Supplementary Information (SI) for Green Chemistry.

Supporting information

CO_2-Enabled Electrochemical Selective Deuterodefluorination of β,γ-Unsaturated α,α-Difluoroesters with Tunable Alkene Deuteration

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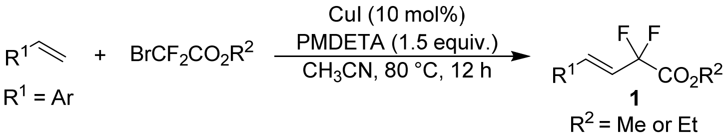
1. General Information

All reagents were purchased from Macklin, Sigma-Aldrich, Adamas-beta, and Energy Chemical of the highest purity grade and used without further purification, unless otherwise indicated. Analytical thin-layer chromatography (TLC) was performed on hexane, visualized by irradiation with UV light. For column chromatography, 300-400 mesh silica gel was used. ^{1}H-NMR and^{13}C-NMR were recorded on a BRUKER 600 MHz spectrometer in $CDCl_3$. ^{19}F-NMR spectra were recorded at BRUKER 400 MHz spectrometer in $CDCl_3$. The residual solvent peak was used as an internal reference: proton ($CDCl_3$ δ 7.26) and carbon ($CDCl_3$ δ 77.16). Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, dd = double doublet, dt = double triplet, m = multiplet), coupling constants (J) are in Hertz (Hz). HRMS spectra were recorded on a Xevo G2-XS QTof (Waters Corporation) using electrospray ionization. DC power supply MT-152D was used for all experiments.

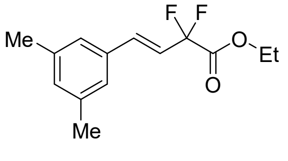
2. Preparation of the substrates

2.1 General procedure A:

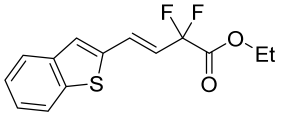
The allyl difluoride substrates **1** are known compounds, and were prepared according to a reported procedure.[1]



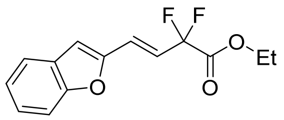
A typical example (Synthesis of **1a**): To a solution of styrene (521 mg, 5.0 mmol, 1.0 equiv.) and ethyl bromodifluoroacetate (1.53 g, 7.5mmol, 1.5 equiv.) in acetonitrile (10 mL) were added PMDETA (pentamethyldiethylenetriamine) (1.30 g, 7.5mmol, 1.5 equiv.) and CuI (95.3 mg, 0.5 mmol, 10 mol%). After stirring at 80 °C in a preheated oil bath for 12 h, water (10 mL) was added and the mixture was extracted with EtOAc (20 mL × 3). The organic layers were combined, washed with brine and water, and dried over anhydrous Na_2SO_4. After removal of solvent, the residue was purified by flash chromatography on silica gel (*n*-hexane/ethyl acetate = 20/1, v/v) to give product **1a** as a colorless oil (1.02 g, 90%). Some allyl difluoride substrates are known compounds,[2-4] characterization of new allyl difluoride substrates **1l, 1p, 1q, 1u** are listed below.



Ethyl (E)-4-(3,5-dimethylphenyl)-2,2-difluorobut-3-enoate (1l). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 20/1) as a yellow oil. Isolated yield: 1.08 g, 85%. **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.13 (s, 2H), 7.10-7.07 (d, *J* = 16.2 Hz, 1H), 7.05 (s, 1H), 6.40-6.33 (m, 1H), 4.43-4.39 (q, *J* = 7.2 Hz, 2H), 2.38 (s, 6H), 1.44-1.41 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$):** δ 164.3 (t, *J* = 36.2 Hz), 138.4, 137.1 (t, *J* = 45.2 Hz), 134.0, 131.4, 125.3, 118.6 (t, *J* = 124.4 Hz), 114.5, 112.9, 111.2, 63.1, 21.2, 14.0. **^{19}F NMR (377 MHz, $CDCl_3$):** δ -102.9 (s, 2F). **HRMS** (ESI): calculated for $C_{14}H_{17}F_2O_2^+$ $[M+H]^+$: 255.1191; found: 255.1192.



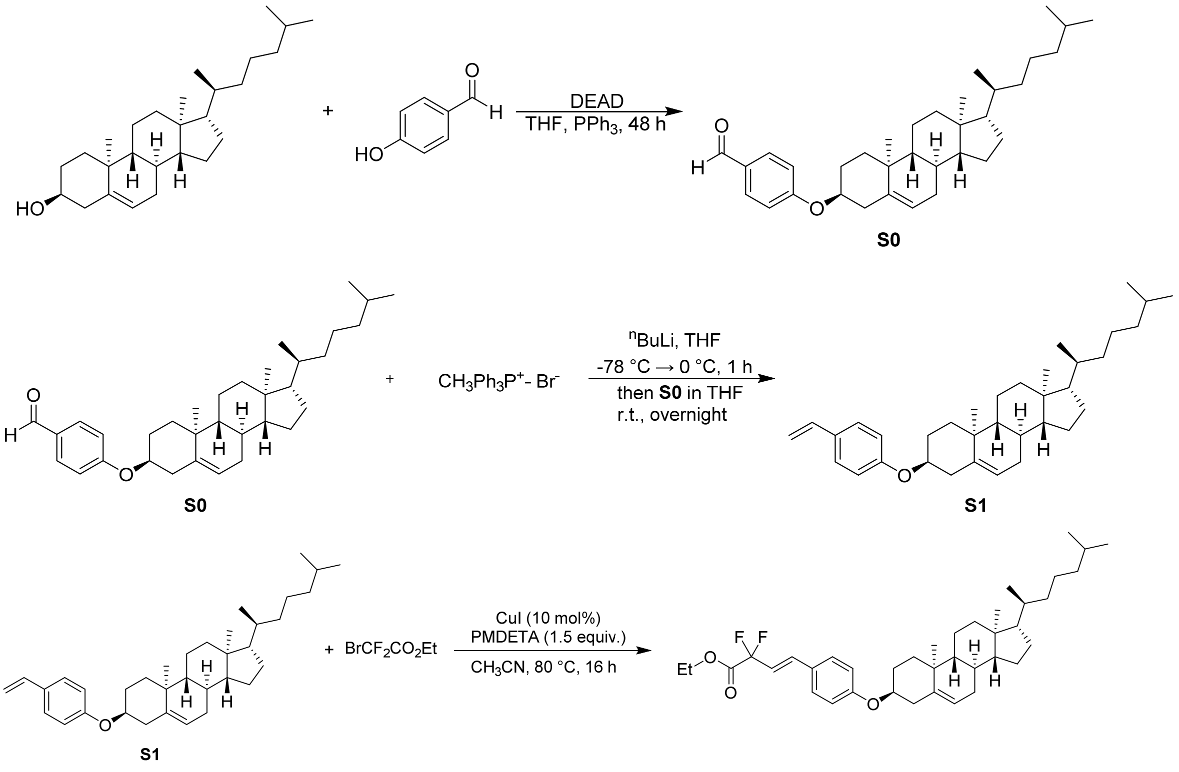
Eethyl (E)-4-(benzo[b]thiophen-2-yl)-2,2-difluorobut-3-enoate (1p). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a yellow oil. Isolated yield: 0.96 g, 68%. **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.81-7.79 (m, 1H), 7.74-7.63 (m, 1H), 7.37-7.33 (m, 2H), 7.21 (s, 1H), 6.99-6.93 (dt, *J* = 16.2, 2.4 Hz, 1H), 6.37-6.30 (m, 1H), 4.37-4.33 (q, *J* = 7.8 Hz, 2H), 1.37-1.35 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$):** δ 164.0 (t, *J* = 36.2 Hz), 144.1, 140.4, 138.6, 124.8, 122.9, 118.6, 114.1, 112.5, 111.6, 110.1, 62.7, 14.0. **^{19}F NMR (377 MHz, $CDCl_3$):** δ -96.4 (s, 2F). **HRMS** (ESI): calculated for $C_{14}H_{13}F_2O_2S^+$ $[M+H]^+$: 283.0599; found: 283.0596.



Ethyl (E)-4-(benzofuran-2-yl)-2,2-difluorobut-3-enoate (1q). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a colorless oil. Isolated yield: 0.85g, 64%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.67-7.63 (m, 1H), 7.54-7.51 (d, *J* = 17.4 Hz, 1H), 7.37-7.33 (m, 2H), 7.07 (s, 1H), 6.95-6.94 (d, *J* = 6.6 Hz, 1H), 6.39-6.33 (m, 1H), 4.40-4.36 (q, *J* = 7.2 Hz, 2H), 1.36-1.34 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 167.2, 149.8, 143.6, 139.9, 126.8, 124.4, 121.6, 120.2, 118.9, 115.6, 113.8, 62.1, 14.3. **^{19}F NMR (377 MHz, CDCl$_3$):** δ -103.0 (s, 2F). **HRMS** (ESI): calculated for $C_{14}H_{13}F_2O_3^+$ $[M+H]^+$: 267.0827; found: 267.0831.

2.2 Procedure B:

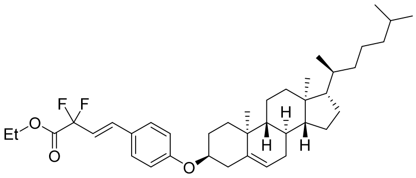
One typical example for the preparation of complex compounds and drug derivatives.[5, 6]



To a solution of DEAD (Diethyl azodicarboxylate) (5.0 mmol, 1.0 equiv.) in THF (Tetrahydrofuran)(31 mL) were added 4-hydroxybenzaldehyde (5.0 mmol, 1.0 equiv.), cholesterol (5.0 mmol, 1.0 equiv.), and triphenylphosphine (5.0 mmol, 1.0 equiv.). The reaction mixture was stirred under N_2 for 48 h at room temperature. The reaction mixture was concentrated in vacuo and the residue was purified by chromatography on silica gel, eluting with *n*-hexane/ethyl acetate to afford the product **S0**.

Then, it is converted to the corresponding alkene via the Wittig reaction. To an oven dried Schlenk flask with a Teflon-coated magnetic stir bar was added Methyltriphenylphosphonium bromide (1.5 equiv.) and Schlenk tube was evacuated and backfilled with nitrogen three times before THF (0.5 M) was added. The reaction was cooled to -78 °C and ^{n}BuLi (1.6 M in hexane, 1.5 equiv.) was added dropwise. The reaction was warmed to room temperature and stirred for 1 h. **S0** was dissolved in THF (1 M) and was added dropwise. The reaction was stirred overnight and afterwards quenched with sat. aq. NH_4Cl solution (5 mL per 1 mmol). The layers were sperarated and the aqueous layer was extracted with EtOAc (5 mL per 1 mmol). The combined organic layers were washed with sat. aq. NaCl (15 ml per 1 mmol), dried over $MgSO_4$ and the solvent was removed under reduced pressure. The product was purified by flash column chromatography on silica gel to yield the corresponding olefine **S1**.

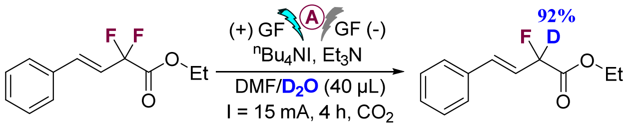
Finally, allyl difluoride substrate **1u** is obtained through general procedure A (40% yield).



Ethyl(E)-4-(4-(((3S,8R,9R,10S,13S,14R,17S)-10,13-dimethyl-17-((S)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl)oxy)phenyl)-2,2-difluorobut-3-enoate (1u). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 20/1) as a pale yellow solid. Isolated yield: 1.68 g, 55%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.72-7.71 (d, 2H), 7.18-7.15 (m, 2H), 6.92 (d, 1H), 6.53-6.51 (d, *J* = 13.2 Hz, 1H), 5.36-5.33 (t, *J* = 7.2 Hz, 1H), 4.36-4.32 (q, *J* = 7.8 Hz, 2H), 3.74 (m, 1H), 2.61-2.59 (m, 1H), 2.29-2.27 (m, 2H), 2.01-1.95 (m, 3H), 1.86-1.82 (m, 3H), 1.80-1.78 (d, *J* = 6.6 Hz, 1H), 1.73-1.69 (m, 2H), 1.66-1.62 (m, 2H), 1.58-1.53 (m, 4H), 1.49-1.45 (m, 2H), 1.42-1.38 (m, 2H), 1.34-1.29 (m, 5H), 1.27-1.25 (m, 4H), 0.98 (s, 3H), 0.93-0.88 (m, 9H), 0.86 (s, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 164.0 (t, *J* = 36.2 Hz), 157.6, 140.8, 134.5, 131.4, 129.3, 122.0, 115.1, 82.3, 62.6, 57.5, 51.1, 43.9, 42.5, 40.2, 38.7, 36.4, 33.5, 30.0, 29.1, 26.3, 25.6, 24.4, 19.5, 14.2, 12.3. **^{19}F NMR (377 MHz, CDCl$_3$):** δ -118.6 (s, 2F). **HRMS** (ESI): calculated for $C_{39}H_{57}F_2O_3^+$ $[M+H]^+$: 611.4270; found: 611.4271.

3. Experimental Procedures

Table S1. Screening of reaction conditions for product 2a [a]

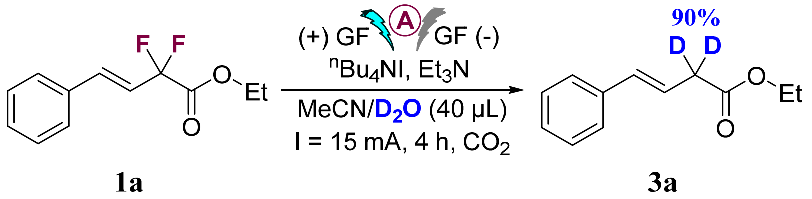


1a **2a**

Entry	Conditions	Yield of 2a (%)[b]	Deuterium content (%)
1	**None**	**68**	**92**
2	Pt (+) | Pt (-)	57	90
3	Zn (+) | Pt (-)	N.D.	—
4	Pt (+) | Ni (-)	40	88
5	Al (+) | GF (-)	N. D.	—
6	$^nBu_4NClO_4$	N.R.	—
7	$^nBu_4NCl$	32	88
8	$^nBu_4NBF_4$	N.D.	—
9	10 mA, 5 h	37	76
10	20 mA, 3 h	38	82
11	0 °C	62	94

[a] Unless otherwise noted, the conditions were as follows: graphite felt anode (10 mm × 15 mm × 0.3 mm), graphite felt cathode (10 mm × 15 mm × 0.3 mm), constant current = 15 mA, **1a** (0.1 mmol), DMF (4.0 mL), D_2O (40.0 µL), Et_3N (5.0 equiv.), $^nBu_4NI$ (1.0 equiv.), room temperature, 4 h, undivided cell, CO_2. [b] yield of isolated product.

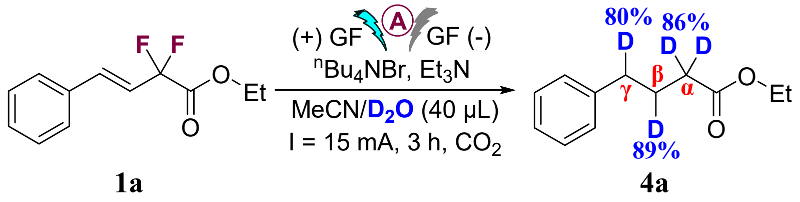
Table S2. Screening of reaction conditions for product 3a [a]



Entry	Conditions	Yield of **3a** (%)[b]	Deuterium content (%)
1	**None**	**94**	**90**
2	Mg (+) | GF (-)	N.D.	—
3	Al (+) | GF (-)	N.D.	—
4	GF (+) | Pb (-)	N.R.	—
5	GF (+) | Ni (-)	43	68
6	Pt (+) | Pt (-)	81	84
7	$^{n}Bu_4NCl$	35	76
8	$^{n}Bu_4NClO_4$/$^{n}Bu_4NPF_6$	N.D.	—
9	NaI/KI	39/32	77/80
10	DMA	58	82/79
11	THF/DCM/DCE/DMSO	N.D.	—
12	10 mA, 4 h/20 mA, 3 h	62/71	72/84
13	CD_3CN instead of D_2O	trace	—
14	Cs_2CO_3 as base	trace	—
15	DIPEA as base	29	73
16	TBD/ DBU as base	N.D.	—
17	No Et_3N	28	66
18	HCOONa/PPh_3/NAP/PHE instead of CO_2	N.R.	—
19	No CO_2	N.R.	—
20	No electricity	N.R.	—

[a] Unless otherwise noted, the conditions were as follows: graphite felt anode (10 mm × 15 mm × 0.3 mm), graphite felt cathode (10 mm × 15 mm × 0.3 mm), constant current = 15 mA, **1a** (0.1 mmol), MeCN (4.0 mL), D_2O (40.0 μL), Et_3N (5.0 equiv.), $^{n}Bu_4NI$ (1.0 equiv.), room temperature, 4 h, undivided cell, CO_2. [b] yield of isolated product. NAP = Naphthalene, PHE = Phenanthrene.

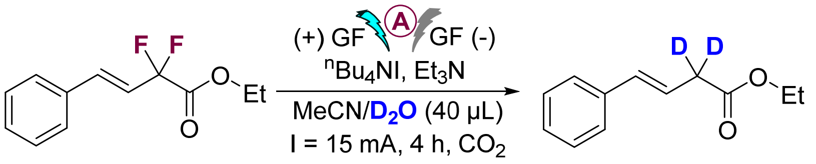
Table S3. Screening of reaction conditions for product 4a [a]



Entry	Conditions	Yield of **4a** (%)[b]	Deuterium content (%)
1	**None**	**82**	**86/89/80**
2	Zn (+) | GF (-)	N.D.	—
3	Mg (+) | GF (-)	N.D.	—
4	Al (+) | GF (-)	N.D.	—
5	Pt (+) | Pt (-)	72	82/86/78
6	$^{n}Bu_4NBF_4$	N.D.	—
7	NaBr	42	75/81/79
8	DMF	66	80/84/82
9	DMA	64	76/82/80
10	THF/DCE/DCM	N.D.	—
11	DMSO	N.R.	—
12	15 mA, 4 h	76	84/86/82
13	20 mA, 3 h	67	78/84/79
14	CD_3CN instead of D_2O	trace	—
15	No Et_3N	22	66/76/68
16	No CO_2	N.R.	—
17	No electricity	N.R.	—

[a] Unless otherwise noted, the conditions were as follows: graphite felt anode (10 mm × 15 mm × 0.3 mm), graphite felt cathode (10 mm × 15 mm × 0.3 mm), constant current = 15 mA, **1a** (0.1 mmol), MeCN (4.0 mL), D_2O (40.0 μL), Et_3N (5.0 equiv.), $^{n}Bu_4NBr$ (1.0 equiv.), room temperature, 3 h, undivided cell, CO_2. [b] yield of isolated product.

Table S4. Reductive mediators instead of CO_2 [a]

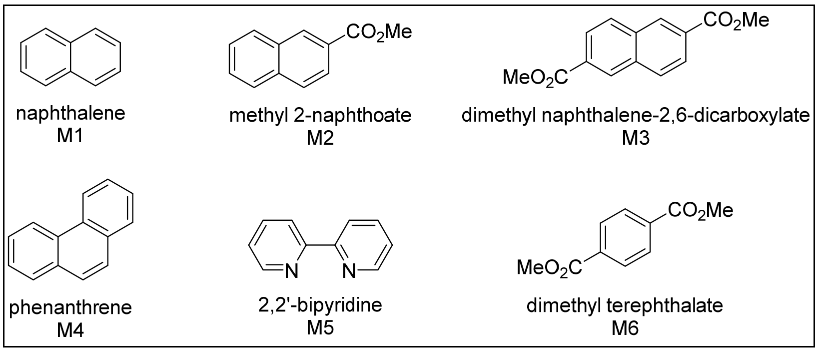


1a **3a**

Entry	Conditions	Yield of 3a (%)[b]
1	HCOONa instead of CO_2	N.R.
2	PPh_3 instead of CO_2	N.R.
2	M1 instead of CO_2	N.R.
3	M2 instead of CO_2	N.R.
4	M3 instead of CO_2	N.R.
5	M4 instead of CO_2	N.R.
6	M5 instead of CO_2	N.R.
7	M6 instead of CO_2	N.R.

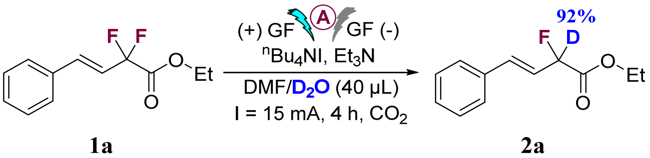
[a] Unless otherwise noted, the conditions were as follows: graphite felt anode (10 mm × 15 mm × 0.3 mm), graphite felt cathode (10 mm × 15 mm × 0.3 mm), constant current = 15 mA, **1a** (0.1 mmol), MeCN (4.0 mL), D_2O (40.0

μL), Et_3N (5.0 equiv.), $^nBu_4NI$ (1.0 equiv.), reductive mediators (20 mol%),[7] room temperature, 4 h, undivided cell, N_2. ^{b} yield of isolated products.



4. General procedure for the synthesis of products

4.1 Electrochemical driven moon-deuterodefluorination



1a **2a**

Ethyl (E)-2,2-difluoro-4-phenylbut-3-enoate **1a** (22.6 mg. 0.1 mmol), $^nBu_4NI$ (1.0 equiv.), Et_3N (5.0 equiv.), DMF (4.0 mL) and D_2O (40.0 μL) were added in a 10 mL hydrogenation tube. The tube was equipped with graphite felt (10 mm × 15 mm × 0.3 mm) as anode and graphite felt (10 mm × 15 mm × 0.3 mm) as cathode. While stirring the reaction mixture, introduce carbon dioxide and bubble for 10 minutes, then switch to carbon dioxide balloons and electrolyze at a constant current of 15 mA for 4 h. When the reaction was finished, the mixture extracted with EtOAc (3 x 10 mL) and the combined organics were washed with H_2O (10 mL), brine (10 mL) and dried over Na_2SO_4. The volatile was removed under reduced pressure and the crude residue was purified by column chromatography using *n*-hexane/EtOAc (15:1, v/v) as the eluent to afford the desired product **2a**.

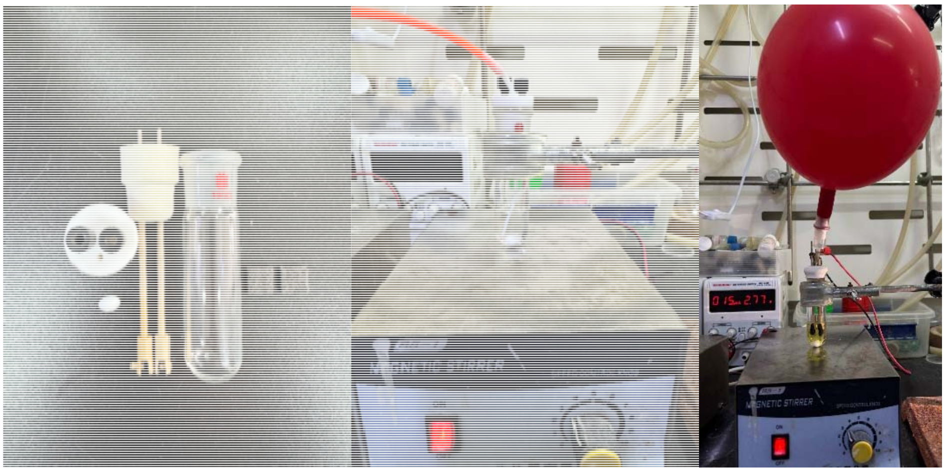
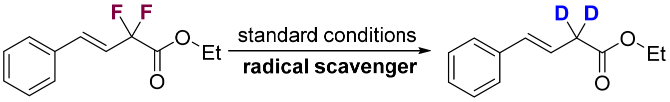


Figure S1. Electrolysis setup for the standard reaction experiment

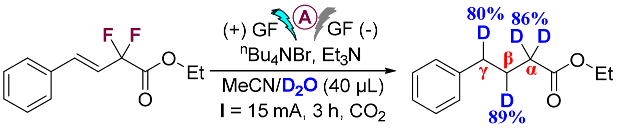
4.2 Electrochemical driven di-deuterodefluorination



1a **3a**

Ethyl (E)-2,2-difluoro-4-phenylbut-3-enoate **1a** (22.6 mg. 0.1 mmol), ${}^{n}Bu_4NI$ (1.0 equiv.), Et_3N (5.0 equiv.), MeCN (4.0 mL) and D_2O (40.0 μL) were added in a 10 mL hydrogenation tube. The tube was equipped with graphite felt (10 mm × 15 mm × 0.3 mm) as anode and graphite felt (10 mm × 15 mm × 0.3 mm) as cathode. While stirring the reaction mixture, introduce carbon dioxide and bubble for 10 minutes, then switch to carbon dioxide balloons and electrolyze at a constant current of 15 mA for 4 h. When the reaction was finished, the mixture extracted with EtOAc (3 x 10 mL) and the combined organics were washed with H_2O (10 mL), brine (10 mL) and dried over Na_2SO_4. The volatile was removed under reduced pressure and the crude residue was purified by column chromatography using *n*-hexane/EtOAc (15:1, v/v) as the eluent to afford the desired product **3a**.

4.3 Electrochemical driven defluorination and polydeuteration

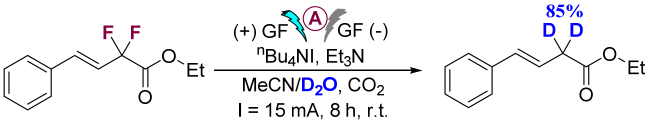


1a **4a**

Ethyl (E)-2,2-difluoro-4-phenylbut-3-enoate **1a** (22.6 mg. 0.1 mmol), ${}^{n}Bu_4NBr$ (1.0 equiv.), Et_3N (5.0 equiv.), MeCN (4.0 mL) and D_2O (40.0 μL) were added in a 10 mL hydrogenation tube. The tube was equipped with graphite felt (10 mm × 15 mm × 0.3 mm) as anode and graphite felt (10 mm × 15 mm × 0.3 mm) as cathode. While stirring the reaction mixture, introduce carbon dioxide and bubble for 10 minutes, then switch to carbon dioxide balloons and electrolyze at a constant current of 15 mA for 3 h. When the reaction was finished, the mixture extracted with EtOAc (3 x 10 mL) and the combined organics were washed with H_2O (10 mL), brine (10 mL) and dried over Na_2SO_4. The volatile was removed under reduced pressure and the crude residue was purified by column chromatography using *n*-hexane/EtOAc (20:1, v/v) as the eluent to afford the desired product **4a**.

4.4 Gram-scale synthesis

4.4.1 Gram-scale synthesis of product 3a

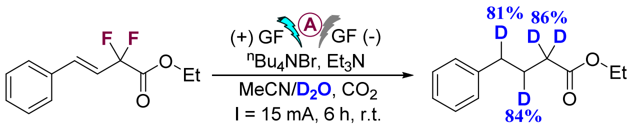


1a (1.13 g, 5 mmol) **3a** (0.79 g, 82% yield)

Ethyl (E)-2,2-difluoro-4-phenylbut-3-enoate **1a** (1.13 g. 5 mmol), ${}^{n}Bu_4NI$ (1.0 equiv.), Et_3N (5.0 equiv.), MeCN (40.0 mL) and D_2O (0.4 mL) were added in a bottle (100.0 mL). The bottle was equipped with graphite felt (40 mm × 40 mm × 0.3 mm) as anode and graphite felt (40 mm × 40 mm × 0.3 mm) as cathode. Then the reaction mixture was stirred and electrolyzed at a constant current of 15 mA for 8 h. When the reaction was finished, the mixture extracted with EtOAc (3 x 10 mL) and the combined organics were washed with H_2O (10 mL), brine (10 mL) and dried over Na_2SO_4. Part of the organics was concentrated and the crude residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 15: 1, v/v) to afford the product **3a**.

Figure S2. Electrolysis setup for the gram scale experiment.

4.4.2 Gram-scale synthesis of product 4a

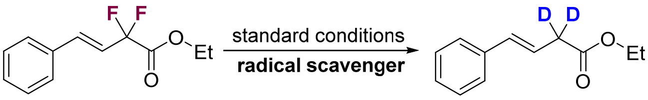


1a (1.13 g, 5 mmol) **4a** (0.69 g, 71% yield)

Ethyl (E)-2,2-difluoro-4-phenylbut-3-enoate **1a** (1.13 g. 5 mmol), ^{n}Bu$_4$NBr (1.0 equiv.), Et_3N (5.0 equiv.), MeCN (40.0 mL) and D_2O (0.4 mL) were added in a bottle (100.0 mL). The bottle was equipped with graphite felt (40 mm × 40 mm × 0.3 mm) as anode and graphite felt (40 mm × 40 mm × 0.3 mm) as cathode. Then the reaction mixture was stirred and electrolyzed at a constant current of 15 mA for 6 h. When the reaction was finished, the mixture extracted with EtOAc (3 x 10 mL) and the combined organics were washed with H_2O (10 mL), brine (10 mL) and dried over Na_2SO_4. Part of the organics was concentrated and the crude residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 20: 1, v/v) to afford the product **4a**.

5. Mechanistic studies

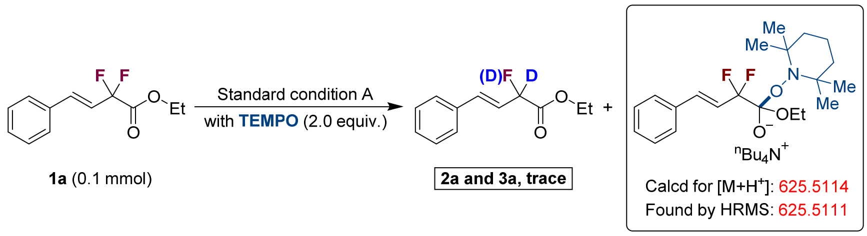
5.1 Radical trapping experiments [a]

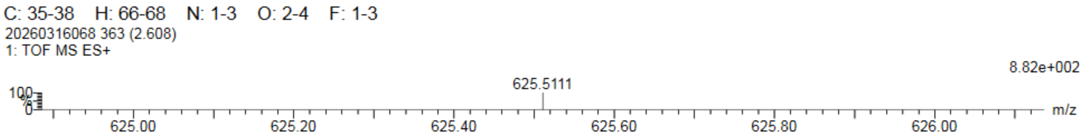


1a **3a**

Entry	Radical scavenger	Yield（%）[b]
1	none	94
2	TMEPO (2.0 equiv.)	trace
3	BHT (2.0 equiv.)	trace

[a] Standard reaction conditions: graphite felt anode (10 mm × 15 mm × 0.3 mm), graphite felt cathode (10 mm × 15 mm × 0.3 mm), constant current = 15 mA, **1a** (0.1 mmol), ^{n}Bu$_4$NI (1.0 equiv.), MeCN (4.0 mL), D_2O (40.0 μL), Et_3N (5.0 equiv.), room temperature, 4 h, undivided cell, CO_2. [b] yield of isolated product.

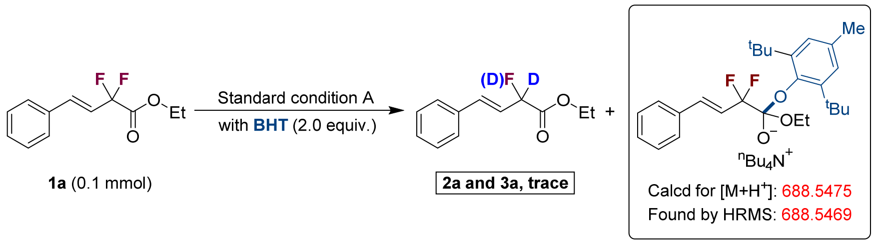


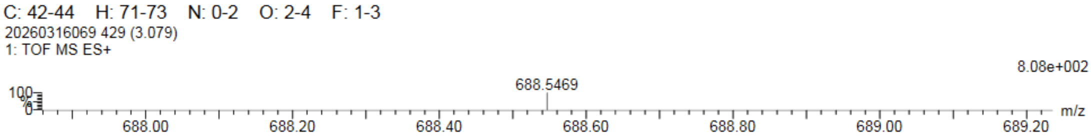


```
Minimum:                          -1.5
Maximum:              5.0    10.0    50.0

Mass       Calc. Mass   mDa    PPM    DBE    i-FIT    Norm   Conf(%)  Formula

625.5111   625.5120    -0.9   -1.4    4.5    24.6     n/a    n/a      C37 H67 N2 O3 F2
```

An undivided cell (10 mL hydrogenation tube) was equipped with a magnet stirrer (3 mm x 5 mm), graphite felt (10 mm × 15 mm × 0.3 mm) as cathode, and graphite felt (10 mm × 15 mm × 0.3 mm) as anode. The electrolyte $^{n}Bu_4NI$ (36.9 mg, 0.1 mmol, 1.0 equiv.), MeCN (4.0 mL), D_2O (40.0 μL), followed by the addition of the substrate **1a** (22.6 mg, 0.1 mmol), a solution of Et_3N (5.0 equiv.) and 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO, 2.0 equiv.). While stirring (1000 rpm) the reaction mixture, introduce carbon dioxide and bubble for 10 minutes, then switch to carbon dioxide balloons and electrolyzed at a constant current of 15 mA flow for 4 h at room temperature. The aqueous layer extracted with EtOAc (3 x 10 mL) and the combined organics were washed with H_2O (10 mL), brine (10 mL) and dried over Na_2SO_4.

When TEMPO was introduced into the model reactions, the desired product **2a** and **3a** was in a trace yield. This result suggests the involvement of radical process in this transformation. The TEMPO-adduct was detected by HRMS (ESI, m/z), calculated for $[C_{37}H_{67}F_2N_2O_3 + H]^+$: 625.5114; Found: 625.5111.





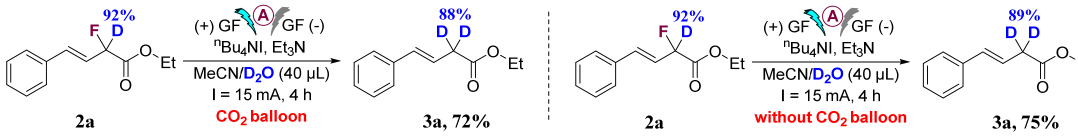
```
Minimum:                          -1.5
Maximum:              5.0    10.0    50.0

Mass       Calc. Mass   mDa    PPM    DBE    i-FIT    Norm   Conf(%)  Formula

688.5469   688.5480    -1.1   -1.6    7.5    24.7     n/a    n/a      C43 H72 N O3 F2
```

An undivided cell (10 mL hydrogenation tube) was equipped with a magnet stirrer (3 mm x 5 mm), graphite felt (10 mm × 15 mm × 0.3 mm) as cathode, and graphite felt (10 mm × 15 mm × 0.3 mm) as anode. The electrolyte $^{n}Bu_4NI$ (36.9 mg, 0.1 mmol, 1.0 equiv.), MeCN (4.0 mL), D_2O (40.0 μL), followed by the addition of the substrate **1a** (22.6 mg, 0.1 mmol), a solution of Et_3N (5.0 equiv.) and 2,6-Di-tert-butyl-4-methylphenol (BHT, 2.0 equiv.). While stirring (1000 rpm) the reaction mixture, introduce carbon dioxide and bubble for 10 minutes, then switch to carbon dioxide balloons and electrolyzed at a constant current of 15 mA flow for 4 h at room temperature. The aqueous layer extracted with EtOAc (3 x 10 mL) and the combined organics were washed with H_2O (10 mL), brine

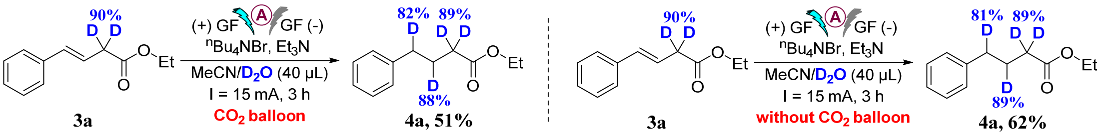
(10 mL) and dried over Na_2SO_4.

When BHT was introduced into the model reactions, the desired product **2a** and **3a** was not detected. This result suggests the involvement of radical process in this transformation. The BHT-adduct was detected by HRMS (ESI, m/z), calculated for $[C_{43}H_{72}F_2NO_3 + H]^+$: 688.5475; Found: 688.5469.

5.2 Step-by-step studies on the stepwise reactions and the role of CO_2

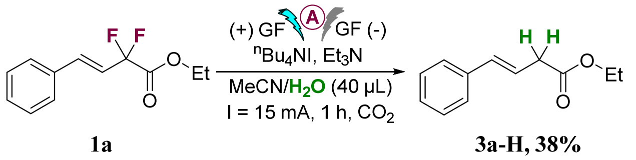


Ethyl (E)-2-fluoro-4-phenylbut-3-enoate-2-d **2a** (20.9 mg. 0.1 mmol), $^nBu_4NI$ (1.0 equiv.), Et_3N (5.0 equiv.), MeCN (4.0 mL) and D_2O (40.0 μL) were added in a 10 mL hydrogenation tube. The tube was equipped with graphite felt (10 mm × 15 mm × 0.3 mm) as anode and graphite felt (10 mm × 15 mm × 0.3 mm) as cathode. While stirring the reaction mixture, introduce carbon dioxide and bubble for 10 minutes, then switch to carbon dioxide balloons and electrolyze at a constant current of 15 mA for 4 h. When the reaction was finished, the mixture extracted with EtOAc (3 x 10 mL) and the combined organics were washed with H_2O (10 mL), brine (10 mL) and dried over Na_2SO_4. The volatile was removed under reduced pressure and the crude residue was purified by column chromatography using *n*-hexane/EtOAc (15:1, v/v) as the eluent to afford the desired product **3a** (yield: 13.8 mg, 72%). When nitrogen is used instead of carbon dioxide, product **3a** can still be obtained (yield: 14.4 mg, 75%).



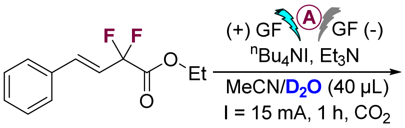
Ethyl (E)-4-phenylbut-3-enoate-2,2-d2 **3a** (19.2 mg. 0.1 mmol), $^nBu_4NBr$ (1.0 equiv.), Et_3N (5.0 equiv.), MeCN (4.0 mL) and D_2O (40.0 μL) were added in a 10 mL hydrogenation tube. The tube was equipped with graphite felt (10 mm × 15 mm × 0.3 mm) as anode and graphite felt (10 mm × 15 mm × 0.3 mm) as cathode. While stirring the reaction mixture, introduce carbon dioxide and bubble for 10 minutes, then switch to carbon dioxide balloons and electrolyze at a constant current of 15 mA for 3 h. When the reaction was finished, the mixture extracted with EtOAc (3 x 10 mL) and the combined organics were washed with H_2O (10 mL), brine (10 mL) and dried over Na_2SO_4. The volatile was removed under reduced pressure and the crude residue was purified by column chromatography using *n*-hexane/EtOAc (20:1, v/v) as the eluent to afford the desired product **4a** (yield: 10.0 mg, 51%). When nitrogen is used instead of carbon dioxide, product **4a** can still be obtained (yield: 12.1 mg, 62%).

5.3 Parallel KIE experiments



Ethyl (E)-2,2-difluoro-4-phenylbut-3-enoate **1a** (22.6 mg. 0.1 mmol), $^nBu_4NI$ (1.0 equiv.), Et_3N (5.0 equiv.), MeCN (4.0 mL) and H_2O (40.0 μL) were added in a 10 mL hydrogenation tube. The tube was equipped with graphite felt (10 mm × 15 mm × 0.3 mm) as anode and graphite felt (10 mm × 15 mm × 0.3 mm) as cathode. While stirring the reaction mixture, introduce carbon dioxide and bubble for 10 minutes, then switch to carbon dioxide balloons and electrolyze at a constant current of 15 mA for 1 h. When the reaction was finished, the mixture extracted with EtOAc (3 x 10 mL) and the combined organics were washed with H_2O (10 mL), brine (10 mL) and dried over

Na_2SO_4. The volatile was removed under reduced pressure and the crude residue was purified by column chromatography using *n*-hexane/EtOAc (15:1, v/v) as the eluent to afford the desired product **3a-H** (yield: 7.2 mg, 38%).

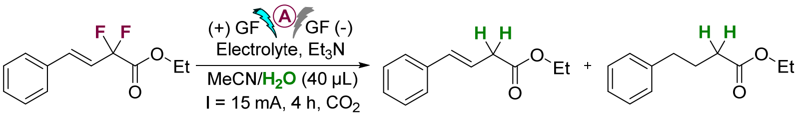


1a **3a, trace**

Ethyl (E)-2,2-difluoro-4-phenylbut-3-enoate **1a** (22.6 mg. 0.1 mmol), $^{n}Bu_4NI$ (1.0 equiv.), Et_3N (5.0 equiv.), MeCN (4.0 mL) and D_2O (40.0 μL) were added in a 10 mL hydrogenation tube. The tube was equipped with graphite felt (10 mm × 15 mm × 0.3 mm) as anode and graphite felt (10 mm × 15 mm × 0.3 mm) as cathode. While stirring the reaction mixture, introduce carbon dioxide and bubble for 10 minutes, then switch to carbon dioxide balloons and electrolyze at a constant current of 15 mA for 1 h. When the reaction was finished, the mixture extracted with EtOAc (3 x 10 mL) and the combined organics were washed with H_2O (10 mL), brine (10 mL) and dried over Na_2SO_4. The yield of the desired product **3a** was observed to be trace by GC-MS.

5.4 Experiment on the influence of the bromine sources

Table S5. The effect of bromine source dosage on products [a]



1a **3a-H** **4a-H**

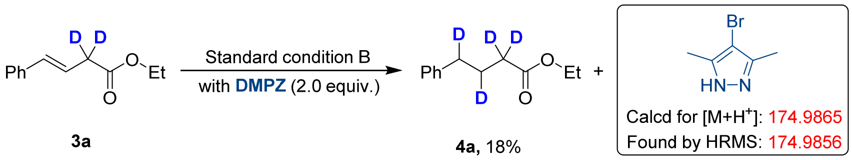
Entry	Conditions	Ratio of **3a-H**/**4a-H**[b]
1	$^{n}Bu_4NI$/ $^{n}Bu_4NBr$ = 1:9	1:11.1
2	$^{n}Bu_4NI$/ $^{n}Bu_4NBr$ = 1:4	1:4.2
3	$^{n}Bu_4NI$/ $^{n}Bu_4NBr$ = 1:1	2:1
4	$^{n}Bu_4NI$/ $^{n}Bu_4NBr$ = 4:1	8.3:1
5	$^{n}Bu_4NI$/ $^{n}Bu_4NBr$ = 9:1	13.3:1

[a] Unless otherwise noted, the conditions were as follows: graphite felt anode (10 mm × 15 mm × 0.3 mm), graphite felt cathode (10 mm × 15 mm × 0.3 mm), constant current = 15 mA, **1a** (0.1 mmol), MeCN (4.0 mL), H_2O (40.0 μL), electrolyte (0.1 mmol), Et_3N (5.0 equiv.), room temperature, 4 h, undivided cell, CO_2. [b] crude NMR yield (using 1,3,5-trimethoxybenzene as an internal standard).

5.5 DMPZ probes $Br_2^{\bullet-}$

An undivided cell (10 mL hydrogenation tube) was equipped with a magnet stirrer (3 mm x 5 mm), graphite felt (10 mm × 15 mm × 0.3 mm) as cathode, and graphite felt (10 mm × 15 mm × 0.3 mm) as anode. The electrolyte $^{n}Bu_4NI$ (36.9 mg, 0.1 mmol, 1.0 equiv.), Br_2 (0.2 equiv.), MeCN (4.0 mL), D_2O (40.0 μL), followed by the addition of the substrate **3a** (19.2 mg, 0.1 mmol), a solution of Et_3N (5.0 equiv.) and 3,5-Dimethylpyrazole (DMPZ, 2.0 equiv.). While stirring (1000 rpm) the reaction mixture, introduce carbon dioxide and bubble for 10 minutes, then switch to carbon dioxide balloons and electrolyze at a constant current of 15 mA flow for 3 h at room temperature. The aqueous layer extracted with EtOAc (3 x 10 mL) and the combined organics were washed with H_2O (10 mL), brine (10 mL) and dried over Na_2SO_4.

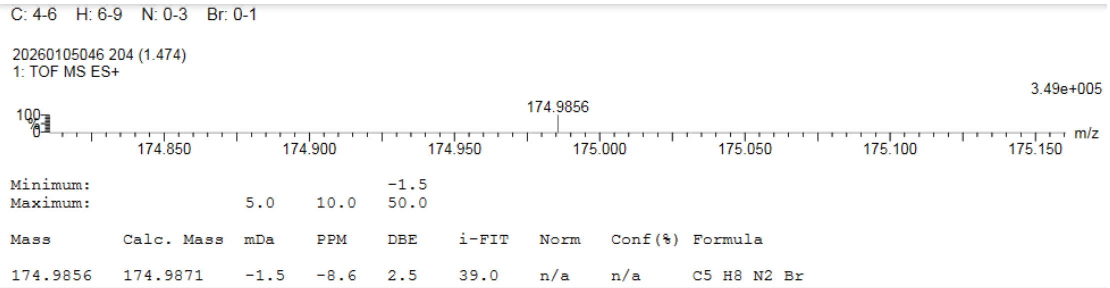
When DMPZ was introduced into the model reactions, the yield of desired product **4a** was 18% and Br-DMPZ is formed. This result suggests the presence of $Br_2^{\bullet-}$ during the reaction[8]. The Br-DMPZ was detected by HRMS (ESI, m/z), calculated for $[C_5H_7BrN_2 + H]^+$: 174.9865; Found: 174.9856.



3a

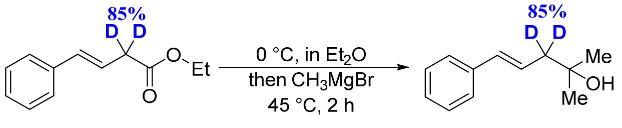
4a, 18%

Calcd for [M+H$^+$]: 174.9865
Found by HRMS: 174.9856



```
C: 4-6   H: 6-9   N: 0-3   Br: 0-1

20260105046 204 (1.474)
1: TOF MS ES+

Minimum:                            -1.5
Maximum:               5.0    10.0  50.0

Mass       Calc. Mass  mDa    PPM   DBE    i-FIT   Norm   Conf(%)  Formula

174.9856   174.9871    -1.5   -8.6  2.5    39.0    n/a    n/a      C5 H8 N2 Br
```

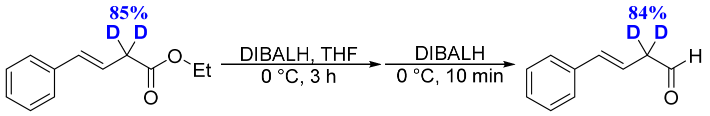
6. Product transformation



3a

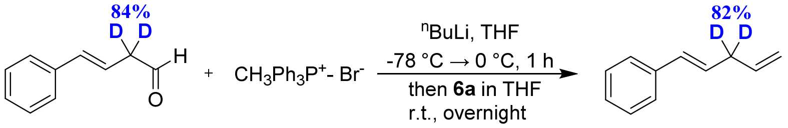
5a, 83%

To a solution of ethyl (E)-4-phenylbut-3-enoate-2,2-d_2 **3a** (0.192 g, 1 mmol) in 5 mL of anhydrous ether, 5 mL of a solution of 3 M methyl magnesium bromide in ether was added drop-wise at 0 °C. The reaction was brought to 45 °C with a warm water bath. After 2 h, TLC (5:1, *n*-hexane/EtOAc) demonstrated complete conversion of the ester to (E)-2-methyl-5-phenylpent-4-en-3,3-d_2-2-ol (**5a**). The reaction mixture was poured slowly into an ice-cooled saturated solution of NH_4Cl, and extracted with EtOAc (3 x 10 mL). The organic phase was washed with brine (2 x 10 mL), dried over Na_2SO_4, filtered and evaporated to afford (E)-2-methyl-5-phenylpent-4-en-3,3-d_2-2-ol **5a** (0.148 g, 83% yield).[9] **^{1}H NMR ($CDCl_3$, 600 MHz):** δ 7.38-7.36 (d, 2H), 7.34-7.32 (m, 2H), 7.26-7.22 (m, 1H), 6.51 (d, *J* = 23.4 Hz, 1H), 6.37-6.29 (m, 1H), 1.54 (s, 1H), 1.29 (s, 6H); **^{13}C NMR ($CDCl_3$, 377 MHz):** δ 138.1, 134.5, 129.4, 128.8, 127.9, 126.1, 63.3, 39.7, 29.8.



3a

6a, 95%

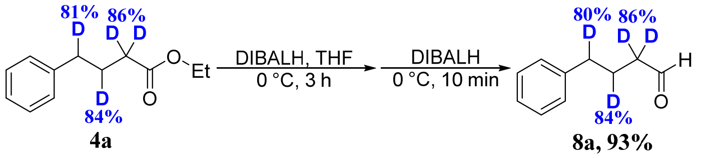


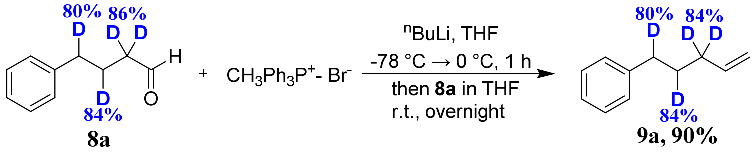
6a

7a, 89%

A dry and nitrogen-flushed flask, equipped with a magnetic stirring bar and a septum, was charged with morpholine (0.18 mL, 2.1 mmol) and THF (10 mL). After cooling to 0 °C, DIBALH (2.0 mL,1.0 M in hexane, 2.0 mmol) was added dropwise and the mixture was stirred for 3 h at the same temperature. Ethyl (E)-4-phenylbut-3-enoate-2,2-d_2 **3a** (0.192 g, 1.0 mmol) was added slowly to the reaction mixture, which was stirred for 10 min. Then, DIBALH (1.5mL, 1.0 M in hexane, 1.5 mmol) was added and the mixture was stirred for 10 min again. The reaction was stopped with aqueous 1 N HCl (10 mL) and extracted with diethyl ether (2 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by short column chromatography on silica gel using Et_2O yielded (E)-4-phenylbut-3-enal-2,2-d_2 **6a** (0.141 g, 95% yield).[10] **^{1}H NMR ($CDCl_3$, 600 MHz):** δ 9.72 (s, 1H), 7.57-7.49 (m, 5H), 6.48 (d, 1H, *J* = 6.6 Hz), 6.38-6.34 (m, 1H); **^{13}C NMR ($CDCl_3$, 377 MHz):** 198.2, 137.7, 134.7, 129.2, 128.1, 126.5, 119.2, 47.1.

Then, it is converted to the corresponding alkene via the Wittig reaction. To an oven dried Schlenk flask with a Teflon-coated magnetic stir bar was added Methyltriphenylphosphonium bromide (1.5 equiv.) and Schlenk tube was evacuated and backfilled with nitrogen three times before THF (0.5 M) was added. The reaction was cooled to -78 °C and ^{n}BuLi (1.6 M in hexane, 1.5 equiv.) was added dropwise. The reaction was warmed to room temperature and stirred for 1 h. (E)-4-phenylbut-3-enal-2,2-d_2 **6a** was dissolved in THF (1 M) and was added dropwise. The reaction was stirred overnight and afterwards quenched with sat. aq. NH_4Cl solution (5 mL per 1 mmol). The layers were sperarated and the aqueous layer was extracted with EtOAc (5 mL per 1 mmol). The combined organic layers were washed with sat. aq. NaCl (15 ml per 1 mmol), dried over Na_2SO_4 and the solvent was removed under reduced pressure. The product was purified by flash column chromatography on silica gel to yield (E)-(penta-1,4-dien-1-yl-3,3-d_2) benzene **7a** (0.130 g, 89% yield). **^{1}H NMR ($CDCl_3$, 600 MHz):** 7.39 (d, *J* = 9.6 Hz, 2H), 7.31 (t, *J* = 9.0 Hz, 2H), 7.23 (t, *J* = 9.6 Hz, 1H), 6.47 (d, *J* = 19.2 Hz, 1H), 6.28-6.23 (m, 1H), 6.03-5.91 (m, 1H), 5.20-5.13 (m, 2H). **^{13}C NMR ($CDCl_3$, 377 MHz):** δ 137.5, 136.4, 130.7, 128.6, 128.1, 127.3, 126.0, 115.9, 37.3.





A dry and nitrogen-flushed flask, equipped with a magnetic stirring bar and a septum, was charged with morpholine (0.18 mL, 2.1 mmol) and THF (10 mL). After cooling to 0 °C, DIBALH (2.0 mL,1.0 M in hexane, 2.0 mmol) was added dropwise and the mixture was stirred for 3 h at the same temperature. Ethyl 4-phenylbutanoate-2,2,3,4-d_4 **4a** (0.196 g, 1.0 mmol) was added slowly to the reaction mixture, which was stirred for 10 min. Then, DIBALH (1.5mL, 1.0 M in hexane, 1.5 mmol) was added and the mixture was stirred for 10 min again. The reaction was stopped with aqueous 1 N HCl (10 mL) and extracted with diethyl ether (2 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by short column chromatography on silica gel using Et_2O yielded 4-phenylbutanal-2,2,3,4-d_4 **8a** (0.141 g, 93% yield). **^{1}H NMR ($CDCl_3$, 600 MHz):** δ 9.76 (s, 1H), 7.29 (t, *J* = 10.8 Hz, 2H), 7.19 (m, 3H), 2.69-2.67 (t, *J* = 7.2 Hz, 1.2H), 2.23-2.20 (m, 0.28H), 1.88-1.86 (t, *J* = 6.6 Hz, 1.16H); **^{13}C NMR ($CDCl_3$, 377 MHz):** δ 201.8, 141.4, 128.2, 127.9, 126.0, 35.6, 28.3, 14.8.

Then, it is converted to the corresponding alkene via the Wittig reaction. To an oven dried Schlenk flask with a Teflon-coated magnetic stir bar was added Triphenylphosphine bromide (1.5 equiv.) and Schlenk tube was evacuated and backfilled with nitrogen three times before THF (0.5 M) was added. The reaction was cooled to -78 °C and ^{n}BuLi (1.6 M in hexane, 1.5 equiv.) was added dropwise. The reaction was warmed to room temperature and stirred for 1 h. 4-phenylbutanal-2,2,3,4-d_4 **8a** was dissolved in THF (1 M) and was added dropwise. The reaction was stirred overnight and afterwards quenched with sat. aq. NH_4Cl solution (5 mL per 1 mmol). The layers were sperarated and the aqueous layer was extracted with EtOAc (5 mL per 1 mmol). The combined organic layers were washed with sat. aq. NaCl (15 ml per 1 mmol), dried over Na_2SO_4 and the solvent was removed under reduced pressure. The product was purified by flash column chromatography on silica gel to yield (pent-4-en-1-yl-1,2,3,3-d_4) benzene **9a** (0.135 g, 90% yield). **^{1}H NMR ($CDCl_3$, 600 MHz):** δ 7.33-7.29 (m, 2H), 7.21-7.17 (m, 3H), 5.92-5.83 (m, 1H), 5.09-5.00 (m, 2H), 2.64-2.62 (t, *J* = 6.6 Hz, 1.2H), 2.28-2.25 (m, 0.32H), 1.92-1.89 (t, *J* = 7.2 Hz, 1.16H); **^{13}C NMR ($CDCl_3$, 377 MHz):** δ 142.6, 138.7, 128.6, 128.3, 125.8, 114.9, 35.5, 24.2, 14.5.

