



Supporting Information

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# Cascade Reactions Using $\text{LiAlH}_4$ or Grignard Reagents in the Presence of Water

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## Materials and Instrumentation

Acetophenone, benzaldehyde, 5-nonanone, 4-methoxyphenylacetone, *p*-toluene sulfonic acid, ethylene glycol, sodium dodecyl sulfate, phenylmagnesium bromide, allylmagnesium bromide, 2-ethylhexylmagnesium bromide, copper (I) iodide, palladium (II) chloride, copper (I) chloride, oxygen, benzylamine, octanol, dicyclohexylcarbodiimide (DCC), pyridinium chlorochromate (PCC), periodic acid, cis cyclooctene, dicyclopentadiene, butyllithium, lithium aluminum hydride, trichloro(1H,1H,2H,2H-perfluorooctyl)silane, and all organic solvents were purchased from Aldrich or Acros Organics at their highest purity. Sylgard 184 was purchased from Dow Corning. Geduran silica gel 60 was purchased from Fisher and used for all purifications. The ketals were synthesized from their respective ketones. Water was taken from the tap.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded at 300 and 75 MHz respectively on a Bruker DPX 300 using  $\text{CDCl}_3$ . The solvent signal or TMS was used as the internal standard.  $^1\text{H}$  NMR spectra were compared to literature precedents.

## Fabrication of Thimbles

Fabrication of PDMS thimbles: A glass vial (19 mm in diameter and 65 mm tall) was placed in a dessicator along with a few drops of trichloro(1H,1H,2H,2H-perfluorooctyl)silane and placed under static vacuum overnight. PDMS was prepared by mixing Sylgard 184 elastomer base and curing agent in a 10:1 ratio respectively and degassed for 30 min. The glass vials were dipped into the PDMS mixture and placed upside down in an oven at 65 °C for 30 min, this process was repeated once. The PDMS was then allowed to cure overnight at 65 °C. The top of the PDMS thimble was cut with a razor blade around the cap of the vial and removed. A small amount of water was added to the inside of the vial and the cap replaced. The vial was then submerged in hexanes to swell the PDMS membrane at which point it delaminated from the glass vial. The PDMS thimbles were dried and used as is.

Fabrication of cyclooctene:dicyclopentadiene thimbles: Cyclooctene (10 mL, 8.46 g, 77 mmol) and dicyclopentadiene (10 mL, 9.86 g, 75 mmol) were added to a vial and mixed. Grubbs' 2<sup>nd</sup> generation catalyst (6.2 mg, 7.3  $\mu\text{mol}$ ) was dissolved in 200  $\mu\text{L}$  dichloromethane, added to the mixture of cyclooctene and dicyclopentadiene, and thoroughly mixed. This solution was then immediately used to fabricate the thimbles. A glass vial with an interior diameter of 19 mm and height of 85 mm was used as the outer shell for the mold. An aluminum rod with a diameter of 18 mm and height of 100 mm was placed in the glass vial suspended approximately 0.5 mm from the bottom of the vial. The void between the aluminum rod and the glass vial was filled with approximately 1.5 mL of the cyclooctene:dicyclopentadiene solution. The mold filled with solution was then placed in a hot water bath at 50-60 °C for 5 min to cure. The mold was wiped dry of water, submerged into liquid  $\text{N}_2$ , and the glass vial was then slid off the thimble and aluminum rod. The thimble, which was rubbery, was warmed to room temperature and then rolled off the aluminum rod. The thimble was swelled in hexanes three times to remove any remaining cyclooctene and dicyclopentadiene from the membrane, and dried under vacuum. The thickness of the thimble walls were approximately 300  $\mu\text{m}$ .

## Cascade Reactions

Molecules previously synthesized and described in the literature have literature references and do not have accompanying HRMS.

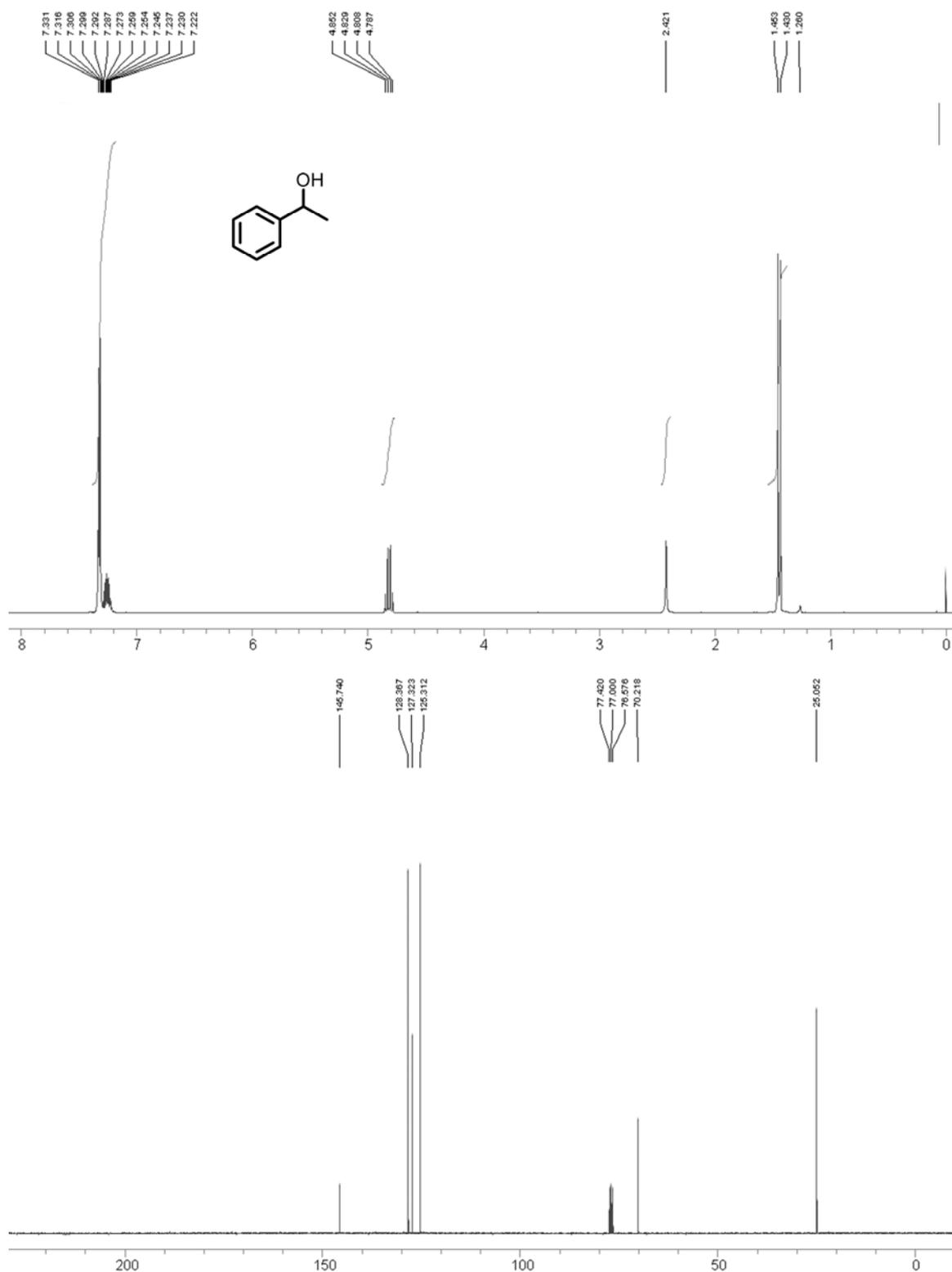
Method 1: One-step cascade reaction procedure. 2-Methyl-2-phenyl-1,3-dioxolane (0.5 g, 3 mmol), sodium dodecyl sulfate (0.2 g, 0.7 mmol) and a stir bar were added to the inside of a PDMS thimble. *p*-Toluene sulfonic acid monohydrate (0.145 g, 0.8 mmol) dissolved in 4 mL  $\text{H}_2\text{O}$  was added to the inside of the PDMS thimble followed by 2 mL of hexanes.  $\text{LiAlH}_4$  (0.145 g, 3.8 mmol) was added to the outside of the PDMS thimble followed by 5 mL hexanes. The reaction was stirred at room temperature for 19 h.  $\text{H}_2\text{O}$  (5mL) was added. The PDMS thimble was swelled with 20 mL hexanes and 2 x 20 mL diethyl ether. The organics were combined and dried over  $\text{MgSO}_4$ . The product was purified by flash chromatography.

