

Chemoselective Deoxygenative α -Arylation of Carboxylic Acids, Amides, and Esters: Synthesis of Anesthetic and Anti-inflammatory Compounds

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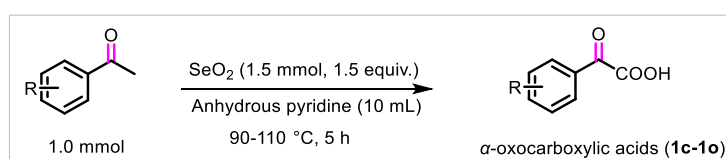
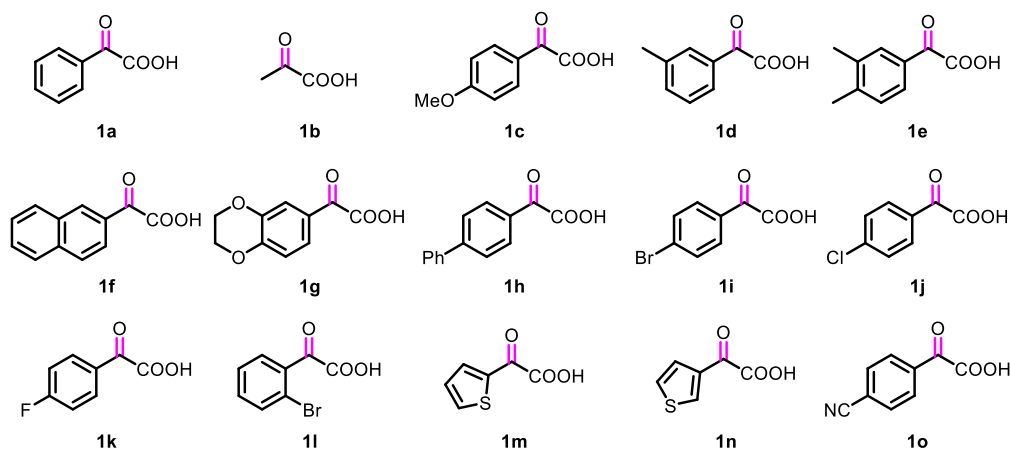
1. General information

All reagents and solvents were of pure analytical grade. All experiments were carried out in a round-bottom flask equipped with a stirring bar. Chemicals were purchased from Sigma-Aldrich, TCI, Alfa-Aesar, and Sisco Research Laboratories (SRL) and used without further purification. Analytical thin-layer chromatography (TLC) was carried out using 0.2 mm commercially available silica gel plates (silica gel 60, F254, EMD Chemical). Visualization of the developed TLC plate was performed by irradiation with UV light. High-resolution mass spectra (HRMS) were recorded on a mass spectrometer using electrospray ionization-time-of-flight (ESI-TOF) reflectron experiments. $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ were recorded on 500 MHz spectrometers and 400 MHz spectrometers, using CDCl_3 and $\text{DMSO-}d_6$ as a solvent; the chemical shifts are reported as parts per million (ppm) referenced to residual protium or carbon of the solvents; CDCl_3 δ H (7.26 ppm) and $\text{DMSO-}d_6$ δ H (2.50 ppm). Coupling constants are reported in Hertz (Hz). Data for $^1\text{H NMR}$ spectra are reported as follows: chemical shift (ppm, referenced to protium; s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sext = sextet, dd = doublet of doublets, td = triplet of doublets, ddd = doublet of doublet of doublets, m = multiplet, coupling constant (Hz), and integration).

2. Synthesis of starting materials

2.1 General procedure for the preparation of α -oxocarboxylic acids (1a–1o)

The α -oxocarboxylic acids (1a-1b) were obtained commercially. The other α -oxocarboxylic acids (1c-1o) can be synthesized by oxidizing the corresponding methyl ketones with SeO_2 , following the method described in the literature.¹

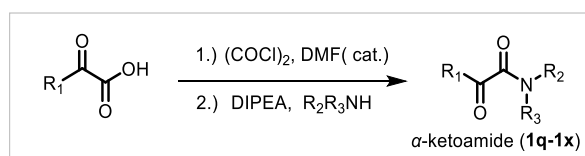
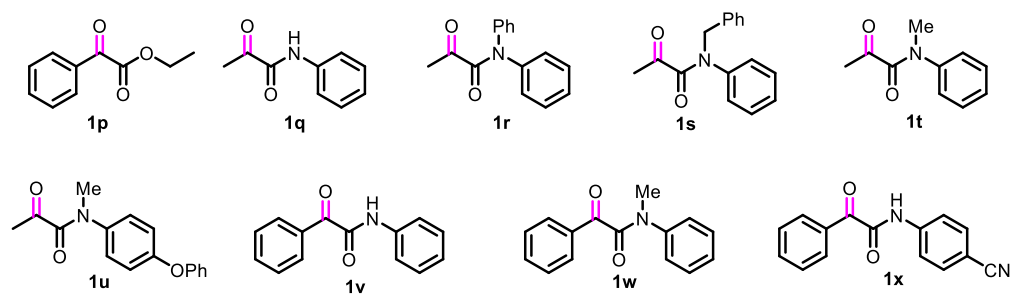


In a dry, round-bottom flask, aryl-methyl ketone (1.0 mmol) was added to a solution of selenium dioxide (SeO_2 , 0.167 g, 1.5 mmol, 1.5 equiv.) in anhydrous pyridine (10 mL). The reaction mixture was heated

in an oil bath at 110 °C for 1 h, then the temperature was reduced to 90 °C and maintained for 4 hours. The solution, which contained precipitated selenium, was filtered using a Buchner funnel, and the residue was washed with ethyl acetate (50 mL). The combined filtrate was treated with 1 N HCl (20 mL), the organic layer was separated, and the aqueous layer was extracted with ethyl acetate (3×50 mL). The combined organic layers were treated with 1 N NaOH (50 mL), and the aqueous layer was separated. The organic layer was then extracted with water (25 mL), and the combined aqueous layers were acidified with 1 N HCl to approximately pH 1.5. The mixture was extracted with ethyl acetate (3×50 mL), and the combined organic layers were dried with anhydrous Na₂SO₄ and concentrated on a rotary evaporator. The crude aryl glyoxylic acid products were purified by silica-gel column chromatography using a MeOH (10:90) solvent system for elution.

2.2 General procedure for the preparation of α -ketoester (**1p**) and α -ketoamide (**1q-1x**)

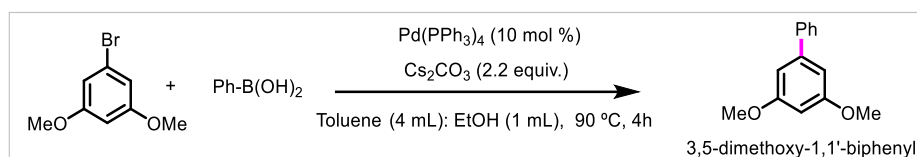
The α -ketoester (**1p**) was purchased from commercial sources. Other α -ketoamide (**1q-1x**) were prepared according to the reported procedure.^{2a}



In a solution of α -ketoacid (30.0 mmol) in CH₂Cl₂ (20 mL), a catalytic amount of DMF (1 drop) and oxalyl chloride (30.0 mmol) were added at 25 °C. The reaction was stirred until the evolution of HCl gas ceased. Then, the primary or secondary amine (45 mmol) and DIPEA (60.0 mmol) were added dropwise to the reaction mixture at 0 °C. The mixture was stirred at room temperature for 3 hours. The reaction was then quenched with water, and the mixture was extracted with CH₂Cl₂ three times. The combined organic layers were washed with brine and dried over Na₂SO₄. The solvent was removed under reduced pressure, and the resulting crude product was purified by column chromatography to yield the desired product in 70-91% yields.

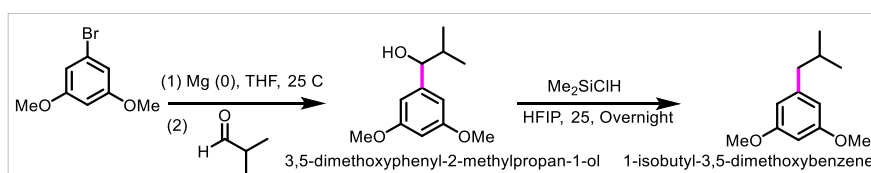
2.3 General procedure for the synthesis of 3,5-dimethoxy-1,1'-biphenyl and 1-isobutyl-3,5-dimethoxybenzene

Synthesis of 3,5-dimethoxy-1,1'-biphenyl:



In a Schlenk tube, 1-bromo-3,5-dimethoxybenzene (1.0 mmol, 1.0 equiv.), phenylboronic acid (3.0 mmol, 1.5 equiv.), Pd(PPh₃)₄ (10 mol %) and Cs₂CO₃ (3.0 mmol, 1.5 equiv.) were added. A vacuum was created using high vacuum pressure and purging with nitrogen using an N₂ balloon. Subsequently, a mixture of toluene and ethanol (4 mL toluene + 1 mL ethanol = 5 mL) was added, and the reaction mixture was stirred at 90 °C in an oil bath for 4 hours. The reaction was then quenched with saturated NaHCO₃ solution and extracted with ethyl acetate. The organic layer was collected, evaporated, and dried over MgSO₄. The crude mixture was purified by column chromatography (SiO₂, Hexane/EtOAc = 95/5) to yield the title compound as a colourless liquid with 80% yield.^{2b}

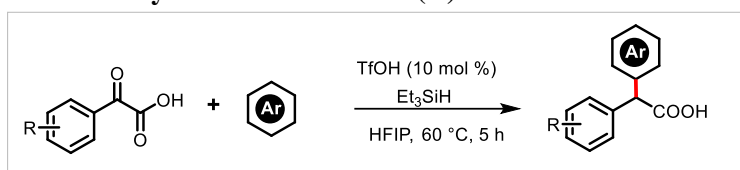
Synthesis of 1-isobutyl-3,5-dimethoxybenzene:



To synthesize 1-isobutyl-3,5-dimethoxybenzene, we used the Grignard reaction. First, we freshly prepared the Grignard reagent by reacting 1-bromo-3,5-dimethoxybenzene (1.0 mmol) with magnesium metal and iodine as an activator in anhydrous THF (3.0 mL). The freshly prepared reagent was then added dropwise to a solution of isobutyraldehyde in anhydrous THF (2.0 mL) at 0 °C. The reaction mixture was stirred at room temperature overnight. Upon completion, the reaction was quenched with NaHCO₃ and extracted with ethyl acetate (3×5 mL). The combined organic layers were washed with brine (20 mL), dried over anhydrous MgSO₄, filtered, and concentrated to yield the crude alcohol. The resulting residue was purified by column chromatography (SiO₂, Hexane/EtOAc = 80:20) to obtain 3,5-dimethoxyphenyl-2-methylpropan-1-ol. To convert this to 1-isobutyl-3,5-dimethoxybenzene, 3,5-dimethoxyphenyl-2-methylpropan-1-ol (1.0 mmol) was dissolved in HFIP (1.0 mL) solvent, and Me₂SiClH (1.5 mmol) was added. After the overnight reaction, the mixture was concentrated, and the resulting residue was purified by column chromatography (SiO₂, Hexane/EtOAc = 95:5) to yield the final product in 65% yield.^{2c}

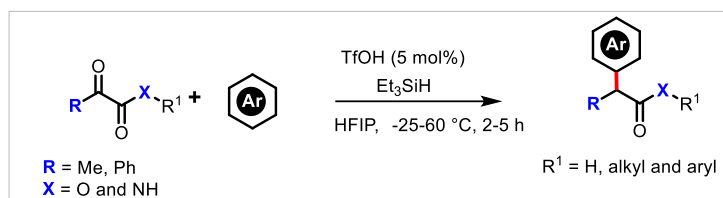
3. General procedure

3.1 General procedure of α -arylation of α -ketoacid (A)



A 10 mL reaction vial was charged with α -ketoacid (0.5 mmol, 1.0 equiv), arene nucleophile (0.75 mmol, 1.5 equiv), triethylsilane (Et_3SiH , 0.75 mmol, 1.5 equiv), and triflic acid (TfOH , 10.0 mol%) in HFIP (0.5 mL) solvent. The reaction mixture was agitated at 60 °C for 5 h. After the reaction was complete (as determined by TLC analysis), the mixture was concentrated under reduced pressure, and the crude product was purified using column chromatography (SiO_2 , $\text{DCM}/\text{MeOH} = 97:3$) to produce the product in good to excellent yield.

3.2 General procedure of α -arylation of α -ketoacid, α -ketoamide and α -ketoester (B)



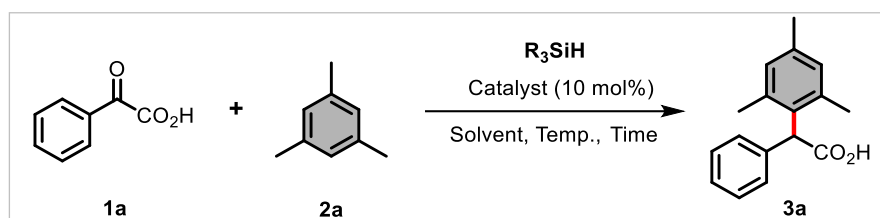
A 10 mL reaction vial is charged with α -ketoacid, α -ketoamide and α -ketoester (0.3 mmol, 1.5 equiv), arenes nucleophile (0.2 mmol, 1.0 equiv), triethyl silane or Me_2SiClH (0.3 mmol, 1.5 equiv), and triflic acid (TfOH , 5.0 mol%) in HFIP (0.5 mL) solvent. The reaction mixture was stirred at -25 to 60 °C for 2-5 h. After completion of the reaction (monitored by TLC analysis), the reaction mixture was concentrated under reduced pressure, and the crude mixture was purified using column chromatography (SiO_2 , $\text{DCM}/\text{MeOH} = 97:03$) in good to excellent product yield.

Note for handling of Triflic acid: When using triflic acid (trifluoromethanesulfonic acid, $\text{CF}_3\text{SO}_3\text{H}$) in a chemical reaction, it is critical to implement rigorous safety measures due to its extreme acidity and reactivity. Personal protective equipment (PPE) is essential: wear chemical-resistant gloves (such as neoprene or nitrile), safety goggles or a full face shield, and acid-resistant clothing, including a lab coat, long pants, closed-toe shoes, and preferably an apron. Conduct all procedures within a fume hood to avoid inhalation of hazardous fumes. Store triflic acid in a cool, dry place away from incompatible substances like water, bases, and organic materials, using non-reactive containers such as Teflon or glass. For spill management, neutralizing agents like sodium bicarbonate or calcium carbonate should be readily available, and proper spill cleanup protocols should be followed while wearing full PPE. When setting up reactions, add triflic acid to other reagents slowly to control exothermic reactions and prevent splashes, ensuring all glassware and connections are secure. Neutralize any waste before disposal in accordance with institutional guidelines and local regulations for hazardous chemical waste. In case of exposure, promptly administer first aid: flush skin contact areas with water for at least 15 minutes and seek medical attention; move to fresh air if inhaled; rinse eyes thoroughly with water for at least 15 minutes if splashed, then obtain medical assistance. Adhering to these safety precautions significantly reduces the risks of handling triflic acid, fostering a safer laboratory environment.

4. Reaction optimization

Our primary goal was to identify a high-yielding synthetic technique for producing α -arylated carboxylic acid (**3a**, Table S1). Initially, reductive Friedel-Crafts alkylation of α -ketoacid **1a** with mesitylene **2a** required a catalyst (entry 1). A realistic synthesis of α -arylated acid (**3a**, 86%, entry 2) was seen utilizing triflic acid (TfOH, 10.0 mol%) as a catalyst and 1.5 equiv. of dimethylchlorosilane (Me_2SiClH) as a reductant in HFIP solvent at 60 °C for 12 h. The achievement was attributed to the in-situ synthesis of the silylium ion ($\text{R}^1\text{R}^2\text{R}^3\text{Si}^+\cdot\text{OTf}$) by activating the Si–H bond of $\text{R}^1\text{R}^2\text{R}^3\text{SiH}$ using triflic acid (TfOH). Replacing HFIP with alternative solvents such as DCE, PhCF_3 , and TFE reduced product yield (entries 3-5). Similarly, additional acid catalysts, such as *p*TSA, TFA, and InCl_3 , resulted in lower yields (entries 6-8).

Table S1: Optimization of the reaction conditions for α -arylation of α -ketoacid.^a



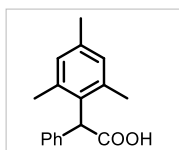
S. N.	Catalyst (10 mol%)	Solvent	Silane	Yield (%)
1	-	HFIP	Me_2SiHCl	<5
2	TfOH	HFIP	Me_2SiHCl	86
3	TfOH	DCE	Me_2SiHCl	10
4	TfOH	PhCF_3	Me_2SiHCl	12
5	TfOH	TFE	Me_2SiHCl	<5
6	<i>p</i> TSA	HFIP	Me_2SiHCl	15
7	TFA	HFIP	Me_2SiHCl	<5
8	InCl_3	HFIP	Me_2SiHCl	<5
9	$[\text{Ph}_3\text{C}][\text{SiEt}_3]$	HFIP	Me_2SiHCl	60
10	TMS·OTf	HFIP	Me_2SiHCl	75
11	TfOH	HFIP	Et_3SiH	88
12	TfOH	HFIP	Ph_3SiH	20
13 ^b	TfOH	HFIP	Et_3SiH	55
14^c	TfOH	HFIP	Et_3SiH	86

^a Reaction conditions: **1a** (0.5 mmol), **2a** (0.75 mmol), Silane (0.75 mmol), HFIP (0.5 mL), 60 °C for 12 h. ^b25 °C. ^c5.0 h.

Alternative Lewis acid catalysts, such as $[\text{Ph}_3\text{C}][\text{SiEt}_3]$ and $\text{TMS}\cdot\text{OTf}$, produced the required product in good yields (entries 9–10). As a result, HFIP was chosen as the standard reaction solvent and TfOH as the standard catalyst because of its greater catalytic activity. Further screening of other silanes revealed that Et_3SiH increased yield to 88% (entry 11), but Ph_3SiH only produced 20% of **3a** (entry 12). As a result, Et_3SiH was chosen as the optimal silane for the process. Lowering the reaction temperature from 60 °C to 25 °C resulted in a 55% reduction in yield (entry 13). Remarkably, shortening the reaction time to 5 h resulted in the required output of 86% yield (entry 14).

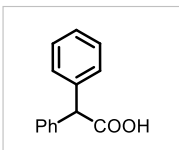
5. Characterization data of products

2-Mesityl-2-phenylacetic acid (**3a**)



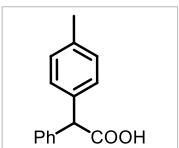
General procedure (A) was followed using 2-oxo-2-phenylacetic acid (75 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO_2 , $R_f = 0.4$; DCM/MeOH = 98/02) to afford the title compound as a white solid (109 mg, 88%); m.p. 96-98 °C; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.32 (t, $J = 7.4$ Hz, 2H), 7.28 (d, $J = 7.5$ Hz, 1H), 7.19 (d, $J = 7.5$ Hz, 2H), 6.96 (s, 2H), 5.49 (s, 1H), 2.34 (s, 3H), 2.25 (s, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 179.3, 137.6, 137.2, 136.2, 131.8, 130.1, 128.8, 128.3, 127.0, 50.8, 21.0; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ calculated for $\text{C}_{17}\text{H}_{18}\text{O}_2\text{Na}$ 277.1204; found: 277.1213.

2,2-Diphenylacetic acid (**3b**).³



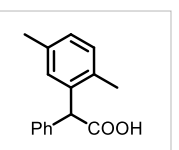
General procedure (A) was followed using 2-oxo-2-phenylacetic acid (75 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO_2 , $R_f = 0.4$; DCM/MeOH = 98/02) to afford the title compound as a white solid (85 mg, 80%); m.p. 148-150 °C; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 9.34 (s, 1H), 7.34 – 7.29 (m, 7H), 7.29 – 7.22 (m, 3H), 5.04 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 178.5, 138.1, 128.81, 128.77, 127.6, 57.2.

2-Phenyl-2-(*p*-tolyl) acetic acid (**3c**).³



General procedure (A) was followed using 2-oxo-2-phenylacetic acid (75 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO_2 , $R_f = 0.4$; DCM/MeOH = 98/02) to afford the title compound as a white solid (96 mg, 85%); m.p. 99-101 °C; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.33 (d, $J = 4.4$ Hz, 4H), 7.30 – 7.26 (m, 1H), 7.22 (d, $J = 8.1$ Hz, 2H), 7.14 (d, $J = 8.1$ Hz, 2H), 5.02 (s, 1H), 2.33 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 178.5, 138.3, 137.4, 135.1, 129.5, 129.1, 128.8, 128.7, 127.5, 56.7, 21.2.

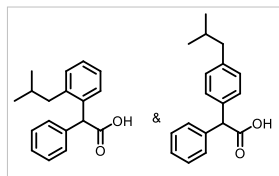
2-(2,5-Dimethylphenyl)-2-phenylacetic acid (**3d**).³



General procedure (A) was followed using 2-oxo-2-phenylacetic acid (75 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO_2 , $R_f = 0.4$; DCM/MeOH = 98/02) to afford the title compound as a yellow viscous (100 mg, 82%); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 10.66 (s, 1H), 7.37 – 7.32 (m, 2H), 7.31 – 7.27 (m, 3H), 7.14 (s, 1H), 7.10 (d, $J = 7.6$ Hz, 1H), 7.04 (d, $J = 5.8$ Hz, 1H), 5.24 (s, 1H), 2.32

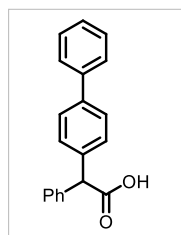
(s, 3H), 2.28 (s, 3H); ^{13}C $\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 178.6, 137.7, 136.3, 135.8, 133.4, 130.7, 129.1, 128.9, 128.6, 128.3, 127.4, 53.8, 21.3, 19.5.

2-(2-Isobutylphenyl)-2-phenylacetic acid & 2-(4-isobutylphenyl)-2-phenylacetic acid (3e).³



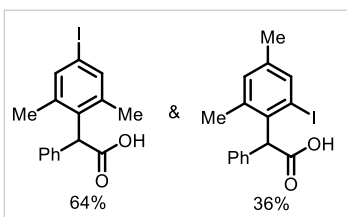
General procedure (A) was followed using 2-oxo-2-phenylacetic acid (75 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO_2 , $R_f = 0.4$; $\text{DCM}/\text{MeOH} = 98/02$) to afford the title compound as a yellow oil (114 mg, 85%, p/o : = 1:0:0.63); ^1H NMR (500 MHz, CDCl_3) δ 7.41 – 7.33 (m, 7H), 7.32 – 7.23 (m, 8H), 7.14 (d, $J = 8.2$ Hz, 2H), 5.38 (s, 1H), 5.06 (s, 1H), 2.60 – 2.51 (m, 1H), 2.48 (d, $J = 7.2$ Hz, 2H), 1.88 (dp, $J = 13.6, 6.8$ Hz, 2H), 0.99 (d, $J = 6.6$ Hz, 2H), 0.93 (d, $J = 6.7$ Hz, 6H); ^{13}C NMR (126 MHz, CDCl_3) δ 179.3, 179.0, 141.1, 140.1, 138.3, 138.1, 135.9, 135.3, 131.0, 129.5, 129.0, 128.9, 128.8, 128.7, 128.7, 128.5, 127.5, 127.4, 126.4, 56.8, 52.8, 45.2, 42.4, 30.3, 29.9, 22.8, 22.6, 22.5, 22.5; HRMS (ESI) m/z : $[\text{M}-\text{H}]^-$ calculated for $\text{C}_{17}\text{H}_{19}$ 223.1487; found: 223.1479.

2-([1,1'-Biphenyl]-4-yl)-2-phenylacetic acid (3f).³



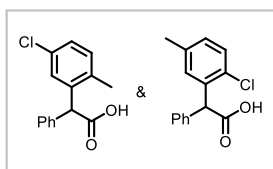
General procedure (A) was followed using 2-oxo-2-phenylacetic acid (75 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO_2 , $R_f = 0.4$; $\text{DCM}/\text{MeOH} = 99/01$) to afford the title compound as a white solid (121 mg, 84%); m.p. 130-132 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.58 (dd, $J = 8.1, 2.9$ Hz, 3H), 7.49 – 7.25 (m, 11H), 5.12 (s, 1H); ^{13}C $\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 178.6, 140.7, 140.6, 138.0, 137.1, 129.2, 128.90, 128.88, 128.8, 127.7, 127.54, 127.50, 127.2, 56.8.

2-(4-Iodo-2,6-dimethylphenyl)-2-phenylacetic acid & 2-(2-iodo-4,6-dimethylphenyl)-2-phenylacetic acid (3g)



General procedure (A) was followed using 2-oxo-2-phenylacetic acid (75 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO_2 , $R_f = 0.4$; $\text{DCM}/\text{MeOH} = 98/02$) to afford the title compound as a yellow viscous (130 mg, 71%, p/o : = 1:0:0.58); m.p. 140-142 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.70 (s, 1H), 7.50 (s, 1H), 7.36 – 7.26 (m, 6H), 7.24 (d, $J = 7.2$ Hz, 2H), 7.16 (d, $J = 7.2$ Hz, 1H), 7.04 (s, 1H), 5.86 (s, 1H), 5.45 (s, 1H), 2.31 (s, 3H), 2.23 (s, 3H), 2.21 (s, 3H); ^{13}C $\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 178.4, 178.0, 140.1, 139.5, 138.81, 138.78, 137.9, 136.1, 135.3, 134.8, 133.0, 128.9, 128.7, 128.5, 128.3, 127.3, 127.2, 104.8, 93.6, 59.9, 50.8, 21.9, 20.7, 20.4; HRMS (ESI) m/z : $[\text{M}-\text{H}]^-$ calculated for $\text{C}_{15}\text{H}_{14}\text{I}$ 321.0140; found: 321.0146.

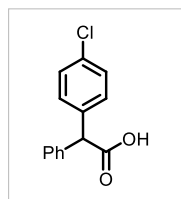
2-(5-Chloro-2-methylphenyl)-2-phenylacetic acid & 2-(2-chloro-5-methylphenyl)-2-phenylacetic acid (3h).³



General procedure (A) was followed using 2-oxo-2-phenylacetic acid (75 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.4; DCM/MeOH = 98/02) to afford the title compound as a white solid (102 mg, 78%, *ortho* of Me/*ortho* of Cl = 1:0:0.65);

m.p. 88-90 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.36 – 7.21 (m, 10H), 7.14 (d, *J* = 8.1 Hz, 1H), 7.08 (d, *J* = 8.1 Hz, 1H), 7.04 – 6.97 (m, 2H), 5.47 (s, 1H), 5.16 (s, 1H), 2.24 (s, 2H), 2.24 (s, 3H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 178.2, 178.1, 138.1, 137.0, 136.6, 135.5, 135.1, 132.0, 131.3, 130.7, 129.8, 129.5, 129.1, 129.0, 128.9, 128.4, 127.83, 127.76, 53.8, 53.6, 21.2, 19.5; HRMS-ESI (*m/z*) [M–H][–] calculated for C₁₄H₁₂Cl 215.0628, found: 215.0618.

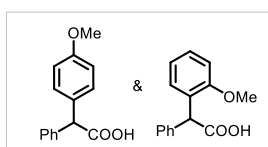
2-(4-Chlorophenyl)-2-phenylacetic acid (3i).³



General procedure (A) was followed using 2-oxo-2-phenylacetic acid (75 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.4; DCM/MeOH = 98/2) to afford the title compound as a yellow viscous (86 mg, 70%); ¹H NMR (500 MHz, CDCl₃) δ 8.79 (s, 1H), 7.36 – 7.24 (m, 9H), 5.00

(s, 1H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 178.0, 137.7, 136.6, 133.6, 130.2, 129.8, 128.9, 128.7, 127.8, 56.5.

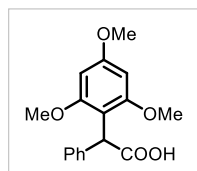
2-(4-Methoxyphenyl)-2-phenylacetic acid & 2-(2-methoxyphenyl)-2-phenylacetic acid (3j).³



General procedure (A) was followed using 2-oxo-2-phenylacetic acid (75 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.3; DCM/MeOH = 98/2) to afford the title compound as a colourless viscous (85 mg, 70%, *p/o* = 1:0:0.53); ¹H NMR

(500 MHz, CDCl₃) δ 7.33 (d, *J* = 9.8 Hz, 5H), 7.28 – 7.21 (m, 4H), 6.87 (dd, *J* = 14.8, 8.4 Hz, 3H), 5.31 (s, 1H), 4.99 (s, 1H), 3.81 (s, 2H), 3.78 (s, 3H); ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 178.8, 159.1, 157.0, 138.4, 137.1, 130.2, 129.9, 129.4, 129.3, 128.84, 128.78, 128.7, 127.6, 127.5, 127.3, 120.7, 114.2, 110.7, 56.3, 55.6, 55.4, 51.2.

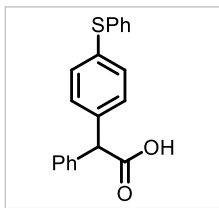
2-Phenyl-2-(2,4,6-trimethoxyphenyl)acetic acid (3k)



General procedure (A) was followed using 2-oxo-2-phenylacetic acid (75 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.3; DCM/MeOH = 98/2) to afford the title compound as a white solid (125 mg, 82%); m.p. 184-186 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.28 (d, *J* = 7.6

Hz, 2H), 7.24 – 7.18 (m, 2H), 7.15 (t, *J* = 7.2 Hz, 1H), 6.11 (s, 2H), 5.35 (s, 1H), 3.76 (s, 3H), 3.74 (s, 6H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 179.1, 160.8, 158.4, 138.5, 129.4, 128.1, 126.8, 109.3, 91.3, 55.9, 55.5, 45.9; HRMS (ESI) *m/z*: [M+Na]⁺ calculated for C₁₇H₁₈O₅Na 325.1052; found: 325.1055.

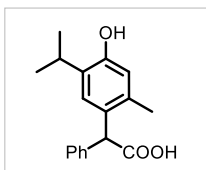
2-Phenyl-2-(4-(phenylthio)phenyl)acetic acid (3l)



General procedure (A) was followed using 2-oxo-2-phenylacetic acid (75 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.4; DCM/MeOH = 99/01) to afford the title compound as a white solid (96 mg, 60%); m.p. 120-122 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.40 – 7.16 (m, 14H), 4.99 (s, 1H); ¹³C {¹H} NMR (126 MHz, CDCl₃)

δ 177.2, 137.9, 136.9, 135.6, 135.2, 131.7, 130.7, 129.6, 129.4, 128.9, 128.8, 127.7, 127.5, 56.6; HRMS (ESI) m/z: [M-H]⁻ calculated for C₁₉H₁₅S 275.0894; found: 275.0895.

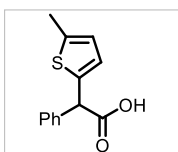
2-(4-hydroxy-5-isopropyl-2-methyl-phenyl)-2-phenylacetic acid (3m)



General procedure (A) was followed using 2-oxo-2-phenylacetic acid (75 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.4; DCM/MeOH = 98/02) to afford the title compound as a light yellow viscous (87.5 mg, 62%); ¹H NMR (500 MHz, CDCl₃) δ 7.33 (t, *J* = 7.3 Hz, 2H), 7.30 – 7.22 (m, 3H), 7.12 (s, 1H), 6.59 (s, 1H), 5.17 (s, 1H), 3.13 (p, *J* = 6.7 Hz, 1H), 2.21 (s, 3H), 1.28 (s, 2H), 1.20 (t, *J* = 6.7 Hz, 4H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 178.2, 152.1,

138.0, 135.2, 132.2, 129.0, 128.7, 127.4, 126.7, 117.7, 53.2, 27.2, 22.7, 22.6, 19.4; HRMS (ESI) m/z: [M-H]⁻ calculated for C₁₈H₁₉O₃ 283.1334; found: 283.1340.

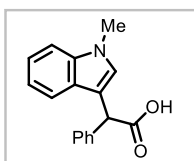
2-(5-Methylthiophen-2-yl)-2-phenylacetic acid (3n)



General procedure (A) was followed using 2-oxo-2-phenylacetic acid (75 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.6; DCM/MeOH = 98/02) to afford the title compound as a colourless viscous (81 mg, 70%); ¹H NMR (500 MHz, CDCl₃) δ 9.68 (s, 1H), 7.45 – 7.31 (m,

5H), 6.79 (d, *J* = 3.7 Hz, 1H), 6.61 (d, *J* = 4.3 Hz, 1H), 5.16 (s, 1H), 2.44 (s, 3H); ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 177.6, 140.1, 138.1, 137.9, 128.9, 128.4, 127.9, 126.6, 124.8, 52.6, 15.4; HRMS (ESI) m/z: [M-H]⁻ calculated for C₁₂H₁₁S 187.0581; found: 187.0583.

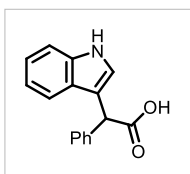
2-(1-Methyl-1*H*-indol-3-yl)-2-phenylacetic acid (3o).⁴



General procedure (A) was followed using 2-oxo-2-phenylacetic acid (75 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.4; DCM/MeOH = 98/02) to afford the title compound as a brown viscous (120 mg, 90%); ¹H NMR (500 MHz, DMSO-*d*₆) δ 7.48 – 7.43 (m, 3H), 7.39

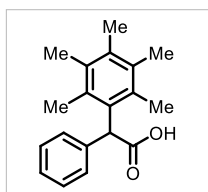
(d, *J* = 8.2 Hz, 1H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.27 (s, 1H), 7.26 – 7.21 (m, 1H), 7.15 (t, *J* = 7.0 Hz, 1H), 7.00 (t, *J* = 6.9 Hz, 1H), 5.23 (s, 1H), 3.74 (s, 3H); ¹³C {¹H} NMR (126 MHz, DMSO-*d*₆) δ 173.9, 139.8, 136.7, 128.4, 128.3, 127.9, 126.83, 126.78, 121.4, 118.9, 118.8, 112.1, 109.8, 48.4, 32.4; HRMS (ESI) m/z: [M-H]⁻ calculated for C₁₆H₁₄N 220.1126; found: 220.1120.

2-(1*H*-Indol-3-yl)-2-phenylacetic acid (3p).⁴



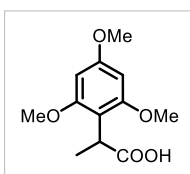
General procedure (A) was followed using 2-oxo-2-phenylacetic acid (75 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.4; DCM/MeOH = 98/2) to afford the title compound as a light pick viscous (100 mg, 80%); ¹H NMR (500 MHz, DMSO-*d*₆) δ 11.01 (s, 1H), 7.41 (d, *J* = 7.5 Hz, 3H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.27 – 7.19 (m, 2H), 7.07 (t, *J* = 7.6 Hz, 1H), 6.94 (t, *J* = 7.4 Hz, 1H), 5.19 (s, 1H); ¹³C {¹H} NMR (101 MHz, DMSO-*d*₆) δ 174.2, 140.0, 136.5, 128.6, 128.4, 127.0, 126.6, 123.8, 121.4, 118.9, 118.8, 113.0, 111.8, 48.7.

2-(2,3,4,5,6-pentamethyl-phenyl)-2-phenylacetic acid (3q)



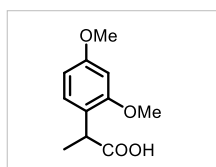
General procedure (A) was followed using 2-oxo-2-phenylacetic acid (75 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.4; DCM/MeOH = 98/04) to afford the title compound as a white solid (108 mg, 76%); ¹H NMR (400 MHz, CDCl₃) δ 7.29 – 7.23 (m, 3H), 7.17 (d, *J* = 7.3 Hz, 2H), 5.51 (s, 1H), 2.27 (s, 3H), 2.23 (s, 6H), 2.14 (s, 6H); ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 179.1, 136.4, 134.8, 133.4, 133.1, 132.4, 129.3, 128.2, 127.0, 52.0, 18.2, 17.2, 17.1; HRMS (ESI) *m/z*: [M-H]⁻ calculated for C₁₈H₂₁ 237.1643; found: 237.1648.

2-(2,4,6-Trimethoxyphenyl)propanoic acid (3r)



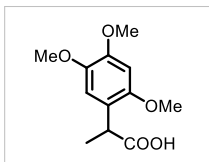
General procedure (B) was followed using 2-oxo propanoic acid (27 mg, 0.3 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.4; DCM/MeOH = 98/02) to afford the title compound as a white solid (41mg, 85%); m.p. 60-62 °C; ¹H NMR (500 MHz, CDCl₃) δ 10.72 (s, 1H), 6.13 (s, 2H), 4.18 (q, *J* = 7.0 Hz, 1H), 3.80 (s, 3H), 3.78 (s, 6H), 1.34 (d, *J* = 7.0 Hz, 3H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 181.6, 160.3, 158.3, 111.1, 91.1, 55.8, 55.4, 34.3, 15.6; HRMS (ESI) *m/z*: [M-H]⁻ calculated for C₁₂H₁₅O₅ 239.0919; found: 239.0923.

2-(2,4-Dimethoxyphenyl)propanoic acid (3s)



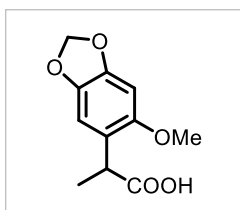
General procedure (B) was followed using 2-oxo propanoic acid (27 mg, 0.3 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.4; DCM/MeOH = 98/02) to afford the title compound as a colorless viscous (25 mg, 60%); ¹H NMR (500 MHz, CDCl₃) δ 7.15 (d, *J* = 8.1 Hz, 1H), 6.50 – 6.43 (m, 2H), 4.00 (q, *J* = 7.2 Hz, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 1.45 (d, *J* = 7.2 Hz, 3H); ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 180.4, 160.2, 157.8, 128.5, 121.4, 104.6, 98.9, 55.7, 55.5, 38.6, 17.1; HRMS (ESI) *m/z*: [M-H]⁻ calculated for C₁₁H₁₃O₄ 209.0814; found: 209.0814.

2-(2,4,5-Trimethoxyphenyl)propanoic acid (3t)



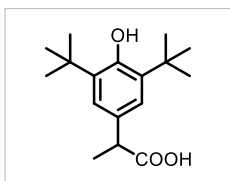
General procedure (**B**) was followed using 2-oxo propanoic acid (27 mg, 0.3 mmol) to give a crude mixture, which was purified by using column chromatography (SiO_2 , $R_f = 0.4$; $\text{DCM/MeOH} = 98/02$) to afford the title compound as a white solid (38.5 mg, 80%); m.p. 58-60 °C; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 6.8 (s, 1H), 6.5 (s, 1H), 4.0 (q, $J = 7.3$ Hz, 1H), 3.9 (s, 3H), 3.8 (s, 3H), 3.8 (s, 3H), 1.5 (d, $J = 7.3$ Hz, 3H); ^{13}C $\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 180.5, 151.2, 149.0, 143.4, 120.4, 112.3, 98.2, 56.84, 56.79, 56.3, 38.5, 17.3; HRMS (ESI) m/z : $[\text{M}-\text{H}]^-$ calculated for $\text{C}_{12}\text{H}_{15}\text{O}_5$ 239.0919; found: 239.0919.

2-(6-Methoxybenzo[*d*][1,3] dioxol-5-yl)propanoic acid (**3u**)



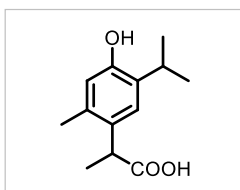
General procedure (**B**) was followed using 2-oxo propanoic acid (27 mg, 0.3 mmol) to give a crude mixture, which was purified by using column chromatography (SiO_2 , $R_f = 0.4$; $\text{DCM/MeOH} = 98/02$) to afford the title compound as a brown solid (37.5 mg, 83%); m.p. 130-132 °C; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 6.76 (s, 1H), 6.53 (s, 1H), 5.90 (d, $J = 4.9$ Hz, 2H), 4.02 (q, $J = 7.2$ Hz, 1H), 3.76 (s, 3H), 1.43 (d, $J = 7.3$ Hz, 3H); ^{13}C $\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 181.0, 152.0, 147.2, 141.4, 121.1, 107.9, 101.3, 95.2, 56.8, 38.7, 17.3; HRMS (ESI) m/z : $[\text{M}-\text{H}]^-$ calculated for $\text{C}_{11}\text{H}_{11}\text{O}_5$ 223.0606; found: 223.0617.

2-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)propanoic acid (**3v**)



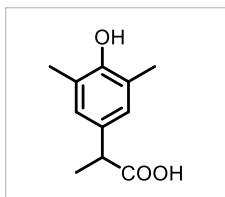
General procedure (**B**) was followed using 2-oxo propanoic acid (27 mg, 0.3 mmol) to give a crude mixture, which was purified by using column chromatography (SiO_2 , $R_f = 0.4$; $\text{DCM/MeOH} = 98/02$) to afford the title compound as a white solid (40.5 mg, 72%); m.p. 160-162 °C; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.13 (s, 2H), 5.16 (s, 1H), 3.65 (q, $J = 7.2$ Hz, 1H), 1.49 (d, $J = 7.2$ Hz, 3H), 1.44 (s, 18H); ^{13}C $\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 181.2, 153.2, 136.1, 130.5, 124.4, 45.3, 34.5, 30.4, 18.4; HRMS (ESI) m/z : $[\text{M}-\text{H}]^-$ calculated for $\text{C}_{17}\text{H}_{25}\text{O}_3$ 277.1804; found: 277.1800.

2-(4-Hydroxy-5-isopropyl-2-methylphenyl)propanoic acid (**3w**)



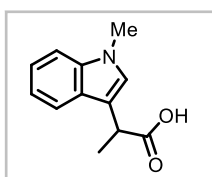
General procedure (**B**) was followed using 2-oxo propanoic acid (27 mg, 0.3 mmol) to give a crude mixture, which was purified by using column chromatography (SiO_2 , $R_f = 0.4$; $\text{DCM/MeOH} = 98/02$) to afford the title compound as a colourless viscous (31 mg, 70%); $^1\text{H NMR}$ (500 MHz, $\text{DMSO}-d_6$) δ 12.02 (s, 1H), 8.99 (s, 1H), 6.91 (s, 1H), 6.55 (s, 1H), 3.70 (q, $J = 7.0$ Hz, 1H), 3.12 (p, $J = 6.9$ Hz, 1H), 2.17 (s, 3H), 1.28 (d, $J = 7.2$ Hz, 3H), 1.12 (t, $J = 6.3$ Hz, 6H); ^{13}C $\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO}-d_6$) δ 176.6, 153.2, 133.7, 132.1, 130.4, 124.3, 117.1, 40.7, 26.8, 23.04, 23.00, 19.3, 18.5; HRMS (ESI) m/z : $[\text{M}-\text{H}]^-$ calculated for $\text{C}_{13}\text{H}_{17}\text{O}_3$ 221.1178; found: 221.1187.

2-(4-Hydroxy-3,5-dimethylphenyl)propanoic acid (3x)



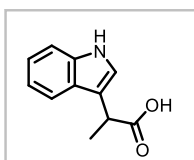
General procedure (B) was followed using 2-oxo propanoic acid (27 mg, 0.3 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.4; DCM/MeOH = 98/02) to afford the title compound as a colourless viscous (17 mg, 44%); ¹H NMR (400 MHz, CDCl₃) δ 6.93 (s, 2H), 3.61 (q, *J* = 7.2 Hz, 1H), 2.23 (s, 6H), 1.46 (d, *J* = 7.1 Hz, 3H); ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 181.0, 151.6, 131.5, 127.8, 123.4, 44.6, 18.3, 16.1; HRMS (ESI) *m/z*: [M-H]⁻ calculated for C₁₁H₁₃O₃ 193.0865, found: 193.0854.

2-(1-Methyl-1H-indol-3-yl) propanoic acid (3y)



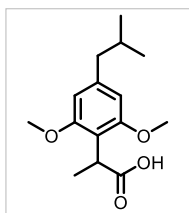
General procedure (B) was followed using 2-oxo propanoic acid (27 mg, 0.3 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.4; DCM/MeOH = 98/02) to afford the title compound as a brown solid (37 mg, 90%); m.p. 122-124 °C; ¹H NMR (400 MHz, CHCl₃) δ 7.66 (d, *J* = 6.6 Hz, 1H), 7.28 – 7.17 (m, 2H), 7.10 (t, *J* = 8.1 Hz, 1H), 6.97 (s, 1H), 4.00 (q, *J* = 7.2 Hz, 1H), 3.69 (s, 3H), 1.59 (d, *J* = 7.2 Hz, 3H); ¹³C {¹H} NMR (101 MHz, CHCl₃) δ 181.6, 137.1, 126.9, 126.6, 121.9, 119.4, 119.3, 113.3, 109.5, 37.0, 32.8, 17.7; HRMS (ESI) *m/z*: [M-H]⁻ calculated for C₁₂H₁₂NO₂ 202.0868; found: 202.0878.

2-(1H-Indol-3-yl)propanoic acid (3z)



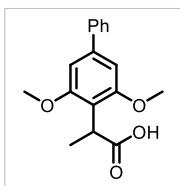
General procedure (B) was followed using 2-oxo propanoic acid (27 mg, 0.3 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.4; DCM/MeOH = 98/02) to afford the title compound as a brown solid (26.5 mg, 70%); m.p. 82-84 °C; ¹H NMR (500 MHz, CDCl₃) δ 8.03 (s, 1H), 7.71 (d, *J* = 8.6 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.21 (t, *J* = 6.9 Hz, 1H), 7.14 (t, *J* = 6.9 Hz, 1H), 7.09 (d, *J* = 3.3 Hz, 1H), 4.05 (q, *J* = 6.8 Hz, 1H), 1.63 (d, *J* = 7.1 Hz, 3H); ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 181.3, 136.3, 126.4, 122.4, 121.9, 119.8, 119.4, 114.9, 111.4, 37.0, 17.6. HRMS (ESI) *m/z*: [M-H]⁻ calculated for C₁₁H₁₀NO₂ 188.0712; found: 188.0721.

2-(4-Isobutyl-2,6-dimethoxy-phenyl) propanoic acid (3za)



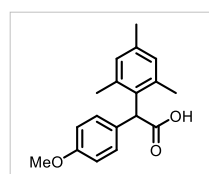
General procedure (B) was followed using 2-oxo propanoic acid (27 mg, 0.3 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.4; DCM/MeOH = 98/02) to afford the title compound as a colorless viscous (52 mg, 92%); ¹H NMR (400 MHz, CDCl₃) δ 6.34 (s, 2H), 4.22 (q, *J* = 7.0 Hz, 1H), 3.78 (s, 6H), 2.43 (d, *J* = 7.2 Hz, 2H), 1.87 (dp, *J* = 13.3, 6.8 Hz, 1H), 1.35 (d, *J* = 7.7 Hz, 3H), 0.92 (d, *J* = 7.3 Hz, 6H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 181.3, 157.3, 142.3, 115.7, 105.2, 55.8, 46.2, 34.5, 30.3, 22.7, 15.5; HRMS (ESI) *m/z*: [M+Na]⁺ calculated for C₁₅H₂₂O₄Na 289.1416; found: 289.1430.

2-(3,5-Dimethoxy-[1,1'-biphenyl]-4-yl)propanoic acid (3zb)



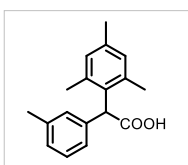
General procedure (B) was followed using 2-oxo propanoic acid (27 mg, 0.3 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.4; EtOAc/Hexane = 30/70) to afford the title compound as a yellow viscous (50 mg, 87%); ¹H NMR (500 MHz, CDCl₃) δ 7.59 (d, *J* = 7.0 Hz, 2H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.37 (t, *J* = 7.4 Hz, 1H), 6.77 (s, 2H), 4.33 (q, *J* = 7.0 Hz, 1H), 3.89 (s, 6H), 1.43 (d, *J* = 7.0 Hz, 3H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 181.6, 157.8, 141.9, 141.7, 128.8, 127.6, 127.3, 117.4, 103.6, 55.9, 34.6, 15.4; HRMS (ESI) *m/z*: [M-H]⁻ calculated for C₁₇H₁₇O₄ 285.1140; found: 285.1140.

2-Mesityl-2-(4-methoxyphenyl)acetic acid (4a)



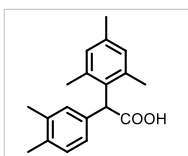
General procedure (A) was followed using 2-(4-methoxyphenyl)-2-oxoacetic acid (90 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.4; DCM/MeOH = 98/02) to afford the title compound as a white solid (137.5 mg, 96%); m.p. 130-132 °C; ¹H NMR (500 MHz, CDCl₃) δ 10.16 (s, 1H), 7.10 (d, *J* = 8.7 Hz, 2H), 6.94 (s, 2H), 6.85 (d, *J* = 7.0 Hz, 2H), 5.41 (s, 1H), 3.80 (s, 3H), 2.33 (s, 3H), 2.24 (s, 6H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 179.7, 158.5, 137.5, 137.1, 132.2, 130.0, 129.9, 128.1, 113.7, 55.3, 50.1, 21.0, 20.9; HRMS (ESI) *m/z*: [M-H]⁻ calculated for C₁₈H₁₉O₃ 283.1334; found: 283.1333.

2-Mesityl-2-(*m*-tolyl)acetic acid (4b)



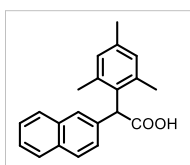
General procedure (A) was followed using 2-oxo-2-(*m*-tolyl)acetic acid (82.5 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.4; DCM/MeOH = 98/02) to afford the title compound as a light yellow solid (125 mg, 93%); m.p. 180-182 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.18 (t, *J* = 7.6 Hz, 1H), 7.07 (d, *J* = 8.1 Hz, 1H), 7.03 (s, 1H), 6.94 (s, 2H), 5.44 (s, 1H), 2.33 (s, 6H), 2.25 (s, 6H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 179.4, 137.9, 137.6, 137.1, 136.2, 132.0, 130.1, 129.6, 128.2, 127.8, 125.8, 50.9, 21.7, 21.1, 21.0; HRMS (ESI) *m/z*: [M-H]⁻ calculated for C₁₈H₁₉O₂ 267.1385; found: 267.1389.

2-(3,4-Dimethylphenyl)-2-mesitylacetic acid (4c)



General procedure (A) was followed using 2-(3,4-dimethylphenyl)-2-oxoacetic acid (90 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.4; DCM/MeOH = 98/02) to afford the title compound as a white solid (135 mg, 94%); m.p. 168-170 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.06 (d, *J* = 7.8 Hz, 1H), 6.99 (s, 1H), 6.94 (s, 2H), 6.86 (d, *J* = 7.8 Hz, 1H), 5.42 (s, 1H), 2.33 (s, 3H), 2.25 (s, 9H), 2.24 (s, 3H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 179.7, 137.6, 137.0, 136.4, 135.3, 133.5, 132.1, 130.2, 130.0, 129.6, 126.1, 50.6, 21.0, 20.0, 19.5; HRMS (ESI) *m/z*: [M-H]⁻ calculated for C₁₉H₂₁O₂ 281.1542; found: 281.1534.

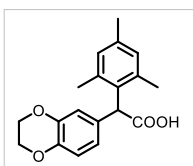
2-Mesityl-2-(naphthalen-2-yl)acetic acid (4d)



General procedure (A) was followed using 2-(naphthalen-2-yl)-2-oxoacetic acid (100 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.4; DCM/MeOH = 98/02) to afford the title compound as a white solid (150 mg, 98%); m.p. 194-196 °C; ¹H NMR (500 MHz, DMSO-*d*₆)

δ 12.70 (s, 1H), 7.98 (dd, *J* = 17.5, 8.1 Hz, 2H), 7.83 (d, *J* = 8.2 Hz, 1H), 7.61 – 7.48 (m, 2H), 7.37 (t, *J* = 7.8 Hz, 1H), 6.93 (s, 2H), 5.75 (s, 1H), 2.26 (s, 3H), 2.15 (s, 6H); ¹³C {¹H} NMR (126 MHz, DMSO-*d*₆) δ 174.5, 137.5, 136.3, 134.0, 133.9, 133.8, 132.7, 130.1, 129.1, 128.0, 126.7, 126.0, 125.8, 125.6, 124.0, 49.1, 21.0, 20.9; HRMS (ESI) *m/z*: [M-H]⁻ calculated for C₂₀H₁₉ 259.1487; found: 259.1490

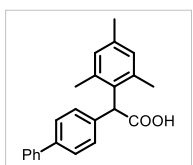
2-(2,3-Dihydrobenzo[*b*][1,4]-dioxin-6-yl)-2-mesitylacetic acid (4e)



General procedure (A) was followed using 2-(2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)-2-oxoacetic acid (105 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.4; DCM/MeOH = 98/02) to afford the title compound as a white solid (145 mg, 92%); m.p. 150-152 °C; ¹H NMR (400 MHz, CDCl₃)

δ 6.91 (s, 2H), 6.79 (d, *J* = 8.6 Hz, 1H), 6.67 – 6.63 (m, 2H), 5.33 (s, 1H), 4.22 (s, 4H), 2.30 (s, 3H), 2.23 (s, 6H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 179.3, 143.2, 142.5, 137.4, 137.1, 132.0, 130.0, 129.4, 122.0, 117.8, 117.0, 64.4, 50.1, 21.0, 20.9; HRMS (ESI) *m/z*: [M-H]⁻ calculated for C₁₉H₁₉O₄ 311.1283; found: 311.1282.

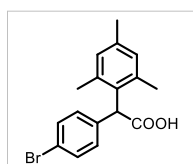
2-([1,1'-Biphenyl]-4-yl)-2-mesitylacetic acid (4f)



General procedure (A) was followed using 2-([1,1'-biphenyl]-4-yl)-2-oxoacetic acid (112.5 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.4; DCM/MeOH = 98/02) to afford the title compound as a white solid (137.5 mg, 83%); m.p. 188-190 °C; ¹H NMR (400 MHz, CDCl₃)

δ 7.60 (d, *J* = 7.9 Hz, 2H), 7.54 (d, *J* = 5.8 Hz, 2H), 7.47 – 7.42 (m, 2H), 7.38 – 7.33 (m, 1H), 7.27 (d, *J* = 8.7 Hz, 2H), 6.97 (s, 2H), 5.52 (s, 1H), 2.34 (s, 3H), 2.29 (s, 6H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 179.3, 140.9, 139.9, 137.6, 137.3, 135.3, 131.8, 130.1, 129.3, 128.8, 127.4, 127.2, 127.0, 50.5, 21.1, 21.0; HRMS (ESI) *m/z*: [M-H]⁻ calculated for C₂₂H₂₁ 285.1643; found: 285.1642.

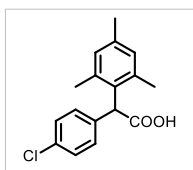
2-(4-Bromophenyl)-2-mesitylacetic acid (4g)



General procedure (A) was followed using 2-(4-bromophenyl)-2-oxoacetic acid (115 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.5; DCM/MeOH = 98/02) to afford the title compound as a white solid (150 mg, 90%); m.p. 194-196 °C; ¹H NMR (500 MHz, CDCl₃)

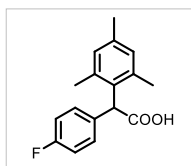
δ 7.40 (d, *J* = 8.5 Hz, 2H), 7.03 (d, *J* = 8.7 Hz, 2H), 6.92 (s, 2H), 5.37 (s, 1H), 2.30 (s, 3H), 2.18 (s, 6H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 178.3, 137.6, 137.5, 135.2, 131.4, 131.3, 130.6, 130.2, 121.1, 50.1, 21.0, 20.9; HRMS (ESI) *m/z*: [M-H]⁻ calculated for C₁₆H₁₆Br 287.0435; found: 287.0426.

2-(4-Chlorophenyl)-2-mesityl-acetic acid (4h)



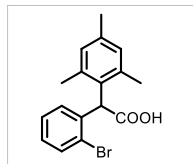
General procedure (A) was followed using 2-(4-chlorophenyl)-2-oxoacetic acid (92.5 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.5; DCM/MeOH = 98/02) to afford the title compound as a white solid (42 mg, 73%); m.p. 190-192 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.28 (d, *J* = 3.7 Hz, 2H), 7.11 (d, *J* = 8.7 Hz, 2H), 6.95 (s, 2H), 5.40 (s, 1H), 2.32 (s, 3H), 2.21 (s, 6H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 177.7, 137.6, 137.5, 134.8, 133.0, 131.4, 130.3, 130.2, 128.5, 49.9, 21.0, 20.9; HRMS (ESI) m/z: [M-H]⁻ calculated for C₁₆H₁₆Cl 273.0941; found: 273.949.

2-(4-Fluorophenyl)-2-mesitylacetic acid (4i)



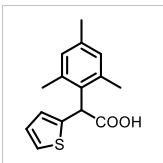
General procedure (A) was followed using 2-(4-fluorophenyl)-2-oxoacetic acid (100 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.5; DCM/MeOH = 98/02) to afford the title compound as a white solid (106 mg, 78%); m.p. 167-169 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.10 (dd, *J* = 8.9, 5.4 Hz, 2H), 6.94 (t, *J* = 8.8 Hz, 2H), 6.91 (s, 2H), 5.37 (s, 1H), 2.29 (s, 3H), 2.18 (s, 6H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 179.1, 161.9 (d, *J* = 245.8 Hz), 137.5, 137.4, 131.8 (d, *J* = 3.3 Hz), 131.7, 130.5 (d, *J* = 7.9 Hz), 130.2, 115.1 (d, *J* = 21.3 Hz), 50.0, 21.0, 20.9; ¹⁹F NMR (471 MHz, CDCl₃) δ -116.1; HRMS (ESI) m/z: [M-H]⁻ calculated for C₁₇H₁₆O₂F 271.1134; found: 271.1141.

2-(2-Bromophenyl)-2-mesityl-acetic acid (4j)



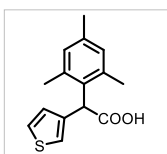
General procedure (A) was followed using 2-(2-bromophenyl)-2-oxoacetic acid (112.5 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.5; DCM/MeOH = 98/02) to afford the title compound as a white solid (87.5 mg, 52%); m.p. 197-199 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.62 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.21 – 7.07 (m, 2H), 6.92 (s, 2H), 6.85 (dd, *J* = 7.3, 2.1 Hz, 1H), 5.62 (s, 1H), 2.29 (s, 3H), 2.23 (s, 6H); ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 177.3, 137.5, 137.4, 135.8, 133.0, 131.8, 130.2, 129.9, 129.1, 127.6, 126.7, 52.4, 21.0; HRMS (ESI) m/z: [M-H]⁻ calculated for C₁₆H₁₆Br 287.0435; found: 287.0428.

2-Mesityl-2-(thiophen-2-yl)acetic acid (4k)



General procedure (A) was followed using 2-oxo-2-(thiophen-2-yl) acetic acid (77.5 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.5; DCM/MeOH = 99/01) to afford the title compound as a white solid (125 mg, 96%); m.p. 141-143 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.24 (d, *J* = 5.2 Hz, 1H), 6.94 (s, 2H), 6.92 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.77 (dt, *J* = 3.6, 1.4 Hz, 1H), 5.55 (s, 1H), 2.33 (s, 3H), 2.28 (s, 6H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 178.2, 139.5, 137.5, 137.1, 132.9, 130.0, 126.4, 126.3, 125.3, 46.6, 21.0, 20.5; HRMS (ESI) m/z: [M-H]⁻ calculated for C₁₅H₁₅O₂S 259.0793; found: 259.0791.

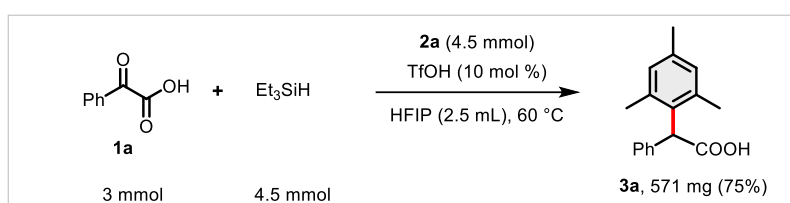
2-Mesityl-2-(thiophen-3-yl) acetic acid (4l)



General procedure (A) was followed using 2-oxo-2-(thiophen-3-yl)acetic acid (77.5 mg, 0.5 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.5; DCM/MeOH = 99/01) to afford the title compound as a white solid (115 mg, 88%); m.p. 170-172 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.25 – 7.23 (m, 1H), 7.01 (dt, *J* = 2.9, 1.4 Hz, 1H), 6.97 (dd, *J* = 5.0, 1.3 Hz, 1H), 6.92 (s, 2H), 5.39 (s, 1H), 2.31 (s, 3H), 2.23 (s, 6H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 178.9, 137.2, 137.1, 136.9, 132.6, 130.0, 128.6, 125.0, 122.8, 46.7, 21.0, 20.6; HRMS (ESI) *m/z*: [M–H][–] calculated for C₁₅H₁₅O₂S 259.0793; found: 259.0785.

