Supporting Information

Manganese-Catalyzed Stereospecific Hydroxymethylation of Alkyl Tosylates

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General Methods and Materials

Proton and carbon magnetic resonance spectra (^{1}H NMR at 400 MHz, 500 MHz, or 600 MHz and ^{13}C NMR at 100 MHz, 126 MHz, or 151 MHz) spectrometer with solvent resonance as the internal standard (^{1}H NMR: $CHCl_3$ at 7.28 ppm; ^{13}C NMR: $CDCl_3$ at 77.0 ppm). ^{1}H NMR data are reported as follows: chemical shift (ppm), multiplicity (s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), and integration. Mass spectra were obtained using a Q Exactive HF-X mass spectrometer with electrospray introduction and external calibration or an or an Agilent Gas Chromatograph-Mass Spectrometer with a 7820A series GC system and a 5977E Network Mass Selective Detector. Percent deuterium incorporation was determined using a ThermoFisher GC Exactive with an Electron Ionization (EI) source. These samples were prepared in methanol. HPLC analysis was performed on a Shimadzu SPD-M20A photodiode array (PDA) system equipped with Daicel Chiralpak IE, IF, IG, and OJ-H columns using a flow rate of 1 mL/min with hexanes and isopropanol as eluent, unless otherwise indicated. Chiral supercritical fluid chromatography analysis was performed on a Waters Acquity UPC2 instrument at 35°C with Phenomenex chiral columns (15 cm) using the conditions detailed for each substrate.

Analytical thin layer chromatography (TLC) was performed on SiliaPlate 250µm thick silica gel purchased from Silicycle. Visualization was accomplished with shortwave UV light (254 nm), iodine, Hanessian's stain, or ethanolic acidic p-anisaldehyde solution followed by heating when necessary. Purification of the reaction products was carried out by flash chromatography using Siliaflash P60 silica gel (40-63µm) purchased from Silicycle. Carbon monoxide, Research grade 99.99% (part number CM R200) was purchased from Airgas. Tetrahydrofuran, diethyl ether, N,N-dimethylformamide, acetonitrile, and dichloromethane were dried by passage through a column of neutral alumina under nitrogen prior to use. t-Amyl alcohol was sparged with argon before storage over 3Å molecular sieves in the glovebox. $Mn_2(CO)_{10}$ was purchased from Sigma-Aldrich. All other reagents were obtained from commercial sources and used without further purification, unless otherwise noted. In addition, all reactions were carried out under an atmosphere of dry argon in flame or oven-dried glassware with magnetic stirring. The glass tubes for carbonylations were purchased from Ace Glass and the gas quick-connect adapters were obtained from Swagelok. An example of the carbonylation setup is shown below.

Swagelok setup for pressurizing reactions

List of Abbreviations

DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene
DCM = dichloromethane
DHP = 3,4-dihydro-2H-pyran
DIAD = diisopropyl azodicarboxylate
DMF = N,N-dimethylformamide EtOAc = ethyl acetate
TEA = triethylamine
THF = tetrahydrofuran
THP = tetrahydropyran
TES = triethylsilyl
TsCl = 4-toluenesulfonyl chloride

Substrate Preparation

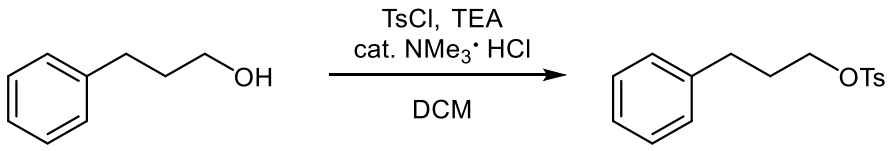
General Procedure A: Tosylation of Alcohols. Tosylates were synthesized using a modified procedure from Tanabe, et. al.[1] To a 0 ^{o}C ice bath cooled solution of TsCl (1.5 equiv) and trimethylamine hydrochloride (0.1 equiv) in DCM (1 M with respect to the alcohol) was added TEA (2.5 equiv) dropwise. To this solution was added a solution of the alcohol in DCM (1 M), the solution was then stirred for 2 hours and allowed to warm to room temperature. The reaction was quenched by addition of N,N-dimethyldiaminopropane (2.0 equiv) and stirred for 15 additional minutes. The reaction mixture was poured into water and separated. The organic layer was washed sequentially with 1 M HCl, a saturated aqueous solution of $NaHCO_3$, and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography.

General Procedure B: Mitsunobu of Phenols. The corresponding alcohol (1 equiv), substituted phenol (1 equiv), and triphenylphosphine (1 equiv), were dissolved in THF (0.5 M) and cooled to 0 ^{o}C. DIAD (1 equiv) was added dropwise and the reaction was warmed to room temperature and stirred overnight. The mixture was filtered through sequential beds of celite and silica, then concentrated under reduced pressure. The crude product was purified by flash chromatography.

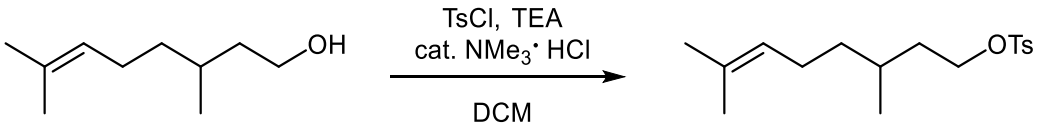
General Procedure C: THP Deprotection. The corresponding THP ether (1 equiv) was combined with pyridinium *p*-toluenesulfonate (0.1 equiv) in methanol (0.4 M) and stirred overnight at room temperature. The mixture was concentrated under reduced pressure and the crude product was purified by flash chromatography.

General Procedure D: Propylene Oxide Opening for Chiral Non-Racemic Alcohol Synthesis. To a -30 °C suspension of CuI (1.5 equiv) in THF (1 M) was added benzyl Grignard. The solution was stirred for five minutes, then (S)-propylene oxide (1 equiv) was added portion-wise and the mixture was warmed to warmed to 0 °C and stirred for an additional 2 hours. The reaction was then quenched with an aqueous saturated solution of NH_4Cl and warmed to room temperature. Ether was added and the layers were separated. The organic layer was washed sequentially with a saturated aqueous solution of $NaHCO_3$ and brine, then dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography.

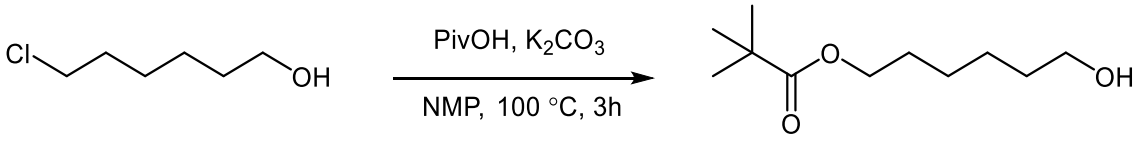
Synthesis of Primary Tosylates



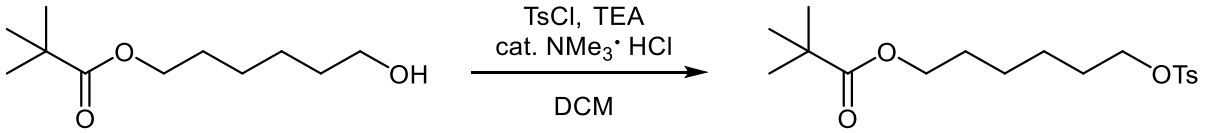
3-phenylpropyl 4-methylbenzenesulfonate (1) was synthesized by tosylating 3-phenyl-1-propanol (2.00 g, 14.7 mmol) according to General Procedure A. The crude product was purified via flash chromatography in 10% EtOAc/hexanes to provide 2.93 g (69%) of tosylate **1** as a clear, colorless oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.85 – 7.78 (m, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.26 (dd, *J* = 8.2, 6.8 Hz, 1H), 7.23 – 7.17 (m, 1H), 7.13 – 7.05 (m, 1H), 4.05 (t, *J* = 6.2 Hz, 1H), 2.67 (t, *J* = 7.6 Hz, 1H), 2.48 (s, 1H), 2.06 – 1.93 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 144.8, 140.4, 133.0, 129.9, 128.5, 128.4, 127.9, 126.2, 69.6, 31.5, 30.5, 21.7. **HRMS** (ESI) calculated for $[C_{10}H_{14}O+Na]^+$ 173.0942, found 173.0942.



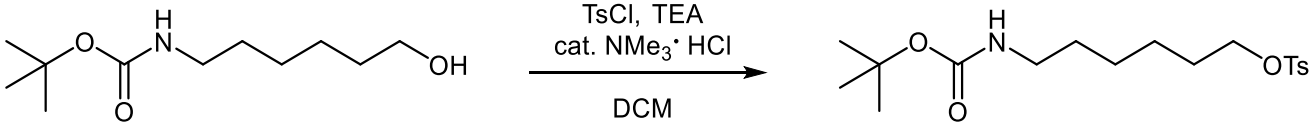
3,7-dimethyloct-6-en-1-yl 4-methylbenzenesulfonate (3) was synthesized by tosylating 3,7-dimethyloct-6-en-1-ol (2.00 g, 12.8 mmol) according to General Procedure A. The crude product was purified via flash chromatography in 10% EtOAc/hexanes to provide 3.30g (83%) of tosylate **3** as a clear, colorless oil. Physical and spectral data were in accordance with the literature.[2]



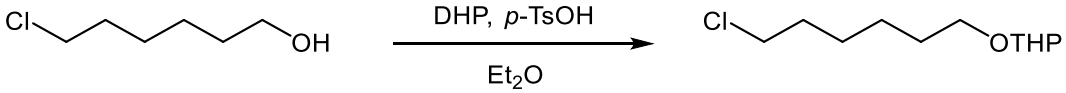
6-hydroxyhexyl pivalate (SI-1) was synthesized by combining 6-chlorohexan-1-ol (1.95 mL, 14.7 mmol, 1 equiv.), pivalic acid (1.70mL, 14.7 mmol, 1 equiv.), and potassium carbonate (4.05 g, 29.3 mmol, 2 equiv.) and heating at 100 °C in an oil bath for 3h. The mixture was cooled to room temperature and partitioned with ether (50 mL) and saturated aqueous NH4Cl (50 mL). The organic phase was washed with brine (3 x 50 mL), dried over $MgSO_4$, and dried under vacuum. The crude oil (2.34 g) was taken to the next step without further purification.



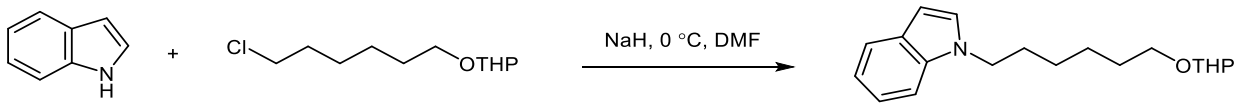
6-(tosyloxy)hexyl pivalate (5) was synthesized by tosylating **SI-1** (2.34 g) according to General Procedure A. The crude product was purified via flash chromatography in 10% EtOAc/hexanes to give 1.13 g of a clear oil, in 22% yield over two steps. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.89 – 7.71 (m, 2H), 7.44 – 7.32 (m, 2H), 4.03 (dt, *J* = 10.1, 6.5 Hz, 4H), 2.47 (s, 3H), 1.67 (dt, *J* = 8.1, 6.5 Hz, 2H), 1.59 (dq, *J* = 8.0, 6.7 Hz, 2H), 1.41 – 1.25 (m, 2H), 1.20 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.6, 144.7, 133.2, 129.8, 127.9, 64.1, 38.7, 28.8, 28.4, 27.2, 25.4, 25.0, 21.6. **HRMS** (ESI) calculated for $[C_{18}H_{28}O_5S+H]^+$ 357.1736, found 357.1726.



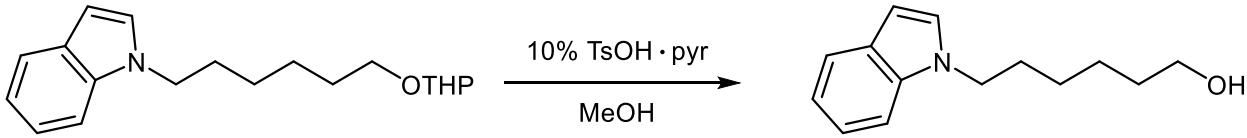
6-((tert-butoxycarbonyl)amino)hexyl 4-methylbenzenesulfonate (7) was synthesized by tosylating tert-butyl (6-hydroxyhexyl)carbamate (1.00 g, 4.60 mmol) according to General Procedure A. The crude product was purified via flash chromatography in 30% EtOAc/hexanes to give 1.25 g (73%) of an off-white solid. **HRMS** (ESI) calculated for $[C_{18}H_{29}NO_5S+Na]^+$ 394.1664, found 394.1655.



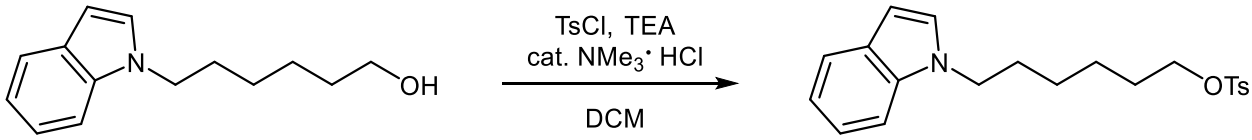
2-((6-chlorohexyl)oxy)tetrahydro-2H-pyran (SI-2) was synthesized by stirring 6-chlorohexan-1-ol (5 g, 36.6 mmol,1 equiv.), 3,4-dihydro-2H-pyran (4.01mL, 43.9 mmol, 1.2 equiv), and p-toluenesulfonic acid monohydrate (70 mg, 0.01 mmol) in ether (100 mL) at room temperature, overnight. The reaction was quenched via addition of a saturated sodium bicarbonate solution. The organic layer was separated and the aqueous layer was extracted twice with Et_2O and the organic layers were combined and dried over $MgSO_4$, filtered, and concentrated under reduced pressure to provide 8.075 g (>99%) of the crude product, which was used without further purification.



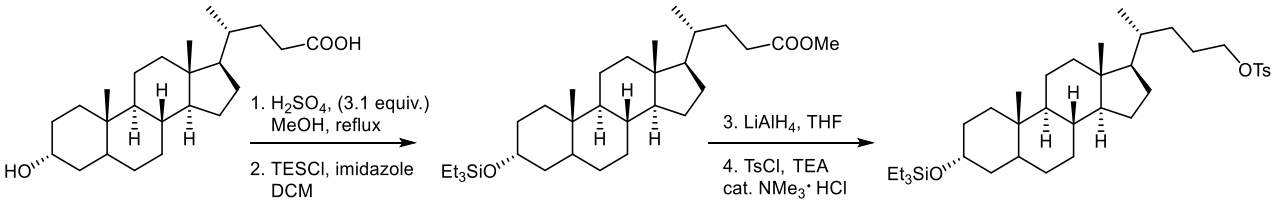
1-(6-((tetrahydro-2H-pyran-2-yl)oxy)hexyl)-1H-indole (SI-3) SI-3 was synthesized cooling a solution of indole (17.0 mmol, 1.99 g) in anhydrous DMF (0.2M with respect to the tosylate or chloride) was added NaH as 60 wt % dispersion in mineral oil (0.91 g, 22.7 mmol) in one portion. After the reaction was stirred at 0 °C for 30 minutes, a solution of chloride (2.50 g, 11.3 mmol) in DMF (0.2M) was added and the reaction was allowed to warm to room temperature, and stirred overnight. The reaction was then quenched with water and diluted with ethyl acetate. The organic layer was collected and the aqueous layer was extracted with ethyl acetate (3 × 20 mL). The organic layers were then combined and washed with DI water (2 × 50 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by gradient flash chromatography in 20% to 30% EtOAc/hexanes to give 1.571 g (46%) of a clear oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.69 (d, *J* = 7.9 Hz, 1H), 7.39 (d, *J* = 8.2 Hz, 1H), 7.26 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.20 – 7.12 (m, 2H), 6.54 (d, *J* = 3.1 Hz, 1H), 4.60 (dd, *J* = 4.6, 2.9 Hz, 1H), 4.16 (t, *J* = 7.1 Hz, 2H), 3.90 (ddd, *J* = 10.9, 7.6, 3.0 Hz, 1H), 3.77 (dt, *J* = 9.6, 6.8 Hz, 1H), 3.58 – 3.48 (m, 1H), 3.41 (dt, *J* = 9.6, 6.5 Hz, 1H), 1.99 – 1.81 (m, 3H), 1.81 – 1.70 (m, 1H), 1.69 – 1.51 (m, 6H), 1.51 – 1.36 (m, 4H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 135.9, 128.6, 127.8, 121.3, 121.0, 119.2, 109.4, 100.9, 98.9, 77.3, 77.1, 76.9, 67.5, 62.5, 46.4, 30.8, 30.2, 29.7, 26.9, 26.0, 25.5, 19.8. **HRMS** (ESI) calculated for $[C_{19}H_{28}NO_2+H]^+$ 302.2120, found 302.2122.



6-(1H-indol-1-yl)hexan-1-ol (SI-4) was synthesized by subjecting **SI-3** (2.50 g, 11.3 mmol) to General Procedure C. The crude product was purified by gradient flash chromatography in 10% EtOAc/hexanes to give 0.4073 g (36%) of a yellow oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.68 (d, *J* = 7.9 Hz, 1H), 7.38 (d, *J* = 8.2 Hz, 1H), 7.27 – 7.17 (m, 1H), 7.19 – 7.06 (m, 2H), 6.53 (d, *J* = 3.1 Hz, 1H), 4.16 (t, *J* = 7.1 Hz, 2H), 3.64 (t, *J* = 6.5 Hz, 2H), 1.90 (q, *J* = 7.2 Hz, 2H), 1.61 – 1.53 (m, 2H), 1.47 – 1.33 (m, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 135.9, 128.6, 127.8, 121.3, 121.0, 119.2, 109.4, 100.9, 62.8, 46.3, 32.6, 30.2, 26.8, 25.4. **HRMS** (ESI) calculated for$[C_{14}H_{20}NO]+$ 218.1545, found 218.1545.



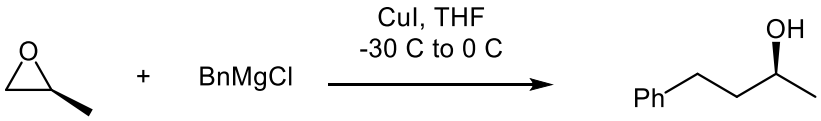
6-(1H-indol-1-yl)hexyl 4-methylbenzenesulfonate (9) was synthesized by **SI-4** (0.4073g 1.874 mmol) according to General Procedure A. The crude product was purified via gradient flash chromatography in 10% to 30% EtOAc/hexanes to give 0.5643 g (81%) of a yellow oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.83 – 7.75 (m, 2H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.34 (t, *J* = 8.5 Hz, 3H), 7.26 – 7.20 (m, 1H), 7.15 – 7.10 (m, 1H), 7.09 (d, *J* = 3.1 Hz, 1H), 6.51 (d, *J* = 3.1 Hz, 1H), 4.11 (t, *J* = 7.0 Hz, 2H), 4.02 (t, *J* = 6.4 Hz, 2H), 2.46 (s, 3H), 1.82 (p, *J* = 7.2 Hz, 2H), 1.68 – 1.58 (m, 2H), 1.41 – 1.23 (m, 4H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 144.71, 135.9, 133.1, 129.8, 128.6, 127.9, 127.7, 121.4, 121.0, 119.2, 109.3, 101.0, 70.4, 46.2, 30.0, 28.7, 26.4, 25.1, 21.7. **HRMS** (ESI) calculated for $[C_{21}H_{25}NO_3S+H]^+$ 372.1633, found 372.1635.



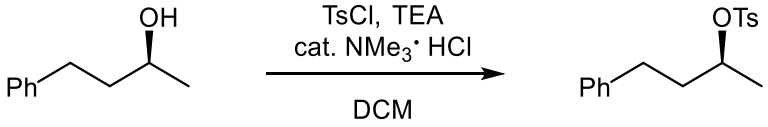
(4R)-4-((3R,8R,9S,10S,13R,14S,17R)-10,13-dimethyl-3-((triethylsilyl)oxy)hexadecahydro-1H-cyclopenta[a]phenanthren-17-yl)pentyl 4-methylbenzenesulfonate (11) To a solution of Lithocholic acid (5.63 g, 15 mmol) in MeOH (59 ml) was added H_2SO_4 (2.5 ml) and the mixture was stirred for 2 hours at reflux. After removing the volatiles, the crude was extracted with dichloromethane (20 ml x 2), dried over $MgSO_4$ and concentrated under vacuum to give 5.71 g of ester (98%). The resulting solid (3.00 g, 7.97 mmol, 1 equiv.) was dissolved in DCM (38 mL). To this solution at 0 ^{o}C was added imidazole (0.814 g, 11.9 mmol, 1.5 equiv.) and trichloroethylsilane (1.60mL, 9.56 mmol, 1.2 equiv.). The solution was warmed to room temperature and stirred overnight. The reaction was quenched with water (50 mL), extracted with DCM (3 x 50 mL), washed with brine (50 mL), dried over $MgSO_4$, filtered, and concentrated under vacuum to give 3.89 g (92%) of the TES-protected alcohol which was used without further purification. The ester was then dissolved in 15 mL THF and added dropwise to a 0 ^{o}C suspension of $LiAlH_4$ (270 mg, 7.1075 mmol, 1 equiv.) in THF (15 mL). The reaction was allowed to warm to room temperature and stirred overnight, after which it was cooled to 0 ^{o}C and quenched by sequential dropwise addition of water (6.4 mL), 2.5 M NaOH (6.4 mL), and water (21.6 mL). The slurry was warmed to room temperature, dried with $MgSO_4$, then stirred for 15 minutes. The mixture was then filtered through a pad of Celite, and concentrated to give 3.24 g (93%) of the crude product, which was used without further purification. The resulting alcohol (3.15g, 6.81 mmol) was tosylated according to General Procedure A and purified by flash chromatography in 10% EtOAc/hexanes

to give 1.20 g (29%) of a white translucent, sticky, amorphous solid. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.90 – 7.73 (d, 2H), 7.46 – 7.32 (d, 2H), 4.03 (tt, *J* = 6.6, 3.2 Hz, 2H), 3.59 (tt, *J* = 10.4, 4.6 Hz, 1H), 2.48 (s, 3H), 1.93 (d, *J* = 12.4 Hz, 1H), 1.89 – 1.63 (m, 5H), 1.65 – 1.49 (m, 4H), 1.36 (d, *J* = 12.4 Hz, 9H), 1.30 – 1.07 (m, 6H), 0.98 (t, *J* = 7.9 Hz, 12H), 0.92 (s, 3H), 0.86 (d, *J* = 6.5 Hz, 3H), 0.62 (q, *J* = 7.9 Hz, 6H), 0.61 (s, 3H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 144.6, 133.3, 129.8, 127.9, 72.4, 71.3, 56.4, 56.0, 42.7, 42.3, 40.2, 40.2, 37.0, 35.9, 35.6, 35.3, 34.6, 31.4, 31.1, 28.2, 27.3, 26.4, 25.6, 24.2, 23.4, 21.7, 20.8, 18.4, 12.0, 6.9, 4.7. **HRMS** (ESI) calculated for $[C_{37}H_{62}O4SSi+Na]^+$ 653.4036, found 653.4039.

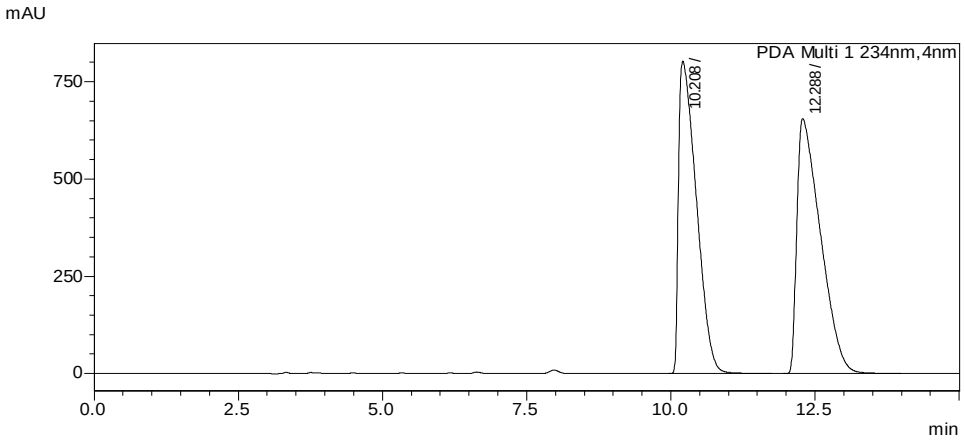
Synthesis of Secondary Tosylates



(S)-4-phenylbutan-2-ol (**SI-5**) was synthesized by subjecting 2.00 g (34.4 mmol) of (S)-propylene oxide to General Procedure D. The crude product was purified via flash chromatography in 20% EtOAc/hexanes to give 4.58 g (88%) of **SI-5** as a clear, colorless oil. Physical and spectral data were in accordance with literature data.[3]



(S)-4-phenylbutan-2-yl 4-methylbenzenesulfonate (**13**) was synthesized by subjecting 1.06 g (7.06 mmol) of **SI-5** to General Procedure A. The crude product was purified via flash chromatography in 10% EtOAc/hexanes to give 1.90 g (88%) of **13** as a pale yellow oil. Physical and spectral data were in accordance with literature data.[3] **Chiral HPLC:** (Chiralpak OJH 70:30 hexanes:isopropanol): ee = >99%.



Ret. Time	Area	Area%
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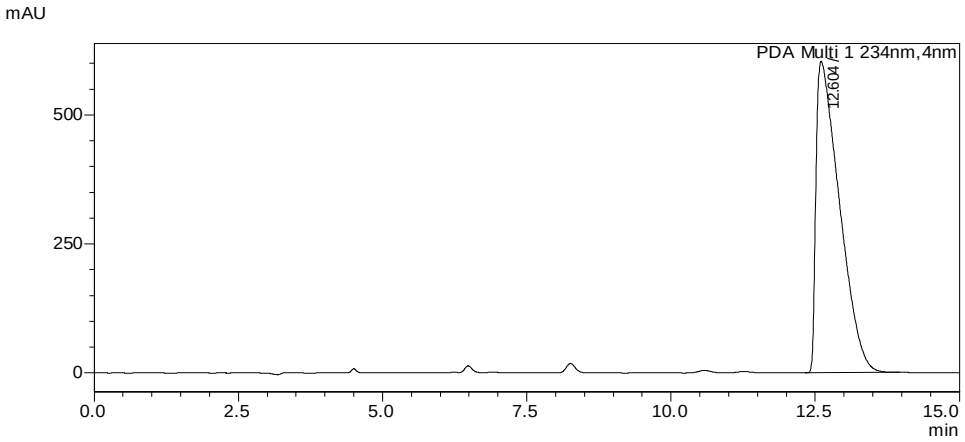
	35825993	100



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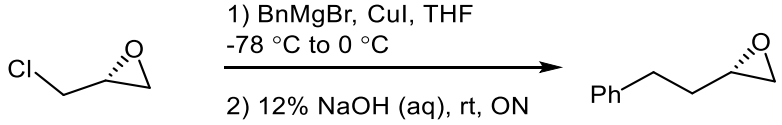
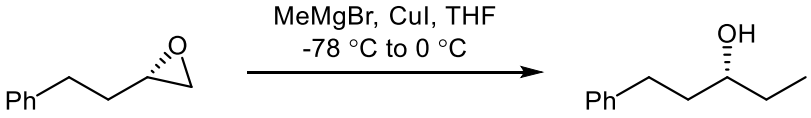
	17083485	100

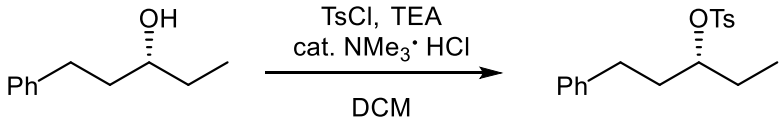


(R)-2-phenethyloxirane (**SI-6**) was synthesized by alkylation of (S)-epichlorohydrin. A dry flask purged with N_2 was charged with CuI (4.63 g, 24.3 mmol) and THF (15 mL). The suspension was cooled to -78 ^{o}C, and a 2.0 M solution of benzylmagnesium bromide in THF (12 mL, 24.3 mmol)

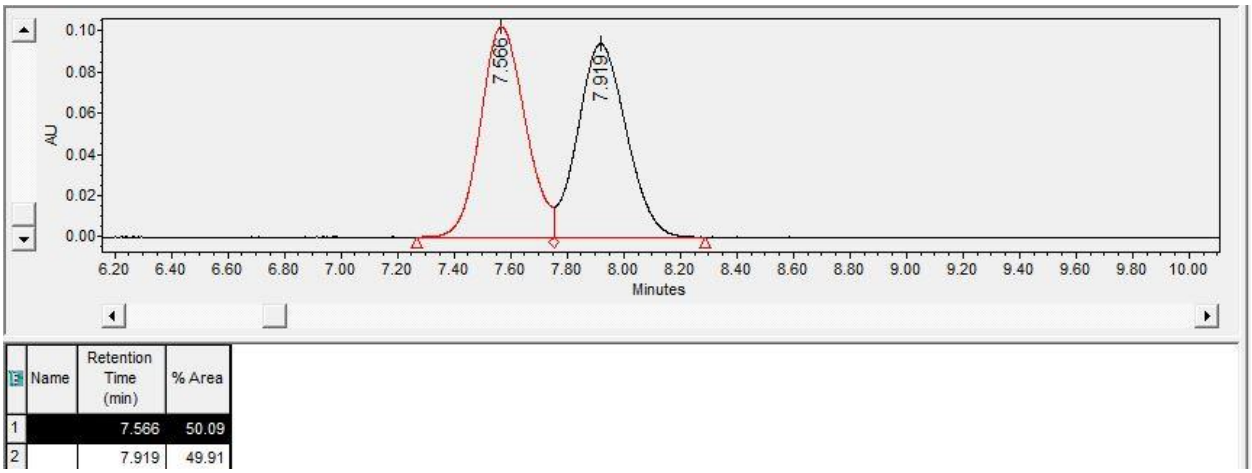
was added to form a yellow-brown solution. After stirring for five minutes, (S)-epichlorohydrin (1.27 mL, 16.2 mmol) was added, dropwise, and the solution turned black. The reaction was allowed to warm to 0 °C and was stirred an additional three hours. The mixture was then allowed to warm to room temperature and was diluted with 15 mL diethyl ether and quenched with 20 mL saturated NH_4Cl (aq). The organic and aqueous phases were separated and the aqueous phase was extracted 3x 10 mL diethyl ether. The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude residue of chloroalcohol was then redissolved in 15 mL THF and stirred with 15 mL of 12% NaOH (aq), overnight at room temperature. The reaction was diluted with 15 mL diethyl ether, and the organic phase was collected. The aqueous layer was extracted 3x 15 mL diethyl ether. The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated to give the epoxide. The crude residue was purified via flash chromatography in 10% EtOAc/hexanes to give 1.29 g (53%) product. Physical and spectral data were in accordance with literature data.[4]



(S)-1-phenylpentan-3-ol (**SI-7**) was synthesized by subjecting **SI-6** (1.21 g, 8.16 mmol) to General Procedure D, using 3.0 M MeMgBr in diethyl ether. The product was purified via flash chromatography in % EtOAc/hexanes to give 0.921 g (69%) of a pale yellow oil. Physical and spectral data were in accordance with literature data.[5]



(S)-1-phenylpentan-3-yl 4-methylbenzenesulfonate (15) was synthesized by tosylating **SI-7** (0.921 g, 5.61 mmol) according to General Procedure A. The crude product was purified via flash chromatography in 10% EtOAc/hexanes to provide 1.44 g (80%) of tosylate **15** as a yellow oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.82 (d, *J* = 8.2 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.28 (m, 2H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.09 (d, *J* = 7.0 Hz, 2H), 4.58 (p, *J* = 5.9 Hz, 1H), 2.61 (ddd, *J* = 13.8, 10.4, 6.0 Hz, 1H), 2.53 (ddd, *J* = 13.9, 10.3, 5.9 Hz, 1H), 2.47 (s, 3H), 1.98 – 1.82 (m, 2H), 1.75 – 1.62 (m, 2H), 0.87 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 144.5, 141.0, 134.6, 129.8, 128.5, 128.3, 127.7, 126.1, 84.7, 35.3, 31.1, 27.1, 21.7, 9.0. **HRMS** (ESI) calculated for $[C_{18}H_{22}O_3S+Na]^+$ 341.1187, found 341.1189. **Chiral SFC:** Phenomenex Cellulose 2 column, 99:1 CO_2:*i*-PrOH, 2 mL/min, 30 °C, 226 nm.



