving the deuterated product as a faint pink solid (50.4 mg, 82%), showing 79% deuteration at C^α and < 4% deuteration at C^{2/6}. ¹H NMR (400 MHz, CDCl₃) δ 11.62 (br s, 0.76 H), 7.60 – 7.53 (m, 2 H), 7.52 – 7.43 (m, 1.96 H), 3.74 – 3.67 (m, 0.42 H). ¹³C NMR (151 MHz, CDCl₃) δ 177.5, 134.2, 134.2, 134.1, 133.0, 131.1 (q, *J* = 32.4 Hz), 129.3, 129.1, 126.3 (q, *J* = 3.1 Hz), 124.5 (q, *J* = 3.5 Hz), 124.1 (q, *J* = 272.1 Hz), 40.5 (sept, *J* = 20.3 Hz). HRMS (ESI, Negative Mode) for C₉H₄D₂F₃O₂ [M-H]⁻ calc. 205.0451, exp. 205.0447.



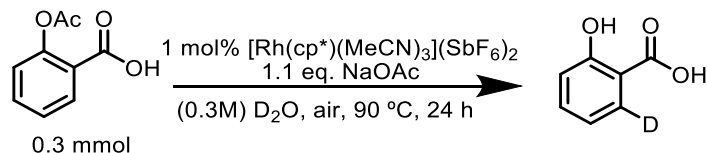
2-(4-Isobutylphenyl-2,6-*d*₂)propanoic Acid (3f): 2-(4-Isobutylphenyl)propanoic Acid (61.9 mg, 0.300 mmol) was used, giving the deuterated product as an orange oil/glass (56.4 mg, 91%), showing 19% deuteration at C^{2/6} and < 4% deuteration at C^α. ¹H NMR (600 MHz, CDCl₃) δ 7.24 (d, *J* = 8.1 Hz, 1.63 H), 7.12 (d, *J* = 7.9 Hz, 2 H), 3.72 (q, *J* = 7.1 Hz, 1 H), 2.46 (d, *J* = 7.2 Hz, 2 H), 1.86 (sept, *J* = 6.6 Hz, 1 H), 1.51 (d, *J* = 7.2 Hz, 3 H), 0.91 (d, *J* = 6.6 Hz, 6

H). ^{13}C NMR (151 MHz, CDCl_3) δ 181.3, 141.0, 137.1, 137.0, 129.5, 129.4, 127.4, 127.1 (t, $J = 23.9$ Hz), 45.2, 45.1, 45.1, 30.3, 22.5, 18.2. HRMS (ESI, Negative Mode) for $\text{C}_{13}\text{H}_{15}\text{D}_2\text{O}_2$ $[\text{M}-\text{H}]^-$ calc. 207.1360, exp. 207.1344.



2-Oxo-2-(phenyl-2,6- d_2)acetic Acid (3g): 2-Oxo-2-phenylacetic Acid (45.0 mg, 0.300 mmol) was used. Due to poor extraction efficiency, product was analyzed by ^1H NMR directly from the crude reaction mixture in D_2O , showing 8% deuteration at $\text{C}^{2/6}$. ^1H NMR (400 MHz, D_2O) δ 7.90 (d, $J = 7.6$ Hz, 1.84 H), 7.68 (t, $J = 7.4$ Hz, 1 H), 7.53 (t, $J = 7.7$ Hz, 2 H).

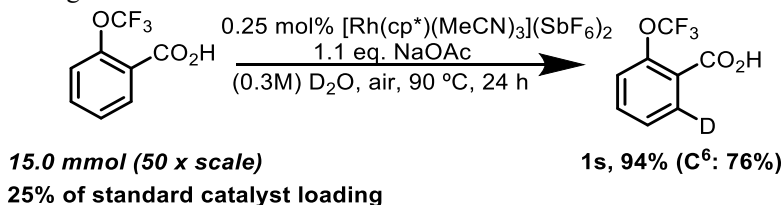
4. Procedure and Characterization for Reaction on Aspirin



Salicylic-6-*d* Acid (1ab): To a 2 dram vial with a PTFE-lined cap and stir bar was added acetylsalicylic acid (54.1 mg, 0.300 mmol), Tris(acetonitrile)pentamethylcyclopentadienylrhodium(III) hexafluoroantimonate (2.5 mg, 3.0 μ mol), sodium acetate (27.1 mg, 0.33 mmol), and D₂O (1.0 mL, 55 mmol), followed by immediately capping. The reaction was then transferred to a pre-heated pie block (90 °C), and heated with stirring (24 h). After completion the reactions were diluted with 1.2 M HCl (3 mL) and dichloromethane (3 mL), followed by stirring for 15 min. The mixture was then poured into additional 1.2 M HCl (15 mL), followed by extracting with dichloromethane (3 x 10 mL). The combined organic phase was dried over Na₂SO₄, then evaporated *in vacuo*, giving product as a tan solid (27.1 mg, 65%) and the level of deuteration was quantified by ¹H NMR, using unexchanged positions as a reference, showing > 99% deuteration at C⁶ with concomitant loss of the acetyl group. Reaction was performed at 80 °C, showing 89% deuteration at C⁶, and at 70 °C, showing 62% deuteration at C⁶, both with loss of the acetyl group. ¹H NMR (400 MHz, CDCl₃) δ 10.39 (br s, 1 H), 7.94 (dd, *J* = 6.5, 1.6 Hz, 0.01 H), 7.54 (dd, *J* = 8.4, 7.3 Hz, 1 H), 7.02 (dd, *J* = 8.4, 1.0 Hz, 1 H), 6.95 (d, *J* = 7.2 Hz, 1 H). ¹³C NMR (151 MHz, CDCl₃) δ 174.8, 162.3, 137.2, 137.1, 130.8 (t, *J* = 25.0 Hz, 119.6, 118.0, 111.3. HRMS (ESI, Negative Mode) for C₇H₄DO₃ [M-H]⁻ calc. 138.0307, exp. 138.0309.

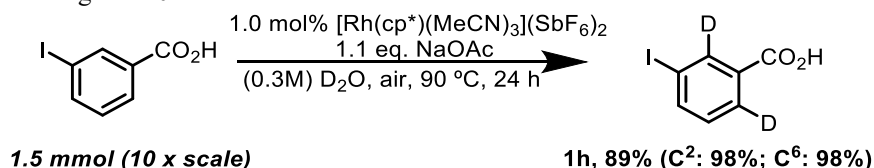
5. Procedure and Characterization for Scale-Up Reactions

a. Reduced Catalyst Loading and 50x Scale



2-(Trifluoromethoxy)benzoic-6-*d* Acid (1s): To a 100 mL round bottom flask with stir bar was added 2-(trifluoromethoxy)benzoic acid (3.092 g, 15.0 mmol), Tris(acetonitrile)pentamethylcyclopentadienylrhodium(III) hexafluoroantimonate (31.2 mg, 37.5 μ mol), sodium acetate (1.353 g, 16.5 mmol), and D₂O (50.0 mL, 2.75 mol), followed by immediately attaching a reflux condenser with attached (empty) balloon. The reaction was then transferred to a pre-heated oil bath (90 °C), and heated with stirring (24 h). After completion the reaction was diluted with 1.2 M HCl (100 mL) and dichloromethane (25 mL), followed by stirring for 15 min. The mixture was then extracted with dichloromethane (3 x 35 mL). The combined organic phase was dried over Na₂SO₄, then evaporated *in vacuo*, giving product as a tan solid (2.92 g, 94%) and the level of deuteration was quantified by ¹H NMR, using unexchanged positions as a reference, showing 76% deuteration at C⁶. ¹H NMR (400 MHz, CDCl₃) δ 8.11 (dd, J = 7.8, 1.7 Hz, 0.24 H), 7.64 (t, J = 7.9 Hz, 1 H), 7.46 – 7.40 (m, 1 H), 7.39 (d, J = 8.2 Hz, 1 H).

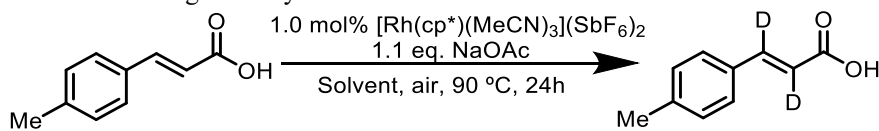
b. Same Catalyst Loading and 10x Scale



3-Iodobenzoic-2,6-*d*₂ Acid (1h): To a 2 dram vial with stir bar was added 3-iodobenzoic acid (372 mg, 1.50 mmol), Tris(acetonitrile)pentamethylcyclopentadienylrhodium(III) hexafluoroantimonate (12.5 mg, 15.0 μ mol), sodium acetate (135 mg, 1.65 mmol), and D₂O (5.00 mL, 275 mmol), followed by capping with a PTFE lined cap. The reaction was then transferred to a pre-heated pie-block (90 °C), and heated with stirring (24 h). After completion the reaction was diluted with 1.2 M HCl (25 mL) and dichloromethane (25 mL), followed by stirring for 15 min. The mixture was then diluted with additional 1.2 M HCl (25 mL), followed by extraction with dichloromethane (3 x 20 mL). The combined organic phase was dried over Na₂SO₄, then evaporated *in vacuo*, giving product as a light orange solid (333 mg, 89%) and the level of deuteration was quantified by ¹H NMR, using unexchanged positions as a reference, showing 98% deuteration at C² and 98% deuteration at C⁶. ¹H NMR (400 MHz, CDCl₃) δ 8.45 (d, J = 1.6 Hz, 0.02 H), 8.08 (d, J = 6.9 Hz, 0.02 H), 7.95 (d, J = 7.9 Hz, 1 H), 7.23 (d, J = 7.9 Hz, 1 H).

6. Co-Solvent Studies

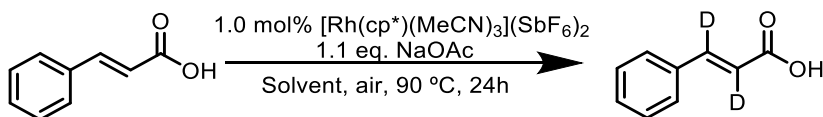
a. Study of Solvent Mixtures Using 4-Methylcinnamic Acid



Entry	Solvent Mixture	C / C Deuteration (%)
1	D ₂ O (750 μL) + CD ₃ OD (250 μL)	87 / 4
2	D ₂ O (500 μL) + CD ₃ OD (500 μL)	93 / 7
3	D ₂ O (750 μL) + DMSO- <i>d</i> ₆ (250 μL)	33 / < 4%
4	D ₂ O (500 μL) + DMSO- <i>d</i> ₆ (500 μL)	10 / < 4%

To a 2 dram vial with a PTFE-lined cap and stir bar was added 4-methylcinnamic acid (48.7 mg, 0.30 mmol), Tris(acetonitrile)pentamethylcyclopentadienylrhodium(III) hexafluoroantimonate (2.5 mg, 3.0 μmol), sodium acetate (27.1 mg, 0.33 mmol), and 1 mL of the solvent mixture. The reactions were then transferred to a pre-heated pie block (90 °C), and heated with stirring (24 h). After completion, the reactions were diluted with 1.2 M HCl (3 mL) and dichloromethane (3 mL), followed by stirring for 15 min. The mixture was then poured into additional 1.2 M HCl (15 mL), followed by extracting with dichloromethane (3 x 10 mL). The combined organic phase was dried over Na₂SO₄, then evaporated *in vacuo*, and the level of deuteration quantified by ¹H NMR, using the aromatic protons as internal standards. Notably, unlike performing the reaction with solely D₂O, **Entries 2 and 3** appeared fully homogeneous at the reaction temperature of 90 °C. Compared to using solely D₂O, increasing amounts of CD₃OD improve the solubility and reaction efficiency of the otherwise insoluble substrate. Meanwhile, addition of DMSO dramatically slows the reaction.

b. Study of Solvent Mixtures Using Cinnamic Acid

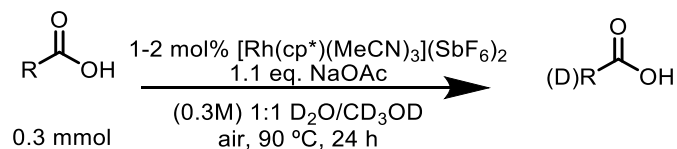


Entry	Solvent Mixture	C / C Deuteration (%)
1	D ₂ O (750 μL) + CD ₃ OD (250 μL)	91 / 8
2	D ₂ O (500 μL) + CD ₃ OD (500 μL)	92 / 7
3	D ₂ O (750 μL) + DMSO- <i>d</i> ₆ (250 μL)	36 / < 4%
4	D ₂ O (500 μL) + DMSO- <i>d</i> ₆ (500 μL)	14 / < 4%

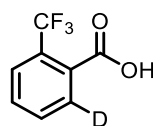
To a 2 dram vial with a PTFE-lined cap and stir bar was added cinnamic acid (44.4 mg, 0.30 mmol), Tris(acetonitrile)pentamethylcyclopentadienylrhodium(III) hexafluoroantimonate (2.5 mg, 3.0 μmol), sodium acetate (27.1 mg, 0.33 mmol), and 1 mL of the solvent mixture. The reactions were then transferred to a pre-heated pie block (90 °C), and heated with stirring (24 h). After completion, the reactions were diluted with 1.2 M HCl (3 mL) and dichloromethane (3 mL), followed by stirring for 15 min. The mixture was then poured into additional 1.2 M HCl (15 mL), followed by extracting with dichloromethane (3 x 10 mL). The combined organic phase was dried over Na₂SO₄, then evaporated *in vacuo*, and the level of deuteration quantified by ¹H NMR, using the aromatic protons as internal

standards. All reactions were observed to be fully homogeneous at the reaction temperature of 90 °C. Compared to using solely D₂O, increasing amounts of CD₃OD seem to slightly slow the rate of the reaction of this soluble substrate, while addition of DMSO dramatically slows the reaction.

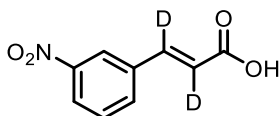
c. Reaction of Poorly Soluble Substrates Using 1:1 D₂O/CD₃OD Solvent Mixture in Place of D₂O



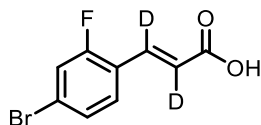
General Procedure: In duplicate, to a 2 dram vial with a PTFE-lined cap and stir bar was added acid (0.300 mmol), Tris(acetonitrile)pentamethylcyclopentadienylrhodium(III) hexafluoroantimonate (2.5 mg, 3.0 μmol), sodium acetate (27.1 mg, 0.33 mmol), D₂O (0.5 mL), and CD₃OD (0.5 mL), followed by immediately capping. The reactions were then transferred to a pre-heated pie block (90 °C), and heated with stirring (24 h). After completion the reactions were diluted with 1.2 M HCl (3 mL) and chloroform (3 mL), followed by stirring for 15 min. The mixture was then poured into additional 1.2 M HCl (15 mL), followed by extracting with chloroform (3 x 10 mL). The combined organic phase was dried over Na₂SO₄, then evaporated *in vacuo*, and the level of deuteration quantified by ¹H NMR, using appropriate unexchanged signals as internal standards.



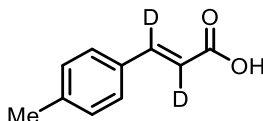
2-(Trifluoromethyl)benzoic-6-*d* Acid (1c): Reaction was homogeneous during the reaction, and gave 88% deuteration at C⁶. See Section 3 for ¹³C, and HRMS data. ¹H NMR (600 MHz, CDCl₃) δ 8.01 – 7.95 (m, 0.12 H), 7.82 (dd, *J* = 5.2, 3.8 Hz, 1 H), 7.71 – 7.63 (m, 2 H).



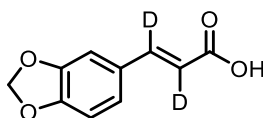
(*E*)-3-(3-Nitrophenyl)acrylic-2,3-*d*₂ Acid (2c): Reaction was homogeneous during the reaction, and gave 20% deuteration at C^β and < 4% deuteration at C^α. See section 3 for HRMS data. ¹H NMR (600 MHz, CD₃OD) δ 8.46 (s, H), 8.25 (dd, *J* = 8.2, 1.4 Hz, 1 H), 8.02 (d, *J* = 7.7 Hz, 1 H), 7.75 (d, *J* = 16.0 Hz, 0.80 H), 7.67 (t, *J* = 8.0 Hz, 1 H), 6.69 – 6.62 (m, 1 H).



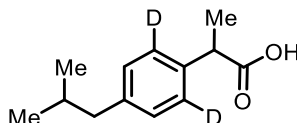
(E)-3-(4-Bromo-2-fluorophenyl)acrylic-2,3-*d*₂ Acid (2d): Reaction was homogeneous during the reaction, and gave 80% deuteration at C^β and < 4% deuteration at C^α. ¹H NMR (600 MHz, CD₃OD) δ 7.72 (d, *J* = 16.2 Hz, 0.20 H), 7.64 (t, *J* = 8.1 Hz, 1 H), 7.45 (d, *J* = 10.4 Hz, 1 H), 7.42 (d, *J* = 8.4 Hz, 1 H), 6.61 – 6.55 (m, 0.97 H). ¹³C NMR (151 MHz, CD₃OD) δ 169.7, 162.2 (d, *J* = 256.1 Hz), 137.0, 136.6 (t, *J* = 24.1 Hz), 131.3, 129.3, 125.5 (d, *J* = 9.8 Hz), 122.9 (d, *J* = 11.8 Hz), 122.7 (d, *J* = 4.9 Hz), 120.7 (d, *J* = 25.7 Hz).



(E)-3-(*p*-Tolyl)acrylic-2,3-*d*₂ Acid (2e): Reaction was homogeneous during the reaction, and gave 93% deuteration at C^β and 5% deuteration at C^α. ¹H NMR (600 MHz, CDCl₃) δ 7.78 (d, *J* = 16.0 Hz, 0.07 H), 7.46 (d, *J* = 8.1 Hz, 2 H), 7.22 (d, *J* = 8.0 Hz, 2 H), 6.45 – 6.37 (m, 0.95 H), 2.39 (s, 3 H). ¹³C NMR (151 MHz, CDCl₃) δ 172.6, 147.2, 146.9 (t, *J* = 23.8 Hz), 141.4, 131.4, 129.8, 128.5, 116.3, 116.2.



(E)-3-(Benzo[*d*][1,3]dioxol-5-yl)acrylic-2,3-*d*₂ Acid (2g): Reaction was heterogeneous during the reaction, and gave 56% deuteration at C^β and < 4% deuteration at C^α. ¹H NMR (600 MHz, DMSO-*d*₆) δ 12.24 (br s, 1 H), 7.50 (d, *J* = 15.9 Hz, 0.44 H), 7.37 (s, 1 H), 7.16 (d, *J* = 7.8 Hz, 1 H), 6.95 (d, *J* = 7.9 Hz, 1 H), 6.40 (m, 0.99 H), 6.07 (s, 2 H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 167.8, 149.1, 148.0, 143.9, 143.6 (t, *J* = 24.1 Hz), 128.7, 128.6, 124.7, 124.7, 117.1, 117.0, 108.5, 106.7, 101.6.



2-(4-Isobutylphenyl-2,6-*d*₂)propanoic Acid (3f): Reaction was homogeneous during the reaction, and gave only 4% deuteration at C^{2/6}. See Section 3 for ¹H NMR, ¹³C NMR, and HRMS data.

7. ^1H and ^{13}C Spectra of Deuterated Compounds

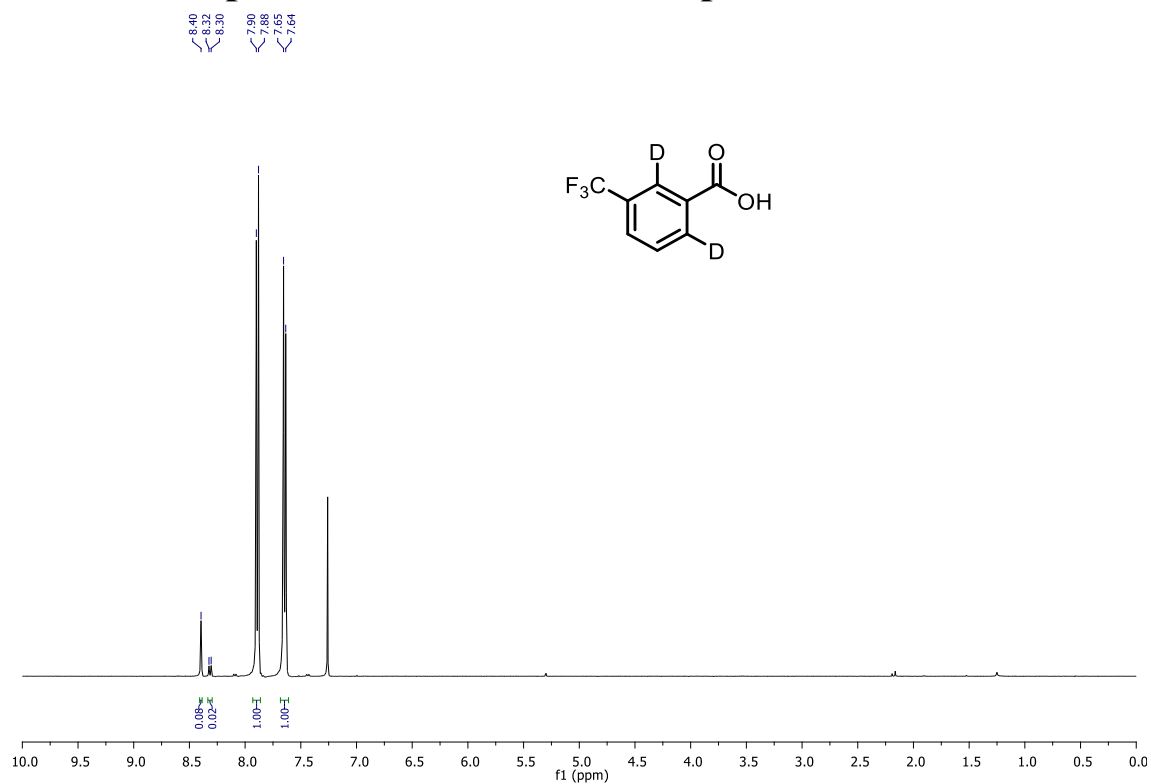


Figure S-1. ^1H NMR spectrum of **1a** (CDCl_3 , 400 MHz, 298 K)

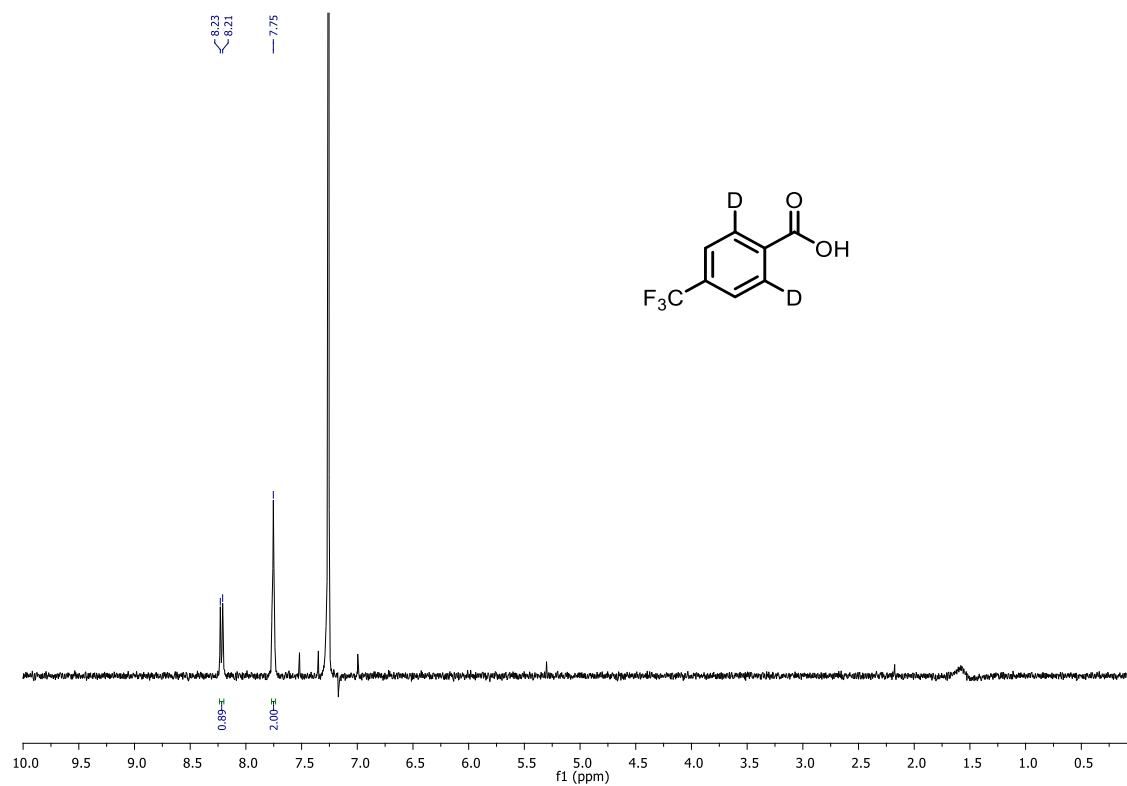


Figure S-2. ^1H NMR spectrum of **1b** from 1 mol% catalyst loading (CDCl_3 , 400 MHz, 298 K)

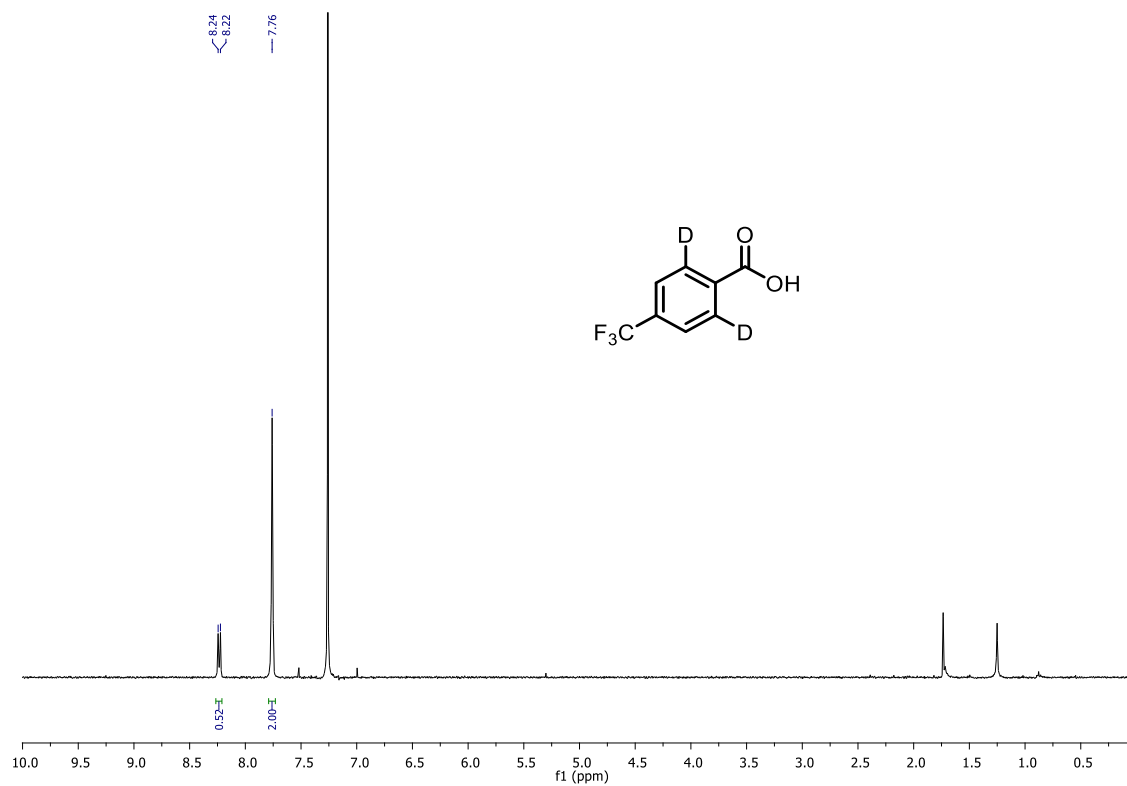


Figure S-3. ¹H NMR spectrum of **1b** from 2 mol% catalyst loading (CDCl₃, 400 MHz, 298 K)

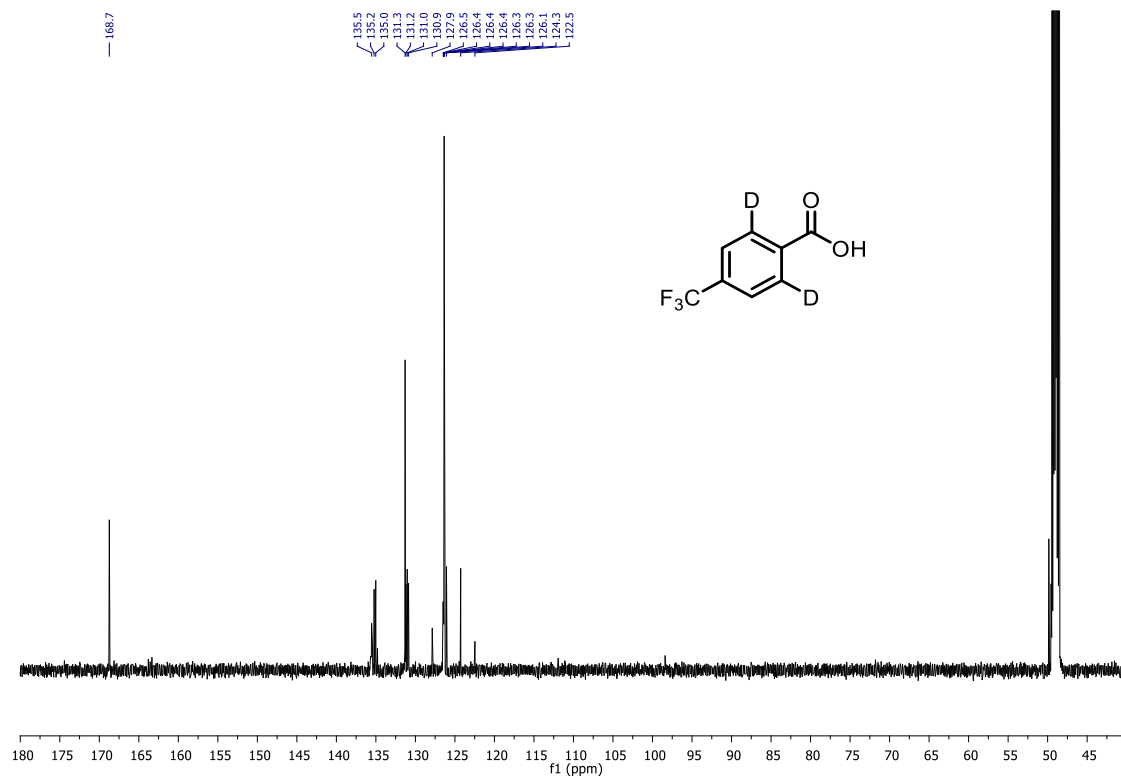


Figure S-4. ¹³C NMR spectrum of **1b** from 2 mol% catalyst loading (CD₃OD, 151 MHz, 298 K)

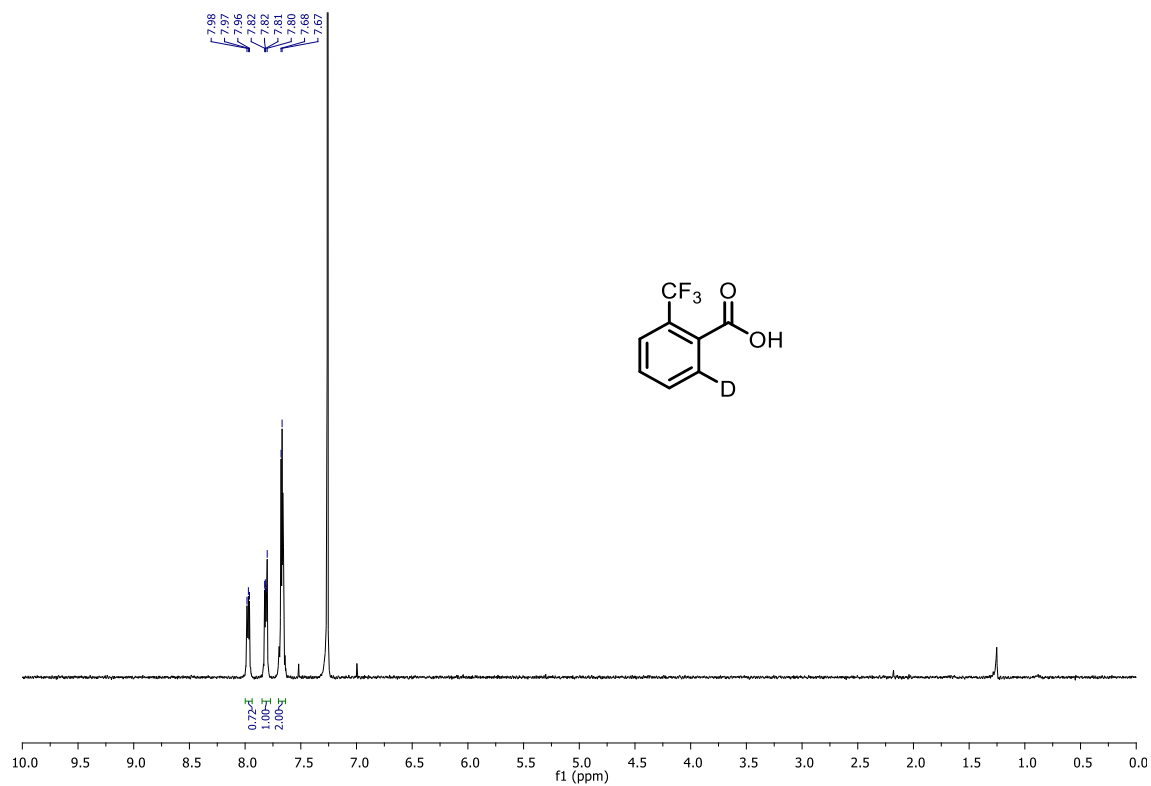


Figure S-5. ¹H NMR spectrum of **1c** from 1 mol% catalyst loading (CDCl₃, 400 MHz, 298 K)

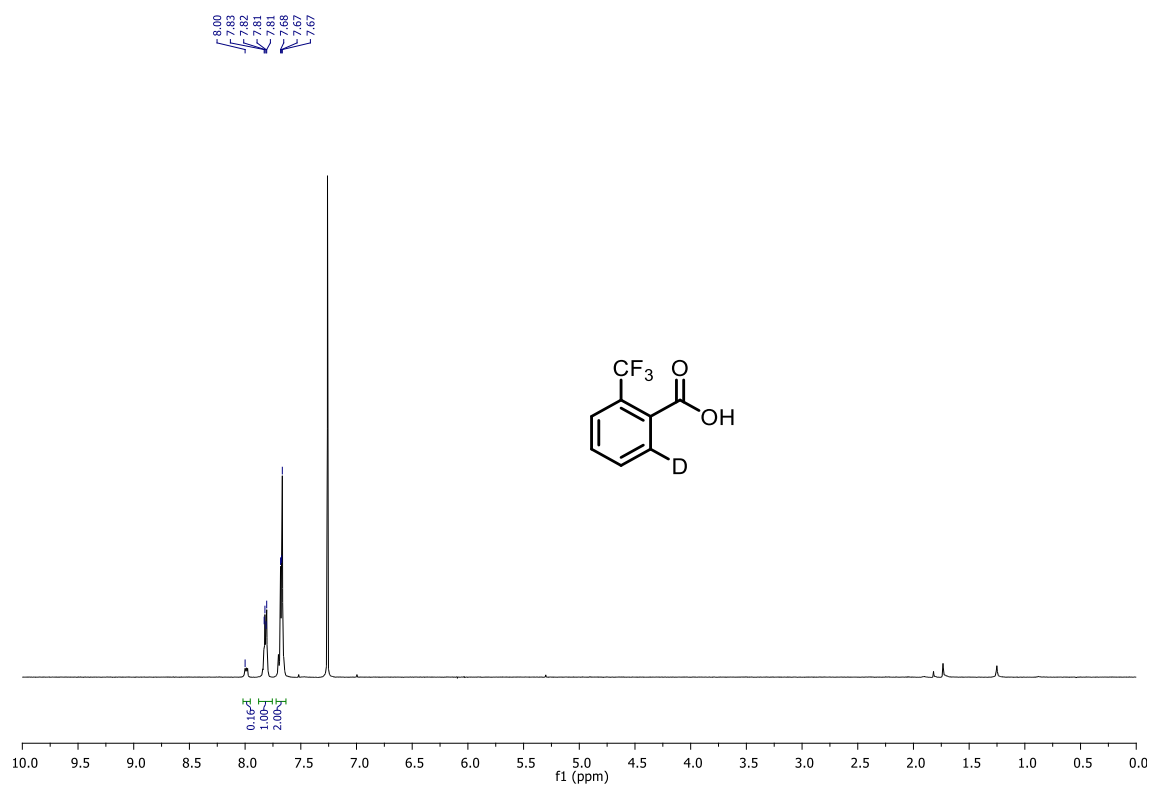


Figure S-6. ¹H NMR spectrum of **1c** from 2 mol% catalyst loading (CDCl₃, 400 MHz, 298 K)

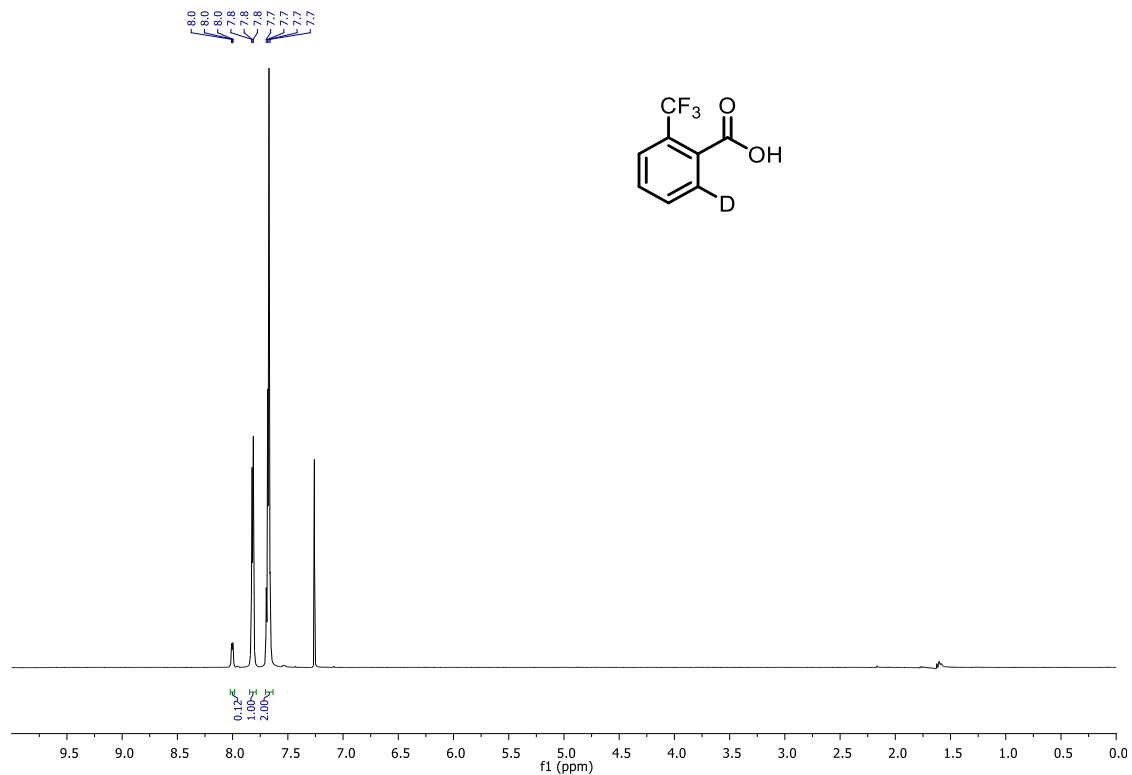


Figure S-7. ¹H NMR spectrum of **1c** from 1:1 D₂O/CD₃OD reaction (CDCl₃, 600 MHz, 298 K)

