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Transition Metal-free Cross-Dehydrogenative Arylation of Unactivated Benzylic C–H Bonds

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1.1 General experimental information

All solvents and reagents were purchased from commercial suppliers and used without further purification unless otherwise stated. Compound **1k** was prepared according to the procedure described by Wu and co-workers.[1]

Column chromatography was performed on silica gel (40-63 μm) unless otherwise stated. $AgNO_3$ impregnated silica gel was prepared by absorbing a solution of $AgNO_3$ in MeCN (10% wt of $AgNO_3$ to silica) on silica. The MeCN was removed under reduced pressure on a rotary evaporator and the silica was further dried at 80 °C and < 1 mbar for 1-2 h (for long term storage, silica was kept in the fridge in the absence of light). Thin layer chromatography (TLC) was carried out on pre-coated silica gel F_{254} plates with visualization under UV light or using an aqueous basic $KMnO_4$ solution.

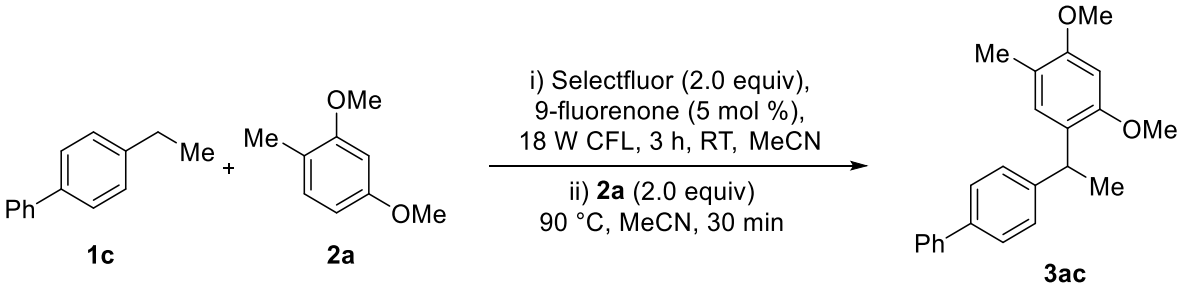
Melting points (mp) are uncorrected and were obtained using a Stuart SMP11 apparatus. IR spectra were recorded using a Thermo Scientific Nicolet iS5 FTIR spectrometer and the relevant peaks are quoted in cm^{-1}. NMR data was collected on a Bruker Avance III 400 MHz or Bruker AvanceII+ 500 MHz spectrometers. Chemical shifts are given in ppm (δ) and are referenced to the residual $CDCl_3$ solvent peak at 7.26 ppm (^{1}H NMR) and 77.16 ppm (^{13}C NMR). Conventional one-dimensional (1D) ^{1}H NMR, ^{19}F NMR, were recorded at room temperature under routine conditions. High Resolution Mass Spectra (HRMS) were performed by the School of Chemistry Mass Spectrometry Service of the University of Manchester on a Thermo Finnigan MAT95XP spectrometer.

1.2 Experimental procedures and characterisation data

General experimental procedure

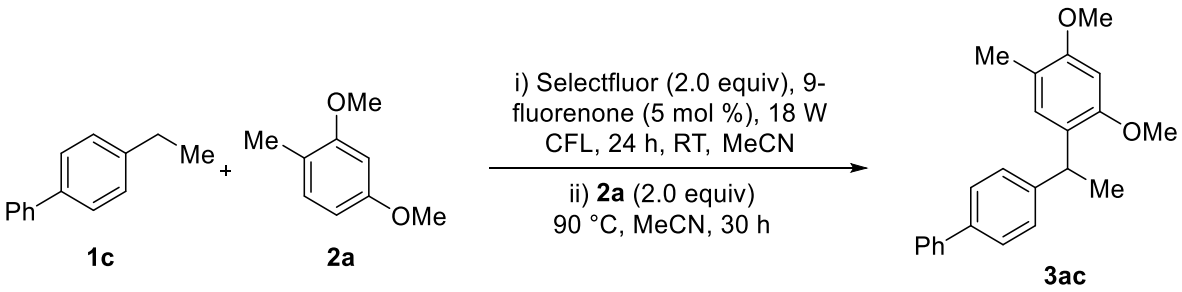
In an argon filled glovebox, a flame-dried crimpable glass schlenk vial (CEM Microwave Technologies, 10 mL volume) was loaded with the ethyl benzene derivative (0.4 mmol), Selectfluor® (354.3 mg, 0.8 mmol), 9-fluorenone (3.60 mg, 0.02 mmol) and MeCN (5 mL). The vial was sealed with a crimpable cap and removed from the glovebox. The reaction was allowed to stir for 24 h at room temperature and irradiated with an 18W CFL bulb. Under a positive pressure of nitrogen, arene (0.8 mmol) was added and the reaction was re-sealed and heated to 90 °C for 30 minutes. After cooling, the reaction mixture was filtered through a short plug of silica with acetone (3 x 15 mL). The products were purified using flash chromatography using the eluents specified.

Glovebox free experimental procedure



A flame-dried crimpable glass schlenk vial (CEM Microwave Technologies, 10 mL volume) was loaded with the 4-ethyl-1,1'-biphenyl **1c** (73.0 mg, 0.4 mmol), Selectfluor® (354.3 mg, 0.8 mmol) and 9-fluorenone (3.60 mg, 0.02 mmol). After evacuating and backfilling 3 times with nitrogen, MeCN that had been degassed three times by *freeze-pump-thaw* cycles (5 mL) was added. The vial was sealed with a crimpable cap and stirred for 3 h at room temperature and irradiated with an 18W CFL bulb. Under a positive pressure of nitrogen, 2,4-dimethoxytoluene **2a** (118 µL, 0.8 mmol) was added and the reaction was re-sealed and heated to 90 °C for 30 minutes. After cooling, the reaction mixture was filtered through a short plug of silica with acetone (3 x 15 mL). A 75% yield of 4-(1-(2,4-dimethoxy-5-methylphenyl)ethyl)-1,1'-biphenyl **3ac** was determined by ^{1}H NMR spectroscopy using CH_2Br_2 as an internal standard.

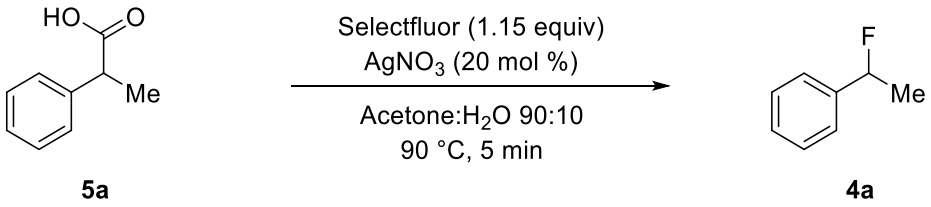
Experimental procedure for 4 mmol scale reaction



In an argon filled glovebox, a 100 mL Ace pressure tube was loaded with the 4-ethyl-1,1'-biphenyl **1c** (730 mg, 4 mmol), Selectfluor® (2.66 g, 6 mmol), 9-fluorenone (36.0 mg, 0.2 mmol) and MeCN (50 mL). The tube was sealed with a screw cap and stirred for 24 h at room temperature and irradiated with two 18W CFL bulbs. Under a stream of nitrogen, 2,4-dimethoxytoluene **2a** (1.18 mL, 8 mmol) was added and the reaction was re-sealed and heated to 90 °C for 3 h. After cooling, the reaction mixture was filtered through a short plug of silica with acetone (3 x 150 mL). The product was purified by flash chromatography with Ag-

impregnated silica using an eluent of 1% to 3% EtOAc:hexanes to afford 4-(1-(2,4-dimethoxy-5-methylphenyl)ethyl)-1,1'-biphenyl **3ac** (1.04 g, 75%) as a yellow solid.

Preparation of (1-fluoroethyl)benzene 4a



5a **4a**

Selectfluor (2.14 g, 5.75 mmol) and a phenylpropanoic acid (0.704 mL, 5 mmol) were weighed into a crimp cap vial and dissolved in a 90:10 solution of acetone:H_2O (37.5 mL:4.2 mL). $AgNO_3$ (0.170 g, 1 mmol) was added and the reaction vessel quickly sealed, covered in foil and stirred in an oil bath for 5 minutes at 90 °C. After this time, the reaction vessel was rapidly cooled in an ice bath and quenched with 1 M HCl to precipitate out AgCl. The reaction mixture diluted in DCM and basified with saturated K_2CO_3 solution. The organic layer was separated and the aqueous layer extracted DCM (20 mL x 2). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo.* The product was purified by column chromatography using an eluent of pentane to afford (1-fluoroethyl)benzene **4a** as a clear oil (0.520 g, 84%).

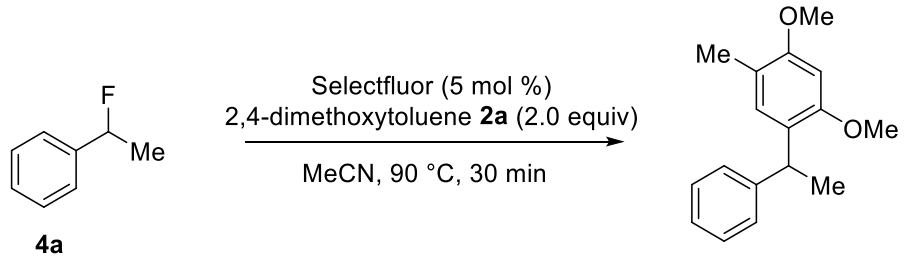
^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.47–7.30 (m, 5H), 5.64 (dq, *J* = 47.7, 6.4 Hz, 1H), 1.66 (dd, *J* = 23.9, 6.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ, ppm: 141.6 (d, *J* = 19.5 Hz), 128.6, 128.3 (d, *J* = 2.0 Hz), 125.4 (d, *J* = 6.7 Hz), 91.1 (d, *J* = 166.9 Hz), 23.1 (d, *J* = 25.3 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ, ppm: −167.1.

Spectroscopic data was in agreement with literature values.[2]

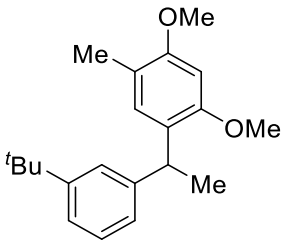
Procedure for the mechanistic experiments



4a **3ab**

Selectfluor (1.77mg, 0.005 mmol) or HF (4.00 μL, 0.005 mmol) and 2,4-dimethoxytoluene (35.4 μL, 0.2 mmol) were weighed into an oven dried 10 mL crimp cap vial and purged with nitrogen. A solution of (1-fluoroethyl)benzene **41** (0.2 mmol) in dry MeCN was added, the overall concentration was adjusted to 0.08 M with additional dry MeCN. The vial sealed and heated to 90 °C for 30 min. After 30 min the reaction vessel was cooled in an ice bath then diluted with Et_2O (5 mL), the crude reaction mixture was filtered through a short plug of silica washing with acetone (3 x 5 mL) and concentrated *in vacuo*. The yield was determined by ^1H NMR using CH_2Br_2 as an internal standard.

1-(1-(3-(tert-butyl)phenyl)ethyl)-2,4-dimethoxy-5-methylbenzene



3aa

Following the general procedure, 1-*tert*-butyl-3-ethylbenzene **1a** (76.0 μL, 0.4 mmol) was irradiated for 24 h then 2,4-dimethoxytoluene **2a** (118 μL, 1.2 mmol) was added. The product was purified by column chromatography using an eluent of 4% to 6% Et_2O:hexanes to afford 1-(1-(3-(tert-butyl)phenyl)ethyl)-2,4-dimethoxy-5-methylbenzene **3aa** (89.0 mg, 71%) as a yellow solid.

m. p. = 42–44°C

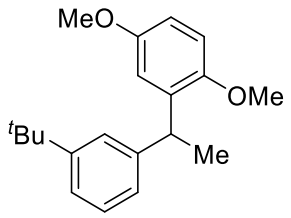
^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.37 (s, 1H), 7.25–7.19 (m, 2H), 7.10–7.04 (m, 1H), 6.93 (s, 1H), 6.45 (s, 1H), 4.51 (q, *J* = 7.3 Hz, 1H), 3.85 (s, 3H), 3.80 (s, 3H), 2.16 (s, 3H), 1.60 (d, *J* = 7.3 Hz, 3H), 1.34 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ, ppm: 156.6, 155.8, 150.7, 146.4, 129.5, 127.8, 126.8, 125.1, 124.7, 122.6, 118.0, 95.7, 56.1, 55.7, 37.2, 34.8, 31.6, 21.3, 15.7.

HRMS m/z calculated for $C_{21}H_{28}O_2Na$, 335.1982, found: 335.1974.

IR (ATR), ν, cm^{-1}: 1298, 1204, 1039, 707, 611, 592, 588, 576, 569.

2-(1-(3-(tert-butyl)phenyl)ethyl)-1,4-dimethoxybenzene



3ba

Following the general procedure, 1-*tert*-butyl-3-ethylbenzene **1a** (76.0 µL, 0.4 mmol) was irradiated for 24 h then 1,4-dimethoxybenzene **2b** (221 mg, 1.6 mmol) was added. The product was purified by flash chromatography using an eluent of 2% diisopropyl ether:hexanes to afford 2-(1-(3-(tert-butyl)phenyl)ethyl)-1,4-dimethoxybenzene **3ba** (47.8 mg, 40%) as a clear oil.

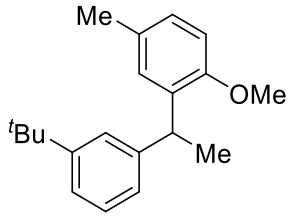
^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.32 (d, *J* = 1.9 Hz, 1H), 7.19 (d, *J* = 5.4 Hz, 2H), 7.04 (td, *J* = 4.6, 1.8 Hz, 1H), 6.80–6.73 (m, 2H), 6.68 (dd, *J* = 8.8, 3.1 Hz, 1H), 4.54 (q, *J* = 7.3 Hz, 1H), 3.73 (s, 3H), 3.73 (s, 3H), 1.57 (d, *J* = 7.2 Hz, 3H), 1.30 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ, ppm: 153.7, 151.4, 150.9, 145.6, 136.8, 127.9, 125.2, 124.8, 122.8, 114.8, 111.8, 110.6, 56.3, 55.8, 38.0, 34.8, 31.6, 21.0.

HRMS m/z calculated for $C_{20}H_{27}O_2$, 299.2006, found: 299.2006.

IR (ATR), ν, cm^{-1}: 1492, 1462, 1214, 1044, 1026, 795, 706.

2-(1-(3-(tert-butyl)phenyl)ethyl)-1-methoxy-4-methylbenzene



3ca

Following the general procedure, 1-*tert*-butyl-3-ethylbenzene **1a** (19.0 µL, 0.1 mmol) was irradiated for 24 h then 1-methoxy-4-methylbenzene **2c** (50.0 µL, 0.4 mmol) was added. The product was purified by preparative thin layer chromatography using an eluent of 100% hexanes to afford 2-(1-(3-(tert-butyl)phenyl)ethyl)-1-methoxy-4-methylbenzene **3ca** (13.5 mg, 48%) as a clear oil.

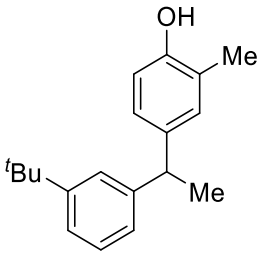
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (dt, *J* = 2.2, 1.1 Hz, 1H), 7.22–7.16 (m, 2H), 7.04 (td, *J* = 4.6, 1.8 Hz, 1H), 6.98–6.92 (m, 2H), 6.75–7.73 (m, 1H), 4.53 (q, *J* = 7.3 Hz, 1H), 3.75 (s, 3H), 2.25 (s, 3H), 1.57 (d, *J* = 7.2 Hz, 3H), 1.30 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 154.9, 150.8, 146.0, 135.1, 129.7, 128.5, 127.8, 127.3, 125.3, 124.8, 122.7, 110.8, 55.8, 37.7, 34.8, 31.6, 21.1, 20.9.

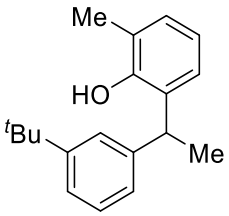
HRMS m/z calculated for $C_{20}H_{26}O$, 282.1978, found: 282.1980.

IR (ATR), ν, cm^{-1}: 1492, 1462, 1277, 1214, 1177, 1044, 1026, 795, 705.

4-(1-(3-(tert-butyl)phenyl)ethyl)-2-methylphenol



3da



3da'

Following the general procedure, 1-*tert*-butyl-3-ethylbenzene **1a** (76.0 µL, 0.4 mmol) was irradiated for 24 h then 2-methylphenol **2d** (124 µL, 1.2 mmol) was added. The product was purified by flash chromatography using an eluent of 0% to 5% EtOAc:hexanes to afford 4-(1-(3-(tert-butyl)phenyl)ethyl)-2-methylphenol **3da** (61.2 mg, 57%) as a red oil. (12% of other regioisomer **3da'** determined by NMR).

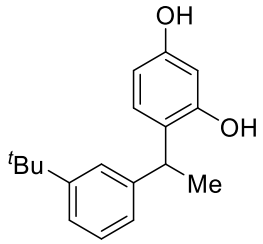
^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.29 (s, 1H), 7.25–7.21 (m, 2H), 7.08–6.98 (m, 2H), 6.95 (dd, *J* = 8.2, 2.3 Hz, 1H), 6.70 (d, *J* = 8.2 Hz, 1H), 4.08 (q, *J* = 7.2 Hz, 1H), 2.23 (s, 3H), 1.62 (d, *J* = 7.2 Hz, 3H), 1.33 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ, ppm: 152.0, 151.1, 146.5, 139.0, 130.4, 128.1, 126.1, 124.8, 124.7, 123.5, 123.0, 114.8, 44.4, 34.8, 31.6, 22.5, 16.0.

HRMS m/z calculated for $C_{19}H_{23}O$, 367.1754, found: 367.1748.

IR (ATR), ν, cm^{-1}: 1505, 1262, 1113, 818, 795, 706.

4-(1-(3-(tert-butyl)phenyl)ethyl)benzene-1,3-diol



3ea

Following the general procedure, 1-*tert*-butyl-3-ethylbenzene **1a** (76.0 µL, 0.4 mmol) was irradiated for 24 h then resorcinol **2e** (88.0 mg, 0.8 mmol) was added. The product was purified by flash chromatography using an eluent of 0% to 20% EtOAc:hexanes to afford 4-(1-(3-(tert-butyl)phenyl)ethyl)benzene-1,3-diol **3ea** (65.0 mg, 60%) as a yellow oil.

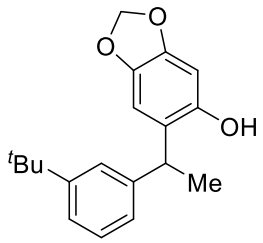
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 2.1 Hz, 1H), 7.30–7.21 (m, 2H), 7.12 (d, *J* = 8.3 Hz, 1H), 7.04 (dt, *J* = 6.3, 2.1 Hz, 1H), 6.44 (dd, *J* = 8.3, 2.5 Hz, 1H), 6.31 (d, *J* = 2.6 Hz, 1H), 4.68 (s, 2H), 4.24 (q, *J* = 7.2 Hz, 1H), 1.62 (d, *J* = 7.2 Hz, 3H), 1.31 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.1, 154.5, 151.7, 144.9, 128.6, 128.5, 124.5, 124.4, 123.6, 107.6, 103.6, 38.8, 34.7, 31.4, 21.4.

HRMS m/z calculated for $C_{18}H_{21}O_2$, 269.1547, found: 269.1540.

IR (ATR), ν, cm^{-1}: 1602, 1451, 1201, 1159, 1108, 971, 836, 797, 706, 628.

6-(1-(3-(*tert*-Butyl)phenyl)ethyl)benzo[*d*][1,3]dioxol-5-ol



3fa

Following the general procedure, 1-*tert*-butyl-3-ethylbenzene **1a** (76.0 µL, 0.4 mmol) was irradiated for 24 h then benzo[*d*][1,3]dioxol-5-ol **2f** (110.5 µL, 0.8 mmol) was added. The product was purified by flash chromatography using an eluent of 97:2:1 hexanes:EtOAc:acetic acid to afford 6-(1-(3-(*tert*-Butyl)phenyl)ethyl)benzo[*d*][1,3]dioxol-5-ol **3fa** (82.7 mg, 69%) as a brown oil.

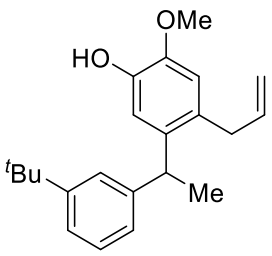
^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm:7.36–7.33 (m, 1H), 7.30–7.21 (m, 2H), 7.05 (dt, *J* = 6.4, 1.9 Hz, 1H), 6.75 (s, 1H), 6.36 (s, 1H), 5.87 (s, 2H), 4.77 (s, 1H), 4.30 (q, *J* = 7.3 Hz, 1H), 1.60 (d, *J* = 7.2 Hz, 3H), 1.32 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ, ppm: 151.7, 147.8, 146.2, 145.0, 141.6, 128.5, 124.5, 124.5, 123.6, 107.4, 101.0, 98.9, 38.8, 34.8, 31.5, 21.4.

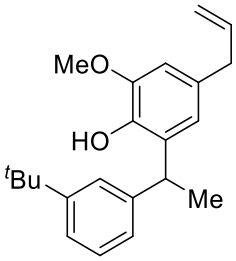
HRMS m/z calculated for $C_{19}H_{21}O_3$, 297.1496, found: 297.1494.

IR (ATR), ν, cm^{-1}: 1482, 1261, 1224, 1167, 1037, 909, 797, 731, 705.

4-allyl-5-(1-(3-(tert-butyl)phenyl)ethyl)-2-methoxyphenol



3ga



3ga'

Following the general procedure, 1-*tert*-butyl-3-ethylbenzene **1a** (76.0 μL, 0.4 mmol) was irradiated for 24 h then 4-allyl-2-methoxyphenol **2g** (124.0 μL, 0.8 mmol) was added. The product was purified by flash chromatography using an eluent of 2% to 4% EtOAc:hexanes to afford 4-allyl-5-(1-(3-(tert-butyl)phenyl)ethyl)-2-methoxyphenol **3ga** (70.2 mg, 54%) as a light brown oil. (17% of minor isomer **3ga'** determined by ^{1}H NMR).

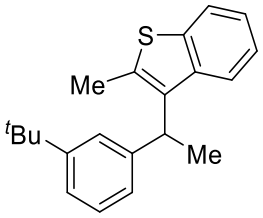
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25–7.21 (m, 1H), 7.20–7.16 (m, 2H), 6.96 (ddd, *J* = 6.6, 3.6, 1.8 Hz, 1H), 6.85 (s, 1H), 6.64 (s, 1H), 5.88 (ddt, *J* = 16.6, 10.1, 6.2 Hz, 1H), 5.43 (s, 1H), 5.10–4.88 (m, 2H), 4.28 (q, *J* = 7.2 Hz, 1H), 3.86 (s, 3H), 3.36 (dt, *J* = 15.8, 1.6 Hz, 1H), 3.27 (dt, *J* = 16.1, 1.5 Hz, 1H), 1.55 (d, *J* = 7.1 Hz, 3H), 1.29 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ, ppm: 151.1, 146.1, 144.7, 144.0, 137.9, 137.6, 129.0, 128.1, 124.9, 124.7, 122.8, 115.5, 113.8, 112.4, 56.1, 40.1, 36.9, 34.8, 31.5, 22.6.

HRMS m/z calculated for $C_{22}H_{29}O_2$, 325.2162, found: 325.2162.

IR (ATR), ν, cm^{-1}: 1508, 1271, 1204, 1093, 878, 795, 706.

3-(1-(3-(tert-butyl)phenyl)ethyl)-2-methylbenzo[b]thiophene



3ha

Following the general procedure, 1-*tert*-butyl-3-ethylbenzene **1a** (76.0 µL, 0.4 mmol) was irradiated for 24 h then 2-methylbenzo[*b*]thiophene **2h** (119 mg, 0.8 mmol) was added. The product was purified by preparative TLC using an eluent of 100% hexanes to afford 3-(1-(3-(tert-butyl)phenyl)ethyl)-2-methylbenzo[b]thiophene **3ha** (80.0 mg, 65%) as a yellow oil.

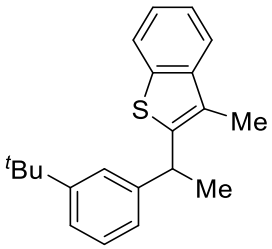
^{1}H NMR (400 MHz, $CDCl_3$): δ, ppm: 7.62 (dt, *J* = 7.1, 1.8 Hz, 1H), 7.36 (dt, *J* = 7.2, 1.2 Hz, 1H), 7.14–7.03 (m, 5H), 6.97 (d, *J* = 6.8 Hz, 1H), 4.55 (q, *J* = 7.3 Hz, 1H), 2.32 (s, 3H), 1.66 (d, *J* = 7.4 Hz, 3H), 1.17 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ, ppm: 151.1, 143.6, 139.8, 138.5, 135.3, 134.7, 128.0, 124.7, 124.0, 123.6, 122.9, 122.5, 122.1, 121.8, 36.8, 34.8, 31.5, 18.8, 14.6.

HRMS m/z calculated for $C_{21}H_{25}S$, 309.1671, found: 309.1674.

IR (ATR), ν, cm^{-1}: 1456, 1433, 761, 730, 706.

2-(1-(3-(tert-butyl)phenyl)ethyl)-3-methylbenzo[b]thiophene



3ia

Following the general procedure, 1-*tert*-butyl-3-ethylbenzene **1a** (76.0 µL, 0.4 mmol) was irradiated for 24 h then 3-methylbenzo[*b*]thiophene **2i** (107 µL, 0.8 mmol) was added. The product was purified by flash chromatography using an eluent of 100% hexanes to afford 2-(1-(3-(tert-butyl)phenyl)ethyl)-3-methylbenzo[b]thiophene **3ia** (57.2 mg, 46%) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.84 (dd, *J* = 8.0, 2.8 Hz, 1H), 7.70 (dd, *J* = 8.3, 2.6 Hz, 1H), 7.51–7.46 (m, 1H), 7.42 (tdd, *J* = 8.0, 2.7, 1.2 Hz, 1H), 7.34 (dddt, *J* = 7.2, 4.5, 3.1, 1.5

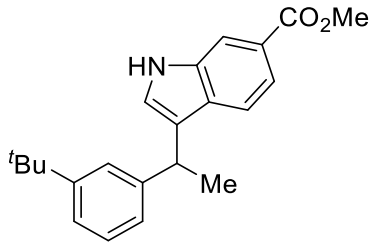
Hz, 3H), 7.23 (d, 1H), 4.68 (q, *J* = 7.2 Hz, 1H), 2.43 (s, 3H), 1.84 (d, *J* = 7.2 Hz, 3H), 1.41 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ, ppm: 151.4, 145.0, 144.7, 141.1, 138.3, 128.3, 126.3, 124.5, 124.4, 123.9, 123.6, 123.5, 122.4, 121.4, 39.5, 34.8, 31.5, 23.0, 12.0.

HRMS m/z calculated for $C_{21}H_{25}S$, 309.1671, found: 309.1675.

IR (ATR), ν, cm^{-1}: 1459, 1435, 794, 752, 737, 706.

methyl 3-(1-(3-(tert-butyl)phenyl)ethyl)-1H-indole-6-carboxylate



3ja

Following the general procedure, 1-*tert*-butyl-3-ethylbenzene **1a** (76.0 µL, 0.4 mmol) was irradiated for 24 h then methyl 1H-indole-6-carboxylate **2j** (140 mg, 0.8 mmol) was added. The product was purified by flash chromatography using an eluent of 40% to 60% DCM:hexanes to afford methyl 3-(1-(3-(tert-butyl)phenyl)ethyl)-1H-indole-6-carboxylate **3ja** (70.2 mg, 52%) as an off white solid.

m. p. = 126–128°C

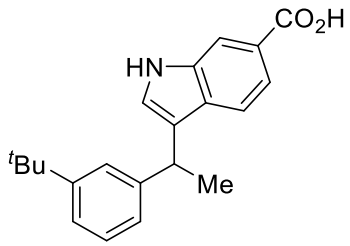
^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 8.35 (s, 1H), 8.12 (s, 1H), 7.72 (dd, *J* = 8.4, 1.5 Hz, 1H), 7.42 (d, *J* = 8.4 Hz, 1H), 7.37 (s, 1H), 7.23–7.20 (m, 2H), 7.15 (s, 1H), 7.07 (d, *J* = 6.6 Hz, 1H), 4.39 (q, *J* = 7.1 Hz, 1H), 3.93 (s, 3H), 1.73 (d, *J* = 7.1 Hz, 3H), 1.31 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ, ppm: 168.4, 151.2, 146.0, 136.0, 130.6, 128.1, 124.8, 124.7 124.4, 123.6, 123.1, 122.3, 120.3, 119.4, 113.6, 52.1, 37.2, 34.8, 31.5, 22.5.

HRMS m/z calculated for $C_{22}H_{25}O_2NNa$, 358.1778, found: 358.1770.

IR (ATR), ν, cm^{-1}: 1689, 1319, 1272, 1210, 775, 707.

