Supporting information

Simultaneous Rapid Reaction Workup and Catalyst Recovery

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1. General

^{1}H and ^{13}C NMR spectra were recorded at 400 MHz and 101 MHz respectively, using $CDCl_3$ as a solvent. The chemical shifts were reported in δ (ppm) values (^{1}H and ^{13}C NMR relative to $CHCl_3$, δ 7.26 ppm for ^{1}H NMR and δ 77.0 ppm for ^{13}C NMR, multiplicities were indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (hextet), m (multiplet) and br (broad). Coupling constants (*J*), were reported in Hertz (Hz). All reagents and solvents were employed without further purification. TLC was developed on silica gel 60 F254 aluminum sheets. A CombiFlash Rf 200 (Teledyne Isco) was used for chromatographic separation. All chemicals were purchased from Aldrich, Alfa Aesar, TCI or Acros.

2. Preparation of porous polymer support (Porelite®)

Organic phase: A solution of divinylbenzene (DVB) (160 mL) and Span 80 (8 mL).

Aqueous phase: A solution of water (1600 mL), calcium chloride dihydrate (20 g) and potassium persulfate (4 g).

Under mechanic stirring (D-shaped PTFE paddle, 300-350 r.p.m), the aqueous phase was slowly added to the organic phase (c.a. 30 min) at room temperature. After addition, the emulsion was further stirred for 15 min. The resultant emulsion, having a consistency similar to that of mayonnaise, was transferred to a 2000 mL polyethylene bottle that was heated at 60°C for 48 hours. After this, the block polymer was removed from its container and extracted in a Soxhlet for 24 hours with 80% ethanol. The block polymer was dried in air and was crushed to powder form (35-120 mesh size) using commercial laboratory blender (from Waring®) and standard sieves.

3. General procedure for a reaction

Step 1. Reaction setup. The reaction is conducted in the usual way with the supported catalyst. Porelite® (typically 1 mL for every 0.1 gram of product) is added to the reaction mixture under stirring,

Step 2. Reaction quench and rigid solvent extraction. If needed, the reaction is quenched with a suitable aqueous solution (e.g. $NaHCO_3$ solution).

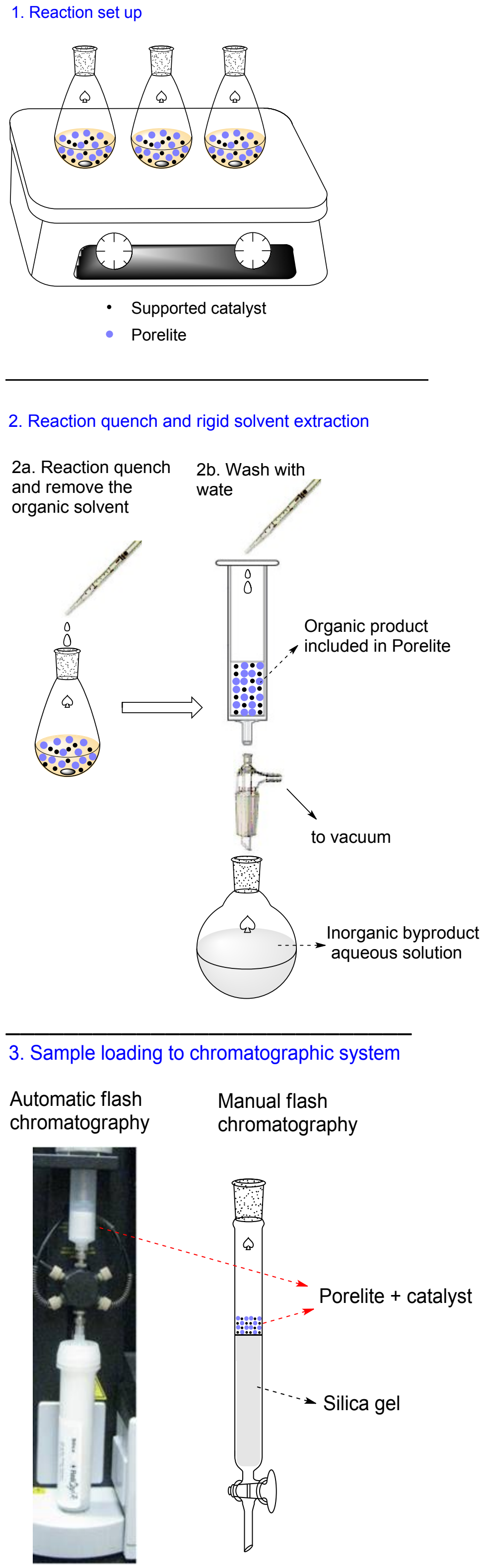
- If the solvent used in the reaction is water-miscible (eg., DMF, methanol, etc.), a minimum amount of water immiscible solvent (e.g. 3 mL ether for every 1 g of product) is added to help organic material become entrenched in Porelite.
- If the reaction is conducted in a water immiscible solvent (e.g. toluene, DCM), no extra solvent is needed in most cases.

The excess amount of solvent is removed by rotavapor or by nitrogen/air purging (no need to remove the water from the mixture). The reaction mixture is filtered to remove aqueous-soluble components (starting materials, by-products, etc.) and washed with water (or HCl or Na_2CO_3 solution to remove basic or acidic byproducts. Vacuum is applied to dry the filtrate for 2 minutes to remove any remaining aqueous and volatile solvents. (*For automatic flash chromatographic separation, an empty loading cartridge can be used, which can be directly attached to the commercial system. For manual chromatographic separation, a regular Büchner filter can be used*).

Step 3. Sample loading to chromatographic system.

- The loading cartridge can be directly attached to the commercial flash chromatographic system (e.g., CombiFlash Rf series).
- For manual chromatographic separation, the polymer powder is loaded directly onto a manual flash silica gel column (dry loading).

Figure S-1.



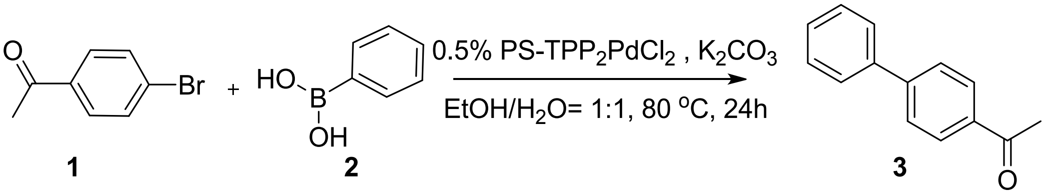
- Because the polymer pad may contain some trapped air, it is recommended to start with the least polar solvent (e.g., hexane) during chromatographic separation to remove the trapped air.

Alternative method: For parallel operations, a commercial filtration station can be used (Figure S-2).

Figure S-2. Use of commercial filtration station.

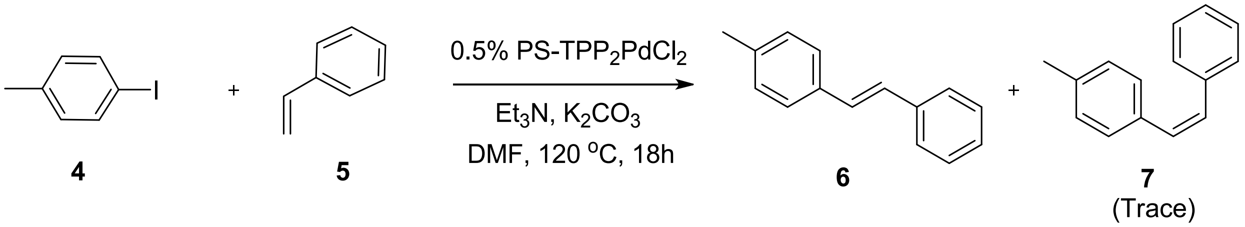
4. Reaction procedures

Suzuki-Miyaura coupling reaction



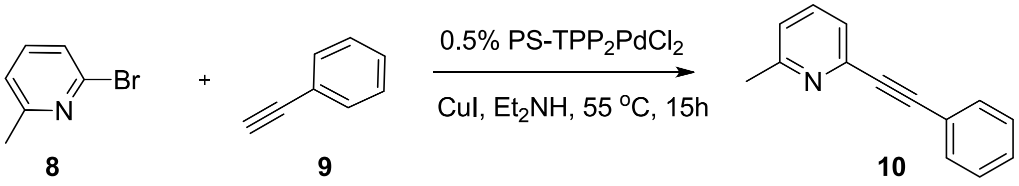
A 50 mL round-bottomed flask fitted with a magnetic stir bar was charged with *p*-bromoacetophenone (1mmol, 199 mg), K_2CO_3 (2 mmol, 276 mg), phenylboronic acid (1.1 mmol, 137 mg), Porelite (180 mg), and a polymer bound catalyst (0.5% mmol). A mixed solvent system (ethanol: deionized water = 1:1, 10 mL) was added and the mixture was purged and backfilled with argon three times. The resulting solution was heated to 80 ^{0}C and stirred at 500 rpm for 24 h. The reaction was allowed to cool down to room temperature after which 10 mL water was added. The resulting mixture was concentrated in a rotovapor to remove the organic solvent (the aqueous phase remained in reaction mixture). The reaction mixture was transferred into an empty loading cartridge, filtered to remove aqueous-soluble components and further washed with water (20 mL). The cartridge was then connected to a flash chromatography apparatus and eluted with a linear gradient of 0 - 10% ethyl acetate/hexanes to yield the product as a white powder. To recycle Porelite and the polymer-bound catalyst, the cartridge were flushed with ethyl acetate for 2 min, and then dried under vacuum to remove the ethyl acetate. The recycled Porelite with the polymer-bound catalyst were used directly in the next run of the reaction. (Additional 10% of Porelite was added to the sample cartridge before filtration in successive reactions due to the loss that occurs during filtration and flash chromatography). The NMR data obtained were in agreement with those reported.[1]