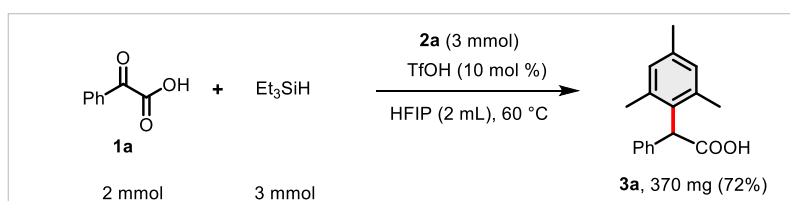
6. Scale-up

1st Reaction



A scale-up reaction was carried out after the general method (A) to illustrate the synthetic efficiency of our developed technique. A reaction was carried out utilizing 2-oxo-2-phenylacetic acid (**1a**, 3.0 mmol, 1.0 equiv.), mesitylene (**2a**, 4.5 mmol, 1.5 equiv.), and Et₃SiH (4.5 mmol, 1.5 equiv.) under optimal reaction conditions. After completing the reaction, the mixture was evaporated in a distillation setup at 60–70 °C to recover the solvent for reuse (Fig. S1). The residue was purified by column chromatography using a gradient of DCM–MeOH (97:03), yielding the product **3a** as a white solid (350 mg, 75% yield).

2nd Reaction



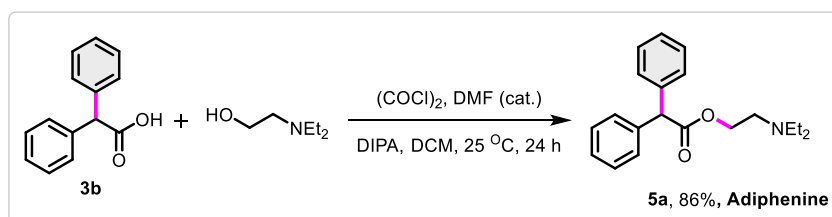
The 2nd reaction uses recovered HFIP (2.0 ml) solvent. To a solution of 2-oxo-2-phenylacetic acid (**1a**, 2.0 mmol, 1.0 equiv.), mesitylene (**2a**, 3.0 mmol, 1.5 equiv.), and Et₃SiH (3.0 mmol, 1.5 equiv.) under optimal reaction conditions. The residue was purified by column chromatography using a gradient of DCM–MeOH (97:03), yielding the product **3a** as a white solid (370 mg, 72% yield).



Fig. 1: Distillation setup after a scale-up reaction to recover the HFIP for reuse.

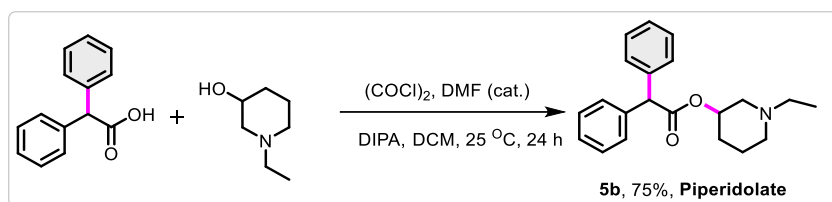
7. Synthesis of drug molecules

7.1 2-(Diethylamino)-ethyl-2,2-diphenylacetate (**5a**).⁵



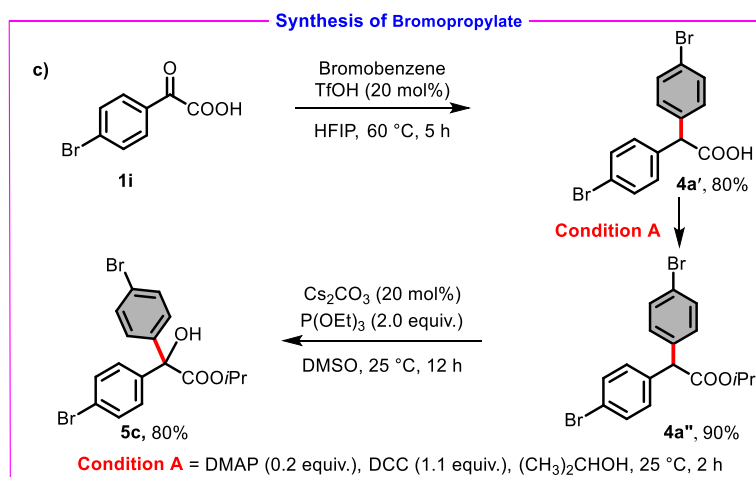
A round bottom flask was charged with 2,2-diphenylacetic acid (**3b**, 1.0 equiv, 0.2 mmol, 42.4 mg), and a catalytic amount of DMF (1 drop), (COCl)₂ (1.0 equiv, 0.2 mmol), in CH₂Cl₂ (1.0 mL), and at room temperature. The reaction mixture was stirred at 25 °C until the generation of gasses ceased. The reaction mixture was cooled to 0 °C and a solution of 2-(diethylamino) ethan-1-ol (0.4 mmol) and DIPEA (0.4 mmol) was then added dropwise. The reaction mixture was stirred at room temperature for 3 hours. Thereafter, the reaction was quenched by water, and the mixture was extracted 3 times with CH₂Cl₂. Then, the reaction is allowed to cool to room temperature and is concentrated under reduced pressure. The residue is purified by column chromatography with a gradient of DCM:MeOH (R_f = 0.3; 97:03) to afford desired product **5a** in 86% yield; ¹H NMR (500 MHz, CDCl₃) δ 7.34 – 7.28 (m, 8H), 7.26 – 7.22 (m, 2H), 5.03 (s, 1H), 4.22 (t, *J* = 6.2 Hz, 2H), 2.67 (t, *J* = 6.2 Hz, 2H), 2.50 (q, *J* = 7.2 Hz, 4H), 0.96 (t, *J* = 7.2 Hz, 6H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 172.6, 138.8, 128.8, 128.7, 127.3, 63.6, 57.2, 51.1, 47.6, 12.0.

7.2 1-Ethylpiperidin-3-yl-2,2-diphenylacetate (**5b**).⁵



In a stirred solution of 2,2-diphenylacetic acid (**3b**, 0.2 mmol) in CH_2Cl_2 (1.0 mL), a catalytic quantity of DMF (1 drop) and oxalyl chloride (0.2 mmol, 1.0 equiv) were added. The reaction mixture was agitated at 25°C until gas evolution stopped. The reaction mixture was then cooled to 0°C before adding a dropwise solution of 1-ethylpiperidin-3-ol (0.3 mmol, 1.5 equiv, 38.8 mg) and DIPEA (0.4 mmol, 2.0 equiv, 51.7 mg). The mixture was stirred at room temperature for five hours. The reaction was quenched with water, and the mixture was extracted three times with CH_2Cl_2 . The mixed organic layers were rinsed with brine and dried on Na_2SO_4 . The solvent was evaporated in vacuo, and the crude product was purified using column chromatography with a gradient of $\text{DCM}:\text{MeOH}$ ($R_f = 0.3$; 97:03), yielding the required product in 5 h with 75% yield; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.38 – 7.32 (m, 8H), 7.32 – 7.24 (m, 2H), 5.05 (s, 1H), 4.98 (hept, $J = 4.0$ Hz, 1H), 2.80 (d, $J = 11.7$ Hz, 1H), 2.60 (dd, $J = 10.8, 4.9$ Hz, 1H), 2.44 (q, $J = 6.1$ Hz, 2H), 2.26 – 2.13 (m, 2H), 1.91 (dd, $J = 12.5, 5.8$ Hz, 1H), 1.76 (dd, $J = 9.8, 3.8$ Hz, 1H), 1.65 – 1.56 (m, 1H), 1.41 (dd, $J = 9.8, 4.0$ Hz, 1H), 1.07 (t, $J = 7.2$ Hz, 3H); ^{13}C $\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 172.0, 139.00, 138.98, 128.68, 128.65, 128.7, 128.6, 127.3, 70.7, 57.2, 56.5, 53.0, 52.4, 29.6, 22.8, 12.0.

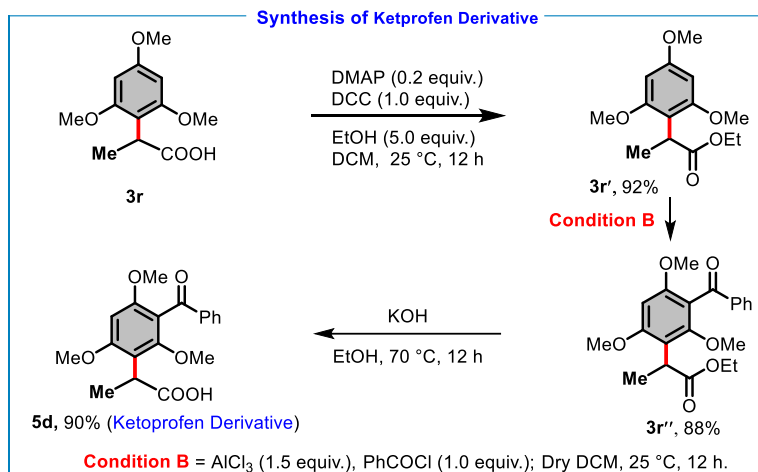
7.3 Isopropyl 2,2-bis(4-bromophenyl)-2-hydroxyacetate (**5c**).⁵



To synthesize bromopropylate (**5c**), we performed the reaction with 2-(4-bromophenyl)-2-oxoacetic acid (**1i**, 1.0 mmol) and bromobenzene (5.0 mmol) as a nucleophile under our optimized reaction condition (general procedure A). After completion of the reaction, we attained **4a'** in 80% yield. Next, we performed esterification of **4a'** with DCC coupling using isopropyl alcohol and after purification by column chromatography, we obtained **4a''**. Then, to introduce the hydroxy group at the α position of the ester (**4a''** 1.0 equiv.), we followed the reported procedure using Cs_2CO_3 (20 mol %) and $\text{P}(\text{OEt})_3$ (2.0 equiv.) in DMSO solvent under O_2 atmosphere.⁶ After 24 h the reaction mixture was extracted with ethyl acetate three times and washed with brine, dried over Na_2SO_4 . The organic layer was concentrated

and purified by column chromatography (SiO₂, R_f = R_f = 0.5; Hexane:EtOAc = 95:05) as a yellow solid in 80% yield; m.p. 86-88 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.45 (d, *J* = 8.5 Hz, 4H), 7.16 (d, *J* = 8.5 Hz, 4H), 5.07 (hept, *J* = 6.2 Hz, 1H), 4.87 (s, 1H), 1.22 (d, *J* = 6.3 Hz, 6H); ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 173.2, 140.8, 131.4, 129.2, 122.5, 80.1, 71.9, 21.6.

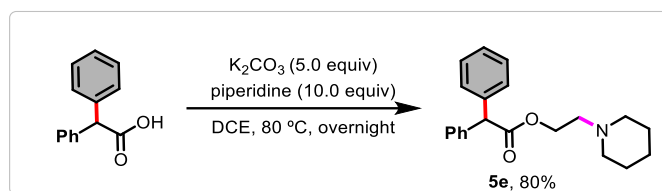
7.4 2-(3-Benzoyl-2,4,6-trimethoxyphenyl)propanoic acid (**5d**)



To synthesize **5d**, we esterified **3r** using a reported procedure, and after purification by column chromatography, we obtained **3r'**. Next, we performed benzylation on **3r'**. In this process, AlCl₃ (1.5 equiv.) was first placed in a round-bottom flask, followed by the addition of dry dichloromethane and benzoyl chloride (PhCOCl, 1.0 equiv.) under an inert atmosphere at 0 °C. After 1 h, the reaction mixture was slowly added to a solution of **3r'** (1.0 equiv.) in dry dichloromethane, also under an inert atmosphere at 0 °C. The reaction mixture was then allowed to warm to room temperature. Upon completion, the crude mixture was poured into an HCl solution. The reaction mixture was extracted with DCM, washed with NaHCO₃, and dried over Na₂SO₄. The organic solvent was removed using a rotavapor, and the crude mixture was purified by column chromatography (SiO₂, EtOAc/Hexane = 20/80) to afford the compound **3r''** as a white solid in 88% yield. Finally, we deprotected the ester using the reported method, obtaining the ketoprofen derivative **5d** in 90% yield as a colorless viscous liquid; ¹H NMR (500 MHz, CDCl₃) δ 7.84 (d, *J* = 7.8 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.41 (t, *J* = 7.7 Hz, 2H), 6.30 (s, 1H), 4.09 (q, *J* = 7.2 Hz, 1H), 3.83 (s, 3H), 3.68 (s, 3H), 3.58 (s, 3H), 1.40 (d, *J* = 7.0 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 195.1, 181.0, 159.5, 157.5, 156.7, 138.1, 133.3, 129.6, 128.5, 116.2, 115.1, 91.7, 62.7, 56.0, 55.8, 35.0, 16.0; HRMS (ESI) *m/z*: [M-H]⁻ calculated for C₁₉H₁₉O₆ 343.1182; found: 343.1187.

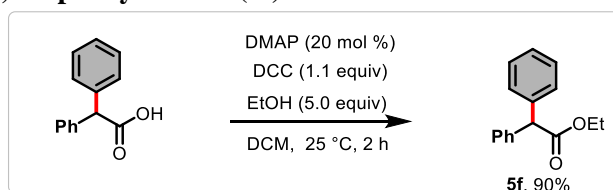
8. Synthetic utility

8.1 Synthesis of 2-(piperidin-1-yl)ethyl 2,2-diphenylacetate (**5e**)



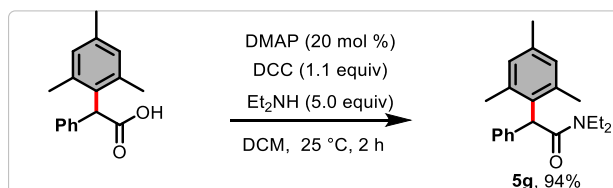
A round bottom flask was charged with 2,2-diphenylacetic acid (**3b**, 1.0 equiv, 0.2 mmol, 42.4 mg), K_2CO_3 (5.0 equiv, 1.0 mmol, 42.4 mg), piperidine (10.0 equiv, 2.0 mmol) and 1,2-DCE (1.0 mL) under air at room temperature. The reaction mixture was heated at 80 °C overnight. Then, the reaction was allowed to cool to room temperature and was concentrated under reduced pressure. The residue was purified by column chromatography with a gradient of DCM:MeOH ($R_f = 0.3$; 97:03) to afford desired colourless viscous (52 mg, 80%); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.33 – 7.29 (m, 8H), 7.27 – 7.24 (m, 2H), 5.04 (s, 1H), 4.28 (t, $J = 5.9$ Hz, 2H), 2.57 (t, $J = 6.0$ Hz, 2H), 2.35 (t, $J = 5.2$ Hz, 4H), 1.52 (p, $J = 5.2$ Hz, 4H), 1.42 – 1.36 (m, 2H); ^{13}C $\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 172.4, 138.8, 128.8, 128.6, 127.3, 62.8, 57.2, 54.7, 25.9, 24.2; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ calculated for $\text{C}_{21}\text{H}_{25}\text{NO}_2\text{Na}$ 346.1783; found: 346.1788.

8.2 Synthesis of ethyl-2,2-diphenylacetate (**5f**)



A reaction vial was charged with 2,2-diphenylacetic acid (**3b**, 0.2 mmol), DCC (0.22 mmol), DMAP (20 mol %), and EtOH (1.0 mmol) in DCM (1.0 mL) at room temperature. Thereafter, in the reaction mixture the diethyl ether was added to quench the reaction. Then the reaction mixture was filtrated through a pad of celite, and the filtrate was washed with a 1N solution of HCl, saturated NaHCO_3 solution, and brine. The collected organic layer was dried and concentrated. The compound was purified by using column chromatography (SiO_2 , $R_f = 0.7$; Hexane/EtOAc = 95/05) to afford the title compound as a white solid (43 mg, 90%); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.33 – 7.30 (m, 8H), 7.27 – 7.22 (m, 2H), 5.01 (s, 1H), 4.20 (q, $J = 7.1$ Hz, 2H), 1.24 (t, $J = 7.1$ Hz, 3H); ^{13}C $\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 172.6, 138.9, 128.70, 128.68, 127.3, 61.3, 57.2, 14.2; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ calculated for $\text{C}_{16}\text{H}_{16}\text{O}_2\text{Na}$ 263.1048; found: 263.1050.

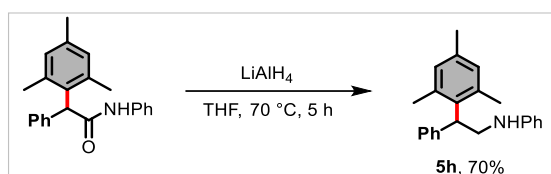
8.3 Synthesis of *N,N*-diethyl-2-mesityl-2-phenylacetamide (**5g**)



A reaction vial was charged with 2-mesityl-2-phenylacetic acid (**3a**, 0.2 mmol), DDC (0.22 mmol), DMAP (0.04 mmol), and ethylenediamine (1.0 mmol) in DCM (1.0 mL) at room

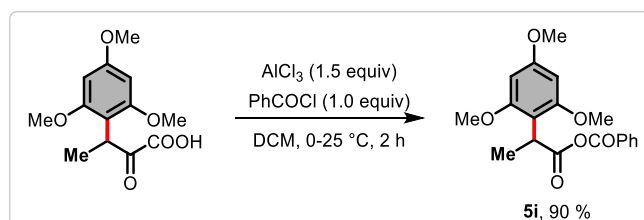
temperature. The diethyl ether was added to quench the reaction in the reaction mixture. Then, the reaction mixture was filtrated through a pad of celite, and the filtrate was washed with a 1*N* solution of HCl, saturated NaHCO₃ solution, and brine. The collected organic layer was dried and concentrated. The compound was purified by using column chromatography (SiO₂, R_f = 0.5; Hexane/EtOAc = 95/05) to afford the title compound as a white solid (58 mg, 94%); m.p. 54-56 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.34 – 7.25 (m, 2H), 7.21 (t, *J* = 7.2 Hz, 1H), 7.05 (d, *J* = 7.5 Hz, 2H), 6.90 (s, 2H), 5.31 (s, 1H), 3.54 (dq, *J* = 14.2, 7.2 Hz, 1H), 3.38 (dq, *J* = 14.0, 7.2 Hz, 1H), 3.17 (qq, *J* = 14.5, 7.1 Hz, 2H), 2.30 (s, 3H), 2.22 (s, 6H), 1.20 (t, *J* = 7.1 Hz, 3H), 0.98 (t, *J* = 7.1 Hz, 3H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 171.8, 138.9, 137.5, 136.6, 133.4, 130.3, 129.3, 128.2, 126.5, 51.4, 41.8, 40.6, 21.3, 20.9, 13.7, 13.0; HRMS (ESI) *m/z*: [M–H][–] calculated for C₂₁H₂₆ON 308.2014; found: 308.2020.

8.4 Synthesis of *N*-(2-mesityl-2-phenylethyl)aniline (5h).⁷



The solution of 2-mesityl-*N*,-2-diphenyl acetamide (66.0 mg, 0.2 mmol, 1.0 equiv.) in dry THF (2.0 mL) was added into LiAlH₄ (43 mg, 1.1 mmol, 5.0 equiv.) dropwise under N₂ atmosphere at 0 °C. After that, the reaction mixture was stirred for 12 h at 70 °C in an oil bath, and then add several drops of saturated brine solution until the evolution of H₂ stopped. Then, the solution was extracted with ethyl acetate. The combined organic layers were dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The reaction mixture was evaporated and purification is done by column chromatography (SiO₂, R_f = 0.4; Hexane/ EtOAc = 90/10) to afford the desired product as a colorless viscous (45 mg, 71% yield); ¹H NMR (500 MHz, CDCl₃) δ 7.32 (t, *J* = 7.6 Hz, 2H), 7.23 (p, *J* = 8.9 Hz, 5H), 6.89 (s, 2H), 6.75 (t, *J* = 7.3 Hz, 1H), 6.65 (d, *J* = 8.2 Hz, 2H), 4.88 (t, *J* = 7.7 Hz, 1H), 4.18 (dd, *J* = 12.1, 6.9 Hz, 1H), 3.73 (dd, *J* = 12.2, 8.2 Hz, 1H), 3.65 (s, 1H), 2.32 (s, 3H), 2.17 (s, 6H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 148.2, 142.4, 137.7, 136.4, 135.8, 129.4, 128.5, 127.4, 126.0, 124.1, 117.6, 113.1, 45.5, 43.7, 21.4, 20.9.

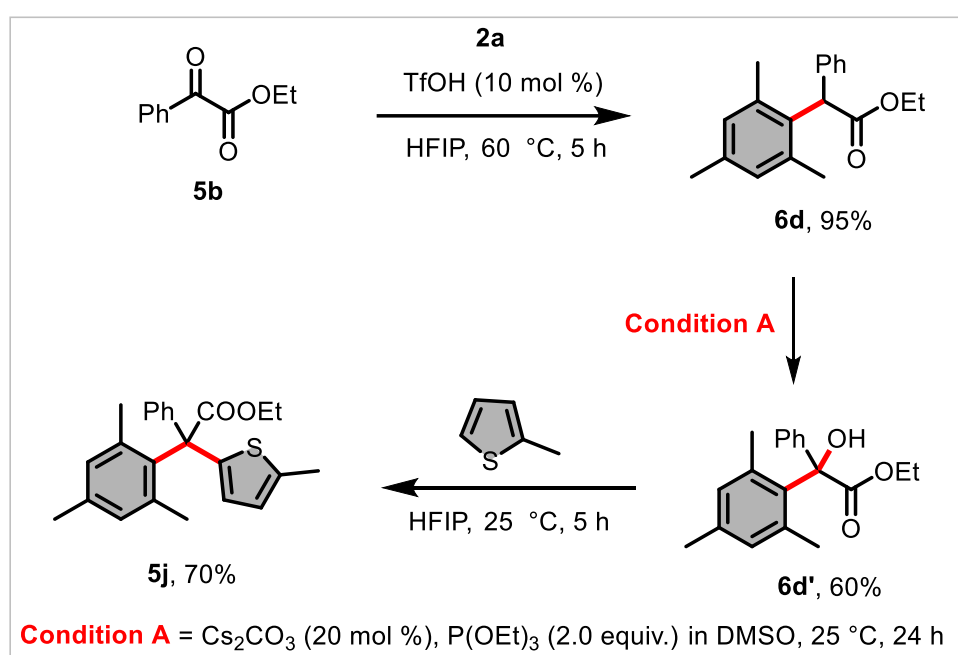
8.5 Synthesis of benzoic-2-(2,4,6-trimethoxyphenyl)propanoic anhydride (5i)



In a round bottle flask, anhydrous AlCl₃ (1.5 equiv.) was taken and dissolved in dichloromethane solvent at 0 °C, and benzoyl chloride (1.1 equiv.) was added. After 1 h, the solution of 2-(2,4,6-

trimethoxyphenyl) propanoic acid in DCM was added dropwise to the reaction mixture. The reaction mixture was allowed to stir for 12 h at room temperature. Thereafter, the reaction was quenched by water, and the mixture was extracted 3 times with CH₂Cl₂; the organic layer was collected and concentrated in vacuo, and the residue was purified by column chromatography (SiO₂, R_f = 0.4; DCM:MeOH = 97/03) to afford the target product **5i** as a colourless viscous (62 mg, 90%); ¹H NMR (500 MHz, CDCl₃) δ 8.12 (d, *J* = 8.1 Hz, 2H), 7.61 (t, *J* = 7.6 Hz, 1H), 7.47 (t, *J* = 7.2 Hz, 2H), 6.16 (s, 2H), 4.23 (q, *J* = 7.3 Hz, 1H), 3.81 (s, 3H), 3.80 (s, 6H), 1.39 (d, *J* = 7.3 Hz, 3H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 182.4, 172.3, 160.3, 158.3, 133.8, 130.3, 129.6, 128.5, 111.1, 91.2, 55.8, 55.4, 34.4, 15.6; HRMS (ESI) *m/z*: [M-H]⁻ calculated for C₁₉H₁₉O₆ 343.1182; found: 343.1185.

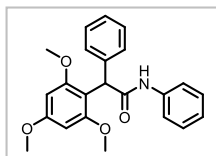
8.6 Ethyl-2-mesityl-2-(5-methylthiophen-2-yl)-2-phenylacetat (**5j**)



In this process, we used ethyl 2-oxo-2-phenylacetate (**5b**, 35 mg, 0.2 mmol) under our optimized reaction conditions and afforded compound **6d** as a colorless viscous, which was purified by using column chromatography (SiO₂, Hexane). Then, we introduced the hydroxy group at the α position of the ester by using a reported method involving Cs₂CO₃ (20 mol%), P(OEt)₃ (2.0 equiv.) in DMSO solvent under an O₂ balloon.⁶ After 24 h, the reaction mixture was extracted with ethyl acetate three times, washed with brine, and dried over Na₂SO₄. The organic layer was concentrated and purified by column chromatography (SiO₂, Hexane: EtOAc= 95:05). Next, we added 2-methylthiophene into the reaction mixture in HFIP solvent, achieving the desired product **5j** in 70% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.44 (d, *J* = 8.5 Hz, 2H), 7.12 – 7.03 (m, 3H), 6.89 (s, 2H), 6.69 (dd, *J* = 3.5, 1.1 Hz, 1H), 5.36 (d, *J* = 4.3 Hz, 1H), 4.28 – 4.12 (m, 2H), 2.48 (s, 3H), 2.29 (s, 3H), 2.18 (s, 6H), 1.23 (t, *J* = 7.1 Hz, 3H); ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 173.3, 141.9, 139.5, 137.5, 136.9, 135.9, 133.2, 132.4, 130.0, 129.2, 126.3, 125.4, 122.9, 61.3, 50.8, 21.0, 15.6, 14.3; HRMS (ESI) *m/z*: [M+Na]⁺ calculated for C₂₄H₂₆O₂NaS 401.1551; found: 401.1561.

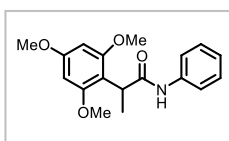
9. α -Arylation of α -keto-amide and α -keto-ester

N,2-Diphenyl-2-(2,4,6-trimethoxyphenyl) acetamide (6a)



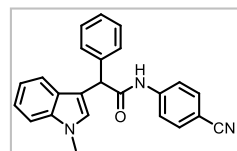
General procedure (B) was followed using 2-oxo-*N*,2-diphenylacetamide (45 mg, 0.2 mmol) to give a crude mixture, which was purified by flash column chromatography (SiO₂, R_f = 0.5; Hexane/ethyl acetate = 60/40) to afford the title compound as a colourless viscous (55 mg, 73%); ¹H NMR (400 MHz, CDCl₃) δ 7.38 (d, *J* = 7.5 Hz, 2H), 7.33 (d, *J* = 6.7 Hz, 2H), 7.30 – 7.18 (m, 5H), 7.01 (t, *J* = 7.4 Hz, 1H), 6.15 (s, 2H), 5.47 (s, 1H), 3.78 (s, 3H), 3.71 (s, 6H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 171.6, 160.9, 159.0, 139.1, 138.5, 129.4, 128.9, 128.6, 127.1, 123.8, 119.7, 109.5, 91.6, 56.1, 55.5, 49.2; HRMS (ESI) *m/z*: [M+Na]⁺ calculated for C₂₃H₂₃O₄NNa 400.1525; found: 400.1531.

N-Phenyl-2-(2,4,6-trimethoxyphenyl) propenamide (6b)



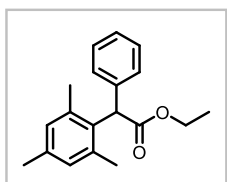
General procedure (B) was followed using 2-oxo-*N*,2-diphenylacetamide (33 mg, 0.2 mmol) to give a crude mixture, which was purified by flash column chromatography (SiO₂, R_f = 0.5; Hexane/ethyl acetate = 60/40) to afford the title compound as a colourless viscous (50 mg, 80%); ¹H NMR (400 MHz, CDCl₃) δ 7.39 (d, *J* = 7.6 Hz, 2H), 7.28 – 7.20 (m, 2H), 7.17 (s, 1H), 7.01 (t, *J* = 7.4 Hz, 1H), 6.17 (s, 2H), 4.23 (q, *J* = 7.0 Hz, 1H), 3.82 (s, 3H), 3.78 (s, 6H), 1.45 (d, *J* = 7.1 Hz, 3H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 173.6, 160.8, 159.0, 138.7, 128.8, 123.5, 119.7, 110.1, 91.1, 55.9, 55.4, 36.2, 15.1; HRMS (ESI) *m/z*: [M+Na]⁺ calculated for C₁₈H₂₁O₄NNa 338.1368, found: 338.1370.

N-(4-Cyanophenyl)-2-(1-methyl-2-oxoindolin-3-yl)-2-phenylacetamide (6c)



General procedure (B) was followed using *N*-(4-cyanophenyl)-2-oxo-2-phenylacetamide (50 mg, 0.2 mmol) to give a crude mixture, which was purified by flash column chromatography (SiO₂, R_f = 0.5; Hexane/ethyl acetate = 60/40) to afford the title compound as a brown viscous (56 mg, 77%); ¹H NMR (500 MHz, CDCl₃) δ 8.01 (s, 1H), 7.51 (q, *J* = 9.0 Hz, 4H), 7.44 (d, *J* = 7.9 Hz, 1H), 7.41 – 7.26 (m, 7H), 7.13 – 7.07 (m, 1H), 6.87 (s, 1H), 5.27 (s, 1H), 3.75 (s, 3H); ¹³C {¹H} NMR (126 MHz, CDCl₃) δ 171.4, 141.9, 138.8, 137.5, 133.3, 129.0, 128.7, 128.6, 127.7, 126.8, 122.6, 120.0, 119.8, 119.0, 118.9, 112.1, 109.9, 107.2, 52.1, 33.0; HRMS (ESI) *m/z*: [M+Na]⁺ calculated for C₂₄H₁₉ON₃Na 388.1426; found: 388.1427.

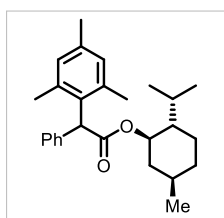
Ethyl-2-mesityl-2-phenylacetate (6d)



General procedure (A) was followed using ethyl 2-oxo-2-phenylacetate (36 mg, 0.2 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.7; Hexane) to afford the title compound as a colorless viscous (54 mg, 95%); ¹H NMR (400 MHz, CDCl₃) δ 7.32 – 7.20 (m, 3H), 7.16 – 7.11 (m, 2H), 6.92 (s, 2H), 5.40 (s, 1H), 4.44 – 3.97 (m, 2H), 2.31 (s, 3H), 2.20 (s, 6H), 1.26 (t, *J* = 7.1 Hz, 3H); ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 173.3, 137.5, 137.1, 136.8, 132.5, 130.0,

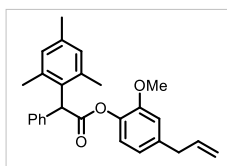
128.7, 128.2, 126.7, 61.2, 51.1, 21.0, 21.0, 14.3; **HRMS-ESI (m/z)** [M+H]⁺ calculated for C₁₉H₂₃O₂ 283.1698, found: 283.1702.

(1*R*,2*R*,5*R*)-2-isopropyl-5-methylcyclohexyl-2-mesityl-2-phenylacetate (6e)



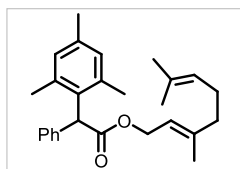
General procedure (A) was followed using (1*R*,2*R*,5*R*)-2-isopropyl-5-methylcyclohexyl 2-oxo-2-phenylacetate (56 mg, 0.2 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.5; Hexane/ethyl acetate = 95/05) to afford the title compound as a colorless viscous (60 mg, 76%); ¹H NMR (400 MHz, CDCl₃) δ 7.17 (t, *J* = 6.6 Hz, 5H), 7.11 (t, *J* = 7.3 Hz, 4H), 7.04 (d, *J* = 6.9 Hz, 2H), 6.78 (s, 2H), 6.77 (s, 2H), 5.33 (s, 1H), 5.30 (s, 1H), 4.68 (td, *J* = 10.8, 4.3 Hz, 1H), 4.59 (td, *J* = 10.8, 4.3 Hz, 1H), 2.19 (s, 3H), 2.18 (s, 3H), 2.09 (s, 6H), 2.08 (s, 6H), 1.89 (dt, *J* = 12.1, 3.6 Hz, 2H), 1.74 (qd, *J* = 7.0, 2.8 Hz, 1H), 1.61 – 1.45 (m, 5H), 1.44 – 1.34 (m, 2H), 1.34 – 1.09 (m, 5H), 1.01 – 0.85 (m, 3H), 0.83 (d, *J* = 6.6 Hz, 3H), 0.77 (dd, *J* = 6.8, 3.3 Hz, 7H), 0.72 (d, *J* = 7.0 Hz, 4H), 0.60 (d, *J* = 7.1 Hz, 3H), 0.48 (d, *J* = 7.0 Hz, 3H); ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 172.5, 172.2, 137.8, 137.73, 137.66, 137.6, 136.7, 136.6, 132.63, 132.59, 129.9, 129.8, 128.6, 128.5, 128.19, 128.18, 126.5, 126.4, 75.1, 75.0, 51.3, 51.0, 47.2, 46.9, 40.9, 40.5, 34.33, 34.30, 31.51, 31.47, 26.5, 25.5, 23.6, 23.1, 22.2, 22.1, 21.18, 21.16, 21.0, 20.9, 20.85, 20.89, 16.6, 16.0. **HRMS-ESI (m/z)** [M+Na]⁺ calculated for C₂₇H₃₆O₂Na 415.2613, found: 415.2599.

4-Allyl-2-methoxyphenyl-2-mesityl-2-phenylacetate (6f)



General procedure (A) was followed using 4-allyl-2-methoxyphenyl 2-oxo-2-phenylacetate (59 mg, 0.2 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.4; Hexane/ethyl acetate = 97/03) to afford the title compound as a colorless viscous (66 mg, 82%); ¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.24 (m, 5H), 6.98 (s, 2H), 6.95 (d, *J* = 8.0 Hz, 1H), 6.82 – 6.75 (m, 2H), 6.07 – 5.90 (m, 1H), 5.78 (s, 1H), 5.16 – 5.12 (m, 1H), 5.11 (t, *J* = 1.5 Hz, 1H), 3.82 (s, 3H), 3.40 (d, *J* = 6.7 Hz, 2H), 2.36 (s, 3H), 2.33 (s, 6H); ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 171.1, 151.1, 138.9, 138.4, 137.9, 137.2, 137.0, 137.0, 132.1, 130.0, 128.6, 128.2, 126.7, 122.5, 120.7, 116.2, 112.9, 55.8, 50.6, 40.1, 21.1, 21.0. **HRMS-ESI (m/z)** [M+Na]⁺ calculated for C₂₇H₂₈O₃Na 423.1936, found: 423.1923.

(*E*)-3,7-dimethylocta-2,6-dien-1-yl-2-mesityl-2-phenylacetate (6g)



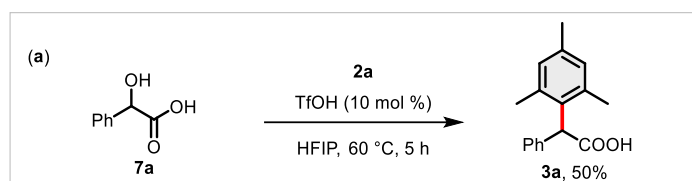
General procedure (A) was followed using (*E*)-3,7-dimethylocta-2,6-dien-1-yl 2-oxo-2-phenylacetate (62 mg, 0.2 mmol) to give a crude mixture, which was purified by using column chromatography (SiO₂, R_f = 0.5; Hexane/ethyl acetate = 95/05) to afford the title compound as a colorless viscous (61 mg, 78%); ¹H NMR (400 MHz, CDCl₃) δ 7.34 – 7.27 (m, 2H), 7.26 – 7.21 (m, 1H), 7.19 – 7.08 (m, 2H), 6.91 (s, 2H), 5.40 (s, 1H), 5.39 – 5.30 (m, 1H), 5.14 – 5.02 (m, 1H), 4.85 – 4.44 (m, 2H), 2.31 (s, 3H), 2.20 (s, 7H), 2.17 – 1.99 (m, 4H), 1.76 (s, 3H), 1.69 (s, 3H), 1.60 (s, 3H); ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 173.3, 142.4, 137.6, 137.2, 136.7, 132.5, 132.2, 129.9, 128.8, 128.8, 128.2, 126.7, 123.8, 119.3, 61.9, 51.1,

32.3, 26.7, 25.8, 23.6, 21.0, 21.0, 17.7. **HRMS-ESI (m/z)** $[M+Na]^+$ calculated for $C_{27}H_{34}O_2Na$ 413.2456, found: 413.2446.

10 Control experiments

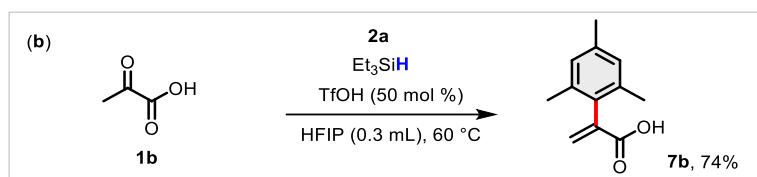
We conducted control experiments to understand the reaction mechanism. Initially, the arylation process utilized **7a** (mandelic acid) instead of **1a** under optimized reaction conditions. The resulting 50% yield of the desired product **3a** suggested that **7a** could be one of the intermediates formed by reducing the carbonyl group in **1a** using silane (Scheme a). Subsequently, 2-oxo propionic acid (**1b**) underwent treatment with mesitylene using TfOH (50 mol%), leading to the formation of alkene **7b** through arylation followed by dehydration (Scheme b). However, this outcome conflicts with the result, i.e., silane first reduced the carbonyl group of ketoacid followed by FC alkylation reaction observed in the control experiment (**a**). To confirm the initial formation of **7a** as an intermediate, substrate **1a** was subjected to reduction with silane, resulting in the production of a trace amount of product **7a** (Scheme c). Based on these control experiments, we can conclude that our reaction involves first FC alkylation followed by reduction. To prove this, we synthesized tertiary alcohol **7c** (a kind of intermediate of FC alkylation). When we subjected this **7c** to 10 mol% TfOH and Et_3SiH , we observed product **5f** in 95% yield, which depicted that the reaction pursued arylation followed by reduction (Scheme d). To check the reactivity of tertiary alcohol towards a competitive arylation or reduction, we performed a reaction of **7c** with **2a** and Et_3SiH under standard conditions, and only the reduced product **5f** was observed in 99% yield, indicating that tertiary alcohols are more susceptible to reduction rather than arylation (Scheme e). This could be the reason for the selective mono-arylation of the keto group under standard conditions.

(a) Synthesis of 2-mesityl-2-phenylacetic acid



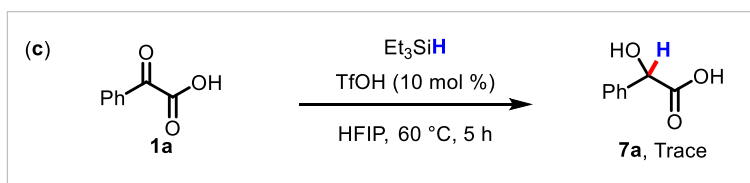
In control experiment (**a**), the arylation process utilized **7a** (mandelic acid) under optimized reaction conditions. After 5 h, the reaction mixture was concentrated under reduced pressure, and the reaction mixture was purified by using column chromatography (SiO_2 , $R_f = 0.4$; DCM/MeOH = 97/03) to afford the **3a** as a white solid. The resulting 50% yield of the desired product **3a** suggested that **7a** could be one of the intermediates formed by reducing the carbonyl group in α -ketoacid (**1a**) using silane.

(b) Synthesis of 2-mesitylacrylic acid (**7b**)⁸



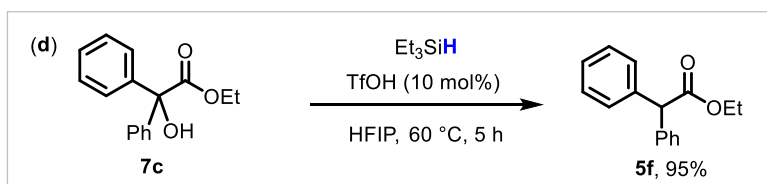
In control experiment (**b**), 2-oxo propanoic acid (**1b**, 27 mg, 0.3 mmol) was treated with mesitylene (**2a**) and Et_3SiH (0.45 mmol) in the presence of TfOH (50 mol %) at 60 °C for 5 h. After 5 h, the reaction mixture was concentrated under reduced pressure, and the reaction mixture was purified by using column chromatography (SiO_2 , $R_f = 0.4$; DCM/MeOH =97/03) and afforded the compound **7b** as a pink viscous (42 mg, 74%); This signifies that in aliphatic α -keto acids, first arylation occur followed by elimination of water. ^1H NMR (500 MHz, CDCl_3) δ 6.89 (s, 2H), 6.75 (s, 1H), 5.74 (s, 1H), 2.29 (s, 3H), 2.16 (s, 6H); ^{13}C { ^1H } NMR (126 MHz, CDCl_3) δ 171.2, 139.4, 137.6, 136.2, 133.3, 131.6, 128.3, 21.2, 20.3.

(c) Synthesis of 2-hydroxy-2-phenylacetic acid



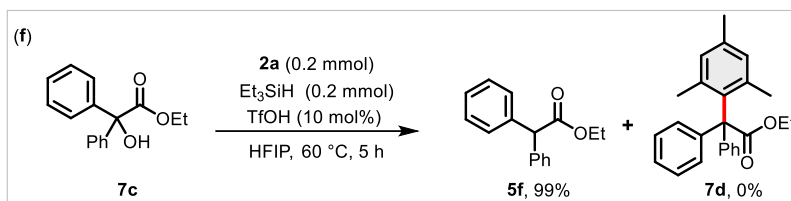
To verify the initial formation of **7a** as an intermediate, we did control experiment (**c**) substrate **1a** underwent reduction with silane under optimized reaction conditions, yielding a trace amount of product **7a**.

(d) Synthesis of ethyl 2,2-diphenylacetate



In this control experiment (**d**), when we subjected **7c** (a kind of intermediate of FC alkylation on **1a**) with 10 mol% triflic acid and Et_3SiH , we observed product **5f** in 95% yield, which depicted that the reaction pursued arylation followed by reduction.

(e) Competition reaction

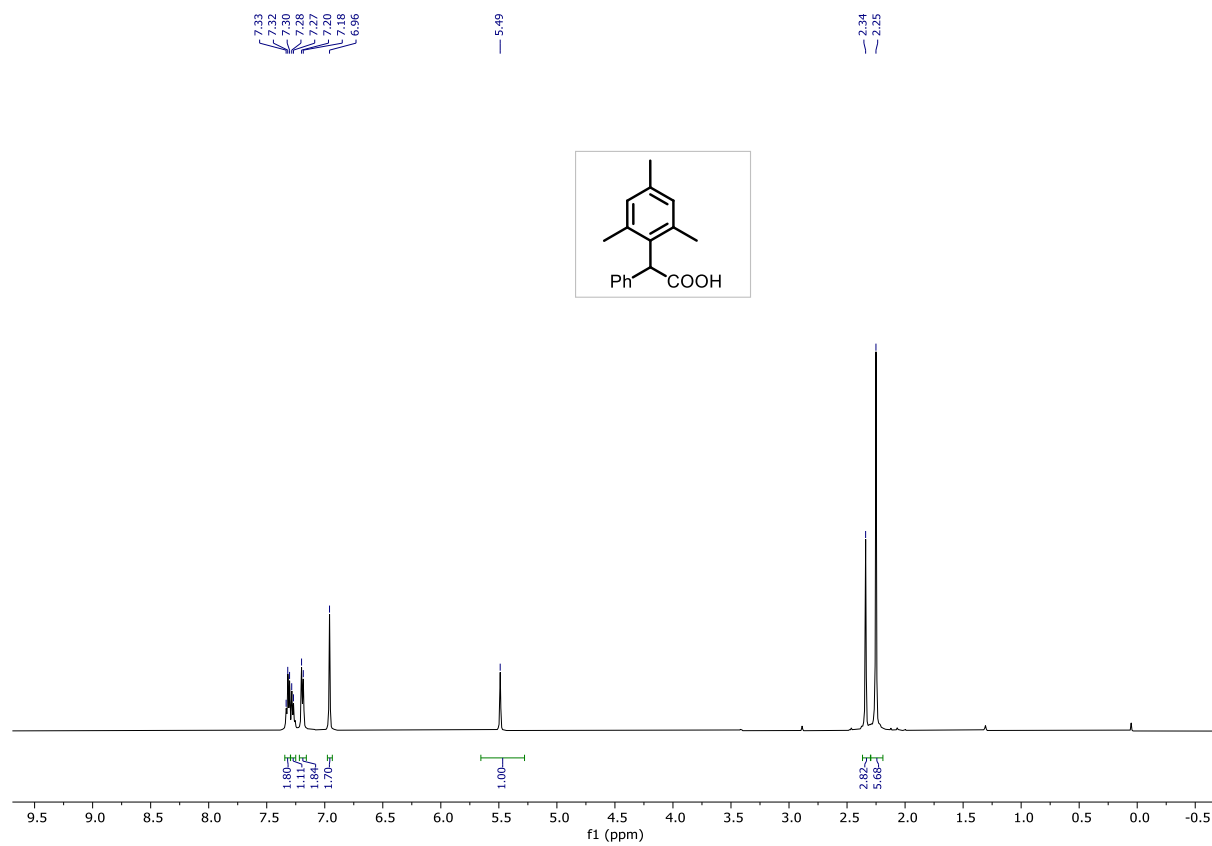


To validate the results of control experiment (**d**), we conducted control experiment (**e**), which involved a competitive reaction between the reduction and arylation of the hydroxy group. In this experiment, compound **7c** was subjected to 10 mol% TfOH , triethylsilane, and mesitylene (**2a**). Upon completion of the reaction and subsequent purification, we identified product **5f** with a yield of 95%. This outcome verifies that the reaction initially proceeded via arylation, followed by reduction.

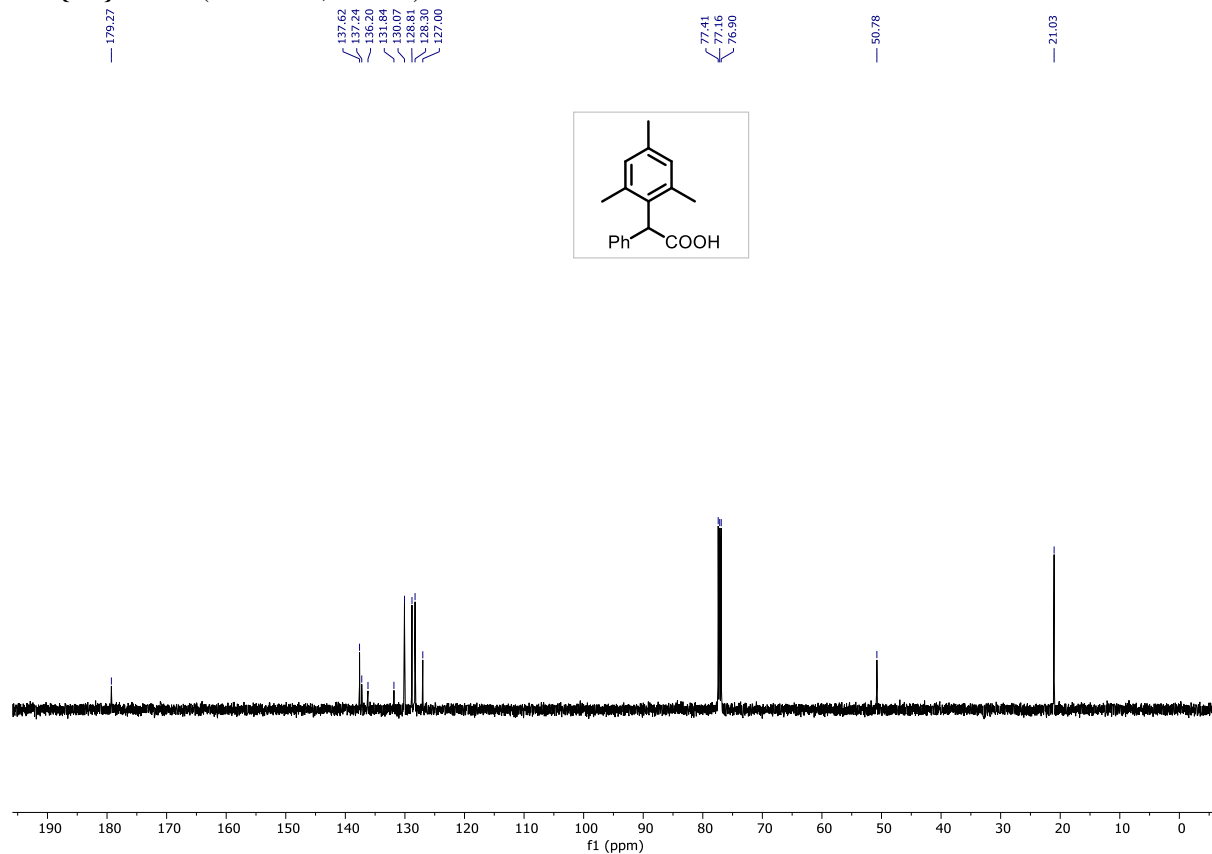
11. Copies of ^1H NMR, ^{13}C $\{^1\text{H}\}$ and ^{19}F NMR spectra of product

2-Mesityl-2-phenylacetic acid (3a)

^1H NMR (500 MHz, CDCl_3)

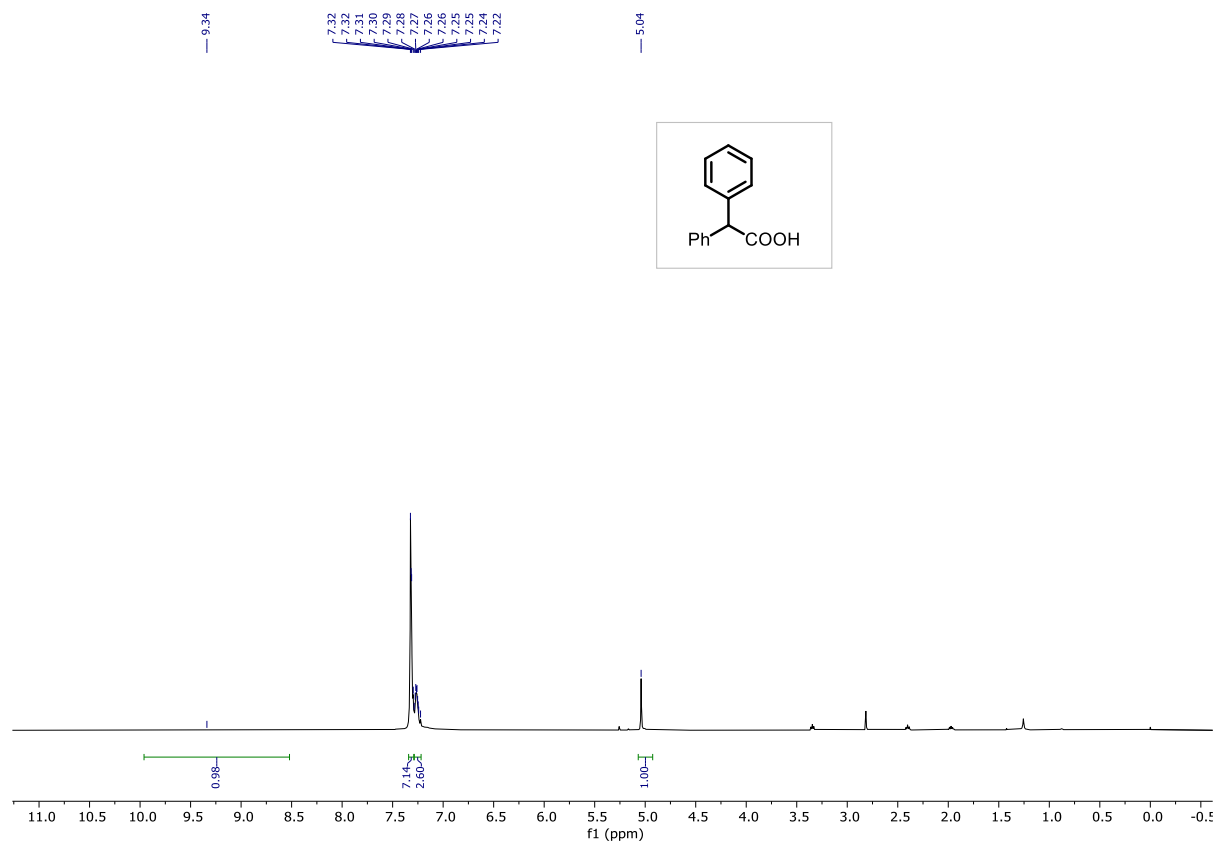


^{13}C { ^1H } NMR (126 MHz, CDCl_3)

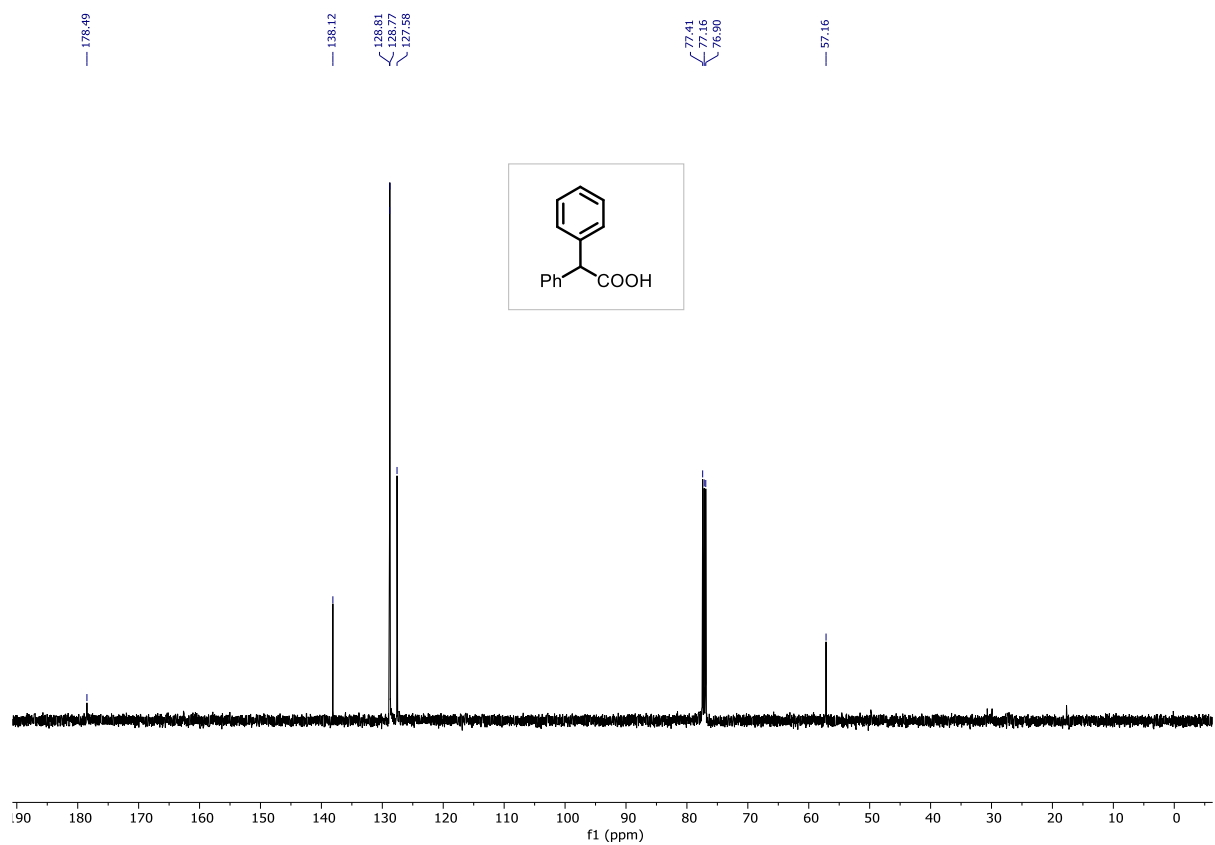


2,2-Diphenylacetic acid (3b)

^1H NMR (500 MHz, CDCl_3)

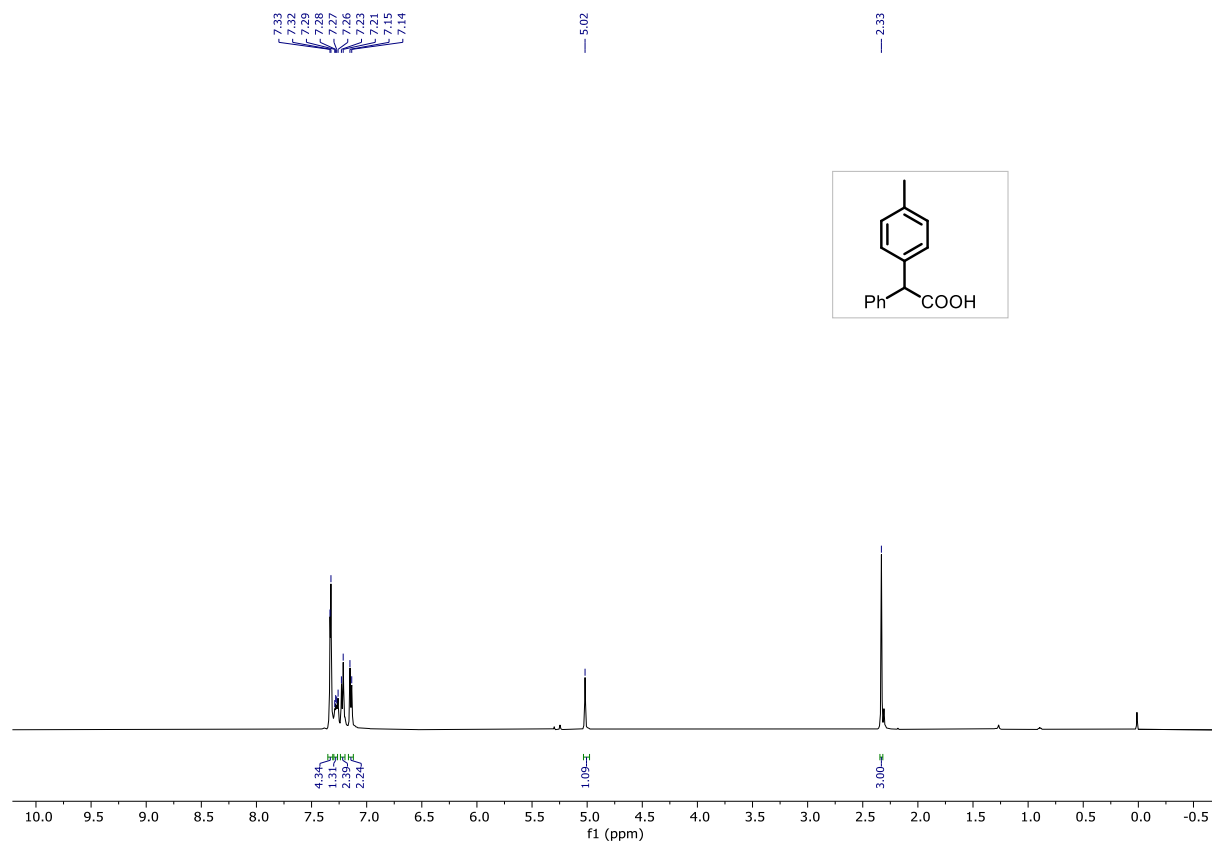


^{13}C $\{^1\text{H}\}$ NMR (126 MHz, CDCl_3)

