Oxazolium Salts as Organocatalysts for the Umpolung of Aldehydes.

Venkata Krishna Rao Garapati and Michel Gravel*

Department of Chemistry, University of Saskatchewan

110 Science Place, Saskatoon, SK, Canada, S7N 5C9

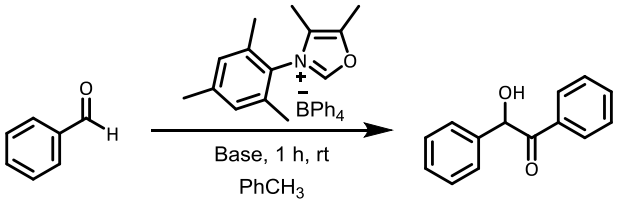
Supporting Information

Table of Contents

General Methods

All chemicals were obtained from commercial suppliers and used without further purification, unless noted otherwise. Anhydrous CH_2Cl_2, diethyl ether, toluene, and THF were dried by using a Braun Solvent Purification System and stored under argon over 4 Å molecular sieves. DMF was dried via distillation over CaH_2. Ethanol was dried over sodium metal. Flash column chromatography (FCC) was performed according to Still et al. with Merck silica gel 60 (0.040–0.063 mm). Thin layer chromatography (TLC) was performed on Merck TLC Silica gel 60 $F_{254.}$ UV light, $KMnO_4$ and iodine on silica gel were used to visualize the TLC. ACS grade solvent was used for column chromatography and TLC. ^{1}H NMR (500 or 600 MHz) and ^{13}C NMR (125 or 150 MHz) were recorded in $CDCl_3$ or DMSO-d_6 as NMR solvent. The ^{1}H NMR and ^{13}C NMR spectra were calibrated to residual solvent peak 7.26 ppm and 77.16 ppm, respectively, for CDCl3 and 2.5 ppm and 39.52 ppm, respectively, for DMSO-$d_{6.}$ High-resolution mass spectra (HRMS) were recorded on a VG 70E double focusing high-resolution spectrometer. Electrospray ionization (EI) was performed at 70 eV on a Qstar XL MS/MS system. Infrared (IR) spectra were obtained on a Fourier transform interferometer using a diffuse reflectance cell (DRIFT); only diagnostic and or intense peaks are reported. All IR samples were prepared as a thin film for liquids on a KBr disk or as a pellet using sample and IR grade KBr. Melting points were measured on a melting point apparatus and are uncorrected. All liquid aldehydes were distilled before use, and solid aldehydes were used without further purification. Chalcone was recrystallized from ethanol.

Screening of bases for the benzoin reaction

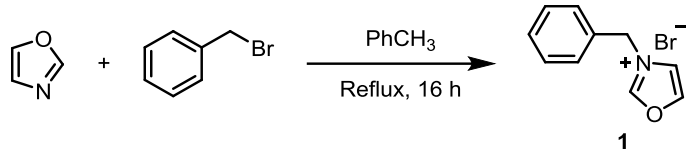


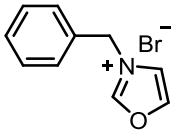
entry	catalyst	base	time (h)	yield (%)
1	3	Et_3N	1	< 5
2	3	*i*-Pr_2NEt	1	< 5
3	3	Cs_2CO_3	1	78
4	3	CsOAc	1	11
5	3	NaHMDS	1	9
6	3	DBU	1	98
7	3	DBU	1	90

Conditions: benzaldehyde (0.25 mmol), catalyst (10 mol %), concn (0.5 M); entries 1 to 5: base (1 equiv), entry 6: base (10 mol %); entry 7: catalyst (5 mol %), base (5 mol %), concn (1 M).

Synthesis of alkyl oxazolium salts

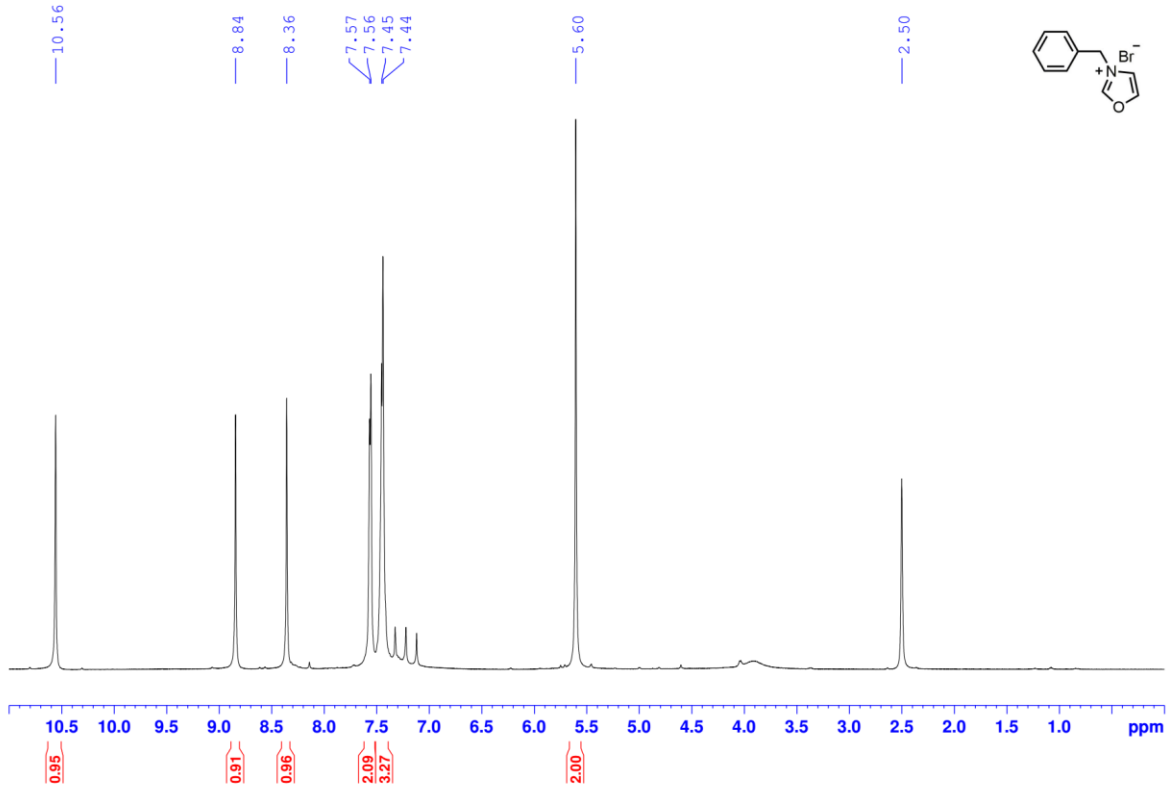
3-benzyloxazol-3-ium bromide (1)[1]



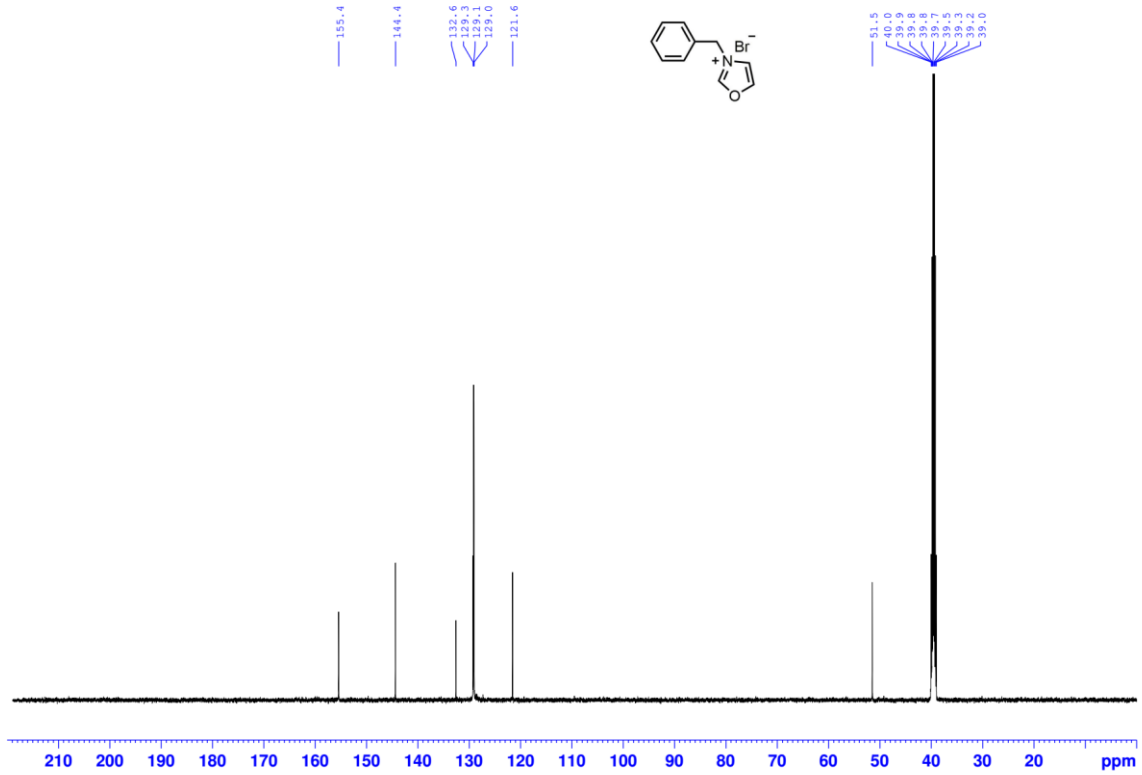


Benzyl bromide (0.54 ml, 4.52 mmol) was added to a stirred solution of oxazole (0.26 g, 3.77 mmol) in toluene (10 ml), then heated to reflux for 16 h. The mixture was cooled to room temperature and concentrated. The crude compound was washed with hexane (3x10 ml) to remove unreacted benzyl bromide, then recrystallized from the acetone-diethyl ether mixture, to obtain 364 mg (40%) of compound **1** as dark brown solid. R_f = 0.2 (10% methanol/CH_2Cl_2); **^{1}H NMR** (500 MHz, DMSO-d_6**)** δ: 10.56 (s, 1H), 8.84 (s, 1H), 8.36 (s, 1H), 7.56 (d, *J* = 6.5 Hz, 1H), 7.45 (d, *J* = 7 Hz, 3H), 5.60 (s, 1H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ: 155.4, 144.4, 132.6, 129.3, 129.1, 129.1, 121.6, 51.5; **HRMS** (EI^+) m/z calculated for $C_{10}H_{10}NO^+$ $[M]^+$: 160.0757; found: 160.0754.

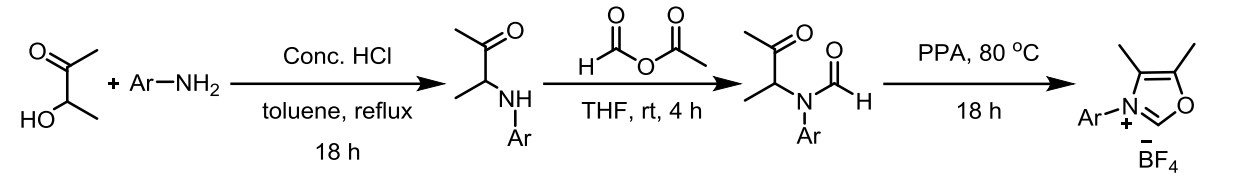
^{1}H NMR spectrum (1)



^{13}C NMR spectrum (1)



Synthesis of aryl oxazolium salts



Ar: a = Phenyl
b = Mesityl
c = 2,6-dimethoxyphenyl

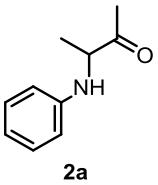
a = 77% (**S1**)
b = 73% (**S2**)
c = 94% (**S3**)

a = 84% (**S4**)
b = 92% (**S5**)
c = 89% (**S6**)

a = 67% (**2**)
b = 65% (**3**)
c = 85% (**4**)

3 is BPh_4 salt

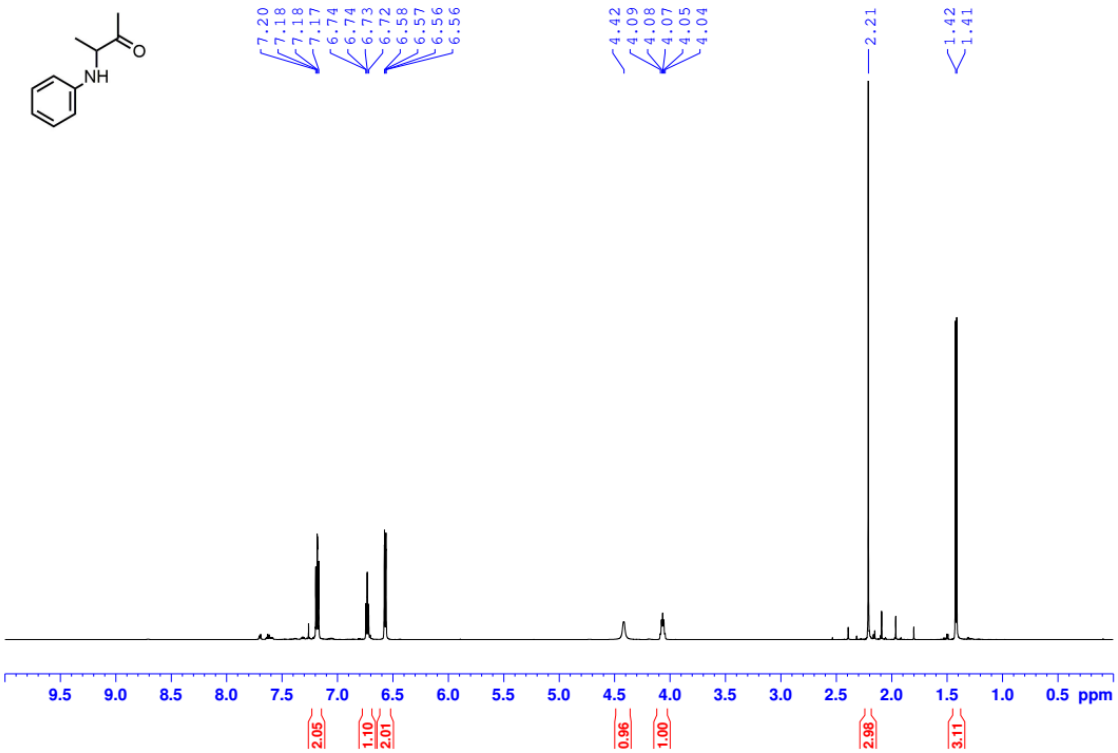
3-(Phenylamino)butan-2-one (S1)[2]



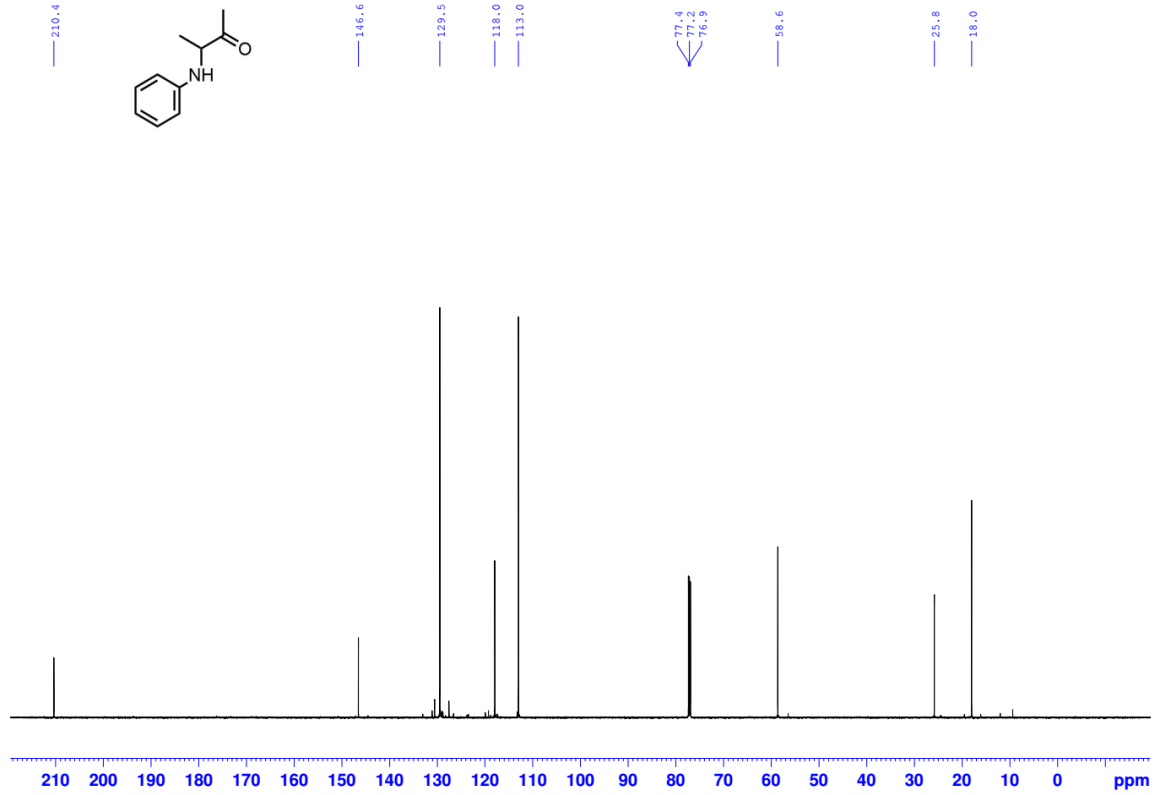
2a

Compounds **S1, S2, S4** and **S5** were prepared using the previously reported procedure.[1] Aniline (3.00 mL, 32.9 mmol) and acetoin (5.80 g, 65.8 mmol) were dissolved in toluene (110 mL), and then 0.1 mL of conc. HCl was added. The formed water from the reaction was removed by using Dean-Stark apparatus for 18 h. The reaction mixture was concentrated and purified by column chromatography (10% EtOAC/hexanes) to obtain 4.15 g (77%) of compound **S1** as a grey solid. R_f = 0.3 (20% EtOAc/Hexanes); **^{1}H NMR** (600 MHz, $CDCl_3$**)** δ: 7.20 – 7.17 (M, 1H), 6.73 (t, *J* = 7.3 Hz, 1H), 6.60 (dd, *J* = 8.6, 0.9 Hz, 2H), 4.42 (br s, 1H), 4.07 (qui, *J* = 6.7 Hz, 1H), 2.21 (s, 3H), 1.42 (d, *J* = 7.0 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 210.4, 146.6, 129.5, 118.0, 113.0, 58.6, 25.8, 18.0

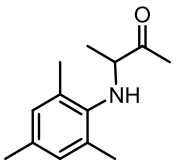
^{1}H NMR spectrum (S1)



^{13}C NMR spectrum (S1)



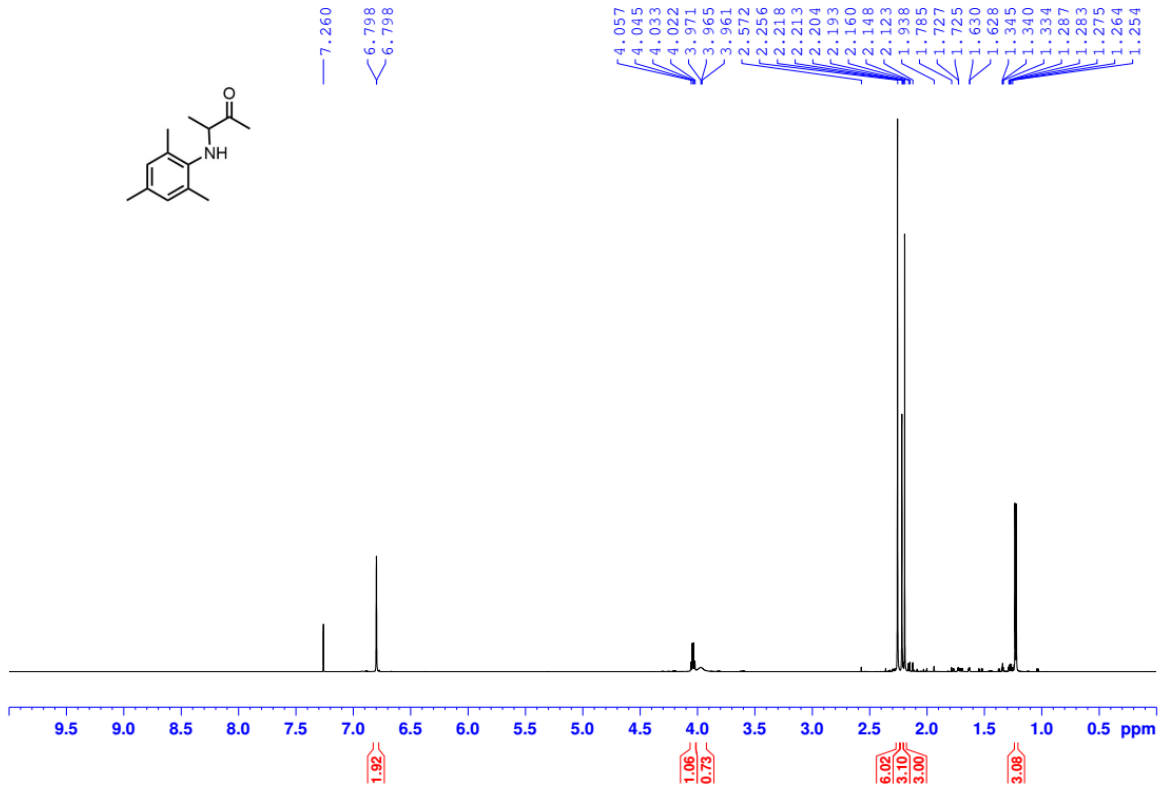
3-(Mesitylamino)butan-2-one (S2)



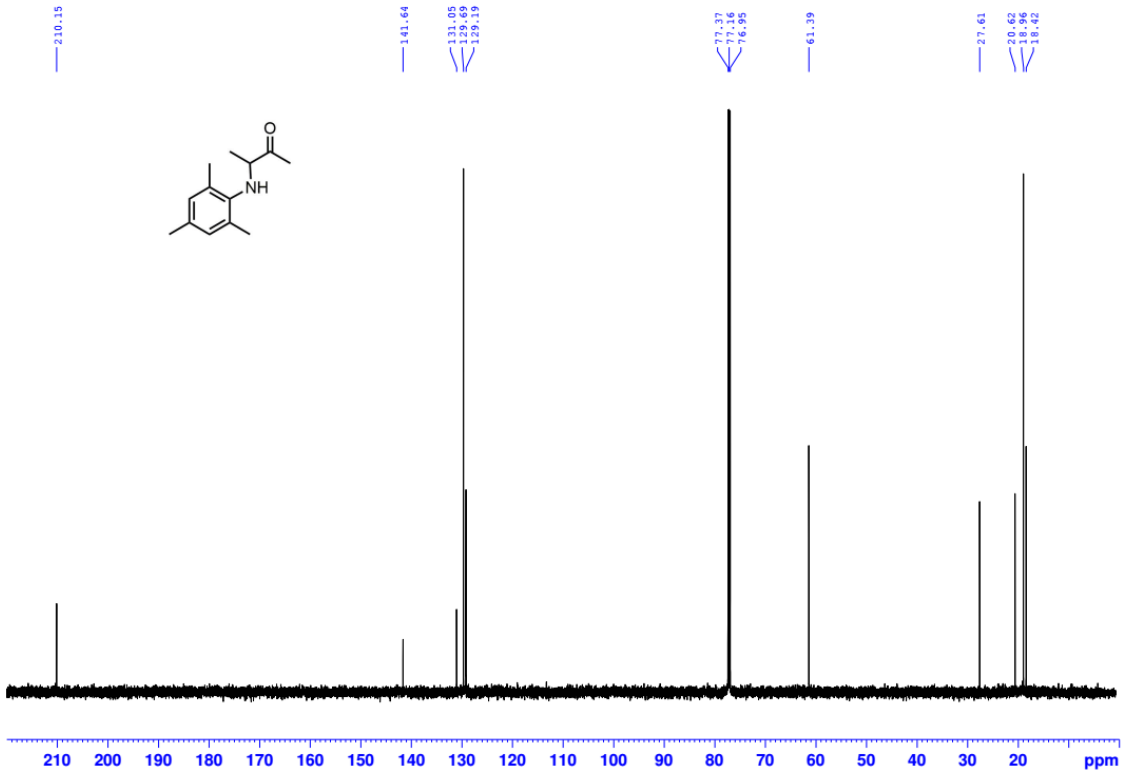
3a

2,4,5-Trimethyl aniline (3.00 mL, 22.2 mmol) and acetoin (3.99 g, 45.3 mmol) were used in this reaction. The crude compound was purified by column chromatography (5% EtOAC/hexanes) to obtain 3.4 g (73%) of compound **S2** as a dark purple solid. R_f = 0.4 (20% EtOAc/Hexanes); **^{1}H NMR** (600 MHz, $CDCl_3$) δ: 6.79 (s, 2H), 4.02 (q, *J* = 7.1 Hz, 1H), 3.96 (br s, 1H), 2.25 (s, 6H), 2.21 (s, 3H), 2.19 (s, 3H), 1.22 (d, *J* = 7 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ: 210.1, 141.6, 131.0, 129.6, 129.1, 61.3, 27.6, 20.6, 18.9, 18.4

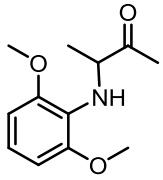
^{1}H NMR spectrum (S2)



^{13}C NMR spectrum (S2)