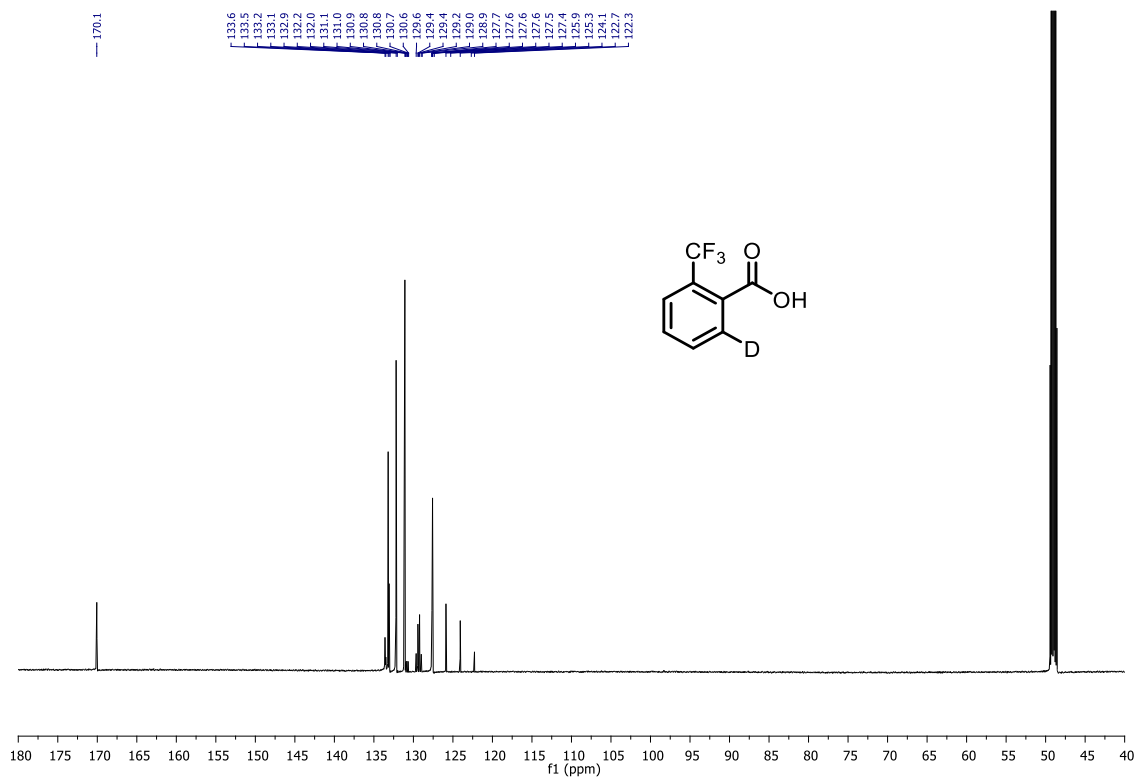
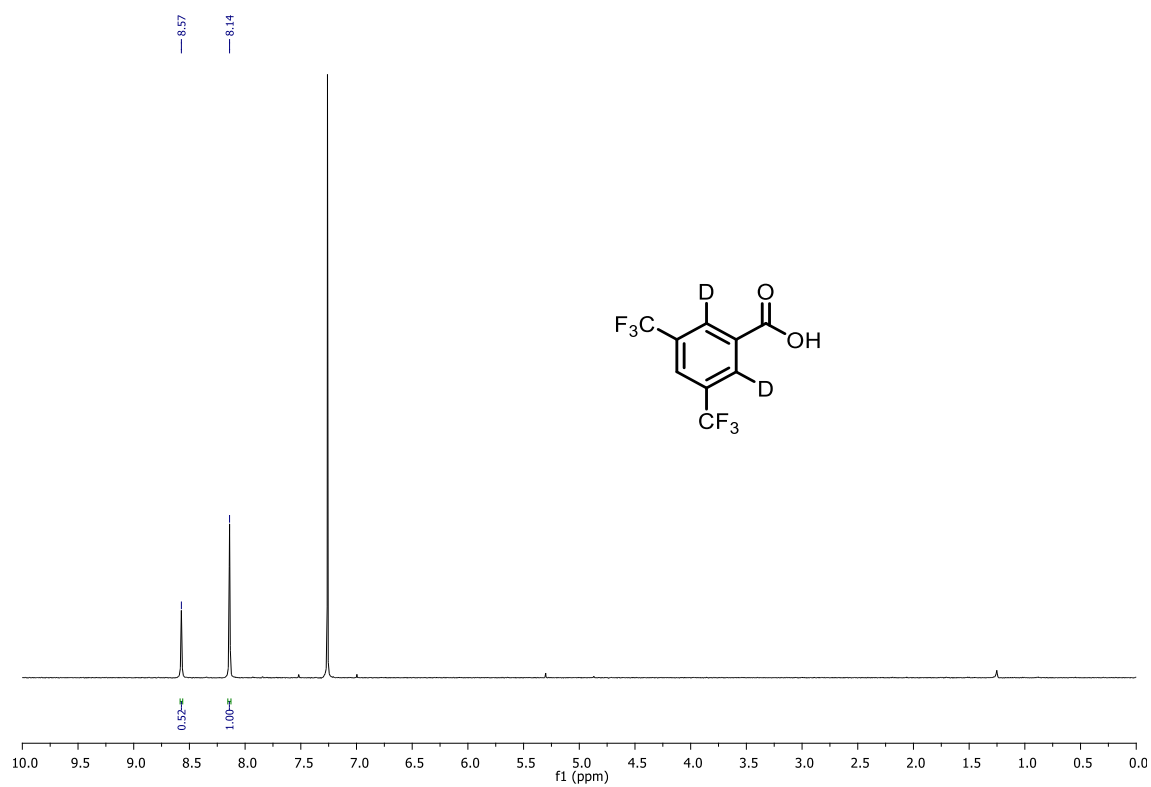
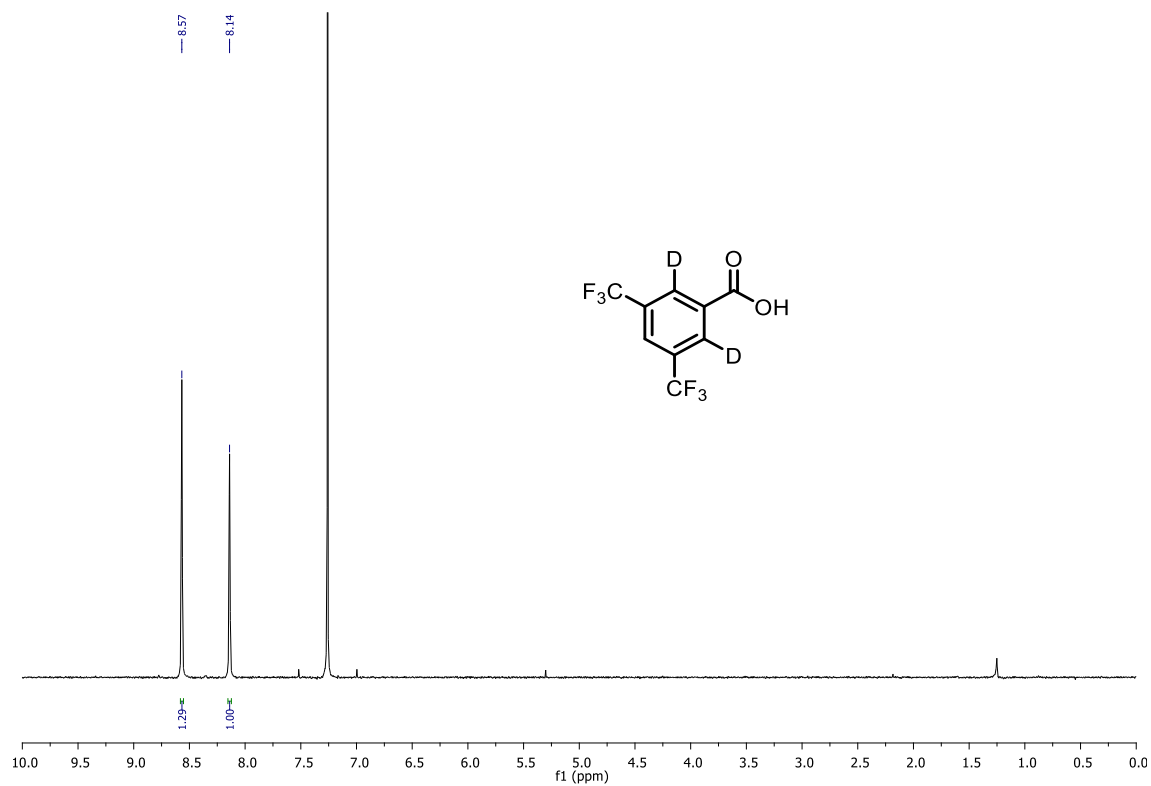


Figure S-8. ¹³C NMR spectrum of **1c** from 2 mol% catalyst loading (CD₃OD, 151 MHz, 298 K)



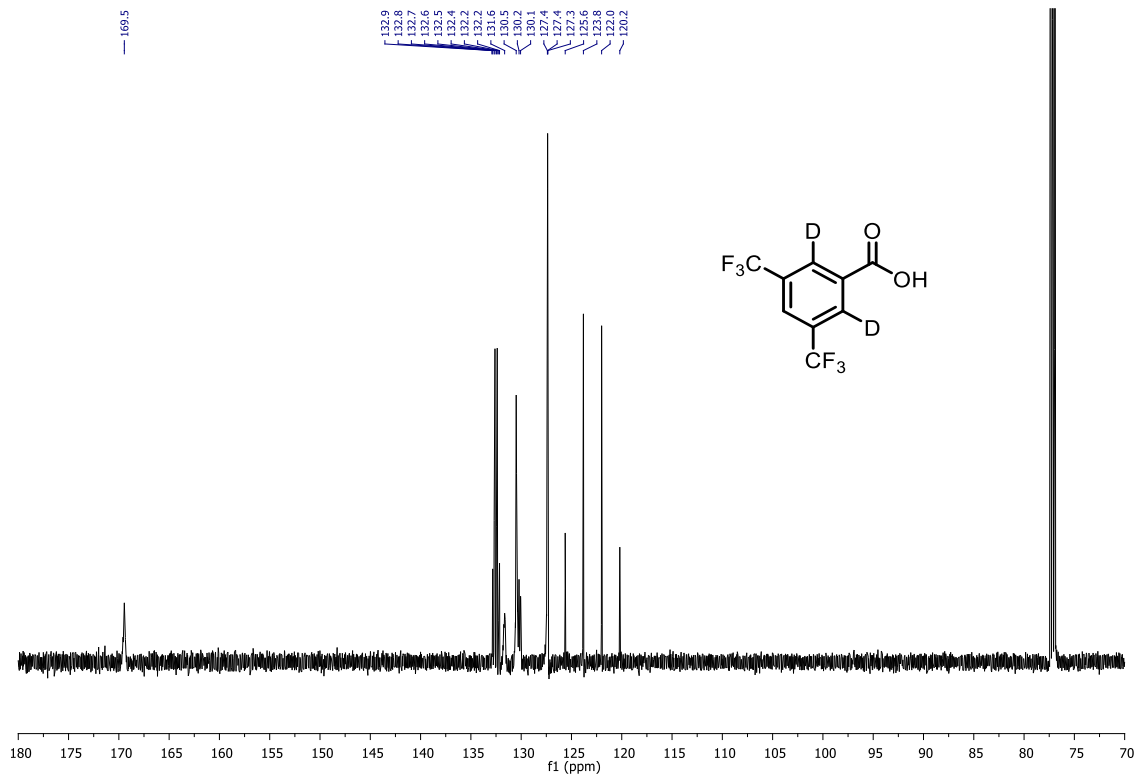


Figure S-11. ^{13}C NMR spectrum of **1d** from 2 mol% catalyst loading (CDCl_3 , 151 MHz, 298 K)

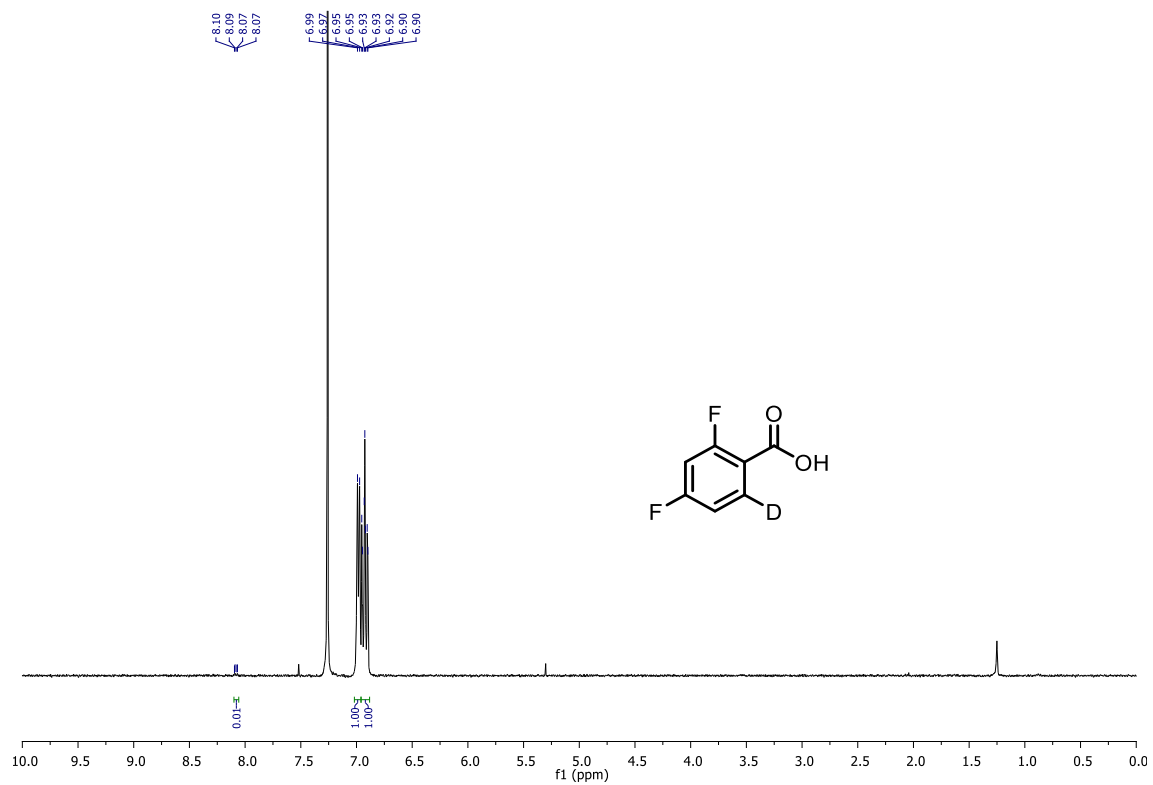


Figure S-12. ^1H NMR spectrum of **1e** (CDCl_3 , 400 MHz, 298 K)

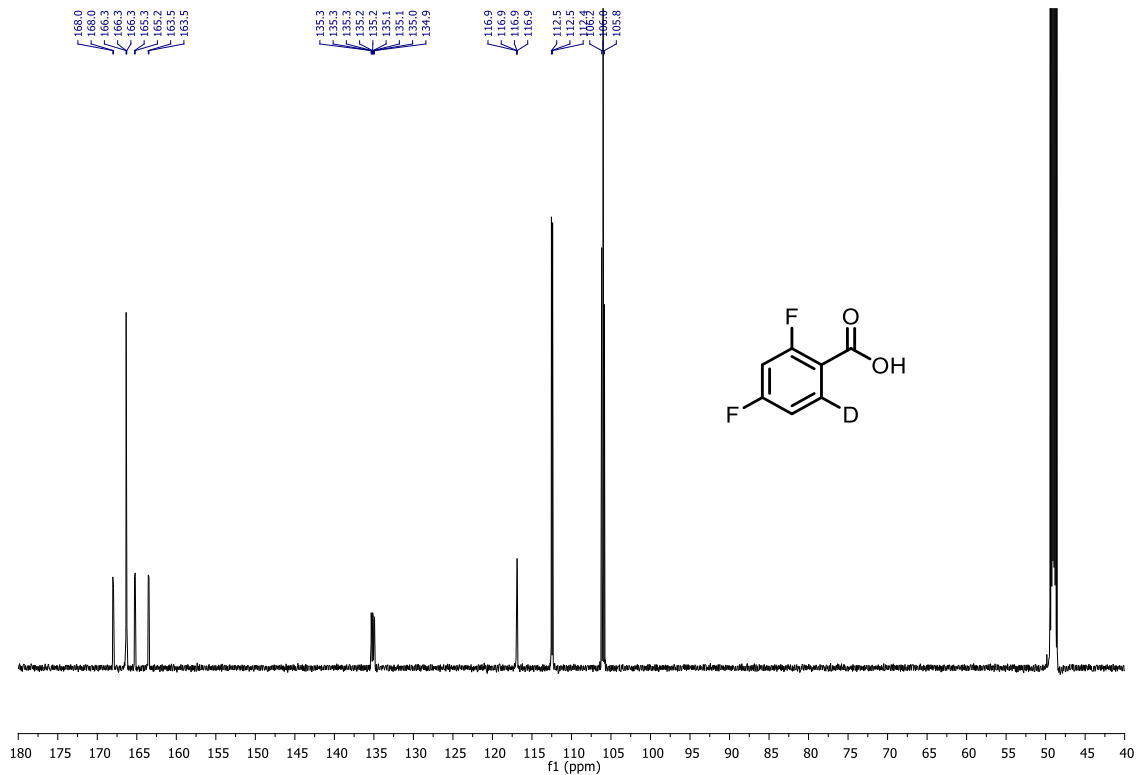


Figure S-13. ^{13}C NMR spectrum of **1e** (CD_3OD , 151 MHz, 298 K)

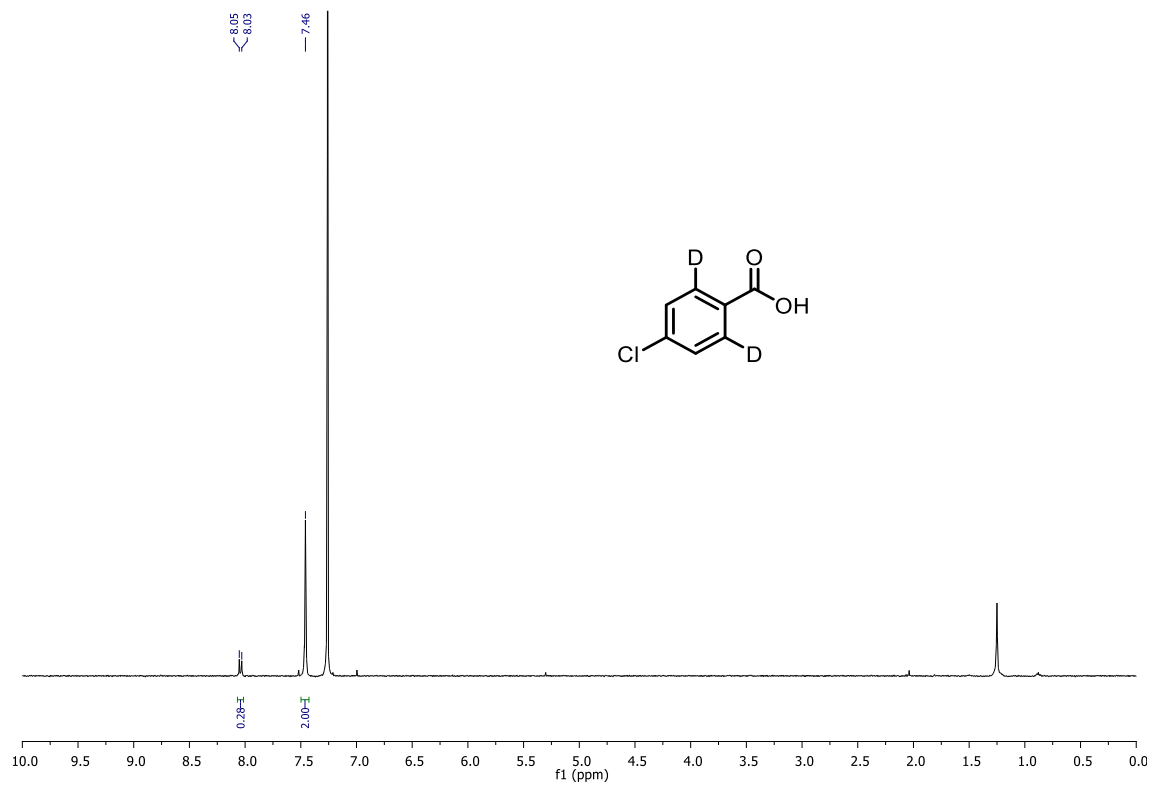


Figure S-14. ^1H NMR spectrum of **1f** (CDCl_3 , 400 MHz, 298 K)

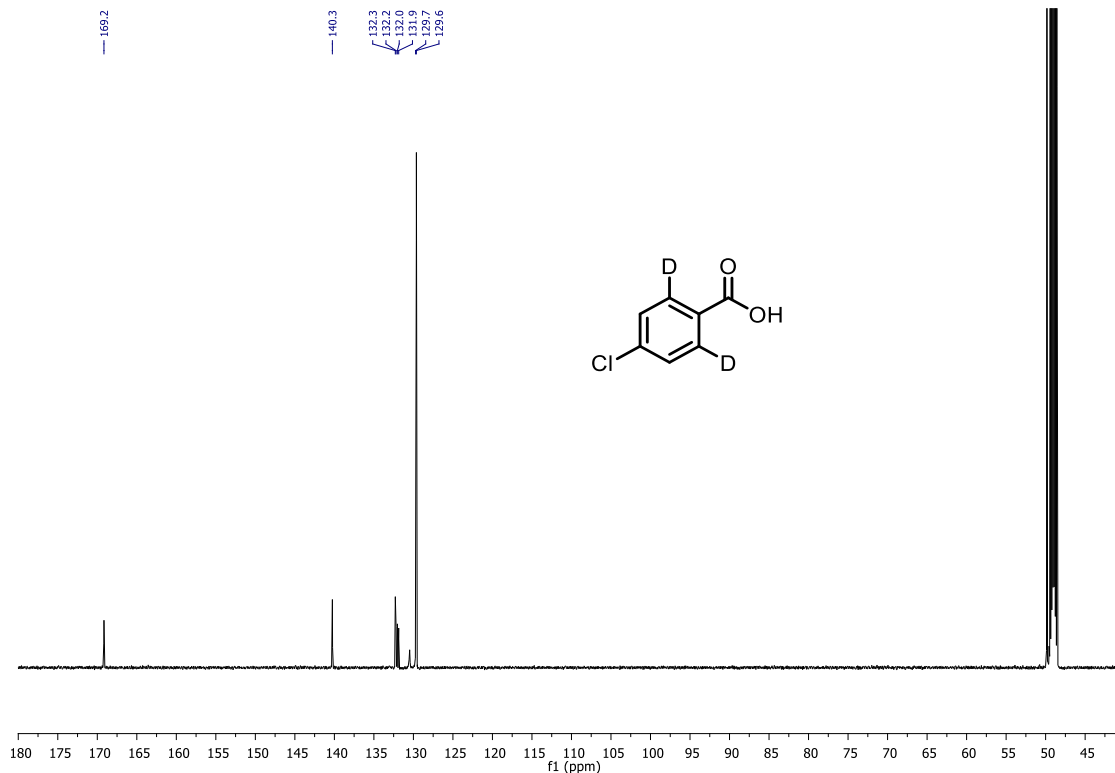


Figure S-15. ^{13}C NMR spectrum of **1f** (CD₃OD, 151 MHz, 298 K)

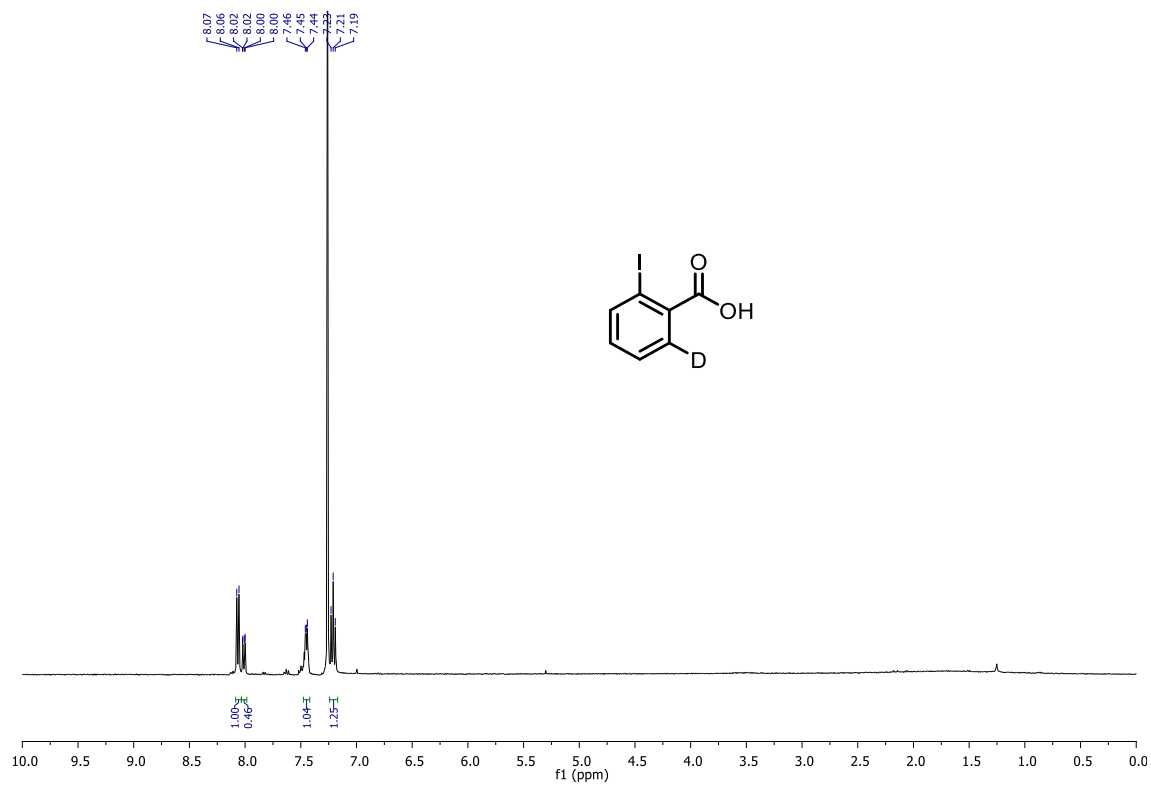


Figure S-16. ^1H NMR spectrum of **1g** (CDCl₃, 400 MHz, 298 K)

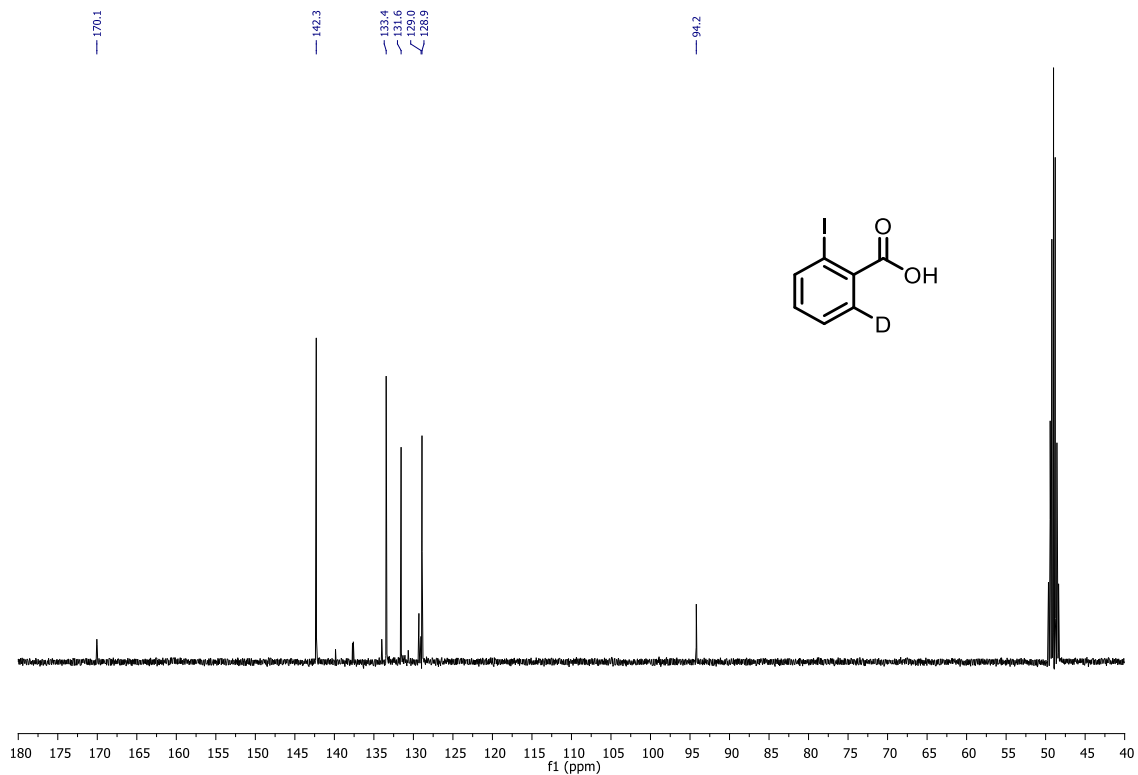


Figure S-17. ¹³C NMR spectrum of **1g** (CDCl₃, 151 MHz, 298 K)

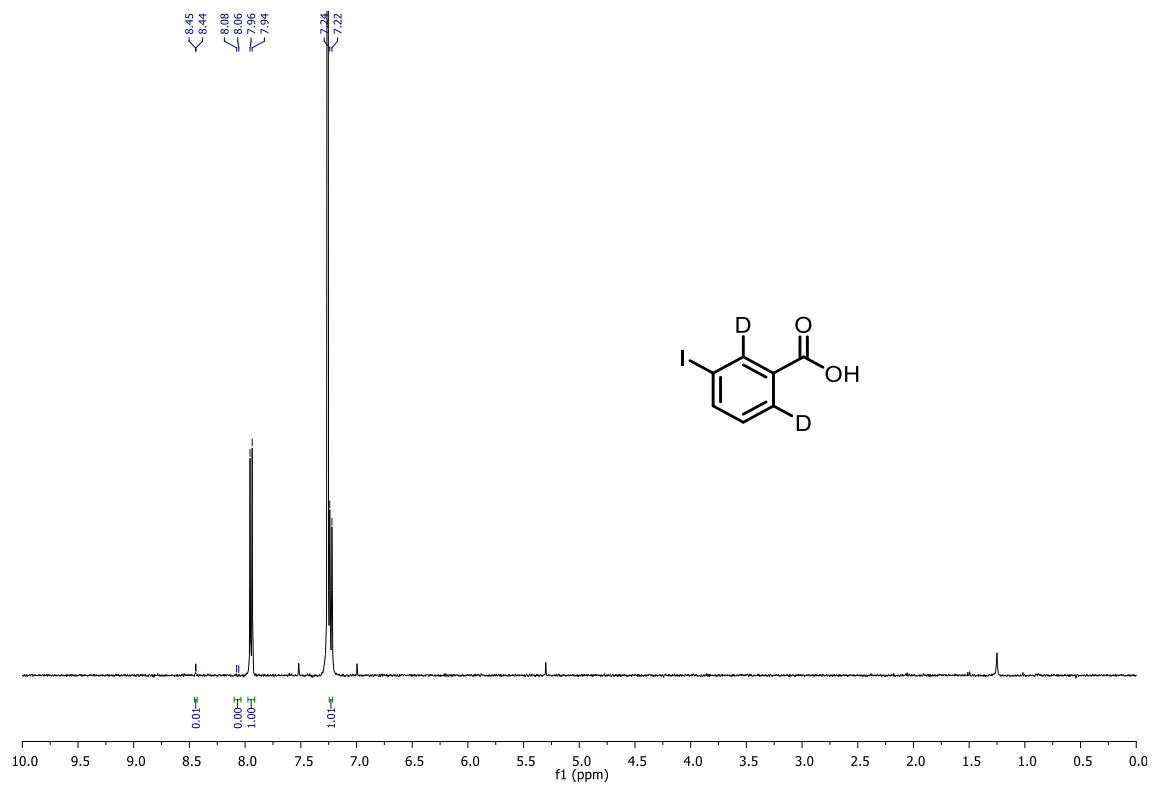


Figure S-18. ¹H NMR spectrum of **1h** (CDCl₃, 400 MHz, 298 K)

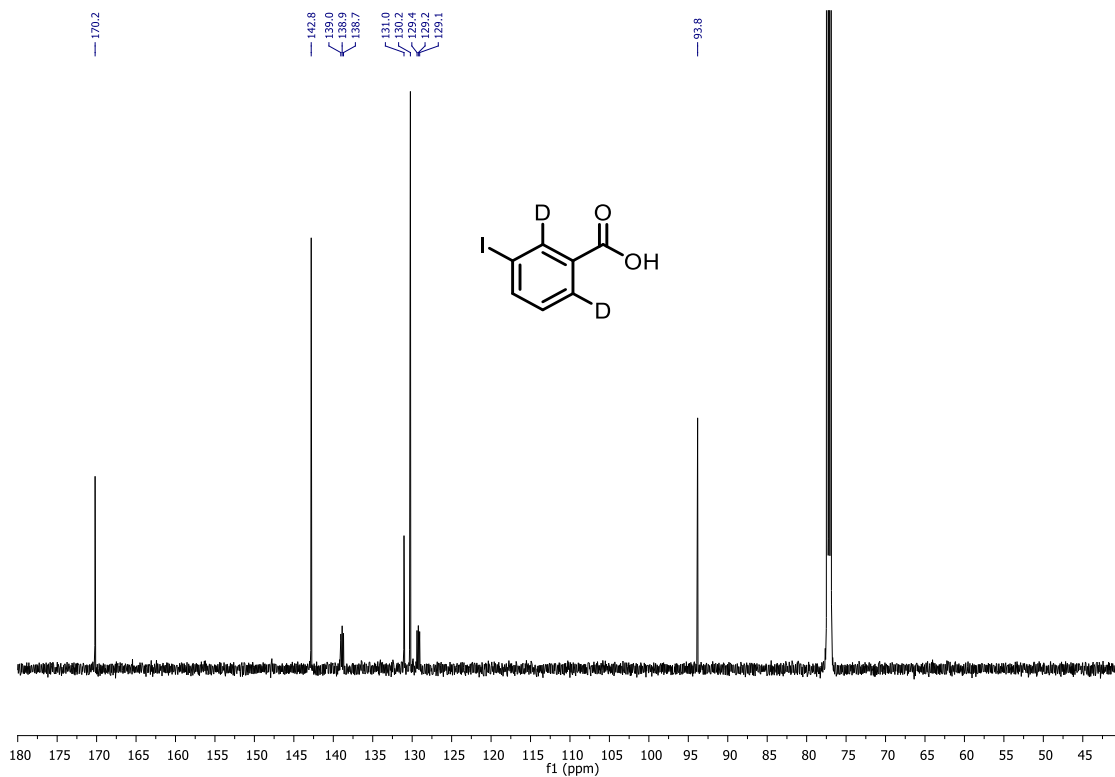


Figure S-19. ¹³C NMR spectrum of **1h** (CDCl₃, 151 MHz, 298 K)

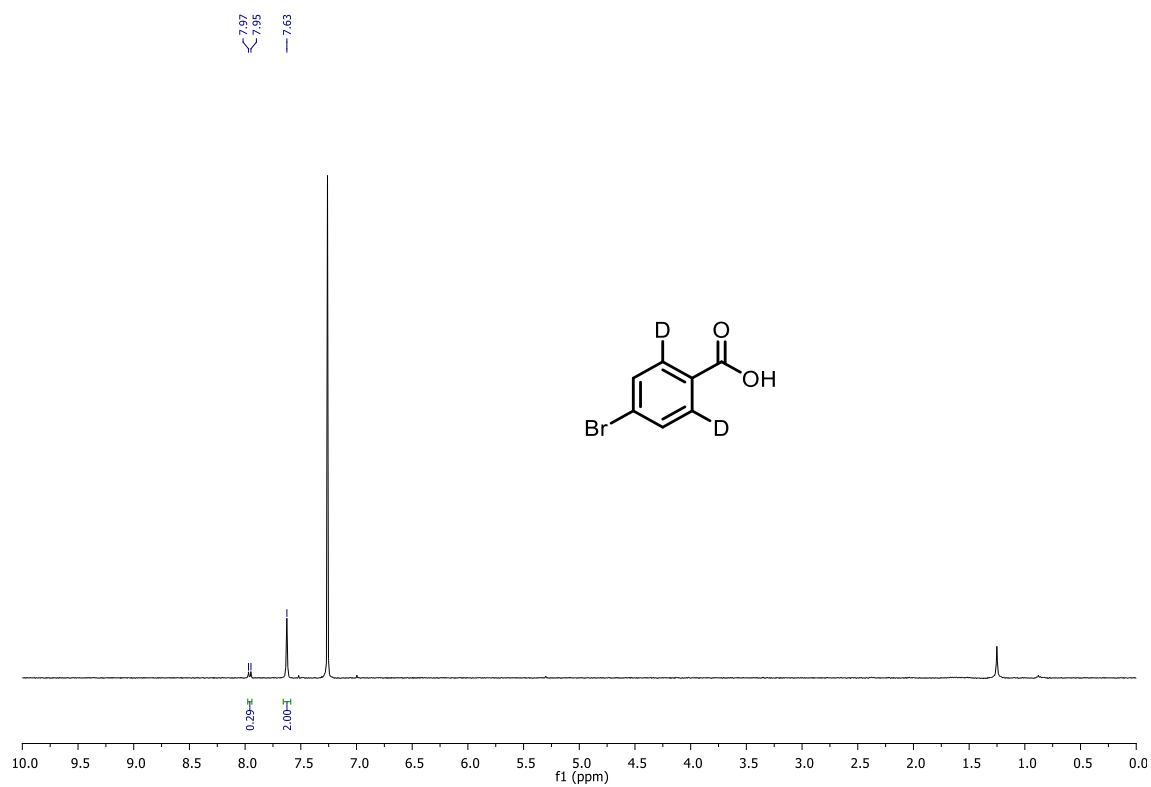


Figure S-20. ¹H NMR spectrum of **1i** (CDCl₃, 400 MHz, 298 K)

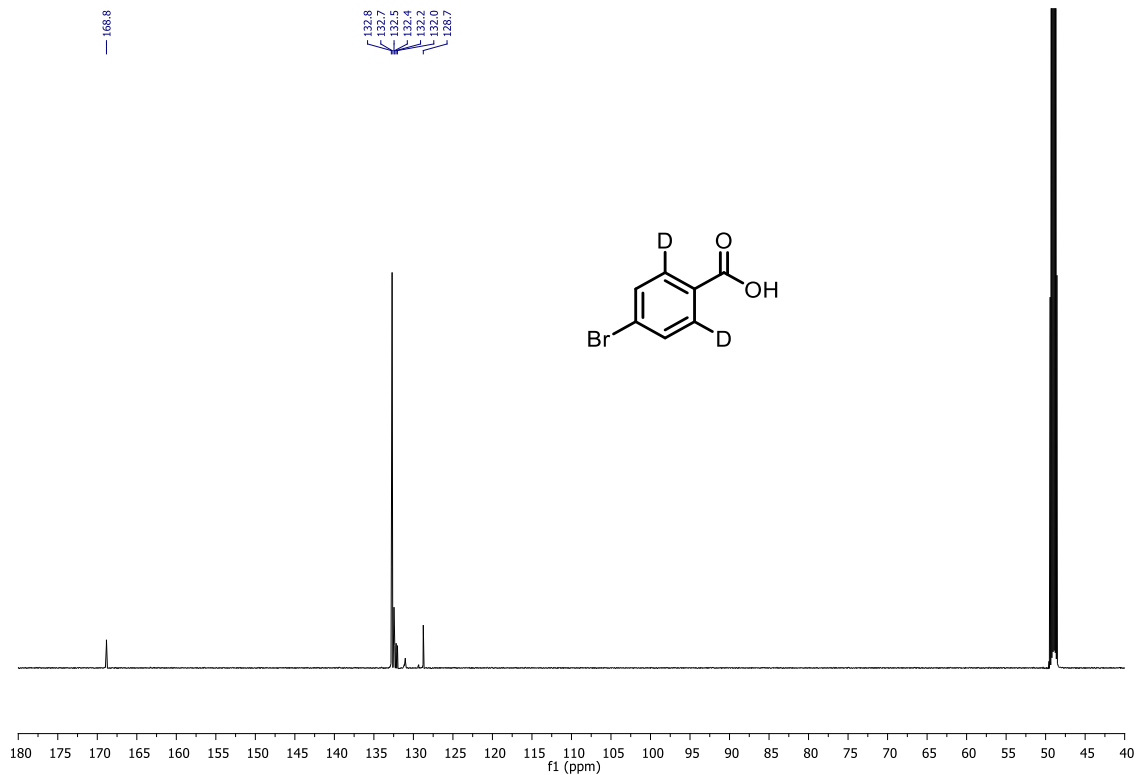


Figure S-21. ^{13}C NMR spectrum of **1i** (CD_3OD , 151 MHz, 298 K)

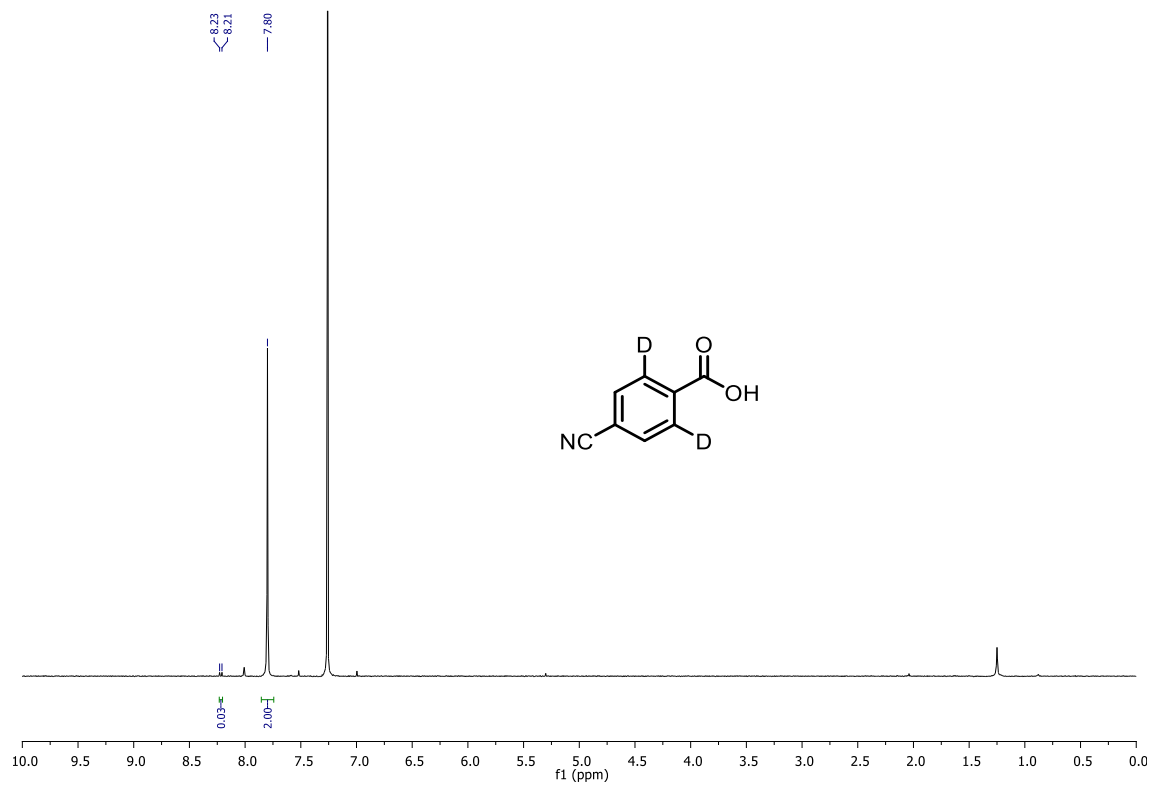


Figure S-22. ^1H NMR spectrum of **1j** (CDCl_3 , 400 MHz, 298 K)