7. Cyclic voltammetry

The cyclic voltammetry was carried out with a Wuhai Corrtest CS310H workstation. A glassy-carbon electrode (3 mm-diameter) was used as the working electrode, a Pt wire (1 mm-diameter) was used as the auxiliary electrode and an Ag/AgCl electrode was used as a reference electrode. The measurements of Ethyl (E)-2,2-difluoro-4-phenylbut-3-enoate **1a** (0.1 M) were carried out at a scan rate of 100 mV s^{-1} in MeCN/$^nBu_4NI$ (0.1 M) (Figure **S3a**) or DMF/$^nBu_4NI$ (0.1 M) (Figure **S3b**).

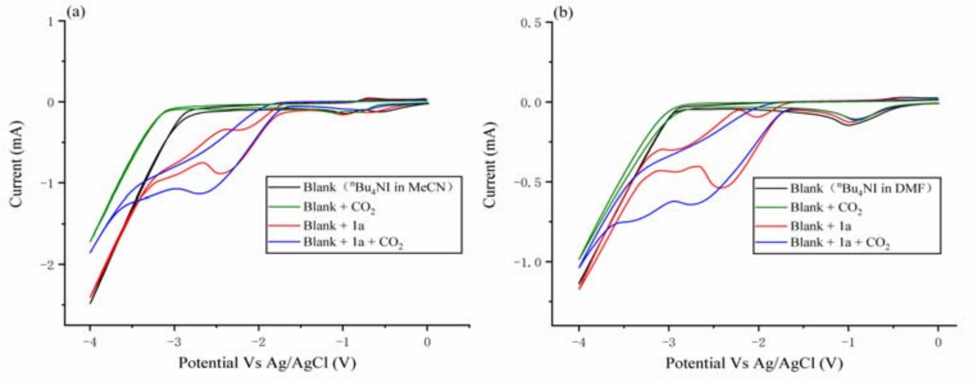
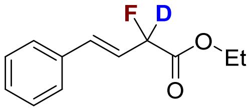
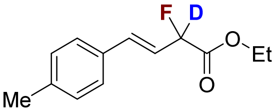


Figure S3. Cyclic voltammetry analysis of 1a in CH_3CN and DMF

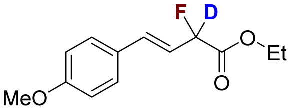
8. Characterization of products



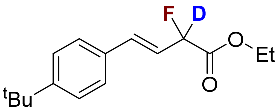
Ethyl (E)-2-fluoro-4-phenylbut-3-enoate-2-d (2a). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a colorless oil. Isolated yield: 13.8 mg, 66%. **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.39-7.38 (d, *J* = 7.2 Hz, 2H), 7.36 (s, 1H), 7.34-7.32 (t, *J* = 7.8 Hz, 2H), 6.89-6.86 (d, *J* = 16.2 Hz, 1H), 6.34-6.29 (t, *J* = 13.8 Hz, 1H), 4.35-4.29 (m, 2H), 1.36-1.34 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$):** δ 171.6 (t, *J* = 37.8 Hz), 136.9, 133.4 (t, *J* = 45.3 Hz), 128.5, 127.5, 126.3, 121.8, 88.6 (d, *J* = 33.2 Hz), 60.8, 14.2. **^{19}F NMR (377 MHz, $CDCl_3$):** δ -183.8 (s, 1F). **HRMS** (ESI): calculated for $C_{12}H_{13}DFO_2^+$ $[M+H]^+$: 210.1035; found: 210.1036.



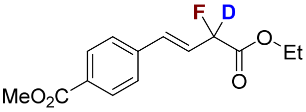
Ethyl (E)-2-fluoro-4-(p-tolyl)but-3-enoate-2-d (2b). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a colorless oil. Isolated yield: 14.1 mg, 63%. **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.32-7.31 (d, *J* = 7.8 Hz, 2H), 7.12-7.10 (d, *J* = 7.8 Hz, 2H), 6.77-6.74 (dd, *J* = 13.8, 6.6 Hz, 1H), 6.31-6.29 (m, 1H), 4.33-4.28 (m, 2H), 2.36 (s, 3H), 1.34-1.32 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$):** δ 170.8 (t, *J* = 37.8 Hz), 139.8, 137.6 (t, *J* = 48.3 Hz), 135.8, 133.6, 128.5, 126.4, 122.1, 89.2 (d, *J* = 31.7 Hz), 61.6, 14.3. **^{19}F NMR (377 MHz, $CDCl_3$):** δ -182.6 (s, 1F). **HRMS** (ESI): calculated for $C_{13}H_{15}DFO_2^+$ $[M+H]^+$: 224.1192; found: 224.1189.



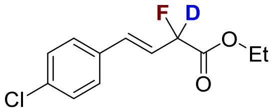
Ethyl (E)-2-fluoro-4-(4-methoxyphenyl)but-3-enoate-2-d (2c). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a colorless oil. Isolated yield: 16.0 mg, 67%. **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.38 (d, *J* = 13.2 Hz, 2H), 6.91 (d, *J* = 14.4 Hz, 2H), 6.83 (dd, *J* = 23.4, 4.8 Hz, 1H), 6.18 (d, *J* = 19.2 Hz, 1H), 4.34-4.27 (m, 2H), 3.85 (s, 3H), 1.32-1.30 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$):** δ 169.0 (t, *J* = 40.8 Hz), 160.6, 136.1 (t, *J* = 10.6 Hz), 128.3, 128.1, 118.8, 114.7, 89.2 (d, *J* = 34.7 Hz), 62.3, 55.8, 14.2. **^{19}F NMR (377 MHz, $CDCl_3$):** δ -181.3 (s, 1F). **HRMS** (ESI): calculated for $C_{13}H_{15}DFO_3^+$ $[M+H]^+$: 240.1141; found: 240.1142.



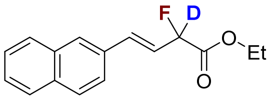
Ethyl (E)-4-(4-(tert-butyl)phenyl)-2-fluorobut-3-enoate-2-d (2d). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a white solid. Isolated yield: 15.9 mg, 60%. **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.40 (m, 4H), 6.86 (m, 1H), 6.31 (m, 1H), 4.34-4.27 (m, 2H), 1.37-1.35 (t, *J* = 7.2 Hz, 3H), 1.33 (s, 9H). **^{13}C NMR (151 MHz, $CDCl_3$):** δ 169.1 (t, *J* = 42.3 Hz), 153.1, 136.7 (t, *J* = 12.2 Hz), 131.4, 127.3, 126.0, 118.2, 89.2 (d, *J* = 31.7 Hz), 63.1, 34.7, 31.2, 14.0. **^{19}F NMR (377 MHz, $CDCl_3$):** δ -182.6 (s, 1F). **HRMS** (ESI): calculated for $C_{16}H_{21}DFO_2^+$ $[M+H]^+$: 266.1661; found: 266.1658.



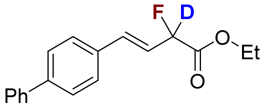
Methyl (E)-4-(4-ethoxy-3-fluoro-4-oxobut-1-en-1-yl-3-d)benzoate (2e). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a white solid. Isolated yield: 9.6 mg, 36%. **^{1}H NMR (600 MHz, $CDCl_3$):** δ 8.09 (d, *J* = 8.4 Hz, 2H), 7.52 (d, *J* = 8.4 Hz, 2H), 6.93 (d, *J* = 16.2 Hz, 1H), 6.47 (m, 1H), 4.37-4.30 (m, 2H), 3.97 (s, 3H), 1.37 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$):** δ 168.4 (t, *J* = 46.8 Hz), 166.9, 140.2, 133.8, 133.6, 130.3, 127.1, 123.8, 88.15 (d, *J* = 43.8 Hz), 62.2, 52.4, 14.1. **^{19}F NMR (377 MHz, $CDCl_3$):** δ -186.1 (s, 1F). **HRMS** (ESI): calculated for $C_{14}H_{15}DFO_4^+$ $[M+H]^+$: 268.1090; found: 268.1092.



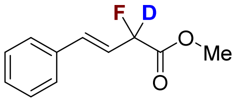
Ethyl (E)-4-(4-chlorophenyl)-2-fluorobut-3-enoate-2-d (2f). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a yellow oil. Isolated yield: 14.1 mg, 58%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.38-7.31 (m, 4H), 6.85 (dd, J = 14.4, 2.4 Hz, 1H), 6.31 (m, 1H), 4.34-4.27 (m, 2H), 1.34-1.32 (t, J = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 168.5 (t, J = 40.8 Hz), 135.1, 134.4 (d, J = 18.1 Hz), 133.9, 129.0, 128.3, 121.8, 88.7 (d, J = 46.8 Hz), 62.1, 14.4. **^{19}F NMR (377 MHz, CDCl$_3$):** δ -184.9 (s, 1F). **HRMS** (ESI): calculated for $C_{12}H_{12}DClFO_2^+$ $[M+H]^+$: 244.0645; found: 244.0652.



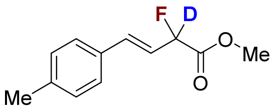
Ethyl (E)-2-fluoro-4-(naphthalen-2-yl)but-3-enoate-2-d (2g). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a white solid. Isolated yield: 15.3 mg, 59%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.85 (m, 4H), 7.61 (dd, J = 8.4, 1.8 Hz, 1H), 7.53-7.49 (m, 2H), 7.00 (dd, J = 16.2, 2.4 Hz, 1H), 6.42 (d, J = 7.2 Hz, 1H), 4.37-4.28 (m, 2H), 1.33-1.31 (t, J = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 170.2 (t, J = 19.6 Hz), 135.8, 133.7, 133.5, 132.9, 128.6, 128.3, 127.7, 126.6, 126.5, 123.4, 121.3 (d, J = 28.7 Hz), 88.6 (d, J = 42.3 Hz), 62.0, 14.1. **^{19}F NMR (377 MHz, CDCl$_3$):** δ -183.5 (s, 1F). **HRMS** (ESI): calculated for $C_{16}H_{15}DFO_2^+$ $[M+H]^+$: 260.1192; found: 260.1190.



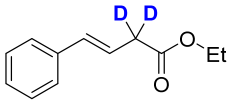
Ethyl (E)-4-([1,1'-biphenyl]-4-yl)-2-fluorobut-3-enoate-2-d (2h). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a colorless oil. Isolated yield: 19.4 mg, 68%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.63-7.59 (m, 4H), 7.53-7.49 (m, 4H), 7.37-7.35 (m, 1H), 6.91 (m, 1H), 6.34 (td, J = 16.8, 6.6 Hz, 1H), 4.35-4.27 (m, 2H), 1.34 (t, J = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 168.8 (t, J = 39.2 Hz), 141.5, 140.7, 135.5 (t, J = 18.1 Hz), 134.2, 129.2, 128.0, 127.7, 127.6, 127.3, 121.7 (d, J = 18.1 Hz), 88.7 (d, J = 43.8 Hz), 62.4, 14.2. **^{19}F NMR (377 MHz, CDCl$_3$):** δ -183.2 (s, 1F). **HRMS** (ESI): calculated for $C_{18}H_{17}DFO_2^+$ $[M+H]^+$: 286.1348; found: 286.1352.



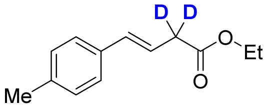
Methyl (E)-2-fluoro-4-phenylbut-3-enoate-2-d (2i). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a colorless oil. Isolated yield: 12.5 mg, 64%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.44 (d, J = 9.6 Hz, 2H), 7.37-7.32 (m, 3H), 6.85-6.82 (dd, J = 15.6, 4.8 Hz, 1H), 6.32-6.26 (m, 1H), 3.84 (s, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 168.6 (t, J = 27.2 Hz), 135.8, 135.4, 129.0, 128.7, 126.7, 120.8 (d, J = 18.1 Hz), 88.4 (d, J = 33.2 Hz), 52.9. **^{19}F NMR (377 MHz, CDCl$_3$):** δ -179.5 (s, 1F). **HRMS** (ESI): calculated for $C_{11}H_{11}DFO_2^+$ $[M+H]^+$: 196.0879; found: 196.0878.



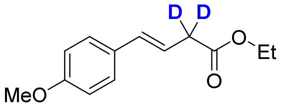
Methyl (E)-2-fluoro-4-(p-tolyl)but-3-enoate-2-d (2j). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a colorless oil. Isolated yield: 12.1 mg, 58%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.33 (d, J = 9.0 Hz, 2H), 7.16 (d, J = 9.0 Hz, 2H), 6.81 (dd, J = 14.4, 2.4 Hz, 1H), 6.26-6.17 (m, 1H), 3.84 (s, 3H), 2.35 (s, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 169.3 (t, J = 27.1 Hz), 138.7, 136.1 (t, J = 16.6 Hz), 132.3, 129.7, 126.8, 120.2 (d, J = 19.6 Hz), 89.1 (d, J = 37.8 Hz), 52.7, 21.1. **^{19}F NMR (377 MHz, CDCl$_3$):** δ -179.1 (s, 1F). **HRMS** (ESI): calculated for $C_{12}H_{13}DFO_2^+$ $[M+H]^+$: 210.1035; found: 210.1036.



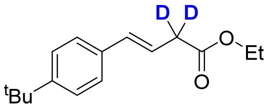
Ethyl (E)-4-phenylbut-3-enoate-2,2-d$_2$ (3a). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a colorless oil. Isolated yield: 18.0 mg, 94%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.38 (d, *J* = 7.2 Hz, 2H), 7.32 (m, 2H), 7.24-7.22 (t, *J* = 7.2, 7.8 Hz, 1H), 6.51 (d, *J* = 15.6 Hz, 1H), 6.34-6.29 (dd, *J* = 15.6, 6.6 Hz, 1H), 4.19-4.16 (q, *J* = 7.2 Hz, 2H), 1.30-1.27 (t, *J* = 13.8 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 171.6, 136.9, 133.4, 128.5, 127.5, 127.5, 126.3, 121.8, 60.8, 14.2. **HRMS** (ESI): calculated for $C_{12}H_{13}D_2O_2^+$ [M+H]$^+$: 193.1192; found: 193.1191.



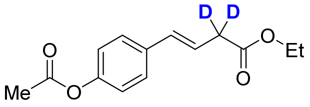
Ethyl (E)-4-(p-tolyl)but-3-enoate-2,2-d$_2$ (3b). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a colorless oil. Isolated yield: 17.7 mg, 86%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.27 (d, *J* = 8.4 Hz, 2H), 7.12 (d, *J* = 7.8 Hz, 2H), 6.47 (d, *J* = 16.2 Hz, 1H), 6.26-6.22 (dd, *J* = 15.6, 6.6 Hz, 1H), 4.19-4.15 (q, *J* = 6.6 Hz, 2H), 2.33 (s, 3H), 1.29-1.27 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 171.7, 137.3, 134.1, 133.3, 129.2, 129.2, 126.2, 120.7, 60.7, 21.2, 14.2. **HRMS** (ESI): calculated for $C_{13}H_{15}D_2O_2^+$ [M+H]$^+$: 207.1349; found: 207.1349.



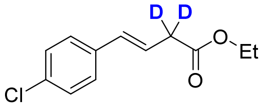
Ethyl (E)-4-(4-methoxyphenyl)but-3-enoate-2,2-d$_2$ (3c). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a colorless oil. Isolated yield: 17.8 mg, 80%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.34 (d, *J* = 8.4 Hz, 2H), 6.88 (d, *J* = 9.0 Hz, 2H), 6.47 (d, *J* = 15.6 Hz, 1H), 6.20-6.16 (dd, *J* = 16.2, 6.6 Hz, 1H), 4.21-4.17 (q, *J* = 7.2 Hz, 2H), 3.83 (s, 3H). 1.31-1.29 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 171.8, 159.2, 132.8, 129.7, 127.4, 127.4, 119.5, 113.9, 60.7, 55.3, 14.2. **HRMS** (ESI): calculated for $C_{13}H_{15}D_2O_3^+$ [M+H]$^+$: 223.1298; found: 223.1296.



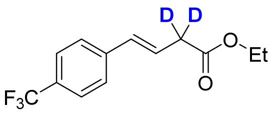
Ethyl (E)-4-(4-(tert-butyl)phenyl)but-3-enoate-2,2-d$_2$ (3d). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a white solid. Isolated yield: 20.5 mg, 83%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.37 (m, 4H), 6.51 (d, *J* = 15.6 Hz, 1H), 6.30-6.26 (dd, *J* = 16.2, 7.2 Hz, 1H), 4.21-4.17 (q, *J* = 7.2 Hz, 2H), 1.34 (s, 9H), 1.31-1.29 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 171.7, 150.6, 134.2, 133.1, 130.0 (d, *J* = 22.7 Hz), 128.2 (d, *J* = 22.7 Hz), 126.0, 125.5, 121.1 (d, *J* = 7.6 Hz), 60.7, 38.6 (d, *J* = 40.8 Hz), 34.6, 31.4 (d, *J* = 16.6 Hz), 14.2. **HRMS** (ESI): calculated for $C_{16}H_{21}D_2O_2^+$ [M+H]$^+$: 249.1818; found: 249.1822.



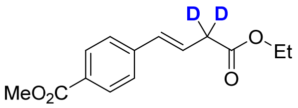
Ethyl (E)-4-(4-acetoxyphenyl)but-3-enoate-2,2-d$_2$ (3e). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a colorless oil. Isolated yield: 15.5 mg, 62%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.35 (d, *J* = 9.0 Hz, 2H), 7.04 (d, *J* = 7.8 Hz, 2H), 6.50 (d, *J* = 15.6 Hz, 1H), 6.28 (m, 1H), 4.19-4.15 (q, *J* = 7.2 Hz, 2H), 2.28 (s, 3H), 1.29-1.27 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 171.4, 169.5, 150.3, 134.6, 132.5, 129.8, 127.4, 122.1, 121.8, 60.7, 37.6, 21.3, 14.2. **HRMS** (ESI): calculated for $C_{14}H_{15}D_2O_4^+$ [M+H]$^+$: 251.1247; found: 251.1242.



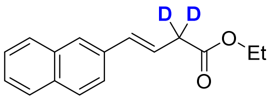
Ethyl (E)-4-(4-chlorophenyl)but-3-enoate-2,2-d$_2$ (3f). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a yellow oil. Isolated yield: 16.7 mg, 74%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.30 (m, 4H), 6.46 (d, *J* = 16.2 Hz, 1H), 6.30-6.26 (dd, *J* = 15.6, 6.6 Hz, 1H), 4.19-4.16 (q, *J* = 7.2 Hz, 2H), 1.29-1.27 (t, *J* = 6.6 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 171.4, 135.4, 133.22, 132.2, 129.0, 128.8, 127.5, 122.6 (d, *J* = 7.6 Hz), 60.9, 14.2. **HRMS** (ESI): calculated for $C_{12}H_{12}D_2ClO_2^+$ $[M+H]^+$: 227.0802; found: 227.0809.



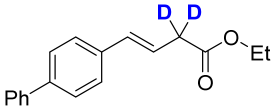
Ethyl (E)-4-(4-(trifluoromethyl)phenyl)but-3-enoate-2,2-d_2 (3g). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 10/1) as a yellow oil. Isolated yield: 15.3 mg, 59%. **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.61 (d, *J* = 7.2 Hz, 2H), 7.53 (d, *J* = 7.2 Hz, 2H), 6.92 (d, *J* = 16.8 Hz, 1H), 6.34-6.29 (dd, *J* = 13.8, 7.2 Hz, 1H), 4.21-4.18 (q, *J* = 7.2 Hz, 2H), 1.29-1.27 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$):** δ 172.5, 141.1, 133.3, 130.2, 127.4, 126.5, 125.6, 122.7, 60.6, 14.2. **^{19}F NMR (377 MHz, $CDCl_3$):** δ -61.9 (s, 3F). **HRMS** (ESI): calculated for $C_{13}H_{12}D_2F_3O_2^+$ $[M+H]^+$: 261.1066; found: 261.1071.



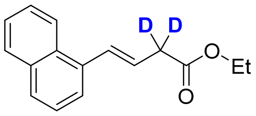
Methyl (E)-4-(4-ethoxy-4-oxobut-1-en-1-yl-3,3-d_2)benzoate (3h). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a white solid. Isolated yield: 12.7 mg, 51%. **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.93 (d, *J* = 8.4 Hz, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 6.55 (d, *J* = 16.2 Hz, 1H), 6.42 (m, 1H), 4.19-4.16 (q, *J* = 7.2 Hz, 2H), 3.89 (s, 3H), 1.30-1.28 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$):** δ 172.1, 168.8, 141.3, 131.7, 130.9, 130.1, 129.8, 129.8, 126.8, 61.2, 52.0, 32.3, 14.1. **HRMS** (ESI): calculated for $C_{14}H_{15}D_2O_4^+$ $[M+H]^+$: 251.1247; found: 251.1244.



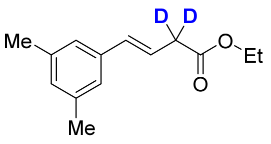
Ethyl (E)-4-(naphthalen-2-yl)but-3-enoate-2,2-d_2 (3i). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a white solid. Isolated yield: 20.3 mg, 84%. **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.82-7.81 (m, 3H), 7.80 (s, 1H), 7.64-7.63 (m, 1H), 7.55-7.52 (m, 2H), 7.25 (d, *J* = 2.4 Hz, 1H), 6.48 (m, 1H), 4.35-4.29 (q, *J* = 7.2 Hz, 2H), 1.42-1.40 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$):** δ 171.8, 134.4, 133.8, 133.7, 133.2, 128.4, 128.3, 127.8, 126.5, 126.3, 126.0, 123.7, 122.3, 60.9, 14.2. **HRMS** (ESI): calculated for $C_{16}H_{15}D_2O_2^+$ $[M+H]^+$: 243.1349; found: 243.1344.



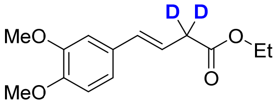
Ethyl (E)-4-([1,1'-biphenyl]-4-yl)but-3-enoate-2,2-d_2 (3j). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a colorless oil. Isolated yield: 22.7 mg, 85%. **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.63 (d, *J* = 7.2 Hz, 2H), 7.59 (d, *J* = 7.8 Hz, 2H), 7.48-7.45 (m, 4H), 7.38-7.35 (m, 1H), 6.57 (d, *J* = 16.2 Hz, 1H), 6.40-6.35 (m, 1H), 4.23-4.20 (q, *J* = 6.6 Hz, 2H), 1.33-1.31 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$):** δ 172.4, 141.2, 140.8, 136.5, 133.7, 129.1, 127.9, 127.9, 127.8, 127.1, 122.3, 60.8, 21.6, 14.3. **HRMS** (ESI): calculated for $C_{18}H_{17}D_2O_2^+$ $[M+H]^+$: 269.1505; found: 269.1504.



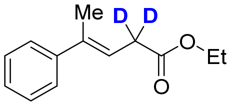
Ethyl (E)-4-(naphthalen-1-yl)but-3-enoate-2,2-d_2 (3k). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a colorless oil. Isolated yield: 19.3 mg, 80%. **^{1}H NMR (600 MHz, $CDCl_3$):** δ 8.12 (d, *J* = 7.8 Hz, 1H), 7.86 (m, 1H), 7.61 (m, 1H), 7.53 (m, 1H), 7.51 (m, 2H), 7.49 (m, 1H), 7.26-7.23 (d, *J* = 12.4 Hz, 1H), 6.35-6.32 (dd, *J* = 15.6, 7.2 Hz, 1H), 4.23-4.20 (q, *J* = 7.2 Hz, 2H), 1.32-1.30 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$):** δ 171.2, 136.7, 135.8, 133.2, 131.5, 130.6, 129.9, 127.8, 127.6, 126.9, 124.4, 123.3, 122.5, 60.8, 22.1, 14.2. **HRMS** (ESI): calculated for $C_{16}H_{15}D_2O_2^+$ $[M+H]^+$: 243.1349; found: 243.1350.



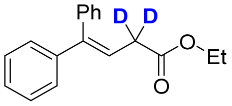
Ethyl (E)-4-(3,5-dimethylphenyl)but-3-enoate-2,2-d$_2$ (3l). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a colorless oil. Isolated yield: 14.7 mg, 67%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.0 (s, 2H), 6.88 (s, 1H), 6.44 (d, *J* = 16.2 Hz, 1H), 6.30 (m, 1H), 4.19-4.15 (m, 2H), 2.30 (s, 6H), 1.29-1.27 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 170.9, 138.5, 135.8, 130.4, 130.3, 124.0, 121.6, 61.3, 22.8, 21.4, 14.1. **HRMS** (ESI): calculated for $C_{14}H_{17}D_2O_2^+$ [M+H]$^+$: 221.1505; found: 221.1509.



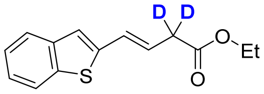
Ethyl (E)-4-(3,4-dimethoxyphenyl)but-3-enoate-2,2-d$_2$ (3m). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a yellow oil. Isolated yield: 15.6 mg, 62%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 6.93 (s, 1H), 6.90 (d, *J* = 8.4 Hz, 1H), 6.81 (d, *J* = 7.8 Hz, 1H), 6.44 (d, *J* = 15.6 Hz, 1H), 6.18-6.14 (dd, *J* = 16.2, 7.2 Hz, 1H), 4.19-4.15 (q, *J* = 6.6 Hz, 2H), 3.89 (d, *J* = 13.2 Hz, 6H), 1.29-1.27 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 171.8, 150.2, 149.7, 134.1, 133.6, 122.0, 120.3, 112.5, 60.8, 57.2, 21.3, 14.2. **HRMS** (ESI): calculated for $C_{14}H_{17}D_2O_4^+$ [M+H]$^+$: 253.1403; found: 253.1401.



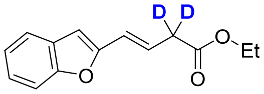
Ethyl (E)-4-phenylpent-3-enoate-2,2-d$_2$ (3n). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a yellow oil. Isolated yield: 15.4 mg, 75%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.39 (d, *J* = 1.8 Hz, 2H), 7.33 (t, *J* = 1.8 Hz, 2H), 7.25-7.23 (m, 1H), 5.95 (d, *J* = 8.4 Hz, 1H), 4.19-4.16 (q, *J* = 7.2 Hz, 2H), 2.07 (d, *J* = 1.2 Hz, 3H), 1.29-1.27 (t, *J* = 6.6 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 171.8, 143.6, 138.1, 128.5, 127.6, 126.2, 119.5, 61.0, 21.1, 16.3, 14.4. **HRMS** (ESI): calculated for $C_{13}H_{15}D_2O_2^+$ [M+H]$^+$: 207.1349; found: 207.1356.



Ethyl 4,4-diphenylbut-3-enoate-2,2-d$_2$ (3o). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a colorless oil. Isolated yield: 20.9 mg, 78%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.40 (m, 2H), 7.34 (m, 1H), 7.31 (m, 3H), 7.24-7.23 (m, 2H), 7.20 (d, *J* = 6.6 Hz, 2H), 6.27 (d, *J* = 7.8 Hz, 1H), 4.17-4.14 (q, *J* = 6.6 Hz, 2H), 1.28-1.25 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 171.9, 144.7 (d, *J* = 6.0 Hz), 143.0, 142.0, 139.3, 129.8, 128.6 (t, *J* = 37.8 Hz), 127.7 (t, *J* = 146.5 Hz), 126.8, 120.5, 60.7, 14.2 (d, *J* = 80.0 Hz). **HRMS** (ESI): calculated for $C_{18}H_{17}D_2O_2^+$ [M+H]$^+$: 269.1505; found: 269.1504.

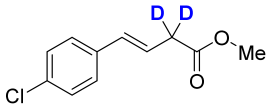


Ethyl (E)-4-(benzo[b]thiophen-2-yl)but-3-enoate-2,2-d$_2$ (3p). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a colorless oil. Isolated yield: 14.8 mg, 60%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.75 (d, *J* = 6.6 Hz, 1H), 7.67 (d, *J* = 6.6 Hz, 1H), 7.34–7.30 (m, 2H), 7.15 (s, 1H), 6.73–6.70 (d, *J* = 16.8 Hz, 1H), 6.28–6.22 (m, 1H), 4.21–4.17 (q, *J* = 7.2 Hz, 2H), 1.31-1.29 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 172.3, 145.1, 141.2, 139.3, 128.8, 128.1, 125.0, 123.7, 123.1, 122.8, 112.1, 61.2, 23.3, 14.1. **HRMS** (ESI): calculated for $C_{14}H_{13}D_2O_2S^+$ [M+H]$^+$: 249.0913; found: 249.0917.

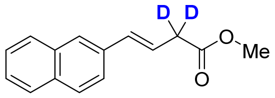


Ethyl (E)-4-(benzofuran-2-yl)but-3-enoate-2,2-d$_2$ (3q). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a colorless oil. Isolated yield: 12.1 mg, 52%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.61 (m, 1H), 7.52 (d, *J* = 7.8 Hz, 1H), 7.31 (m, 1H), 7.24 (m, 1H), 6.81 (s, 1H), 6.58 (d, *J* = 16.2 Hz, 1H), 6.30 (d, 7.8 Hz, 1H), 4.20-4.17 (q, *J* = 7.2 Hz, 2H), 1.33-1.31 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 171.6, 158.6, 158.5, 129.7, 125.6, 124.4, 121.6, 120.8, 113.6, 109.9, 61.4, 21.7, 14.1. **HRMS** (ESI): calculated for $C_{14}H_{13}D_2O_3^+$ [M+H]$^+$:

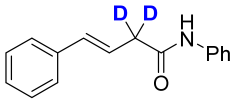
233.1141; found: 233.1137.



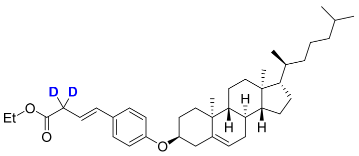
Methyl (E)-4-(4-chlorophenyl)but-3-enoate-2,2-d$_2$ (3r). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a yellow oil. Isolated yield: 16.5 mg, 78%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.30-7.28 (m, 4H), 6.48 (d, *J* = 18.0 Hz, 1H), 6.31 (m, 1H), 3.73 (s, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 172.2, 135.5, 133.3, 132.6, 128.9, 127.7, 122.7, 52.5, 23.1. **HRMS** (ESI): calculated for $C_{11}H_{10}D_2ClO_2^+$ [M+H]$^+$: 213.0646; found: 213.0651.



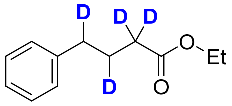
Methyl (E)-4-(naphthalen-2-yl)but-3-enoate-2,2-d$_2$ (3s). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a colorless oil. Isolated yield: 17.5 mg, 77%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.81 (m, 3H), 7.76-7.71 (m, 1H), 7.63-7.61 (m, 1H), 7.54-7.46 (m, 2H), 6.67 (d, *J* = 15.6 Hz, 1H), 6.48 (dd, *J* = 16.2, 7.2 Hz, 1H), 3.79 (s, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 172.6, 134.7, 134.1, 133.5, 131.6, 128.8, 128.2, 127.9, 126.6, 126.3, 125.9, 123.7, 122.4, 52.1, 23.3. **HRMS** (ESI): calculated for $C_{15}H_{13}D_2O_2^+$ [M+H]$^+$: 229.1192; found: 229.1192.



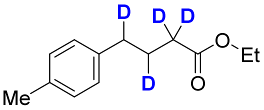
(E)-N,4-diphenylbut-3-enamide-2,2-d$_2$ (3t). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a yellow oil. Isolated yield: 14.5 mg, 61%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.53-7.51 (d, *J* = 8.4 Hz, 1H), 7.45-7.42 (m, 2H), 7.34-7.21 (m, 8H), 6.52 (dd, *J* = 15.6, 1.2 Hz, 1H), 6.28 (dd, *J* = 15.6, 6.0 Hz, 1H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 169.4, 137.6, 136.3, 135.4, 129.1, 128.6, 127.8, 126.6, 124.5, 122.0, 120.1, 21.7. **HRMS** (ESI): calculated for $C_{16}H_{14}D_2NO^+$ [M+H]$^+$: 240.1352; found: 240.1355.



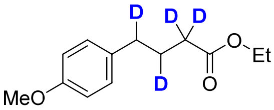
Ethyl(E)-4-(4-(((3S,8R,9R,10S,13S,14R,17S)-10,13-dimethyl-17-((S)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl)oxy)phenyl)but-3-enoate-2,2-d$_2$ (3u). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 20/1) as a colorless oil. Isolated yield: 27.6 mg, 48%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.61 (d, *J* = 10.8 Hz, 2H), 6.88 (d, *J* = 9.6 Hz, 2H), 6.58 (d, *J* = 13.2 Hz, 1H), 6.31 (d, *J* = 12.6 Hz, 1H), 5.28 (t, *J* = 6.6 Hz, 1H), 4.24-4.21 (q, *J* = 7.2 Hz, 2H), 3.63 (m, 1H), 2.44-2.41 (m, 1H), 2.19-2.14 (m, 2H), 1.94-1.90 (m, 3H), 1.75-1.62 (m, 6H), 1.58-1.53 (m, 4H), 1.53-1.50 (m, 2H), 1.50-1.45 (m, 2H), 1.38-1.33 (m, 2H), 1.31-1.25 (m, 1H), 1.19-1.17 (m, 5H), 1.11-1.02 (m, 3H), 0.94 (s, 3H), 0.88-0.87 (m, 9H), 0.84 (s, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 170.6, 156.8, 141.1, 131.2, 130.0, 128.6, 121.8, 121.1, 81.8, 62.1 56.5, 56.2, 50.9, 42.8, 40.0, 39.3, 37.7, 37.5, 36.2, 36.0, 32.2, 32.0, 29.3, 28.2, 26.4, 25.8, 24.6, 23.3, 21.4, 21.1, 19.4, 14.1, 12.1. **HRMS** (ESI): calculated for $C_{39}H_{57}D_2O_3^+$ [M+H]$^+$: 577.4584; found: 577.4586.



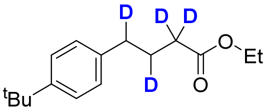
Ethyl 4-phenylbutanoate-2,2,3,4-d$_4$ (4a). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 20/1) as a colorless oil. Isolated yield: 16.0 mg, 82%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.29-7.27 (m, 2H), 7.20-7.17 (m, 3H), 4.14-4.11 (q, *J* = 7.2 Hz, 2H), 2.65-2.62 (t, *J* = 7.8 Hz, 1.2H), 2.32-2.29 (t, *J* = 7.8 Hz, 0.28H), 1.94-1.91 (t, *J* = 8.4 Hz, 1.11H), 1.27 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 173.6, 141.6, 128.6, 128.5, 125.9, 60.6, 34.1, 21.4, 17.4, 14.2. **HRMS** (ESI): calculated for $C_{12}H_{13}D_4O_2^+$ [M+H]$^+$: 197.1474; found: 197.1477.



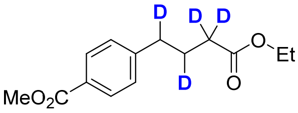
Ethyl 4-(p-tolyl)butanoate-2,2,3,4-d$_4$ (4b). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 20/1) as a colorless oil. Isolated yield: 17.8 mg, 85%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.16 (m, 4H), 4.21-4.18 (q, *J* = 7.2 Hz, 2H), 2.69-2.66 (t, *J* = 7.8 Hz, 1.16H), 2.38-2.34 (t, *J* = 8.4 Hz, 3.28H), 2.01-1.98 (t, *J* = 8.4 Hz, 1.1H), 1.31-1.28 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 173.7, 138.5, 135.4, 129.2, 128.5, 60.4, 34.4, 22.6, 21.2, 17.6, 14.3. **HRMS** (ESI): calculated for $C_{13}H_{15}D_4O_2^+$ [M+H]$^+$: 211.1631; found: 211.1629.



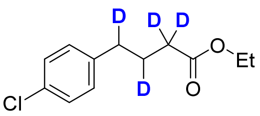
Ethyl 4-(4-methoxyphenyl)butanoate-2,2,3,4-d$_4$ (4c). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 20/1) as a colorless oil. Isolated yield: 18.1 mg, 80%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.10 (d, *J* = 10.8 Hz, 2H), 6.85 (d, *J* = 6.6 Hz, 2H), 4.15-4.12 (q, *J* = 7.2 Hz, 2H), 3.79 (s, 3H), 2.59-2.57 (t, *J* = 7.2 Hz, 1.15H), 2.30-2.28 (t, *J* = 7.2 Hz, 0.24H), 1.96-1.93 (t, *J* = 7.8 Hz, 1.11H), 1.28-1.25 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 173.8, 157.9, 133.7, 129.3, 113.9, 60.3, 55.6, 35.1, 21.3, 17.4, 14.2. **HRMS** (ESI): calculated for $C_{13}H_{15}D_4O_3^+$ [M+H]$^+$: 227.1580; found: 227.1579.



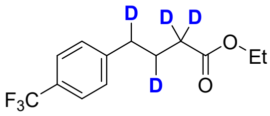
Ethyl 4-(4-(tert-butyl)phenyl)butanoate-2,2,3,4-d$_4$ (4d). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 20/1) as a colorless oil. Isolated yield: 20.7 mg, 82%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.23-7.21 (d, *J* = 10.8 Hz, 2H), 7.05-7.03 (d, *J* = 10.2 Hz, 2H), 4.09-4.05 (q, *J* = 7.2 Hz, 2H), 2.56-2.53 (t, *J* = 7.2 Hz, 1.2H), 2.26-2.23 (d, *J* = 7.8 Hz, 0.24H), 1.90-1.87 (t, *J* = 7.8 Hz, 1.14H), 1.24 (s, 9H), 1.21-1.19 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 173.4, 148.7, 138.5, 128.3, 125.4, 60.1, 34.7 (d, *J* = 39.3 Hz), 31.5, 21.7, 17.8, 14.0. **HRMS** (ESI): calculated for $C_{16}H_{21}D_4O_2^+$ [M+H]$^+$: 253.2100; found: 253.2104.



Methyl 4-(4-ethoxy-4-oxobutyl-1,2,3,3-d$_4$)benzoate (4e). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 20/1) as a colorless oil. Isolated yield: 11.2 mg, 44%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.98 (d, *J* = 6.6 Hz, 2H), 7.28 (d, *J* = 7.2 Hz, 2H), 4.17-4.13 (q, *J* = 7.2 Hz, 2H), 3.93 (s, 3H), 2.71-2.68 (t, *J* = 7.8 Hz, 1.24H), 2.33-2.31 (d, *J* = 7.2 Hz, 0.4H), 2.00-1.98 (t, *J* = 7.2 Hz, 1.21H), 1.27-1.24 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 173.5, 167.3, 147.2, 129.9, 128.6, 128.1, 60.3, 52.2, 35.1, 21.6, 17.4, 14.2. **HRMS** (ESI): calculated for $C_{14}H_{15}D_4O_4^+$ [M+H]$^+$: 255.1529; found: 255.1527.

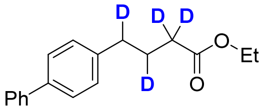


Ethyl 4-(4-chlorophenyl)butanoate-2,2,3,4-d$_4$ (4f). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 20/1) as a colorless oil. Isolated yield: 16.1 mg, 70%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.27-7.25 (m, 2H), 7.13-7.11 (m, 2H), 4.12-4.09 (q, *J* = 7.2 Hz, 2H), 2.61-2.59 (t, *J* = 7.8 Hz, 1.2H), 2.29-2.27 (t, *J* = 7.8 Hz, 0.44H), 1.93-1.90 (t, *J* = 8.4 Hz, 1.19H), 1.26-1.23 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 173.6, 139.8, 131.8, 130.2, 128.8, 60.6, 34.3, 21.6, 17.4, 14.3. **HRMS** (ESI): calculated for $C_{12}H_{12}D_4ClO_2^+$ [M+H]$^+$: 231.1084; found: 231.1081.

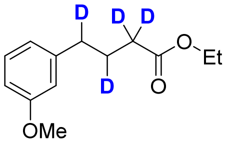


Ethyl 4-(4-(trifluoromethyl)phenyl)butanoate-2,2,3,4-d$_4$ (4g). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a yellow oil. Isolated yield: 14.2 mg, 54%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.58 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 6.0 Hz, 2H), 4.19-4.15 (q, *J* = 6.6 Hz, 2H), 2.75-2.72 (t, *J*

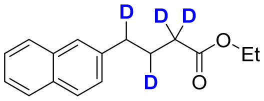
= 8.4 Hz, 1.25H), 2.38-2.35 (t, *J* = 7.8 Hz, 0.42H), 2.02-1.99 (t, *J* = 9.0 Hz, 1.22H), 1.30-1.27 (t, *J* = 7.8 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 173.3, 145.7, 129.1, 128.3, 125.5, 123.6, 121.3, 60.4, 35.1, 21.7, 17.7, 14.3. **^{19}F NMR (377 MHz, CDCl$_3$):** δ -62.7 (s, 3F). **HRMS** (ESI): calculated for $C_{13}H_{12}D_4F_3O_2^+$ [M+H]$^+$: 265.1348; found: 265.1351.



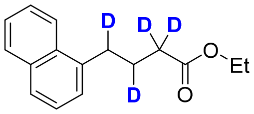
Ethyl 4-([1,1'-biphenyl]-4-yl)butanoate-2,2,3,4-d_4 (4h). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a colorless oil. Isolated yield: 18.7 mg, 69%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.62 (m, 2H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.45-7.43 (m, 2H), 7.35-7.33 (m, 1H), 7.31-7.26 (m, 2H), 4.16-4.13 (q, *J* = 7.2 Hz, 2H), 2.72-2.70 (t, *J* = 7.2 Hz, 1.2H), 2.38-2.35 (t, *J* = 7.8 Hz, 0.36H), 2.03-2.00 (t, *J* = 7.8 Hz, 1.2H), 1.29-1.27 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 173.5, 141.3, 140.9, 139.3, 128.9, 128.7, 127.2 (m), 127.0, 60.4, 34.8, 21.6, 17.8, 14.4. **HRMS** (ESI): calculated for $C_{18}H_{17}D_4O_2^+$ [M+H]$^+$: 273.1787; found: 273.1788.



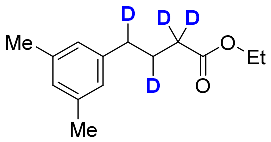
Ethyl 4-(3-methoxyphenyl)butanoate-2,2,3,4-d_4 (4i). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 20/1) as a colorless oil. Isolated yield: 16.5 mg, 73%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.22-7.18 (m, 1H), 6.79-6.75 (m, 3H), 4.15-4.11 (t, *J* = 7.8 Hz, 2H), 3.79 (s, 3H), 2.65-2.62 (t, *J* = 6.6 Hz, 1.2H), 2.33-2.31 (t, *J* = 7.2 Hz, 0.38H), 1.99-1.96 (t, *J* = 7.2 Hz, 1.17H), 1.26-1.24 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 173.6, 159.9, 143.2, 129.4, 121.1, 114.4, 111.2, 60.5, 55.6, 35.3, 21.7, 17.5, 14.2. **HRMS** (ESI): calculated for $C_{13}H_{15}D_4O_3^+$ [M+H]$^+$: 227.1580; found: 227.1584.



Ethyl 4-(naphthalen-2-yl)butanoate-2,2,3,4-d_4 (4j). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 20/1) as a colorless oil. Isolated yield: 17.2 mg, 70%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.81 (m, 3H), 7.59 (s, 1H), 7.47-7.40 (m, 2H), 7.33-7.31 (m, 1H), 4.15-4.11 (q, *J* = 7.2 Hz, 2H), 2.82-2.79 (d, *J* = 7.8 Hz, 1.18H), 2.35-2.33 (t, *J* = 7.2 Hz, 0.32H), 2.05-2.03 (t, *J* = 7.2 Hz, 1.18H), 1.26-1.24 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 173.7, 139.1, 133.8, 132.2, 128.2, 127.7 (m), 126.8, 126.1, 125.5, 60.3, 35.7, 21.8, 17.9, 14.2. **HRMS** (ESI): calculated for $C_{16}H_{15}D_4O_2^+$ [M+H]$^+$: 247.1631; found: 247.1635.

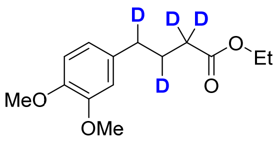


Ethyl 4-(naphthalen-1-yl)butanoate-2,2,3,4-d_4 (4k). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 20/1) as a colorless oil. Isolated yield: 19.4 mg, 79%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 8.06 (d, *J* = 8.4 Hz, 1H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.72 (d, *J* = 8.4 Hz, 1H), 7.52-7.46 (m, 2H), 7.39 (t, *J* = 7.8 Hz, 1H), 7.33 (d, *J* = 6.6 Hz, 1H), 4.16-4.13 (q, *J* = 7.2 Hz, 2H), 3.11-3.07 (t, *J* = 7.8 Hz, 1.19H), 2.41-2.39 (t, *J* = 7.2 Hz, 0.24H), 2.09-2.07 (t, *J* = 7.2 Hz, 1.17H), 1.27-1.25 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 173.5, 137.6, 134.3, 132.1, 129.0, 127.2, 126.4, 125.9, 125.4, 123.8, 60.6, 35.2, 22.1, 17.8, 14.4. **HRMS** (ESI): calculated for $C_{16}H_{15}D_4O_2^+$ [M+H]$^+$: 247.1631; found: 247.1633.

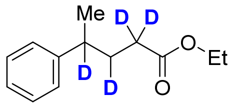


Ethyl 4-(3,5-dimethylphenyl)butanoate-2,2,3,4-d_4 (4l). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 20/1) as a colorless oil. Isolated yield: 16.3 mg, 73%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 6.85-6.81 (d, *J* = 21.6 Hz, 3H), 4.18-4.14 (q, *J* = 7.8 Hz, 2H), 2.59-2.57 (t, *J* = 7.2 Hz, 1.2H), 2.35-2.32 (t, *J* = 6.6 Hz, 0.28H), 2.30 (s, 6H), 1.97-1.95 (t, *J* = 7.8 Hz, 1.18H), 1.28-1.26 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 173.6, 141.3, 137.9, 127.7, 126.4, 60.8, 34.4, 21.6, 21.2, 17.1, 14.2. **HRMS** (ESI):

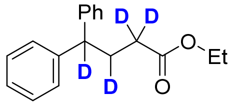
calculated for $C_{14}H_{17}D_4O_2^+$ [M+H]$^+$: 225.1787; found: 225.1784.



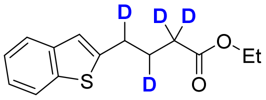
Ethyl 4-(3,4-dimethoxyphenyl)butanoate-2,2,3,4-d_4 (4m). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 20/1) as a colorless oil. Isolated yield: 17.6 mg, 69%. **^{1}H NMR (600 MHz, $CDCl_3$):** δ 6.91-6.86 (m, 3H), 4.16-4.12 (q, *J* = 7.2 Hz, 2H), 3.87 (s, 6H), 2.71-2.69 (t, *J* = 6.6 Hz, 1.2H), 2.52-2.49 (t, *J* = 7.8 Hz, 0.34H), 2.02-2.00 (t, *J* = 7.2 Hz, 1.22H), 1.29-1.27 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$):** δ 173.9, 149.9, 147.3, 132.0, 121.5, 113.4, 112.9, 61.1, 56.3, 33.8, 21.9, 17.6, 14.2. **HRMS** (ESI): calculated for $C_{14}H_{17}D_4O_4^+$ [M+H]$^+$: 257.1685; found: 257.1688.



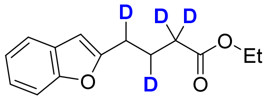
Ethyl 4-phenylpentanoate-2,2,3,4-d_4 (4n). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 20/1) as a colorless oil. Isolated yield: 13.0 mg, 62%. **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.35-7.31 (m, 2H), 7.24-7.21 (m, 3H), 4.14-4.10 (q, *J* = 7.2 Hz, 2H), 2.82-2.76 (m, 0.18H), 2.24-2.21 (t, *J* = 8.4 Hz, 0.32H), 1.98-1.95 (t, *J* = 7.8 Hz, 1.11H), 1.32-1.31 (d, *J* = 6.6 Hz, 3H), 1.27-1.25 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$):** δ 173.9, 146.5, 128.5, 127.0, 126.5, 126.2, 60.2, 25.8, 20.9, 20.7, 20.1, 14.2. **HRMS** (ESI): calculated for $C_{13}H_{15}D_4O_2^+$ [M+H]$^+$: 211.1631; found: 211.1633.



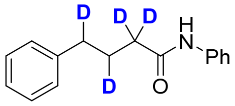
Ethyl 4,4-diphenylbutanoate-2,2,3,4-d_4 (4o). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 20/1) as a colorless oil. Isolated yield: 17.9 mg, 66%. **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.30-7.22 (m, 8H), 7.19 (m, 2H), 4.12-4.09 (q, *J* = 7.2 Hz, 2H), 3.96-3.94 (t, *J* = 6.6 Hz, 0.21H), 2.42-2.39 (t, *J* = 9.0 Hz, 0.4H), 2.29-2.26 (t, *J* = 7.8 Hz, 1.18H), 1.25-1.22 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$):** δ 173.5, 144.3, 128.6, 127.9, 126.5, 60.4, 33.1, 29.6, 17.7, 14.3. **HRMS** (ESI): calculated for $C_{18}H_{17}D_4O_2^+$ [M+H]$^+$: 273.1787; found: 273.1786.



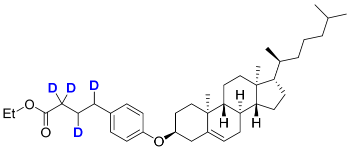
Ethyl 4-(benzo[b]thiophen-2-yl)butanoate-2,2,3,4-d_4 (4p). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a colorless oil. Isolated yield: 11.8 mg, 47%. **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.85 (m, 1H), 7.79 (m, 1H), 7.39 (s, 1H), 7.34-7.31 (m, 2H), 4.19-4.15 (q, *J* = 7.2 Hz, 2H), 2.65-2.62 (t, *J* = 6.6 Hz, 1.26H), 2.30-2.28 (t, *J* = 7.2 Hz, 0.36H), 1.97-1.95 (t, *J* = 6.6 Hz, 1.24H), 1.36-1.33 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$):** δ 172.2, 146.3, 139.4, 139.3, 124.5 (d, *J* = 15.1 Hz), 123.3, 122.9, 118.1, 61.0, 34.7, 22.1, 17.9, 14.1. **HRMS** (ESI): calculated for $C_{14}H_{13}D_4O_2S^+$ [M+H]$^+$: 253.1195; found: 253.1199.



Ethyl 4-(benzofuran-2-yl)butanoate-2,2,3,4-d_4 (4q). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 15/1) as a colorless oil. Isolated yield: 10.6 mg, 45%. **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.59 (m, 1H), 7.50 (m, 1H), 7.29-7.24 (m, 2H), 6.74 (s, 1H), 4.17-4.13 (q, *J* = 7.8 Hz, 2H), 2.72-2.69 (t, *J* = 7.2 Hz, 1.24H), 2.29-2.27 (t, *J* = 6.6 Hz, 0.32H), 1.92-1.90 (t, *J* = 6.6 Hz, 1.2H), 1.27-1.25 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$):** δ 171.7, 160.1, 154.0, 127.2, 124.9, 123.5, 121.0, 111.7, 103.3, 61.5, 35.8, 20.4, 16.5, 14.1. **HRMS** (ESI): calculated for $C_{14}H_{13}D_4O_3^+$ [M+H]$^+$: 237.1423; found: 237.1419.



N,4-diphenylbutanamide-2,2,3,4-d_4 (4r). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 20/1) as a yellow oil. Isolated yield: 16.3 mg, 67%. **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.51-7.49 (d, *J* = 7.8 Hz, 2H), 7.35 (m, 4H), 7.20 (m, 4H), 7.10 (m, 1H), 2.69-2.67 (t, *J* = 7.2 Hz, 1.2H), 2.34-2.32 (t, *J* = 7.8 Hz, 0.36H), 2.07-2.05 (t, *J* = 7.2 Hz, 1.32H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 170.9, 141.3, 137.7, 129.1, 128.5, 128.3, 126.3, 124.5, 119.9, 31.9, 21.5, 18.0. **HRMS** (ESI): calculated for $C_{16}H_{14}D_4NO^+$ [M+H]$^+$: 244.1634; found: 244.1638.



Ethyl4-(4-(((3S,8R,9R,10S,13S,14R,17S)-10,13-dimethyl-17-((S)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl)oxy)phenyl)butanoate-2,2,3,4-d$_4$ (4s). The title compound was isolated through preparative TLC on silica gel (*n*-Hexane/EtOAc = 20/1) as a colorless oil. Isolated yield: 23.8 mg, 41%. **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.18 (d, *J* = 6.0 Hz, 2H), 6.82 (d, *J* = 6.6 Hz, 2H), 5.26 (t, *J* = 7.2 Hz, 1H), 4.21-4.17 (q, *J* = 7.2 Hz, 2H), 3.65 (m, 1H), 2.73-2.71 (t, *J* = 7.2 Hz, 1.18H), 2.43 (m, 1H), 2.33-2.30 (t, *J* = 7.8 Hz, 0.32H), 2.19 (m, 2H), 2.02-2.00 (t, *J* = 6.6 Hz, 1.18H), 1.94-1.90 (m, 5H), 1.78-1.73 (m, 2H), 1.65-1.62 (m, 4H), 1.59-1.50 (m, 3H), 1.38-1.27 (m, 6H), 1.25-1.19 (m, 5H), 1.11-1.08 (m, 1H), 1.06-1.04 (m, 2H), 0.93 (s, 3H), 0.88-0.86 (m, 9H), 0.83 (s, 3H). **^{13}C NMR (151 MHz, CDCl$_3$):** δ 172.3, 155.1, 141.1, 130.4, 129.2, 121.9, 114.7, 81.9, 61.1, 56.6, 51.0, 42.9, 40.0, 39.4, 37.9, 36.6, 32.2, 31.9, 29.3, 28.2, 26.5, 26.1, 24.7, 23.4, 21.2, 19.5, 17.6, 17.4, 14.1, 12.0. **HRMS** (ESI): calculated for $C_{39}H_{57}D_4O_3^+$ [M+H]$^+$: 581.4866; found: 581.4862.