Method 2: Two step/one pot cascade reaction procedure. 2-Methyl-2-phenyl-1,3-dioxolane (0.5 g, 3 mmol), sodium dodecyl sulfate (0.2 g, 0.7 mmol) and a stir bar were added to the inside of a PDMS thimble. *p*-Toluene sulfonic acid monohydrate

(0.145 g, 0.8 mmol) dissolved in 4 mL H<sub>2</sub>O was added to the inside of the PDMS thimble followed by 2 mL of 1:3 CH<sub>2</sub>Cl<sub>2</sub>:hexanes. The reaction was stirred for 5 h at room temperature. LiAlH<sub>4</sub> (0.145 g, 3.8 mmol) was added to the outside of the PDMS thimble with 5 mL 1:3 CH<sub>2</sub>Cl<sub>2</sub>:hexanes. The reaction was stirred at room temperature for 17 h. 5 mL of H<sub>2</sub>O was added. The PDMS thimble was swelled with 20 mL hexanes and 2 x 20 mL diethyl ether. The organics were combined and dried over MgSO<sub>4</sub>. The product was purified by flash chromatography. Products were verified by comparison of <sup>1</sup>H NMR spectra in literature.

## 1-phenylethanol

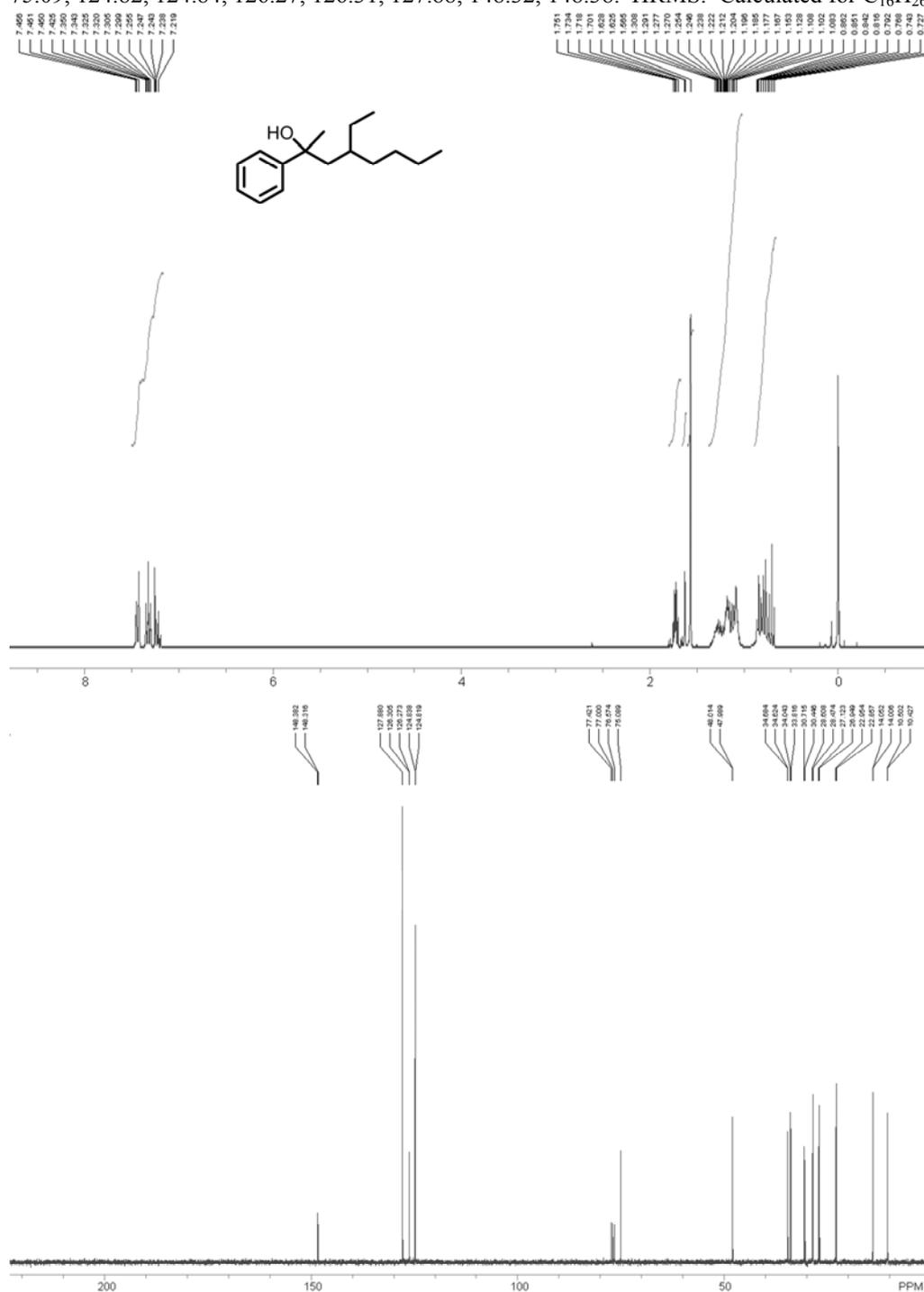
2-Methyl-2-phenyl-1,3-dioxolane (0.5 g, 3 mmol), sodium dodecyl sulfate (0.2 g, 0.7 mmol) and a stir bar were added to the inside of a PDMS thimble. *p*-Toluene sulfonic acid monohydrate (0.145 g, 0.8 mmol) was dissolved in 4 mL H<sub>2</sub>O and added to the inside of the PDMS thimble followed by 2 mL of hexanes. LiAlH<sub>4</sub> (0.145 g, 3.8 mmol) was added to the outside of the PDMS thimble with 5 mL hexanes. The reaction was stirred at 25 °C for 19 h. H<sub>2</sub>O (5 mL) was added. The PDMS thimble was swelled with 20 mL hexanes and 2 x 20 mL diethyl ether. The organics were combined and dried over MgSO<sub>4</sub>. The product was purified by column chromatography eluting with 1:4 ethyl acetate:hexanes to yield a colorless liquid (0.33 g, 89% yield). <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.44 (d, *J* = 6.9 Hz, 3H), 2.42 (s, 1H), 4.81 (q, *J* = 6.9 Hz, 1H), 7.22-7.33 (m, 5H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 25.05, 70.22, 125.31, 127.32, 128.37, 145.74.<sup>1</sup>