Heck coupling reaction



A 50 mL round-bottomed flask fitted with a magnetic stir bar was charged with iodotoluene (1 mmol, 218 mg), styrene (1.5 mmol, 156 mg), K_2CO_3 (2 mmol, 276 mg), triethylamine (2 mmol, 202 mg), Porelite (180 mg), polymer bound catalyst (0.5% mmol). DMF (5 mL) was added and the mixture was purged and backfilled with argon three times. The solution was heated to 120 ^{0}C and stirred at 500 rpm for 18 h. 5% LiCl aqueous solution (10 mL) was then added to the reaction. The resulting mixture was transferred into a 250 mL flask and concentrated to remove the DMF. The resulting mixture was concentrated in a rotovapor to remove the organic solvent (the aqueous phase remained in reaction mixture). The reaction mixture was transferred into an empty loading cartridge, filtered to remove aqueous-soluble components and further washed with water (20 mL). The cartridge was then connected to a flash chromatography apparatus and eluted with a linear gradient eluting with hexanes to furnish product as a white powder. Porelite and the catalyst in the cartridge were recycled by flushing with ethyl acetate for 2 min, and then dried under vacuum to remove ethyl acetate. The recycled Porelite with the catalyst were used directly in the next reaction run. (Additional 10% of Porelite was added to the sample cartridge before filtration in successive reactions due to the loss that occurs during filtration and flash chromatography). The NMR data obtained were in agreement with those reported.[2]

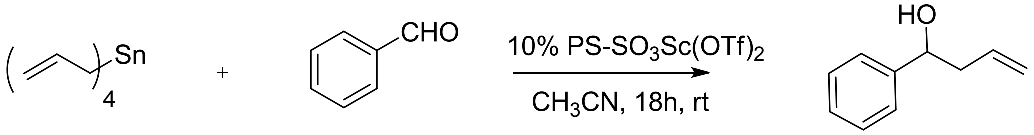
Sonogashira coupling reaction



A 50 mL round-bottomed flask fitted with a magnetic stir bar was charged with 2-bromo-6-methylpyridine (1.5 mmol, 263 mg), ethynylbenzene (3 mmol, 313 mg), cuprous iodide (0.015 mmol, 3 mg), Porelite (270 mg) and polymer bound catalyst (0.5% mmol). Diethylamine (8 mL) was added and the mixture was purged and backfilled with argon three times. The reaction was heated to 55 ^{0}C and stirred at 500 rpm for 15 h. Water (10 mL) was added and the resulting mixture was concentrated in a rotovapor to remove diethylamine. The reaction mixture was transferred into an empty loading cartridge, filtered to remove aqueous-soluble components and further washed with water (20 mL). The cartridge was then connected to a flash chromatography apparatus and eluted with a linear gradient of 0 - 10% ethyl acetate/hexanes to yield the product as a yellow oil. Porelite and the catalyst in the cartridge were recycled by flushing with ethyl acetate for 2 min, and then dried under vacuum to remove ethyl acetate.

The recycled Porelite with the catalyst were used directly in the next reaction run. (Additional 10% of Porelite was added to the sample cartridge before filtration in successive reactions due to the loss that occurs during filtration and flash chromatography). The NMR data obtained were in agreement with those reported.[3]

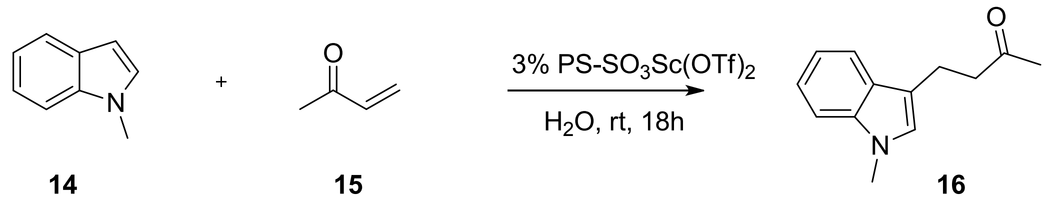
Allylation reaction



11 **12** **13**

An 8 mL-vial fitted with a magnetic stir bar was charged with polymer bound-Sc(OTf)$_3$ (0.1 mmol, 100 mg), benzaldehyde (1 mmol, 106 mg), Porelite (100 mg) and CH_3CN (3 mL). Tetraallyl tin (0.3 mmol, 88.4 mg) was added at room temperature and the mixture was stirred at 500 rpm for 18 h. The reaction mixture was transferred into a 50 mL-flask with ethyl acetate (10 mL) and water (10 mL). The result mixture was concentrated under reduced pressure to remove THF and was transferred into an empty loading cartridge, filtered to remove aqueous-soluble components and further washed with water (20 mL). The cartridge was then connected to a flash chromatography apparatus and eluted with a linear gradient of 0 - 30% ethyl acetate/hexanes to give the product as a colorless oil. Porelite and the catalyst in the cartridge were recycled by flushing with ethyl acetate for 2 min, and then dried under vacuum to remove ethyl acetate. The recycled Porelite with the catalyst were used directly in the next reaction run. (Additional 10% of Porelite was added to the sample cartridge before filtration in successive reactions due to the loss that occurs during filtration and flash chromatography). The NMR data obtained were in agreement with those reported.[4]

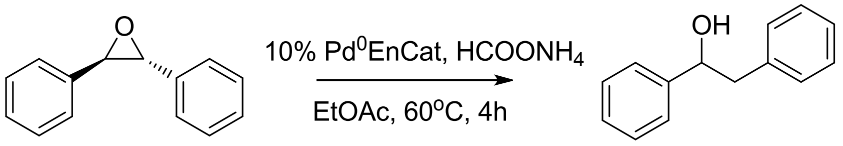
Michael addition



14 **15** **16**

Into a suspension of polymer bound Sc(OTf)$_3$ (0.03 mmol, 30 mg) and Porelite (100 mg) in water (5 mL) in an 8 mL-vial was added 1-methylindole (1 mmol, 131 mg) and methyl vinyl ketone (3 mmol, 210 mg) at room temperature. The reaction mixture was stirred at 500 rpm for 18 h. The reaction mixture was transferred into an empty loading cartridge, filtered to remove aqueous-soluble components and further washed with water (20 mL). The cartridge was then connected to a flash chromatography apparatus and eluted with a linear gradient of 0 - 30% ethyl acetate/hexanes to give the product as an amber oil. Porelite and the catalyst in the cartridge were recycled by flushing with ethyl acetate for 2 min, and then dried under vacuum to remove ethyl acetate. The recycled Porelite with the catalyst were used directly in the next reaction run. (Additional 10% of Porelite was added to the sample cartridge before filtration in successive reactions due to the loss that occurs during filtration and flash chromatography). The NMR data obtained were in agreement with those reported.[5]

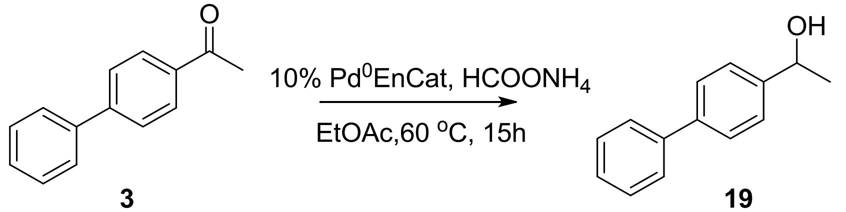
Epoxide hydrogenolysis



17 **18**

An 8 mL-vial fitted with a magnetic stir bar was charged with the trans-stilbene oxide [6] (0.5 mmol, 98.1 mg), Pd^{0}EnCat (0.025 mmol, 62.5 mg), ammonium formate (2.5 mmol, 158 mg) and Porelite (150 mg). Ethyl acetate (3 mL) was then introduced and the reaction was stirred at 60 °C at 500 rpm for 4 hours. The reaction mixture was transferred into a 50 mL-flask with ethyl acetate (10 mL) and water (10 mL). The resulting mixture was concentrated under reduced pressure to remove ethyl acetate. The reaction mixture was transferred into an empty loading cartridge, filtered to remove aqueous-soluble components and further washed with water (20 mL). The cartridge was then connected to a flash chromatography apparatus and eluted with a linear gradient of 0 - 50% ethyl acetate/hexanes to furnish the product as a white powder. Porelite and the catalyst in the cartridge were recycled by flushing with ethyl acetate for 2 min, and then dried under vacuum to remove ethyl acetate. The recycled Porelite with the catalyst were used directly in the next reaction run. (Additional 10% of Porelite was added to the sample cartridge before filtration in successive reactions due to the loss that occurs during filtration and flash chromatography). The NMR data obtained were in agreement with those reported.[7]