3-(1-(3-(tert-butyl)phenyl)ethyl)-1H-indole-6-carboxylic acid



3ka

Following the general procedure, 1-*tert*-butyl-3-ethylbenzene **1a** (76.0 µL, 0.4 mmol) was irradiated for 24 h then 1H-indole-6-carboxylic acid **2k** (193 mg, 1.2 mmol) was added. The product was purified by flash chromatography using an eluent of 89:10:1 Hexane:EtOAc: AcOH to afford methyl 3-(1-(3-(tert-butyl)phenyl)ethyl)-1H-indole-6-carboxylic acid **3ka** (70.7 mg, 55%) as an off white solid.

m. p. = 201–204°C

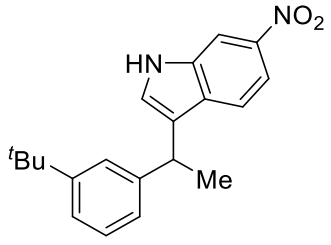
^{1}H NMR (400 MHz, DMSO-d_6) δ, ppm: 12.43 (s, 1H), 11.22 (s, 1H), 7.97 (d, *J* = 1.4 Hz, 1H), 7.51–7.43 (m, 2H), 7.38 (d, *J* = 9.4 Hz, 2H), 7.17–7.13 (m, 2H), 7.09–7.02 (m, 1H), 4.34 (q, *J* = 7.1 Hz, 1H), 1.64 (d, *J* = 7.1 Hz, 3H), 1.24 (s, 9H).

^{13}C NMR (101 MHz, DMSO-d_6) δ, ppm: 168.4, 150.4, 146.5, 135.7, 129.6, 127.9, 125.4, 124.1, 124.2, 123.1, 122.5, 120.3, 119.1, 118.4, 113.5, 36.4, 34.3, 31.2, 22.3.

HRMS m/z calculated for $C_{21}H_{22}O_2N$, 320.1656, found: 320.1652.

IR (ATR), ν, cm^{-1}: 1671, 1318, 1281, 1257, 1233, 772, 746, 723, 706.

3-(1-(3-(tert-butyl)phenyl)ethyl)-6-nitro-1H-indole



3la

Following the general procedure, 1-*tert*-butyl-3-ethylbenzene **1a** (76.0 µL, 0.4 mmol) was irradiated for 24 h then 6-nitro-1H-indole **2l** (130 mg, 0.8 mmol) was added. The product was purified by flash chromatography using an eluent of 0% to 11% EtOAc:hexanes to afford 3-(1-(3-(tert-butyl)phenyl)ethyl)-6-nitro-1H-indole **3la** (78.8 mg, 61%) as a yellow solid.

m. p. = 194–197°C

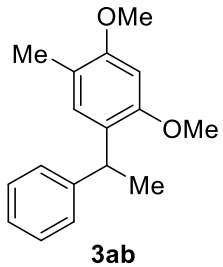
^{1}H NMR (400 MHz, DMSO-d_6) δ, ppm: 11.65 (s, 1H), 8.28 (d, *J* = 2.1 Hz, 1H), 7.77 (dd, *J* = 8.8, 2.1 Hz, 1H), 7.71 (s, 1H), 7.48 (d, *J* = 8.8 Hz, 1H), 7.39 (s, 1H), 7.20–7.12 (m, 2H), 7.09–7.02 (m, 1H), 4.38 (q, *J* = 7.2 Hz, 1H), 1.65 (d, *J* = 7.2 Hz, 3H), 1.24 (s, 9H).

^{13}C NMR (101 MHz, DMSO-d_6) δ, ppm: 150.5, 146.1, 141.7, 134.8, 131.0, 129.0, 128.0, 124.1, 124.0, 122.7, 121.2, 119.0, 113.3, 108.2, 36.1, 34.3, 31.2, 22.3.

HRMS m/z calculated for $C_{20}H_{21}O_2N_2$, 321.1609, found: 321.1605.

IR (ATR), ν, cm^{-1}: 1502, 1324, 1298, 1067, 1058, 803, 735, 710, 686.

1,5-dimethoxy-2-methyl-4-(1-phenylethyl)benzene



3ab

Following the general procedure, ethyl benzene **1b** (49.0 µL, 0.4 mmol) was irradiated for 48 h then 2,4-dimethoxytoluene **2a** (118 µL, 0.8 mmol) was added. The product was purified by flash chromatography using an eluent of 0% to 8% EtOAc:hexanes to afford 1,5-dimethoxy-2-methyl-4-(1-phenylethyl)benzene **3ab** (69.7 mg, 68%) as a white solid .

m. p. = 101–104°C

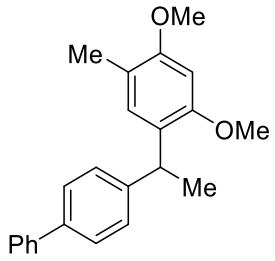
^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.29–7.24 (m, 4H), 7.20–7.11 (m, 1H), 6.91 (s, 1H), 6.43 (s, 1H), 4.50 (q, *J* = 7.3 Hz, 1H), 3.83 (s, 3H), 3.78 (s, 3H), 2.14 (s, 3H), 1.57 (d, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ, ppm: 156.7, 155.8, 147.1, 129.6, 128.2, 127.7, 126.5, 125.7, 118.1, 95.7, 56.1, 55.7, 36.9, 21.2, 15.7.

HRMS m/z calculated for $C_{17}H_{20}O_2Na$, 279.1356, found: 279.1347.

IR (ATR), ν, cm^{-1}: 1509, 1297, 1204, 1117, 1036, 814, 698.

4-(1-(2,4-dimethoxy-5-methylphenyl)ethyl)-1,1'-biphenyl



3ac

Following the general procedure, 4-ethyl-1,1'-biphenyl **1c** (73.0 mg, 0.4 mmol) was irradiated for 3 h then 2,4-dimethoxytoluene **2a** (118 µL, 0.8 mmol) was added. The product was purified by flash chromatography using an eluent of 1% to 3% EtOAc:hexanes to afford 4-(1-(2,4-dimethoxy-5-methylphenyl)ethyl)-1,1'-biphenyl **3ac** (103.1 mg, 78%) as a yellow solid.

m. p. = 54–56°C

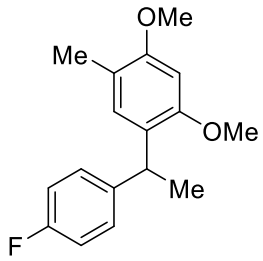
^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.64–7.60 (d, *J* = 8.3 Hz, 2H), 7.55 (d, *J* = 8.3 Hz, 2H), 7.45 (t, *J* =6.9 Hz, 2H), 7.40–7.30 (m, 3H), 7.00 (s, 1H), 6.48 (s, 1H), 4.59 (q, *J* = 7.3 Hz, 1H), 3.86 (s, 3H), 3.83 (s, 3H), 2.20 (s, 3H), 1.65 (d, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ, ppm: 156.7, 155.8, 146.2, 141.3, 138.5, 129.5, 128.8, 128.1, 127.1, 127.0, 126.9, 126.3, 118.1, 95.6, 56.1, 55.6, 36.6, 21.2, 15.7.

HRMS m/z calculated for $C_{23}H_{24}O_2$, 332.1771, found: 332.1774.

IR (ATR), ν, cm^{-1}: 1295, 1203, 1106, 1037, 846, 760, 742, 693.

1-(1-(4-fluorophenyl)ethyl)-2,4-dimethoxy-5-methylbenzene



3ad

Following the general procedure, 1-ethyl-4-fluorobenzene **1d** (51.0 µL, 0.4 mmol) was irradiated for 24 h then 2,4-dimethoxytoluene **2a** (118 µL, 0.8 mmol) was added. The product was purified by flash chromatography using an eluent of 1% to 8% EtOAc:hexanes to afford 1-(1-(4-fluorophenyl)ethyl)-2,4-dimethoxy-5-methylbenzene **3ad** (84.0 mg, 77%) as a yellow solid.

m. p. = 46–48°C

^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.25–7.18 (m, 2H), 6.96 (t, *J* = 8.8 Hz, 2H), 6.91 (s, 1H), 6.45 (s, 1H), 4.48 (q, *J* = 7.3 Hz, 1H), 3.85 (s, 3H), 3.79 (s, 3H), 2.16 (s, 3H), 1.57 (d, *J* = 7.3 Hz, 3H).

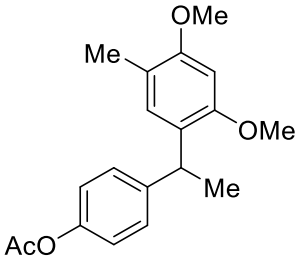
^{13}C NMR (101 MHz, $CDCl_3$) δ, ppm: 161.4 (d, *J* = 242.9 Hz), 157.1, 156.1, 142.7 (d, *J* = 3.0 Hz) 129.7, 129.3 (d, *J* = 7.6 Hz), 126.5, 118.4, 115.1 (d, *J* = 21.0 Hz), 95.9, 56.3, 55.9, 36.6, 21.6, 16.0.

^{19}F NMR (376 MHz, $CDCl_3$) δ −118.28 (tt, *J* = 8.9, 5.5 Hz).

HRMS m/z calculated for $C_{17}H_{19}O_2F$, 274.1364, found: 274.1367.-

IR (ATR), ν, cm^{-1}: 1505, 1300, 1205, 1190, 1120, 1037, 834, 821, 812.

4-(1-(2,4-dimethoxy-5-methylphenyl)ethyl)phenyl acetate



3ae

Following the general procedure, 4-ethylphenyl acetate **1e** (63.8 µL, 0.4 mmol) was irradiated for 24 h using 15 mol % 9-fluorenone then 2,4-dimethoxytoluene **2a** (118 µL, 0.8 mmol) was added and the reaction was heated to 90 °C for 3 hours. The product was purified by flash chromatography using an eluent of 3% to 5% EtOAc:hexanes to afford 4-(1-(2,4-dimethoxy-5-methylphenyl)ethyl)phenyl acetate **3ae** (59.2 mg, 47%) as a yellow solid.

m. p. = 63–64°C

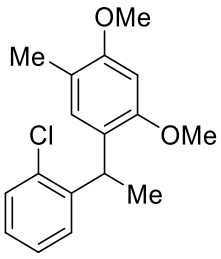
^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.23 (d, *J* = 8.6 Hz, 2H), 6.97 (d, *J* = 8.6 Hz, 2H), 6.89 (s, 1H), 6.42 (s, 1H), 4.47 (q, *J* = 7.3 Hz, 1H), 3.82 (s, 3H), 3.76 (s, 3H), 2.28 (s, 3H), 2.13 (s, 3H), 1.55 (d, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ, ppm: 169.8, 156.7, 155.8, 148.6, 144.6, 129.5, 128.6, 126.1, 121.1, 118.1, 95.6, 56.0, 55.7, 36.4, 21.3, 21.2, 15.6.

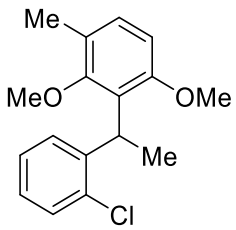
HRMS m/z calculated for $C_{19}H_{22}O_4Na$, 337.1410, found: 237.1397.

IR (ATR), ν, cm^{-1}: 1754, 1505, 1293, 1216, 1196, 1162, 1115, 1034, 1018, 912, 845, 836, 831.

1-(1-(2-chlorophenyl)ethyl)-2,4-dimethoxy-5-methylbenzene



3af



3af'

Following the general procedure, 1-chloro-2-ethylbenzene **1e** (56.2 mg, 0.4 mmol) was irradiated for 24 h then 2,4-dimethoxytoluene **2a** (283 µL, 2.0 mmol) was added and the reaction was heated to 90 °C for 16 hours. The product was purified by flash chromatography using an eluent of 1% to 5% EtOAc:hexanes to afford 1-(1-(2-chlorophenyl)ethyl)-2,4-dimethoxy-5-methylbenzene as a mixture of isomers **3af** and **3af'** (59.2 mg, 51% (r.r = 6.3:1)) as an orange solid.

m. p. = 98–102°C

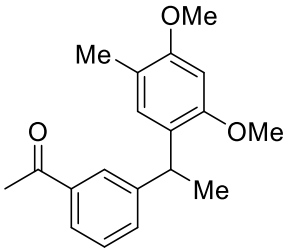
^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.56 (dd, *J* = 7.9, 1.7 Hz, 1H Minor), 7.36–7.31 (m, 1H Major), 7.29 (dd, *J* = 7.9, 1.4 Hz, 1H Minor), 7.22 (dd, *J* = 7.7, 1.5 Hz, 1H Minor), 7.20–7.15 (m, 2H Major), 7.15 (d, *J* = 1.3 Hz, 1H Minor), 7.11 (ddd, *J* = 7.6, 6.0, 3.0 Hz, 1H Major), 7.02 (d, *J* = 8.4 Hz, 1H Minor), 6.87 (s, 1H Major), 6.62 (d, *J* = 8.4 Hz, 1H Minor), 6.43 (s, 1H Major), 4.99 (q, *J* = 7.2 Hz, 1H Minor), 4.84 (q, *J* = 7.2 Hz, 1H Major), 3.83 (s, 3H Major), 3.75 (s, 3H Major), 3.73 (s, 3H Minor), 3.33 (s, 3H Minor), 2.22 (s, 3H Minor), 2.15 (s, 3H Major), 1.67 (d, *J* = 7.2 Hz, 3H Minor), 1.52 (d, *J* = 7.2 Hz, 3H Major).

^{13}C NMR (101 MHz, $CDCl_3$) δ, ppm: 157.6 (Minor), 157.2 (Minor), 156.8 (Major), 156.1 (Major), 144.5 (Major), 143.8 (Minor), 134.1 (Minor), 134.0 (Major), 129.8 (Minor), 129.5 (Major), 129.4 (Minor), 129.4 (Major), 129.3 (Minor), 128.5 (Major), 126.9 (Major), 126.8 (Minor), 126.7 (Major), 126.6 (Minor), 126.3 (Minor), 125.1 (Major), 123.5 (Minor), 117.8 (Major), 107.5 (Minor), 95.7 (Major), 60.1 (Minor), 56.1 (Major), 55.9 (Minor), 55.6 (Major), 34.4 (Major), 33.5 (Minor), 20.4 (Major), 19.4 (Minor), 16.3 (Minor), 15.7 (Major).

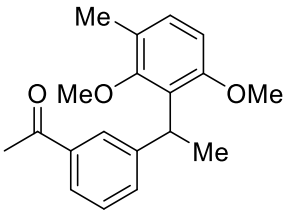
HRMS m/z calculated for $C_{17}H_{19}O_2Cl$, 290.1068, found: 290.1070.

IR (ATR), ν, cm^{-1}: 1470, 1450, 1296, 1205, 1113, 1034, 824, 767.

1-(3-(1-(2,4-dimethoxy-5-methylphenyl)ethyl)phenyl)ethan-1-one



3ag



3ag'

Following the general procedure, 1-(3-ethylphenyl)ethan-1-one **1g** (59.3 mg, 0.4 mmol) was irradiated for 24 h then 2,4-dimethoxytoluene **2a** (283 µL, 2.0 mmol) was added and the reaction was heated to 90 °C for 16 hours. The product was purified by flash chromatography using an eluent of 3% to 5% EtOAc:hexanes to afford 1-(3-(1-(2,4-dimethoxy-5-methylphenyl)ethyl)phenyl)ethan-1-one **3ag** (83.3 mg, 70%) as a yellow oil. (12% of minor isomer **3ag'** determined by ^{1}H NMR)

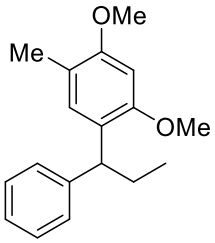
^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.88 (t, *J* = 1.9 Hz, 1H), 7.74 (dt, *J* = 7.8, 1.5 Hz, 1H), 7.43 (dt, *J* = 7.7, 1.6 Hz, 1H), 7.34 (t, *J* = 7.7 Hz, 1H), 6.90 (s, 1H), 6.42 (s, 1H), 4.52 (q, *J* = 7.3 Hz, 1H), 3.82 (s, 3H), 3.76 (s, 3H), 2.58 (s, 3H), 2.13 (s, 3H), 1.59 (d, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ, ppm: 198.5, 156.7, 155.7, 147.6, 137.0, 132.5, 129.3, 128.3, 127.3, 125.9, 125.5, 118.0, 95.4, 55.8, 55.5, 36.9, 26.7, 20.9, 15.5.

HRMS m/z calculated for $C_{19}H_{22}O_3Na$, 321.1461, found: 321.1447.

IR (ATR), ν, cm^{-1}: 1681, 1510, 1436, 1271, 1204, 1191, 1115, 1035, 816, 695.

1,5-dimethoxy-2-methyl-4-(1-phenylpropyl)benzene



3ah

Following the general procedure, propylbenzene **1h** (56.0 µL, 0.4 mmol) was irradiated for 48 h then 2,4-dimethoxytoluene **2a** (118 µL, 0.8 mmol) was added. The product was purified by flash chromatography using an eluent of 1% to 3% EtOAc:hexanes to afford 1,5-dimethoxy-2-methyl-4-(1-phenylpropyl)benzene **3ah** (56.2 mg, 52%) as a white solid.

m. p. = 58–59°C

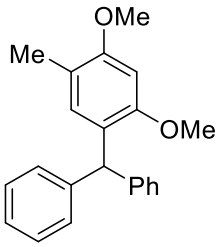
^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.29–7.21 (m, 4H), 7.13 (m, 1H), 6.96 (s, 1H), 6.41 (s, 1H), 4.19 (t, *J* = 7.8 Hz, 1H), 3.81 (s, 3H), 3.76 (s, 3H), 2.14 (s, 3H), 2.0 –1.94 (m, 2H), 0.89 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ, ppm: 156.5, 156.2, 145.8, 129.5, 128.2, 128.2, 125.6, 125.3, 118.1, 95.7, 56.2, 55.6, 44.6, 28.2, 15.7, 13.0.

HRMS m/z calculated for $C_{18}H_{22}O_2Na$, 293.1512, found: 293.1501.

IR (ATR), ν, cm^{-1}: 1519, 1461, 1296, 1205, 1119, 1035, 812, 764, 699.

((2,4-dimethoxy-5-methylphenyl)methylene)dibenzene



3ai

Following the general procedure, diphenylmethane **1i** (67.0 µL, 0.4 mmol) was irradiated for 24 h then 2,4-dimethoxytoluene **2a** (118 µL, 0.8 mmol) was added. The product was purified by flash chromatography using an eluent of 8% to 10% DCM:hexanes to afford ((2,4-dimethoxy-5-methylphenyl)methylene)dibenzene **3ai** (87.4 mg, 69%) as a white solid.

m. p. = 133–134°C

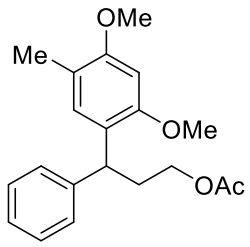
^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.28–7.22 (m, 4H), 7.22–7.15 (m, 2H), 7.13–7.08 (m, 4H), 6.62 (s, 1H), 6.45 (s, 1H), 5.85 (s, 1H), 3.83 (s, 3H), 3.70 (s, 3H), 2.06 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ, ppm: 157.0, 156.1, 144.5, 132.1, 129.5, 128.2, 126.0, 124.2, 117.9, 95.6, 56.2, 55.6, 49.1, 15.7.

HRMS m/z calculated for $C_{22}H_{22}O_2Na$, 341.1512, found: 341.1501.

IR (ATR), ν, cm^{-1}: 1508, 1436, 1297, 1207, 1172, 1104, 1037, 817, 737, 699.

3-(2,4-dimethoxy-5-methylphenyl)-3-phenylpropyl acetate



3aj

Following the general procedure, 3-phenylpropyl acetate **1j** (72.0 µL, 0.4 mmol) was irradiated for 48 h then 2,4-dimethoxytoluene **2a** (118 µL, 0.8 mmol) was added. The product was purified by flash chromatography using an eluent of 2% to 4% EtOAc:hexanes to afford 3-(2,4-dimethoxy-5-methylphenyl)-3-phenylpropyl acetate **3aj** (80.4 mg, 61%) as an off white solid.

m. p. = 76–77°C

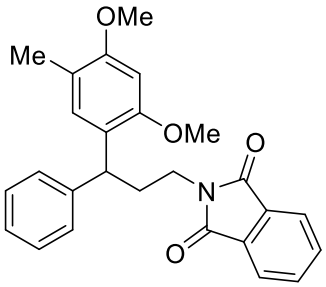
^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.36–7.23 (m, 4H), 7.17 (ddd, *J* = 8.7, 5.3, 3.3 Hz, 1H), 6.95 (s, 1H), 6.42 (s, 1H), 4.44 (t, *J* = 7.9 Hz, 1H), 4.04 (qt, *J* = 11.0, 6.9 Hz, 2H), 3.82 (s, 3H), 3.78 (s, 3H), 2.36 (qd, *J* = 7.0, 3.3 Hz, 2H), 2.15 (s, 3H), 2.03 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ, ppm: 171.2, 156.9, 156.0, 144.7, 129.5, 128.3, 128.0, 126.0, 123.9, 118.2, 95.6, 63.5, 56.0, 55.6, 39.5, 33.8, 21.1, 15.7.

HRMS m/z calculated for $C_{20}H_{25}O_4$, 329.1747, found: 329.1738.

IR (ATR), ν, cm^{-1}: 1744, 1733, 1298, 1246, 1206, 1034, 813, 700.

2-(3-(2,4-dimethoxy-5-methylphenyl)-3-phenylpropyl)isoindoline-1,3-dione



3ak

Following the general procedure, 2-(3-phenylpropyl)isoindoline-1,3-dione **1k** (106 mg, 0.4 mmol) was irradiated for 48 h then 2,4-dimethoxytoluene **2a** (118 µL, 0.8 mmol) was added. The product was purified by flash chromatography using an eluent of 8% to 12% EtOAc:hexanes to afford 2-(3-(2,4-dimethoxy-5-methylphenyl)-3-phenylpropyl)isoindoline-1,3-dione **3ak** (107.0 mg, 64%) as a white solid.

m. p. = 156–159°C

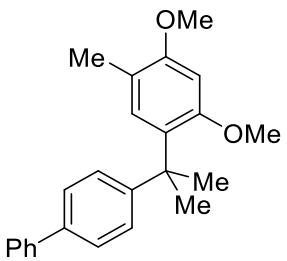
^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.80–7.73 (m, 2H), 7.70–7.62 (m, 2H), 7.30 (d, *J* = 7.7 Hz, 2H), 7.22 (t, *J* = 7.5 Hz, 2H), 7.08 (t, *J* = 7.3 Hz, 1H), 6.96 (s, 1H), 6.32 (s, 1H), 4.40 (t, *J* = 7.8 Hz, 1H), 3.76 (s, 3H), 3.74 (s, 4H), 3.70 (t, *J* = 7.0 Hz, 2H), 2.49–2.34 (m, 2H), 2.07 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ, ppm: 168.3, 156.7, 155.8, 144.6, 133.7, 132.3, 129.5, 128.0, 125.9, 123.8, 123.0, 118.1, 95.5, 55.9, 55.5, 41.1, 37.5, 33.1, 15.6.

HRMS m/z calculated for $C_{26}H_{25}O_4NNa$, 438.1676, found: 438.1662.

IR (ATR), ν, cm^{-1}: 1703, 1395, 1354, 1300, 1206, 1119, 1035, 882, 814, 720, 701.

4-(2-(2,4-dimethoxy-5-methylphenyl)propan-2-yl)-1,1'-biphenyl



3al

Following the general procedure, 4-isopropyl-1,1'-biphenyl **1l** (56.4 µL, 0.4 mmol) was irradiated for 6 h then 2,4-dimethoxytoluene **2a** (283 µL, 2.0 mmol) was added and the reaction

was heated to 90 °C for 16 hours. The product was purified by flash chromatography using an eluent of 1% to 6% EtOAc:hexanes to afford 1,5-dimethoxy-2-methyl-4-(1-phenylethyl)benzene **3al** (62.2 mg, 45%) as a yellow solid.

m. p. = 126–129°C

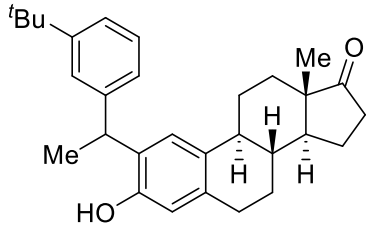
^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.59 (d, *J* = 8.4 Hz, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.41 (t, *J* = 7.7 Hz, 2H), 7.33–7.28 (m, 1H), 7.26–7.24 (m, 2H), 7.22 (s, 1H), 6.39 (s, 1H), 3.81 (s, 3H), 3.32 (s, 3H), 2.23 (s, 3H), 1.68 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ, ppm: 156.9, 151.4, 141.3, 137.4, 130.4, 128.8, 128.7, 127.0, 126.9, 126.3, 126.3, 117.5, 97.8, 56.0, 55.6, 41.2, 30.0, 15.9.

HRMS m/z calculated for $C_{24}H_{26}O_2Na$, 369.1825, found: 369.1814.

IR (ATR), ν, cm^{-1}: 623, 589, 579, 575, 565.

(8R,9S,13S,14S)-2-(1-(3-(tert-butyl)phenyl)ethyl)-3-hydroxy-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one



3ma

Following the general procedure, 1-*tert*-butyl-3-ethylbenzene **1a** (76.0 µL, 0.4 mmol) was irradiated for 24 h then (8R,9S,13S,14S)-3-hydroxy-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one **2m** (216 mg, 0.8 mmol) was added. The product was purified by flash chromatography using an eluent of 2% to 5% EtOAc:hexanes to afford (8R,9S,13S,14S)-2-(1-(3-(tert-butyl)phenyl)ethyl)-3-hydroxy-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one **3ma** (110.1 mg, 64%) as a white solid.

m. p. = 168–171°C

^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.39–7.34 (m, 1H), 7.25–7.20 (m, 2H), 7.15 (s, 1H), 7.05–7.00 (m, 1H), 6.52 (d, *J* = 5.0 Hz, 1H), 4.70 (d, *J* = 5.1 Hz, 1H), 4.31 (q, *J* = 7.2 Hz, 1H),

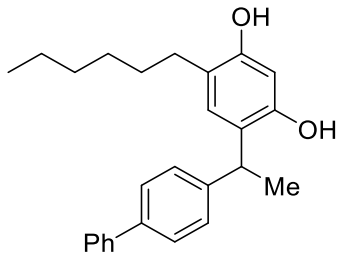
2.93 – 2.77 (m, 2H), 2.51 (dd, *J* = 18.9, 8.6 Hz, 1H), 2.43–2.34 (m, 1H), 2.31–2.23 (m, 1H), 2.20–2.11 (m, 1H), 2.10 – 1.92 (m, 3H), 1.70 – 1.38 (m, 9H), 1.31 (s, 9H), 0.93 (d, *J* = 4.4 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ, ppm: 221.1 (d, *J* = 2.1 Hz), 151.5 (dd, *J* = 23.7, 6.5 Hz), 144.8 (d, *J* = 6.8 Hz), 135.7 (d, *J* = 2.7 Hz), 131.9 (d, *J* = 2.5 Hz), 129.5 (d, *J* = 14.2 Hz), 128.5 (d, *J* = 3.5 Hz), 125.0, 124.8, 124.6 (d, *J* = 3.5 Hz), 124.5 (d, *J* = 5.1 Hz), 123.5 (d, *J* = 3.7 Hz), 116.1, 50.4 (d, *J* = 1.9 Hz), 48.1, 44.1 (d, *J* = 8.3 Hz), 39.4 (d, *J* = 11.8 Hz), 38.4, 35.9, 34.7, 31.6 (d, *J* = 1.7 Hz), 31.4 (d, *J* = 1.0 Hz), 29.1 (d, *J* = 2.6 Hz), 26.6, 26.1 (d, *J* = 7.9 Hz), 21.6, 21.2 (d, *J* = 21.7 Hz), 13.9 (d, *J* = 2.3 Hz).

HRMS m/z calculated for $C_{30}H_{37}O_2$, 429.2799, found: 429.2797.

IR (ATR), ν, cm^{-1}: 1718, 1420, 1256, 1204, 893, 705.

4-(1-([1,1'-biphenyl]-4-yl)ethyl)-6-hexylbenzene-1,3-diol



3na

Following the general procedure, 4-ethyl-1,1'-biphenyl **1c** (73.0 mg, 0.4 mmol) was irradiated for 3 h then 4-hexylbenzene-1,3-diol **2n** (233 mg, 1.2 mmol.) was added and the reaction was heated to 90 °C for 3 hours. The product was purified by Ag impregnated silica gel chromatography using an eluent of 12% to 14% EtOAc:hexanes to afford 4-(1-([1,1'-biphenyl]-4-yl)ethyl)-6-hexylbenzene-1,3-diol **3na** (46.3 mg, 31%) as an orange solid.

m. p. = 53–55°C

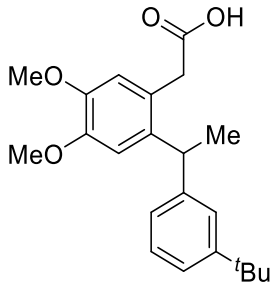
^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.60–7.56 (m, 2H), 7.53 (d, *J* = 8.2 Hz, 2H), 7.43 (t, *J* = 7.7 Hz, 2H), 7.38–7.29 (m, 3H), 7.00 (s, 1H), 6.26 (s, 1H), 4.65 (s, 1H), 4.56 (s, 1H), 4.30 (q, *J* = 7.2 Hz, 1H), 2.58–2.53 (m, 2H), 1.70–1.54 (m, 5H), 1.46–1.26 (m, 6H), 1.00–0.85 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ, ppm: 152.3, 151.9, 144.7, 140.7, 139.1, 129.0, 128.5, 127.6, 127.3, 126.9, 126.8, 123.7, 120.4, 103.5, 37.9, 31.6, 30.0, 29.3, 29.0, 22.5, 21.1, 13.9.

HRMS m/z calculated for $C_{26}H_{29}O_2$, 373.2160, found: 373.2160.

IR (ATR), ν, cm^{-1}: 1191, 1110, 835, 690, 608, 595, 584.

