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Supporting Online Material

Primary Alcohols from Terminal Olefins: Formal Anti-Markovnikov Hydration via Triple Relay Catalysis

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I. Materials and Methods:

All reactions unless otherwise specified were carried out in a Vacuum Atmospheres Glovebox under a nitrogen atmosphere. All substrates were passed through a column of basic alumina prior to usage except for 1-octene, which was distilled over CaH_2 before being passed through a column of basic alumina under a nitrogen atmosphere. $PdCl_2(MeCN)_2$ was prepared following literature procedures(*34)*. Benzoquinone was recrystallized from *i*-PrOH prior to usage. Shvo's catalyst [1-Hydroxytetraphenyl-cyclopentadienyl(tetraphenyl-2,4-cyclopentadien-1-one)-μ-hydrotetracarbonyldiruthenium(II)] was purchased from Strem and $CuCl_2$ was from Aldrich. Both were used as received. H_2O was distilled under argon. Anhydrous *i*-PrOH from Aldrich was freeze-pump-thawed three times under argon and anhydrous *t*-BuOH also from Aldrich, was degassed, before use. ^1H and ^{13}C NMR spectra were recorded on a Varian 500 Mhz, Varian 400 Mhz or a Varian 300 Mhz spectrometer. High resolution mass spectra were provided by the California Institute of Technology Mass Spectrometry Facility using JEOL JMS-600H High Resolution Mass Spectrometer. GC-MS data was also provided through the California Institute of Technology Mass Spectrometry Facility using HP 5970 series MSD with HP 5890 GC.

Gas chromatography data was obtained using an Agilent 6850 FID gas chromatograph equipped with a HP-5 (5%-phenyl)-methylpolysiloxane capillary column (Agilent). Instrument conditions-inlet temperature: 250 ^oC; detector temperature: 250 ^oC; hydrogen flow: 30 ml/min; air flow: 400 ml/min; constant col + makeup flow: 25 ml/min. Method: 50^oC for 2 min., followed by a temperature increase of 10 ^oC/min to 115^oC, hold for 0.5 min., another temperature increase of 1^oC/min. to 125 ^oC, hold for 0.5 min., then a temperature increase of 5 ^oC/min to 140 ^oC, hold 0.5 min. and a final temperature increase of 60 ^oC/min to 300 ^oC and hold at 300 ^oC for 5 min. (total run time = 30.67 min). Response factors were collected for styrene (**1a**), 2-phenylethanol (**2a**), ethylbenzene (**3a**), 1-phenylethanol (**4a**), phenylacetaldehyde (**5a**) and acetophenone (**6a**) following literature procedures(*35)*.

Condition A: Procedure for hydration of styrene (for [styrene] = 0.25 M): $PdCl_2(MeCN)_2$ (0.01 mmol, 0.0026 g), Shvo's catalyst (0.01 mmol, 0.0109 g), $CuCl_2$ (0.02 mmol, 0.0027 g) and

benzoquinone (0.08 mmol, 0.0088 g) were weighed into a 1 dram vial in the glovebox, followed by the addition of *i*-PrOH (0.2 ml) and *t*-BuOH (0.2 ml). Styrene (0.1 mmol, 11.5µl) was added to the mixture followed by addition of H_2O (0.11 mmol, 2 µl). The resulting mixture was stirred in the glovebox at 85 ^oC for 6 h.

GC sample preparation: Tridecane (0.00123 mmol, 3 µl) was added to the reaction mixture as an internal standard. The mixture was then diluted with diethylether (3 ml) and *ca.* 0.5 ml of the resultant mixture was filtered through a plug of silica gel followed by flushing with ethyl acetate (*ca.* 1 ml). GC retention times (min) were as follows: ethylbenzene **3a** (5.31), styrene **1a** (5.80), phenylacetaldehyde **5a** (8.37), 1-phenylethanol **4a** (8.67), acetophenone **6a** (8.75), 2-phenylethanol **2a** (9.62) and tridecane (14.35).

Condition B: Procedure for hydration of other substrates (for [substrate] = 0.125 M): $PdCl_2(MeCN)_2$ (0.04 mmol, 0.0104 g), Shvo's catalyst (0.04 mmol, 0.0436 g), $CuCl_2$ (0.08 mmol, 0.0108 g) and benzoquinone (0.32 mmol, 0.0352 g) were weighed into a 20 ml vial in the glovebox, followed by the addition of *i*-PrOH (1.1 ml) and *t*-BuOH (2.2 ml). The substrate (0.4 mmol) was added to the mixture followed by addition of H_2O (0.4 mmol, 8.1 µl). After the resulting mixture was stirred in the glovebox at 85 ^oC for 6 h, it was diluted with pentane (6 ml) and filtered through a plug of silica gel followed by flushing with ethyl acetate (6 ml). The solvent was removed under vacuum, and the desired primary alcohol product was purified via a standard silica gel flash chromatography.

Condition C: Procedure for hydration of other substrates (for [substrate] = 0.067 M): $PdCl_2(MeCN)_2$ (0.04 mmol, 0.0104 g), Shvo's catalyst (0.04 mmol, 0.0436 g), $CuCl_2$ (0.08 mmol, 0.0108 g) and benzoquinone (0.4 mmol, 0.0432 g) were weighed into a 20 ml vial in the glovebox, followed by the addition of *i*-PrOH (2 ml) and *t*-BuOH (4 ml). The substrate (0.4 mmol) was added to the mixture followed by addition of H_2O (0.4 mmol, 8.1 µl). After the resulting mixture was stirred in the glovebox at 85 ^oC for 6 h, it was diluted with pentane (6 ml) and filtered through a plug of silica gel followed by flushing with ethyl acetate (6 ml). The solvent was removed under vacuum, and the desired primary alcohol product was purified via a standard silica gel flash chromatography.

Condition D: Procedure for hydration of 1-octene (for [1-octene] = 0.067 M): $PdCl_2(MeCN)_2$ (0.04 mmol, 0.0104g), Shvo's catalyst (0.04 mmol, 0.0436 g), $CuCl_2$ (0.08 mmol, 0.0108 g) and benzoquinone (0.4 mmol, 0.432 g) were weighed into a 20 ml vial in the glovebox, followed by the addition of *i*-PrOH (3 ml) and *t*-BuOH (3 ml). 1-octene (0.4 mmol, 62.8 µl) was added to the mixture followed by addition of H_2O (0.4 mmol, 8.1 µl). After the resulting mixture was stirred in the glovebox at 85 ^oC for 6 h, it was diluted with pentane (6 ml) and filtered through a plug of silica gel followed by flushing with ethyl acetate (6 ml). The solvent was removed under vacuum, and purification of the alcohol products were attempted via a standard silica gel flash chromatography.