	Name	Retention Time (min)	% Area
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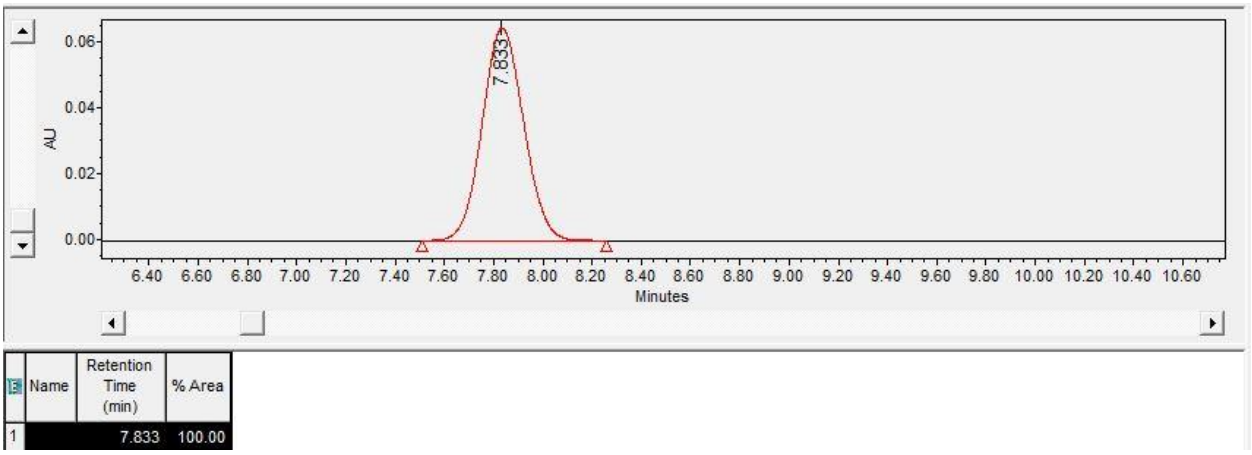
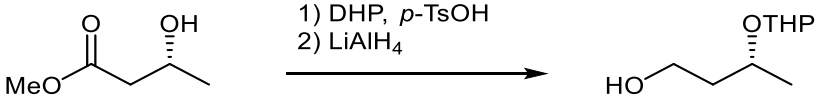
2		7.919	49.91

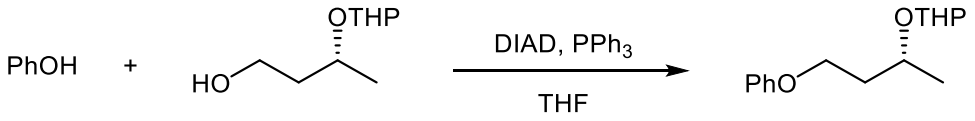


	Name	Retention Time (min)	% Area
1		7.833	100.00

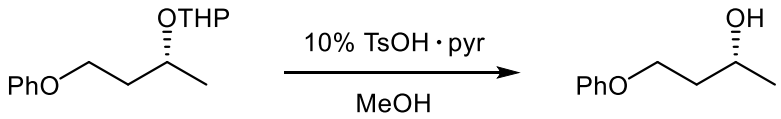


(R)-3-((tetrahydro-2H-pyran-2-yl)oxy)butan-1-ol (SI-8) was synthesized by the 2 step sequence shown above. (R)-methyl 3-hydroxybutanoate (20 g, 169 mmol), 3,4-dihydro2H-pyran (18.5 mL, 203 mmol), and p-toluenesulfonic acid monohydrate (0.3 g, 1.7 mmol) were combined in Et2O and allowed to stir overnight at room temperature. The reaction was quenched via addition of a saturated sodium bicarbonate solution. The organic layer was separated and the aqueous layer was extracted twice with Et2O and the organic layers were combined and dried over MgSO4, filtered, and concentrated under reduced pressure to provide 34.2 g of the crude product (100%)**.** A solution of the crude product (34.2 g, 169 mmol) in Et_2O (450 mL) was added dropwise to a suspension of $LiAlH_4$ (6.42 g, 169 mmol) in Et2O (mL) at 0 ^oC. The reaction was allowed to warm to room temperature and stirred overnight. The reaction was cooled to 0 ^oC and quenched by sequential dropwise addition of water (6.4 mL), 2.5 M NaOH (6.4 mL), and water (21.6 mL). The slurry was warmed to room temperature, dried with $MgSO_4$, then stirred for 15 minutes. The

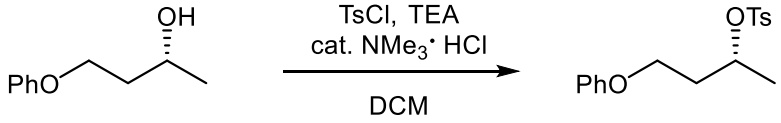
mixture was then filtered through a pad of Celite, and concentrated. The crude product **SI-8** (26.7g, 91%) was used without further purification.



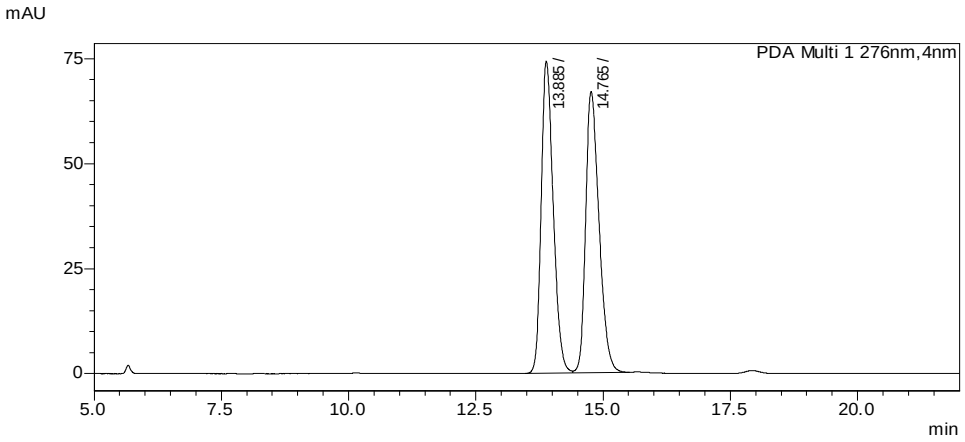
2-(((R)-4-phenoxybutan-2-yl)oxy)tetrahydro-2H-pyran (SI-9) was synthesized by subjecting **SI-8** (1.50 g, 8.61 mmol) and phenol (0.68 g, 7.2 mmol) to General Procedure B. The crude product was purified via flash chromatography in 10% EtOAc/hexanes to provide 1.0 g (56%) of **SI-9** as a clear oil in a 1:1 mixture of diastereomers. Physical and spectral data were in accordance with literature data.[3]



(R)-4-phenoxybutan-2-ol (SI-10) was synthesized by subjecting **SI-9** (1.00 g, 3.99 mmol) to General Procedure C. The crude product was purified via flash chromatography in 20% EtOAc/hexanes to provide 0.56 g (84%) of **SI-10** as a colorless oil. Physical and spectral data were in accordance with literature data.[3]



(R)-4-phenoxybutan-2-yl 4-methylbenzenesulfonate (17) was synthesized by tosylating **SI-10** (0.56 g, 3.08 mmol) according to General Procedure A. The crude product was purified via flash chromatography in 10% EtOAc/hexanes to provide 1.5 g (76%) of tosylate **17** as a white solid. Physical and spectral data were in accordance with the literature.[3] **Chiral HPLC:** (ChiralPak IF, 95:5 hexanes:isopropanol): ee = >99%.



Ret. Time	Area	Area%
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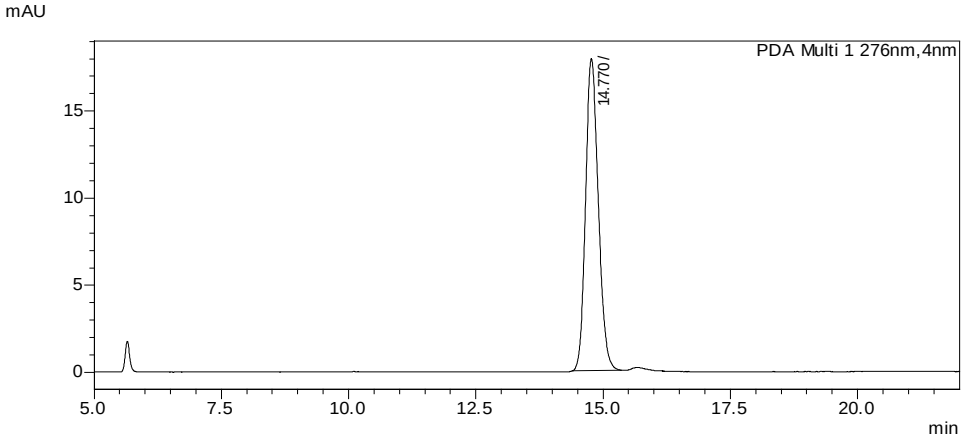
14.765	1224450	50.024
	2447745	100



Ret. Time	Area	Area%
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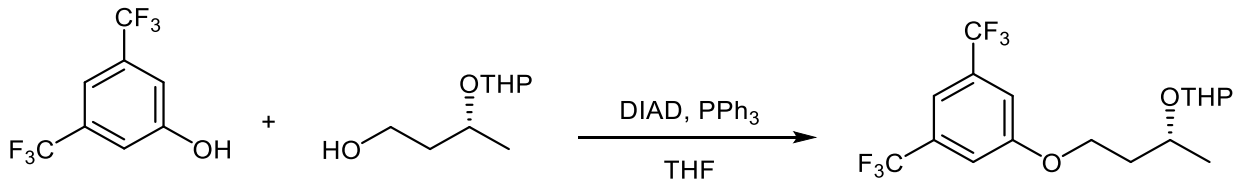
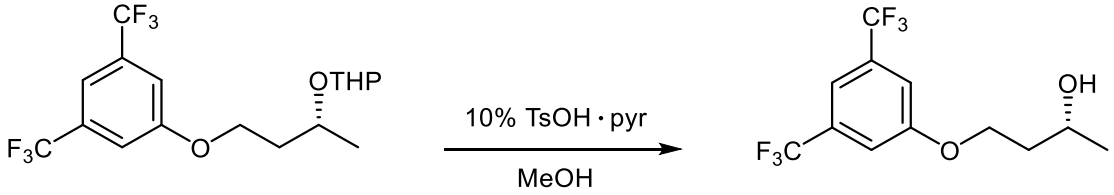
	415103	100

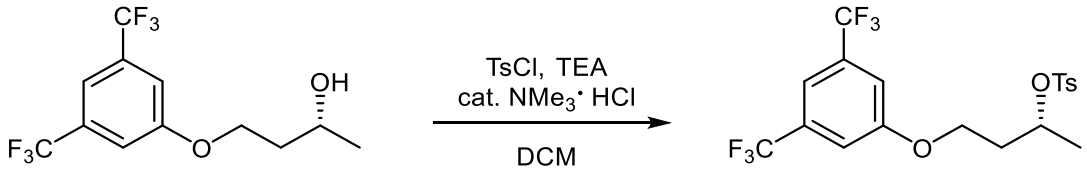


2-(((R)-4-(3,5-bis(trifluoromethyl)phenoxy)butan-2-yl)oxy)tetrahydro-2H-pyran (SI-11) was synthesized by subjecting **SI-9** (1.50 g, 8.60 mmol) and 3,5-(bis)trifluoromethylphenol (1.65 g, 7.17 mmol) to General Procedure B. The crude product was purified via flash chromatography in

5% EtOAc/hexanes to provide 2.21g (80%) of a pink oil as a 1:1 mixture of diasteromers. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.45 (d, *J* = 9.0 Hz, 2H), 7.35 – 7.29 (m, 4H), 4.69 (dd, *J* = 5.0, 3.1 Hz, 1H), 4.65 (dd, *J* = 5.0, 2.9 Hz, 1H), 4.28 (dt, *J* = 9.2, 6.9 Hz, 1H), 4.22 – 4.05 (m, 4H), 4.02 (p, *J* = 6.3 Hz, 1H), 3.95 (ddd, *J* = 11.4, 7.3, 3.8 Hz, 1H), 3.75 (ddd, *J* = 11.0, 7.3, 3.0 Hz, 1H), 3.51 (dtd, *J* = 11.5, 4.1, 2.2 Hz, 1H), 3.43 (ddd, *J* = 11.5, 5.7, 3.1 Hz, 1H), 2.07 – 1.94 (m, 4H), 1.91 – 1.77 (m, 2H), 1.71 (dtt, *J* = 20.9, 8.0, 3.0 Hz, 2H), 1.61 – 1.42 (m, 8H), 1.35 (d, *J* = 6.4 Hz, 3H), 1.23 (d, *J* = 6.2 Hz, 3H). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 159.7, 159.5, δ 132.8 (q, *J* = 33.2 Hz), δ 132.7 (q, *J* = 33.3 Hz), 123.2 (q, *J* = 272.6 Hz), 123.2 (q, *J* = 272.7 Hz), 114.9 (q, *J* = 4.0 Hz), 114.7 (q, *J* = 3.9 Hz), 114.1 (hept, *J* = 3.8 Hz), 113.9 (hept, *J* = 3.8 Hz), 99.4, 96.3, 71.2, 68.0, 65.7, 65.4, 62.9, 62.9, 36.6, 36.0, 31.2, 31.1, 25.4, 25.4, 21.9, 20.0, 19.9, 19.5. **^{19}F NMR** (565 MHz, $CDCl_3$) δ -63.16, -63.17. **HRMS** (ESI) calculated for $[C_{17}H_{20}F_6O_3+Na]^+$ 409.1214, found 409.1217.

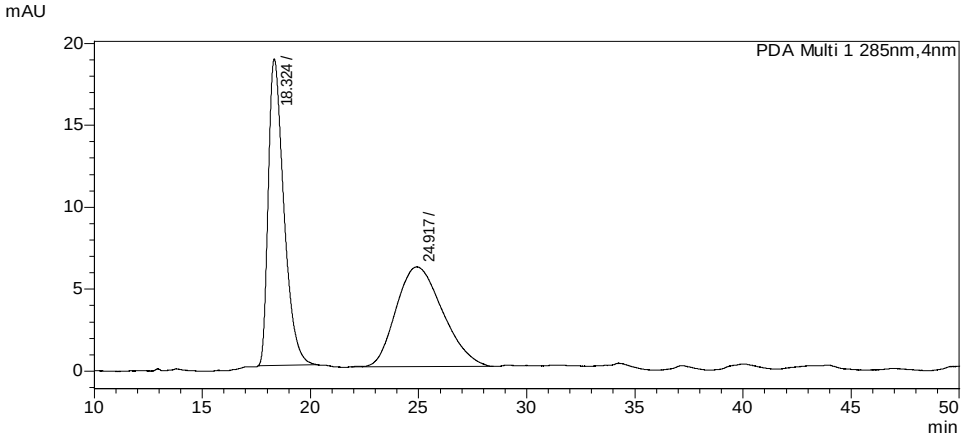


(R)-4-(3,5-bis(trifluoromethyl)phenoxy)butan-2-ol (SI-12) was synthesized by subjecting **SI-11** (2.21 g, 5.72 mmol) to General Procedure C. The crude product was purified via flash chromatography in 20% EtOAc/hexanes to provide 1.36 g (79%) of **SI-12** as a clear oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.48 (s, 1H), 4.27 (ddd, *J* = 9.3, 7.6, 5.3 Hz, 1H), 4.19 (dt, *J* = 9.2, 5.7 Hz, 1H), 4.14 (m, 1H), 2.07 – 1.90 (m, 2H), 1.70 – 1.61 (m, 1H), 1.33 (d, *J* = 6.2 Hz, 3H). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 159.4, 132.8 (q, *J* = 33.4 Hz), 123.2 (q, *J* = 272.9 Hz), 116.5 – 112.6 (m), 65.7 (d, *J* = 126.1 Hz), 37.9, 24.0. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.05. **HRMS** (ESI) calculated for $[C_{12}H_{12}F_6O_2+Na]^+$ 325.0639, found 325.0640.

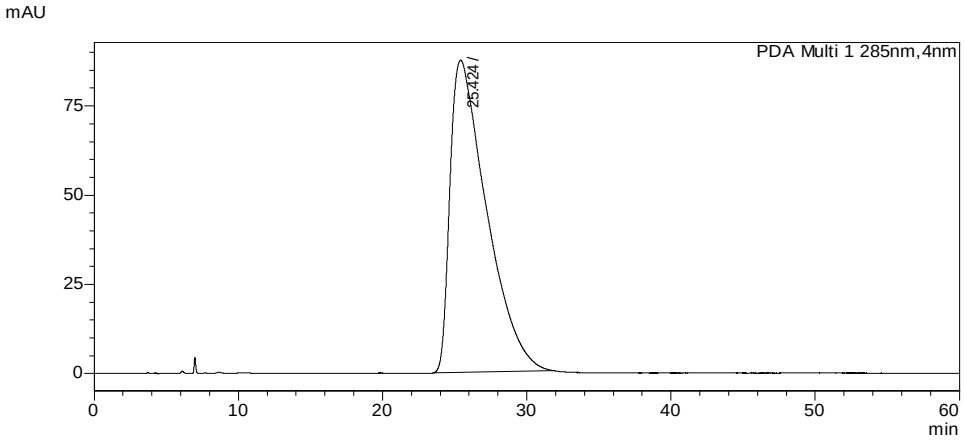


(R)-4-(3,5-bis(trifluoromethyl)phenoxy)butan-2-yl 4-methylbenzenesulfonate (19) was synthesized by tosylating **SI-12** (0.56 g, 3.08 mmol) according to General Procedure A. The crude product was purified via flash chromatography in 10% EtOAc/hexanes to provide 1.53 g (76%) of tosylate **19** as a white solid. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 8.3 Hz, 2H), 7.47 (s, 1H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.09 (s, 1H), 4.95 – 4.81 (m, 1H), 3.91 (dt, *J* = 9.3, 4.7 Hz, 1H), 3.77 (td, *J* = 9.0, 4.6 Hz, 1H), 2.23 (s, 3H), 2.06 (tt, *J* = 8.7, 4.4 Hz, 2H), 1.49 (d, *J* = 6.3 Hz, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 158.9, 144. 7, 133.8, 132.7 (q, *J* = 33.3 Hz), 129.7, 127.6, 124.5, 121.8,

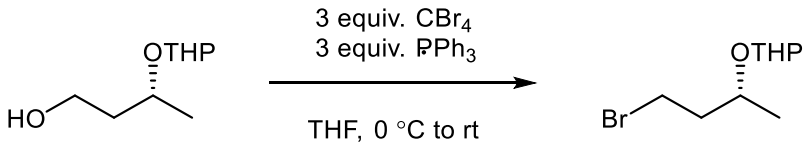
114.4 (d, *J* = 20.0 Hz), 63.9, 35.9, 21.7, 21.4. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -63.00. **HRMS** (ESI) calculated for [$C_{19}H_{18}F_6O_4S$+Na]+ 479.0728, found 479.0715. **Chiral HPLC:** (Daicel OJH, 99.9:0.1 hexanes:isopropanol): ee = >99%.



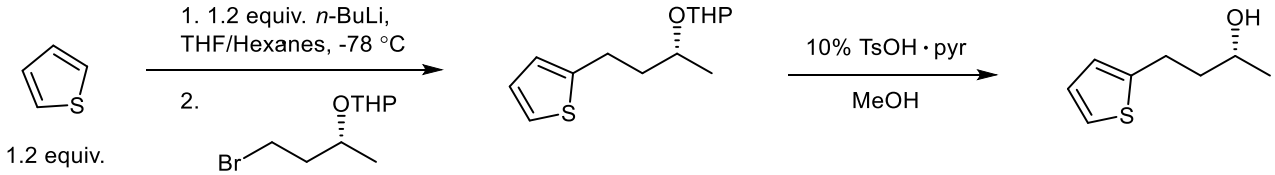
Ret. Time	Area	Area%
18.324	937505	50.712
24.917	911197	49.288
	1848702	100



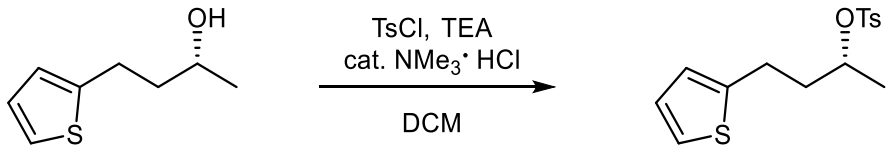
Ret. Time	Area	Area%
25.424	15402398	100
	15402398	100



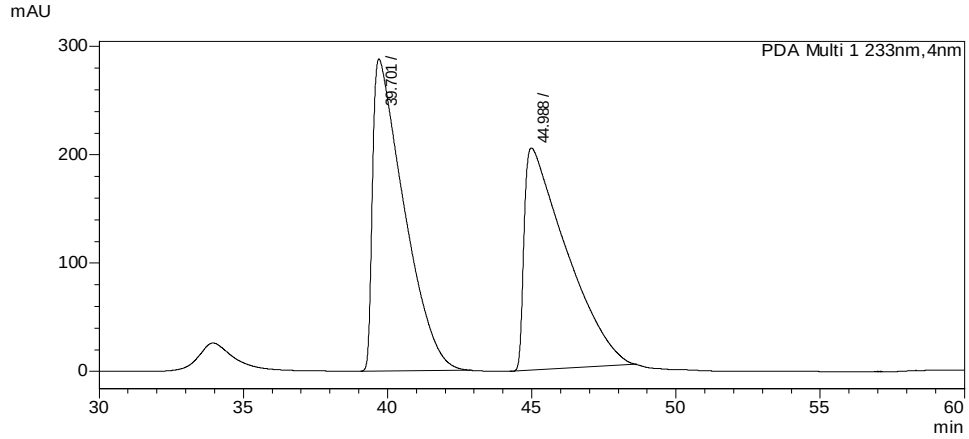
2-(((R)-4-bromobutan-2-yl)oxy)tetrahydro-2H-pyran (SI-13) was synthesized according to the following procedure. To a 0°C solution of triphenylphosphine (15.8 g, 60.3 mmol) in THF (115 mL) was added CBr_4 (20.0 g, 60.3 mmol). This solution was stirred at 0°C for 5 minutes until the solution turned bright yellow. The alcohol (3.50 g, 20.1 mmol) was then added dropwise, and the reaction mixture was allowed to warm to ambient temperature and was stirred ON. The reaction was stirred with hexanes to crash out TPPO and was filtered through a bed of celite and concentrated. The residue was dissolved in 1:1 Hexanes:EtOAc and filtered through a silica pad, and concentrated to give a pale yellow oil. The crude product was purified via gradient flash chromatography in 30:1 Hexanes:EtOAc to 3.82 g (80%) of a clear, colorless oil. The product was obtained as a mixture of diastereomers. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 4.60 (dd, *J* = 4.5, 2.8 Hz, 1H), 4.55 (t, *J* = 5.0 Hz, 1H), 4.11 (ddd, *J* = 11.4, 5.0, 1.4 Hz, 1H), 3.87 (ddd, *J* = 11.1, 7.6, 3.4 Hz, 1H), 3.84 – 3.68 (m, 4H), 3.48 (t, *J* = 6.8 Hz, 2H), 3.43 (t, *J* = 6.9 Hz, 2H), 2.09 – 1.96 (m, 4H), 1.90 (dt, *J* = 14.1, 6.9 Hz, 2H), 1.75 (ddt, *J* = 16.5, 9.1, 5.9 Hz, 4H), 1.70 – 1.50 (m, 9H), 1.25 (d, *J* = 6.2 Hz, 3H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 101.6, 98.9, 72.8, 66.6, 66.5, 62.4, 34.2, 33.8, 33.7, 33.0, 32.7, 30.7, 29.8, 28.4, 25.5, 22.9, 21.8, 19.6. **HRMS** (ESI) calculated for $[C_9H_{17}BrO_2+Na]+$ 259.0310, found 259.0304.



(R)-4-(thiophen-2-ylmethoxy)butan-2-ol (SI-14) was synthesized by the 2 step sequence shown above. To a solution of thiophene (1.35g, 16.0 mmol) in THF (6mL), *n*-BuLi in hexanes (6.4mL, 2.50 M, 16.0 mmol) was slowly added dropwise at -78 ^{o}C. The solution was warmed to 0 ^{o}C and stirred for 1 hour, after which the bromide was added slowly, dropwise. The reaction was then allowed to warm to room temperature and was stirred overnight. It was then diluted with ether and quenched with saturated ammonium chloride. The aqueous and organic phases were separated and the aqueous phase was extracted 3 x 50 mL with ether. The organic layers were combine dand dried with MgSO4, filtered, and concentrated to give a black oil. The crude residue was passed through silica with 30:1 Hexanes:EtOAc to give 1.91 g (59%) of a pale yellow oil, which was used immediately in the next step without further characterization. The title compound **SI-14** was then synthesized by deprotection using General Procedure C. The crude product was purified three times via flash chromatography in 20% EtOAc/hexanes to provide 0.368 g (30%) of the alcohol, containing 22% inseparable byproduct from thiophene hydrolysis. The alcohol was carried onto the next step without further purification. Physical and spectral data were in accordance with literature data.[7]



(R)-4-(thiophen-2-ylmethoxy)butan-2-yl 4-methylbenzenesulfonate (21) was synthesized by tosylating **SI-14** (0.368 g, 2.36 mmol) according to General Procedure A. The crude product was purified via flash chromatography in 10% EtOAc/hexanes, then again in a gradient 10% EtOAc/hexanes to 5% EtOAc/hexanes, and a third time in 5% EtOAc/hexanes, to provide 0.580 g (79%) of tosylate **21** as a clear oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.92 – 7.72 (m, 2H), 7.51 – 7.31 (m, 2H), 7.12 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.91 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.72 (dq, *J* = 3.4, 1.1 Hz, 1H), 4.70 (dqd, *J* = 7.6, 6.3, 4.6 Hz, 1H), 2.86 (dddd, *J* = 15.4, 9.7, 5.9, 1.0 Hz, 1H), 2.76 (dddd, *J* = 15.0, 9.6, 6.2, 1.0 Hz, 1H), 2.47 (s, 3H), 2.02 (dddd, *J* = 13.7, 9.6, 7.7, 5.9 Hz, 1H), 1.89 (dddd, *J* = 14.3, 9.7, 6.2, 4.6 Hz, 1H), 1.32 (d, *J* = 6.3 Hz, 3H).**^{13}C NMR** (151 MHz, $CDCl_3$) δ 144.7, 143.5, 134.3, 129.9, 127.7, 126.8, 124.5, 123.3, 79.4, 38.4, 25.4, 21.7, 21.7, 20.9, 20.9. **HRMS** (ESI) calculated for $[C_{15}H_{18}O_3S_2+Na]^+$ 333.0595, found 333.0590. **Chiral HPLC:** (Daicel OJH, 98:2 hexanes:isopropanol): ee = >99%.