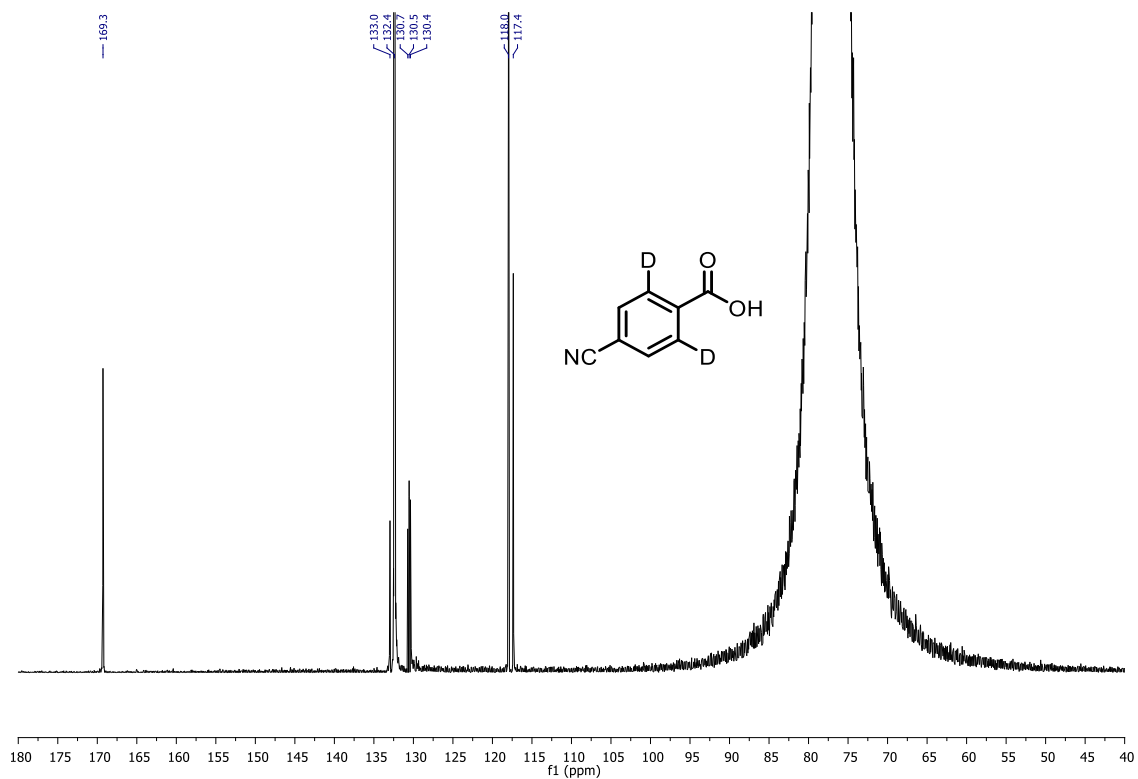


Figure S-23. ^{13}C NMR spectrum of **1j** (CDCl_3 , 151 MHz, 298 K)

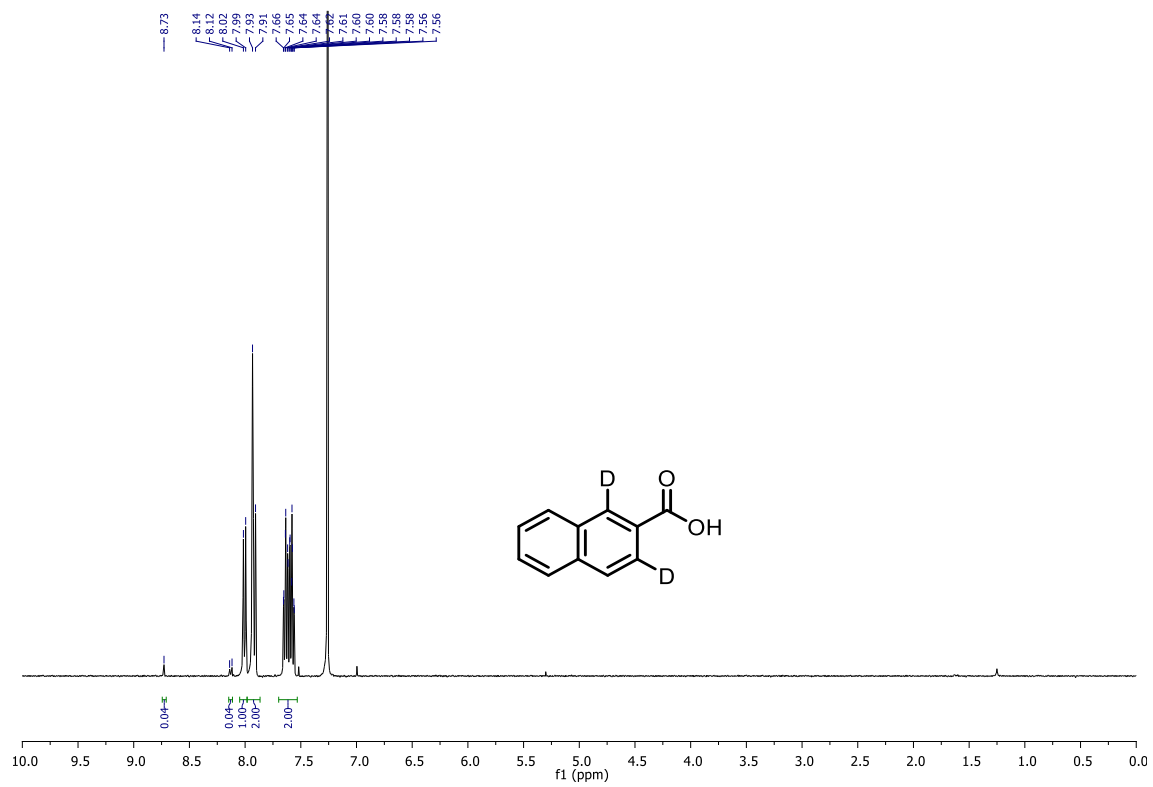


Figure S-24. ^1H NMR spectrum of **1k** (CDCl_3 , 400 MHz, 298 K)

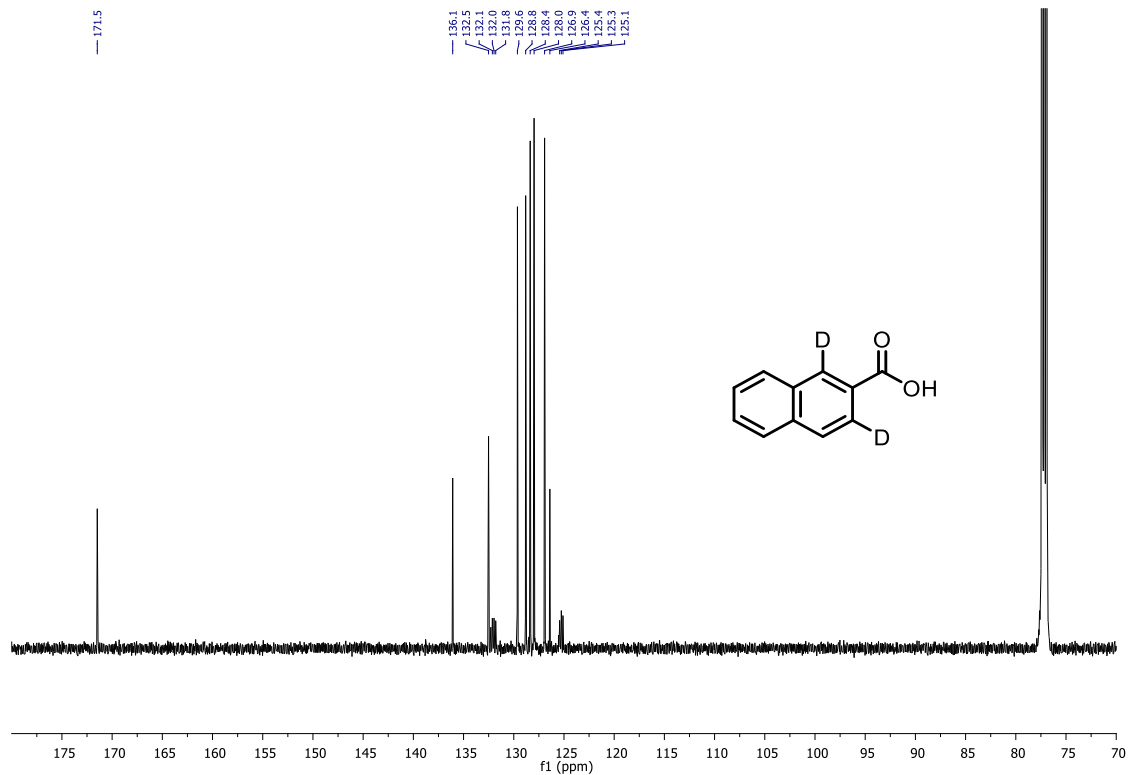


Figure S-25. ^{13}C NMR spectrum of **1k** (CDCl_3 , 151 MHz, 298 K)

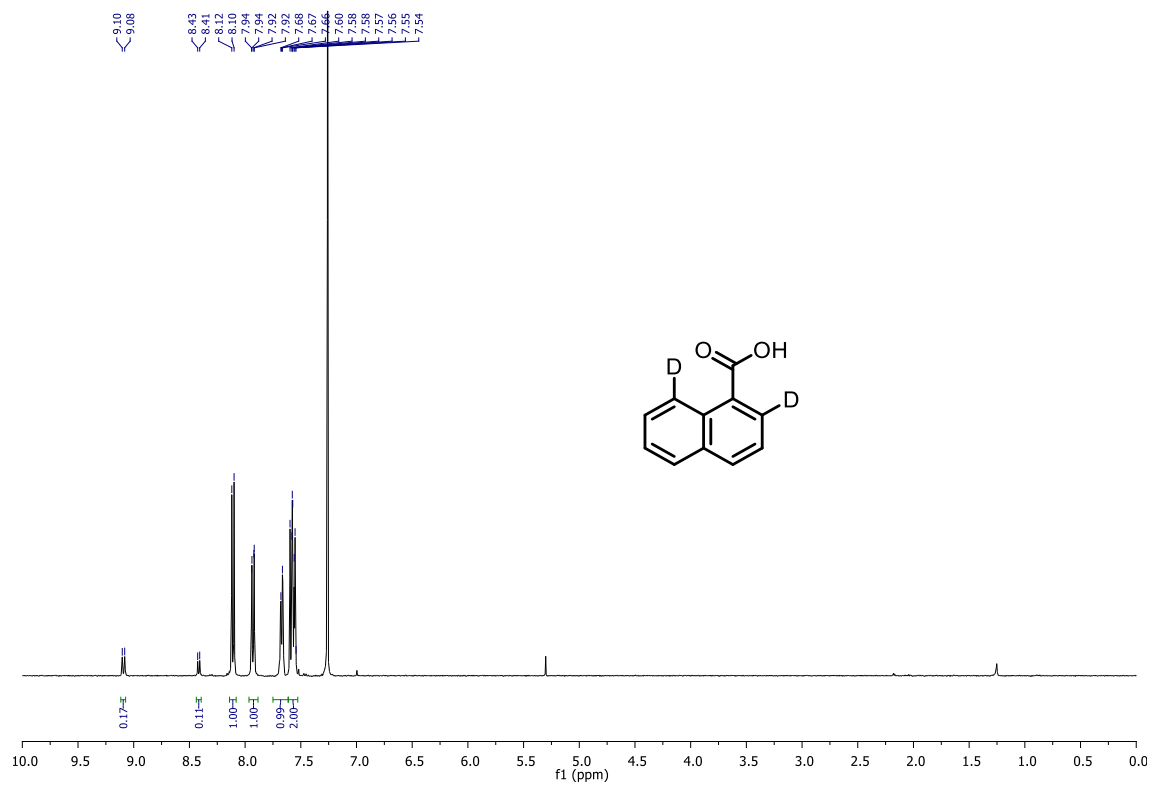


Figure S-26. ^1H NMR spectrum of **1l** (CDCl_3 , 400 MHz, 298 K)

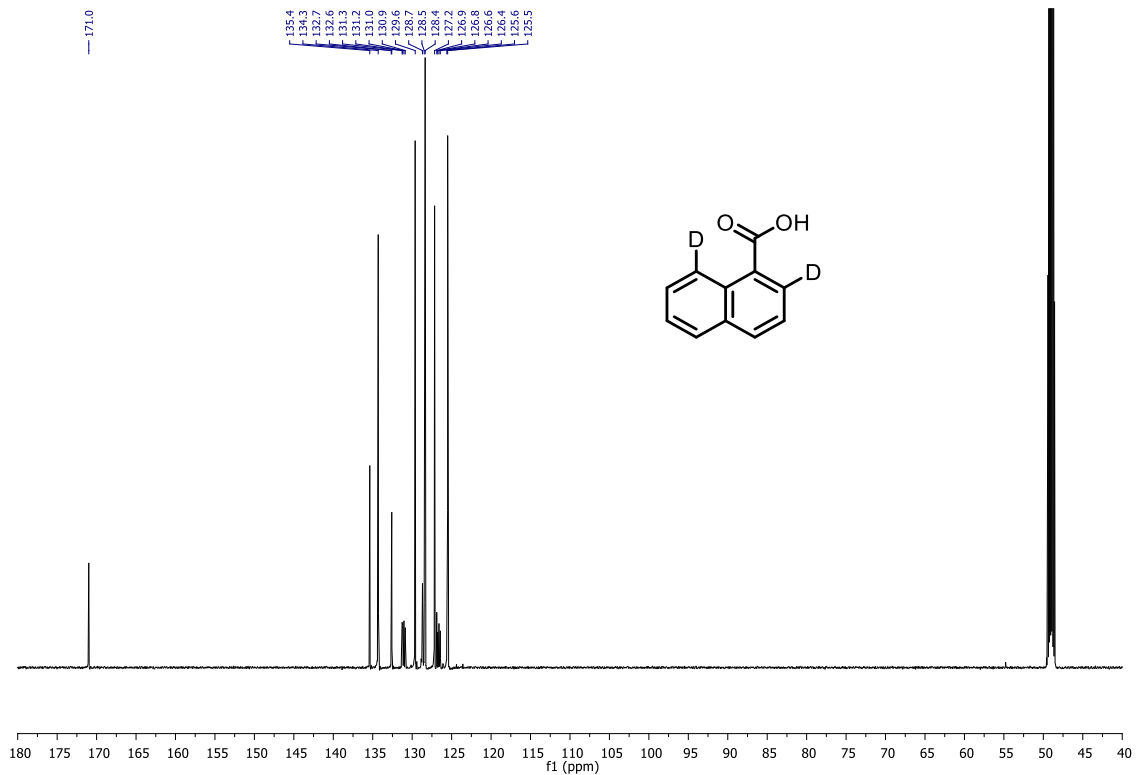


Figure S-27. ^{13}C NMR spectrum of **11** (CD_3OD , 151 MHz, 298 K)

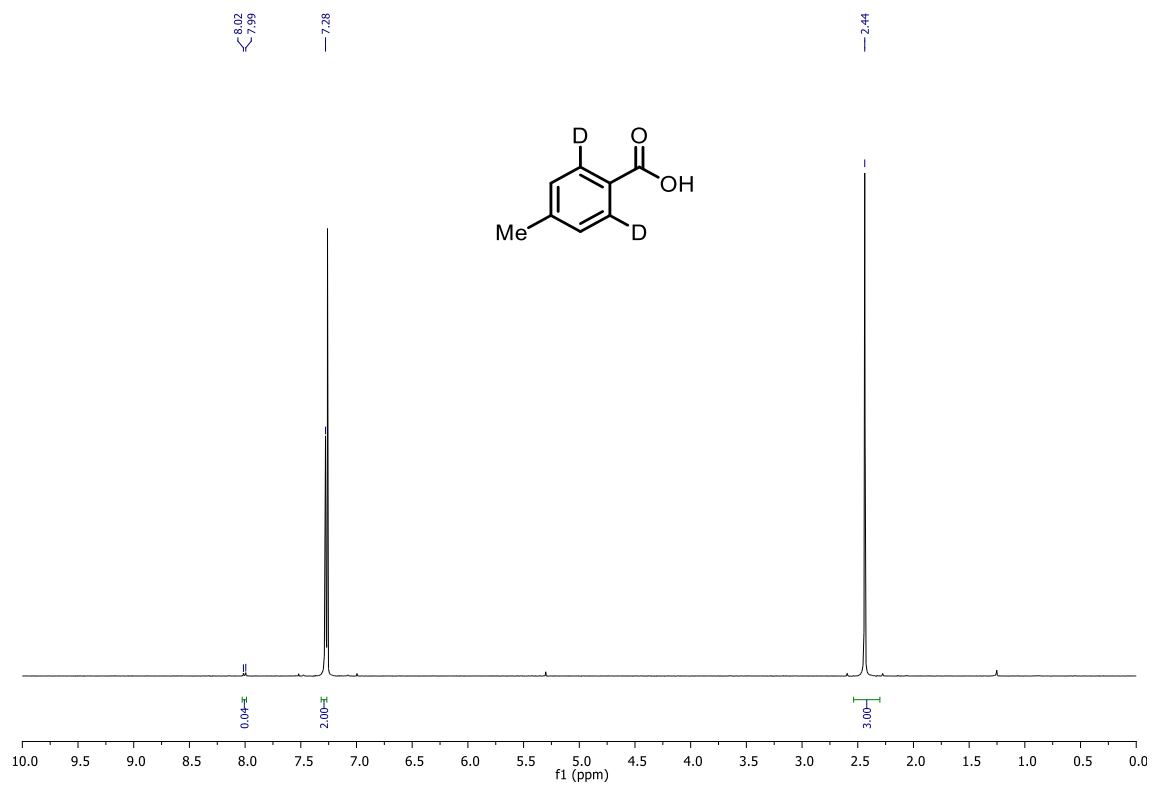


Figure S-28. ^1H NMR spectrum of **1m** (CDCl_3 , 400 MHz, 298 K)

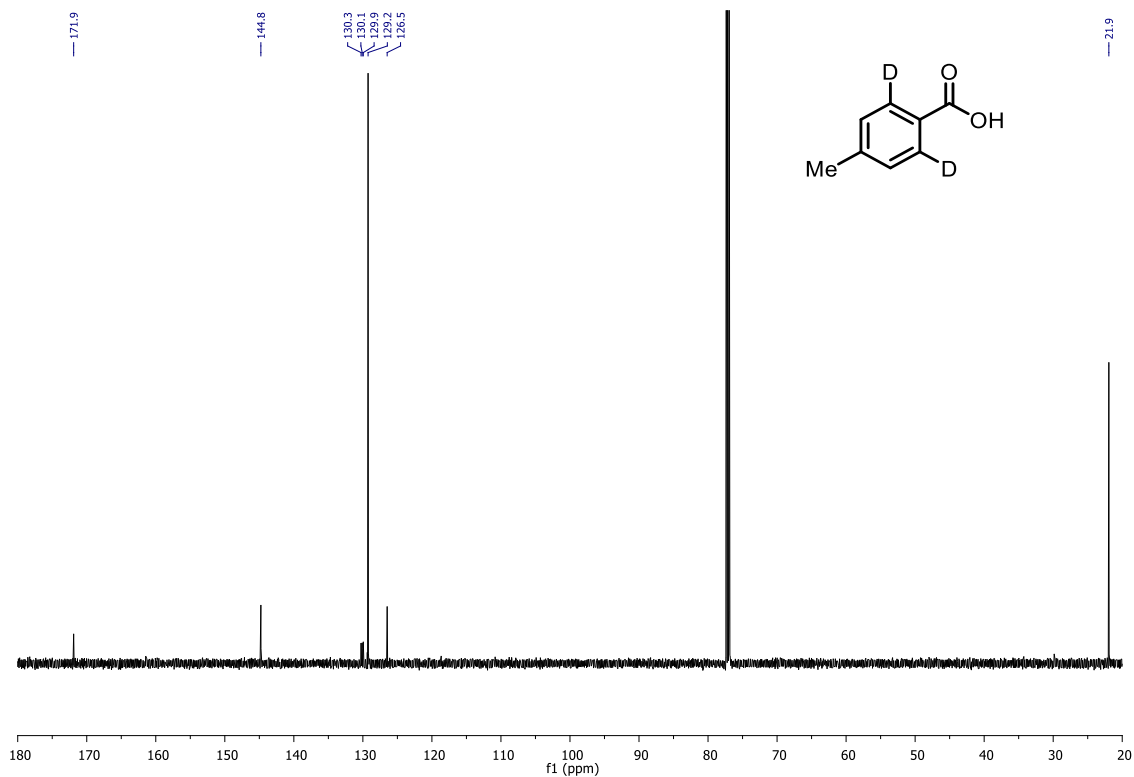


Figure S-29. ^{13}C NMR spectrum of **1m** (CDCl_3 , 151 MHz, 298 K)

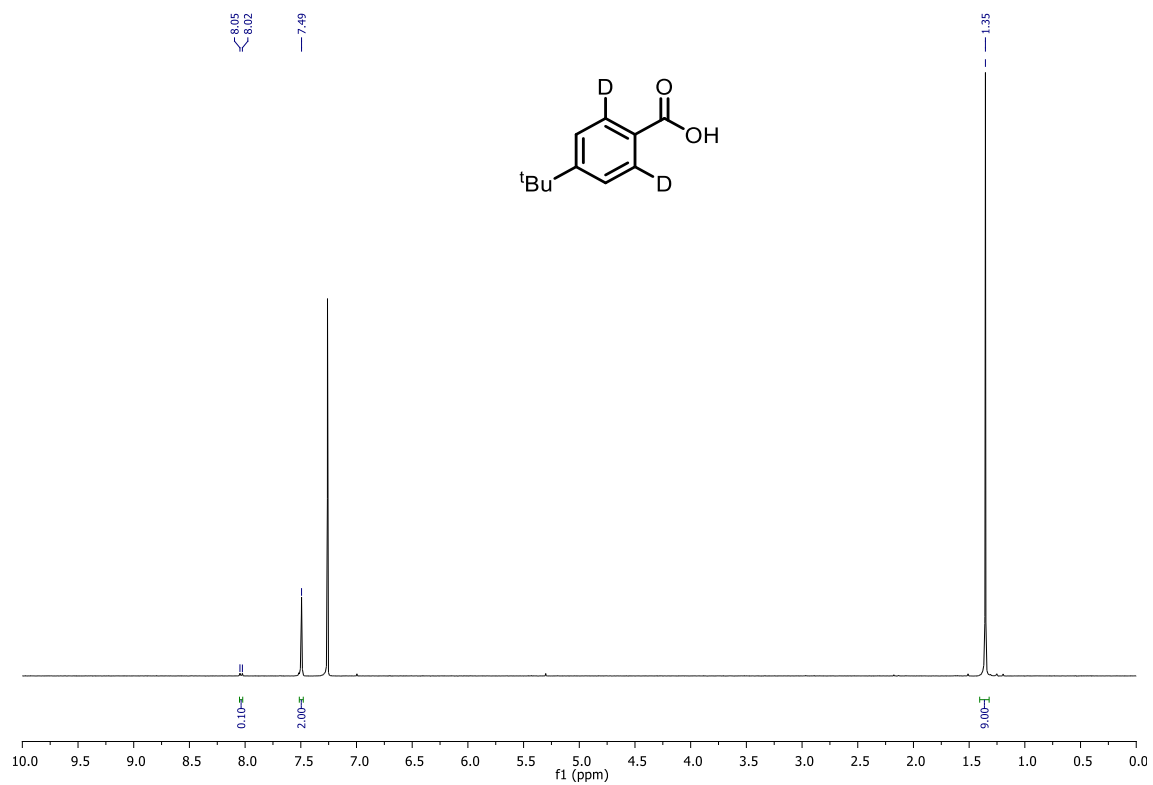


Figure S-30. ^1H NMR spectrum of **1n** (CDCl_3 , 400 MHz, 298 K)

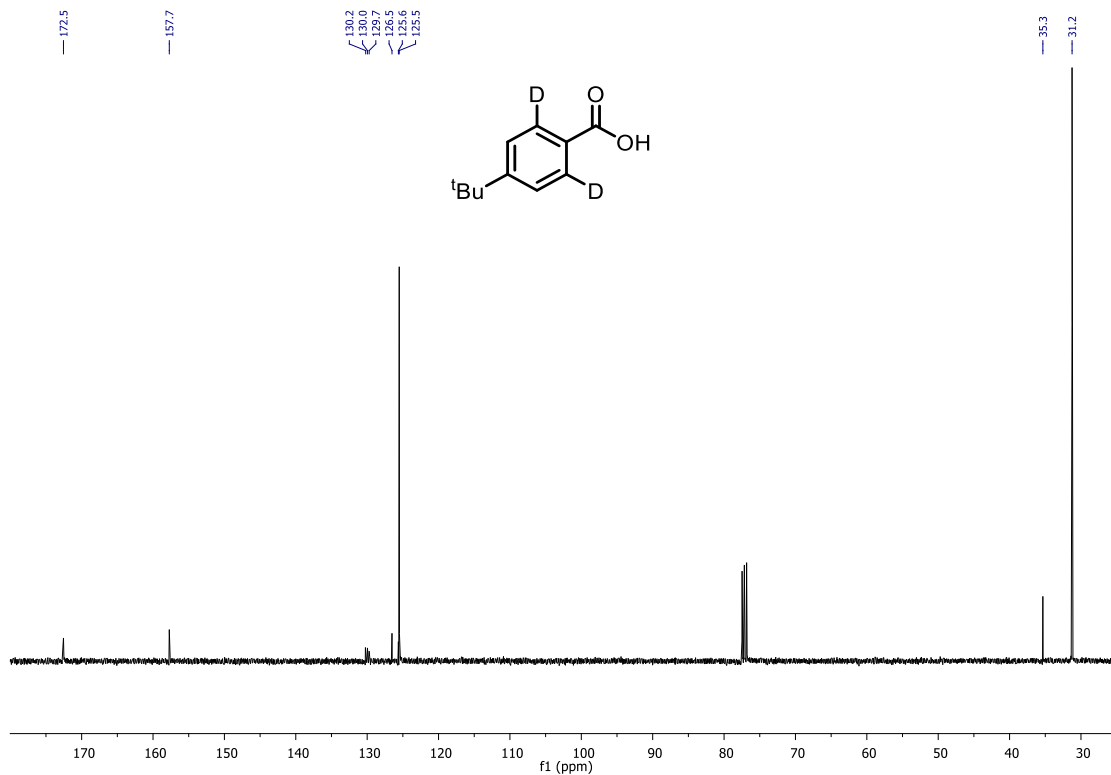


Figure S-31. ^{13}C NMR spectrum of **1n** (CDCl_3 , 151 MHz, 298 K)

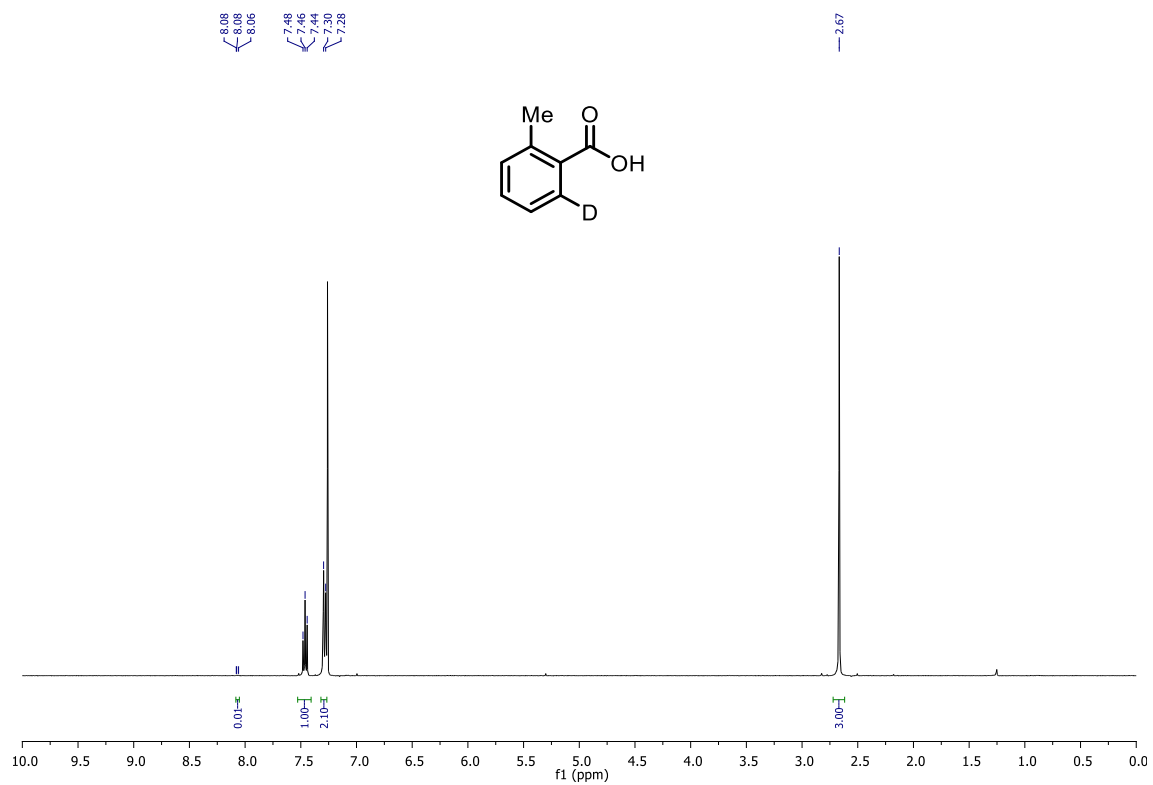


Figure S-32. ^1H NMR spectrum of **1o** (CDCl_3 , 400 MHz, 298 K)

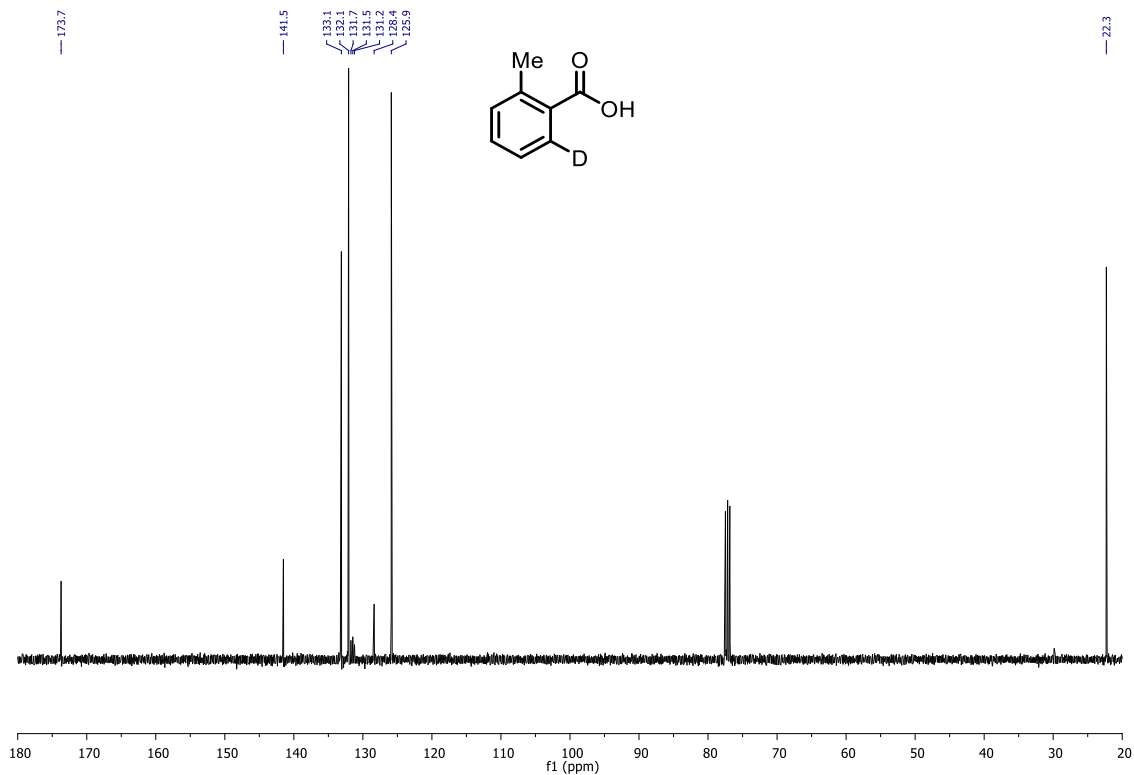


Figure S-33. ^{13}C NMR spectrum of **1o** (CDCl_3 , 151 MHz, 298 K)

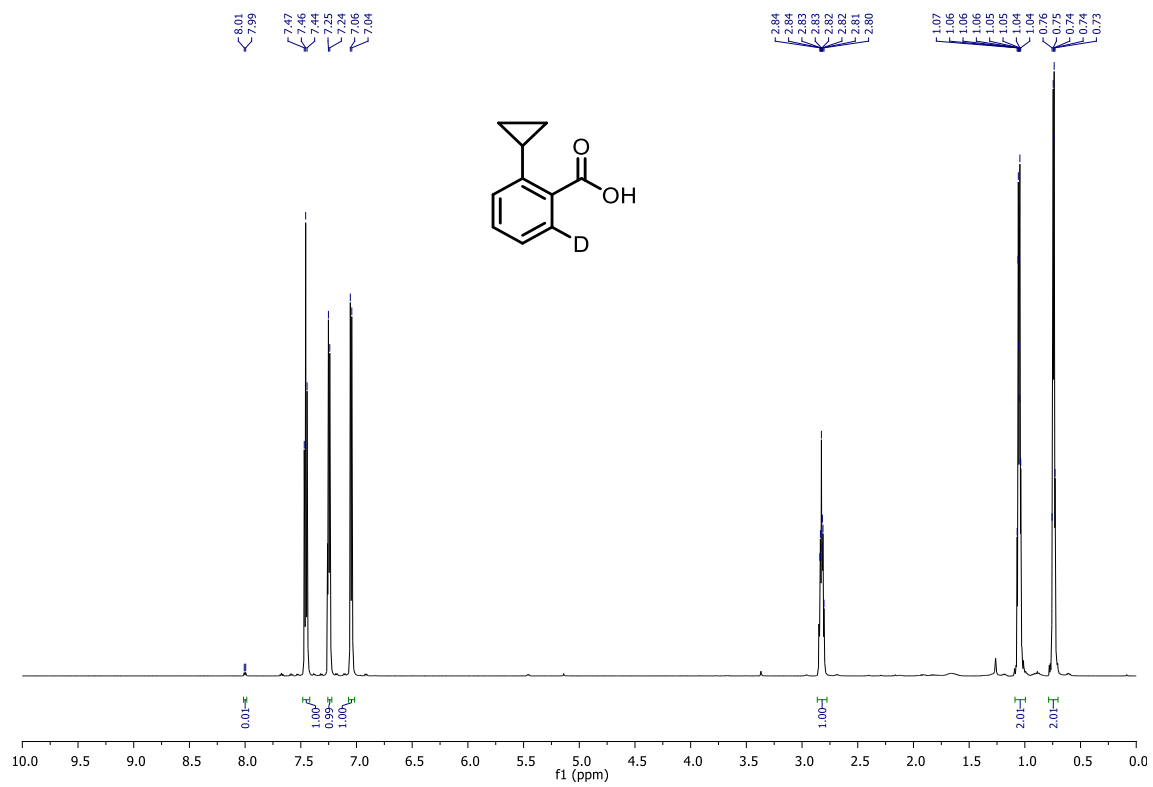


Figure S-34. ^1H NMR spectrum of **1p** (CDCl_3 , 400 MHz, 298 K)

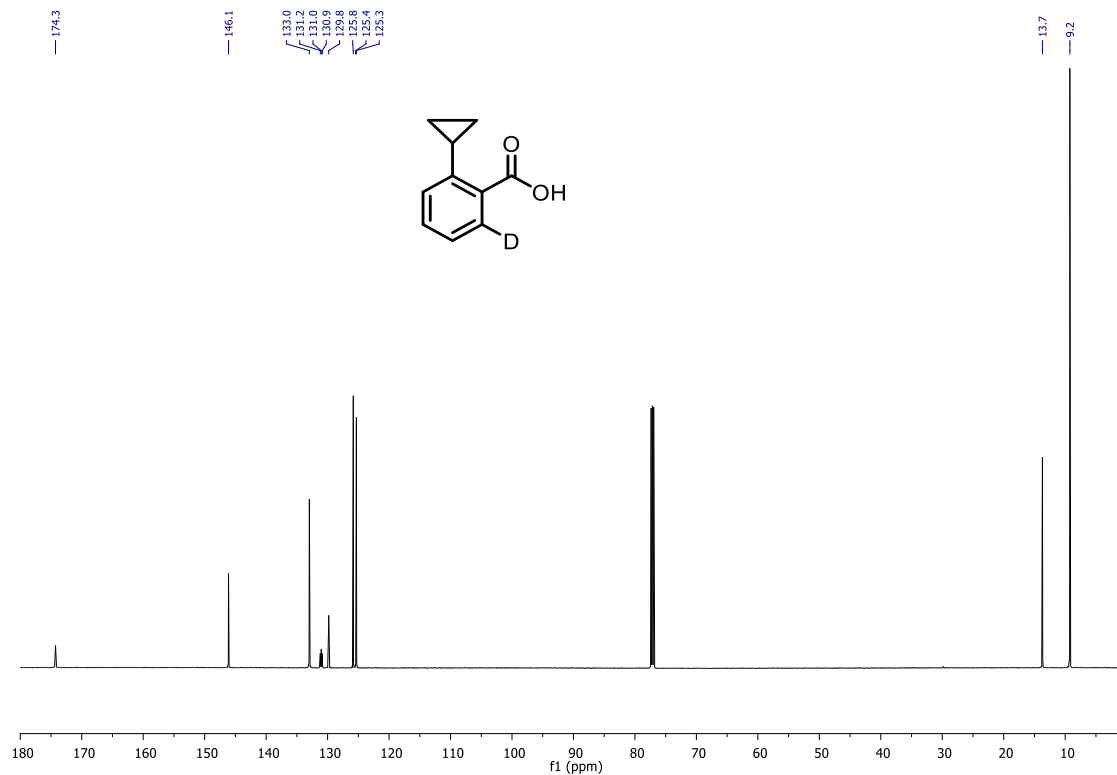


Figure S-35. ^{13}C NMR spectrum of **1p** (CDCl_3 , 151 MHz, 298 K)

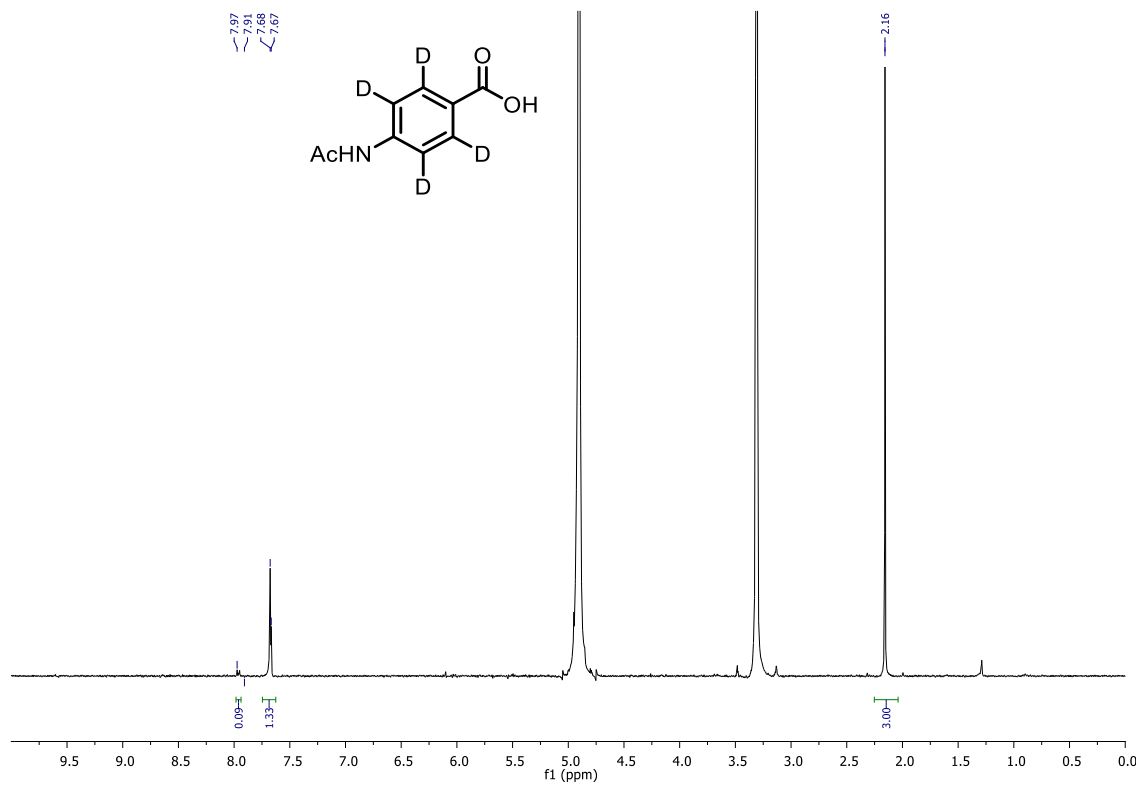


Figure S-36. ^1H NMR spectrum of **1q** (CD_3OD , 400 MHz, 298 K)