Ketone hydrogenation

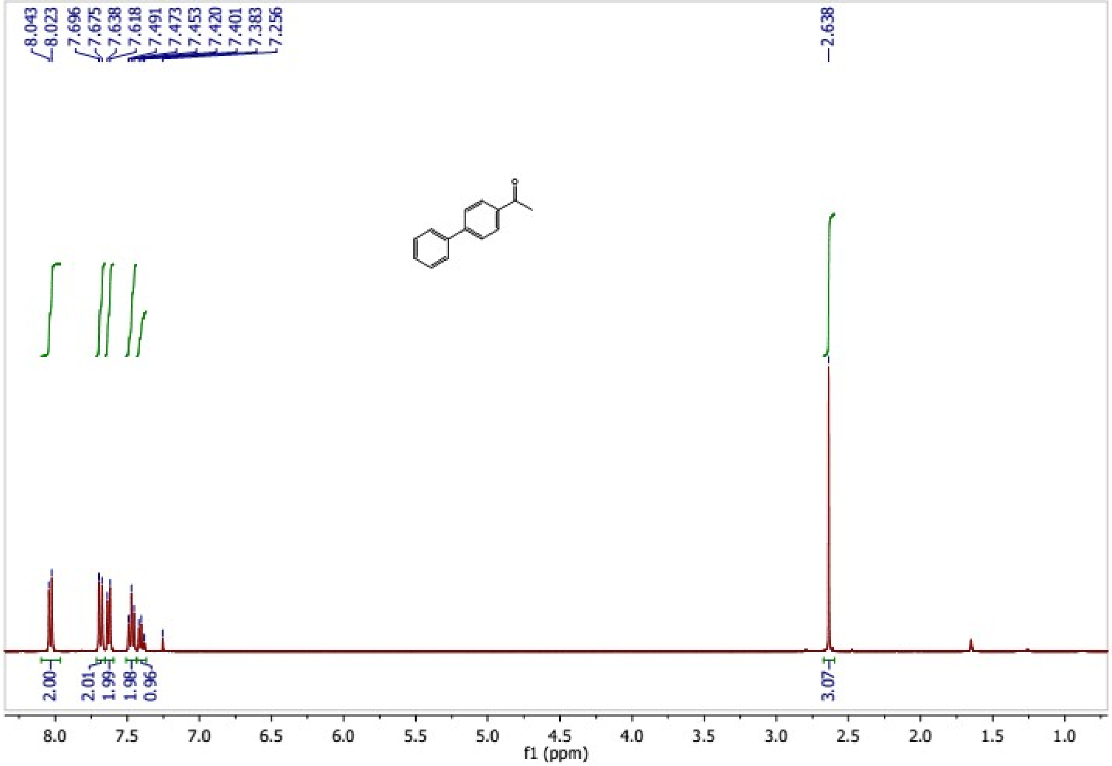


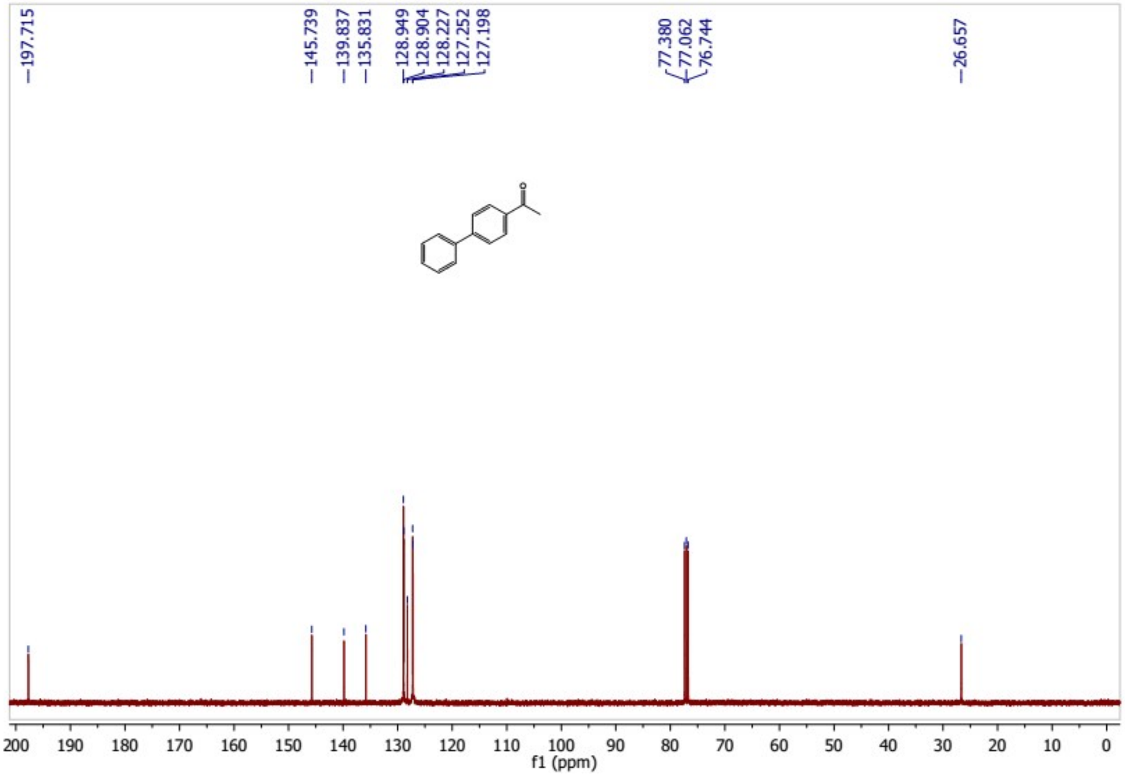
3 **19**

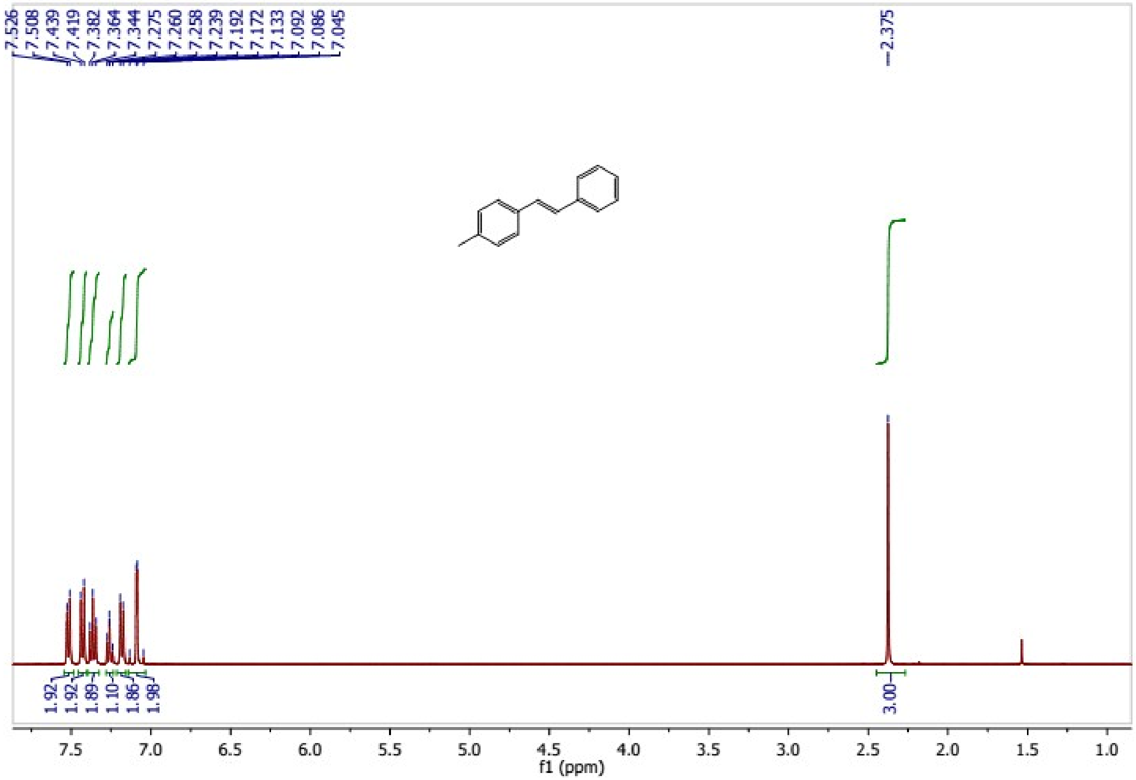
An 8 mL-vial fitted with a magnetic bar was charged with 4-acetylbiphenyl (0.5 mmol, 98.1 mg), Pd^{0}EnCat (0.05 mmol, 125 mg), ammonium formate (2.5 mmol, 158 mg) and Porelite (150 mg). Ethyl acetate (3 mL) was then introduced and the reaction was stirred at 60 °C for 15 hour. The reaction solution was transferred into a 50 mL-flask with EtOAc (10 mL) and H_2O (10 mL). The resulting mixture was concentrated under reduced pressure to remove ethyl acetate. The mixture was transferred into an empty loading cartridge, filtered to remove aqueous-soluble components and further washed with water (20 mL). The cartridge was then connected to a flash chromatography apparatus and eluted with a linear gradient of

0 - 40% ethyl acetate/hexanes to furnish the product as a white powder. Porelite and the catalyst in the cartridge were recycled by flushing with ethyl acetate for 2 min, and then dried under vacuum to remove ethyl acetate. The recycled Porelite with the catalyst were used directly in the next reaction run. (Additional 10% of Porelite was added to the sample cartridge before filtration in successive reactions due to the loss that occurs during filtration and flash chromatography). The NMR data obtained were in agreement with those reported. [8]