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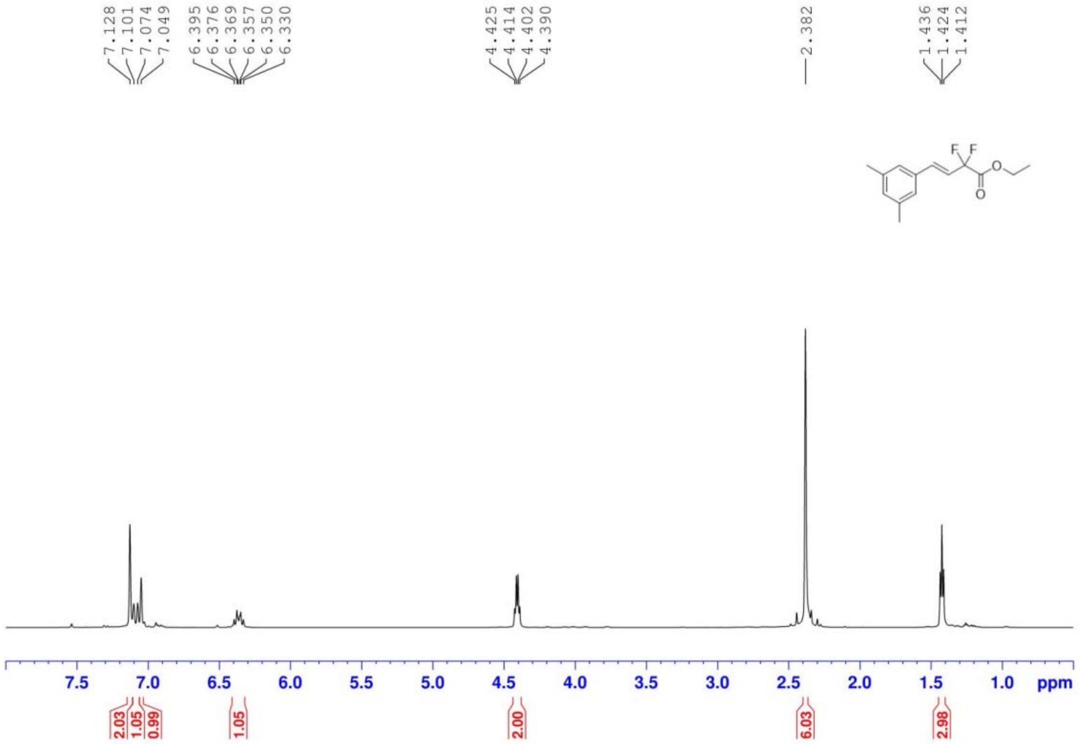
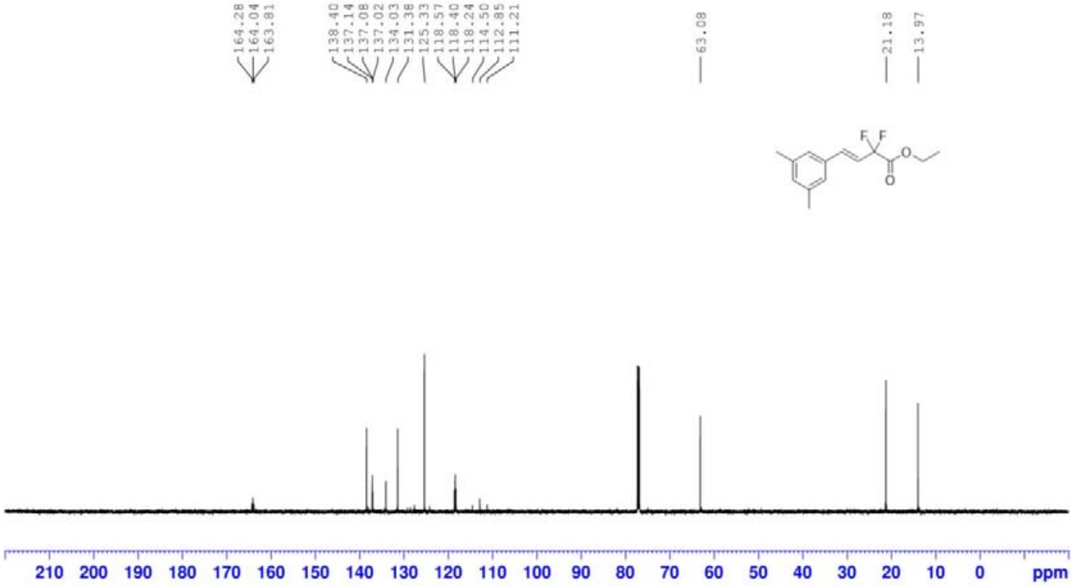
10. NMR Spectra

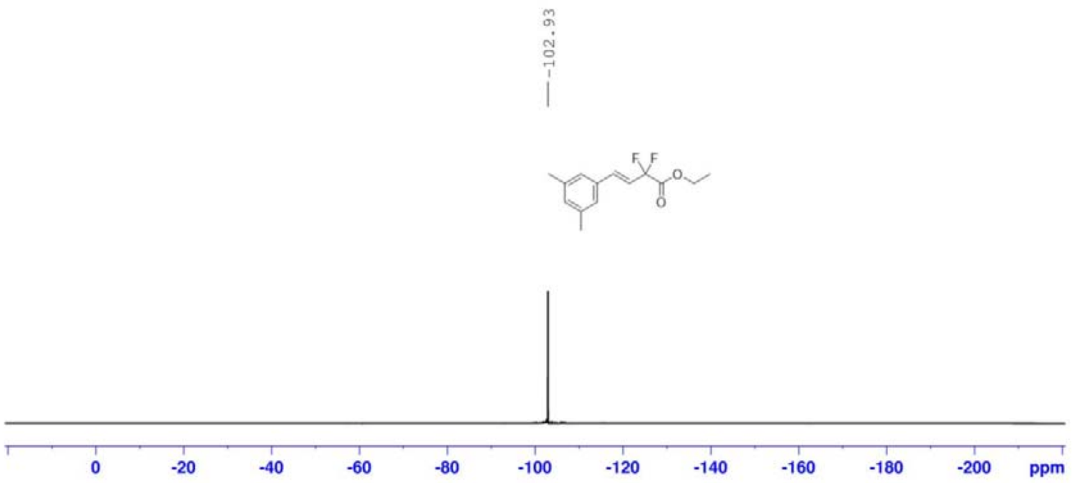
^{1}H NMR Spectra of **1l** (600 MHz, CDCl$_3$)



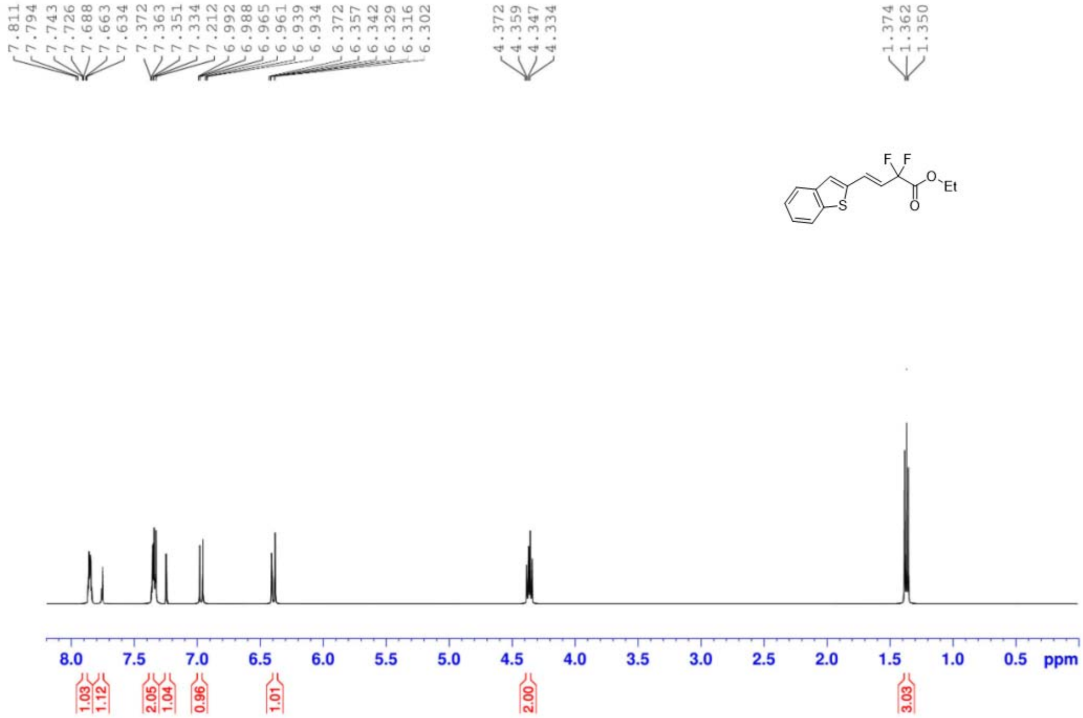
^{13}C NMR Spectra of **1l** (151 MHz, CDCl$_3$)



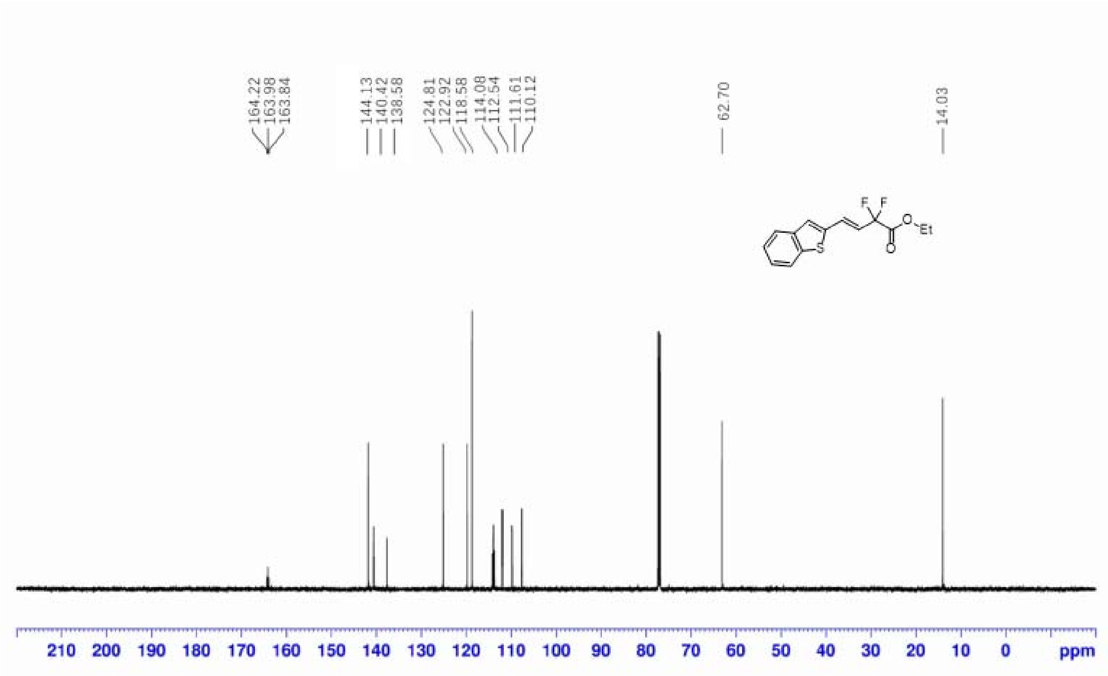
^{19}F NMR Spectra of **1l** (377 MHz, CDCl$_3$)



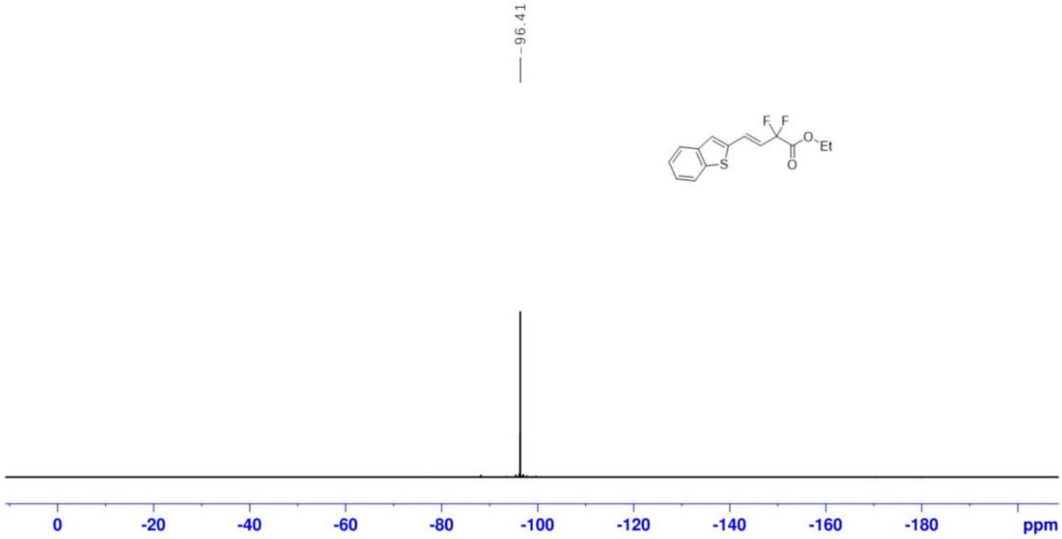
^{1}H NMR Spectra of **1p** (600 MHz, $CDCl_3$)



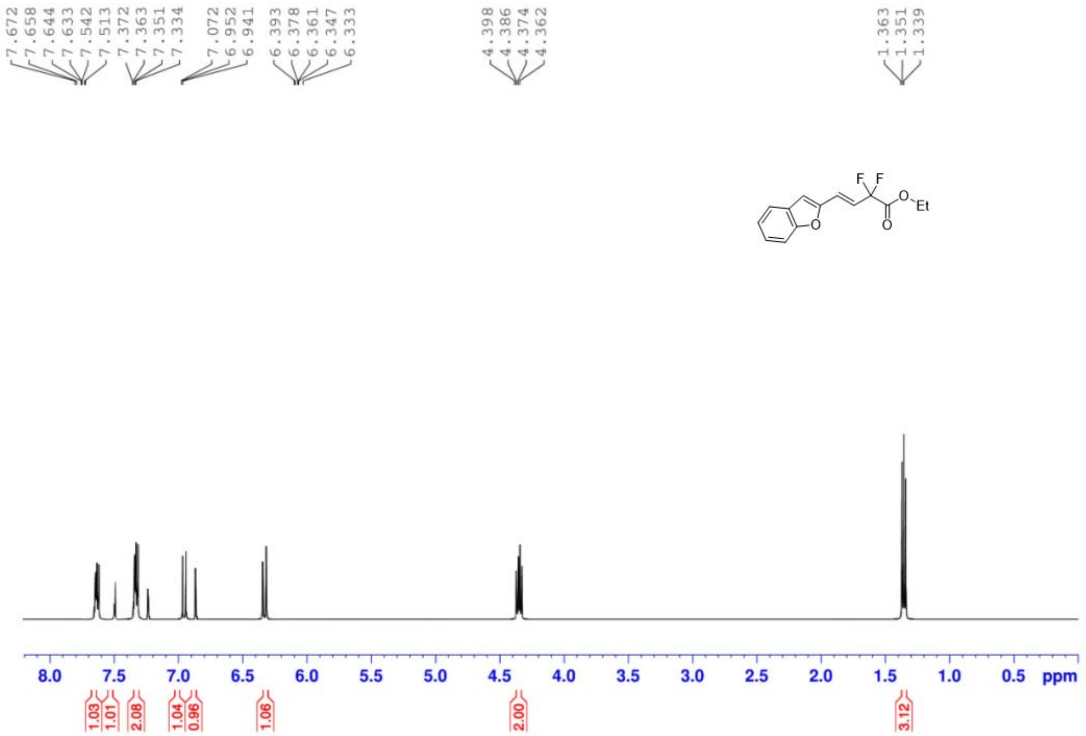
^{13}C NMR Spectra of **1p** (151 MHz, $CDCl_3$)



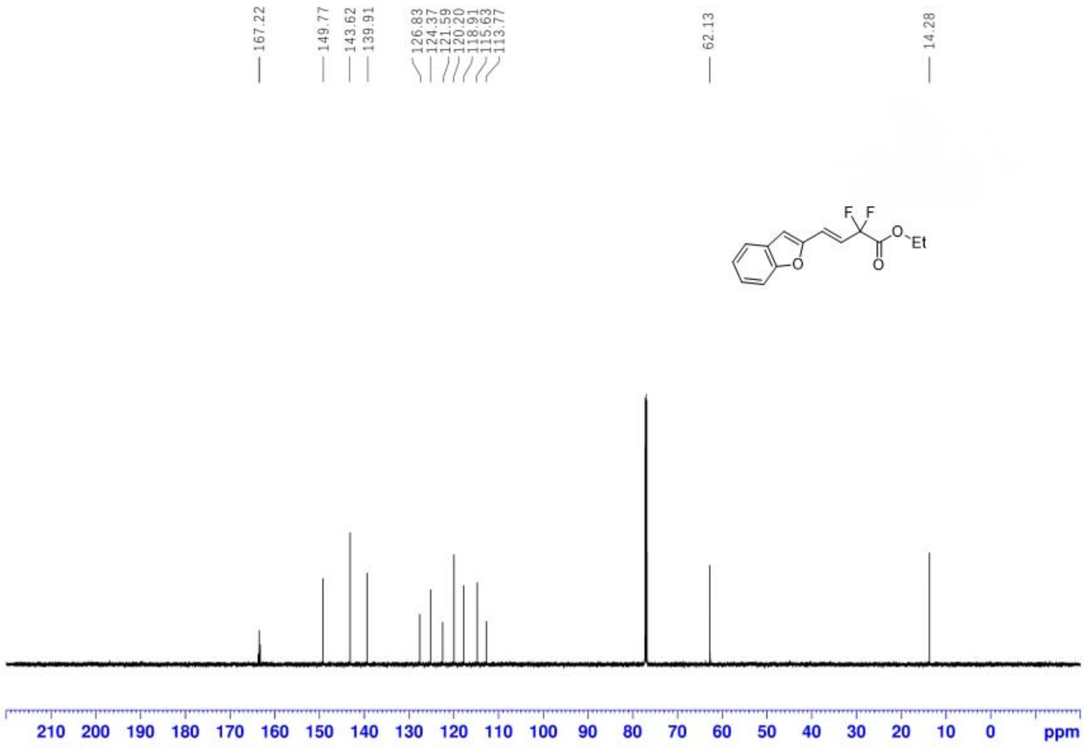
^{19}F NMR Spectra of **1p** (377 MHz, $CDCl_3$)



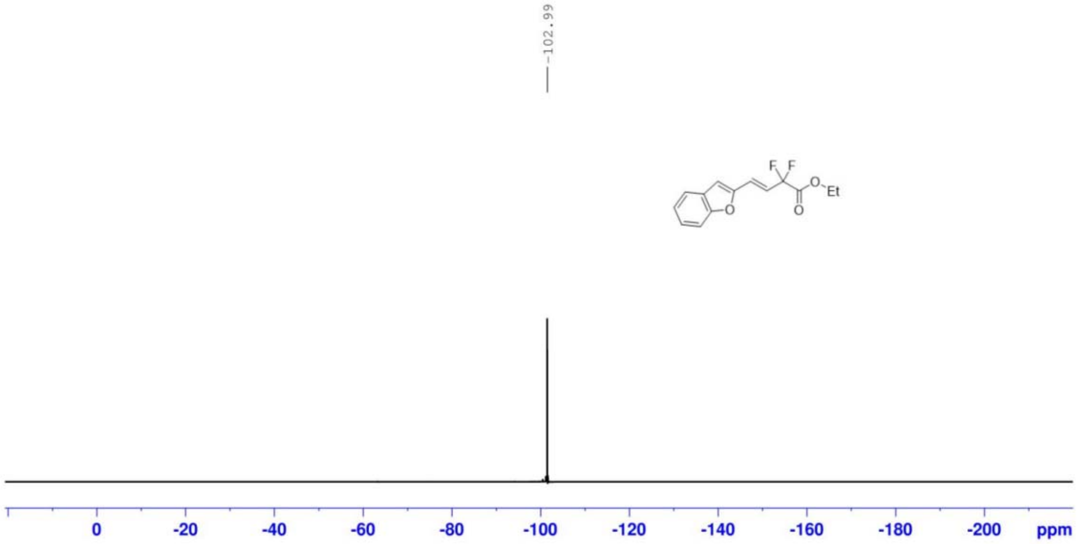
^{1}H NMR Spectra of **1q** (600 MHz, $CDCl_3$)



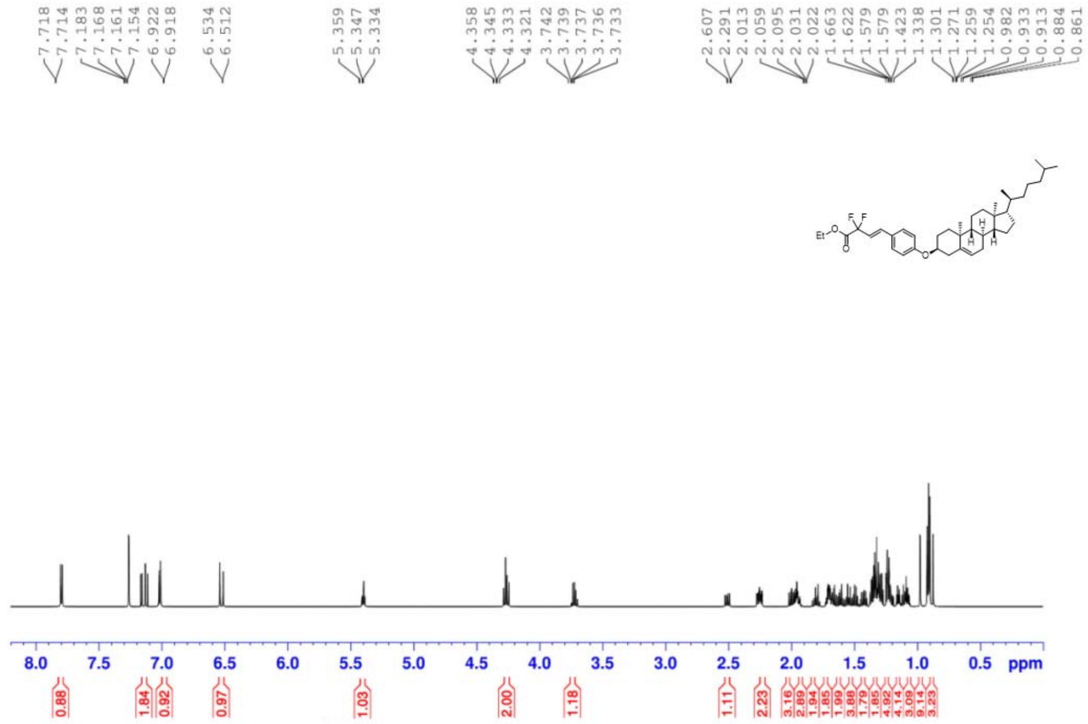
^{13}C NMR Spectra of **1q** (151 MHz, CDCl$_3$)



^{19}F NMR Spectra of **1q** (377 MHz, CDCl$_3$)



^{1}H NMR Spectra of **1u** (600 MHz, CDCl$_3$)



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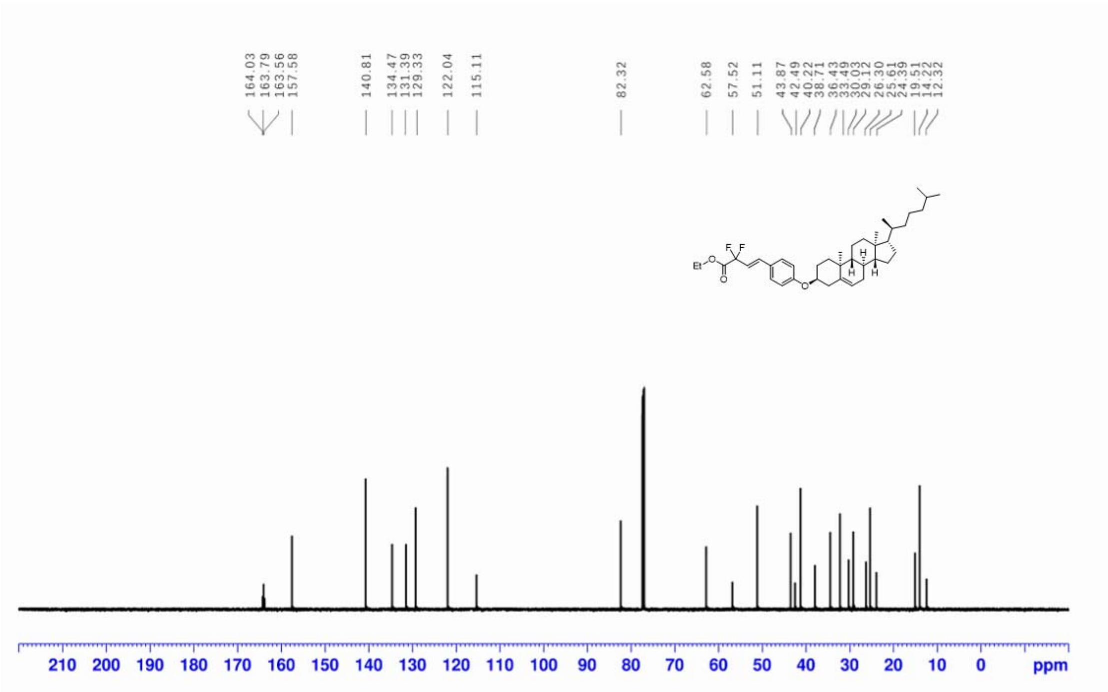

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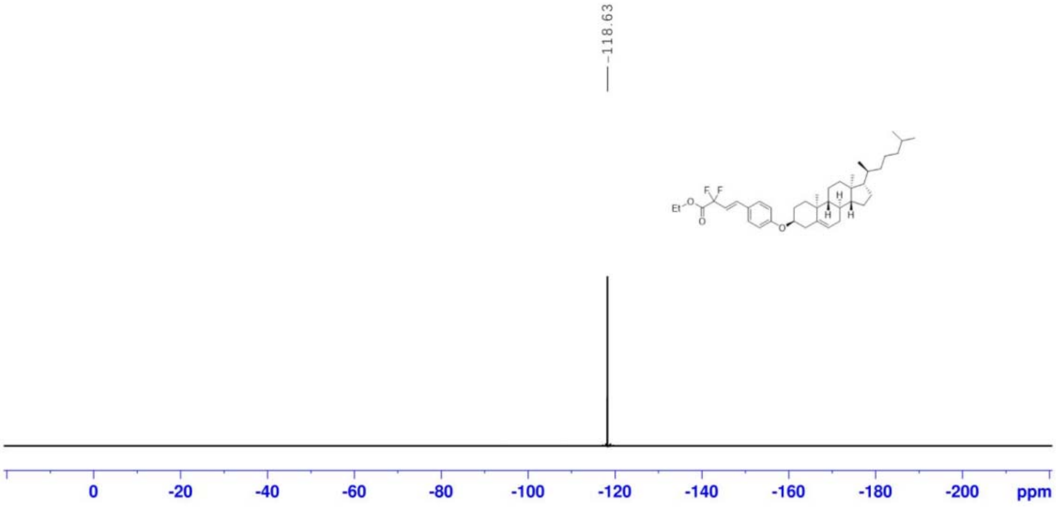
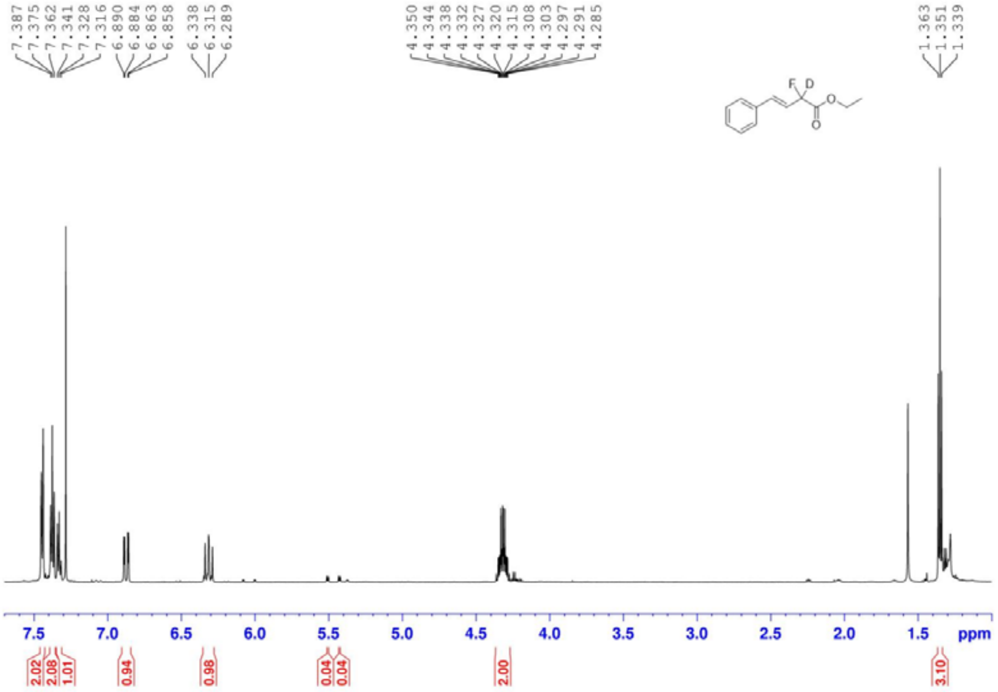
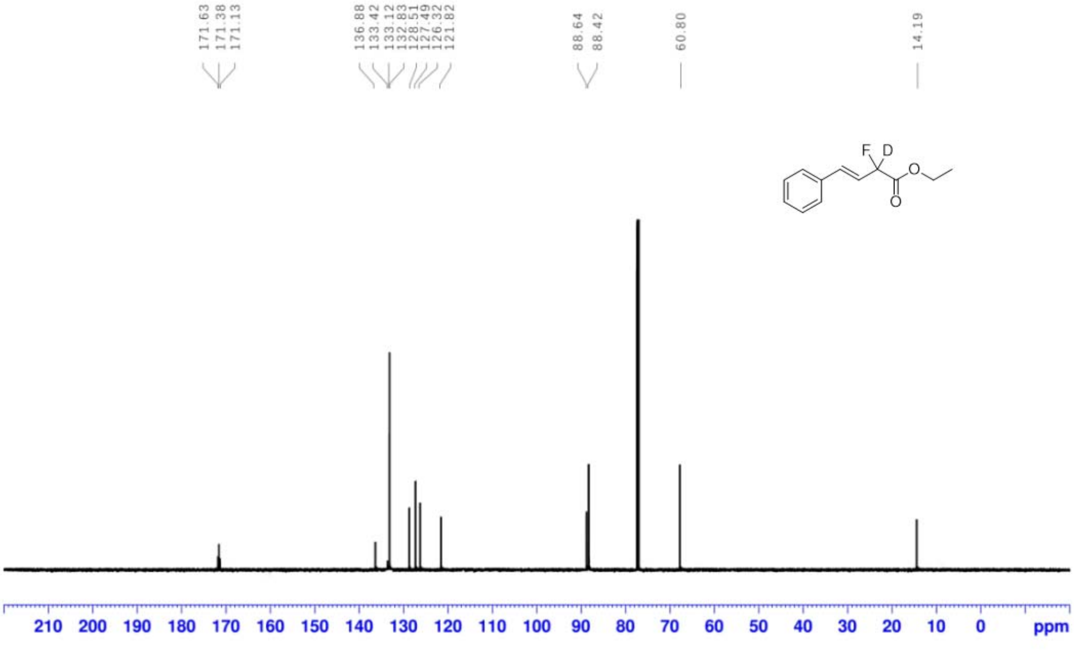


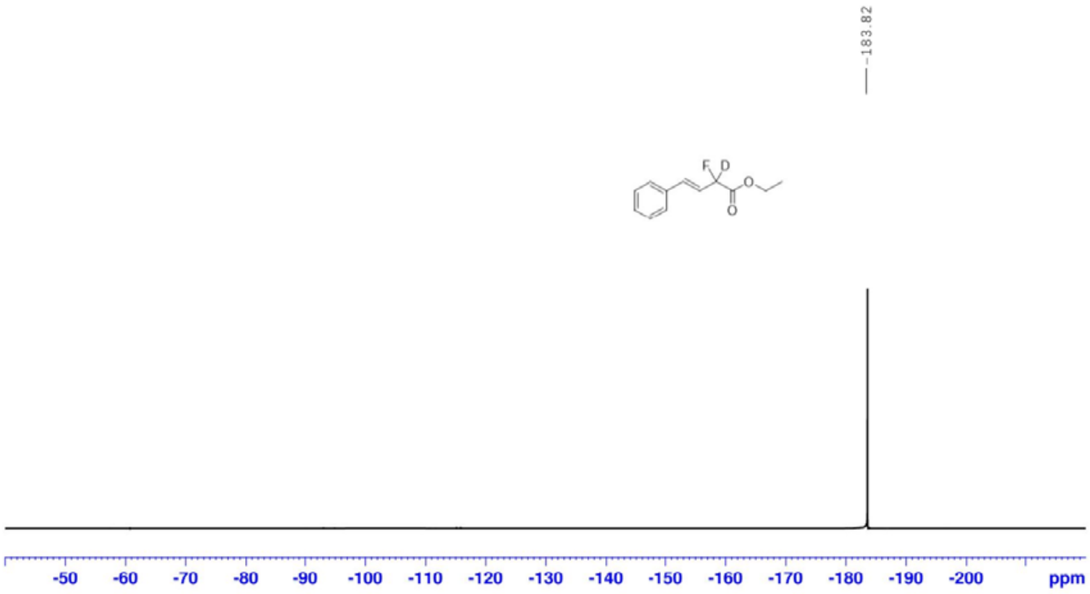
^{1}H NMR Spectra of **2a** (600 MHz, CDCl$_3$)



^{13}C NMR Spectra of **2a** (151 MHz, CDCl$_3$)



^{19}F NMR Spectra of **2a** (377 MHz, CDCl$_3$)



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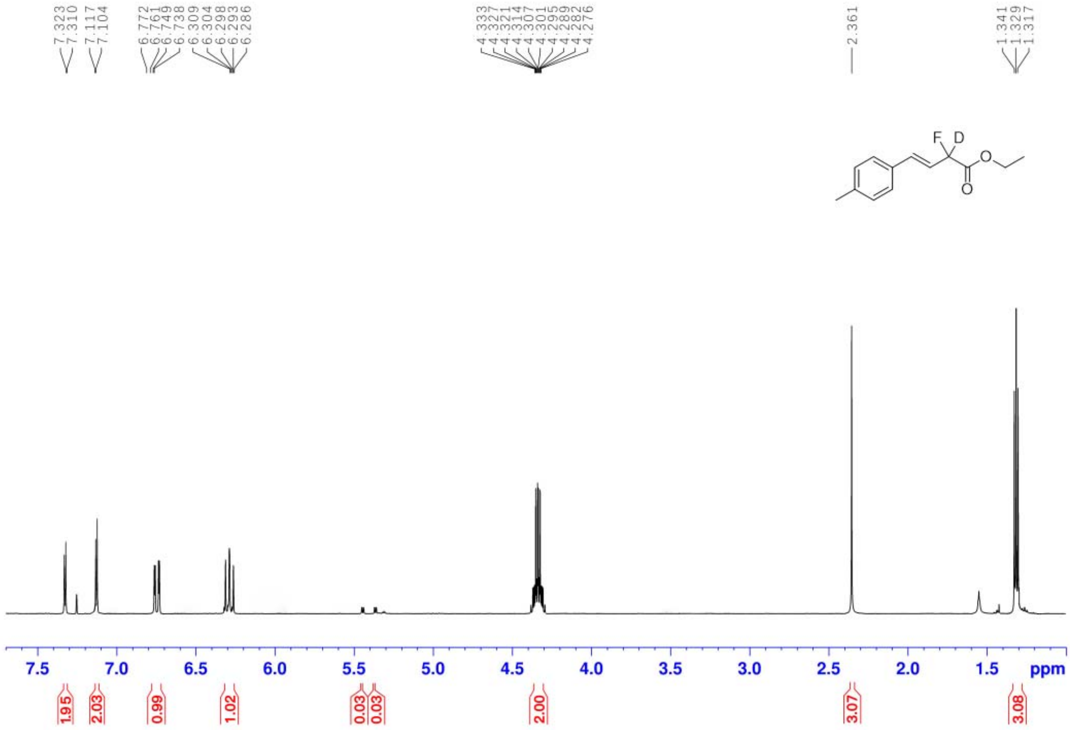

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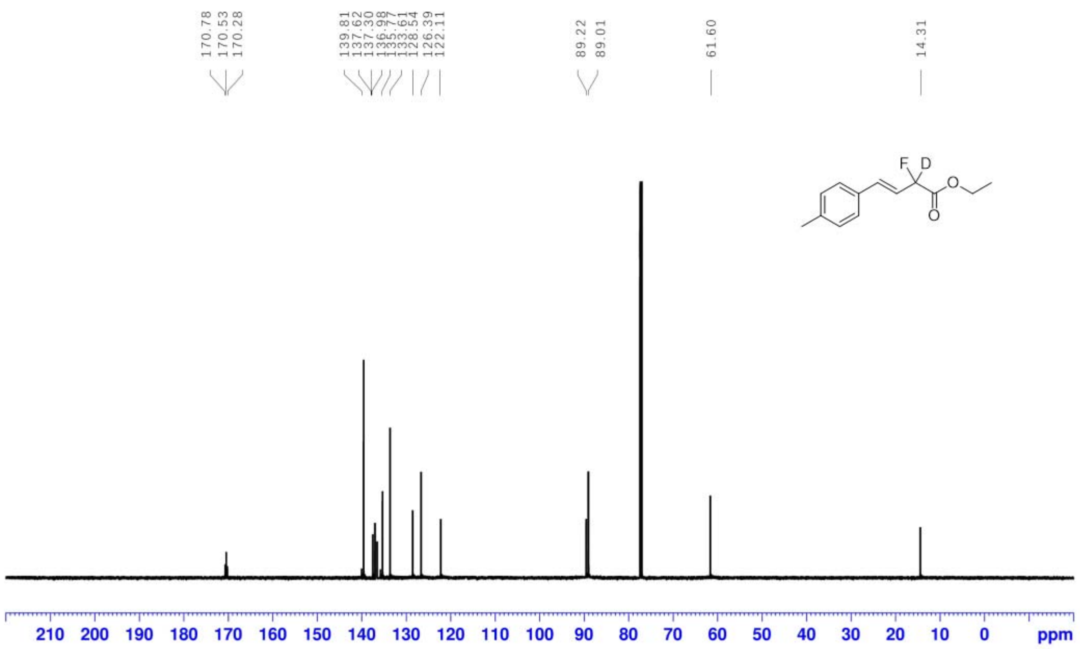
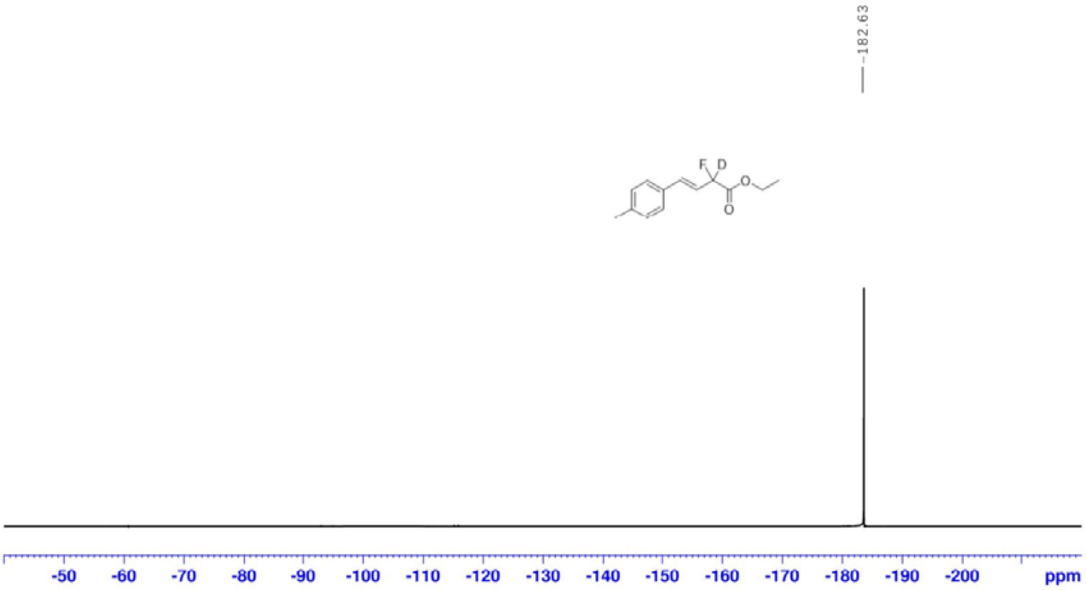
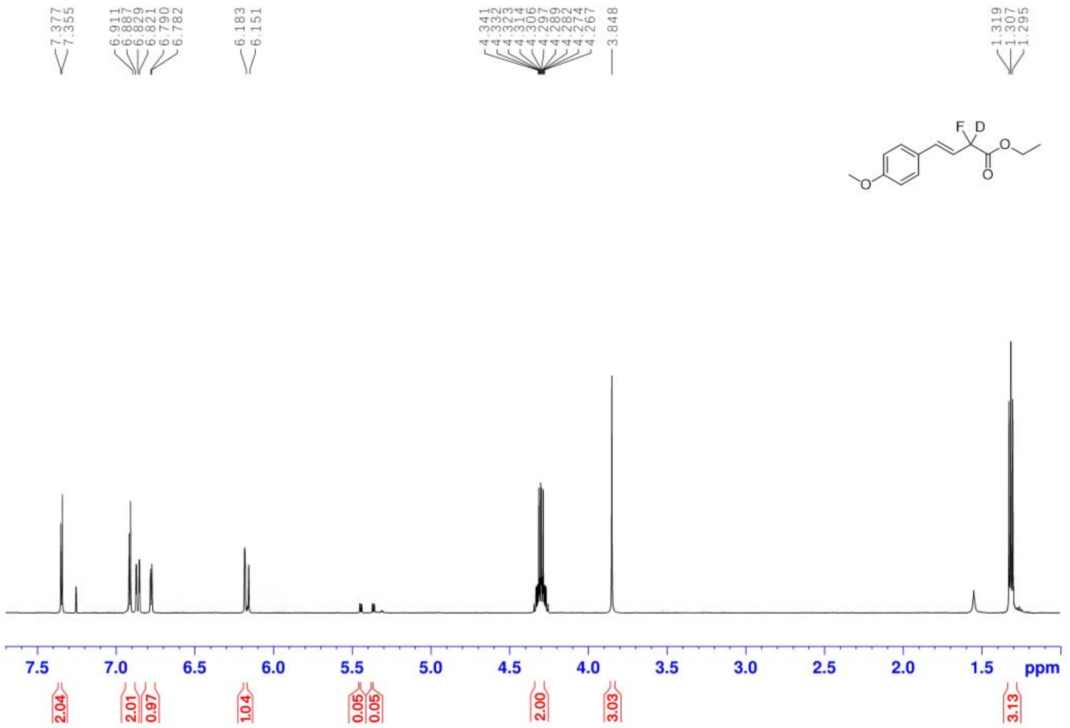


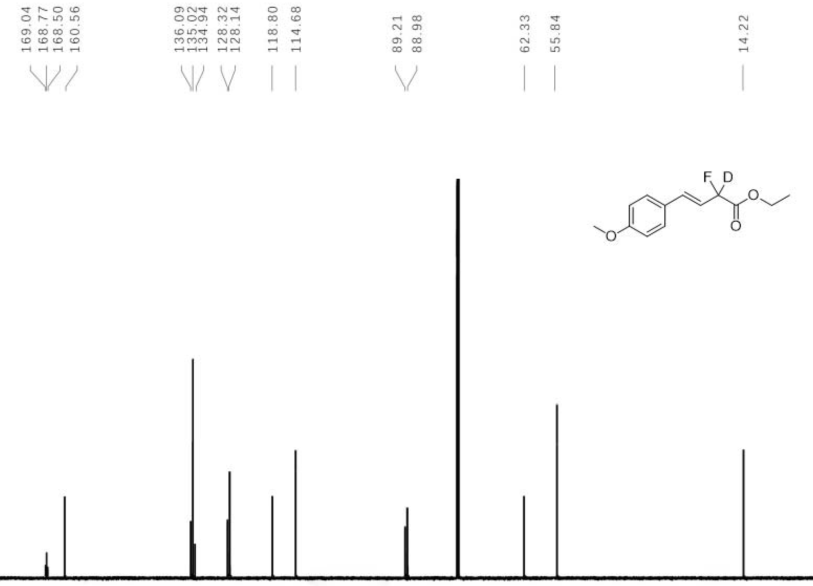
^{19}F NMR Spectra of **2b** (377 MHz, CDCl$_3$)



^{1}H NMR Spectra of **2c** (600 MHz, CDCl$_3$)



^{13}C NMR Spectra of **2c** (151 MHz, CDCl$_3$)



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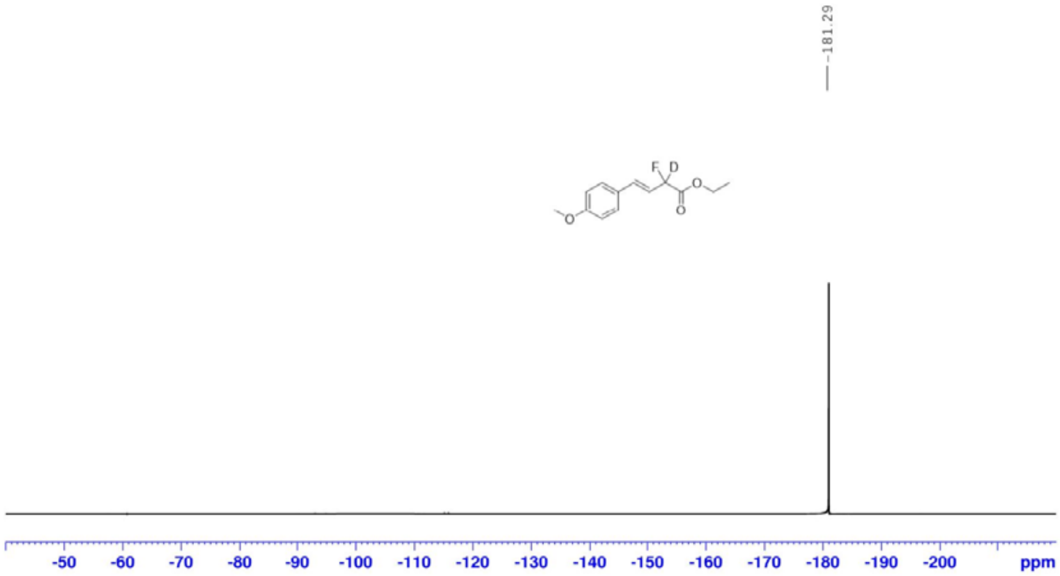

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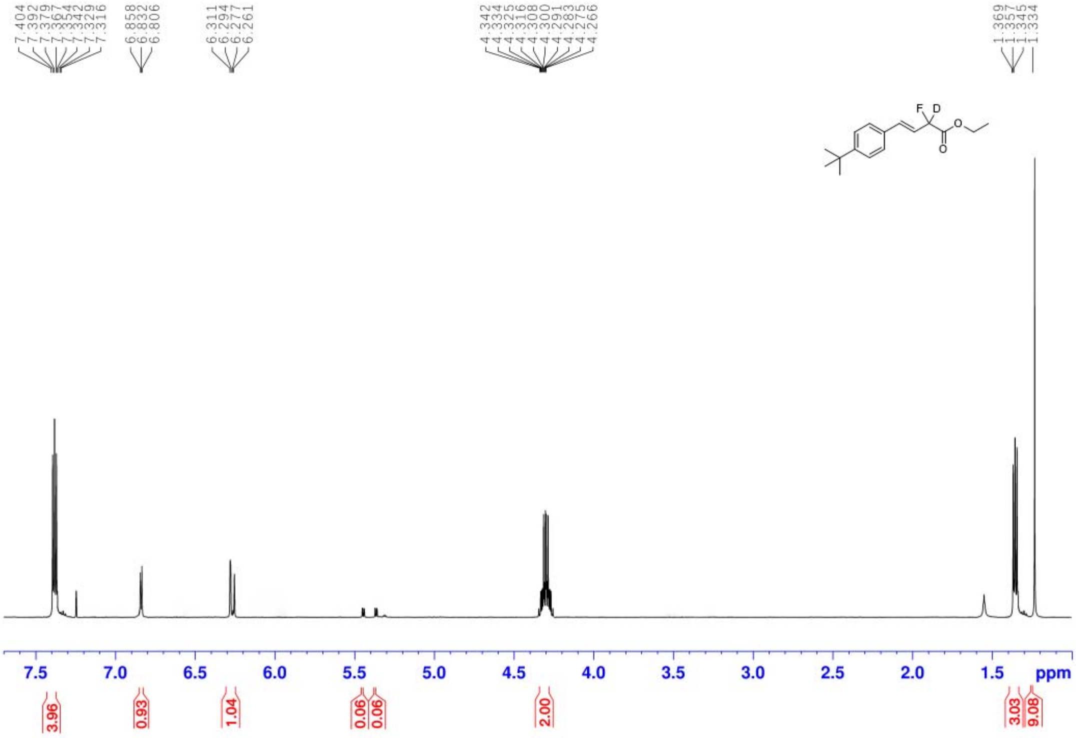

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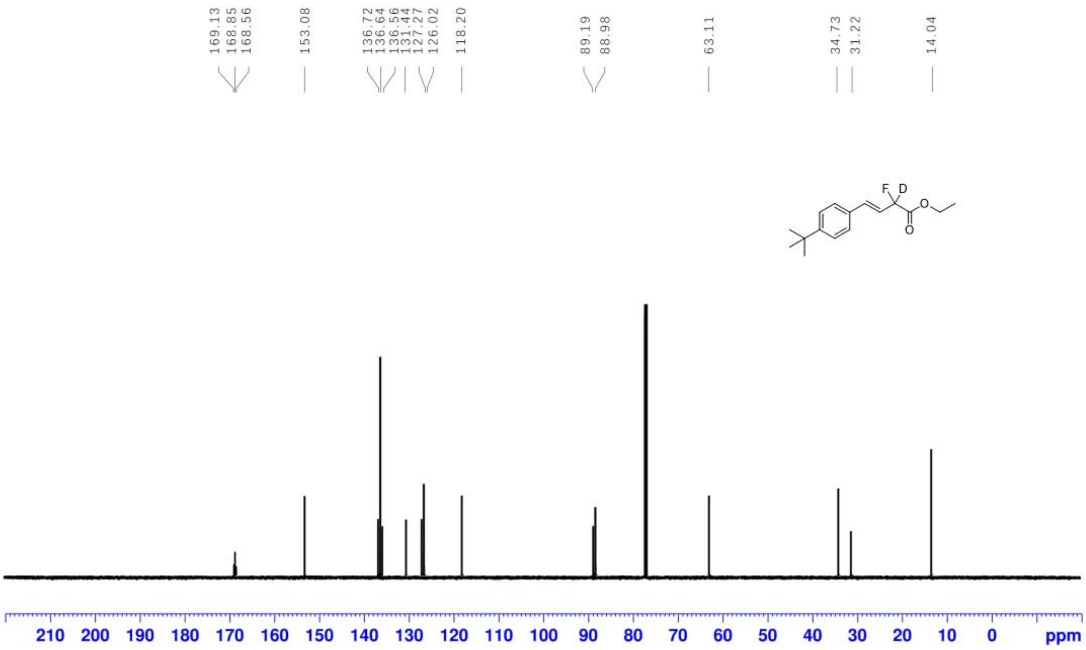

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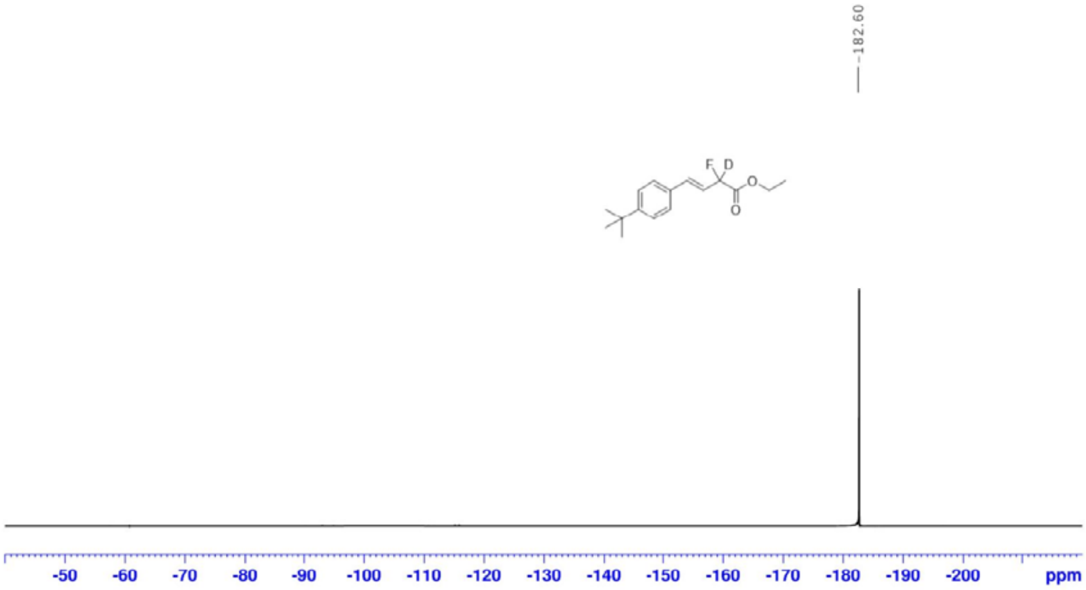

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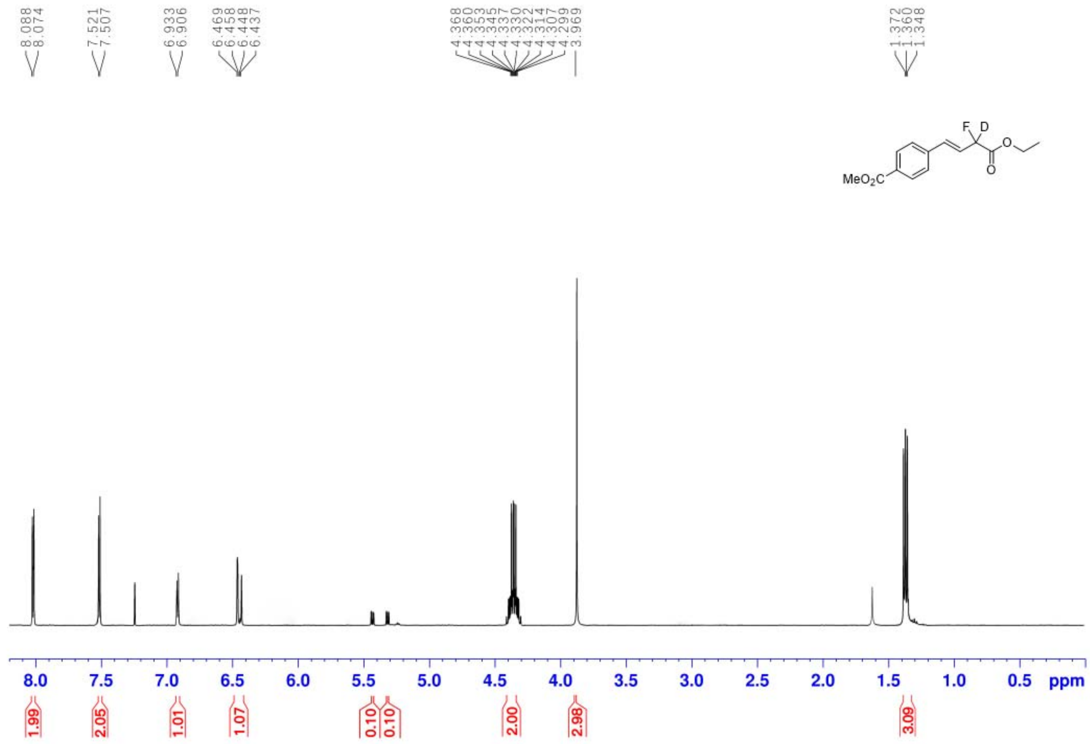