2-(2-(1-(3-(tert-butyl)phenyl)ethyl)-4,5-dimethoxyphenyl)acetic acid



3oa

Following the general procedure, 1-*tert*-butyl-3-ethylbenzene **1a** (76.0 µL, 0.4 mmol) was irradiated for 24 h then 2-(3,4-dimethoxyphenyl)acetic acid **2o** (157 mg, 0.8 mmol) was added. The product was purified by flash chromatography using an eluent of 86.5:12.5:1 EtOAc:hexanes:AcOH to afford 2-(2-(1-(3-(tert-butyl)phenyl)ethyl)-4,5-dimethoxyphenyl)acetic acid **3oa** (40.1 mg, 28%) as a yellow solid.

m. p. = 114–119°C

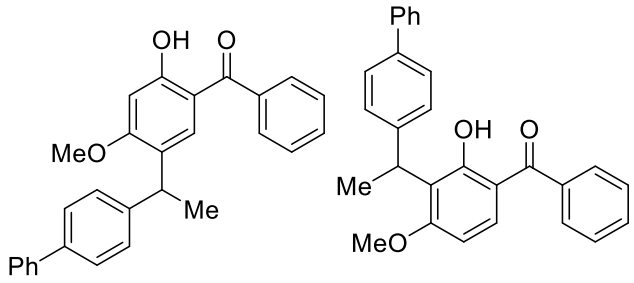
^{1}H NMR (400 MHz, Acetone-d_6) δ, ppm: 7.38 (s, 1H), 7.23–7.13 (m, 2H), 7.04 (dt, *J* = 6.7, 1.9 Hz, 1H), 6.85 (s, 1H), 6.83 (s, 1H), 4.38 (q, *J* = 7.2 Hz, 1H), 3.76 (s, 3H), 3.73 (s, 3H), 3.64 (d, *J* = 15.9 Hz, 1H), 3.53 (d, *J* = 15.9 Hz, 1H), 1.57 (d, *J* = 7.1 Hz, 3H), 1.27 (s, 9H).

^{13}C NMR (126 MHz, Acetone-d_6) δ, ppm: 173.4, 151.6, 149.3, 148.2, 146.8, 138.3, 128.8, 126.0, 125.5, 125.4, 123.5, 115.8 (d, *J* = 2.4 Hz), 112.4 (d, *J* = 2.4 Hz), 56.2 (d, *J* = 4.1 Hz), 56.1 (d, *J* = 4.5 Hz), 41.1 (d, *J* = 2.4 Hz), 38.5, 35.1, 31.7 (d, *J* = 2.4 Hz), 22.5 (d, *J* = 2.3 Hz).

HRMS m/z calculated for $C_{22}H_{27}O_4$, 355.1915, found: 355.1921.

IR (ATR), ν, cm^{-1}: 1718, 1517, 1268, 1218, 1172, 1200, 1108, 864, 805, 711.

(5-(1-([1,1'-biphenyl]-4-yl)ethyl)-2-hydroxy-4-methoxyphenyl)(phenyl)methanone



3pa **3pa'**

Following the general procedure, 4-ethyl-1,1'-biphenyl **1c** (73.0 mg, 0.4 mmol) was irradiated for 3 h then (2-hydroxy-4-methoxyphenyl)(phenyl)methanone **2p** (183 mg, 0.8 mmol) was added. The product was purified by Ag impregnated silica gel chromatography using an eluent of 5.5% EtOAc:hexanes to afford (5-(1-([1,1'-biphenyl]-4-yl)ethyl)-2-hydroxy-4-methoxyphenyl)(phenyl)methanone **3pa** (58.8 mg, 36%) as a yellow oil. (17% of other isomer **3pa'** determined by ^{1}H NMR).

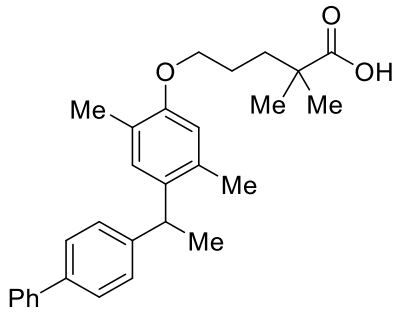
^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 12.67 (s, 1H), 7.61–7.53 (m, 4H), 7.51–7.47 (m, 3H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.42–7.32 (m, 4H), 7.24 (d, *J* = 8.1 Hz, 2H), 6.52 (s, 1H), 4.47 (q, *J* = 7.2 Hz, 1H), 3.88 (s, 3H), 1.50 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ, ppm: 200.2, 165.4, 164.1, 145.4, 141.4, 139.3, 138.6, 133.3, 131.9, 129.5, 129.2, 128.6, 128.4, 127.5, 127.4, 127.4, 127.0, 112.7, 99.8, 56.3, 37.2, 21.1.

HRMS m/z calculated for $C_{28}H_{23}O_3$, 407.1646, found: 407.1647.

IR (ATR), ν, cm^{-1}: 1623, 1344, 1250, 1204, 837, 764, 730, 696, 595.

5-(4-(1-([1,1'-biphenyl]-4-yl)ethyl)-2,5-dimethylphenoxy)-2,2-dimethylpentanoic acid



3qa

Following the general procedure, 4-ethyl-1,1'-biphenyl **1c** (73.0 mg, 0.4 mmol) was irradiated for 3 h then (2-hydroxy-4-methoxyphenyl)(phenyl)methanone **2q** (183 mg, 0.8 mmol) was

added. The product was purified by Ag impregnated silica gel chromatography using an eluent of 5:94:1 EtOAc:hexanes:AcOH to afford 5-(4-(1-([1,1'-biphenyl]-4-yl)ethyl)-2,5-dimethylphenoxy)-2,2-dimethylpentanoic acid **3qa** (115.4 mg, 67%) as an off white solid.

m. p. = 116–119°C

^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.60–7.54 (m, 2H), 7.49 (d, *J* = 8.3 Hz, 2H), 7.41 (t, *J* = 7.7 Hz, 2H), 7.35–7.29 (m, 1H), 7.22 (d, *J* = 8.3 Hz, 2H), 7.05 (s, 1H), 6.59 (s, 1H), 4.27 (q, *J* = 7.2 Hz, 1H), 3.93 (t, *J* = 5.8 Hz, 2H), 2.22 (s, 3H), 2.21 (s, 3H), 1.85–1.72 (m, 4H), 1.61 (d, *J* = 7.2 Hz, 3H), 1.26 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ, ppm: 184.1, 155.3, 146.1, 141.2, 138.7, 135.5, 134.3, 129.1, 128.8, 128.1, 127.1, 124.0, 113.4, 68.1, 42.1, 40.1, 37.0, 25.3, 25.1 (d, *J* = 1.9 Hz), 22.4, 19.9, 16.1.

HRMS m/z calculated for $C_{29}H_{33}O_3$, 429.2427, found: 429.2431.

IR (ATR), ν, cm^{-1}: 1694, 1102, 833, 764, 695, 583, 574.

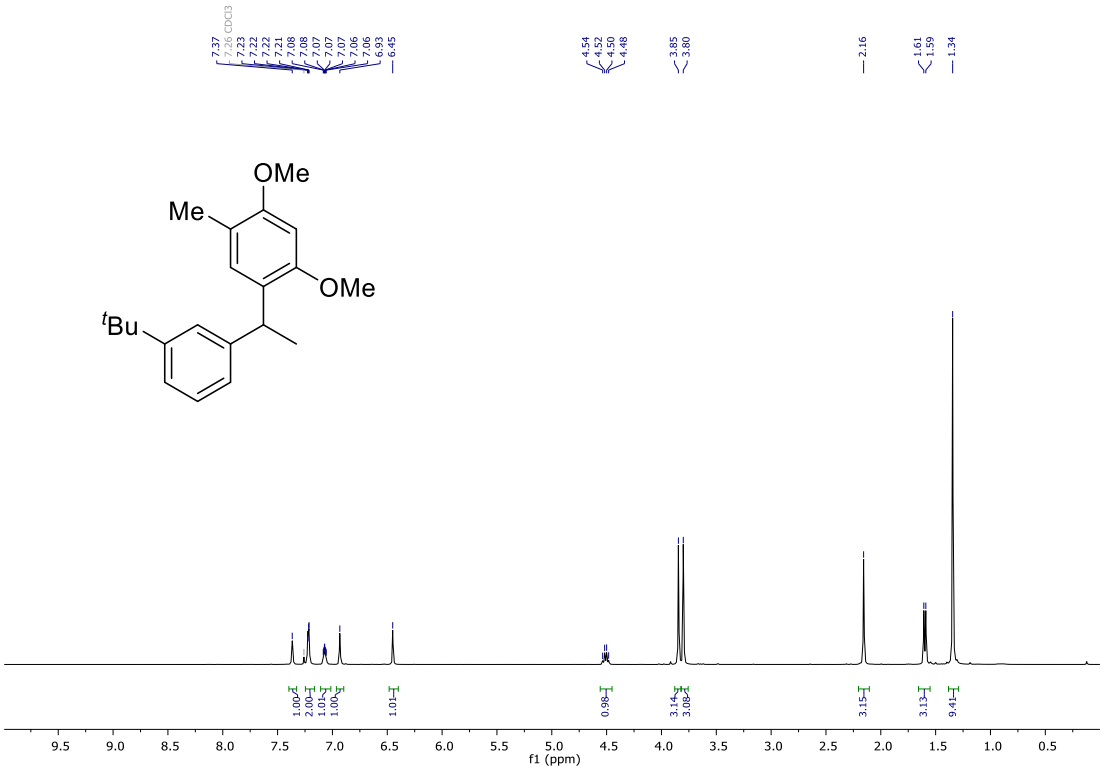
1.3 References

1. M. Xiang, Z.-K. Xin, B. Chen, C.-H. Tung and L.-Z. Wu, *Org. Lett*., 2017, **19**, 3009-3012.

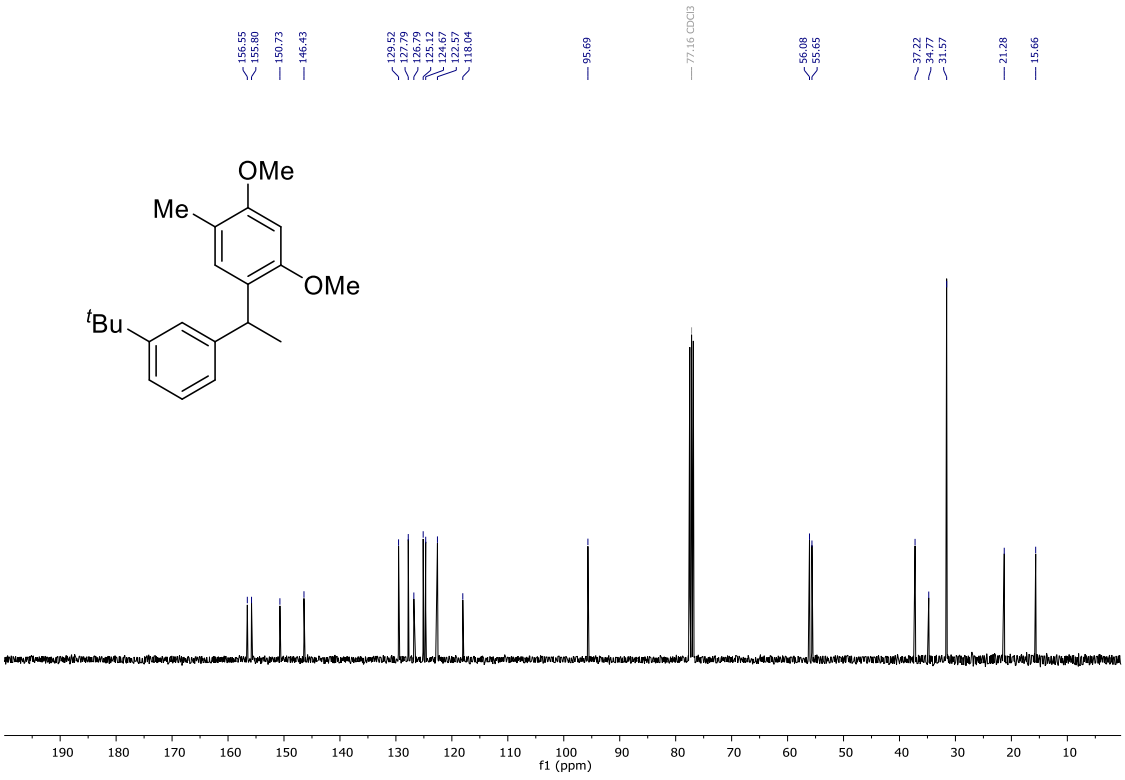
2. S. Bresciani and D. O'Hagan, *Tetrahedron Lett.*, 2010, **51**, 5795-5797.

1.4 NMR spectral data

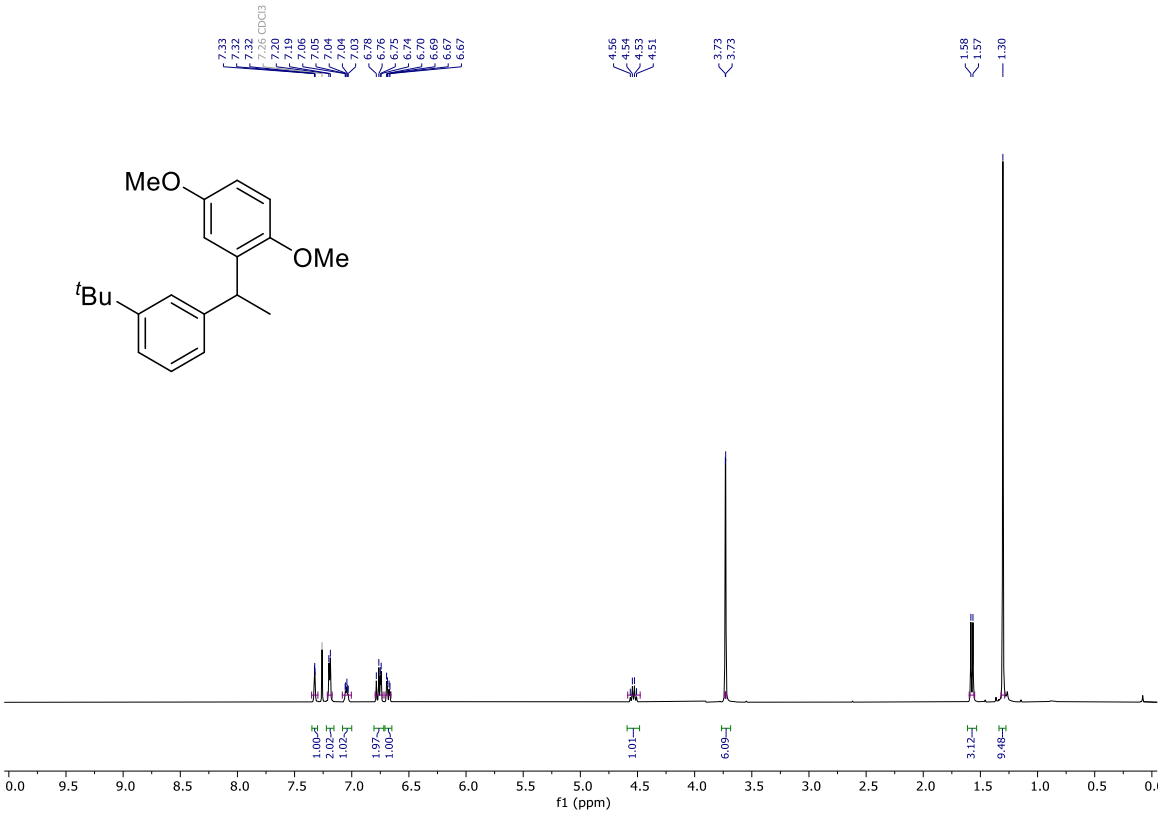
^{1}H NMR (400 MHz, $CDCl_3$)



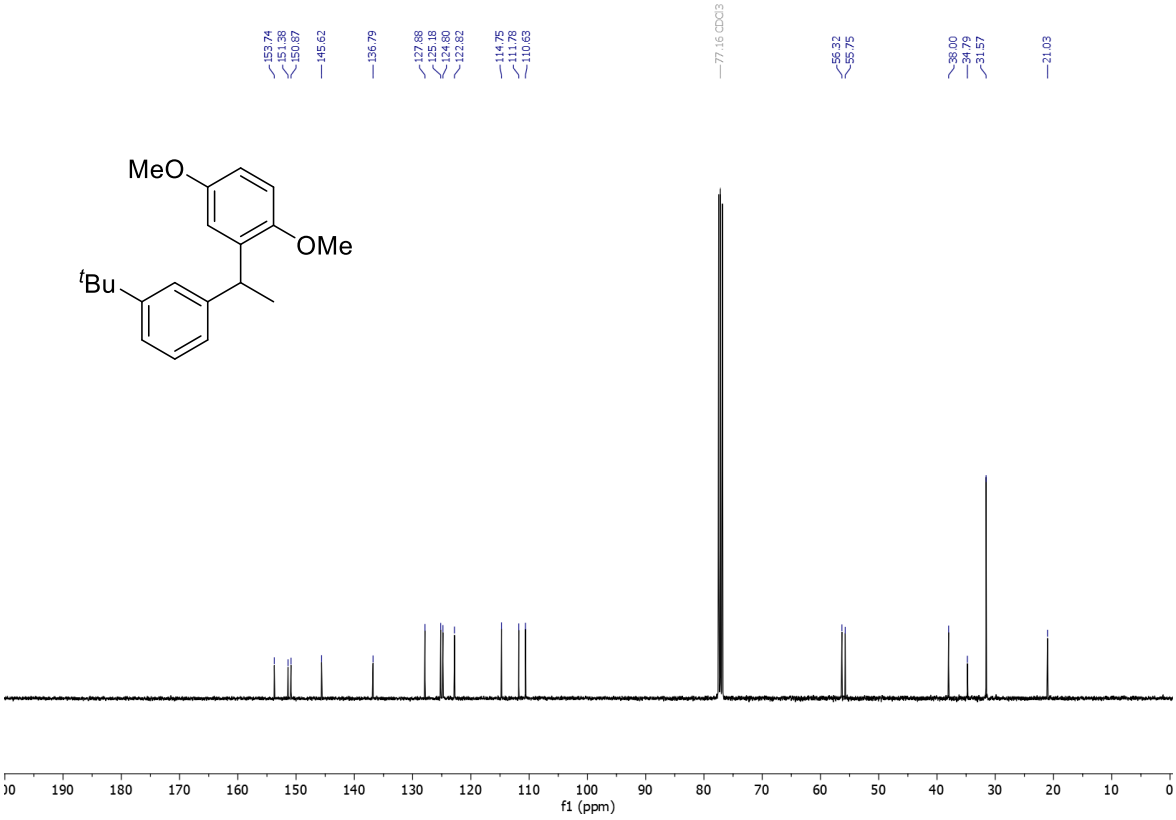
^{13}C NMR (101 MHz, $CDCl_3$)



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



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



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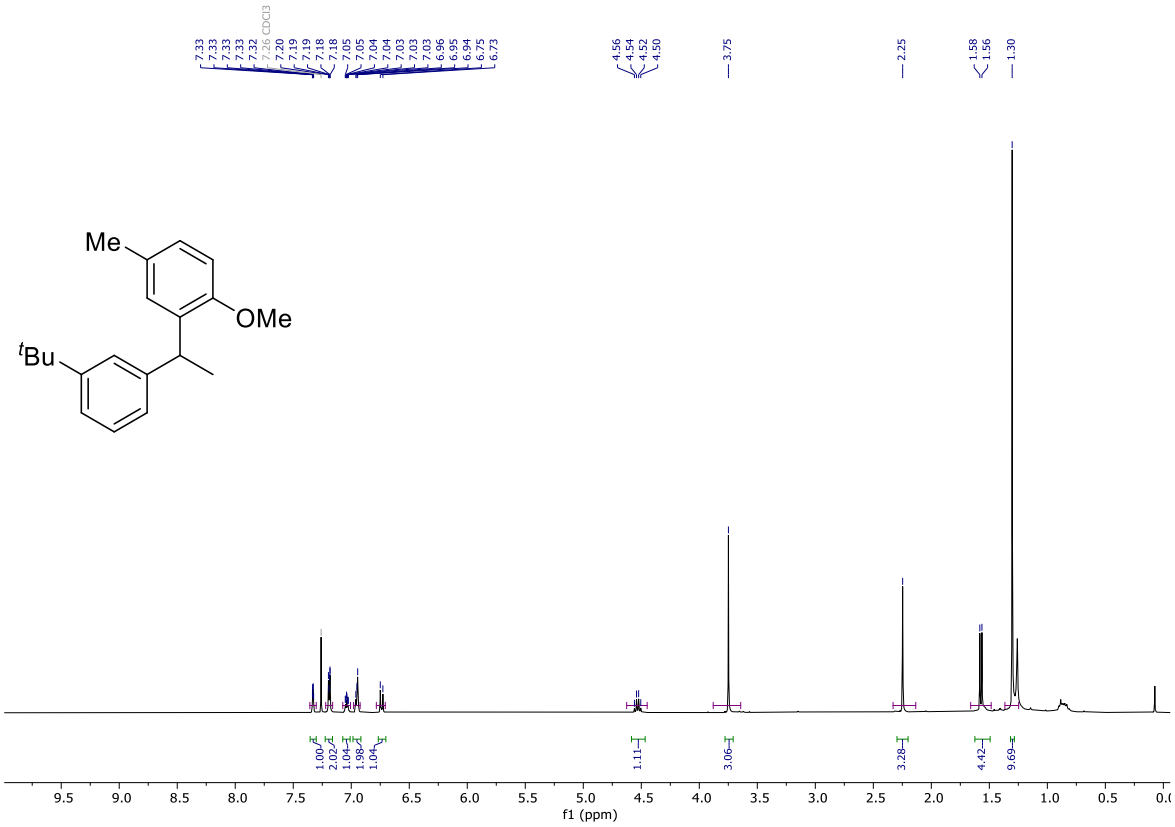

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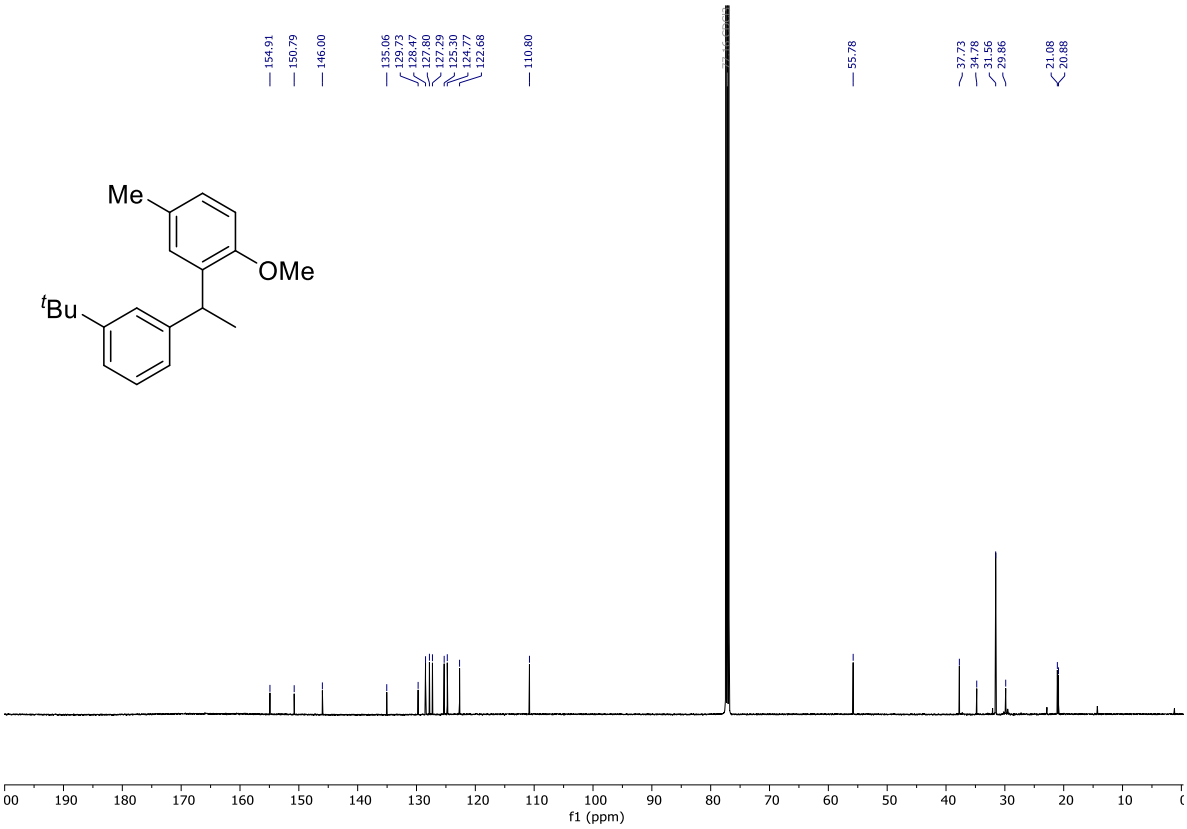
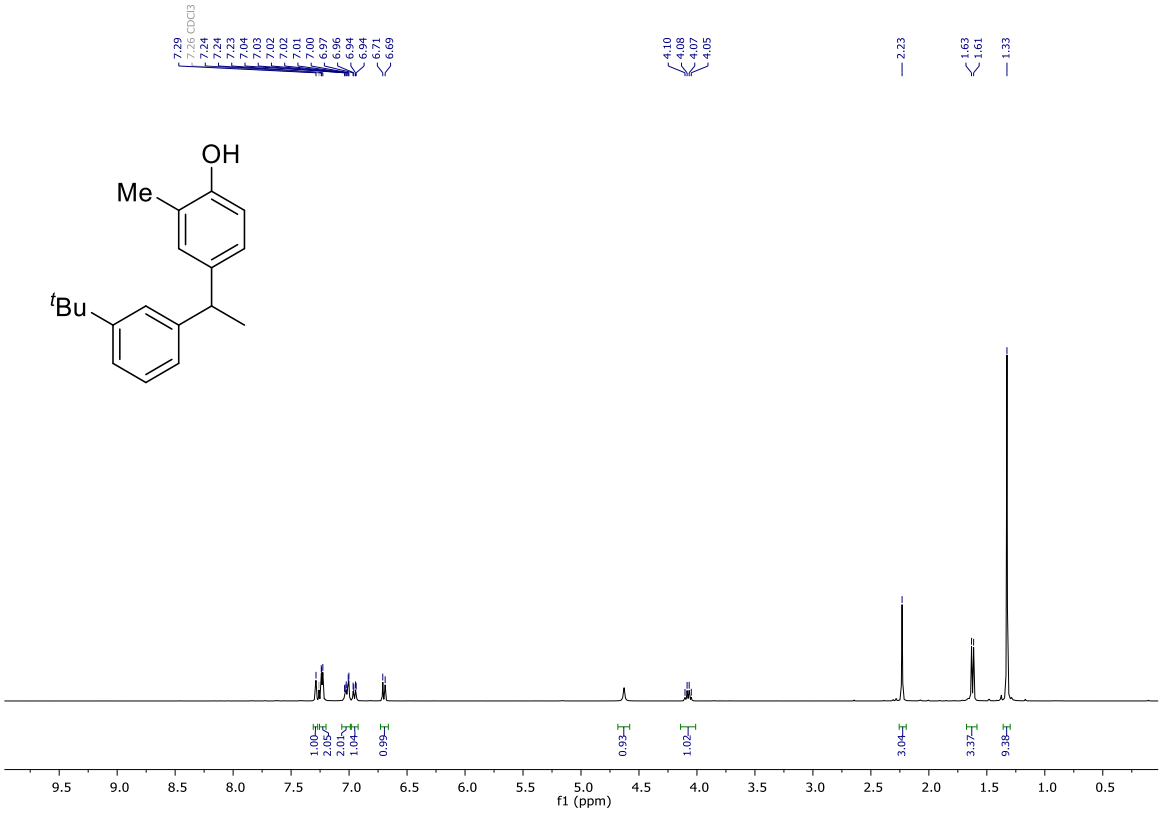
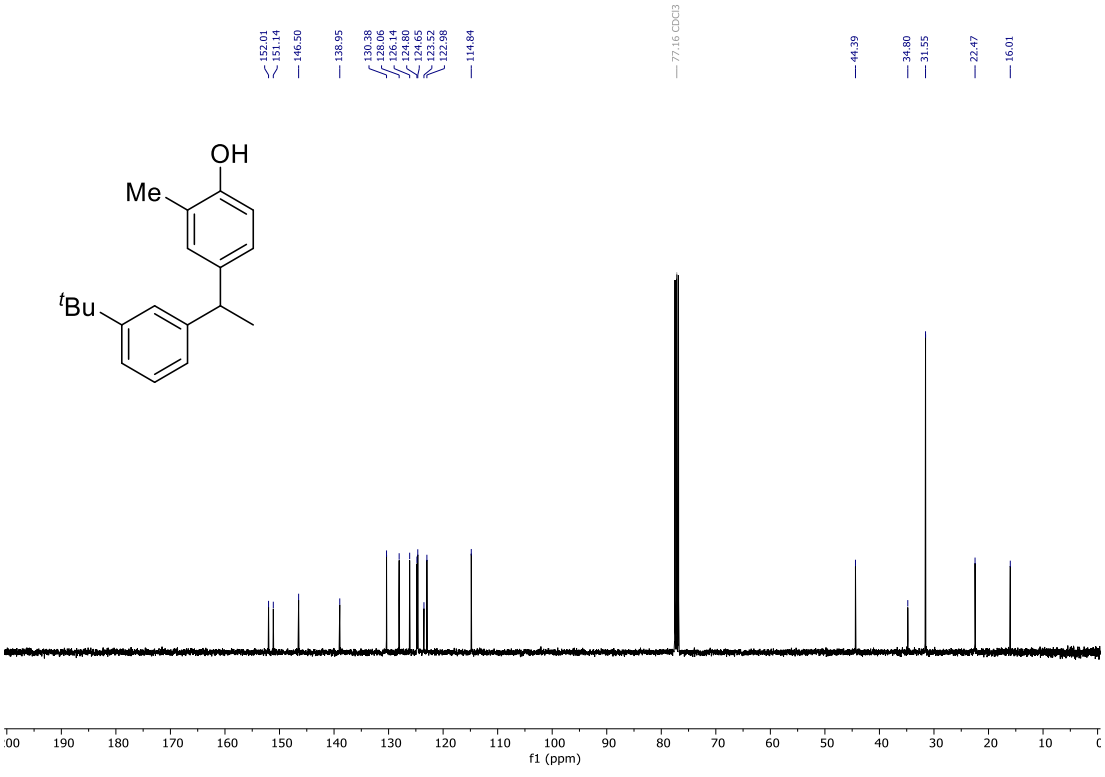