5. NMR Copies for compounds



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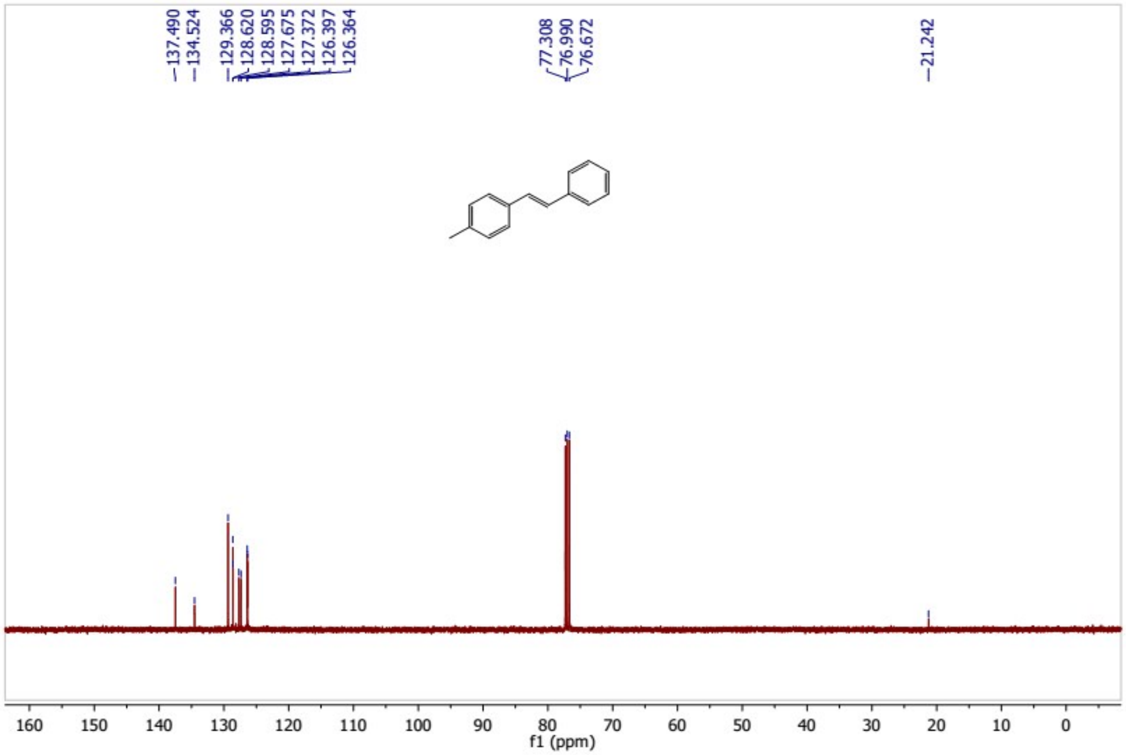
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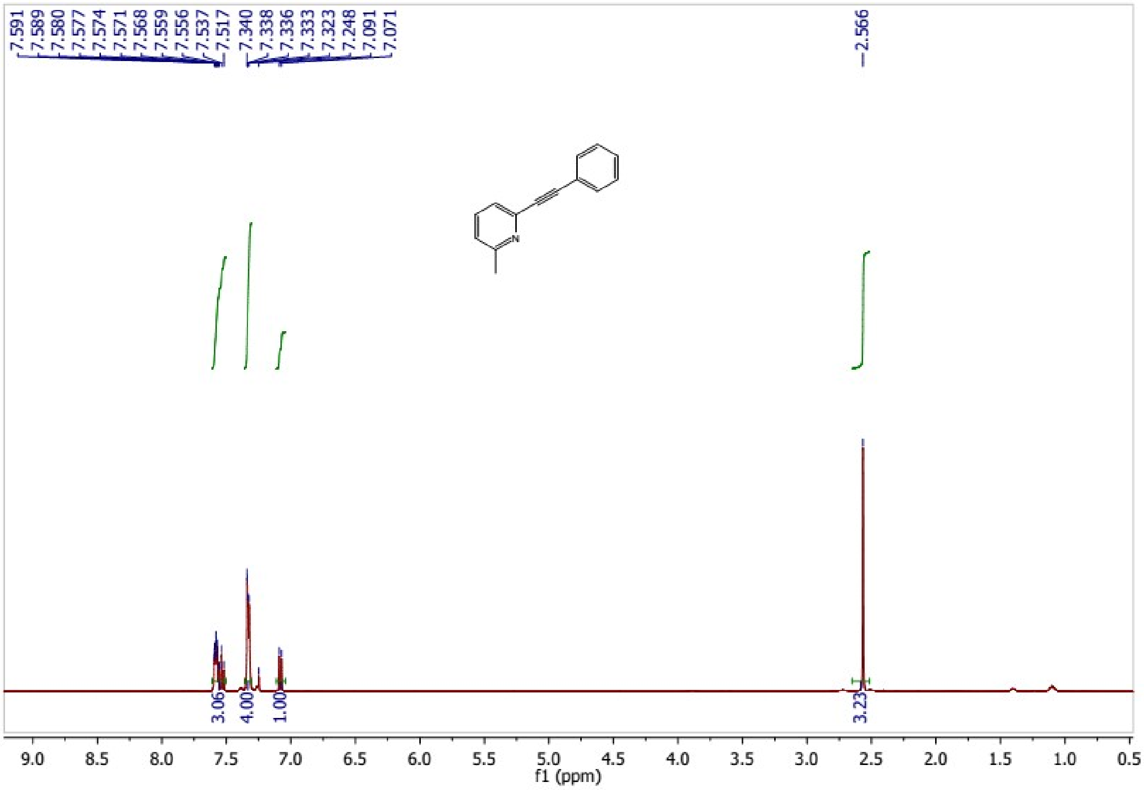
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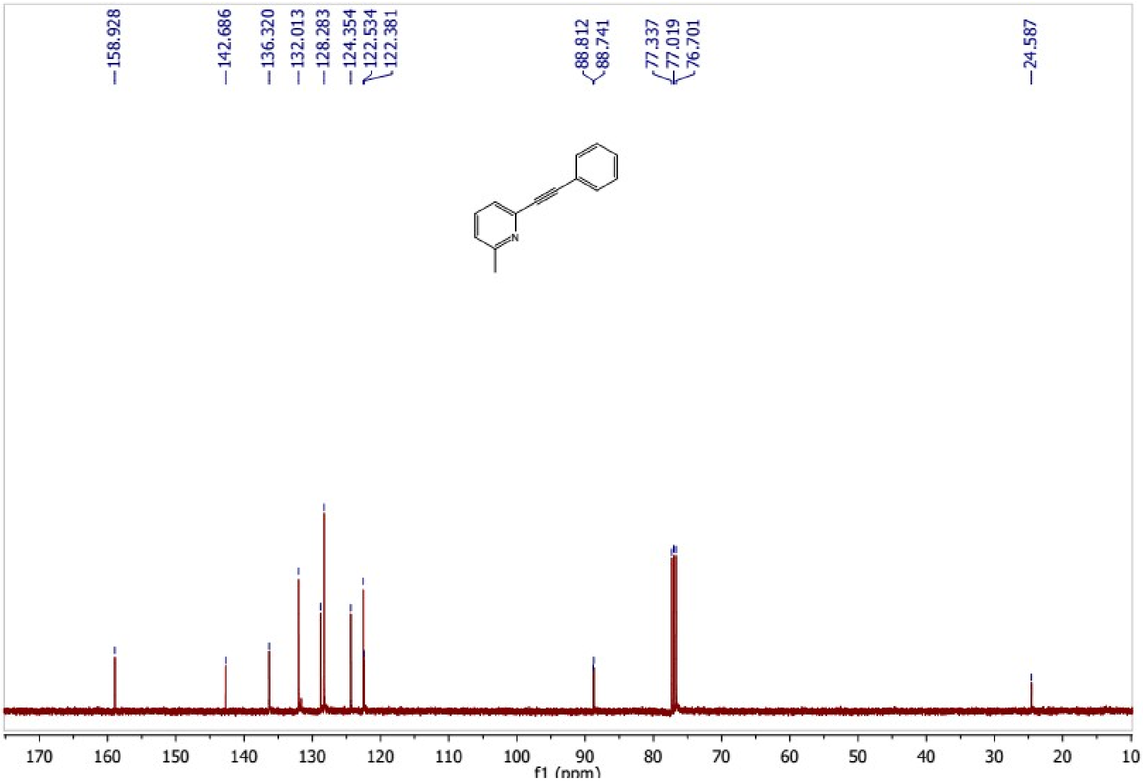