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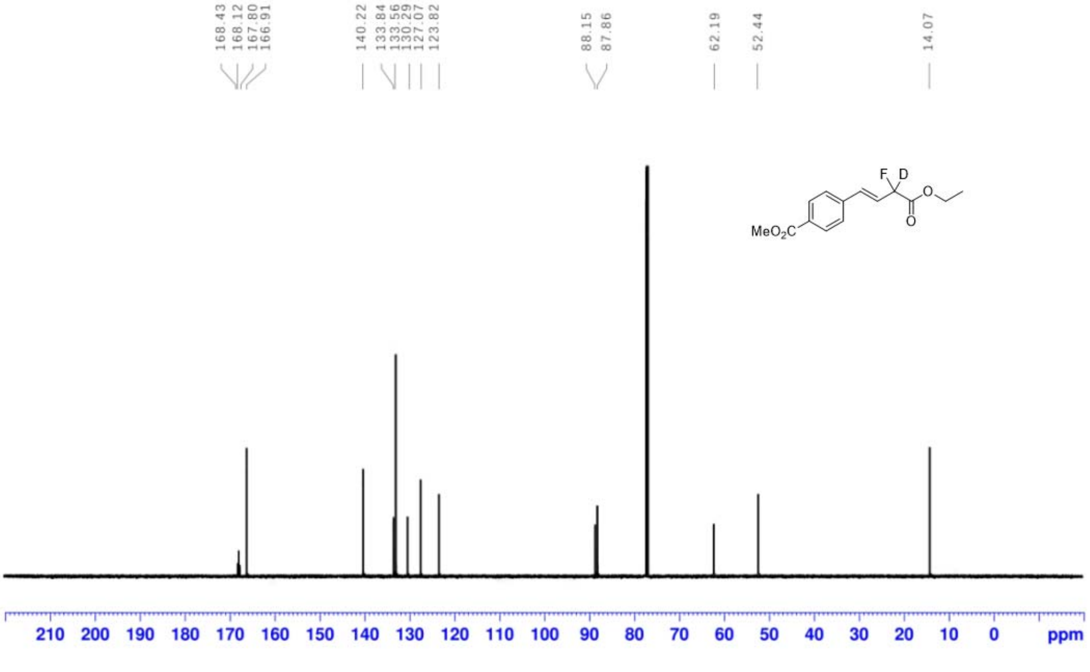
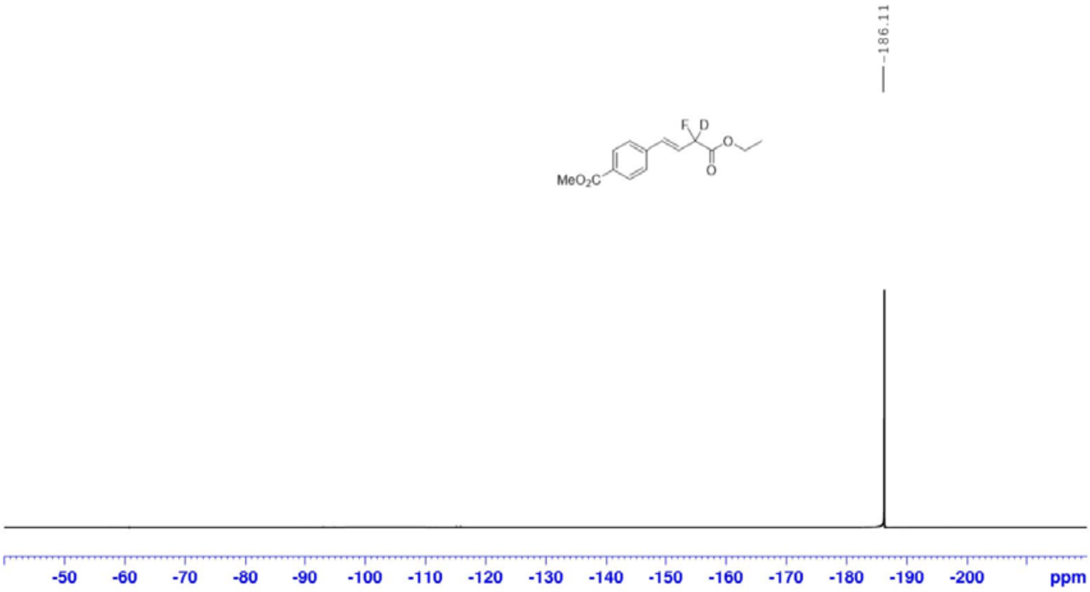
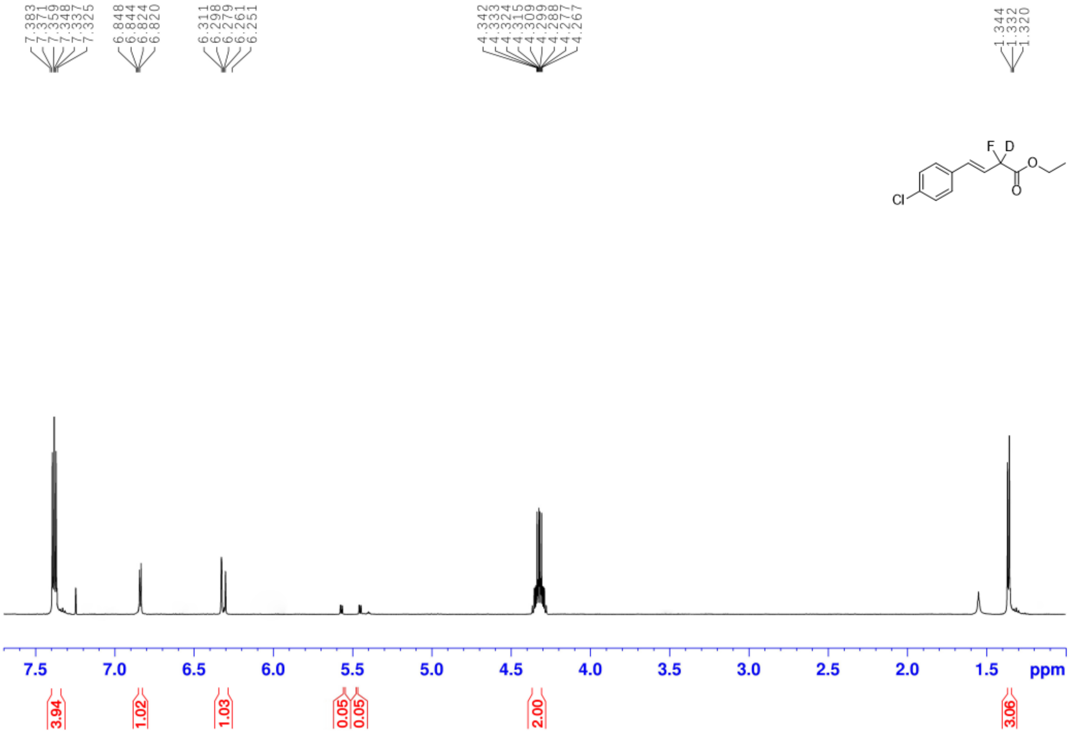


^{19}F NMR Spectra of **2e** (377 MHz, CDCl$_3$)



^{1}H NMR Spectra of **2f** (600 MHz, CDCl$_3$)



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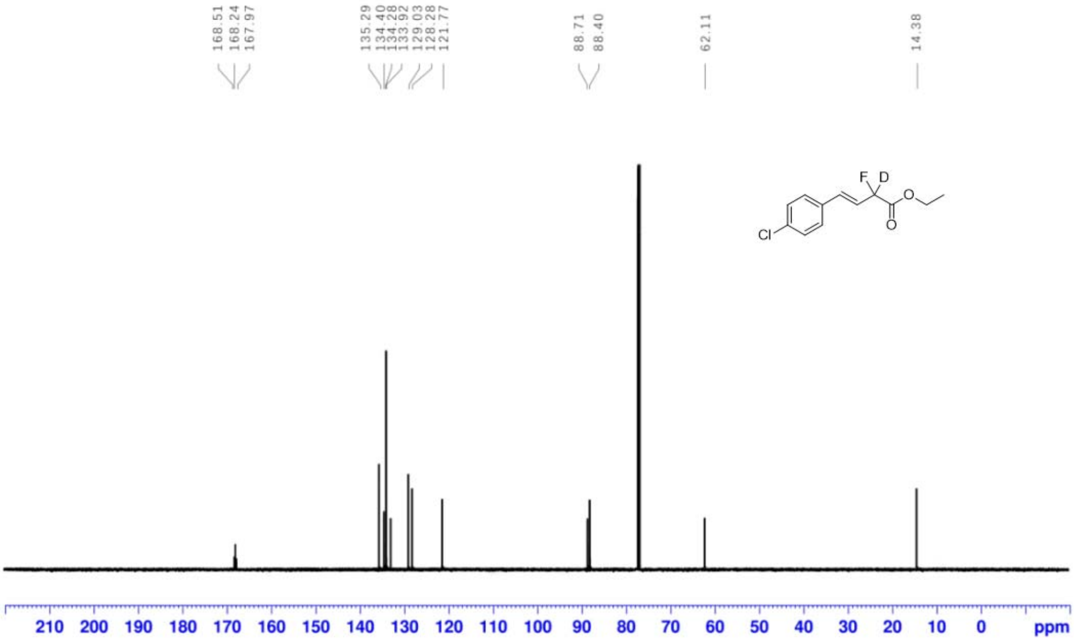

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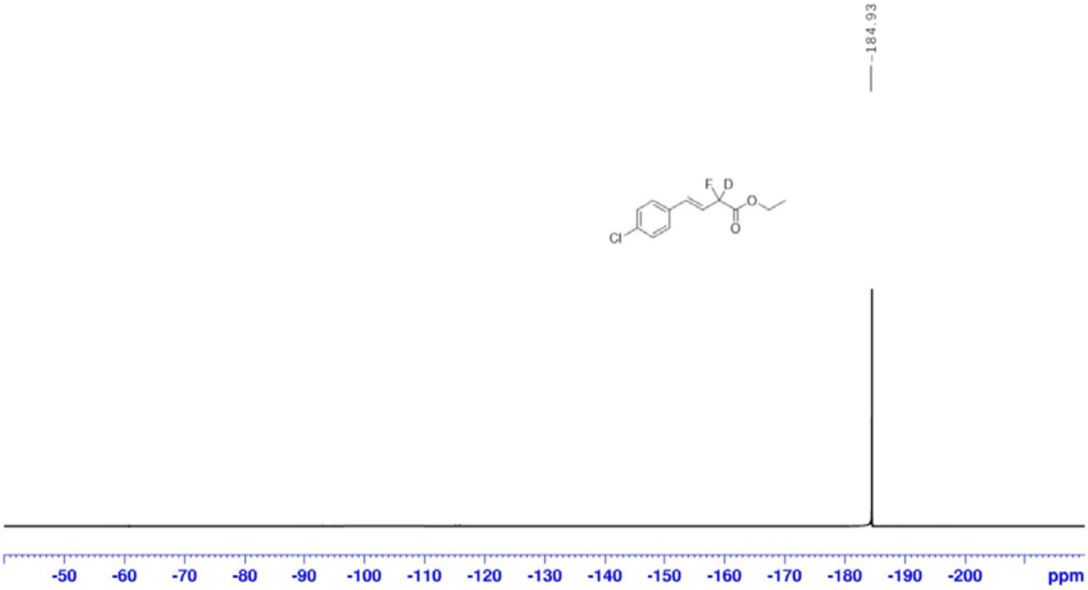
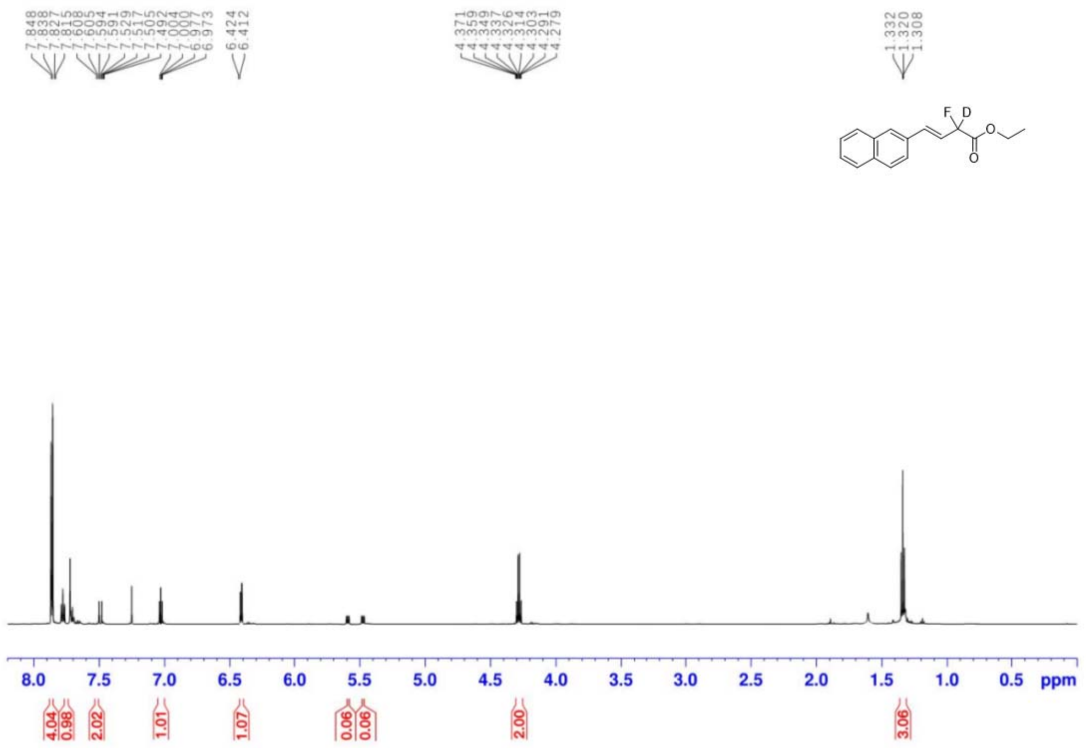
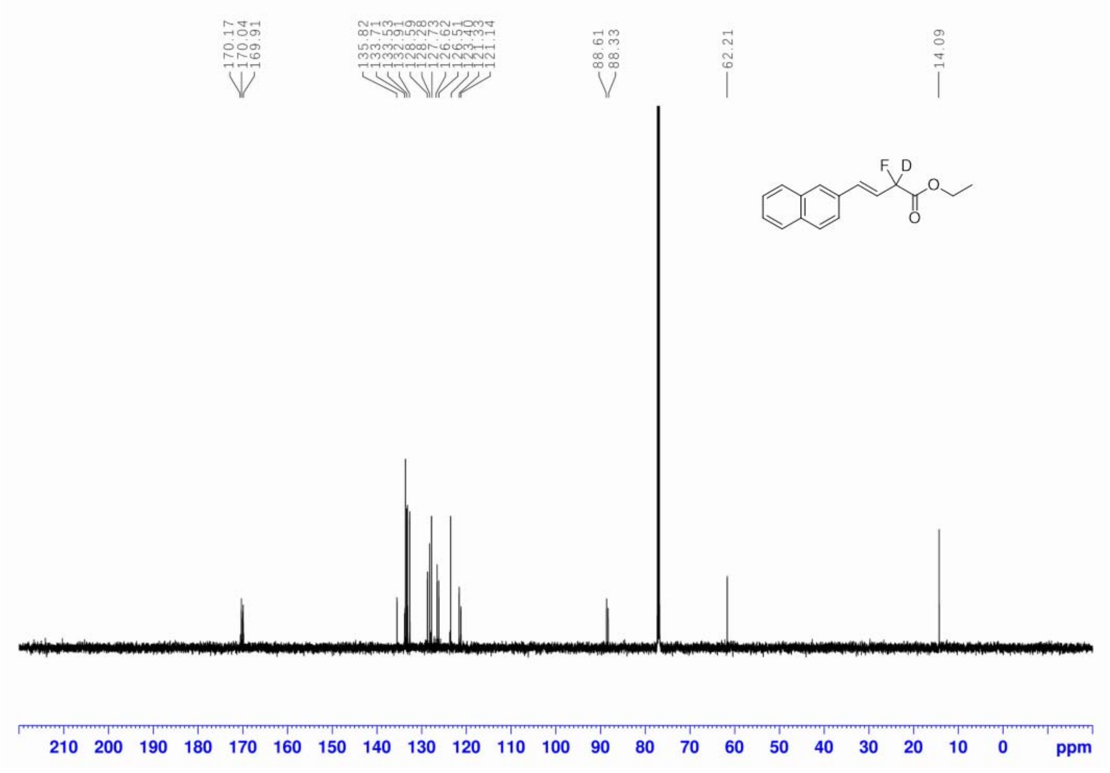


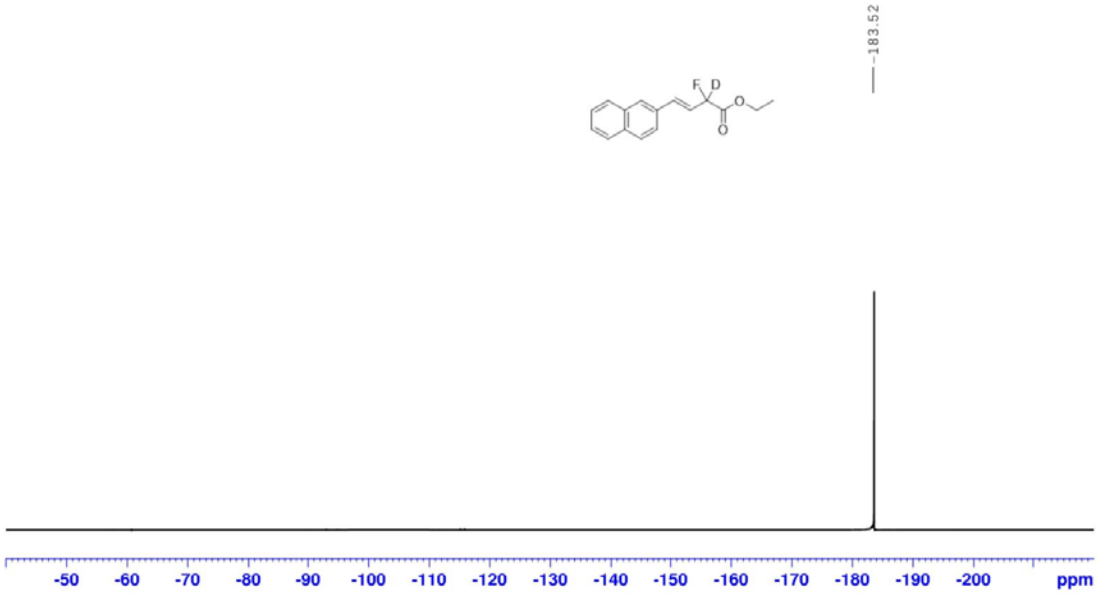
^{1}H NMR Spectra of **2g** (600 MHz, CDCl$_3$)



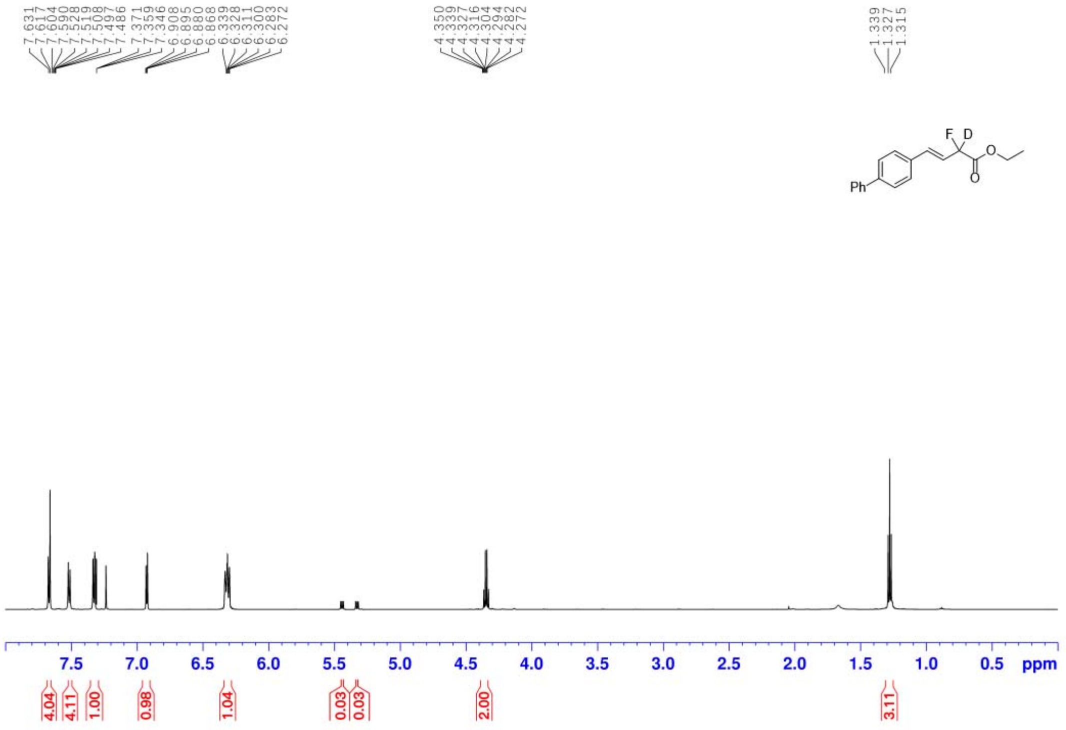
^{13}C NMR Spectra of **2g** (151 MHz, CDCl$_3$)



^{19}F NMR Spectra of **2g** (377 MHz, CDCl$_3$)



^{1}H NMR Spectra of **2h** (600 MHz, CDCl$_3$)



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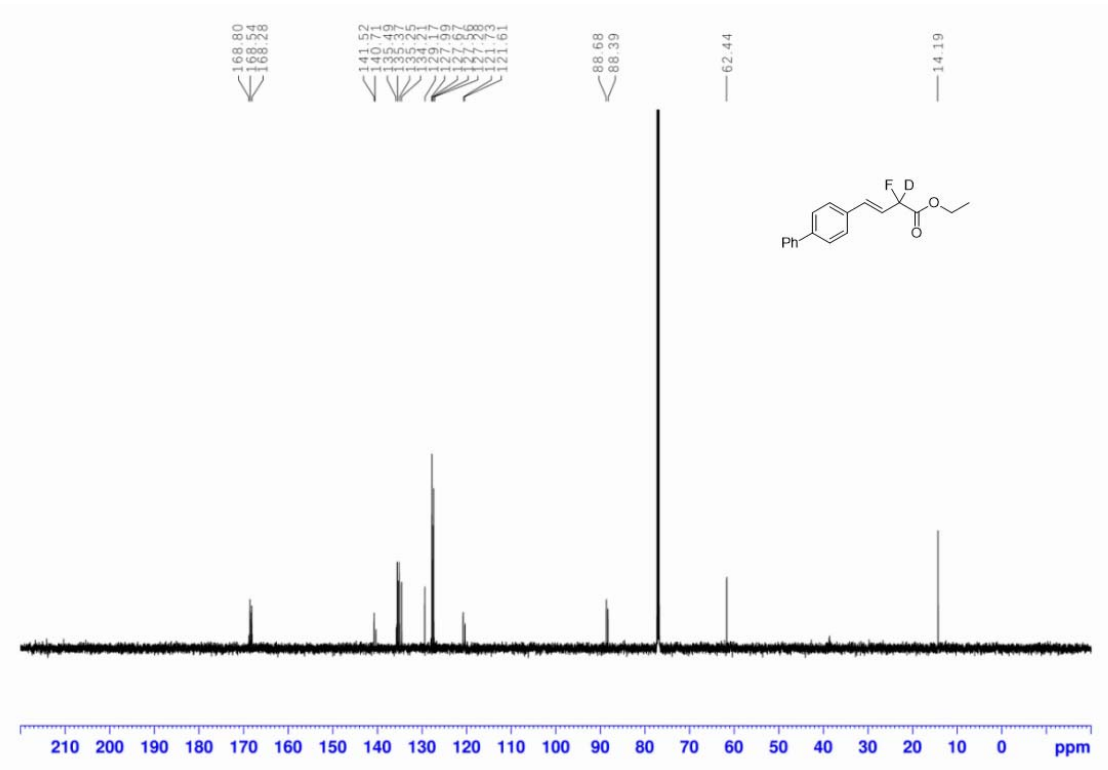
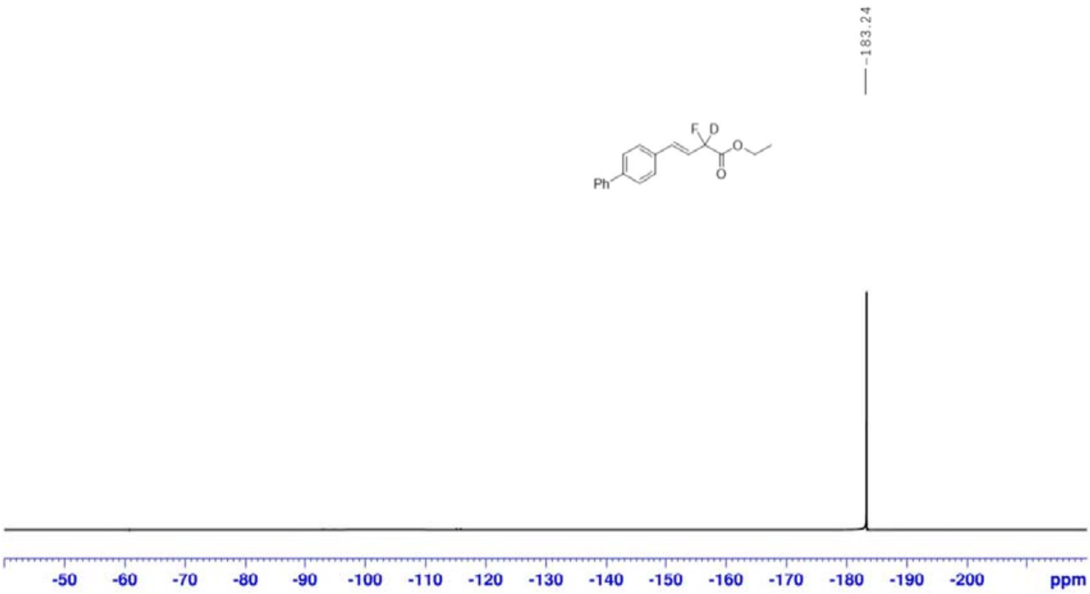
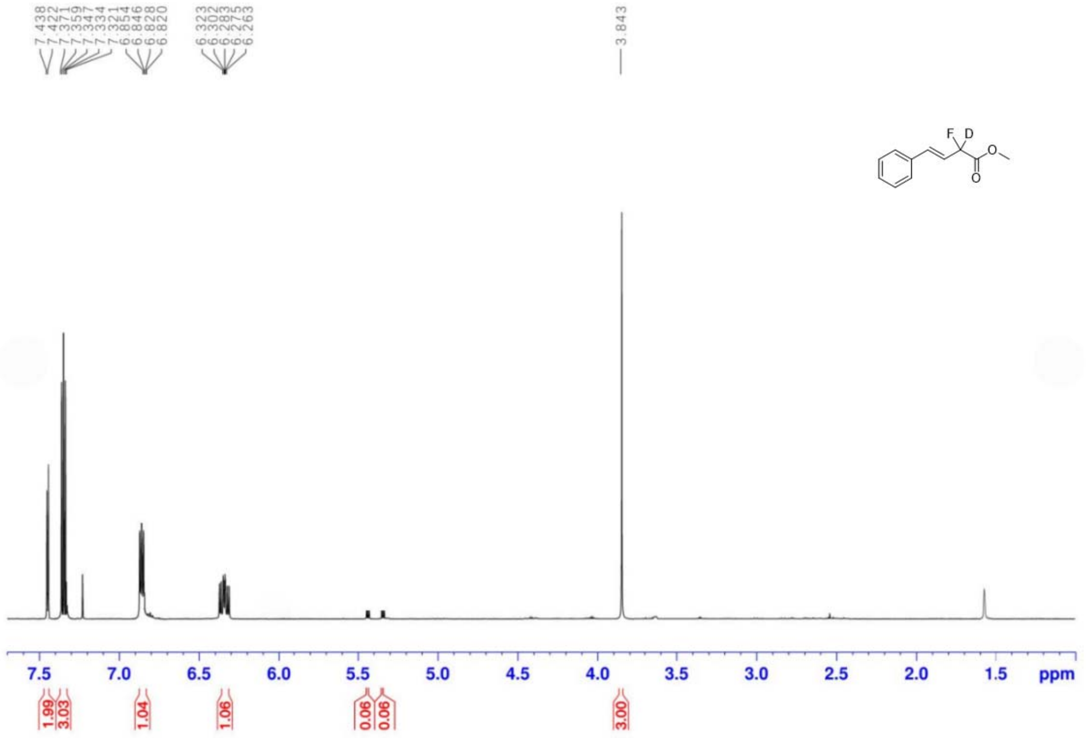


^{19}F NMR Spectra of **2h** (377 MHz, CDCl$_3$)



^{1}H NMR Spectra of **2i** (600 MHz, CDCl$_3$)



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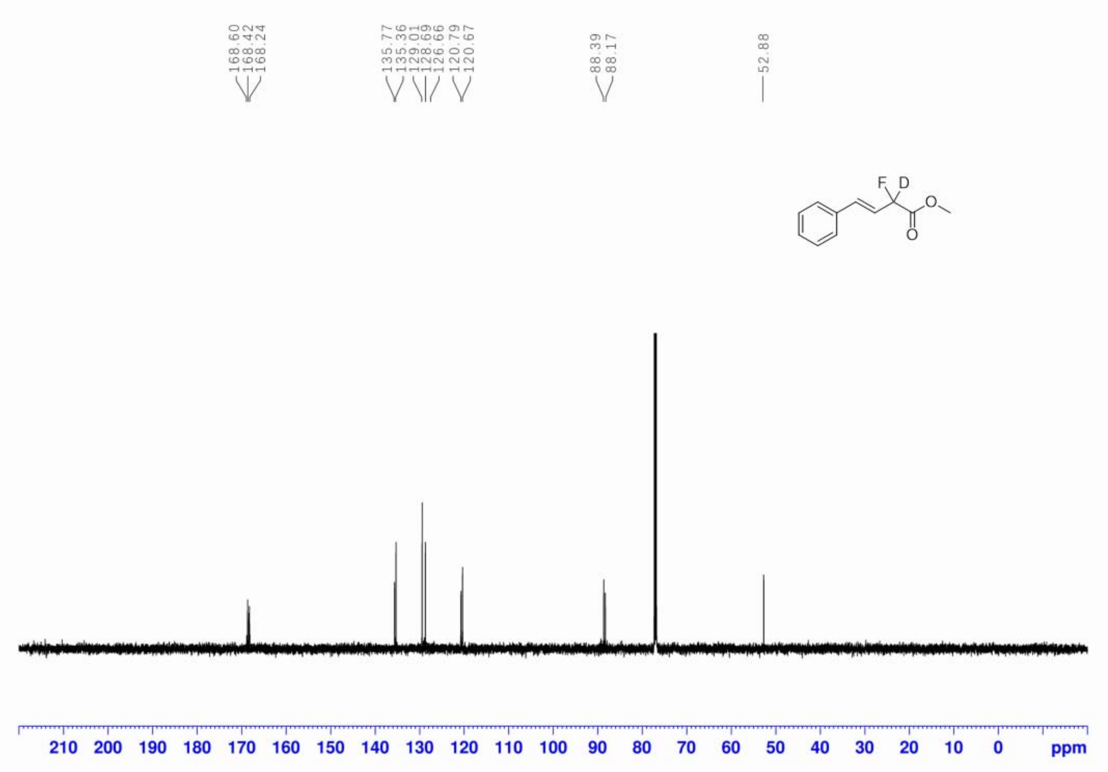

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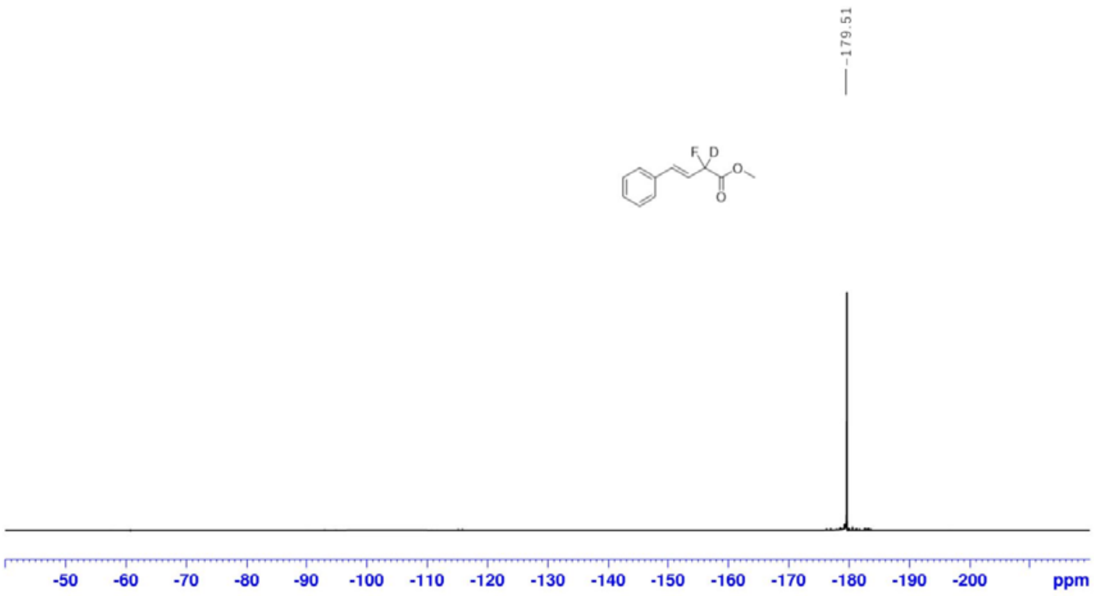

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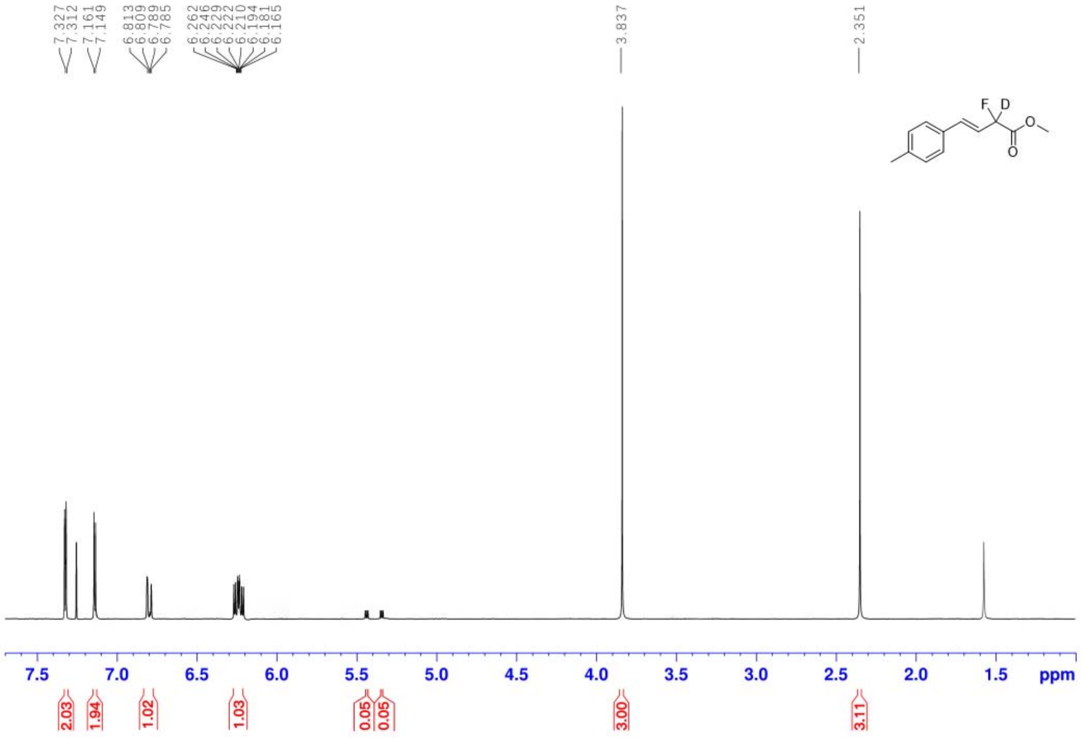
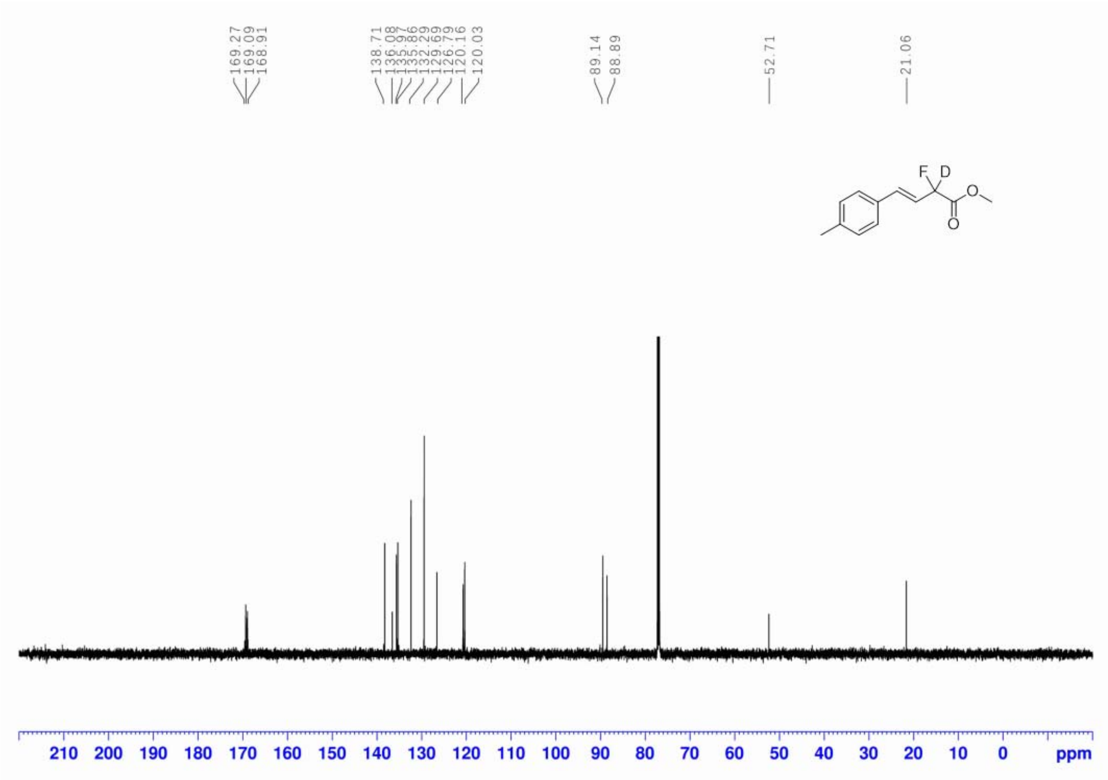


^{13}C NMR Spectra of **2j** (151 MHz, $CDCl_3$)



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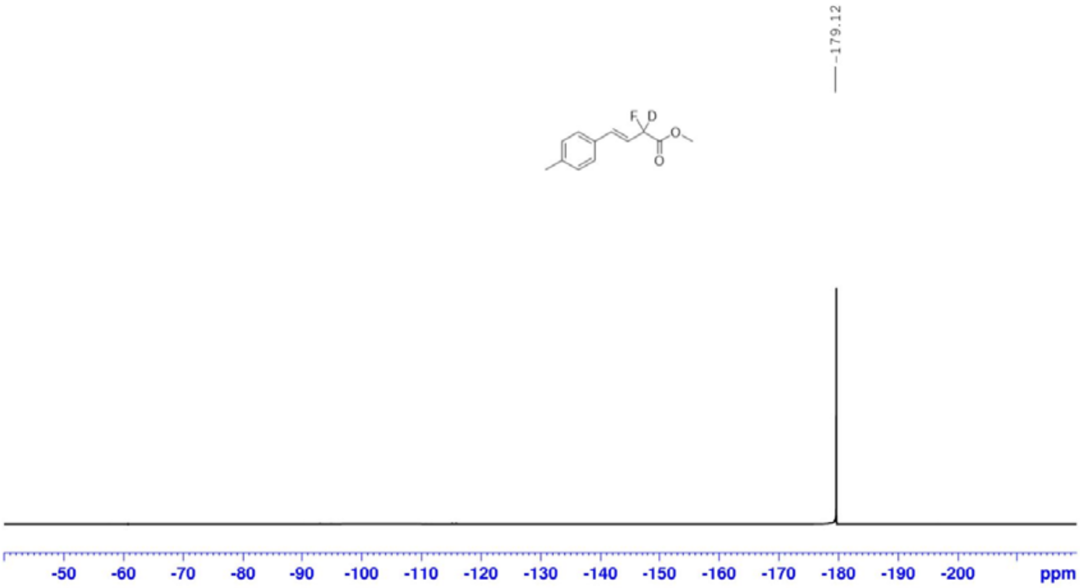
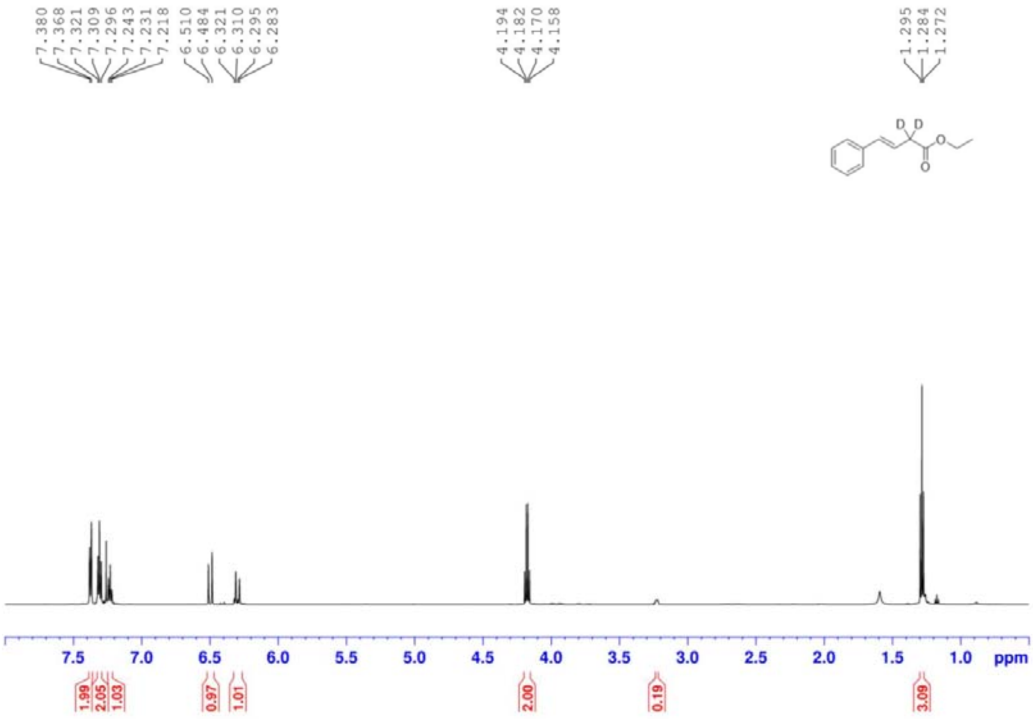
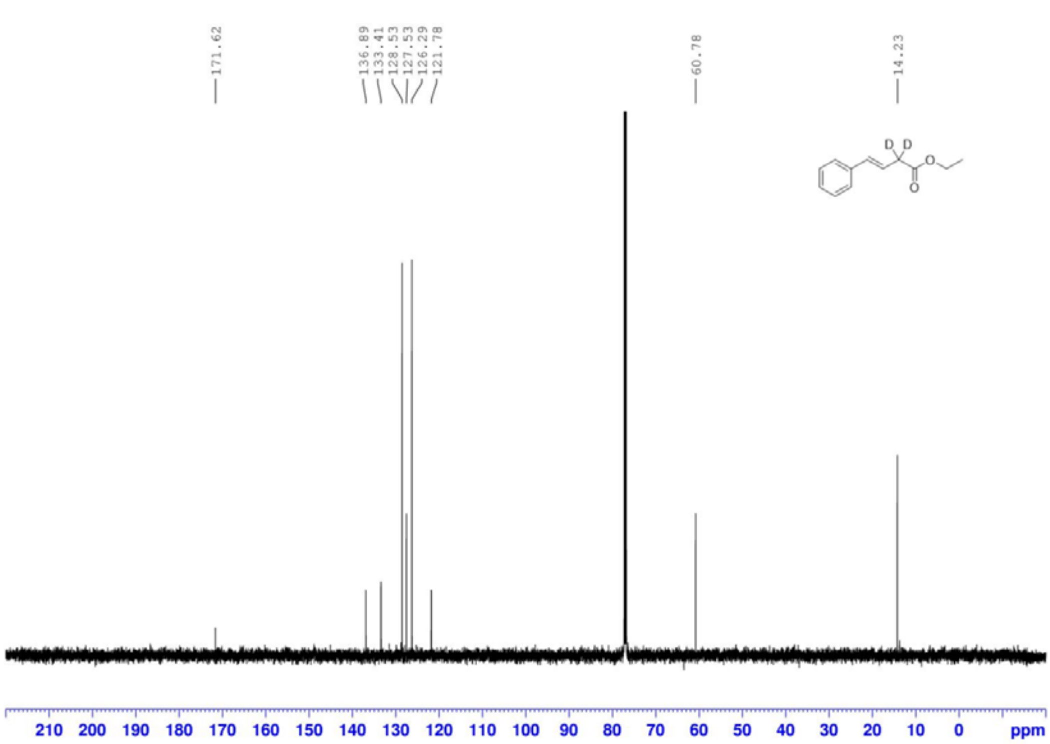


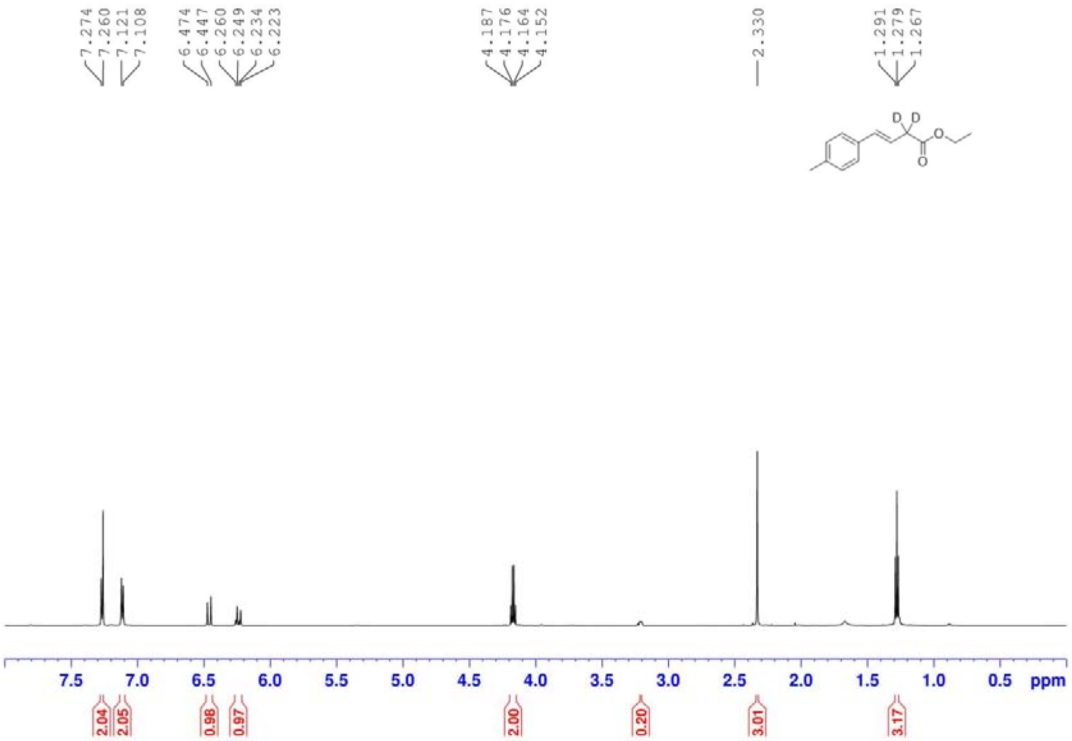
^{1}H NMR Spectra of **3a** (600 MHz, CDCl$_3$)



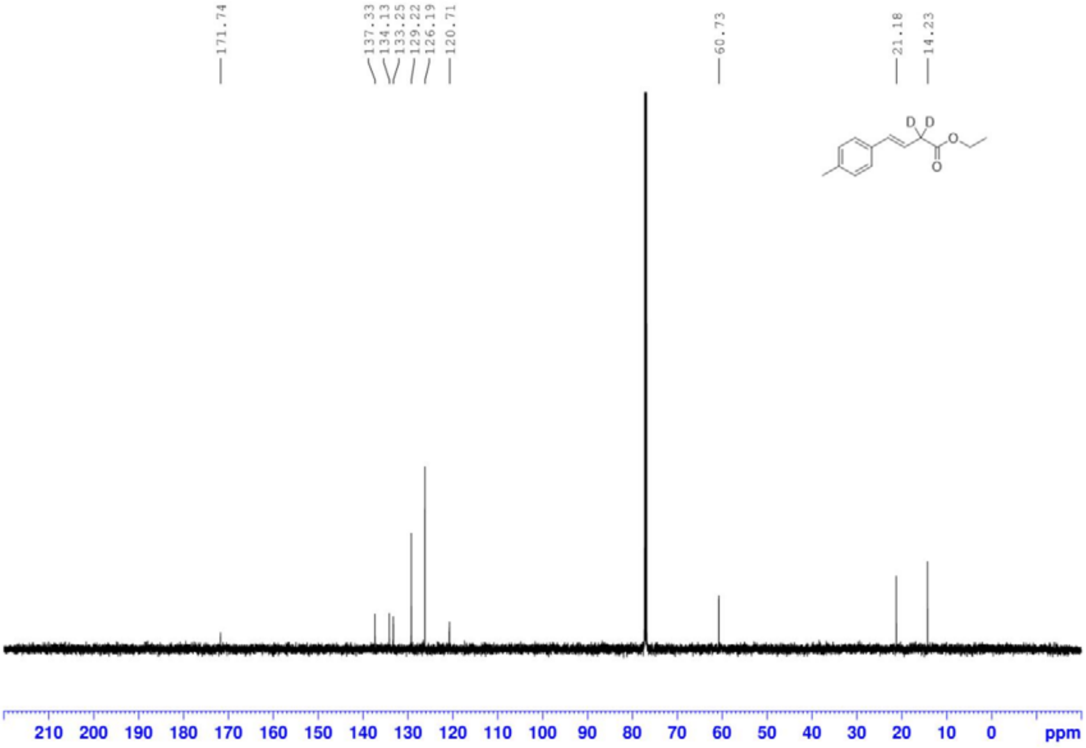
^{13}C NMR Spectra of **3a** (151 MHz, CDCl$_3$)



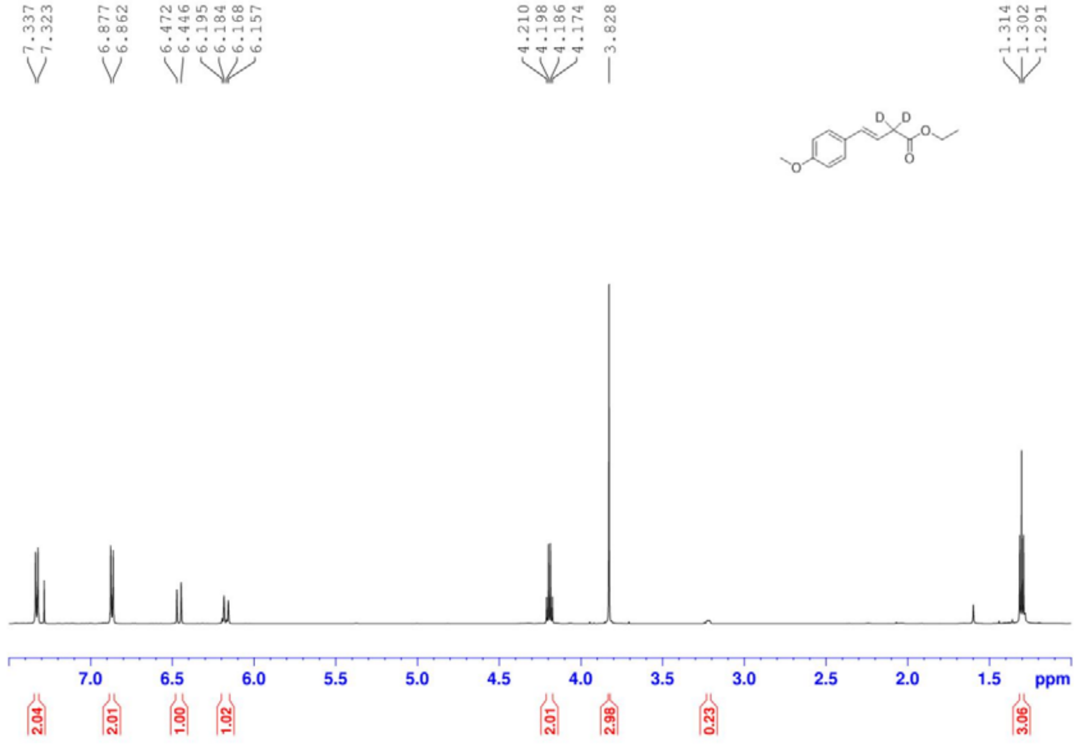
^{1}H NMR Spectra of **3b** (600 MHz, CDCl$_3$)



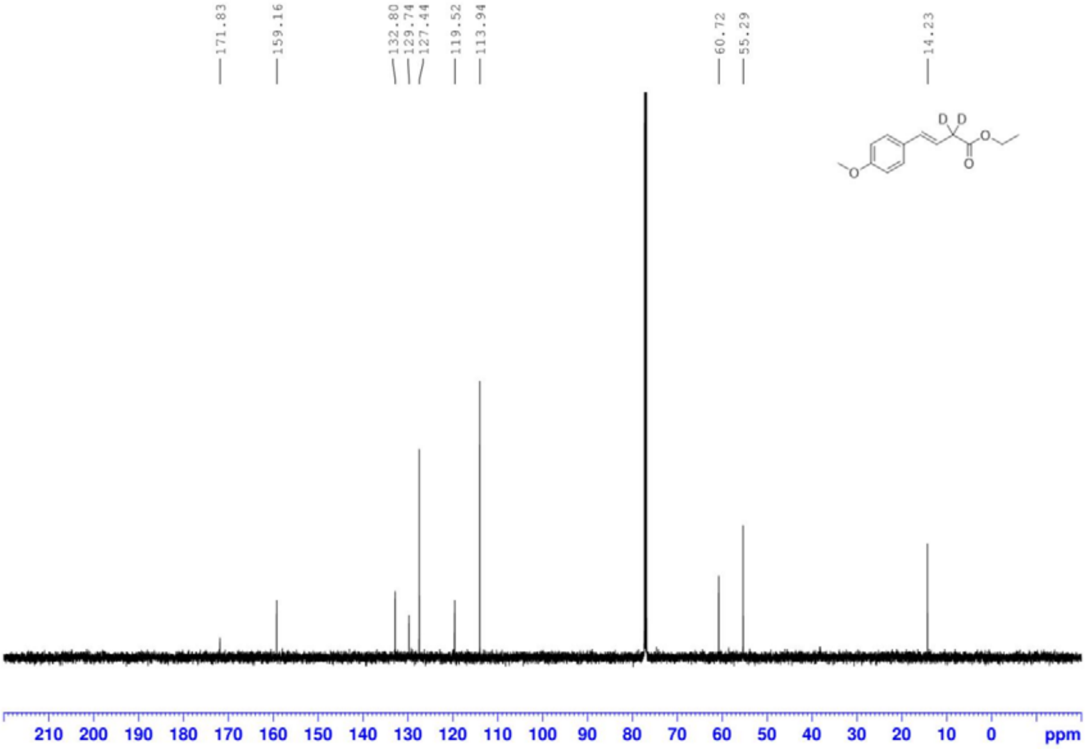
^{13}C NMR Spectra of **3b** (151 MHz, CDCl$_3$)