Peak#	Ret. Time	Area	Area%
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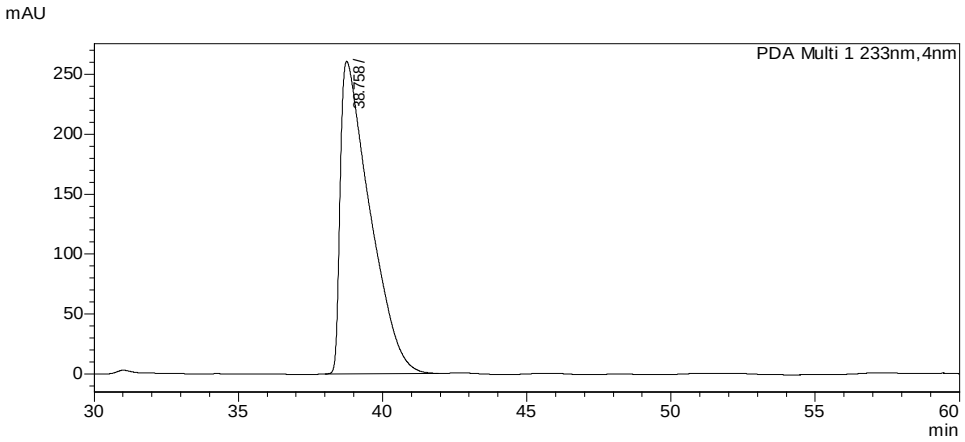
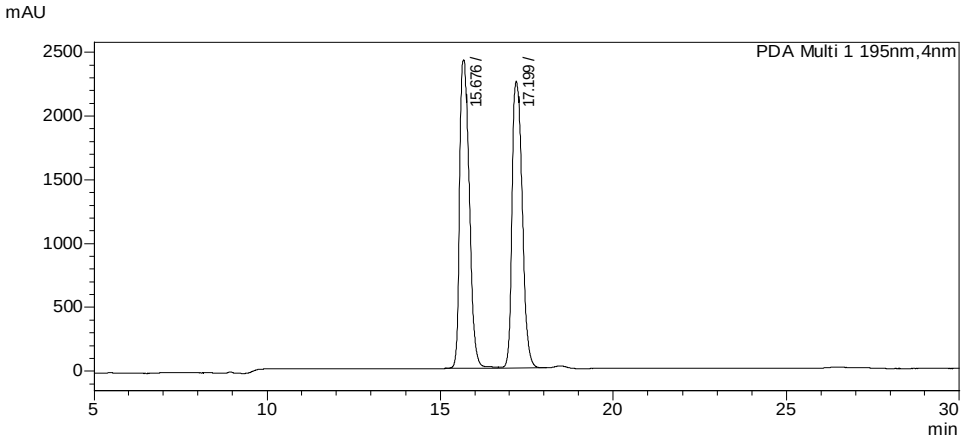
2	44.988	20924212	49.024
Total		42681963	100



Peak#	Ret. Time	Area	Area%
1	38.758	18544664	100
Total		18544664	100

(S)-octan-2-yl 4-methylbenzenesulfonate (23) was synthesized by tosylating (S)-octan-2-ol (3.40 g, 12.3 mmol) according to General Procedure A. The crude product was purified via flash chromatography in 10% EtOAc/hexanes to provide 3.2 g (94%) of tosylate 27 as a clear, colorless oil. Physical and spectral data were in accordance with literature data.[8] **Chiral HPLC:** (ChiralPak IG 95:5 hexanes:isopropanol) ee = 99%.



Peak#	Ret. Time	Area	Area%
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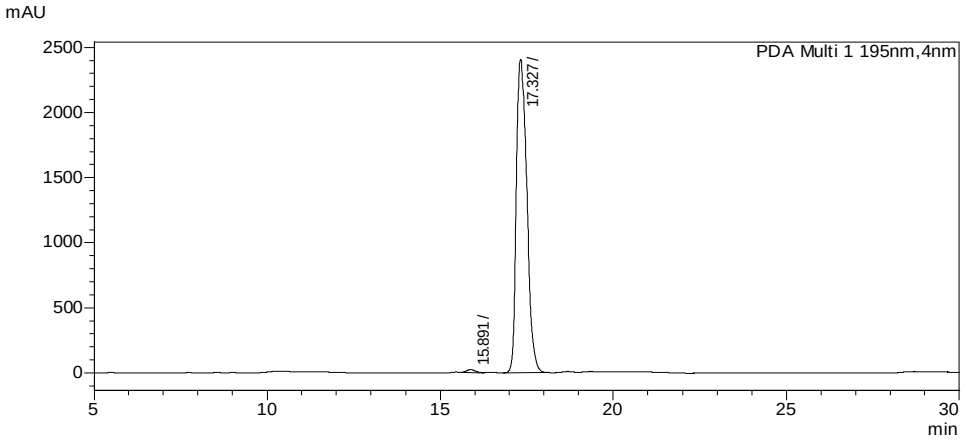
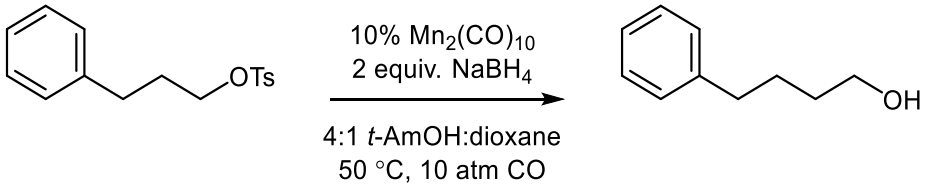
2	17.199	46094846	49.359
Total		93386017	100



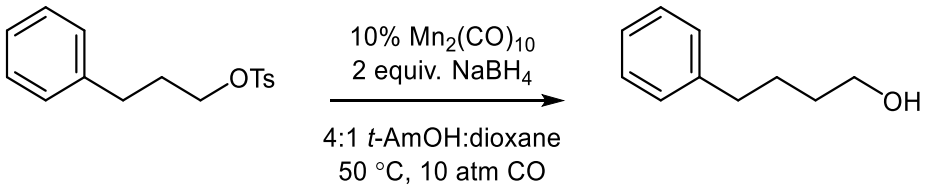
Peak#	Ret. Time	Area	Area%
1	15.891	368388	0.717
2	17.327	51041381	99.283
Total		51409769	100

Manganese-catalyzed reactions:

General Carbonylation Procedure: In a glovebox under an argon atmosphere, alkyl tosylate (0.25 mmol) was combined with $Mn_2(CO)_{10}$ (10.5 mg, 0.05 mmol), sodium borohydride (18.9mg, 0.50 mmol), t-amyl alcohol (0.4 mL) and dioxane (0.1mL) in an Ace Glass pressure tube (20 mL total volume). The tube was sealed with a Swagelok gas quick-connect adapter and removed from the glovebox. Subsequently, the tube was purged three times with 10 atm CO and then set to 10 atm CO and the reaction was stirred at 50 ^{o}C in an oil bath. After 18 hours, the tube was removed from the bath, cooled to room temperature, and depressurized. The reaction was allowed to stir for at least 2 hours with 8-10 drops of DBU, after which it was diluted with EtOAc and quenched with brine for at least 20 minutes. The aqueous layer was then extracted with EtOAc (3 × 2mL). The combined organic layers were dried with $MgSO_4$, filtered through a cotton plug, and concentrated under reduced pressure. The crude mixture was then diluted with 8-10mL 20% EtOAc/Hexanes and filtered through a short silica plug to remove manganese, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography.

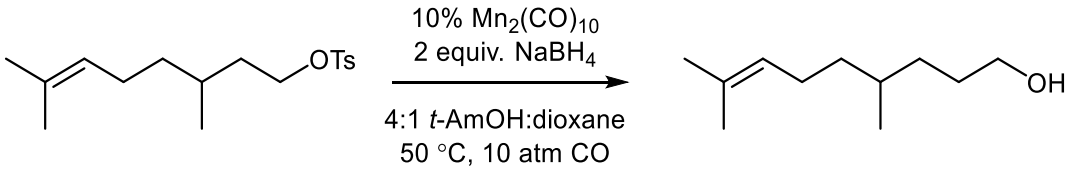


4-phenylbutan-1-ol (2) was obtained from the General Carbonylation Procedure and the crude product was dry-loaded onto silica and flashed in a gradient of hexanes to 30% EtOAc/hexanes yielding **2** as a colorless oil (24.8 mg, 66%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.37 – 7.26 (m, 2H), 7.26 – 7.15 (m, 3H), 3.68 (t, *J* = 6.5 Hz, 2H), 2.68 (t, *J* = 7.6 Hz, 2H), 1.73 (dddd, *J* = 12.2, 10.7, 5.4, 1.8 Hz, 2H), 1.68 – 1.58 (m, 2H), 1.50 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.4, 128.4, 128.4, 128.3, 128.3, 125.8, 77.4, 77.1, 76.8, 62.8, 35.7, 32.3, 27.6. **HRMS** (ESI) calculated for $[C_{10}H_{14}O+Na]^+$ 173.0942, found 173.0942.

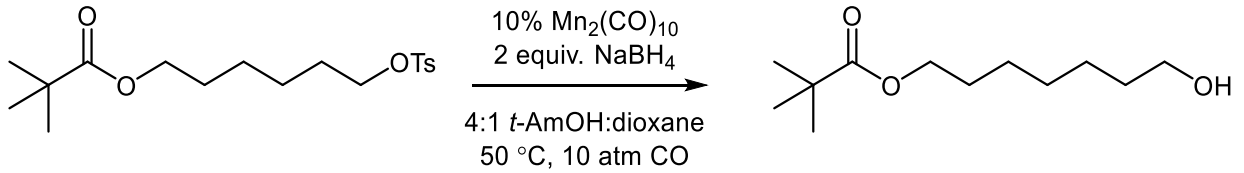


4-phenylbutan-1-ol (2) was obtained from scaling the General Carbonylation Procedure to 1 mmol with respect to the tosylate. In a glovebox under an argon atmosphere, alkyl tosylate (0.290 g, 1.00 mmol) was combined with $Mn_2(CO)_{10}$ (39 mg, 0.100 mmol), sodium borohydride (75.7 mg, 2.00 mmol), t-amyl alcohol (1.6 mL) and dioxane (0.4 mL) in an Ace Glass pressure tube (20 mL total volume). The tube was sealed with a Swagelok gas quick-connect adapter and removed

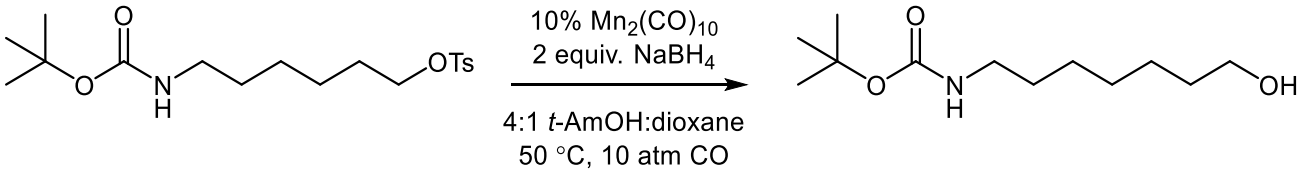
from the glovebox. Subsequently, the tube was purged three times with 10 atm CO and then set to 10 atm CO and the reaction was stirred at 50 ^{o}C in an oil bath. After 18 hours, the tube was removed from the bath, cooled to room temperature, and depressurized. The reaction was allowed to stir for at least 2 hours with 8-10 drops of DBU, after which it was diluted with EtOAc and quenched with brine for at least 20 minutes. The aqueous layer was then extracted with EtOAc (3 × 2mL). The combined organic layers were dried with $MgSO_4$, filtered through a cotton plug, and concentrated under reduced pressure. The crude mixture was then diluted with 8-10mL 20% EtOAc/Hexanes and filtered through a short silica plug to remove manganese, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography in 20% EtOAc/hexanes yielding **2** as a colorless oil (84.3 mg, 56%).



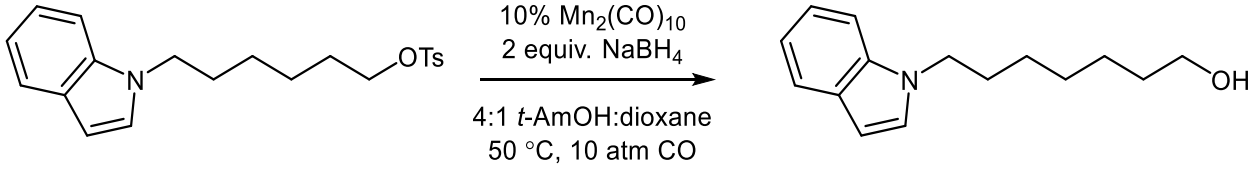
4,8-dimethylnon-7-en-1-ol (4) was obtained from the General Carbonylation and the crude product was flashed by silica gel chromatography in a gradient of hexanes to 30% EtOAc/hexanes yielding **4** as a clear oil (22.3 mg, 52%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 5.11 (tt, *J* = 7.2, 1.7 Hz, 1H), 3.64 (t, *J* = 6.7 Hz, 2H), 1.99 (td, *J* = 16.2, 14.2, 7.1 Hz, 2H), 1.71 – 1.68 (s, 3H), 1.62 (s, 3H), 1.66-1.51 (m, 1H), 1.50 – 1.23 (m, 4H), 1.24 – 1.03 (m, 2H), 0.90 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 131.1, 124.9, 63.5, 37.1, 32.9, 32.3, 30.3, 25.7, 25.5, 19.5, 17.7. **HRMS** (ESI) calculated for $[C_{11}H_{22}O+Na]^+$ 193.1568, found 193.1566.



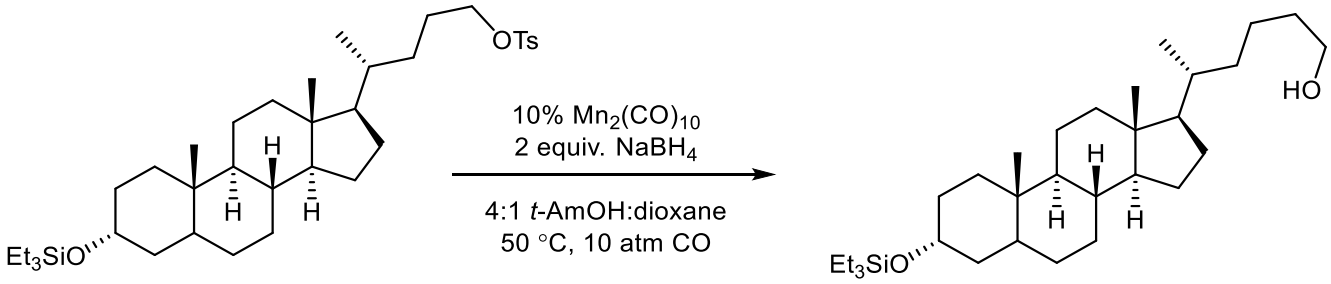
7-hydroxyhexylpivalate (6) was obtained from the General Carbonylation Procedure and the crude product was dry-loaded onto silica and flashed in a gradient of hexanes to 30% EtOAc/hexanes yielding **6** as a yellow oil (30.8 mg, 57%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 4.05 (t, *J* = 6.6 Hz, 2H), 3.64 (t, *J* = 6.6 Hz, 2H), 1.63 (qd, *J* = 7.3, 3.6 Hz, 2H), 1.60 – 1.53 (m, 2H), 1.43 – 1.31 (m, 6H), 1.20 (s, 9H).**^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.7, 64.4, 62.9, 38.7, 32.6, 29.0, 28.5, 27.2, 25.9, 25.6. **HRMS** (ESI) calculated for $[C_{12}H_{24}O_3+Na]^+$ 239.1623, found 239.1624.



***tert*-butyl (7-hydroxyheptyl)carbamate (8)** was obtained from the General Carbonylation Procedure, quenched with DI H_2O instead of brine. The crude product was flashed in a gradient of 30% EtOAc/hexanes to 50% EtOAc/hexanes yielding **8** as a clear, slightly brown oil (30.5 mg, 53%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 4.57 (s, 1H), 3.64 (t, *J* = 6.6 Hz, 2H), 3.11 (q, *J* = 6.8 Hz, 2H), 1.73 – 1.54 (m, 3H), 1.45 (s, 11H), 1.41-1.30 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.0, 79.1, 62.9, 40.5, 32.6, 30.0, 29.0, 28.4, 26.7, 25.6. **HRMS** (ESI) calculated for $[C_{12}H_{25}NO_3+Na]^+$ 254.1732, found 254.1731.

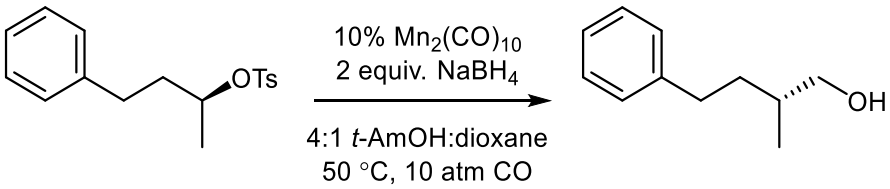


7-(1H-indol-1-yl)heptan-1-ol (10) was obtained from the General Carbonylation and the crude product was dry-loaded onto silica and flashed in a gradient of hexanes to 30% EtOAc/hexanes yielding **10** as a slightly reddish oil (33.4 mg, 58%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.67 (d, *J* = 7.9 Hz, 1H), 7.38 (d, *J* = 8.2 Hz, 1H), 7.28 – 7.20 (m, 1H), 7.19 – 7.09 (m, 2H), 6.53 (d, *J* = 3.0 Hz, 1H), 4.15 (t, *J* = 7.1 Hz, 2H), 3.63 (t, *J* = 6.6 Hz, 2H), 1.88 (p, *J* = 7.0 Hz, 2H), 1.56 (p, *J* = 6.6 Hz, 2H), 1.36 (m, 7H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 136.0, 128.6, 127.8, 121.3, 121.0, 119.2, 109.4, 100.9, 62.9, 46.4, 32.6, 30.2, 29.0, 27.0, 25.6. **HRMS** (ESI) calculated for $[C_{15}H_{21}NO+Na]^+$ 254.1521, found 254.1519.

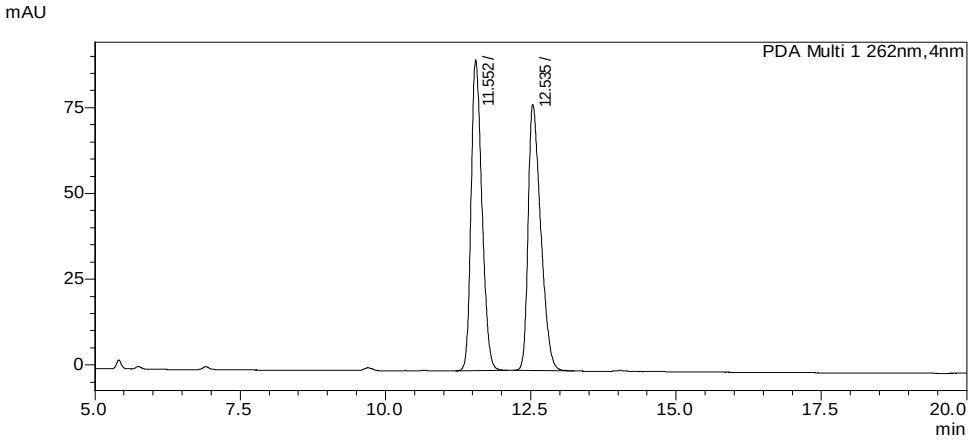


(5R)-5-((3R,8R,9S,10S,13R,14S,17R)-10,13-dimethyl-3-((triethylsilyl)oxy)hexadecahydro-1H-cyclopenta[a]phenanthren-17-yl)hexan-1-ol (12) was obtained from the General Carbonylation Procedure, quenched with DI H_2O instead of brine. The crude product was flashed by gradient

silica gel chromatography in hexanes to 30% EtOAc/hexanes yielding **12** as a clear oil (66.7 mg, 56%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 3.72 – 3.44 (m, 3H), 1.96 (dt, *J* = 12.3, 3.1 Hz, 1H), 1.91 – 1.67 (m, 4H), 1.67 – 1.50 (m, 4H), 1.50 – 1.31 (m, 11H), 1.31 – 1.18 (m, 5H), 1.15 – 1.01 (m, 6H), 0.97 (t, *J* = 7.9 Hz, 9H), 0.94 – 0.87 (m, 6H), 0.61 (dd, *J* = 16.1, 8.2 Hz, 9H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 72.5, 63.1, 56.5, 56.2, 42.7, 42.4, 40.2, 37.0, 35.9, 35.8, 35.8, 35.7, 35.6, 34.6, 33.3, 31.1, 28.4, 27.3, 26.4, 24.3, 23.4, 22.3, 20.8, 18.6, 12.0, 6.9, 4.9. **HRMS** (ESI) calculated for $[C_{31}H_{58}O_2Si+Na]^+$ 513.4104, found 513.4113.



(R)-2-methyl-4-phenylbutan-1-ol (14) was obtained from the General Carbonylation Procedure and the crude product was dry-loaded onto silica and flashed in a gradient of hexanes to 30% EtOAc/hexanes yielding **14** as a clear oil (24 mg, 58%). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.30 (q, *J* = 6.5, 5.4 Hz, 1H), 7.26 – 7.17 (m, 2H), 3.56 (dd, *J* = 10.5, 5.8 Hz, 1H), 3.49 (dd, *J* = 10.6, 6.4 Hz, 1H), 2.74 (ddd, *J* = 13.6, 10.3, 5.6 Hz, 1H), 2.63 (ddd, *J* = 13.7, 10.0, 6.3 Hz, 1H), 1.85 – 1.75 (m, 1H), 1.69 (dp, *J* = 12.8, 6.5 Hz, 1H), 1.47 (dddd, *J* = 13.6, 10.2, 8.1, 5.6 Hz, 1H), 1.02 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.6, 128.3, 125.7, 77.4, 77.1, 76.7, 68.2, 35.4, 35.0, 33.3, 16.5. **HRMS** (ESI) calculated for $[C_{11}H_{16}O+Na]^+$ 187.1099, found 187.1099. **Chiral HPLC:** (ChiralPak IF 99:1 hexanes:isopropanol): ee = 96%, es = 97%.



Ret. Time	Area	Area%
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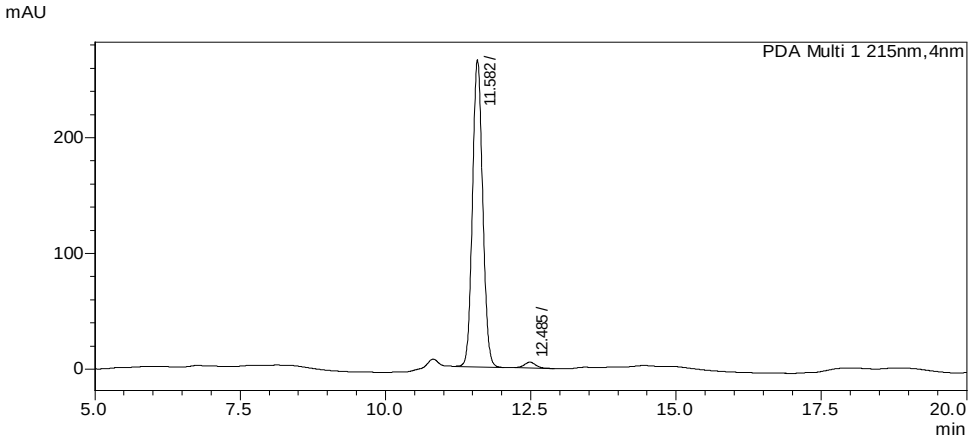
12.535	21444855	52.387
	3311488	100



Ret. Time	Area	Area%
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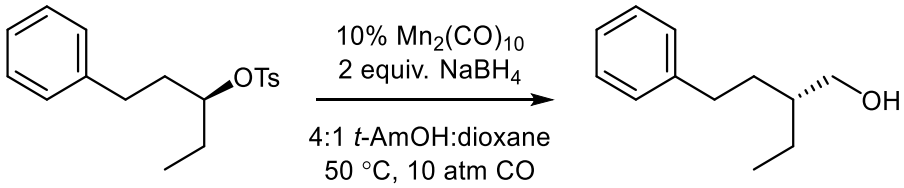
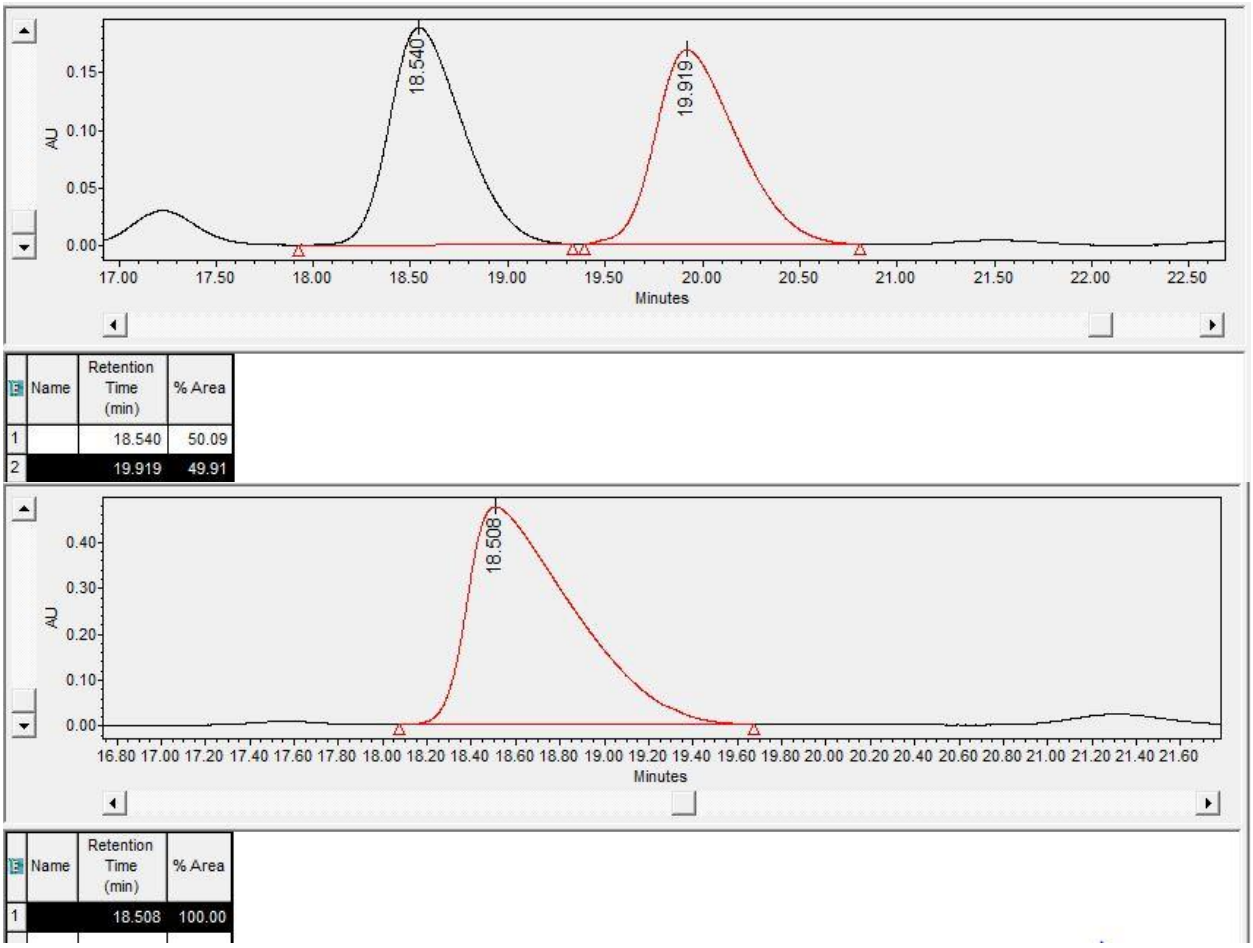
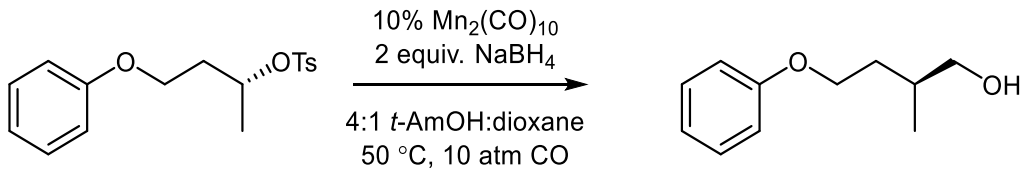
	3311488	100

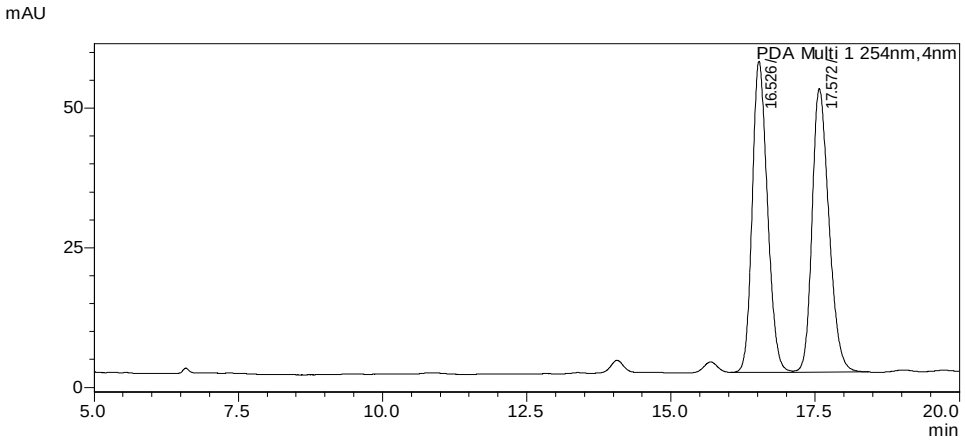


(R)-2-ethyl-4-phenylbutan-1-ol (16) was obtained from the General Carbonylation Procedure (40% NMR yield) and the crude product was flashed in 20 % EtOAc/hexanes to obtain yielding **16** as a colorless oil (13.8 mg, 31%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.30 (q, *J* = 7.6 Hz, 2H), 7.25 – 7.17 (m, 3H), 3.66 – 3.60 (m, 2H), 2.67 (t, *J* = 8.2 Hz, 2H), 1.84 – 1.57 (m, 2H), 1.57 – 1.39 (m, 3H), 0.95 (t, *J* = 7.4 Hz, 3H).**^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.7, 128.4, 125.7, 77.3, 77.1, 76.8, 65.1, 41.6, 33.3, 32.4, 23.3, 11.1. **HRMS** (ESI) calculated for $[C_{12}H_{18}O+Na]^+$ 201.1255, found 201.1255. **Chiral SFC:** Phenomenex Amylose 1 column, 99:1 CO_2:*i*-PrOH, 2 mL/min, 35 ^{o}C, 210 nm. ee = >99%, es = >99%.





(S)-2-methyl-4-phenoxybutan-1-ol (18) was obtained from the General Carbonylation Procedure the crude product was dry-loaded onto silica and flashed in a gradient of hexanes to 30% EtOAc/hexanes yielding **18** as a colorless oil (21.5 mg, 48%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.31 (dd, *J* = 8.7, 7.3 Hz, 2H), 6.97 (tt, *J* = 7.3, 1.1 Hz, 1H), 6.93 (d, *J* = 7.6 Hz, 2H), 4.10 (dt, *J* = 9.4, 5.8 Hz, 1H), 4.05 (ddd, *J* = 9.4, 7.1, 5.5 Hz, 1H), 3.58 (d, *J* = 5.6 Hz, 2H), 1.95 (ttd, *J* = 11.8, 6.1, 2.8 Hz, 2H), 1.76 – 1.67 (m, 1H), 1.03 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.8, 129.5, 120.8, 114.5, 68.0, 66.0, 33.4, 32.9, 16.8. **HRMS** (ESI) calculated for $[C_{11}H_{16}O_2+Na]^+$ 203.1048, found 203.1054. **Chiral HPLC:** (ChiralPak IF 99:1 hexanes:isopropanol): ee = 94%, es = 95%.