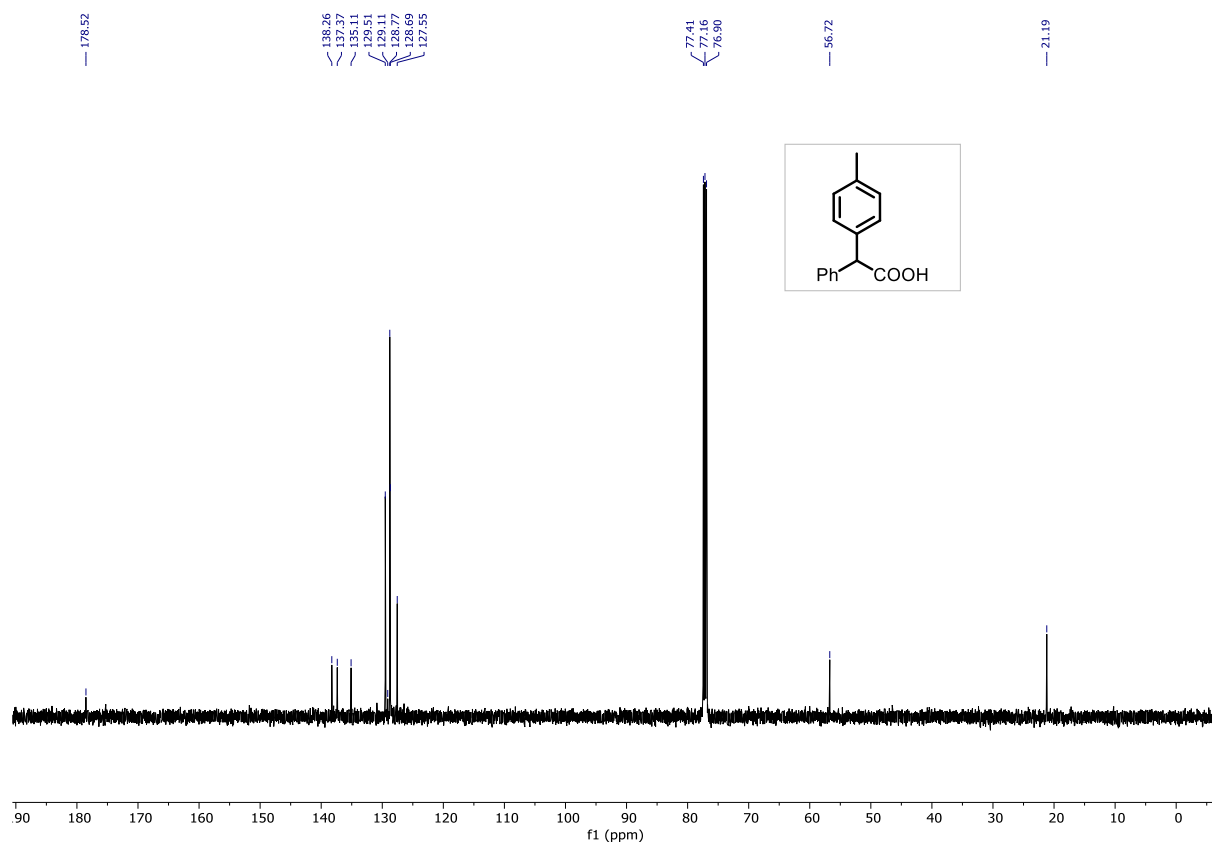


2-Phenyl-2-(*p*-tolyl) acetic acid (3c)

^1H NMR (500 MHz, CDCl_3)

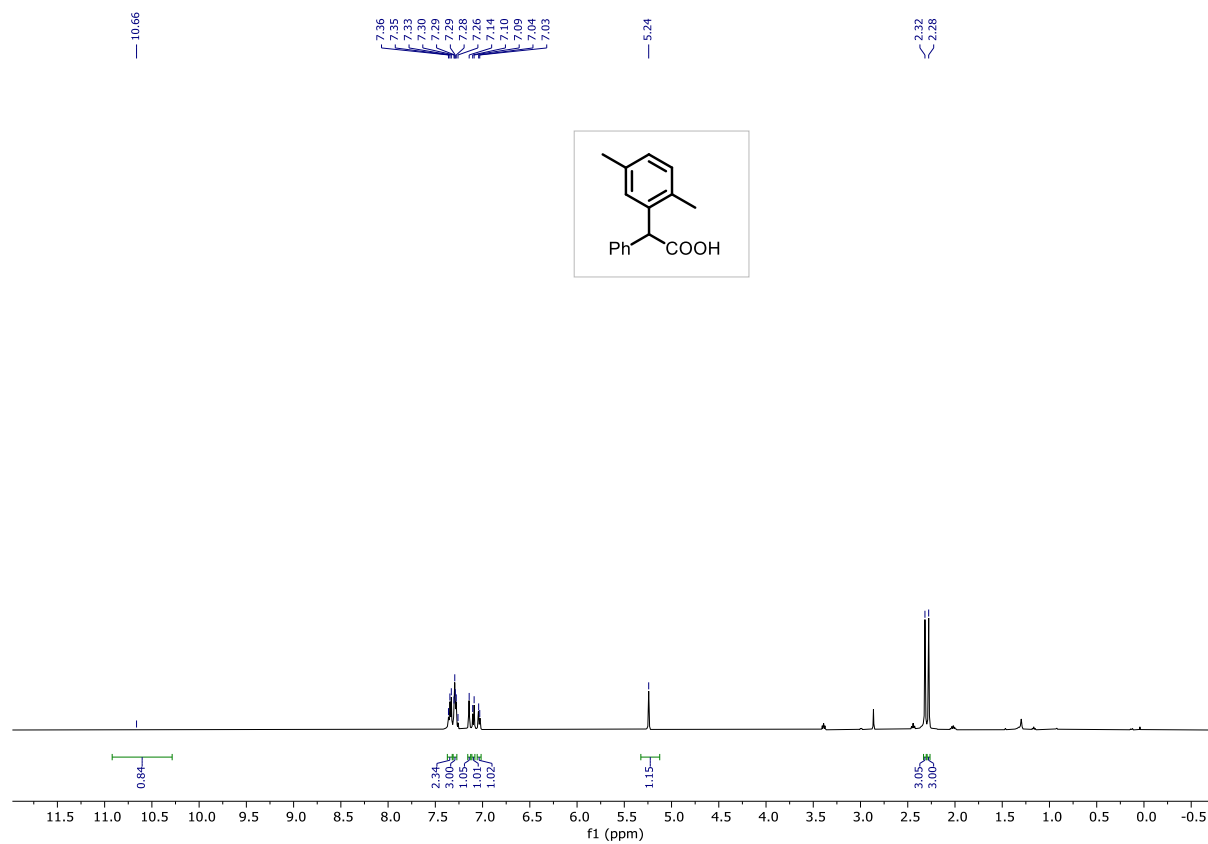


^{13}C { ^1H } NMR (126 MHz, CDCl_3)

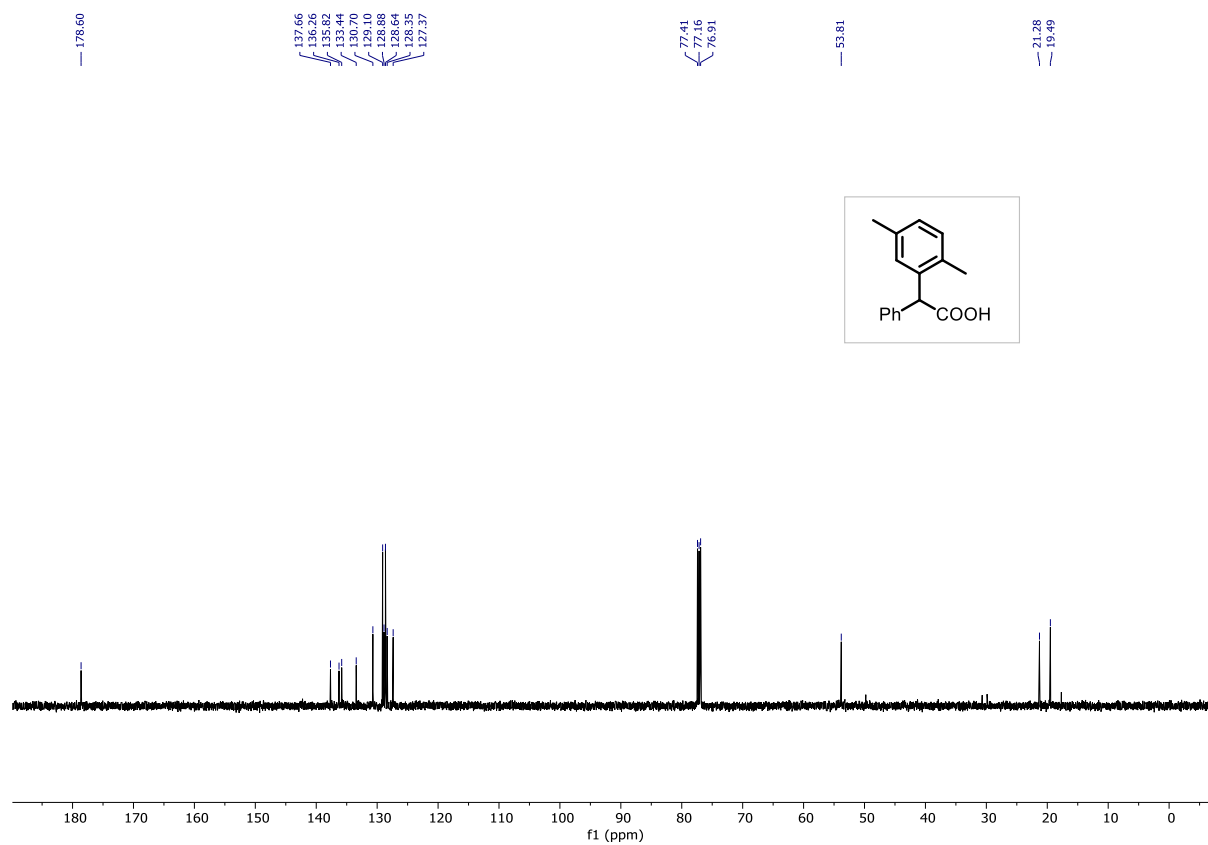


2-(2,5-Dimethylphenyl)-2-phenylacetic acid (3d)

^1H NMR (500 MHz, CDCl_3)

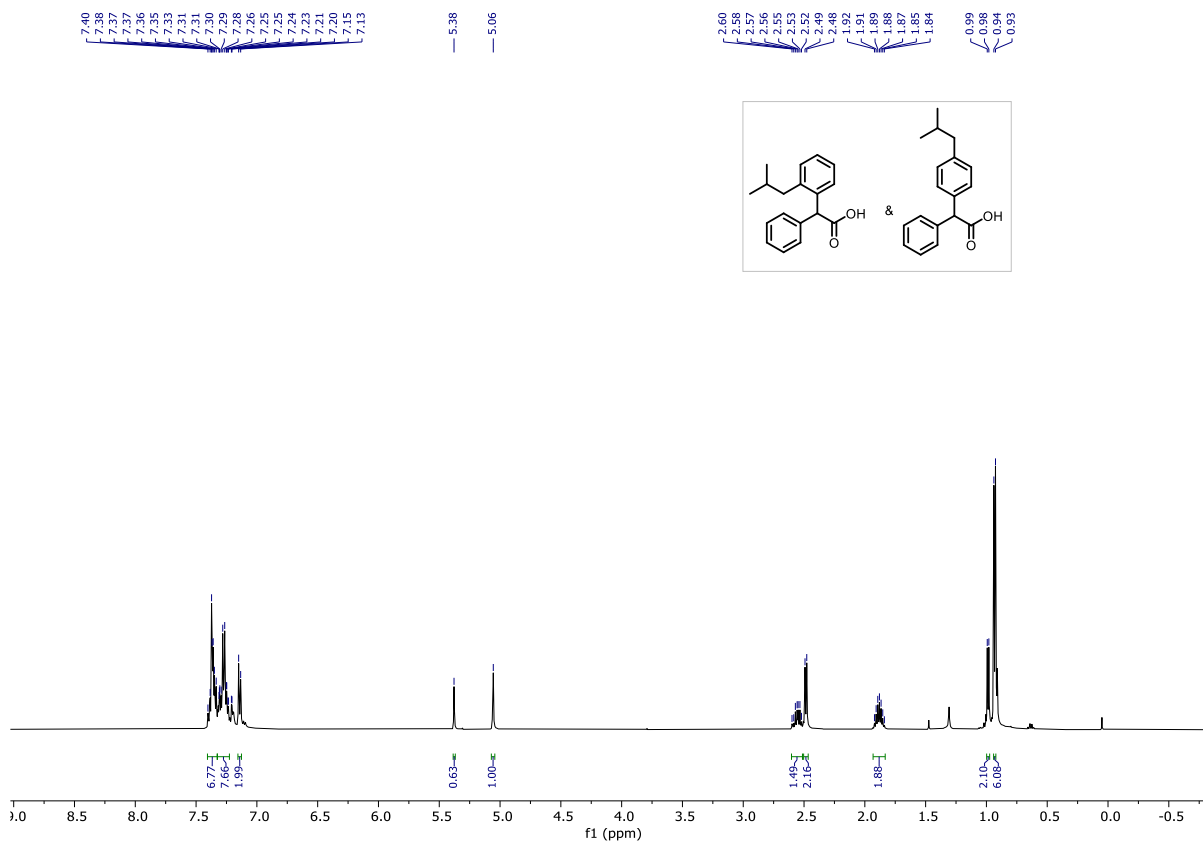


^{13}C { ^1H } NMR (126 MHz, CDCl_3)

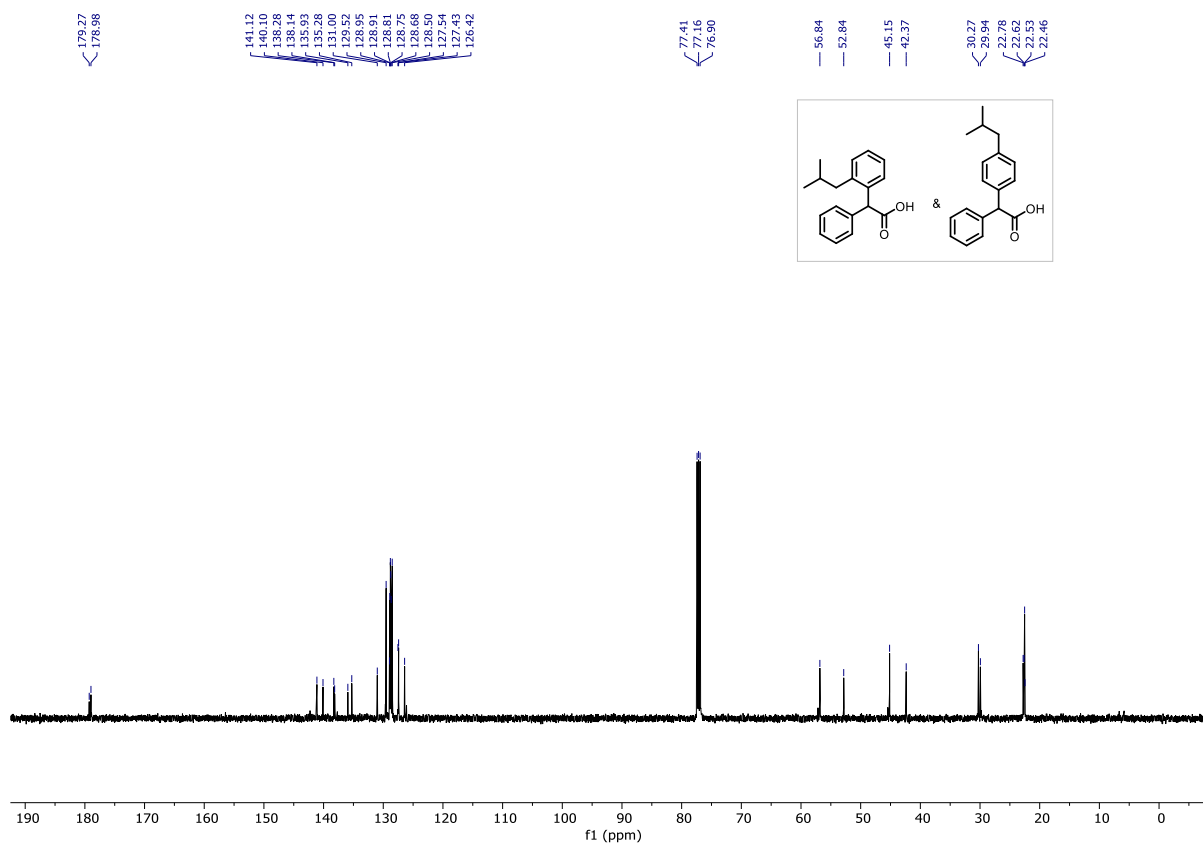


2-(2-Isobutylphenyl)-2-phenylacetic acid & 2-(4-isobutylphenyl)-2-phenylacetic acid

^1H NMR (500 MHz, CDCl_3)

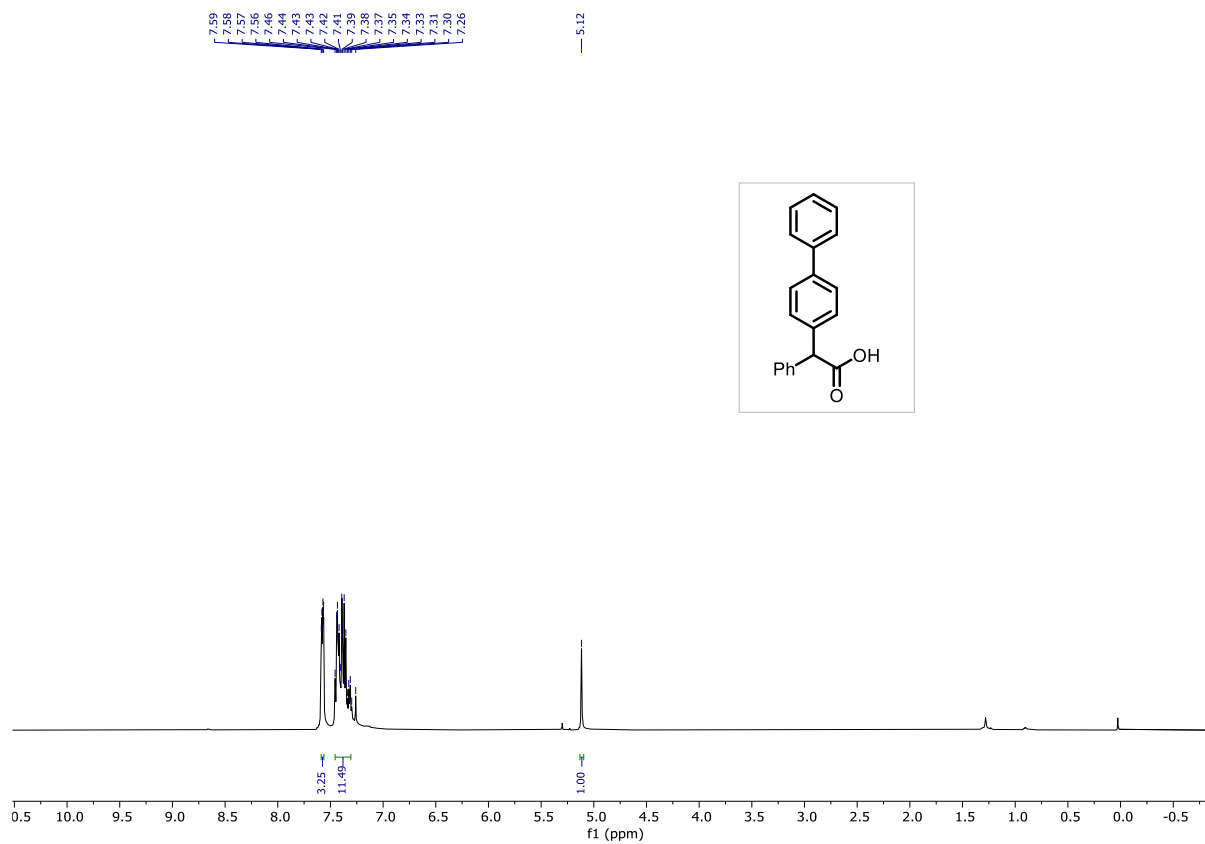


^{13}C { ^1H } NMR (126 MHz, CDCl_3)

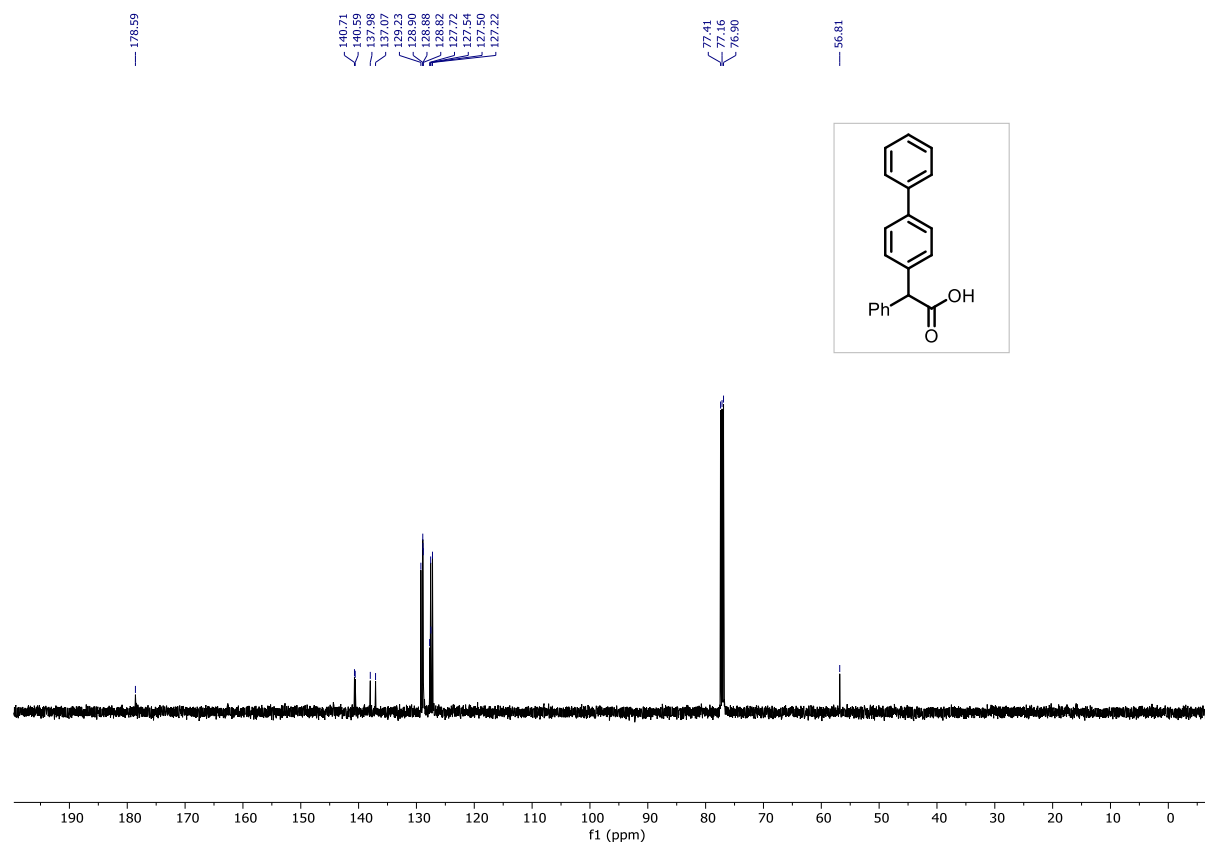


2-([1,1'-Biphenyl]-4-yl)-2-phenylacetic acid (3f)

^1H NMR (500 MHz, CDCl_3)

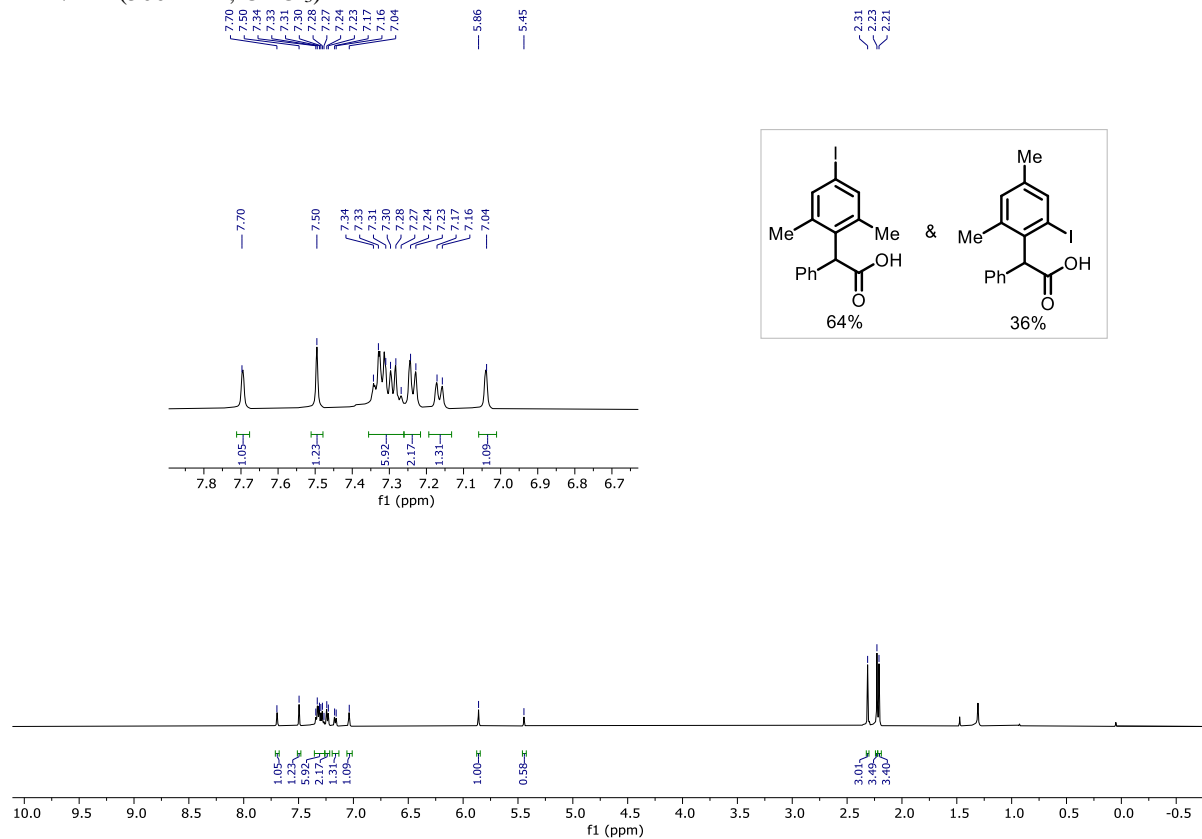


^{13}C { ^1H } NMR (126 MHz, CDCl_3)

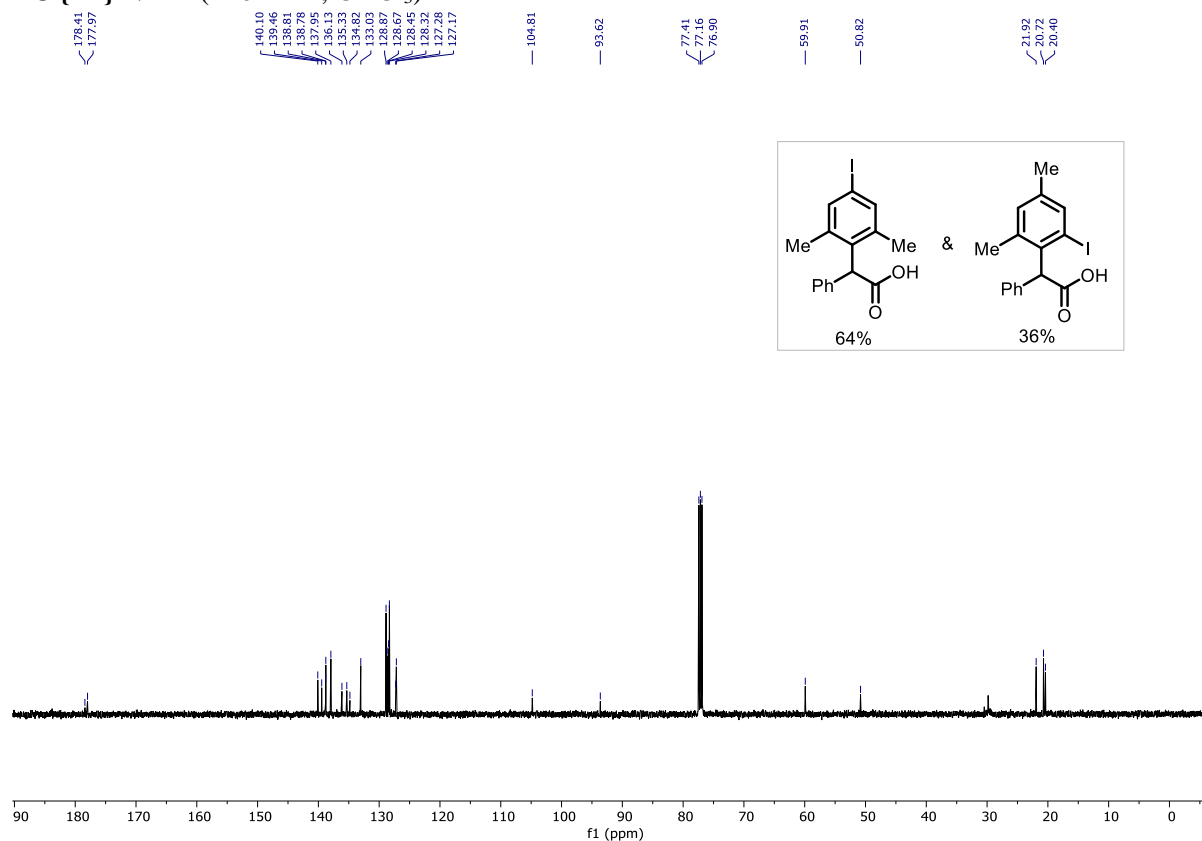


2-(4-Iodo-2,6-dimethylphenyl)-2-phenylacetic acid & 2-(2-iodo-4,6-dimethylphenyl)-2-phenylacetic acid (3g)

^1H NMR (500 MHz, CDCl_3)

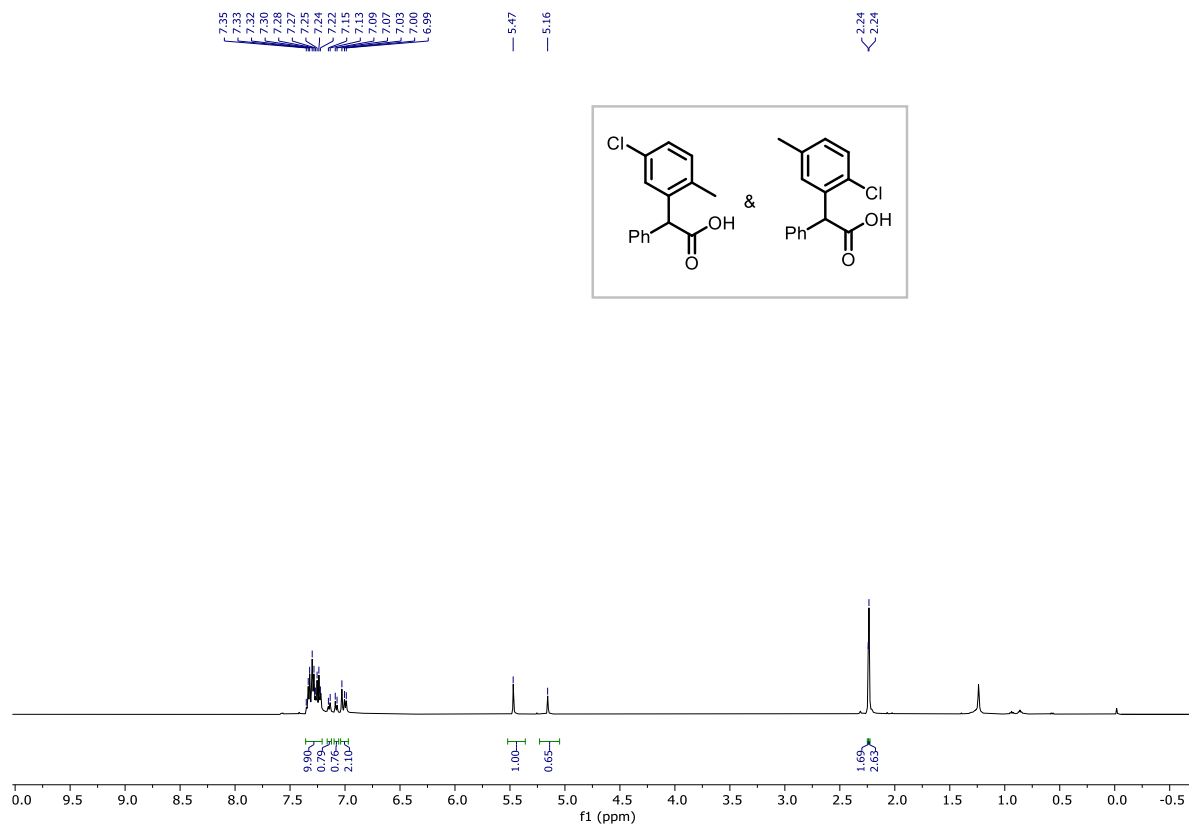


^{13}C { ^1H } NMR (126 MHz, CDCl_3)

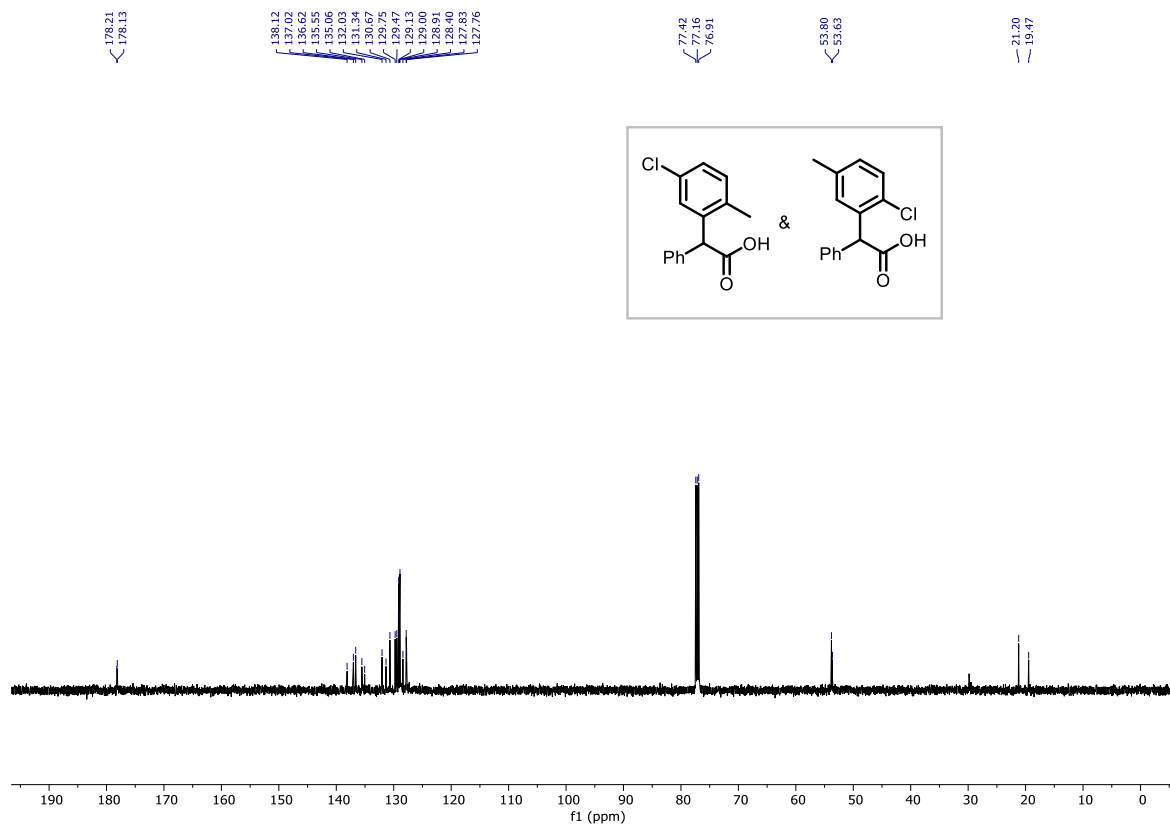


2-(5-Chloro-2-methylphenyl)-2-phenylacetic acid & 2-(2-chloro-5-methylphenyl)-2-phenylacetic acid (3h)

^1H NMR (500 MHz, CDCl_3)

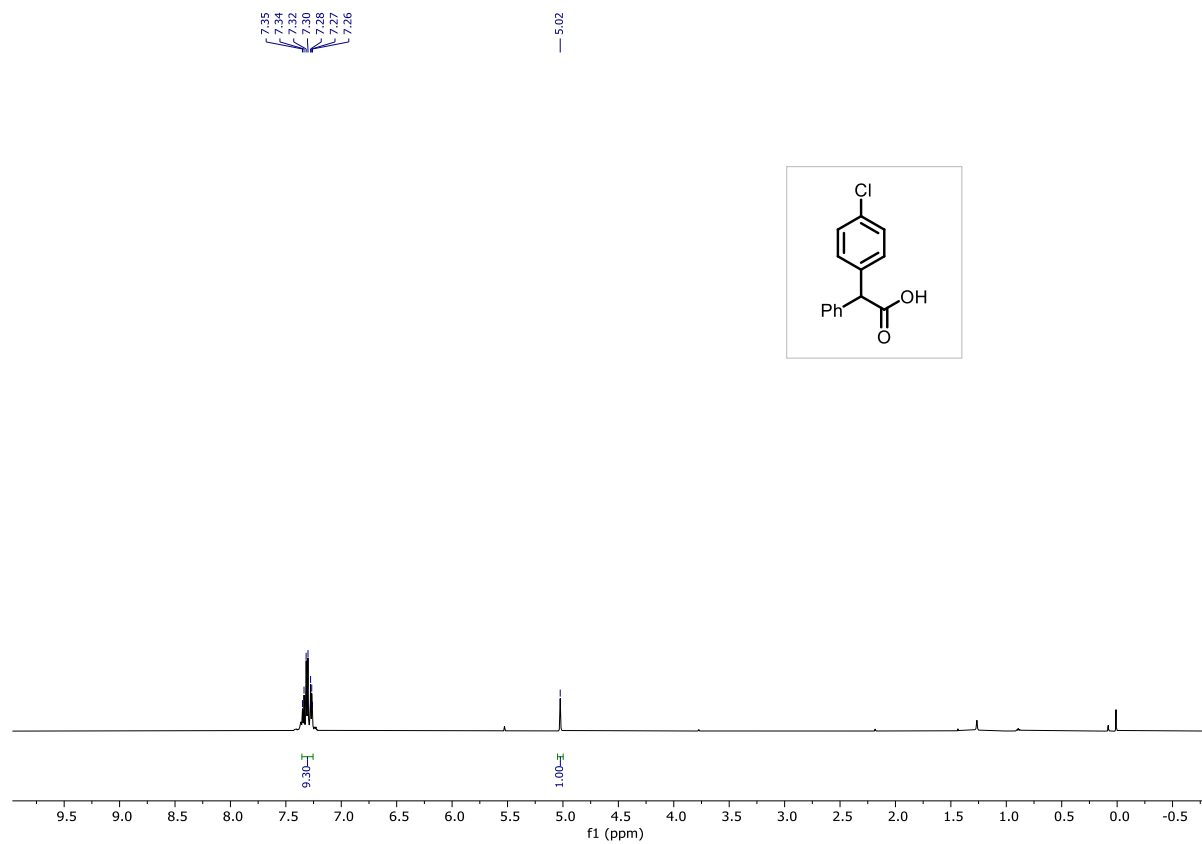


^{13}C $\{^1\text{H}\}$ NMR (126 MHz, CDCl_3)



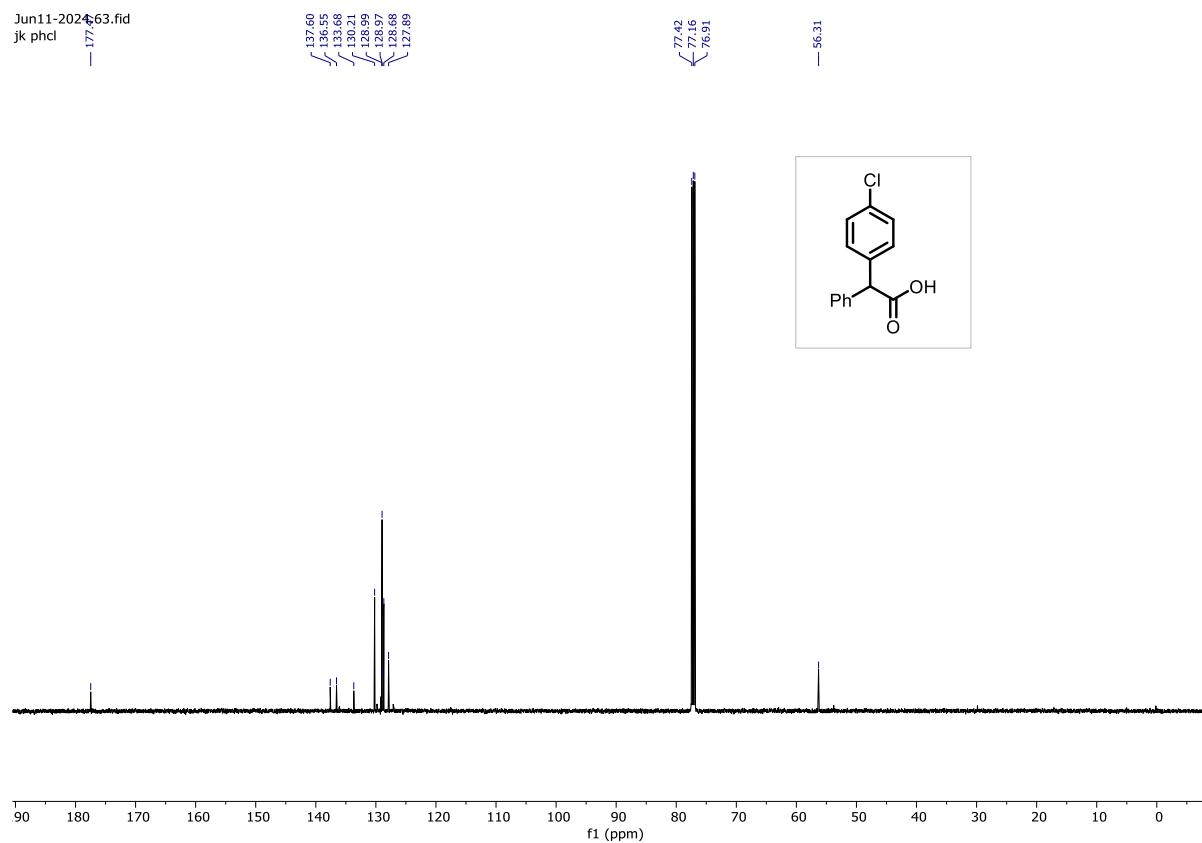
2-(4-Chlorophenyl)-2-phenylacetic acid (3i)

^1H NMR (500 MHz, CDCl_3)

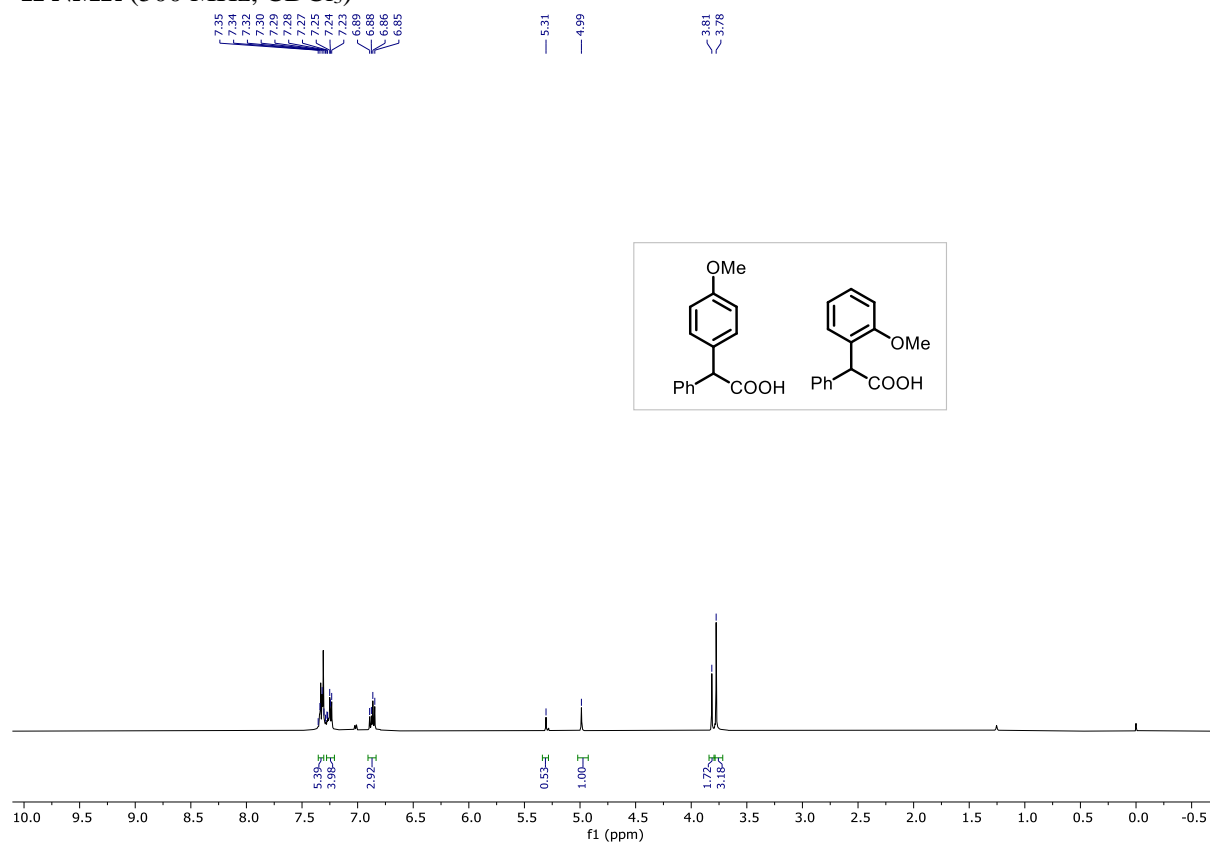


^{13}C { ^1H } NMR (126 MHz, CDCl_3)

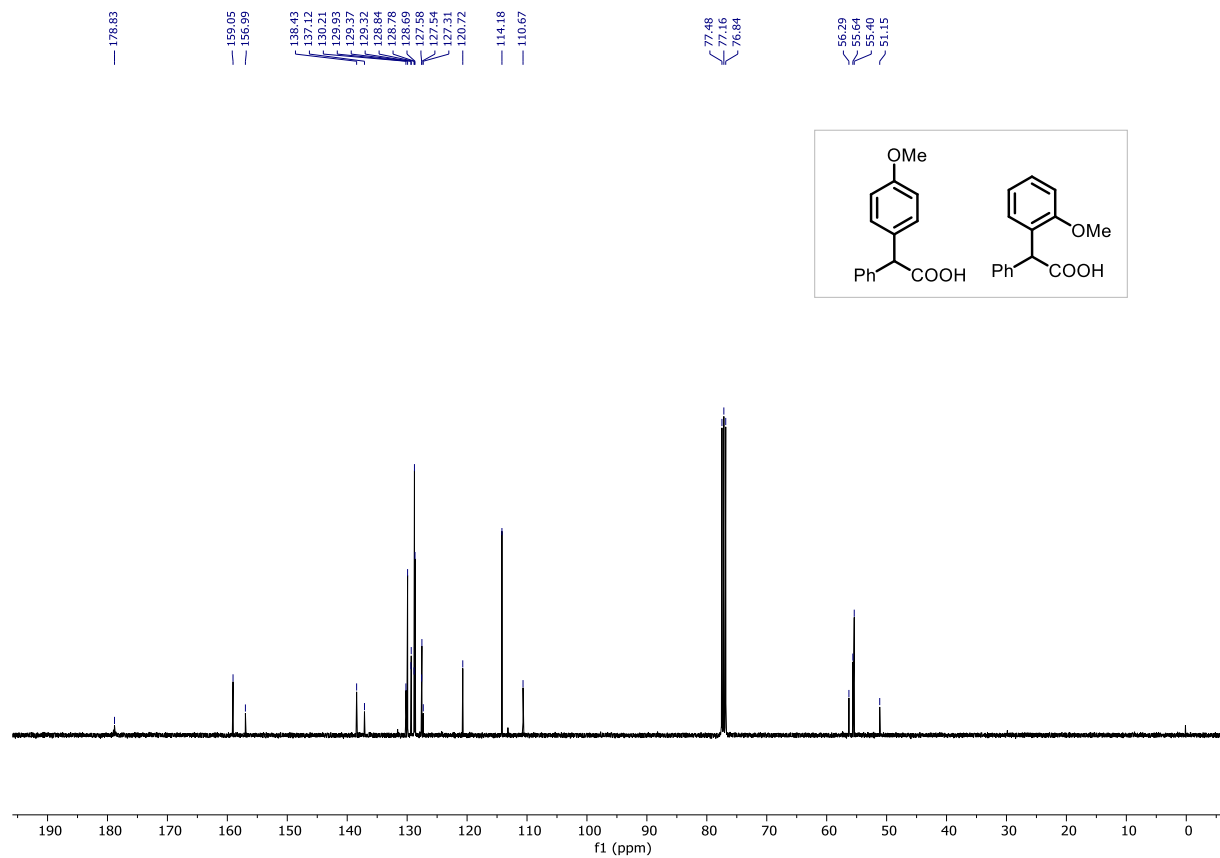
Jun11-2024_63.fid
jk phcl



2-(4-Methoxyphenyl)-2-phenylacetic acid & 2-(2-methoxyphenyl)-2-phenylacetic acid (3j)
¹H NMR (500 MHz, CDCl₃)

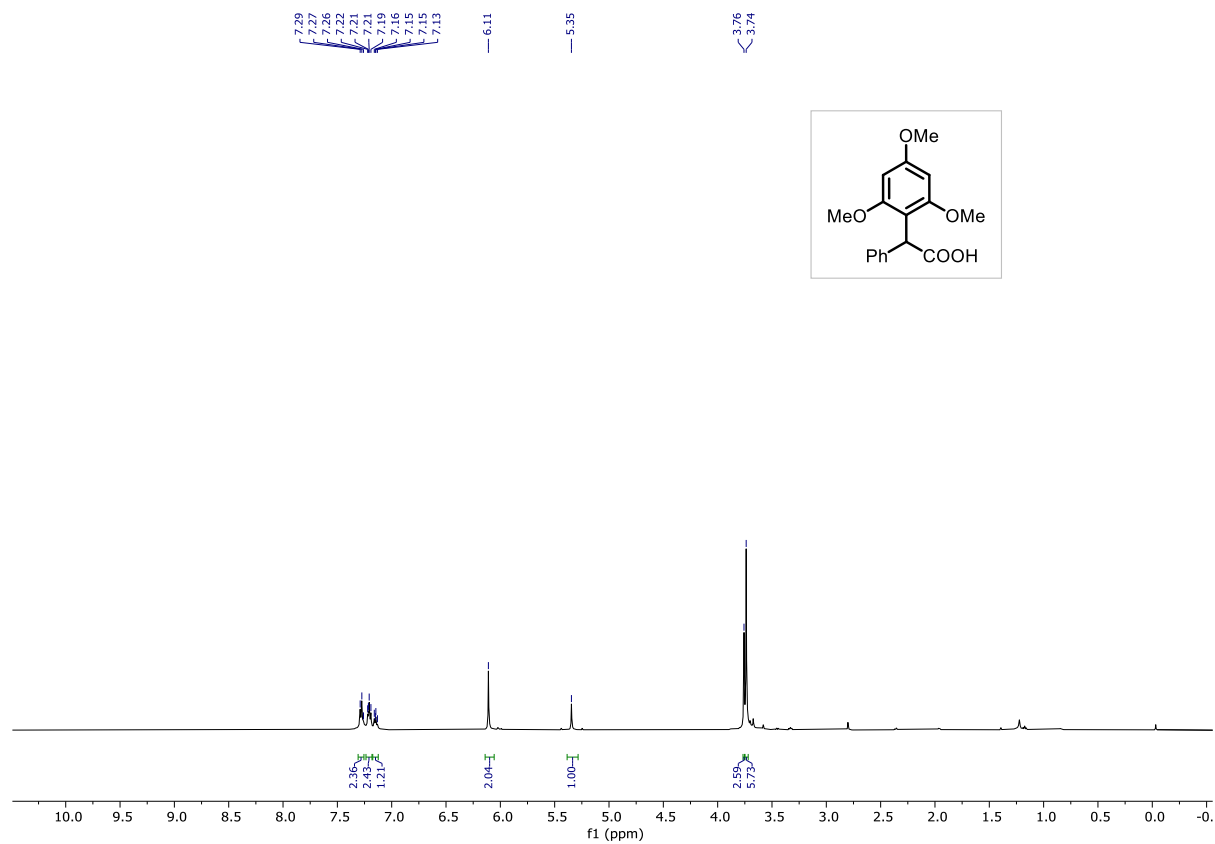


¹³C {¹H} NMR (101 MHz, CDCl₃)

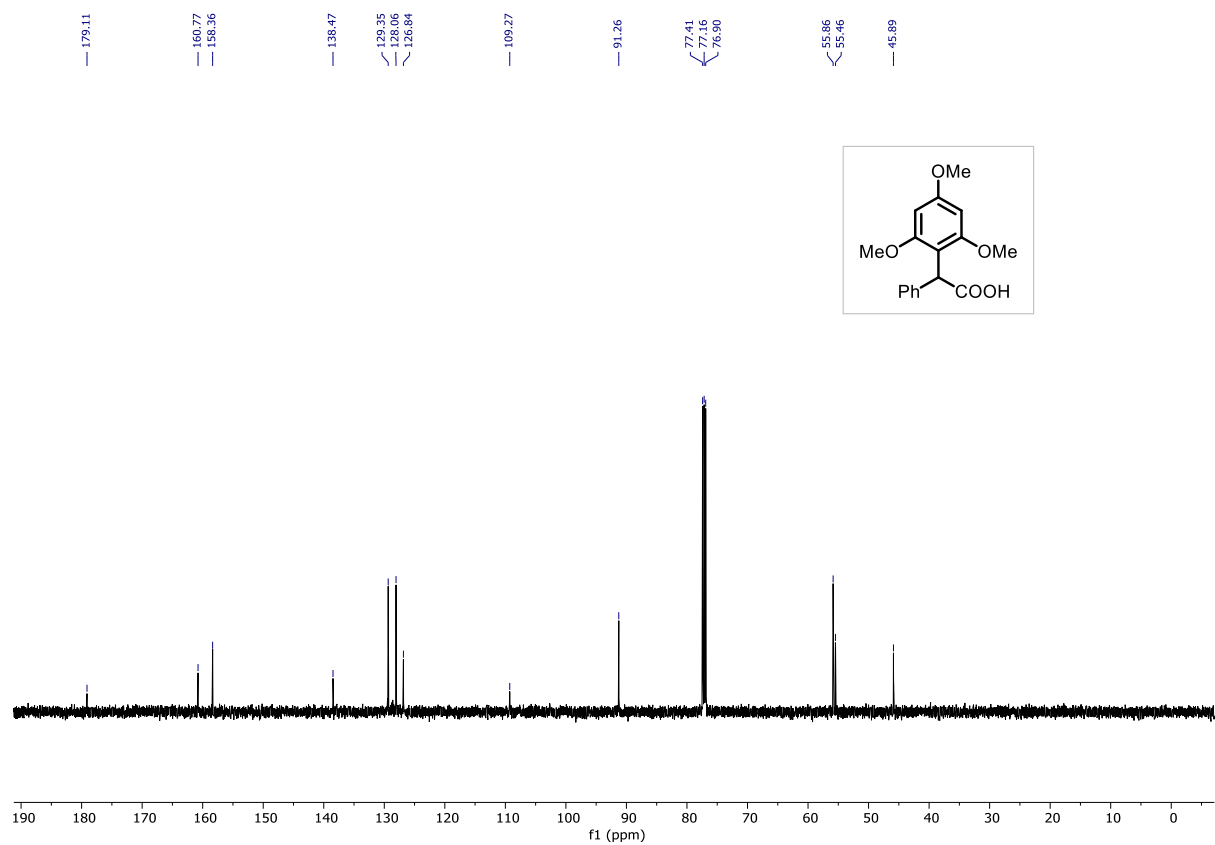


2-Phenyl-2-(2,4,6-trimethoxyphenyl) acetic acid (3k)

^1H NMR (500 MHz, CDCl_3)

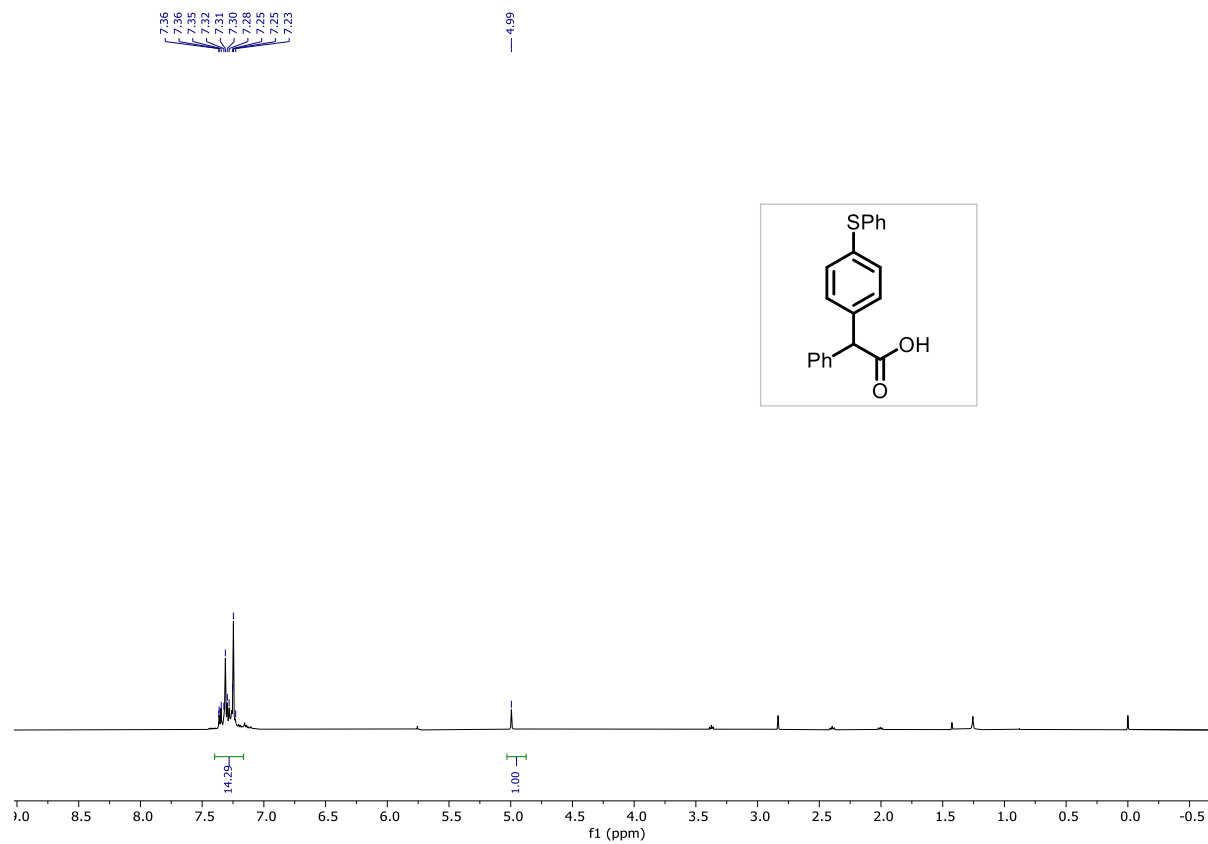


^{13}C { ^1H } NMR (126 MHz, CDCl_3)