II. Characterization Data

Except **2-(3,5-bis(trifluoromethyl)phenyl)ethanol** (**2j**), all the alcohols products are either known compounds or commercially available. **^{1}H NMR** and **HRMS** data were provided for all the primary alcohol compounds. We further checked the **^{13}C NMR** data of known compounds **2a**, **2b**, **2c**, **2e** and **2g**. Full characterization data was provided for compound **2j**.

2-phenethanol (2a) (36)**:** 41 mg, 84% yield. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.35 – 7.29 (m, 2H), 7.27 – 7.21 (m, 3H), 3.86 (t, *J* = 6.6 Hz, 2H), 2.88 (t, *J* = 6.6 Hz, 2H); **^{13}C NMR** (126 MHz,

$CDCl_3$) δ 138.46, 129.02, 128.58, 126.47, 63.67, 39.20; **HRMS** (EI+) calcd for $C_8H_{10}O$ 122.0732, found 122.0730.

2-(4-(tert-butyl)phenyl)ethanol (2b) (36)**:** 30 mg, 42% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.1 Hz, 2H), 7.17 (d, *J* = 8.1 Hz, 2H), 3.86 (t, *J* = 6.4 Hz, 2H), 2.85 (t, *J* = 6.5 Hz, 2H), 1.32 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.30, 135.27, 128.66, 125.47, 63.66, 38.61, 34.38, 31.34; **HRMS** (EI+) calcd for $C_{12}H_{18}O$ 178.1361, found 178.1358.

2-(4-methylpehenyl)ethanol (2c) (36)**:** 33 mg, 61% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.13 (s, 2H), 3.84 (t, *J* = 6.5 Hz, 2H), 2.84 (t, *J* = 6.6 Hz, 2H), 2.33 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 136.18, 135.41, 129.44, 129.05, 63.94, 38.91, 21.17; **HRMS** (EI+) calcd for $C_9H_{12}O$ 136.0886, found 136.0888

2-(2-Naphthyl)ethanol (2d) (*37*)**:** 41 mg, 60% yield. **^{1}H NMR** (300 MHz, $CDCl_3$ 7.84 – 7.76 (m, 3H), 7.69 (s, 1H), 7.51 – 7.41 (m, 2H), 7.37 (d, *J* = 8.3 Hz, 1H), 3.96 (brs, 2H), 3.05 (t, *J* = 6.5 Hz, 2H), 1.42 (s, 1H); **HRMS** (EI+) calcd for $C_{12}H_{12}O$ 172.0888, found 172.0892.

2-(2-methylpehenyl)ethanol (2e) (*38*)**:** 39 mg, 72% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.21 – 7.09 (m, 4H), 3.85 (t, *J* = 6.6 Hz, 2H), 2.90 (t, *J* = 6.9 Hz, 2H), 2.34 (s, 3H), 1.49 – 1.35 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 136.65, 136.56, 130.57, 129.75, 126.74, 126.19, 62.78, 36.53, 29.84, 19.58; **HRMS** (EI+) calcd for $C_9H_{12}O$ 136.0888, found 138.0888.

2-(4-chlorophenyl)ethanol (2f) (*39*)**:** 46.3 mg, 60% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.31 – 7.26 (m, 2H), 7.20 – 7.14 (m, 2H), 3.85 (q, *J* = 6.3 Hz, 2H), 2.84 (t, *J* = 6.5 Hz, 2H), 1.36 (t, *J* = 5.6 Hz, 1H); **HRMS** (EI+) calcd for C_8H_9ClO 156.0342, found 156.0340.

2-(4-bromophenyl)ethanol (2g) (*40*)**:** 58 mg, 72% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.3 Hz, 2H), 7.11 (d, *J* = 8.4 Hz, 2H), 3.83 (t, *J* = 6.5 Hz, 2H), 2.82 (t, *J* = 6.5 Hz, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 137.69, 131.74, 130.89, 120.44, 63.50, 38.66; **HRMS** (EI+) calcd for C_8H_9BrO 199.9839, found 199.9837.

2-(4-fluorophenyl)ethanol (2h) (*38*)**:** 47 mg, 84% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.23 – 7.15 (m, 2H), 7.05 – 6.95 (m, 2H), 3.85 (t, 6.3 Hz, 2H), 2.85 (t, *J* = 6.5 Hz, 2H); **HRMS** (EI+) calcd for C_8H_9FO 140.0638, found 140.0637.

2-(4-nitrophenyl)ethanol (2i) (*41*)**:** 55.4 mg, 83% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.7 Hz, 2H), 7.38 (d, *J* = 8.7 Hz, 2H), 3.90 (dd, *J* = 6.5, 4.8 Hz, 2H), 2.95 (t, *J* = 6.4 Hz, 2H), 1.40 (t, *J* = 4.7 Hz, 1H); **HRMS** (EI+) calcd for $C_8H_9NO_3$ 167.0582, found 167.0590.

2-(3,5-bis(trifluoromethyl)phenyl)ethanol (2j): 87 mg, 84% yield. R_f: 0.3 (30% ethyl acetate in hexane); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.4 Hz, 1H), 7.71 (s, 2H), 3.94 (t, *J* = 6.3 Hz, 2H), 3.00 (t, *J* = 6.3 Hz, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 141.54, 131.80 (q, *J* = 33.2 Hz), 129.35, 123.50 (q, *J* = 272.7 Hz), 120.72 – 120.54 (m), 62.90, 38.71; **^{19}F NMR** (282 MHz, $CDCl_3$) δ -62.87; **IR** (NaCl plate) 3382 (br), 2919, 2849, 1995, 1624, 1461, 1278, 1137 cm^{-1}; **HRMS** (EI+) calcd for $C_{10}H_8F_3O$ 258.0479, found 258.0487.

1-octanol (**2k**) and **2-octanol** (**4k**): The yield of compounds **2k** and **4k** was determined via crude ^{1}H NMR using mesitylene as an internal standard by comparing the integration of the α protons of the alcohols with the methyl peaks of mestylene. Purification of compounds **2k** and **4k** was attempted via silica gel flash chromatography, and a mixture of compounds **2k** and **4k** with an unknown aromatic impurity was isolated. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.79 (m, 1H, compound

4k) 3.64 (t, *J* = 7.0 Hz, 2H, compound **2k**), 1.56 (m, 2H, compound **2k**), 1.45-1.28 (CH_2 protons for both **2k** and **4k**), 1.18 (d, *J* = 6.5 Hz, 3H, compound **4k**), 0.88 (t, *J* = 6.5 Hz, 3H, for both compounds **2k** and **4k**); **HRMS** (M-H) calcd for $C_8H_{17}O$ 129.1279, found 129.1276. The identity of compound **4m** was further confirmed by GC-MS, in which the synthetic sample gave an identical retention time (8.6 min for **4k** and 9.9 min for **2k**) and mass spec as the authentic sample: for **2k**, m/z 129 (M-1), 112, 97, 84, 69, 56, 41; for **2k**, m/z 129 (M-1), 115, 97, 84, 69, 55, 45, 41.

