Supporting Information

Palladium-Catalyzed Nondirected Late-Stage C–H Deuteration of Arenes

Mirxan Farizyan,[†,‡] Arup Mondal, [†,‡] Sourjya Mal,[†,§] Fritz Deufel,[†,§]
and Manuel van Gemmeren[*,†]

† Organisch-Chemisches Institut, Westfälische Wilhelms-Universität Münster,
Corrensstraße 36, 48149 Münster, Germany

‡ These authors contributed equally to this work

§ These authors contributed equally to this work

* mvangemmeren@uni-muenster.de

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1 General Experimental Methods

Solvents, Reagents, and Techniques

Unless otherwise noted, all reactions were carried out in oven-dried glassware. Reaction temperatures are reported as the temperature of the metal block surrounding the vessel.

The following solvents were dried by distillation over the drying agents indicated in parentheses: HFIP (activated 3Å molecular sieves), toluene (CaH_2). Additional anhydrous solvents (<50 ppm water) were purchased from Acros Organics, Sigma-Aldrich, or Carl Roth and stored over molecular sieves under an argon atmosphere. A strong and homogeneous stirring was also found to be crucial for the optimal yield.

Commercially available chemicals were obtained from ABCR, Acros Organics, Aldrich Chemical Co., Alfa Aesar, Combi-Blocks, Carbolution, Fluorochem, and TCI Europe and used as received unless otherwise stated.

Chromatography

Analytical thin layer chromatography (TLC) was performed on silica gel 60 F254 aluminum plates (Merck). Visualization was achieved by exposure to ultraviolet light (254 nm, 366 nm) and/or by staining. For staining the TLC plates were dipped into a solution of $KMnO_4$ (1 g $KMnO_4$, 6 g K_2CO_3 and 0.1 g KOH in 100 mL H_2O) and developed with a heat gun if necessary. Flash column chromatography was performed on silica gel (35-70 μm mesh, 60A, Acros) with a positive argon overpressure.

Nuclear Magnetic Resonance (NMR) Spectroscopy

^1H, ^{13}C, and ^{19}F NMR spectra were recorded at room temperature on a Bruker Avance II 300 MHz, Bruker Avance II 400 MHz, Agilent DD2 500 or Agilent DD2 600 spectrometer. Chemical shifts (δ) of ^1H and ^{13}C NMR spectra are given in ppm relative to tetramethylsilane (TMS) using the residual solvent peaks for calibration ($CDCl_3$: δ_H = 7.26 ppm, δ_C = 77.16 ppm).[1] ^{19}F NMR spectra are reported relative to CCl_3F. Rather than calibrating with an internal standard, the spectra are referenced to the proton resonance of TMS as the primary reference for the unified chemical shift scale as recommended by the IUPAC since 2001.[2] Chemical shifts are generally reported with two (^1H) or one (all other nuclei) digits after the decimal point. NMR-data are reported as follows: chemical shift (multiplicity [s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sept = septet, m = multiplet, br = broad], coupling constants (*J*, Hz) and integration). All spectra were processed using the MestReNova program. The ^{13}C-NMR spectra of deuterated compounds are reported as observed. Due to the low signal intensity and potentially an overlap of signals, the number of signals can deviate from the hypothetical value and C–D coupling constants could not be determined.

Mass Spectrometry (MS)

High resolution mass spectra (HRMS) were recorded on a Bruker Daltonics MicroTof or on a Thermo-Fisher Scientific Orbitrap LTQ XL spectrometer using electrospray ionization (ESI) and on a Exactive GC Orbitrap using electron impact ionization (EI).

Infrared Spectroscopy (IR)

Infrared spectra were recorded neat on a Shimadzu FTIR 8400S or a Varian Associates FTIR 3100 Excalibur spectrometer. The wave numbers (ν) of recorded IR-signals are quoted in cm^{-1}.

Gas Chromatography with Flame Ionization Detection (GC-FID)

GC-FID analyses were performed using an Agilent Technologies 7890B setup equipped with an HP5 column (30 m, 0.32mm × 0.25 μm).

Gas Chromatography coupled with Mass Spectrometry (GC-MS)

GC-MS spectra were recorded on an Agilent Technologies 7890A GC-system with an Agilent 5975C VL MSD or an Agilent 5975 inert Mass Selective Detector (EI) and an HP-5MS column (30 m, 0.32mm × 0.25 μm).

Determination of Deuteration Degrees by NMR Spectroscopy

For NMR analysis the decrease of the proton signal intensity was measured and compared with the values obtained from non-deuterated starting materials. The decrease in signal intensities was calibrated relative to positions in which no proton-deuterium exchange was observed. Only positions which undergo H/D exchange to 10% or more are reported as deuterated due to the experimental precision of NMR integration analysis. For comparison, the ^{1}H and ^{13}C-spectra of the non-deuterated compounds were recorded and are shown alongside the deuterated samples in the characterization of the respective products. For the optimization studies the degree of de-deuteration was determined by ^{1}H-NMR analysis. Additionally, the yield of deuterated material was determined using 1,3,5-trimethoxybenzene or 1,3,5-trimethylbenzene as internal standard.

Determination of Deuteration Degrees by Mass Spectrometry

The determination of deuteration degrees by mass spectrometric analysis was performed by the service department of the University of Münster using the automated program Universal Mass Calculator (UMC Version 3.11.0.70, Dr. Matthias C. Letzel, WWU Münster, Org.-Chem. Institut, Germany. https://www.uni-muenster.de/Chemie.oc/ms/downloads.html). For improved readability, the original data are shown explicitly. The diagrams show the measured m/z values and the experimental relative intensities of the isolated compounds (top row) followed by theoretically generated mass diagrams for selected degrees of deuteration considering the natural abundance of isotopes (bottom rows, in selected cases). The degree of deuteration was determined by fitting the experimentally observed pattern with the best possible linear combination of predicted isotopologue spectra.

Determination of Yields

For the determination of yields the mean molecular mass of the compound derived from mass spectrometry was used.

2 Preparation of Starting Materials and Ligands

General Procedure A:[3]

To a solution of the corresponding benzoic acid (10.0 mmol, 1.0 equiv.) in CH_2Cl_2 (40 mL, 0.25 M) $SOCl_2$ (0.87 mL, 12.0 mmol, 1.2 equiv.) was added slowly at 0 °C. DMF (30 µL, 0.39 mmol, 0.04 equiv.) was added as catalyst and the mixture was stirred for 4 h at 50 °C. Solvent and volatiles were removed under reduced pressure and the product was used in the following step without further purification.

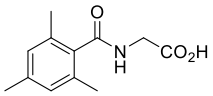
The product from the previous step was dissolved in CH_2Cl_2 (5 mL) and slowly added to a mixture of ethyl glycinate hydrochloride (1.40 g, 10.0 mmol, 1.0 equiv.) and triethylamine (3.10 mL, 22.0 mmol, 2.2 equiv.) in CH_2Cl_2 (10 mL) at 0°C. The reaction mixture was stirred for further 30 min at 0 °C and was then allowed to slowly warm to room temperature overnight. The mixture was washed with 1 M aq. HCl (2 × 20 mL) 1 M aq. HCl, subsequently with sat. aq. $NaHCO_3$ (2 × 20 mL) and finally with sat NaCl solution (2 × 20 mL). The combined organic phases were dried over Na_2CO_3 and the solvent was removed under reduced pressure. The product was used in the following step without further purification.

The product from the previous step was dissolved in a mixture of MeOH (20 mL) and aq. NaOH solution (20 wt%, 20 mL) and the resulting mixture was stirred at 80 °C overnight. MeOH was removed under reduced pressure and the solution was washed with CH_2Cl_2. The aqueous phase was acidified with conc. aq. HCl to reach a pH value of 1 and extracted with CH_2Cl_2. (2 × 20 mL) The extracts were concentrated and the crude product was purified via flash column chromatography.

General Procedure B:[4,5]

DMAP (489 mg, 4.00 mmol, 2.0 equiv.) was added to a suspension of EDC·HCl (499 mg, 2.40 mmol, 1.2 equiv.) in CH_2Cl_2 (5 mL, 0.4 M). The mixture was stirred at room temperature until all the solids dissolved. The mixture was cooled to 0 °C, the corresponding acid (2.00 mmol, 1.0 equiv.) was added, followed by the corresponding sulfonamide (2.20 mmol, 1.1 equiv.) and the mixture was stirred at rt for 24 h. The aqueous phase was acidified with conc. aq. HCl to reach a pH value of 1 and extracted with CH_2Cl_2 (4 × 20 mL). The combined organic phases were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified via flash column chromatography.

(2,4,6-trimethylbenzoyl)glycine (L2)



Following the general procedure A using 2,4,6-trimethylbenzoic acid (1.64 g, 10.0 mmol) and purification via silica gel column chromatography using pentane:EtOAc = 1:1 as the eluent, the target compound **L2** was obtained as colorless solid (1.68 g, 7.60 mmol, 76%).

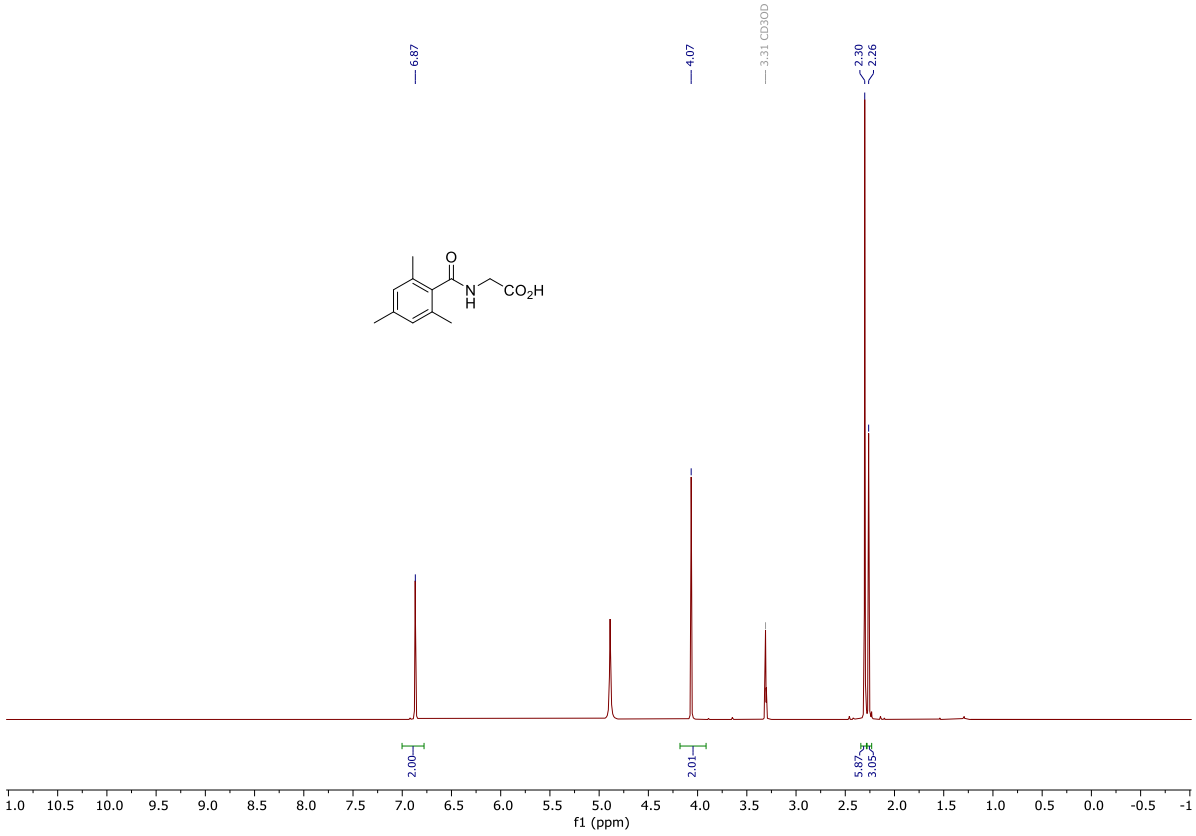
^{1}H NMR (400 MHz, CD_3OD) δ = 6.87 (s, 2H), 4.07 (s, 2H), 2.30 (s, 6H), 2.26 (s, 3H) ppm.

^{13}C NMR (101 MHz, CD_3OD) δ = 174.0, 172.7, 139.8, 135.7, 135.6, 129.0, 41.7, 21.2, 19.2 ppm.

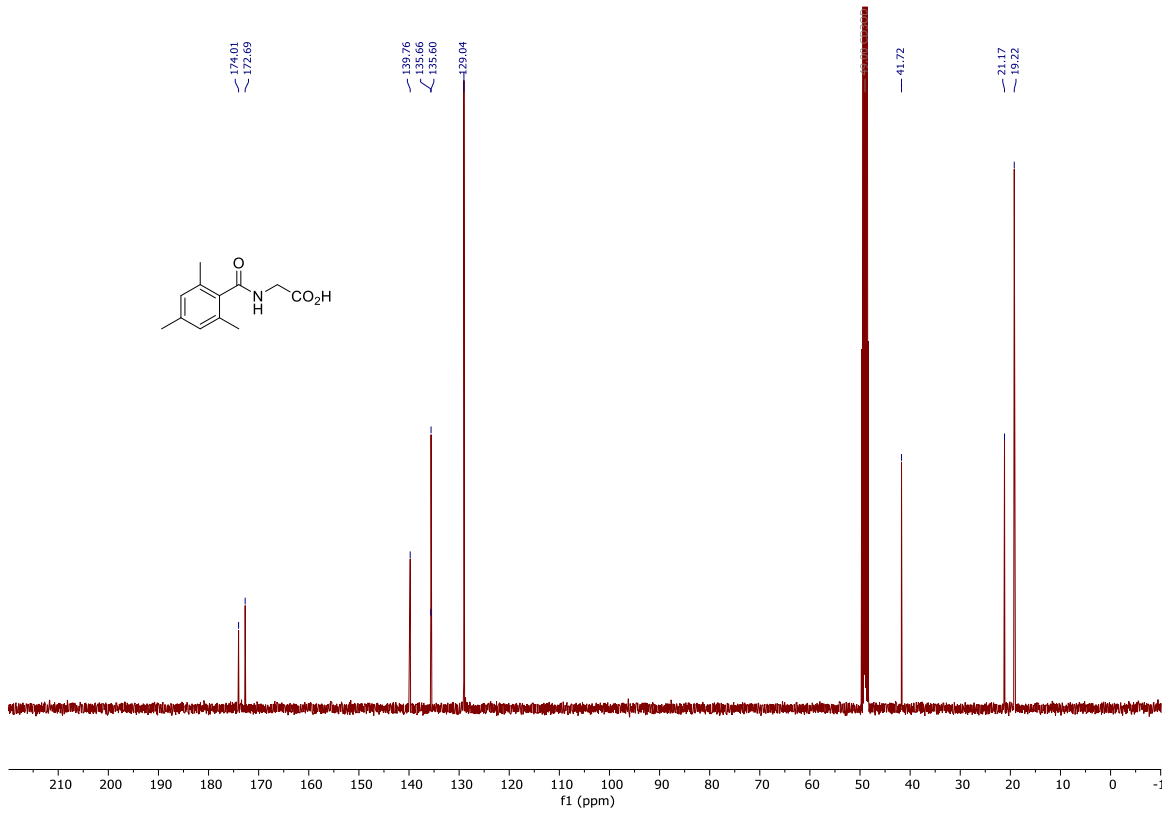
HRMS (ESIneg) m/z: Calcd for $C_{12}H_{14}NO_3$ 220.09682, Found 220.09760.

IR (cm^{-1}): 2460, 2240, 2209, 2071, 1122, 1089, 1068, 973, 820.

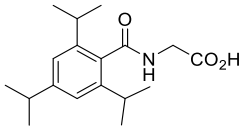
^{1}H-NMR spectrum in CD_3OD:



^{13}C-NMR spectrum in CD_3OD:



(2,4,6-triisopropylbenzoyl)glycine (L3)



Following the general procedure A using 2,4,6-triisopropylbenzoic acid (2.48 g, 10.0 mmol), and purification via silica gel column chromatography using pentane:EtOAc = 1:1 as the eluent, the target compound **L3** was obtained as colorless solid (2.02 g, 6.60 mmol, 66%).

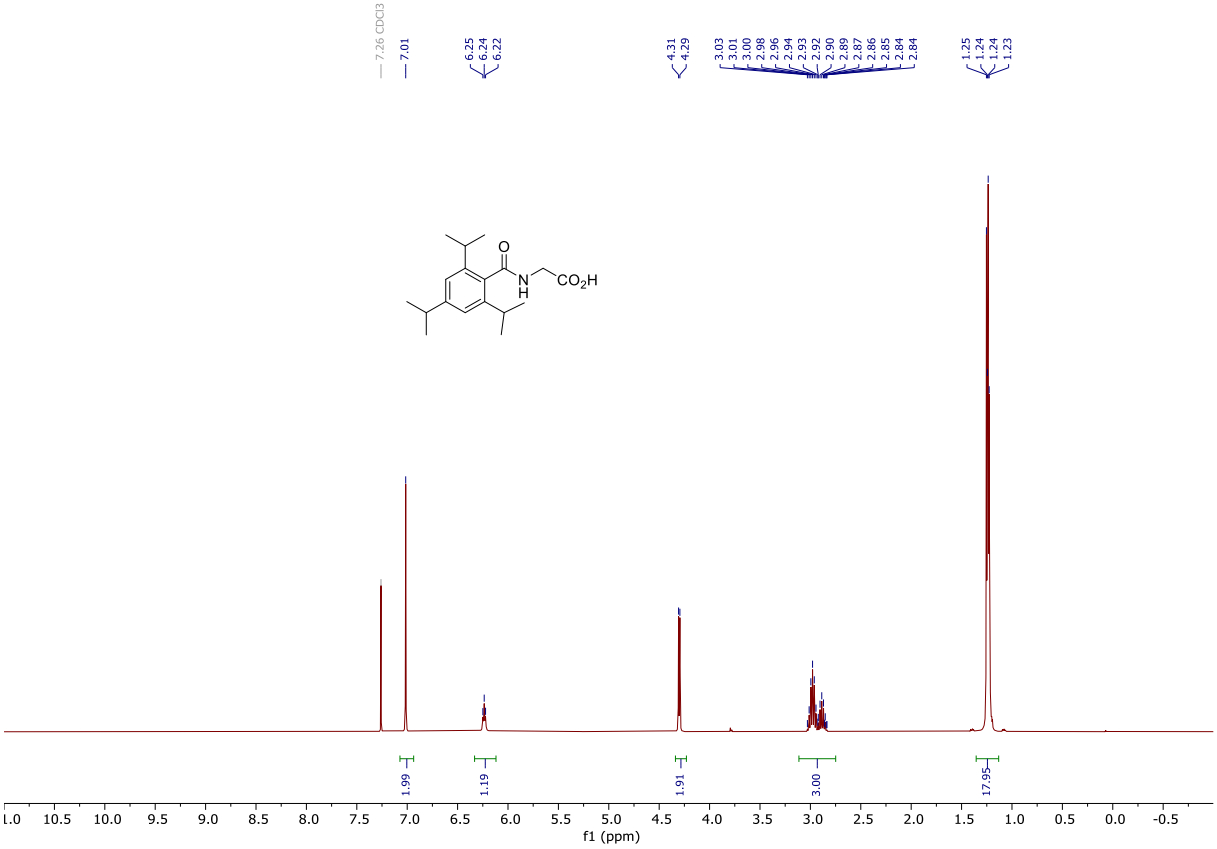
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.01 (s, 2H), 6.24 (t, *J* = 5.3 Hz, 1H), 4.30 (d, *J* = 5.2 Hz, 2H), 3.07-2.80 (m, 3H), 1.31-1.14 (m, 18H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 173.5, 171.7, 150.4, 145.3, 132.3, 121.2, 41.5, 34.6, 31.1, 24.9-24.4 (4C), 24.1 ppm.

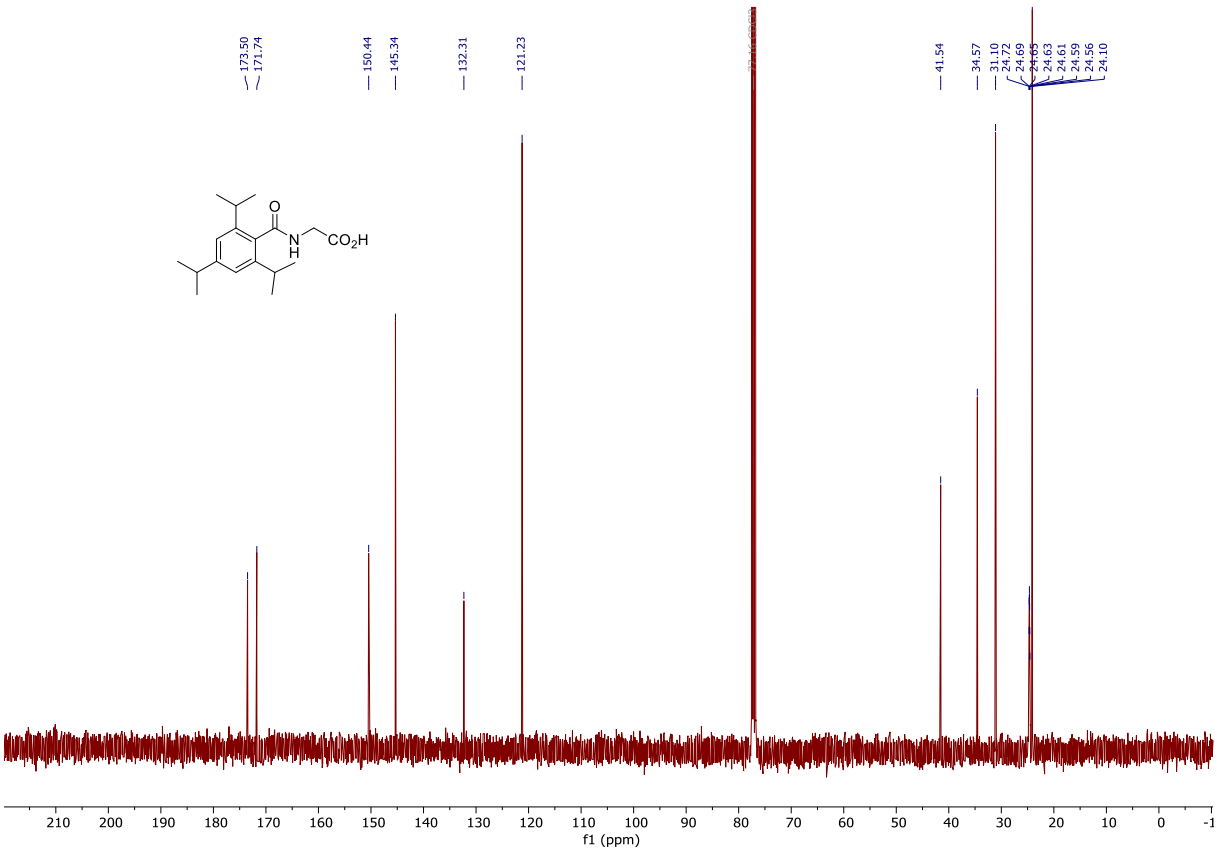
HRMS (ESIneg) m/z: Calcd for $C_{18}H_{26}NO_3$ 304.19072, Found 304.19116.

IR (cm^{-1}): 1506, 1465, 1379, 1340, 1312, 1160, 1128, 1108, 951, 917, 650.

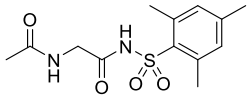
^{1}H-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



2-acetamido-*N*-(mesitylsulfonyl)acetamide (L4)



Following the general procedure B using acetylglycine (234 mg, 2.00 mmol) and 2,4,6-trimethylbenzenesulfonamide (439 mg, 2.20 mmol, 1.1 equiv.), and purification via silica gel column chromatography using MeOH:CH_2Cl_2 = 1:19 as the eluent, the target compound **L4** was obtained as colorless solid (378 mg, 1.27 mmol, 63%).

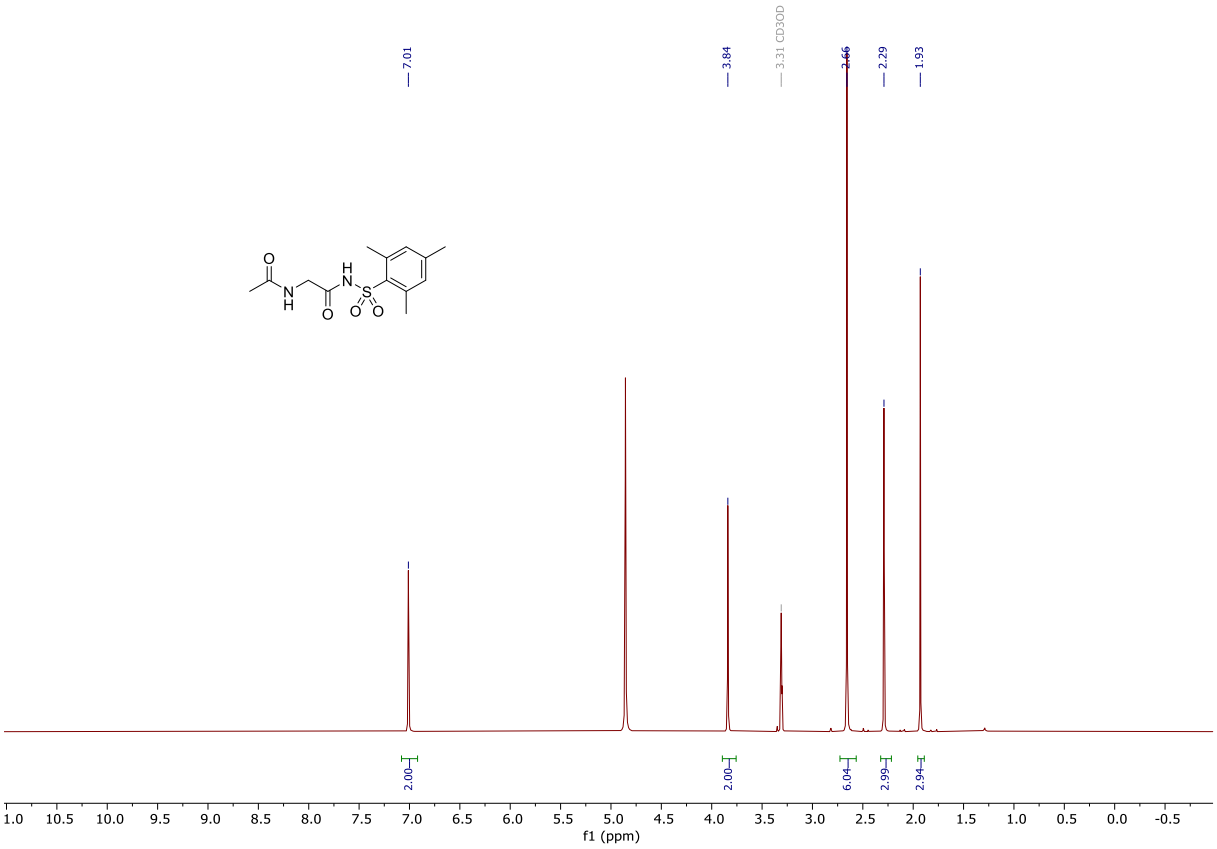
^{1}H NMR (400 MHz, CD_3OD) δ = 7.01 (s, 2H), 3.84 (s, 2H), 2.66 (s, 6H), 2.29 (s, 3H), 1.93 (s, 3H) ppm.

^{13}C NMR (101 MHz, CD_3OD) δ = 173.8, 169.9, 144.7, 141.6, 134.5, 132.8, 43.3, 22.8, 22.2, 21.0 ppm.

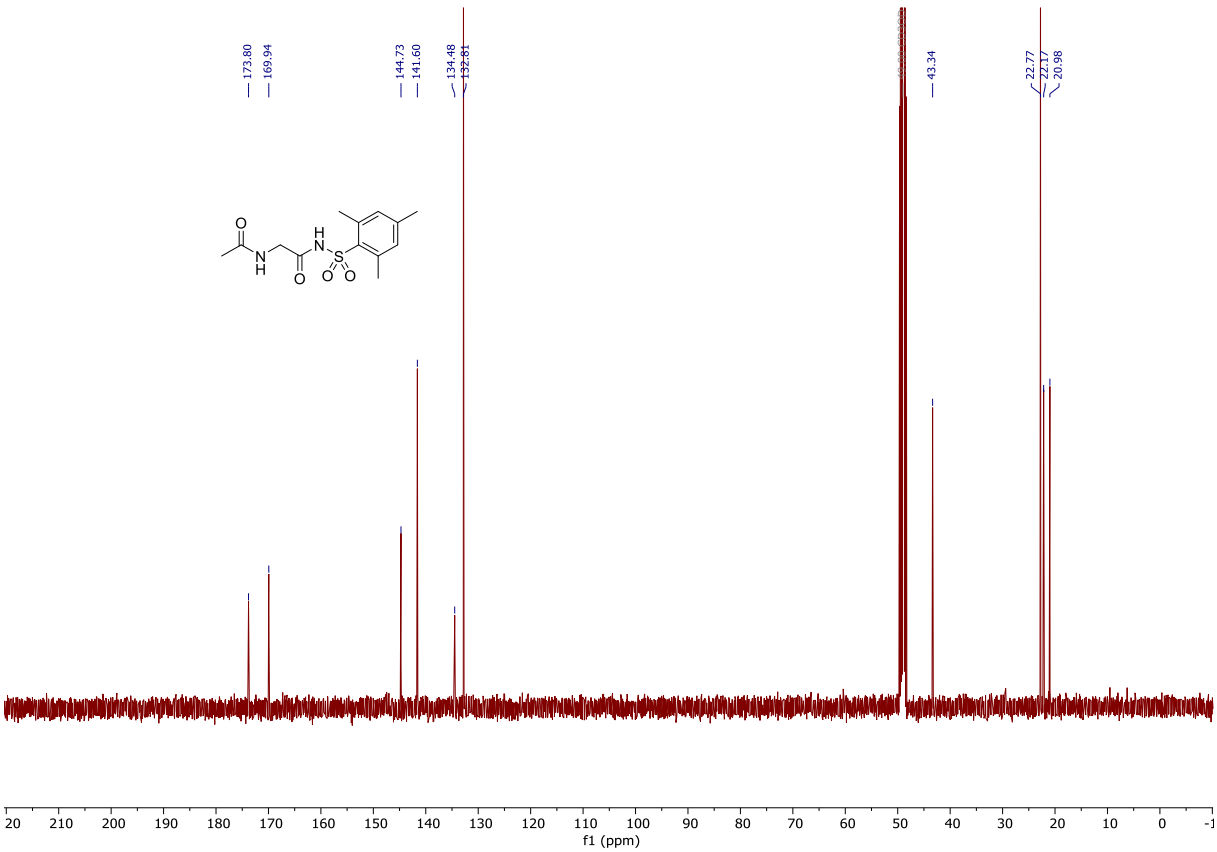
HRMS (ESIneg) m/z: Calcd for $C_{13}H_{17}N_2O_4S$ 297.09035, Found 297.09072.

IR (cm^{-1}): 2460, 2240, 2211, 2071, 1507, 1122, 1092, 973, 819.

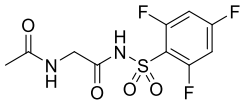
^{1}H-NMR spectrum in CD_3OD:



^{13}C-NMR spectrum in CD_3OD:



2-acetamido-*N*-((2,4,6-trifluorophenyl)sulfonyl)acetamide (L5)



Following the general procedure B using acetylglycine (234 mg, 2.00 mmol, 1.0 equiv.) and 2,4,6-trifluorobenzenesulfonamide (465 mg, 2.20 mmol, 1.1 equiv.), and purification via silica gel column chromatography using MeOH:CH_2Cl_2 = 1:19 with 0.3% formic acid as the eluent, the target compound **L5** was obtained as colorless solid (549 mg, 1.77 mmol, 89%).

^{1}H NMR (500 MHz, CD_3OD) δ = 7.10 (s, 2H), 3.89 (s, 2H), 1.95 (s, 3H) ppm.

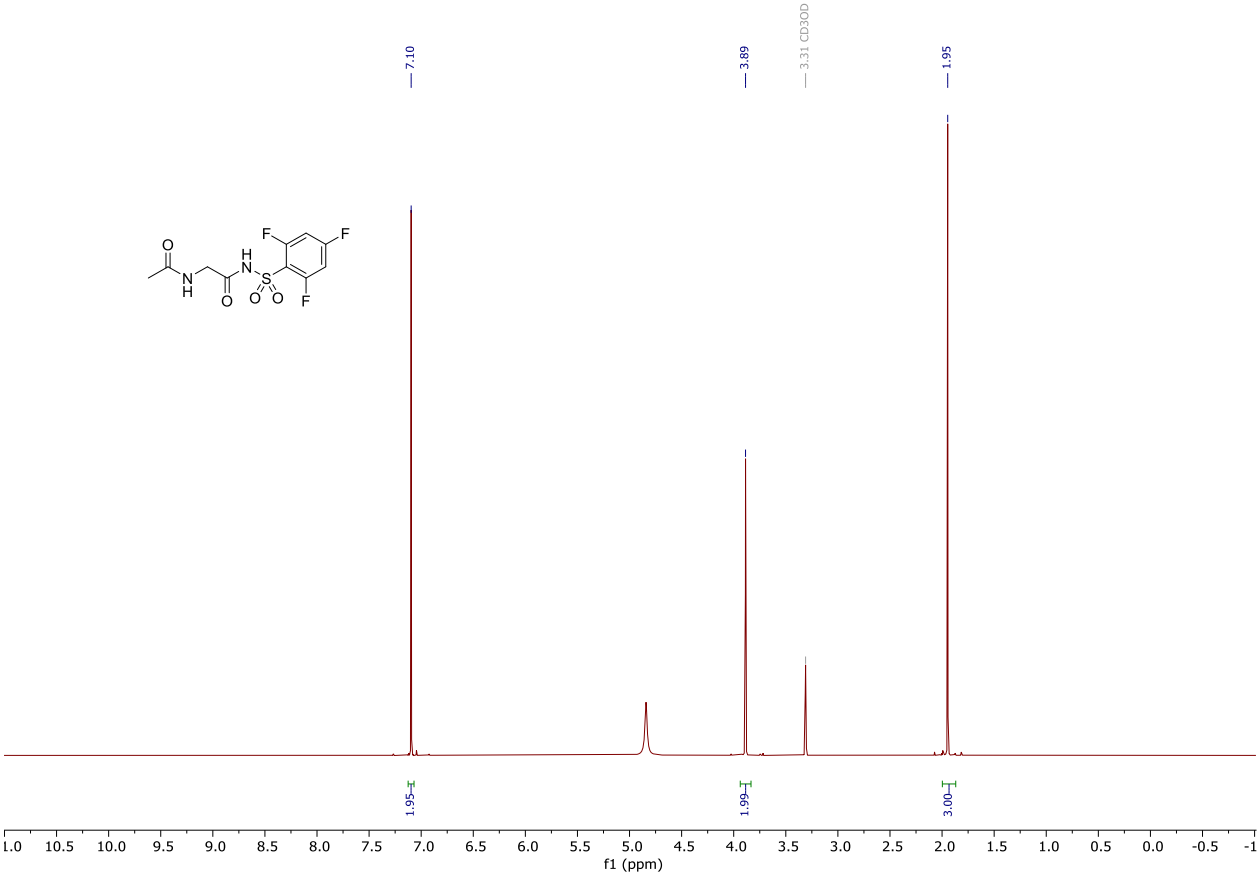
^{13}C NMR (126 MHz, CD_3OD) δ = 173.8, 170.2, 167.4, 162.5, 115.5, 103.2, 43.6, 22.1 ppm.

^{19}F NMR (470 MHz, CD_3OD) δ = –99.5 (t, *J* = 11.9 Hz), –104.3 (d, *J* = 11.9 Hz) ppm.

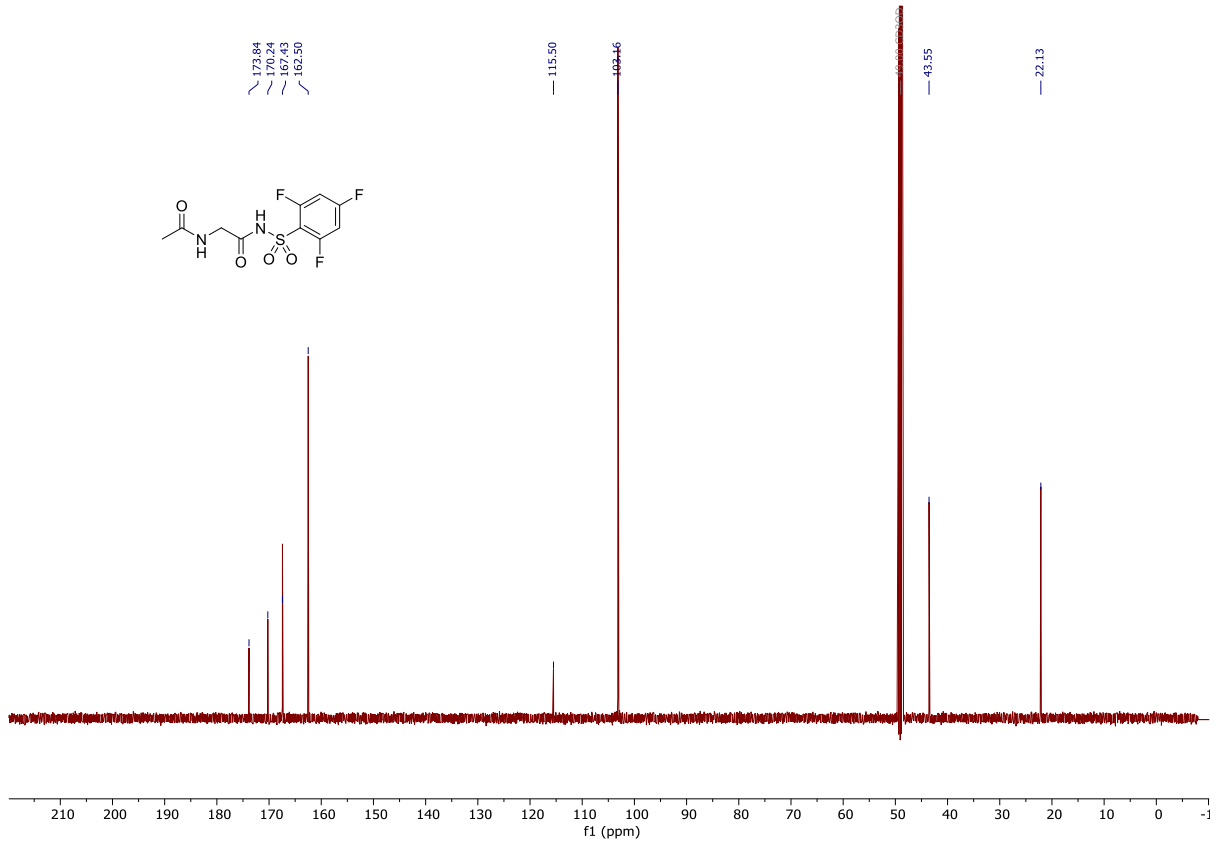
HRMS (ESIneg) m/z: Calcd for $C_{10}H_8F_3N_2O_4S$ 309.01514, Found 309.01571.

IR (cm^{-1}): 2464, 2209, 2071, 1559, 1507, 1122, 1092, 973, 819.

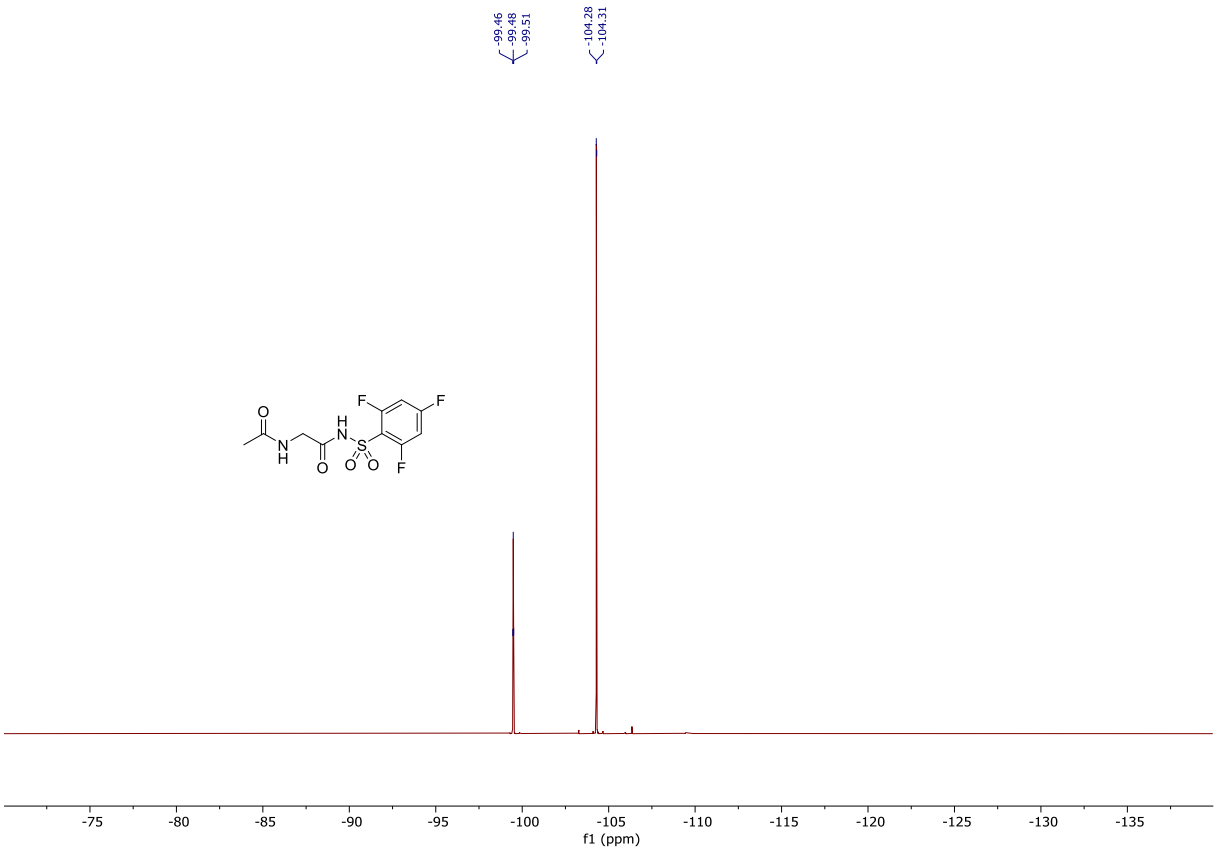
^{1}H-NMR spectrum in CD_3OD:



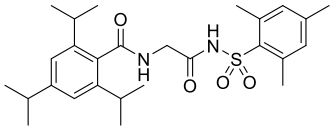
^{13}C-NMR spectrum in CD_3OD:



^{19}F-NMR spectrum in CD_3OD:



2,4,6-triisopropyl-*N*-(2-oxo-2-((2,4,6-trimethylphenyl)sulfonamido)ethyl)benzamide (L6)



Following the general procedure B using (2,4,6-triisopropylbenzoyl)glycine **L3** (611 mg, 2.00 mmol, 1.0 equiv.) and 2,4,6-trimethylbenzenesulfonamide (439 mg, 2.20 mmol, 1.1 equiv.), and purification via silica gel column chromatography using MeOH:CH_2Cl_2 = 1:49 with 0.3% formic acid as the eluent, the target compound **L6** was obtained as colorless solid (740 mg, 1.52 mmol, 76%)

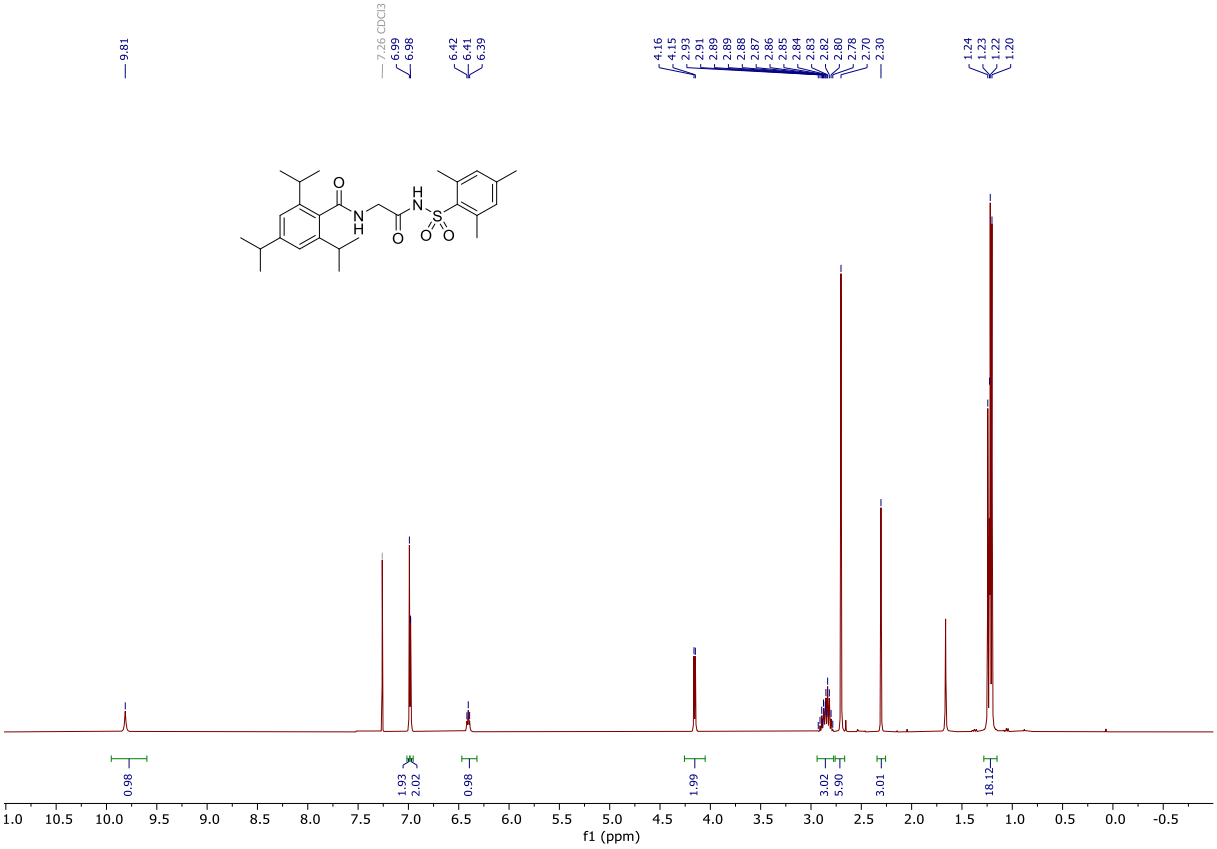
^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.81 (s, 1H), 6.99 (s, 2H), 6.98 (s, 2H), 6.41 (t, *J* = 5.4 Hz, 1H), 4.16 (d, *J* = 5.5 Hz, 2H), 2.96-2.76 (m, 3H), 2.70 (s, 6H), 2.30 (s, 3H), 1.28-1.18 (m, 18H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 172.8, 167.4, 150.7, 145.2, 143.9, 140.8, 132.6, 132.2, 131.7, 121,2, 44.7, 34.6, 31.4, 25.2-24.2 (4C), 24.1, 22.9, 21.2 ppm.

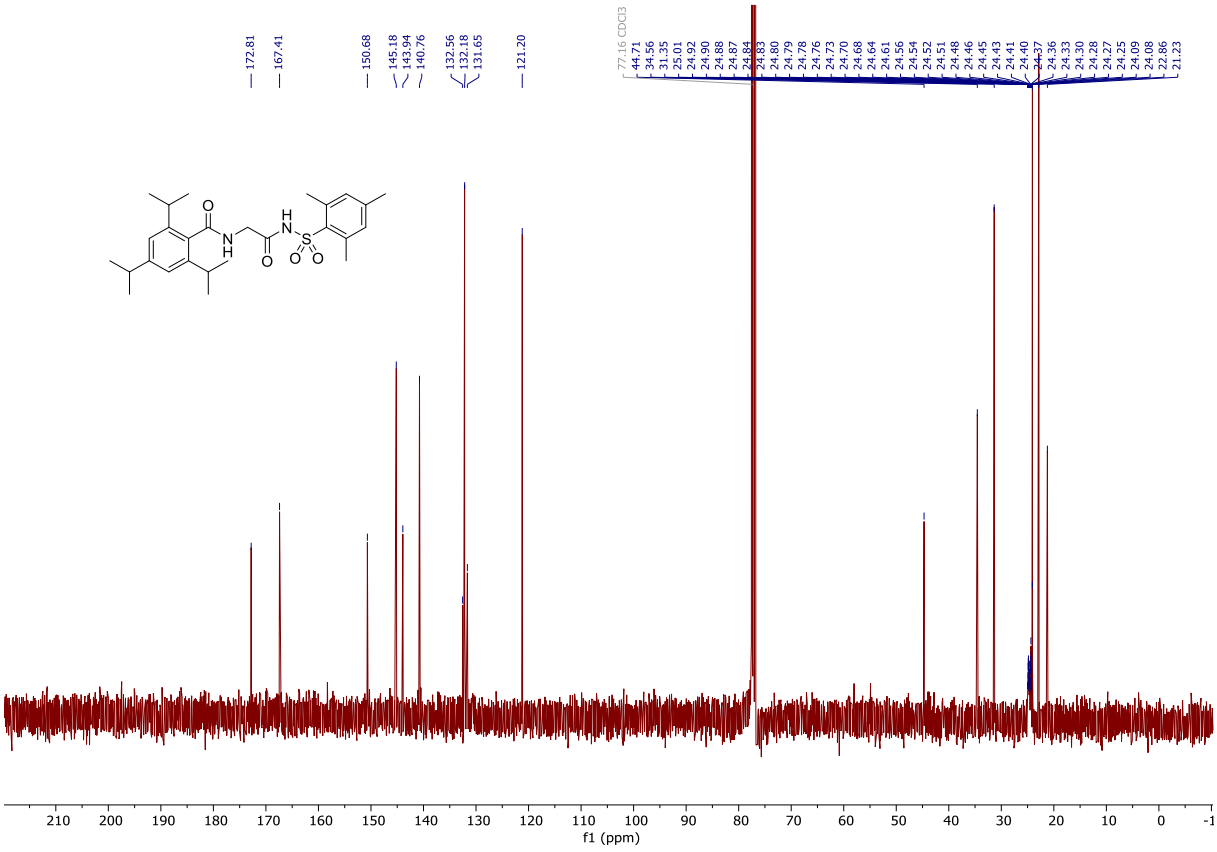
HRMS (ESIneg) m/z: Calcd for $C_{27}H_{37}N_2O_4S$ 485.24685 , Found 485.24696.

IR (cm^{-1}): 1559, 1539, 1507, 1457, 1379, 1369, 1340, 1313, 1160, 1128, 1107, 951, 922, 910, 816, 733, 646.

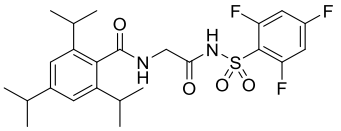
^{1}H-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



2,4,6-triisopropyl-*N*-(2-oxo-2-((2,4,6-trifluorophenyl)sulfonamido)ethyl)benzamide (L7)



Following the general procedure B using (2,4,6-triisopropylbenzoyl)glycine **L3** (611 mg, 2.00 mmol, 1.0 equiv.) and 2,4,6-trifluorobenzenesulfonamide (465 mg, 2.20 mmol, 1.2 equiv.), and purification via silica gel column chromatography using MeOH:CH_2Cl_2 = 1:49 with 0.3% formic acid as the eluent, the target compound **L7** was obtained as colorless solid (879 mg, 1.76 mmol, 88%).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.00 (s, 2H), 6.81 (t, *J* = 8.5 Hz, 2H), 6.43 (t, *J* = 5.5 Hz,1H), 4.22 (d, *J* = 5.5 Hz, 2H), 2.95-2.68 (m, 3H), 1.31-1.13 (m, 18H) ppm.

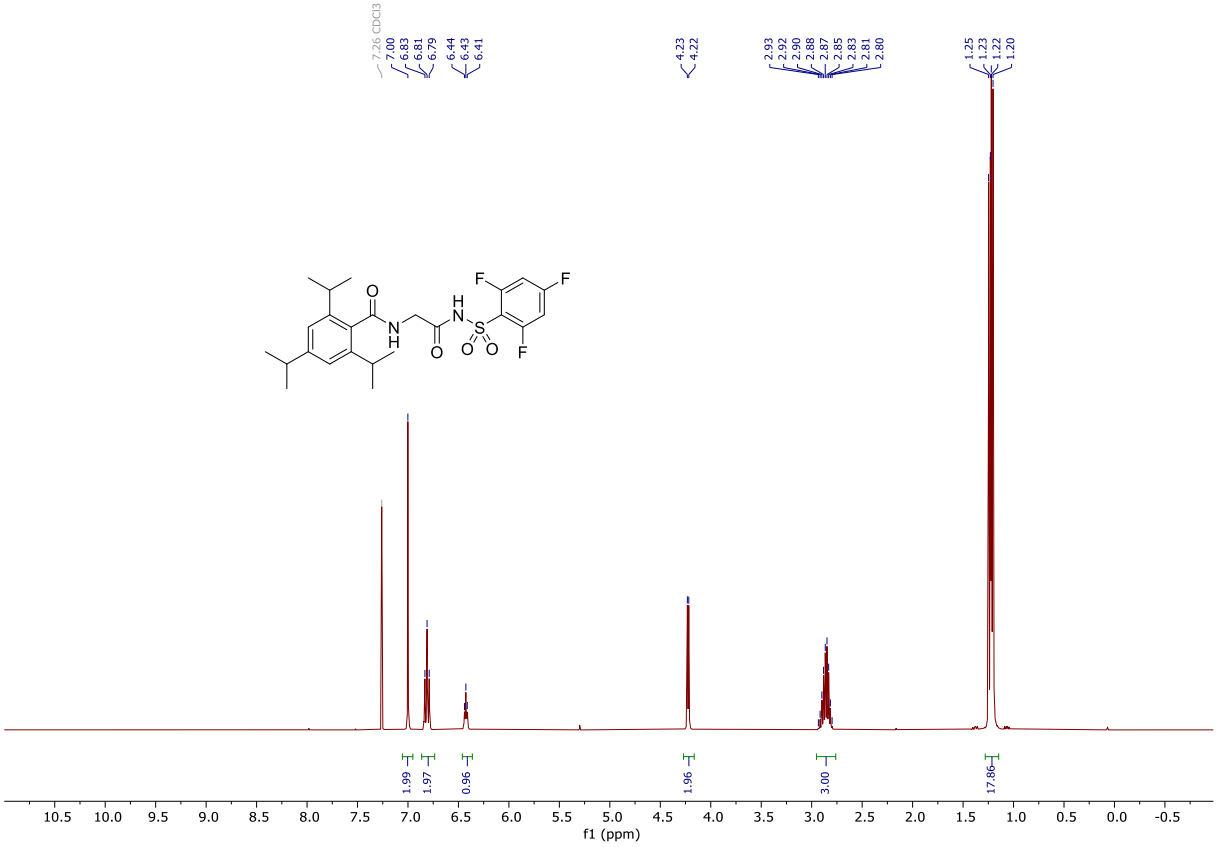
^{13}C NMR (126 MHz, $CDCl_3$) δ = 172.9, 168.2, 166.1, 161.3, 150.7, 145.3, 131.5, 121.2, 114.0, 102.3, 44.5, 34.6, 31.3, 27.0-22.4 (3C) ppm.

^{19}F NMR (470 MHz, $CDCl_3$) δ = –100.0 (t, *J* = 12.1 Hz), –105.7 (d, *J* = 12.2 Hz) ppm.

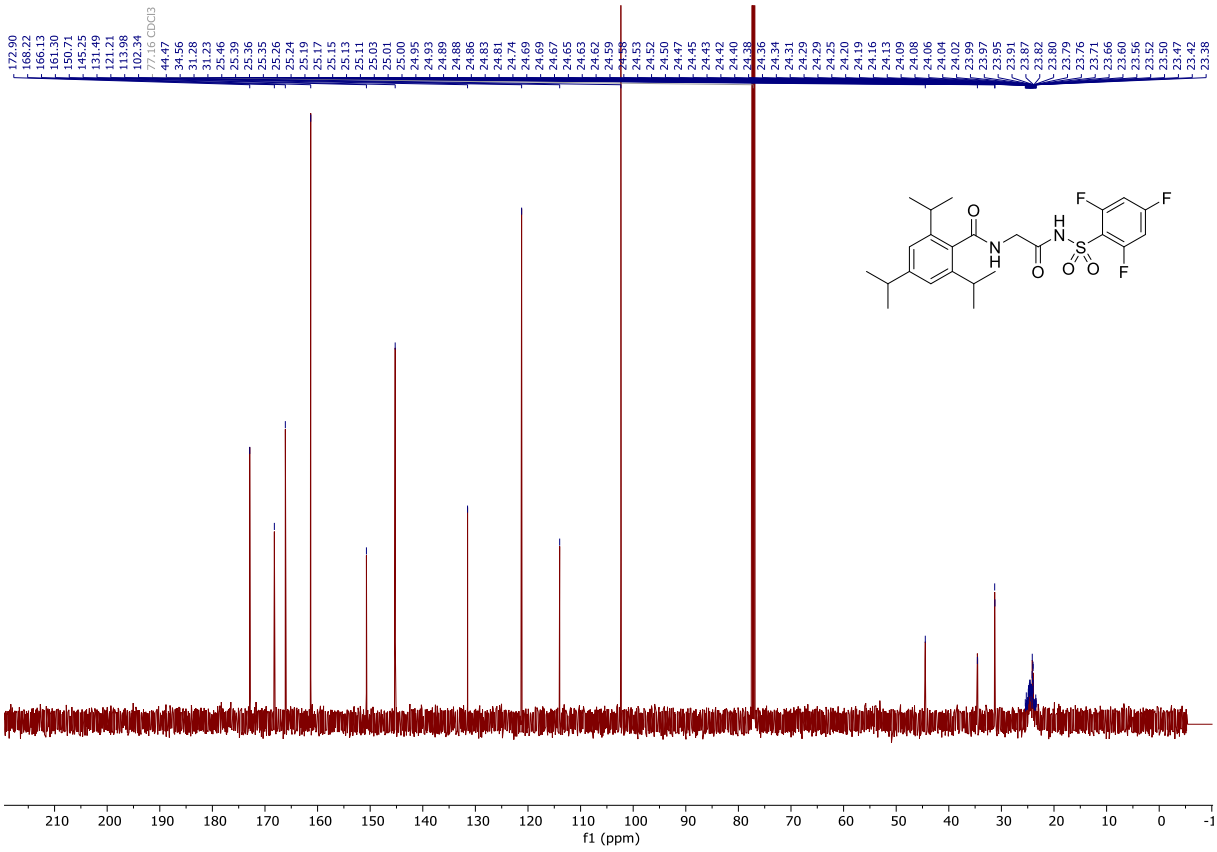
HRMS (ESIneg) m/z: Calcd for $C_{24}H_{28}F_3N_2O_4S$ 497.17164 , Found 497.17165.

IR (cm^{-1}): 1653, 1559, 1507, 1457, 904, 849, 723, 665, 650.

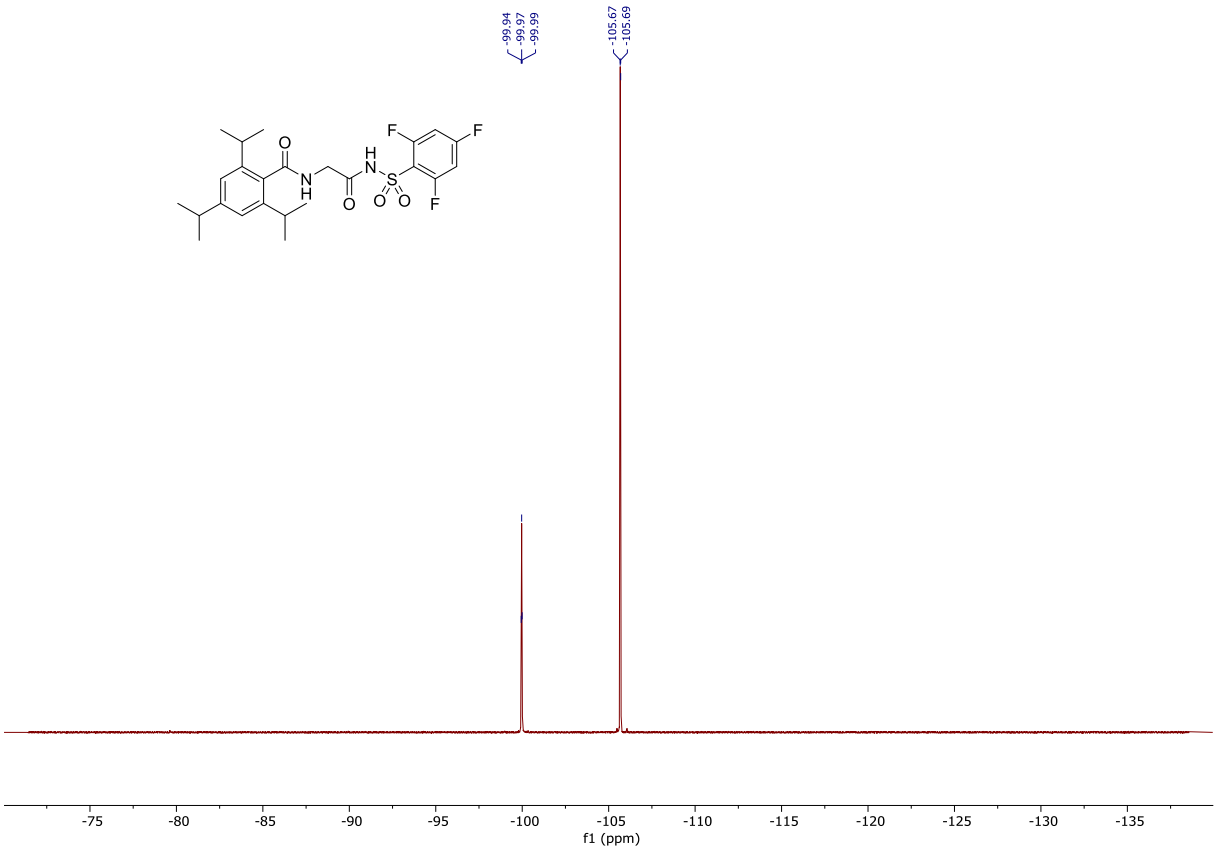
^{1}H-NMR spectrum in $CDCl_3$:



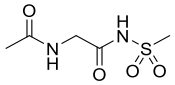
^{13}C-NMR spectrum in $CDCl_3$:



^{19}F-NMR spectrum in $CDCl_3$:



2-acetamido-*N*-(methylsulfonyl)acetamide (L8)



Following the general procedure B using acetylglycine (234 mg, 2.00 mmol, 1.0 equiv.) and methanesulfonamide (209 mg, 2.20 mmol, 1.1 equiv.), and purification via silica gel column chromatography using MeOH:CH_2Cl_2 = 1:19 with 0.3% formic acid as the eluent, the target compound **L4** was obtained as colorless solid (307 mg, 1.58 mmol, 79%).

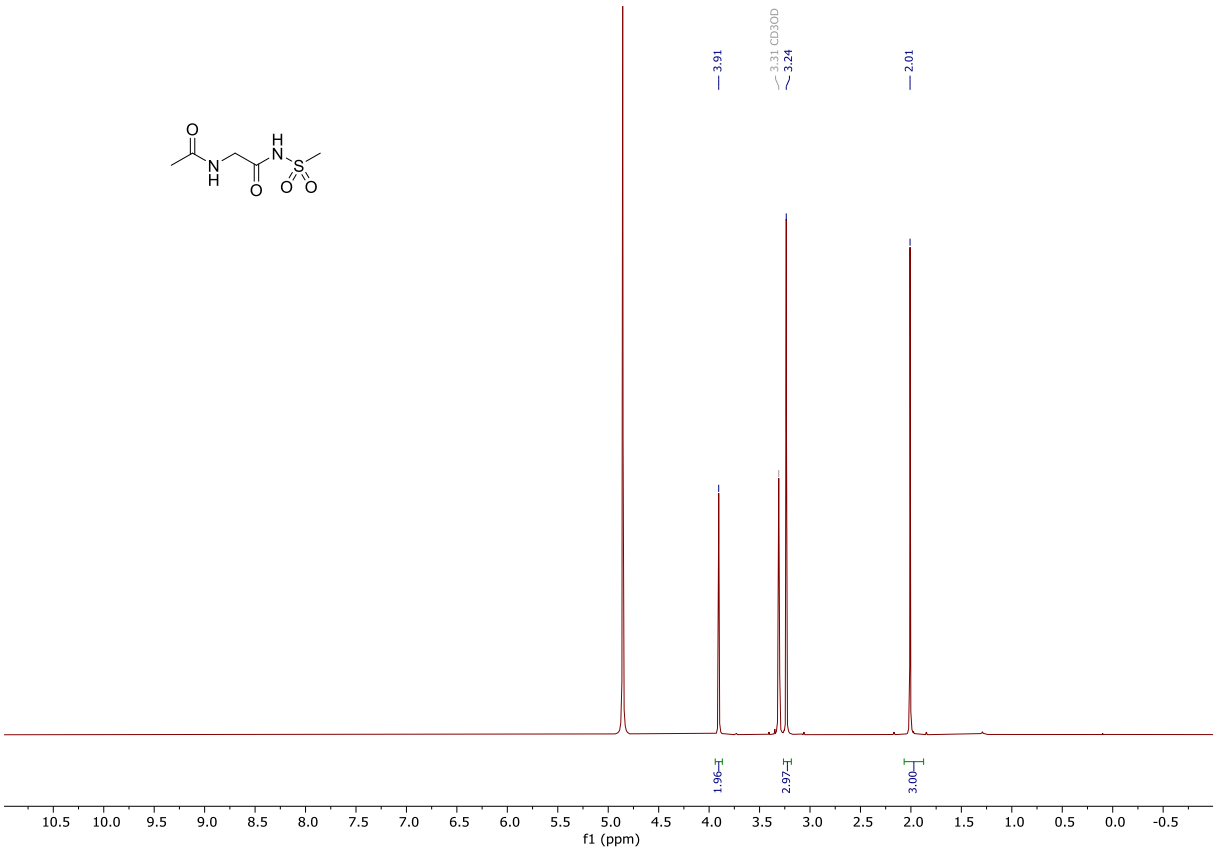
^{1}H NMR (400 MHz, CD_3OD) δ = 3.91 (s, 2H), 3.24 (s, 3H), 2.01 (s, 1H) ppm.

^{13}C NMR (101 MHz, CD_3OD) δ = 174.0, 170.7, 43.7, 41.4, 22.2 ppm.

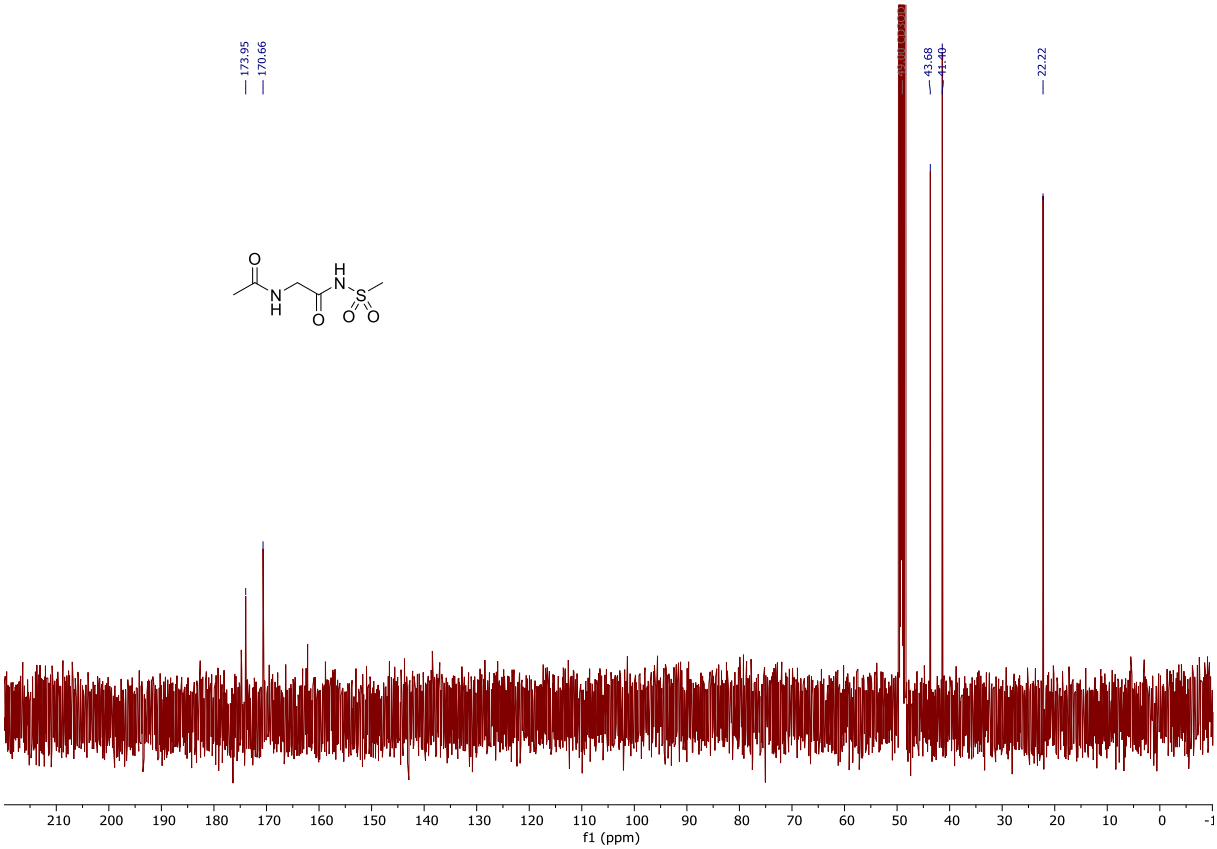
HRMS (ESIneg) m/z: Calcd for $C_5H_9N_2O_4S$ 193.02775, Found 193.02861.

IR (cm^{-1}): 2468, 2241, 2208, 2071, 1507, 1122, 1090, 973, 925.

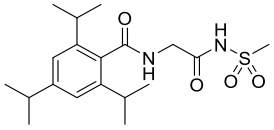
^{1}H-NMR spectrum in CD_3OD:



^{13}C-NMR spectrum in CD_3OD:



2,4,6-triisopropyl-*N*-(2-(methylsulfonamido)-2-oxoethyl)benzamide (L9)



Following the general procedure B using (2,4,6-triisopropylbenzoyl)glycine **L3** (611 mg, 2.00 mmol, 1.0 equiv.) and methanesulfonamide (209 mg, 2.20 mmol, 1.1 equiv.), and purification via silica gel column chromatography using MeOH:CH_2Cl_2 = 1:49 with 0.3% formic acid as the eluent, the target compound **L6** was obtained as colorless solid (543 mg, 1.42 mmol, 71%).

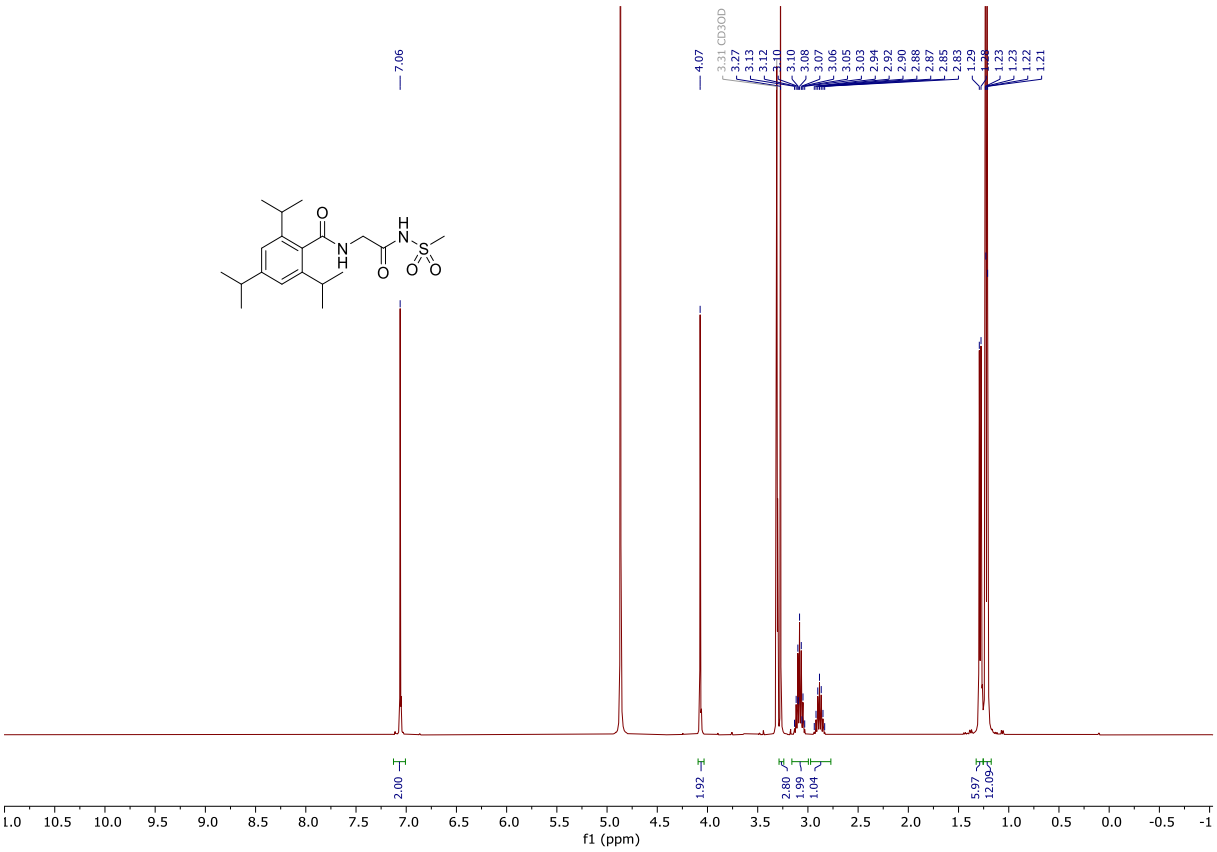
^{1}H NMR (400 MHz, CD_3OD) δ = 7.06 (s, 2H), 4.07 (s, 2H), 3.27 (s, 3H), 3.08 (hept, *J* = 6.7 Hz, 2H), 2.88 (hept, *J* = 6.9 Hz, 1H), 1.28 (d, *J* = 6.8 Hz, 6H), 1.22 (dd, *J* = 6.9, 1.9 Hz, 12H) ppm.

^{13}C NMR (101 MHz, CD_3OD) δ = 174.4, 170.1, 151.4, 146.6, 134.0, 121.9, 43.6, 41.4, 35.7, 32.0, 24.9, 24.6, 24.4 ppm.

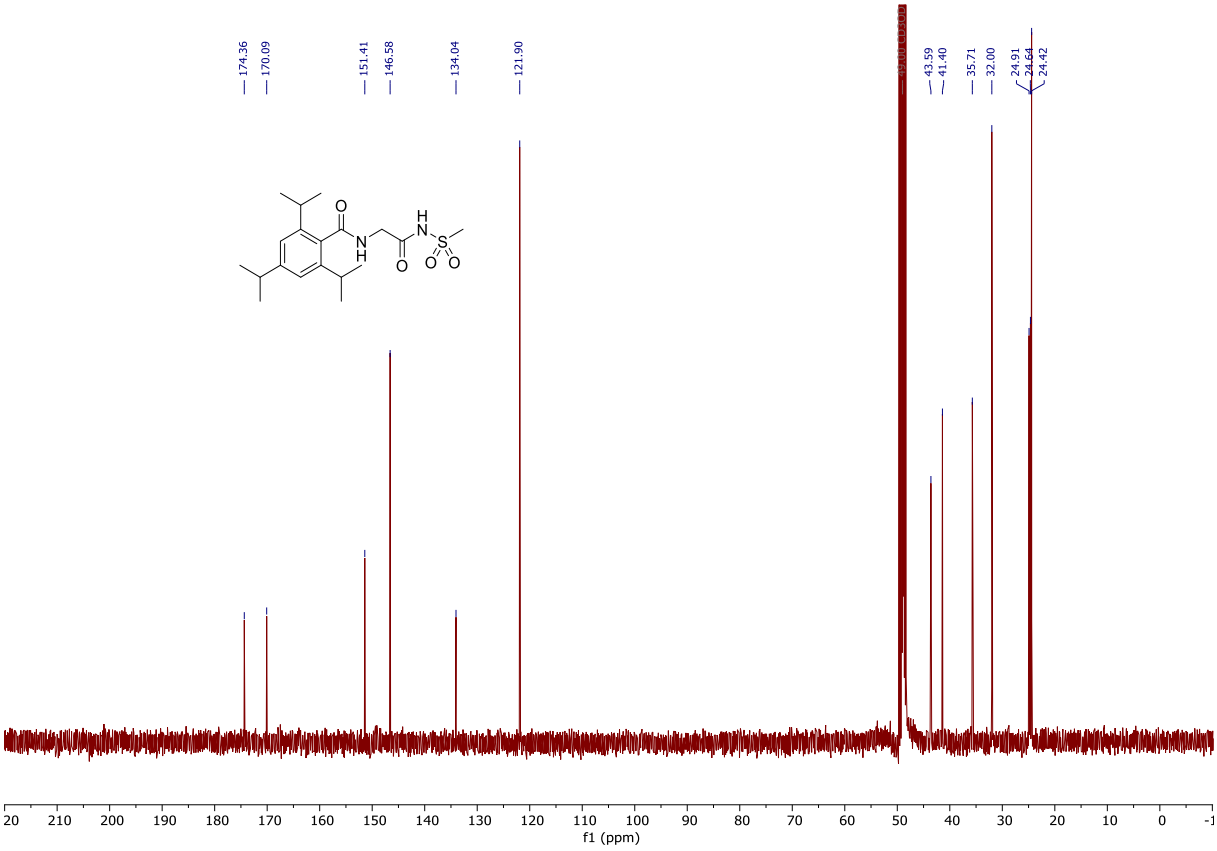
HRMS (ESIneg) m/z: Calcd for $C_{19}H_{29}N_2O_4S$ 381.18425, Found 381.18463.

IR (cm^{-1}): 2467, 2240, 2207, 2071, 1559, 1507, 1122, 1090, 973, 824.

^{1}H-NMR spectrum in CD_3OD:



^{13}C-NMR spectrum in CD_3OD:

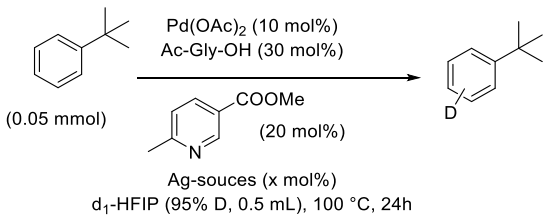


3 Optimization of the Reaction Conditions with Electron-Donating Substitutents

General Procedure C:

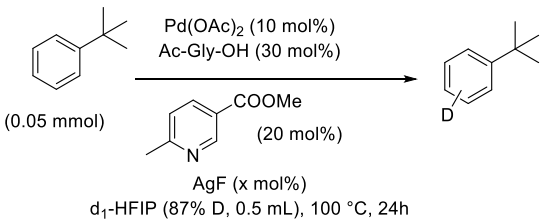
An oven dried 10 mL Schlenk tube was charged with a $Pd(OAc)_2$, a bidentate ligand, a pyridine ligand, if indicated an Ag-source, *tert*-butyl benzene or anisole (0.100 mmol), and solvent. The reaction vessel was tightly sealed then placed into the inside circle of a preheated aluminum block with a tightly fitting recess on a magnetic stirrer and stirred at the indicated temperature until completion of the reaction. The reaction mixture was allowed to cool to room temperature. 1,3,5-trimethoxybenzene or 1,3,5-trimethylbenzene was added as an internal standard. The reaction mixture was filtered over a pad of Celite® and the residue was washed with dichloromethane. The overall solution was concentrated under reduced pressure and $CDCl_3$ (0.9 mL) was added. All yields and deuteration degrees during the optimization study were determined via ^{1}H-NMR of the crude reaction using 1,3,5-trimethoxybenzene or 1,3,5-trimethylbenzene as an internal standard.

Scheme S3.1: Screening of silver salts.



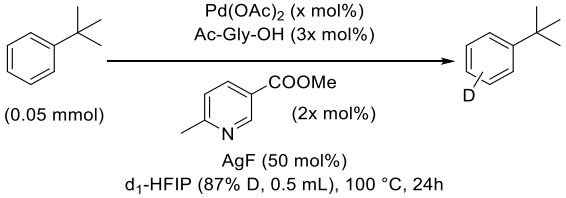
Entry	Ag-sources	Yield of starting material and product (%, GC-FID)	D-content after reaction (NMR)
1	AgOAc (50 mol%)	92	Ortho - 3% meta - 93% para - 94%
2	AgF (50 mol%)	quant	Ortho - 7% meta - 96% para - 95%
3	Ag_2CO_3 (25 mol%)	93	Ortho - 11% meta - >99% para - 97%

Scheme S3.2: Screening of the amount of silver salt.



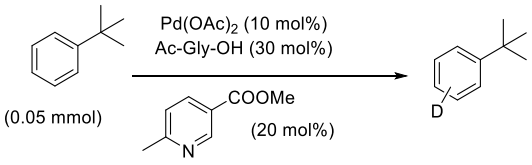
Entry	AgF amount	Yield of starting material and product (%, GC-FID)	D-content after reaction (NMR)
1	50 mol%	-	Ortho - 6% meta - 94% para - 95%
2	30 mol%	quant	Ortho - 4% meta - 94% para - 96%
3	10 mol%	86	Ortho - 4% meta - 93% para - 93%
4	w/o Ag	93	Ortho - 0% meta - >50% para - 61%

Scheme S3.3: Screening of the amount of catalyst.



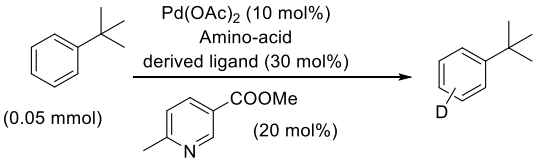
Entry	Amount of $Pd(OAc)_2$	Yield of starting material and product (%, GC-FID)	D-content after reaction (NMR)
1	10 mol%	quant	Ortho - 5% meta - 91% para - 92%
2	5 mol%	quant	Ortho - 4% meta - 94% para - 96%

Scheme S3.4: Screening of temperature.



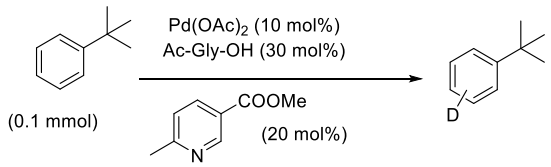
Entry	Temperature	Yield of starting material and product (%, GC-FID)	D-content after reaction (NMR)
1	100	quant	Ortho - 5% meta - 92% para - 94%
2	80	81	Ortho - 4% meta - 94% para - 95%
3	60	80	Ortho - 5% meta - >92% para - 96%

Scheme S3.5: Initial screening of amino-acid derived ligand.



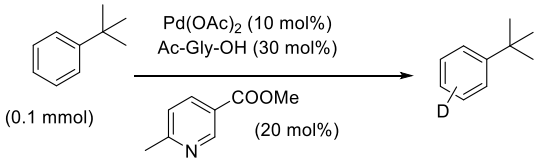
Entry	Amino-acid derived ligand	Yield of starting material and product (%, NMR)	D-content after reaction (NMR)
1	Ac-Gly-OH	97	Ortho - 5% meta - 92% para - 94%
2	Ac-Phe-OH	72	Ortho - 3% meta - 91% para - 93%
3	Ac-Ala-OH	77	Ortho - 5% meta - >92% para - 96%

Scheme S3.6: Re-screening of silver salts.



Entry	Ag-Sources	Yield of starting material and product (%, NMR)	D-content after reaction (NMR)
1	AgF (30 mol%)	97	Ortho - 3% meta - >95% para - 94%
2	Ag_2CO_3 (15 mol%)	90	Ortho - 4% meta - >95% para - 95%

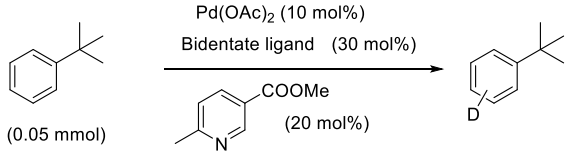
Scheme S3.7: Screening towards lowering of silver salt amount, temperature simultaneously.

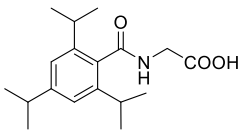
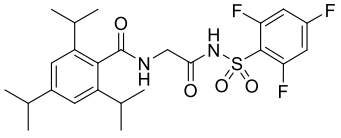


Entry	Ag-loading (mol%)	Temperature (°C)	Yield of starting material and product (%, NMR)	D-content after reaction (NMR)
1	30	80	97	Ortho - 3% meta - >95% para - 94%
2	30	60	97	Ortho - 3% meta - 89% para - 85%
3	10	80	98	Ortho - 0% meta - 52% para - 64%

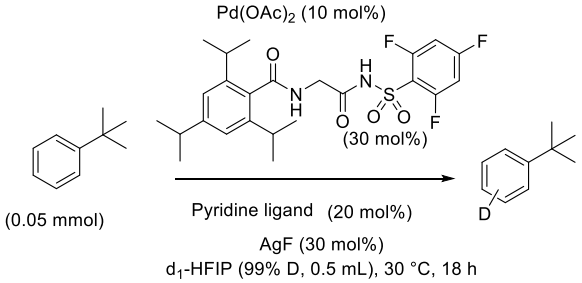
After **Scheme S3.7**, we were interested to see if the electron-donating substrates can be deuterated at lower temperatures. Unfortunately, simple Ac-Gly-OH failed to deliver good results (**Scheme S3.8**, entry 1). Hence in **Scheme S3.8** (entry 2 and entry 3), we chose the two best ligands from the optimization of electron-withdrawing substrate, which proved more efficient than Ac-Gly-OH (*cf.* **Scheme S4.4** and **Scheme S4.7**).

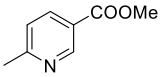
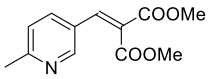
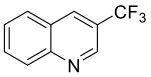
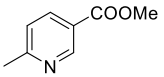
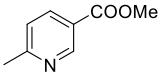
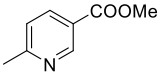
Scheme S3.8: Screening towards comparison between the bidentate ligands.



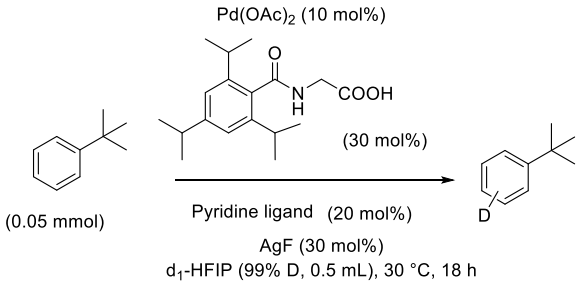
Entry	Bidentate ligand	Yield of starting material and product (%, NMR)	D-content after reaction (NMR)
1	Ac-Gly-OH	91	Ortho - 0% meta - 10% para - 13%
2		93	Ortho - 3% meta - 56.5% para - 71%
3		96	Ortho - 1.5% meta - 19.5% para - 31%

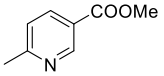
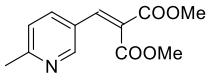
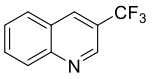
Scheme S3.9: Screening of pyridine ligand with 2,4,6-triisopropyl-*N*-(2-oxo-2-((2,4,6-trifluorophenyl)sulfonamide)ethyl)benzamide as bidentate ligand.



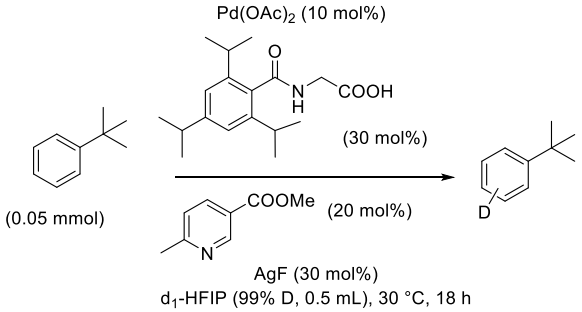
Entry	Pyridine ligand	Yield of starting material and product (%, NMR)	D-content after reaction (NMR)
1		96	Ortho - 1.5% meta - 19.5% para - 31%
2		96	Ortho - 0% meta - < 20% para - < 30%
3		100	Ortho - 1% meta - 24% para - 35%
4		100	Ortho - 6% meta - 24% para - 34%
5	 and 120 °C	96	Ortho - 4% meta - 90% para - 90%
6	 and 48 h	93	Ortho - 0% meta - 55% para - 71%
7	 and without AgF	60	Ortho - 2% meta - 24% para - 34%

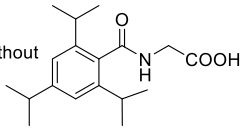
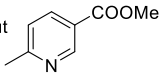
Scheme S3.10: Screening of pyridine ligands with (2,4,6-triisopropylbenzoyl)glycine as amino-acid derived ligand.



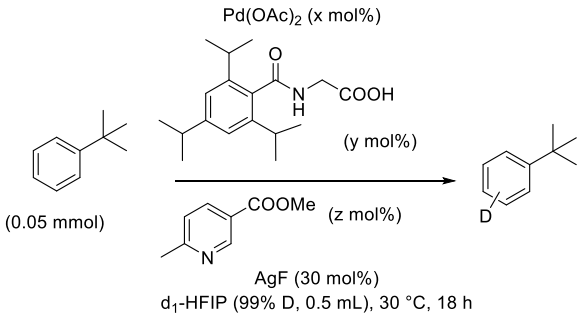
Entry	Pyridine ligand	Yield of starting material and product (%, NMR)	D-content after reaction (NMR)
1		93	Ortho - 3% meta - 56.5% para - 71%
2		89	Ortho - 0% meta - 9% para - 12%
3		94	Ortho - 0% meta - 22% para - 27%
4		98	Ortho - 0.5% meta - 23.5% para - 30%

Scheme S3.11: Control experiments.



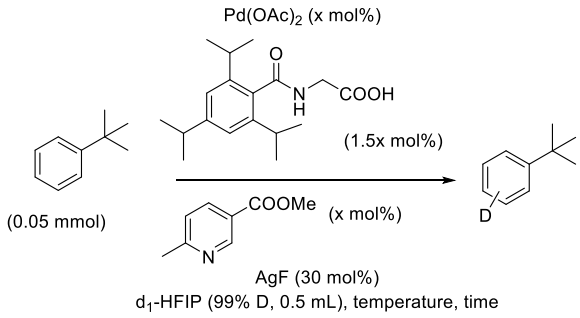
Entry	Deviation from standard conditions	Yield of starting material and product (%, NMR)	D-content after reaction (NMR)
1	No deviation	93	Ortho - 3% meta - 56.5% para - 71%
2	without $Pd(OAc)_2$	0	Ortho - 0% meta - 0% para - 0%
3	without AgF	55	Ortho - 4% meta - 50% para - 42%
4	without 	90	Ortho - 0% meta - 0% para - 0%
5	without 	100	Ortho - 5% meta - 12% para - 12%

Scheme S3.12: Screening of ratio between catalyst components.



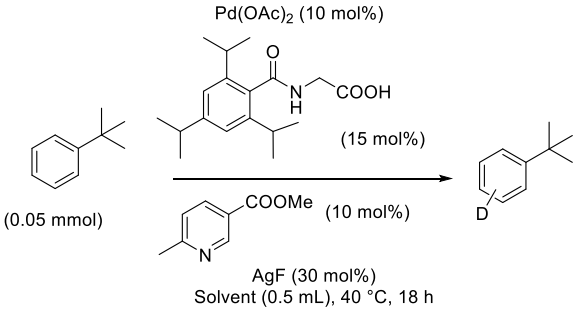
Entry	$Pd(OAc)_2$ (mol%)	Bidentate ligand (mol%)	Pyridine ligand (mol%)	Yield of starting material and product (%, NMR)	D-content after reaction (NMR)
1	10	30	20	93	Ortho - 3% meta - 56.5% para - 71%
2	10	15	10	92	Ortho - 2.5% meta - 55% para - 69%
3	10	10	10	95	Ortho - 0% meta - 23% para - 28%
4	10	15	5	99	Ortho - 1% meta -24% para - 31%

Scheme S3.13: Screening of time and catalyst loading.



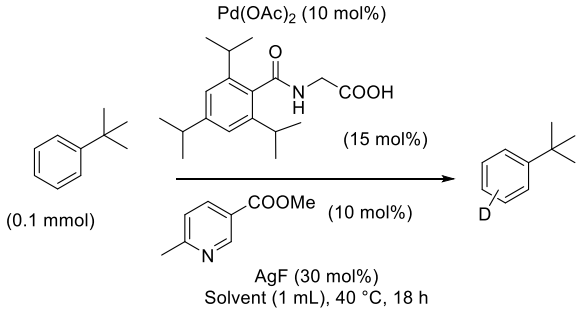
Entry	Catalyst loading (x mol%)	reaction temperature (°C)	reaction time (h)	Yield of starting material and product (%, NMR)	D-content after reaction (NMR)
1	10	30	18	93	Ortho - 3% meta - 56.5% para - 71%
2	10	30	72	97	Ortho - 5% meta - 70.5% para - 78%
3	10	40	48	100	Ortho - 6% meta - < 90% para - < 90%
4	10	40	72	97	Ortho - 6% meta - 93% para - 93%
5	5	40	72	95	Ortho - 4% meta - < 85% para - < 90%

Scheme S3.14: Screening of reaction solvent.



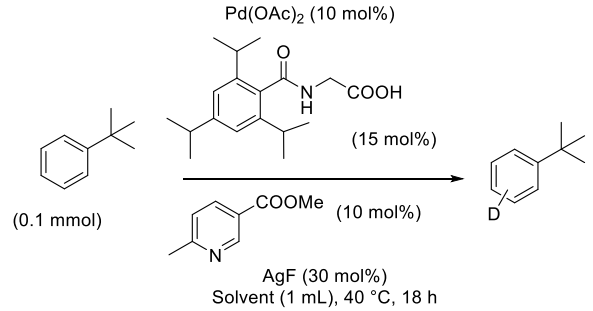
Entry	Solvent	Yield of starting material and product (%, NMR)	D-content after reaction (NMR)
1	d_4-MeOH	95	ortho - 6% meta - 8% para - 7%
2	d_1-AcOH	99	ortho - 0% meta - 2.5% para - 6%
3	d_1-TFA	-	ortho - 1% meta - 1.5% para - 5%
4	HFIP:D_2O (1:1)	92	ortho - 0% meta - 46% para - 60%
5	d_1-HFIP:DCE	-	ortho - 1.5% meta - 20.5% para - 26%
6	d_1-HFIP:MeCN	99	ortho - 0% meta - 0% para - 4%
7	d_1-HFIP:$CHCl_3$	100	ortho - 0% meta - 0% para - 0%
8	d_1-HFIP:CH_2Cl_2	99	ortho - 4% meta - 22% para - 28%
9	d_1-HFIP:THF	-	ortho - 6% meta - 11.5% para - 17%
10	d_1-HFIP:d_4-MeOH	100	ortho - 4% meta - 5.5% para - 28%
11	d_1-HFIP:d_1-AcOH	100	ortho - 0% meta - 0% para - 4%
12	d_1-HFIP	97	ortho - 4% meta - 69% para - 77%

Scheme S3.15: Screening of ratio of solvent mixture.



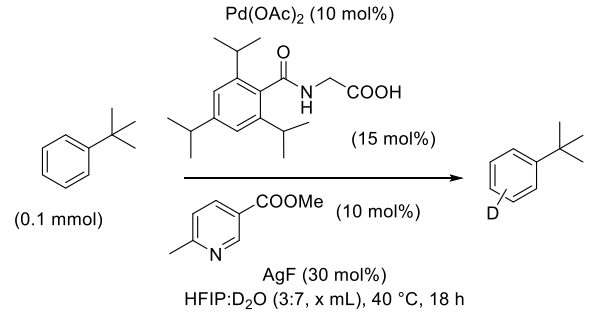
Entry	D_2O:HFIP ratio	Yield of starting material and product (%, NMR)	D-content after reaction (NMR)
1	1 mL D_2O + 2 equiv HFIP	92	ortho - 3.5% meta - 13% para - 18%
2	9:1	90	ortho - 2% meta - 47.5% para - 65%
3	8:2	92	ortho - 0% meta - 57% para - 76%
4	7:3	93	ortho - 2% meta - 57% para - 75%
5	6:4	87	ortho - 0% meta - 49% para - 66%
6	5:5	98	ortho - 0% meta - 50% para - 68%
7	3:7	100	ortho - 4% meta - 30.5% para - 43%

Scheme S3.16: Comparison with d_1-HFIP and D_2O as solvent system.



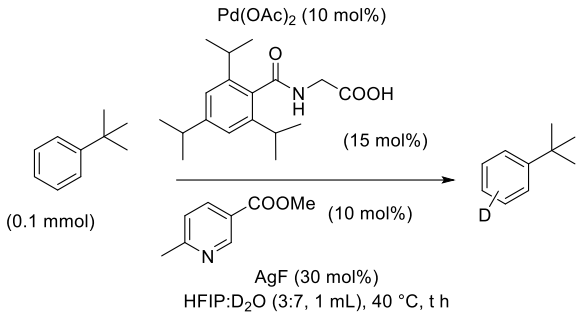
Entry	D_2O:d_1-HFIP ratio	Yield of starting material and product (%, NMR)	D-content after reaction (NMR)
1	7:3	93	ortho - 2% meta - 58% para - 73%
2	5:5	92	ortho - 1.5% meta - 56% para - 74%
3	3:7	90	ortho - 0% meta - 48% para - 68%

Scheme S3.17: Effect of dilution.



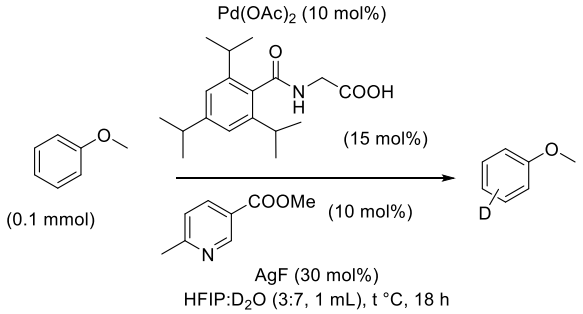
Entry	Amount of Solvent	Yield of starting material and product (%, NMR)	D-content after reaction (NMR)
1	1	93	ortho - 0% meta - 55% para - 72%
2	1.5	92	ortho - 0% meta - 60% para - 76%
3	2	82	ortho - 4% meta - 68% para - 83%
4	3	92	ortho - 1% meta - 62% para - 77%

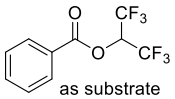
Scheme S3.18: Screening of time.



Entry	Time	Further changes	Yield of starting material and product (%, NMR)	D-content after reaction (NMR)
1	18	none	93	ortho - 0% meta - 55% para - 72%
2	48	none	89	ortho - 2% meta - 84% para - 92%
3	48	only d_1-HFIP	100	Ortho - 6% meta - < 90% para - < 90%
4	48	2 mL of solvent mixture	> 90	ortho - 2% meta - 85-88% para - >93%
5	72	none	92	ortho - 4% meta - 92% para - 95%
6	72	only d_1-HFIP	97	Ortho - 6% meta - 93% para - 93%

Scheme S3.19: Screening of temperature with anisole.



Entry	Temperature	Further changes	Yield of starting material and product (%, NMR)	D-content after reaction (NMR)
1	40	none	100	ortho - 13.5% meta - >90% para - >90%
2	40	72 h	100	ortho - 15-20% meta - 95-100% para - 95-100%
3	60	none	89	ortho - 45% meta - 95-100% para - 95-100%
4	80	none	94	ortho - 92% meta - 95-100% para - 95-100%
6	80	 as substrate	92	ortho - 2.5% meta - 20% para - 7%

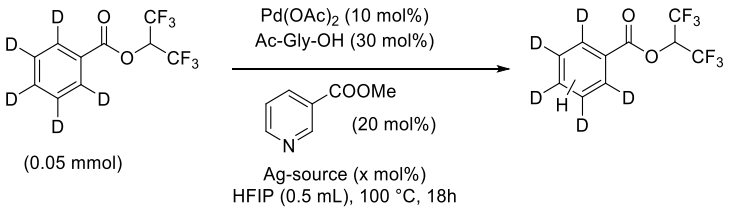
Note: A reaction mixture obtained under the optimized reaction Conditions A was analyzed by mass spectrometry and revealed that no deuteration incorporation occurs at the glycine-CH_2-position of the bidentate ligand.

4 Optimization of the Reaction Conditions with Electron-Withdrawing Substituents

General Procedure D:

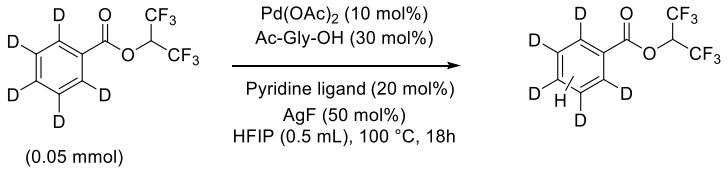
An oven dried 10 mL Schlenk tube was charged with a $Pd(OAc)_2$, a bidentate ligand, a pyridine ligand, if indicated an Ag-source, 1,1,1,3,3,3-hexafluoropropan-2-yl benzoate-d_5 or 1,1,1,3,3,3-hexafluoropropan-2-yl benzoate (0.100 mmol), and solvent. The reaction vessel was tightly sealed then placed into the inside circle of a preheated aluminum block with a tightly fitting recess on a magnetic stirrer and stirred at the indicated temperature until completion of the reaction. The reaction mixture was allowed to cool to room temperature and 1,3,5-trimethylbenzene was added as an internal standard. The reaction mixture was filtered over a pad of Celite® and the residue was washed with dichloromethane. The overall solution was concentrated under reduced pressure and $CDCl_3$ (0.9 mL) was added. All yields and deuteration degrees during the optimization study were determined via ^{1}H-NMR of the crude reaction using 1,3,5-trimethylbenzene as an internal standard.

Scheme S4.1: Screening of silver salts.

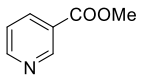
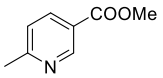
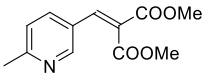
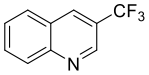
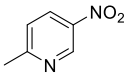
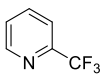


Entry	Ag-source	Yield of starting material and product (%, NMR)	H-content after reaction (NMR)
1	AgOAc (50 mol%)	66	Ortho - 4% meta - 7% para - 2%
2	AgF (50 mol%)	-	Ortho - 7.5% meta - 12.5% para - 4%
3	Ag_2CO_3 (25 mol%)	81	Ortho - 4% meta - 7% para - 2%
4	$AgNO_3$ (50 mol%)	89	Ortho - 4.5% meta - 8.5% para - 3%

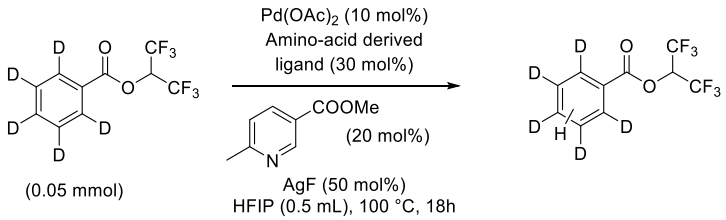
Scheme S4.2: Screening of pyridine ligands.

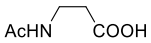
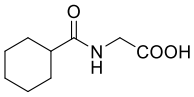
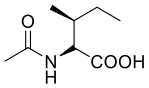
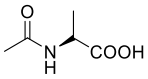
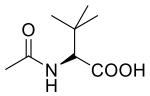
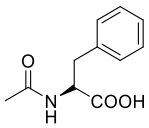
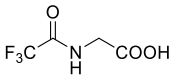


(0.05 mmol)

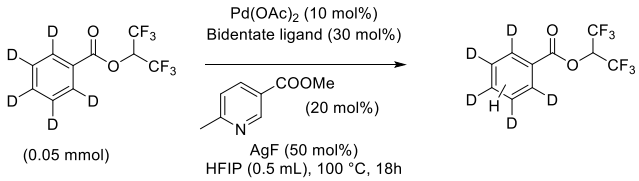
Entry	Pyridine ligand	Yield of starting material and product (%, NMR)	H-content after reaction (NMR)
1		84	Ortho - 7% meta - 11% para - 3%
2		83	Ortho - 6.5% meta - 23.5% para - 6%
3		83	Ortho - 2.5% meta - 10% para - 6%
4		87	Ortho - 4.5% meta - 17% para - 7.5%
5		93	Ortho - 2.5% meta - 7% para - No data
6		88	Ortho - 7% meta - 8.5% para - 2%
7		74	Ortho - 6.5% meta - 15.5% para - 4%
8		76	Ortho - 7% meta - 22.5% para - 5%
9		76	Ortho - 1.5% meta - 16% para - No data

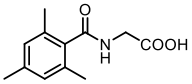
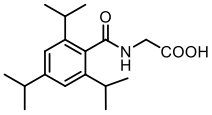
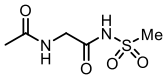
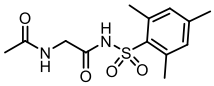
Scheme S4.3: Screening of amino-acid derived ligands.



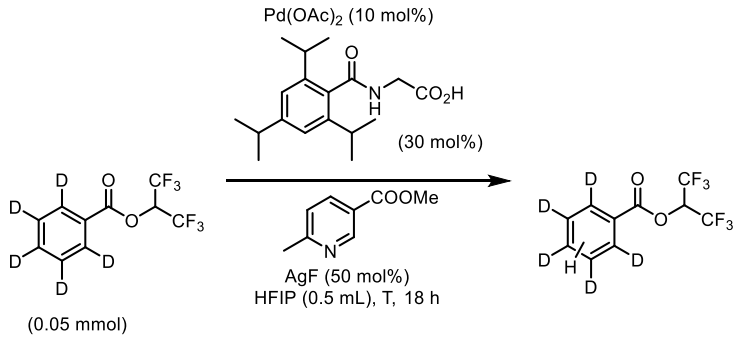
Entry	Amino-acid derived ligand	Yield of starting material and product (%, NMR)	H-content after reaction (NMR)
1	Ac-Gly-OH	83	Ortho - 6.5% meta - 23.5% para - 9%
2		78	Ortho - 1% meta - 4.5% para - 1%
3		22	Ortho - 1.5% meta - 7% para - 4%
4		68	Ortho - 1% meta - 5.5% para - 1%
5		64	Ortho - 3% meta - 13% para - 4%
6		85	Ortho - 2% meta - 20% para - 4%
7		20	Ortho - 3.5% meta - 22% para - 5%
8		80	Ortho - 1% meta - 3.5% para - 1%

Scheme S4.4: Screening of bidentate ligands.



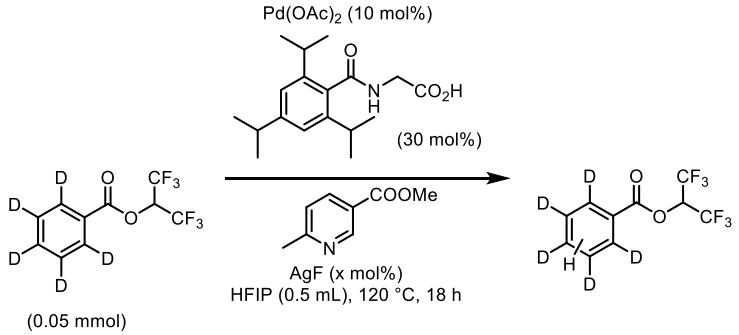
Entry	Bidentate ligand	Yield of starting material and product (in %, NMR)	H-content after reaction (NMR)
1	Ac-Gly-OH	80	Ortho - 7% meta - 24% para - 8%
2		76	Ortho - 6% meta - 28.5% para - 10%
3		78	Ortho - 7.5% meta - 32.5% para - 12%
4		78	Ortho - 2.5% meta - 16% para - 5%
5		92	Ortho - 3% meta - 22% para - 7%

Scheme S4.5: Screening of temperature.



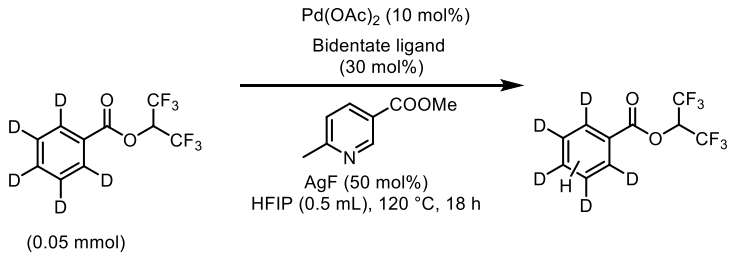
Entry	Temperature	Yield of starting material and product (%, NMR)	H-content after reaction (NMR)
1	90	74	Ortho - 5% meta - 20% para - 7%
2	100	86	Ortho - 7.5% meta - 32% para - 12%
3	110	88	Ortho - 10% meta - 41% para - 16%
4	120	84	Ortho - 16.5% meta - 59% para - 26%
5	130	92	Ortho - 17.5% meta - 58.5% para - 26%

Scheme S4.6: Screening of amount of Ag-source.

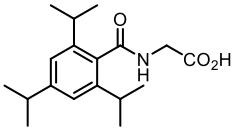
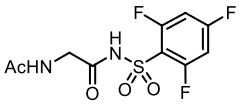
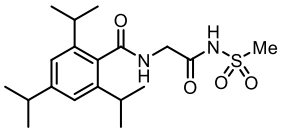
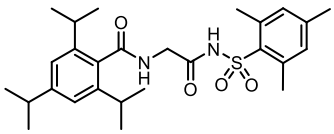
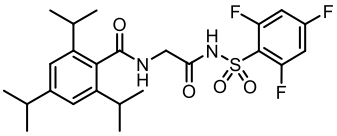


Entry	Amount of AgF	Yield of starting material and product (%, NMR)	H-content after reaction (NMR)
1	0	74	Ortho - 10.5% meta - 41% para - 16%
2	10	88	Ortho - 11.5% meta - 46% para - 17%
3	20	84	Ortho - 12% meta - 49% para - 20%
4	30	90	Ortho - 13% meta - 51% para - 19%
5	40	90	Ortho - 15% meta - 55% para - 23%
6	50	94	Ortho - 16% meta - 57% para - 25%
7	60	92	Ortho - 15% meta - 56% para - 26%

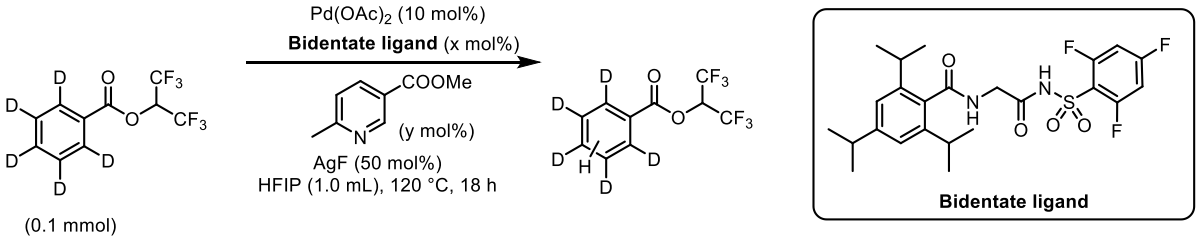
Scheme S4.7: Re-screening of bidentate ligands.



(0.05 mmol)

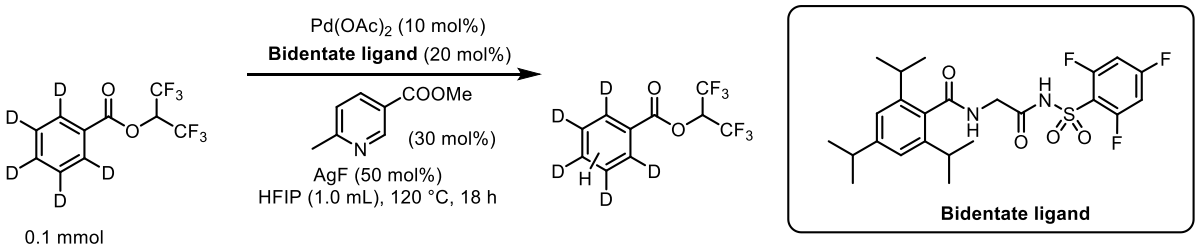
Entry	Bidentate ligand	Yield of starting material and product (%, NMR)	H-content after reaction (NMR)
1		86	Ortho - 14% meta - 54% para - 22%
2		90	Ortho - 4% meta - 25.5% para - 9%
3		92	Ortho - 4% meta - 37% para - 13%
4		92	Ortho - 5% meta - 52% para - 18%
5		96	Ortho - 7% meta - 72% para - 30%

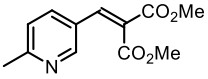
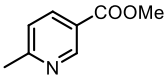
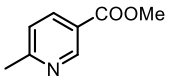
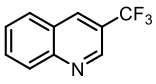
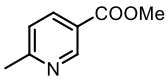
Scheme S4.8: Screening of ratio between catalyst components.



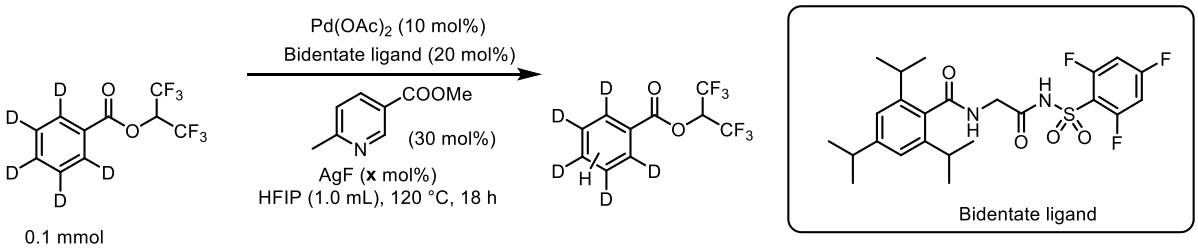
Entry	$Pd(OAc)_2$	Bidentate ligand	Pyridine ligand	Yield of starting material and product (%, NMR)	H-content after reaction (NMR)
1	1	1	1	88	Ortho - 3.5% meta - 45% para - 16%
2	1	1	2	83	Ortho - 5.5% meta - 59.5% para - 24%
3	1	1	3	85	Ortho - 5% meta - 59% para - 23%
4	1	2	1	91	Ortho - 4% meta - 49% para - 17%
5	1	2	2	89	Ortho - 7% meta - 68.5% para - 31%
6	1	2	3	91	Ortho - 9% meta - 73% para - 34%
7	1	3	1	88	Ortho - 4.5% meta - 55.5% para - 21%
8	1	3	2	94	Ortho - 6.5% meta - 72.5% para - 30%
9	1	3	3	96	Ortho - 7.5% meta - 72.5% para - 33%

Scheme S4.9: Control experiments.