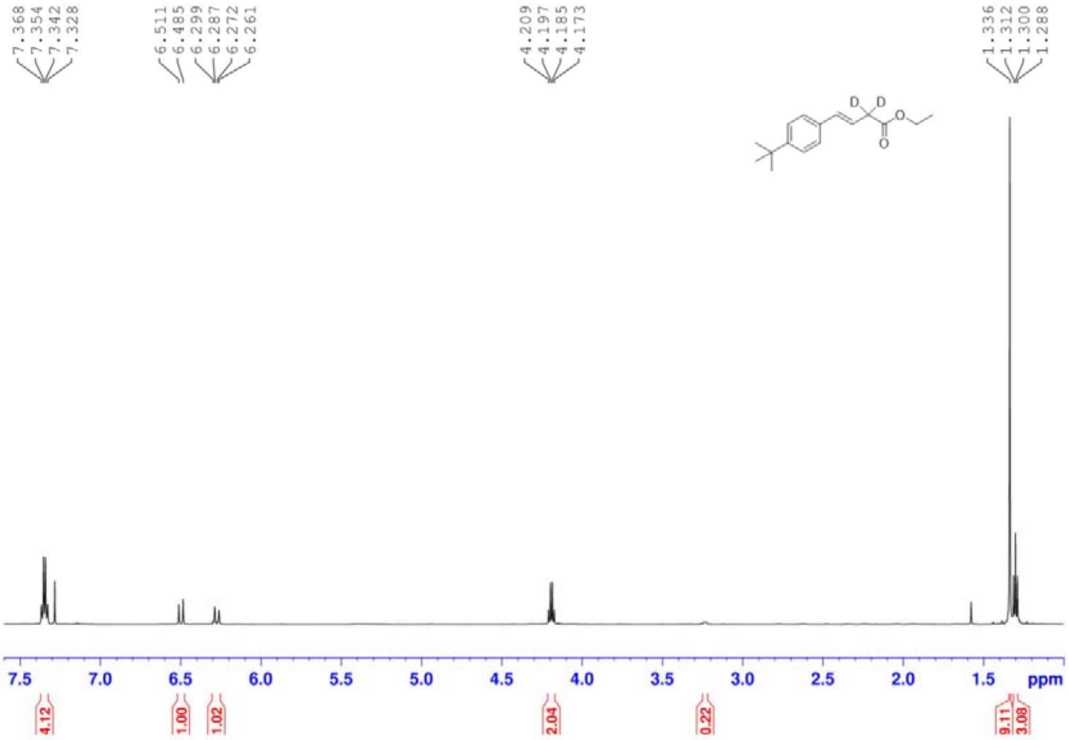
^{1}H NMR Spectra of **3c** (600 MHz, CDCl$_3$)



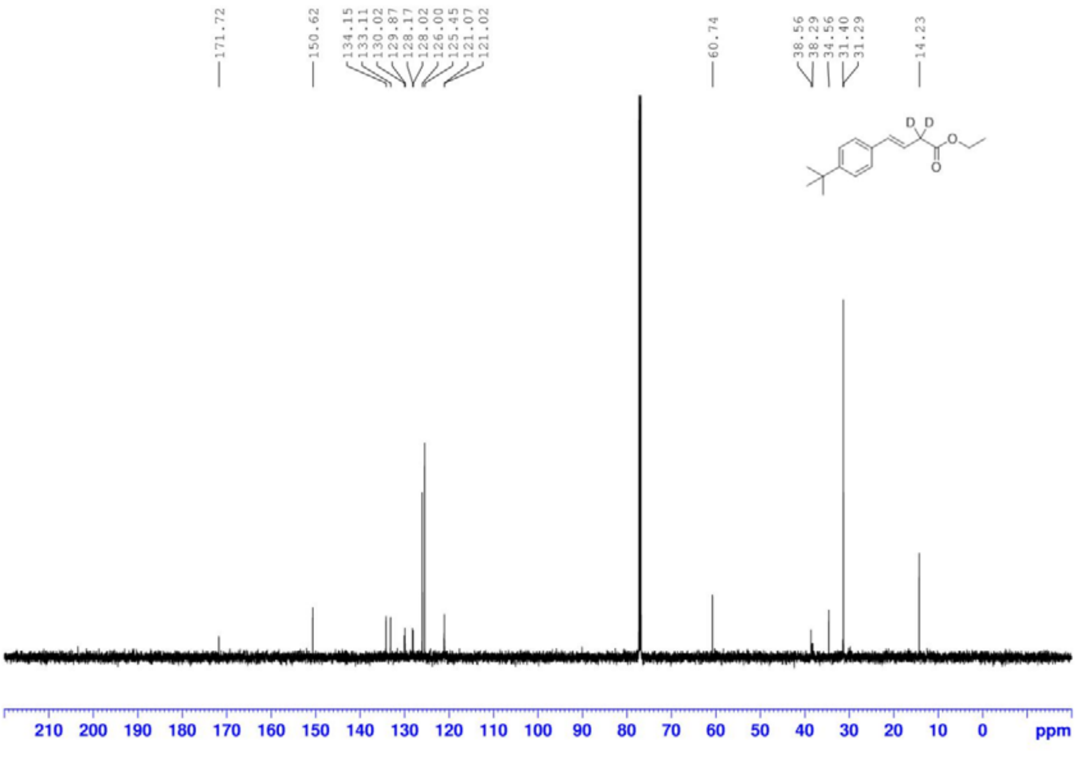
^{13}C NMR Spectra of **3c** (151 MHz, $CDCl_3$)



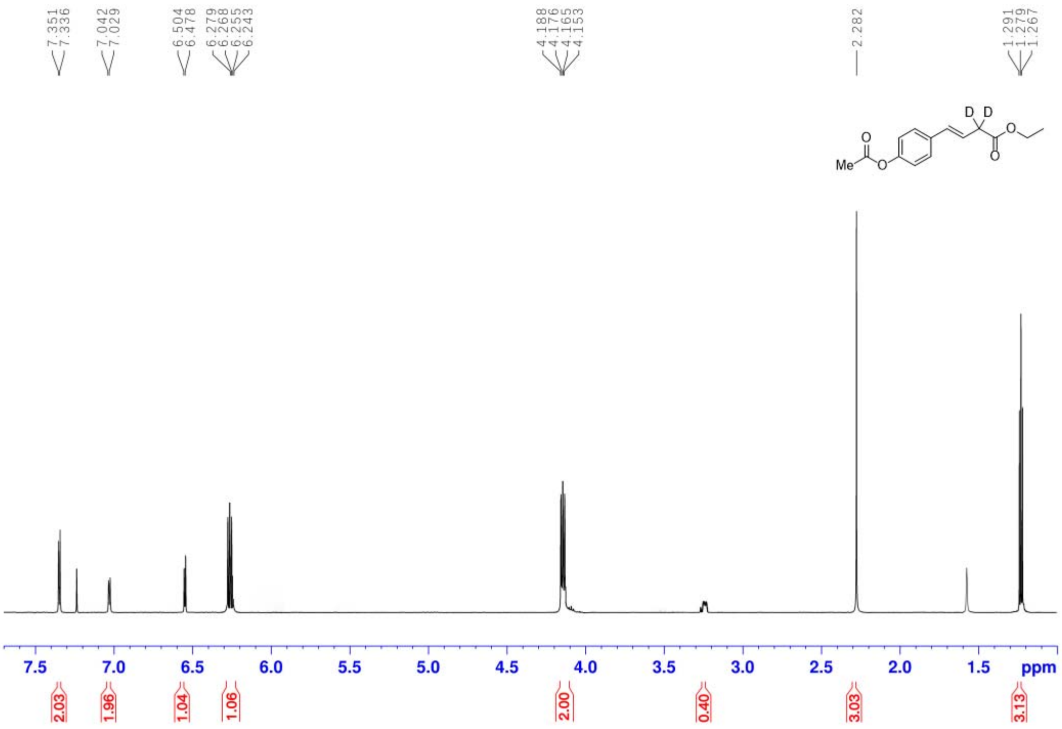
^{1}H NMR Spectra of **3d** (600 MHz, $CDCl_3$)



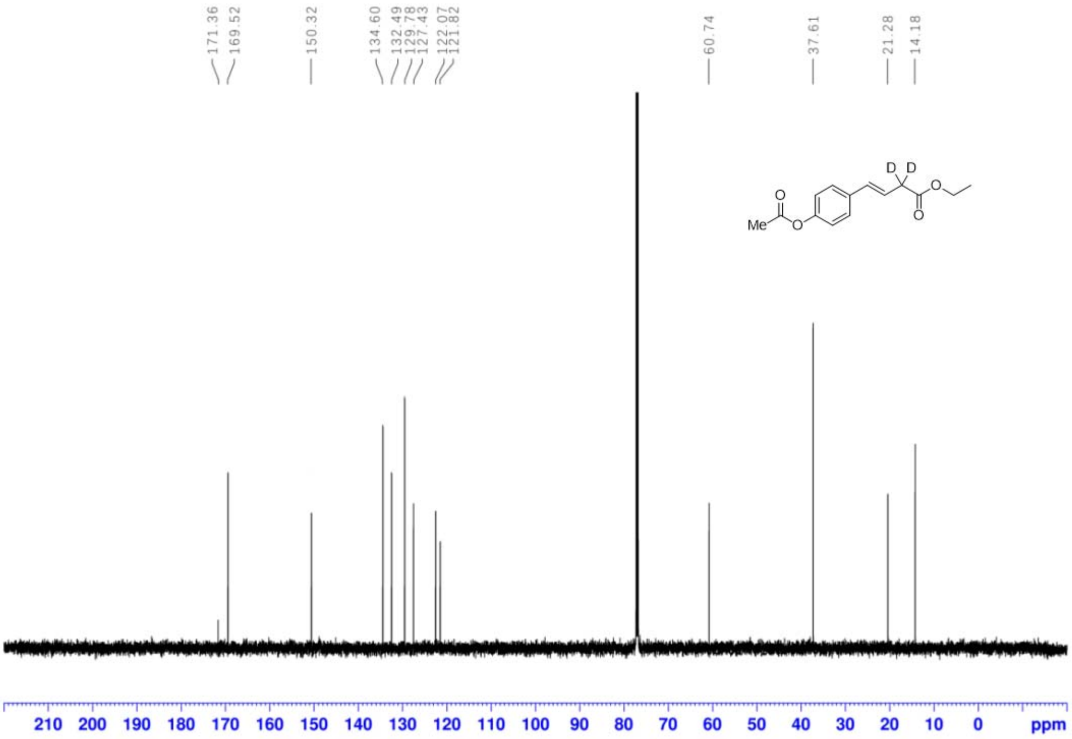
^{13}C NMR Spectra of **3d** (151 MHz, CDCl$_3$)



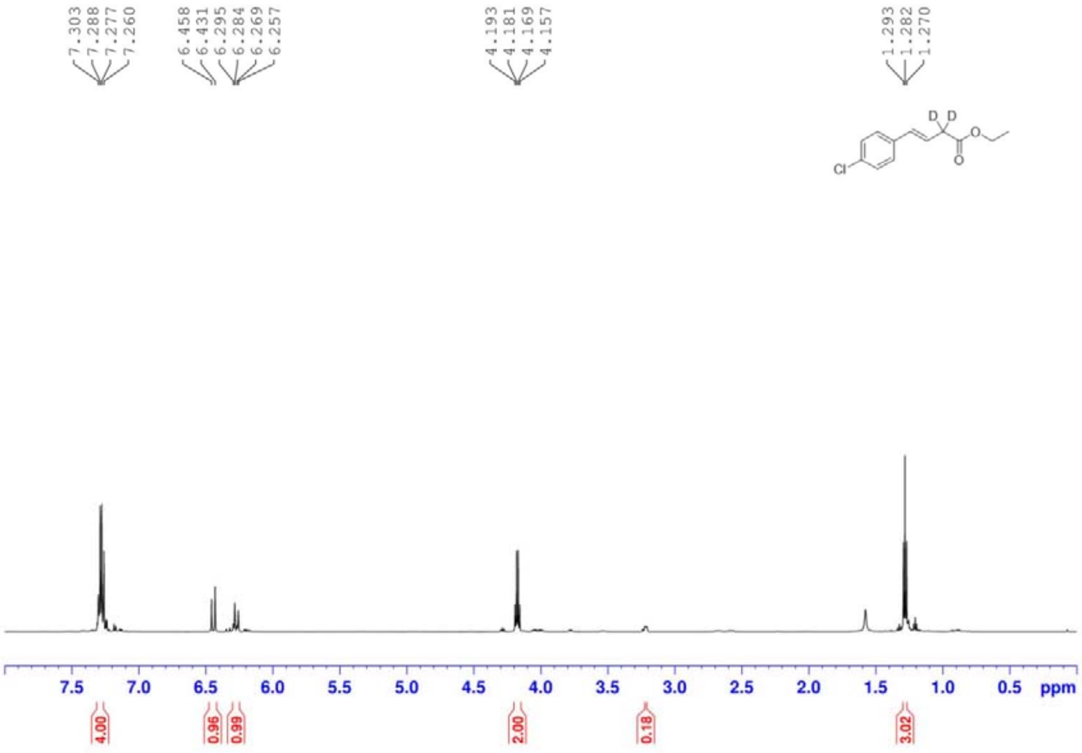
^{1}H NMR Spectra of **3e** (600 MHz, CDCl$_3$)



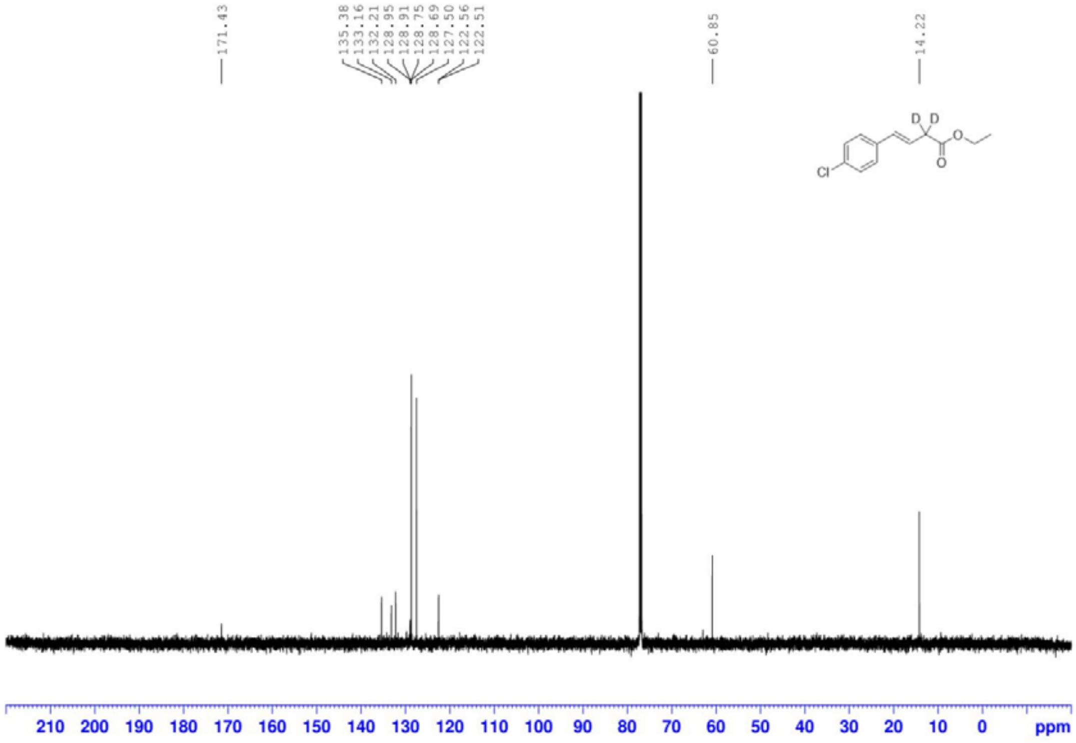
^{13}C NMR Spectra of **3e** (151 MHz, CDCl$_3$)



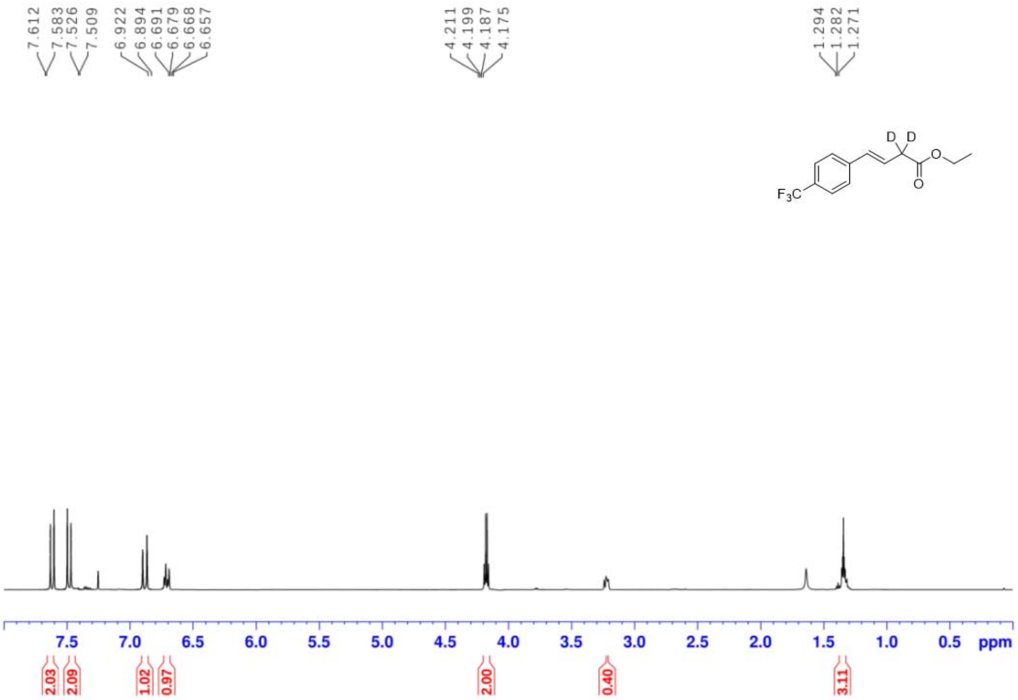
^{1}H NMR Spectra of **3f** (600 MHz, CDCl$_3$)



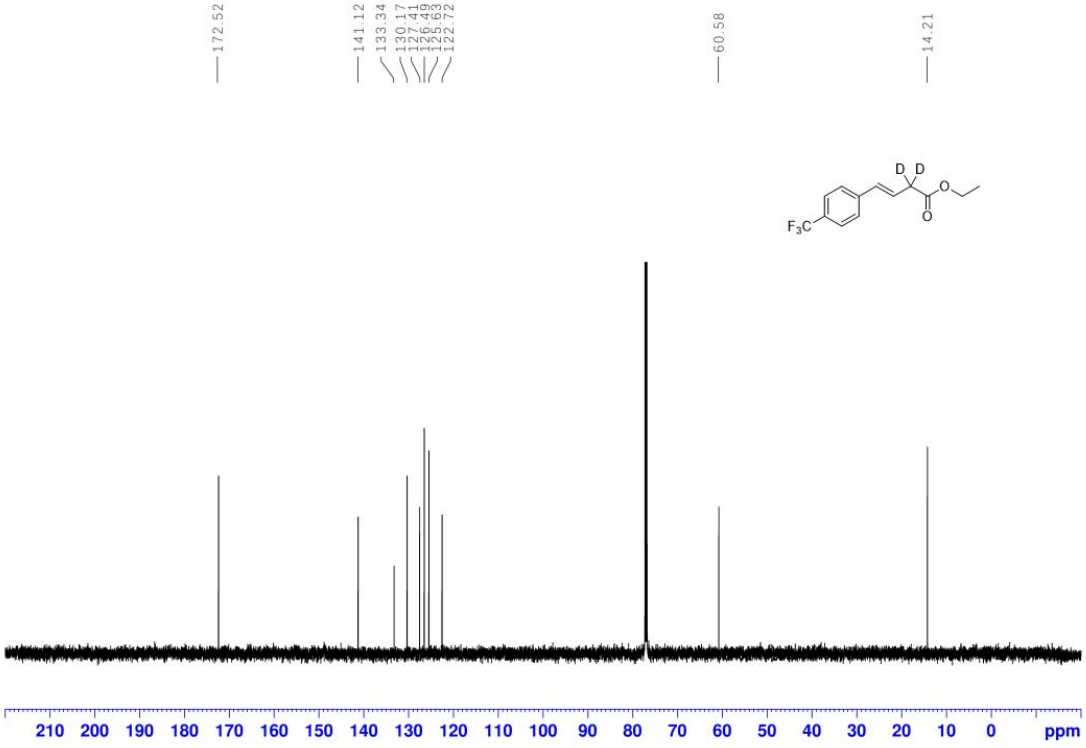
^{13}C NMR Spectra of **3f** (151 MHz, $CDCl_3$)



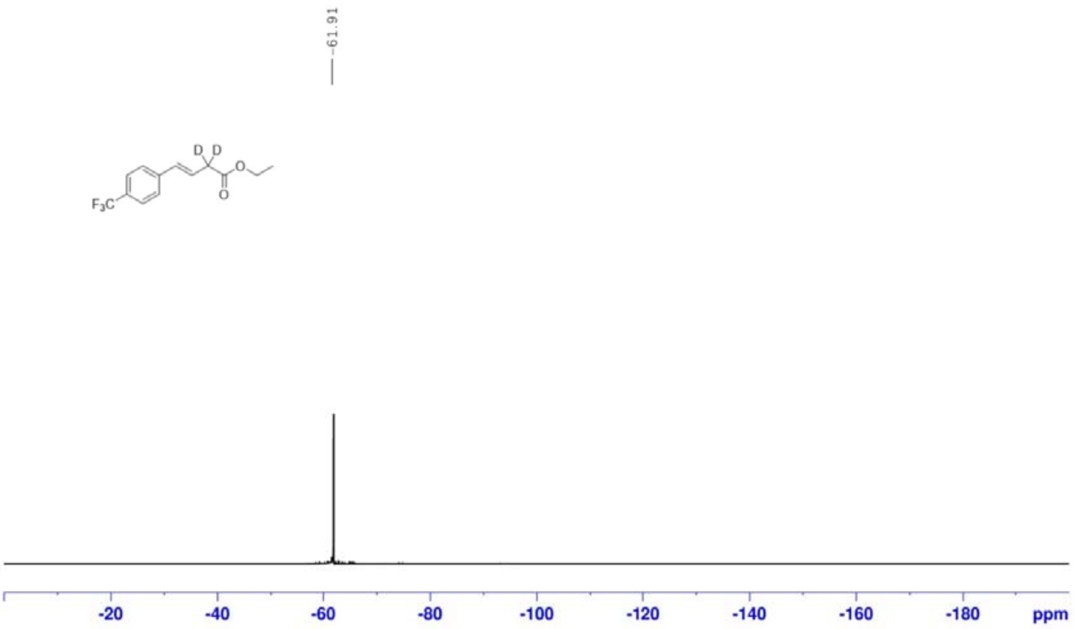
^{1}H NMR Spectra of **3g** (600 MHz, $CDCl_3$)



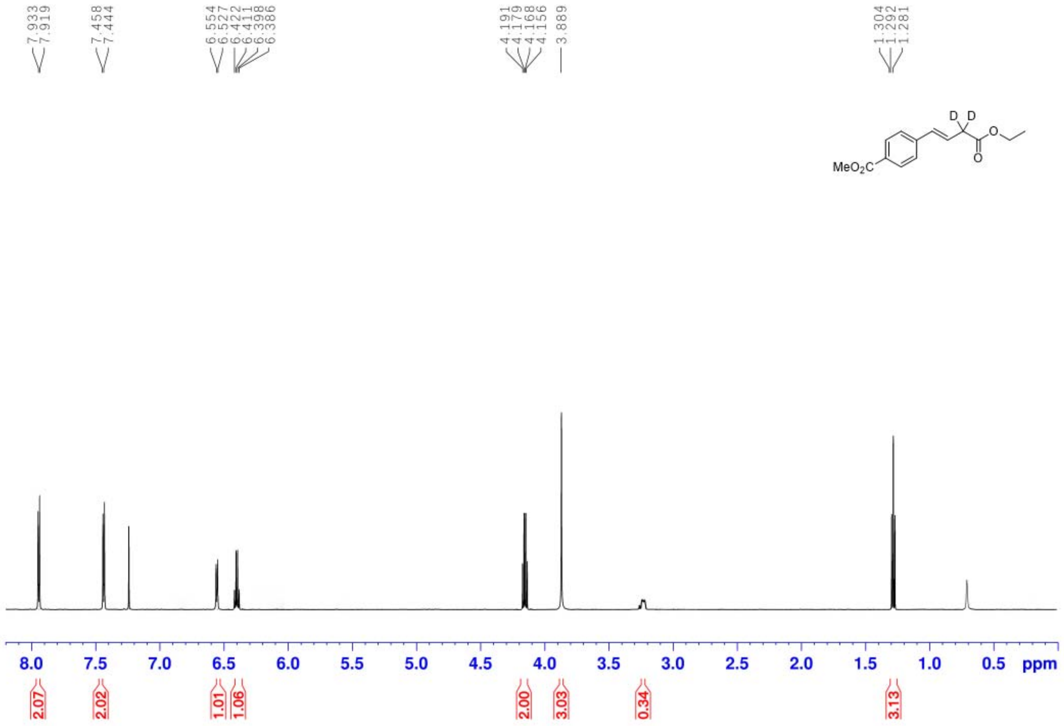
^{13}C NMR Spectra of **3g** (151 MHz, $CDCl_3$)



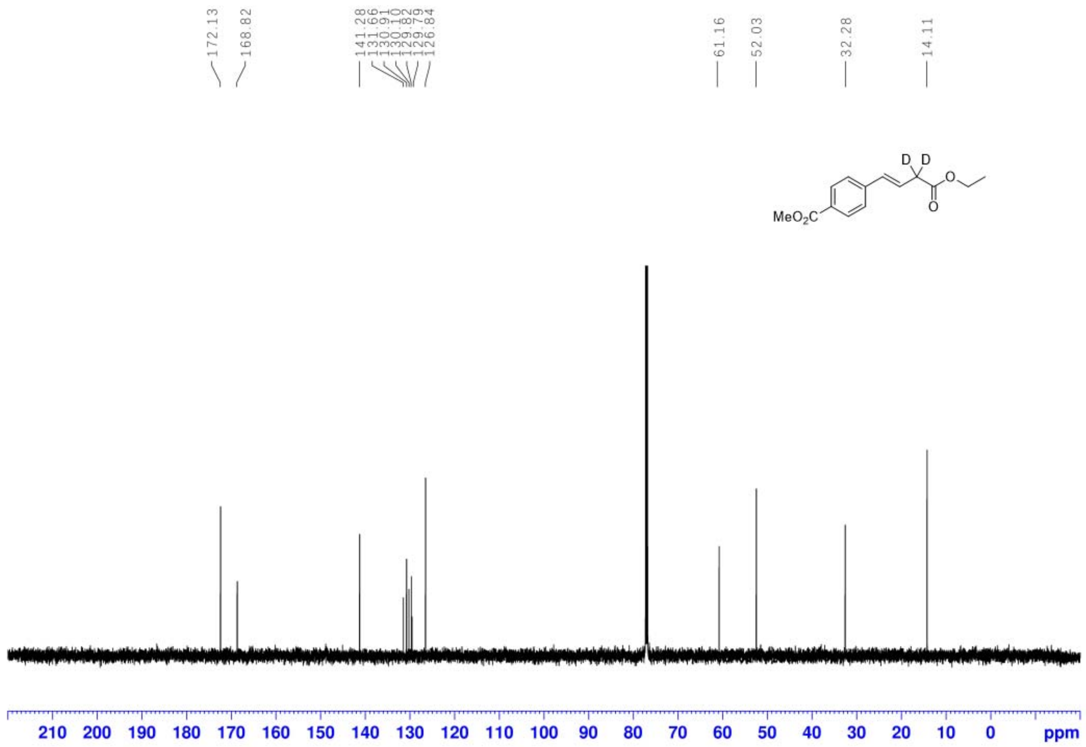
^{19}F NMR Spectra of **3g** (377 MHz, $CDCl_3$)



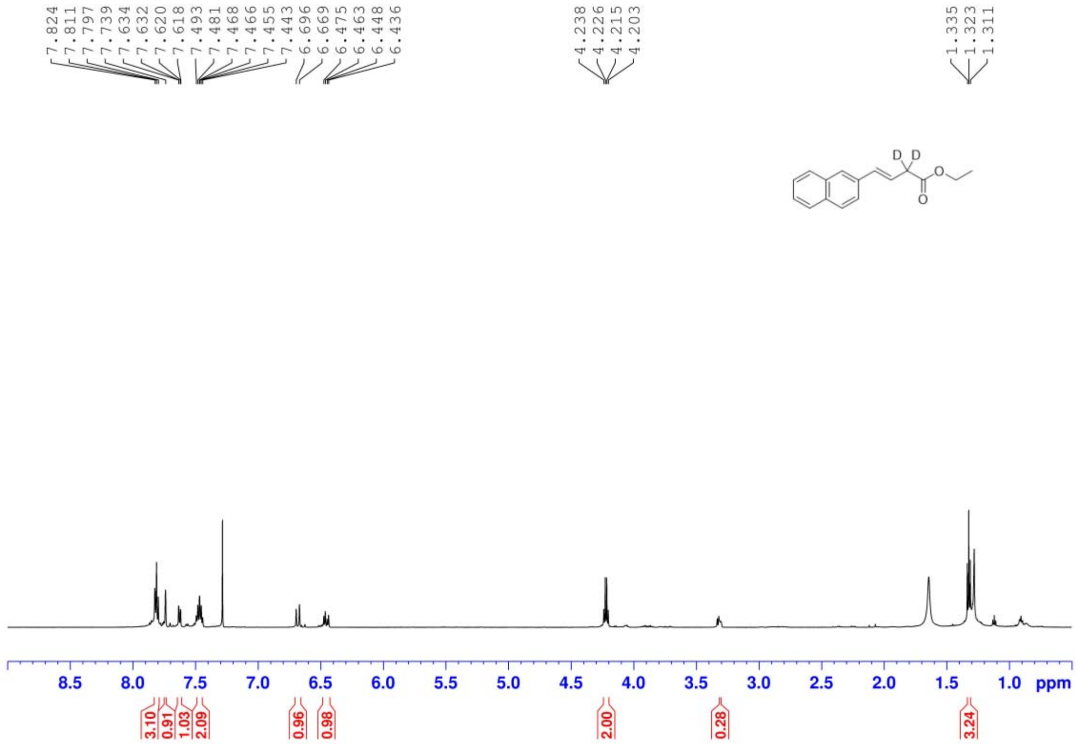
^{1}H NMR Spectra of **3h** (600 MHz, CDCl$_3$)



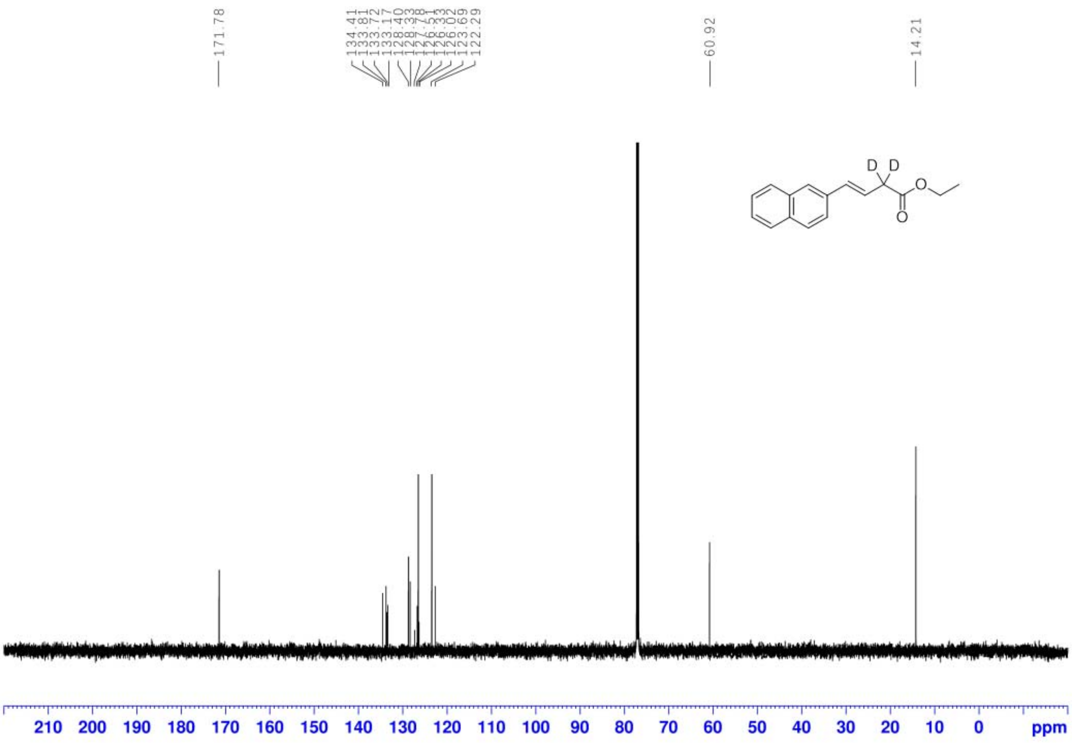
^{13}C NMR Spectra of **3h** (151 MHz, CDCl$_3$)



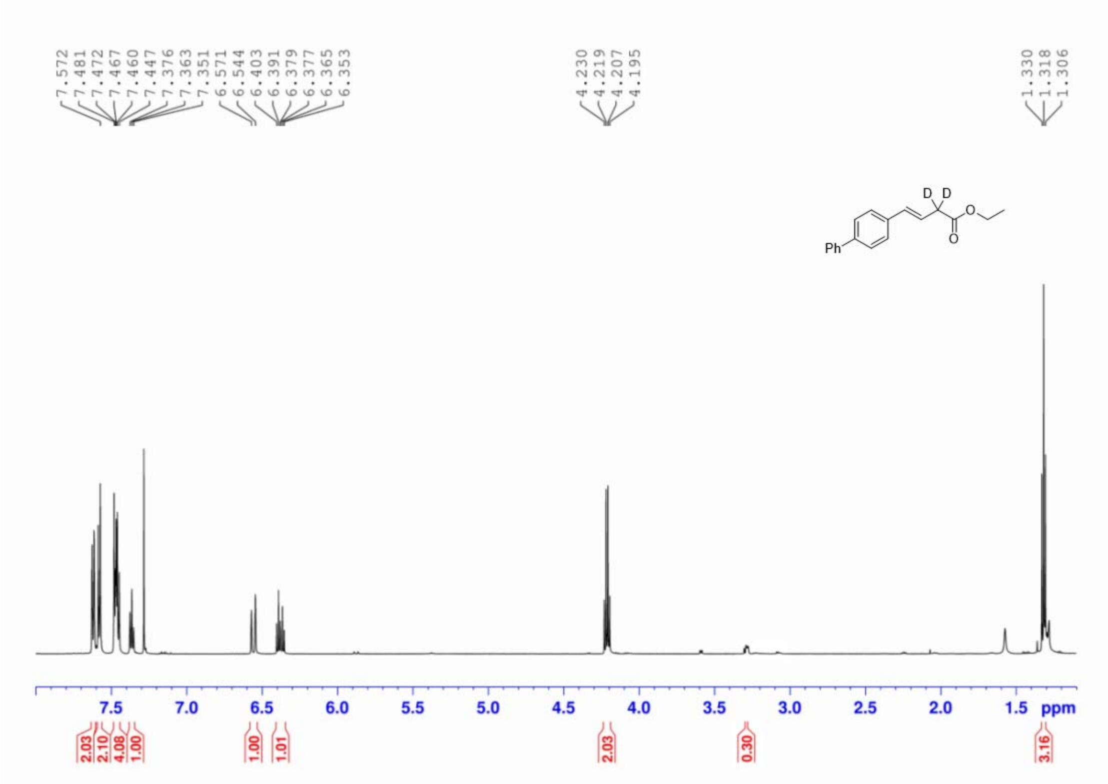
^{1}H NMR Spectra of **3i** (600 MHz, CDCl$_3$)



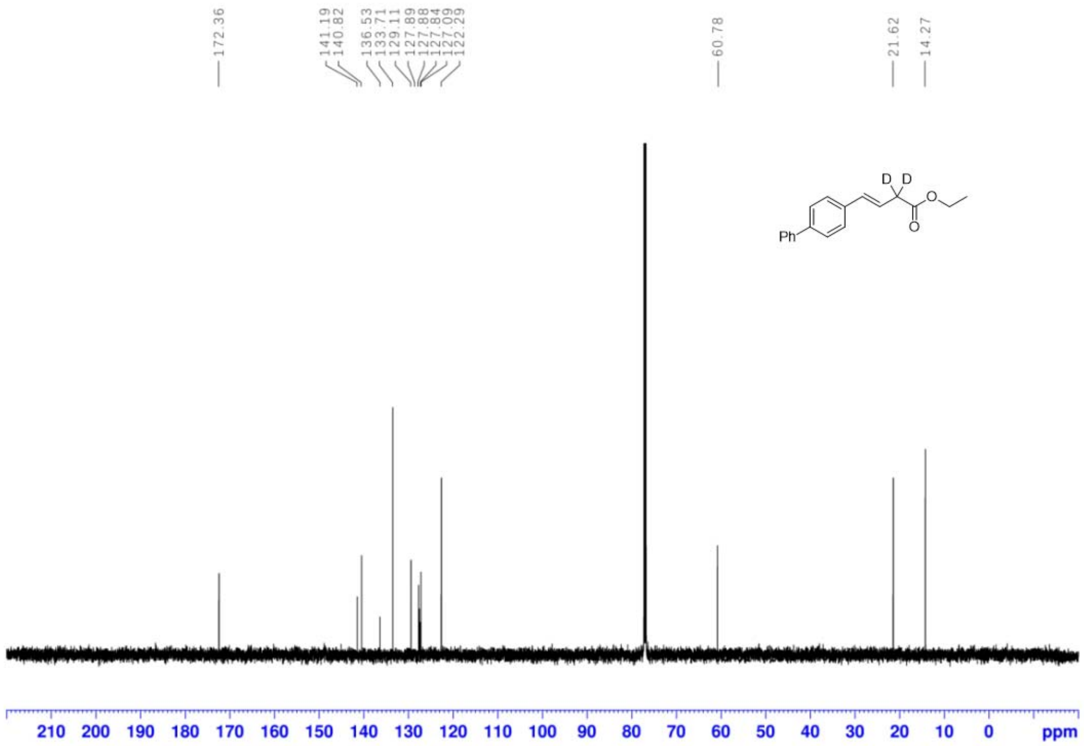
^{13}C NMR Spectra of **3i** (151 MHz, CDCl$_3$)



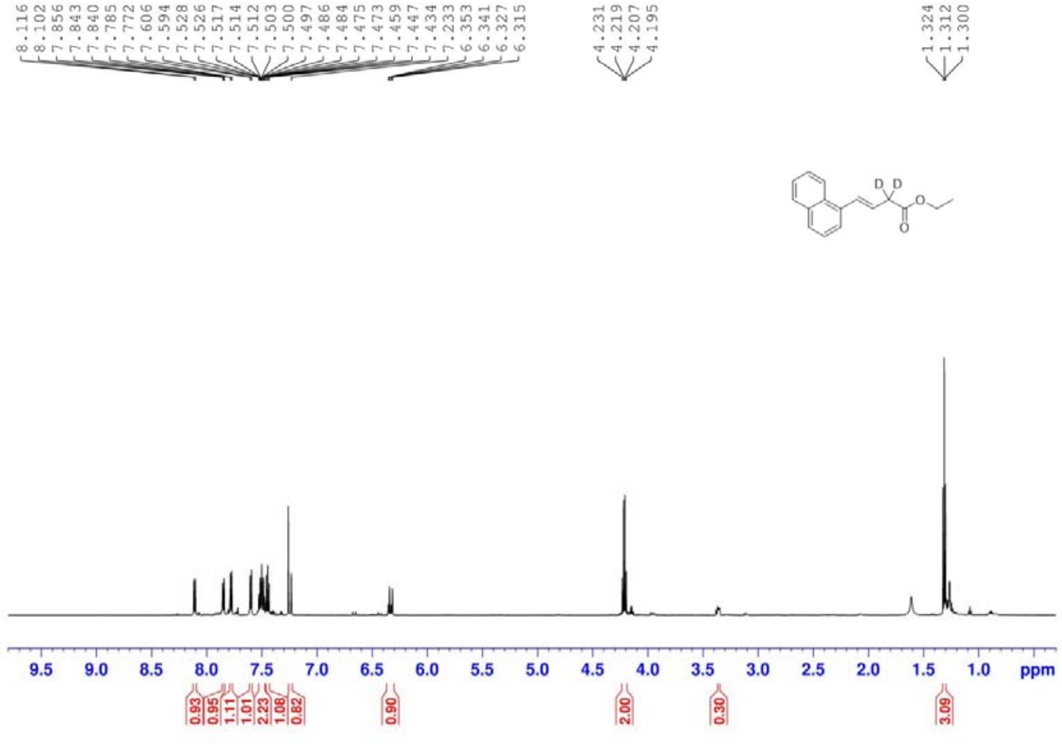
^{1}H NMR Spectra of **3j** (600 MHz, CDCl$_3$)



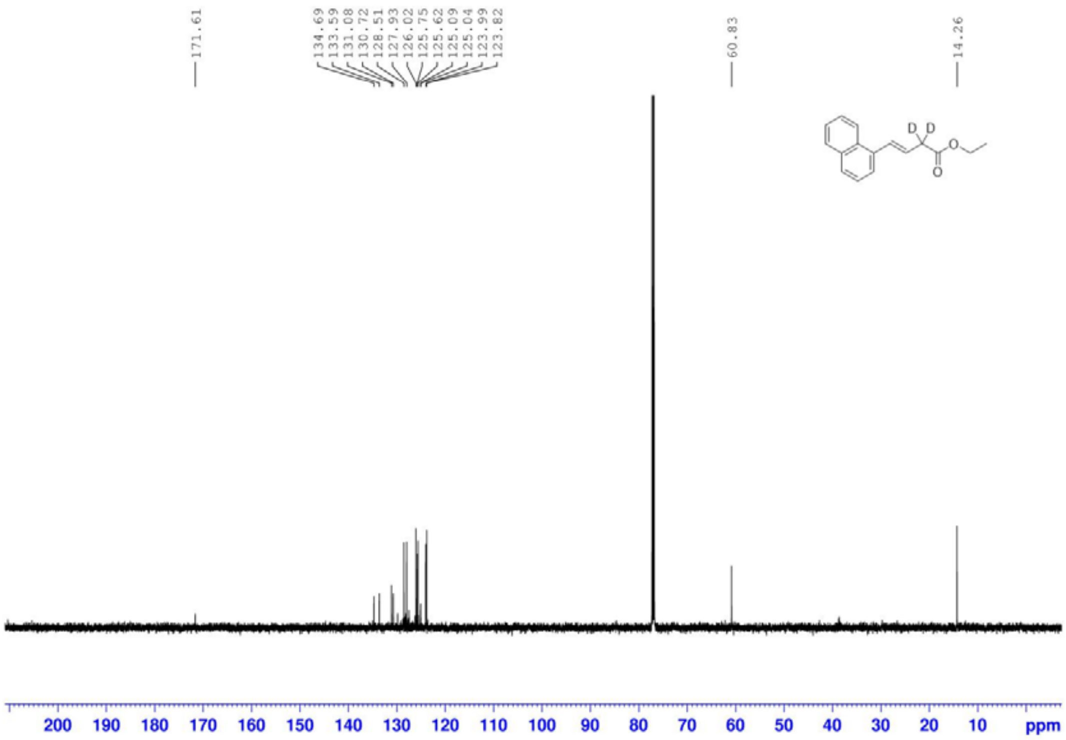
^{13}C NMR Spectra of **3j** (151 MHz, CDCl$_3$)



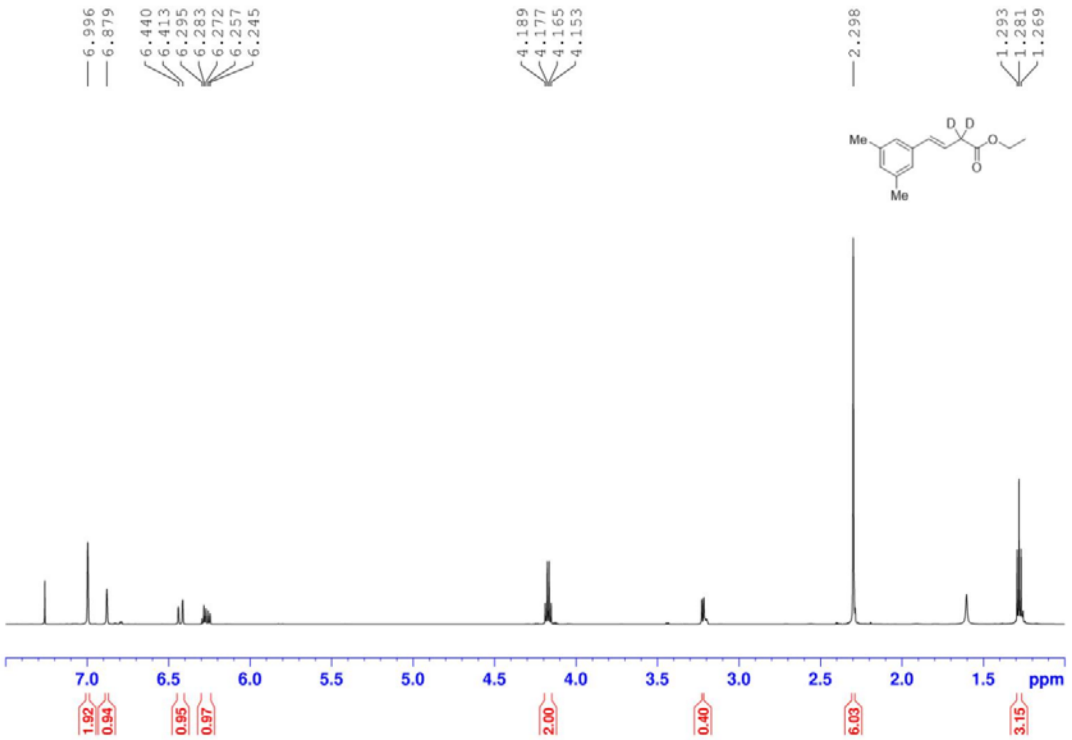
^{1}H NMR Spectra of **3k** (600 MHz, CDCl$_3$)



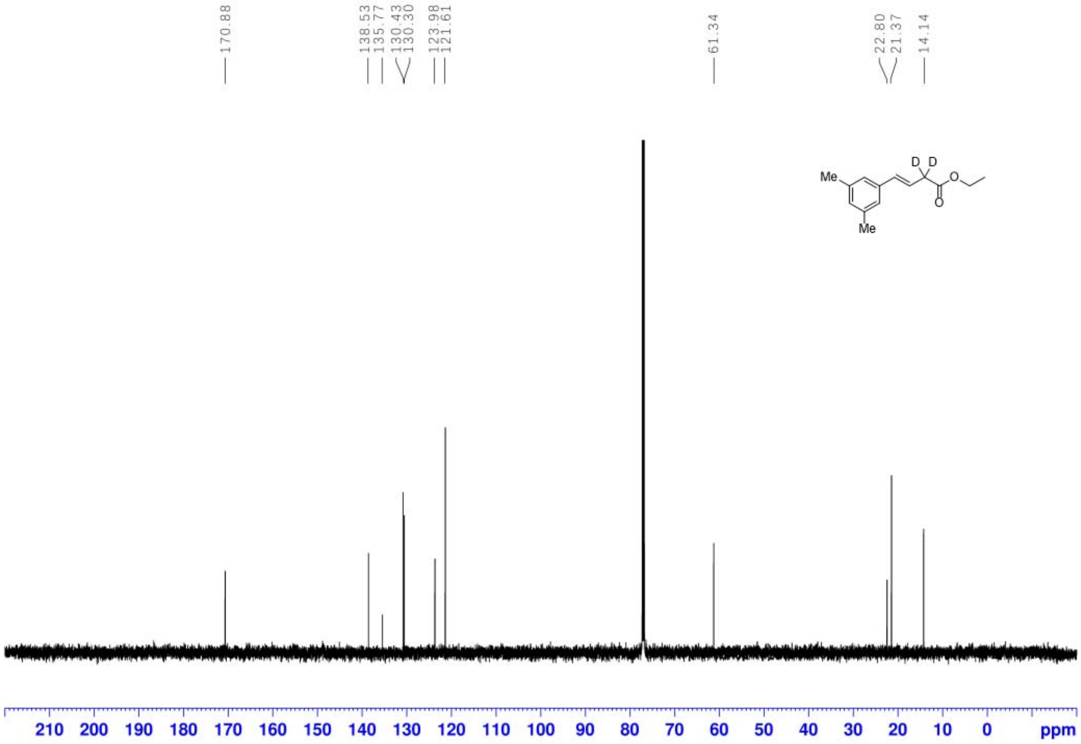
^{13}C NMR Spectra of **3k** (151 MHz, CDCl$_3$)



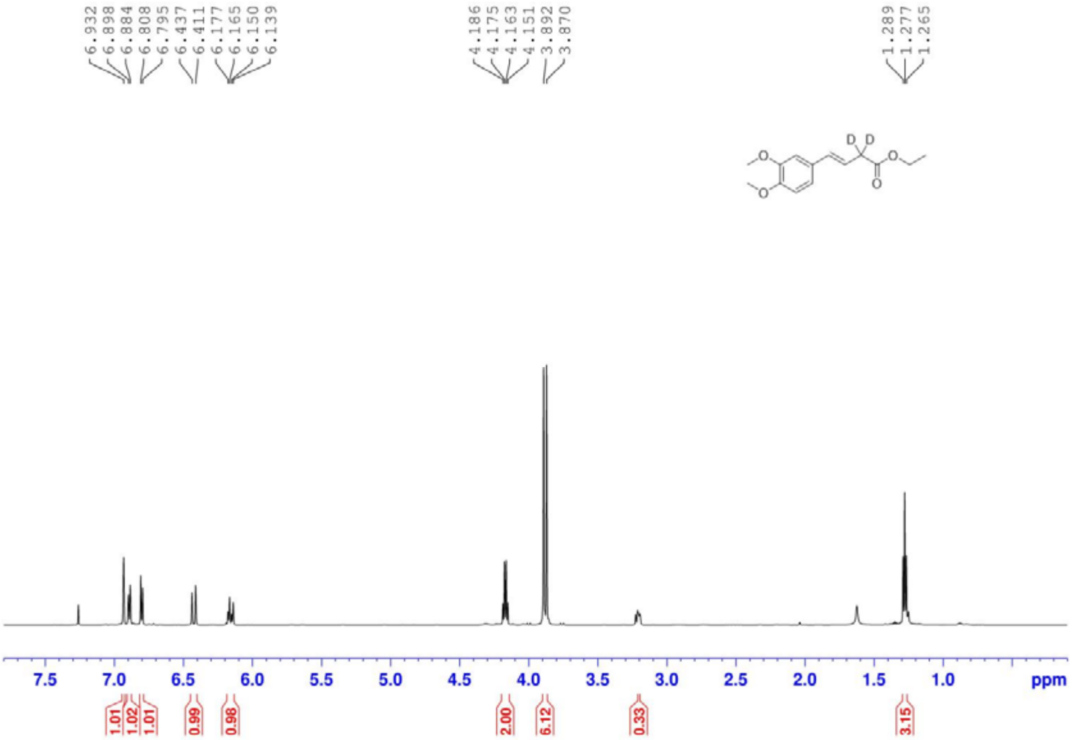
^{1}H NMR Spectra of **3l** (600 MHz, CDCl$_3$)



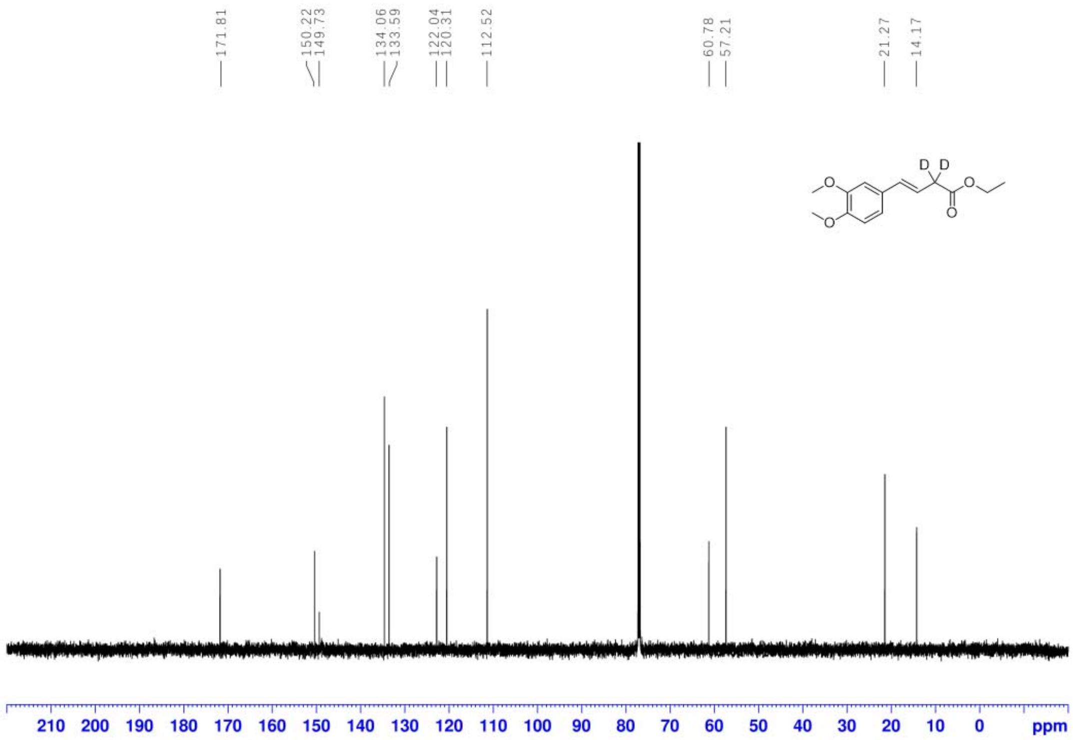
^{13}C NMR Spectra of **3l** (151 MHz, CDCl$_3$)