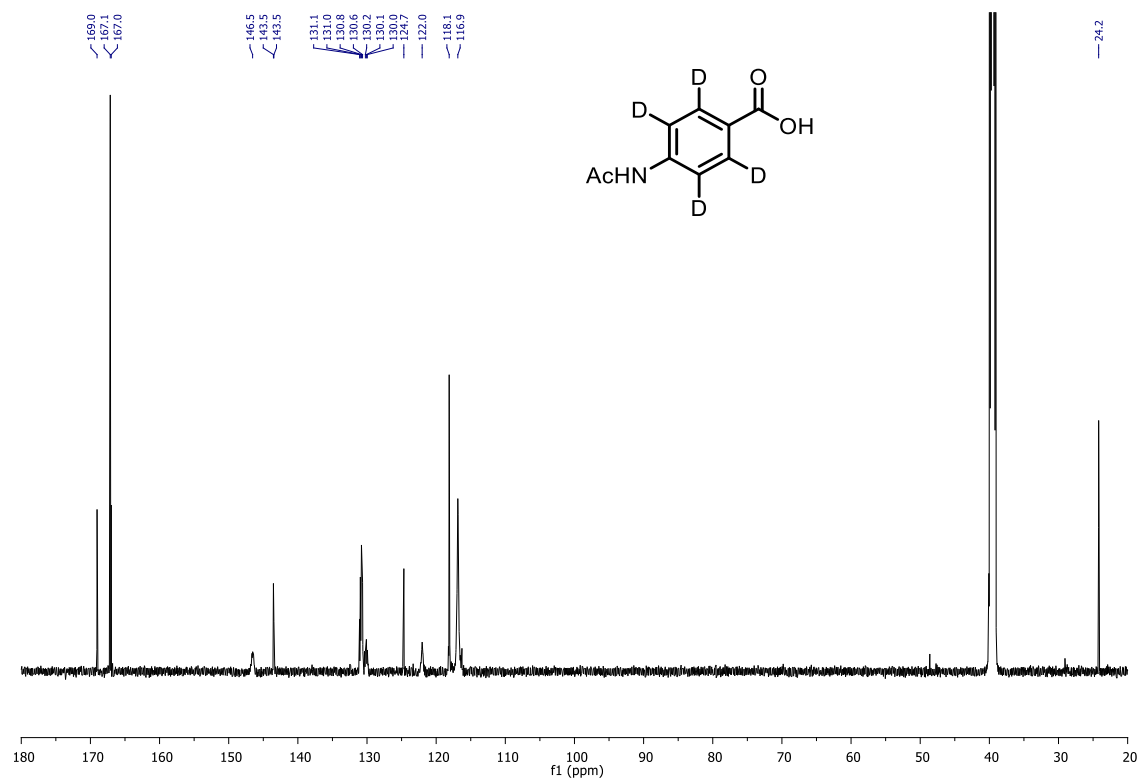


Figure S-37. ¹³C NMR spectrum of **1q** (DMSO-*d*₆, 151 MHz, 298 K)

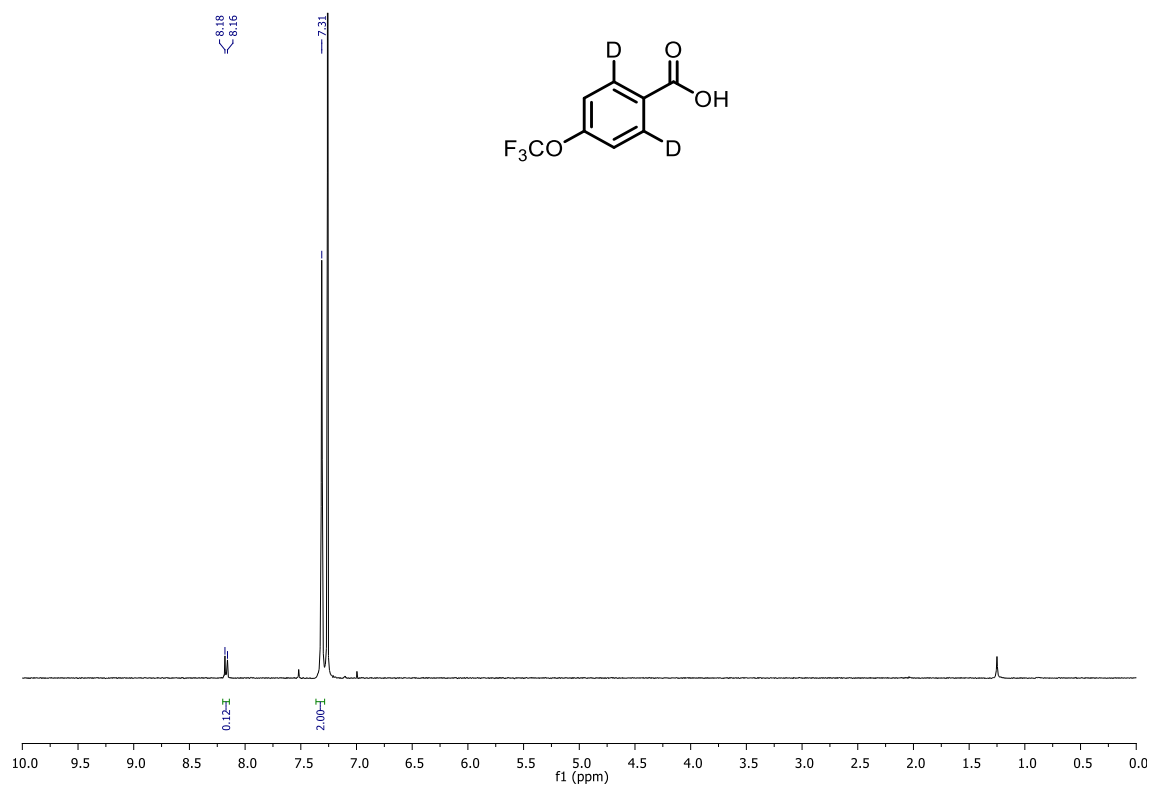


Figure S-38. ¹H NMR spectrum of **1r** (CDCl₃, 400 MHz, 298 K)

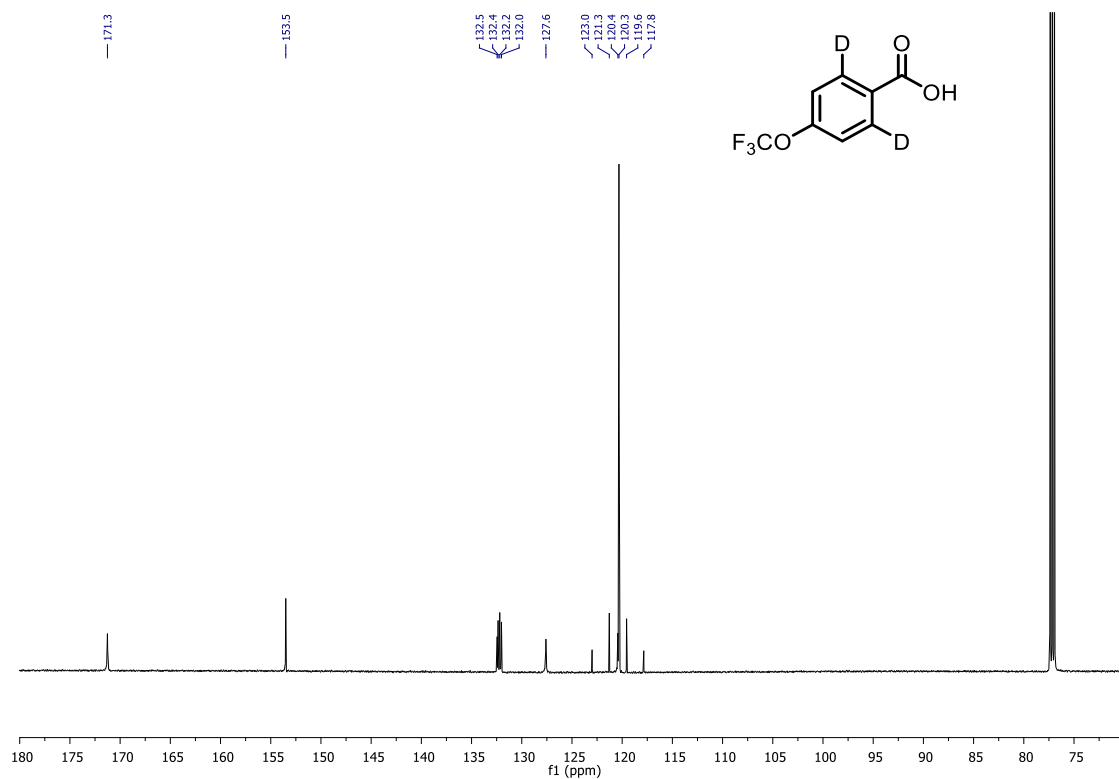


Figure S-39. ^{13}C NMR spectrum of **1r** (CDCl_3 , 151 MHz, 298 K)

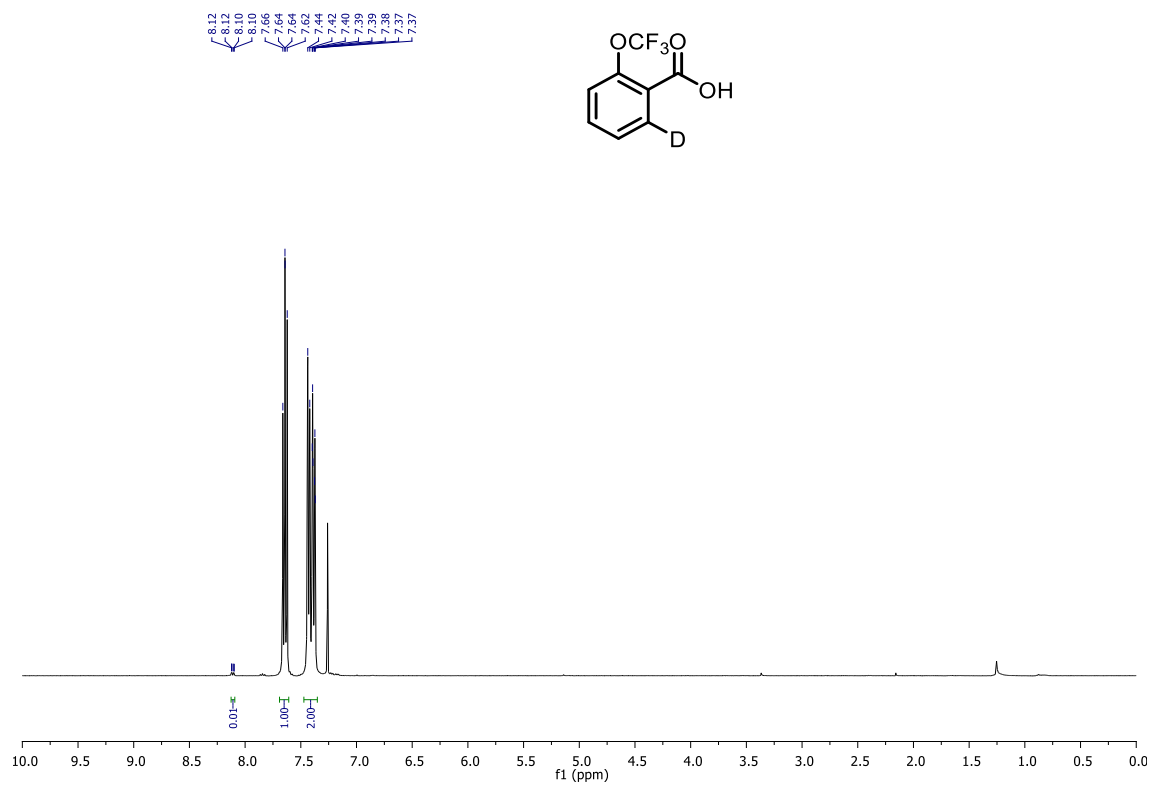


Figure S-40. ^1H NMR spectrum of **1s** (CDCl_3 , 400 MHz, 298 K)

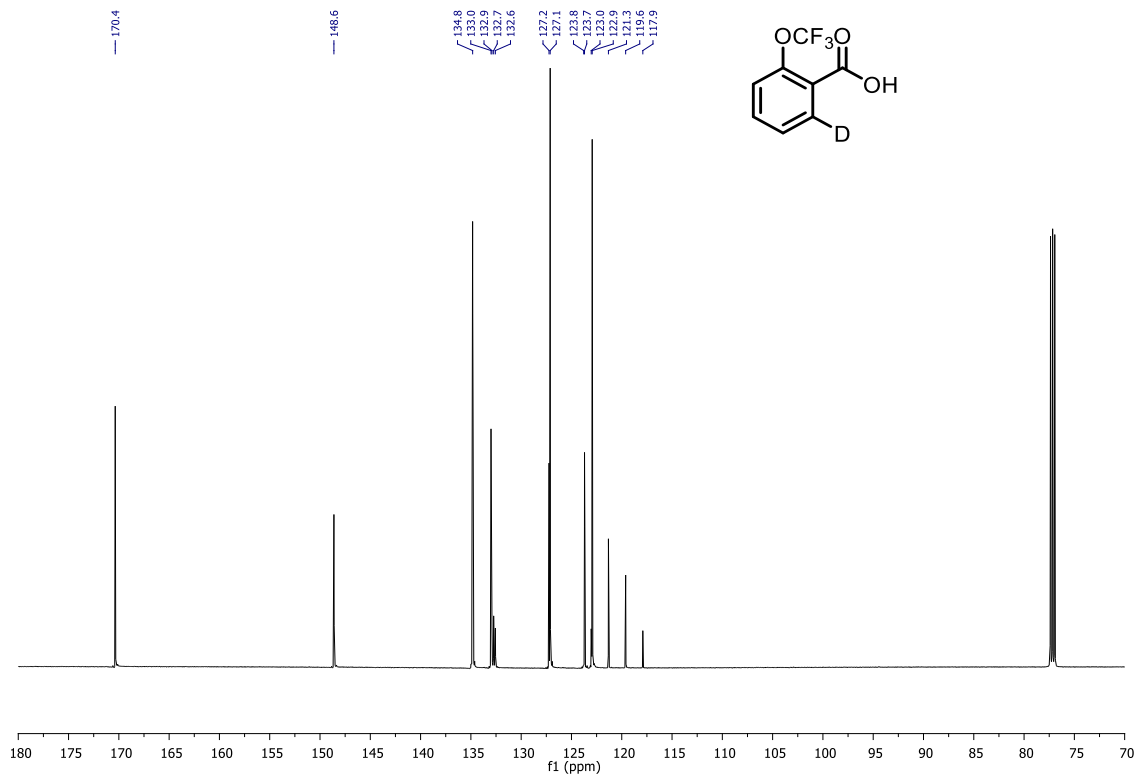


Figure S-41. ^{13}C NMR spectrum of **1s** (CDCl_3 , 151 MHz, 298 K)

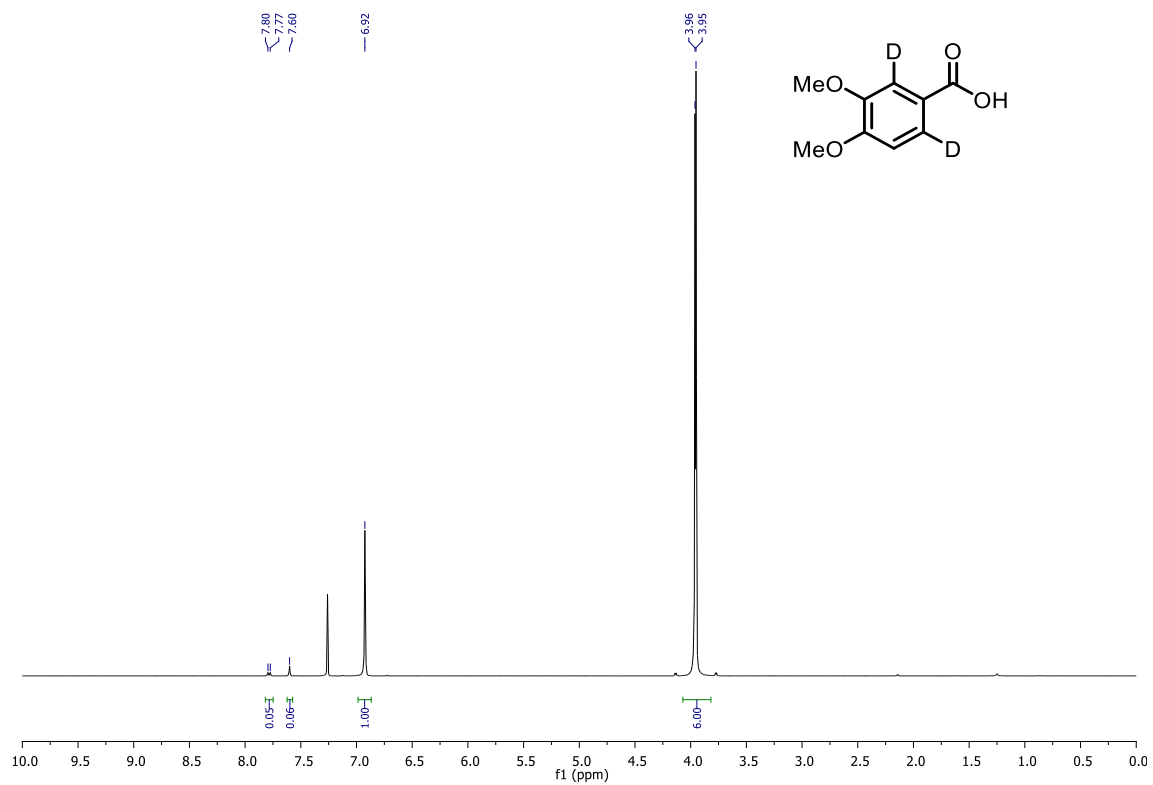


Figure S-42. ^1H NMR spectrum of **1t** (CDCl_3 , 400 MHz, 298 K)

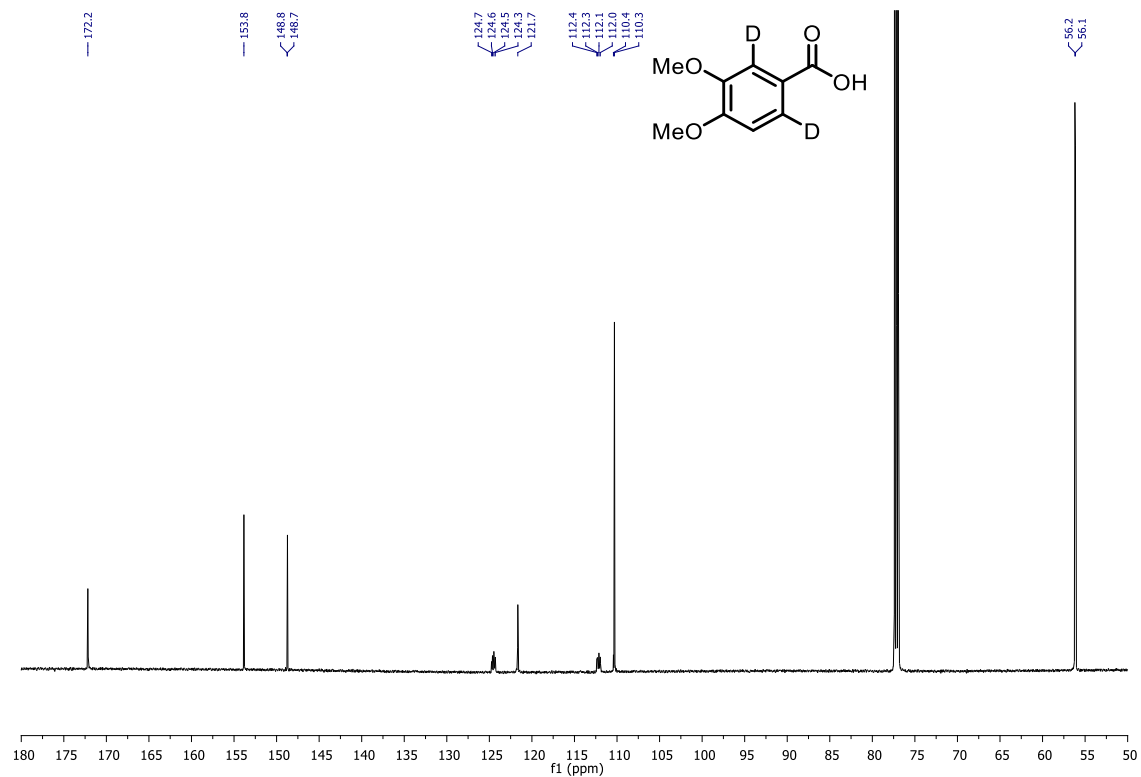


Figure S-43. ¹³C NMR spectrum of **1t** (CDCl₃, 151 MHz, 298 K)

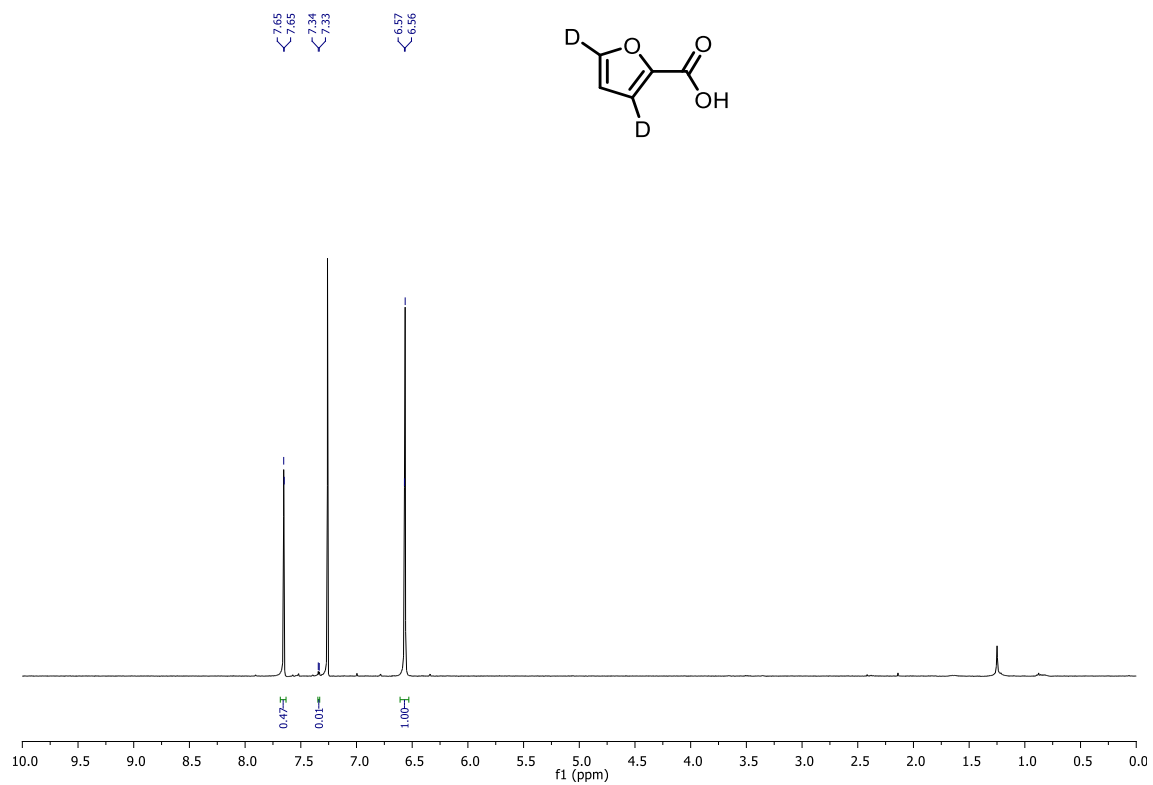


Figure S-44. ¹H NMR spectrum of **1u** (CDCl₃, 400 MHz, 298 K)

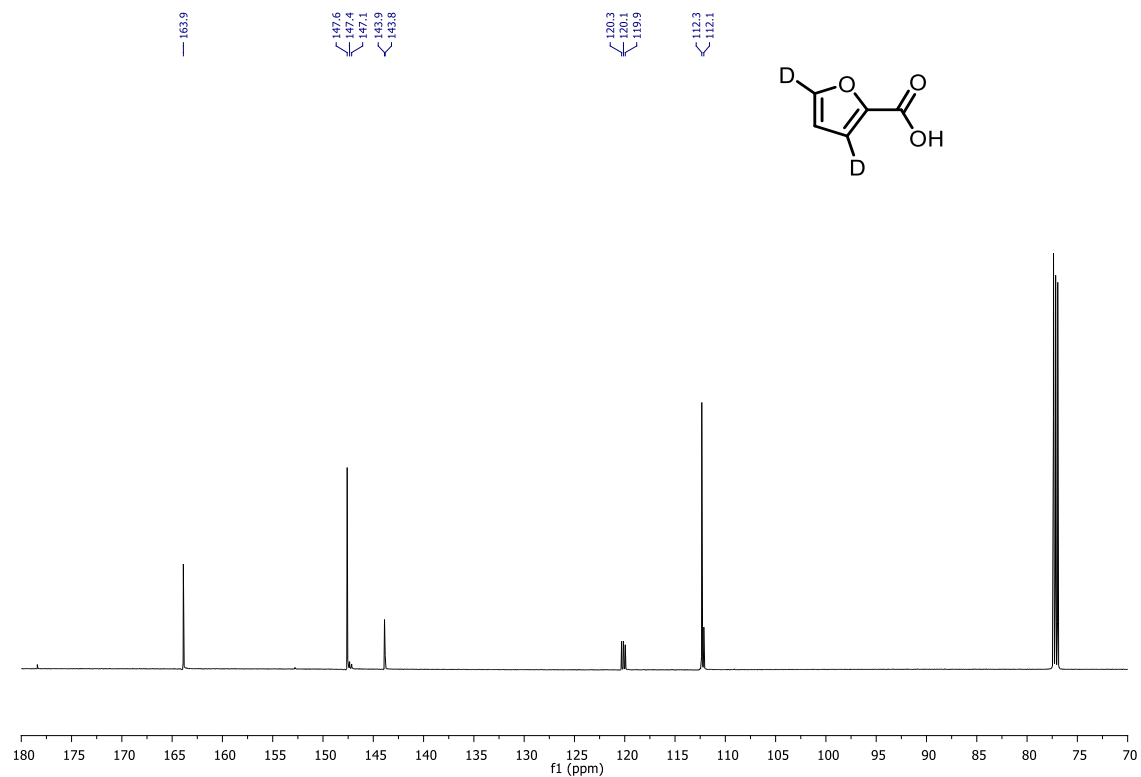


Figure S-45. ^{13}C NMR spectrum of **1u** (CDCl₃, 151 MHz, 298 K)

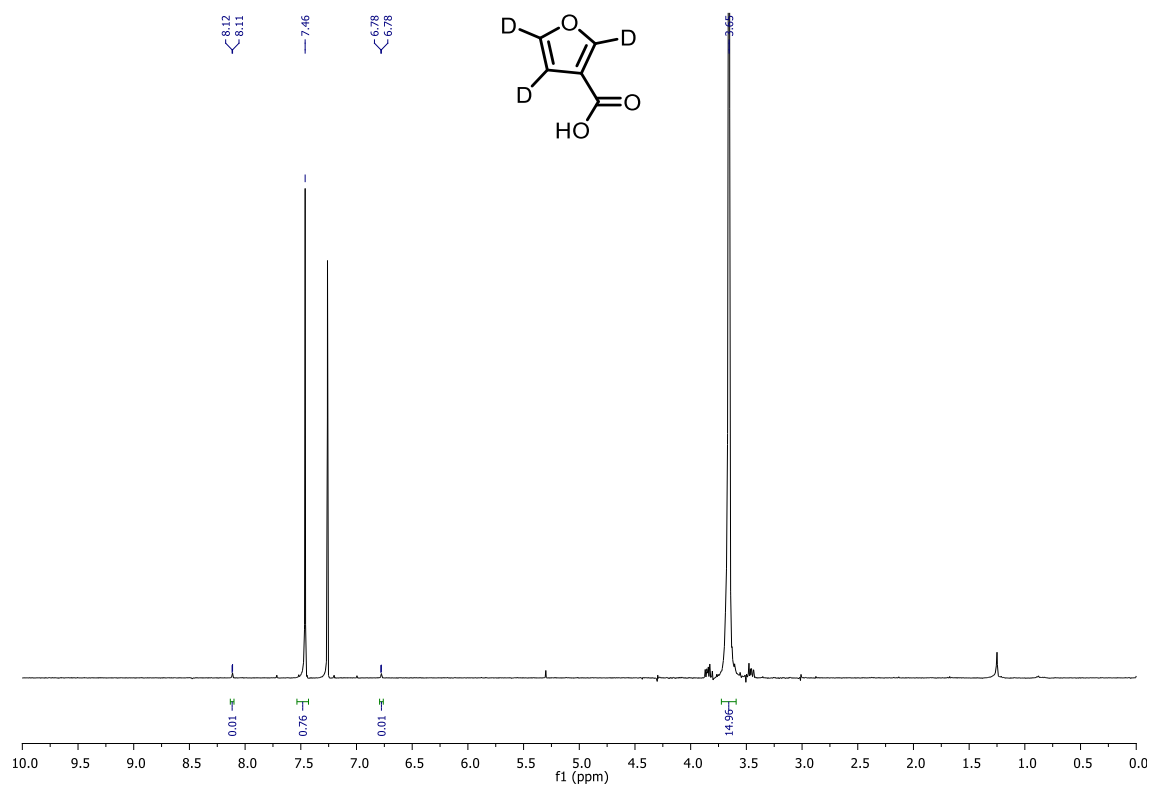


Figure S-46. ^1H NMR spectrum of **1v** with 1,2-dibromoethane (59.0 mg) as internal standard (CDCl₃, 400 MHz, 298 K)

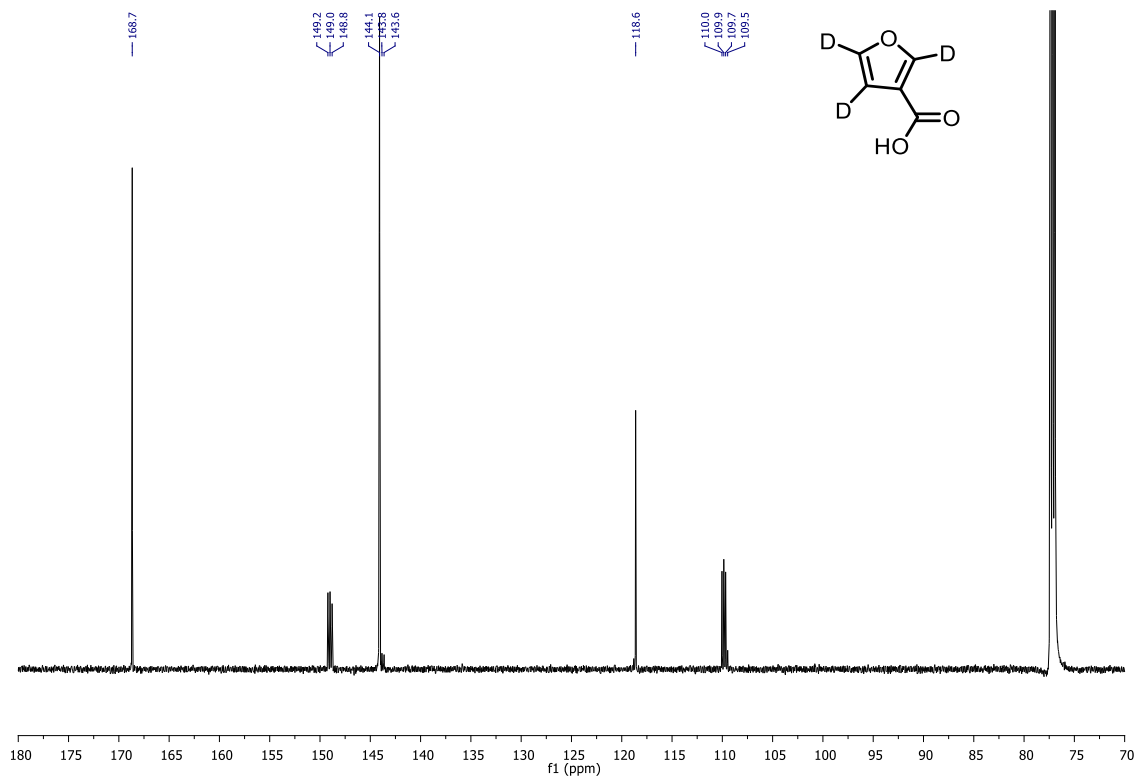


Figure S-47. ^{13}C NMR spectrum of **1v** (CDCl_3 , 151 MHz, 298 K)

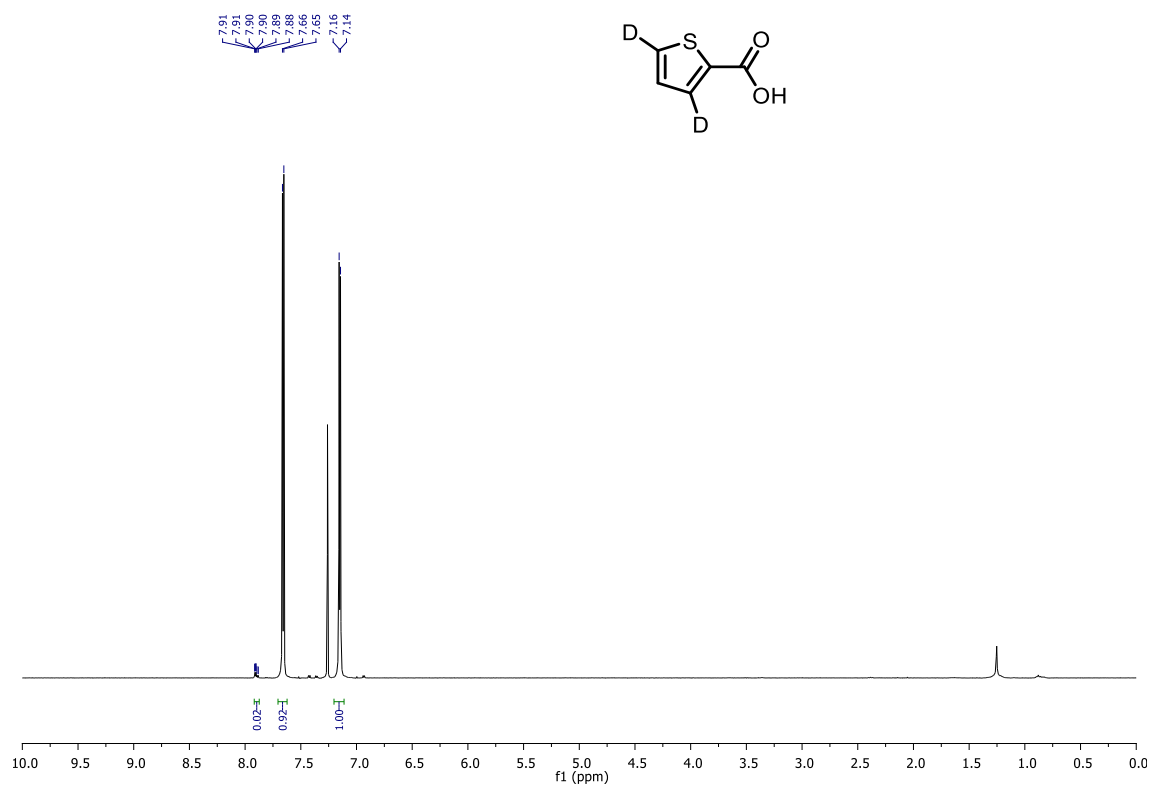


Figure S-48. ^1H NMR spectrum of **1w** (CDCl_3 , 400 MHz, 298 K)

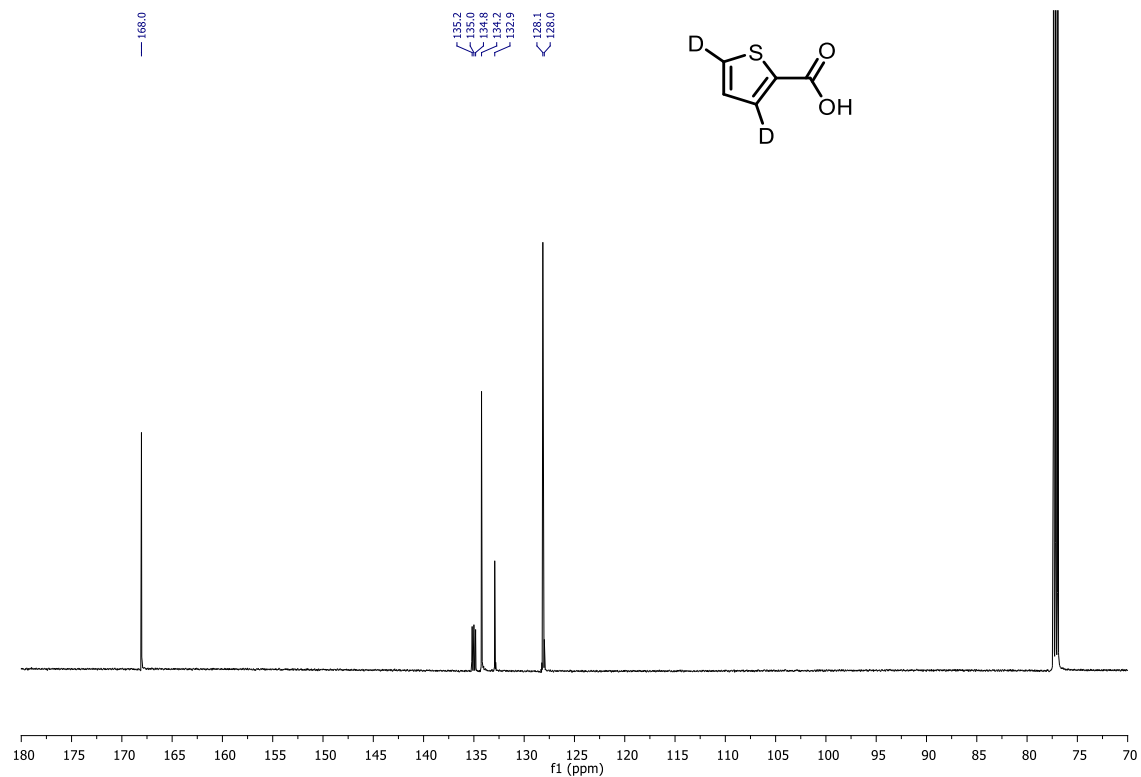


Figure S-49. ^{13}C NMR spectrum of **1w** (CDCl_3 , 151 MHz, 298 K)

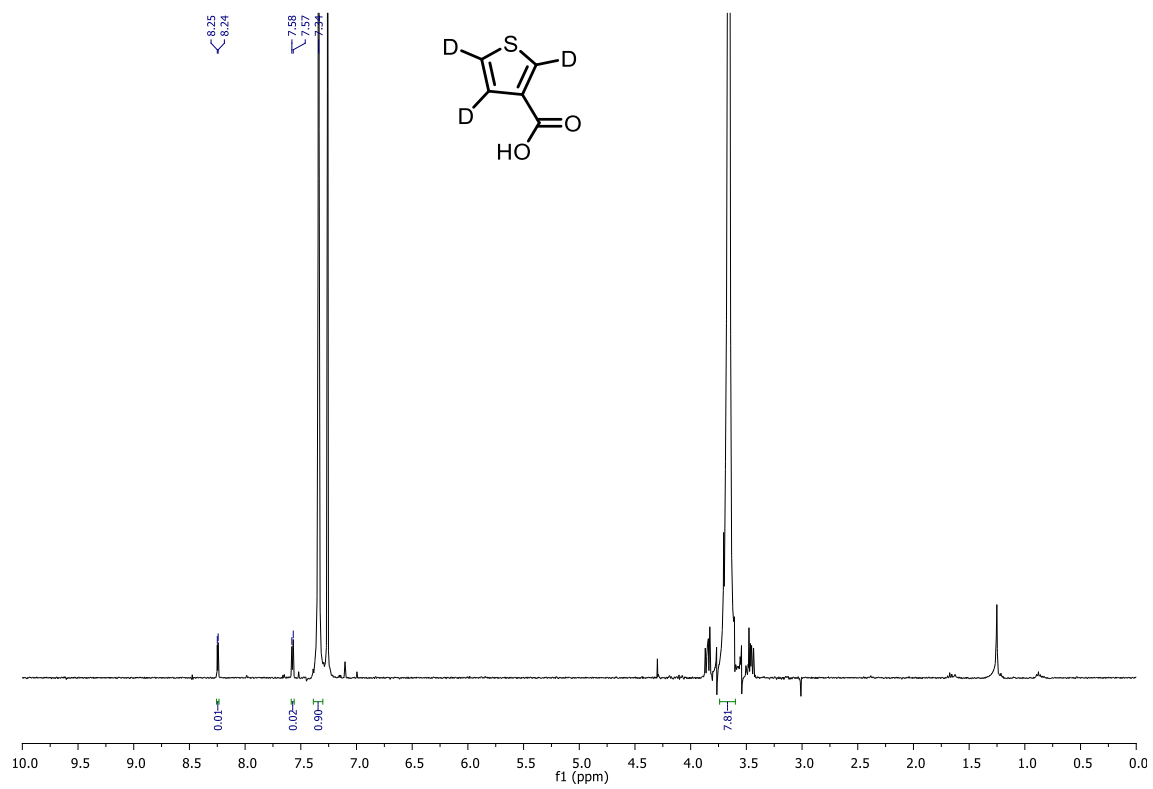


Figure S-50. ^1H NMR spectrum of **1x** with 1,2-dibromoethane (89.0 mg) as internal standard (CDCl_3 , 400 MHz, 298 K)