Ret. Time	Area	Area%
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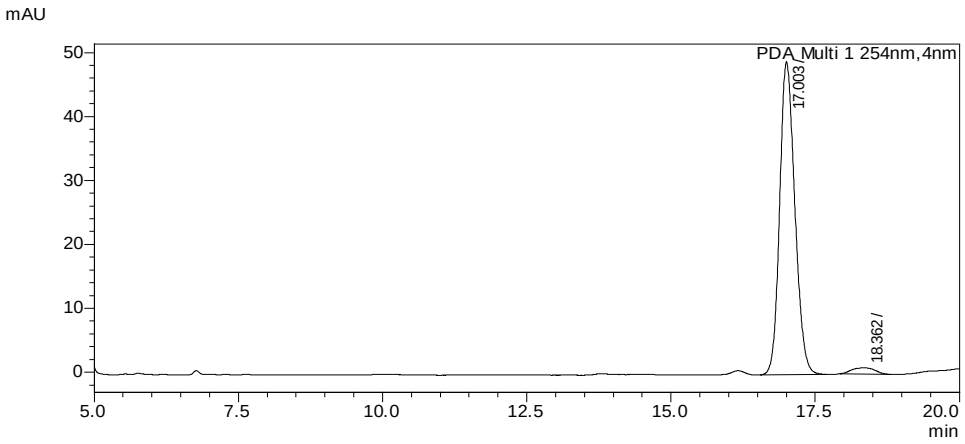
	4973760	100



Ret. Time	Area	Area%
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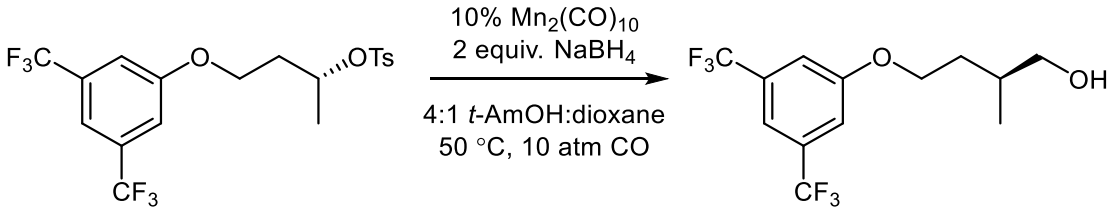
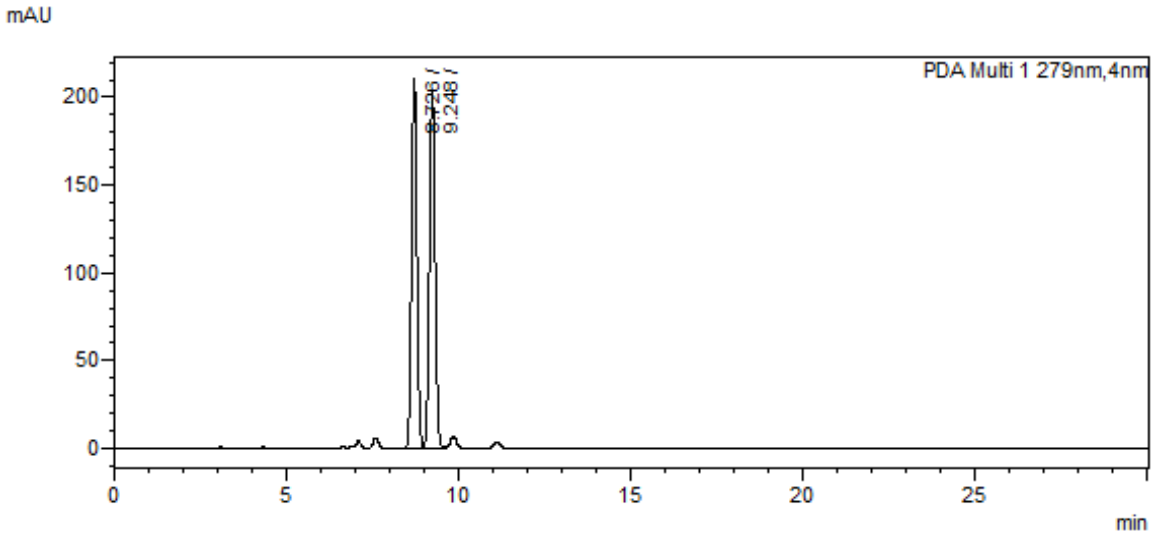
18.362	26791	2.902
	923101	100



(S)-4-(3,5-bis(trifluoromethyl)phenoxy)-2-methylbutan-1-ol (20) was obtained from the General Carbonylation Procedure the crude product was dry-loaded onto silica and flashed in a gradient of hexanes to 30% EtOAc/hexanes yielding 20 as a colorless oil (40 mg, 50%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.47 (s, 1H), 7.32 (d, *J* = 1.5 Hz, 2H), 4.19 – 4.10 (m, 2H), 3.59 (dt, *J* = 7.6, 3.6 Hz, 2H), 2.06 – 1.90 (m, 2H), 1.76 – 1.61 (m, 2H), 1.04 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 159.5, 132.8 (q, *J* = 33.4 Hz), 123.2 (q, *J* = 272.7 Hz), 114.8 (q, *J* = 3.9 Hz), 114.2 (apparent p, *J* = 3.9 Hz), 67.9, 67.01, 32.9, 32.5, 16.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.05. **HRMS** (ESI) calculated for $[C_{13}H_{14}F_6O_2+H]^+$ 317.0976, found 317.0973. **Chiral HPLC:** (ChiralPak IG 99:1 hexanes:isopropanol): ee = 94%, es = 94%.



Ret. Time	Area	Area%
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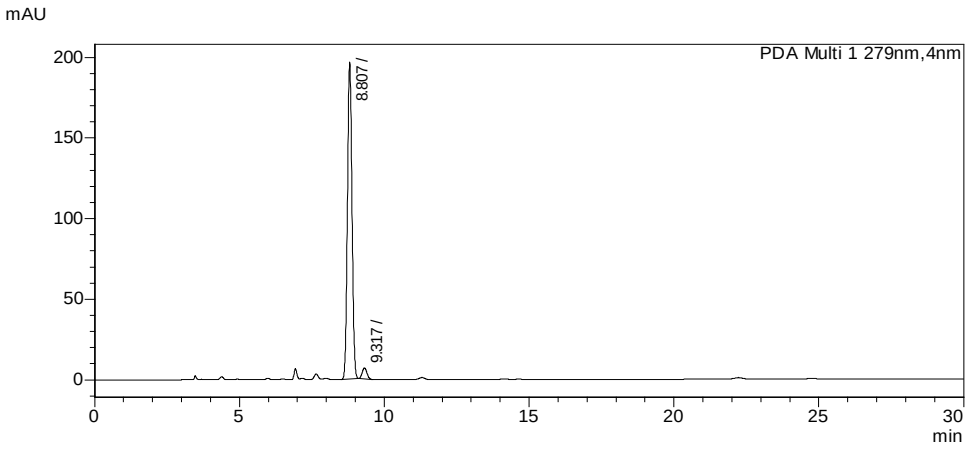
9.248	2327563	50.9
	4572783	100



Ret. Time	Area	Area%
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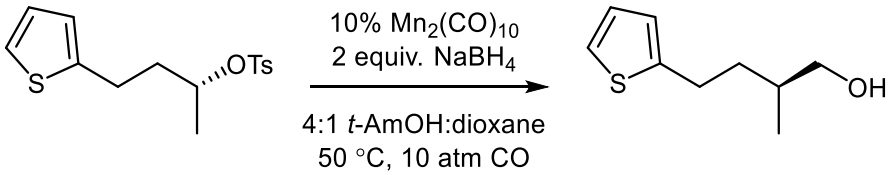
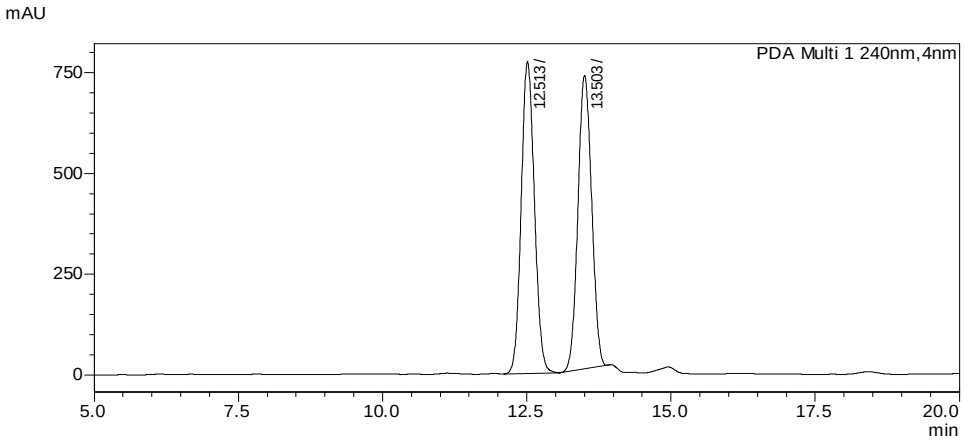
9.317	77108	3.481



(S)-2-methyl-4-(thiophen-2-yl)butan-1-ol (22) was obtained from the General Carbonylation Procedure and the crude product was flashed in 10% EtOAc in hexanes yielding **24** as a clear oil (22 mg, 52%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.14 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.94 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.82 (dq, *J* = 3.4, 1.1 Hz, 1H), 3.56 (dd, *J* = 10.6m, 5.9 Hz, 1H), 3.50 (dd, *J* = 10.6, 6.3 Hz, 1H), 2.95 (dddd, *J* = 15.4, 9.9, 5.7, 1.0 Hz, 1H), 2.86 (dddd, *J* = 14.9, 9.7, 6.5, 0.9 Hz, 1H), 1.86 (dddd, *J* = 13.3, 9.8, 6.6, 5.2 Hz, 1H), 1.78 – 1.69 (m, 1H), 1.54 (dddd, *J* = 13.6, 9.7, 8.2, 5.6 Hz, 1H), 1.01 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 145.5, 126.7, 124.0, 122.9, 68.1, 35.2, 35.2, 27.4, 16.4. **HRMS** (EI) calculated for [$C_9H_{14}OS$] 170.0765, found 170.0760. **Chiral HPLC:** (ChiralPak IF 99:1 hexanes:isopropanol): ee = 99%, es = 99%.



Peak#	Ret. Time	Area	Area%
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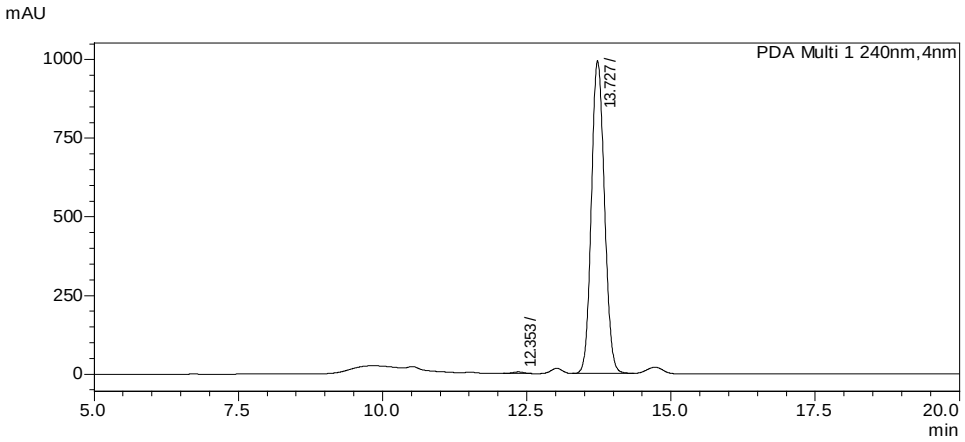
2	13.503	12032978	49.384
Total		24365989	100



Peak#	Ret. Time	Area	Area%
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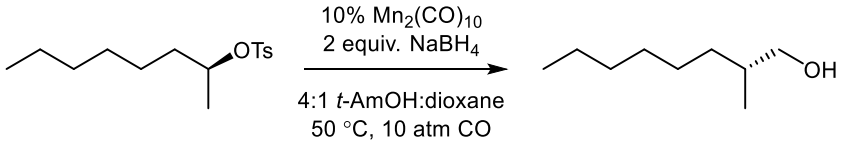
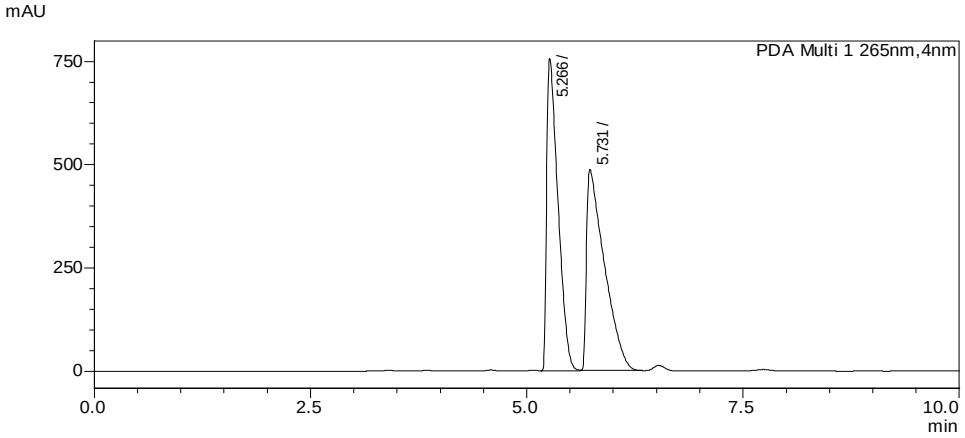


(R)-2-methyloctan-1-ol (24) was obtained from the General Carbonylation Procedure (51% NMR yield) and the crude product was flashed in 10% EtOAc/hexanes yielding 28 as a colorless oil (17

mg, 47%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 3.53 (dd, *J* = 10.5, 5.8 Hz, 1H), 3.44 (dd, *J* = 10.5, 6.5 Hz, 1H), 1.72 – 1.50 (m, 1H), 1.50 – 1.36 (m, 3H), 1.29 (dt, *J* = 8.8, 4.2 Hz, 10H), 1.17 – 1.01 (m, 1H), 1.01 – 0.69 (m, 8H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 68.4, 35.8, 33.2, 31.9, 29.6, 27.0, 22.7, 16.6, 14.1. **HRMS** (ESI) calculated for $[C_9H_{20}O+Na]^+$ 167.1412, found 167.1545. To obtain a chiral HPLC trace, the compound was derivatized to (R)-2-methyloctyl 4-methylbenzenesulfonate via General Procedure A. **Chiral HPLC:** (Daicel OJH 90:10 hexanes:isopropanol): ee = 86%, es = 87%.



Ret. Time	Area	Area%
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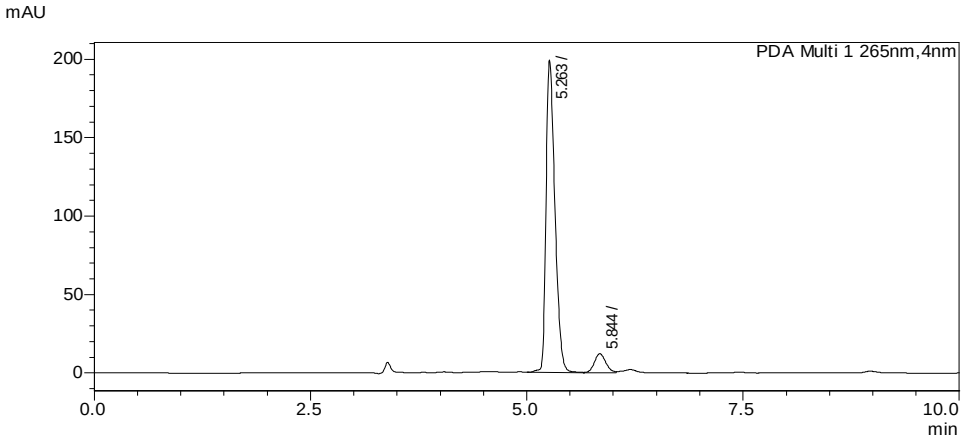
5.731	7323286	50.511
	14498494	100



Ret. Time	Area	Area%
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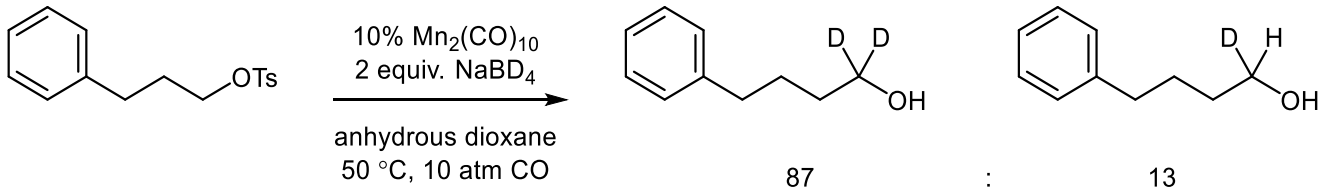


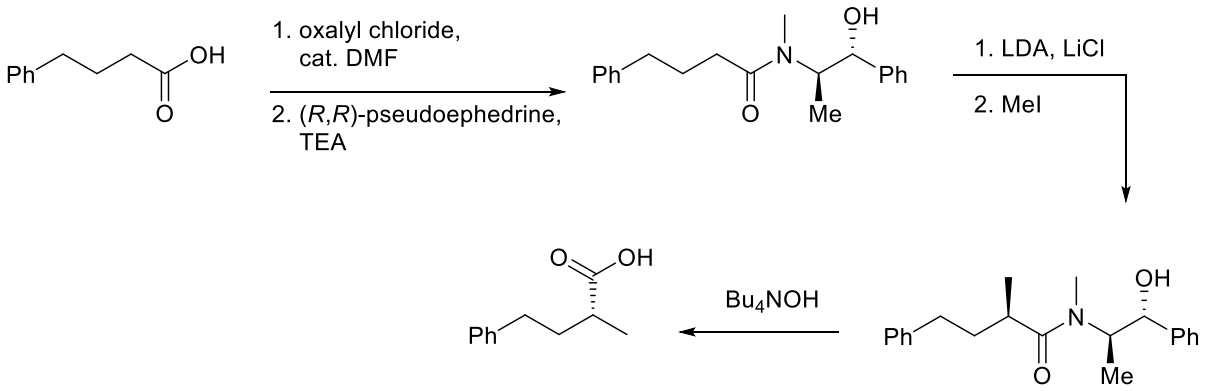
4-phenylbutan-1,1-d_2-1-ol (SI-15) was obtained from the General Carbonylation Procedure to give 57% NMR yield and the crude product was flashed in 20% EtOAc/hexanes yielding **SI-15** as a colorless oil (19.1 mg, 50%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.35 – 7.26 (m, 3H), 7.21 (dd, *J* = 7.8, 5.4 Hz, 3H), 2.67 (t, *J* = 7.6 Hz, 2H), 1.79 – 1.69 (m, 2H), 1.68 – 1.58 (m, 2H). **^{2}H NMR** (77 MHz, $CDCl_3$) δ 3.66. **^{13}C NMR** (151 MHz, $CDCl_3$) δ142.3, 128.4, 128.3, 125.8, 77.3, 77.1, 76.8, 35.7, 32.1, 27.5. **HRMS** (ESI) calculated for $[C_{10}H_{12}D_2O+Na]^+$ 175.1068, found 175.1050.

Deuterium incorporation was determined by isotopic abundance. Samples were analyzed with a ThermoFisher GC Exactive with an Electron Ionization (EI) source and acquired in positive mode with a scan range of 50-600 m/z and a resolution of 60,000. The ion source was set to 280 °C and the MS transfer line was set to 250 °C.

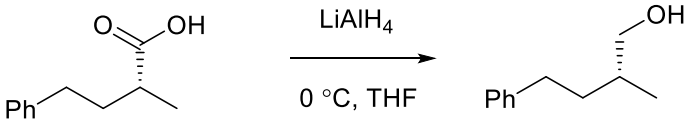
Mechanistic Experiments

Absolute Stereochemistry Determination

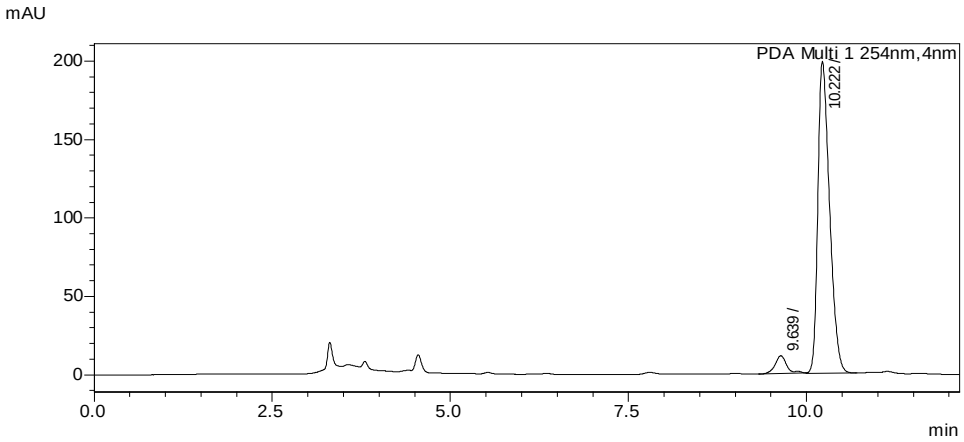
An independent HPLC standard of primary alcohol product was obtained by reduction of the corresponding enantiopure morpholine amide, synthesized according to literature procedure[8] to show that the carbonylation reaction proceeds via inversion. This suggests an S_N2 oxidative addition is operative in the reaction mechanism.



(R)-2-methyl-4-phenylbutanoic acid (SI-16) was prepared according to a published procedure and used without further purification.[8]



2-methyl-4-phenylbutan-1-ol (14) was synthesized according to the following procedure. The carboxylic acid **SI-16** (10.5mg, 0.059 mmol) was dissolved in 0.25 mL diethyl ether and added dropwise to a 0 ^oC suspension of $LiAlH_4$ (8.9 mg, .236 mmol) in diethyl ether (0.25 mL). The reaction was allowed to warm to room temperature and stirred overnight, after which it was cooled to 0 ^oC and quenched by sequential dropwise addition of water (9 µL), 2.5 M NaOH (9 µL), and water (27 µL). The slurry was warmed to room temperature, dried with $MgSO_4$, then stirred for 15 minutes. The mixture was then filtered through a plug of Celite, and concentrated to give 8.7 mg (90%) of the crude product, which was characterized by HPLC analysis without further purification.



Ret. Time	Area	Area%
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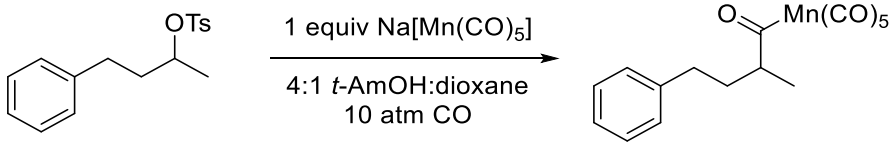
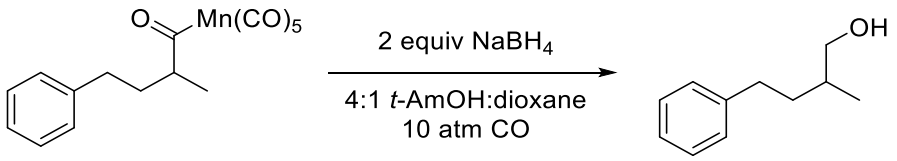
10.222	2278410	94.651
	2407173	100

Isolation and Reaction of Proposed Intermediates



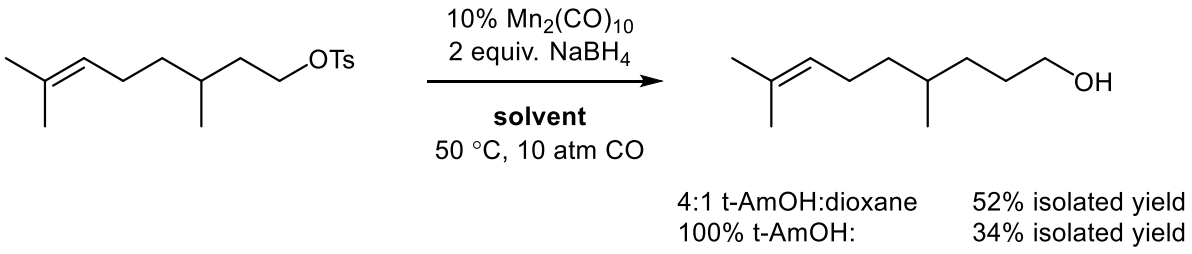
(25) In a glovebox under an argon atmosphere, alkyl tosylate (152mg, 0.500 mmol) was combined with $Na[Mn(CO)_5]$ (109 mg, 0.500 mmol), and t-amyl alcohol (0.8 mL) and dioxane (0.2mL) in an Ace Glass pressure tube. The tube was sealed with a Swagelok gas quick-connect adapter and removed from the glovebox. Subsequently, the tube was purged three times with 10 atm CO and then set to 10 atm CO and the reaction was stirred at 50 ^{o}C. After 16 hours, the tube was removed from the bath, cooled to room temperature, and depressurized. The crude reaction mixture was dissolved in DCM and adsorbed onto silica by rotary evaporation at temperatures no greater than 0^{o}C. The resulting yellow powder was purified immediately by gradient silica gel chromatography in hexanes to 2.5% Et_2O/hexanes. A bright yellow band ($Mn_2(CO)_{10}$) eluted first in hexanes, followed by a second band containing the acyl manganese product. This product was concentrated at temperatures no greater than 0 ^{o}C to give 85 mg (48% yield) of a mixture of shiny white and yellow crystals. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.28 (s, 6H), 7.21 (dd, *J* = 8.4, 6.8 Hz, 3H), 3.14 (h, *J* = 6.7 Hz, 1H), 2.71 – 2.56 (m, 2H), 2.02 (ddt, *J* = 13.2, 10.3, 6.3 Hz, 1H), 1.55 – 1.41 (m, 1H), 1.10 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 262.19, 209.58, 141.90, 128.43, 128.31, 125.94, 77.26, 77.05, 76.84, 68.59, 34.11, 33.48, 15.46. **HRMS** (ESI) calculated for $[C_{16}H_{13}MnO_6+Na]^+$ 378.9990, found 378.9953.



2-methyl-4-phenylbutan-1-ol (14) was synthesized according to the following procedure. In a glovebox under an argon atmosphere, acyl manganese **25** (89.1mg, 0.25 mmol) was combined with sodium borohydride (18.9mg, 0.50 mmol), *t*-amyl alcohol (0.4 mL) and dioxane (0.1mL) in an Ace Glass pressure tube. The tube was sealed with a Swagelok gas quick-connect adapter and removed from the glovebox. Subsequently, the tube was purged three times with 10 atm CO and then set to 10 atm CO and the reaction was stirred at 50 ^{o}C. After 16 hours, the tube was removed from the bath, cooled to room temperature, and depressurized. The reaction was allowed to stir for 8 hours with 8-10 drops of DBU, after which it was diluted with EtOAc and quenched with brine for at least 20 minutes. The aqueous layer was then extracted with EtOAc (3 × 2mL). The combined organic layers were dried with $MgSO_4$, filtered through a cotton plug, and concentrated under reduced pressure and heat (approx. 45 ^{o}C water bath). The crude mixture was then diluted with 8-10mL 20% EtOAc/Hexanes and filtered through a short silica plug to remove manganese, and concentrated under reduced pressure to give 56% NMR yield, determined using HMDSO as an internal standard.