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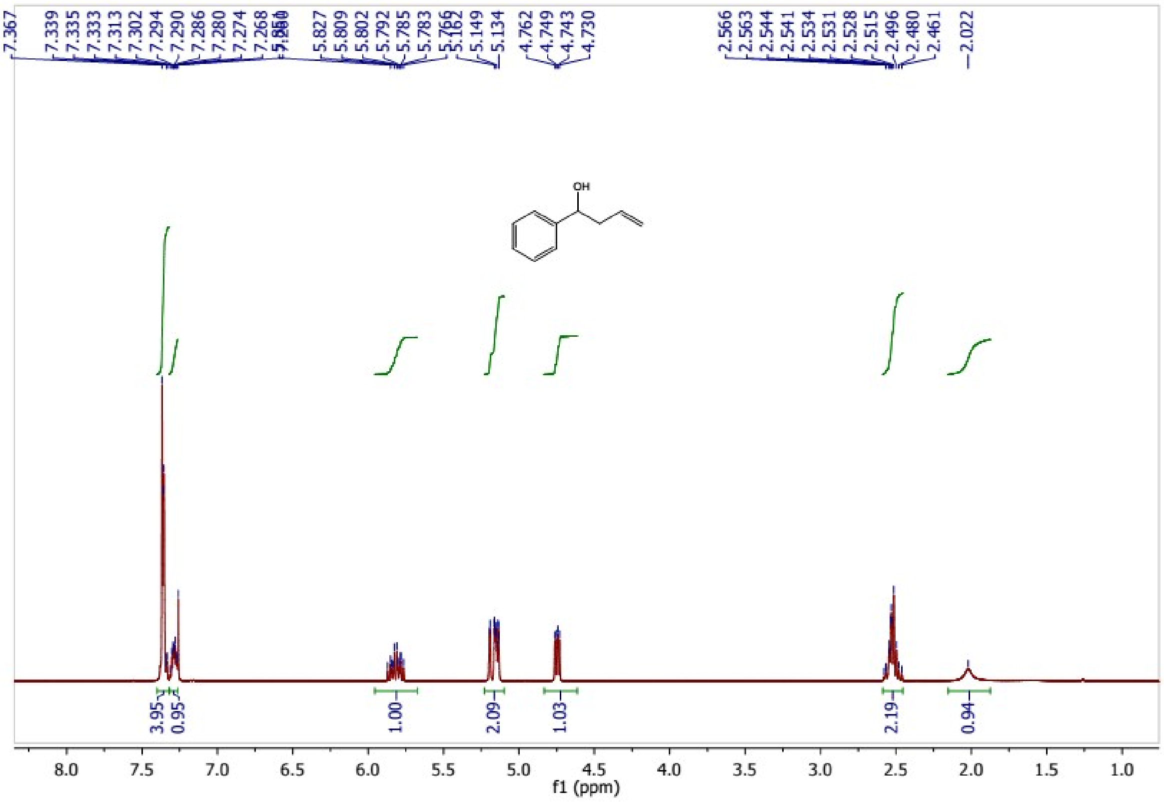
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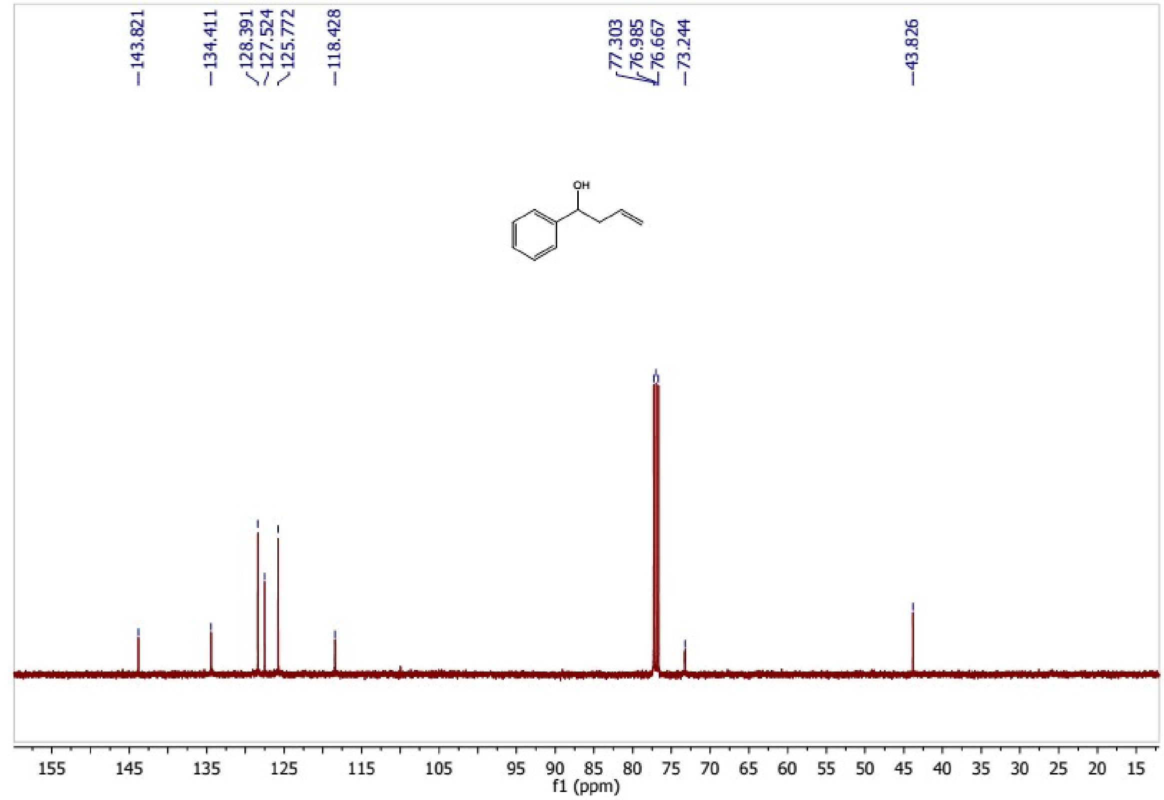
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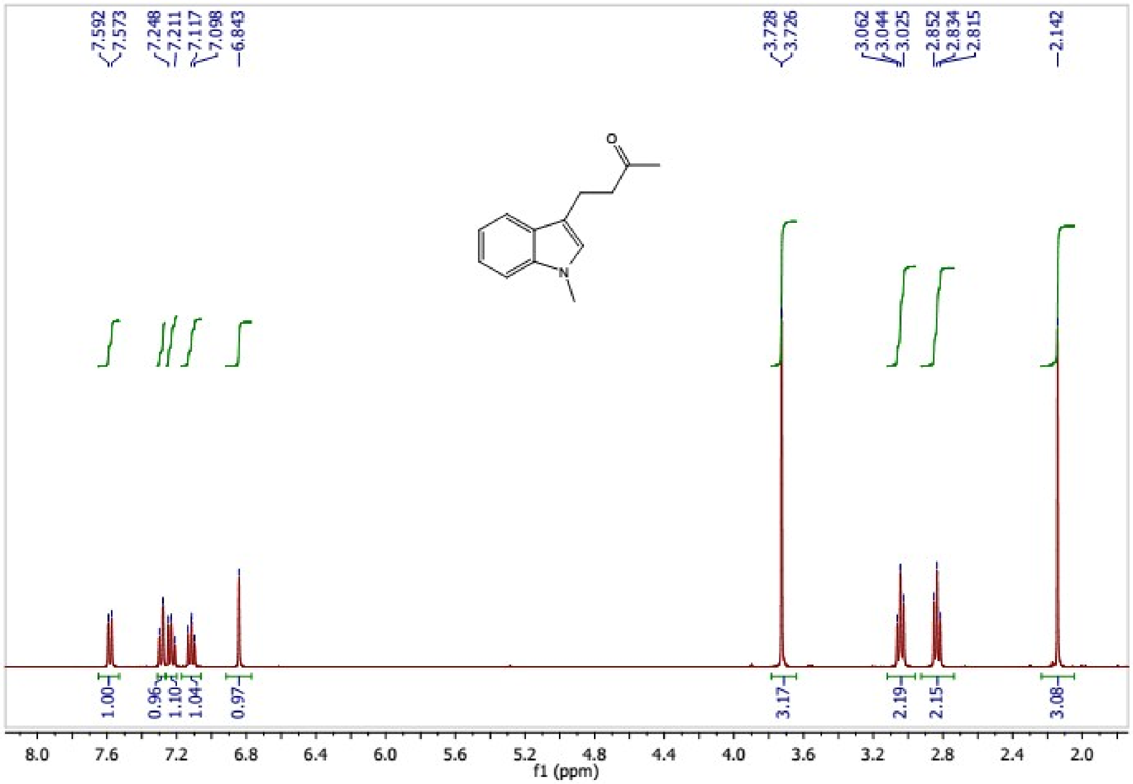
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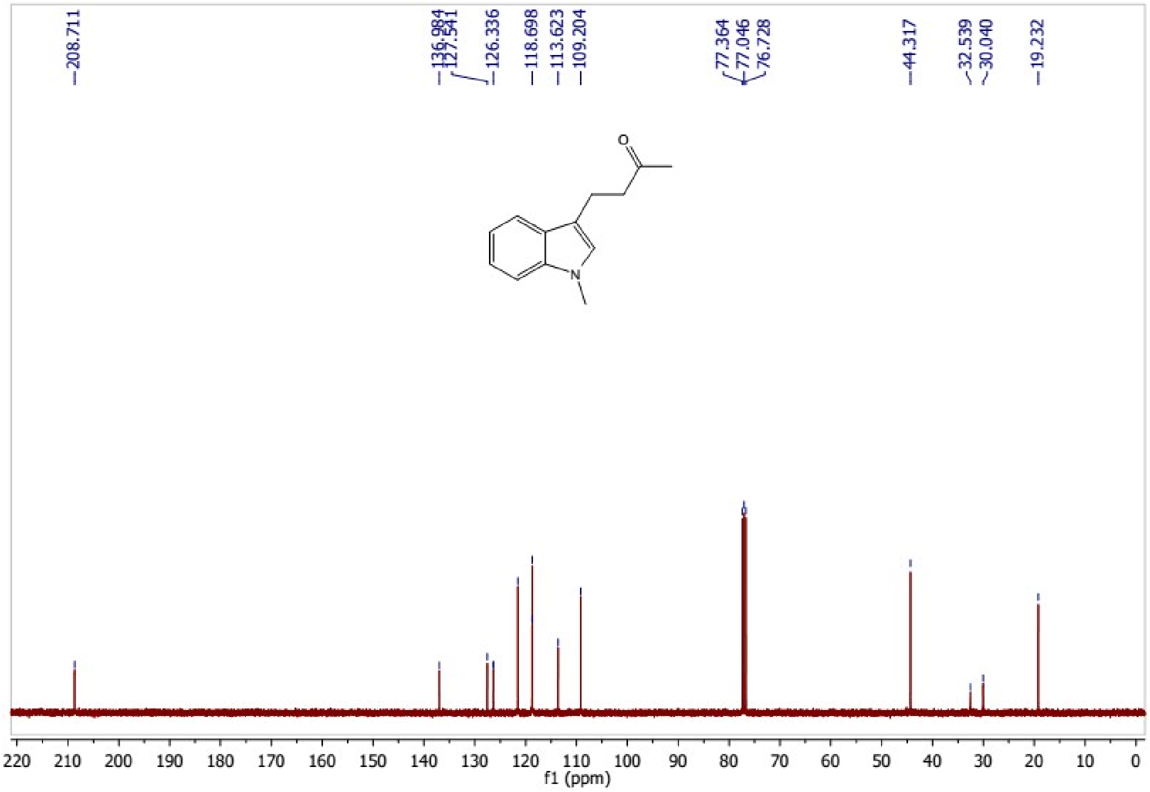
