Supporting Information

Palladium-catalyzed substrate-switchable C-H alkenylation and alkylation of benzoic acids using MBH alcohols

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General Information. Pd(OAc)$_2$, Ag$_2$CO$_3$, Ag$_2$O, AgOAc (≥99.99%), NaOAc (98%), KOAc (98%), Na$_2$CO$_3$, K$_2$CO$_3$, Cs$_2$CO$_3$, 2,2,2-trifluoroethanol (TFE), 2,2,2-trichloroethanol (TCE), 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) and benzoic acids of Sigma-Aldrich, BLD Pharm and TCI chemicals were used as received. MeOH, CH$_2$Cl$_2$ and (CH$_2$Cl)$_2$ were dried prior as per the standard procedure. Silica gel-G/GF254 plates (Merck) were used for TLC analysis with a mixture of hexane and EtOAc as the eluent. Column chromatography was carried out using Rankem silica gel (60-120 mesh). Bruker Avance III 400, 500 and 600 MHz NMR spectrometers were used to record (^{1}H, ^{13}C and ^{19}F) spectra using CDCl$_3$ and DMSO-d$_6$ as the solvent and tetramethylsilane (TMS) as an internal standard. Chemical shifts (δ) and spin-spin coupling constant (*J*) are reported in parts per million and hertz (Hz), respectively, and to describe peak patterns following abbreviations were used when appropriate: s = singlet, d = doublet, t = triplet, dd = doublet of doublets and m = multiplet. Melting point of the products was measured on Büchi melting point apparatus, MPB-540. Open capillary tubes were used for the measurements and are uncorrected. Mestre nova software was used throughout the spectral analysis. Q-Tof ESI-MS instrument (model HAB273) was used for recording HRMS data. Infrared spectra were recorded on Perkin Elmer FT-IR instrument. Single crystal X-ray data were collected on a Bruker SMART APEX equipped with a CCD area detector using Mo/Kα radiation and the structure was solved by direct method using SHELXL-18 (Göttingen, Germany).

Crystal Data and Structure Refinement for 3oa.

Sample Preparation for Crystal Growth. The compound **3oa** was dissolved in minimum volume of acetonitrile and kept at room temperature for slow evaporation (2 days). Block shaped crystals were formed. The single crystal was subjected to X-ray diffraction.

Crystal Data and Structure Refinement for 3oa.

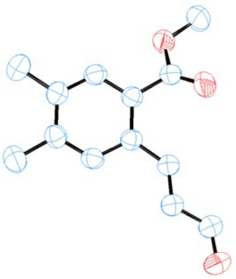
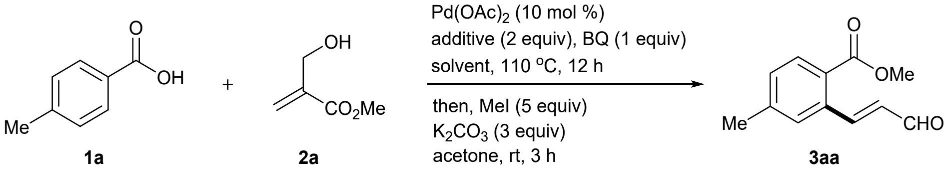


Figure S1. ORTEP diagram of **Methyl (*E*)-4,5-dimethyl-2-(3-oxoprop-1-en-1-yl)benzoate 3oa** (CCDC No 2368719) with 50% ellipsoid. H-Atoms are omitted for clarity.

CCDC	**2368719**
Identification code	**3oa**
Empirical formula	$C_{13}H_{14}O_3$
Formula weight	218.24
Crystal habit, colour	Block, Colorless
Temperature, *T*/K	298 K
Wavelength, λ/Å	0.71073 Å
Crystal system	Triclinic
Space group	P -1
Unit cell dimensions	a = 8.402(3) Å b = 8.472(3) Å c = 9.245(4) Å α= 109.344(11) β= 101.143(11) γ = 100.258(11)
Volume, *V*/Å^3	588.0
Z	2
Calculated density, Mg·m^{-3}	1.233
Absorption coefficient, μ/mm^{-1}	0.087
F(000)	232
θ range for data collection	2.426 to 26.001
Limiting indices	$-10 \leq h \leq 10$, $-10 \leq k \leq 10$, $-11 \leq l \leq 11$
Reflection collected / unique	2304/ 1770
Completeness to θ	99.3%
Absorption correction	Multi-scan
Refinement method	SHELXL 2018/3 (Sheldrick, 2015)
Data / restraints / parameters	2304/ 0/ 148
Goodness−of−fit on F^2	1.087
Final *R* indices [I >2sigma(I)]	R1 = 0.0548, *w*R2 = 0.1271
R indices (all data)	R1 = 0.0734, *w*R2 = 0.1416

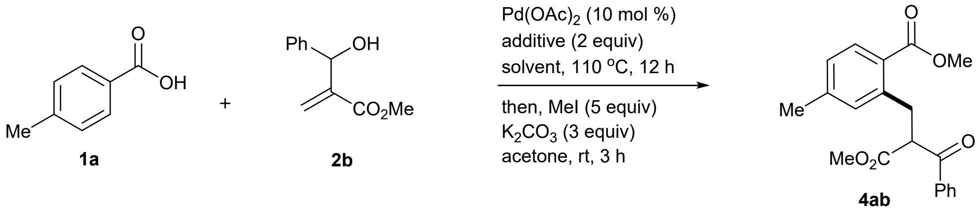
Table S1. Optimization of Reaction Conditions: C-H Alkenylation[a]



entry	additive	solvent	yield of 3aa[b] (%)
1	**Ag_2CO_3**	**HFIP**	**72**
2	Na_2CO_3	HFIP	trace
3	K_2CO_3	HFIP	24
4	Cs_2CO_3	HFIP	30
5	Ag_2O	HFIP	n.d.
6	AgOAc	HFIP	n.d.
7	NaOAc	HFIP	n.d.
8	KOAc	HFIP	n.d.
9	Ag_2CO_3	TFE	58
10	Ag_2CO_3	TCE	56
11	Ag_2CO_3	MeOH	35
12	Ag_2CO_3	EtOH	20
13	Ag_2CO_3	$PhCF_3$	n.d.
14	Ag_2CO_3	$(CH_2Cl)_2$	n.d.
15	-	HFIP	n.d.
16[c]	Ag_2CO_3	HFIP	n.d.
17[d]	Ag_2CO_3	HFIP	n.d.
18[e]	Ag_2CO_3	HFIP	55
19[f]	Ag_2CO_3	HFIP	45
20[g]	Ag_2CO_3	HFIP	n.d.
21[h]	Ag_2CO_3	HFIP	n.d.
22[i]	Ag_2CO_3	HFIP	n.d.

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.11 mmol), $Pd(OAc)_2$ (10 mol %), Ag_2CO_3 (2 equiv), BQ (1 equiv), Solvent (1 mL), 110 °C, 12 h, then MeI (5 equiv), K_2CO_3 (3 equiv), acetone (1.5 mL) rt, 3h. [b]Isolated yield. [c]In absence of BQ. [d]In absence of $Pd(OAc)_2$. [e]Ag_2CO_3 (1 equiv). [f]At 80 °C. [g]$Pd(TFA)_2$ (10 mol %) used. [h] $PdCl_2$ (10 mol %) used. [i]$Pd_2(dba)_3$ (10 mol %) used. n.d. = not detected. TFE = 2,2,2-trifluoroethanol. TCE = 2,2,2-trichloroethanol. HFIP = 1,1,1,3,3,3-hexafluoroisopropanol. BQ = 1,4-benzoquinone.

Table S2. Optimization of Reaction Conditions: C-H Alkylation[a]

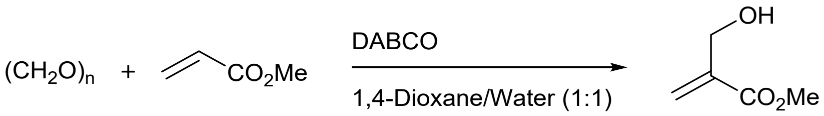


entry	additive	solvent	yield of 4ab[b] (%)
1[c]	Ag_2CO_3	HFIP	54
2	Ag_2CO_3	HFIP	67
3	$\mathbf{Ag_2CO_3}$	**TFE**	**77**
4	Ag_2CO_3	TCE	44
5	Ag_2CO_3	MeOH	27
6	Ag_2CO_3	EtOH	25
7	Ag_2CO_3	$PhCF_3$	n.d.
8	Ag_2CO_3	$(CH_2Cl)_2$	30
9	-	TFE	n.d.
10[d]	Ag_2CO_3	TFE	n.d.
11[e]	Ag_2CO_3	TFE	50
12[f]	Ag_2CO_3	TFE	41
13[g]	Ag_2CO_3	TFE	n.d.
14[h]	Ag_2CO_3	TFE	n.d.
15[i]	Ag_2CO_3	TFE	n.d.

[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.11 mmol), $Pd(OAc)_2$ (10 mol %), Ag_2CO_3 (2 equiv), Solvent (1 mL), 110 °C, 12 h, then MeI (5 equiv), K_2CO_3 (3 equiv), acetone (1.5 mL) rt, 3h. [b] Isolated yield. [c] In presence of BQ (1 equiv). [d] In absence of $Pd(OAc)_2$. [e] Ag_2CO_3 (1 equiv). [f] At 80 °C. [g] $Pd(TFA)_2$ (10 mol%) used. [h] $PdCl_2$ (10 mol %) used. [i] $Pd_2(dba)_3$ (10 mol %) used. n.d. = not detected. TFE = 2,2,2-trifluoroethanol. TCE = 2,2,2-trichloroethanol. HFIP = 1,1,1,3,3,3-hexafluoroisopropanol. BQ = 1,4-benzoquinone.

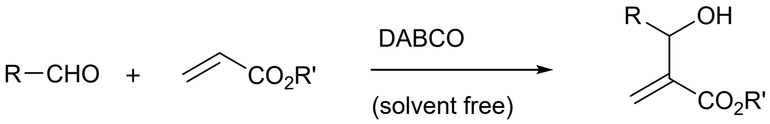
Benzoic Acids **1a-r** of Sigma-Aldrich, TCI Chemicals and BLD pharm were utilized for the reactions as received.

General Procedure for the Preparation of MBH Alcohol 2a.[1]



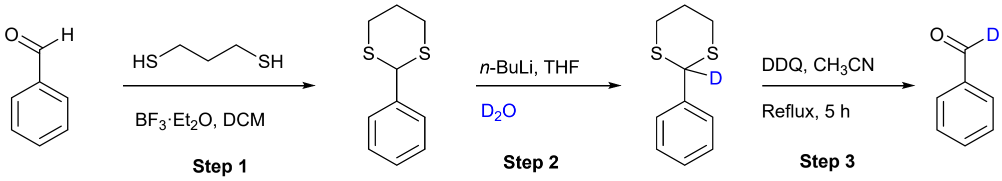
To a solution of paraformaldehyde (20 mmol, 600 mg, 1.0 equiv) in dioxane/water (1:1) (30 mL, 0.6 M), methyl acrylate (60 mmol, 1.72 g, 3.0 equiv) and DABCO (20 mmol, 2.240 g, 1.0 equiv) were added and stirred at room temperature for 12 h. After completion (monitored by TLC), the reaction mixture was diluted with EtOAc (20 mL) and washed successively with saturated solution of $NaHCO_3$ (2 x 20 mL) and brine (1 x 10 mL). Drying of the organic layer over Na_2SO_4 and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using n-hexane and EtOAc as an eluent to afford the MBH alcohol **2a**.

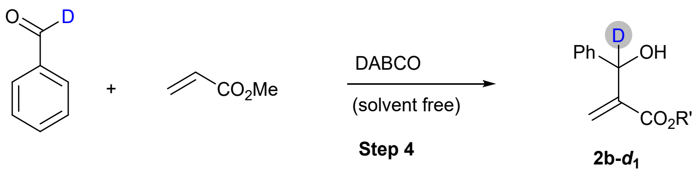
General Procedure for the Preparation of MBH Alcohols 2b-o.[1]



Aldehyde (20 mmol, 1.0 equiv), acrylate (60 mmol, 3.0 equiv) and DABCO (20 mmol, 2.24 g, 1.0 equiv) were stirred at room temperature under solvent free condition for 3 h to 7 days. After completion (monitored by TLC), the reaction mixture was diluted with EtOAc (20 mL) and washed successively with saturated solution of $NaHCO_3$ (2 x 20 mL) and brine (1 x 10 mL). Drying of the organic layer over Na_2SO_4 and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using n-hexane and EtOAc as an eluent to afford the MBH alcohol **2b-o**.

Procedure for the Preparation of Deuterated MBH Alcohol 2b-*d*$_1$.[2]





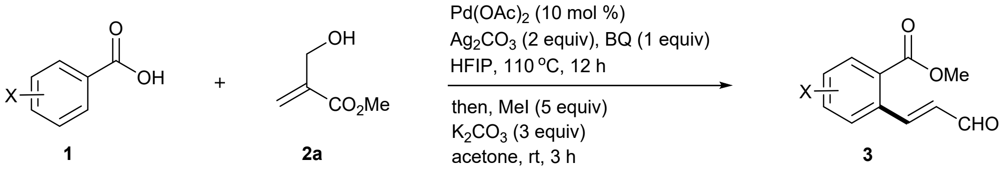
Step 1: To a stirred solution of benzaldehyde (6.0 mmol, 636 mg, 1.0 equiv) and propane-1,3-dithiol (6.0 mmol, 649 mg, 1.0 equiv) in CH_2Cl_2 (20 mL, 0.3 M) were slowly added $BF_3{\cdot}Et_2O$ (3 mmol, 0.37 mL, 0.3 equiv) at 0 °C. The resulting mixture was allowed to warm to room temperature and continued to the stirring for 30 min until the disappearance of benzaldehyde was determined by TLC analysis. The reaction was quenched with H_2O (20 mL) and extracted with CH_2Cl_2 (3 x 20 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using n-hexane and EtOAc as an eluent to afford the corresponding 2-phenyl-1,3-dithiane in 91% (1.1 g) yield.

Step 2: To a stirred solution of 2-phenyl-1,3-dithiane (3 mmol, 589 mg, 1 equiv) in THF (15 mL, 0.2 M) was added *n*-BuLi (1.6 M in hexane solution, 6 mmol, 5.5 mL, 2 equiv) at -35 °C under N_2 atmosphere. After stirring for 3 h, D_2O (34.4 mmol, 0.6 mL, 4 equiv) was added into the reaction mixture. After completion (monitored by TLC), the mixture was diluted with H_2O (5 mL) and extracted with EtOAc (3 x 15 mL). Drying (Na_2SO_4) and evaporation of the solvent gave deuterated 2-phenyl-1,3-dithiane residue, which was used for the next step without further purification.

Step 3: To a stirred solution of deuterated 2-phenyl-1,3-dithiane (3 mmol, 592 mg, 1.0 equiv) in CH_3CN (15 mL, 0.2 M) was added DDQ (3.3 mmol, 749 mg, 1.0 equiv) and the resulting mixture was refluxed at 90 °C for 5 h. After completion, the solvent was evaporated under reduced pressure and the residue was dissolved in CH_2Cl_2 (10 mL) and passed through a short pad of celite. Evaporation of the solvent gave a residue that was purified on silica gel column chromatography using n-hexane and EtOAc as an eluent to afford the deuterated benzaldehyde in 85% (273 mg) yield.

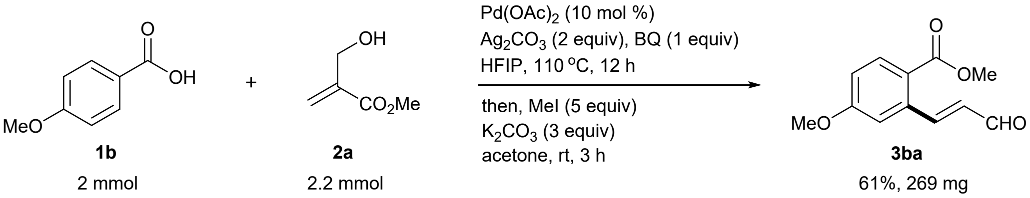
Step 4: The deuterated benzaldehyde (step 3) was reacted with methyl acrylate as described in the general procedure for the preparation of MBH alcohol to produce the deuterated MBH alcohol **2b-*d*₁**.

General Procedure for the Pd-Catalyzed C-H Alkenylation of Benzoic acids with MBH Alcohols.



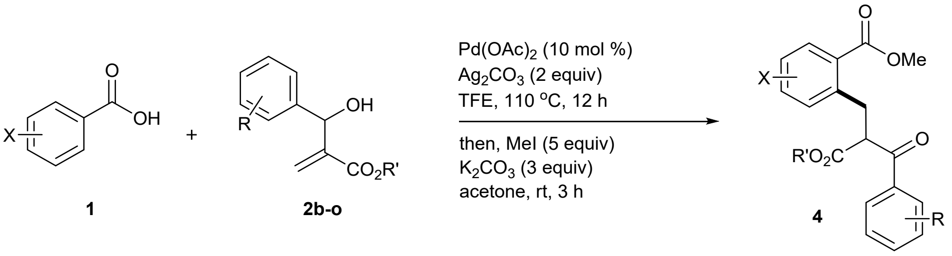
Benzoic acid **1** (0.1 mmol, 1.0 equiv), MBH alcohol **2a** (0.11 mmol, 1.1 equiv), $Pd(OAc)_2$ (0.01 mmol, 2.3 mg, 0.1 equiv), Ag_2CO_3 (0.2 mmol, 55 mg, 2.0 equiv) and 1,4-benzoquinone (0.1 mmol, 11 mg, 1.0 equiv) were stirred in 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) (1 mL, 0.1 M) at 110 ° C (in a pre-heated oil bath) in a sealed tube for 12 h. The reaction mixture was cooled to room temperature, diluted with EtOAc (5 mL) and passed through a short celite pad. Evaporation of the solvent gave a residue, which was stirred with K_2CO_3 (0.3 mmol, 41.5 mg, 3.0 equiv) and MeI (0.5 mmol, 31 μL, 5 equiv) in acetone (2 mL, 0.05 M) at room temperature for 3 h. After completion (monitored by TLC), the solvent was evaporated under reduced pressure and resulting residue was mixed with water (10 mL) and extracted with EtOAc (2 x 10 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using n-hexane and EtOAc as an eluent to afford **3**.

Scale-up Synthesis of 3ba.



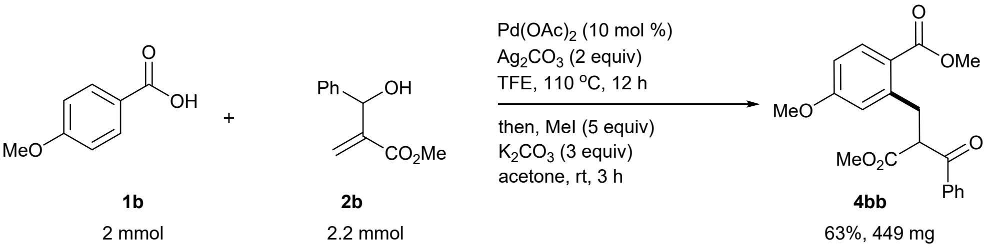
4-Methoxybenzoic acid **1b** (2 mmol, 304 mg, 1.0 equiv), MBH alcohol **2a** (2.2 mmol, 255 mg, 1.1 equiv), $Pd(OAc)_2$ (0.2 mmol, 45 mg, 0.1 equiv), Ag_2CO_3 (4 mmol, 1.1 g, 2.0 equiv) and 1,4-benzoquinone (2 mmol, 216 mg, 1.0 equiv) were stirred in 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) (10 mL, 0.2 M) at 110 ° C (in a pre-heated oil bath) in a sealed tube for 12 h. The reaction mixture was cooled to room temperature, diluted with EtOAc (20 mL) and passed through a short celite pad. Evaporation of the solvent gave a residue that was stirred with K_2CO_3 (6 mmol, 828 mg, 3.0 equiv) and MeI (10 mmol, 0.6 mL, 5.0 equiv) in acetone (20 mL, 0.1 M) at room temperature for 3 h. After completion (monitored by TLC), the solvent was evaporated under reduced pressure and resulting residue was mixed with water (30 mL) and extracted with EtOAc (2 x 30 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using n-hexane and EtOAc as an eluent to afford **3ba** in 61% (269 mg) yield.

General Procedure for the Pd-Catalyzed C-H Alkylation of Benzoic acids with MBH Alcohols.



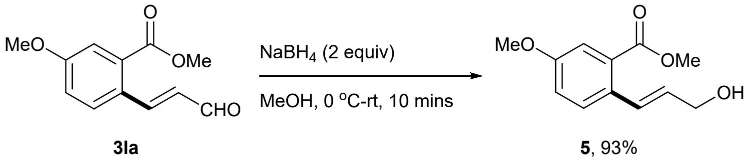
Benzoic acid **1** (0.1 mmol, 1.0 equiv), MBH alcohol **2b-o** (0.11 mmol, 1.1 equiv), Pd(OAc)$_2$ (0.01 mmol, 2.3 mg, 0.1 equiv) and Ag$_2$CO$_3$ (0.2 mmol, 55 mg, 2.0 equiv) were stirred in 2,2,2-trifluoroethanol (TFE) (1 mL, 0.1 M) at 110 °C (in a pre-heated oil bath) in a sealed tube for 12 h. The reaction mixture was cooled to room temperature, diluted with EtOAc (5 mL) and passed through a short pad of celite. Evaporation of the solvent gave a residue that was stirred with K$_2$CO$_3$ (0.3 mmol, 41.5 mg, 3.0 equiv) and MeI (0.5 mmol, 31 μL, 5.0 equiv) in acetone (2 mL, 0.05 M) at room temperature for 3 h. After completion (monitored by TLC), the solvent was evaporated under reduced pressure and resulting residue was mixed with water (10 mL) and extracted with EtOAc (2 x 10 mL). Drying (Na$_2$SO$_4$) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using n-hexane and EtOAc as an eluent to afford **4**.

Scale-up Synthesis of 4bb.



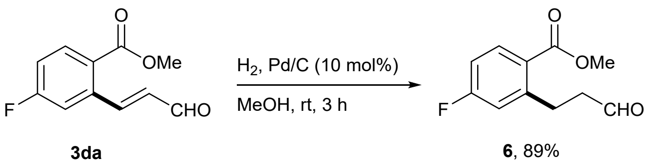
4-Methoxybenzoic acid **1b** (2 mmol, 304 mg, 1.0 equiv), MBH alcohol **2b** (2.2 mmol, 384 mg, 1.1 equiv), Pd(OAc)$_2$ (0.2 mmol, 45 mg, 0.1 equiv), Ag$_2$CO$_3$ (4 mmol, 1.1 g, 2.0 equiv) were stirred in 2,2,2- trifluoroethanol (TFE) (10 mL, 0.2 M) at 110 °C (in a pre-heated oil bath) in a sealed tube for 12 h. The reaction mixture was cooled to room temperature, diluted with EtOAc (20 mL) and passed through a small celite pad. Evaporation of the solvent gave a residue that was stirred with K_2CO_3 (6 mmol, 828 mg, 3.0 equiv) and MeI (10 mmol, 0.6 mL, 5.0 equiv) in acetone (20 mL, 0.1 M) at room temperature for 3 h. After completion (monitored by TLC), the solvent was evaporated under reduced pressure and resulting residue was mixed with water (30 mL) and extracted with EtOAc (2 x 30 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using n-hexane and EtOAc as an eluent to afford **4bb** in 63% (449 mg) yield.

Synthesis of 5.



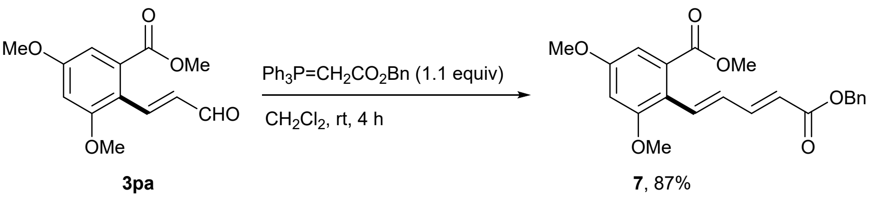
To a stirred solution of **3la** (0.1 mmol, 20.4 mg, 1.0 equiv) in MeOH (2 mL, 0.05 M) was added $NaBH_4$ (0.2 mmol, 7.6 mg, 2.0 equiv) at 0 °C under N_2 atmosphere. The reaction was allowed to stir for 10 minutes at room temperature. After completion (monitored by TLC), the solvent was evaporated and the residue was purified on silica gel column chromatography using n-hexane and EtOAc as an eluent to afford **5** in 93% (20.7 mg) yield.

Synthesis of 6.



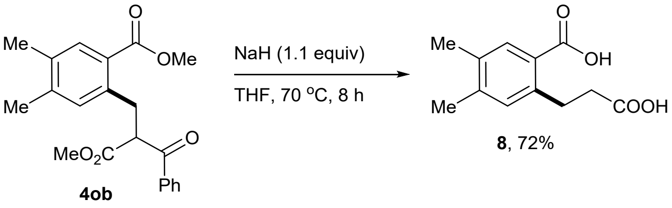
To a stirred solution of **3da** (0.1 mmol, 18.5 mg, 1.0 equiv) in MeOH (2 mL, 0.05 M), Pd/C (10 mol %, 1 mg) was added under hydrogen balloon and allowed to stir for 3 h at room temperature. After completion (monitored by TLC), the reaction mixture was passed through a short celite pad using EtOAc (10 mL). Evaporation of the solvent gave a residue that was purified on silica gel column chromatography to afford **6** in 89% (18.7 mg) yield.

Synthesis of 7.



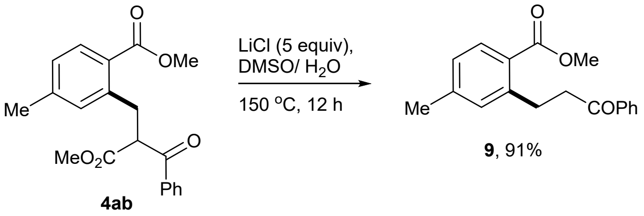
To a stirred solution of **3pa** (0.1 mmol, 25 mg, 1.0 equiv) in CH_2Cl_2 (1 mL, 0.1 M), $Ph_3P=CH_2CO_2Bn$ (0.11 mmol, 45 mg, 1.1 equiv) was added and the reaction was allowed to stir for 4 h at room temperature. After completion (monitored by TLC), the solvent was evaporated under reduced pressure and the residue was purified on silica gel chromatography using n-hexane and EtOAc as an eluent to afford **7** in 87% (33 mg) yield.

Synthesis of 8.



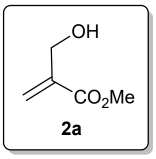
A solution of **4ob** (0.1 mmol, 35.5 mg, 1.0 equiv) and a suspension of NaH (0.11 mmol, 4.5 mg, 60 % dispersion in mineral oil, 1.1 equiv) in THF (2 mL, 0.05 M) was stirred at 70 °C for 12 h. After completion (monitored by TLC), the reaction mixture was quenched with saturated aq. NH_4Cl (5 mL) and the aqueous layer was extracted using EtOAc (2 x 10 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using n-hexane and EtOAc as an eluent to afford **8** in 72% (16 mg) yield.

Synthesis of 9.

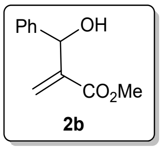


To a stirred solution of **4ab** (0.1 mmol, 34 mg, 1.0 equiv) in DMSO (1 mL, 0.1 M) and H_2O (0.5 mmol, 10 µL, 5.0 equiv), LiCl (0.5 mmol, 21 mg, 5.0 equiv) was added. The resultant solution was stirred at 150 °C for 12 h under argon atmosphere. After completion (monitored by TLC), the reaction mixture was cooled to room temperature and extracted with EtOAc (2 x 10 mL). The organic layer was washed with brine (1 x 10 mL) and water (1 x 10 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using n-hexane and EtOAc as an eluent to afford **9** in 91% (25.7 mg) yield.

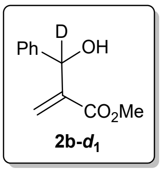
Characterization Data of the MBH Alcohols



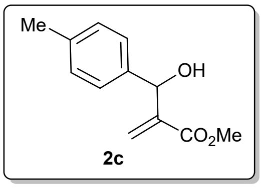
Methyl 2-(hydroxymethyl)acrylate 2a.[3] Analytical TLC on silica gel, 1:5 EtOAc/hexane $R_f = 0.41$; colorless liquid; yield 75% (870 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.25 (s, 1H), 5.83 (s, 1H), 4.31 (s, 2H), 3.77 (s, 3H), 2.50 (bs, 1H).



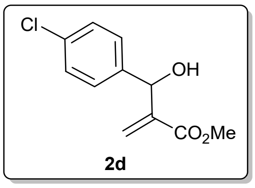
Methyl 2-(hydroxy(phenyl)methyl)acrylate 2b.[4] Analytical TLC on silica gel, 1:5 EtOAc/hexane $R_f = 0.44$; colorless liquid; yield 79% (1.52 g); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.31 (m, 4H), 7.29-7.26 (m, 1H), 6.33 (s, 1H), 5.84 (s, 1H), 5.55 (s, 1H), 3.71 (s, 3H), 3.14 (bs, 1H).



Methyl 2-(hydroxy(phenyl)methyl-*d*)acrylate 2b-*d*$_1$.[5] Analytical TLC on silica gel, 1:5 EtOAc/hexane $R_f = 0.44$; colorless liquid; yield 71% (411 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.26 (m, 5H), 6.34 (s, 1H), 5.84 (s, 1H), 3.72 (s, 3H), 3.02 (bs, 1H).

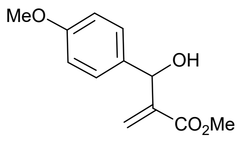


Methyl 2-(hydroxy(p-tolyl)methyl)acrylate 2c.[6] Analytical TLC on silica gel, 1:5 EtOAc/hexane $R_f = 0.50$; colorless liquid; yield 79% (1.63 g); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, $J = 8.0$ Hz, 2H), 7.14 (d, $J = 8.0$ Hz, 2H), 6.32 (s, 1H), 5.85 (s, 1H), 5.53-5.52 (m, 1H), 3.71 (s, 3H), 2.97 (bs, 1H), 2.33 (s, 3H).



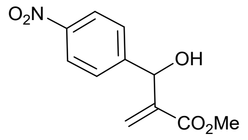
Methyl 2-((4-chlorophenyl)(hydroxy)methyl)acrylate 2d.[4] Analytical TLC on silica gel, 1:5 EtOAc/hexane $R_f = 0.51$; colorless liquid; yield 80% (1.81 g); ^{1}H NMR

(400 MHz, $CDCl_3$) δ 7.30 (s, 4H), 6.33 (s, 1H), 5.83 (s, 1H), 5.52-5.51 (m, 1H), 3.72 (s, 3H), 3.17 (bs, 1H).



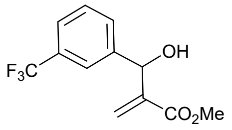
2e

Methyl 2-(hydroxy(4-methoxyphenyl)methyl)acrylate 2e.[4] Analytical TLC on silica gel, 1:5 EtOAc/hexane $R_f = 0.41$; colorless liquid; yield 66% (1.47 g); ^1H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, $J = 8.5$ Hz, 2H), 6.86 (d, $J = 8.8$ Hz, 2H), 6.32 (s, 1H), 5.85 (s, 1H), 5.52-5.51 (m, 1H), 3.79 (s, 3H), 3.71 (s, 3H), 2.96-2.95 (m, 1H).



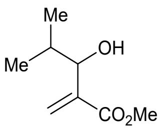
2f

Methyl 2-(hydroxy(4-nitrophenyl)methyl)acrylate 2f.[6] Analytical TLC on silica gel, 1:5 EtOAc/hexane $R_f = 0.45$; yellow liquid; yield 85% (2.0 g); ^1H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, $J = 8.4$ Hz, 2H), 7.55 (d, $J = 8.4$ Hz, 2H), 6.39 (s, 1H), 5.87 (s, 1H), 5.63 (s, 1H), 3.73 (s, 3H), 3.40 (bs, 1H).



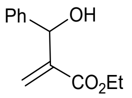
2g

Methyl 2-(hydroxy(3-(trifluoromethyl)phenyl)methyl)acrylate 2g.[6] Analytical TLC on silica gel, 1:5 EtOAc/hexane $R_f = 0.52$; colorless liquid; yield 82% (2.15 g); ^1H NMR (400 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.56 (t, $J = 8.0$ Hz, 2H), 7.47 (t, $J = 7.6$ Hz, 1H), 6.38 (s, 1H), 5.84 (s, 1H), 5.62-5.60 (m, 1H), 3.74 (s, 3H), 3.19 (d, $J = 6.0$ Hz, 1H).



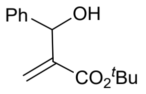
2h

Methyl 3-hydroxy-4-methyl-2-methylenepentanoate 2h.[7] Analytical TLC on silica gel, 1:5 EtOAc/hexane $R_f = 0.50$; colorless liquid; yield 68% (1.1 g); ^1H NMR (400 MHz, $CDCl_3$) δ 6.18 (d, $J = 6.9$ Hz, 1H), 5.72 (s, 1H), 4.04 (d, $J = 6.6$ Hz, 1H), 3.71 (s, 3H), 2.74 (bs, 1H), 1.88-1.81 (m, 1H), 0.88-0.82 (m, 6H).



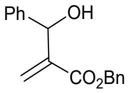
2i

Ethyl 2-(hydroxy(phenyl)methyl)acrylate 2i.[8] Analytical TLC on silica gel, 1:5 EtOAc/hexane R_f = 0.44; colorless liquid; yield 82% (1.7 g); ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.37-7.32 (m, 4H), 7.29-7.26 (m, 1H), 6.33 (s, 1H), 5.82 (s, 1H), 5.55-5.54 (m, 1H), 4.16 (q, J = 7.2 Hz, 2H), 3.17 (bs, 1H), 1.23 (t, J = 7.2 Hz, 3H).



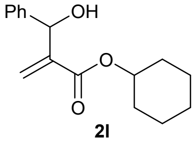
2j

***tert*-Butyl 2-(hydroxy(phenyl)methyl)acrylate 2j.**[9] Analytical TLC on silica gel, 1:5 EtOAc/hexane R_f = 0.51; colorless liquid; yield 70% (1.64 g); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.38-7.32 (m, 4H), 7.29-7.25 (m, 1H), 6.25 (s, 1H), 5.72 (s, 1H), 5.49 (d, J = 5.6 Hz, 1H), 3.12 (d, J = 6.0 Hz, 1H), 1.39 (s, 9H).



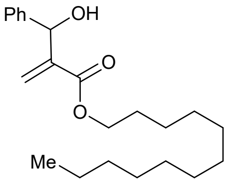
2k

Benzyl 2-(hydroxy(phenyl)methyl)acrylate 2k.[9] Analytical TLC on silica gel, 1:5 EtOAc/hexane R_f = 0.44; colorless liquid; yield 81% (2.17 g); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.35-7.20 (m, 10H), 6.37 (s, 1H), 5.86 (s, 1H), 5.54 (s, 1H), 5.14-5.07 (m, 2H), 3.13 (bs, 1H).



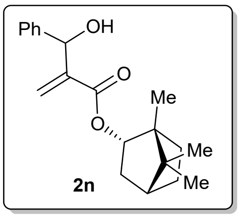
2l

Cyclohexyl 2-(hydroxy(phenyl)methyl)acrylate 2l.[10] Analytical TLC on silica gel, 1:5 EtOAc/hexane R_f = 0.44; colorless liquid; yield 71% (1.85 g); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.38-7.31 (m, 4H), 7.29-7.25 (m, 1H), 6.34 (s, 1H), 5.80 (s, 1H), 5.54 (s, 1H), 4.81-4.76 (m, 1H), 3.16 (bs, 1H), 1.79-1.52 (m, 5H), 1.50-1.23 (m, 6H).



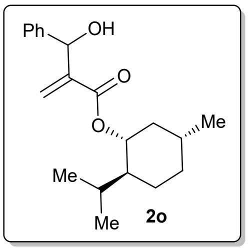
2m

Dodecyl 2-(hydroxy(phenyl)methyl)acrylate 2m. Analytical TLC on silica gel, 1:10 EtOAc/hexane R_f = 0.47; colorless liquid; yield 81% (281 mg); ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.36 (d, J = 7.2 Hz, 2H), 7.34 (t, J = 7.2 Hz, 2H), 7.29-7.26 (m, 1H), 6.34 (s, 1H), 5.82 (s, 1H), 5.55 (s, 1H), 4.13-4.06 (m, 2H), 3.11 (bs, 1H), 1.60-1.58 (m, 2H), 1.31-1.26 (m, 18H), 0.88 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 166.5, 142.3, 141.5, 128.5, 127.9, 126.7, 126.0, 73.5, 65.2, 32.0, 29.8, 29.7, 29.68, 29.60, 29.5, 29.3, 28.6, 26.0, 22.8, 14.2; FT-IR (neat) 3447, 2923, 2854, 1711, 1630, 1456, 1269, 1149, 1040, 955 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M+Na]$^+$ calcd for $C_{22}H_{34}O_3Na$ 369.2400; Found 369.2399.



2n

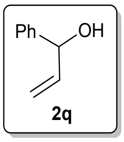
(1R,2S,4R)-1,7,7-Trimethylbicyclo[2.2.1]heptan-2-yl 2-(hydroxy-(phenyl)methyl)acrylate 2n. Analytical TLC on silica gel, 1:10 EtOAc/hexane R$_f$ = 0.41; colorless liquid; yield 79% (248 mg); 1:1 mixture of diastereomers; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.38-7.31 (m, 8H), 7.29-7.25 (m, 2H), 6.38 (s, 2H), 5.85 (t, *J* = 1.6 Hz, 1H), 5.84 (t, *J* = 1.2 Hz, 1H), 5.56-5.54 (m, 2H), 4.91-4.86 (m, 2H), 3.11 (d, *J* = 5.6 Hz, 1H), 3.05 (d, *J* = 5.6 Hz, 1H), 2.36-2.24 (m, 2H), 1.84-1.61 (m, 7H), 1.32-1.23 (m, 2H), 1.18-1.05 (m, 2H), 0.93-0.88 (m, 1H), 0.87-0.84 (m, 12H), 0.77 (s, 3H), 0.70 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 166.7, 166.6, 142.5, 142.4, 141.5, 128.6, 128.5, 128.0, 127.9, 126.8, 126.7, 126.0, 125.7, 80.9, 80.8, 73.5, 73.4, 48.9, 47.9, 44.9, 36.7, 36.6, 28.0, 27.9, 27.4, 27.3, 19.7, 18.9, 13.5, 13.4; FT-IR (neat) 3450, 2953, 2879, 1705, 1630, 1453, 1267, 1152, 1022, 955 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M+Na]$^+$ calcd for $C_{20}H_{26}O_3Na$ 337.1774; Found 337.1772.



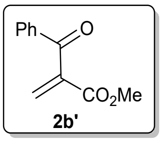
2o

(1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl 2-(hydroxy(phenyl)-methyl)acrylate 2o.[11] Analytical TLC on silica gel, 1:10 EtOAc/hexane R$_f$ = 0.40; colorless solid; yield 74% (268 mg); 1.11:1 mixture of diastereomers; ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.40-7.35 (m, 7.6H, major + minor), 7.31-7.28 (m, 1.9H, major + minor), 6.36 (s, 1H, major), 6.34 (s, 0.9H, minor), 5.85 (s, 1H, major), 5.80 (s, 0.9H, minor), 5.57-5.56 (m, 1.9H, major + minor), 4.76-4.71 (m, 1.9H, major + minor), 3.11 (d, *J* = 6.6 Hz, 0.9H, minor), 3.08 (d, *J* = 6.6 Hz, 1H, major), 1.96-1.90 (m, 1.9H, major + minor), 1.69-1.65 (m, 4.9H, major + minor), 1.51-1.46 (m, 2.7H, minor), 1.38-1.32 (m, 1.9H, major + minor), 1.08-1.02 (m, 1.9H, major + minor), 1.00-0.94 (m, 1.9H, major + minor), 0.91-0.88 (m, 5.8H, major + minor), 0.83 (d, *J* =

7.2 Hz, 2.7H, minor), 0.78 (d, *J* = 7.2 Hz, 3H, major), 0.68 (d, *J* = 6.6 Hz, 2.7H, minor), 0.63 (d, *J* = 6.6 Hz, 3H, major).

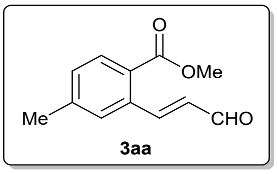

2q

1-Phenylprop-2-en-1-ol 2q.[12] Analytical TLC on silica gel, 1:10 EtOAc/hexane R_f = 0.35; colorless solid; yield 82% (154 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.24 (m, 5H), 6.08-6.00 (m, 1H), 5.36-5.32(m, 1H), 5.20-5.17 (m, 2H), 2.12 (bs, 1H).

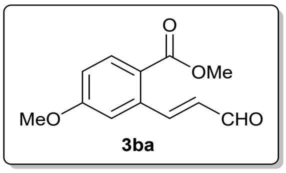

2b'

Methyl 2-benzoylacrylate 2b′.[13] Analytical TLC on silica gel, 1:10 EtOAc/hexane R_f = 0.42; colorless solid; yield 77% (231 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.4 Hz, 2H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.7 Hz, 2H), 6.72 (s, 1H), 6.05 (s, 1H), 3.76 (s, 3H).

Characterization Data of the Products

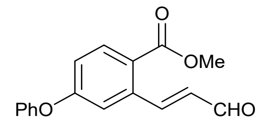

3aa

Methyl (*E*)-4-methyl-2-(3-oxoprop-1-en-1-yl)benzoate 3aa. Analytical TLC on silica gel, 1:9 EtOAc/hexane R_f = 0.50; colorless solid; mp 77-78 °C; yield 72% (15 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.75 (d, *J* = 8.0 Hz, 1H), 8.44 (d, *J* = 16.0 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.44 (s, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 6.60 (dd, *J* = 16.0, 8.0 Hz, 1H), 3.93 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.3, 167.2, 152.0, 143.5, 136.2, 131.4, 131.2, 131.1, 128.8, 126.8, 52.4, 21.7; FT-IR (neat) 2924, 1712, 1678, 1604, 1438, 1267, 1207, 1121, 1081 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{12}H_{13}O_3$ 205.0859; Found 205.0859.


3ba

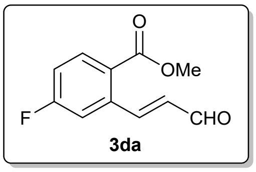
Methyl (*E*)-4-methoxy-2-(3-oxoprop-1-en-1-yl)benzoate 3ba. Analytical TLC on silica gel, 1:9 EtOAc/hexane R_f = 0.34; colorless solid; mp 82-83 °C; yield 73% (16 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.77 (d, *J* = 7.8 Hz, 1H), 8.50 (d, *J* = 16.2 Hz, 1H), 8.02 (d, *J* = 9.0 Hz, 1H), 7.08 (d, *J* = 2.4 Hz, 1H), 6.98 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.58 (dd,

J = 16.2, 7.8 Hz, 1H), 3.91 (s, 3H), 3.89 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 194.3, 166.8, 162.8, 152.1, 138.5, 133.5, 131.3, 121.7, 115.6, 113.2, 55.8, 52.3; FT-IR (neat) 2925, 1704, 1678, 1594, 1440, 1332, 1238, 1123, 1031 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{12}H_{13}O_4$ 221.0808; Found 221.0808.



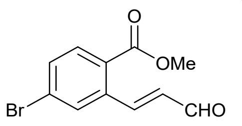
3ca

Methyl (*E*)-2-(3-oxoprop-1-en-1-yl)-4-phenoxybenzoate 3ca. Analytical TLC on silica gel, 1:9 EtOAc/hexane R_f = 0.41; brown sticky liquid; yield 65% (18 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.74 (d, J = 7.8 Hz, 1H), 8.46 (d, J = 16.2 Hz, 1H), 8.02 (d, J = 9.0 Hz, 1H), 7.42 (t, J = 7.8 Hz, 2H), 7.24 (t, J = 7.2 Hz, 1H), 7.16-7.15 (m, 1H), 7.07 (d, J = 7.8 Hz, 2H), 7.04-7.03 (m, 1H), 6.47 (dd, J = 15.6, 7.8 Hz, 1H), 3.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.1, 166.6, 161.5, 155.1, 151.3, 138.6, 133.6, 131.6, 130.4, 125.2, 123.4, 120.4, 118.9, 116.4, 52.5; FT-IR (neat) 2925, 2878, 1709, 1678, 1594, 1445, 1332, 1238, 1123, 1033 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{17}H_{15}O_4$ 283.0965; Found 283.0964.



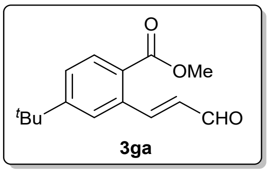
3da

Methyl (*E*)-4-fluoro-2-(3-oxoprop-1-en-1-yl)benzoate 3da. Analytical TLC on silica gel, 1:9 EtOAc/hexane R_f = 0.53; colorless solid; mp 94-95 °C; yield 74% (15 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (d, J = 7.6 Hz, 1H), 8.47-8.42 (m, 1H), 8.08 (dd, J = 8.8, 5.6 Hz, 1H), 7.32 (dd, J = 9.6, 2.8 Hz, 1H), 7.20-7.15 (m, 1H), 6.58 (dd, J = 15.6, 7.6 Hz, 1H), 3.94 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.8, 166.3, 166.2 (J_{C-F} = 249.0 Hz), 150.2, 139.2 (J_{C-F} = 8.5 Hz), 134.0 (J_{C-F} = 9.2 Hz), 132.0, 125.7 (J_{C-F} = 3.2 Hz), 117.4 (J_{C-F} = 21.4 Hz), 115.1 (J_{C-F} = 22.9 Hz), 52.7; ^{19}F NMR (565 MHz, $CDCl_3$) δ -105.18; FT-IR (neat) 2920, 1716, 1686, 1559, 1439, 1274, 1238, 1124, 1033 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{11}H_{10}O_3F$ 209.0608; Found 209.0595.



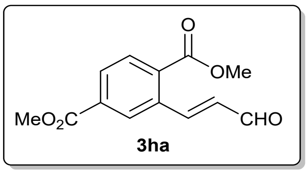
3ea

Methyl (*E*)-4-bromo-2-(3-oxoprop-1-en-1-yl)benzoate 3ea. Analytical TLC on silica gel, 1:9 EtOAc/hexane R_f = 0.48; yellow solid; mp 127-128 °C; yield 51% (14 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (d, J = 7.6 Hz, 1H), 8.36 (d, J = 16.0 Hz, 1H), 7.90 (d, J = 8.4 Hz, 1H), 7.77 (d, J = 2.0 Hz, 1H), 7.63 (dd, J = 8.4, 1.6 Hz, 1H), 6.59 (dd, J = 16.0, 7.6 Hz, 1H), 3.94 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.7, 166.5, 149.9, 138.1, 133.3, 132.7, 132.1, 131.1, 128.2, 127.7, 52.8; FT-IR (neat) 2922, 1714, 1686, 1557, 1438, 1274, 1238, 1123, 1030 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{11}H_{10}O_3Br$ 268.9808; Found 268.9804.



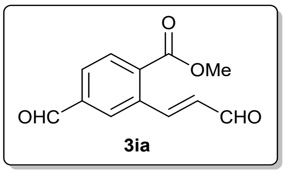
3ga

Methyl (*E*)-4-(*tert*-butyl)-2-(3-oxoprop-1-en-1-yl)benzoate 3ga. Analytical TLC on silica gel, 1:9 EtOAc/hexane R_f = 0.55; yellow sticky liquid; yield 45% (11 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (d, J = 7.6 Hz, 1H), 8.47 (d, J = 16.0 Hz, 1H), 7.96 (d, J = 8.4 Hz, 1H), 7.64-7.63 (m, 1H), 7.52 (dd, J = 8.4, 2.0 Hz, 1H), 6.63 (dd, J = 15.6, 7.6 Hz, 1H), 3.93 (s, 3H), 1.36 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.4, 167.2, 156.5, 152.5, 136.0, 131.2, 131.1, 127.6, 126.8, 125.1, 52.5, 35.3, 31.1; FT-IR (neat) 2934, 1716, 1677, 1605, 1438, 1265, 1207, 1121, 1079 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{15}H_{19}O_3$ 247.1329; Found 247.1329.



3ha

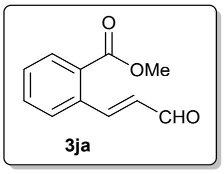
Dimethyl (*E*)-2-(3-oxoprop-1-en-1-yl)terephthalate 3ha. Analytical TLC on silica gel, 1:9 EtOAc/hexane R_f = 0.44; yellow solid; mp 114-115 °C; yield 75% (18.6 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (d, J = 7.6 Hz, 1H), 8.36 (d, J = 16.0 Hz, 1H), 8.31-8.30 (m, 1H), 8.14-8.11 (m, 1H), 8.08-8.06 (m, 1H), 6.70 (dd, J = 15.6, 7.6 Hz, 1H), 3.97 (s, 3H), 3.96 (s, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.8, 166.5, 165.6, 150.1, 136.2, 133.9, 133.1, 132.1, 131.3, 130.9, 129.2, 52.9, 52.8; FT-IR (neat) 2922, 1715, 1711, 1675, 1594, 1439, 1333, 1238, 1123, 1029 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{13}H_{13}O_5$ 249.0757; Found 249.0767.



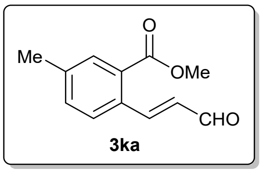
3ia

Methyl (*E*)-4-formyl-2-(3-oxoprop-1-en-1-yl)benzoate 3ia. Analytical TLC on silica gel, 1:9 EtOAc/hexane R_f = 0.43; yellow solid; mp 79-80 °C; yield

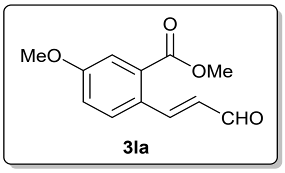
64% (14 mg); ^{1}H NMR (400 MHz, CDCl$_3$) δ 10.12 (s, 1H), 9.80 (d, *J* = 7.6 Hz, 1H), 8.37 (d, *J* = 16.0 Hz, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 8.13-8.12 (m, 1H), 7.99 (dd, *J* = 8.0, 1.6 Hz, 1H), 6.71 (dd, *J* = 16.0, 7.6 Hz, 1H), 3.99 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 193.6, 190.9, 166.3, 149.7, 138.9, 137.0, 134.2, 132.4, 132.0, 130.5, 129.2, 53.1; FT-IR (neat) 2953, 1725, 1670, 1600, 1460, 1332, 1210, 1159, 1056 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M+H]$^+$ calcd for $C_{12}H_{11}O_4$ 219.0652; Found 219.0639.



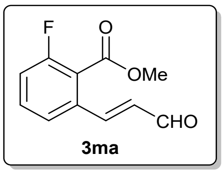
Methyl (*E*)-2-(3-oxoprop-1-en-1-yl)benzoate 3ja. Analytical TLC on silica gel, 1:9 EtOAc/hexane R$_f$ = 0.43; yellow liquid; yield 66% (25 mg); ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.76 (d, *J* = 7.8 Hz, 1H), 8.43 (d, *J* = 15.9 Hz, 1H), 8.02 (d, *J* = 7.8 Hz, 1H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 6.62 (dd, *J* = 15.9, 7.8 Hz, 1H), 3.95 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 194.2, 167.2, 151.6, 136.1, 132.8, 131.3, 131.2, 130.4, 129.7, 128.1, 52.6; FT-IR (neat) 2955, 1723, 1674, 1460, 1332, 1210, 1159 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M+H]$^+$ calcd for $C_{11}H_{11}O_3$ 191.0703; Found 191.0703.



Methyl (*E*)-5-methyl-2-(3-oxoprop-1-en-1-yl)benzoate 3ka. Analytical TLC on silica gel, 1:9 EtOAc/hexane R$_f$ = 0.50; colorless solid; mp 69-70 °C; yield 70% (14 mg); ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.74 (d, *J* = 8.0 Hz, 1H), 8.38 (d, *J* = 16.0 Hz, 1H), 7.83 (s, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.37 (d, *J* = 9.6 Hz, 1H), 6.61 (dd, *J* = 16.0, 7.6 Hz, 1H), 3.94 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 194.3, 167.4, 151.6, 141.1, 133.5, 133.1, 131.8, 130.6, 129.7, 128.0, 52.6, 21.4; FT-IR (neat) 2925, 1712, 1678, 1606, 1438, 1267, 1208, 1121, 1079 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M+H]$^+$ calcd for $C_{12}H_{13}O_3$ 205.0859; Found 205.0866.

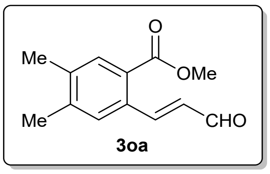


Methyl (*E*)-5-methoxy-2-(3-oxoprop-1-en-1-yl)benzoate 3la. Analytical TLC on silica gel, 1:9 EtOAc/hexane R$_f$ = 0.44; colorless solid; mp 74-76 °C; yield 75% (16.5 mg); ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.70 (d, *J* = 8.0 Hz, 1H), 8.34 (d, *J* = 15.6 Hz, 1H), 7.63 (d, $J = 8.8$ Hz, 1H), 7.49 (d, $J = 2.8$ Hz, 1H), 7.10 (dd, $J = 8.8, 2.8$ Hz, 1H), 6.57 (dd, $J = 15.6, 7.6$ Hz, 1H), 3.95 (s, 3H), 3.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.3, 167.0, 161.2, 151.0, 131.4, 129.5, 128.0, 118.7, 116.0, 55.8, 52.7; FT-IR (neat) 2955, 1720, 1677, 1599, 1496, 1273, 1231, 1122, 1071 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{12}H_{13}O_4$ 221.0808; Found 221.0808.



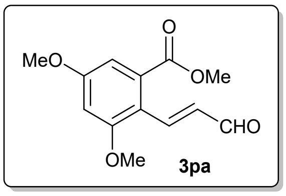
3ma

Methyl (*E*)-2-fluoro-6-(3-oxoprop-1-en-1-yl)benzoate 3ma. Analytical TLC on silica gel, 1:9 EtOAc/hexane $R_f = 0.54$; colorless solid; mp 87-88 °C; yield 56% (11.6 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.71 (d, $J = 8.0$ Hz, 1H), 7.70 (d, $J = 16.0$ Hz, 1H), 7.52-7.47 (m, 2H), 7.21 (t, $J = 9.0$ Hz, 1H), 6.67 (dd, $J = 16.0, 8.0$ Hz, 1H), 4.00 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.4, 165.2, 161.6 ($J_{C-F} = 250.0$ Hz), 148.2 ($J_{C-F} = 3.0$ Hz), 135.3 ($J_{C-F} = 2.9$ Hz), 132.4 ($J_{C-F} = 8.8$ Hz), 132.0, 123.0 ($J_{C-F} = 3.4$ Hz), 121.6 ($J_{C-F} = 16.1$ Hz), 118.4 ($J_{C-F} = 22.2$ Hz), 53.2; ^{19}F NMR (470 MHz, $CDCl_3$) δ -111.71; FT-IR (neat) 2922, 1715, 1685, 1557, 1438, 1274, 1238, 1123, 1031 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{11}H_{10}O_3F$ 209.0608; Found 209.0606.



3oa

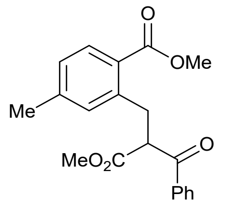
Methyl (*E*)-4,5-dimethyl-2-(3-oxoprop-1-en-1-yl)benzoate 3oa. Analytical TLC on silica gel, 1:9 EtOAc/hexane $R_f = 0.45$; yellow solid; mp 94-95 °C; yield 72% (16 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 (d, $J = 8.0$ Hz, 1H), 8.41 (d, $J = 16.0$ Hz, 1H), 7.80 (s, 1H), 7.43 (s, 1H), 6.60 (dd, $J = 15.6, 7.6$ Hz, 1H), 3.92 (s, 3H), 2.34-2.33 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.4, 167.4, 151.9, 142.1, 139.8, 133.5, 132.4, 130.4, 129.2, 127.2, 52.4, 20.1, 19.8; FT-IR (neat) 2926, 1715, 1676, 1604, 1438, 1267, 1207, 1120, 1080 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{13}H_{15}O_3$ 219.1016; Found 219.1014.



3pa

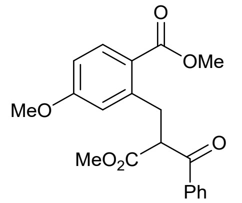
Methyl (*E*)-3,5-dimethoxy-2-(3-oxoprop-1-en-1-yl)benzoate 3pa. Analytical TLC on silica gel, 1:9 EtOAc/hexane $R_f = 0.31$; yellow solid; mp 104-105 °C; yield

74% (18.5 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.62 (d, *J* = 8.0 Hz, 1H), 7.90 (d, *J* = 16.0 Hz, 1H), 6.96-6.87 (m, 2H), 6.63 (d, *J* = 2.4 Hz, 1H), 3.93 (s, 3H), 3.89 (s, 3H), 3.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.1, 168.0, 161.9, 160.8, 147.2, 134.7, 132.4, 116.1, 106.8, 101.7, 56.0, 55.8, 52.9; FT-IR (KBr) 2953, 1722, 1672, 1597, 1460, 1330, 1209, 1159, 1057 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{13}H_{15}O_5$ 251.0914; Found 251.0913.



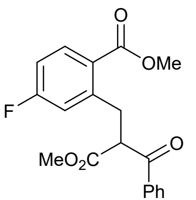
4ab

Methyl 2-(2-benzoyl-3-methoxy-3-oxopropyl)-4-methylbenzoate 4ab. Analytical TLC on silica gel, 1:9 EtOAc/hexane R_f = 0.37; colorless liquid; yield 77% (26 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.2 Hz, 2H), 7.82 (d, *J* = 8.4 Hz, 1H), 7.53 (t, *J* = 7.2 Hz, 1H), 7.40 (t, *J* = 8.0 Hz, 2H), 7.05-7.03 (m, 2H), 4.95 (t, *J* = 7.6 Hz, 1H), 3.85 (s, 3H), 3.61-3.59 (m, 5H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.3, 170.1, 167.8, 143.0, 140.4, 136.6, 133.5, 133.3, 131.4, 128.9, 128.7, 127.8, 126.6, 55.1, 52.5, 52.1, 34.3, 21.5; FT-IR (neat) 2954, 1720, 1686, 1585, 1437, 1266, 1242, 1122, 1082 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{20}H_{20}O_5Na$ 363.1203; Found 363.1203.