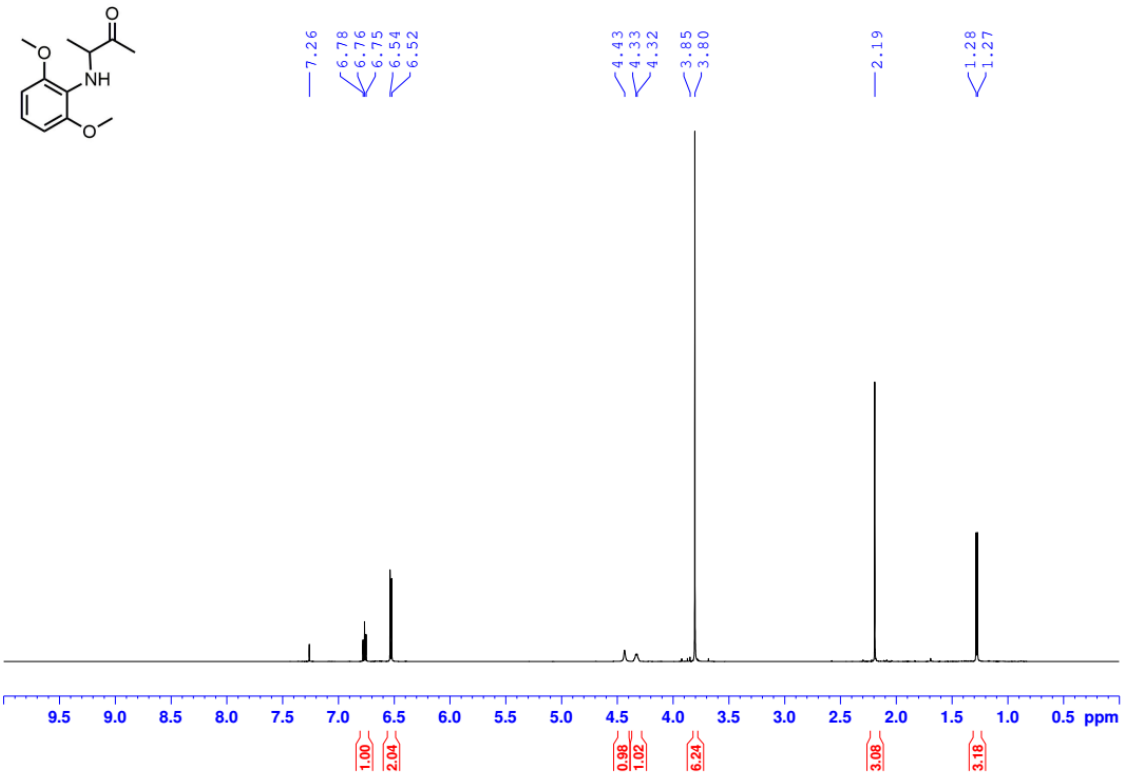


3-((2,6-Dimethoxyphenyl)amino)butan-2-one (S3)

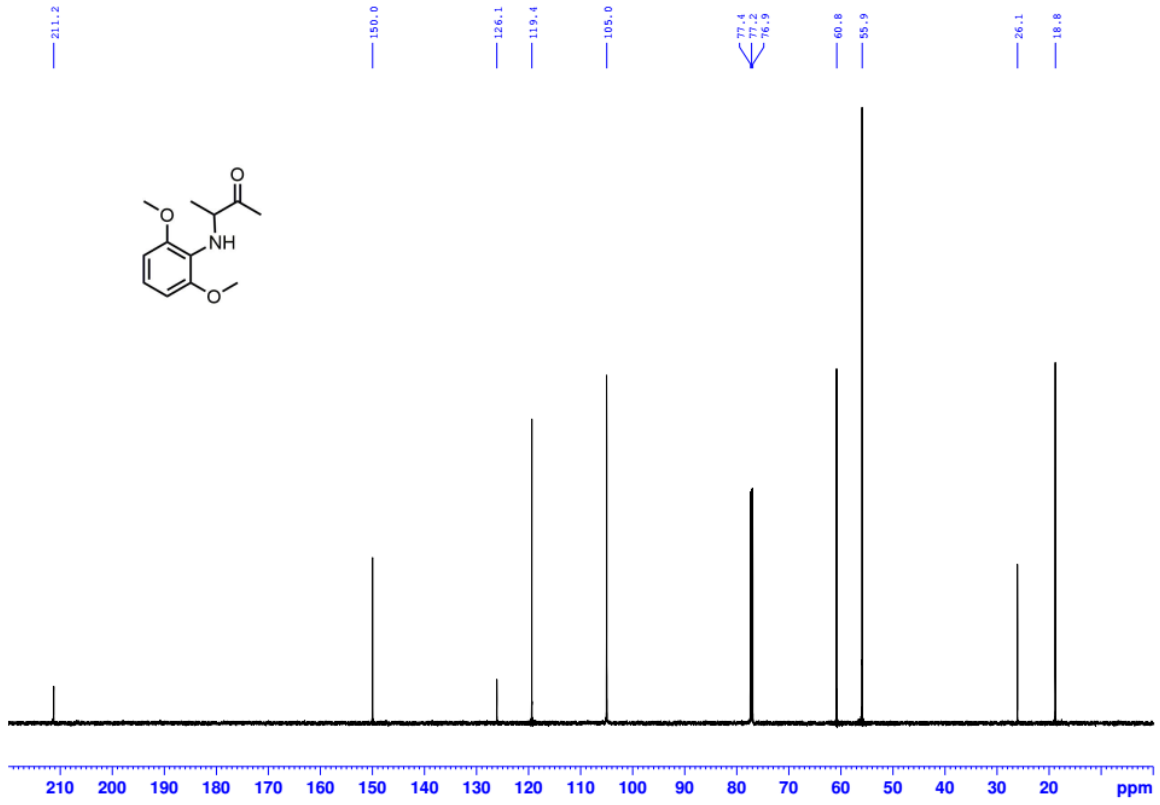


Acetoin (0.80 g, 5.2 mmol) and 2,6-dimethoxy aniline (0.69 g, 7.8 mmol) were used in this reaction. The crude compound was purified by column chromatography (15% EtOAc/Hexanes) offered (1.1 g, 94%) of compound **S3** as light pale pink solid. R_f = 0.4 (25% EtOAc/Hexanes); mp = 50.5-52.5 ^oC; **^{1}H NMR** (600 MHz, $CDCl_3$) δ: 6.76 (t, *J* = 8.3 Hz, 1H), 6.53 (d, *J* = 8.3 Hz, 2H), 4.43 (br s, 1H), 4.33 (d, *J* = 6.6 Hz, 1H), 3.80 (s, 6H), 2.19 (s, 3H), 1.28 (d, *J* = 7.1 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ: 211.2, 150.2, 126.1, 119.4, 105.0, 60.8, 55.9, 26.1, 18.8; **FTIR** (KBr thin film) νmax (cm^{-1}) : 3366, 2967, 2939, 2836, 1716, 1597, 1494, 1466, 1108; **HRMS** (EI^+) m/z calculated for $C_{12}H_{17}NO_3$ $[M]^+$: 223.1208; found: 223.1276

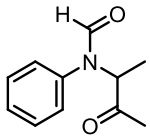
^{1}H NMR spectrum (S3)



^{13}C NMR spectrum (S3)



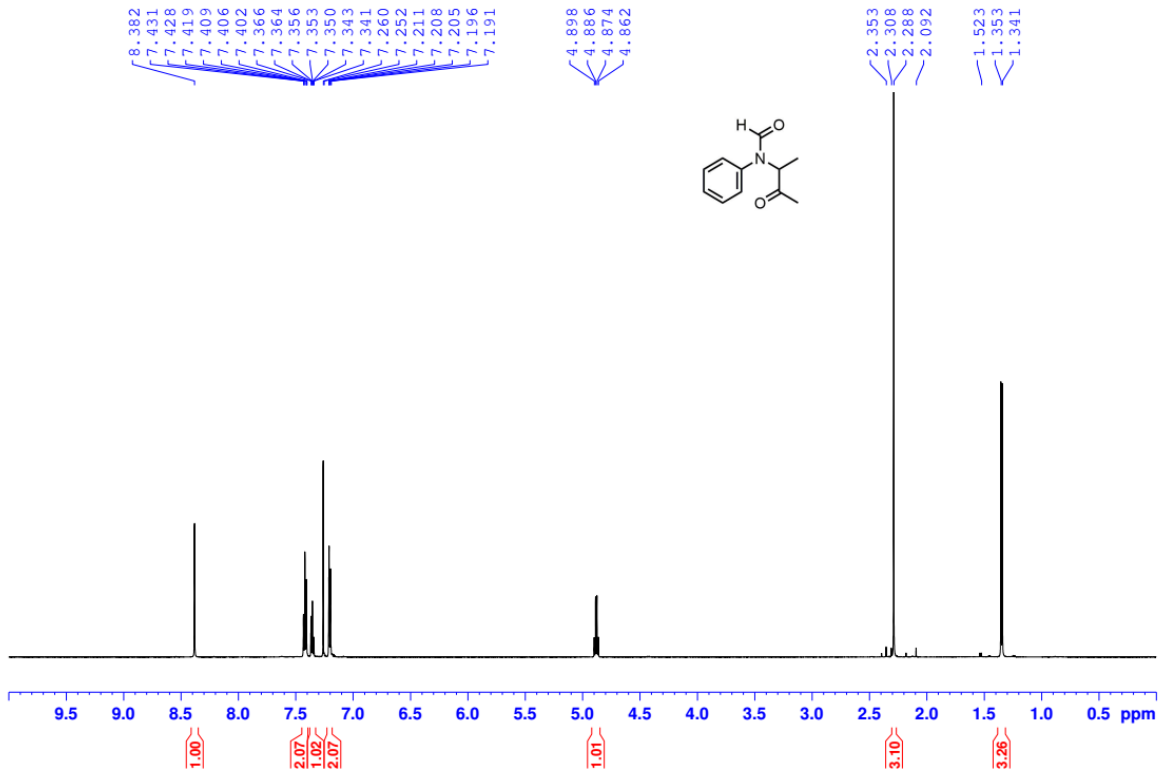
N-(3-oxobutan-2-yl)-N-phenylformamide (S4) [2]



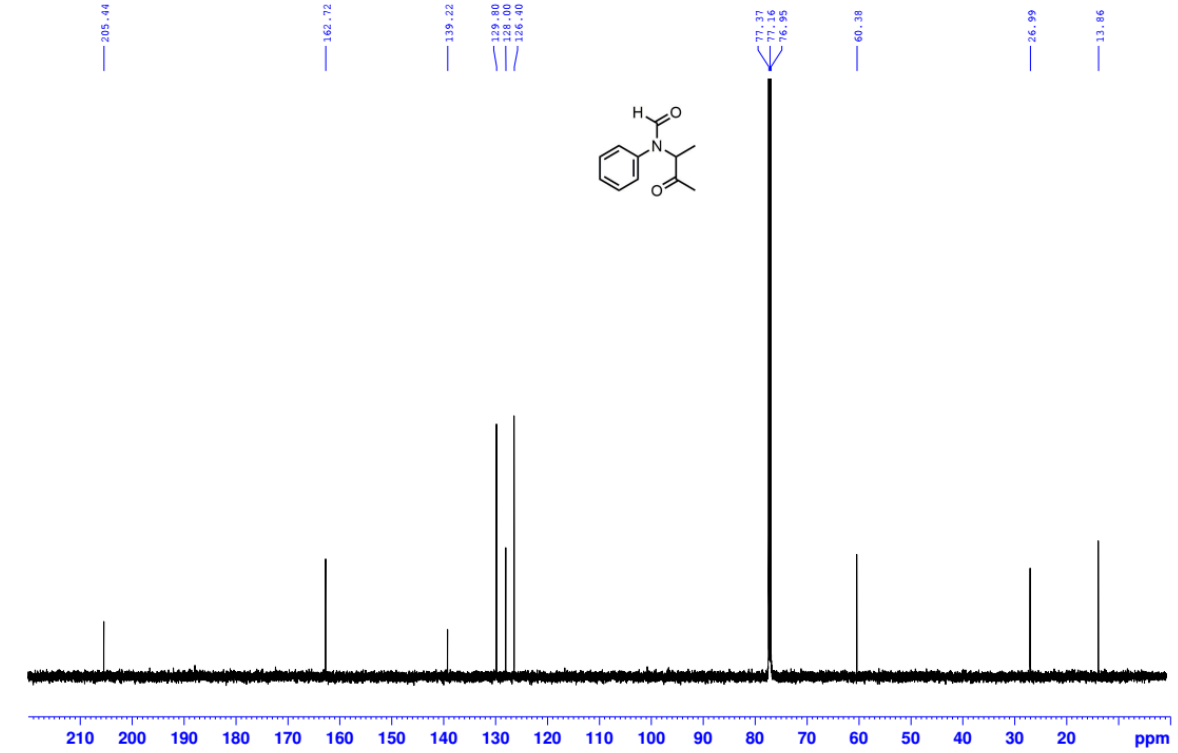
2b

Formic acid (1.16 mL, 30.4 mmol) was added to acetic anhydride (2.17 mL, 23.0 mmol), then stirred at 60 ^{o}C for 2 hours. The resulting mixed anhydride was added slowly to a stirred solution of amino ketone **S4** (2.50 g, 15.3 mmol) in THF (51 mL), then stirred at room temperature for 16h. The reaction mixture was concentrated, followed by co-concentration with toluene (3x50 ml). The crude compound was purified by column chromatography (25% EtOAc/hexanes) to obtain (2.45 g, 84%) of compound **S4** as a dark brown solid. R_f = 0.3 (30% EtOAc/Hexanes); **^{1}H NMR** (600 MHz, $CDCl_3$) δ: 8.38 (s, 1H), 7.43-7.40 (m, 2H), 7.37-7.34 (m, 2H), 7.21-7.19 (m, 1H), 4.86 (q, *J* = 7.3 Hz), 2.29 (s, 3H), 1.34 (d, *J* = 7.3 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ: 205.4, 162.7, 139.2, 129.8, 128.0, 126.4, 60.4, 27.0

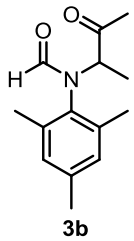
^{1}H NMR spectrum (S4)



^{13}C NMR spectrum (S4)



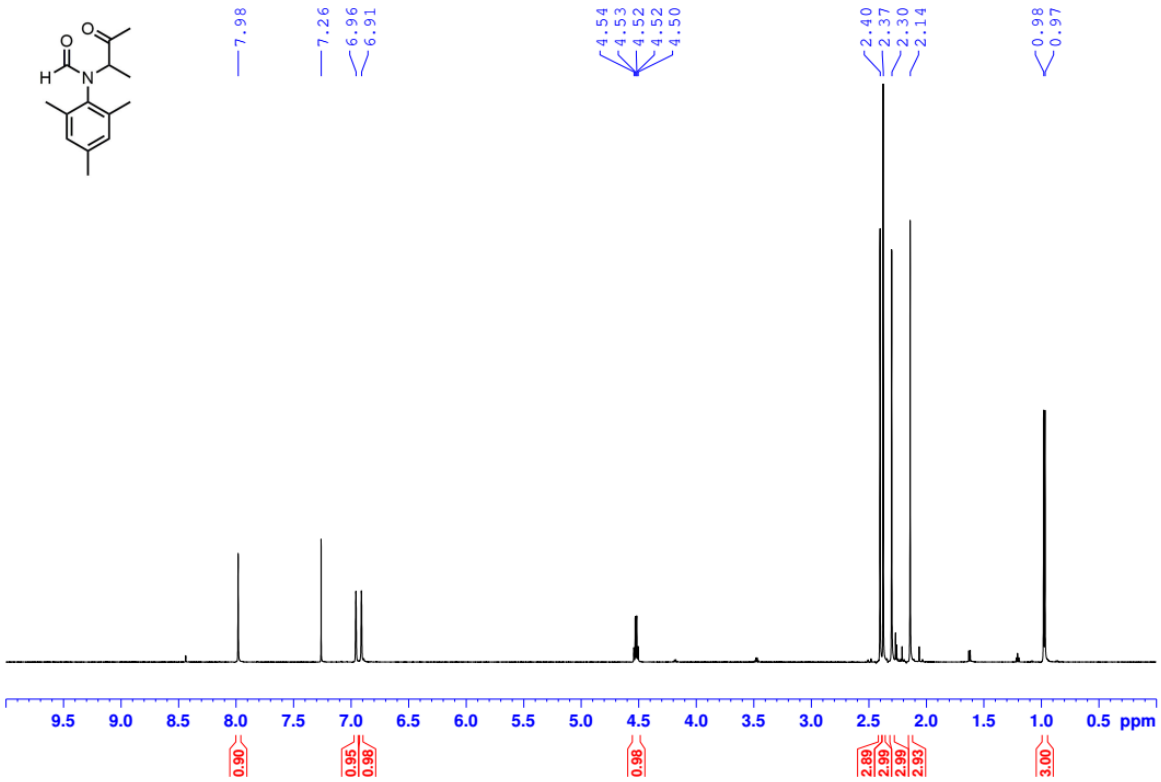
***N*-mesityl-*N*-(3-oxobutan-2-yl)formamide (S5)**



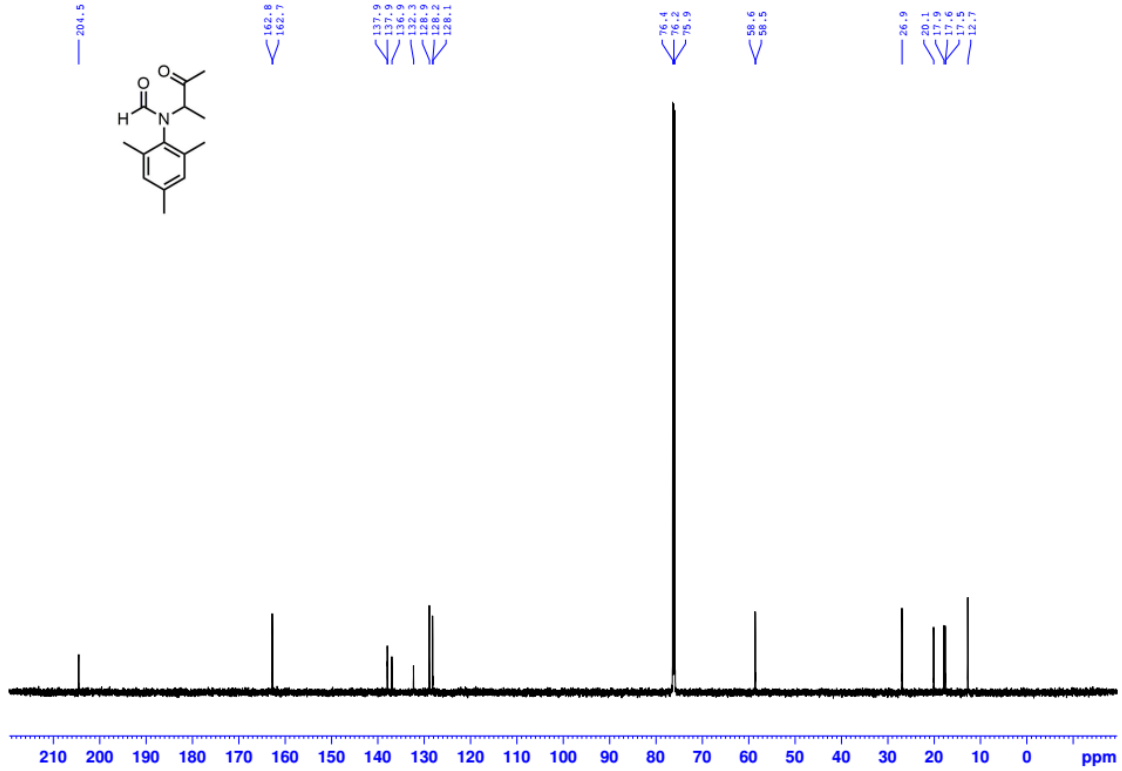
3b

Amino ketone **S2** (3.00 g, 14.6 mmol) was used for this reaction. The crude compound was purified by column chromatography (20% EtOAc/hexanes) to obtain 3.15g (92%) of compound **S5** as a dark brown solid. R_f = 0.3 (25% EtOAc/Hexanes); **^{1}H NMR** (600 MHz, $CDCl_3$) δ: 7.98 (s, 1H), 6.96 (s, 1H), 6.91 (s, 1H), 4.52 (q, *J* = 7.4 Hz, 1H), 2.40 (s, 3H), 2.37 (s, 3H), 2.30 (s, 3H), 2.14 (s, 3H), 0.98 (d, *J* = 7.5 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ: 204.5, 162.8, 162.7, 137.9, 137.9, 136.9, 132.3, 128.9, 128.2, 128.1, 58.6, 58.5, 26.9, 20.1, 17.9, 17.6, 17.5, 12.7

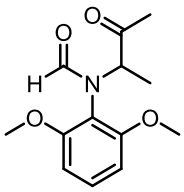
^{1}H NMR spectrum (S5)



^{13}C NMR spectrum (S5)

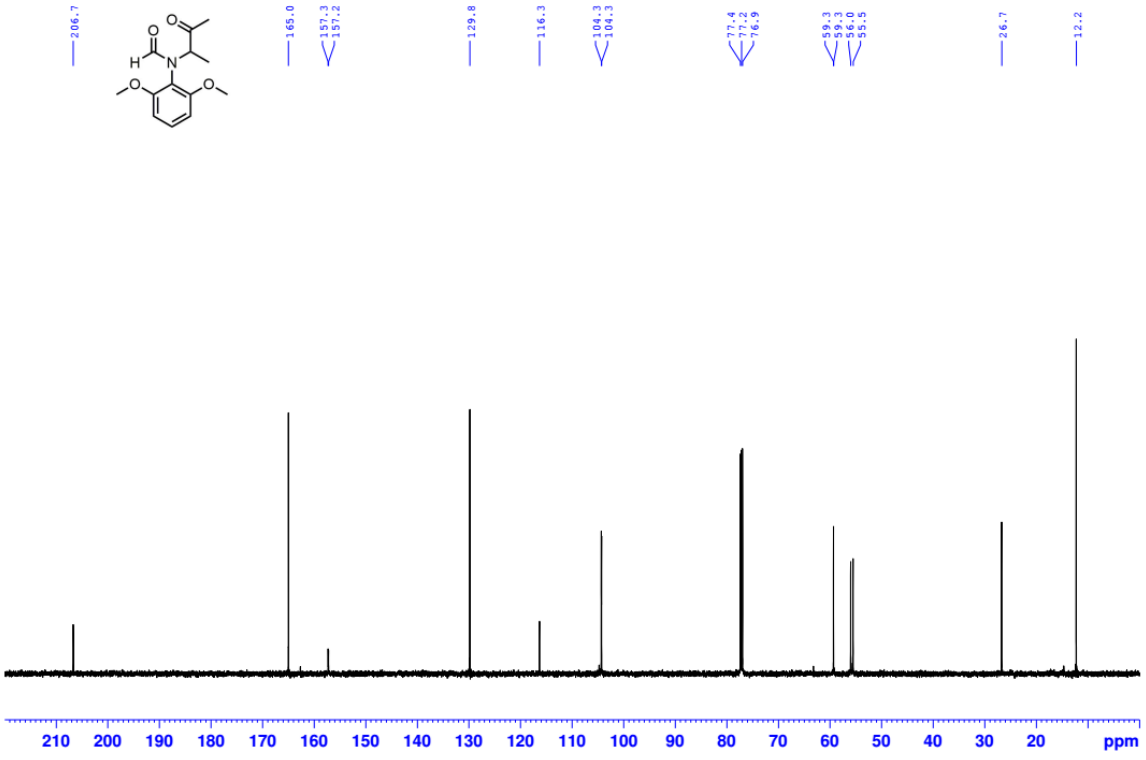


***N*-(2,6-dimethoxyphenyl)-*N*-(3-oxobutan-2-yl)formamide (S6)**

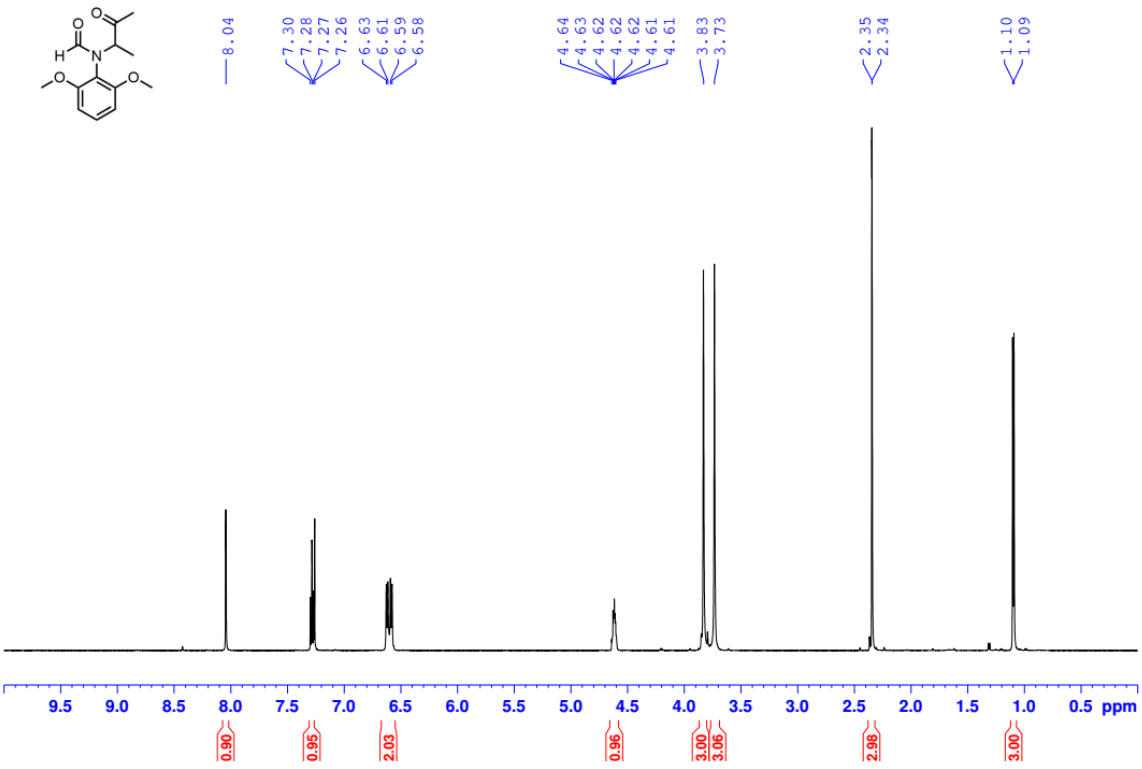


Compound **S3** (1.10 g, 4.4 mmol) was used in this reaction. The crude product was purified by chromatography (25% EtOAc/hexanes) to obtain 1.15 g (89%) of compound **S6** as a light brown solid. R_f = 0.3 (30% EtOAc/Hexanes); mp = 94-97 ^oC; **^{1}H NMR** (600 MHz, $CDCl_3$) δ: 8.04 (s, 1H), 7.28 (t, *J* = 8.4 Hz, 1H), 6.60 (dd, *J* = 22, 8.4 Hz, 2H), 4.64 – 4.61 (m, 1H), 3.83 (s, 3H), 3.73 (s, 3H), 2.35 (d, *J* = 1.3 Hz, 3H), 1.1 (d, *J* = 7.0 Hz, 3H); **^{13}C NMR** (600 MHz, $CDCl_3$) δ: 206.7, 165.0, 157.3, 157.2, 129.8, 116.3, 104.3, 104.3, 59.3, 59.3, 56.0, 55.5, 26.7, 12.2; **FTIR** (KBr thin film) νmax (cm^{-1}) : 2941, 1781, 1676, 1479, 1300, 1111; **HRMS** (EI^+) m/z calculated for $C_{13}H_{17}NO_4$ $[M]^+$: 251.1158; found: 251.1165.