Solvent Effect

It was noted that yields of certain substrates were solvent-dependent. The following is a representative example:



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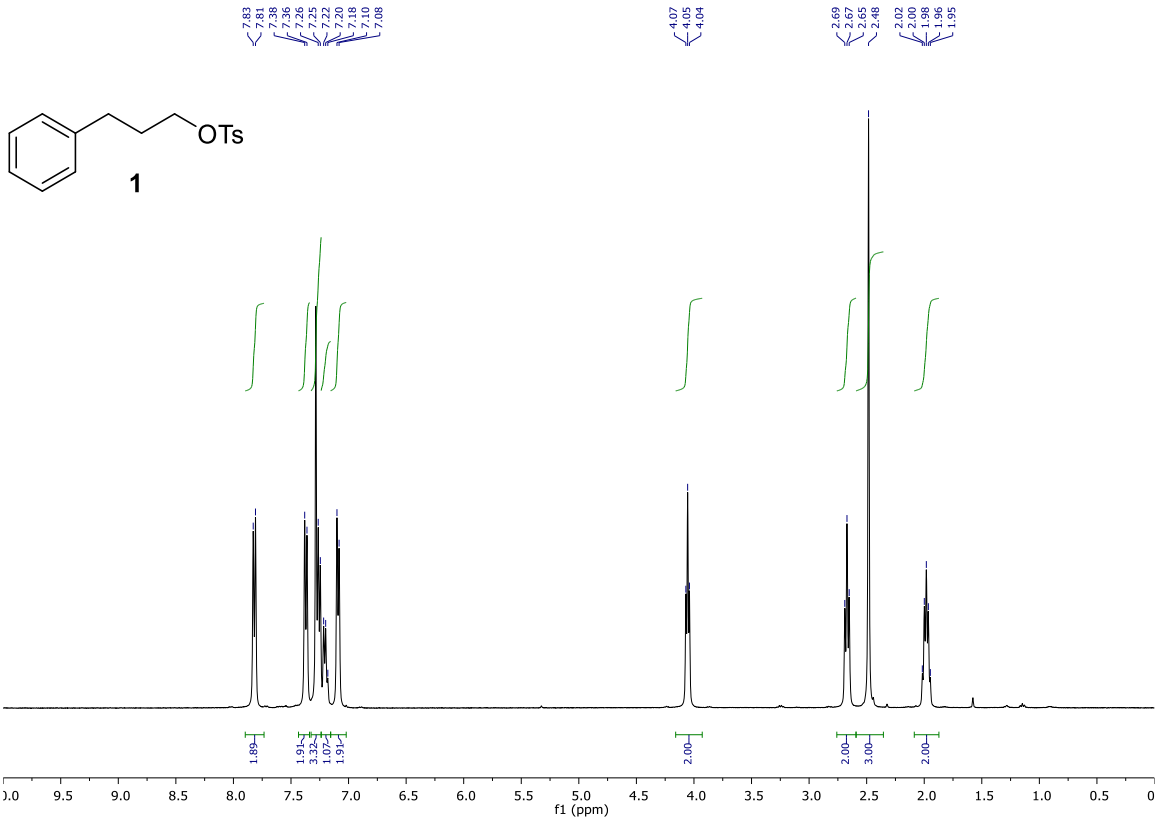
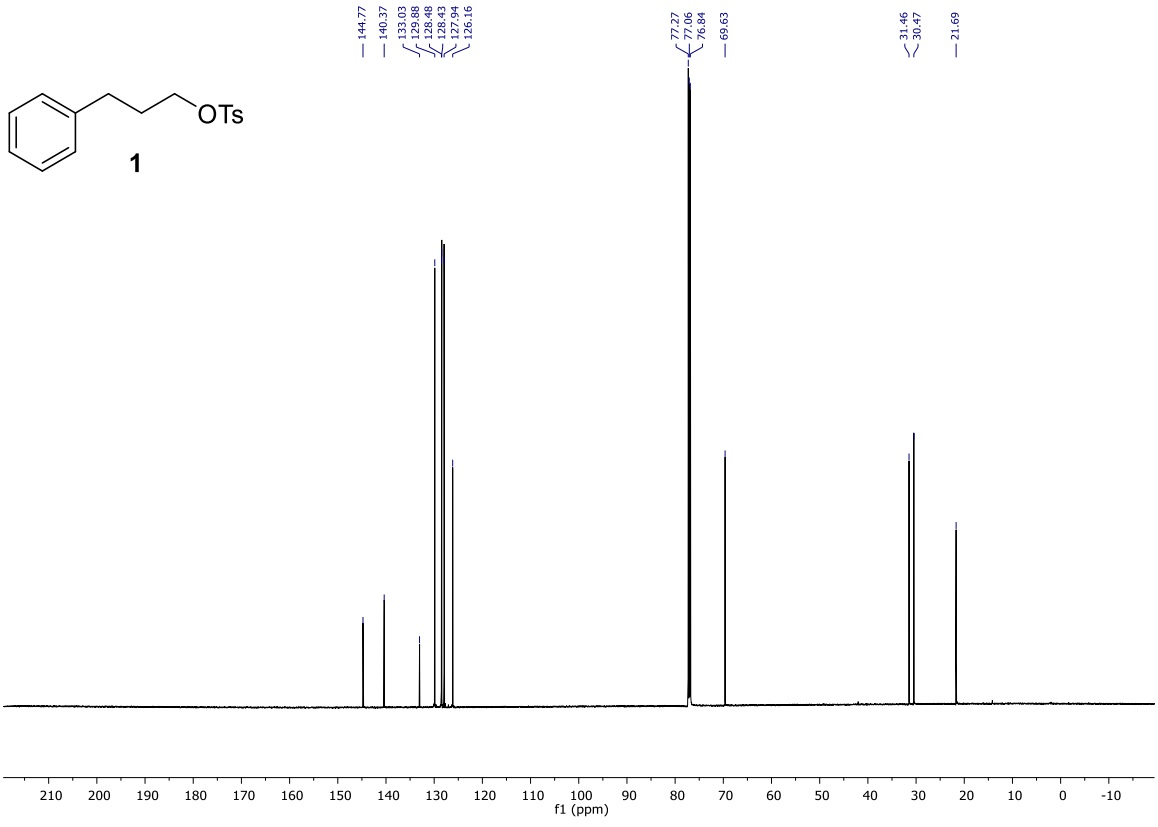
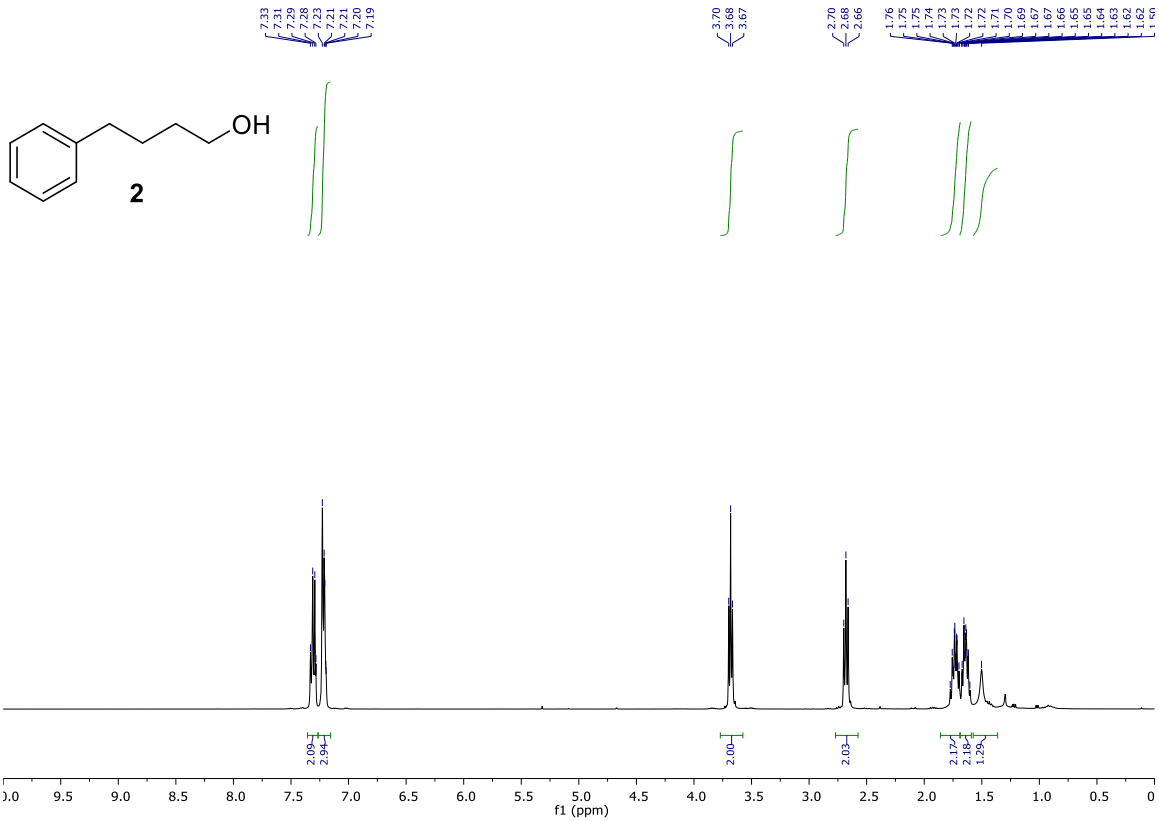
8. Sargent, B. T., Alexanian, E. J. Cobalt-Catalyzed Aminocarbonylation of Alkyl Tosylates: Stereospecific Synthesis of Amides. *Angewandte Chemie International Edition* **2019**, *58*, 9533–9536.

^{1}H and ^{13}C NMR Spectra



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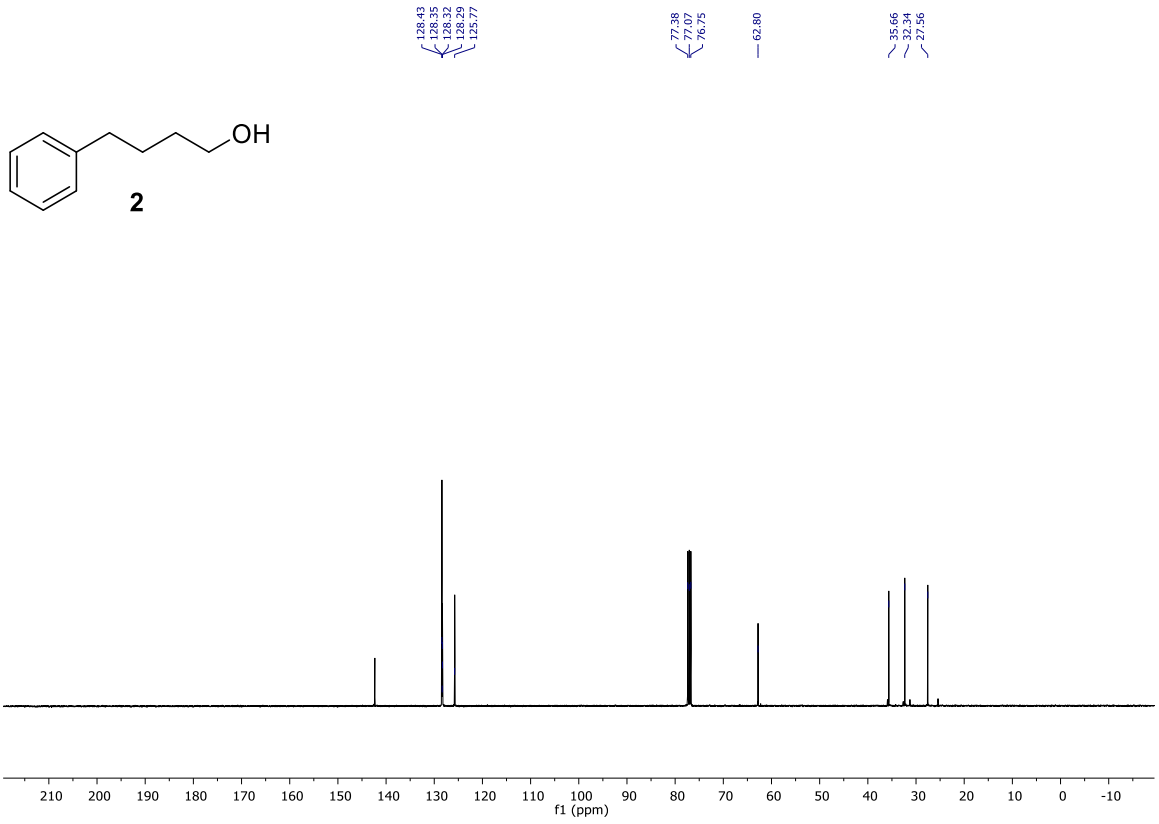
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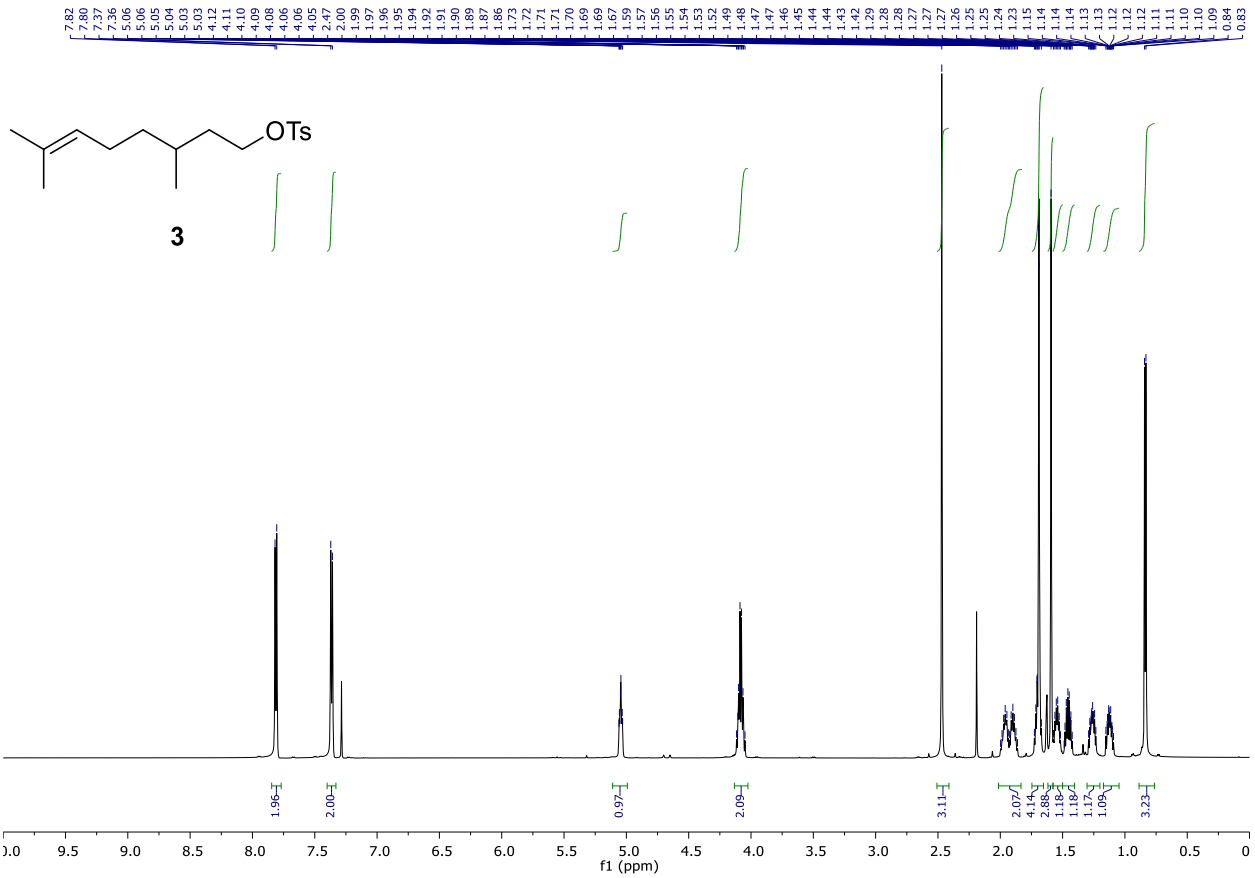
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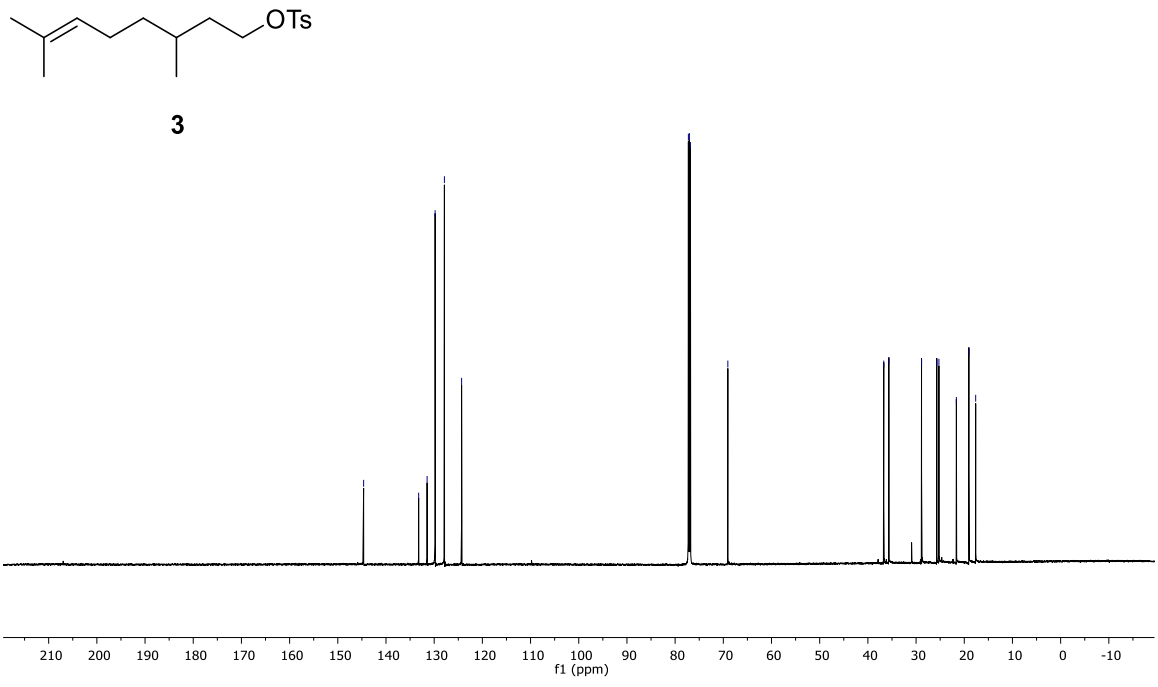
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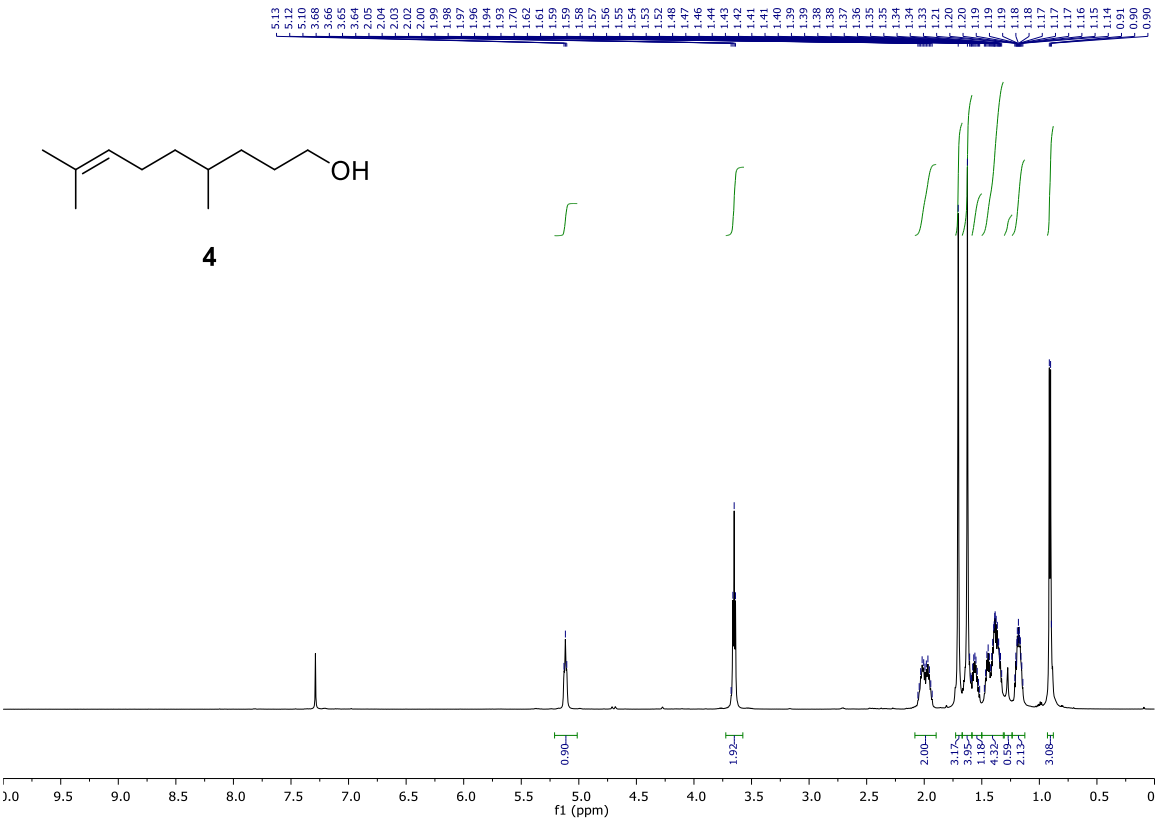
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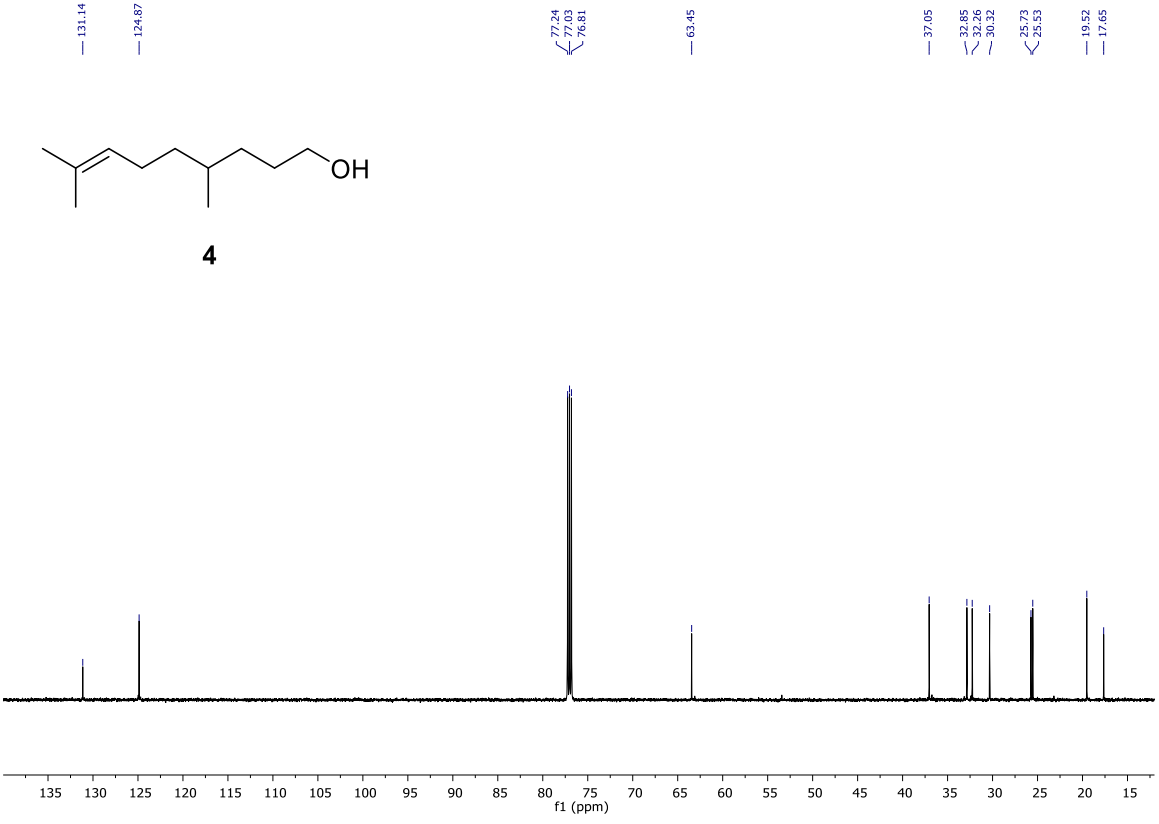
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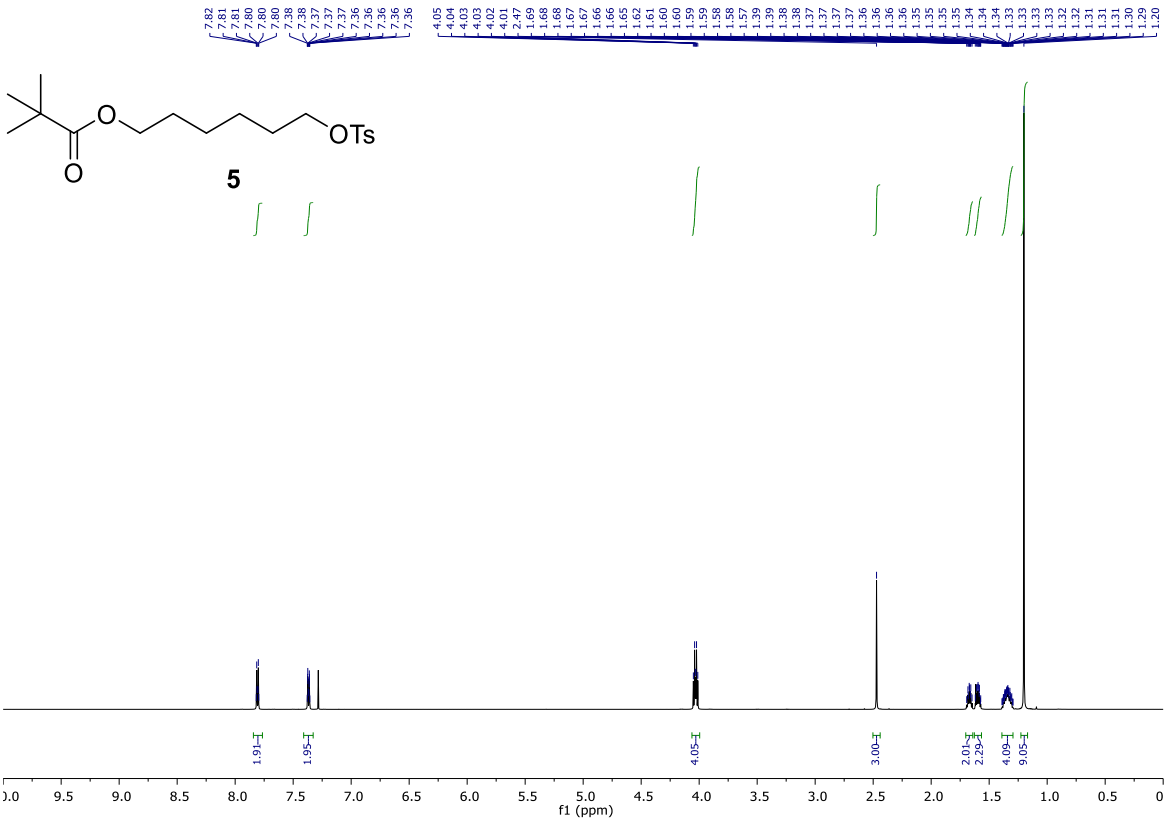
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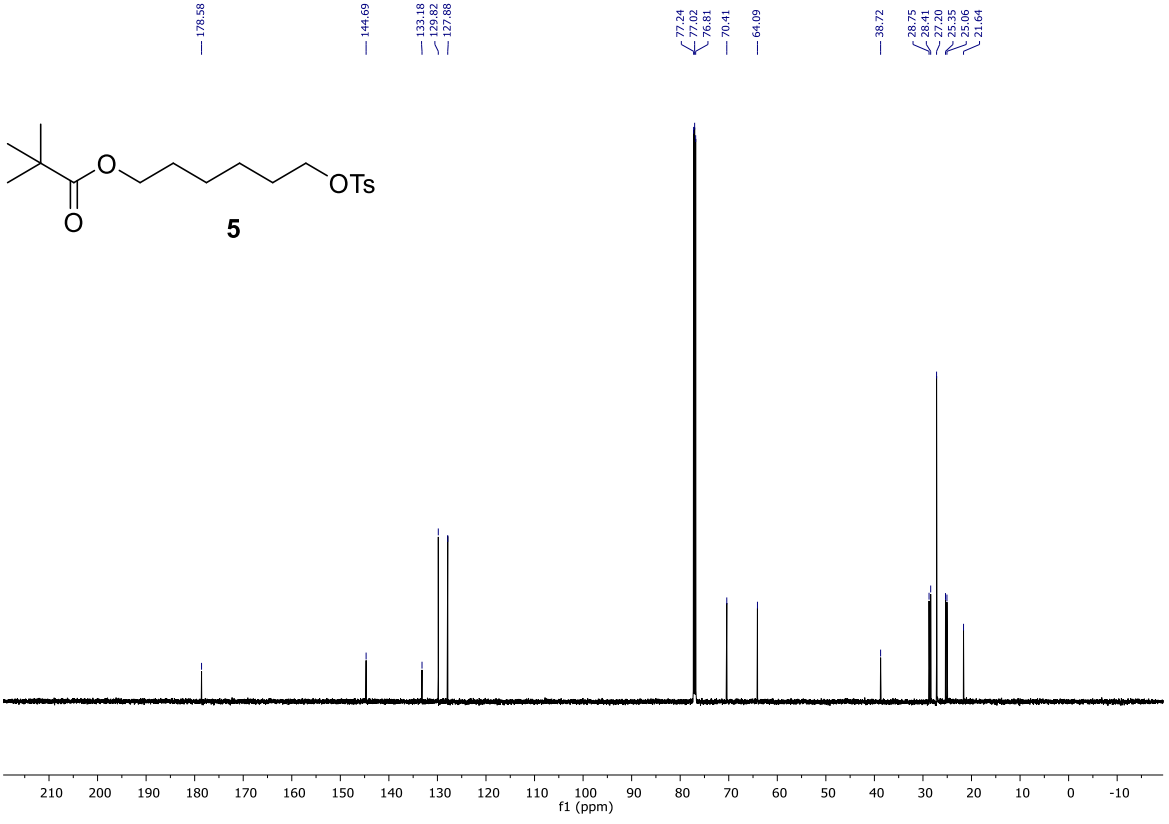
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OTs
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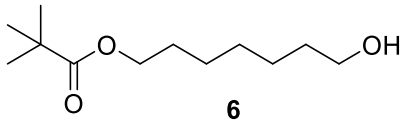
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OH
O