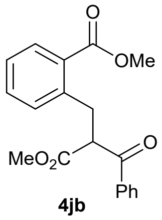


4bb

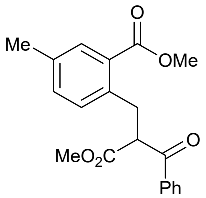
Methyl 2-(2-benzoyl-3-methoxy-3-oxopropyl)-4-methoxybenzoate 4bb. Analytical TLC on silica gel, 1:9 EtOAc/hexane R_f = 0.30; colorless liquid; yield 73% (26 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.94-7.92 (m, 3H), 7.53 (t, *J* = 7.2 Hz, 1H), 7.41 (t, *J* = 8.4 Hz, 2H), 6.76 (d, *J* = 2.4 Hz, 1H), 6.74 (dd, *J* = 8.4, 2.4 Hz, 1H), 4.97 (t, *J* = 7.8 Hz, 1H), 3.83 (s, 3H), 3.77 (s, 3H), 3.65-3.61 (m, 5H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.3, 170.1, 167.2, 162.4, 143.0, 136.6, 133.6, 133.5, 128.9, 128.7, 121.4, 117.6, 112.6, 55.5, 54.9, 52.6, 52.0, 34.7; FT-IR (neat) 3003, 2291, 2253, 1712, 1633, 1441, 1375, 1039 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{20}H_{20}O_6Na$ 379.1152; Found 379.1152.


4db

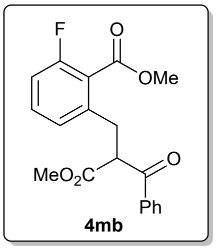
Methyl 2-(2-benzoyl-3-methoxy-3-oxopropyl)-4-fluorobenzoate 4db. Analytical TLC on silica gel, 1:9 EtOAc/hexane $R_f = 0.42$; colorless liquid; yield 66% (23 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98-7.94 (m, 3H), 7.55 (t, $J = 7.6$ Hz, 1H), 7.43 (t, $J = 8.0$ Hz, 2H), 7.02 (dd, $J = 9.6, 2.4$ Hz, 1H), 6.96-6.92 (m, 1H), 4.94 (t, $J = 7.32$ Hz, 1H), 3.86 (s, 3H), 3.68-3.57 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.8, 169.8, 166.8, 165.7 ($J_{C\text{-}F} = 252.0$ Hz), 144.0 ($J_{C\text{-}F} = 8.6$ Hz), 136.4, 133.9 ($J_{C\text{-}F} = 9.3$ Hz), 133.7, 128.9, 128.8, 125.6 ($J_{C\text{-}F} = 2.8$ Hz), 119.6 ($J_{C\text{-}F} = 21.7$ Hz), 114.3 ($J_{C\text{-}F} = 15.0$ Hz), 54.9, 52.7, 52.3, 34.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.41; FT-IR (neat) 2954, 1721, 1687, 1587, 1437, 1269, 1242, 1122, 1081 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{19}H_{18}O_5F$ 345.1133; Found 345.1134.


4jb

Methyl 2-(2-benzoyl-3-methoxy-3-oxopropyl)benzoate 4jb. Analytical TLC on silica gel, 1:9 EtOAc/hexane $R_f = 0.51$; colorless liquid; yield 70% (23 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (t, $J = 7.8$ Hz, 3H), 7.53 (t, $J = 7.4$ Hz, 1H), 7.41 (t, $J = 7.7$ Hz, 2H), 7.36 (t, $J = 7.5$ Hz, 1H), 7.29-7.24 (m, 2H), 4.97 (t, $J = 7.3$ Hz, 1H), 3.88 (s, 3H), 3.62 (d, $J = 11.4$ Hz, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.2, 170.1, 167.8, 140.2, 136.6, 133.6, 132.6, 132.3, 131.2, 129.6, 128.9, 128.7, 127.1, 55.1, 52.6, 52.3, 34.2; FT-IR (neat) 2954, 1721, 1687, 1587, 1437, 1265, 1242, 1145, 1077 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{19}H_{18}O_5Na$ 349.1046; Found 349.1051.

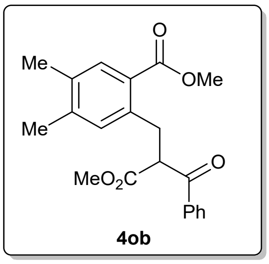

4kb

Methyl 2-(2-benzoyl-3-methoxy-3-oxopropyl)-5-methylbenzoate 4kb. Analytical TLC on silica gel, 1:9 EtOAc/hexane $R_f = 0.39$; colorless liquid; yield 75% (25.5 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, $J = 7.2$ Hz, 2H), 7.73 (s, 1H), 7.53 (t, $J = 7.2$ Hz, 1H), 7.41 (t, *J* = 8.0 Hz, 2H), 7.16 (s, 2H), 4.94 (t, *J* = 7.2 Hz, 1H), 3.86 (s, 3H), 3.61-3.53 (m, 5H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.2, 170.1, 168.0, 137.1, 136.8, 136.6, 133.5, 133.1, 132.5, 131.7, 129.4, 128.9, 128.7, 55.3, 52.5, 52.2, 33.8, 21.0; FT-IR (neat) 2955, 1719, 1686, 1587, 1438, 1269, 1240, 1123, 1080 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{20}H_{20}O_5Na$ 363.1203; Found 363.1203.



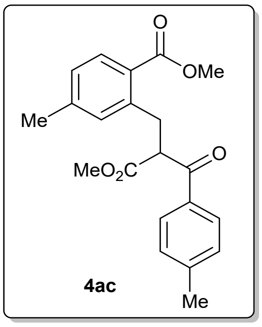
4mb

Methyl 2-(2-benzoyl-3-methoxy-3-oxopropyl)-6-fluorobenzoate 4mb. Analytical TLC on silica gel, 1:9 EtOAc/hexane R_f = 0.45; colorless liquid; yield 55% (19 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.5 Hz, 2H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.43 (t, *J* = 8.0 Hz, 2H), 7.24-7.23 (m, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.95 (t, *J* = 8.5 Hz, 1H), 4.88 (t, *J* = 7.5 Hz, 1H), 3.92 (s, 3H), 3.63 (s, 3H), 3.38 (d, *J* = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.7, 169.6, 166.2, 161.3 (J_{C-F} = 250.7 Hz), 139.3 (J_{C-F} = 2.0 Hz), 136.3, 133.8, 131.8 (J_{C-F} = 9.1 Hz), 128.9, 128.8, 126.7 (J_{C-F} = 3.2 Hz), 121.7 (J_{C-F} = 15.5 Hz), 114.8 (J_{C-F} = 21.8 Hz), 55.0, 52.8, 52.7, 33.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ -113.06; FT-IR (neat) 2954, 1718, 1687, 1587, 1439, 1264, 1244, 1123, 1081 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{19}H_{18}O_5F$ 345.1133; Found 345.1133.

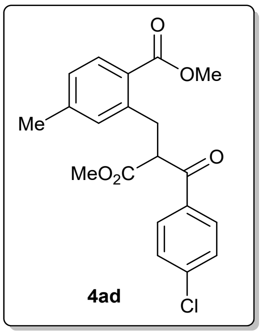


4ob

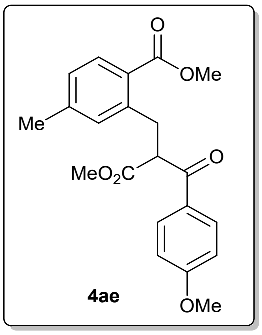
Methyl 2-(2-benzoyl-3-methoxy-3-oxopropyl)-4,5-dimethylbenzoate 4ob. Analytical TLC on silica gel, 1:9 EtOAc/hexane R_f = 0.44; colorless liquid; yield 81% (29 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.5 Hz, 2H), 7.70 (s, 1H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.01 (s, 1H), 4.92 (t, *J* = 7.5 Hz, 1H), 3.84 (s, 3H), 3.61 (s, 3H), 3.59-3.54 (m, 2H), 2.21 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.4, 170.2, 167.9, 141.6, 137.7, 136.7, 135.4, 133.9, 133.5, 132.4, 128.9, 128.7, 126.7, 55.3, 52.5, 52.0, 33.8, 19.8, 19.3; FT-IR (neat) 2958, 1721, 1687, 1587, 1437, 1269, 1242, 1123, 1081, cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{21}H_{23}O_5$ 355.1540; Found 355.1542.



Methyl 2-(3-methoxy-2-(4-methylbenzoyl)-3-oxopropyl)-4-methylbenzoate 4ac. Analytical TLC on silica gel, 1:9 EtOAc/hexane $R_f = 0.44$; colorless liquid; yield 65% (23 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84-7.82 (m, 3H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.05-7.04 (m, 2H), 4.91 (t, *J* = 7.5 Hz, 1H), 3.85 (s, 3H), 3.60-3.58 (m, 5H), 2.38 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.8, 170.3, 167.8, 144.5, 142.9, 140.5, 134.1, 133.3, 131.4, 129.4, 129.0, 127.8, 126.6, 55.0, 52.5, 52.1, 34.2, 21.8, 21.5; FT-IR (neat) 2954, 1722, 1687, 1587, 1437, 1269, 1242, 1122, 1081, cm^{-1}; HRMS (ESI-TOF) *m/z*: [M+H]$^+$ calcd for $C_{21}H_{23}O_5$ 355.1540; Found 355.1538.

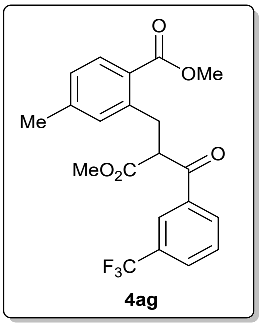


Methyl 2-(2-(4-chlorobenzoyl)-3-methoxy-3-oxopropyl)-4-methylbenzoate 4ad. Analytical TLC on silica gel, 1:9 EtOAc/hexane $R_f = 0.42$; colorless liquid; yield 68% (25.5 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.8 Hz, 2H), 7.82 (d, *J* = 7.8 Hz, 1H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.06-7.04 (m, 2H), 4.92 (t, *J* = 7.2 Hz, 1H), 3.86 (s, 3H), 3.61 (s, 3H), 3.58-3.54 (m, 2H), 2.29 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 194.3, 169.9, 167.7, 143.1, 140.2, 140.1, 135.0, 133.4, 131.4, 130.3, 129.1, 127.9, 126.5, 55.1, 52.6, 52.1, 34.2, 21.5; FT-IR (neat) 2953, 1721, 1685, 1587, 1437, 1269, 1242, 1123, 1081, cm^{-1}; HRMS (ESI-TOF) *m/z*: [M+H]$^+$ calcd for $C_{20}H_{20}O_5Cl$ 375.0994; Found 375.0994.



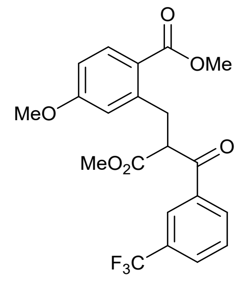
4ae

Methyl 2-(3-methoxy-2-(4-methoxybenzoyl)-3-oxopropyl)-4-methylbenzoate 4ae. Analytical TLC on silica gel, 1:9 EtOAc/hexane $R_f = 0.37$; colorless liquid; yield 60% (22 mg); ^{1}H NMR ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 9.0 Hz, 2H), 7.82 (d, J = 7.9 Hz, 1H), 7.09-7.01 (m, 2H), 6.87 (d, J = 9.0 Hz, 2H), 4.89 (t, J = 7.2 Hz, 1H), 3.85 (d, J = 3.3 Hz, 6H), 3.63-3.56 (m, 5H), 2.28 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 193.6, 170.3, 167.8, 163.9, 142.9, 140.5, 133.3, 131.4, 131.3, 129.8, 127.7, 126.7, 113.9, 55.6, 54.9, 52.4, 52.1, 34.3, 21.5; FT-IR (neat) 2957, 1721, 1689, 1587, 1440, 1269, 1244, 1123, 1081, cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{21}H_{22}O_6Na$ 393.1309; Found 393.1310.



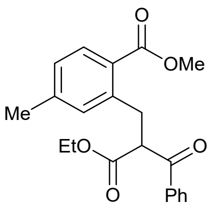
4ag

Methyl 2-(3-methoxy-3-oxo-2-(3-(trifluoromethyl)benzoyl)propyl)-4-methylbenzoate 4ag. Analytical TLC on silica gel, 1:9 EtOAc/hexane $R_f = 0.34$; colorless liquid; yield 55% (22.5 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 8.08 (d, J = 8.0 Hz, 1H), 7.82 (d, J = 8.8 Hz, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.54 (t, J = 8.0 Hz, 1H), 7.05-7.04 (m, 2H), 5.00 (t, J = 7.6 Hz, 1H), 3.86 (s, 3H), 3.63 (s, 3H), 3.58 (d, J = 7.6 Hz, 2H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.6, 169.8, 167.7, 143.1, 140.1, 137.2, 134.9 ($J_{C\text{-}F}$ =36.3 Hz), 133.5, 131.9, 131.5 ($J_{C\text{-}F}$ = 271.9 Hz), 131.4, 129.9 ($J_{C\text{-}F}$ =3.6 Hz), 129.4, 128.0, 126.4, 125.8 ($J_{C\text{-}F}$ =3.9 Hz), 55.0, 52.6, 52.1, 34.4, 21.5; ^{19}F NMR (565 MHz, $CDCl_3$) δ -62.86; FT-IR (neat) 2954, 1721, 1686, 1587, 1437, 1270, 1242, 1122, 1080, cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{21}H_{20}O_5F_3$ 409.1257; Found 409.1266.



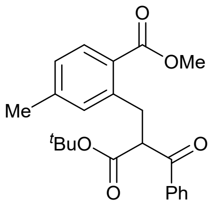
4bg

Methyl 4-methoxy-2-(3-methoxy-3-oxo-2-(3-(trifluoromethyl)benzoyl)propyl)benzoate 4bg. Analytical TLC on silica gel, 1:9 EtOAc/hexane R_f = 0.34; colorless liquid; yield 58% (24.6 mg); ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.21 (s, 1H), 8.10 (d, J = 8.0 Hz, 1H), 7.92 (d, J = 8.8 Hz, 1H), 7.77 (d, J = 8.4 Hz, 1H), 7.55 (t, J = 7.6 Hz, 1H), 6.77-6.73 (m, 2H), 5.02 (t, J = 7.2 Hz, 1H), 3.85 (s, 3H), 3.78 (s, 3H), 3.64-3.61 (m, 5H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 194.5, 169.7, 167.2, 162.5, 142.7, 137.1, 135.5 ($J_{\text{C-F}}$ =32.3 Hz), 133.6, 132.0 ($J_{\text{C-F}}$ = 265.7 Hz), 131.9, 129.9 ($J_{\text{C-F}}$ = 3.7 Hz), 129.4, 125.9 ($J_{\text{C-F}}$ = 3.7 Hz), 121.3, 118.0, 112.6, 55.5, 54.9, 52.7, 52.0, 34.8; ^{19}F NMR (565 MHz, CDCl$_3$) δ -62.87; FT-IR (neat) 3001, 2294, 2256, 1712, 1633, 1441, 1375, 1081 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M+H]$^+$ calcd for $C_{21}H_{20}O_6F_3$ 425.1206; Found 425.1205.



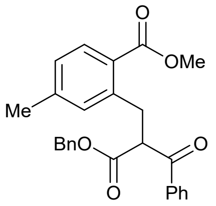
4ai

Methyl 2-(2-benzoyl-3-ethoxy-3-oxopropyl)-4-methylbenzoate 4ai. Analytical TLC on silica gel, 1:9 EtOAc/hexane R_f = 0.48; colorless liquid; yield 72% (25.5 mg); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.94 (d, J = 7.2 Hz, 2H), 7.84 (d, J = 7.9 Hz, 1H), 7.52 (t, J = 7.4 Hz, 1H), 7.41 (t, J = 7.7 Hz, 2H), 7.10-7.01 (m, 2H), 4.94-4.85 (m, 1H), 4.10-4.03 (m, 2H), 3.84 (s, 3H), 3.66-3.61 (m, 1H), 3.55 (dd, J = 13.2, 7.8 Hz, 1H), 2.29 (s, 3H), 1.08 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 195.3, 169.7, 167.8, 142.9, 140.5, 136.7, 133.4, 133.3, 131.4, 128.8, 128.7, 127.8, 126.6, 61.4, 55.4, 52.0, 34.2, 21.5, 14.1; FT-IR (neat) 2952, 1715, 1687, 1610, 1444, 1266, 1231, 1186, 1083 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M+H]$^+$ calcd for $C_{21}H_{23}O_5$ 355.1540; Found 355.1540.



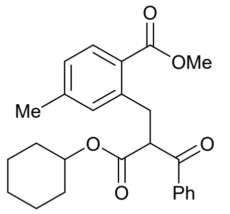
4aj

Methyl 2-(2-benzoyl-3-(*tert*-butoxy)-3-oxopropyl)-4-methylbenzoate 4aj. Analytical TLC on silica gel, 1:9 EtOAc/hexane $R_f = 0.51$; colorless liquid; yield 75% (29 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, J = 7.8 Hz, 2H), 7.84 (d, J = 8.0 Hz, 1H), 7.52 (t, J = 7.4 Hz, 1H), 7.41 (t, J = 7.7 Hz, 2H), 7.09 (s, 1H), 7.06 (d, J = 8.1 Hz, 1H), 4.75 (dd, J = 8.1, 6.4 Hz, 1H), 3.84 (s, 3H), 3.65 (dd, J = 13.3, 6.3 Hz, 1H), 3.47 (dd, J = 13.3, 8.3 Hz, 1H), 2.30 (s, 3H), 1.25 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.5, 168.8, 167.8, 142.7, 140.7, 136.9, 133.5, 133.2, 131.4, 128.8, 128.6, 127.6, 126.6, 81.9, 56.7, 52.0, 33.9, 27.8, 21.5; FT-IR (neat) 2977, 2924, 1719, 1692, 1594, 1447, 1267, 1147, 1083 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{23}H_{26}O_5Na$ 405.1672; Found 405.1672.



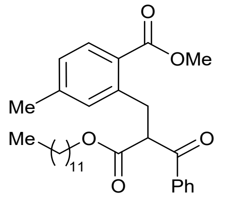
4ak

Methyl 2-(2-benzoyl-3-(benzyloxy)-3-oxopropyl)-4-methylbenzoate 4ak. Analytical TLC on silica gel, 1:9 EtOAc/hexane $R_f = 0.44$; colorless liquid; yield 72% (30 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 7.2 Hz, 2H), 7.82 (d, J = 8.0 Hz, 1H), 7.52 (t, J = 7.2 Hz, 1H), 7.38 (t, J = 8.0 Hz, 2H), 7.26-7.23 (m, 3H), 7.10-7.08 (m, 2H), 7.05-7.02 (m, 2H), 5.07-5.00 (m, 2H), 4.98-4.94 (m, 1H), 3.82 (s, 3H), 3.70-3.64 (m, 1H), 3.59-3.54 (m, 1H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.1, 169.5, 167.7, 143.0, 140.4, 136.6, 135.5, 133.5, 133.4, 131.4, 128.9, 128.7, 128.5, 128.3, 128.0, 127.8, 126.6, 67.0, 55.5, 52.1, 34.2, 21.5; FT-IR (neat) 2951, 1715, 1687, 1610, 1448, 1267, 1218, 1161, 1083 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{26}H_{25}O_5$ 417.1697; Found 417.1697.



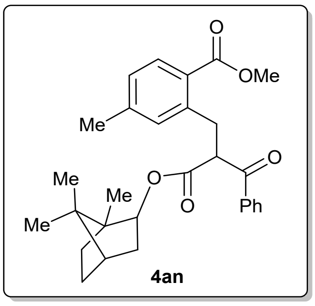
4al

Methyl 2-(2-benzoyl-3-(cyclohexyloxy)-3-oxopropyl)-4-methylbenzoate 4al. Analytical TLC on silica gel, 1:9 EtOAc/hexane $R_f = 0.49$; colorless liquid; yield 67% (27.4 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, $J = 7.2$ Hz, 2H), 7.83 (d, $J = 8.0$ Hz, 1H), 7.52 (t, $J = 7.2$ Hz, 1H), 7.41 (t, $J = 8.0$ Hz, 2H), 7.08-7.05 (m, 2H), 4.86-4.83 (m, 1H), 4.72-4.66 (m, 1H), 3.84 (s, 3H), 3.71-3.66 (m, 1H), 3.52-3.47 (m, 1H), 2.29 (s, 3H), 1.53-1.14 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.2, 169.2, 167.7, 142.8, 140.6, 136.7, 133.4, 131.4, 128.8, 128.6, 127.7, 126.6, 73.6, 55.9, 52.0, 34.0, 31.24, 31.22, 25.4, 23.45, 23.38, 21.5; FT-IR (neat) 2979, 2926, 1718, 1692, 1594, 1448, 1268, 1147, 1081 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{25}H_{29}O_5$ 409.2010; Found 409.2008.



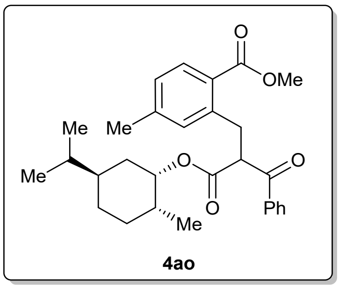
4am

Methyl 2-(2-benzoyl-3-(dodecyloxy)-3-oxopropyl)-4-methylbenzoate 4am. Analytical TLC on silica gel, 1:9 EtOAc/hexane $R_f = 0.52$; colorless liquid; yield 71% (35 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, $J = 7.9$ Hz, 2H), 7.84 (d, $J = 7.9$ Hz, 1H), 7.52 (t, $J = 7.0$ Hz, 1H), 7.41 (t, $J = 7.7$ Hz, 2H), 7.09-7.03 (m, 2H), 4.90 (t, $J = 7.2$ Hz, 1H), 3.98 (td, $J = 6.5, 2.7$ Hz, 2H), 3.84 (s, 3H), 3.64 (dd, $J = 13.2, 6.6$ Hz, 1H), 3.55 (dd, $J = 13.3, 7.8$ Hz, 1H), 2.29 (s, 3H), 1.45-1.41 (m, 2H), 1.25-1.09 (m, 18H), 0.88 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.2, 169.7, 167.8, 142.9, 140.6, 136.7, 133.4, 133.4, 131.4, 128.9, 128.7, 127.8, 126.6, 65.6, 55.5, 52.1, 34.1, 32.1, 29.8, 29.8, 29.7, 29.6, 29.5, 29.3, 28.5, 25.8, 22.8, 21.5, 14.3; FT-IR (neat) 2933, 2917, 1719, 1692, 1594, 1447, 1268, 1147, 1083 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{31}H_{43}O_5$ 495.3105; Found 495.3110.



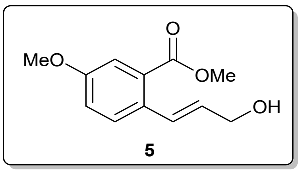
4an

Methyl 2-(2-benzoyl-3-oxo-3-(((1S,4S)-1,7,7-trimethyl-bicyclo-[2.2.1]heptan-2-yl)oxy)propyl)-4-methylbenzoate 4an. Analytical TLC on silica gel, 1:9 EtOAc/hexane R$_f$ = 0.44; colorless liquid; yield 64% (29.6 mg); 1:1 mixture of diastereomers; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.97 (t, J = 7.0 Hz, 4H), 7.87-7.84 (m, 2H), 7.53 (t, J = 7.0 Hz, 2H), 7.44-7.40 (m, 4H), 7.10-7.05 (m, 4H), 4.89 (t, J = 7.0 Hz, 2H), 4.73 (t, J = 9.5 Hz, 2H), 3.85-3.83 (m, 6H), 3.74-3.68 (m, 2H), 3.53-3.47 (m, 2H), 2.30 (s, 6H), 2.24-2.12 (m, 2H), 1.66-1.63 (m, 2H), 1.56-1.51 (m, 4H), 1.15-1.02 (m, 4H), 0.90-0.84 (m, 2H), 0.80-0.78 (m, 12H), 0.72 (s, 3H), 0.50 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 194.97, 194.95, 170.0, 169.9, 167.7, 142.9, 140.7, 140.6, 136.8, 133.43, 133.38, 133.3, 131.5, 128.9, 128.8, 128.7, 127.8, 126.63, 126.60, 81.3, 81.2, 56.0, 55.8, 52.0, 48.8, 47.9, 47.8, 44.9, 44.8, 36.4, 36.3, 34.0, 33.8, 28.0, 27.8, 27.0, 21.5, 19.7, 18.9, 13.5, 13.1; FT-IR (neat) 2953, 1719, 1690, 1610, 1449, 1267, 1233, 1187, 1083 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M+H]$^+$ calcd for C$_{29}$H$_{35}$O$_5$ 463.2479; Found 463.2477.

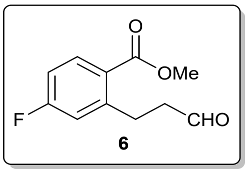


4ao

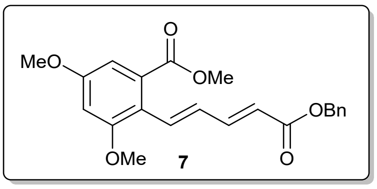
Methyl 2-(2-benzoyl-3-(((1S,2R,5R)-5-isopropyl-2-methyl-cyclohexyl)oxy)-3-oxopropyl)-4-methylbenzoate 4ao. Analytical TLC on silica gel, 1:9 EtOAc/hexane R$_f$ = 0.44; colorless liquid; yield 61% (28.3 mg); 1:1 mixture of diastereomers; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.98 (d, J = 7.5 Hz, 2H), 7.92 (d, J = 7.5 Hz, 2H), 7.86 (t, J = 8.5 Hz, 2H), 7.55-7.51 (m, 2H), 7.43-7.38 (m, 4H), 7.10-7.06 (m, 4H), 4.88-4.85 (m, 2H), 4.56-4.49 (m, 2H), 3.84 (s, 6H), 3.76-3.68 (m, 2H), 3.51-3.41 (m, 2H), 2.31-2.30 (m, 6H), 1.80-1.78 (m, 1H), 1.67-1.65 (m, 1H), 1.56-1.52 (m, 6H), 1.40-1.32 (m, 2H), 1.23-1.16 (m, 4H), 0.93-0.86 (m, 4H), 0.84 (d, J = 6.5 Hz, 3H), 0.80 (d, J = 6.5 Hz, 3H), 0.72 (d, J = 7.5 Hz, 3H), 0.62 (d, J = 7.0 Hz, 3H), 0.53 (d, J = 7.0 Hz, 3H), 0.33 (d, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 195.2, 194.7, 169.4, 169.1, 167.8, 167.7, 142.9, 140.6, 136.8, 136.6, 133.5, 133.43, 133.41, 133.3, 131.54, 131.46, 128.9, 128.8, 128.64, 128.58, 127.8, 127.7, 126.6, 126.5, 75.6, 75.5, 56.4, 55.8, 52.05, 52.02, 46.8, 40.7, 40.5, 34.22, 34.19, 34.16, 34.0, 31.4, 31.3, 25.73, 25.67, 23.1, 22.9, 22.11, 22.07, 21.5, 20.9, 20.8, 15.7; FT-IR (neat) 2953, 2869, 1718, 1688, 1611, 1449, 1266, 1231, 1185, 1083 $\mathrm{cm^{-1}}$; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{29}H_{37}O_5$ 465.2636; Found 465.2636.



Methyl (*E*)-2-(3-hydroxyprop-1-en-1-yl)-5-methoxybenzoate 5. Analytical TLC on silica gel, 1:9 EtOAc/hexane $R_f = 0.36$; colorless liquid; yield 93% (20.7 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.5 Hz, 1H), 7.38-7.37 (m, 1H), 7.30 (d, *J* = 15.5 Hz, 1H), 7.04-7.02 (m, 1H), 6.20-6.15 (m, 1H), 4.32 (d, *J* = 6.0 Hz, 2H), 3.90 (s, 3H), 3.86-3.84 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.8, 158.8, 131.3, 129.8, 129.7, 129.6, 128.9, 118.8, 114.8, 64.1, 55.6, 52.3; FT-IR (neat) 3440, 2954, 1720, 1594, 1438, 1256, 1207, 1137, 1072 $\mathrm{cm^{-1}}$; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{12}H_{14}O_4Na$ 245.0784; Found 245.0787.

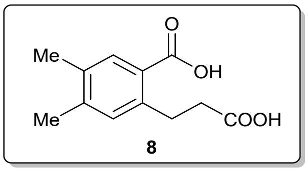


Methyl 4-fluoro-2-(3-oxopropyl)benzoate 6. Analytical TLC on silica gel, 1:9 EtOAc/hexane $R_f = 0.42$; colorless liquid; yield 89% (18.7 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.82 (t, *J* = 1.2 Hz, 1H), 8.00-7.96 (m, 1H), 7.01-6.94 (m, 2H), 3.88 (s, 3H), 3.28 (t, *J* = 9.0 Hz, 2H), 2.84-2.80 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.3, 166.8, 166.2 ($J_{C\text{-}F}$ = 252.0 Hz), 146.5 ($J_{C\text{-}F}$ = 8.4 Hz), 134.0 ($J_{C\text{-}F}$ = 9.3 Hz), 125.3 ($J_{C\text{-}F}$ = 3.0 Hz), 118.3 ($J_{C\text{-}F}$ = 21.4 Hz), 113.8 ($J_{C\text{-}F}$ = 21.2 Hz), 52.2, 45.3, 27.4; ^{19}F NMR (470 MHz, $CDCl_3$) δ -106.59; FT-IR (neat) 2956, 1717, 1630, 1594, 1442, 1256, 1208, 1137, 1072 $\mathrm{cm^{-1}}$; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{11}H_{12}O_3F$ 211.0765; Found 211.0761.



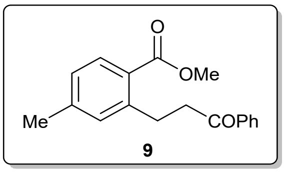
Methyl 2-((1*E*,3*E*)-5-(benzyloxy)-5-oxopenta-1,3-dien-1-yl)-3,5-dimethoxybenzoate 7. Analytical TLC on silica gel, 1:9 EtOAc/hexane $R_f = 0.44$; yellow solid; mp 75-76 °C; yield 87% (33 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 15.5, 11.5

Hz, 1H), 7.40-7.31 (m, 5H), 7.19 (d, *J* = 15.5 Hz, 1H), 6.95 (dd, *J* = 15.5, 11.0 Hz, 1H), 6.82-6.81 (m, 1H), 6.59-6.58 (m, 1H), 5.95 (d, *J* = 15.5 Hz, 1H), 5.21 (s, 2H), 3.88 (s, 3H), 3.86 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.9, 167.2, 160.3, 159.8, 147.1, 136.4, 134.9, 133.8, 130.5, 128.7, 128.3, 128.2, 120.1, 118.2, 105.8, 101.8, 66.2, 56.0, 55.7, 52.7; FT-IR (neat) 2949, 1712, 1596, 1457, 1327, 1241, 1210, 1125, 1058 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{22}H_{23}O_6$ 383.1489; Found 383.1489.



8

2-(2-Carboxyethyl)-4,5-dimethylbenzoic acid 8. Analytical TLC on silica gel, 6:4 EtOAc/hexane R_f = 0.30; colorless solid; mp >200 °C; yield 72% (16 mg); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.36 (bs, 2H), 7.60 (s, 1H), 7.09 (s, 1H), 3.06 (t, *J* = 7.6 Hz, 2H), 2.46 (t, *J* = 8.0 Hz, 2H), 2.22 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.9, 168.5, 140.7, 139.6, 134.2, 132.1, 131.6, 127.3, 35.5, 28.8, 19.3, 18.8; FT-IR (neat) 3440, 2954, 1710, 1594, 1438, 1256, 1207, 1137 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{12}H_{15}O_4$ 223.0965; Found 223.0960.



9

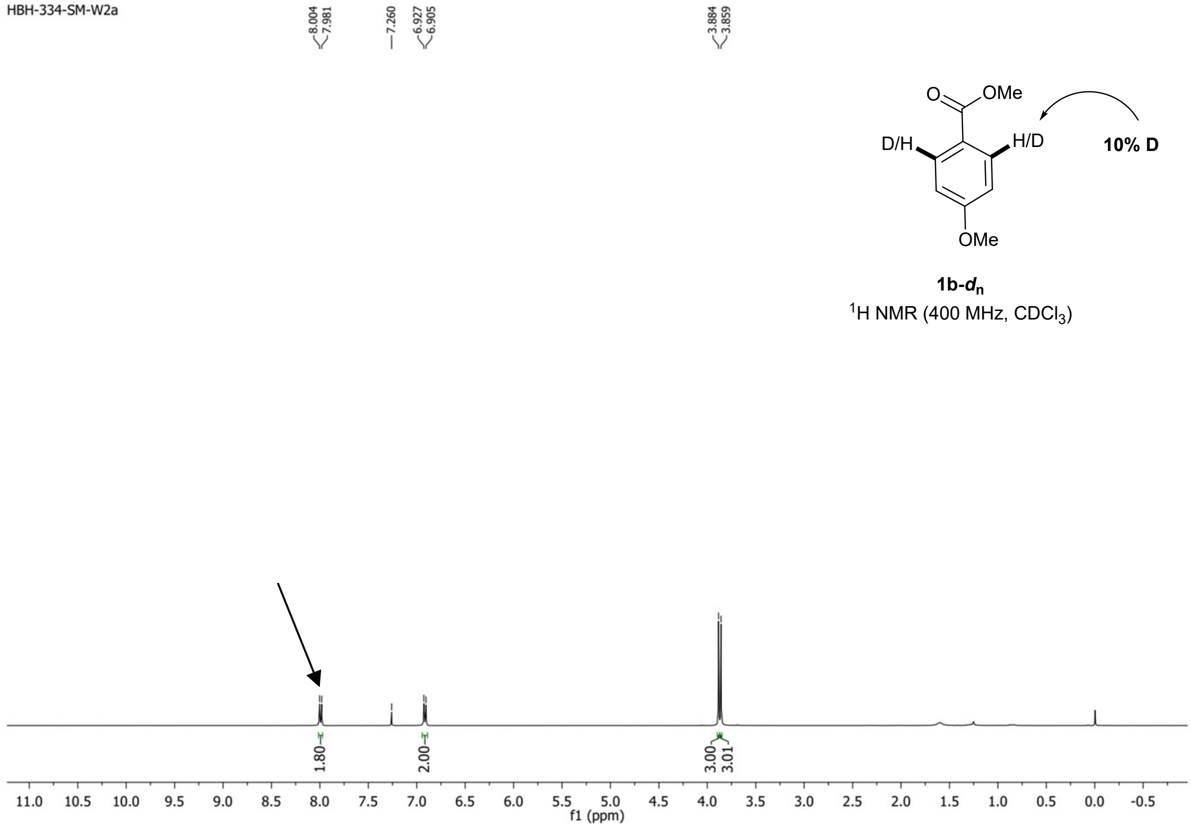
Methyl 4-methyl-2-(3-oxo-3-phenylpropyl)benzoate 9. Analytical TLC on silica gel, 1:9 EtOAc/hexane R_f= 0.32; colorless liquid; yield 91% (25.7 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.5 Hz, 2H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.54 (t, *J* = 7.0 Hz, 1H), 7.44 (t, *J* = 8.0 Hz, 2H), 7.15 (s, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 3.87 (s, 3H), 3.35-3.34 (m, 4H), 2.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.7, 167.9, 143.7, 143.0, 137.1, 133.1, 132.4, 131.3, 128.7, 128.3, 127.2, 126.6, 52.0, 40.8, 29.6, 21.6; FT-IR (neat) 2926, 1717, 1685, 1448, 1268, 1204, 1082, 973 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{18}H_{19}O_3$ 283.1329; Found 283.1328.

H/D Exchange Experiments

C-H Alkenylation

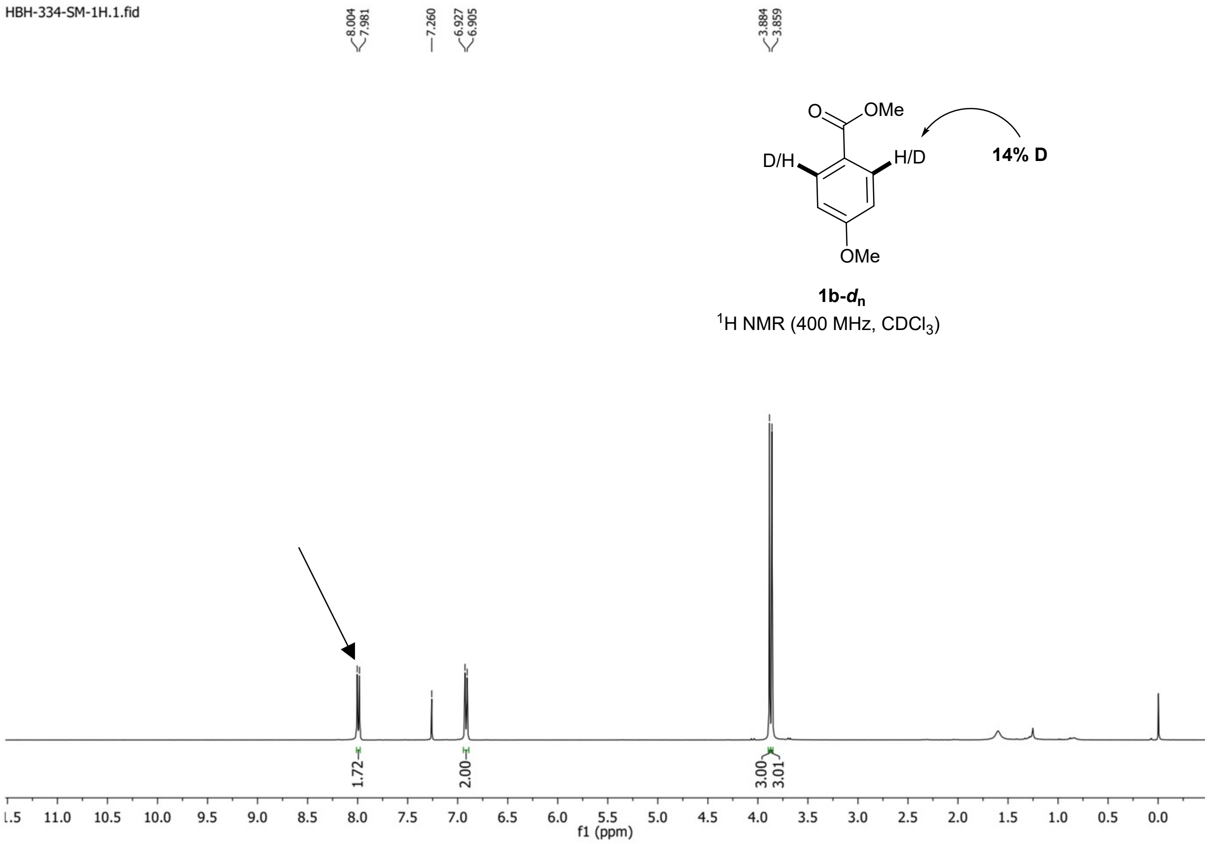
H/D Exchange Experiment of 1b with D_2O in Absence of 2a. 4-Methoxybenzoic acid **1b** (0.1 mmol, 15.2 mg), $Pd(OAc)_2$ (0.01 mmol, 2.3 mg), Ag_2CO_3 (0.2 mmol, 55 mg), 1,4-benzoquinone (0.1 mmol, 11 mg) and D_2O (1 mmol, 18 μL) were stirred in HFIP (1 mL) at

110 ° C (in a pre-heated oil bath) in a sealed tube for 6 h. The reaction mixture was cooled to room temperature, diluted with EtOAc (5 mL) and passed through a short pad of celite. Evaporation of the solvent gave a residue that was stirred with K_2CO_3 (0.3 mmol, 41.5 mg) and MeI (0.5 mmol, 31 μL) in acetone (2 mL) at room temperature for 3 h. After completion (monitored by TLC), the solvent was evaporated under reduced pressure and residue was mixed with water (10 mL) and extracted with EtOAc (2 x 10 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using n-hexane and EtOAc as an eluent to afford **1b-*d*$_n$**. The deuterium incorporation of **1b-*d$_n$*** was calculated based on its 400 MHz ^{1}H NMR spectrum (See the following ^{1}H NMR spectrum).



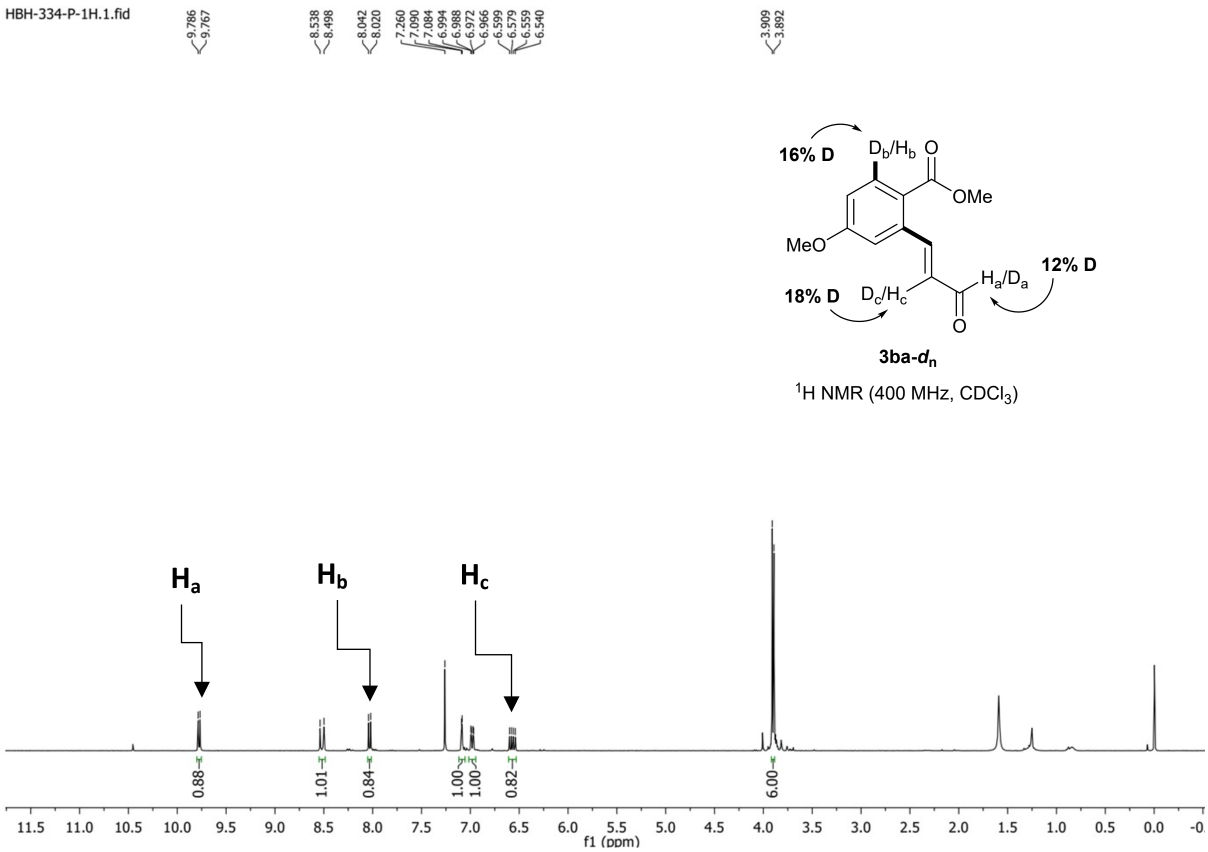
C-H Alkenylation

H/D Exchange Experiment of 1b with D_2O in Presence of 2a. 4-Methoxybenzoic acid **1b** (0.1 mmol, 15.2 mg), MBH alcohol **2a** (0.11 mmol, 12.8 mg), $Pd(OAc)_2$ (0.01 mmol, 2.3 mg), Ag_2CO_3 (0.2 mmol, 55 mg), 1,4-benzoquinone (0.1 mmol, 11 mg) and D_2O (1 mmol, 18 μL) were stirred in HFIP (1 mL) at 110 ° C (in a pre-heated oil bath) in a sealed tube for 6 h. The reaction mixture was cooled to room temperature, diluted with EtOAc (5 mL) and passed through a short pad of celite. Evaporation of the solvent gave a residue that was stirred with K_2CO_3 (0.3 mmol, 41.5 mg) and MeI (0.5 mmol, 31 μL) in acetone (2 mL) at room temperature for 3 h. After completion (monitored by TLC), the solvent was evaporated under reduced pressure and the residue was mixed with water (10 mL) and extracted with EtOAc (2 x 10 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using n-hexane and EtOAc as an eluent to afford **3ba-d_n** and **1b-d_n**. The deuterium incorporation of **1b-d_n** and **3ba-d_n** were calculated based on their respective 400 MHz ^1H NMR spectrum (See the following ^1H NMR spectrums).



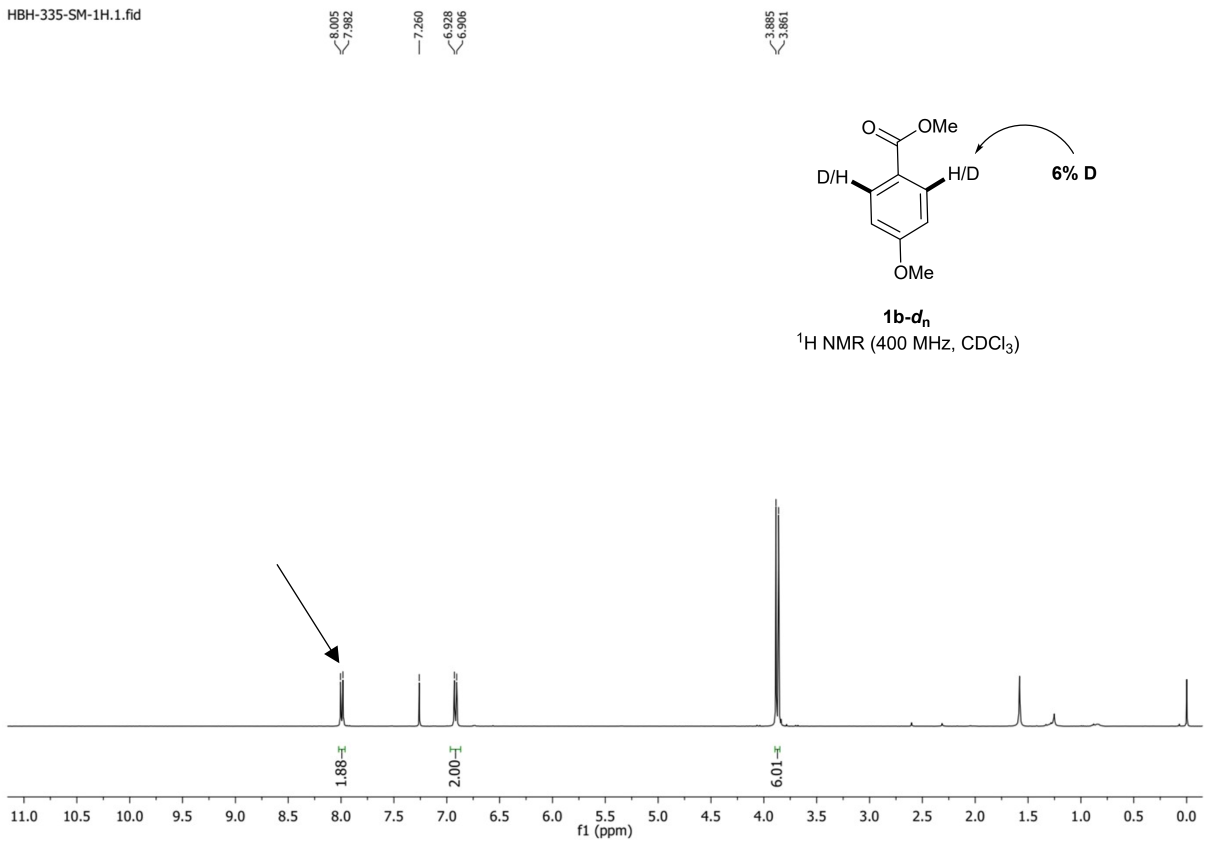
1b-d_n

^1H NMR (400 MHz, $CDCl_3$)



C-H Alkylation

H/D Exchange Experiment of 1b with D_2O in Absence of 2b. 4-Methoxybenzoic acid **1b** (0.1 mmol, 15.2 mg), $Pd(OAc)_2$ (0.01 mmol, 2.3 mg), Ag_2CO_3 (0.2 mmol, 55 mg) and D_2O (1 mmol, 18 μL) were stirred in TFE (1 mL) at 110 °C (in a pre-heated oil bath) in a sealed tube for 6 h. The reaction mixture was cooled to room temperature, diluted with EtOAc (5 mL) and passed through a short pad of celite. Evaporation of the solvent gave a residue that was stirred with K_2CO_3 (0.3 mmol, 41.5 mg) and MeI (0.5 mmol, 31 μL) in acetone (2 mL) at room temperature for 3 h. After completion (monitored by TLC), the solvent was evaporated under reduced pressure and the residue was mixed with water (10 mL) and extracted with EtOAc (2 x 10 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using n-hexane and EtOAc as an eluent to afford **1b-*d*$_n$**. The deuterium incorporation of **1b-*d*$_n$** was calculated based on its 400 MHz ^{1}H NMR spectrum (See the following ^{1}H NMR spectrum).

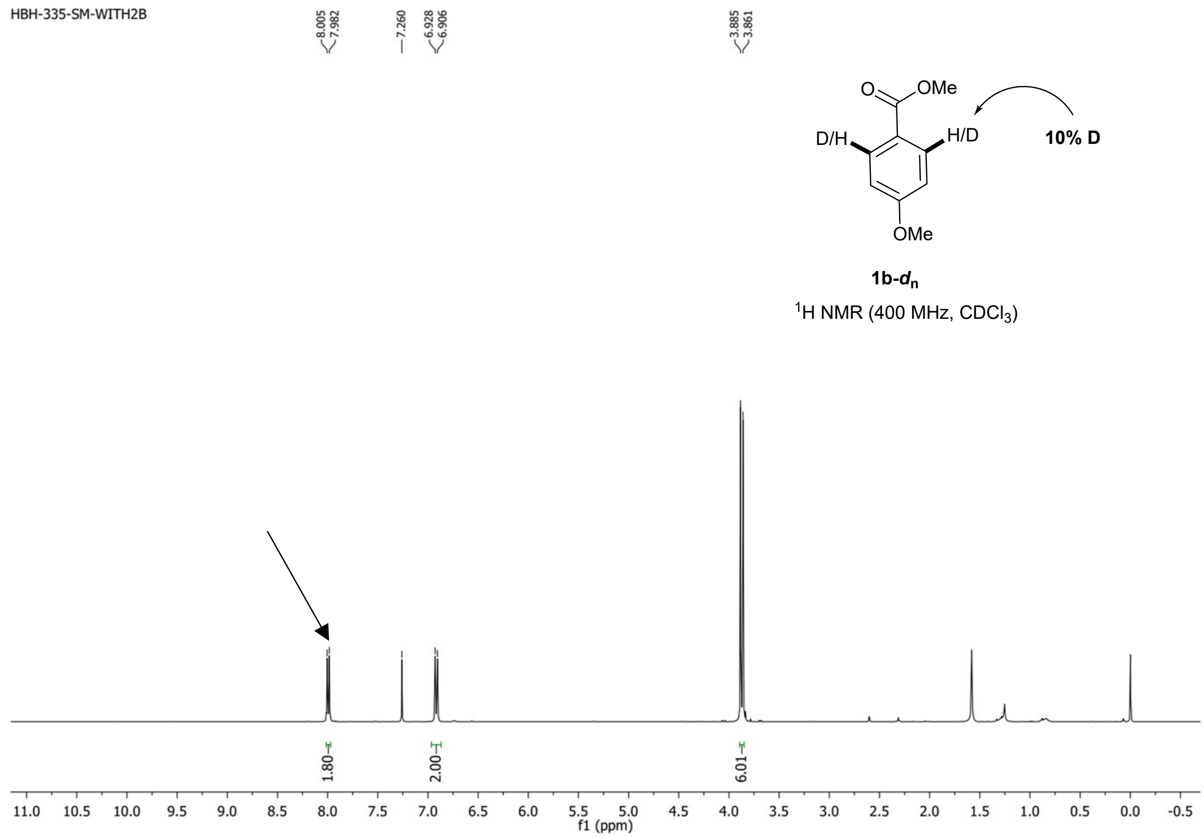


1b-*d*$_n$

^{1}H NMR (400 MHz, $CDCl_3$)

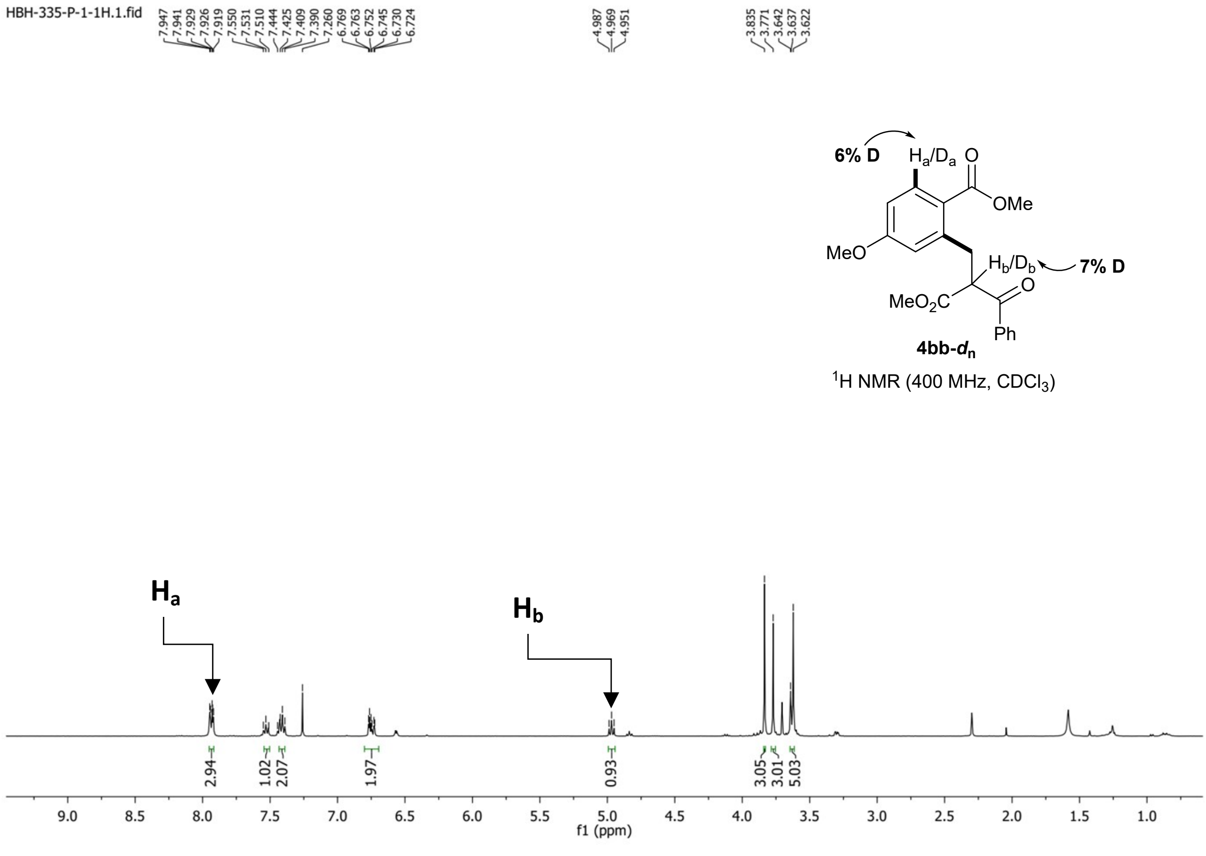
C-H Alkylation

H/D Exchange Experiment of 1b with D_2O in Presence of 2b. 4-Methoxybenzoic acid **1b** (0.1 mmol, 15.2 mg), MBH alcohol **2b** (0.11 mmol, 21 mg), $Pd(OAc)_2$ (10 mol %, 0.01 mmol, 2.3 mg), Ag_2CO_3 (0.2 mmol, 55 mg) and D_2O (1 mmol, 18 μL) were stirred in TFE (1 mL) at 110 °C (in a pre-heated oil bath) in a sealed tube for 6 h. The reaction mixture was cooled to room temperature, diluted with EtOAc (5 mL) and passed through a short celite pad. Evaporation of the solvent gave a residue that was stirred with K_2CO_3 (0.3 mmol, 41.5 mg) and MeI (0.5 mmol, 31 μL) in acetone (2 mL) at room temperature for 3 h. After completion (monitored by TLC), the solvent was evaporated under reduced pressure and the residue was mixed with water (10 mL) and extracted using EtOAc (2 x 10 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using n-hexane and EtOAc as an eluent to afford **4bb-*d*$_n$** and **1b-*d*$_n$**. The deuterium incorporation of **1b-*d*$_n$** and **4bb-*d*$_n$** were calculated based on their respective 400 MHz ^{1}H NMR spectrum (See the following ^{1}H NMR spectrums).



1b-d_n

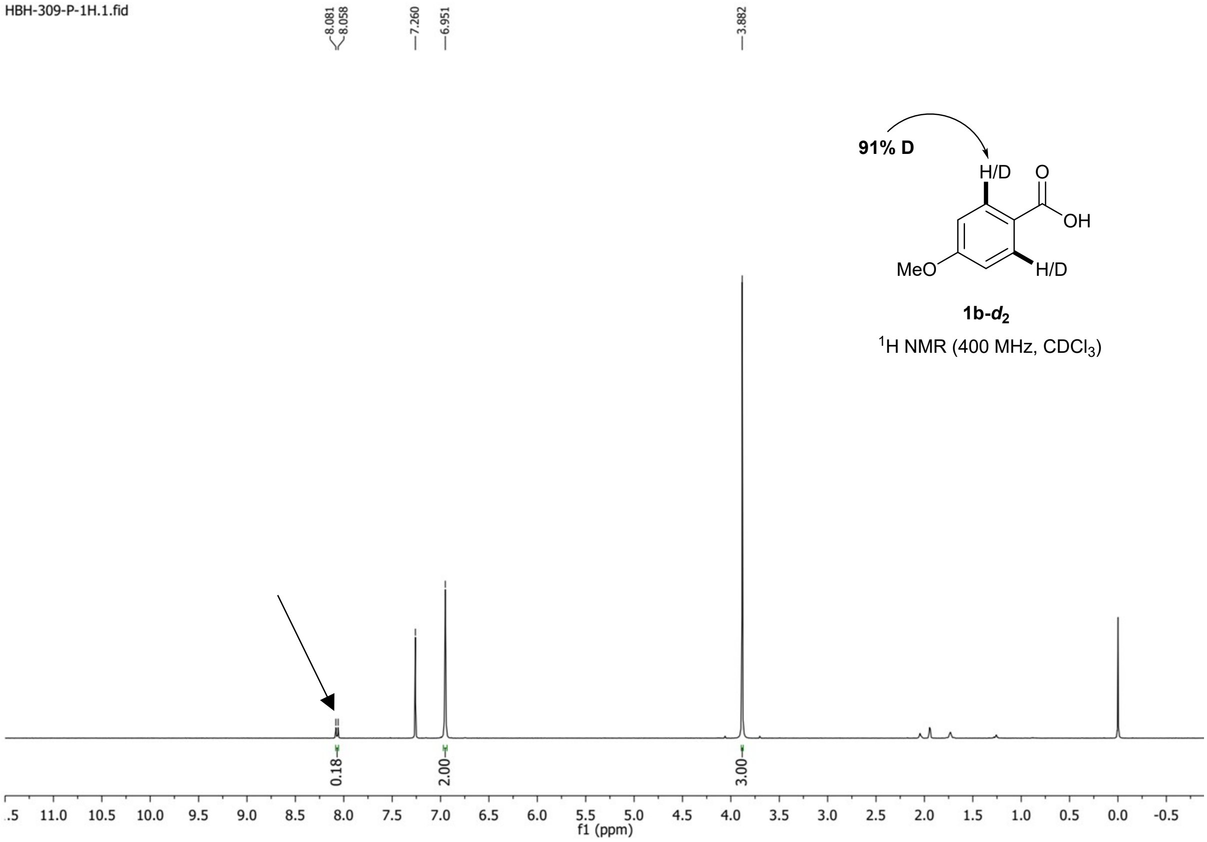
^{1}H NMR (400 MHz, CDCl$_3$)



4bb-d_n

^{1}H NMR (400 MHz, CDCl$_3$)

Preparation of 4-Methoxylbenzoic-2,6-*d*$_2$ acid 1b-*d*$_2$.[14] 4-Methoxylbenzoic acid **1b** (0.50 mmol, 68 mg), [Ru(O_2CAd)$_2$(*p*-cymene)] (5 mol %, 14.9 mg) and D_2O (5 mmol, 90 μL) were stirred in 1,4-dioxane (1 mL) at 100 °C for 16 h under N_2 atmosphere. After cooling to room temperature, the residue was diluted with CH_2Cl_2 (8 mL) and passed through a short pad of celite and all the volatiles were removed under reduced pressure and the residue was purified using silica gel column chromatography with n-hexane and EtOAc as an eluent to afford **1b-*d*$_2$** [91% D].