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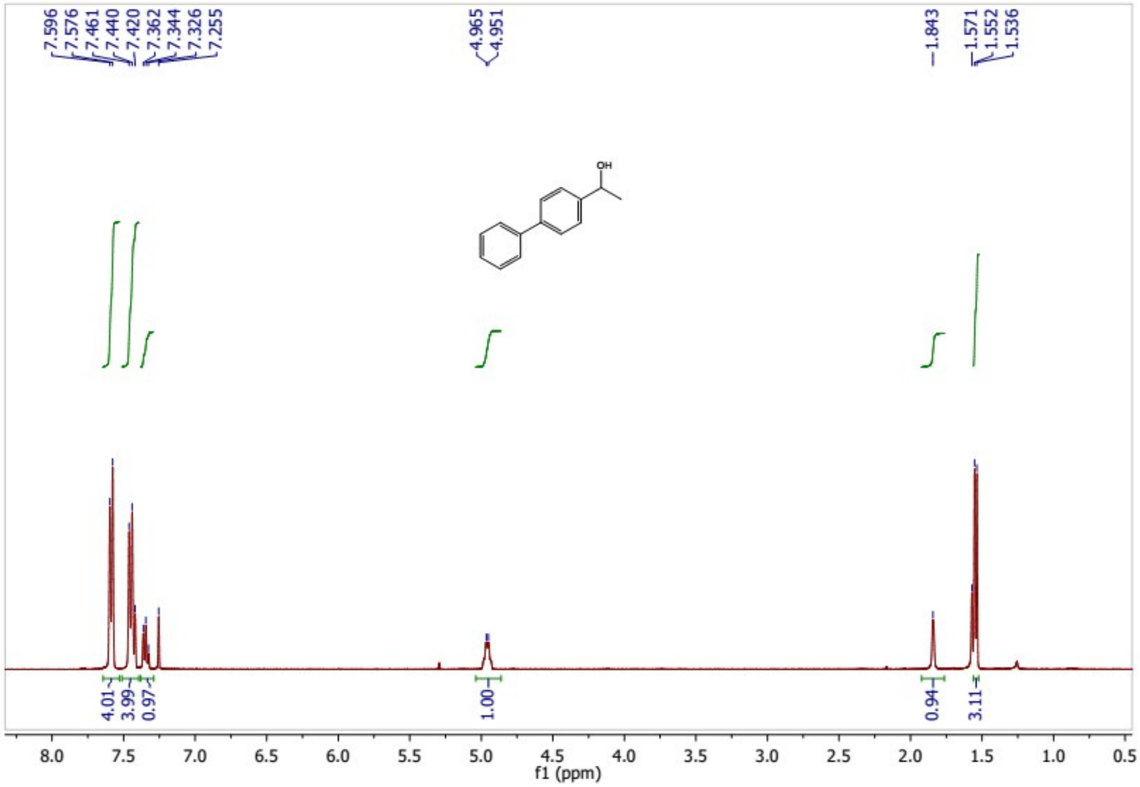
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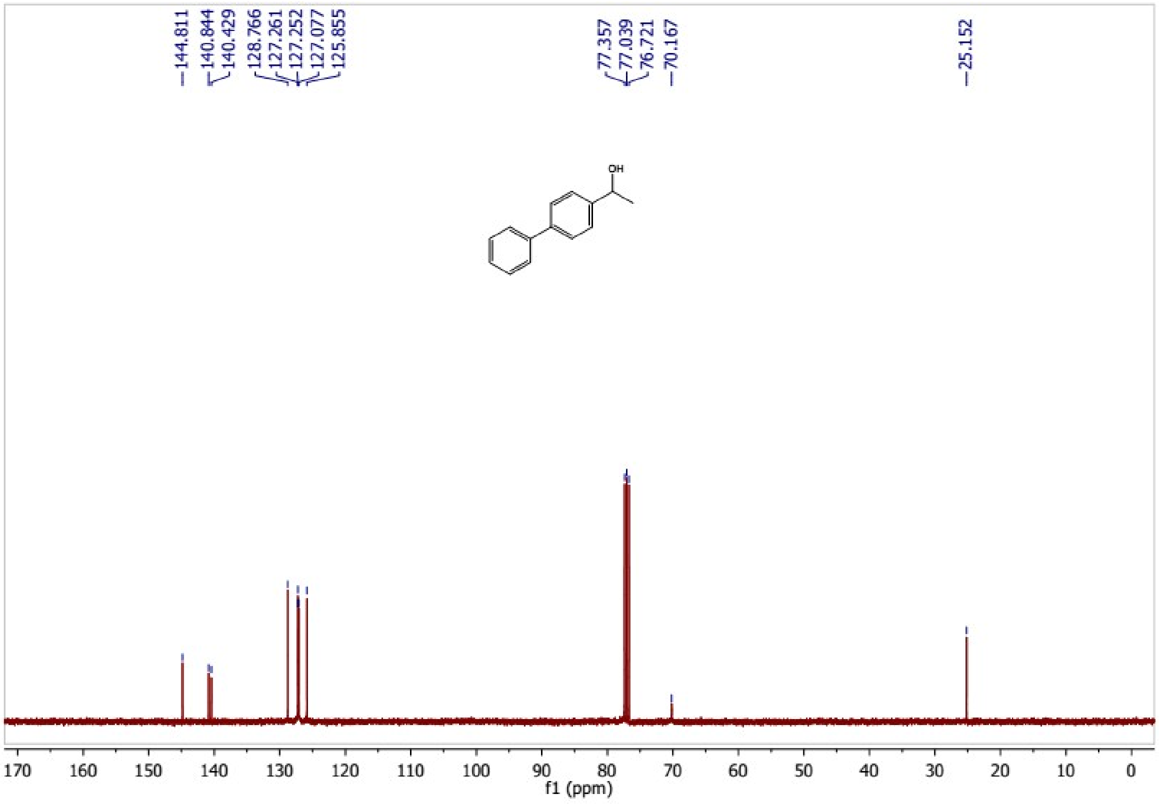
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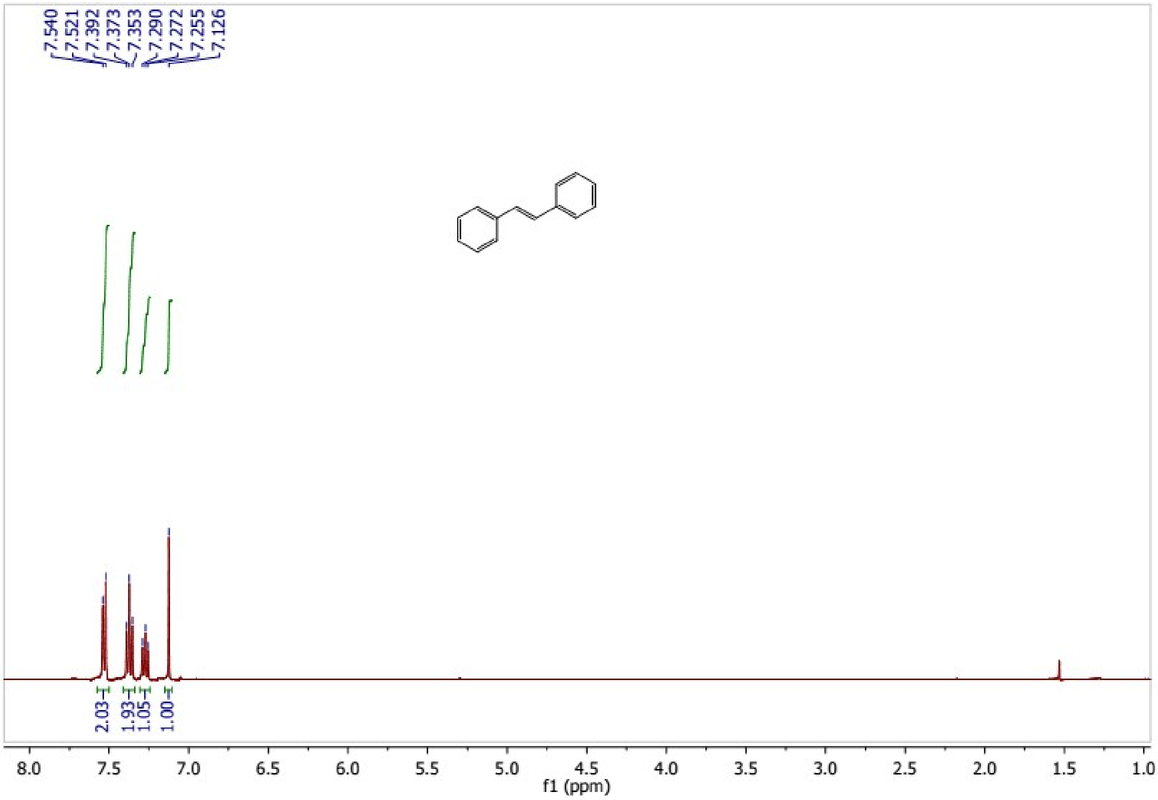
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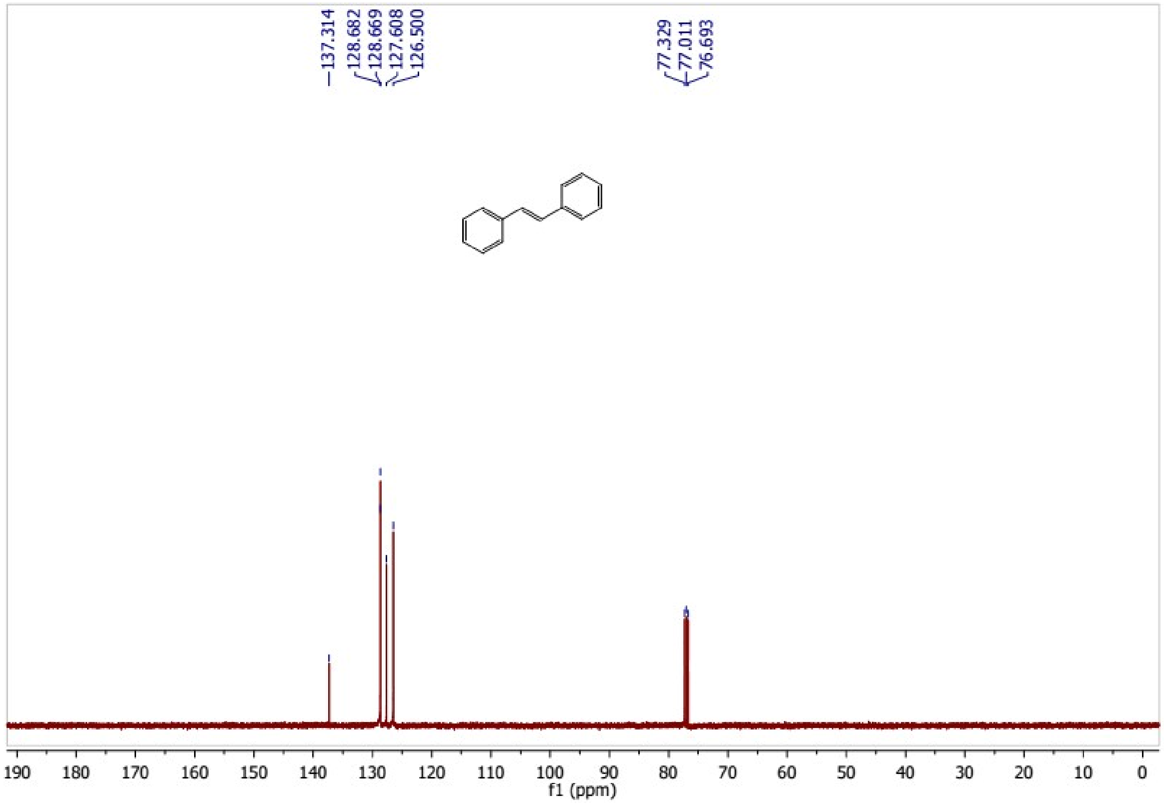