3-phenylpropan-1-ol (2m): 6.4 mg, 12% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.33 – 7.26 (m, 2H), 7.24 – 7.16 (m, 3H), 3.69 (q, *J* = 6.3 Hz, 2H), 2.72 (t, 6.3 2H), 1.97 – 1.85 (m, 2H), 1.25 (t, *J* = 5.3 Hz, 1H). **HRMS** (EI+) calcd for $C_9H_{12}O$ 136.0888, found 136.0884. The ratio between compounds **2m** and **4m** was determined via crude ^{1}H NMR by comparing the integration of the α protons of the alcohols. Isolation of pure compound **4m** was unsuccessful due to contamination of an unknown impurity. The identity of compound **4m** was further confirmed by GC-MS, in which the synthetic sample gave an identical retention time (11.1 min) and mass spec as the authentic sample: m/z 136 (M), 121, 117, 103, 92, 91, 77, 65, 51, 45, 39.

Recovery of hydroquinone:

$PdCl_2(MeCN)_2$ (0.04 mmol, 0.0104g), Shvo's catalyst (0.04 mmol, 0.0436 g), $CuCl_2$ (0.08 mmol, 0.0108 g) and benzoquinone (0.37 mmol, 0.040 g) were weighed into a 20 ml vial in the glovebox, followed by the addition of *i*-PrOH (2 ml) and *t*-BuOH (4 ml). Styrene (46 µL, 0.4 mmol) was added to the mixture followed by addition of H_2O (0.4 mmol, 8.1 µl). The resulting mixture was stirred in the glovebox at 85 ^{o}C for 6 h. Crude reaction mixture was washed three times with toluene (2 ml) and filtered through a celite plug. The celite plug was subsequently washed with ethyl acetate (ca 5 ml). The ethyl acetate fraction was recombined with the remaining material after the toluene wash. After removal of the solvent, pure hydroquinone was obtained as a white crystal (30mg, 74% yield). **^{1}H NMR** (300 MHz, CD_3CN) δ 6.64; **HRMS** (EI+) calcd for $C_6H_6O_2$ 110.0368, found 110.0390.

Synthesis and characterization of vinyl enol ether:

$PdCl_2(MeCN)_2$ (0.04 mmol, 0.0104 g), $CuCl_2$ (0.08 mmol, 0.0108 g) and benzoquinone (0.4 mmol, 0.432 g) were weighed into a 20 ml vial in the glovebox, followed by the addition of *t*-BuOH (6 ml). Styrene (46 µl, 0.4 mmol) was added to the mixture and the resulting mixture was stirred in the glovebox at 85 ^{o}C for 6 h. Yield was determined via crude NMR using mesitylene as an internal standard. The olefin peaks for the *cis* and *trans* isomers were both observed by crude NMR: **^{1}H NMR** (300 MHz, $CDCl_3$) *trans isomer*: δ 7.02 (d, *J* = 12.4 Hz, 1H), 5.99 (d, *J* = 12.4 Hz, 1H); *cis isomer* 6.45 (d, *J* = 7.1 Hz, 1H), 6.45 (d, *J* = 5.24 Hz, 1H). The ratio between *trans* and *cis* isomers is 1.5:1. This data fits with previously reported values for these vinyl enol ethers (*42*). GC/HRMS was additionally employed to characterize the compounds ([$C_{12}H_{16}O$] cald 176.1201, found 176.1216).

Labeling studies:

Synthesis of deuterated products **9** and **10:** General procedure (styrene as the substrate, Condition C) was followed using *i*-C_3H_7OD and *t*-butanol-OD. Deuterated 2-phenylethanol products were isolated by silica gel chromatography as an inseparable mixture of **9** and **10**. The yield (77%) was determined via GC using response factors calculated for **2a** relative to tridecane. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.35 – 7.29 (m, 2H), 7.27 – 7.21 (m, 3H), (m, *J* = 6.6 Hz, 2H), 2.88 (m, 0.68H). **HRMS HRMS (EI+)** calcd for $C_8H_8OD_2$ 124.0857, found 124.0860; calcd for C_8H_9OD 123.0794, found 123.0796. Integration analysis indicates the β-position incorporated one deuterium in 69%

of the product and two deuterium atoms in 31% of the product. This calculation approximates that no **2a** was formed.

Synthesis of deuterated products **11** and **12:** General procedure (styrene as the substrate, Condition C) was following using *i*-propanol-d8 and *t*-butanol-OD. Deuterated 2-phenylethanol products were isolated by silica gel chromatography as an inseparable mixture. The yield (67%) was determined via GC using response factors calculated for **2a** relative to tridecane. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.35 – 7.29 (m, 2H), 7.27 – 7.21 (m, 3H), (m, J = 6.6 Hz, 1.13H), 2.88 (m, 0.65H). Integration analysis indicates the α position incorporated one deuterium in 87% of the product and the β position incorporated one deuterium in 65% of the product and two deuterium atoms in 35% of the product. These calculation approximates that no **2a** was formed. Both compounds **11** and **12** do not get ionized on **HRMS (EI+)**. GC-MS spectrum indicates a single peak matched the retention time with compound **2a**, but shows a mass of m/z 124 and 125 along with m/z 123 as a minor peak (the m/z 122 peak was only observed marginally).