Entry	Deviation from standard conditions	Yield of starting material and product (%, NMR)	H-content after reaction (NMR)
1	None	87	ortho - 7.5% meta - 70% para - 30%
2	no bidentate ligand	86	ortho - 0% meta - 0% para - 0%
3	no pyridine ligand	83	ortho - 1% meta - 2% para - 1%
4	no $Pd(OAc)_2$	94	ortho - 1% meta - 2% para - 1%
5	no catalyst	97	ortho - 1% meta - 0.5% para - 0.5%
6	no AgF	97	ortho - 8.5% meta - 74% para - 34%
7	 instead of 	93	ortho - 4.5% meta - 54% para - 26%
8	 instead of 	90	ortho - 13% meta - 36% para - 13%
9	 instead of 	96	ortho - 10.5% meta - 73% para - 35%

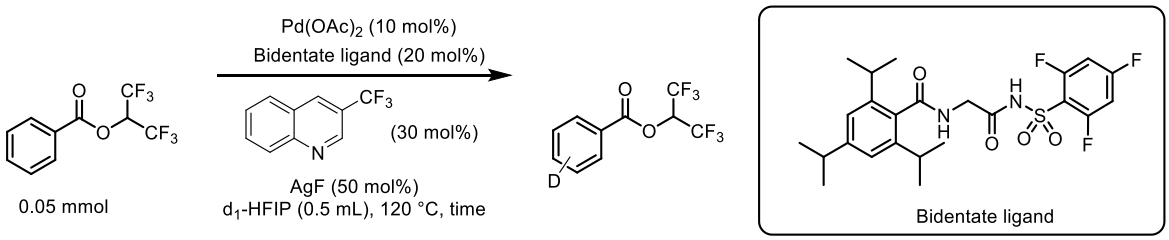
Scheme S4.10: Screening of silver-salt loading.



Entry	AgF (mol%)	Yield of starting material and product (%, NMR)	H-content after reaction (NMR)
1	0	83	ortho - 7% meta - 70% para - 30%
2	10	83	ortho - 7% meta - 70.5% para - 32%
3	20	87	ortho - 7% meta - 71% para - 32%
4	30	88	ortho - 7% meta - 71.5% para - 32%
5	40	91	ortho - 7.5% meta - 69% para - 30%
6	50	91	ortho - 6% meta - 66% para - 29%
7	60	95	ortho - 7% meta - 65% para - 30%
8	70	98	ortho - 6% meta - 63% para - 26%
9[a]	0	97	ortho - 10% meta - 72% para - 36%
10[a]	10	92	ortho - 10% meta - 71% para - 34%

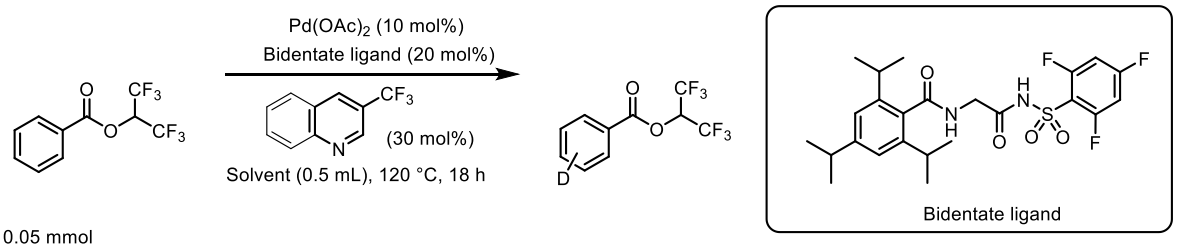
a: 3-Trifluoroquinoline was used as Ligand

Scheme S4.11: Deuteration reaction at different reactions times.



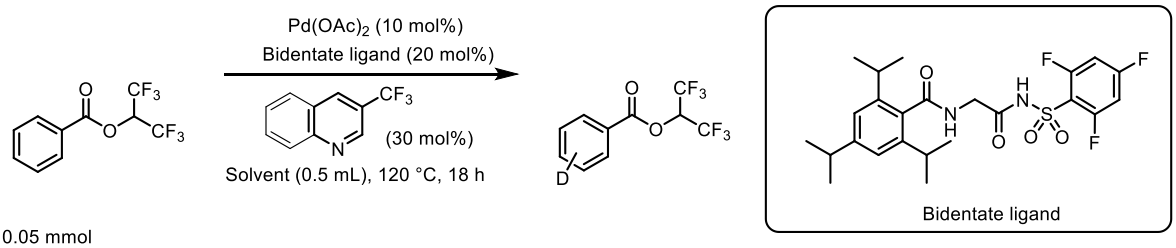
Entry	Time (in h)	Yield of starting material and product (%, NMR)	D-content after reaction (NMR)
1	18	quant	ortho - 18.5% meta - 86% para - 62%
2	48	quant	ortho - 36% meta -86% para - 86%

Scheme S4.12: Deuteration reaction with different solvents.



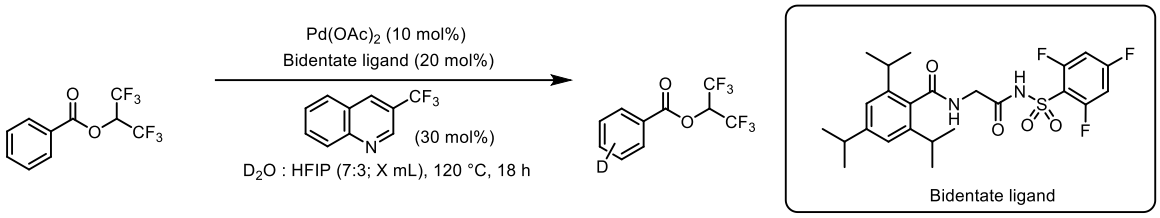
Entry	Solvent	Yield of starting material and product (%, NMR)	D-content after reaction (NMR)
1	d_4-MeOH	88	ortho - 2.5% meta - 16% para - 3%
2	d_1-AcOH	100	ortho - 6% meta - 15% para - 7%
3	d_1-TFA	86	ortho - 0% meta - 0% para - 0%
4	HFIP:D_2O (1:1)	96	ortho - 31.5% meta - 89% para - 75%
5	HFIP:D_2O (9:1)	98	ortho - 19% meta - 58% para - 40%
6	d_1-HFIP:DCE	100	ortho - 23.5% meta - 84% para - 70%
7	d_1-HFIP:MeCN	100	ortho - 7% meta - 22% para - 6%
8	d_1-HFIP:$CHCl_3$	84	ortho - 18.5% meta - 82% para - 60%
9	d_1-HFIP:CH_2Cl_2	88	ortho - 15% meta - 76% para - 45%
10	d_1-HFIP:THF	95	ortho - 12% meta - 64% para - 30%
11	d_1-HFIP:d_4-MeOH	86	ortho - 8% meta - 46% para - 10%
12	d_1-HFIP:d_1-AcOH	94	ortho - 4.5% meta - 26% para - 8%

Scheme S4.13: Screening of different D_2O:HFIP ratios.



Entry	D_2O:HFIP ratio	Yield of starting material and product (%, NMR)	D-content after reaction (NMR)
1	100% D_2O	100	ortho - 0% meta - 5% para - 0%
2	9:1	100	ortho - 0% meta - 3% para - 3%
3	8:2	96	ortho - 28.5% meta - 92% para - 75%
4	7:3	94	ortho - 39% meta - 94.5% para - 89%
5	6:4	96	ortho - 36% meta - 92.5% para - 86%
6	1:1	100	ortho - 33% meta - 92% para - 77%
7	4:6	94	ortho - 15% meta - 77.5% para - 52%
8	3:7	98	ortho - 20% meta - 77% para - 54%

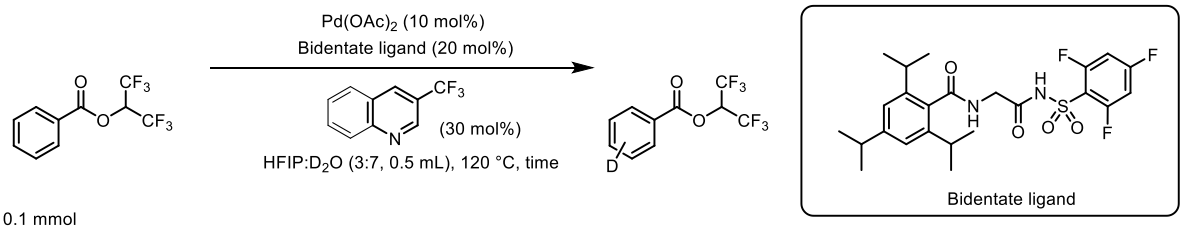
Scheme S4.14: Screening of the reaction concentration.



0.1 mmol

Entry	Amount ofsolvent / Concentration	Yield of starting material and product (%, NMR)	D-content after reaction (NMR)
1	0.5 mL / 0.2 M	quant	ortho - 42% meta - 94% para - 87%
2	1.0 mL / 0.1 M	97	ortho - 41% meta - 95% para - 88%
3	1.5 mL / 0.075 M	quant	ortho - 47% meta - 96% para - 88%
4	2.0 mL / 0.05 M	quant	ortho - 37.5% meta - 95.5% para - 82%

Scheme S4.15: Cross-screening of different D_2O:HFIP volumes and reaction times.

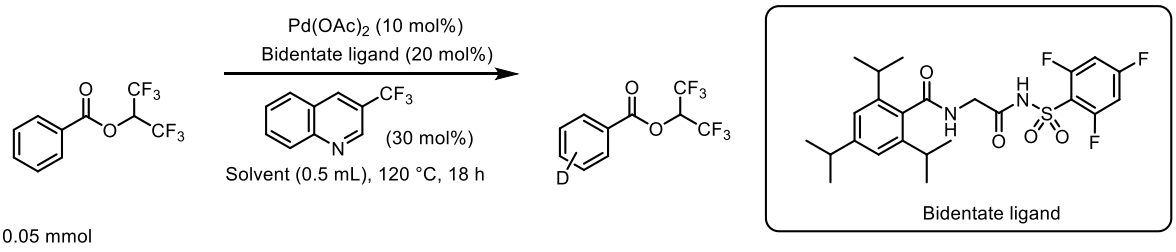


0.1 mmol

Entry	Concentration (M)	Reaction time (h)	Yield of starting material and product (%, NMR)	D-content after reaction (NMR)
1	0.1	18	94	ortho - 40% meta - 95.5% para - 90%
2	0.1	48	91	ortho - 69% meta - 95% para - 95%
3	0.1	72	90	ortho - 67% meta - 95% para - 94%
4	0.075	18	97	ortho - 44% meta - 95% para - 91%
5	0.075	48	93	ortho - 60% meta - 95.5% para - 94%
6	0.075	72	90	ortho - 59% meta - 95% para - 93%

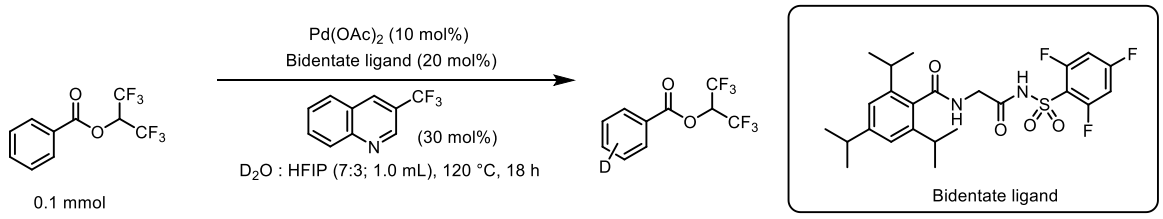
Note: A reaction mixture obtained under the optimized Conditions B was analyzed by mass spectrometry: No bidentate ligand was detected. Since this ligand can in principle be characterized through mass spectrometry, this result implies that the ligand decomposes in the reaction mixture after the reaction is completed. It could therefore not be evaluated if deuterium incorporation occurs in the bidentate ligand backbone.

Scheme S4.16: Use of d_1-HFIP with D_2O.



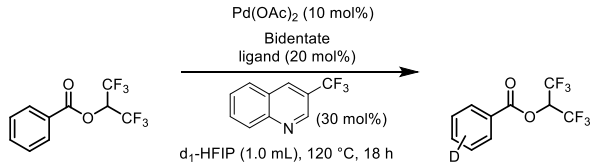
Entry	D_2O : d_1-HFIP ratio	Yield of starting material and product (%, NMR)	D-content after reaction (NMR)
1	9:1	98	ortho - 0% meta - 8% para - 5%
2	7:3	96	ortho - 35% meta - 95% para - 88%
3	1:1	100	ortho - 32.5% meta - 94.5% para - 86%

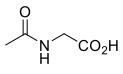
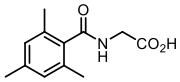
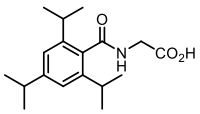
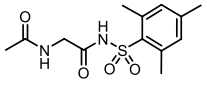
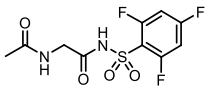
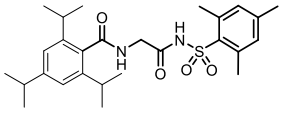
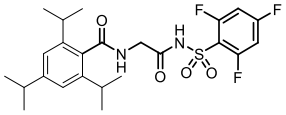
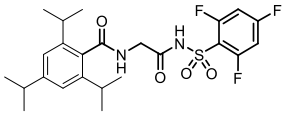
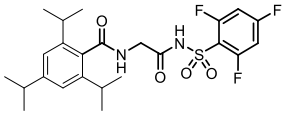
Scheme S4.17: Control experiments.



Entry	Deviation from standard conditions	Yield of starting material and product (%, NMR)	D-content after reaction (NMR)	D Total (MS)
1	none	95	ortho - 39% meta - 95% para - 84%	3.51
2	no 3-trifluoromethyl quinoline	99	ortho - 34% meta - 60% para - 32%	2.15
3	no bidentate ligand	98	-	0
4	no ligands added	92	-	0

Scheme S4.18: Comparison of amino acid-derived ligand.



Entry	Bidentate ligand	Yield of starting material and product (%, NMR)	H-content after reaction (NMR)
1		99	Ortho - 11% meta - 50% para - 23%
2		95	Ortho - 22% meta - 73% para - 41%
3		97	Ortho - 24.5% meta - 79% para - 47%
4		98	Ortho - 5% meta - 46% para - 23%
5		98	Ortho - 7% meta - 35% para - 21%
6		97	Ortho - 5% meta - 72% para - 46%
7		97	Ortho - 17% meta - 90% para - 74%
8[a]		95	Ortho - 32% meta - 90% para - 85%
9[a,b]		94	Ortho - 62% meta - 95% para - 95%

a: Reaction was conducted with 48 h reaction time
b: Reaction was conducten with D_2O:HFIP (7:3) as solvent

5 Scope of the Reaction

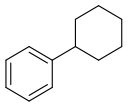
General Procedure E:

An oven dried 10 mL Schlenk tube was charged with $Pd(OAc)_2$ (4.5 mg, 10 mol%), (2,4,6-triisopropylbenzoyl)glycine (**L3**) (9.2 mg, 15 mol%), methyl 6-methylnicotinate (3.0 mg, 10 mol%), AgF (7.6 mg, 30 mol%), and arene (0.200 mmol). HFIP (0.6 mL) and D_2O (1.4 mL) were added, the reaction vessel was tightly sealed and placed into the inside circle of a preheated aluminum block with a tightly fitting recess at 80 °C on a magnetic stirrer and stirred for 18 h. The reaction mixture was allowed to cool to room temperature, transferred into a 100 mL round-bottom flask, and concentrated under reduced pressure. The product was then purified according to the procedure described for the respective substrate.

General Procedure F:

An oven dried 10 mL Schlenk tube was charged with $Pd(OAc)_2$ (4.5 mg, 10 mol%), (2,4,6-triisopropyl-*N*-(2-oxo-2-((2,4,6-trifluorophenyl)sulfonamido)ethyl)benzamide (**L7**) (20.0 mg, 20 mol%), 3-(trifluoromethyl)quinoline (11.8 mg, 30 mol%), and arene (0.200 mmol). HFIP (0.6 mL) and D_2O (1.4 mL) were added, the reaction vessel was tightly sealed and placed into the inside circle of a preheated aluminum block with a tightly fitting recess at 120 °C on a magnetic stirrer and stirred for 48 h. The reaction mixture was allowed to cool to room temperature, transferred into a 100 mL round-bottom flask, and concentrated under reduced pressure. The product was then purified according to the procedure described for the respective substrate.

Deuteration of cyclohexylbenzene (2):



Following the general procedure E, but at 40 °C for 72 h, using cyclohexylbenzene (**2**) (32.0 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane as the eluent the target compound **[D]2** was obtained as colorless liquid (29.4 mg, 89%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 4.22 D/molecule [Mass]; 4.25 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.36-7.30 (m, 1H), 7.28-7.23 (m, 1H), 7.24-7.19 (m, 1H), 2.59-2.49 (m, 1H), 1.99-1.84 (m, 4H), 1.84-1.76 (m, 1H), 1.54-1.39 (m, 4H), 1.37-1.26 (m, 1H) ppm.

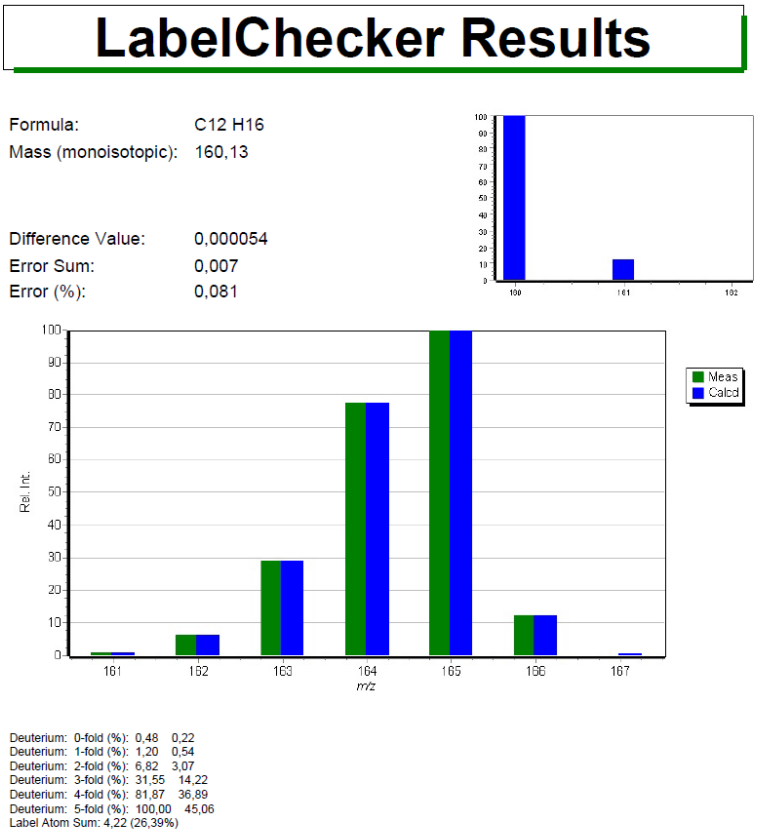
^{13}C NMR (100 MHz, $CDCl_3$) δ = 148.2, 128.4, 126.9, 125.9, 44.8, 34.6, 27.1, 26.3 ppm.

NMR Data of Product:

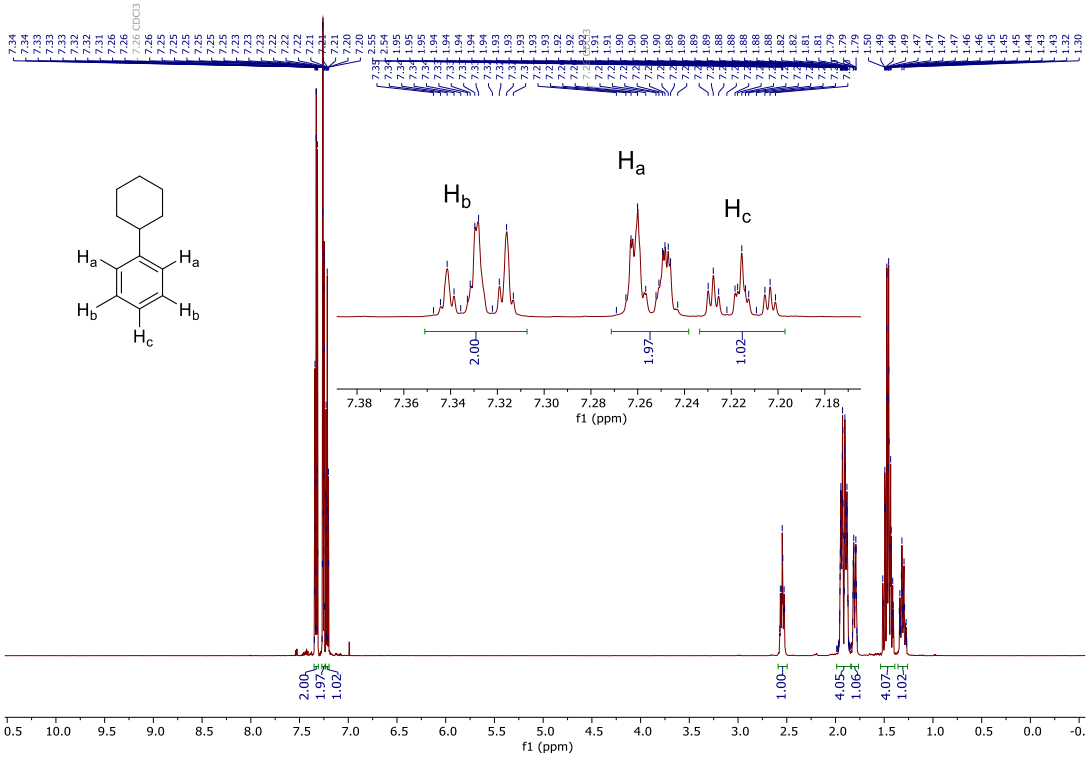
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.34-7.28 (m, 0.21H, 89.5% D), 7.26-7.20 (m, 0.45H, 77.5% D), 7.20 (s, 0.09H, 91% D), 2.60-2.45 (m, 1H), 1.95-1.82 (m, 4H), 1.81-1.72 (m, 1H), 1.51-1.35 (m, 4H), 1.34-1.23 (m, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ = 148.4-147.9 (1C), 128.4-125.0 (5C), 44.8-44.6 (1C), 34.6, 27.1, 26.3 ppm.

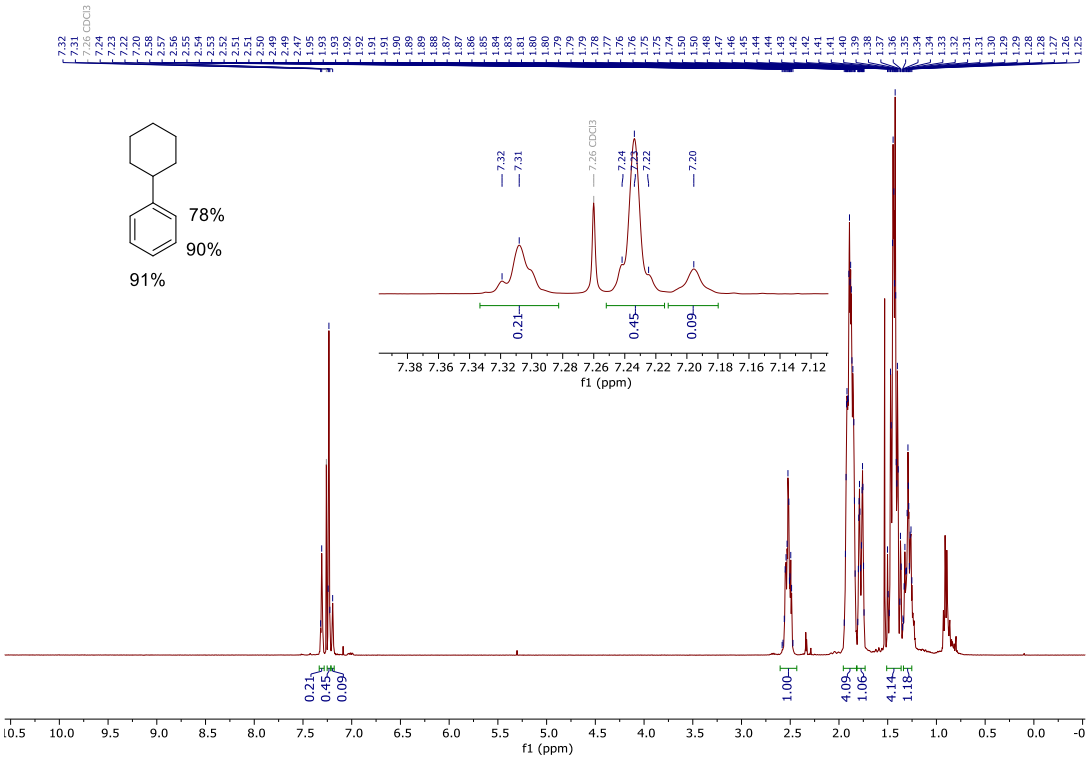
Mass Data:



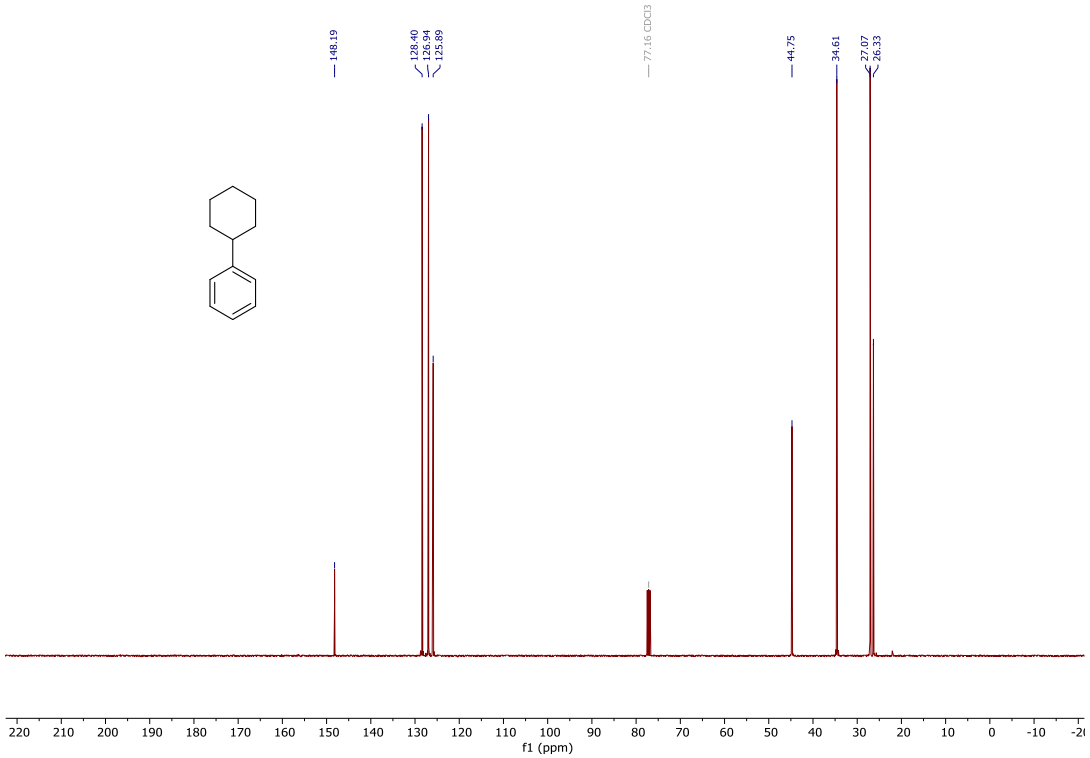
^{1}H-NMR spectrum in $CDCl_3$:



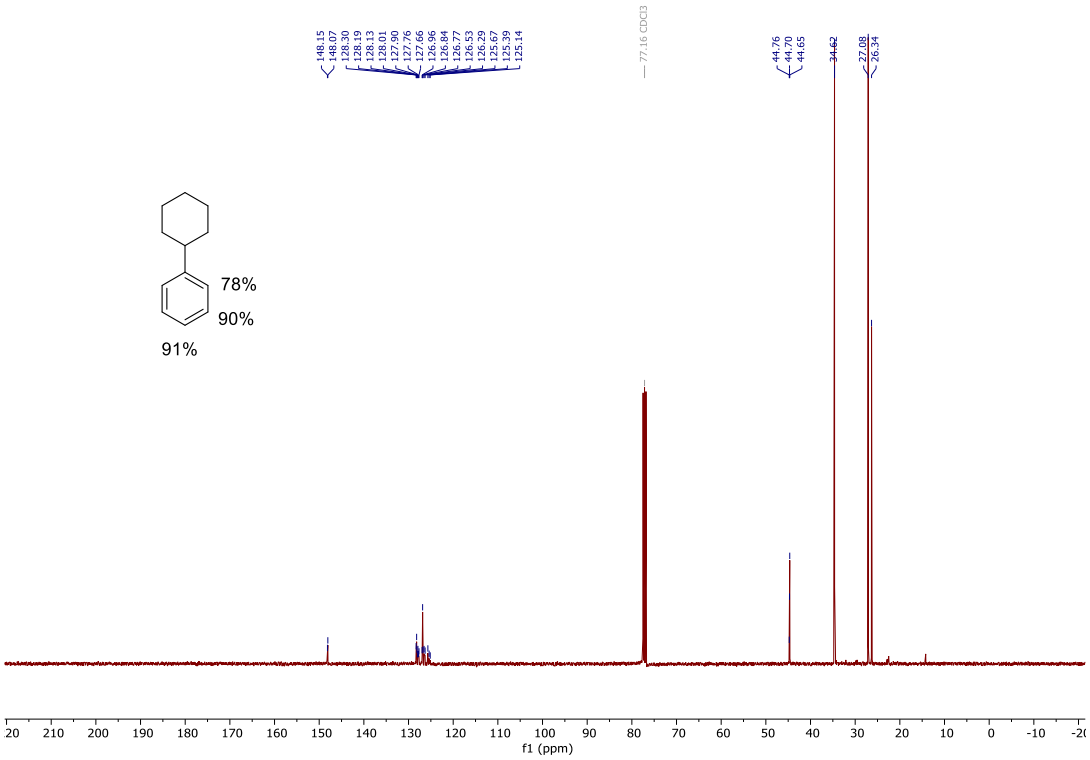
^{1}H-NMR spectrum in $CDCl_3$:



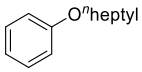
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of (heptyloxy)benzene (3):



Following the general procedure E, using (heptyloxy)benzene (**3**) (38.5 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:Et_2O = 50:1 as the eluent the target compound **[D]3** was obtained as colorless liquid (32.8 mg, 83%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 4.76 D/molecule [Mass]; 4.73 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.30-7.25 (m, 2H), 6.95-6.91 (m, 1H), 6.91-6.88 (m, 2H), 3.96 (t, *J* = 6.6 Hz, 2H), 1.83-1.74 (m, 2H), 1.49-1.42 (m, 2H), 1.40-1.27 (m, 6H), 0.93-0.86 (m, 3H) ppm.

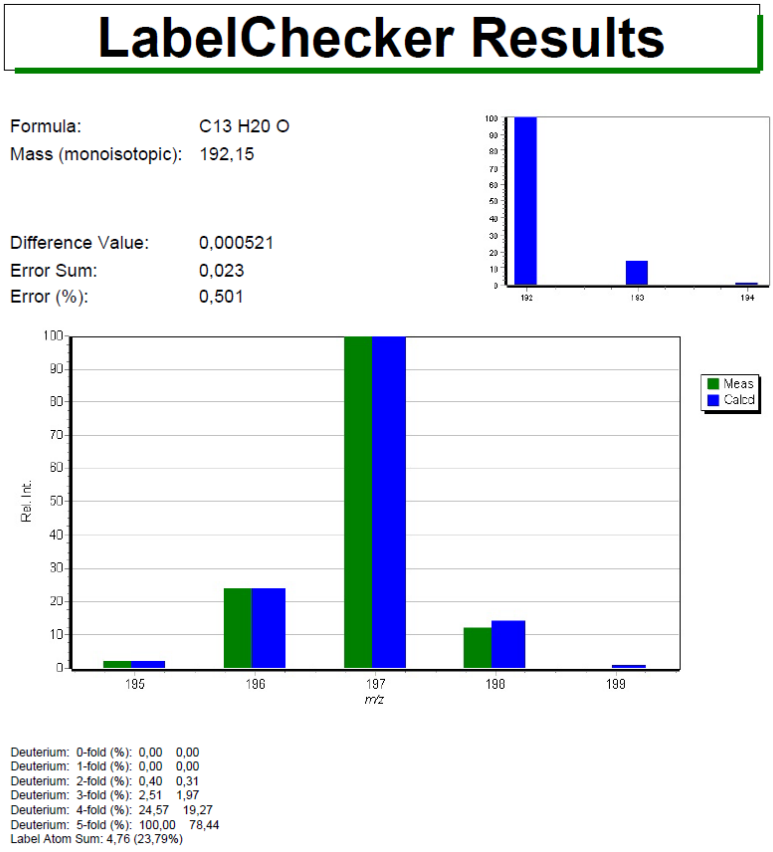
^{13}C NMR (125 MHz, $CDCl_3$) δ = 159.3, 129.5, 120.6, 114.7, 68.0, 32.0, 29.5, 29.2, 26.2, 22.8, 14.2 ppm.

NMR Data of Product:

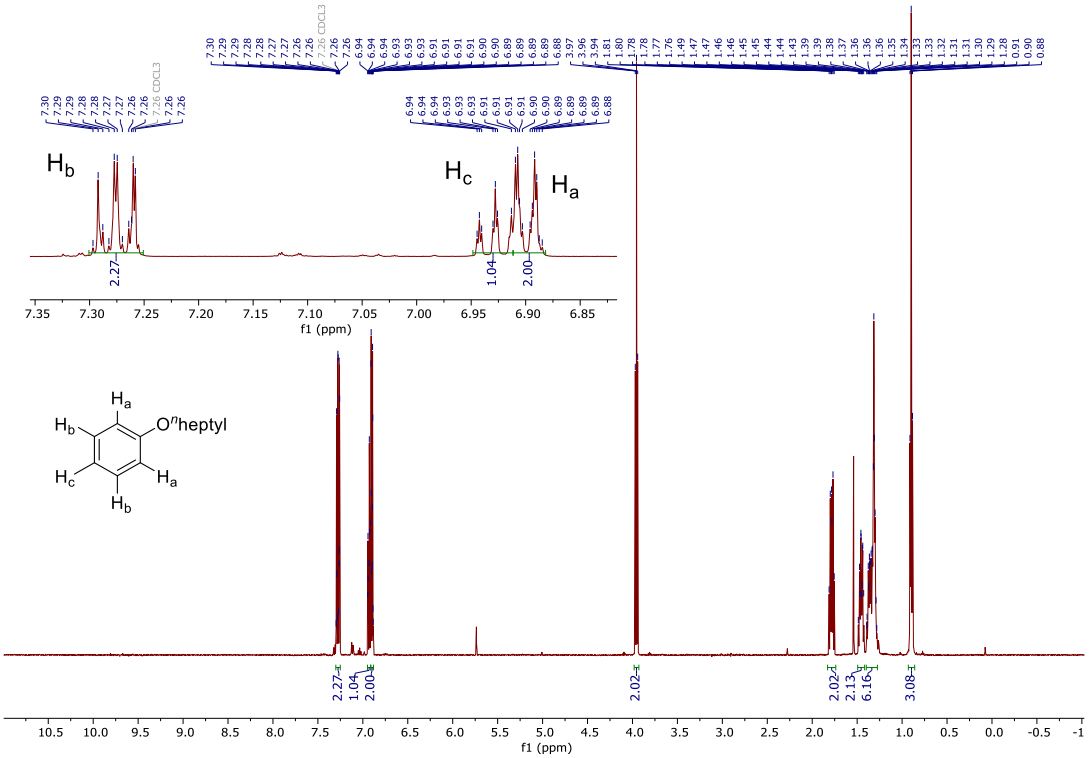
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.28 (s, 0.12H, 94% D), 6.93 (s, 0.05H, 95% D), 6.91 (s, 0.09H, 95% D), 3.96 (t, *J* = 6.6 Hz, 2H), 1.83-1.75 (m, 2H), 1.51-1.42 (m, 2H), 1.38-1.29 (m, 6H), 0.91 (t, *J* = 6.9 Hz, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.2, 129.6-113.9 (5C), 68.0, 32.0, 29.5, 29.2, 26.2, 22.8, 14.2 ppm.

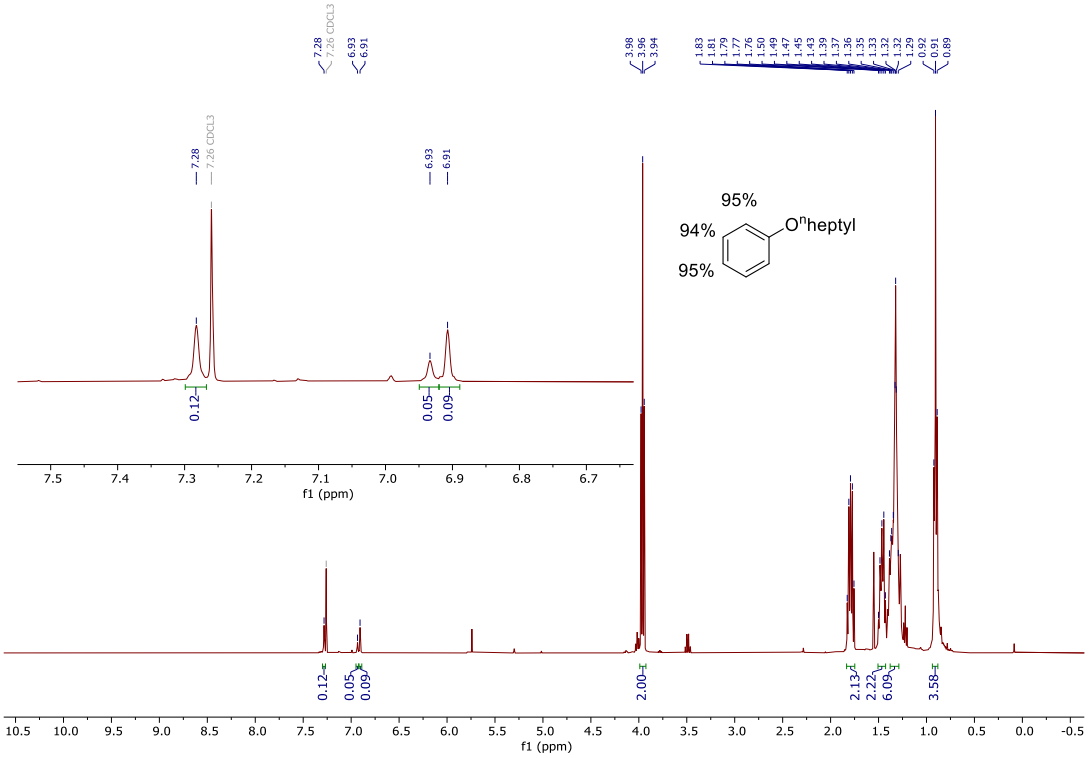
Mass Data:



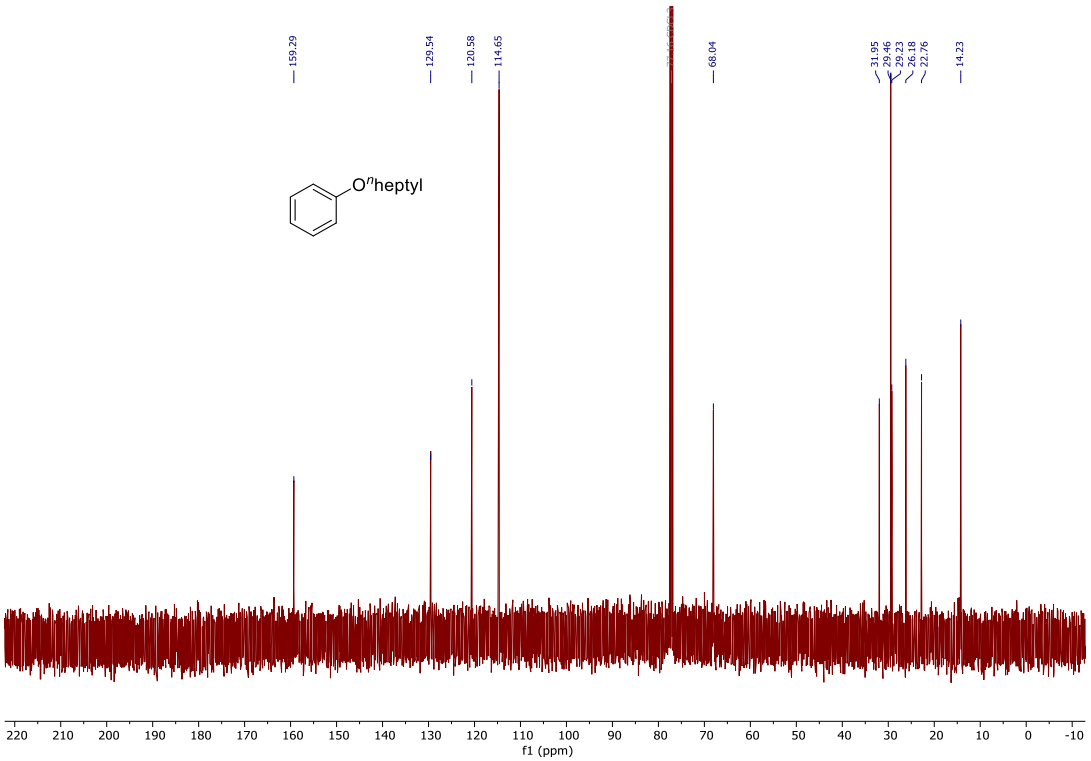
^{1}H-NMR spectrum in $CDCl_3$:



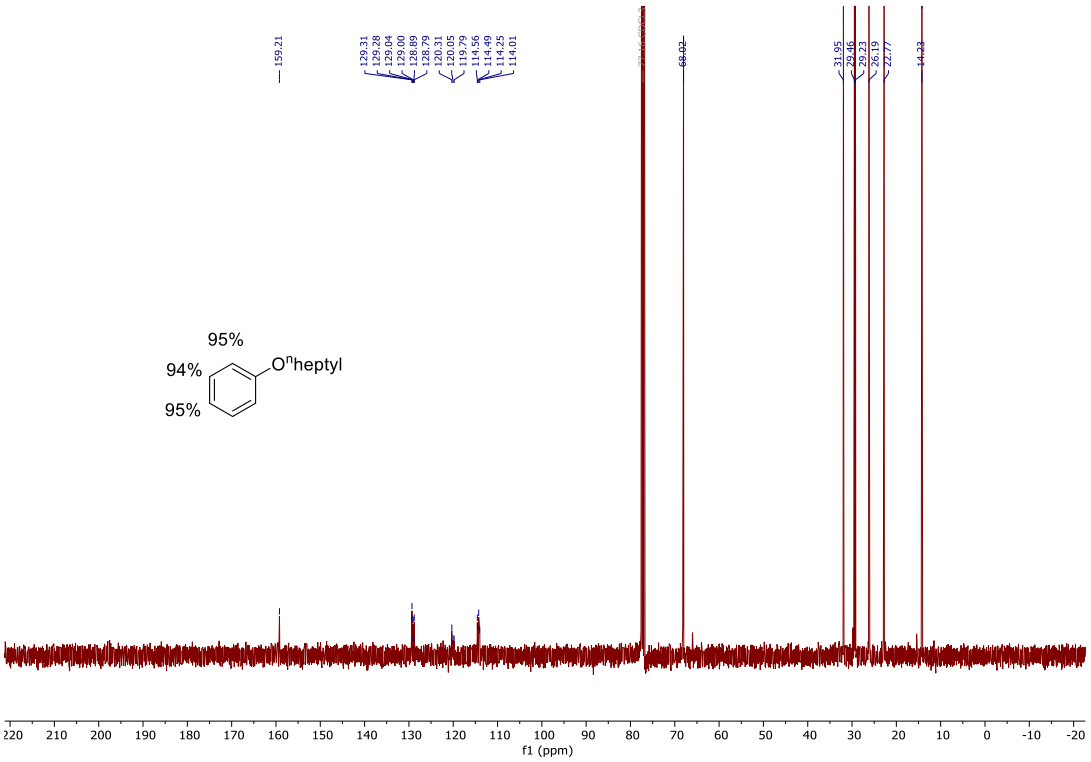
^{1}H-NMR spectrum in $CDCl_3$:



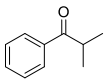
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of 2-methyl-1-phenylpropan-1-one (4):



Following the general procedure F and using 2-methyl-1-phenylpropan-1-one (**4**) (29.6 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:Et_2O = 50:1 as the eluent, the target compound **[D]4** was obtained as light-yellow liquid (22.5 mg, 74%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 4.30 D/molecule [Mass]; 4.42 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.00-7.92 (m, 2H), 7.59-7.52 (m, 1H), 7.50-7.42 (m, 2H), 3.56 (hept, *J* = 6.8 Hz, 1H), 1.22 (d, *J* = 6.8 Hz, 6H) ppm.

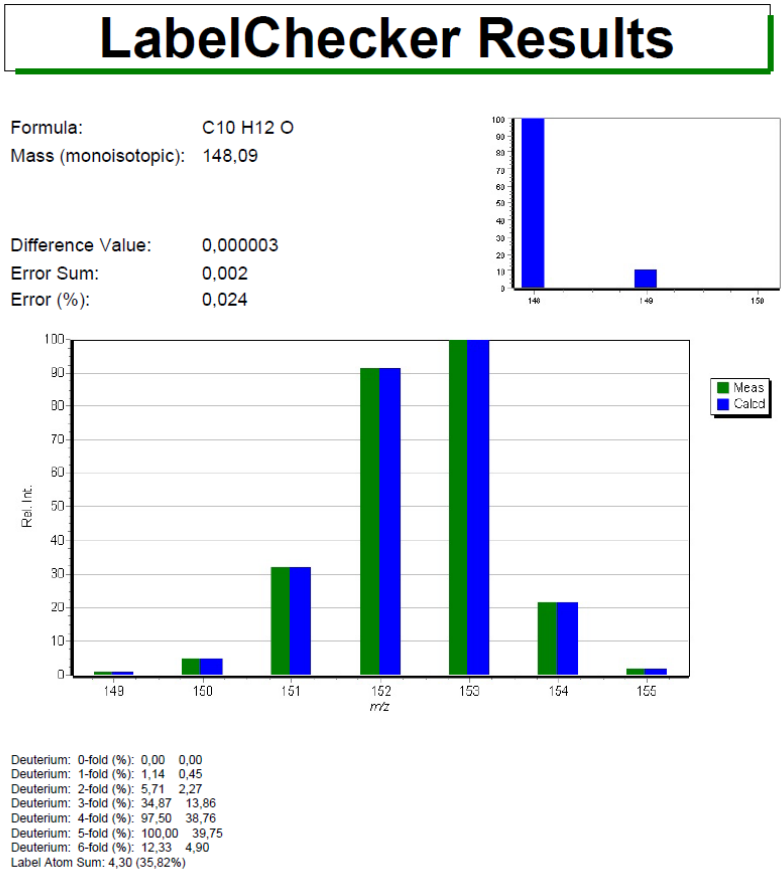
^{13}C NMR (101 MHz, $CDCl_3$) δ = 204.6, 136.4, 132.9, 128.7, 128.5, 35.5, 19.3 ppm.

NMR Data of Product:

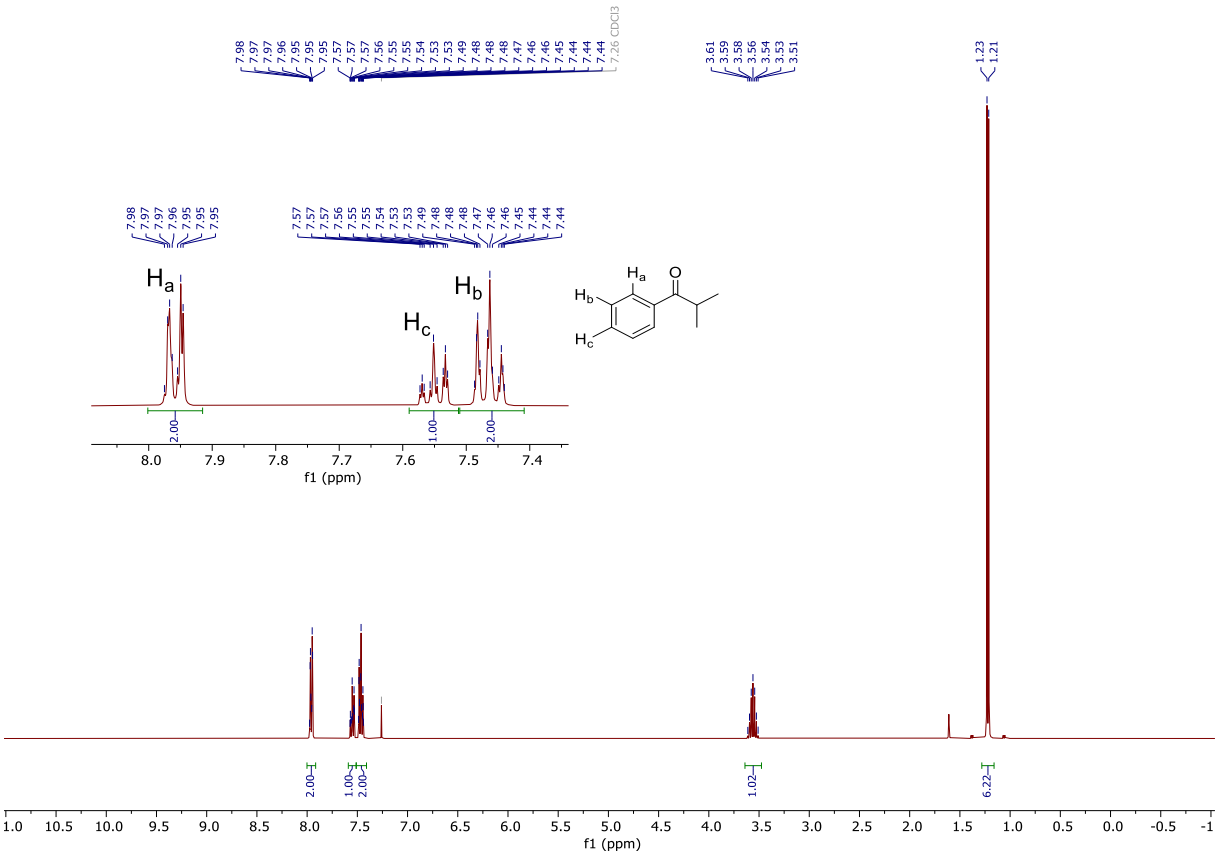
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.96 (s, 0.54H, 73% D), 7.55 (s, 0.06H, 94% D), 7.49-7.44 (m, 0.11H, 94.5% D), 3.63-3.49 (m, 0.87H, 13% D), 1.22 (d, *J* = 6.8 Hz, 6H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 204.7, 136.7-135.2 (1C), 133.5-130.7 (1C), 129.4-126.9 (4C), 36.8-33.2 (1C), 22.4-13.2 (2C) ppm.

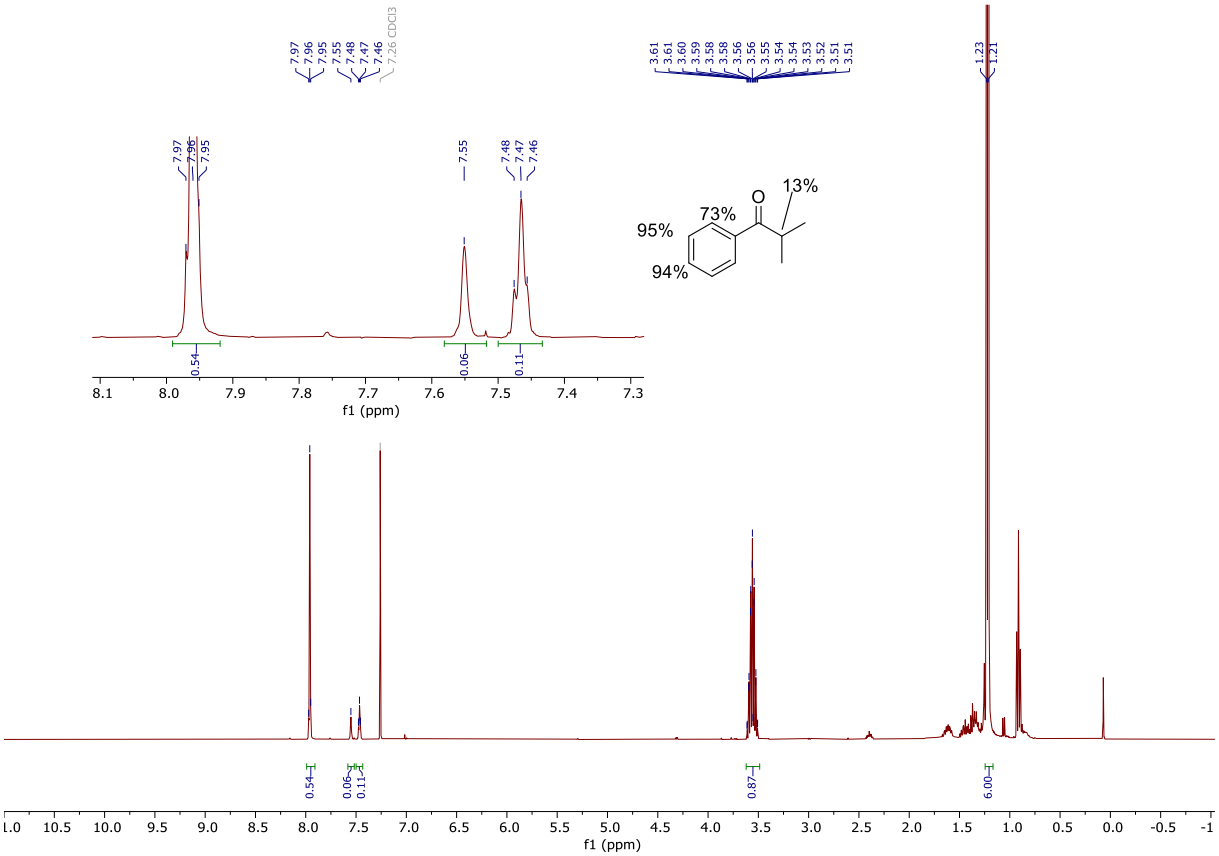
Mass Data:



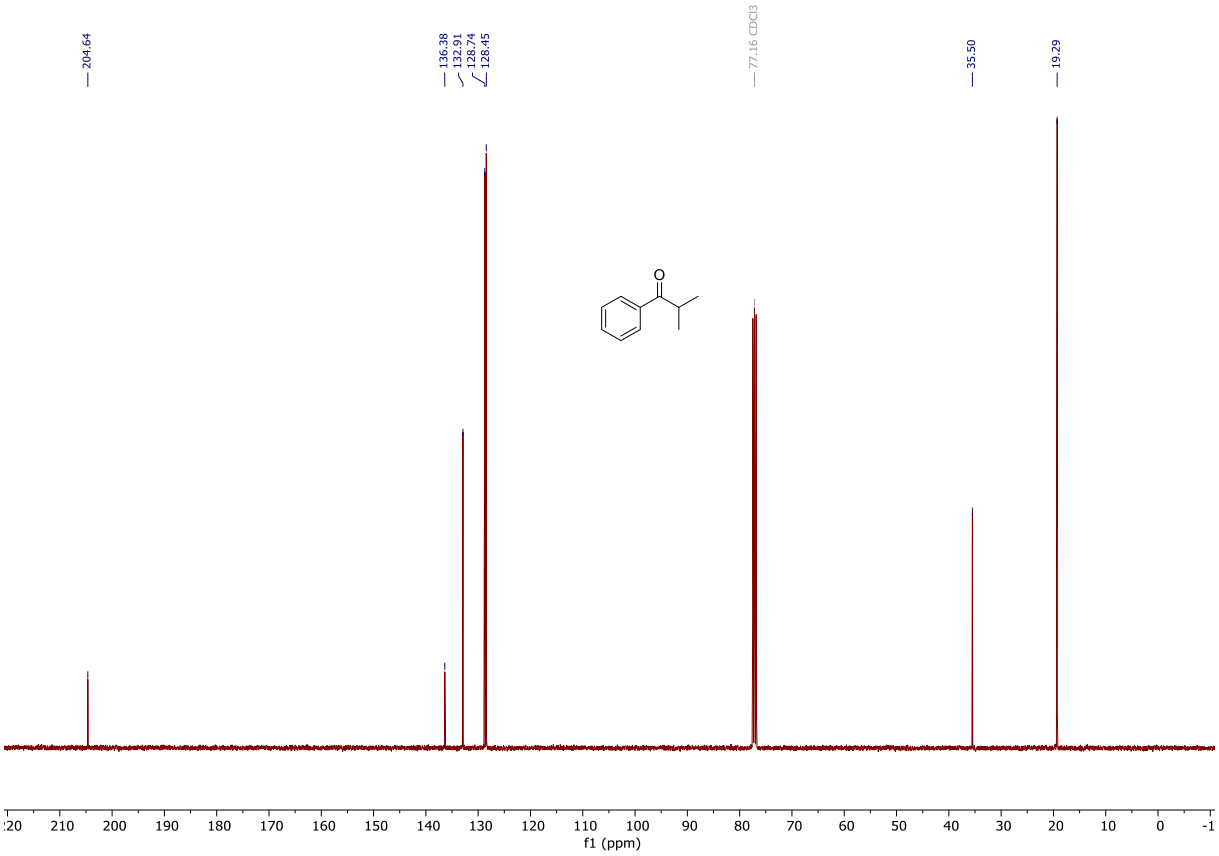
^{1}H-NMR spectrum in $CDCl_3$:



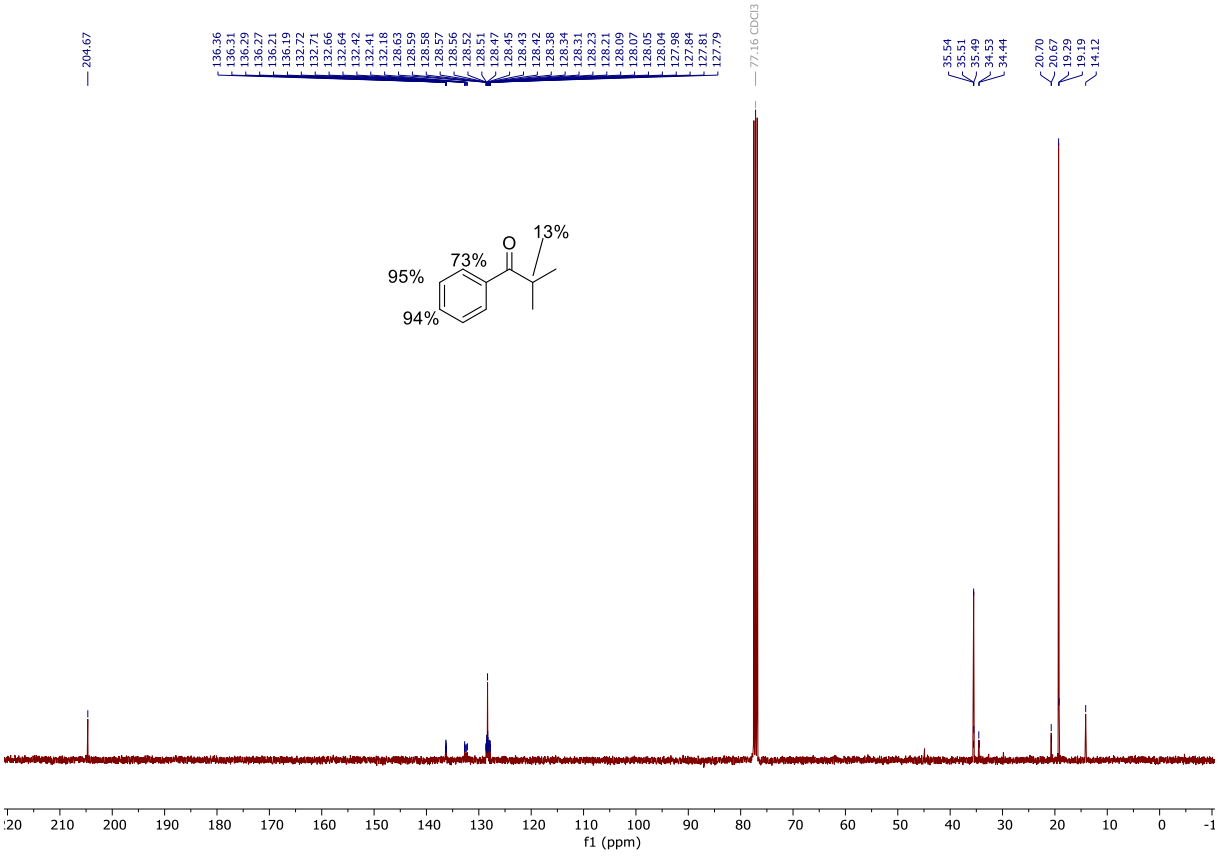
^{1}H-NMR spectrum in $CDCl_3$:



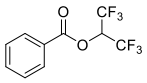
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of 1,1,1,3,3,3-hexafluoropropan-2-yl benzoate (1):



Following the general procedure F and using 1,1,1,3,3,3-hexafluoropropan-2-yl benzoate (**1**) (54.4 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:Et_2O = 50:1 as the eluent, the target compound **[D]1** was obtained as colorless solid (41.9 mg, 76%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 4.03 D/molecule [Mass]; 4.13 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.17-8.08 (m, 2H), 7.72-7.65 (m, 1H), 7.57-7.48 (m, 2H), 6.02 (hept, *J* = 6.1 Hz, 1H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 163.4, 134.9, 130.7, 129.0, 127.0, 120.7 (q, *J* = 282.3 Hz), 67.1 (hept, *J* = 34.8 Hz) ppm.

^{19}F NMR (286 MHz, $CDCl_3$) δ = –73.2 ppm.

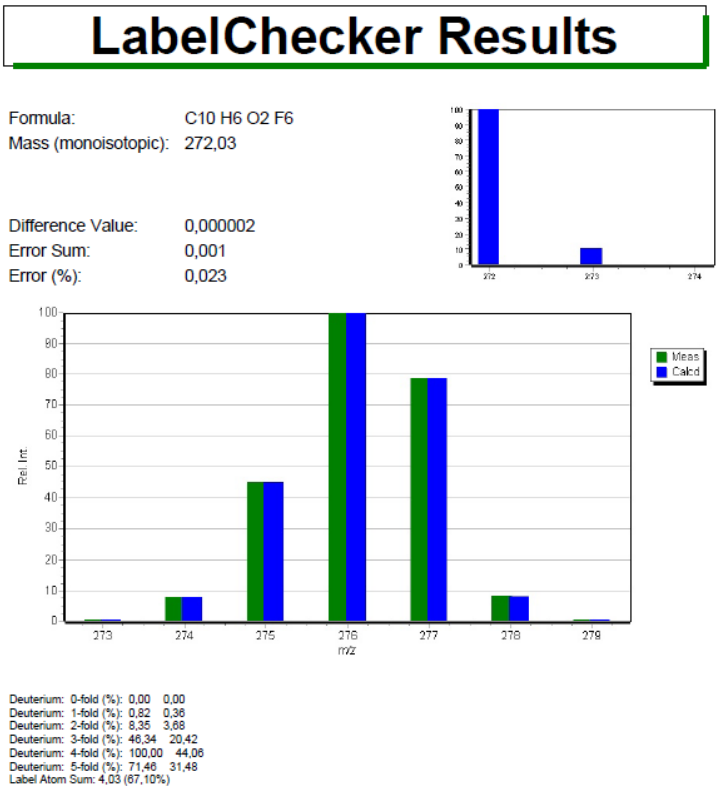
NMR Data of Product:

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.16-8.08 (m, 0.72H, 64% D), 7.68 (s, 0.07H, 93% D), 7.56-7.49 (m, 0.12H, 94% D), 6.03 (hept, *J* = 6.1 Hz, 1H) ppm.

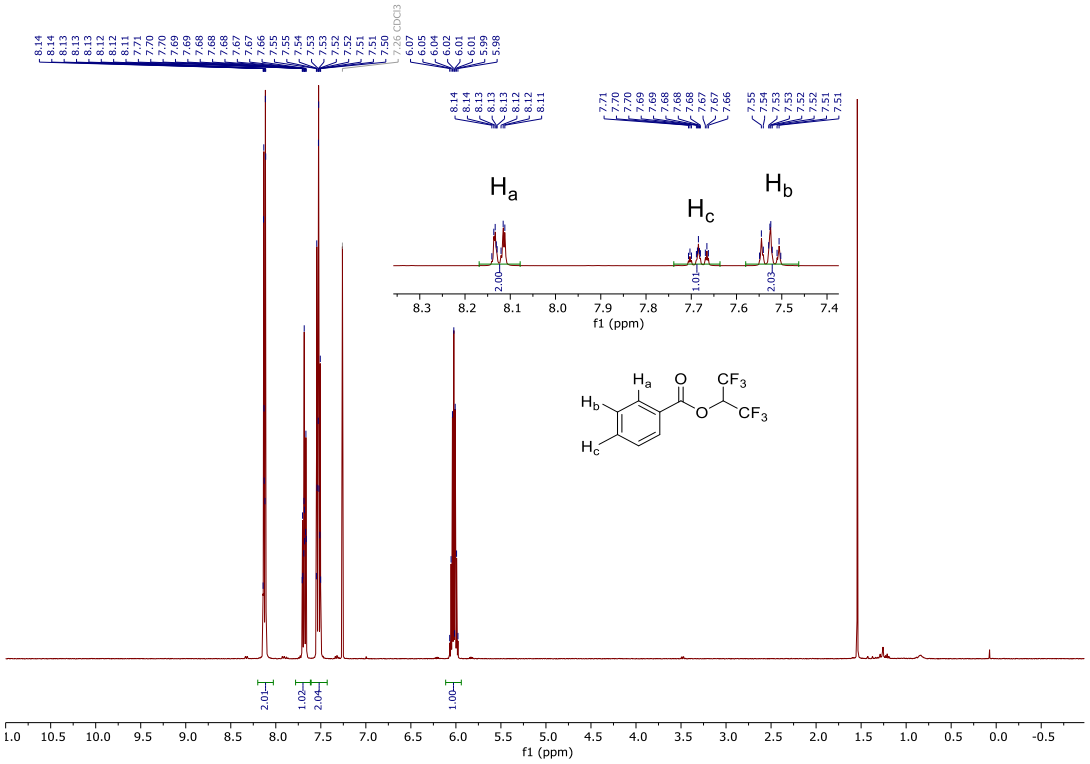
^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.4, 135.4-133.6 (1C), 131.0-129.5 (2C), 129.3-127.8 (2C), 126.9, 120.7 (q, *J* = 282.3 Hz), 67.1 (hept, *J* = 34.8 Hz) ppm.

^{19}F NMR (377 MHz, $CDCl_3$) δ = –73.2 ppm.

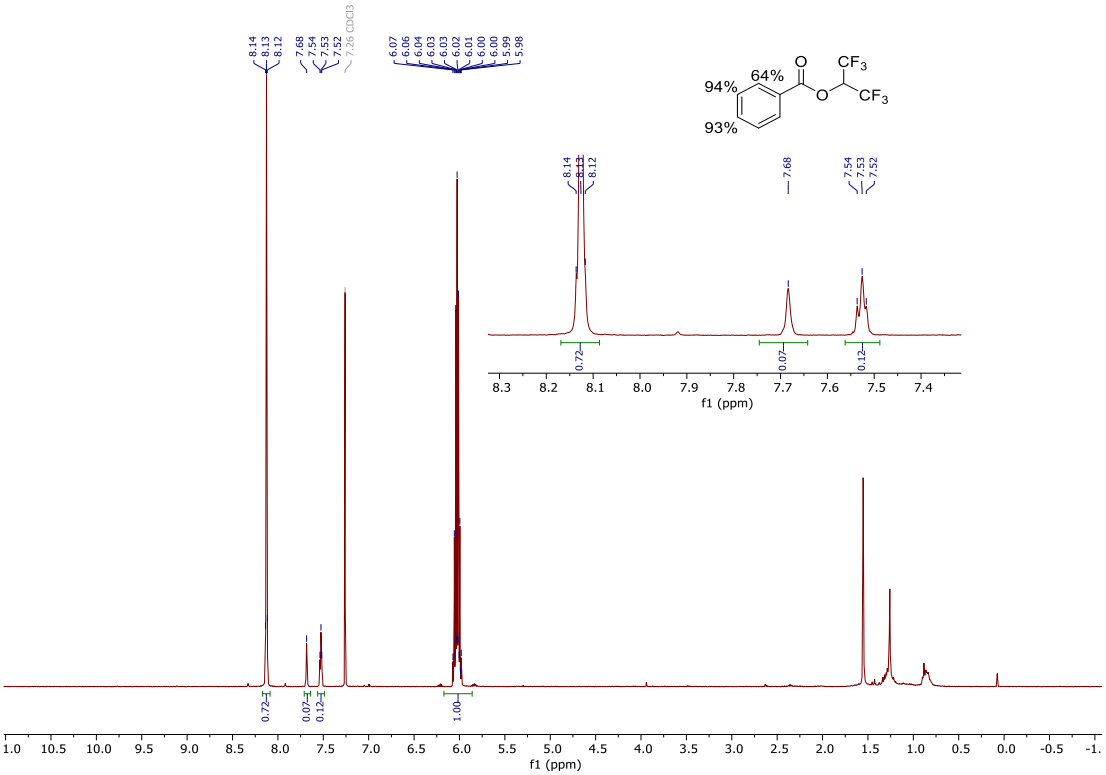
Mass Data:



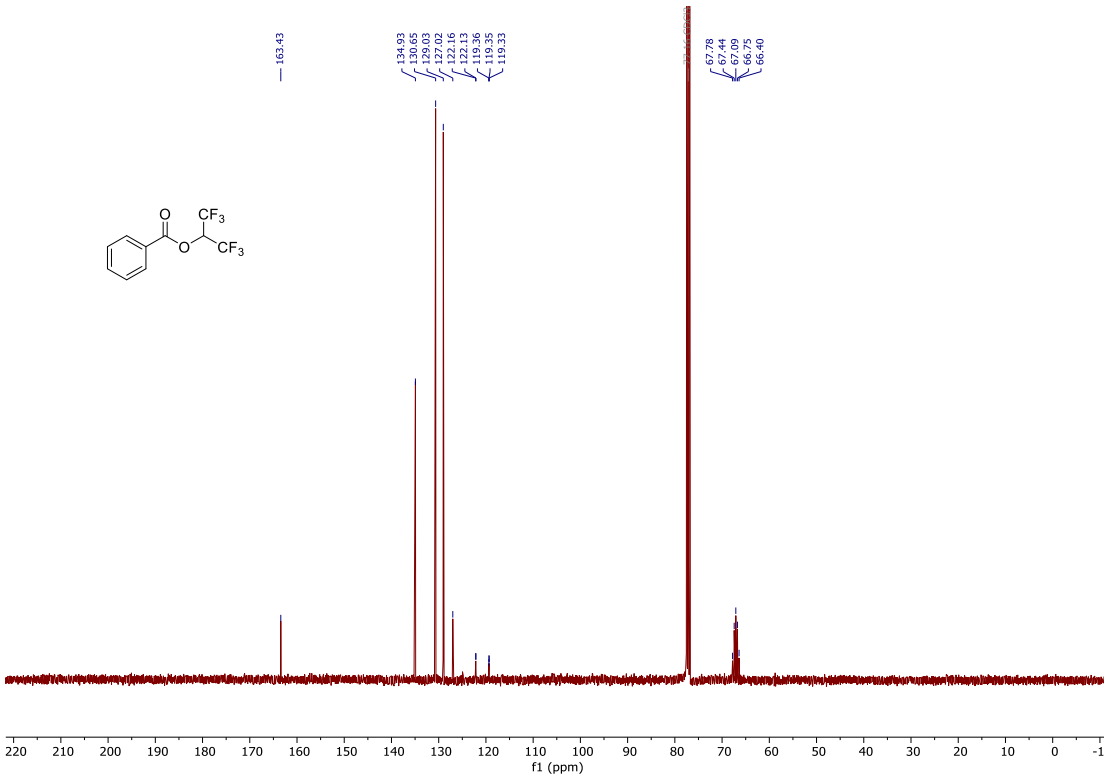
^{1}H-NMR spectrum in $CDCl_3$:



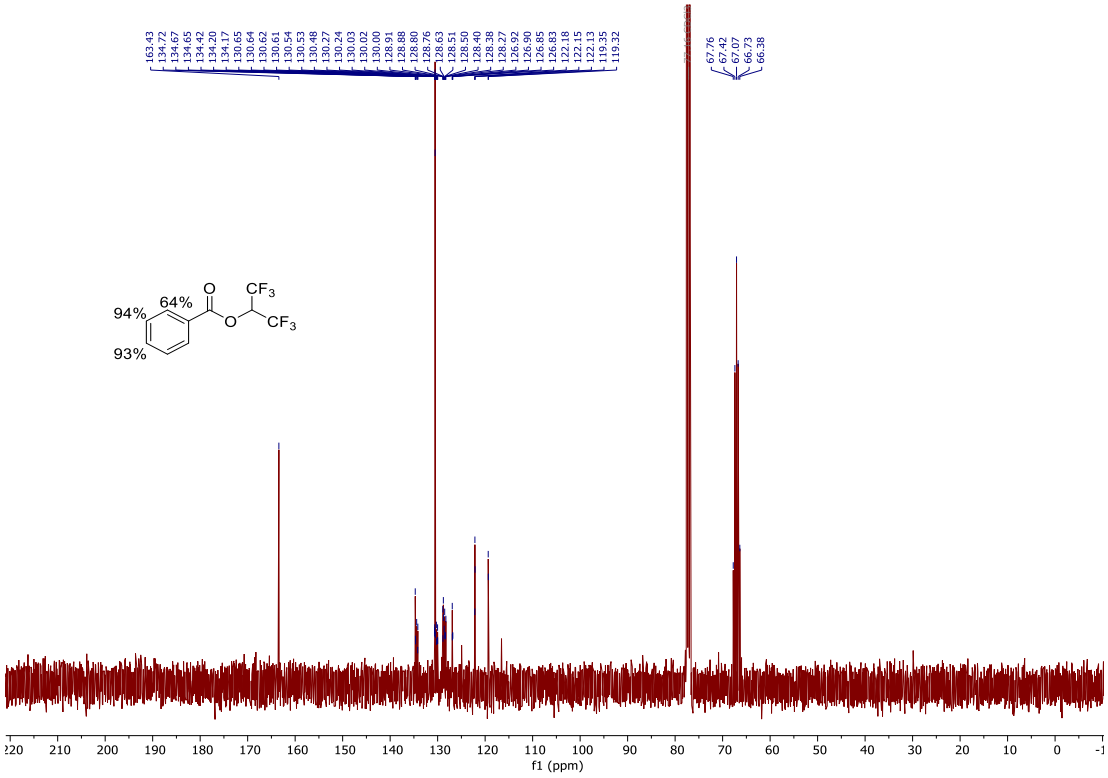
^{1}H-NMR spectrum in $CDCl_3$:



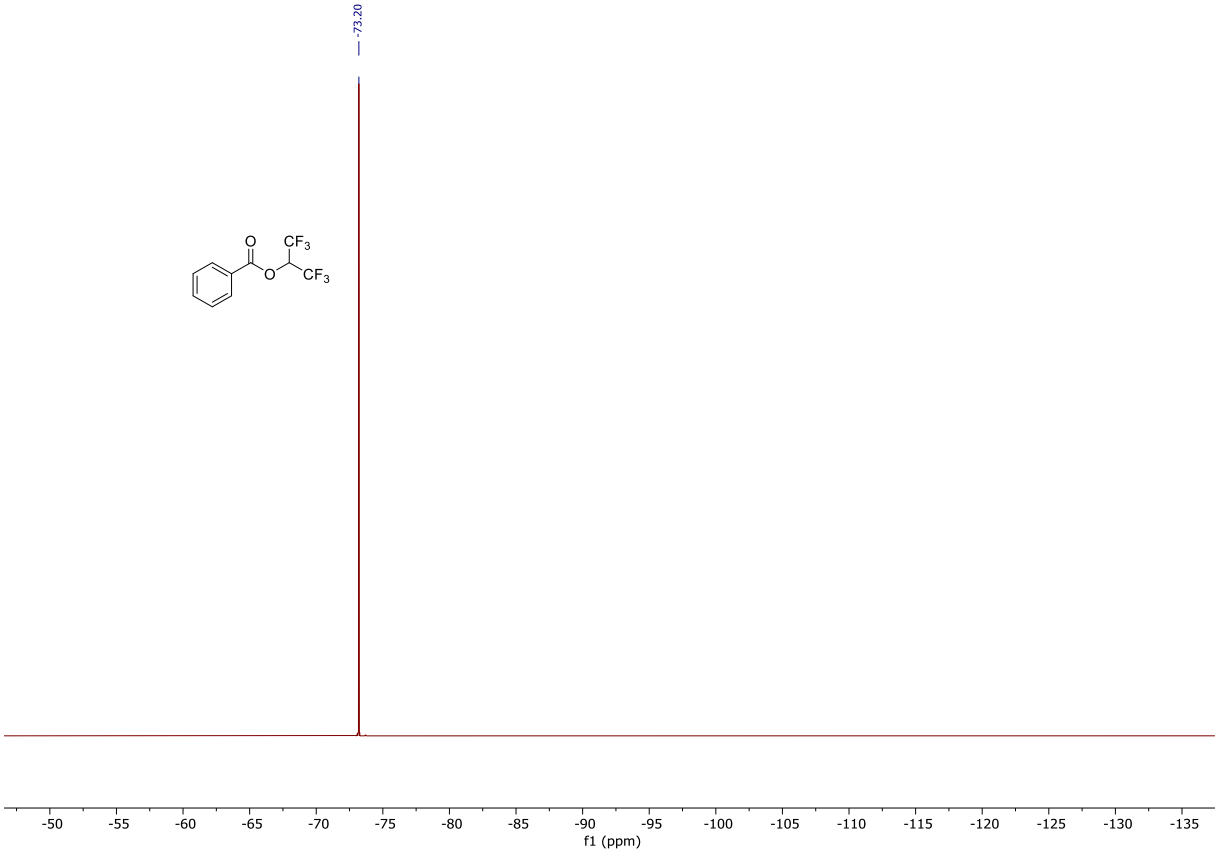
^{13}C-NMR spectrum in $CDCl_3$:



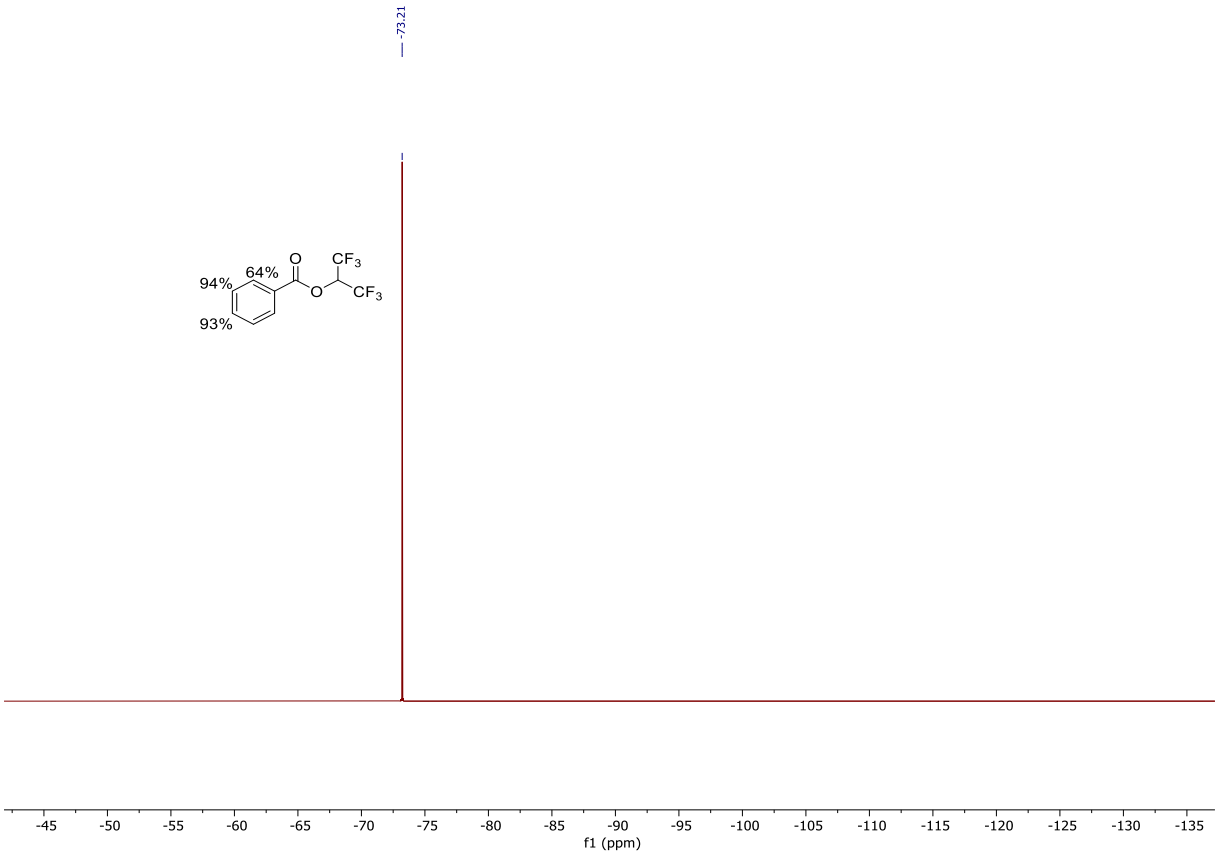
^{13}C-NMR spectrum in $CDCl_3$:



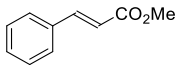
^{19}F-NMR spectrum in $CDCl_3$:



^{19}F-NMR spectrum in $CDCl_3$:



Deuteration of methyl cinnamate (5):



Following the general procedure F and using methyl cinnamate (**5**) (32.4 mg, 0.200 mmol) and purification by silica gel column chromatography using Pentane: Et_2O = 90:10 as the eluent, the target compound **[D]5** was obtained as colorless liquid (22.0 mg, 66%). The degree of deuteration was determined by HRMS studies.

Deuterium Incorporation: 4.52 D/molecule [HRMS]; 4.54 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (600 MHz, C_6D_6) δ = 7.78 (d, *J* = 16.1 Hz, 1H), 7.10-7.06 (m, 2H), 7.01-6.93 (m, 3H), 6.42 (d, *J* = 16.0 Hz, 1H), 3.48 (s, 3H).

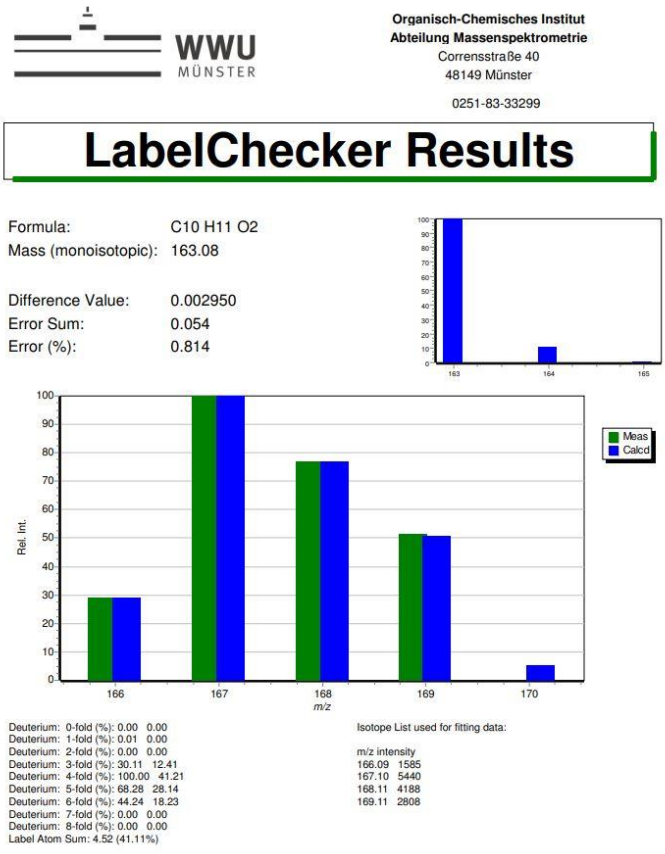
^{13}C NMR (150 MHz, C_6D_6) δ = 166.9, 144.8, 134.8, 130.1, 129.0, 128.3, 118.5, 51.2 ppm.

NMR Data of Product:

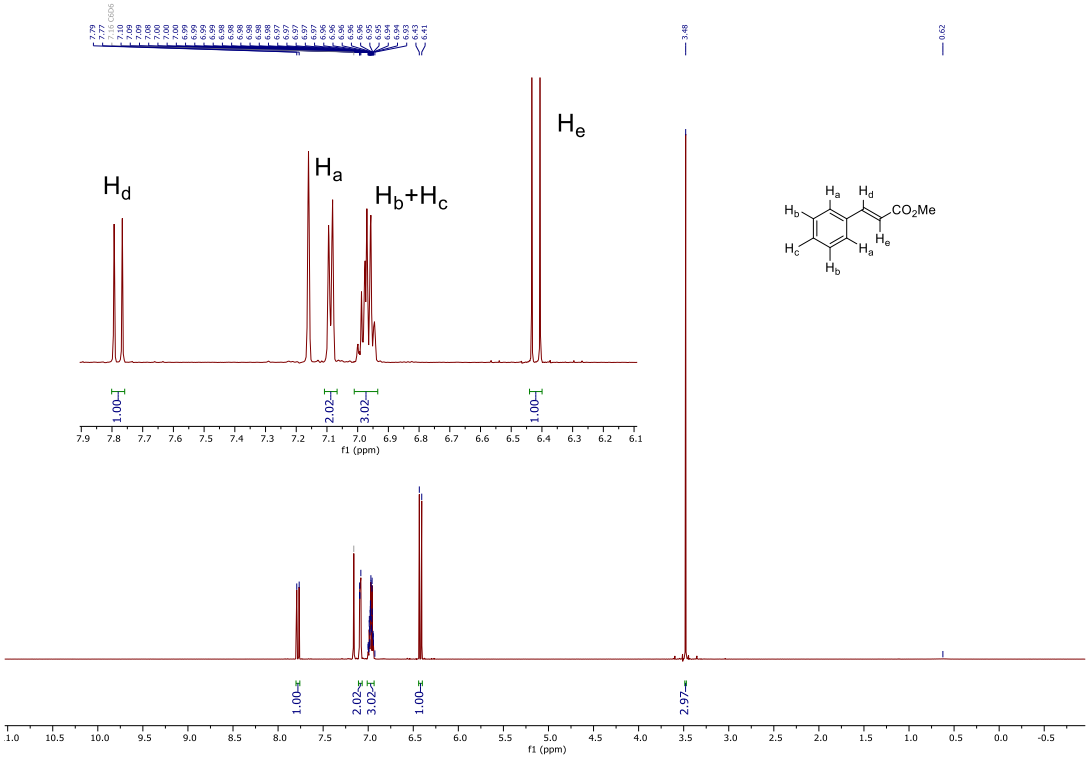
^{1}H NMR (400 MHz, C_6D_6) δ = 7.83-7.73 (m, 0.97H, 3% D), 7.10-7.04 (m, 0.61H, 70% D), 7.00-6.91 (m, 0.69H, 77% average D), 6.42 (d, 0.19H, 81% D), 3.48 (s, 3H) ppm.

^{13}C NMR (100 MHz, C_6D_6) δ = 166.9, 144.8-144.7(1C), 134.8-134.5 (1C), 130.0-129.7 (1C), 129.4-129.2 (2C),128.9-128.7 (2C), 118.5-118.4(1C), 51.2 ppm.

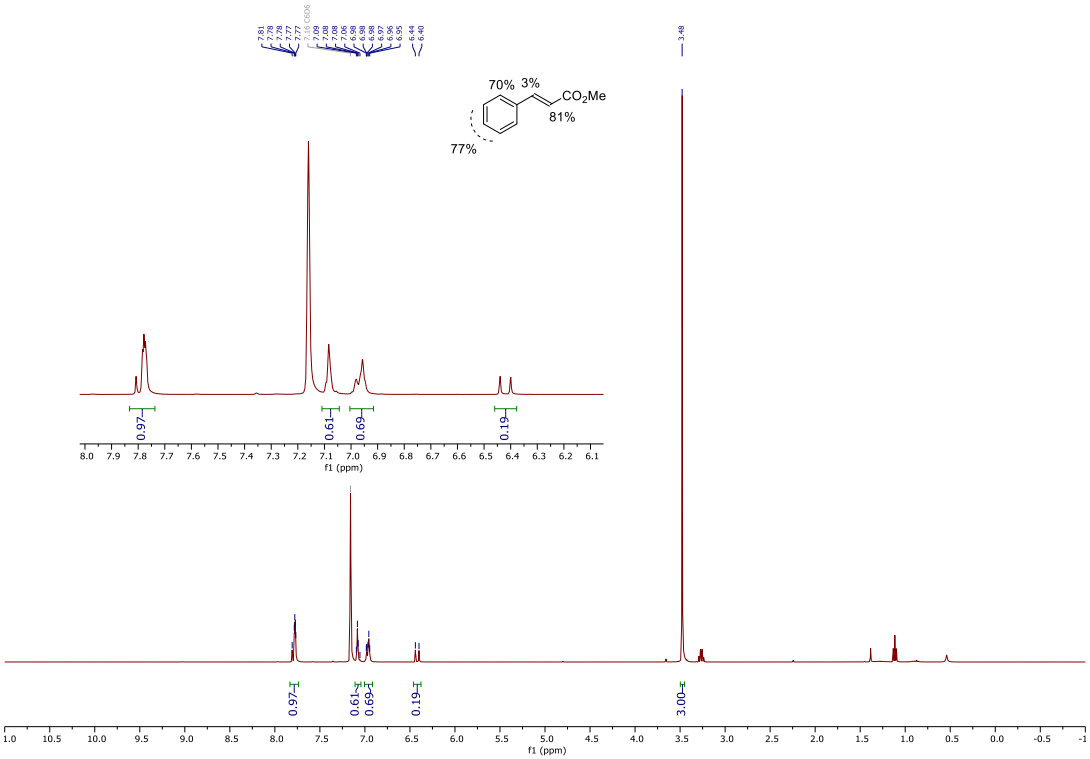
Mass Data:



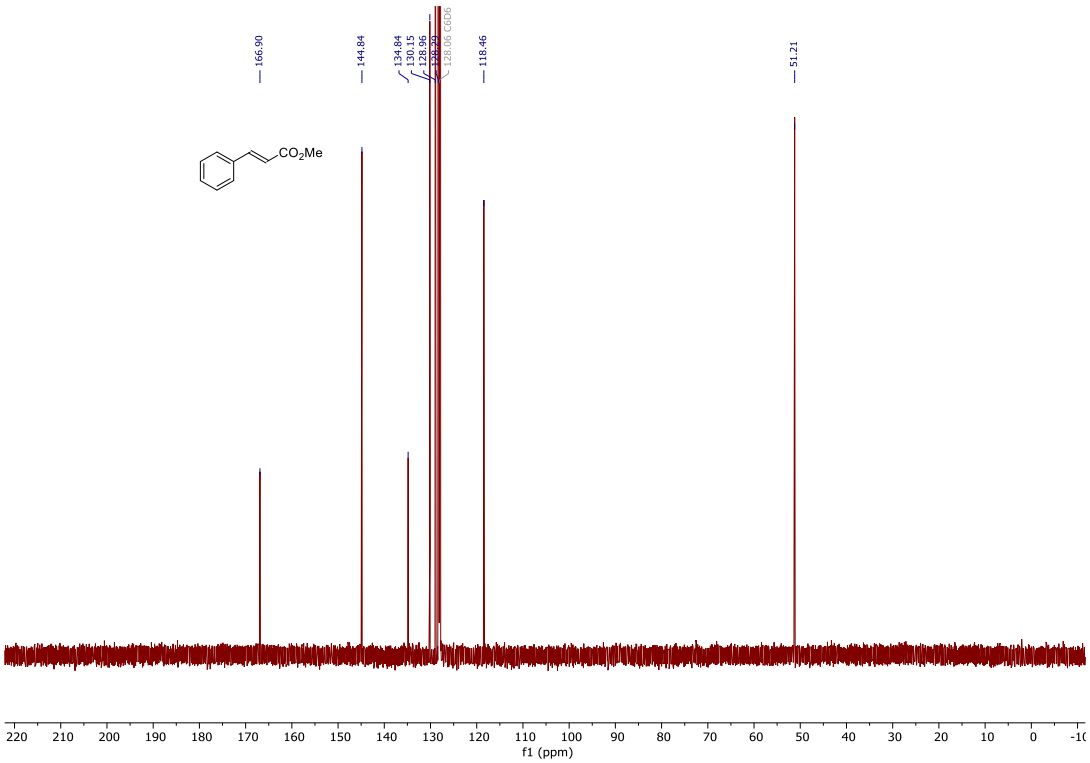
^{1}H-NMR spectrum in C_6D_6:



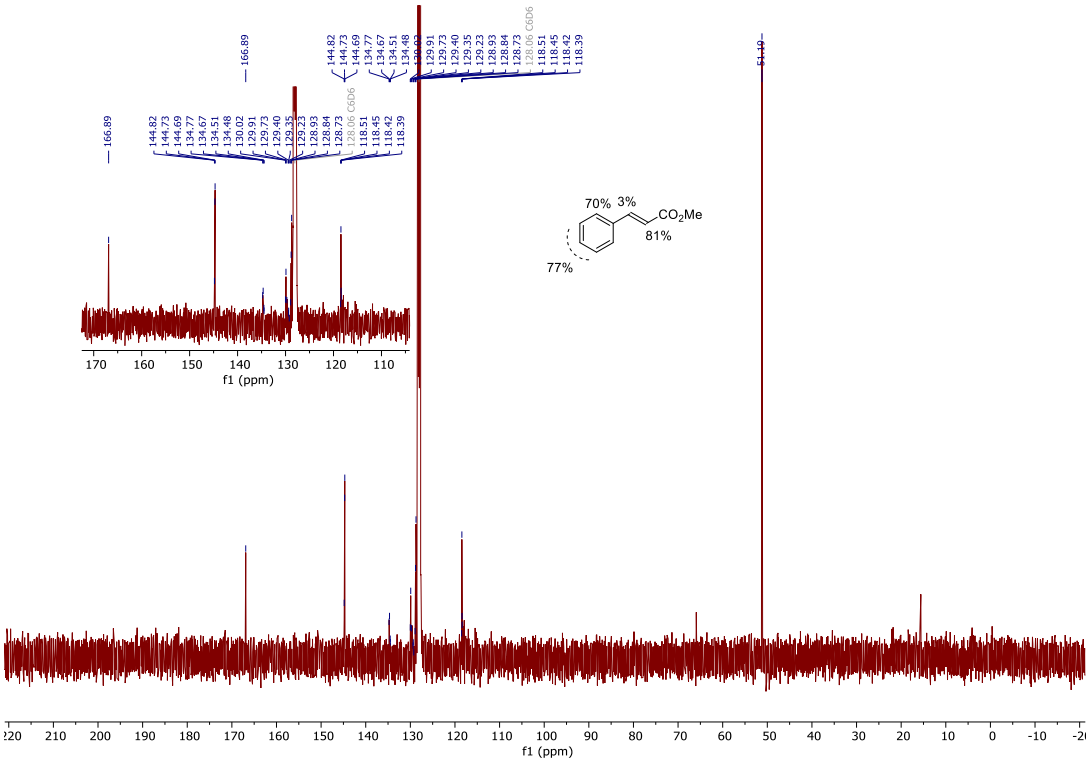
^{1}H-NMR spectrum in C_6D_6:



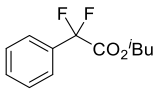
^{13}C-NMR spectrum in C_6D_6:



^{13}C-NMR spectrum in C_6D_6:



Deuteration of isobutyl 2,2-difluoro-2-phenylacetate (6):



Following the general procedure F and using isobutyl 2,2-difluoro-2-phenylacetate (**6**) (45.6 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:Et_2O = 50:1 as the eluent, the target compound **[D]6** was obtained as light-yellow liquid (25.1 mg, 54%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 3.09 D/molecule [Mass]; 3.23 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.66-7.58 (m, 2H), 7.54-7.46 (m, 1H), 7.46-7.40 (m, 2H), 4.02 (d, *J* = 6.6 Hz, 2H), 1.96 (dh, *J* = 13.4, 6.7 Hz, 1H), 0.88 (d, *J* = 6.8 Hz, 6H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 164.4 (t, *J* = 35.4 Hz), 133.1 (t, 25.5 Hz), 131.1 (t, *J* = 1.8 Hz), 128.8, 125.6 (t, *J* = 6.2 Hz), 113.6 (t, *J* = 252.0 Hz), 72.8, 27.8, 18.9 ppm.

^{19}F NMR (377 MHz, $CDCl_3$) δ = –104.1 ppm.

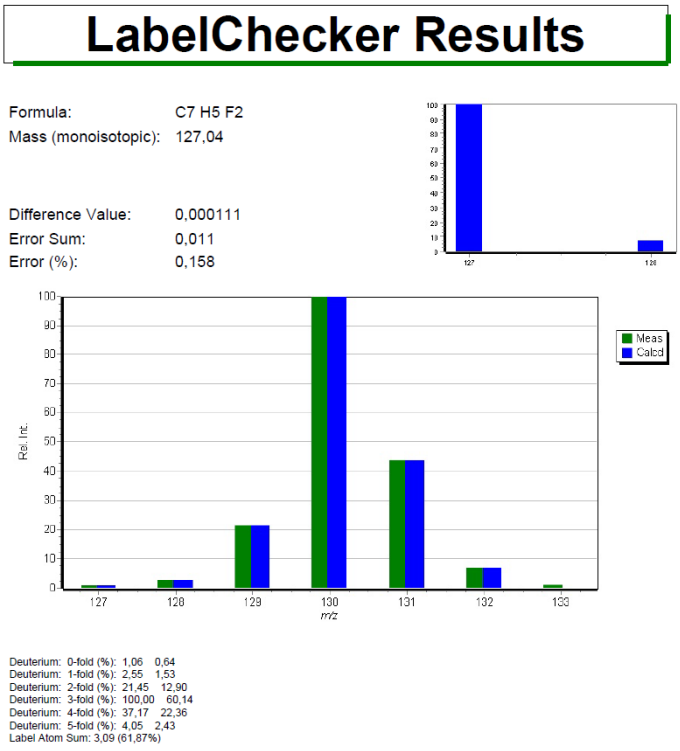
NMR Data of Product:

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.62 (s, 1.59H, 20.5% D), 7.49 (s, 0.07H, 93% D), 7.46-7.39 (m, 0.12H, 94% D), 4.02 (d, *J* = 6.6 Hz, 2H), 1.96 (dh, *J* = 13.4, 6.7 Hz, 1H), 0.88 (d, *J* = 6.8 Hz, 6H) ppm.

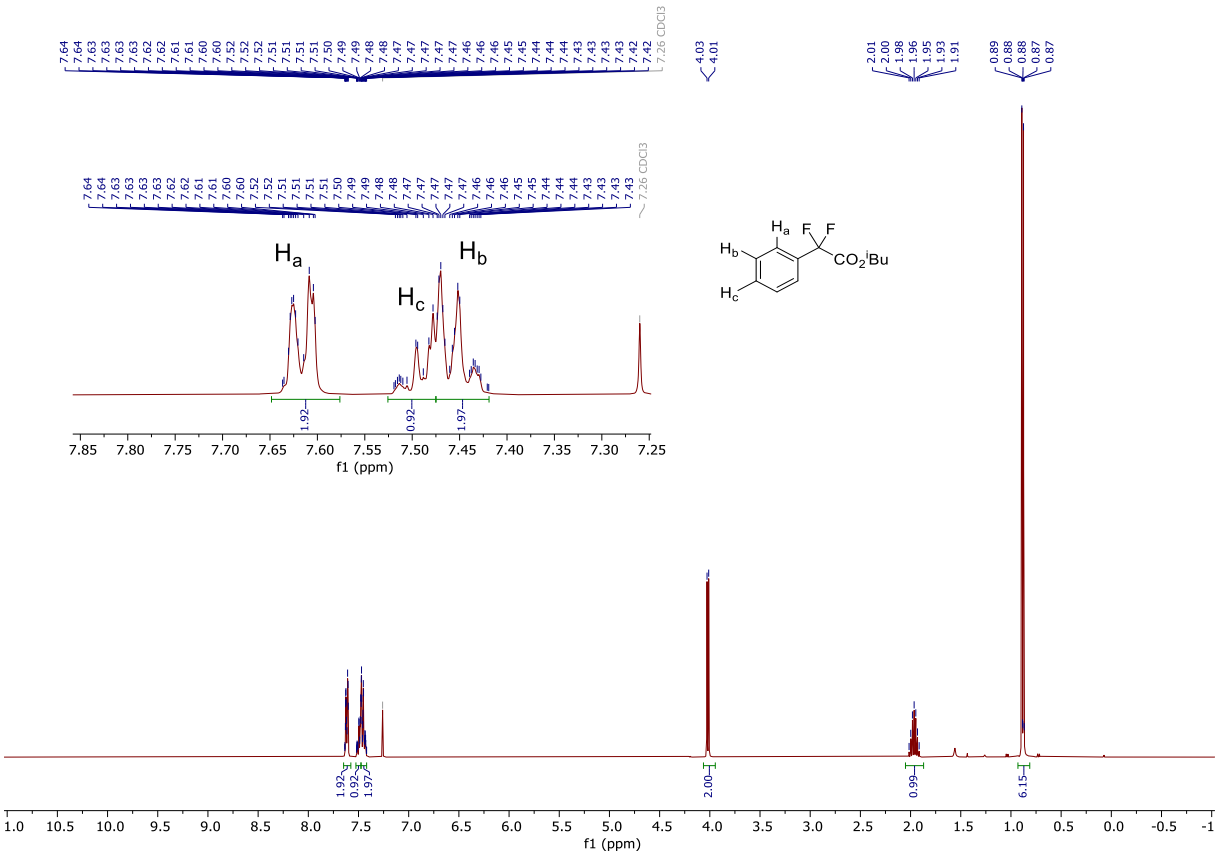
^{13}C NMR (101 MHz, $CDCl_3$) δ = 164.4 (t, *J* = 35.4 Hz), 134.4-127.2 (5C), 125.5 (t, *J* = 6.1 Hz), 113.6 (t, *J* = 252.0 Hz), 72.8, 27.8, 18.9 ppm.

^{19}F NMR (377 MHz, $CDCl_3$) δ = –104.1 ppm.

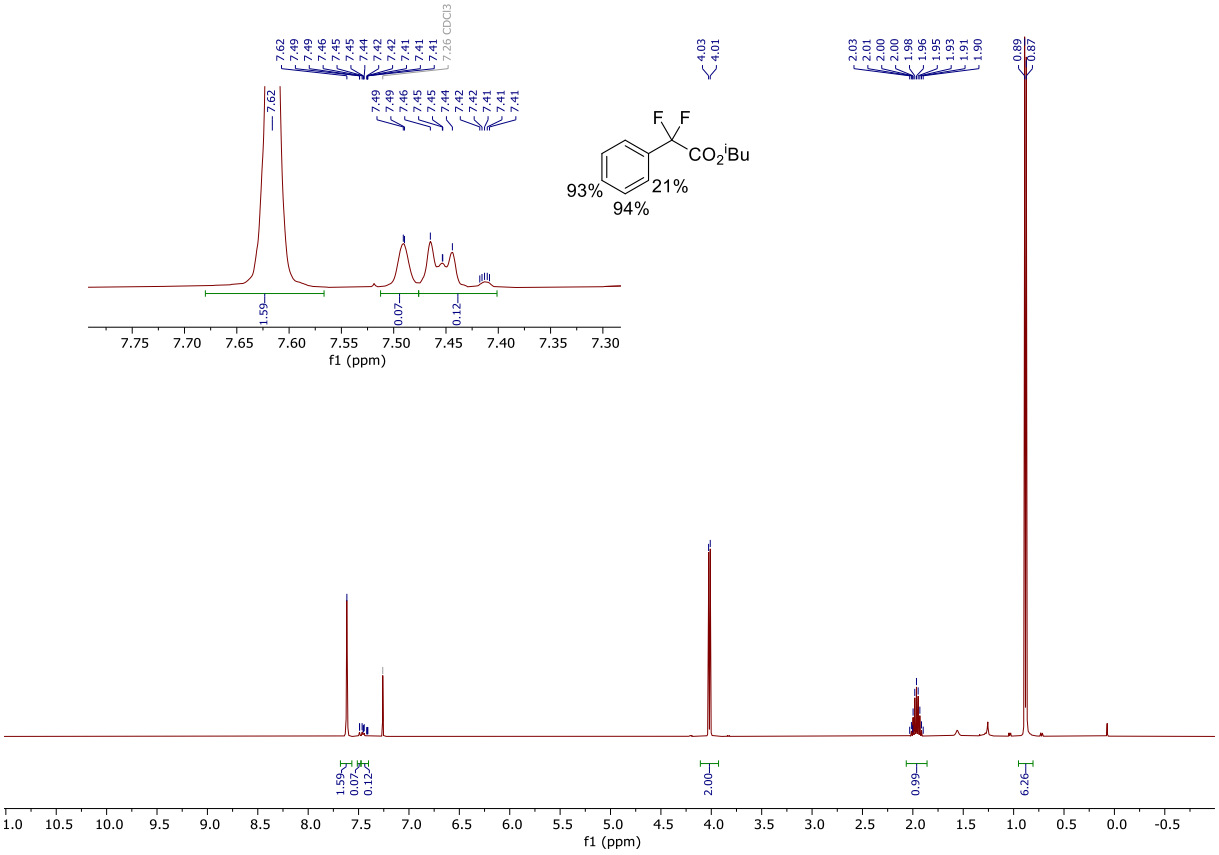
Mass Data:



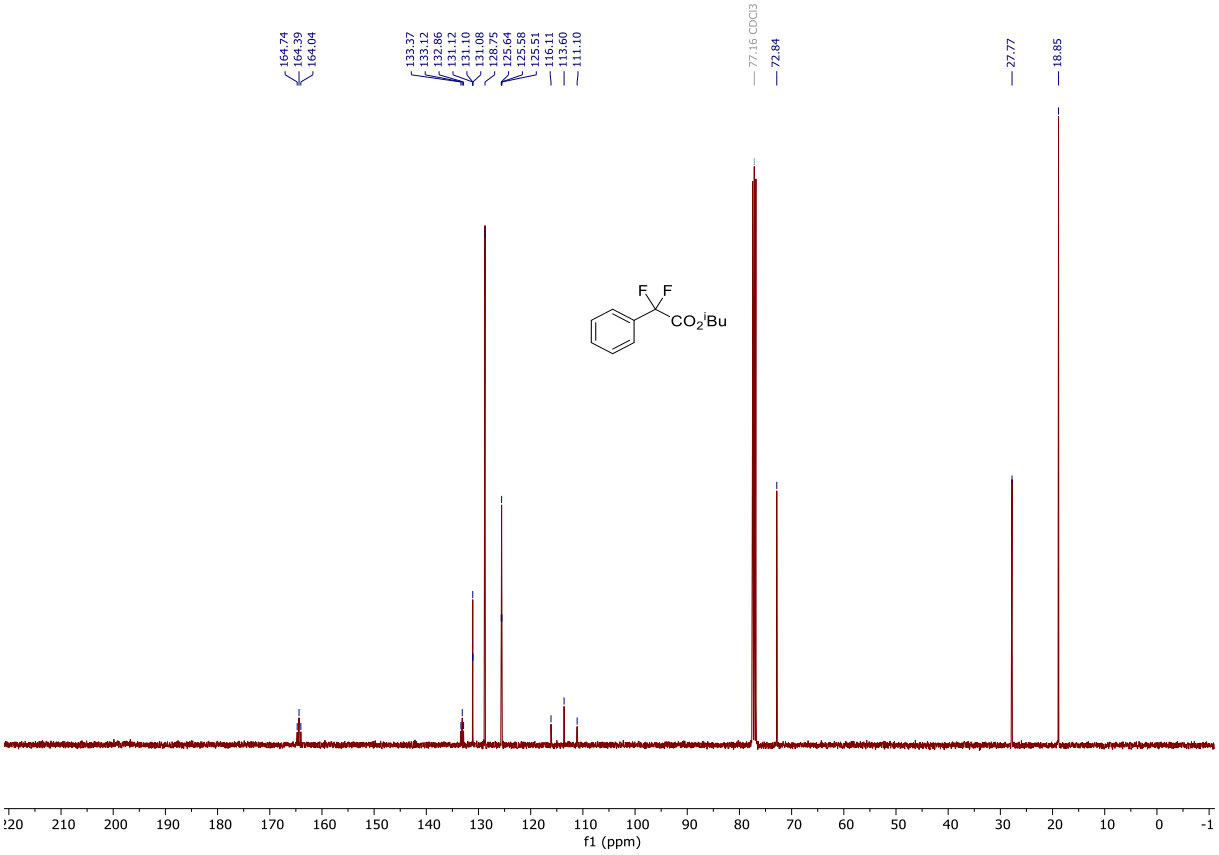
^{1}H-NMR spectrum in $CDCl_3$:



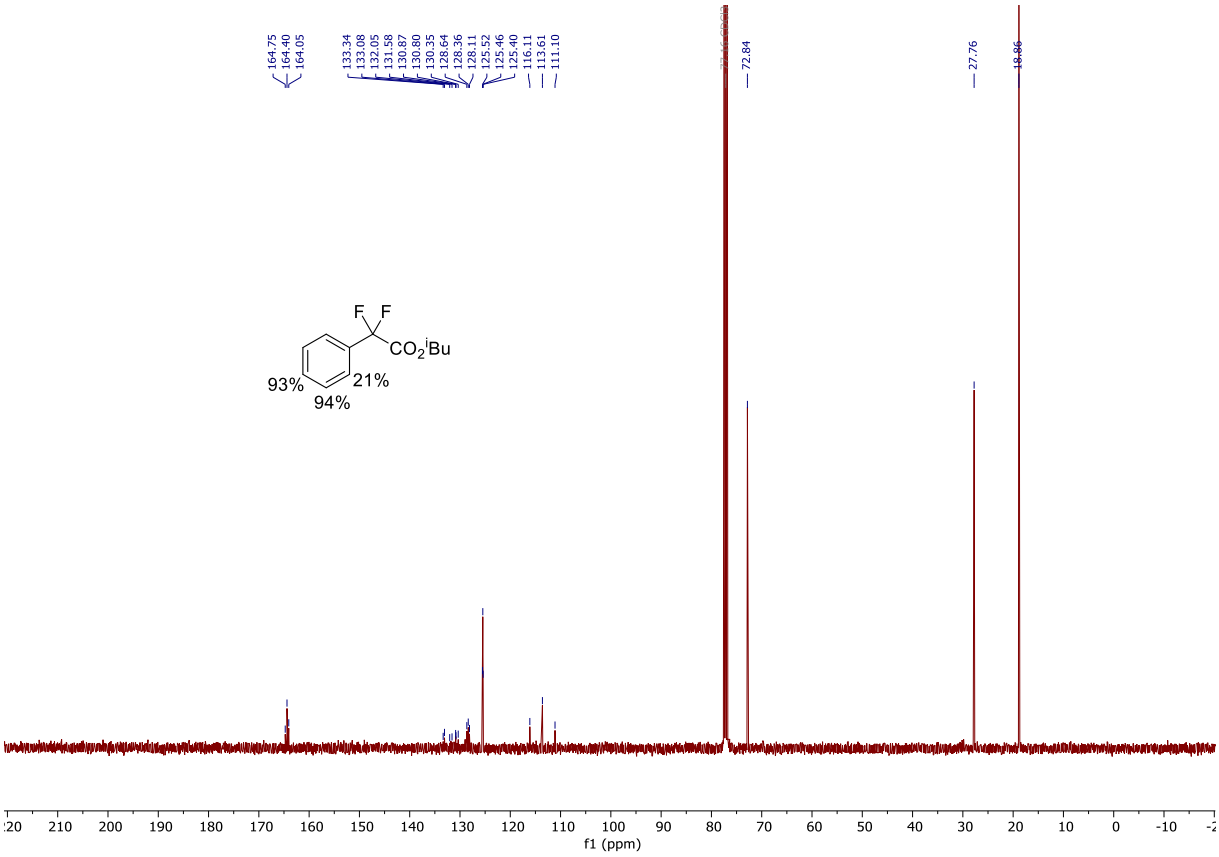
^{1}H-NMR spectrum in $CDCl_3$:



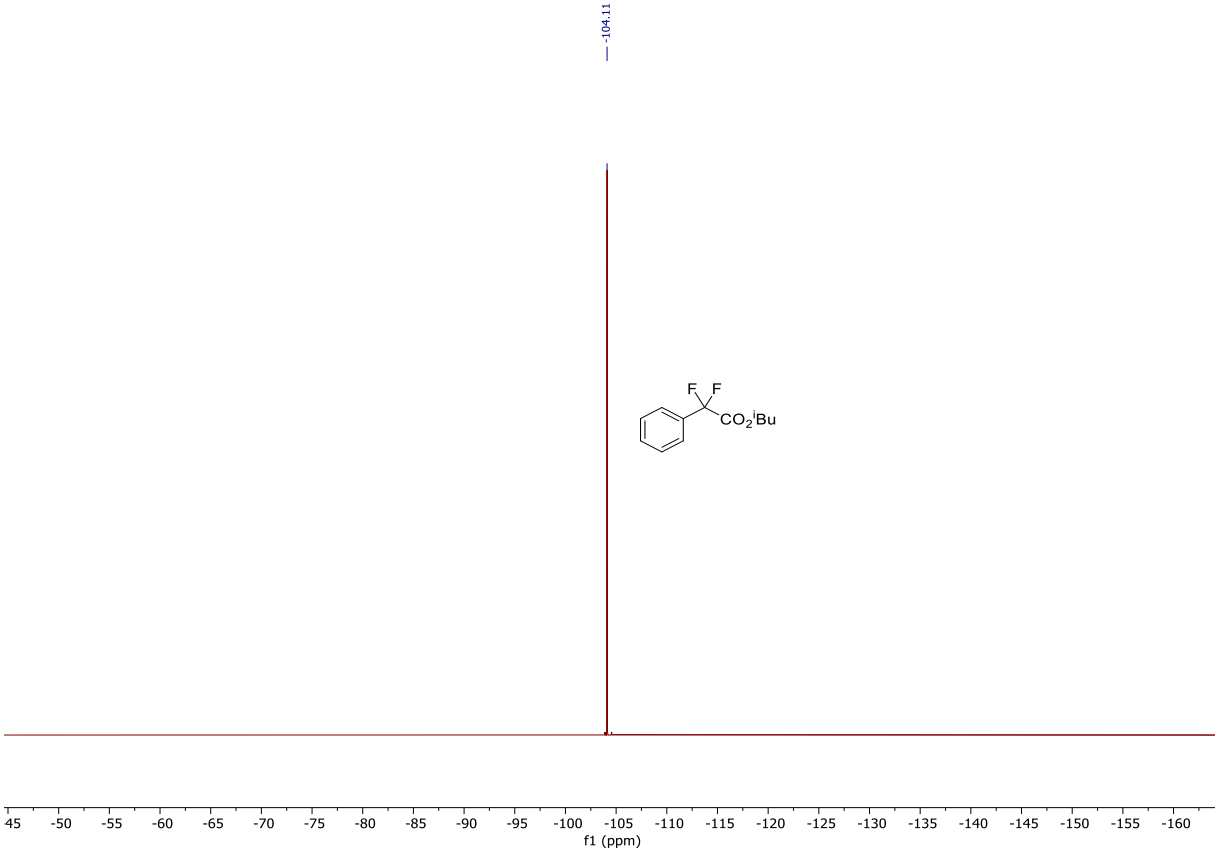
^{13}C-NMR spectrum in $CDCl_3$:



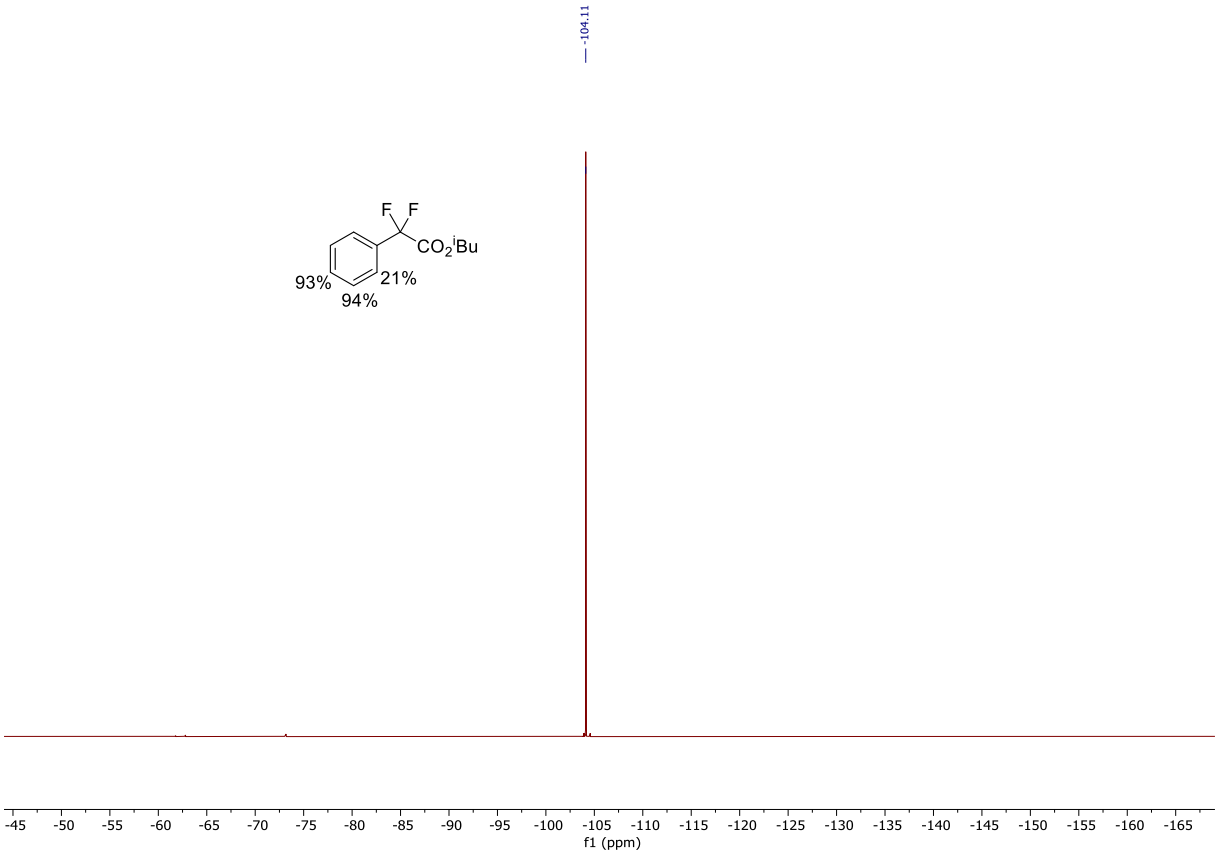
^{13}C-NMR spectrum in $CDCl_3$:



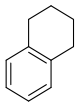
^{19}F-NMR spectrum in $CDCl_3$:



^{19}F-NMR spectrum in $CDCl_3$:



Deuteration of 1,2,3,4-tetrahydronaphthalene (7):



Following the general procedure E, but at 40 °C for 72 h, using 1,2,3,4-tetrahydronaphthalene (**7**) (26.4 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane as the eluent, the target compound **[D]7** was obtained as colorless liquid (16.3 mg, 60%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 3.40 D/molecule [Mass]; 3.77 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.23-7.15 (m, 4H), 2.93-2.85 (m, 4H), 1.96-1.88 (m, 4H) ppm.