6

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1.58
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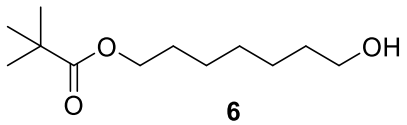
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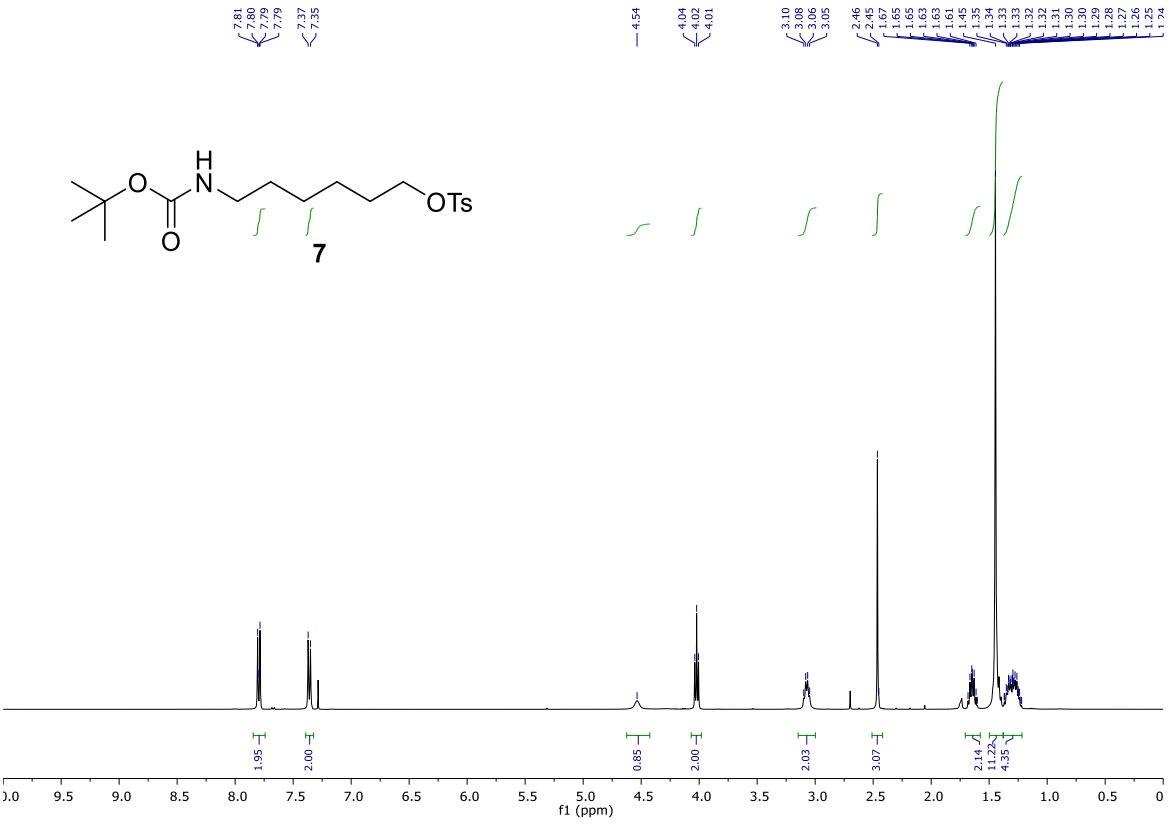
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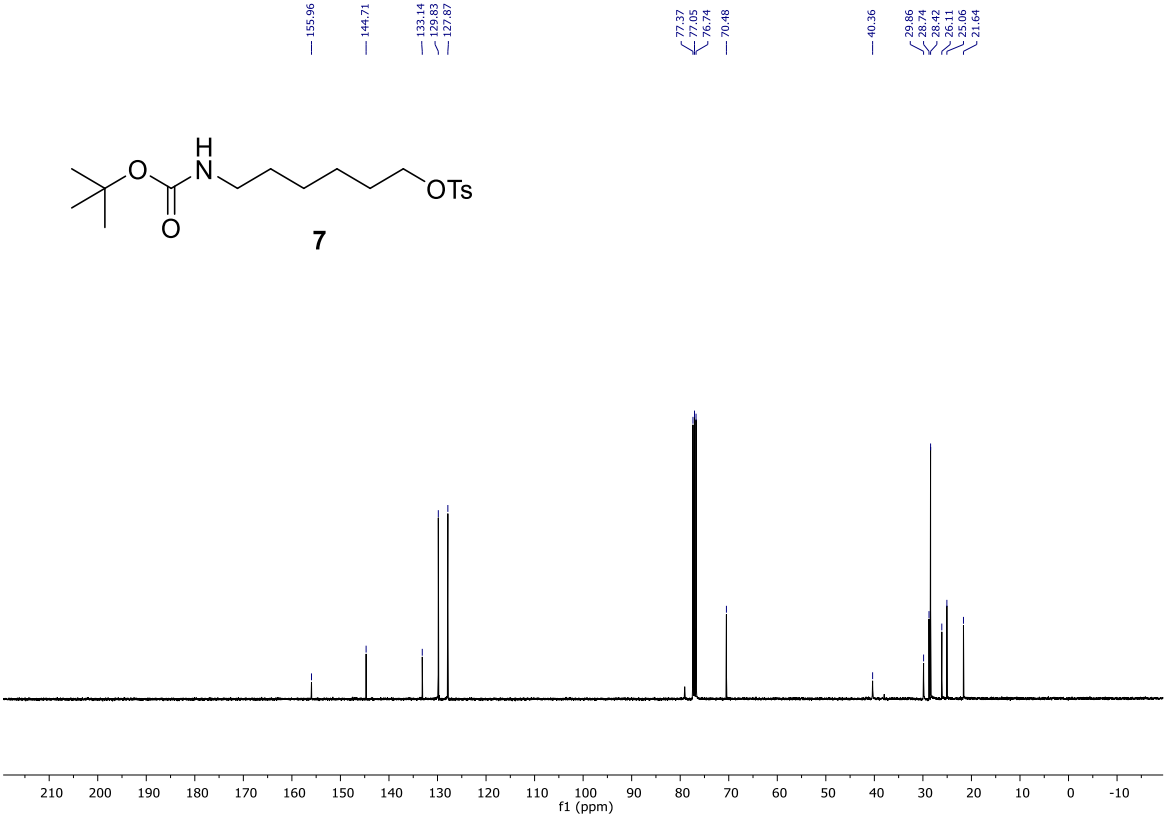
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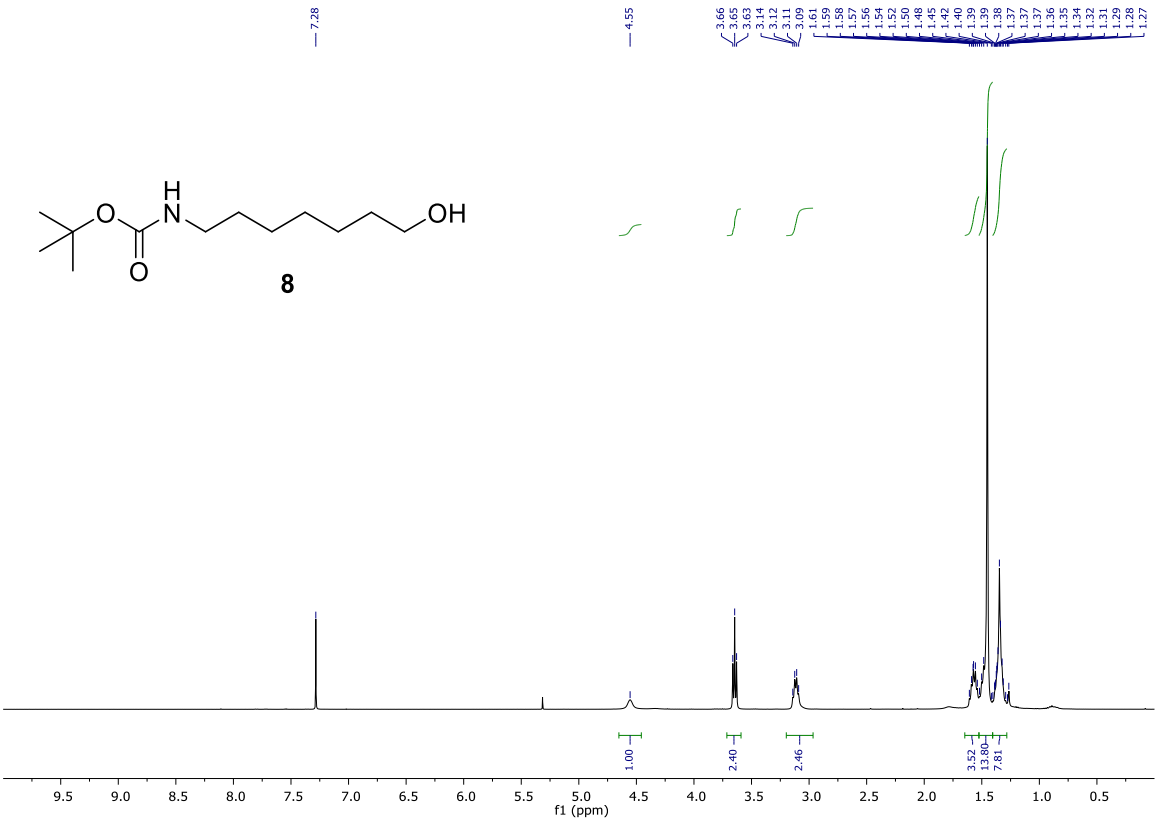
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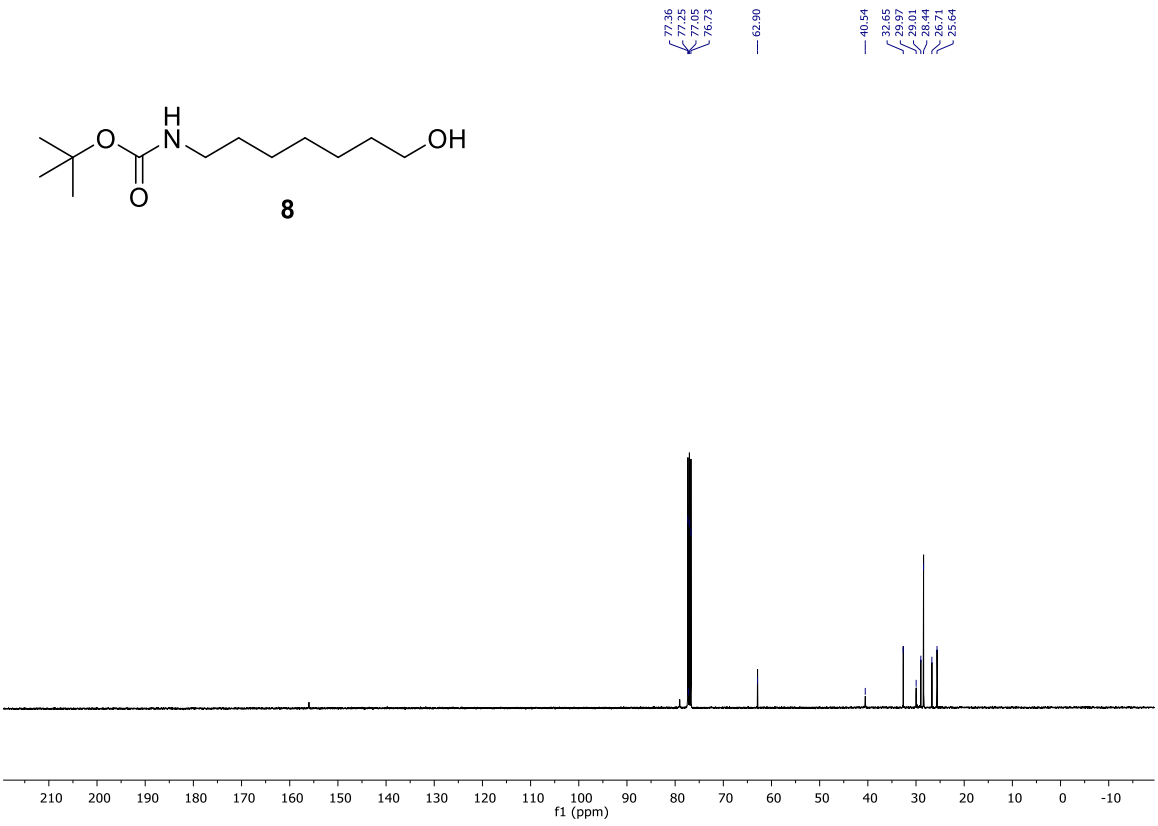
7.81
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)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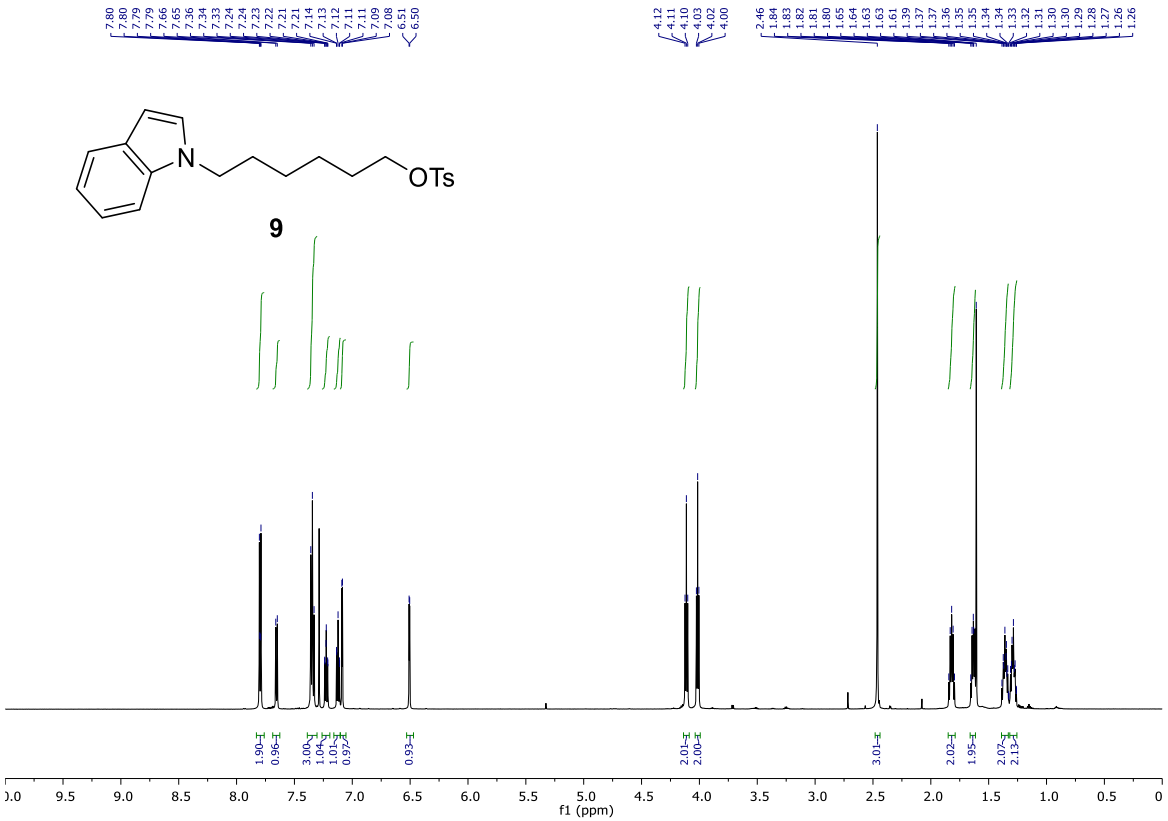
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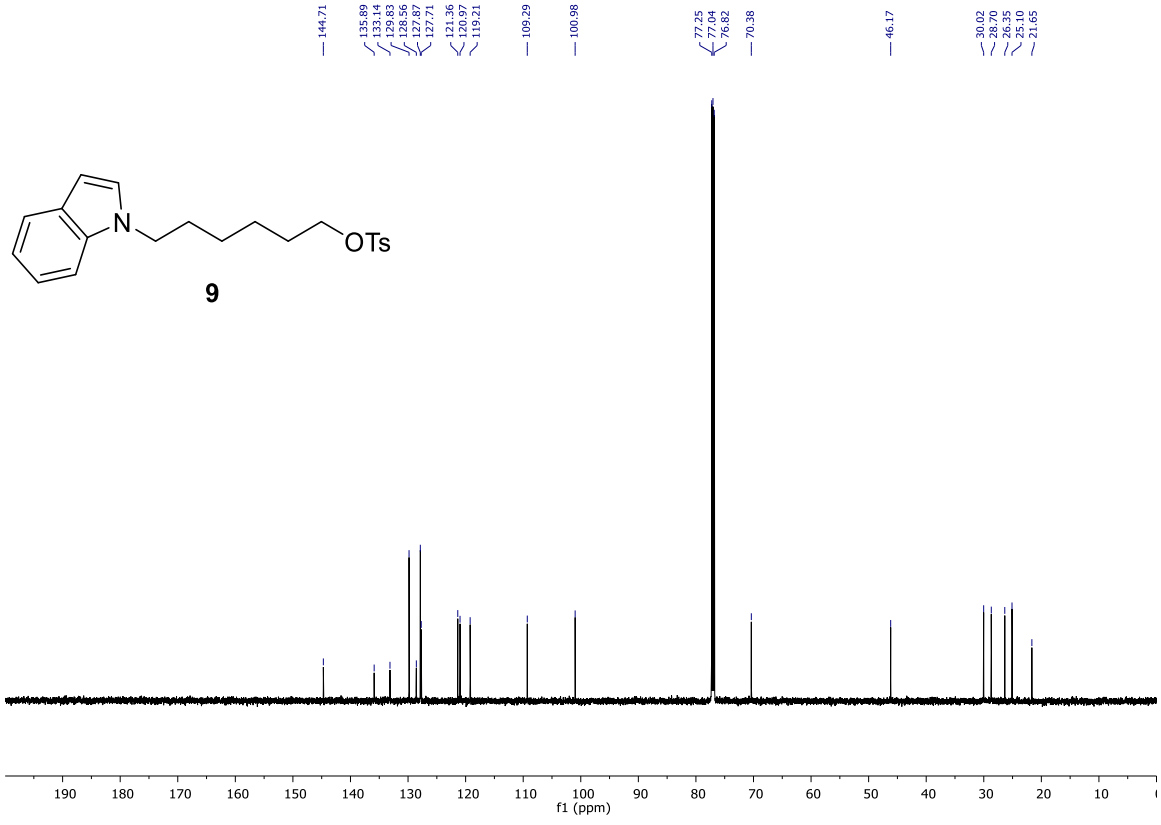
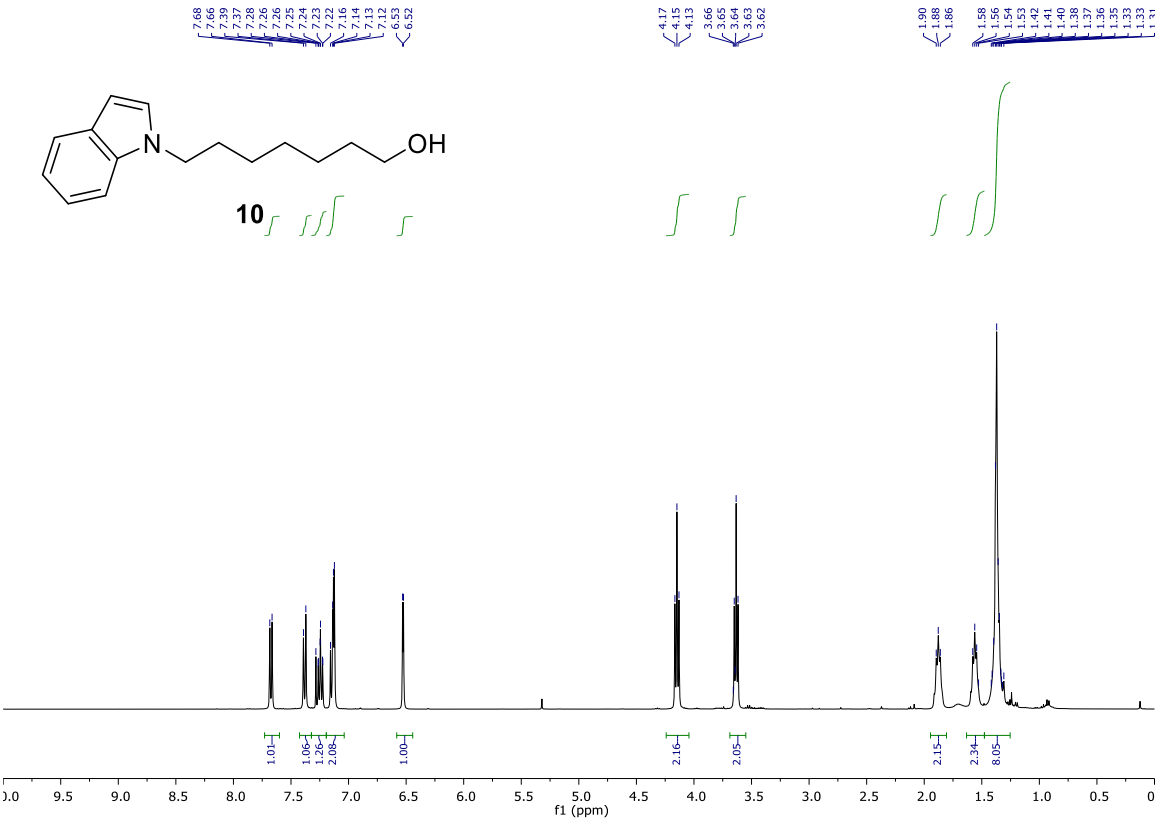
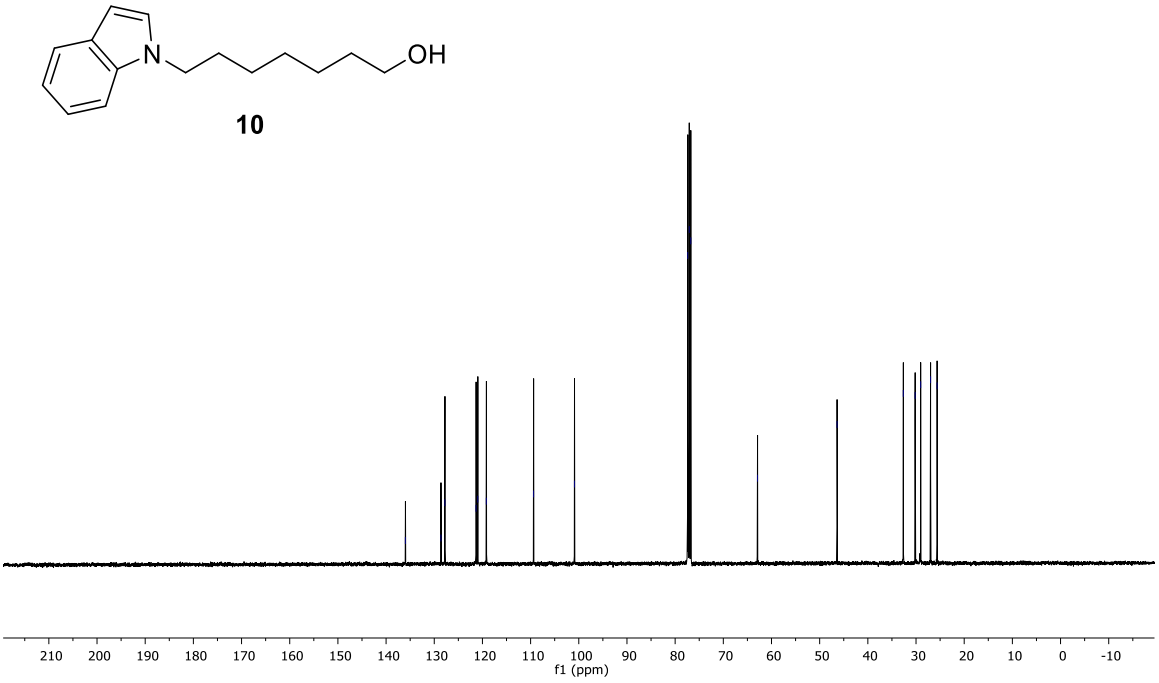
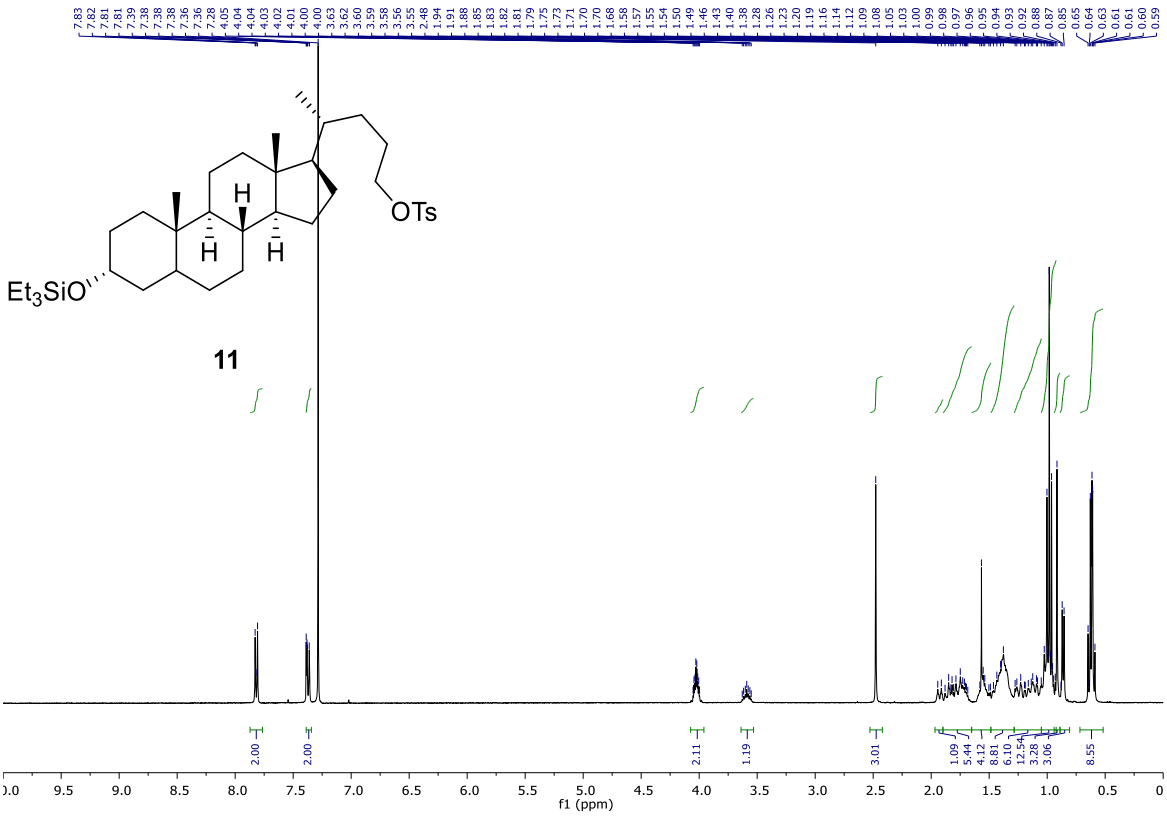
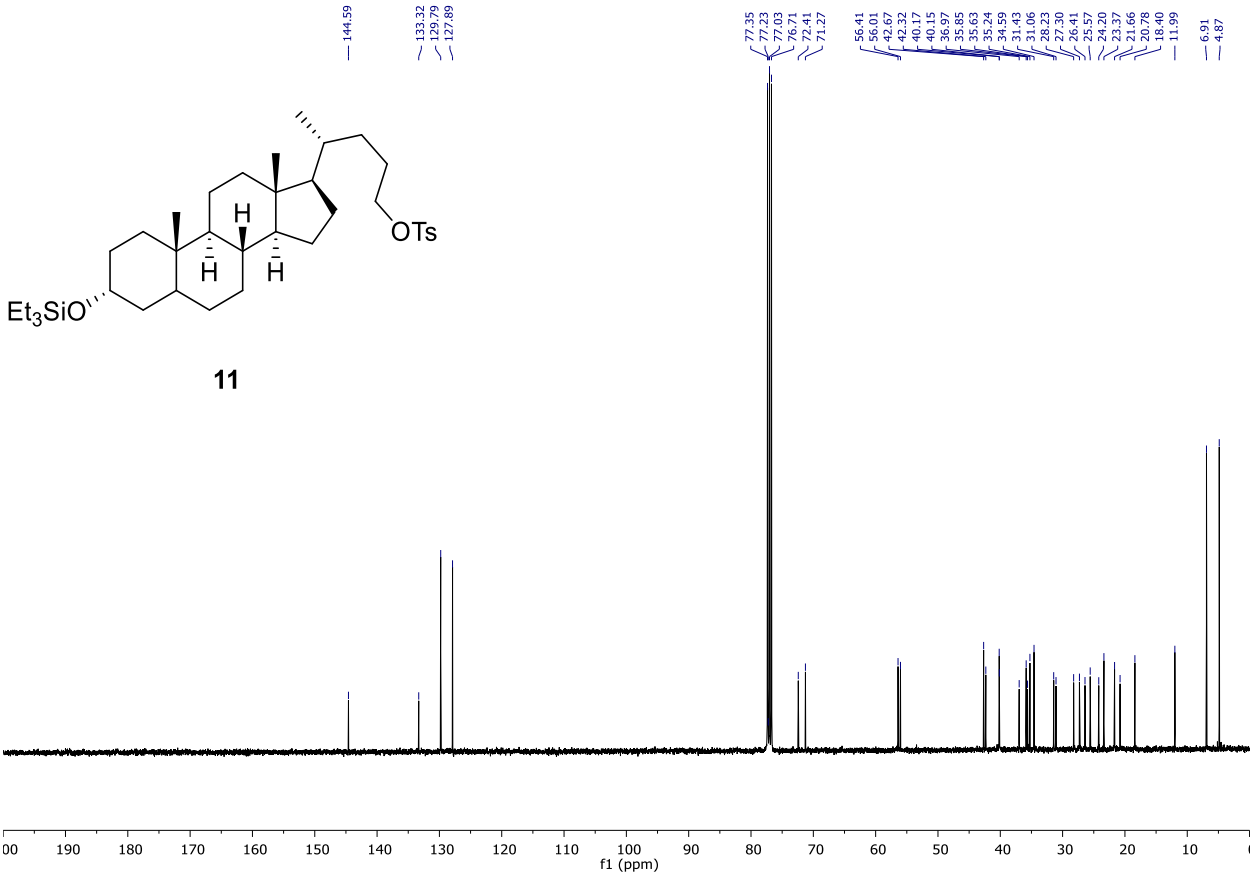
2.13
f1 (ppm)