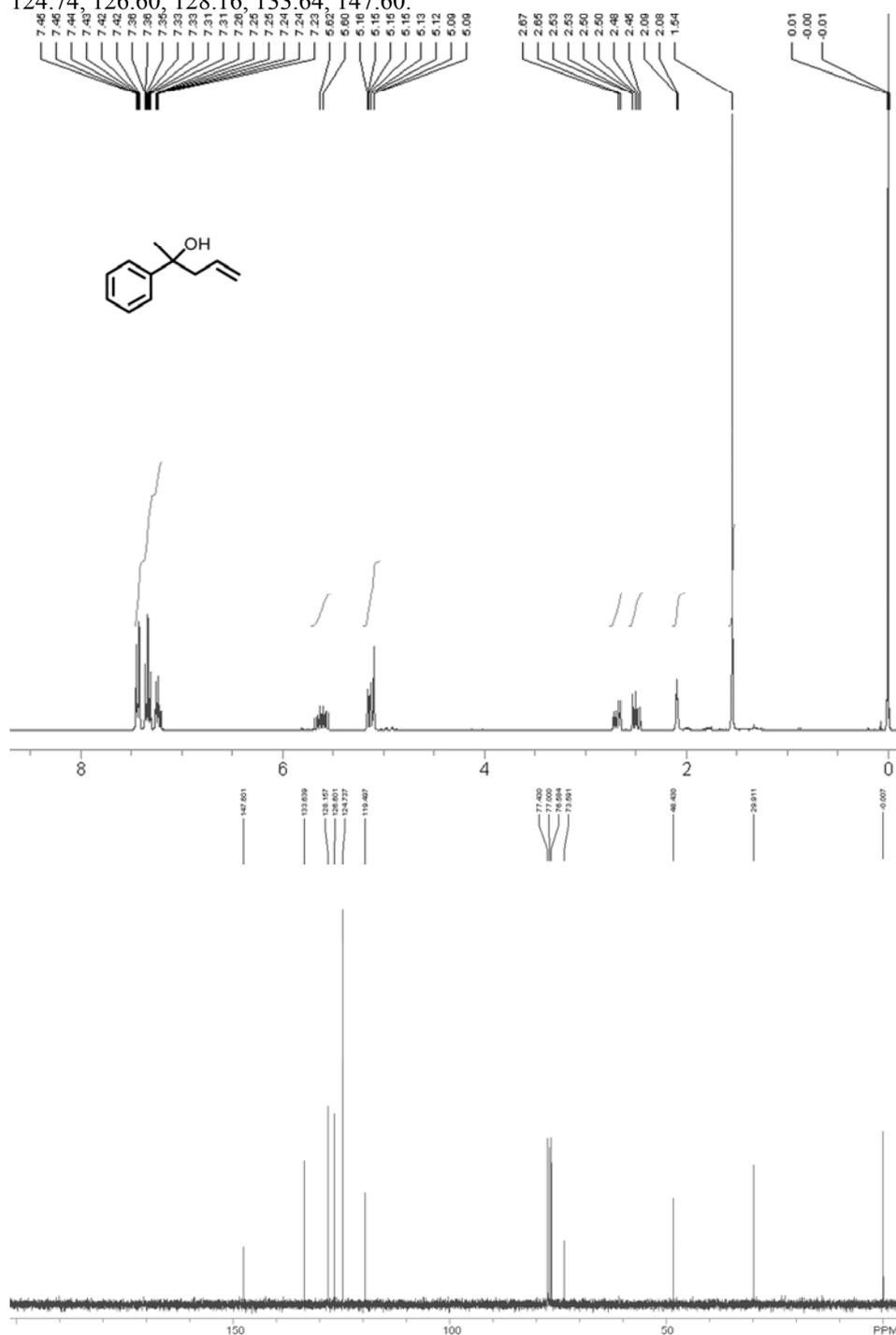
## 4-ethyl-2-phenyloctan-2-ol

2-Methyl-2-phenyl-1,3-dioxolane (0.25 g, 1.5 mmol), sodium dodecyl sulfate (0.1 g, 0.35 mmol) and a stir bar were added to the inside of a PDMS thimble. *p*-Toluene sulfonic acid monohydrate (72.4 mg, 0.38 mmol) dissolved in 2 mL H<sub>2</sub>O was added to the inside of the PDMS thimble followed by 1 mL of hexanes. The reaction was stirred at 25 °C for 4 h. Hexanes (2.5 mL) was added to the outside of the PDMS thimble followed by 12 mL of 1 M 2-ethylhexylmagnesium bromide (2.6 g, 12 mmol). The reaction was stirred for an additional 12 h after which 5 mL H<sub>2</sub>O was added. The PDMS thimble was swelled with 20 mL hexanes and 2 x 20 mL diethyl ether. The organics were combined and dried over MgSO<sub>4</sub>. The product was purified by column chromatography, eluting with 100% hexanes to yield a colorless oil (0.28 g, 80% yield). <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 0.68-0.86 (m, 6H), 1.08-1.29 (m, 9H), 1.57 (s, 3H), 1.63 (s, 1H), 1.70-1.75 (m, 2H), 7.19-7.46 (m, 5H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 10.43, 10.49, 14.00, 14.05, 22.86, 22.95, 26.95, 27.12, 28.48, 28.61, 30.45, 30.72, 33.82, 34.04, 34.62, 34.68, 47.99, 48.01, 75.07, 75.09, 124.82, 124.84, 126.27, 126.31, 127.88, 148.32, 148.38. HRMS: Calculated for C<sub>16</sub>H<sub>26</sub>O: 234.1984. Found: 234.1981.