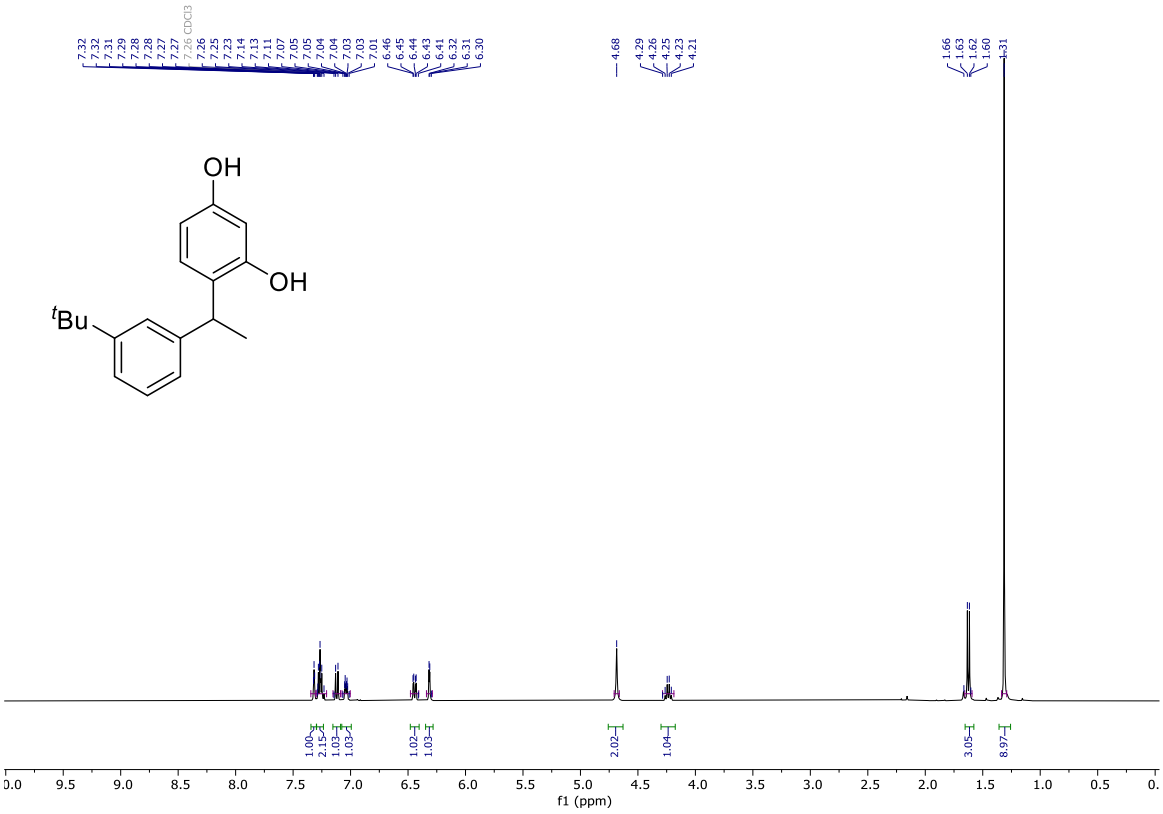
^{1}H NMR (400 MHz, $CDCl_3$)



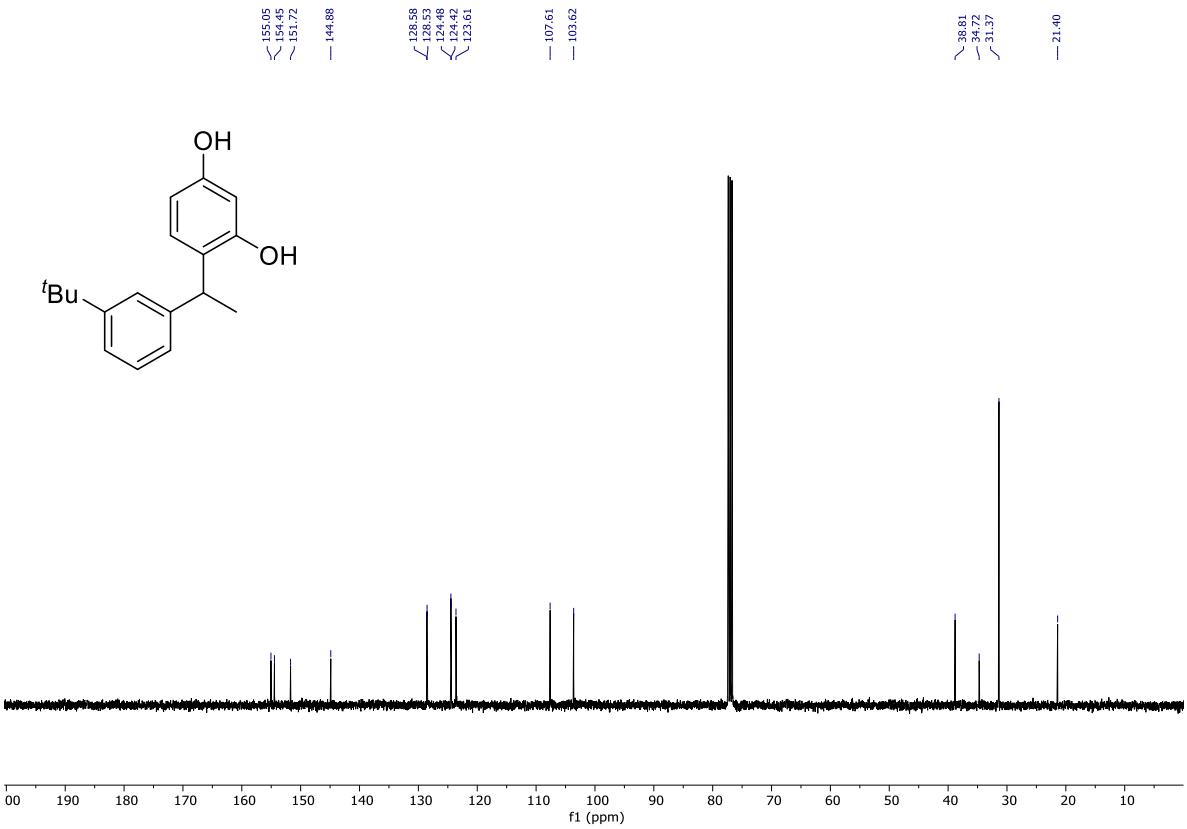
^{13}C NMR (101 MHz, $CDCl_3$)



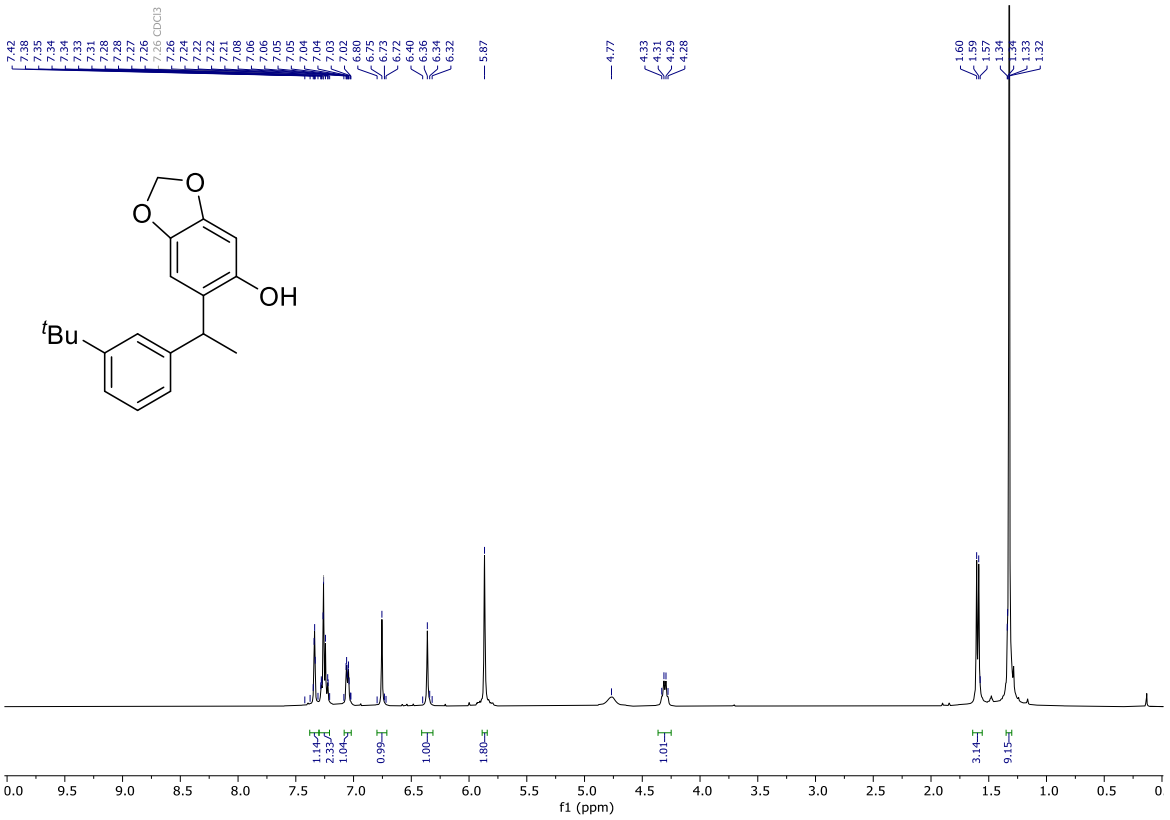
^{1}H NMR (400 MHz, $CDCl_3$)



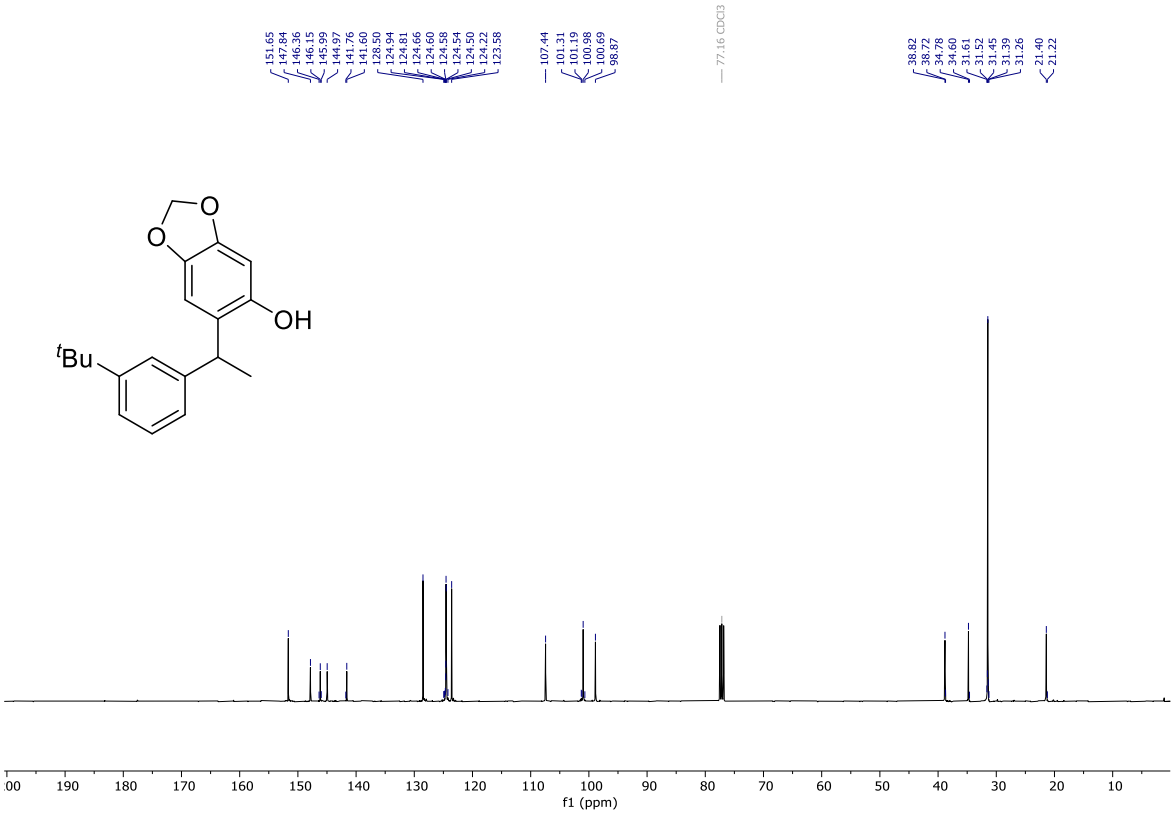
^{13}C NMR (101 MHz, $CDCl_3$)



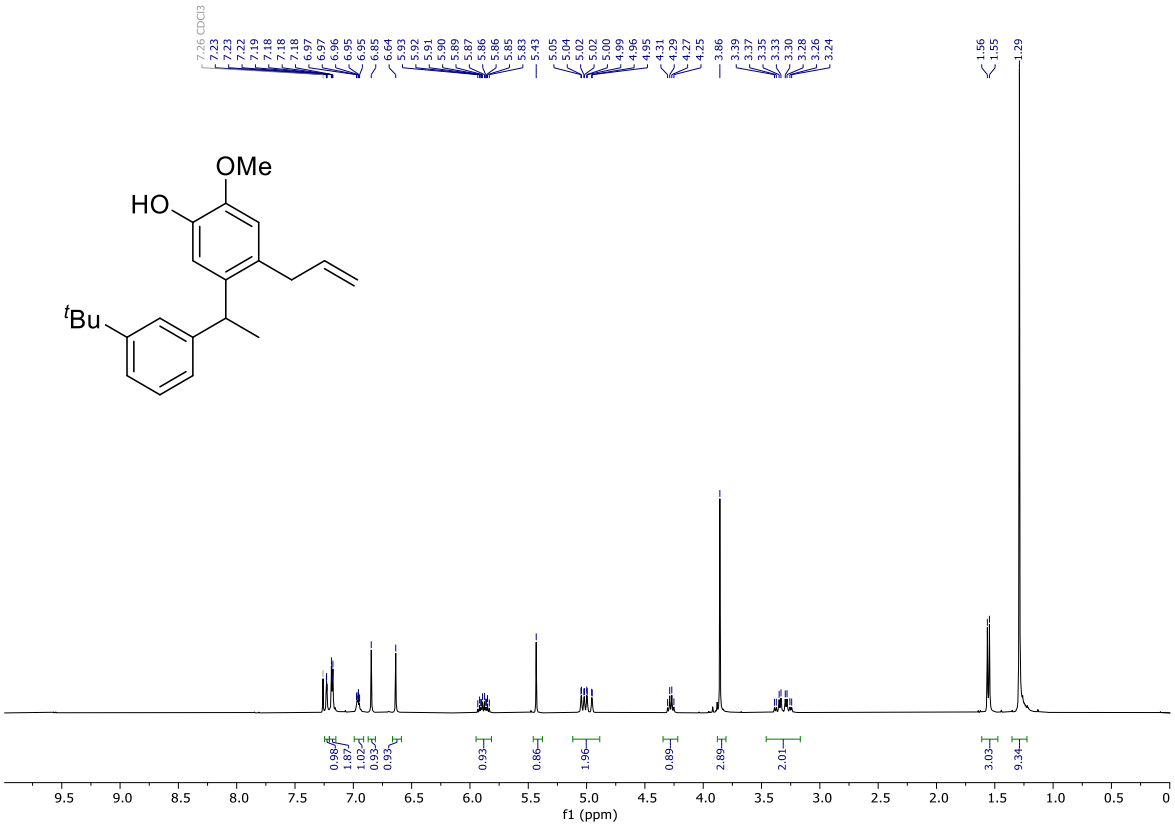
^{1}H NMR (400 MHz, $CDCl_3$)



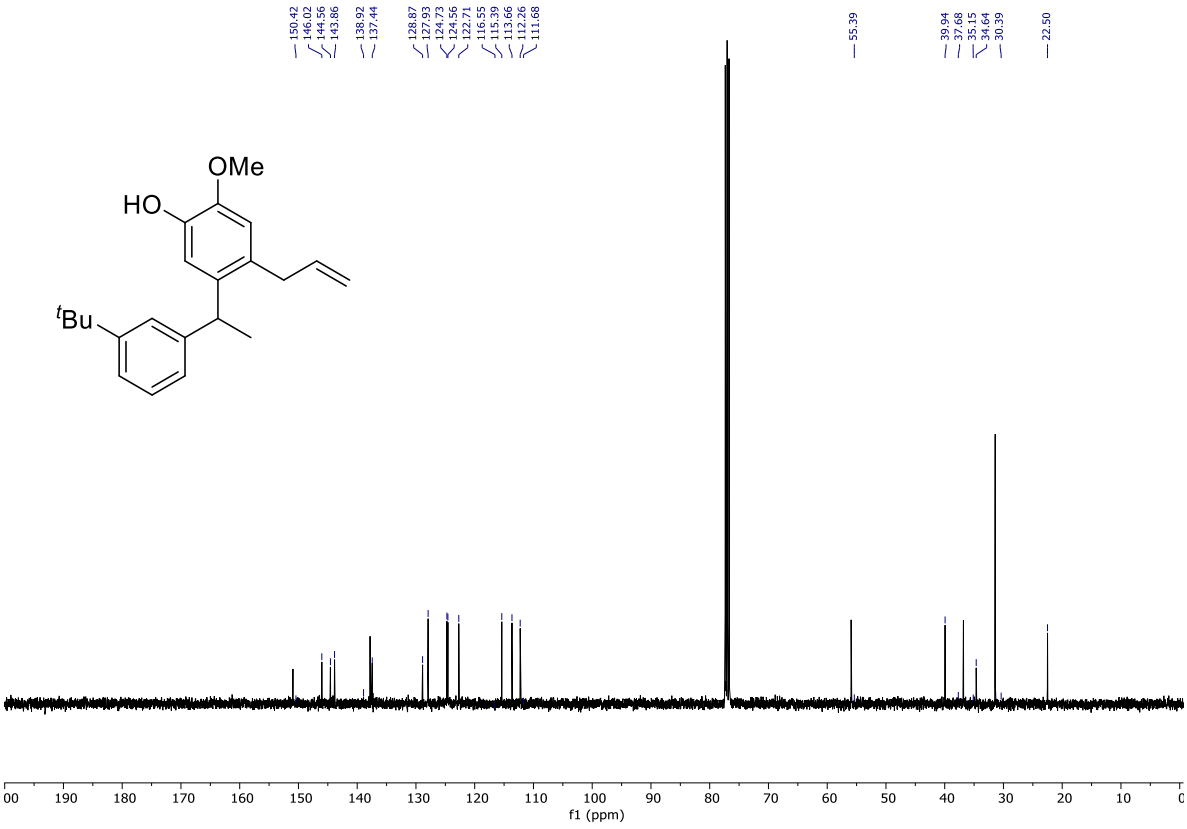
^{13}C NMR (101 MHz, $CDCl_3$)



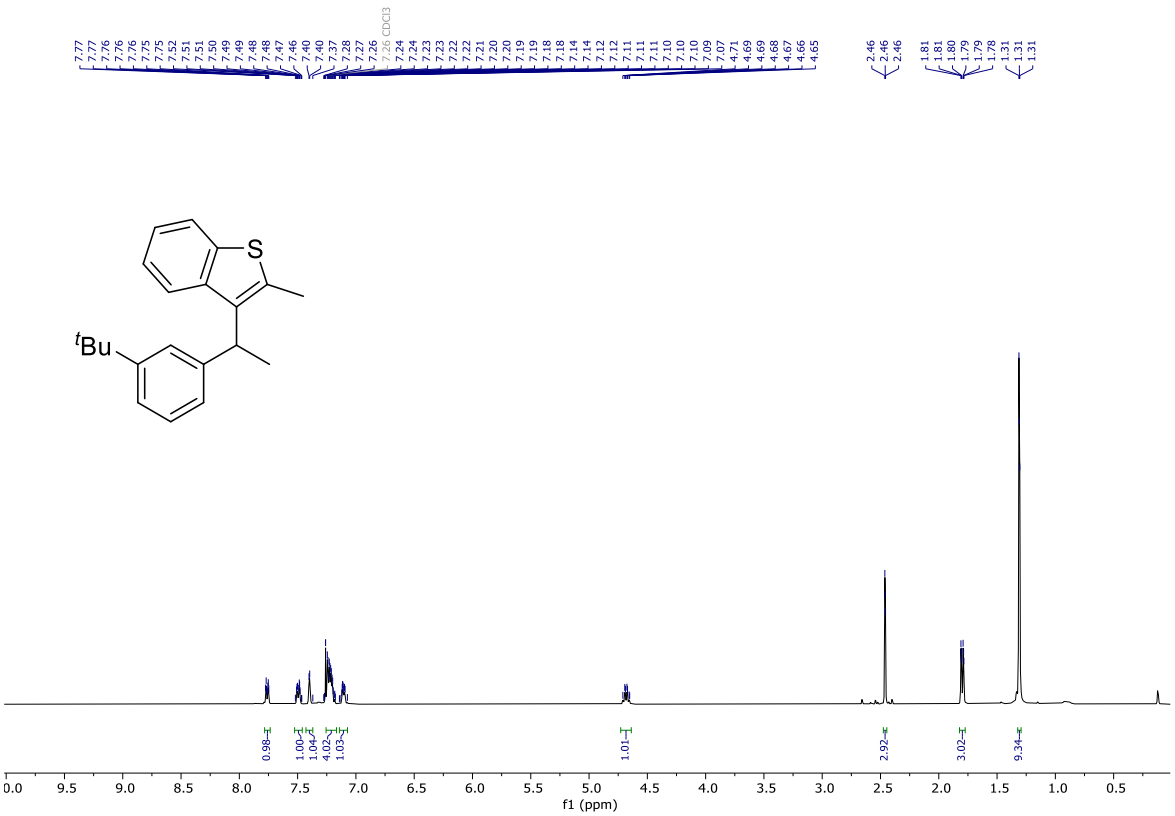
^{1}H NMR (400 MHz, $CDCl_3$)



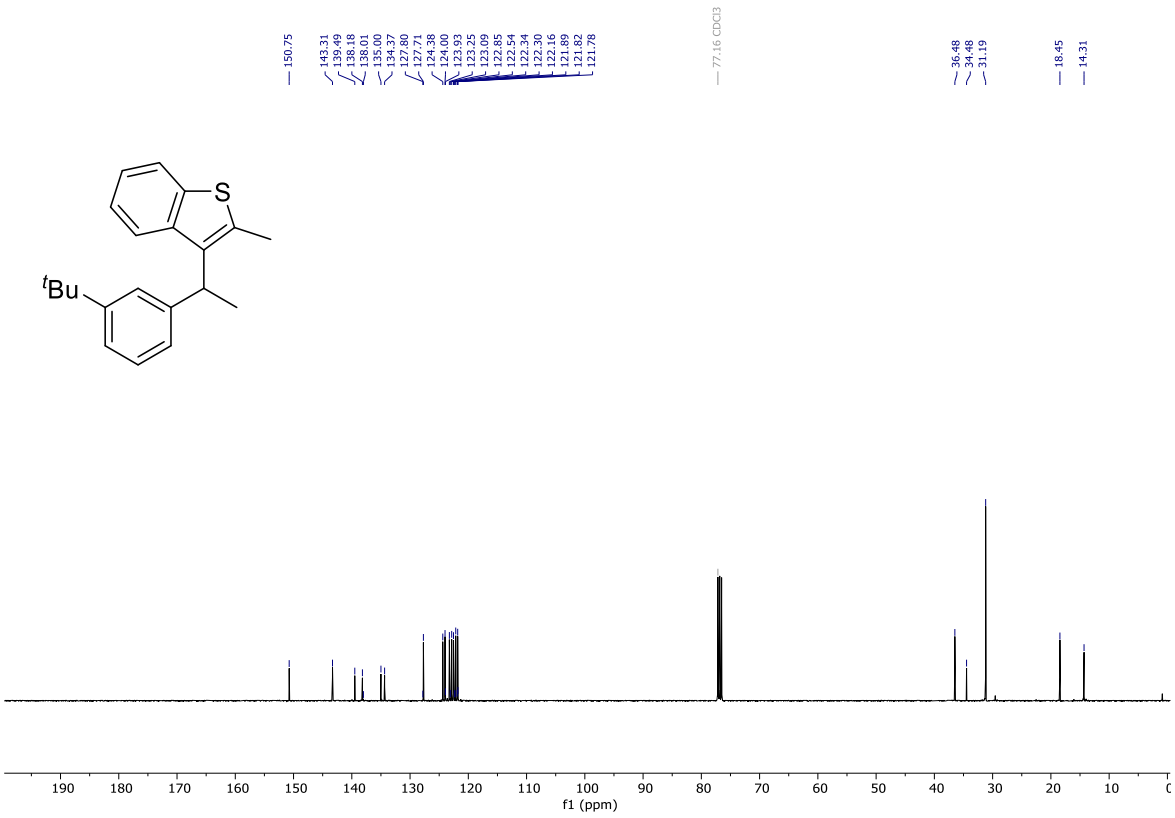
^{13}C NMR (101 MHz, $CDCl_3$)



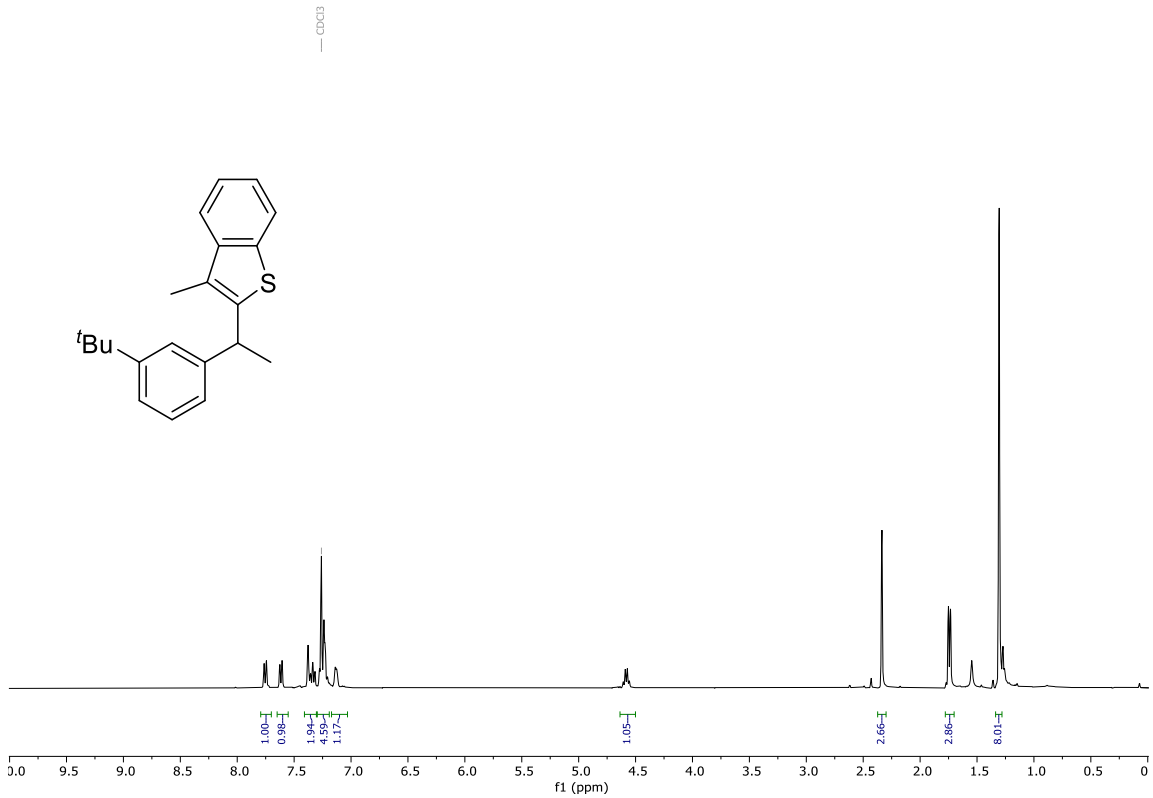
^{1}H NMR (400 MHz, $CDCl_3$)