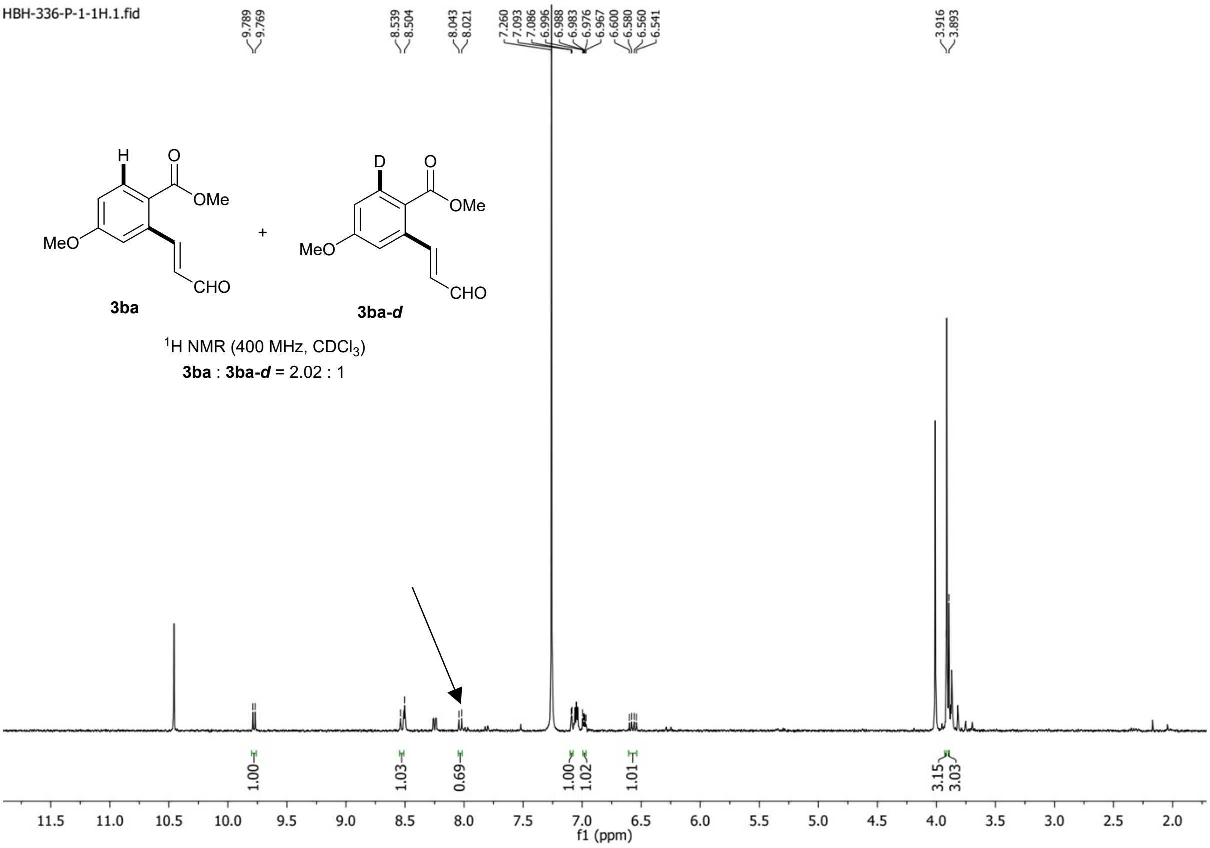


Kinetic Isotope Effect Experiments

For C-H Alkenylation

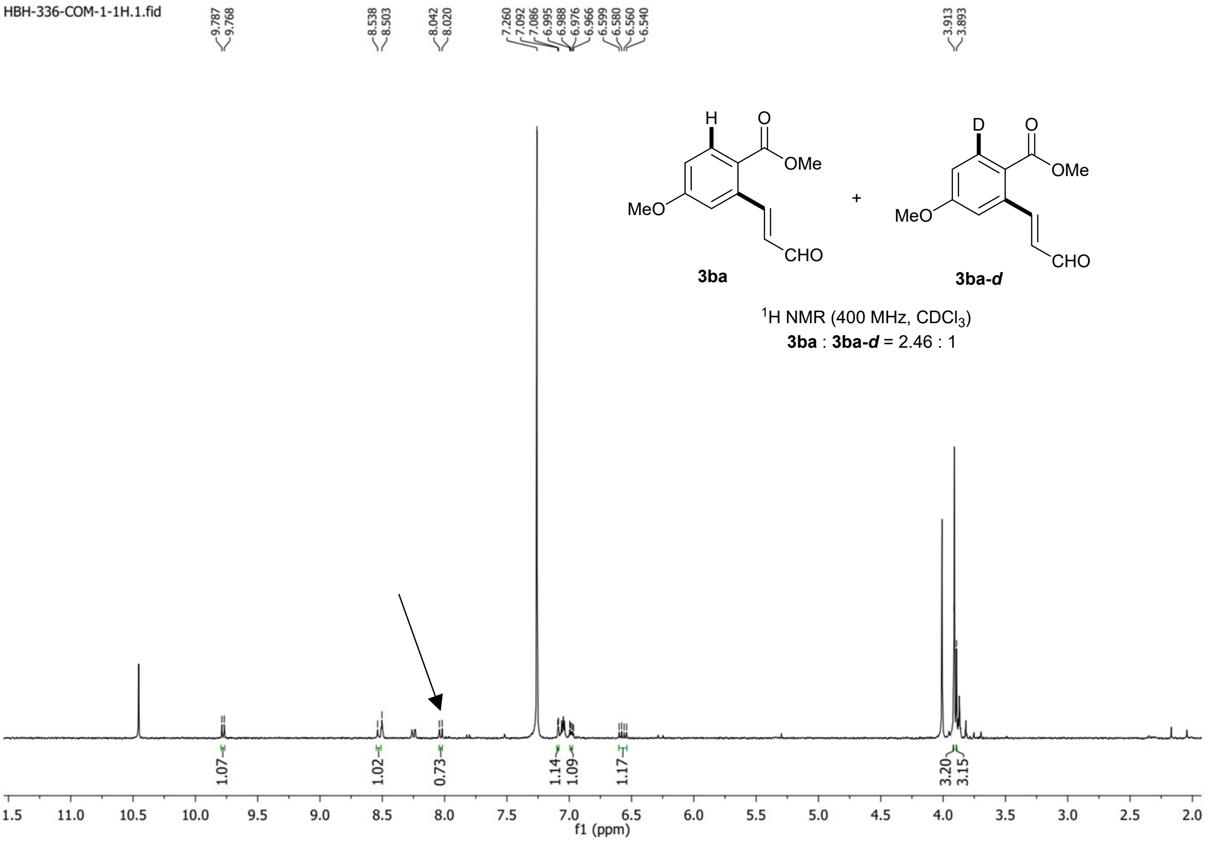
Parallel Experiment: 4-Methoxylbenzoic acid **1b** (15.2 mg) or **1b-*d*$_2$** [91% D] (15.4 mg), 0.1 mmol), MBH alcohol **2a** (0.11 mmol, 12.8 mg), Pd(OAc)$_2$ (10 mol %, 0.01 mmol, 2.3 mg), Ag_2CO_3 (0.2 mmol, 55 mg) and 1,4-benzoquinone (0.1 mmol, 11 mg) were stirred in HFIP (1 mL) at 110 ° C (in a pre-heated oil bath) in a sealed tube for 2 h. The reaction mixture was cooled to room temperature, diluted with EtOAc (10 mL) and passed through a short celite pad. Evaporation of the solvent gave a residue that was stirred with K_2CO_3 (0.3 mmol, 41.5 mg) and

MeI (0.5 mmol, 31 μL) in acetone (2 mL) at room temperature for 1 h. The solvent was removed under vacuum and purification was performed as described in the general procedure to afford **3ba** and **3ba-*d***. The KIE value was determined to be $k_H/k_D = 2.02$ on the basis of ^{1}H NMR analysis.



For C-H Alkenylation

Competitive Experiment: 4-Methoxylbenzoic acid **1b** (0.05 mmol, 7.6 mg), 4-methoxylbenzoic acid-d_2 **1b-*d*₂** [91% D] (0.05 mmol, 7.7 mg), MBH alcohol **2a** (0.11 mmol, 12.8 mg), $Pd(OAc)_2$ (10 mol %, 0.01 mmol, 2.3 mg), Ag_2CO_3 (0.2 mmol, 55 mg) and 1,4-benzoquinone (0.1 mmol, 11 mg) were stirred in HFIP (1 mL) at 110 °C (in a pre-heated oil bath) in a sealed tube for 2 h. The reaction mixture was cooled to room temperature, diluted with EtOAc (10 mL) and passed through a short celite pad. Evaporation of the solvent gave a residue that was stirred with K_2CO_3 (0.3 mmol, 41.5 mg) and MeI (0.5 mmol, 31 μL) in acetone (2 mL) at room temperature for 1 h. The solvent was removed under vacuum and purification was performed as described in the general procedure to afford a mixture of **3ba**/**3ba-*d***. The KIE value was determined to be $k_H/k_D = 2.46$ on the basis of ^{1}H NMR analysis.



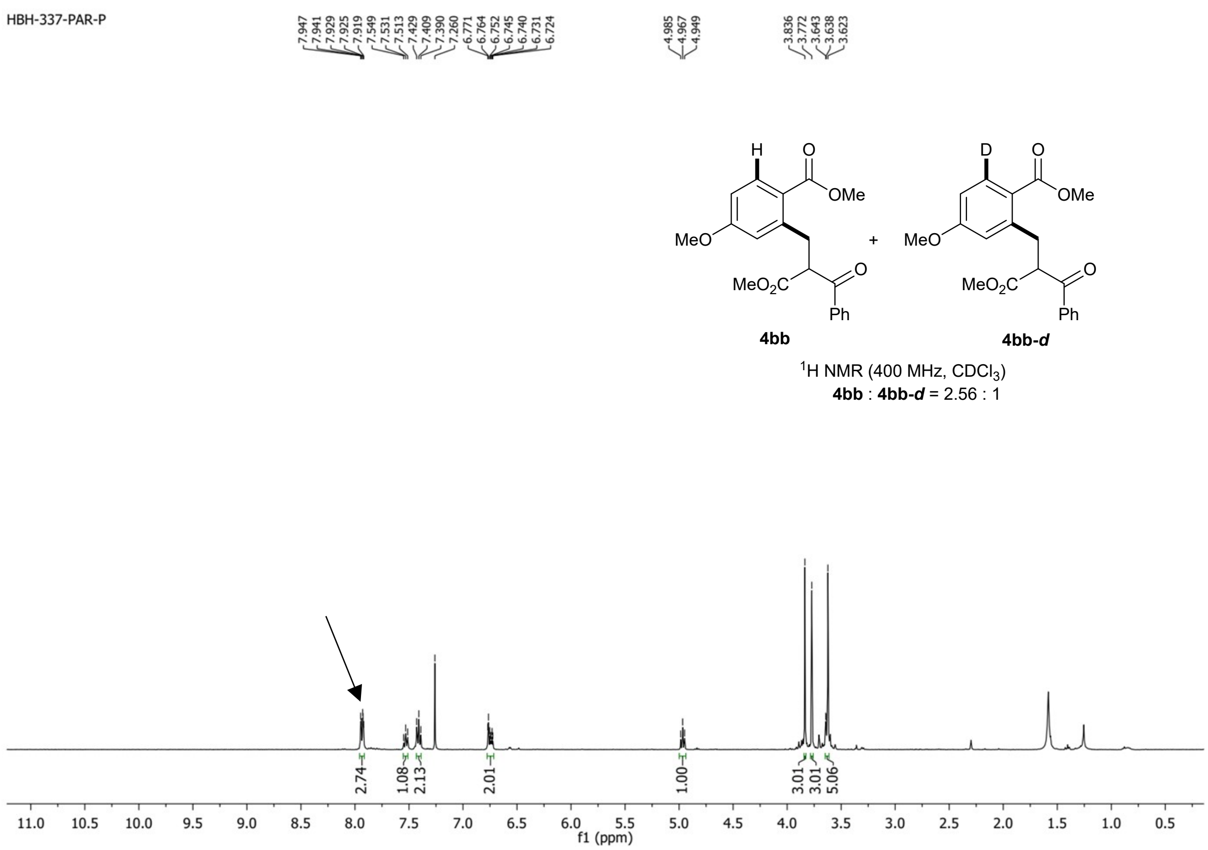
3ba **3ba-*d***

^{1}H NMR (400 MHz, $CDCl_3$)

3ba : **3ba-*d*** = 2.46 : 1

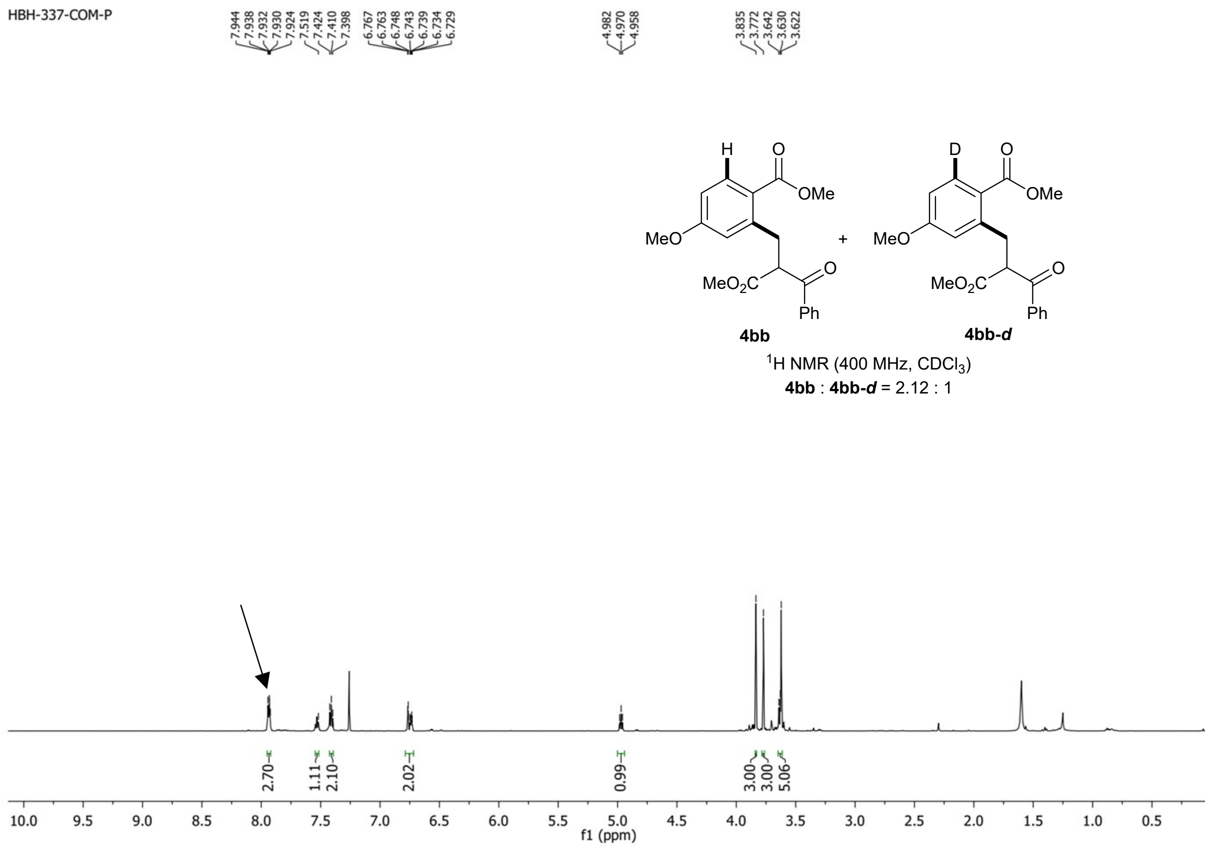
For C-H Alkylation

Parallel Experiment 4-Methoxylbenzoic acid (**1b** (15.2 mg) or **1b-*d*$_2$** [91% D] (15.4 mg), 0.1 mmol), MBH alcohol **2b** (0.11 mmol, 21 mg), $Pd(OAc)_2$ (10 mol %, 0.01 mmol, 2.3 mg) and Ag_2CO_3 (0.2 mmol, 55 mg) were stirred in TFE (1 mL) at 110 °C (in a pre-heated oil bath) in a sealed tube for 2 h. The reaction mixture was cooled to room temperature, diluted with EtOAc (10 mL) and passed through a short celite pad. Evaporation of the solvent gave a residue that was stirred with K_2CO_3 (0.3 mmol, 41.5 mg) and MeI (0.5 mmol, 31 μL) in acetone (2 mL) at room temperature for 1 h. The solvent was removed under vacuum and purification was performed as described in the general procedure to afford **4bb** and **4bb-*d***. The KIE value was determined to be $k_H/k_D = 2.56$ on the basis of ^{1}H NMR analysis.



For C-H Alkylation

Competitive Experiment: 4-Methoxylbenzoic acid **1b** (0.05 mmol, 7.6 mg), 4-methoxylbenzoic acid-d_2 **1b-*d*$_2$** [91% D] (0.05 mmol, 7.7 mg), MBH alcohol **2a** (0.11 mmol, 21 mg), Pd(OAc)$_2$ (10 mol %, 0.01 mmol, 2.3 mg) and Ag$_2$CO$_3$ (0.2 mmol, 55 mg) were stirred in TFE (1 mL) at 110 °C (in a pre-heated oil bath) in a sealed tube for 2 h. The reaction mixture was cooled to room temperature, diluted with EtOAc (20 mL) and passed through a short celite pad. Evaporation of the solvent gave a residue that was stirred with K$_2$CO$_3$ (0.3 mmol, 41.5 mg) and MeI (0.5 mmol, 31 μL) in acetone (2 mL) at room temperature for 1 h. The solvent was removed under vacuum and purification was performed as described in the general procedure to afford a mixture of **4bb**/**4bb-*d***. The KIE value was determined to be $k_H/k_D = 2.12$ on the basis of ^{1}H NMR analysis.



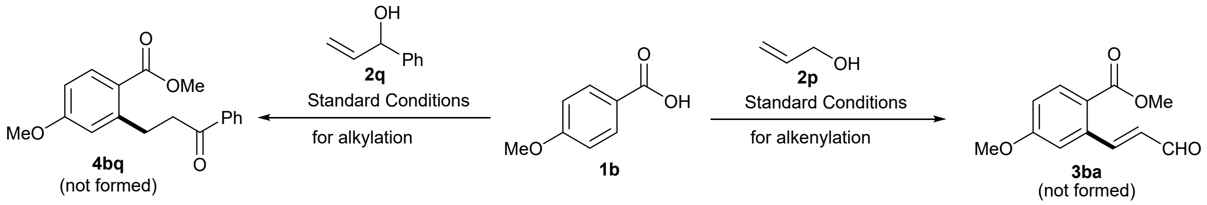
Control Experiment (1)

For C-H Alkenylation: 4-Methoxylbenzoic acid **1b** (0.1 mmol, 15.2 mg, 1.0 equiv), prop-2-en-1-ol **2p** (0.11 mmol, 6.4 mg, 1.1 equiv), $Pd(OAc)_2$ (0.01 mmol, 2.3 mg, 0.1 equiv), Ag_2CO_3 (0.2 mmol, 55 mg, 2.0 equiv) and 1,4-benzoquinone (0.1 mmol, 11 mg, 1.0 equiv) were stirred in HFIP (1 mL) at 110 ° C (in a pre-heated oil bath) in a sealed tube for 12 h. The reaction mixture was cooled to room temperature, diluted with EtOAc (20 mL) and passed through a short celite pad. Evaporation of the solvent gave a residue that was stirred with K_2CO_3 (0.3 mmol, 41.5 mg, 3.0 equiv) and MeI (0.5 mmol, 31 μL, 5.0 equiv) in acetone (2 mL) at room temperature for 3 h. The formation of **3ba** was not observed.

For C-H Alkylation: 4-Methoxylbenzoic acid **1b** (0.1 mmol, 15.2 mg, 1.0 equiv), 1-phenylprop-2-en-1-ol **2q** (0.11 mmol, 14.8 mg, 1.1 equiv)**,** $Pd(OAc)_2$ (0.01 mmol, 2.3 mg, 0.1 equiv) and Ag_2CO_3 (0.2 mmol, 55 mg, 2.0 equiv) were stirred in TFE (1 mL) at 110 °C (in a pre-heated oil bath) in a sealed tube for 12 h. The reaction mixture was cooled to room temperature, diluted with EtOAc (20 mL) and passed through a short celite pad. Evaporation of the solvent gave a residue that was stirred with K_2CO_3 (0.3 mmol, 41.5 mg, 3.0 equiv) and

MeI (0.5 mmol, 31 µL, 5.0 equiv) in acetone (2 mL) at room temperature for 3 h. The formation of **4bq** was not observed.

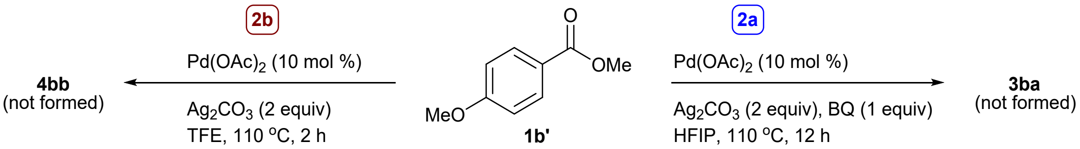
This outcome highlights that the ester moiety plays an essential role of in the reaction by aiding the migratory insertion step in the catalytic cycle.



Control Experiment (2)

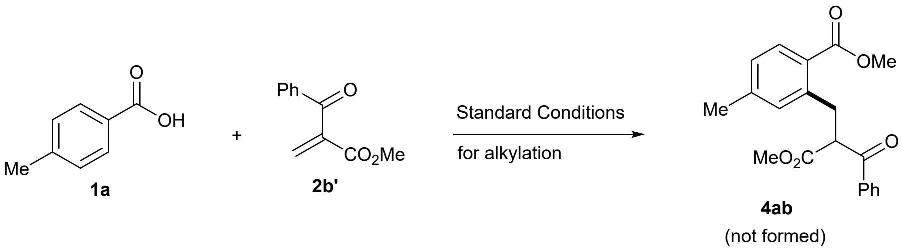
For C-H Alkenylation: Methyl 4-methoxybenzoate **1b′** (0.1 mmol, 16.6 mg, 1.0 equiv), methyl 2-(hydroxymethyl)acrylate **2a** (0.11 mmol, 12.8 mg, 1.1 equiv), Pd(OAc)$_2$ (0.01 mmol, 2.3 mg, 0.1 equiv), Ag$_2$CO$_3$ (0.2 mmol, 55 mg, 2.0 equiv) and 1,4-benzoquinone (0.1 mmol, 11 mg, 1.0 equiv) were stirred in HFIP (1 mL) at 110 ° C (in a pre-heated oil bath) in a sealed tube for 12 h. The formation of **3ba** was not observed.

For C-H Alkylation: Methyl 4-methoxybenzoate **1b′** (0.1 mmol, 16.6 mg, 1.0 equiv), methyl 2-(hydroxy(phenyl)methyl)acrylate **2b** (0.11 mmol, 21 mg, 1.1 equiv)**,** Pd(OAc)$_2$ (0.01 mmol, 2.3 mg, 0.1 equiv) and Ag$_2$CO$_3$ (0.2 mmol, 55 mg, 2.0 equiv) were stirred in TFE (1 mL) at 110 °C (in a pre-heated oil bath) in a sealed tube for 12 h. The formation of **4bb** was not observed.



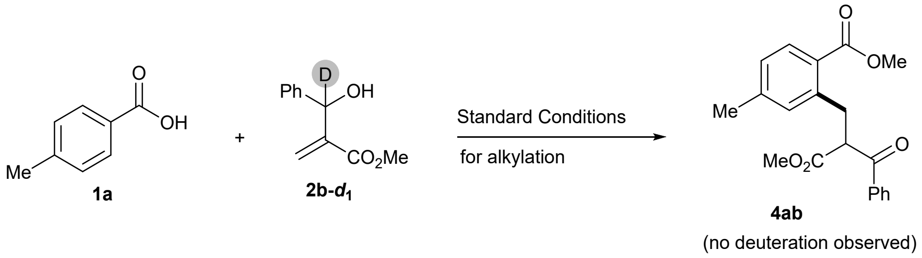
Control Experiment (3)

4-Methylbenzoic acid **1a** (0.1 mmol, 13.6 mg, 1.0 equiv), methyl 2-benzoylacrylate **2b′** (0.11 mmol, 21mg, 1.1 equiv), Pd(OAc)$_2$ (0.01 mmol, 2.3 mg, 0.1 equiv) and Ag$_2$CO$_3$ (0.2 mmol, 55 mg, 2.0 equiv) were stirred in TFE (1 mL) at 110 °C (in a pre-heated oil bath) in a sealed tube for 12 h. The formation of alkylated **4ab** was not formed.



Control Experiment (4)

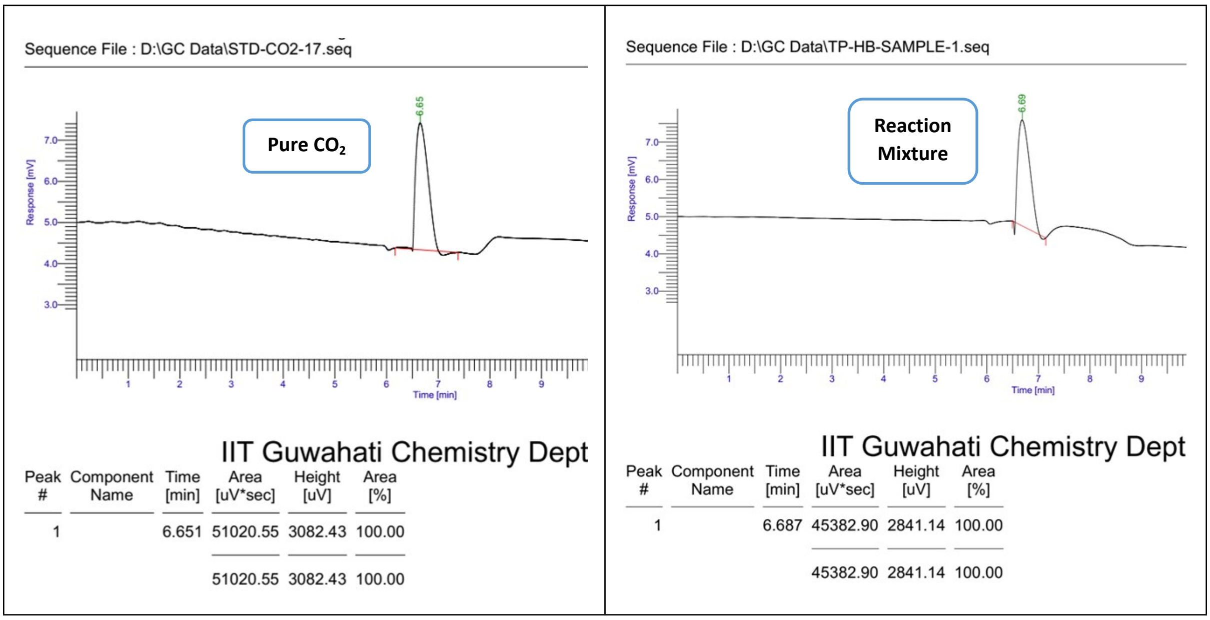
4-Methylbenzoic acid **1a** (0.1 mmol, 13.6 mg, 1.0 equiv), methyl 2-(hydroxy(phenyl)methyl-*d*) acrylate **2b-*d*$_1$** (0.11 mmol, 21.2 mg, 1.1 equiv), Pd(OAc)$_2$ (0.01 mmol, 2.3 mg, 0.1 equiv) and Ag$_2$CO$_3$ (0.2 mmol, 55 mg, 2.0 equiv) were stirred in TFE (1 mL) at 110 °C (in a pre-heated oil bath) in a sealed tube for 12 h. In the isolated alkylated product **4ab**, no deuteration incorporation was observed.



Determination of CO$_2$ Evolution using GC Analysis. 4-Methylbenzoic acid **1a** (2.0 mmol, 272 mg, 1.0 equiv), methyl 2-(hydroxymethyl)acrylate **2a** (2.2 mmol, 255 mg, 1.1 equiv), Pd(OAc)$_2$ (0.2 mmol, 45 mg, 0.1 equiv), Ag$_2$CO$_3$ (4 mmol, 1.1 g, 2.0 equiv) and 1,4-benzoquinone (2 mmol, 216 mg, 1.0 equiv) were stirred in HFIP (5 mL) at 110 °C (in a pre-heated oil bath) in a sealed tube for 12 h. The pressure tube was cooled to 0 °C, the evolved gas was syringed out and detected by PerkinElmer clarus590 GC instrument using Elite Plot-Q column (30 m length x 530 µm x 20 µm ID) with the following conditions:

TCD starting temperature: 40 °C
Oven temperature: 60 °C
Time at starting temperature: 0 min
Hold time: 5 min
Ramp: 28 °C/ min up to 200 °C
Flow rate: 5 ml/ min (N$_2$)
Split ration: 20
Inlet temperature: 40 °C
Detector temperature TCD: 200 °C

Gas Chromatograms:



Sequence File : D:\GC Data\STD-CO2-17.seq

IIT Guwahati Chemistry Dept

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		6.651	51020.55	3082.43	100.00
			51020.55	3082.43	100.00

Sequence File : D:\GC Data\TP-HB-SAMPLE-1.seq

IIT Guwahati Chemistry Dept

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		6.687	45382.90	2841.14	100.00
			45382.90	2841.14	100.00

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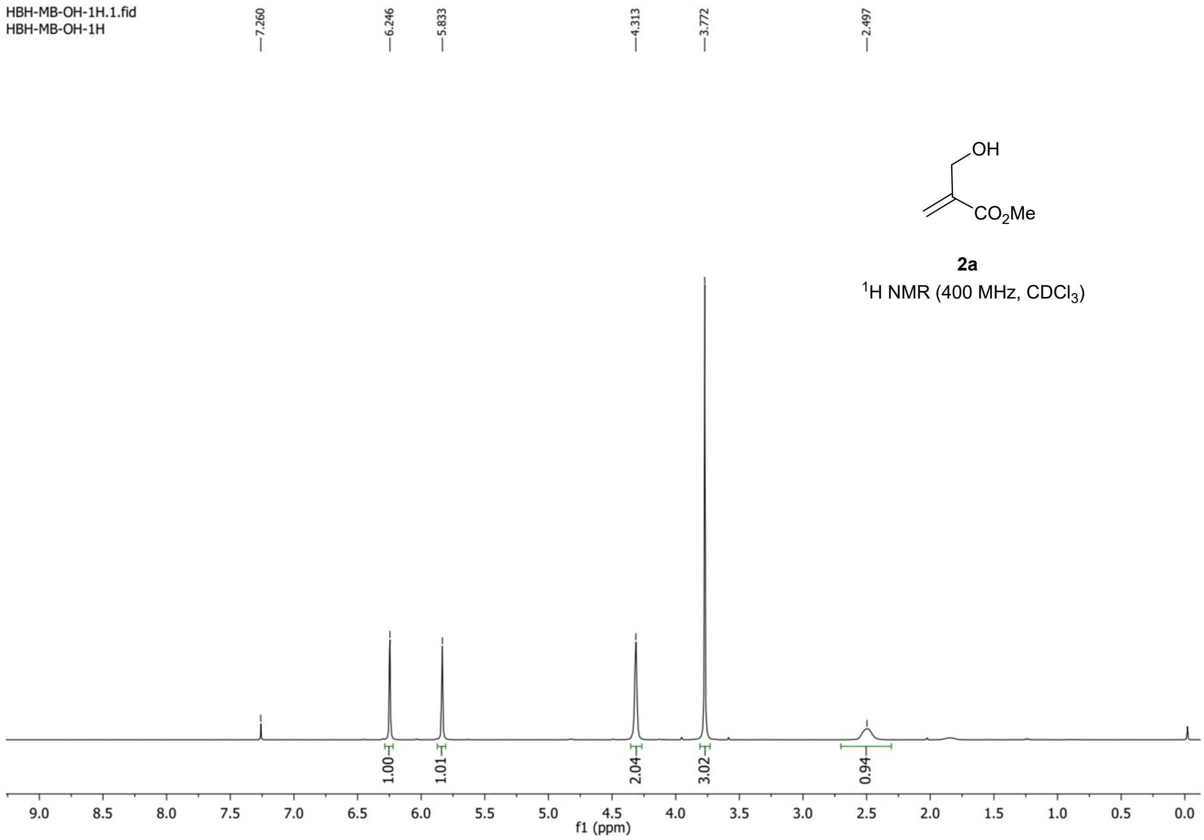
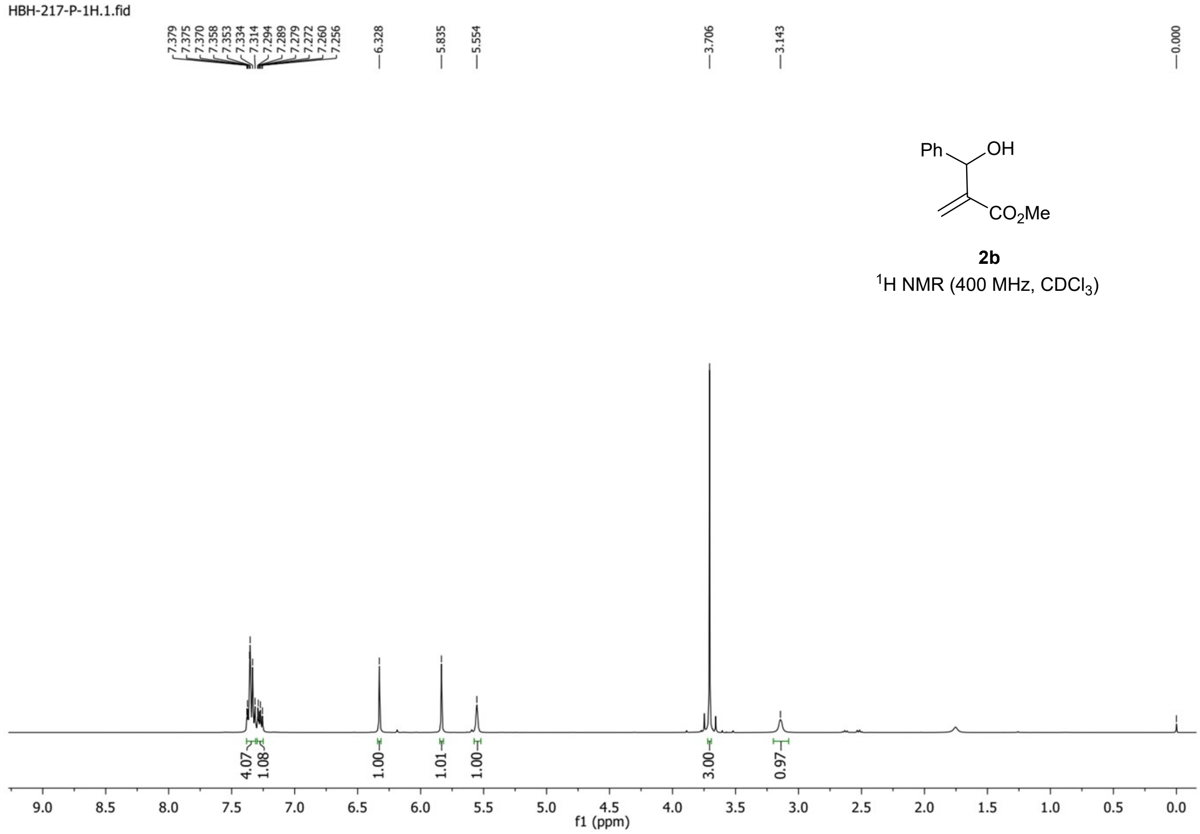
NMR (^{1}H, ^{13}C and ^{19}F) Spectra



2a

^{1}H NMR (400 MHz, CDCl$_3$)



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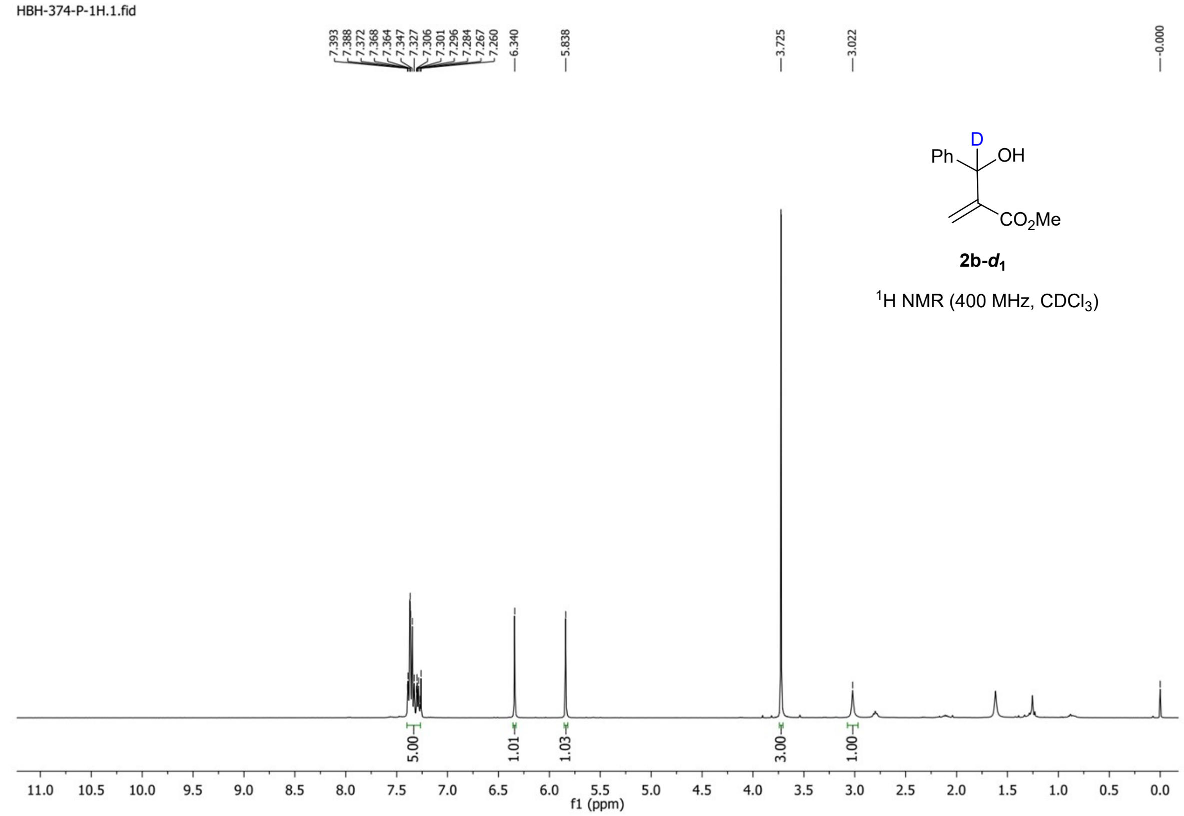

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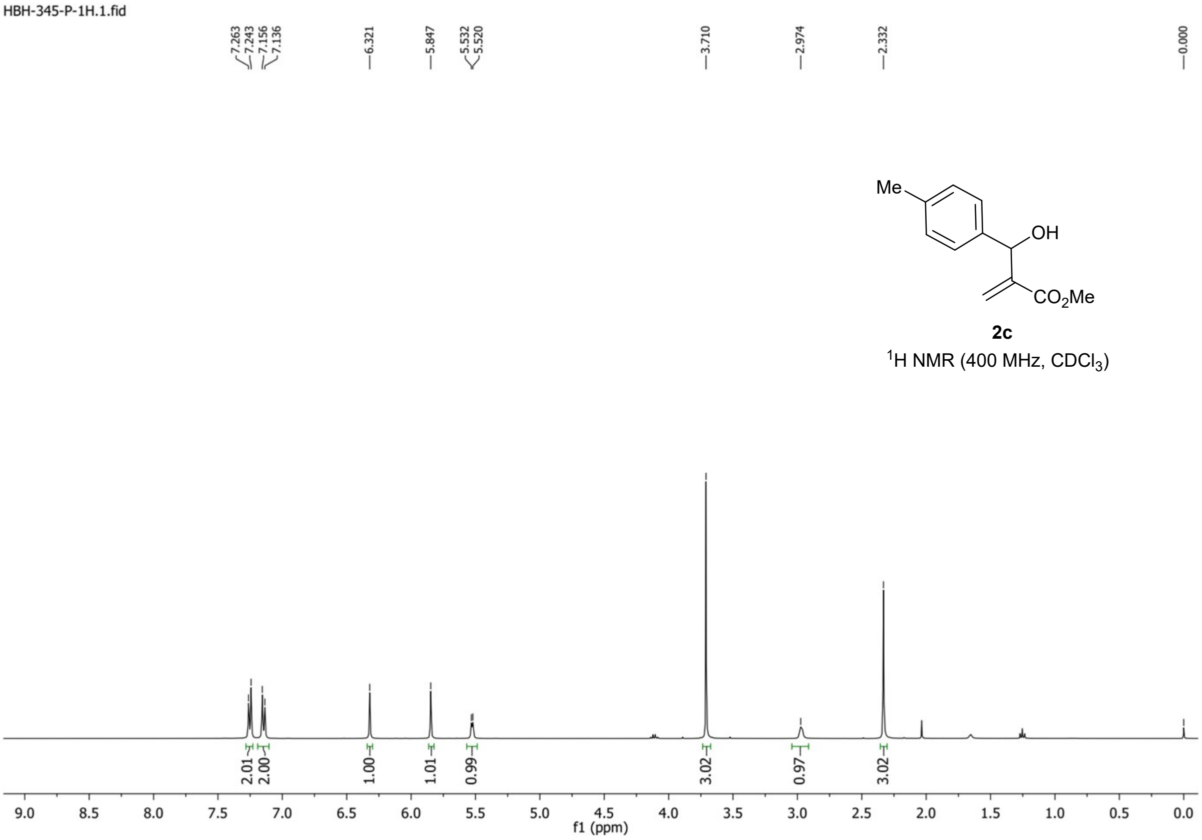

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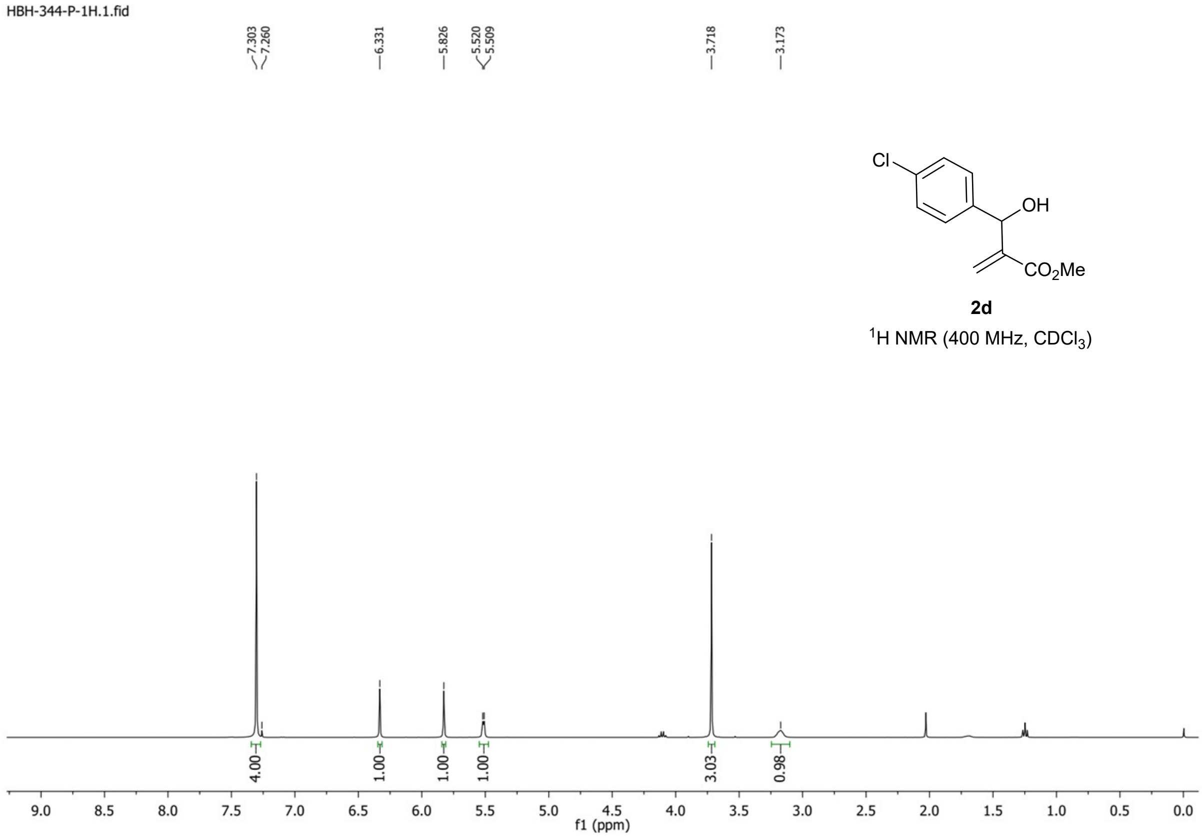

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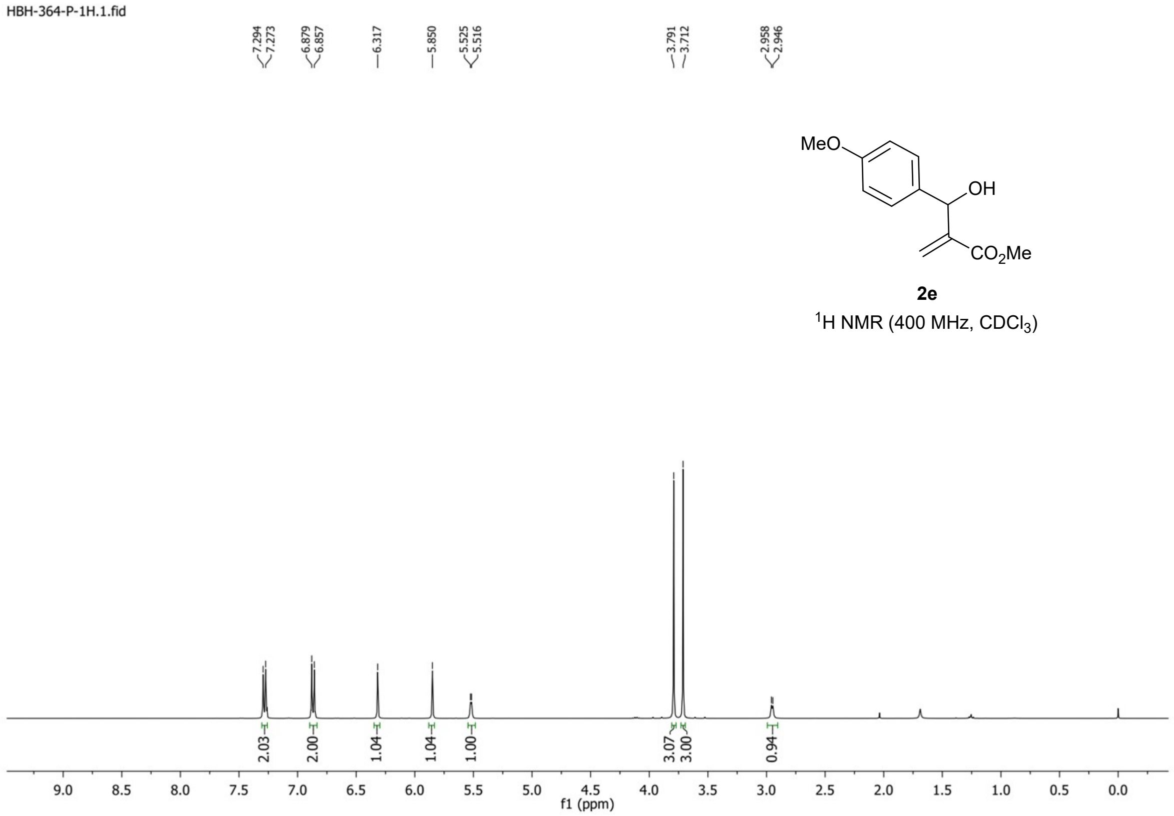

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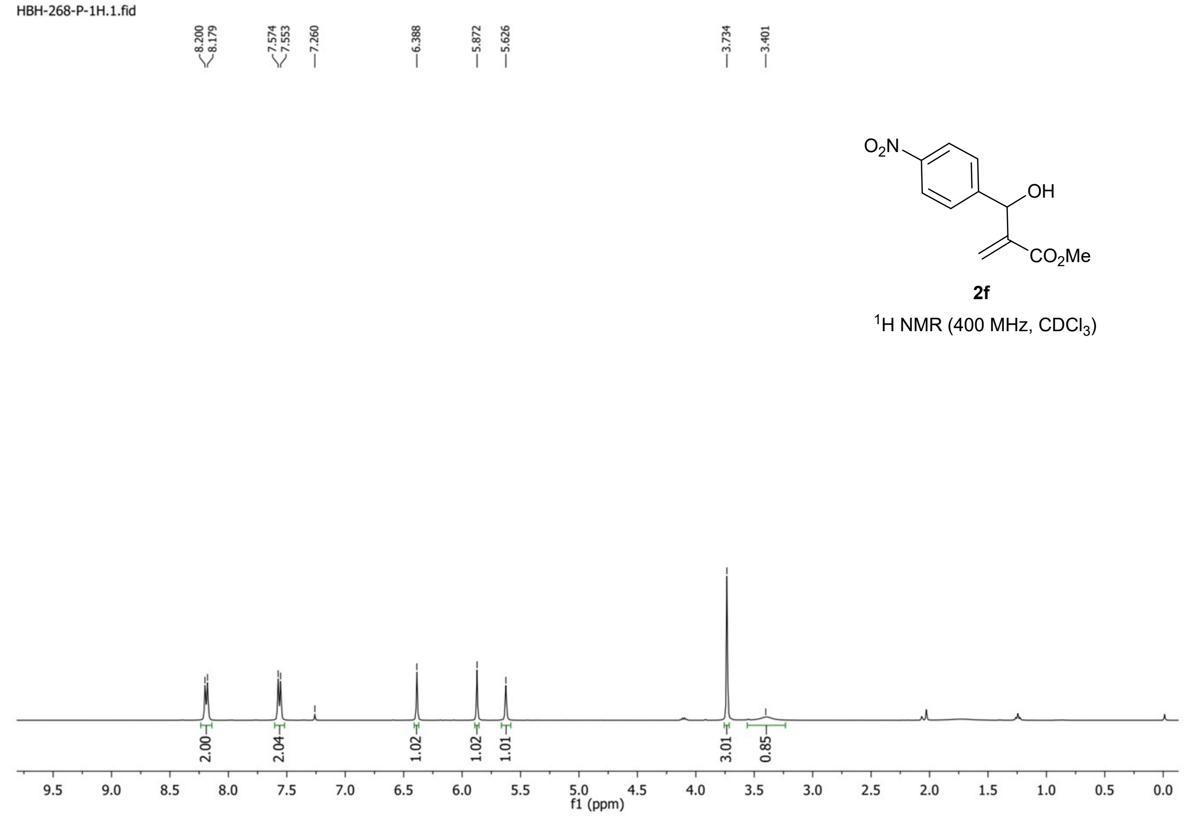

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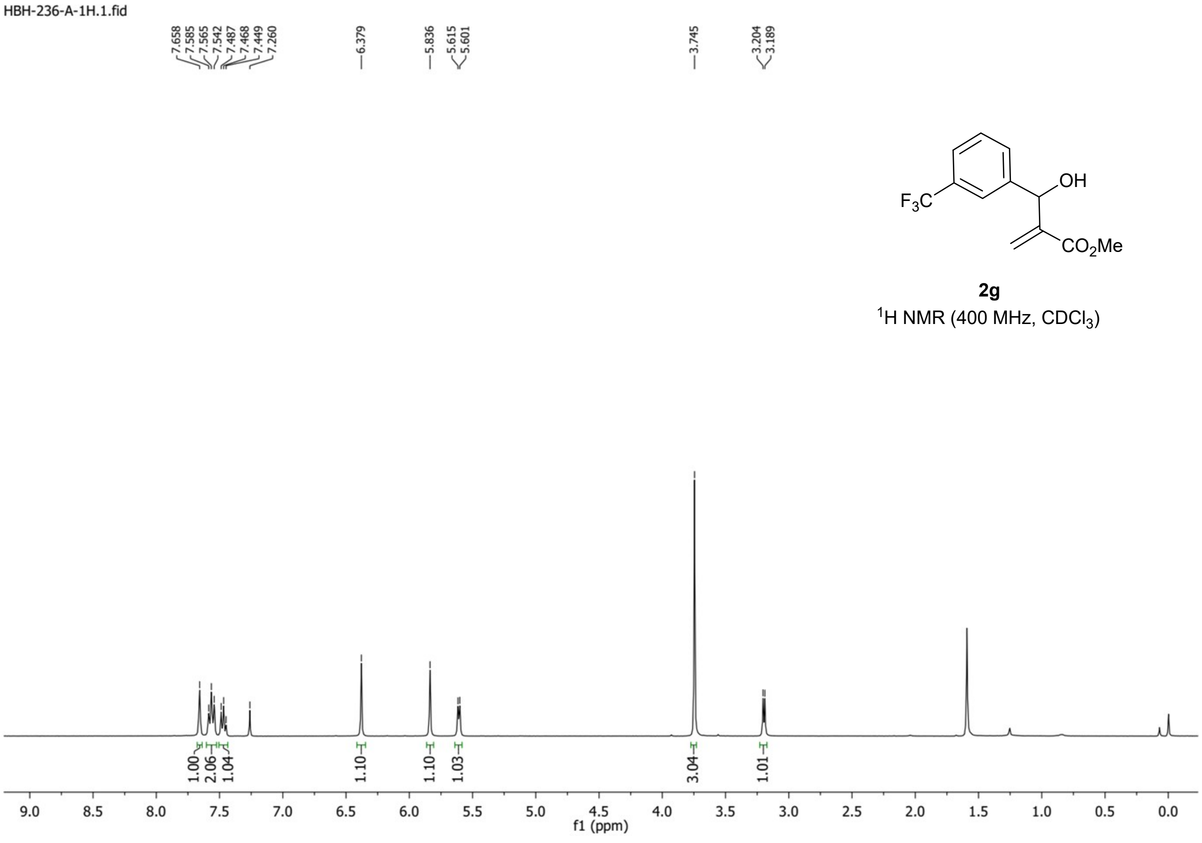

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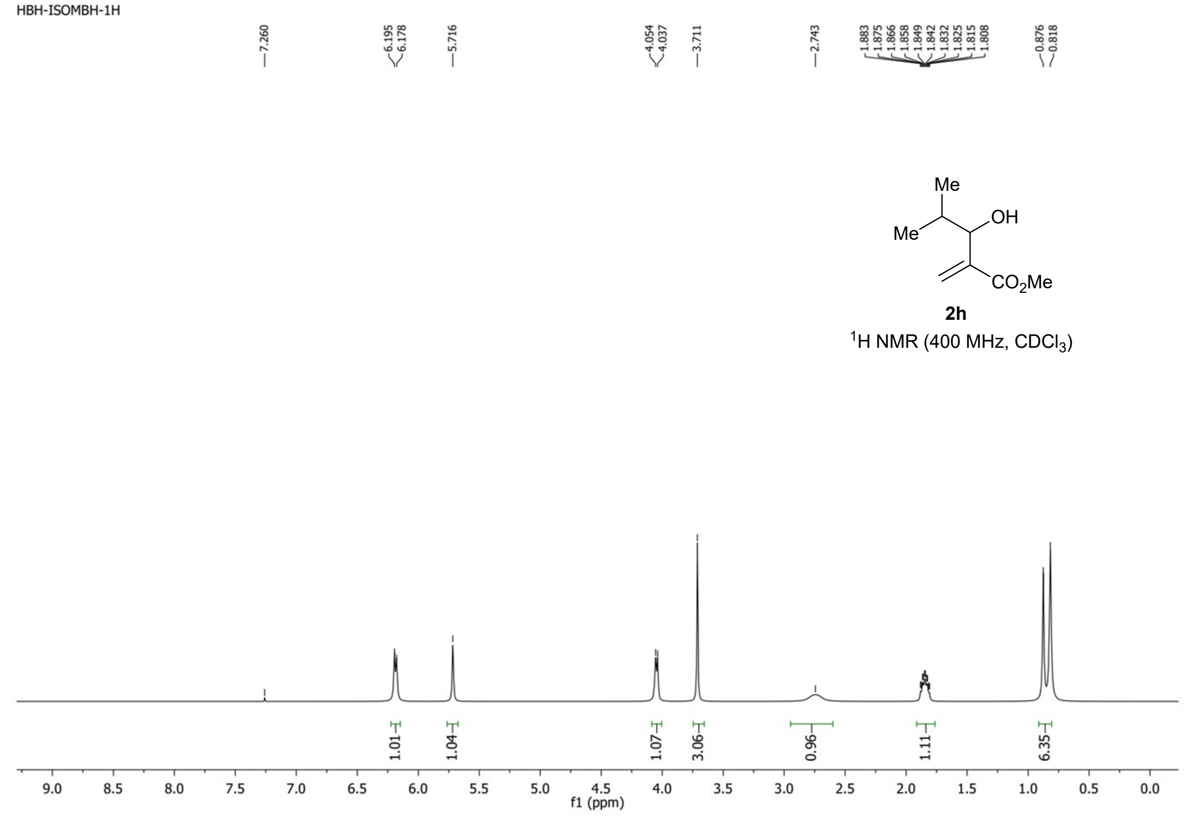