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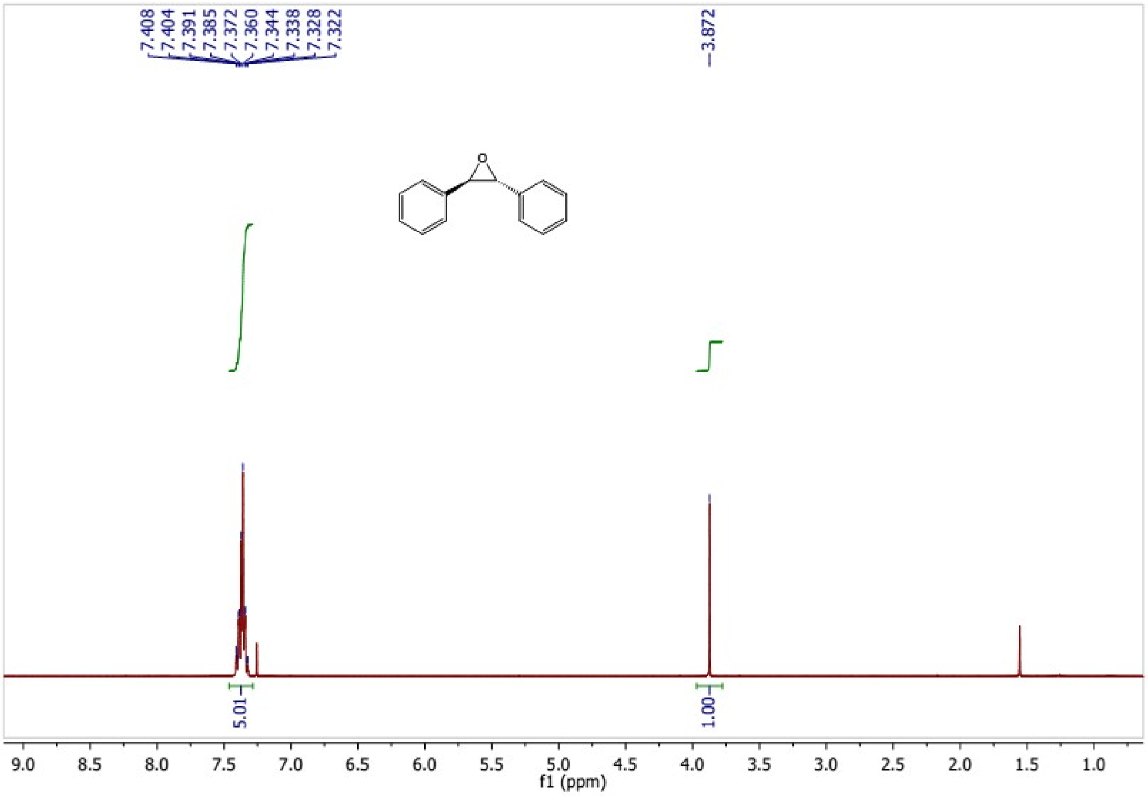
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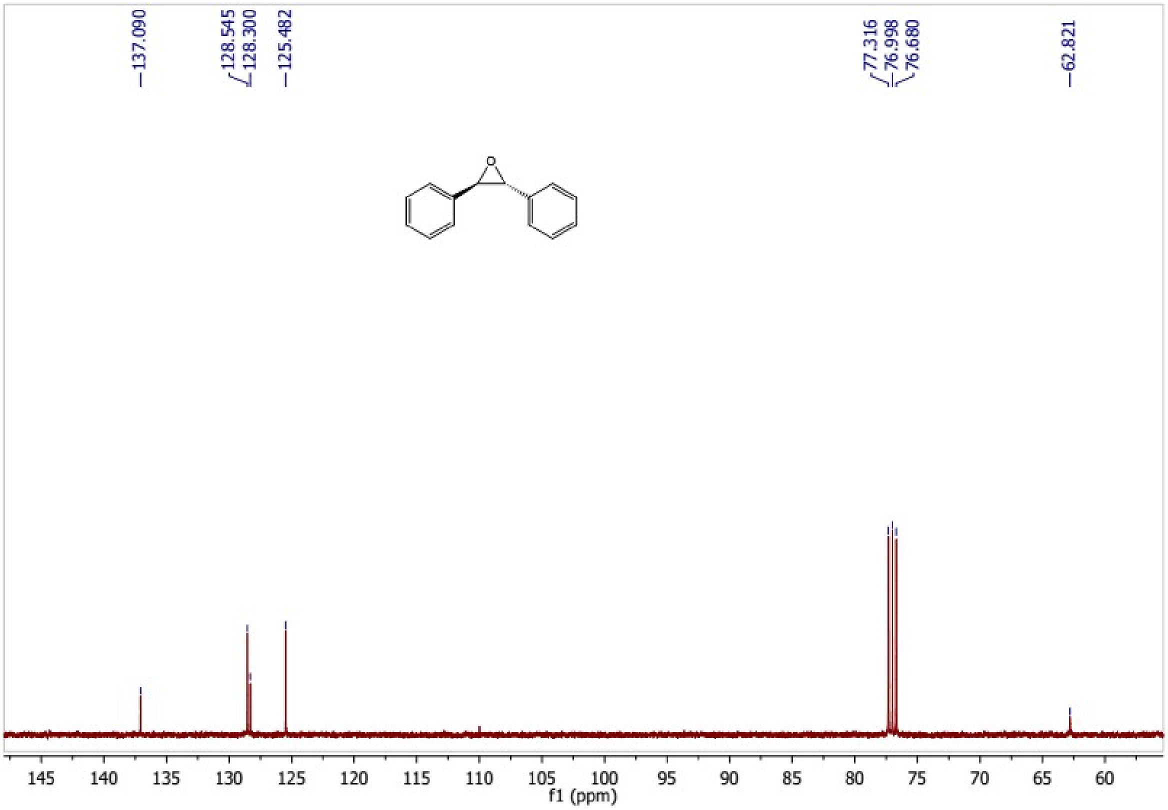
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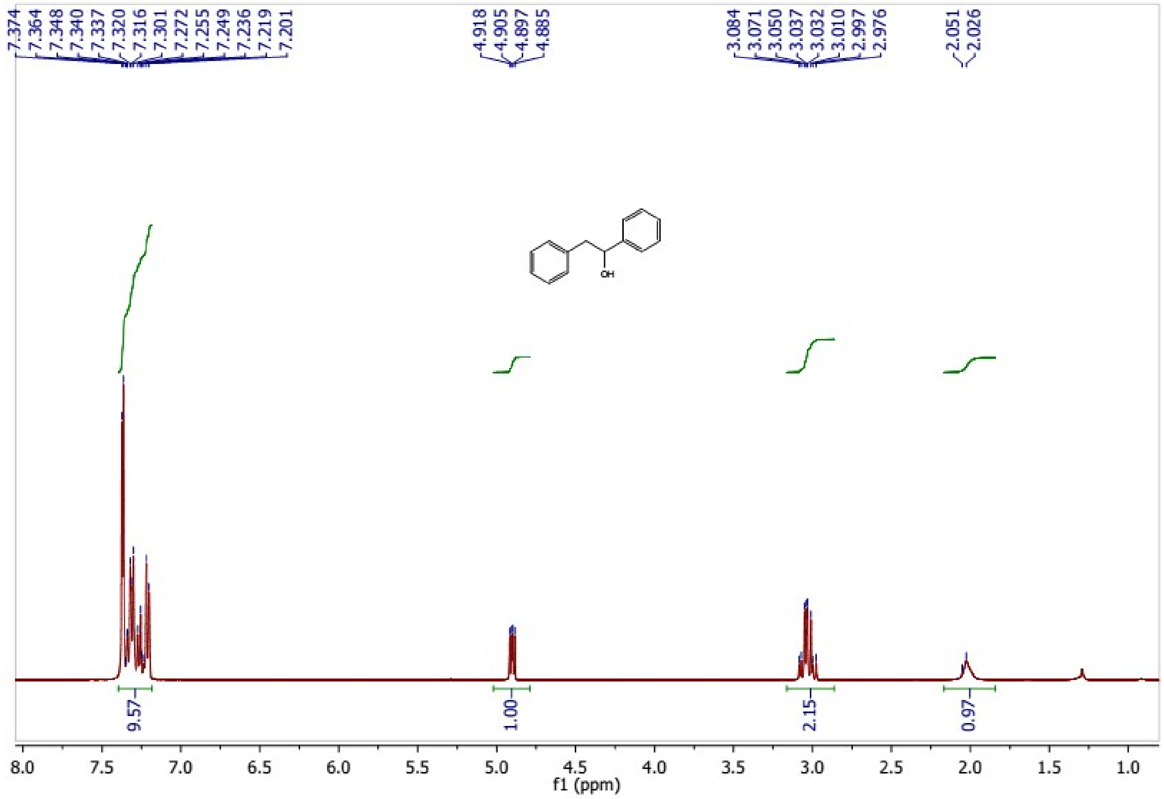
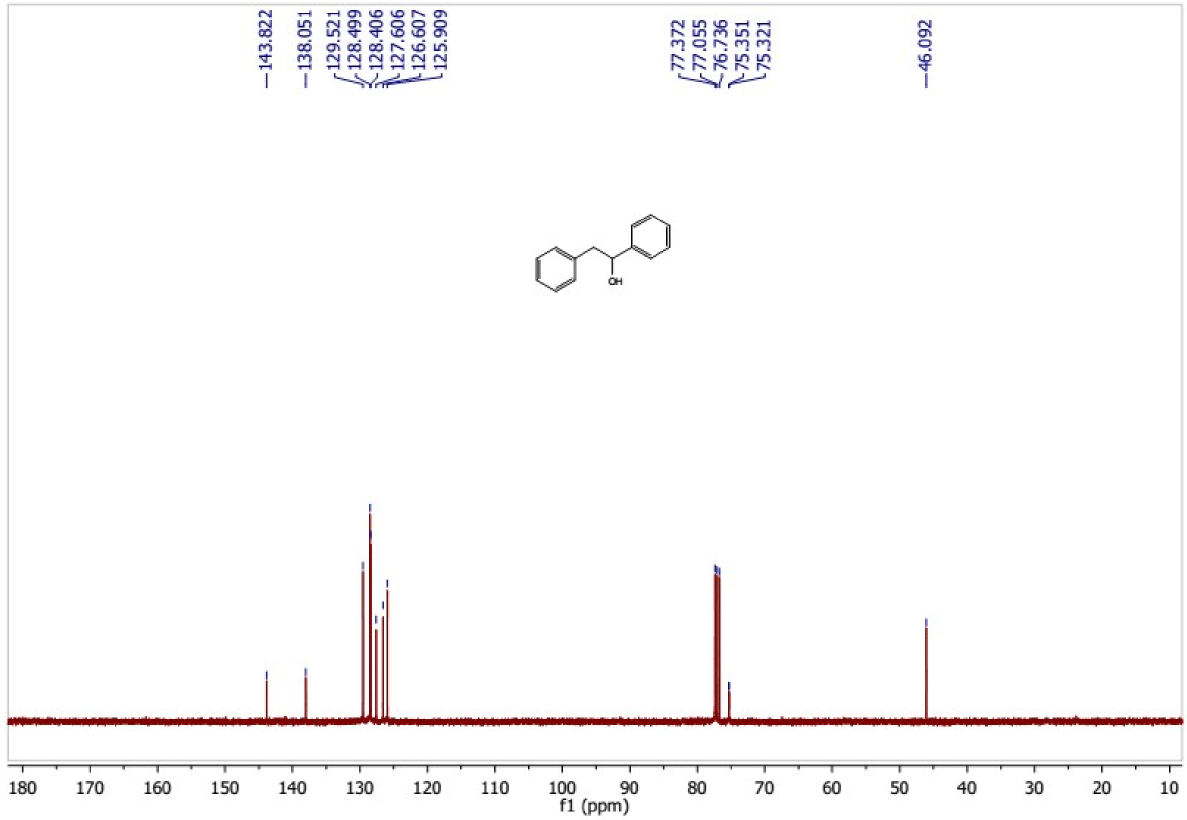
60
f1 (ppm)