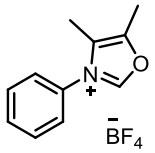
^{1}H NMR spectrum (S6)



^{13}C NMR spectrum (S6)



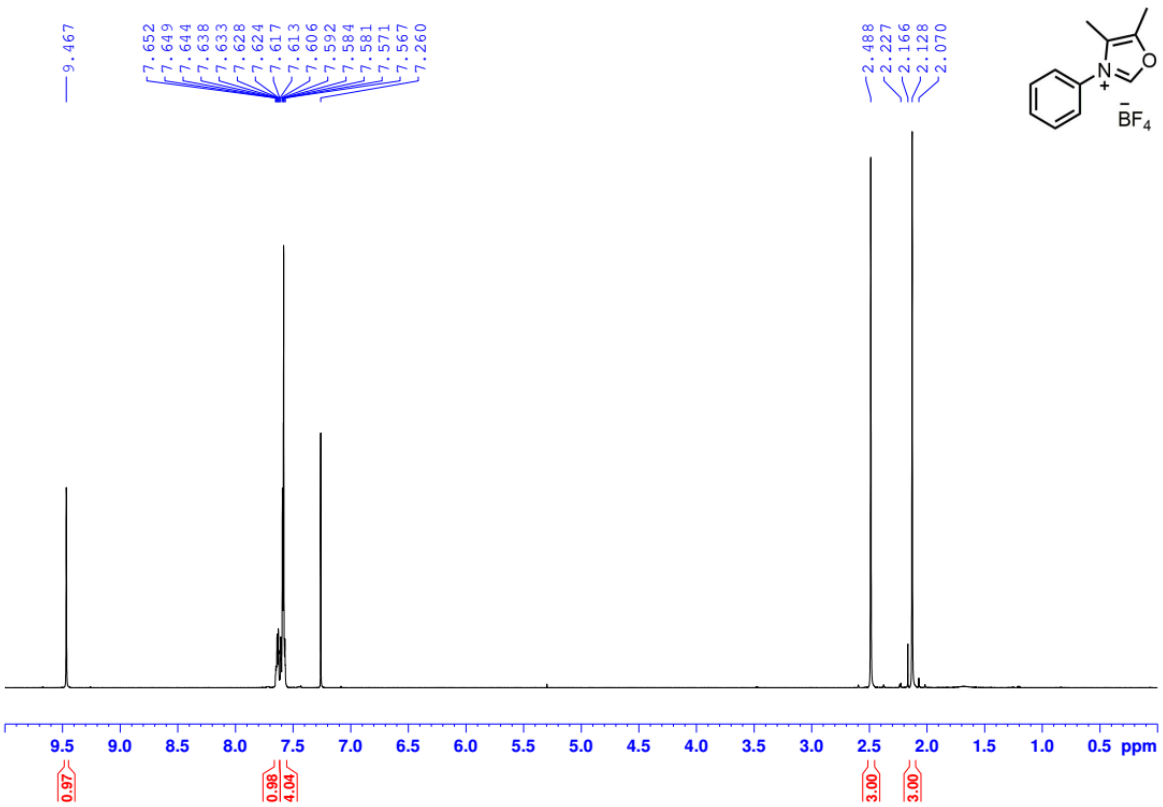
4,5-dimethyl-3-phenyloxazol-3-ium tetrafluoroborate (2) [3,4]



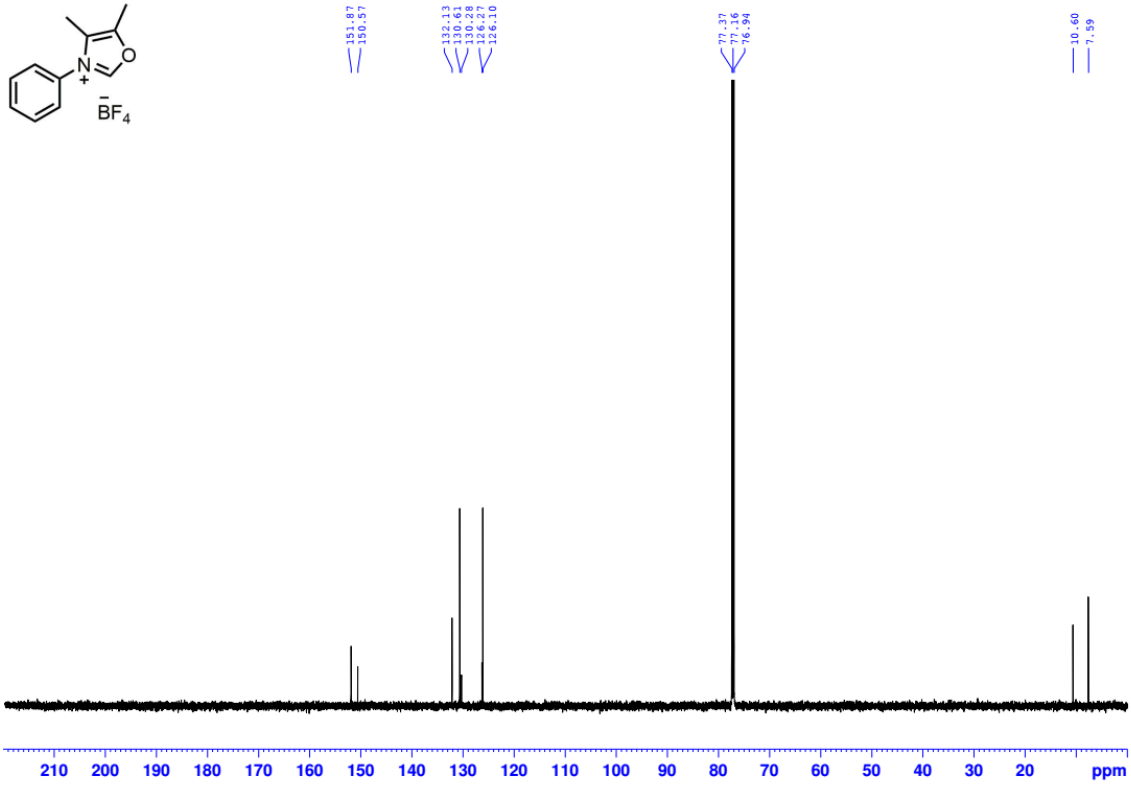
2

The keto amide **S4** (1.20 g, 6.28 mmol) in polyphosphoric acid (PPA) (6.0 mL) was heated at 80 ^{o}C for 18 h. The mixture was cooled to room temperature and a solution of $NaBF_4$ (1.41 g, 18.83 mmol) in distilled water (15 ml) was slowly added. The mixture was extracted with CH_2Cl_2 (4x30 ml), dried over anhydrous $NaSO_4$ and concentrated. The crude compound was obtained as a gummy liquid and recrystallized from diethyl ether to obtain 1.10 g (67%) of compound **2** as a beige solid. R_f = 0.3 (10% methanol/ CH_2Cl_2); mp = 90.5-94 ^{o}C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ: 9.47 (s, 1H), 7.65-7.62 (m, 1H), 7.61-7.57 (m, 4H), 2.49 (s, 3H), 2.13 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ: 151.9, 150.6, 132.1, 130.6, 130.3, 126.3, 126.1, 10.6, 7.6; **FTIR** (KBr thin film) νmax (cm^{-1}): 3134, 2932, 1680, 1492, 1053, 729; **HRMS** (EI^+) m/z calculated for $C_{11}H_{12}NO^+$ $[M]^+$: 174.0913; found: 174.0912.

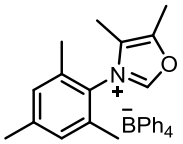
^{1}H NMR spectrum (2)



^{13}C NMR spectrum (2)



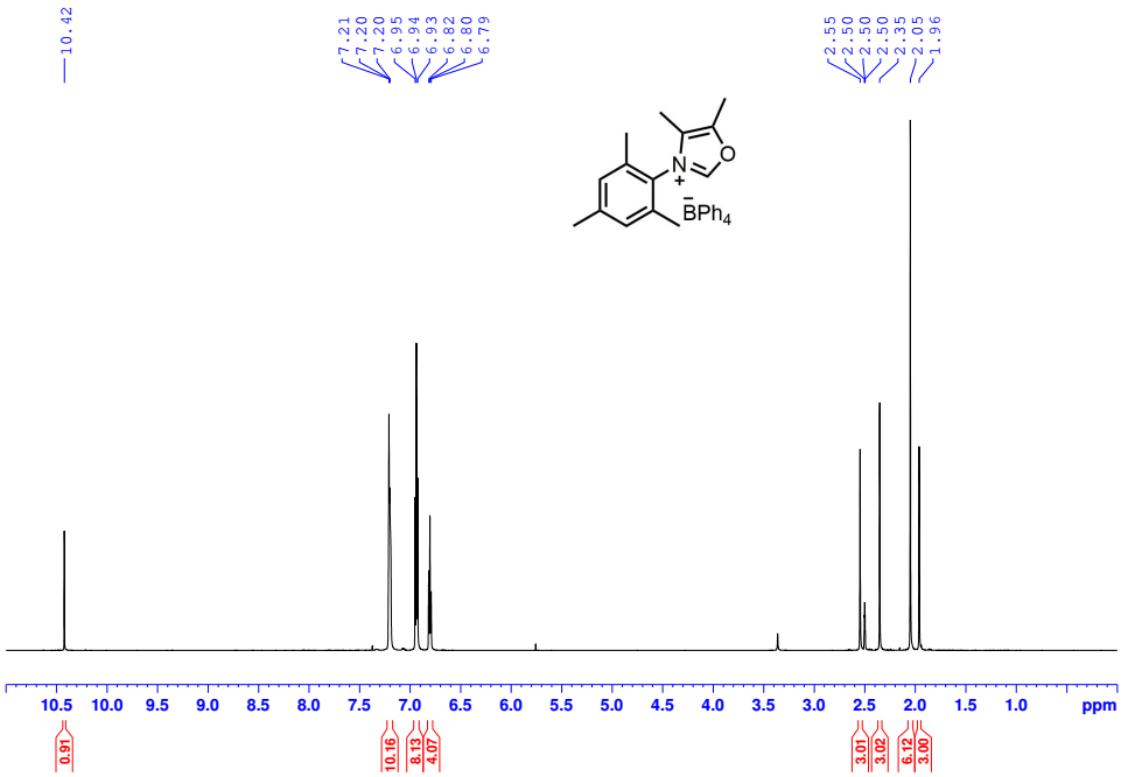
3-mesityl-4,5-dimethyloxazol-3-ium tetraphenylborate (3)



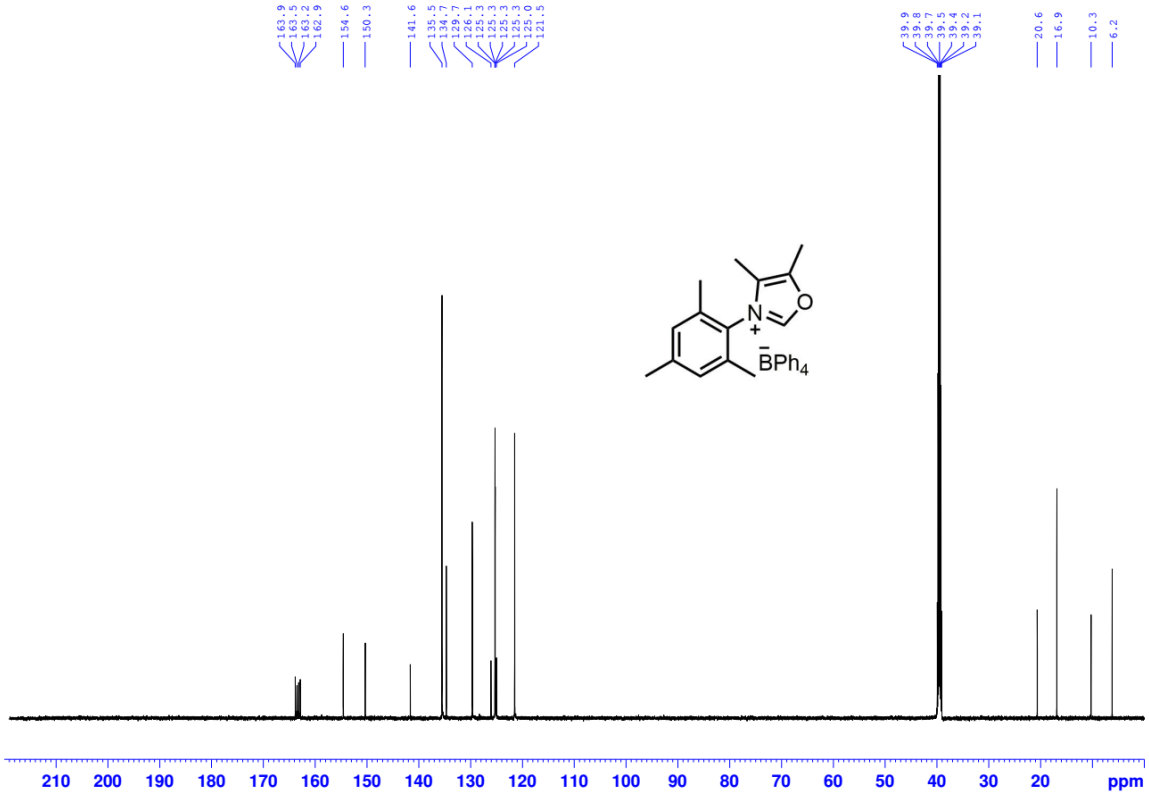
3

Compound **S5** (1.00 g, 4.29 mmol) and sodium tetraphenylborate (1.47g, 4.29 mmol) were used in this reaction. The crude product was recrystallized form diethyl ether. The title compound **3** was obtained as a beige solid (1.49 g, 65%). R_f = 0.5 (5% methanol/ CH_2Cl_2); mp = 228-230 ^oC; **^{1}H NMR** (600 MHz, DMSO-d_6) δ: 10.42 (s, 1H), 7.21 – 7.20 (m, 10H), 6.94 (t, *J* = 7.4 Hz, 8H), 6.80 (t, *J* = 7.2 Hz, 4H), 2.55 (s, 3H), 2.35 (s, 3H), 2.05 (s, 6H), 1.96 (s, 3H); **^{13}C NMR** (150 MHz, DMSO-d_6) δ: 163.9, 163.5, 163.2, 162.9, 154.6, 150.3, 141.6, 135.5, 134.7, 129.7, 126.1, 125.3, 125.3, 125.3, 125.3, 125.0, 121.5, 20.6, 16.9, 10.3, 6.2; **FTIR** (KBr thin film) νmax (cm^{-1}): 3094, 3058, 3037, 1670, 1477, 1424, 1031, 745, 733, 706; **HRMS** (EI^+) m/z calculated for $C_{14}H_{18}NO^+$ $[M]^+$: 216.1383; found: 216.1395.

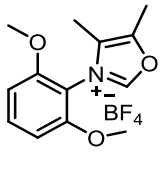
^{1}H NMR spectrum (3)



^{13}C NMR spectrum (3)



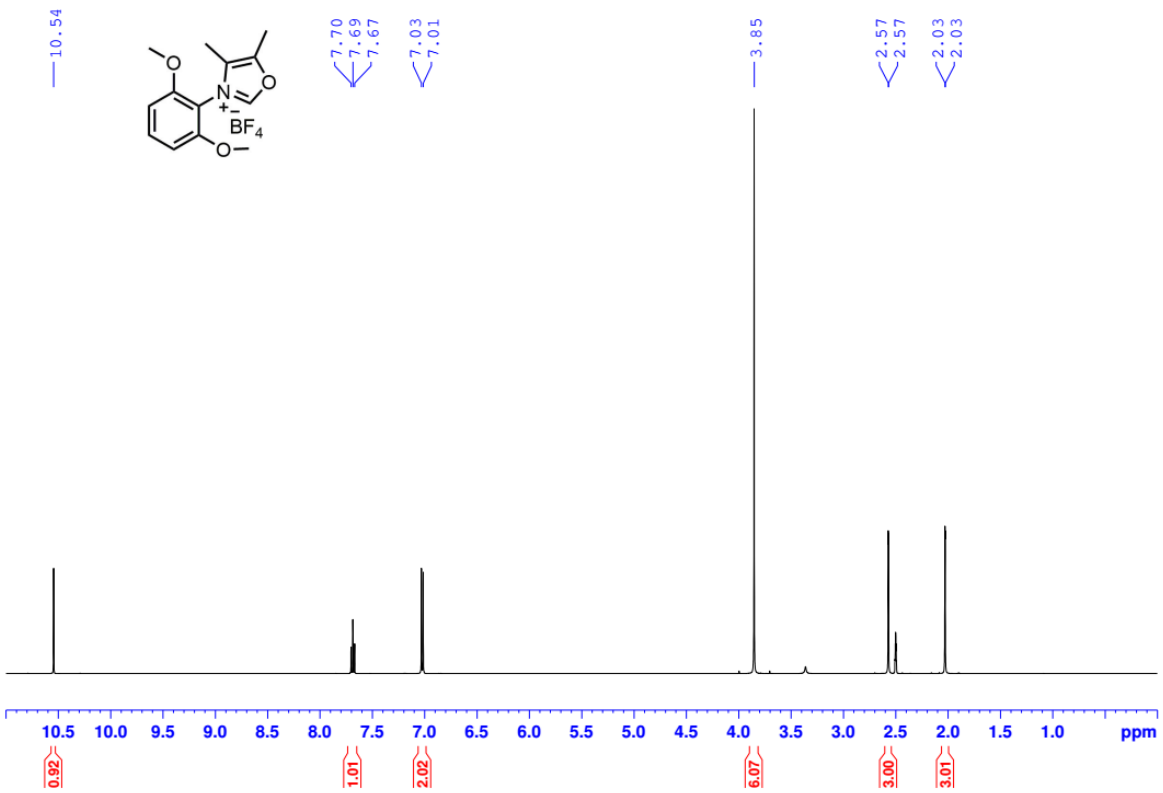
3-(2,6-dimethoxyphenyl)-4,5-dimethyloxazol-3-ium tetrafluoroborate (4)



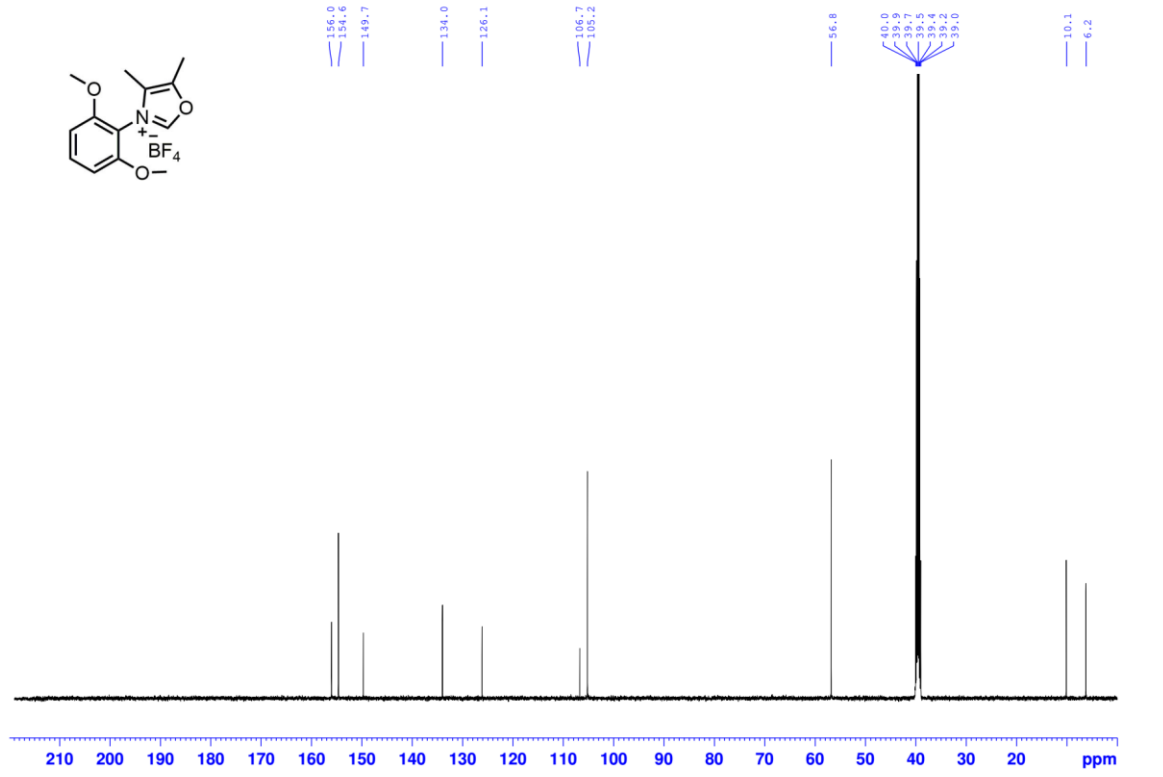
4

This reaction was started with compound **S6** (1.00 g, 3.98 mmol). The crude product was recrystallized from acetone/diethyl ether to obtain the title compound **4** (1.04 g, 85%) as a grey solid. R_f = 0.4 (10% methanol/ CH_2Cl_2); mp = 131-133 ^oC; **^{1}H NMR** (500 MHz, DMSO-d_6) δ: 10.54 (s, 1H), 7.69 (t, *J* = 8.6 Hz, 1H), 7.02 (d, *J* = 8.7 Hz, 2H), 3.9 (s, 6H), 2.57 (d, *J* = 0.9 Hz, 3H), 2.03 (d, *J* = 0.9 Hz, 3H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ: 156.0, 154.6, 149.7, 134.0, 126.1, 106.7, 105.2, 56.8, 10.1, 6.2; **FTIR** (KBr thin film) νmax (cm^{-1}): 2921, 1676, 1602, 1553, 1486, 1300, 1262, 1108, 784, 533, 521; **HRMS** (EI^+) m/z calculated for $C_{13}H_{16}NO_3^+$ $[M]^+$: 234.1125; found: 234.1127.