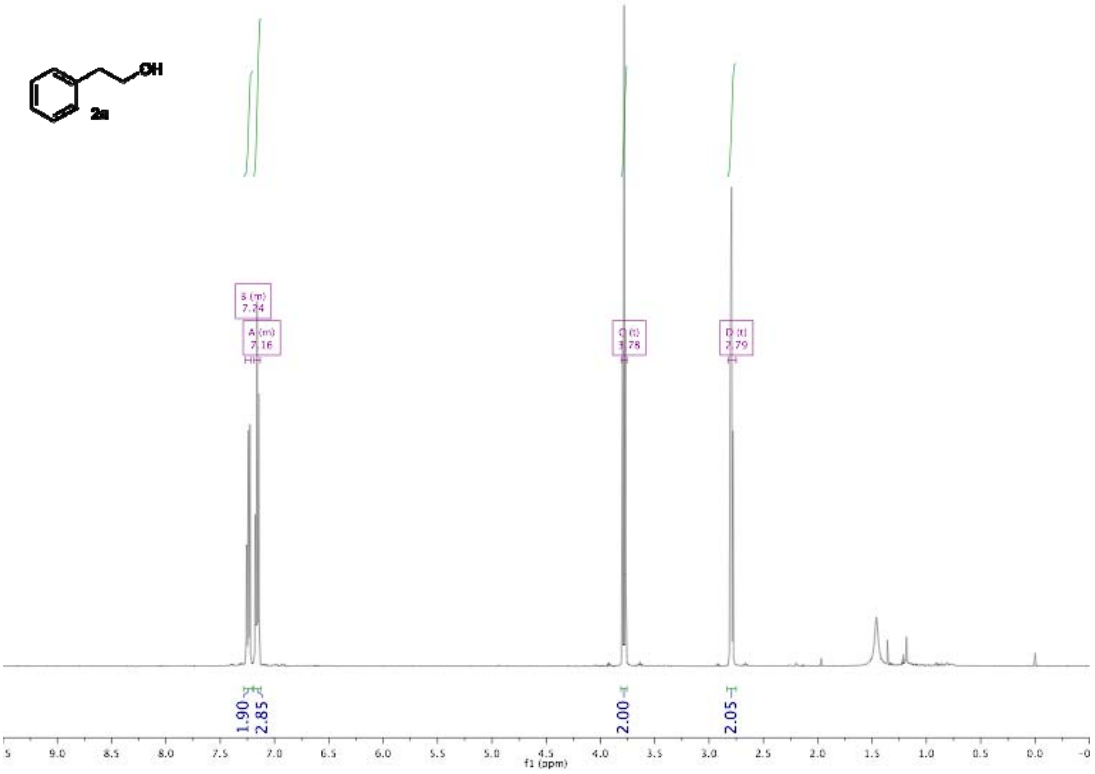
III. Supporting Table

Table 1S. Studies with styrene as the substrate. The Reaction concentration is 0.25M. Yields and conversions were determined by GC analysis, using tridecane as the internal standard. (BQ: 1,4-Benzoquinone; MS: Molecular sieves)[*,†]

Entry	Change from the "standard conditions"	Conversion (%)	Yield of **2a** (%)	Yield of byproducts (%)			
				3a	**4a**	**5a**	**6a**
1	none	89	77	1.3	0.7	1.5	1.4
2	no $PdCl_2(CH_3CN)_2$	34	0	26	0	0	0
3	no Shvo's catalyst	80	0	0.2	0	42	0
4	no $CuCl_2$	>99	48	32	5.9	0.5	1.4
5	no BQ	58	0	0.9	0	0	0
6	no i-PrOH	88	0	0.5	0	57	0
7	no t-BuOH	48	18	2.0	trace	trace	trace
8	no *t*-BuOH, but 28 equiv H_2O	75	64	2.0	4.9	0.96	9.9
9	replace H_2O with 4 Å MS	>99	0	57	0	0	0

[*]The loss of mass balance in entry 5 is unclear but presumably caused by either styrene oligomerization or complexation with metal catalysts. [†] The loss of mass balance in entry 6 (57% vs 88%) is presumably caused by the lability of the benzylic α proton and the reactivity of the aldehyde to form oligomers and aldol condensation products.