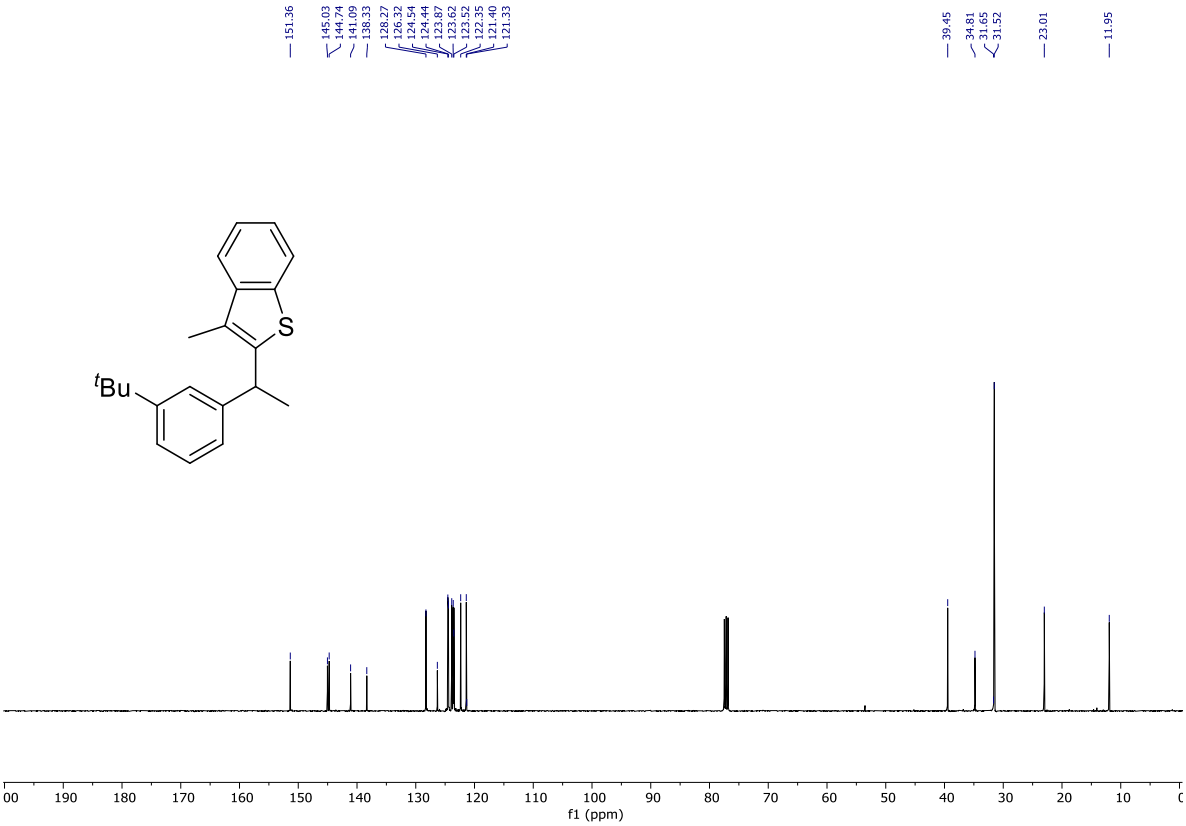
^{13}C NMR (101 MHz, $CDCl_3$)



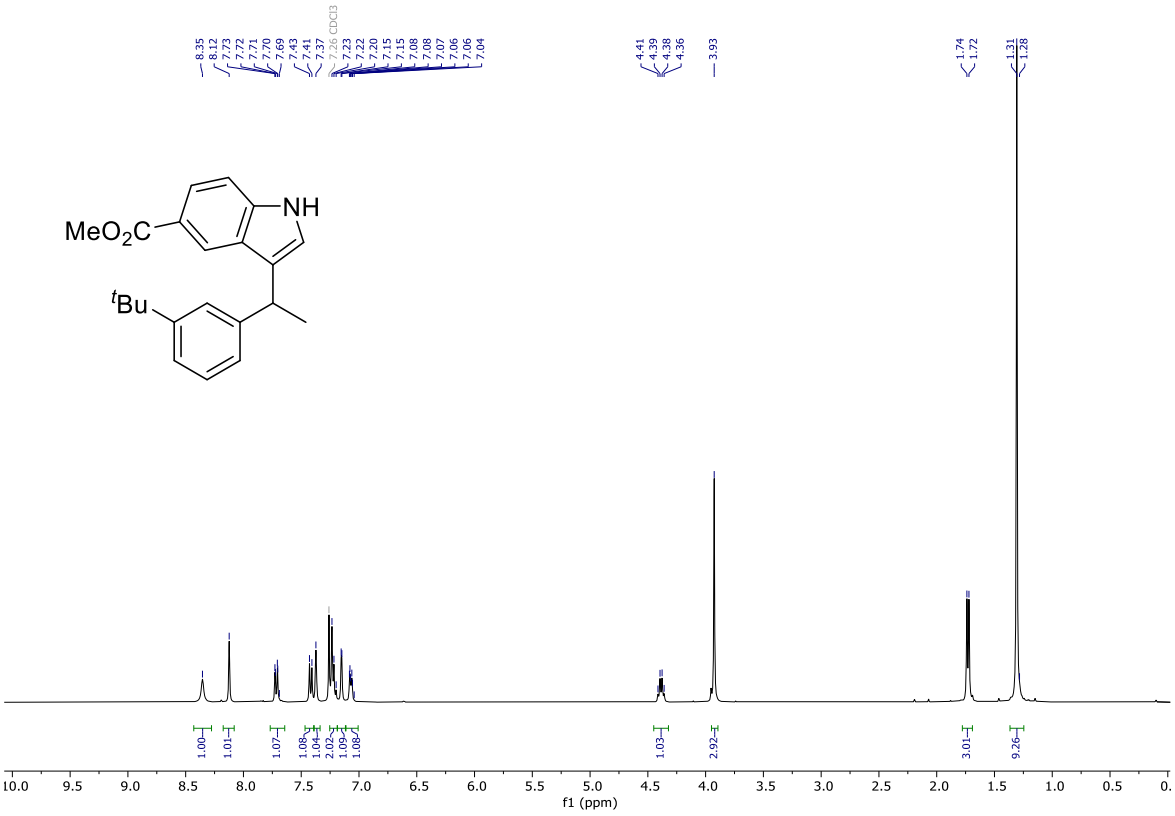
^{1}H NMR (400 MHz, $CDCl_3$)



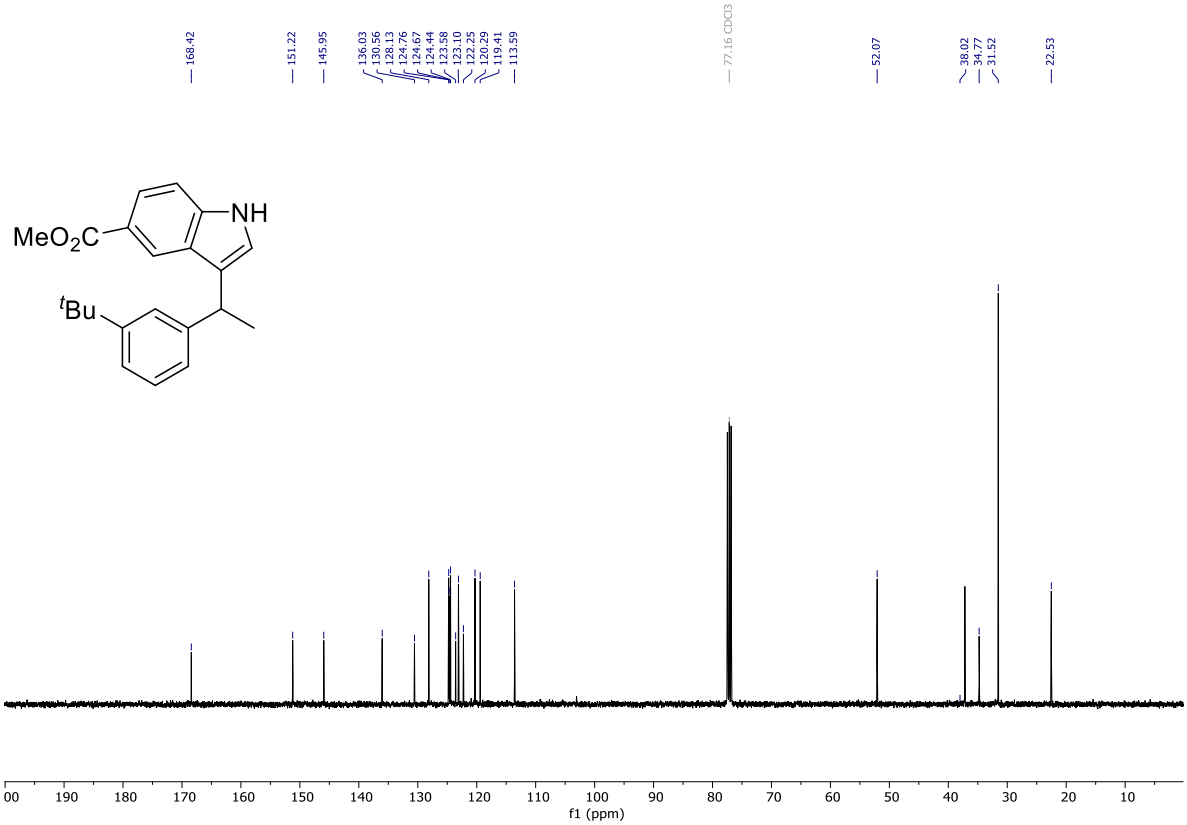
^{13}C NMR (101 MHz, $CDCl_3$)



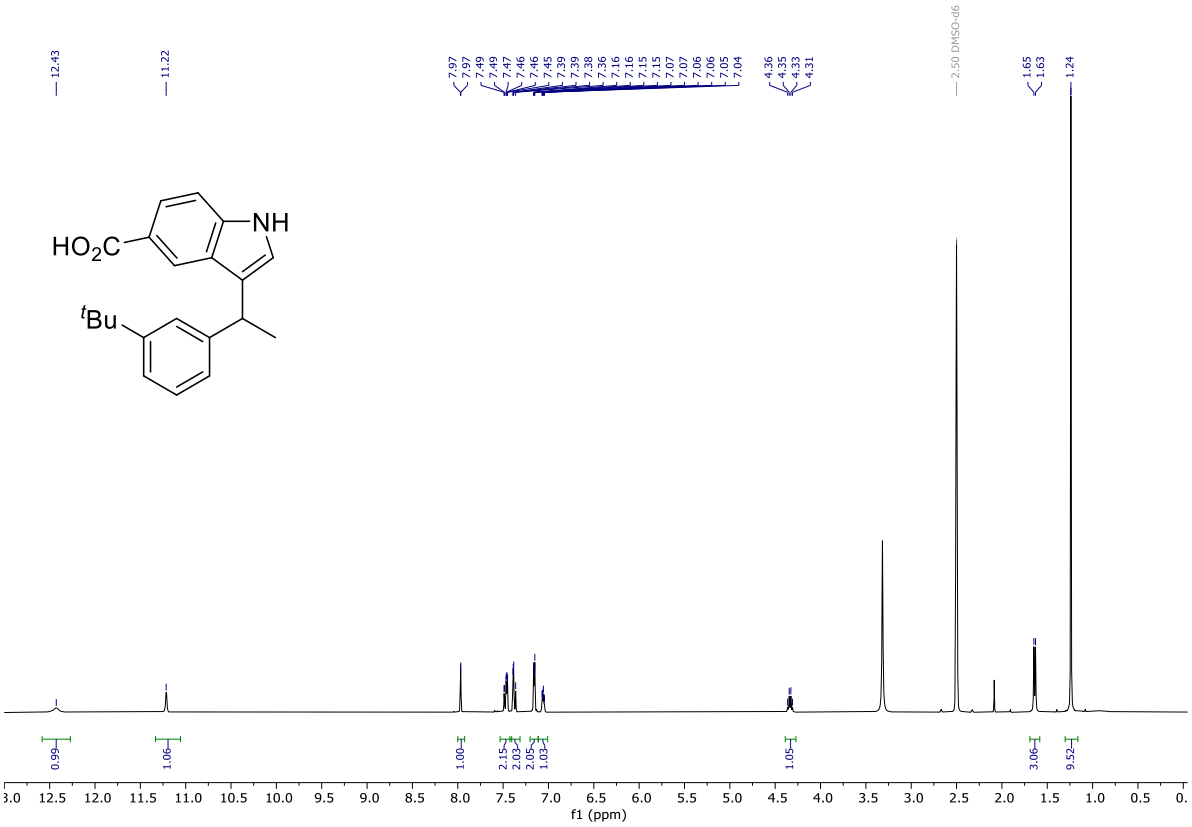
^{1}H NMR (400 MHz, $CDCl_3$)



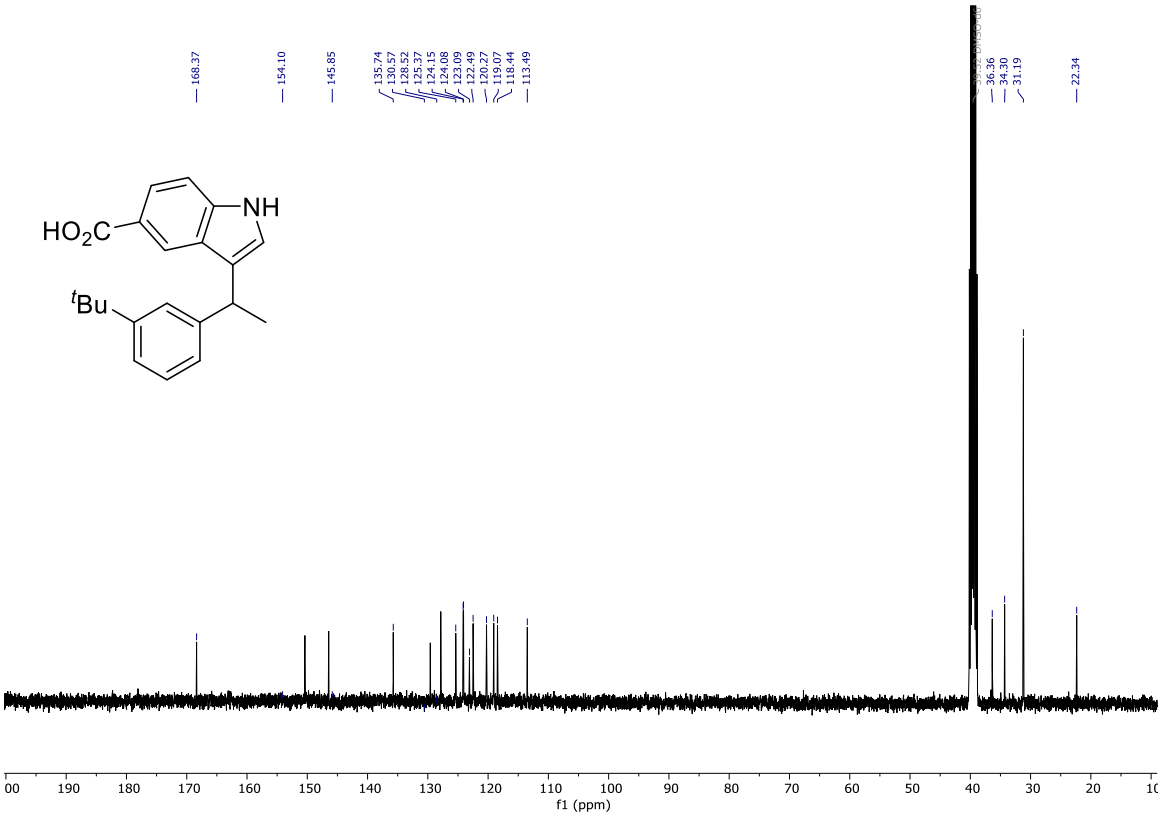
^{13}C NMR (101 MHz, $CDCl_3$)



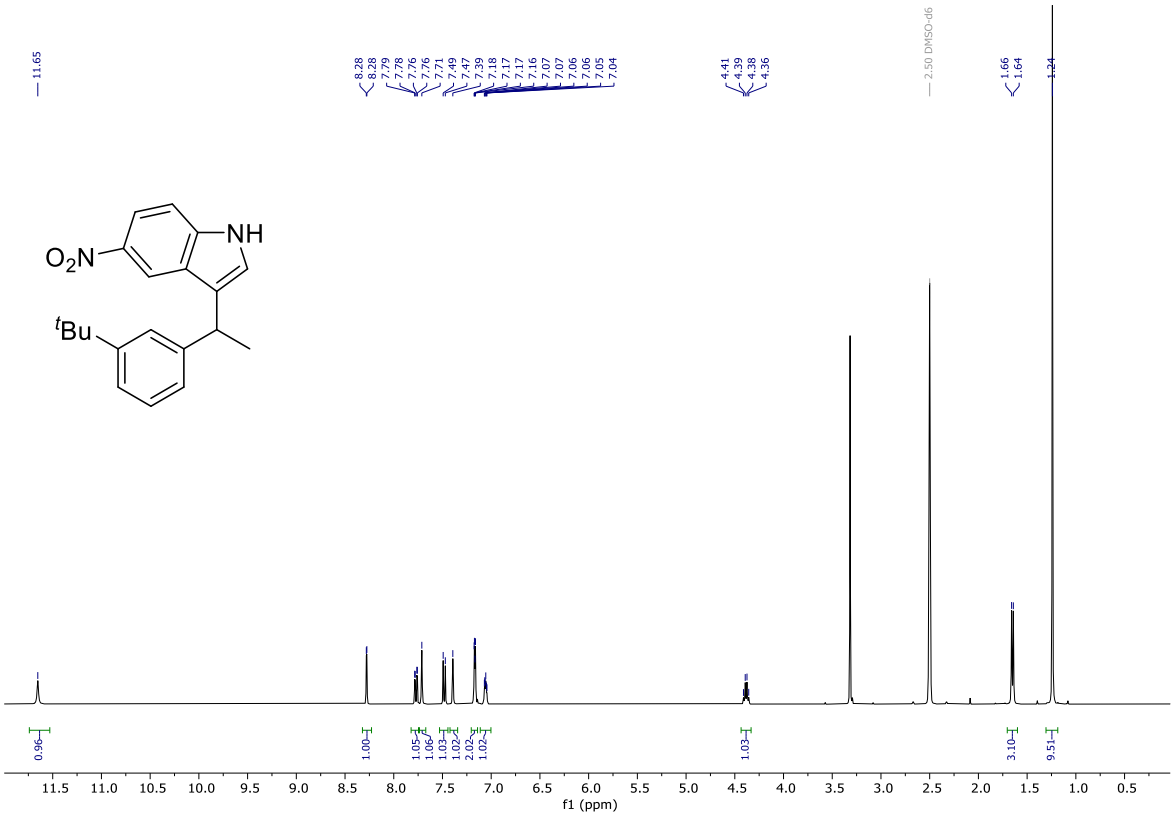
^{1}H NMR (400 MHz, DMSO-d_6)



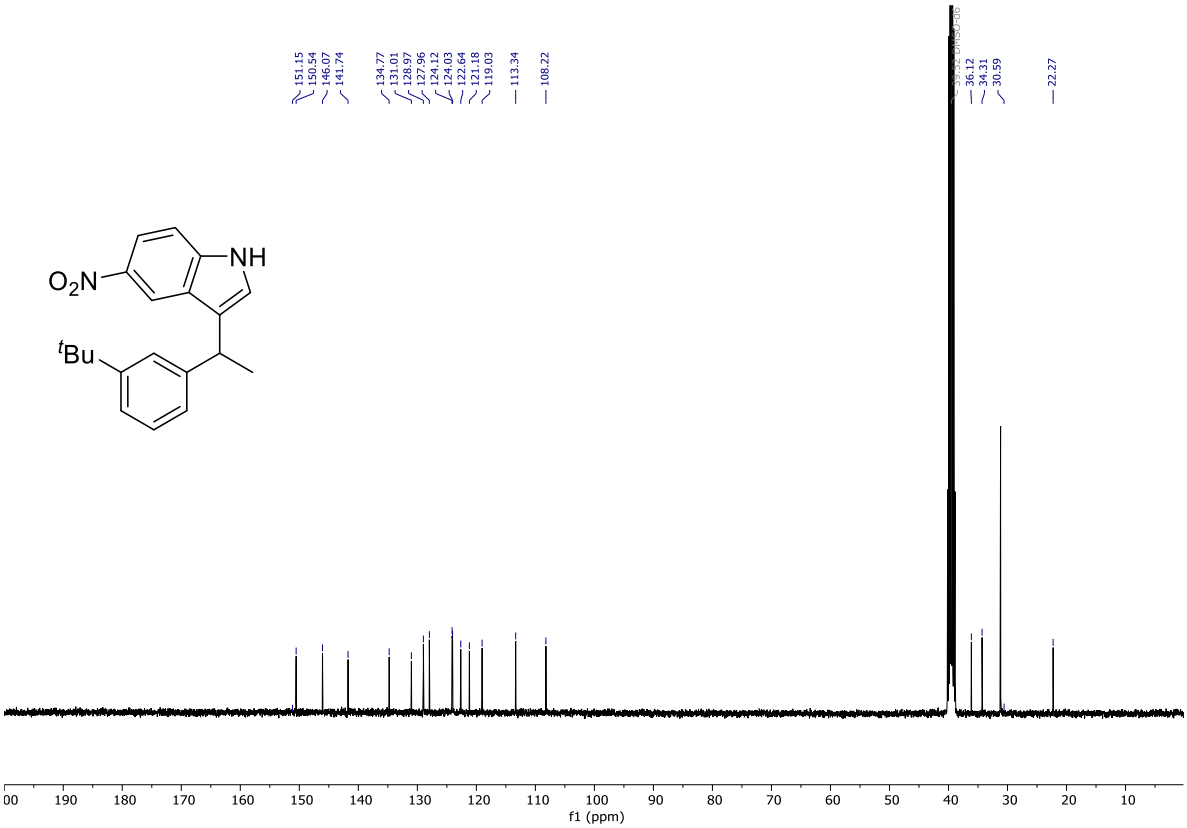
^{13}C NMR (101 MHz, DMSO-d_6)



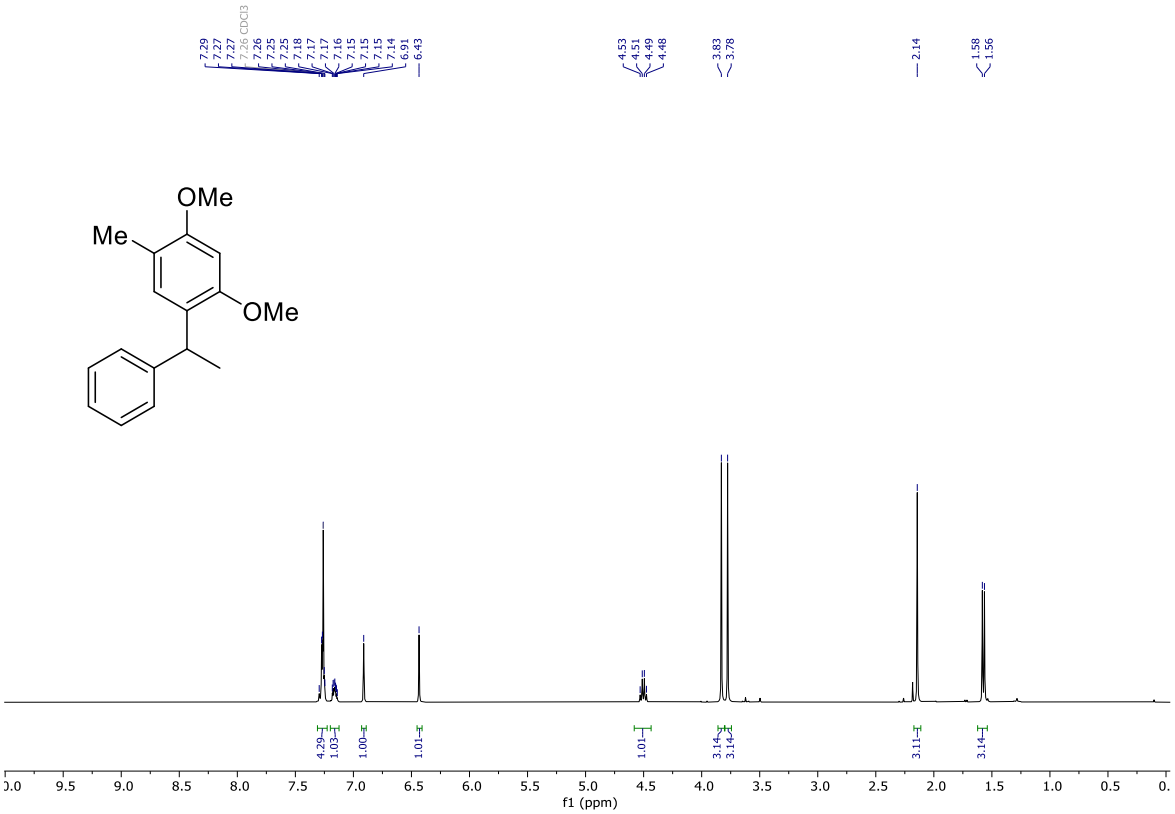
^{1}H NMR (400 MHz, DMSO-d_6)



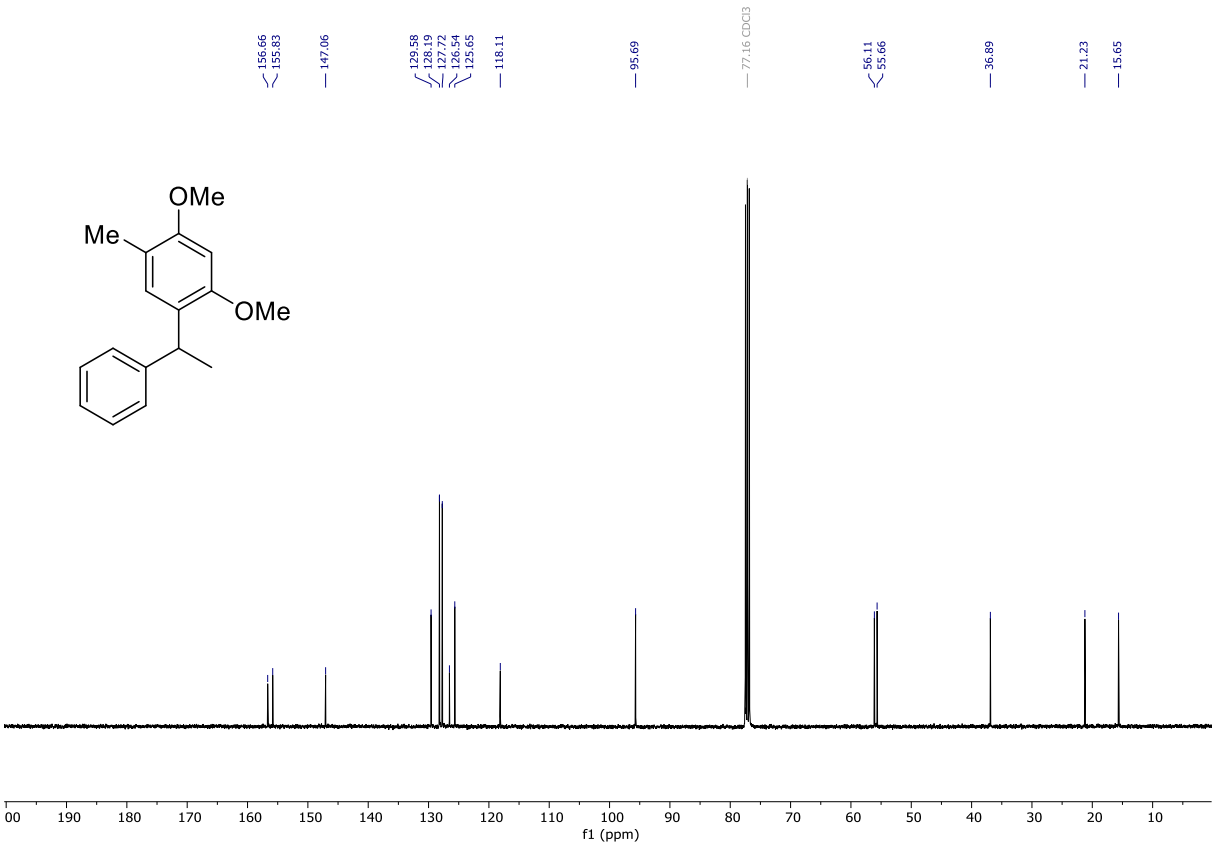
^{13}C NMR (101 MHz, DMSO-d_6)



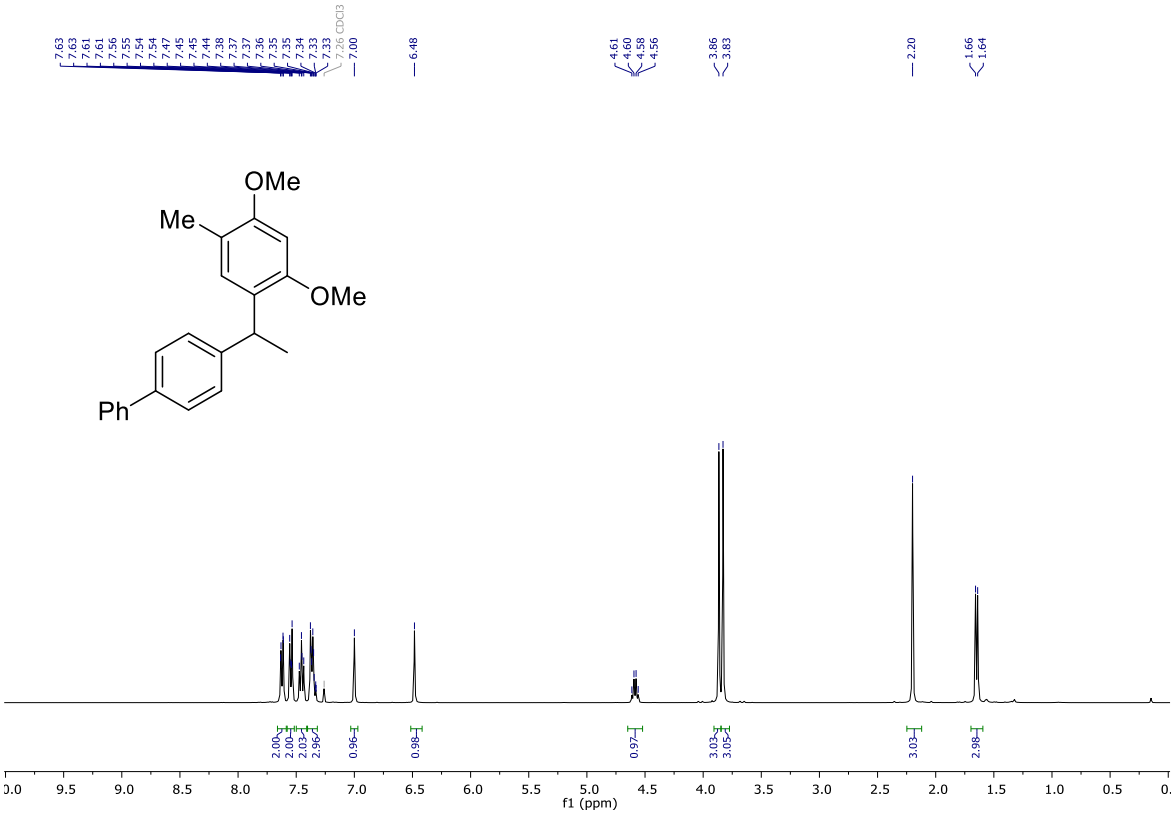
^{1}H NMR (400 MHz, $CDCl_3$)