2h

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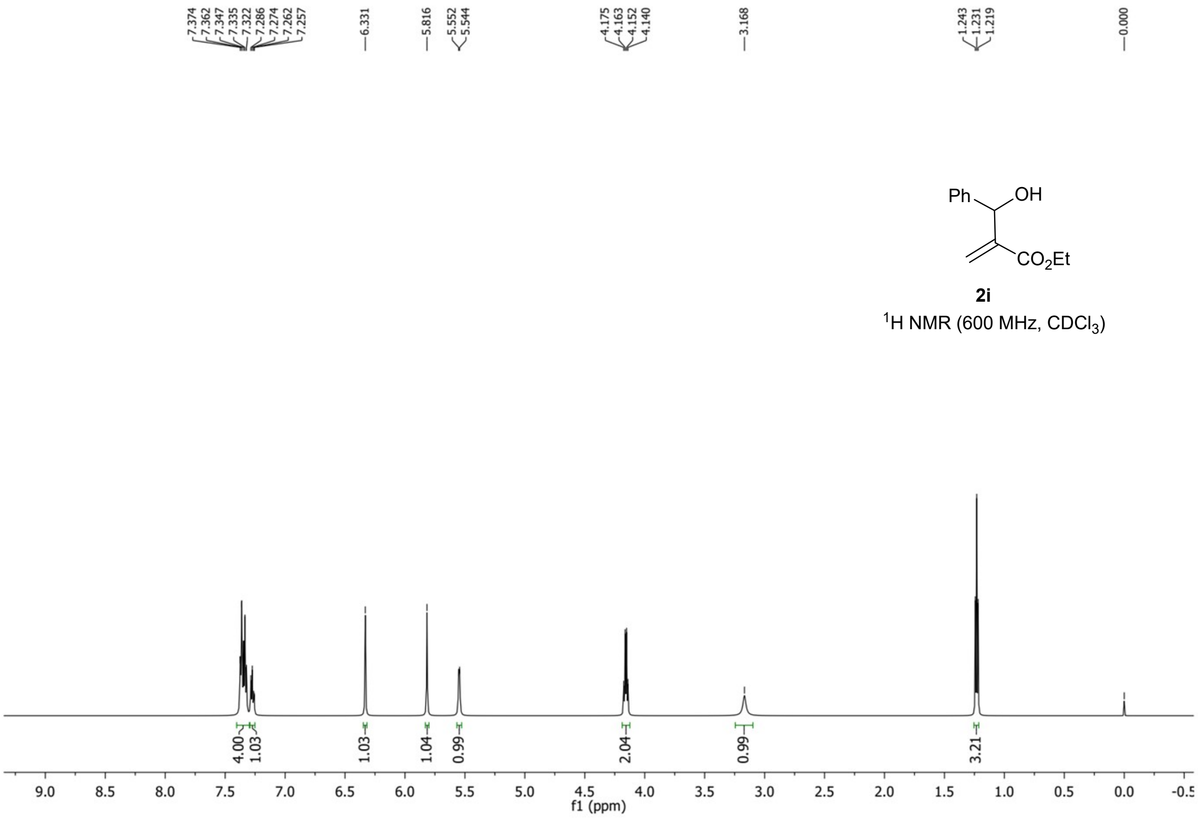

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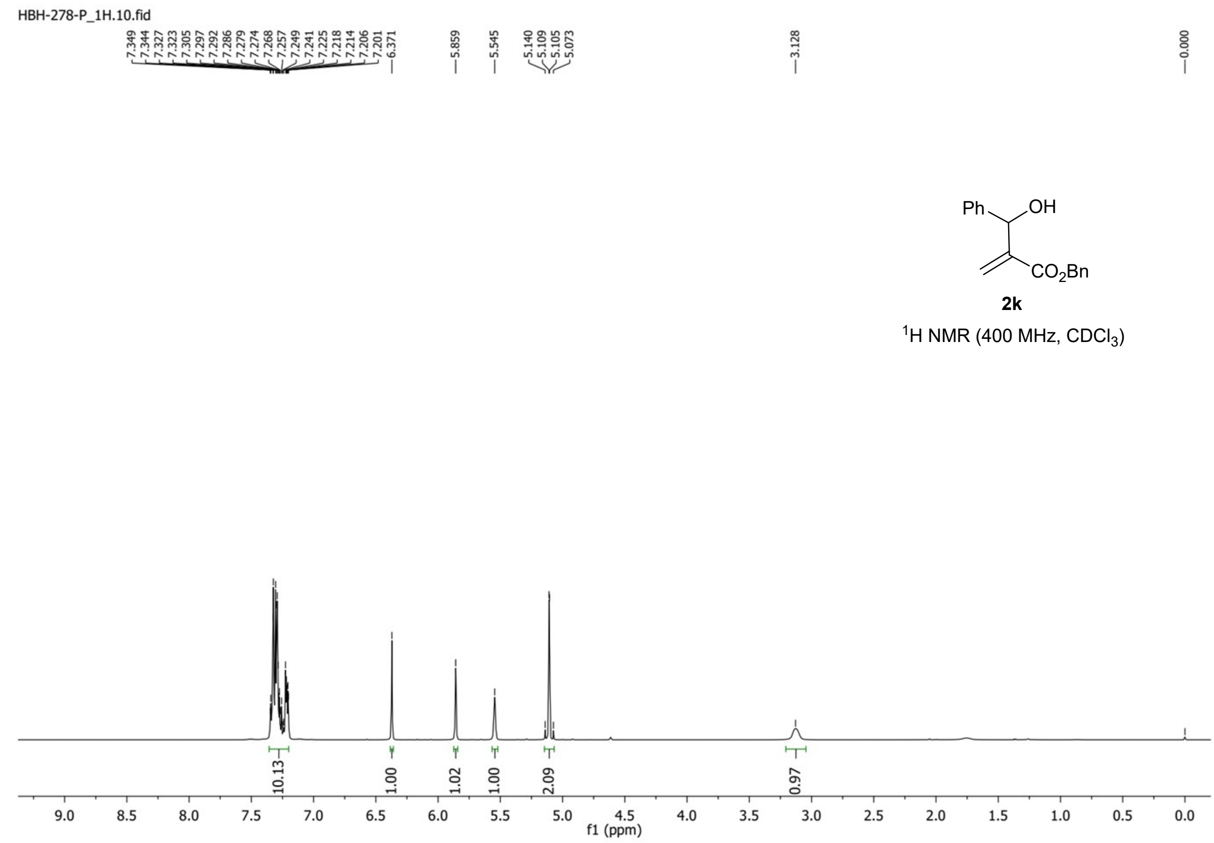

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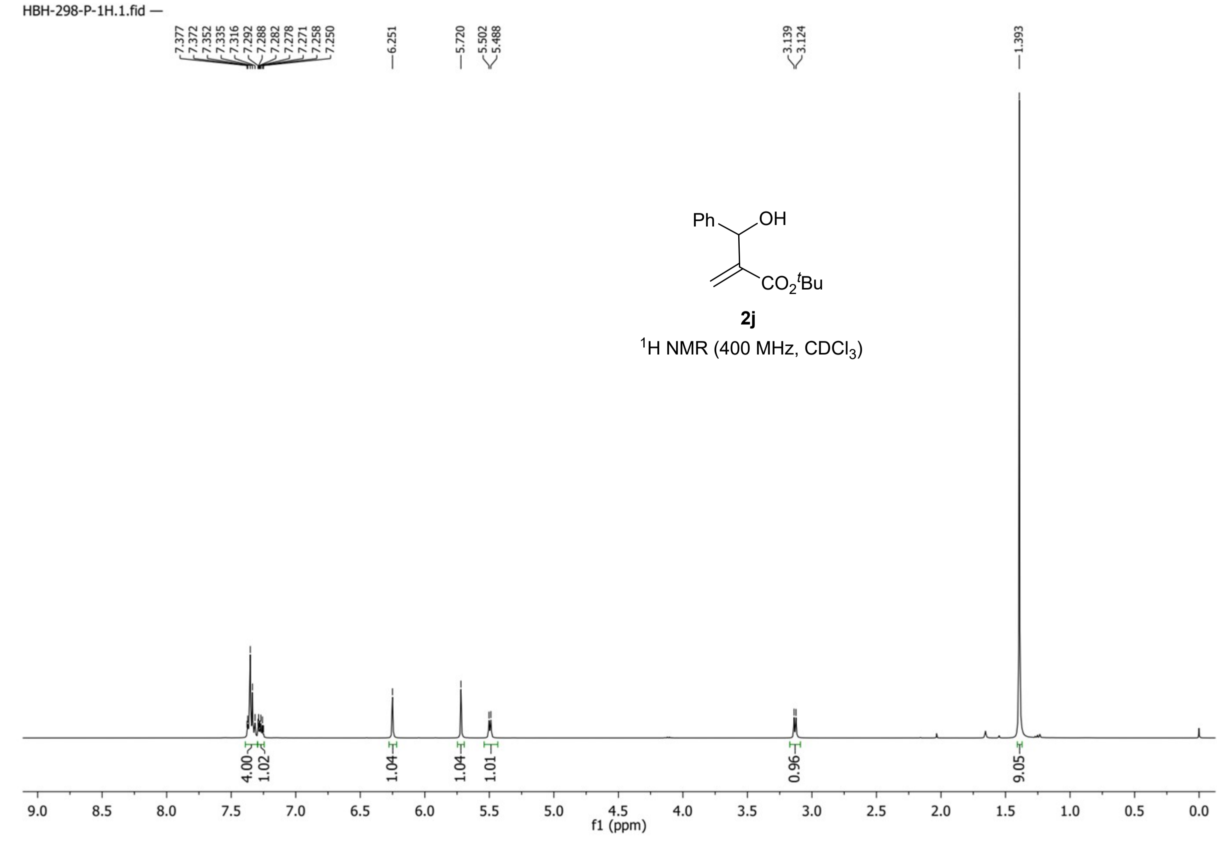

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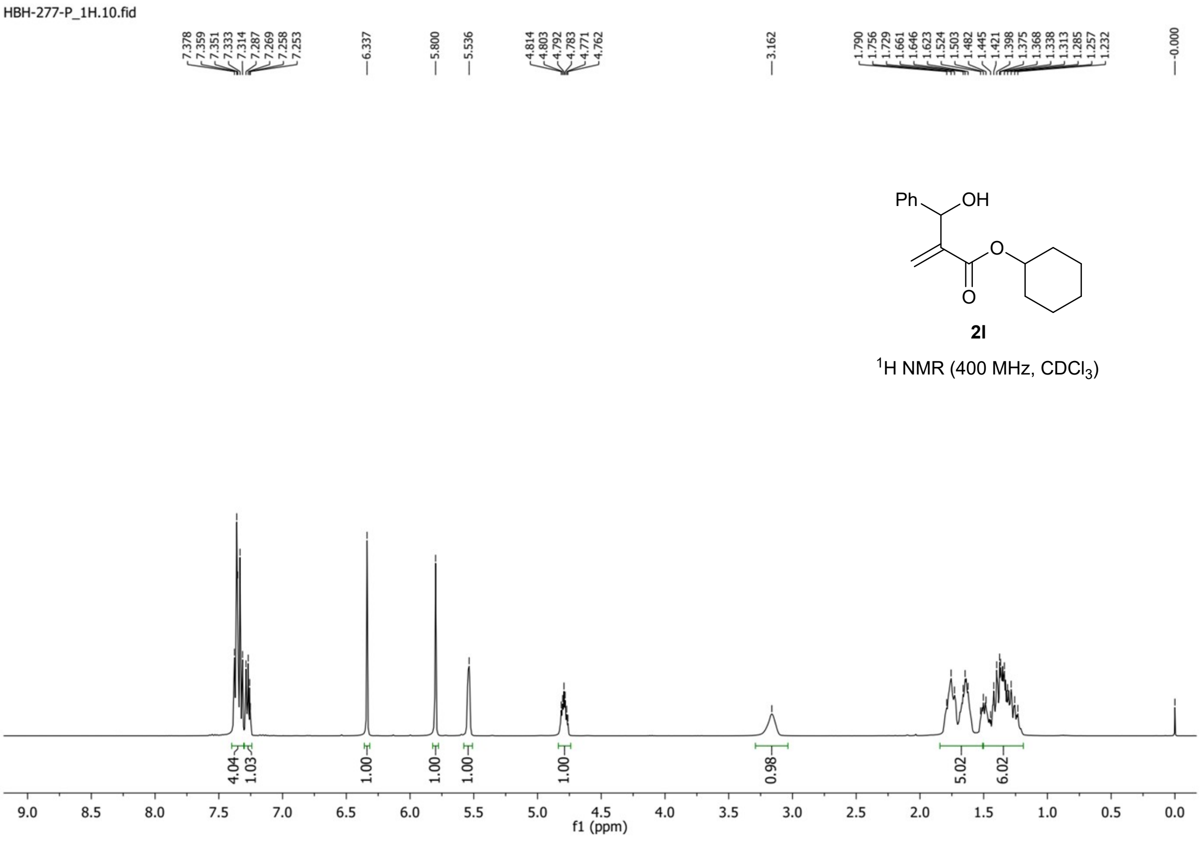

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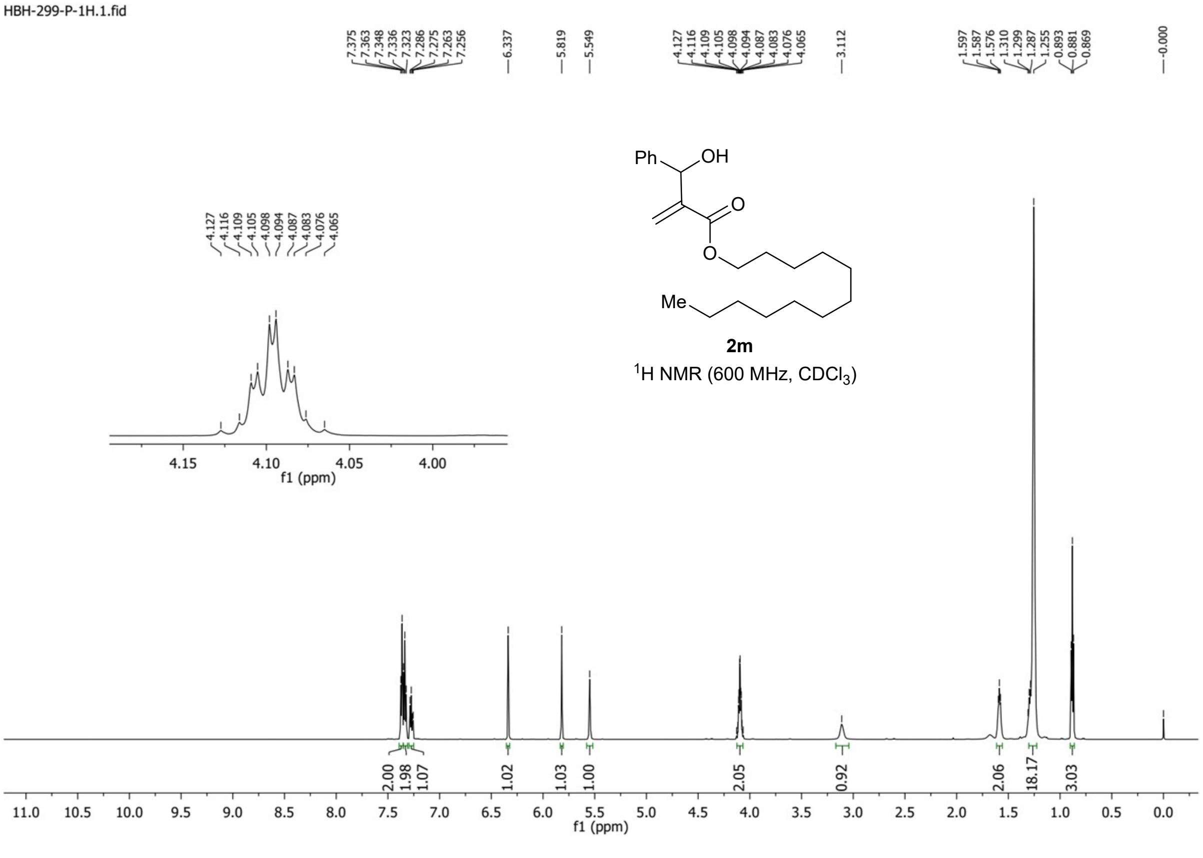

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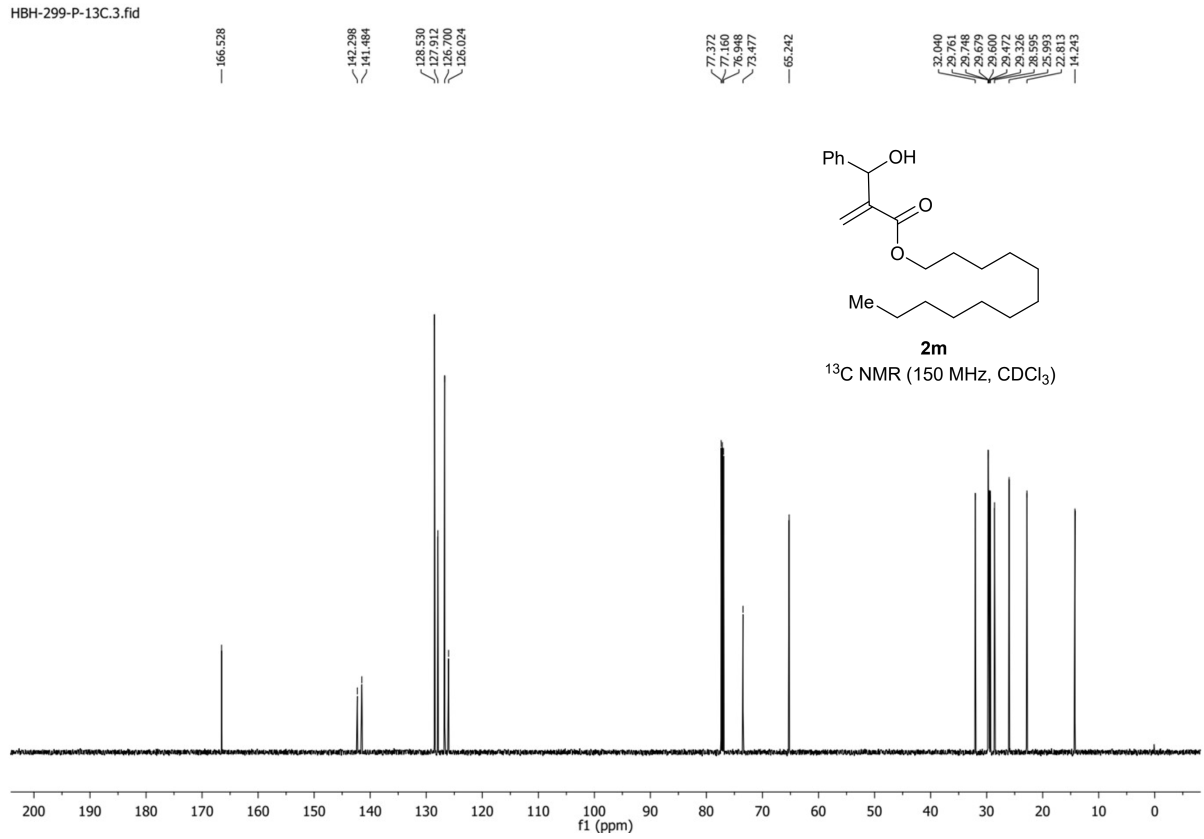

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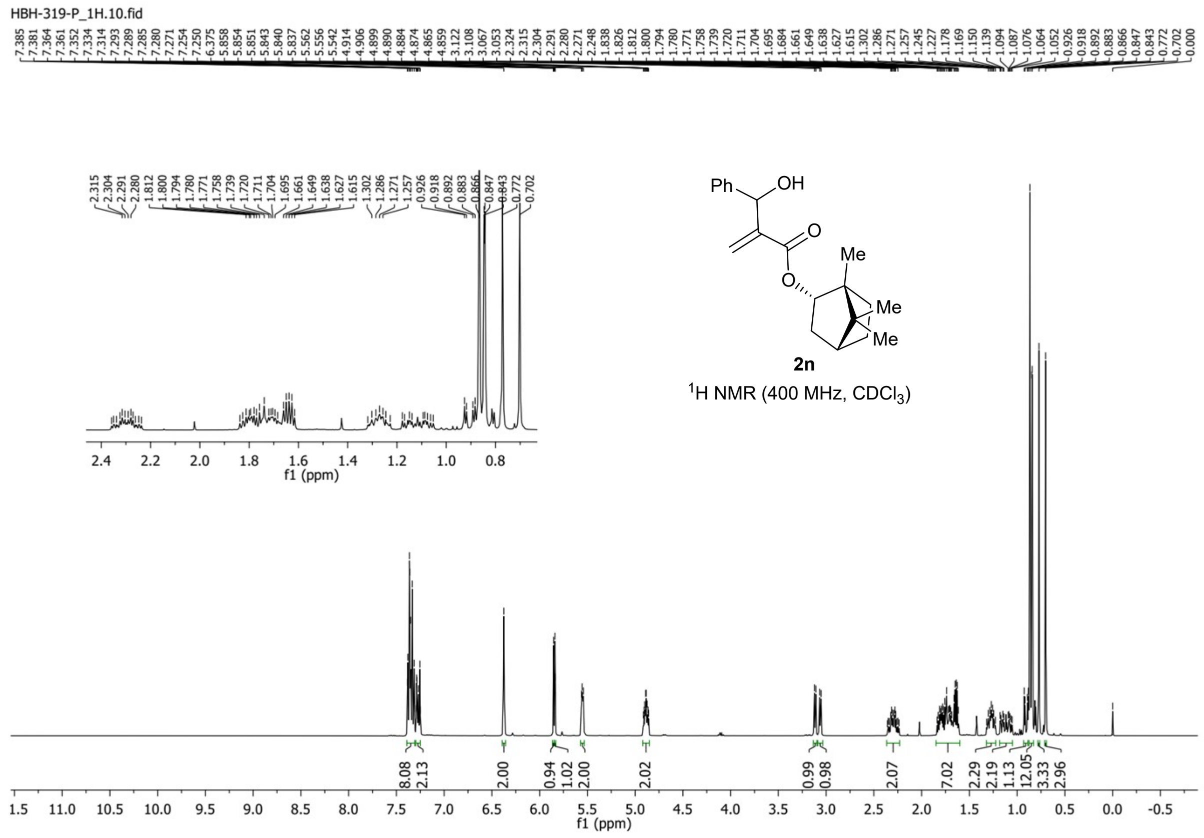

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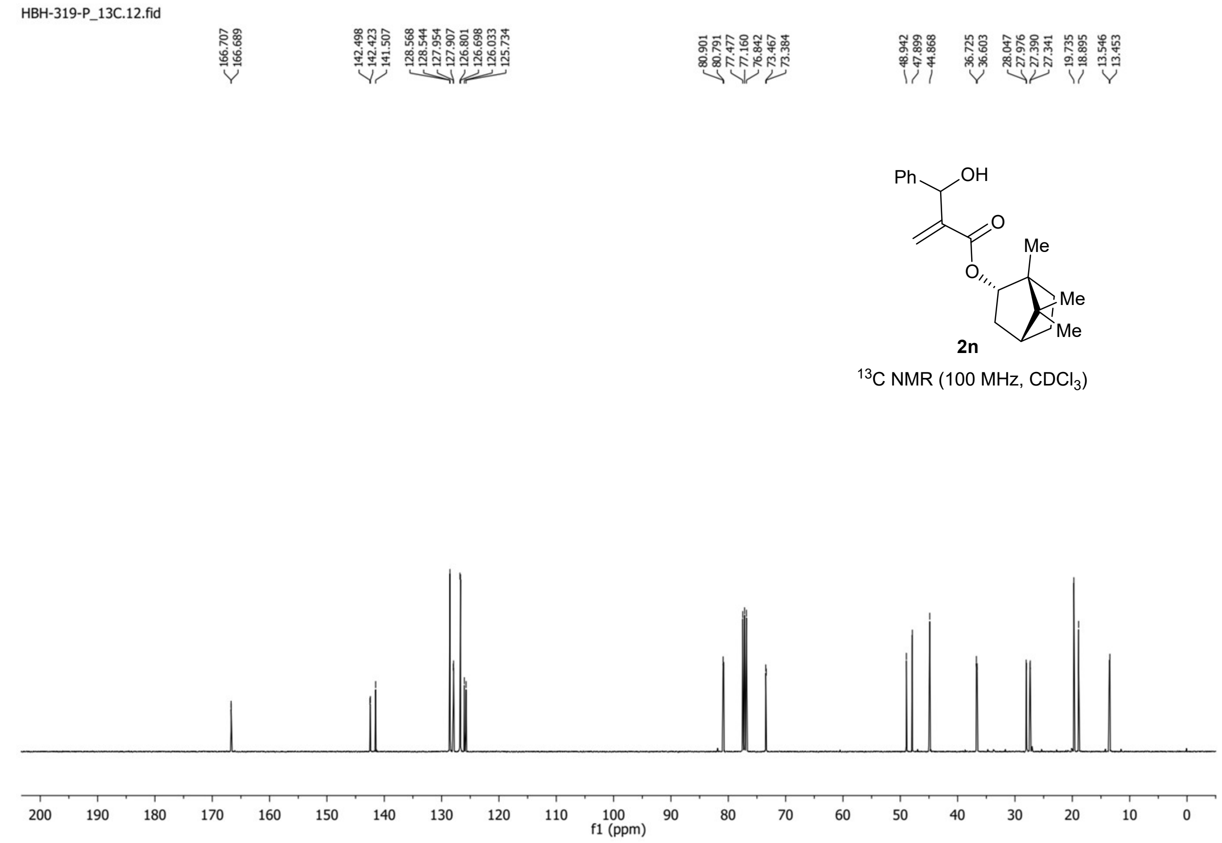

2n

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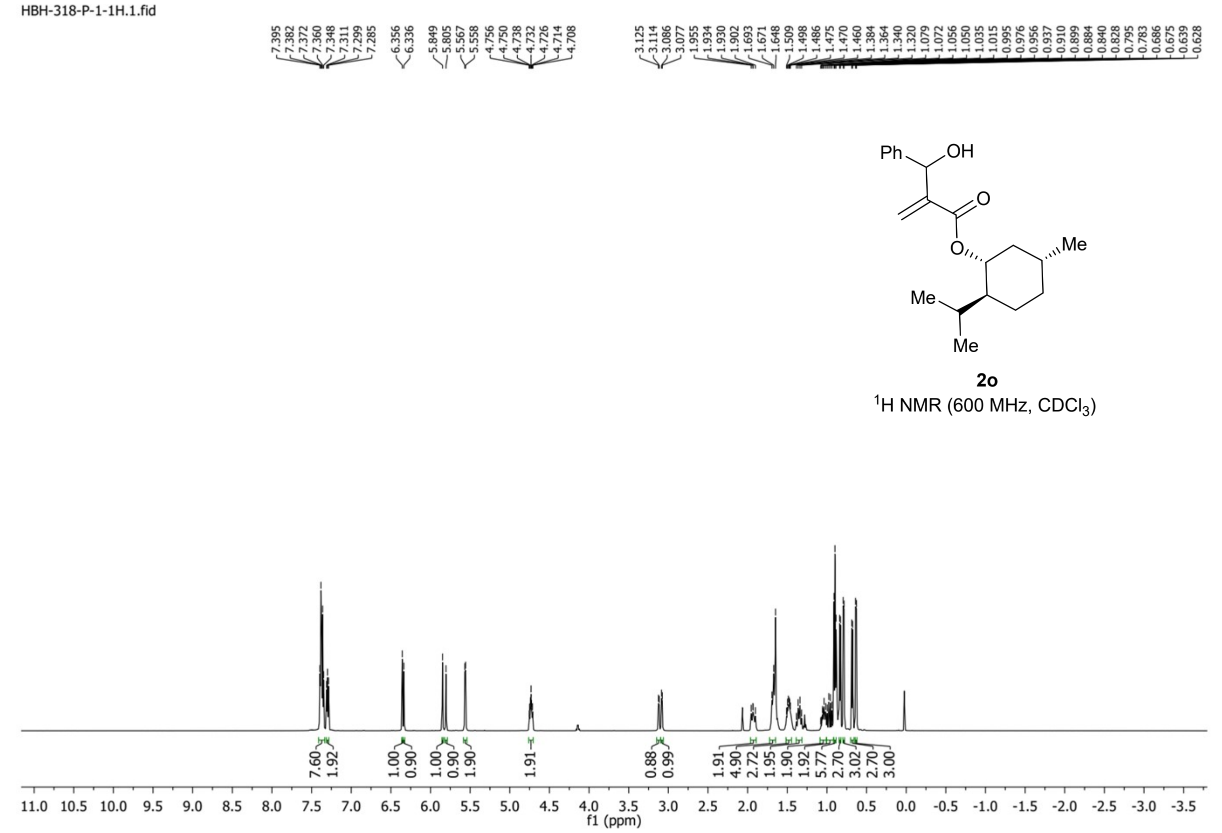
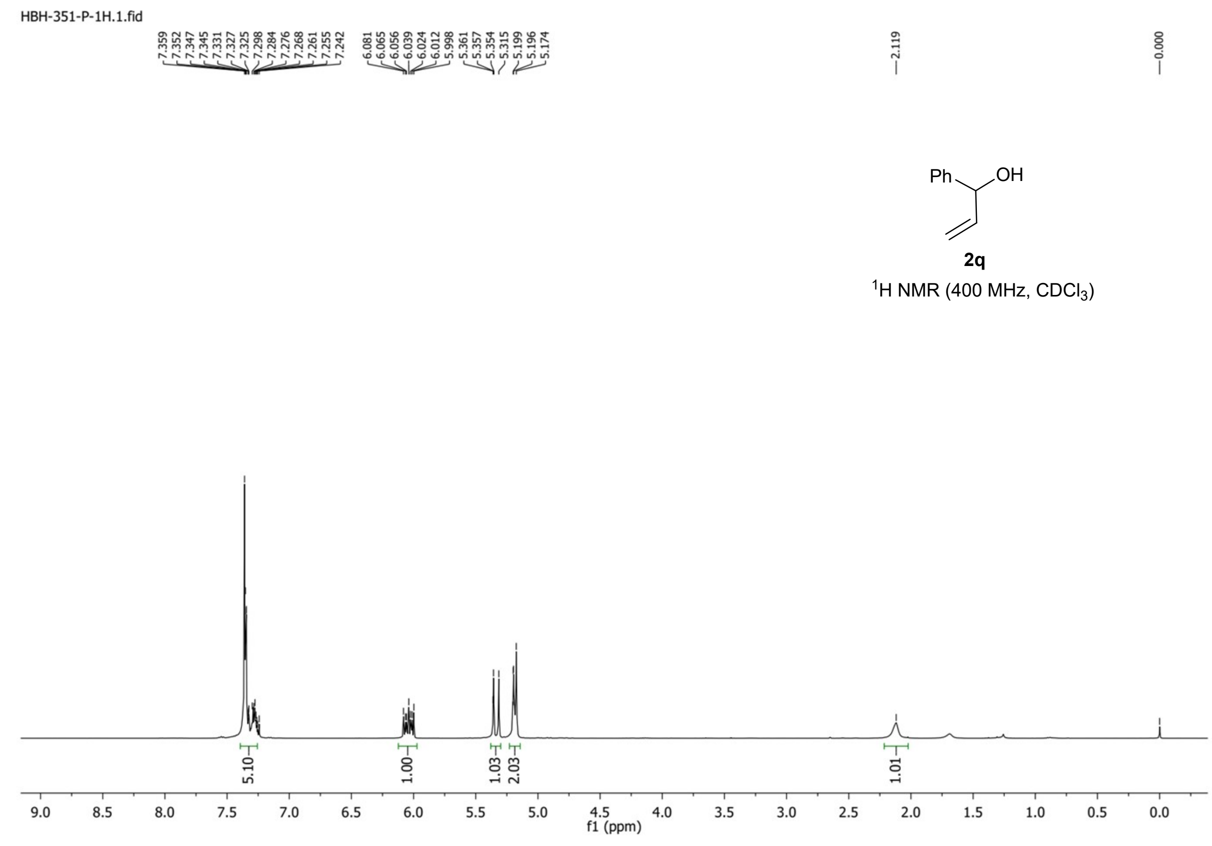


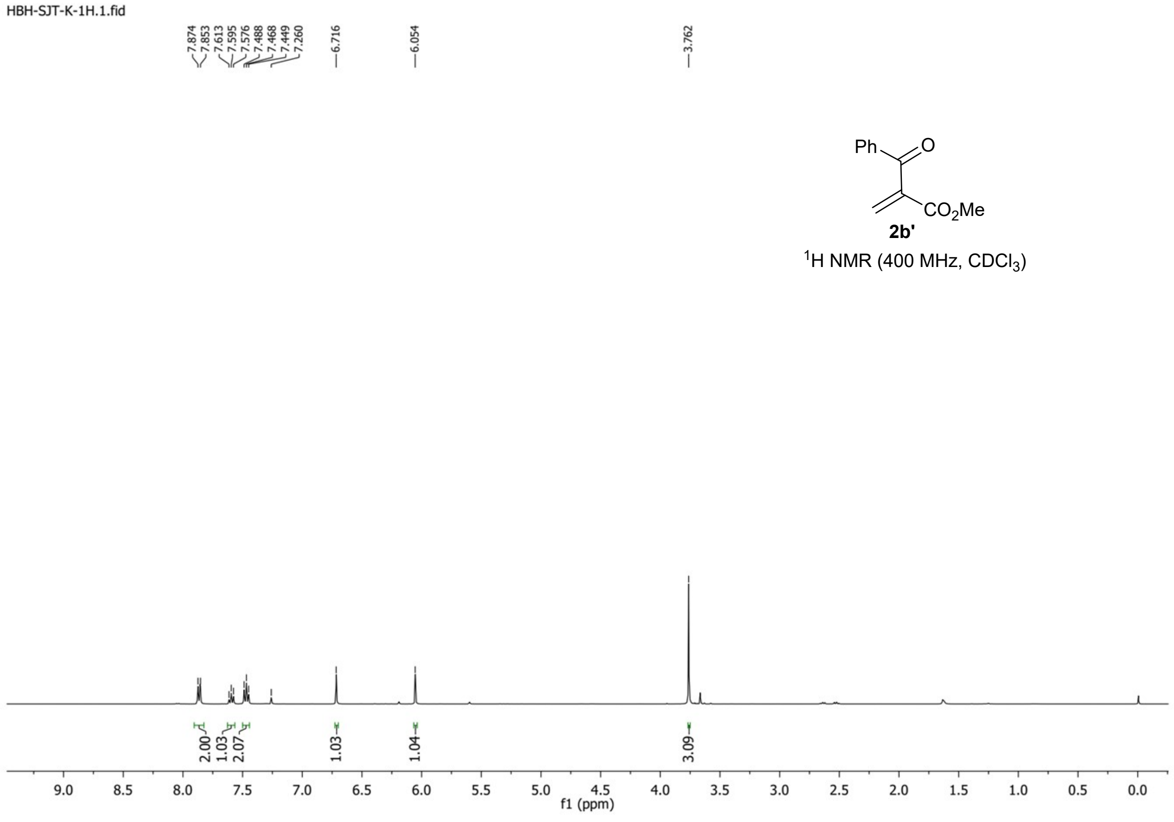
2o

^{1}H NMR (600 MHz, $CDCl_3$)



2q

^{1}H NMR (400 MHz, $CDCl_3$)



2b'

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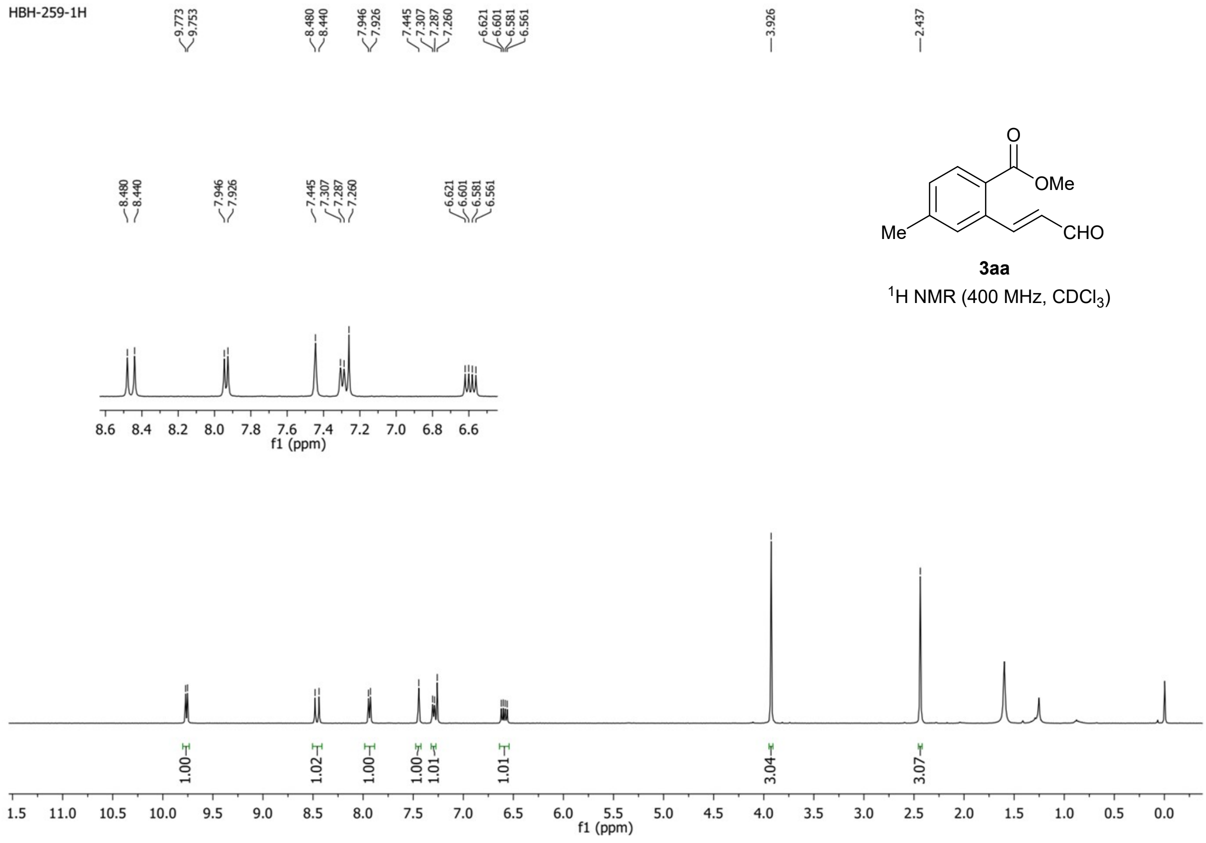

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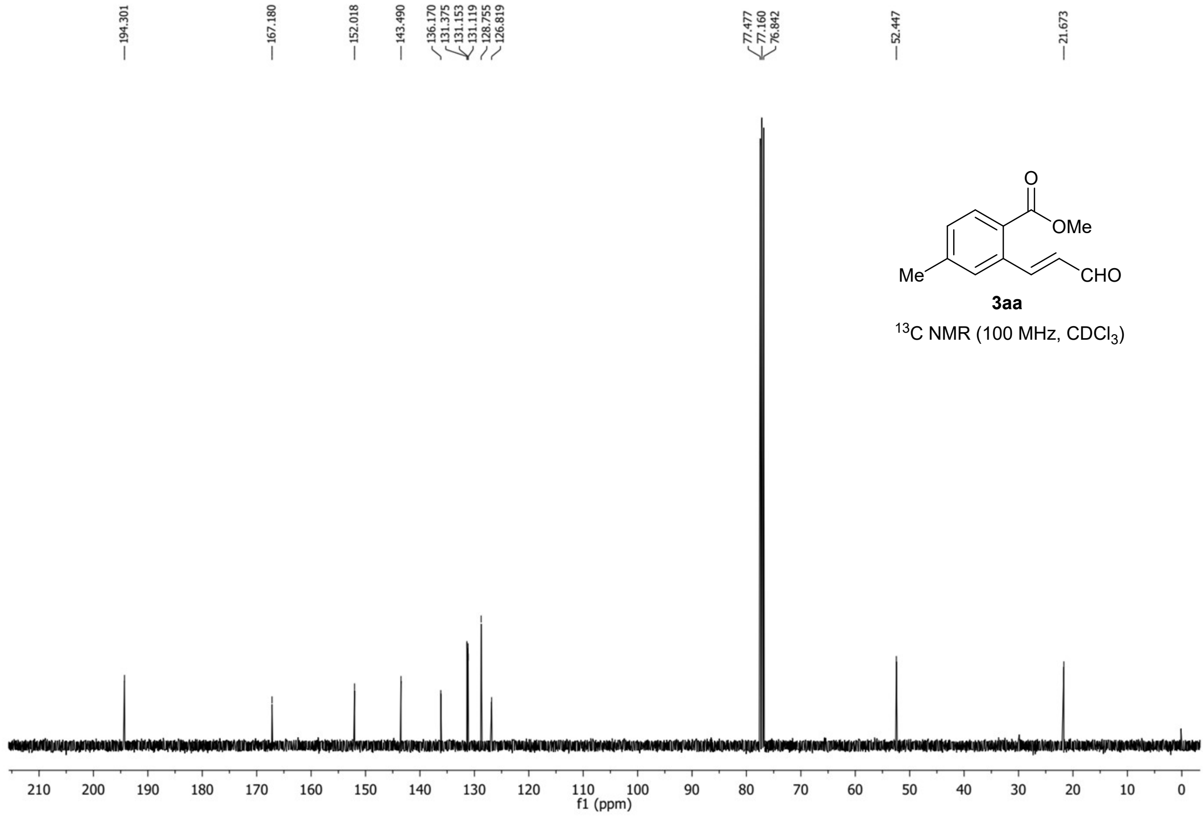
^{1}H NMR (400 MHz, $CDCl_3$)



3aa

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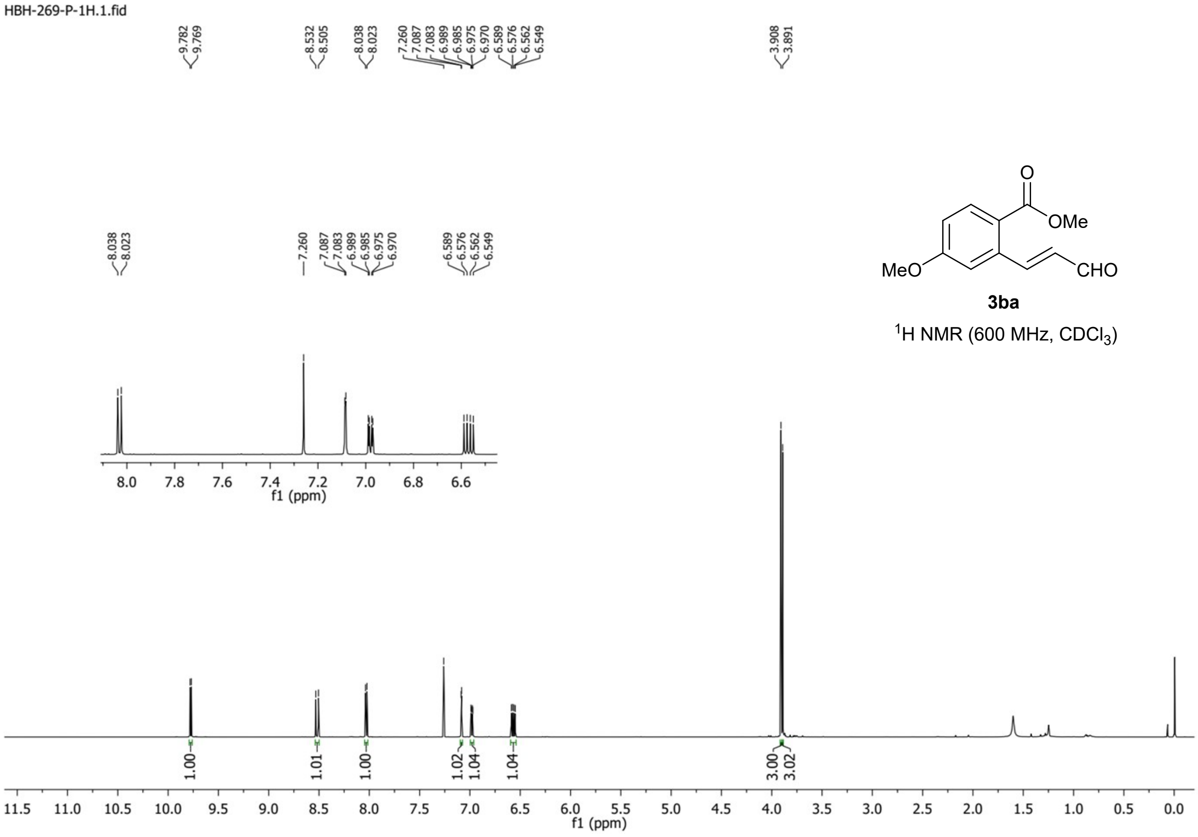

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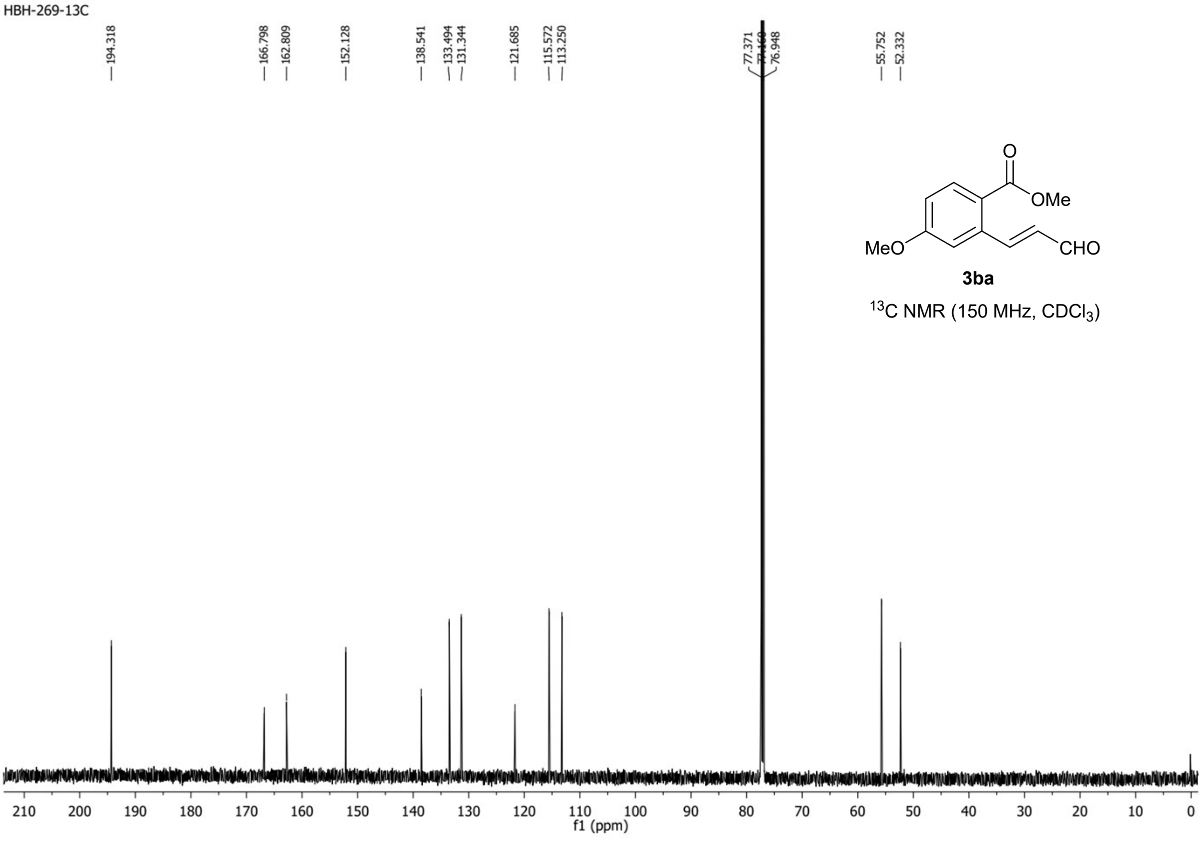

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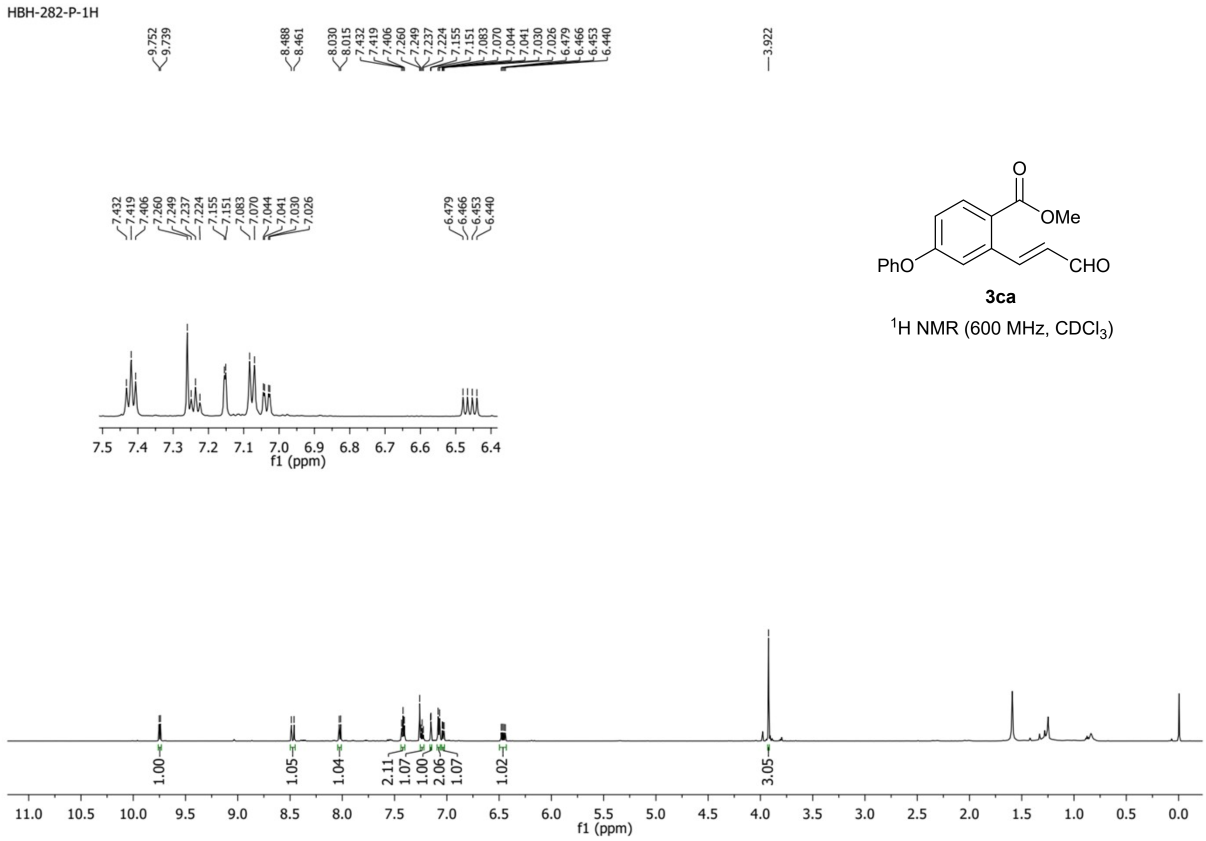

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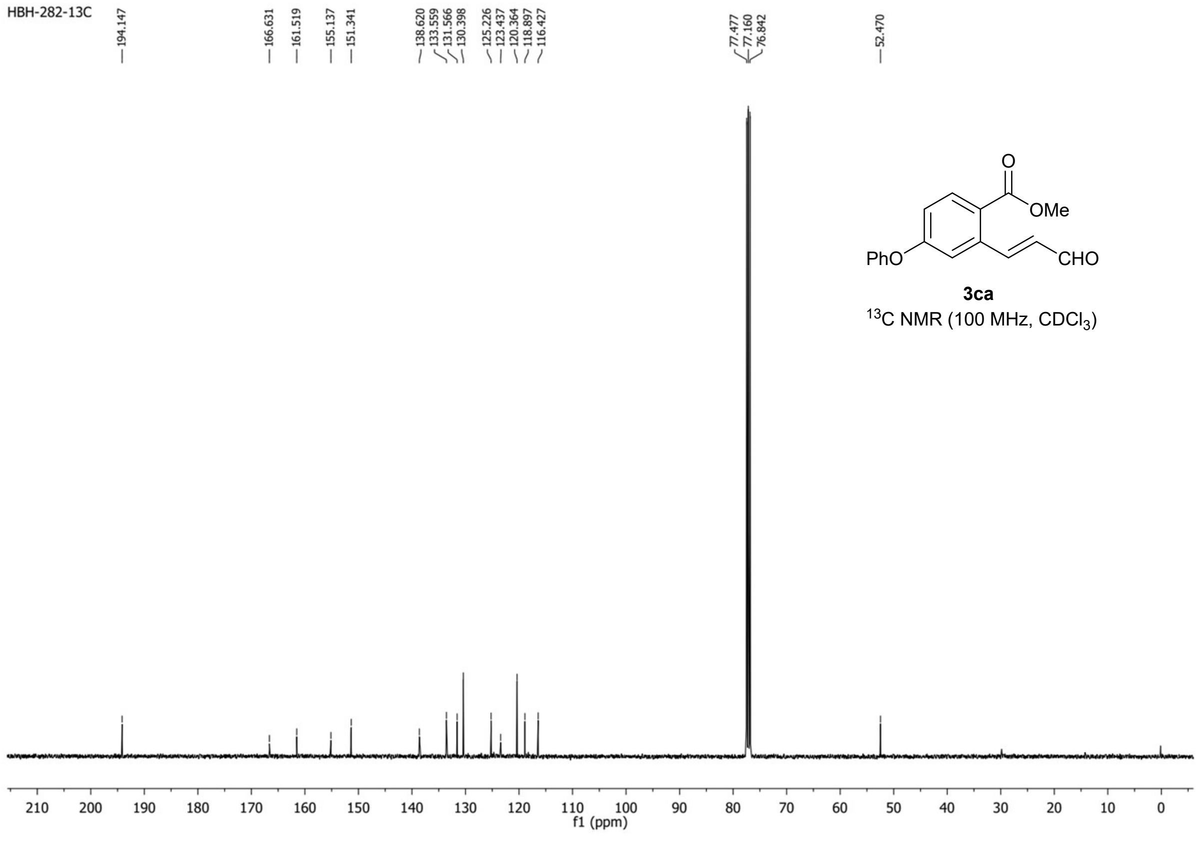

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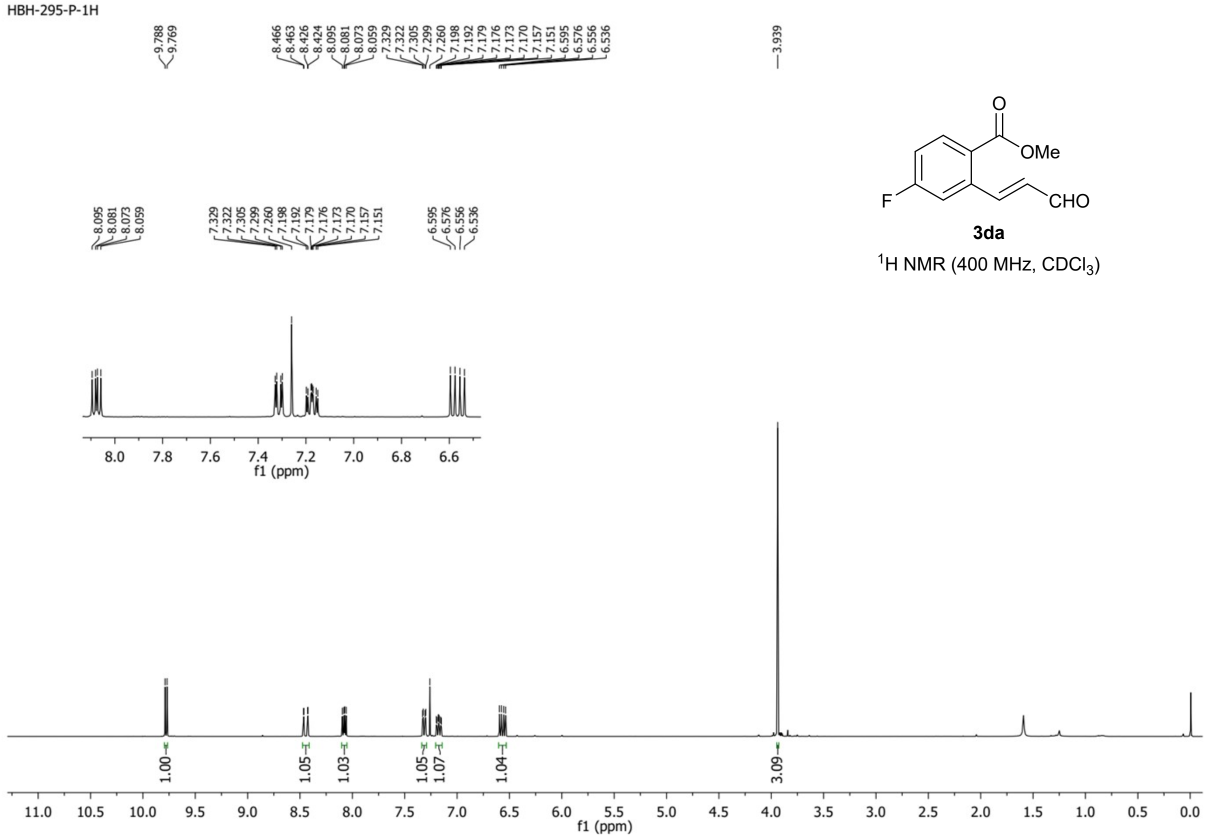