IV. NMR Spectra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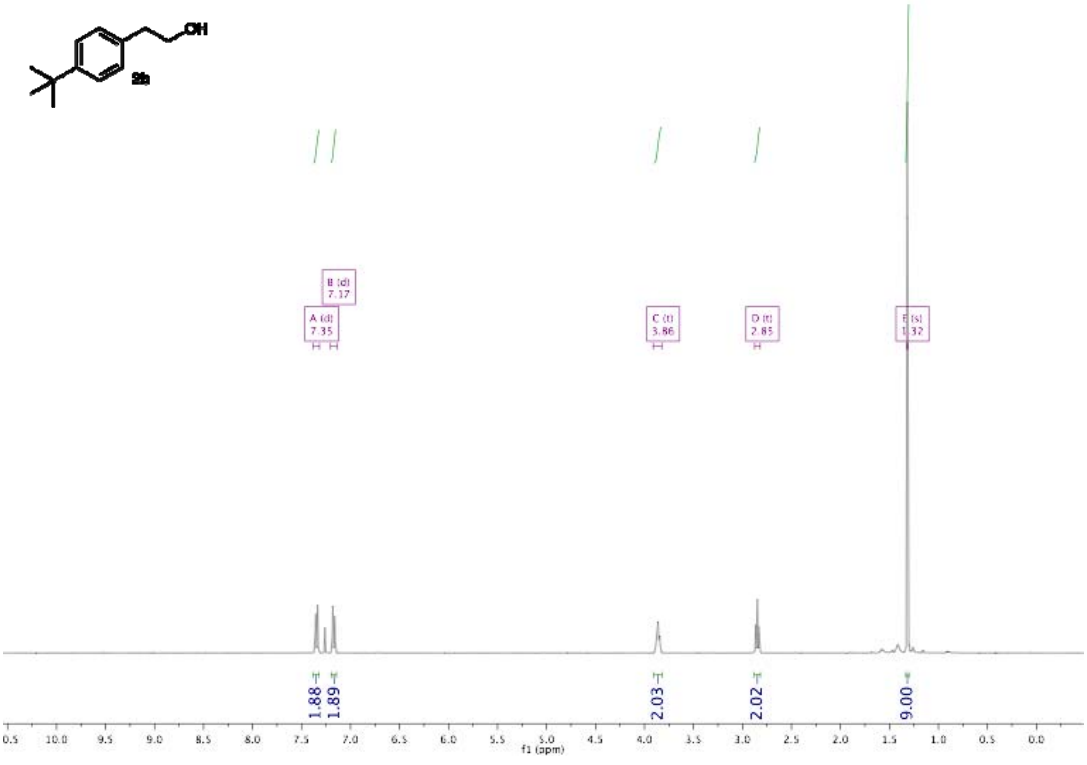
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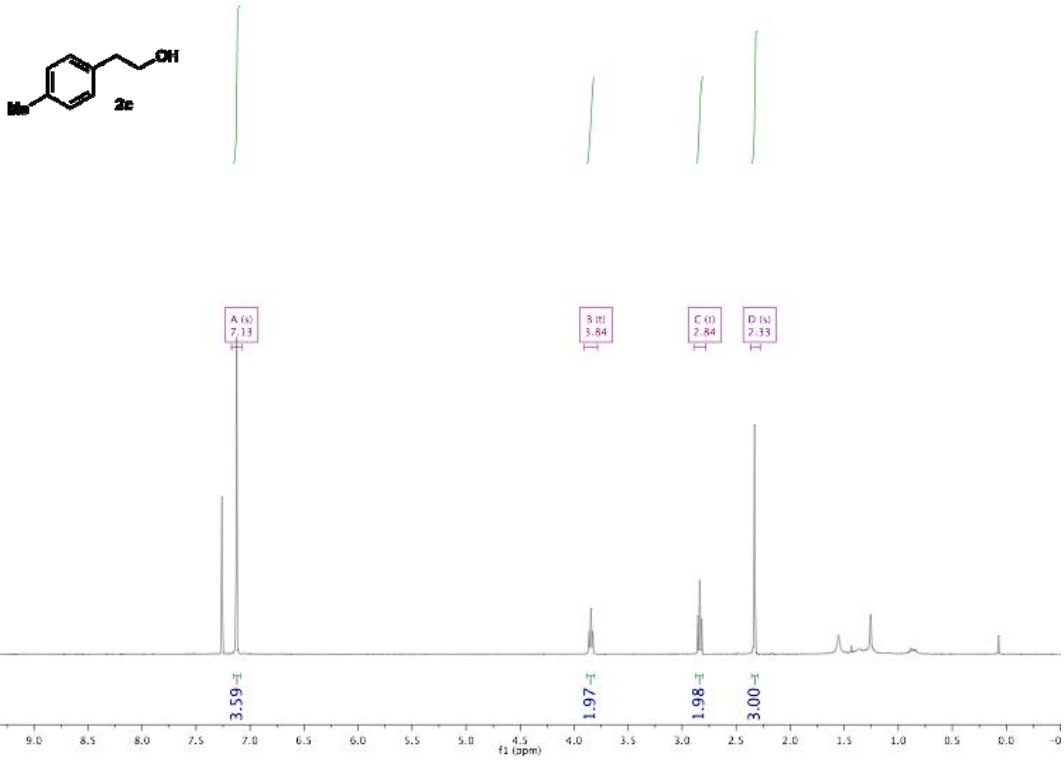
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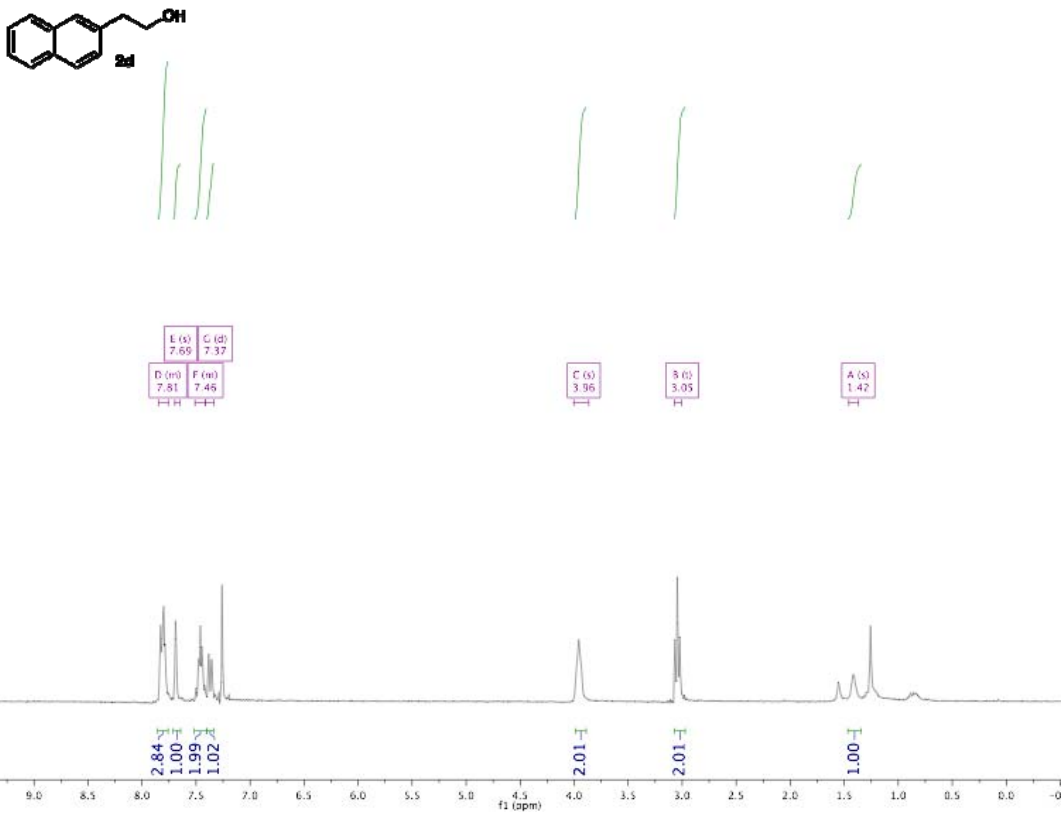
f1 (ppm)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D (m) 7.81