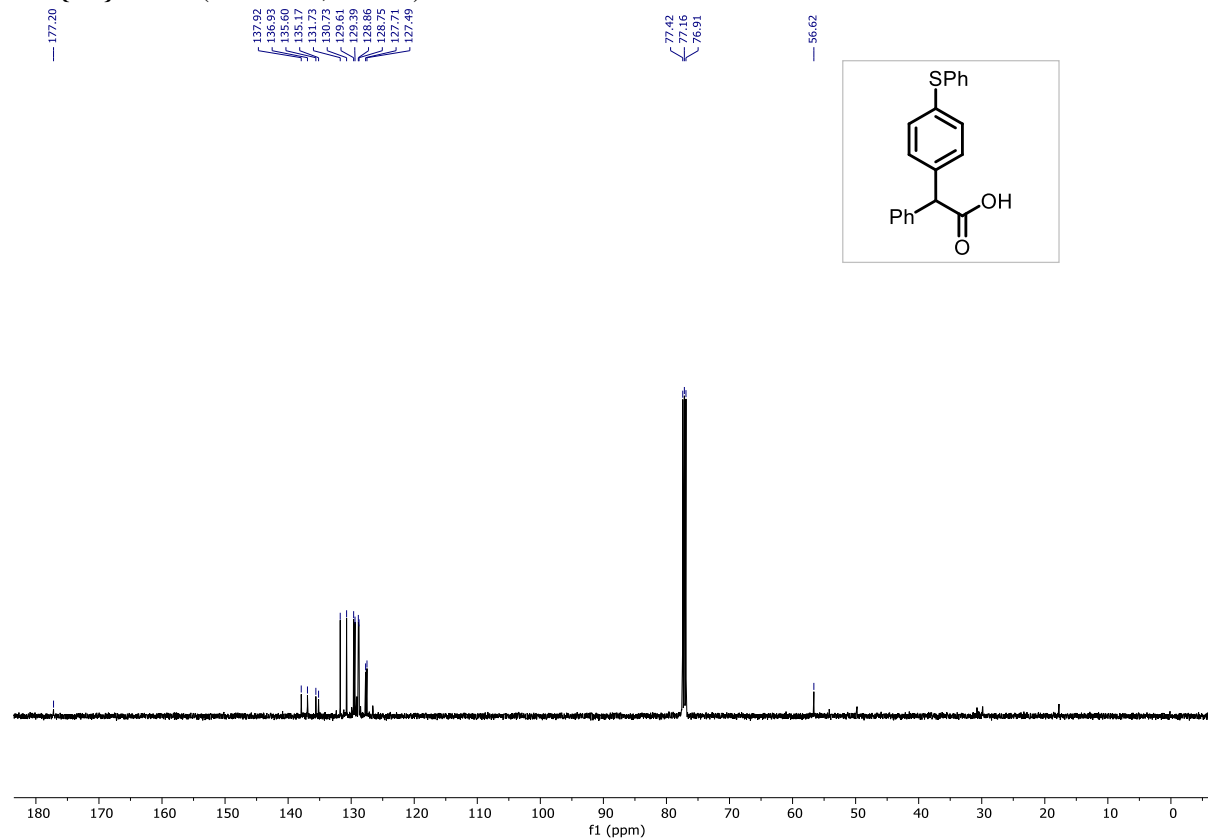


2-Phenyl-2-(4-(phenylthio) phenyl) acetic acid (3l)

^1H NMR (500 MHz, CDCl_3)

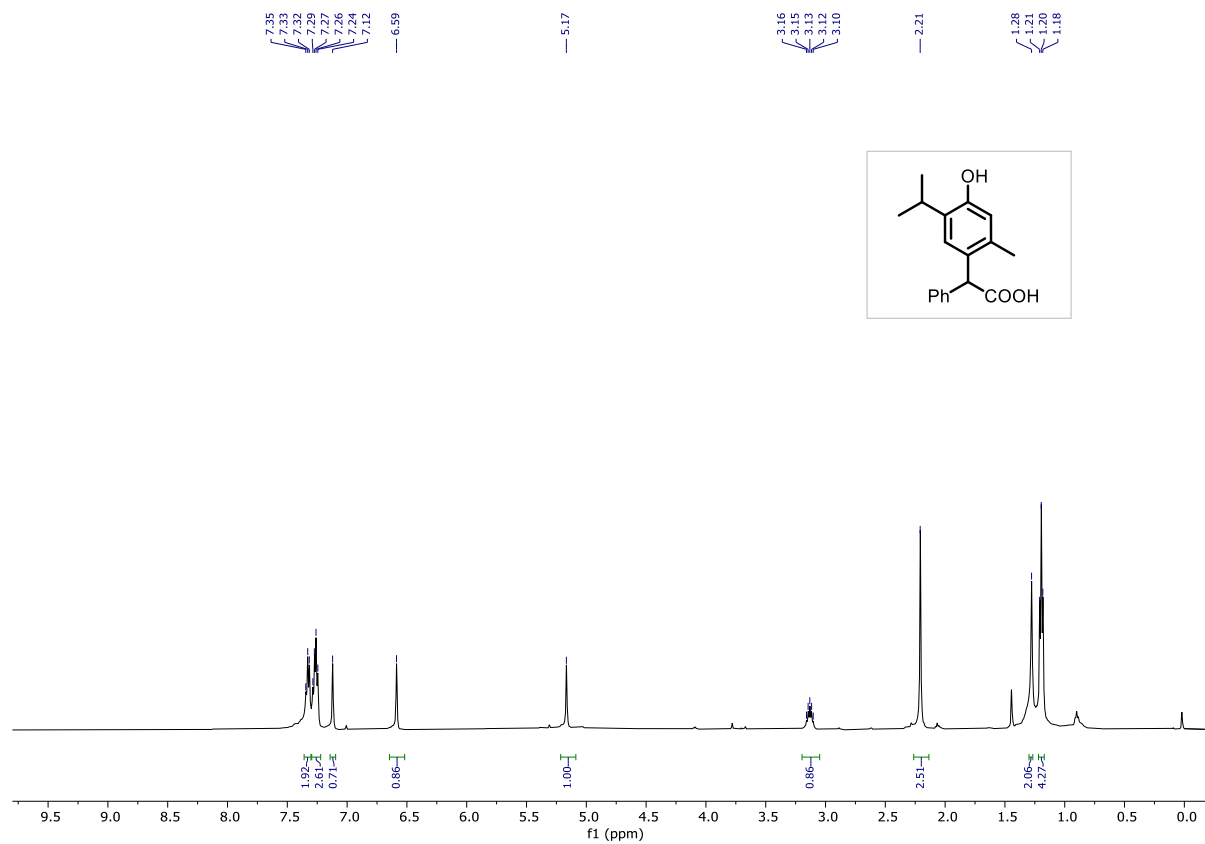


^{13}C $\{^1\text{H}\}$ NMR (126 MHz, CDCl_3)

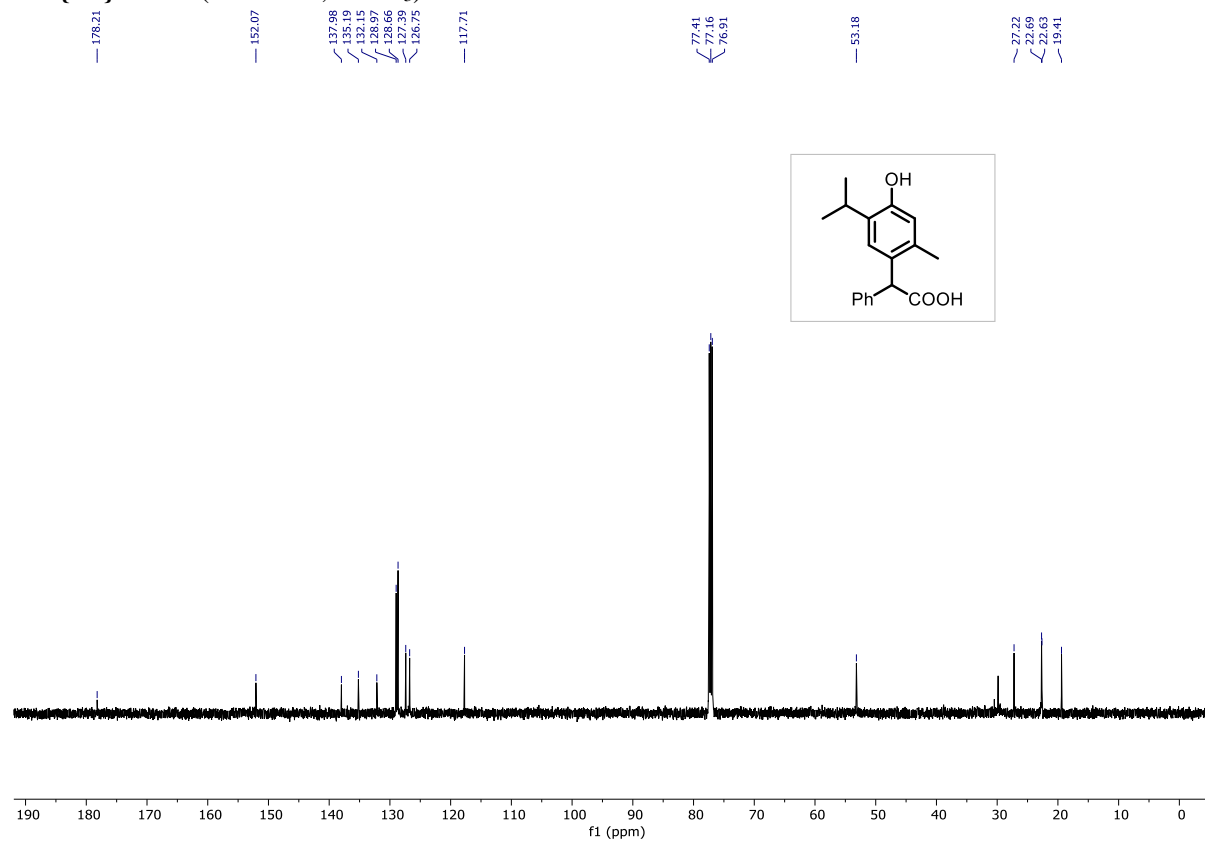


2-(4-Hydroxy-5-isopropyl-2-methylphenyl)-2-phenylacetic acid (3m)

^1H NMR (500 MHz, CDCl_3)

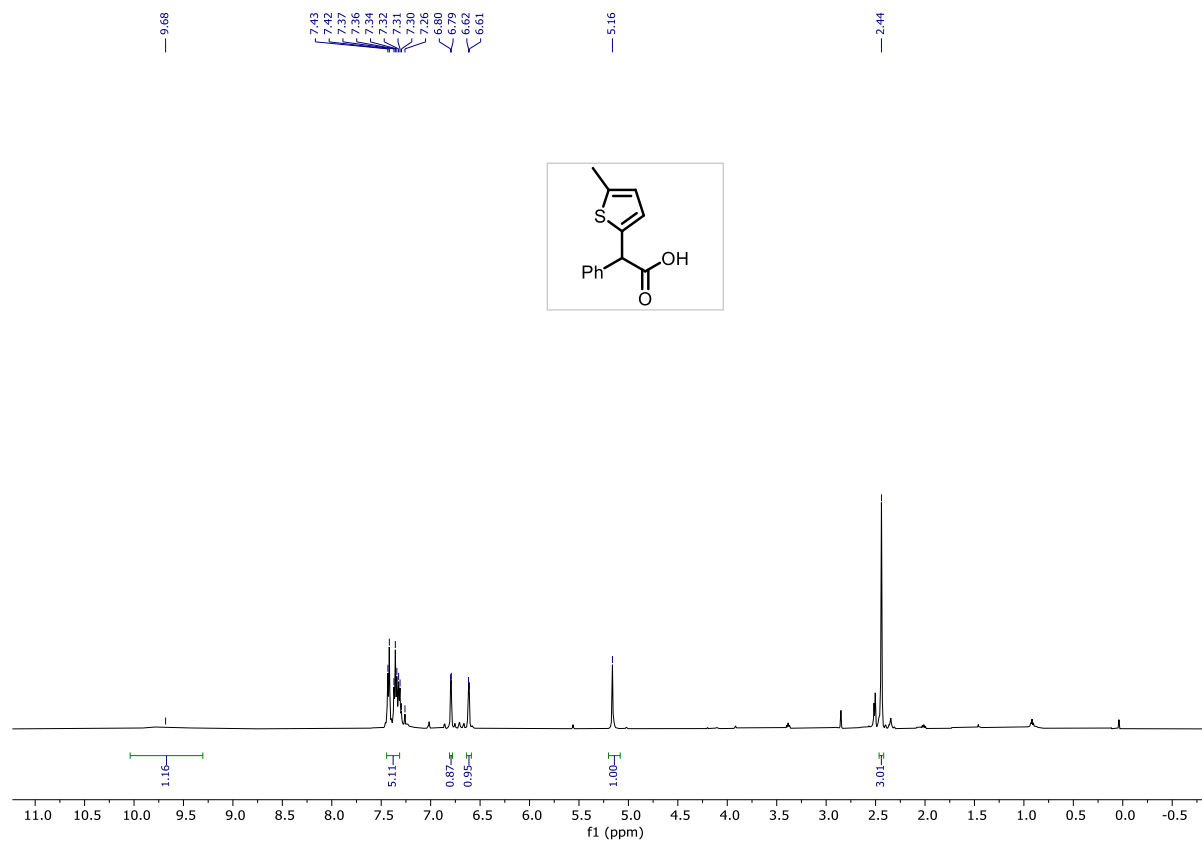


^{13}C { ^1H } NMR (126 MHz, CDCl_3)

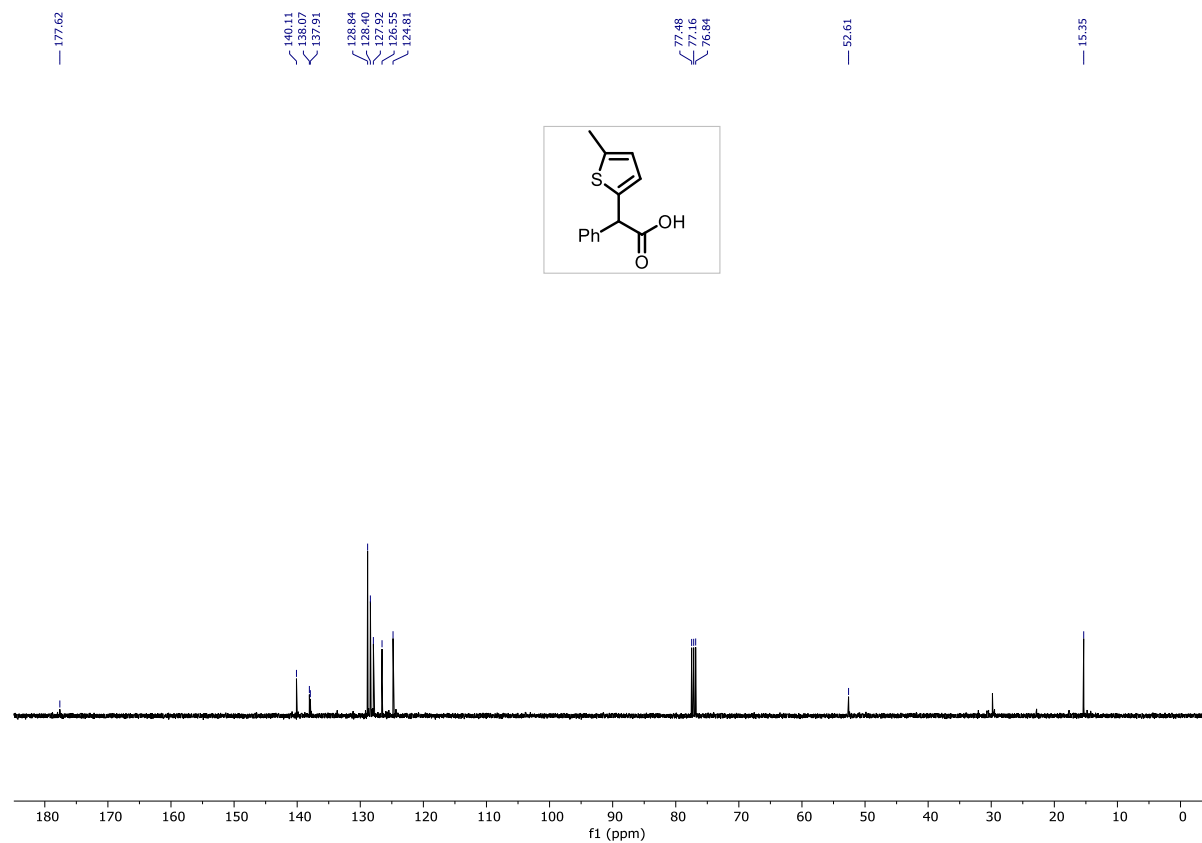


2-(5-Methylthiophen-2-yl)-2-phenylacetic acid (3n)

^1H NMR (500 MHz, CDCl_3)

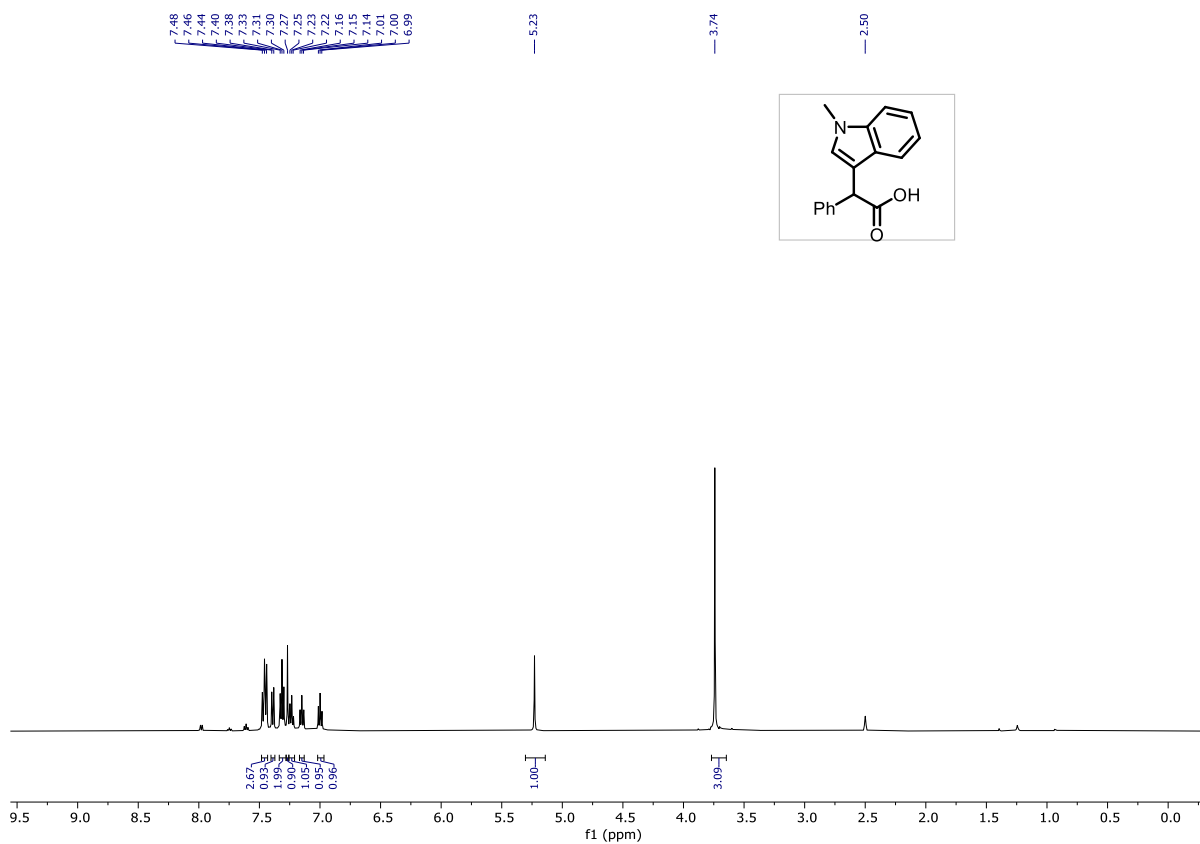


^{13}C { ^1H } NMR (126 MHz, CDCl_3)

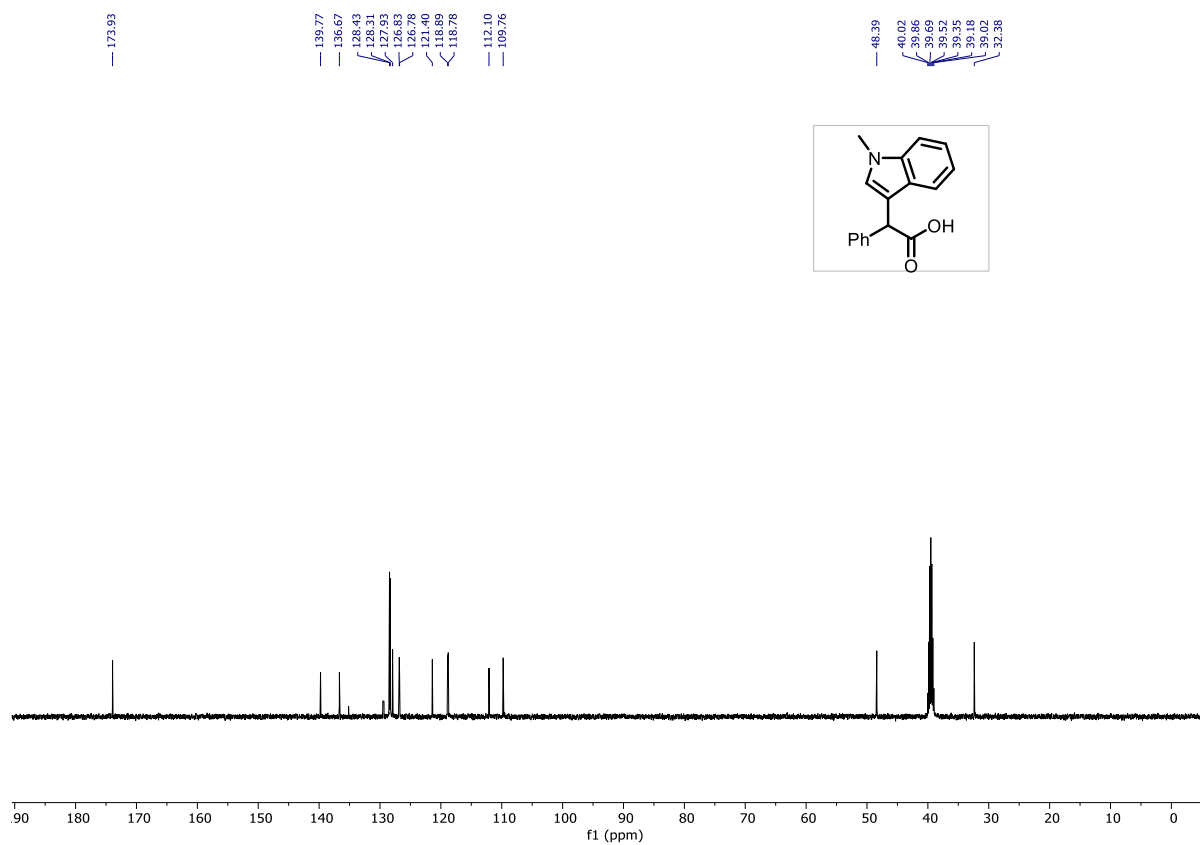


2-(1-Methyl-1*H*-indol-3-yl)-2-phenylacetic acid (3o)

^1H NMR (500 MHz, $\text{DMSO-}d_6$)

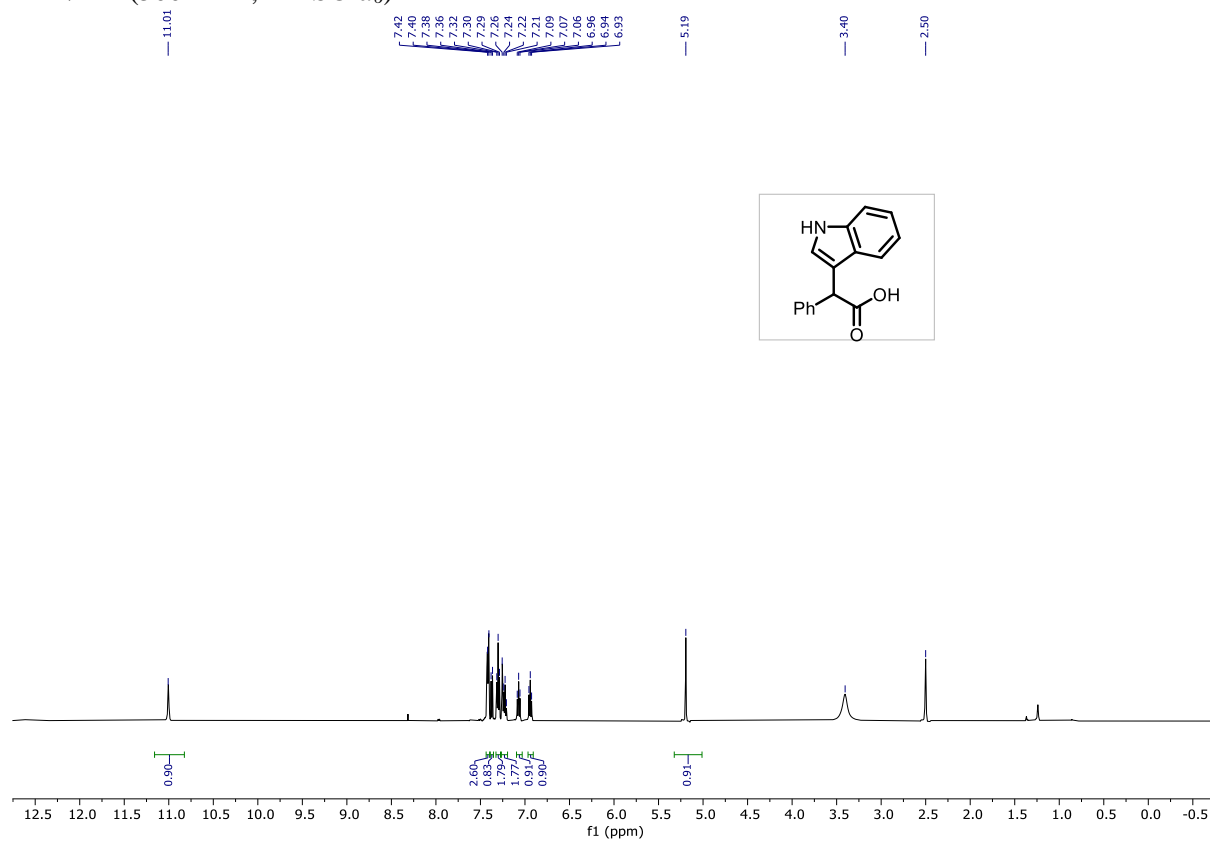


^{13}C NMR (126 MHz, $\text{DMSO-}d_6$)

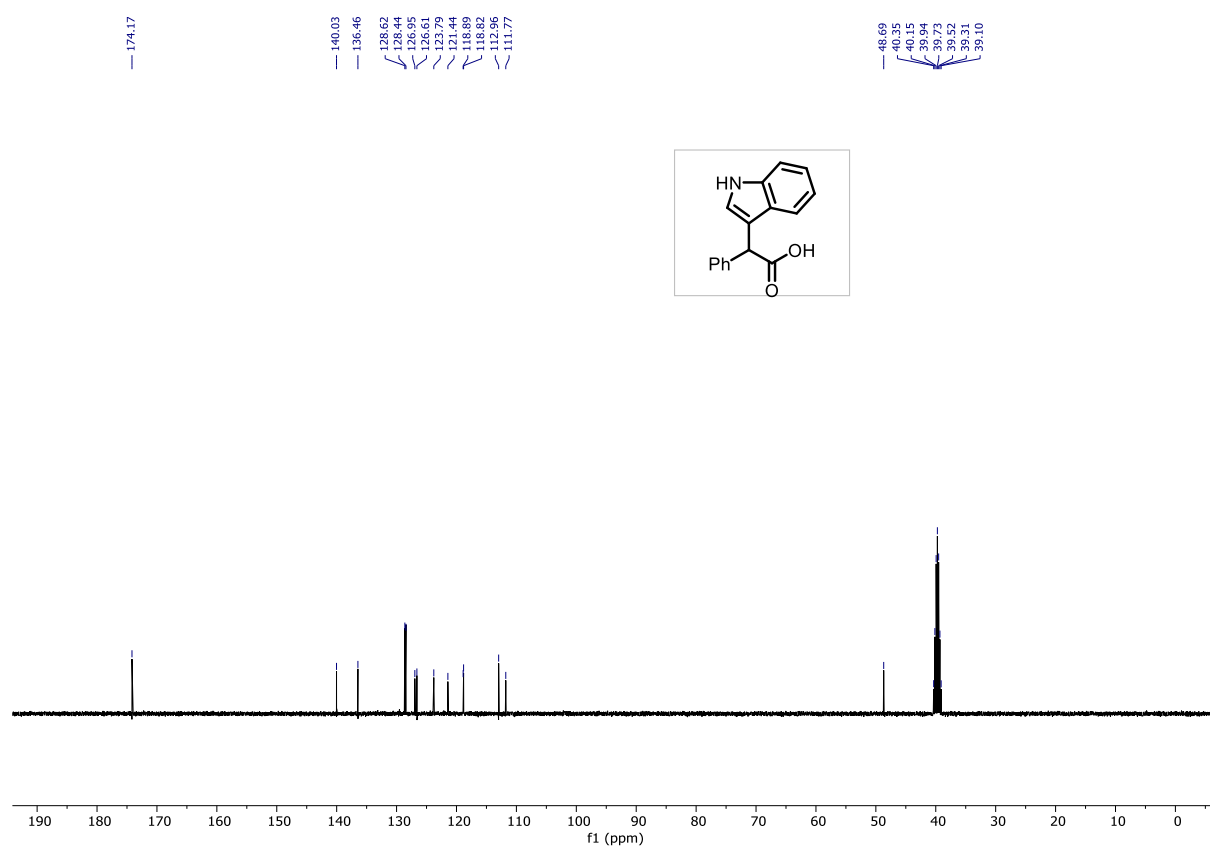


2-(1*H*-indol-3-yl)-2-phenylacetic acid (3p)

¹H NMR (500 MHz, DMSO-*d*₆)

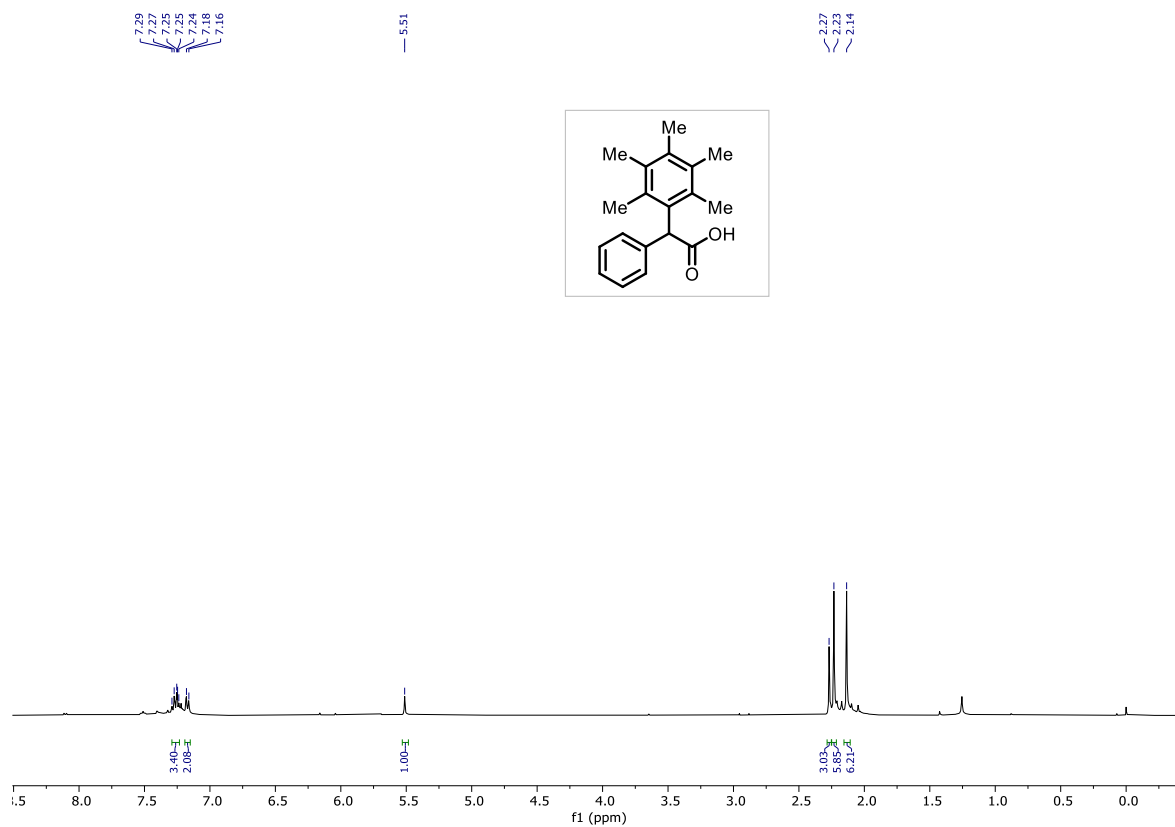


¹³C NMR (101 MHz, DMSO-*d*₆)

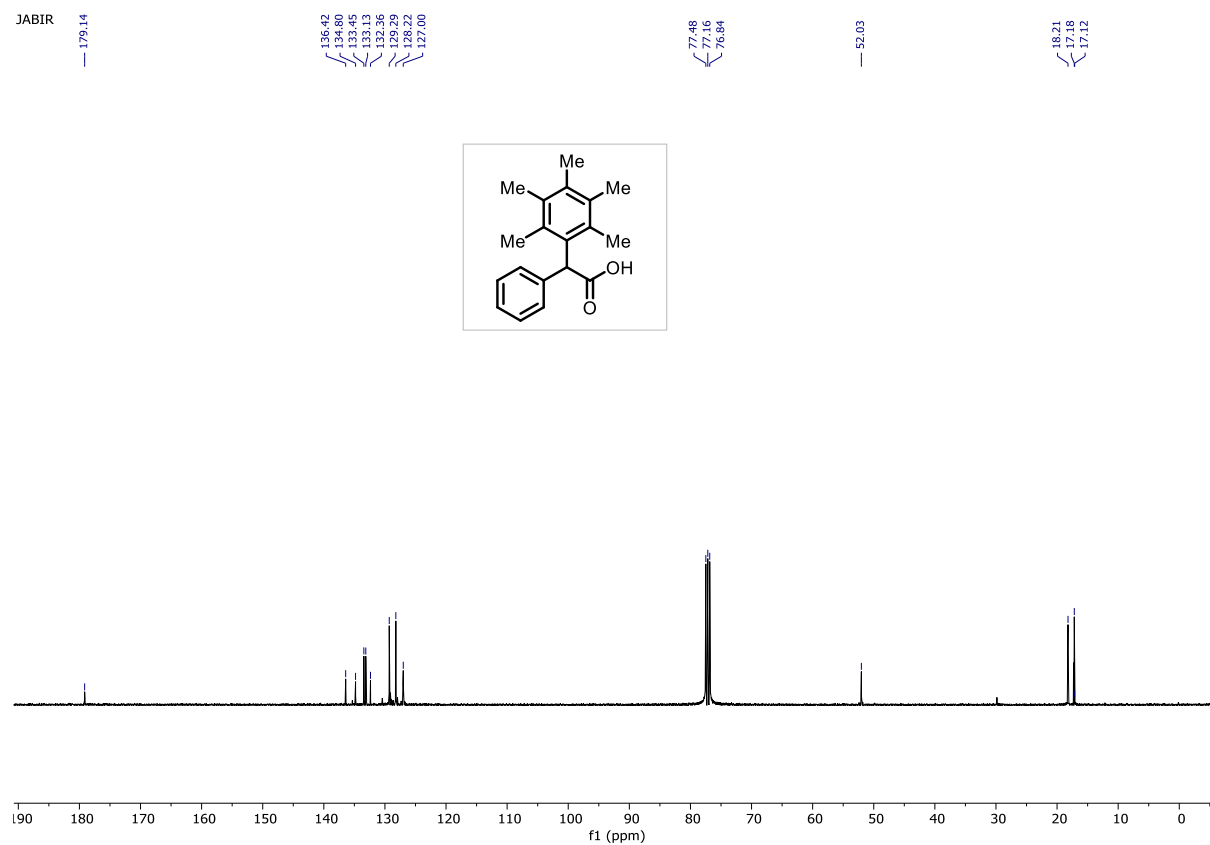


2-(2,3,4,5,6-pentamethyl-phenyl)-2-phenylacetic acid (3q)

^1H NMR (400 MHz, CDCl_3)

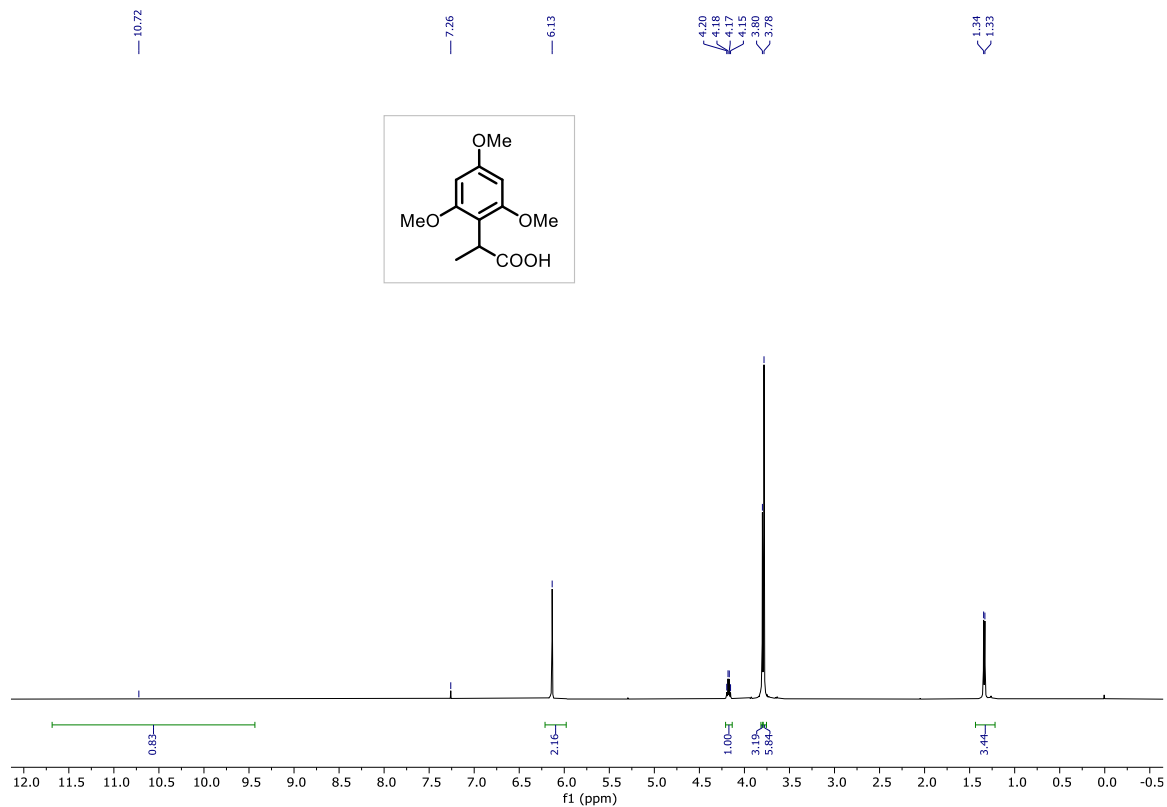


^{13}C $\{^1\text{H}\}$ NMR (101 MHz, CDCl_3)

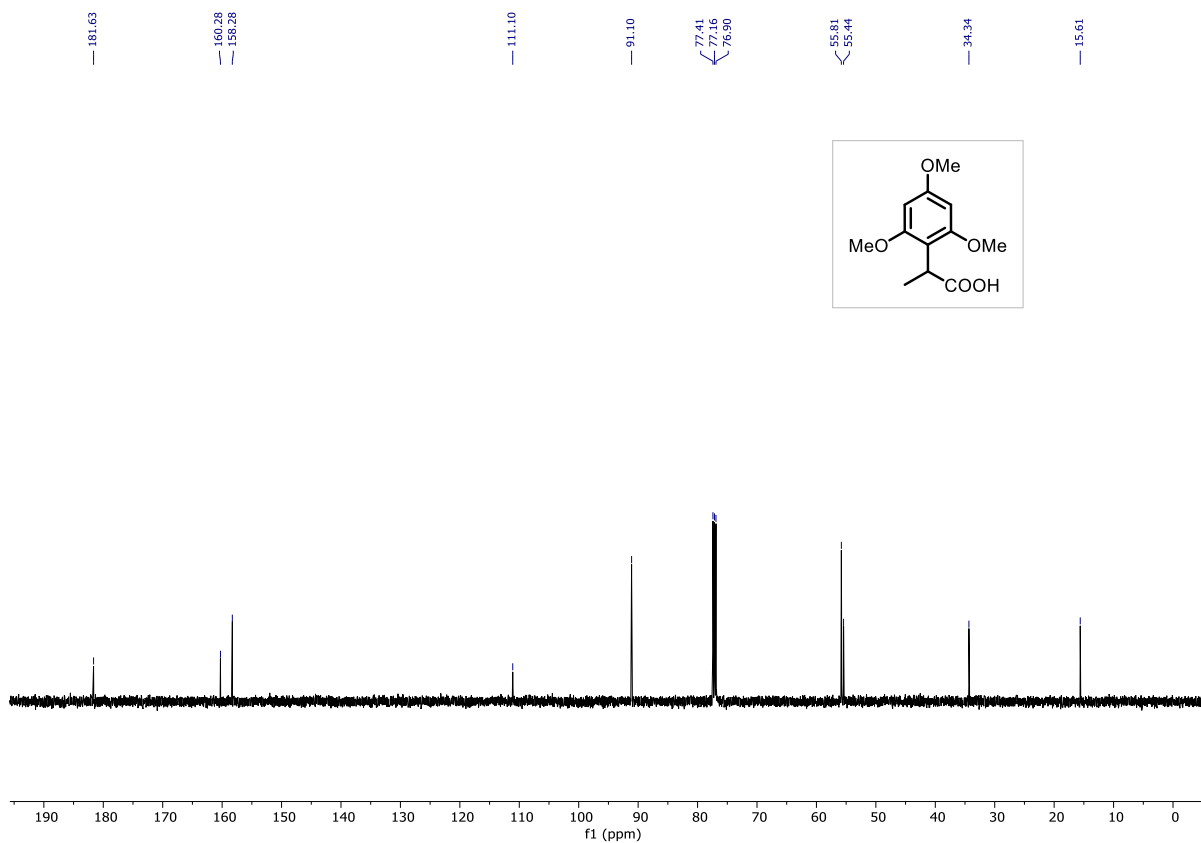


2-(2,4,6-Trimethoxyphenyl) propanoic acid (3r)

^1H NMR (500 MHz, CDCl_3)

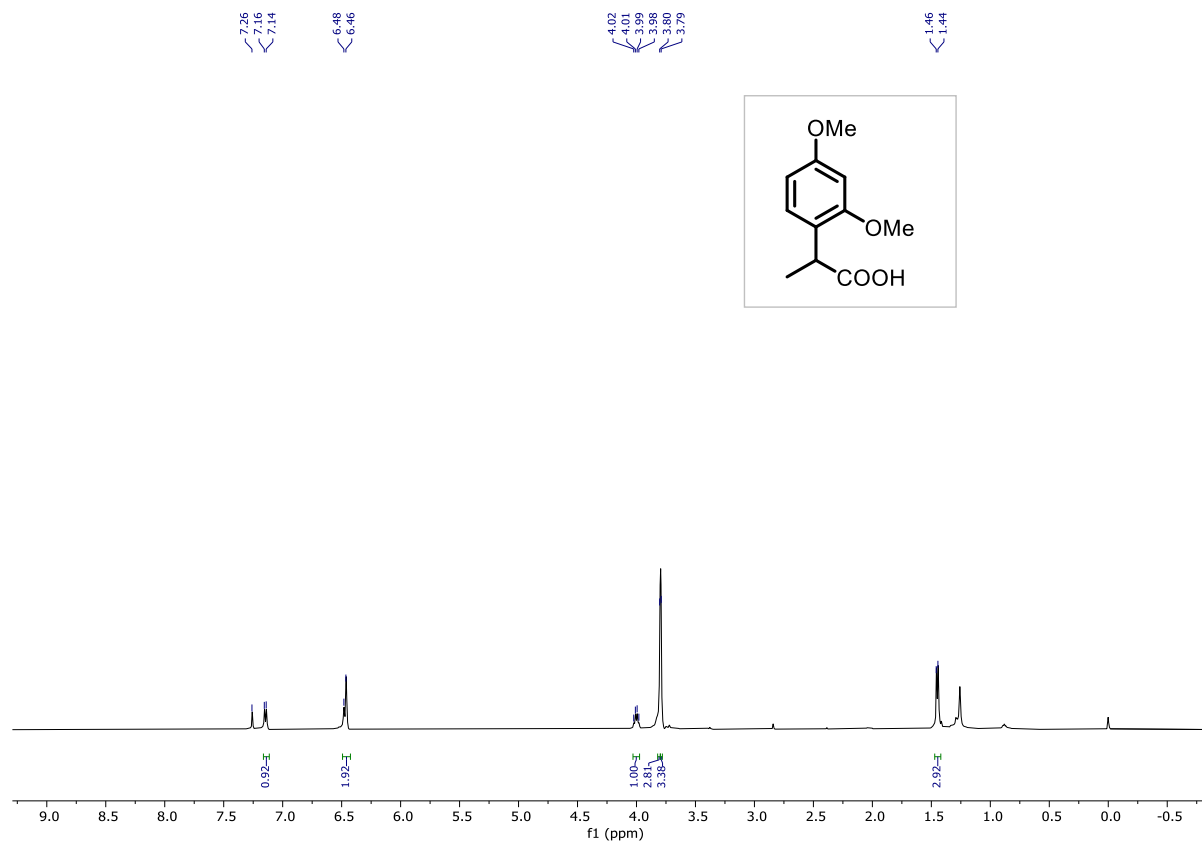


^{13}C { ^1H } NMR (126 MHz, CDCl_3)

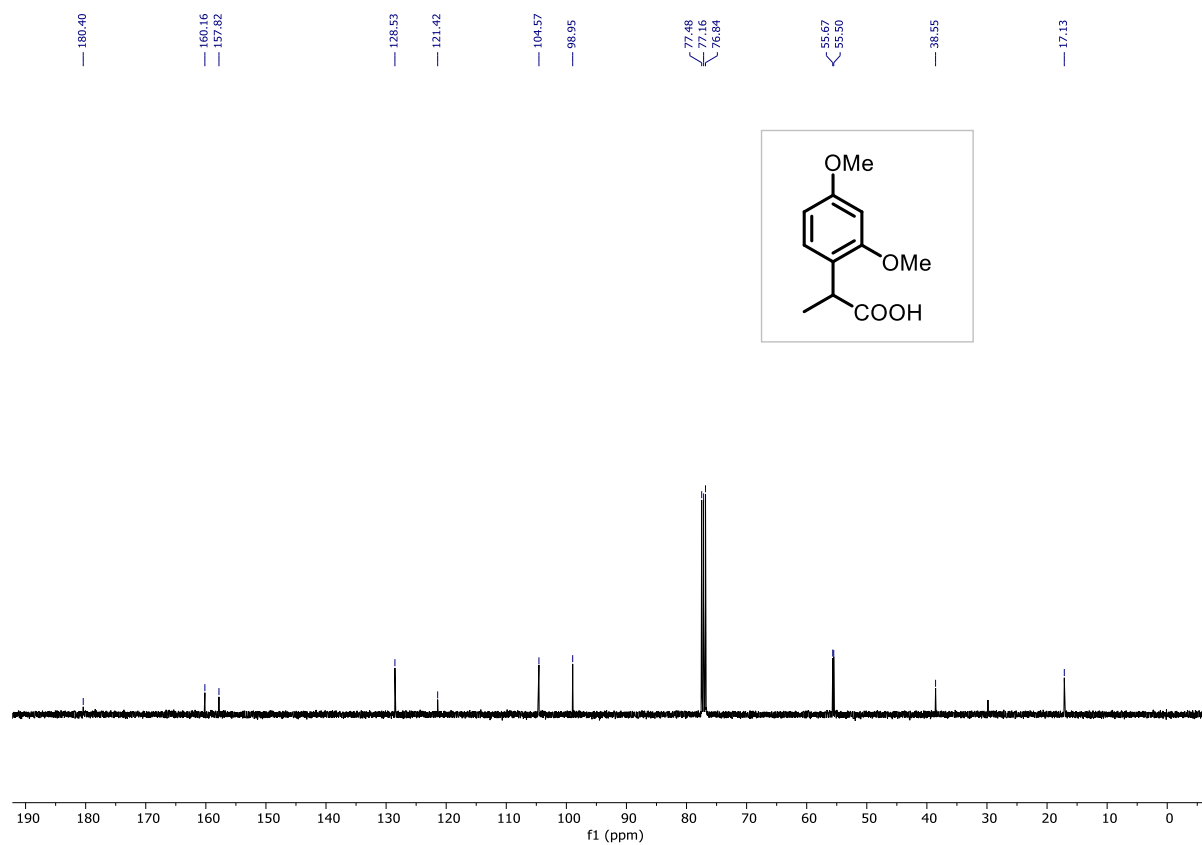


2-(2,4-Dimethoxyphenyl) propanoic acid (3s)

^1H NMR (500 MHz, CDCl_3)

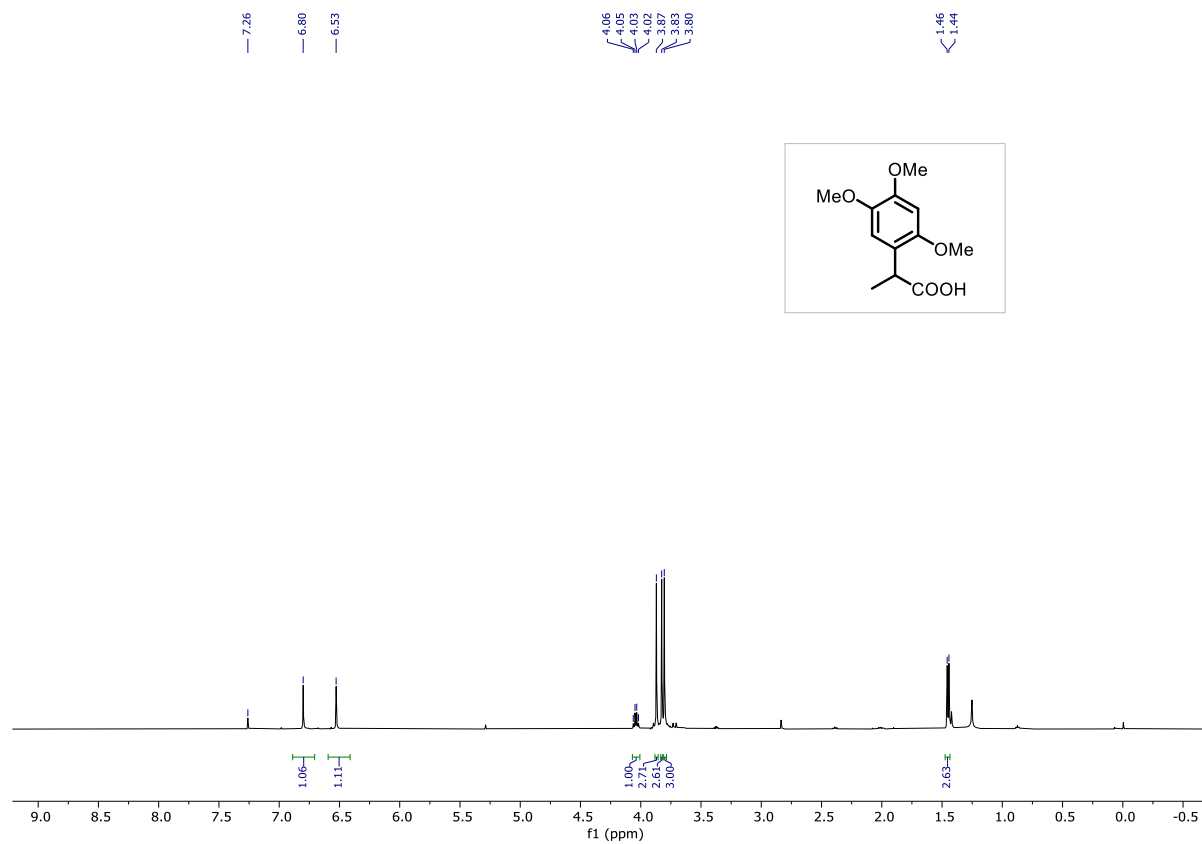


^{13}C $\{^1\text{H}\}$ NMR (101 MHz, CDCl_3)

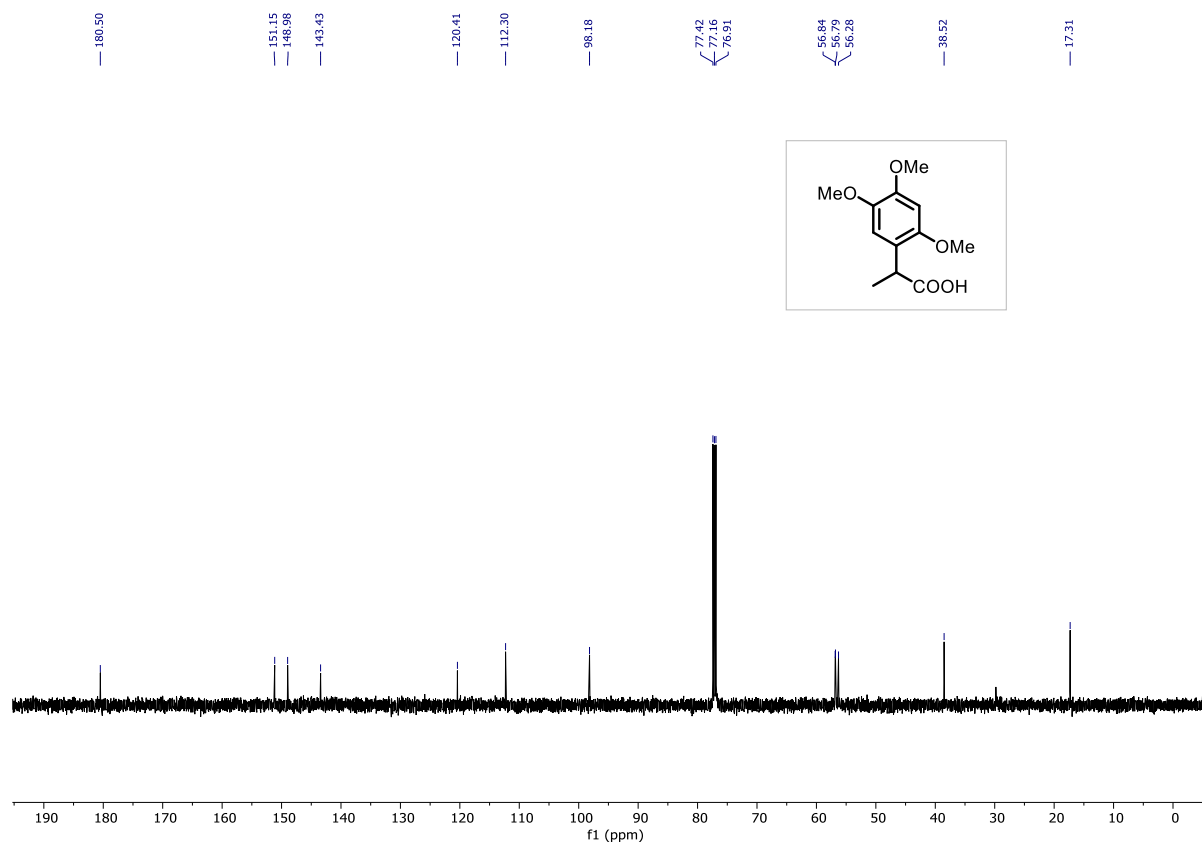


2-(2,4,5-Trimethoxyphenyl) propanoic acid (3t)

^1H NMR (500 MHz, CDCl_3)

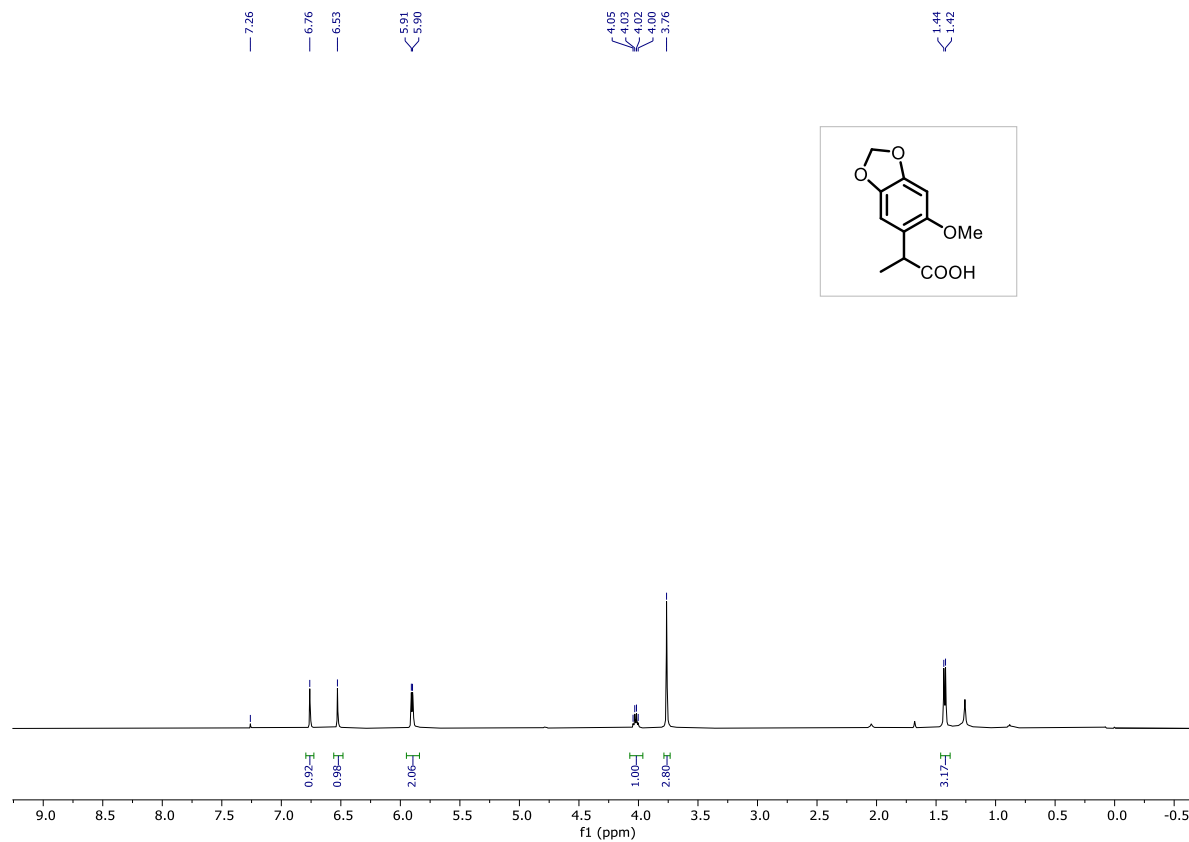


^{13}C $\{^1\text{H}\}$ NMR (126 MHz, CDCl_3)

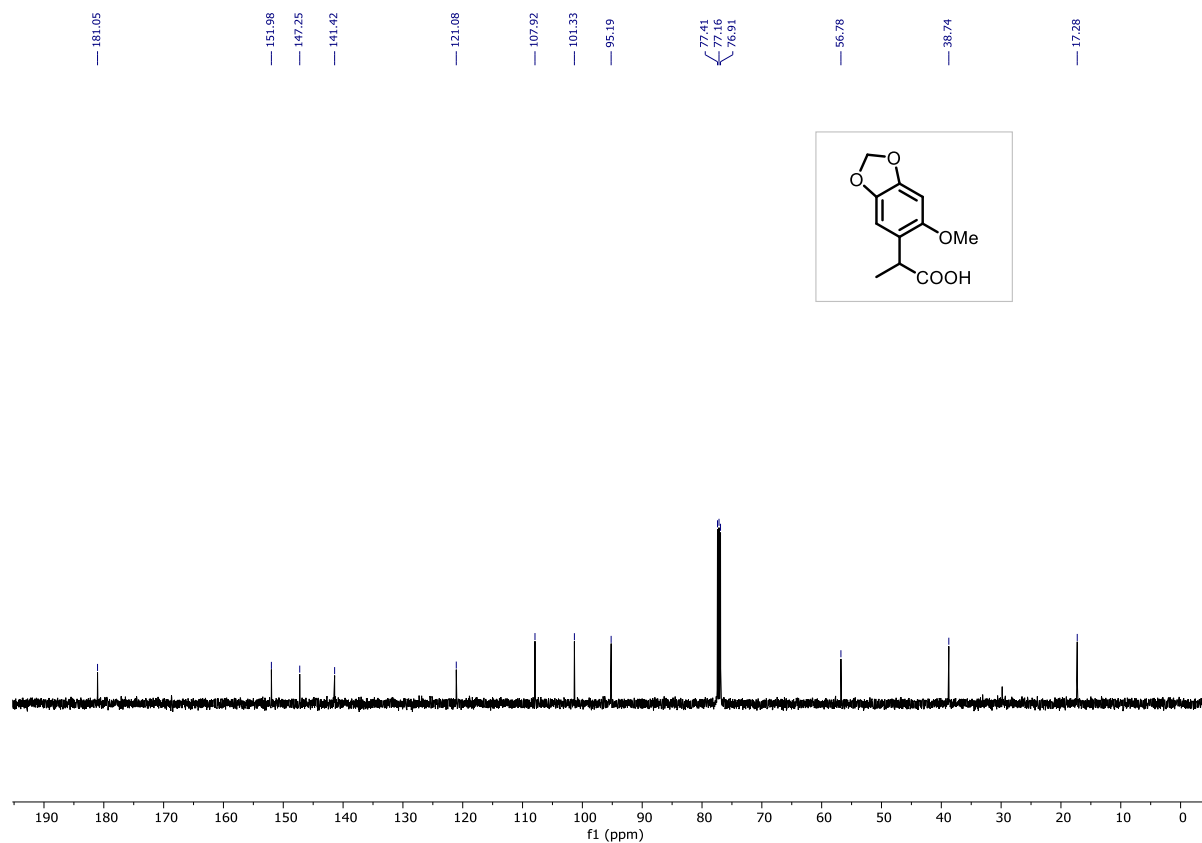


2-(6-Methoxybenzo[d][1,3]-dioxol-5-yl)propanoic acid (3u)