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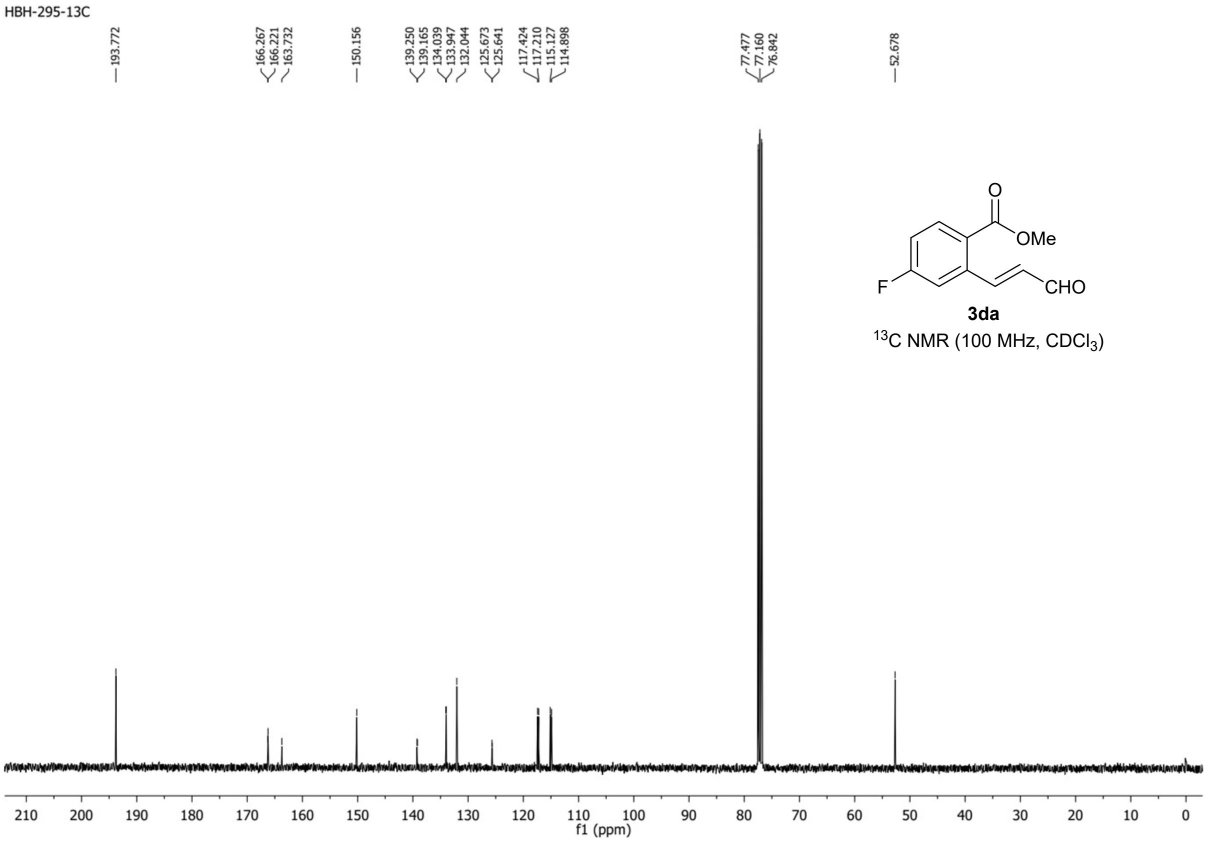

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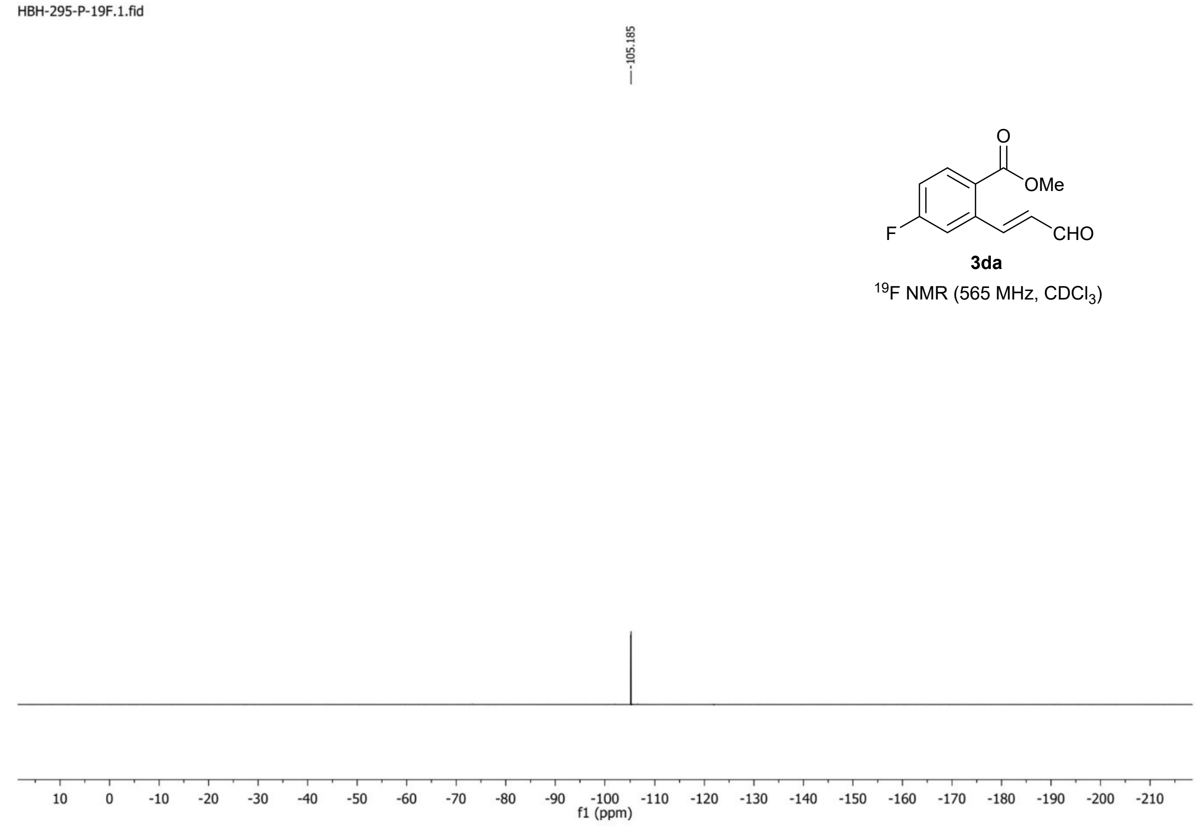

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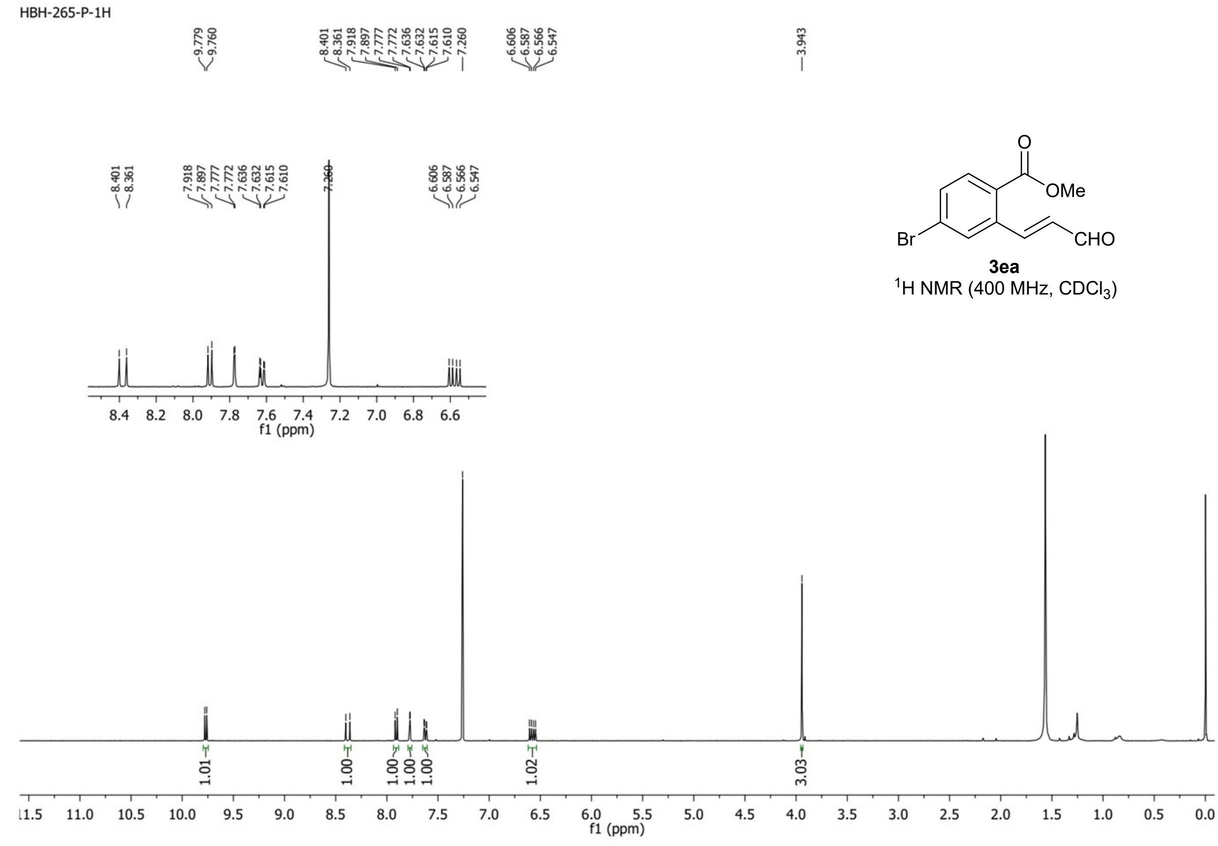

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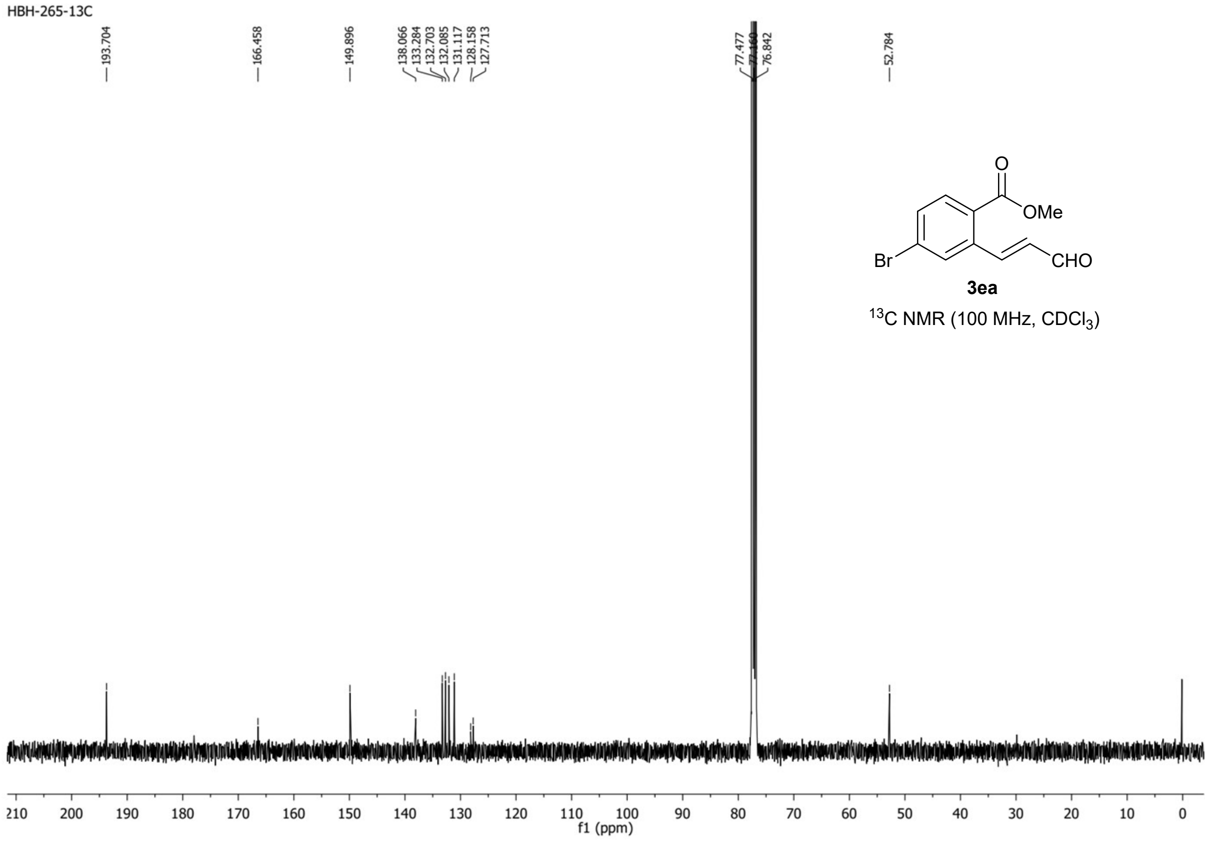
^{1}H NMR (400 MHz, $CDCl_3$)



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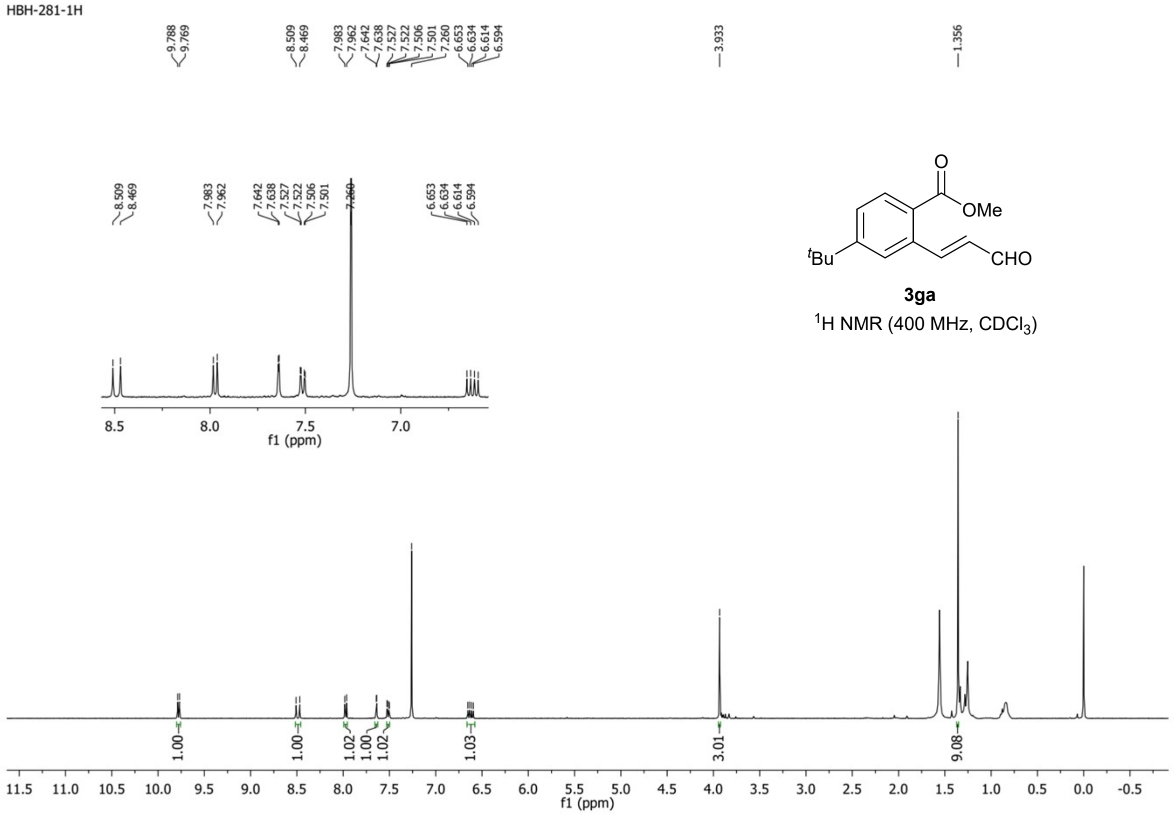

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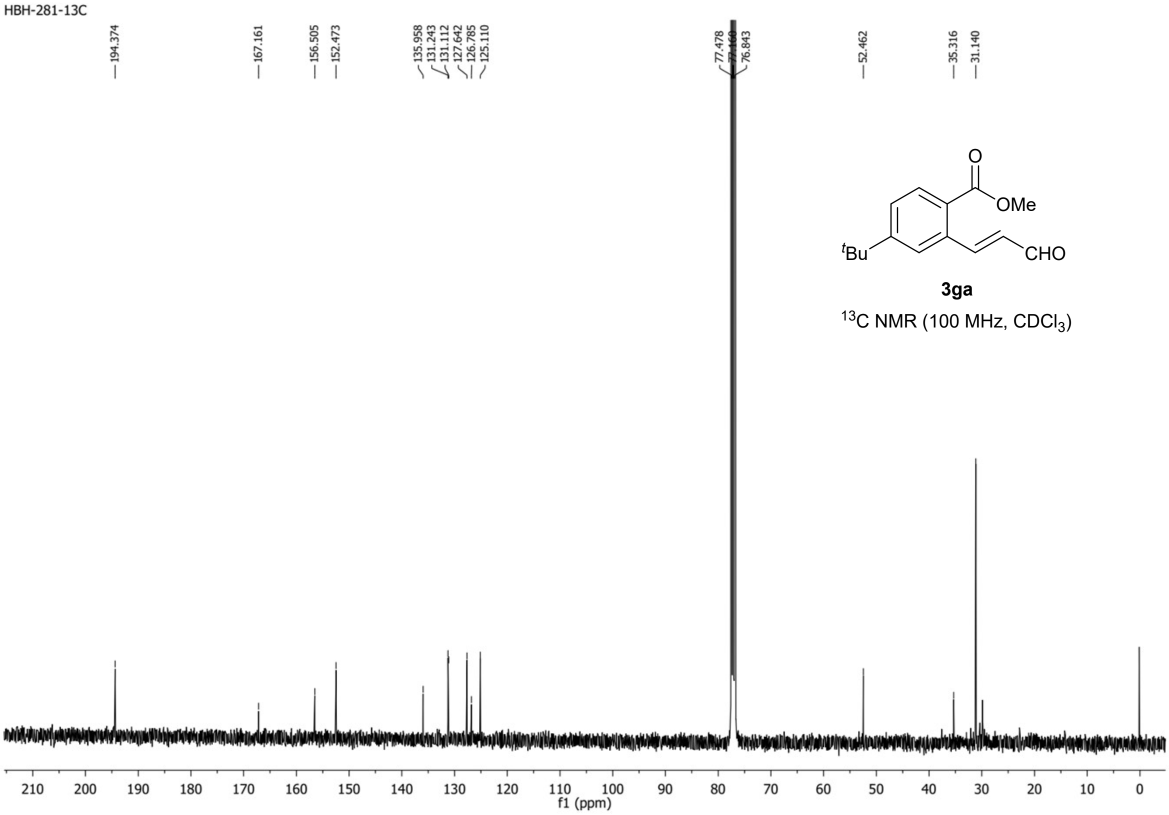

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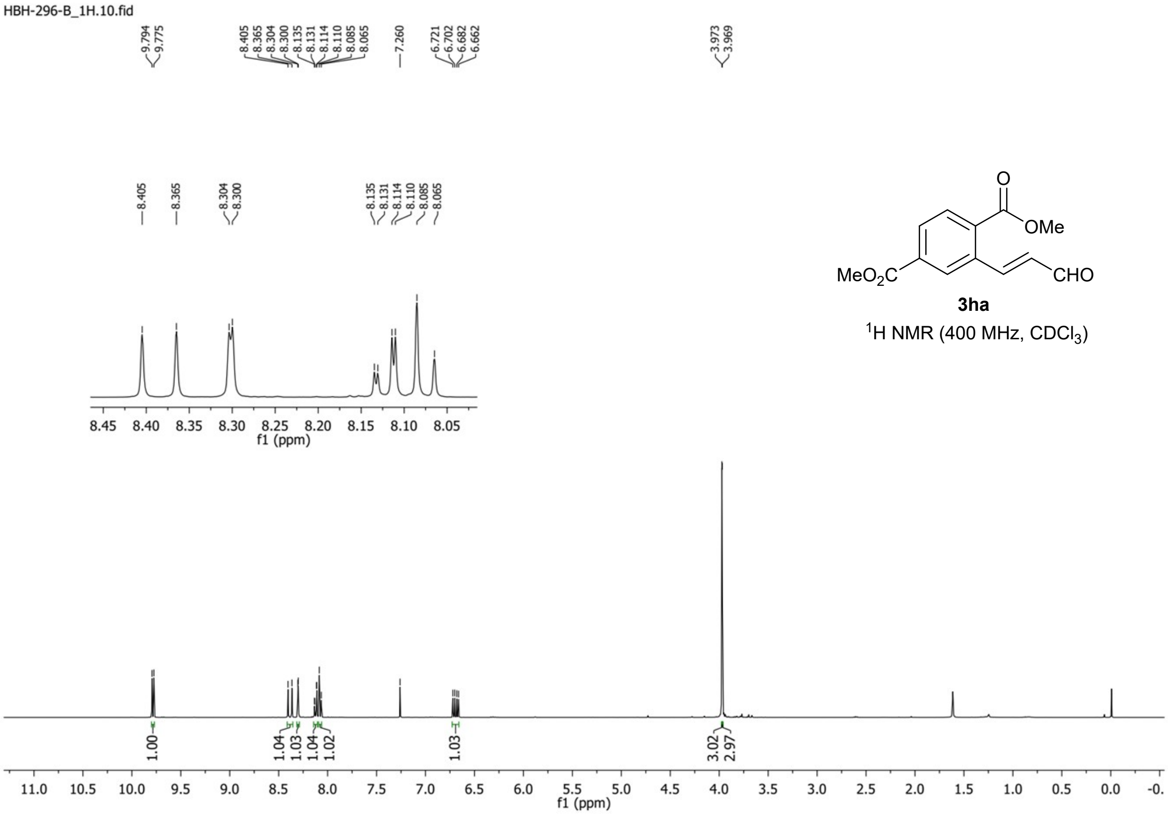

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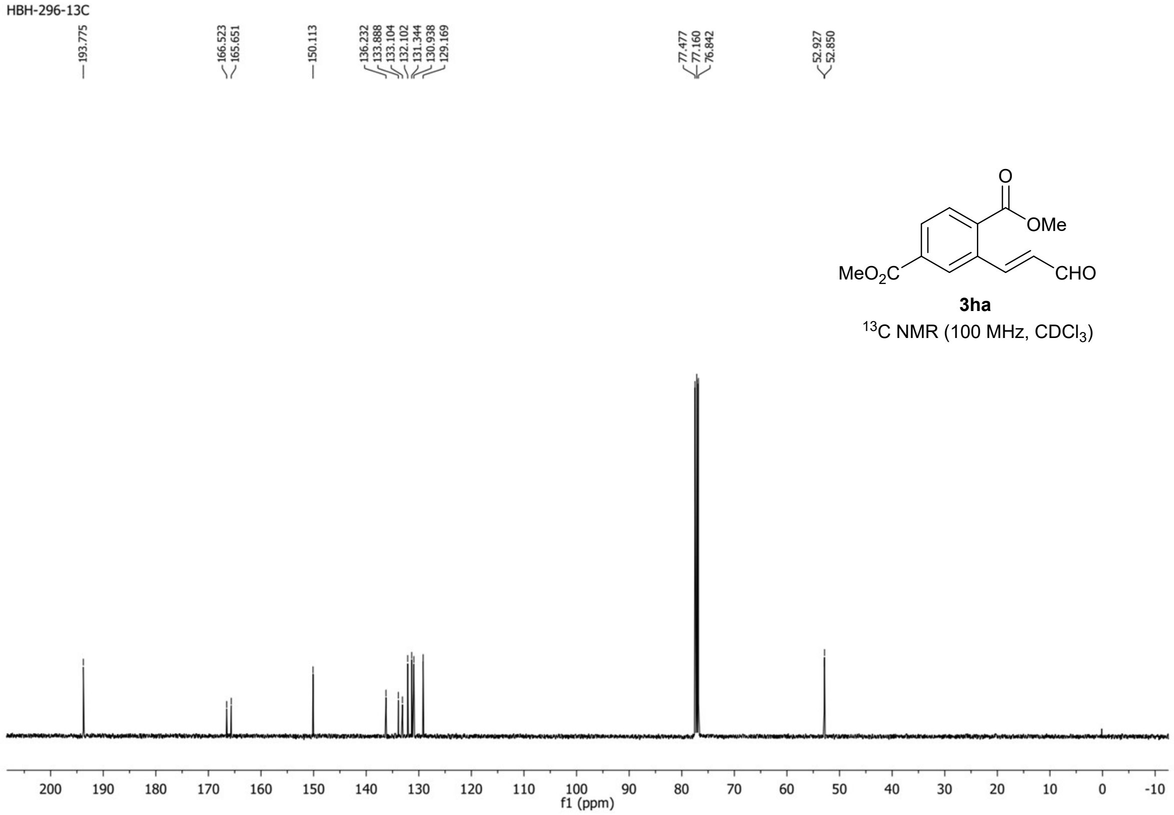

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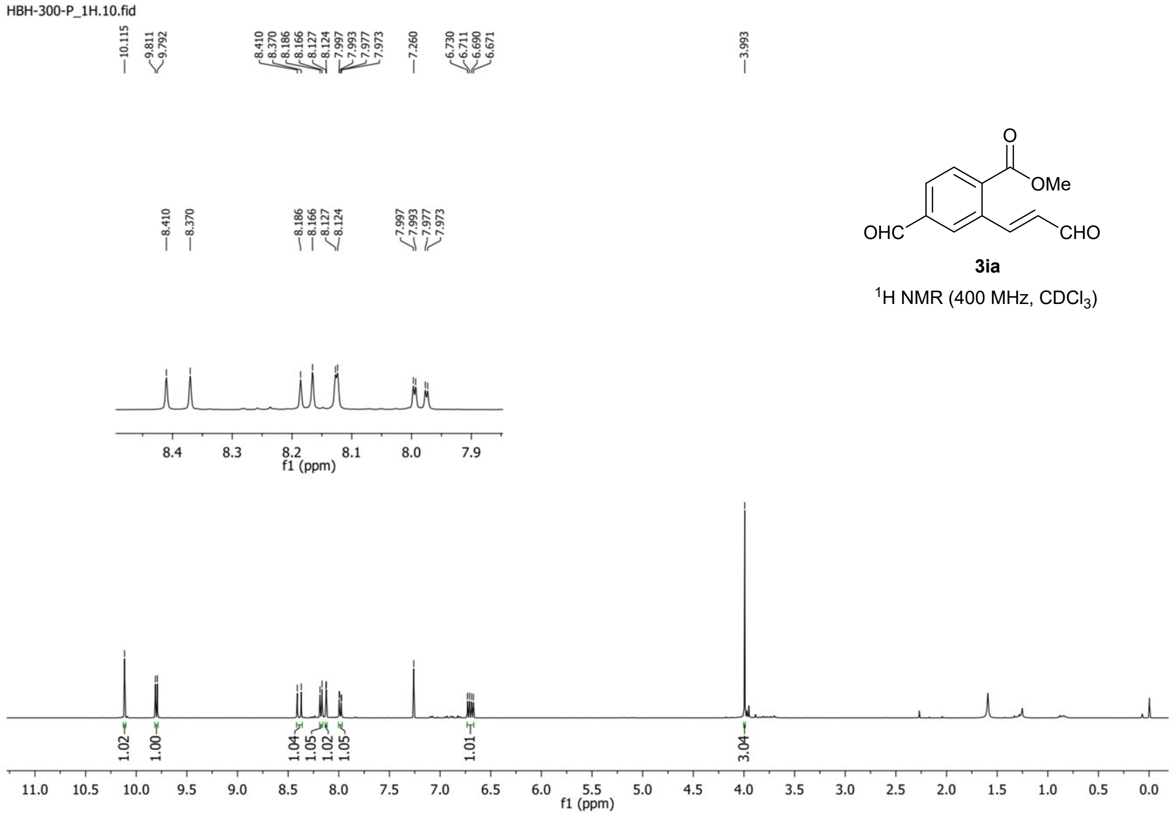

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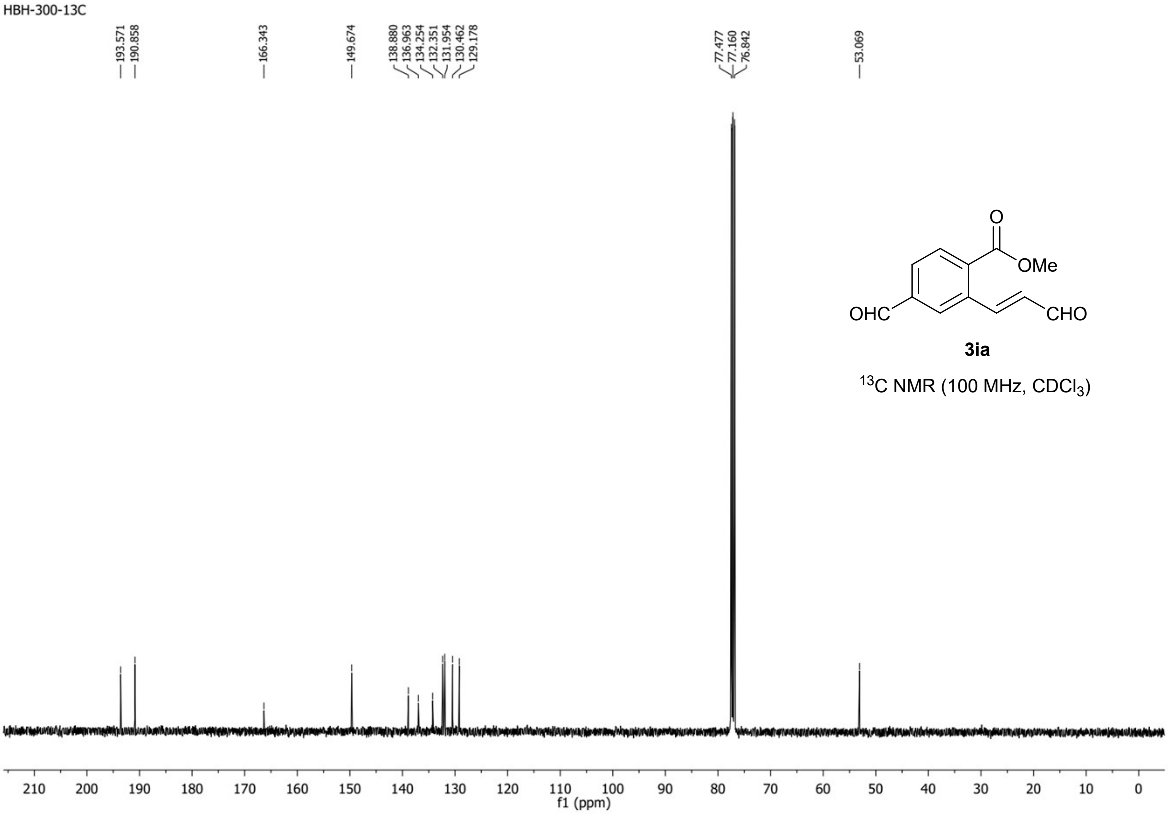

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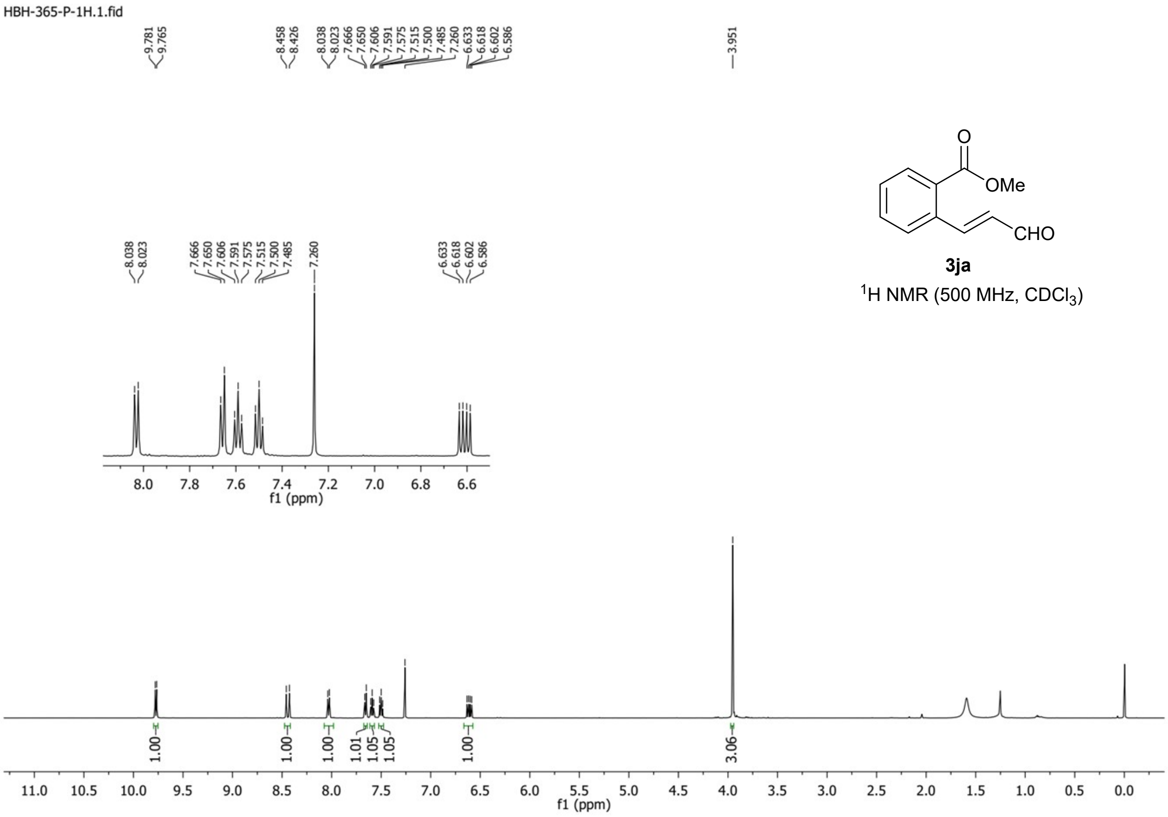

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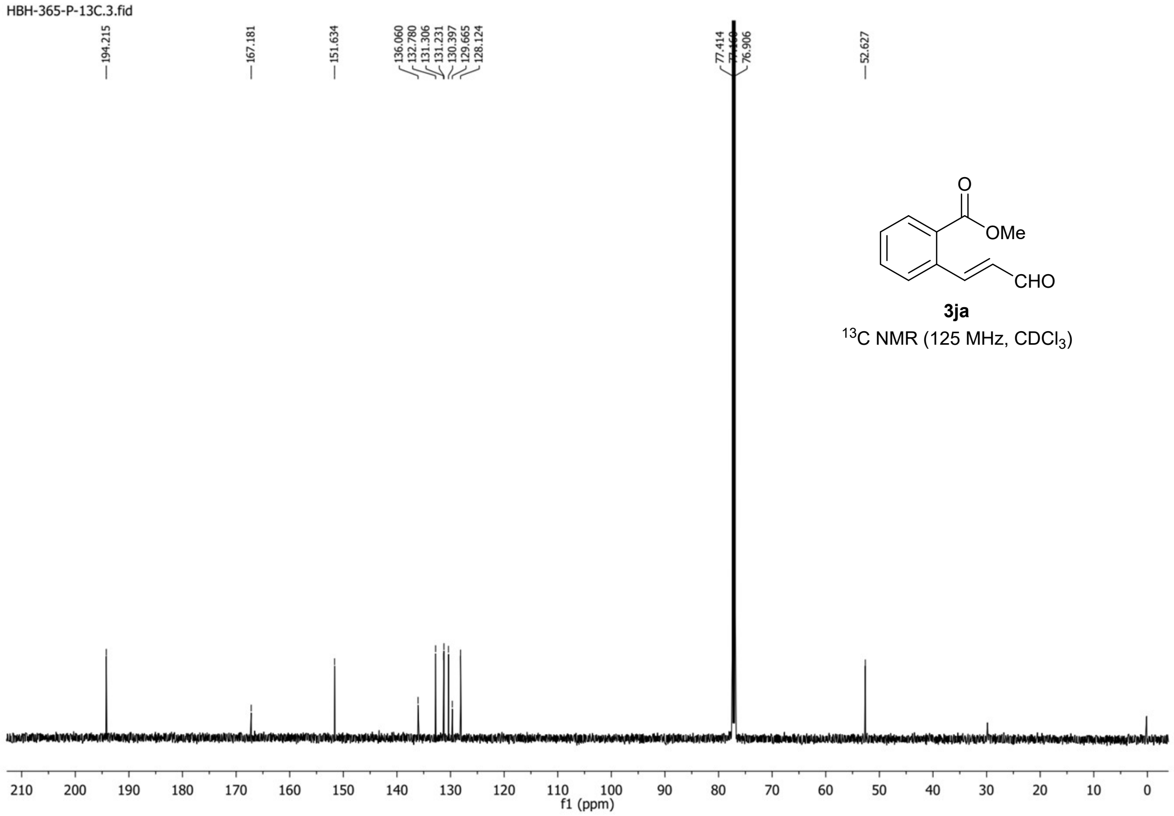

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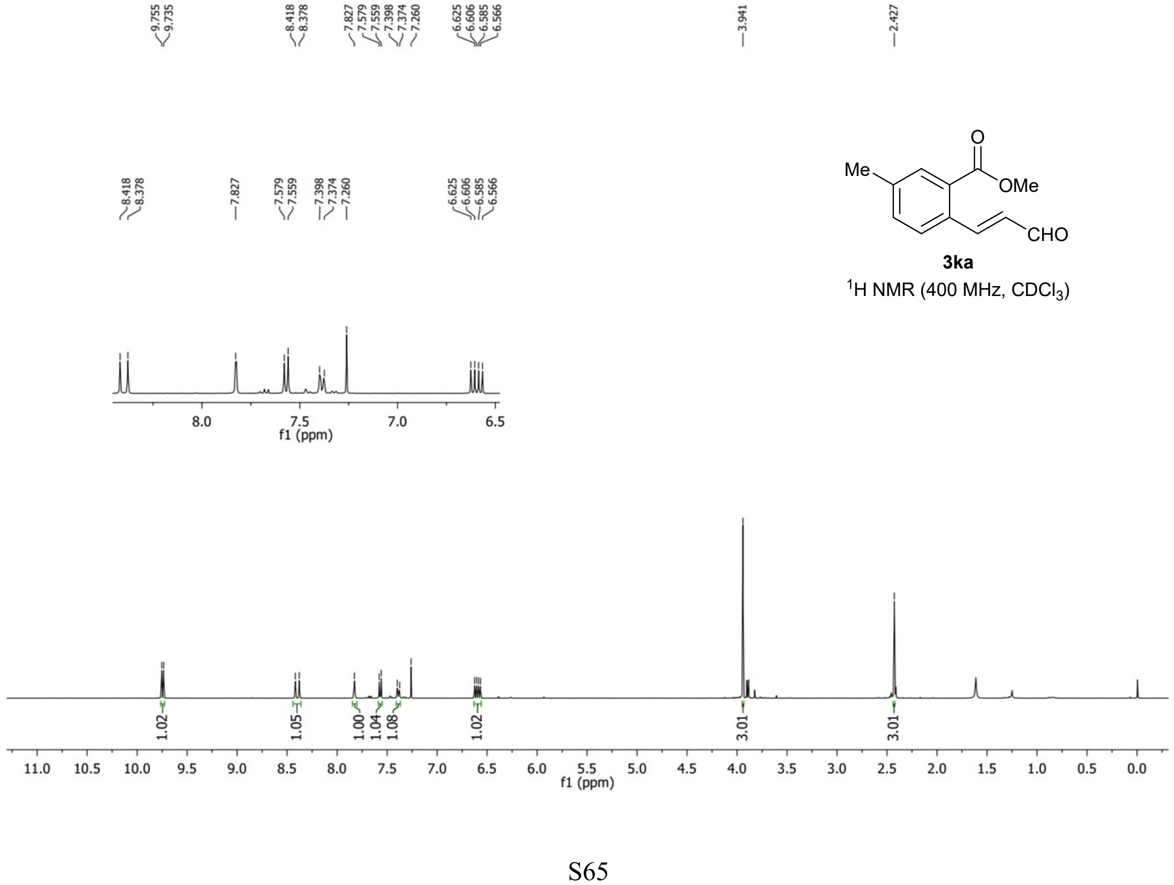

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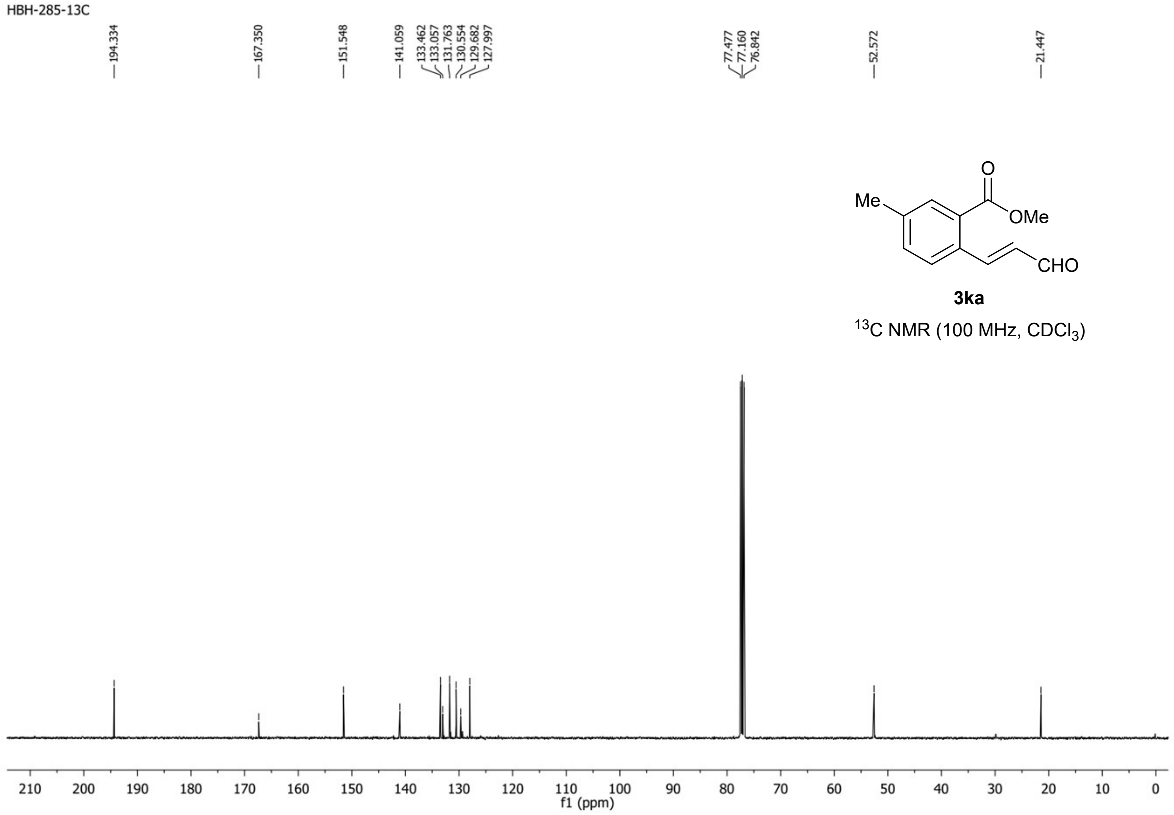

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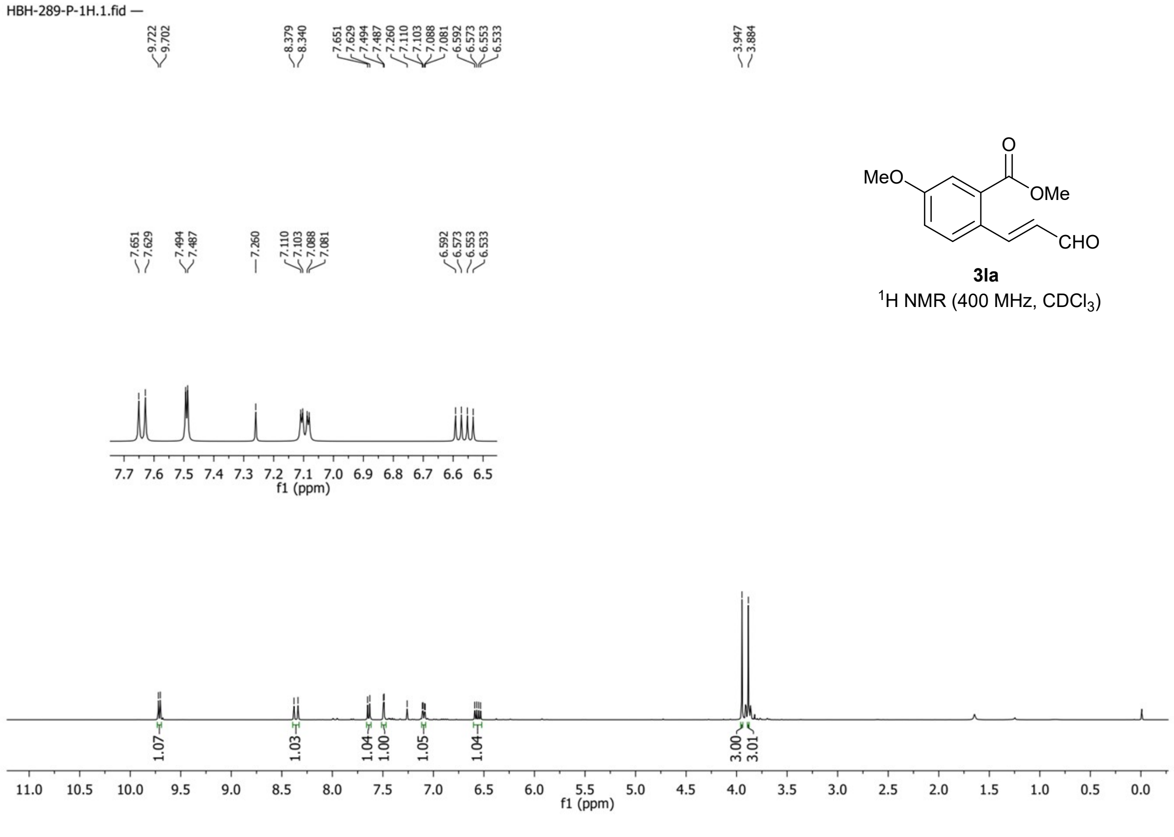

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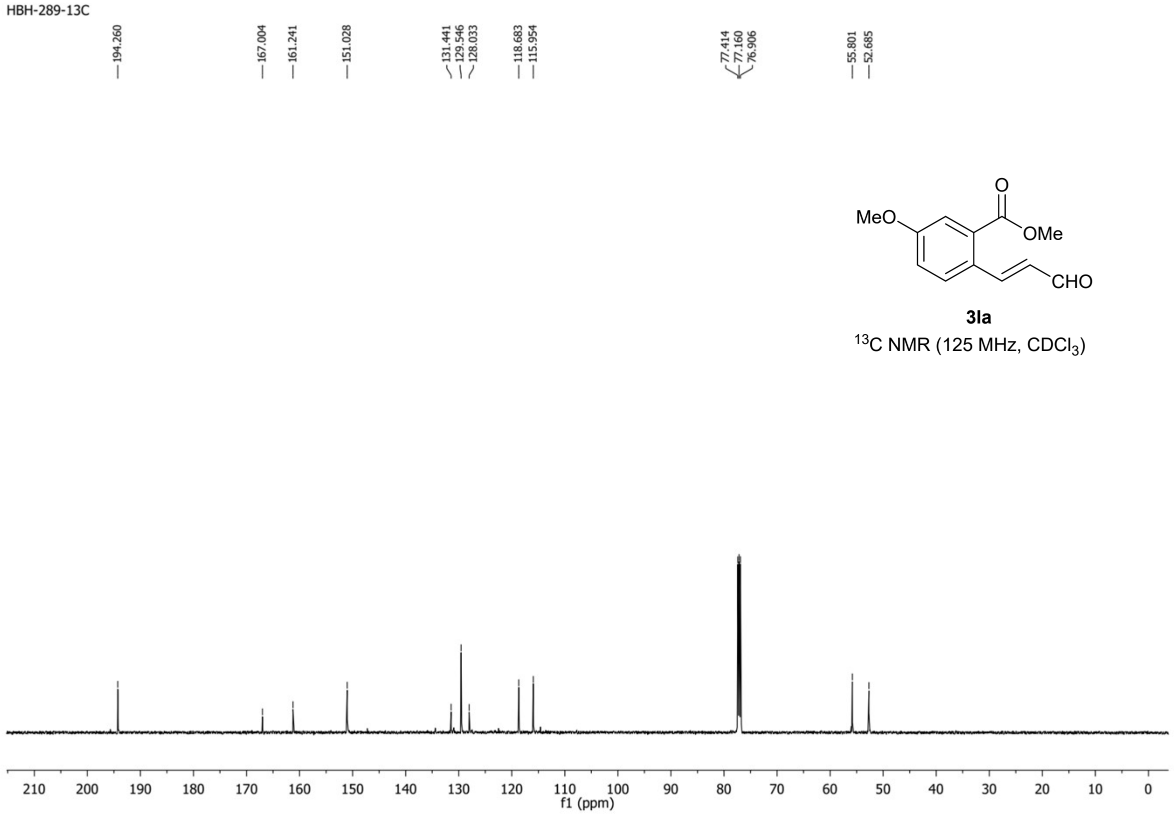

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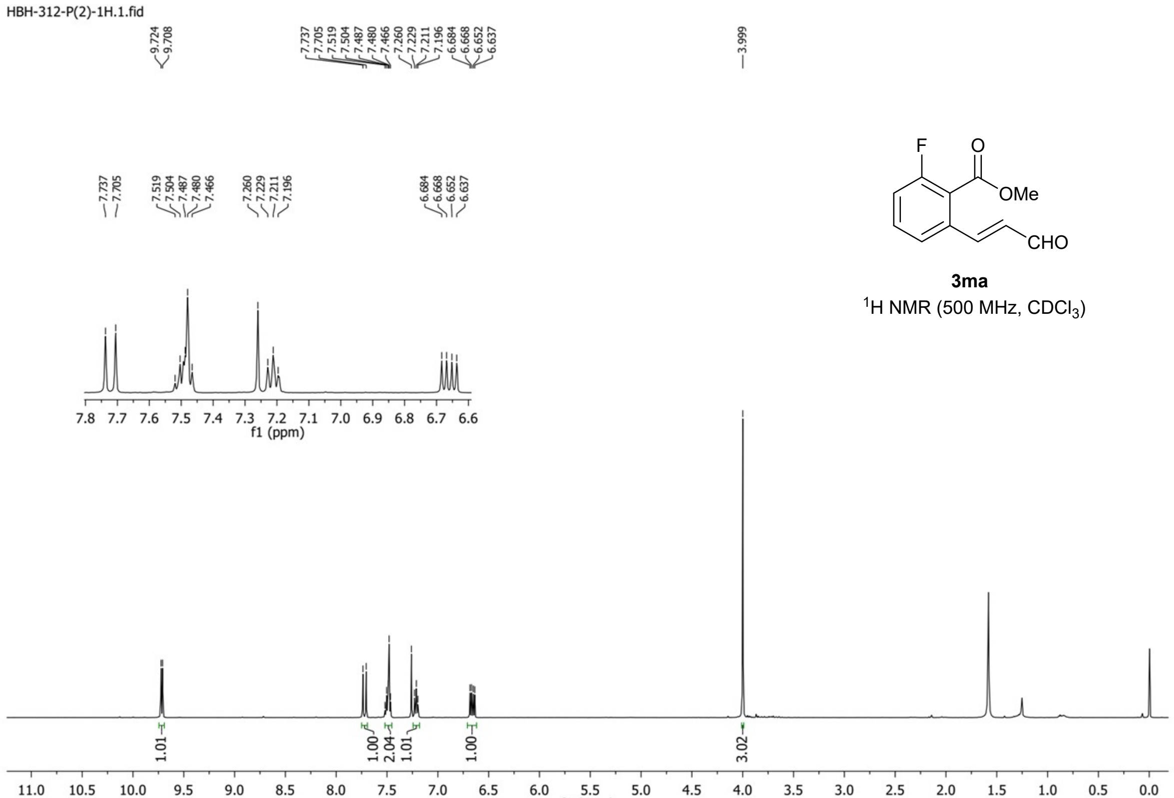

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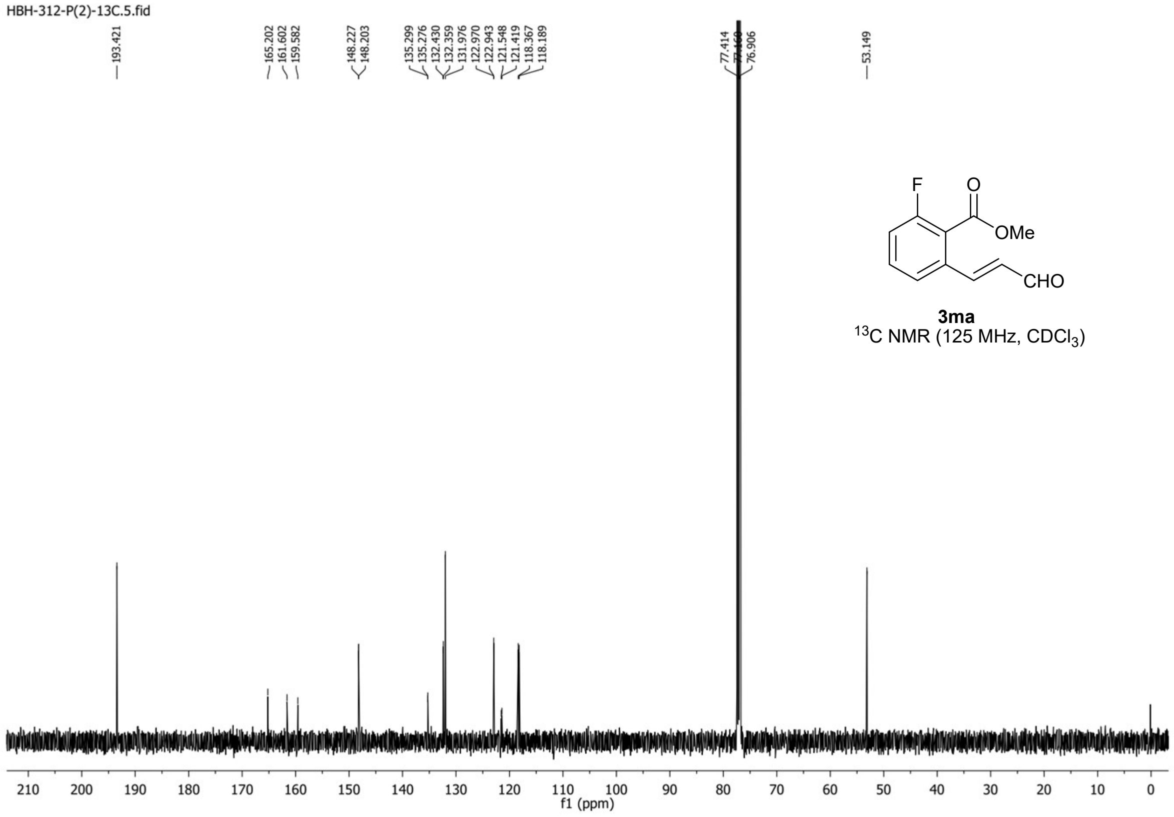

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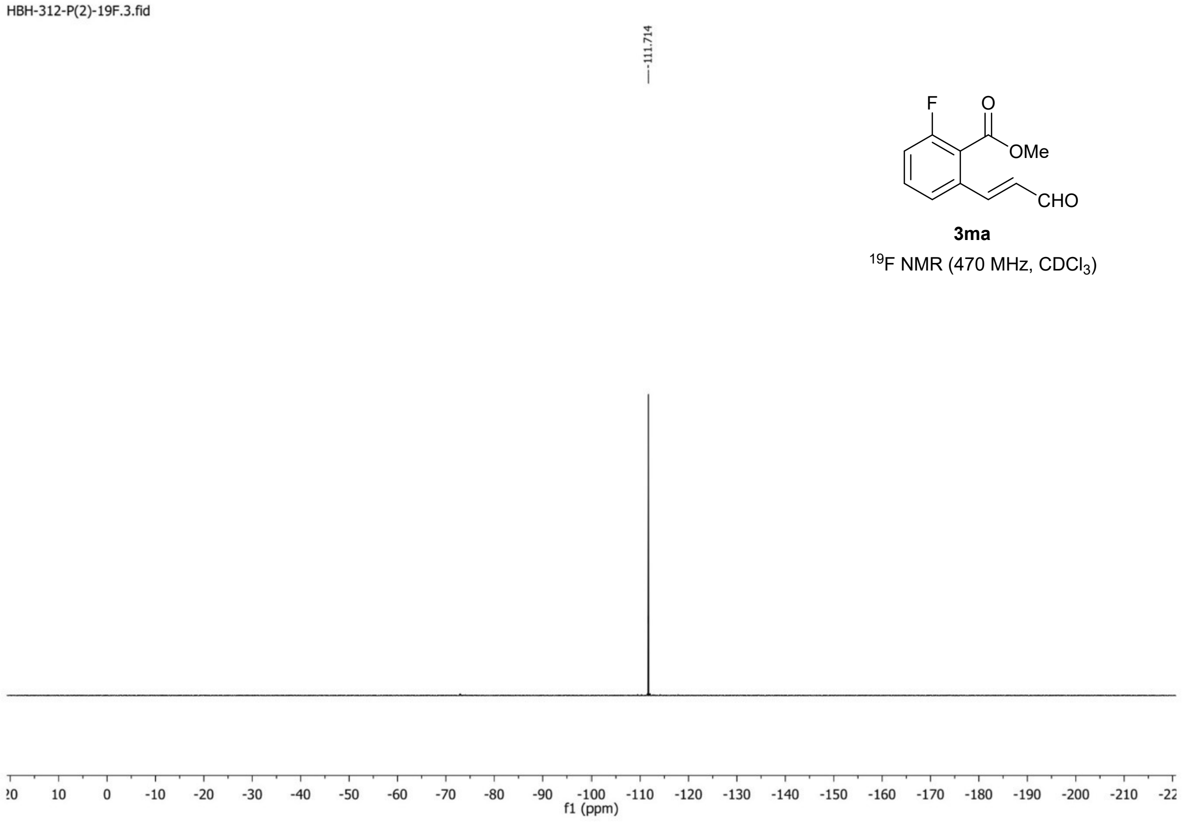

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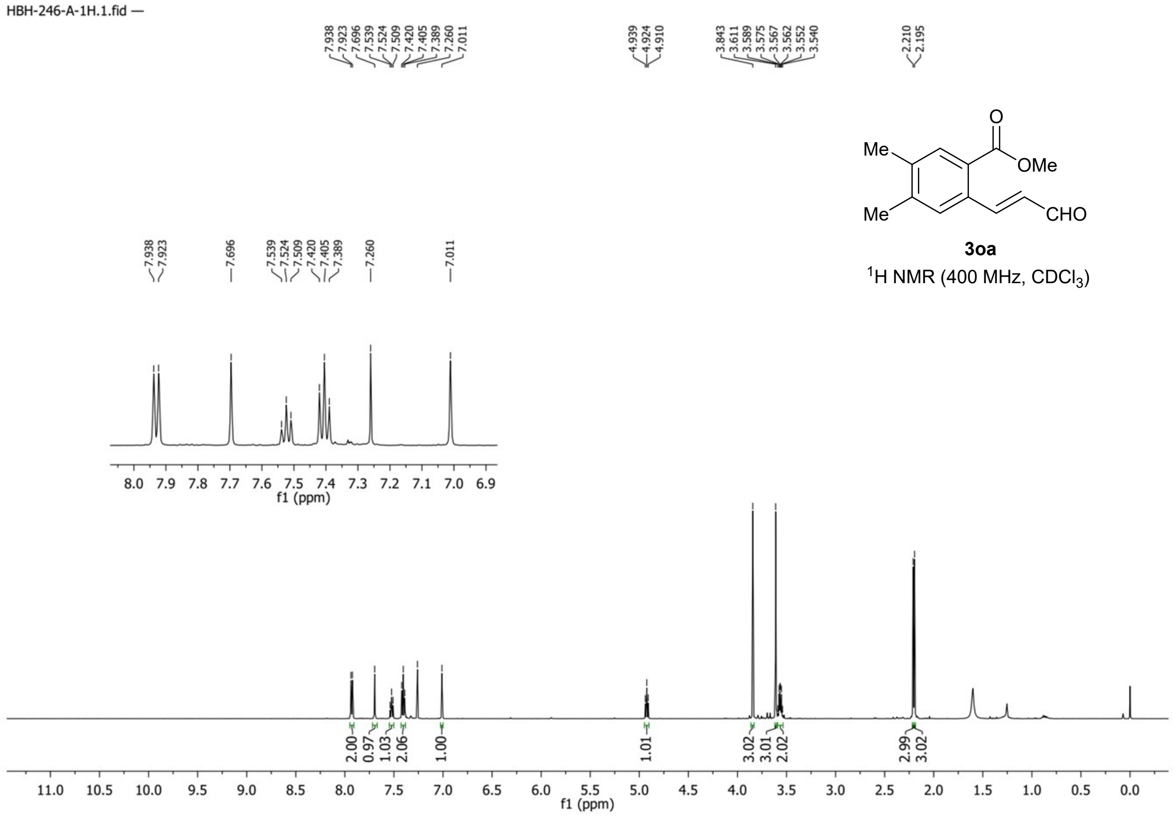