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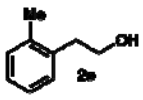
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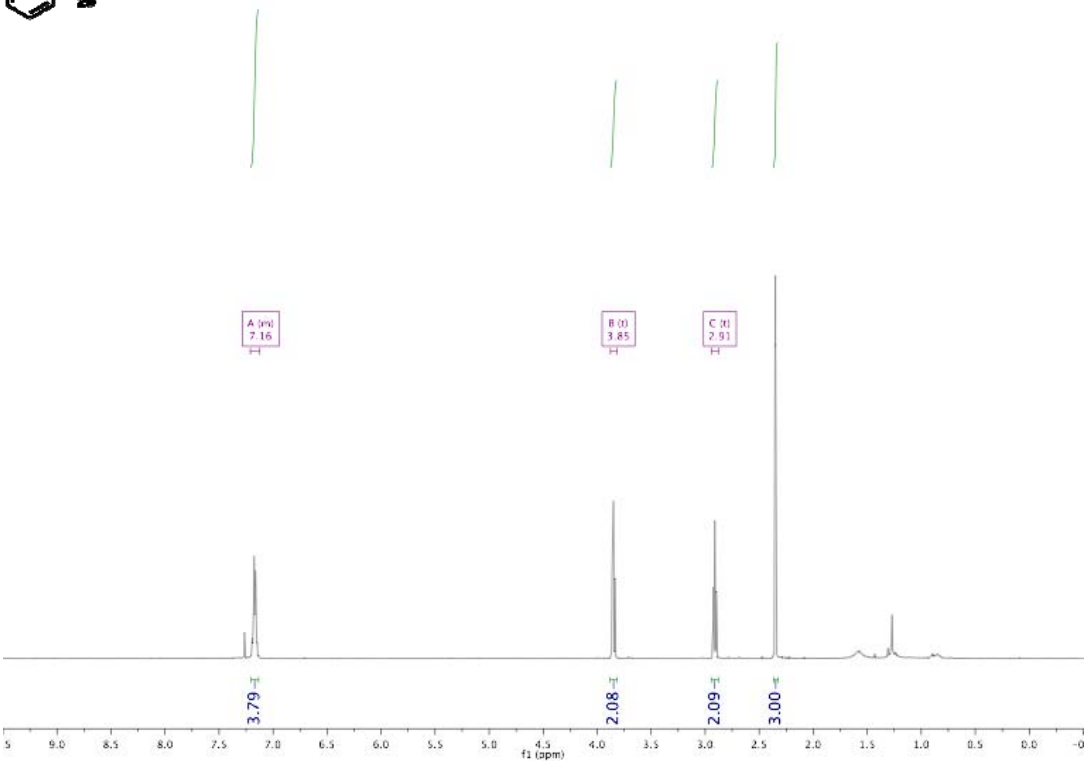
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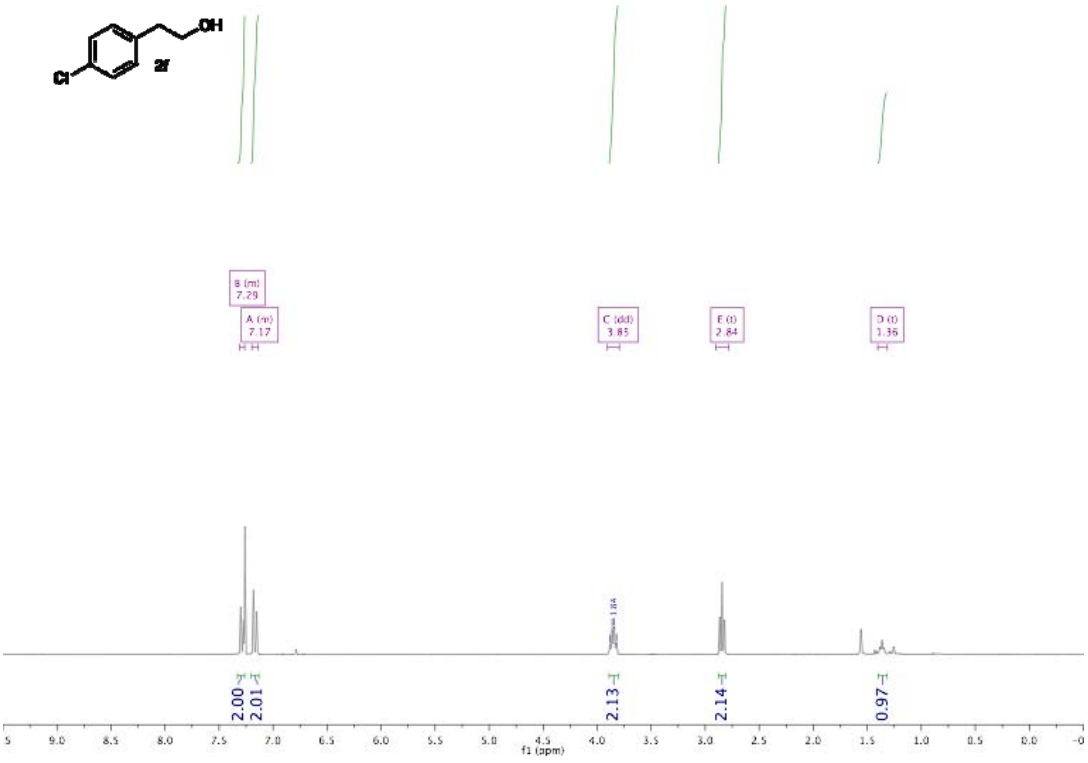
2.09
3.00
f1 (ppm)