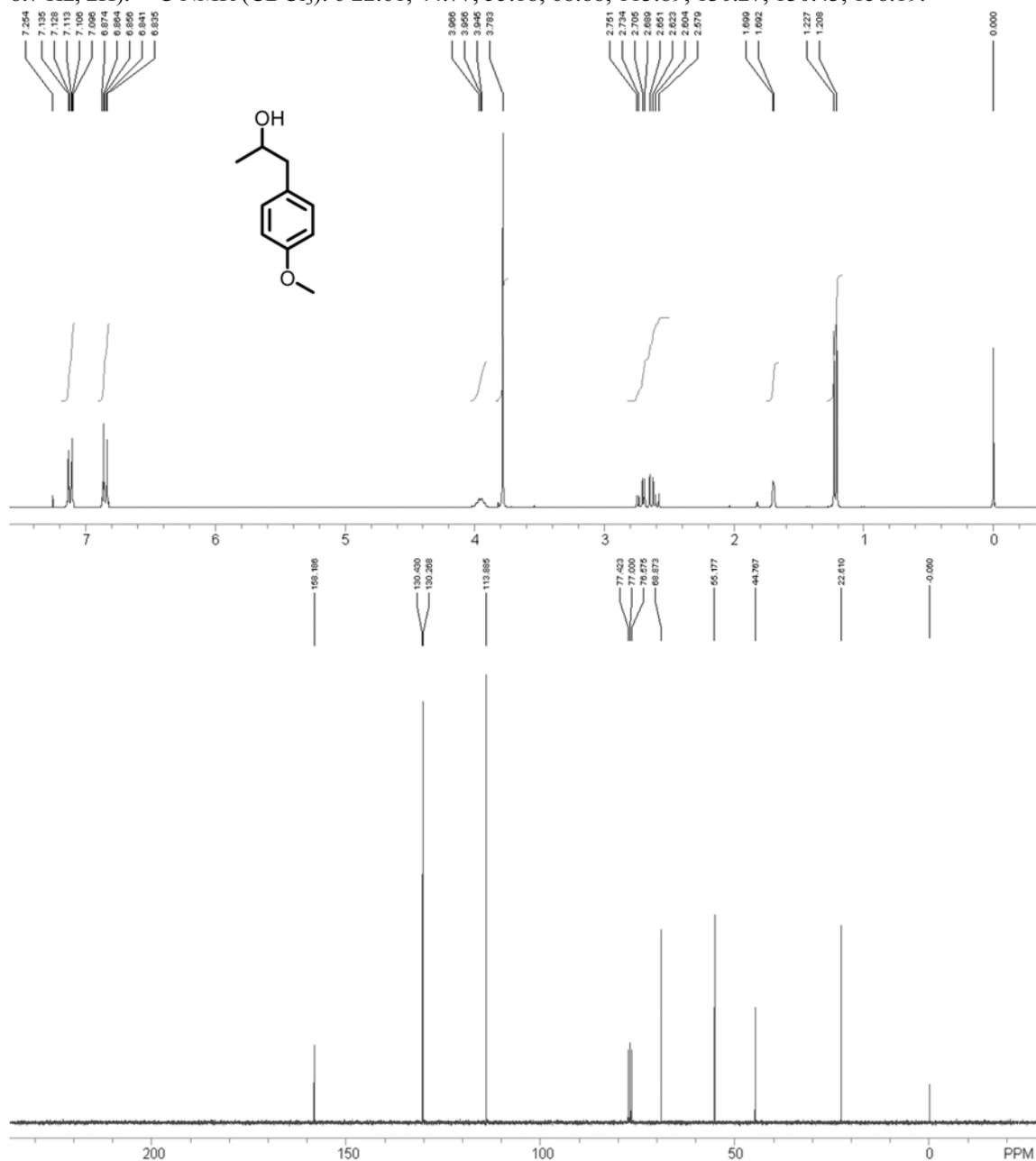
## 2-phenylpent-4-en-2-ol

2-Methyl-2-phenyl-1,3-dioxolane (0.5 g, 3 mmol), sodium dodecyl sulfate (0.2 g, 0.7 mmol) and a stir bar were added to the inside of a PDMS thimble. *p*-Toluene sulfonic acid monohydrate (0.145 g, 0.8 mmol) dissolved in 4 mL H<sub>2</sub>O was added to the inside of the PDMS thimble followed by 2 mL of hexanes. The reaction was stirred at 25 °C for 5 h. Hexanes (5 mL) and 24 mL of 1 M allylmagnesium bromide (3.49 g, 24 mmol) in diethyl ether was added to the outside of the PDMS thimble and the reaction was stirred for 14 h. H<sub>2</sub>O (5 mL) was added. The PDMS thimble was swelled with 20 mL hexanes and 2 x 20 mL diethyl ether, the organics were combined and dried over MgSO<sub>4</sub>. The product was purified by flash chromatography eluting with 100 % hexanes initially and then increasing to 1:49 ethyl acetate:hexanes to yield a colorless oil (0.39 g, 79% yield). <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.54 (s, 3H), 2.09 (s, 1H), 2.49 (dd, *J* = 13.8, 8.4 Hz, 1H), 2.68 (dd, *J* = 13.5, 6.3 Hz, 1H), 5.09-5.16 (m, 2H), 5.55-5.66 (m, 1H), 7.21-7.26 (m, 1H), 7.31-7.36 (m, 2H), 7.41-7.45 (m, 2H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 29.91, 48.43, 73.59, 119.50, 124.74, 126.60, 128.16, 133.64, 147.60.<sup>3</sup>



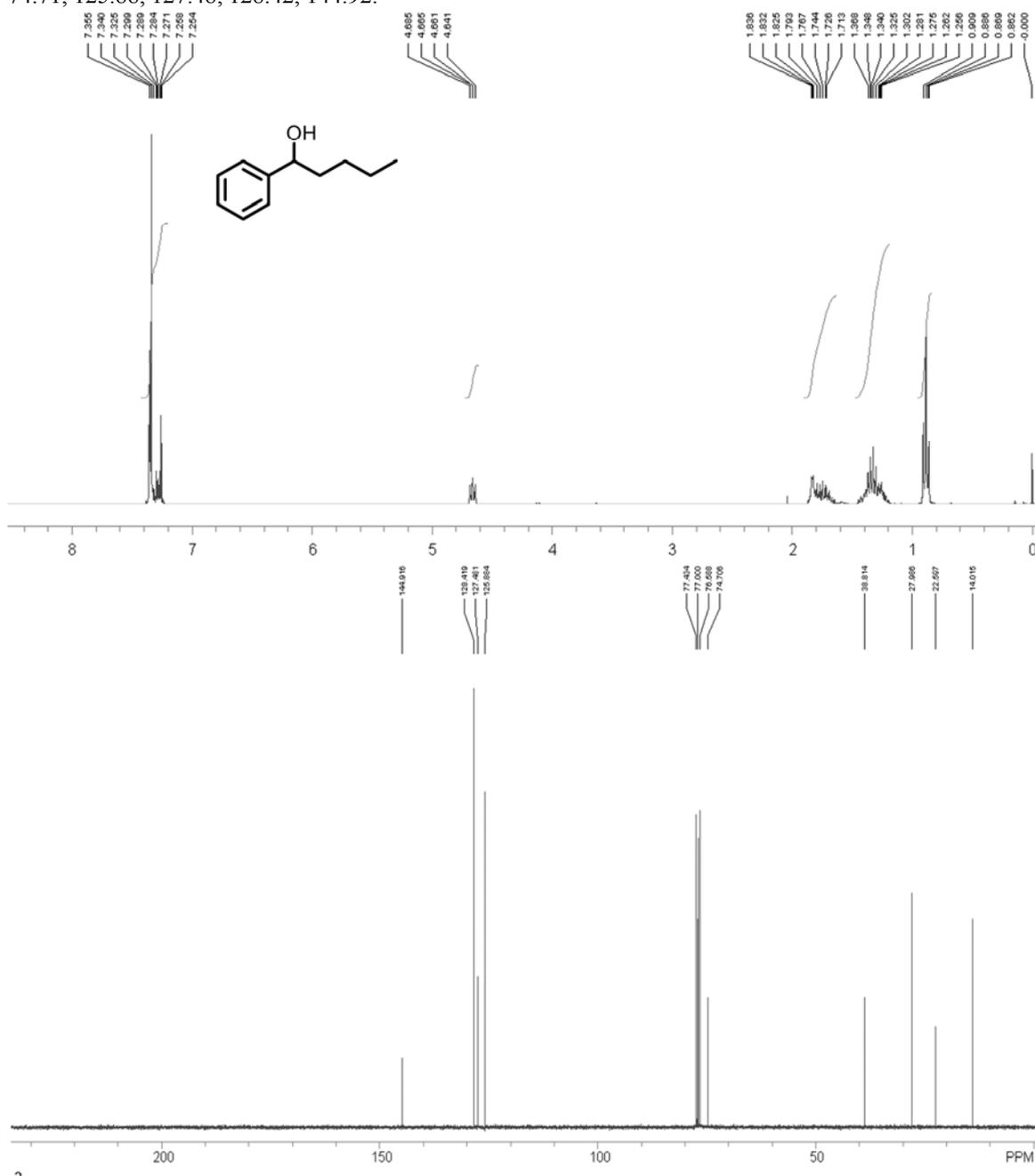
## 1-(4-methoxyphenyl)propan-2-ol

2-(4-Methoxybenzyl)-2-methyl-1,3-dioxolane (0.64 g, 3 mmol), sodium dodecyl sulfate (0.2 g, 0.7 mmol) and a stir bar were added to the inside of a PDMS thimble. *p*-Toluene sulfonic acid monohydrate (0.145 g, 0.8 mmol) dissolved in 4 mL H<sub>2</sub>O was added to the inside of the PDMS thimble followed by 2 mL of THF. The reaction was stirred at 25 °C for 5 h. LiAlH<sub>4</sub> (0.229 g, 6 mmol) and 5 mL hexanes were added to the outside of the PDMS thimble and the reaction proceeded for 24 h. 5 mL H<sub>2</sub>O was added. The PDMS thimble was swelled with 20 mL hexanes and 2 x 20 mL diethyl ether, the organics were combined and dried over MgSO<sub>4</sub> and evaporated. The product was purified by flash chromatography eluting with 1:4 ethyl acetate:hexanes to yield a pale yellow oil (0.43 g, 83% yield). <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.22 (d, *J* = 5.7 Hz, 3H), 1.69 (s, 1H), 2.61 (dd, *J* = 13.5, 7.5 Hz, 1H), 2.72 (dd, *J* = 13.5, 4.8 Hz, 1H), 3.78 (s, 3H), 3.93-3.98 (m, 1H), 6.85 (d, *J* = 8.4, 2H), 7.12 (d, *J* = 8.7 Hz, 2H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 22.61, 44.77, 55.18, 68.88, 113.89, 130.27, 130.43, 158.19.<sup>4</sup>