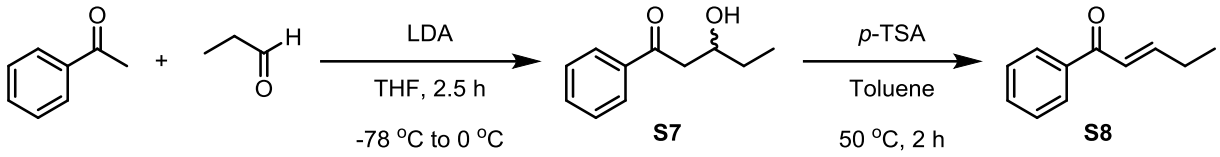
^{1}H NMR spectrum (4)



^{13}C NMR spectrum (4)



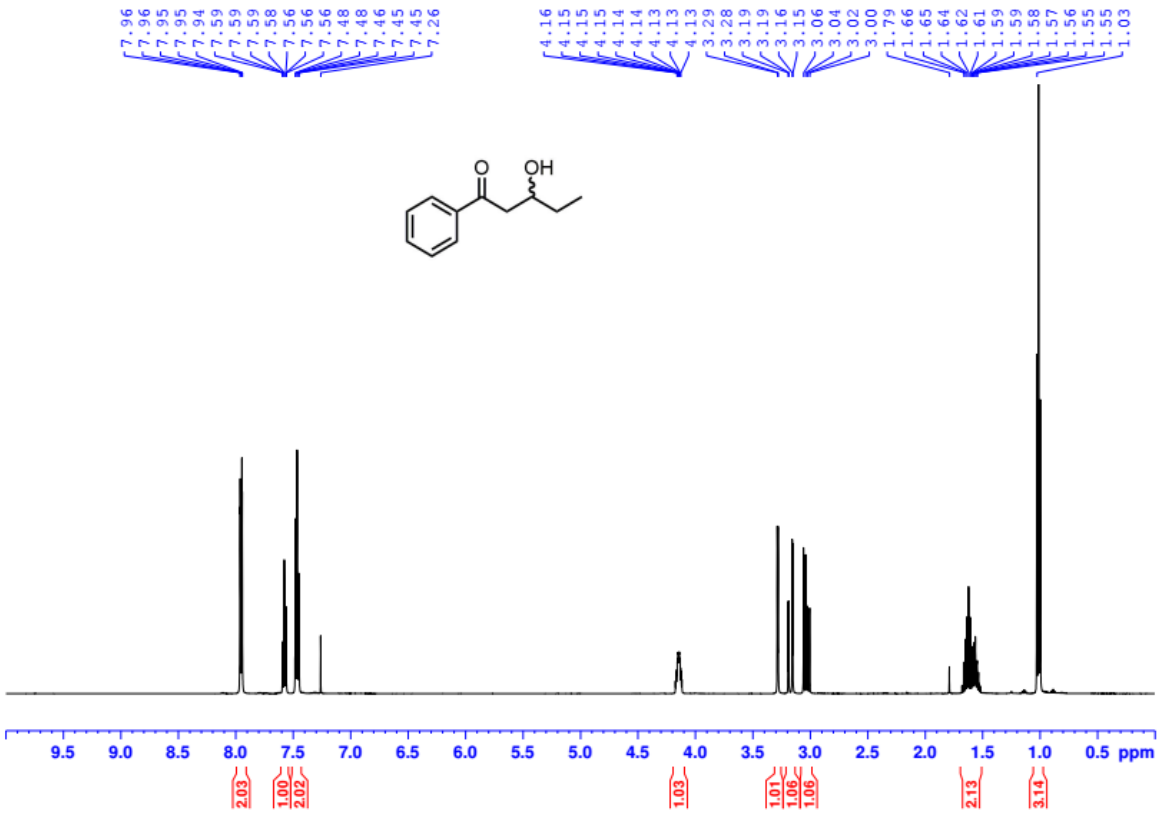
Synthesis of (*E*)-1-phenylpent-2-en-1-one (S8)[5]



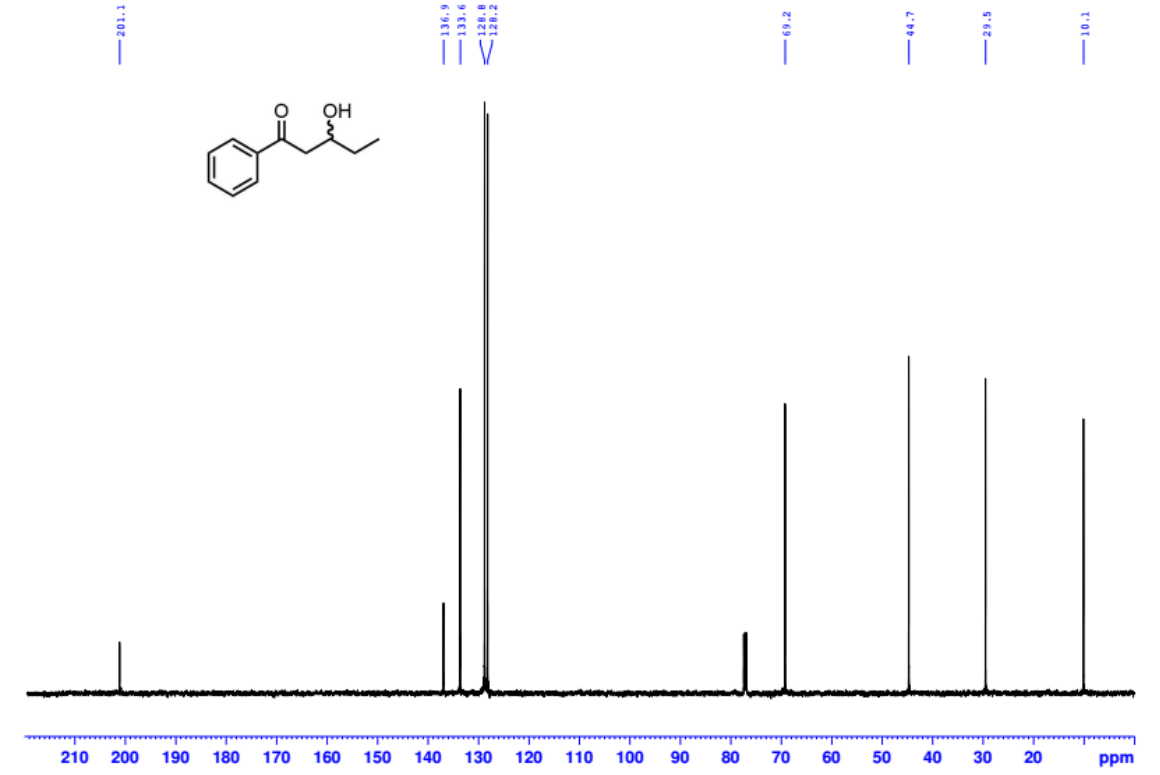
2.5 M *n*-butyl lithium in hexane (11.3 mL, 28.3 mmol) was slowly added to a stirred solution of diisopropyl amine (3.99 ml, 28.3 mmol) in dry THF (64 mL) at -78 °C. The reaction mixture was slowly warmed to 0 °C in 10 minutes and stirred for another 10 min at this temperature to generate LDA. The mixture was again cooled to -78 °C, then acetophenone (3.00 mL, 25.7 mmol) was added and stirred for another 30 minutes. Then freshly distilled propionaldehyde (1.94 mL, 27.0 mmol) was added and stirring continued for another 1.5 hour at -78 °C. The reaction was quenched with 1:1 AcOH/water (10 mL) at -78 °C, warmed to room temperature and concentrated. The crude mixture was diluted with CH_2Cl_2 (50 ml) and 30 mL of water, the organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2x50 ml). The combined organic layers were washed with a saturated $NaHCO_3$ solution and brine, then dried over anhydrous Na_2SO_4 and concentrated. The crude compound was purified by column chromatography (20% EtOAc/Hexanes) to afford 3.04 g (66%) of compound **S7** as a colorless liquid. R_f = 0.3 (30% EtOAc/Hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.96 – 7.94 (m, 2H), 7.59 – 7.56 (m, 1H), 7.48 – 7.45 (m, 2H), 4.16 – 4.13 (m, 1H), 3.28 (d, *J* = 3.4 Hz, 1H), 3.17 (dd, *J* = 17.6, 2.6 Hz, 1H), 3.03 (dd, *J* = 17.6, 9.1 Hz, 1H), 1.68 – 1.52 (m, 2H), 1.01 (t, *J* =7.5 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 201.1, 136.9, 133.6, 128.8, 128.2, 69.2, 44.7, 29.5, 10.1; **HRMS** (EI^+) m/z calculated for $C_{11}H_{14}O_2$ + Na $[M]^+$: 201.0886; found: 201.0887.

The β-hydroxy ketone **S7** (3.00 g, 16.8 mmol) was dissolved in toluene (56 mL), then *p*-toluene sulfonic acid (3.20 g, 16.8 mmol) was added. The mixture was heated to 50 °C for 2 hours, then the mixture was diluted with hexanes, filtered through celite and concentrated. The crude product was purified by using chromatography (5% EtOAc/Hexanes) to afford 2.45 g (91%) of compound **S8** as a colorless liquid. R_f = 0.2 (10 % EtOAc/Hexanes); **^{1}H NMR** (600 MHz, $CDCl_3$) δ: 7.94 – 7.92 (m, 2H), 7.57 – 7.54 (m, 1H), 7.48 – 7.46 (m, 2H), 7.11 (dt, *J* = 15.4, 6.4 Hz, 1H), 6.88 (dt, *J* = 15.4, 1.7 Hz, 1H), 2.38 – 2.33 (m, 2H), 1.15 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ: 191.1, 151.4, 138.1, 132.6, 128.7, 128.7, 128.6, 128.6, 128.5, 125.1, 26.0, 12.4; **HRMS** (EI^+) m/z calculated for $C_{11}H_{12}O$ + Na $[M]^+$: 183.0780; found: 183.0790.

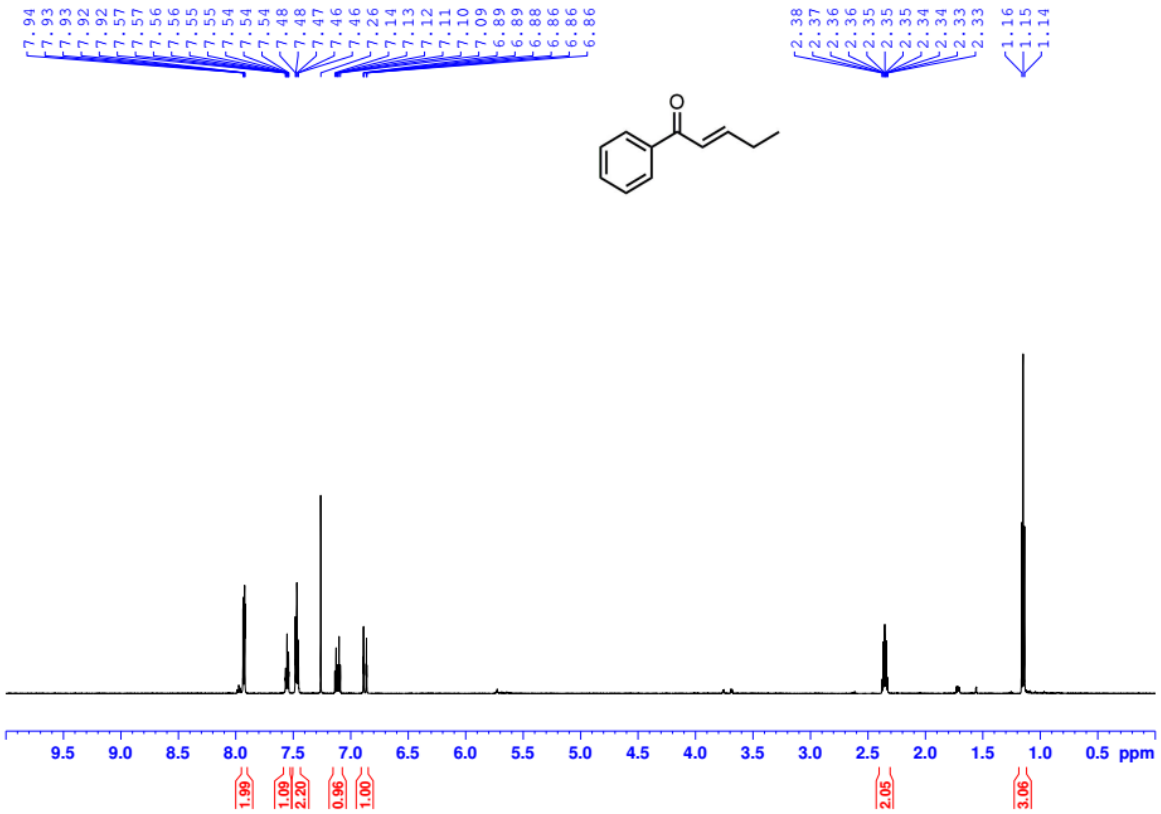
^{1}H NMR spectrum (S7)



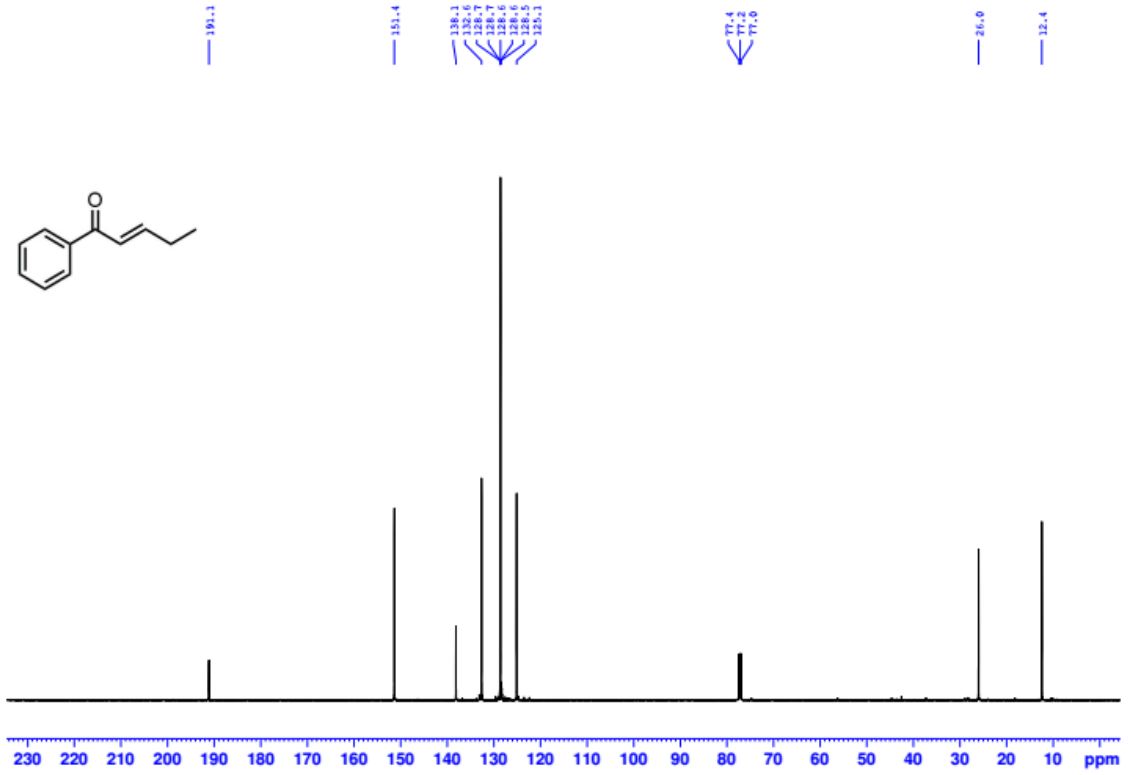
^{13}C NMR spectrum (S7)



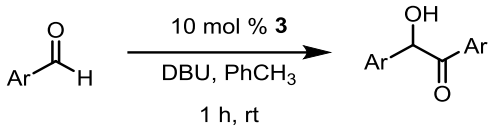
^{1}H NMR spectrum (S8)



^{13}C NMR spectrum (S8)



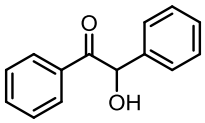
Benzoin reaction



General method for benzoin reaction

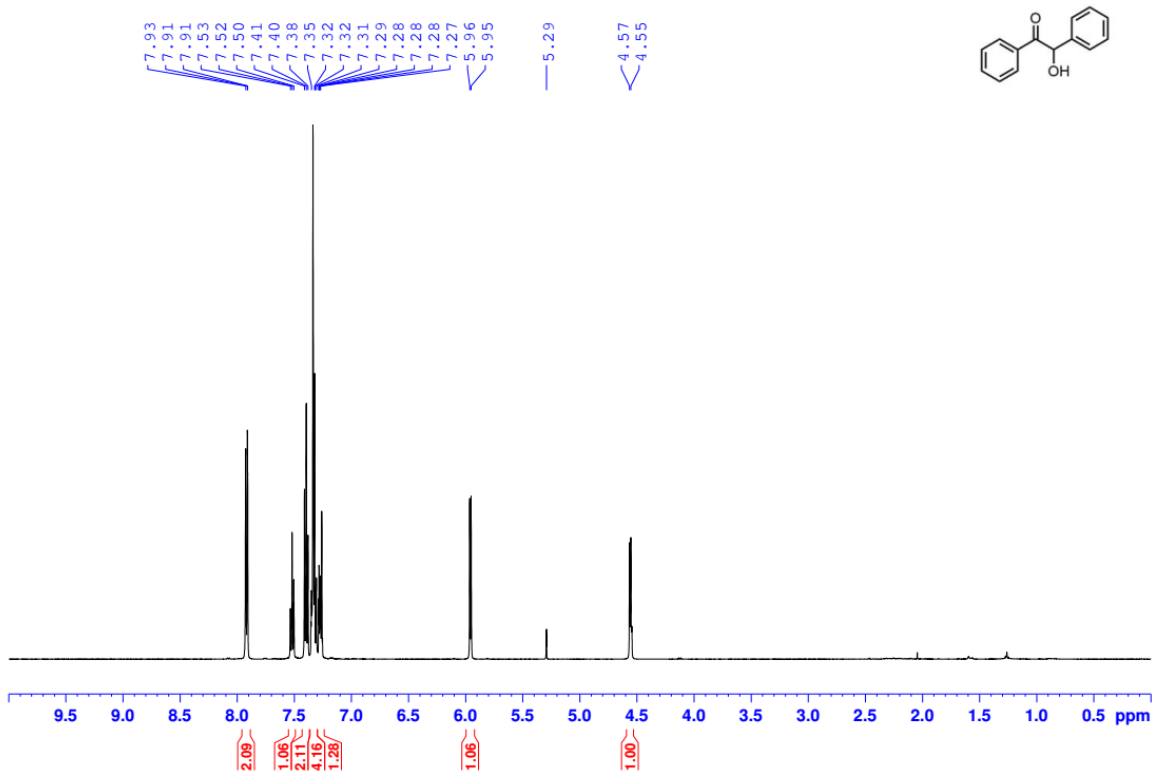
Catalyst **3** (13.4 mg, 0.025 mmol) was added to an oven dried Schlenk tube containing a magnetic stir bar and a septum, then the side arm was connected to a double manifold. The Schlenk tube was evacuated and refilled with argon three times. Aldehyde (0.5 mmol), toluene (0.5 ml) and DBU (3.7 µl, 0.025 mmol) were added sequentially under an argon atmosphere. The reaction mixture was stirred at room temperature for 1 h. The reaction progress was monitored by TLC. The reaction mixture was passed through containing plug of silica gel, eluted with EtOAc and concentrated under reduced pressure. Crude compounds were purified by silica gel column chromatography..

2-Hydroxy-1,2-diphenylethan-1-one (5)

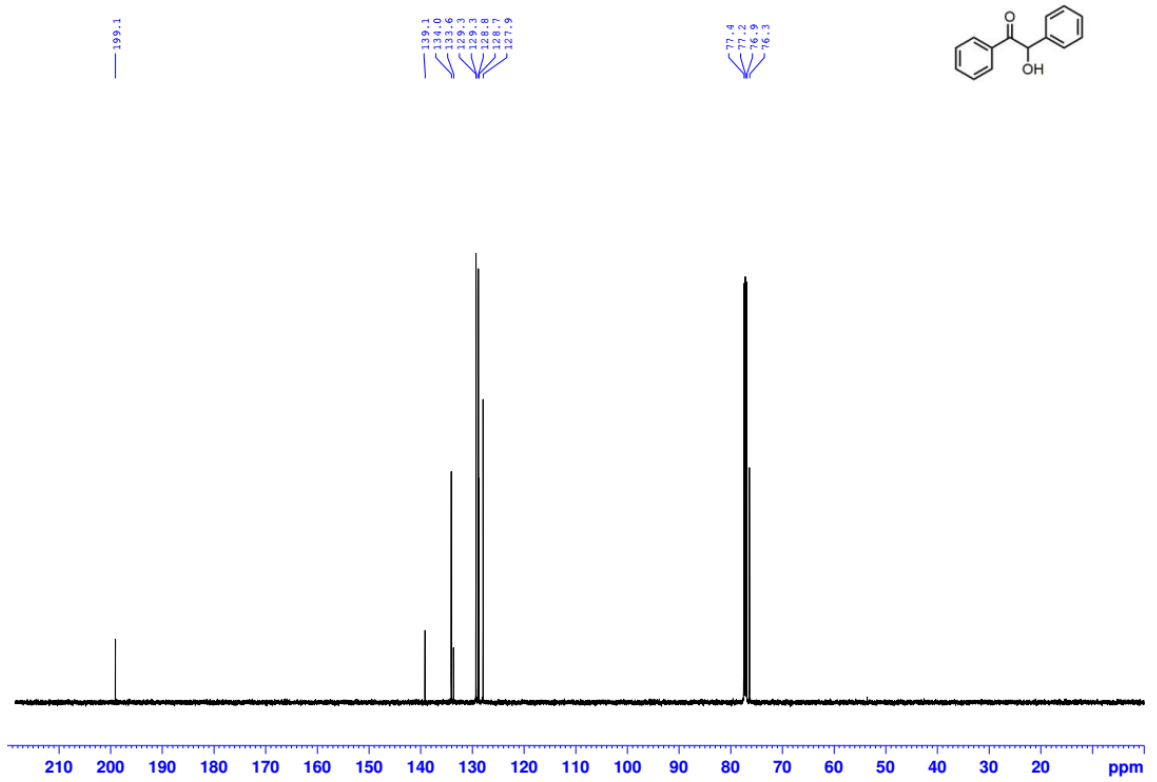


The crude product was purified by column chromatography (20% EtOAc/Hexanes) to afford 52 mg (97%) of compound **5** as a white solid. The same reaction on a 2 mmol scale (212 mg of benzaldehyde) furnished 207 mg of product (97%). R_f = 0.3 (25% EtOAc/Hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.93 -7.91 (m, 2 H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.41-7.38 (m, 2H), 7.35-7.31 (m, 4H), 7.29-7.27 (m, 1H), 5.95 (d, *J* = 6.1 Hz, 1H), 4.57-4.55 (d, *J* = 6.1 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 199.1, 139.1, 134.0, 133.6, 129.3, 129.3, 128.8, 128.7, 127.9, 76.3

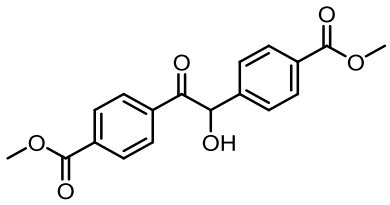
^{1}H NMR spectrum (5)



^{13}C NMR spectrum (5)

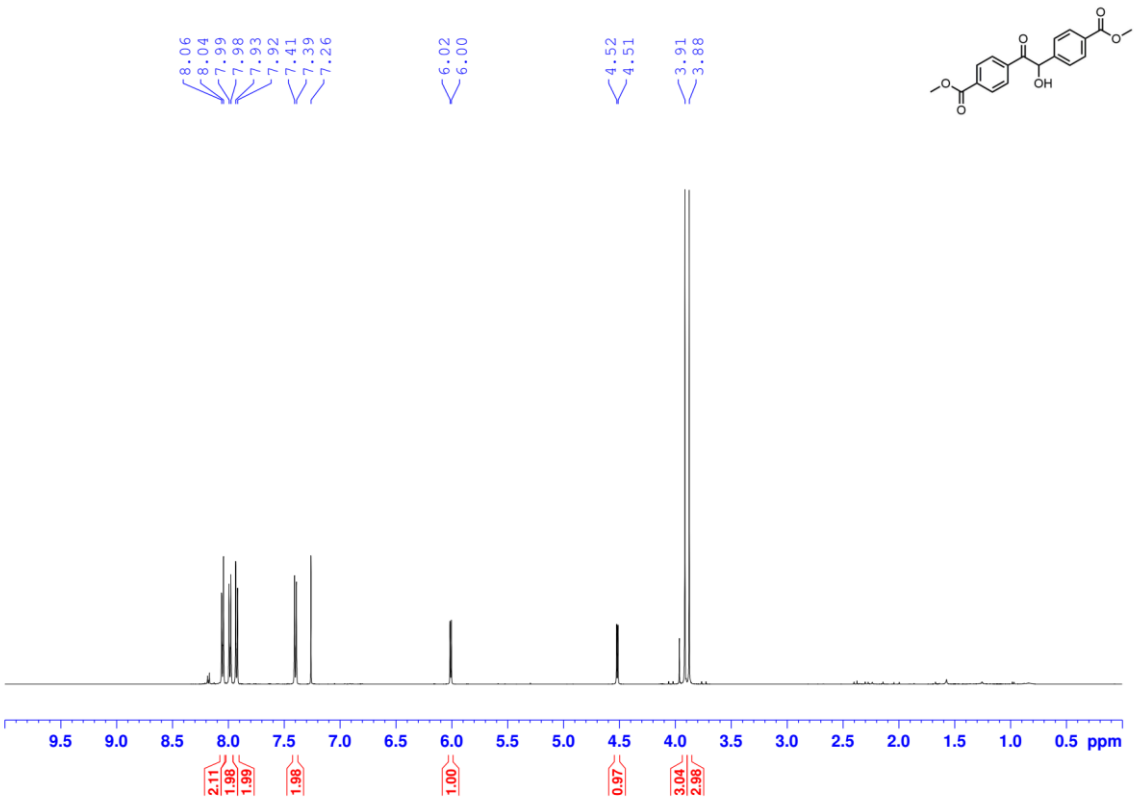


Dimethyl 4,4'-(1-hydroxy-2-oxoethane-1,2-diyl)dibenzoate (6)

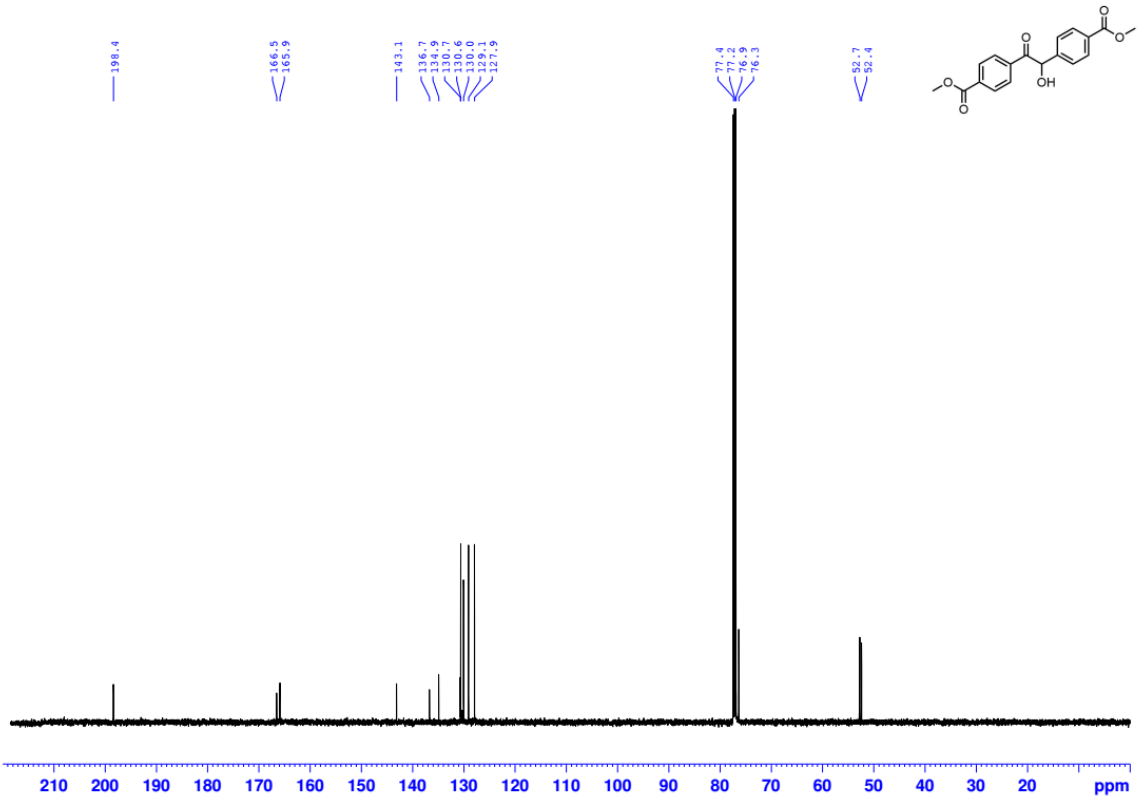


The crude product was purified by column chromatography (30% EtOAc/Hexanes) to afford 81 mg (99%) of compound **6** as a white solid. R_f = 0.3 (30% EtOAc/Hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 8.05 (d, *J* = 8.6 Hz, 2H), 7.98 (d, *J* = 8.4 Hz, 2H), 7.93 (d, *J* = 8.6 Hz, 2H), 7.39 (d, *J* = 8.3 Hz, 2H), 6.01 (d, *J* = 5.9 Hz, 1H), 4.51 (d, *J* = 5.9 Hz, 1H), 3.91 (s, 3H), 3.88 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 198.4, 166.5, 165.9, 143.1, 136.7, 134.9, 130.7, 130.6, 130.0, 129.1, 127.9, 76.3, 52.7, 52.4.