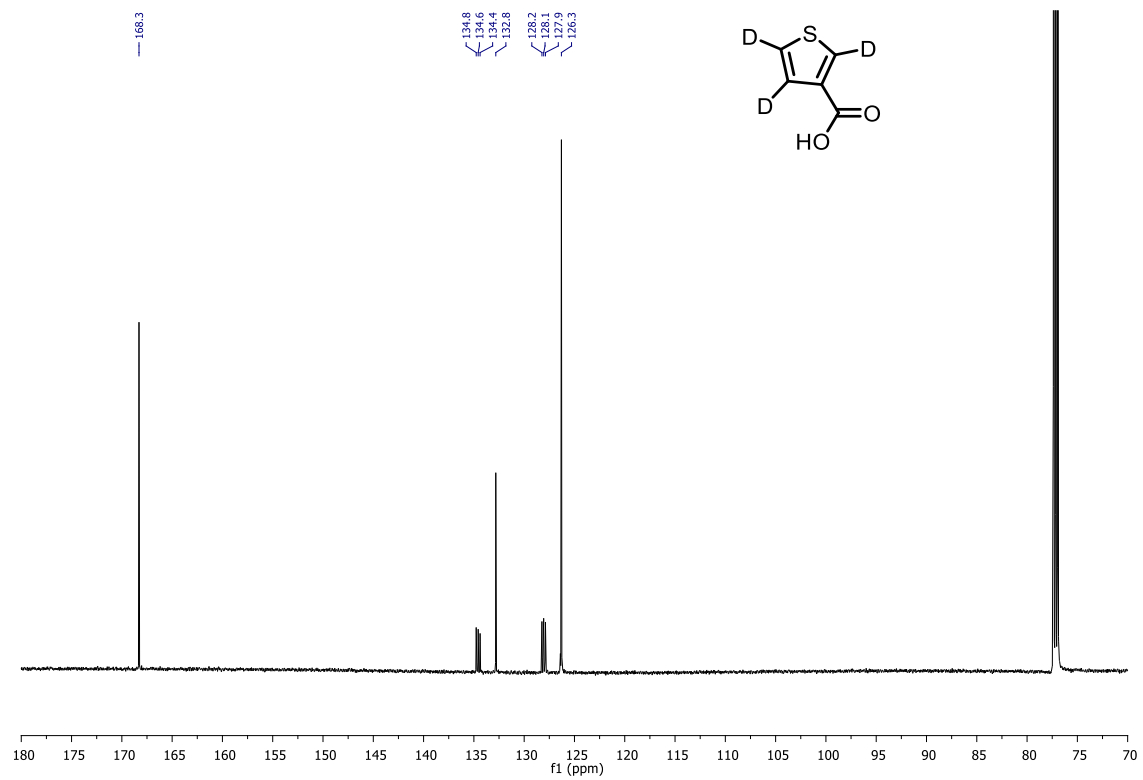


Figure S-51. ^{13}C NMR spectrum of **1x** (CDCl_3 , 151 MHz, 298 K)

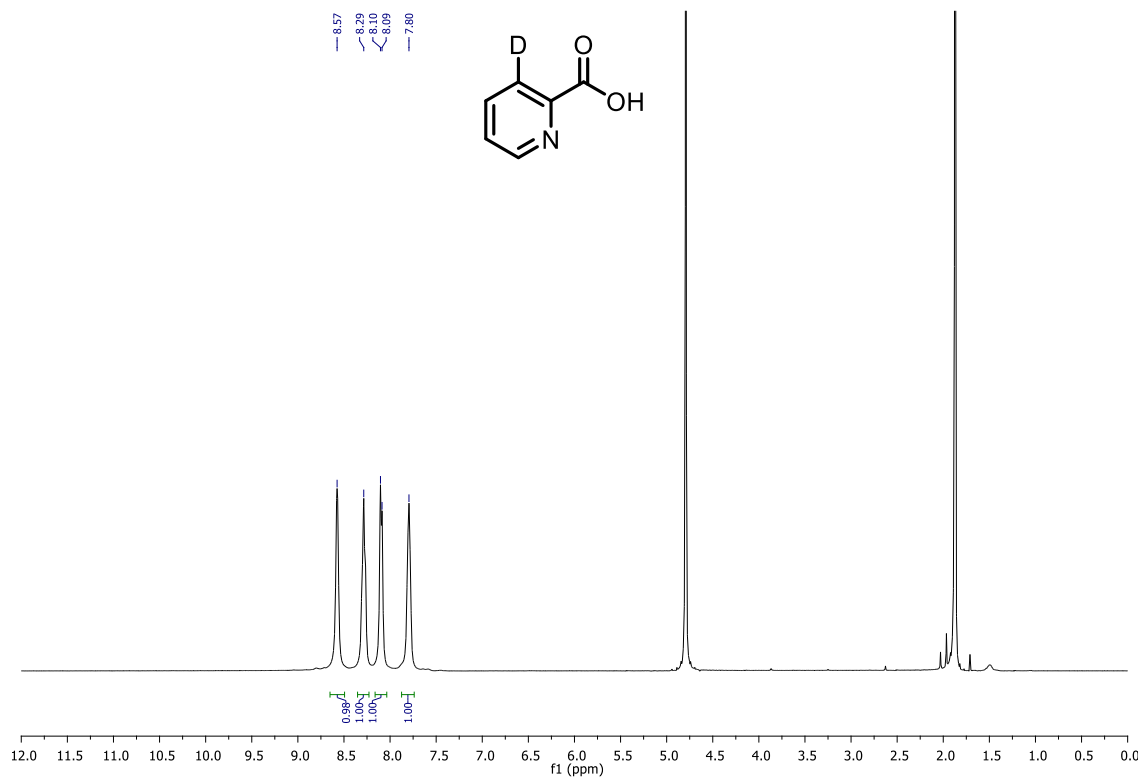


Figure S-52. ^1H NMR spectrum of **1y** (D_2O , 400 MHz, 298 K)

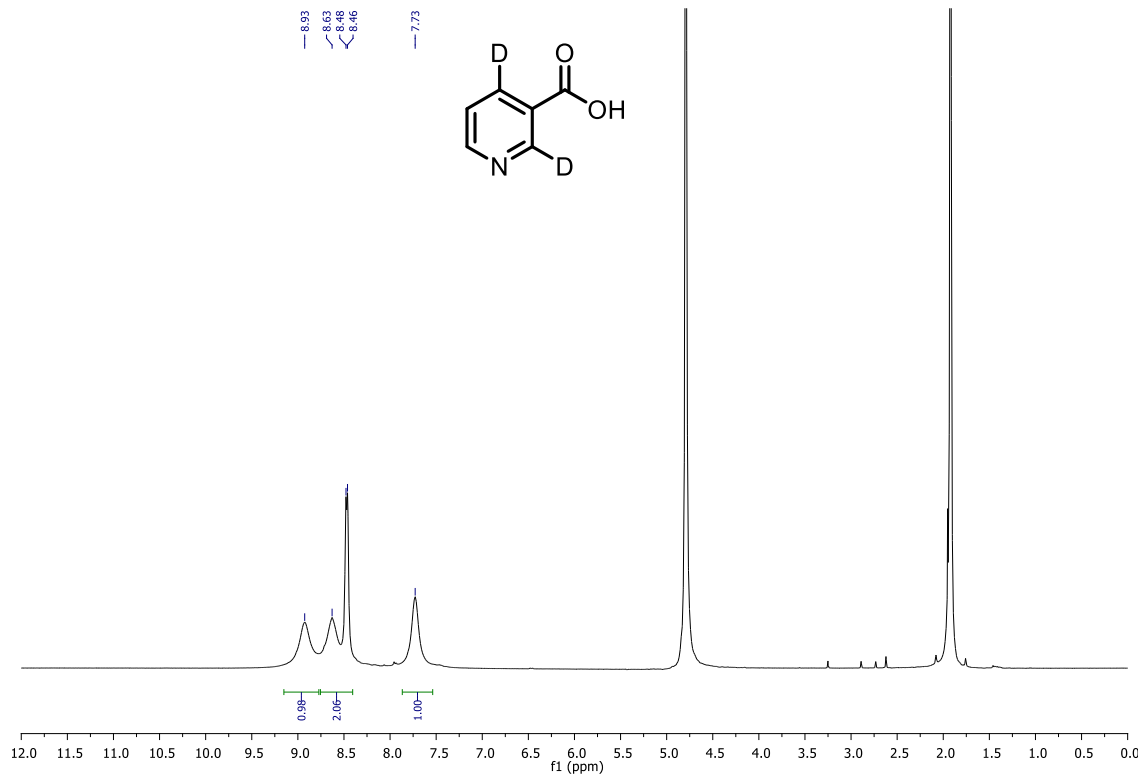


Figure S-53. ^1H NMR spectrum of **1z** (D_2O , 400 MHz, 298 K)

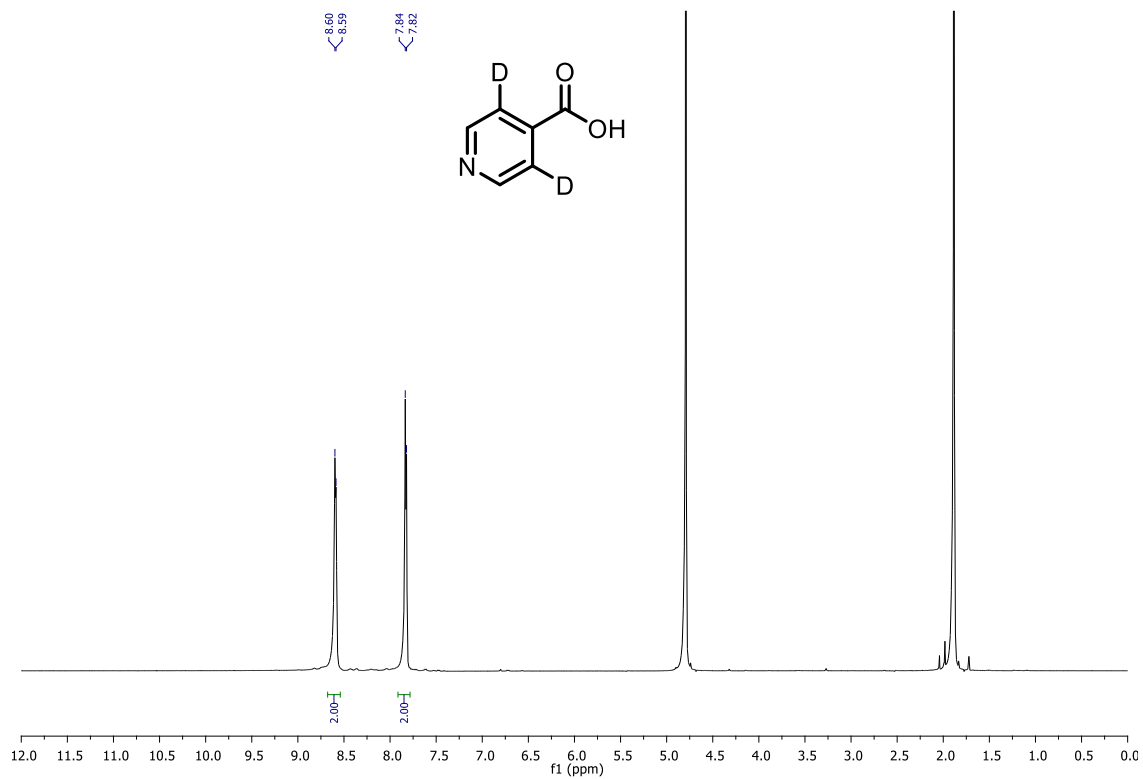


Figure S-54. ^1H NMR spectrum of **1aa** (D_2O , 400 MHz, 298 K)

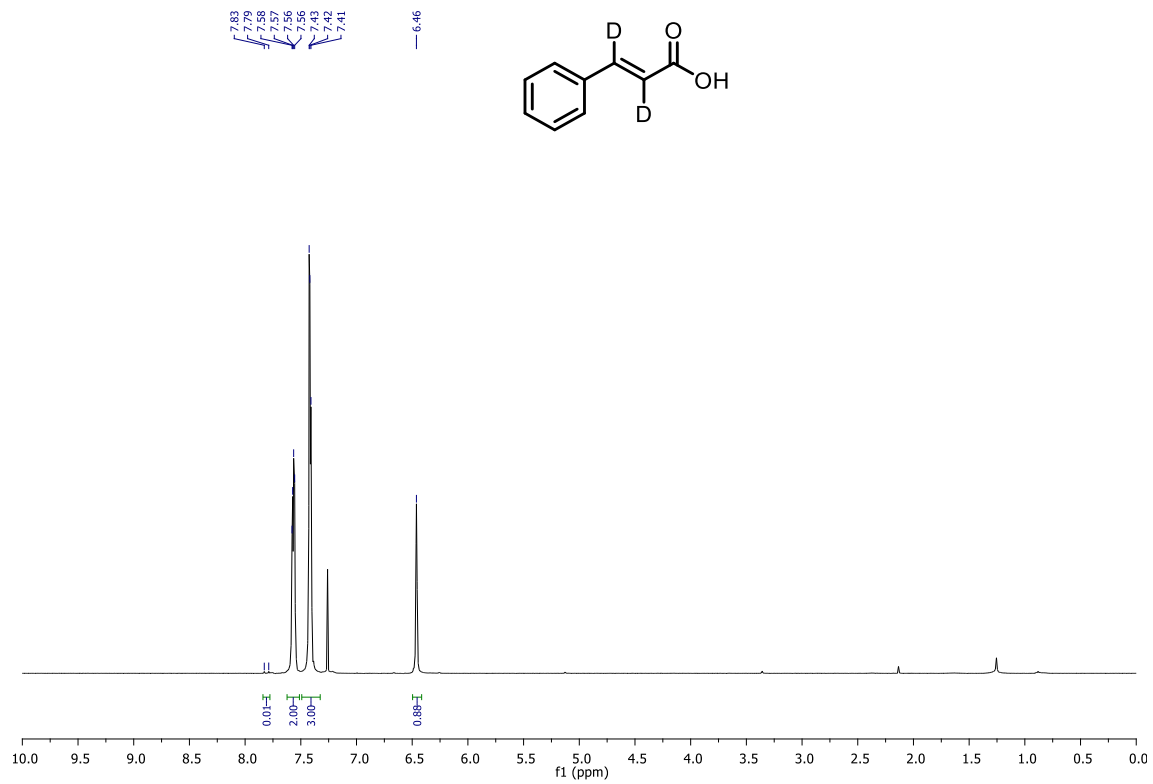


Figure S-55. ¹H NMR spectrum of **2a** (CDCl₃, 400 MHz, 298 K)

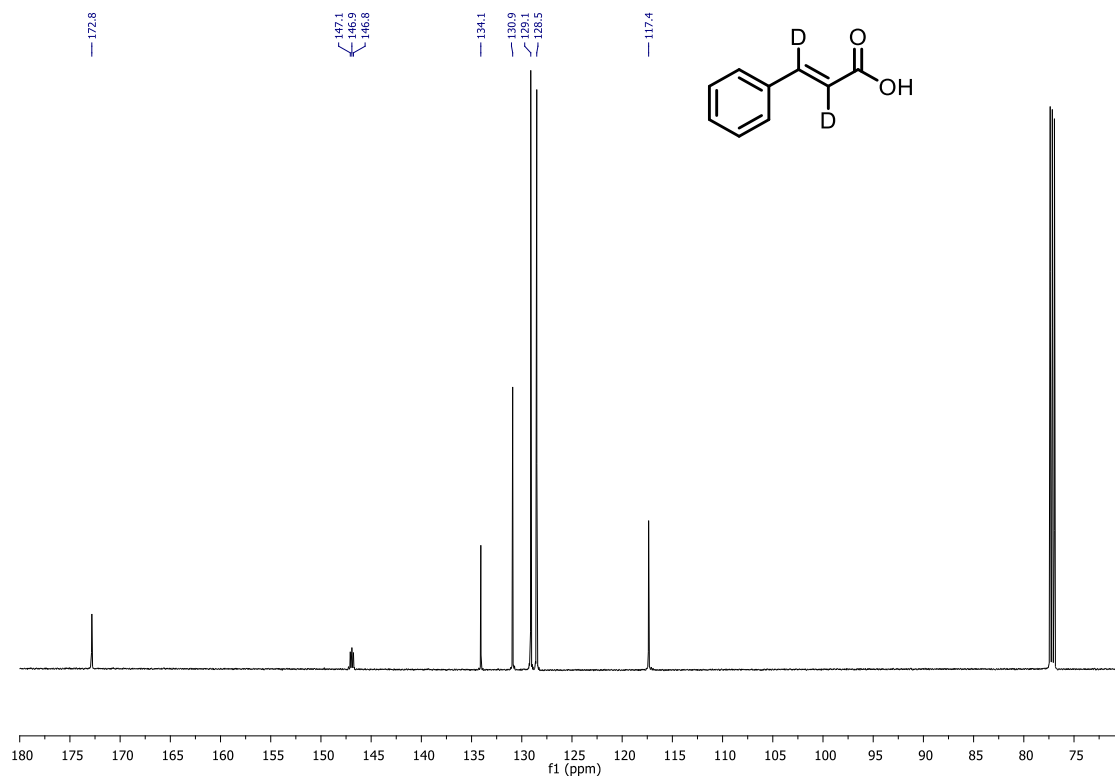
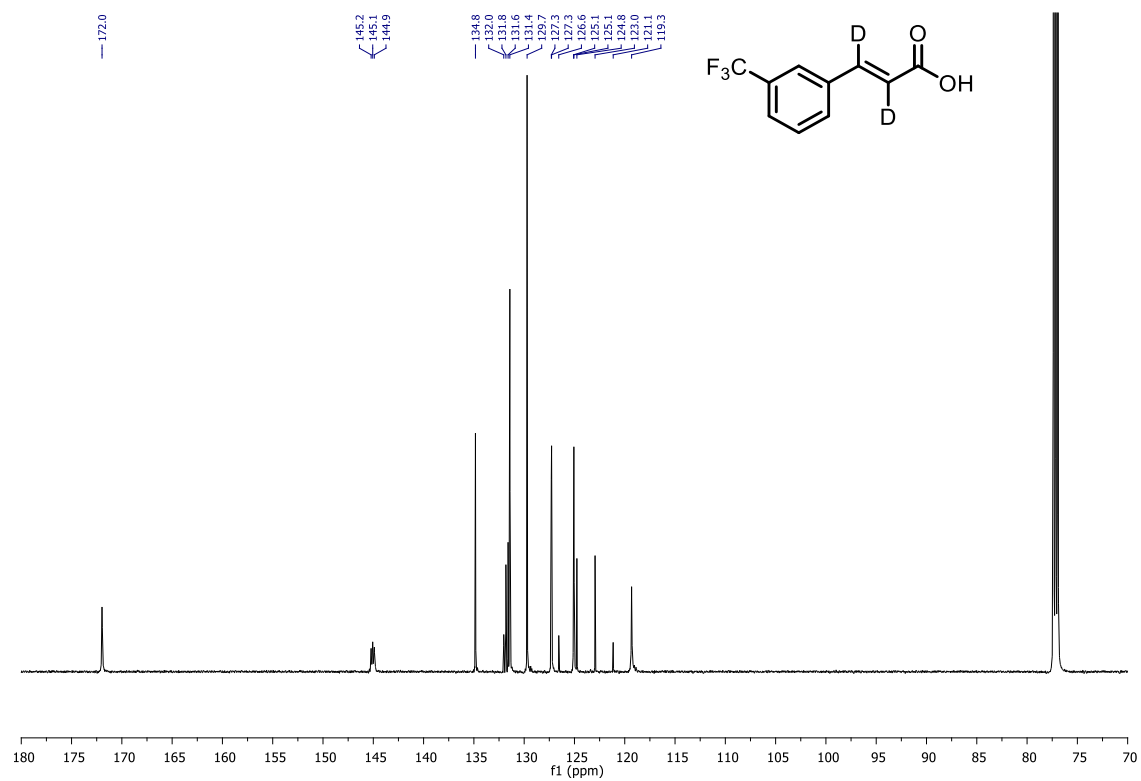
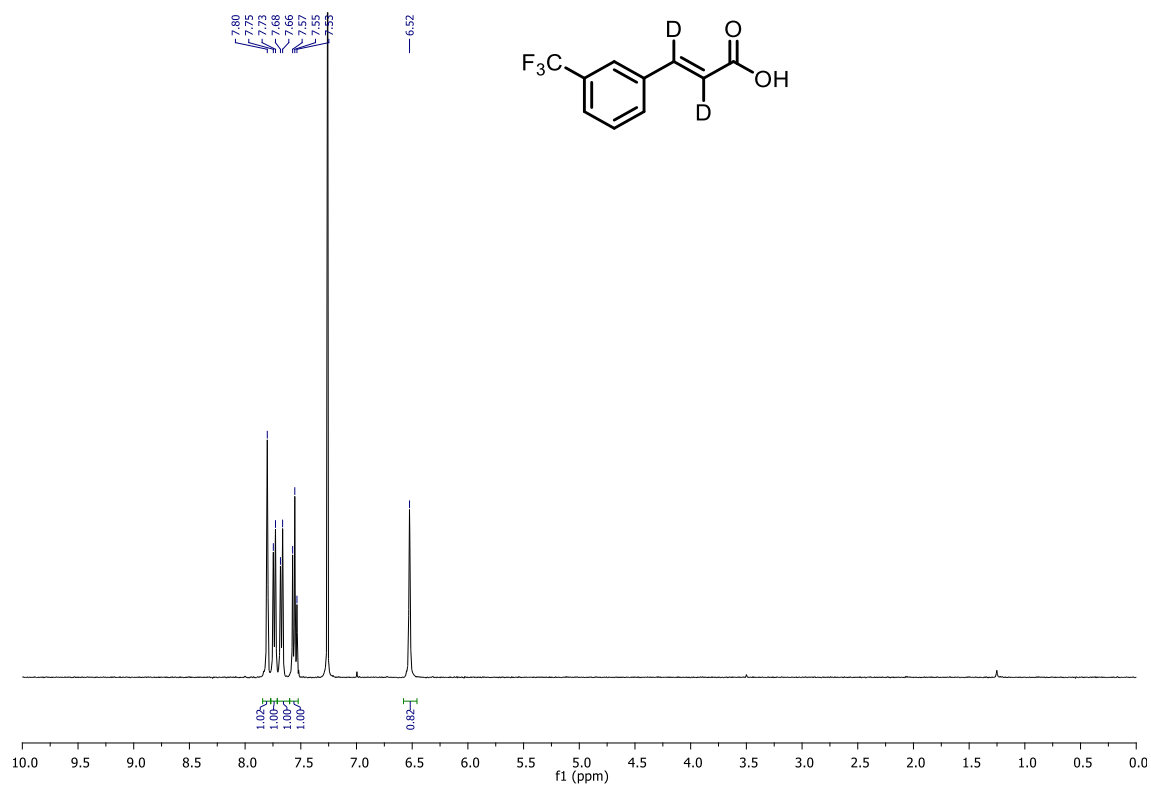


Figure S-56. ¹³C NMR spectrum of **2a** (CDCl₃, 151 MHz, 298 K)



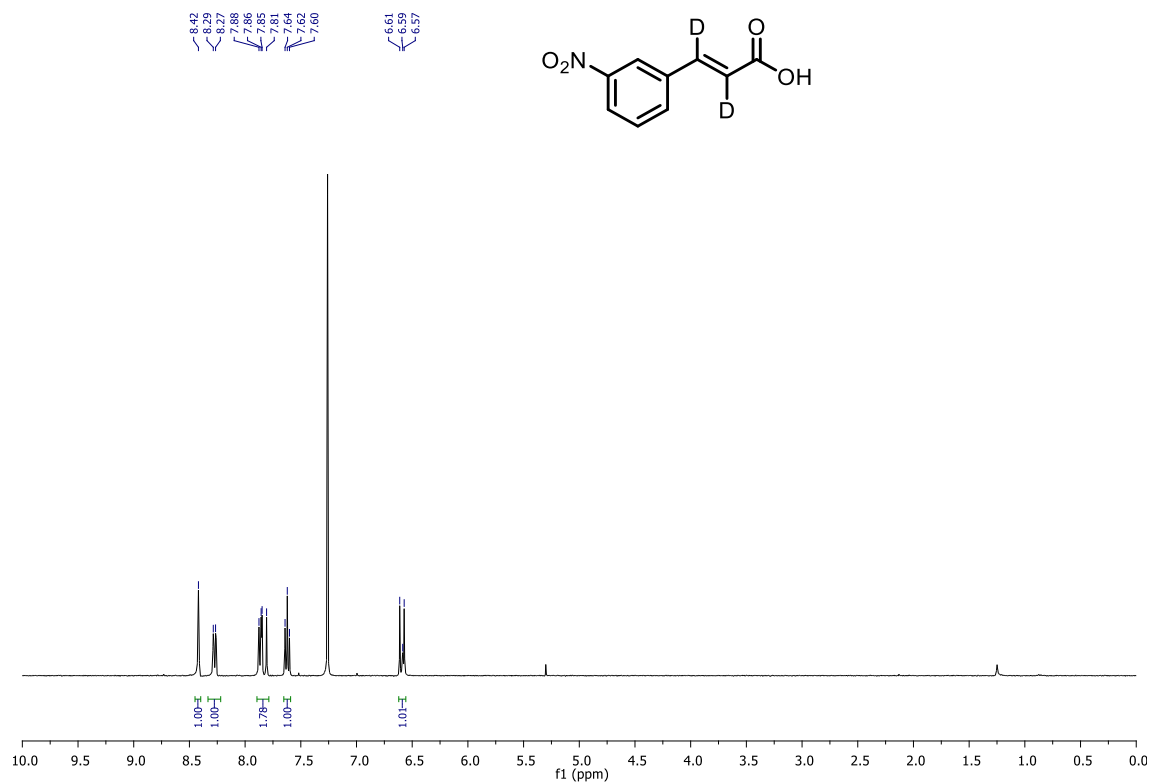


Figure S-59. ¹H NMR spectrum of 2c (CDCl₃, 400 MHz, 298 K)

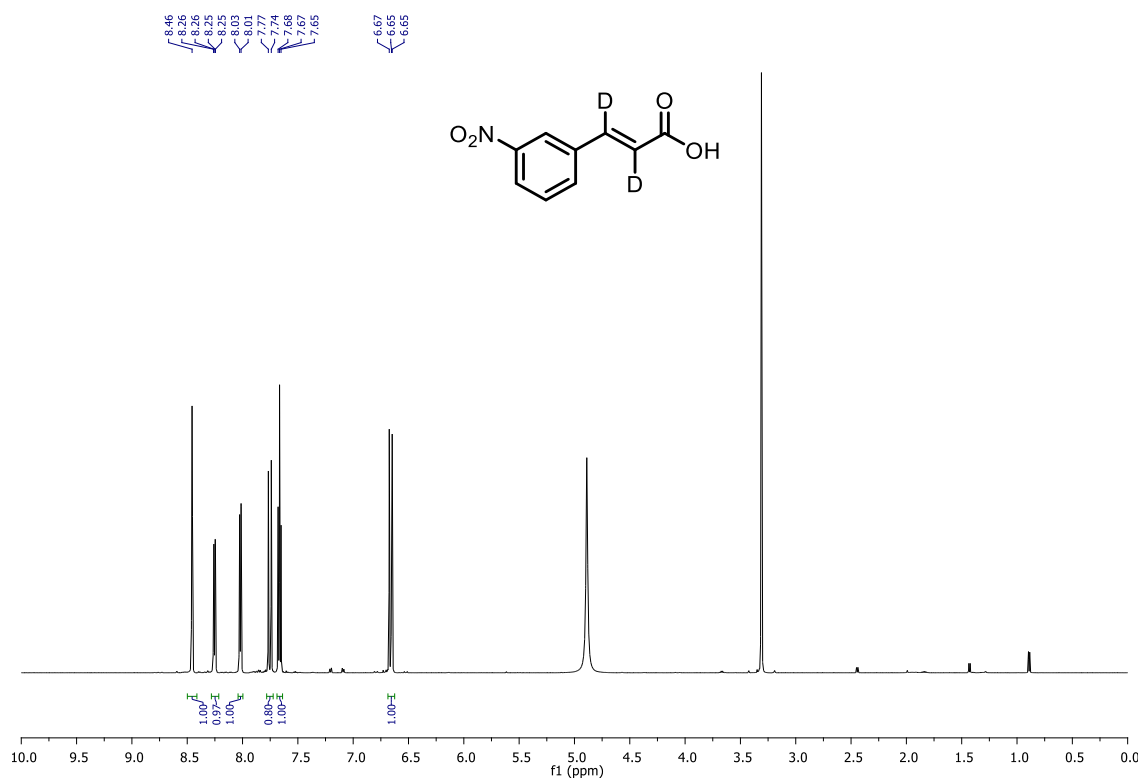


Figure S-60. ¹H NMR spectrum of 2c from 1:1 D₂O/CD₃OD reaction (CD₃OD, 600 MHz, 298 K)

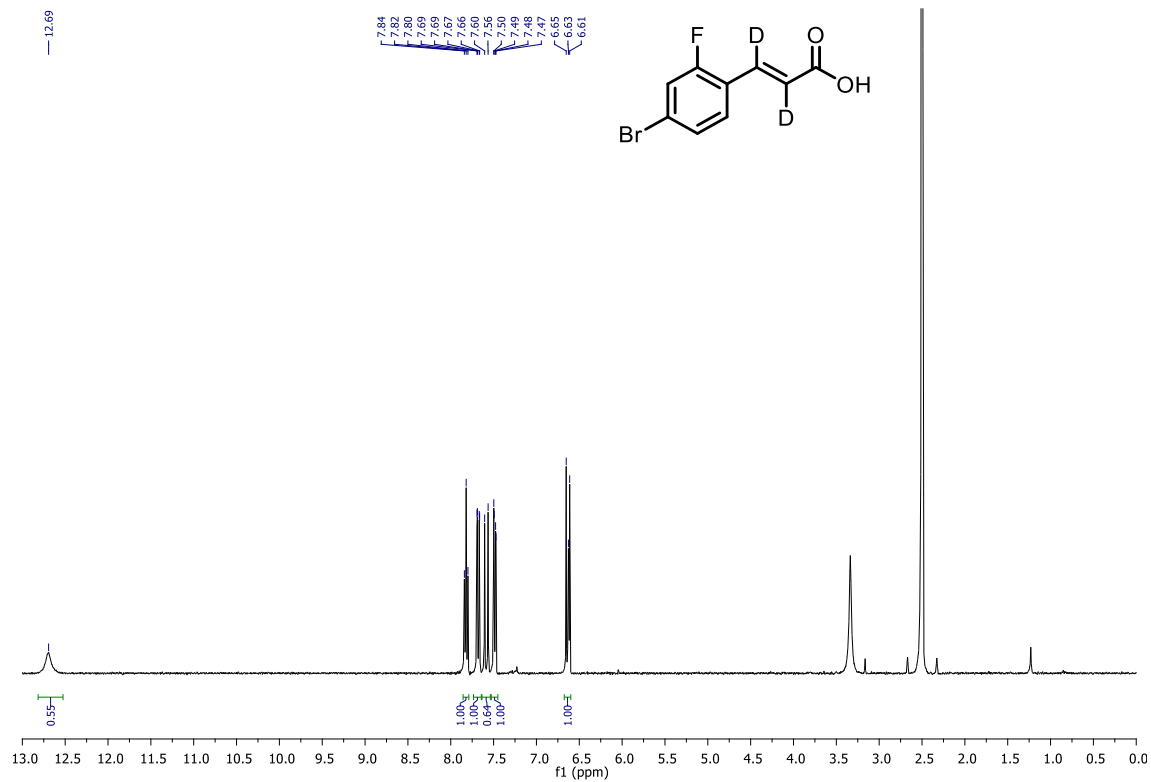


Figure S-61. ^1H NMR spectrum of **2d** (DMSO- d_6 , 400 MHz, 298 K)

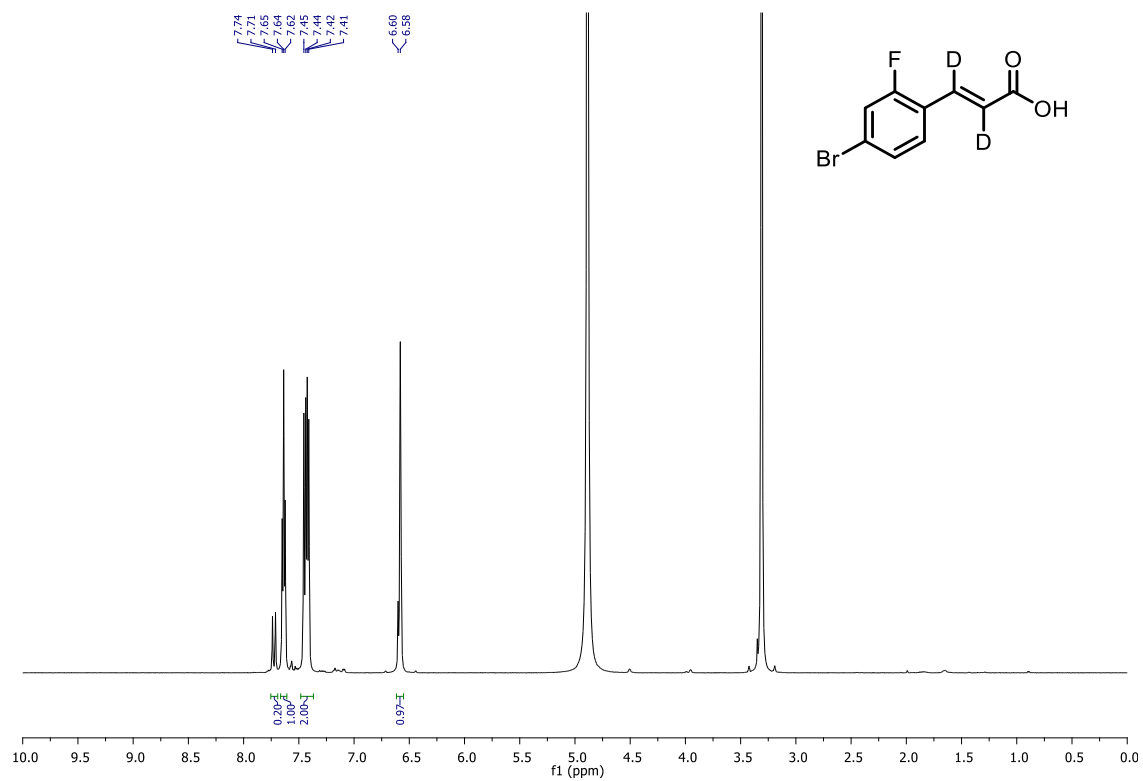


Figure S-62. ^1H NMR spectrum of **2d** from 1:1 $\text{D}_2\text{O}/\text{CD}_3\text{OD}$ reaction (CD_3OD , 600 MHz, 298 K)

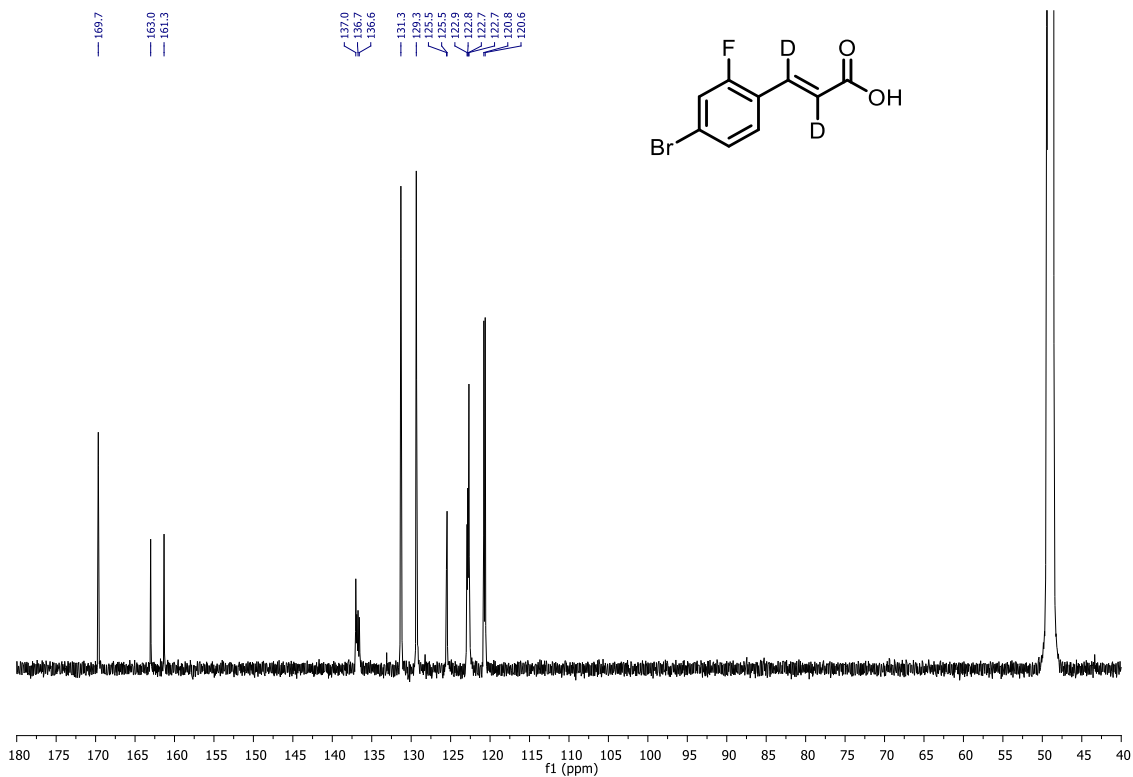


Figure S-63. ¹³C NMR spectrum of **2d** from 1:1 D₂O/CD₃OD reaction (CD₃OD, 151 MHz, 298 K)

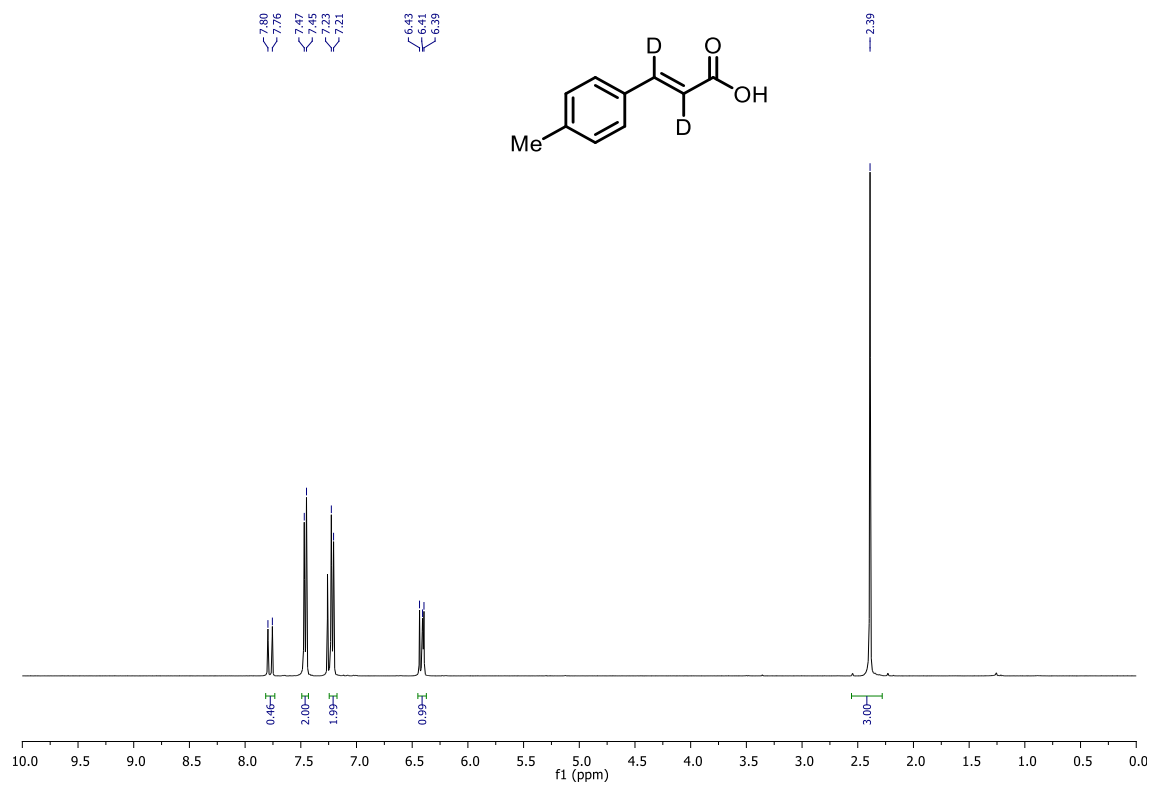


Figure S-64. ¹H NMR spectrum of **2e** (CDCl₃, 400 MHz, 298 K)