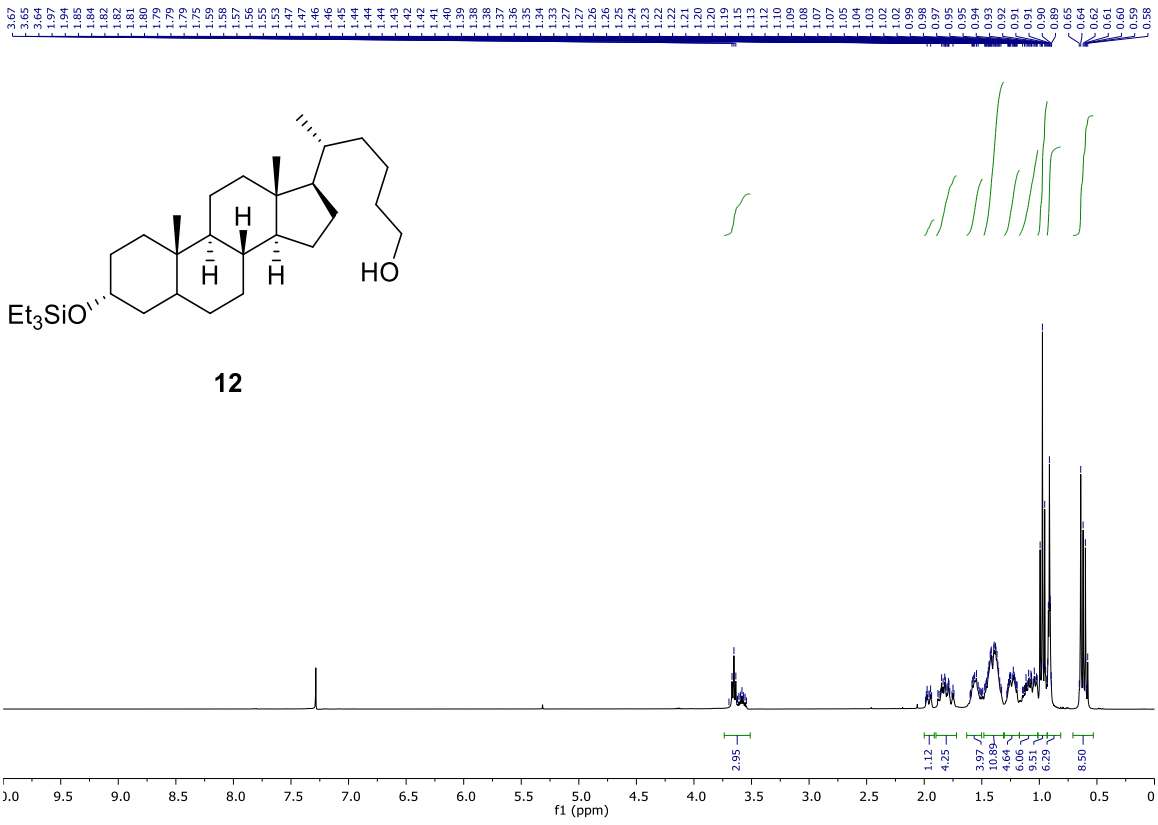

144.71
135.89
133.14
129.83
128.56
127.87
127.71
121.36
120.97
119.21
109.29
100.98
77.25
77.04
76.82
70.38
46.17
30.02
28.70
26.35
25.10
21.65
N
OTs
9
f1 (ppm)


7.68
7.66
7.39
7.37
7.28
7.26
7.26
7.25
7.24
7.23
7.22
7.16
7.14
7.13
7.12
6.53
6.52
4.17
4.15
4.13
3.66
3.65
3.64
3.63
3.62
1.90
1.88
1.86
1.58
1.56
1.54
1.53
1.42
1.41
1.40
1.38
1.37
1.36
1.35
1.33
1.33
N
OH
10
1.01
1.06
1.26
2.08
1.00
2.16
2.05
2.15
2.34
8.05
f1 (ppm)

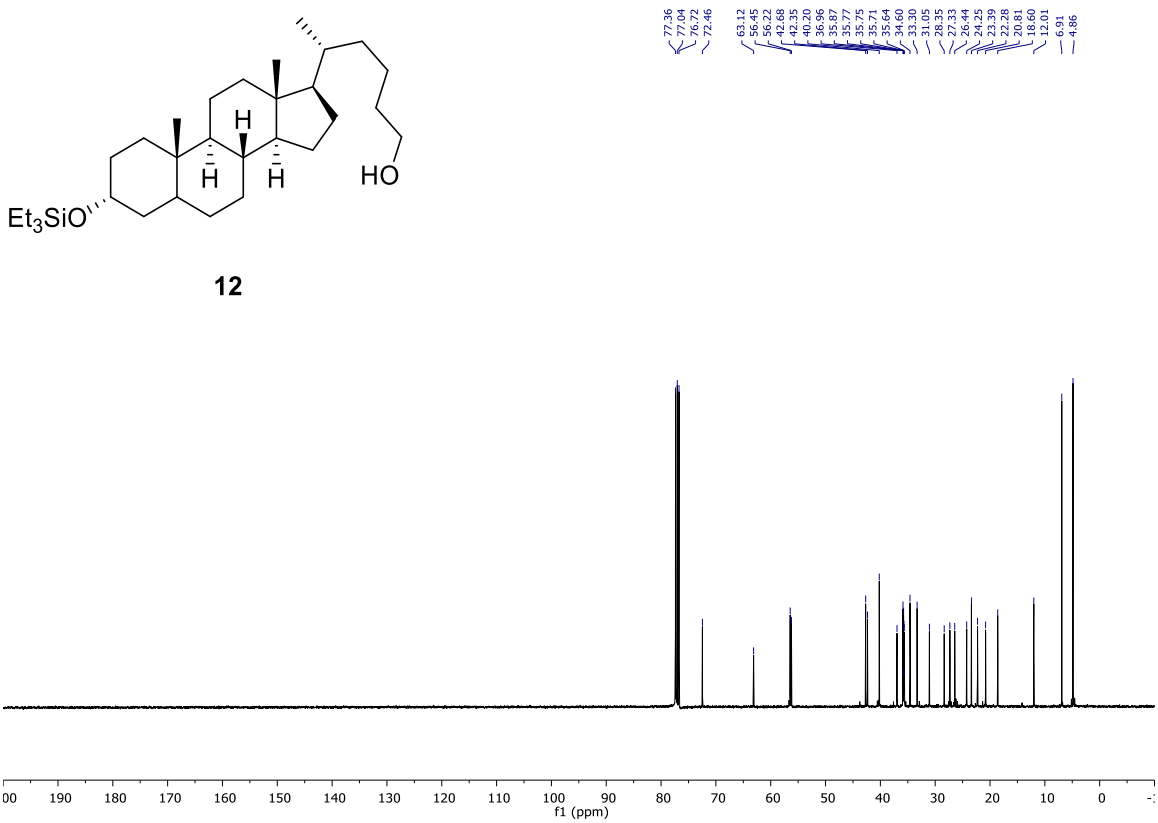

135.99
128.62
127.79
121.33
120.97
119.18
109.39
100.90
77.40
77.08
76.76
62.90
46.39
32.63
30.18
29.04
26.98
25.62
N
OH
10
f1 (ppm)


OTs
H
H
H
Et3SiO
11
f1 (ppm)

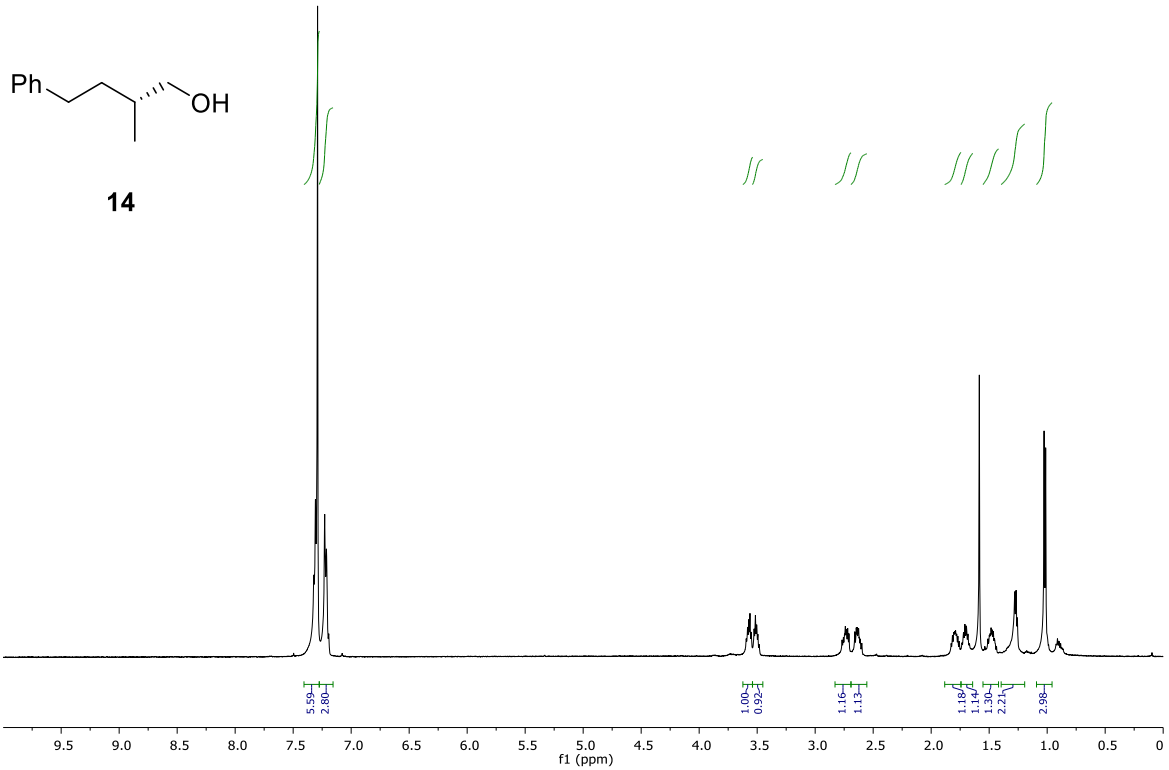

OTs
H
H
H
Et3SiO
11
f1 (ppm)

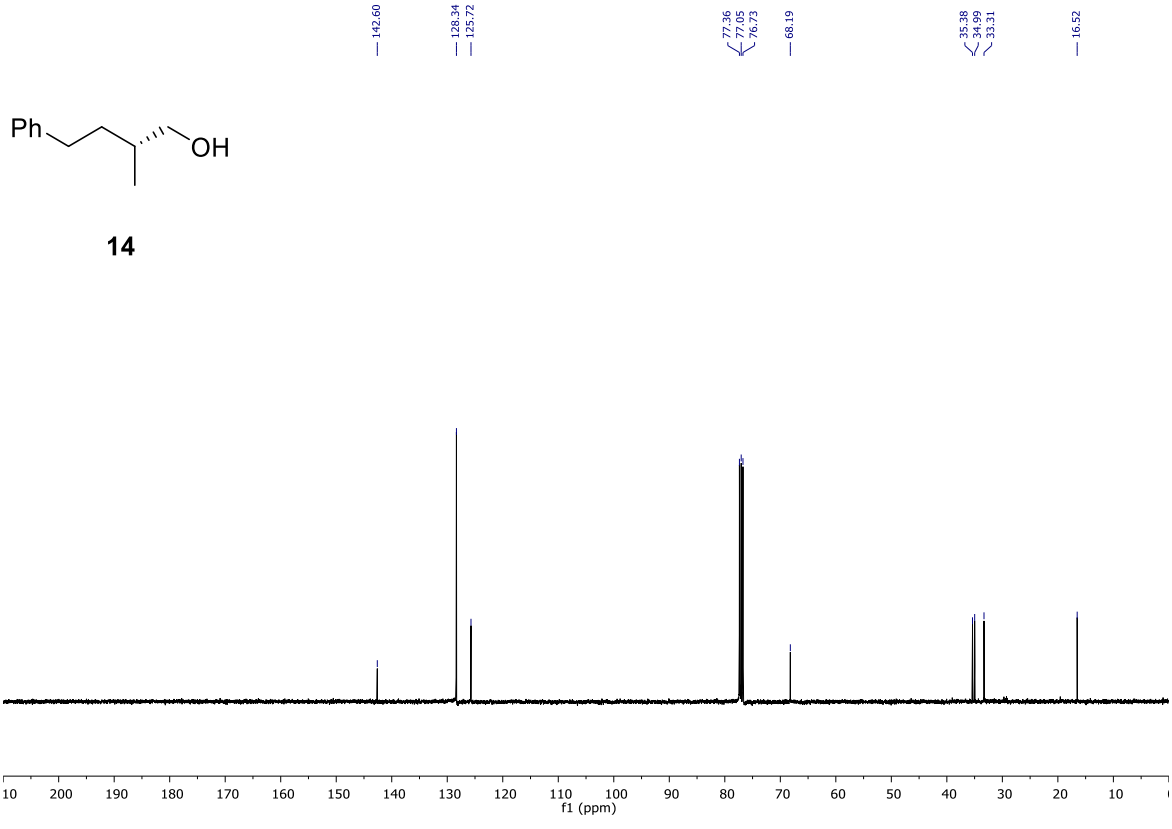


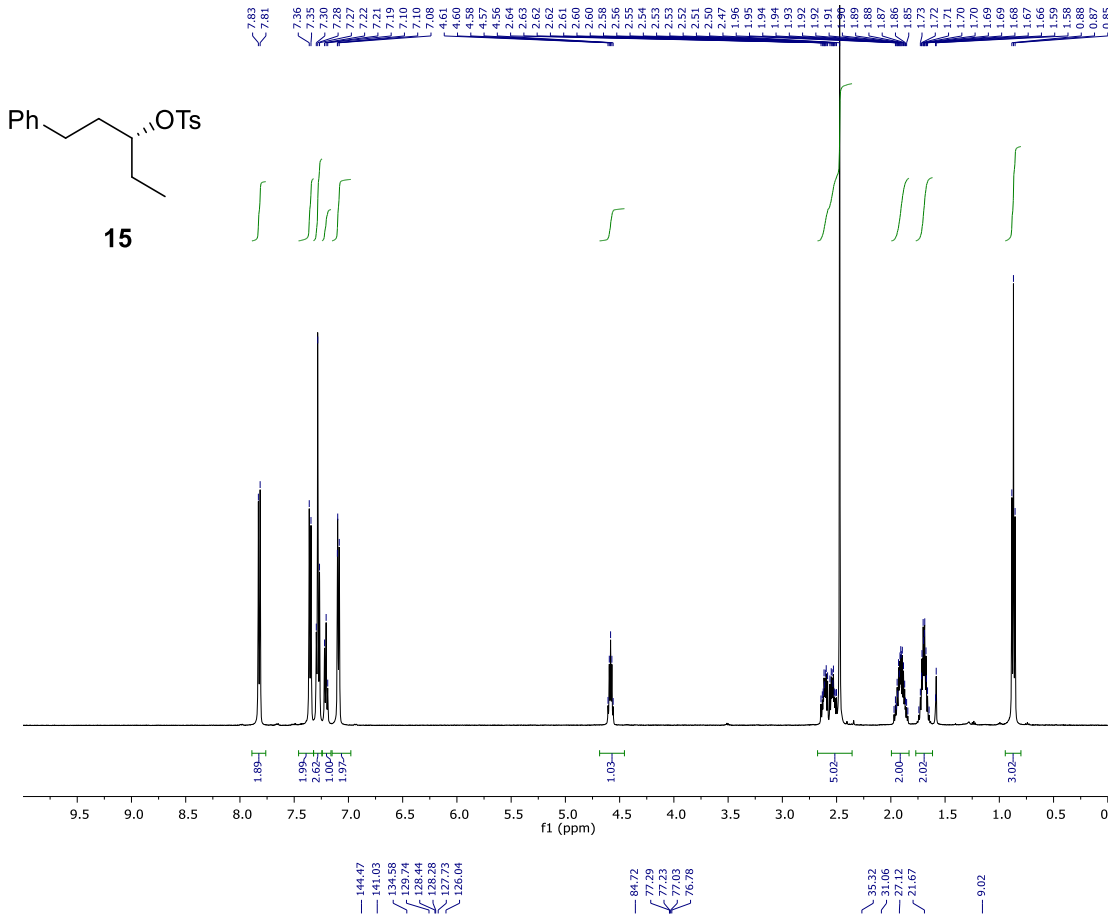
12

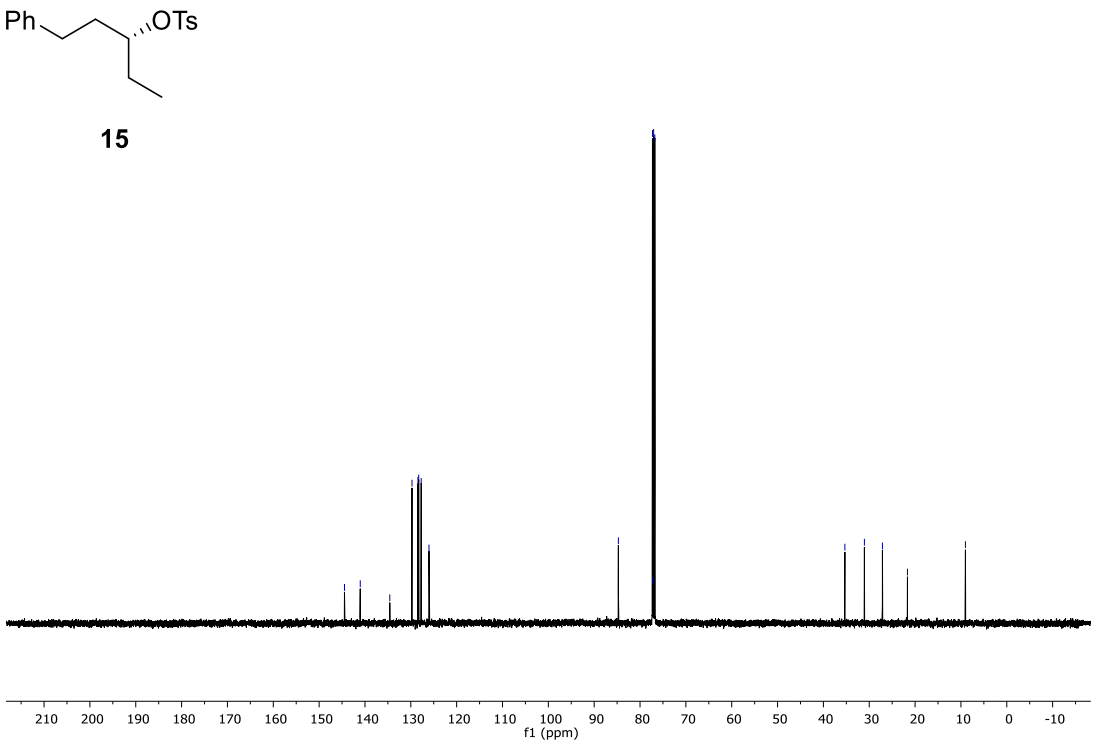


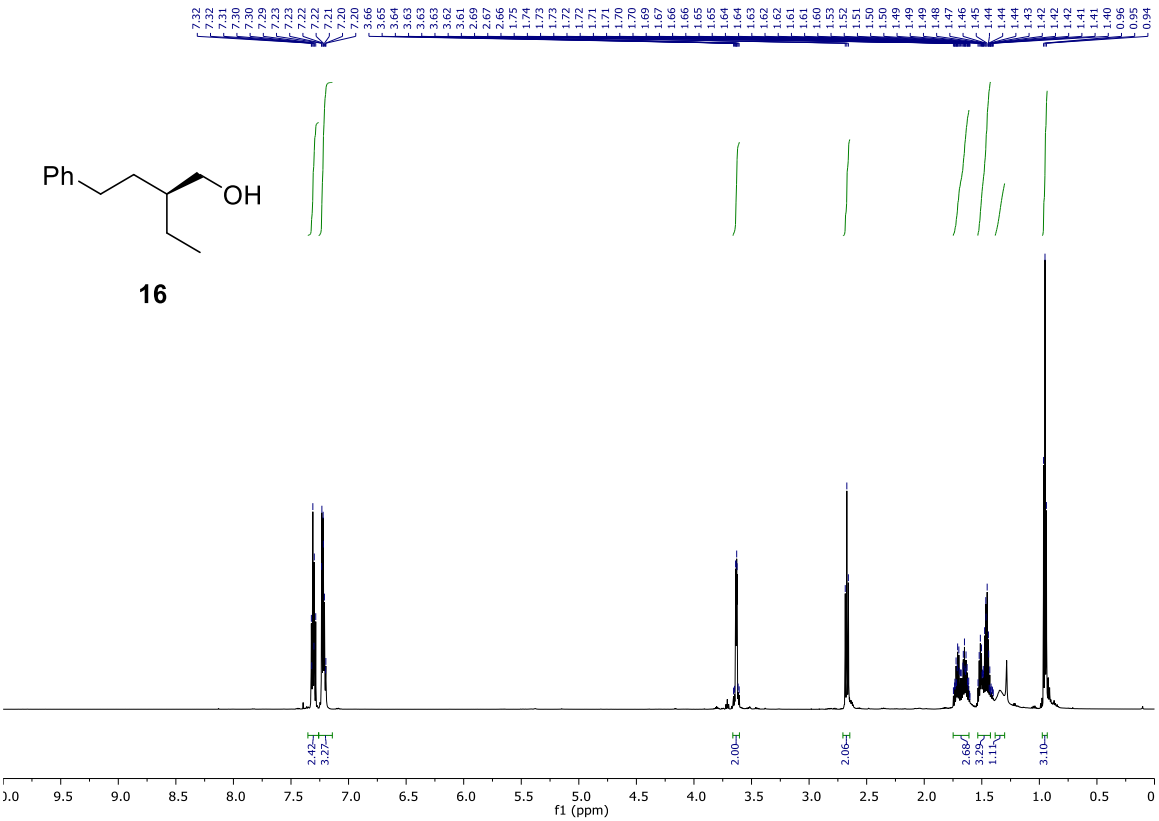
12

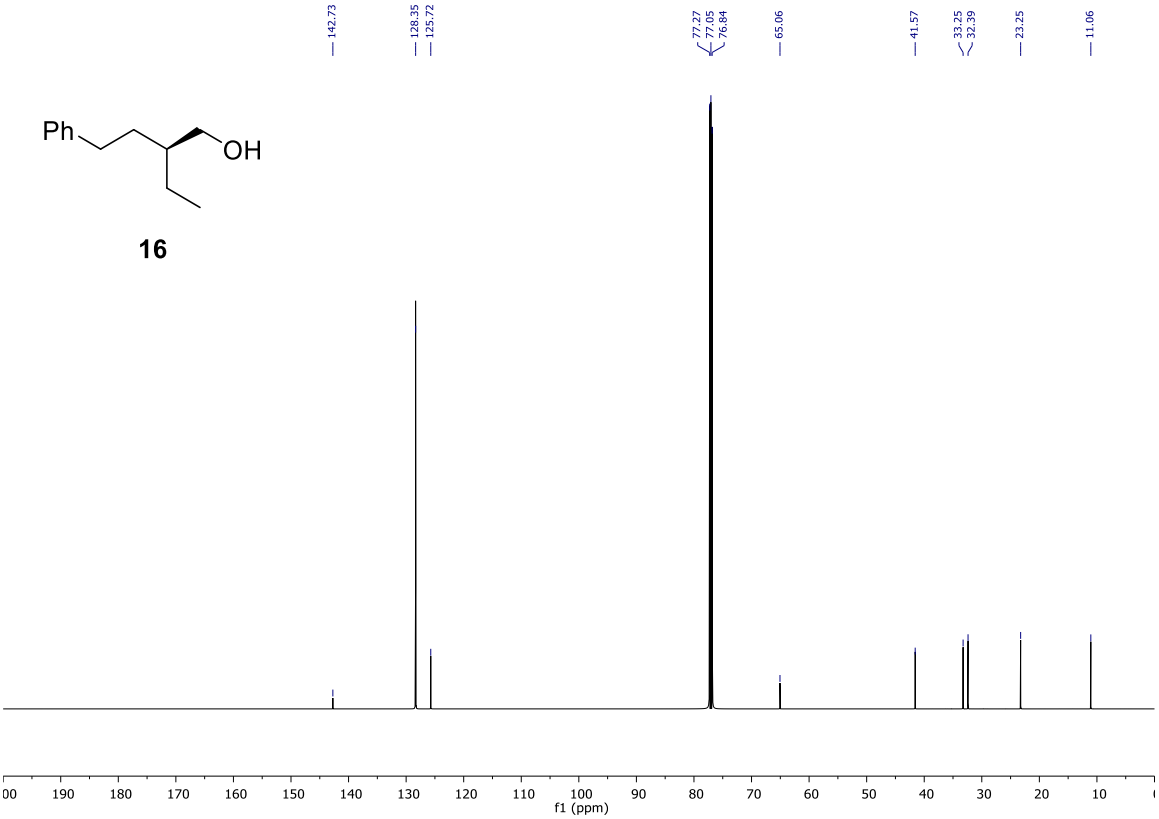

Ph
OH
14
5.59
2.80
1.00
0.92
1.16
1.13
1.18
1.14
1.30
2.21
2.98
f1 (ppm)

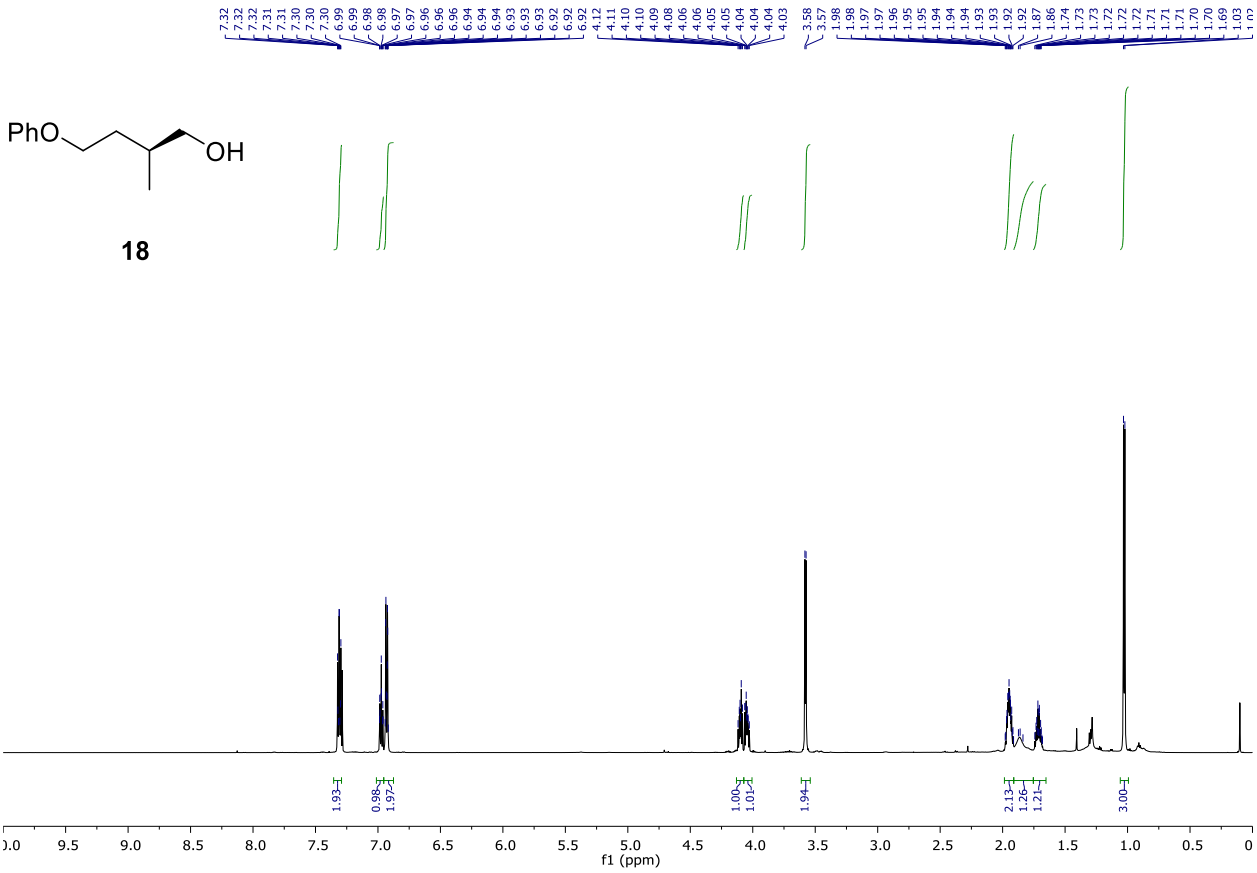

142.60
128.34
125.72
77.36
77.05
76.73
68.19
35.38
34.99
33.31
16.52
Ph
OH
14
f1 (ppm)

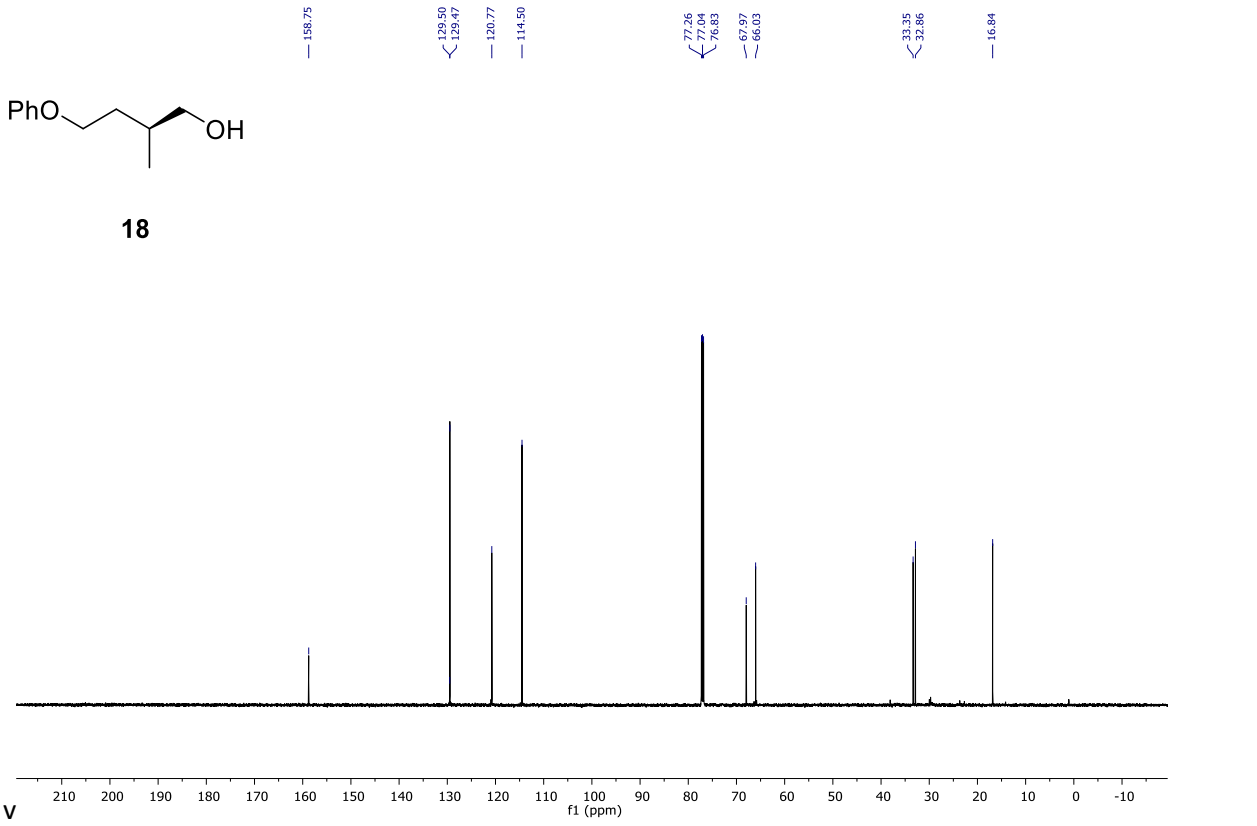

Ph
OTs
15
f1 (ppm)