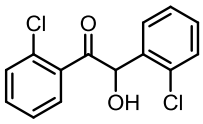
^{1}H NMR spectrum (6)



^{13}C NMR spectrum (6)

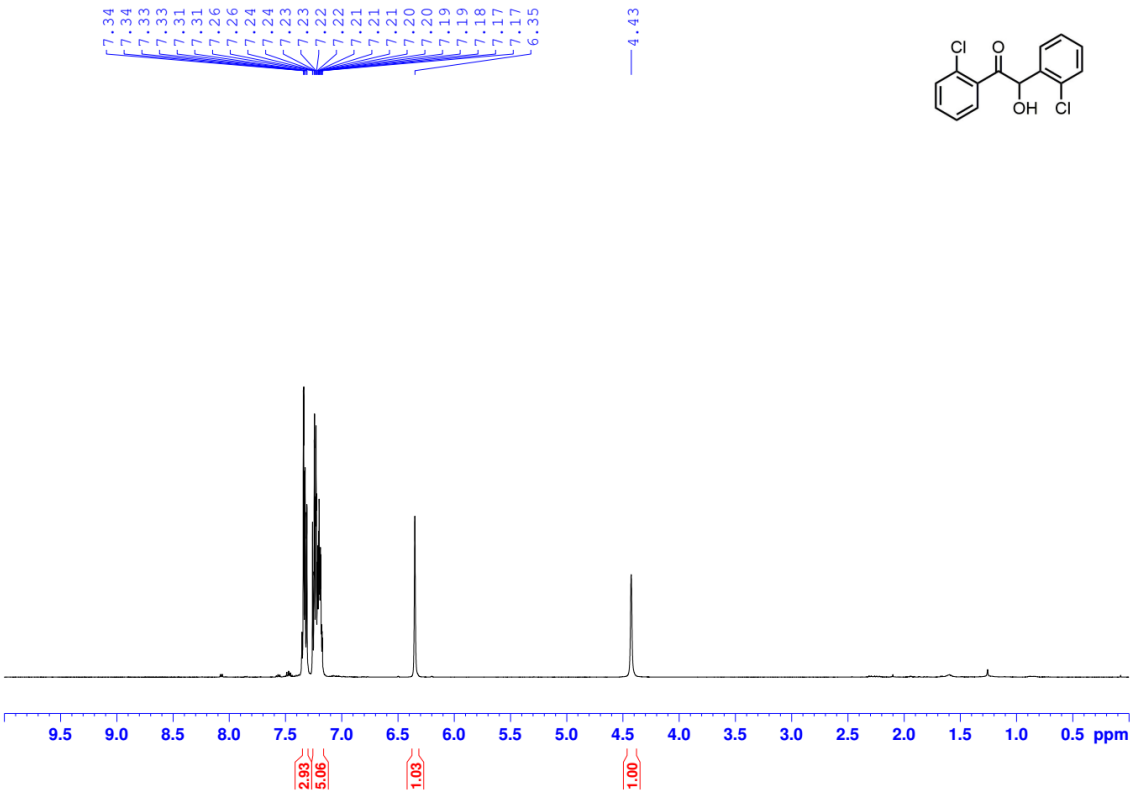


1,2-bis(2-chlorophenyl)-2-hydroxyethan-1-one (7)

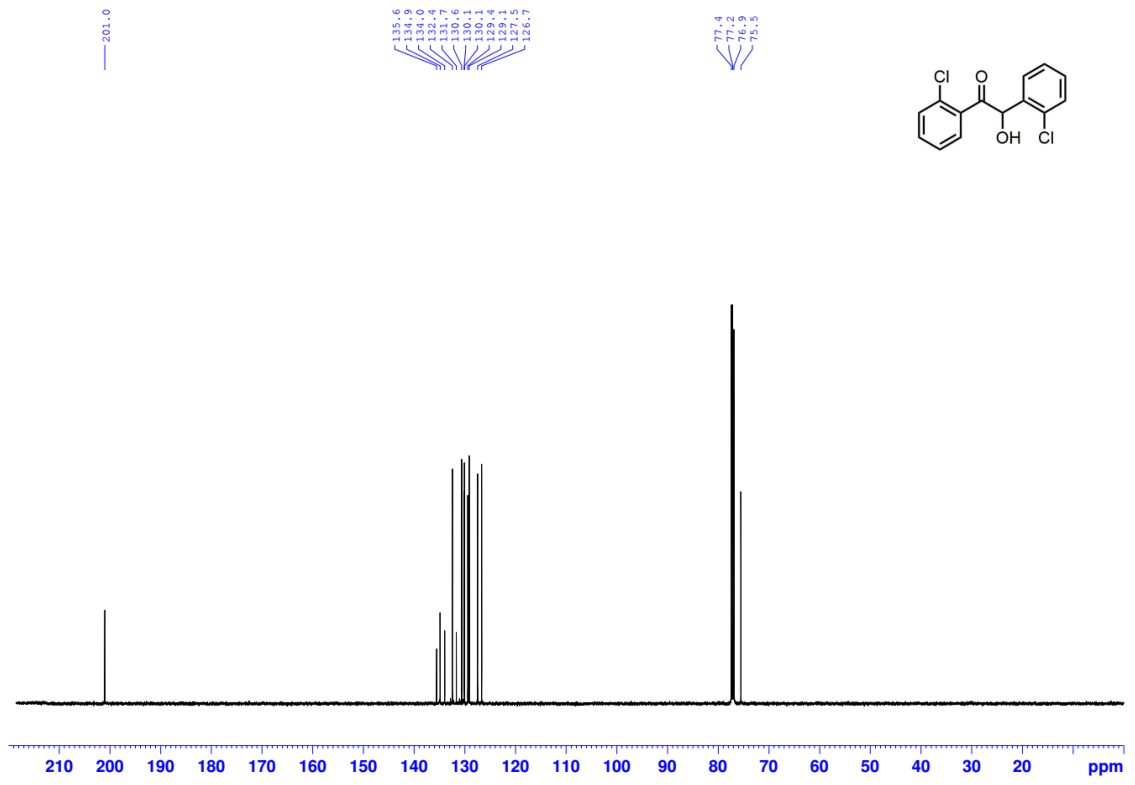


This reaction was stirred for 6 hours at room temperature. The crude product was purified by column chromatography (10% EtOAc/Hexanes) afford 53 mg (75%) of compound **7** as a white solid. R_f = 0.3 (15% EtOAc/Hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.34 – 7.31 (m, 3H), 7.26 – 7.17 (m, 5H) 6.35 (s, 1H), 4.43 (s, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 201.0, 135.6, 134.9, 134.0, 132.4, 131.7, 130.6, 130.1, 130.1, 129.4, 129.1, 127.5, 126.7, 75.5

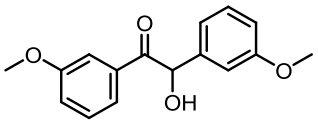
^{1}H NMR spectrum (7)



^{13}C NMR spectrum (7)

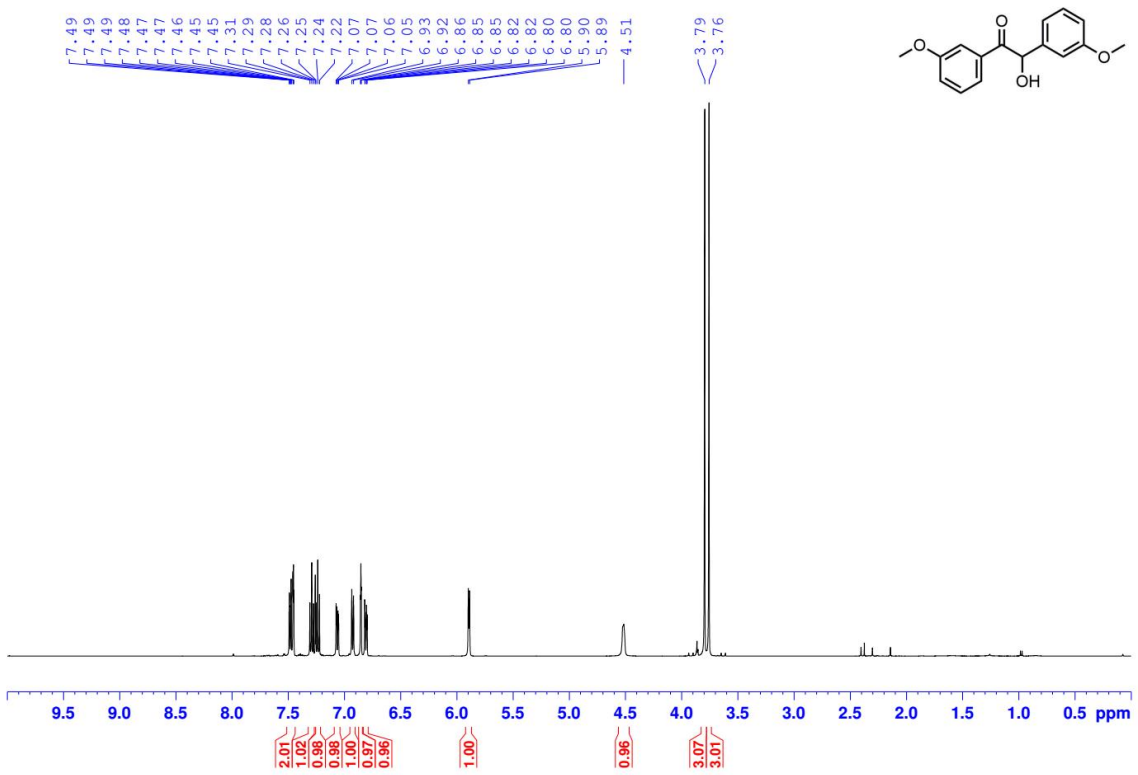


2-hydroxy-1,2-bis(3-methoxyphenyl)ethan-1-one (8)

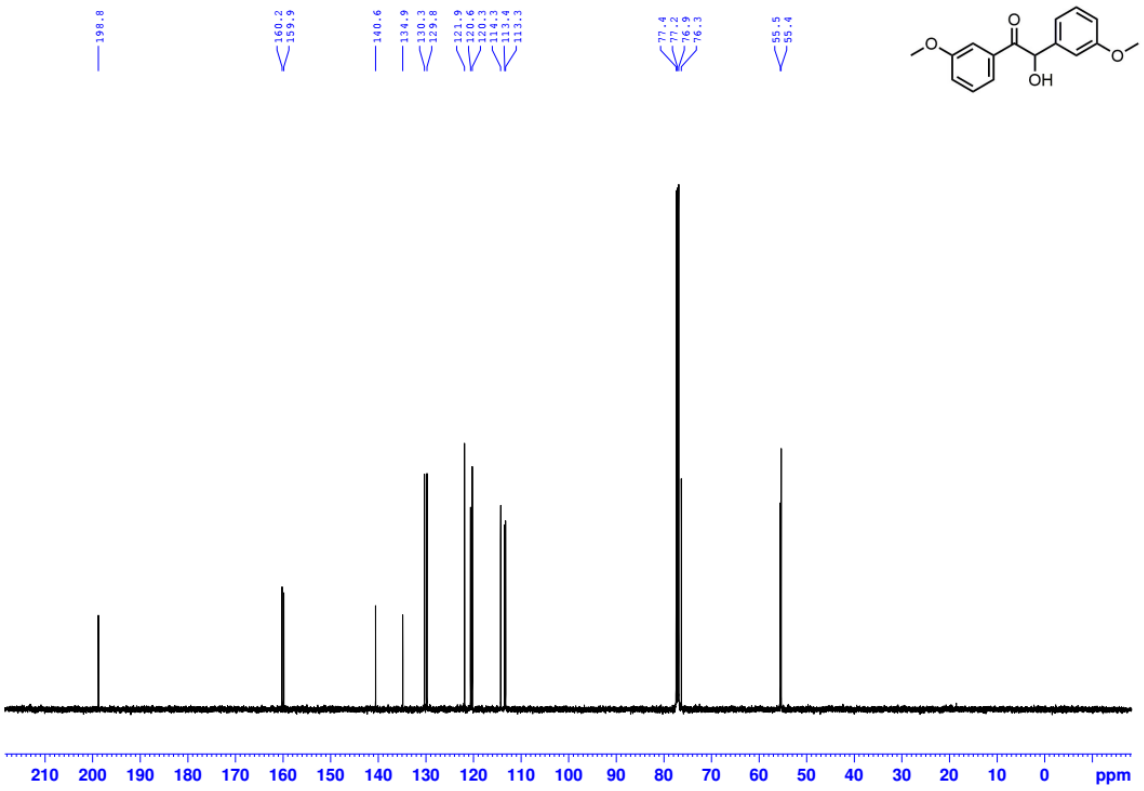


The crude product was purified by column chromatography (30% EtOAc/Hexanes) to afford 67 mg (98%) of compound **8** as a white solid. R_f = 0.3 (25% EtOAc/Hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.49 – 7.45 (m, 2H), 7.29 (t, *J* = 8.0 Hz, 1H), 7.24 (t, *J* = 7.9 Hz, 1H), 7.06 (dd, *J* = 8.2, 2.6 Hz, 1H), 6.93 (d, *J* = 7.7 Hz, 1H), 6.85 (t, *J* = 1.7 Hz, 1H), 6.81 (dd, *J* = 8.3, 2.5 Hz, 1H), 5.89 (d, *J* = 5.7 Hz, 1H), 4.52 (br s, 1H), 3.97 (s, 3H), 3.76 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 198.8, 160.2, 159.9, 140.6, 134.9, 130.3, 129.8, 121.9, 120.6, 120.3, 114.3, 113.4, 113.3, 77.3, 55.5, 55.4.

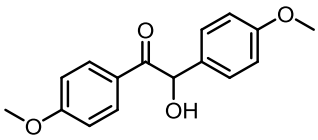
^{1}H NMR spectrum (8)



^{13}C NMR spectrum (8)

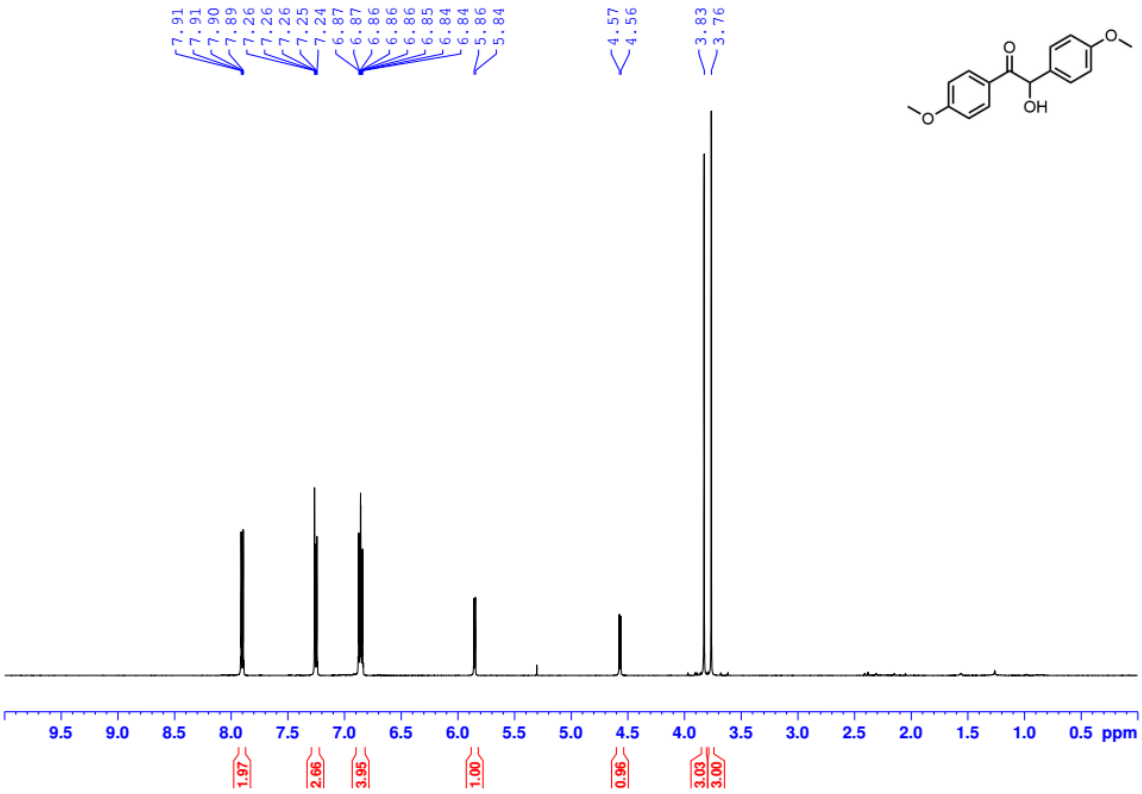


2-Hydroxy-1,2-bis(4-methoxyphenyl)ethan-1-one (9)

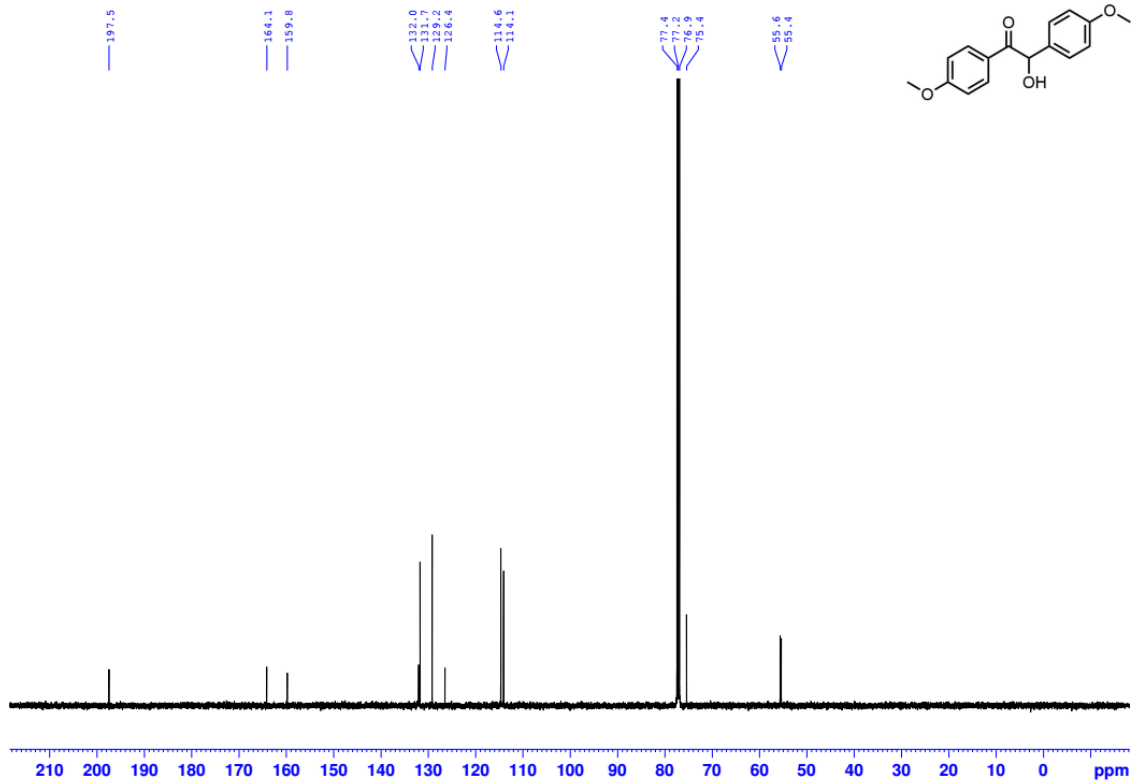


The crude product was purified by column chromatography (30% EtOAc/Hexanes) to afford 46 mg (67%) of compound **9** as a white solid. R_f = 0.3 (30% EtOAc/Hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.91-7.89 (m, 2H), 7.26 – 7.26 (m, 2H), 6.87 – 6.84 (m, 4H), 5.85 (d, *J* = 6.0 Hz, 1H), 4.57 (d, *J* = 6.0 Hz, 1H), 3.87 (s, 3H), 3.76 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 197.5, 164.1, 159.8, 132.0, 131.7, 129.2, 126.4, 114.6, 114.1, 75.4, 55.6, 55.4

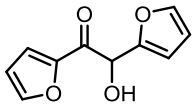
^{1}H NMR spectrum (9)



^{13}C NMR spectrum (9)

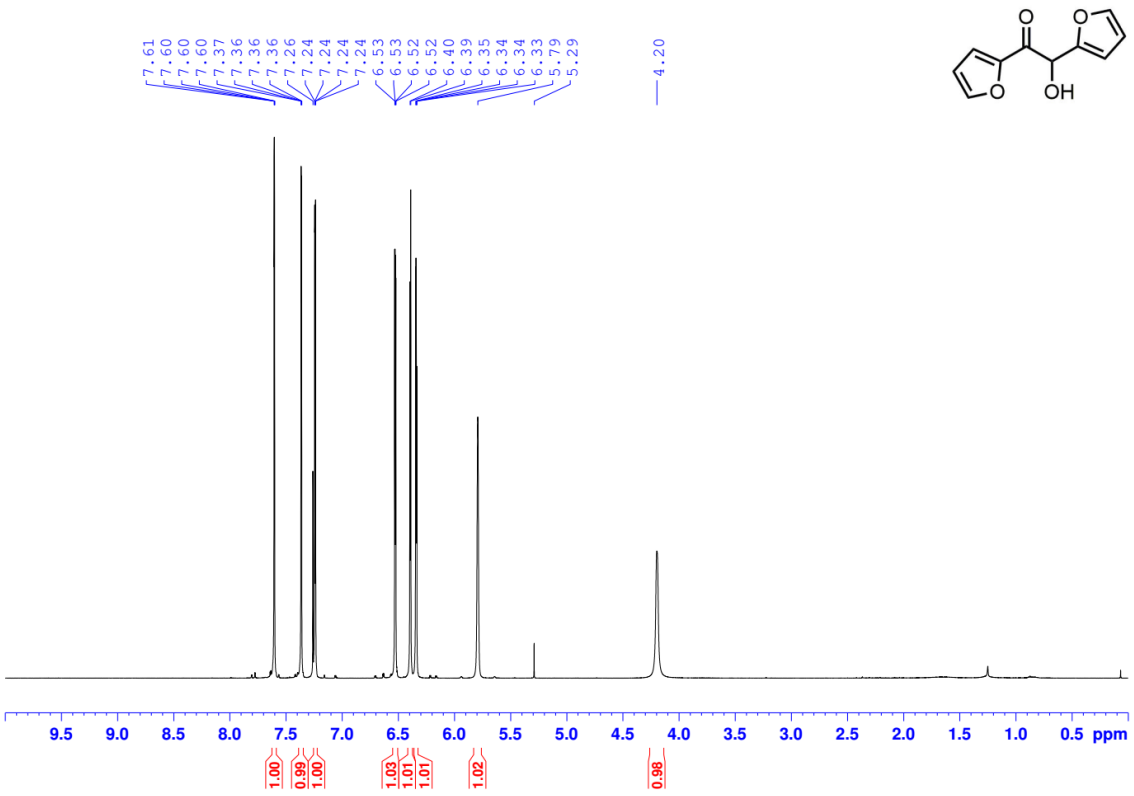


1,2-di(furan-2-yl)-2-hydroxyethan-1-one (10)

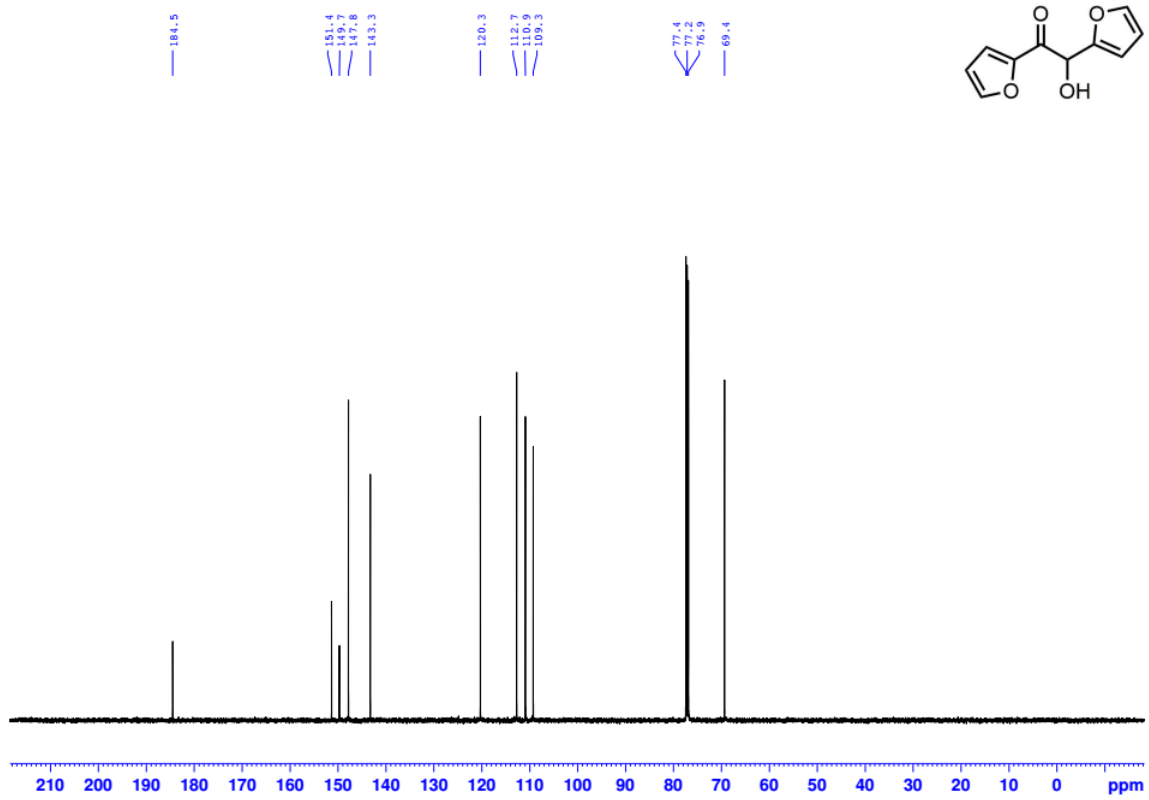


The crude product was purified by column chromatography (30% EtOAc/Hexanes) to afford 47 mg (97%) of compound **10** as a white solid. R_f = 0.3 (25% EtOAc/Hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.60 (dd, *J* = 1.6, 0.6 Hz, 1H), 7.36 (dd, *J* = 1.8, 0.7 Hz, 1H), 7.24 (dd, *J* = 3.7, 0.5 Hz, 1H), 6.53 (dd, *J* = 3.7, 1.7 Hz, 1H), 6.39 (d, *J* = 3.3 Hz, 1H), 6.34 (dd, *J* = 3.3, 1.8 Hz, 1H), 5.79 (s, 1H), 4.20 (br s, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 184. 5, 151.4, 149.7, 147.8, 143.3, 120.3, 112.7, 110.9, 109.3, 69.4.