^1H NMR (500 MHz, CDCl_3)

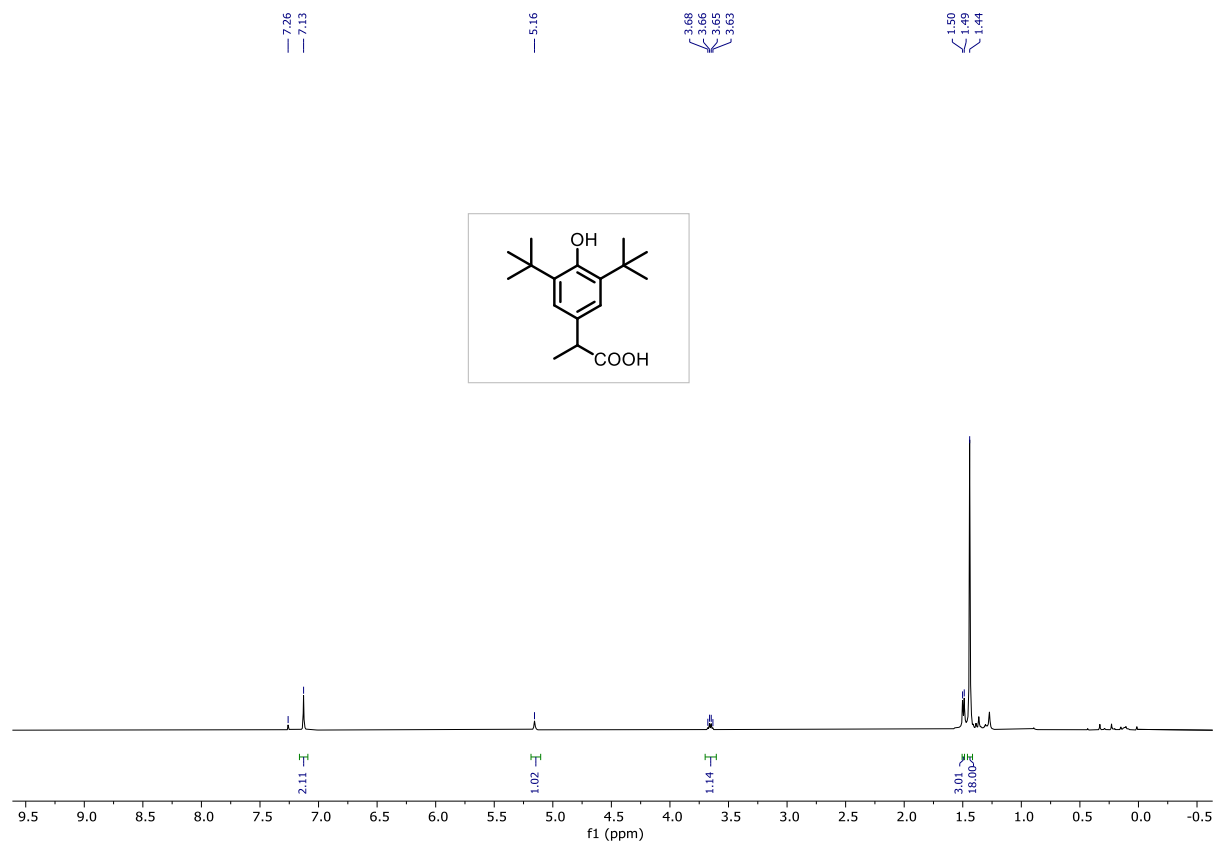


^{13}C { ^1H } NMR (126 MHz, CDCl_3)

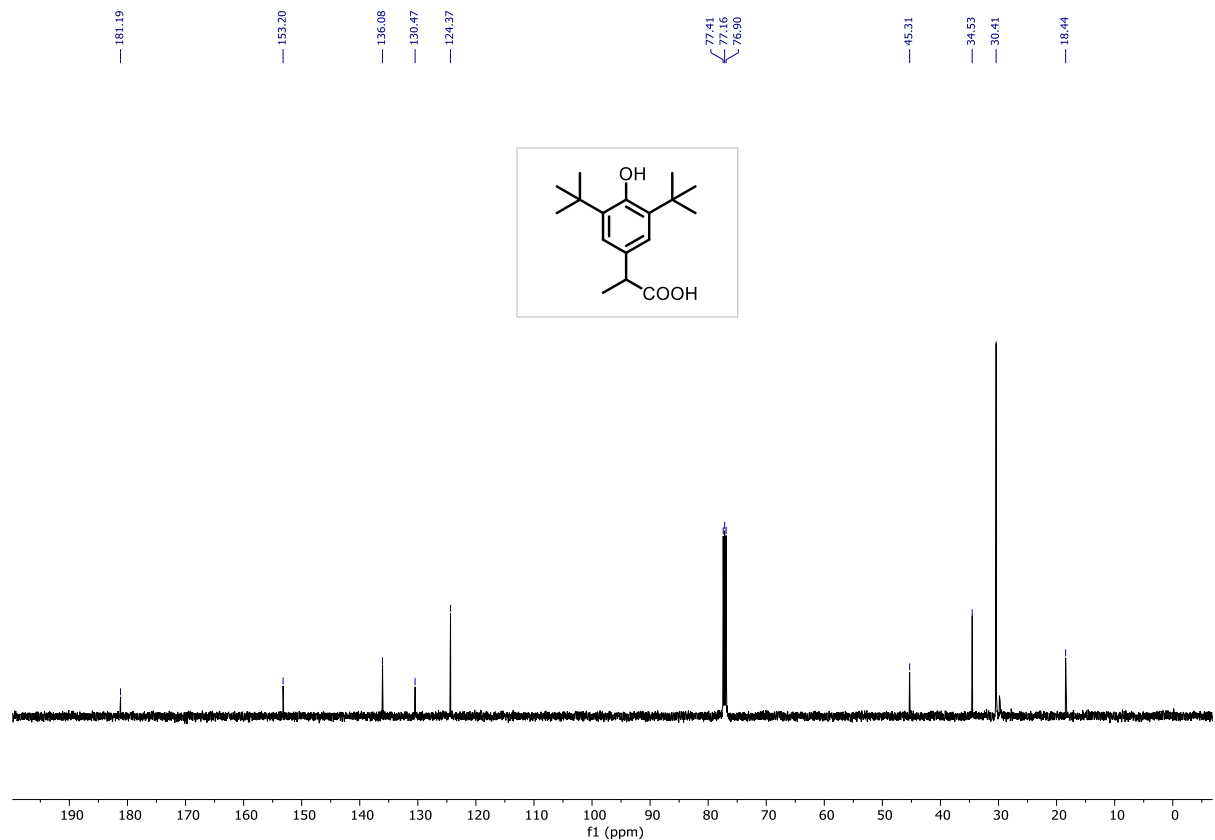


2-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)propanoic acid (3v)

^1H NMR (500 MHz, CDCl_3)

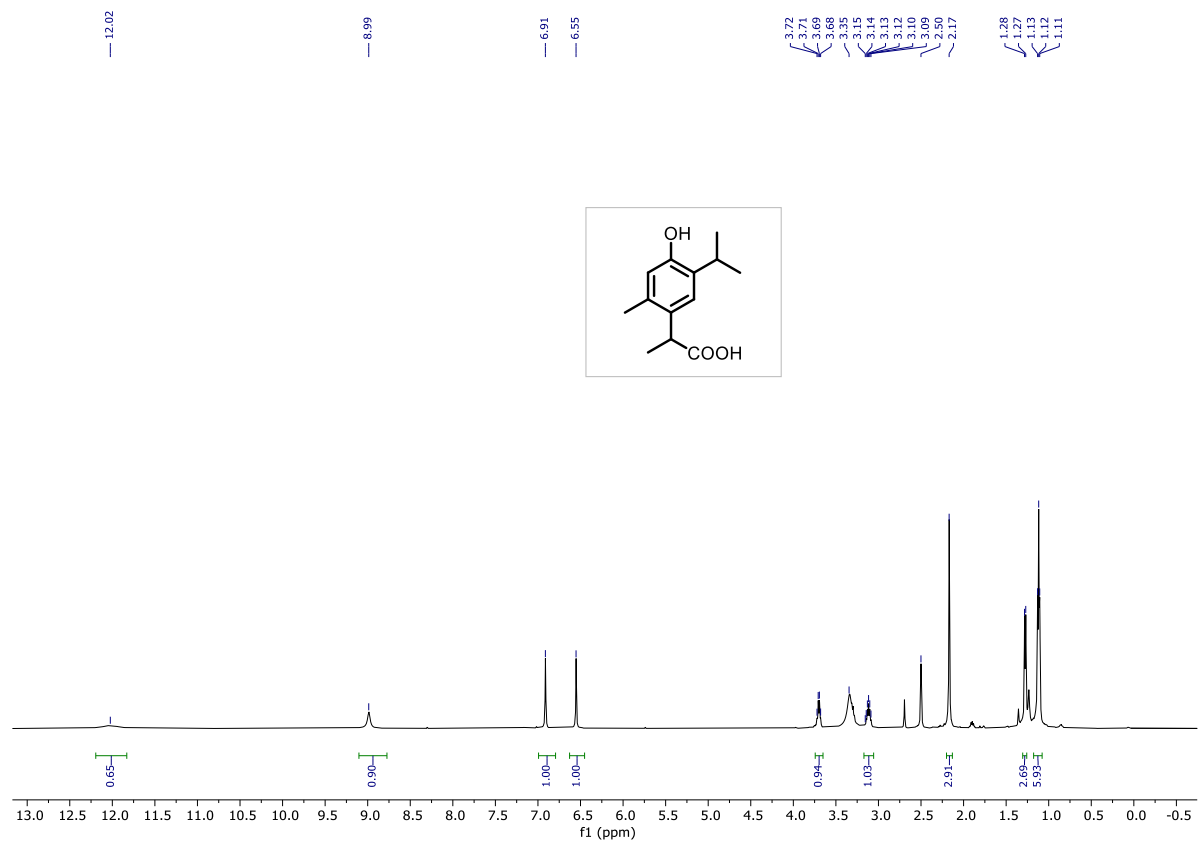


^{13}C { ^1H } NMR (101 MHz, CDCl_3)

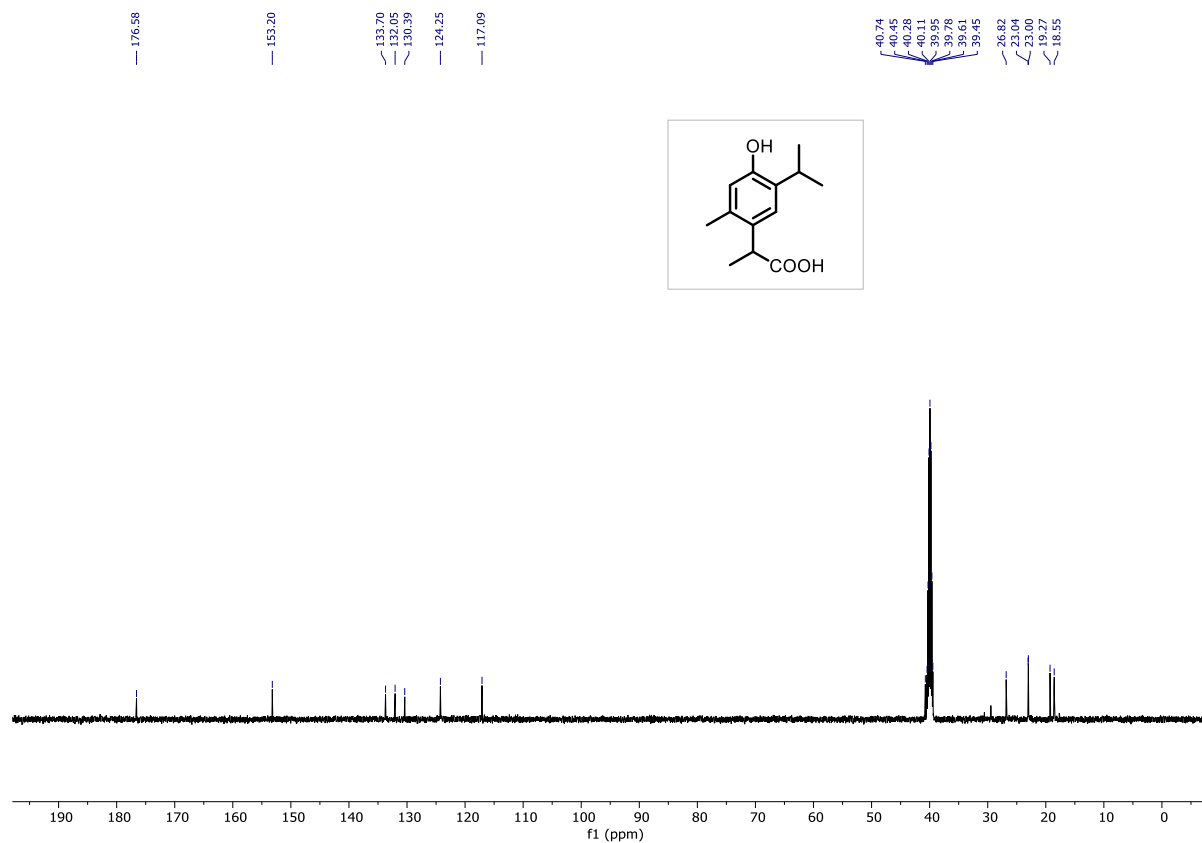


2-(4-Hydroxy-5-isopropyl-2-methylphenyl)propanoic acid (3w)

^1H NMR (500 MHz, $\text{DMSO-}d_6$)

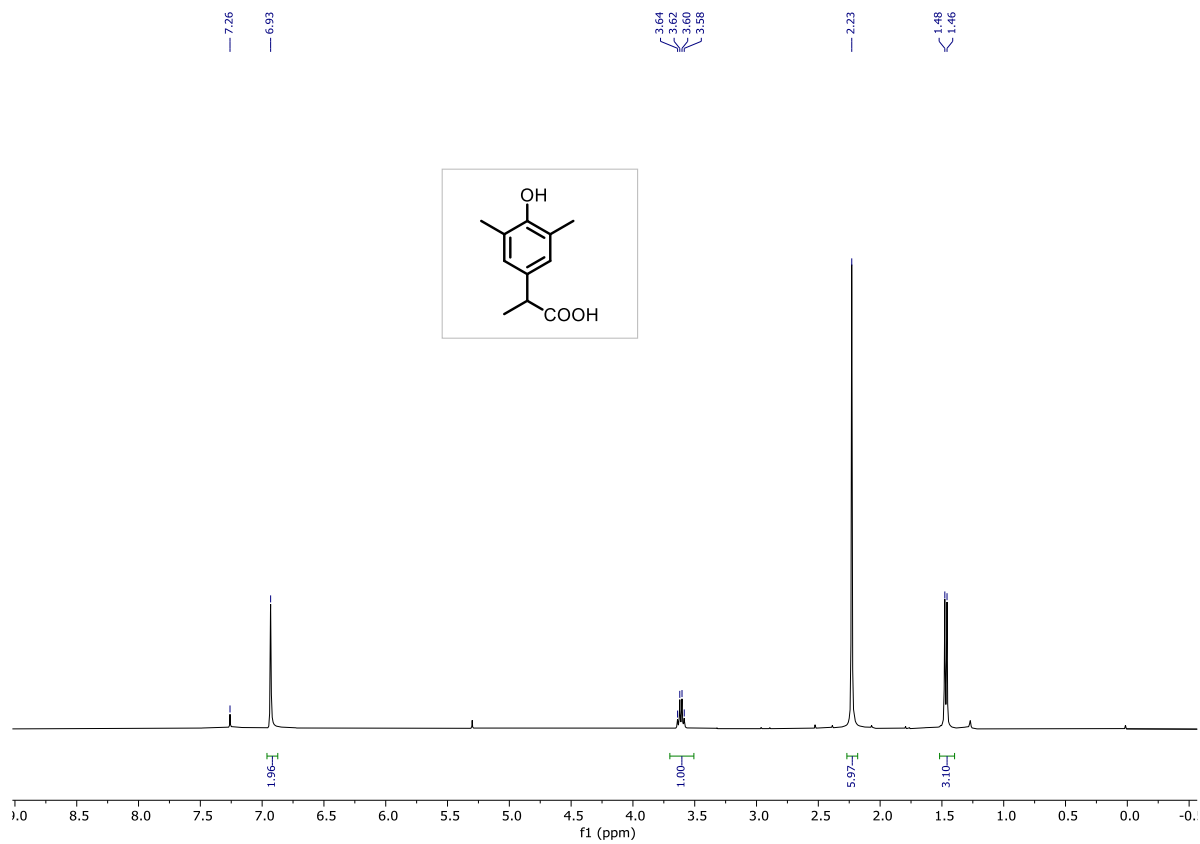


^{13}C { ^1H } NMR (126 MHz, $\text{DMSO-}d_6$)

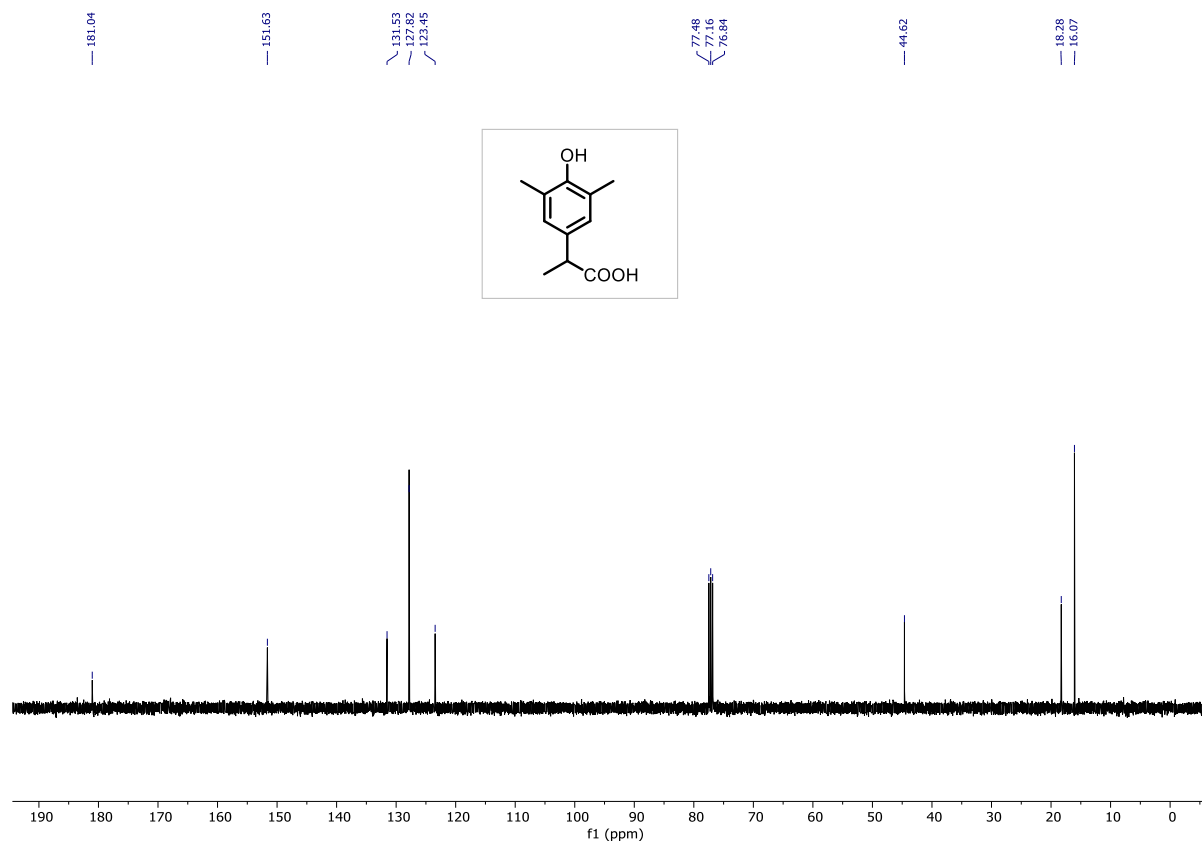


2-(4-Hydroxy-3,5-dimethylphenyl) propanoic acid (3x)

^1H NMR (500 MHz, CDCl_3)

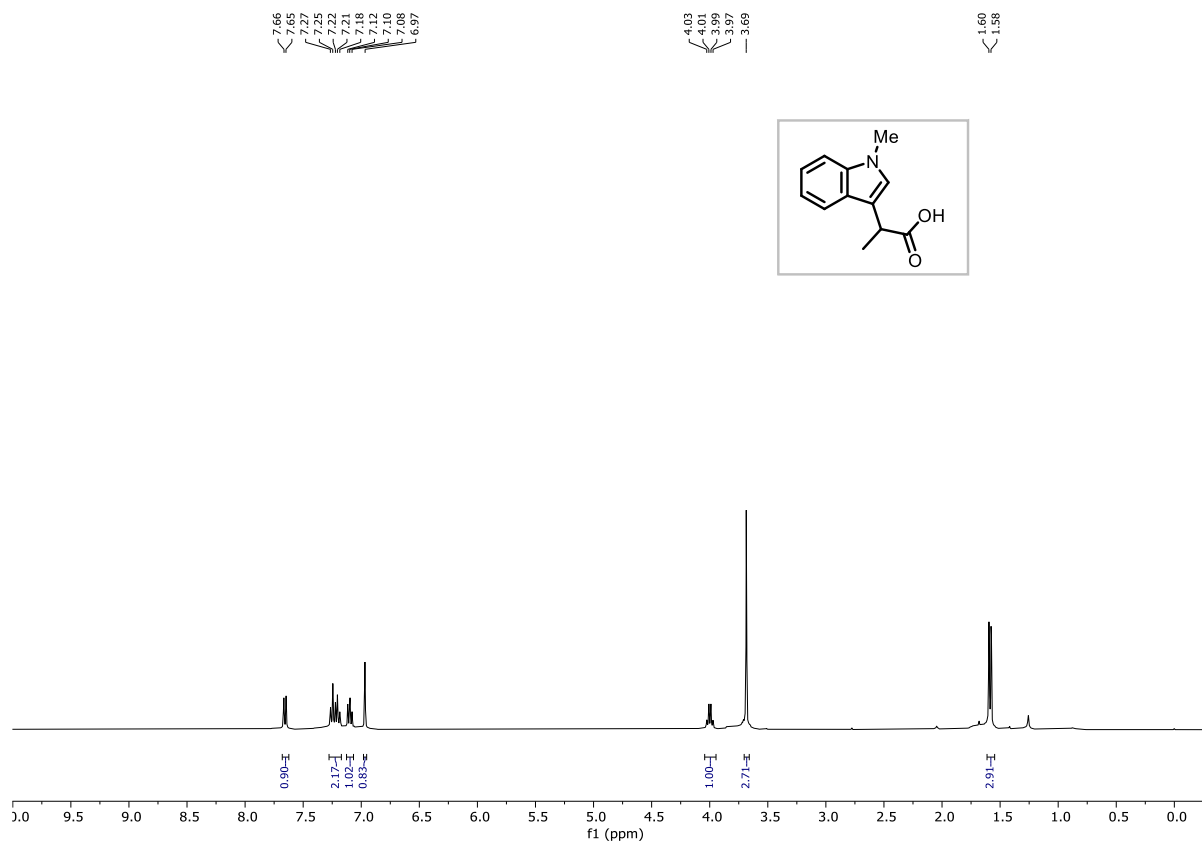


^{13}C { ^1H } NMR (126 MHz, CDCl_3)

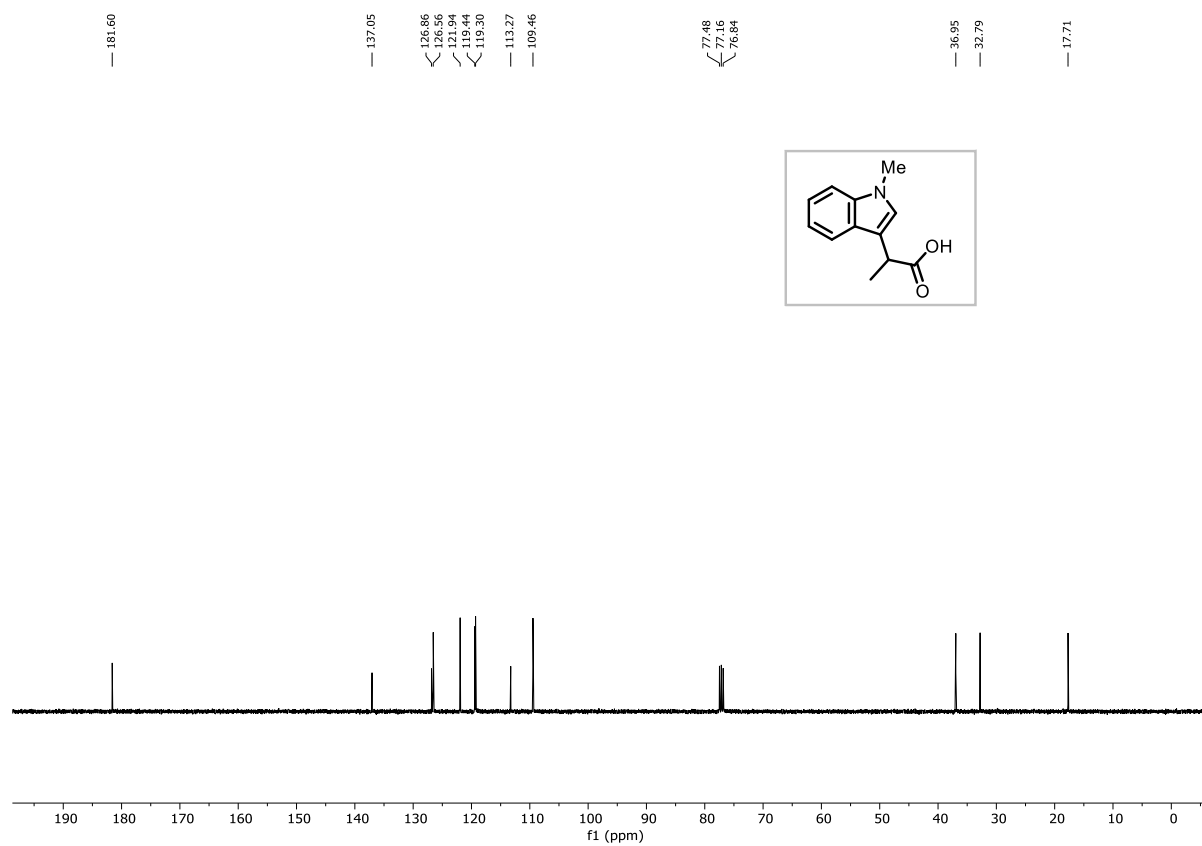


2-(1-Methyl-1*H*-indol-3-yl) propanoic acid (**3y**)

^1H NMR (400 MHz, CHCl_3)

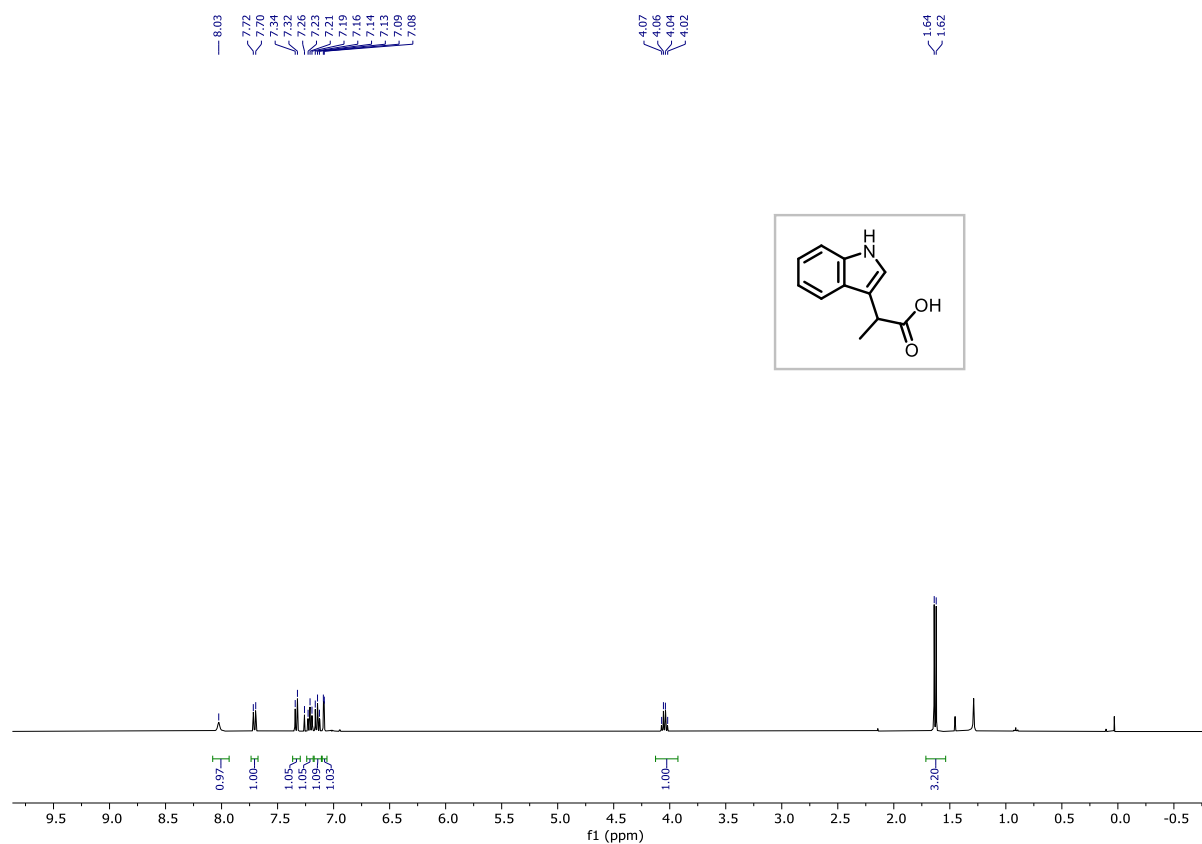


$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3)

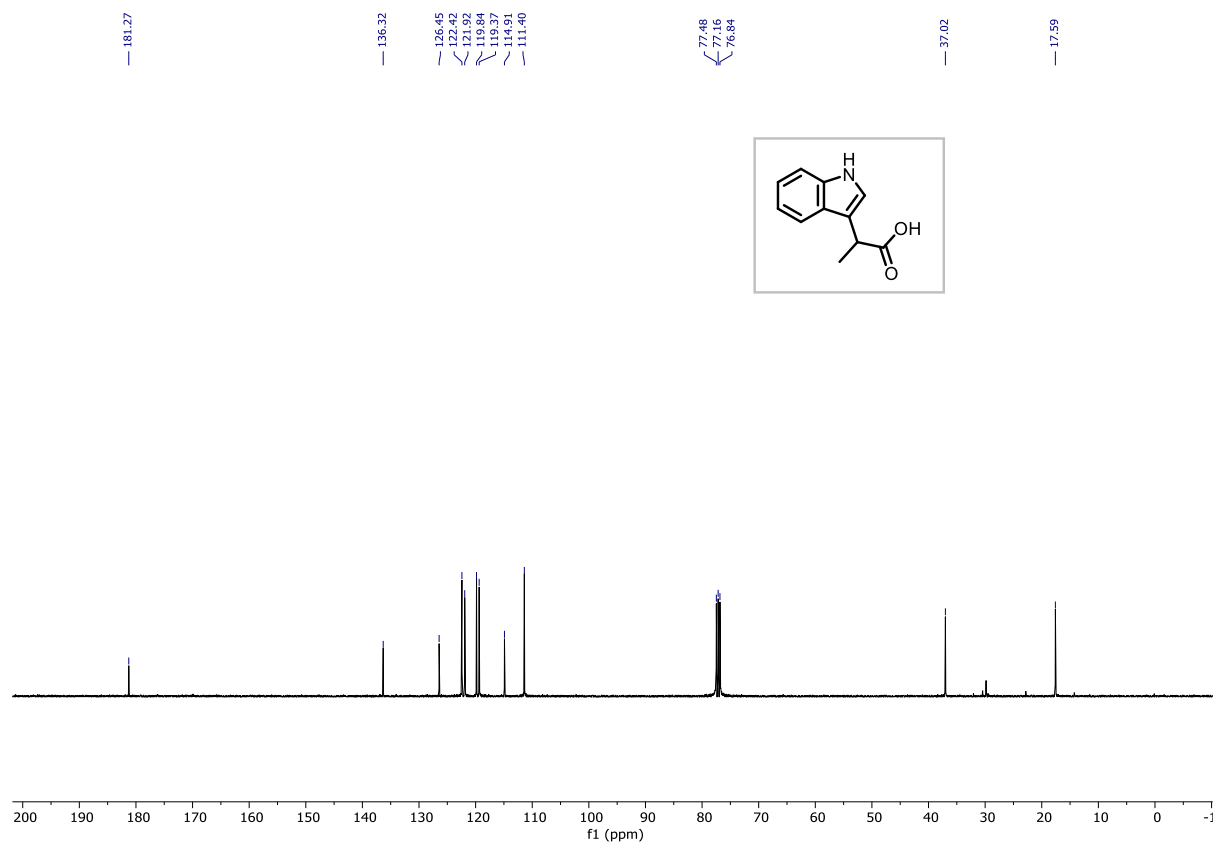


2-(1*H*-indol-3-yl) propanoic acid (3z)

¹H NMR (400 MHz, CHCl₃)

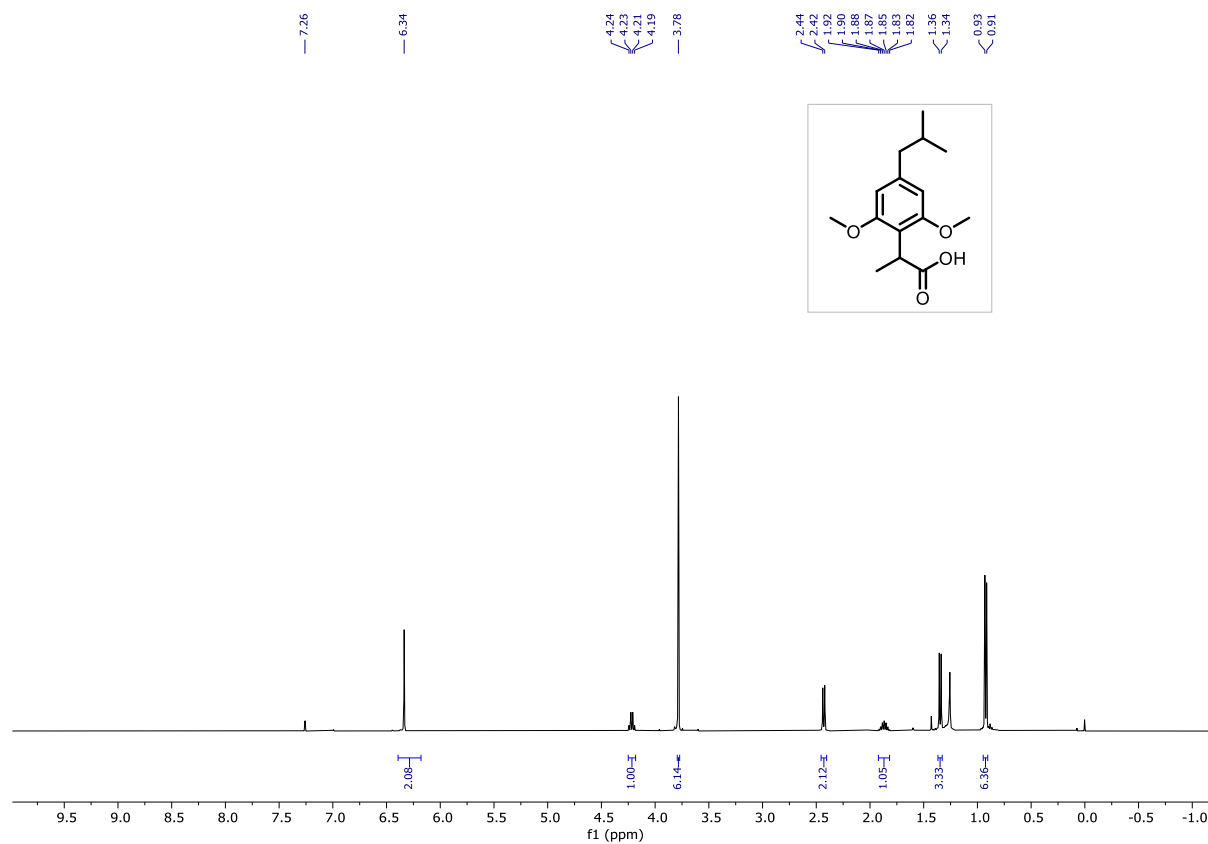


¹³C{¹H} NMR (101 MHz, CDCl₃)

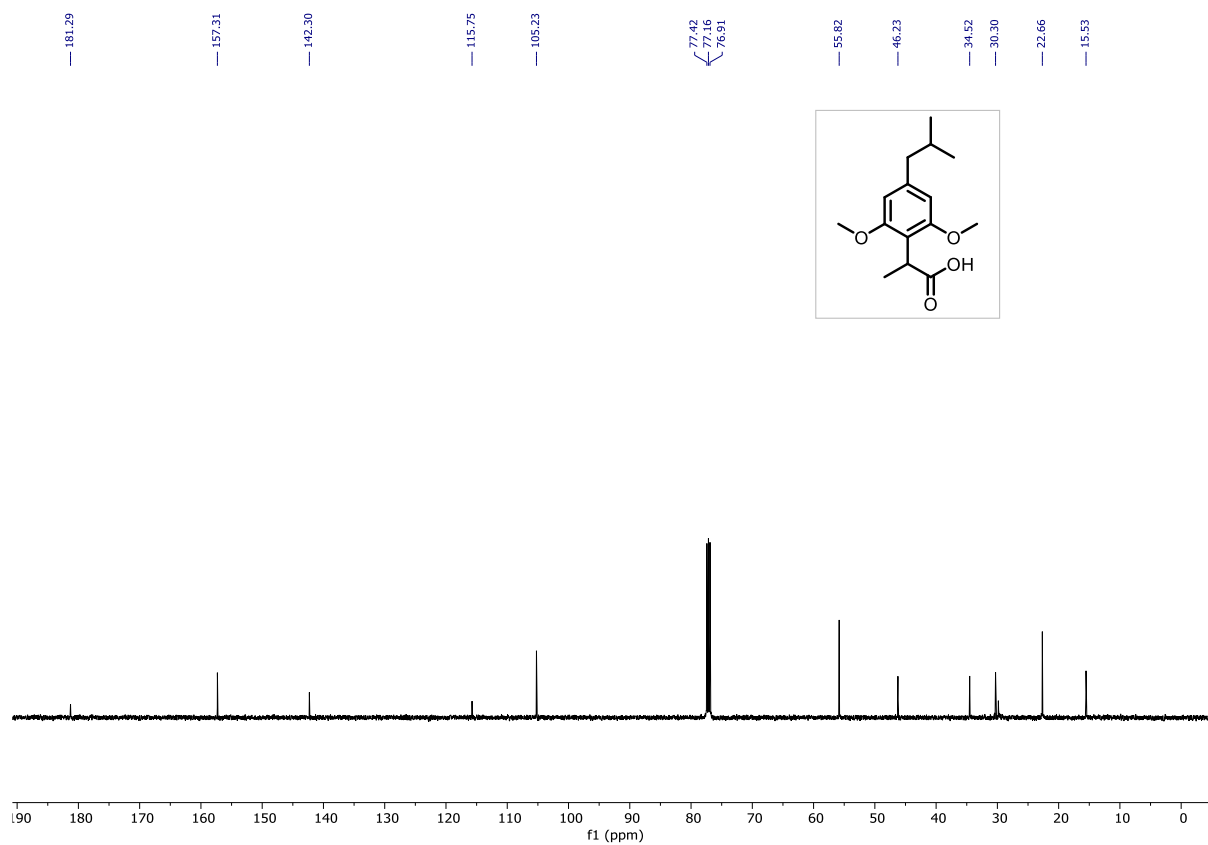


2-(4-Isobutyl-2,6-dimethoxy phenyl) propanoic acid (3za)

^1H NMR (400 MHz, CDCl_3)

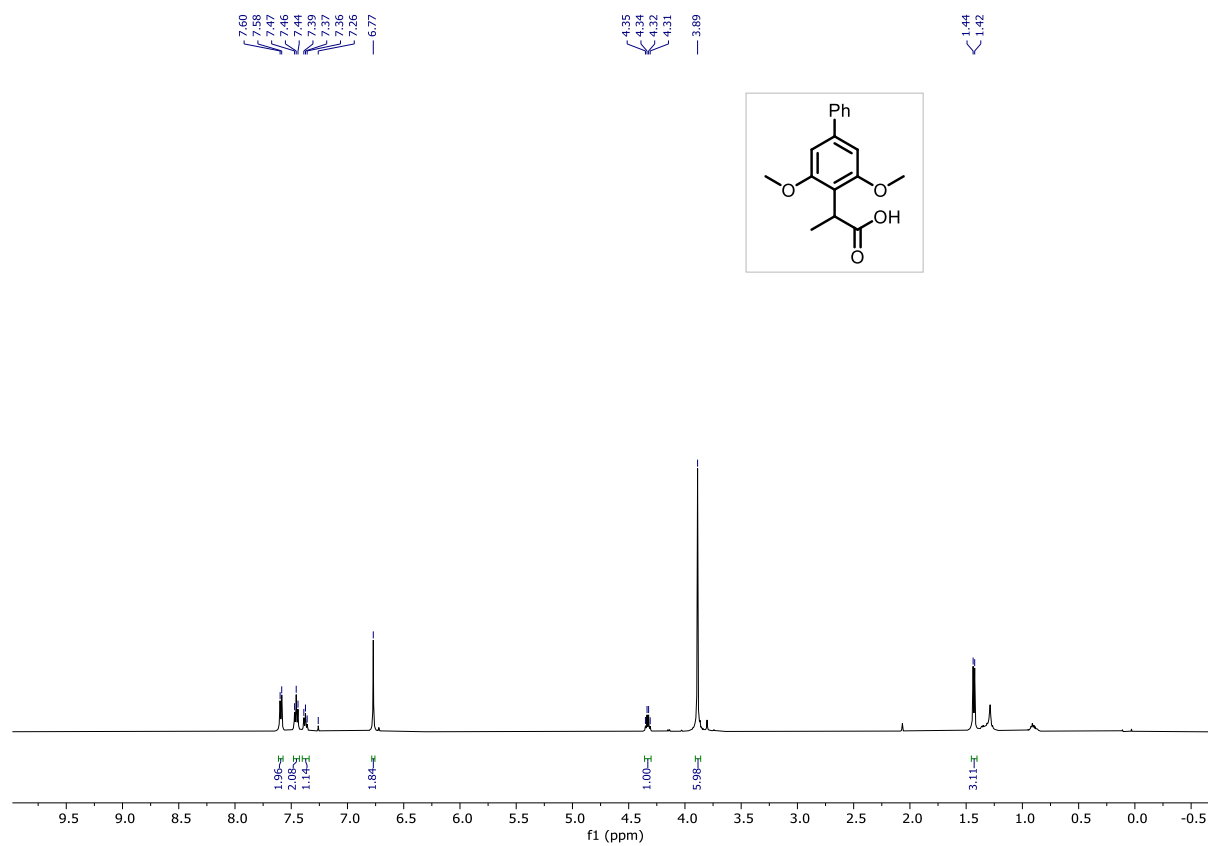


$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3)

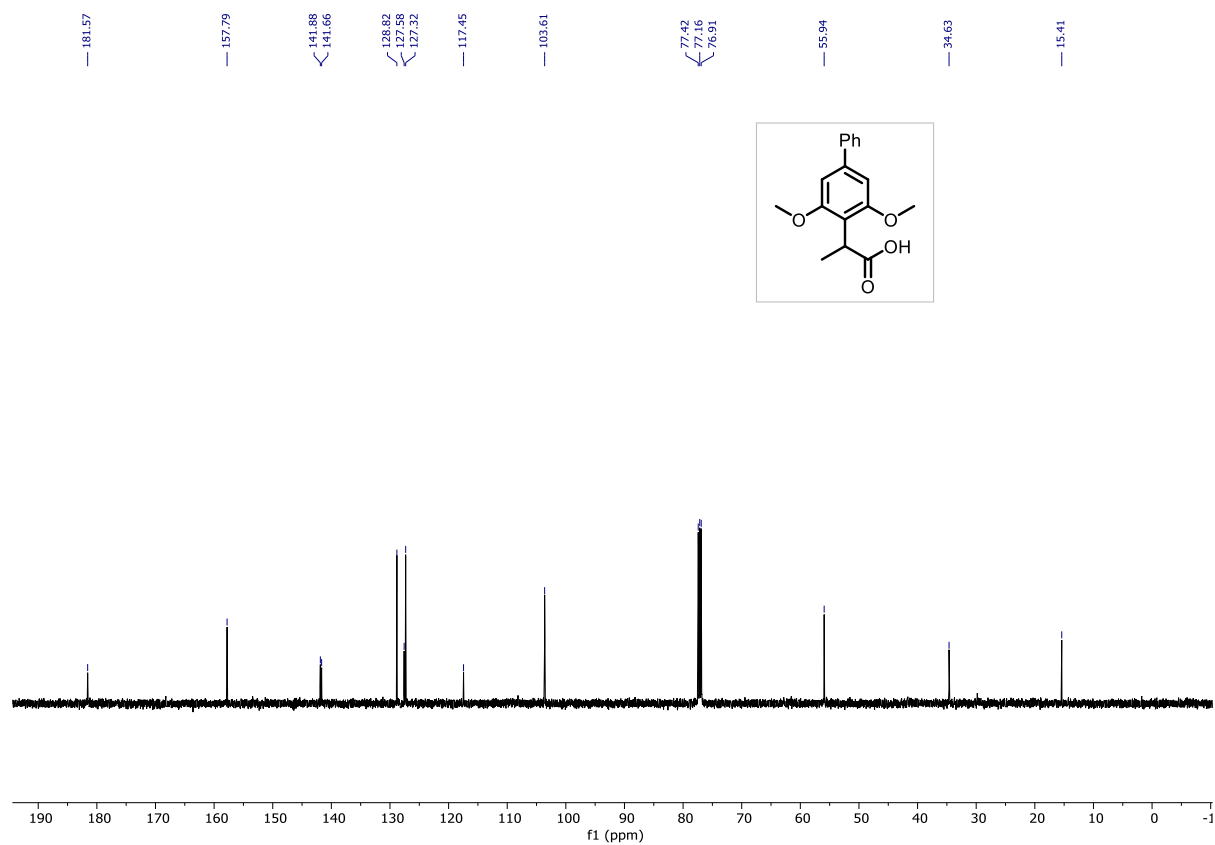


2-(3,5-Dimethoxy-[1,1'-biphenyl]-4-yl) propanoic acid (3zb)

^1H NMR (500 MHz, CDCl_3)

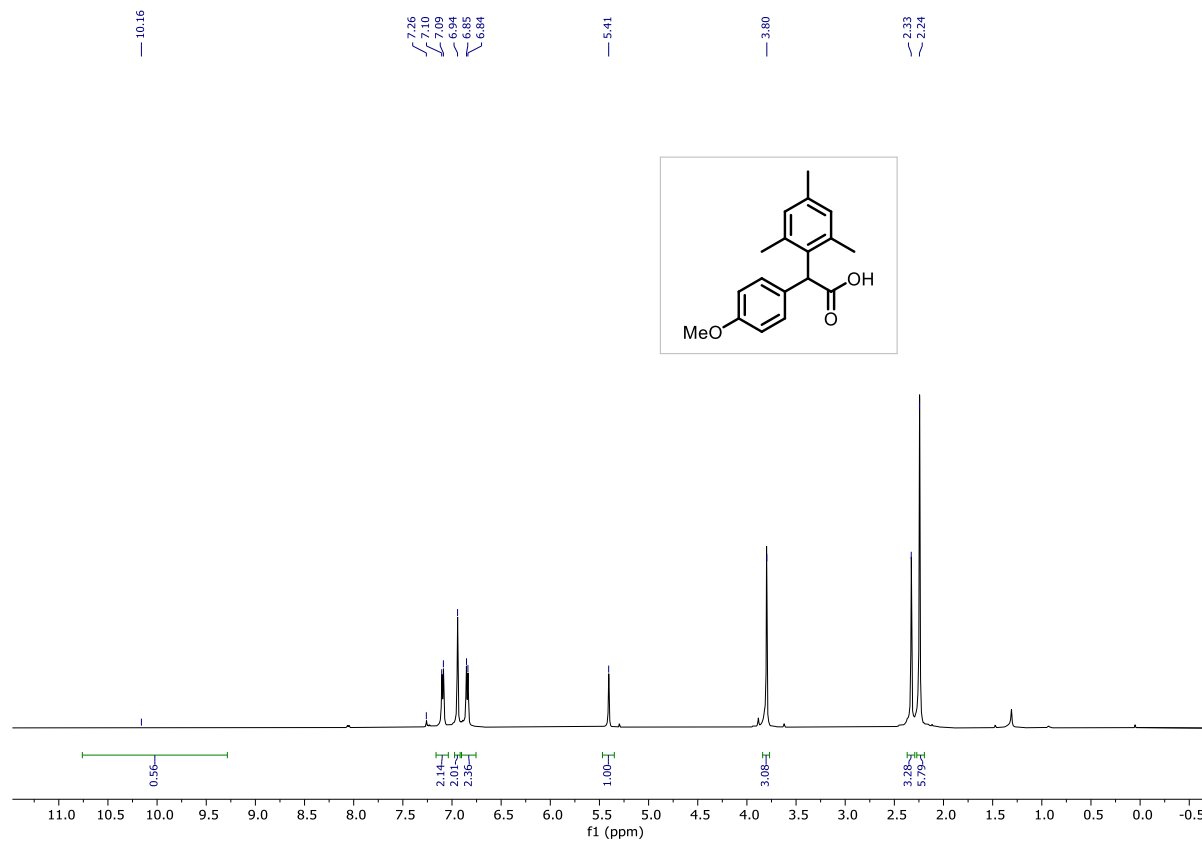


^{13}C $\{^1\text{H}\}$ NMR (126 MHz, CDCl_3)

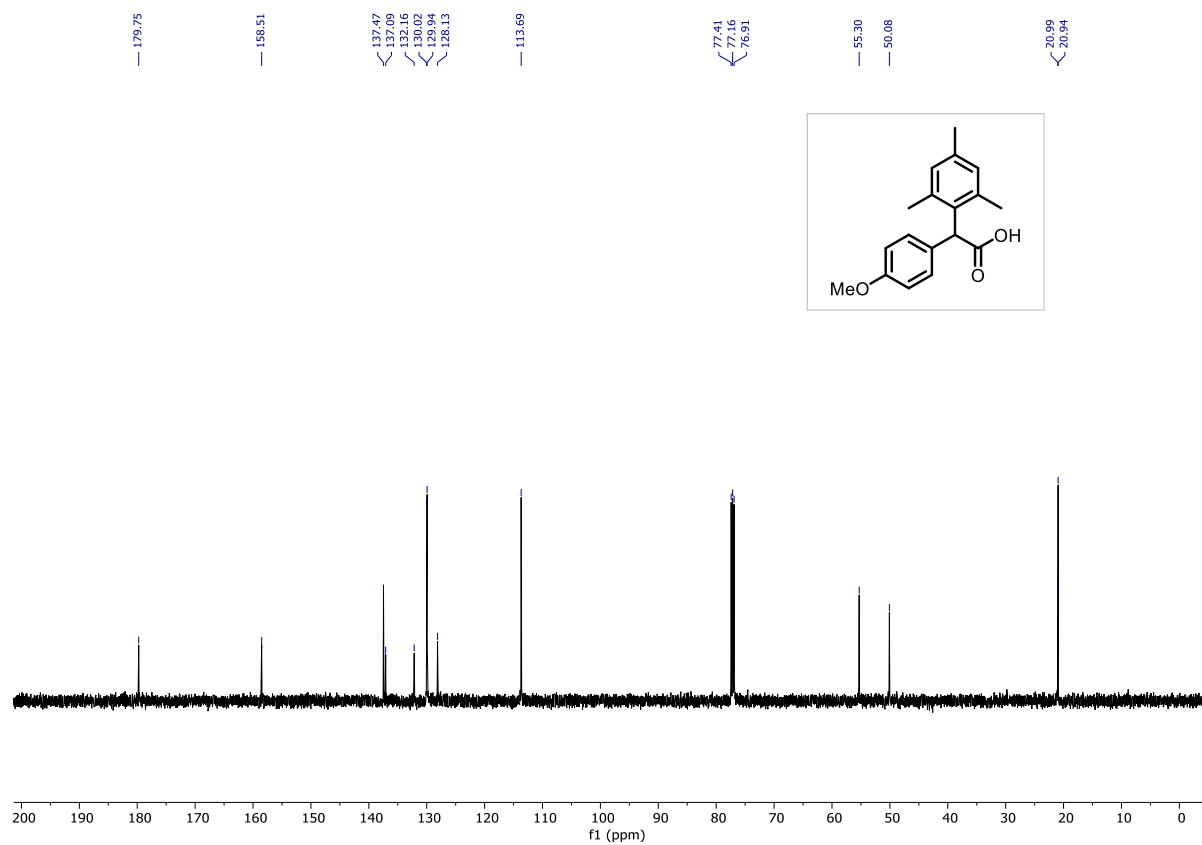


2-Mesityl-2-(4-methoxyphenyl) acetic acid (4a)

^1H NMR (500 MHz, CDCl_3)

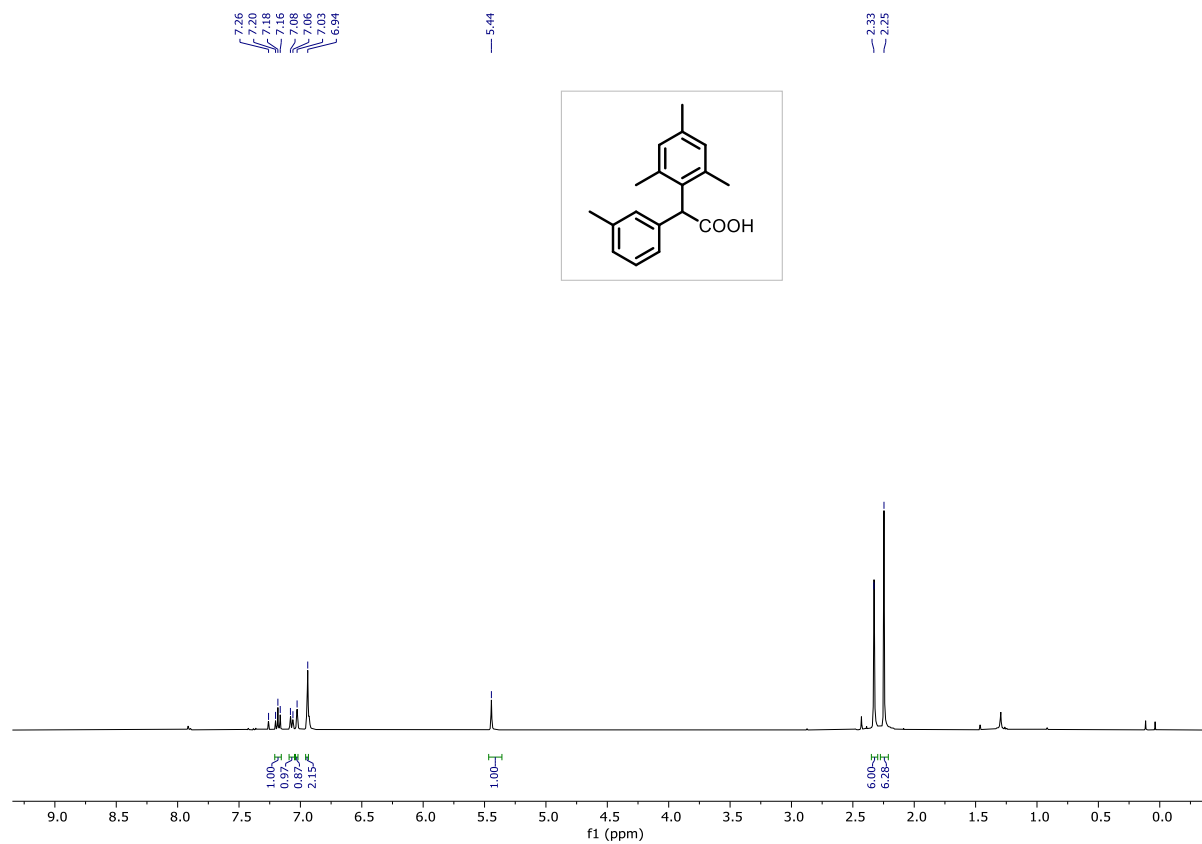


^{13}C { ^1H } NMR (126 MHz, CDCl_3)

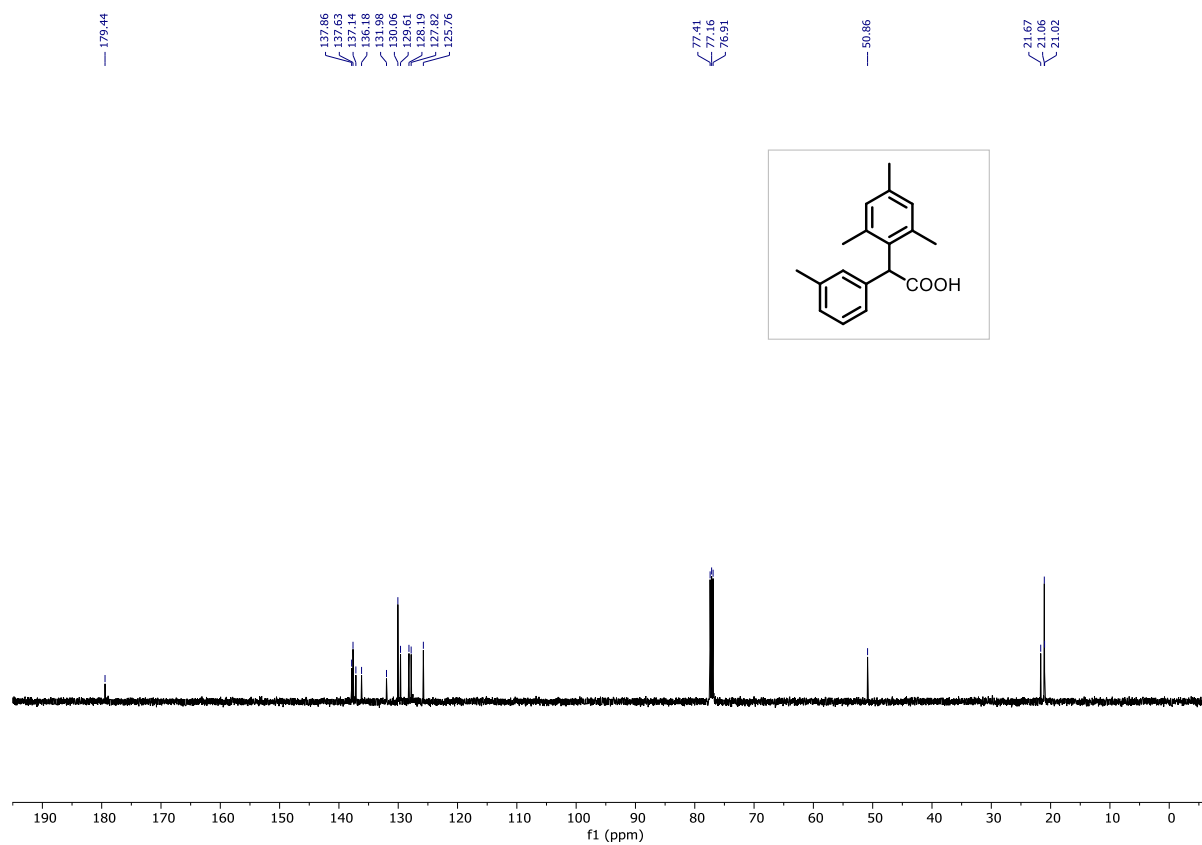


2-Mesityl-2-(*m*-tolyl) acetic acid (4b)

^1H NMR (400 MHz, CDCl_3)