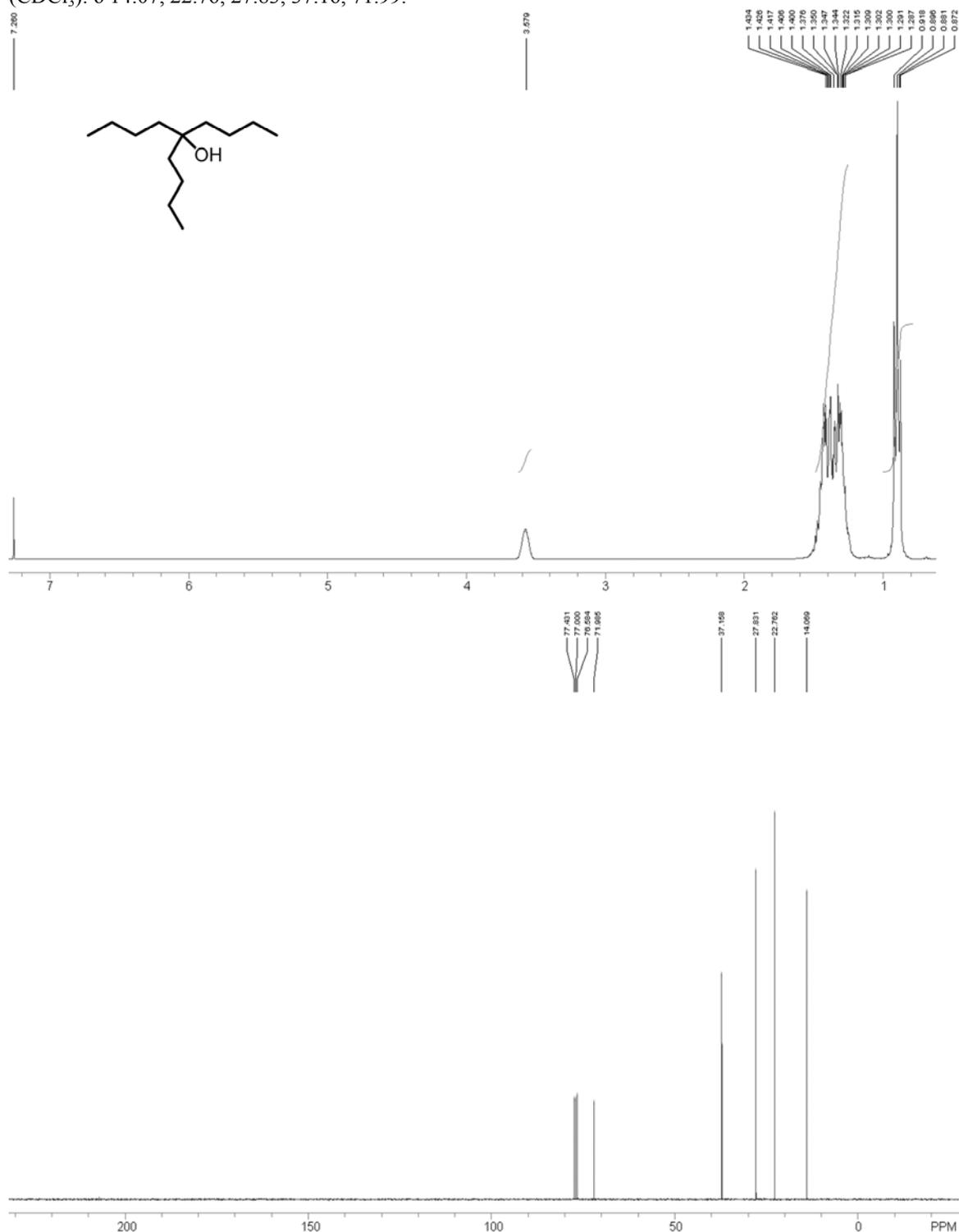
## 1-phenylpentan-1-ol

Sodium dodecyl sulfate (0.2 g, 0.7 mmol), *p*-toluene sulfonic acid monohydrate (0.145 g, 0.8 mmol) and a stir bar were added to the inside of a PDMS thimble. All solvents were purged with Argon. H<sub>2</sub>O (4 mL) was added to the inside of the PDMS thimble followed by 2 mL of THF. 2-phenyl-1,3-dioxolane (0.46 g, 3 mmol) was added to the inside of the PDMS thimble. The reaction was stirred at 25 °C for 3.5 h. Separately, the cuprate was synthesized under N<sub>2</sub> utilizing standard Schlenk line techniques. CuI (2.88 g, 15 mmol) was placed in an Schlenk flask under N<sub>2</sub>, 42 mL diethyl ether was added and the suspension was cooled in a brine bath for 20 min. 12 mL of 2.5 M butyllithium (1.92 g, 30 mmol) in hexanes was added and the reaction was stirred for 30 minutes in the brine bath. The cuprate solution was then transferred to the outside of the PDMS thimble and the reaction proceeded for 12 h. H<sub>2</sub>O (5 mL) was added. The PDMS thimble was swelled with 3 x 20 mL diethyl ether, the organics were combined and dried over MgSO<sub>4</sub> and evaporated. The product was purified by flash chromatography eluting with 1:4 ethyl acetate:hexanes to yield a colorless oil (0.44 g, 87% yield). <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 0.89 (t, *J* = 7.2 Hz, 3H), 1.21-1.42 (m, 4H), 1.66-1.84 (m, 3H), 4.66 (t, *J* = 6.6 Hz, 1H), 7.25-7.36 (m, 5H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 14.02, 22.60, 27.99, 38.81, 74.71, 125.88, 127.48, 128.42, 144.92.<sup>5,6</sup>



## 5-butylnonan-5-ol

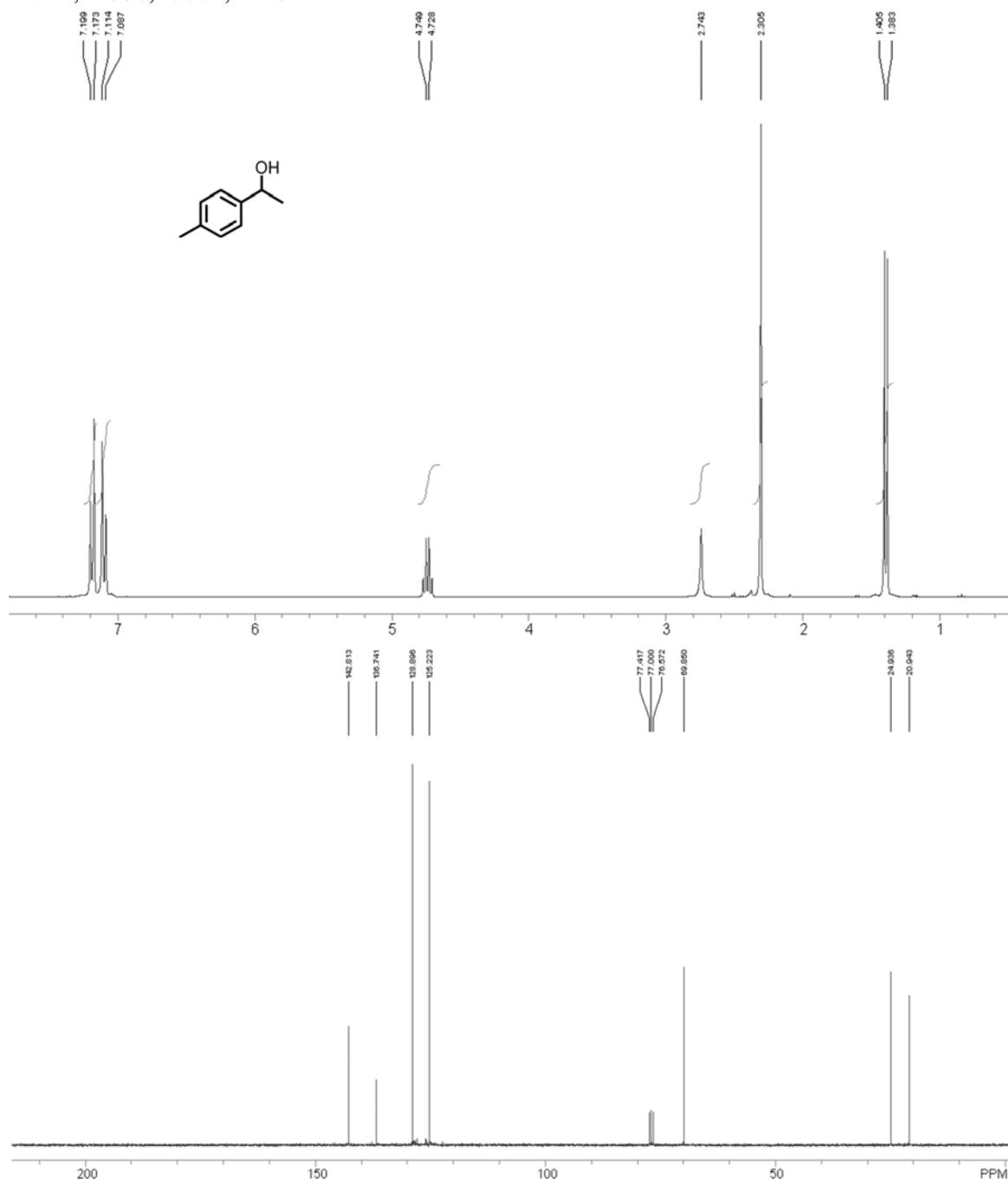
Sodium lauryl sulfate (0.2 g, 0.7 mmol), *p*-toluene sulfonic acid monohydrate (0.290 g, 1.5 mmol) and a stir bar were added to the inside of a PDMS thimble and placed under N<sub>2</sub>. All solvents were purged with Argon. H<sub>2</sub>O (2 mL) was added to the inside of the PDMS thimble followed by 6 mL THF. 2,2-dibutyl-1,3-dioxolane was added and the reaction was stirred for 12 h. Separately, the cuprate was synthesized under N<sub>2</sub> utilizing standard Schlenk line techniques. CuI (2.88 g, 15 mmol) was placed in an Schlenk flask under N<sub>2</sub>, 26 mL diethyl ether was added and the suspension was cooled in a brine bath for 20 min. 12 mL of 2.5 M butyllithium (1.92 g, 30 mmol) in hexanes was added and the reaction was stirred for 30 minutes in the brine bath. The cuprate solution was then transferred to the outside of the PDMS thimble and the reaction proceeded for 22 h. H<sub>2</sub>O (5 mL) was added. The PDMS thimble was swelled with 3 x 20 mL diethyl ether, the organics were combined and dried over MgSO<sub>4</sub> and evaporated. The product was purified by flash chromatography eluting with 1:19 ethyl acetate:hexanes to yield a colorless oil (0.47 g, 77% yield). <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 0.89 (t, *J* = 7.2 Hz, 9H), 1.3-1.43 (m, 18H), 3.58 (s, 1H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 14.07, 22.76, 27.83, 37.16, 71.99.