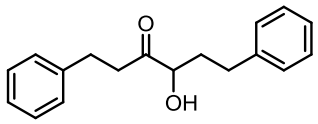
^{1}H NMR spectrum (10)



^{13}C NMR spectrum (10)

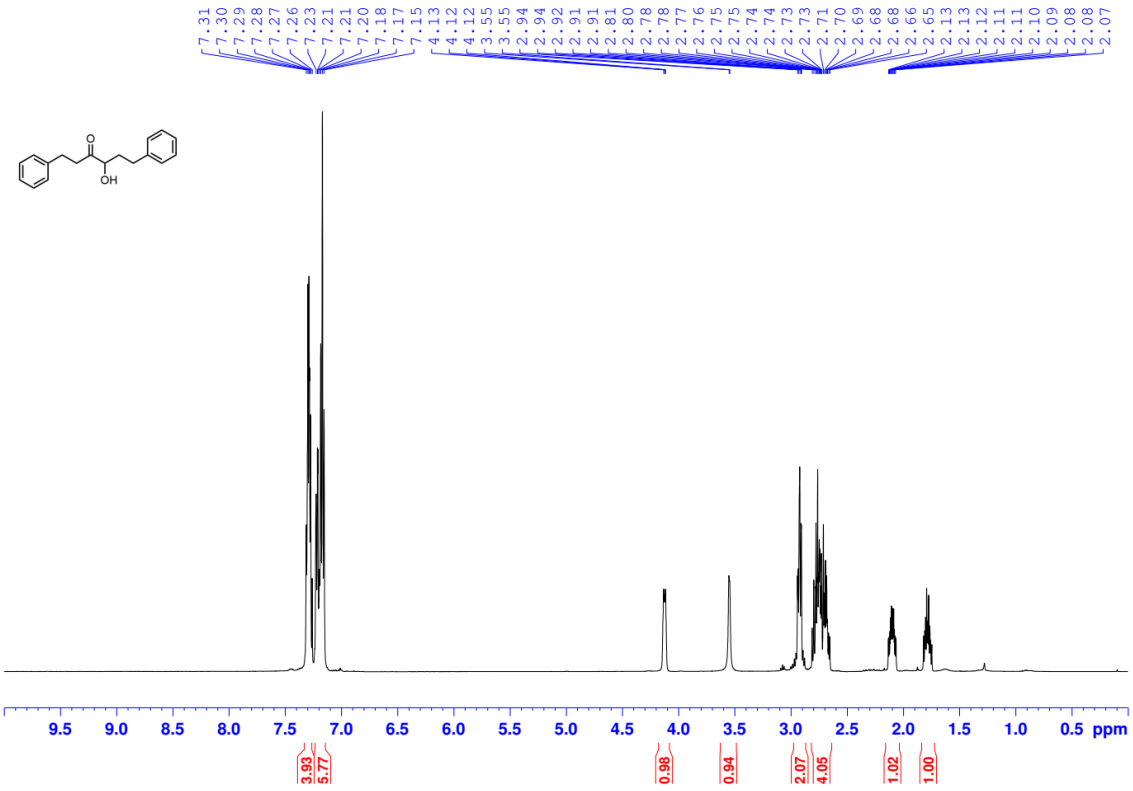


4-hydroxy-1,6-diphenylhexan-3-one (11)

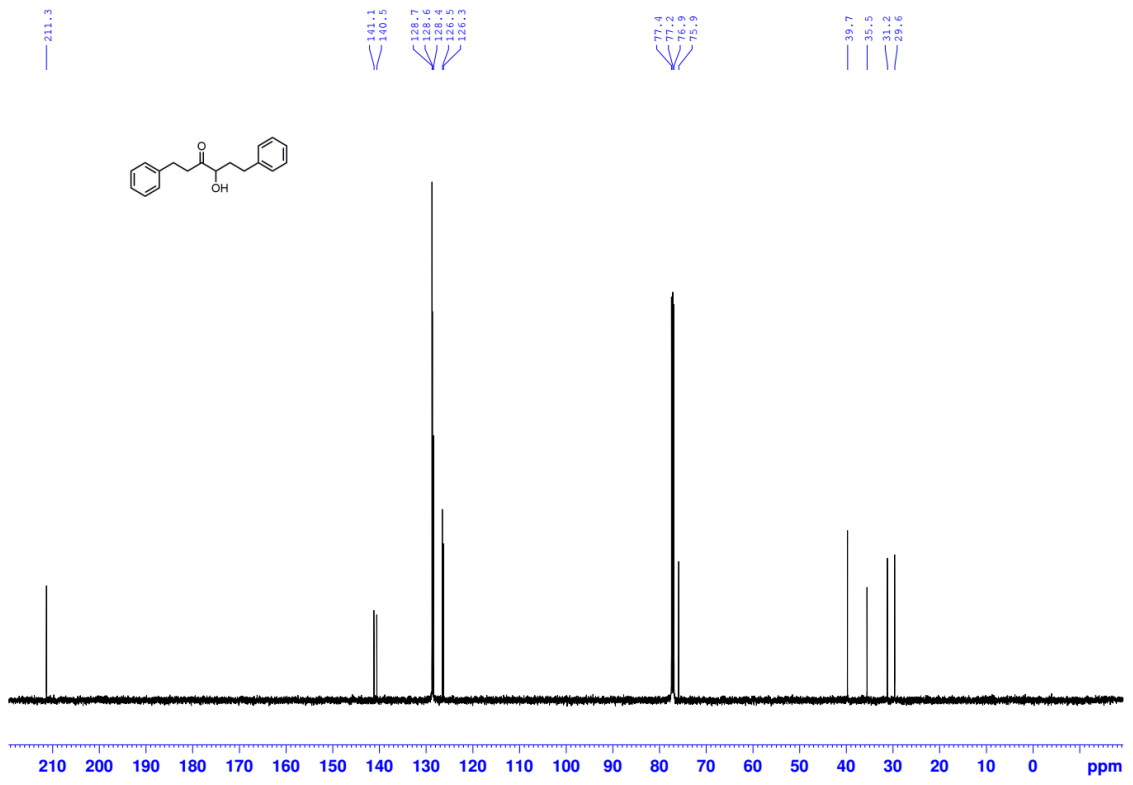


The crude product was purified by column chromatography (15% EtOAc/Hexanes) to afford 64 mg (96%) of compound **11** as a pale yellow liquid. R_f = 0.4 (25% EtOAc/Hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.31 – 7.27 (m, 4H), 7.23 – 7.16 (m, 6H), 4.12 (t, *J* = 4 Hz, 1H), 3.55 (d, *J* = 3.1 Hz, 1H), 2.97 – 2.88 (m, 2H), 2.81 – 2.65 (m, 4H), 2.13 – 2.06 (m, 1H), 1.82 – 1.75 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 211.3, 141.1, 140.5, 128.7, 128.6, 128.4, 126.5, 126.3, 75.9, 39.7, 35.5, 31.2, 29.6.

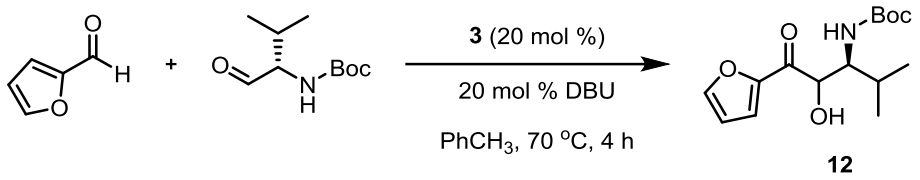
^{1}H NMR spectrum (11)



^{13}C NMR spectrum (11)



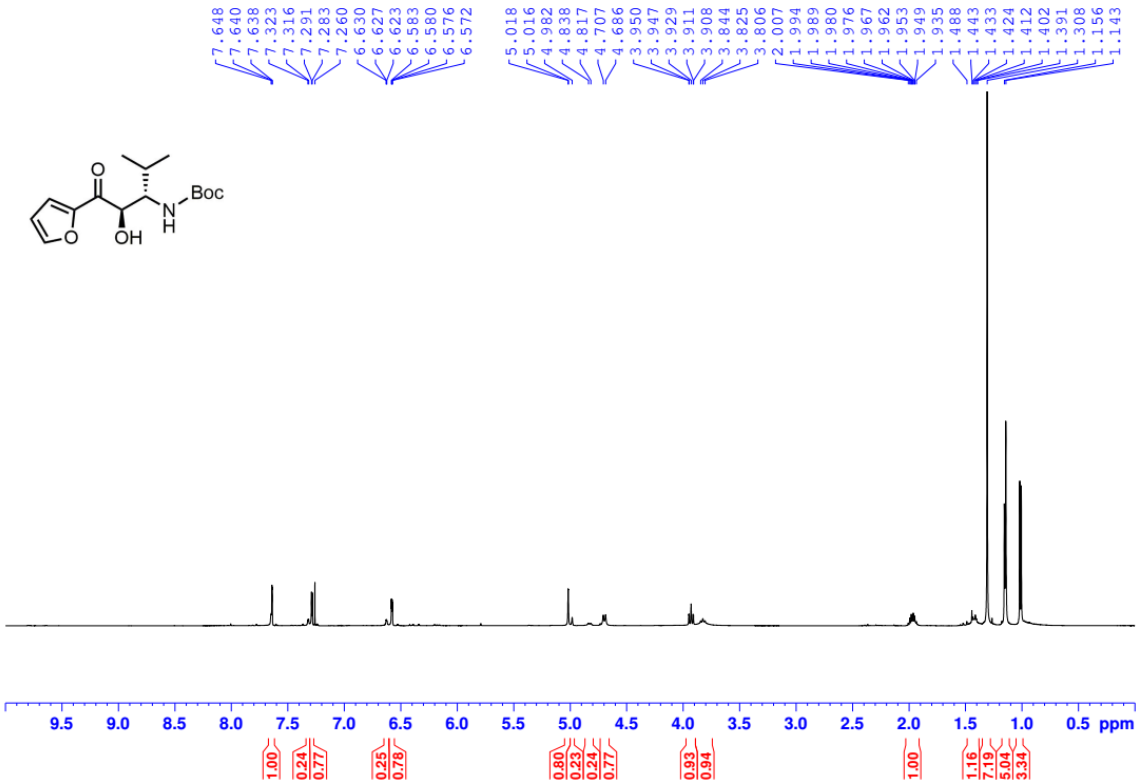
Tert-butyl ((3S)-1-(furan-2-yl)-2-hydroxy-4-methyl-1-oxopentan-3-yl)carbamate (12)[6]



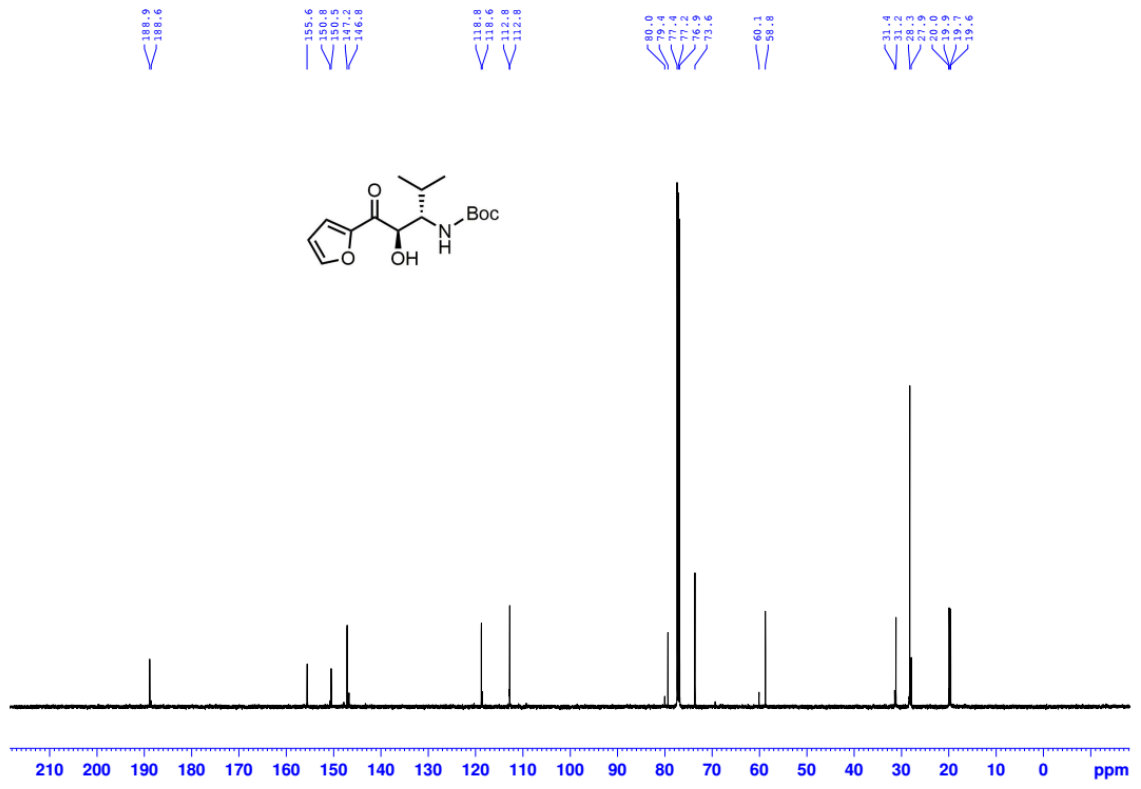
12

To an oven dried 10 mL Schlenk tube containing a stir bar, the catalyst **3** (26.8 mg, 0.5 mmol) and *N*-boc valinal (50.3 mg, 0.25 mmol) were added. The Schlenk tube was closed with a septum and attached to a double manifold. The tube was evacuated and refilled with argon three times. Then furfural (31 µl, 0.38 mmol) and dry toluene (0.5 mL) followed by DBU (7.5 µl, 0.05 mmol) were added sequentially. The septum was replaced with a cold finger condenser under argon, and the reaction mixture was heated to 70 ^{o}C and stirred for 4 hours. The mixture was cooled to room temperature, diluted with EtOAc (1 mL), the mixture was passed through pad of silica gel using EtOAc as eluent (2 mL) and concentrated. The crude product was purified by column chromatography (15% EtOAc/Hexanes) to afford 42 mg (56%) of compound **12** as a white solid. R_f = 0.3 (25% EtOAc/Hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.65 – 7.64 (m, 1H), 7.32 (d, *J* = 3.5 Hz, 0.24H), 7.29 (d, *J* = 3.6 Hz, 0.77H), 6.63 - 6.62 (m, 0.25H), 6.58 – 6.57 (m, 0.78H), 5.01 (s, 0.80H), 4.98 (s, 0.23 H), 4.83 (d, *J* = 10.6 Hz, 0.24H), 4.70 (d, *J* = 10.3 Hz, 0.77H), 3.95 – 3.90 (m, 1H), 3.83 (t, *J* = 9.6 Hz, 1H), 2.00 – 1.94 (m, 1H), 1.44 – 1.39 (m, 1H), 1.31 (s, 7H), 1.15 (d, *J* = 6.6 Hz, 5H), 1.01 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 188.9, 188.6, 155.6, 150.8, 150.5, 147.2, 146.8, 188.8, 118.6, 112.8, 12.8, 80.0, 79.4, 73.6, 60.1, 58.8, 31.4, 31.2, 28.3, 27.9, 20.0, 19.9, 19.7, 19.6.

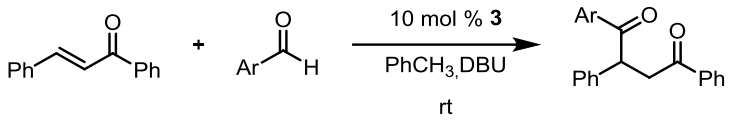
^{1}H NMR spectrum (12)



^{13}C NMR spectrum (12)



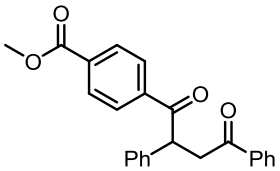
Stetter reaction



General Procedure for Stetter reaction

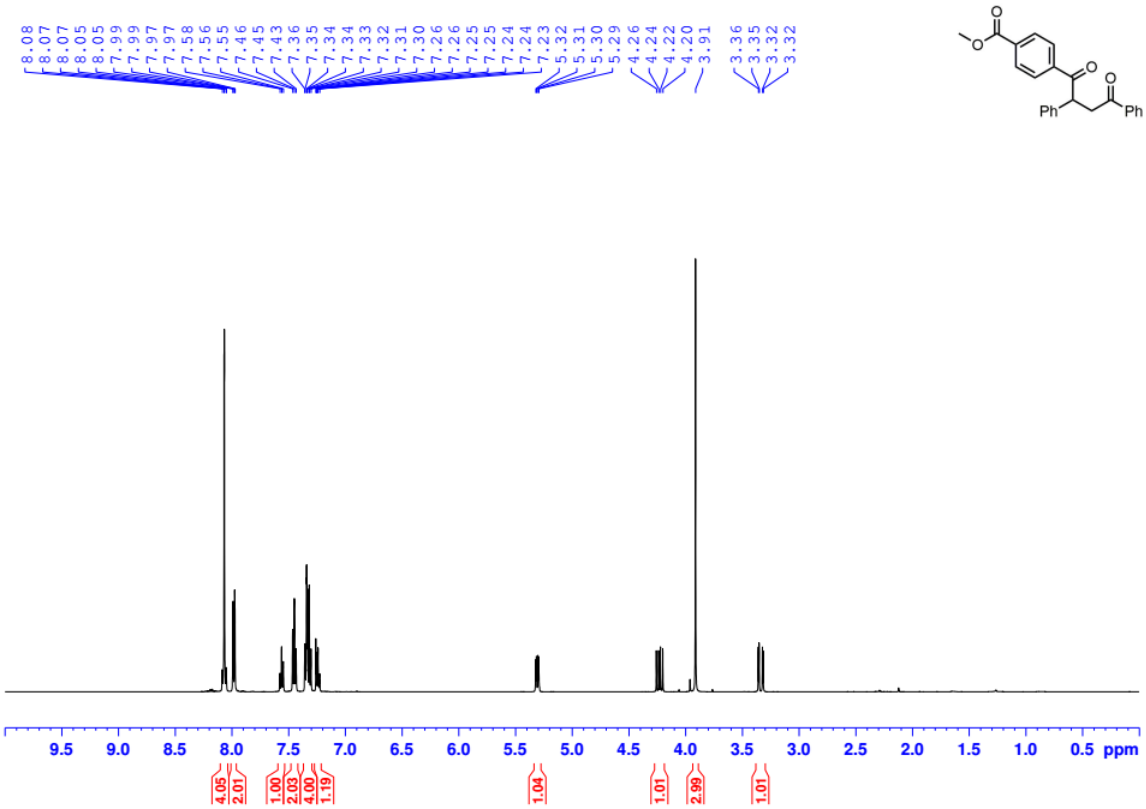
Chalcone (52 mg, 0.25 mmol) and catalyst **3** (13.4 mg, 0.025 mmol) were added to oven dried Schlenk tube equipped with magnetic stir bar and septum, then side arm was connected to the double manifold. The Schlenk tube was evacuated and refilled with argon for three cycles. Aldehyde (0.33 mmol), toluene (0.5 ml) and DBU (3.7 µl, 0.025 mmol) were added to the Schlenk tube under argon. The reaction mixture was stirred at room temperature for 3-5 h, and its progress was monitored by tlc. The reaction mixture was passed through a Pasteur pipette containing a pad of silica gel using ethyl acetate as eluent and concentrated. The resulting crude compound was purified by FCC with ethyl acetate in hexanes as an eluent.

Methyl 4-(4-oxo-2,4-diphenylbutanoyl)benzoate (13)

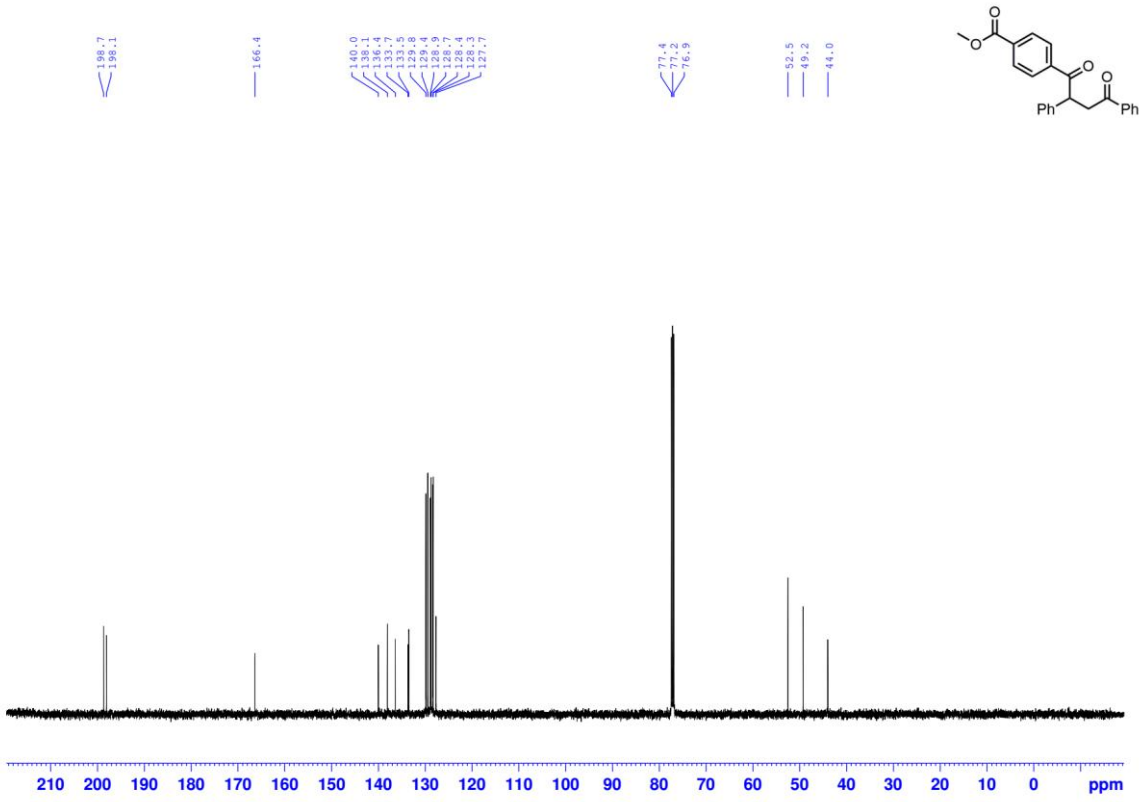


The crude product was purified by column chromatography (15% EtOAc/Hexanes) to afford 91 mg (98%) of compound **13** as a beige solid. R_f = 0.3 (20% EtOAc/Hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 8.09 – 8.05 (m, 4H), 7.99 – 7.97 (m, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.36 – 7.30 (m, 4H), 7.26 – 7.23 (m, 1H), 5.31 (dd, *J* = 10.2, 3.5 Hz, 1H), 4.23 (dd, *J* = 18.1, 10.2 Hz, 1H), 3.91 (s, 3H), 3.34 (dd, *J* = 18.1, 3.6 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 198.7, 198.1, 166.4, 140.0, 138.1, 136.4, 133.7, 133.5, 129.8, 129.4, 128.9, 128.7, 128.4, 128.3, 127.7, 52.5, 49.2, 44.0.