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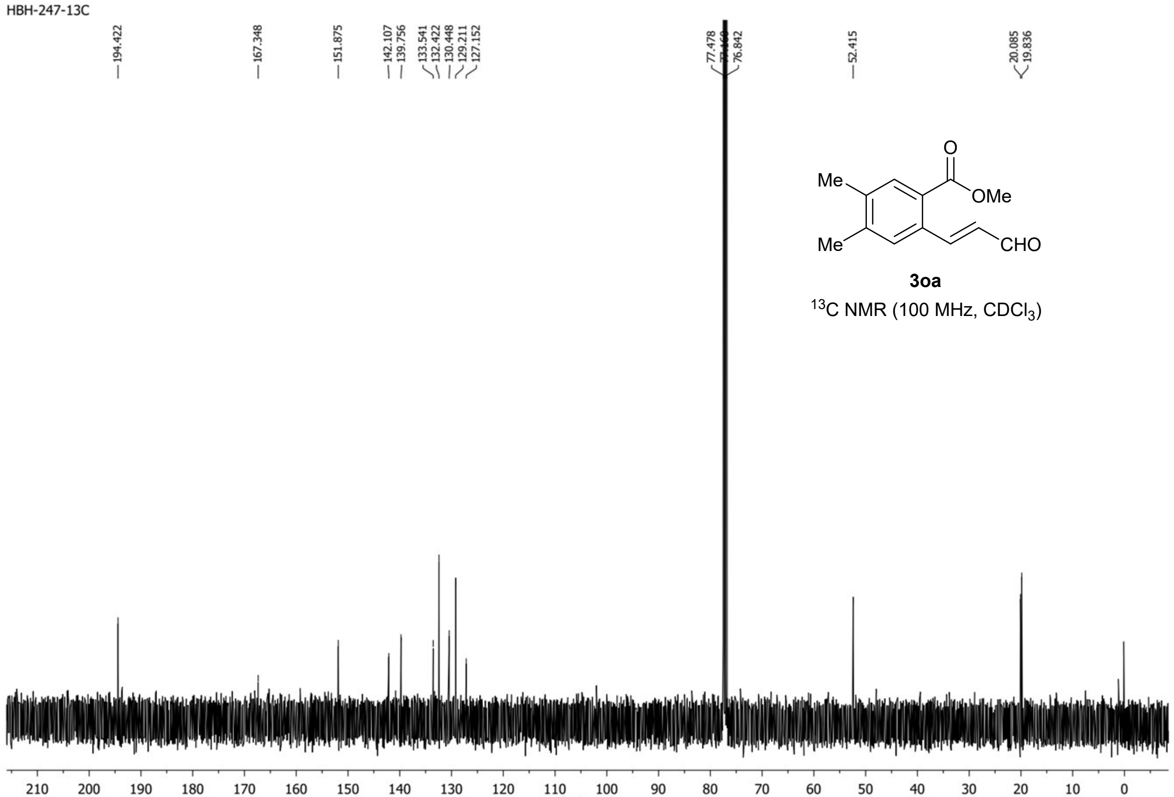

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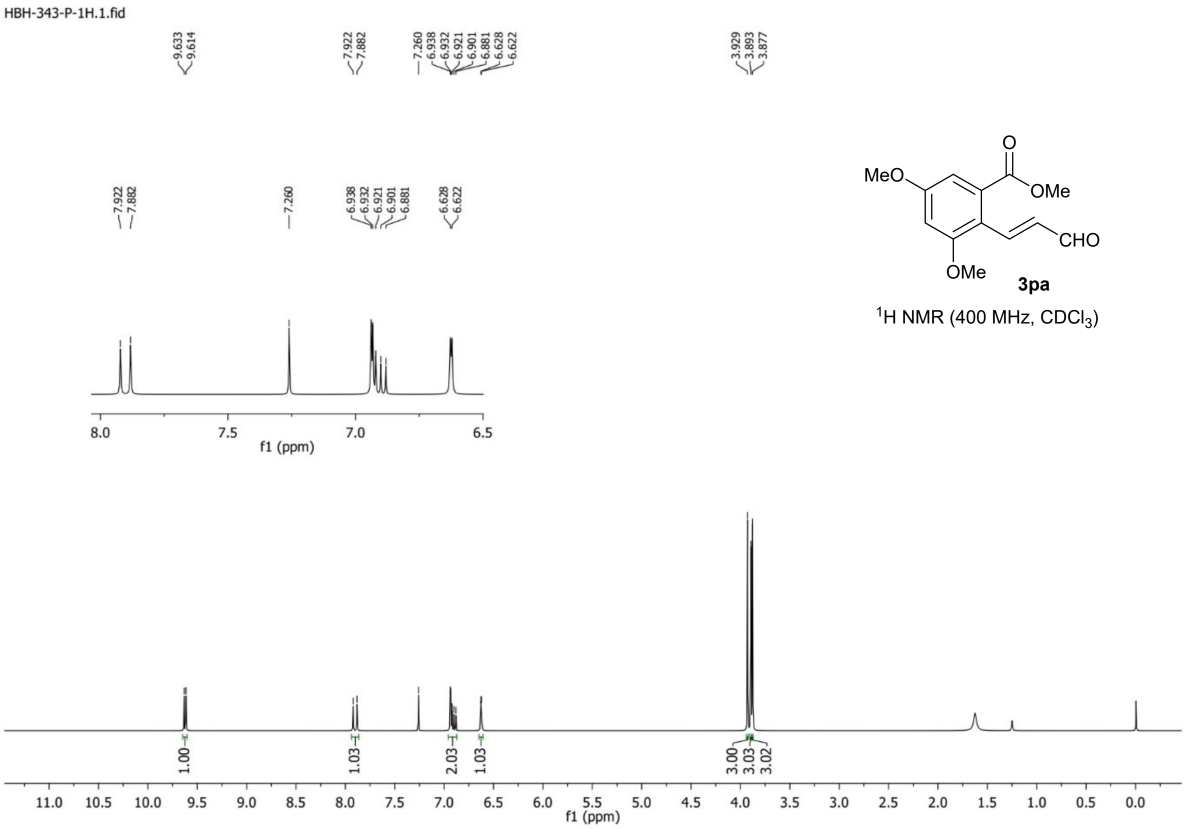

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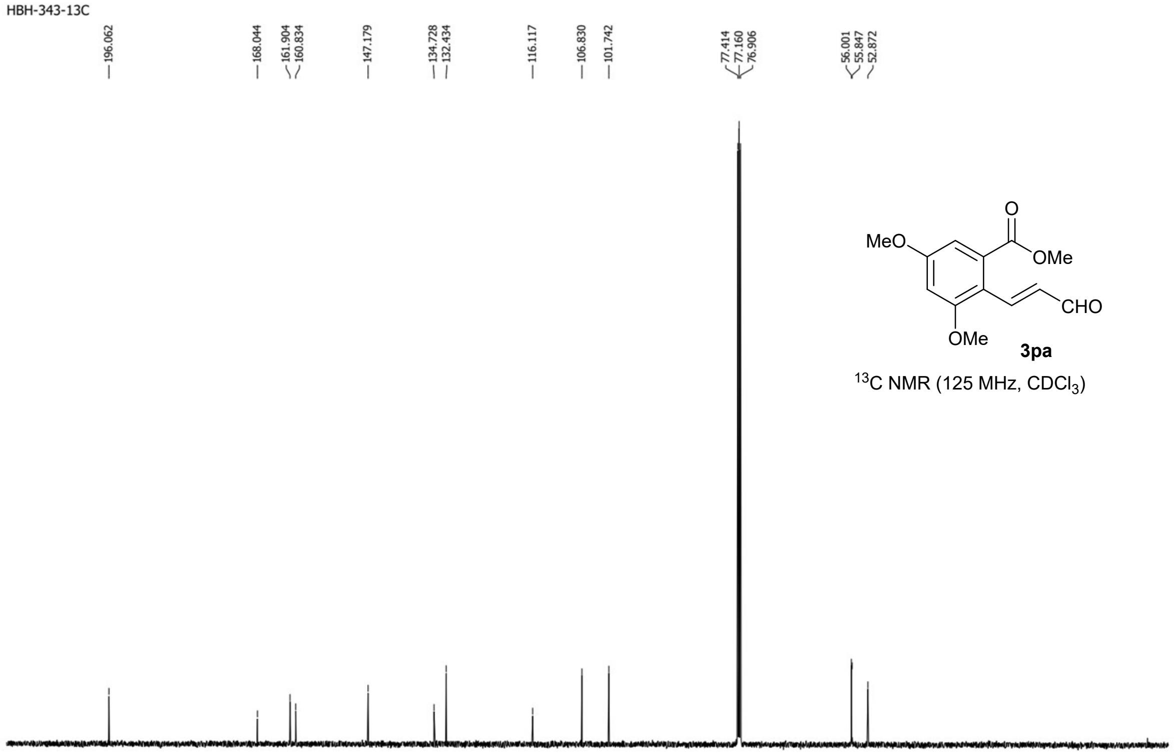

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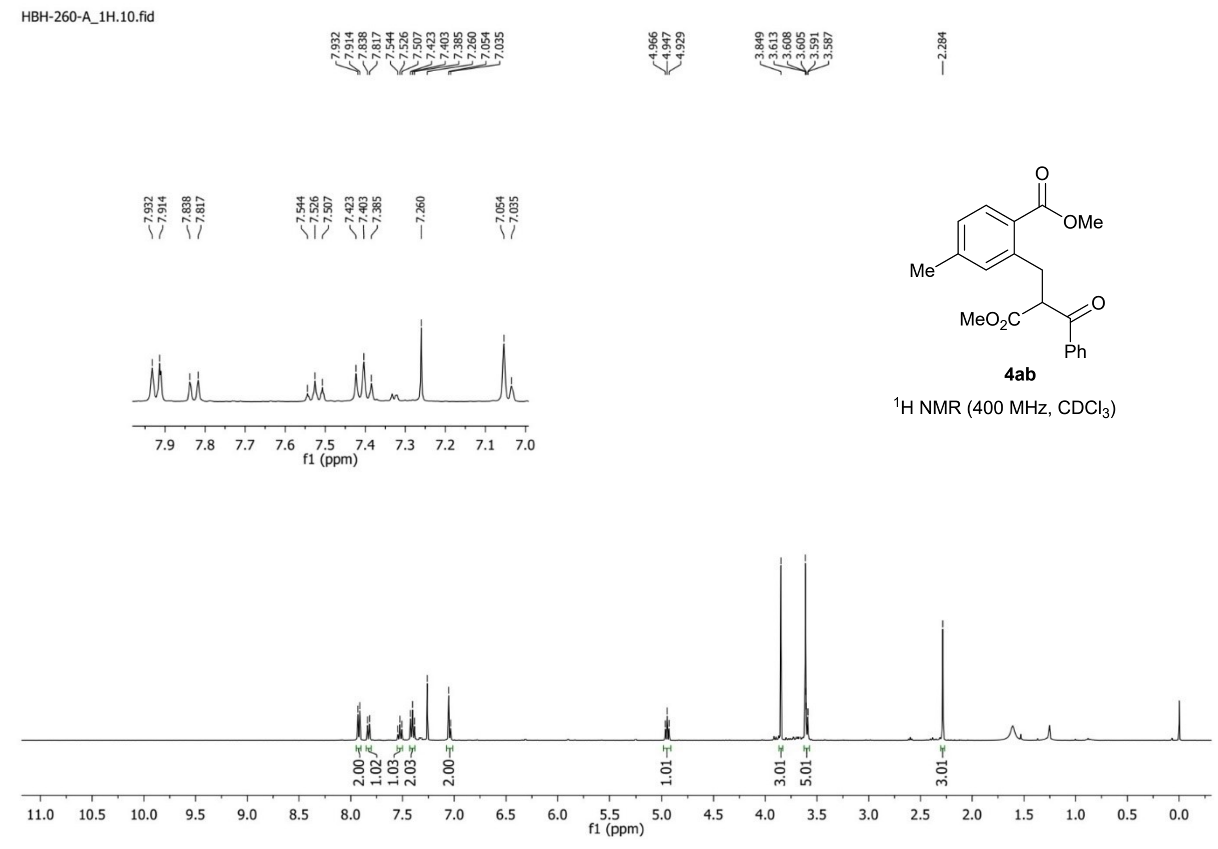

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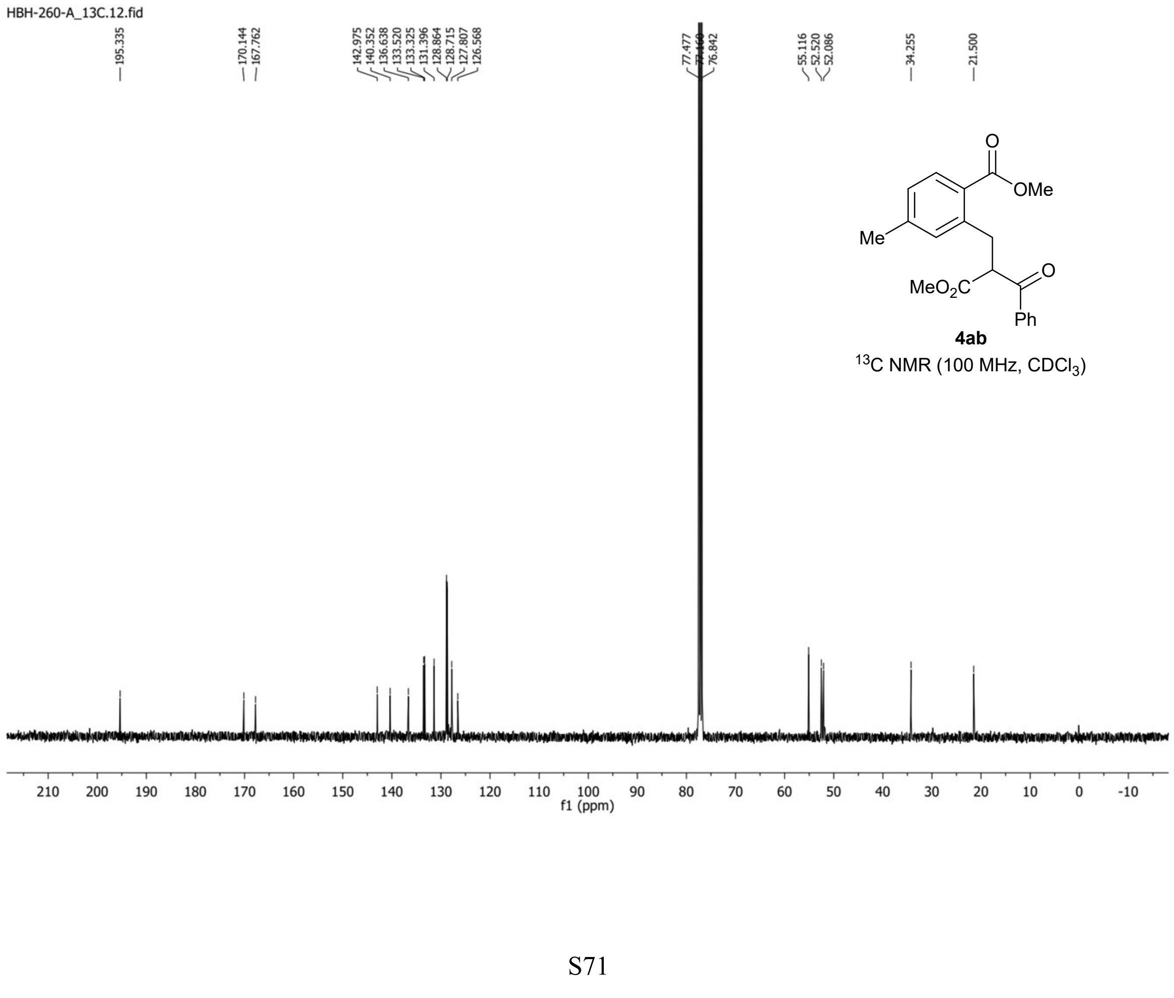

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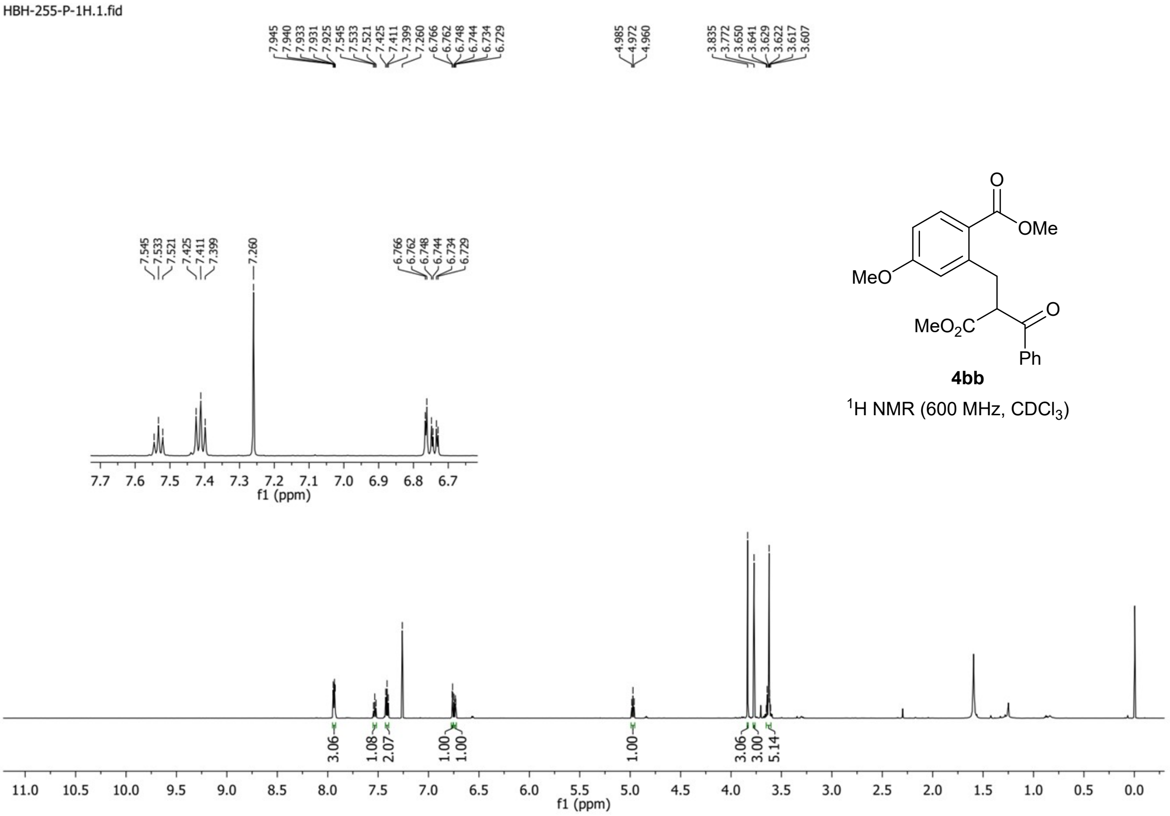

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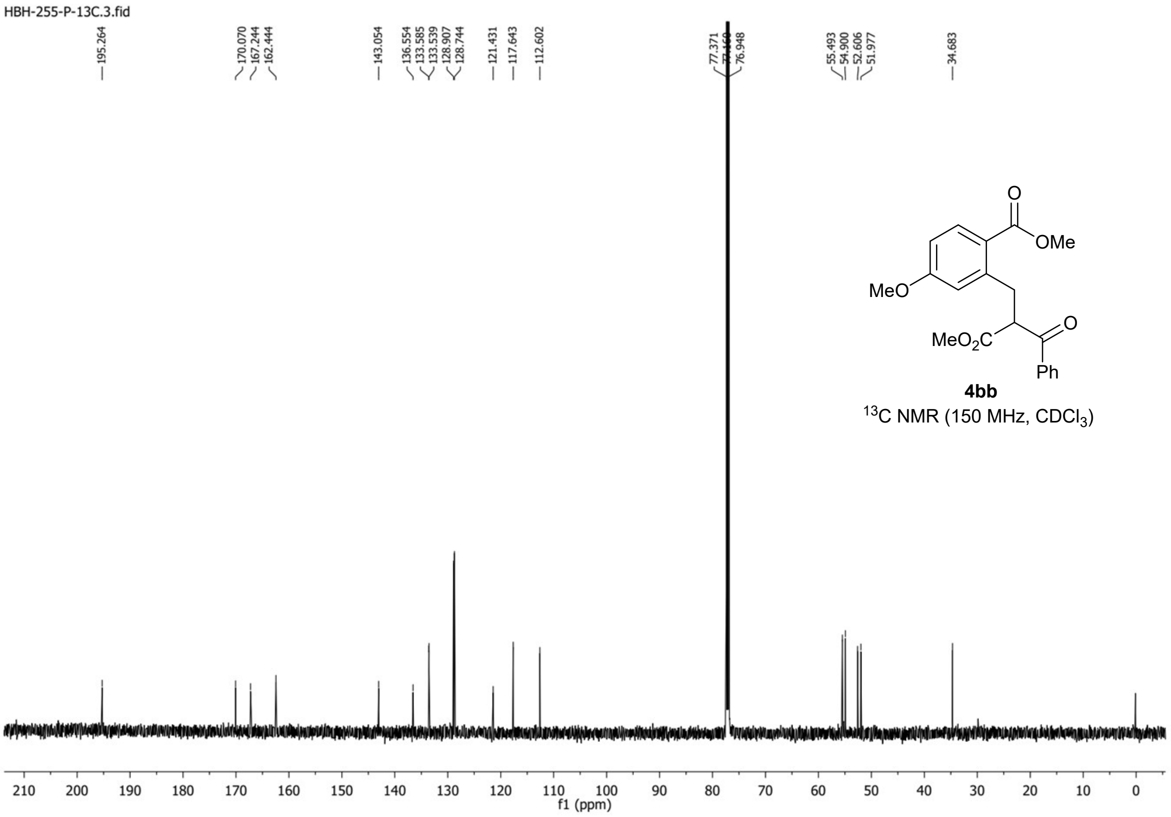

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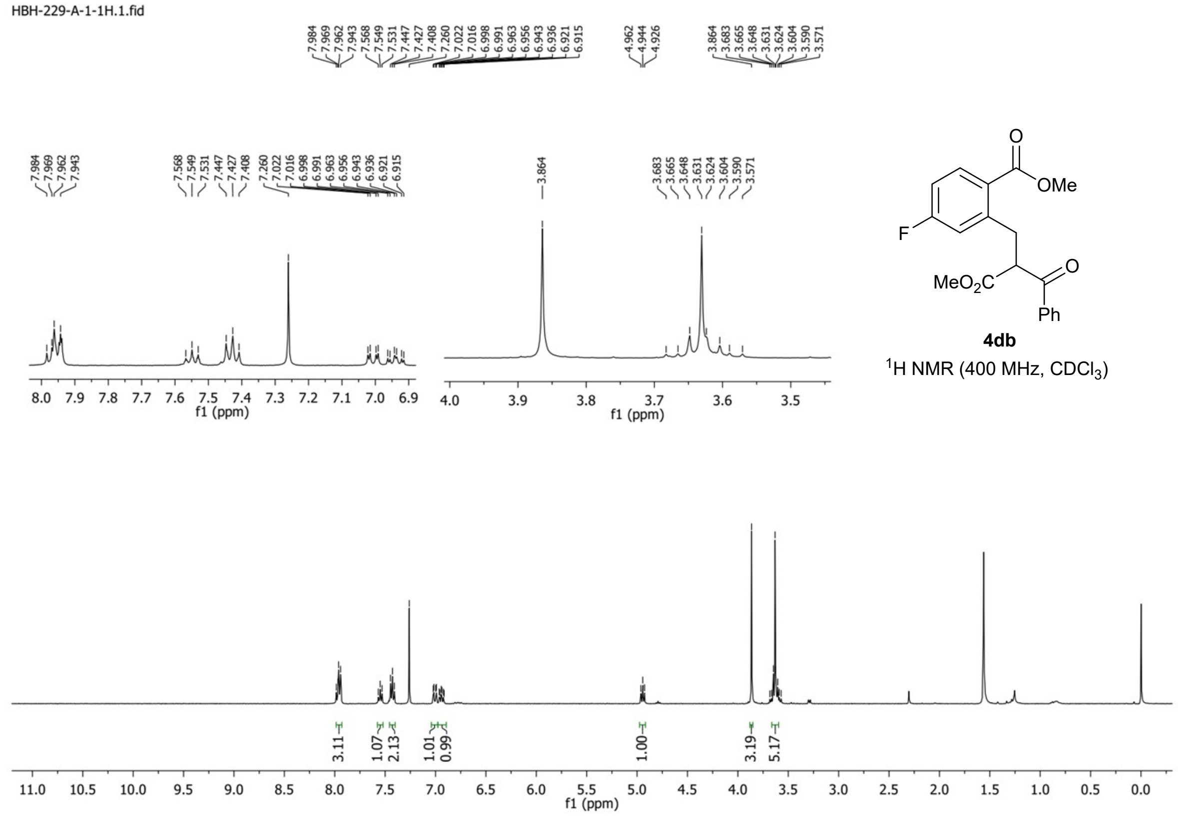
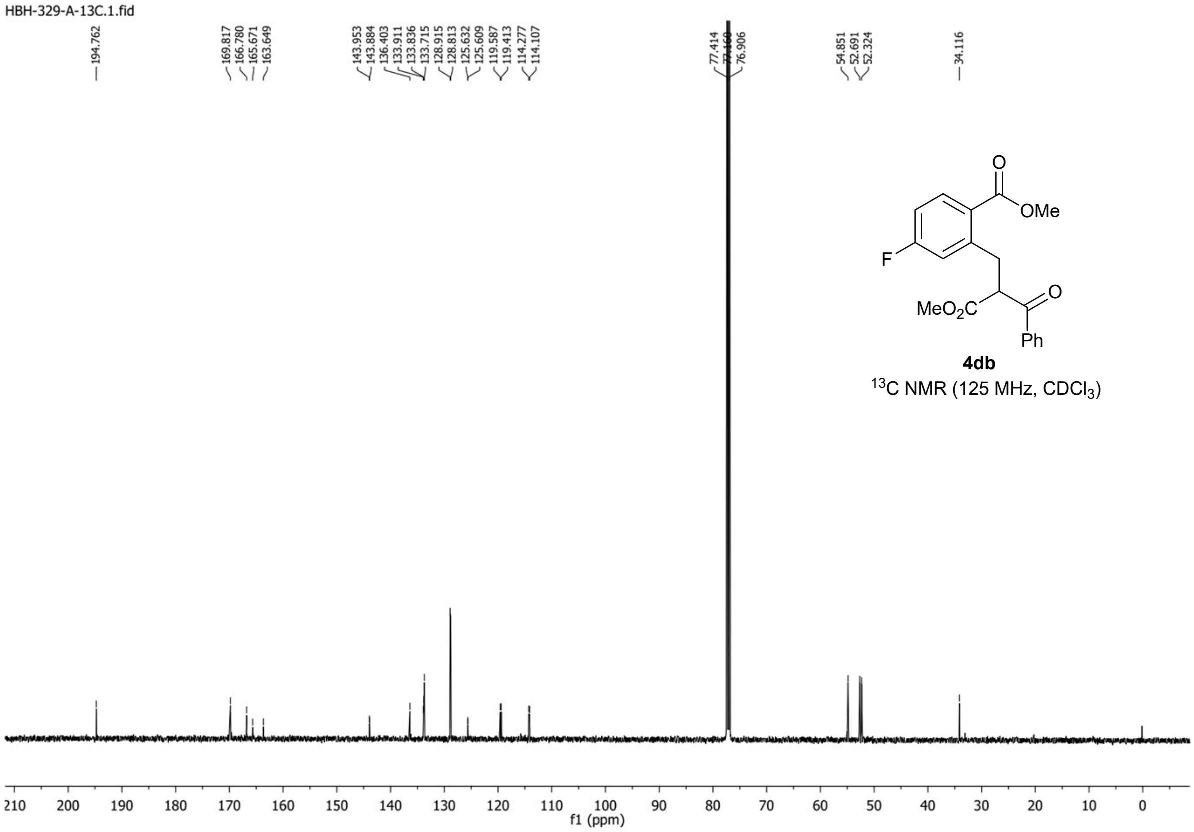


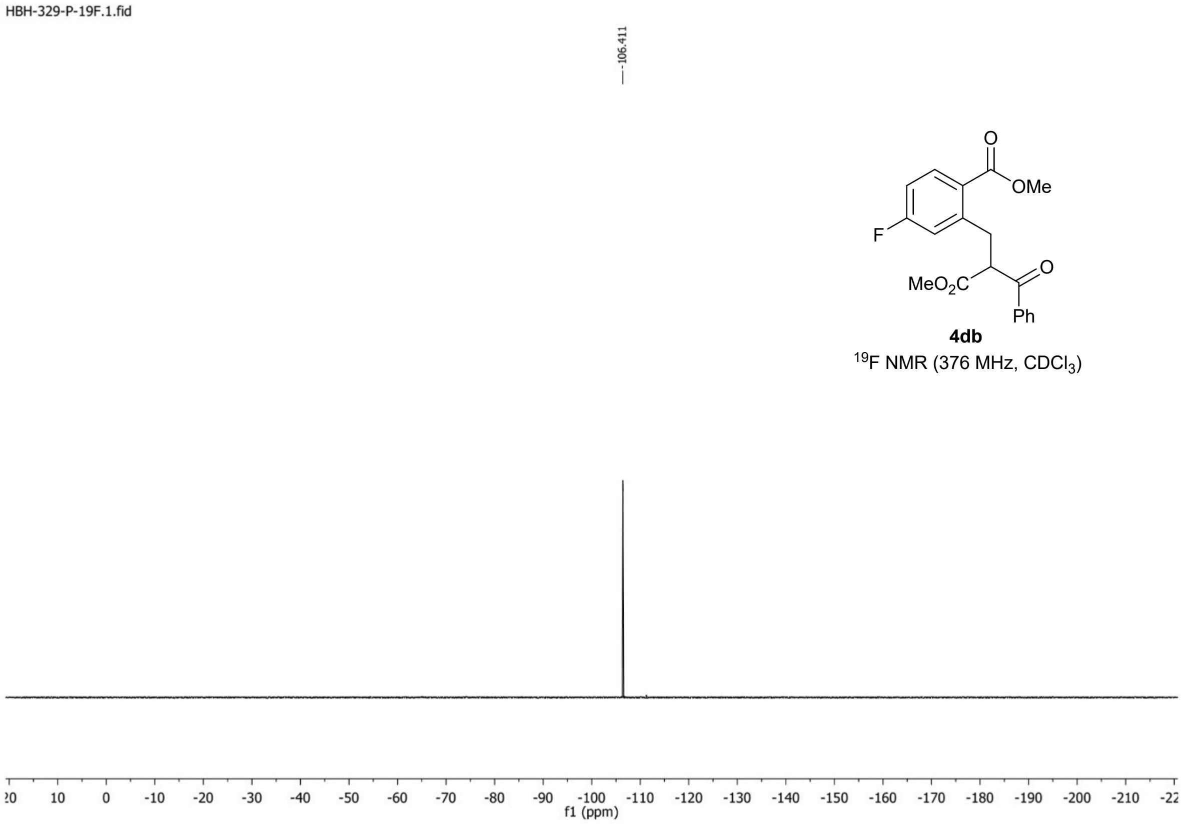
4db

^{1}H NMR (400 MHz, CDCl$_3$)



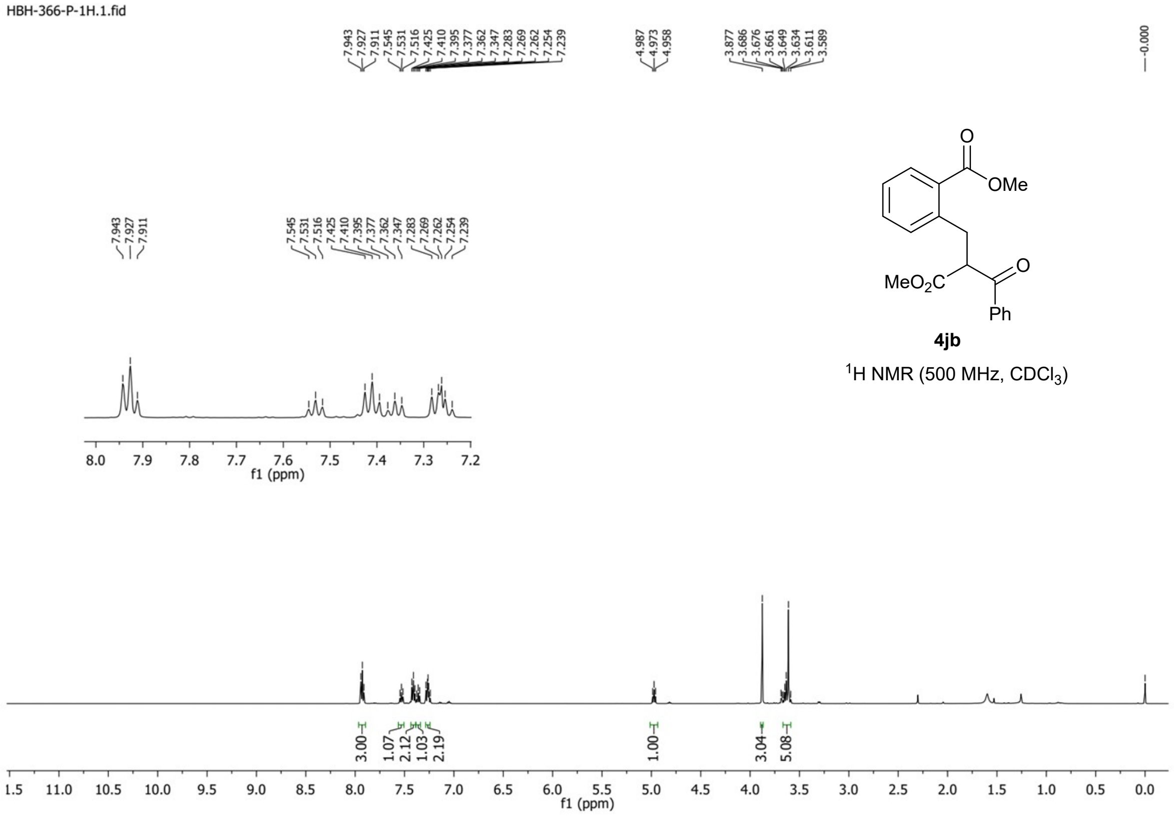
4db

^{13}C NMR (125 MHz, CDCl$_3$)



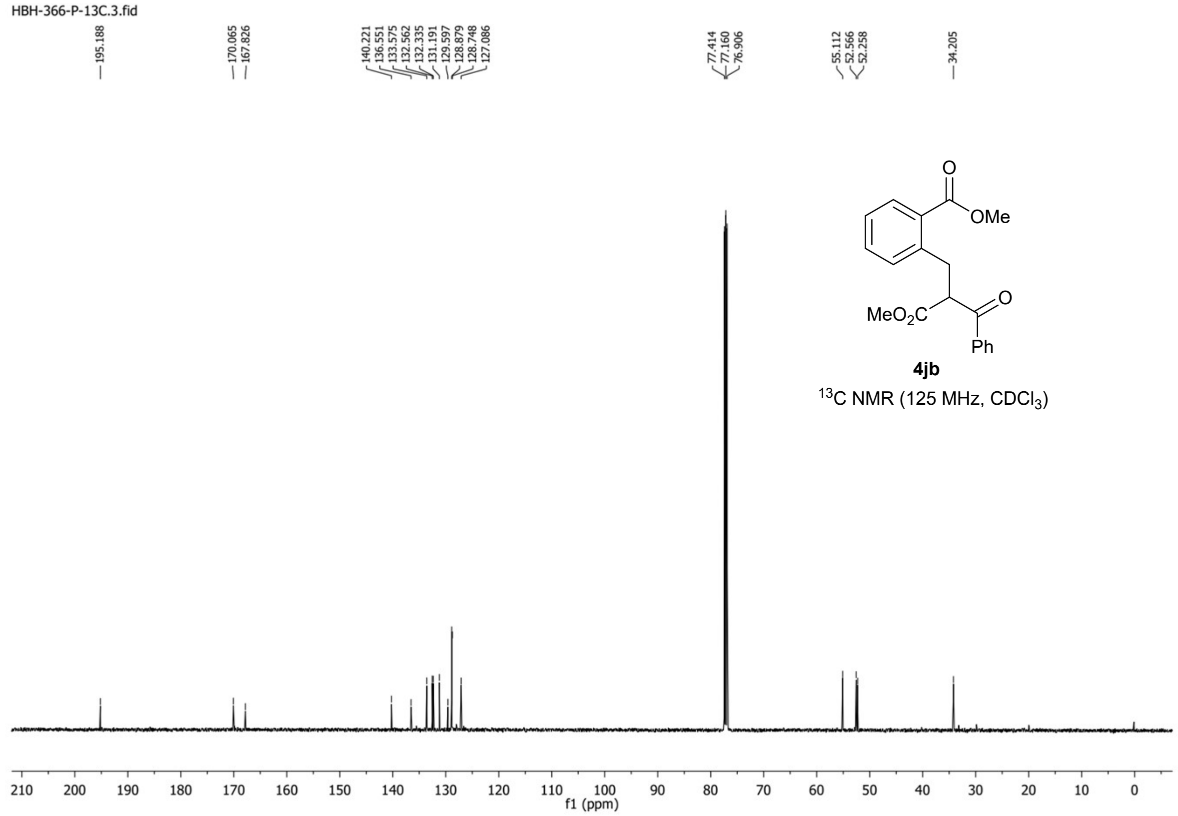
4db

^{19}F NMR (376 MHz, CDCl$_3$)



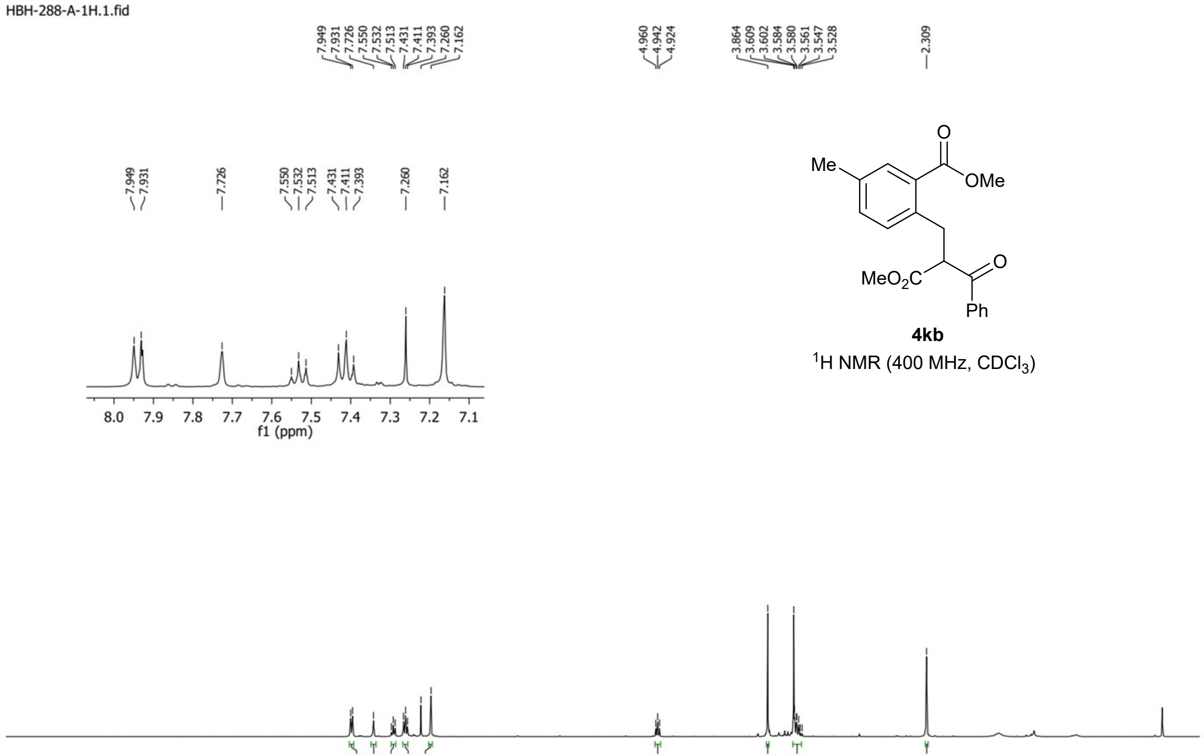
4jb

^{1}H NMR (500 MHz, CDCl$_3$)



4jb

^{13}C NMR (125 MHz, CDCl$_3$)



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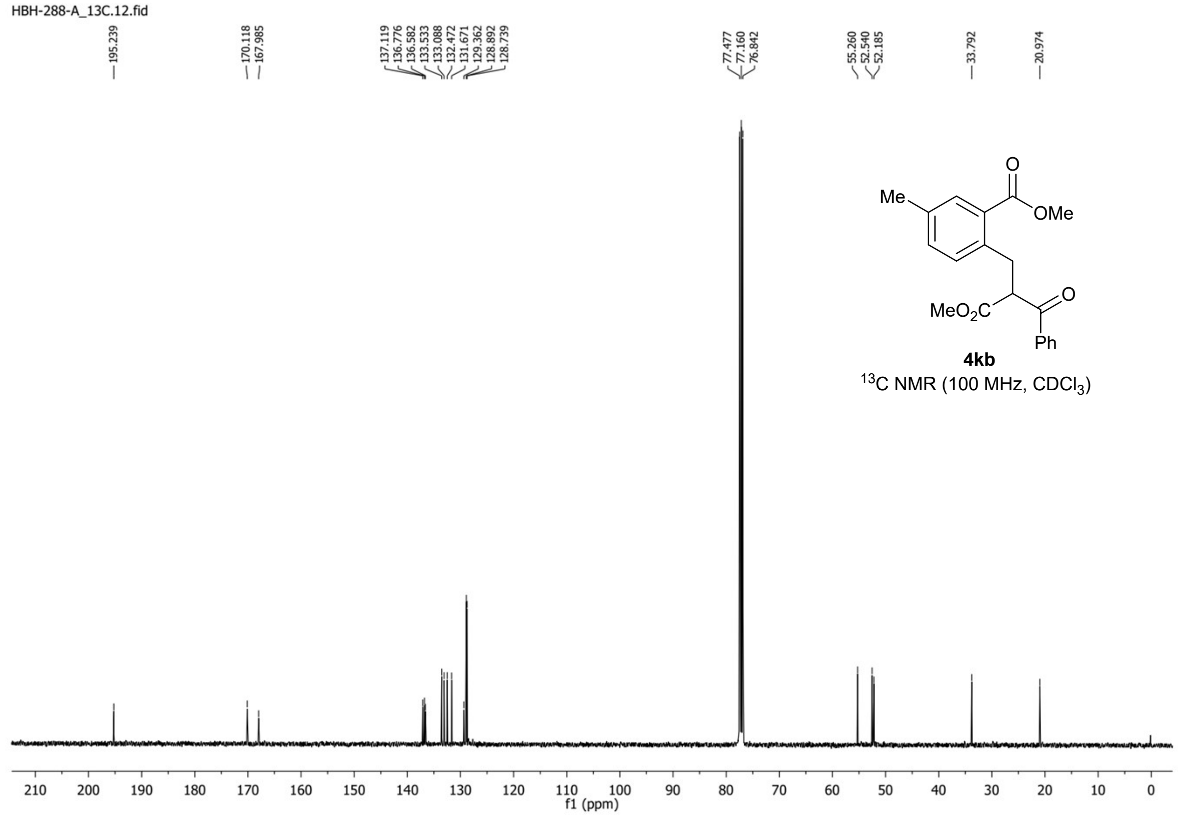
^{1}H NMR (400 MHz, CDCl$_3$)



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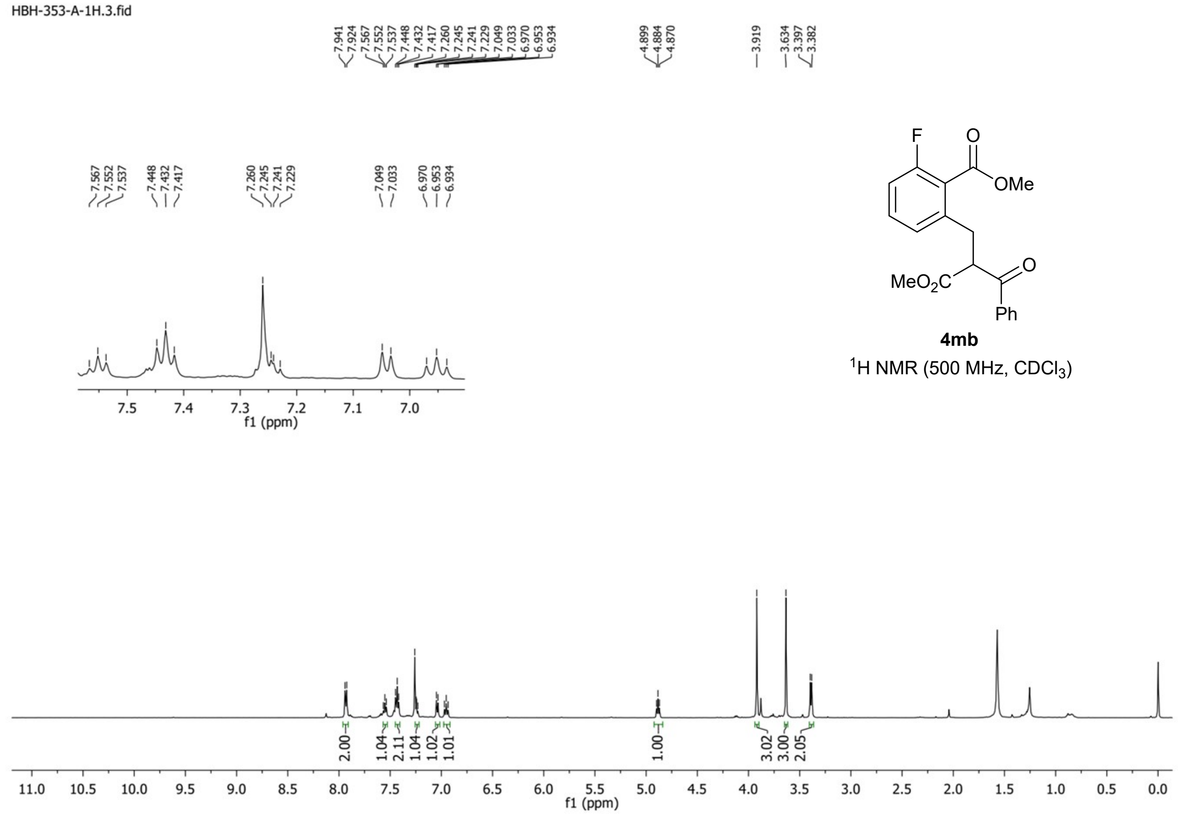
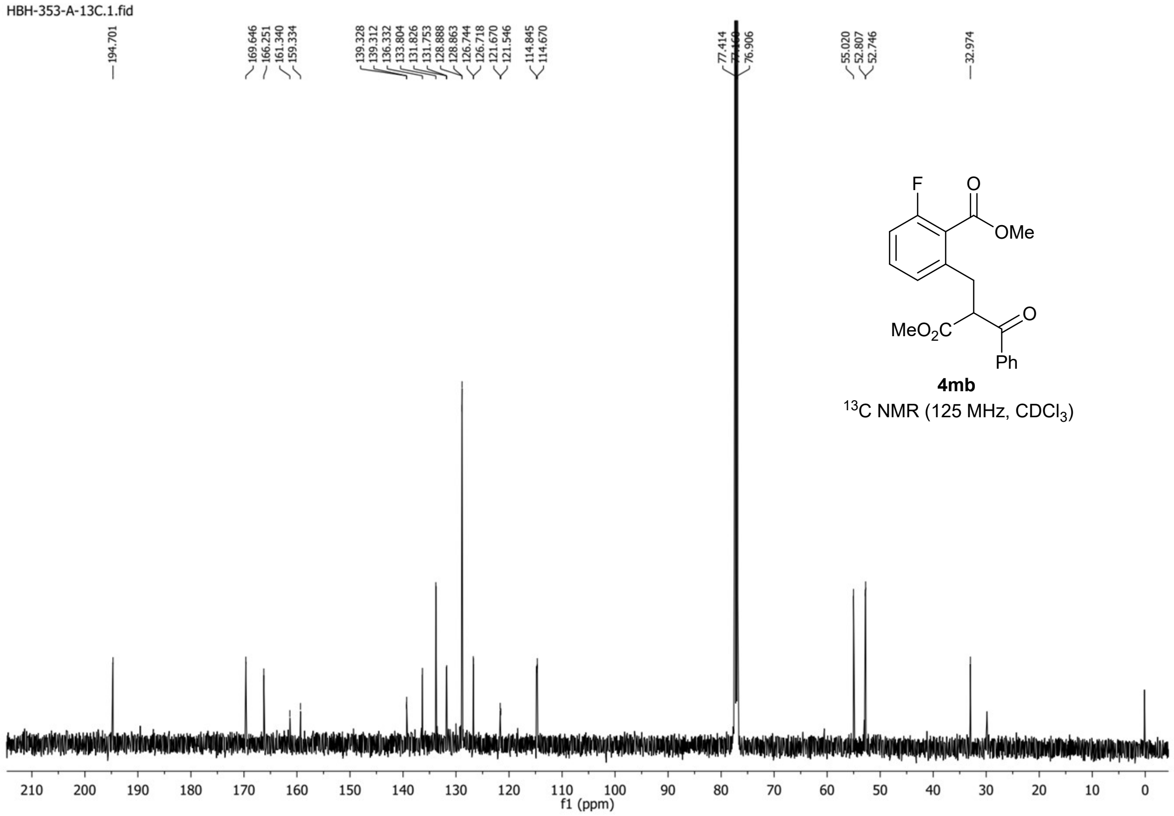
^{13}C NMR (100 MHz, CDCl$_3$)



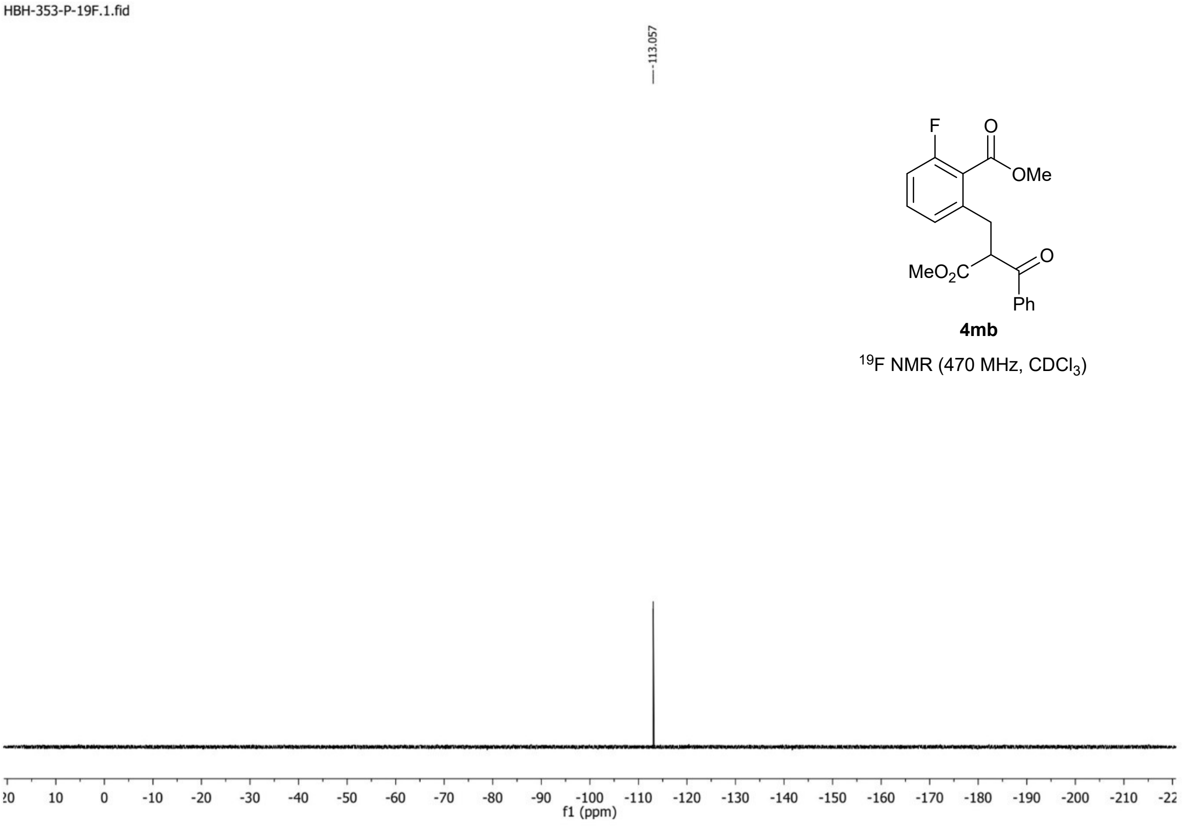
4mb

^{1}H NMR (500 MHz, CDCl$_3$)



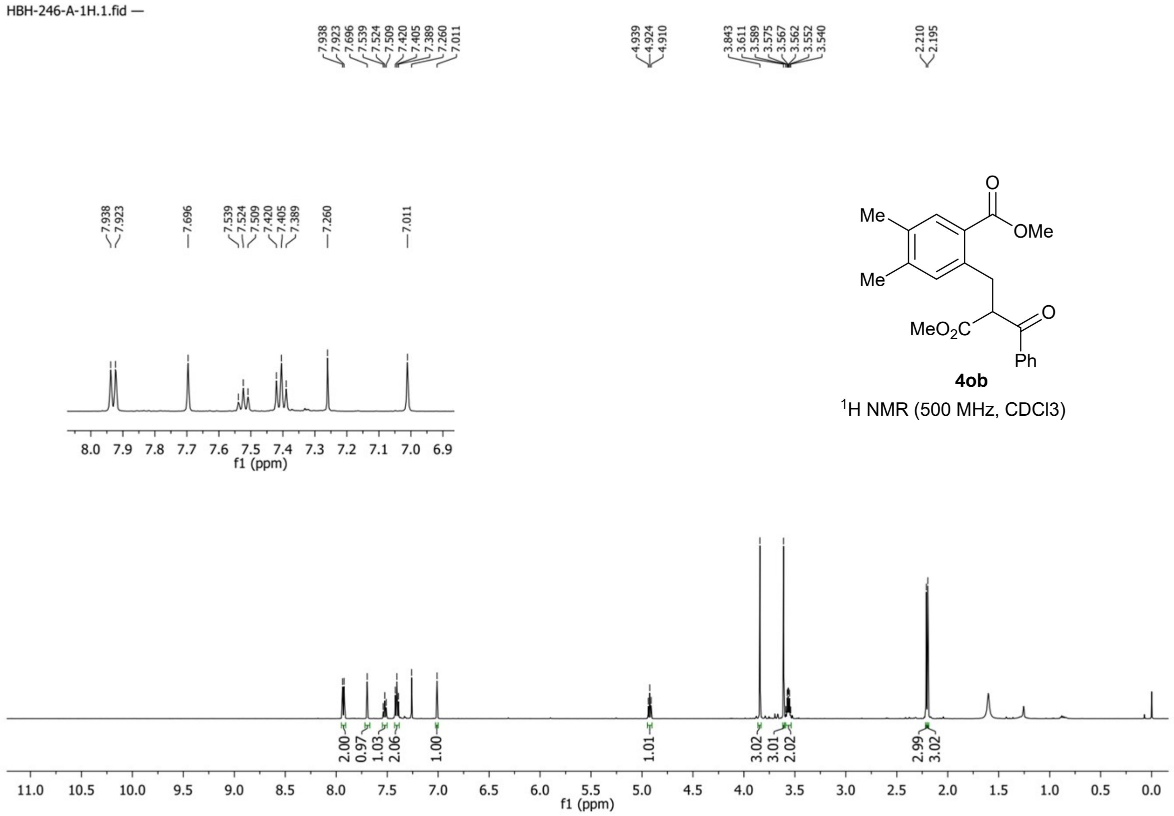
4mb

^{13}C NMR (125 MHz, CDCl$_3$)



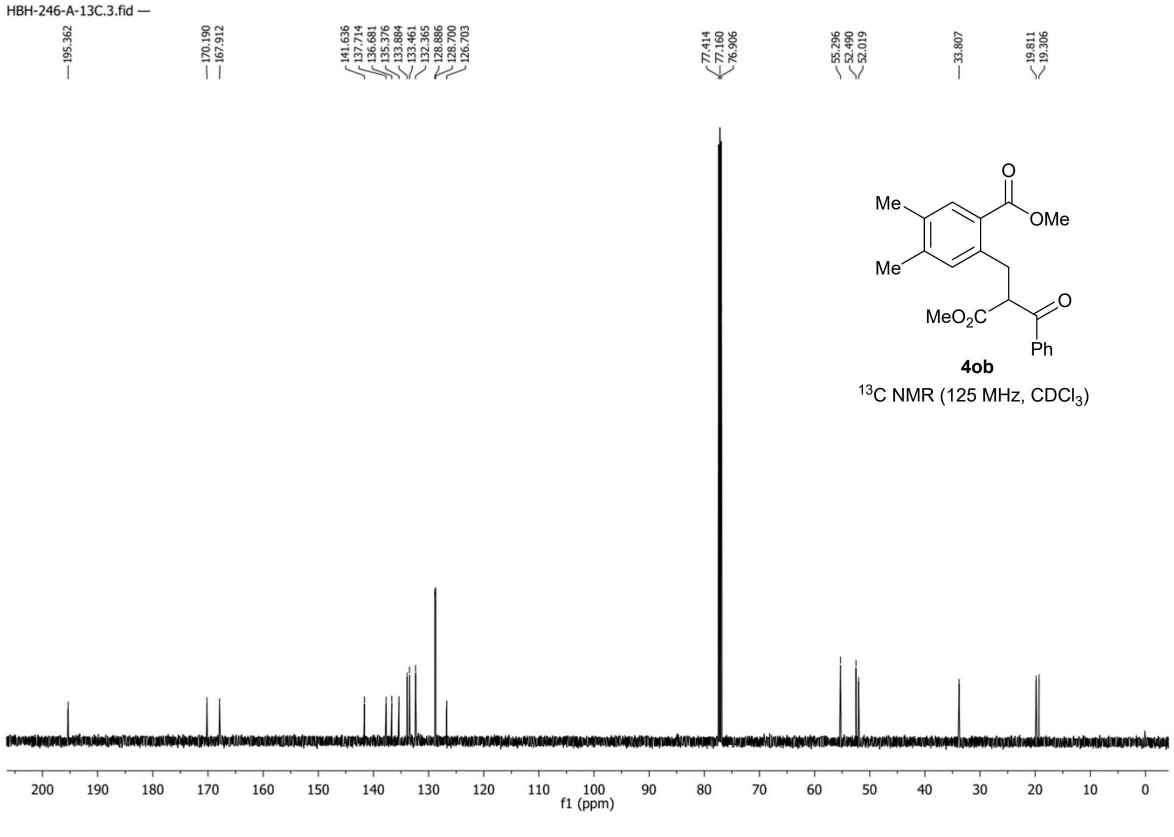
4mb

^{19}F NMR (470 MHz, CDCl$_3$)