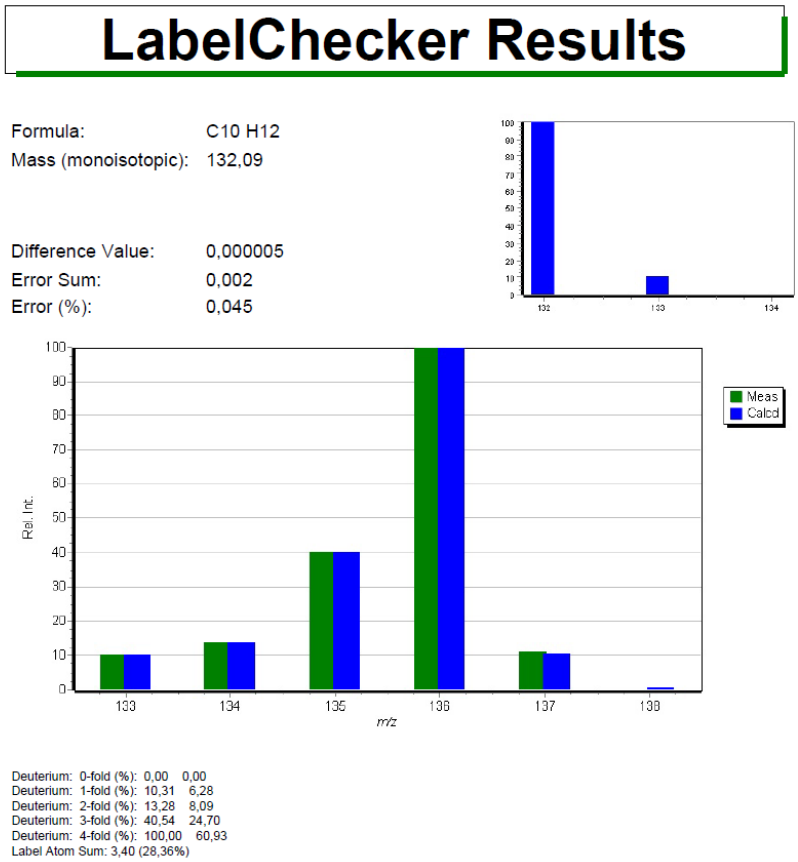
^{13}C NMR (150 MHz, $CDCl_3$) δ = 137.2, 129.2, 125.5, 29.5, 23.4 ppm.

NMR Data of Product:

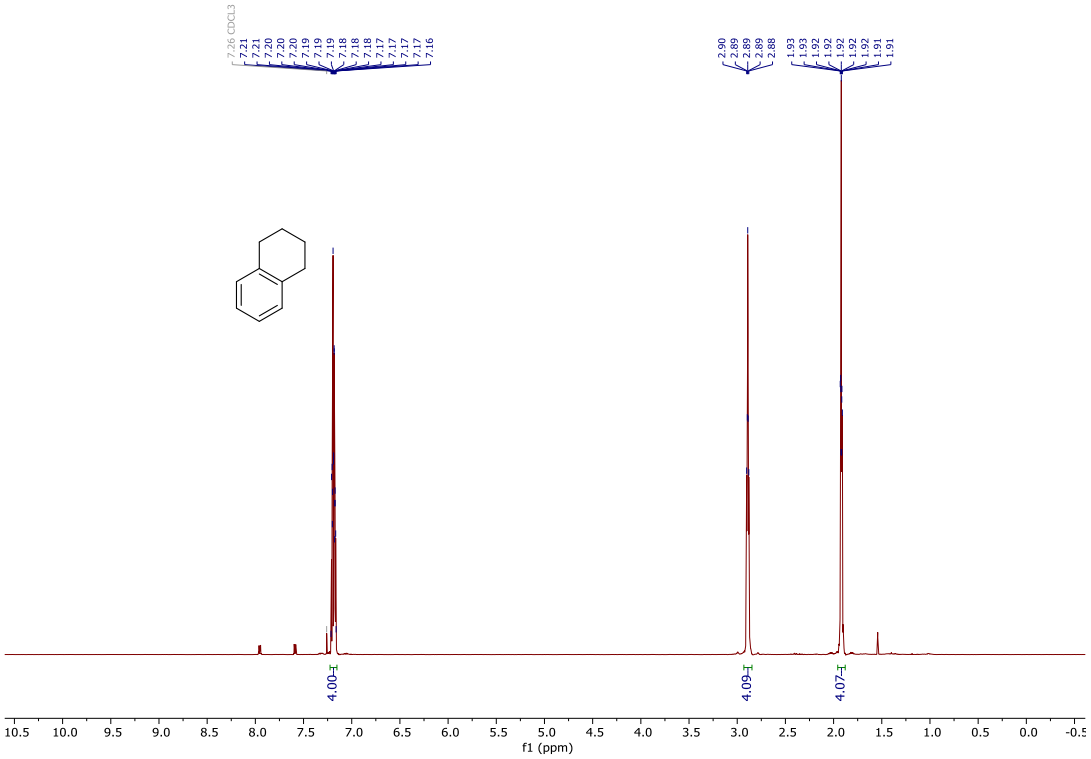
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.09 (s, 0.10H, 95% D), 7.07 (s, 0.13H, 93% D), 2.85-2.71 (m, 4H), 1.88-1.73 (m, 4H). ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ = 137.2, 129.4-128.3 (2C), 125.7-124.4 (2C), 29.5, 23.4 ppm.

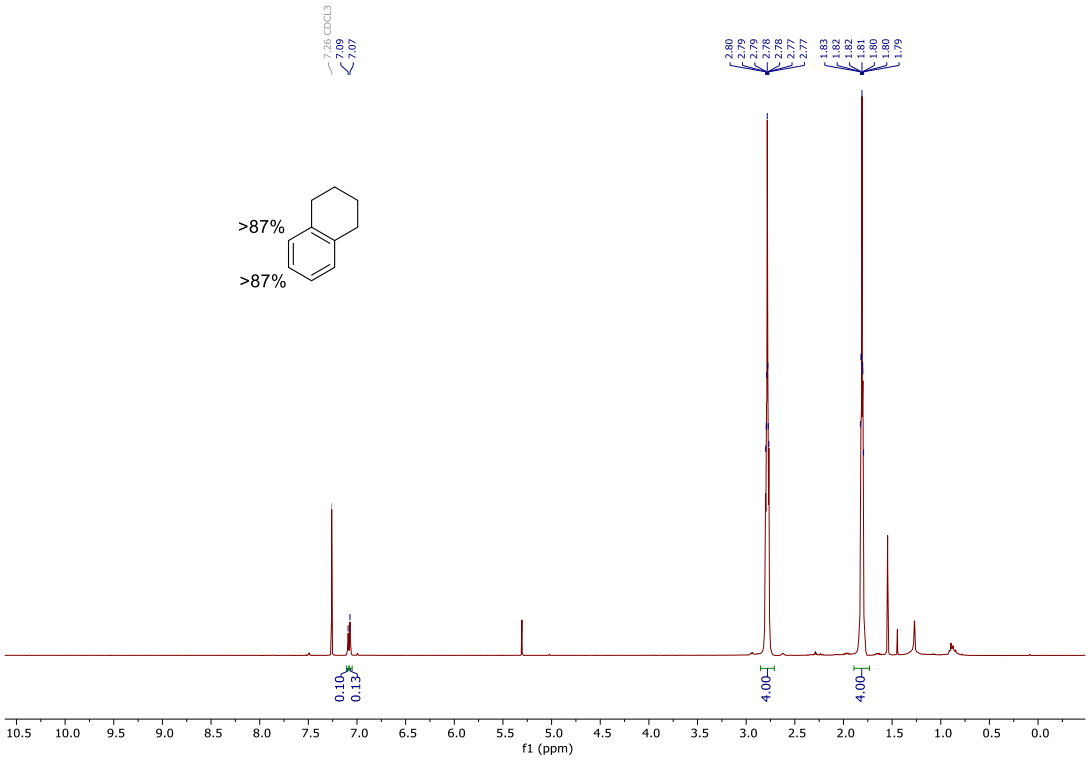
Mass Data:



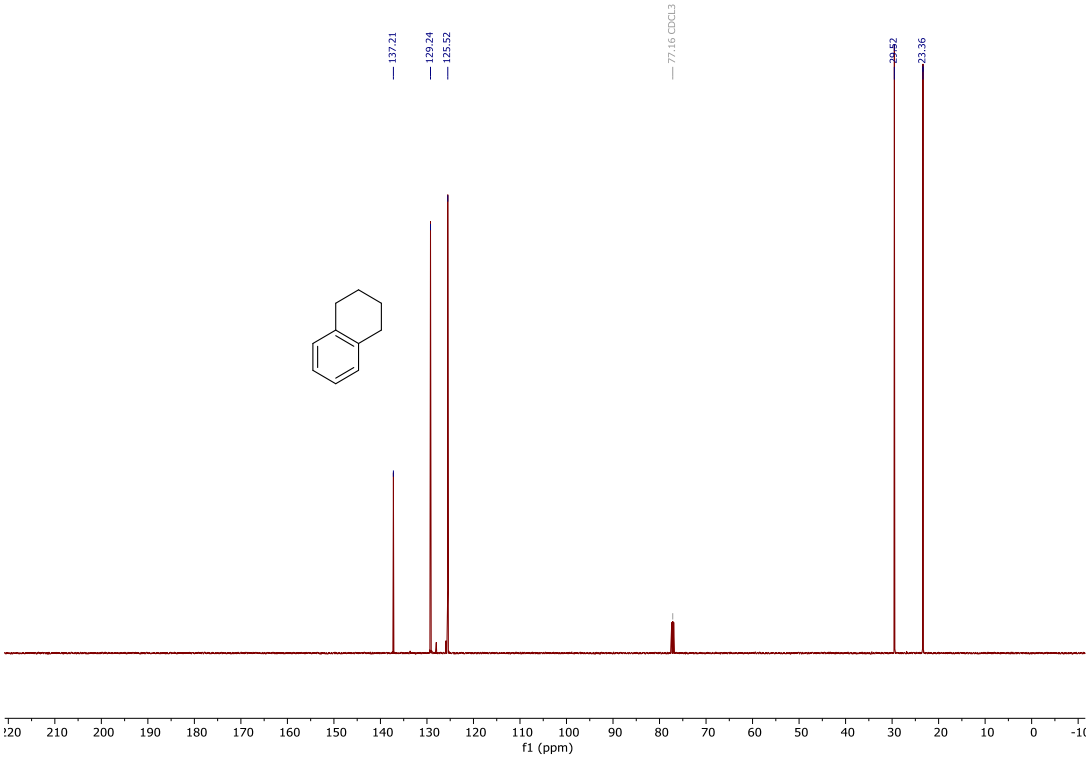
^{1}H-NMR spectrum in $CDCl_3$:



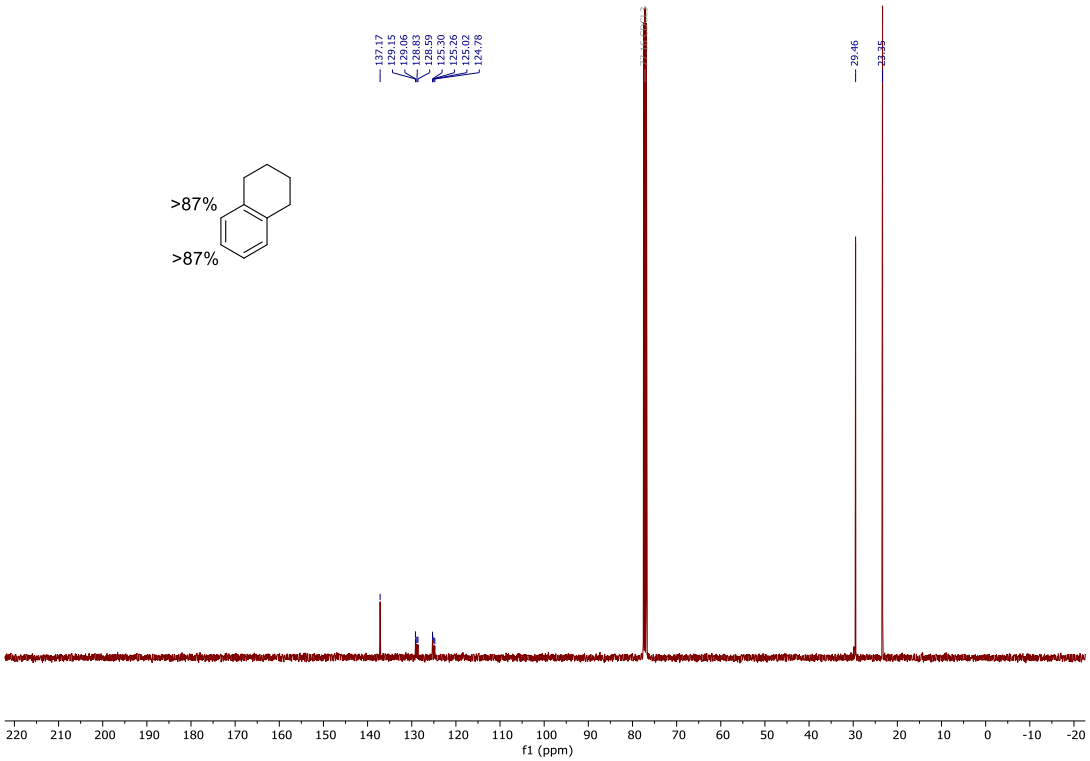
^{1}H-NMR spectrum in $CDCl_3$:



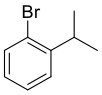
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of 1-bromo-2-isopropylbenzene (8):



Following the general procedure E and using 1-bromo-2-isopropylbenzene (**8**) (39.8 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane as the eluent, the target compound **[D]8** was obtained as colorless liquid (23.5 mg, 58%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 2.84 D/molecule [Mass]; 2.90 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (600 MHz, C_6D_6) δ = 7.44-7.38 (m, 1H), 7.00 (dd, *J* = 7.8, 1.8 Hz, 1H), 6.98-6.93 (m, 1H), 6.68 (ddd, *J* = 7.9, 7.3, 1.8 Hz, 1H), 3.38 (hept, *J* = 6.9 Hz, 1H), 1.07 (d, *J* = 6.9 Hz, 3H) ppm.

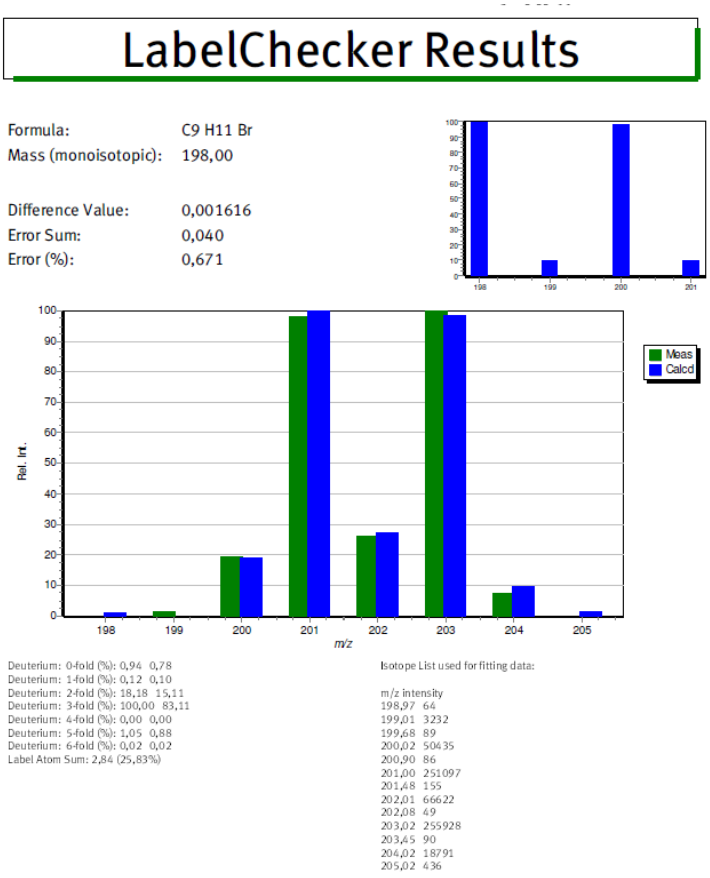
^{13}C NMR (150 MHz, C_6D_6) δ = 147.5, 133.2, 127.9, 127.6, 127.0, 124.7, 33.1, 22.8 ppm.

NMR Data of Product:

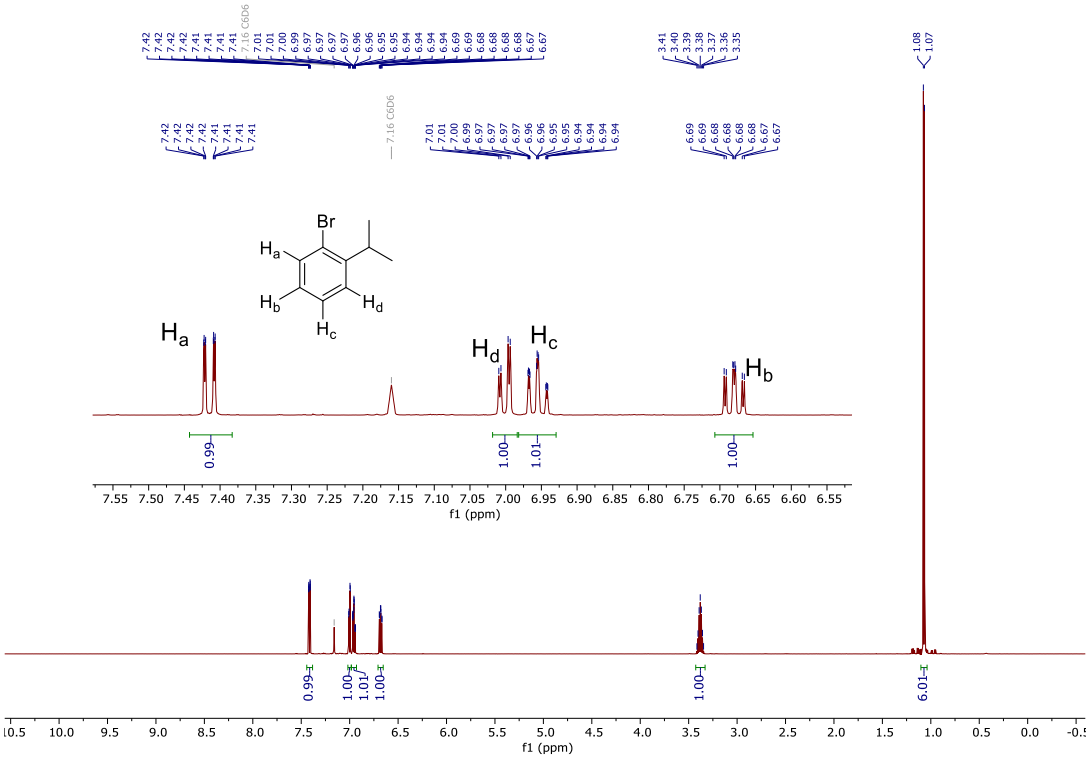
^{1}H NMR (600 MHz, C_6D_6) δ = 7.42 (s, 0.05H, 95% D), 7.00 (s, 0.94H, 6% D), 6.95 (d, *J* = 7.7 Hz, 0.06H, 94% H), 6.67 (s, 0.05H, 95% D), 3.39 (hept, *J* = 6.8 Hz, 1H), 1.07 (d, *J* = 6.9 Hz, 6H) ppm.

^{13}C NMR (150 MHz, C_6D_6) δ = 147.5, 132.9-132.4 (1C), 128.6-124.5 (4C), 33.1, 22.8 ppm.

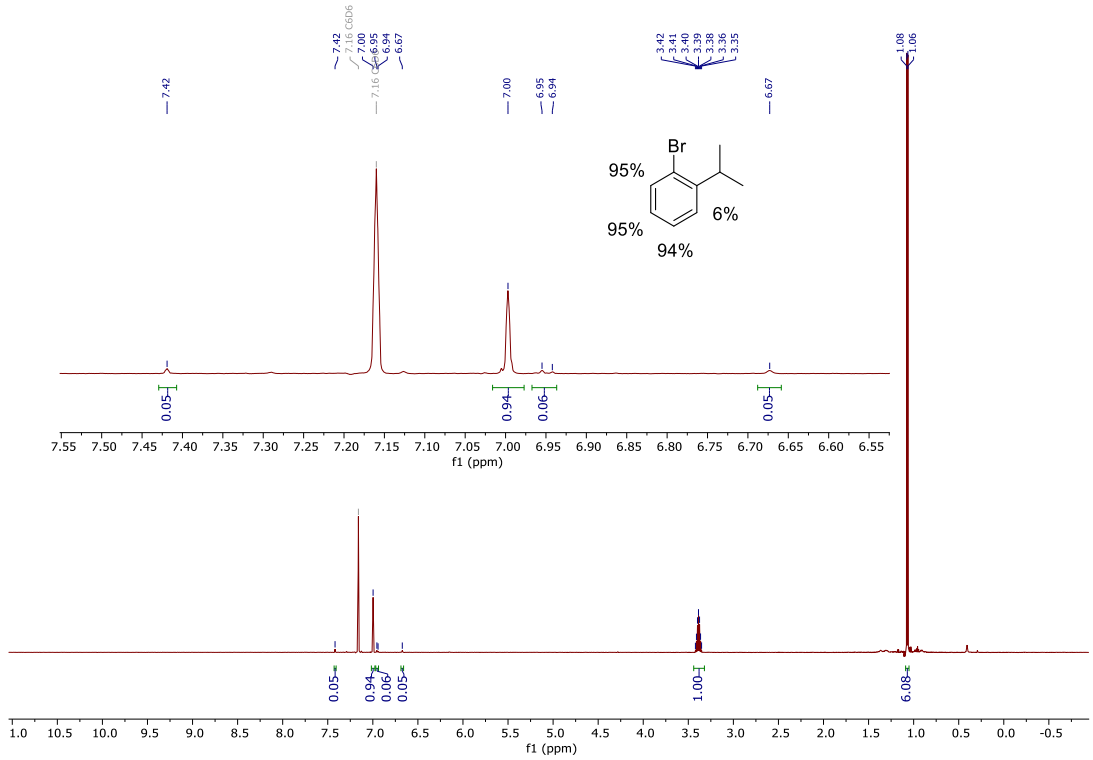
Mass Data:



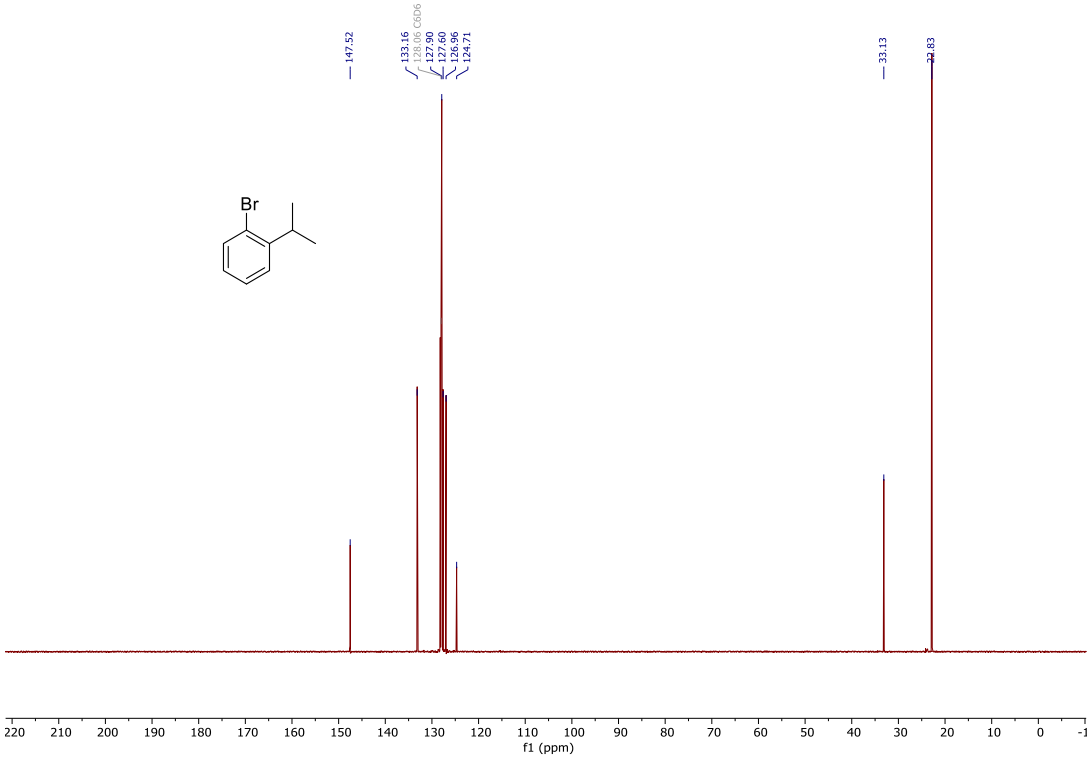
^{1}H-NMR spectrum in C_6D_6:



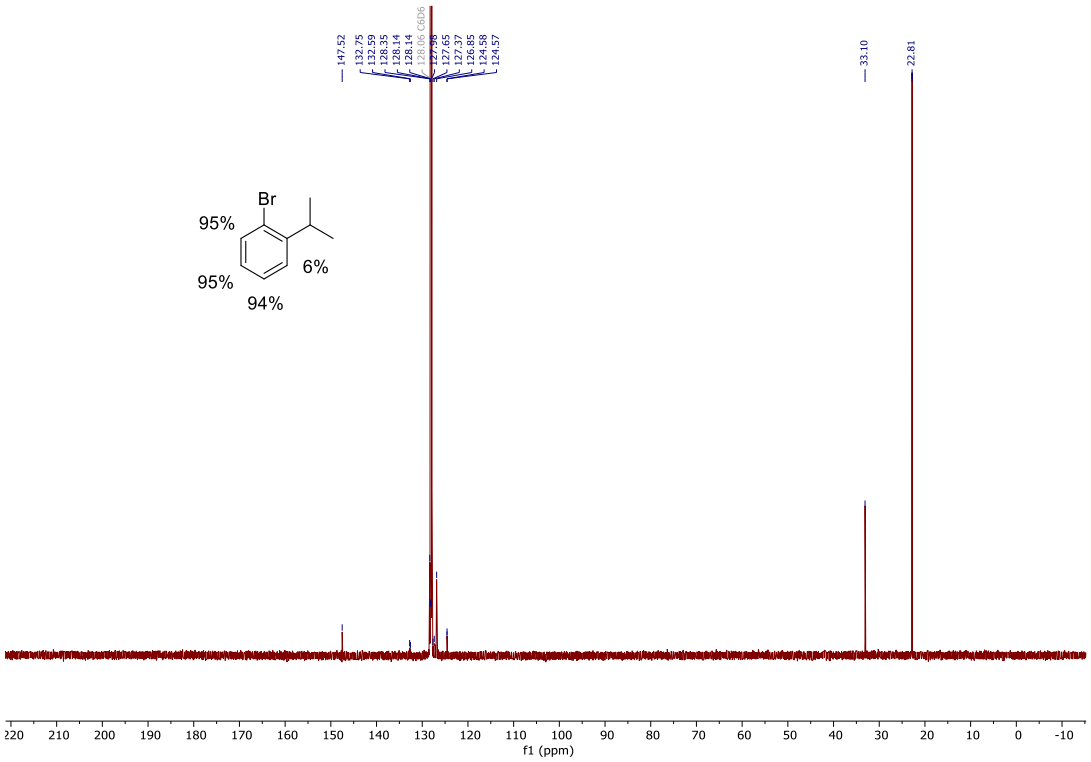
^{1}H-NMR spectrum in C_6D_6:



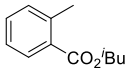
^{13}C-NMR spectrum in C_6D_6:



^{13}C-NMR spectrum in C_6D_6:



Deuteration of isobutyl 2-methylbenzoate (9):



Following the general procedure F and using isobutyl 2-methylbenzoate (**9**) (38.5 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:Et_2O = 50:1 as the eluent, the target compound **[D]9** was obtained as colorless liquid (34.0 mg, 87%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 3.97 D/molecule [Mass]; 3.76 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.98-7.84 (m, 1H), 7.43-7.36 (m, 1H), 7.28-7.20 (m, 2H), 4.09 (d, *J* = 6.6 Hz, 2H), 2.61 (s, 3H), 2.07 (dh, *J* = 13.4, 6.7 Hz, 1H), 1.03 (d, *J* = 6.8 Hz, 6H) ppm.

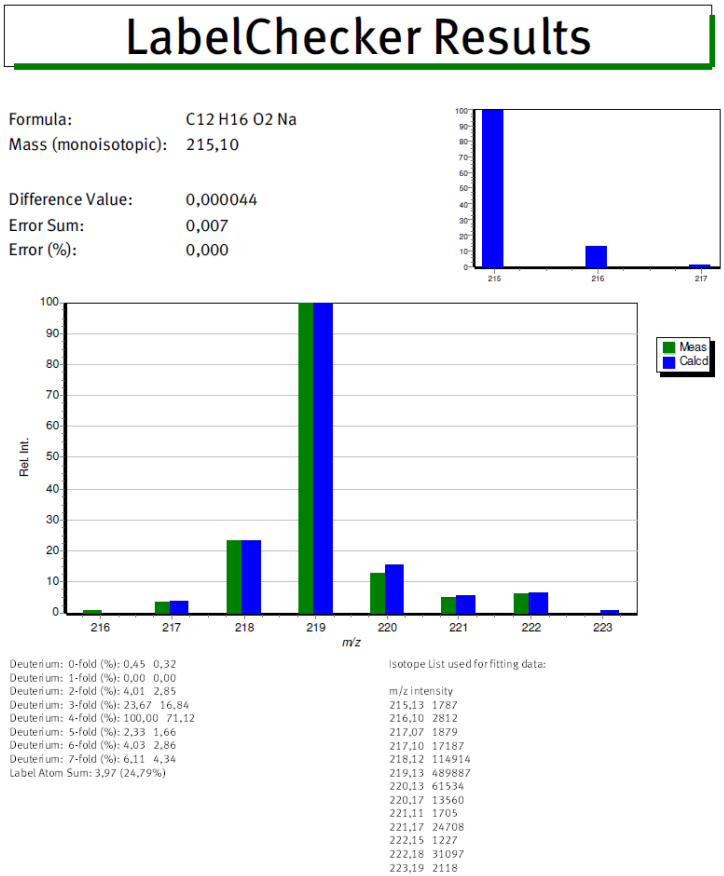
^{13}C NMR (101 MHz, $CDCl_3$) δ = 167.9, 140.2, 132.0, 131.8, 130.7, 130.1, 125.8, 71.1, 28.0, 22.0, 19.5 ppm.

NMR Data of Product:

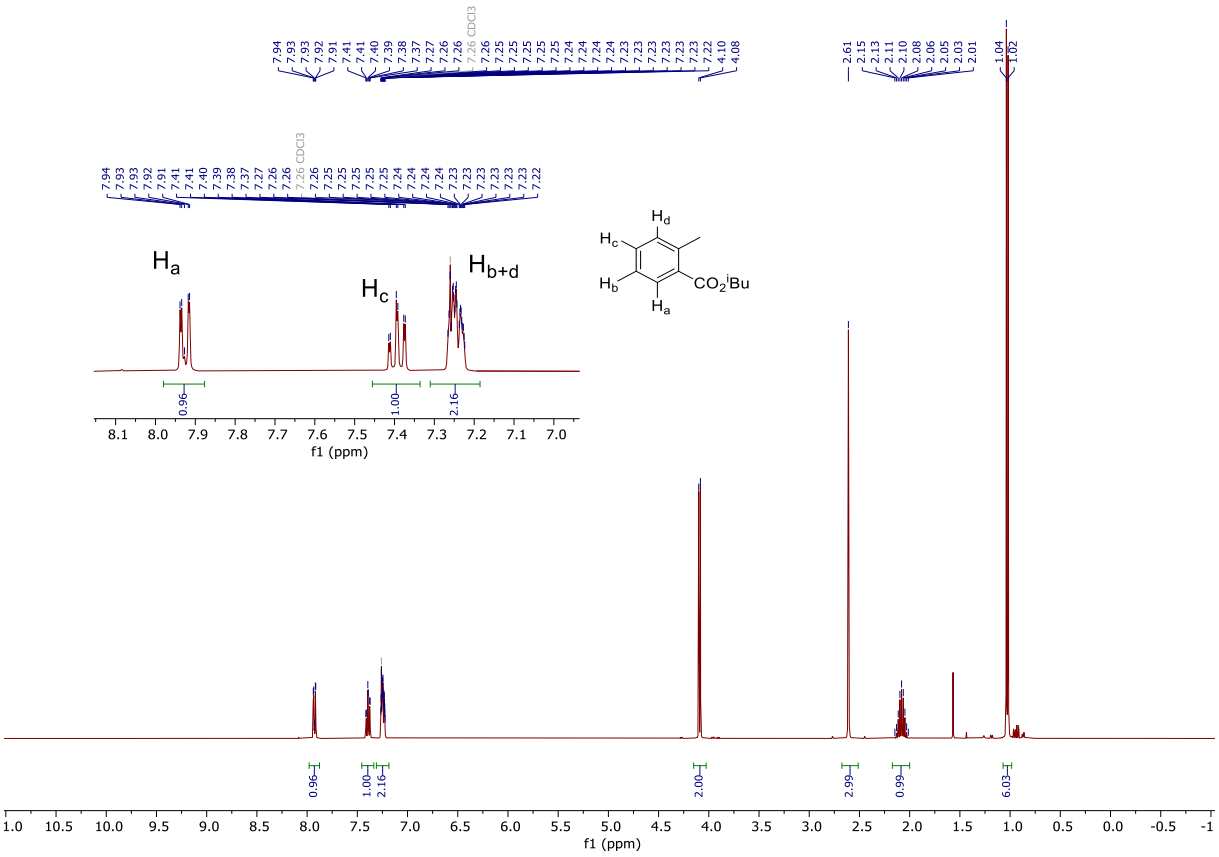
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.93 (s, 0.06H, 94% D), 7.39 (s, 0.06H, 94% D), 7.25 (s, 0.12H, 94% D), 4.09 (d, *J* = 6.5 Hz, 2H), 2.61 (s, 3H), 2.07 (dh, *J* = 13.4, 6.7 Hz, 1H), 1.03 (d, *J* = 6.8 Hz, 6H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ = 167.9, 140.1, 132.0-130.8 (2C), 130.8-130.0 (1C), 130.0, 125.8-124.7 (1C), 71.1, 28.0, 21.9, 19.4 ppm.

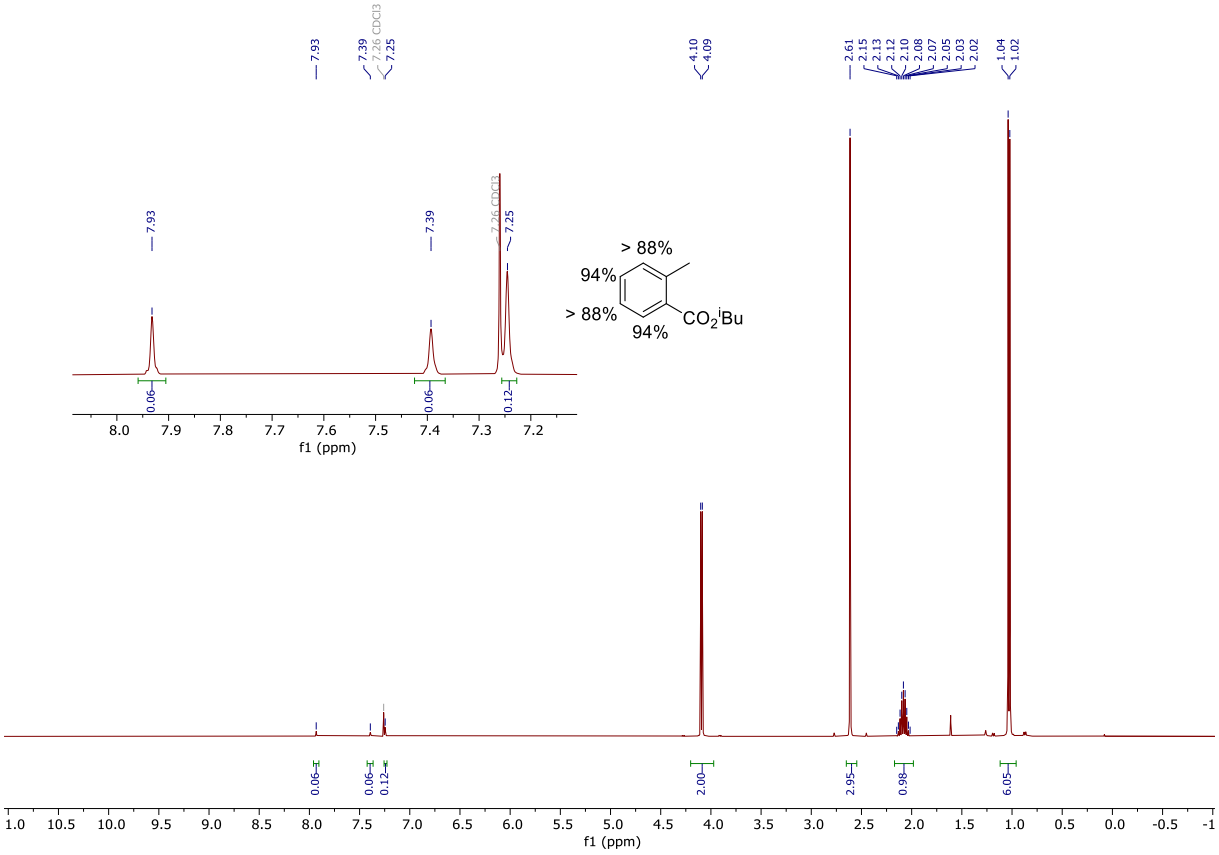
Mass Data:



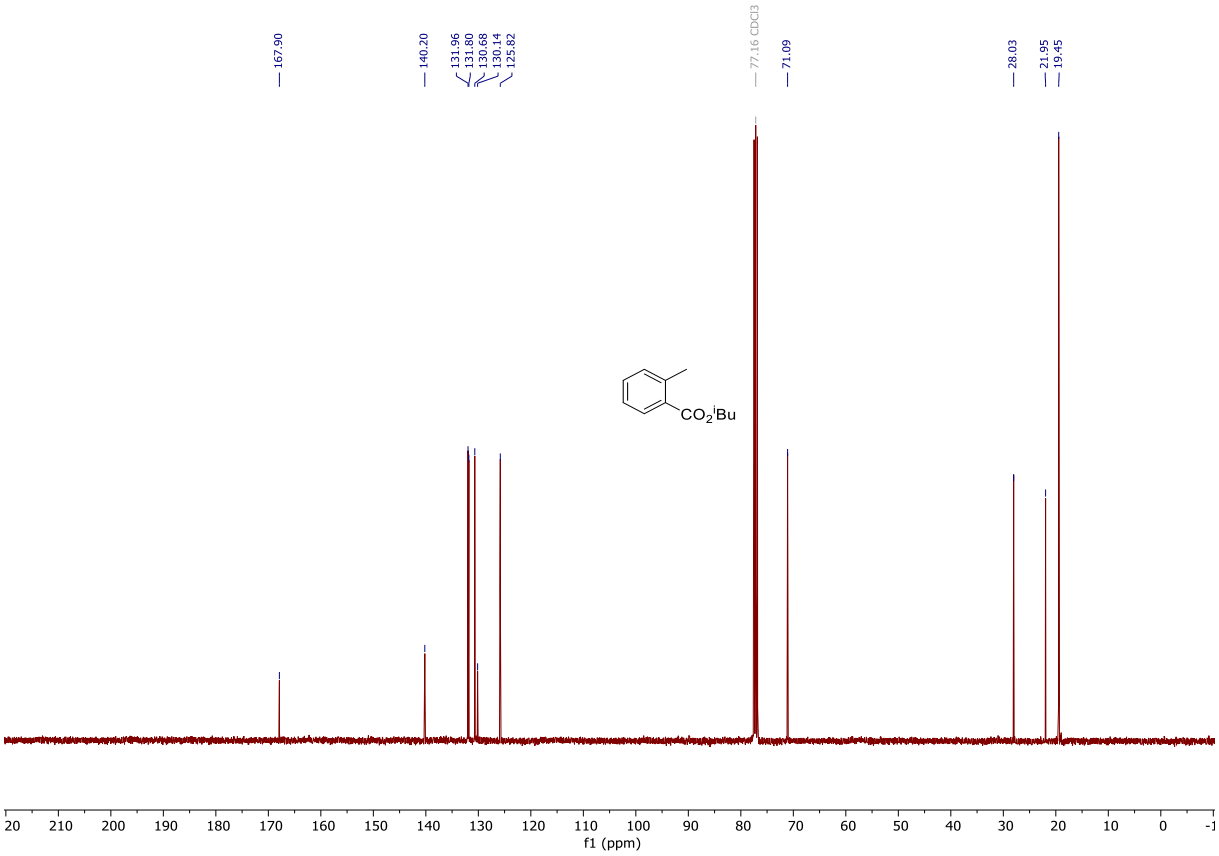
^{1}H-NMR spectrum in $CDCl_3$:



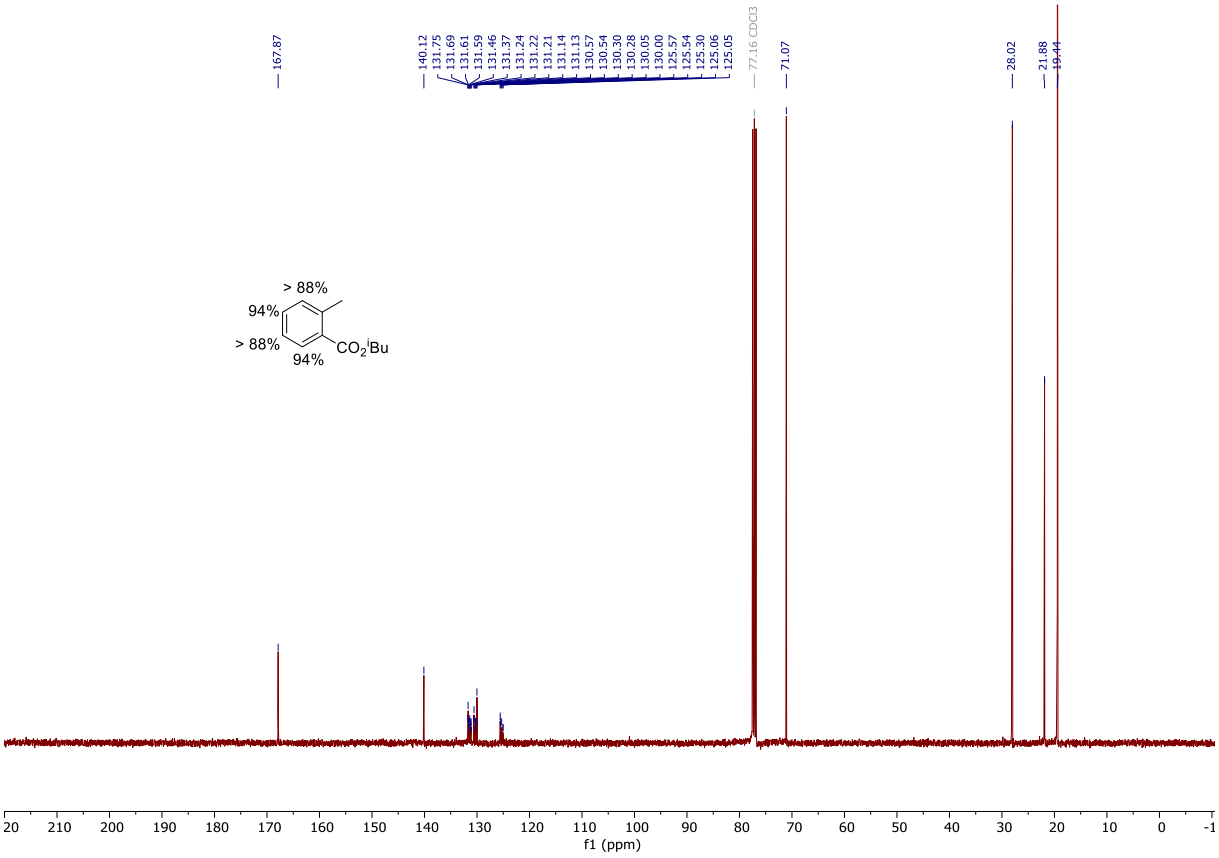
^{1}H-NMR spectrum in $CDCl_3$:



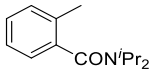
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of *N*,*N*-diisopropyl-2-methylbenzamide (10):



Following the general procedure F and using *N*,*N*-diisopropyl-2-methylbenzamide (**10**) (43.9 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAc = 9:1 as the eluent, the target compound **[D]10** was obtained as colorless liquid (41.2 mg, 93%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 3.32 D/molecule [Mass]; 3.36 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.25-7.20 (m, 1H), 7.20-7.14 (m, 2H), 7.10-7.07 (m, 1H), 3.66 (hept, *J* = 6.8 Hz, 1H), 3.51 (hept, *J* = 6.8 Hz, 1H), 2.31 (s, 3H), 1.58 (d, *J* = 6.8 Hz, 6H), 1.12 (d, *J* = 6.7 Hz, 3H), 1.08 (d, *J* = 6.7 Hz, 3H) ppm.

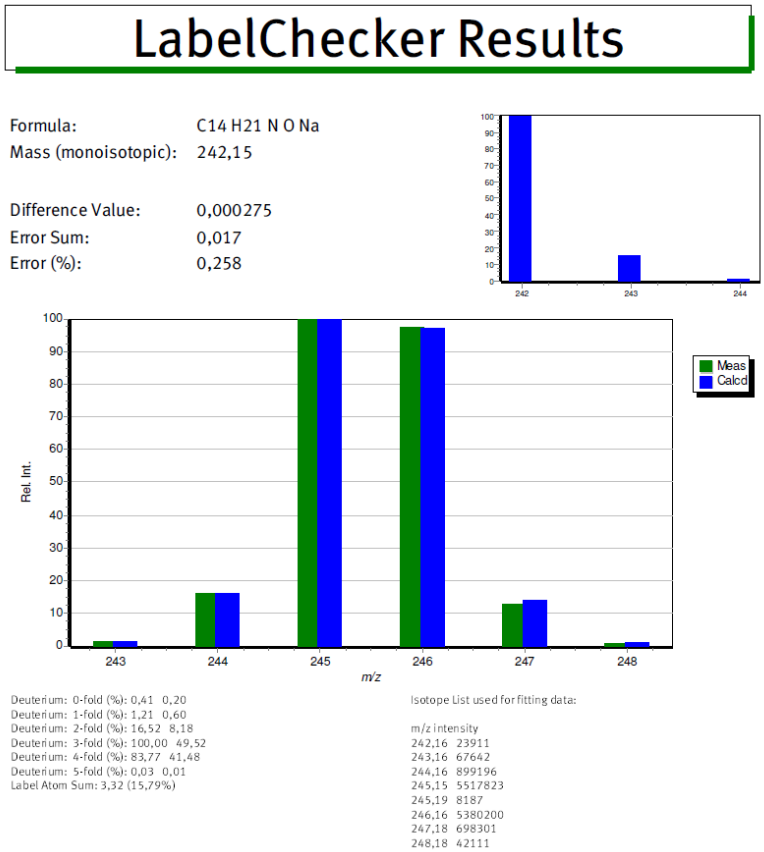
^{13}C NMR (126 MHz, $CDCl_3$) δ = 170.8, 138.8, 133.7, 130.5, 128.2, 125.9, 124.8, 50.9, 45.9, 21.1, 20.90, 20.86, 20.7, 18.9 ppm.

NMR Data of Product:

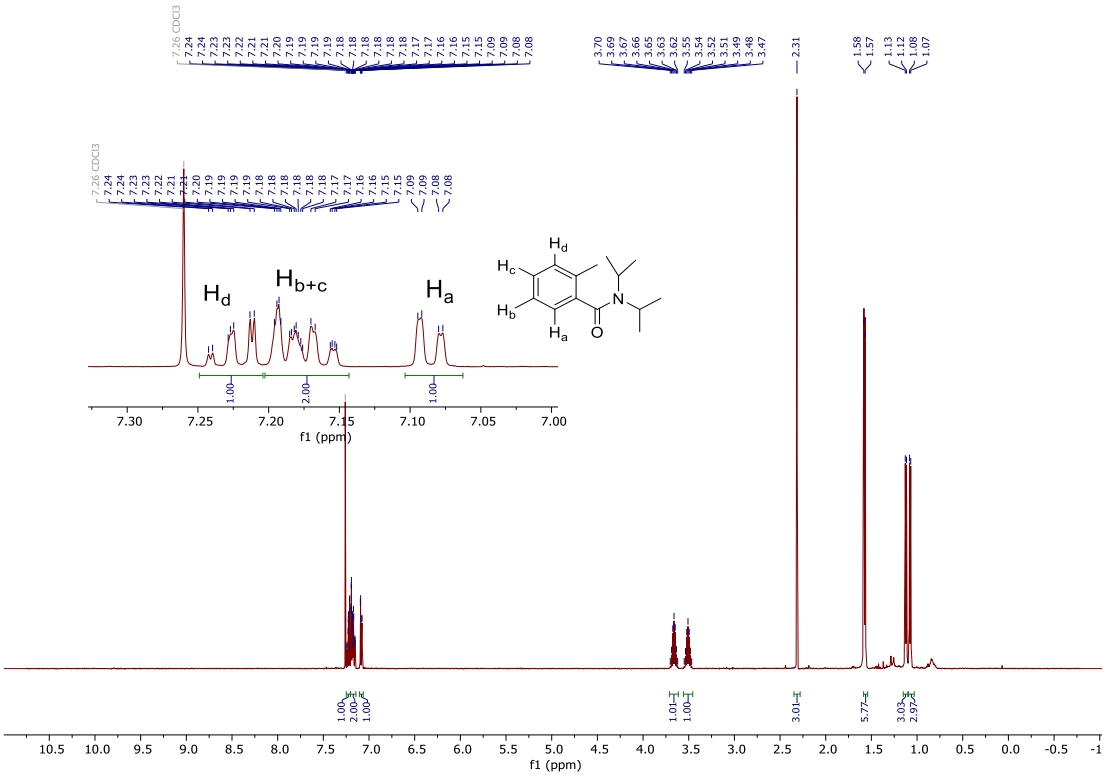
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.21 (s, 0.05H, 95% D), 7.19-7.14 (m, 0.12H, 94% D), 7.08 (s, 0.46H, 54% D), 3.65 (hept, *J* = 6.7 Hz, 1H), 3.50 (hept, *J* = 6.8 Hz, 1H), 2.31 (s, 3H), 1.57 (d, *J* = 6.5 Hz, 6H), 1.11 (d, *J* = 6.7 Hz, 3H), 1.07 (d, *J* = 6.7 Hz, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.8, 138.7, 133.6, 130.4-129.5 (1C), 128.0-127.3 (1C), 125.9-124.9 (1C), 124.8-123.9 (1C), 50.8, 45.8, 21.0, 20.84, 20.80, 20.7, 18.8 ppm.

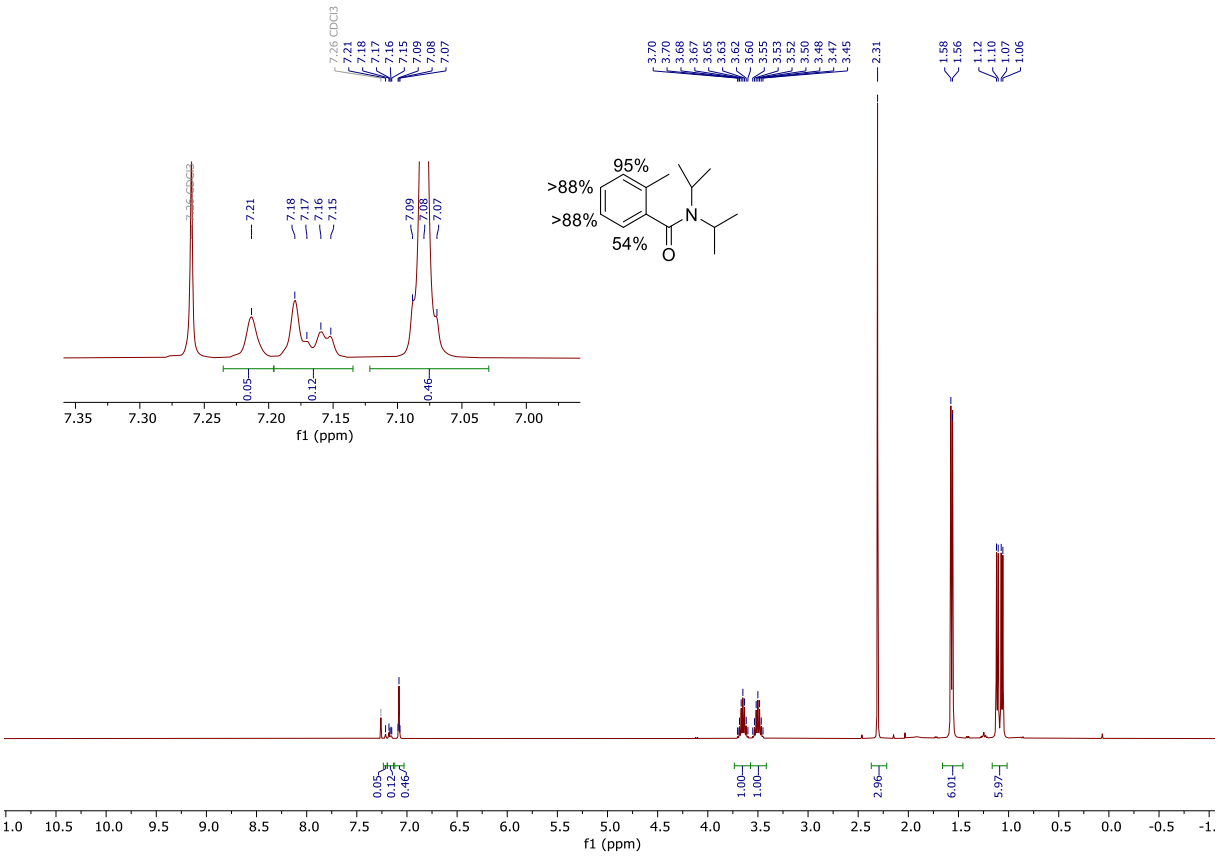
Mass Data:



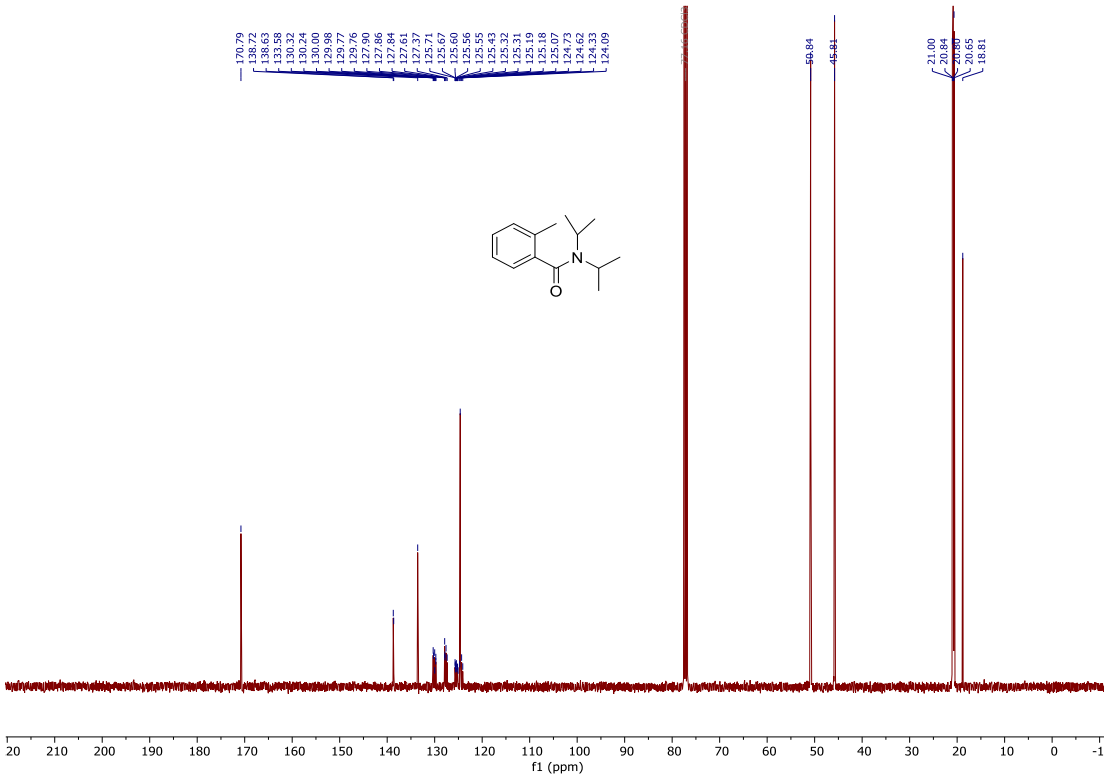
^{1}H-NMR spectrum in $CDCl_3$:



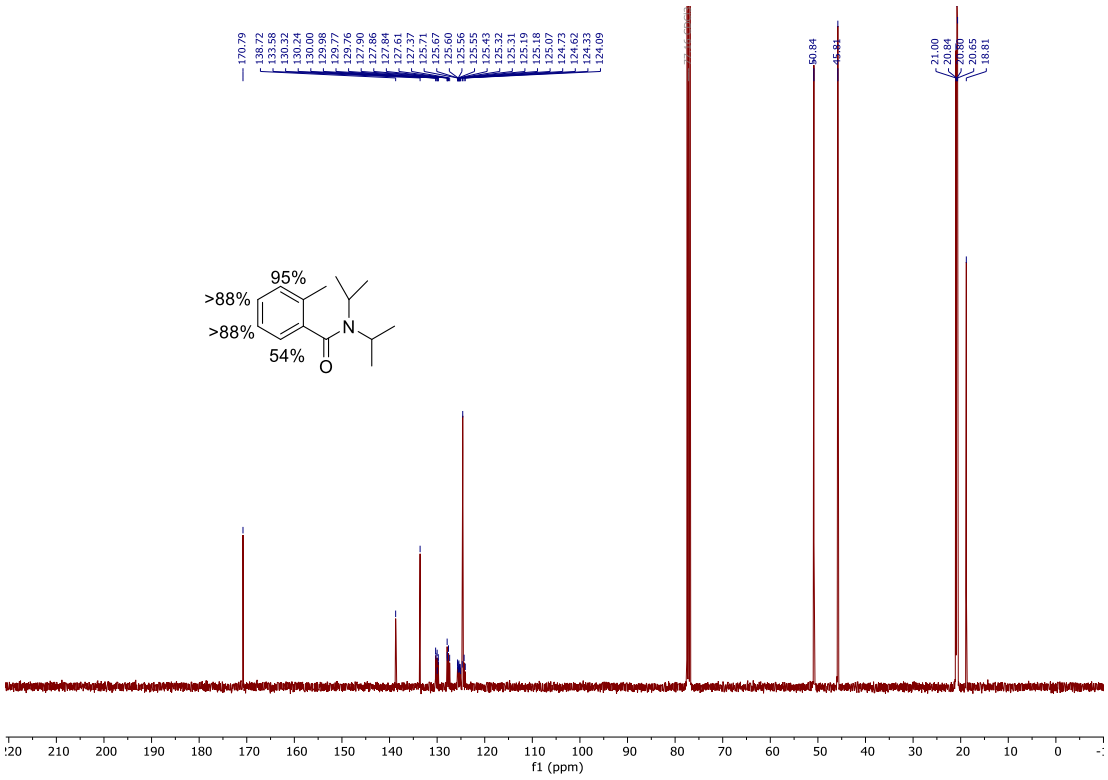
^{1}H-NMR spectrum in $CDCl_3$:



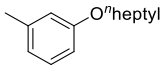
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of 1-(heptyloxy)-3-methylbenzene (11):



Following the general procedure E and using 1-(heptyloxy)-3-methylbenzene (**11**) (41.3 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:Et_2O = 50:1 as the eluent, the target compound **[D]11** was obtained as colorless liquid (33.6 mg, 80%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 3.82 D/molecule [Mass]; 3.80 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.19 (t, *J* = 7.8 Hz, 1H), 6.78 (d, *J* = 7.5 Hz, 1H), 6.76 (s, 1H), 6.74 (d, *J* = 8.3 Hz, 1H), 3.97 (t, *J* = 6.6 Hz, 2H), 2.36 (s, 3H), 1.81 (p, *J* = 6.7 Hz, 2H), 1.49 (p, *J* = 7.7, 7.3 Hz, 2H), 1.44-1.29 (m, 6H), 0.94 (t, *J* = 6.8 Hz, 3H) ppm.

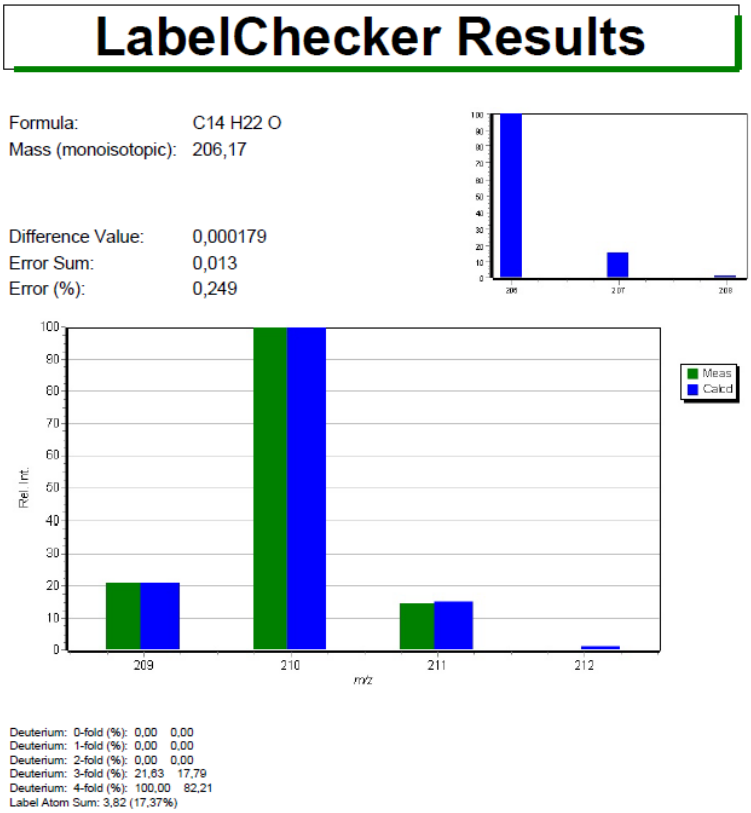
^{13}C NMR (150 MHz, $CDCl_3$) δ = 159.3, 139.5, 129.3, 121.4, 115.5, 111.5, 68.0, 32.0, 29.5, 29.2, 26.2, 22.8, 21.7, 14.2 ppm.

NMR Data of Product:

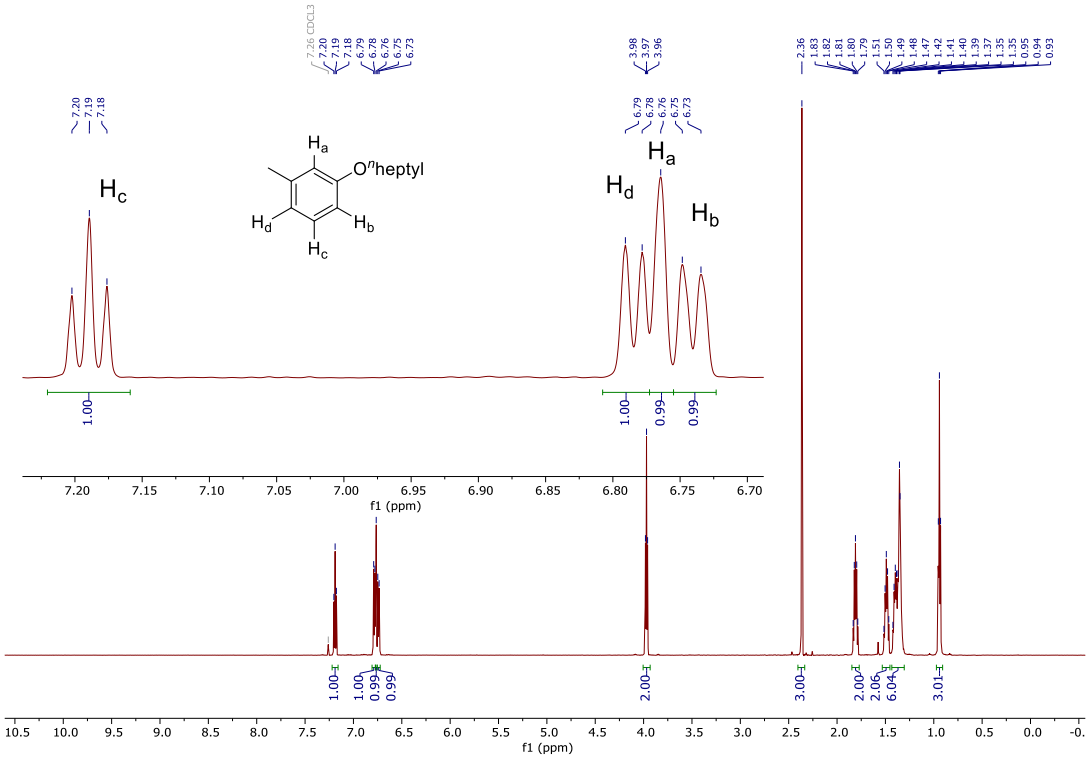
^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.16 (s, 0.05H, 95% D), 6.76 (s, 0.05H, 95% D), 6.74 (s, 0.05H, 95% D), 6.71 (s, 0.05H, 95% D), 3.94 (t, *J* = 6.6 Hz, 2H), 2.33 (s, 3H), 1.81-1.75 (m, 2H), 1.49-1.43 (m, 2H), 1.39-1.29 (m, 6H), 0.91 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C NMR (150 MHz, $CDCl_3$) δ = 159.2, 139.4, 129.2-128.3 (1C), 121.5-120.4 (1C), 115.9-114.7 (1C), 111.7-110.6 (1C), 68.0, 32.0, 29.5, 29.2, 26.2, 22.8, 21.6, 14.2 ppm.

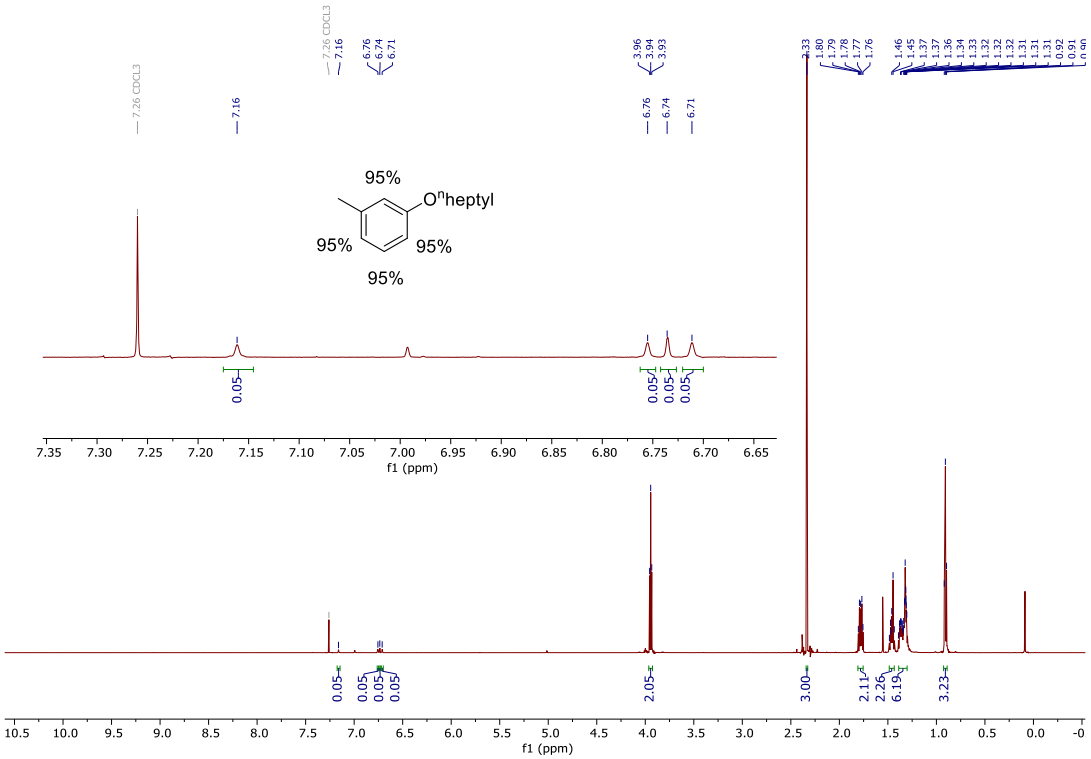
Mass Data:



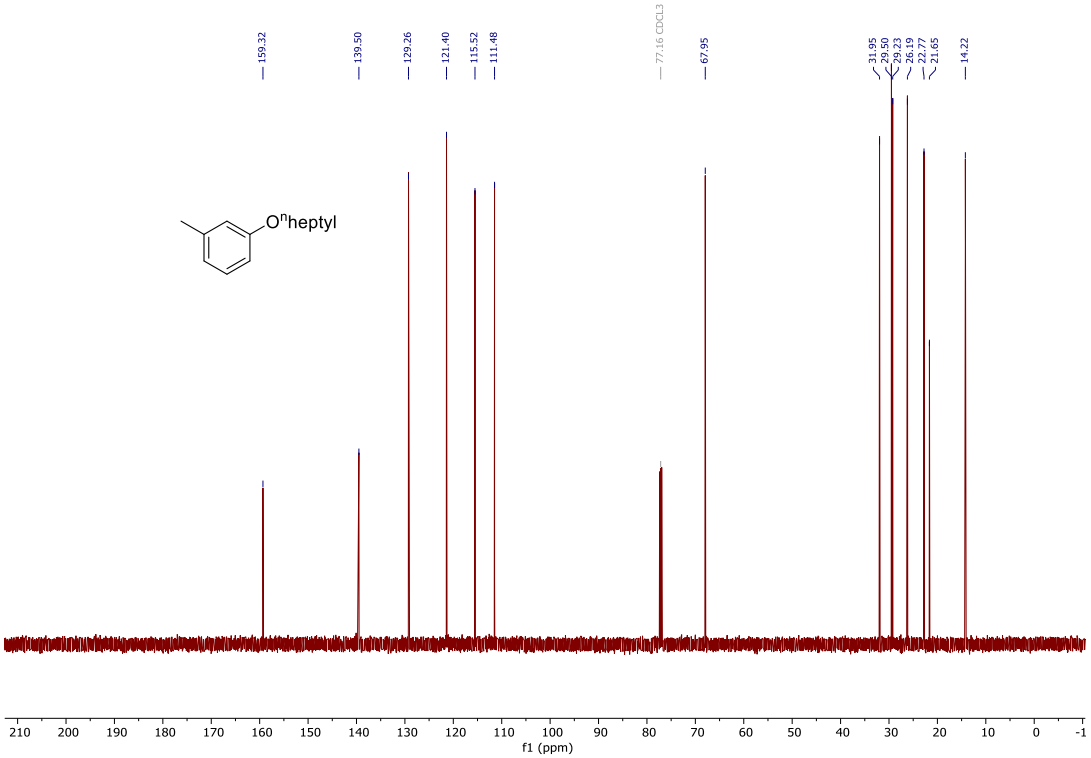
^{1}H-NMR spectrum in $CDCl_3$:



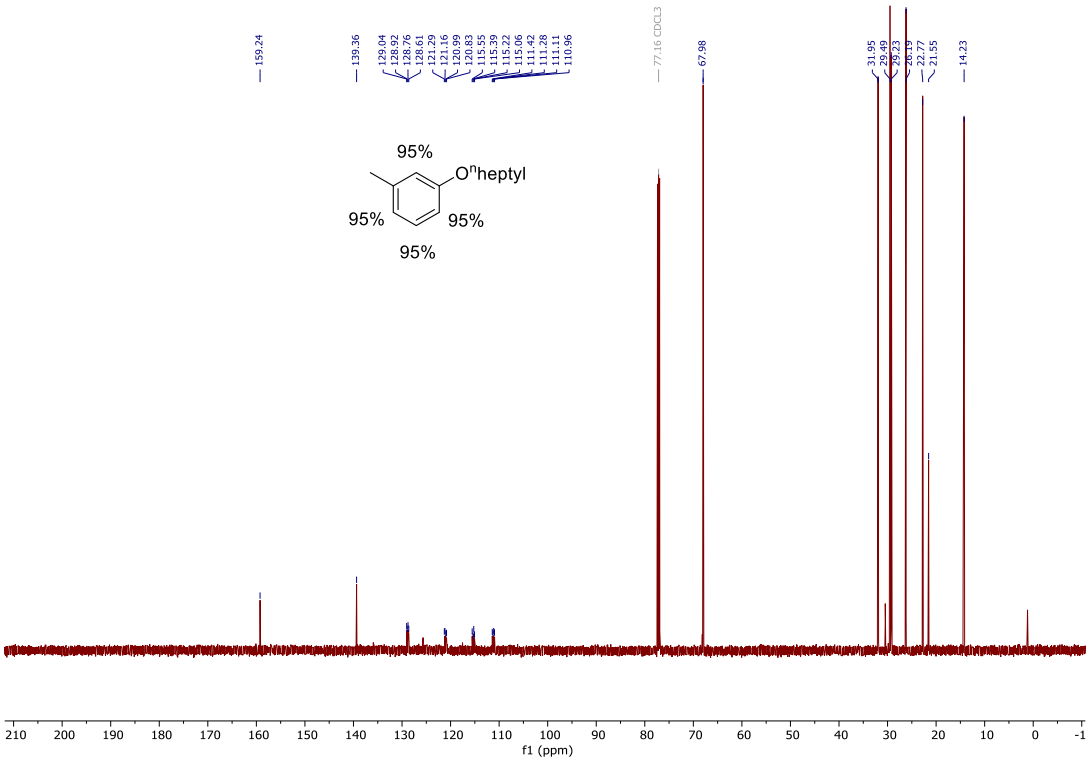
^{1}H-NMR spectrum in $CDCl_3$:



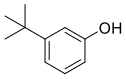
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of 3-(*tert*-butyl)phenol (12) using Conditions A:



Following the general procedure E, using 3-(*tert*-butyl)phenol (**12**) (30.0 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAc = 19:1 as the eluent the target compound **[D]12** was obtained as light-yellow liquid (23.7 mg, 79%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 1.99 D/molecule [Mass]; 2.18 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.18 (t, *J* = 7.9 Hz, 1H), 7.00-6.95 (m, 1H), 6.89-6.85 (m, 1H), 6.68-6.62 (m, 1H), 4.56 (s, br s, OH), 1.31 (s, 9H) ppm.

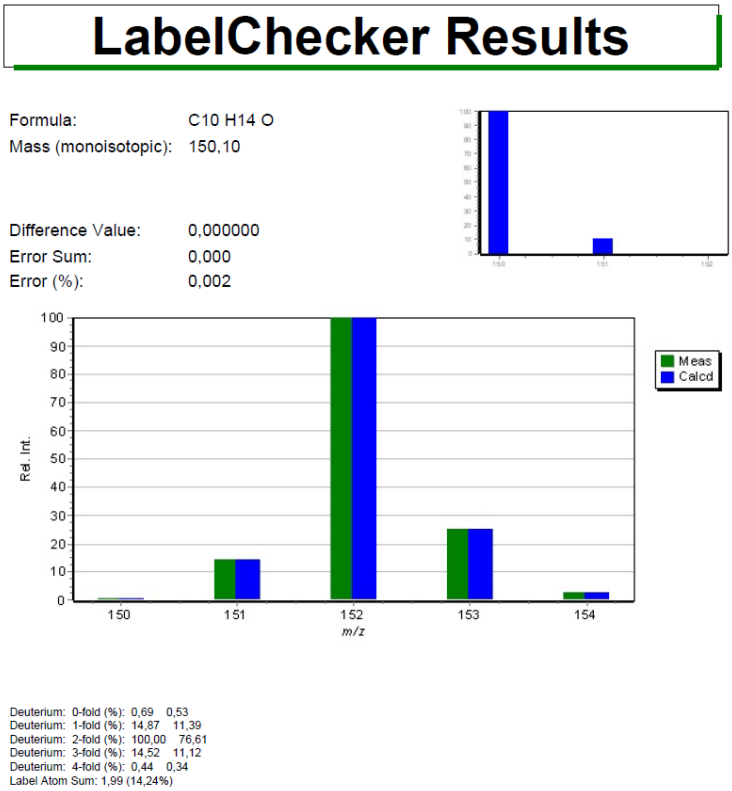
^{13}C NMR (101 MHz, $CDCl_3$) δ = 155.4, 153.5, 129.3, 118.0, 112.7, 112.4, 34.8, 31.4 ppm.

NMR Data of Product:

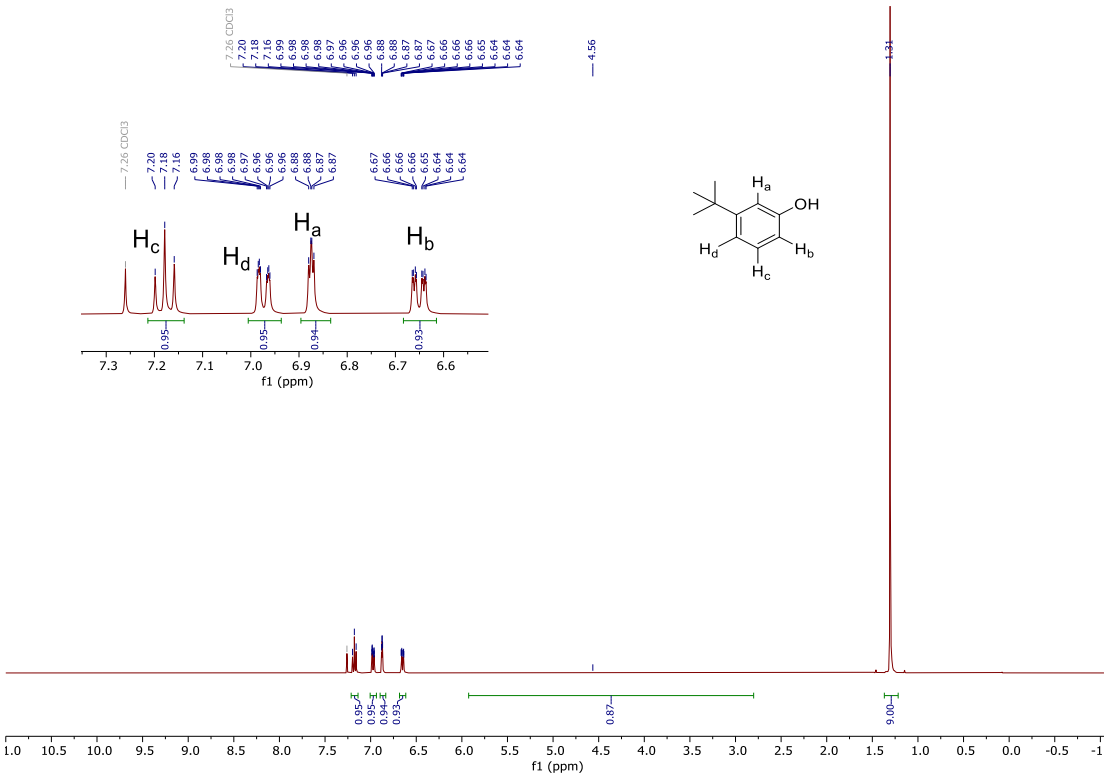
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.21-7.15 (m, 0.05H, 95% D), 6.99-6.95 (m, 0.86H, 14% D), 6.90-6.84 (m, 0.85H, 15% D), 6.69-6.63 (m, 0.06H, 94% D), 4.70 (s, br s, OH), 1.31 (s, 9H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 155.3, 153.5, 129.7-128.2 (1H), 118.2-117.5 (1H), 112.7, 112.4-111.6 (1H), 34.8, 31.4 ppm.

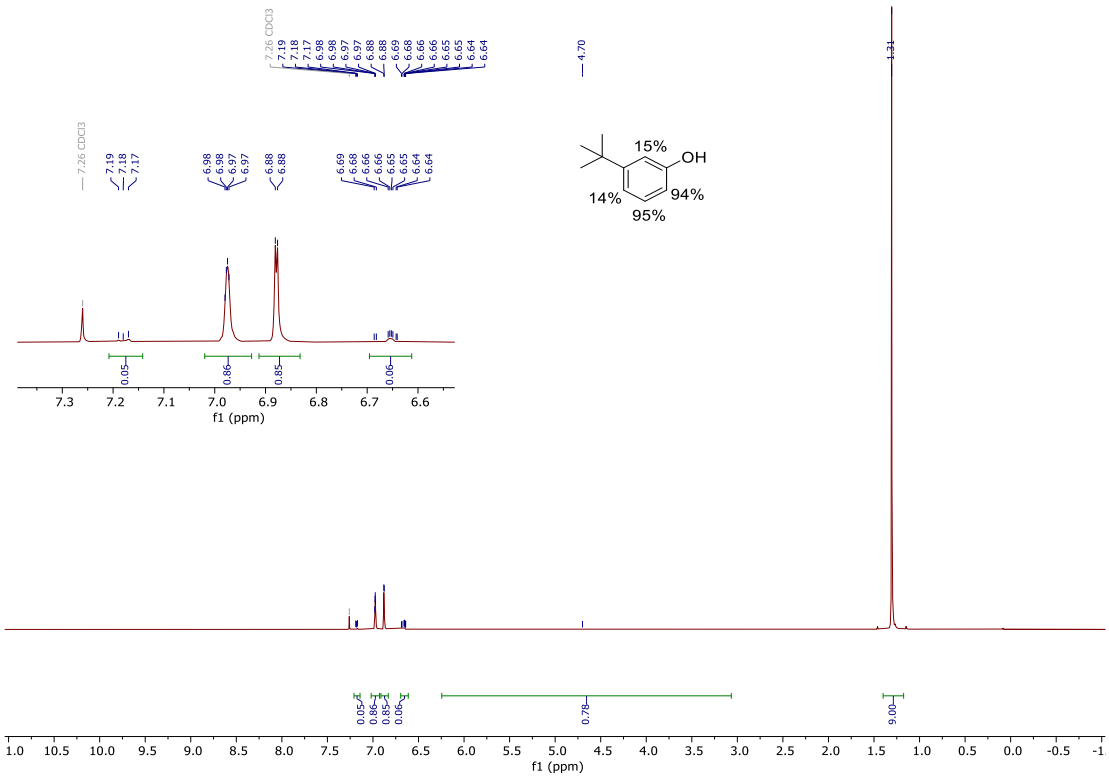
Mass Data:



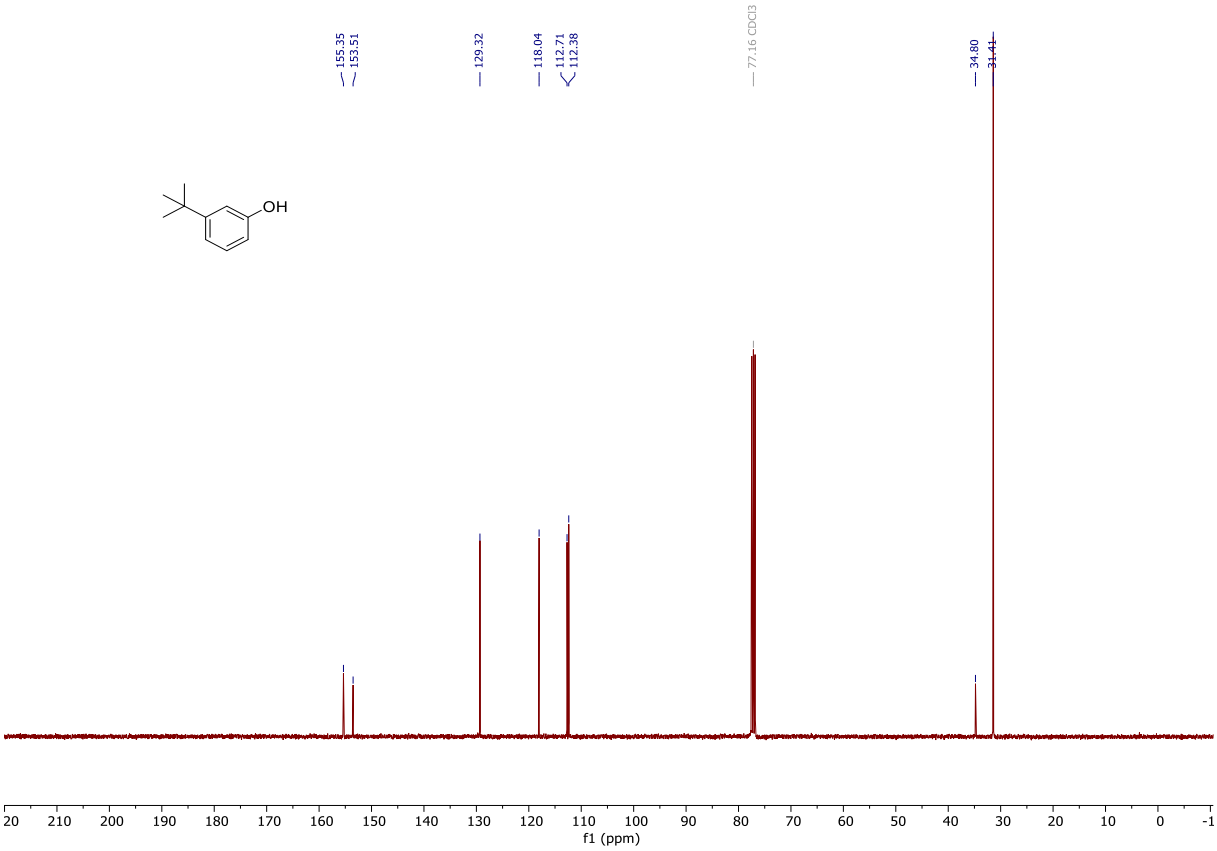
^{1}H-NMR spectrum in $CDCl_3$:



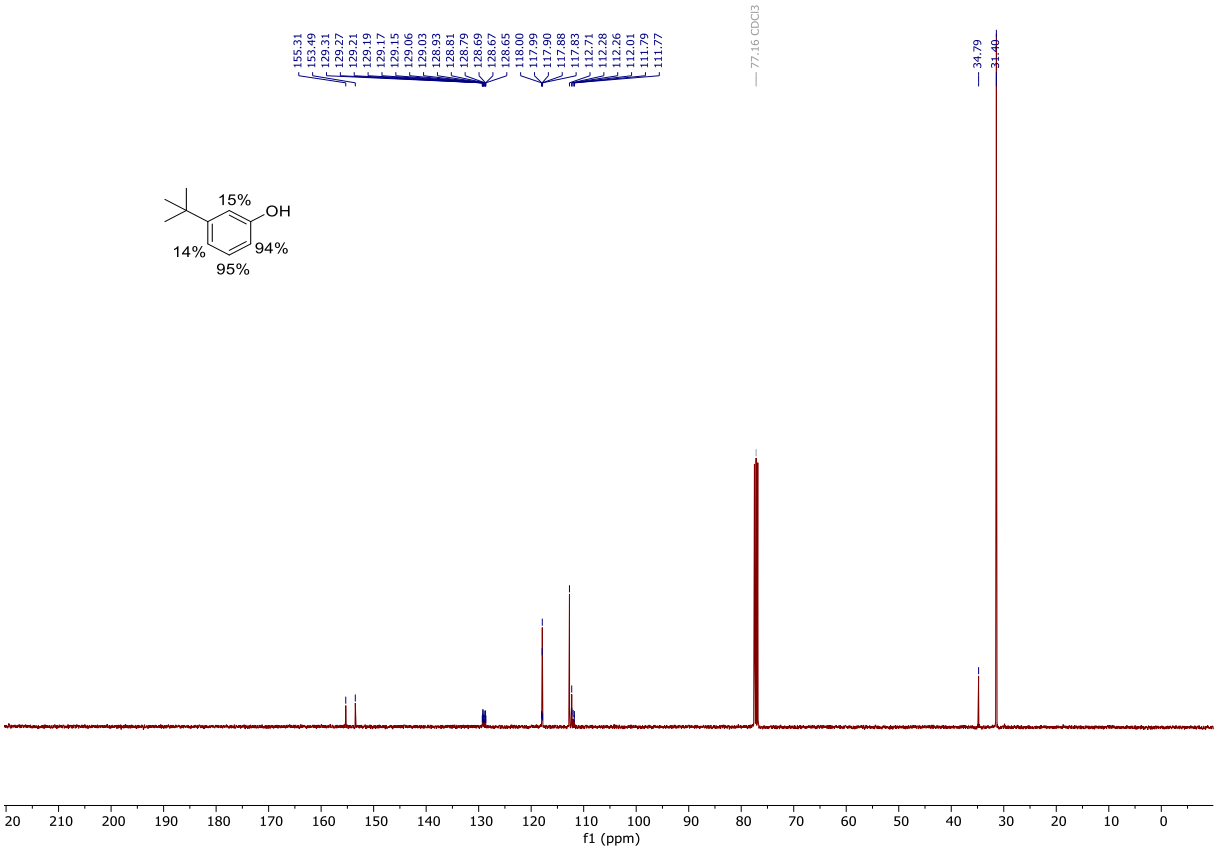
^{1}H-NMR spectrum in $CDCl_3$:



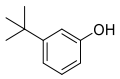
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of 3-(*tert*-butyl)phenol (12) using Conditions B:



Following the general procedure F, using 3-(*tert*-butyl)phenol (**12**) (30.0 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAc = 19:1 as the eluent the target compound **[D]12** was obtained as light-yellow liquid (27.7 mg, 92%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 3.34 D/molecule [Mass]; 3.43 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.18 (t, *J* = 7.9 Hz, 1H), 7.00-6.95 (m, 1H), 6.89-6.85 (m, 1H), 6.68-6.62 (m, 1H), 4.56 (s, br s, OH), 1.31 (s, 9H) ppm.

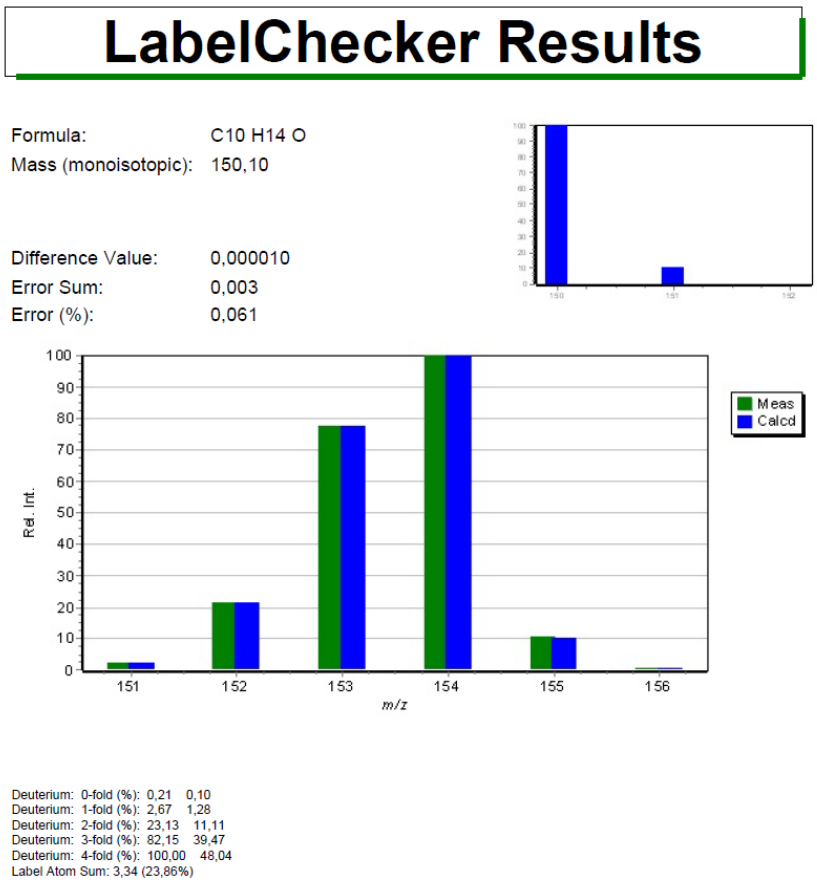
^{13}C NMR (101 MHz, $CDCl_3$) δ = 155.4, 153.5, 129.3, 118.0, 112.7, 112.4, 34.8, 31.4 ppm.

NMR Data of Product:

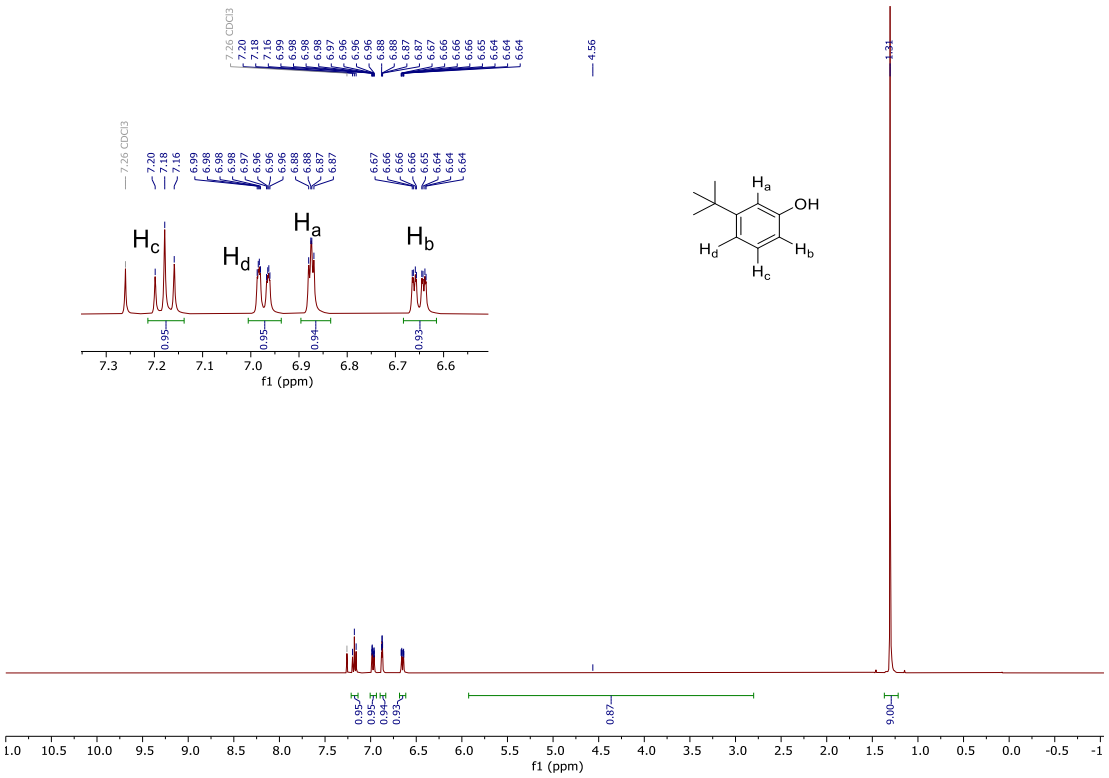
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.20-7.16 (m, 0.05H, 95% D), 6.99-6.95 (m, 0.22H, 78% D), 6.90-6.87 (m, 0.25H, 75% D), 6.66 (s, 0.05H, 95% D), 5.05 (s, br s, OH), 1.30 (s, 9H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.3, 153.3, 129.8-128.0 (1H), 118.3-116.6 (1H), 112.8-111.7 (2H), 34.8, 31.4 ppm.

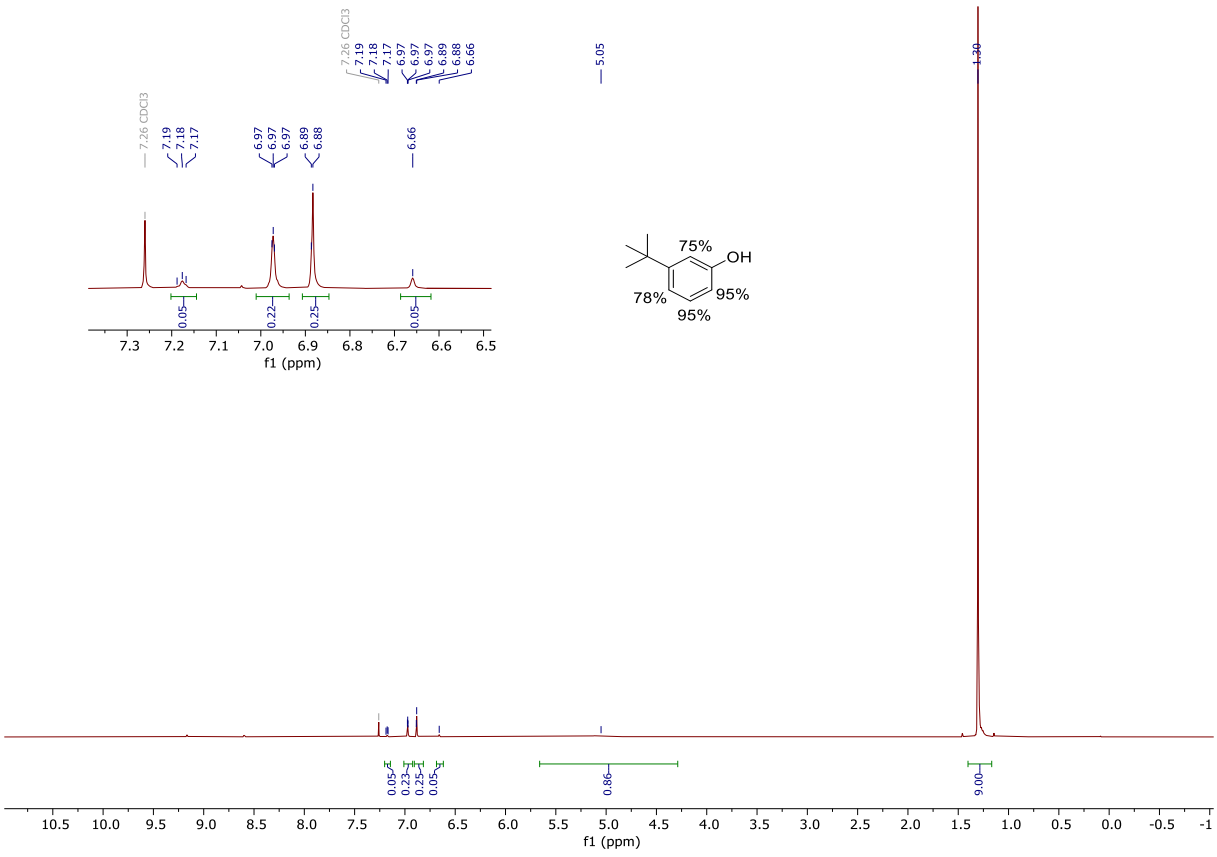
Mass Data:



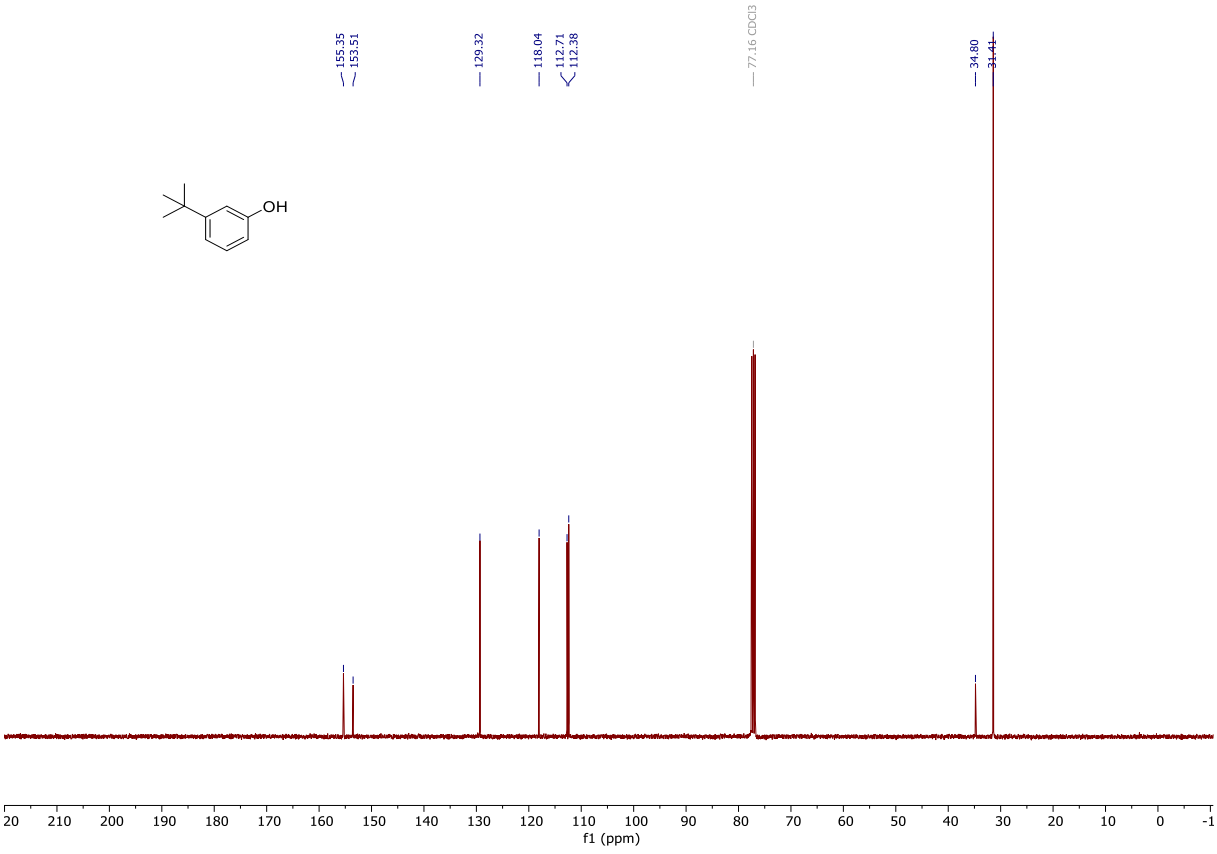
^{1}H-NMR spectrum in $CDCl_3$:



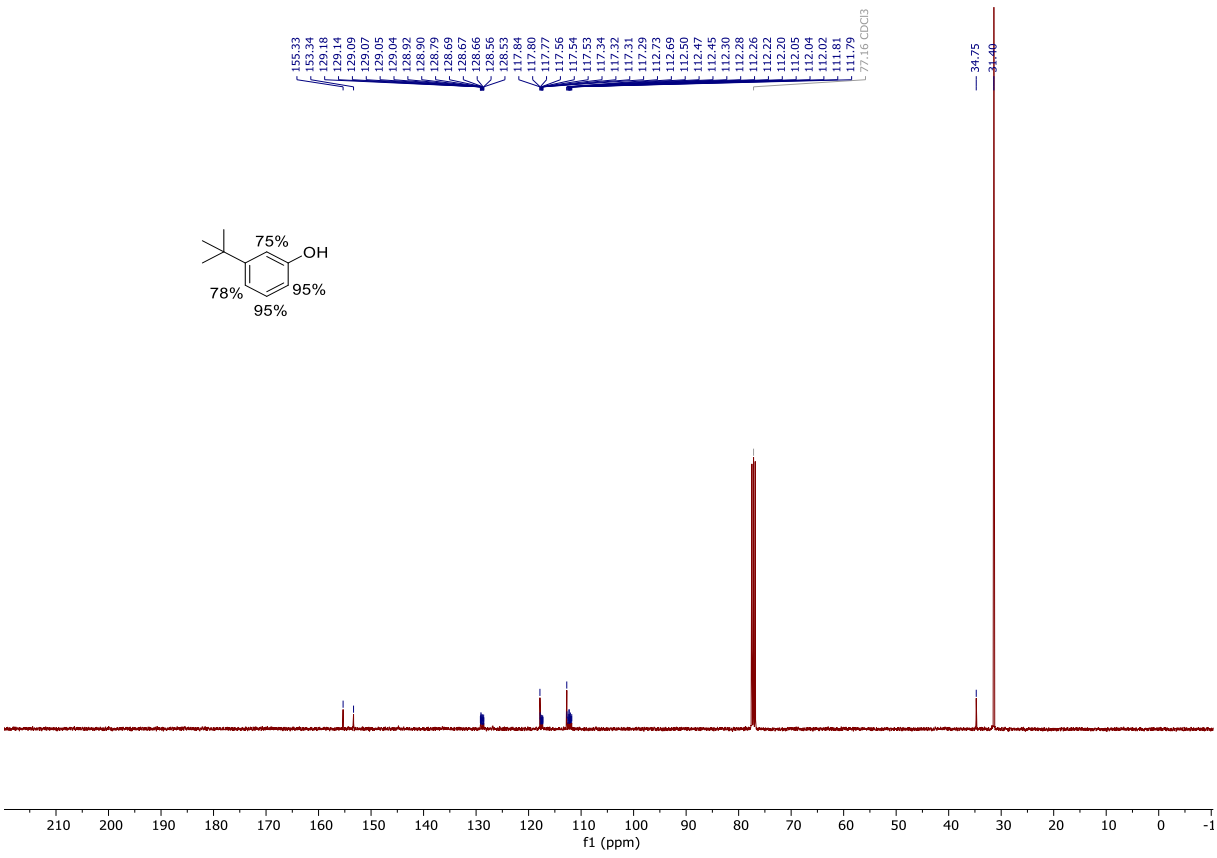
^{1}H-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of 3-methylbenzoic acid (13):

Following the general procedure F and using 3-methylbenzoic acid (**13**) (27.2 mg, 0.200 mmol) and purification by silica gel column chromatography using Pentane:EtOAc = 90:10 as the eluent, the target compound **[D]13** was obtained as colorless solid (21 mg, 76%). The degree of deuteration was determined by HRMS studies.

Deuterium Incorporation: 2.91 D/molecule [HRMS]; 2.95 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.95-7.91 (m, 2H), 7.43 (d, *J* = 7.5 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 2.43 (s, 3H) ppm.

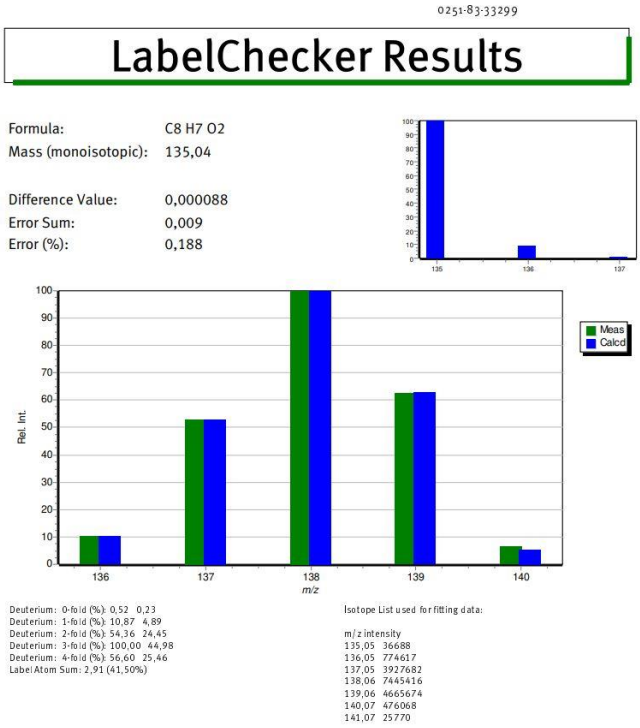
^{13}C NMR (151 MHz, $CDCl_3$) δ = 172.5, 138.5, 134.7, 130.9, 129.4, 128.5, 127.5, 21.4 ppm.

NMR Data of Product:

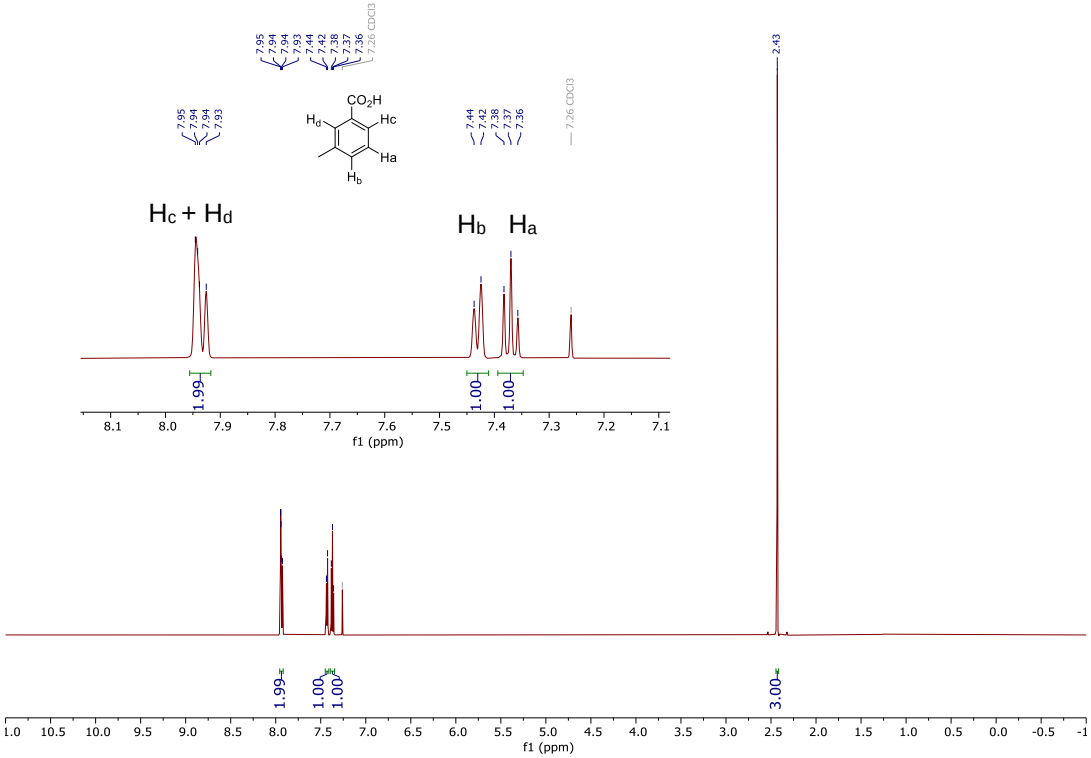
^{1}H NMR (600 MHz, CDCl3) δ = 7.94 (d, *J* = 0.8 Hz, 0.55H, 45% D)7.93 (s, 0.15H, 85% D) 7.43 (s, 0.3H, 70% D), 7.38-7.35 (0.06H, 94% D), 2.43-2.42 (m, 3H) ppm.