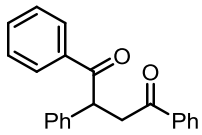
^{1}H NMR spectrum (13)



^{13}C NMR spectrum (13)

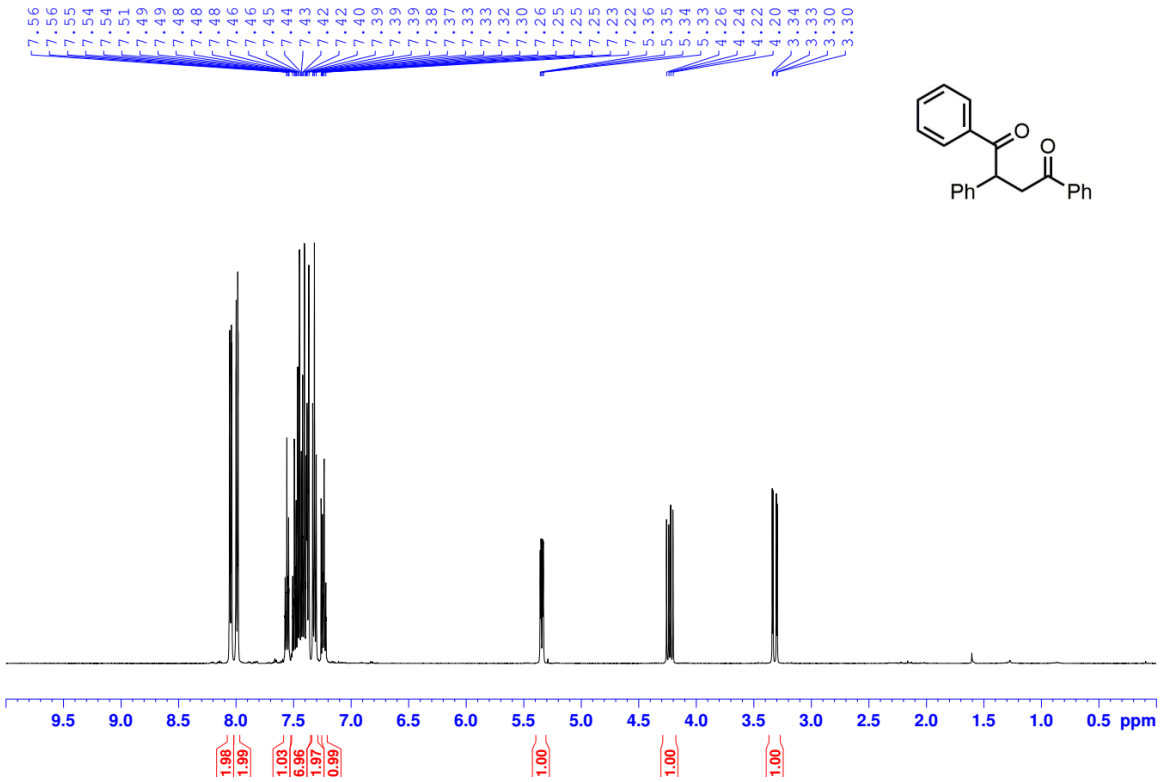


1,2,4-triphenylbutane-1,4-dione (14)

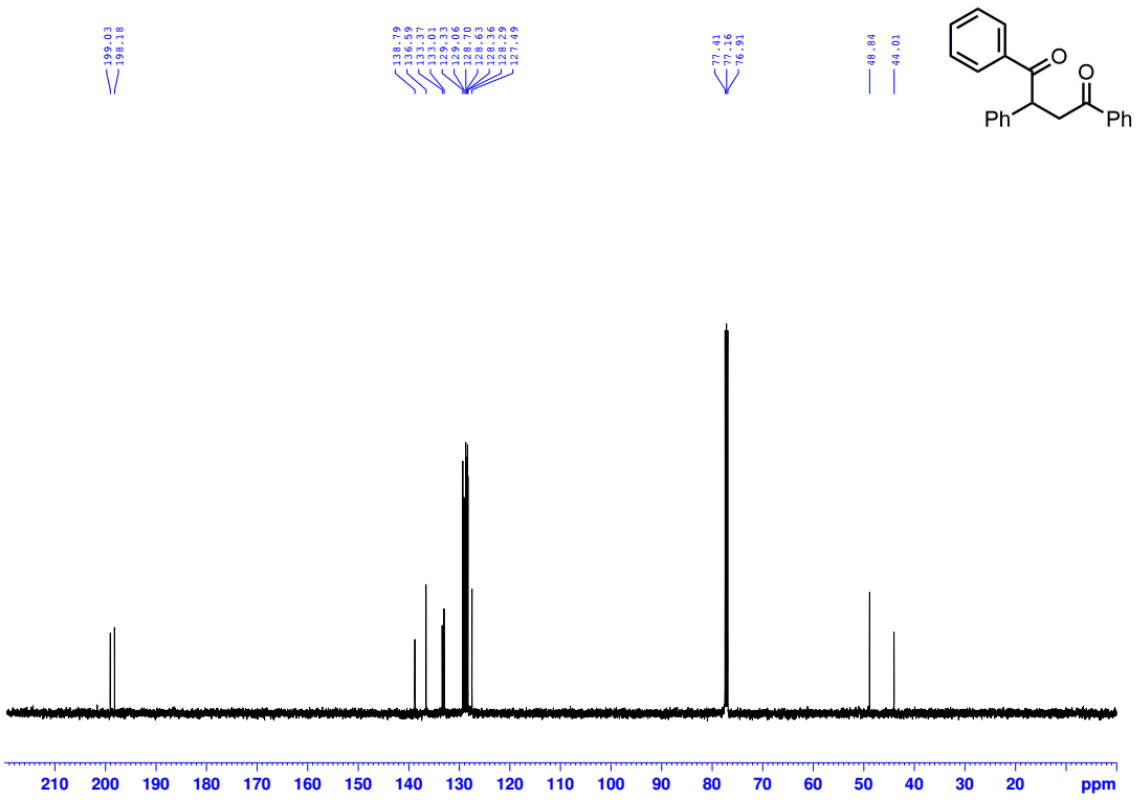


The crude product was purified by column chromatography (12% EtOAc/Hexanes) to afford 78 mg (99%) of compound **14** as a white solid. The same reaction on a 1 mmol scale (208 mg of chalcone) furnished 310 mg of product (97%). R_f = 0.4 (25% EtOAc/Hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 8.05 – 8.04 (m, 2H), 8.00 – 7.98 (m, 2H), 7.57 – 7.54 (m, 1H), 7.51 – 7.37 (m, 7H), 7.33 – 7.30 (m, 2H), 7.25 – 7.21 (m, 1H), 5.34 (dd, *J* = 10.1, 3.7 Hz, 1H), 4.23 (dd, *J* = 18.1, 10.1 Hz, 1H), 3.32 (dd, *J* = 18.1, 3.7 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 199.0, 198.2, 138.8, 136.6, 133.4, 133.0, 129.3, 129.1, 128.7, 128.6, 128.4, 128.3, 127.5, 48.8, 44.0

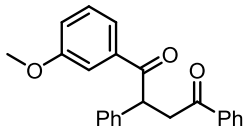
^{1}H NMR spectrum (14)



^{13}C NMR spectrum (14)

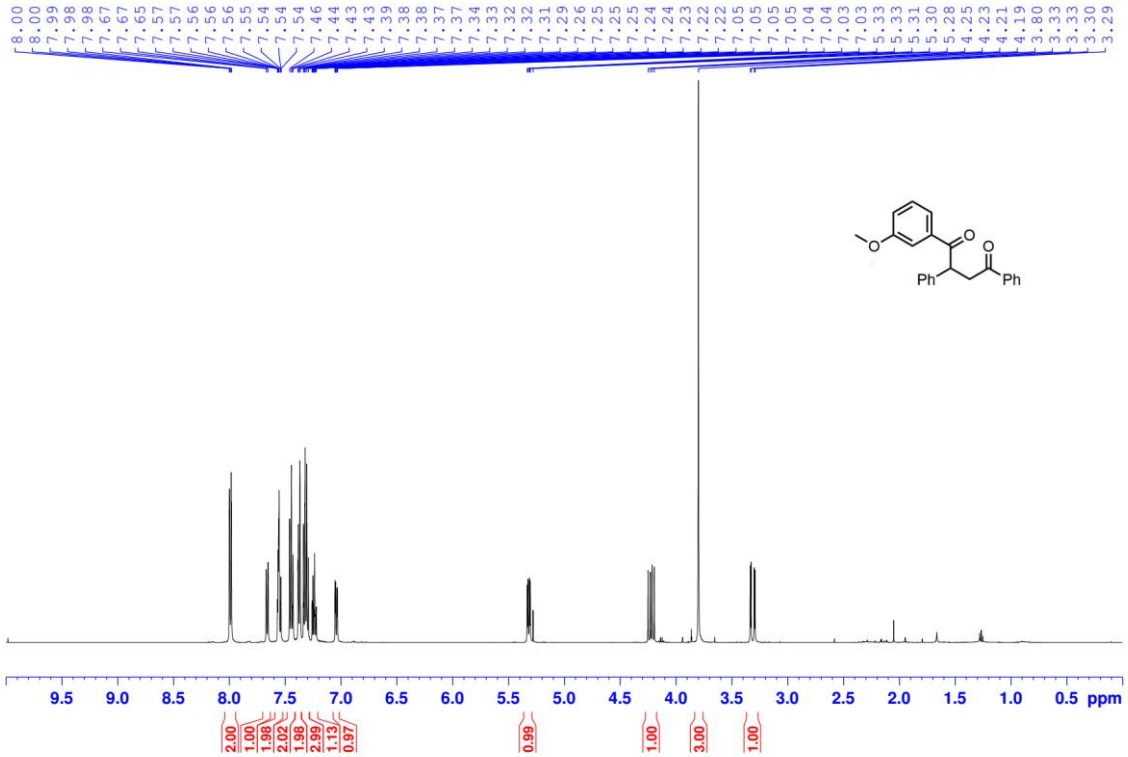


1-(3-methoxyphenyl)-2,4-diphenylbutane-1,4-dione (15)

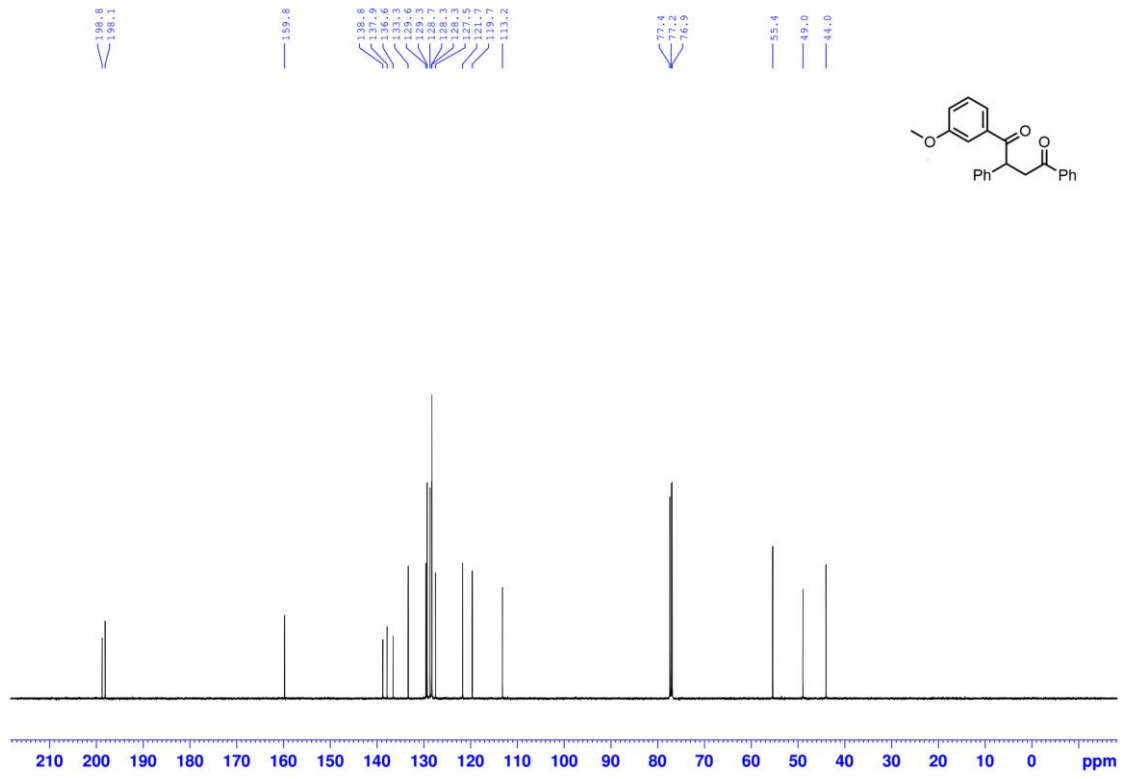


The crude product was purified by column chromatography (12% EtOAc/Hexanes) to afford 83 mg (97%) of compound **15** as a white solid. R_f = 0.3 (25% EtOAc/Hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 8.00 – 7.98 (m, 2H), 7.67 – 7.65 (m, 1H), 7.57 – 7.54 (m, 2H), 7.46 – 7.43 (m, 2H), 7.39 – 7.37 (m, 2H), 7.34 – 7.31 (m, 3H), 7.25 – 7.22 (m, 1H), 7.04 (ddd, *J* = 8.3, 2.7, 0.8 Hz, 1H), 5.32 (dd, *J* = 10.1, 3.7 Hz, 1H), 4.22 (*J* = 18.0, 10.2 Hz, 1H), 3.80 (s, 3H), 3.32 (dd, *J* = 18, 3.7 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 198.8, 198.1, 159.8, 138.8, 137.9, 136.6, 133.3, 129.6, 129.3, 128.7, 128.3, 128.3, 127.5, 121.7, 119.7, 113.2, 55.4, 49.0, 44.0

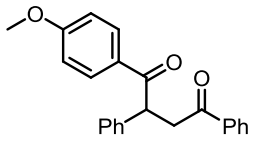
^{1}H NMR spectrum (15)



^{13}C NMR spectrum (15)

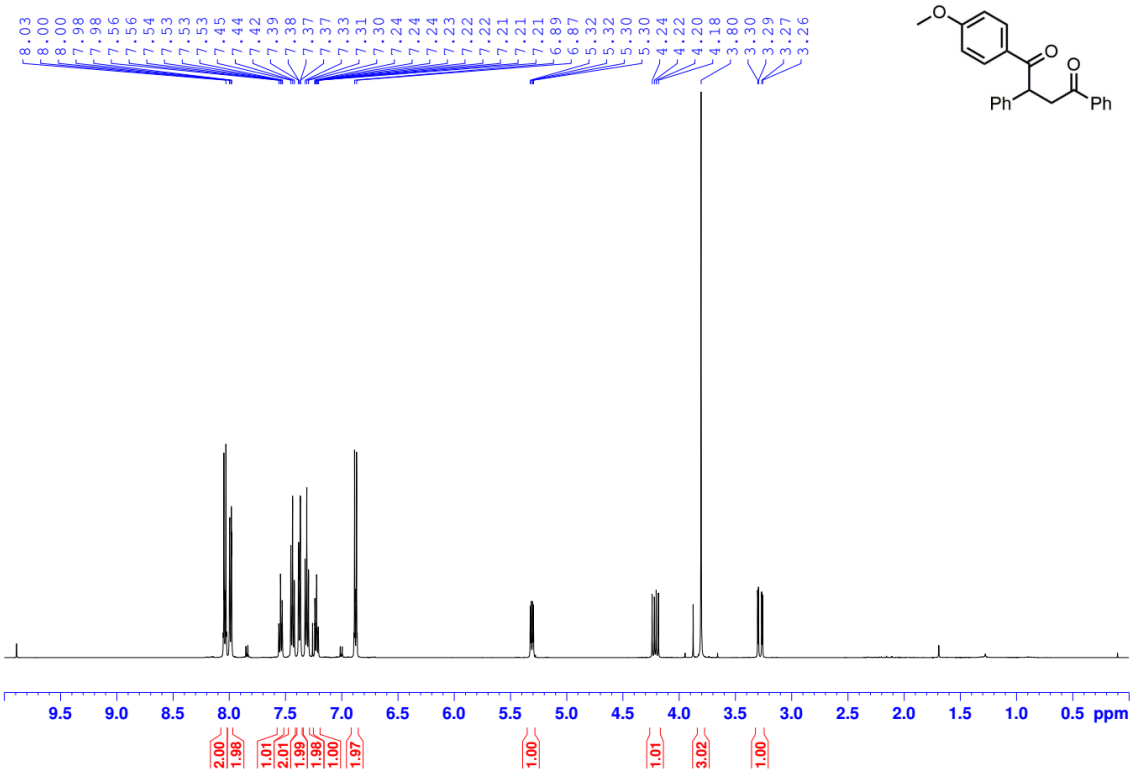


1-(4-methoxyphenyl)-2,4-diphenylbutane-1,4-dione (16)

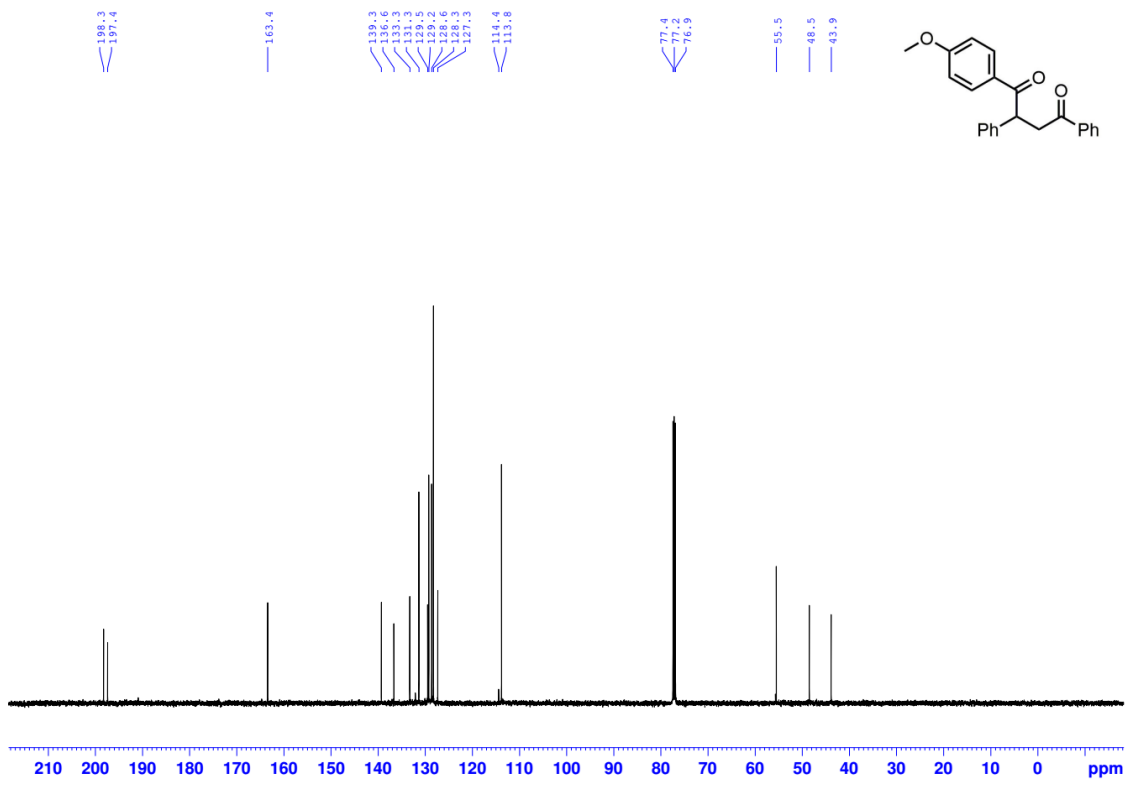


The crude product was purified by column chromatography (15 % EtOAc/Hexanes) to afford 84 mg (98%) of compound **16** as a white solid. R_f = 0.3 (25% EtOAc/Hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 8.05 - 8.03 (m, 2H), 8.00 – 7.98 (m, 2H), 7.56 – 7.53 (m, 1H), 7.46 – 7.42 (m, 2H), 7.39 – 7.37 (m, 2H), 7.33 – 7.30 (m, 2H), 7.24 – 7.21 (m, 1H), 6.89 – 6.87 (m ,2H), 5.31 (dd, *J* = 10.0, 3.8 Hz, 1H), 4.21 (dd, *J* = 17.8, 9.9 Hz, 1H), 3.80 (s, 3H), 3.28 (dd, *J* = 17.8, 3.8 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 198.3, 197.4, 163.4, 139.3, 136.6, 133.3, 131.3, 129.5, 129.2, 128.6, 128.3, 127.3, 114.4, 113.8, 55.5, 48.5, 43.9

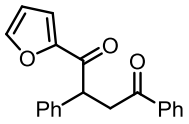
^{1}H NMR spectrum (16)



^{13}C NMR spectrum (16)

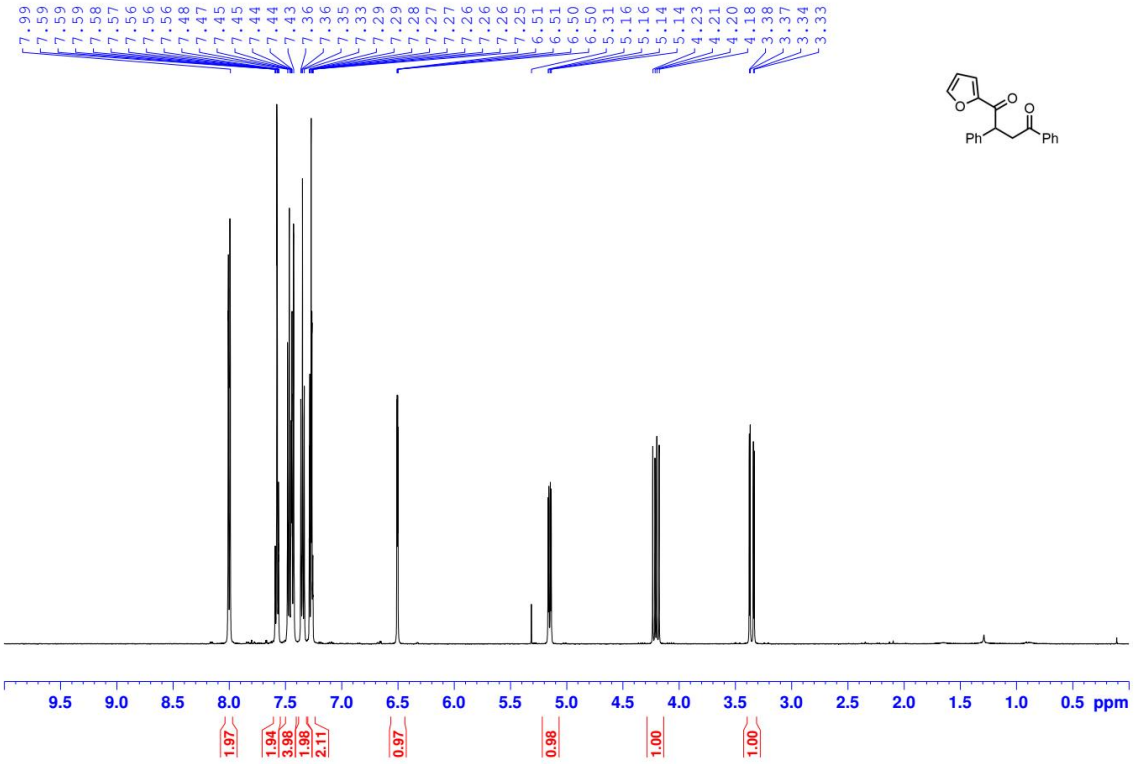


1-(furan-2-yl)-2,4-diphenylbutane-1,4-dione (17)

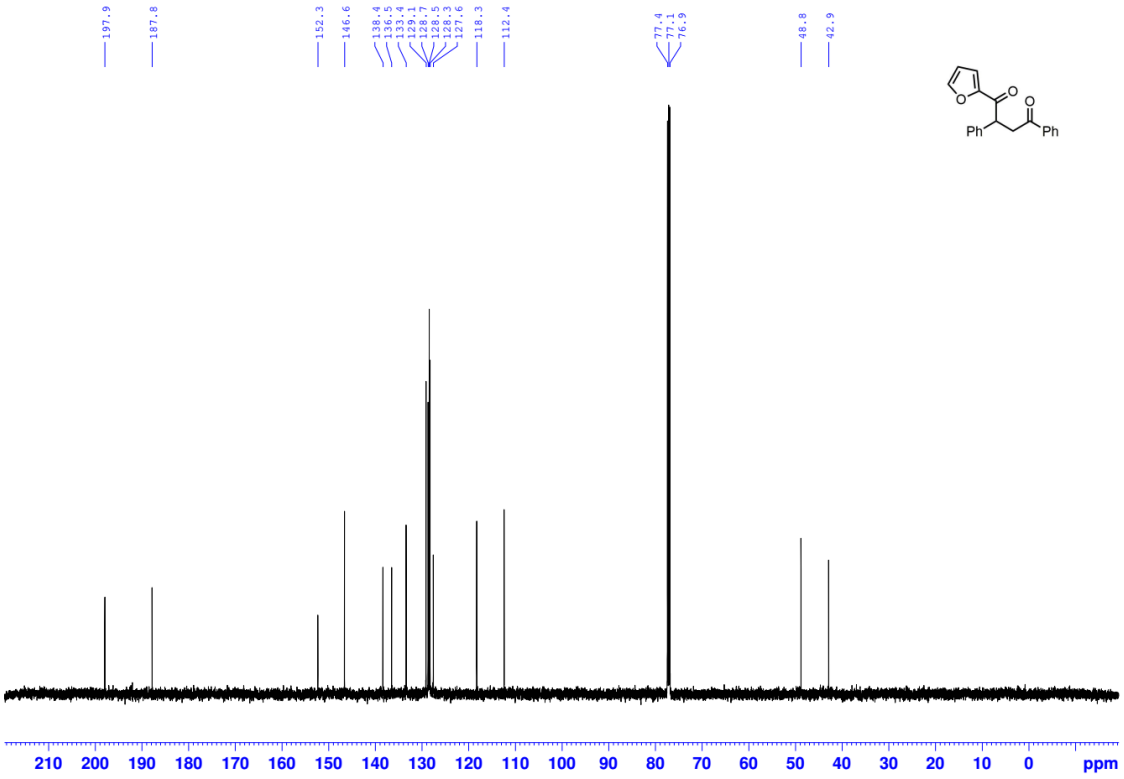


The crude product was purified by column chromatography (15% EtOAc/Hexanes) to afford 75 mg (98%) of compound **17** as a white solid. R_f = 0.3 (25% EtOAc/Hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.98 – 7.96 (m, 2H), 7.57 – 7.53 (m, 2H), 7.46 – 7.40 (m, 4H), 7.34 -7.31 (m, 2H), 7.26 – 7.23 (m, 2H), 6.48 (dd, *J* = 3.6, 1.7 Hz, 1H), 5.13 (dd, *J* = 10.2, 3.8 Hz, 1H), 4.18 (dd, *J* = 18.1, 10.3 Hz, 1H), 3.33 (dd, *J* = 18.1, 3.8 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 197.9, 187.8, 152.3, 146.6, 138.4, 136.5, 133.4, 129.1, 128.7, 128.5, 128.3, 127.6, 118.3, 112.4, 48.8, 42.9

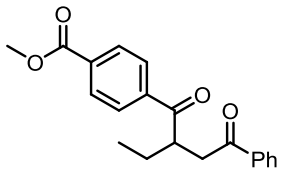
^{1}H NMR spectrum (17)



^{13}C NMR spectrum (17)