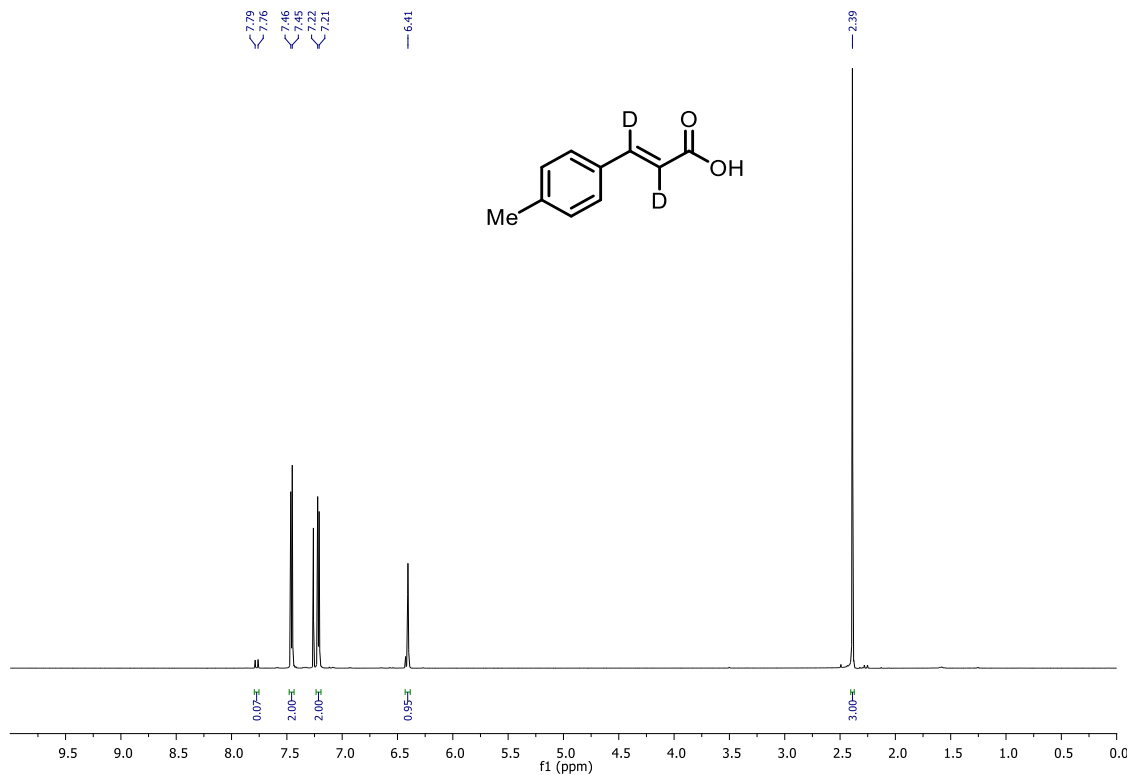


Figure S-65. ¹H NMR spectrum of **2e** from 1:1 D₂O/CD₃OD reaction (CDCl₃, 600 MHz, 298 K)

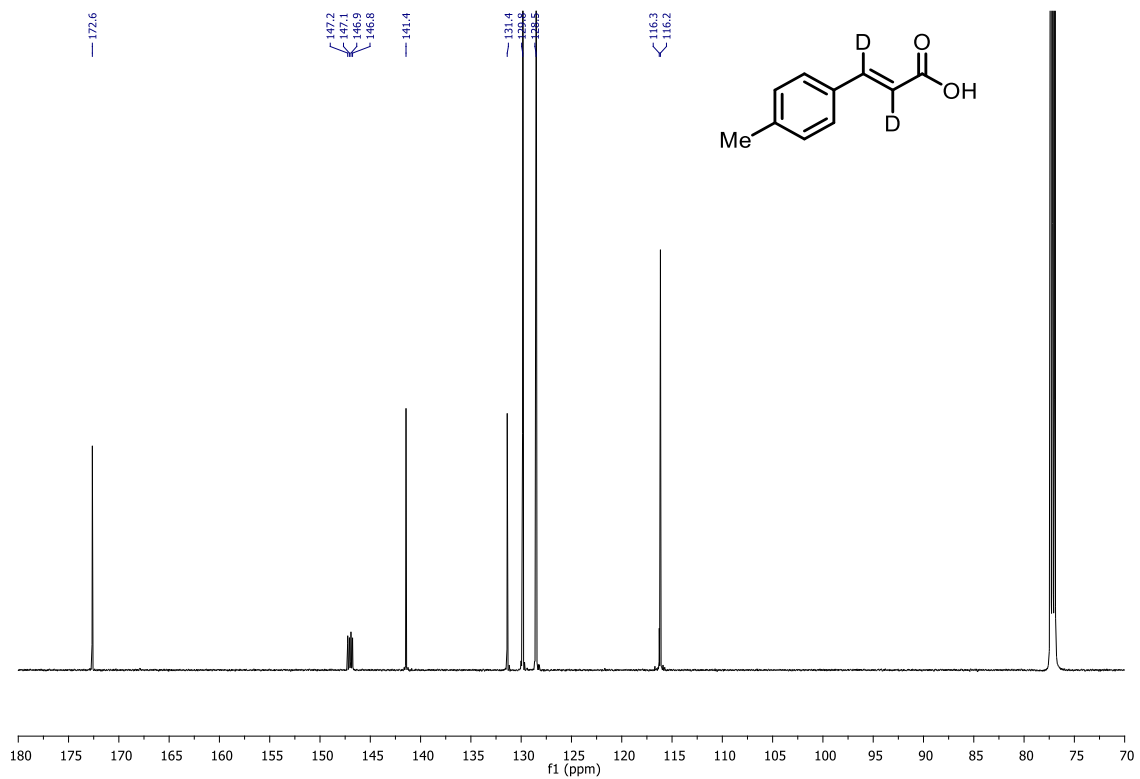


Figure S-66. ¹³C NMR spectrum of **2e** from 1:1 D₂O/CD₃OD reaction (CDCl₃, 151 MHz, 298 K)

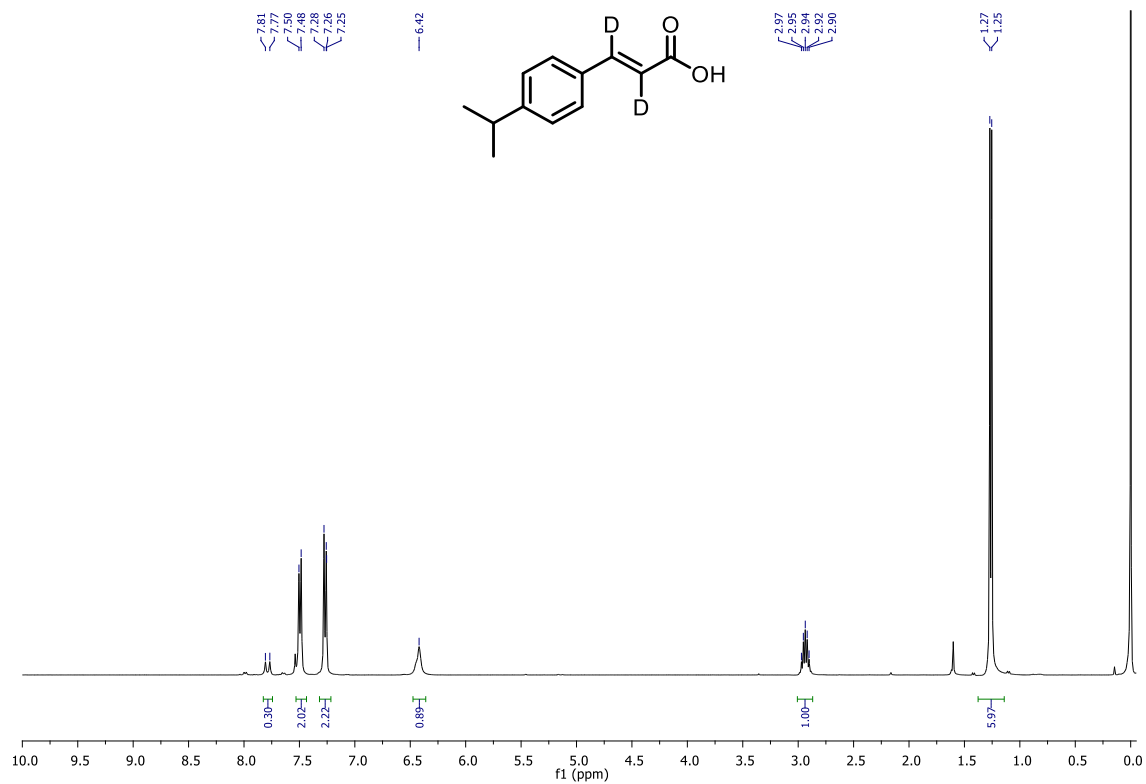


Figure S-67. ¹H NMR spectrum of **2f** from 1 mol% catalyst loading (CDCl₃ with TMS, 400 MHz, 298 K)

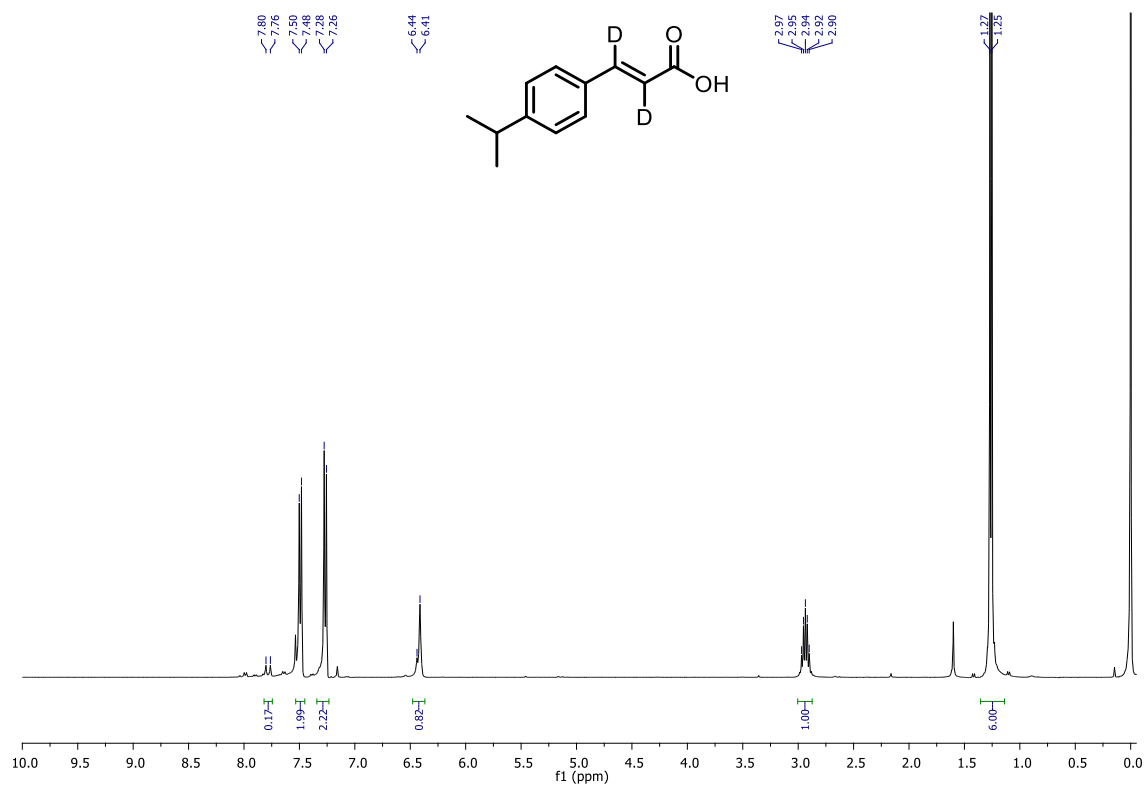


Figure S-68. ¹H NMR spectrum of **2f** from 3 mol% catalyst loading (CDCl₃ with TMS, 400 MHz, 298 K)

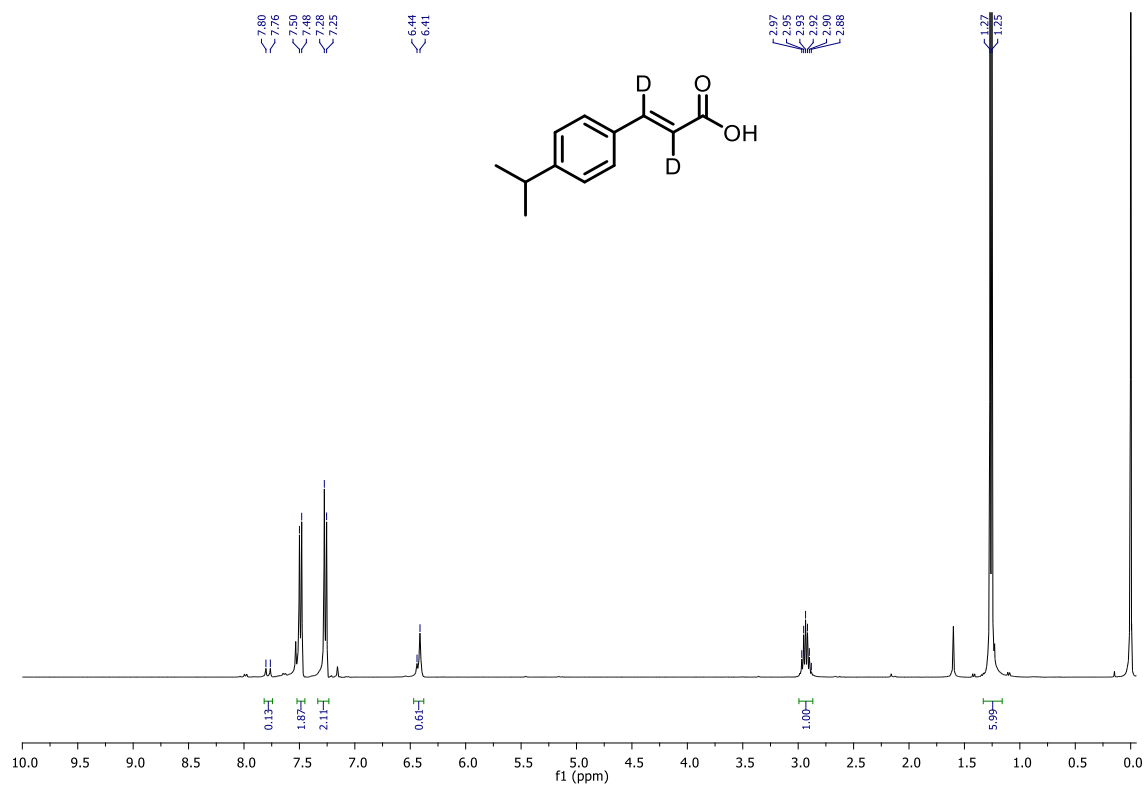


Figure S-69. ¹H NMR spectrum of **2f** from 5 mol% catalyst loading (CDCl₃ with TMS, 400 MHz, 298 K)

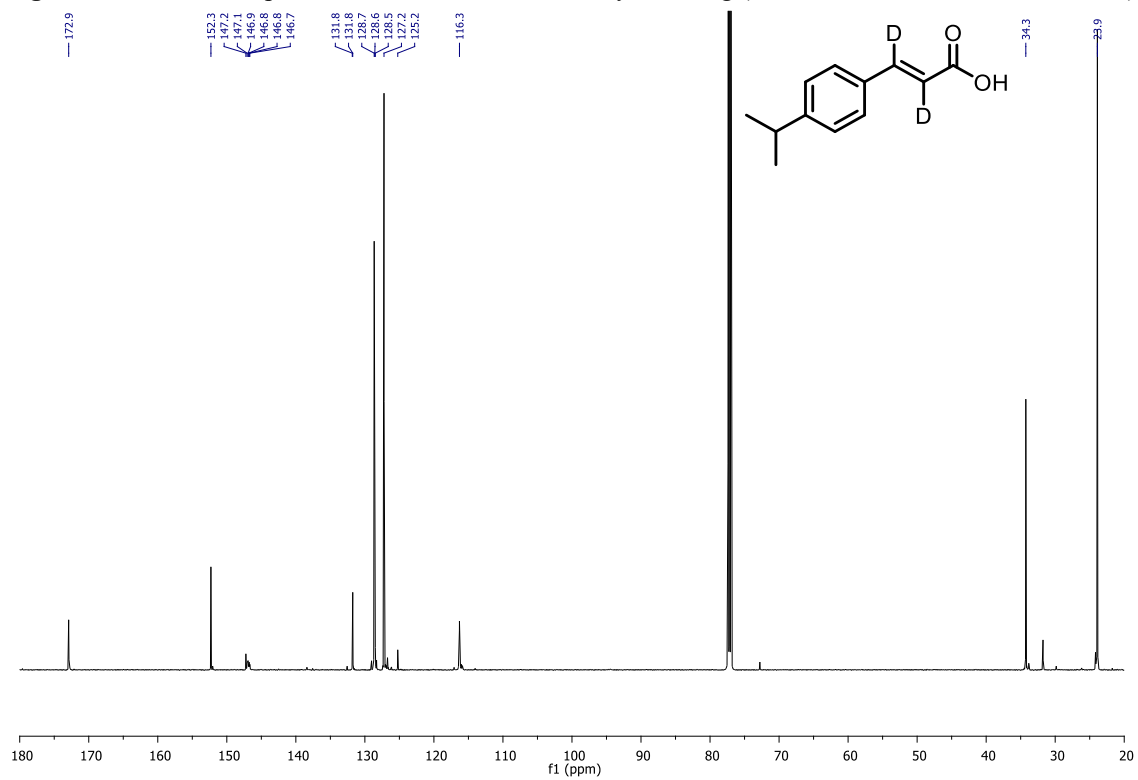


Figure S-70. ¹³C NMR spectrum of **2f** from 5 mol% catalyst loading (CDCl₃, 151 MHz, 298 K)

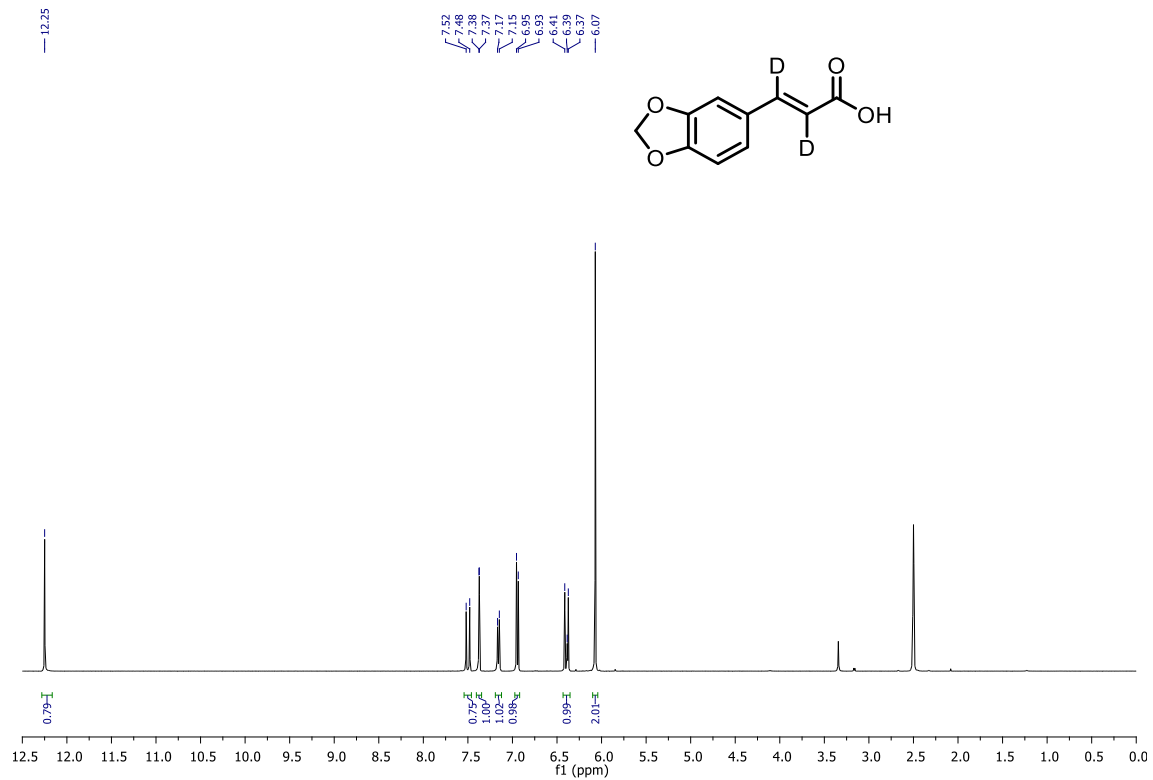


Figure S-71. ¹H NMR spectrum of **2g** (DMSO-*d*₆, 400 MHz, 298 K)

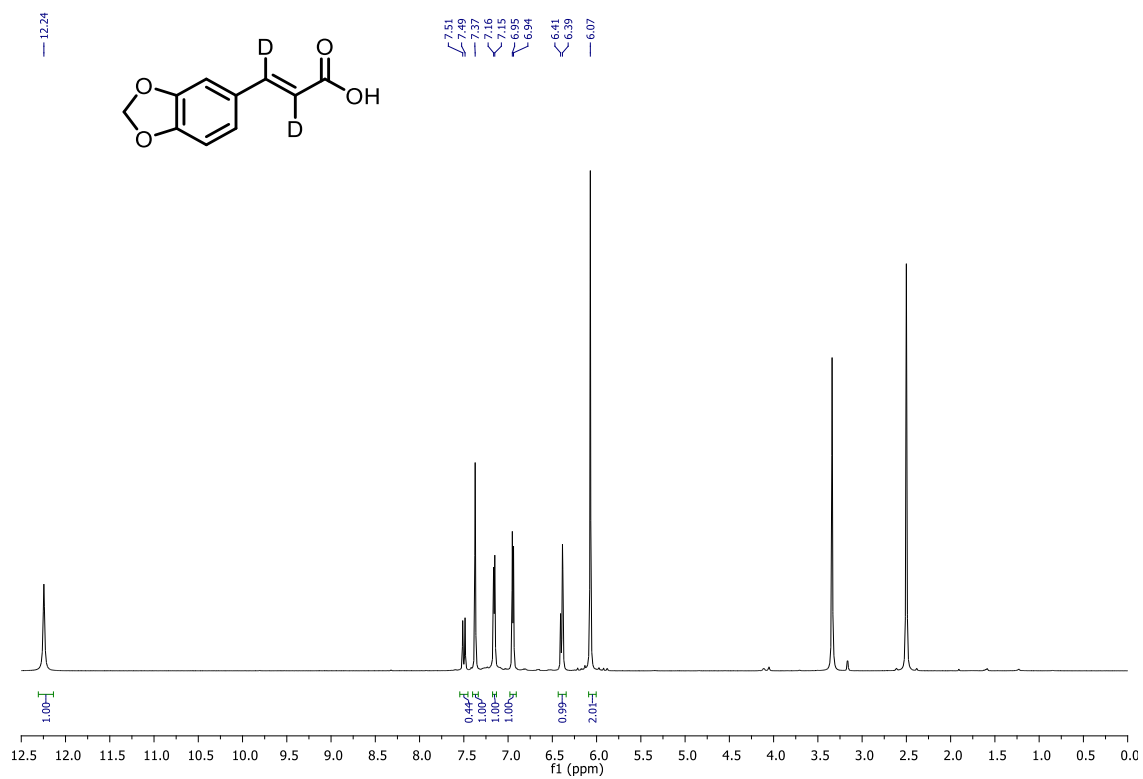


Figure S-72. ¹H NMR spectrum of **2g** from 1:1 D₂O/CD₃OD reaction (DMSO-*d*₆, 600 MHz, 298 K)

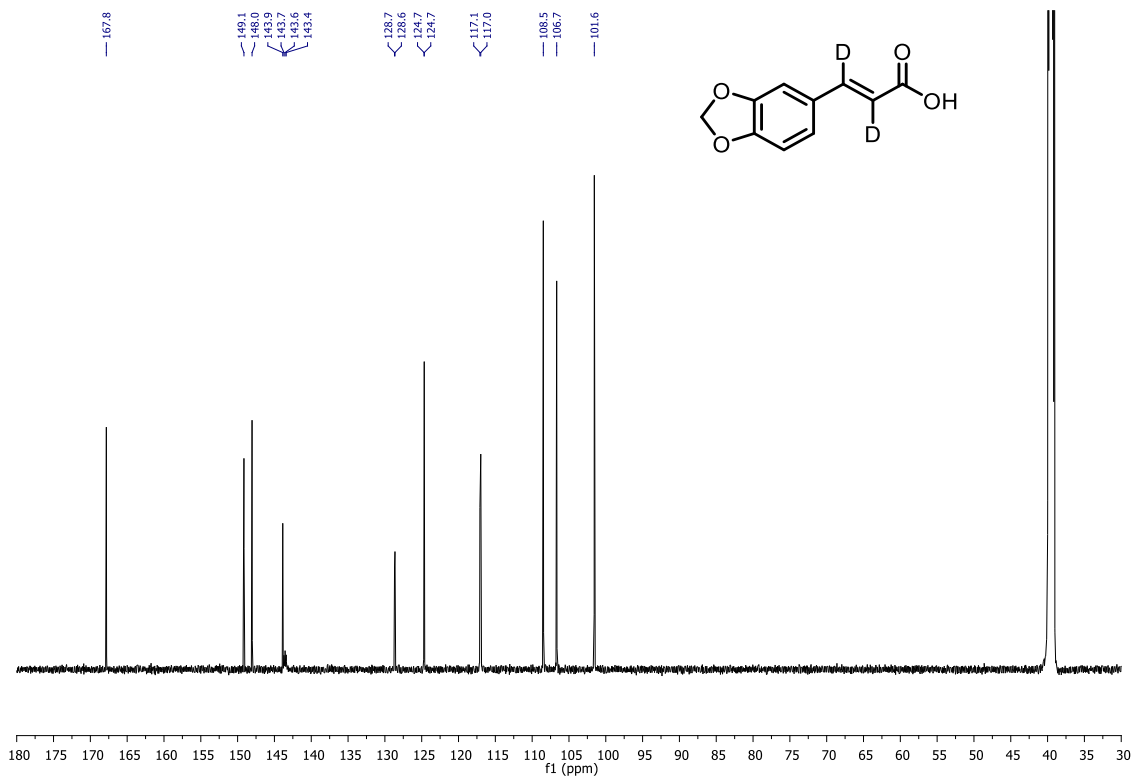


Figure S-73. ^{13}C NMR spectrum of **2g** from 1:1 $\text{D}_2\text{O}/\text{CD}_3\text{OD}$ reaction ($\text{DMSO-}d_6$, 151 MHz, 298 K)

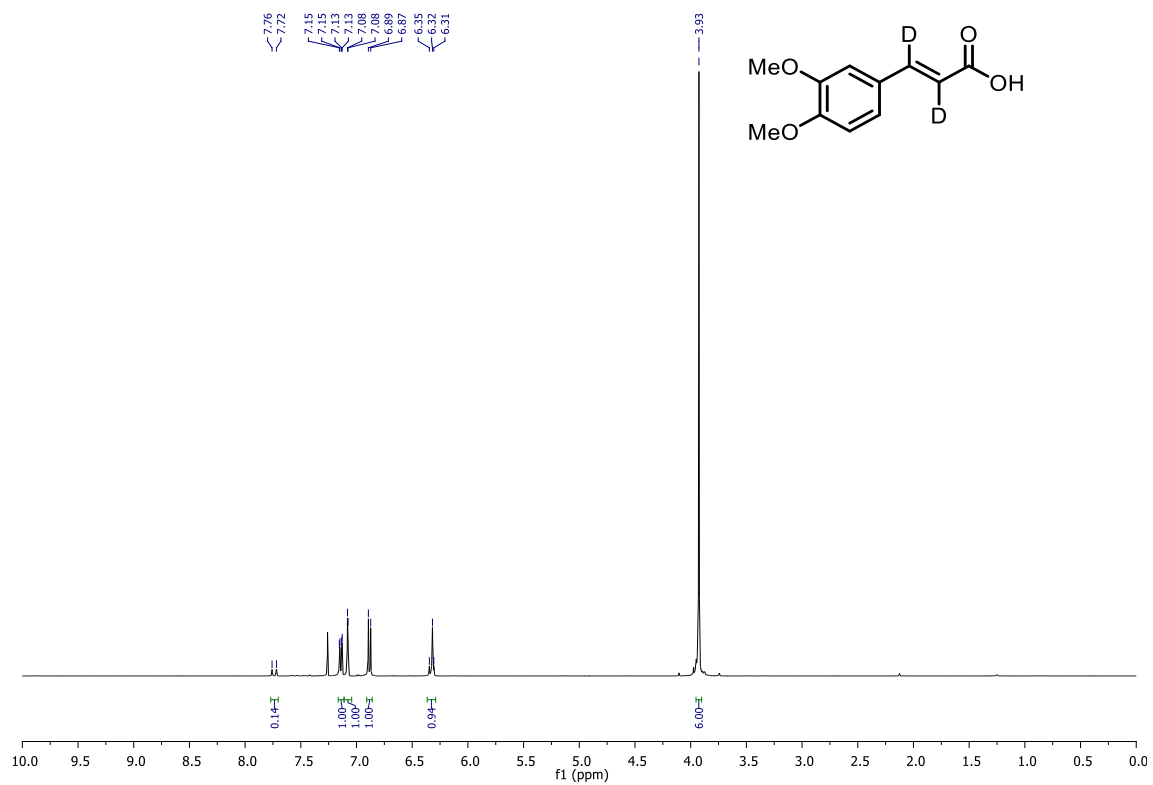


Figure S-74. ^1H NMR spectrum of **2h** (CDCl_3 , 400 MHz, 298 K)

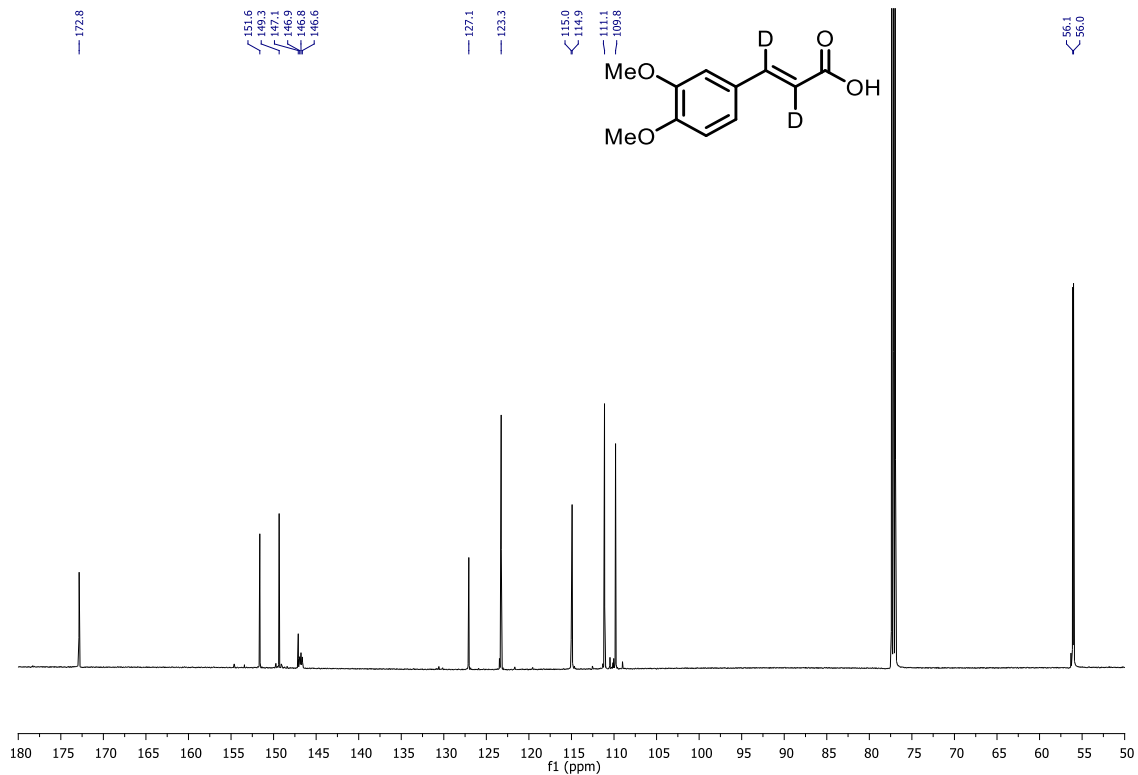


Figure S-75. ¹³C NMR spectrum of **2h** (CDCl₃, 151 MHz, 298 K)

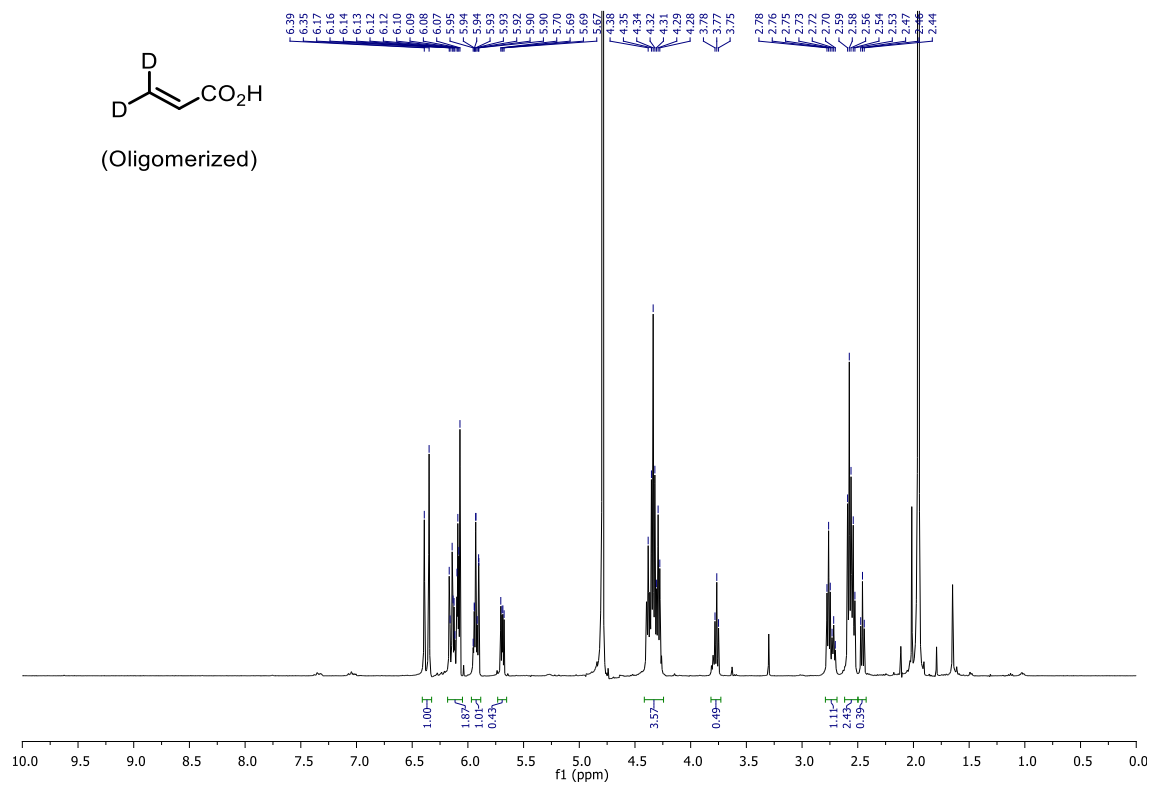


Figure S-76. ¹H NMR spectrum of **2i** (D₂O, 400 MHz, 298 K)

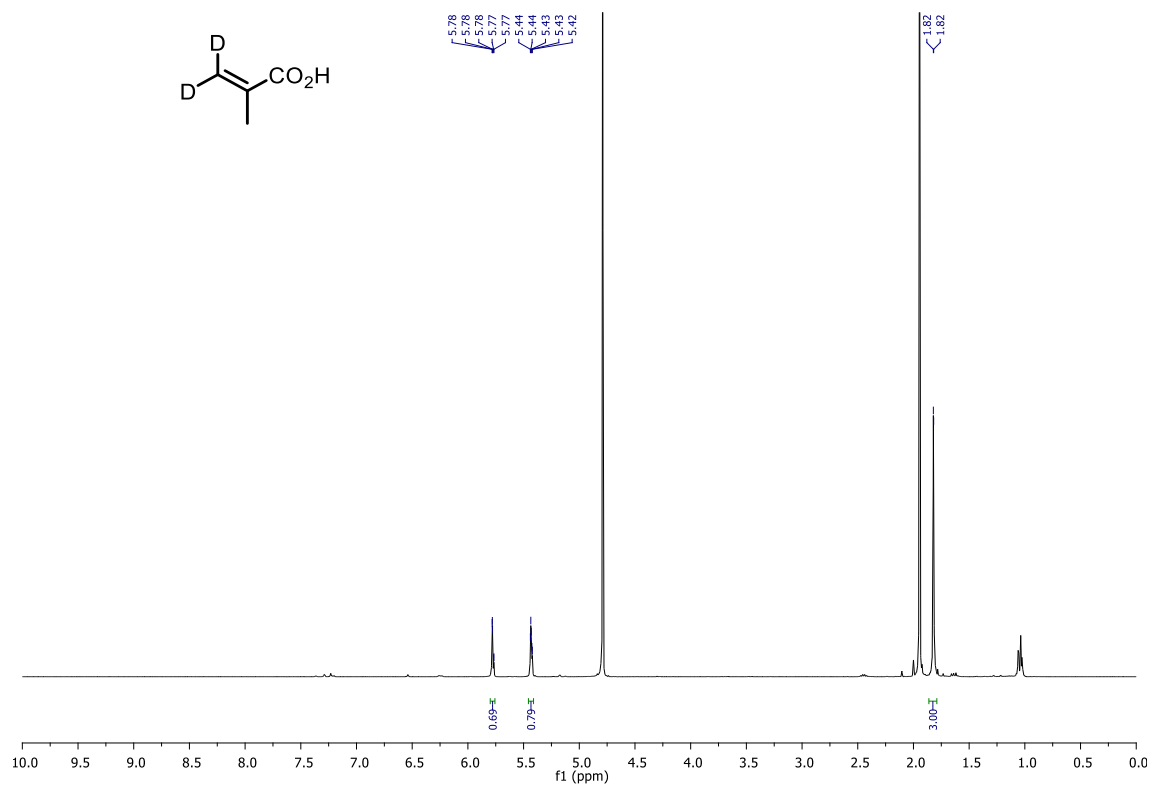


Figure S-77. ¹H NMR spectrum of 2j (D₂O, 400 MHz, 298 K)

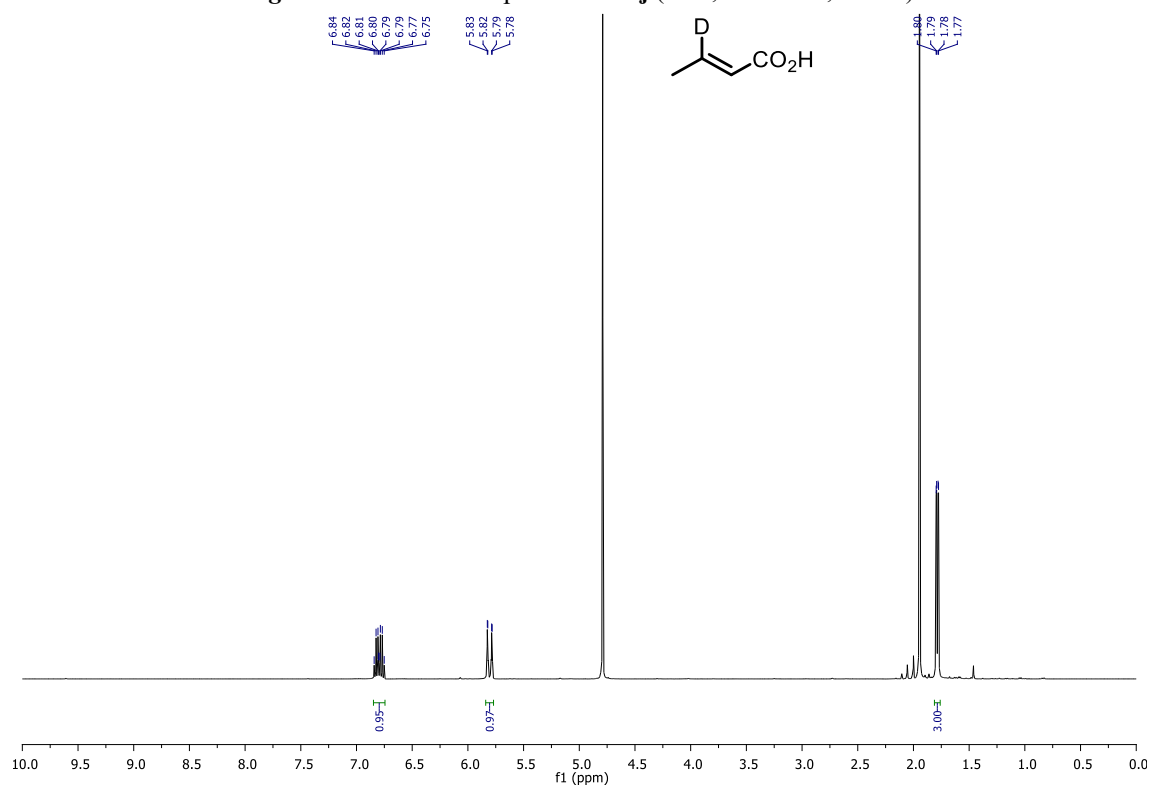


Figure S-78. ¹H NMR spectrum of 2k (D₂O, 400 MHz, 298 K)



Figure S-79. ^1H NMR spectrum of **2l** with 10 second acquisition time (CDCl_3 , 400 MHz, 298 K)