^{13}C NMR (151 MHz, $CDCl_3$) δ = 172.4, 138.4-138.3(1C), 134.6, 130.8, 129.4-129.2(1C), 128.4-128.1(1C), 127.5-127.3(1C), 21.4-21.3(1C) ppm.

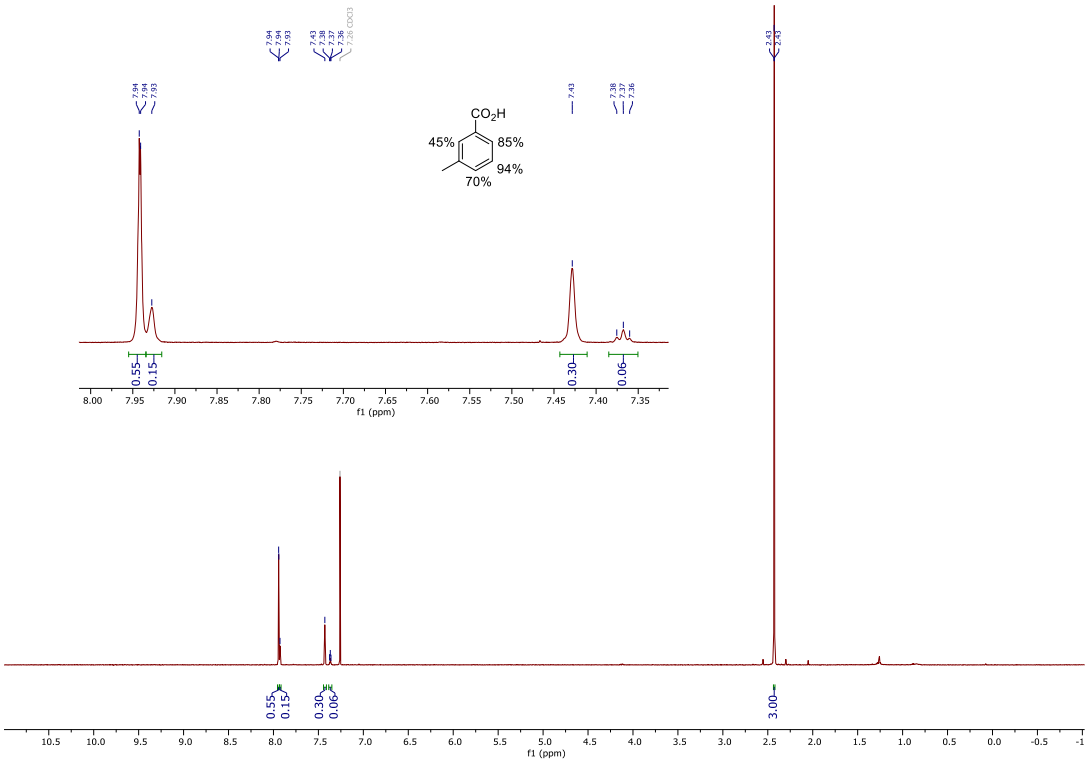
Mass Data:



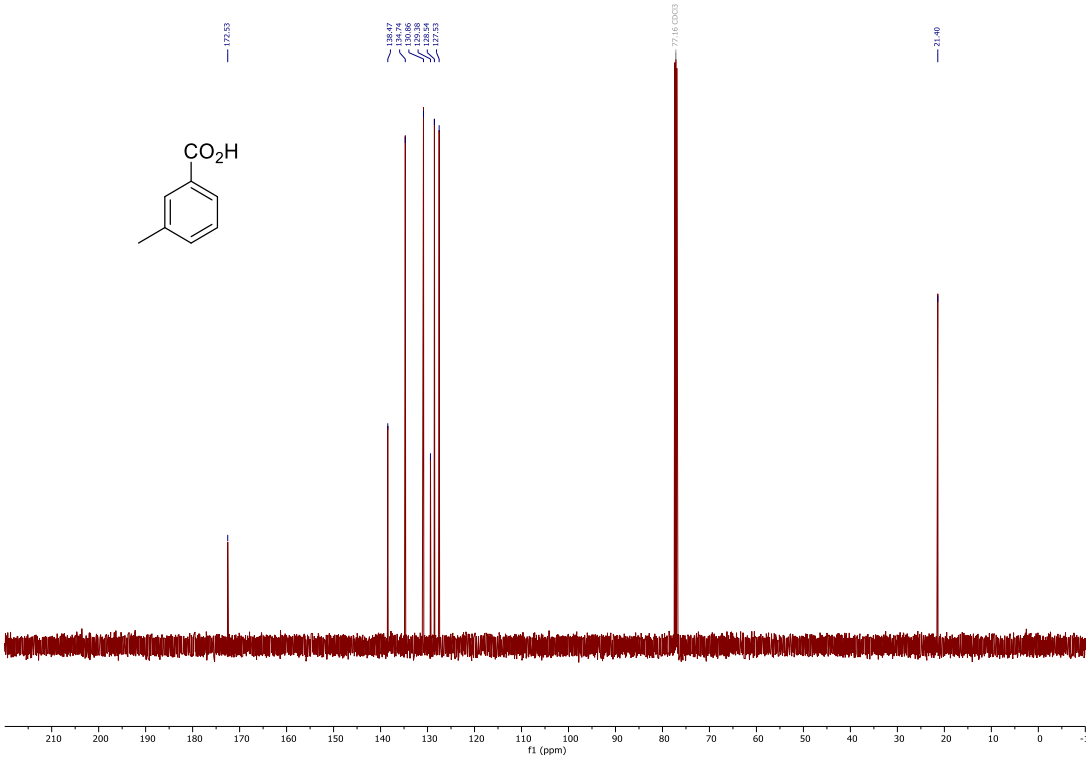
^{1}H-NMR spectrum in $CDCl_3$:



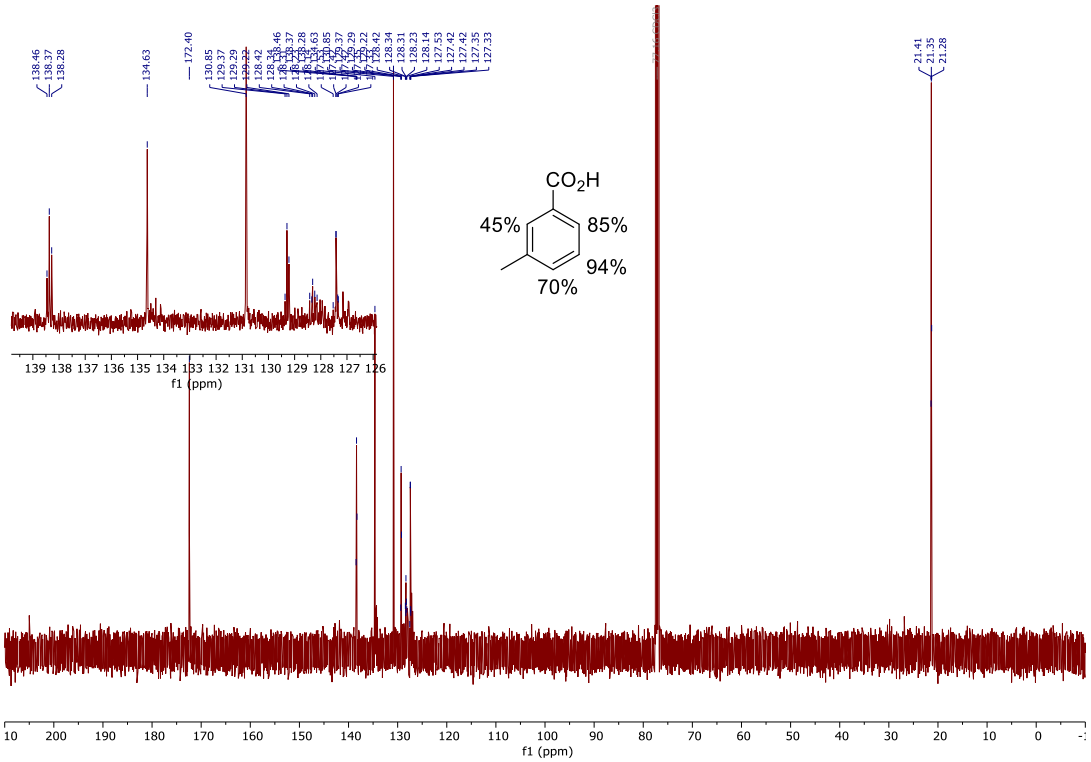
^{1}H-NMR spectrum in $CDCl_3$:



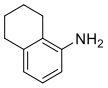
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of 5,6,7,8-tetrahydronaphthalen-1-amine (14) using Conditions A:



Following the general procedure E, using 5,6,7,8-tetrahydronaphthalen-1-amine (**14**) (29.4 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAc = 19:1 as the eluent the target compound **[D]14** was obtained as red liquid (18.1 mg, 61%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 1.80 D/molecule [Mass]; 1.99 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (599 MHz, $CDCl_3$) δ = 6.96 (t, *J* = 7.7 Hz, 1H), 6.63-6.59 (m, 2H), 4.45 (br s, NH_2), 2.74 (t, *J* = 6.3 Hz, 2H), 2.51 (t, *J* = 6.5 Hz, 2H), 1.90-1.84 (m, 2H), 1.79-1.74 (m, 2H) ppm.

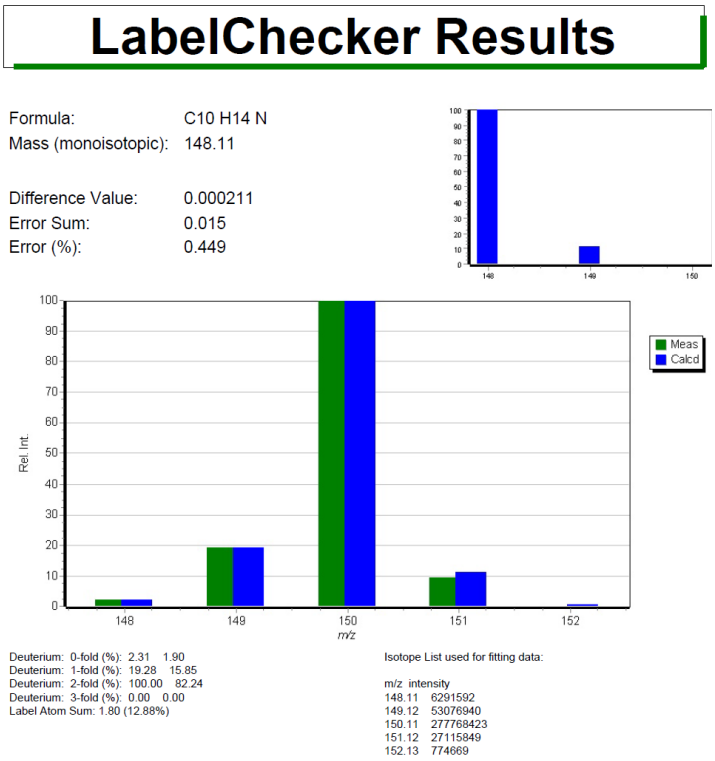
^{13}C NMR (151 MHz, $CDCl_3$) δ = 143.0, 138.4, 126.1, 122.8, 120.7, 113.1, 30.1, 24.3, 23.2, 22.9 ppm.

NMR Data of Product:

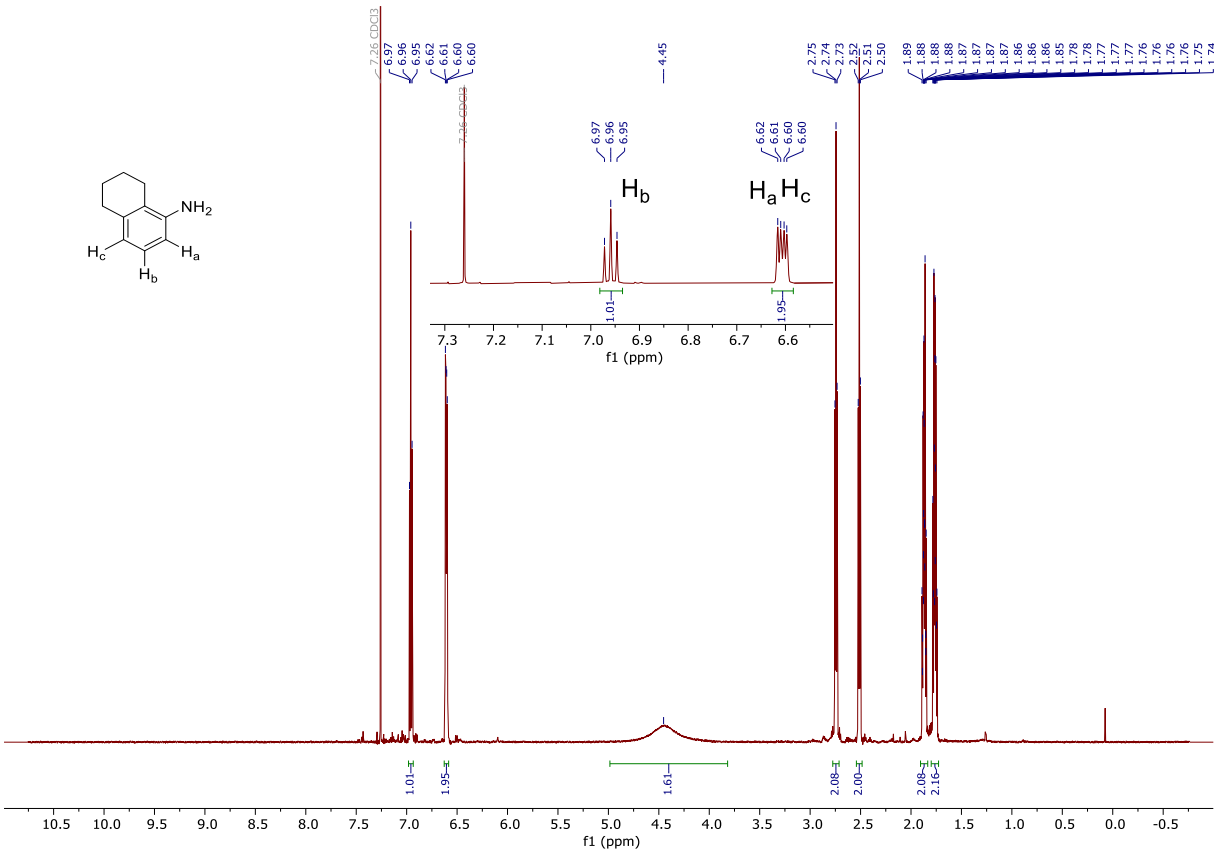
^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.95 (s, 0.91H, 9% D), 6.57 (t, *J* = 7.5 Hz, 0.10H, >90% D), 3.80 (br s, NH_2), 2.75 (t, *J* = 6.2 Hz, 2H), 2.49 (t, *J* = 6.4 Hz, 2H), 1.93-1.82 (m, 2H), 1.82-1.71 (m, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.8, 138.2, 126.4-125.4 (1H), 122.2, 120.4-119.2 (1H), 112.9-111.4 (1H), 30.0, 24.2, 23.2, 22.9 ppm.

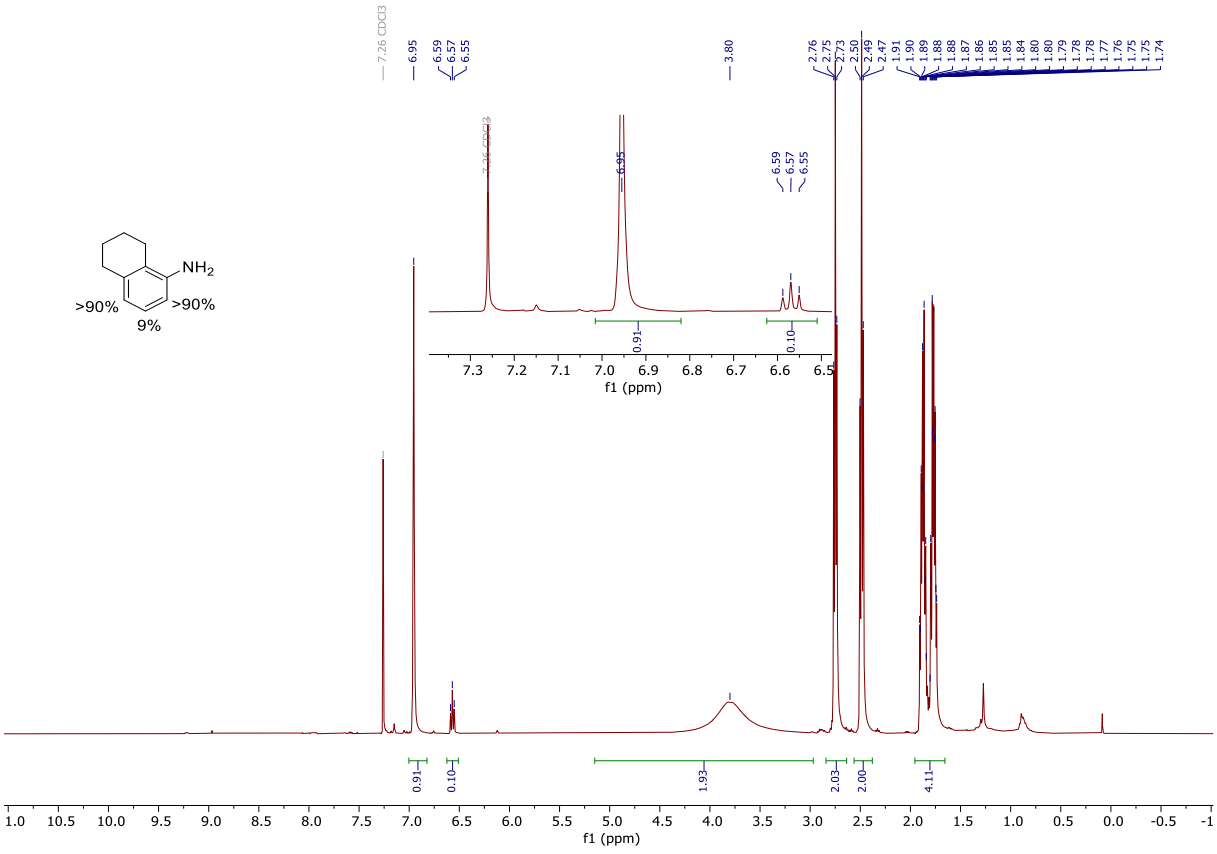
Mass Data:



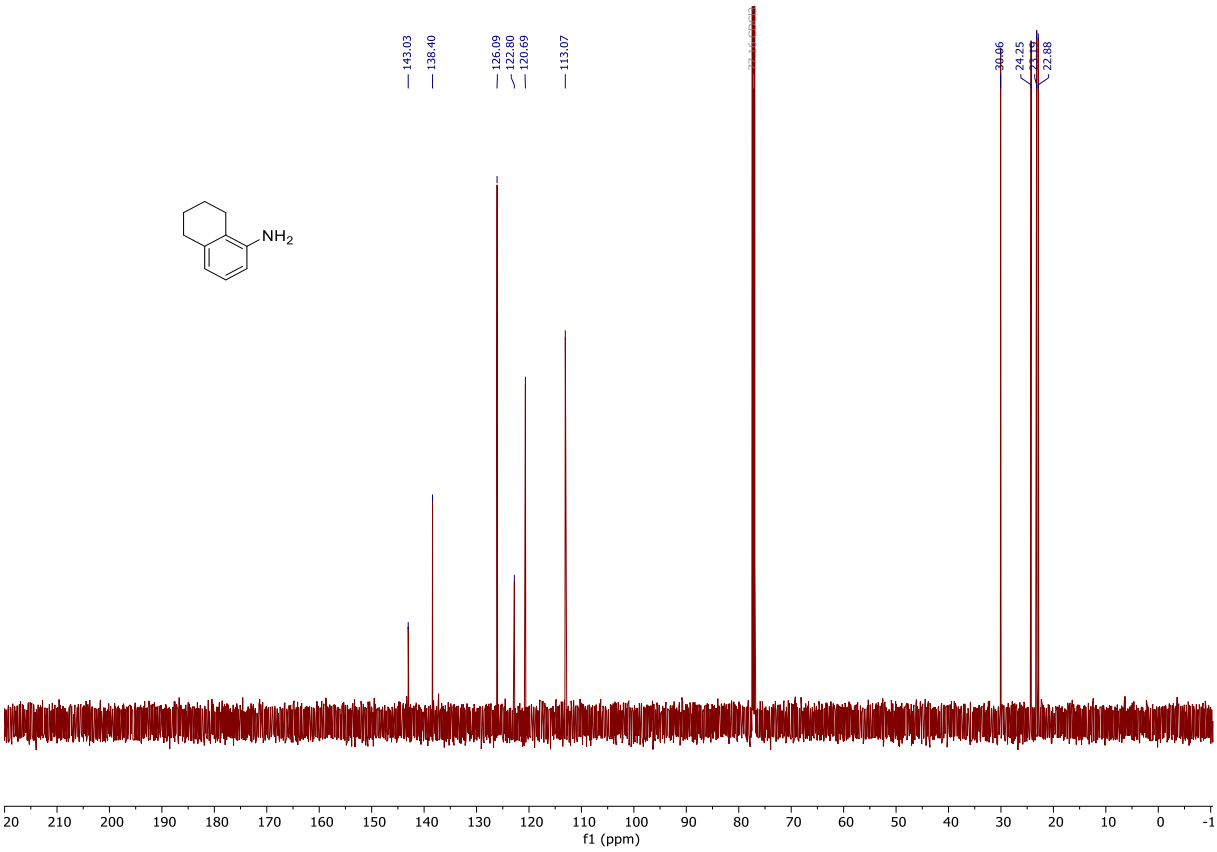
^{1}H-NMR spectrum in $CDCl_3$:



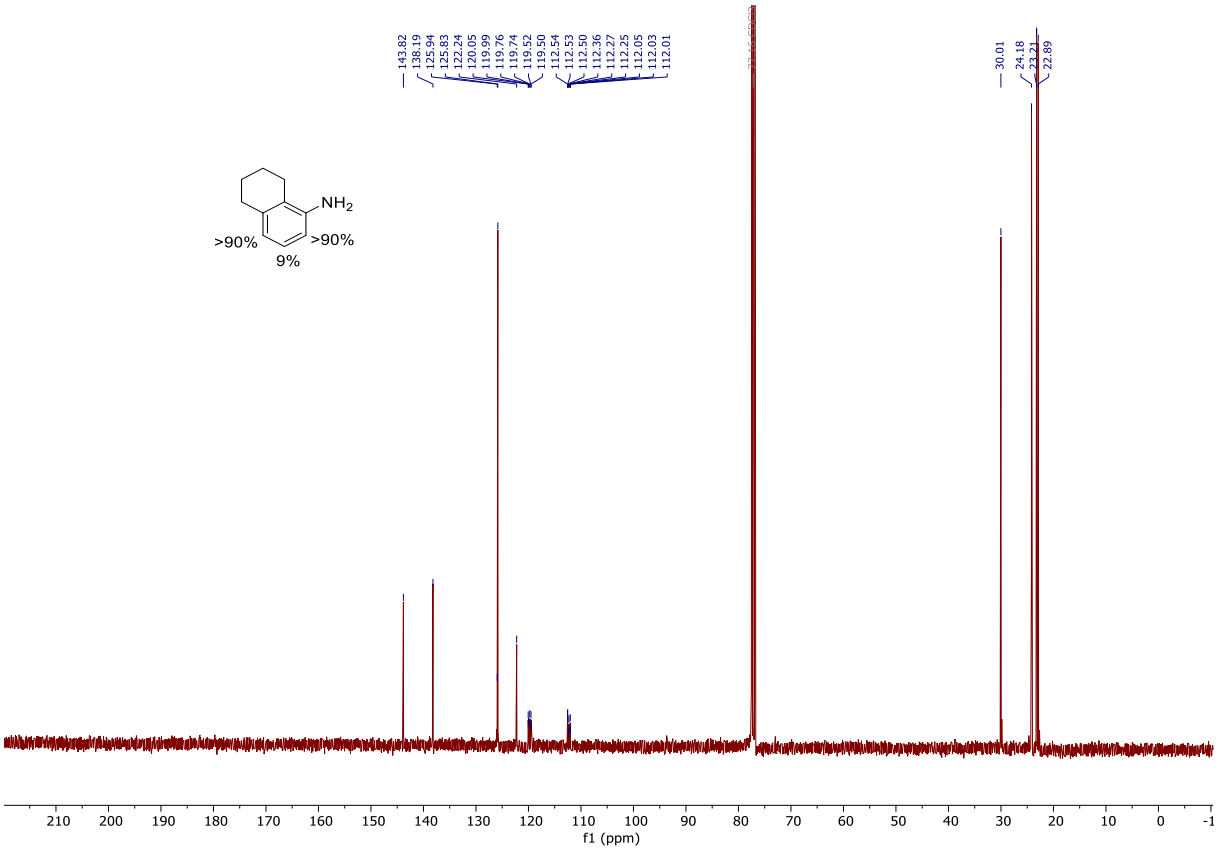
^{1}H-NMR spectrum in $CDCl_3$:



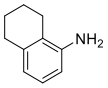
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of 5,6,7,8-tetrahydronaphthalen-1-amine (14) using Conditions B:



Following the general procedure F, using 5,6,7,8-tetrahydronaphthalen-1-amine (**14**) (29.4 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAc = 19:1 as the eluent the target compound **[D]14** was obtained as red liquid (16.6 mg, 56%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 1.98 D/molecule [Mass]; 2.19 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (599 MHz, $CDCl_3$) δ = 6.96 (t, *J* = 7.7 Hz, 1H), 6.63-6.59 (m, 2H), 4.45 (br s, NH_2), 2.74 (t, *J* = 6.3 Hz, 2H), 2.51 (t, *J* = 6.5 Hz, 2H), 1.90-1.84 (m, 2H), 1.79-1.74 (m, 2H) ppm.

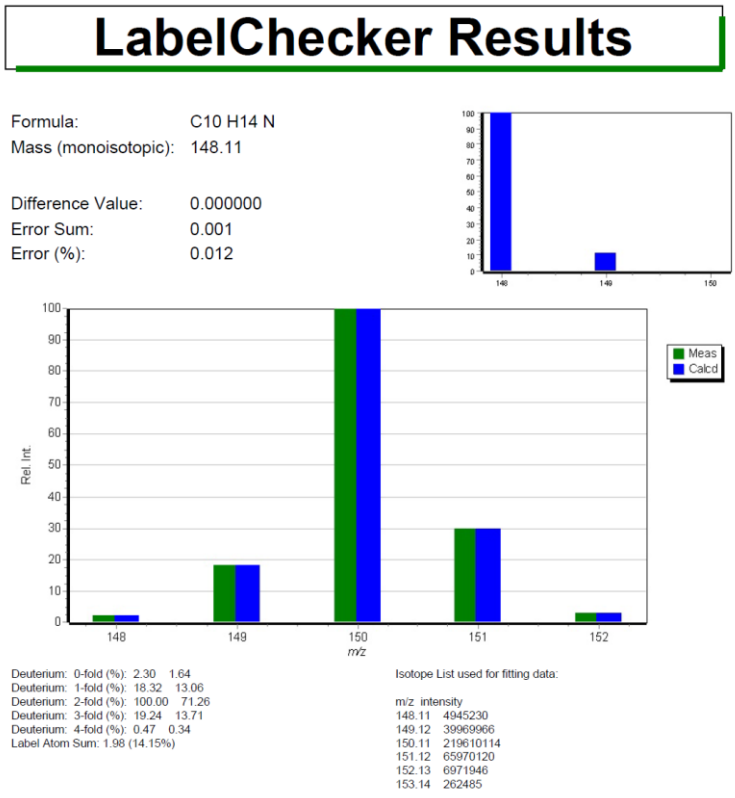
^{13}C NMR (151 MHz, $CDCl_3$) δ = 143.0, 138.4, 126.1, 122.8, 120.7, 113.1, 30.1, 24.3, 23.2, 22.9 ppm.

NMR Data of Product:

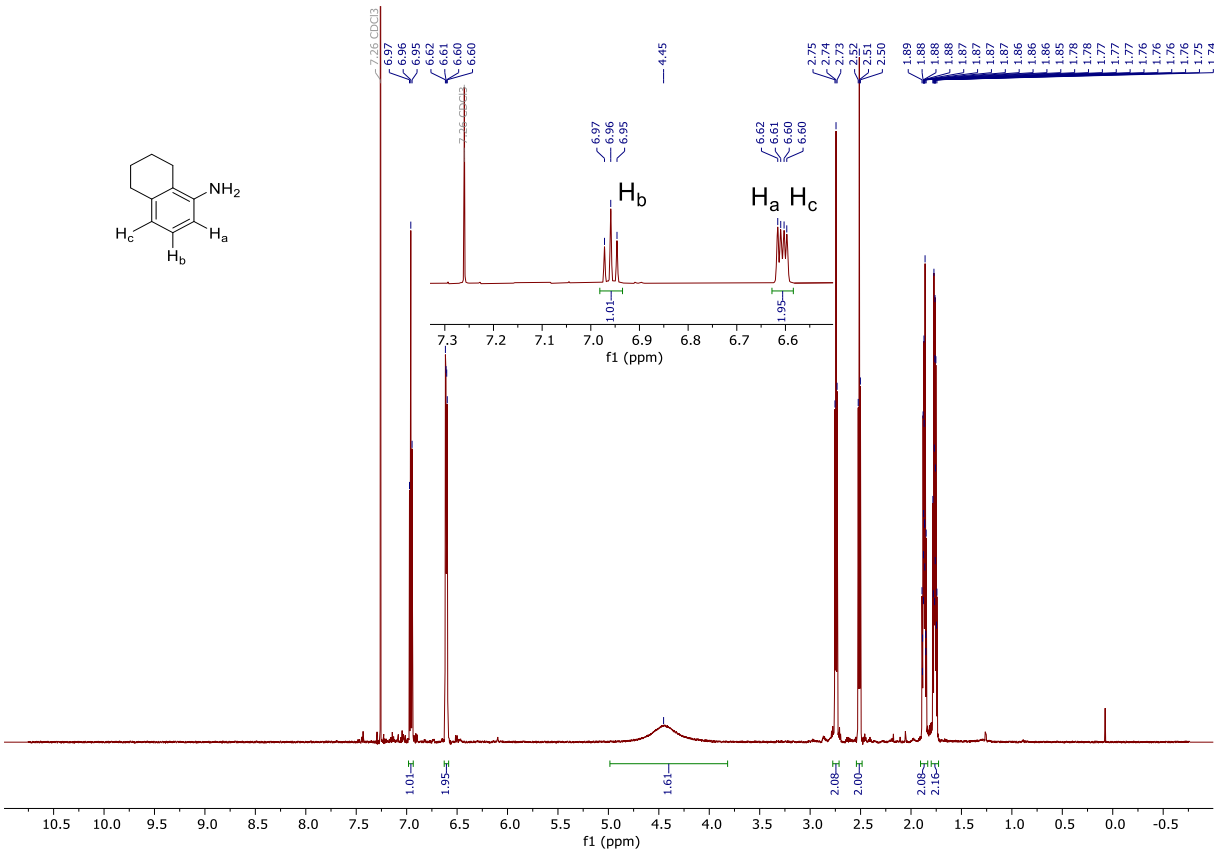
^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.95 (s, 0.71H, 29% D), 6.57 (t, *J* = 7.3 Hz, 0.10H, >90% D), 3.81 (br s, NH_2), 2.75 (t, *J* = 6.2 Hz, 2H), 2.49 (t, *J* = 6.5 Hz, 2H), 1.94-1.83 (m, 2H), 1.83-1.70 (m, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.8, 138.2, 126.4-125.2 (1H), 122.3, 120.3-119.1 (1H), 113.4-111.4 (1H), 30.0, 24.2, 23.2, 22.9 ppm.

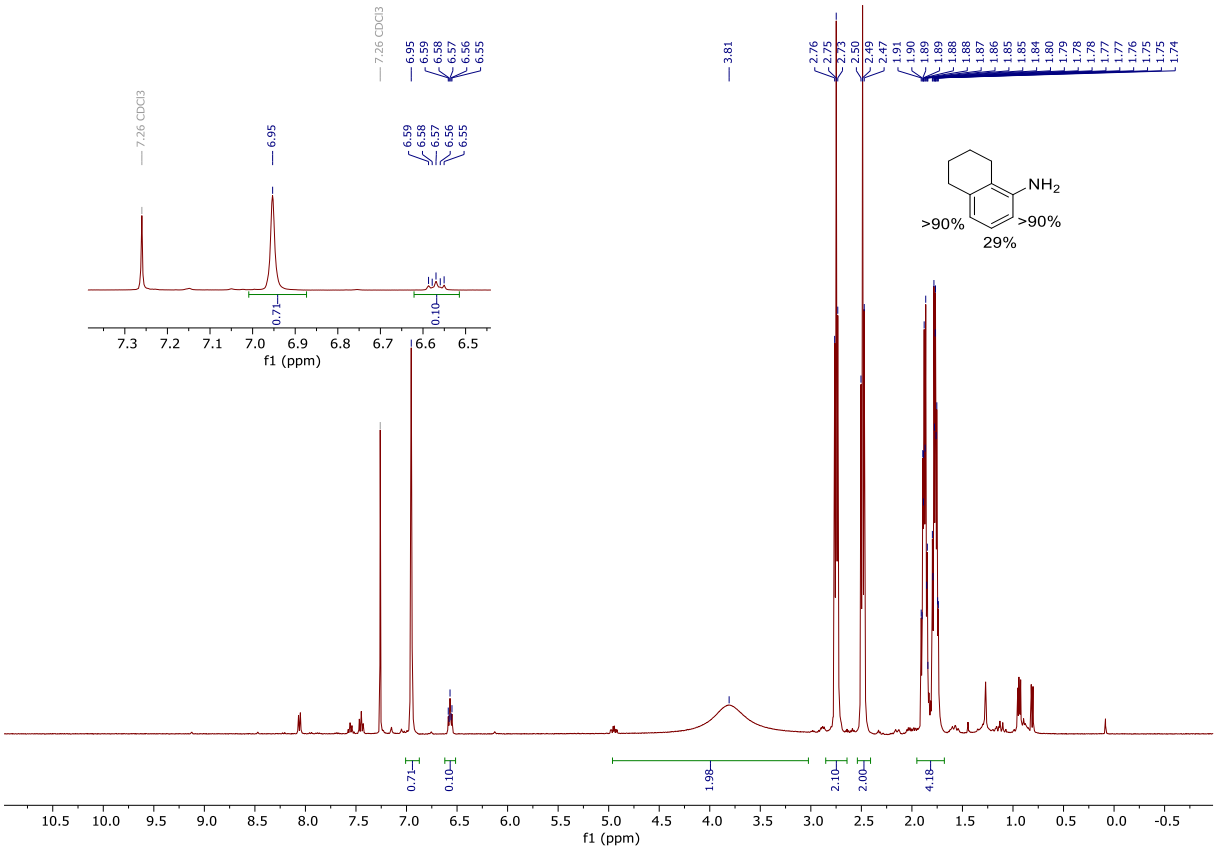
Mass Data:



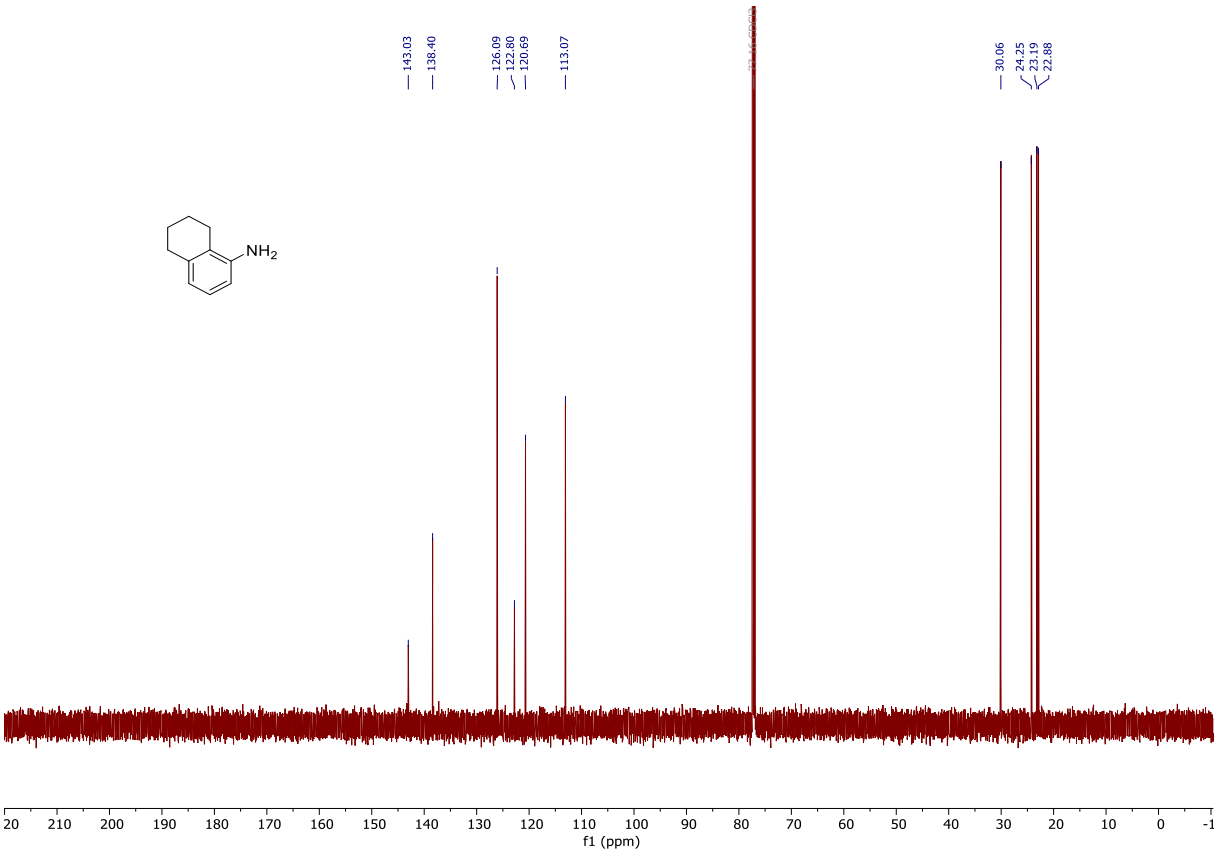
^{1}H-NMR spectrum in $CDCl_3$:



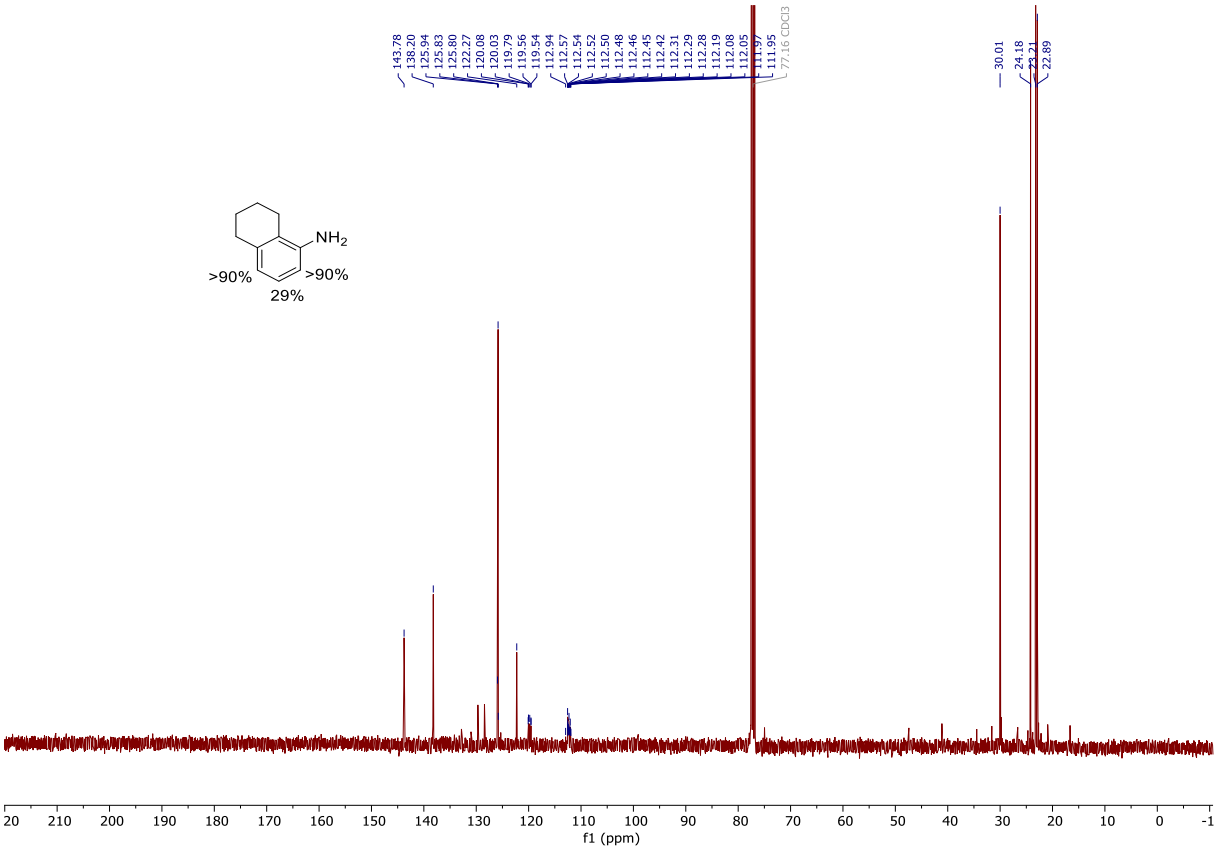
^{1}H-NMR spectrum in $CDCl_3$:



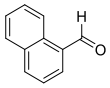
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of 1-naphthaldehyde (15):



Following the general procedure F, using 1-naphthaldehyde (**15**) (31.2 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAc = 19:1 as the eluent the target compound **[D]15** was obtained as yellow liquid (18.7 mg, 60%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 3.95 D/molecule [Mass]; 4.28 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (599 MHz, $CDCl_3$) δ = 10.41 (s, 1H), 9.26 (d, J = 8.7 Hz, 1H), 8.11 (d, J = 8.2 Hz, 1H), 8.00 (dd, J = 7.0, 1.3 Hz, 1H), 7.93 (d, J = 8.4 Hz, 1H) 7.70 (ddd, J = 8.5, 6.9, 1.4 Hz, 1H), 7.64 (dd, J = 8.2, 7.0 Hz, 1H), 7.60 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H) ppm.

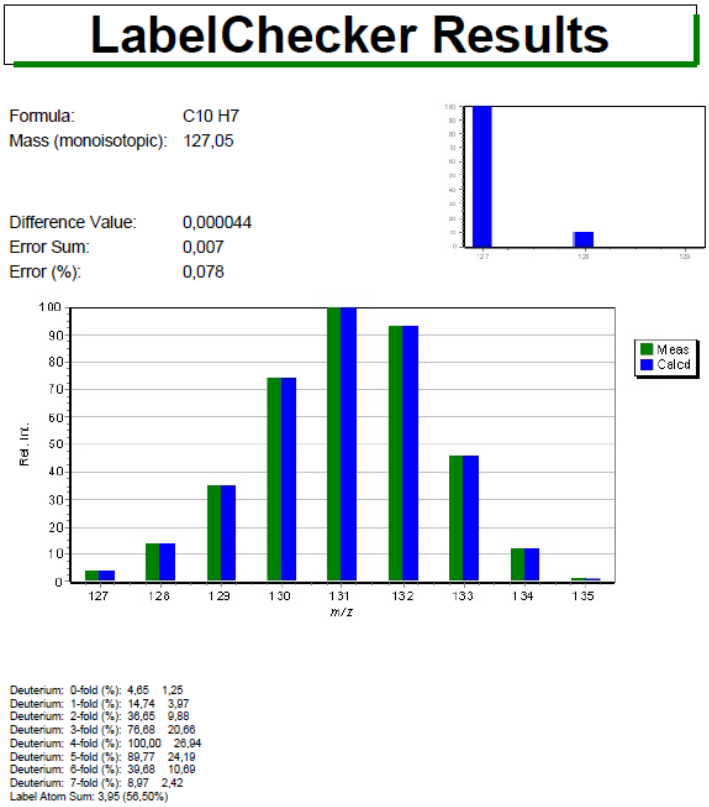
^{13}C NMR (151 MHz, $CDCl_3$) δ = 193.7, 136.8, 135.5, 133.9, 131.6, 130.7, 129.2, 128.6, 127.1, 125.0(4), 125.0(3) ppm.

NMR Data of Product:

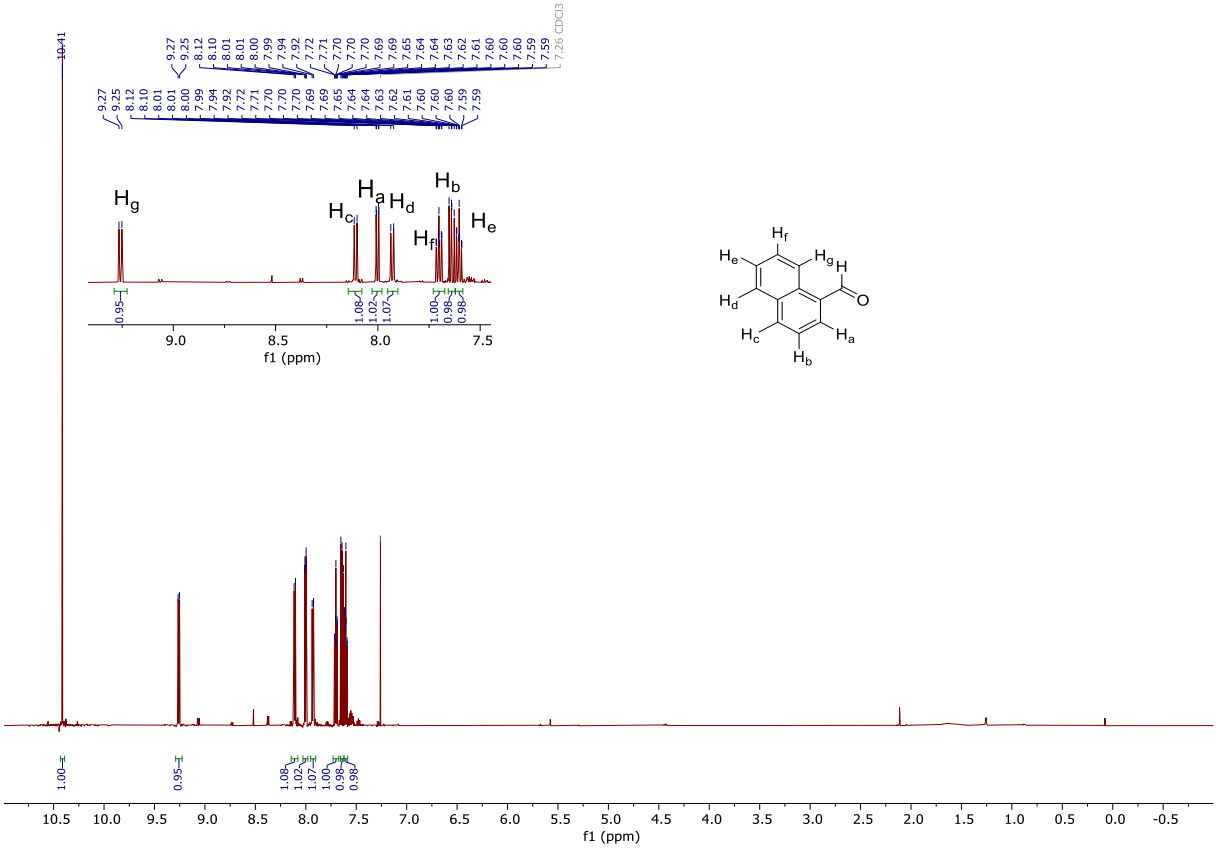
^{1}H NMR (400 MHz, $CDCl_3$) δ = 10.41 (s, 1H), 9.29-9.24 (m, 0.67H, 33% D), 8.14-8.09 (m, 0.42H, 58% D), 8.02-7.98 (m, 0.91H, 9% D), 7.95-7.90 (m, 0.11H, 89%) 7.73-7.67 (m, 0.17H, 83% D), 7.66-7.58 (m, 0.44H, >77% D) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 193.7, 136.9-136.5 (1H), 135.5-135.1 (1H), 133.9-133.6 (1H), 131.6, 130.7, 129.3-129.0 (1H), 128.7-128.3 (1H), 127.1-126.7 (1H), 125.1-124.7 (2H) ppm.

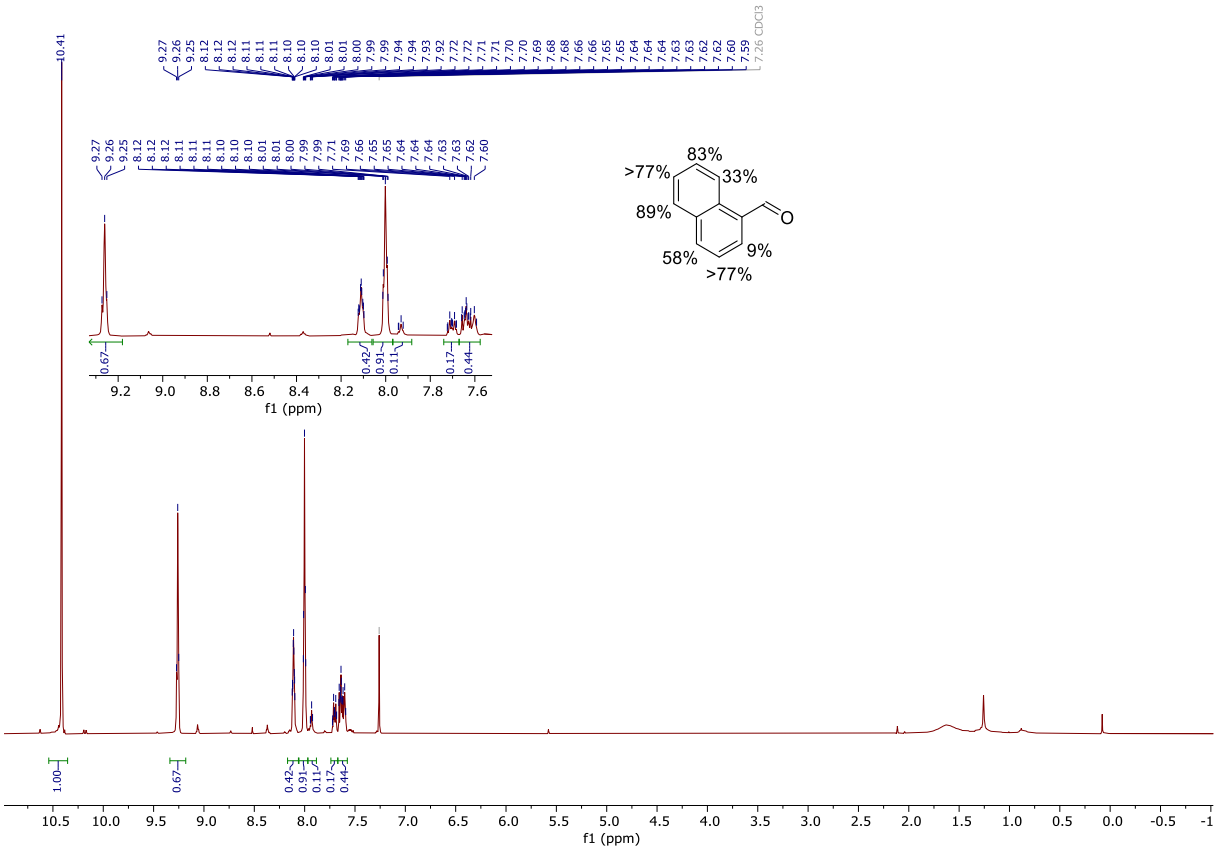
Mass Data:



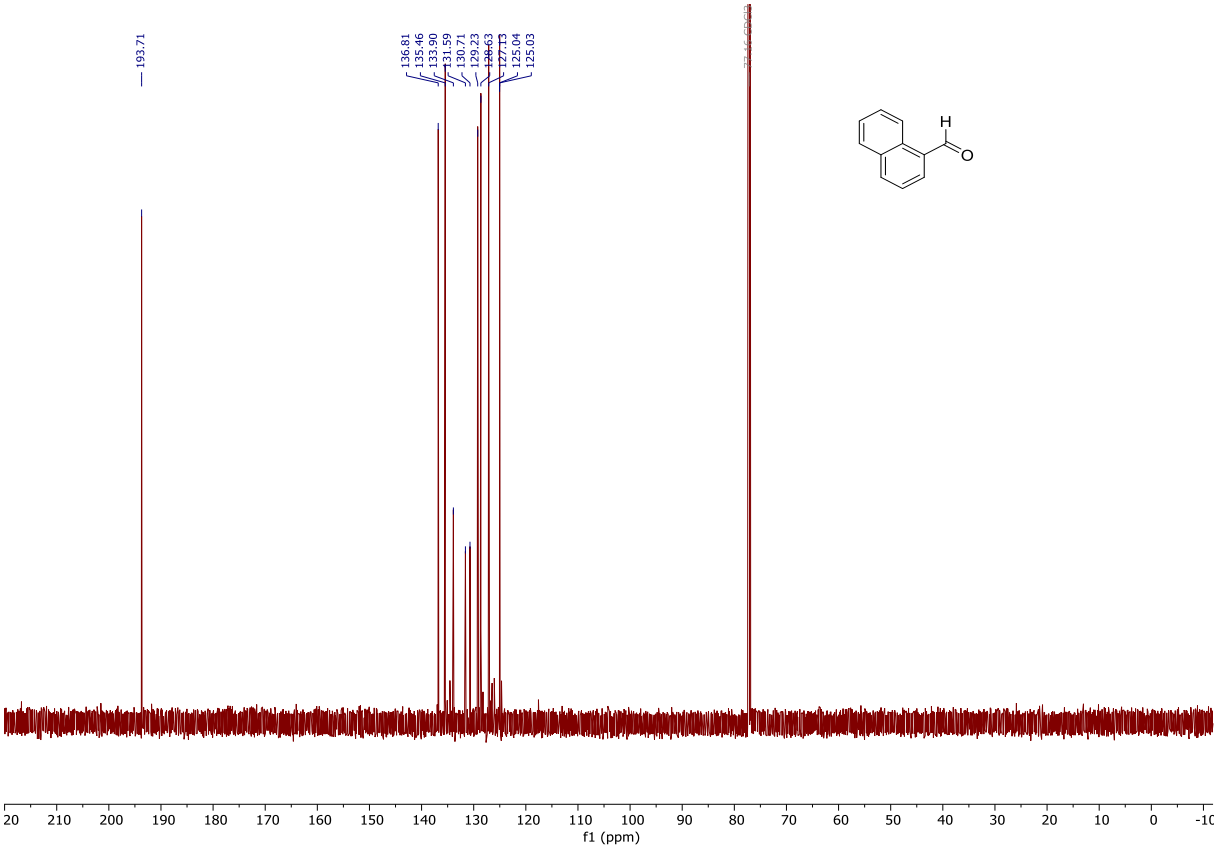
^{1}H-NMR spectrum in $CDCl_3$:



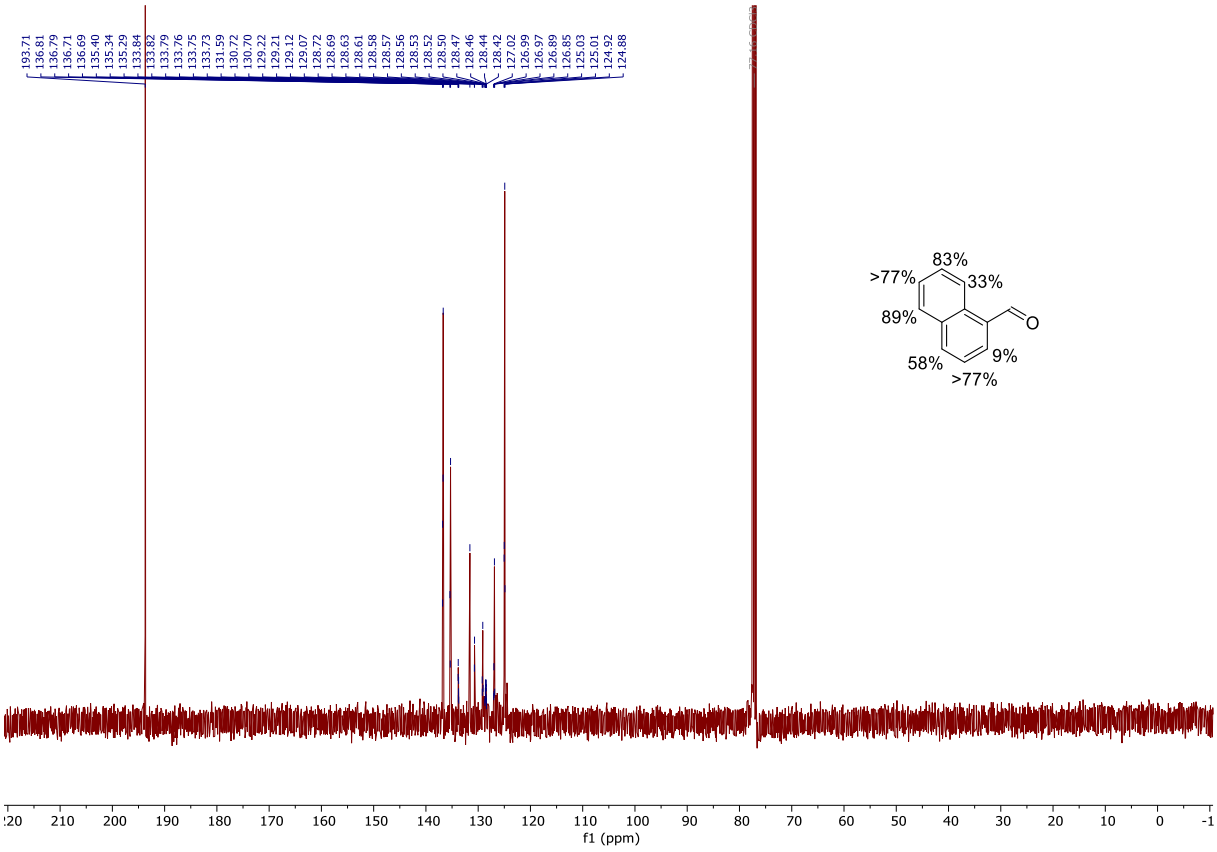
^{1}H-NMR spectrum in $CDCl_3$:



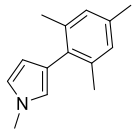
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of 3-mesityl-1-methyl-1*H*-pyrrole (16):



Following the general procedure E and using 3-mesityl-1-methyl-1*H*-pyrrole (**16**) (39.9 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAc = 100:1 as the eluent, the target compound **[D]16** was obtained as a colorless solid (21.2 mg, 53%). The degree of deuteration was determined by NMR-spectroscopy.

Deuterium Incorporation: 0.56 D/molecule [^{1}H-NMR].[1]

NMR Data of Starting Material:

^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.9 (s, 2H), 6.7 (dd, *J* = 2.5, 2.5 Hz, 1H), 6.4 (dd, *J* = 2.0, 2.0 Hz, 1H), 6.0 (dd, J = 2.1, 2.1 Hz, 1H), 3.7 (s, 3H), 2.3 (s, 3H), 2.2 (s, 6H). ppm.

^{13}C NMR (151 MHz, $CDCl_3$): δ = 137.7, 135.9, 133.8, 128.0, 122.3, 121.3, 120.4, 110.0, 36.3, 21.4, 21.1 ppm.

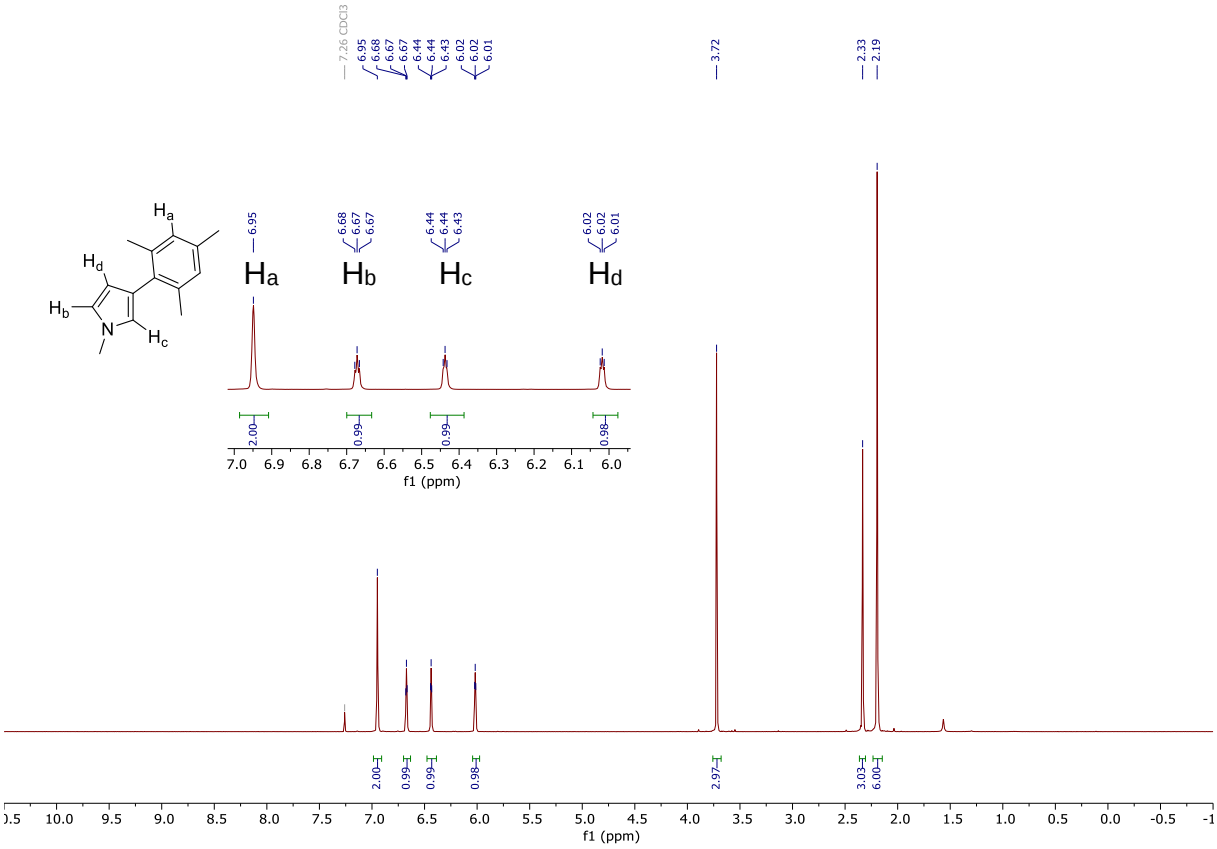
NMR Data of Product:

^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.93 (s, 2H), 6.65 (s, 0.82H, 18% D), 6.42 (s, 0.78 H, 22% D), 5.99 (s, 0.84H, 16% D), 3.70 (s, 3H), 2.31 (s, 4H), 2.17 (s, 6H). ppm.

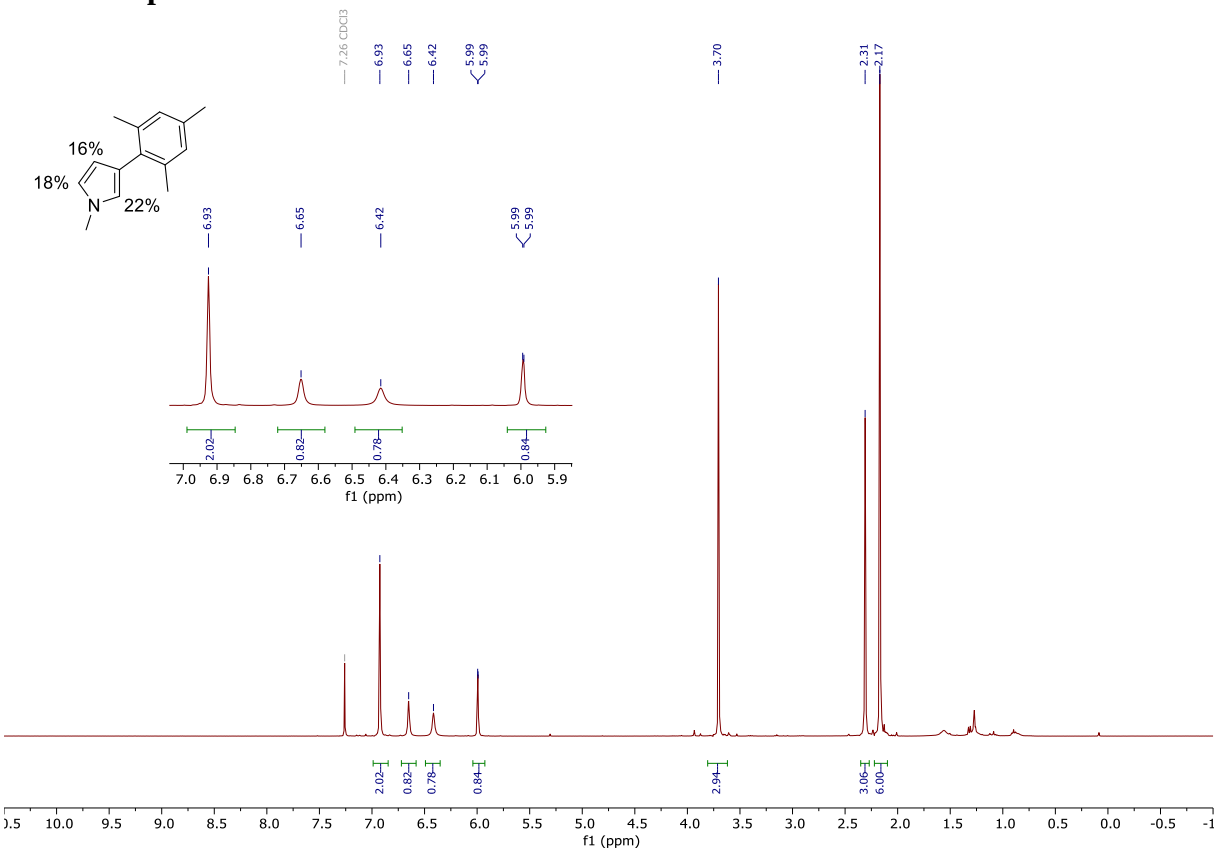
^{13}C NMR (101 MHz, $CDCl_3$) δ = 137.7, 135.9, 133.8, 128.0, 122.2 121.4-121.1 (1C), 120.5-120.3 (1C), 110.1-109.7 (1C), 36.3, 21.4, 21.1 ppm.

[1] The degree of deuteration could not be determined through mass spectrometry for this compound, which proved unsuitable for ESI analysis and gave inconclusive deuteration values from the fragments observed after EI ionization.

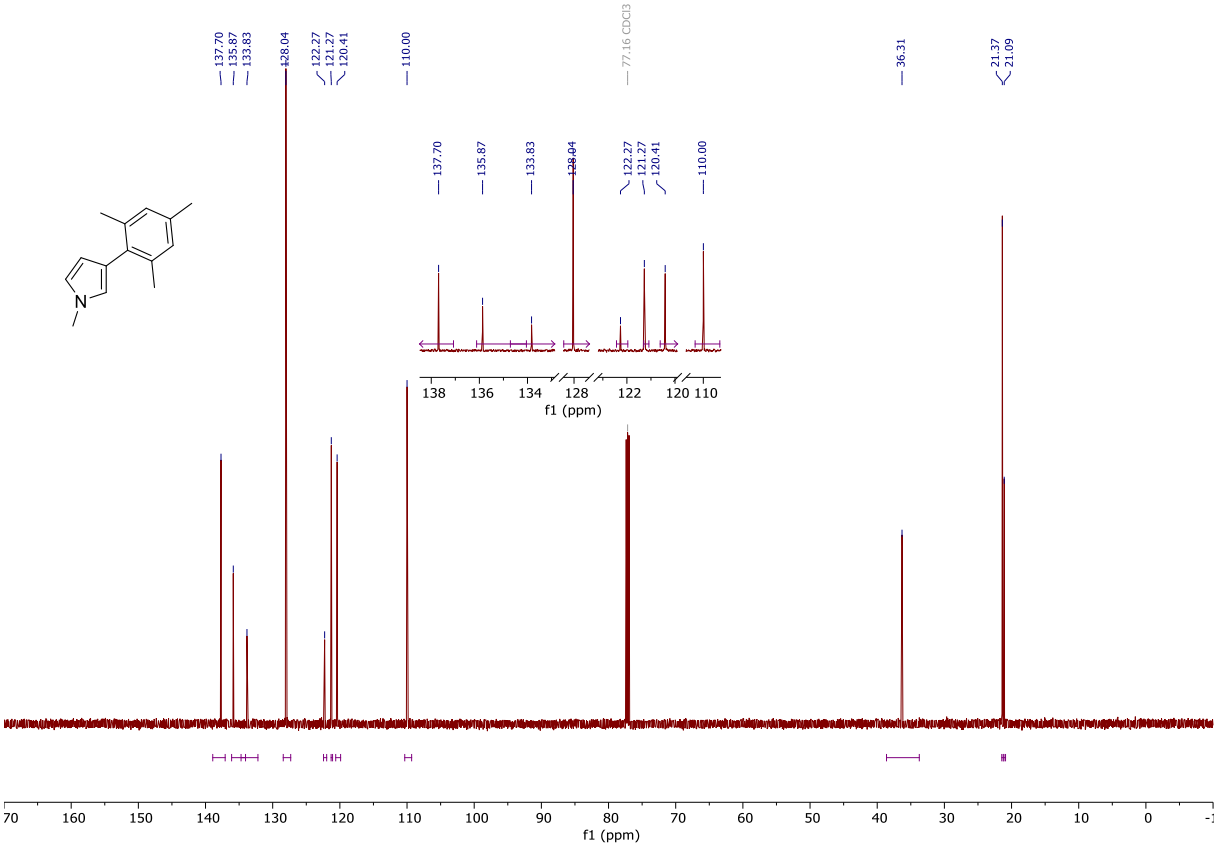
^{1}H-NMR spectrum in $CDCl_3$:



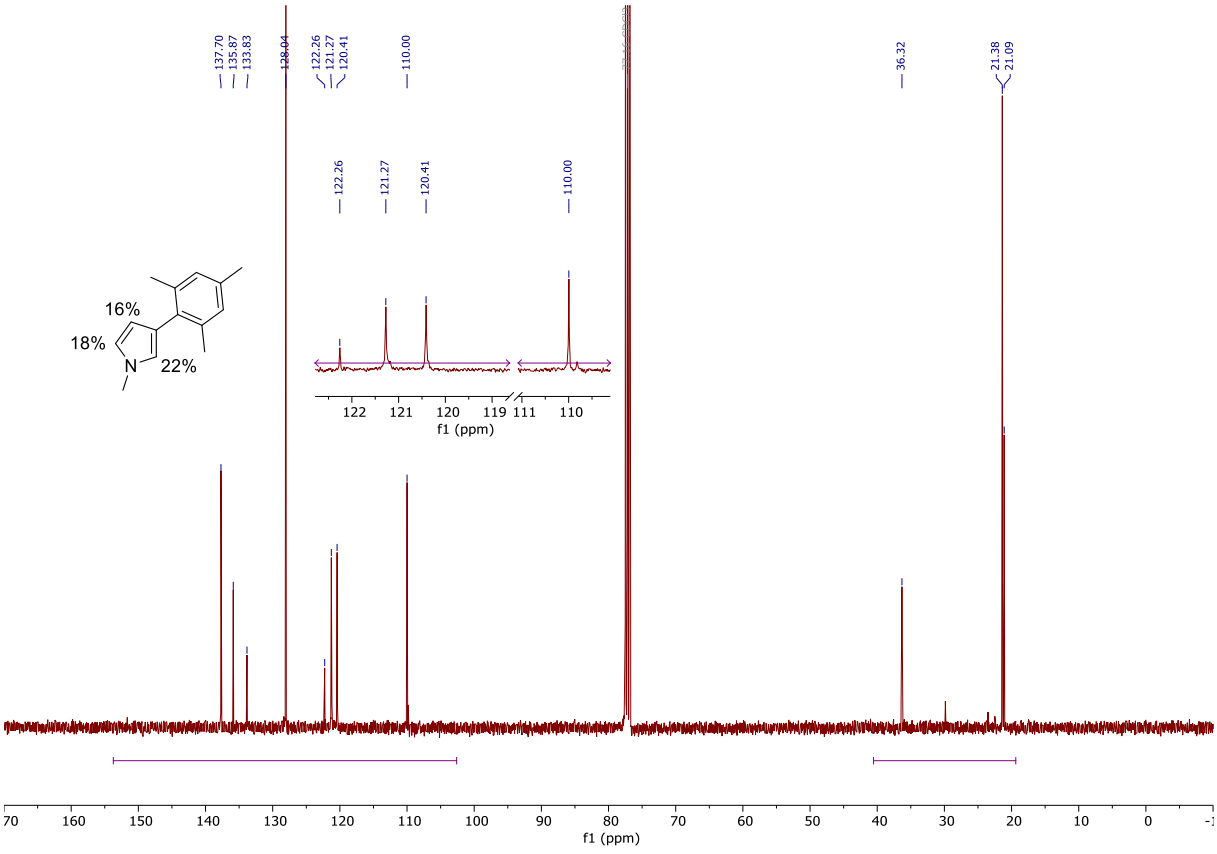
^{1}H-NMR spectrum in $CDCl_3$:



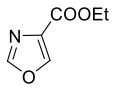
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of ethyl oxazole-4-carboxylate (17):



Following the general procedure F and using ethyl oxazole-4-carboxylate (**17**) (28.2 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:Et_2O = 20:1 as the eluent, the target compound **[D]17** was obtained as colorless liquid (32%)[a]. The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 1.18 D/molecule [Mass]; 1.17 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.30-8.23 (m, 1H), 7.93 (s, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H). ppm.

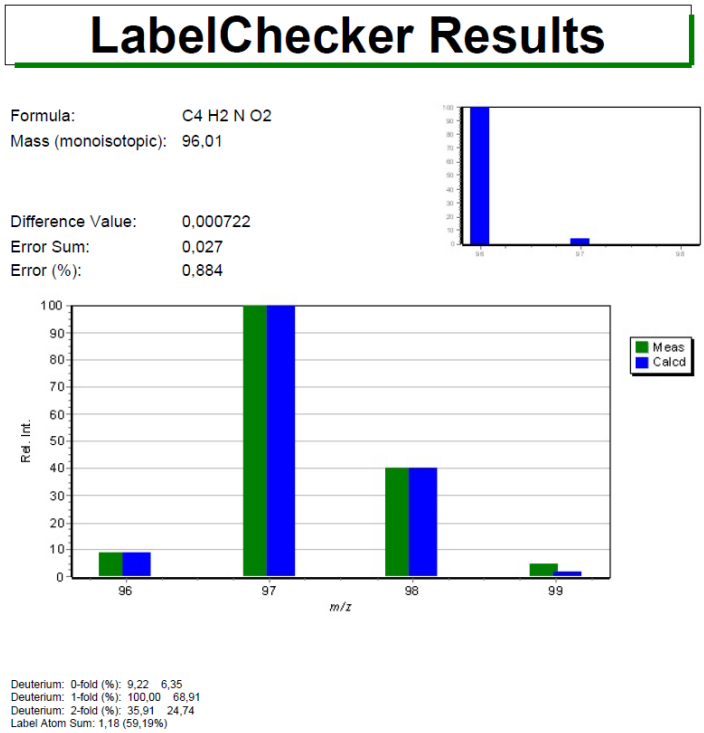
^{13}C NMR (100 MHz, $CDCl_3$) δ = 161.1, 151.5, 144.1, 133.5, 61.5, 14.4.ppm.

NMR Data of Product:

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.27 (s, 0.79H, 21% D), 7.93 (s, 0.04H, 96% D), 4.44-4.36 (m, 2H), 1.39 (t, *J* = 7.1 Hz, 3H) ppm.

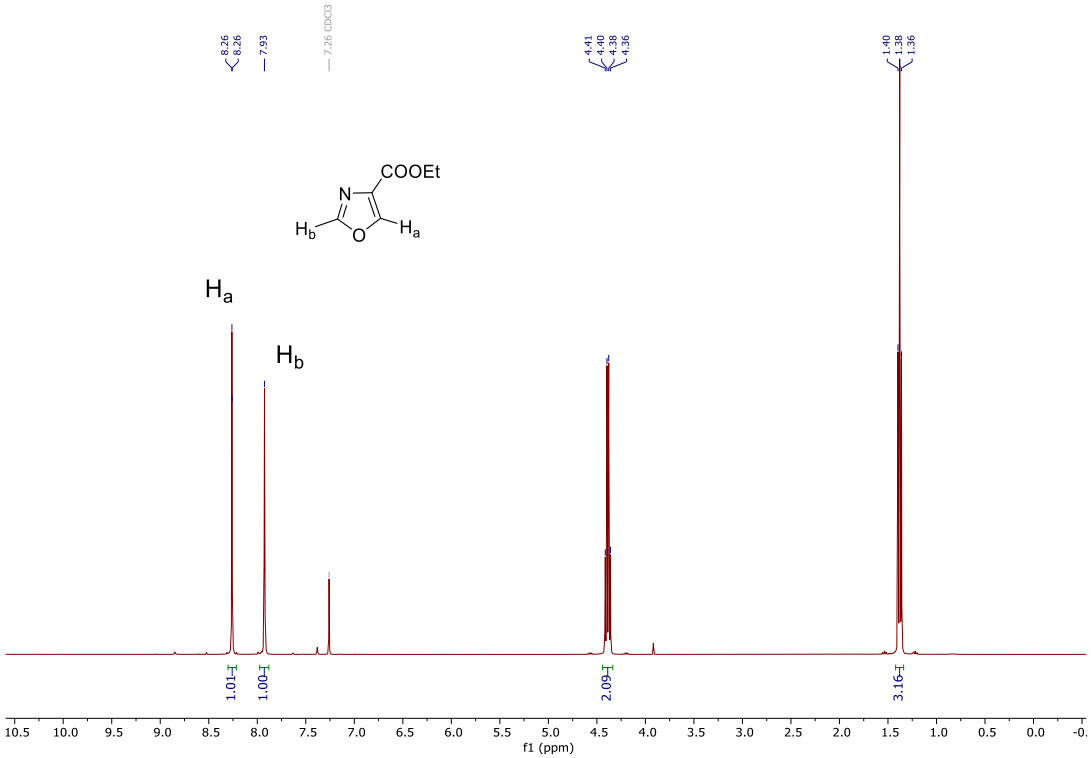
^{13}C NMR (150 MHz, $CDCl_3$) δ = 161.1, 151.0-149.9 (1C), 144.1, 133.5, 61.5, 14.4 ppm.

Mass Data:

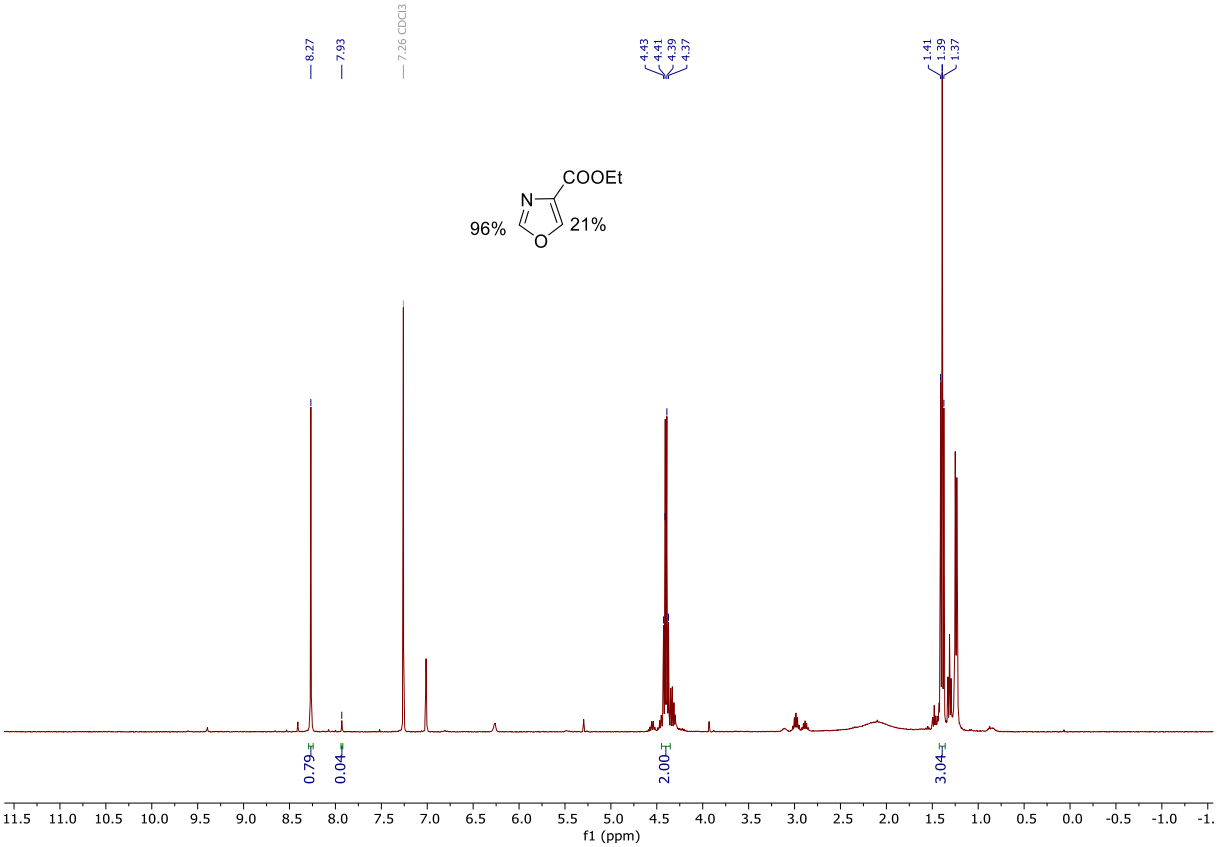


a The isolated product was obtained with an unknown impurity, which could not be separated by column chromatography. Therefore, after isolation, 1,3,5-trimethyl benzene was added as an internal standard and the product yield was calculated. The spectra presented are those after isolation with unknown impurity, but before the addition of the internal standard.

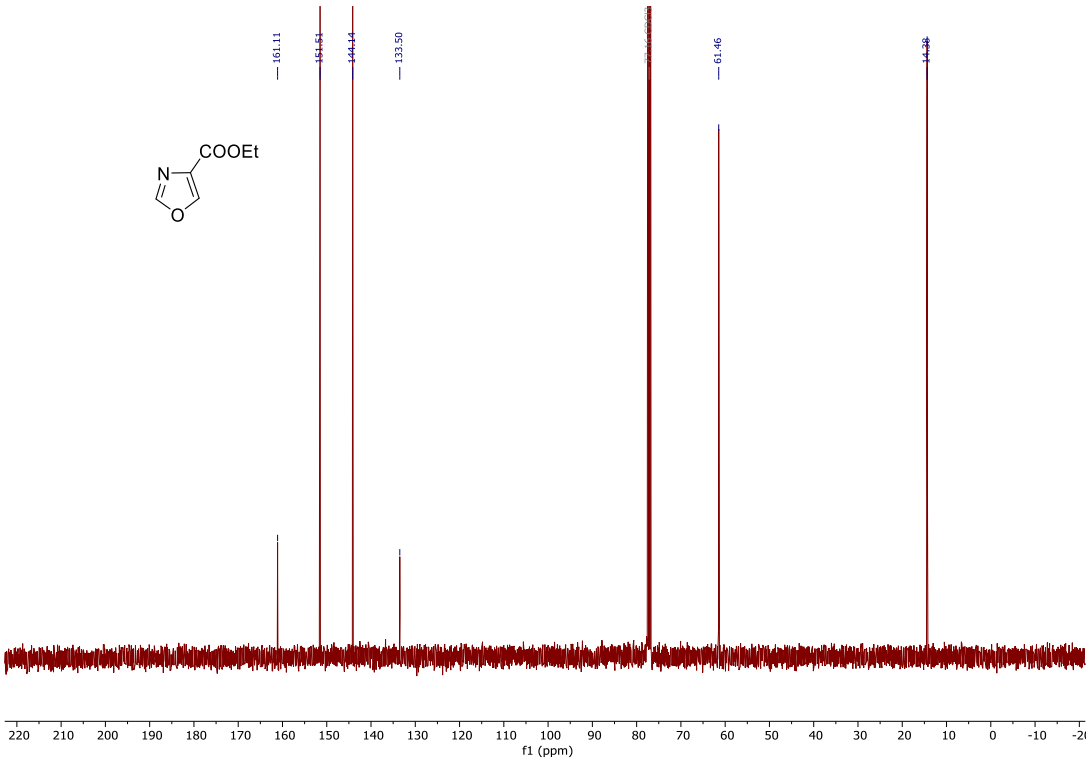
^{1}H-NMR spectrum in $CDCl_3$:



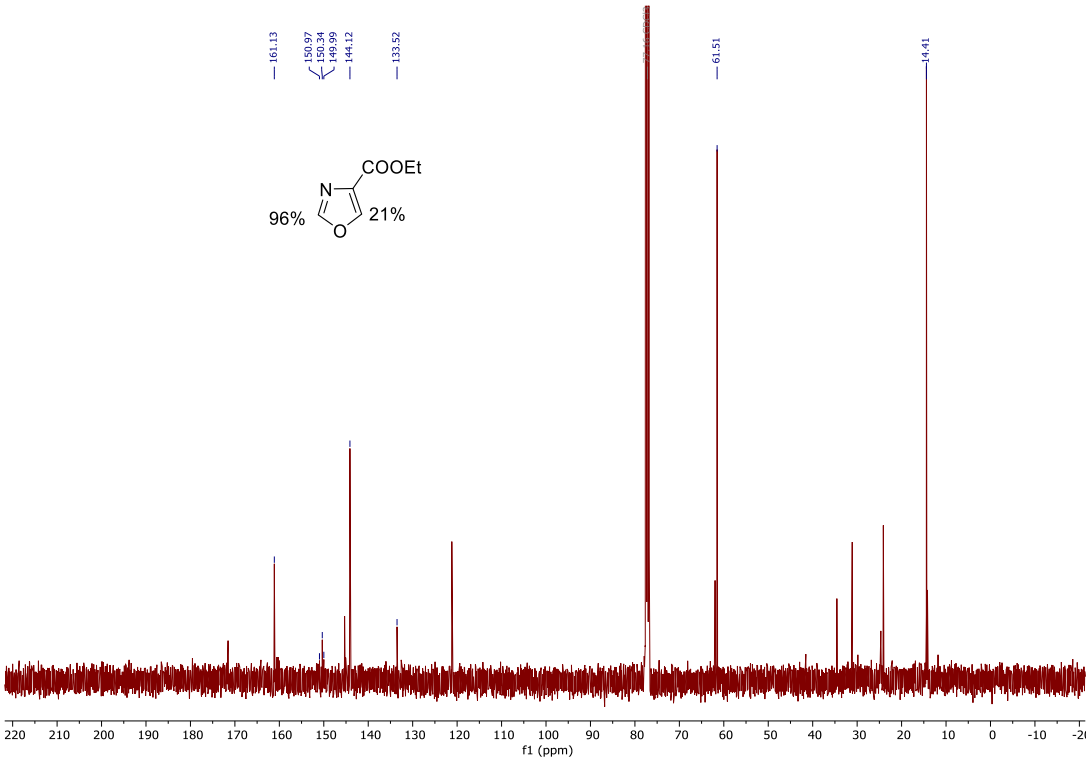
^{1}H-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of 2-methoxythiazole (18):

Following the general procedure F and using 2-methoxythiazole (**18**) (23.0 mg, 0.200 mmol), the yield of the target compound **[D]18** was determined using crude reaction mixture and 1,3,5-trimethyl benzene as an internal standard (85%)[b]. The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 0.46 D/molecule [Mass]; 0.53 D/molecule [^{1}H-NMR].

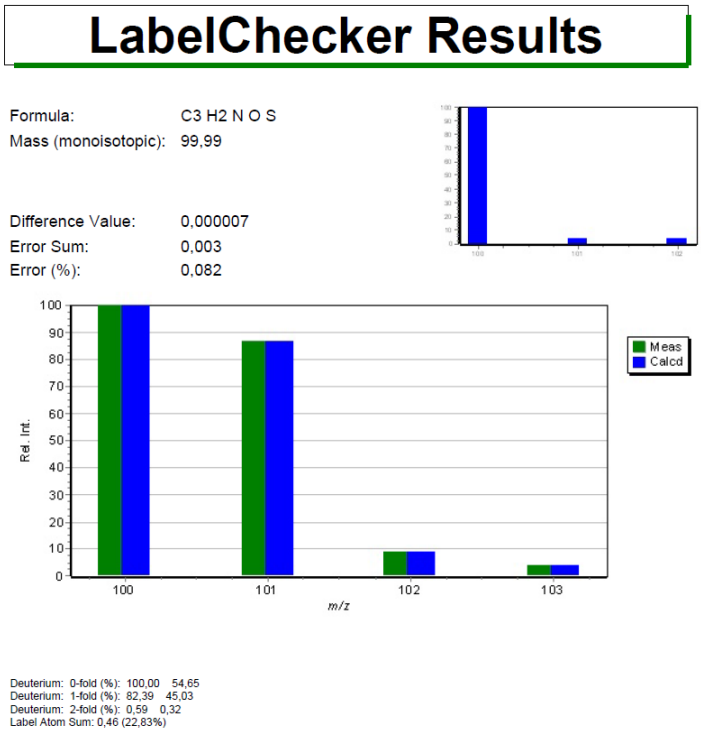
NMR Data of Starting Material:

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.16-7.01 (m, 1H), 6.72-6.55 (m, 1H), 4.08-3.99 (m, 3H) ppm.

NMR Data of Product in Crude Reaction Mixture:

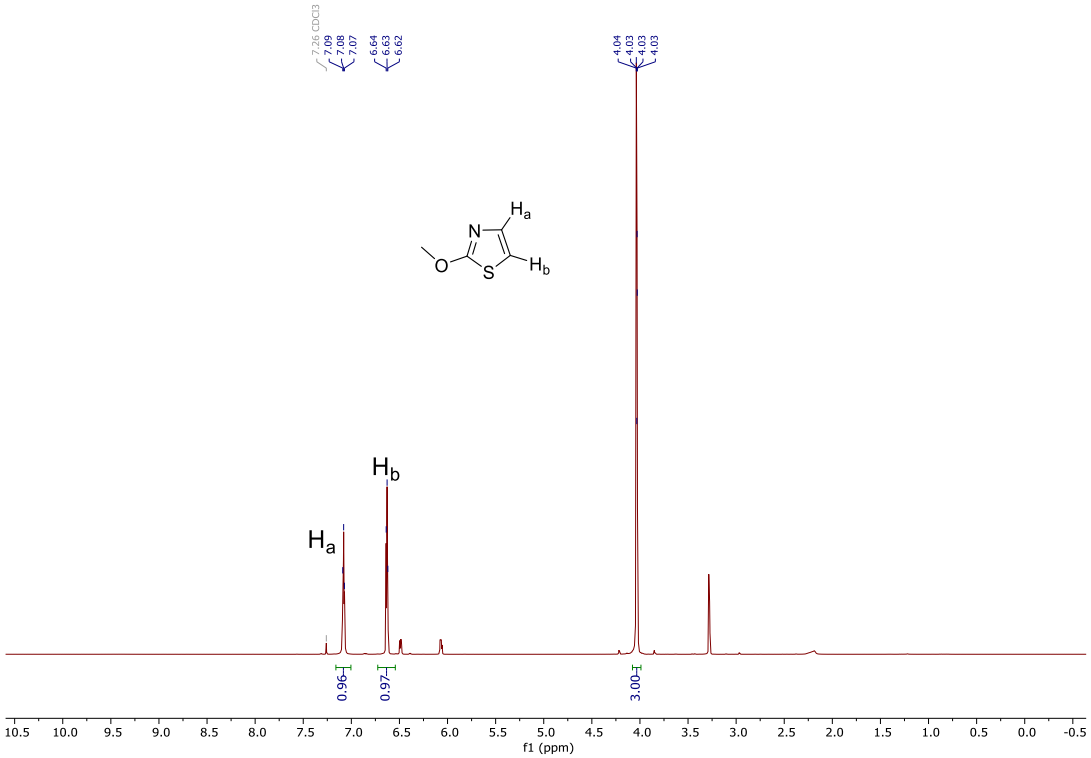
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.12-7.06 (m, 0.96H, 4% D), 6.62-6.57 (m, 0.51H, 49% D), 4.06 (s, 3H) ppm.

Mass Data:

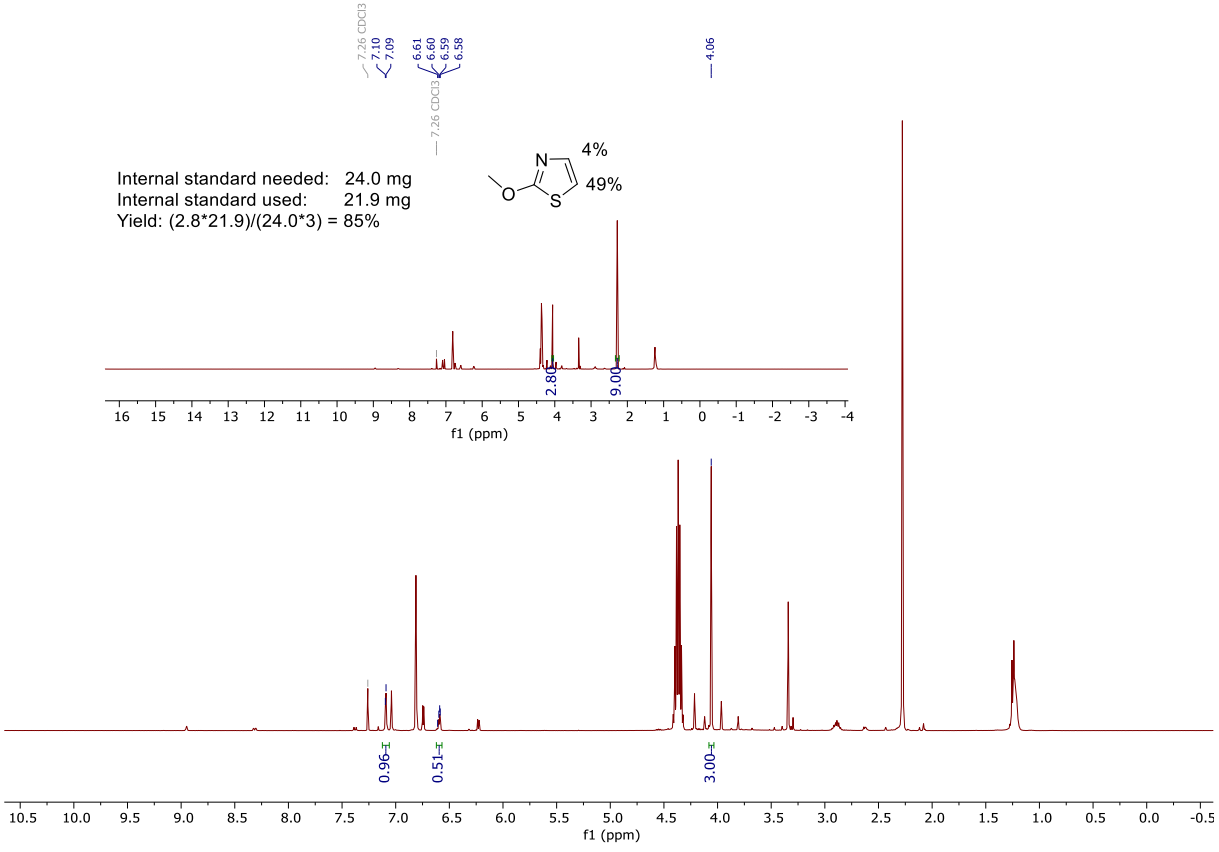


b The NMR yield was used in this case due to difficulties in the isolation of this product caused by its volatility.

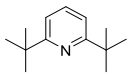
^{1}H-NMR spectrum in $CDCl_3$:



^{1}H-NMR spectrum in $CDCl_3$:



Deuteration of 2,6-di-*tert*-butylpyridine (19):



Following the general procedure F and using 2,6-di-*tert*-butylpyridine (**19**) (38.3 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAc = 9:1 as the eluent, the target compound **[D]19** was obtained as colorless solid (26.4 mg, 69%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 0.89 D/molecule [Mass]; 1.02 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.51 (t, *J* = 7.8 Hz, 1H), 7.09 (d, *J* = 7.8 Hz, 2H), 1.35 (s, 18H) ppm.

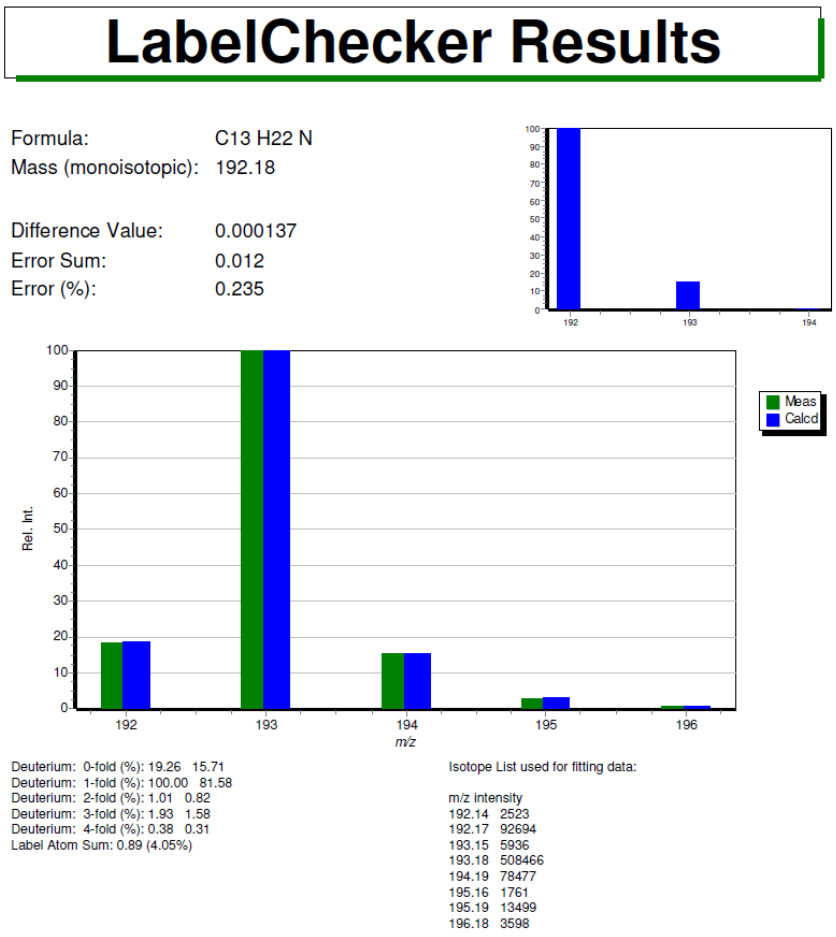
^{13}C NMR (101 MHz, $CDCl_3$) δ = 167.7, 136.1, 115.3, 37.8, 30.3 ppm.

NMR Data of Product:

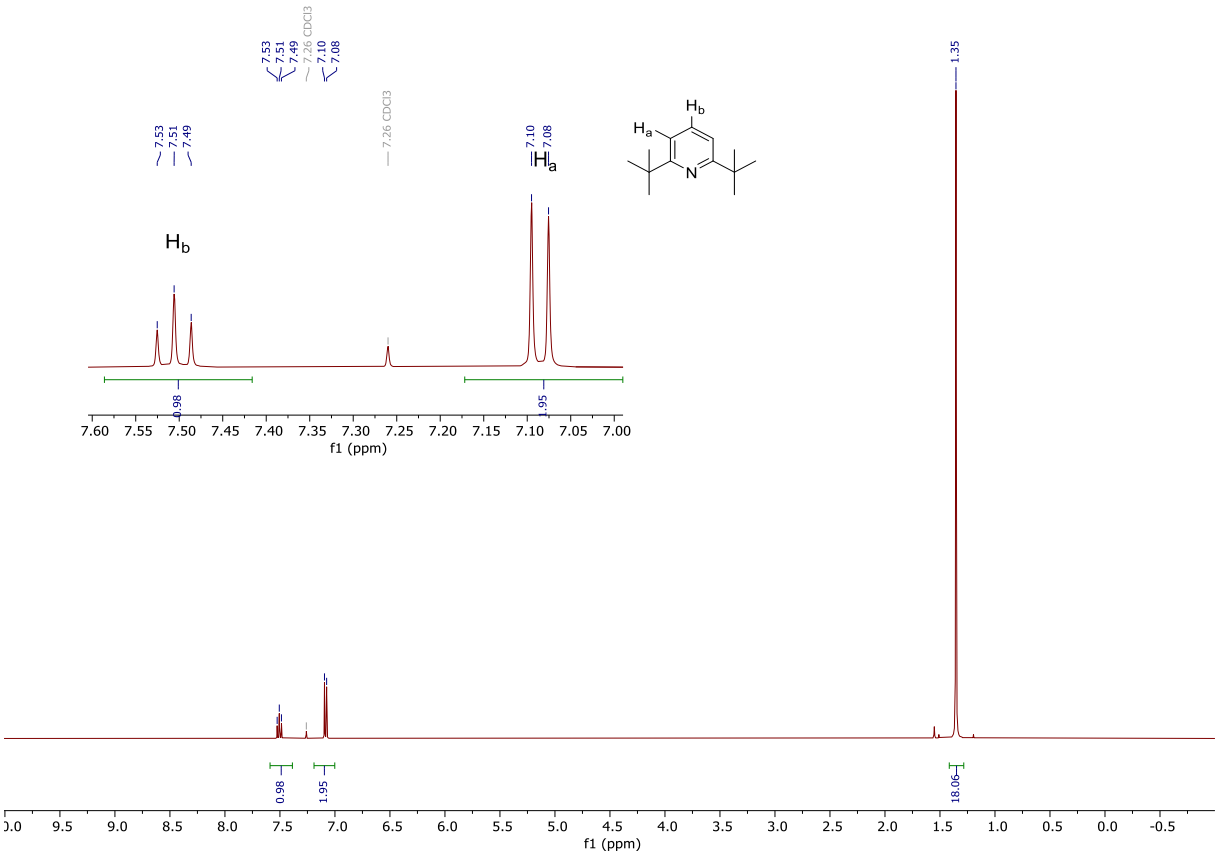
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.54-7.46 (m, 0.17H, 83% D), 7.11-7.05 (m, 1.80H, 10% D), 1.35 (s, 18H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 167.7, 136.9-134.0 (1C), 116.2-114.0 (2C), 37.8, 30.3 ppm

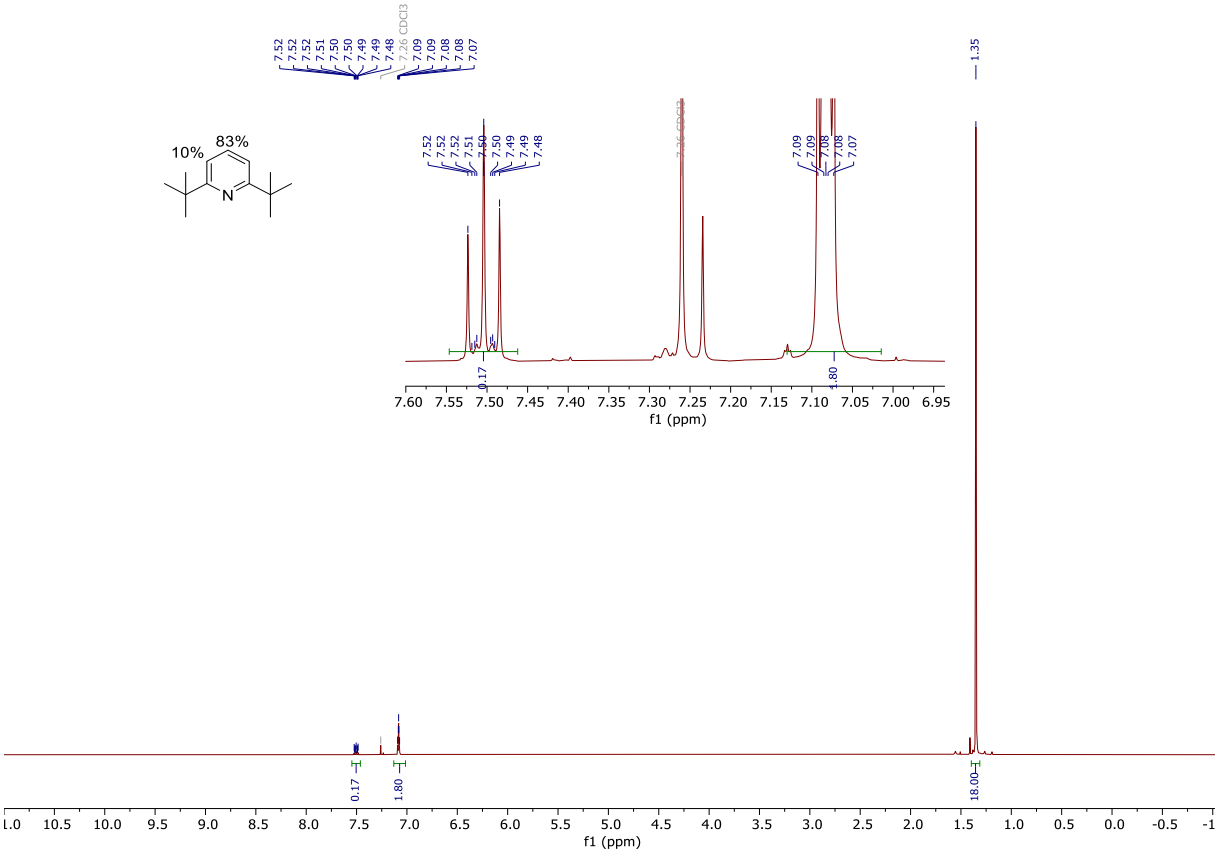
Mass Data:



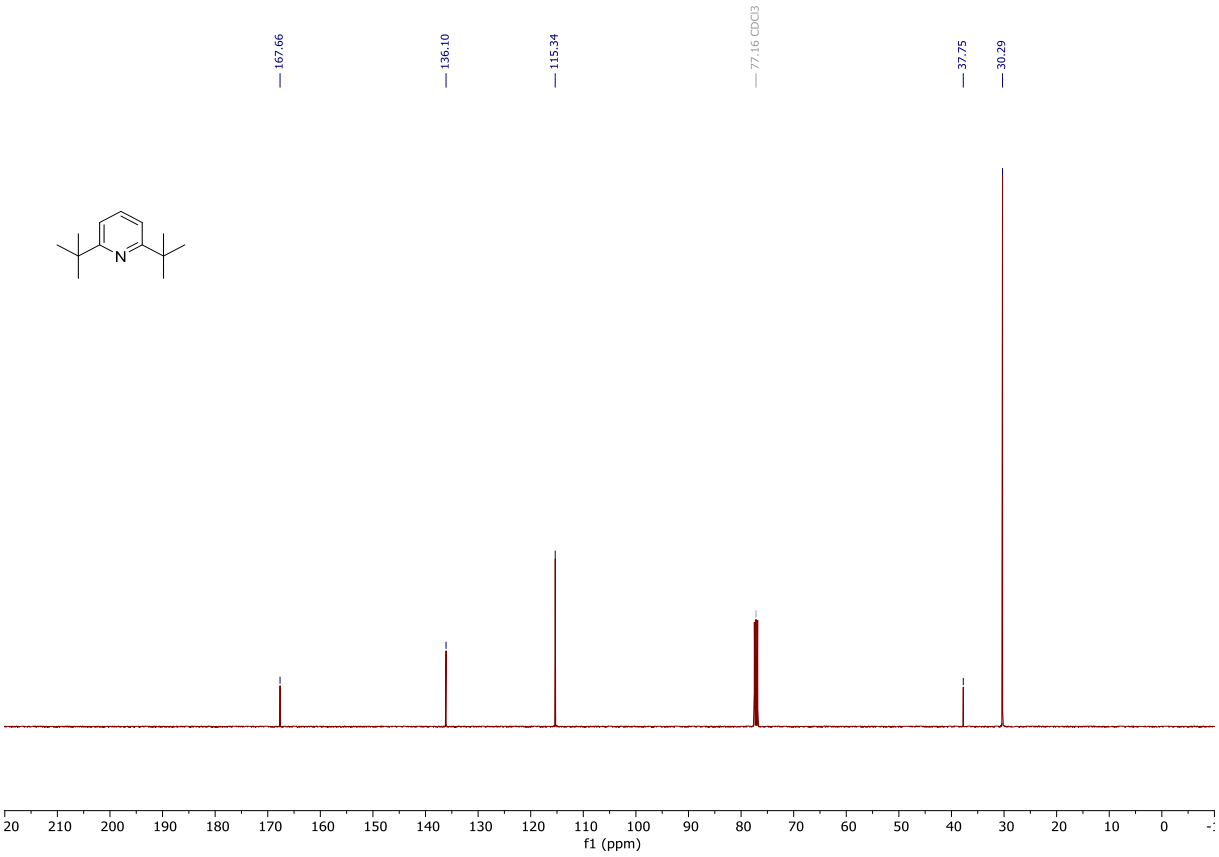
^{1}H-NMR spectrum in $CDCl_3$:



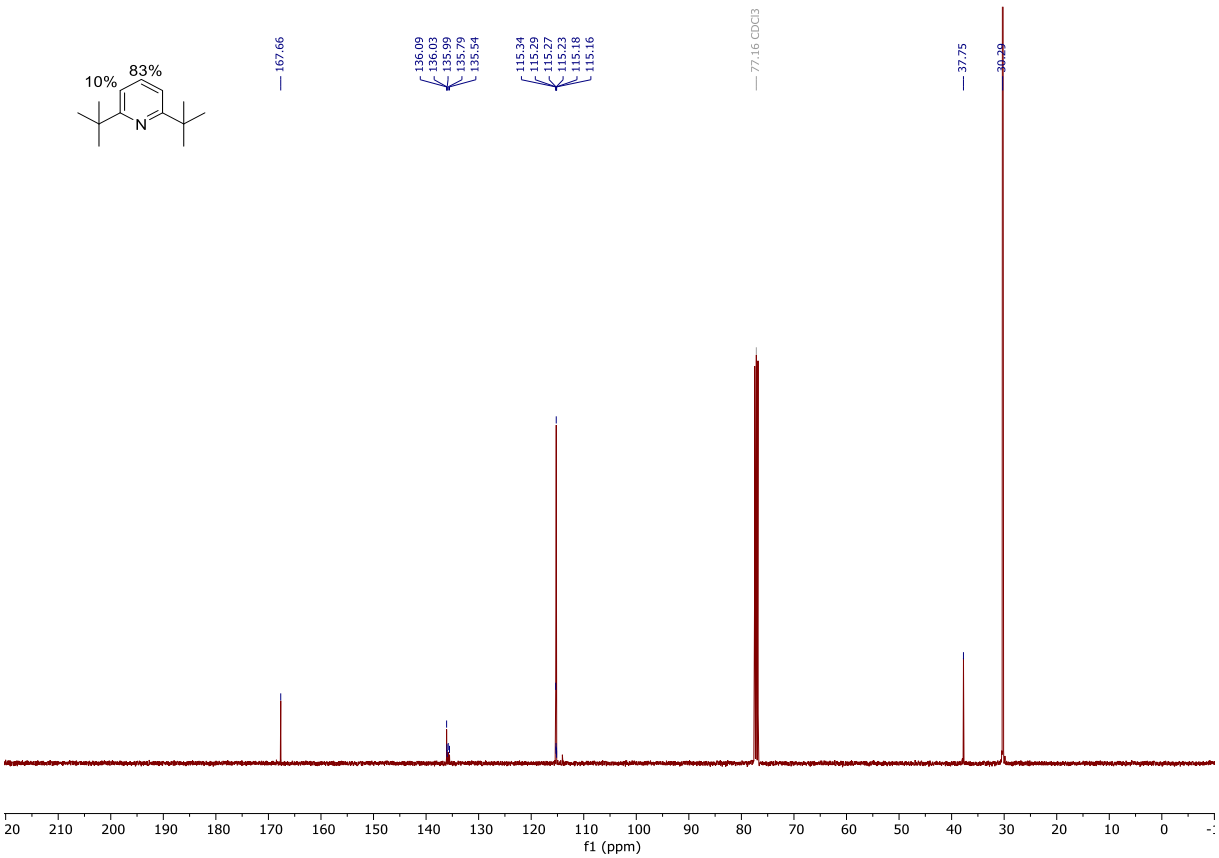
^{1}H-NMR spectrum in $CDCl_3$:



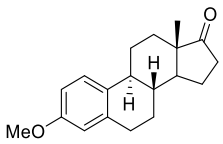
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of (8*R*,9*S*,13*S*)-3-methoxy-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[*a*]phenanthren-17-one (20):



Following the general procedure E and using (8*R*,9*S*,13*S*)-3-methoxy-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[*a*]phenanthren-17-one (**20**) (56.9 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAc = 3:1 as the eluent, the target compound **[D]20** was obtained as colorless solid (49.3 mg, 86%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 2.21 D/molecule [HRMS]; 2.29 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.21 (d, *J* = 8.7 Hz, 1H), 6.72 (dd, *J* = 8.6, 2.8 Hz, 1H), 6.65 (d, *J* = 2.7 Hz, 1H), 3.78 (s, 3H), 2.94-2.86 (m, 2H), 2.50 (ddd, *J* = 19.1, 8.9, 1.0 Hz, 1H), 2.43-2.37 (m, 1H), 2.26 (td, *J* = 10.7, 4.4 Hz, 1H), 2.14 (dt, *J* = 19.0, 9.0 Hz, 1H), 2.09-1.98 (m, 2H), 1.97-1.93 (m, 1H), 1.67-1.56 (m, 2H), 1.54-1.40 (m, 4H), 0.91 (s, 3H) ppm.