OH
Cl
2f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A (m)
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D (t)
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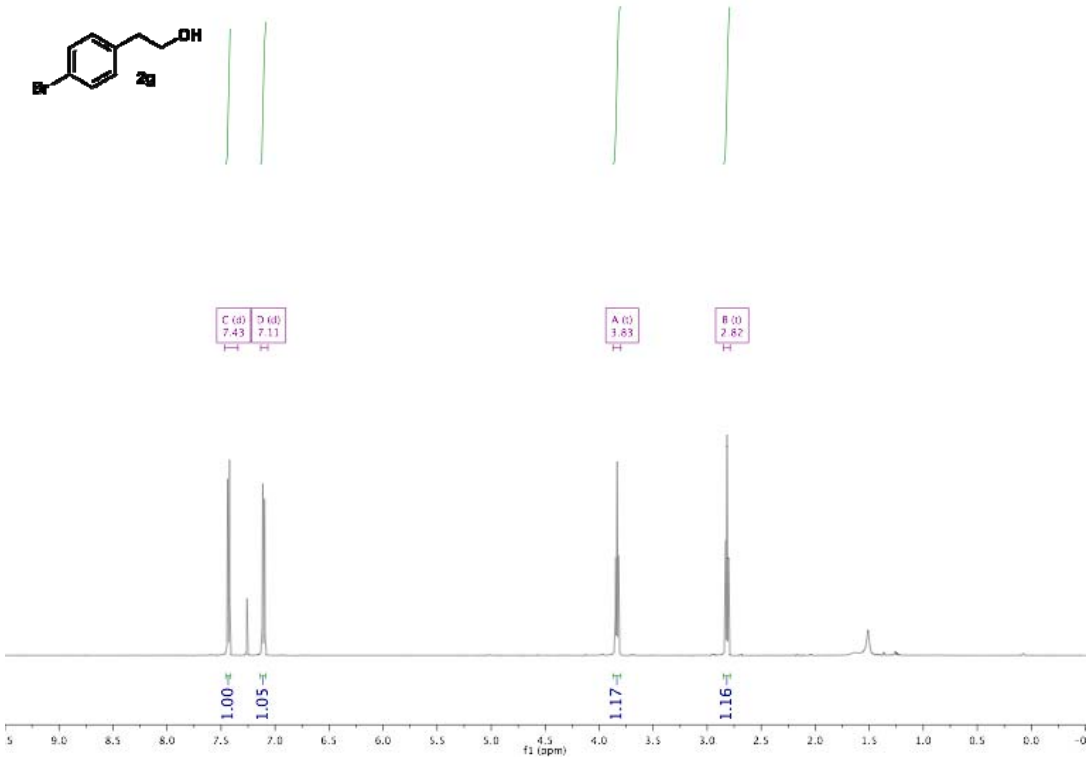
2.14
0.97
f1 (ppm)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Br
2g
C (d) 7.43
D (d) 7.11
A (t) 3.83
B (t) 2.82
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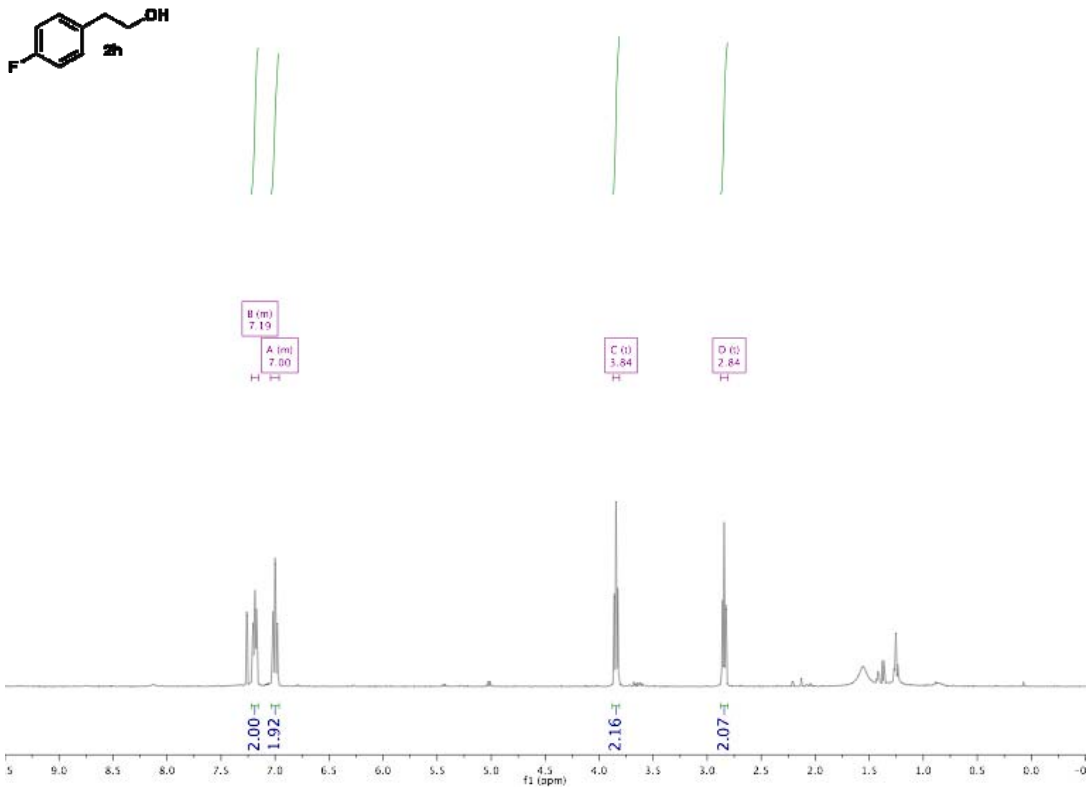
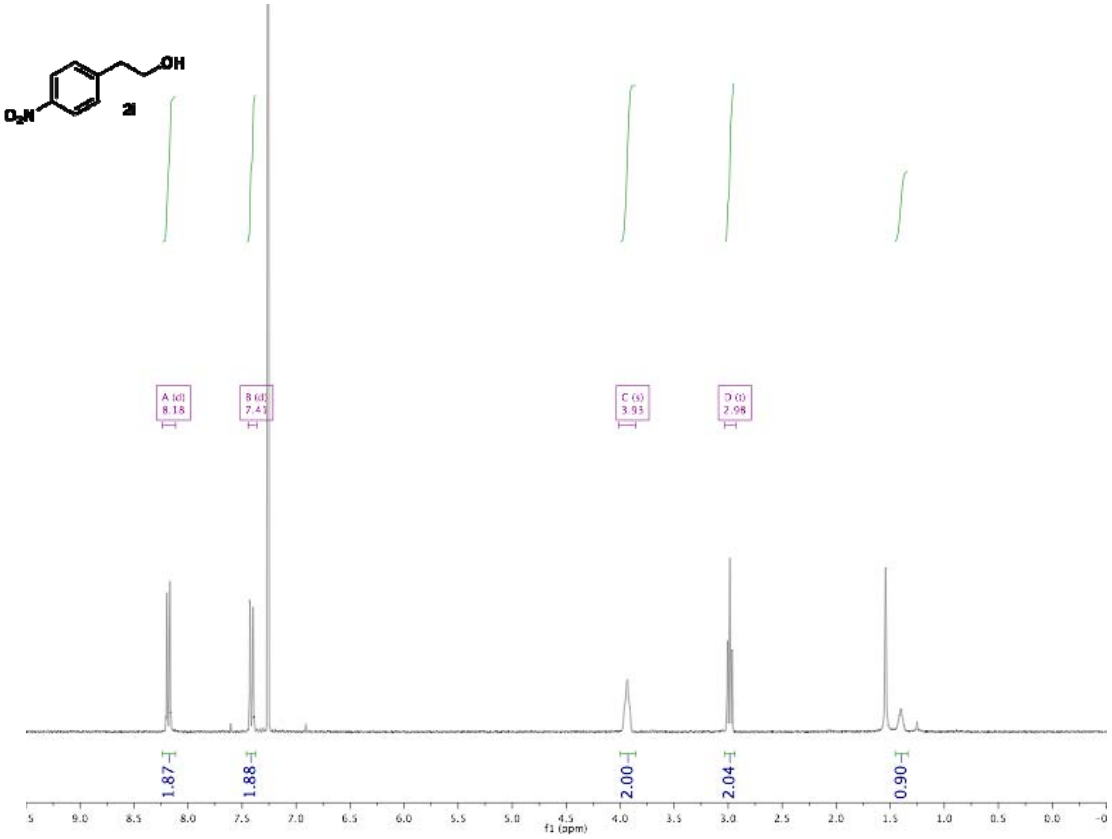
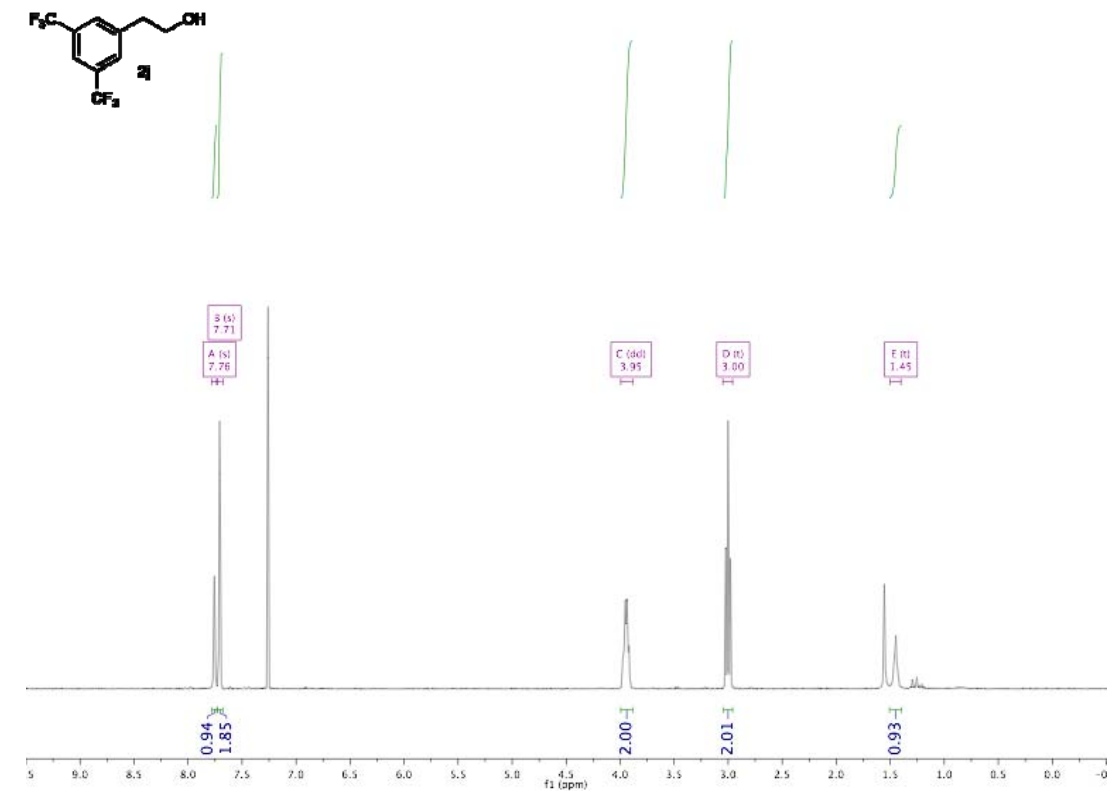
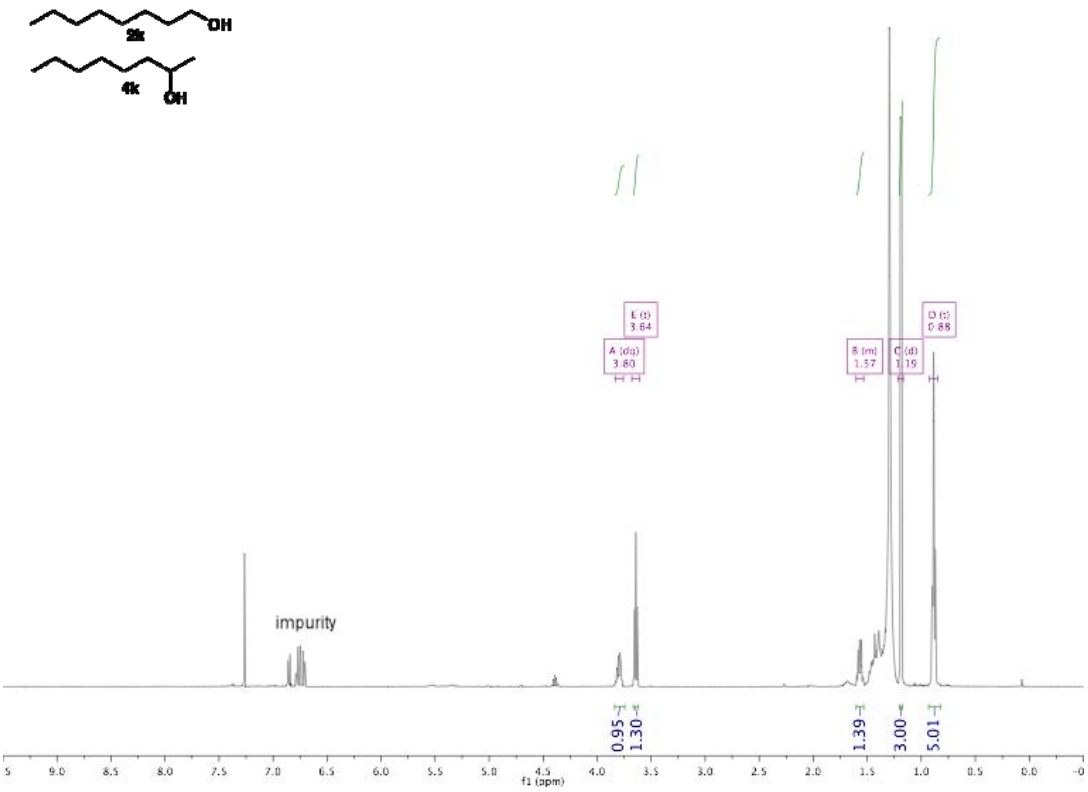
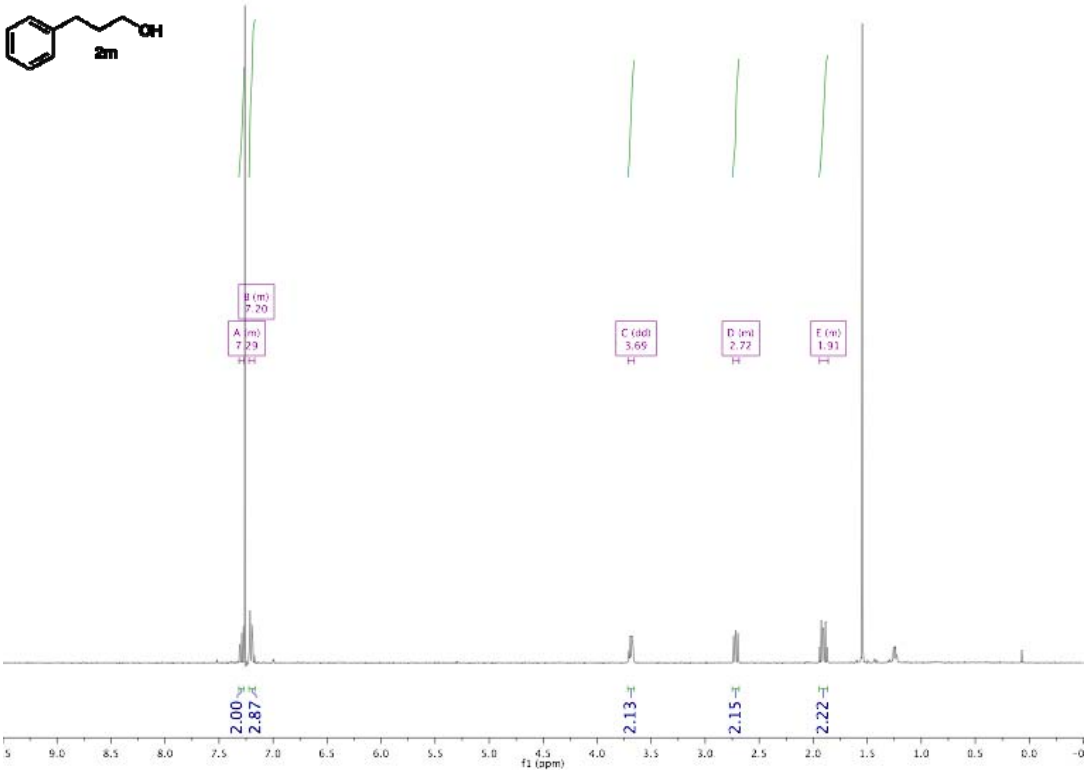
1.05
1.17
1.16
f1 (ppm)


OH
F
2h
B (m) 7.19
A (m) 7.00
C (t) 3.84
D (t) 2.84
2.00
1.92
2.16
2.07
f1 (ppm)


OH
O2N
2l
A (d) 8.18
B (d) 7.43
C (s) 3.93
D (t) 2.98
1.87
1.88
2.00
2.04
0.90
f1 (ppm)


F3C
OH
CF3
2j
B (s) 7.71
A (s) 7.76
C (dd) 3.95
D (t) 3.00
E (t) 1.45
0.94
1.85
2.00
2.01
0.93
f1 (ppm)


2k
4k
OH
OH
impurity
E (t) 3.64
A (dq) 3.80
B (m) 1.57
C (d) 1.19
D (t) 0.88
0.95
1.30
1.39
3.00
5.01
f1 (ppm)


2m
OH
B (m) 7.20
A (m) 7.29
C (dd) 3.69
D (m) 2.72
E (m) 1.91
2.00
2.87
2.13
2.15
2.22
f1 (ppm)

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