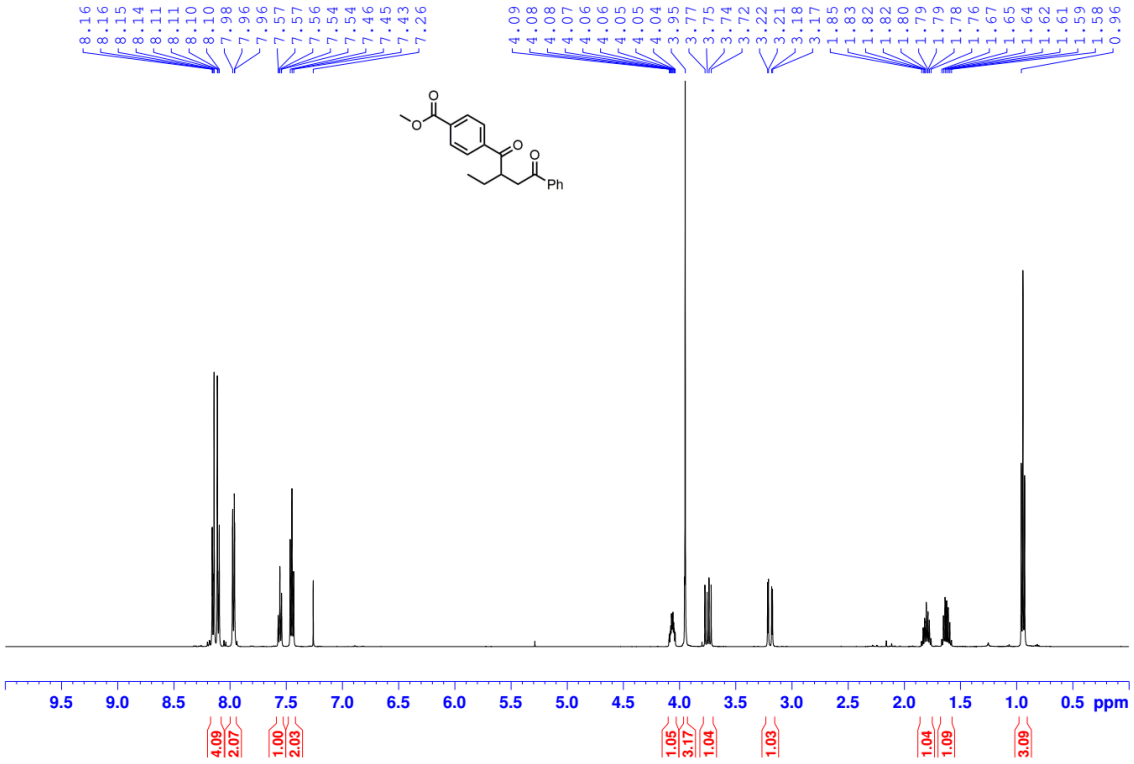


methyl 4-(2-ethyl-4-oxo-4-phenylbutanoyl)benzoate (18)

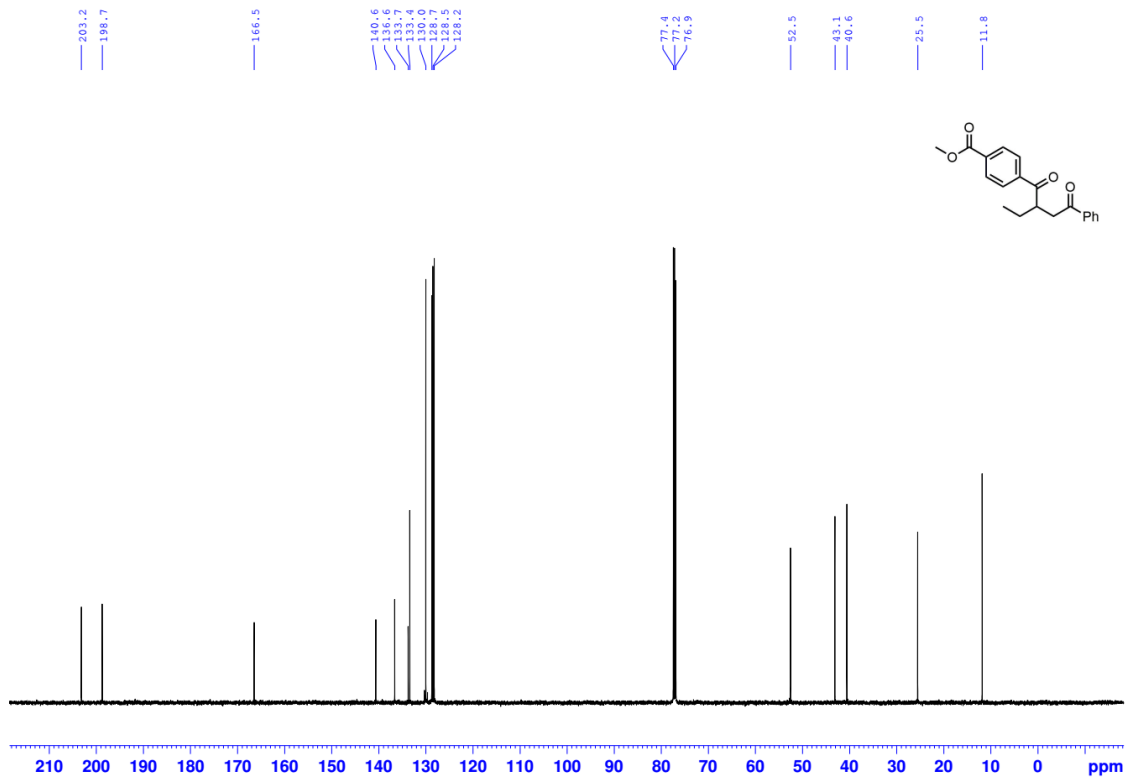


The crude product was purified by column chromatography (15% EtOAc/Hexanes) to afford 78 mg (96%) of compound **18** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 8.16 – 8.10 (m, 4H), 7.98 – 7.96 (m, 2H), 7.57 – 7.54 (m, 1H),7.47 – 7.43 (m, 2H), 4.09 – 4.04 (m, 1H0, 3.95 (s, 1H), 3.75 (dd, *J* = 18.1, 9.6 Hz, 1H), 3.19 (dd, *J* = 18.1, 3.9 Hz, 1H), 1.85 – 1.76 (m, 1H), 1.67 – 1.58 (m, 1H), 0.94 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 203.4, 198.9, 166.7, 140.8, 136.8, 134.0, 133.6, 130.2, 128.9, 128.7, 128.4, 52.7, 43.3, 40.8, 25.7, 12.02.

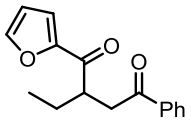
^{1}H NMR spectrum (18)



^{13}C NMR spectrum (18)

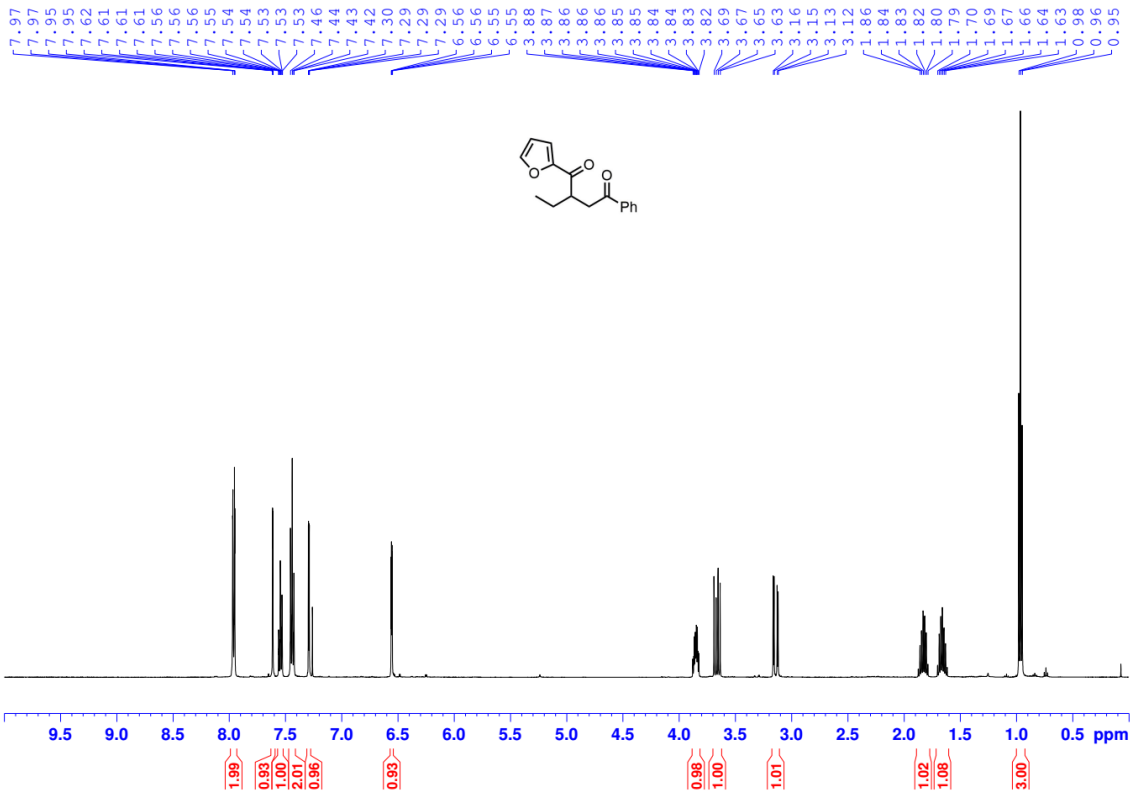


2-ethyl-1-(furan-2-yl)-4-phenylbutane-1,4-dione (19)

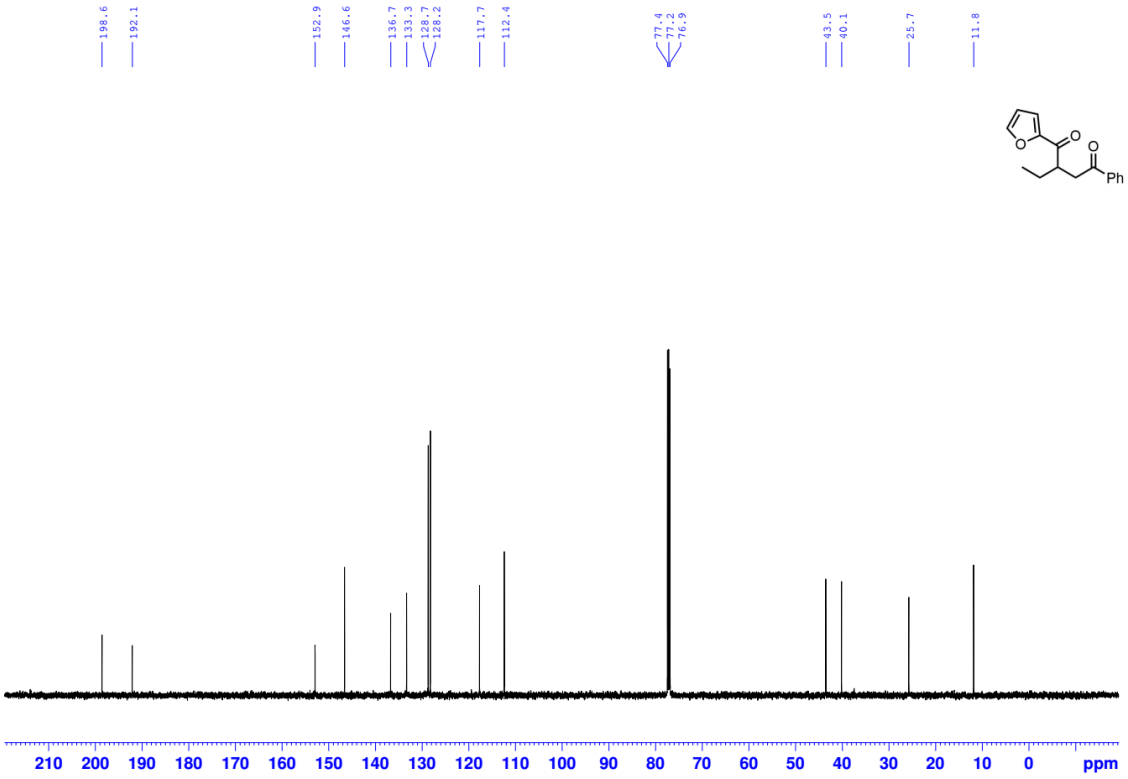


This reaction was done with 20 mol % catalyst and base at 125 ºC for 1h. The crude product was purified by column chromatography (30% EtOAc/Hexanes) to afford 27 mg (42%) of compound **19** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.97 – 7.95 (m, 2H), 7.62 – 7.61 (m, 1H), 7.55 (tt, *J* = 8.6, 1.2 Hz, 1H), 7.46 – 7.42 (m, 2H), 7.29 (dd, *J* = 3.5, 0.5 Hz, 1H), 6.56 (dd, *J* = 3.6, 1.7 Hz, 1H), 3.88 – 3.82 (m, 1H), 3.66 (dd, *J* = 18.0, 9.3 Hz, 1H), 3.14 (dd, *J* = 18.0, 4.3 Hz, 1H), 1.87 – 1.79 (m, 1H), 1.70 – 1.62 (m, 1H), 0.96 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 198.6, 192.1, 152.9, 146.6, 136.7, 133.3, 128.7, 128.2, 117.7, 112.4, 43.5, 40.1, 25.7, 11.8; **FTIR** (KBr thin film) νmax (cm-1): 2966, 1672; **HRMS** (EI+) m/z calculated for $C_{16}H_{16}O_3$ [M]+: 256.1099; found: 256.1096.

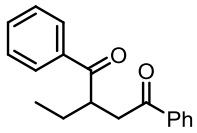
^{1}H NMR spectrum (19)



^{13}C NMR spectrum (19)

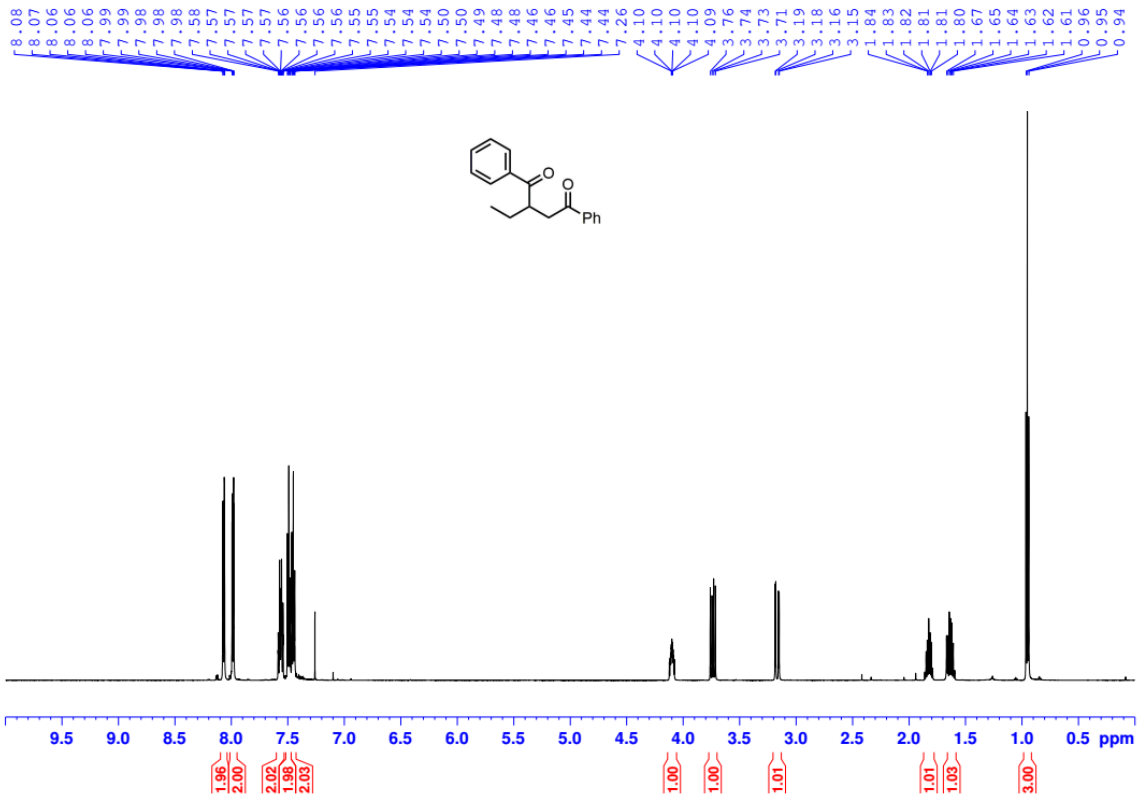


2-ethyl-1,4-diphenylbutane-1,4-dione (20)

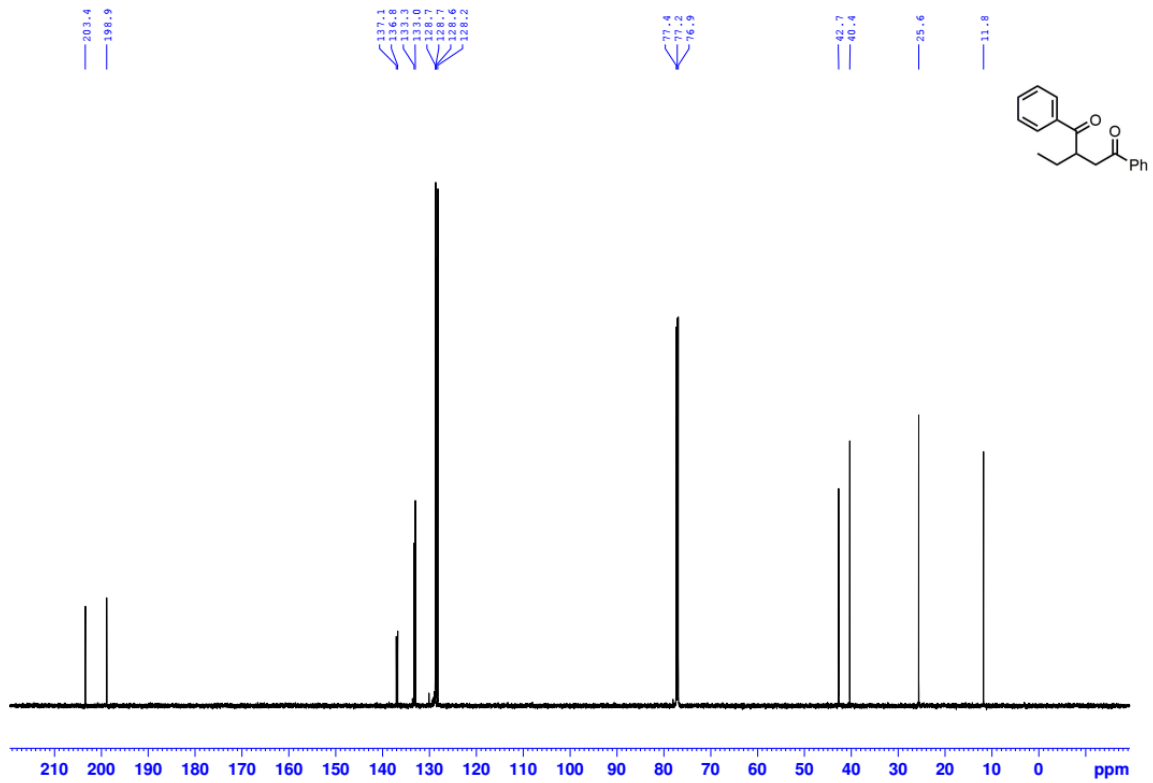


This reaction was done with 20 mol % catalyst and base at 125 ^{o}C for 1h. The crude product was purified by column chromatography (20% EtOAc/Hexanes) to afford 36 mg (54%) of compound **20** as a colorless liquid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ: 8.08 - 8.06 (m, 2H), 8.00 – 7.98 (m, 2H), 7.59 – 7.54 (m, 2H). 7.50 – 7.48 (m, 2H), 7.46 – 7.44 (m, 2H), 4.12 -4.08 (m, 1H), 3.74 (dd, *J* = 18.0, 9.2 Hz, 1H), 3.17 (dd, *J* = 18.0, 4.1 Hz, 1H), 1.86 – 1.79 (m, 1H), 1.67 – 1.59 (m, 1H), 0.95 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ: 203.4, 198.9, 137.1, 136.8, 133.3, 133.0, 128.8, 128.7, 128.6, 128.2, 42.7, 40.4, 25.6, 11.8; **FTIR** (KBr thin film) νmax (cm^{-1}): 2965, 1679; **HRMS** (EI+) m/z calculated for $C_{18}H_{18}O_2$ [M]+: 266.1307; found: 266.1307.

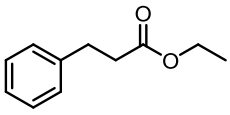
^{1}H NMR spectrum (20)



^{13}C NMR spectrum (20)

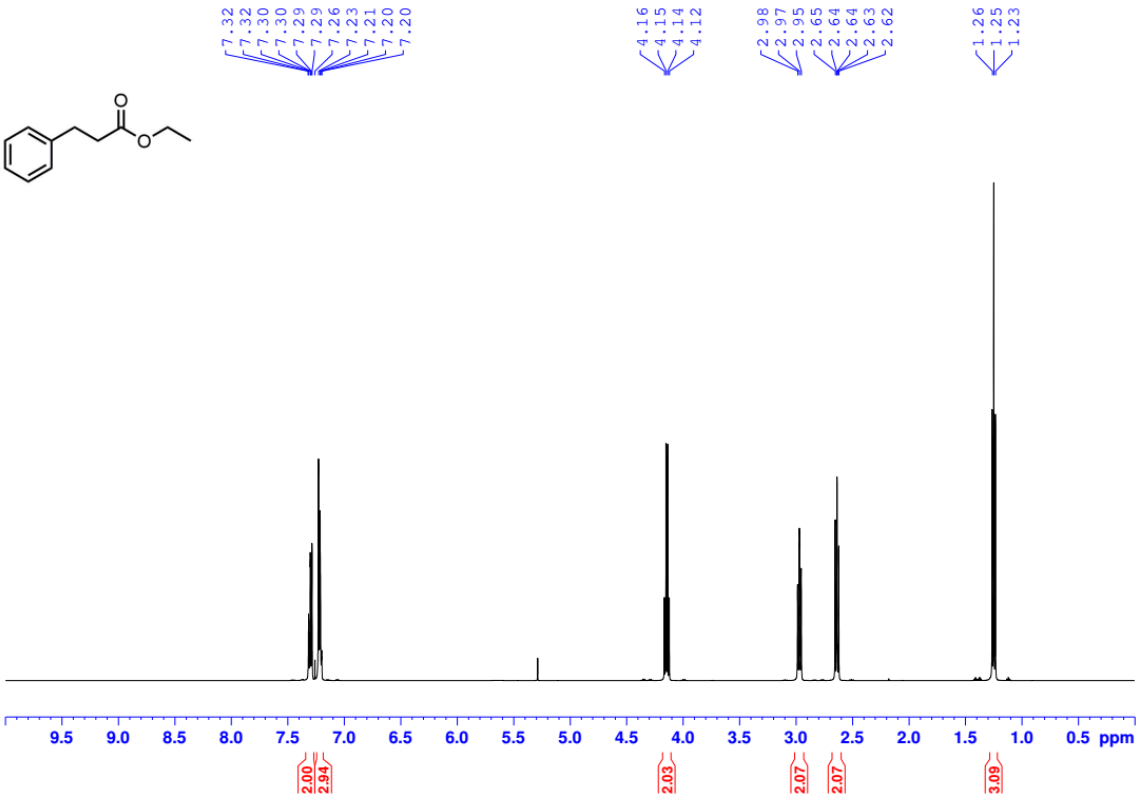


Ethyl 3-phenylpropanoate (23)[7]

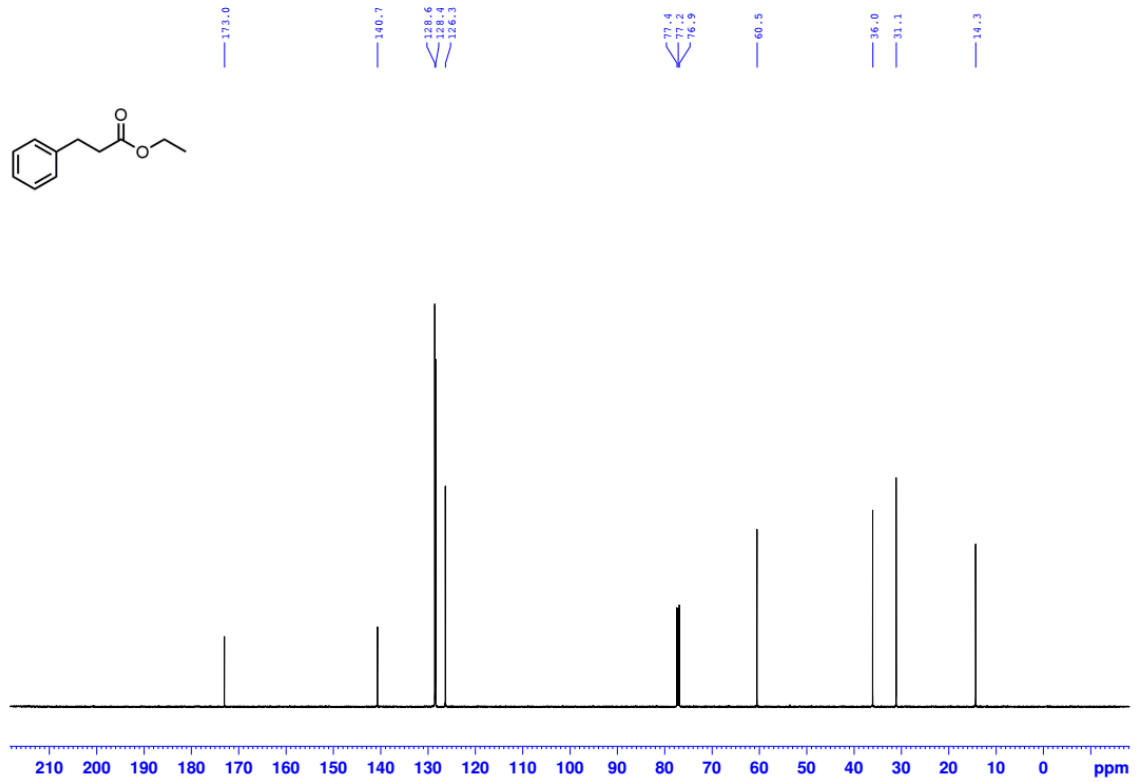


The crude product was purified by column chromatography (10% EtOAc/Hexanes) to afford 38 mg (85%) of product as a colorless liquid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.32 – 7.29 (m, 2H), 7.23 – 7.20 (m, 3H), 4.14 (q, *J* = 7.2 Hz, 2H), 2.97 (t, *J* = 7.7 Hz, 2H), 2.64 (t, *J* = 8.2 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 173.0, 140.7, 128.6, 128.4, 126.3, 60.5, 36.0, 31.1, 14.3

^{1}H NMR spectrum (23)



^{13}C NMR spectrum (23)



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