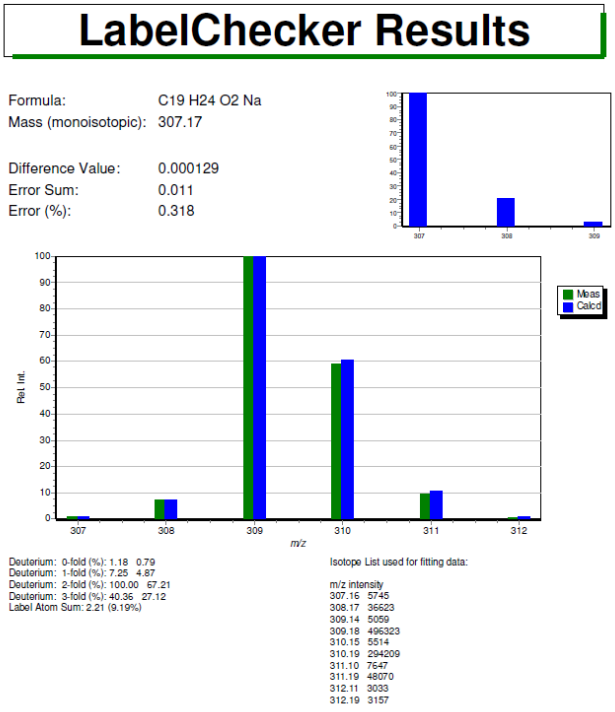
^{13}C NMR (100 MHz, $CDCl_3$) δ = 221.1, 157.7, 137.9, 132.2, 126.5, 114.0, 111.7, 55.4, 50.6, 48.2, 44.1, 38.5, 36.0, 31.7, 29.8, 26.7, 26.1, 21.7, 14.0 ppm.

NMR Data of Product:

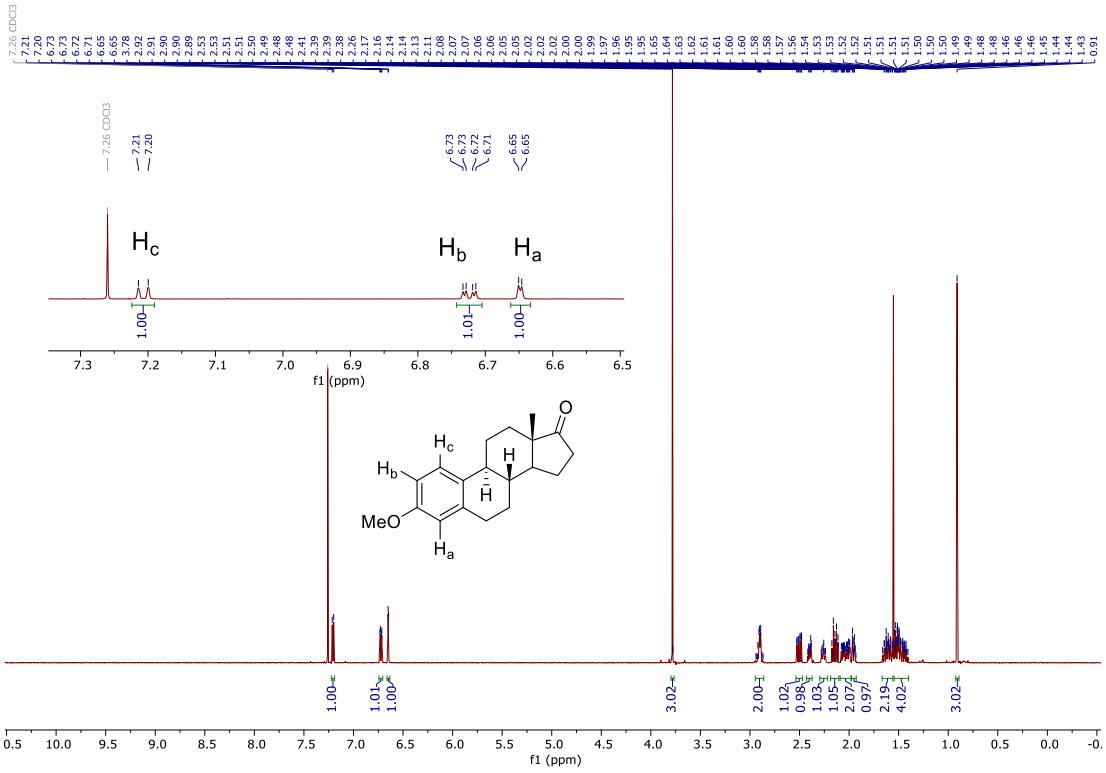
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.21 (s, 0.63H, 37% H), 6.75-6.70 (m, 0.04H, 96% H), 6.65 (s, 0.04H, 96% H), 3.78 (s, 3H), 2.96-2.85 (m, 2H), 2.55-2.46 (m, 1H), 2.44-2.35 (m, 1H), 2.26 (td, *J* = 10.8, 3.9 Hz, 1H), 2.20-1.90 (m, 4H), 1.70-1.36 (m, 6H), 0.91 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ = 221.0, 157.6, 137.8, 132.2-131.9 (1C), 126.3, 114.2-113.3 (1C), 111.8-111.2 (1C), 55.3, 50.5, 48.1, 44.1, 44.1, 38.5, 36.0, 31.7, 29.7, 26.7, 26.0, 21.7, 14.0 ppm.

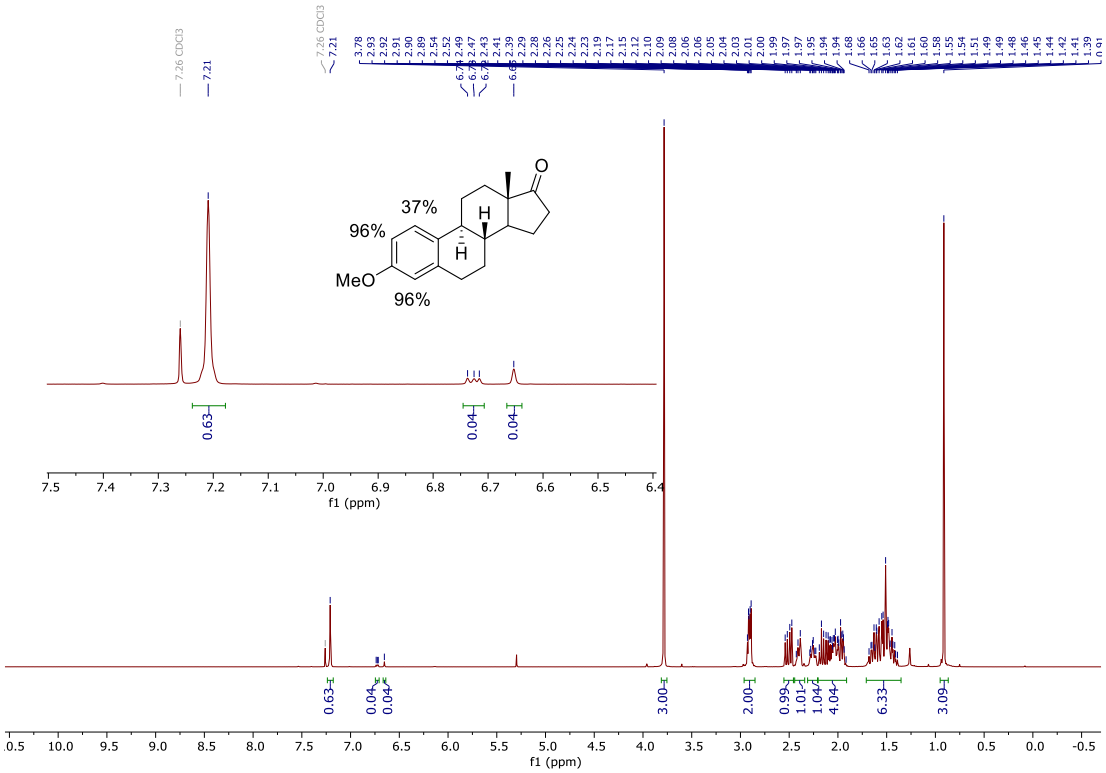
Mass Data:



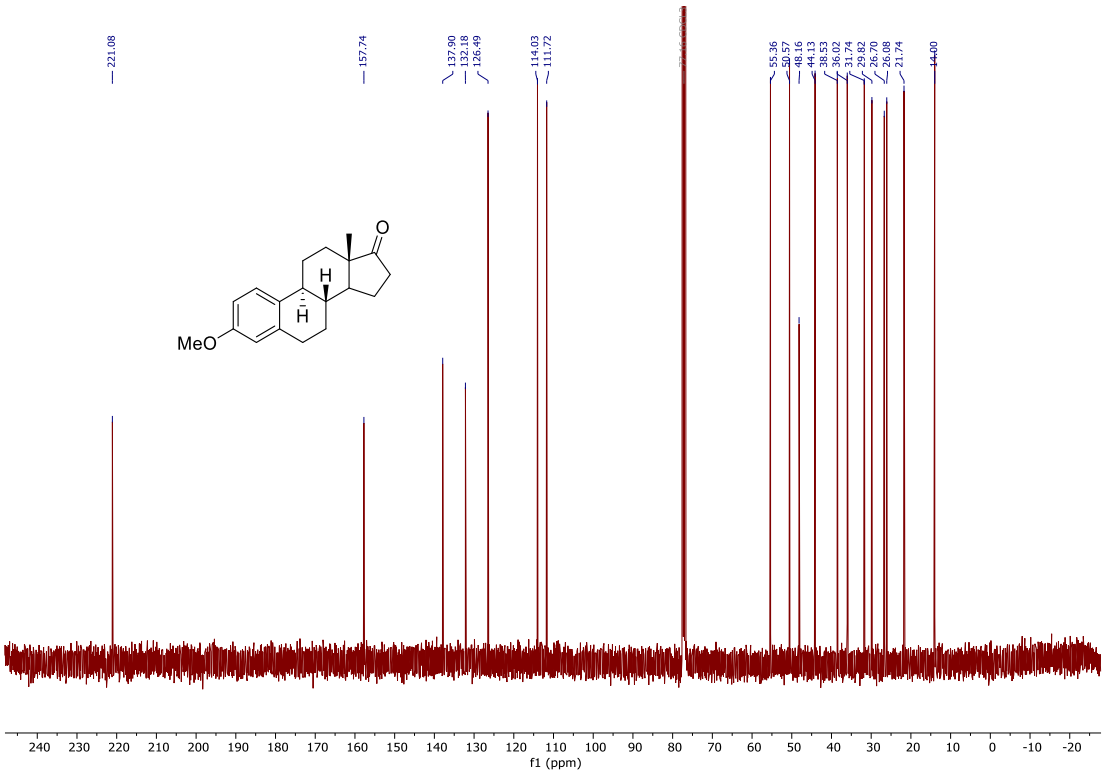
^{1}H-NMR spectrum in $CDCl_3$:



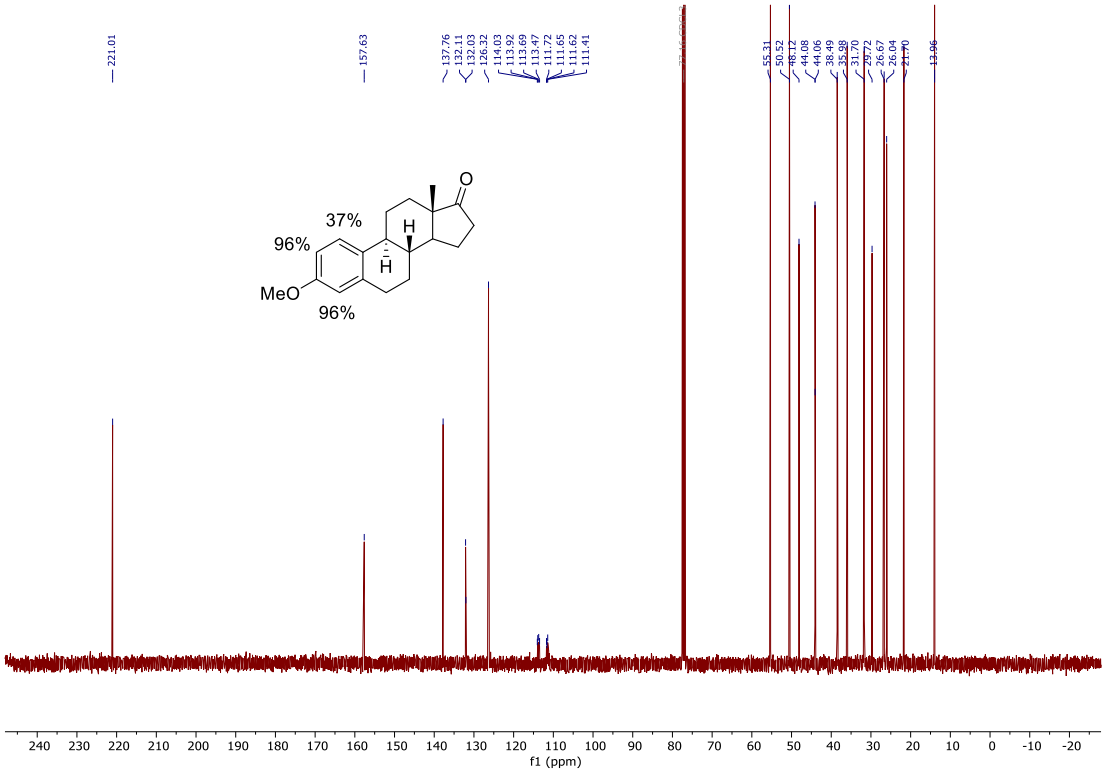
^{1}H-NMR spectrum in $CDCl_3$:



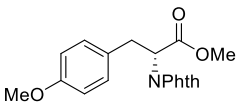
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of methyl (*R*)-2-(1,3-dioxoisoindolin-2-yl)-3-(4-methoxyphenyl)propanoate (21):



Following the general procedure E and using methyl (*R*)-2-(1,3-dioxoisoindolin-2-yl)-3-(4-methoxyphenyl)propanoate **(21)** (67.9 mg, 0.200 mmol), and purification via silica gel column chromatography using EtOAc as the eluent, the target compound **[D]21** was obtained as colorless solid (66.5 mg, 97%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 2.80 D/molecule [HRMS]; 2.81 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.78 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.69 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.07 (d, *J* = 8.7 Hz, 2H), 6.71 (d, *J* = 8.7 Hz, 2H), 5.11 (dd, *J* = 11.3, 5.3 Hz, 1H), 3.77 (s, 3H), 3.70 (s, 3H), 3.57-3.45 (m, 2H) ppm.

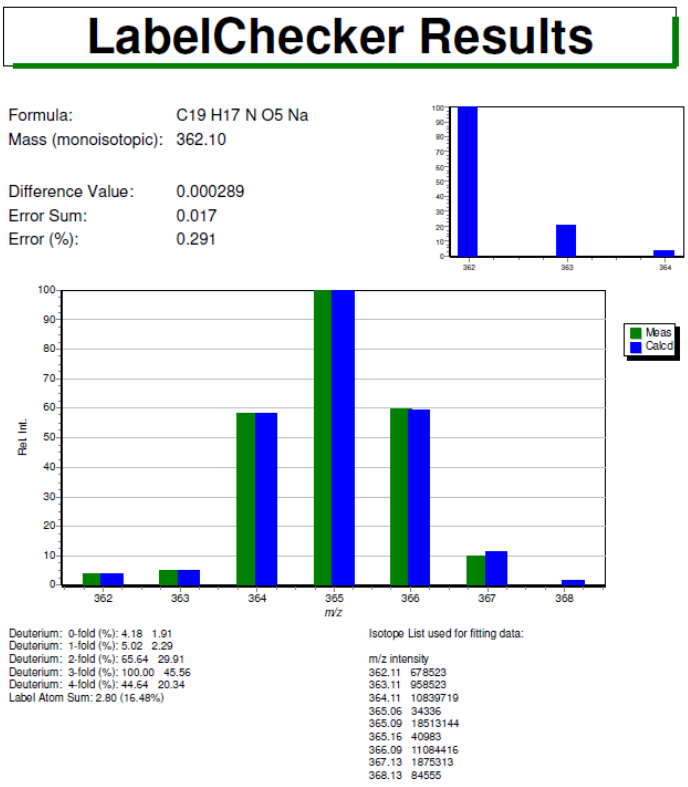
^{13}C NMR (100 MHz, $CDCl_3$) δ = 169.5, 167.6, 158.5, 134.2, 131.8, 130.0, 128.8, 123.6, 114.1, 55.2, 53.6, 53.0, 33.9 ppm.

NMR Data of Product:

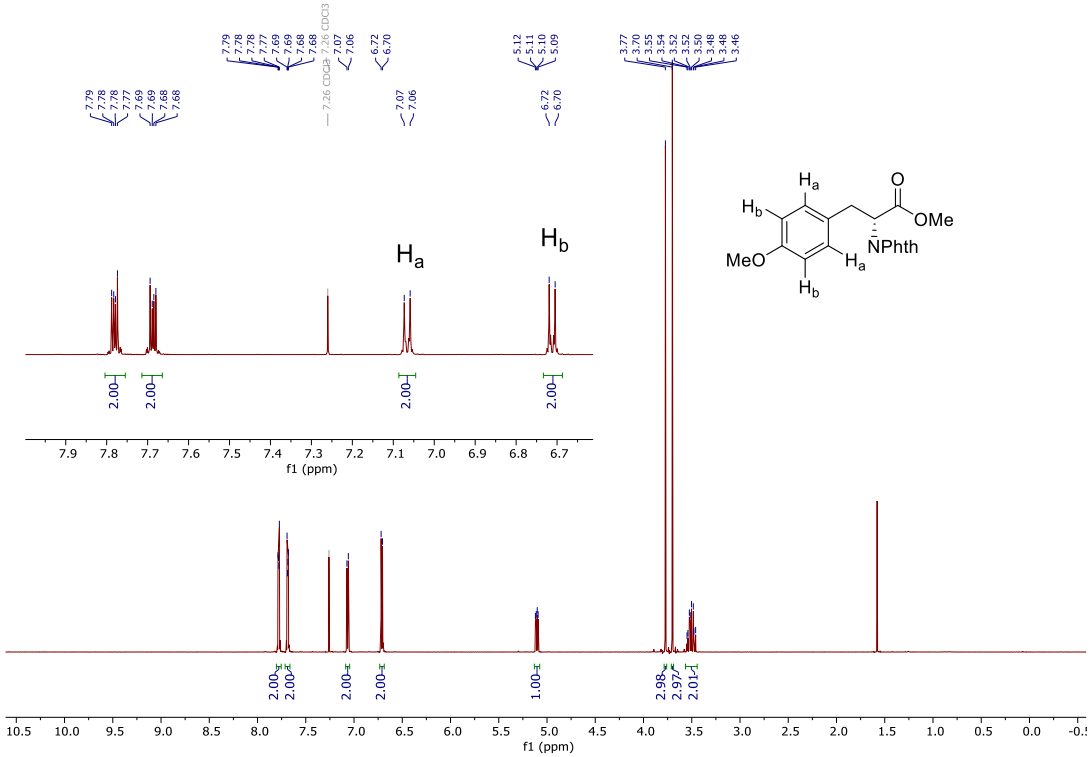
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.77 (dd, *J* = 5.4, 3.1 Hz, 1H), 7.68 (dd, *J* = 5.5, 3.0 Hz, 1H), 7.06 (s, 1.10H, 45% D), 6.73-6.69 (m, 0.09H, 96% D), 5.11 (dd, *J* = 10.9, 5.7 Hz, 1H), 3.77 (s, 3H), 3.69 (s, 3H), 3.57-3.43 (m, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ = 169.5, 167.6, 158.4, 134.2, 131.7, 129.8, 128.7-128.3 (2C), 123.6, 114.2-113.2 (2C), 55.2, 53.5, 53.0, 33.9-33.5 (1C) ppm.

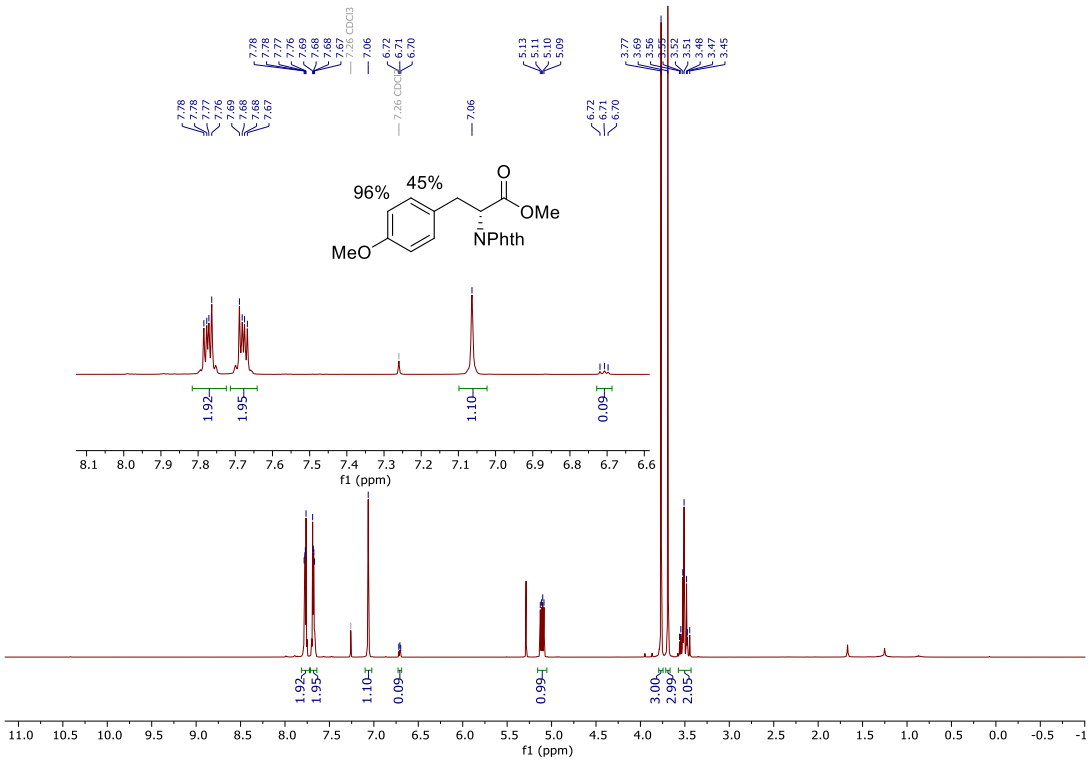
Mass Data:



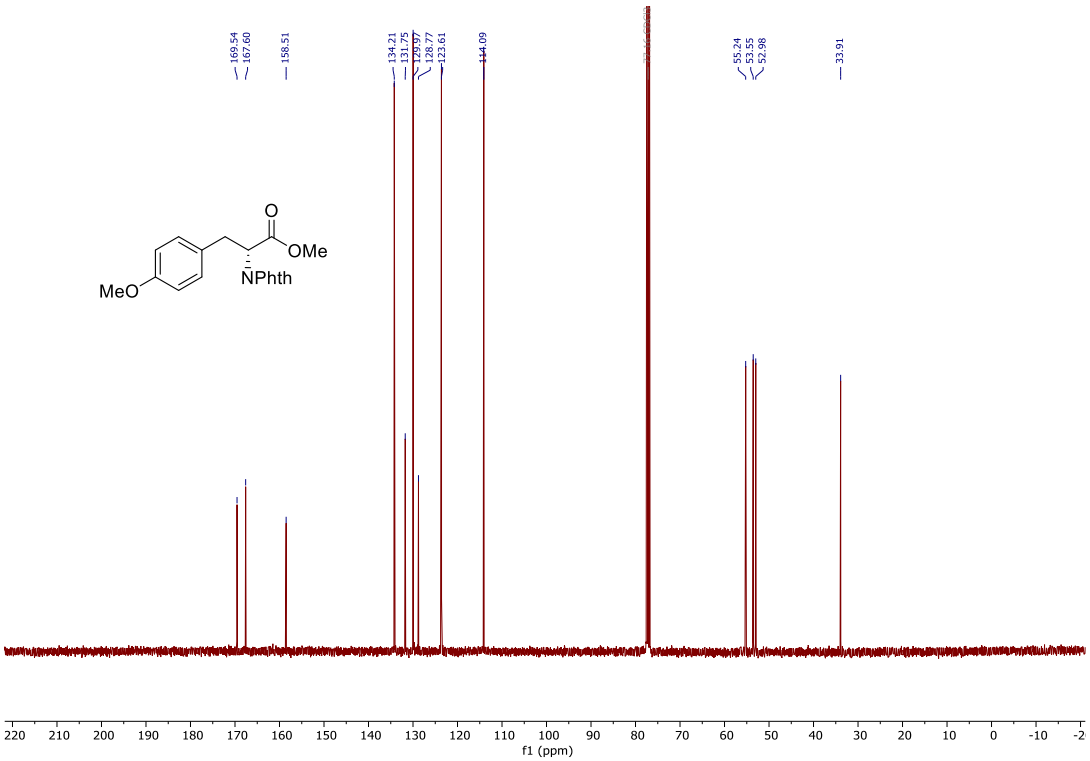
^{1}H-NMR spectrum in $CDCl_3$:



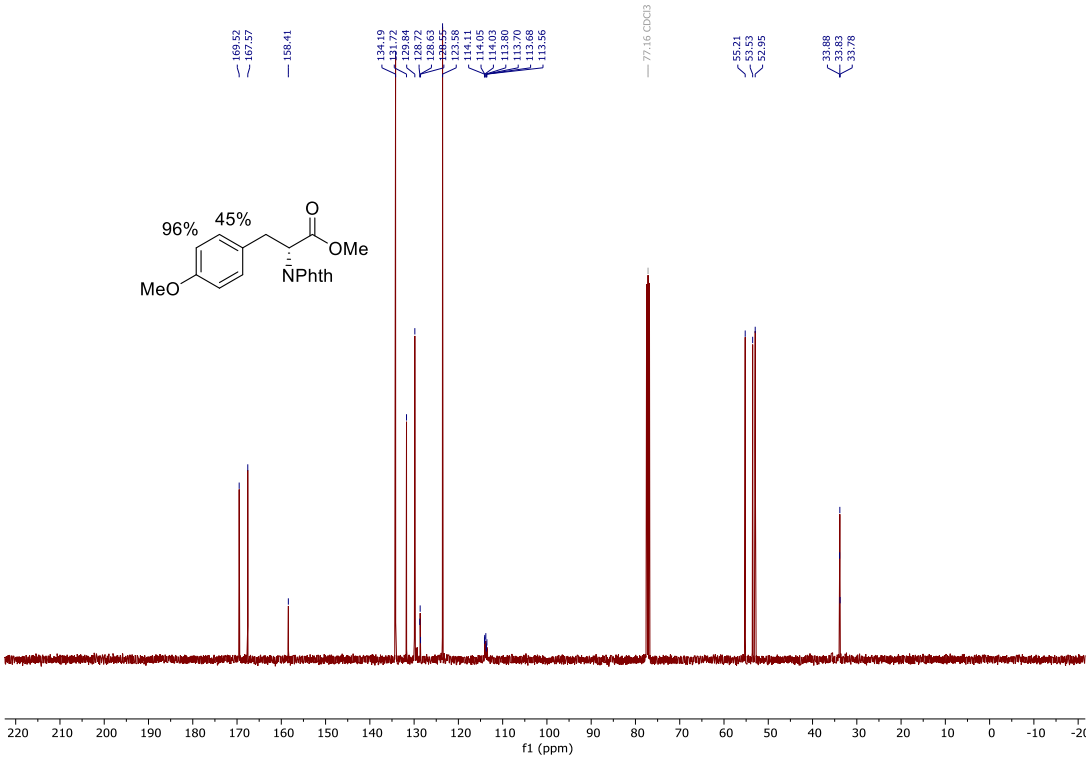
^{1}H-NMR spectrum in $CDCl_3$:



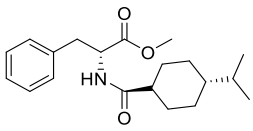
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of (*R*)-2-rel-((1*r*,4*R*)-4-Isopropylcyclohexanecarboxamido)-3-phenylpropanoate (22):



Following the general procedure E and using (*R*)-2-rel-((1*r*,4*R*)-4-Isopropylcyclohexanecarboxamido)-3-phenylpropanoate **(22)** (66.3 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAc = 80:20 as the eluent, the target compound **[D]22** was obtained as colorless liquid (62 mg, 92%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 4.42 D/molecule [HRMS]. 4.38 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.30-7.26 (m, 2H), 7.26-7.22 (m, 1H), 7.09-7.05 (m, 2H), 5.87 (d, *J* = 7.7 Hz, 1H), 4.91-4.86 (m, 1H), 3.73 (s, 3H), 3.18-3.06 (m, 2H), 2.04-1.95 (m, 1H), 1.92-1.82 (m, 2H), 1.80-1.73 (m, 2H), 1.45-1.33 (m, 3H), 1.09-0.91 (m, 3H), 0.85 (d, *J* = 6.8 Hz, 6H) ppm.

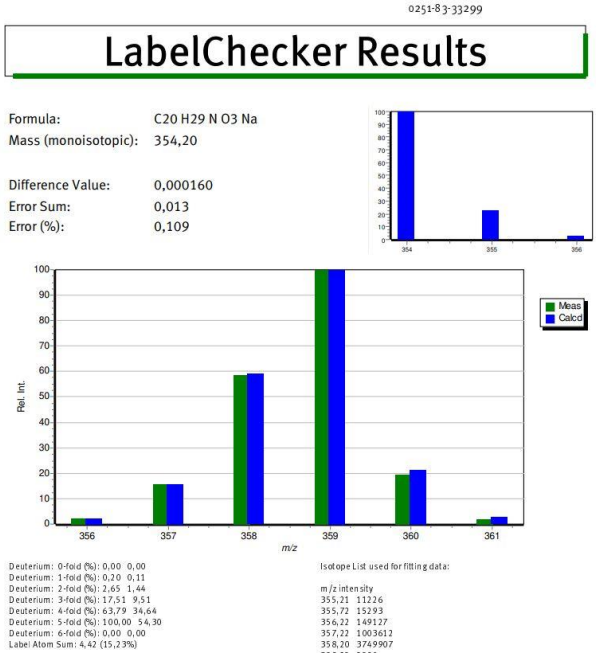
^{13}C NMR (125 MHz, $CDCl_3$) δ = 175.7, 172.4, 136.1, 129.5, 128.6, 127.2, 52.8, 52.4, 45.6, 43.4, 38.0, 32.9, 29.9, 29.6, 29.1, 29.0, 19.8(65), 19.8(61) ppm.

NMR Data of Product:

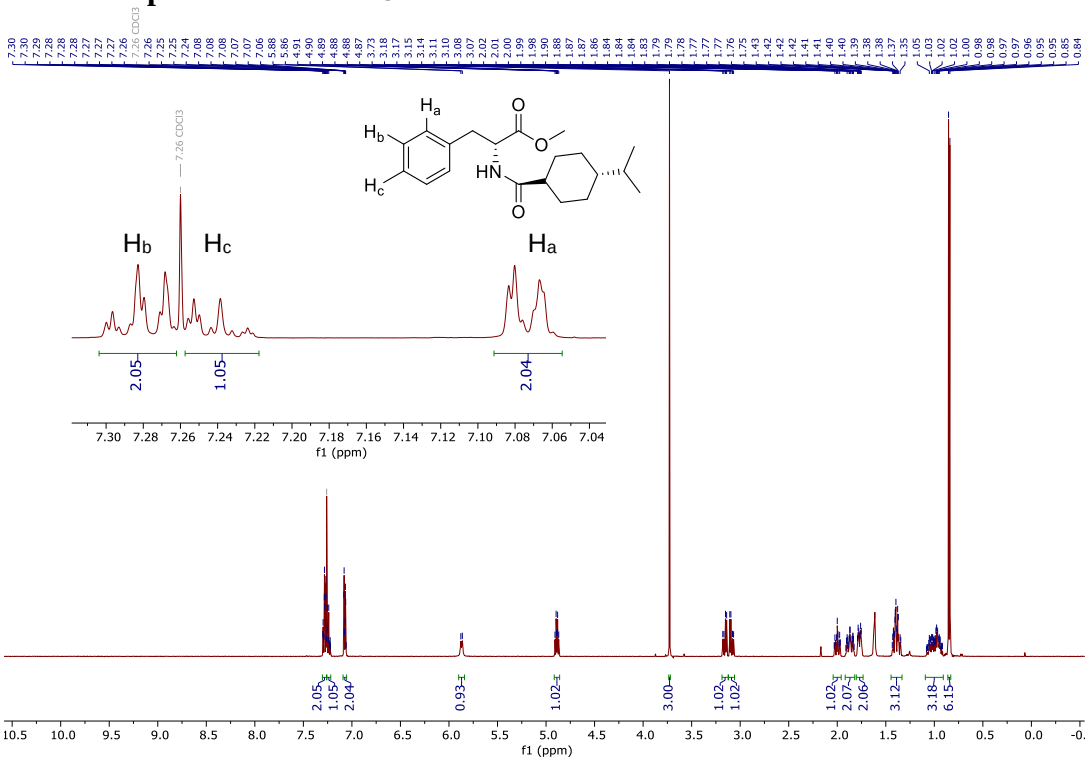
^{1}H NMR (600 MHz, CDCl3) δ = 7.30-7.26 (m, 0.29H, 85.5% D), 7.25-7.21 (m, 0.09H, 91% D, 7.09-7.05 (m, 0.24H, 88% D), 5.87 (d, *J* = 7.8 Hz, 1H), 4.91-4.86 (m, 1H), 3.73 (s, 3H), 3.20-3.05 (m, 1H), 2.04-1.96 (m, 1H), 1.92-1.82 (m, 2H), 1.80-1.74 (m, 2H), 1.44-1.34 (m, 3H), 1.09-0.91 (m, 3H), 0.85 (d, *J* = 6.8 Hz, 6H) ppm.

^{13}C NMR (126 MHz, $CDCl_3$) δ =175.7, 172.3, 136.0-135.9(1C), 129.3-127.4 (5C), 52.9, 52.4, 45.7, 43.4, 38.0-37.9(1C), 32.9, 29.9, 29.6, 29.1, 29.0, 19.8, 19.8(7)-19.8(6) ppm.

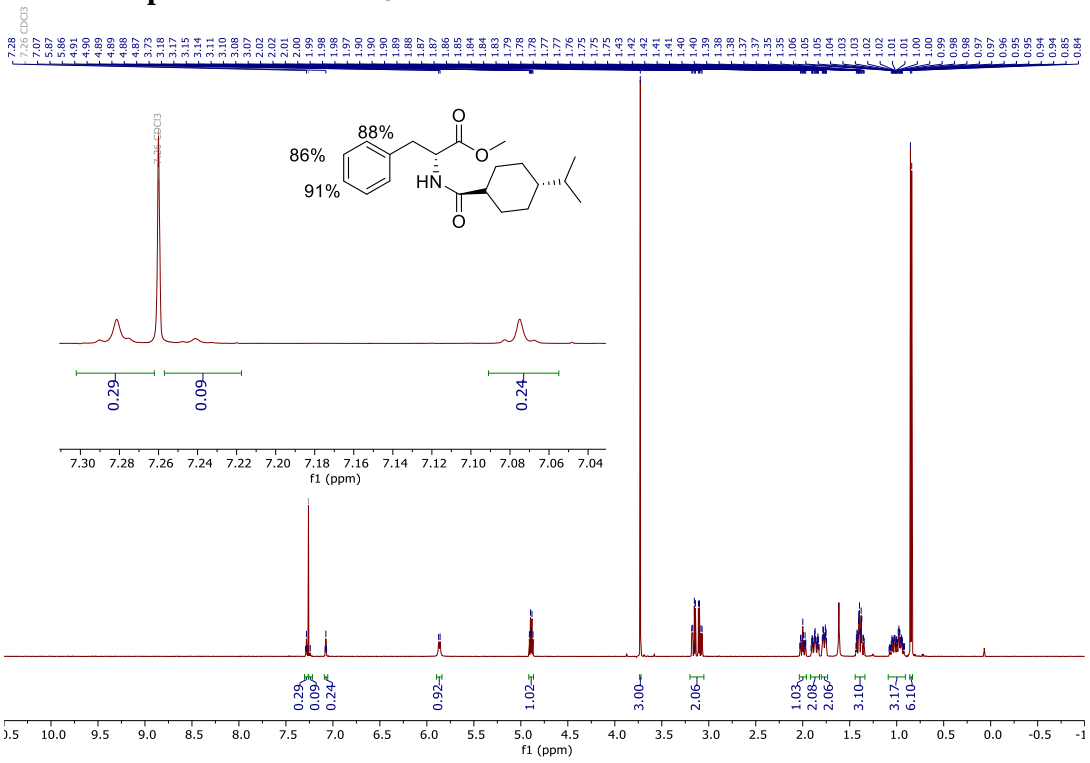
Mass Data:



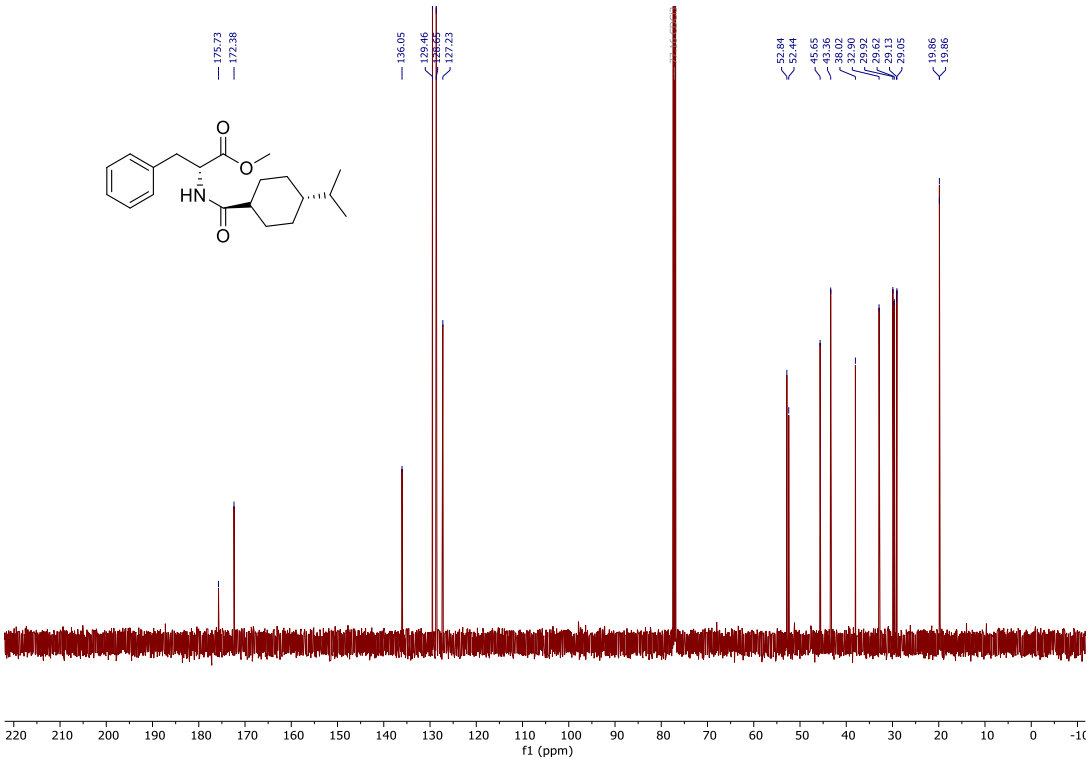
^{1}H-NMR spectrum in $CDCl_3$:



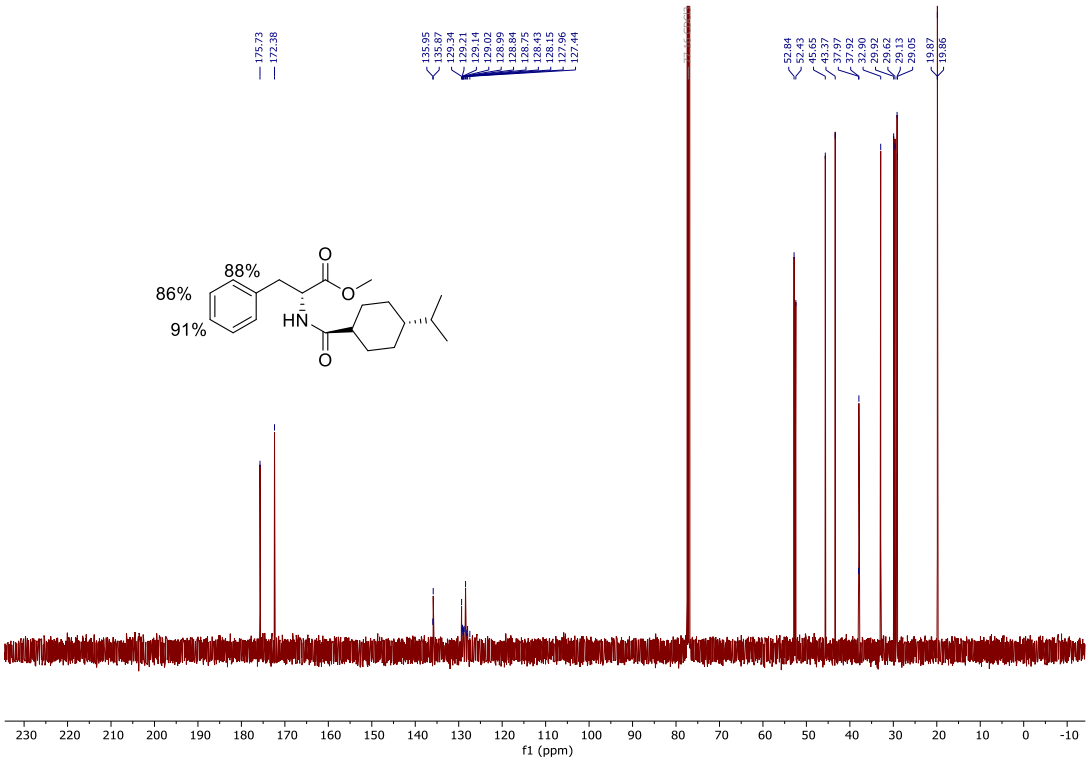
^{1}H-NMR spectrum in $CDCl_3$:



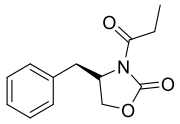
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of (*R*)-4-benzyl-3-propionyloxazolidin-2-one (23):



Following the general procedure E and using (*R*)-4-benzyl-3-propionyloxazolidin-2-one (**23**) (46.7 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAc = 80:20 as the eluent, the target compound **[D]23** was obtained as colorless liquid (46.5 mg, 98%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 3.63 D/molecule [HRMS]; 3.78 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.36-7.31 (m, 2H), 7.30-7.26 (m, 1H), 7.22-7.19 (m, 2H), 4.70-4.64 (m, 1H), 4.22-4.15 (m, 2H), 3.31 (dd, *J* = 13.4, 3.4 Hz, 1H), 3.04-2.88 (m, 2H), 2.77 (dd, *J* = 13.4, 9.6 Hz, 1H), 1.21 (t, *J* = 7.4 Hz, 3H) ppm.

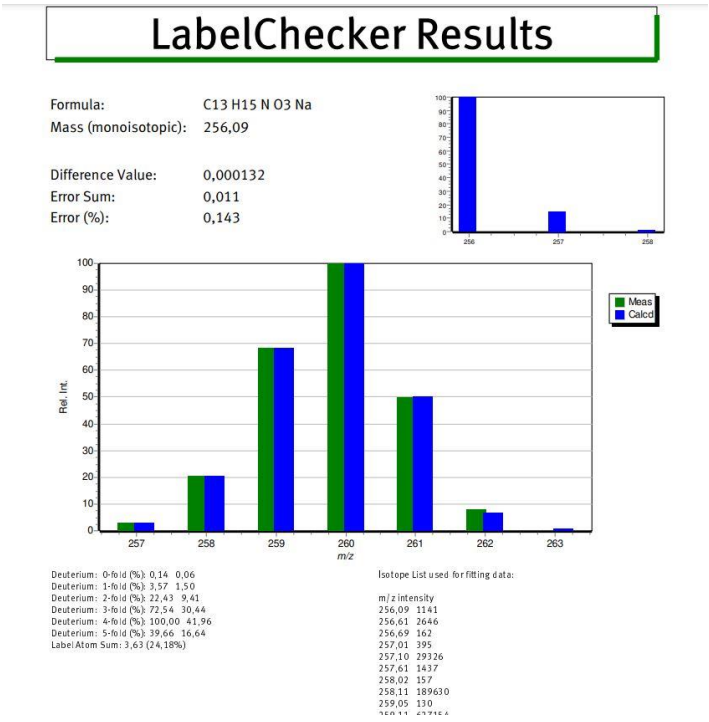
^{13}C NMR (126 MHz, $CDCl_3$) δ = 174.2, 153.7, 135.5, 129.6, 129.1, 127.5, 66.4, 55.3, 38.1, 29.3, 8.4 ppm.

NMR Data of Product:

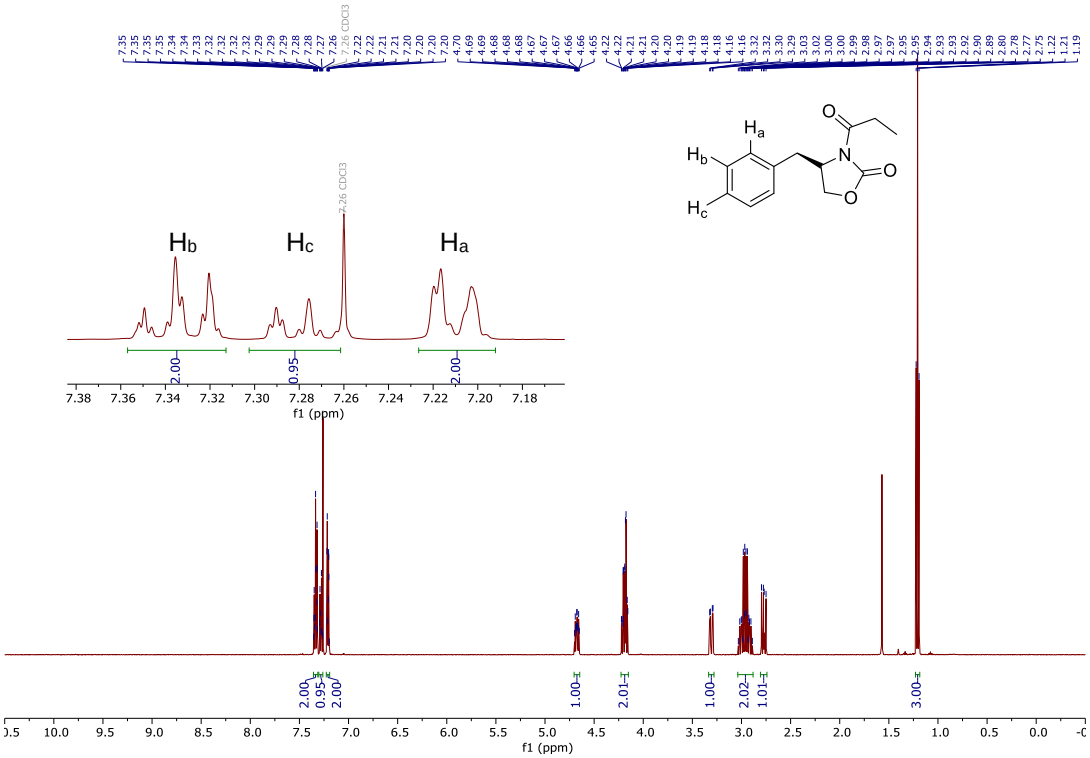
^{1}H NMR (600 MHz, CDCl3) δ = 7.35-7.31 (m, 0.32H, 84% D), 7.28-7.26 (m, 0.06H, 94% D), 7.23-7.18 (m, 0.84H, 58% D) 4.70-4.64 (m, 1H), 4.22-4.13 (m, 2H), 3.31 (dd, *J* = 13.4, 3.4 Hz, 1H), 3.03-2.88 (m, 2H), 2.77 (dd, *J* = 13.4, 9.6 Hz, 1H), 1.20 (t, *J* = 7.4 Hz, 3H) ppm.

^{13}C NMR (126 MHz, $CDCl_3$) δ = 174.2, 153.6, 135.4-135.3(1C), 129.5-128.3(4C), 127.3-126.7(1C), 66.3, 55.3, 38.0-37.9(1C), 29.3, 8.4 ppm.

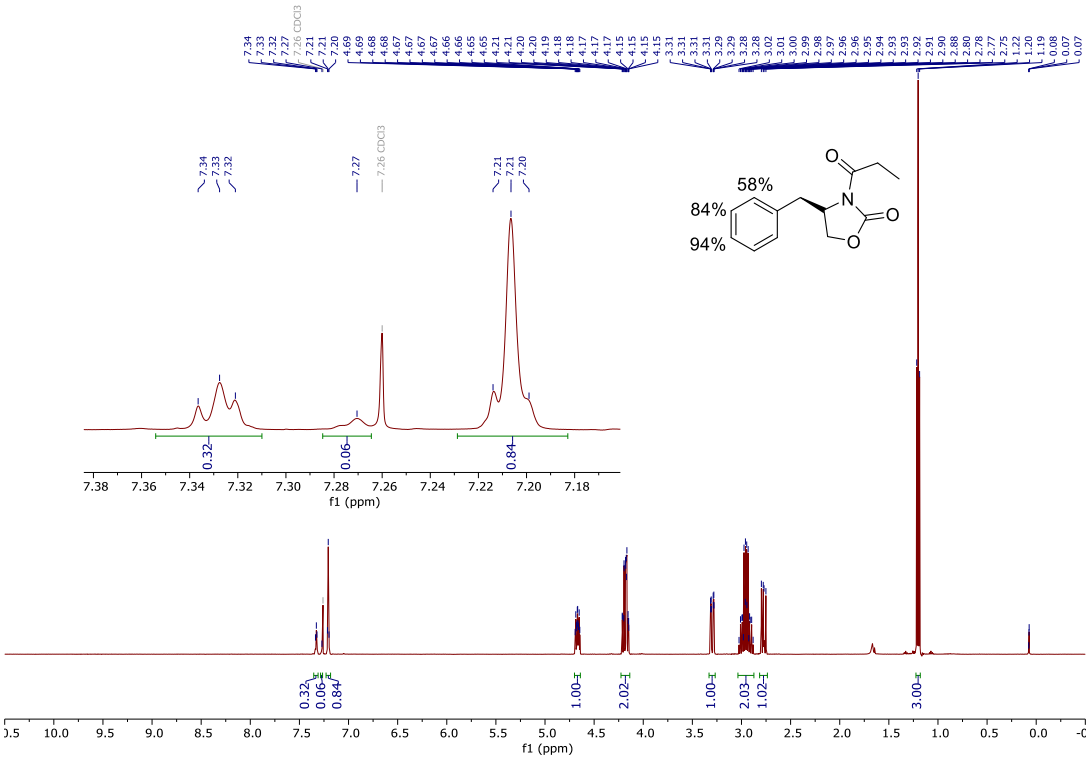
Mass Data:



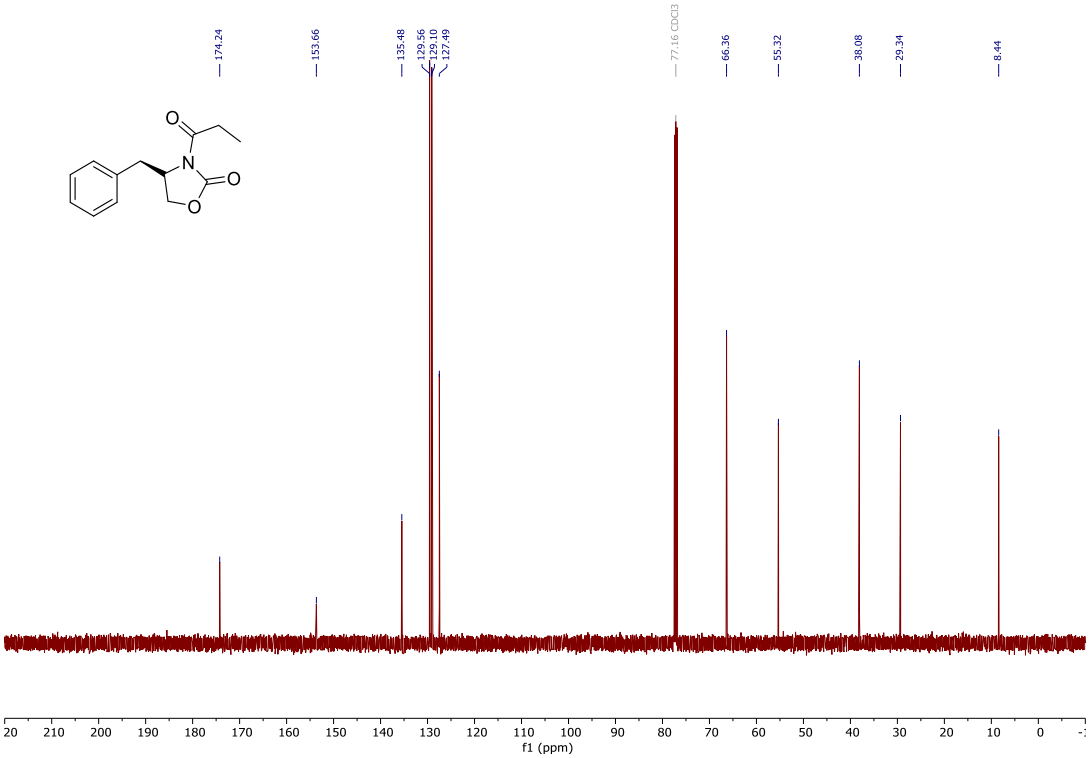
^{1}H-NMR spectrum in $CDCl_3$:



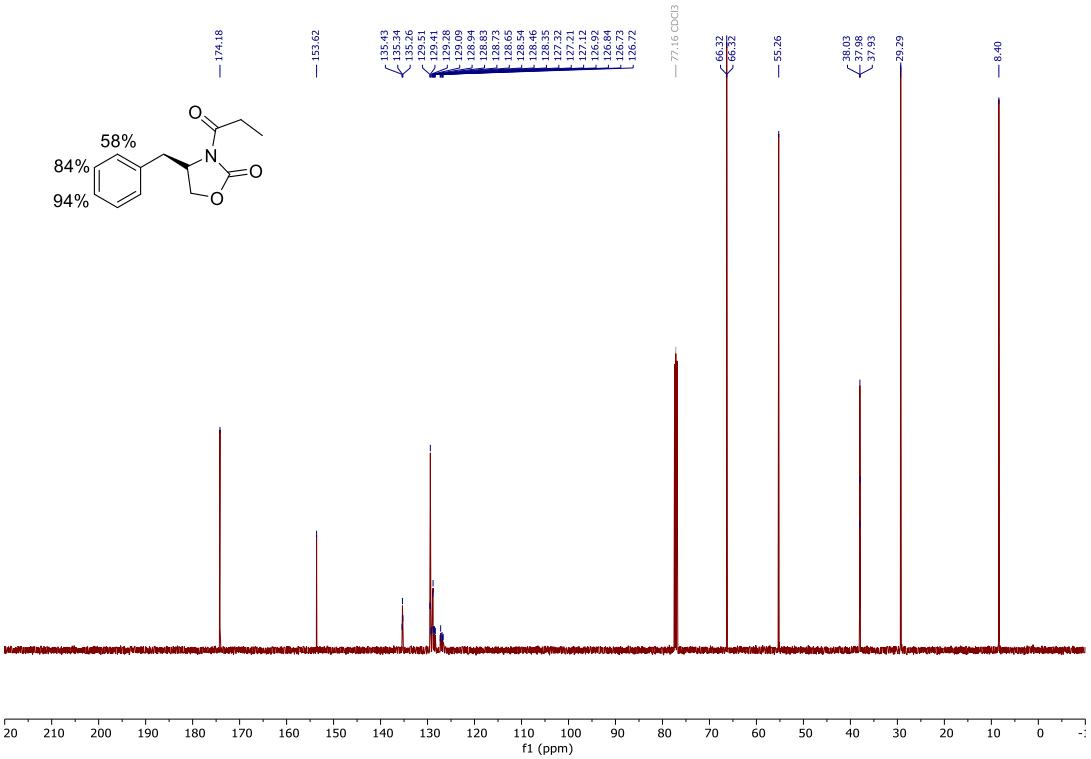
^{1}H-NMR spectrum in $CDCl_3$:



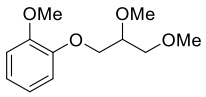
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of 1-(2,3-dimethoxypropoxy)-2-methoxybenzene (24)



Following the general procedure E and using 1-(2,3-dimethoxypropoxy)-2-methoxybenzene (**24**) (45.3 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAc = 80:20 as the eluent, the target compound **[D]24** was obtained as colorless liquid (41.8 mg, 91%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 3.85 D/molecule [HRMS]; 3.84 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

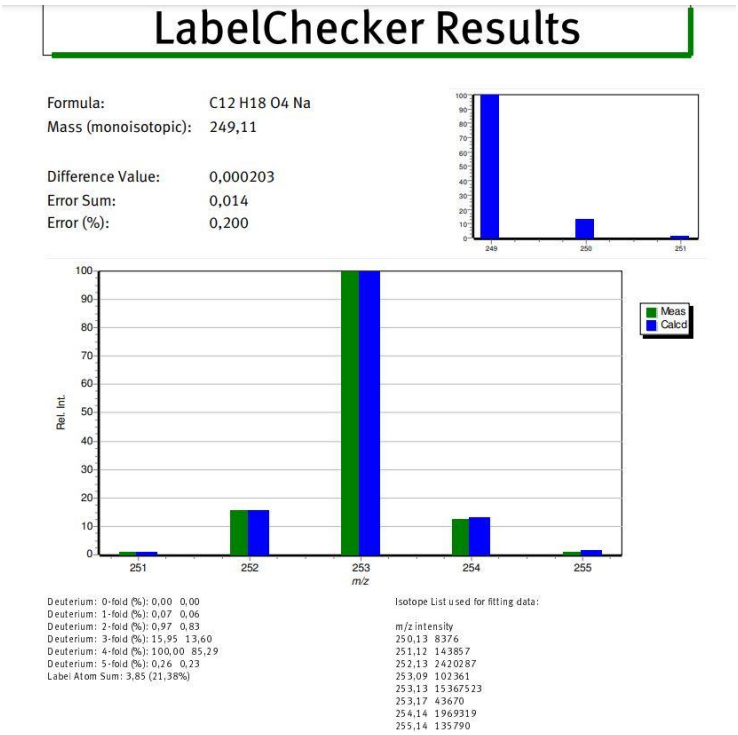
^{1}H NMR (599 MHz, C_6D_6) δ = 6.85-6.81 (m, 1H), 6.81-6.78 (m, 2H), 6.65-6.62 (m, 1H), 4.07-3.99 (m, 2H), 3.71 (p, *J* = 5.2 Hz, 1H), 3.51-3.43 (m, 2H), 3.39 (s, 3H), 3.34 (s, 3H), 3.09 (s, 3H) ppm.

^{13}C NMR (151 MHz, C_6D_6) δ = 150.6, 149.6, 121.6, 121.2, 114.6, 112.9, 79.3, 72.8, 69.6, 58.9, 58.1, 55.6 ppm.

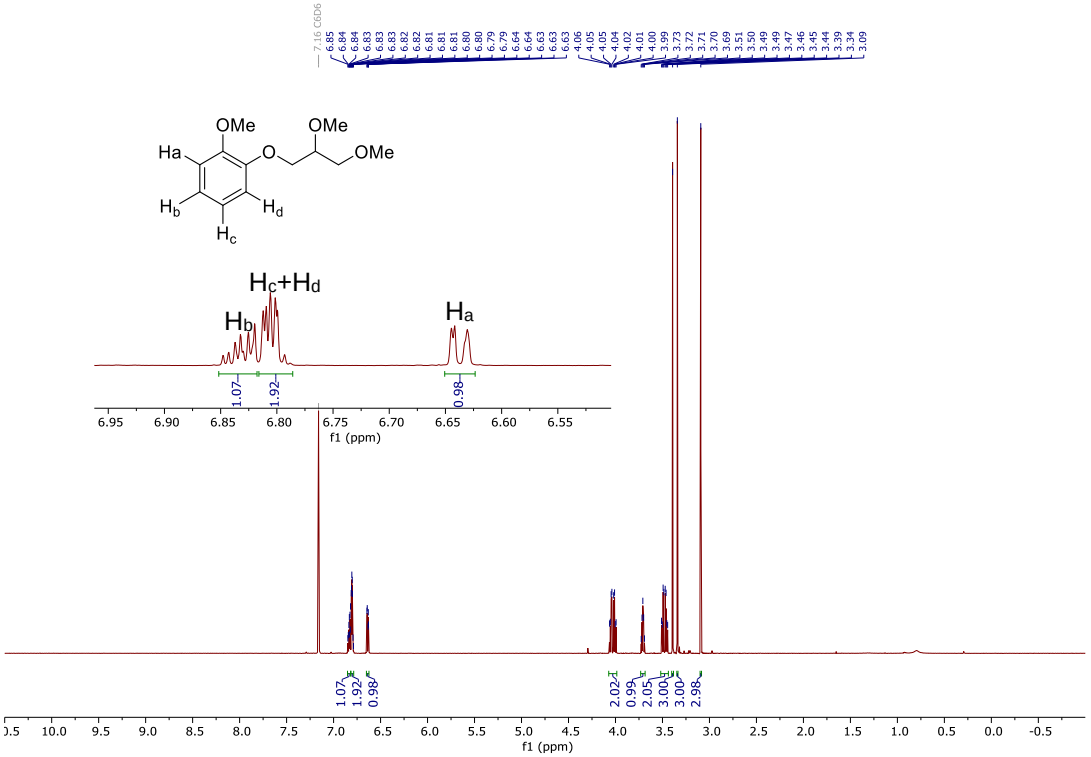
^{1}H NMR (599 MHz, C_6D_6) δ = 6.84-6.82 (m, 0.04H, 96% D), 6.81-6.79 (m, 0.08H, 96% D), 6.65-6.63 (m, 0.04H, 96% D), 4.07-3.98 (m, 2H), 3.71 (p, *J* = 5.2 Hz, 1H), 3.52-3.43 (m, 2H), 3.40 (s, 3H), 3.34 (s, 3H), 3.09 (s, 3H) ppm.

^{13}C NMR (151 MHz, C_6D_6) δ = 150.1, 149.1, 121.0-120.8(2C), 114.1-113.6(1C), 112.4-111.9(1C), 78.9, 72.4, 69.1, 58.5, 57.7, 55.2 ppm.

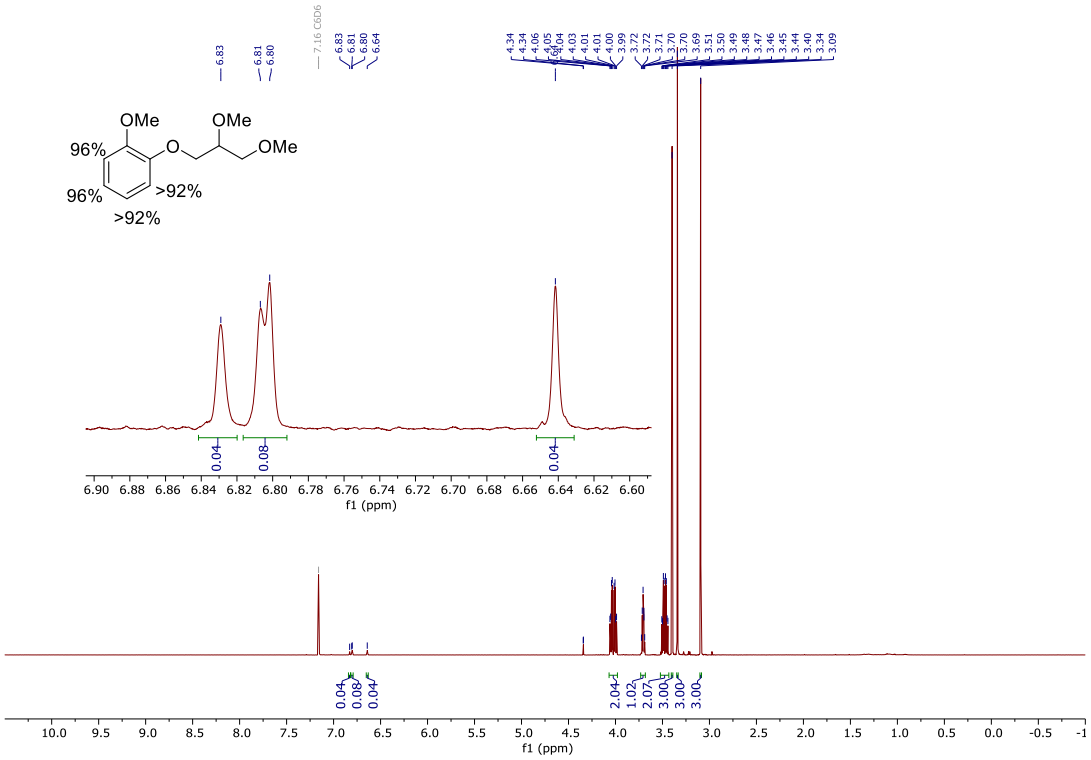
Mass Data:



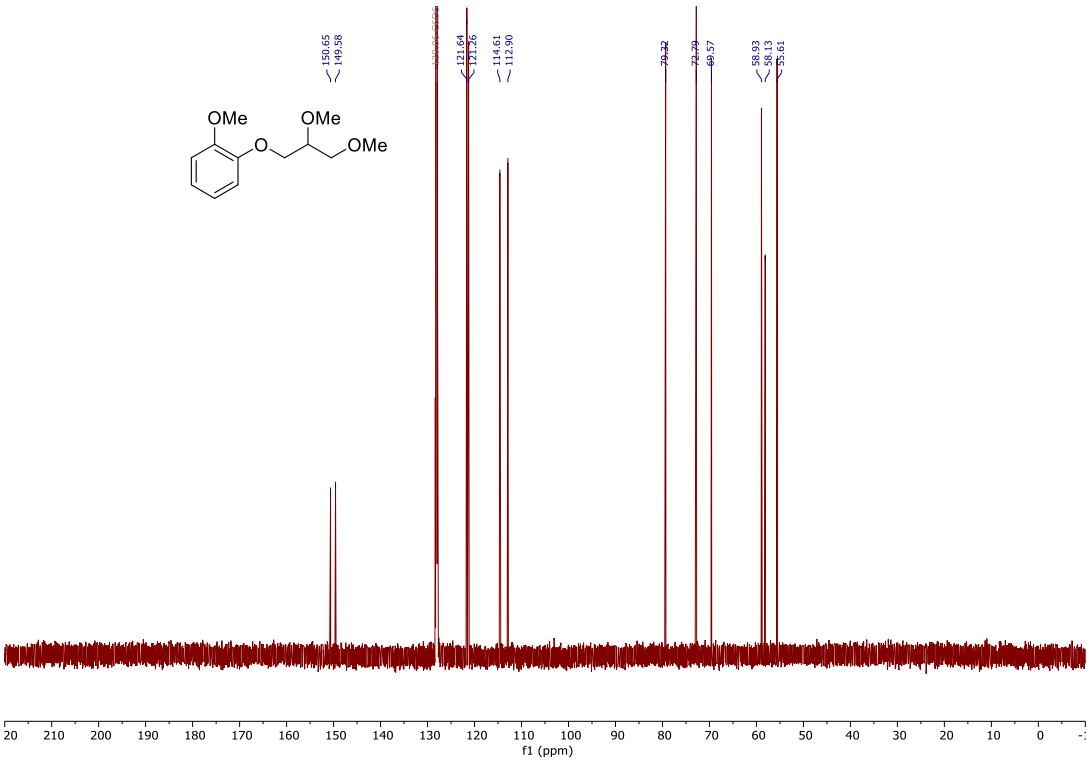
^{1}H-NMR spectrum in C_6D_6:



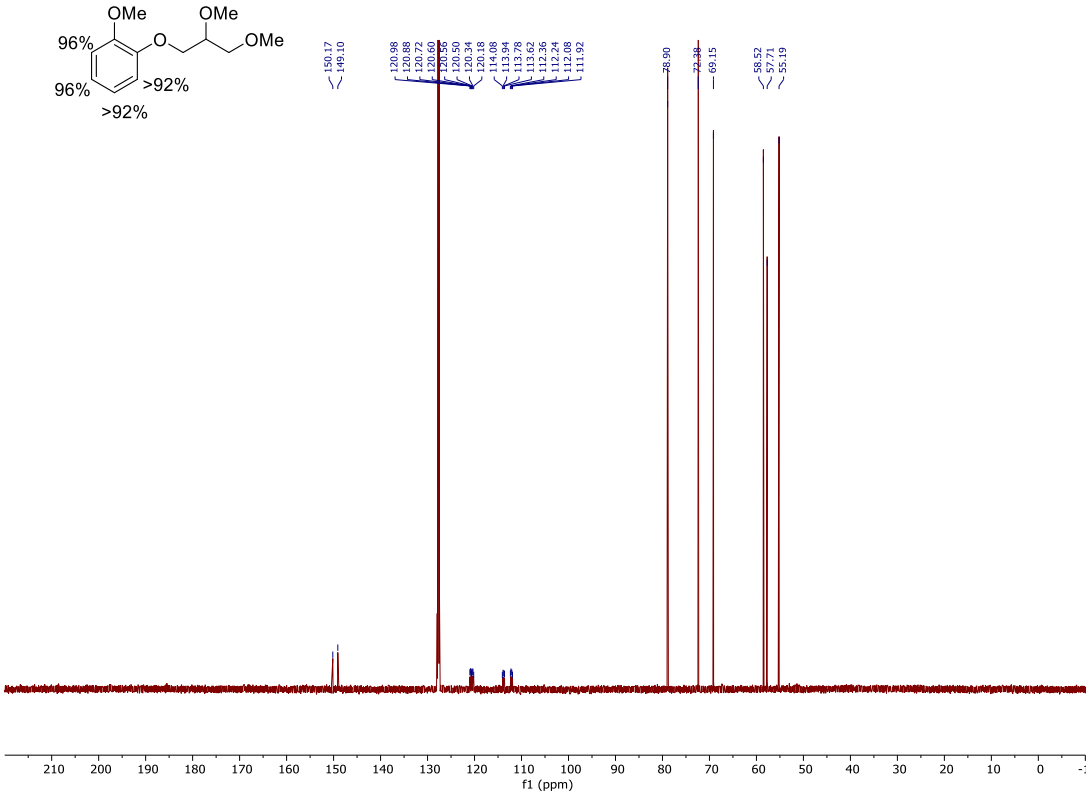
^{1}H-NMR spectrum in C_6D_6



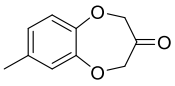
^{13}C-NMR spectrum in C_6D_6:



^{13}C-NMR spectrum in C_6D_6:



Deuteration of 7-methyl-2*H*-benzo[*b*][1,4]dioxepin-3(4*H*)-one (25):



Following the general procedure E and using 7-methyl-2*H*-benzo[*b*][1,4]dioxepin-3(4*H*)-one **(25)** (35.6 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAc = 15:1 as the eluent, the target compound **[D]25** was obtained as a colorless solid (31.2 mg, 86%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 2.44 D/molecule [HRMS]; 2.37 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.89 (d, *J* = 8.2 Hz, 1H), 6.81 (d, *J* = 2.1 Hz, 1H), 6.77 (dd, *J* = 8.2, 2.1 Hz, 1H), 4.70 (s, 2H), 4.67 (s, 2H), 2.27 (s, 3H) ppm.

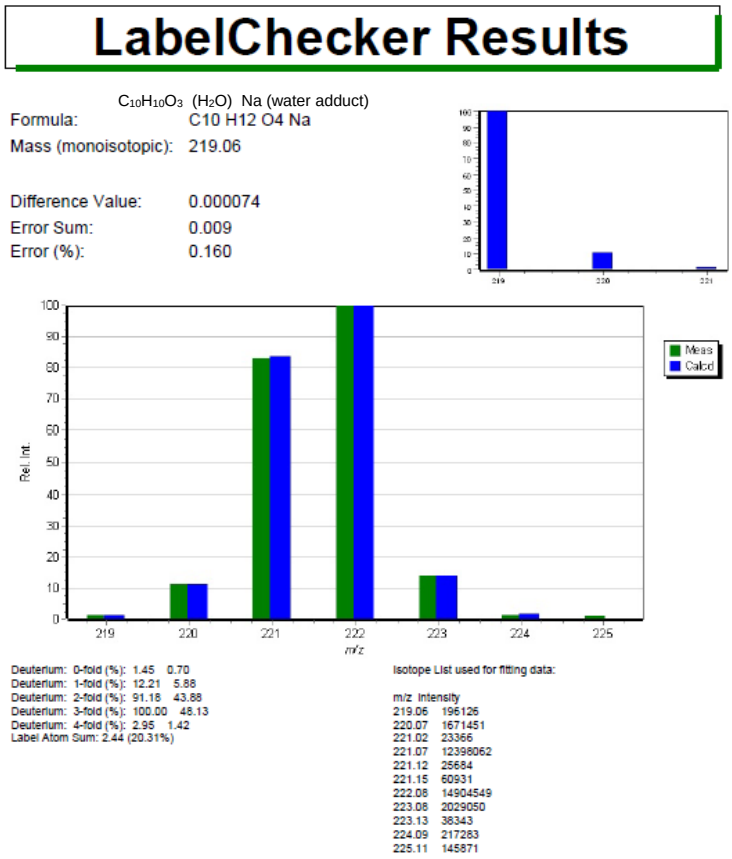
^{13}C NMR (101 MHz, $CDCl_3$) δ = 204.9, 148.1, 146.2, 133.9, 124.4, 121.3, 120.8, 75.9, 75.6, 20.6 ppm.

NMR Data of Product:

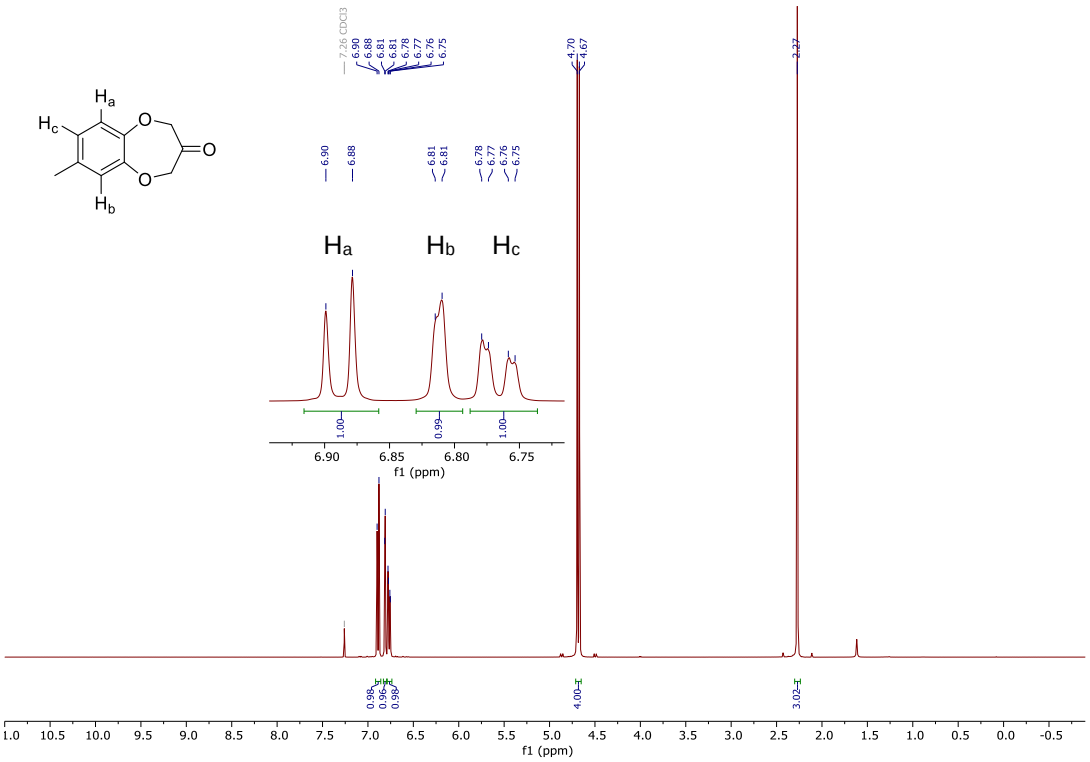
^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.91-6.87 (m, 0.06H, 94%D), 6.82-6.70 (m, 0.45H, 65%D), 6.78-6.75 (m, 0.12H, 88%D), 4.70 (s, 2H), 4.68 (s, 2H), 2.27 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 205.0, 148.1, 146.2, 134.0-133.6 (1C), 124.5-123.8 (1C), 121.3, 121.0-120.4 (1C), 75.9, 75.6, 20.6-20.5 (1C) ppm.

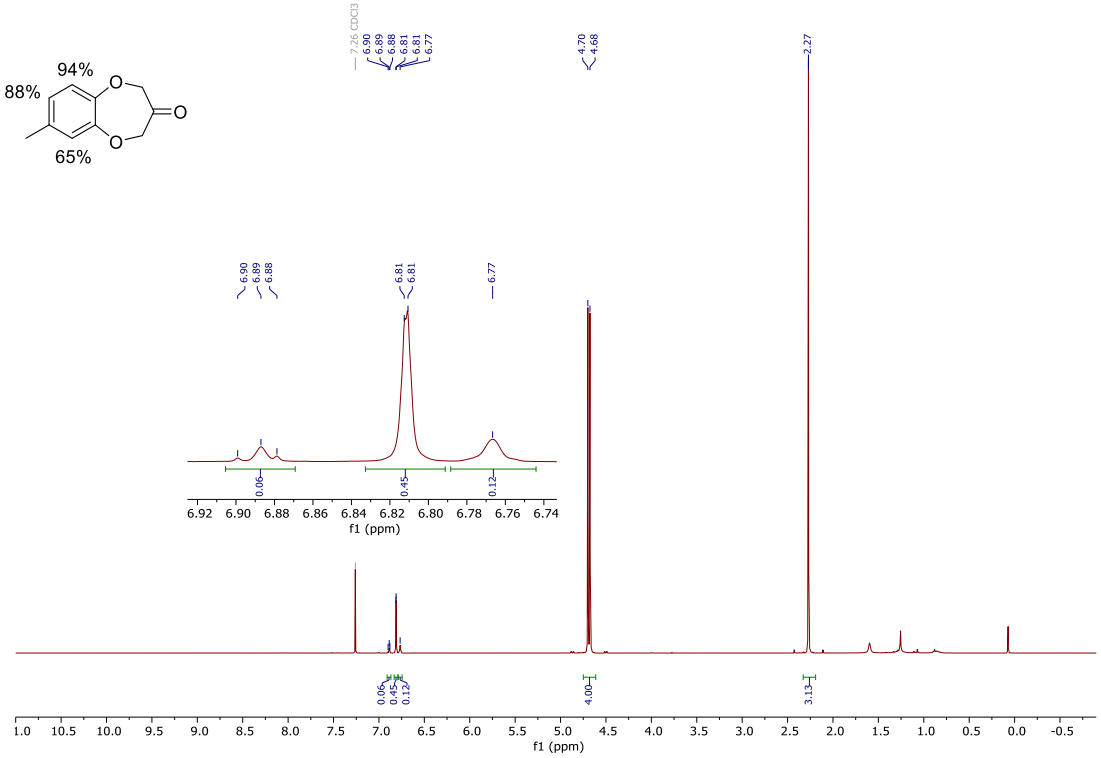
Mass Data:



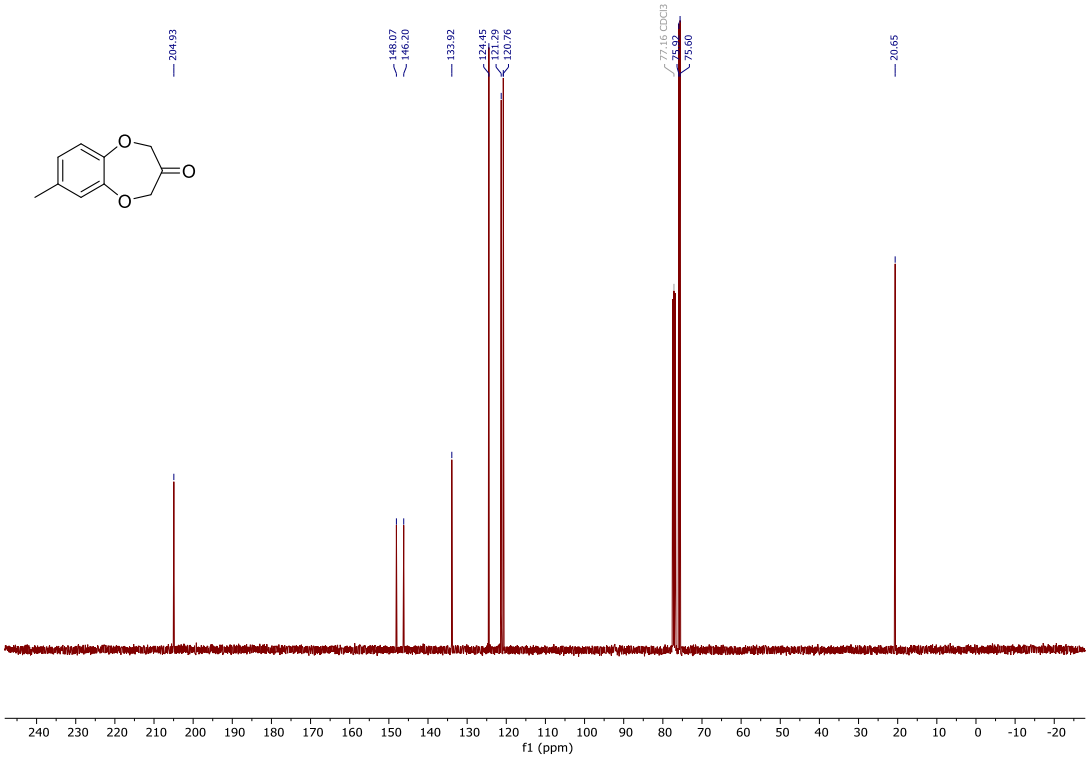
^{1}H-NMR spectrum in $CDCl_3$:



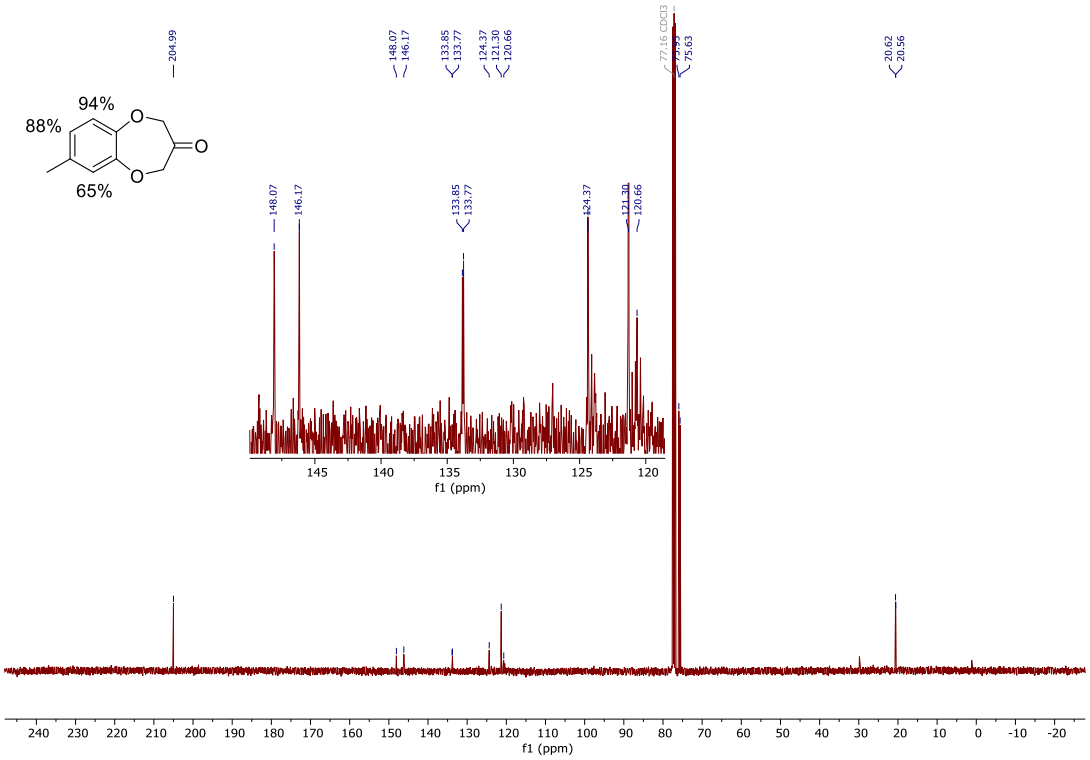
^{1}H-NMR spectrum in $CDCl_3$:



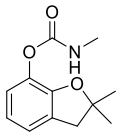
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of 2,2-dimethyl-2,3-dihydrobenzofuran-7-yl methylcarbamate (26):



Following the general procedure E and using 2,2-dimethyl-2,3-dihydrobenzofuran-7-yl methylcarbamate **(26)** (44.3 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAc = 10:3 as the eluent, the target compound **[D]26** was obtained as a colorless solid (38.1 mg, 85%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 2.86 D/molecule [HRMS]; 2.86 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.97 (d, *J* = 7.8 Hz, 1H), 6.94 (d, *J* = 7.8 Hz, 1H), 6.78 (dd, *J* = 7.8, 7.8 Hz, 1H), 5.05 (br s, 1H)*, 3.03 (s, 2H), 2.88 (d, *J* = 4.9 Hz, 3H)*, 1.49 (s, 6H) ppm.

*major rotamer peak reported

^{13}C NMR (101 MHz, $CDCl_3$) δ = 154.7, 150.3, 134.8, 129.5, 122.1, 121.9, 120.1, 88.2, 43.1, 28.2, 27.8 ppm.

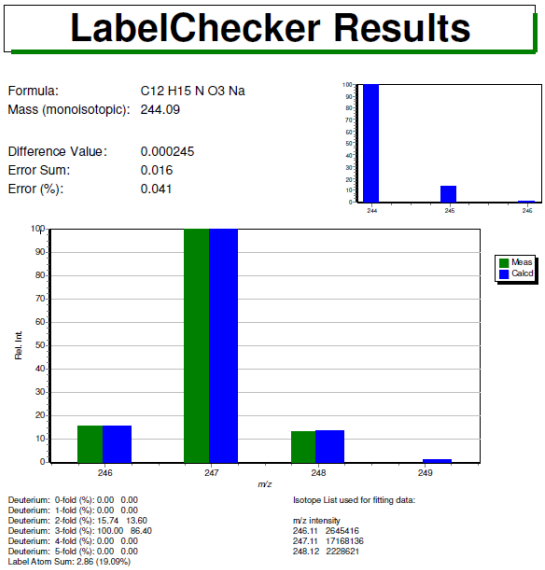
NMR Data of Product:

^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.97 (s, 0.06H, 94% D), 6.94 (s, 0.04H, 96% D), 6.78 (s, 0.04H, 96% D), 5.05 (br. s, 1H)*, 3.03 (s, 2H), 2.88 (d, *J* = 4.9 Hz, 3H)*, 1.49 (s, 6H) ppm.

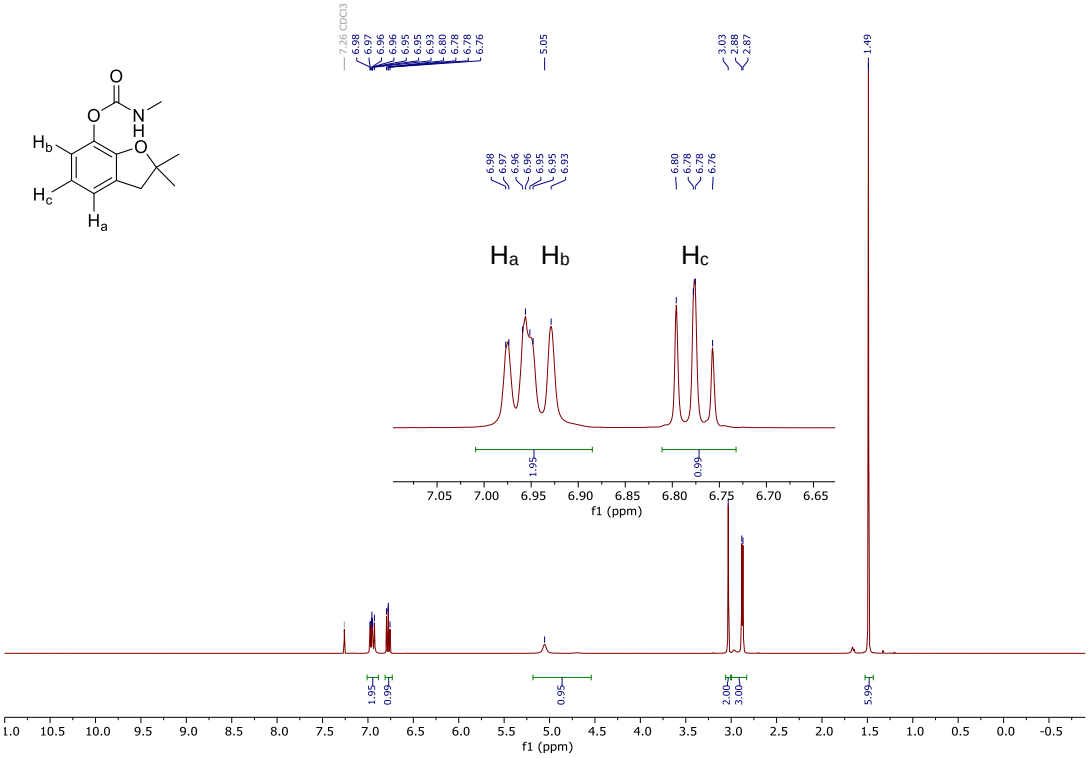
*major rotamer peak reported

^{13}C NMR (101 MHz, $CDCl_3$) δ = 154.7, 150.3, 134.8, 129.5, 122.1-121.2 (2C), 120.2-119.3(1C), 88.2, 43.1, 28.2, 27.8 ppm.

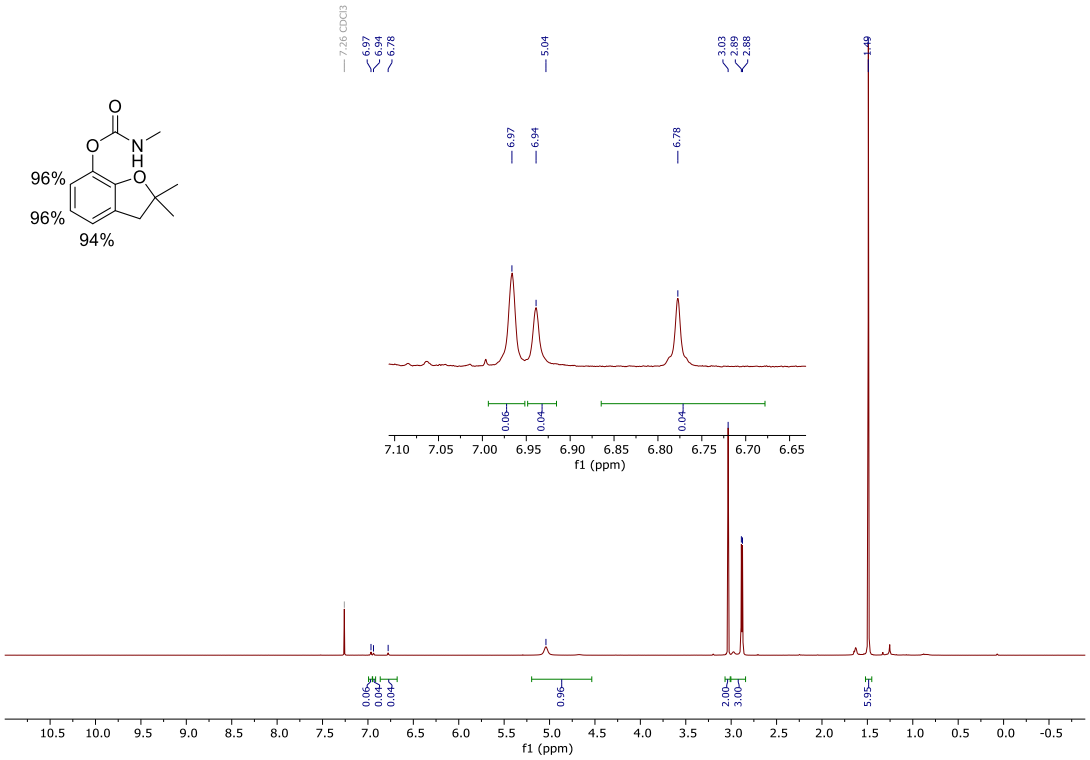
Mass Data:



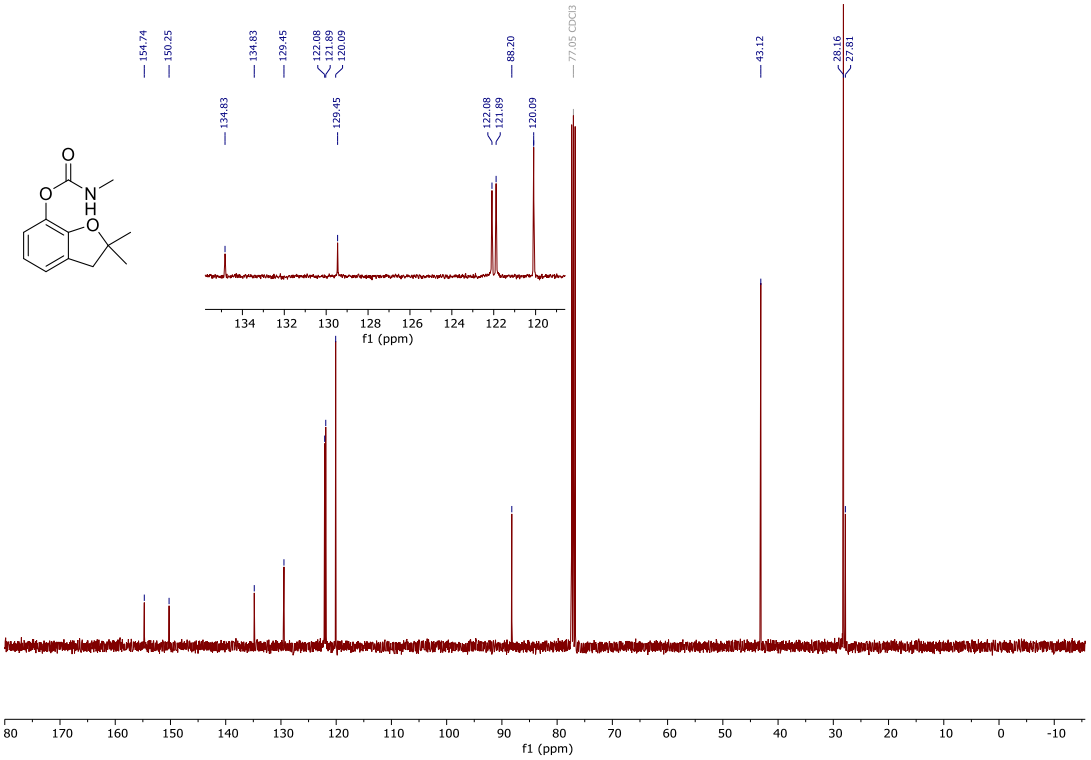
^{1}H-NMR spectrum in $CDCl_3$:



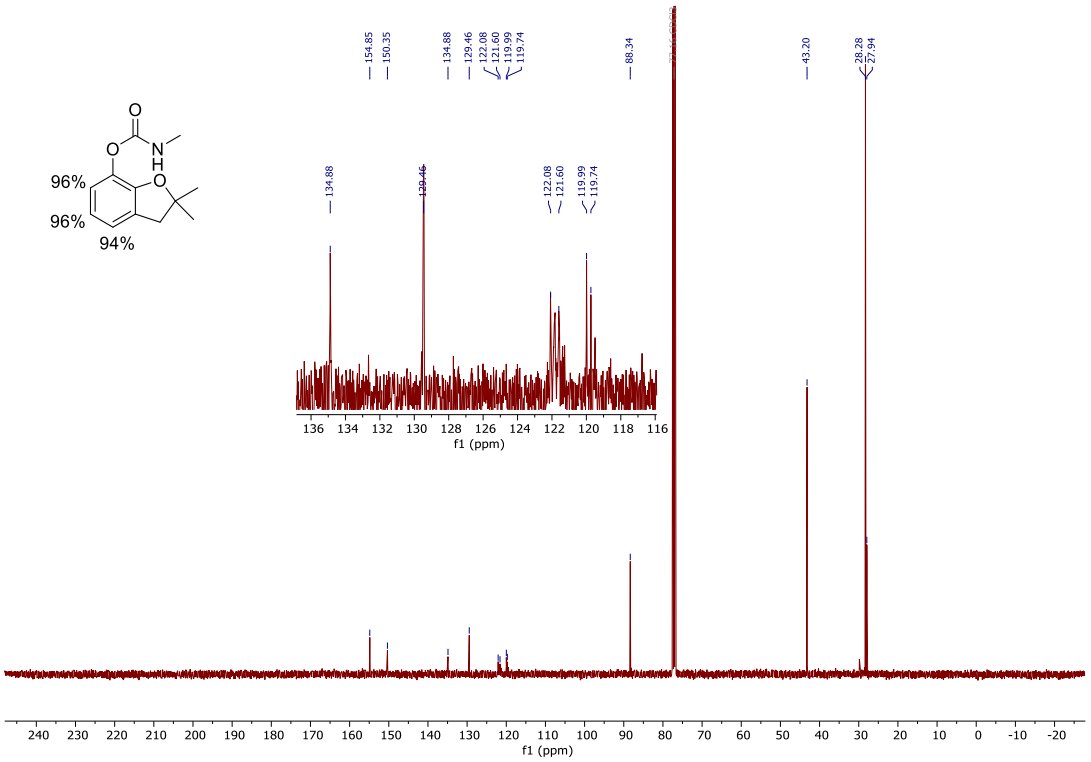
^{1}H-NMR spectrum in $CDCl_3$:



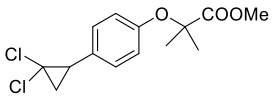
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of methyl 2-(4-(2,2-dichlorocyclopropyl)phenoxy)-2-methylpropanoate (27):



Following the general procedure E and using methyl 2-(4-(2,2-dichlorocyclopropyl)phenoxy)-2-methylpropanoate **(27)** (60.6 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAc = 3:1 as the eluent, the target compound **[D]27** was obtained as colorless solid (46.6 mg, 76%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 3.23 D/molecule [HRMS]; 3.24 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.11 (d, *J* = 8.5 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 3.76 (s, 3H), 2.83 (dd, *J* = 10.7, 8.4 Hz, 1H), 1.93 (dd, *J* = 10.7, 7.4 Hz, 1H), 1.77 (dd, *J* = 8.2, 7.5 Hz, 1H), 1.59 (s, 6H) ppm.

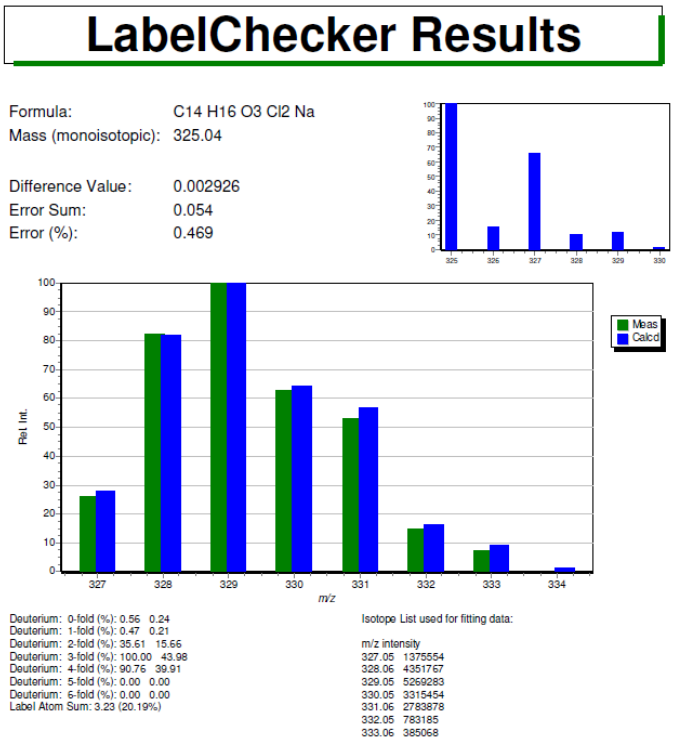
^{13}C NMR (150 MHz, $CDCl_3$) δ = 174.9, 155.0, 129.8, 128.4, 118.9, 79.3, 61.0, 52.6, 35.0, 26.0, 25.5(2), 25.5(0) ppm.

NMR Data of Product:

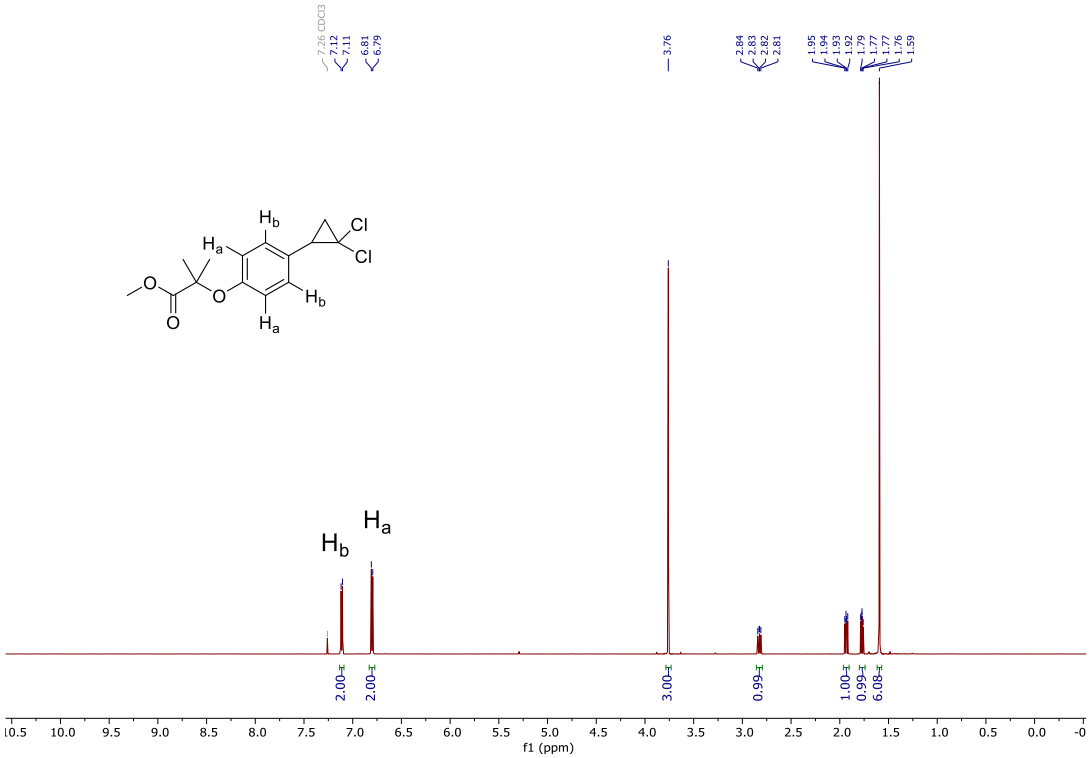
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.11 (s, 0.66H, 67% D), 6.83-6.77 (m, 0.10H, 95% D), 3.76 (s, 3H), 2.83 (dd, *J* = 10.6, 8.4 Hz, 1H), 1.93 (dd, *J* = 10.7, 7.4 Hz, 1H), 1.82-1.71 (m, 1H), 1.59 (s, 6H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ = 174.9, 154.9, 130.3-127.9 (3C), 119.2-117.9 (2C), 79.3, 61.0, 52.6, 35.1-34.7 (1C), 26.0, 25.5(0), 25.4(9) ppm.

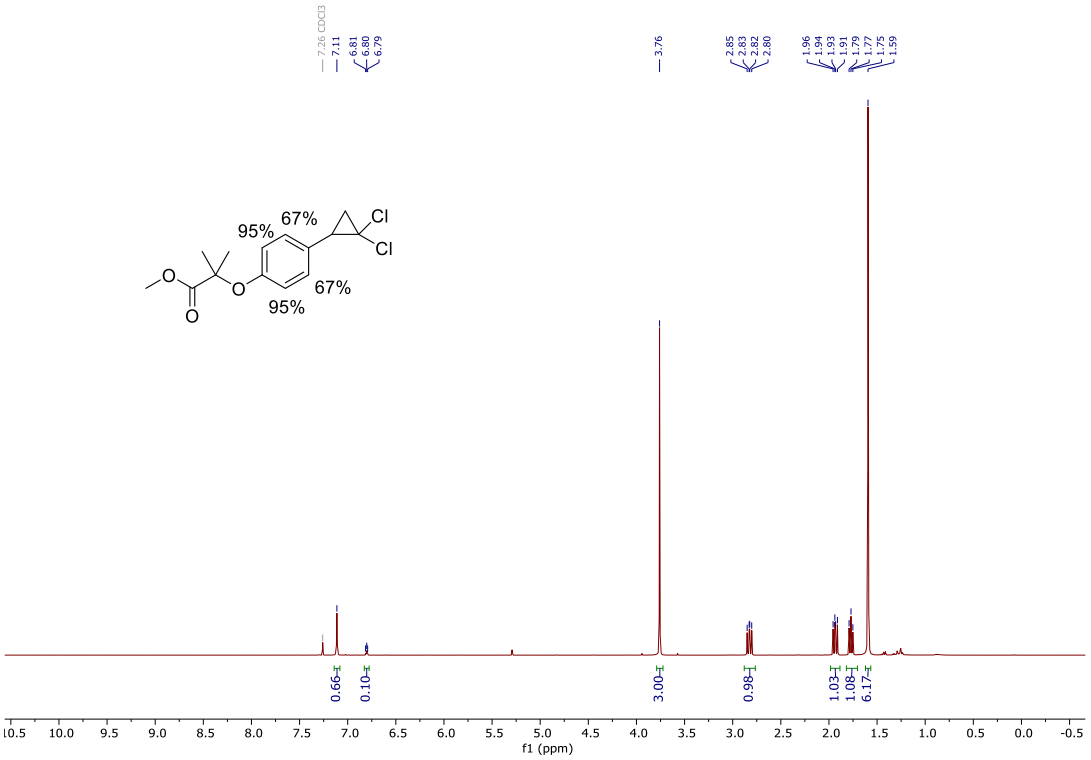
Mass Data:



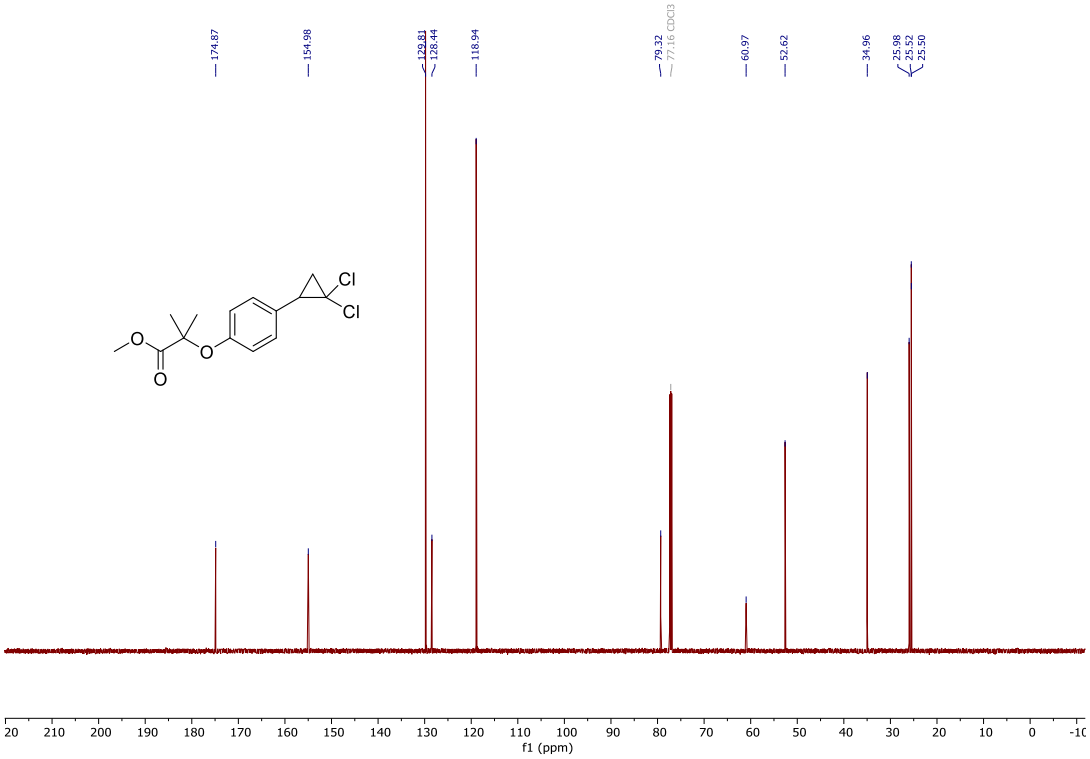
^{1}H-NMR spectrum in $CDCl_3$:



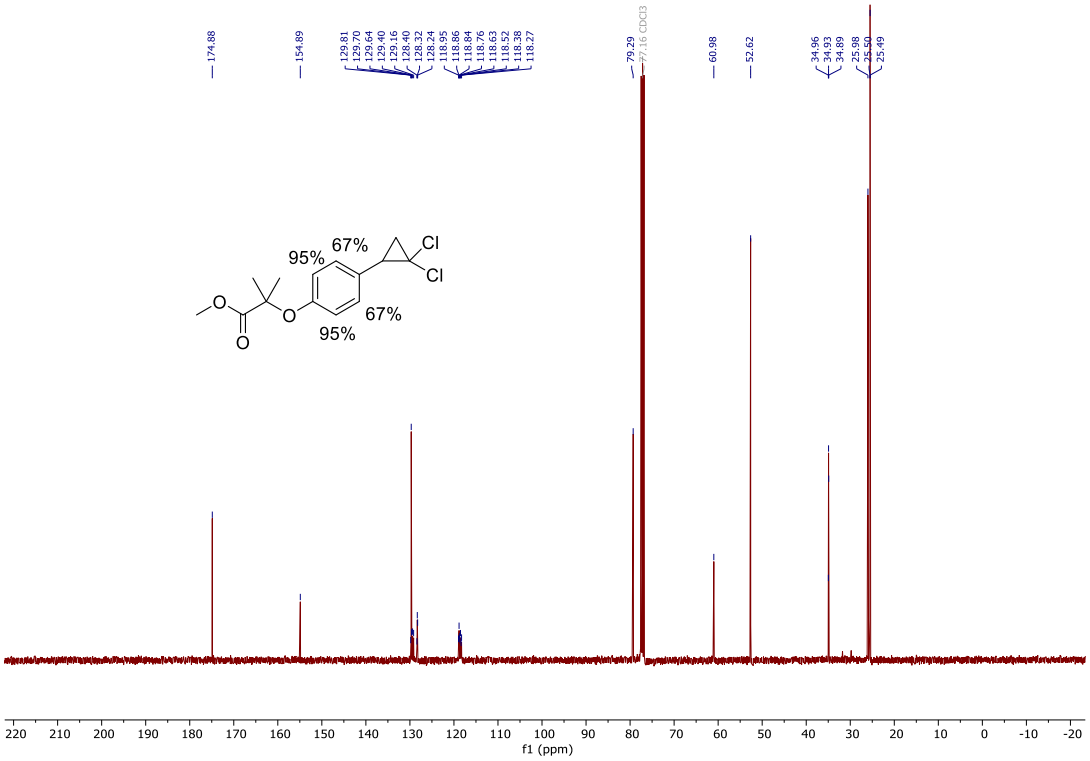
^{1}H-NMR spectrum in $CDCl_3$:



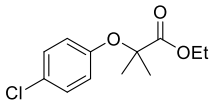
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of ethyl 2-(4-chlorophenoxy)-2-methylpropanoate (28):



Following the general procedure E and using ethyl 2-(4-chlorophenoxy)-2-methylpropanoate **(28)** (48.5 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAc = 5:1 as the eluent, the target compound **[D]28** was obtained as yellowish liquid (29.6 mg, 60%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 3.71 D/molecule [HRMS]; 3.76 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.20-7.15 (m, 2H), 6.79-6.76 (m, 2H), 4.24-4.18 (m, 2H), 1.58-1.54 (m, 6H), 1.25-1.20 (m, 3H) ppm.

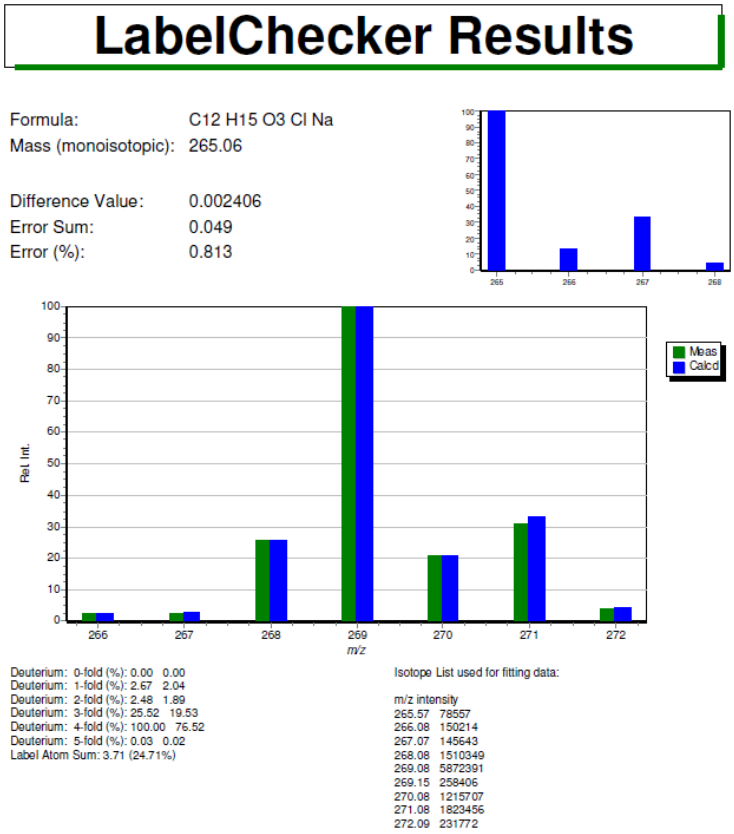
^{13}C NMR (125 MHz, $CDCl_3$) δ = 174.0, 154.2, 129.2, 127.3, 120.6, 79.6, 61.6, 25.4, 14.1 ppm.