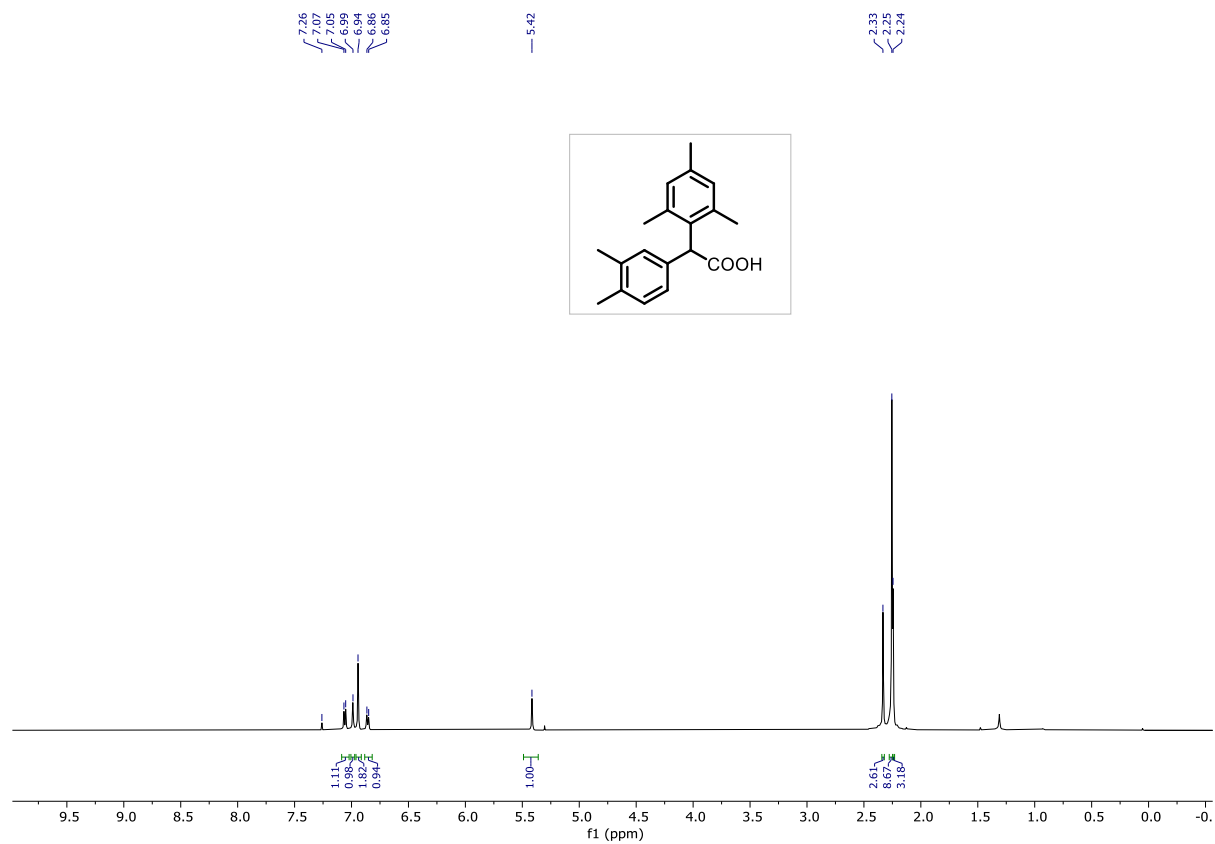


^{13}C { ^1H } NMR (126 MHz, CDCl_3)

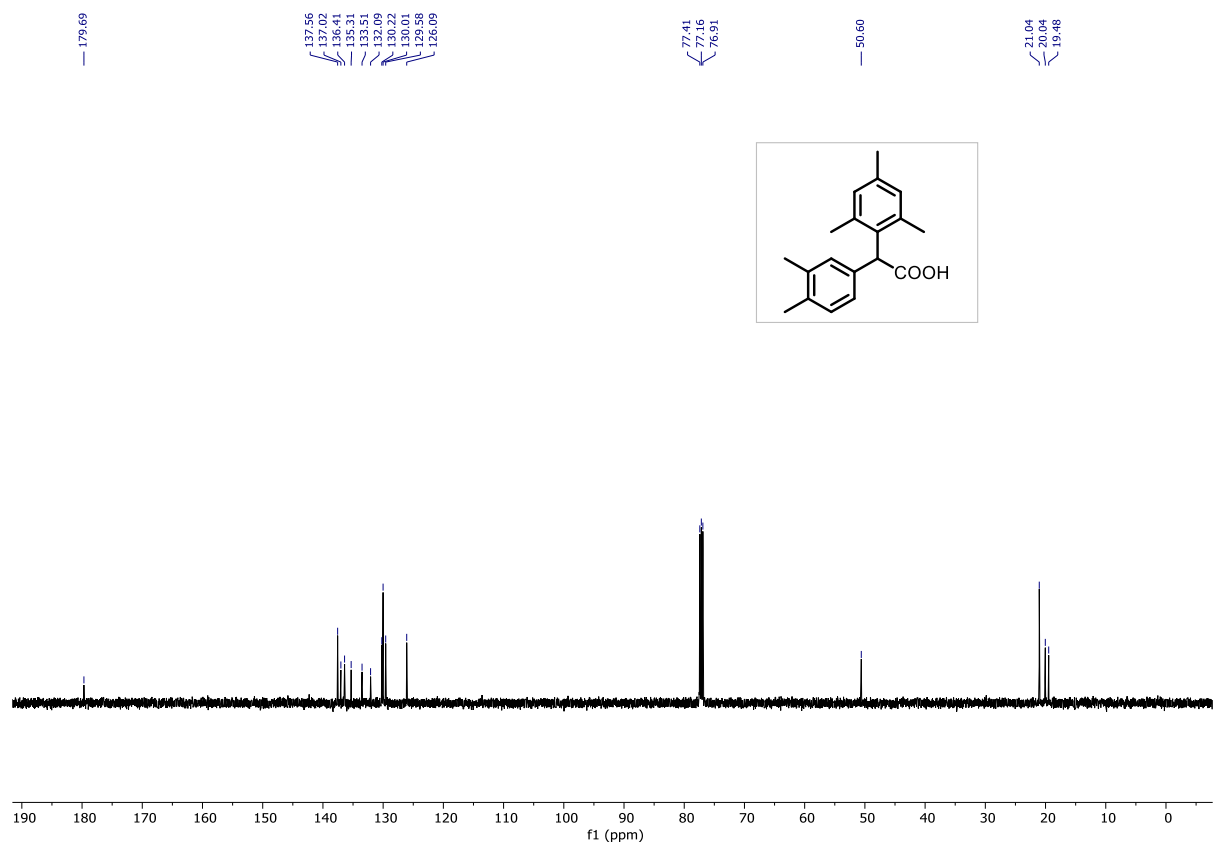


2-(3,4-Dimethylphenyl)-2-mesitylacetic acid (4c)

^1H NMR (500 MHz, CDCl_3)

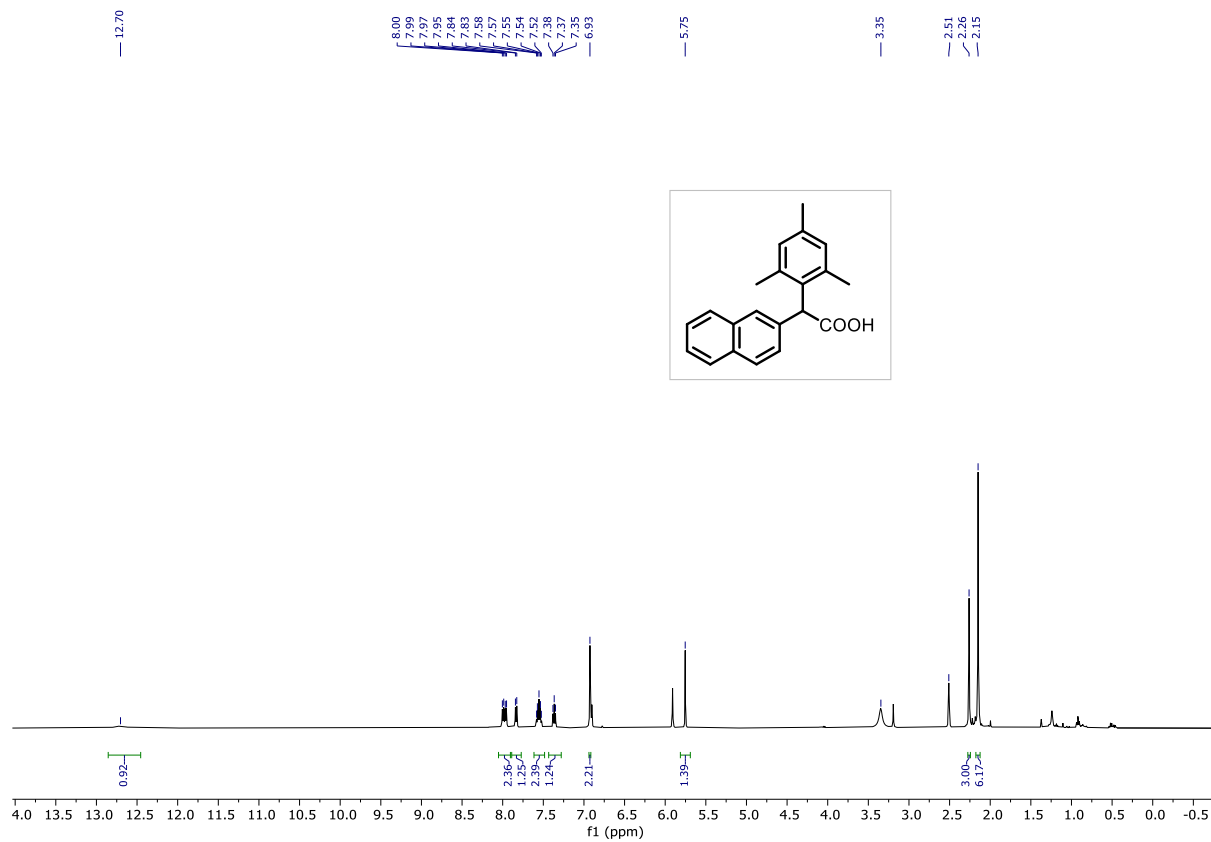


^{13}C { ^1H } NMR (126 MHz, CDCl_3)

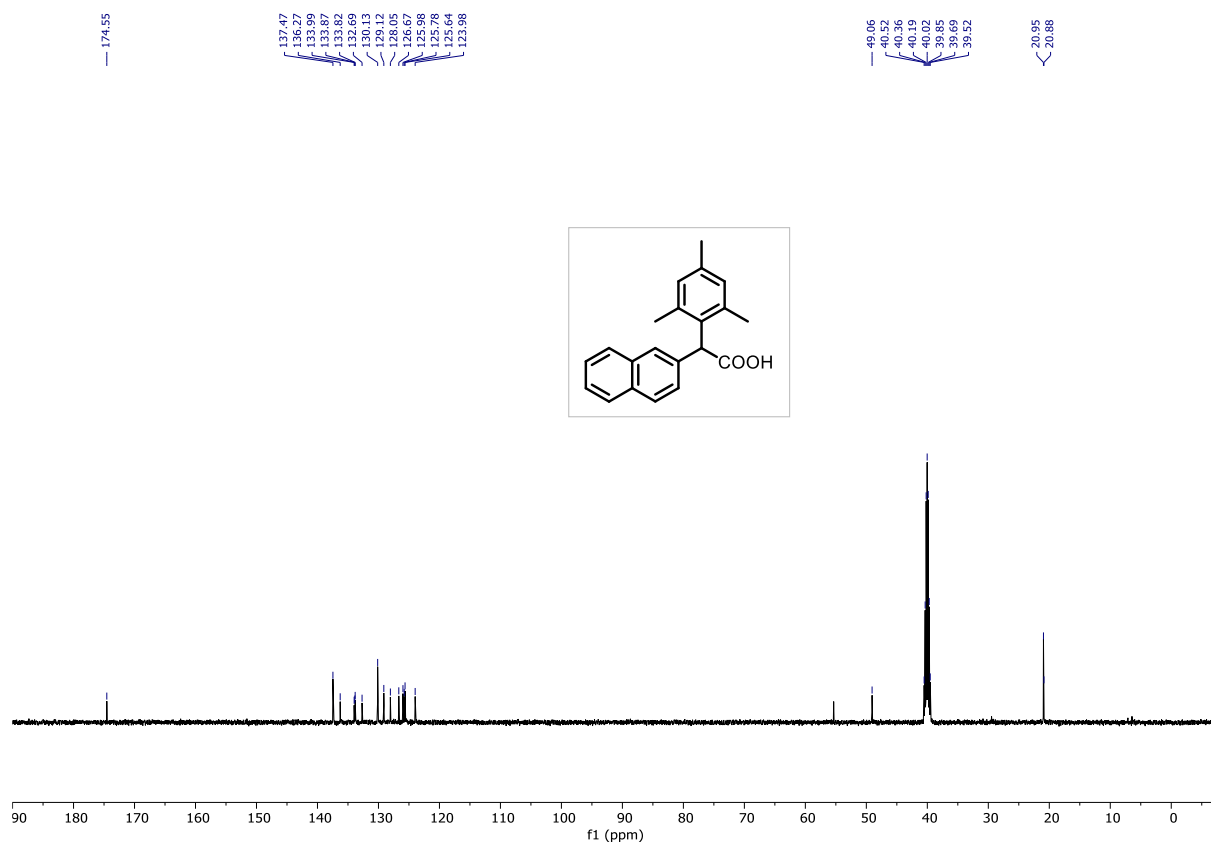


2-Mesityl-2-(naphthalen-2-yl) acetic acid (4d)

^1H NMR (500 MHz, $\text{DMSO-}d_6$)

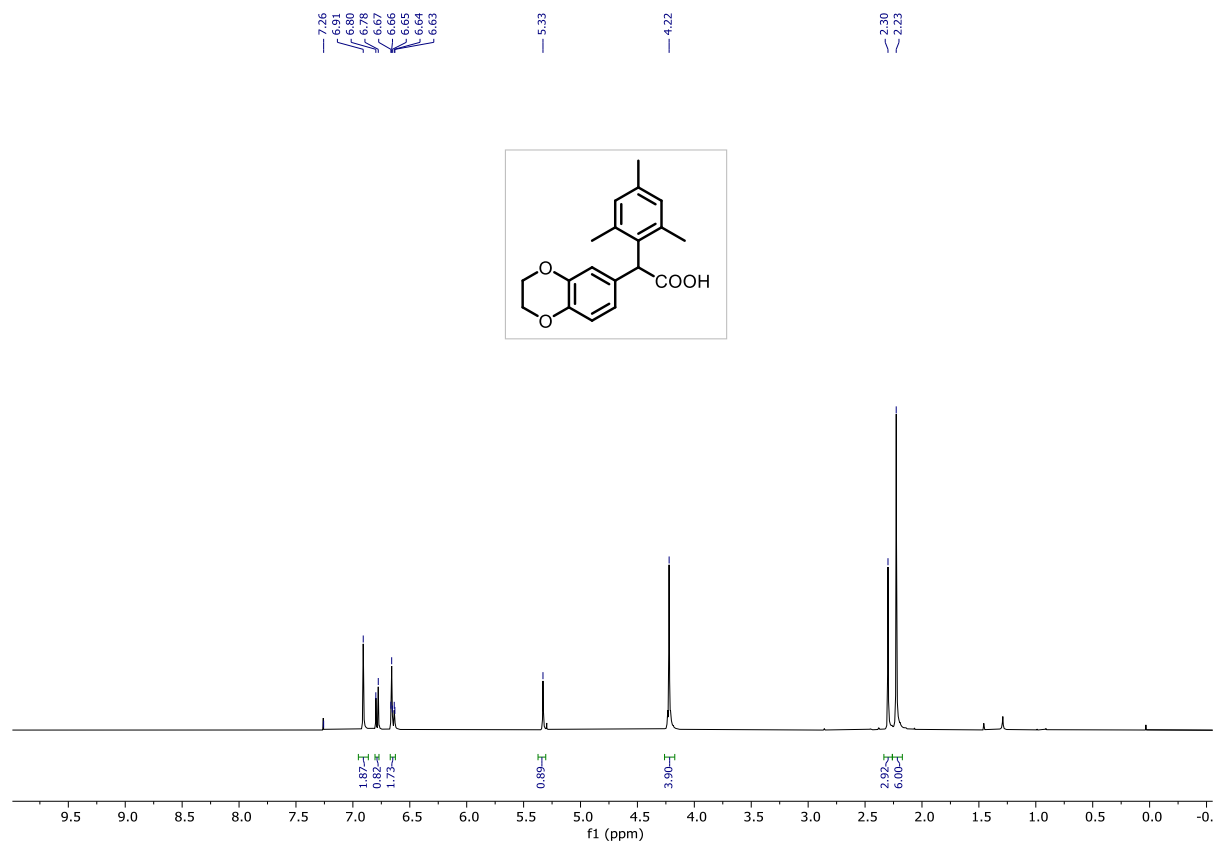


^{13}C $\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$)

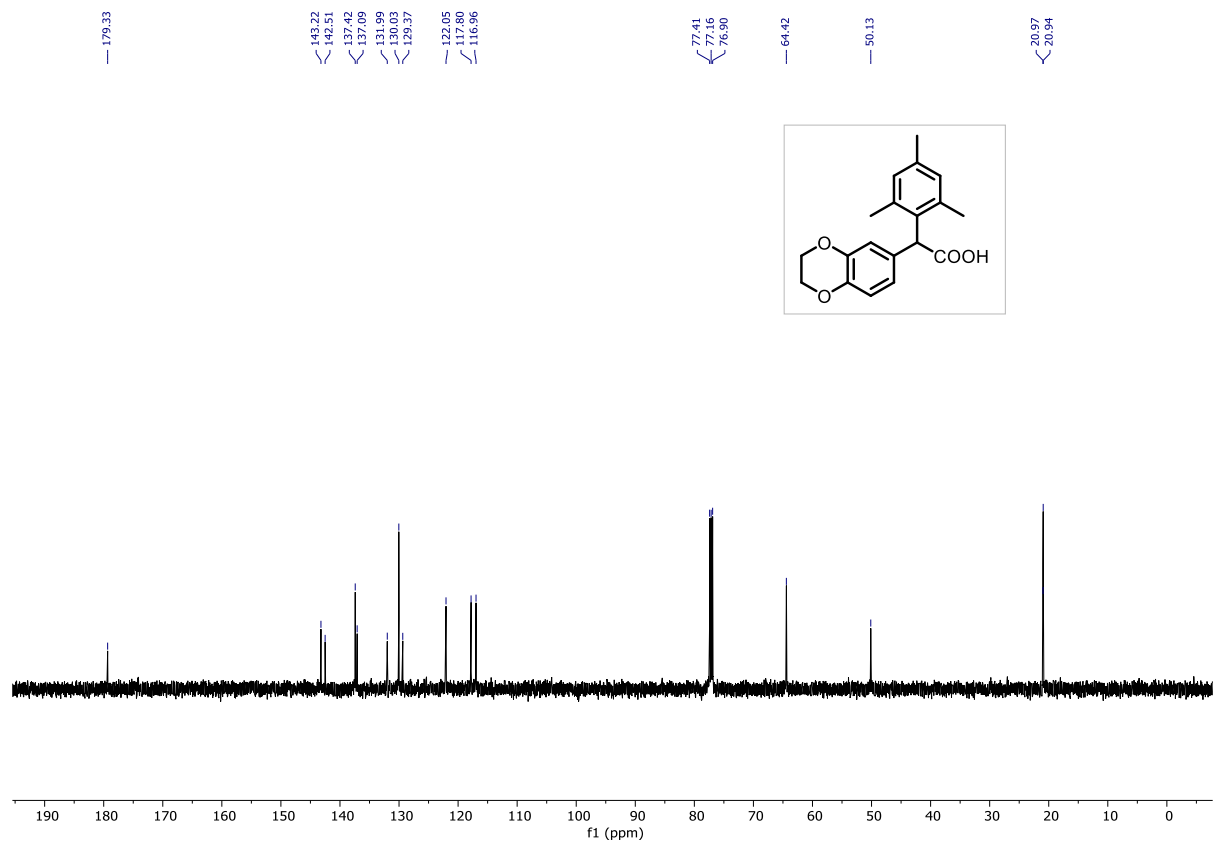


2-(2,3-Dihydrobenzo[b][1,4] dioxin-6-yl)-2-mesitylacetic acid (4e)

^1H NMR (400 MHz, CDCl_3)

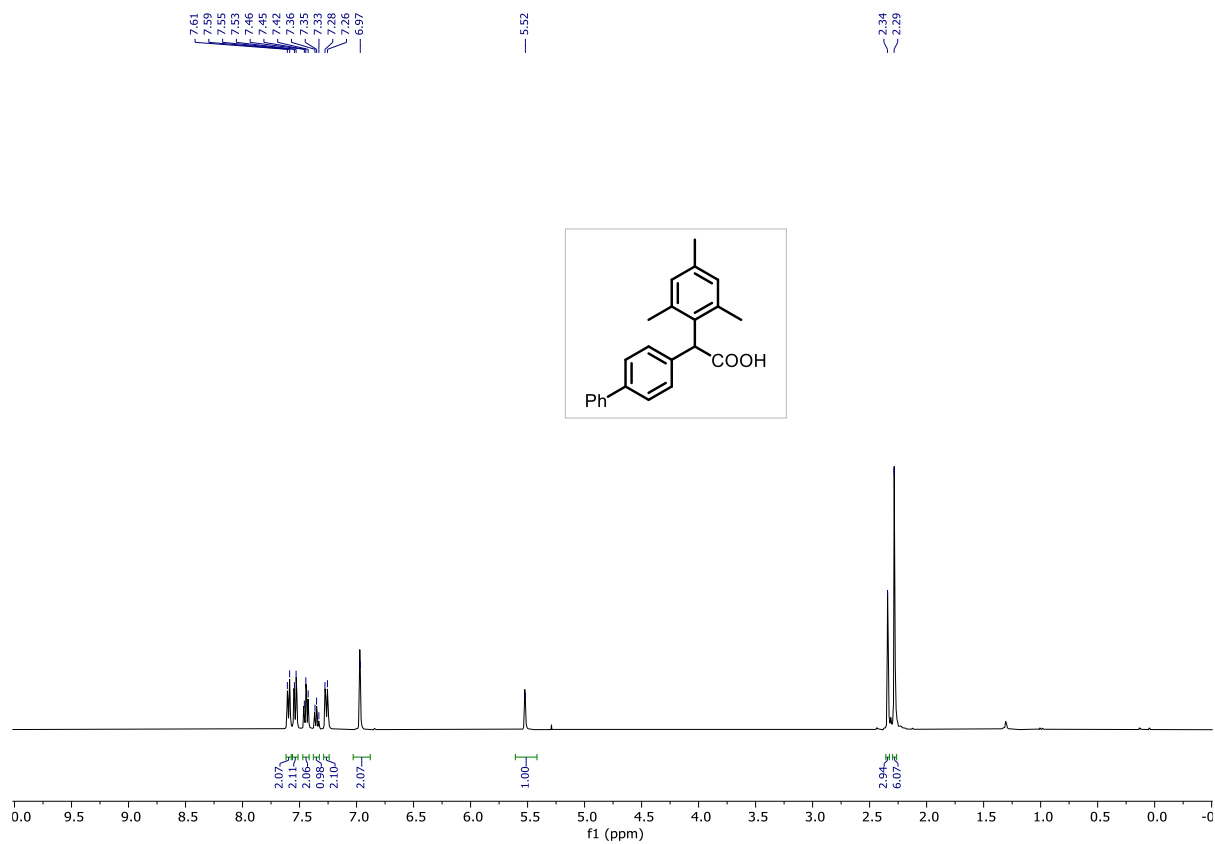


^{13}C { ^1H } NMR (126 MHz, CDCl_3)

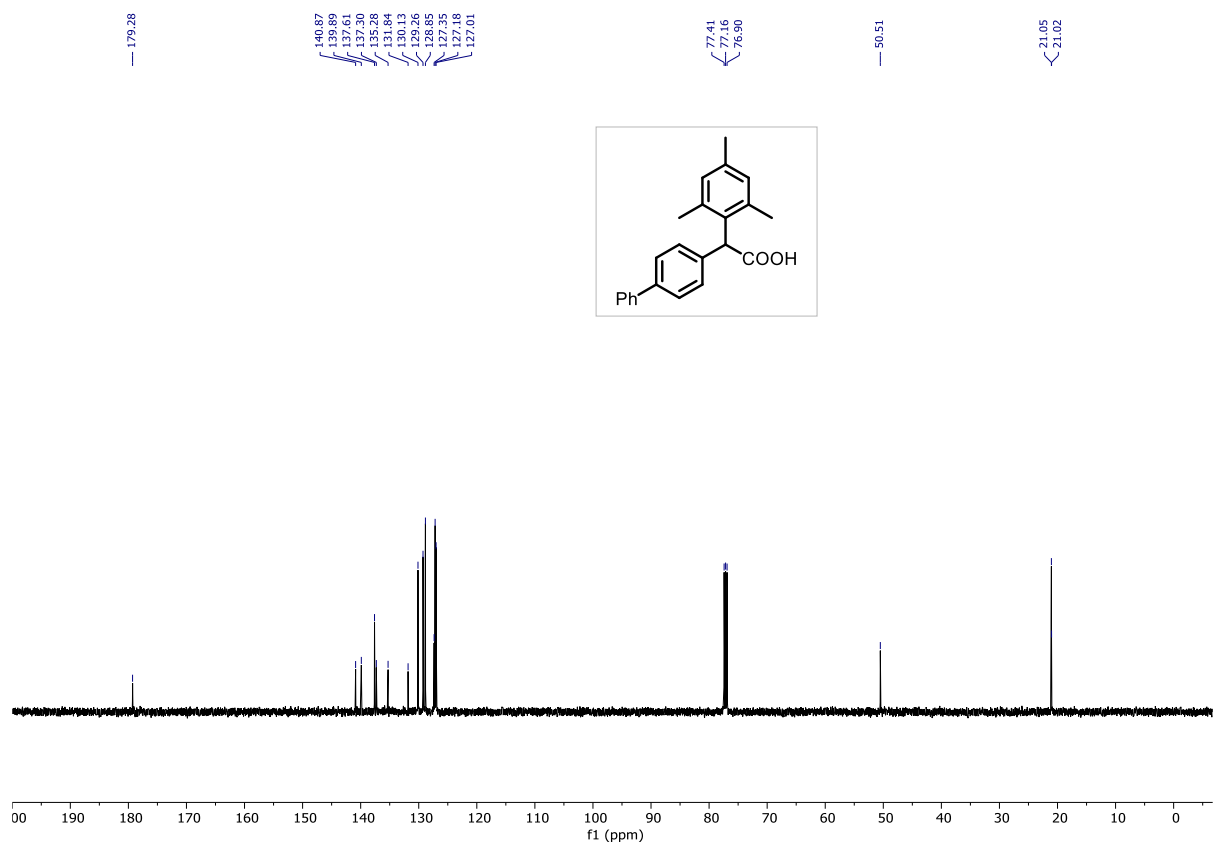


2-([1,1'-Biphenyl]-4-yl)-2-mesitylacetic acid (4f)

^1H NMR (400 MHz, CDCl_3)

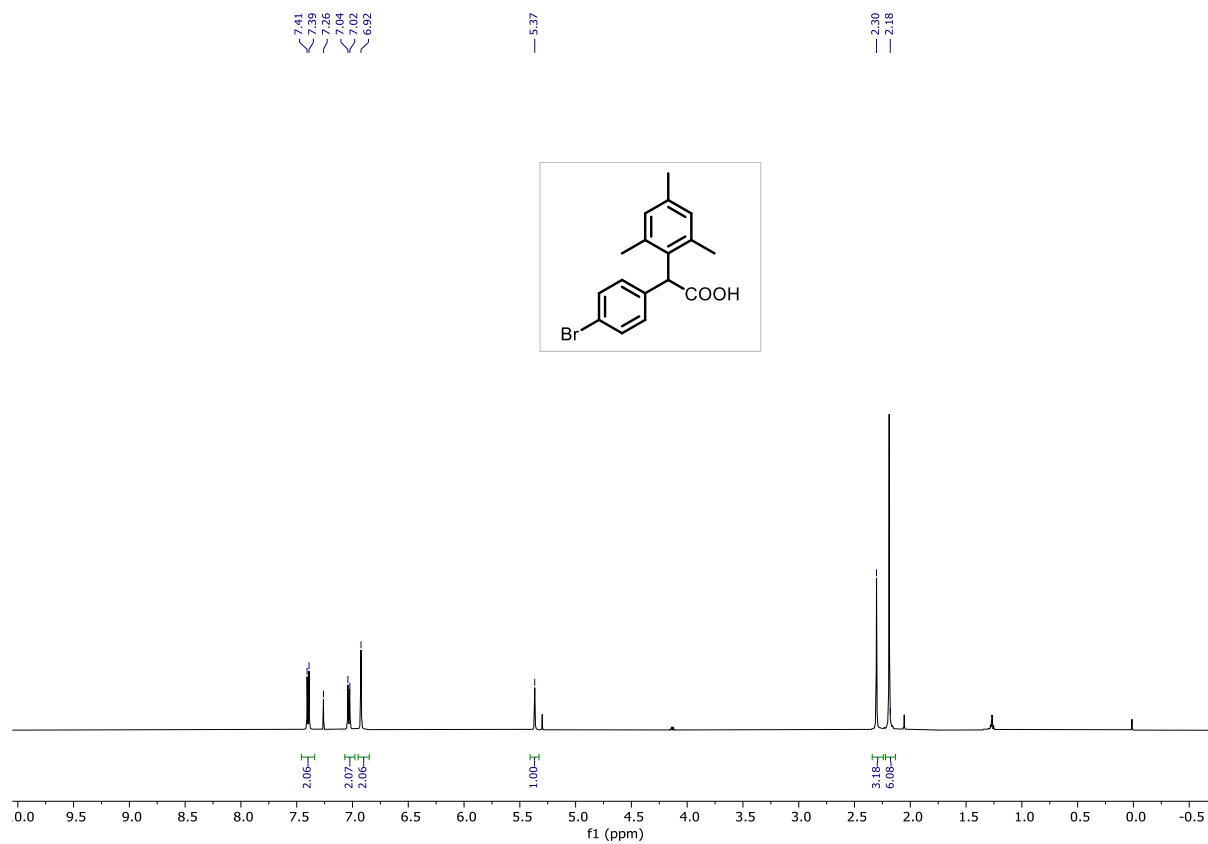


^{13}C $\{^1\text{H}\}$ NMR (126 MHz, CDCl_3)

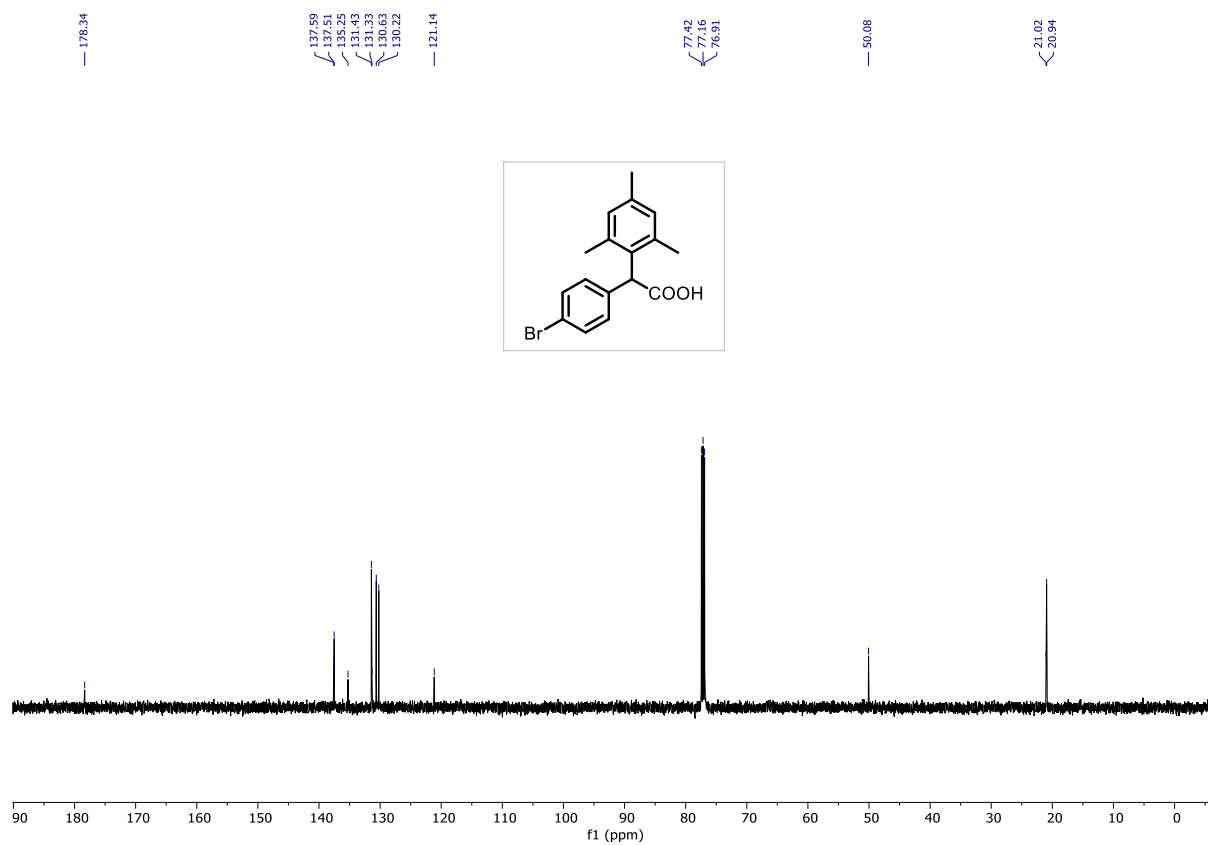


2-(4-Bromophenyl)-2-mesitylacetic acid (4g)

^1H NMR (500 MHz, CDCl_3)

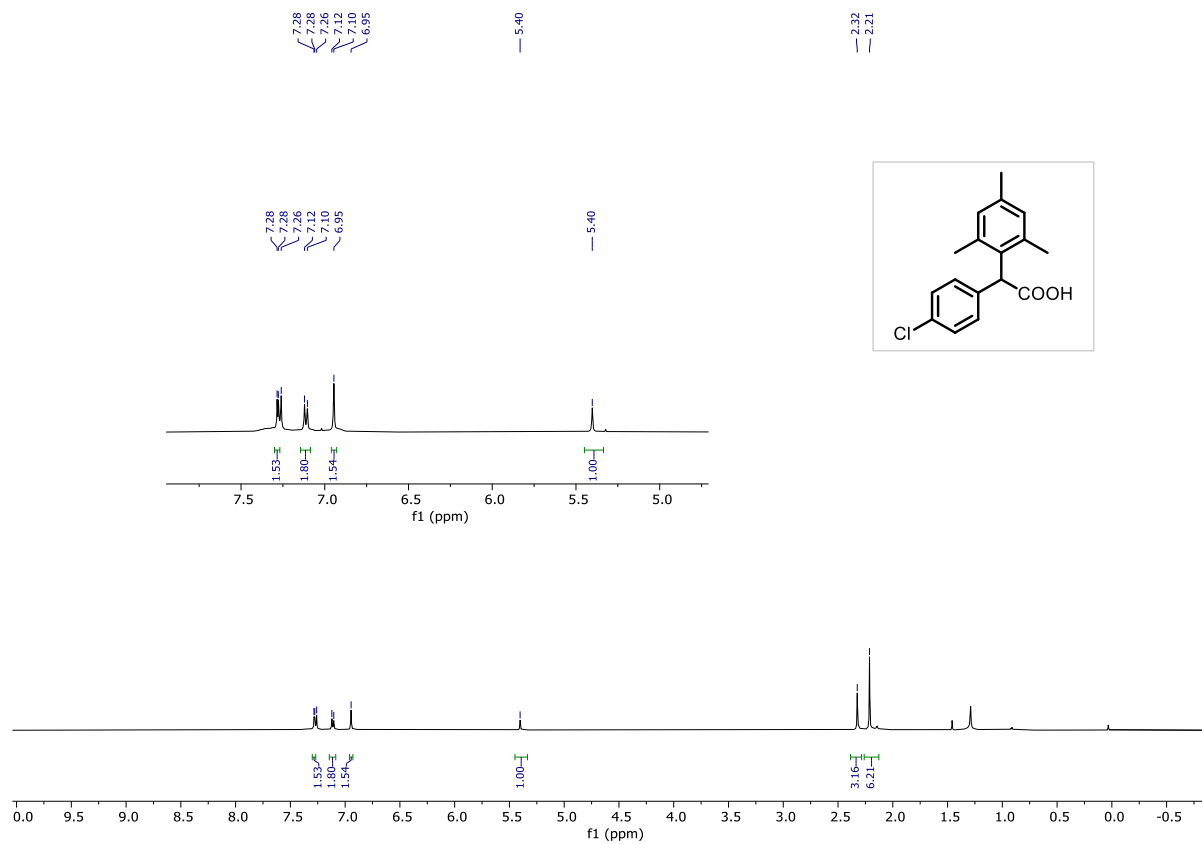


^{13}C { ^1H } NMR (126 MHz, CDCl_3)

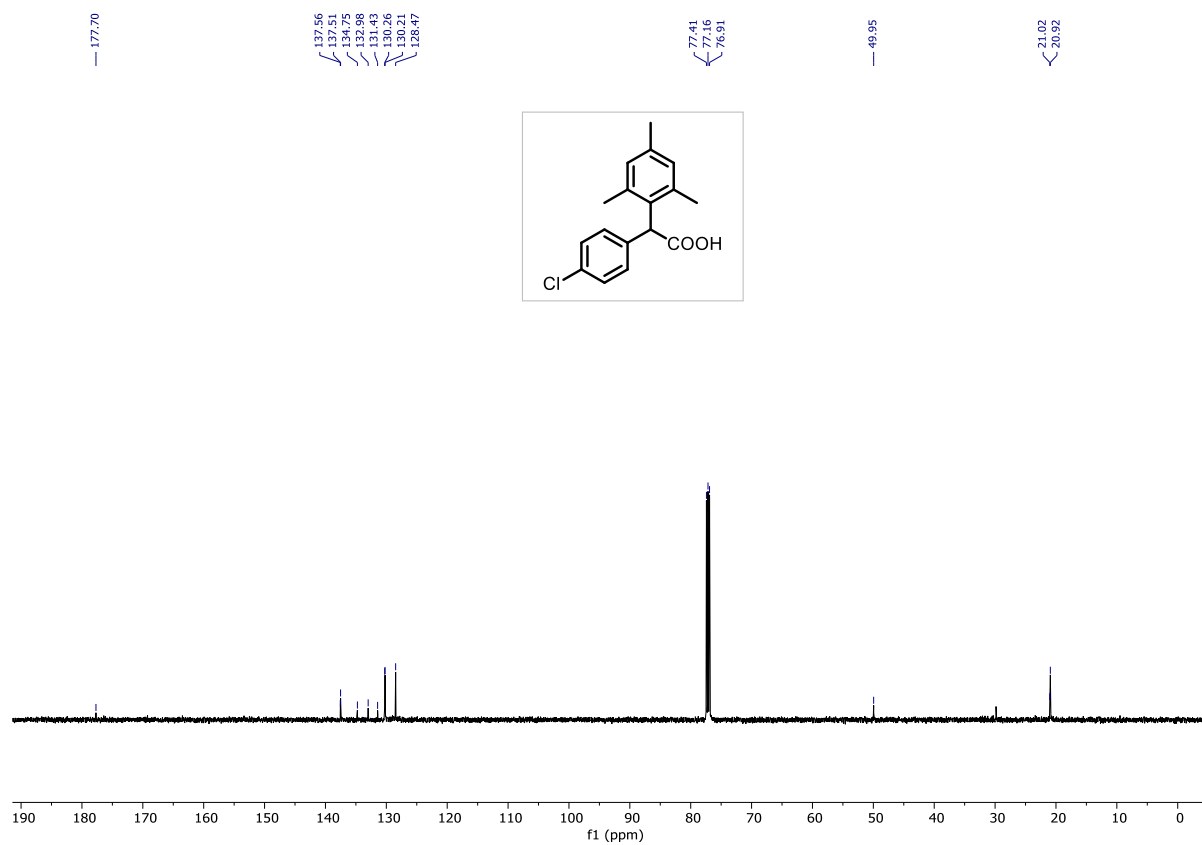


2-(4-Chlorophenyl)-2-mesitylacetic acid (4h)

^1H NMR (500 MHz, CDCl_3)

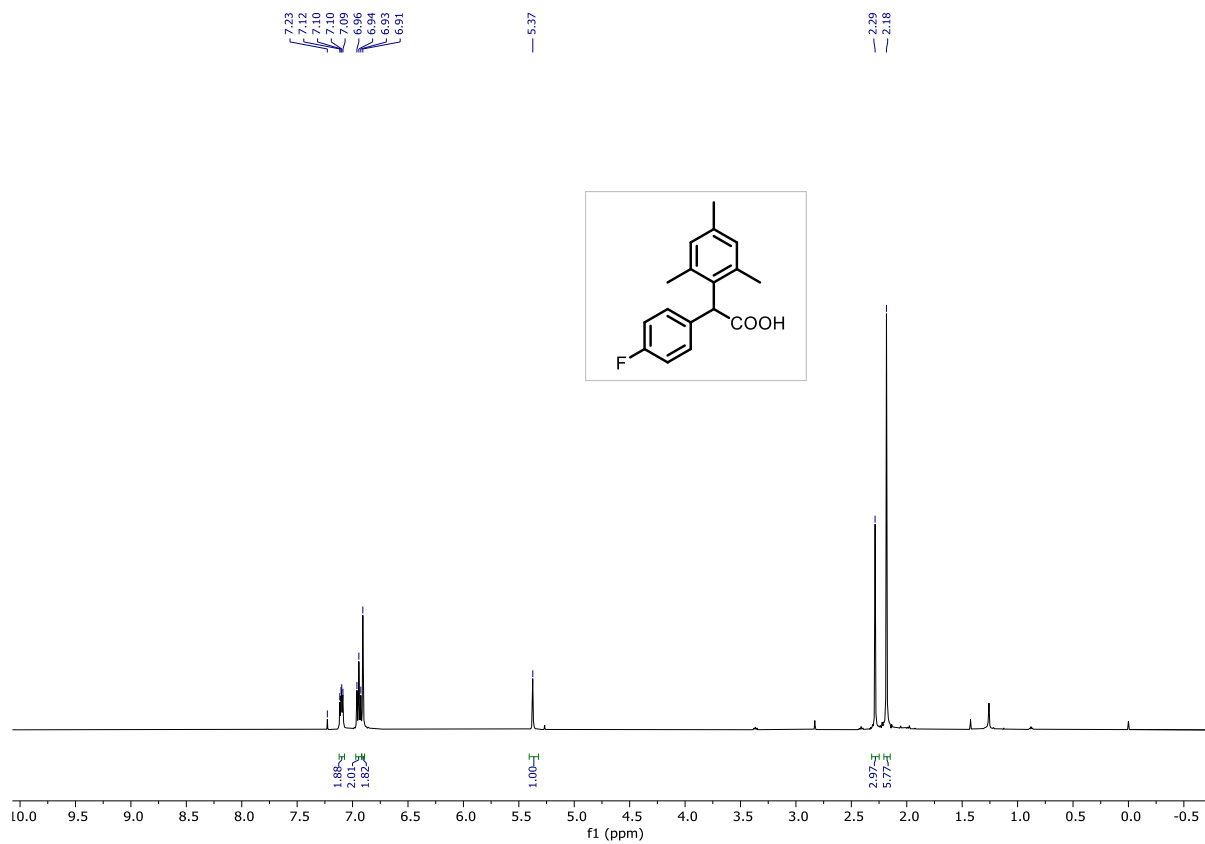


^{13}C $\{^1\text{H}\}$ NMR (126 MHz, CDCl_3)

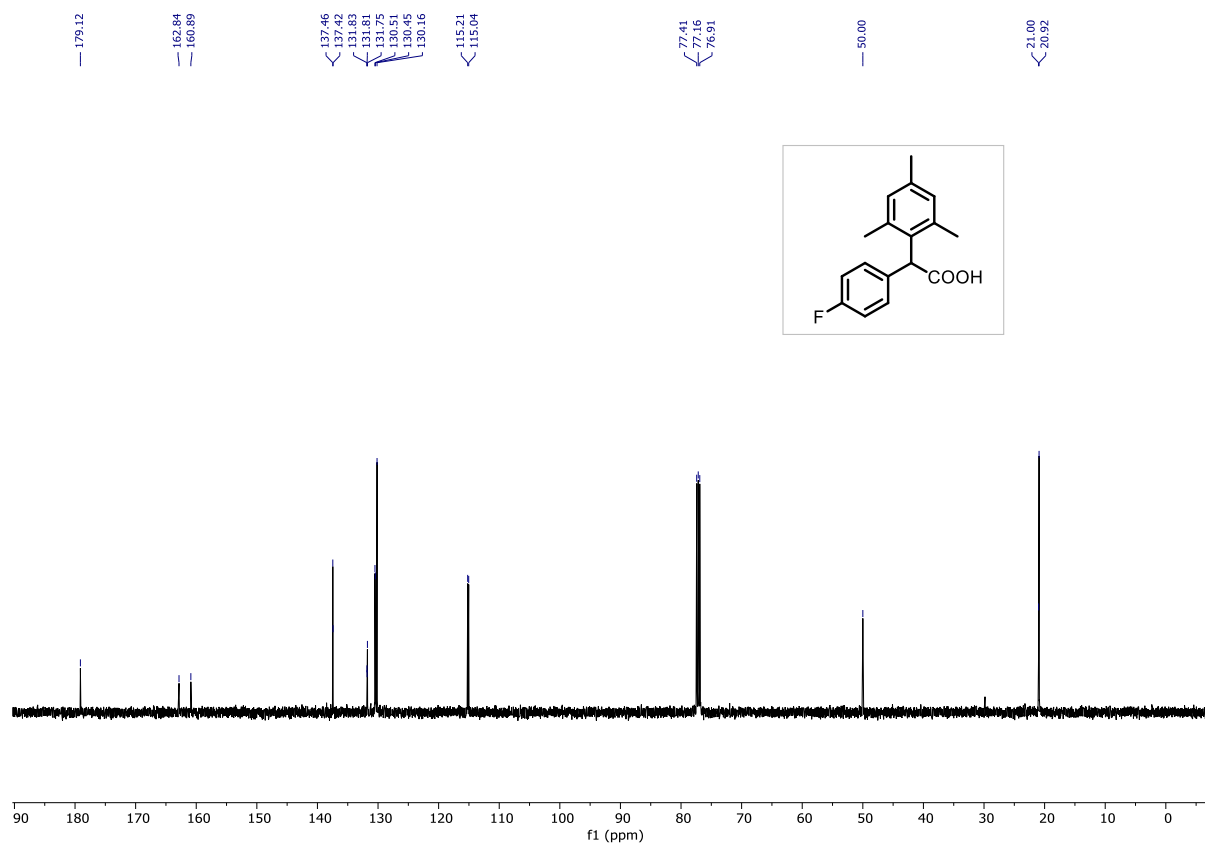


2-(4-Fluorophenyl)-2-mesitylacetic acid (4i)

^1H NMR (500 MHz, CDCl_3)

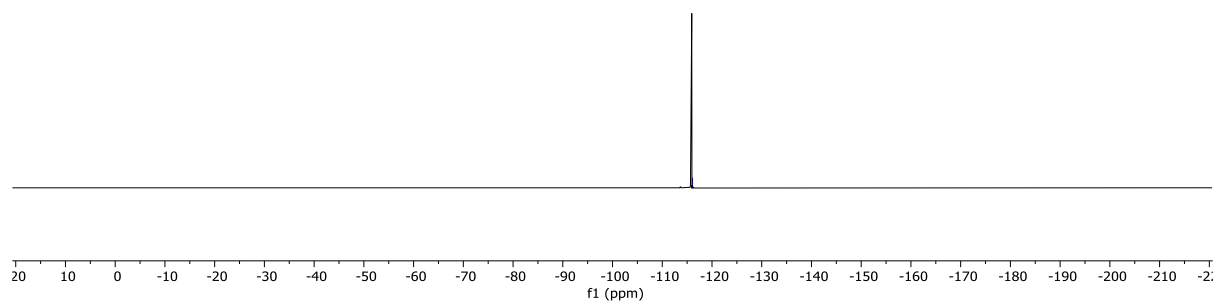
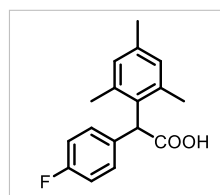


^{13}C { ^1H } NMR (126 MHz, CDCl_3)



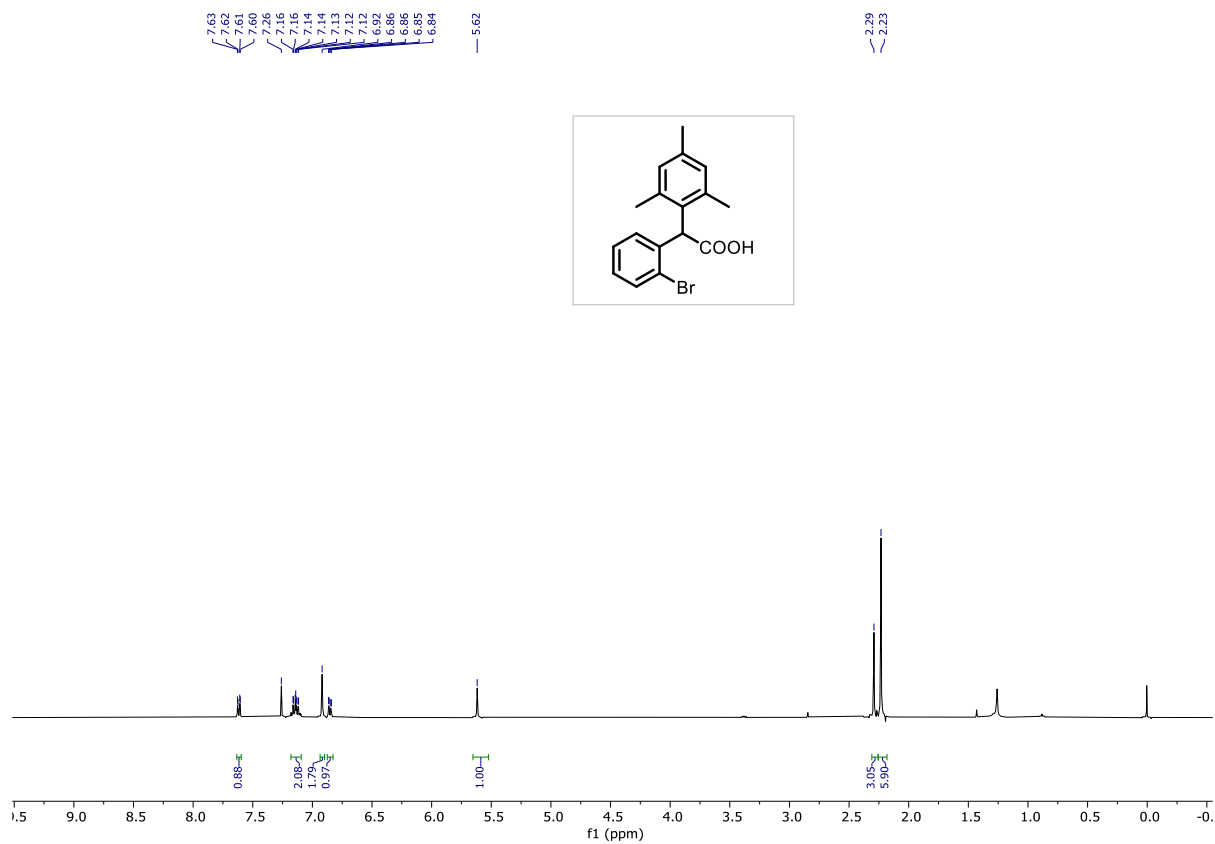
¹⁹F NMR (471 MHz, CDCl₃)

116.09

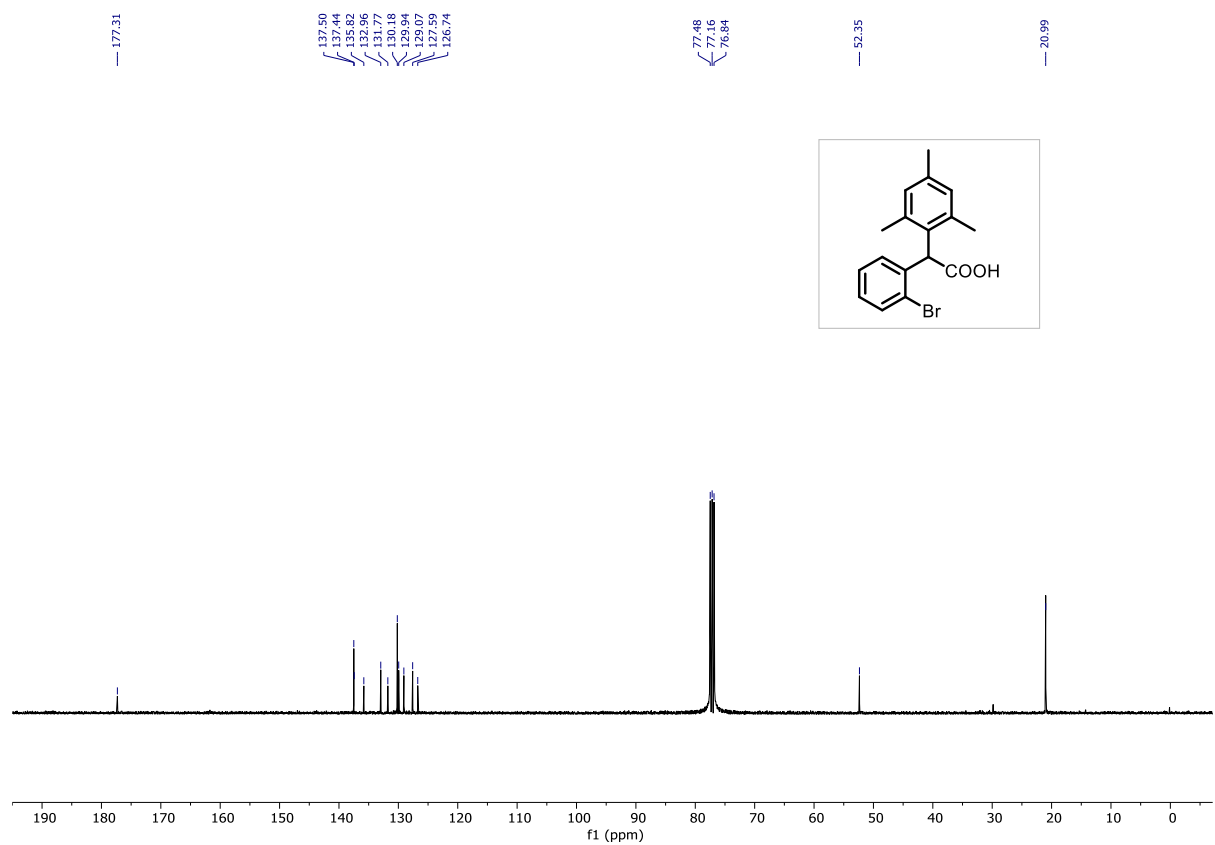


2-(2-Bromophenyl)-2-mesitylacetic acid (4j)

^1H NMR (400 MHz, CDCl_3)

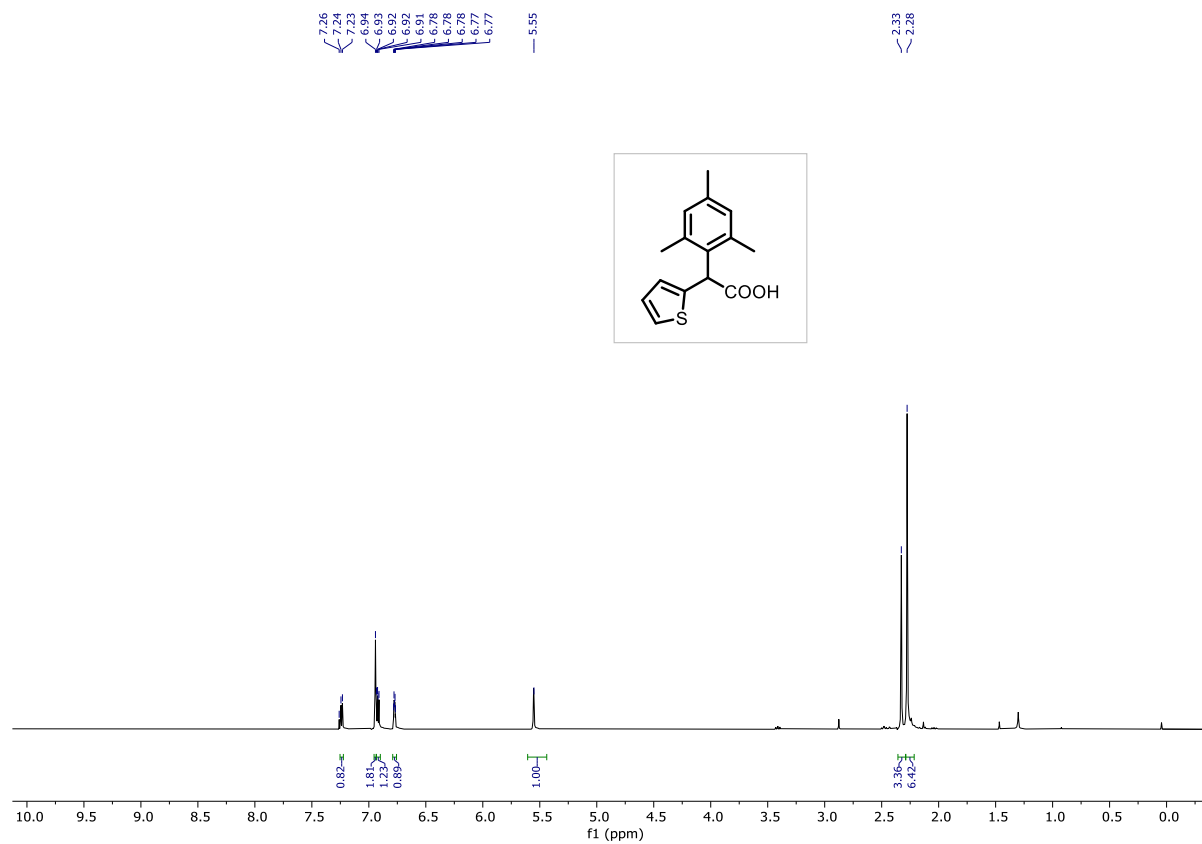


^{13}C { ^1H } NMR (126 MHz, CDCl_3)

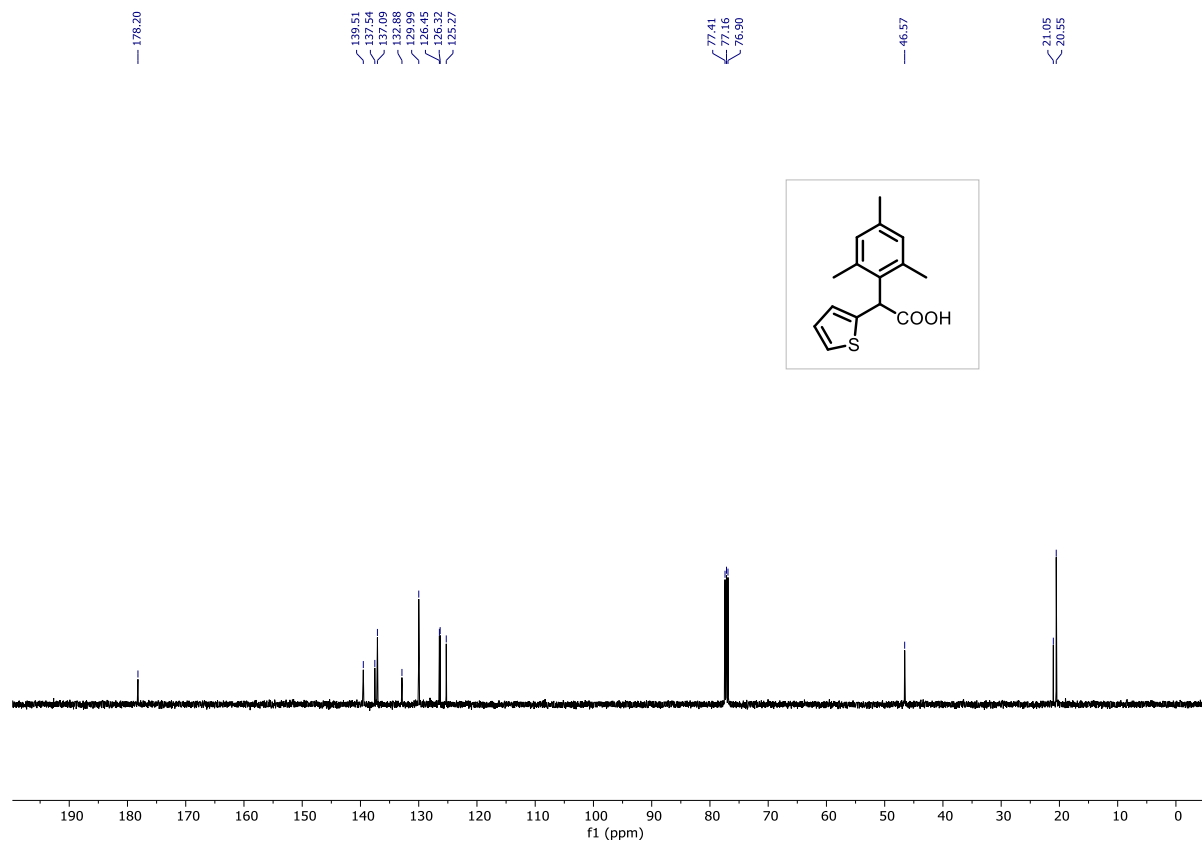


2-Mesityl-2-(thiophen-2-yl)acetic acid (4k)