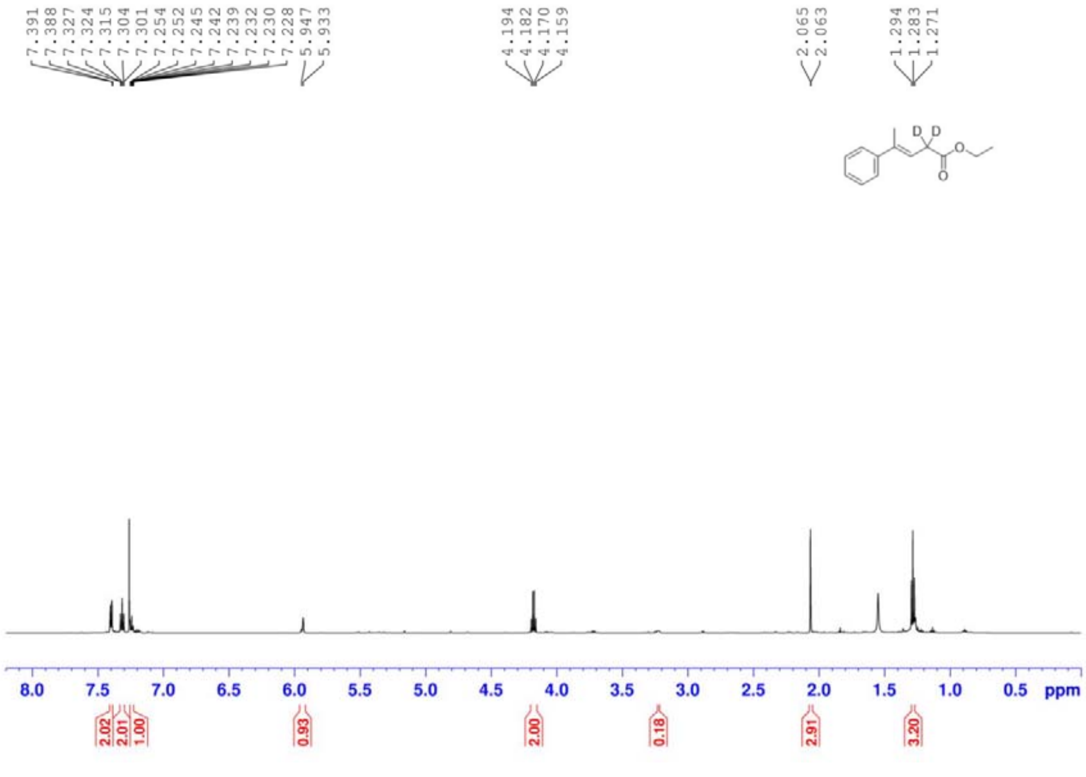
^{1}H NMR Spectra of **3m** (600 MHz, CDCl$_3$)



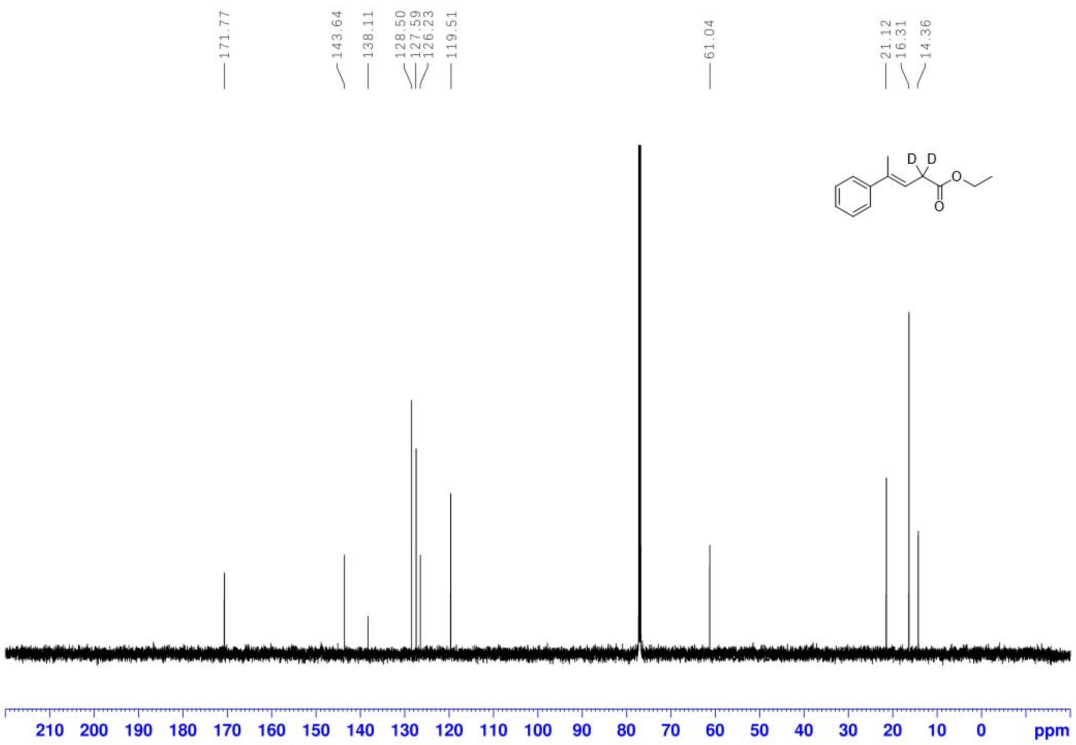
^{13}C NMR Spectra of **3m** (151 MHz, CDCl$_3$)



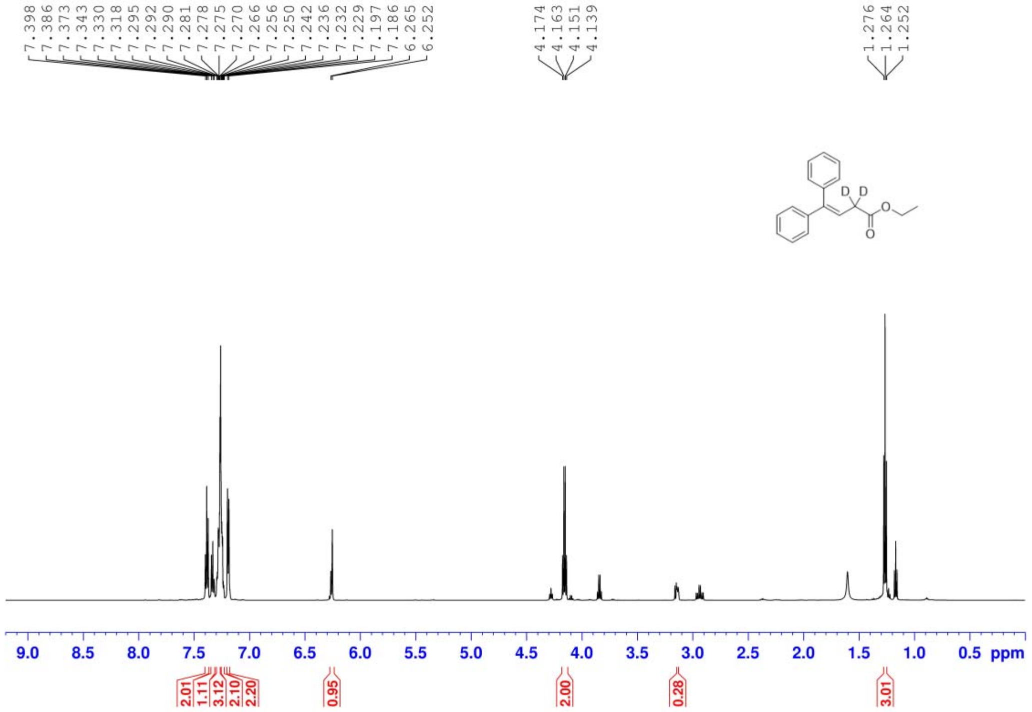
^{1}H NMR Spectra of **3n** (600 MHz, CDCl$_3$)



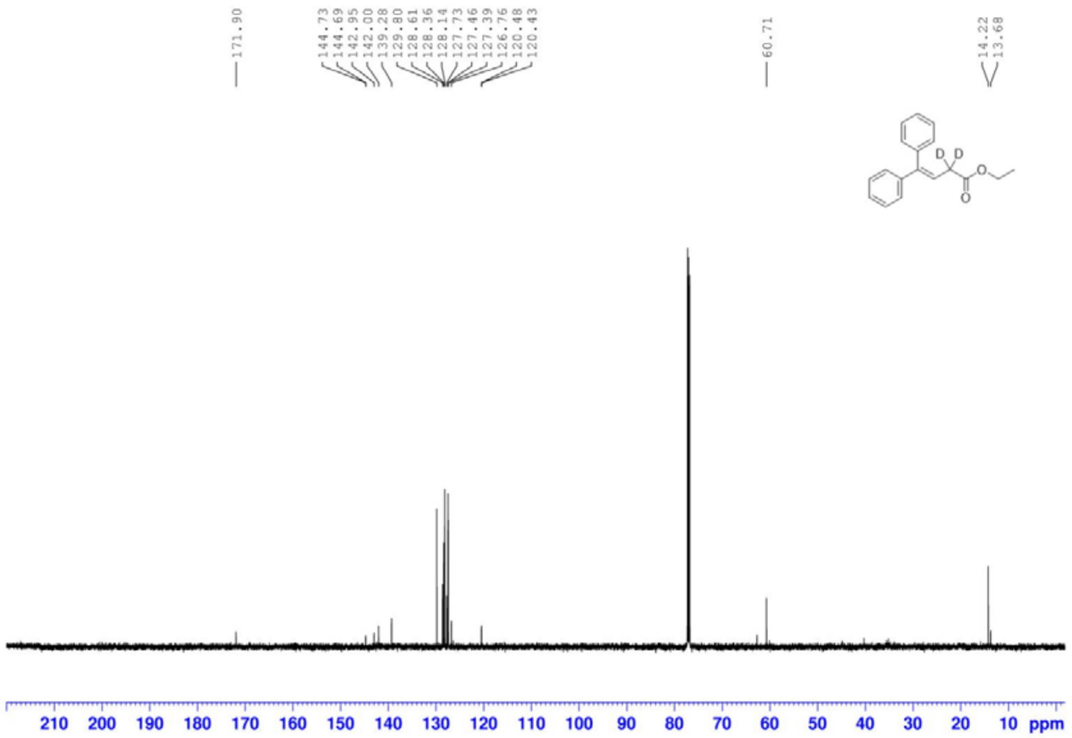
^{13}C NMR Spectra of **3n** (151 MHz, CDCl$_3$)



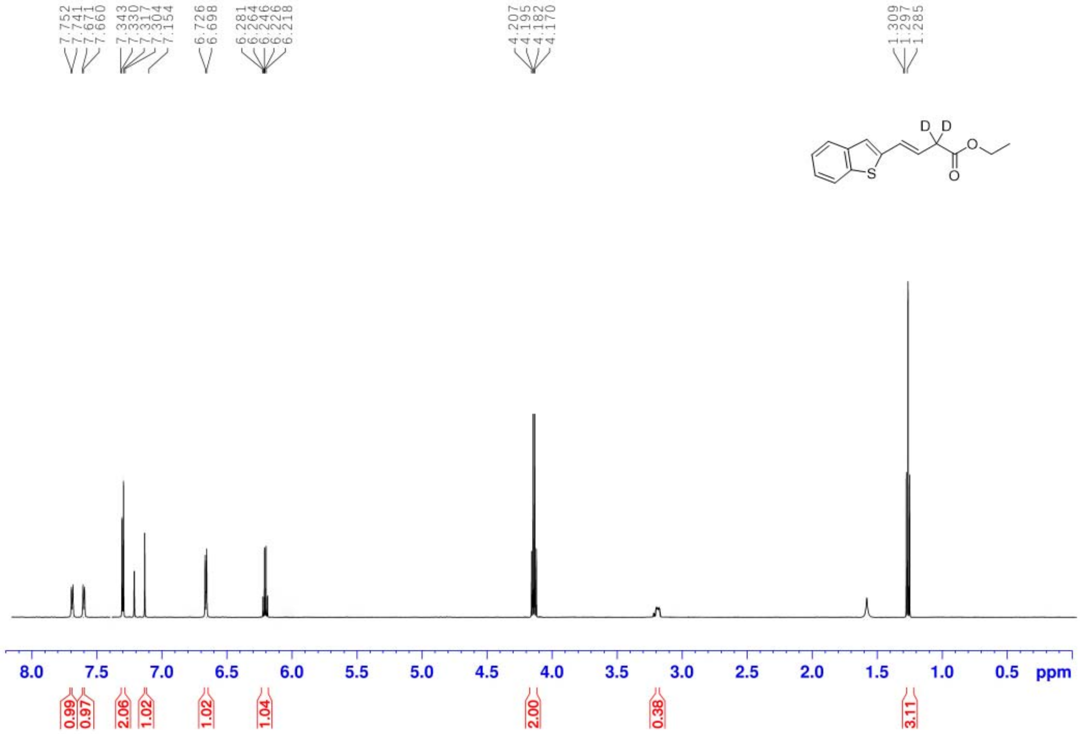
^{1}H NMR Spectra of **3o** (600 MHz, $CDCl_3$)



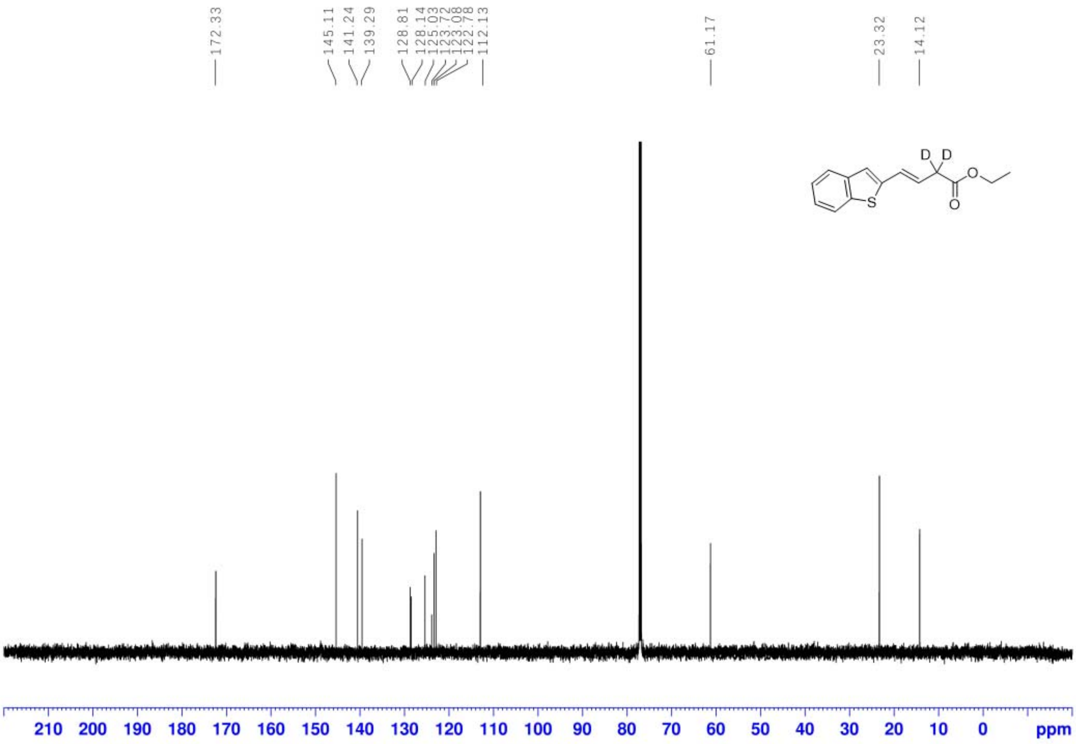
^{13}C NMR Spectra of **3o** (151 MHz, $CDCl_3$)



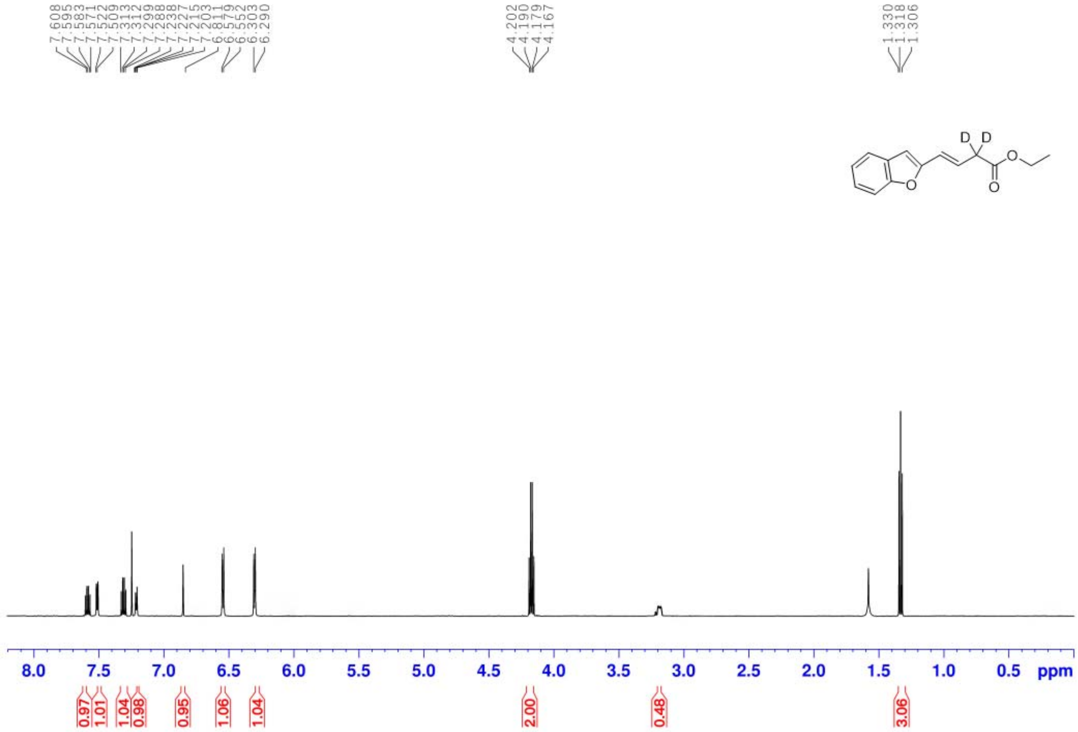
^{1}H NMR Spectra of **3p** (600 MHz, CDCl$_3$)



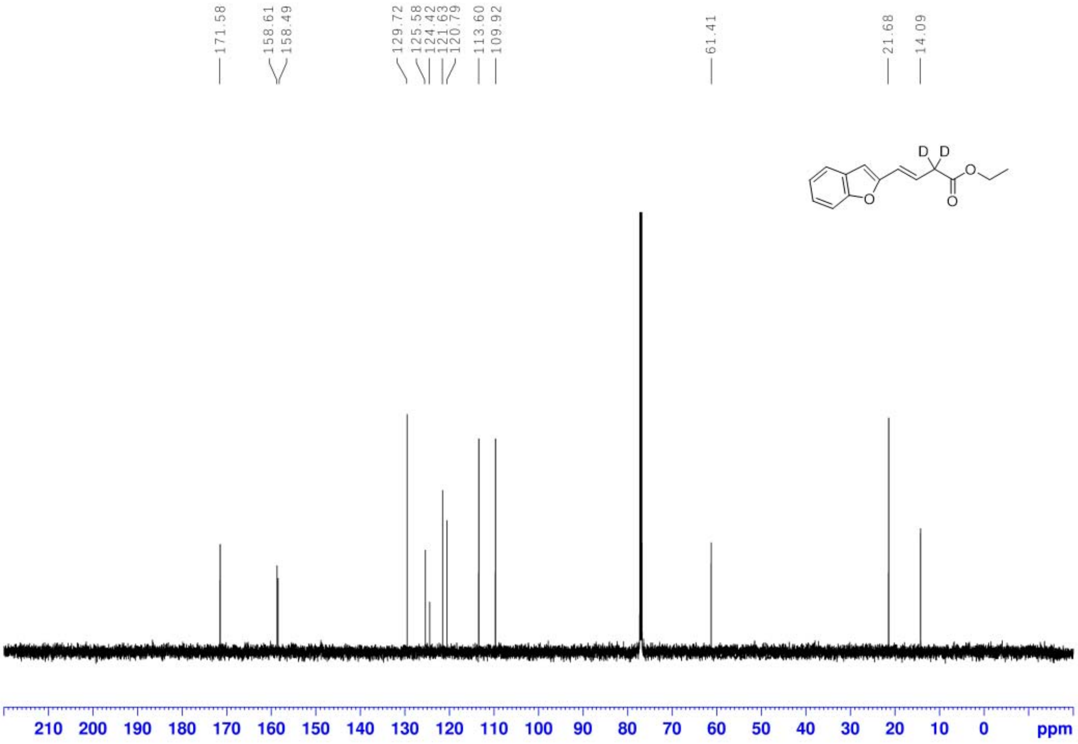
^{13}C NMR Spectra of **3p** (151 MHz, CDCl$_3$)



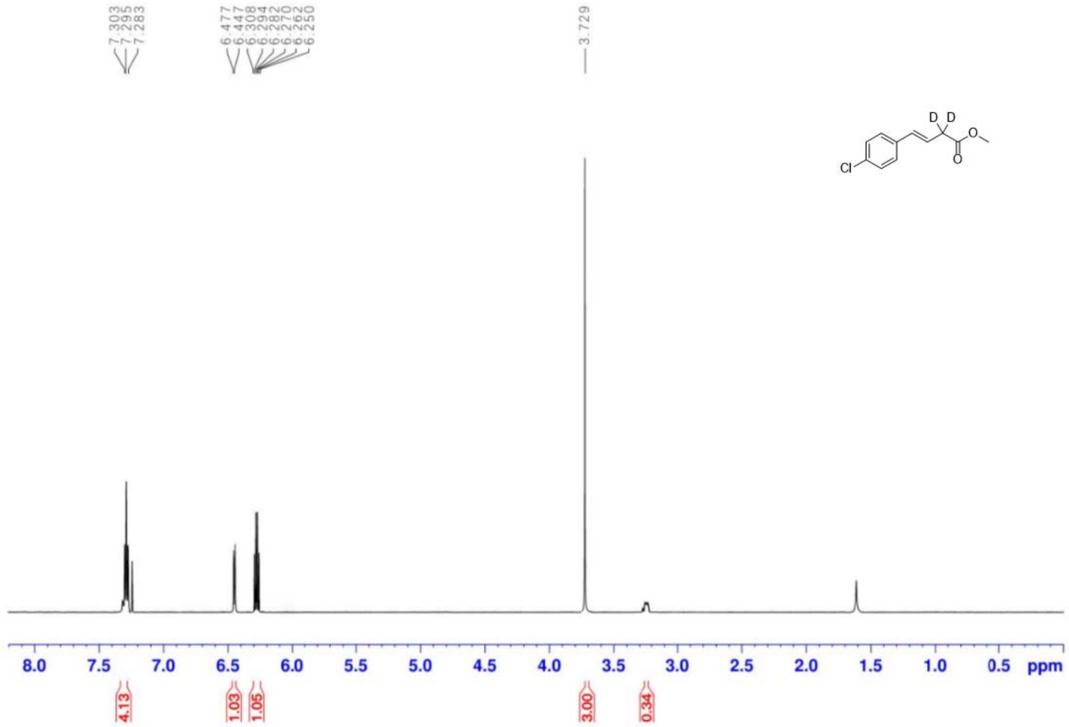
^{1}H NMR Spectra of **3q** (600 MHz, CDCl$_3$)



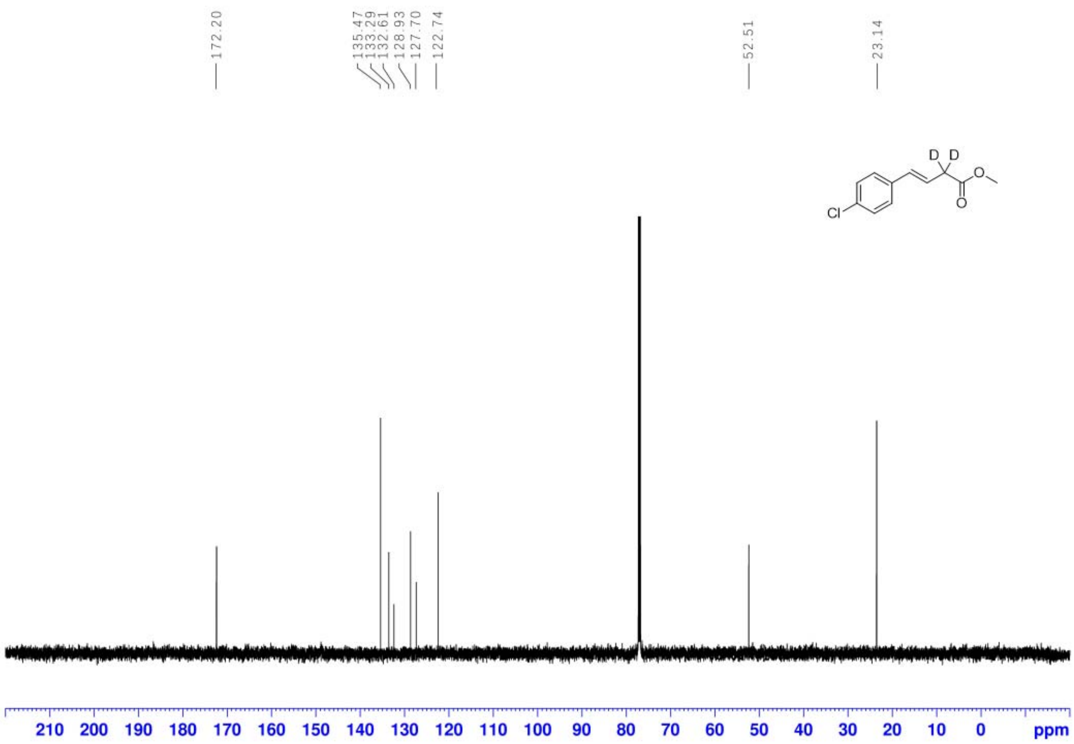
^{13}C NMR Spectra of **3q** (151 MHz, CDCl$_3$)



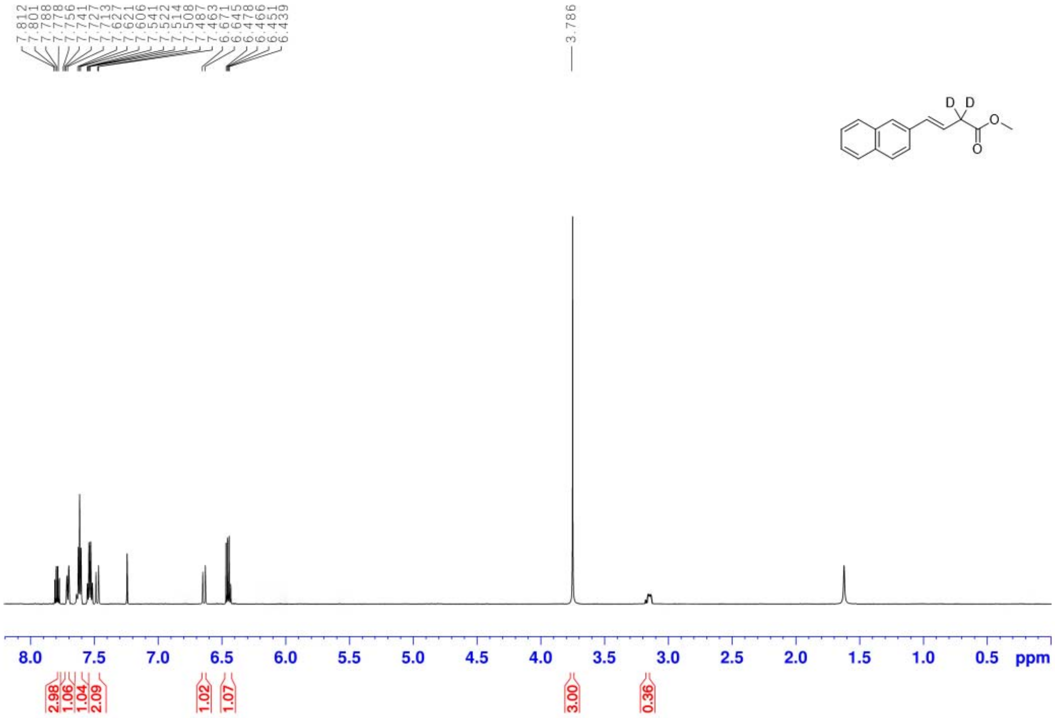
^{1}H NMR Spectra of **3r** (600 MHz, CDCl$_3$)



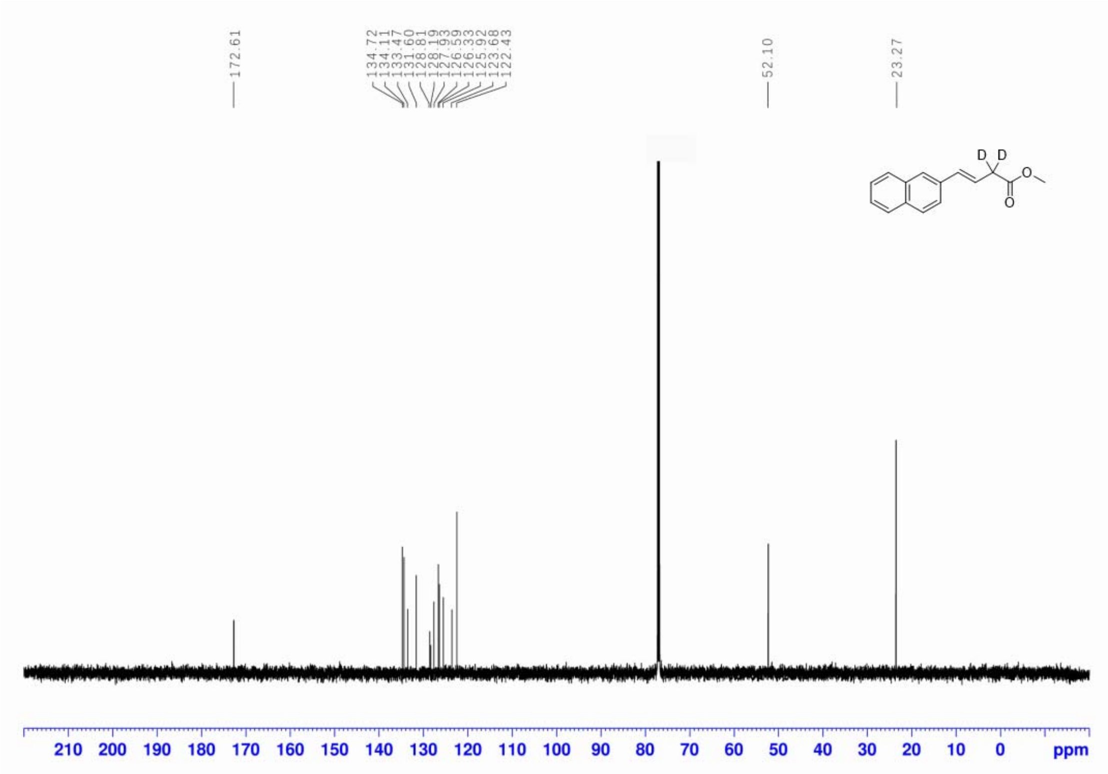
^{13}C NMR Spectra of **3r** (151 MHz, CDCl$_3$)



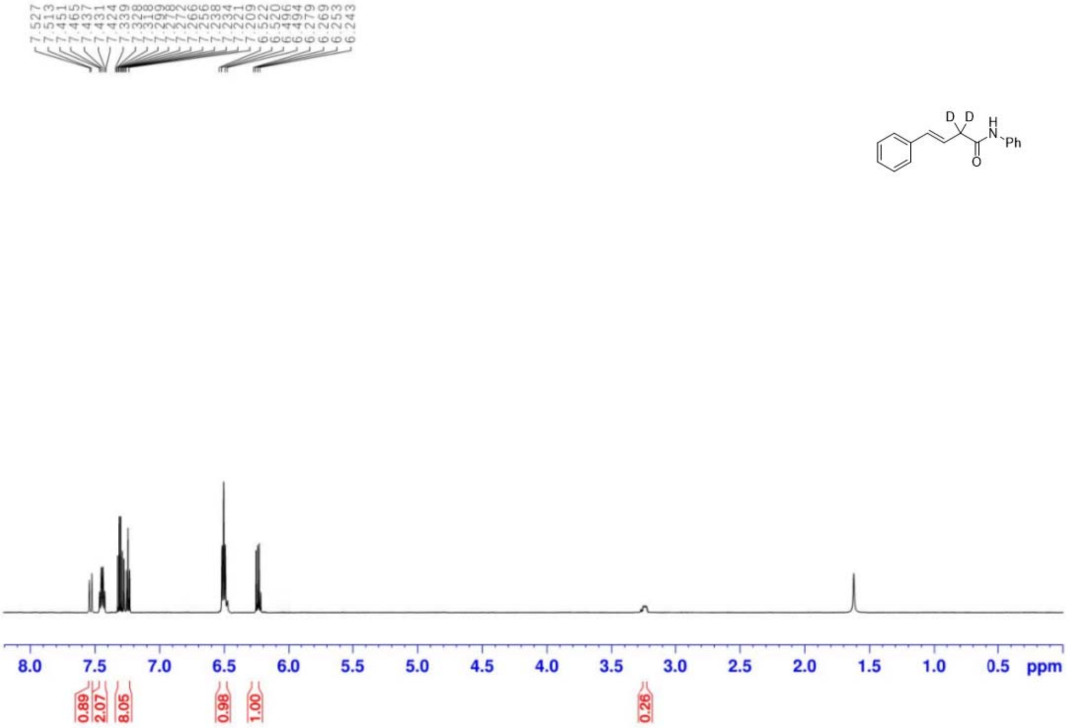
^{1}H NMR Spectra of **3s** (600 MHz, CDCl$_3$)



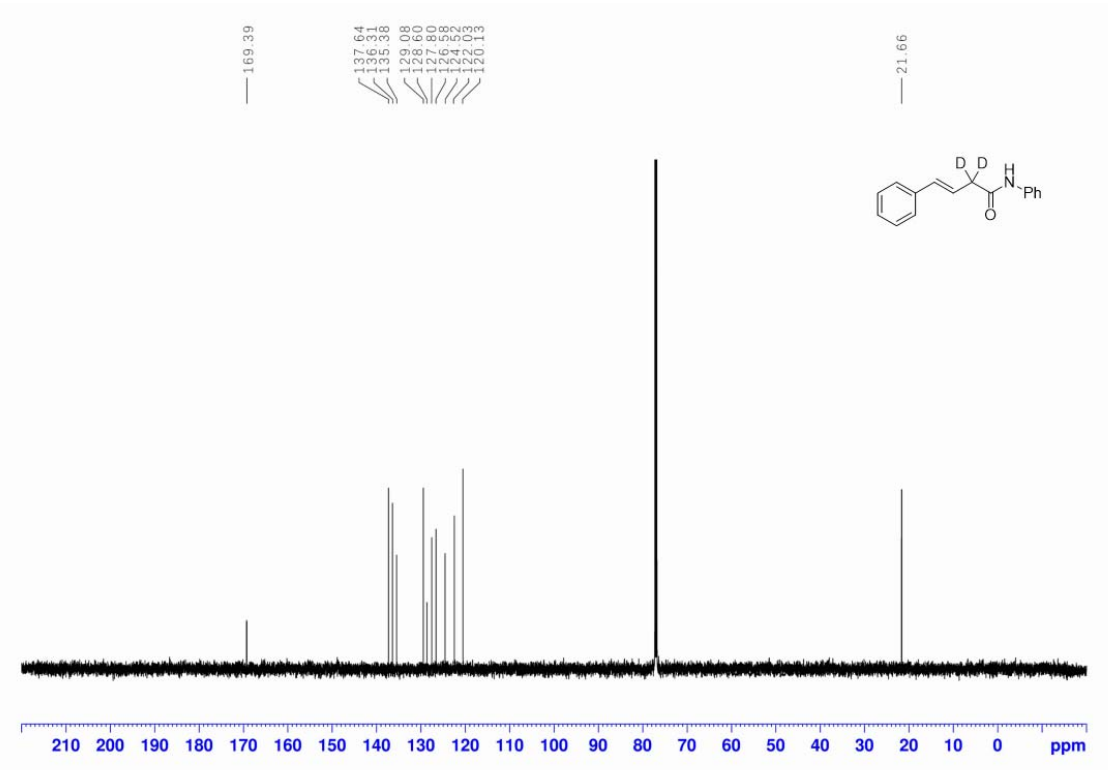
^{13}C NMR Spectra of **3s** (151 MHz, CDCl$_3$)



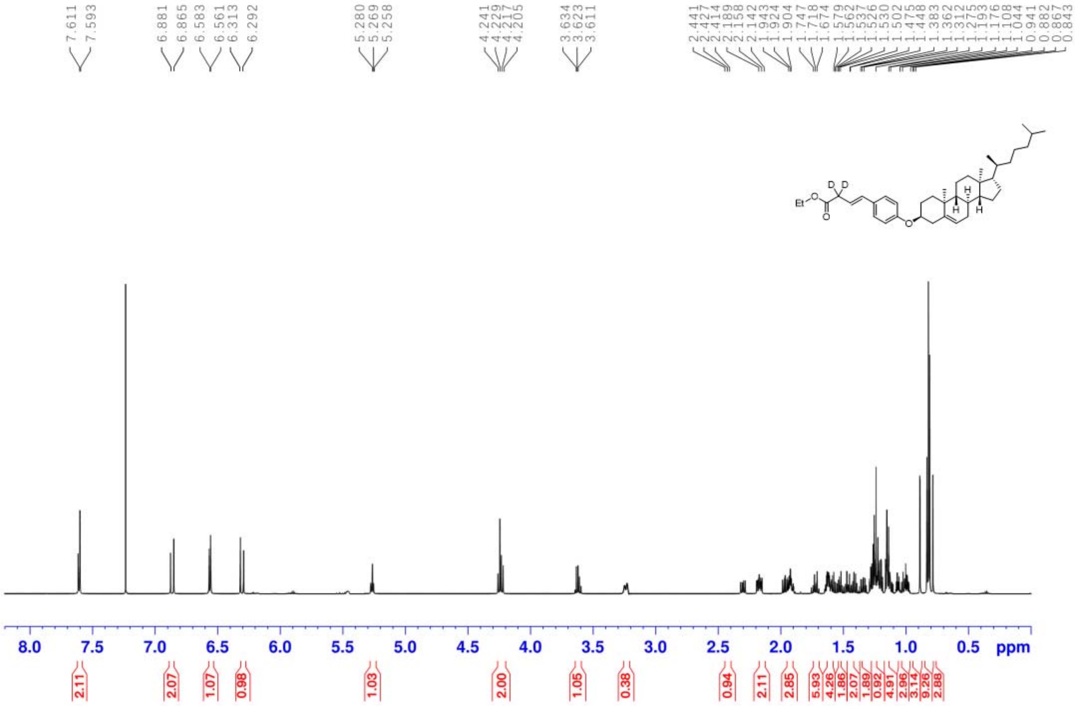
^{1}H NMR Spectra of **3t** (600 MHz, $CDCl_3$)



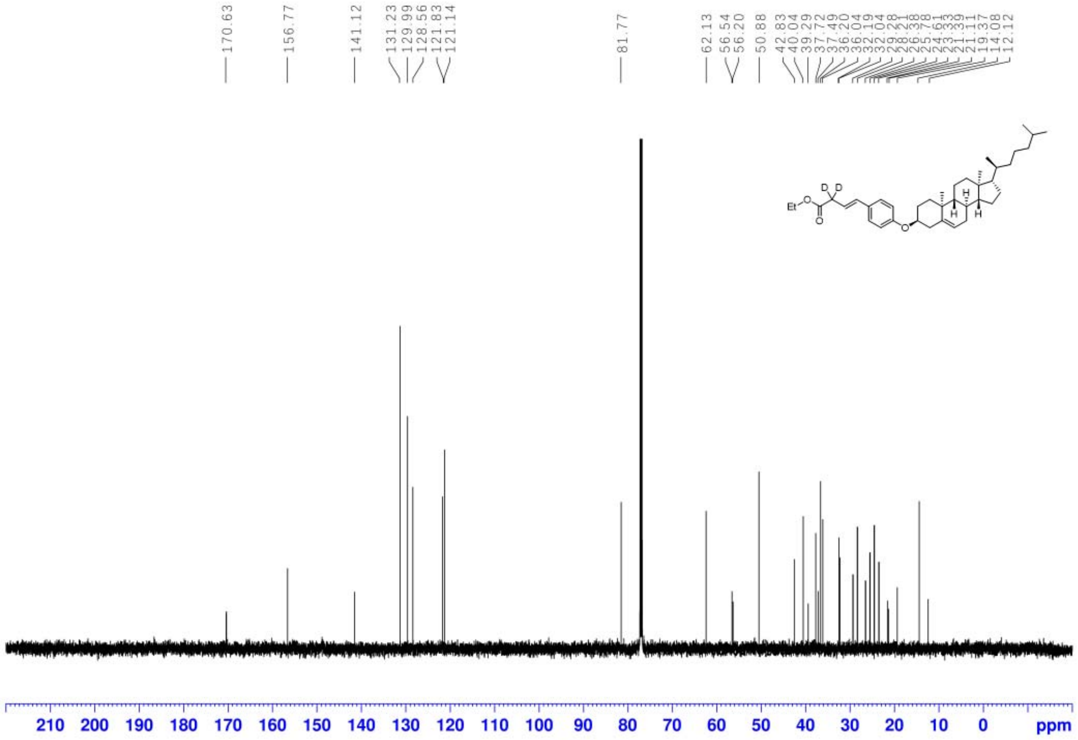
^{13}C NMR Spectra of **3t** (151 MHz, $CDCl_3$)



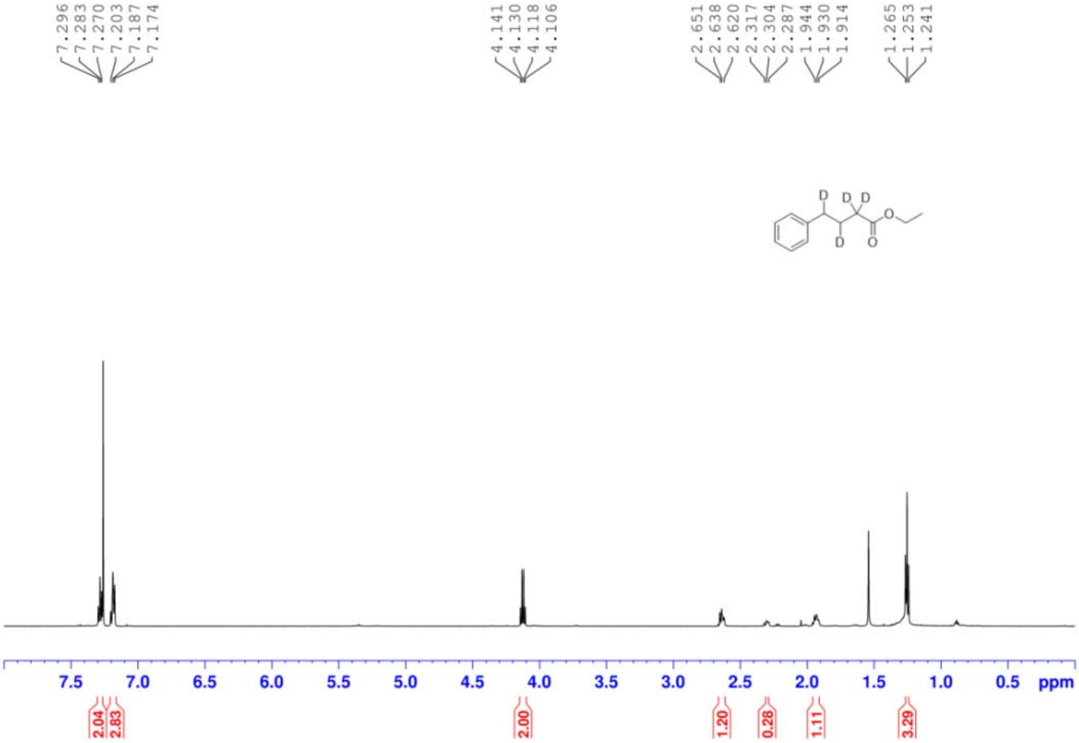
^{1}H NMR Spectra of **3u** (600 MHz, CDCl$_3$)



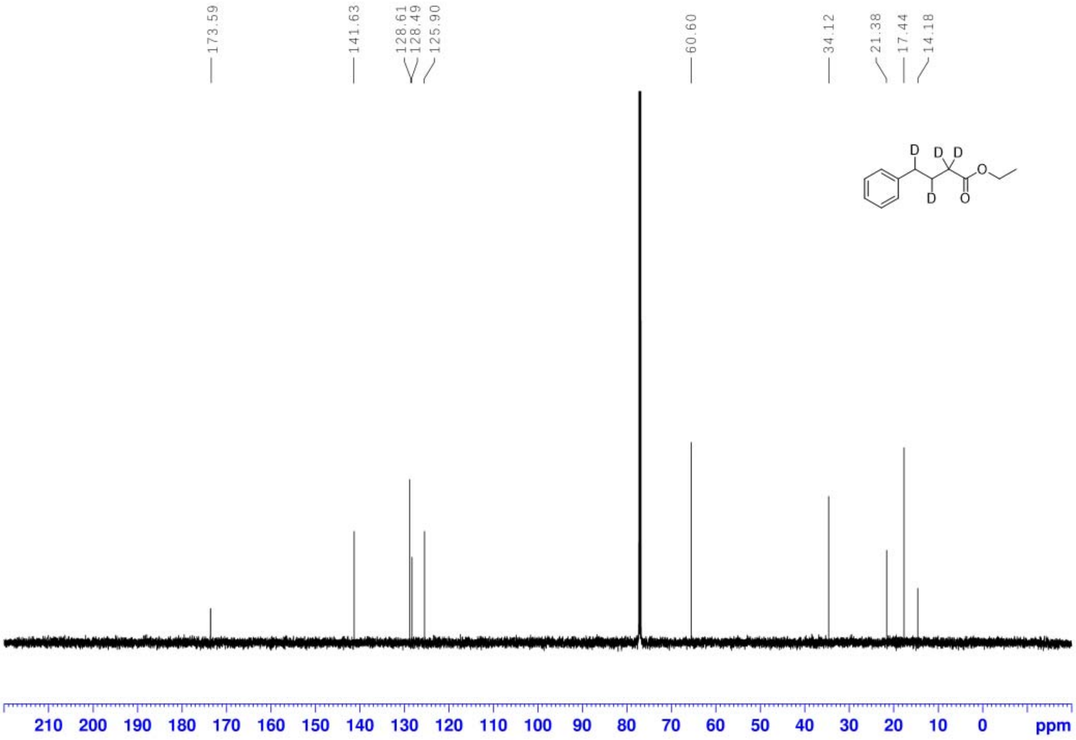
^{13}C NMR Spectra of **3u** (151 MHz, CDCl$_3$)



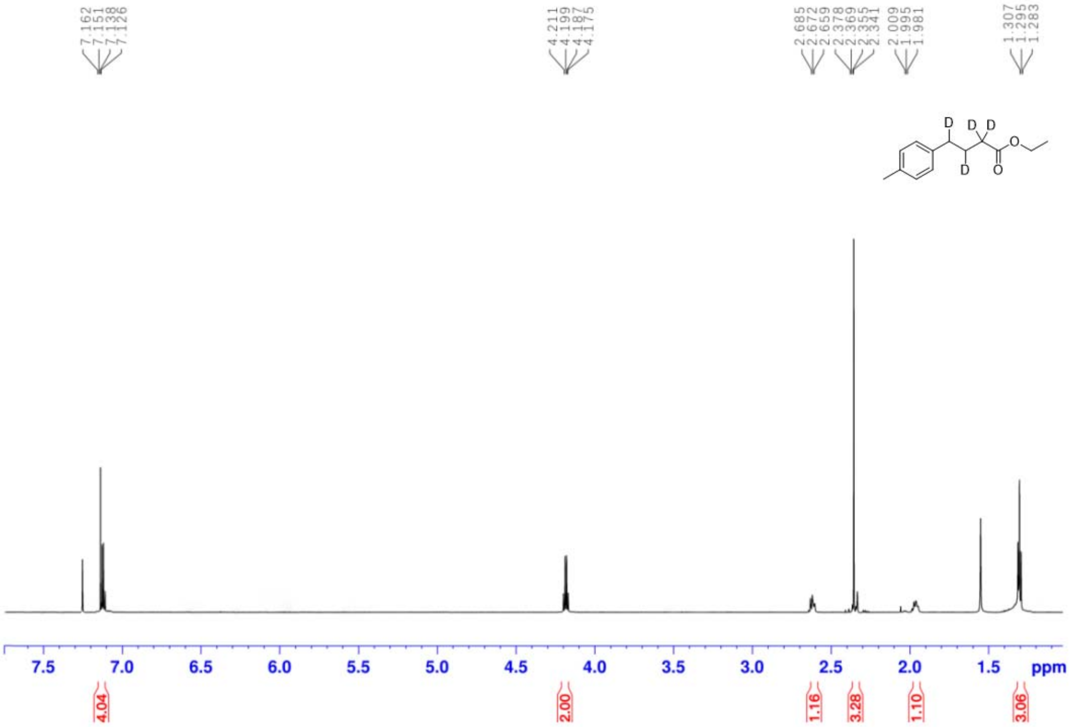
^{1}H NMR Spectra of **4a** (600 MHz, CDCl$_3$)



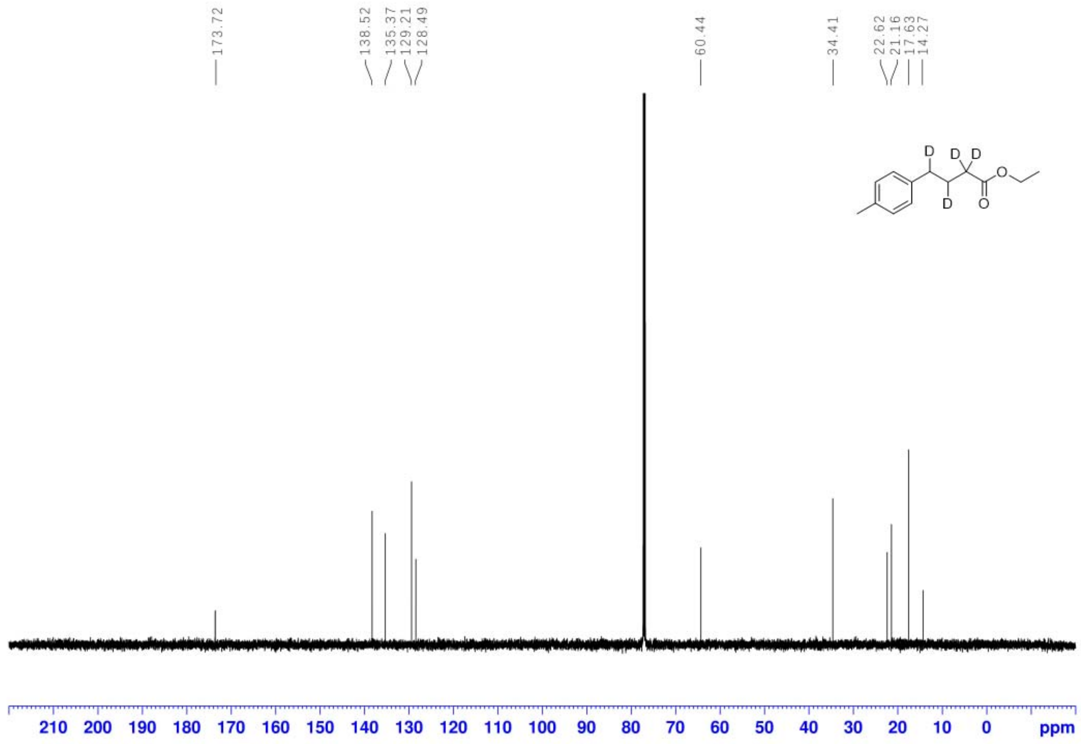
^{13}C NMR Spectra of **4a** (151 MHz, CDCl$_3$)



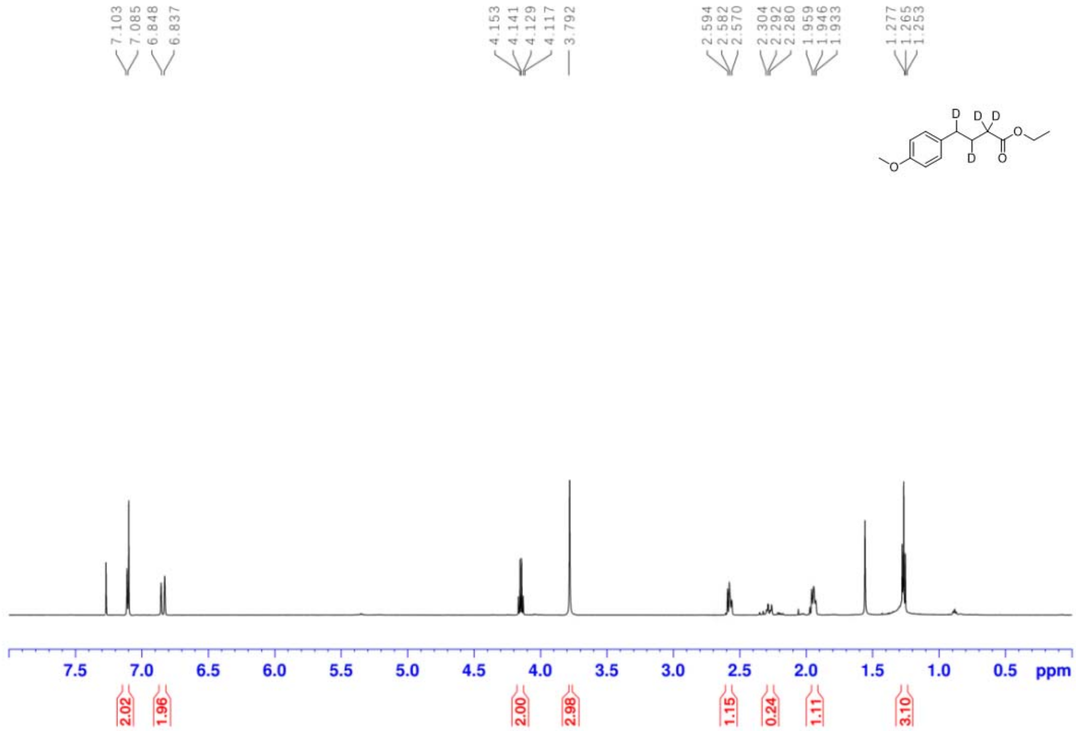
^{1}H NMR Spectra of **4b** (600 MHz, CDCl$_3$)