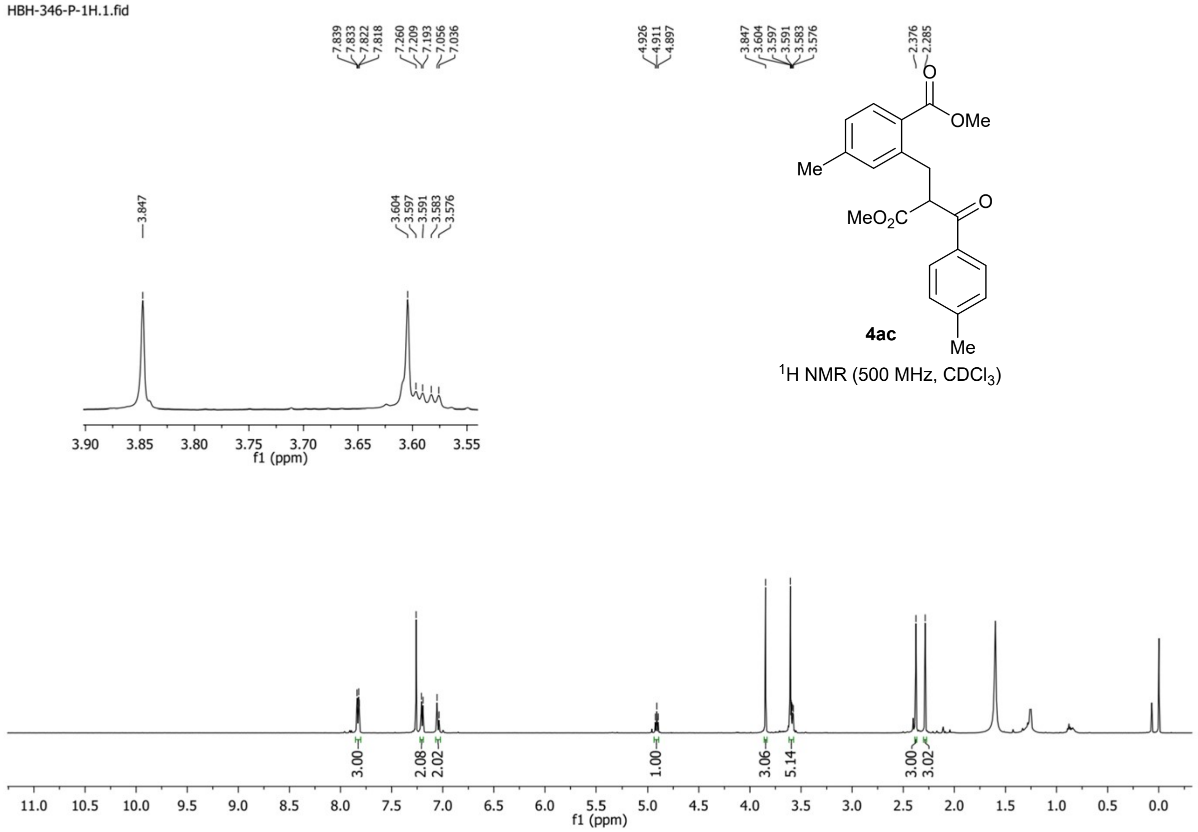
4ob

^{1}H NMR (500 MHz, CDCl3)



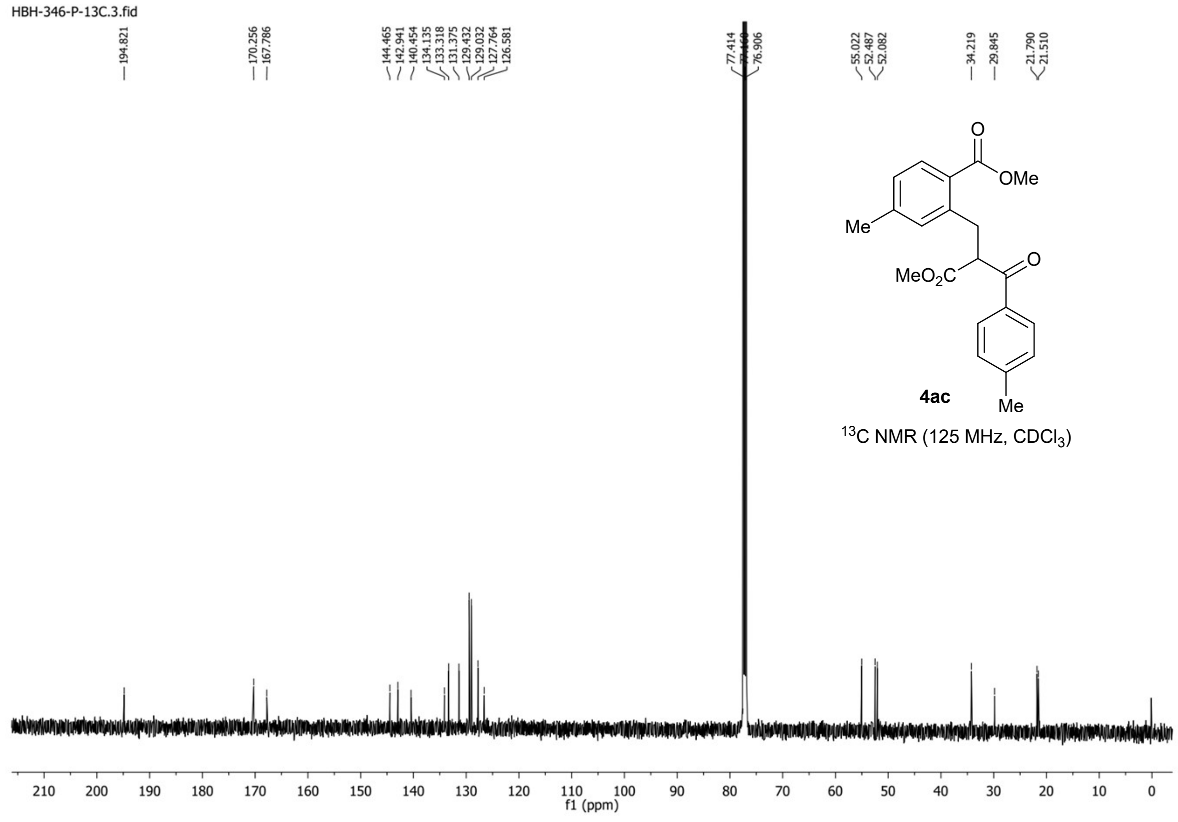
4ob

^{13}C NMR (125 MHz, CDCl$_3$)



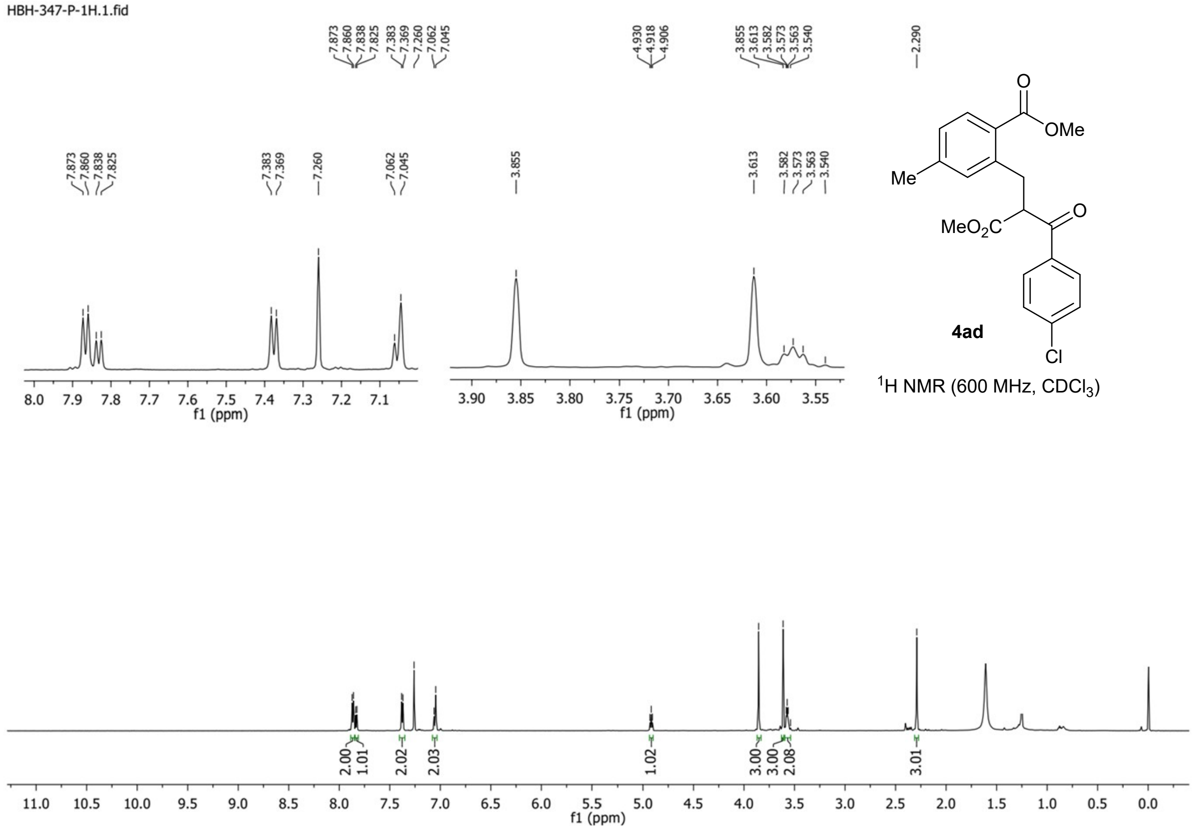
4ac

^{1}H NMR (500 MHz, CDCl$_3$)



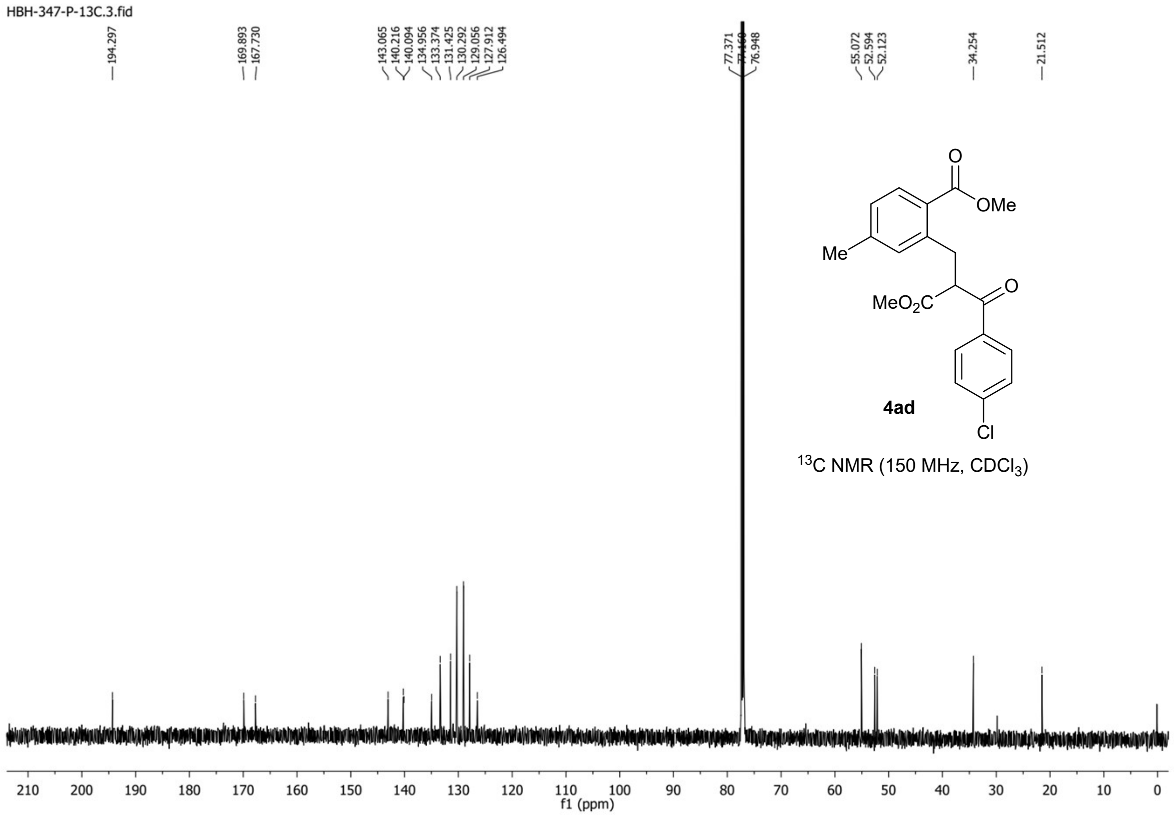
4ac

^{13}C NMR (125 MHz, CDCl$_3$)



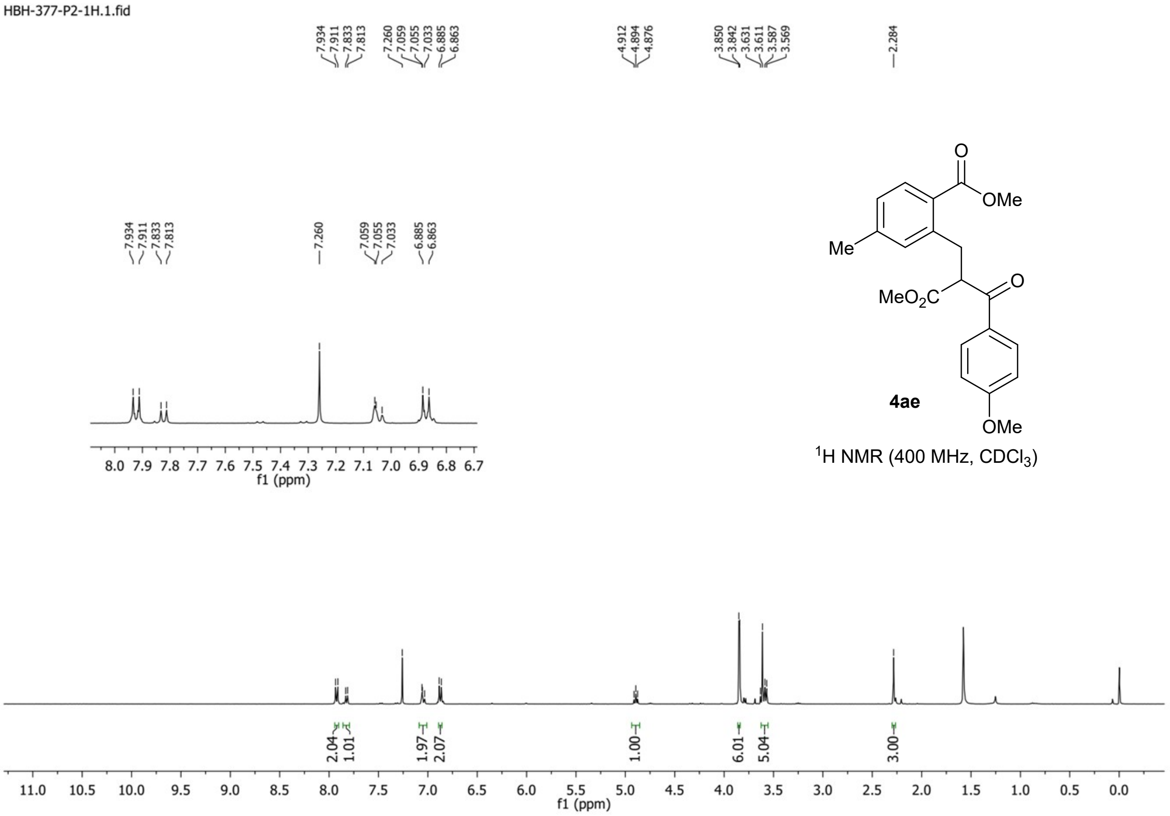
4ad

^{1}H NMR (600 MHz, CDCl$_3$)



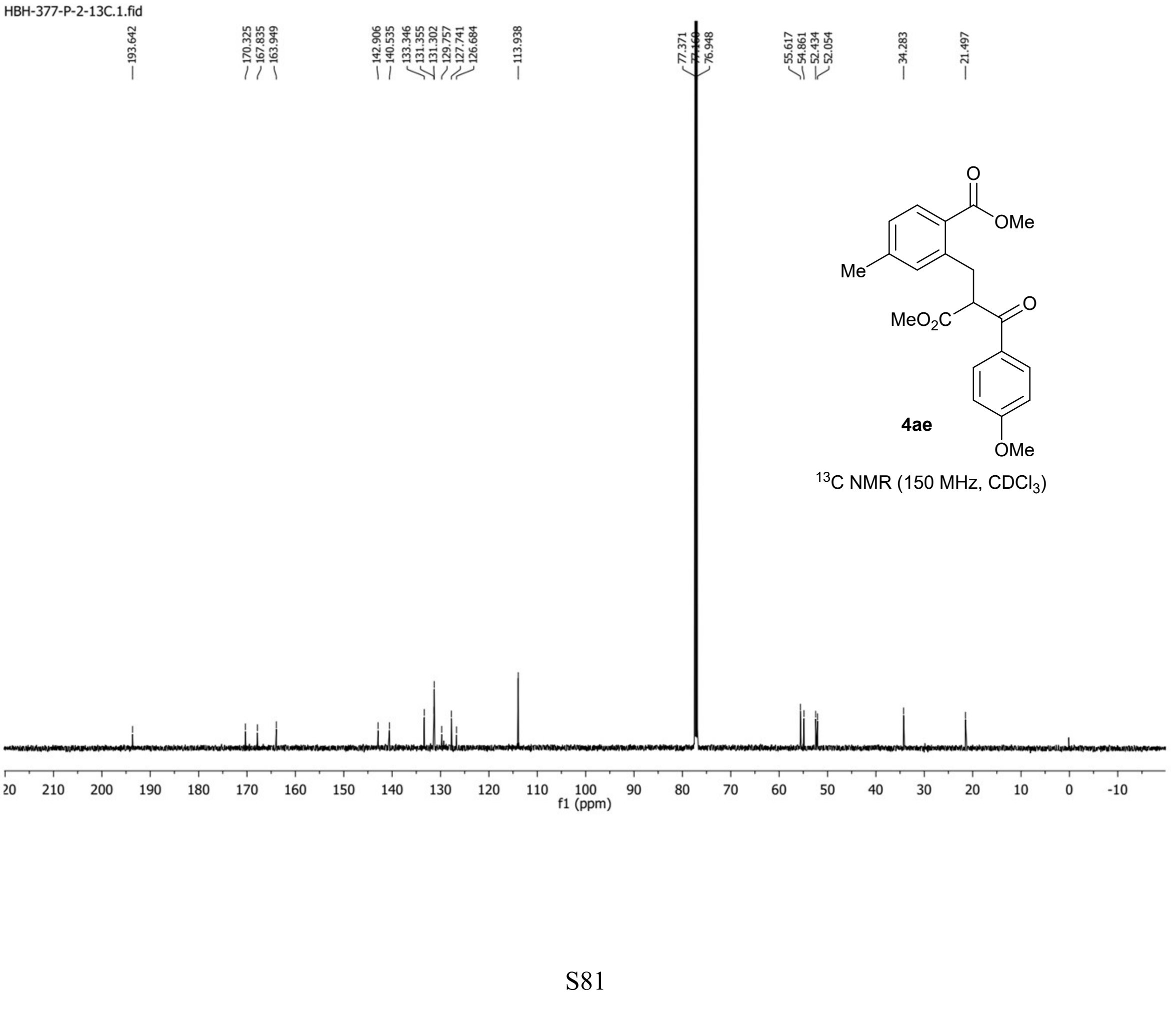
4ad

^{13}C NMR (150 MHz, CDCl$_3$)



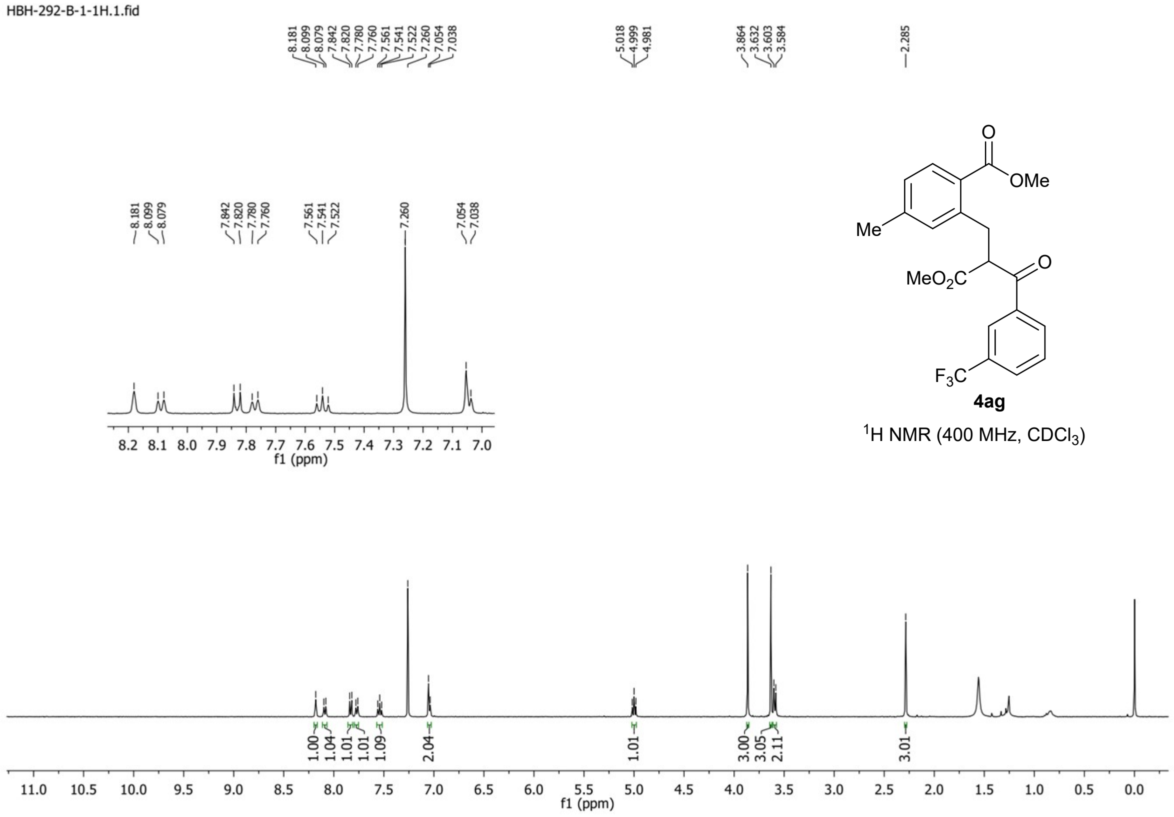
4ae

^{1}H NMR (400 MHz, CDCl$_3$)



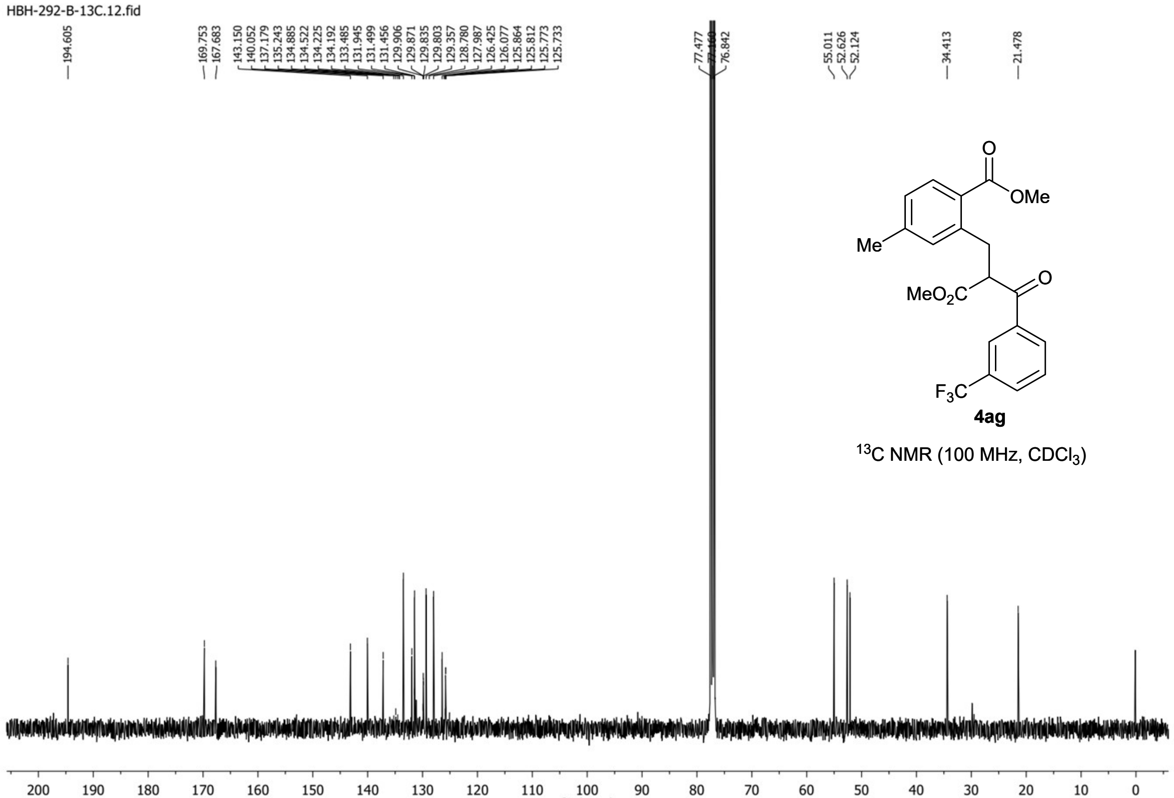
4ae

^{13}C NMR (150 MHz, CDCl$_3$)



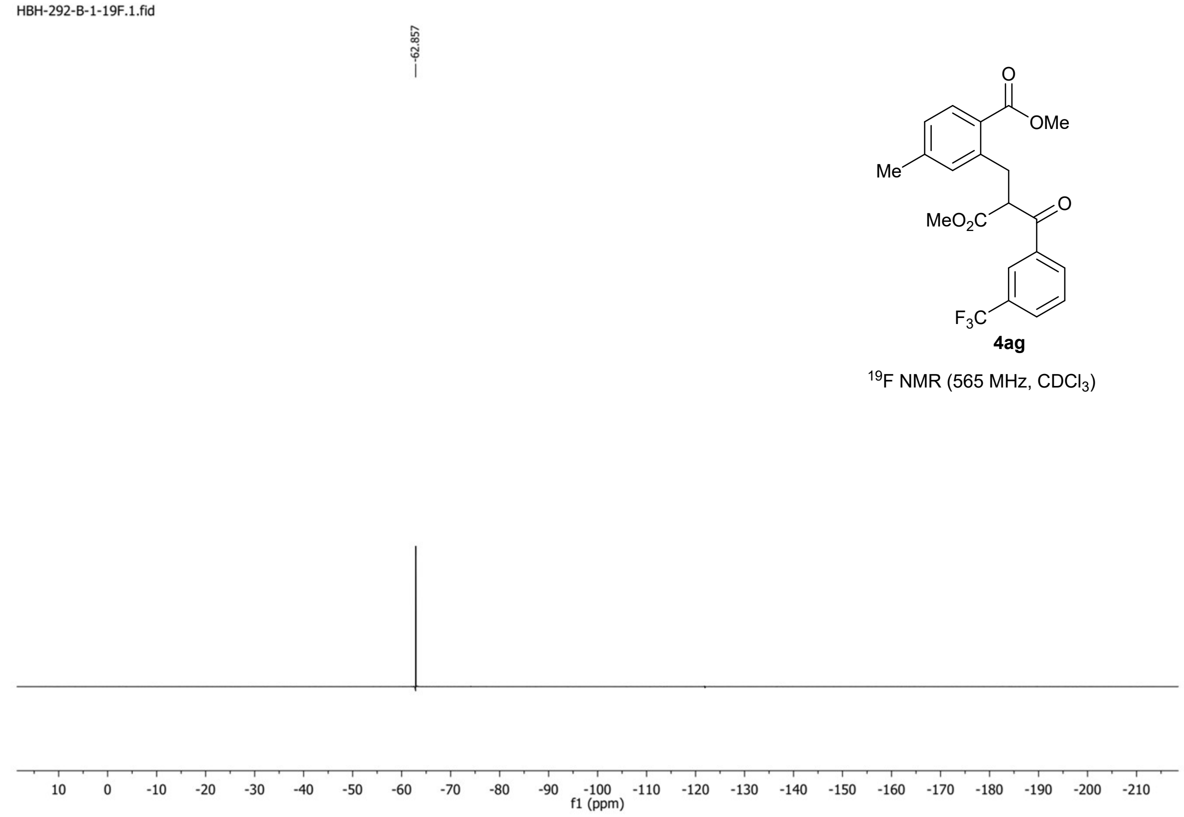
4ag

^{1}H NMR (400 MHz, CDCl$_3$)



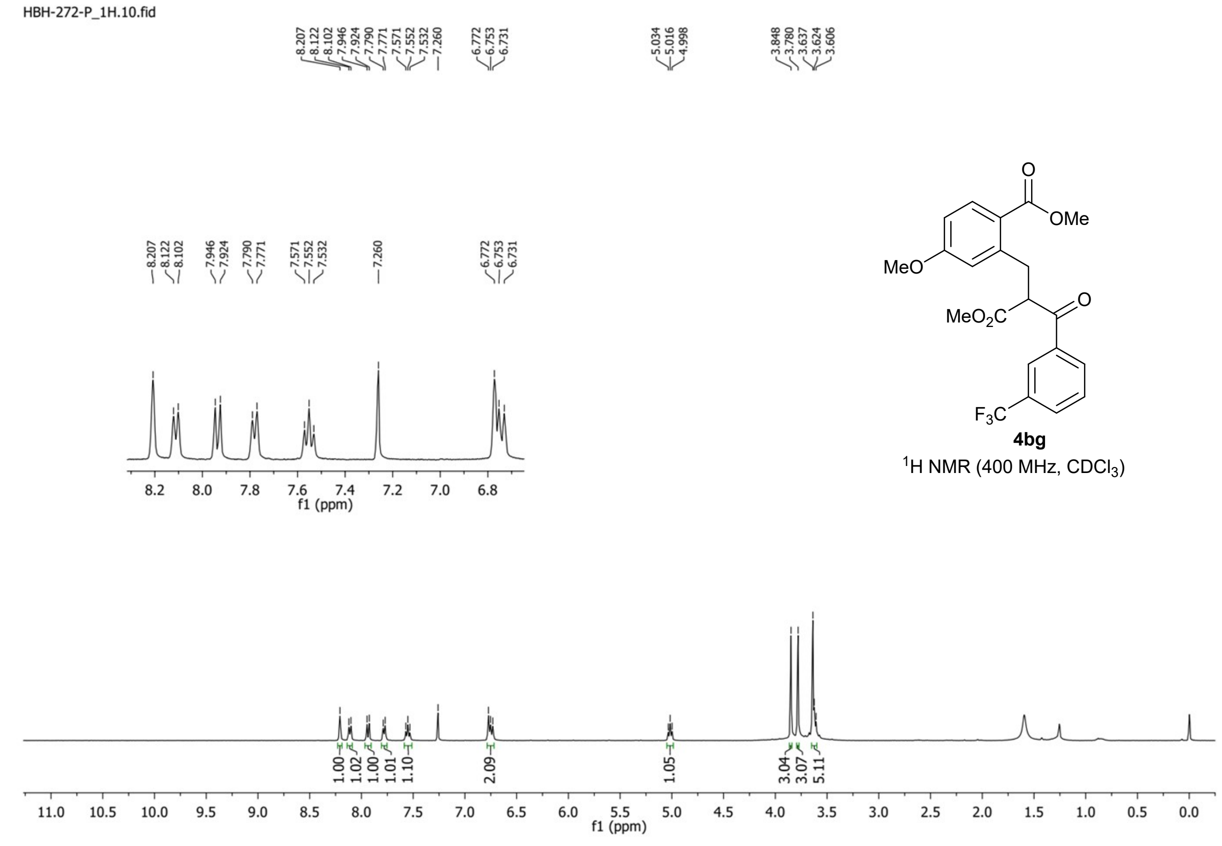
4ag

^{13}C NMR (100 MHz, CDCl$_3$)



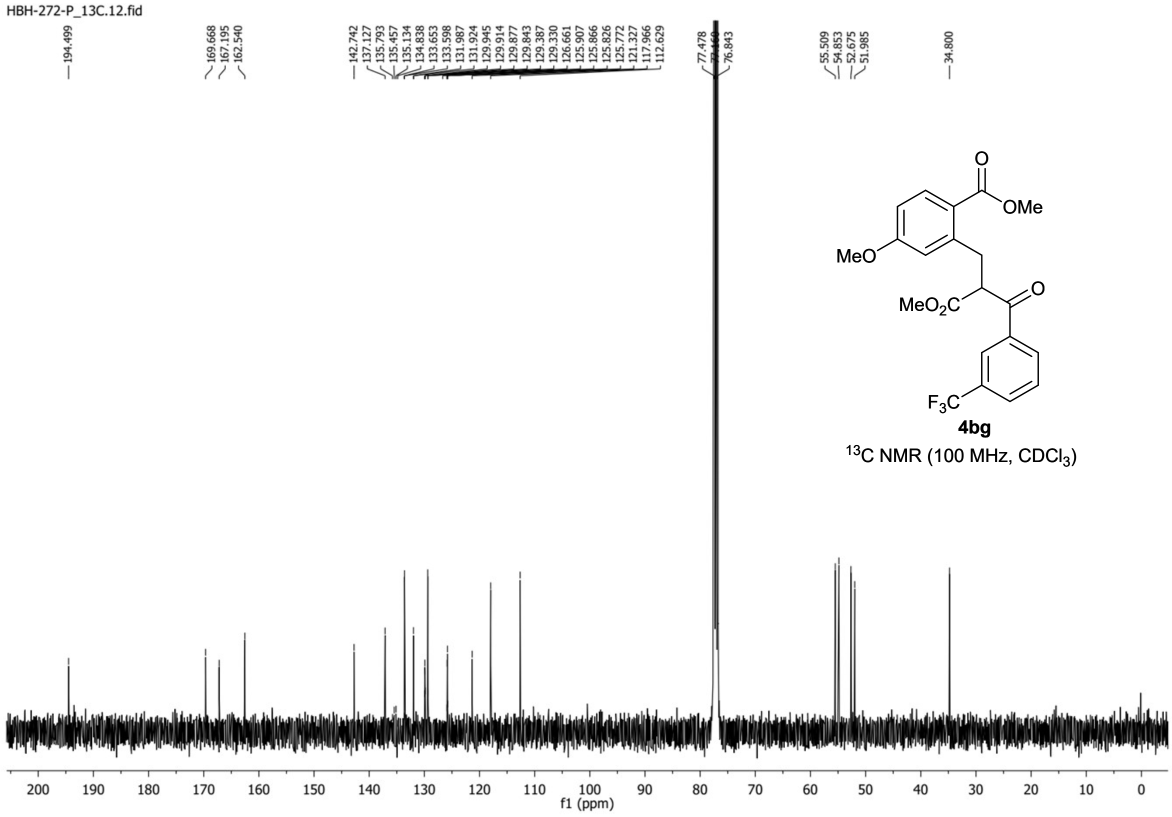
4ag

^{19}F NMR (565 MHz, CDCl$_3$)



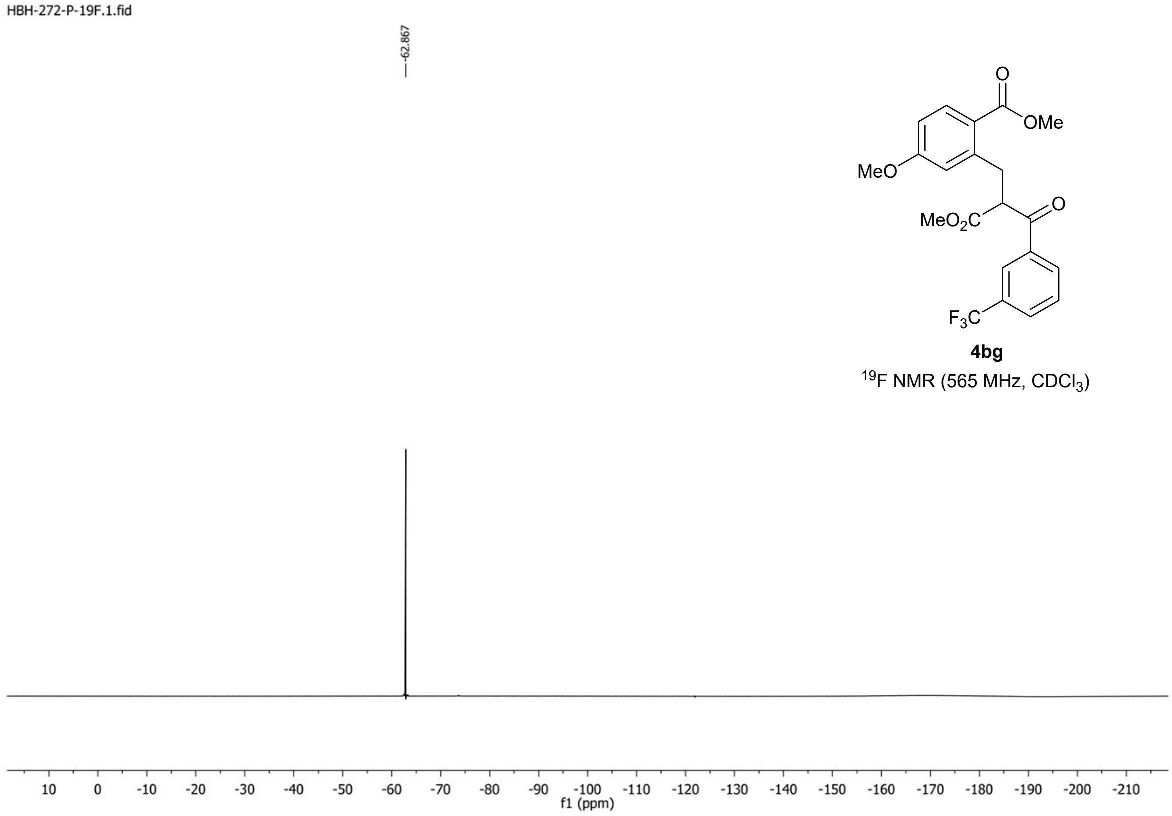
4bg

^{1}H NMR (400 MHz, CDCl$_3$)



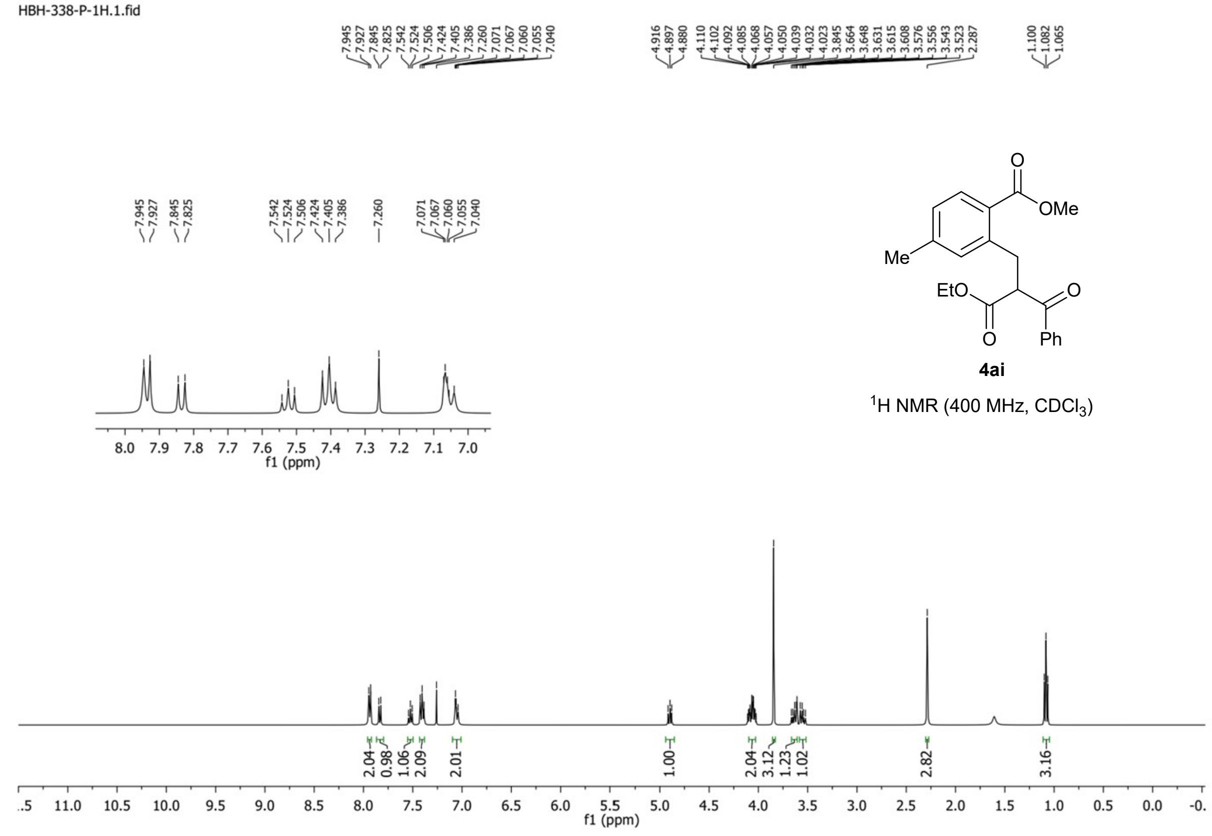
4bg

^{13}C NMR (100 MHz, $CDCl_3$)



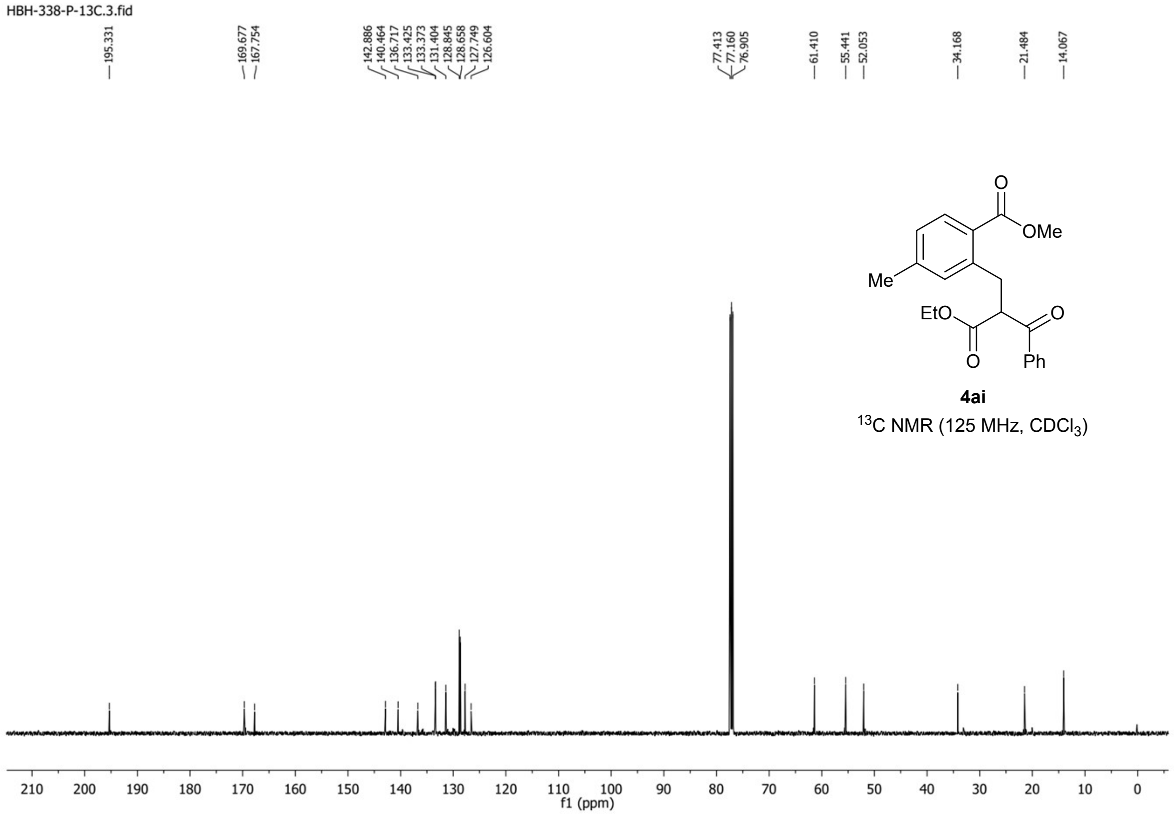
4bg

^{19}F NMR (565 MHz, $CDCl_3$)



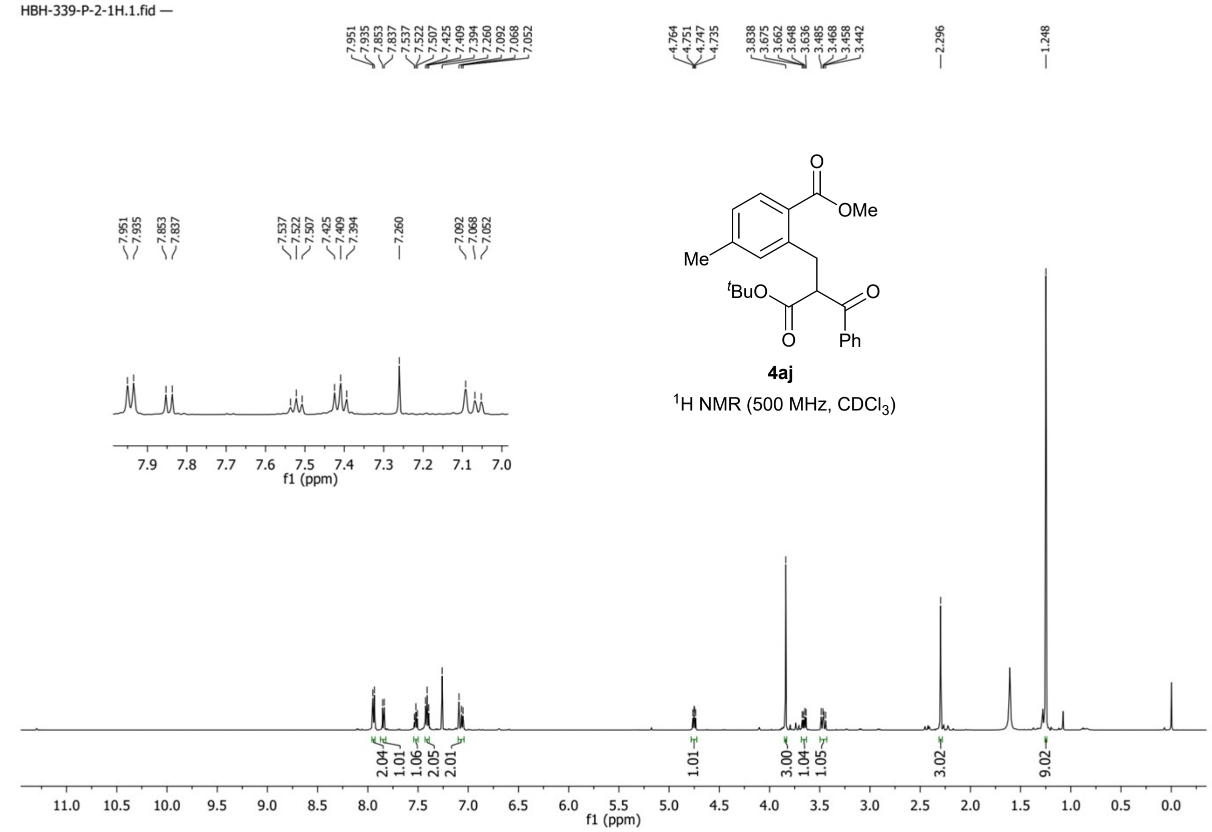
4ai

^{1}H NMR (400 MHz, CDCl$_3$)



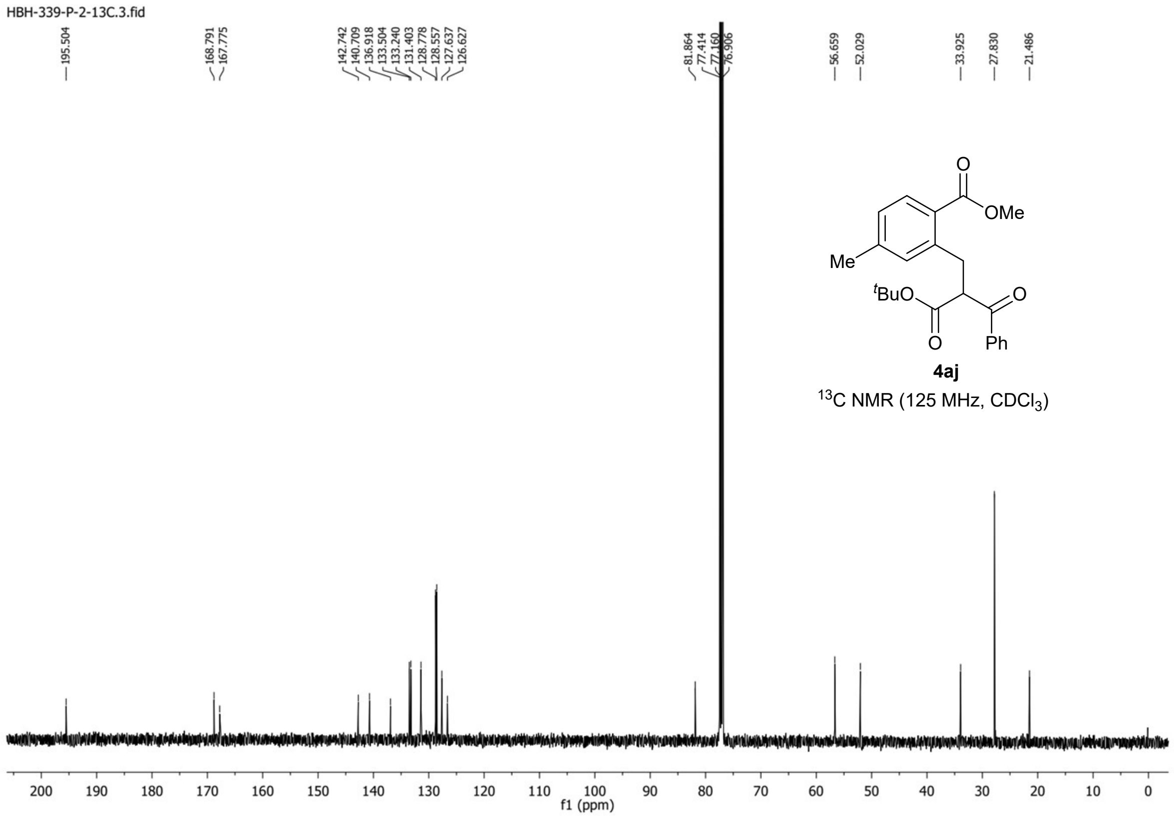
4ai

^{13}C NMR (125 MHz, CDCl$_3$)



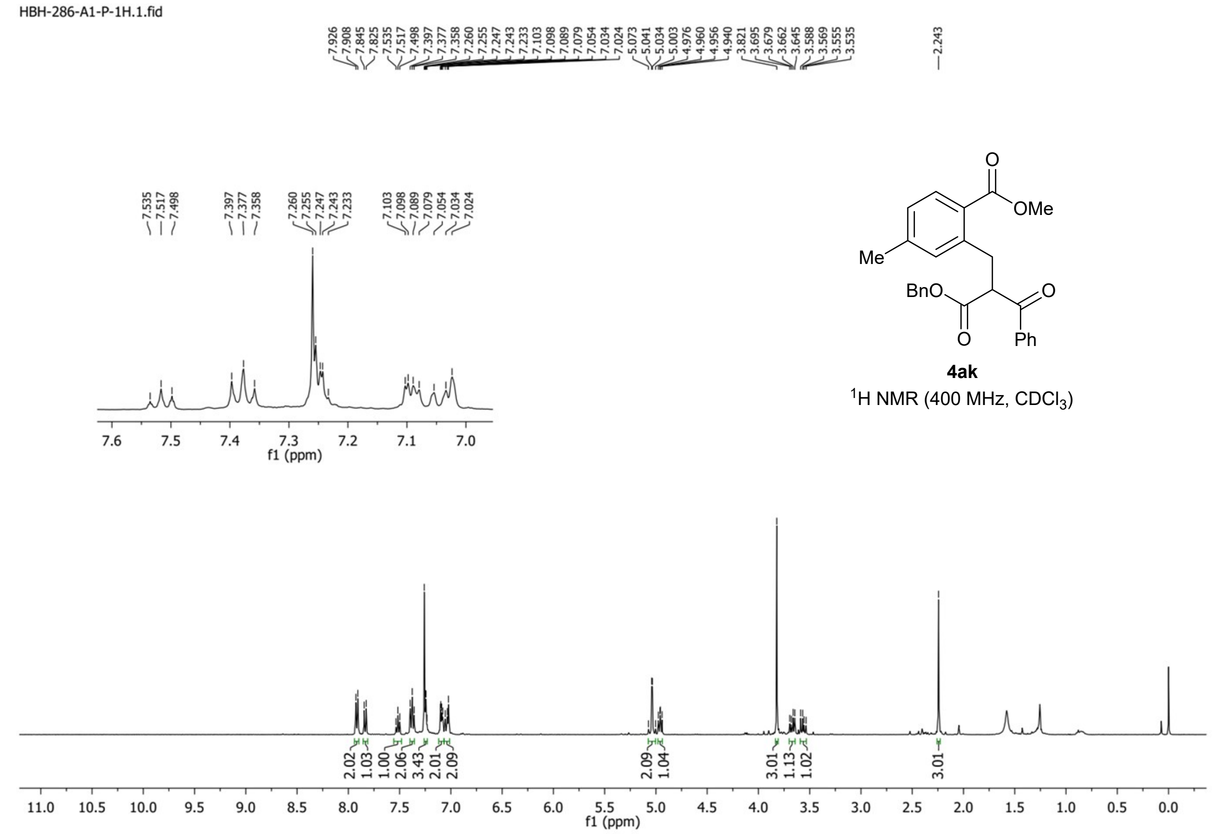
4aj

^{1}H NMR (500 MHz, $CDCl_3$)



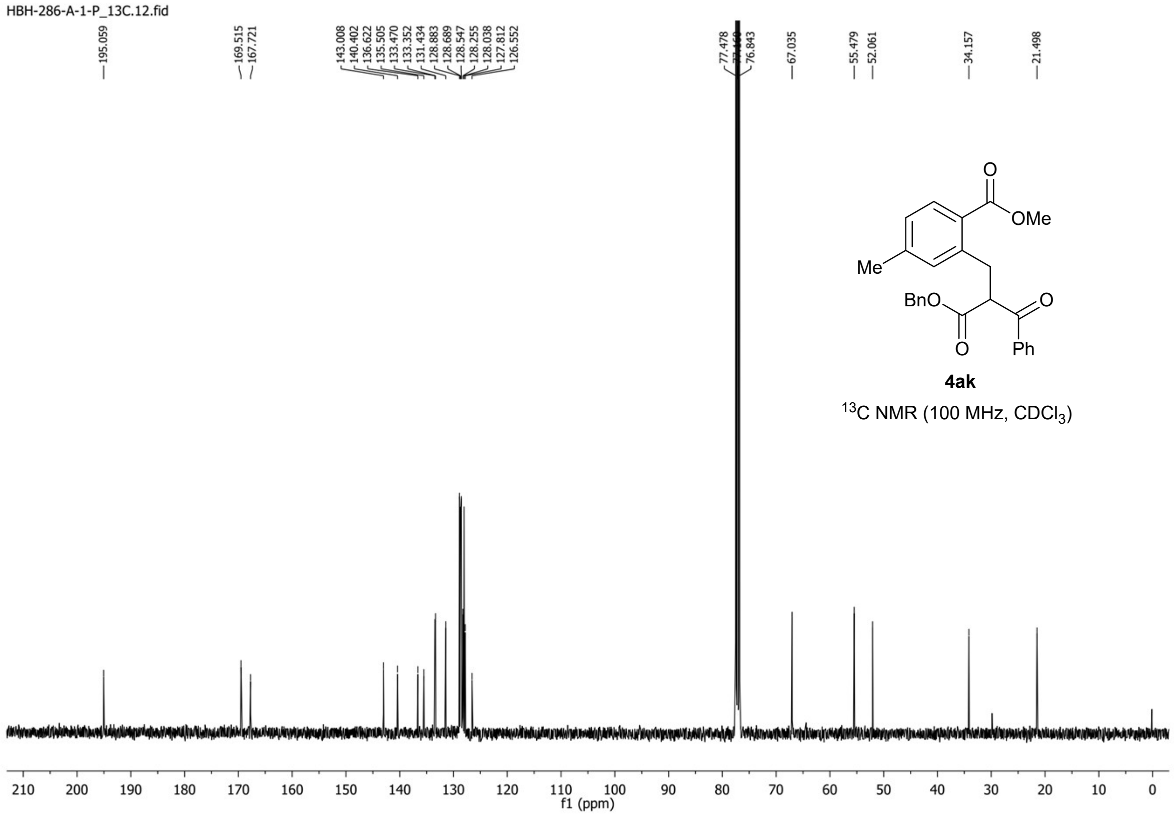
4aj

^{13}C NMR (125 MHz, $CDCl_3$)