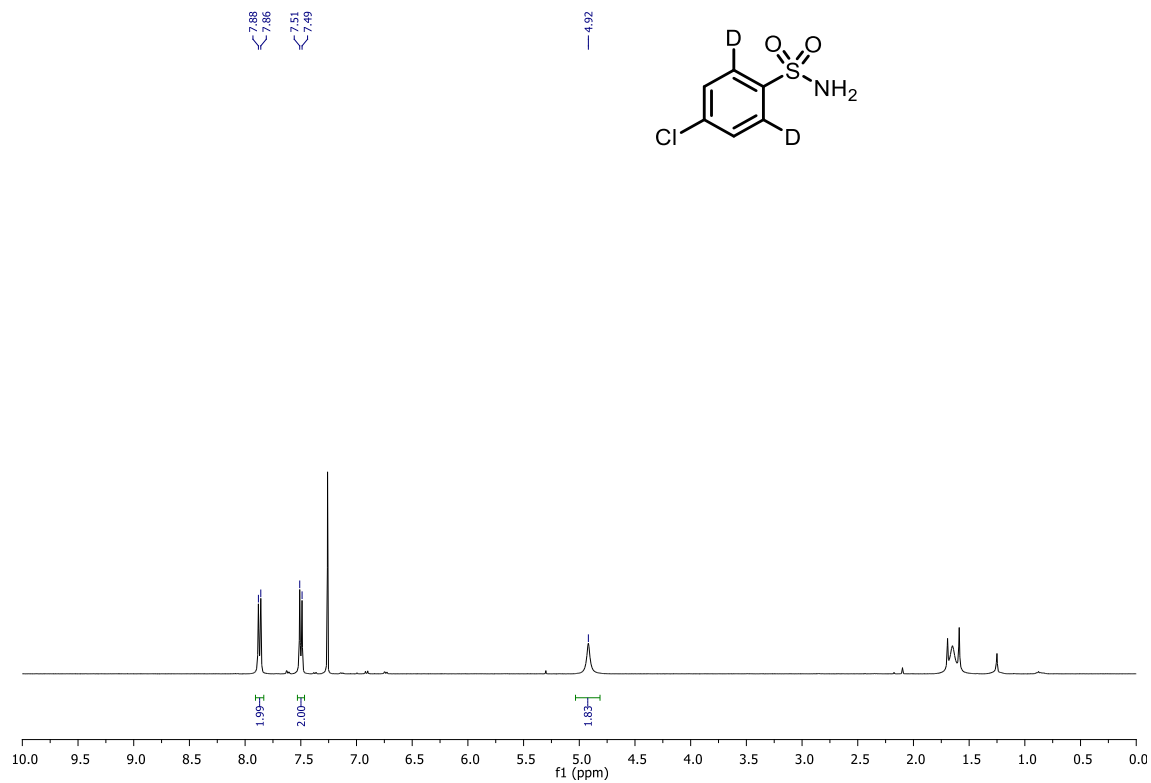


Figure S-80. ^1H NMR spectrum of **3a** (CDCl_3 , 400 MHz, 298 K)

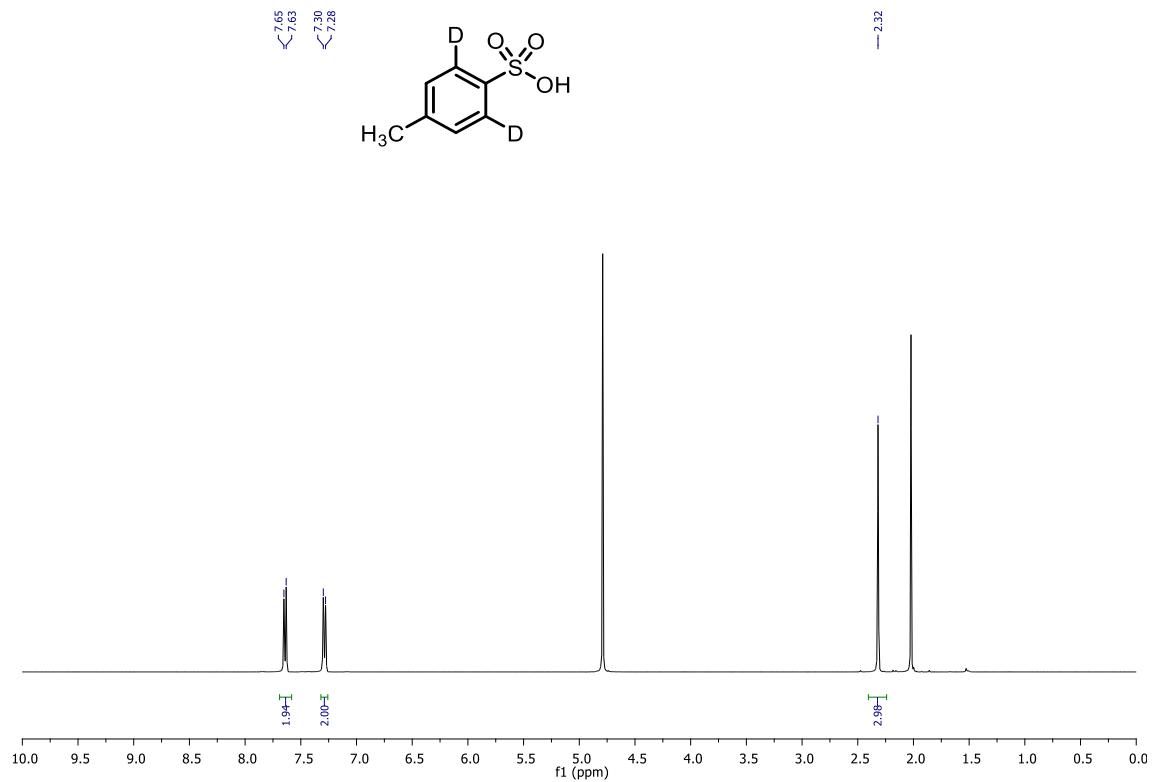


Figure S-81. ^1H NMR spectrum of **3b** (D_2O , 400 MHz, 298 K)

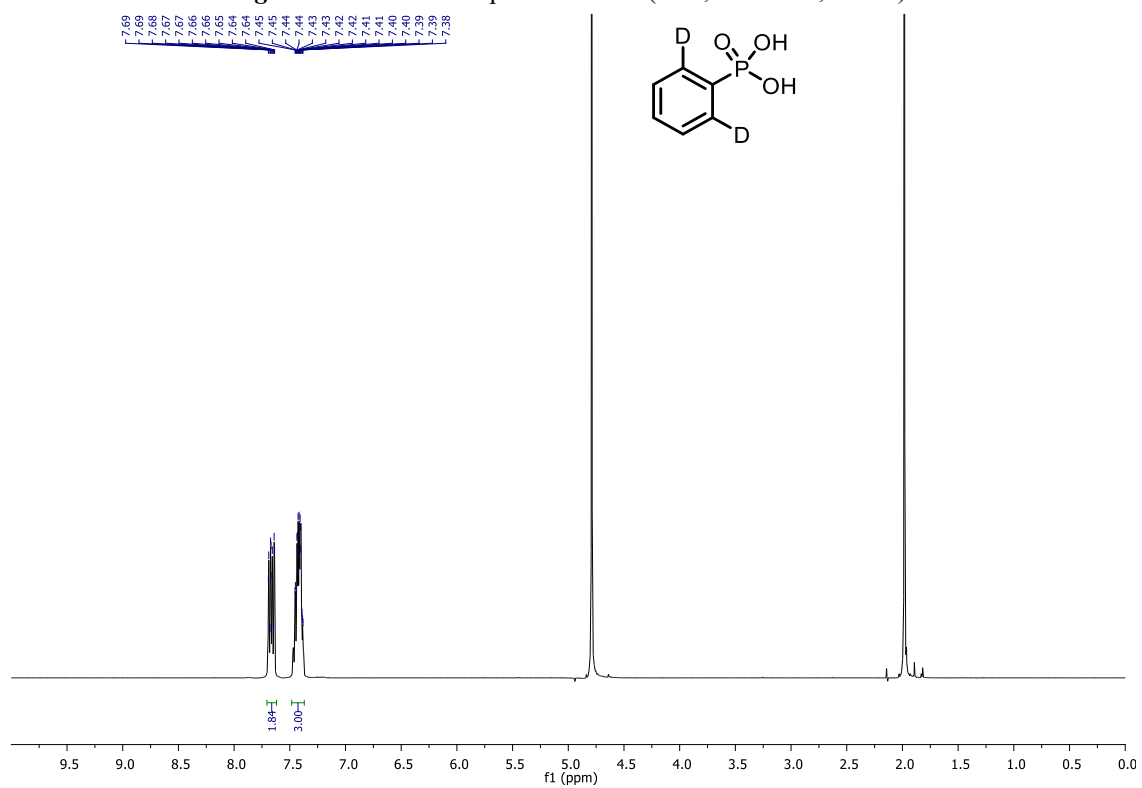


Figure S-82. ^1H NMR spectrum of **3c** (D_2O , 400 MHz, 298 K)

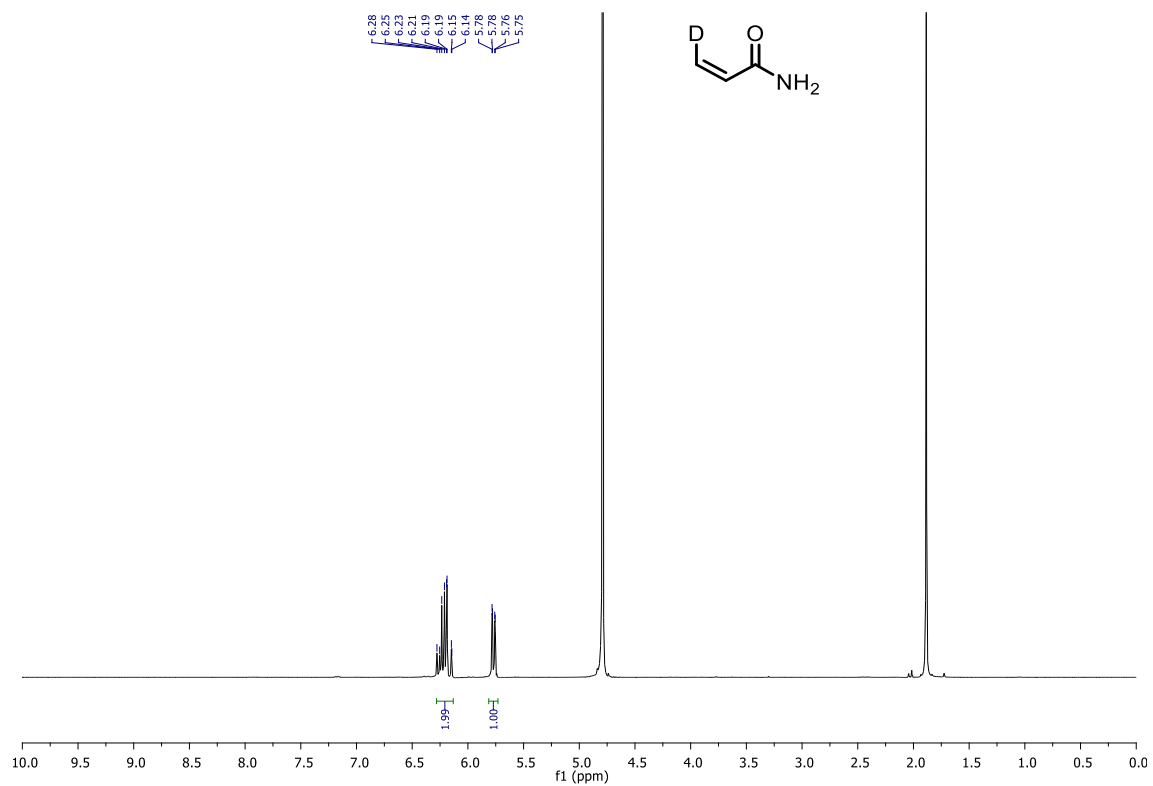


Figure S-83. ^1H NMR spectrum of 3d (D_2O , 400 MHz, 298 K)

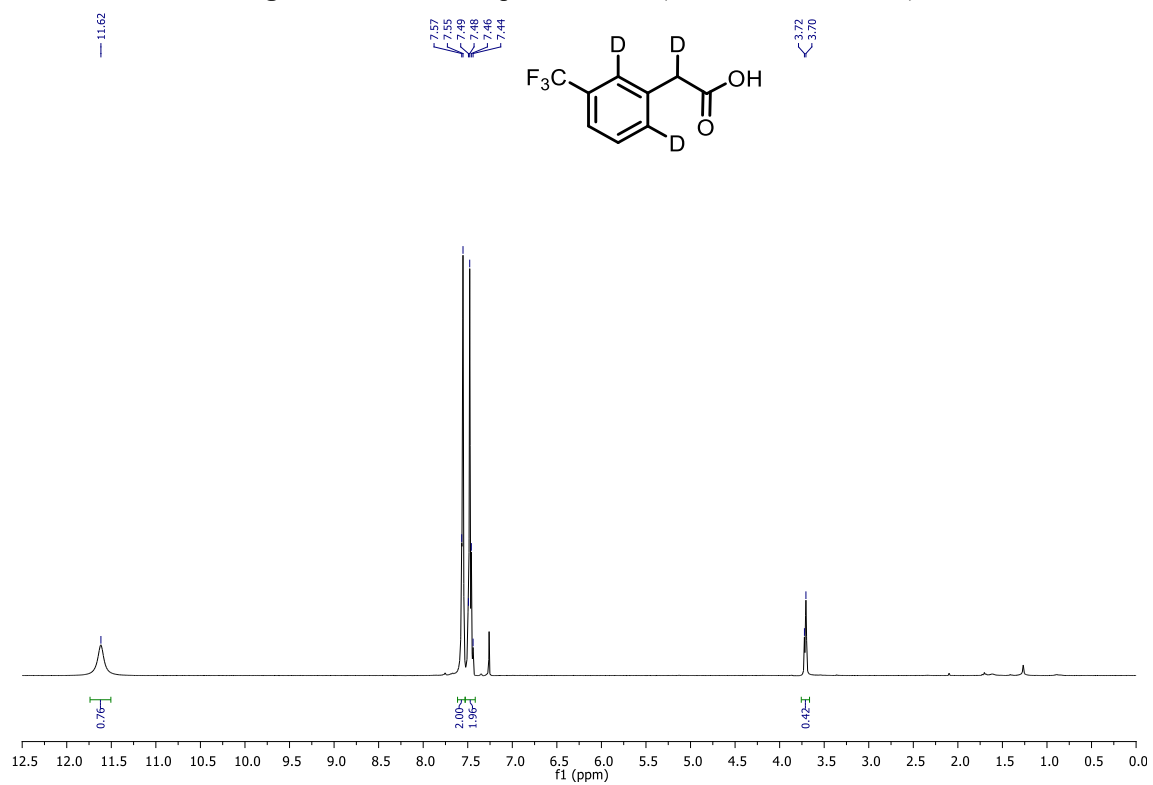


Figure S-84. ^1H NMR spectrum of 3e (CDCl_3 , 400 MHz, 298 K)

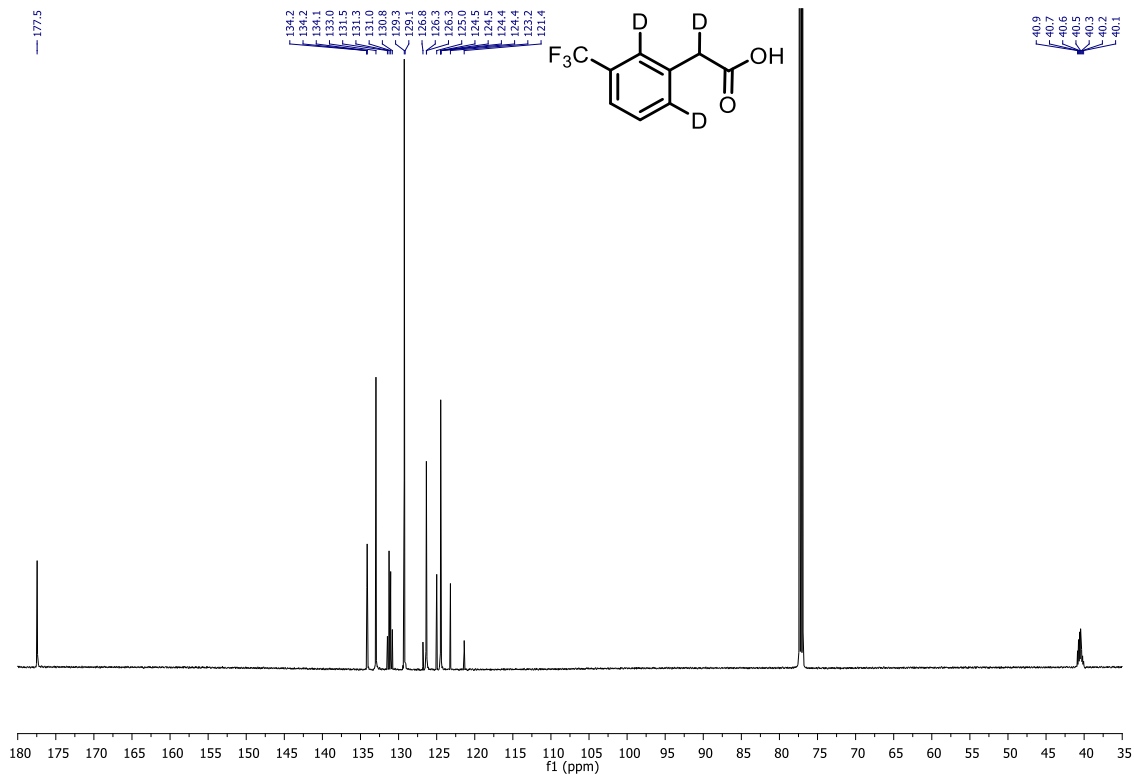


Figure S-85. ^{13}C NMR spectrum of **3e** (CDCl_3 , 151 MHz, 298 K)

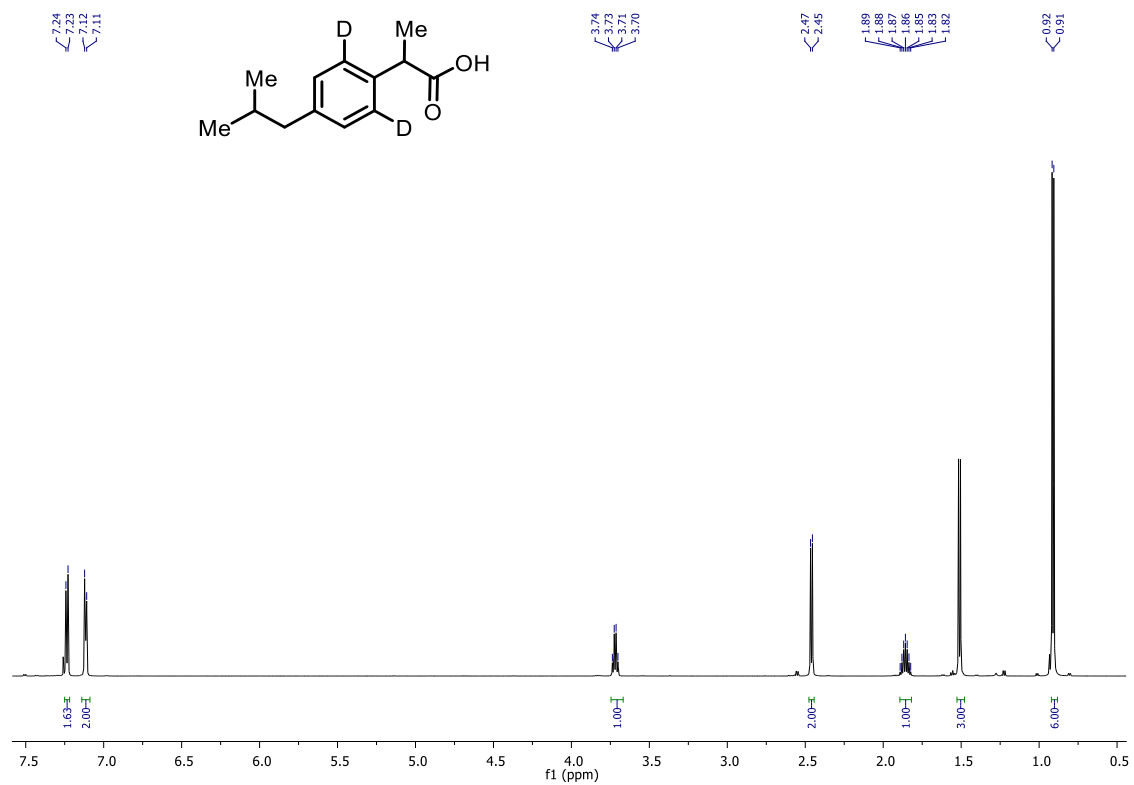


Figure S-86. ^1H NMR spectrum of **3f** with a 10 sec acquisition time (CDCl_3 , 600 MHz, 298 K)

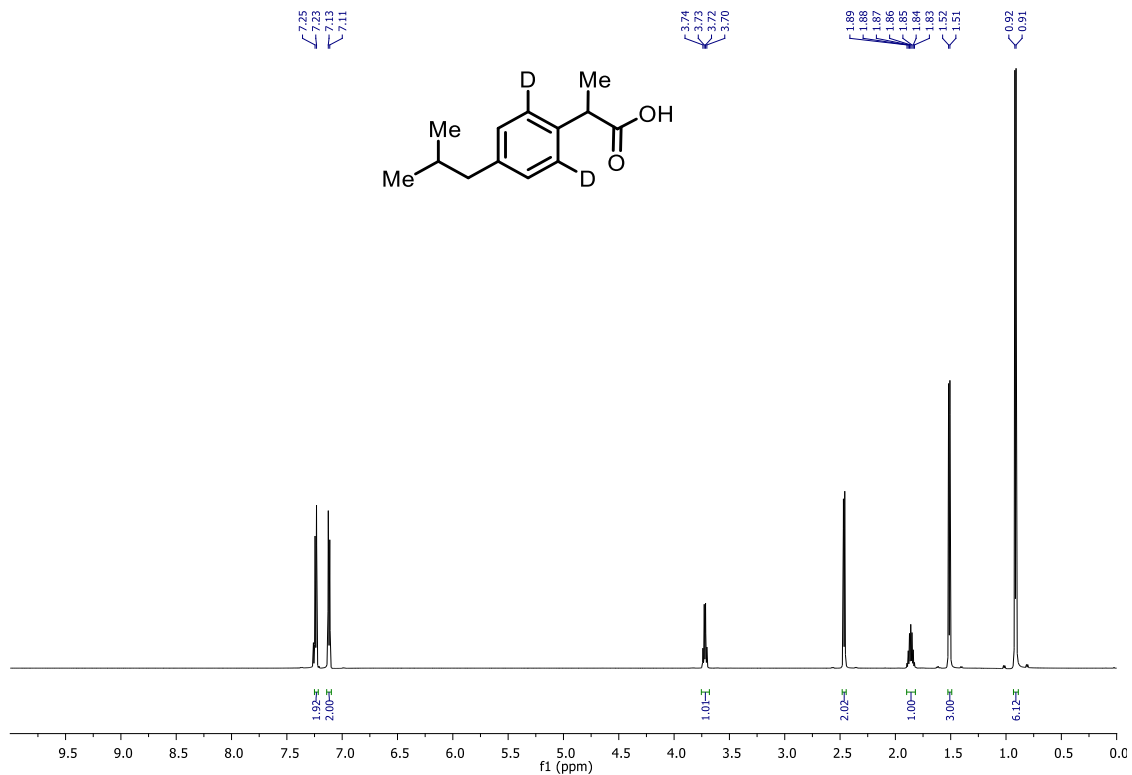


Figure S-87. ¹H NMR spectrum of **3f** from 1:1 D₂O/CD₃OD reaction (CDCl₃, 600 MHz, 298 K)

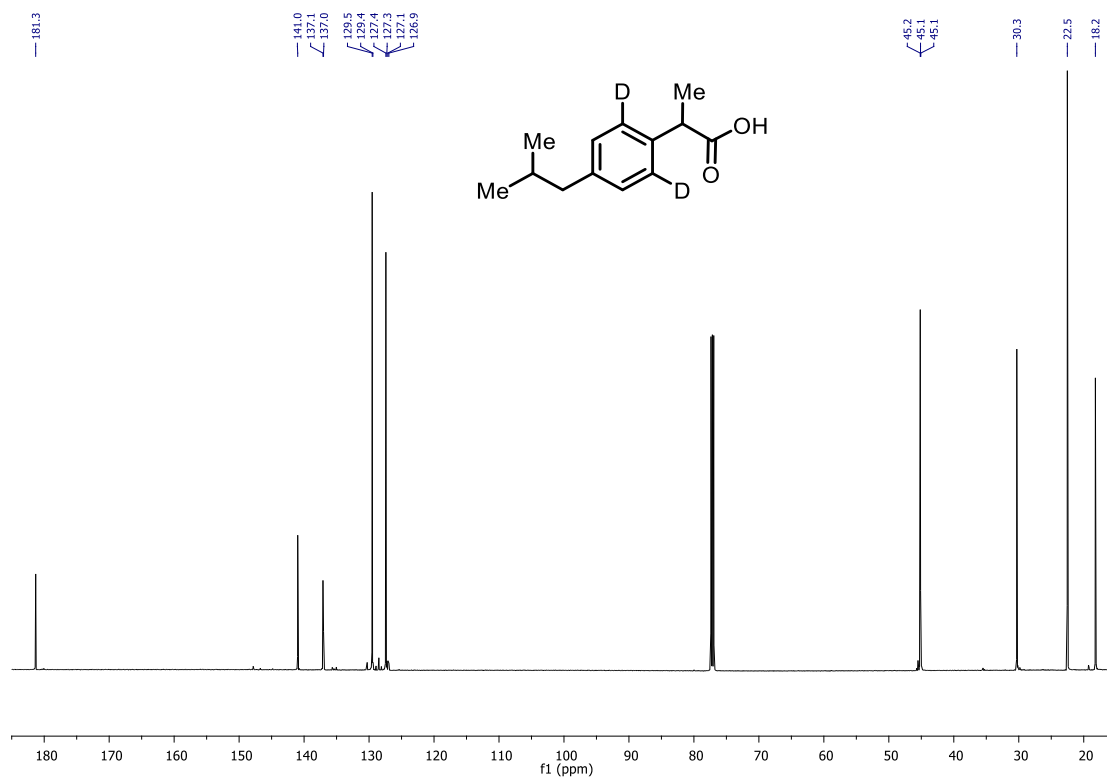


Figure S-88. ¹³C NMR spectrum of **3f** (CDCl₃, 151 MHz, 298 K)

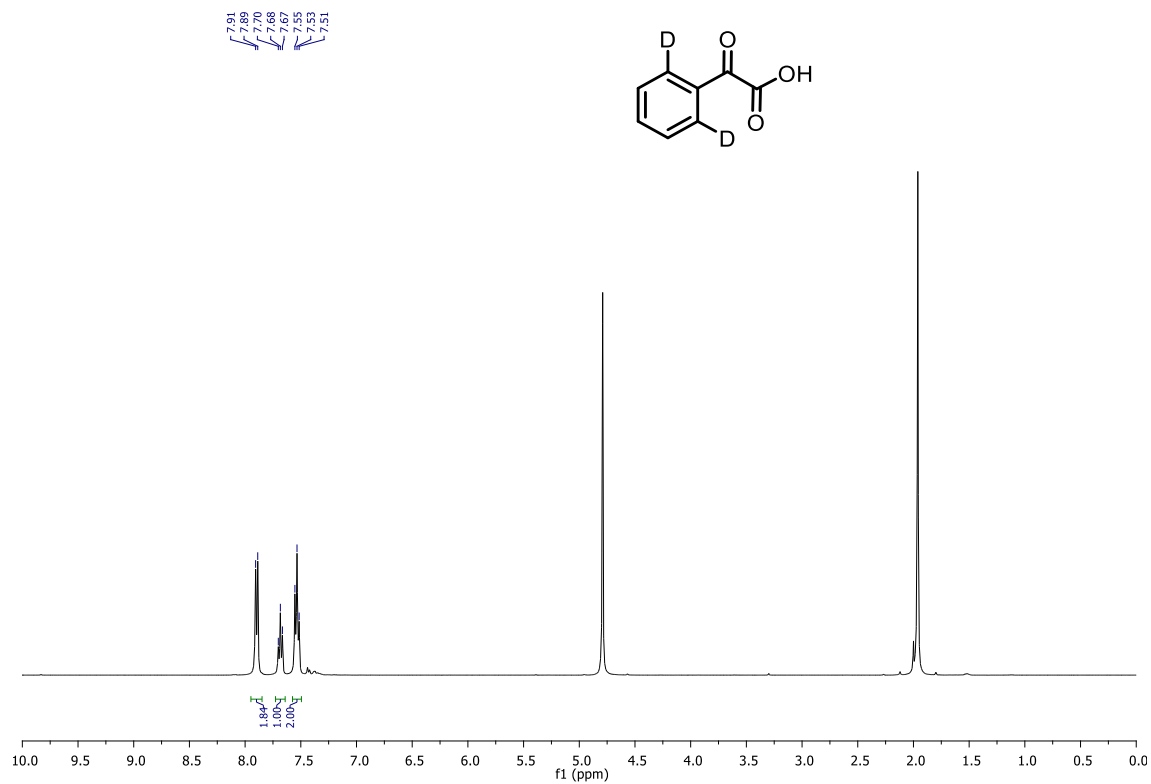


Figure S-89. ^1H NMR spectrum of **3g** (D_2O , 400 MHz, 298 K)

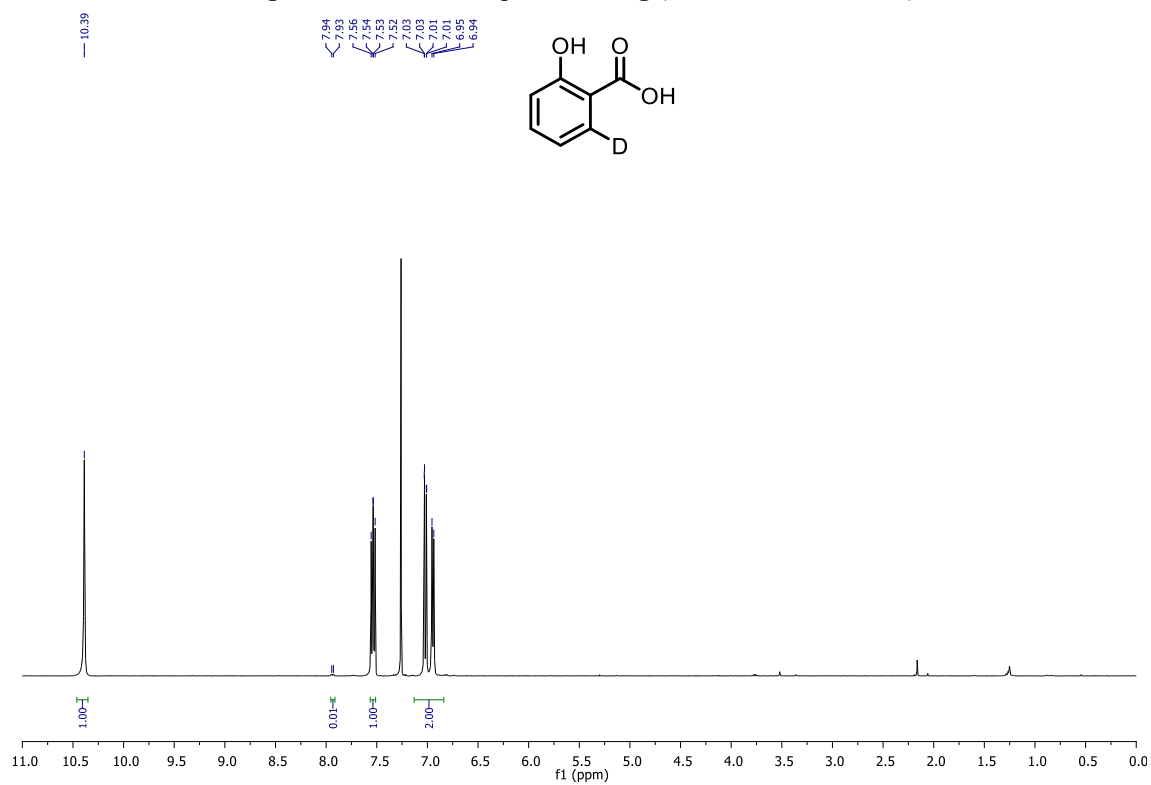


Figure S-90. ^1H NMR spectrum of **1ab** from reaction at 90 °C (CDCl_3 , 400 MHz, 298 K)

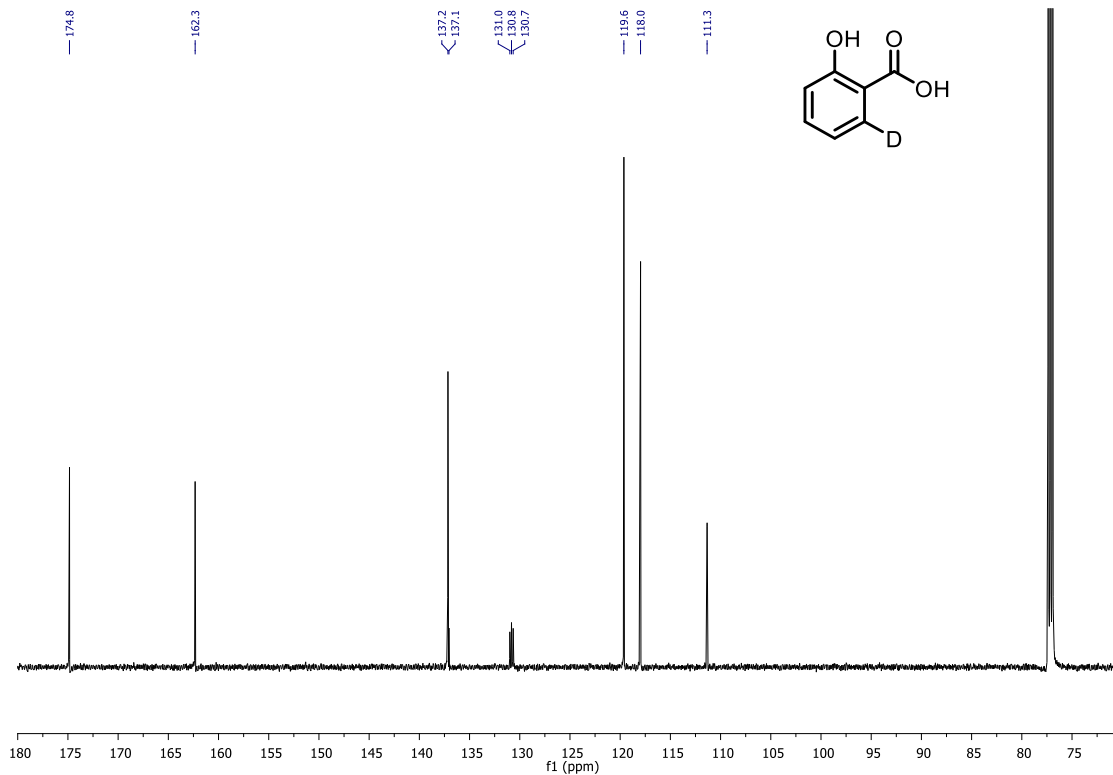


Figure S-91. ^{13}C NMR spectrum of **1ab** from reaction at 90 °C (CDCl_3 , 151 MHz, 298 K)

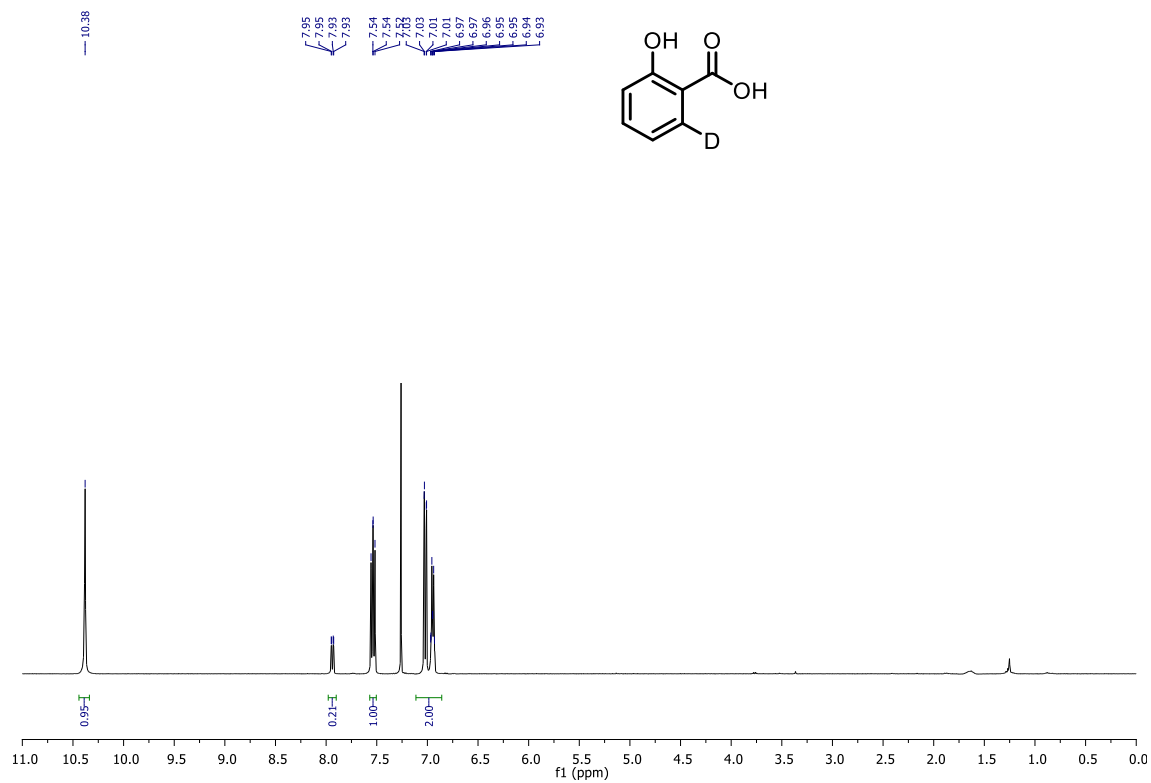


Figure S-92. ^1H NMR spectrum of **1ab** from reaction at 80 °C (CDCl_3 , 400 MHz, 298 K)

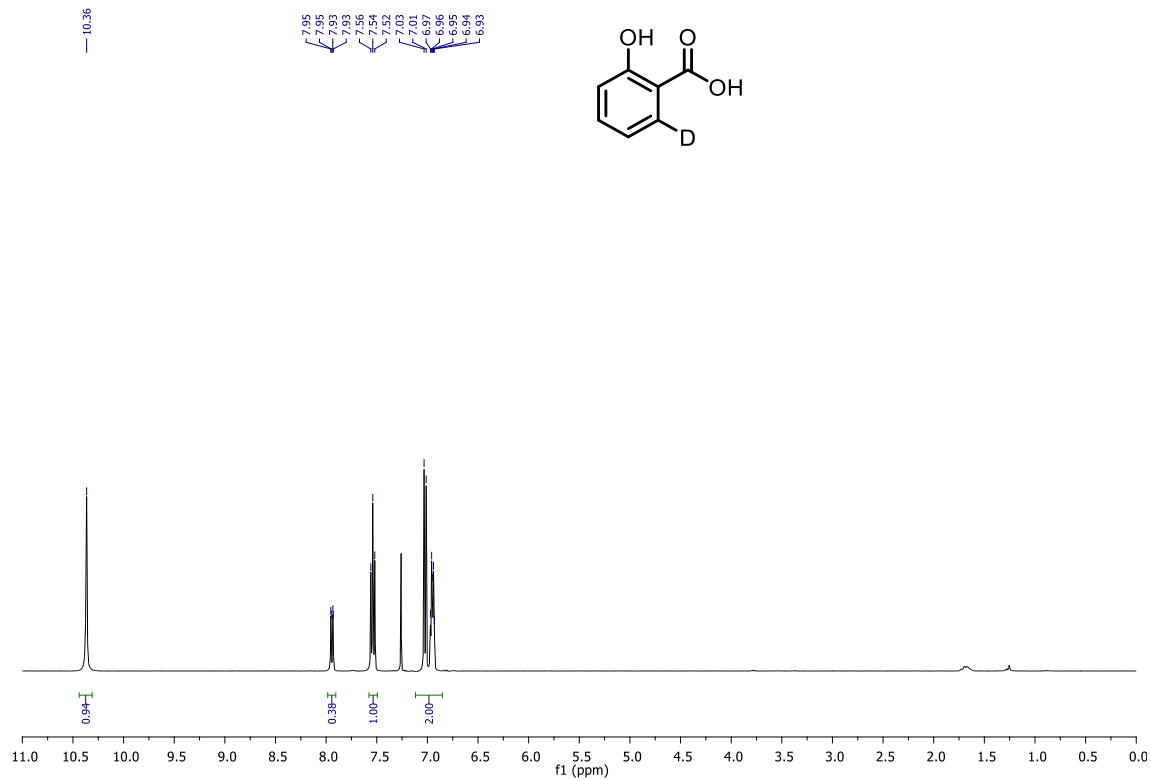


Figure S-93. ¹H NMR spectrum of **1ab** from reaction at 70 °C (CDCl₃, 400 MHz, 298 K)