NMR Data of Product:

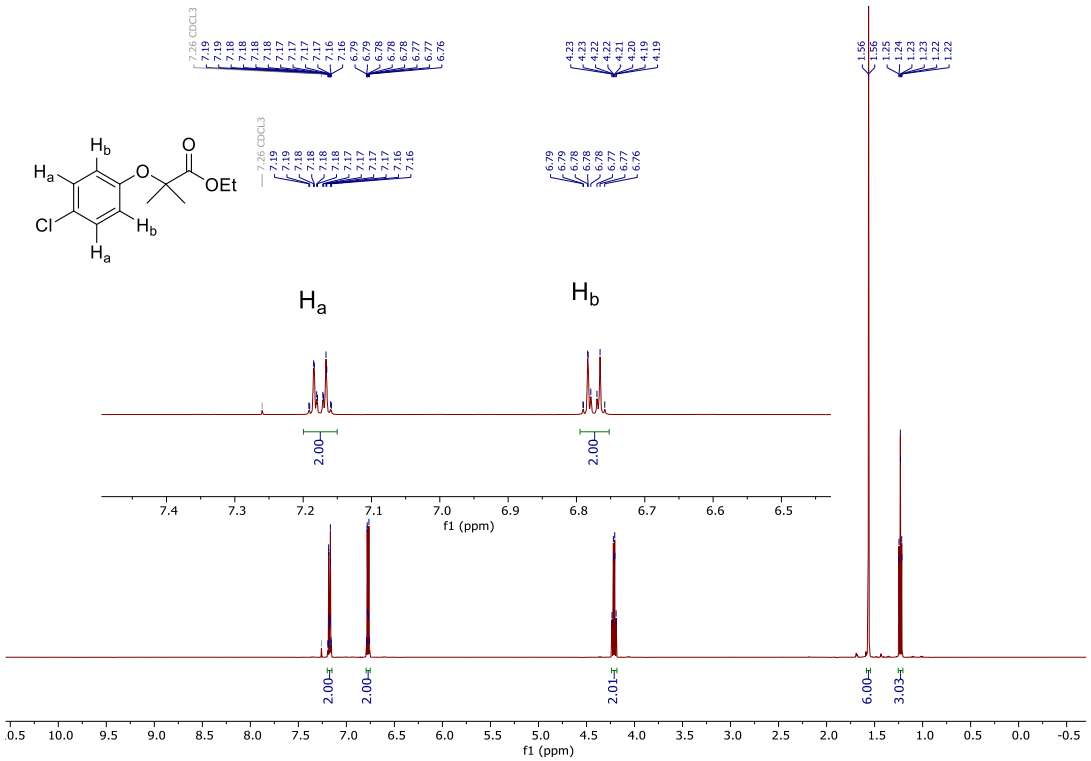
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.19 (s, 0.15H, 93% D), 6.78 (s, 0.09H, 96% D), 4.23 (q, *J* = 7.1 Hz, 2H), 1.58 (s, 6H), 1.24 (t, *J* = 7.1 Hz, 3H) ppm.

^{13}C NMR (150 MHz, $CDCl_3$) δ = 174.1, 154.1, 129.4-128.3 (2C), 127.7-126.6 (2C), 121.0-119.5 (1C), 79.6, 61.7, 25.4, 14.2 ppm.

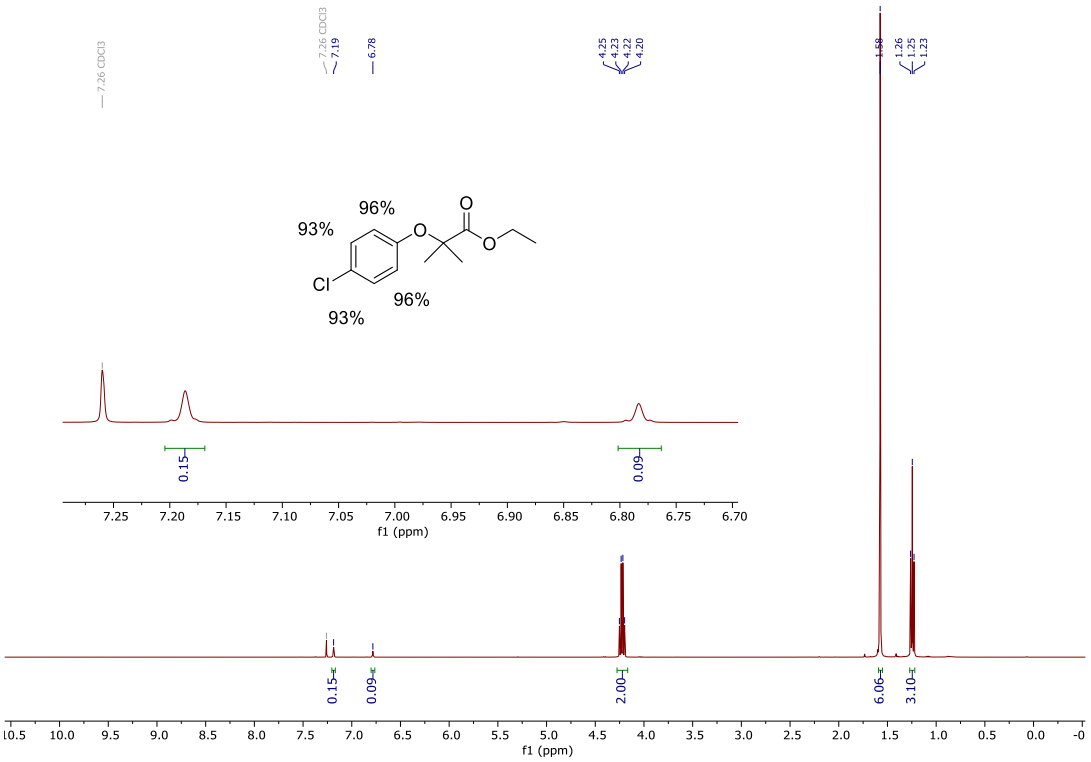
Mass Data:



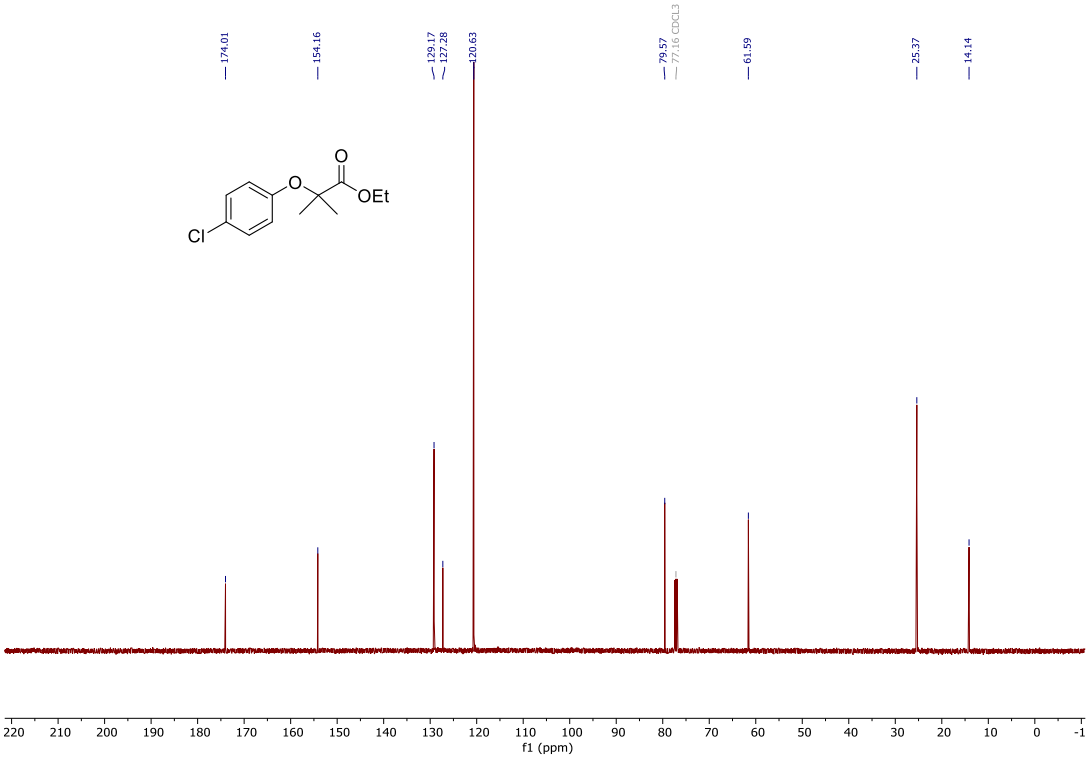
^{1}H-NMR spectrum in $CDCl_3$:



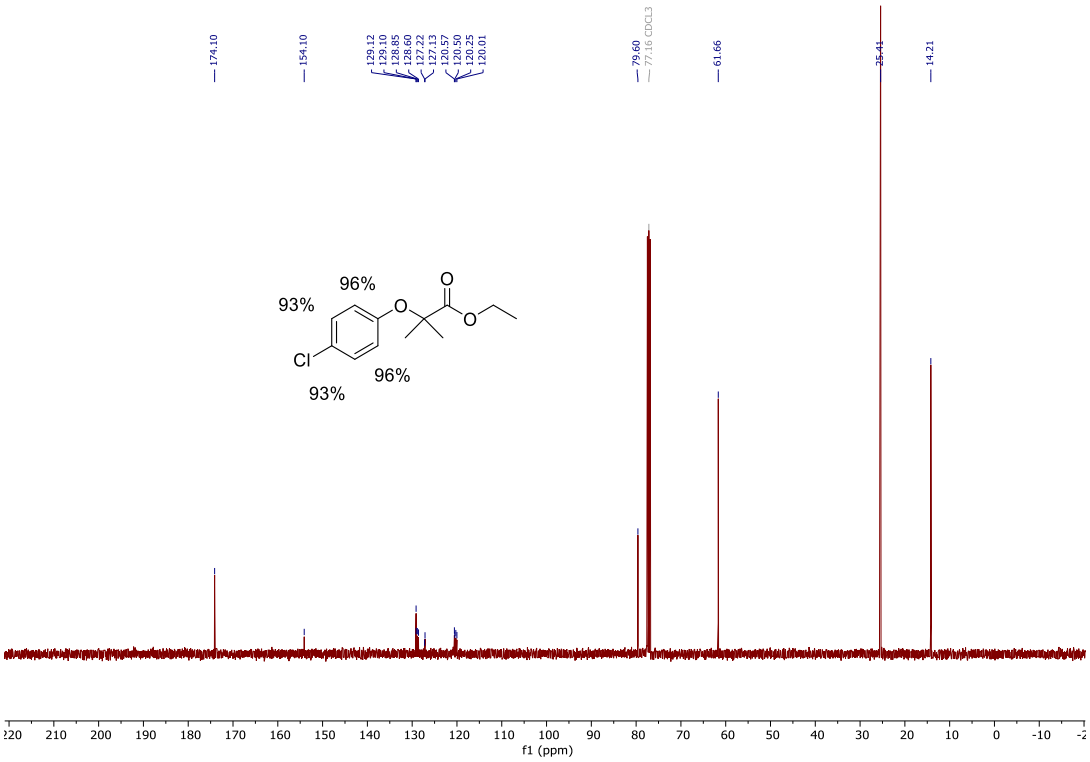
^{1}H-NMR spectrum in $CDCl_3$:



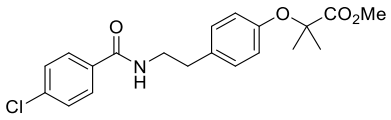
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of methyl 2-(4-(2-(4-chlorobenzamido)ethyl)phenoxy)-2-methylpropanoate (29) Using Conditions A:



Following the general procedure E and using methyl 2-(4-(2-(4-chlorobenzamido)ethyl)phenoxy)-2-methylpropanoate (**29**) (75.2 mg, 0.200 mmol), and purification via silica gel column chromatography using CH_2Cl_2:MeOH = 99:1 as the eluent, the target compound **[D]29** was obtained as colorless liquid (75.0 mg, 99%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 1.77 D/molecule [HRMS]; 1.69 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.62-7.59 (m, 2H), 7.39-7.35 (m, 2H), 7.11-7.07 (m, 2H), 6.81-6.78 (m, 2H), 3.77 (s, 3H), 3.68-3.63 (m, 2H), 2.86 (t, *J* = 6.9 Hz, 2H), 1.58 (s, 6H) ppm.

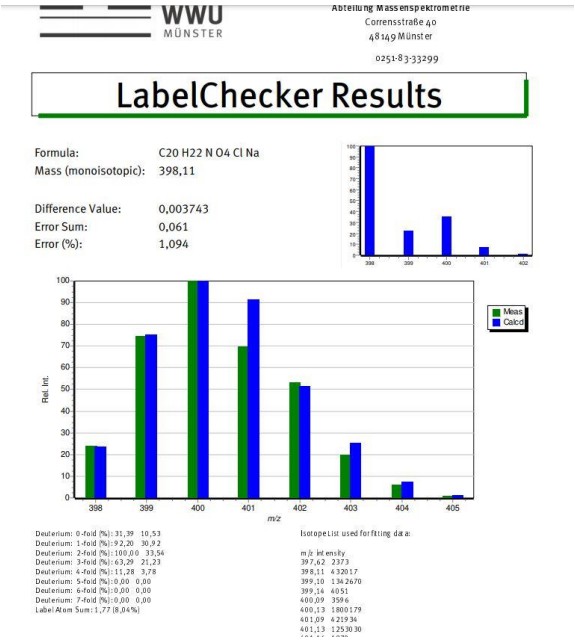
^{13}C NMR (126 MHz, $CDCl_3$): δ = 174.9, 166.5, 154.2, 137.8, 133.1, 132.6, 129.7, 129.0, 128.4, 119.7, 79.3, 52.6, 41.3, 34.9, 25.5 ppm.

NMR Data of Product:

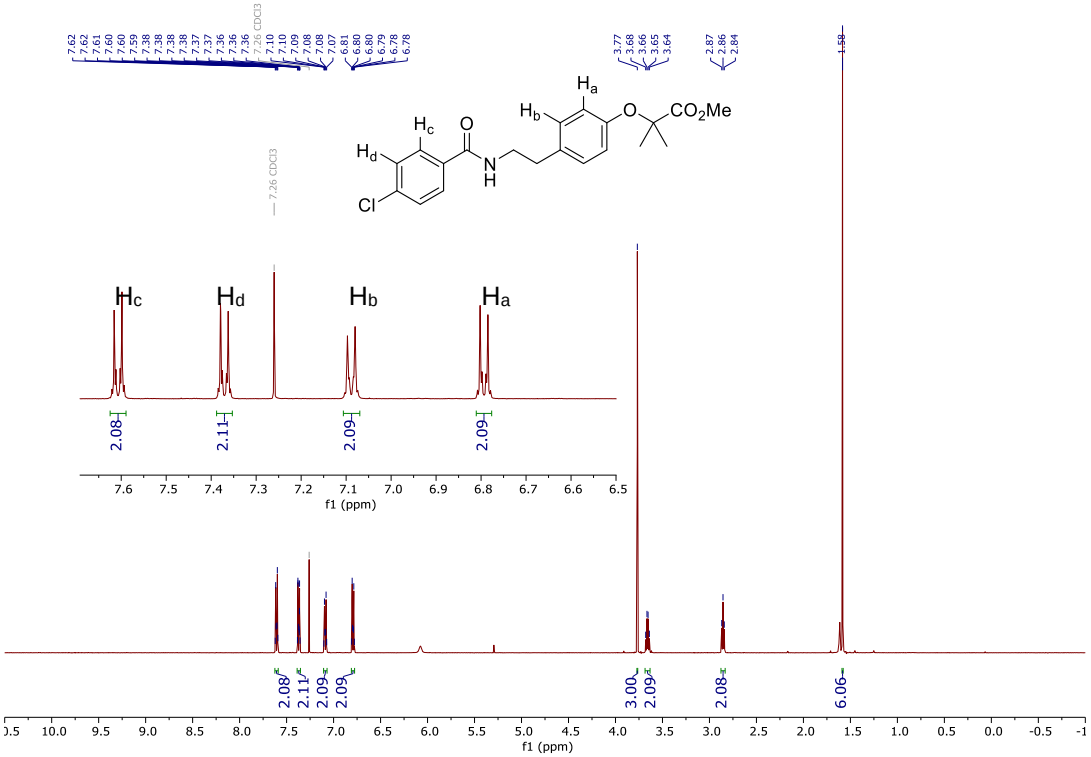
^{1}H NMR (600 MHz, CDCl3) δ = 7.62-7.59 (m, 2H), 7.39-7.36 (m, 1.87H, 6.5% D), 7.11-7.07 (m, 1.62H, 19% D), 6.81-6.78 (m, 0.82H, 59% D), 3.77 (s, 3H), 3.69-3.63 (m, 2H), 2.86 (t, *J* = 6.9 Hz, 2H), 1.59 (s, 6H) ppm.

^{13}C NMR (126 MHz, $CDCl_3$) δ = 174.9, 166.5, 154.2, 137.8, 133.1-128.3(8C), 119.8-119.7 (2C), 79.3, 52.6, 41.3-41.2(1C), 34.9-34.8(1C), 25.5 ppm.

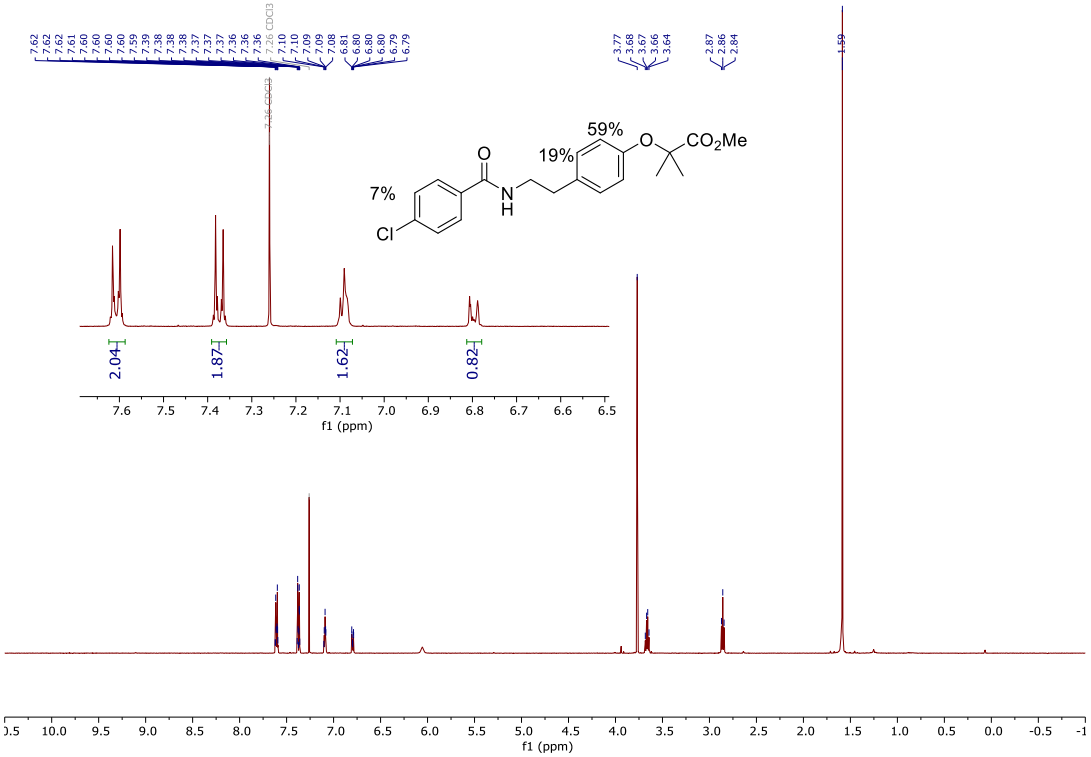
Mass Data:



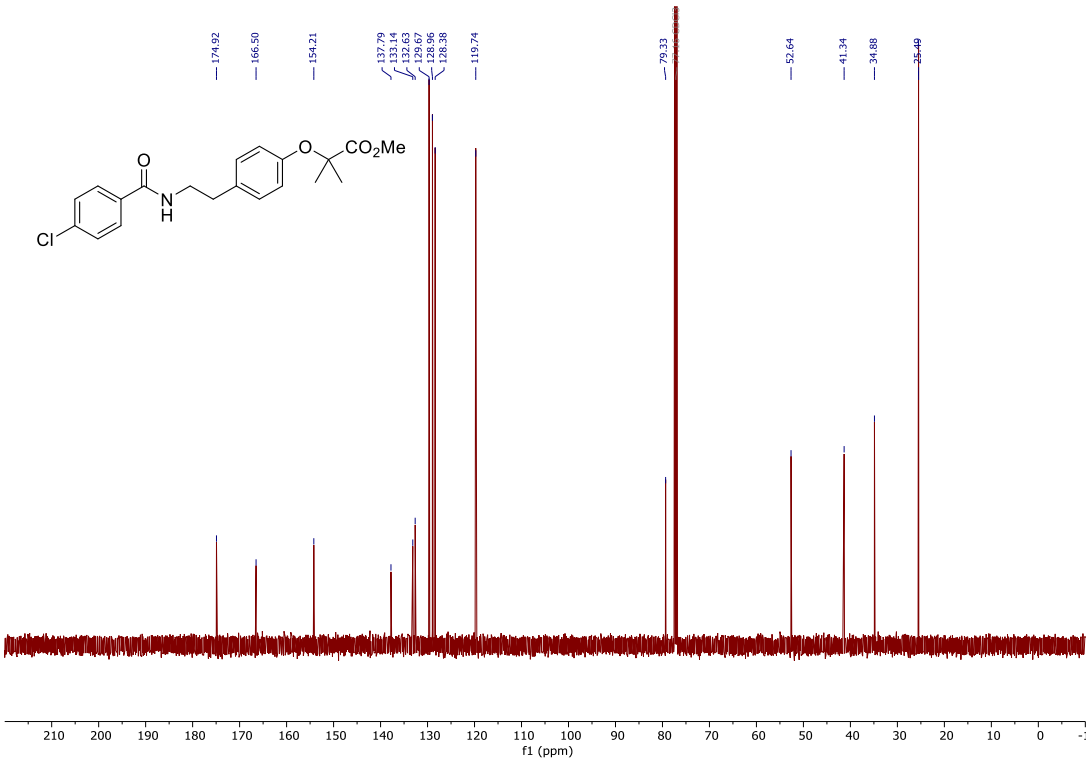
^{1}H-NMR spectrum in $CDCl_3$:



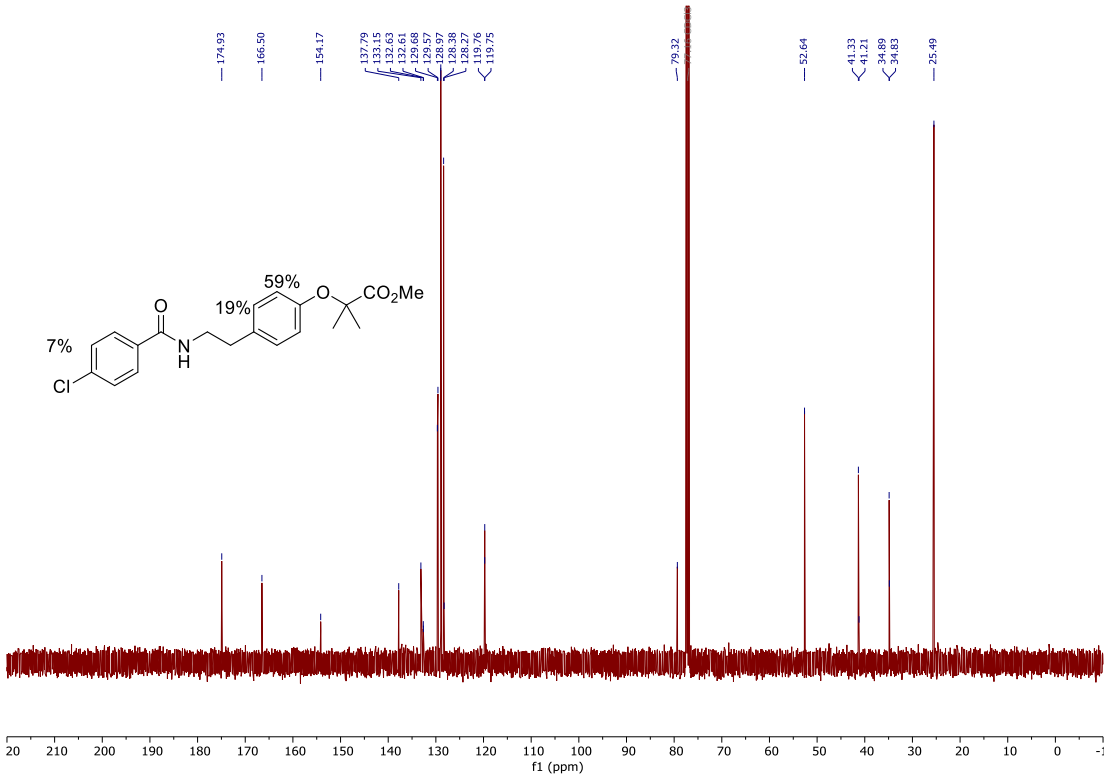
^{1}H-NMR spectrum in $CDCl_3$:



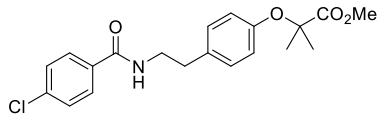
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of methyl 2-(4-(2-(4-chlorobenzamido)ethyl)phenoxy)-2-methylpropanoate (29) Using Conditions B:



Following the general procedure F and using methyl 2-(4-(2-(4-chlorobenzamido)ethyl)phenoxy)-2-methylpropanoate (**29**) (75.2 mg, 0.200 mmol), and purification via silica gel column chromatography using CH_2Cl_2:MeOH = 99:1 as the eluent, the target compound **[D]29** was obtained as colorless liquid (74.8 mg, 98%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 5.96 D/molecule [HRMS]; 5.79 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.62-7.59 (m, 2H), 7.39-7.35 (m, 2H), 7.11-7.07 (m, 2H), 6.81-6.78 (m, 2H), 3.77 (s, 3H), 3.68-3.63 (m, 2H), 2.86 (t, *J* = 6.9 Hz, 2H), 1.58 (s, 6H) ppm.

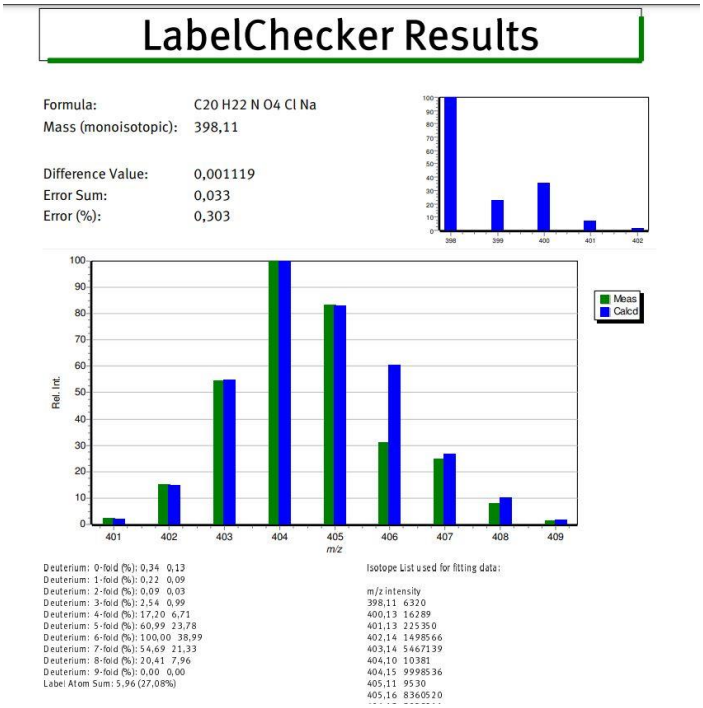
^{13}C NMR (126 MHz, $CDCl_3$ δ = 174.9, 166.5, 154.2, 137.8, 133.1, 132.6, 129.7, 129.0, 128.4, 119.7, 79.3, 52.6, 41.3, 34.9, 25.5 ppm.

NMR Data of Product:

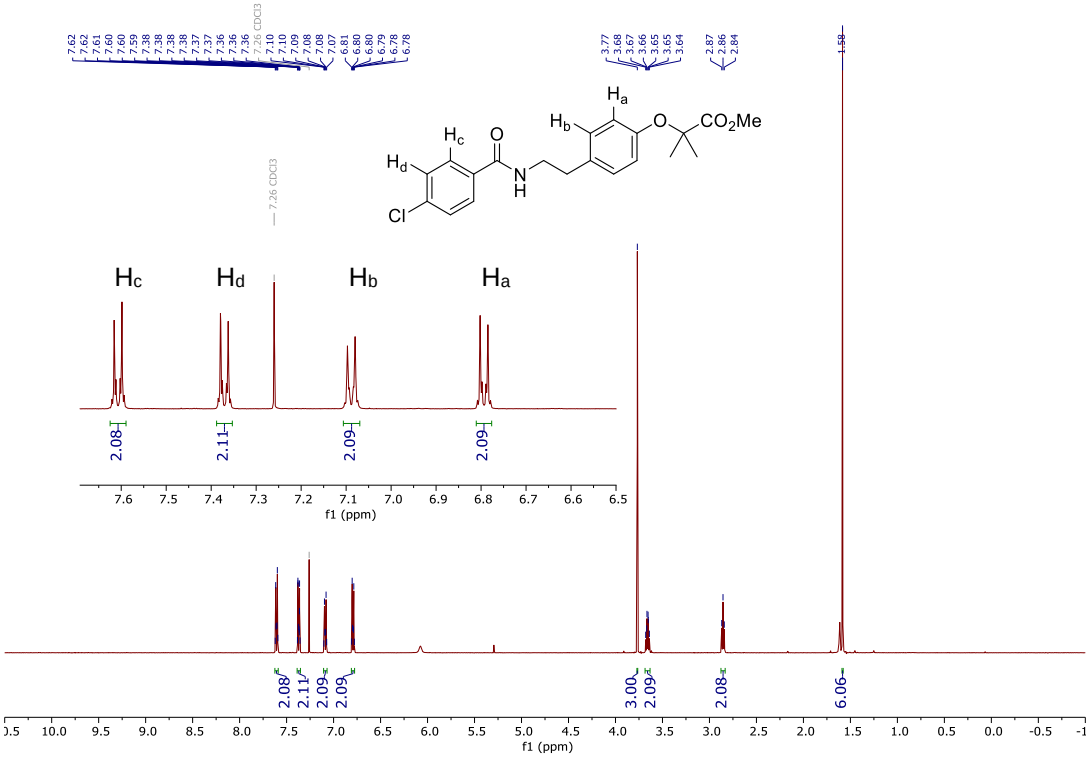
^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.62-7.58 (m, 1.24H, 38% D), 7.38-7.35 (m, 0.39H, 80.5% D), 7.10-7.07 (m, 0.23H, 88.5%), 6.82-6.76 (m, 0.35H, 82.5%D), 3.77 (s, 3H), 3.68-3.63 (m, 2H), 2.86 (t, *J* = 6.9 Hz, 2H), 1.58 (s, 6H) ppm.

^{13}C NMR (126 MHz, $CDCl_3$) δ = 174.9, 166.5, 154.1, 137.7-137.6 (1C), 133.1-128.3(8C), 120.1-118.7 (2C), 79.3, 52.6, 41.3-41.2(1C), 34.8-34.7(1C), 25.5 ppm.

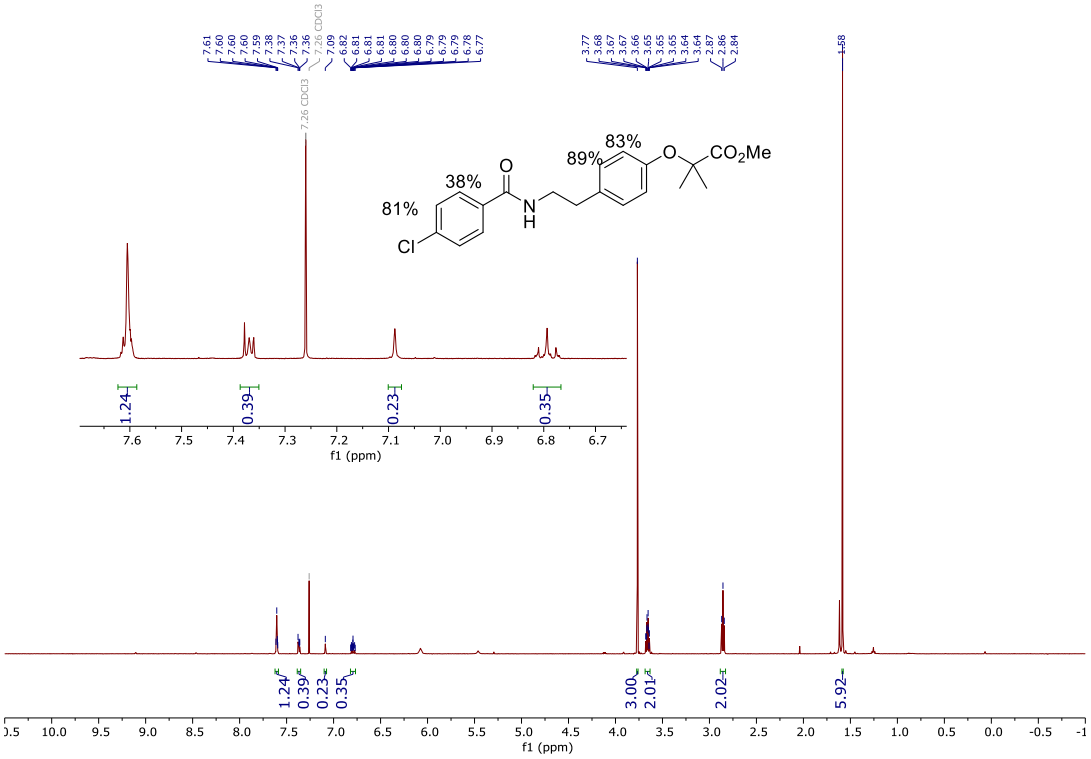
Mass Data:



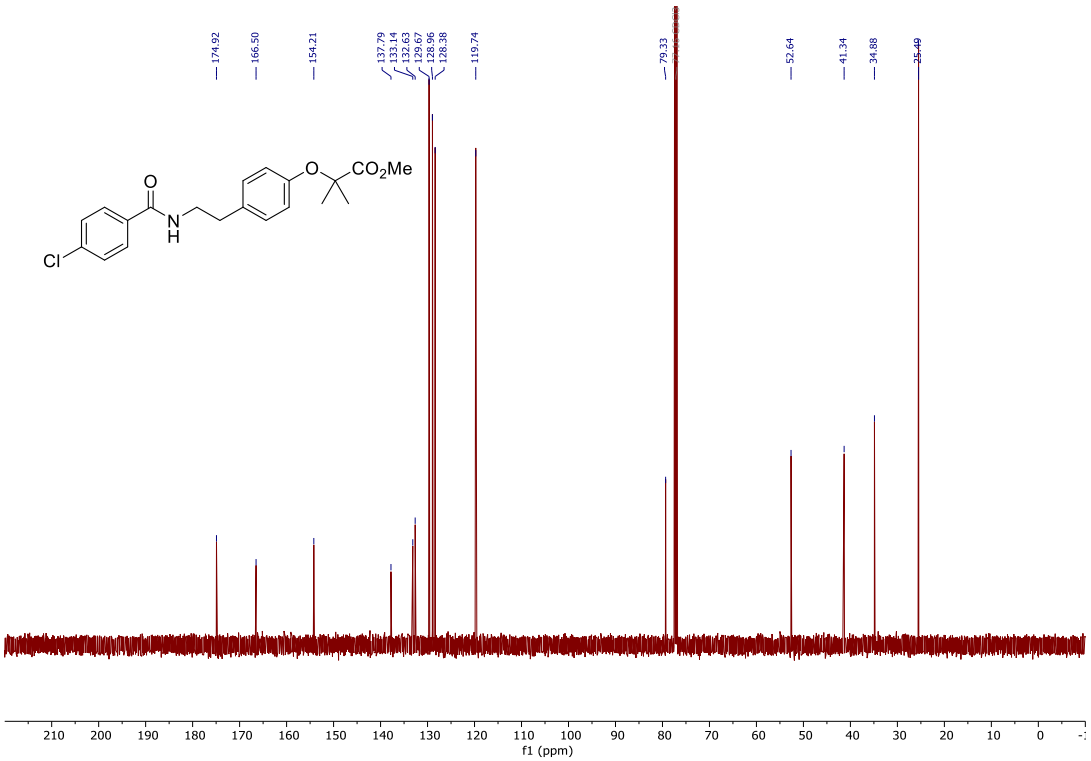
^{1}H-NMR spectrum in $CDCl_3$:



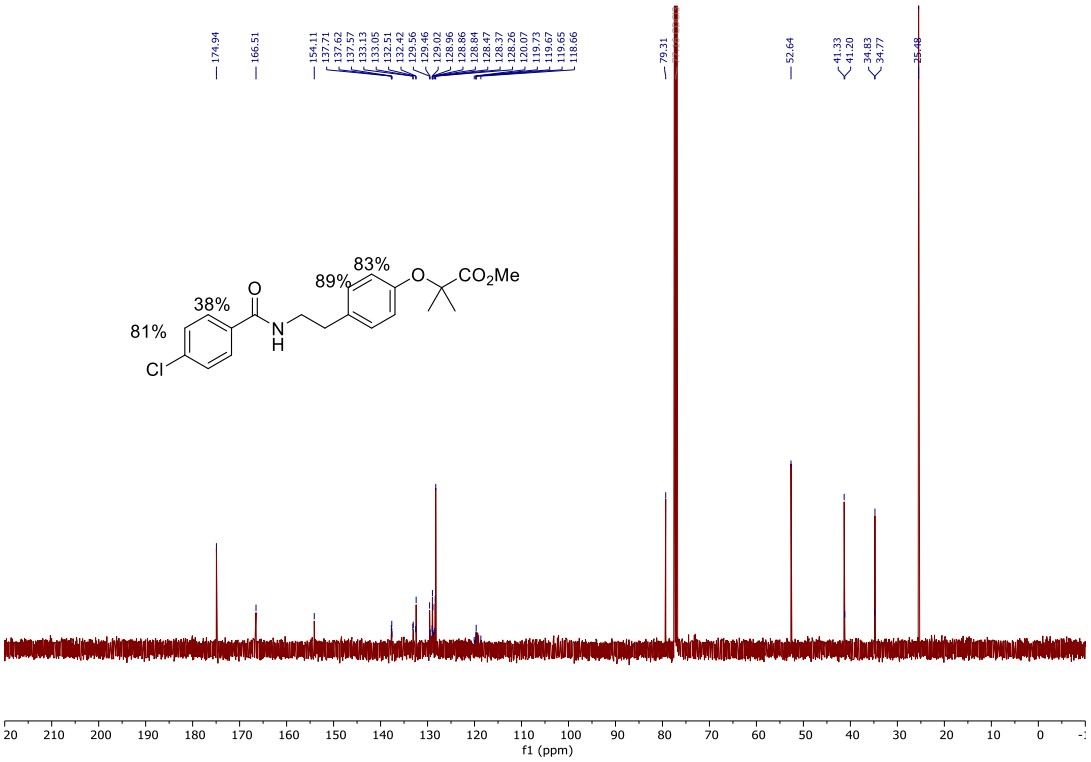
^{1}H-NMR spectrum in $CDCl_3$:



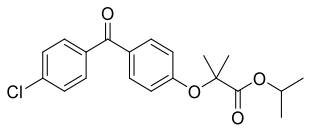
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of isopropyl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate (30) Using Conditions A:



Following the general procedure E and using isopropyl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate **(30)** (72.2 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAC = 20:1 as the eluent, the target compound **[D]30** was obtained as a colorless solid (66.0 mg, 91%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 1.18 D/molecule [HRMS]; 1.40 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (599 MHz, $CDCl_3$) δ = 7.74-7.71 (m, 2H), 7.71-7.68 (m, 2H), 7.46-7.42 (m, 2H), 6.88-6.84 (m, 2H), 5.08 (hept, *J* = 6.3 Hz, 1H), 1.66 (s, 6H), 1.20 (d, *J* = 6.2 Hz, 6H) ppm.

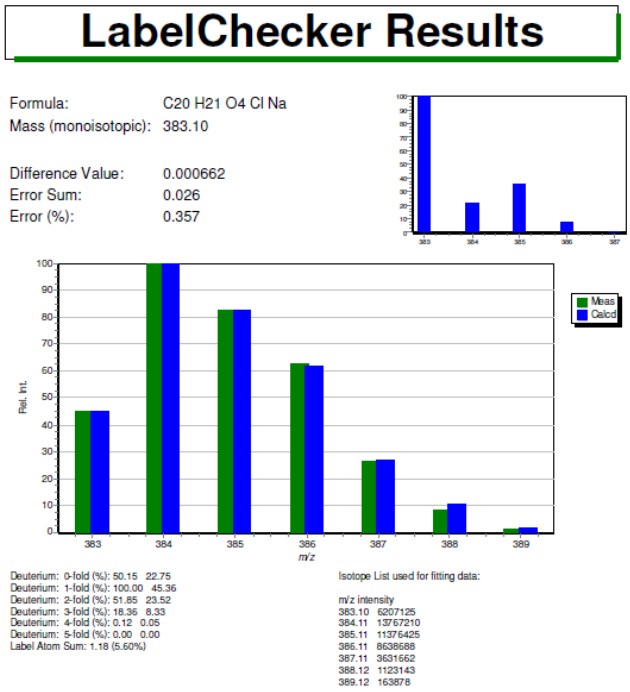
^{13}C NMR (101 MHz, $CDCl_3$) δ = 194.4, 173.2, 159.9, 138.5, 136.6, 132.1, 131.3, 130.4, 128.7, 117.4, 79.6, 69.5, 25.5, 21.7 ppm.

NMR Data of Product:

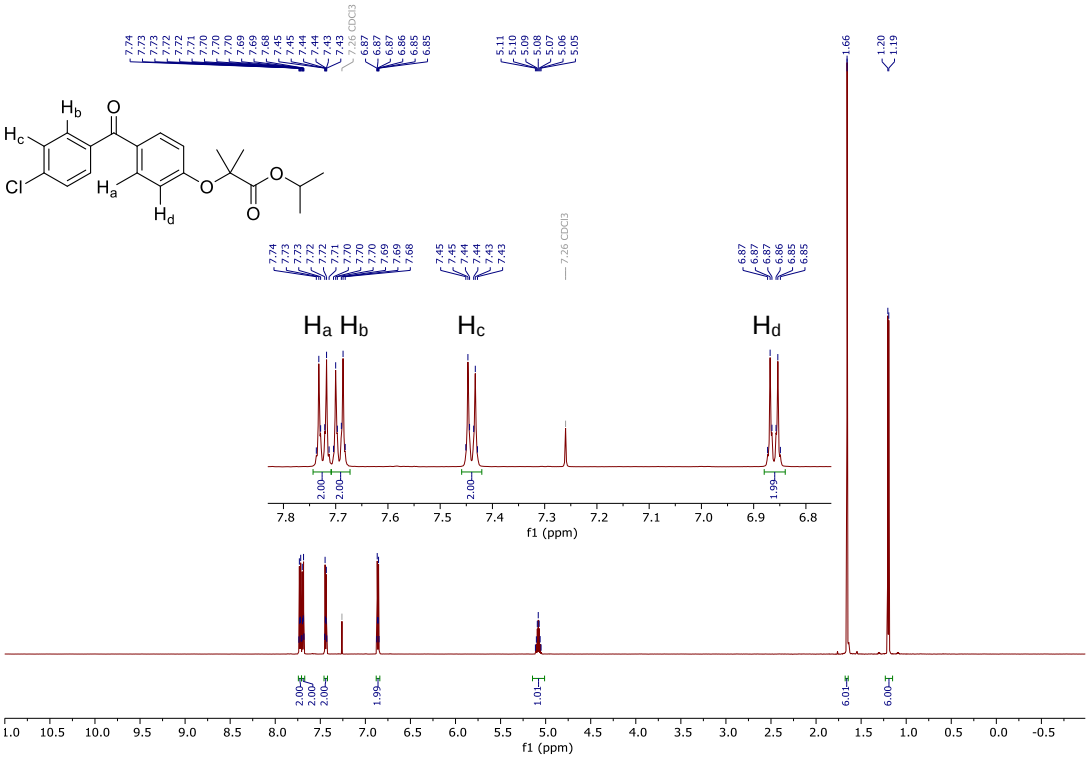
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.74-7.71 (m, 1.94H, 3%D), 7.71-7.68 (m, 1.92H, 4%D), 7.47-7.41 (m, 1.62H, 19%D), 6.88-6.84 (m, 1.12H, 44%D), 5.08 (hept, *J* = 6.3 Hz, 1H), 1.66 (s, 6H), 1.20 (d, *J* = 6.3 Hz, 6H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 194.4, 173.2, 159.9-159.7 (1C), 138.5-128.7 (9H), 117.5-117.4 (2C), 79.6, 69.5, 25.5, 21.7 ppm.

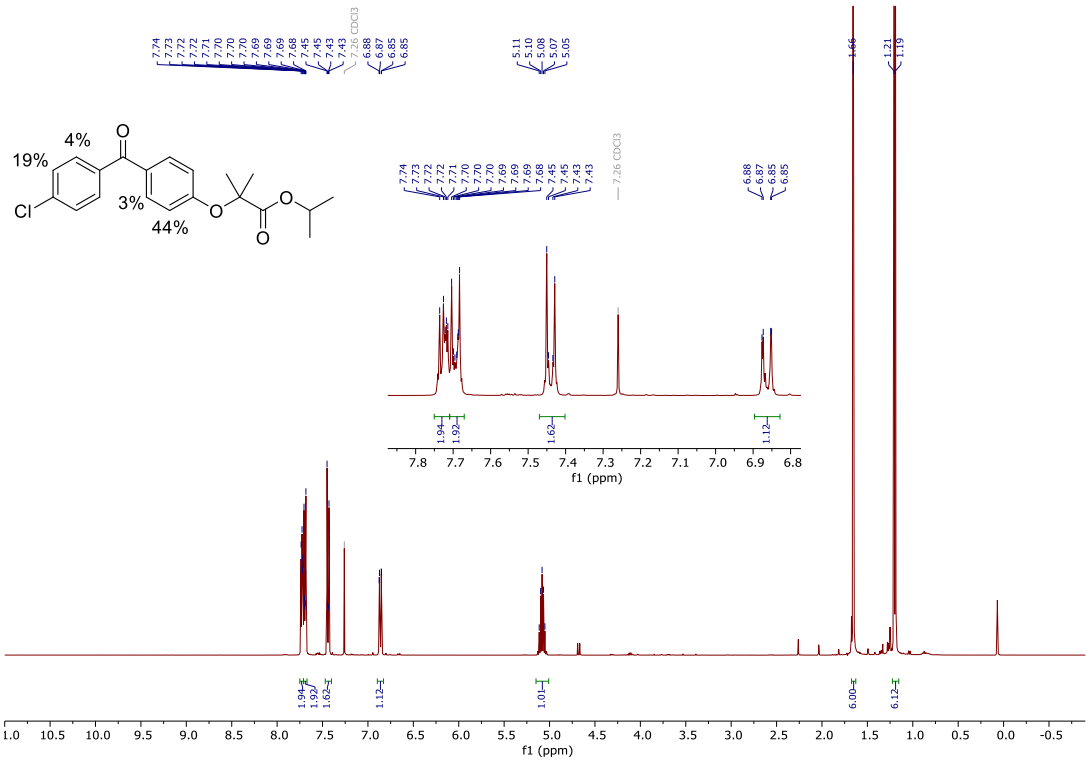
Mass Data:



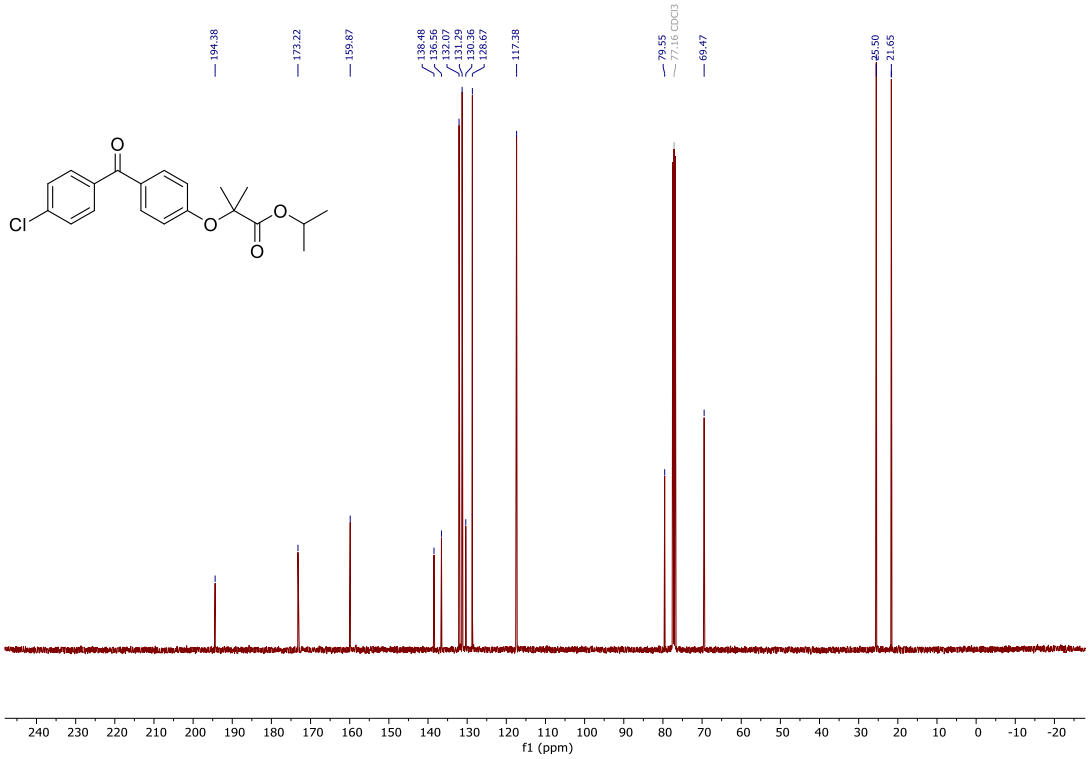
^{1}H-NMR spectrum in $CDCl_3$:



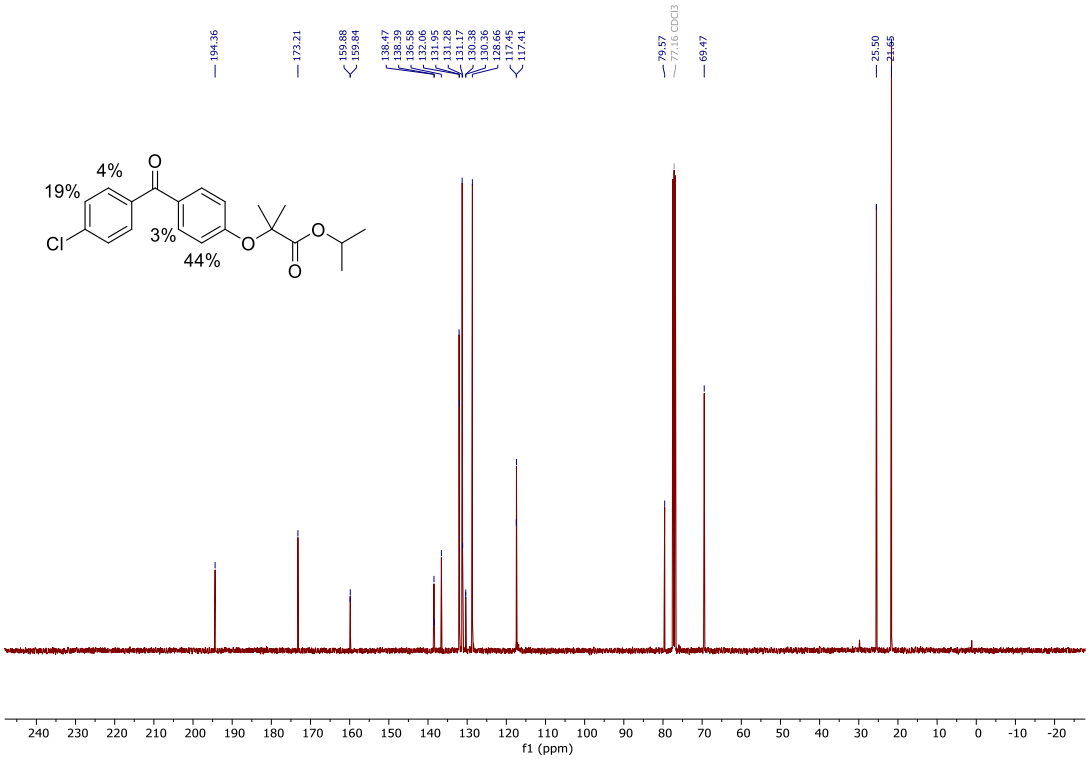
^{1}H-NMR spectrum in $CDCl_3$:



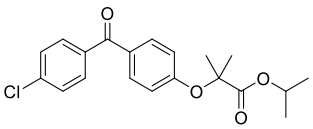
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of isopropyl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate (30) Using Conditions B:



Following the general procedure F and using isopropyl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate **(30)** (72.2 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAC = 20:1 as the eluent, the target compound **[D]30** was obtained as a colorless solid (66.7 mg, 92%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 6.12 D/molecule [HRMS]; 6.25 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (599 MHz, $CDCl_3$) δ = 7.74-7.71 (m, 2H), 7.71-7.68 (m, 2H), 7.46-7.42 (m, 2H), 6.88-6.84 (m, 2H), 5.08 (hept, *J* = 6.3 Hz, 1H), 1.66 (s, 6H), 1.20 (d, *J* = 6.2 Hz, 6H) ppm.

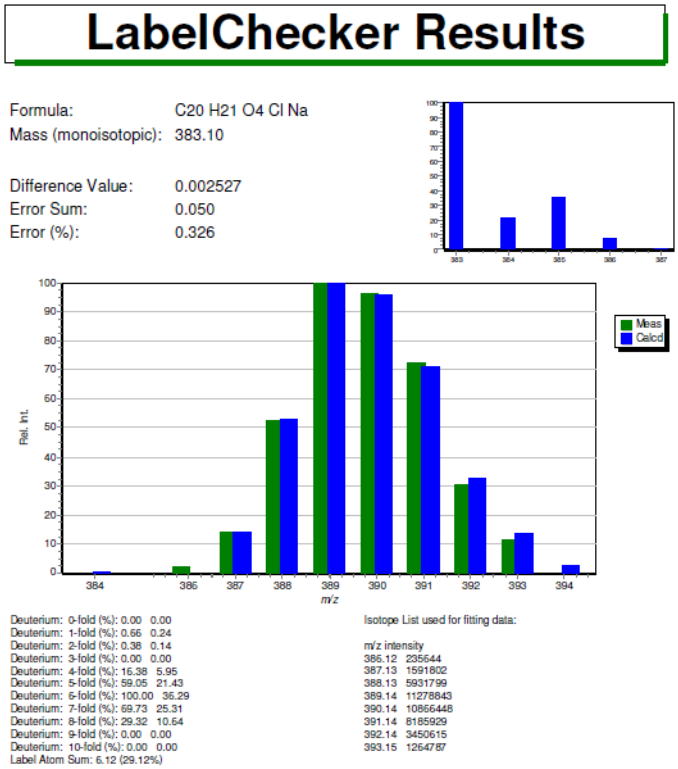
^{13}C NMR (101 MHz, $CDCl_3$) δ = 194.4, 173.2, 159.9, 138.5, 136.6, 132.1, 131.3, 130.4, 128.7, 117.4, 79.6, 69.5, 25.5, 21.7 ppm.

NMR Data of Product:

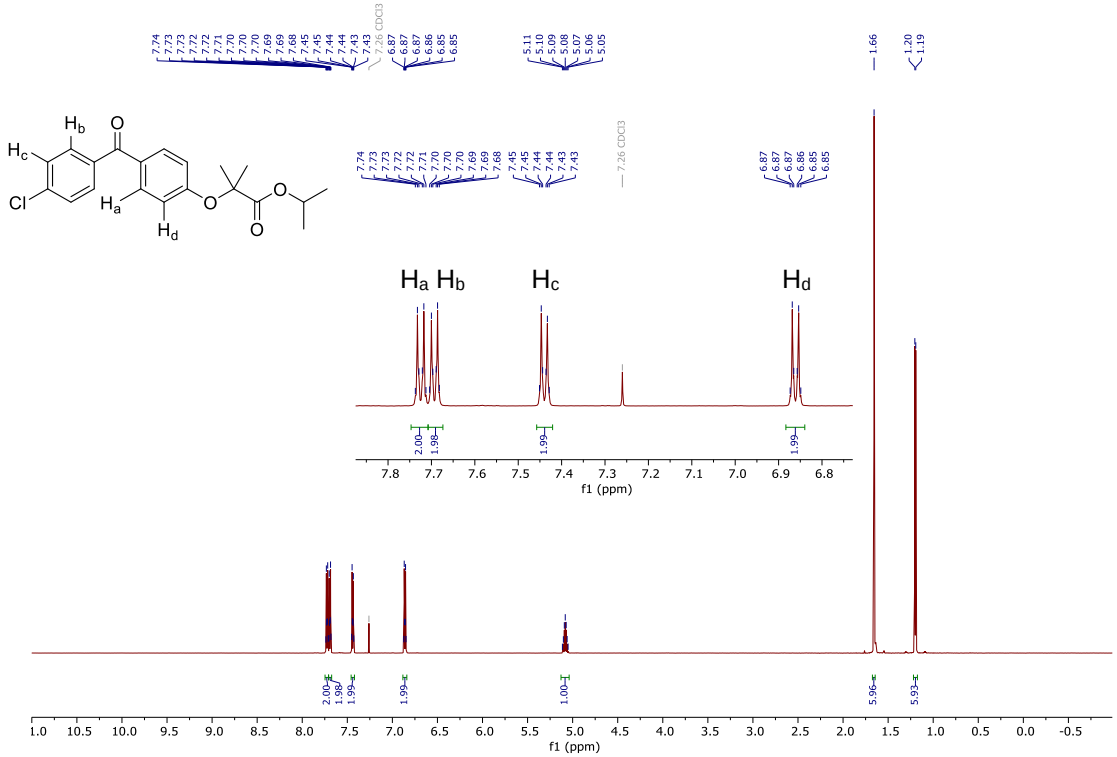
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.72 (s, 0.88H, 56%D), 7.69 (s, 0.65H, 68%D), 7.45-7.43 (m, 0.12H, 94%D), 6.88-6.84 (m, 0.10H, 95%D), 5.08 (hept, *J* = 6.3 Hz, 1H), 1.65 (s, 3H), 1.19 (d, *J* = 6.3 Hz, 6H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 194.3, 173.2, 159.8, 138.3, 136.6-136.4 (1C), 132.2-131.6 (2C), 131.3-130.7 (2C), 130.4-130.0(1C), 128.7-128.0 (2C), 117.4-117.0 (2C), 79.5, 69.5, 25.5, 21.6 ppm.

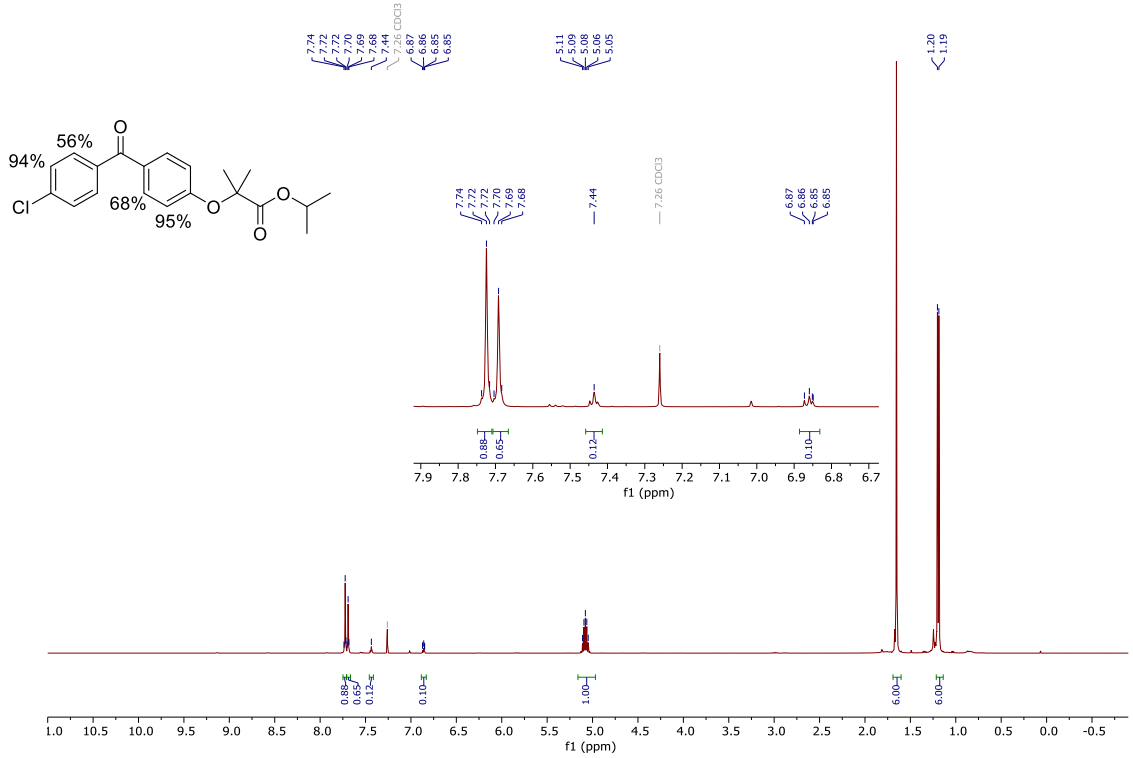
Mass Data:



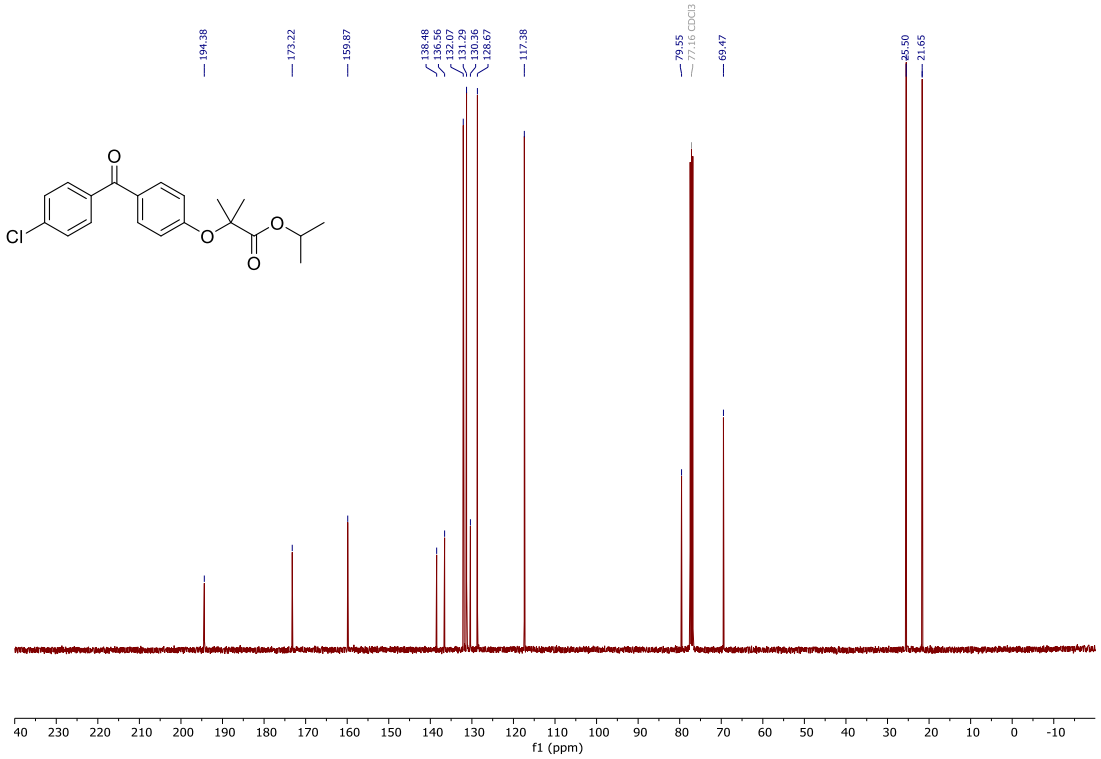
^{1}H-NMR spectrum in $CDCl_3$:



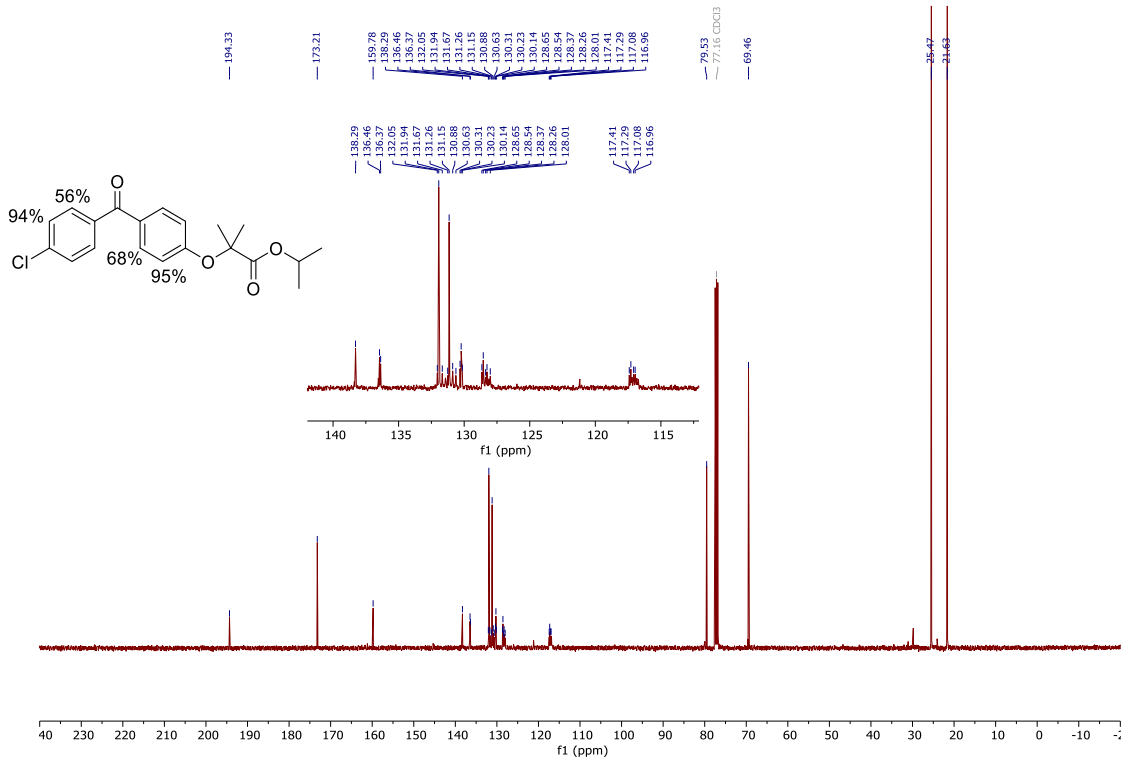
^{1}H-NMR spectrum in $CDCl_3$:



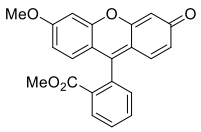
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of methyl 2-(6-methoxy-3-oxo-3*H*-xanthen-9-yl)benzoate (31) Using Conditions A:



Following the general procedure E and using methyl 2-(6-methoxy-3-oxo-3H-xanthen-9-yl)benzoate (**31**) (72.1 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAC = 9:1 as the eluent, the target compound **[D]31** was obtained as colorless solid (62.5 mg, 86%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 2.49 D/molecule [Mass]; 2.45 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.02 (d, *J* =7.5 Hz, 1H), 7.66 (td, *J* = 7.4, 1.2 Hz, 1H), 7.61 (td, *J* = 7.4, 1.1 Hz, 1H), 7.16 (d, *J* = 7.5 Hz, 1H), 6.78 (d, *J* = 2.5 Hz, 2H), 6.69 (d, *J* = 8.7 Hz, 2H), 6.61 (dd, *J* = 8.8, 2.6 Hz, 2H), 3.84 (s, 6H) ppm.

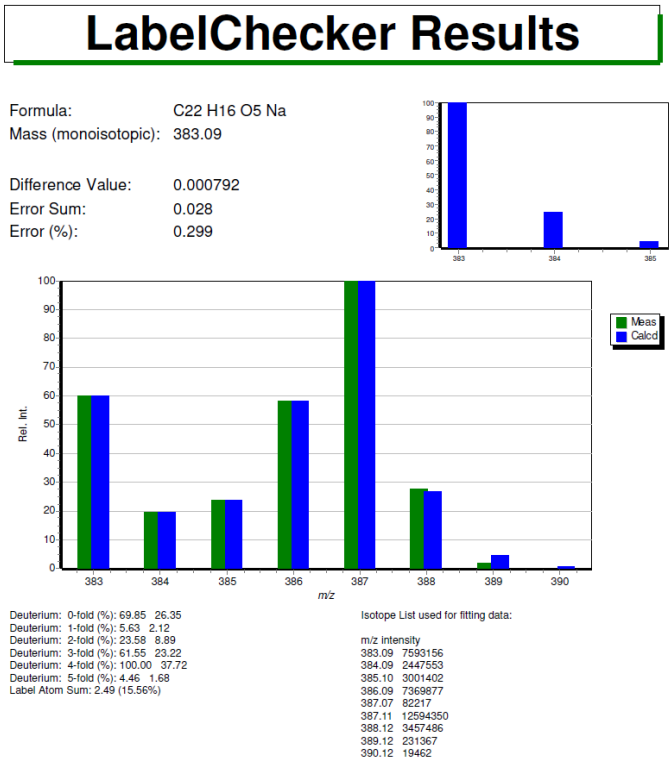
^{13}C NMR (126 MHz, $CDCl_3$) δ = 169.6, 161.5, 153.4, 152.7, 135.1, 129.8, 129.3, 127.0, 125.2, 124.1, 111.8, 111.4, 101.0, 83.4, 55.7(3), 55.7(0) ppm.

NMR Data of Product:

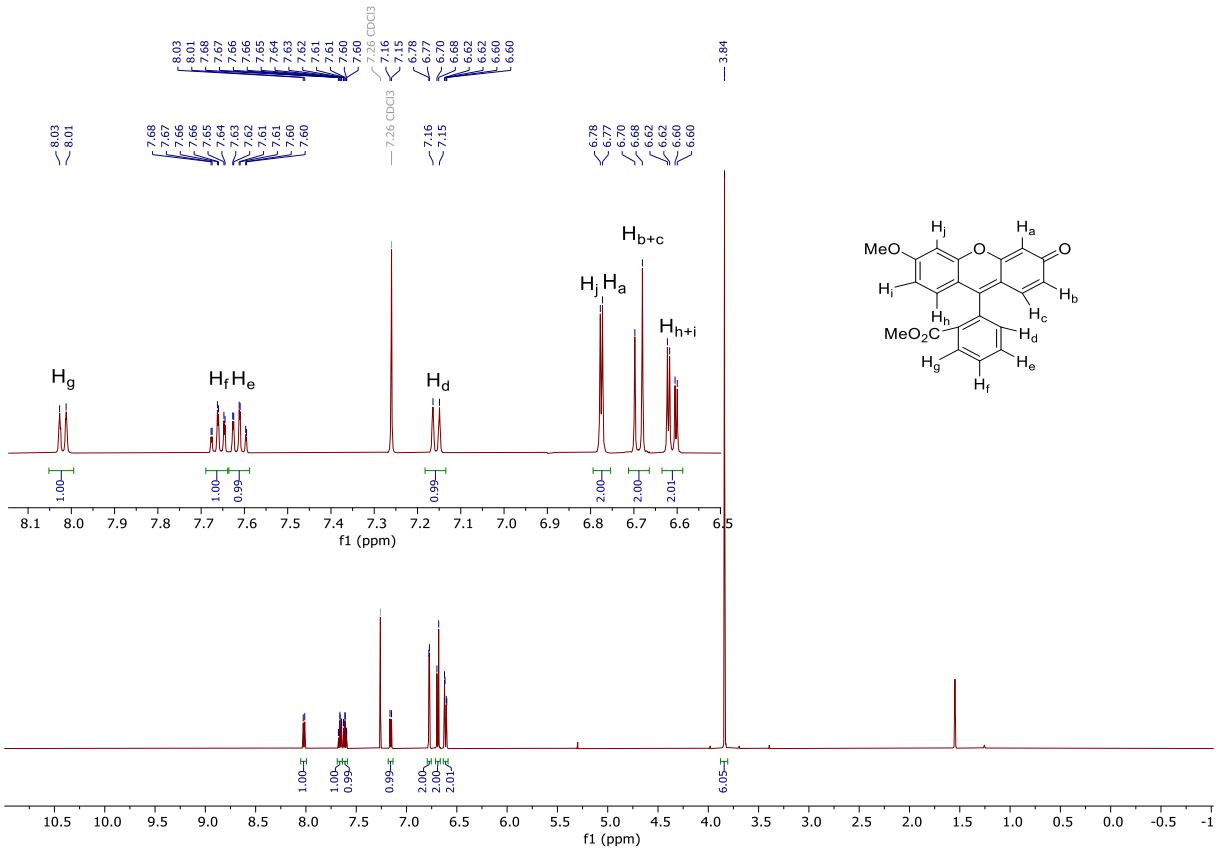
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.02 (d, *J* =7.8 Hz, 1H), 7.66 (td, *J* = 7.4, 1.3 Hz, 1H), 7.61 (td, *J* = 7.4, 1.2 Hz, 1H), 7.16 (d, *J* = 7.5 Hz, 1H), 6.80-6.74 (m, 0.91H, 95% D), 6.71-6.67 (m, 1.85H, 7.5%), 6.61 (dd, *J* = 8.8, 2.5 Hz, 0.59H, 71% D), 3.83 (s, 6H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 169.6, 162.8-160.3 (1C), 153.3, 152.8-152.4, 135.1, 129.8, 129.3-128.9 (2C), 127.0, 125.1, 124.0, 111.7, 111.4-111-3 (1C), 101.3-100.7 (1C), 83.4, 55.7 ppm.

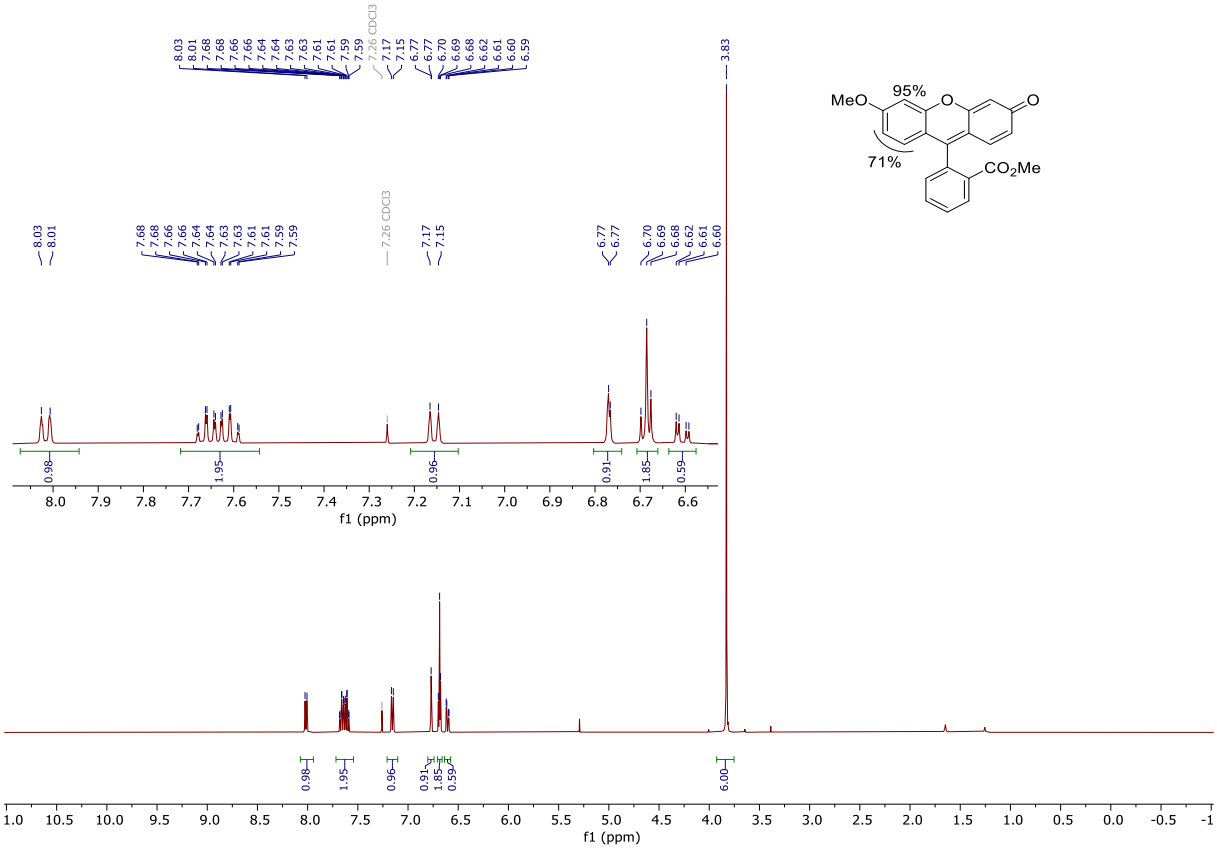
Mass Data:



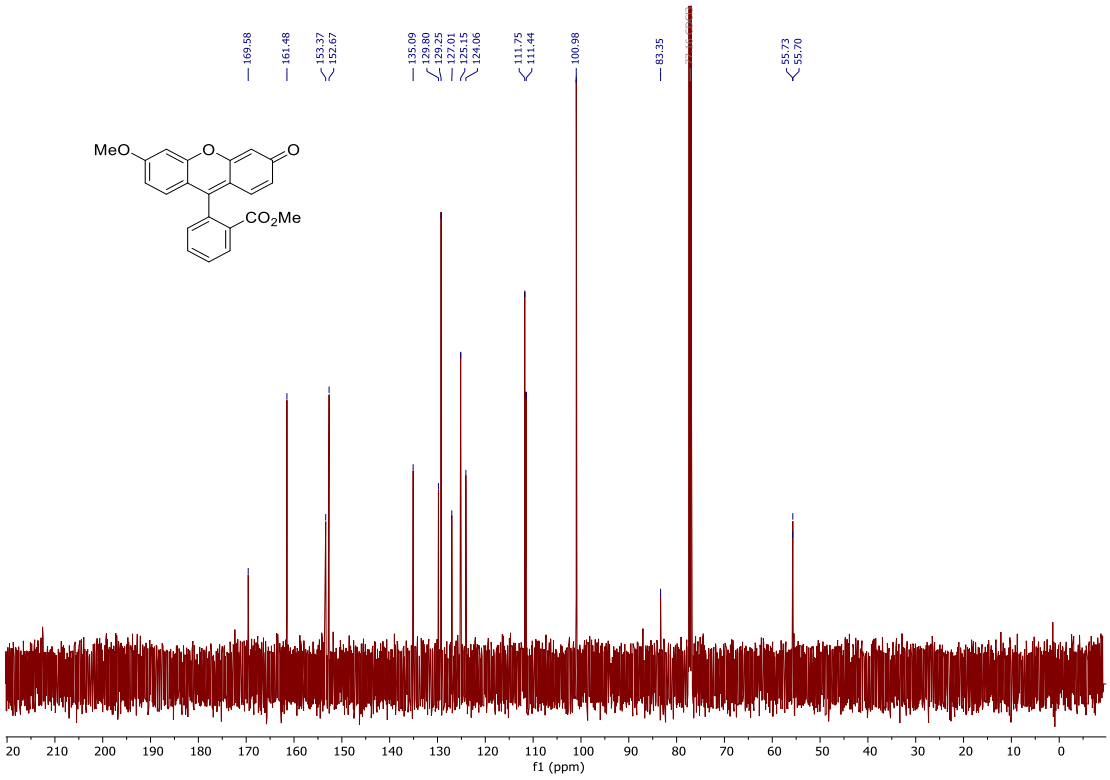
^{1}H-NMR spectrum in $CDCl_3$:



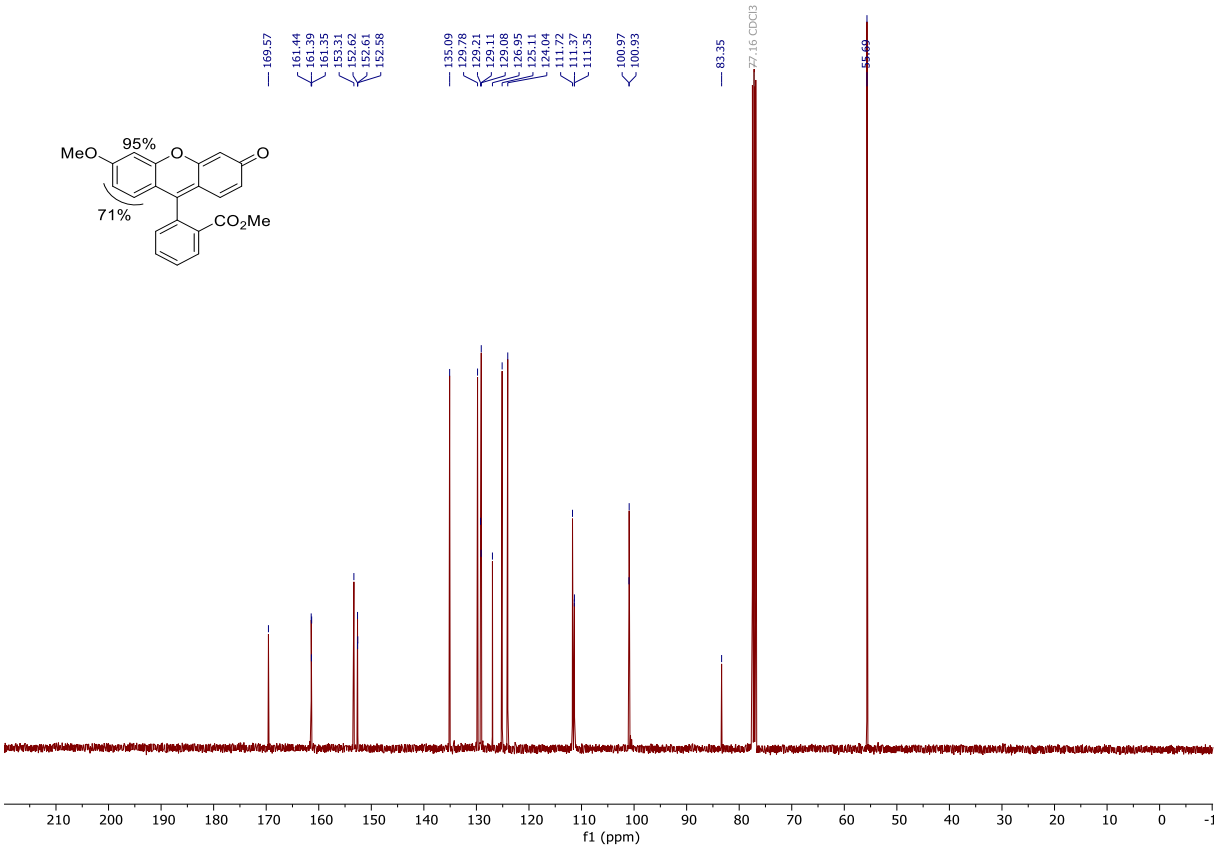
^{1}H-NMR spectrum in $CDCl_3$:



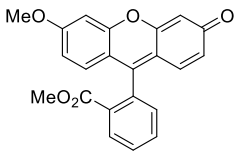
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of methyl 2-(6-methoxy-3-oxo-3*H*-xanthen-9-yl)benzoate (31) Using Conditions B:



Following the general procedure F and using methyl 2-(6-methoxy-3-oxo-3H-xanthen-9-yl)benzoate (**31**) (72.1 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAC = 9:1 as the eluent, the target compound **[D]31** was obtained as colorless solid (64.2 mg, 88%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 4.57 D/molecule [Mass]; 4.85 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.02 (d, *J* =7.5 Hz, 1H), 7.66 (td, *J* = 7.4, 1.2 Hz, 1H), 7.61 (td, *J* = 7.4, 1.1 Hz, 1H), 7.16 (d, *J* = 7.5 Hz, 1H), 6.78 (d, *J* = 2.5 Hz, 2H), 6.69 (d, *J* = 8.7 Hz, 2H), 6.61 (dd, *J* = 8.8, 2.6 Hz, 2H), 3.84 (s, 6H) ppm.

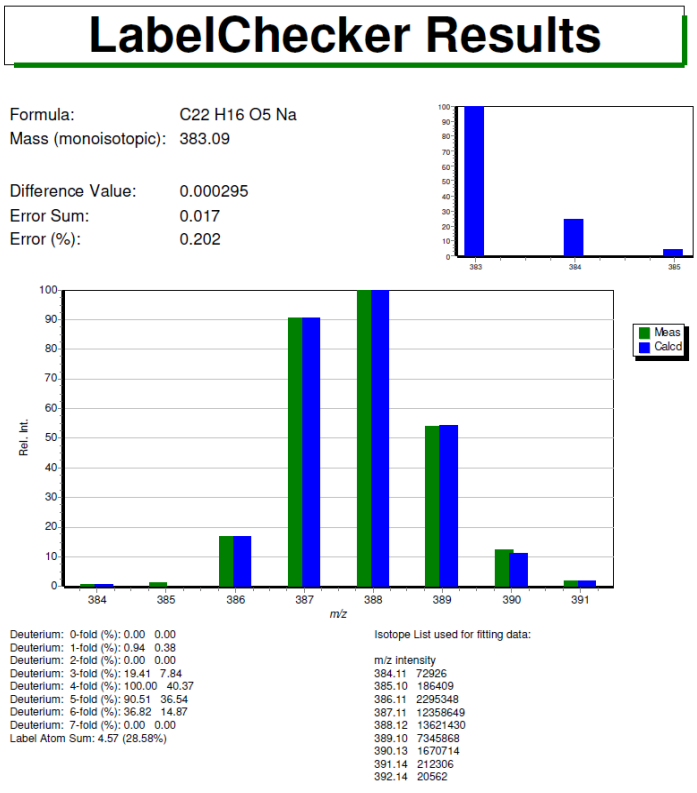
^{13}C NMR (126 MHz, $CDCl_3$) δ = 169.6, 161.5, 153.4, 152.7, 135.1, 129.8, 129.3, 127.0, 125.2, 124.1, 111.8, 111.4, 101.0, 83.4, 55.7(3), 55.7(0) ppm.

NMR Data of Product:

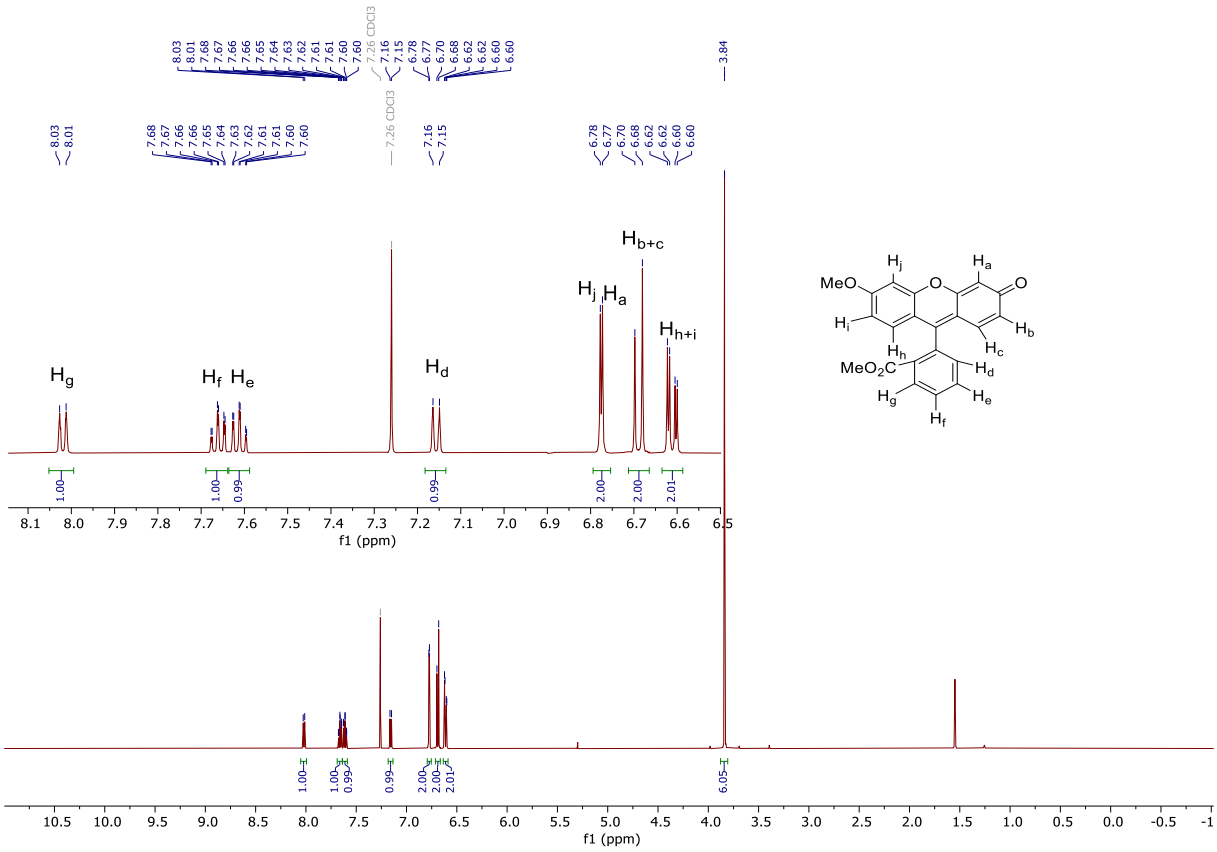
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.05-7.99 (m, 0.74H, 26% D), 7.69-7.63 (m, 0.75H, 25% D), 7.63-7.58 (m, 0.68H, 32% D), 7.19-7.12 (m, 1H), 6.77 (s, 0.11H, 95% D), 6.72-6.65 (m, 1.75H, 12.5% D), 6.60 (d, J = 8.8 Hz, 0.10H, 95% D), 3.82 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 169.6, 161.4, 153.3, 152.7, 135.4-134.4 (1C), 130.0-129.5 (1C), 129.2-128.9 (2C), 127.0-126.8 (1C), 125.2-124.9 (1C), 124.2-123.7 (1C), 112.4-110.9 (1C), 101.3-100.0 (2C), 83.4, 55.7 ppm.

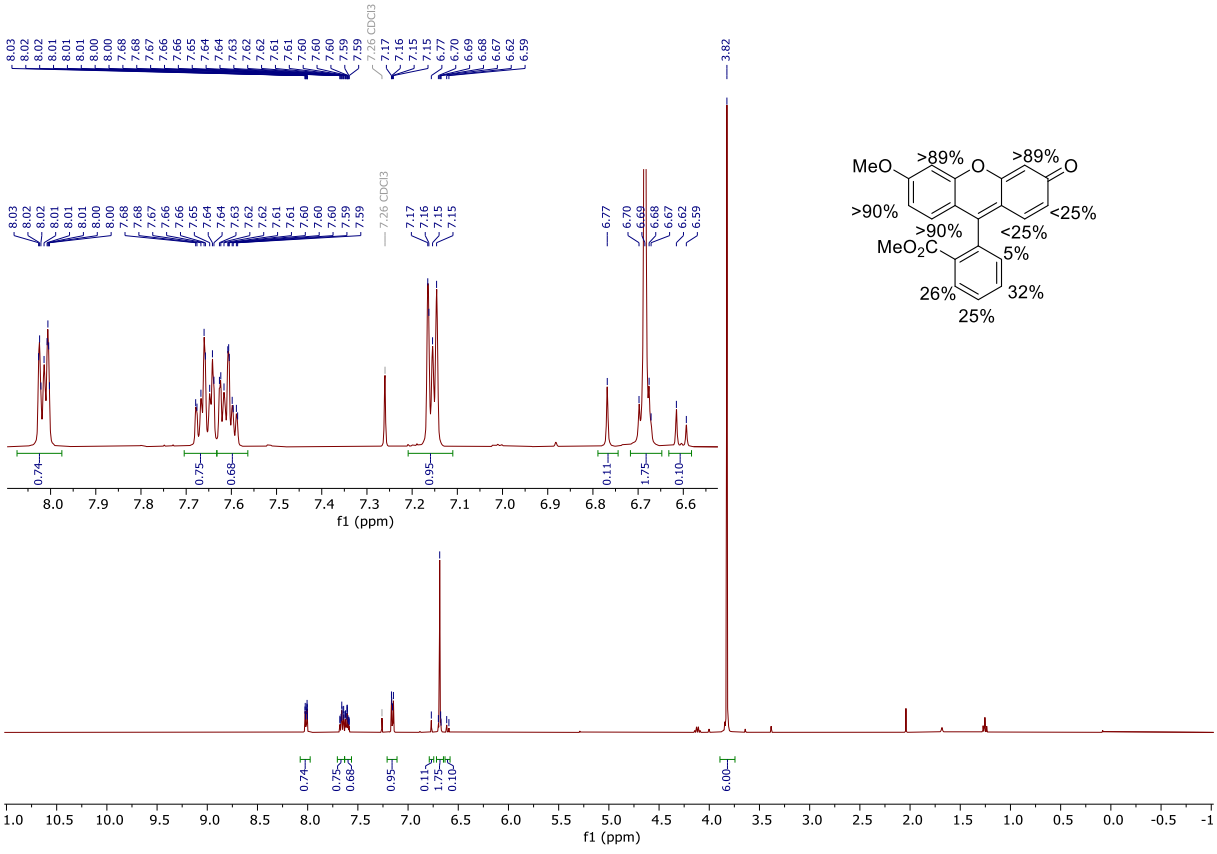
Mass Data:



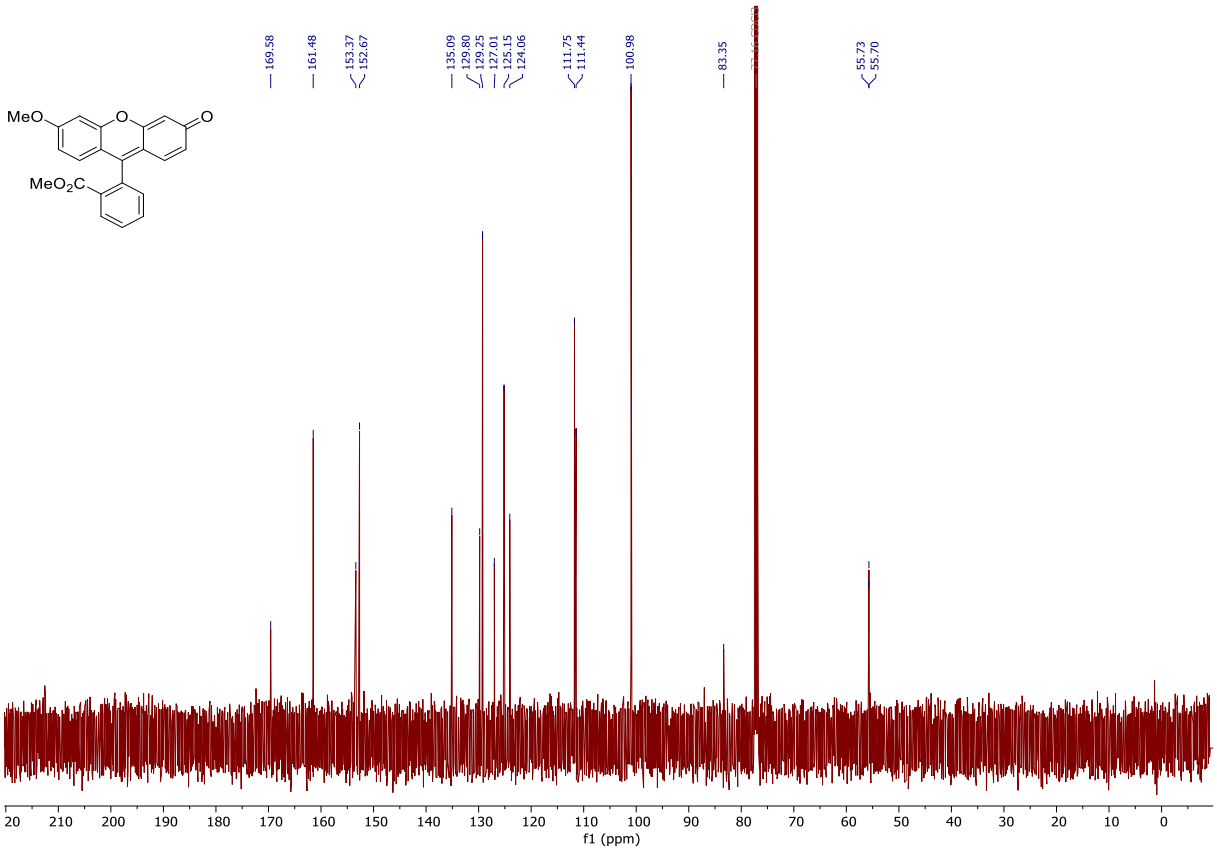
^{1}H-NMR spectrum in $CDCl_3$:



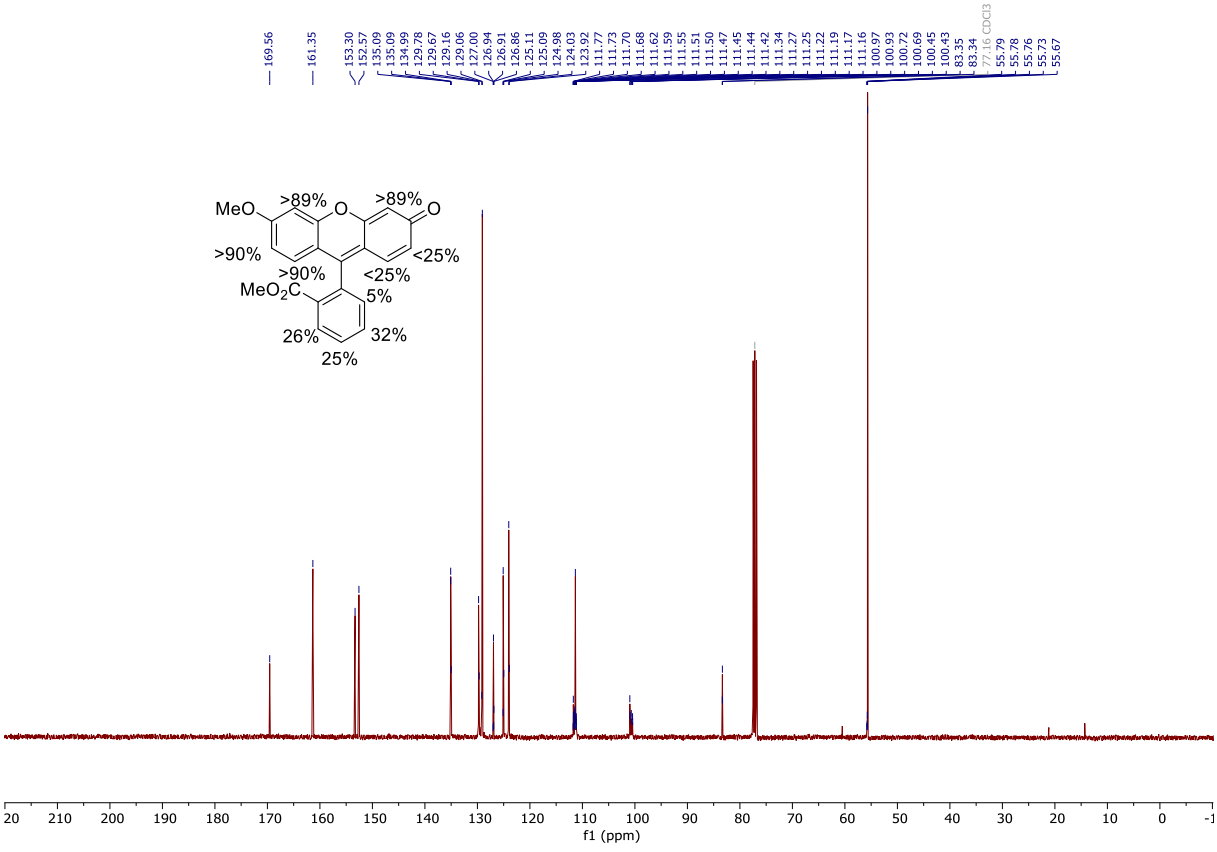
^{1}H-NMR spectrum in $CDCl_3$:



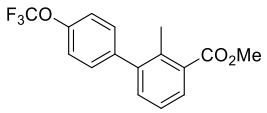
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of methyl 2-methyl-4'-(trifluoromethoxy)-[1,1'-biphenyl]-3-carboxylate (32):



Following the general procedure F and using methyl methyl 2-methyl-4'-(trifluoromethoxy)-[1,1'-biphenyl]-3-carboxylate (**32**) (62.1 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:Et_2O = 50:1 as the eluent, the target compound **[D]32** was obtained as light-yellow liquid (56.2 mg, 89%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 6.06 D/molecule [Mass]; 6.02 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (500 MHz, C_6D_6) δ = 7.84 (dd, *J* = 7.6, 1.7 Hz, 1H), 6.99 (dd, *J* = 7.8, 1.6 Hz, 1H) 6.94 (t, *J* = 7.6 Hz, 1H), 6.92-6.89 (m, 2H), 6.83-6.79 (m, 2H), 3.51 (s, 3H), 2.42 (s, 3H) ppm.

^{13}C NMR (126 MHz, C_6D_6) δ = 168.2, 148.7 (q, *J* = 1.7 Hz), 142.7, 140.6, 137.2, 133.3, 132.2, 131.0, 130.0, 125.6, 121.3 (q, *J* = 257 Hz), 120.9 (d, *J* = 1.0 Hz), 51.6, 18.6 ppm.

^{19}F NMR (470 MHz, C_6D_6) δ = –57.7 ppm.

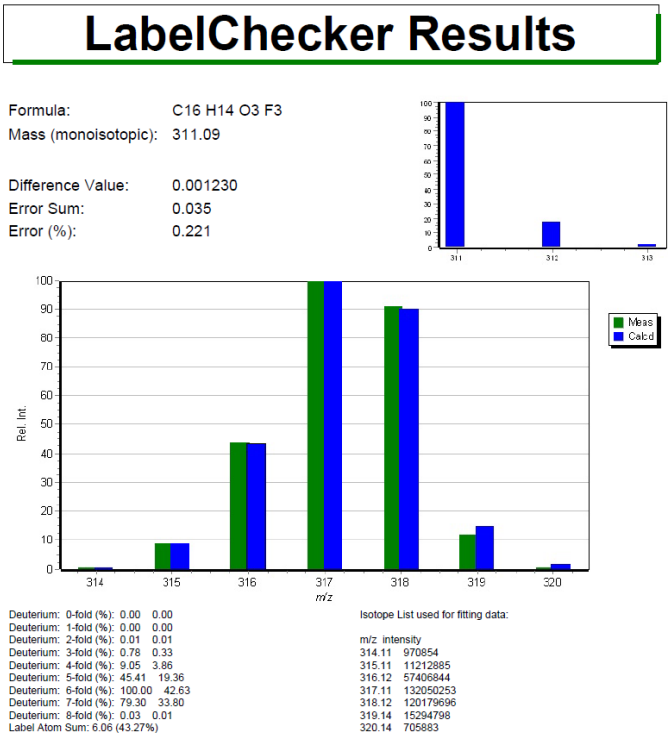
NMR Data of Product:

^{1}H NMR (400 MHz, C_6D_6) δ = 7.84 (s, 0.06H, 94% D), 6.99 (s, 0.09H, 91% D), 6.95 (s, 0.07H, 93% D), 6.91 (s, 0.12H, 94% D), 6.82 (s, 0.58H, 71% D), 3.52 (s, 3H), 2.42 (s, 3H) ppm.

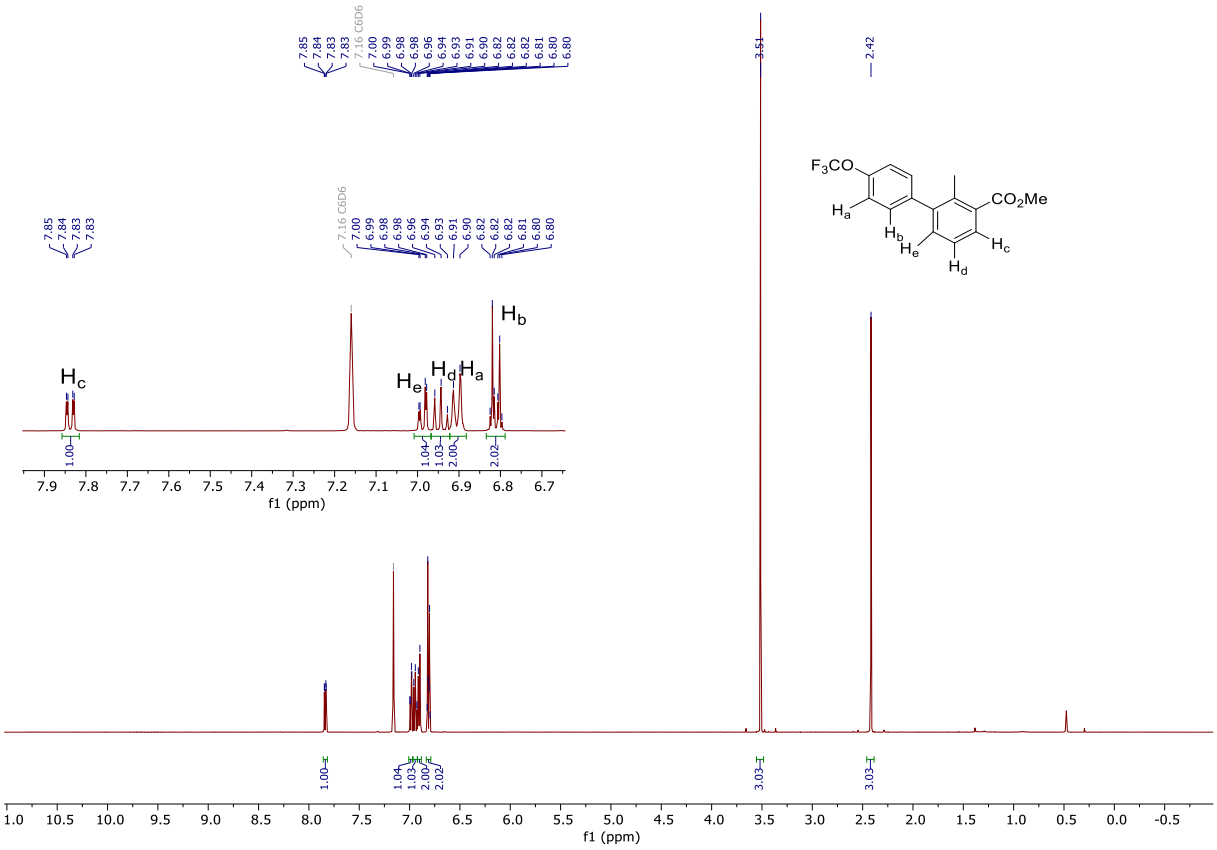
^{13}C NMR (101 MHz, C_6D_6) δ = 168.2, 148.6 (d, *J* = 2.2 Hz), 143.3-141.6 (1C), 140.3-140.5 (1C), 137.2, 133.7-132.4 (1C), 132.1, 131.4-130.2 (1C), 130.2-129.2 (1C), 125.6-124.5 (1C), 121.3 (q, *J* = 257 Hz), 121.2-121.1 (1C), 51.6, 18.6 ppm.

^{19}F NMR (377 MHz, C_6D_6) δ = –57.7 ppm.