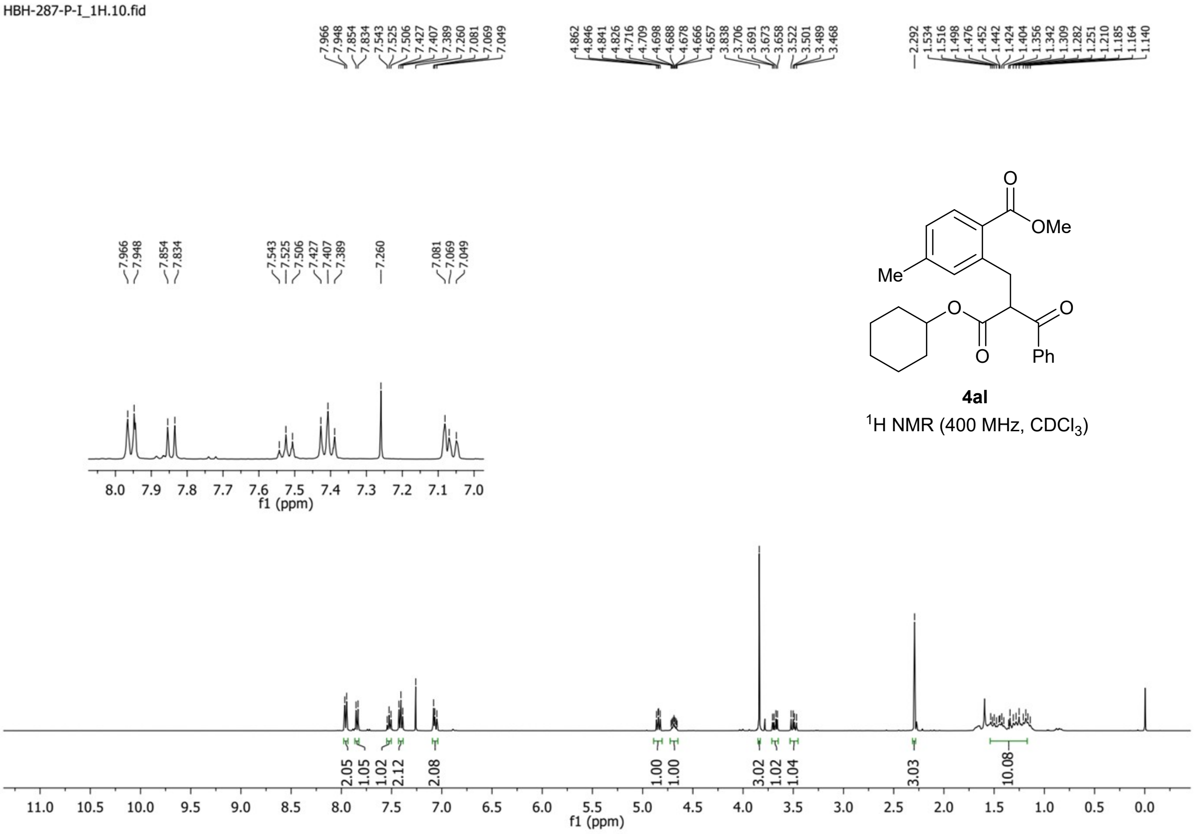
4ak

^{1}H NMR (400 MHz, CDCl$_3$)



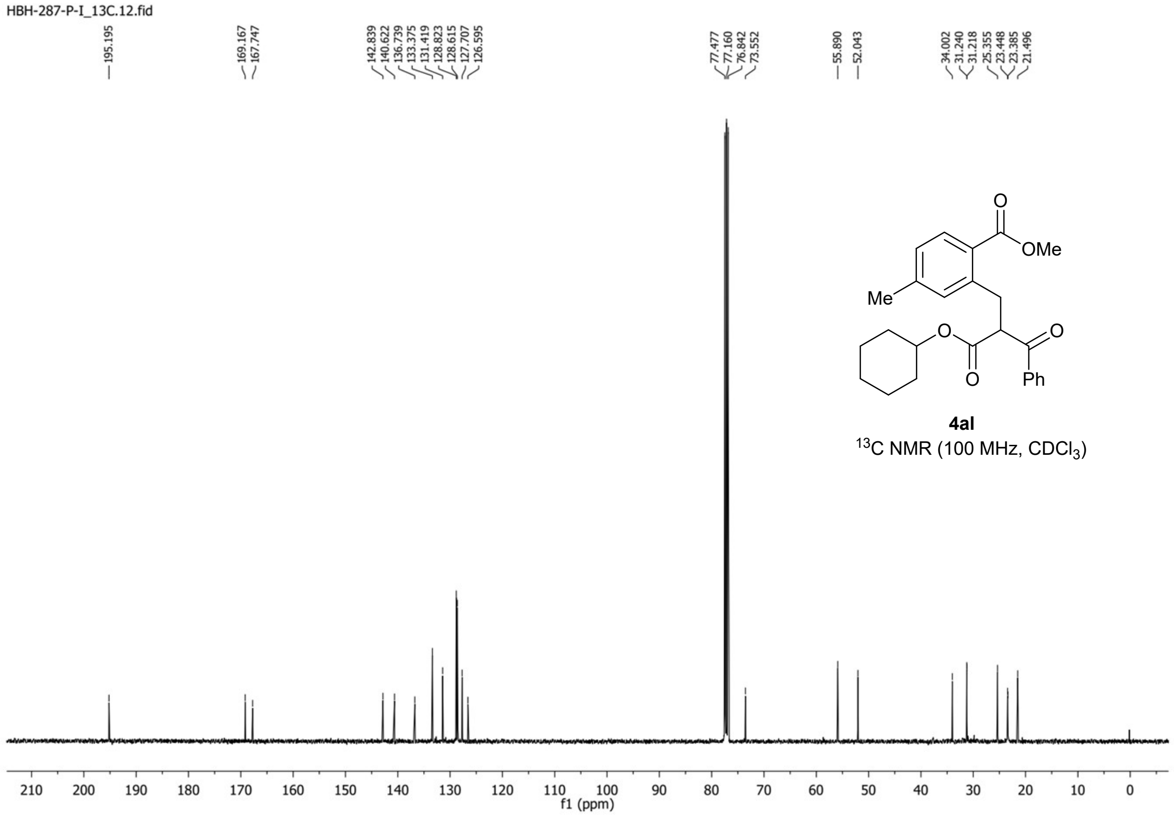
4ak

^{13}C NMR (100 MHz, CDCl$_3$)



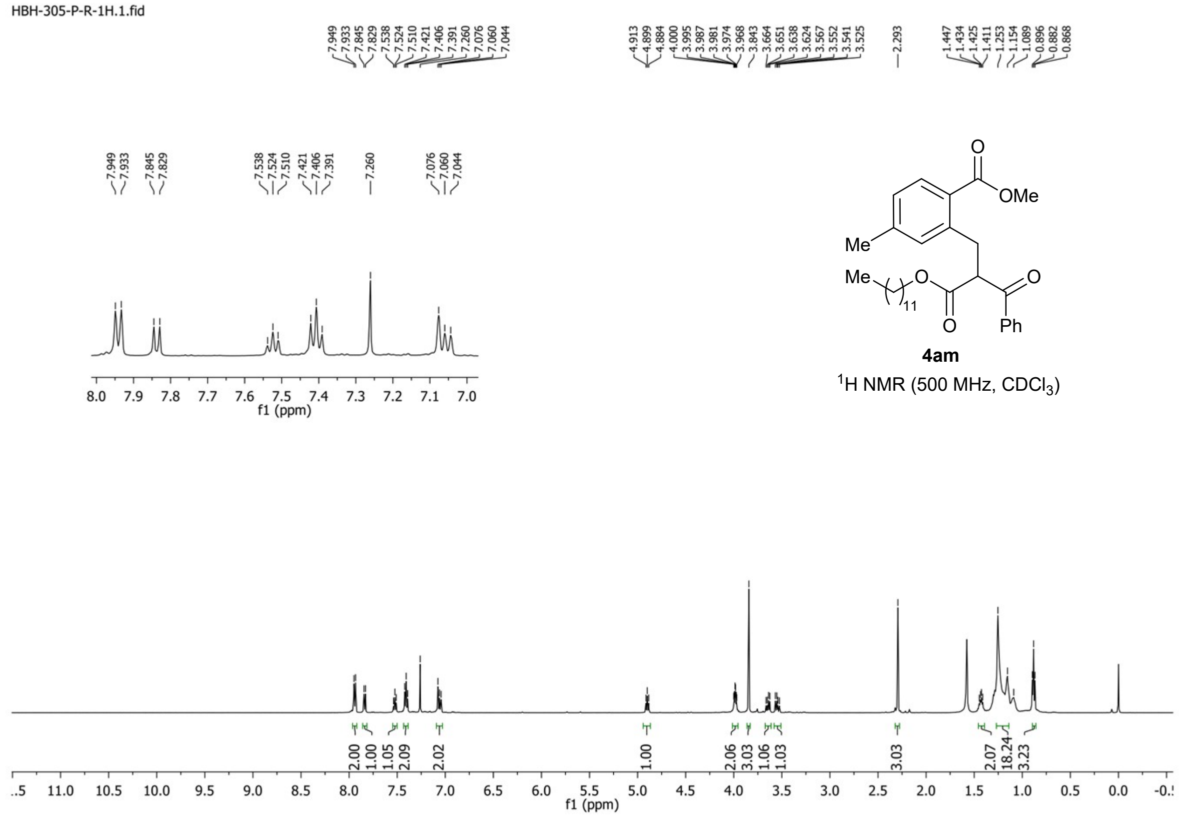
4al

^{1}H NMR (400 MHz, CDCl$_3$)



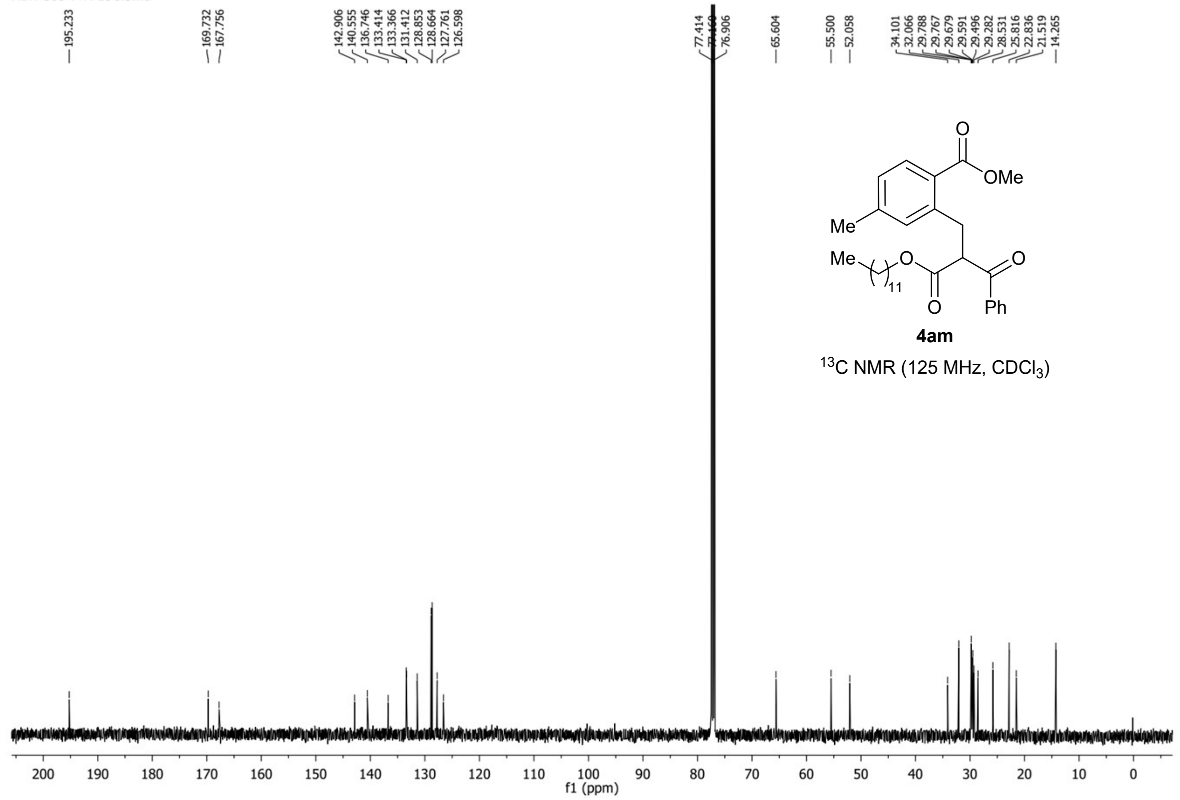
4al

^{13}C NMR (100 MHz, CDCl$_3$)



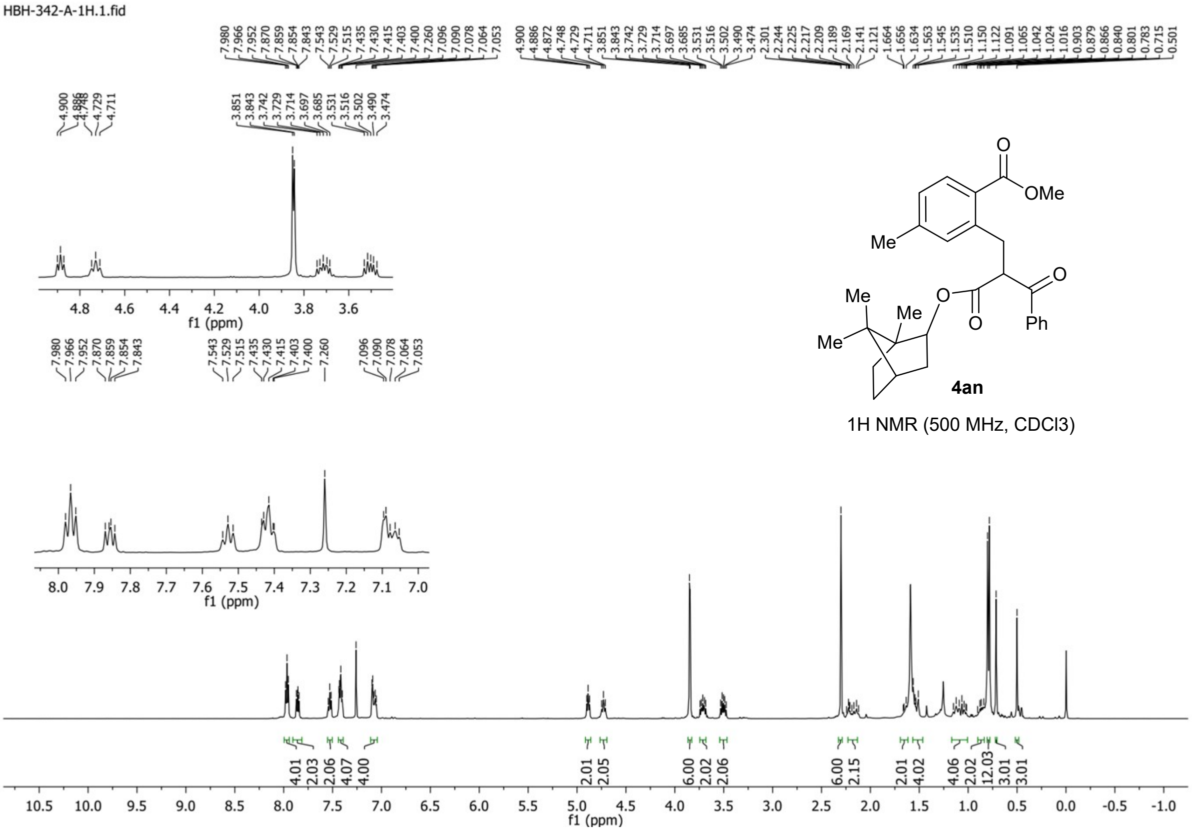
4am

^{1}H NMR (500 MHz, $CDCl_3$)

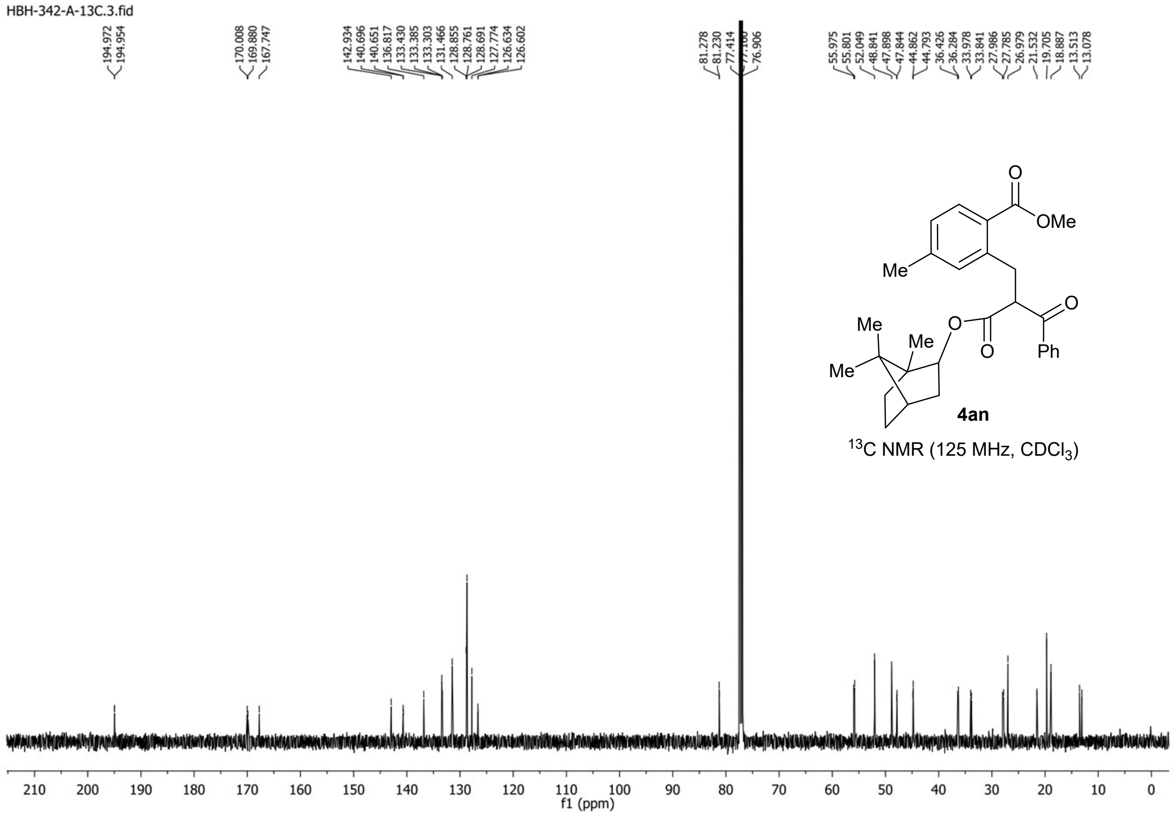


4am

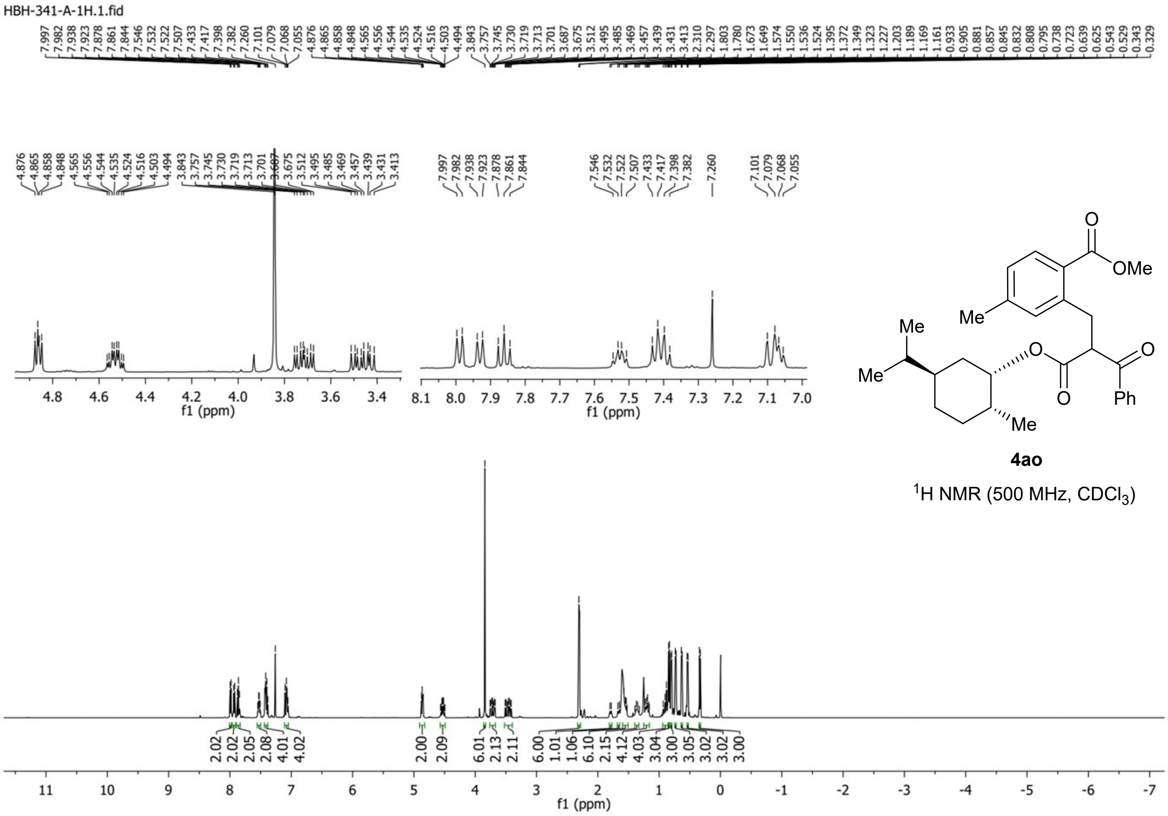
^{13}C NMR (125 MHz, $CDCl_3$)



1H NMR (500 MHz, CDCl3)

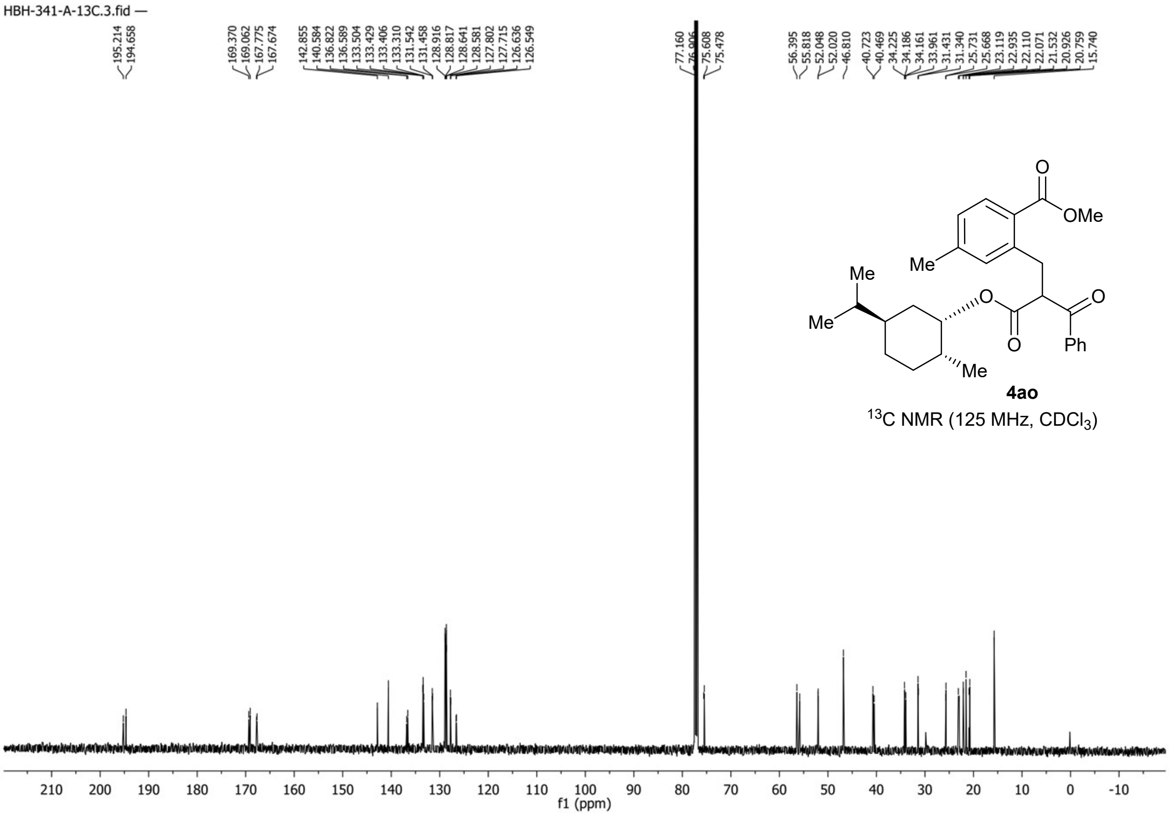


^{13}C NMR (125 MHz, CDCl$_3$)



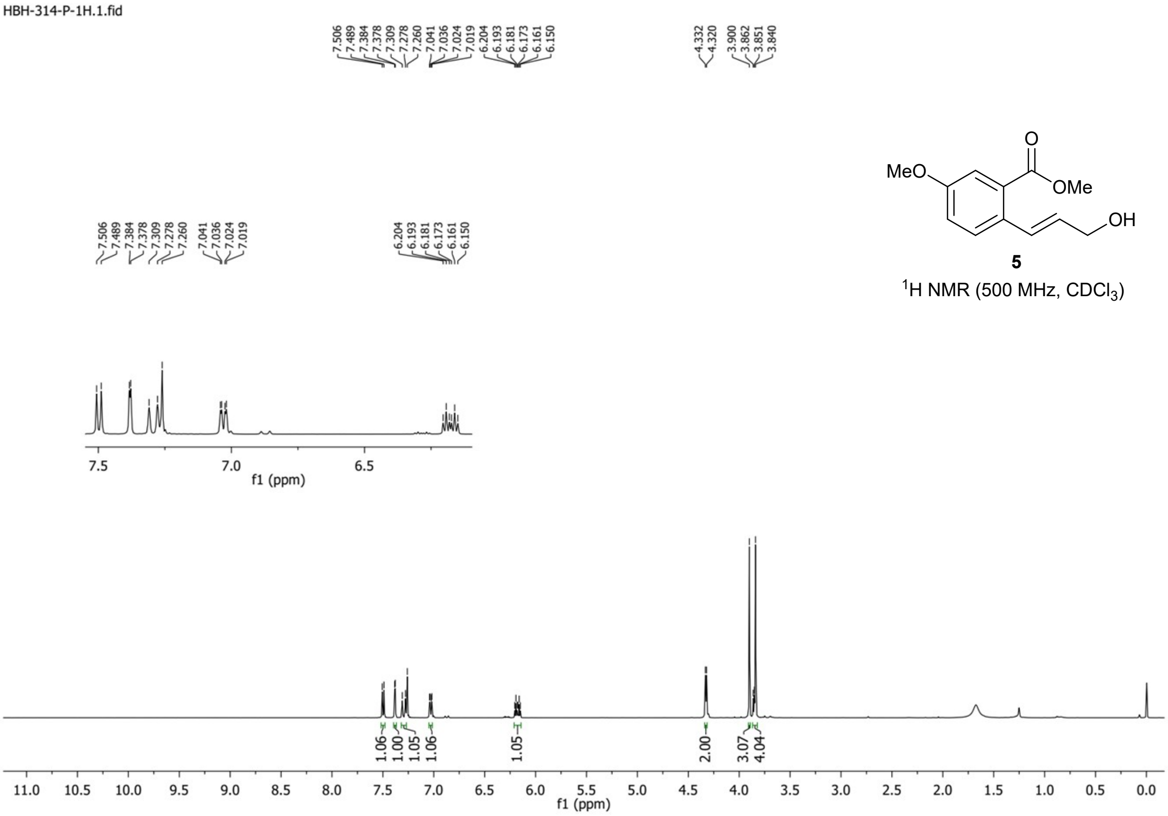
4ao

^{1}H NMR (500 MHz, CDCl$_3$)



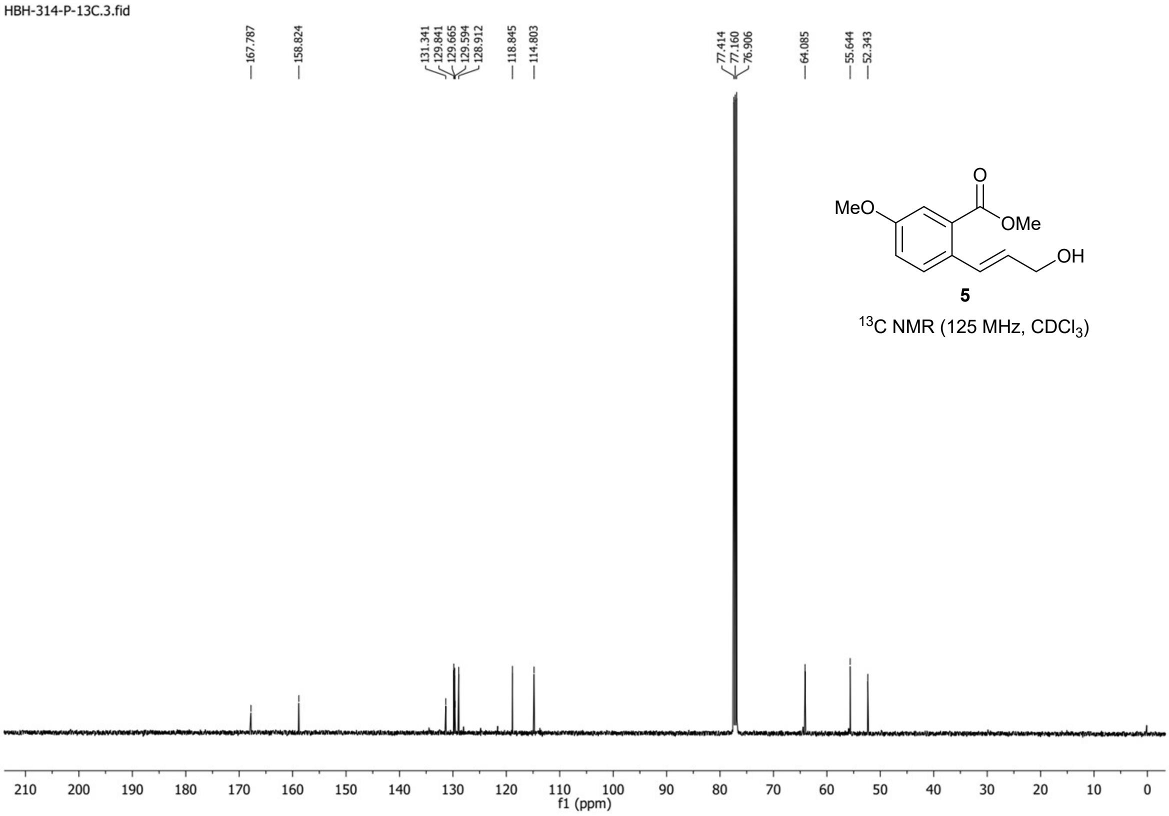
4ao

^{13}C NMR (125 MHz, CDCl$_3$)



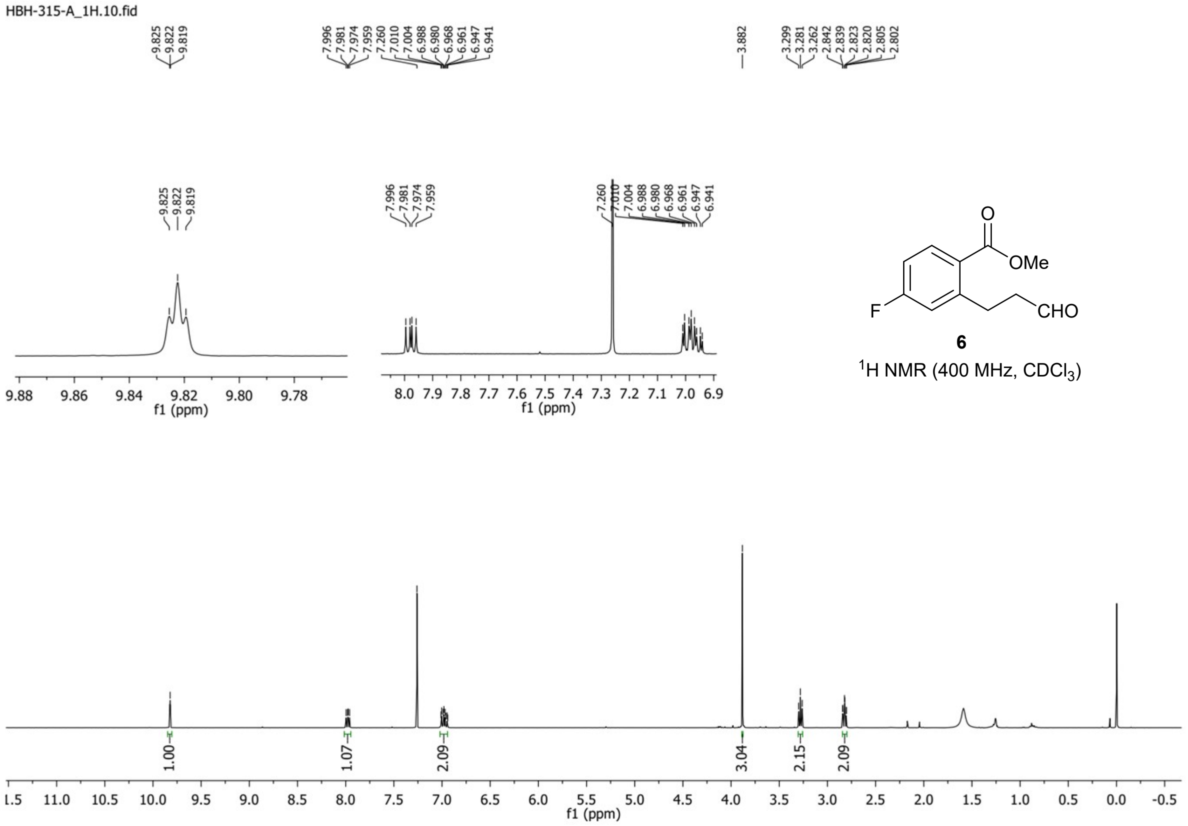
5

^{1}H NMR (500 MHz, $CDCl_3$)



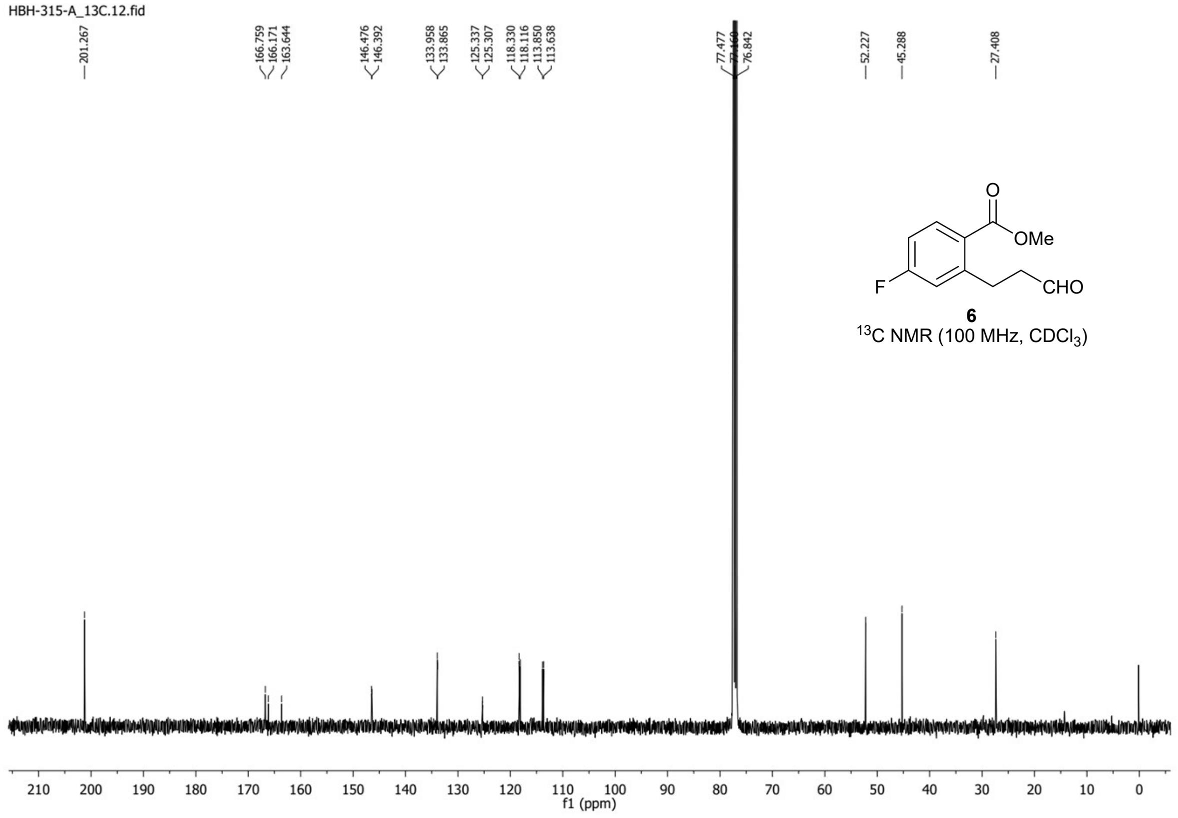
5

^{13}C NMR (125 MHz, $CDCl_3$)



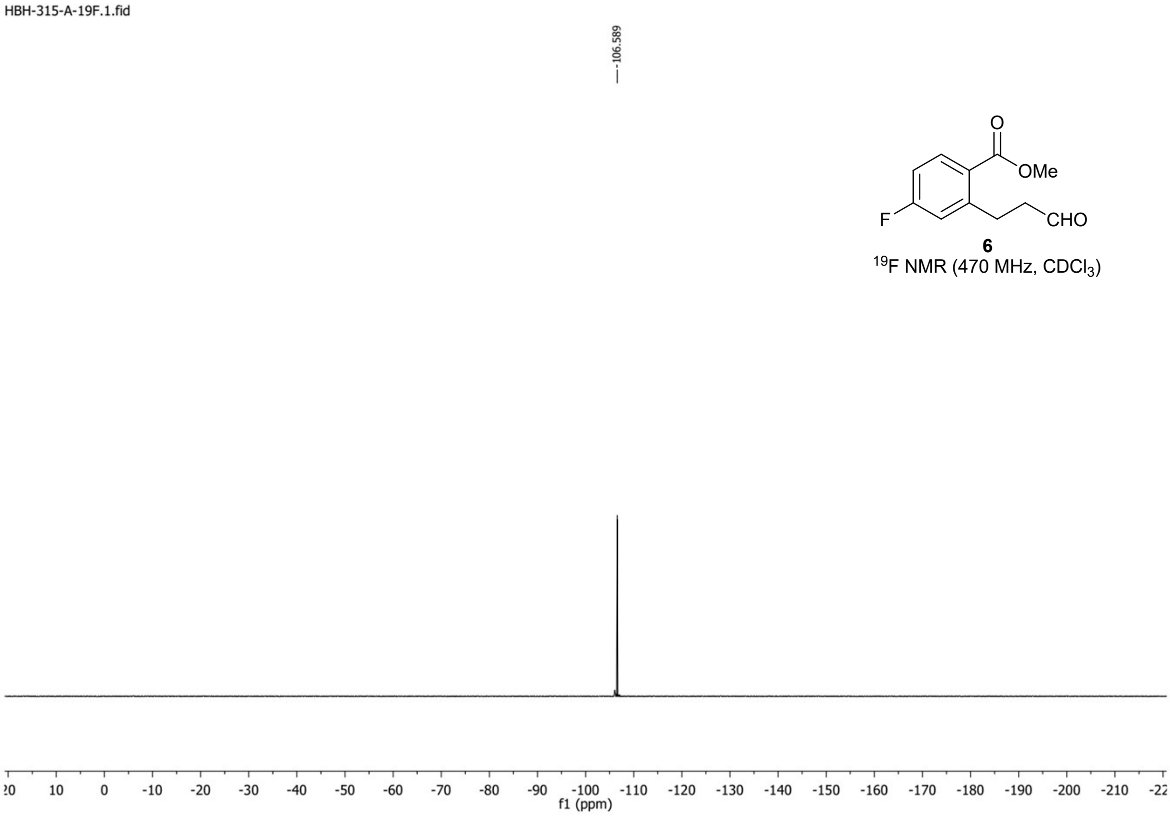
6

^{1}H NMR (400 MHz, CDCl$_3$)



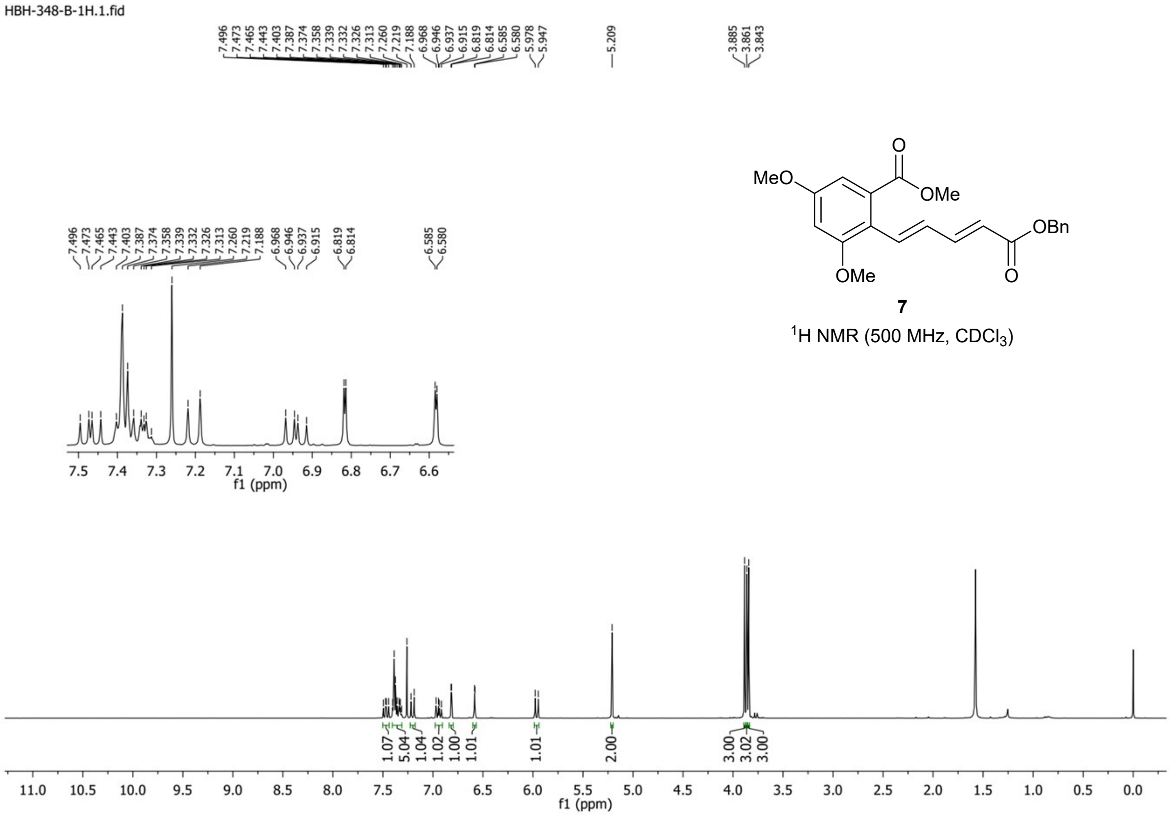
6

^{13}C NMR (100 MHz, CDCl$_3$)



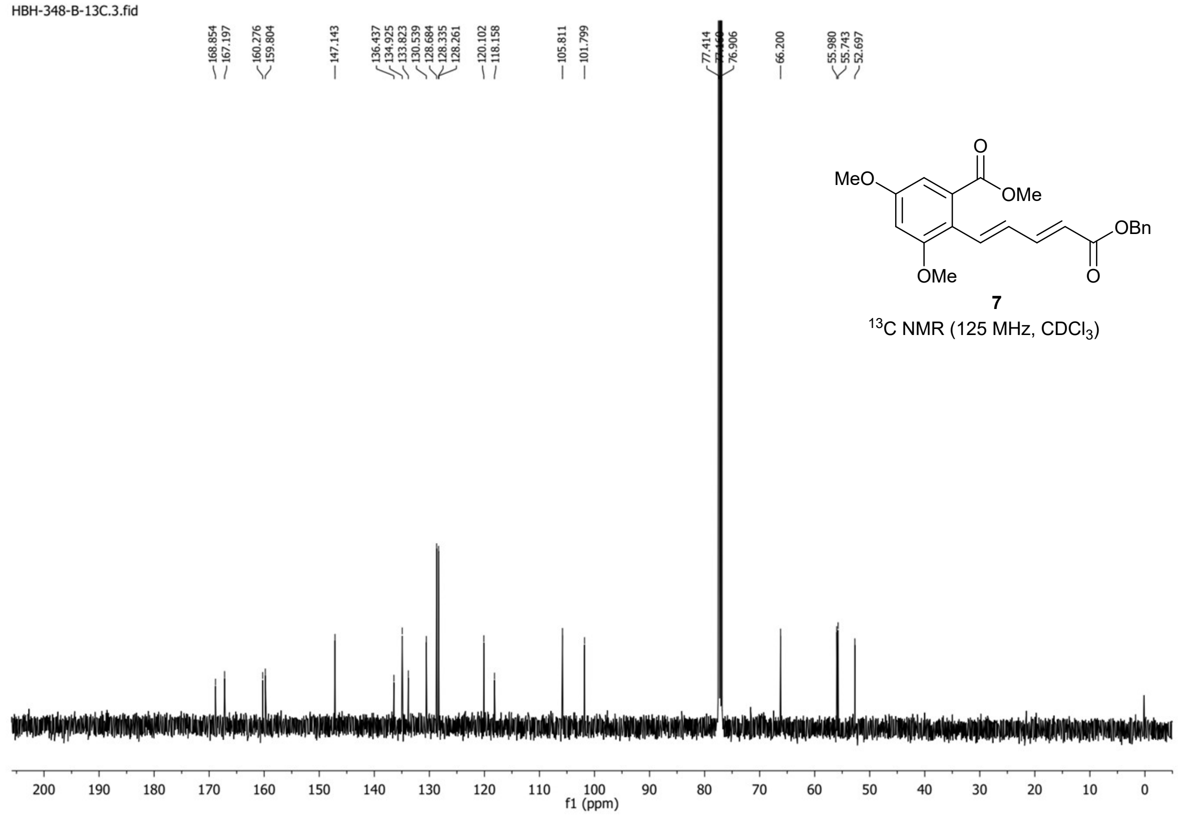
6

^{19}F NMR (470 MHz, CDCl$_3$)



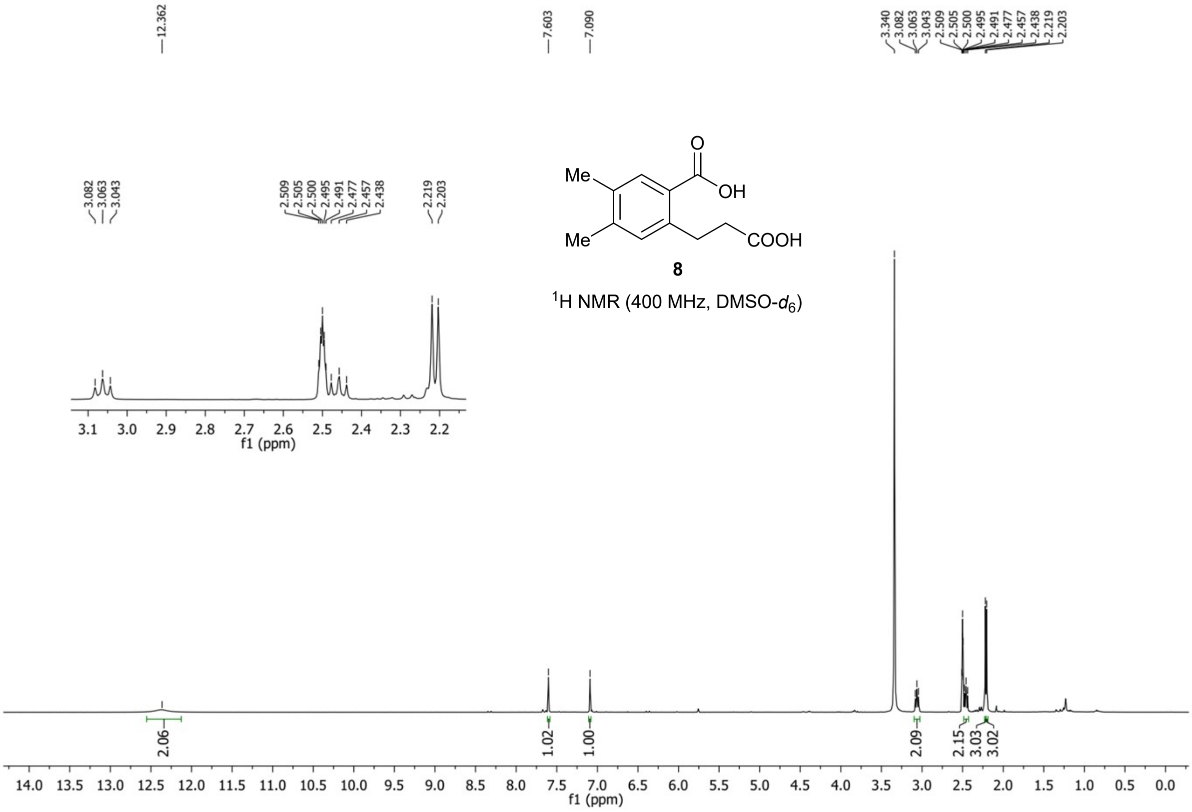
7

^{1}H NMR (500 MHz, CDCl$_3$)



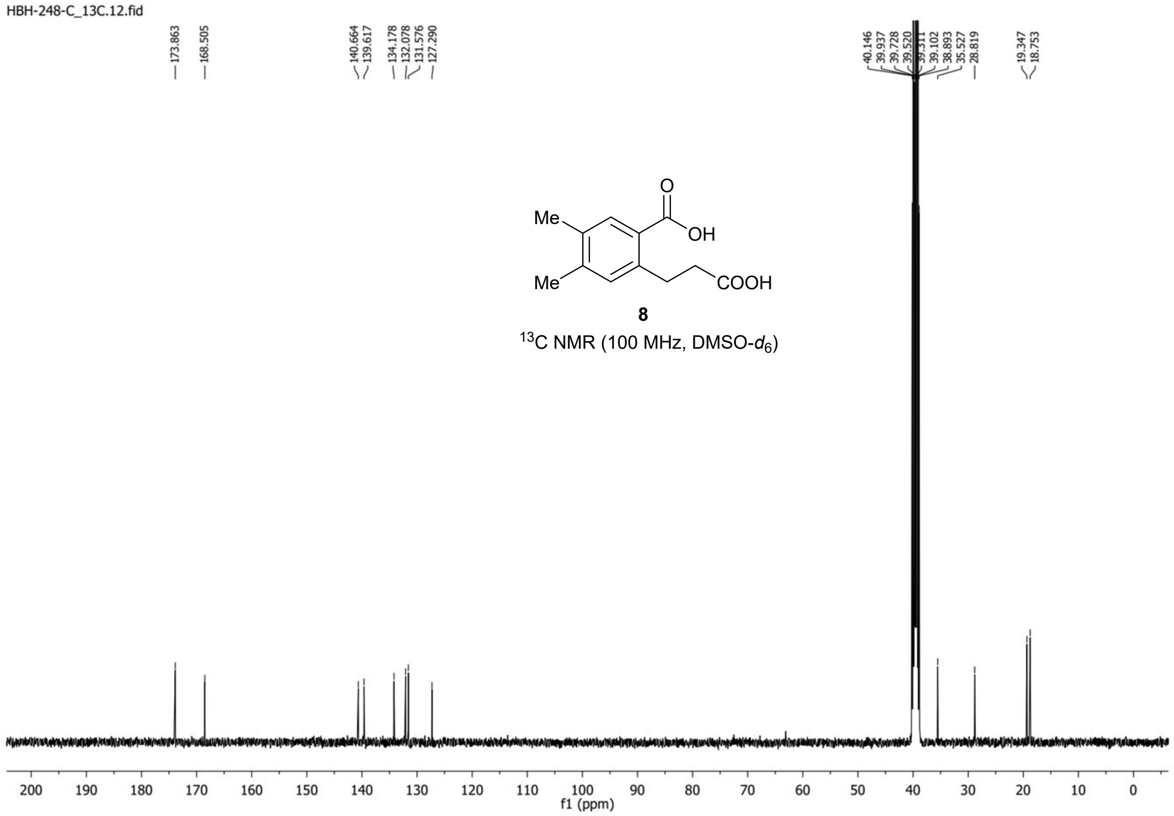
7

^{13}C NMR (125 MHz, CDCl$_3$)



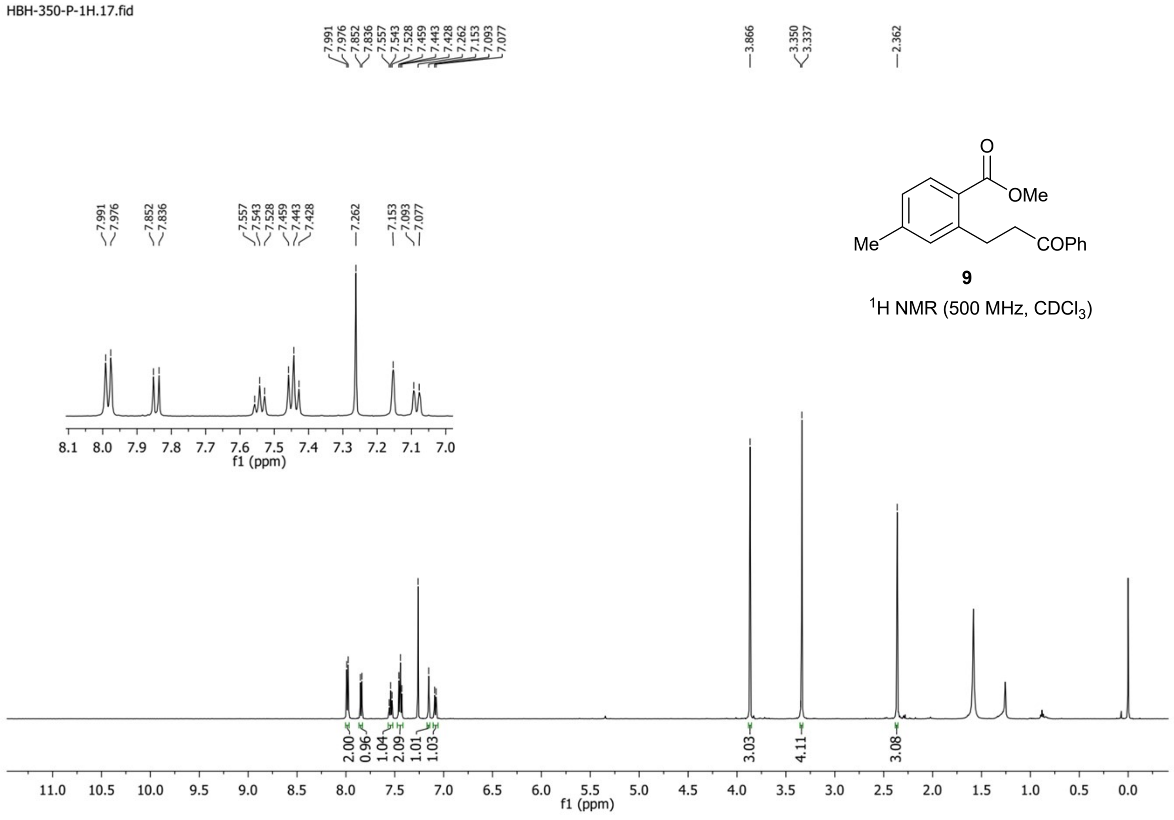
8

^{1}H NMR (400 MHz, DMSO-d_6)



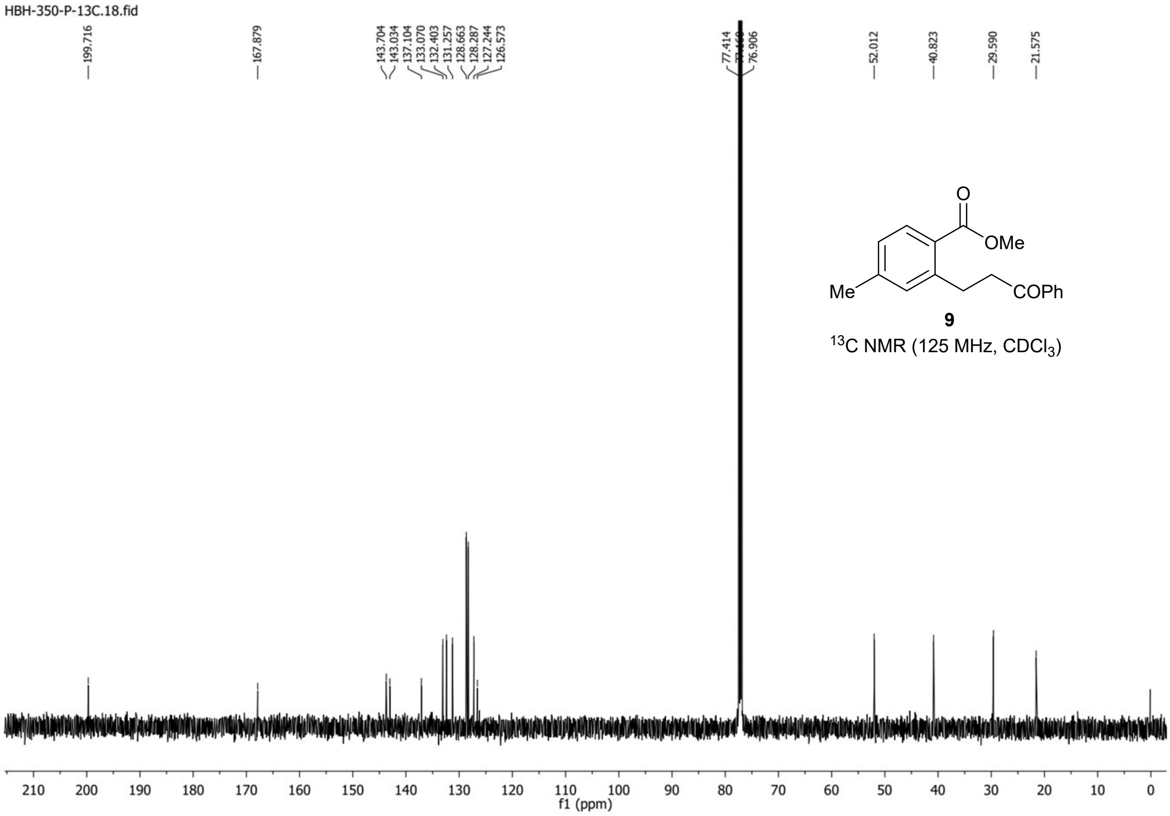
8

^{13}C NMR (100 MHz, DMSO-d_6)



9

^{1}H NMR (500 MHz, CDCl$_3$)



9

^{13}C NMR (125 MHz, CDCl$_3$)