## 1-(4-methylphenyl)ethanol

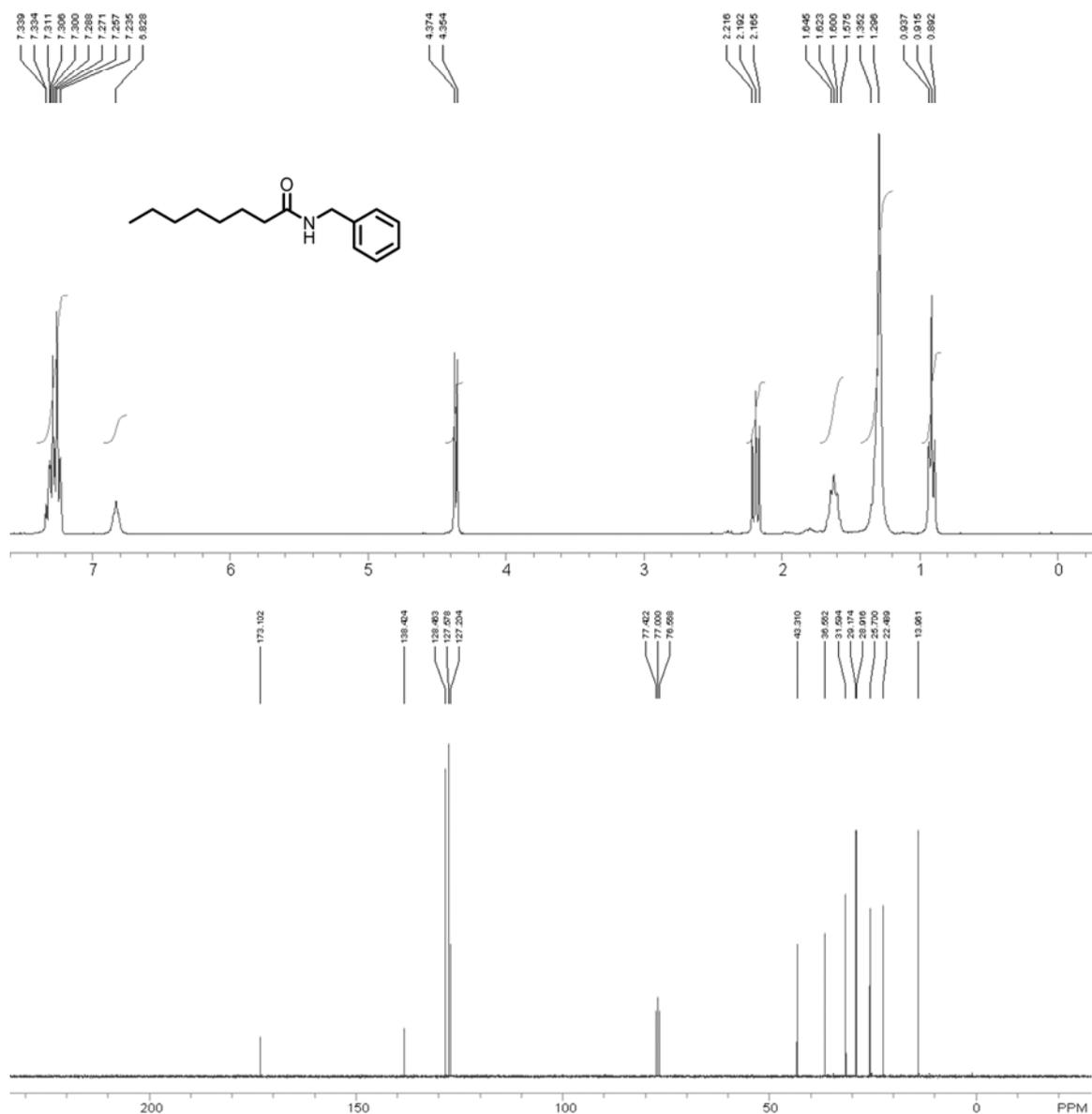
Cascade sequence of Wacker oxidation followed by reduction with  $\text{LiAlH}_4$ .

$\text{PdCl}_2$  (0.100 g, 0.564 mmol) and  $\text{CuCl}$  (0.560 g, 5.64 mmol) were placed in a PDMS thimble and the thimble was put into a flame-dried Schlenk flask under  $\text{N}_2$ . DMF (3.95 mL) and  $\text{H}_2\text{O}$  (0.56 mL) were subsequently transferred into the PDMS capsule. A rubber septum was stoppered to the top of the Schlenk flask and a balloon containing  $\text{O}_2$  was attached via a syringe. After 1 hour, *p*-methylstyrene (0.742 mL, 5.64 mmol) was added inside the PDMS thimble and the reaction was allowed to stir at room temperature under  $\text{O}_2$  for 24 hours. The Schlenk flask was then flushed with  $\text{N}_2$  gas and  $\text{LiAlH}_4$  (0.268 g, 7.05 mmol) was added to the outside the PDMS capsule followed by 10 mL hexanes and the reaction mixture was stirred for 24 hours at room temperature. Next the hexanes was pipetted out and the PDMS capsule was soaked in  $\text{Et}_2\text{O}$  4 x 50 mL. The  $\text{Et}_2\text{O}$  and hexanes were combined and extracted with 3 x 100 mL 3N HCl. The organic layer was dried over  $\text{MgSO}_4$  and the solvent was removed by evaporation. The product was purified by flash chromatography eluting with 1:4 ethyl acetate:hexanes to yield a pale yellow oil (0.505 g, 66% yield).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ): 1.39 (d,  $J= 6.6$ , 3H,  $\text{OCHCH}_3$ ), 2.31 (s, 3H,  $\text{ArCH}_3$ ), 2.74 (s, 1H, OH), 4.74 (q,  $J= 6.6$ , 1H,  $\text{OCHCH}_3$ ), 7.10 (d,  $J= 8.0$ , 2H, Ar), 7.19 (d,  $J= 8.0$ , 2H, Ar).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ): 20.94, 24.94, 69.85, 125.22, 128.90, 136.74, 142.81.<sup>1</sup>