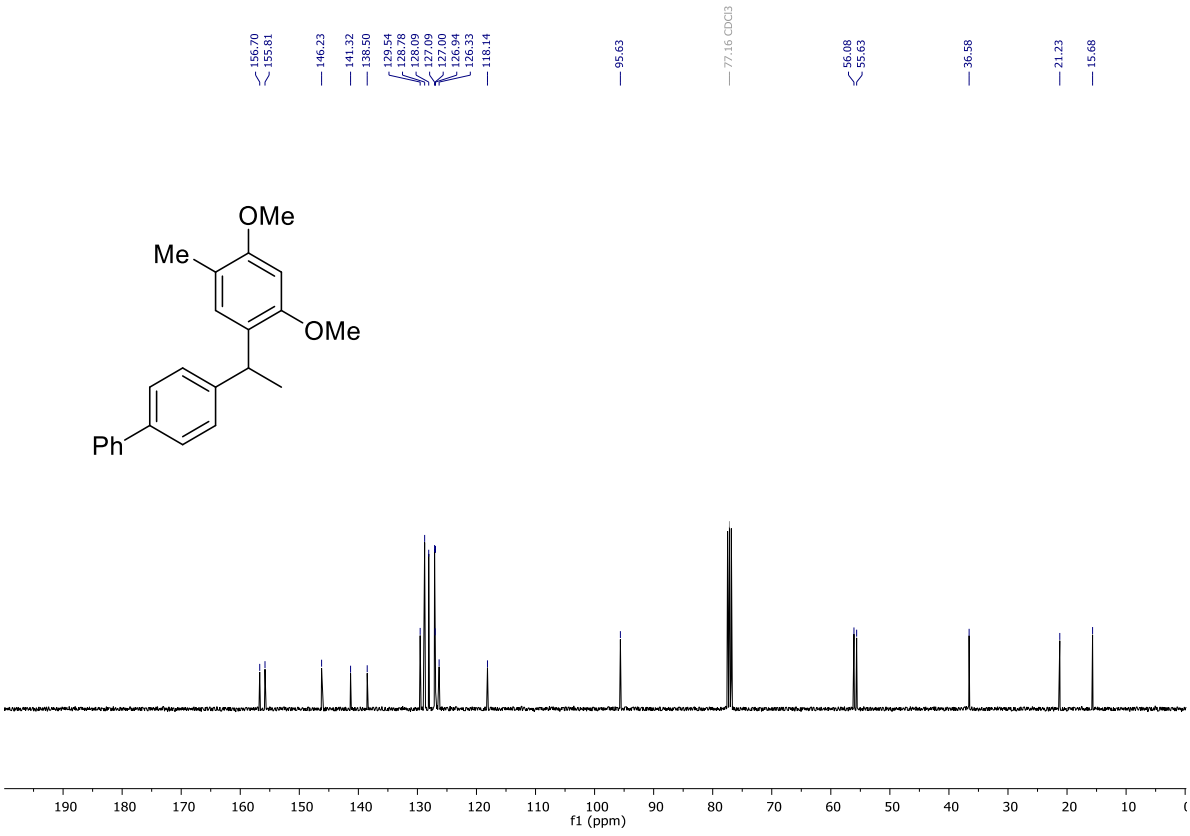
^{13}C NMR (101 MHz, $CDCl_3$)



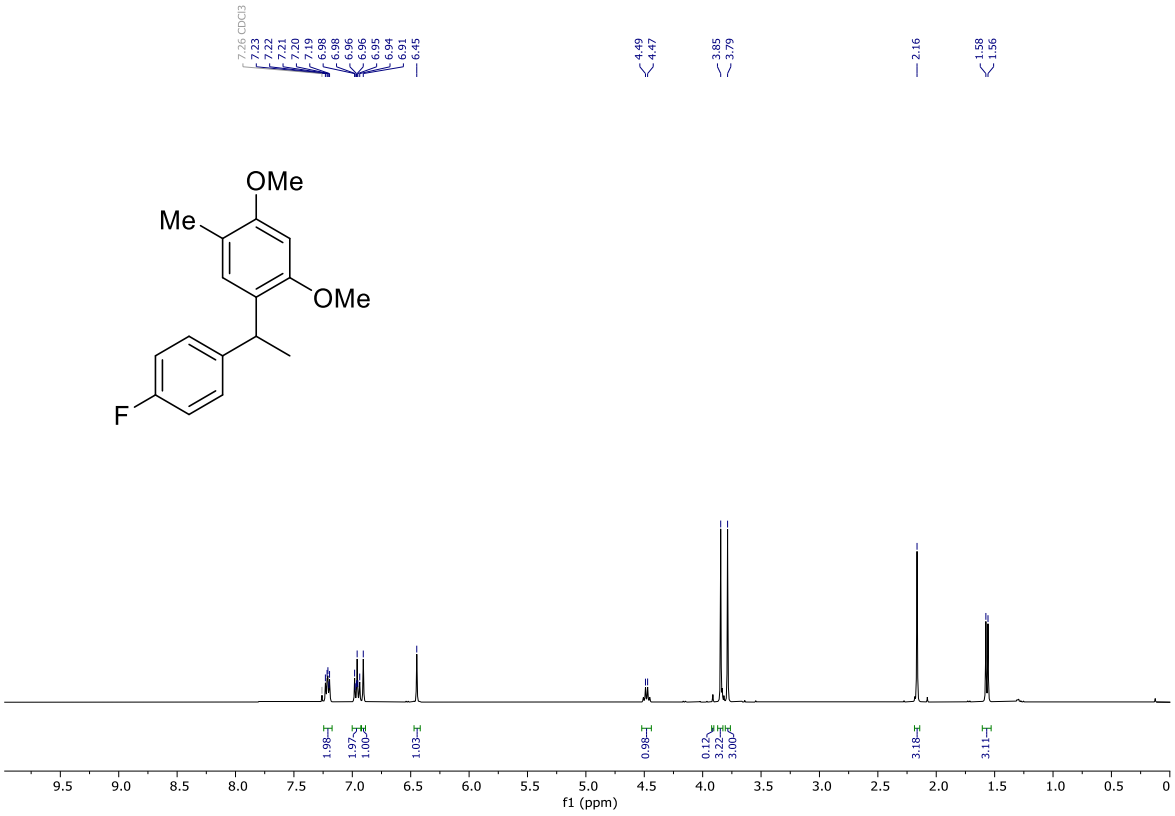
^{1}H NMR (400 MHz, $CDCl_3$)



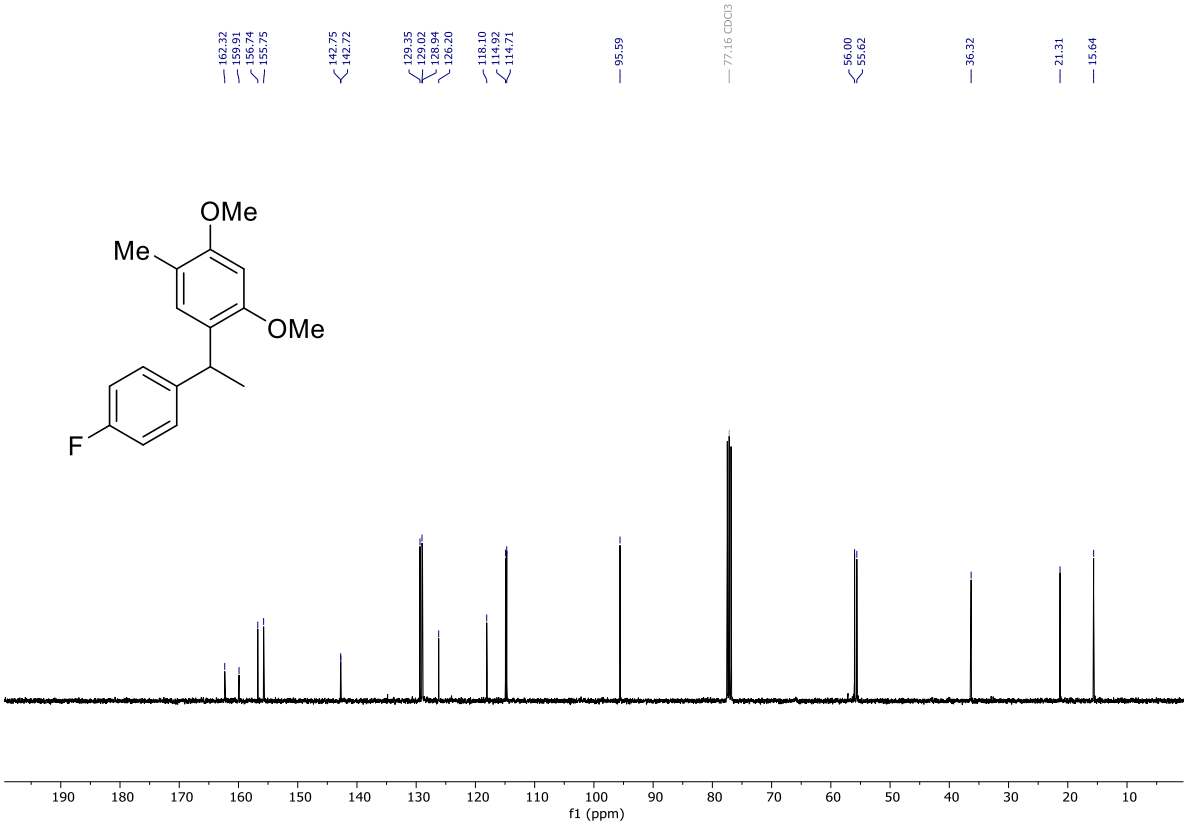
^{13}C NMR (101 MHz, $CDCl_3$)



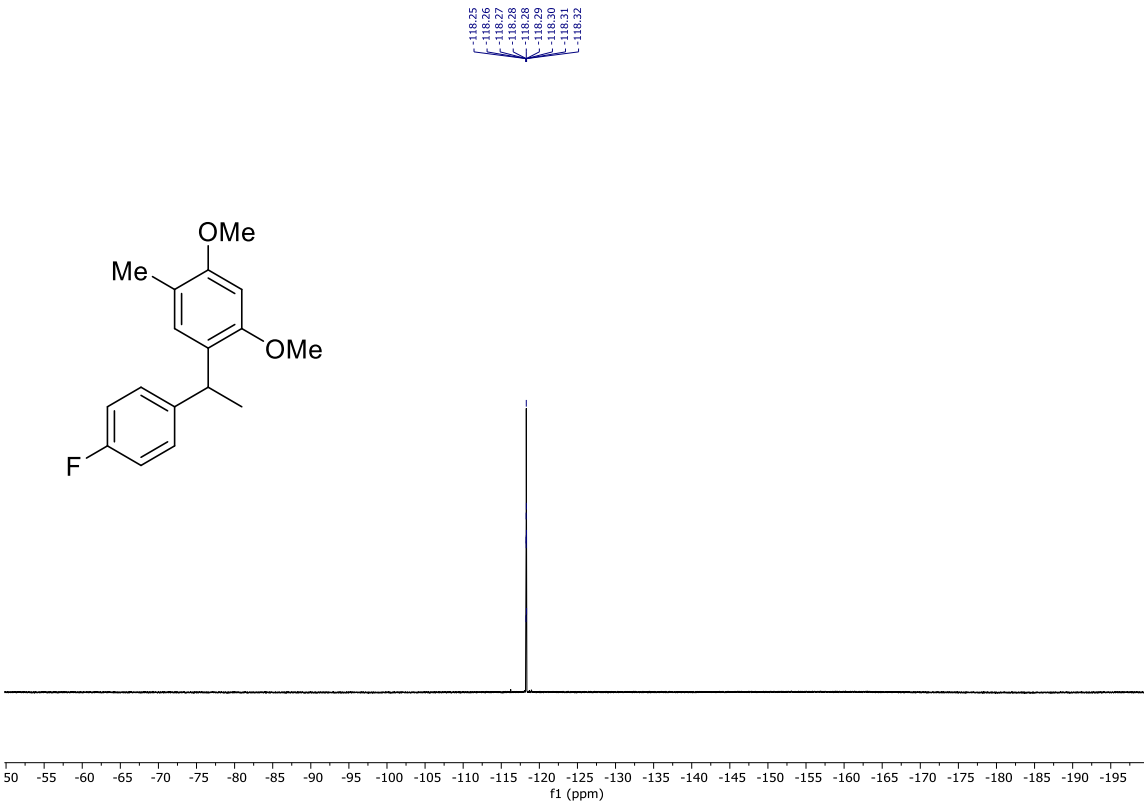
^{1}H NMR (400 MHz, $CDCl_3$)



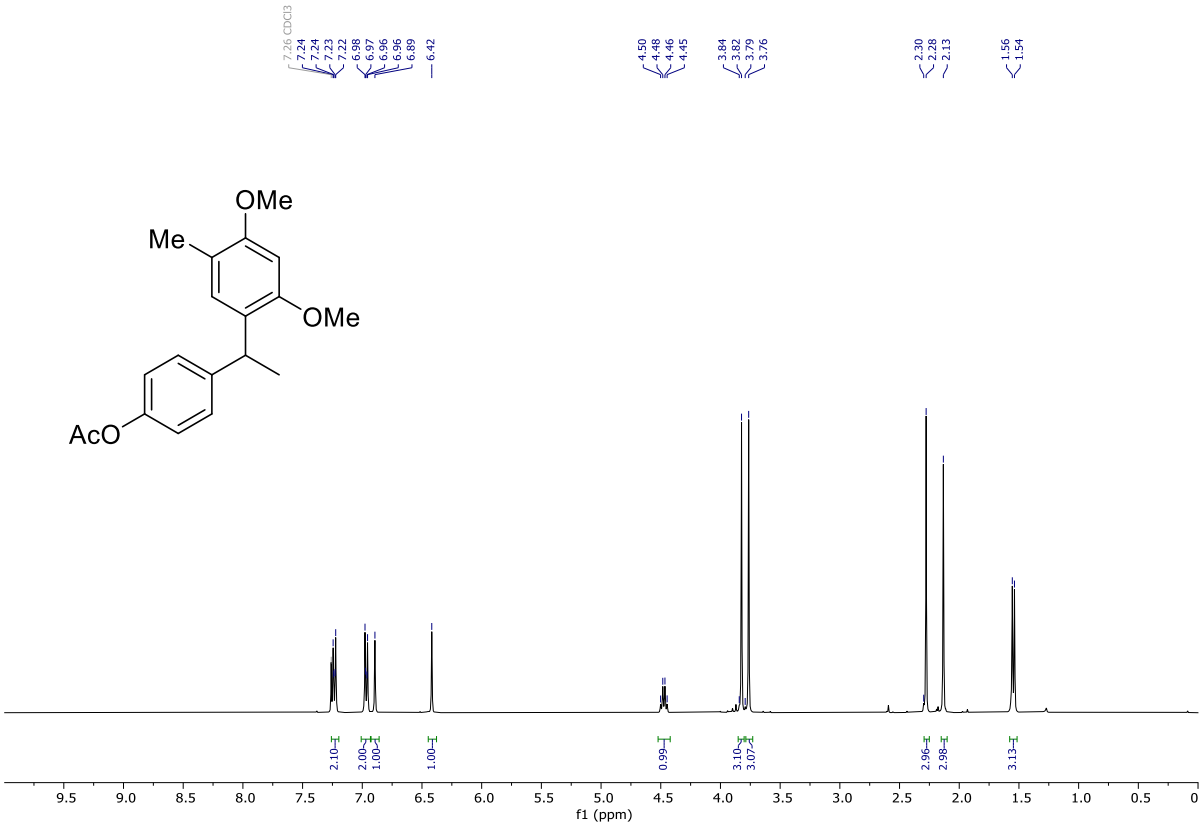
^{13}C NMR (101 MHz, $CDCl_3$)



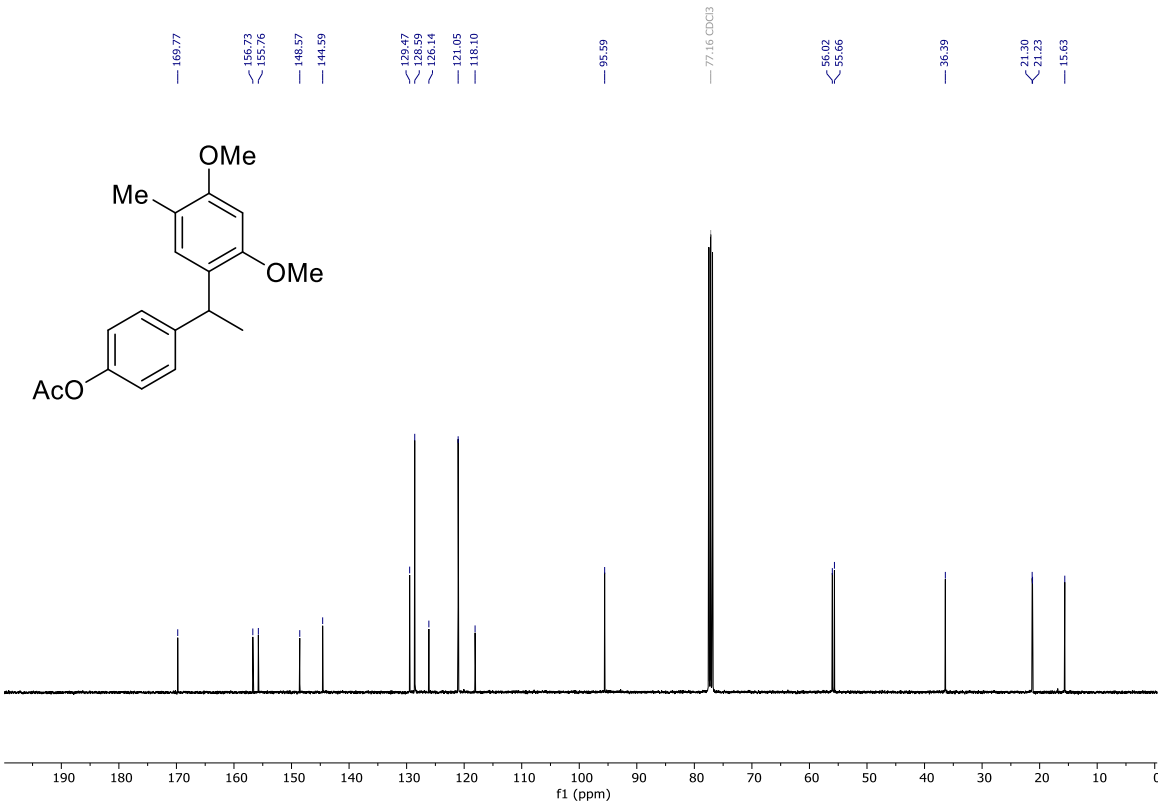
^{19}F NMR (376 MHz, $CDCl_3$)



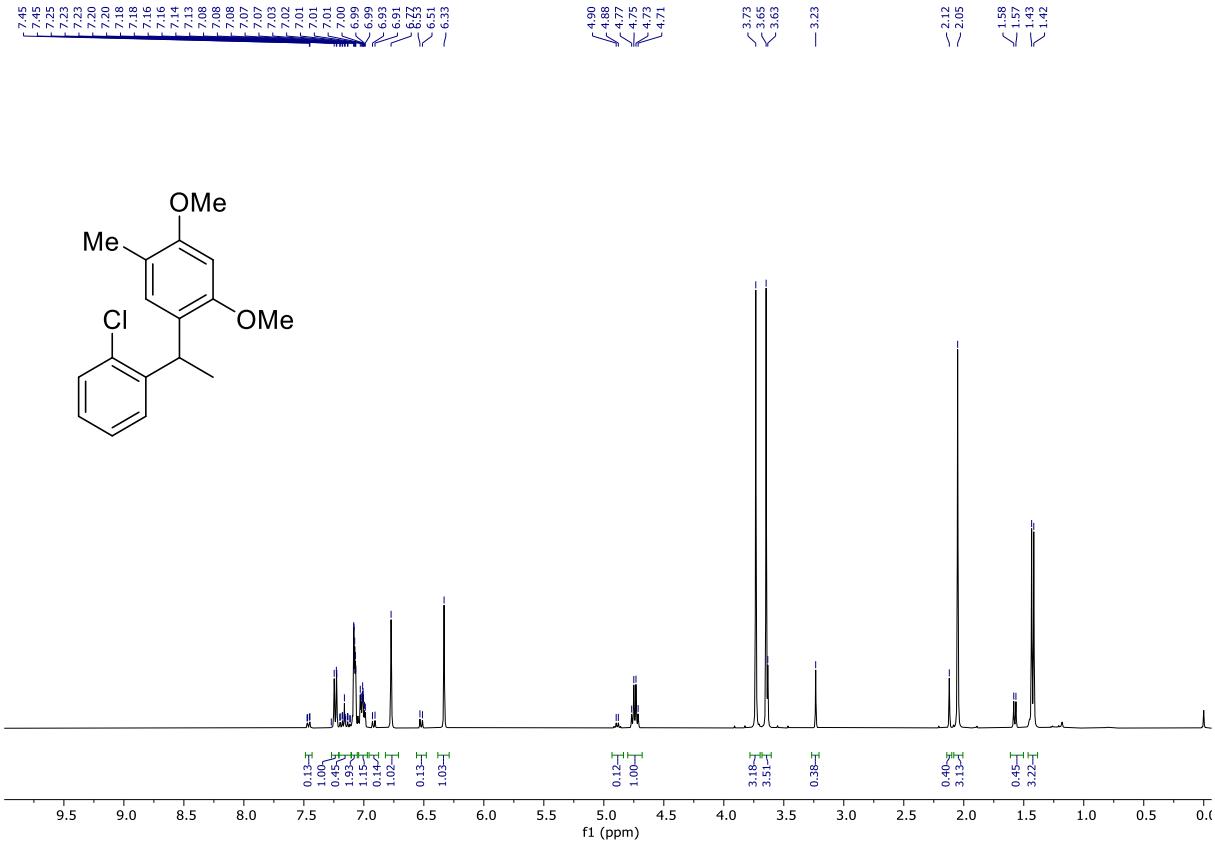
^{1}H NMR (400 MHz, $CDCl_3$)



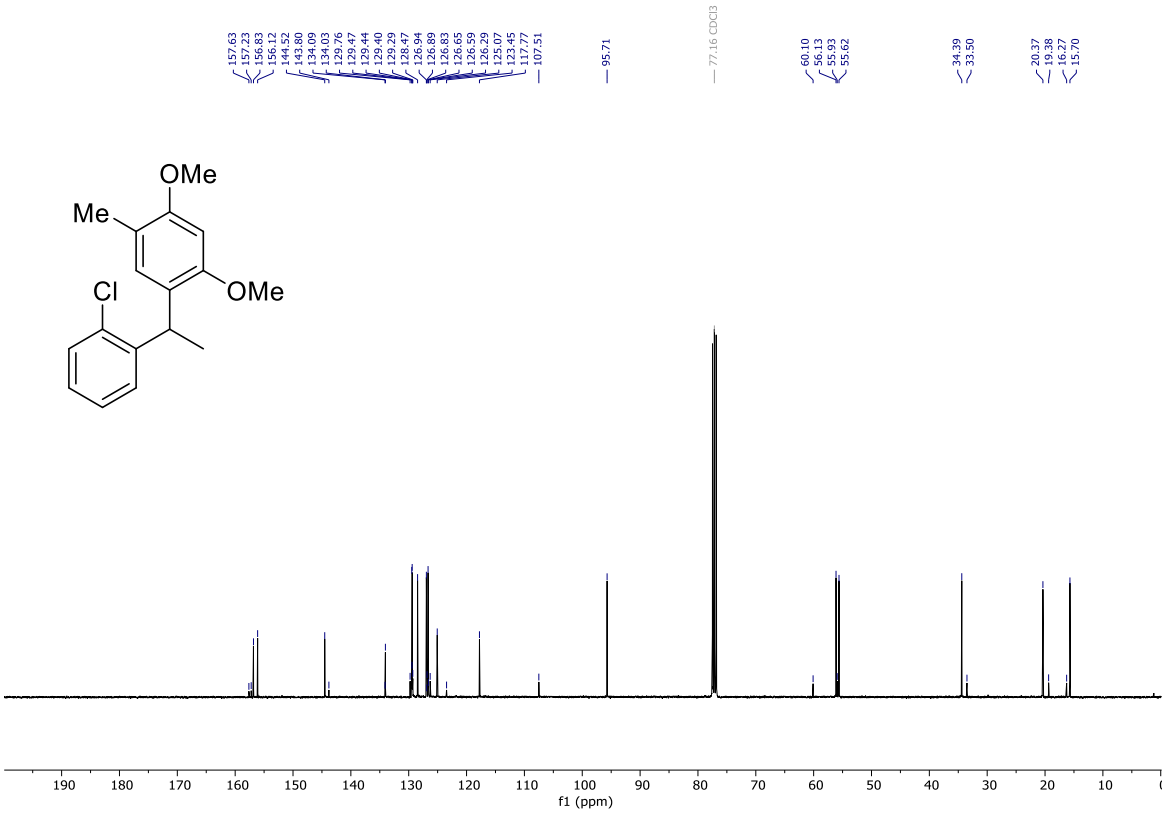
^{13}C NMR (101 MHz, $CDCl_3$)



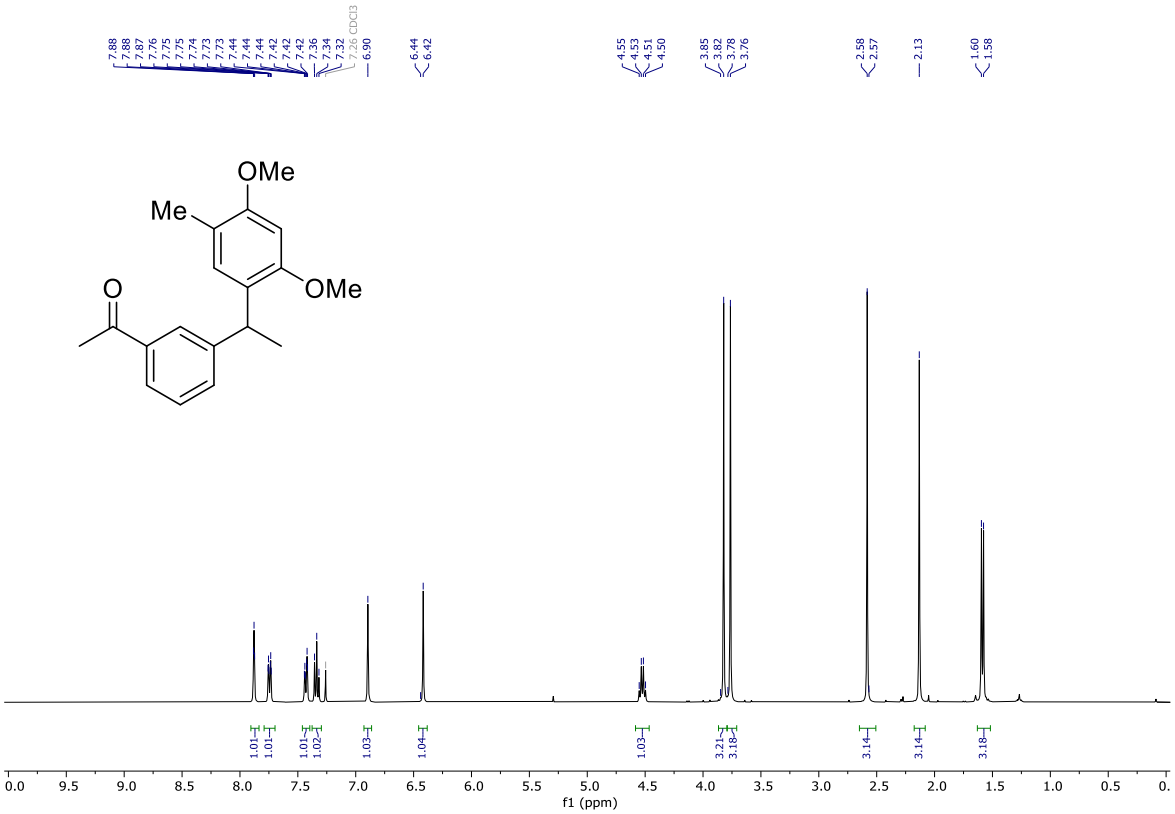
^{1}H NMR (400 MHz, $CDCl_3$)