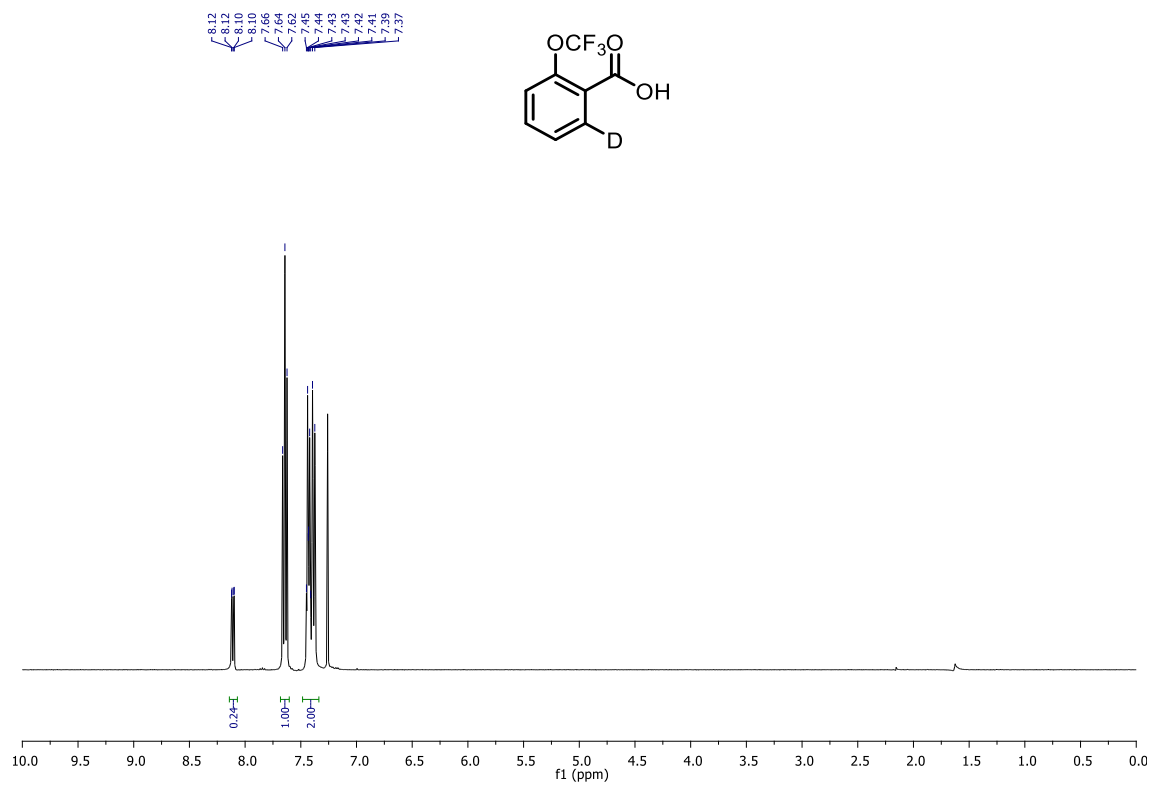


Figure S-94. ¹H NMR spectrum of **1s** from reaction at 50x scale (CDCl₃, 400 MHz, 298 K)

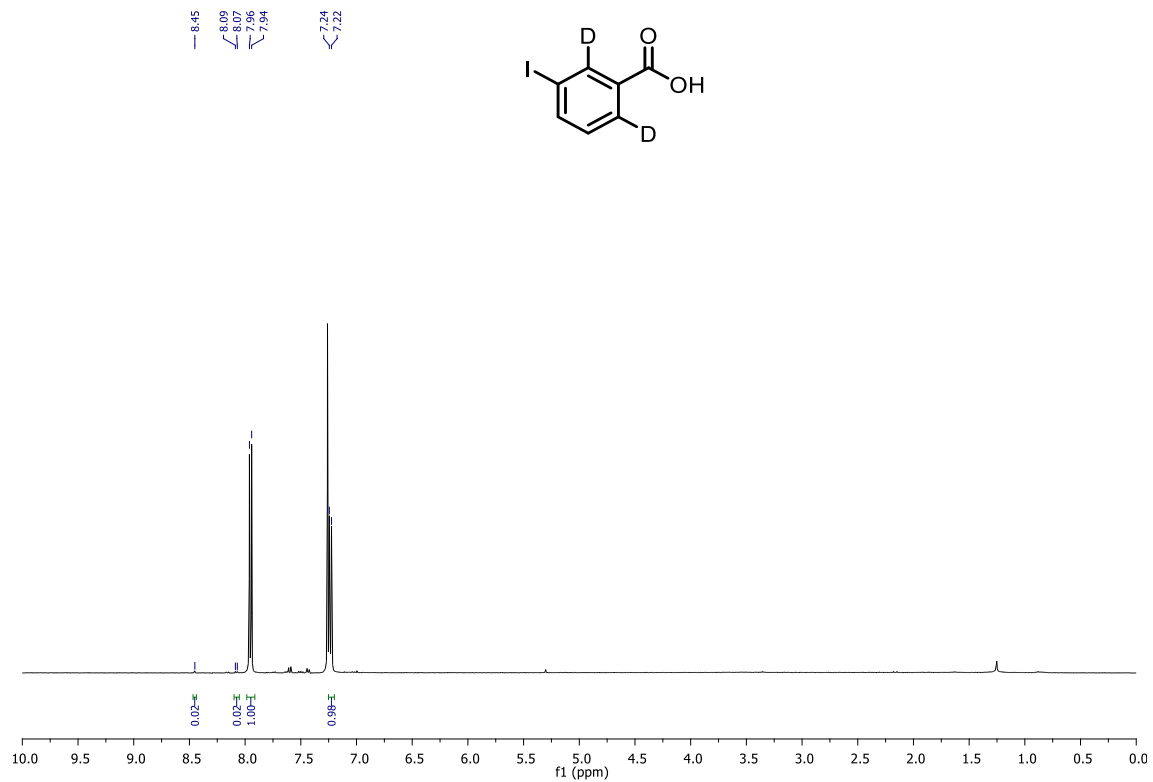


Figure S-95. ^1H NMR spectrum of **1h** from reaction at 10x scale (CDCl_3 , 400 MHz, 298 K)

8. Select ^2H Spectra of Deuterated Compounds

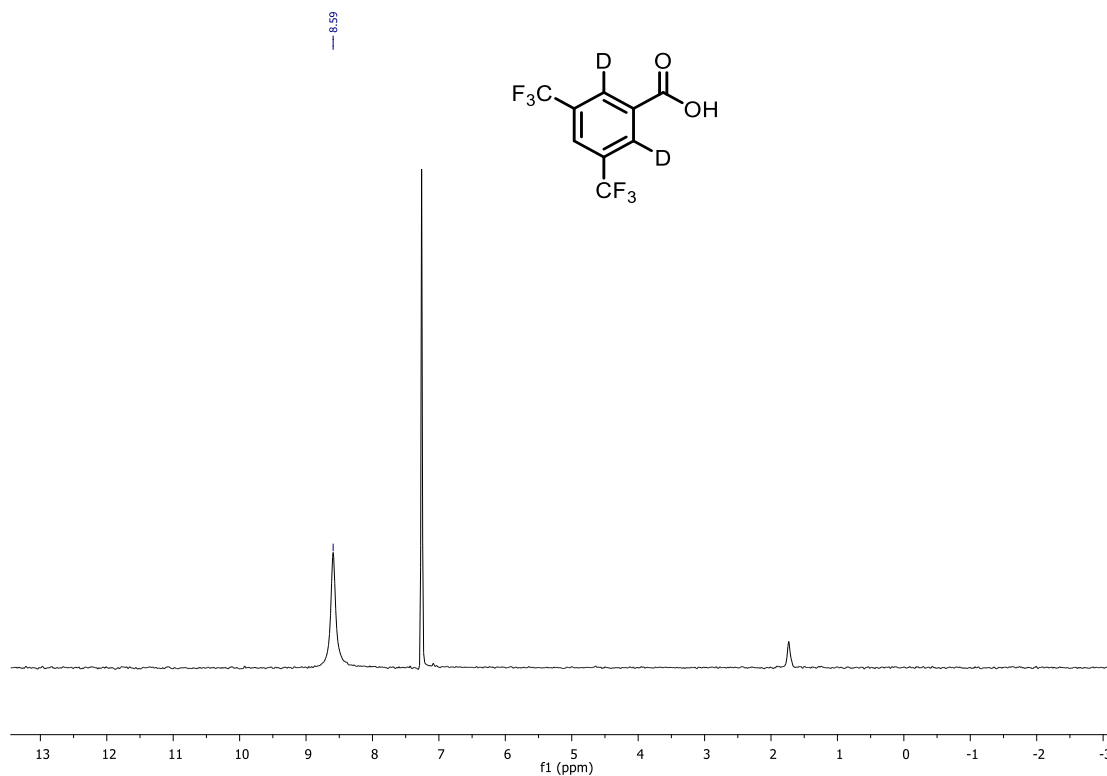


Figure S-96. ^2H NMR spectrum of **1d** (CHCl_3 , 92.1 MHz, 298 K)

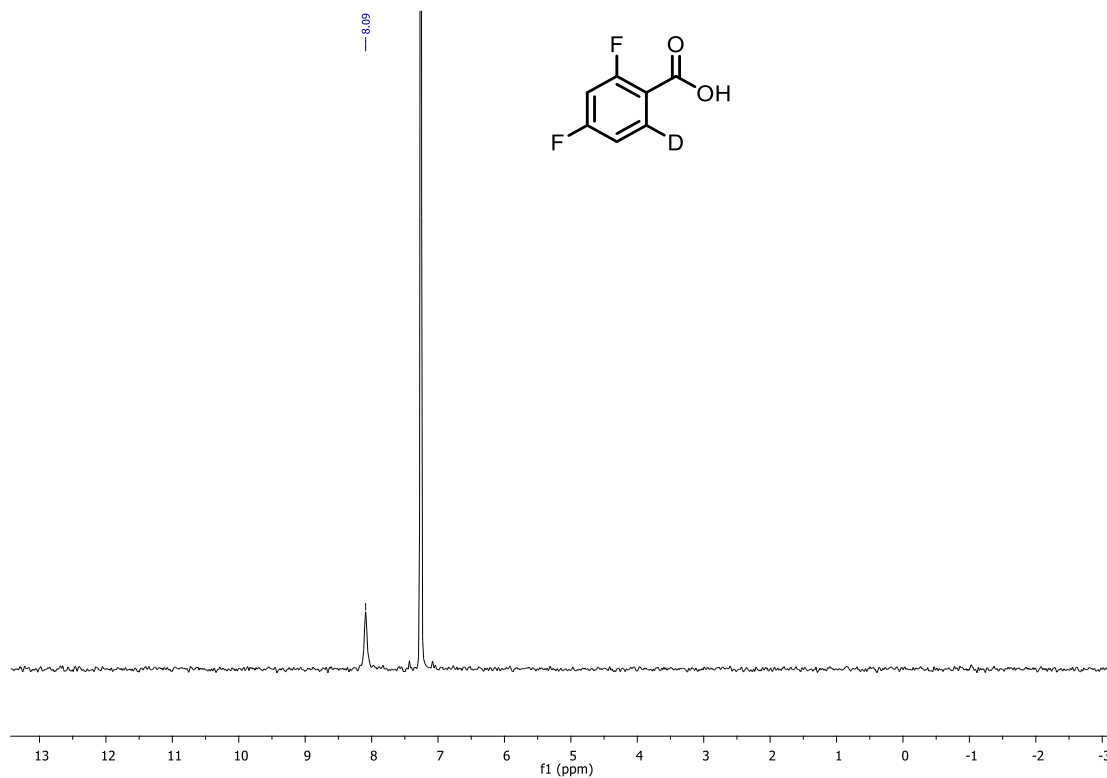


Figure S-97. ^2H NMR spectrum of **1e** (CHCl_3 , 92.1 MHz, 298 K)

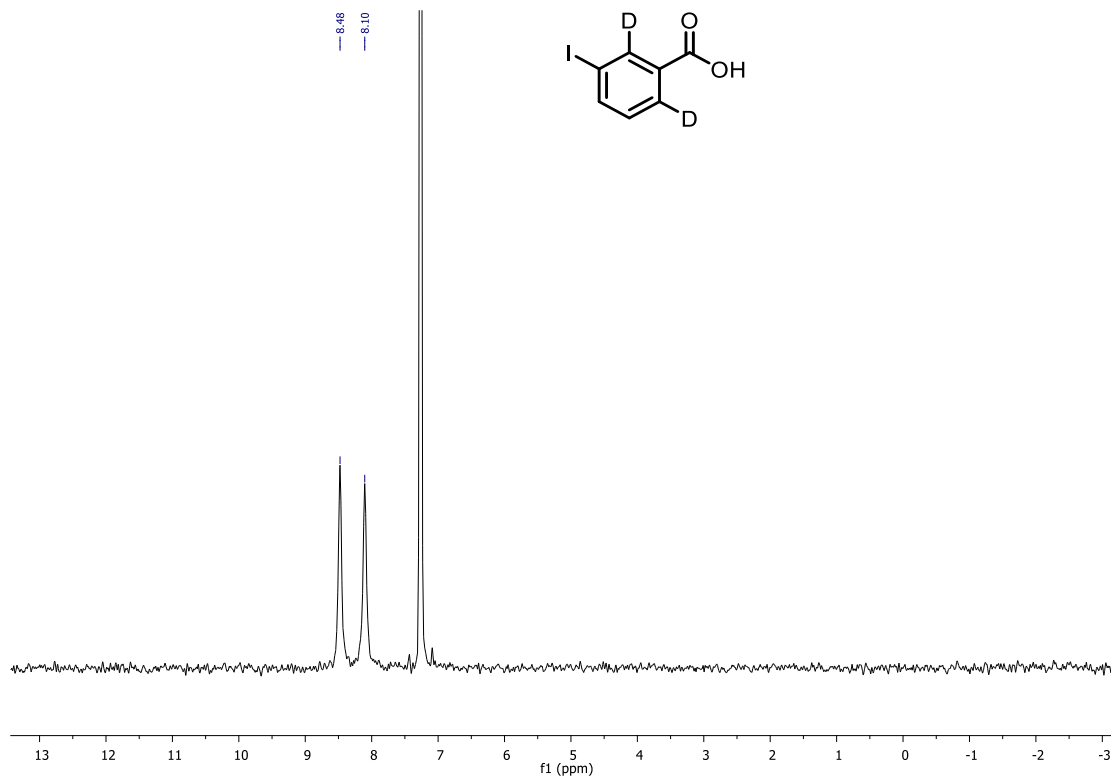


Figure S-98. ^2H NMR spectrum of **1h** (CHCl_3 , 92.1 MHz, 298 K)

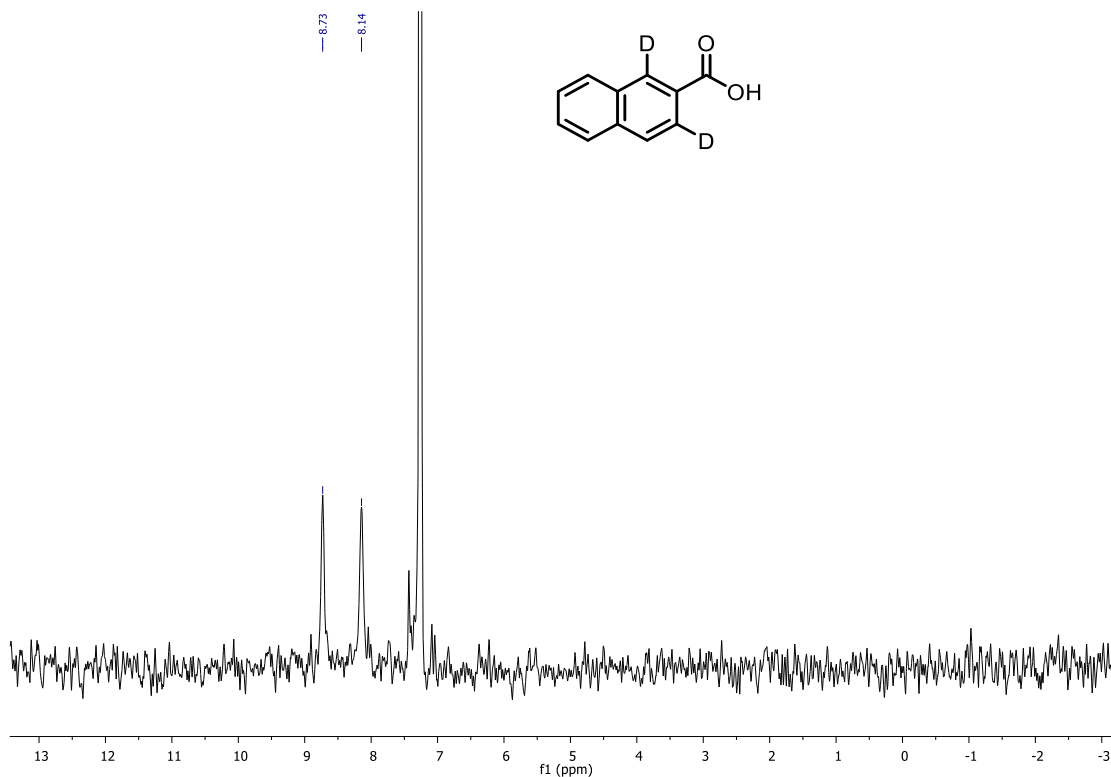


Figure S-99. ^2H NMR spectrum of **1k** (CHCl_3 , 92.1 MHz, 298 K)

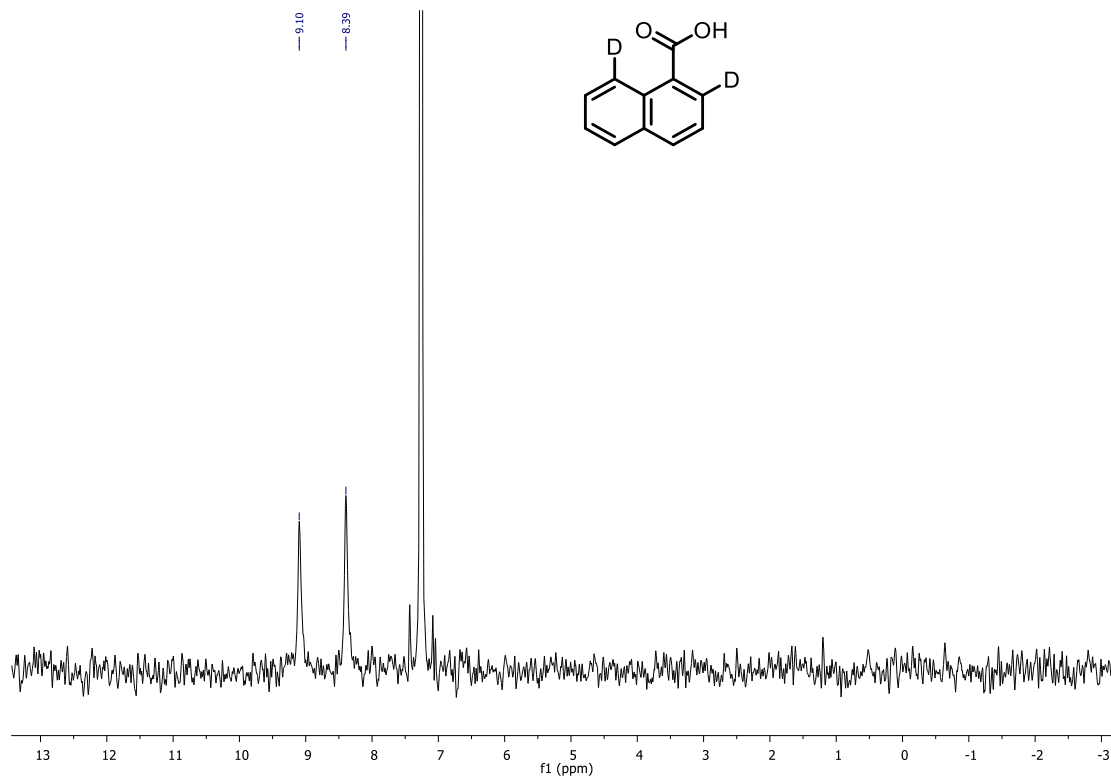


Figure S-100. ^2H NMR spectrum of **11** (CHCl_3 , 92.1 MHz, 298 K)

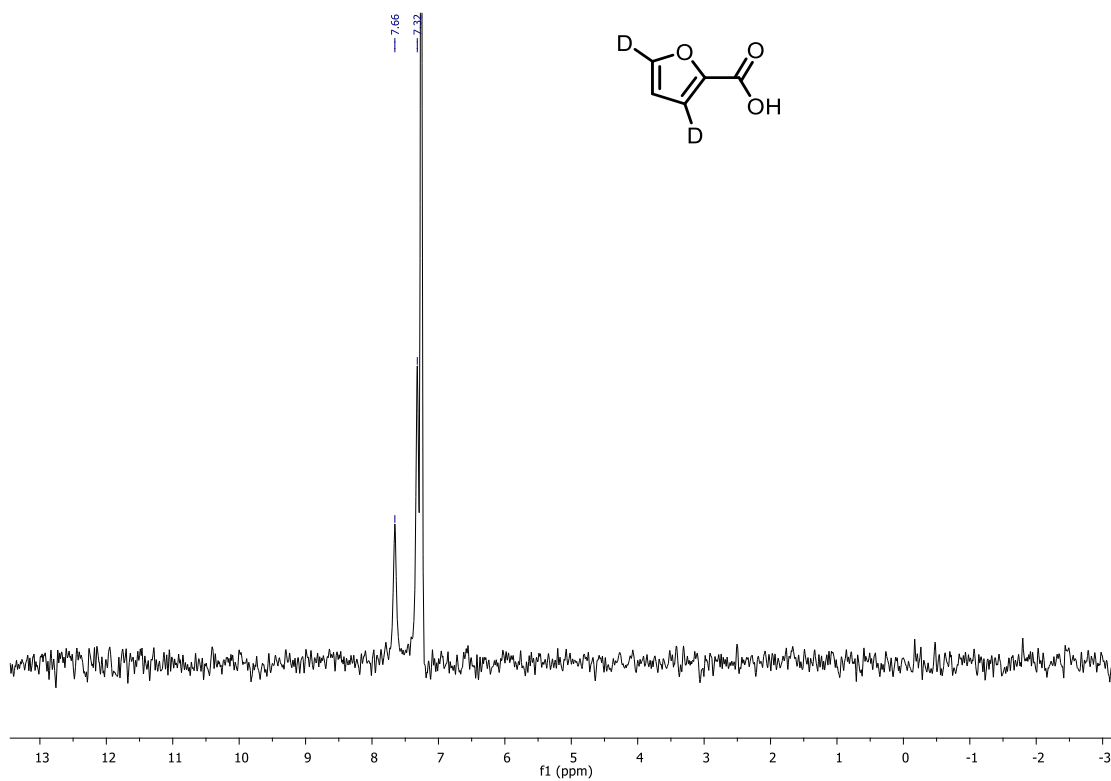


Figure S-101. ^2H NMR spectrum of **1u** (CHCl_3 , 92.1 MHz, 298 K)

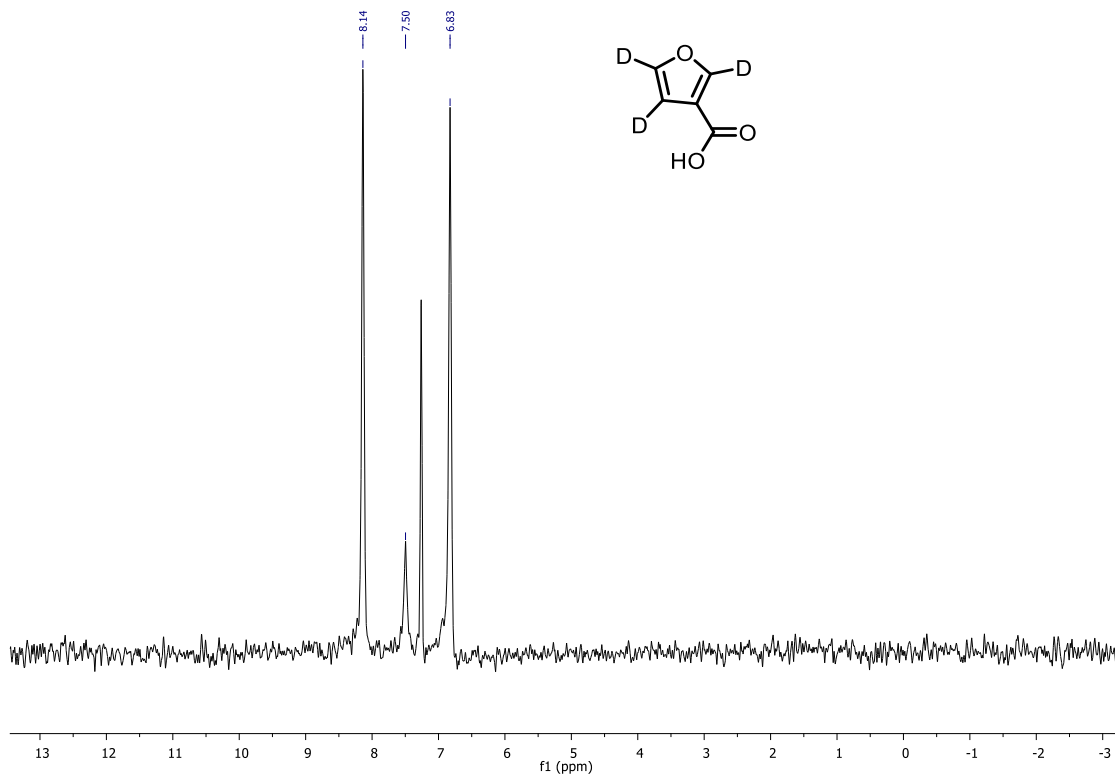


Figure S-102. ^2H NMR spectrum of **1v** (CHCl_3 , 92.1 MHz, 298 K)

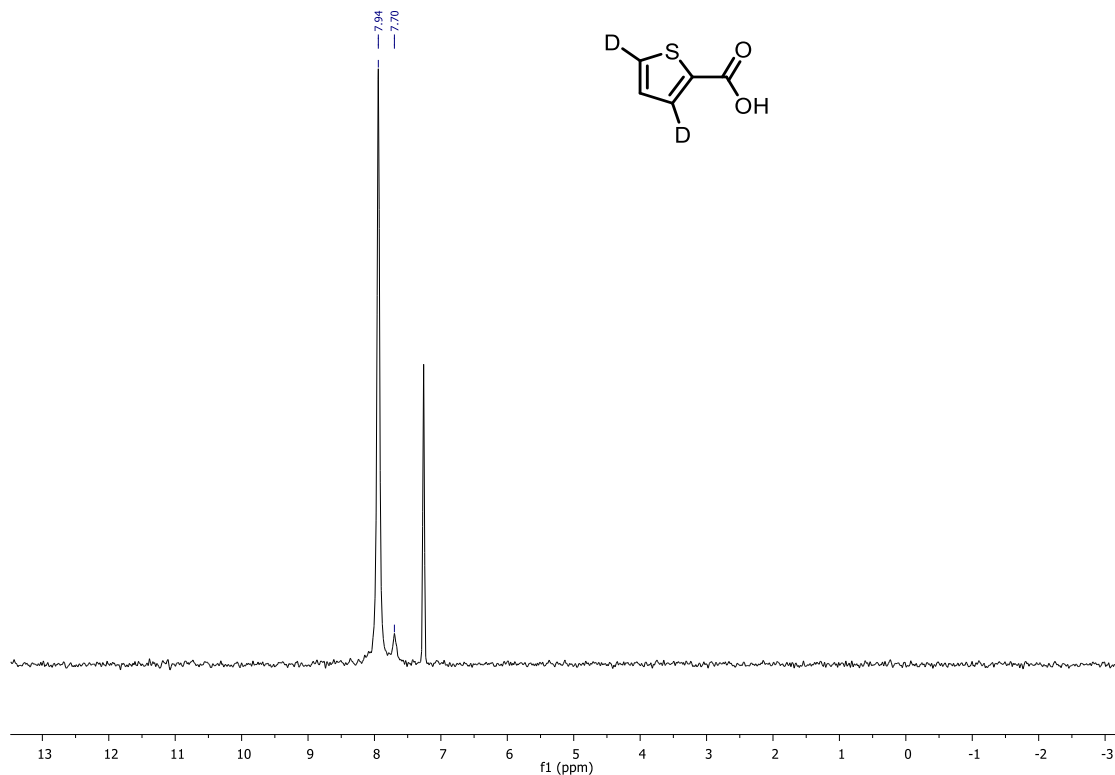


Figure S-103. ^2H NMR spectrum of **1w** (CHCl_3 , 92.1 MHz, 298 K)

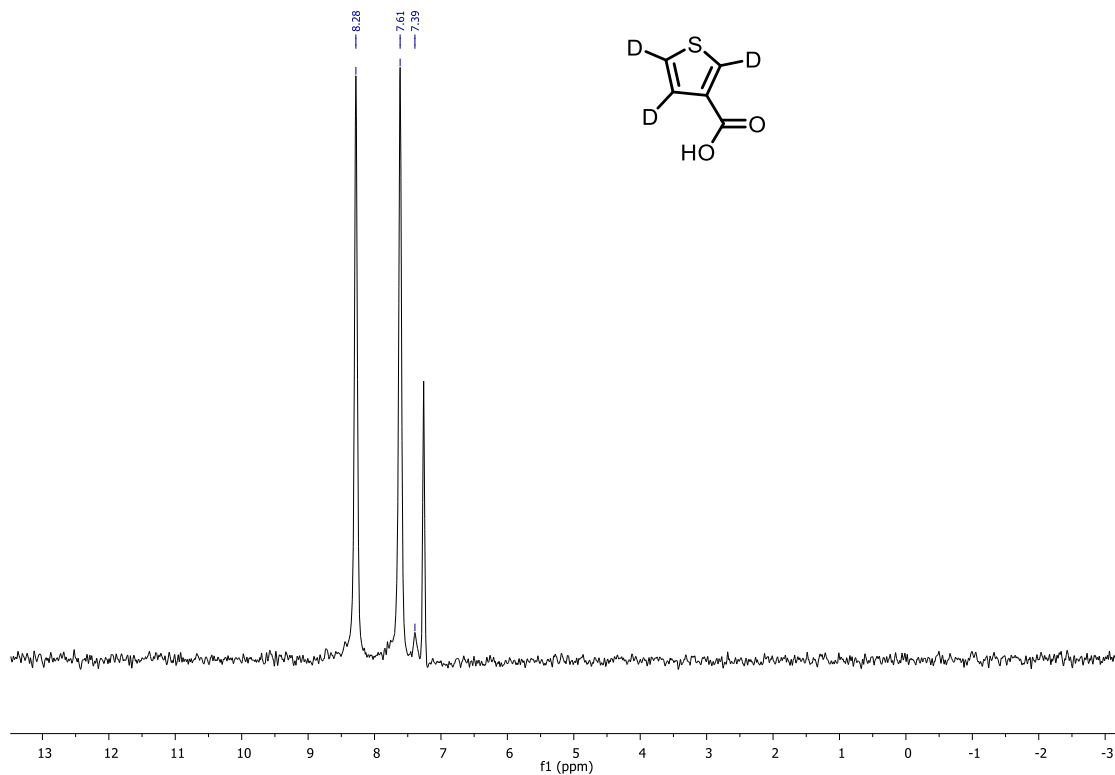


Figure S-104. ^2H NMR spectrum of **1x** (CHCl_3 , 92.1 MHz, 298 K)

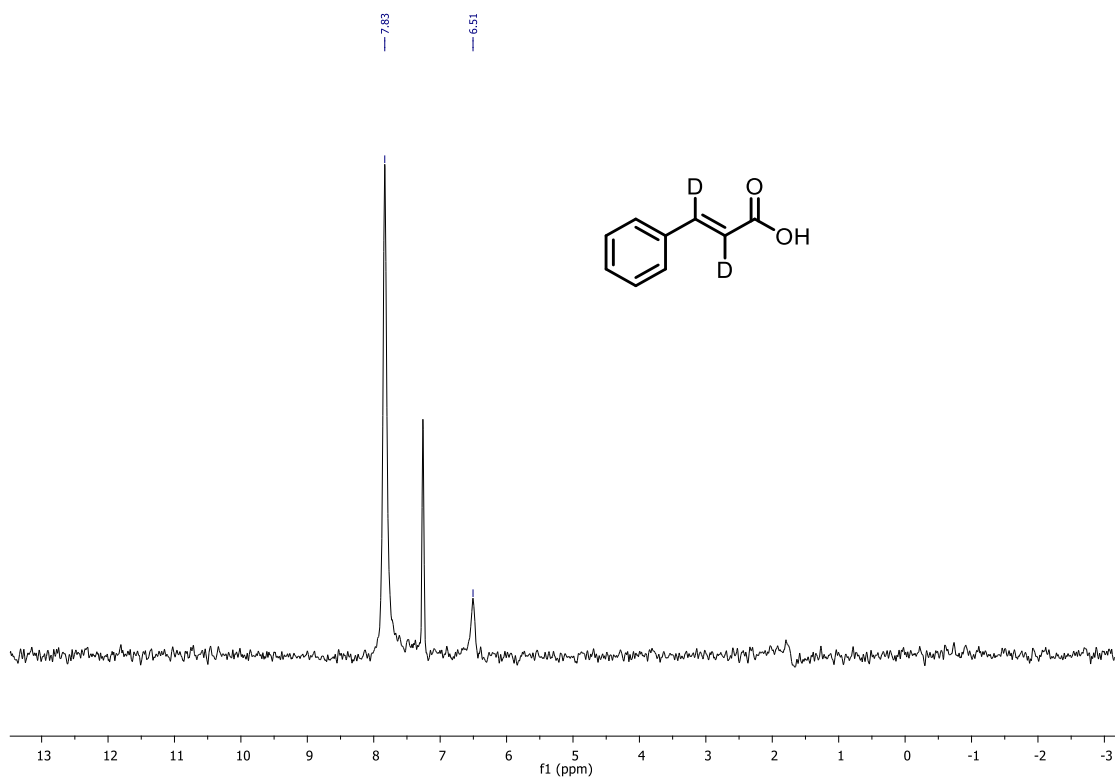


Figure S-105. ^2H NMR spectrum of **2a** (CHCl_3 , 92.1 MHz, 298 K)

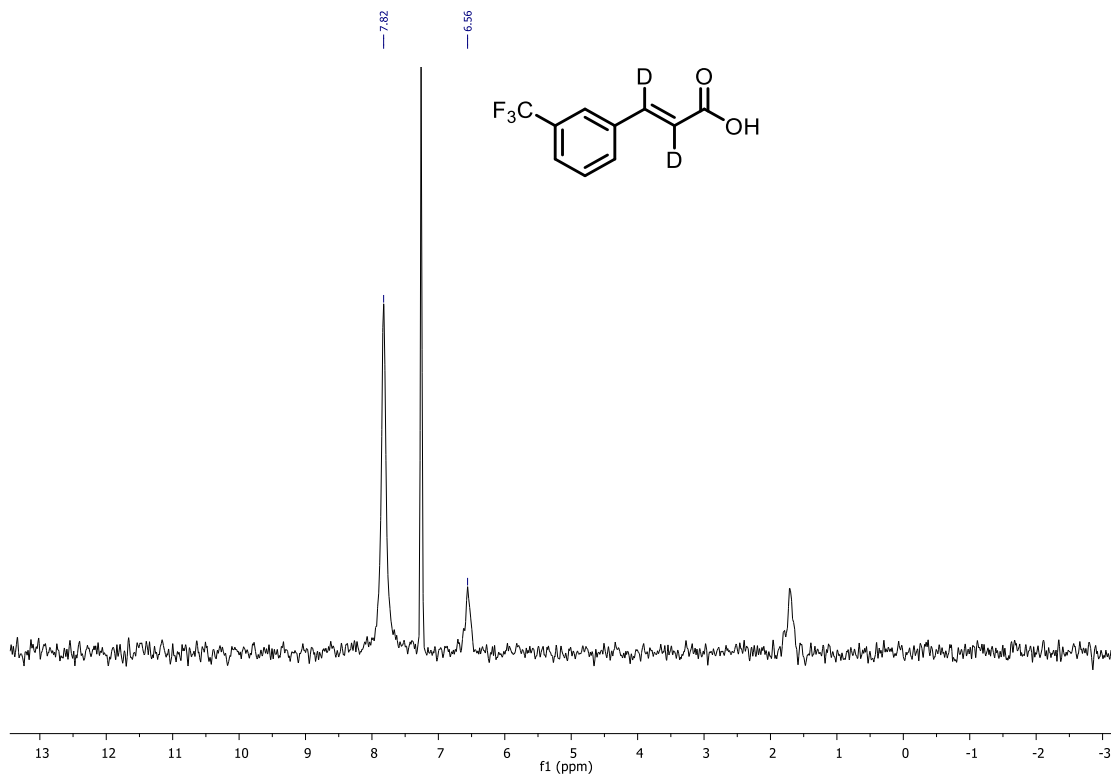


Figure S-106. ^2H NMR spectrum of **2b** (CHCl_3 , 92.1 MHz, 298 K)

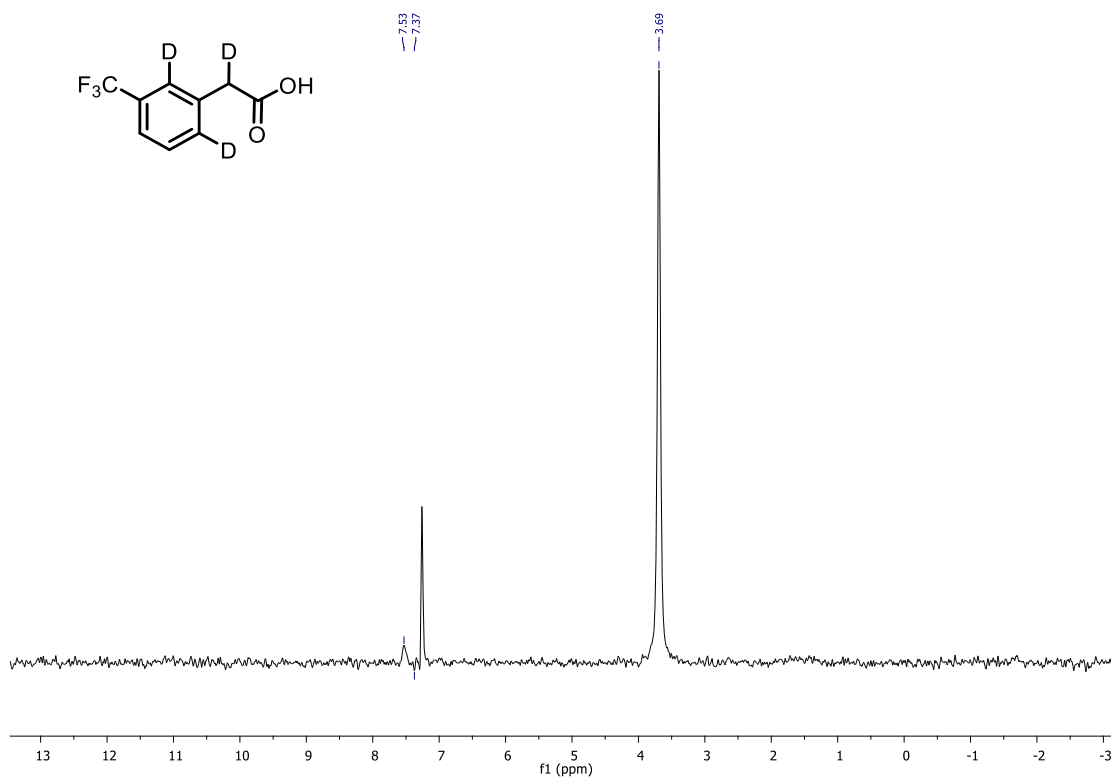


Figure S-107. ^2H NMR spectrum of **3e** (CHCl_3 , 92.1 MHz, 298 K)

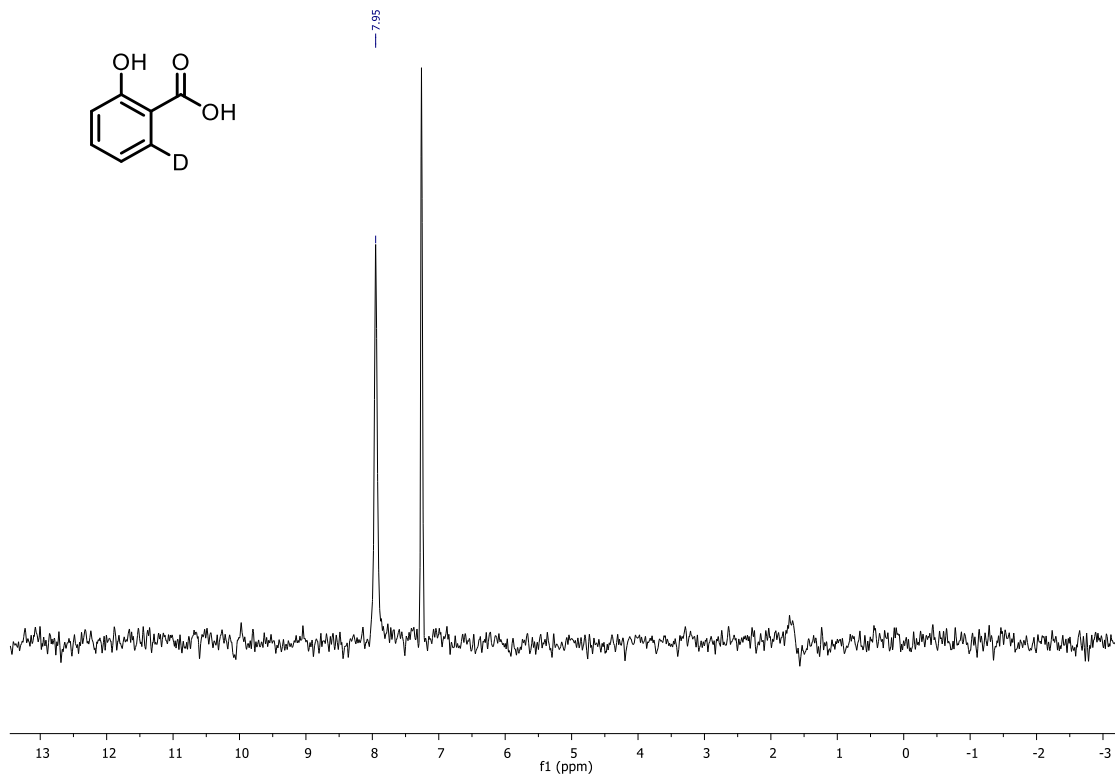


Figure S-108. ^2H NMR spectrum of **1ab** (CHCl_3 , 92.1 MHz, 298 K)

9. References

1. Fulmer, G. R.; Miller, A. J. M.; Sherden, N. H.; Gottlieb, H. E.; Nudelman, A.; Stoltz, B. M.; Bercaw, J. E.; Goldberg, K. I. *Organometallics*, **2010**, *29*, 2176.
2. Kapoor, M.; Chand-Thakuri, P.; Young, M. C. *J. Am. Chem. Soc.* **2019**, *141*, 7980.