## N-Benzyl octanamide

A PDMS thimble was placed in a Schlenk flask. The Schlenk flask was then placed under  $N_2$  and periodic acid (2.35 g, 8.45 mmol), and pyridinium chlorochromate (17 mg, 0.08 mmol) dissolved in 4 mL of 1:1 dichloromethane:*N,N*-dimethyl formamide were added to the interior of the thimble. The flask and thimble were then cooled in an ice bath and 1-octanol (0.5 g, 3.84 mmol) was slowly added into the thimble while vigorously stirring under nitrogen. The reaction mixture was then slowly warmed to room temperature and allowed to stir for a further 2 h. To the flask was then added 40 mL of 1:1 dichloromethane:*N,N*-dimethyl formamide and allowed to stir for 10 h after which the thimble was removed. DCC (0.95 g, 4.6 mmol), DMAP (0.188 g, 1.54 mmol), and benzyl amine (0.82 g, 7.68 mmol) were added to the solution remaining in the flask and the mixture continued stirring for a further 12 h under nitrogen. The reaction mixture was diluted with 20 mL of water and extracted with 3 X 50 mL diethyl ether. The organics were combined, backwashed with brine, dried over  $Na_2SO_4$ , and the solvent was evaporated. The product was purified by flash chromatography eluting with dichloromethane. The product was recovered as a white crystalline solid (0.63 g, 71 % yield).  $^1H$  NMR ( $CDCl_3$ ):  $\delta$  0.92 (t,  $J = 6.75$  Hz, 3H), 1.30 (m, 8H), 1.62 (m, 2H), 2.19 (t,  $J = 7.8$  Hz, 2H) 4.36 (d,  $J = 6$  Hz, 2H), 6.63 (br s, 1H, CONH) 7.24 – 7.31 (m, 5H).  $^{13}C$  NMR ( $CDCl_3$ ):  $\delta$  13.96, 22.49, 25.70, 28.92, 29.17, 31.59, 36.56, 43.31, 127.21, 127.58, 128.46, 138.42, 173.10.<sup>7</sup>



## N-Benzyl octanamide Control Experiments

1) Does the PCC/H<sub>5</sub>IO<sub>6</sub> interfere with the coupling reaction?

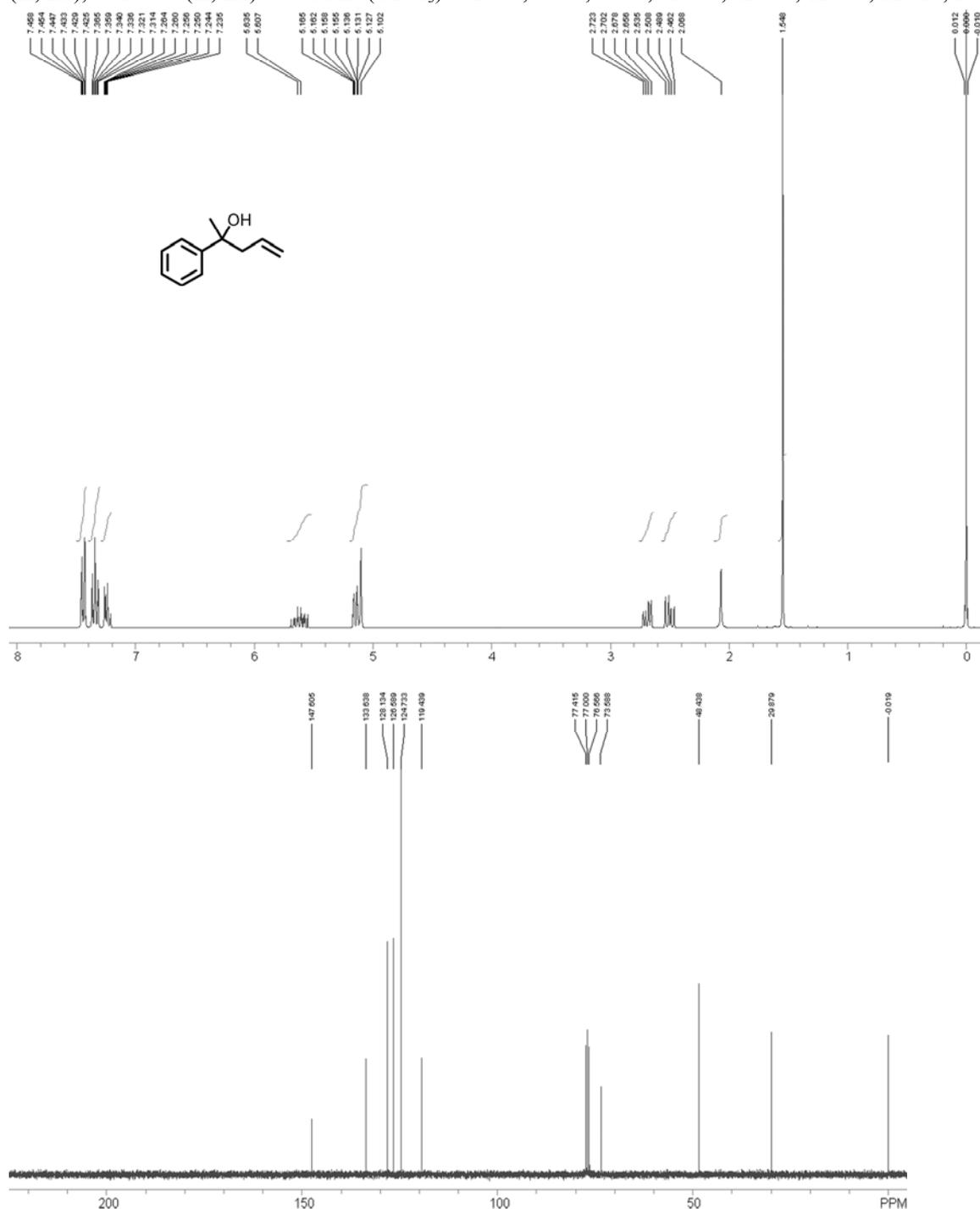
PCC (6.7 mg, 0.031 mmol) and H<sub>5</sub>IO<sub>6</sub> (770 mg, 3.4 mmol) dissolved in 5 mL of 1/1 DMF/dichloromethane were added to a previously flamed dried Schlenk flask under N<sub>2</sub>. After stirring for 10 min, octanol (0.2 g, 1.5 mmol) was slowly added. The mixture was allowed to stir for 40 min. To this mixture was added DCC (412 mg, 2.1 mmol) followed by benzyl amine (868 mg, 7.7 mmol). The mixture was allowed to stir for 13 h after which the reaction mixture was dissolved in 100 mL 3N HCl. The organics were then extracted with dichloromethane 3 x 50 mL, dried over MgSO<sub>4</sub>, and the solvent was removed in *vacuo*. The residue analyzed by <sup>1</sup>H NMR and all of the alcohol had been converted to the acid, but no amide formation was observed.

2) Does the H<sub>5</sub>IO<sub>6</sub> oxidant react with DCC?

DCC (0.95 g, 4.61 mmol) and DMAP (0.19 g, 1.54 mmol) dissolved in 5 mL dichloromethane were added to a vial. To this was added H<sub>5</sub>IO<sub>6</sub> (1.5 g, 5.4 mmol) and an exothermic process immediately started giving a yellow coloration and an off-white precipitate. The mixture was allowed to continue stirring for a further 2 h. <sup>1</sup>H NMR analysis of the reaction mixture showed the disappearance of DCC and the formation of DCU as the main product. Similarly, when this reaction was repeated and benzyl amine (0.49 g, 4.57 mmol) was added, the <sup>1</sup>H NMR was too complex to interpret.