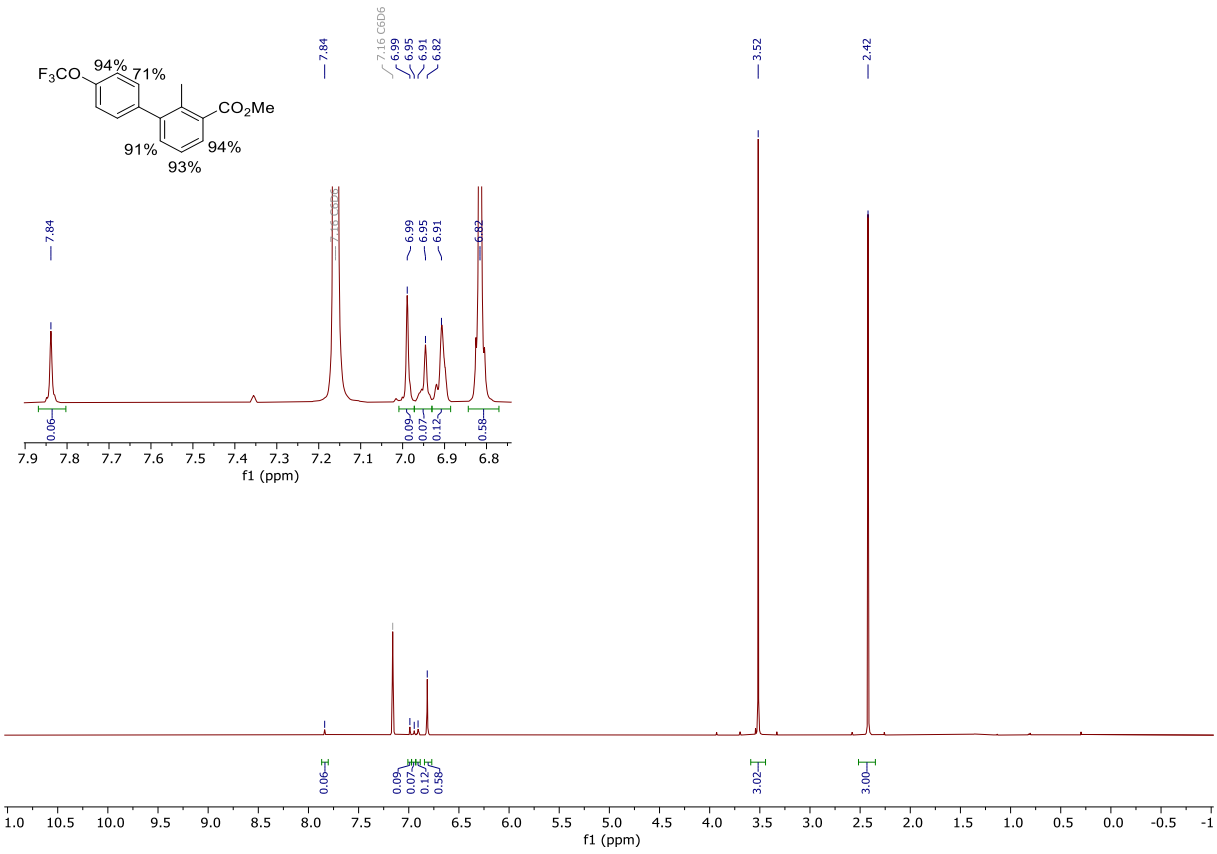
Mass Data:



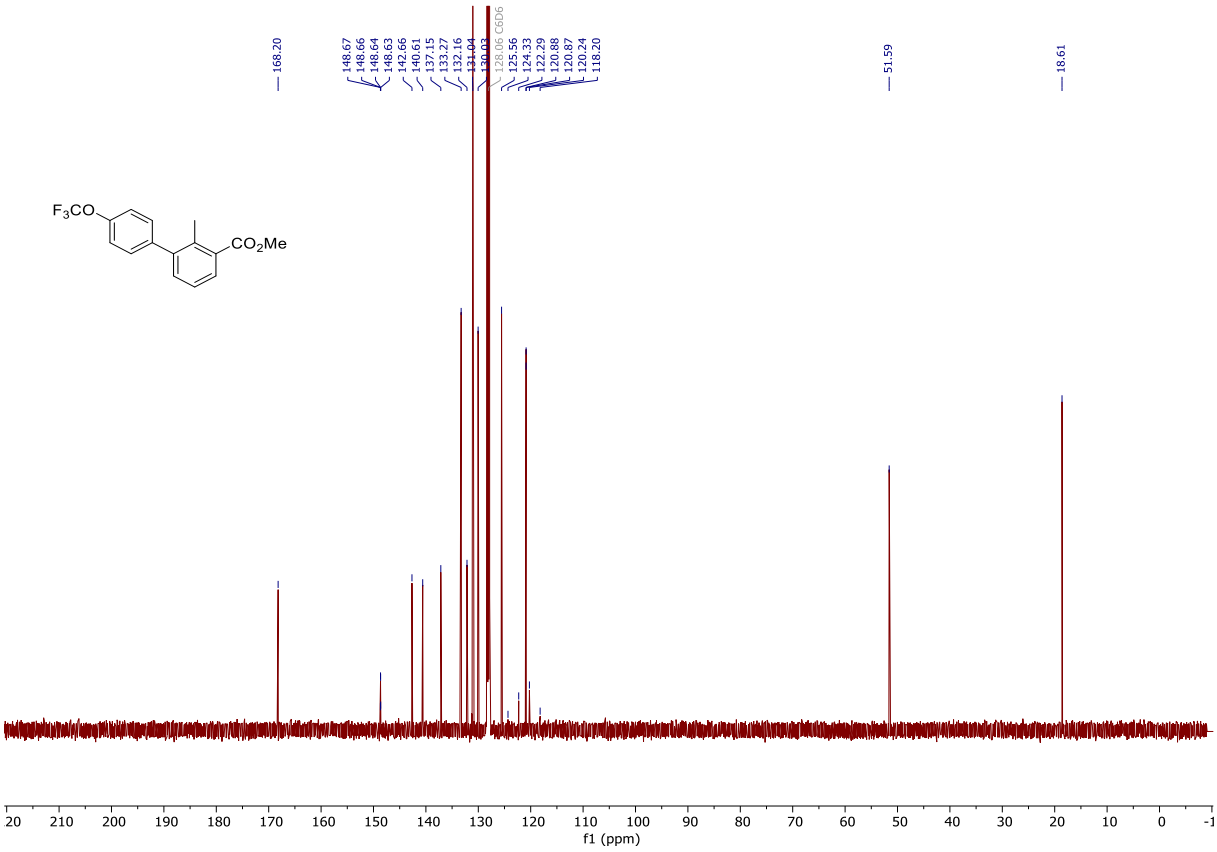
^{1}H-NMR spectrum in C_6D_6:



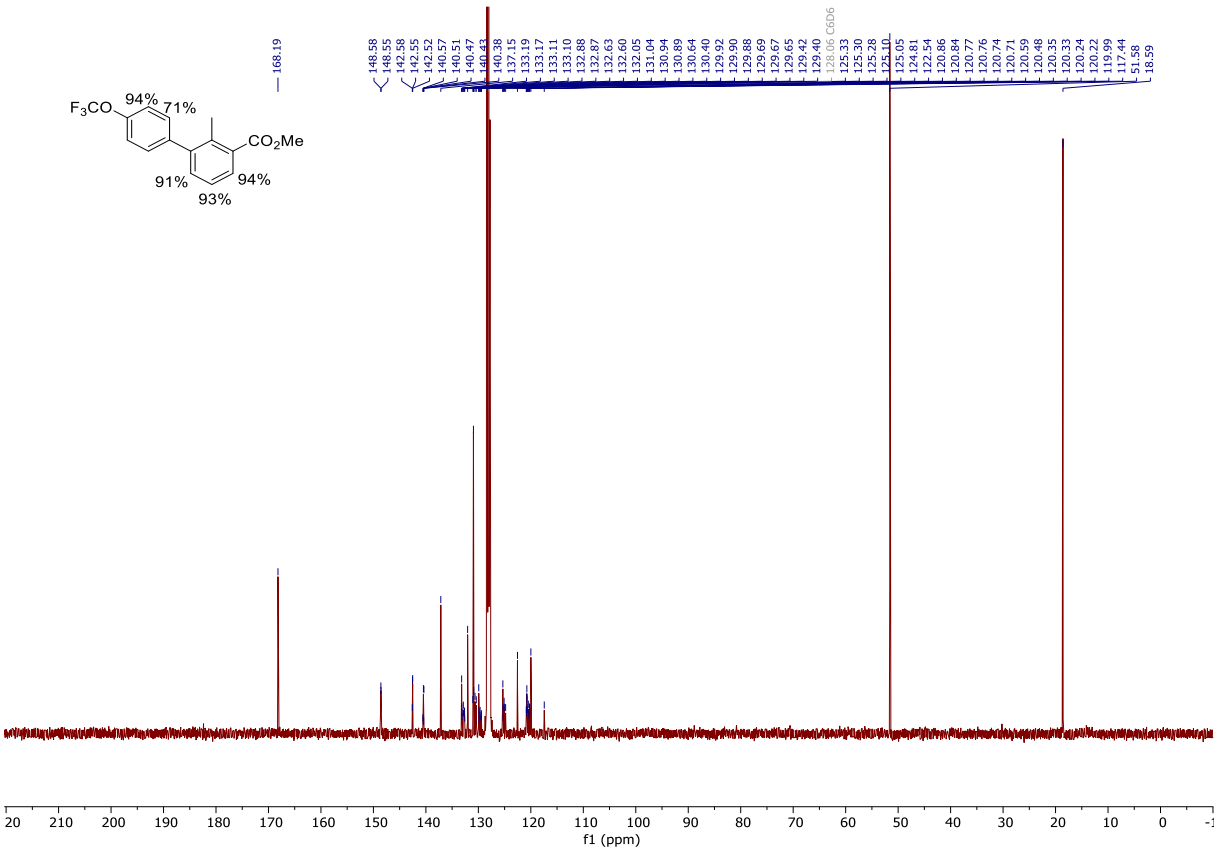
^{1}H-NMR spectrum in C_6D_6:



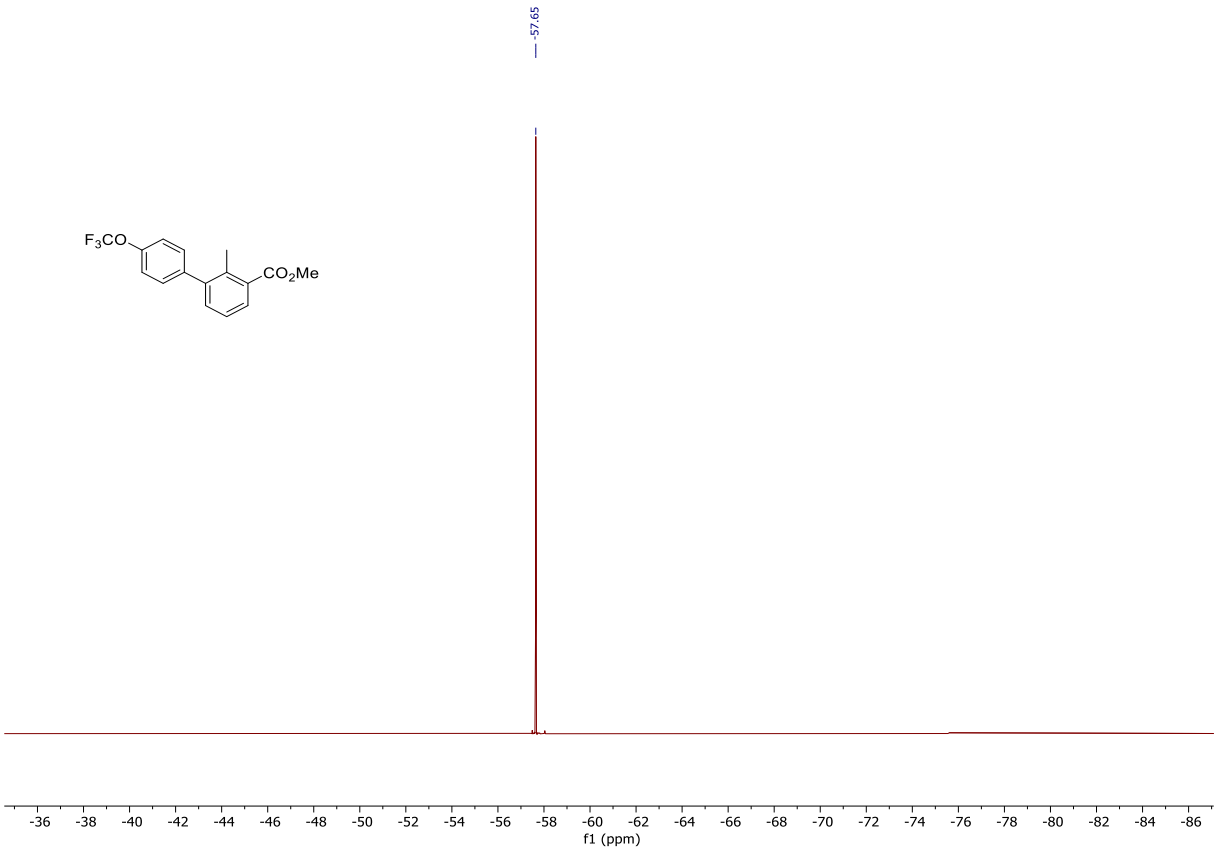
^{13}C-NMR spectrum in C_6D_6:



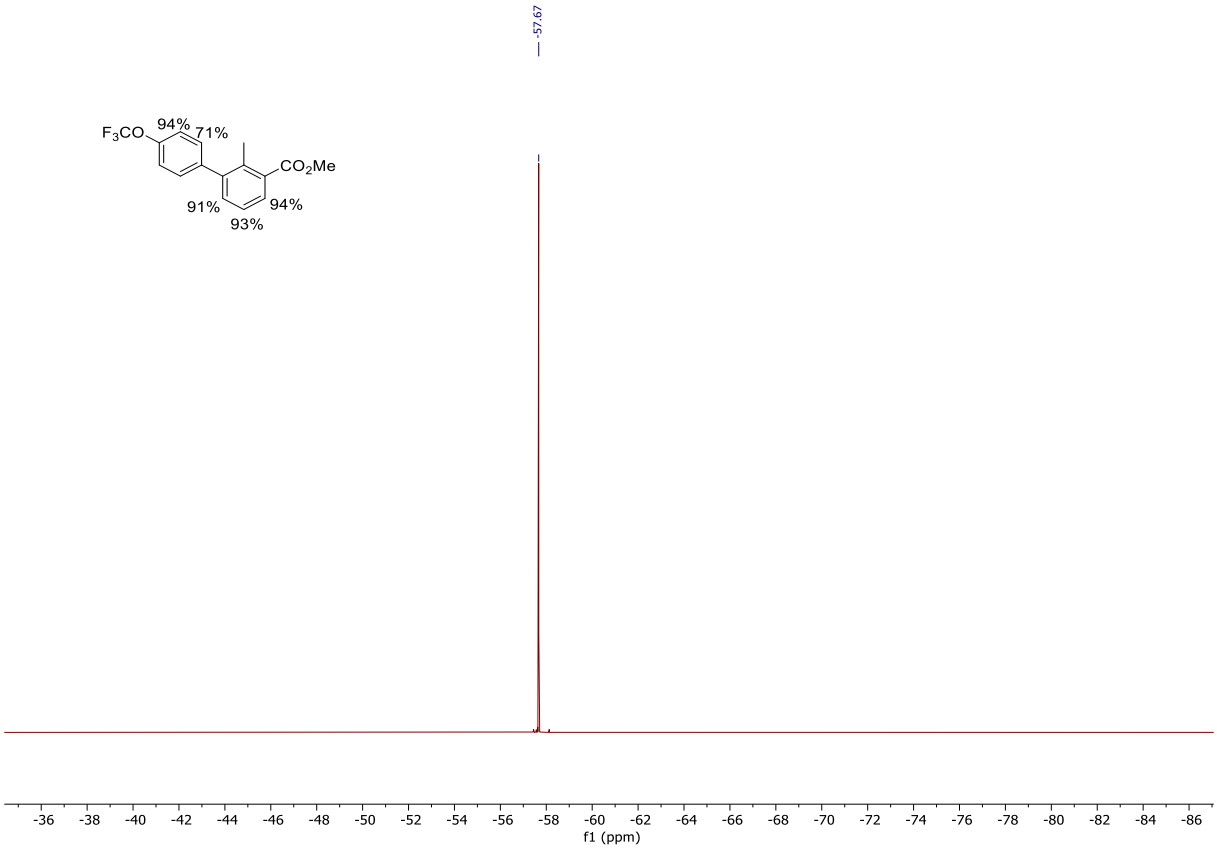
^{13}C-NMR spectrum in C_6D_6:



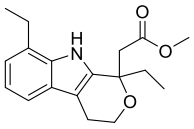
^{19}F-NMR spectrum in C_6D_6:



^{19}F-NMR spectrum in C_6D_6:



Deuteration of 2,2-dimethyl-2,3-dihydrobenzofuran-7-yl methylcarbamate (33):



Following the general procedure E and using 2,2-dimethyl-2,3-dihydrobenzofuran-7-yl methylcarbamate **(33)** (60.3 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAC = 20:1→10:1 as the eluent, the target compound **[D]33** was obtained as a colorless solid (47.4 mg, 78%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 2.31 D/molecule [HRMS]; 2.28 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (599 MHz, $CDCl_3$) δ = 9.06 (br. s, 1H), 7.37 (d, *J* = 7.6 Hz, 1H), 7.07 (dd, *J* = 7.6 Hz, 1H), 7.02 (d, J = 7.6 Hz, 1H), 4.06 (dd, *J* = 11.2, 4.8, 4.8 Hz, 1H), 3.95 (ddd, *J* = 11.6, 7.6, 4.3 Hz, 1H), 3.73 (s, 3H), 3.03 (d, *J* = 16.5 Hz, 1H), 2.93 (d, *J* = 16.5 Hz, 1H), 2.89 (qd, *J* = 7.6, 2.0 Hz, 2H), 2.85 (ddd, *J* = 15.1, 7.6, 4.9 Hz, 1H), 2.76 (ddd, *J* = 15.2, 4.6, 4.6 Hz, 1H), 2.18 (dq, *J* = 14.8, 7.4 Hz, 1H), 2.02 (dq, *J* = 14.6, 7.3 Hz, 1H), 1.39 (t, *J* = 7.6 Hz, 3H), 0.85 (dd, *J* = 7.4 Hz, 3H) ppm.

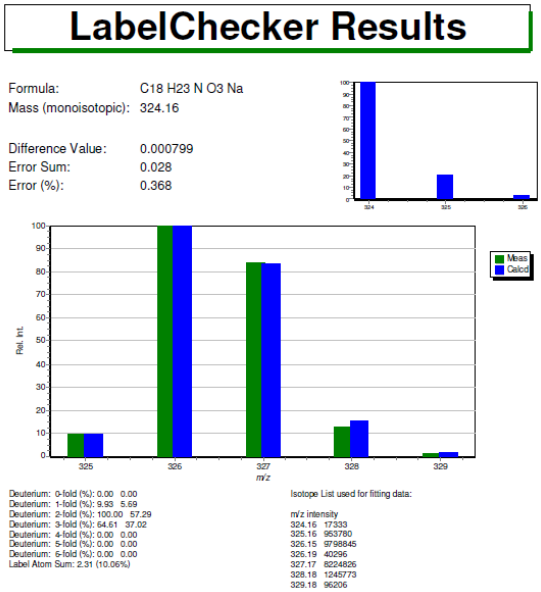
^{13}C NMR (101 MHz, $CDCl_3$) δ = 173.4, 136.0, 134.6, 126.8, 126.3, 120.5, 119.7, 116.1, 108.6, 74.7, 60.8, 52.1, 42.9, 30.8, 24.3, 22.5, 13.9, 7.7 ppm.

NMR Data of Product:

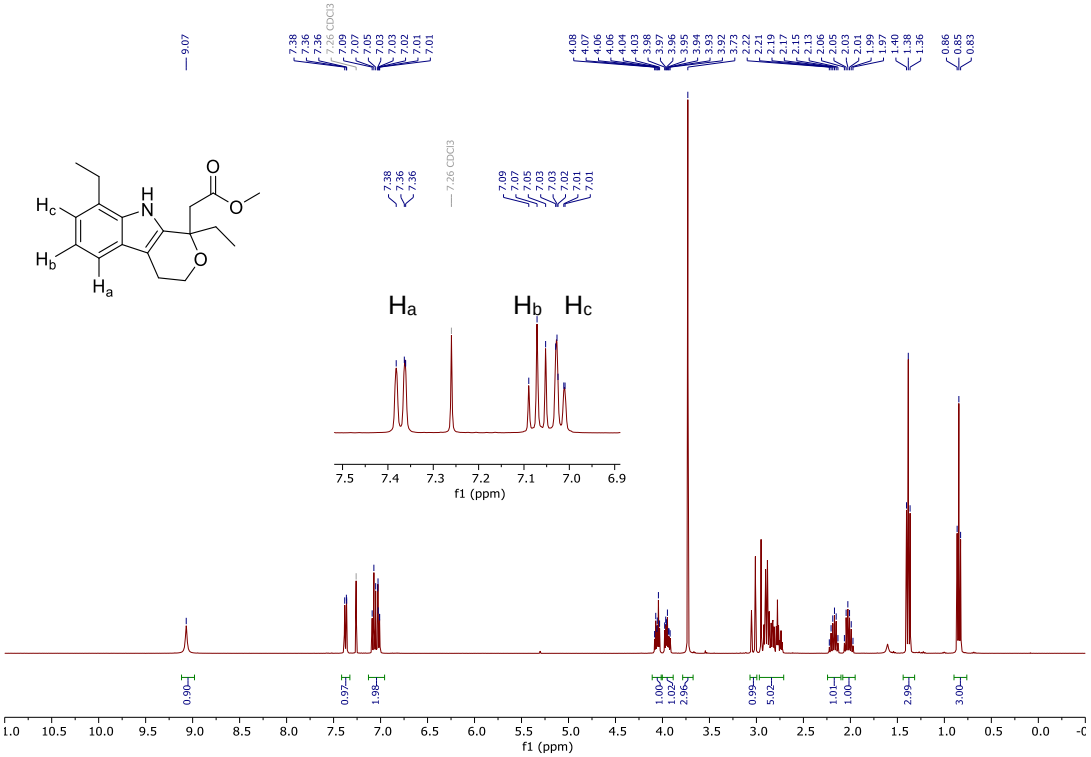
^{1}H NMR (599 MHz, $CDCl_3$) δ = 9.06 (br. s, 1H), 7.40-35 (m, 0.07H, 93%D), 7.08-7.05 (m, 0.05H, 95%), 7.02 (s, 0.60H, 40%D), 4.06 (dd, *J* = 11.2, 4.8, 4.8 Hz, 1H), 3.95 (ddd, *J* = 11.6, 7.6, 4.3 Hz, 1H), 3.73 (s, 3H), 3.03 (d, *J* = 16.5 Hz, 1H), 2.93 (d, *J* = 16.5 Hz, 1H), 2.89 (qd, *J* = 7.6, 2.0 Hz, 2H), 2.85 (ddd, *J* = 15.1, 7.6, 4.9 Hz, 1H), 2.76 (ddd, *J* = 15.2, 4.6, 4.6 Hz, 1H), 2.18 (dq, *J* = 14.8, 7.4 Hz, 1H), 2.02 (dq, *J* = 14.6, 7.3 Hz, 1H), 1.38 (t, *J* = 7.6 Hz, 3H), 0.84 (dd, *J* = 7.4 Hz, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 173.4, 136.0, 134.6, 126.8-126.4 (1C), 126.3-126.1 (1C), 120.4, 119.8-119.4 (1C), 116.2-115.7 (1C), 108.5, 74.8, 60.8, 52.1, 43.0, 30.8, 24.3-24.2 (1C), 22.6, 13.9-13.8 (1C), 7.7 ppm.

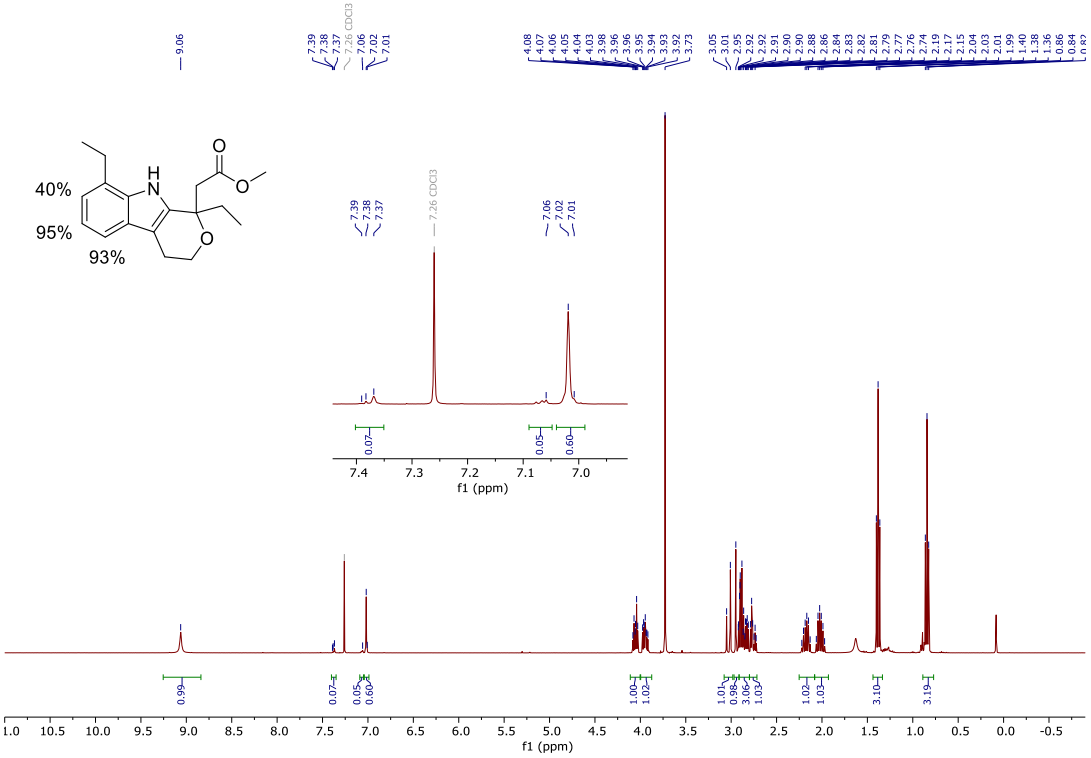
Mass Data:



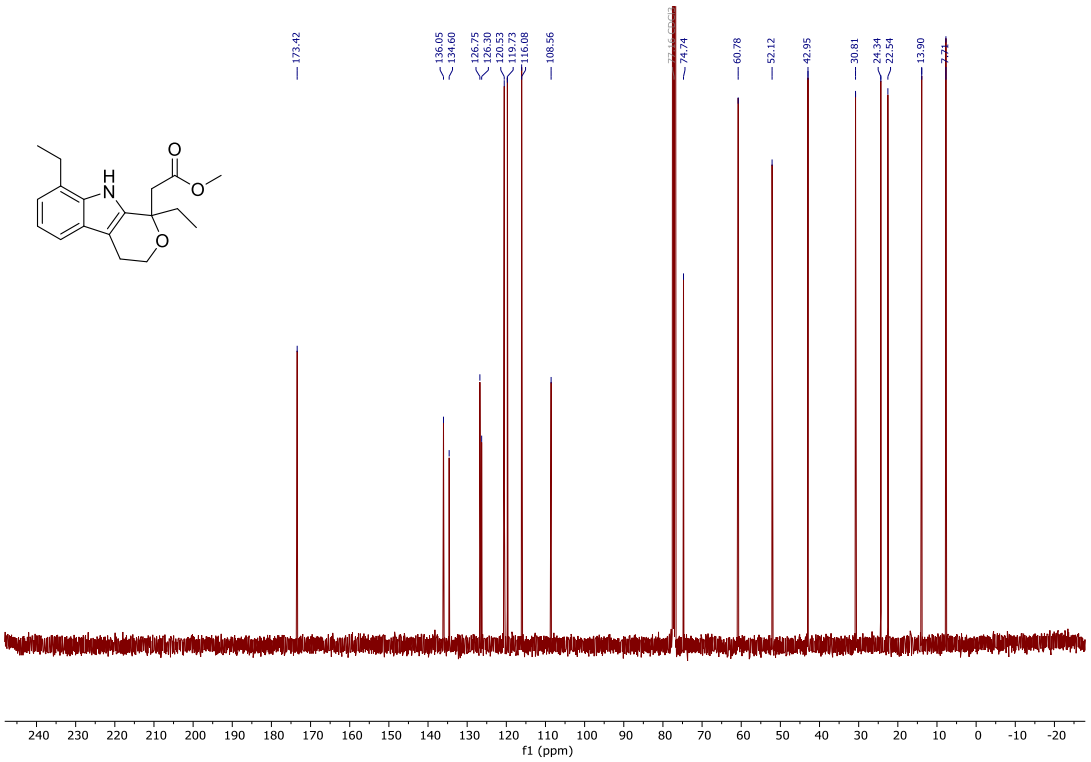
^{1}H-NMR spectrum in $CDCl_3$:



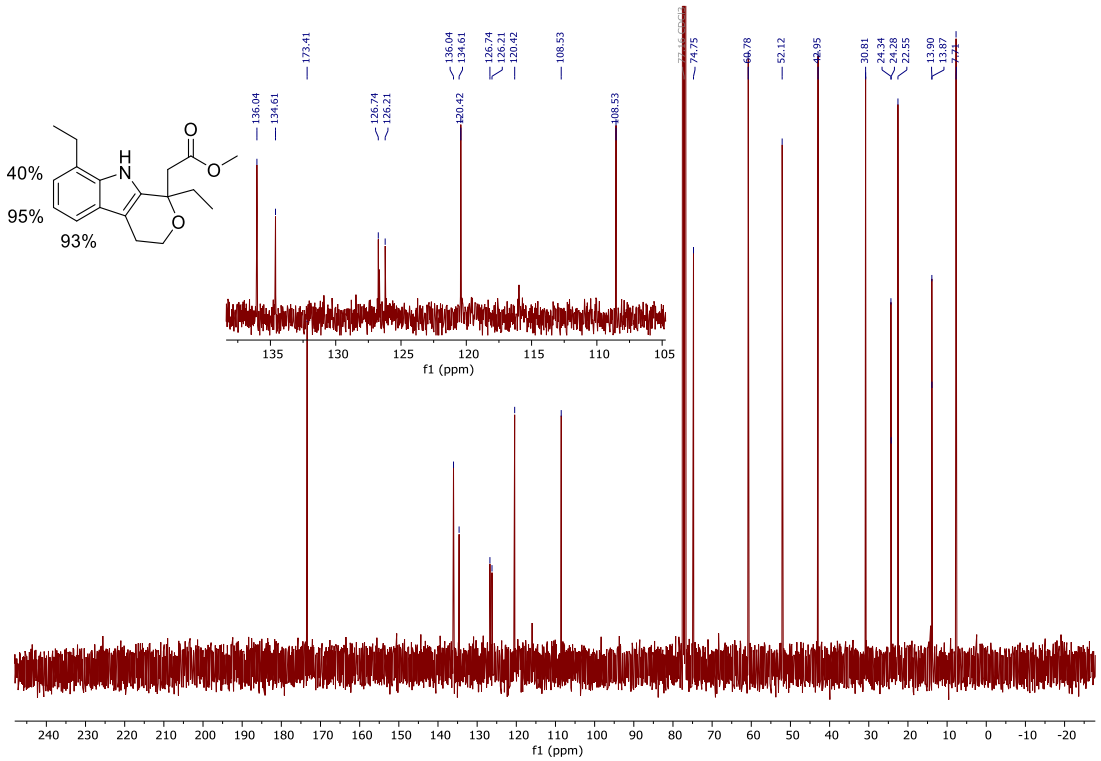
^{1}H-NMR spectrum in $CDCl_3$:



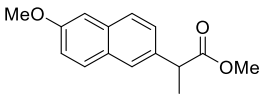
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of methyl 2-(6-methoxynaphthalen-2-yl)propanoate (34):



Following the general procedure E and using methyl 2-(6-methoxynaphthalen-2-yl)propanoate **(34)** (48.9 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAc = 4:1 as the eluent, the target compound **[D]34** was obtained as colorless solid (40.2 mg, 80%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 5.54 D/molecule [HRMS]; 5.68 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.70 (d, *J* = 8.6 Hz, 2H), 7.66 (d, *J* = 1.6 Hz, 1H), 7.40 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.14 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.11 (d, *J* = 2.5 Hz, 1H), 3.91 (s, 3H), 3.86 (q, *J* = 7.3 Hz, 1H), 3.67 (s, 3H), 1.60-1.56 (m, 3H) ppm.

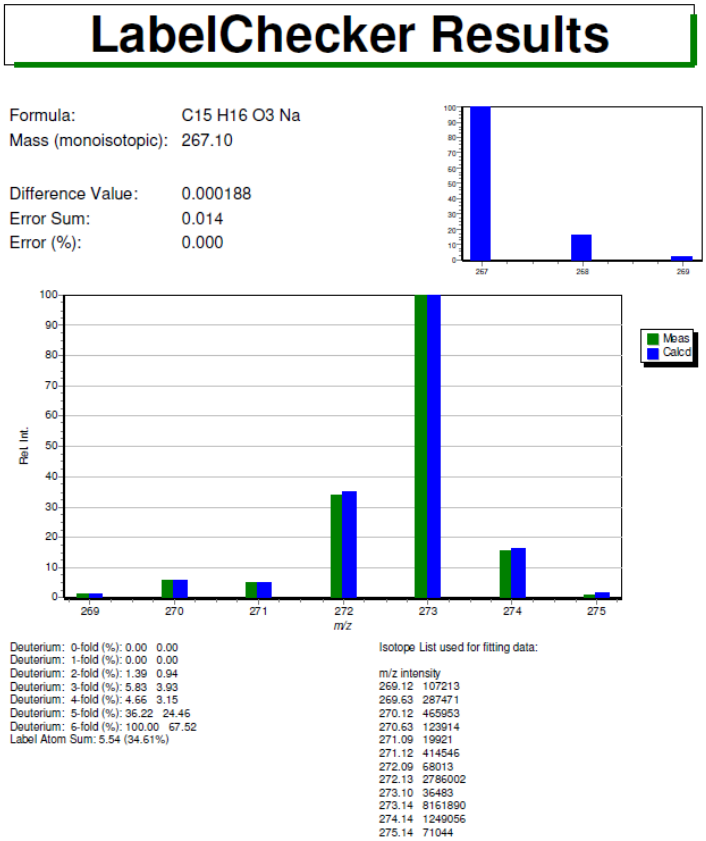
^{13}C NMR (150 MHz, $CDCl_3$) δ = 175.3, 157.8, 135.8, 133.9, 129.4, 129.1, 127.3, 126.3, 126.1, 119.1, 105.8, 55.5, 52.2, 45.5, 18.7 ppm.

NMR Data of Product:

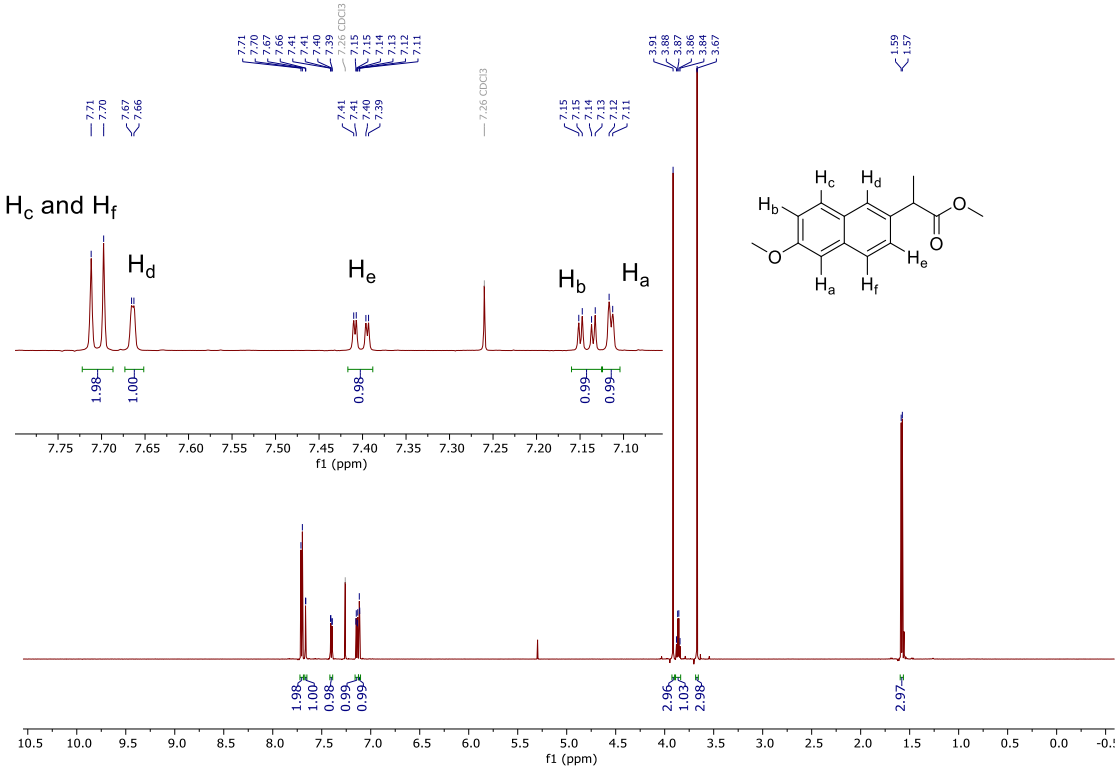
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.71 (s, 0.09H, 91.0-95.5% D), 7.67 (s, 0.05H, 95% D), 7.41 (s, 0.08H, 92% D), 7.15 (s, 0.05H, 95% D), 7.12 (s, 0.05H, 95% D), 3.91 (s, 3H), 3.87 (q, *J* = 7.2 Hz, 1H), 3.67 (s, 3H), 1.59 (d, *J* = 7.2 Hz, 3H) ppm.

^{13}C NMR (150 MHz, $CDCl_3$) δ = 175.3, 157.7, 135.6, 133.7, 129.7-128.1 (2C), 127.7-124.8 (3C), 119.5-117.7 (1C), 106.5-104.6 (1C), 55.4, 52.2, 45.4, 18.7 ppm.

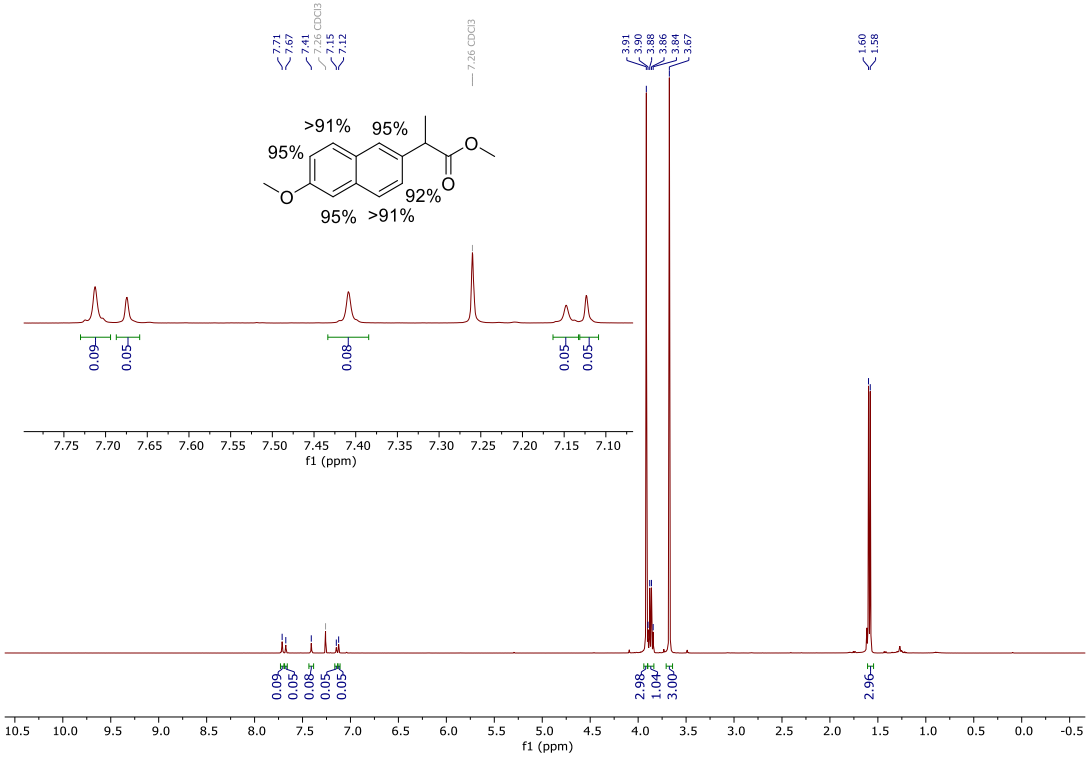
Mass Data:



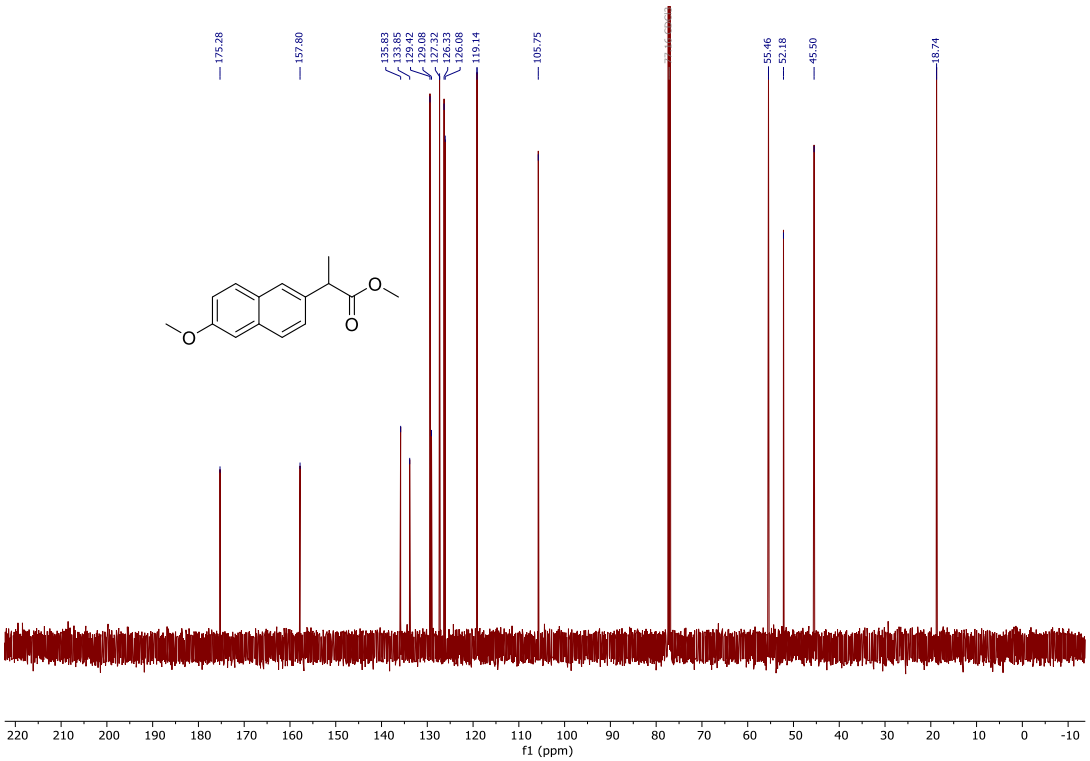
^{1}H-NMR spectrum in $CDCl_3$:



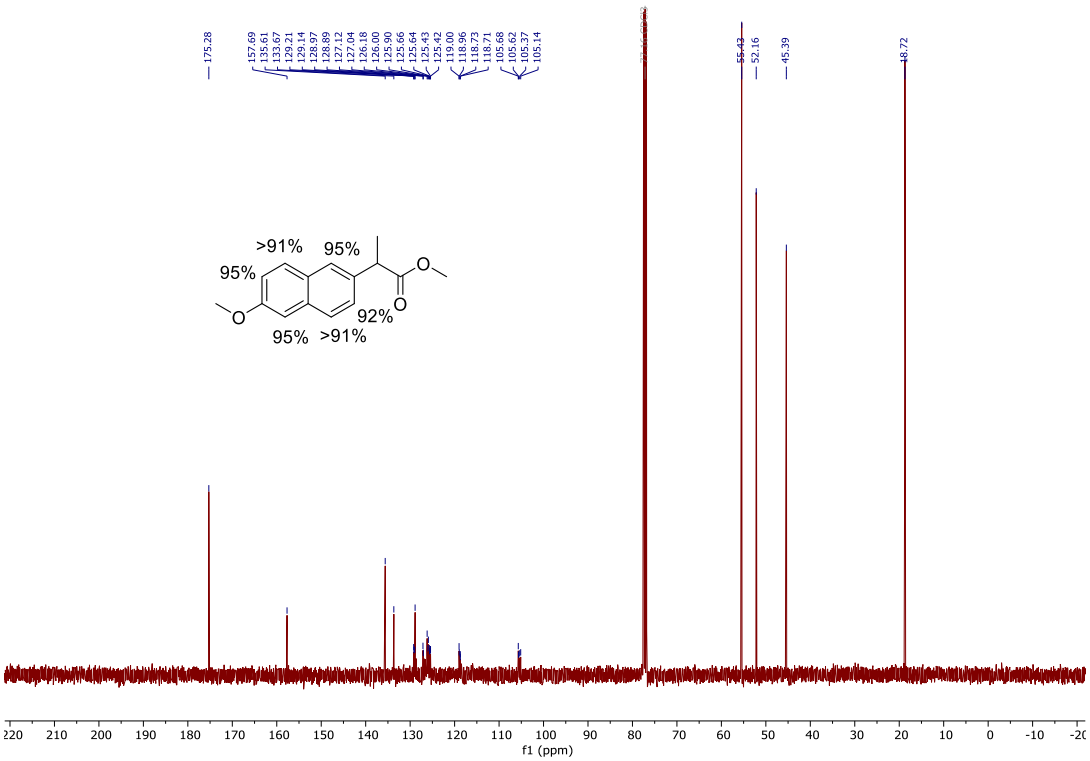
^{1}H-NMR spectrum in $CDCl_3$:



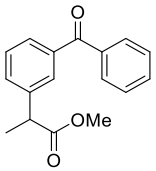
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of methyl 2-(3-benzoylphenyl)propanoate (35):



Following the general procedure F and using methyl 2-(3-benzoylphenyl)propanoate (**35**) (53.7 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAc = 9:1 as the eluent, the target compound **[D]35** was obtained as colorless solid (34.7 mg, 63%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 7.25 D/molecule [Mass]; 7.37 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (599 MHz, $CDCl_3$) δ = 7.82-7.78 (m, 2H), 7.75 (t, *J* = 1.8 Hz, 1H), 7.68 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.62-7.57 (m, 1H), 7.54 (dt, *J* = 7.7, 1.6 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 2H), 7.44 (t, *J* = 7.7 Hz, 1H), 3.81 (q, *J* = 7.2 Hz, 1H), 3.68 (s, 3H), 1.54 (d, *J* = 7.2 Hz, 3H) ppm.

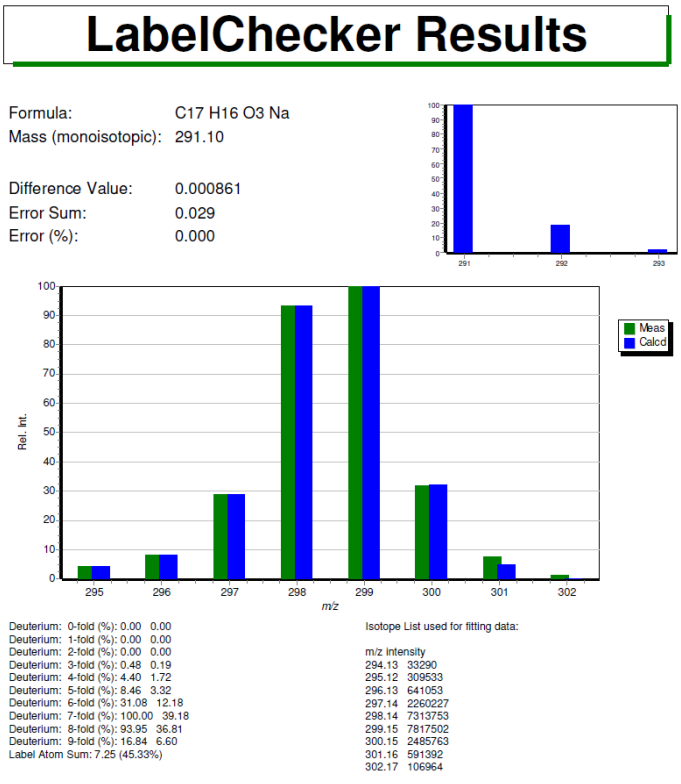
^{13}C NMR (151 MHz, $CDCl_3$) δ = 196.6, 174.7, 141.0, 138.1, 137.7, 132.6, 131.6, 130.2, 129.4, 129.2, 128.7, 128.4, 52.3, 45.4, 18.6 ppm.

NMR Data of Product:

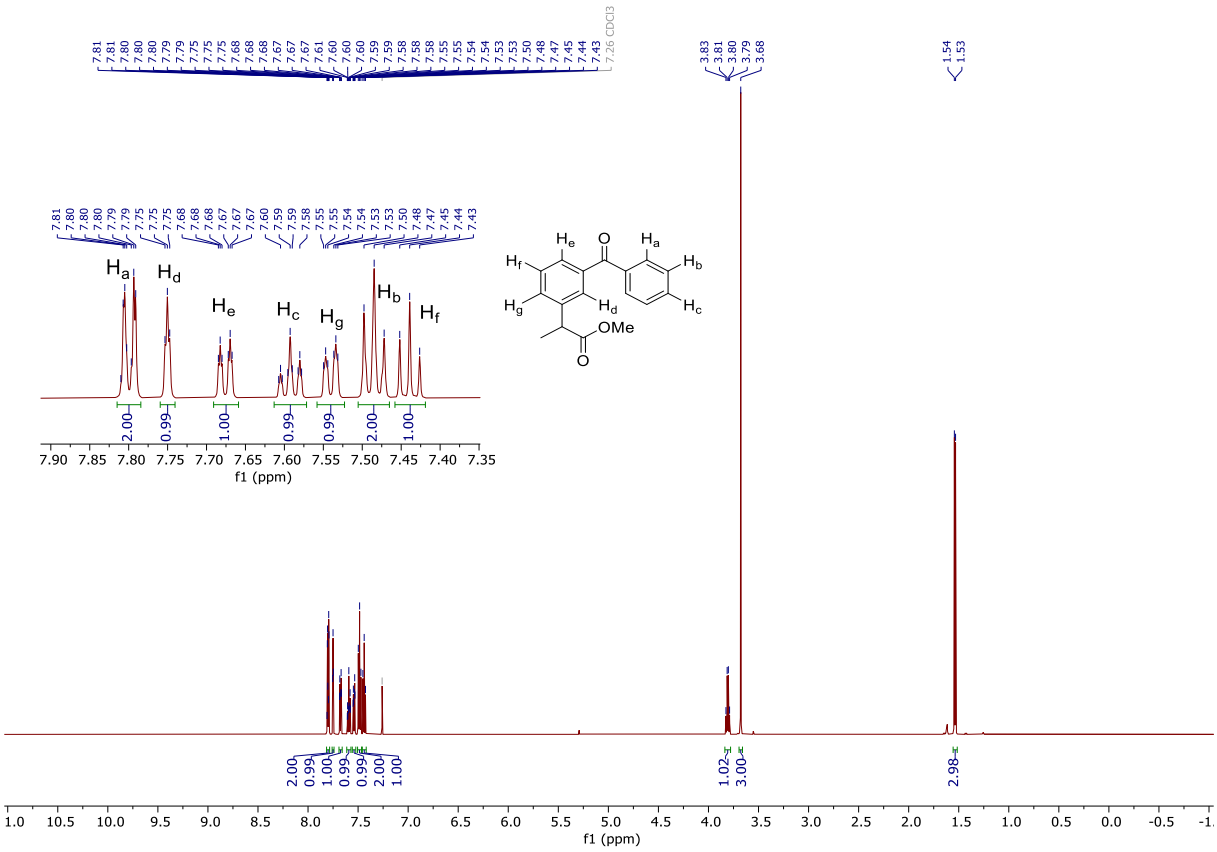
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.80 (s, 0.12H, 94% D), 7.75 (s, 0.80H, 20% D), 7.68 (s, 0.05H, 95% D), 7.59 (s, 0.06H, 94% D), 7.54 (s, 0.44H, 56% D), 7.48 (s, 0.11H, 94% D), 7.45-7.41 (m, 0.06H, 94% D), 3.81 (q, *J* = 7.2 Hz, 1H), 3.68 (s, 3H), 1.54 (d, *J* = 7.2 Hz, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 196.6, 174.7, 140.9 (d, *J* = 8.4 Hz), 138.0, 137.5, 132.6-127.5 (9C), 52.3, 45.4 (d, *J* = 4.4 Hz), 18.6 ppm.

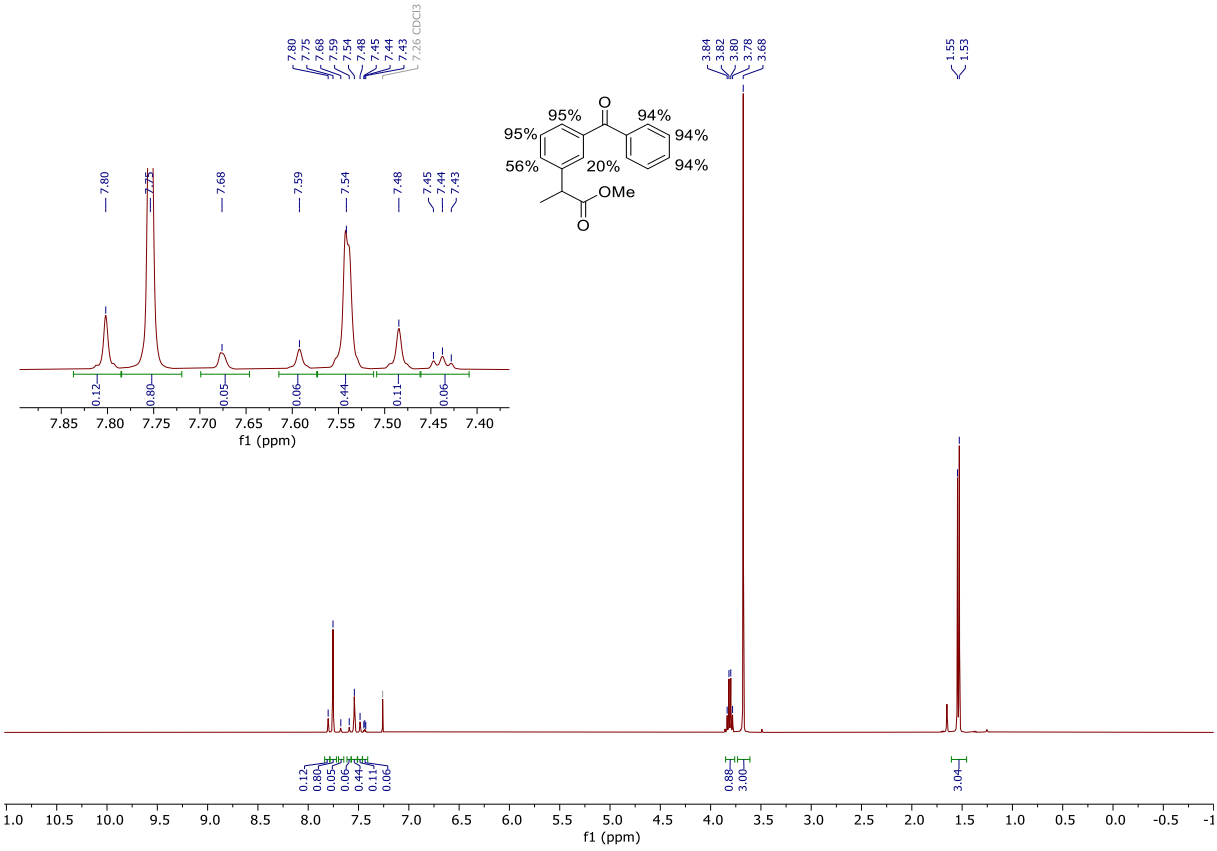
Mass Data:



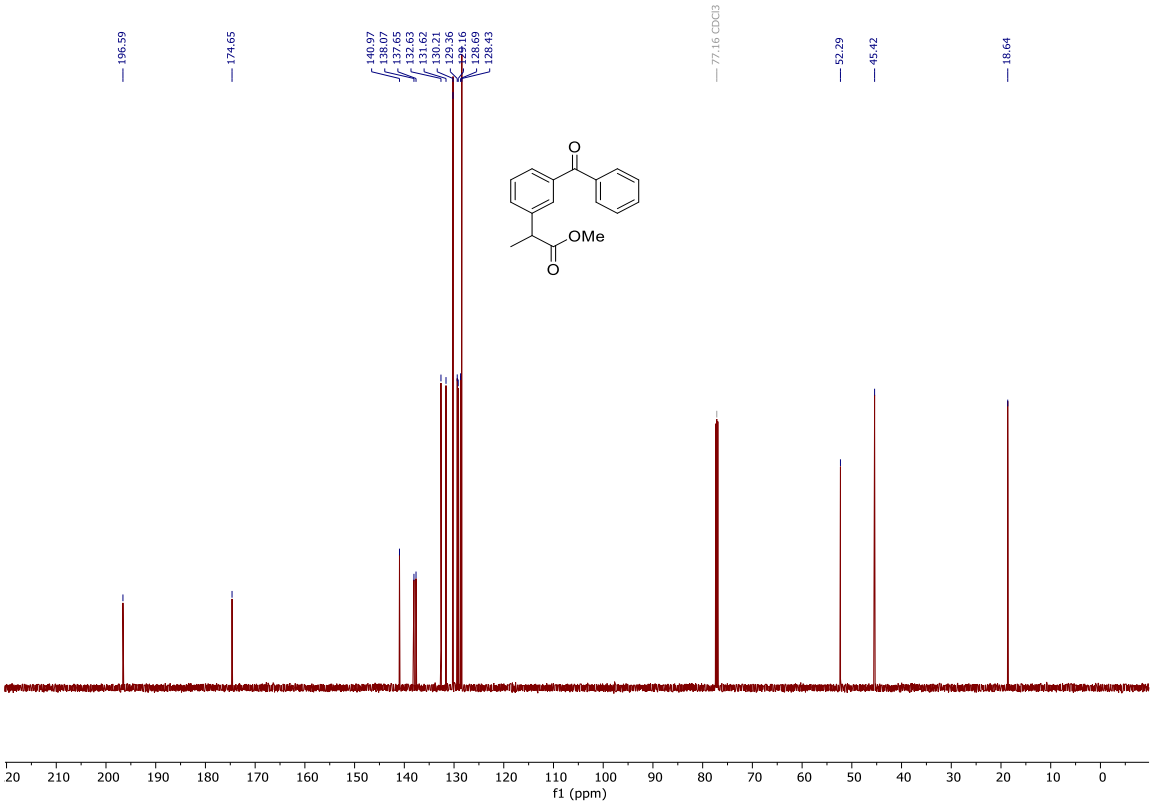
^{1}H-NMR spectrum in $CDCl_3$:



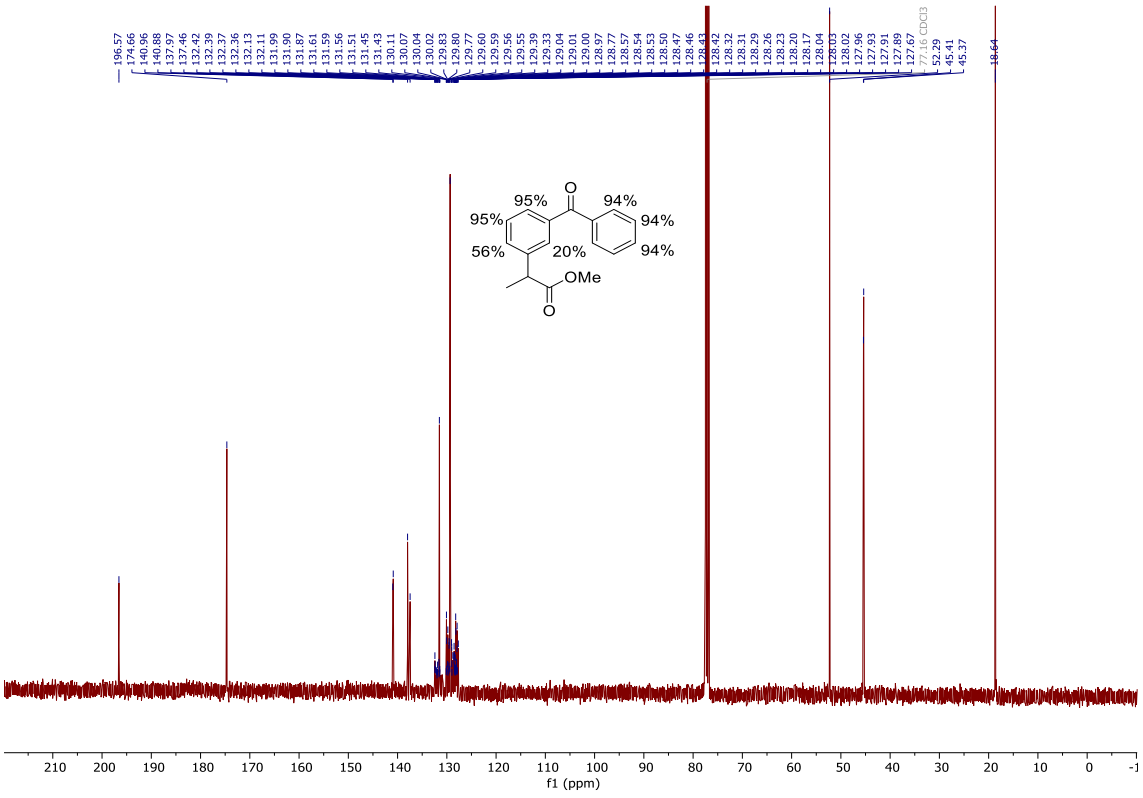
^{1}H-NMR spectrum in $CDCl_3$:



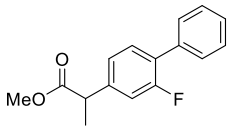
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of methyl 2-(2-fluoro-[1,1'-biphenyl]-4-yl)propanoate (36):



Following the general procedure F and using methyl 2-(2-fluoro-[1,1'-biphenyl]-4-yl)propanoate (**36**) (51.7 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAc = 9:1 as the eluent, the target compound **[D]36** was obtained as colorless solid (43.7 mg, 82%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 7.57 D/molecule [Mass]; 7.59 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR 599 MHz, $CDCl_3$) δ = 7.56-7.52 (m, 2H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.40 (t, *J* = 8.0 Hz, 1H), 7.38-7.35 (m, 1H), 7.15 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.13 (dd, *J* = 11.4, 1.7 Hz, 1H), 3.77 (q, *J* = 7.2 Hz, 1H), 3.71 (s, 3H), 1.54 (d, *J* = 7.2 Hz, 3H) ppm.

^{13}C NMR (151 MHz, $CDCl_3$) δ = 174.6, 159.8 (d, *J* = 248.4 Hz), 142.0 (d, *J* =7.6 Hz), 135.6 (d, *J* = 1.3 Hz), 131.0 (d, *J* = 4.0 Hz), 129.1 (d, *J* = 3.0 Hz), 128.6, 128.0 (d, *J* = 13.6 Hz), 127.8, 123.7 (d, *J* = 3.4 Hz), 115.4 (d, *J* = 23.7 Hz), 52.4, 45.1 (d, *J* = 1.5 Hz), 18.6 ppm.

^{19}F NMR (564 MHz, $CDCl_3$) δ = –117.6 ppm

NMR Data of Product:

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.54 (s, 0.10H, 95% D), 7.44 (s, 0.10H, 95% D), 7.42-7.38 (m, 0.05H, 95% D), 7.37 (s, 0.05H, 95% D), 7.17-7.14 (m, 0.08H, 92% D), 7.11 (s, 0.03H, 97% D), 3.77 (q, *J* = 7.2 Hz, 1H), 3.71 (s, 3H), 1.55 (d, *J* = 7.2 Hz, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 174.6, 159.8 (d, *J* = 248.1 Hz), 141.8 (d, *J* = 7.8 Hz), 135.4, 131.3-130.0 (1C), 129.4-126.8 (5C), 123.8-122.6 (1C), 115.8-114.2 (1C), 52.4, 45.0 (d, *J* = 1.6 Hz), 18.6 ppm.

^{19}F NMR (377 MHz, $CDCl_3$) δ = –117.7, –118.0 ppm.[2]

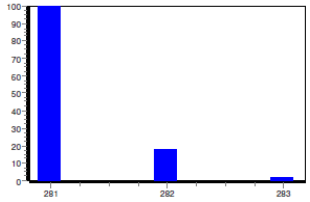
[2] The ^{19}F-NMR spectrum shows the presence of a trace impurity with a signal at δ = –61.8 ppm.

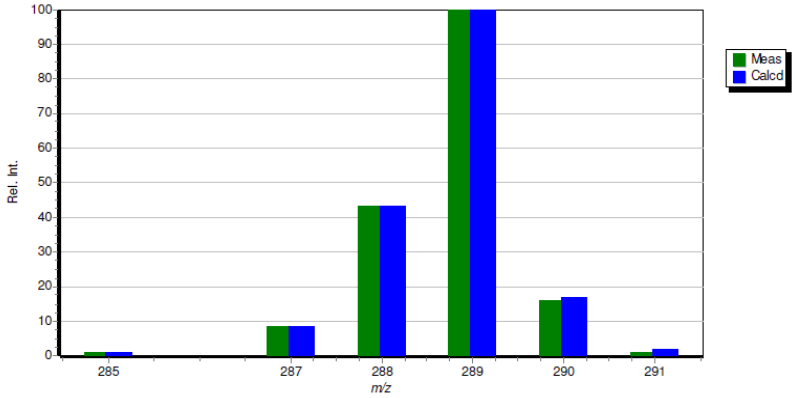
Mass Data:

LabelChecker Results

Formula: C16 H15 O2 F Na
Mass (monoisotopic): 281.10

Difference Value: 0.000144
Error Sum: 0.012
Error (%): 0.054



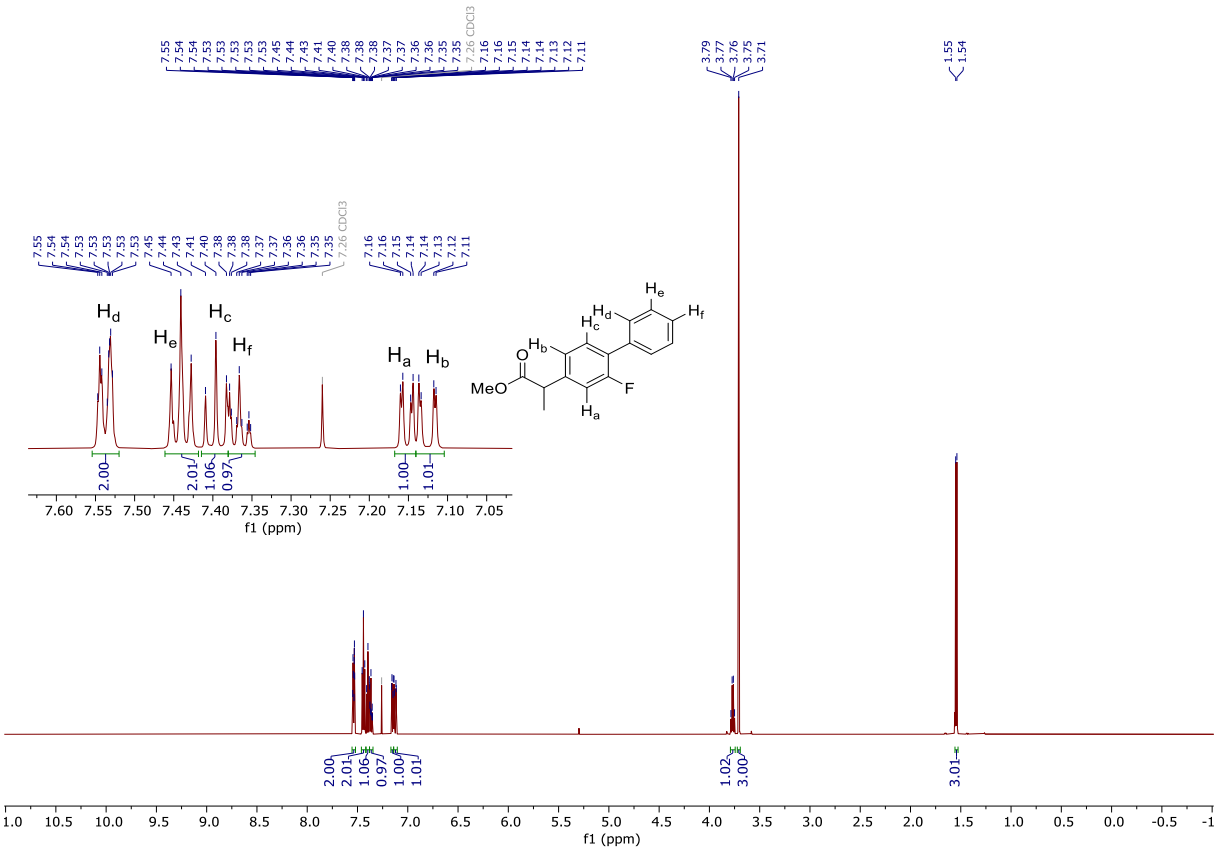


Deuterium: 0-fold (%): 0.00 0.00
Deuterium: 1-fold (%): 0.00 0.00
Deuterium: 2-fold (%): 0.00 0.00
Deuterium: 3-fold (%): 0.00 0.00
Deuterium: 4-fold (%): 1.05 0.68
Deuterium: 5-fold (%): 0.00 0.00
Deuterium: 6-fold (%): 9.08 5.85
Deuterium: 7-fold (%): 45.03 29.02
Deuterium: 8-fold (%): 100.00 64.44
Deuterium: 9-fold (%): 0.00 0.00
Deuterium: 10-fold (%): 0.00 0.00
Label Atom Sum: 7.57 (50.44%)

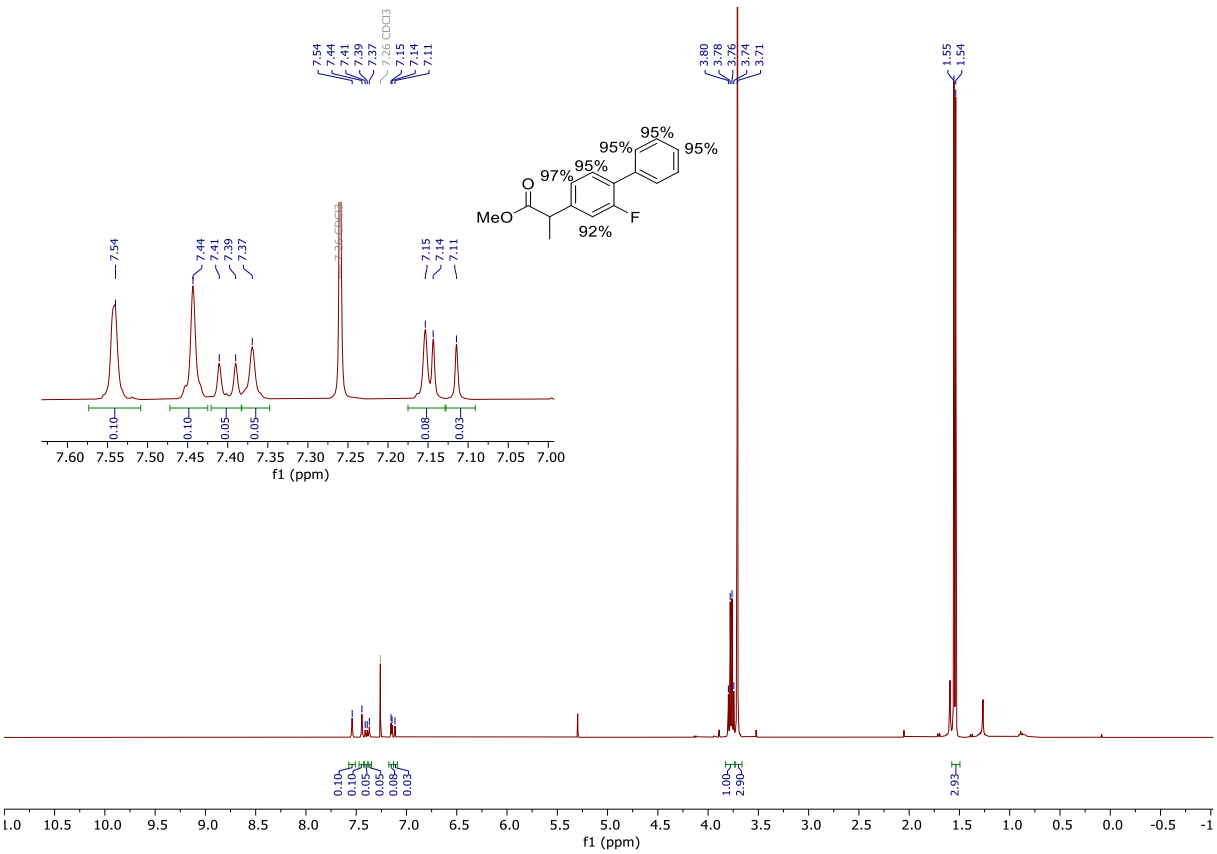
Isotope List used for fitting data:

m/z	intensity
285.13	40352
287.13	338602
288.14	1733683
289.14	4018966
290.15	642062
291.15	43857

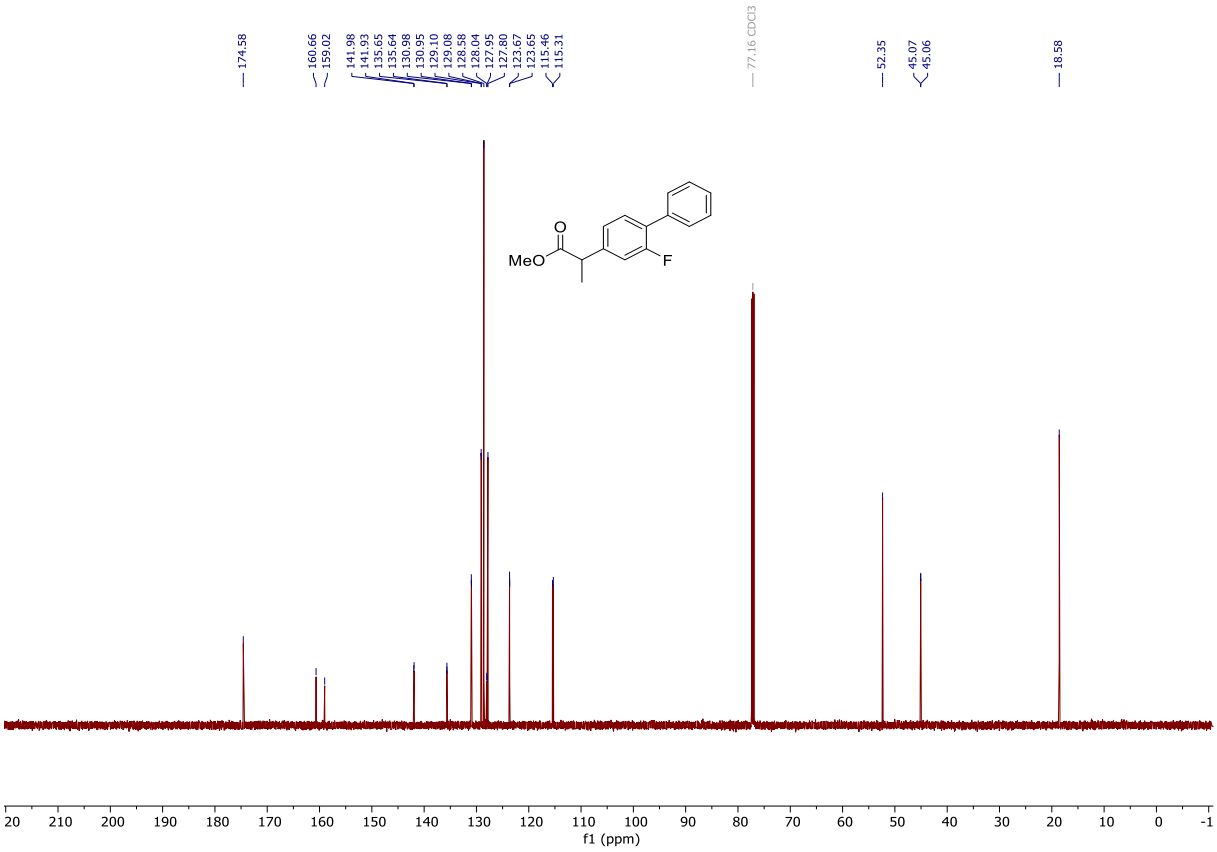
^{1}H-NMR spectrum in $CDCl_3$:



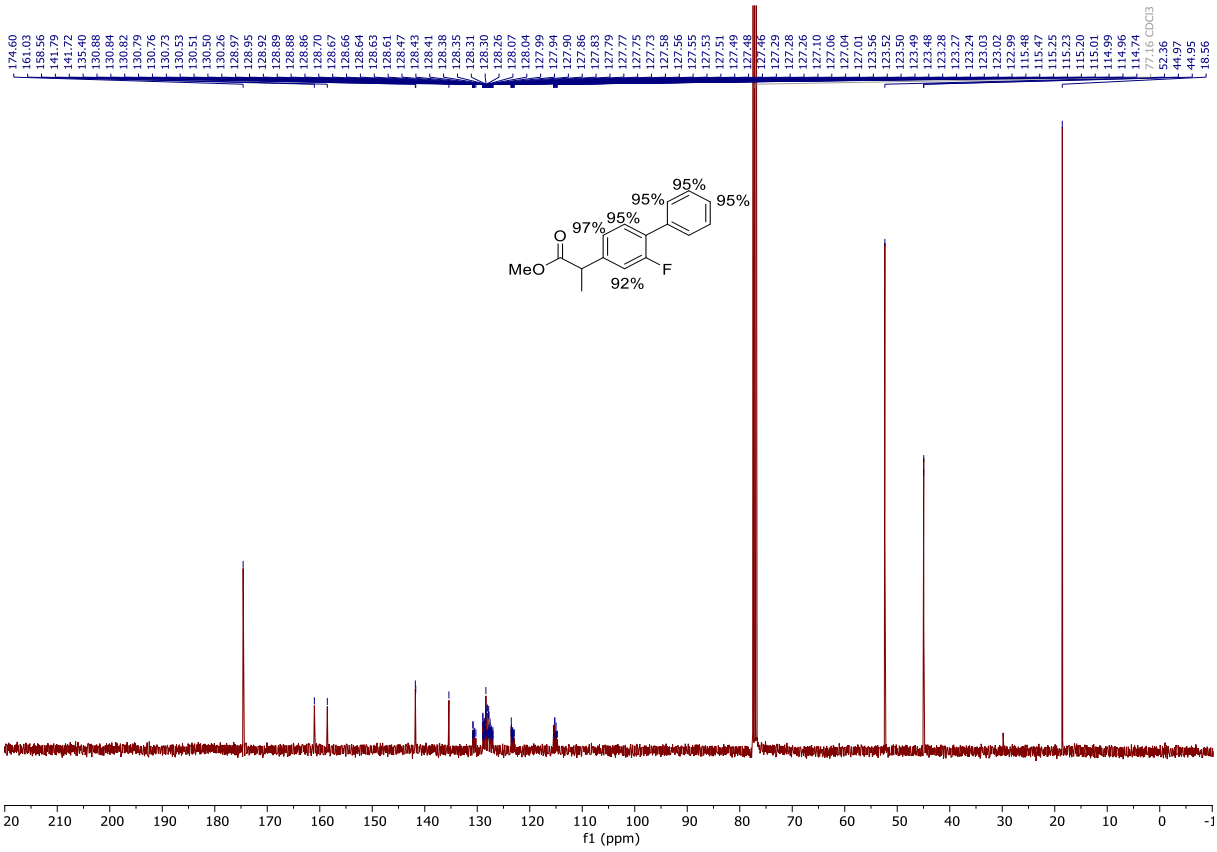
^{1}H-NMR spectrum in $CDCl_3$:



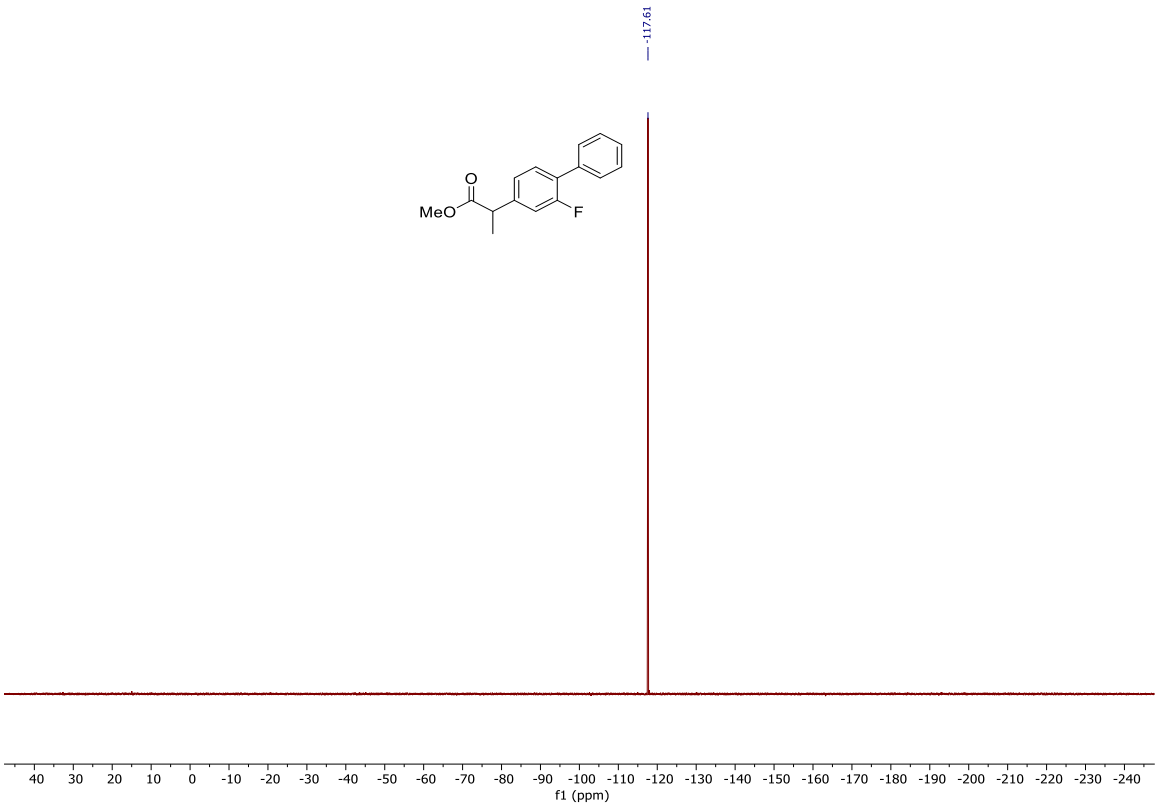
^{13}C-NMR spectrum in $CDCl_3$:



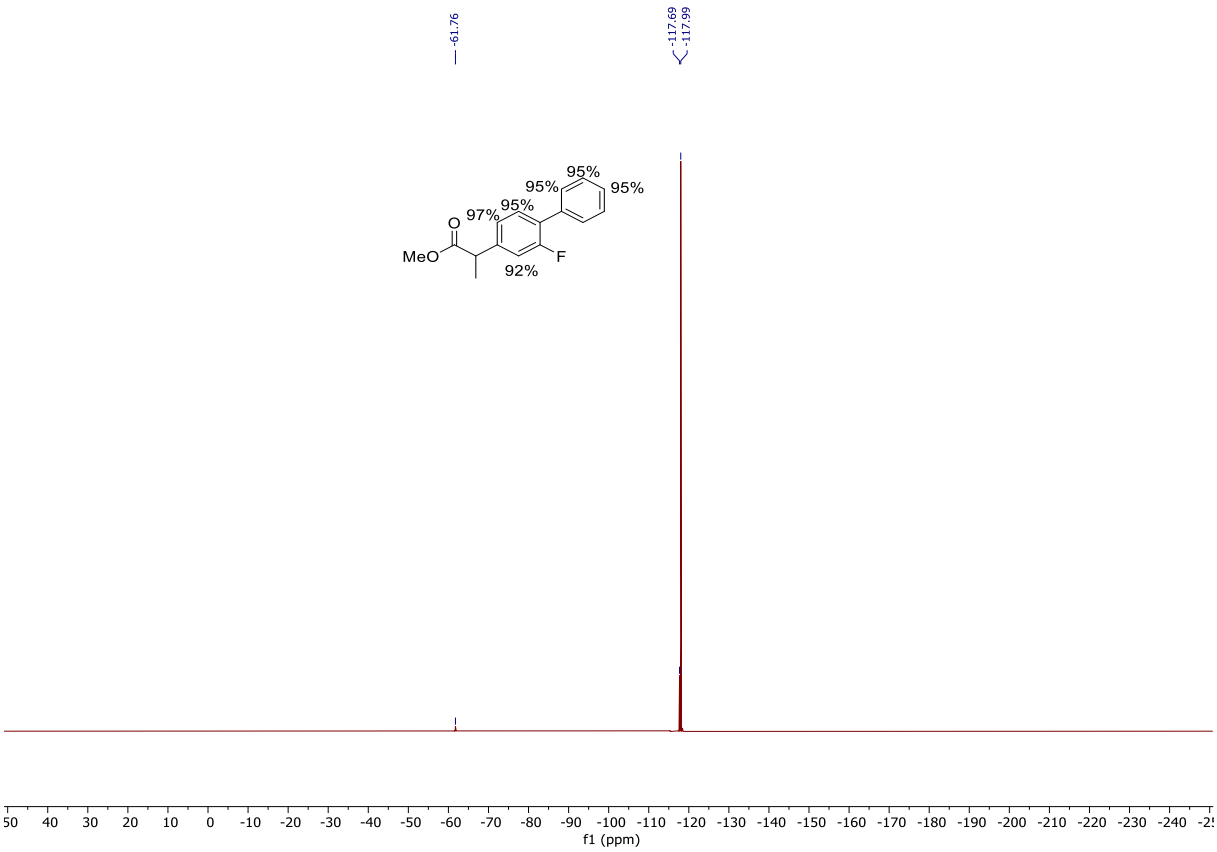
^{13}C-NMR spectrum in $CDCl_3$:



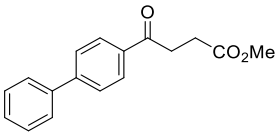
^{19}F-NMR spectrum in $CDCl_3$:



^{19}F-NMR spectrum in $CDCl_3$:



Deuteration of methyl 4-([1,1'-biphenyl]-4-yl)-4-oxobutanoate (37):



Following the general procedure F and using methyl 4-([1,1'-biphenyl]-4-yl)-4-oxobutanoate (**37**) (53.7 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAc = 9:1 as the eluent, the target compound **[D]37** was obtained as colorless solid (33.3 mg, 60%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 9.88 D/molecule [Mass]; 9.99 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (599 MHz, $CDCl_3$) δ = 8.08-8.04 (m, 2H), 7.72-7.67 (m, 2H), 7.65-7.61 (m, 2H), 7.50-7.45 (m, 2H), 7.43-7.38 (m, 1H), 3.72 (s, 3H), 3.36 (t, *J* = 6.7 Hz, 2H), 2.80 (t, *J* = 6.7 Hz, 2H) ppm.

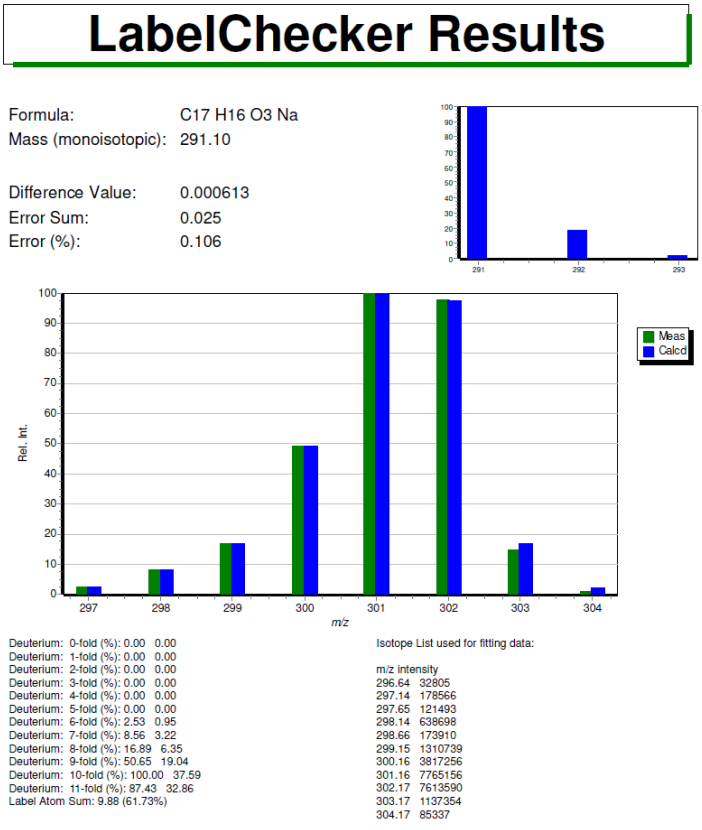
^{13}C NMR (151 MHz, $CDCl_3$) δ = 197.8, 173.5, 146.1, 140.0, 135.4, 129.1, 128.8, 128.4, 127.4, 52.0, 33.6, 28.2 ppm.

NMR Data of Product:

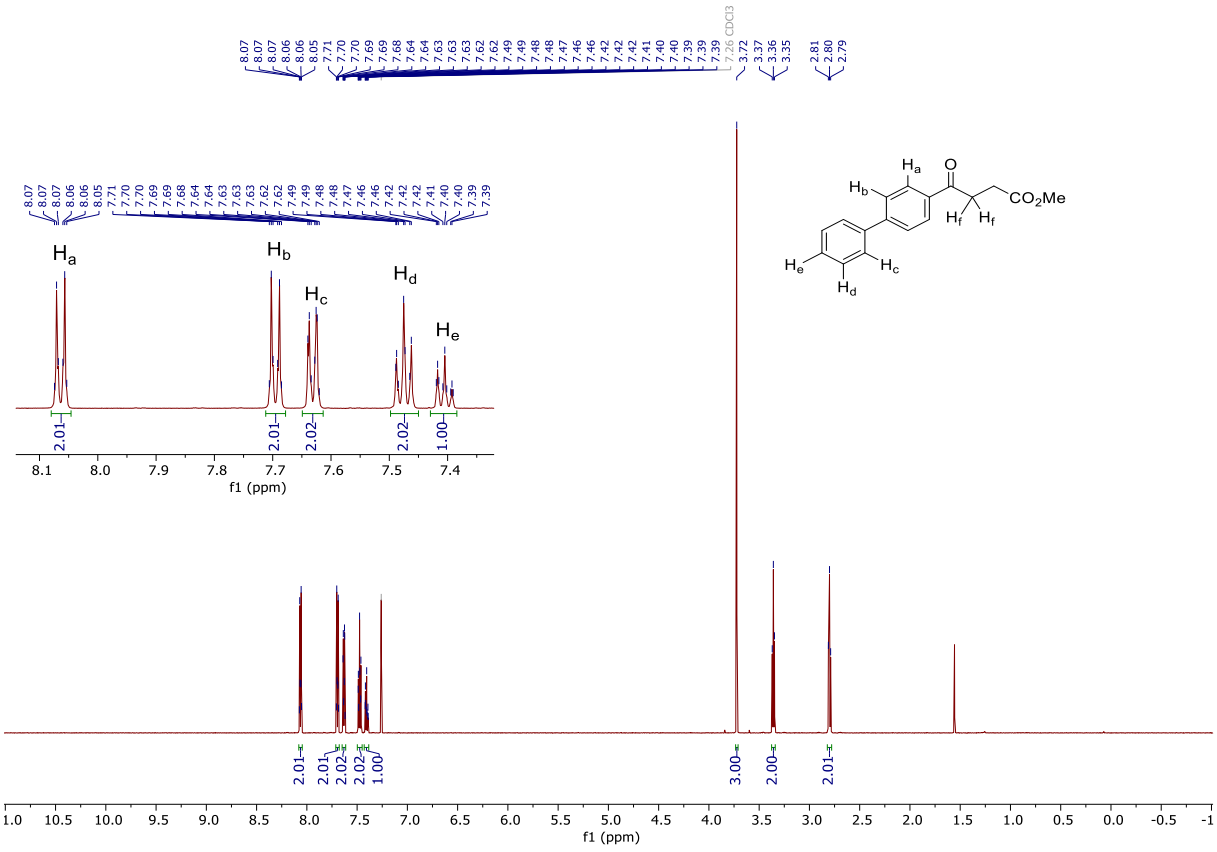
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.06 (s, 0.43H, 79% D), 7.73-7.66 (m, 0.11H, 95% D), 7.63 (s, 0.11H, 95% D), 7.47 (s, 0.11H, 95% D), 7.41 (s, 0.05H, 95% D), 3.72 (s, 3H), 3.42-3.25 (m, 0.21H, 90% D), 2.79 (s, 2H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 197.9, 173.5, 145.8, 139.7, 135.2, 129.9-125.6 (9C), 52.0, 34.8-31.6 (1C), 28.2 ppm.

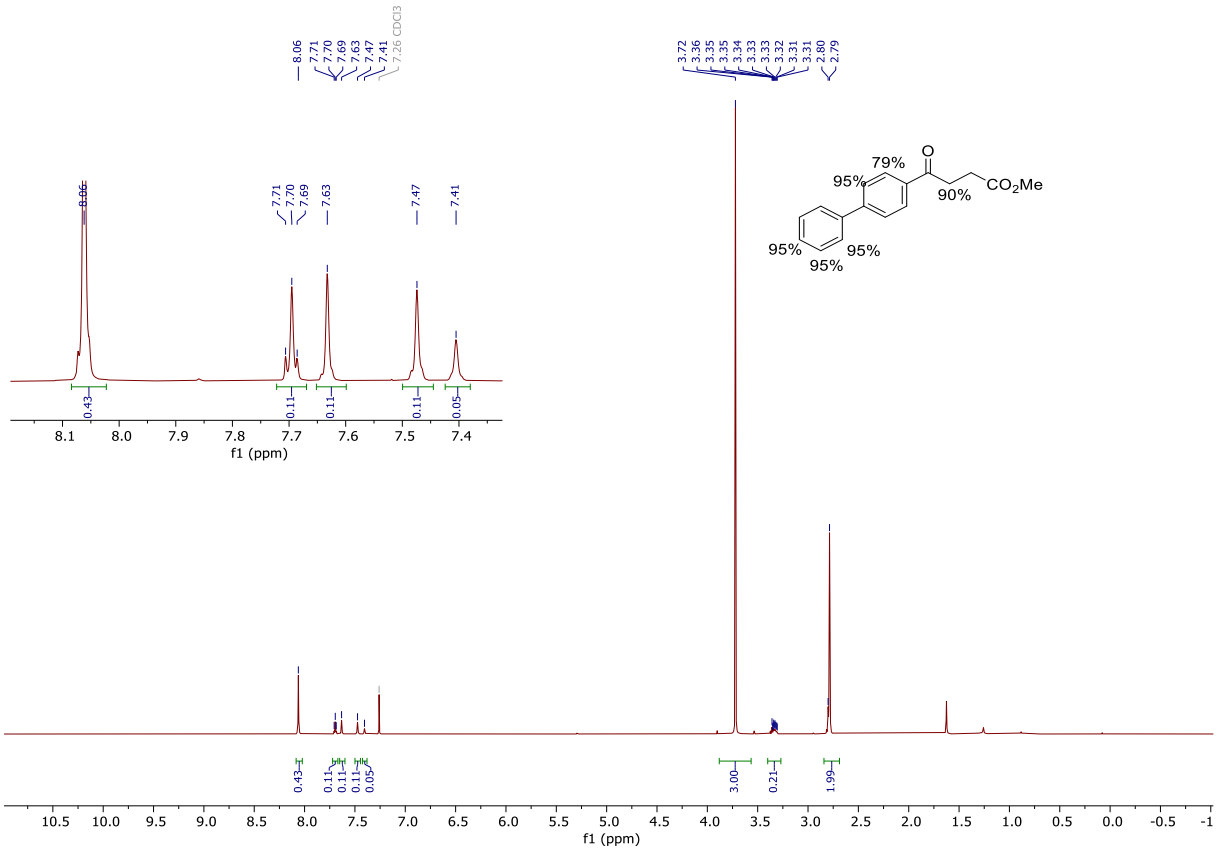
Mass Data:



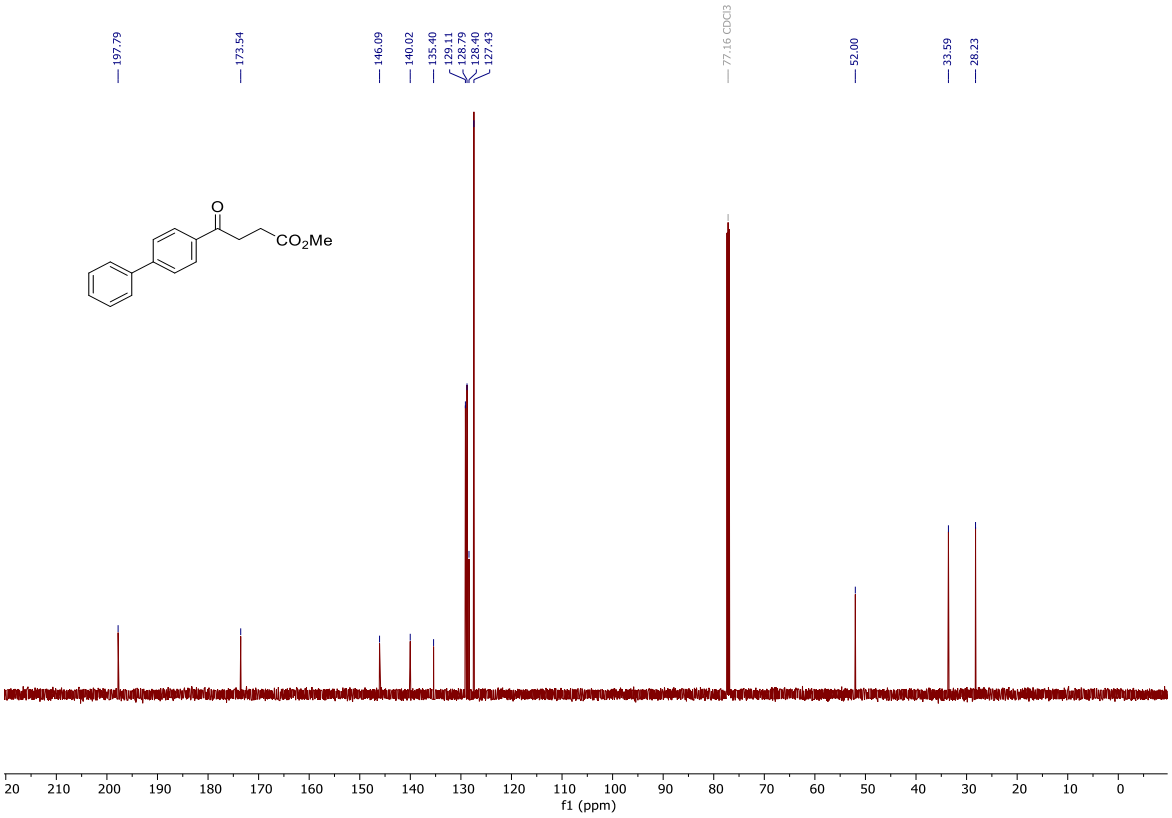
^{1}H-NMR spectrum in $CDCl_3$:



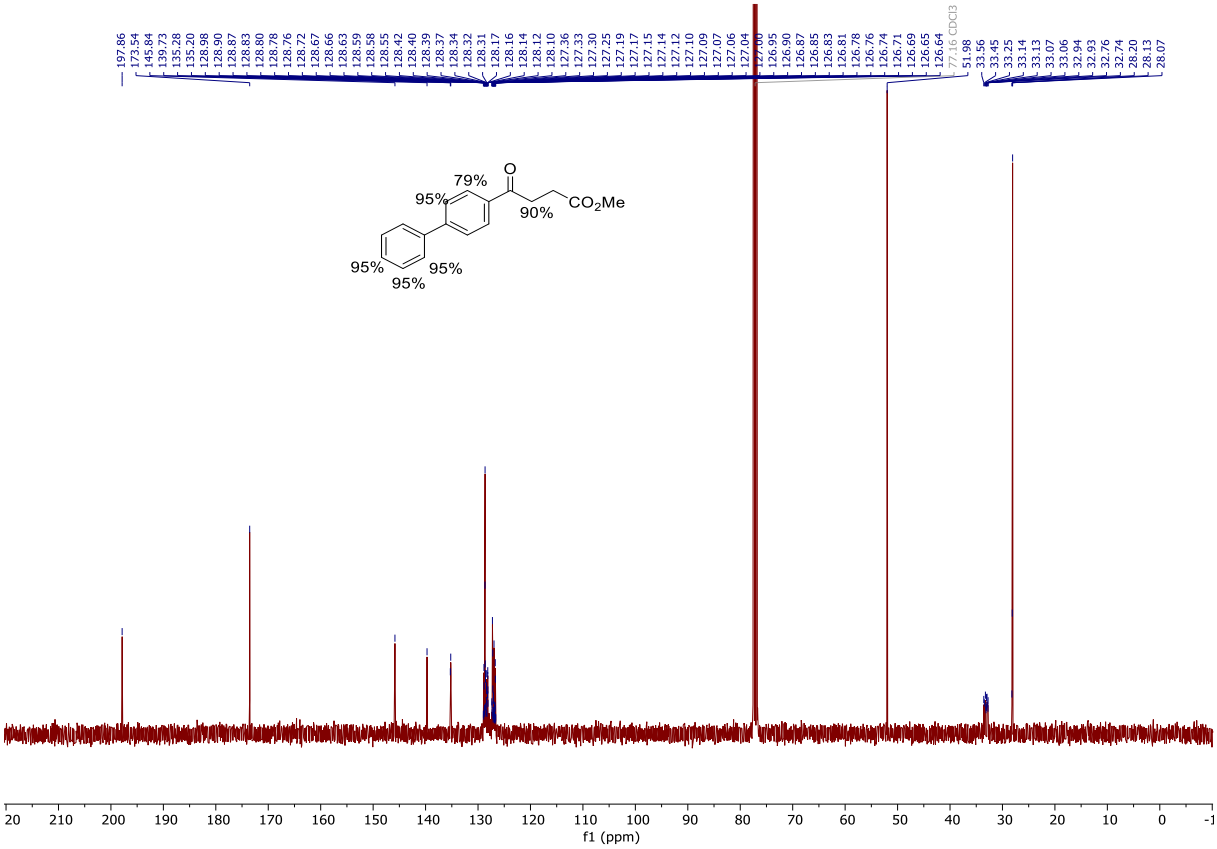
^{1}H-NMR spectrum in $CDCl_3$:



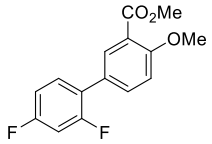
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of methyl 2',4'-difluoro-4-methoxy-[1,1'-biphenyl]-3-carboxylate (38):



Following the general procedure F and using methyl 2',4'-difluoro-4-methoxy-[1,1'-biphenyl]-3-carboxylate (**38**) (55.7 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAc = 9:1 as the eluent, the target compound **[D]38** was obtained as light-yellow solid (51.5 mg, 91%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 5.10D/molecule [Mass]; 5.16 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR 599 MHz, $CDCl_3$) δ = 7.93 (dd, *J* = 2.4, 1.2 Hz, 1H), 7.62 (ddd, *J* = 8.7,2.4, 1.8 Hz, 1H), 7.38 (td, *J* = 8.7, 6.3 Hz, 1H), 7.05 (d, *J* = 8.7 Hz, 1H), 6.96-6.92 (m, 1H), 6.92-6.88 (m, 1H), 3.95 (s, 3H), 3.91 (s, 3H) ppm.

^{13}C NMR (151 MHz, $CDCl_3$) δ = 166.5, 162.4, 159.8, 158.9, 134.0, 132.2, 131.3, 127.1, 124.1, 120.3, 112.3, 111.8, 104.5, 56.3, 52.3 ppm.

^{19}F NMR (564 MHz, $CDCl_3$) δ = –111.4 - –111.5 (m), –113.7 - –113.8 (m) ppm

NMR Data of Product:

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.93 (d, *J* =1.2 Hz, 0.53H, 47% D), 7.62 (s, 0.08H, 92% D), 7.38 (dd, *J* = 8.7, 6.6 Hz, 0.08H, 92% D), 7.05 (s, 0.05H, 95% D), 6.94 (d, *J* = 8.0 Hz, 0.06H, 94%), 6.90 (dd, *J* = 10.7, 8.9 Hz, 0.04H, 96%), 3.95 (s, 3H), 3.91 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 166.5 (d, *J* = 2.2 Hz), 163.5-161.0 (1C), 159.5-157.7 (2C), 135.2-132.8 (1C), 132.2 (d, *J* = 2.7 Hz), 131.2-130.1 (1C), 127.8-125.9 (1C), 124.9-122.5 (1C), 120.2 (d, *J* = 9.7 Hz), 113.5-110.3 (2C), 105.7-102.4 (1C), 56.3, 52.3 ppm.

^{19}F NMR (377 MHz, $CDCl_3$) δ = –111.6 - –111.7 (m), –111.8 - – 112.2 (m), –113.7 - – 113.9 (m), –114.0 - –114.3 (m) ppm.[3]

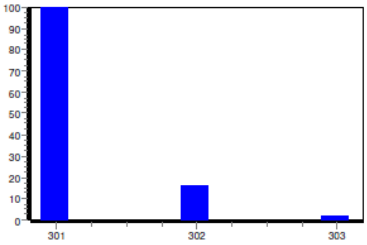
[3] The 19F-NMR spectrum shows the presence of trace impurities with signals at: δ = –59.3, –61.8, –61.9, –73.1, –73.2, –75.6 (d, *J* = 1.3 Hz) ppm.

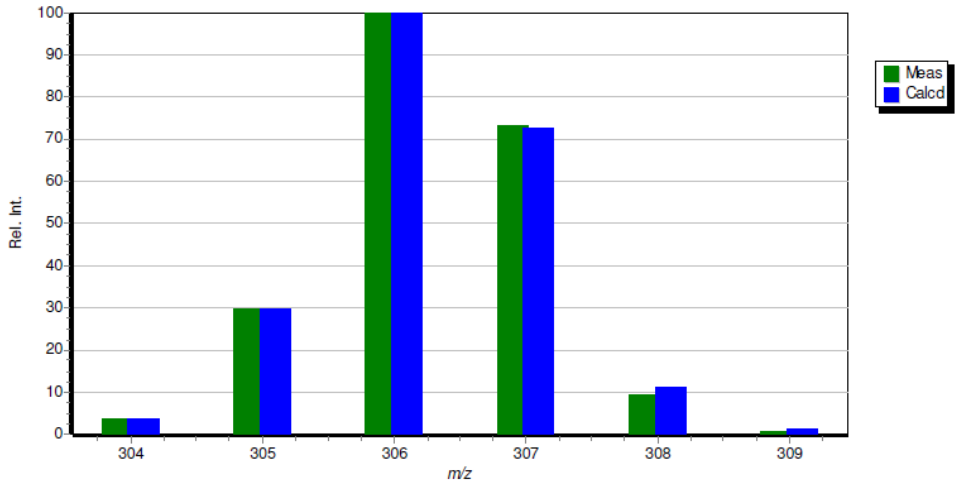
Mass Data:

LabelChecker Results

Formula: C15 H12 O3 F2 Na
Mass (monoisotopic): 301.07

Difference Value: 0.000362
Error Sum: 0.019
Error (%): 0.239



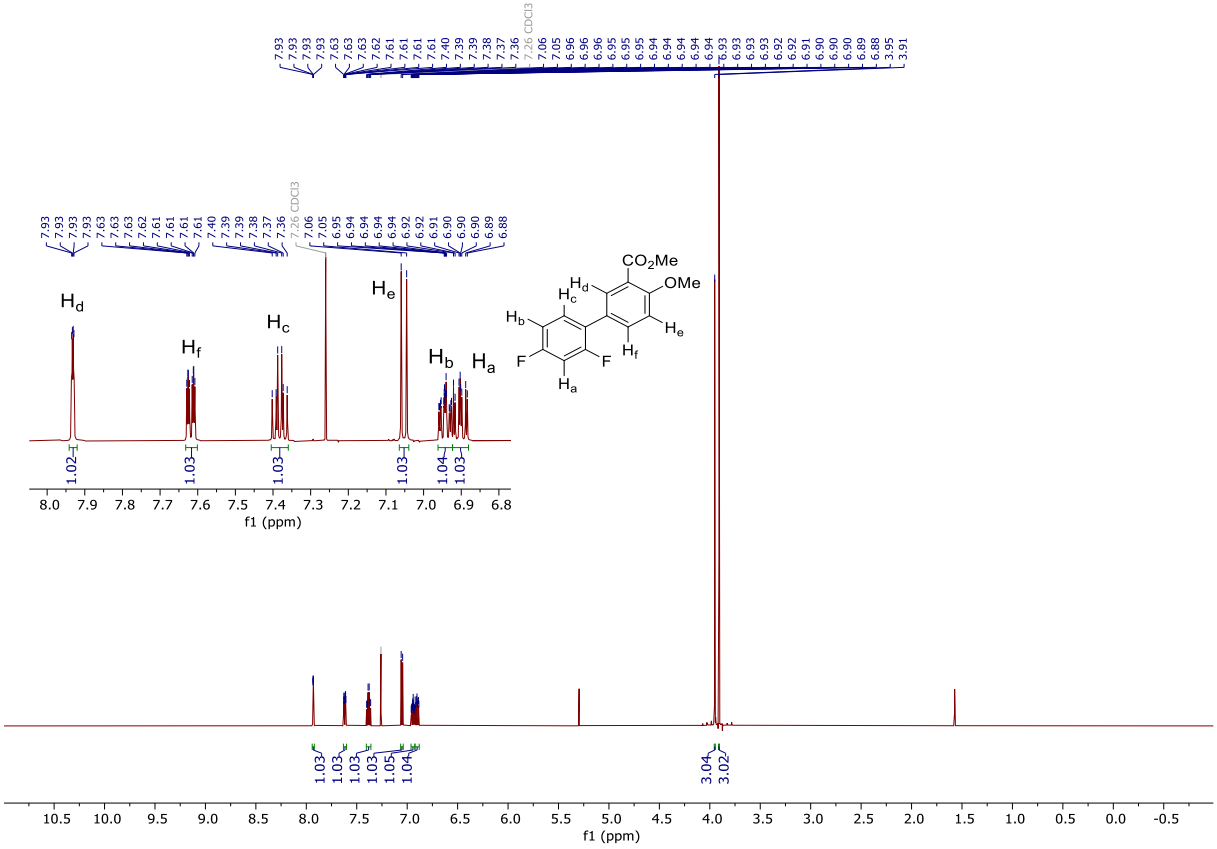


Deuterium: 0-fold (%): 0.00 0.00
Deuterium: 1-fold (%): 0.00 0.00
Deuterium: 2-fold (%): 0.30 0.16
Deuterium: 3-fold (%): 3.98 2.05
Deuterium: 4-fold (%): 30.67 15.75
Deuterium: 5-fold (%): 100.00 51.36
Deuterium: 6-fold (%): 59.73 30.68
Label Atom Sum: 5.10 (42.53%)

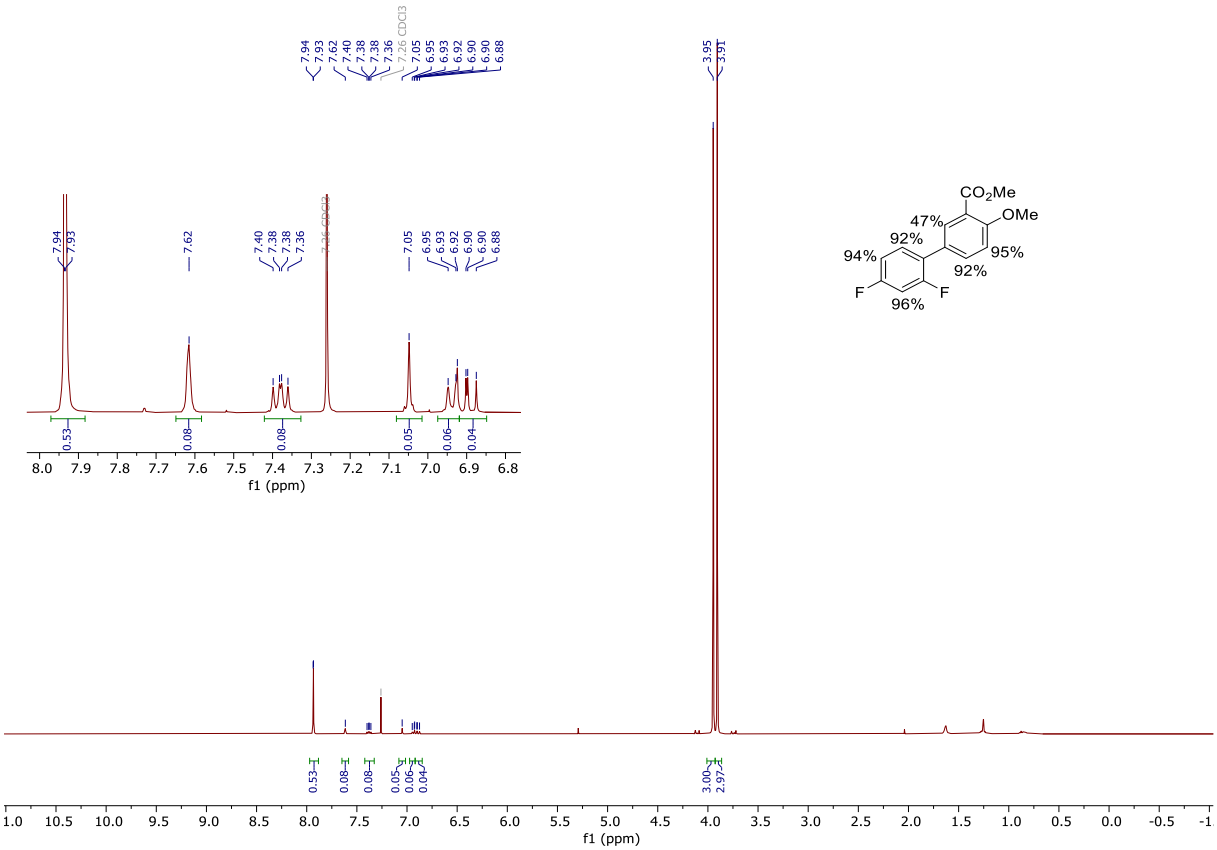
Isotope List used for fitting data:

m/z	intensity
303.08	23541
304.08	364893
305.09	2810844
306.10	9418557
307.10	6904133
308.11	883481
309.11	58565

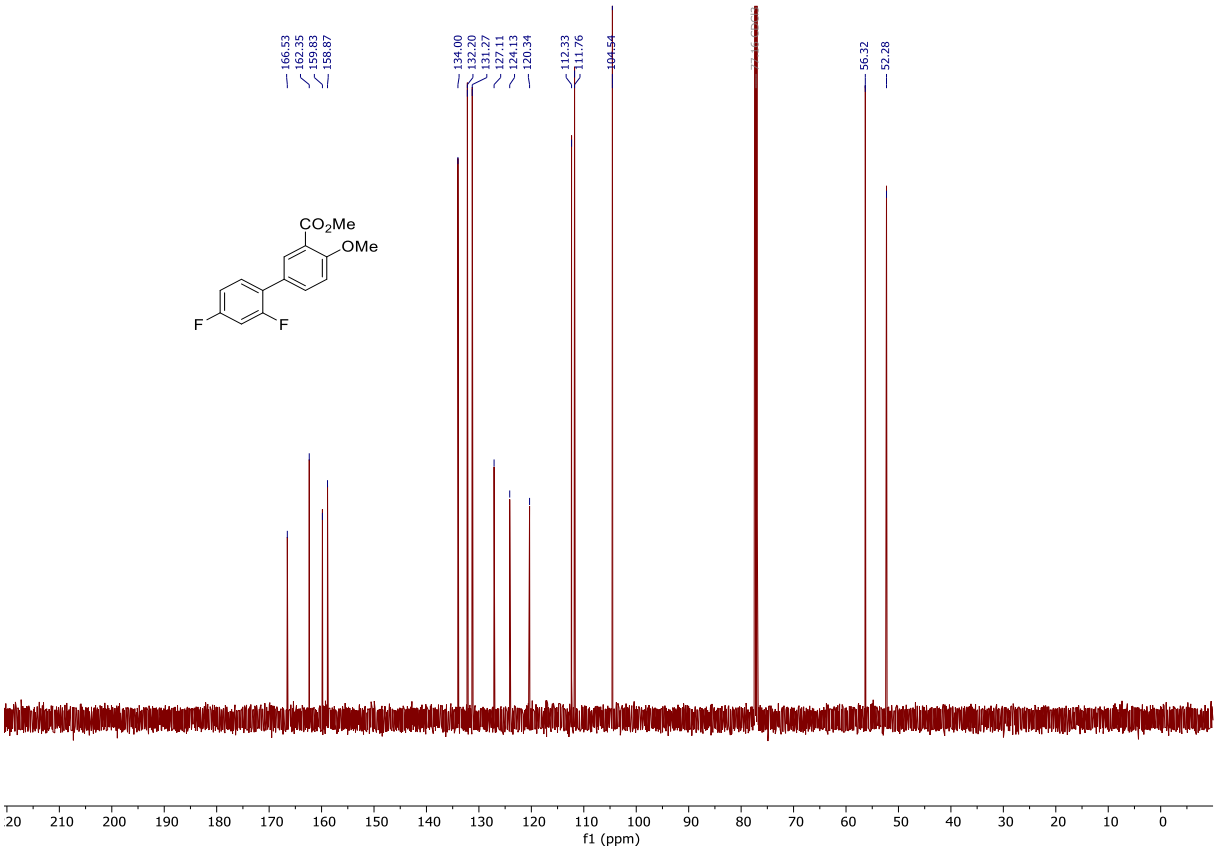
^{1}H-NMR spectrum in $CDCl_3$:



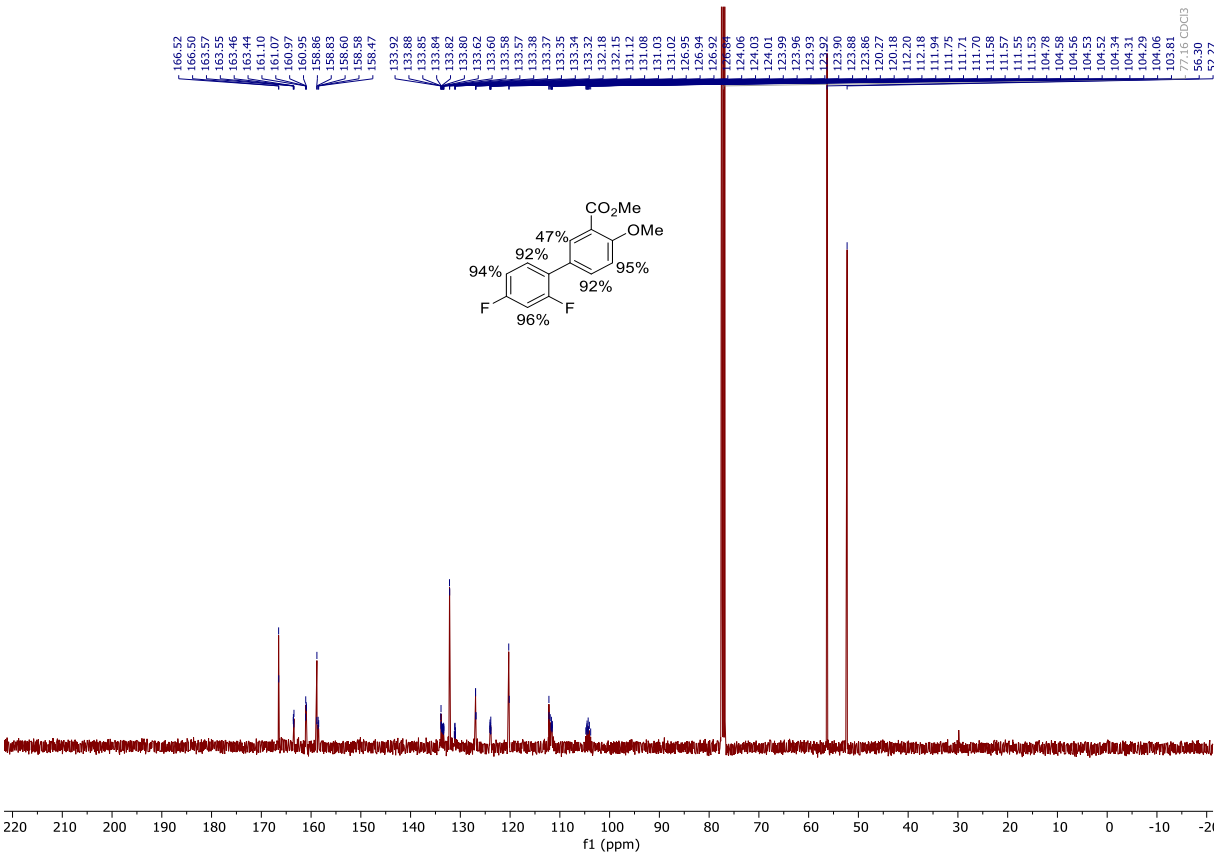
^{1}H-NMR spectrum in $CDCl_3$:



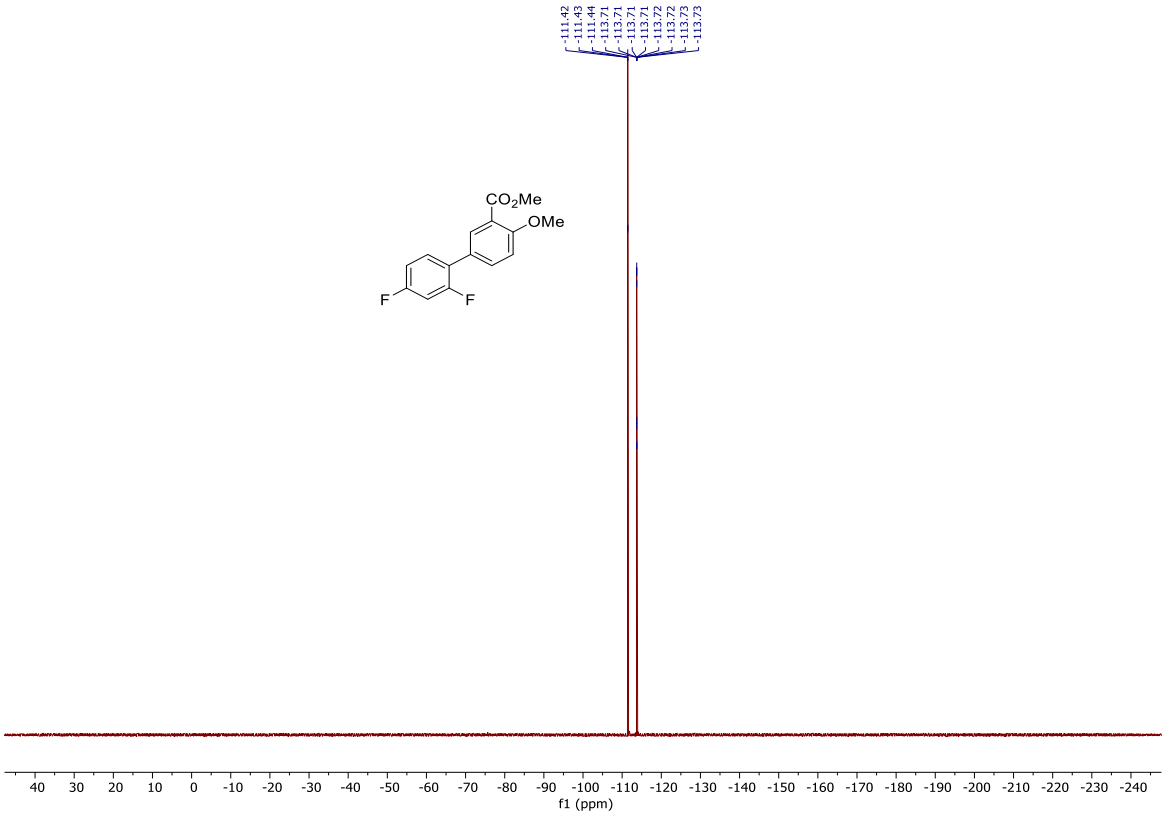
^{13}C-NMR spectrum in $CDCl_3$:



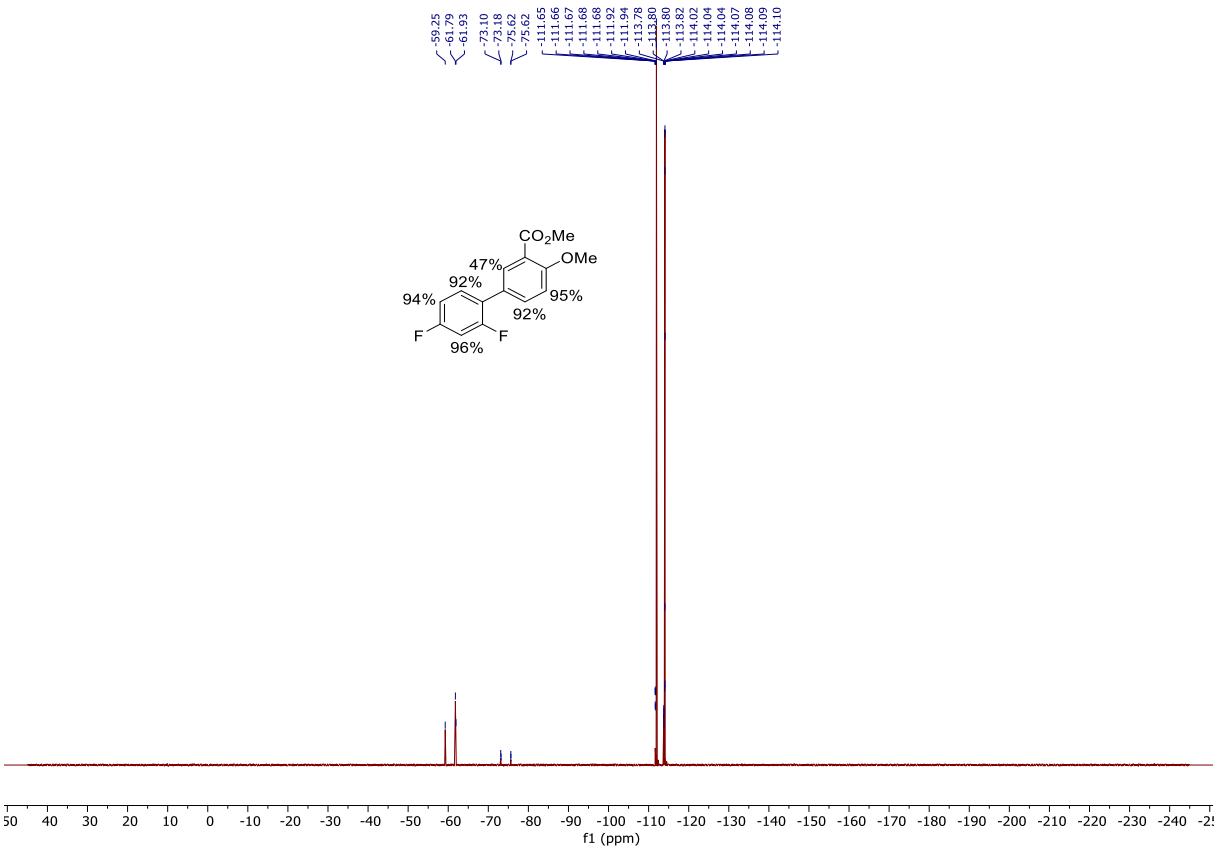
^{13}C-NMR spectrum in $CDCl_3$:



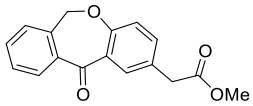
^{19}F-NMR spectrum in $CDCl_3$:



^{19}F-NMR spectrum in $CDCl_3$:



Deuteration of methyl 2-(11-oxo-6,11-dihydrodibenzo[*b,e*]oxepin-2-yl)acetate (39):



Following the general procedure F and using methyl 2-(11-oxo-6,11-dihydrodibenzo[*b,e*]oxepin-2-yl)acetate (**39**) (56.5 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAc = 80:20 as the eluent, the target compound **[D]39** was obtained as colorless liquid (42.8 mg, 75%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 3.46 D/molecule [HRMS]; 3.58 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.11 (d, *J* = 2.4 Hz, 1H), 7.89 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.59-7.52 (m, 1H), 7.50-7.44 (m, 1H), 7.42 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.36 (d, *J* = 7.4 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 5.18 (s, 2H), 3.70 (s, 3H), 3.65 (s, 2H) ppm.