^1H NMR (400 MHz, CDCl_3)

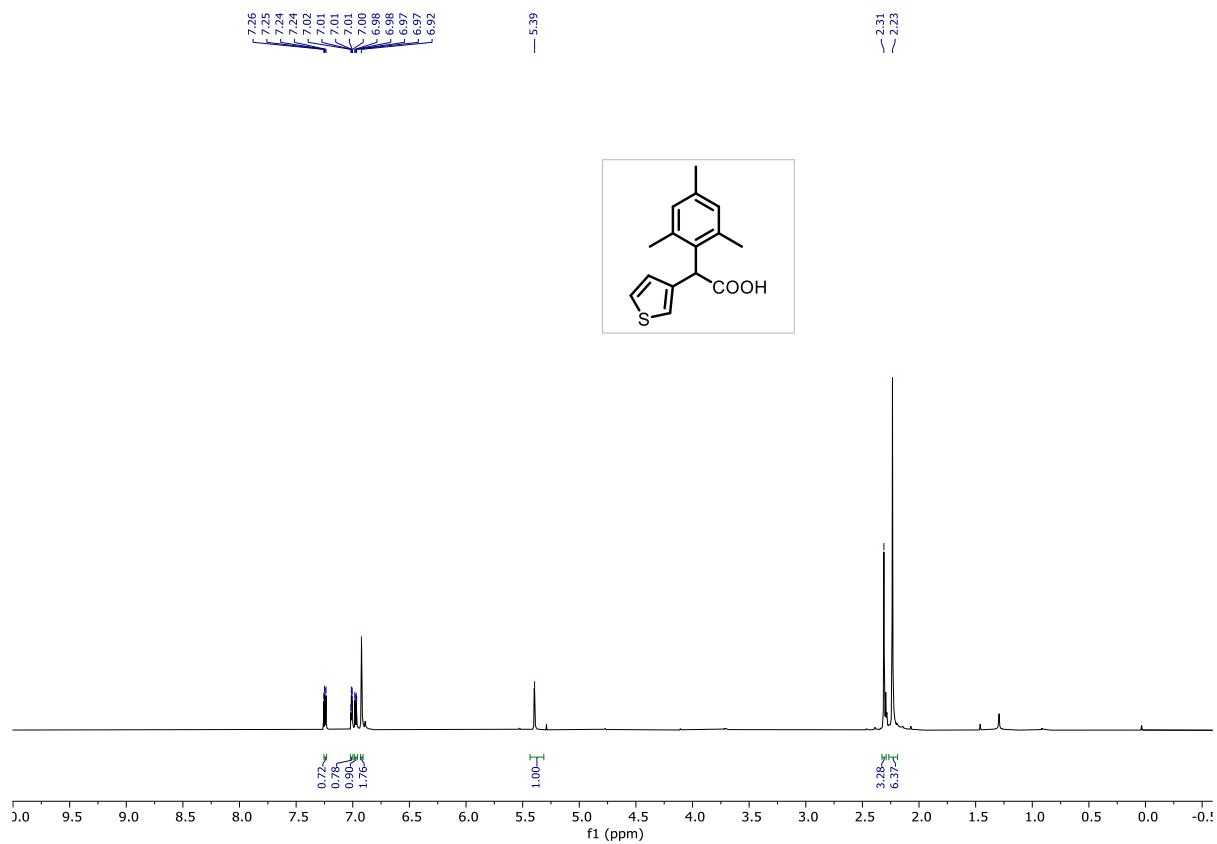


^{13}C { ^1H } NMR (126 MHz, CDCl_3)

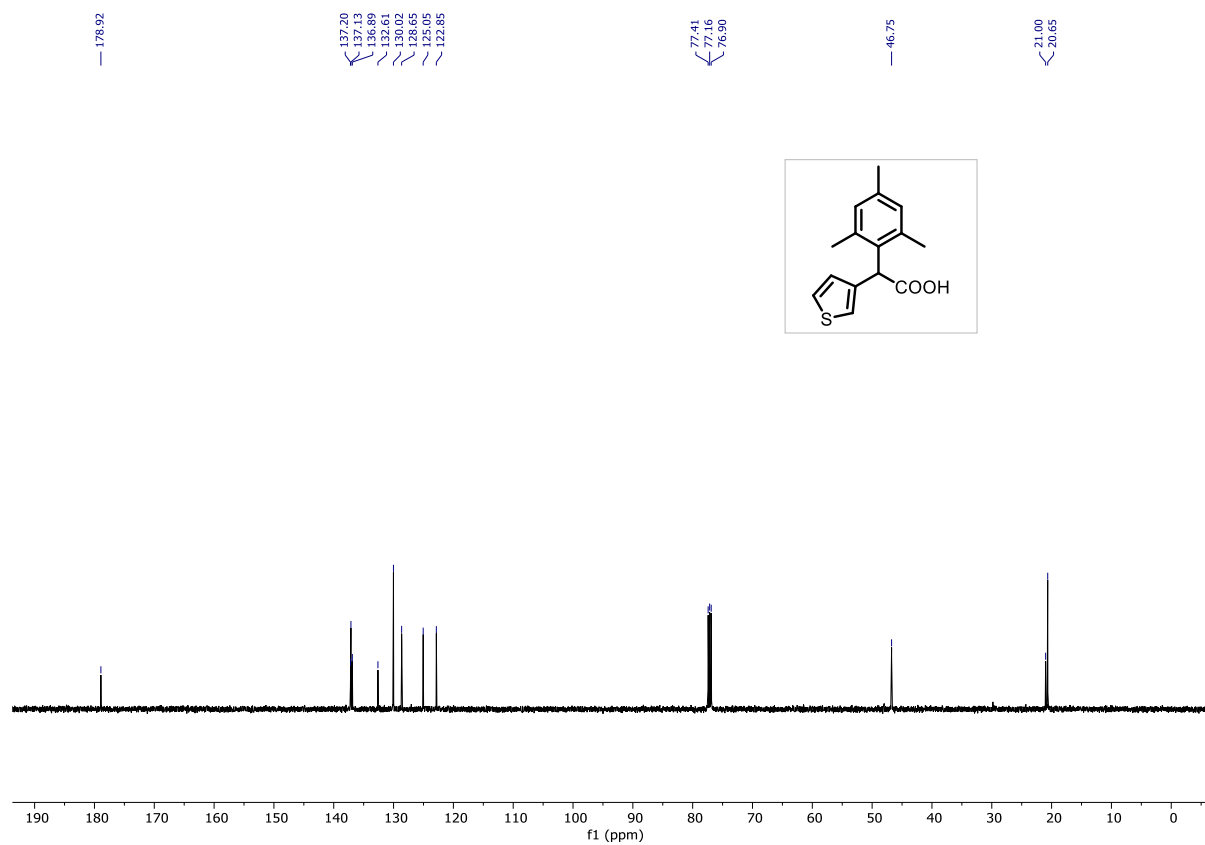


2-Mesityl-2-(thiophen-3-yl)acetic acid (4l)

^1H NMR (400 MHz, CDCl_3)

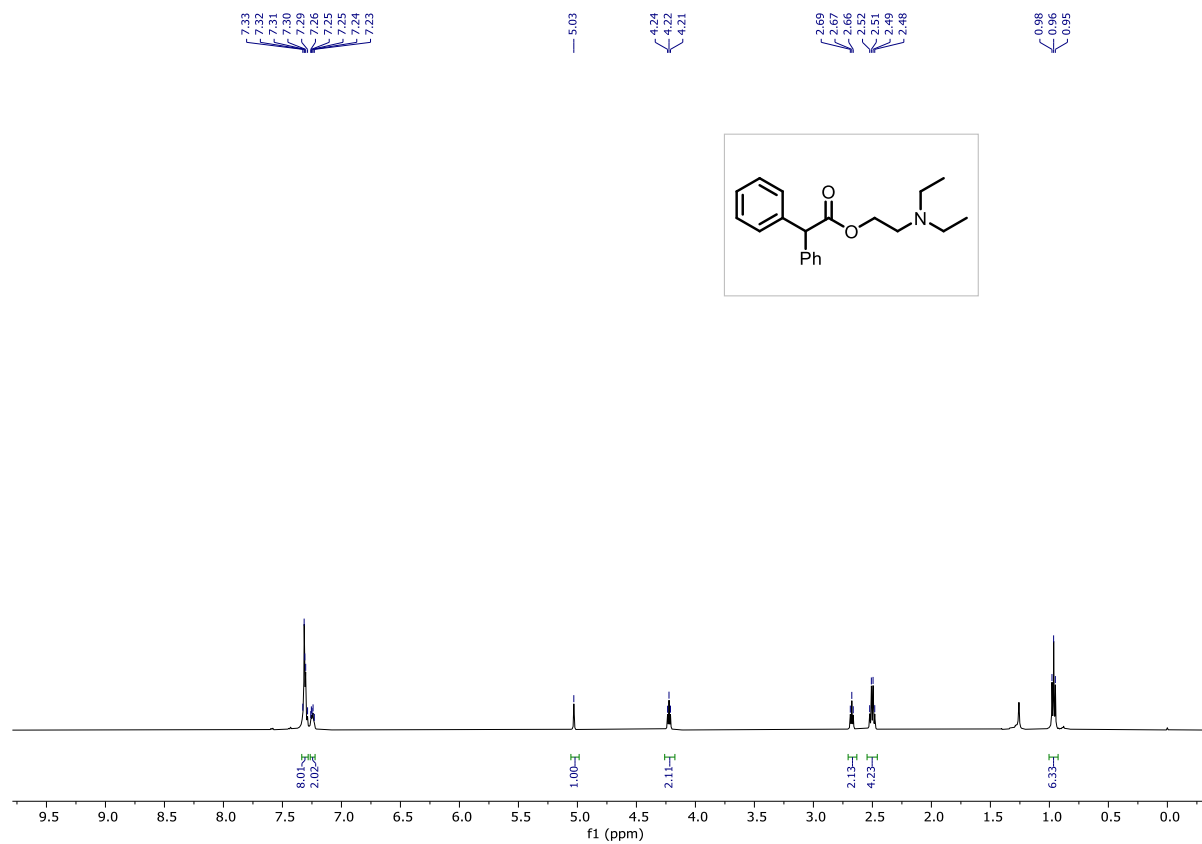


^{13}C { ^1H } NMR (126 MHz, CDCl_3)

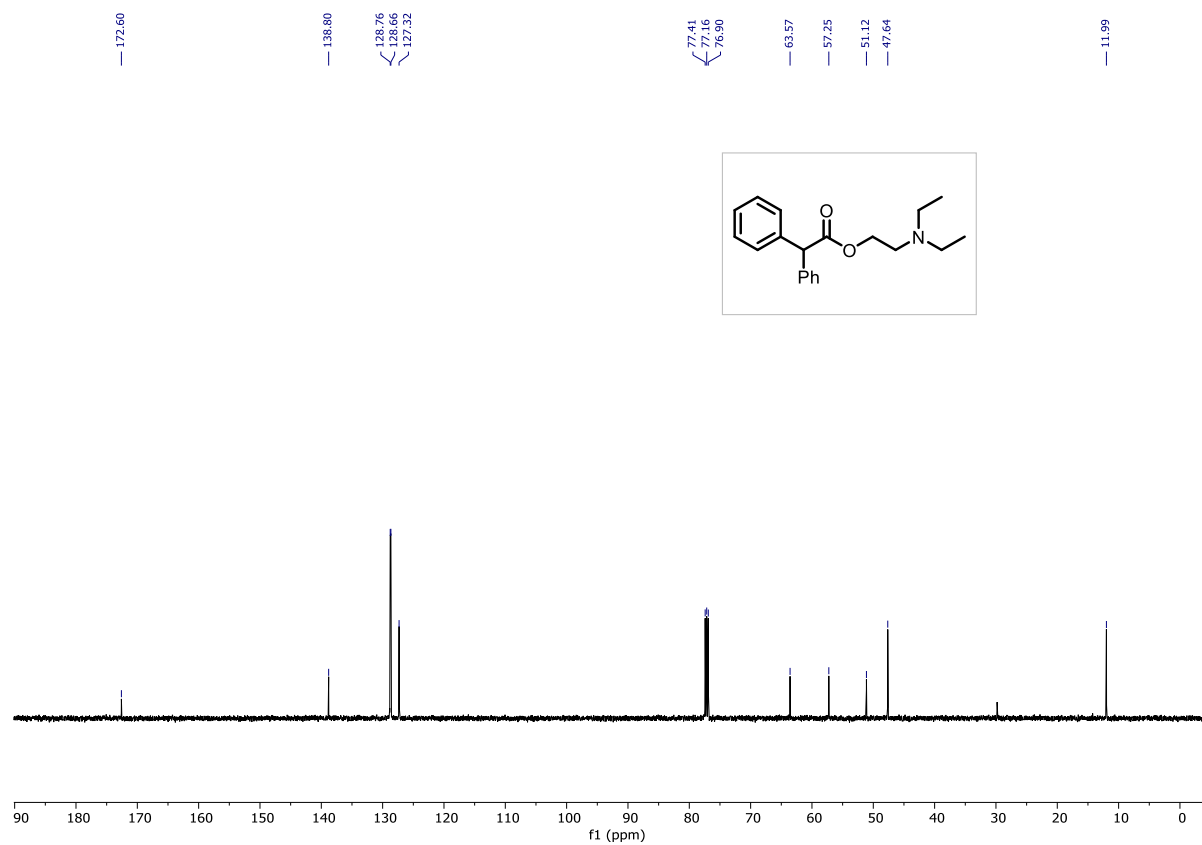


2-(Diethylamino)-ethyl 2,2-diphenylacetate (5a)

^1H NMR (500 MHz, CDCl_3)

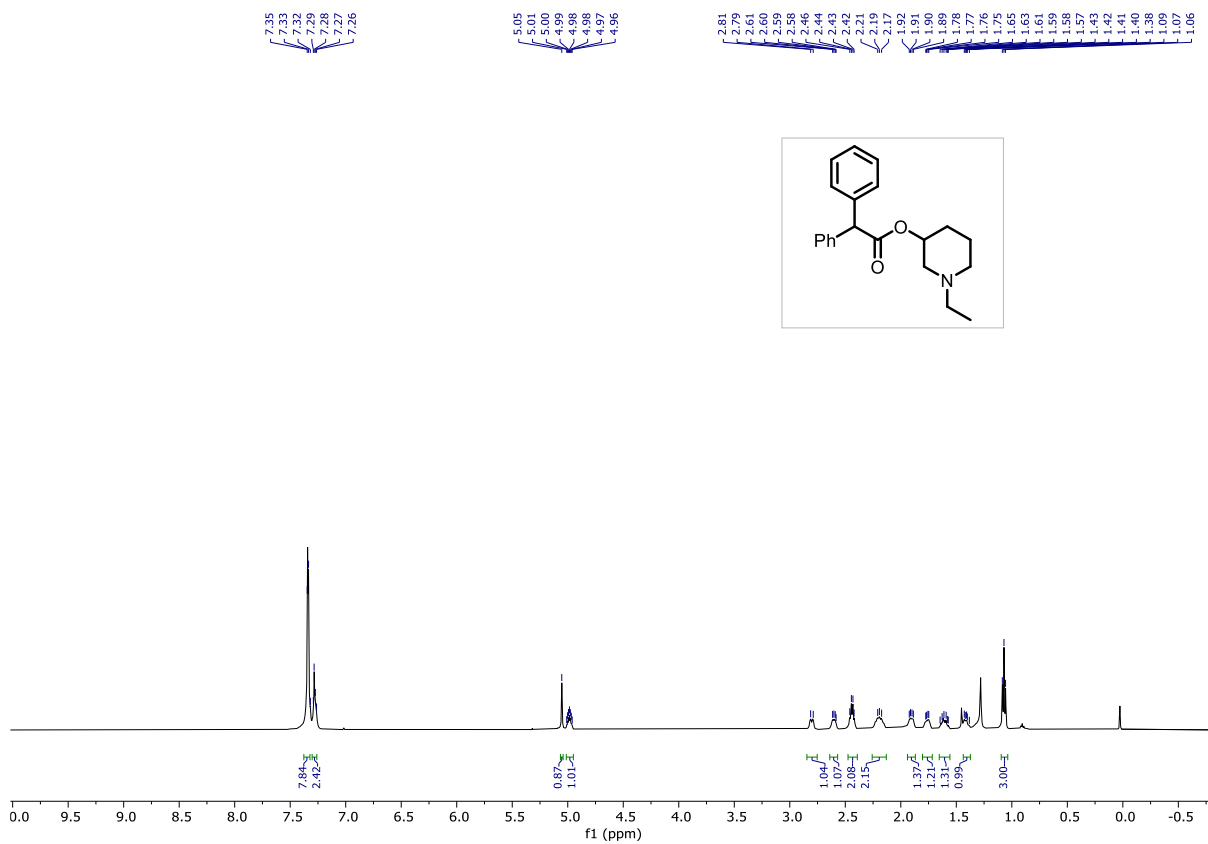


^{13}C { ^1H } NMR (126 MHz, CDCl_3)

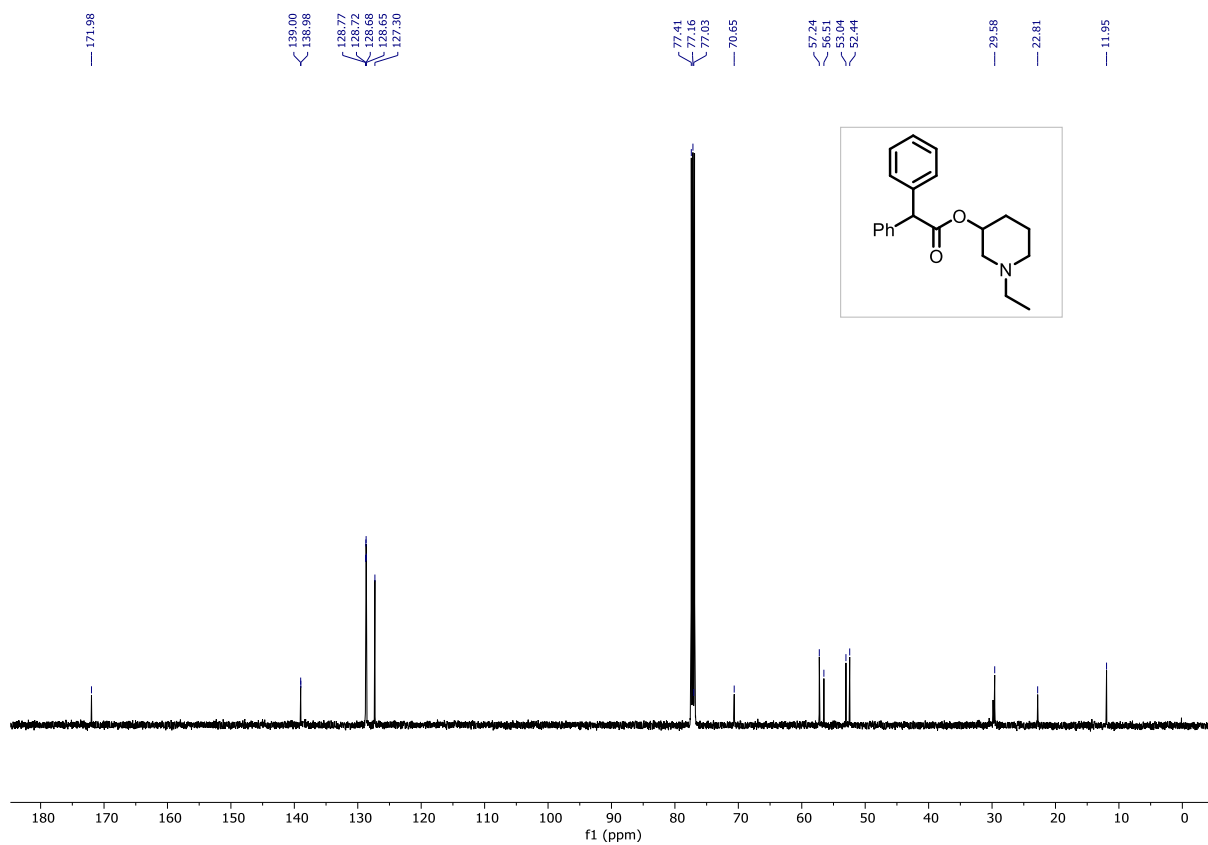


1-Ethylpiperidin-3-yl-2,2-diphenylacetate (5b)

^1H NMR (500 MHz, CDCl_3)

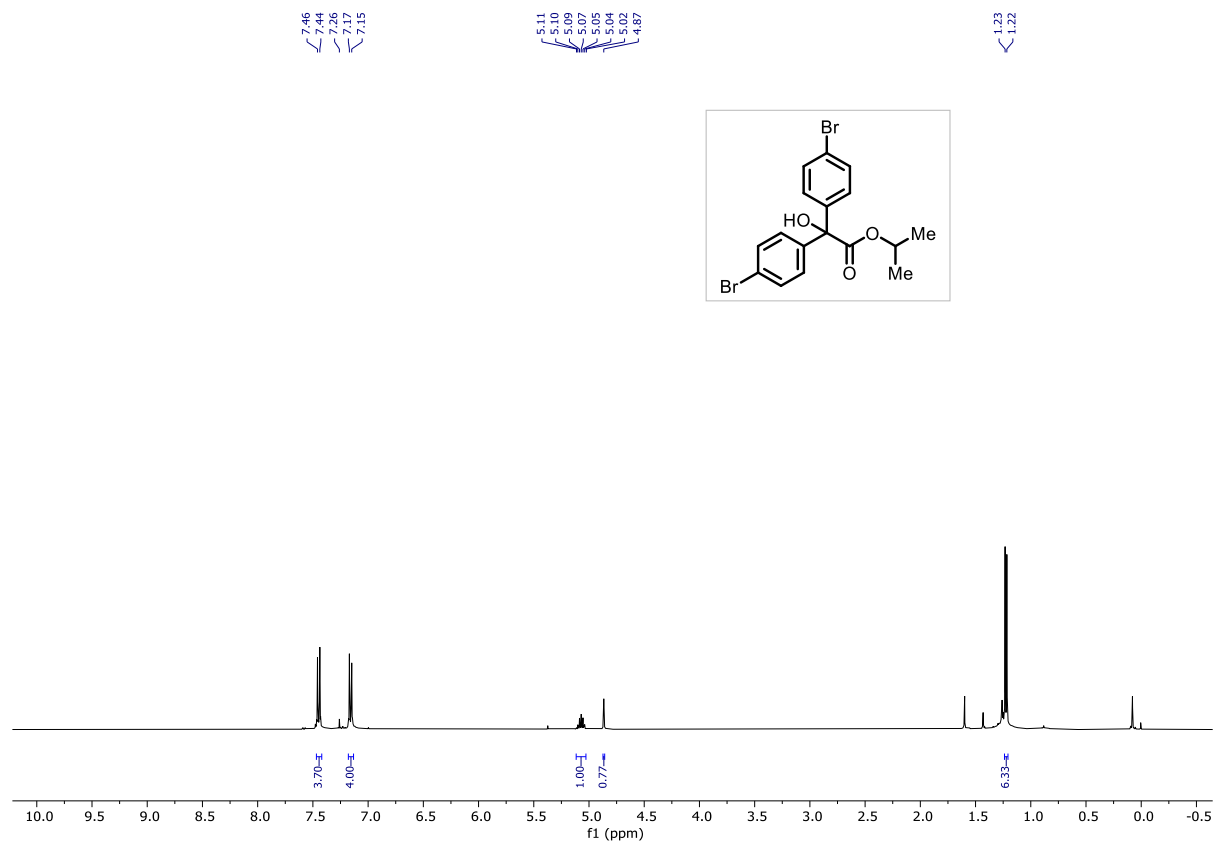


^{13}C { ^1H } NMR (126 MHz, CDCl_3)

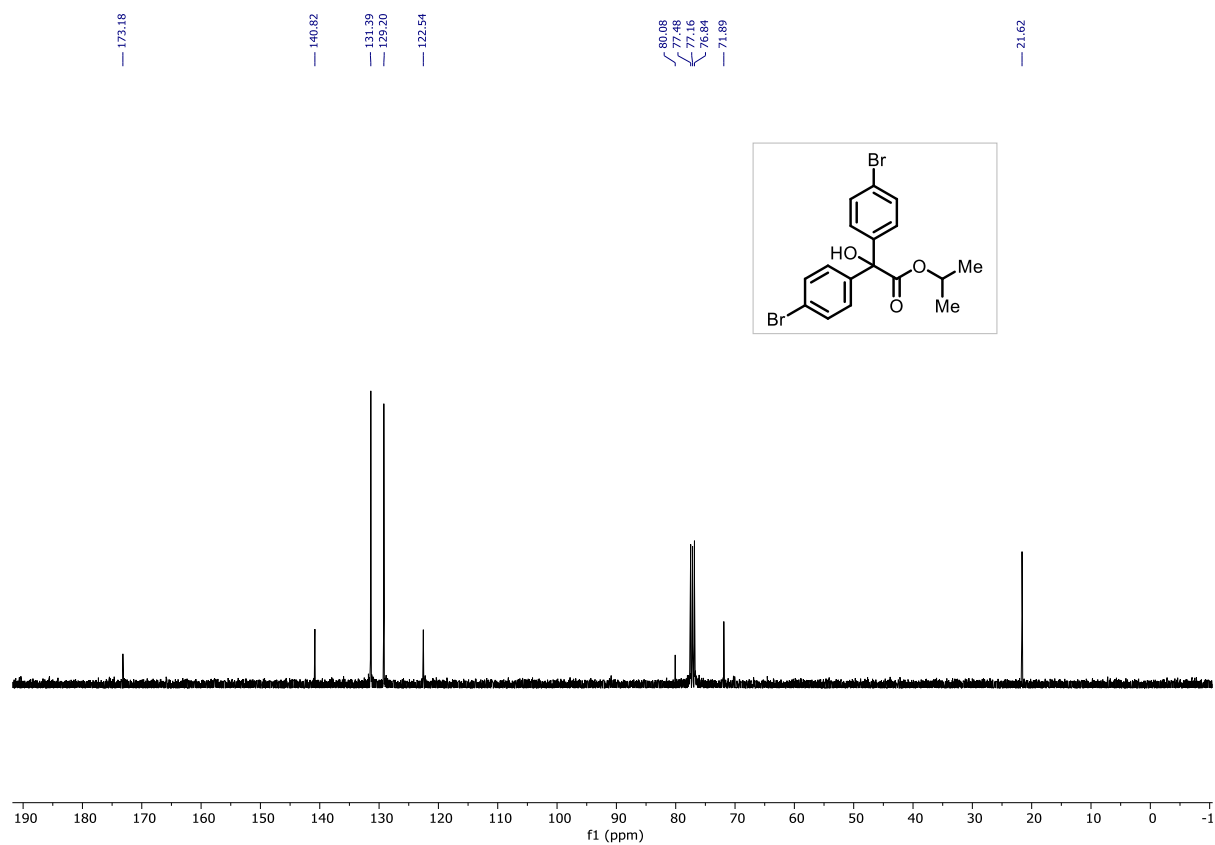


Isopropyl-2,2-bis(4-bromophenyl)-2-hydroxyacetate (5c)

^1H NMR (400 MHz, CDCl_3)

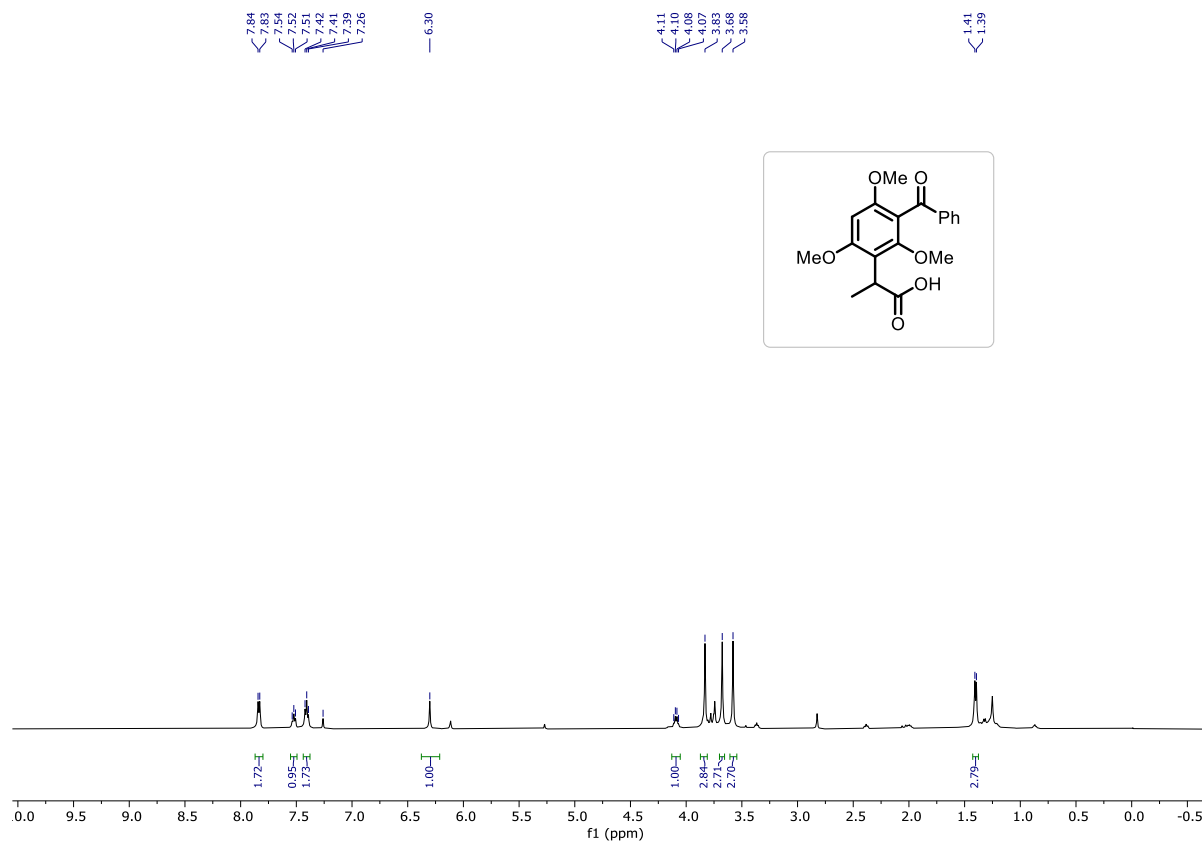


^{13}C { ^1H } NMR (101 MHz, CDCl_3)

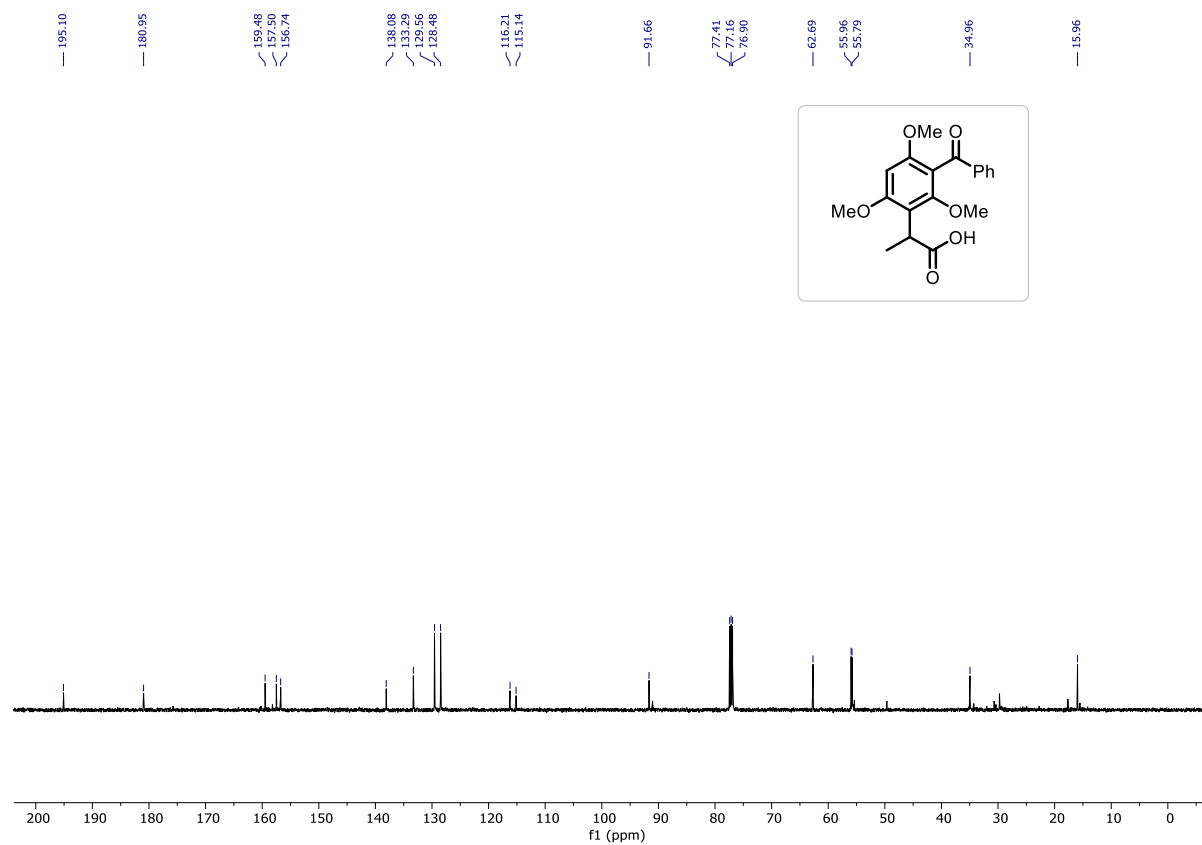


2-(3-Benzoyl-2,4,6-trimethoxyphenyl)propanoic acid (5d)

^1H NMR (500 MHz, CDCl_3)



^{13}C { ^1H } NMR (126 MHz, CDCl_3)



2-(Piperidin-1-yl)ethyl 2,2-diphenylacetate (5e)

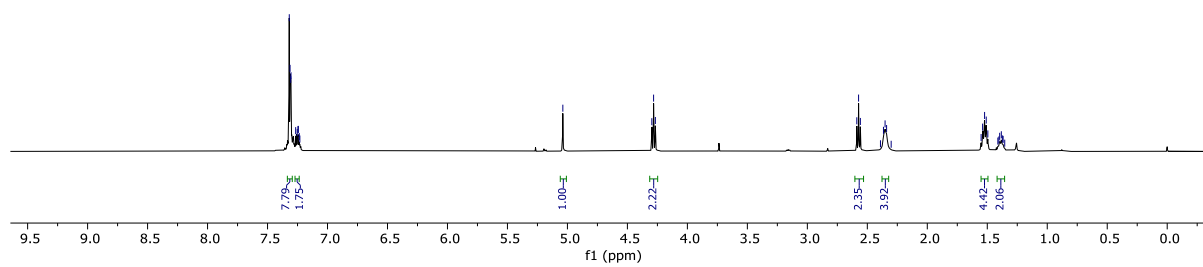
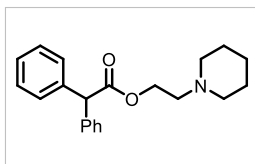
^1H NMR (400 MHz, CDCl_3)

7.33
7.31
7.31
7.30
7.27
7.25
7.24
7.24
7.23

5.04

4.30
4.28
4.27

2.59
2.56
2.56
2.37
2.35
2.34
2.30
1.55
1.54
1.54
1.51
1.50
1.41
1.40
1.38
1.37
1.35



^{13}C { ^1H } NMR (126 MHz, CDCl_3)

172.45

138.76

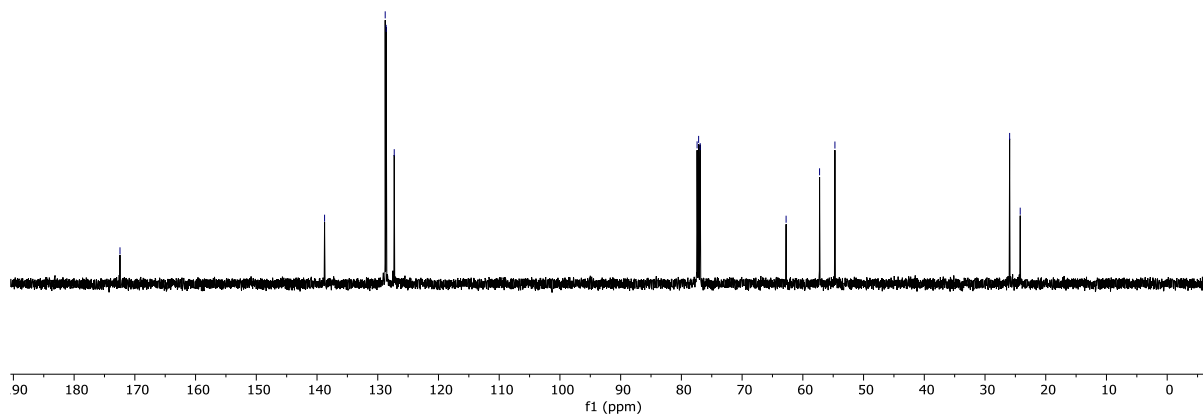
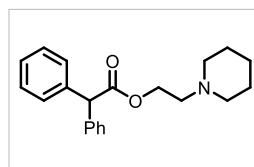
138.77
138.67
127.29

77.41
77.16
76.91

62.76

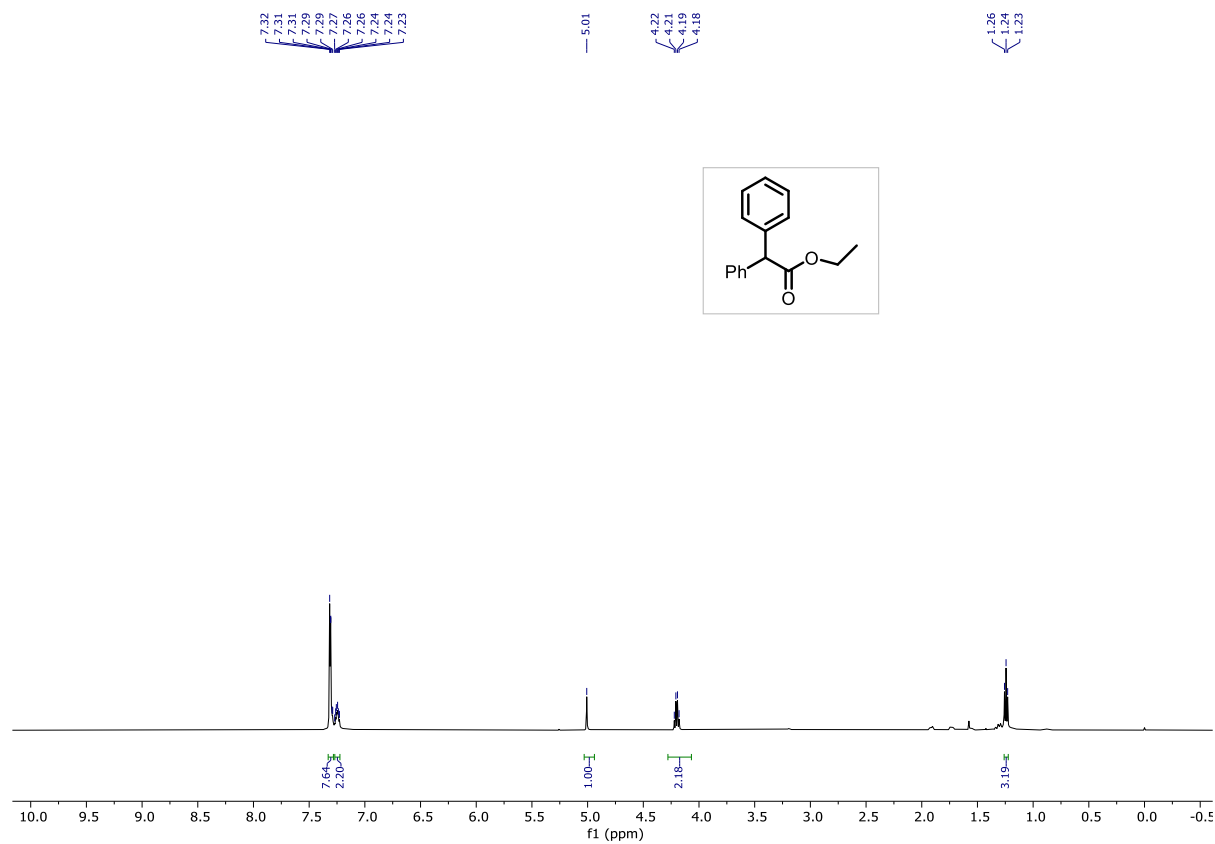
57.24
54.72

25.94
24.20

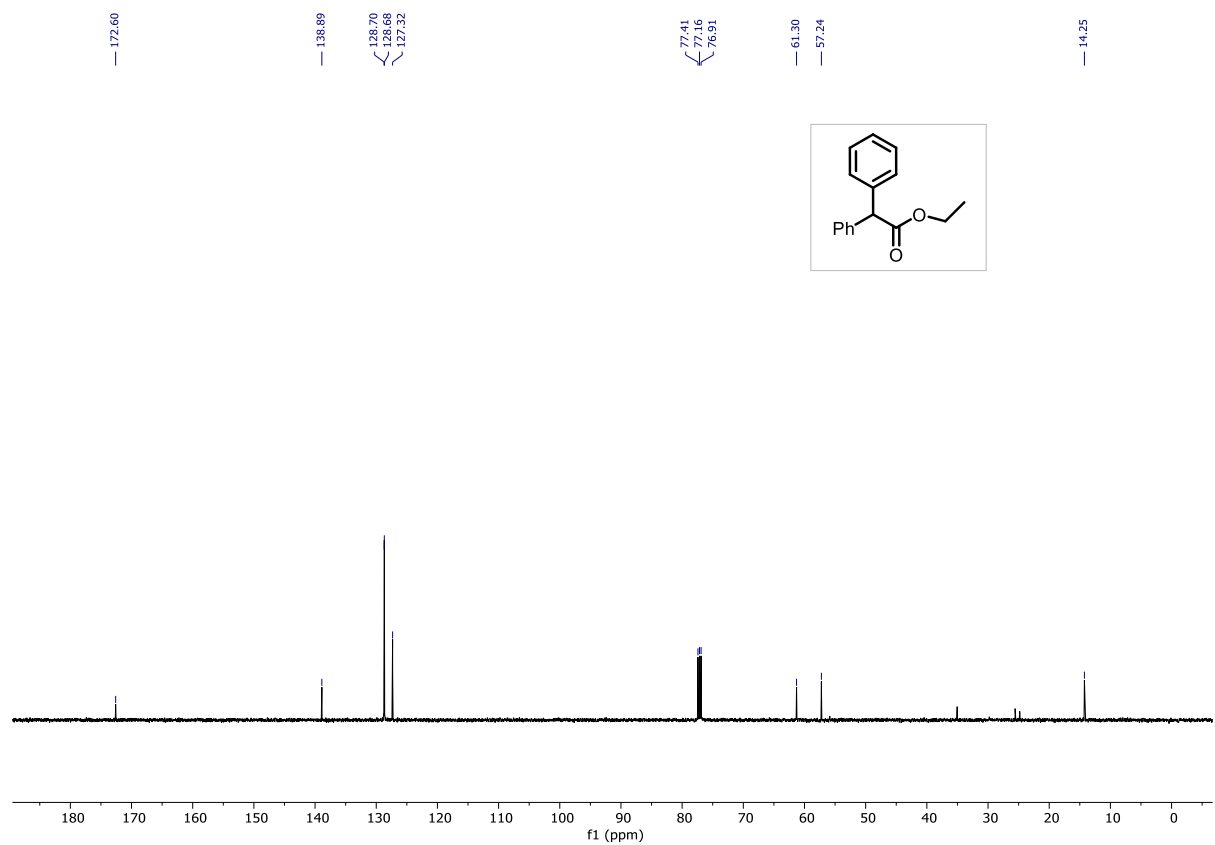


Ethyl-2,2-diphenylacetate (5f)

^1H NMR (500 MHz, CDCl_3)

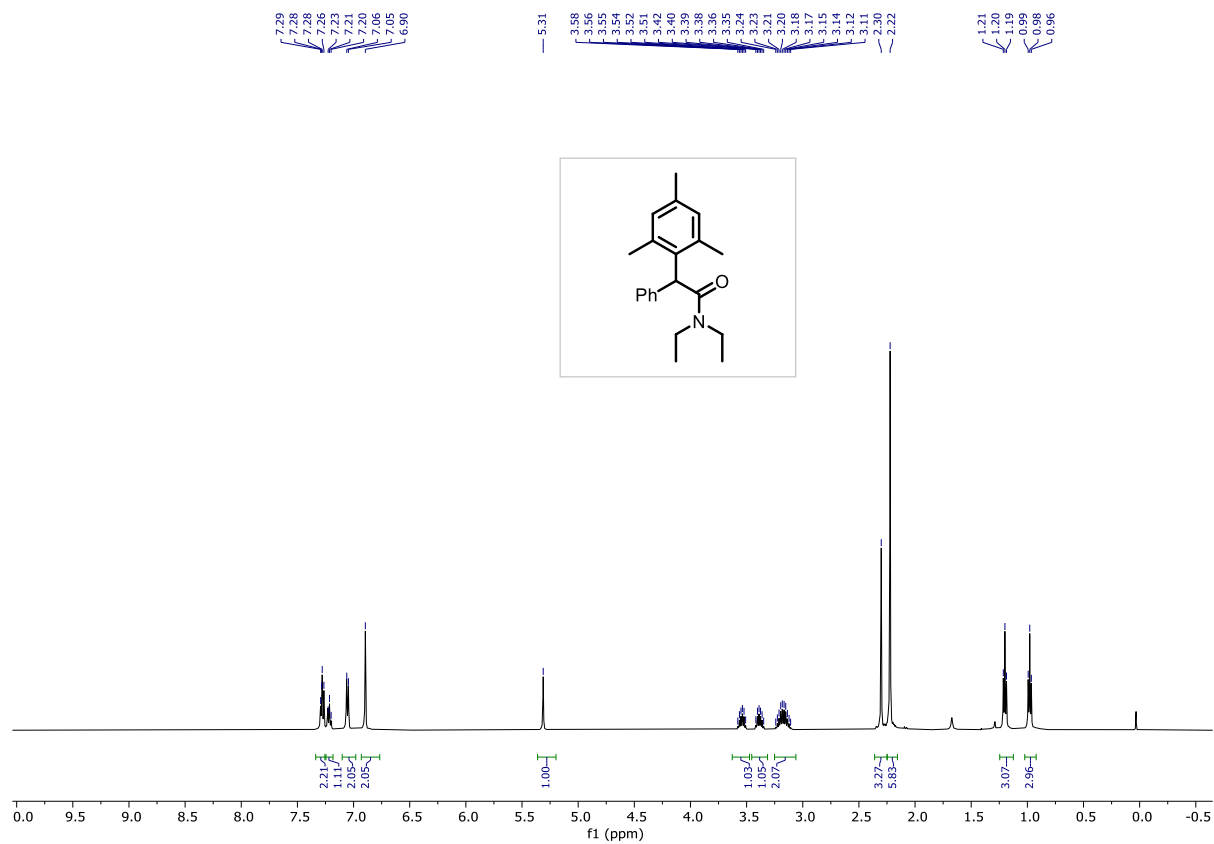


^{13}C { ^1H } NMR (126 MHz, CDCl_3)

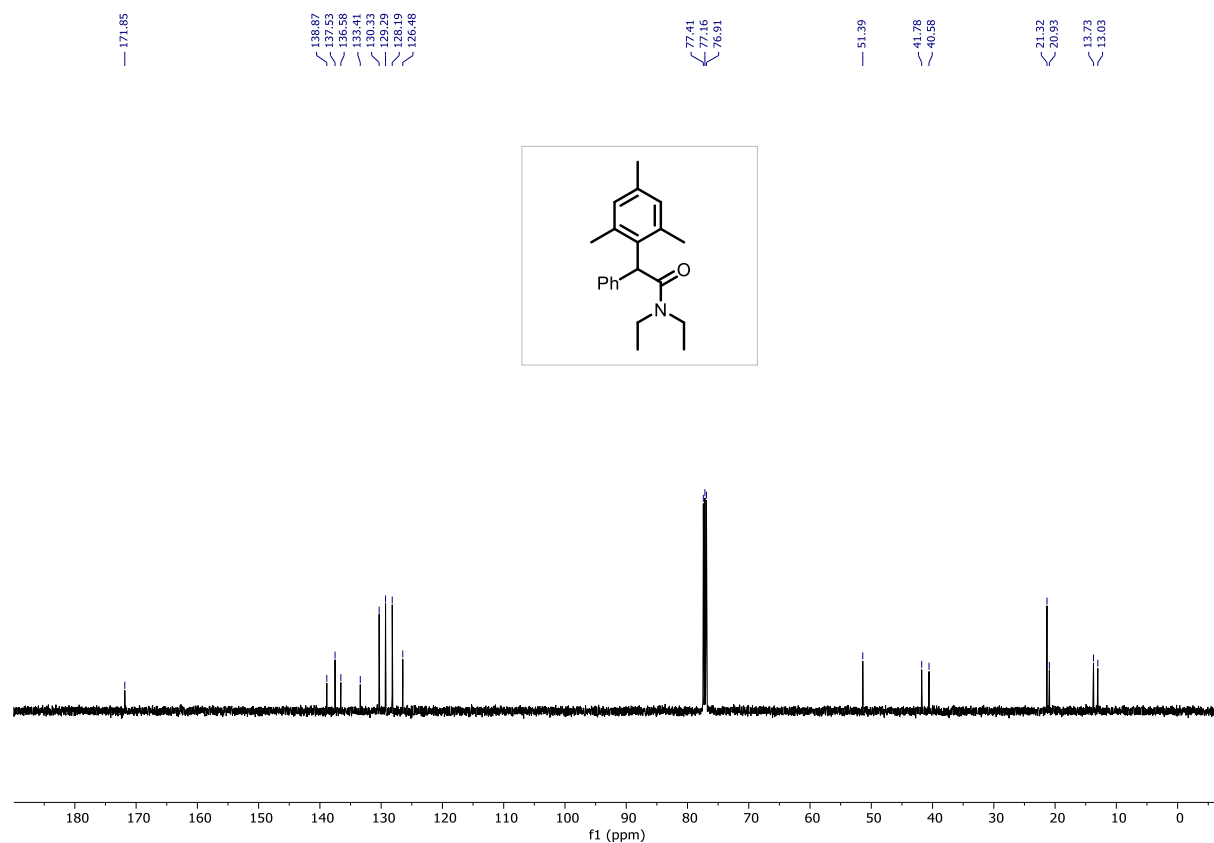


N,N-Diethyl-2-mesityl-2-phenylacetamide (5g)

^1H NMR (500 MHz, CDCl_3)

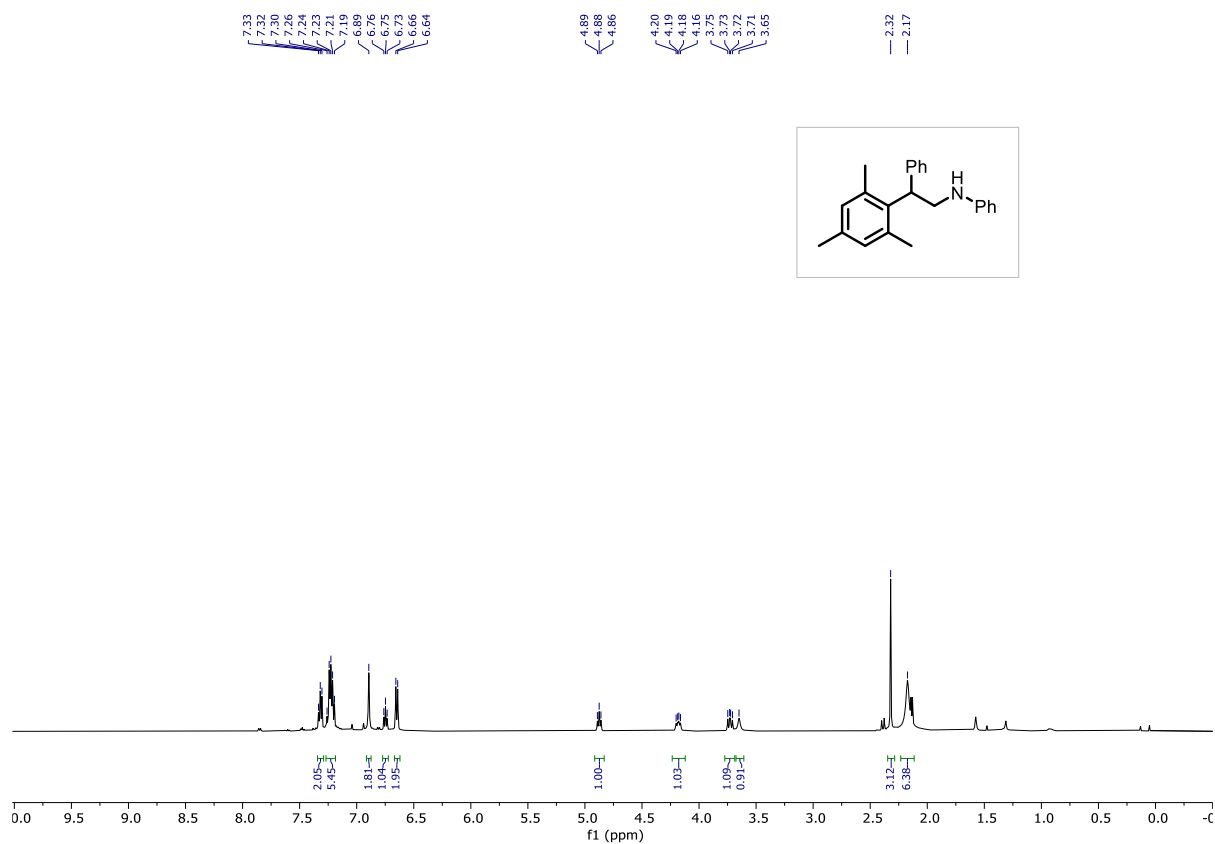


^{13}C $\{^1\text{H}\}$ NMR (126 MHz, CDCl_3)

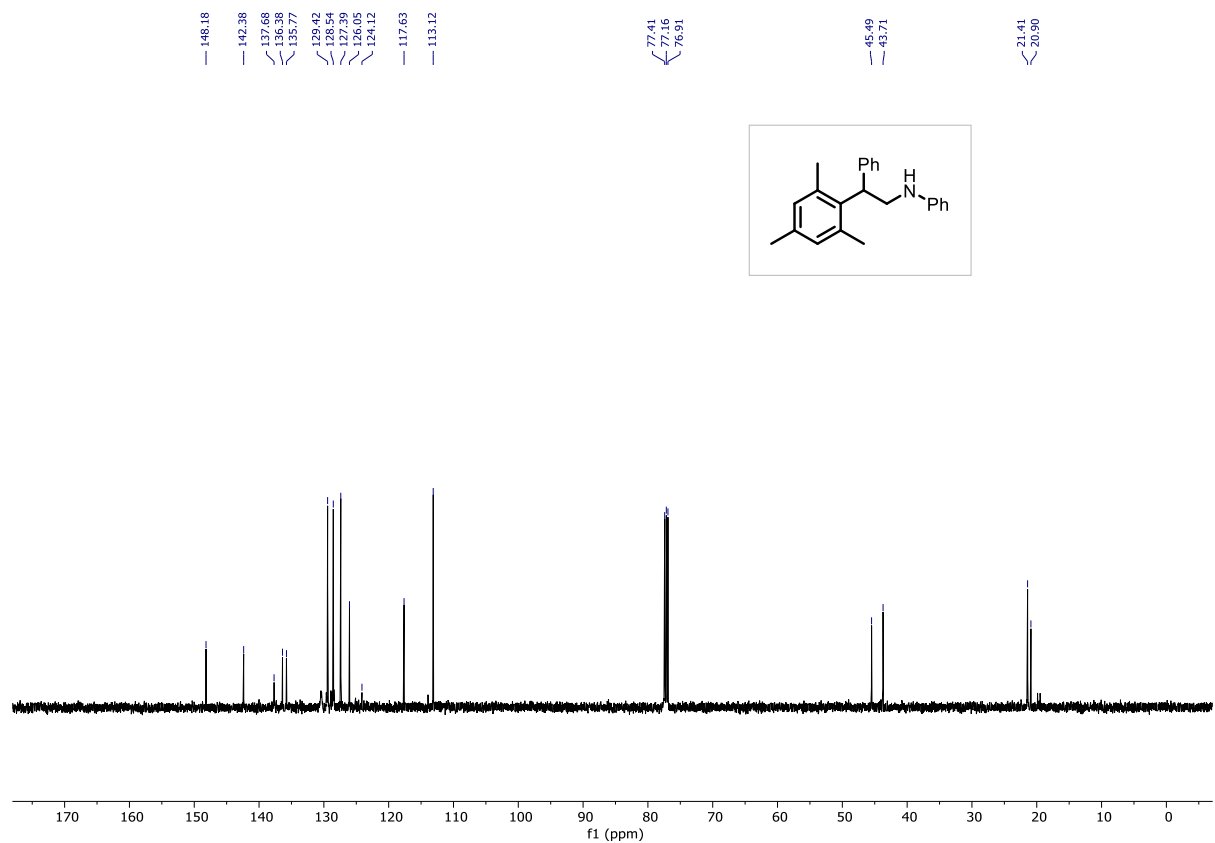


N-(2-mesityl-2-phenylethyl)aniline (5h)

^1H NMR (500 MHz, CDCl_3)

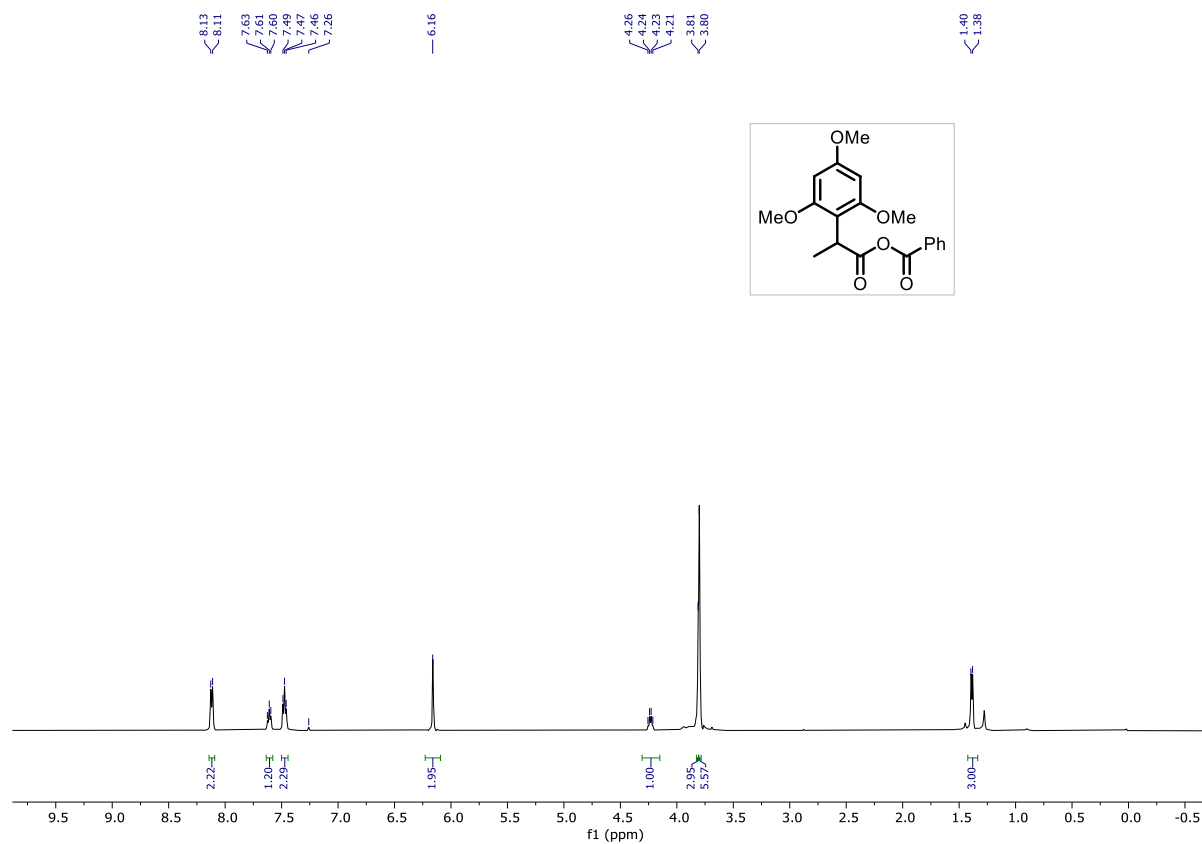


^{13}C { ^1H } NMR (126 MHz, CDCl_3)