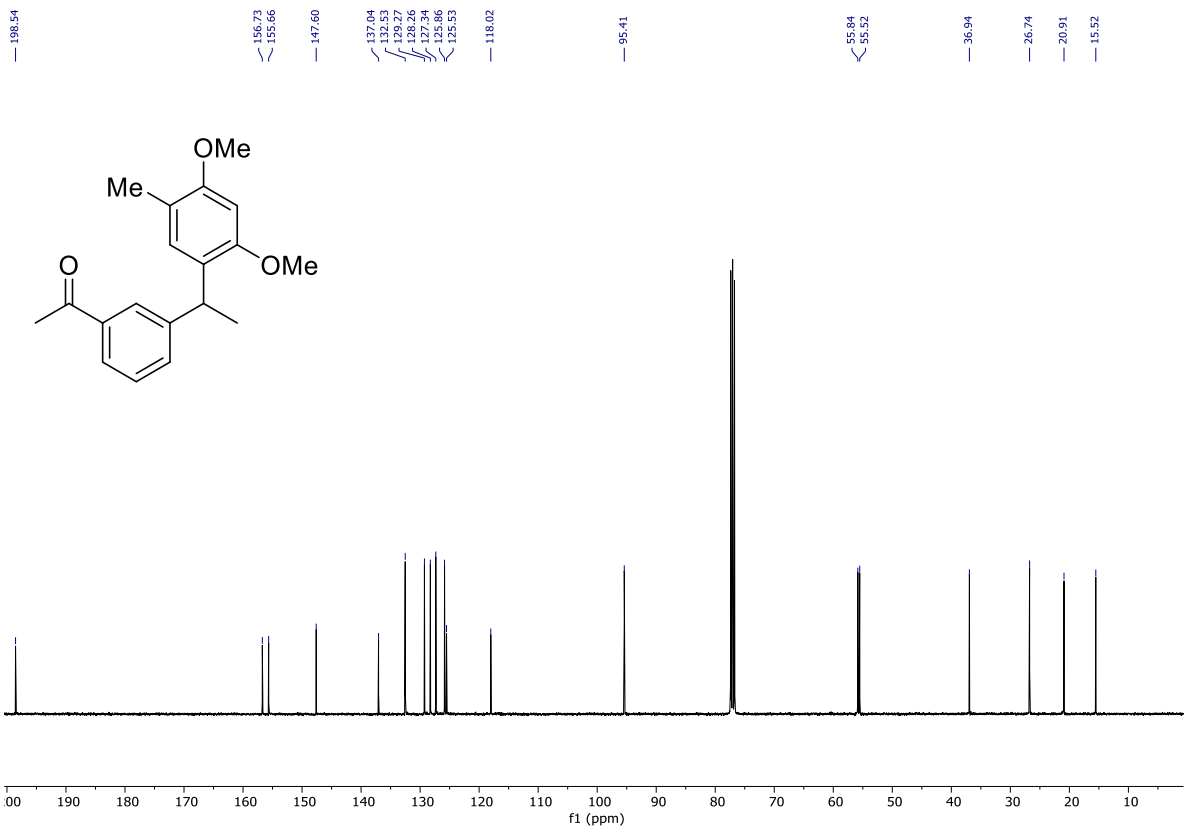
^{13}C NMR (101 MHz, $CDCl_3$)



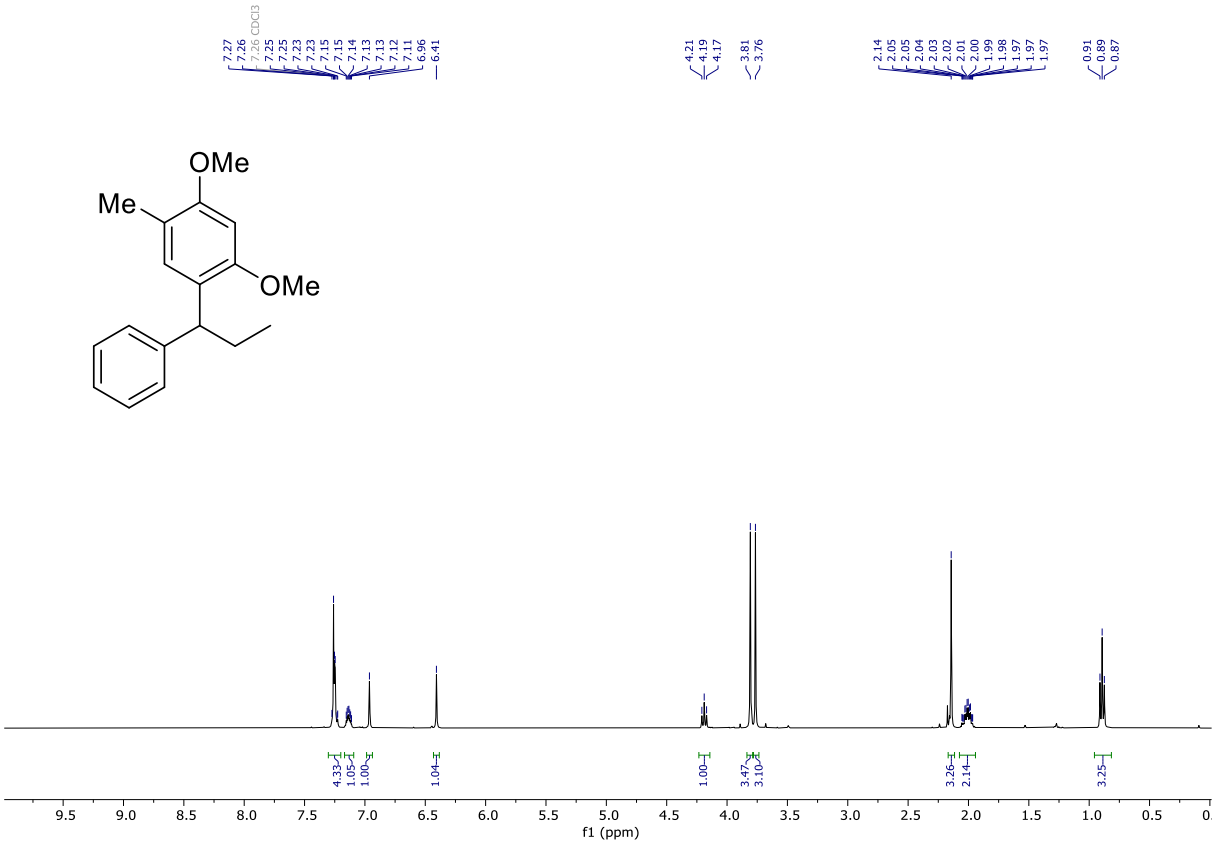
^{1}H NMR (400 MHz, $CDCl_3$)



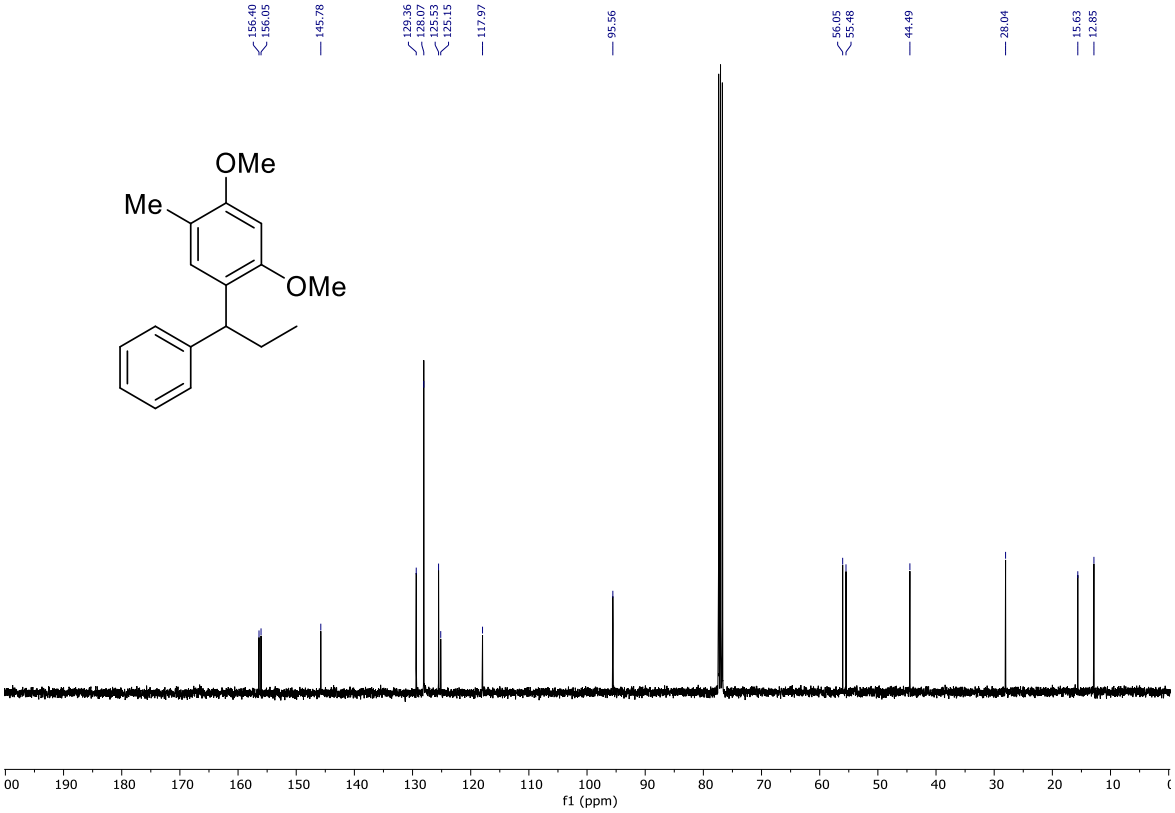
^{13}C NMR (101 MHz, $CDCl_3$)



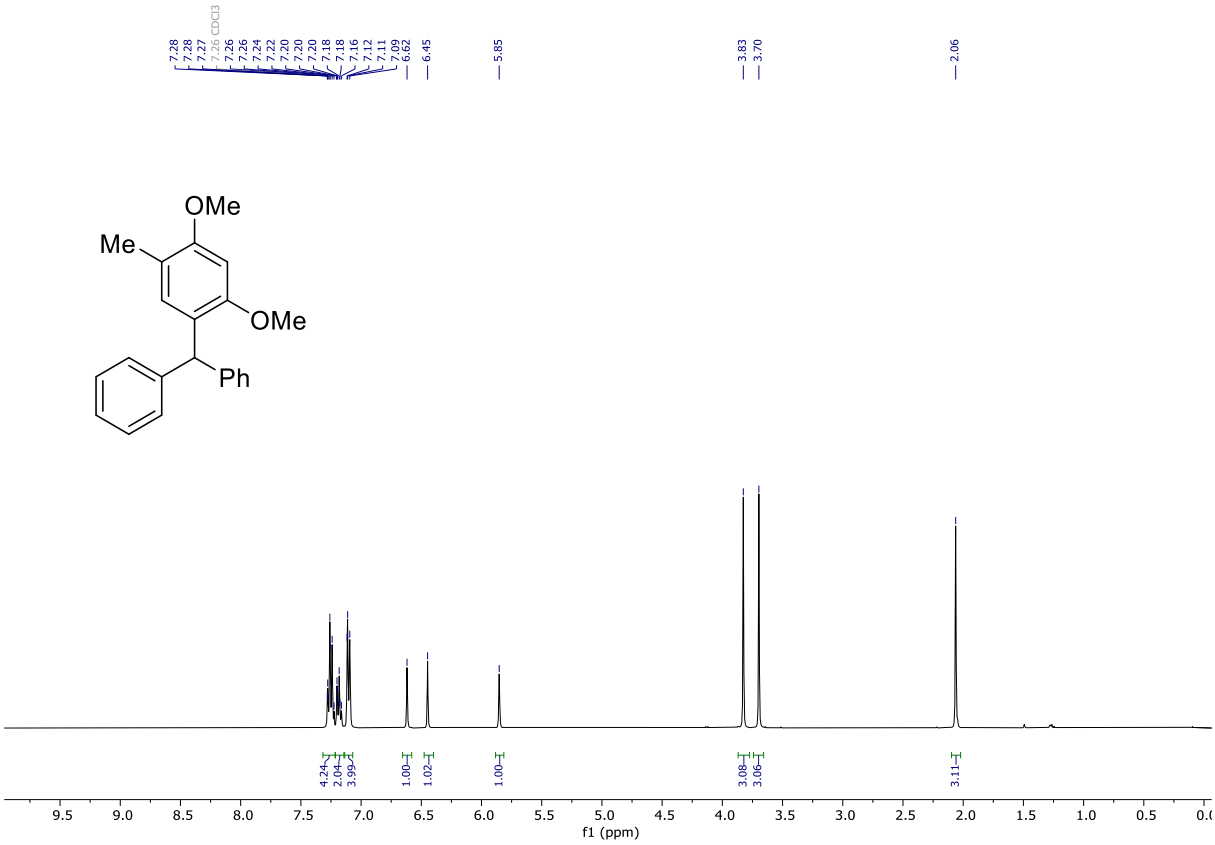
^{1}H NMR (400 MHz, $CDCl_3$)



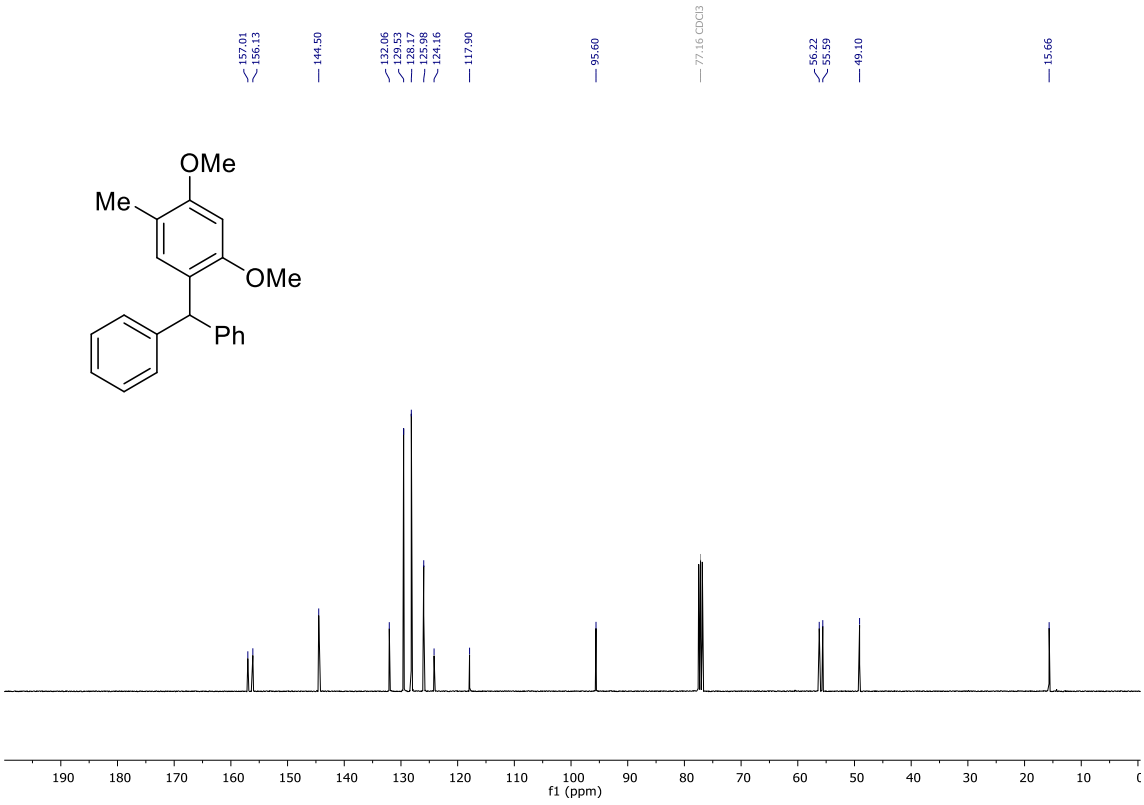
^{13}C NMR (101 MHz, $CDCl_3$)



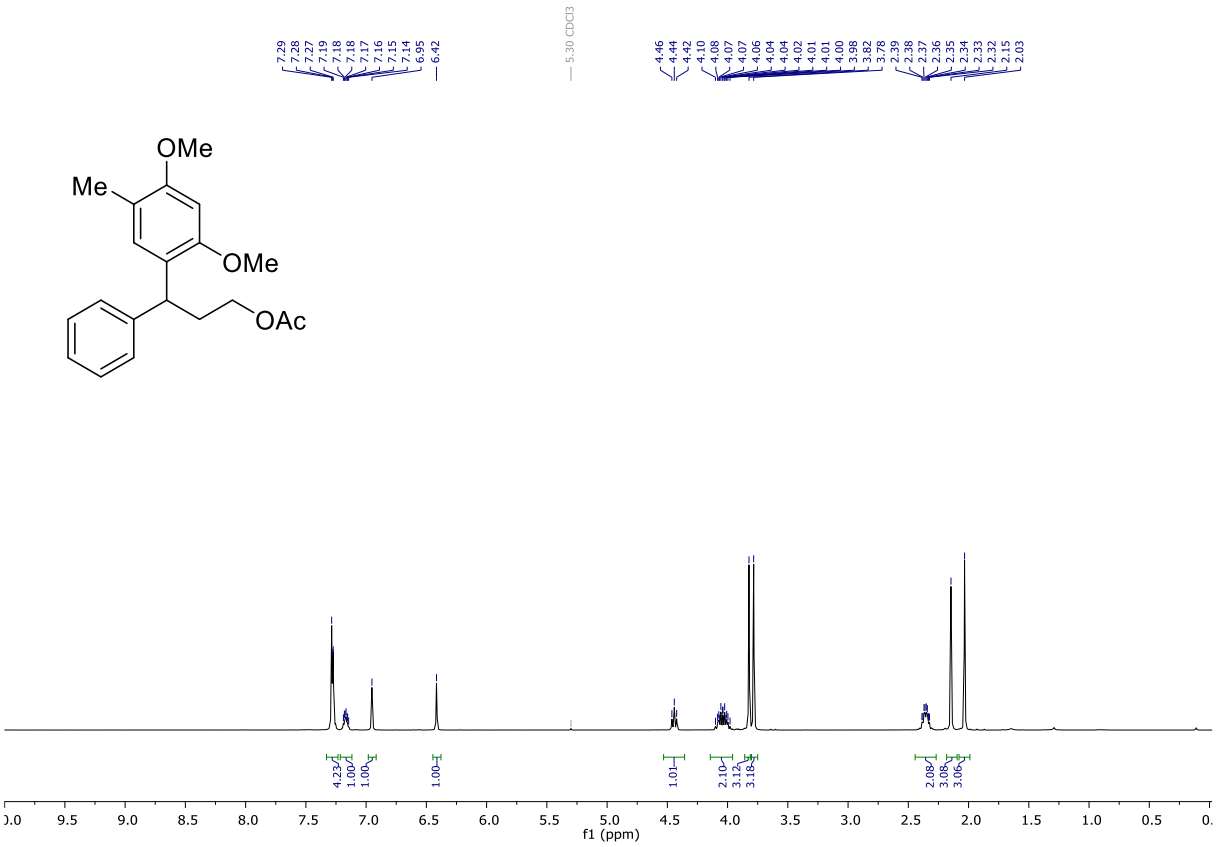
^{1}H NMR (400 MHz, $CDCl_3$)



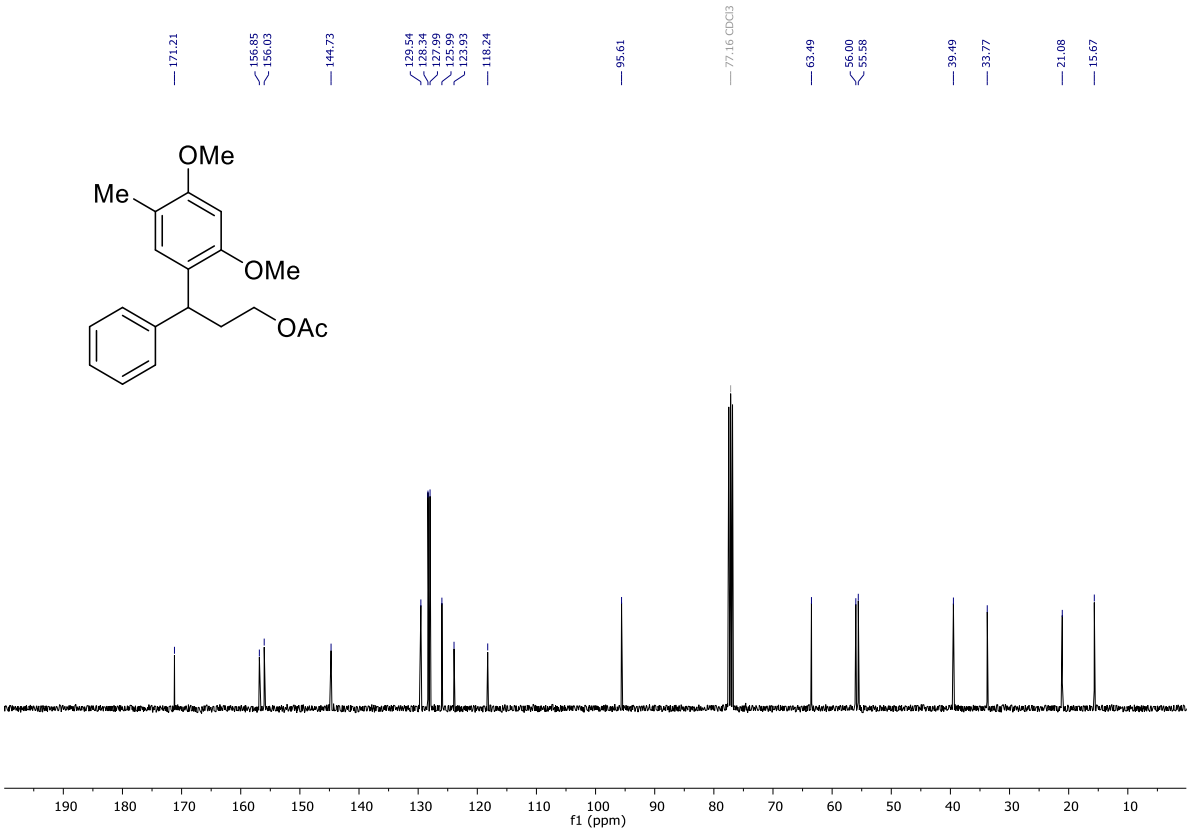
^{13}C NMR (101 MHz, $CDCl_3$)



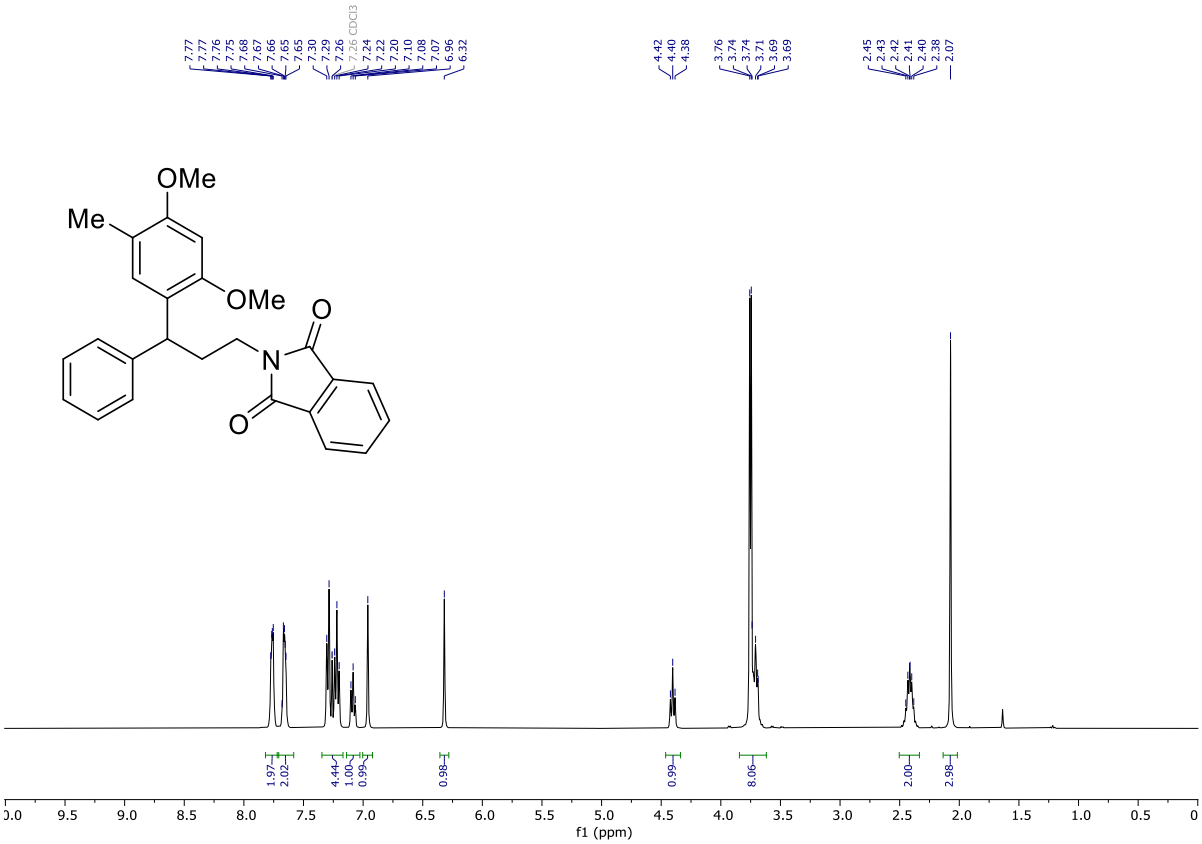
^{1}H NMR (400 MHz, $CDCl_3$)



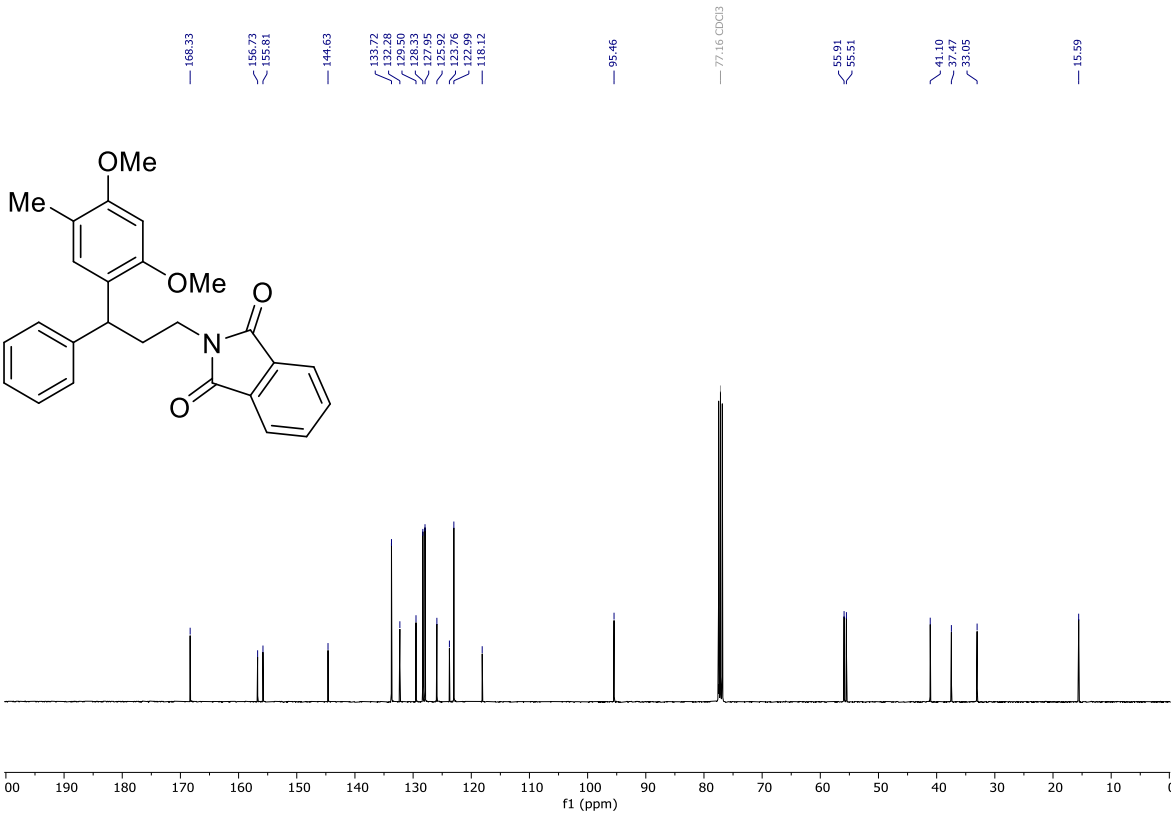
^{13}C NMR (101 MHz, $CDCl_3$)



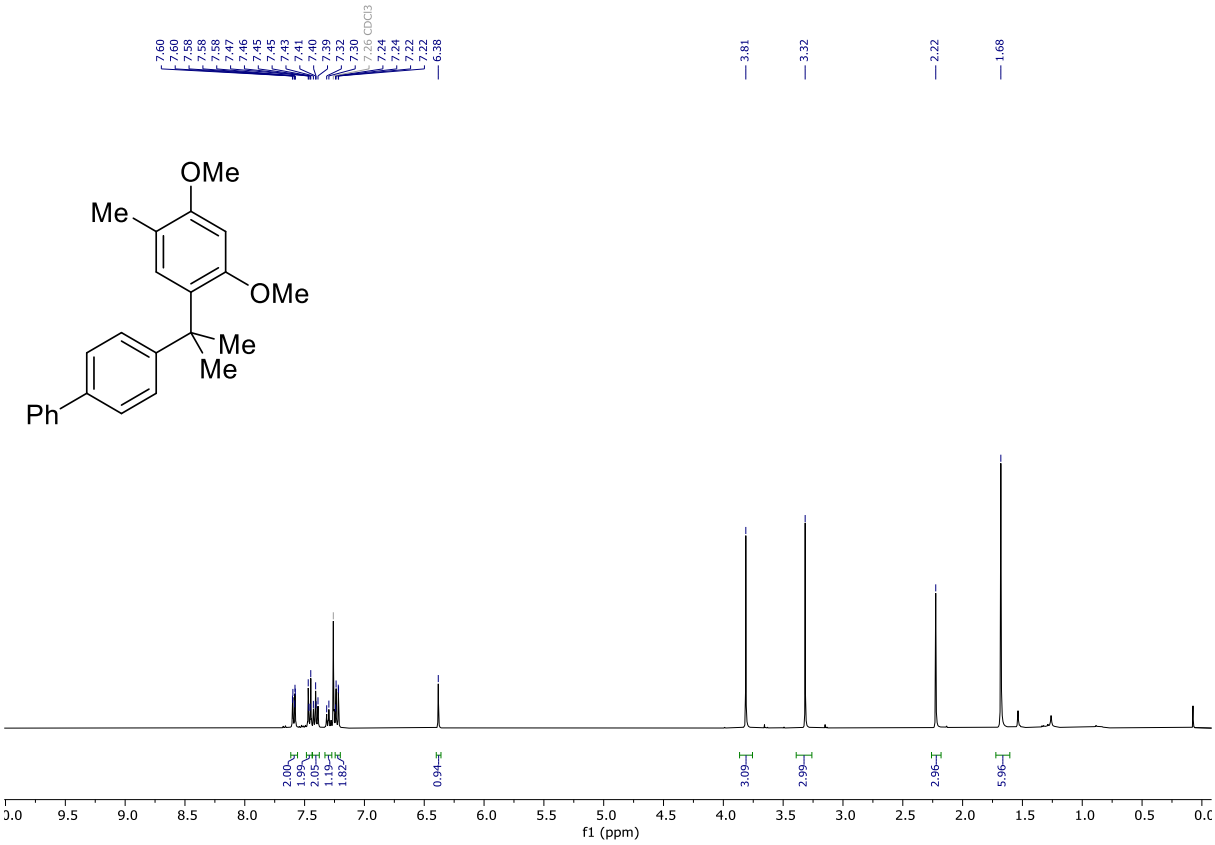
^{1}H NMR (400 MHz, $CDCl_3$)