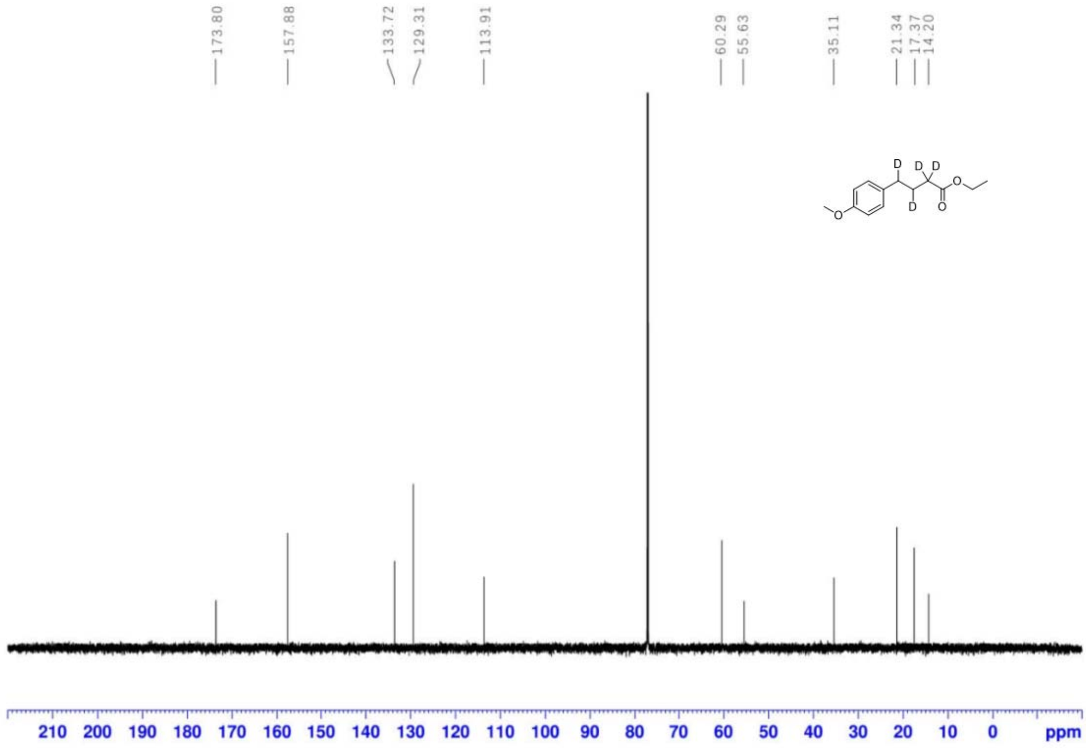
^{13}C NMR Spectra of **4b** (151 MHz, CDCl$_3$)



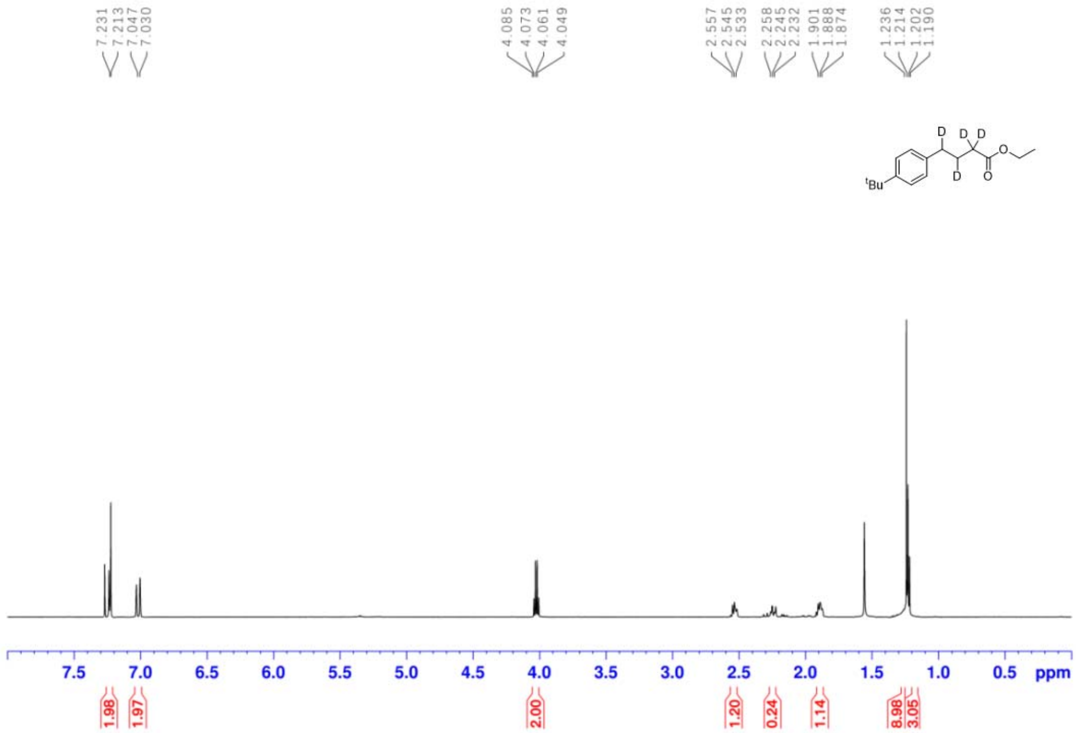
^{1}H NMR Spectra of **4c** (600 MHz, CDCl$_3$)



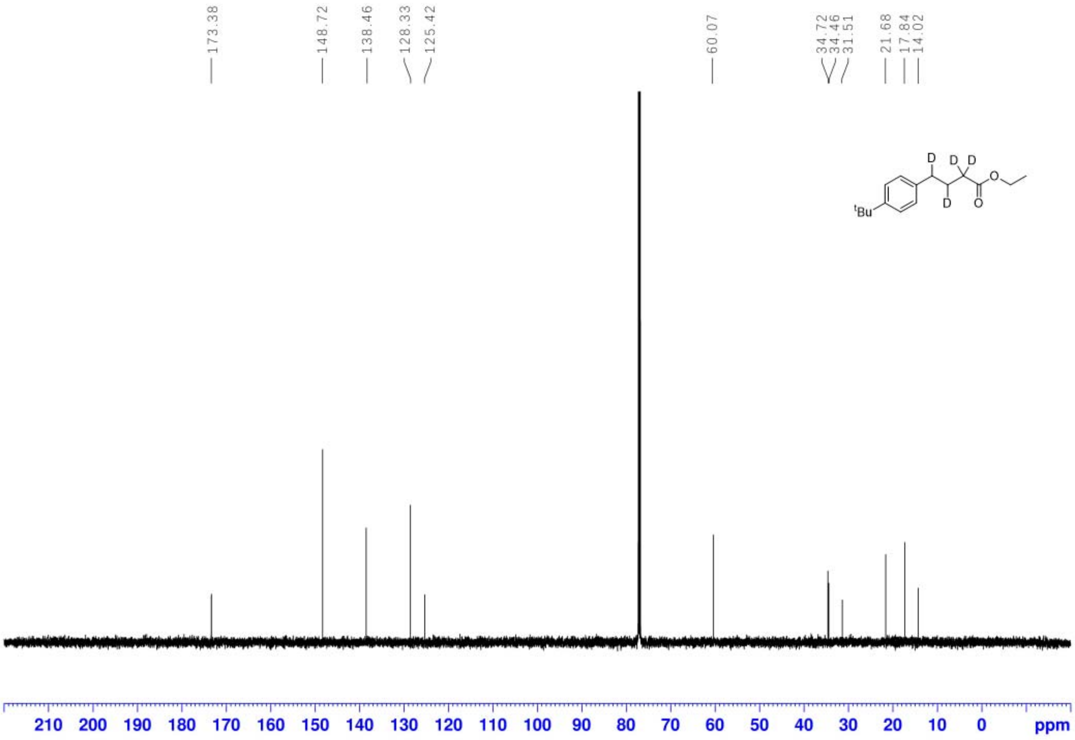
^{13}C NMR Spectra of **4c** (151 MHz, CDCl$_3$)



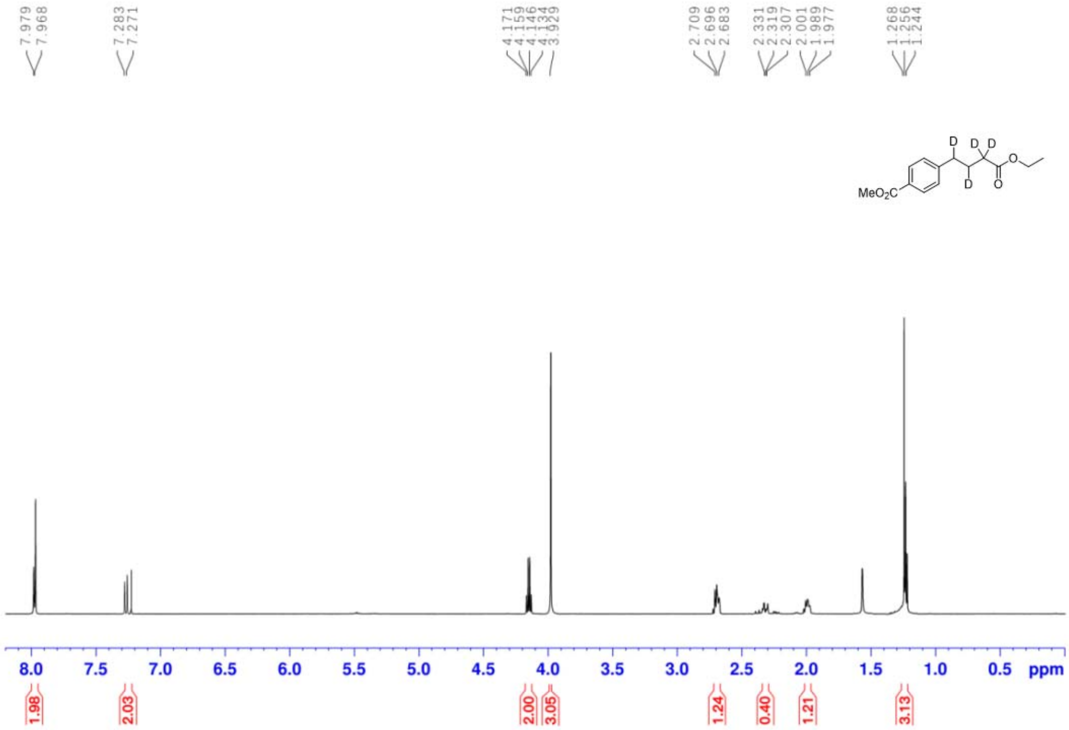
^{1}H NMR Spectra of **4d** (600 MHz, $CDCl_3$)



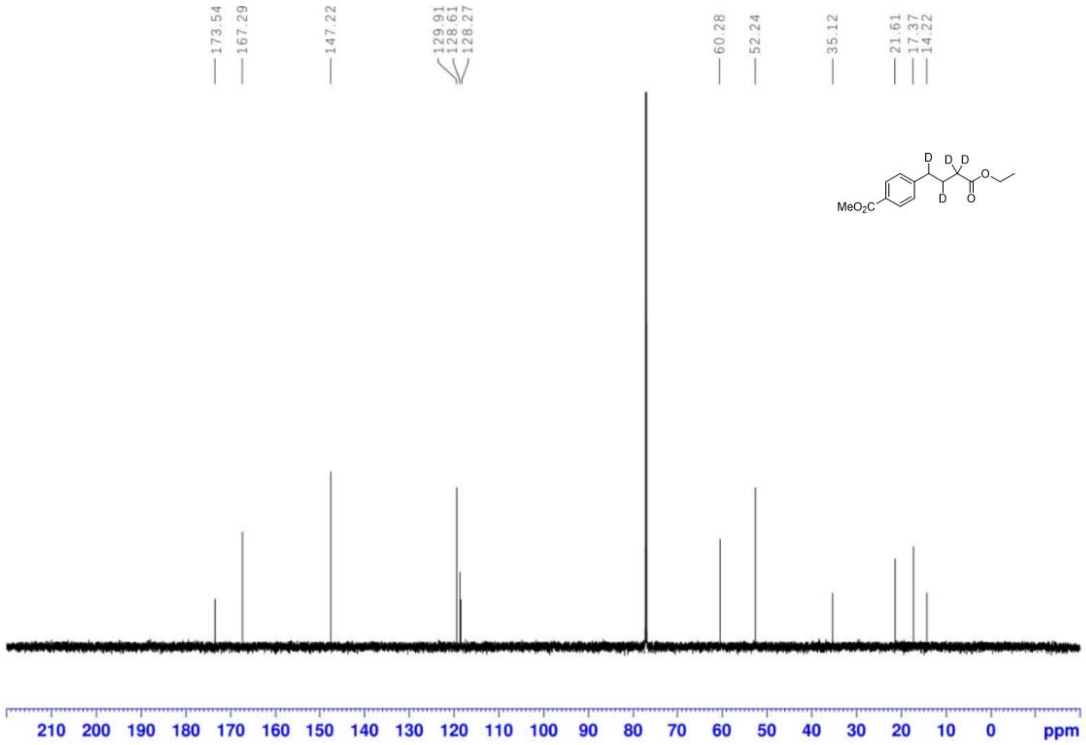
^{13}C NMR Spectra of **4d** (151 MHz, $CDCl_3$)



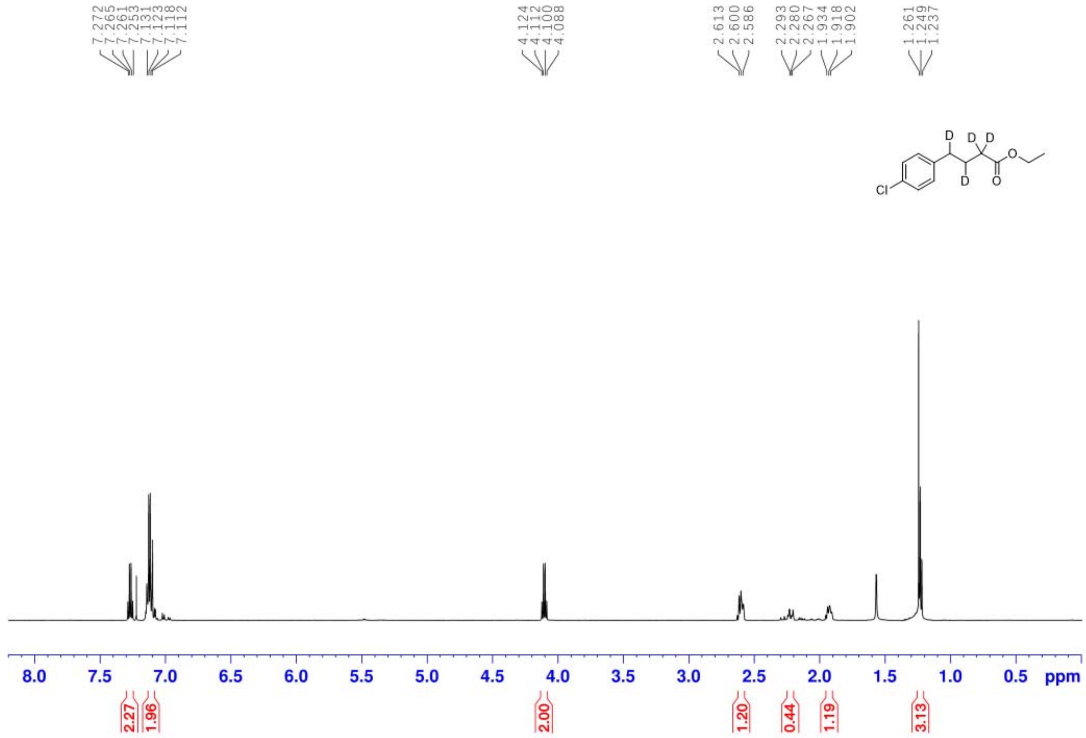
^{1}H NMR Spectra of **4e** (600 MHz, $CDCl_3$)



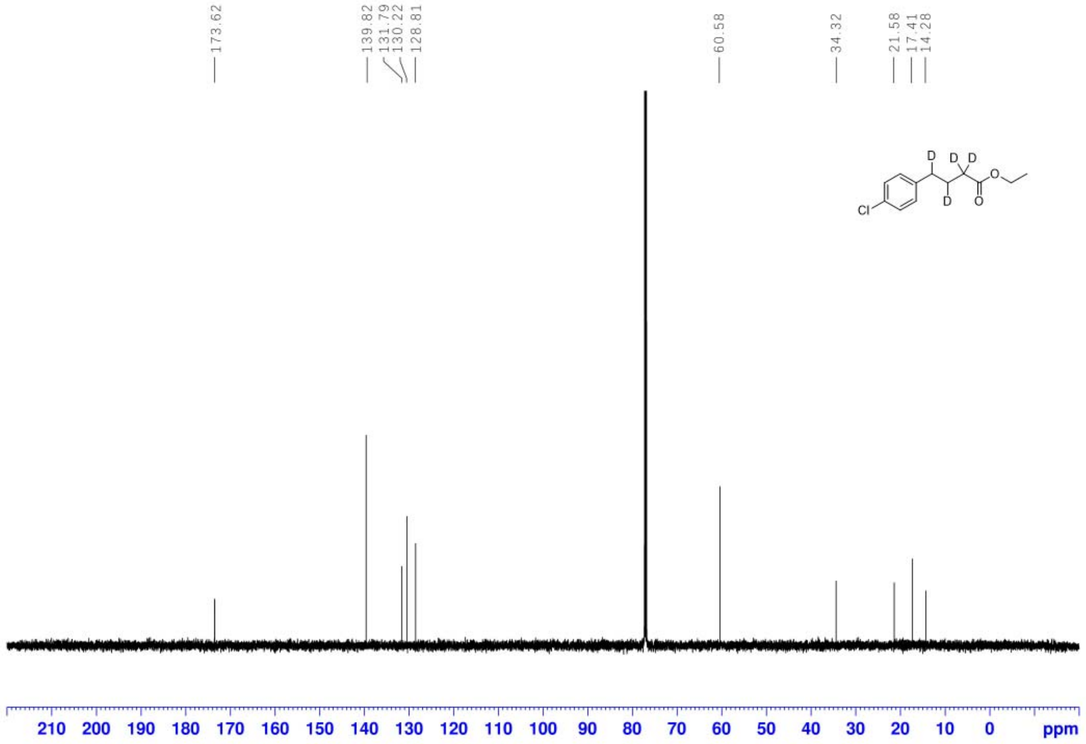
^{13}C NMR Spectra of **4e** (151 MHz, $CDCl_3$)



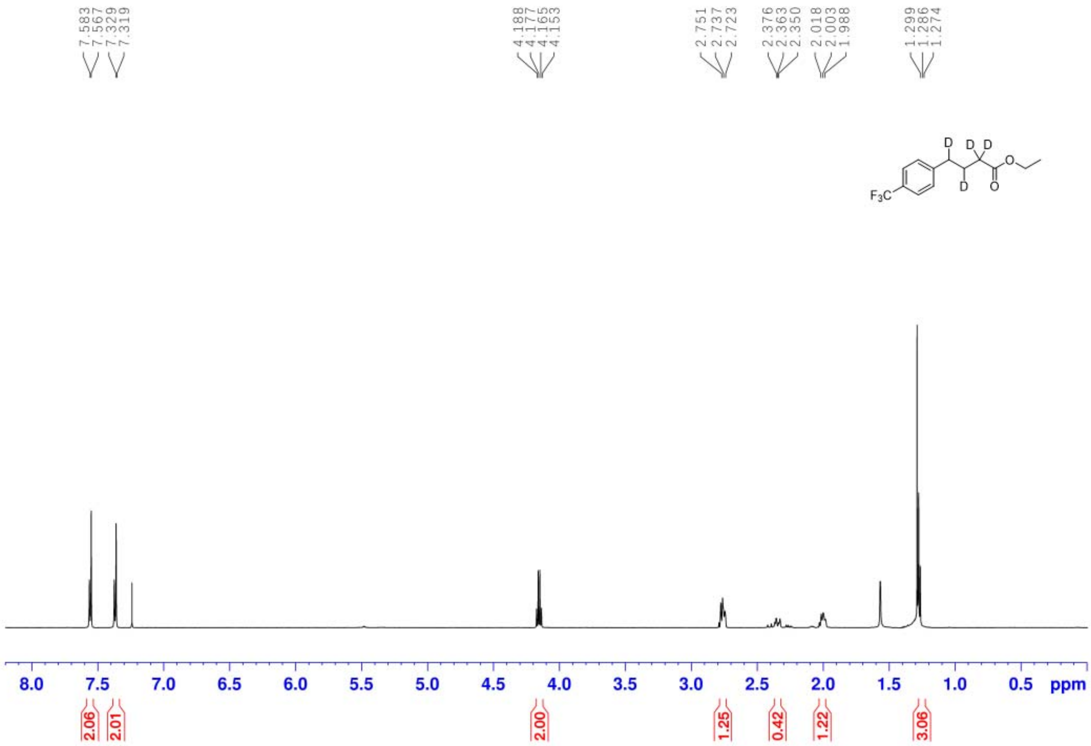
^{1}H NMR Spectra of **4f** (600 MHz, CDCl$_3$)



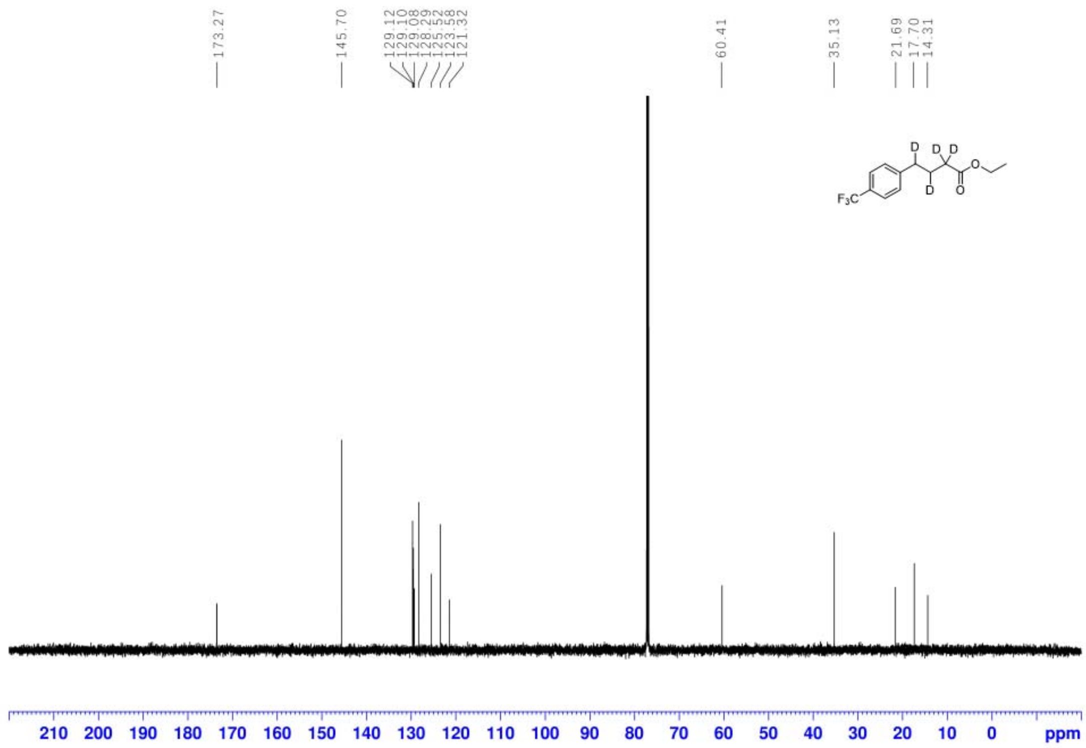
^{13}C NMR Spectra of **4f** (151 MHz, CDCl$_3$)



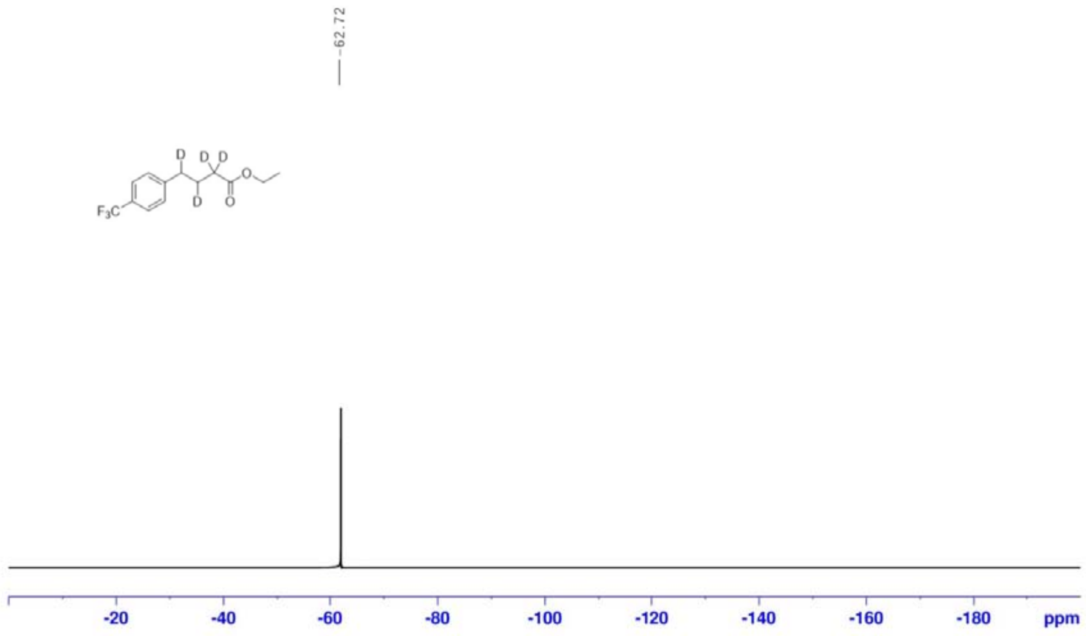
^{1}H NMR Spectra of **4g** (600 MHz, $CDCl_3$)



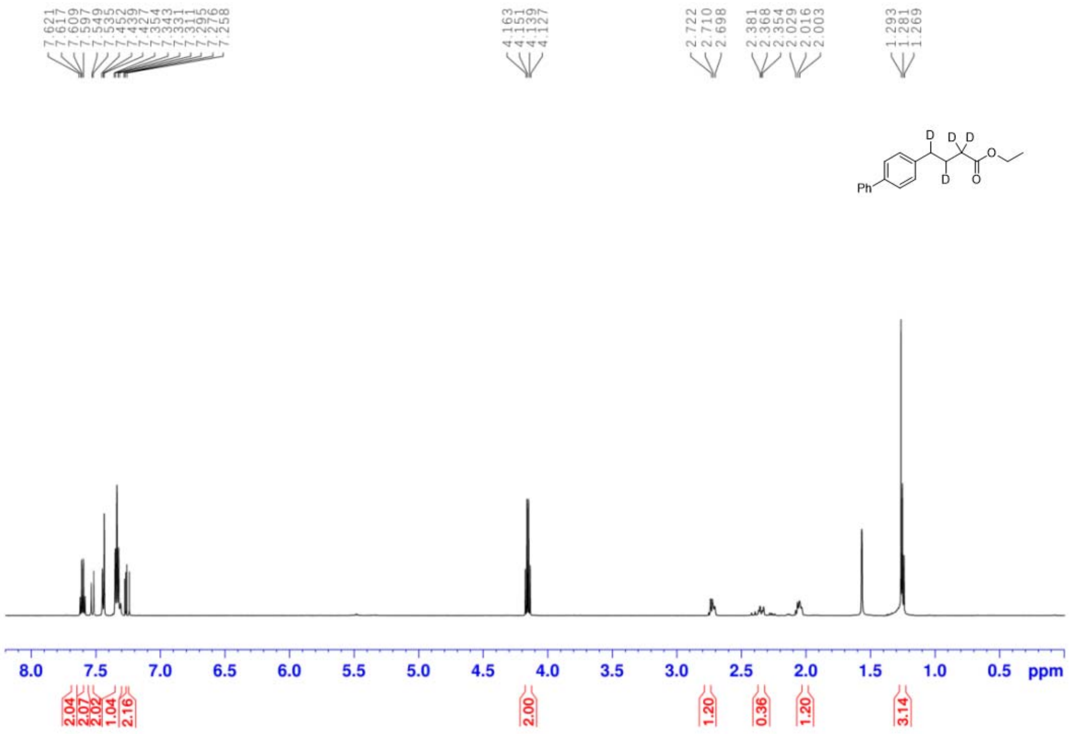
^{13}C NMR Spectra of **4g** (151 MHz, $CDCl_3$)



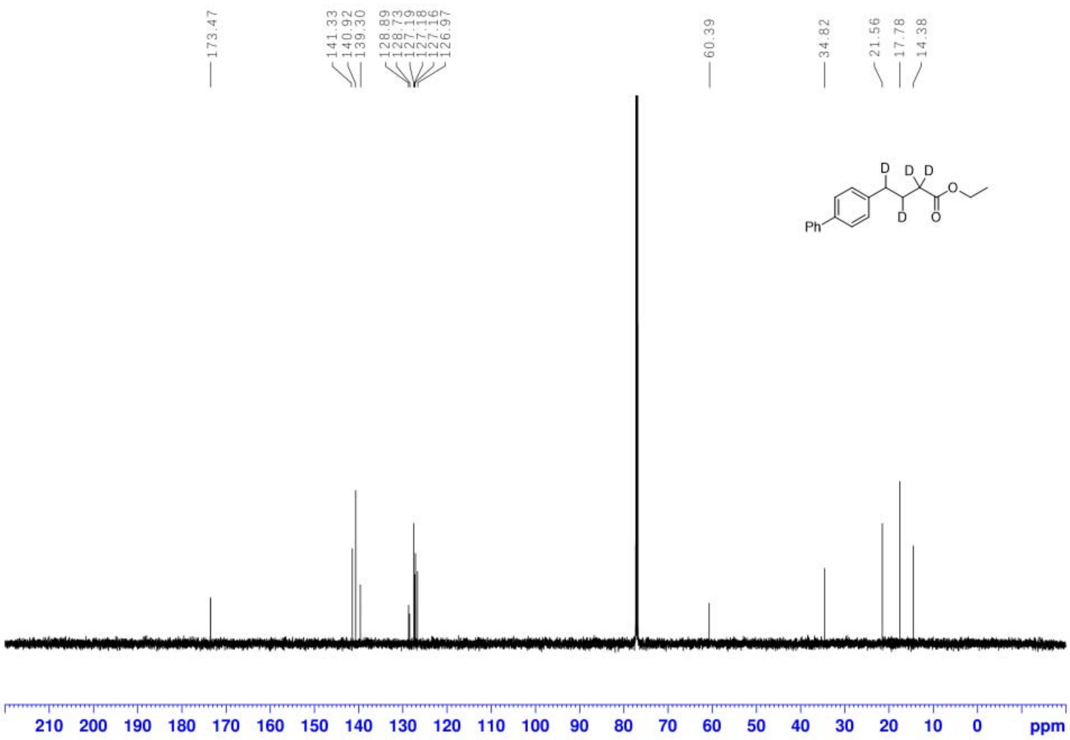
^{19}F NMR Spectra of **4g** (377 MHz, CDCl$_3$)



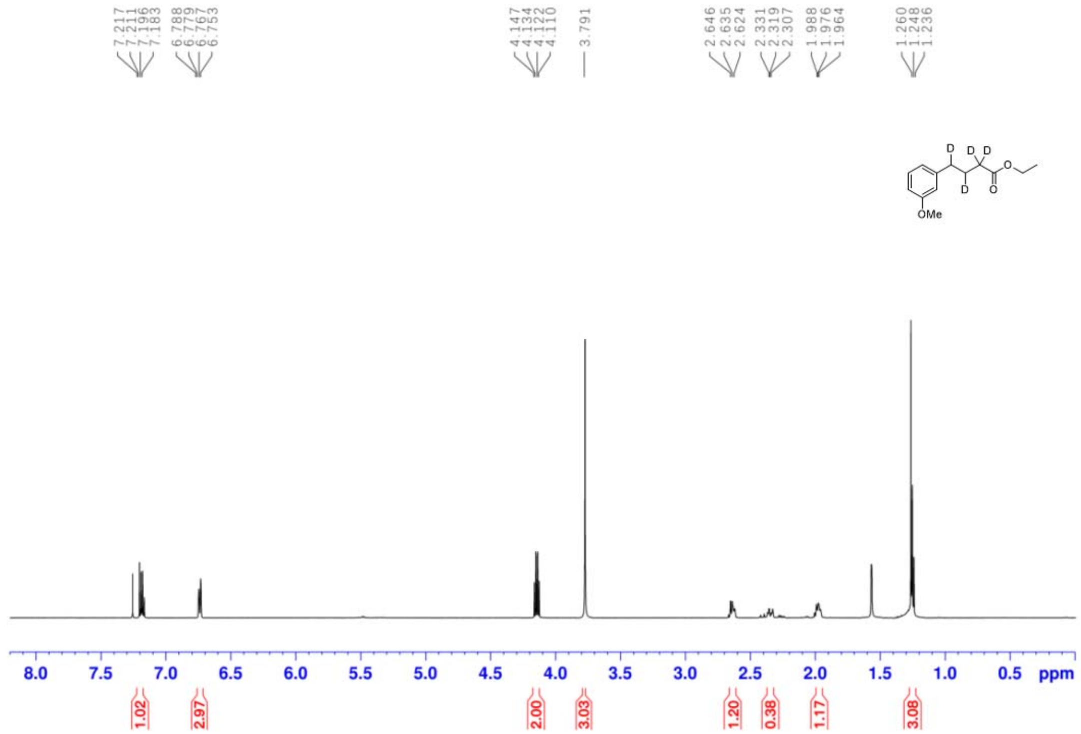
^{1}H NMR Spectra of **4h** (600 MHz, CDCl$_3$)



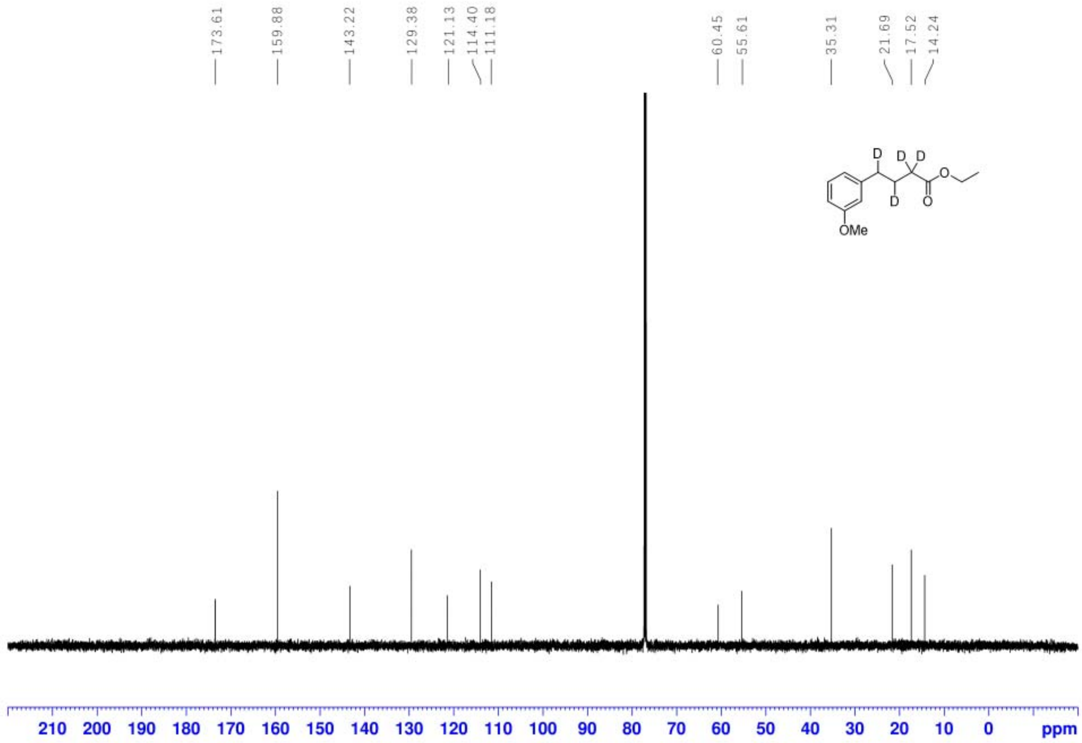
^{13}C NMR Spectra of **4h** (151 MHz, CDCl$_3$)



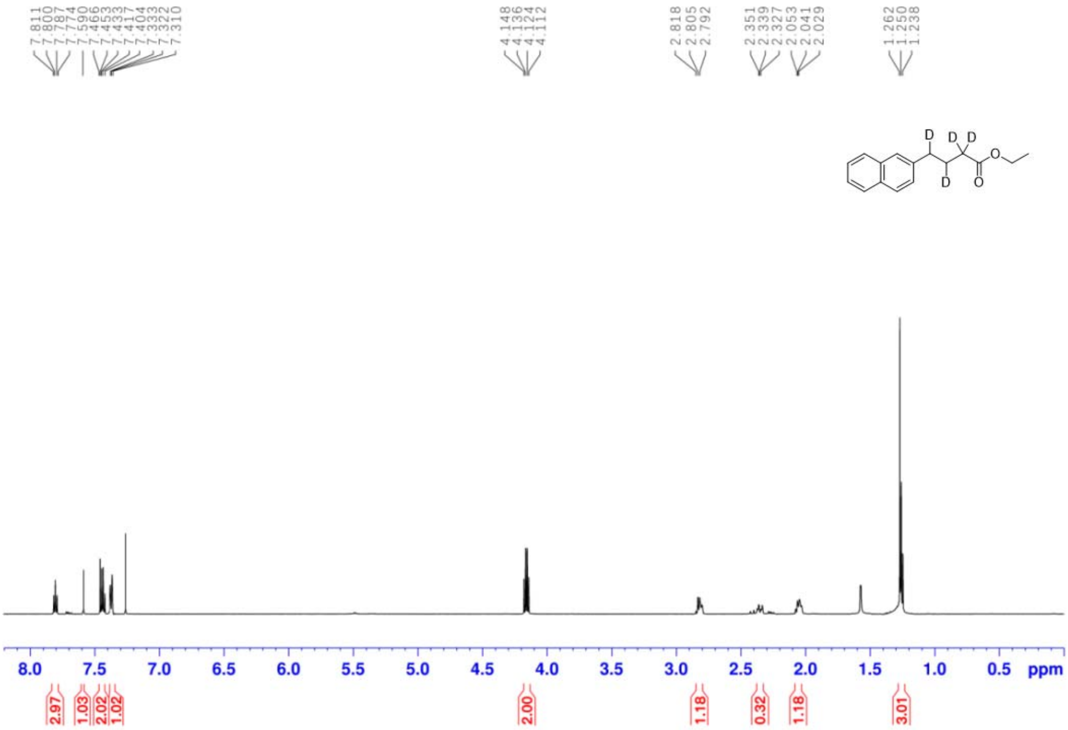
^{1}H NMR Spectra of **4i** (600 MHz, CDCl$_3$)



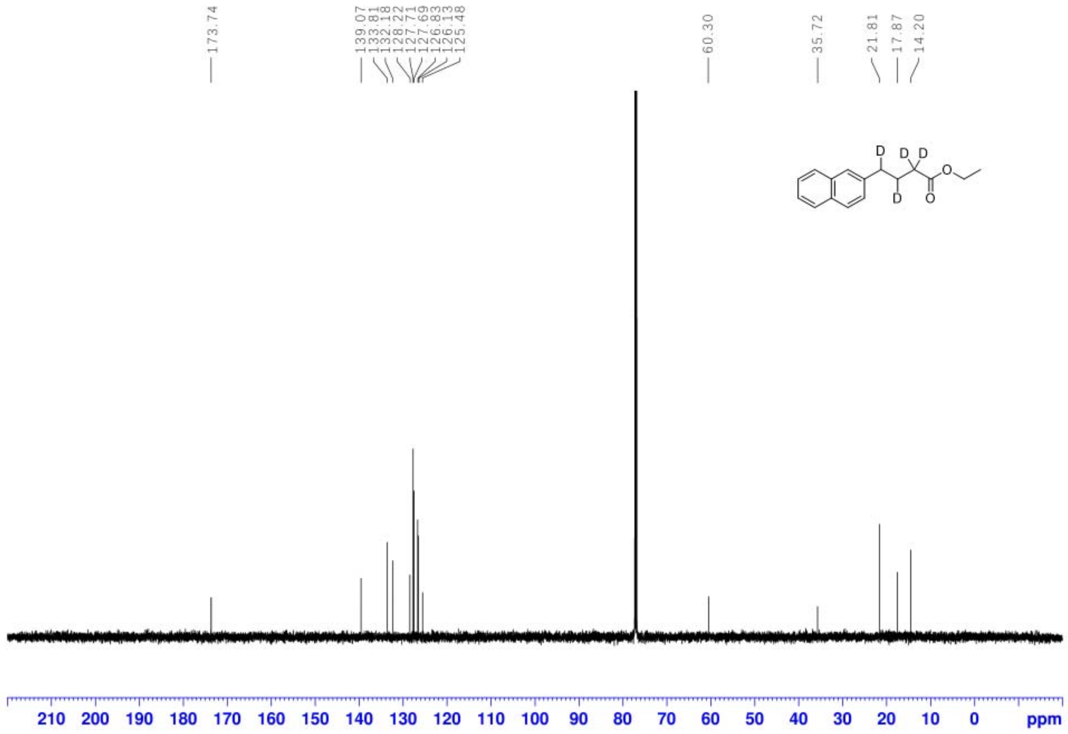
^{13}C NMR Spectra of **4i** (151 MHz, $CDCl_3$)



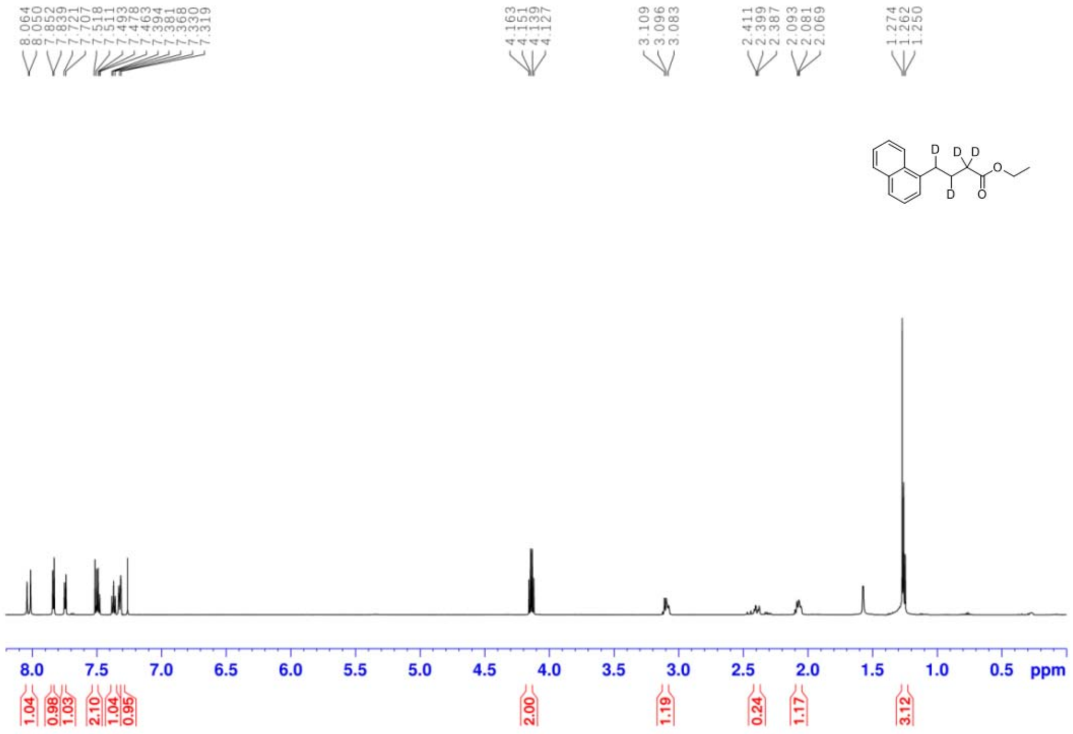
^{1}H NMR Spectra of **4j** (600 MHz, $CDCl_3$)



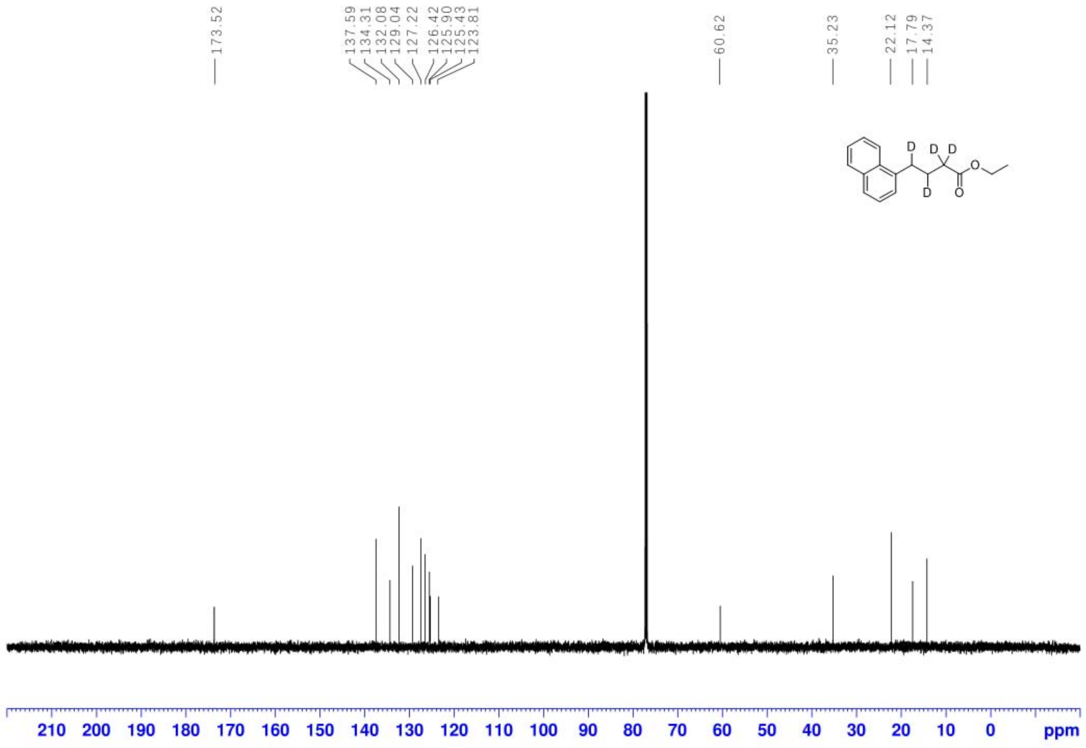
^{13}C NMR Spectra of **4j** (151 MHz, $CDCl_3$)



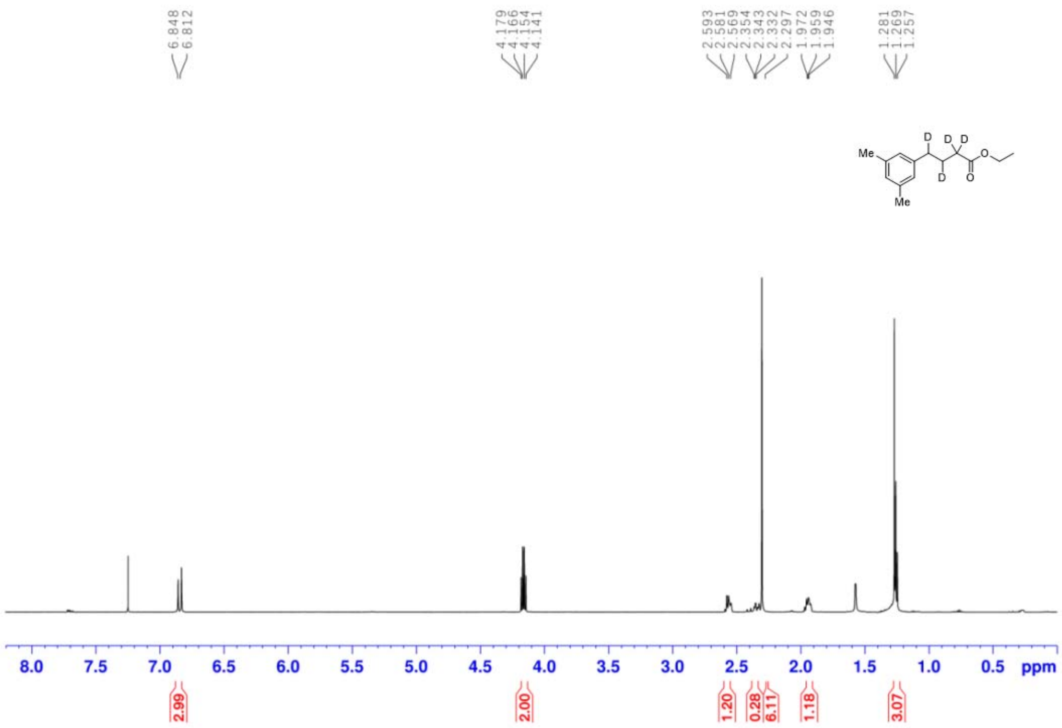
^{1}H NMR Spectra of **4k** (600 MHz, $CDCl_3$)



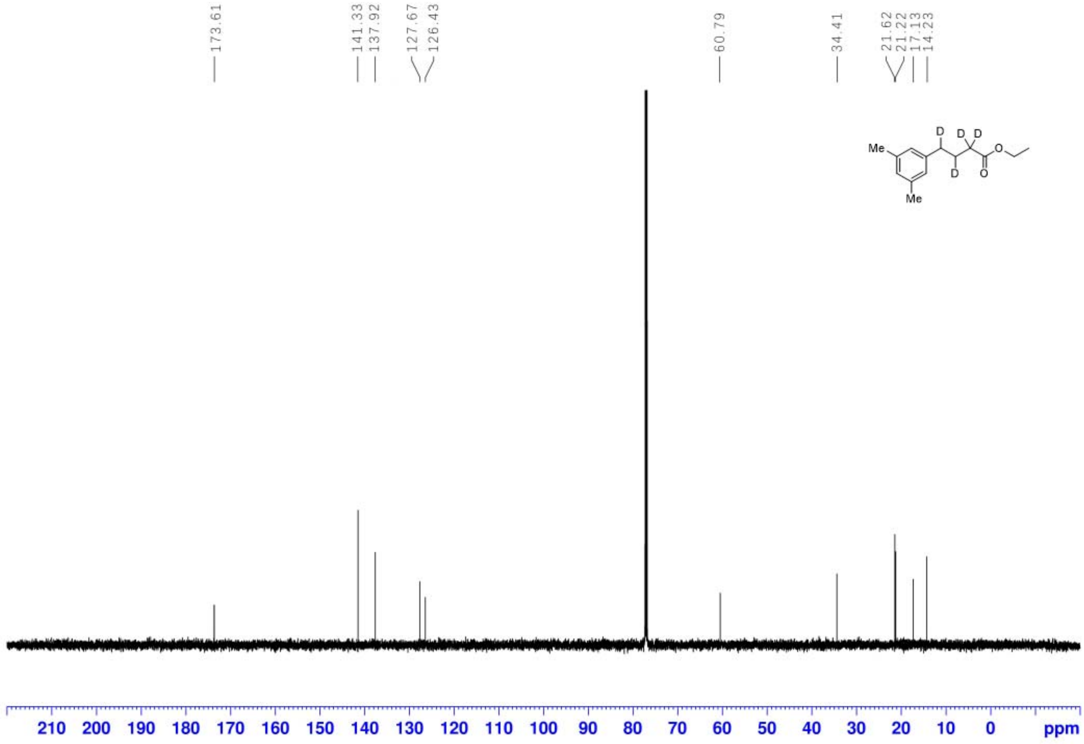
^{13}C NMR Spectra of **4k** (151 MHz, $CDCl_3$)



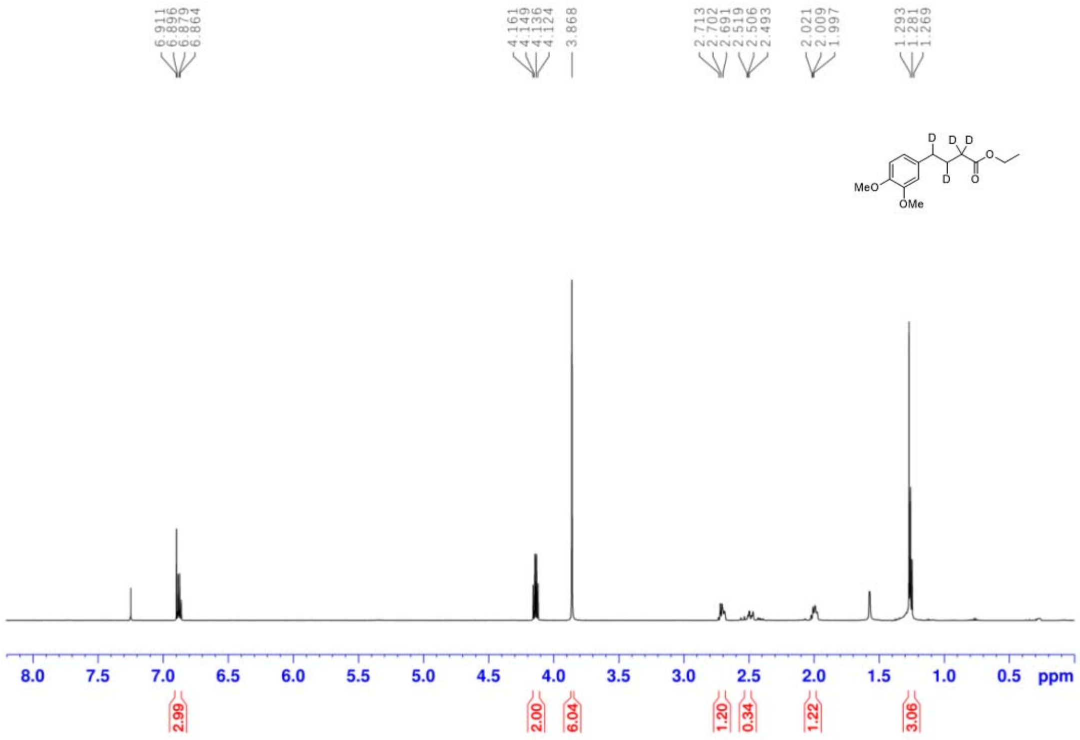
^{1}H NMR Spectra of **4l** (600 MHz, $CDCl_3$)



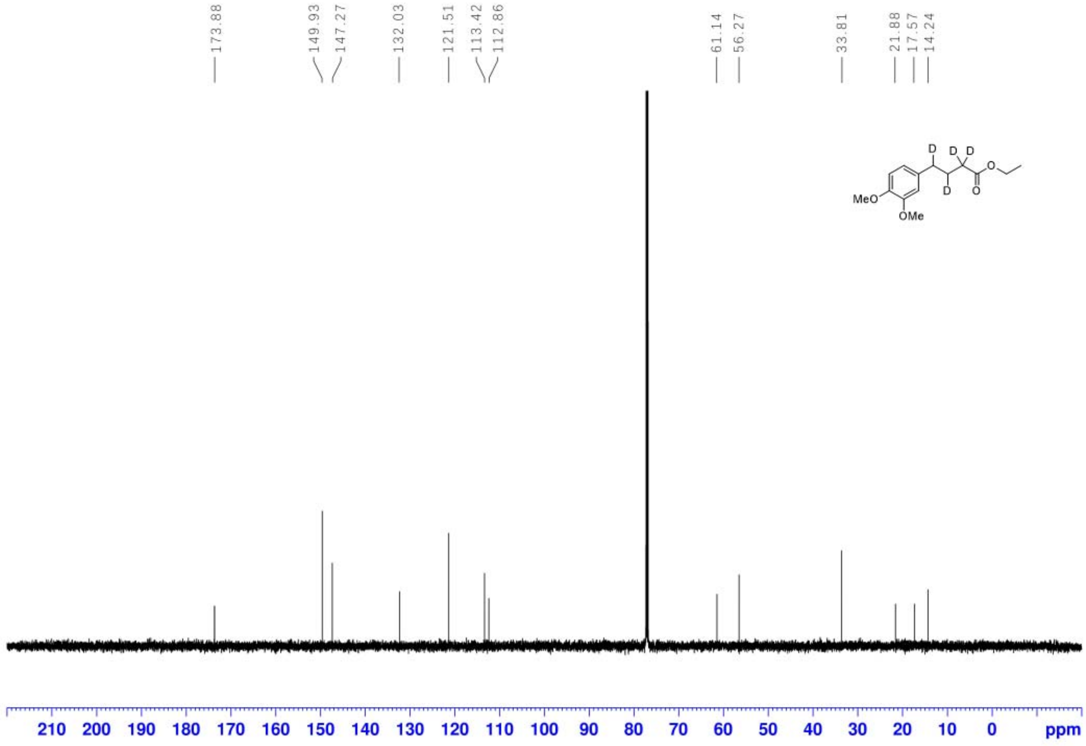
^{13}C NMR Spectra of **4l** (151 MHz, CDCl$_3$)