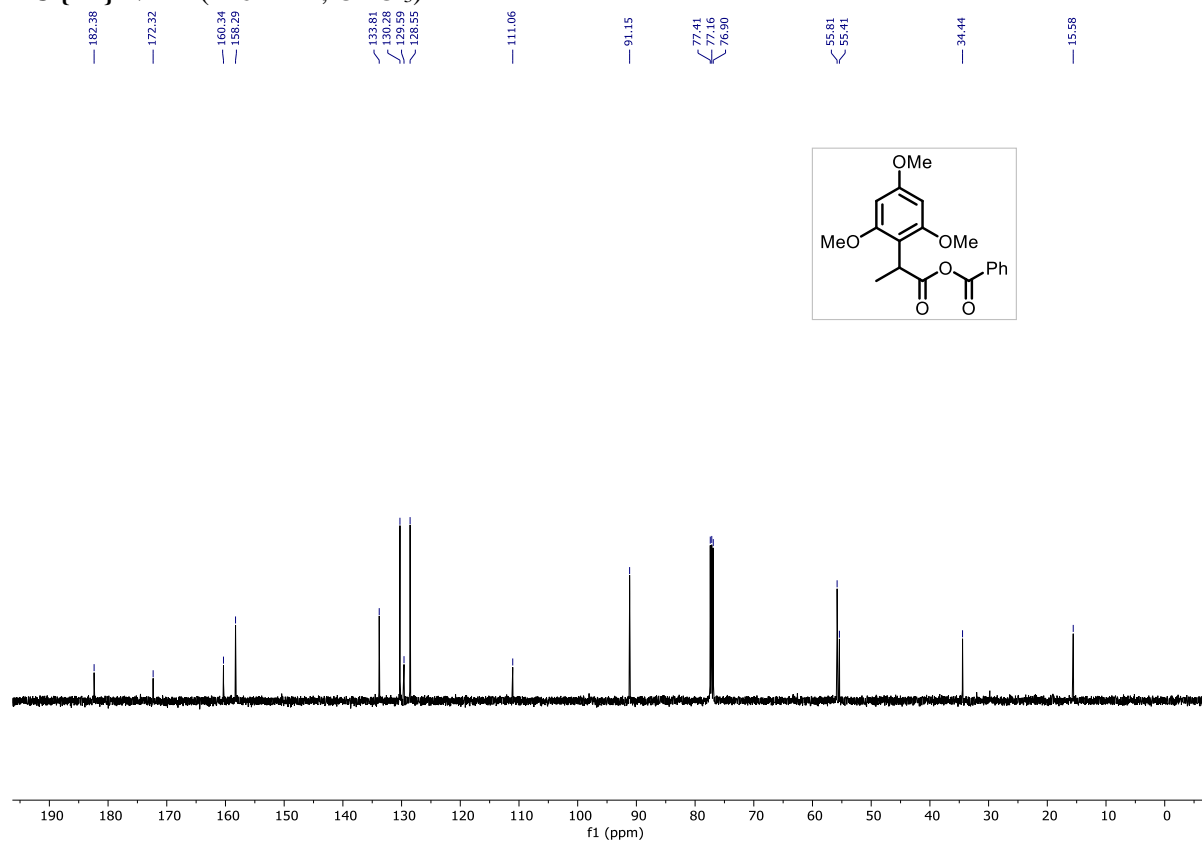


Benzoic-2-(2,4,6-trimethoxyphenyl) propanoic anhydride (5i)

^1H NMR (500 MHz, CDCl_3)

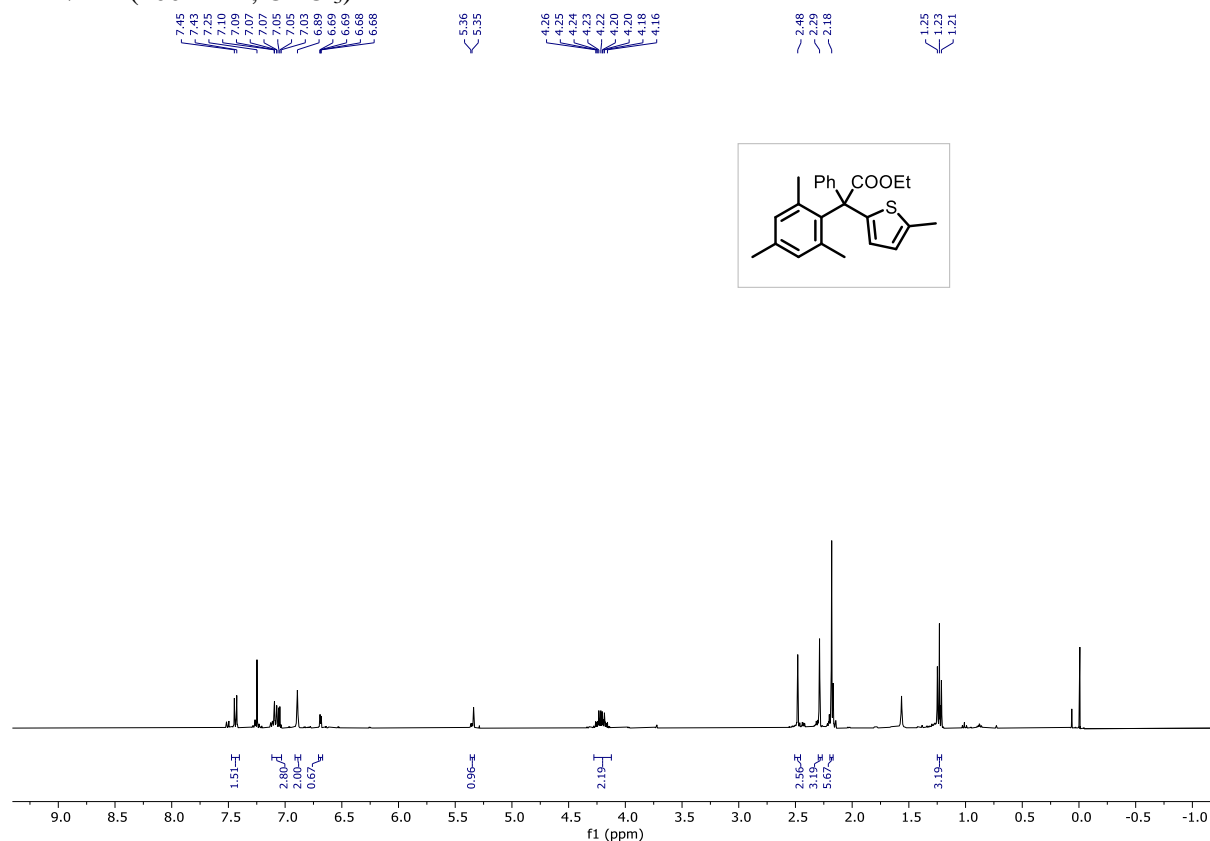


^{13}C $\{^1\text{H}\}$ NMR (126 MHz, CDCl_3)

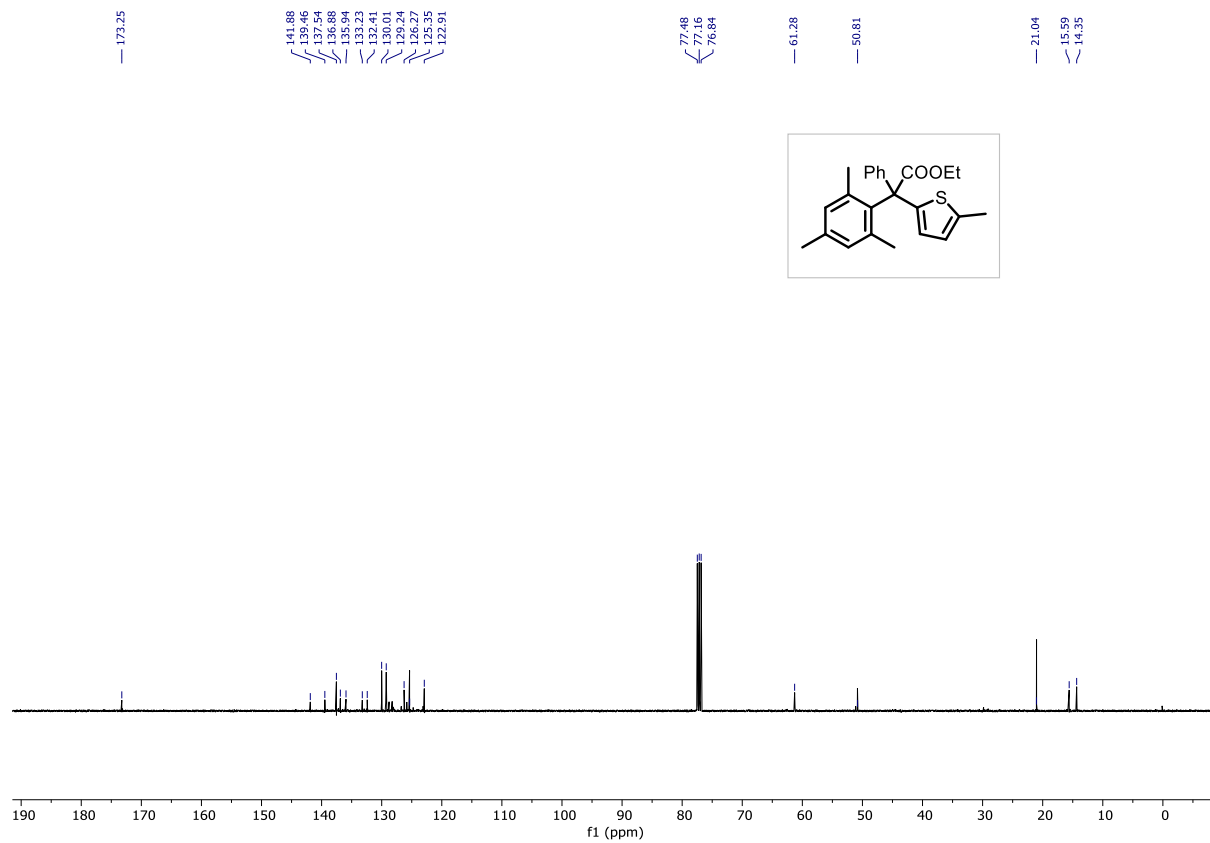


Ethyl-2-mesityl-2-(5-methylthiophen-2-yl)-2-phenylacetate (5j)

^1H NMR (400 MHz, CDCl_3)

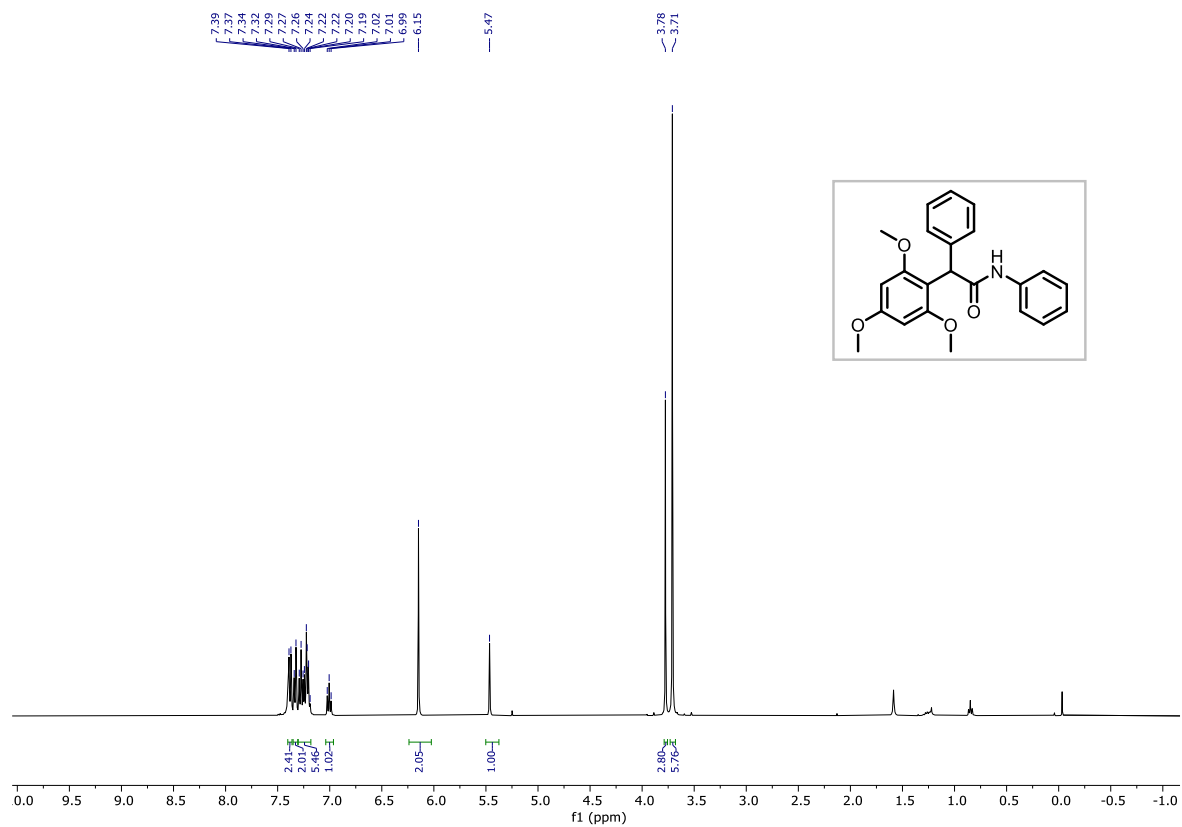


^{13}C { ^1H } NMR (101 MHz, CDCl_3)

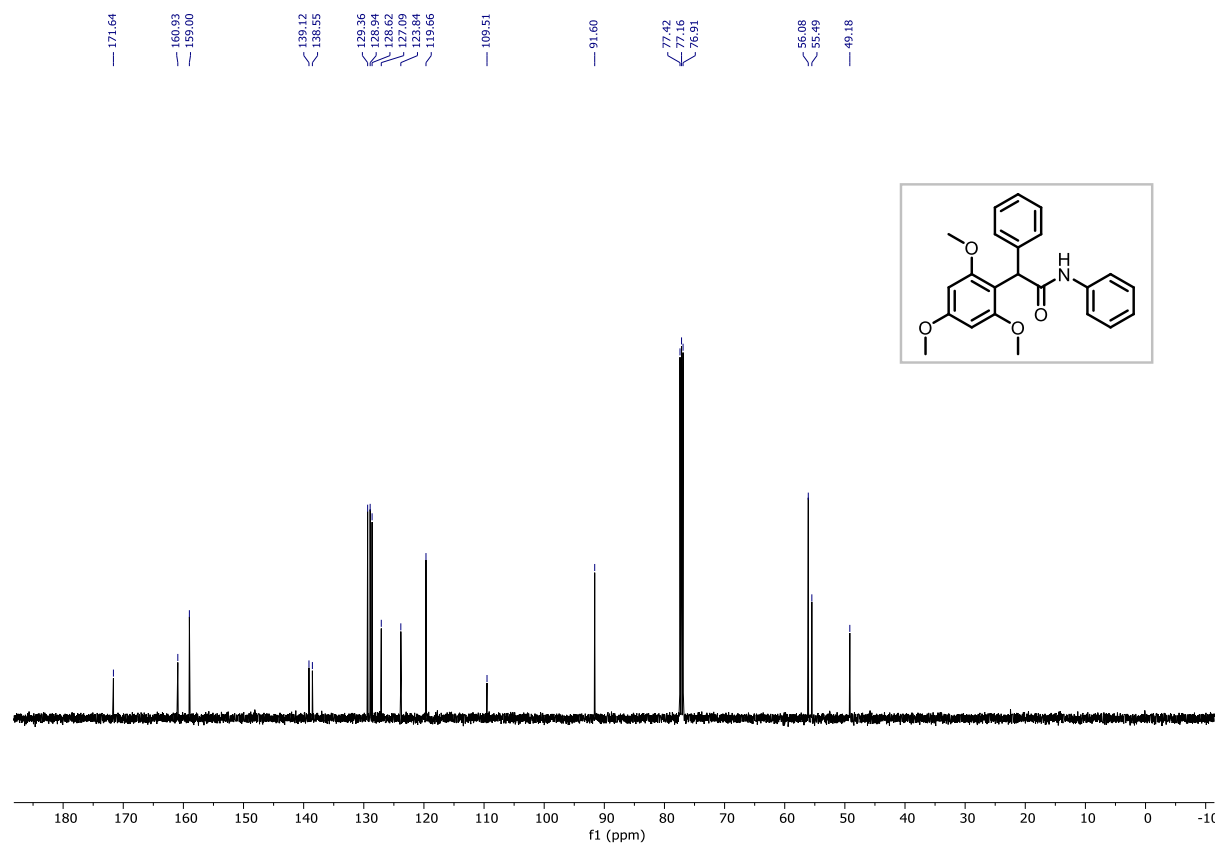


N,2-Diphenyl-2-(2,4,6-trimethoxyphenyl) acetamide (6a)

^1H NMR (400 MHz, CDCl_3)

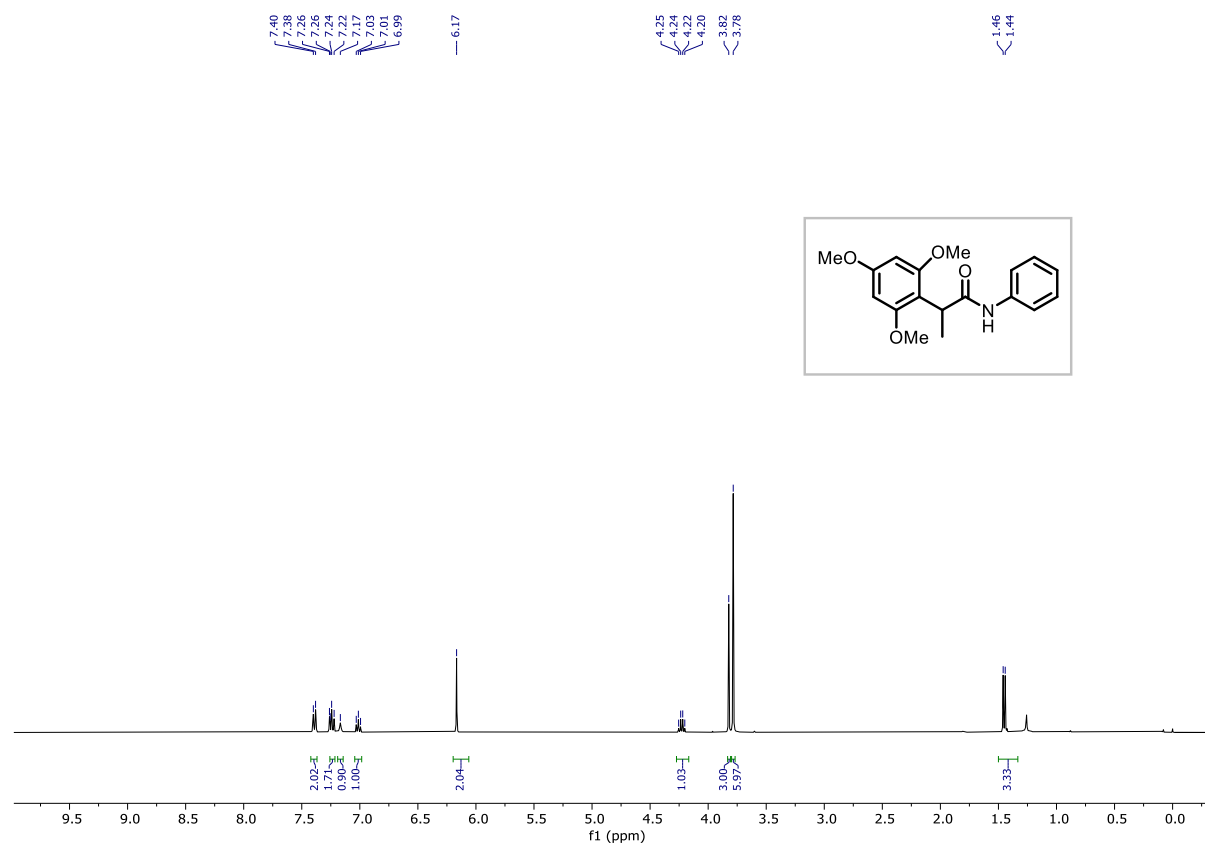


$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3)

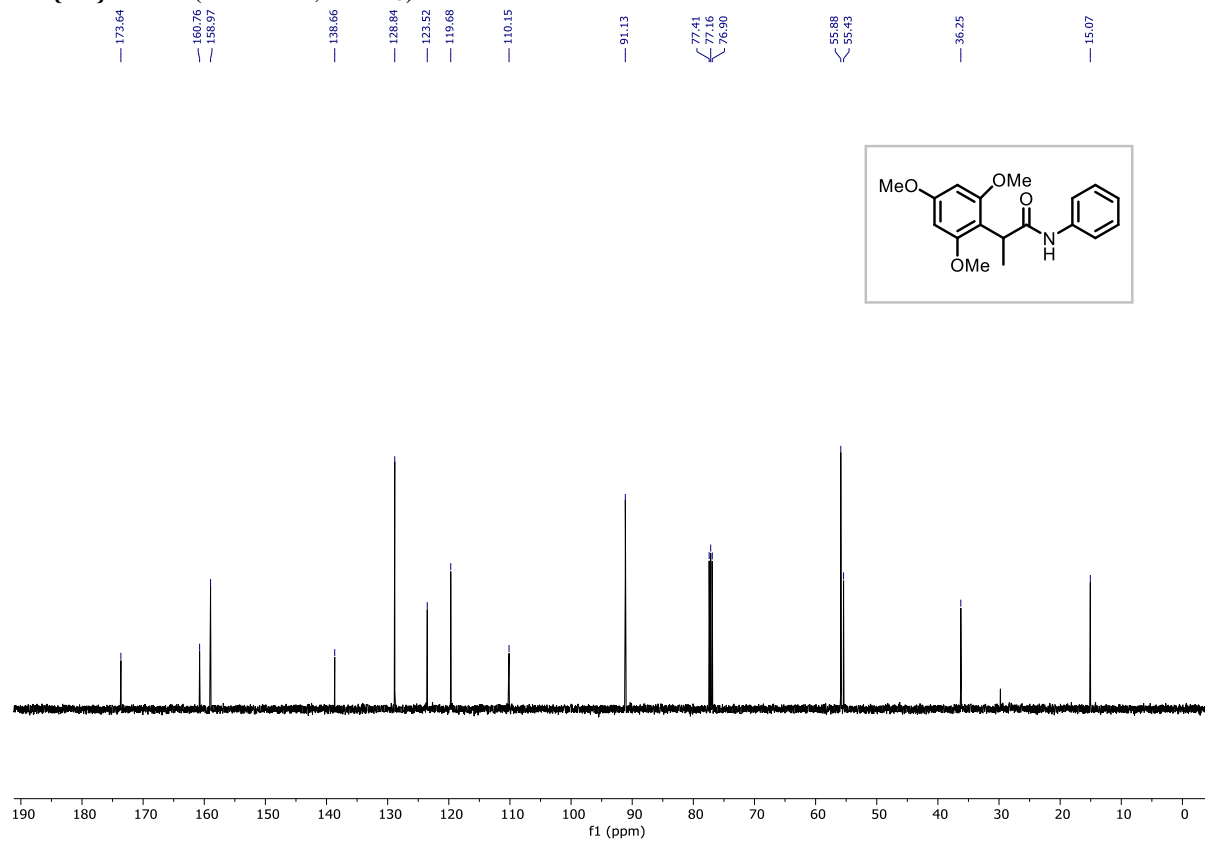


N-Phenyl-2-(2,4,6-trimethoxyphenyl) propenamide (6b)

^1H NMR (400 MHz, CDCl_3)

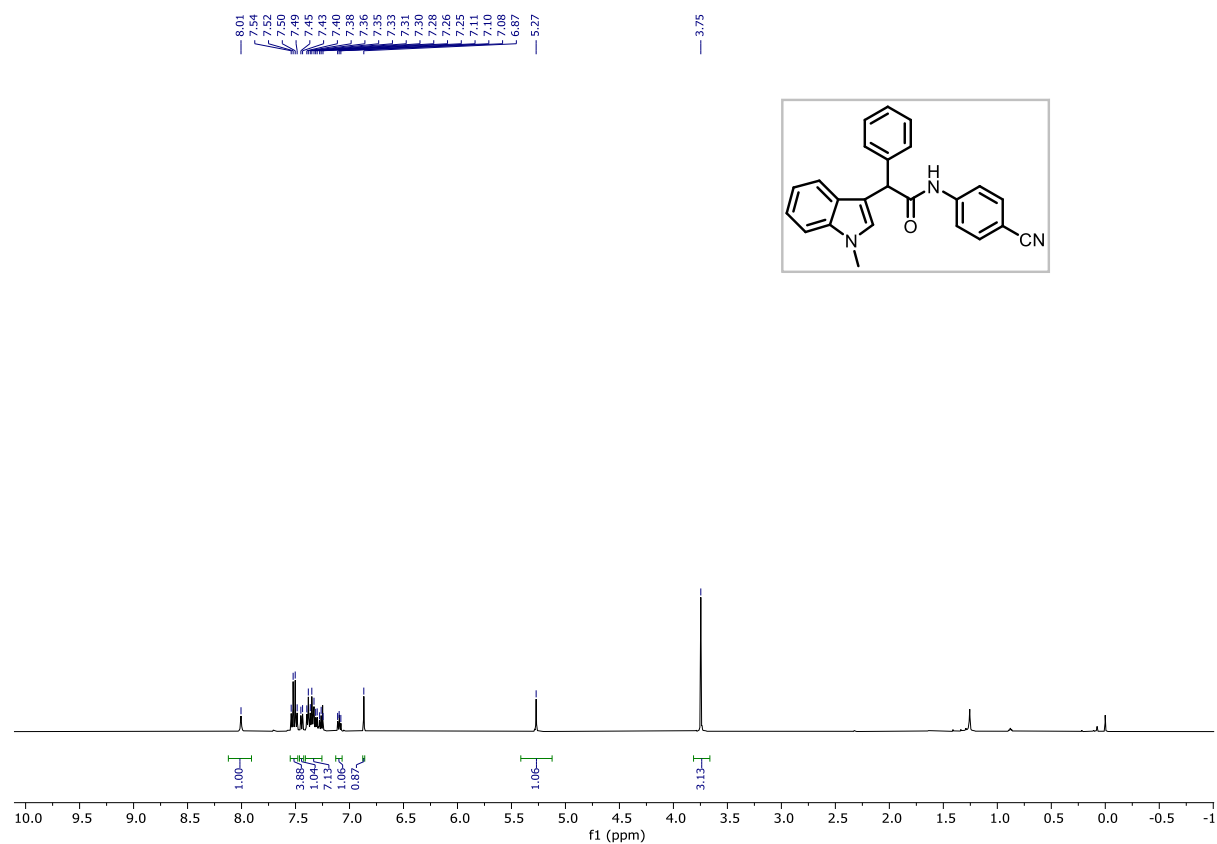


$^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3)

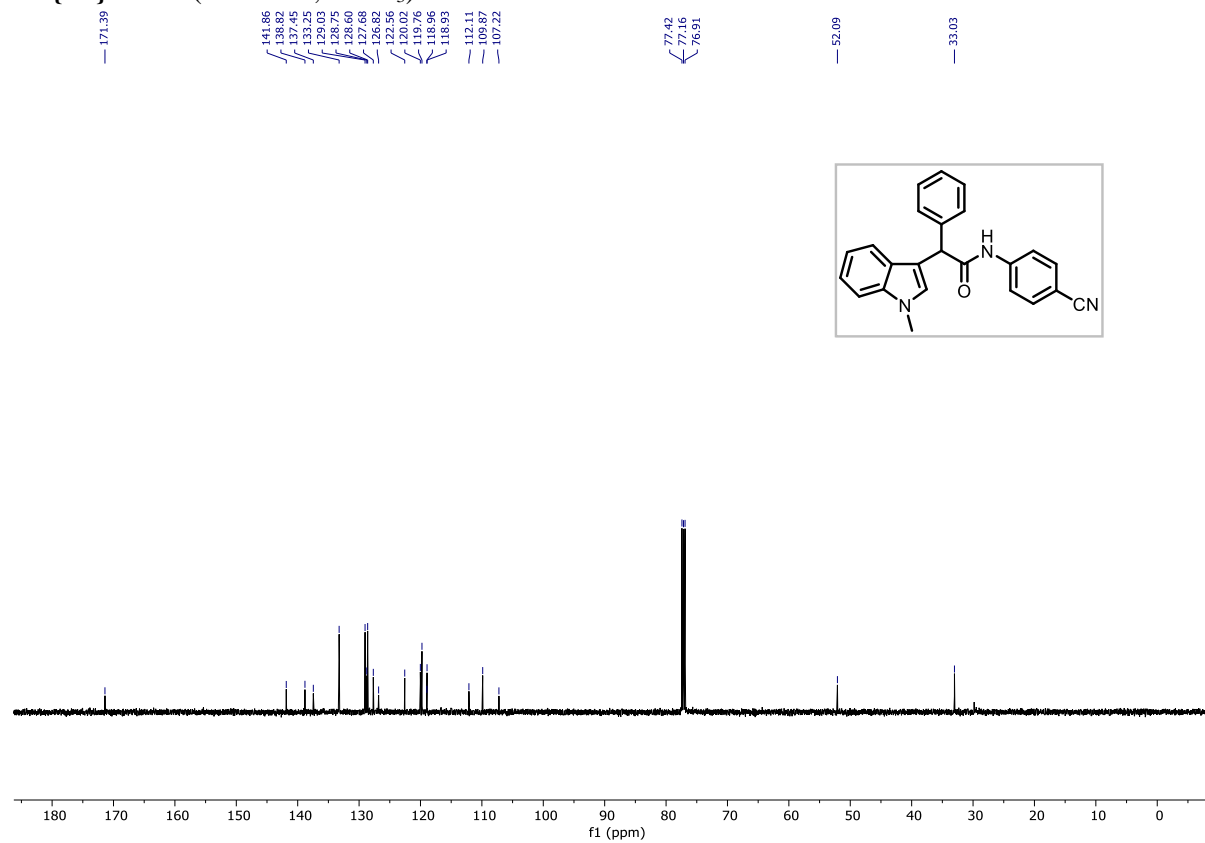


N-(4-Cyanophenyl)-2-(1-methyl-1*H*-indol-3-yl)-2-phenylacetamide (**6c**)

¹H NMR (500 MHz, CDCl₃)

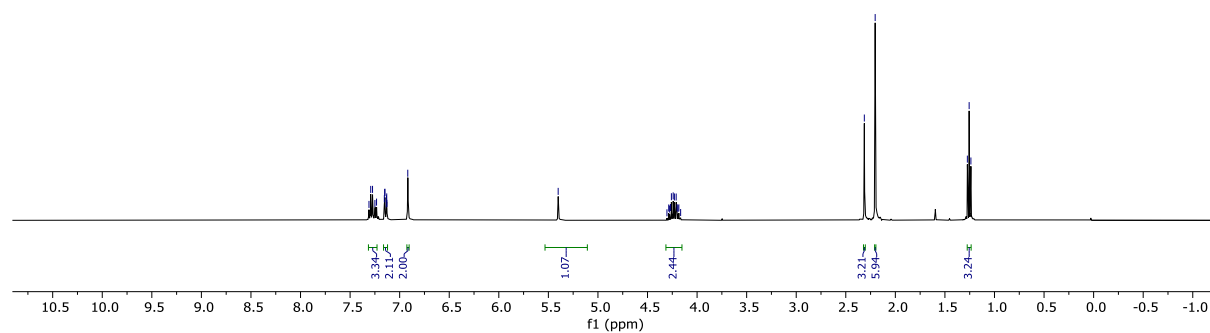
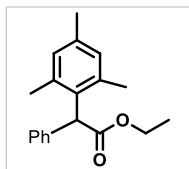


¹³C{¹H} NMR (126 MHz, CDCl₃)

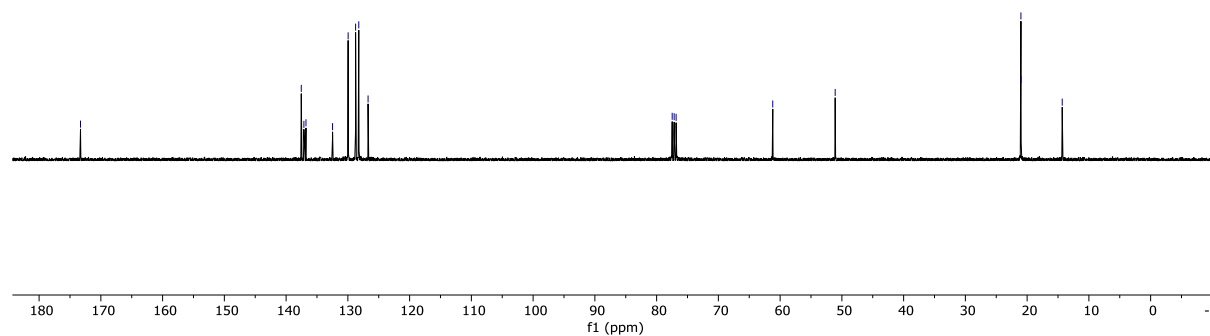


Ethyl-2-mesityl-2-phenylacetate (6d)

^1H NMR (400 MHz, CDCl_3)

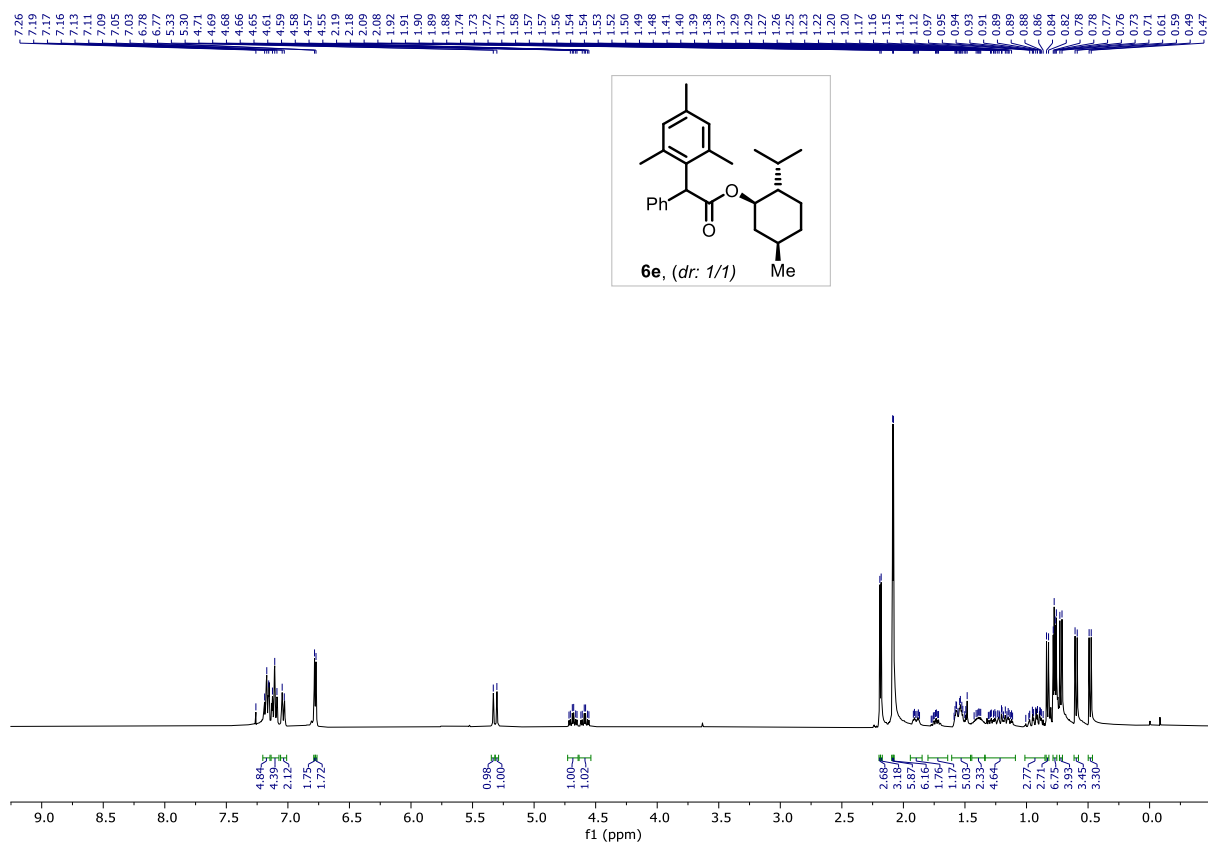


$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3)

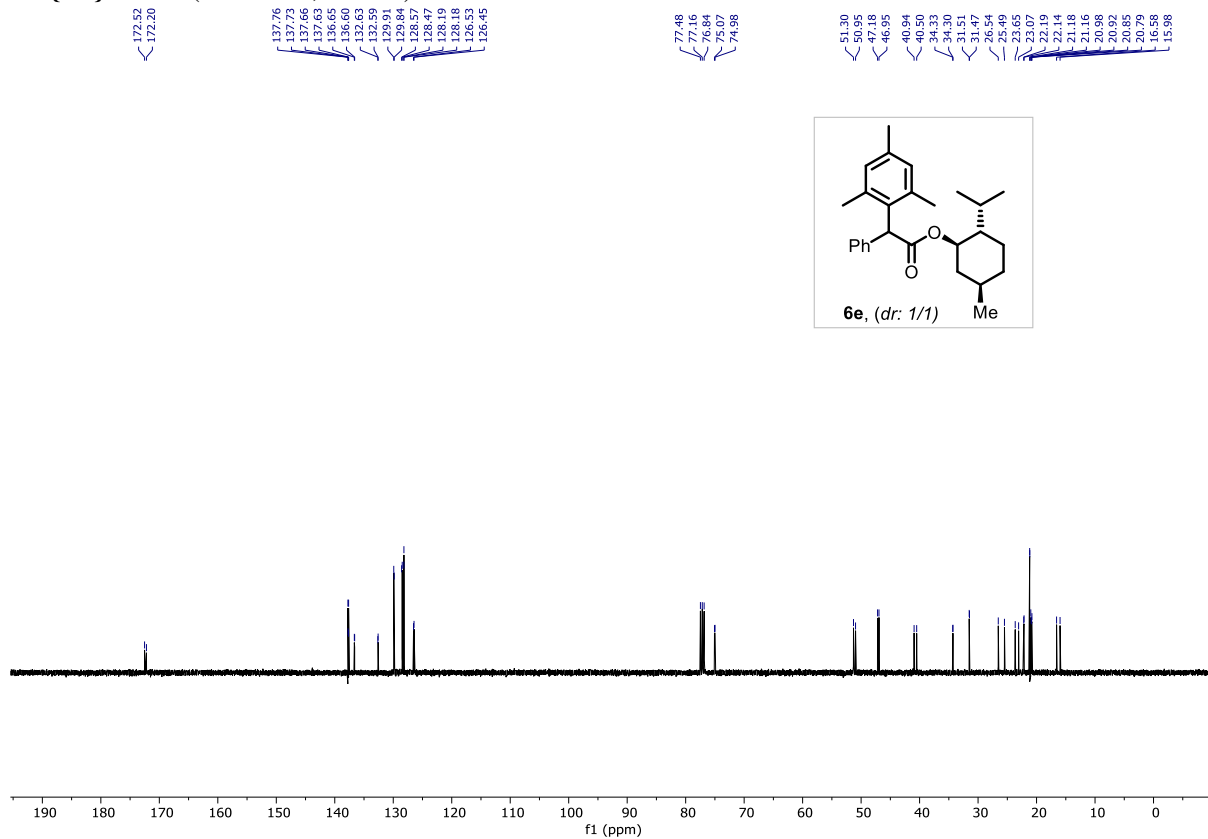


(1*R*,2*R*,5*R*)-2-isopropyl-5-methylcyclohexyl-2-mesityl-2-phenylacetate (**6e**)

¹H NMR (400 MHz, CDCl₃)

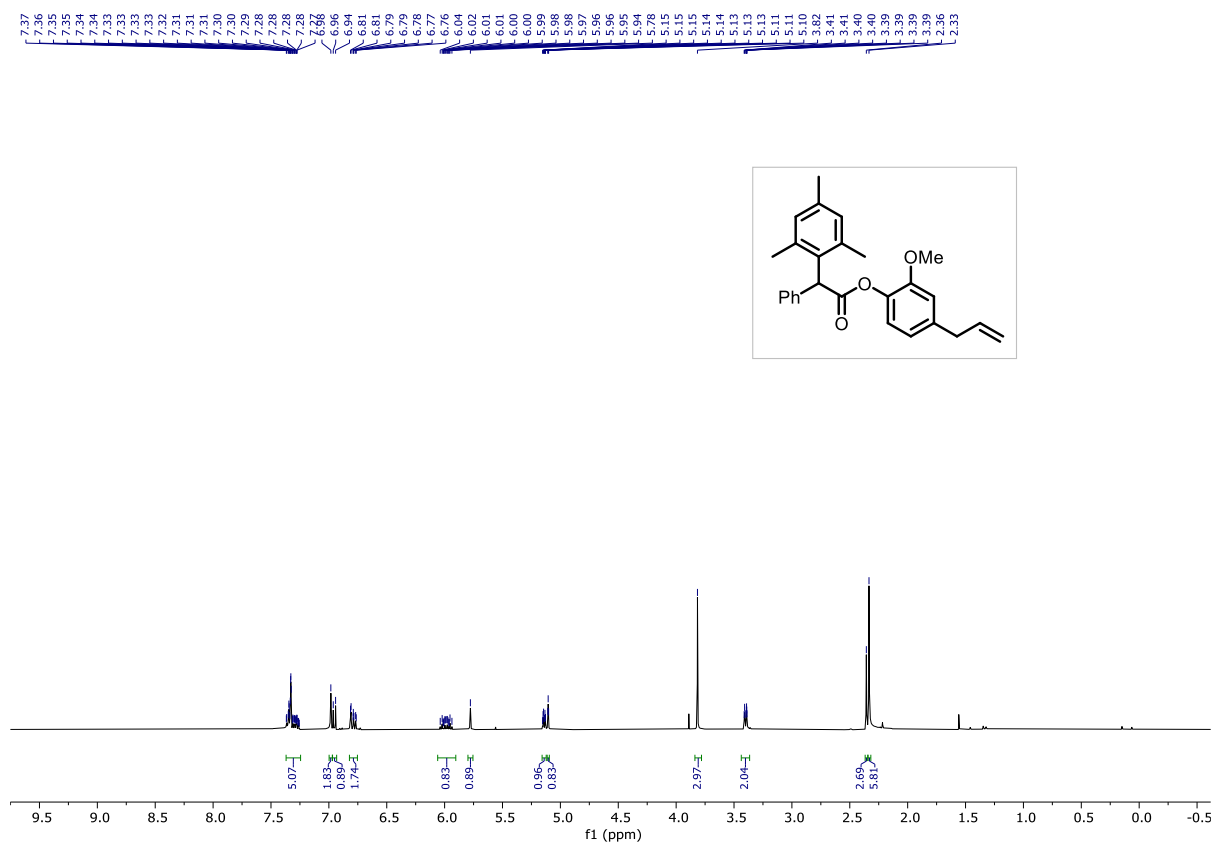


¹³C{¹H} NMR (101 MHz, CDCl₃)

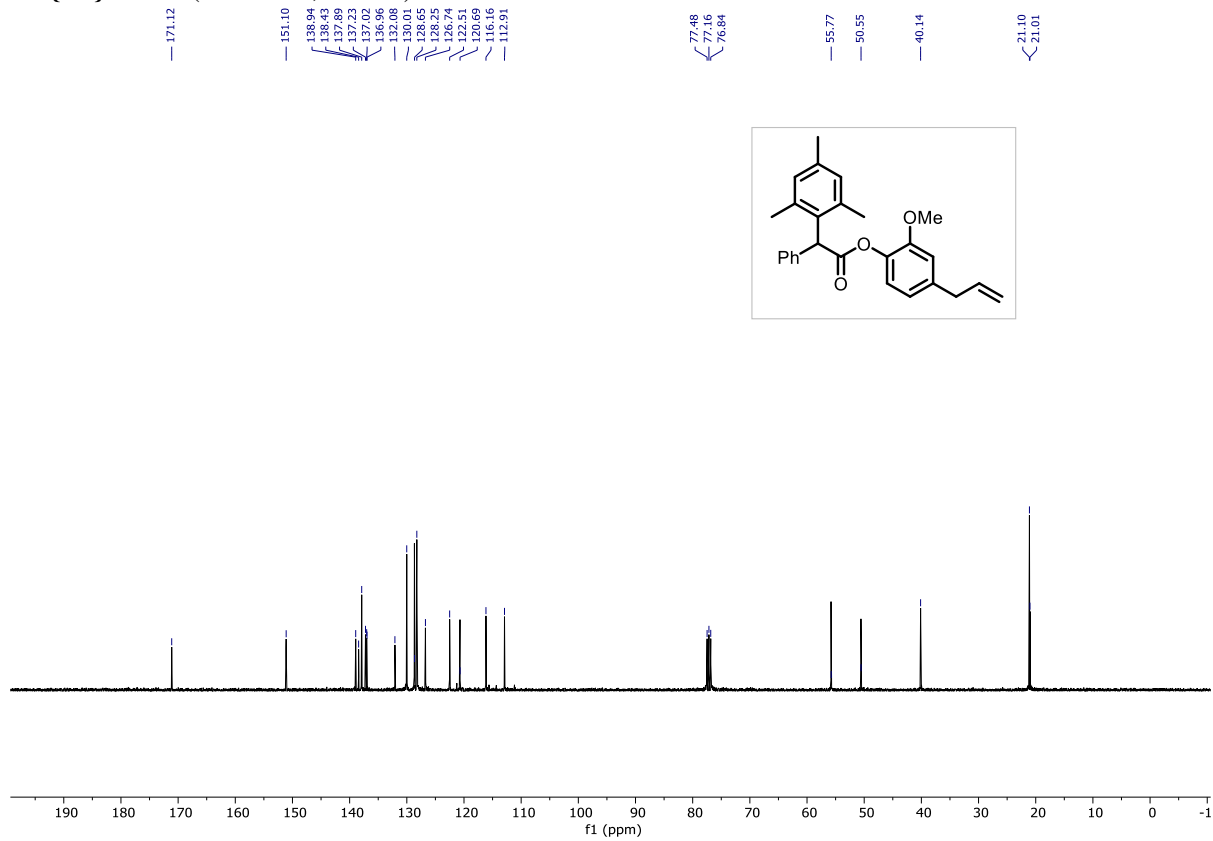


4-Allyl-2-methoxyphenyl 2-mesityl-2-phenylacetate (6f)

^1H NMR (400 MHz, CDCl_3)

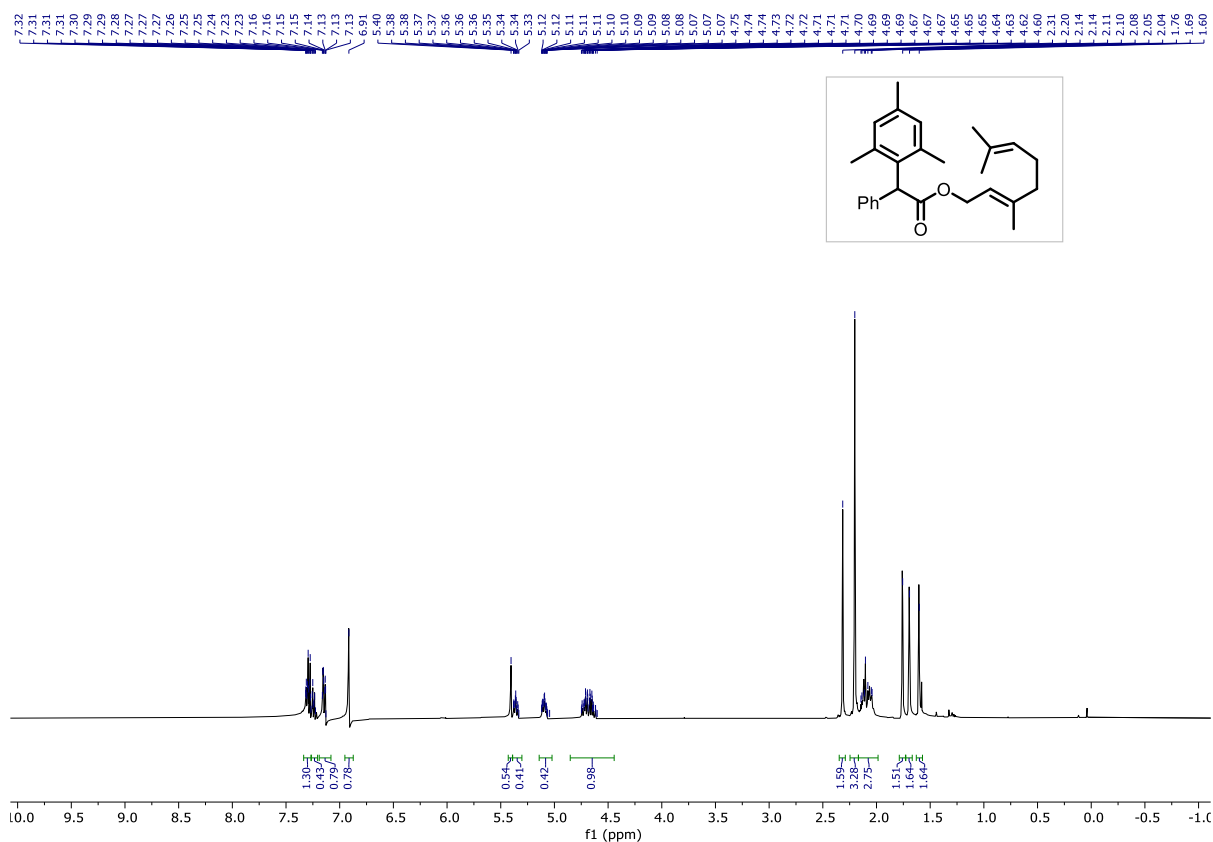


$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3)

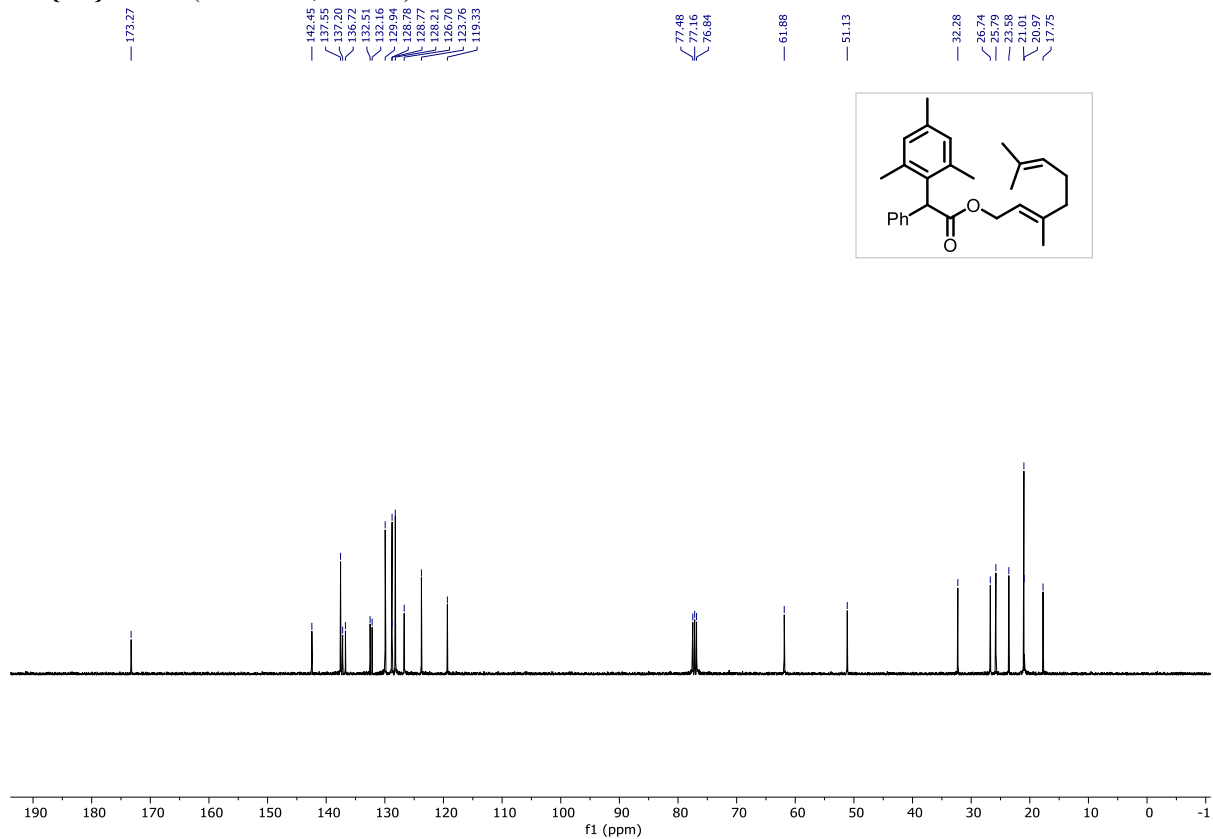


(E)-3,7-dimethylocta-2,6-dien-1-yl 2-mesityl-2-phenylacetate (6g)

¹H NMR (400 MHz, CDCl₃)

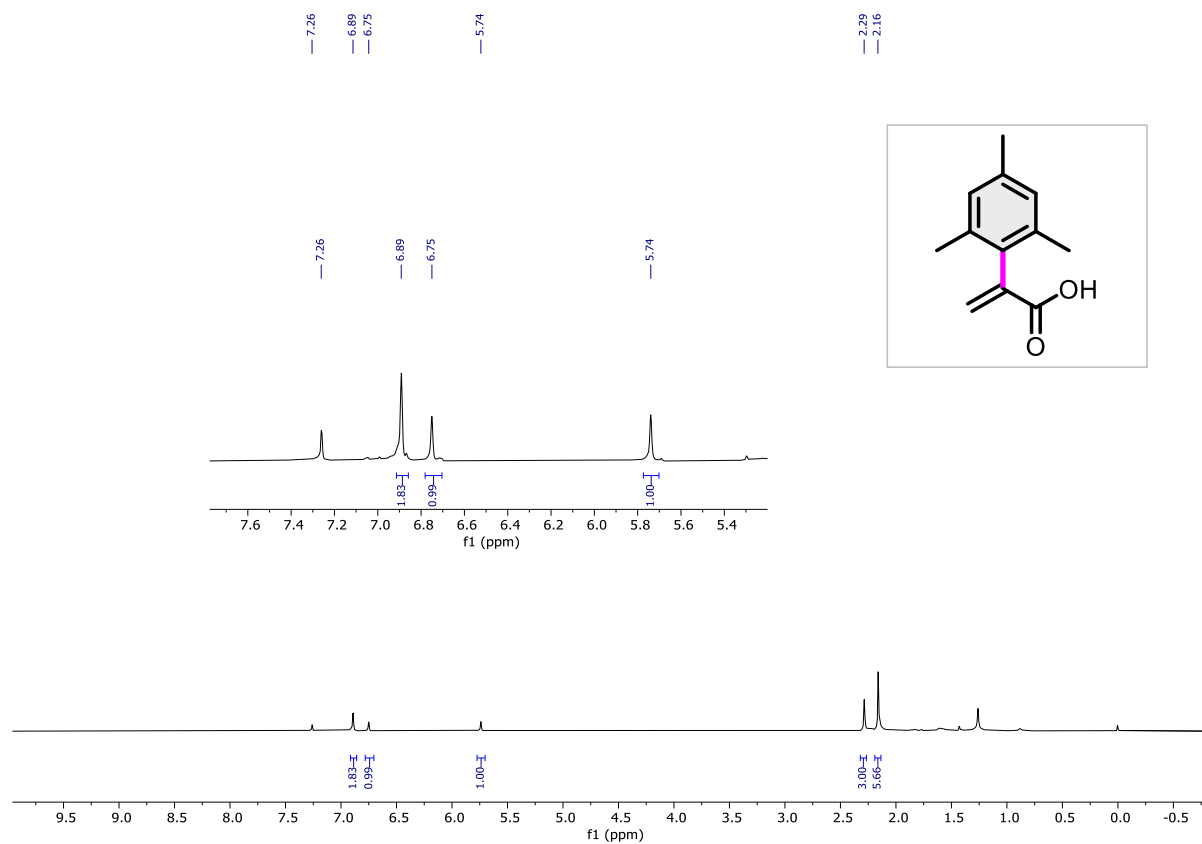


¹³C{¹H} NMR (101 MHz, CDCl₃)

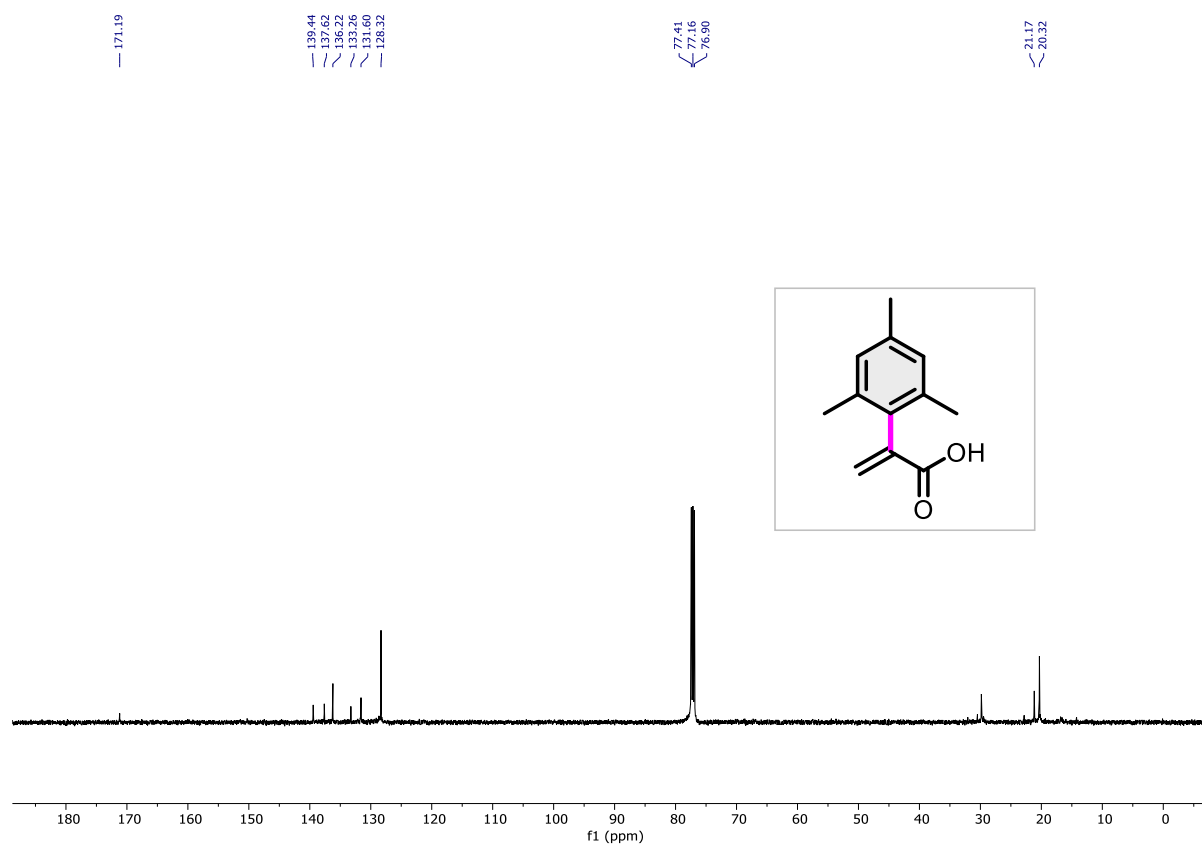


2-Mesitylacrylic acid (7b)

^1H NMR (500 MHz, CDCl_3)



^{13}C $\{^1\text{H}\}$ NMR (126 MHz, CDCl_3)



12. References

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