7.374
7.364
7.348
7.340
7.337
7.320
7.316
7.301
7.272
7.255
7.249
7.236
7.219
7.201
4.918
4.905
4.897
4.885
3.084
3.071
3.050
3.037
3.032
3.010
2.997
2.976
2.051
2.026
OH
9.57
1.00
2.15
0.97
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)


143.822
138.051
129.521
128.499
128.406
127.606
126.607
125.909
77.372
77.055
76.736
75.351
75.321
46.092
OH
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

6. Reference

1. Han, W.; Liu, C.; Jin, Z.-L. *Organic Letters* **2007,** *9*, 4005-4007.
2. Li, P.; Wang, L.; Zhang, L.; Wang, G.-W. *Adv. Synth. Catal.* **2012,** *354*, 1307-1318.
3. Reddy, P. V.; Srinivas, P.; Annapurna, M.; Bhargava, S.; Wagler, J.; Mirzadeh, N.; Kantam, M. L. *Adv. Synth. Catal.* **2013,** *355*, 705-710.
4. Das, M.; O'Shea, D. F. *J. Org. Chem.* **2014,** *79*, 5595-5607.
5. Huang, L.; Qi, J.; Wu, X.; Wu, W.; Jiang, H. *Chem. Eur. J.* **2013,** *19*, 15462-15466.
6. (a) Crotti, P.; Ferretti, M.; Macchia, F.; Stoppioni, A. *J. Org. Chem.* **1984,** *49*, 4706-4711; (b) Mai, E.; Schneider, C. *Chem. Eur. J.* **2007,** *13*, 2729-2741.
7. Zhao, Y.; Weix, D. J. *J. Am. Chem. Soc.* **2014,** *136*, 48-51.
8. Zhu, K.; Shaver, M. P.; Thomas, S. P. *Eur. J. Org. Chem.* **2015,** *2015*, 2119-2123.