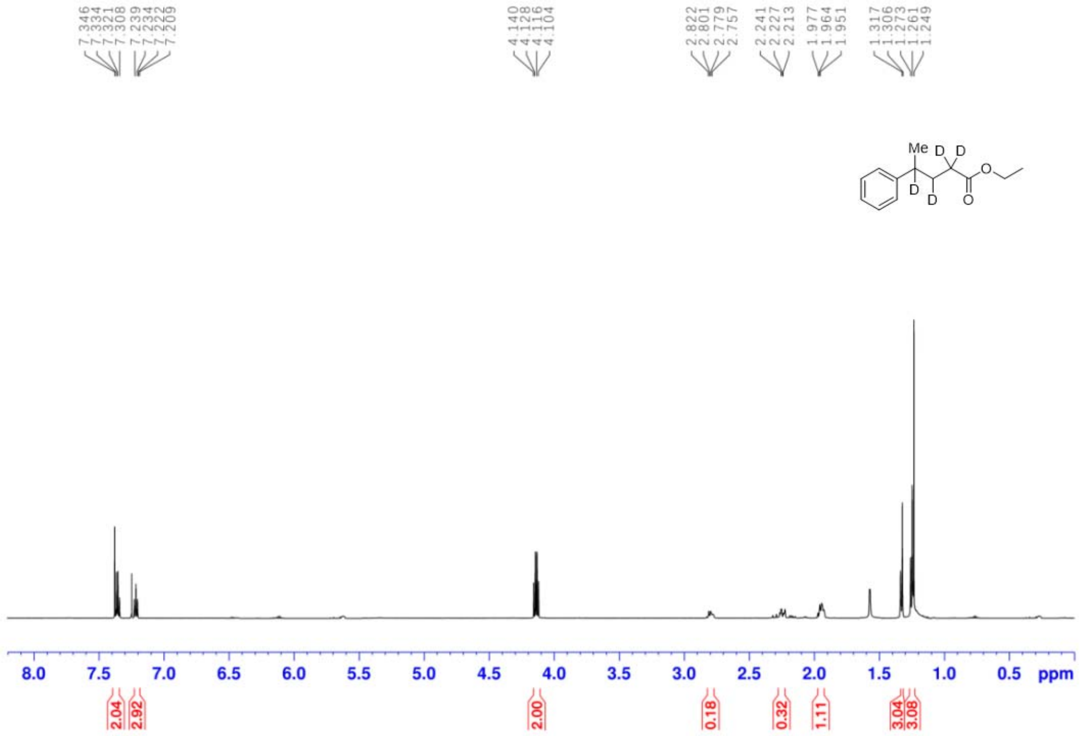
^{1}H NMR Spectra of **4m** (600 MHz, CDCl$_3$)



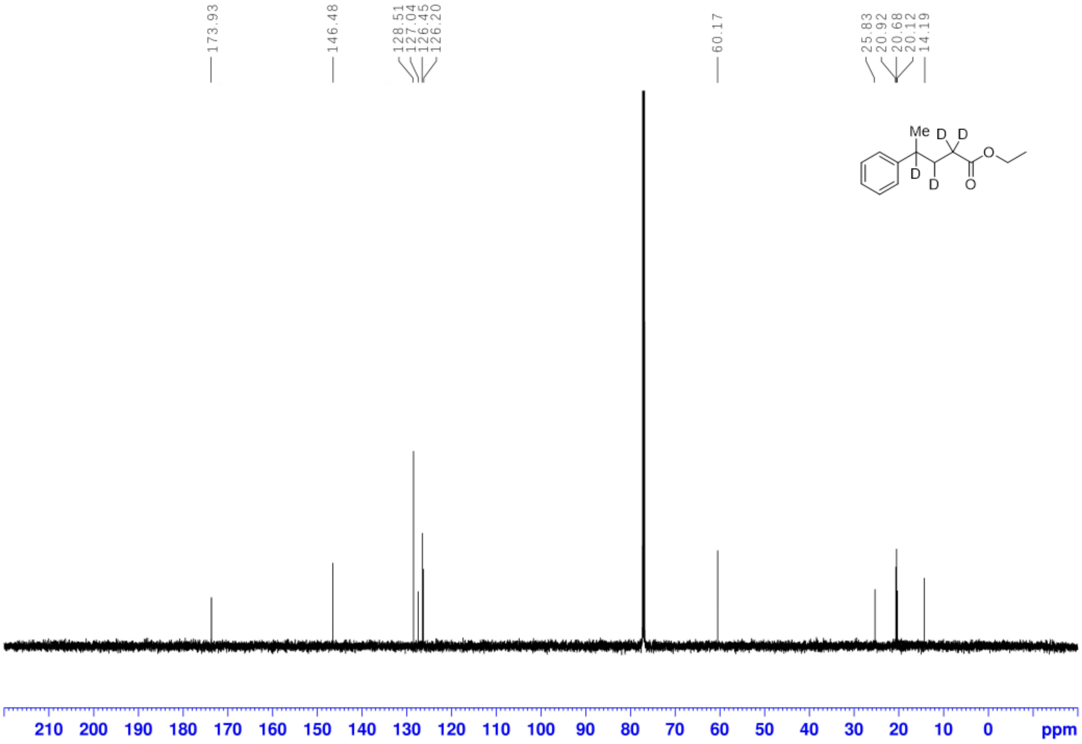
^{13}C NMR Spectra of **4m** (151 MHz, CDCl$_3$)



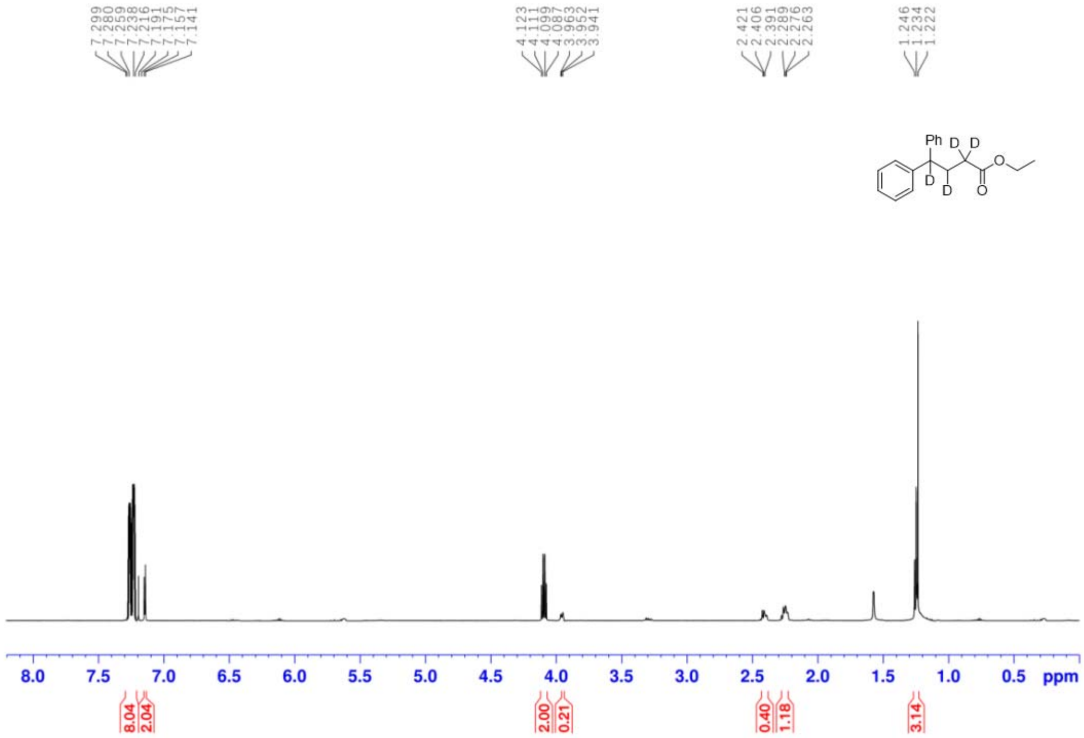
^{1}H NMR Spectra of **4n** (600 MHz, CDCl$_3$)



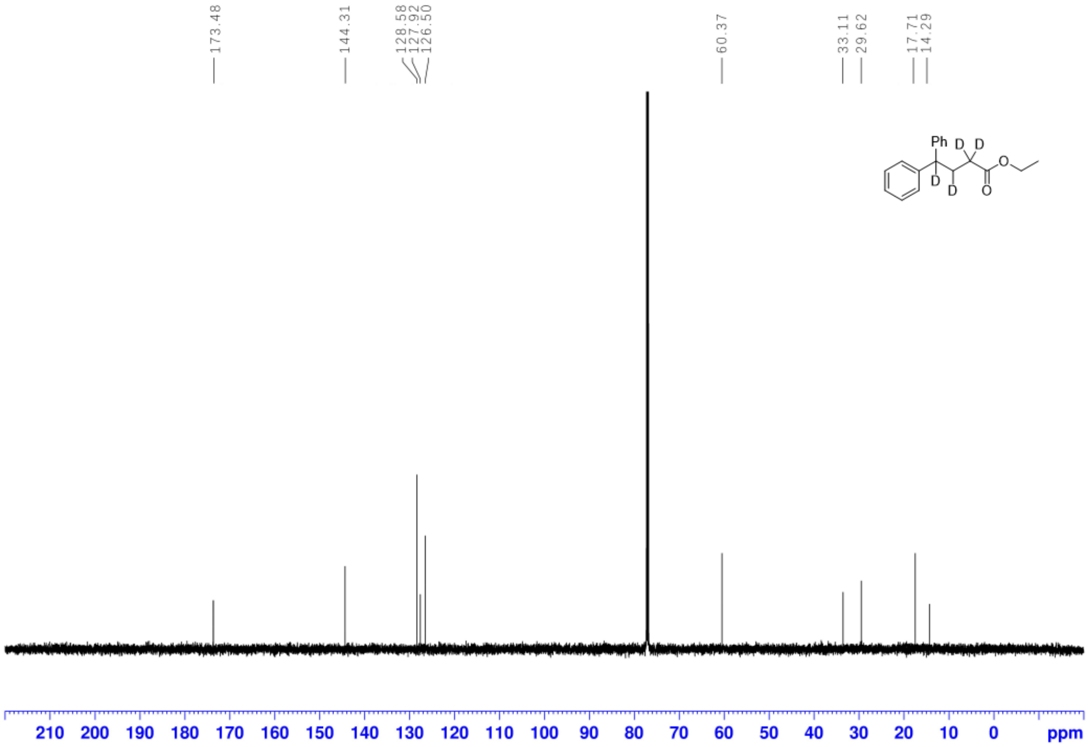
^{13}C NMR Spectra of **4n** (151 MHz, CDCl$_3$)



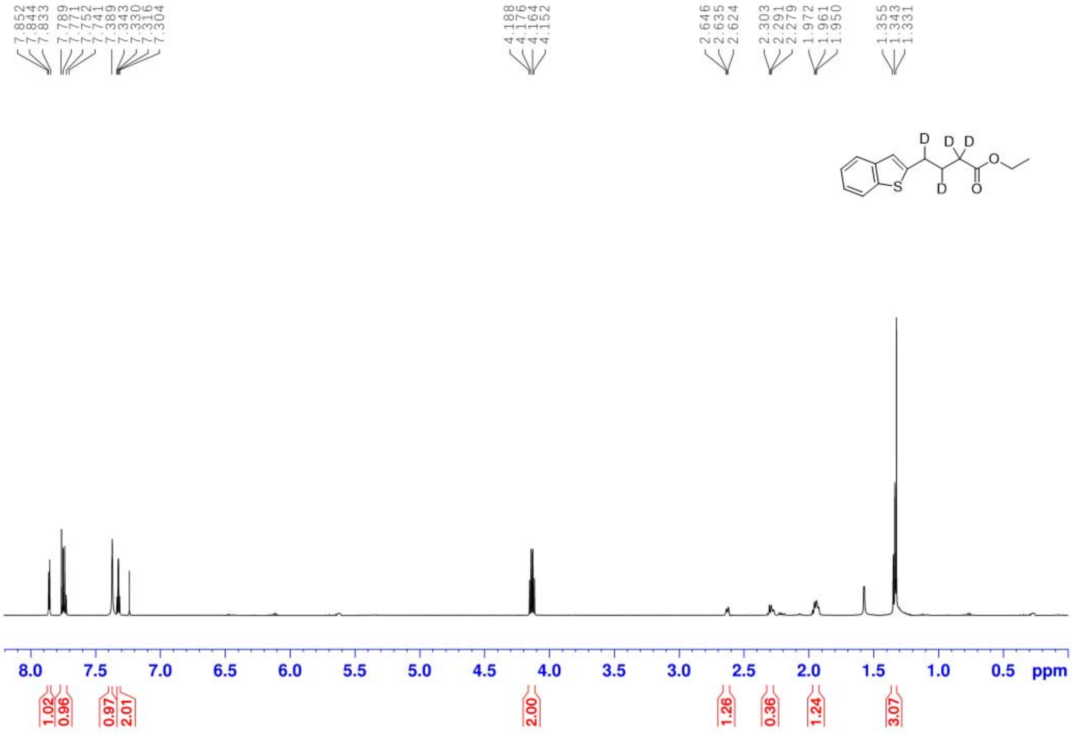
^{1}H NMR Spectra of **4o** (600 MHz, CDCl$_3$)



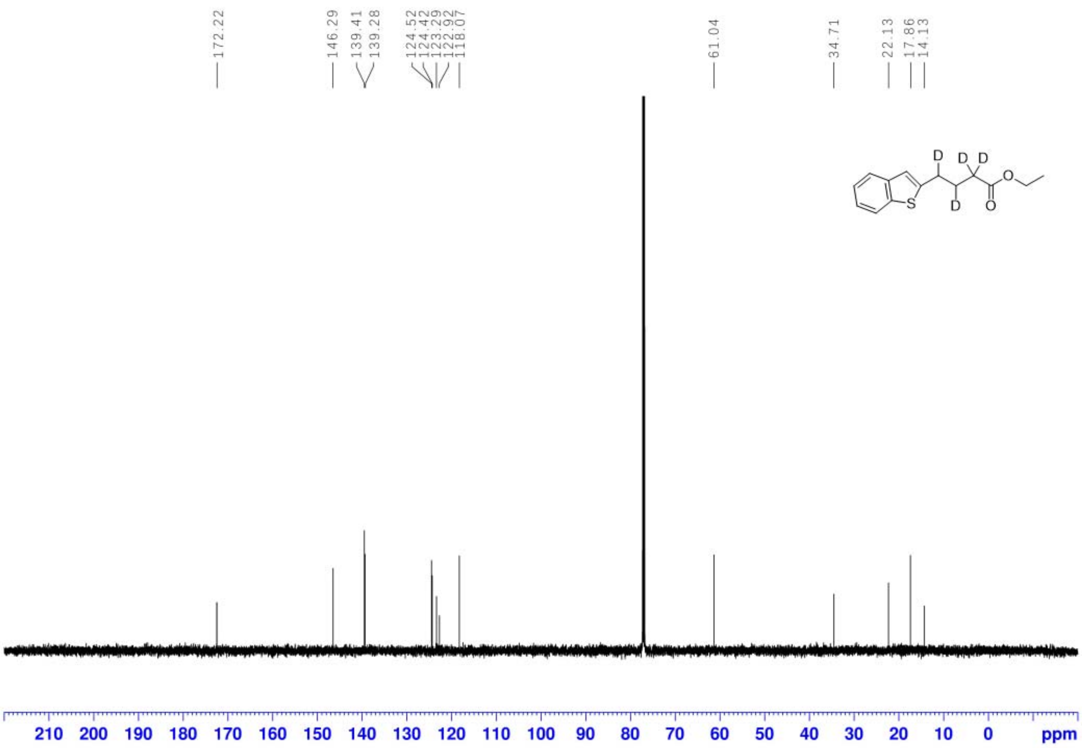
^{13}C NMR Spectra of **4o** (151 MHz, $CDCl_3$)



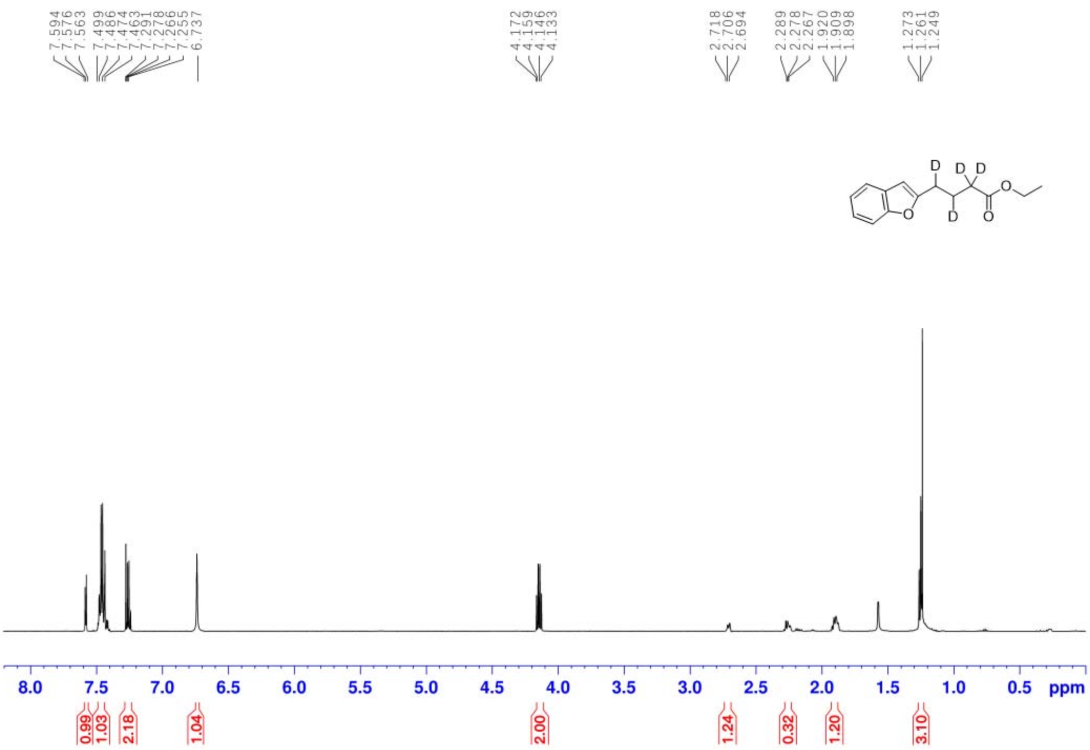
^{1}H NMR Spectra of **4p** (600 MHz, $CDCl_3$)



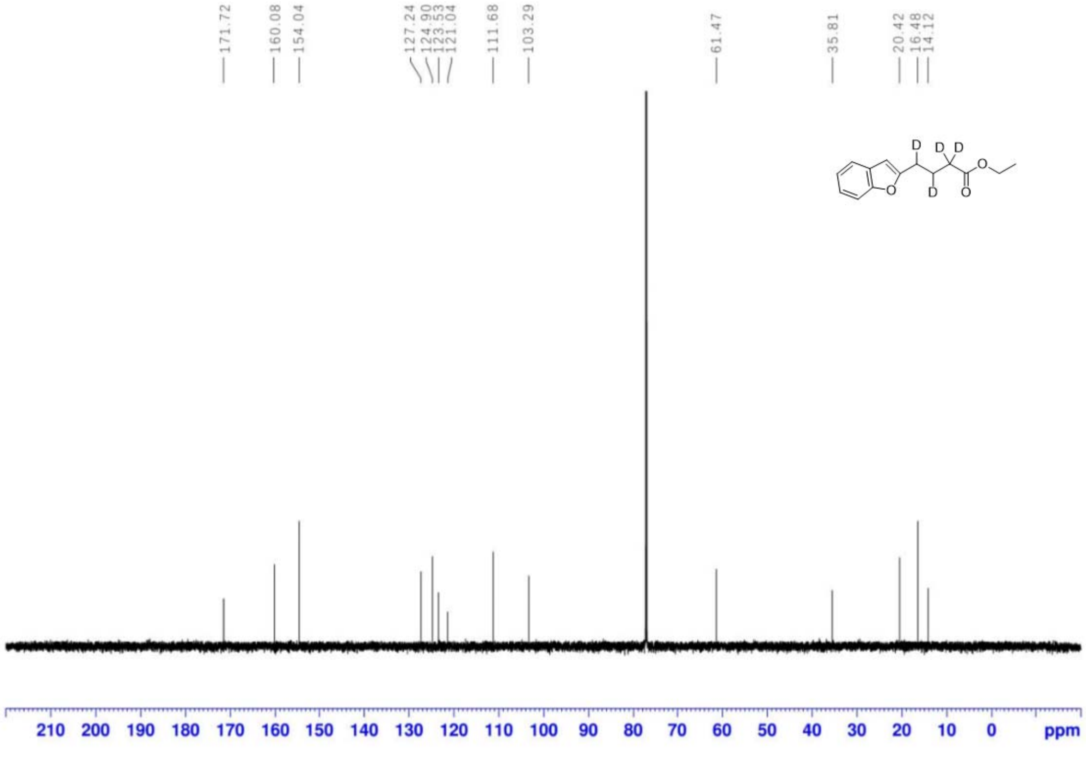
^{13}C NMR Spectra of **4p** (151 MHz, CDCl$_3$)



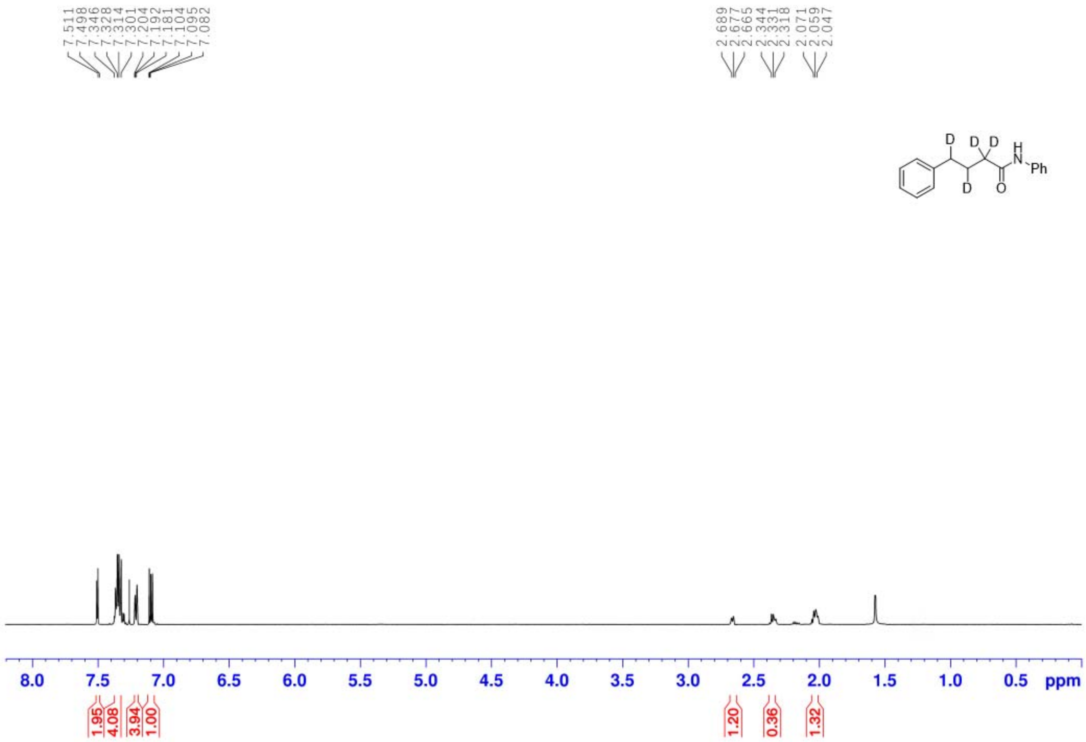
^{1}H NMR Spectra of **4q** (600 MHz, CDCl$_3$)



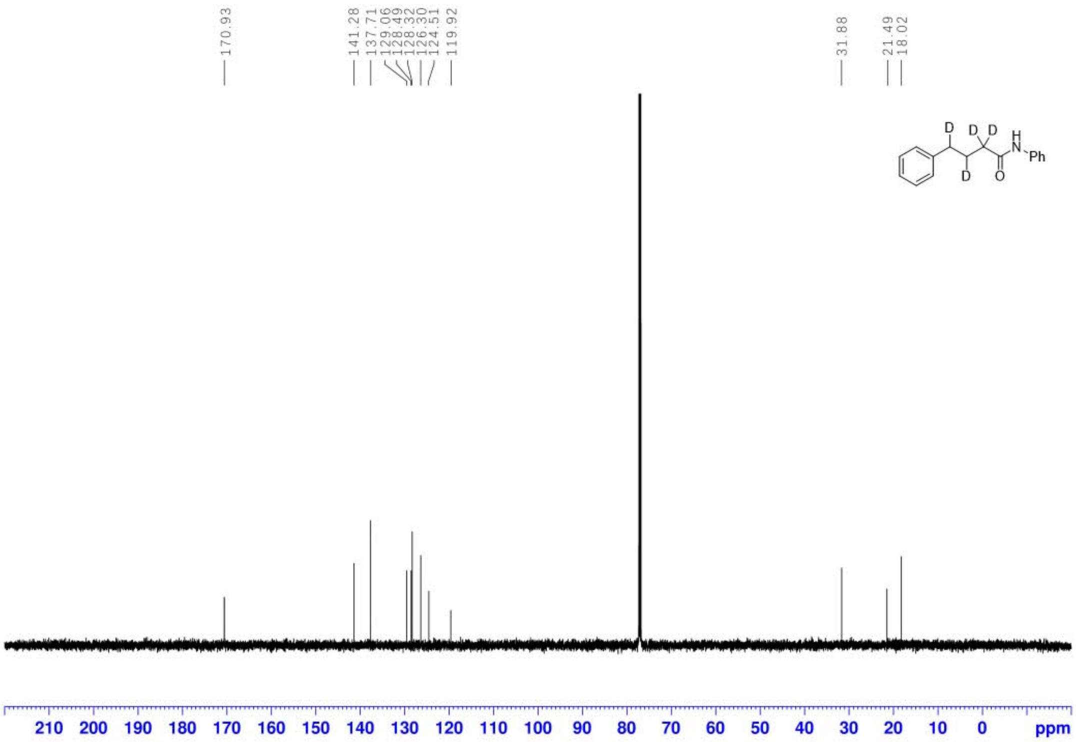
^{13}C NMR Spectra of **4q** (151 MHz, CDCl$_3$)



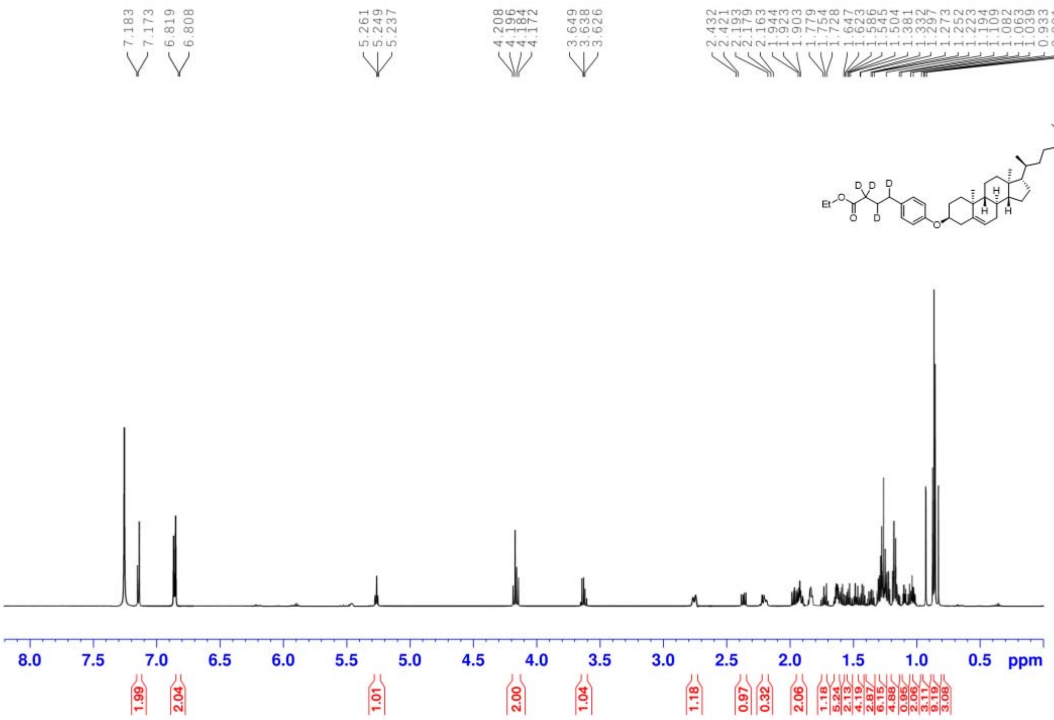
^{1}H NMR Spectra of **4r** (600 MHz, CDCl$_3$)



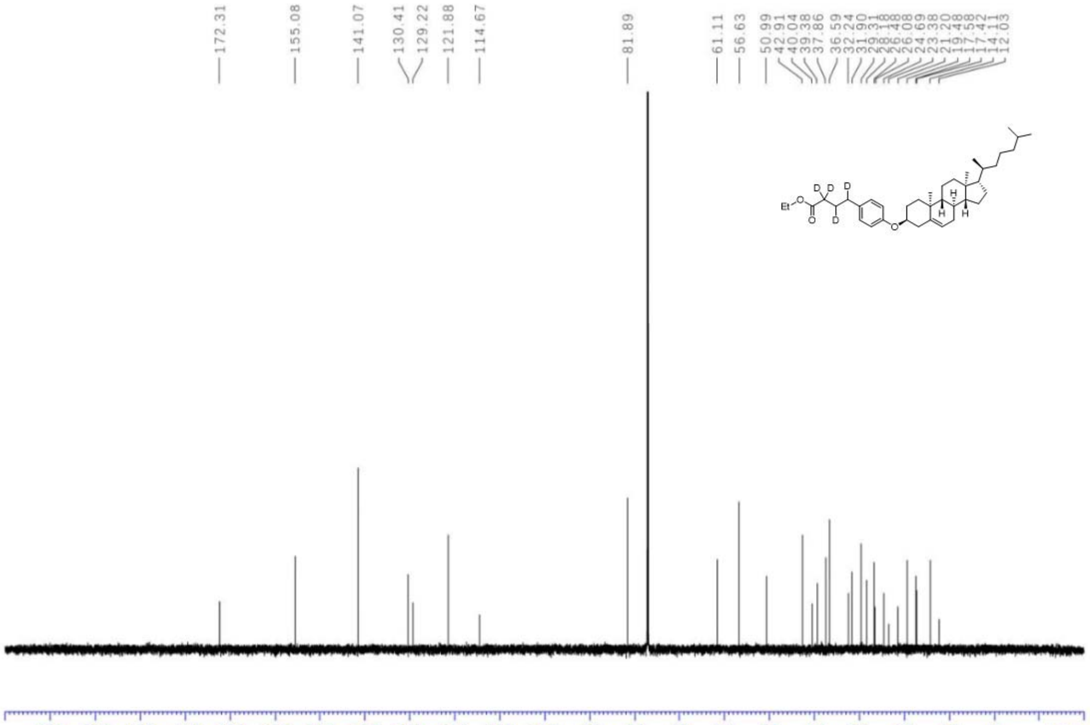
^{13}C NMR Spectra of **4r** (151 MHz, $CDCl_3$)



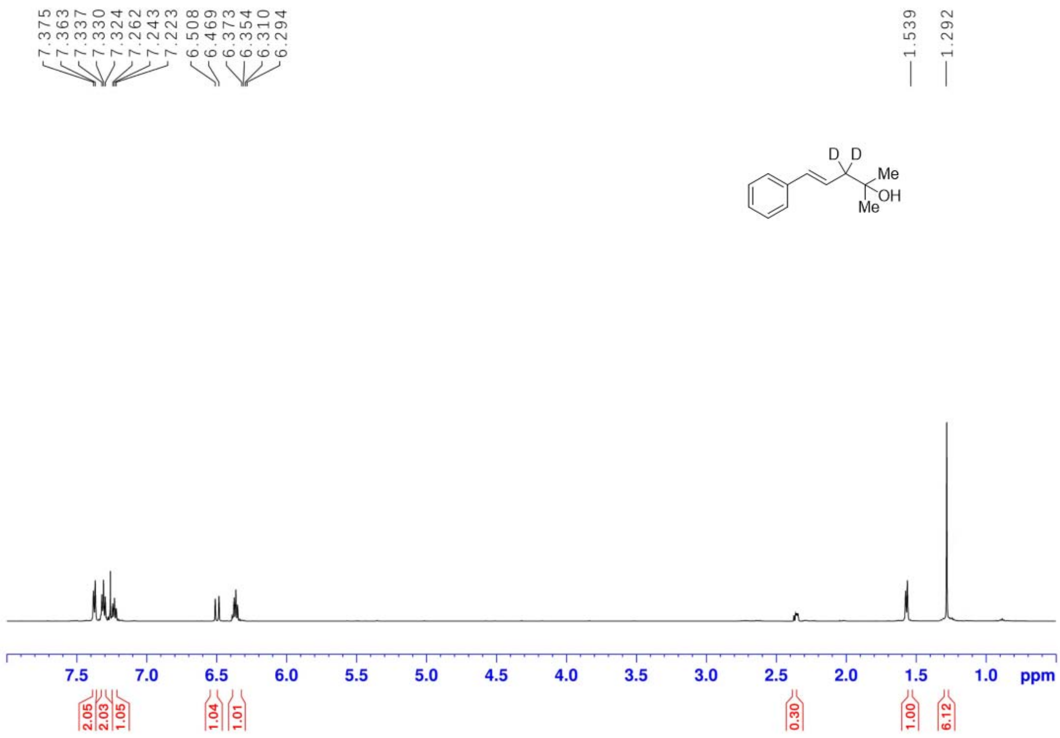
^{1}H NMR Spectra of **4s** (600 MHz, $CDCl_3$)



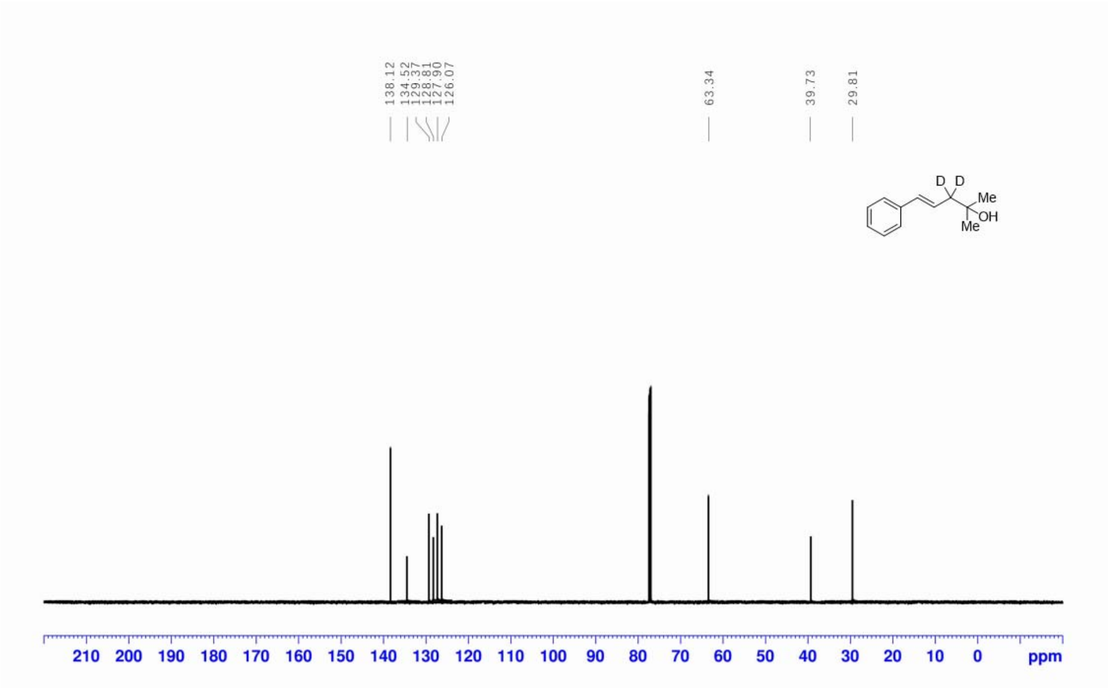
^{13}C NMR Spectra of **4s** (151 MHz, CDCl$_3$)



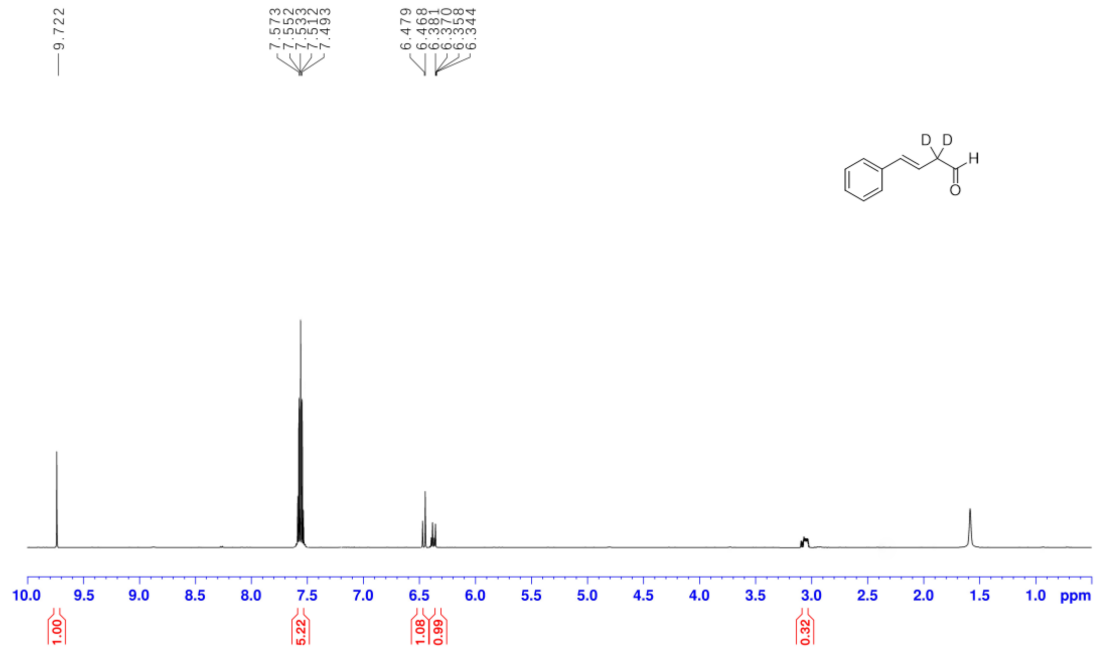
^{1}H NMR Spectra of **5a** (600 MHz, CDCl$_3$)



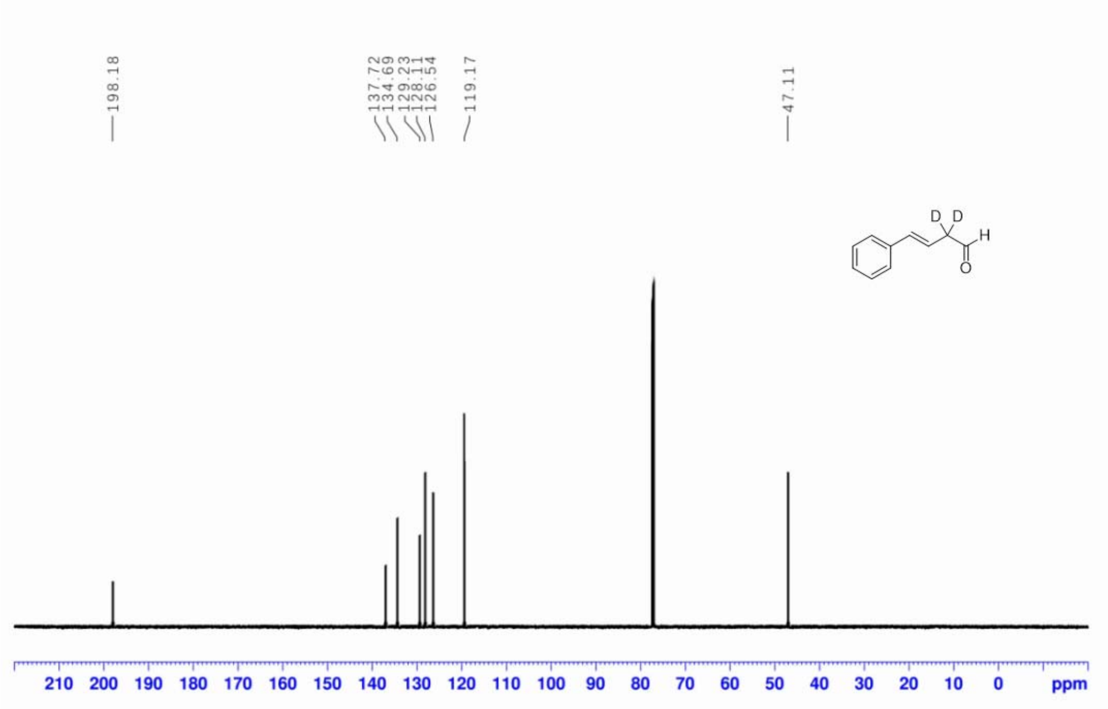
^{13}C NMR Spectra of **5a** (151 MHz, $CDCl_3$)



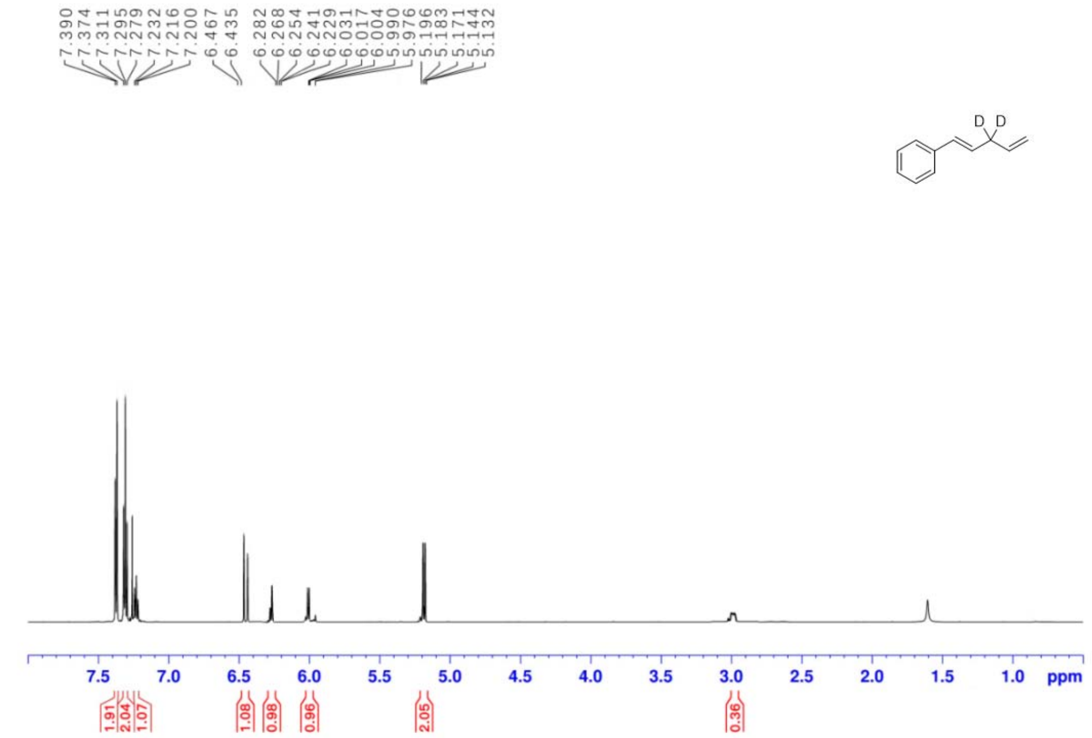
^{1}H NMR Spectra of **6a** (600 MHz, $CDCl_3$)



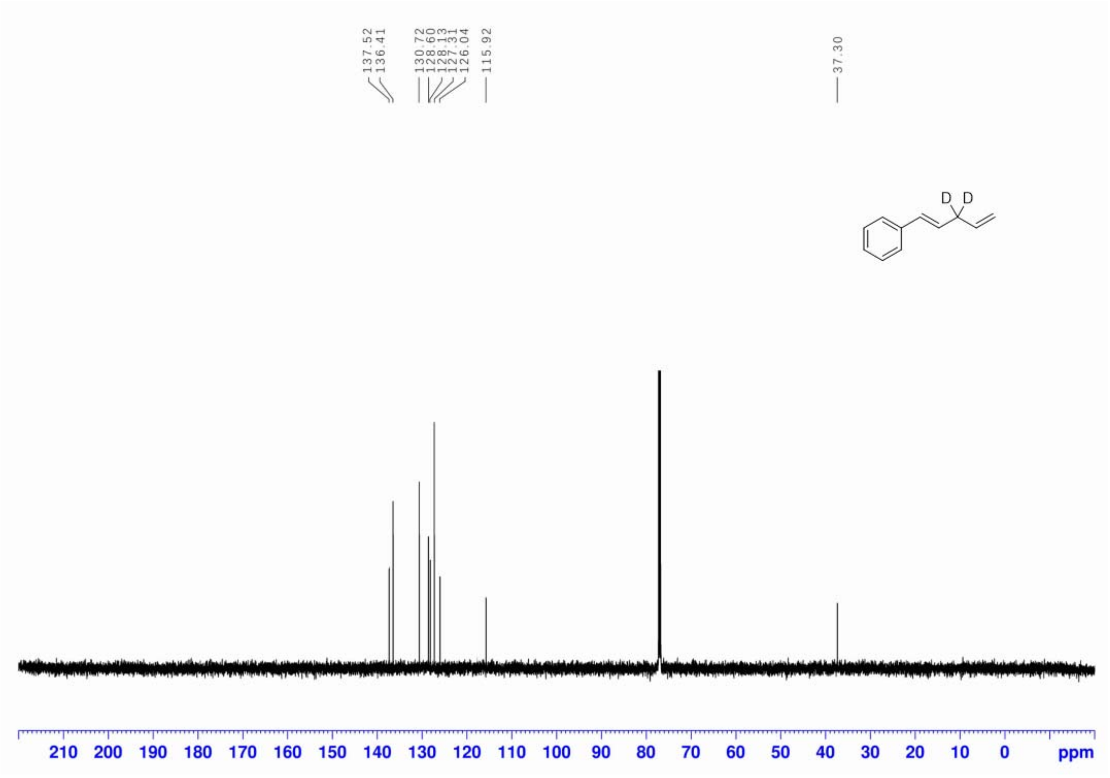
^{13}C NMR Spectra of **6a** (151 MHz, $CDCl_3$)



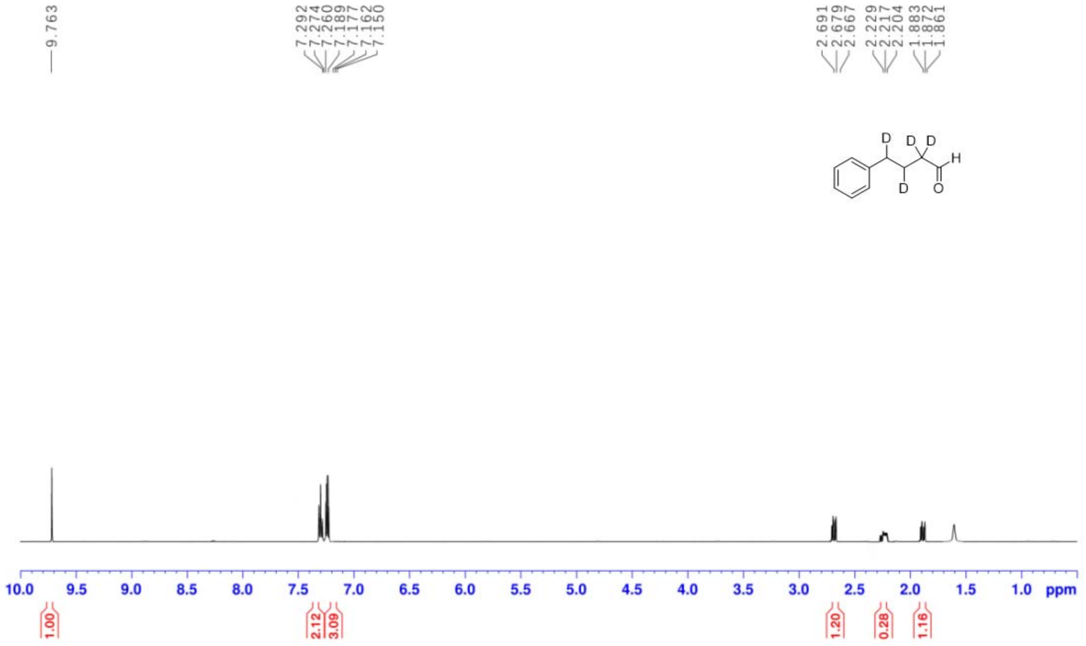
^{1}H NMR Spectra of **7a** (600 MHz, $CDCl_3$)



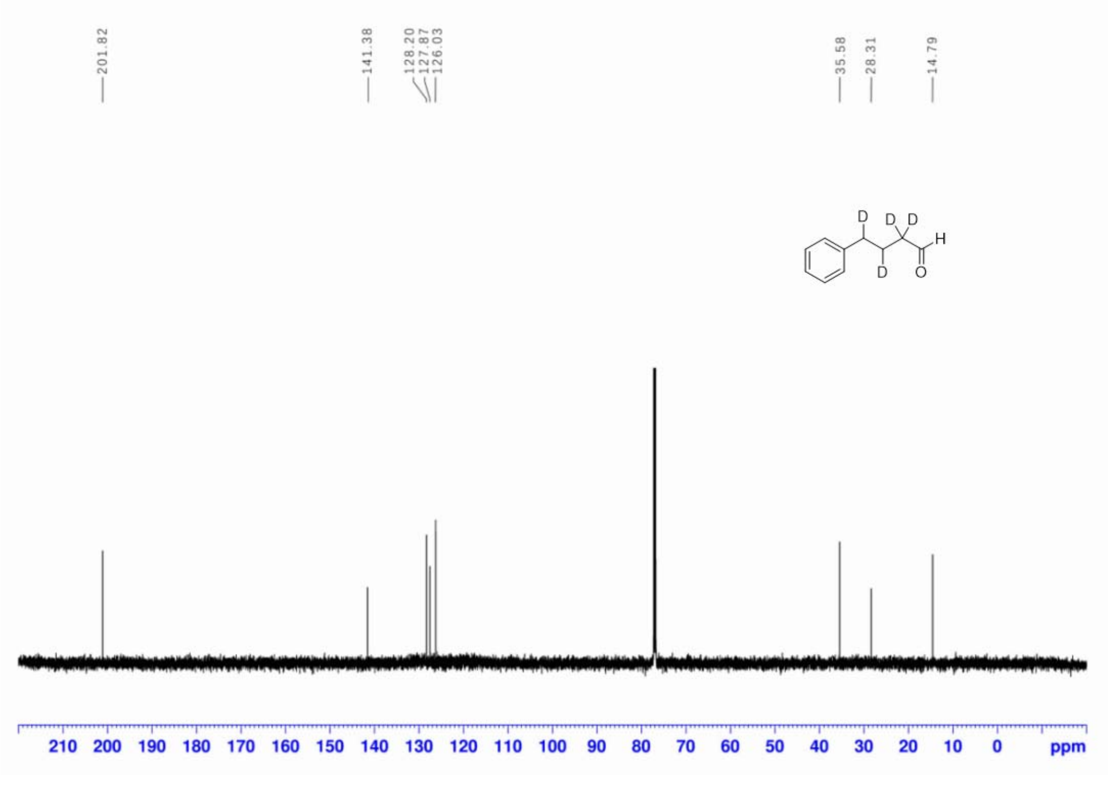
^{13}C NMR Spectra of **7a** (151 MHz, $CDCl_3$)



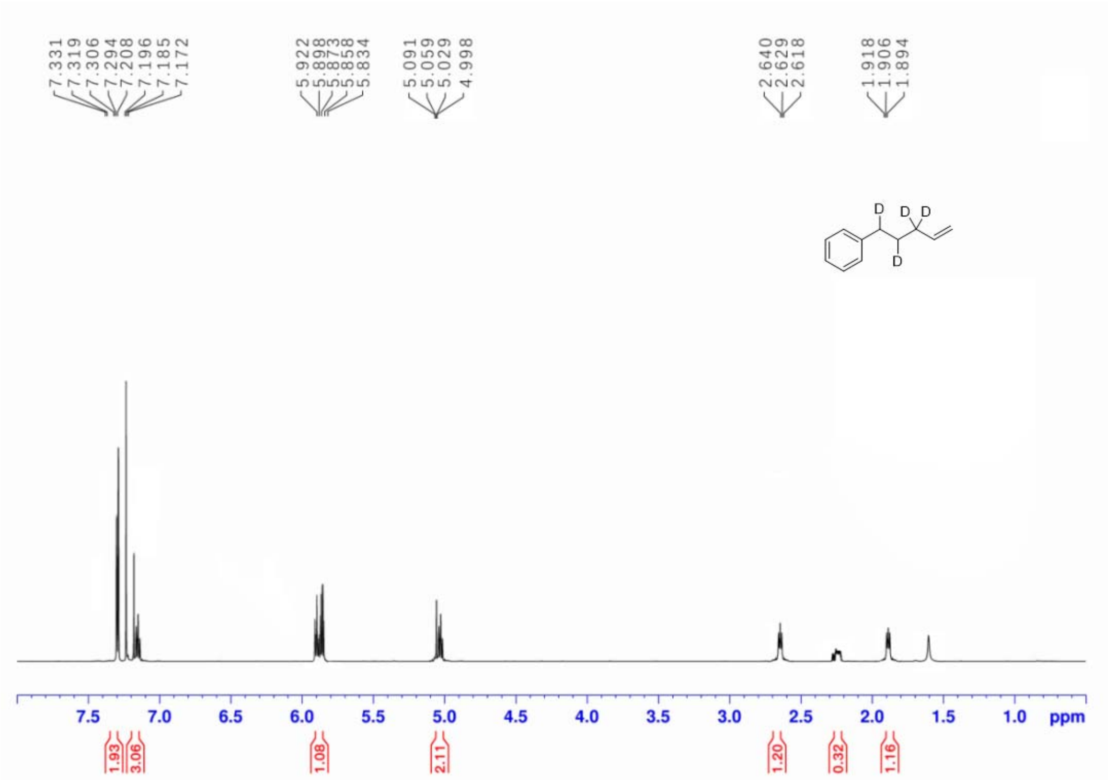
^{1}H NMR Spectra of **8a** (600 MHz, $CDCl_3$)



^{13}C NMR Spectra of **8a** (151 MHz, $CDCl_3$)



^{1}H NMR Spectra of **9a** (600 MHz, $CDCl_3$)



^{13}C NMR Spectra of **9a** (151 MHz, $CDCl_3$)