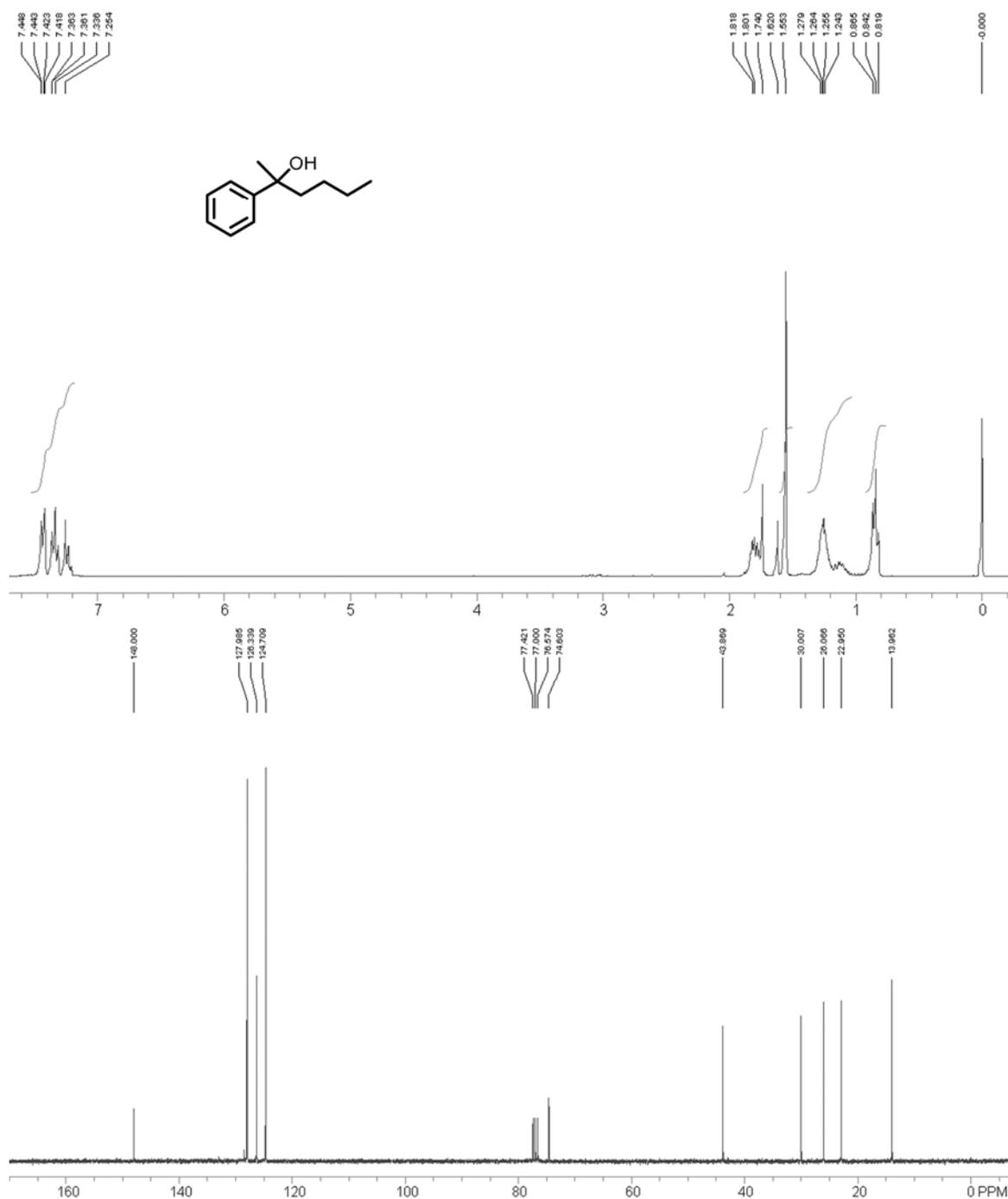
## 2-phenylpent-4-en-2-ol (cyclooctene/dicyclopentadiene thimbles)

2-methyl-2-phenyl-1,3-dioxolane (0.5 g, 3 mmol), sodium dodecyl sulfate (0.1 g, 0.35 mmol), *p*-toluene sulfonic acid monohydrate (0.145 g, 0.8 mmol), and a stir bar were added to the interior of a thimble prepared from a mixture of cyclooctene and dicyclopentadiene. 2 mL of water and 1 mL of hexanes were added to the inside of the thimble. The thimble was placed inside a Schlenk flask that had been flamed dried under N<sub>2</sub>. The reaction was allowed to stir for 4.25 h before 30 mL of 1:3 tetrahydrofuran:hexanes was added to the outside of the thimble followed by 12 mL of 1 M allylmagnesium bromide (1.75 g, 12 mmol) in diethyl ether. The reaction was left overnight (16 h) at which time 75 mL of 3N HCl was added to quench any remaining Grignard reagent and dissolve the magnesium salts. The thimble was extracted with 3 x 40 mL tetrahydrofuran. The organics and water layers were combined and the resulting mixture was extracted with 3 x 40 mL of methylene chloride. The organics were dried over MgSO<sub>4</sub> and evaporated. The crude product was purified by flash chromatography eluting with 1:19 ethylacetate:hexanes resulting in a colorless oil (0.466 g, 95% yield). <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.54 (s, 3H), 2.07 (s, 1H), 2.49 (dd, *J* = 13.5, 8.4 Hz, 1H), 2.68 (dd, *J* = 13.5, 6.3 Hz, 1H), 5.09-5.16 (m, 2H), 5.55-5.66 (m, 1H), 7.21-7.26 (m, 1H), 7.31-7.36 (m, 2H), 7.41-7.45 (m, 2H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 29.88, 48.44, 73.59, 119.44, 124.73, 126.59, 128.13, 133.64, 147.60.<sup>3</sup>

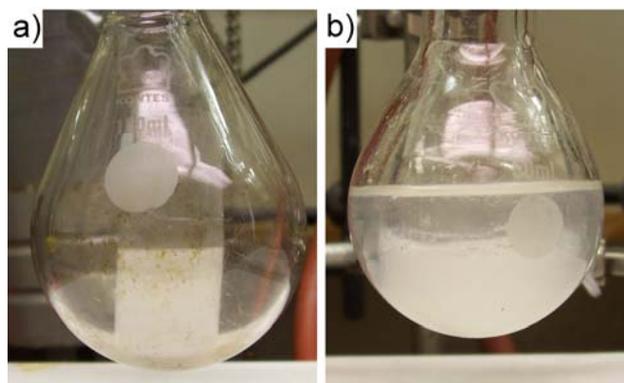


## 2-phenylhexan-2-ol (cyclooctene/dicyclopentadiene thimbles)

2-methyl-2-phenyl-1,3-dioxolane (0.5 g, 3 mmol), sodium dodecyl sulfate (0.2 g, 0.69 mmol), *p*-toluene sulfonic acid monohydrate (0.145 g, 0.8 mmol), and a stir bar were added to the interior of a thimble prepared from a mixture of cyclooctene and dicyclopentadiene. 4 mL of water and 2 mL of hexanes were added to the inside of the thimble. The thimble was placed inside a Schlenk flask that had been flamed dried under N<sub>2</sub>. The reaction was allowed to stir for 4.25 h before 25 mL of hexanes were added to the outside of the thimble followed by 2.4 mL of 2.5M butyllithium (0.38 g, 6 mmol) in hexanes, followed by another 20 mL of hexanes to bring the solvent level to near the top of the thimble. The reaction proceeded for 9 h at which time 30 mL of water was added to quench any remaining butyllithium. The solvent was decanted off, and the thimble swelled with 30 mL hexanes and 2 x 30 mL of diethyl ether. The water layer was extracted with dichloromethane 3 x 30 mL and the organics were combined and evaporated. The resulting crude mixture was purified by flash chromatography eluting with 1:9 ethylacetate:hexanes resulting in a colorless liquid (0.43 g, 81% yield). <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 0.84 (t, *J*= 6.9 Hz, 3H), 1.09-1.30 (m, 4H), 1.55 (s, 3H), 1.74-1.83 (m, 3H), 7.21-7.26 (m, 1H), 7.31-7.36 (m, 2H), 7.42-7.45 (m, 2H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 13.96, 22.95, 26.07, 30.01, 43.87, 74.60, 124.71, 126.34, 127.99, 148.00.<sup>8</sup>



## Supporting Figures



**Figure S1.** Optical micrographs of a) the deprotection of ketal with water/hexane solution on the inside and nothing on the outside. b) after the addition of a Grignard as the 2<sup>nd</sup> reagent in the cascade sequence.

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