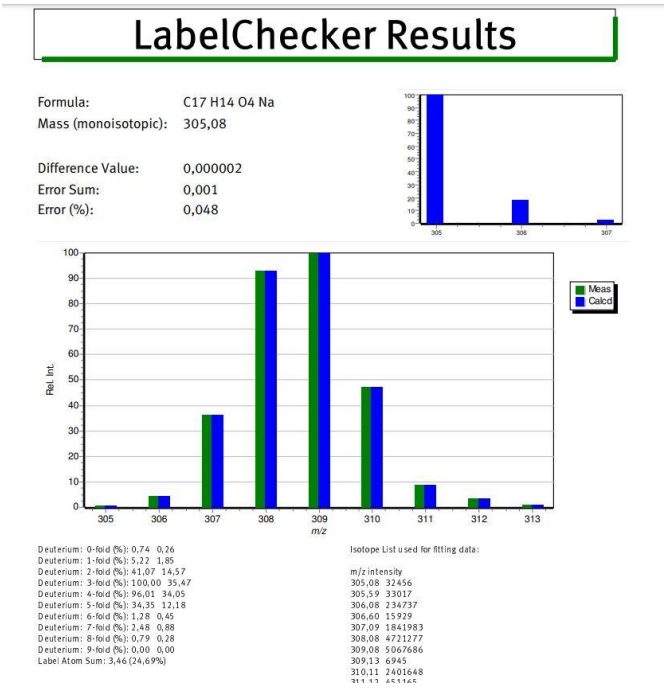
^{13}C NMR (101 MHz, $CDCl_3$) δ = 191.0, 172.0, 160.6, 140.6, 136.5, 135.7, 132.9, 132.6, 129.6, 129.4, 127.9(3), 127.9(1), 125.3, 121.2, 73.8, 52.3, 40.2 ppm.

NMR Data of Product:

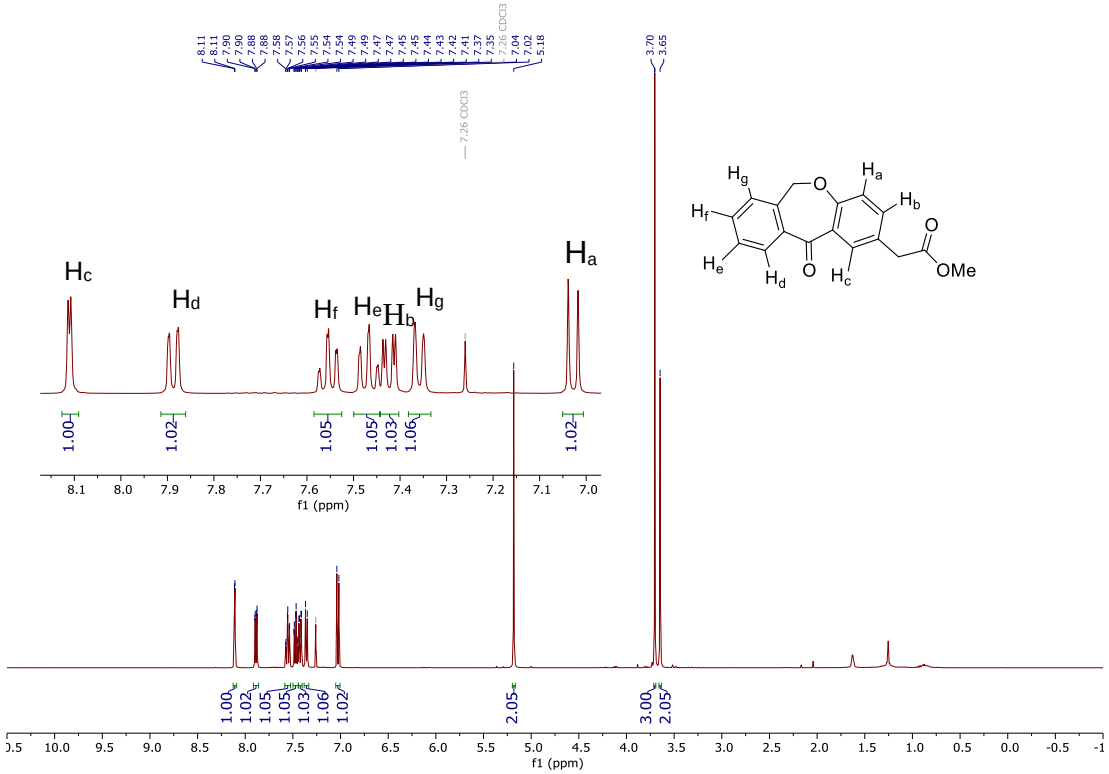
^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.12-8.10 (m, 0.94H, 6% D), 7.90-7.87 (m, 0.61H, 39% D), 7.57-7.53 (m, 0.41H, 59% D), 7.48-7.44 (m, 0.14H, 86% D), 7.44-7.40 (m, 0.84H, 16% D), 7.37-7.34 (m, 0.54H, 46% D), 7.04-7.00 (m, 0.05H, 95% D), 5.18 (s, 2H), 3.70 (s, 3H), 3.64 (s, 1.89H, 6% D) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 191.0, 172.0, 160.6, 140.6-140.5 (1C), 136.4-136.3 (1C), 135.7-135.6 (1C), 132.9-132.8 (1C), 132.7-132.6(1C), 129.6-129.5 (1C), 129.3-129.2 (1C), 127.9-127.8 (2C), 125.3, 121.2-120.7 (1C), 73.7(4)-73.6(9)(1C), 52.2, 40.2-40.1(1C) ppm.

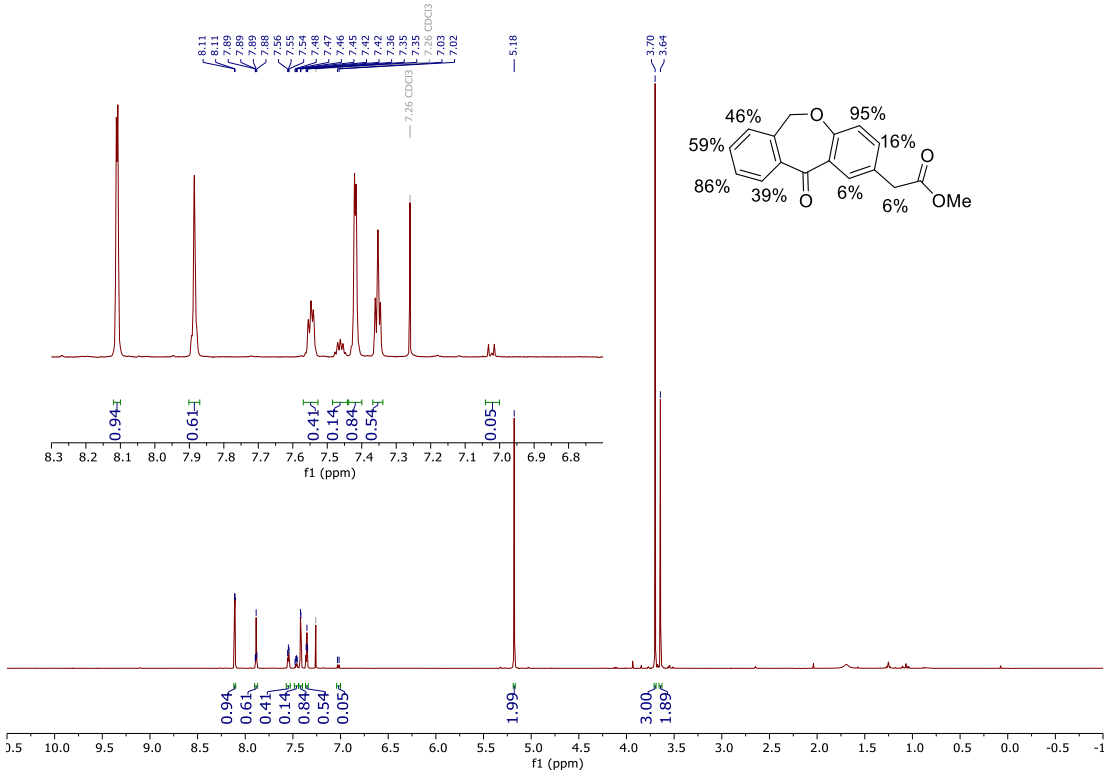
Mass Data:



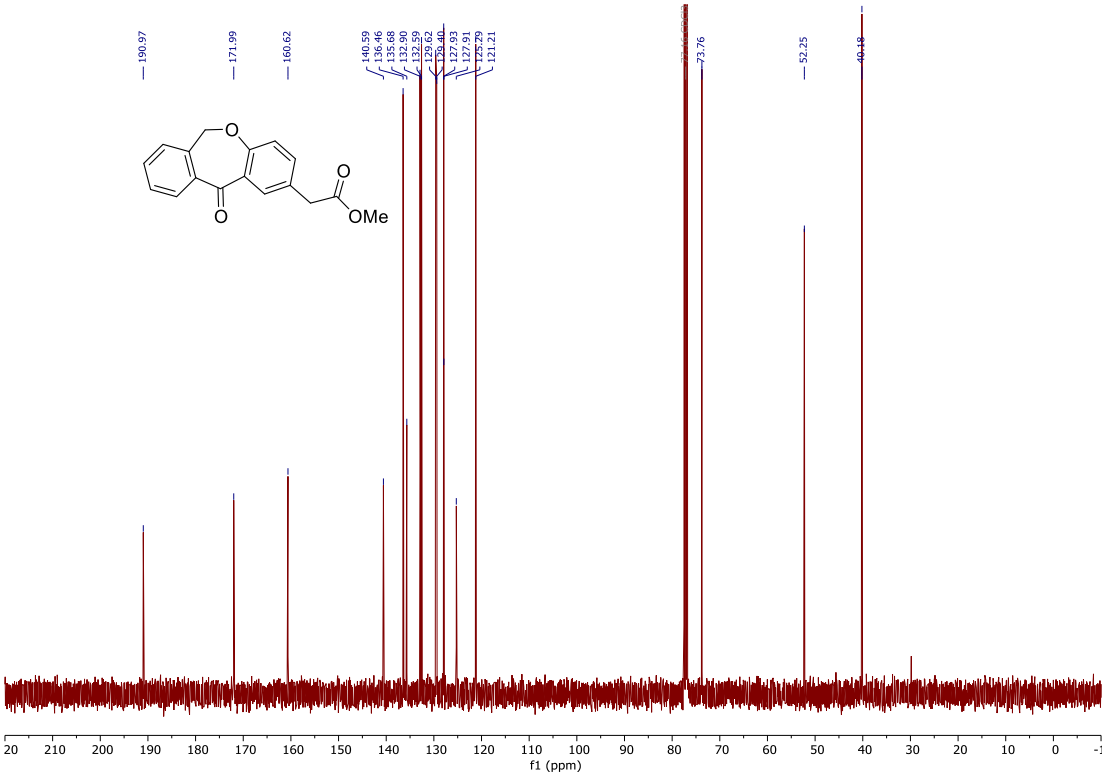
^{1}H-NMR spectrum in $CDCl_3$:



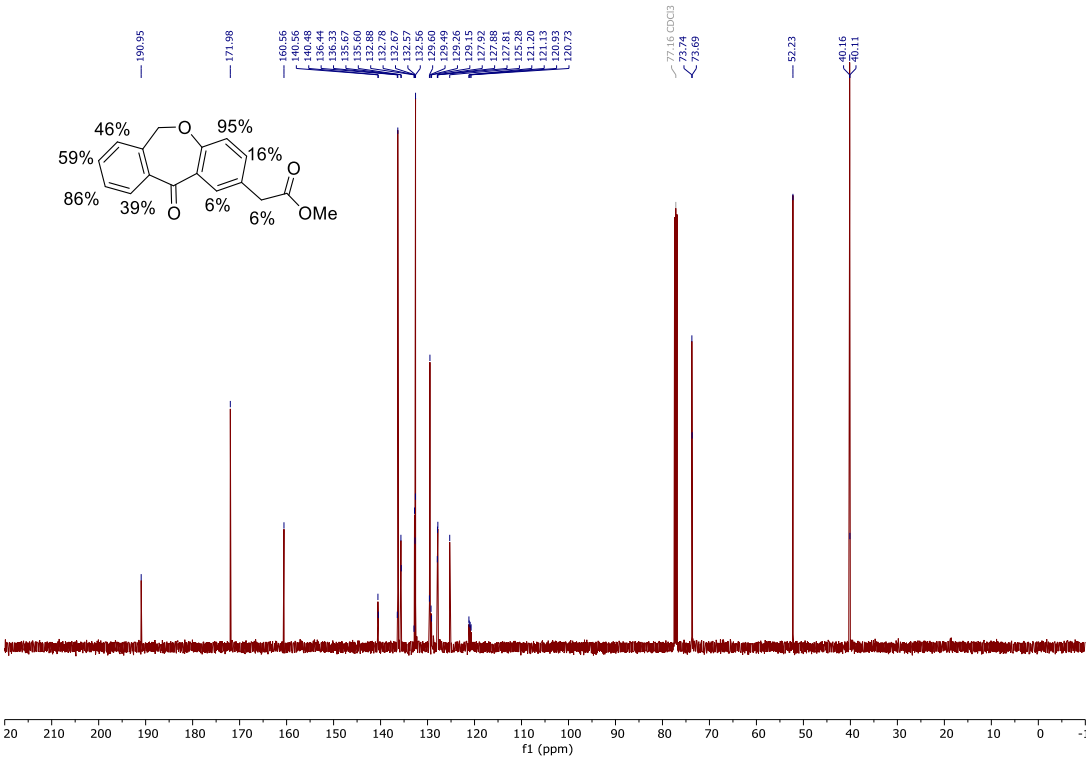
^{1}H-NMR spectrum in $CDCl_3$:



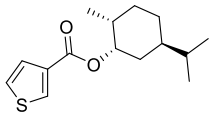
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of (1*S*,2*R*,5*R*)-5-isopropyl-2-methylcyclohexyl thiophene-3-carboxylate (40):



Following the general procedure F and using (1*S*,2*R*,5*R*)-5-isopropyl-2-methylcyclohexyl thiophene-3-carboxylate (**40**) (53.3 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAc = 100:1 as the eluent, the target compound **[D]40** was obtained as a colorless liquid (44.9 mg, 83%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 2.86 D/molecule [HRMS]; 2.85 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.08 (dd, *J* = 3.1, 1.2 Hz, 1H), 7.52 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.29 (dd, *J* = 5.1, 3.1 Hz, 1H), 4.87 (td, *J* = 10.9, 4.4 Hz, 1H), 2.11 (dddd, J = 12.0, 4.2, 3.5, 1.8 Hz, 1H), 1.94 (ttd, J = 7.0, 7.0, 2.8 Hz, 1H), 1.75 – 1.67 (m, 2H), 1.61 – 1.46 (m, 2H), 1.17-1.06 (m, 2H), 0.98-0.89 (m, 1H), 0.93 (d, J = 6.8 Hz, 3H), 0.92 (d, *J* = 7.0 Hz, 3H), 0.82 (d, *J* = 6.9 Hz, 3H) ppm.

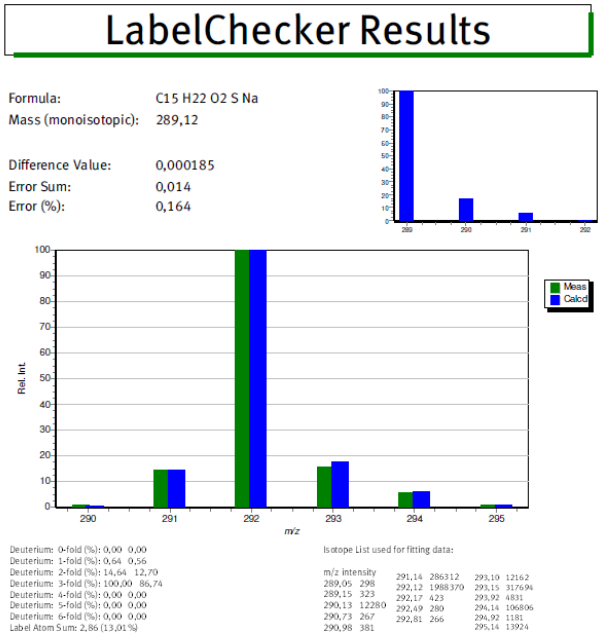
^{13}C NMR (126 MHz, $CDCl_3$): δ = 162.5, 134.5, 132.4, 128.1, 125.9, 74.7, 47.4, 41.1, 34.4, 31.6, 26.7, 23.8, 22.2, 20.9, 16.7 ppm.

NMR Data of Product:

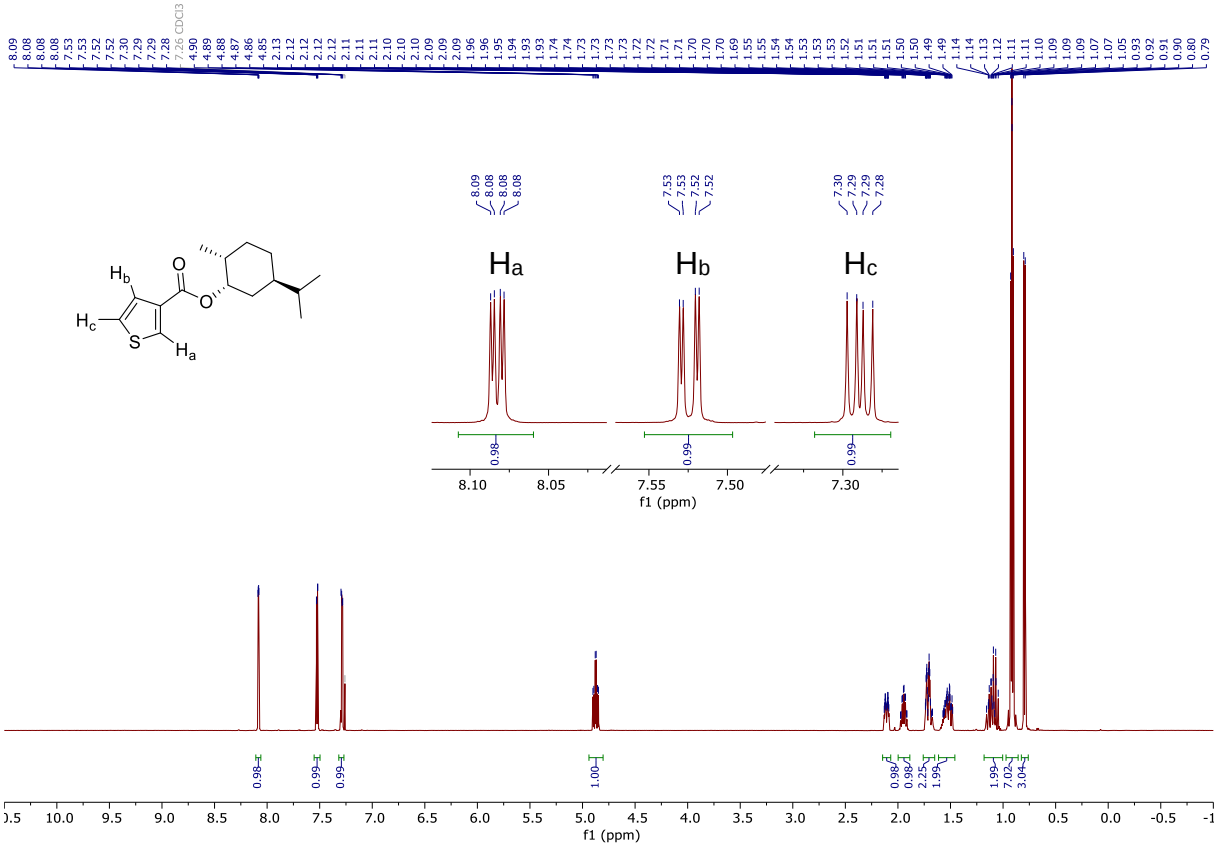
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.08 (s, 0.05H, 95% D), 7.52 (s, 0.05H, 95% D), 7.29 (s, 0.05H, 95% D), 4.87 (td, *J* = 10.9, 4.4 Hz, 1H), 2.11 (dddd, *J* = 12.0, 4.0, 4.0, 1.7 Hz, 1H), 1.95 (ttd, J = 7.0, 2.7 Hz, 1H), 1.77 – 1.66 (m, 2H), 1.60-1.46 (m, 2H), 1.19-1.04 (m, 2H), 0.99 – 0.84 (m, 1H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.91 (d, *J* = 6.9 Hz, 3H), 0.80 (d, *J* = 7.0 Hz, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 162.5, 134.4-131.8 (1C), 128.0-127.5 (1C), 125.9-125.2 (1C), 74.7, 47.4, 41.2, 34.5, 31.6, 26.7, 23.9, 22.2, 20.9, 16.7 ppm.

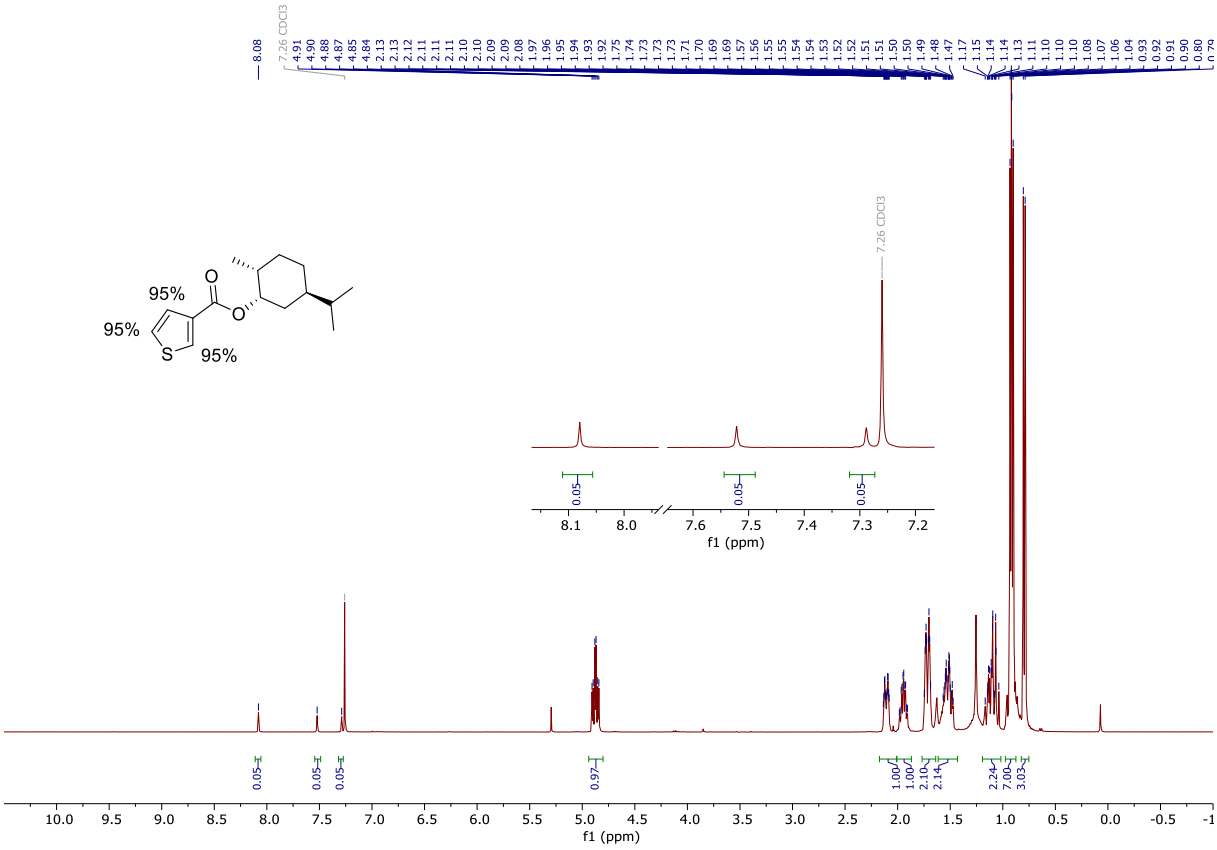
Mass Data:



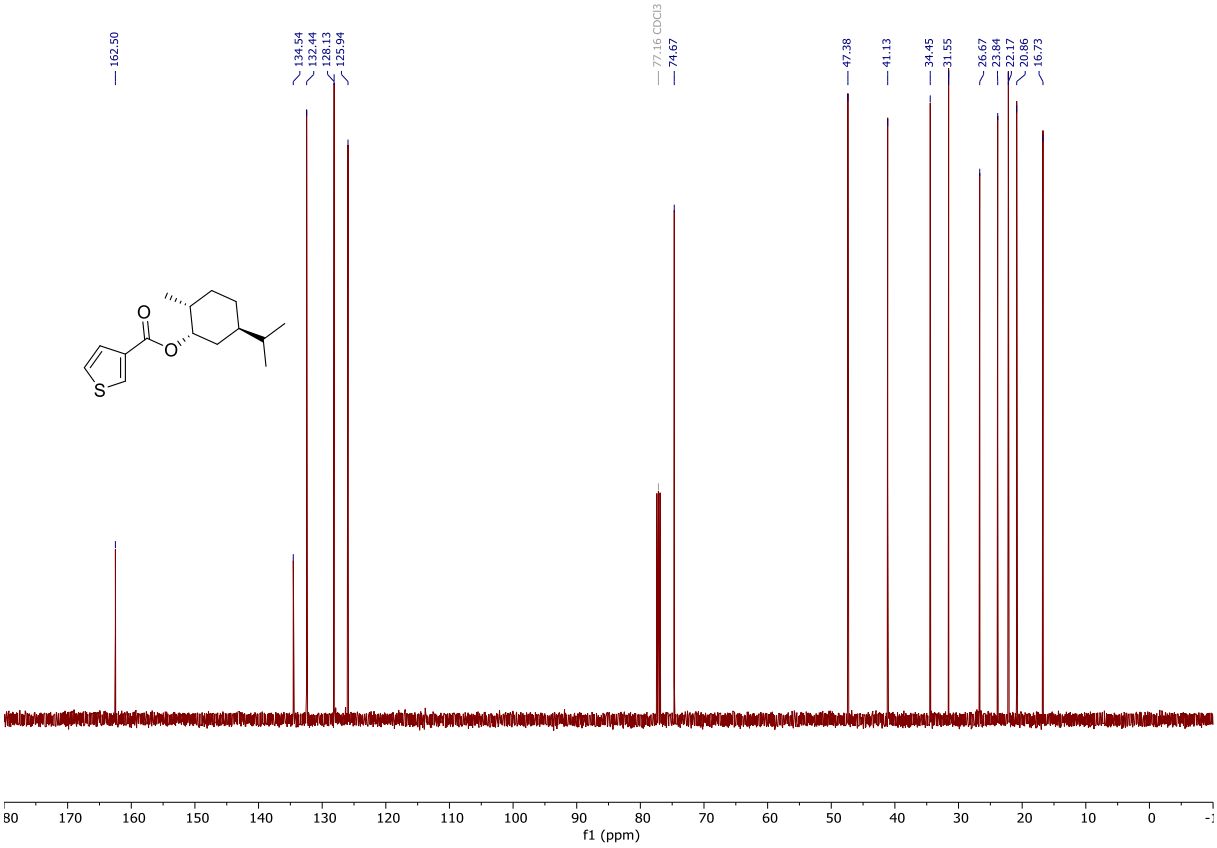
^{1}H-NMR spectrum in $CDCl_3$:



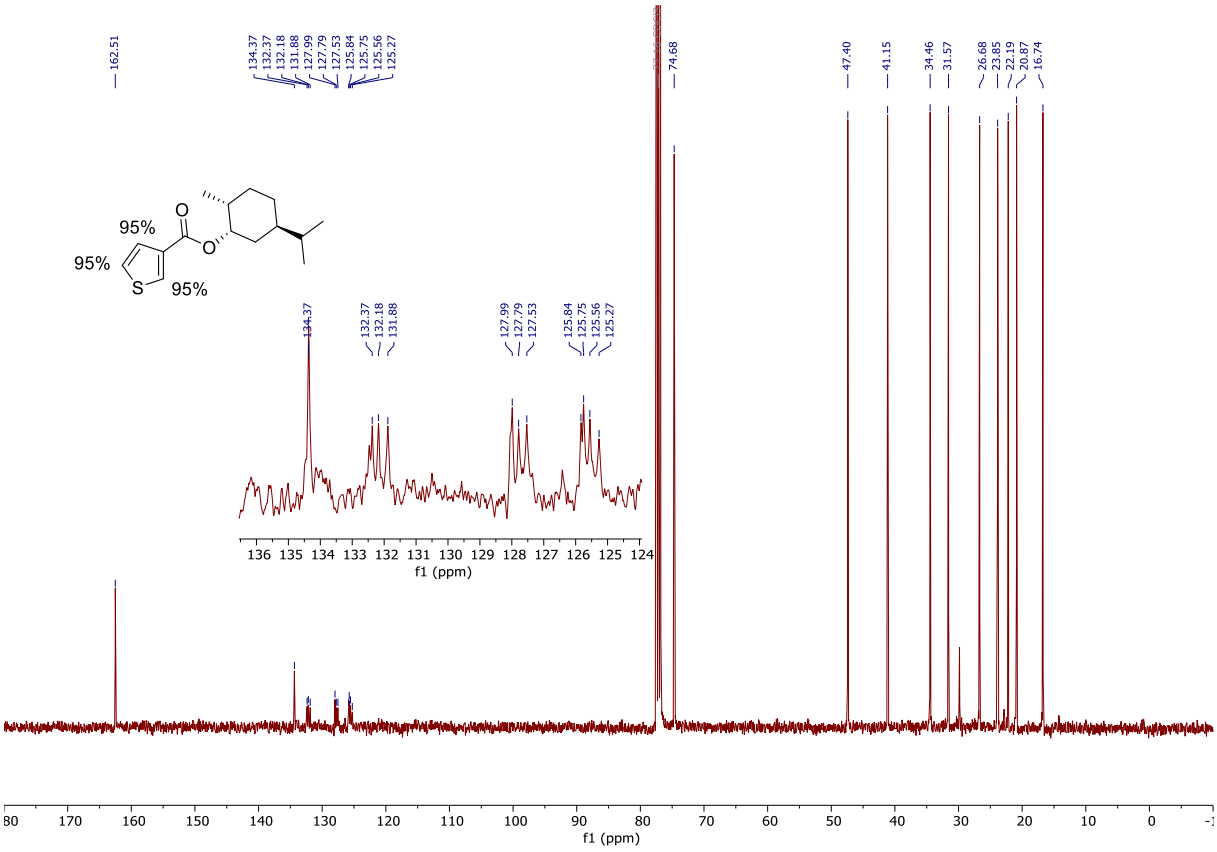
^{1}H-NMR spectrum in $CDCl_3$:



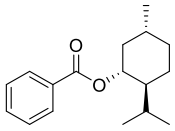
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of methyl (1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl benzoate (41):



Following the general procedure F and using (1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl benzoate (**41**) (52.1 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:Et_2O = 50:1 as the eluent, the target compound **[D]41** was obtained as colorless solid (45.5 mg, 86%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 4.68D/molecule [Mass]; 4.69 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.07-8.01 (m, 2H), 7.58-7.52 (m, 1H), 7.48-7.40 (m, 2H), 4.94 (td, J = 10.9, 4.4 Hz, 1H), 2.25-2.06 (m, 1H), 2.06-1.90 (m, 1H), 1.80-1.68 (m, 2H), 1.65-1.48 (m, 2H), 1.21-1.04 (m, 2H), 0.93 (dd, J = 6.8, 4.4 Hz, 7H), 0.80 (d, J = 7.0 Hz, 3H) ppm.

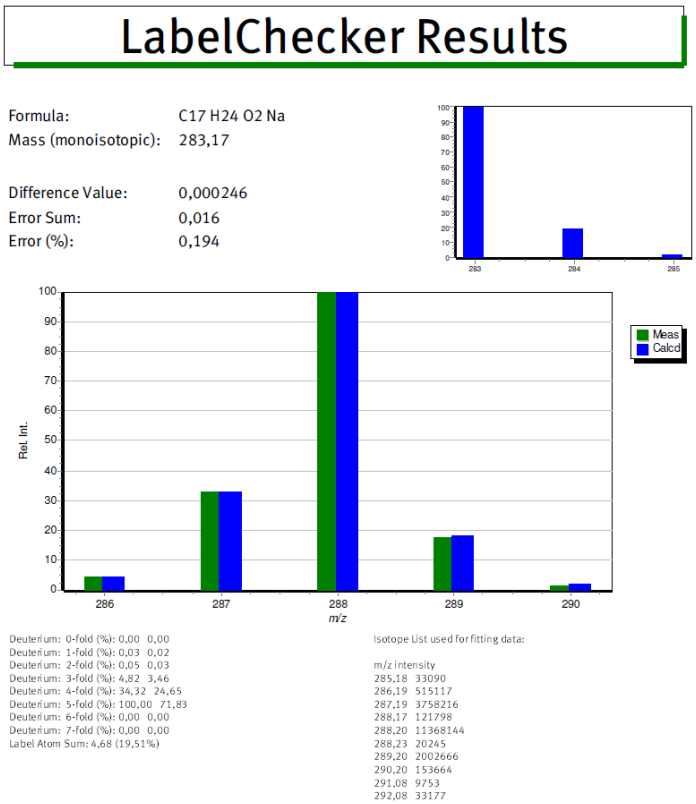
^{13}C NMR (101 MHz, $CDCl_3$) δ = 166.3, 132.8, 131.1, 129.7, 128.4, 75.0, 47.5, 41.1, 34.5, 31.6, 26.7, 23.8, 22.2, 20.9, 16.7 ppm.

NMR Data of Product:

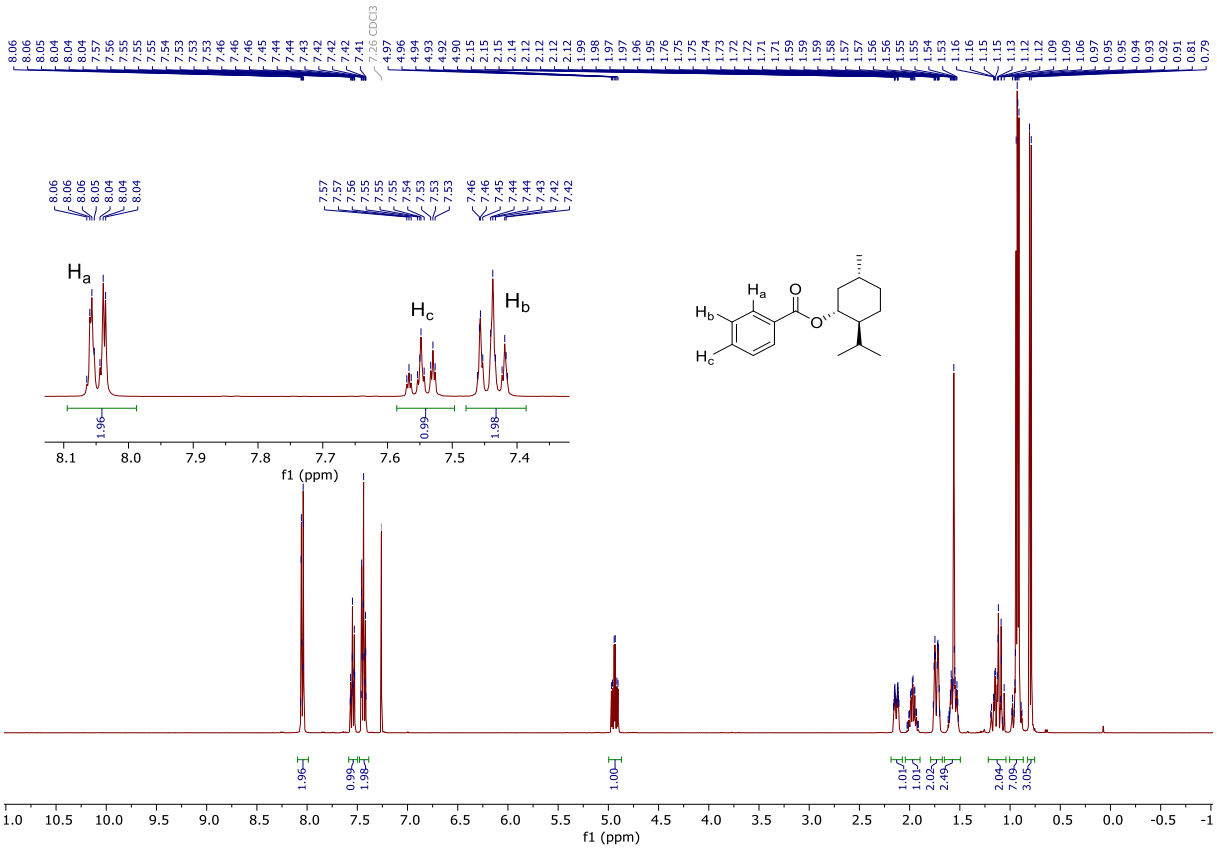
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.05 (s, 0.15H, 92.5% D), 7.55 (s, 0.06H, 94% D), 7.44 (s, 0.11H, 94.5% D), 4.94 (td, *J* = 10.9, 4.4 Hz, 1H), 2.17-2.09 (m, 1H), 1.97 (pd, *J* = 7.0, 2.8 Hz, 1H), 1.79-1.68 (m, 2H), 1.65-1.48 (m, 2H), 1.21-1.04 (m, 2H), 1.01-0.84 (m, 7H), 0.80 (d, *J* = 7.0 Hz, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 166.2, 133.1-131.5 (1C), 130.9, 129.9-128.7 (2C), 128.6-127.3 (2C), 74.9, 47.4, 41.1, 34.5, 31.6, 26.6, 23.8, 22.2, 20.9, 16.7 ppm.

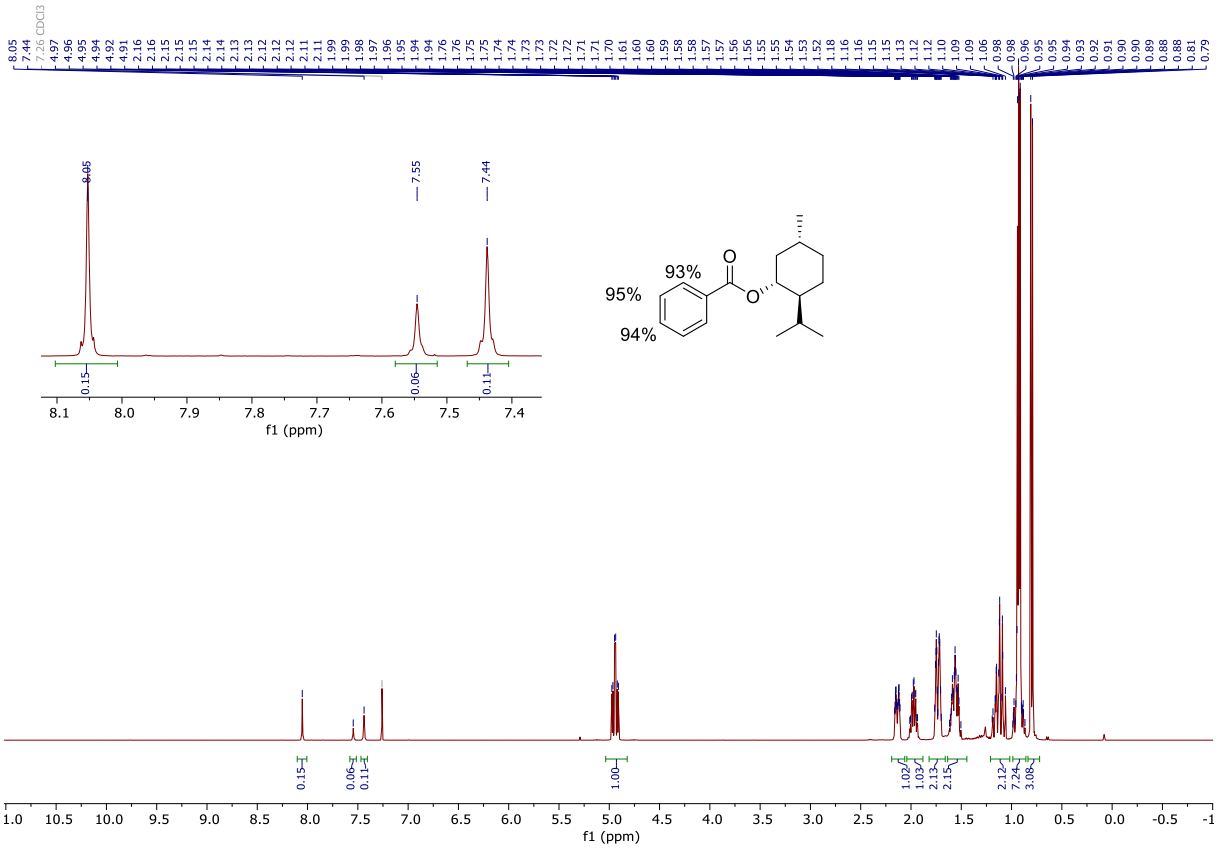
Mass Data:



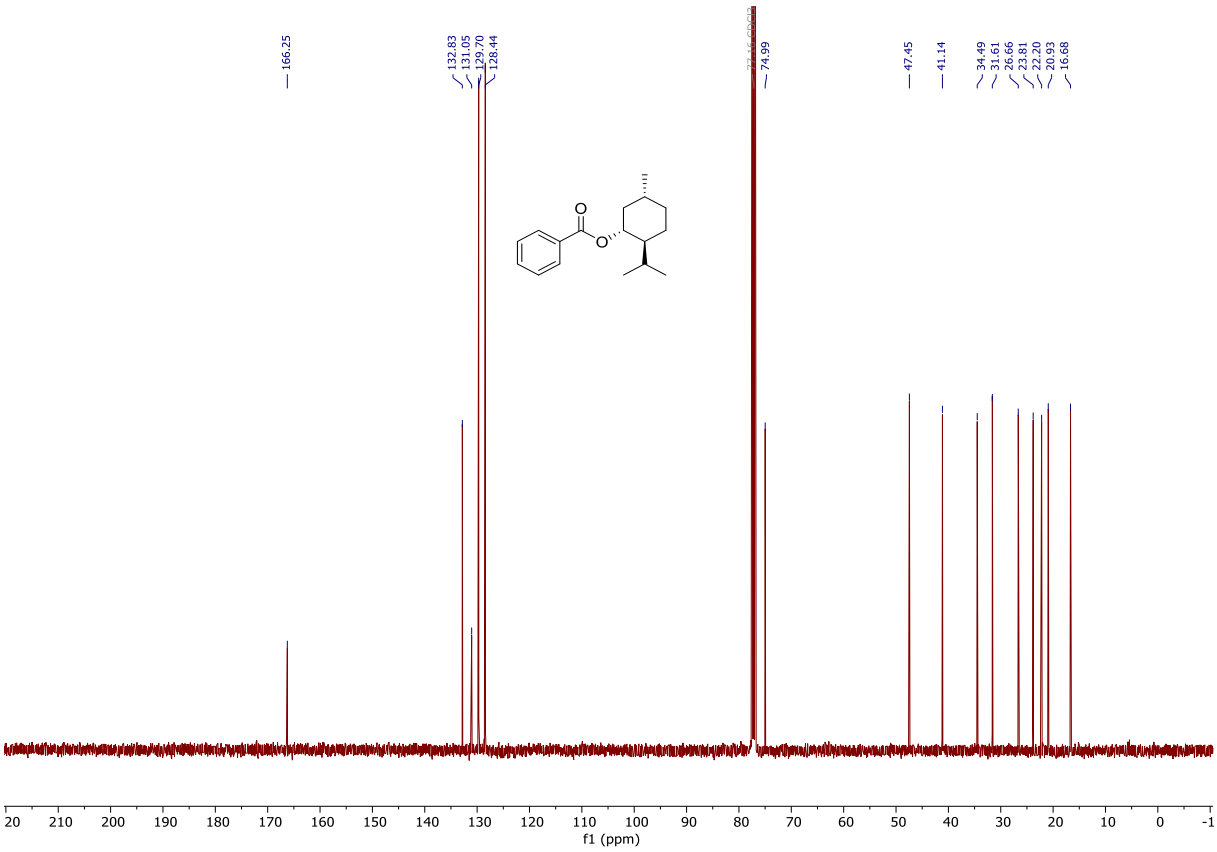
^{1}H-NMR spectrum in $CDCl_3$:



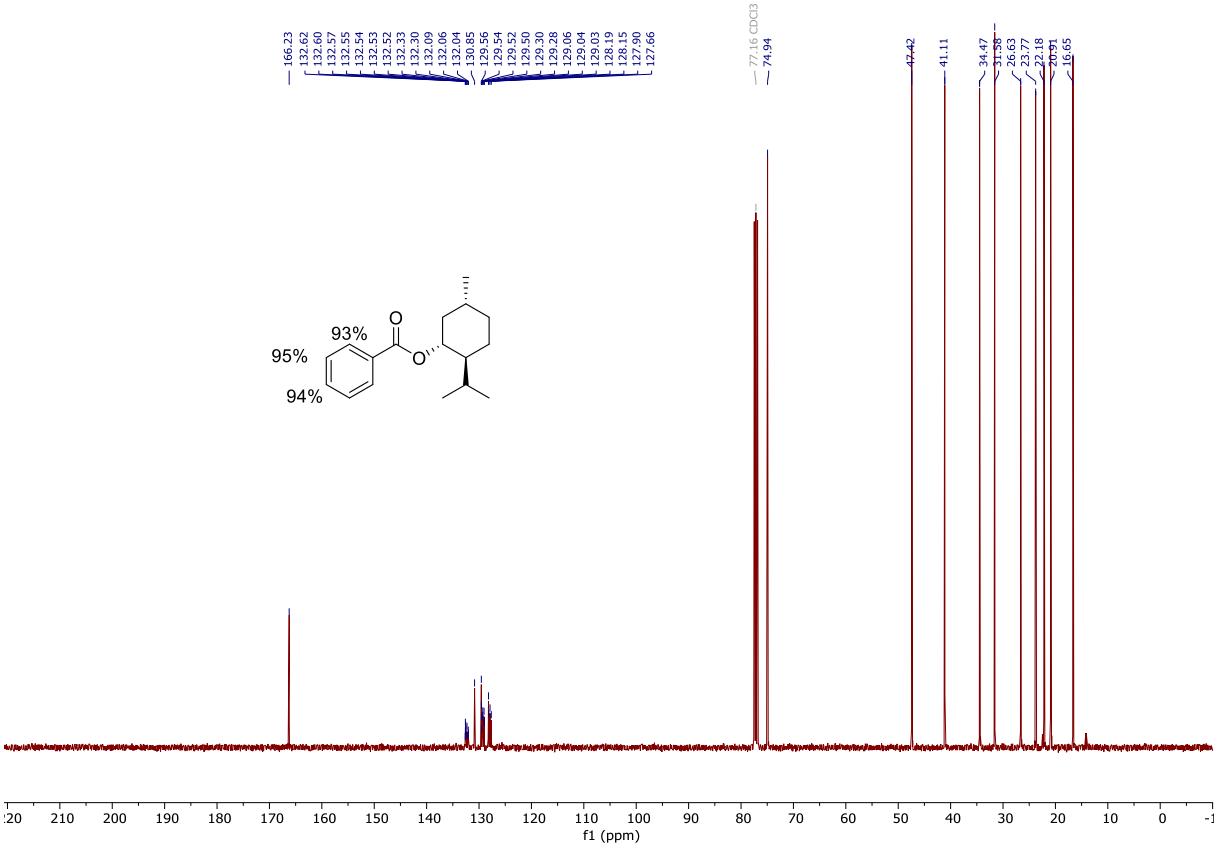
^{1}H-NMR spectrum in $CDCl_3$:



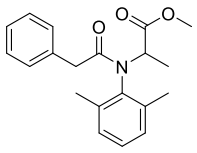
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of methyl *N*-(2,6-dimethylphenyl)-*N*-(2-phenylacetyl)alaninate (42):



Following the general procedure F and using methyl *N*-(2,6-dimethylphenyl)-*N*-(2-phenylacetyl)alaninate (**42**) (65.1 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAc = 80:20 as the eluent, the target compound **[D]42** was obtained as colorless liquid (63.0 mg, 95%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 7.70 D/molecule [Mass]; 7.60 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.24-7.20 (m, 1H), 7.20-7.15 (m, 4H), 7.06-7.03 (m, 1H), 6.97-6.92 (m, 2H), 4.44 (q, *J* = 7.4 Hz, 1H), 3.78 (s, 3H), 3.37-3.18 (m, 2H), 2.40 (s, 3H), 1.88 (s, 3H), 0.99 (d, *J* = 7.4 Hz, 3H) ppm.

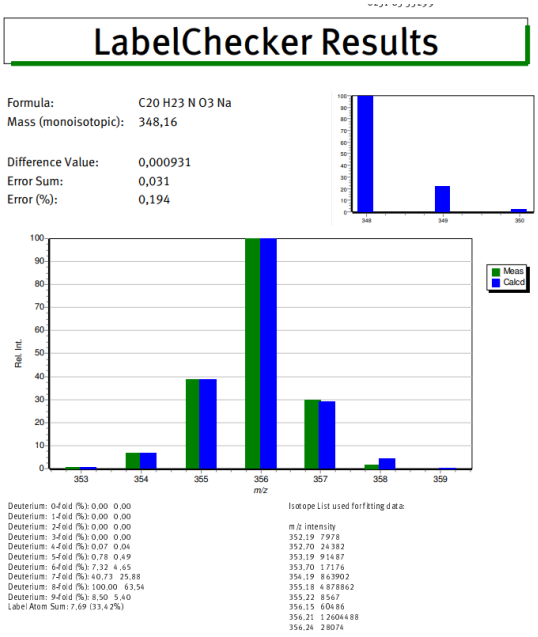
^{13}C NMR (126 MHz, $CDCl_3$) δ = 173.3, 171.9, 139.0, 138.1, 137.4, 134.4, 129.5, 129.3, 128.9, 128.7, 128.3, 126.9, 55.7, 52.2, 41.3, 18.8, 18.2, 15.2 ppm.

NMR Data of Product:

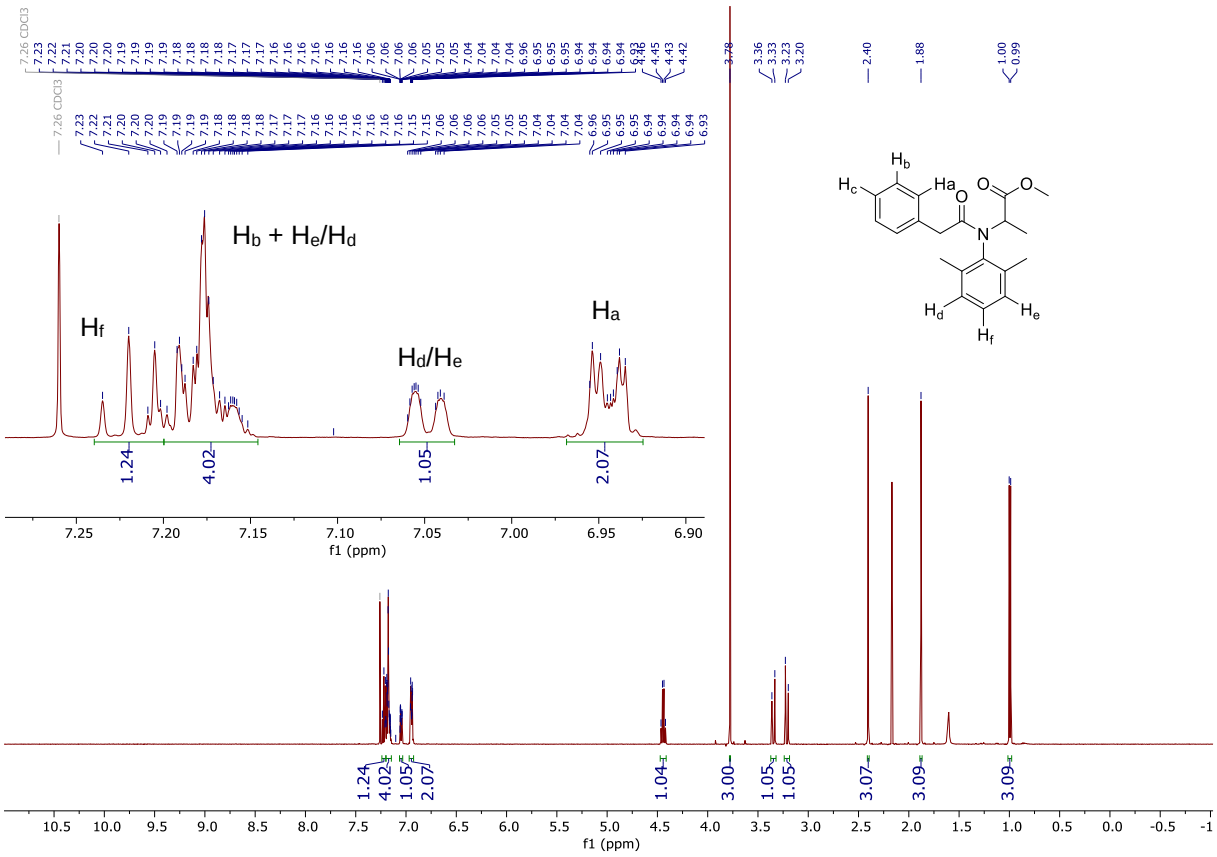
^{1}H NMR (600 MHz, CDCl3) δ = 7.23-7.20 (m, 0.05H, 95% D), 7.19-7.15 (m, 0.20H, > 85% D), 7.06-7.03 (m, 0.05H, 95% D), 6.95-6.92 (m, 0.1H, 95% D) 4.44 (q, *J* = 7.4 Hz, 1H), 3.78 (s, 3H), 3.37-3.18 (m, 1.90H, 5% D), 2.40 (s, 3H), 1.87 (s, 3H), 0.99 (d, *J* = 7.4 Hz, 3H) ppm.

^{13}C NMR (126 MHz, $CDCl_3$) δ = 173.2, 171.9, 138.8, 137.9, 137.3, 134.1, 129.3-127.6 (7C), 126.6-126.1 (1C), 55.6, 52.2, 41.2-41.1(1C), 18.7(4)-18.6(8)(1C), 18.2-18.1(1C), 15.2 ppm.

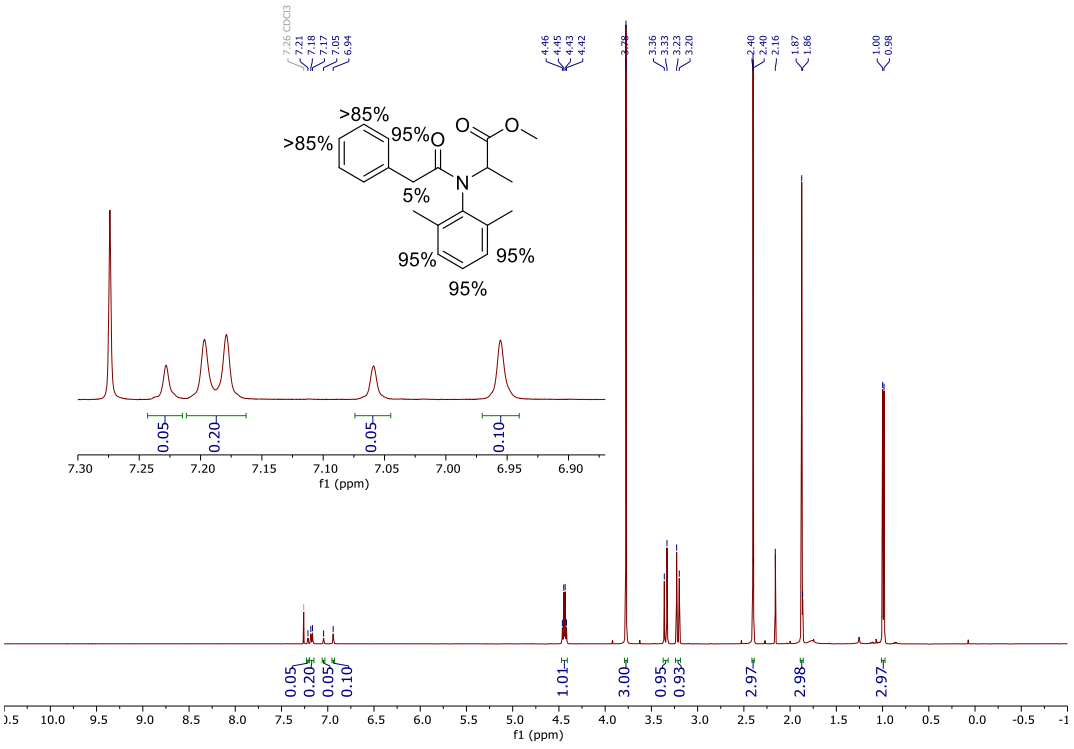
Mass Data:



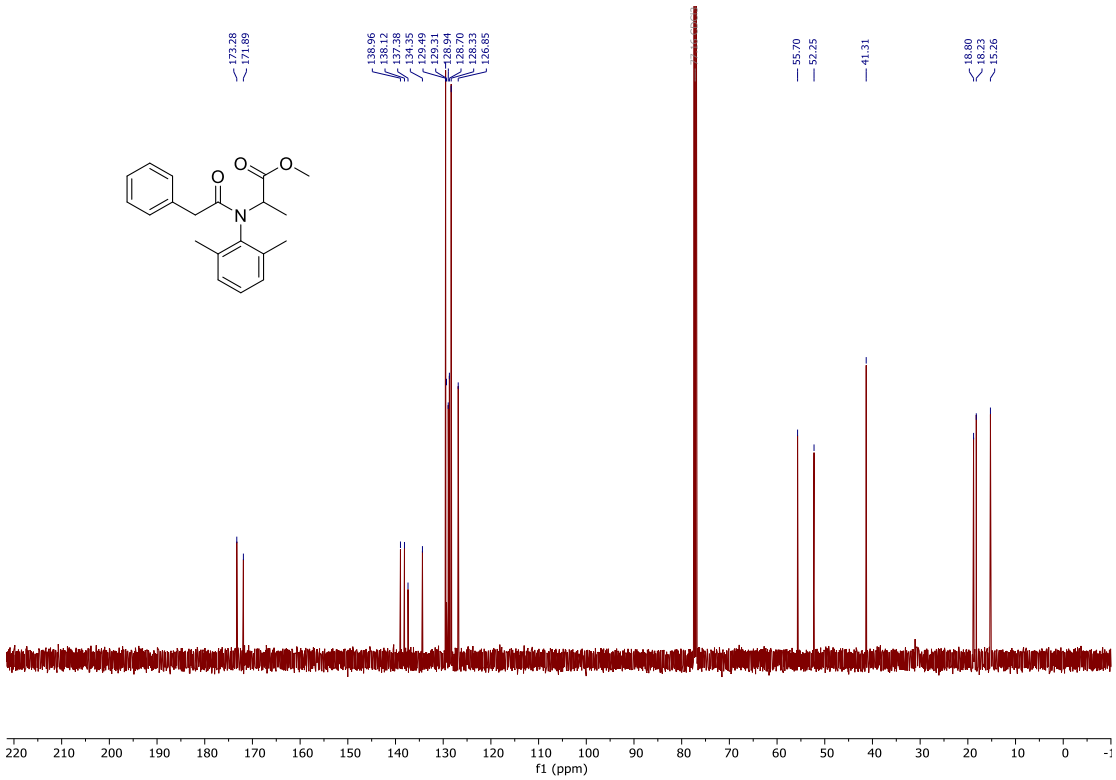
^{1}H-NMR spectrum in $CDCl_3$:



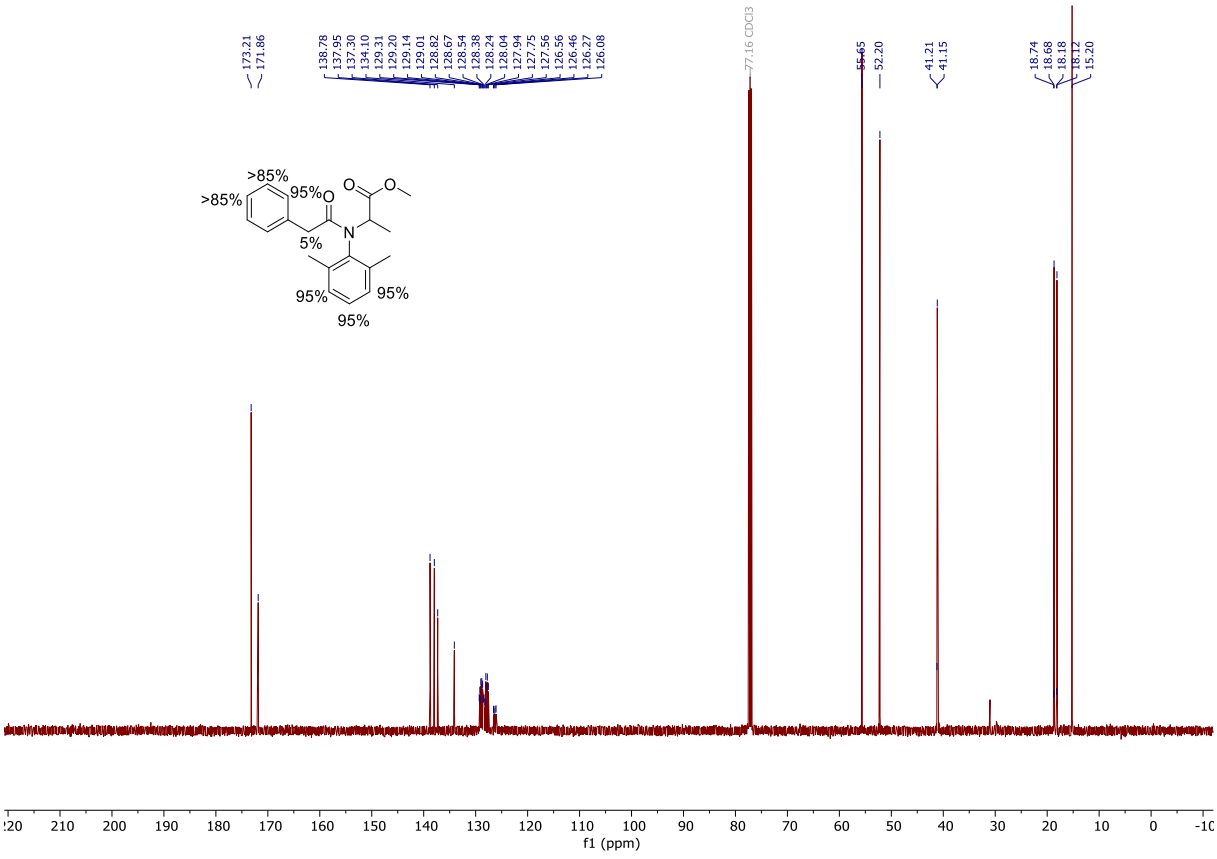
^{1}H-NMR spectrum in $CDCl_3$:



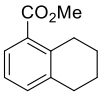
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of methyl 5,6,7,8-tetrahydronaphthalene-1-carboxylate (43):



Following the general procedure F and using methyl 5,6,7,8-tetrahydronaphthalene-1-carboxylate (**43**) (38.1 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:Et_2O = 50:1 as the eluent, the target compound **[D]43** was obtained as colorless liquid (34.9 mg, 90%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 2.85 D/molecule [Mass]; 2.84 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.65 (d, *J* = 7.7 Hz, 1H), 7.21 (d, *J* = 7.6 Hz, 1H), 7.13 (t, *J* = 7.6 Hz, 1H), 3.87 (s, 3H), 3.06 (t, *J* = 5.6 Hz, 2H), 2.82 (t, *J* = 5.6 Hz, 2H), 1.84-1.75 (m, 4H) ppm.

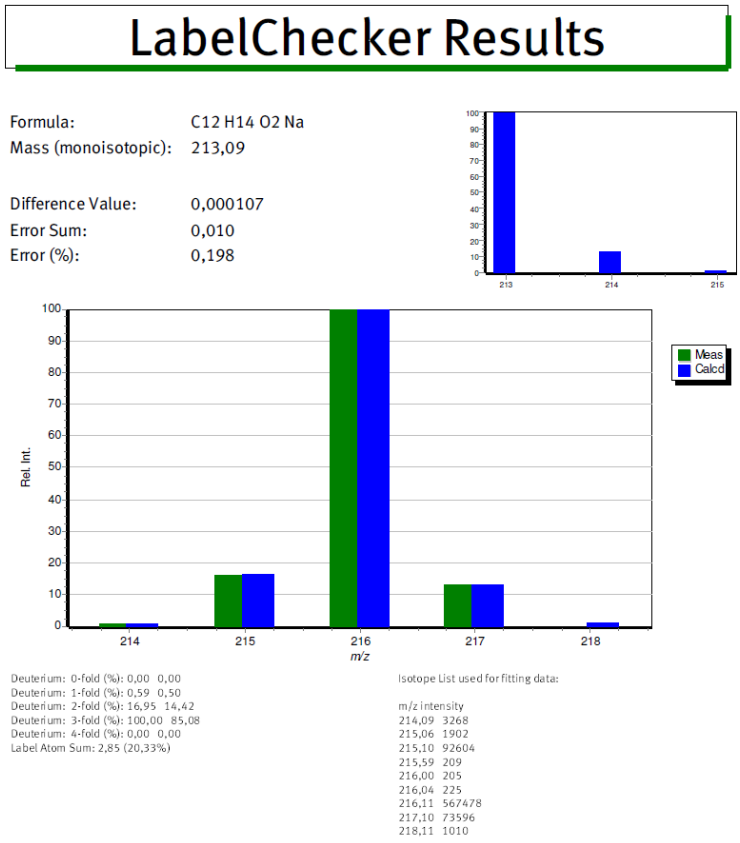
^{13}C NMR (151 MHz, $CDCl_3$) δ = 168.7, 138.7, 138.5, 133.2, 130.4, 127.9, 125.1, 51.9, 30.3, 27.9, 23.2, 22.6 ppm.

NMR Data of Product:

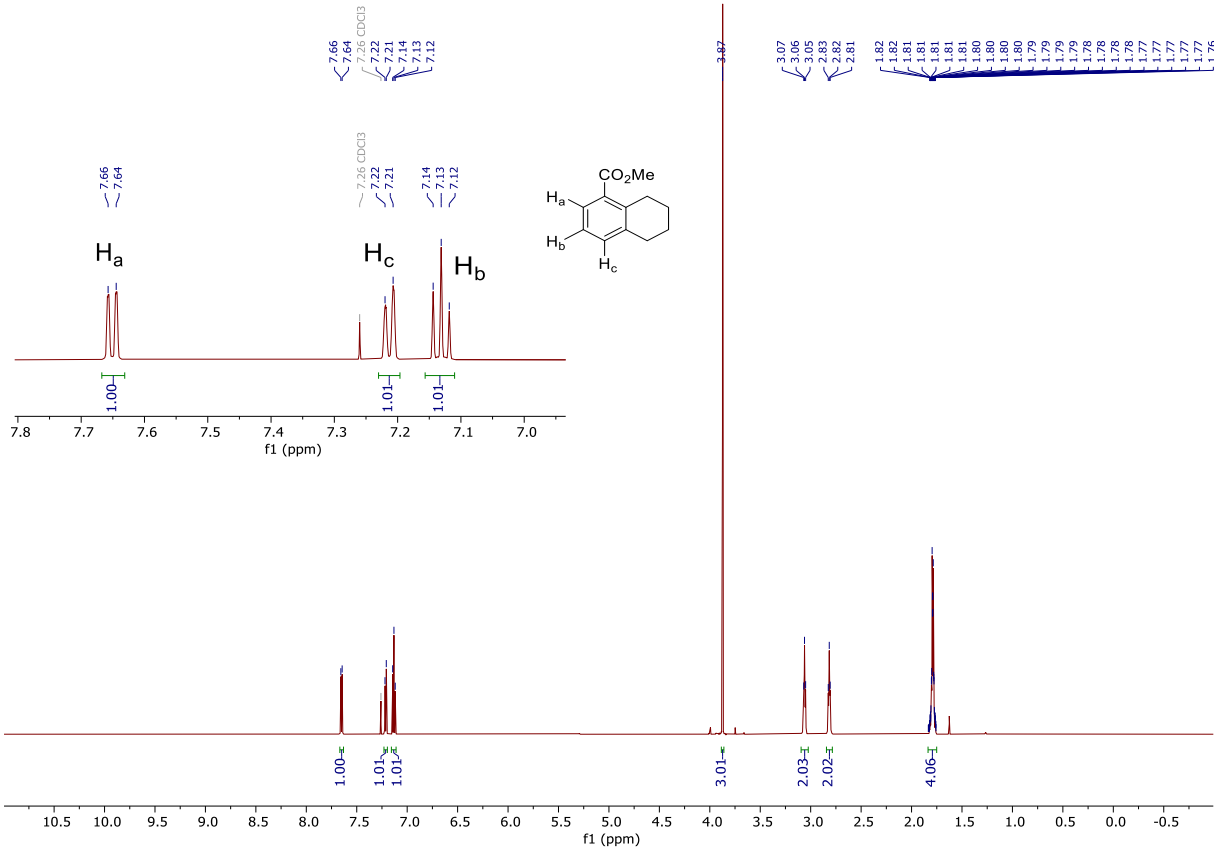
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.65 (s, 0.05H, 95% D), 7.21 (s, 0.06H, 94% D), 7.13 (s, 0.05H, 95% D), 3.87 (s, 3H), 3.14-2.98 (m, 2H), 2.90-2.80 (m, 2H), 1.87-1.70 (m, 4H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 168.7, 138.7, 138.4, 133.5-131.9 (1C), 130.2, 128.3-127.0 (1C), 125.6-122.7 (1C), 51.9, 30.3, 27.9, 23.2, 22.6 ppm.

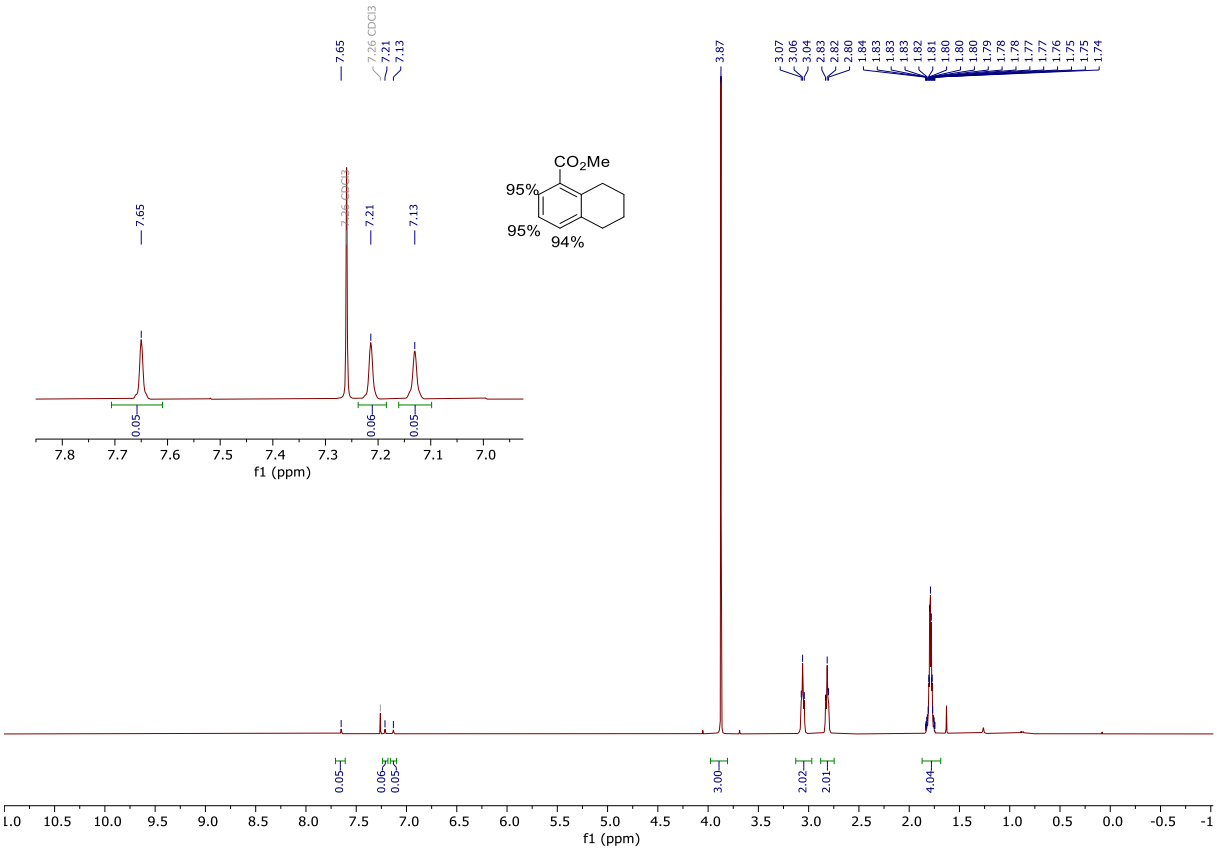
Mass Data:



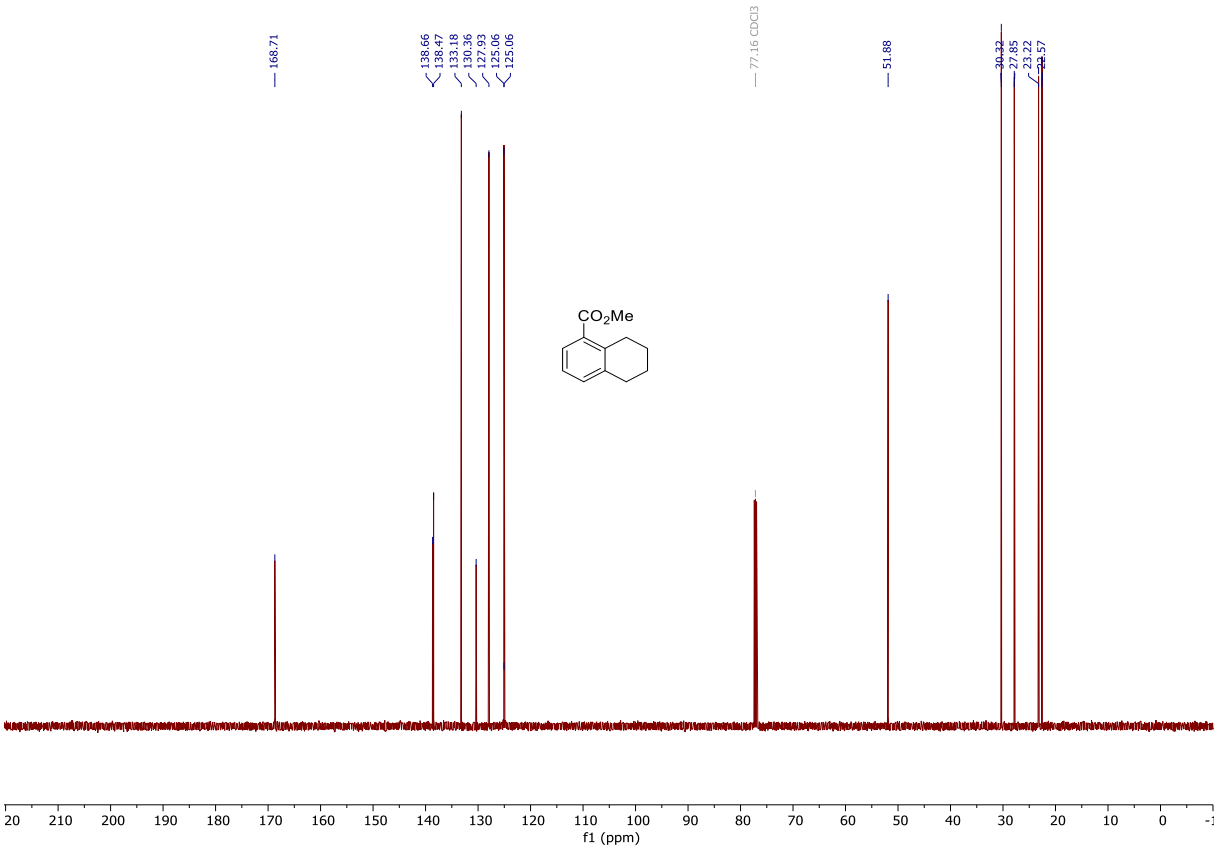
^{1}H-NMR spectrum in $CDCl_3$:



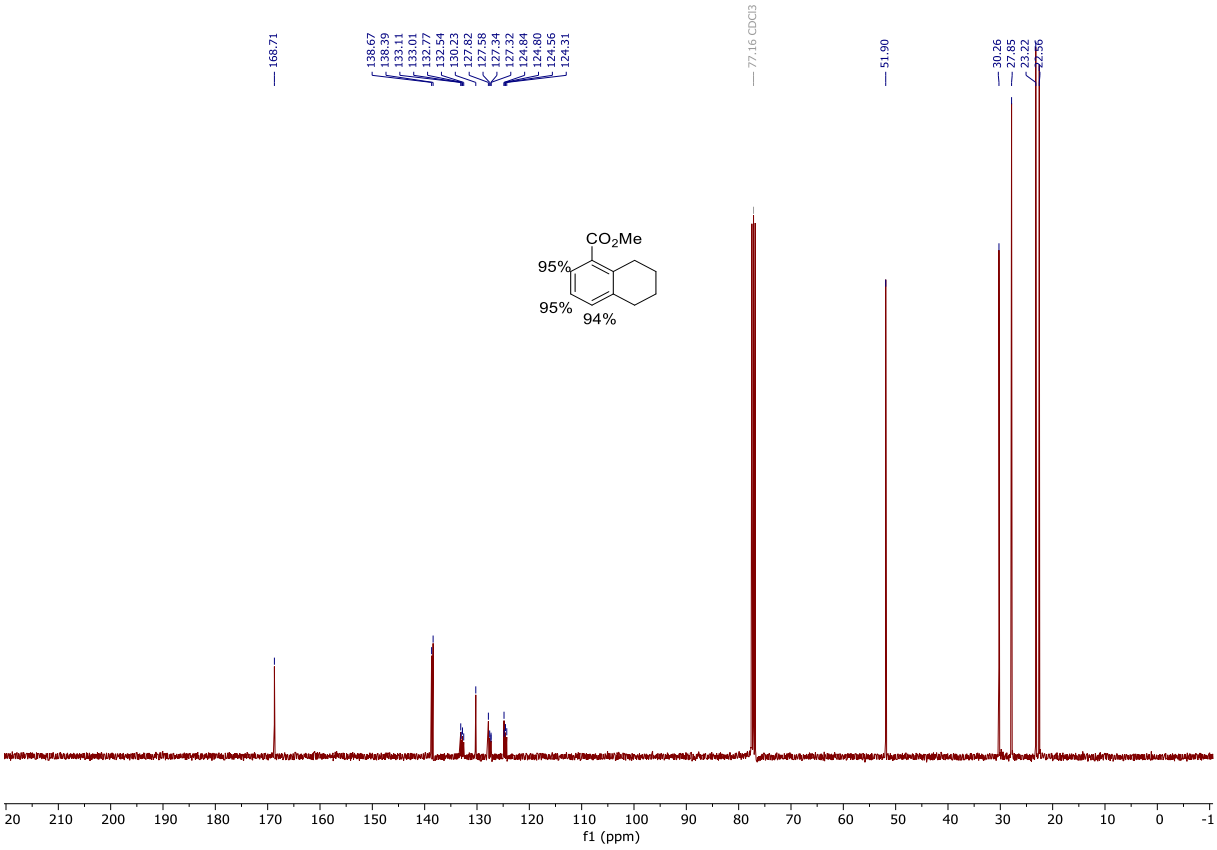
^{1}H-NMR spectrum in $CDCl_3$:



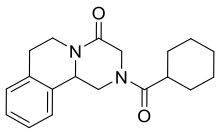
^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



Deuteration of 2-(cyclohexanecarbonyl)-1,2,3,6,7,11b-hexahydro-4*H*-pyrazino[2,1-*a*]isoquinolin-4-one (44):



Following the general procedure F and using 2-(cyclohexanecarbonyl)-1,2,3,6,7,11b-hexahydro-4*H*-pyrazino[2,1-*a*]isoquinolin-4-one **(44)** (62.5 mg, 0.200 mmol), and purification via silica gel column chromatography using EtOAc as the eluent, the target compound **[D]44** was obtained as colorless solid (37.8 mg, 60%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 3.38 D/molecule [HRMS]; 3.33 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (400 MHz, CD_3OD) δ = 7.48-7.10 (m, 4H), 5.08-4.91 (m, 1H), 4.86-4.42 (m, 3H), 4.03 (dd, *J* = 124.6, 17.8 Hz, 1H), 3.50-2.54 (m, 5H), 1.92-1.68 (m, 5H), 1.61-1.18 (m, 5H) ppm.

^{13}C NMR (100 MHz, CD_3OD) δ = 178.0, 168.6, 167.8, 137.5, 137.2, 135.1, 134.6, 131.3, 131.2, 129.6, 129.4, 128.9(5), 128.8(9), 127.6, 127.4, 57.8, 56.9, 51.0, 50.6, 50.4, 50.2, 50.0, 47.9, 47.3, 42.7, 42.4, 41.3, 41.2, 31.5, 31.2, 31.1, 30.5(1), 30.4(5), 27.9, 27.5(2), 27.4(8) ppm.*

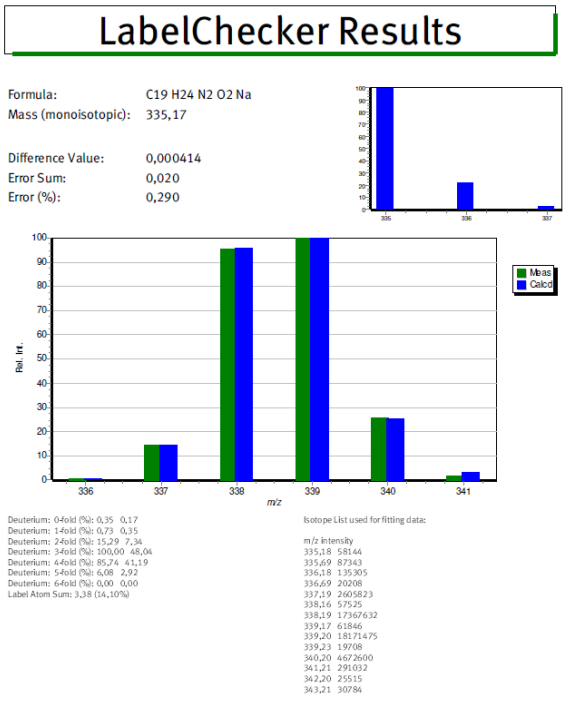
NMR Data of Product:

^{1}H NMR (400 MHz, CD_3OD) δ = 7.44-7.16 (m, 0.67H, 83% D average), 5.07-4.90 (m, 1H), 4.85-4.39 (m, 3H), 4.03 (dd, *J* = 125.2, 17.8 Hz, 1H), 3.46-2.56 (m, 5H), 1.91-1.66 (m, 5H), 1.58-1.18 (m, 5H) ppm.

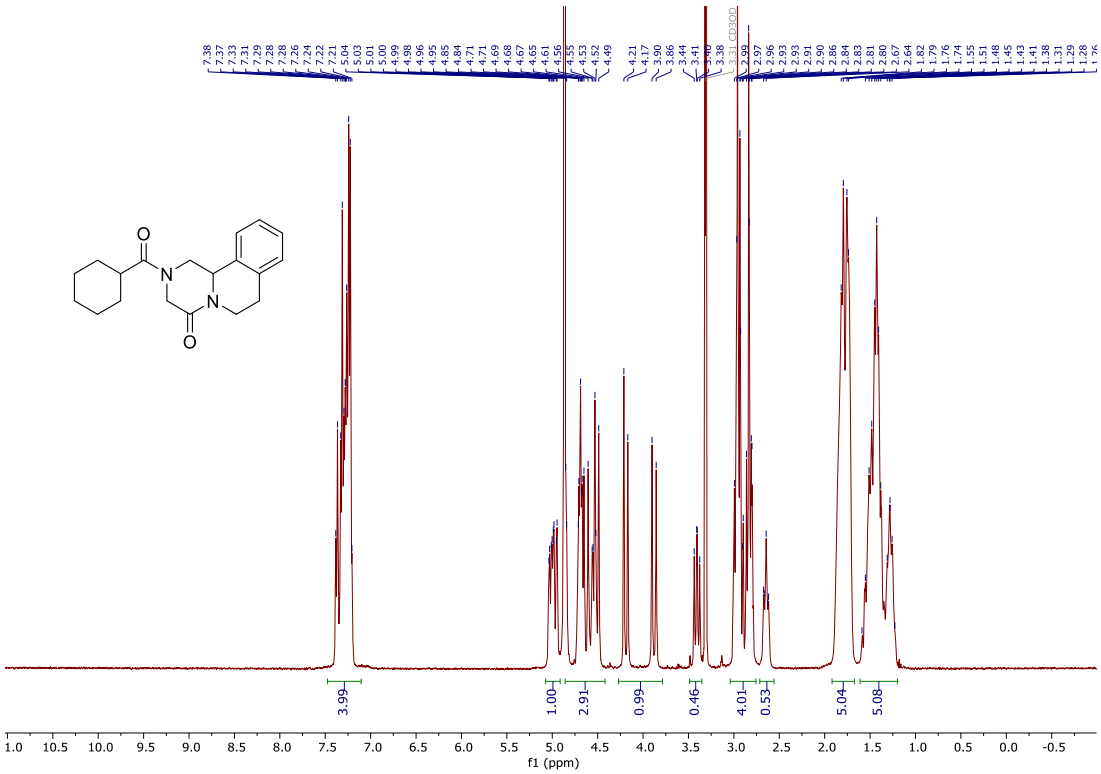
^{13}C NMR (100 MHz, CD_3OD) δ = 178.0, 168.6, 167.7, 137.4, 137.1, 135.4-134.2 (2C), 131.5-127.9 (6C), 127.5, 127.3, 57.7-55.7 (2H), 51.0, 50.6, 50.4, 50.2, 50.0, 47.9, 47.3, 42.6, 42.3, 41.3, 41.2, 31.5, 31.2, 31.1, 30.4(4), 30.3(8), 27.9, 27.5(1), 27.4(7) ppm.*

*the peaks are reported as observed.

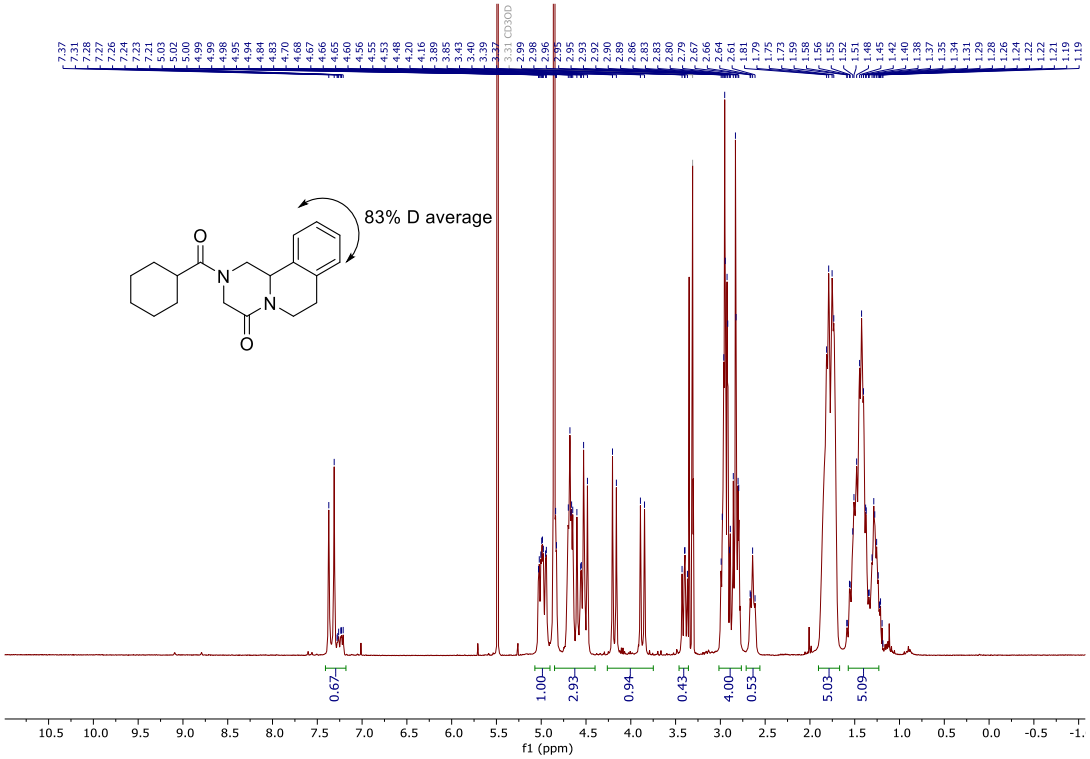
Mass Data:



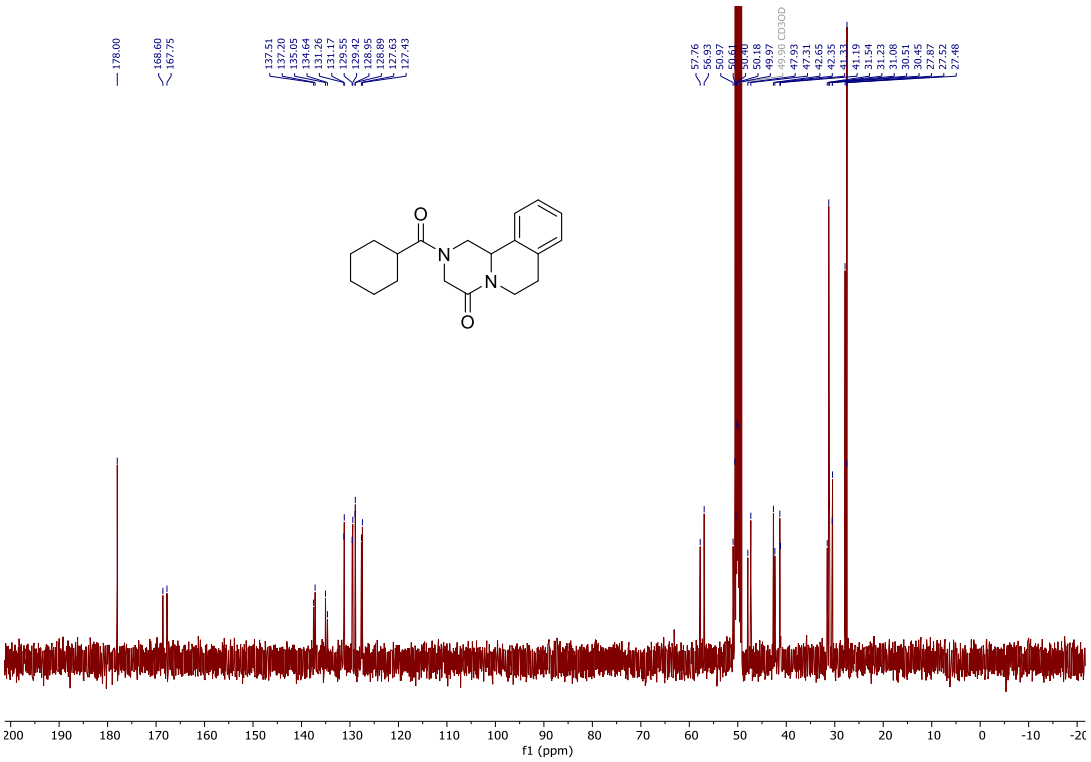
^{1}H-NMR spectrum in CD_3OD:



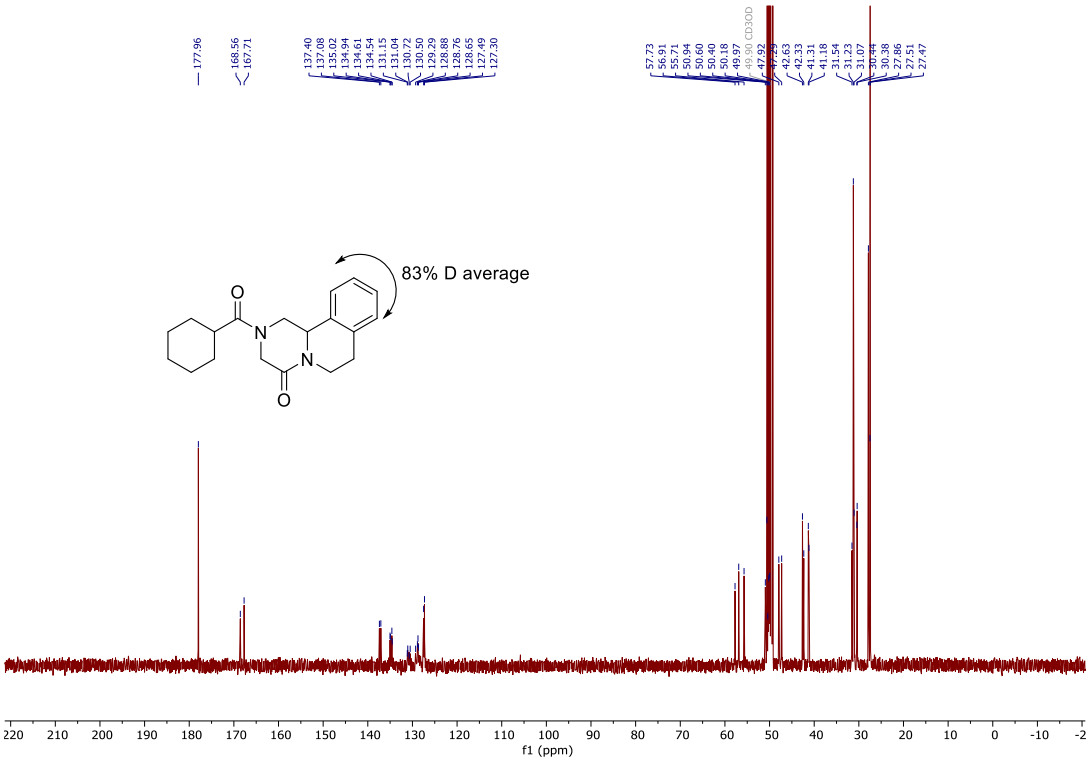
^{1}H-NMR spectrum in CD_3OD:



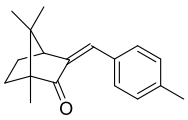
^{13}C-NMR spectrum in CD_3OD:



^{13}C-NMR spectrum in CD_3OD:



Deuteration of (4*S*)-1,7,7-trimethyl-3-((*Z*)-4-methylbenzylidene)bicyclo[2.2.1]heptan-2-one (45):



Following the general procedure F and using (4*S*)-1,7,7-trimethyl-3-((*Z*)-4-methylbenzylidene)bicyclo[2.2.1]heptan-2-one **(45)** (50.9 mg, 0.200 mmol), and purification via silica gel column chromatography using pentane:EtOAC = 40:1 as the eluent, the target compound **[D]45** was obtained as a colorless solid (47.7 mg, 92%). The degree of deuteration was determined by mass spectrometry.

Deuterium Incorporation: 4.74 D/molecule [HRMS]; 4.74 D/molecule [^{1}H-NMR].

NMR Data of Starting Material:

^{1}H NMR (599 MHz, $CDCl_3$) δ = 7.38 (d, *J* = 8.1 Hz, 2H), 7.22 (s, 1H), 7.20 (d, *J* = 7.9 Hz, 2H), 3.10 (d, *J* = 4.3 Hz, 1H), 2.37 (s, 3H), 2.17 (dddd, *J* = 11.7, 11.7, 4.5, 4.5 Hz, 1H), 1.78 (ddd, *J* = 13.2, 11.3, 3.7 Hz, 1H), 1.59 (ddd, *J* = 12.2, 9.3, 3.7 Hz, 1H), 1.52 (ddd, *J* = 13.7, 9.3, 4.6 Hz, 1H), 1.03 (s, 3H), 1.00 (s, 3H), 0.80 (s, 3H) ppm.

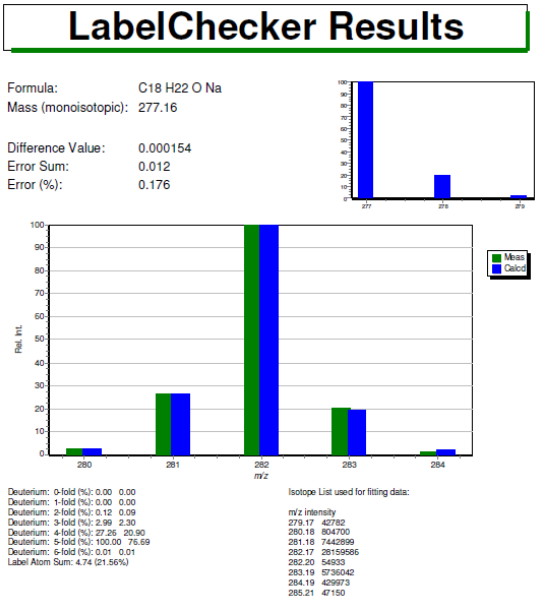
^{13}C NMR (101 MHz, $CDCl_3$) δ = 208.5, 141.4, 139.1, 133.0, 129.9, 129.5, 127.7, 57.2, 49.4, 46.9, 30.9, 26.1, 21.5, 20.7, 18.5, 9.4 ppm.

NMR Data of Product:

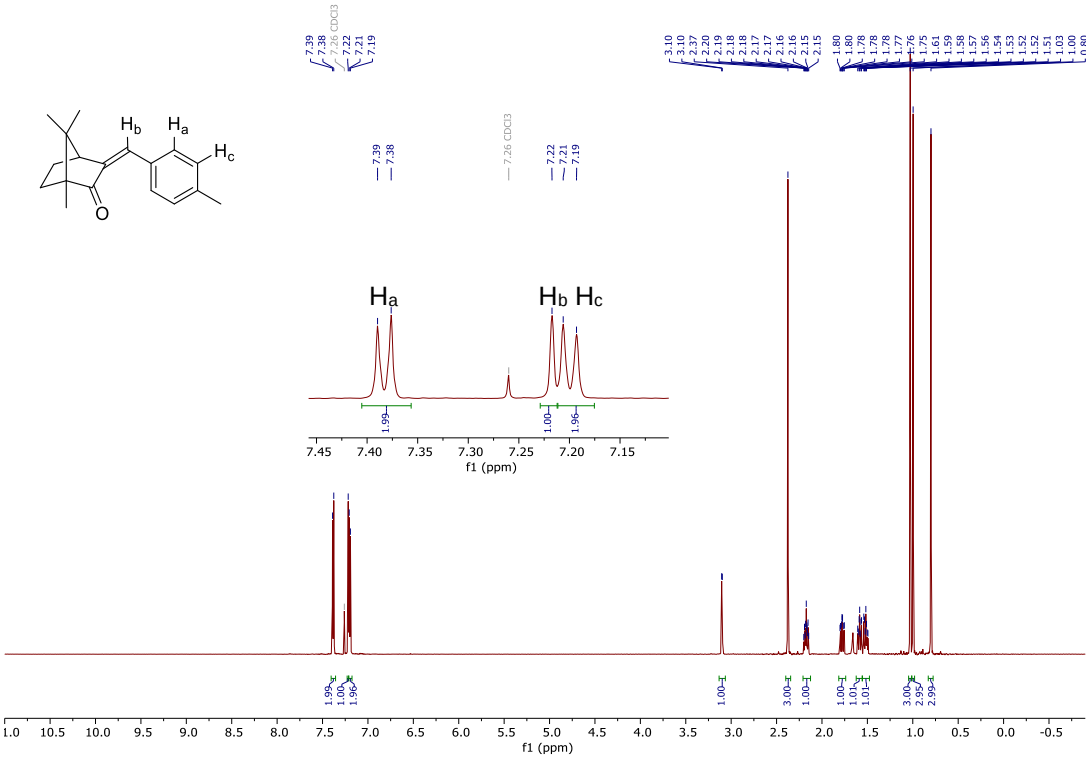
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.39 (s, 0.10H, 95%D), 7.22 (s, 0.05H, 95%D), 7.20 (s, 0.11H, 95%D), 3.10 (d, *J* = 4.2 Hz, 1H), 2.37 (s, 3H), 2.17 (dddd, *J* = 10.8, 10.8, 4.2, 4.2 Hz, 1H), 1.78 (ddd, *J* = 12.4, 12.4, 3.3 Hz, 1H), 1.58 (ddd, *J* = 12.3, 9.1, 3.6 Hz, 1H), 1.51 (ddd, *J* = 13.5, 9.3, 4.2 Hz, 1H), 1.03 (s, 3H), 1.00 (s, 3H), 0.80 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 208.5, 141.3, 138.9, 132.7, 129.9-128.8 (2C), 127.7-126.9 (1C), 57.2, 49.4, 46.9, 30.9, 26.1, 21.4, 20.7, 18.5, 9.4 ppm.

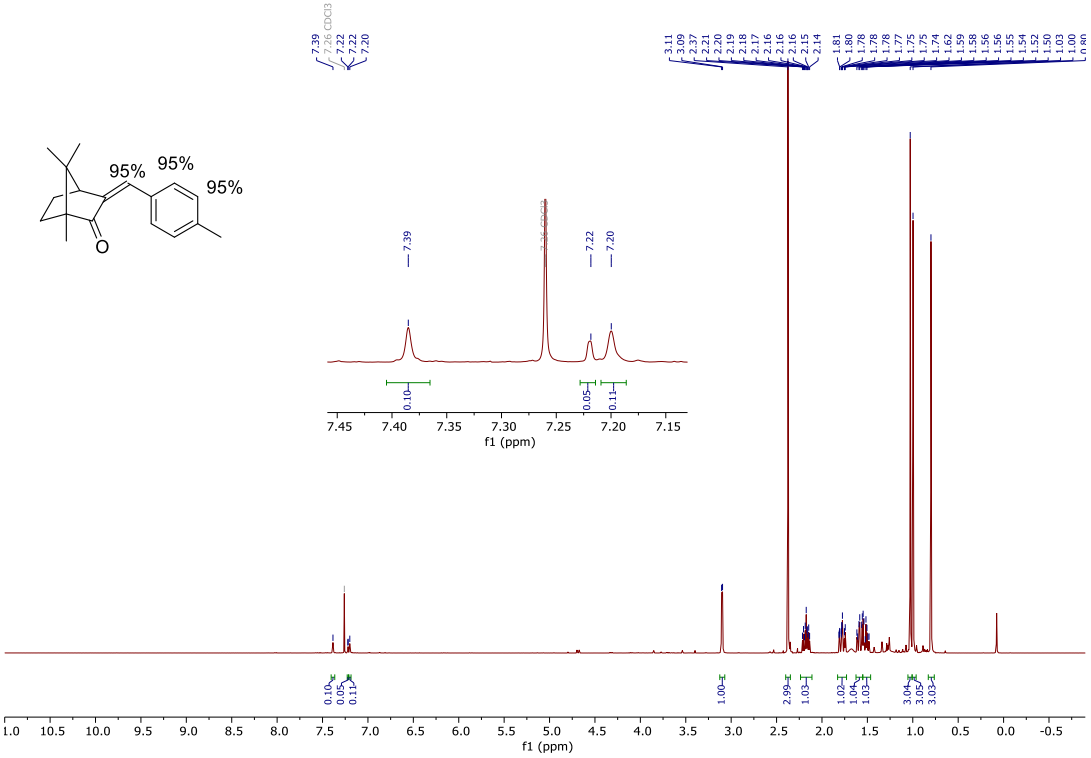
Mass Data:



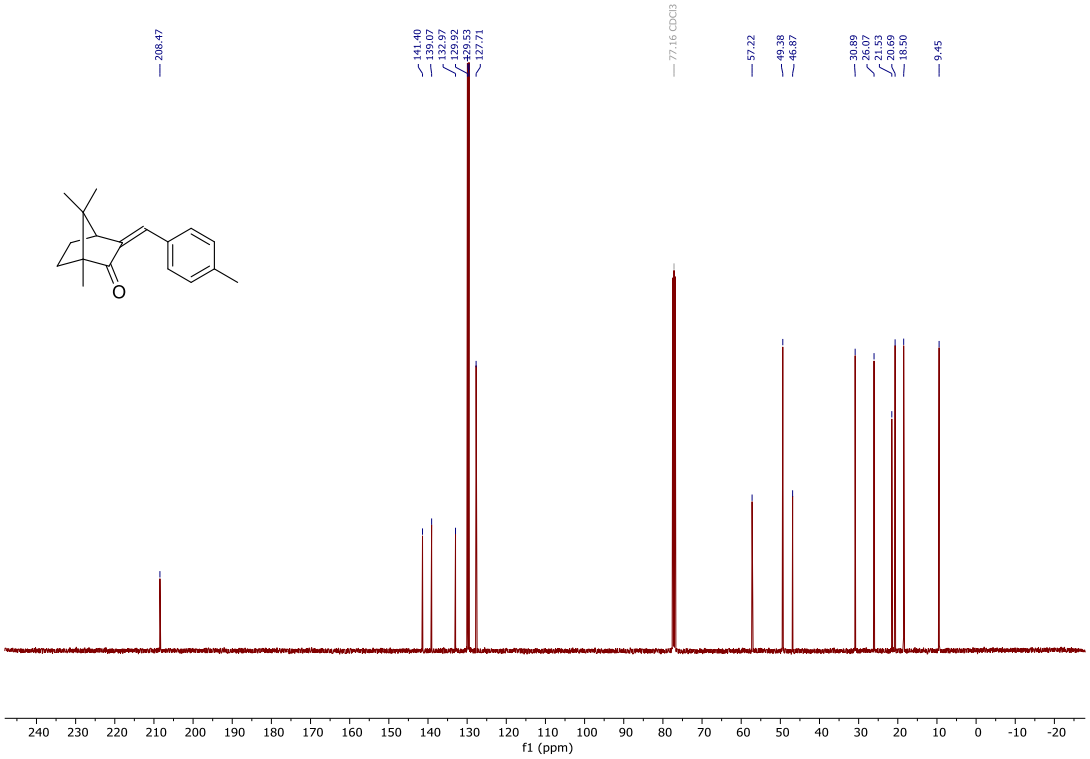
^{1}H-NMR spectrum in $CDCl_3$:



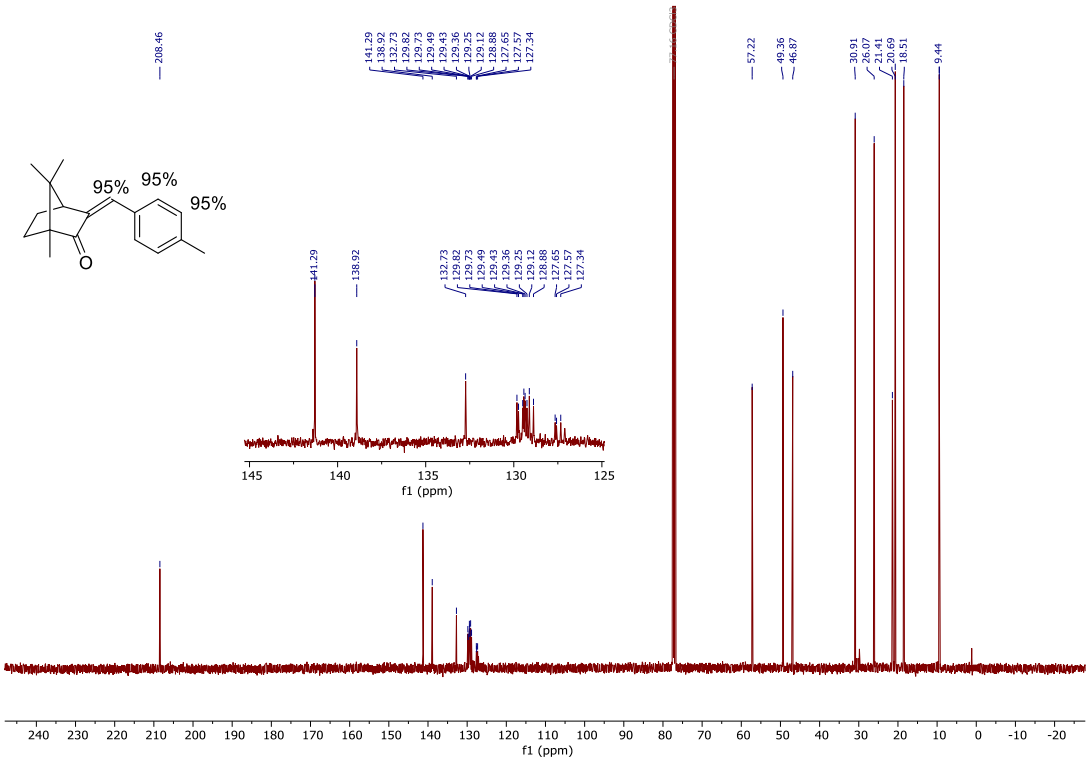
^{1}H-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



^{13}C-NMR spectrum in $CDCl_3$:



6. References

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