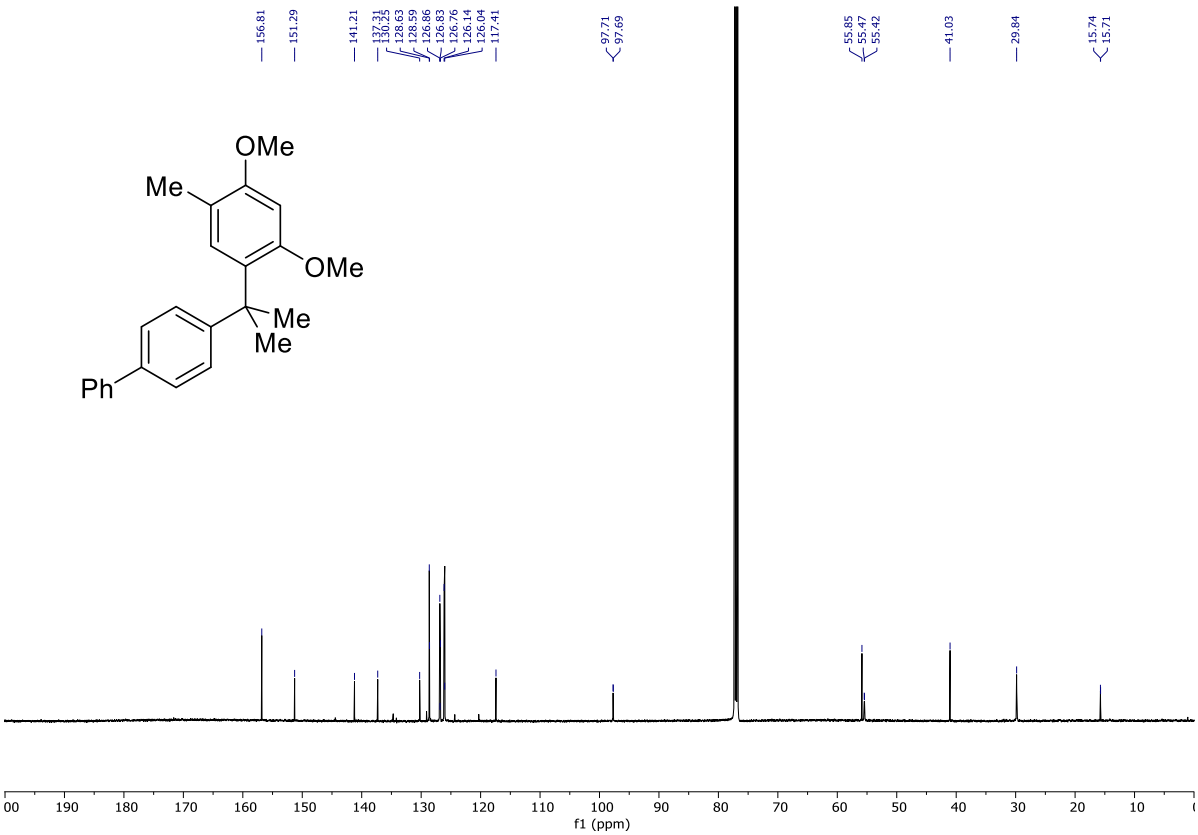
^{13}C NMR (101 MHz, $CDCl_3$)



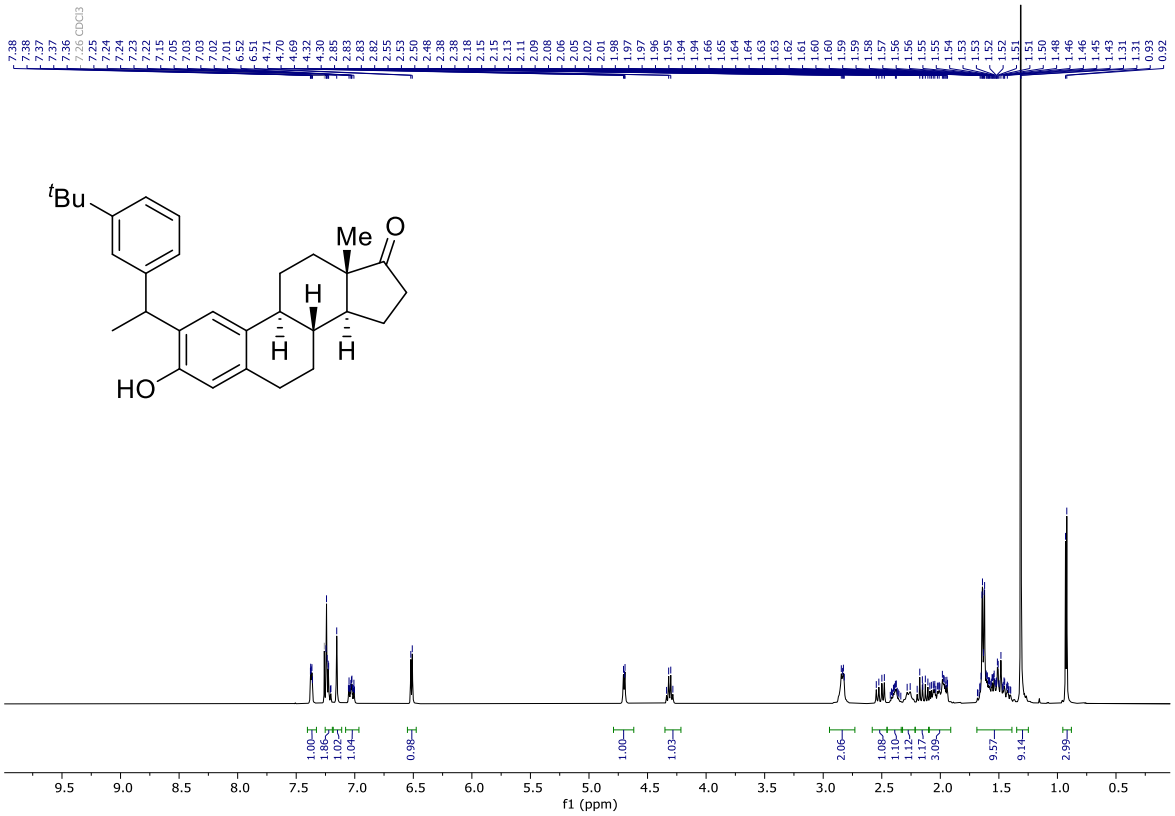
^{1}H NMR (400 MHz, $CDCl_3$)



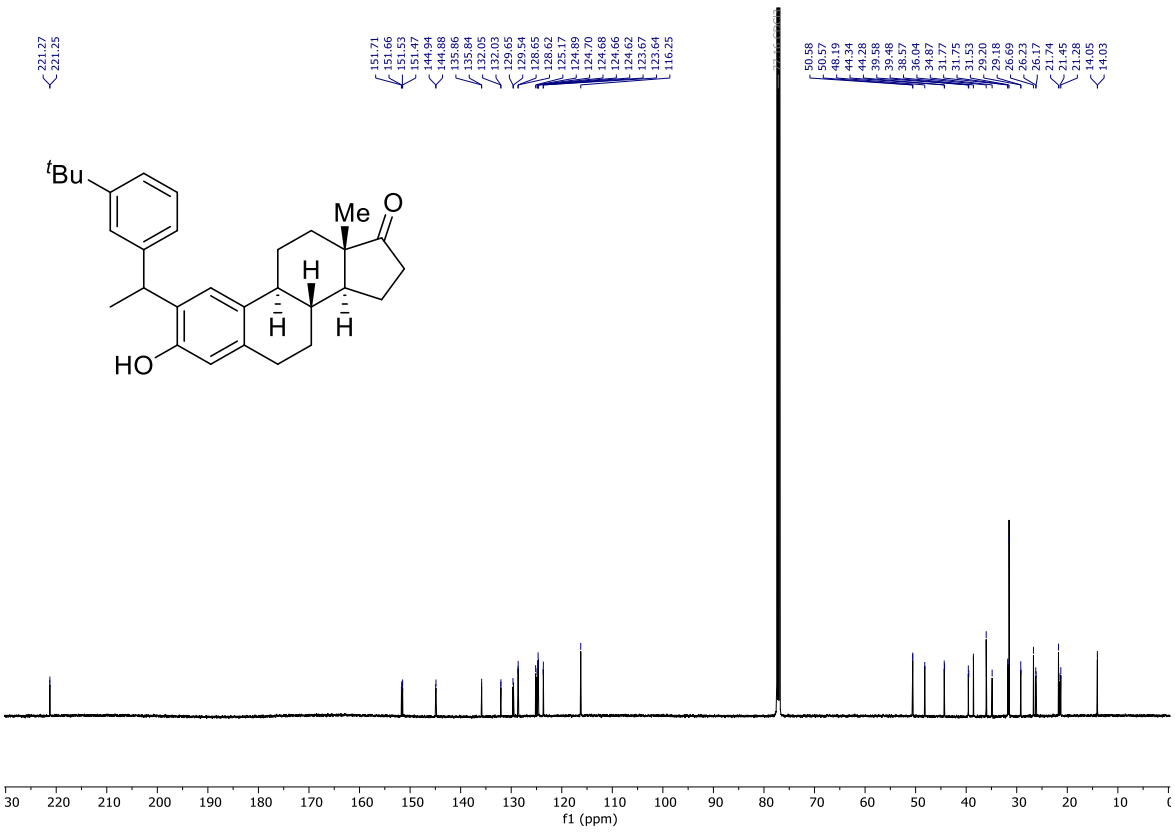
^{13}C NMR (126 MHz, $CDCl_3$)



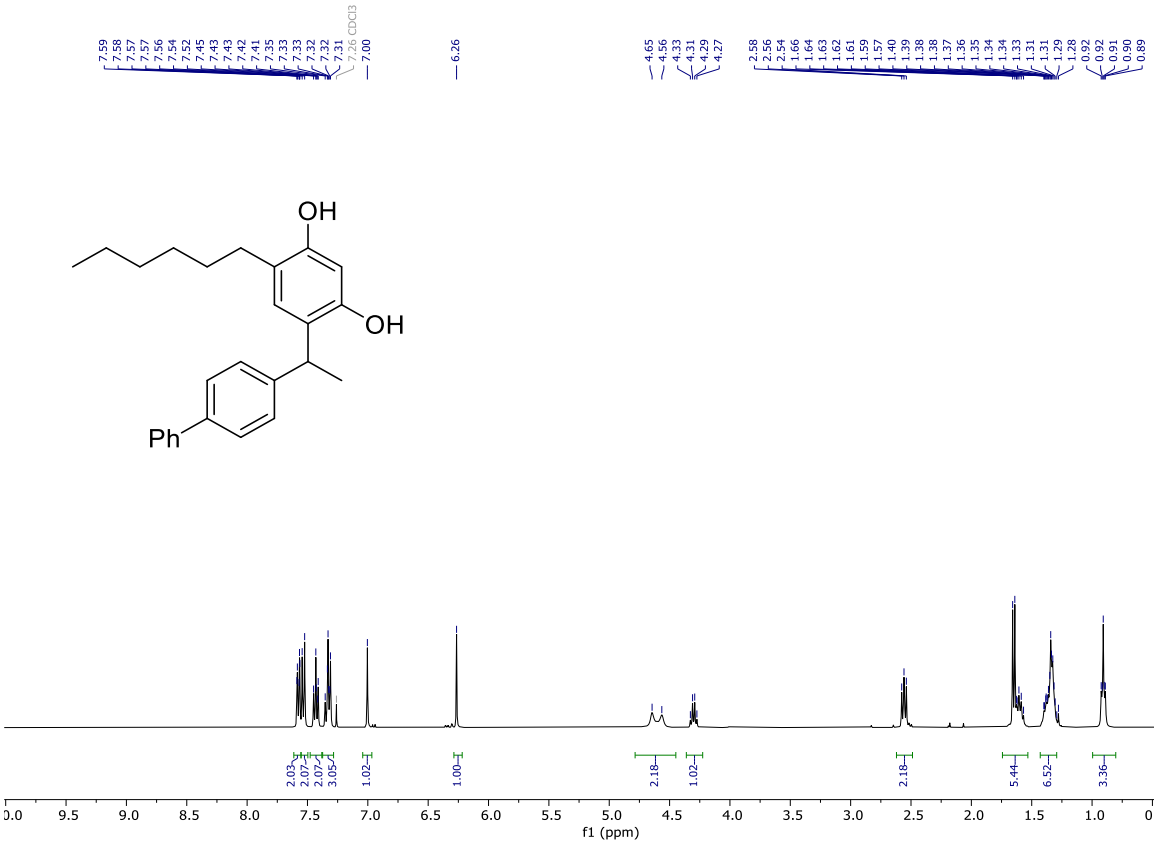
^{1}H NMR (400 MHz, $CDCl_3$)



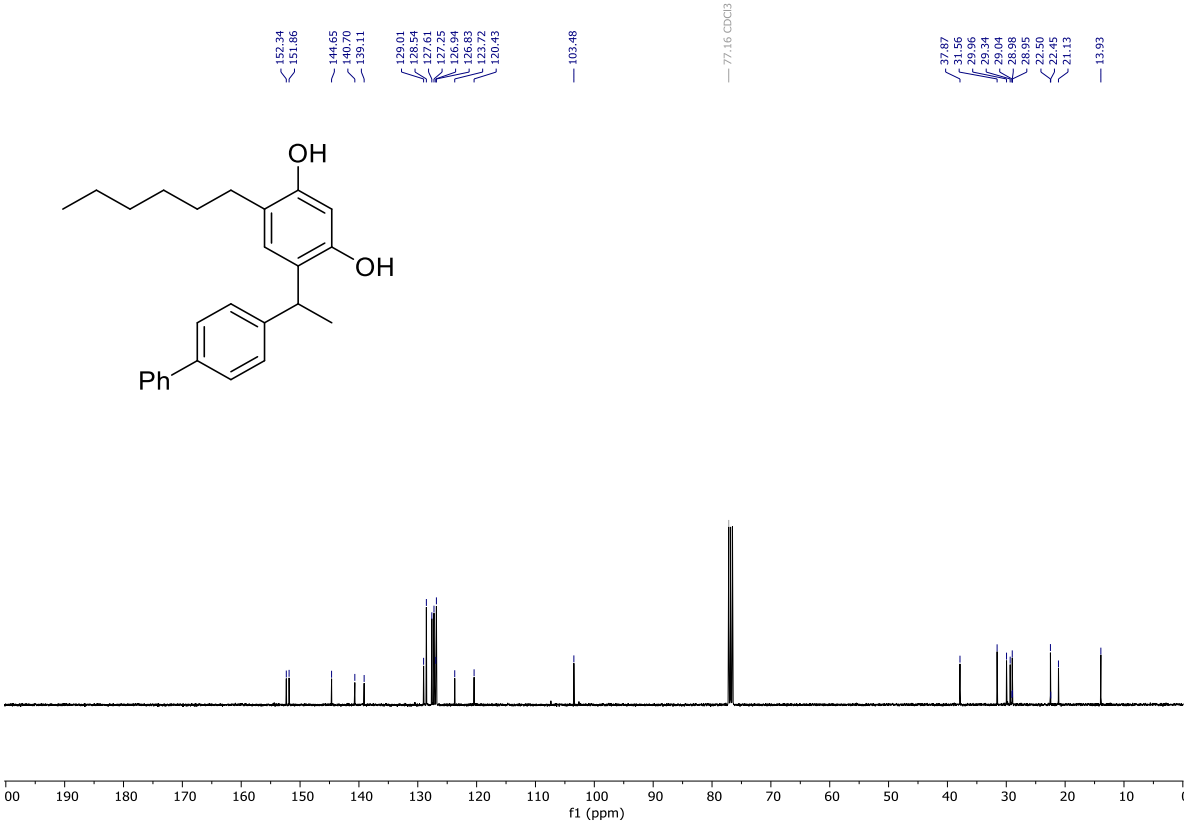
^{13}C NMR (126 MHz, $CDCl_3$)



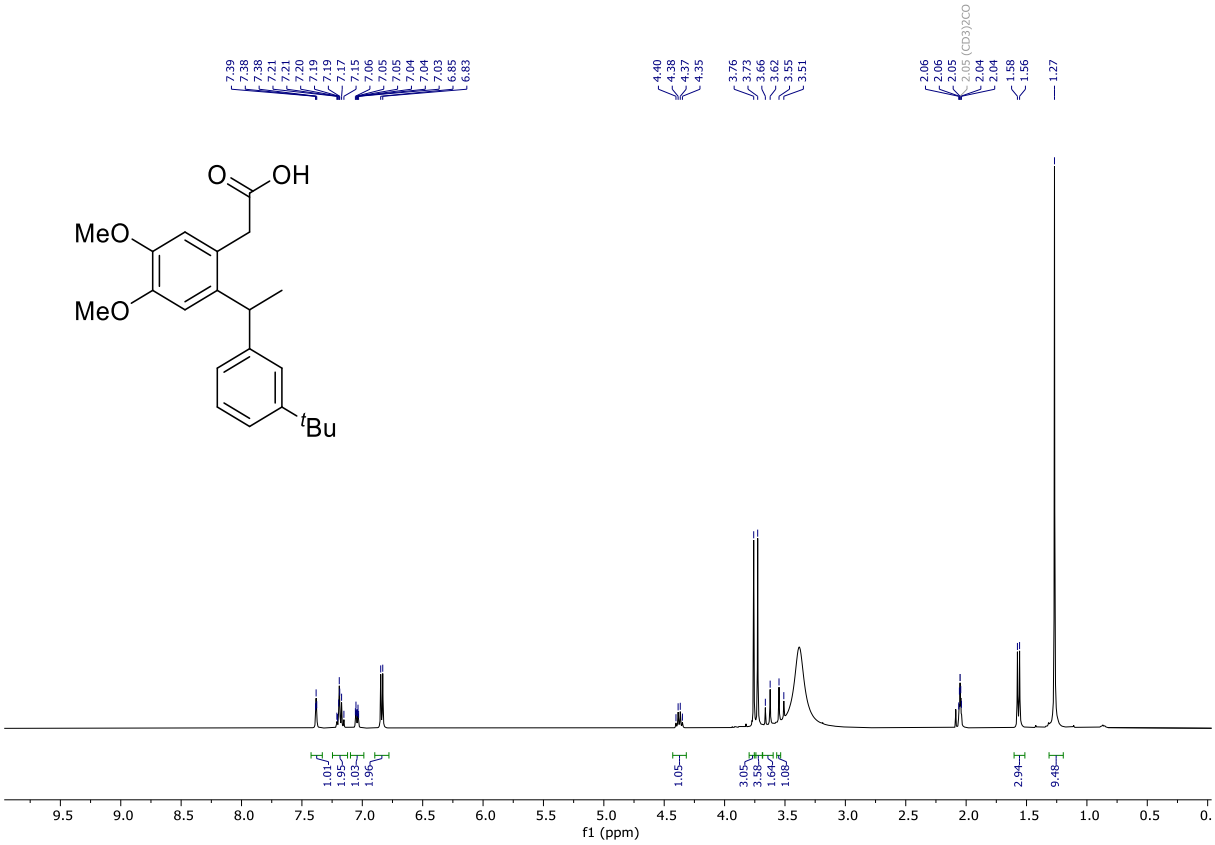
^{1}H NMR (400 MHz, $CDCl_3$)



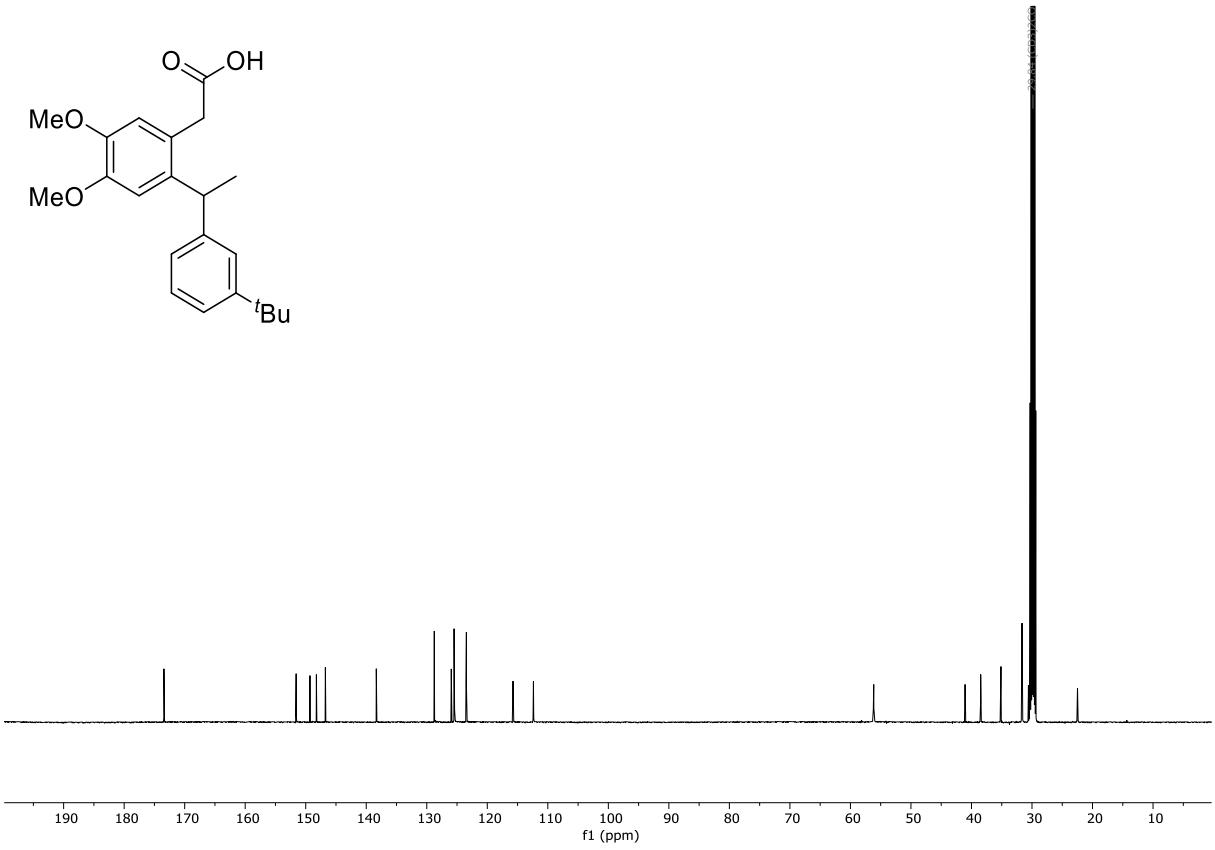
^{13}C NMR (101 MHz, $CDCl_3$)



^{1}H NMR (400 MHz, Acetone)

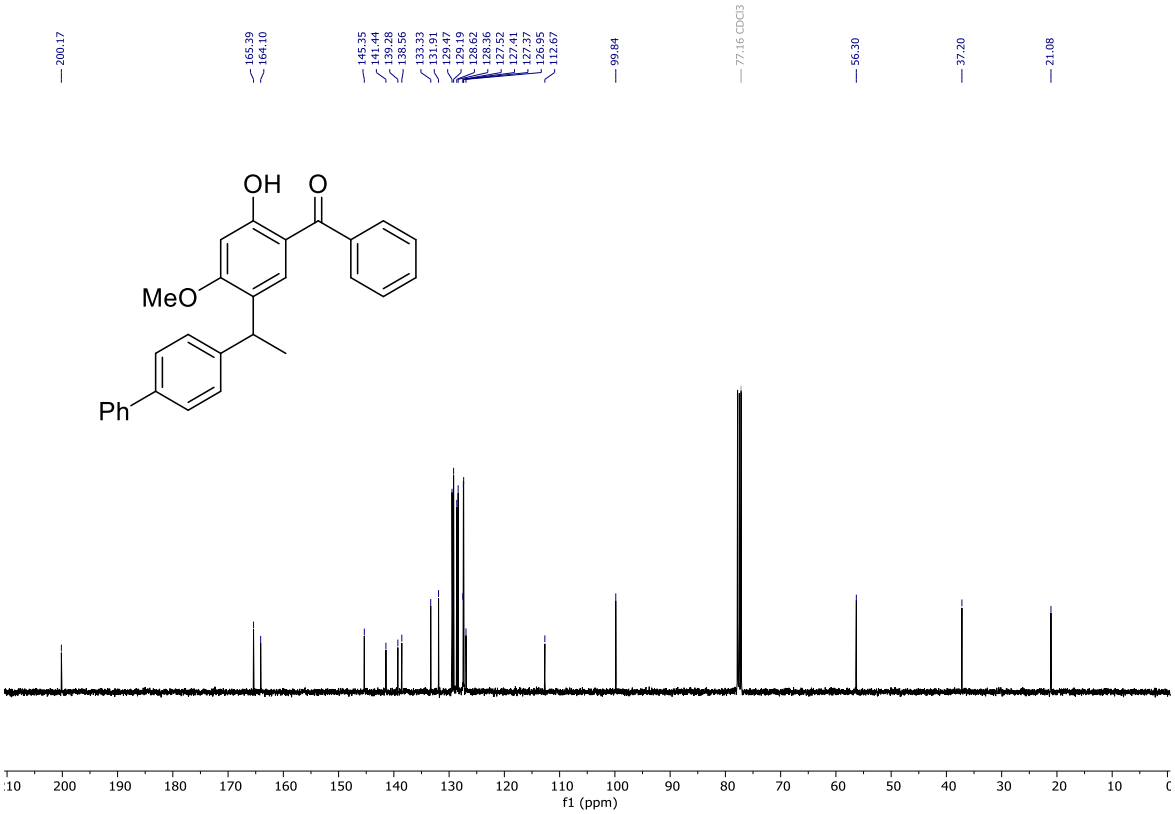


^{13}C NMR (400 MHz, Acetone)

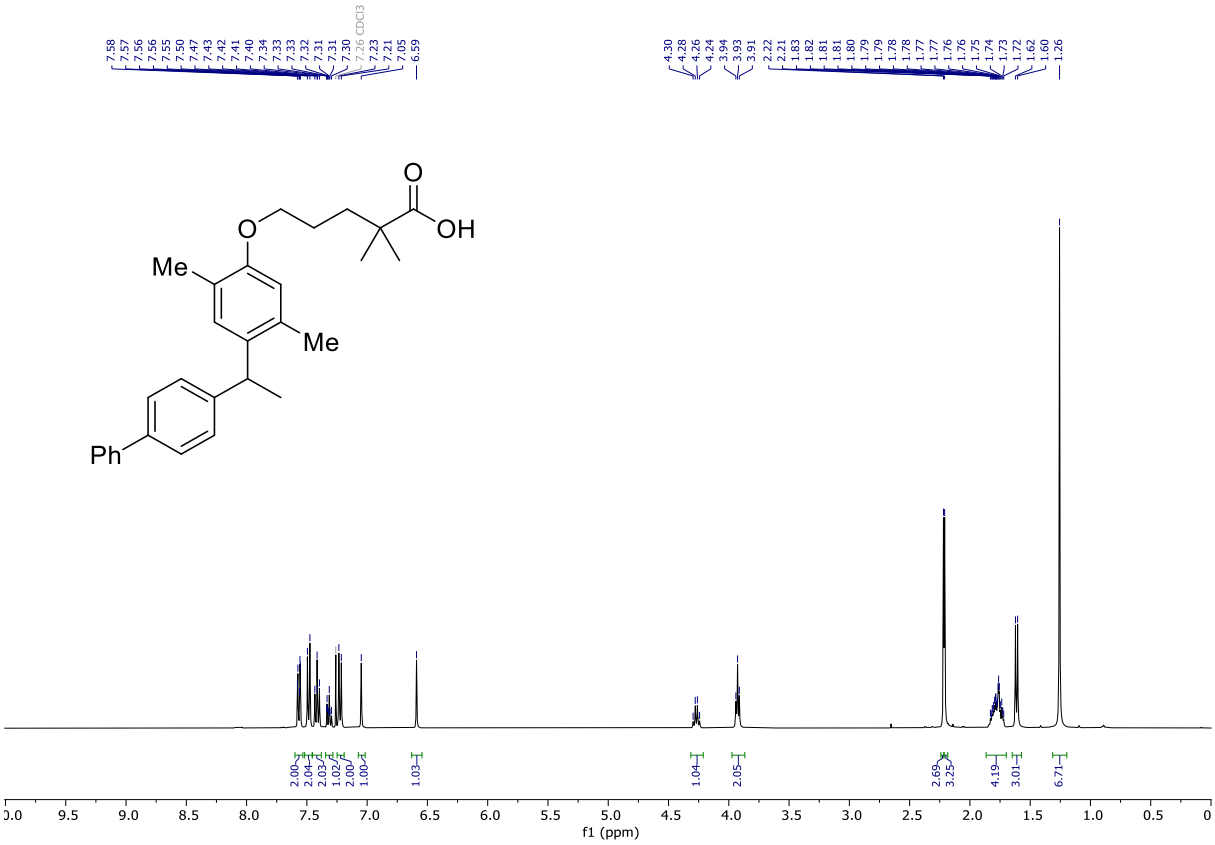


^{1}H NMR (400 MHz, $CDCl_3$)

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



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



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