Ph
OTs
15
f1 (ppm)

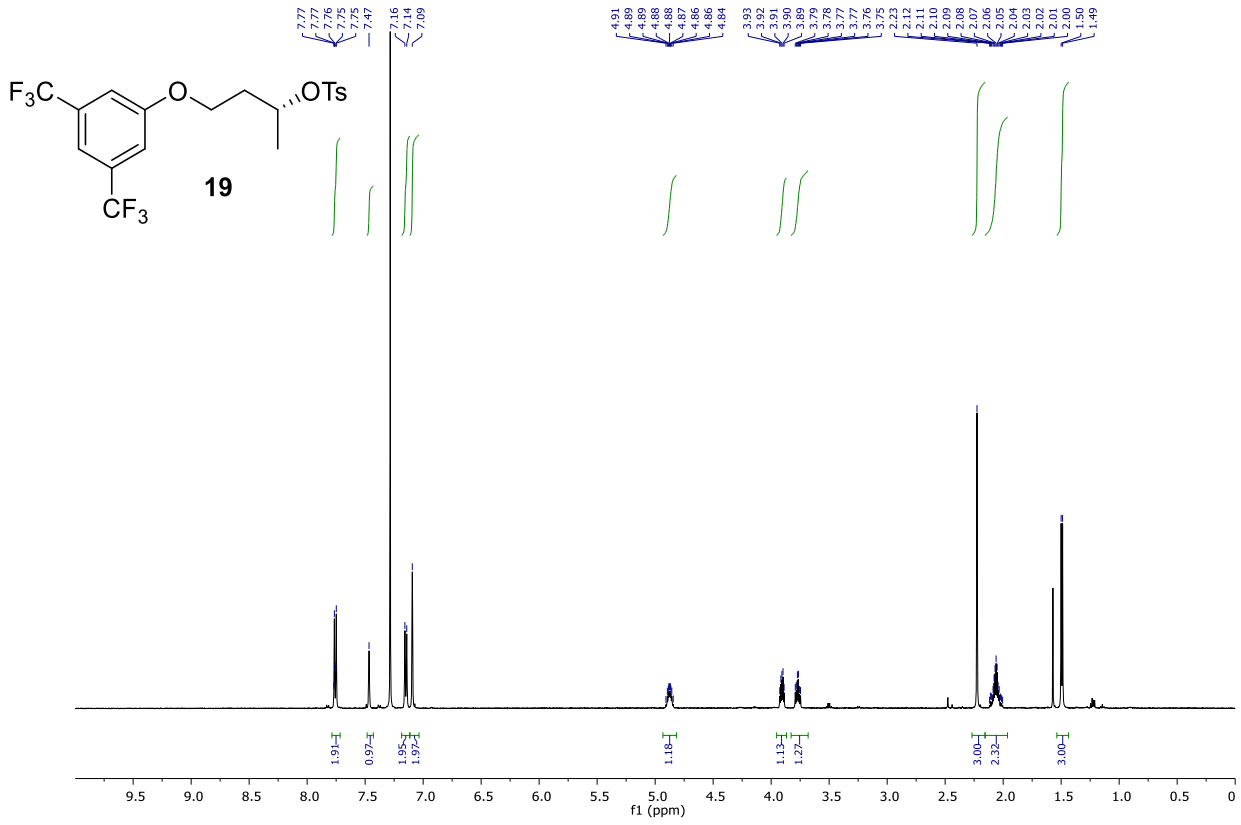

Ph
OH
16
f1 (ppm)

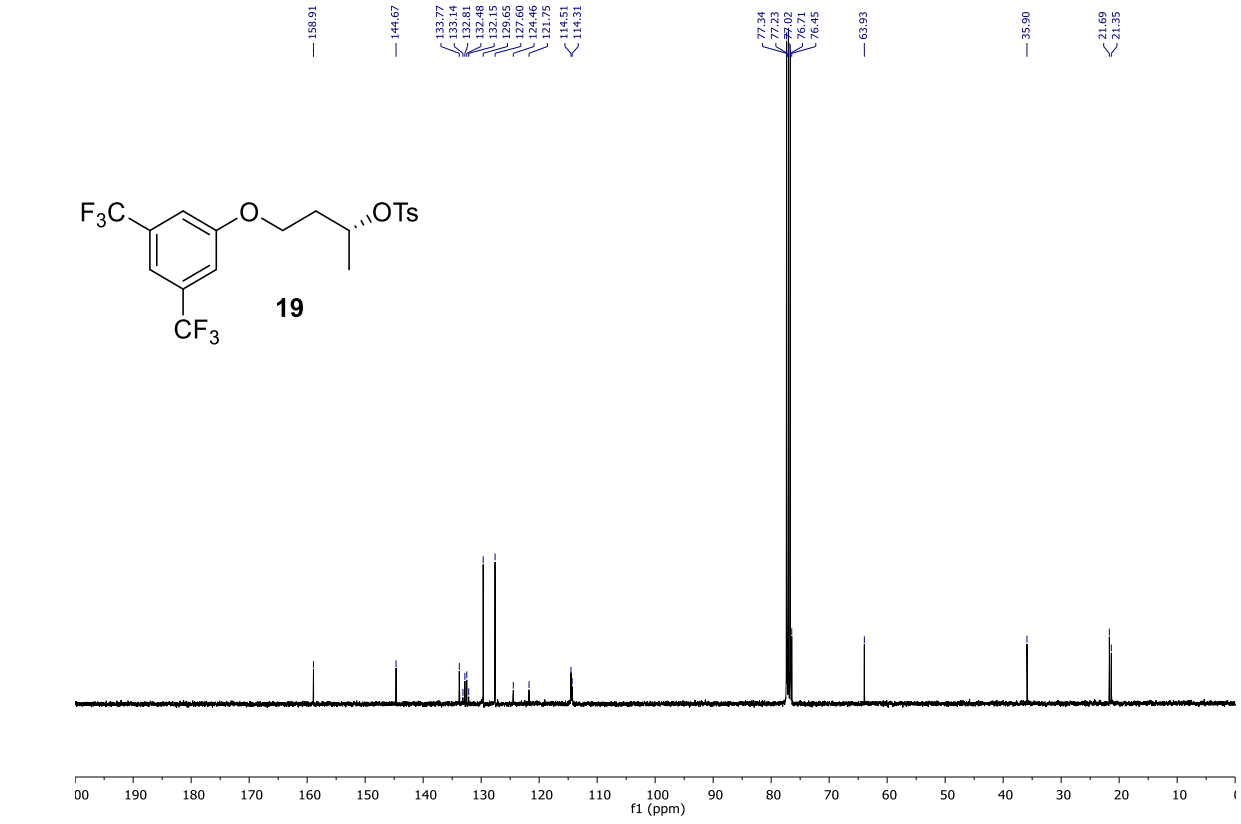

Ph
OH
16
f1 (ppm)

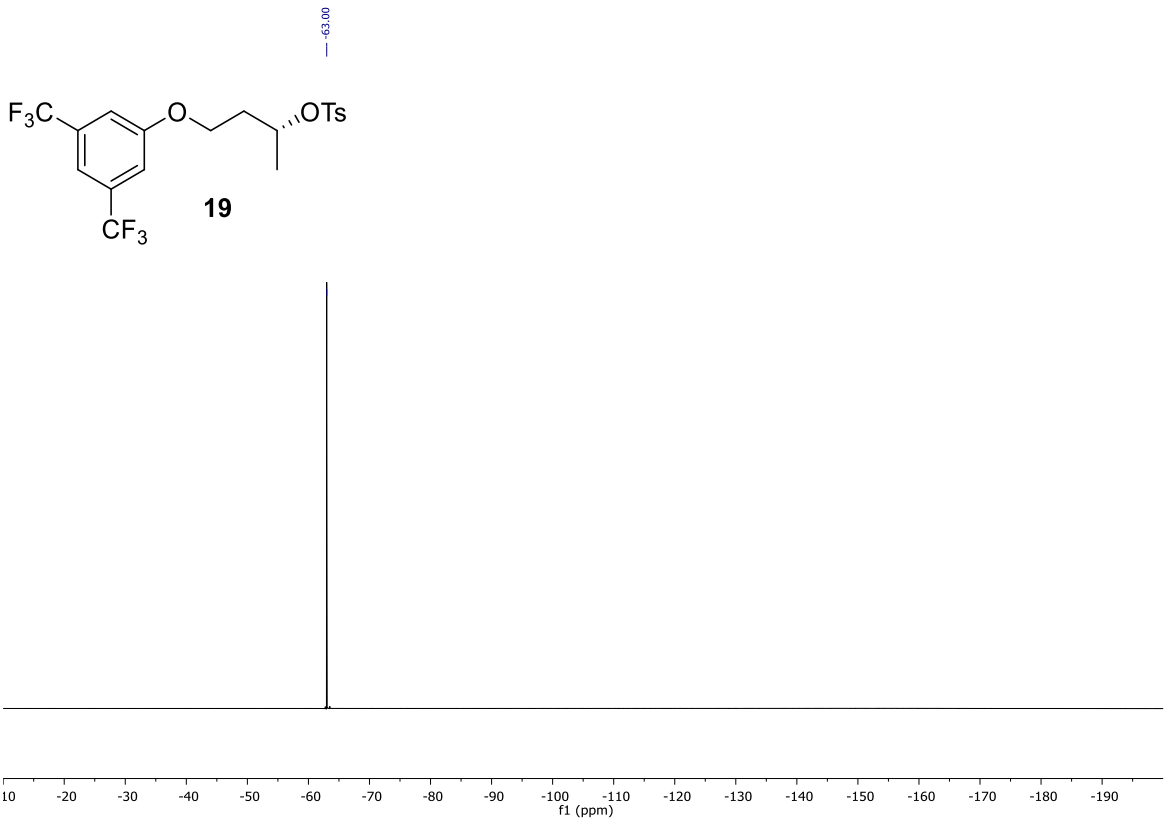


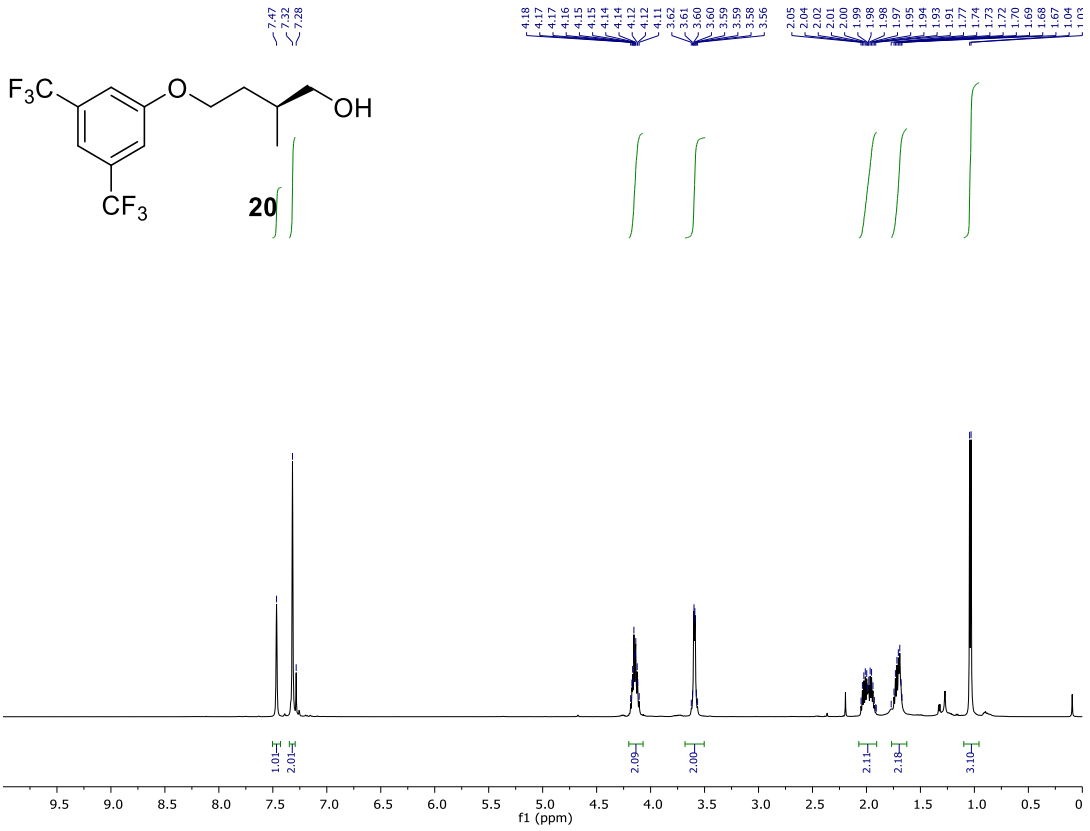


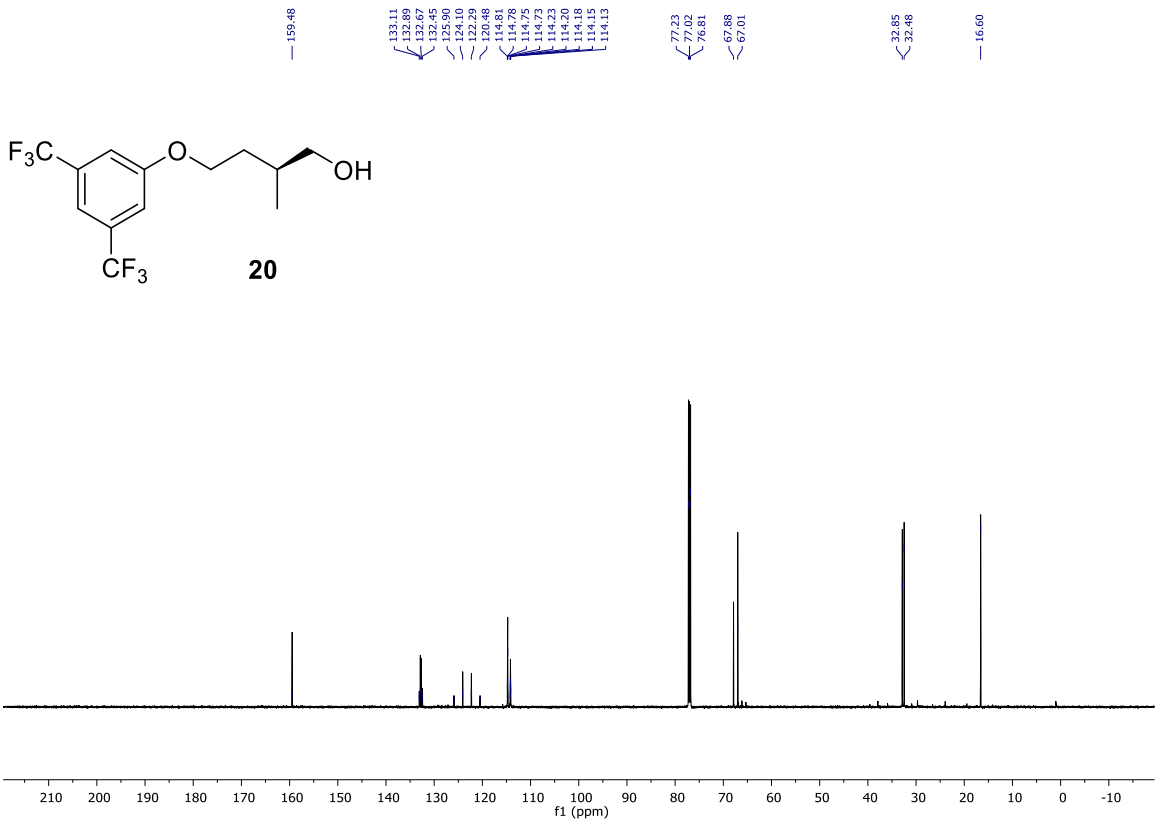
V

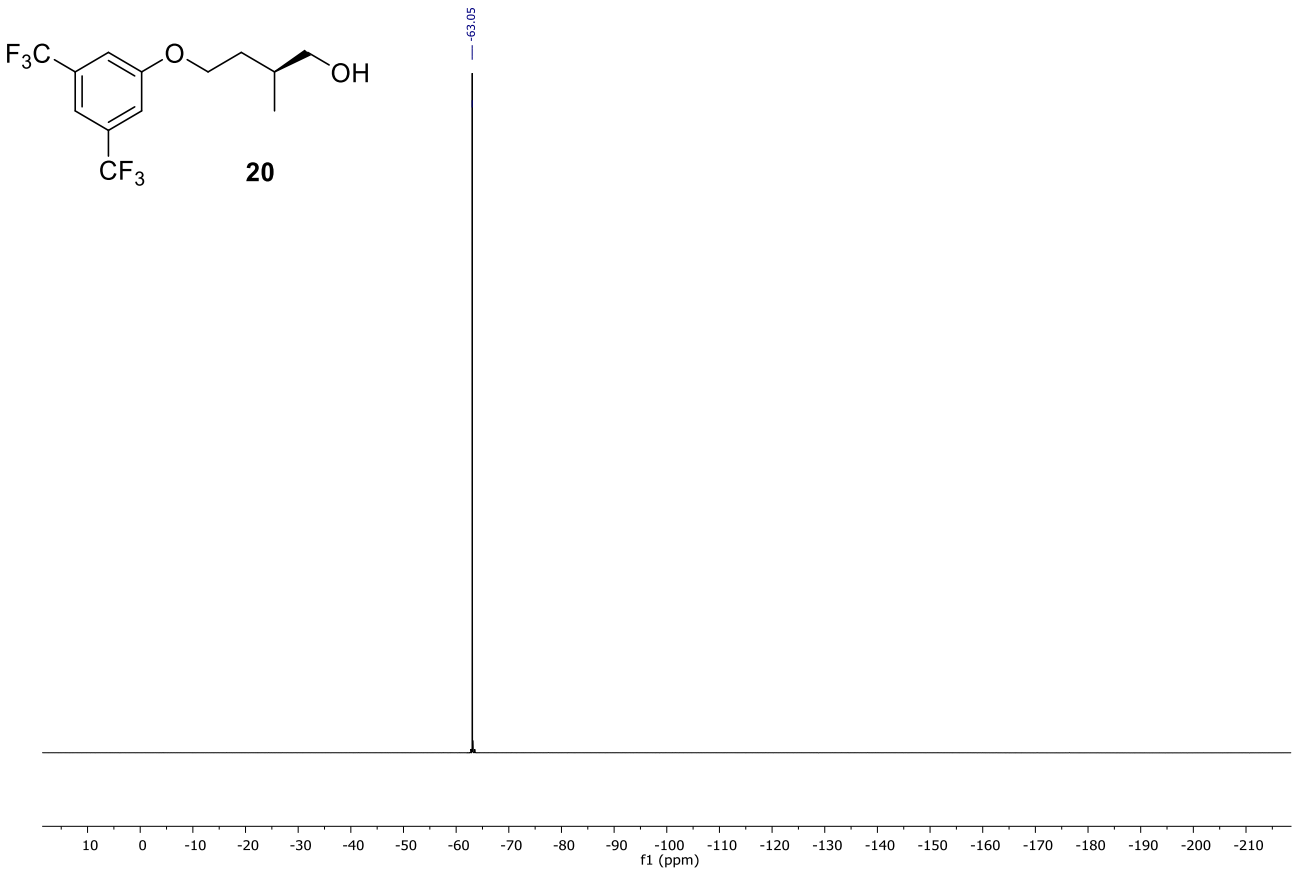

F3C
O
OTs
CF3
19
f1 (ppm)

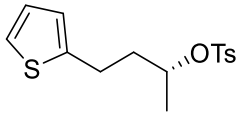

F3C
O
OTs
CF3
19
f1 (ppm)


-63.00
F3C
O
OTs
CF3
19
10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)


F3C
O
OH
CF3
20
7.47
7.32
7.28
4.18
4.17
4.17
4.16
4.15
4.15
4.14
4.14
4.12
4.12
4.11
3.62
3.61
3.60
3.60
3.59
3.59
3.58
3.56
2.05
2.04
2.02
2.01
2.00
1.99
1.98
1.98
1.97
1.95
1.94
1.93
1.91
1.77
1.74
1.73
1.72
1.70
1.69
1.68
1.67
1.04
1.01
2.01
2.09
2.00
2.11
2.18
3.10
f1 (ppm)

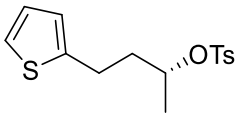

159.48
133.11
132.89
132.67
132.45
125.90
124.10
122.29
120.48
114.81
114.78
114.75
114.73
114.23
114.20
114.18
114.15
114.13
77.23
77.02
76.81
67.88
67.01
32.85
32.48
16.60
F3C
O
OH
CF3
20
f1 (ppm)


F3C
O
OH
CF3
20
-63.05
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

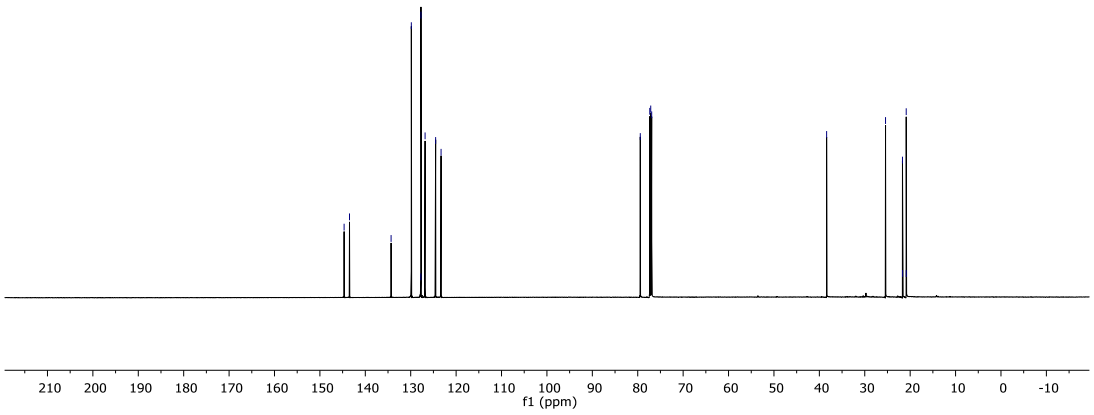

S
OTs

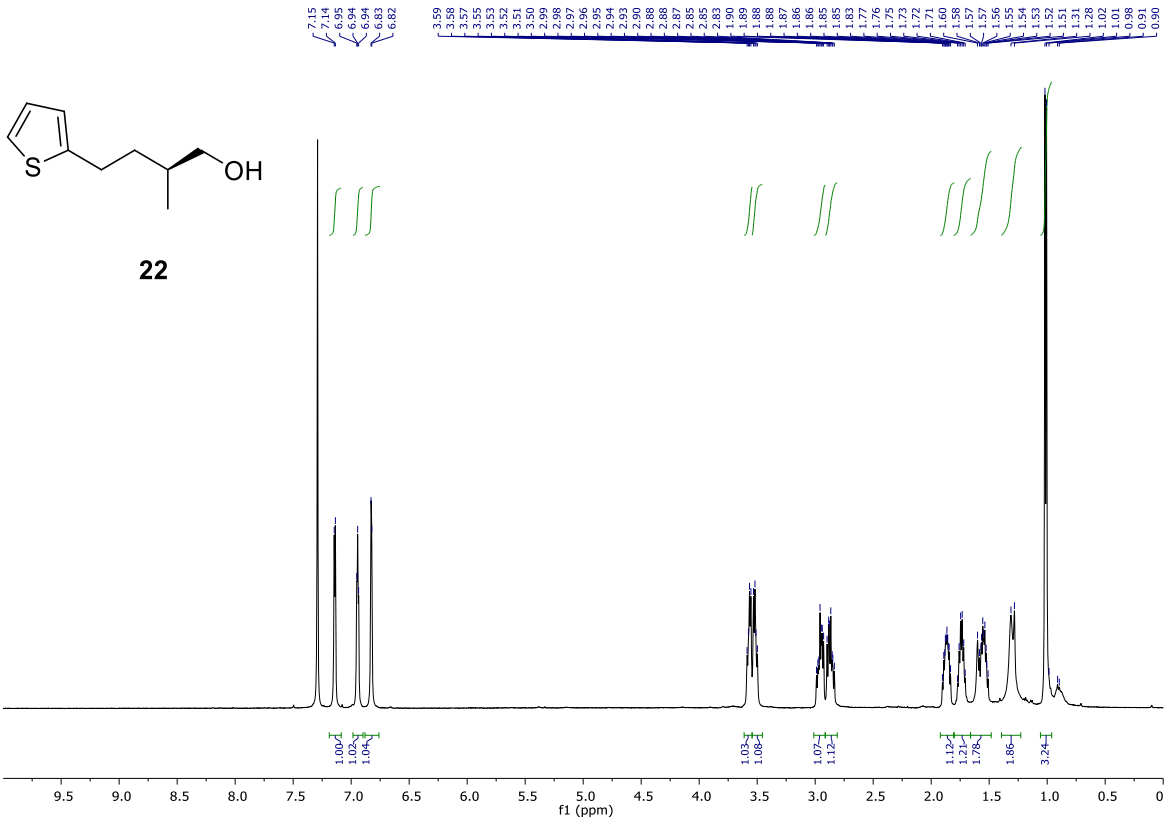
21

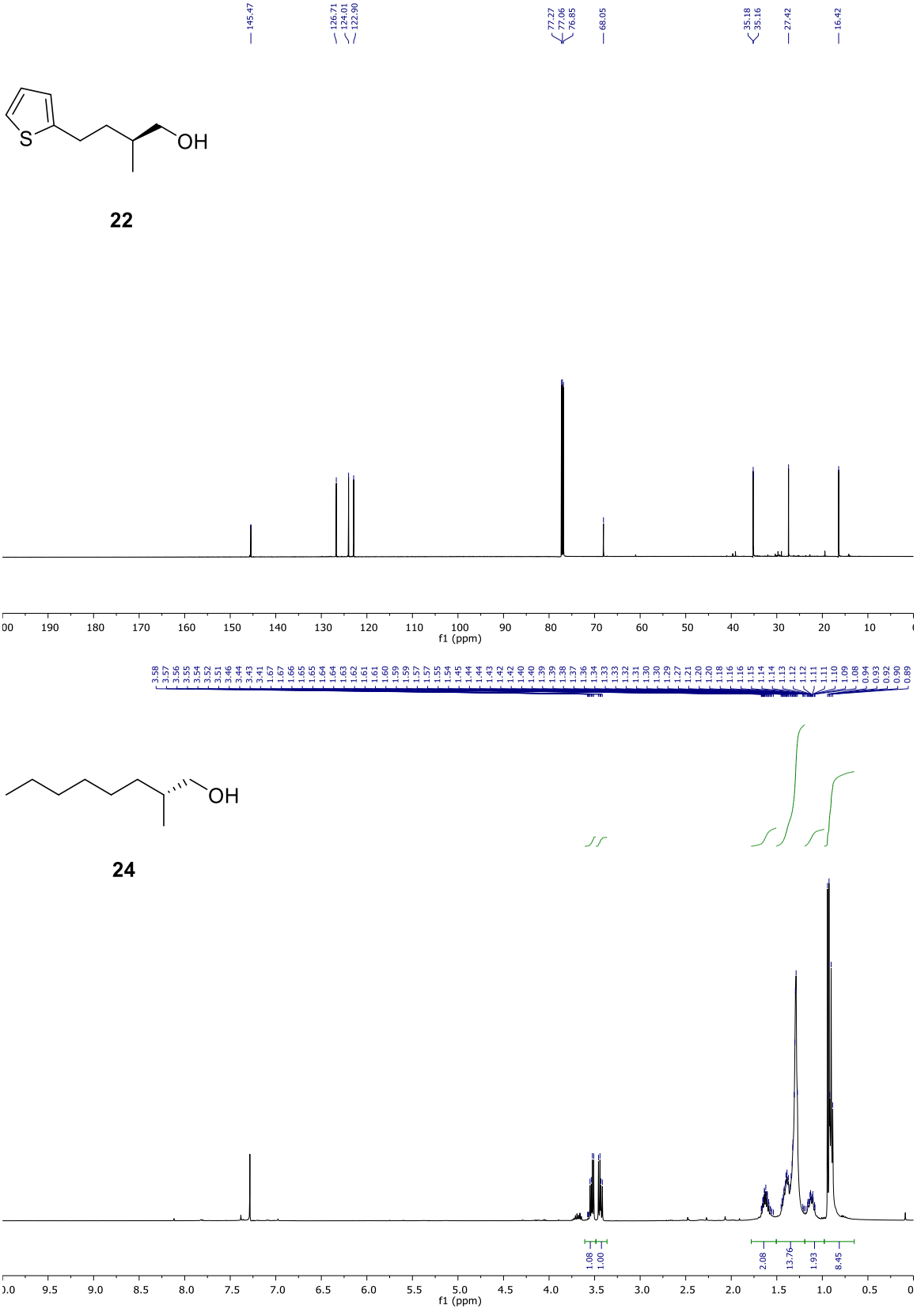
1.99
2.02
0.92
0.97
0.96
1.00
1.02
1.05
3.14
1.06
1.08
3.29
f1 (ppm)
144.67
143.48
134.32
129.86
127.77
127.74
126.83
124.51
123.31
79.44
77.35
77.14
76.93
38.40
25.42
21.69
21.68
20.87
20.85

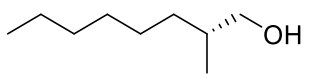

S
OTs

21


f1 (ppm)

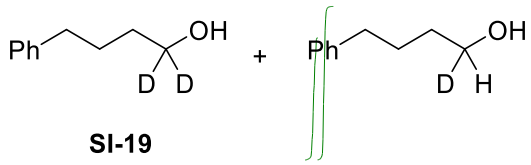

S
OH
22
f1 (ppm)


145.47
126.71
124.01
122.90
77.27
77.06
76.85
68.05
35.18
35.16
27.42
16.42
S
OH
22
f1 (ppm)
OH
24
1.08
1.00
2.08
13.76
1.93
8.45
f1 (ppm)


OH

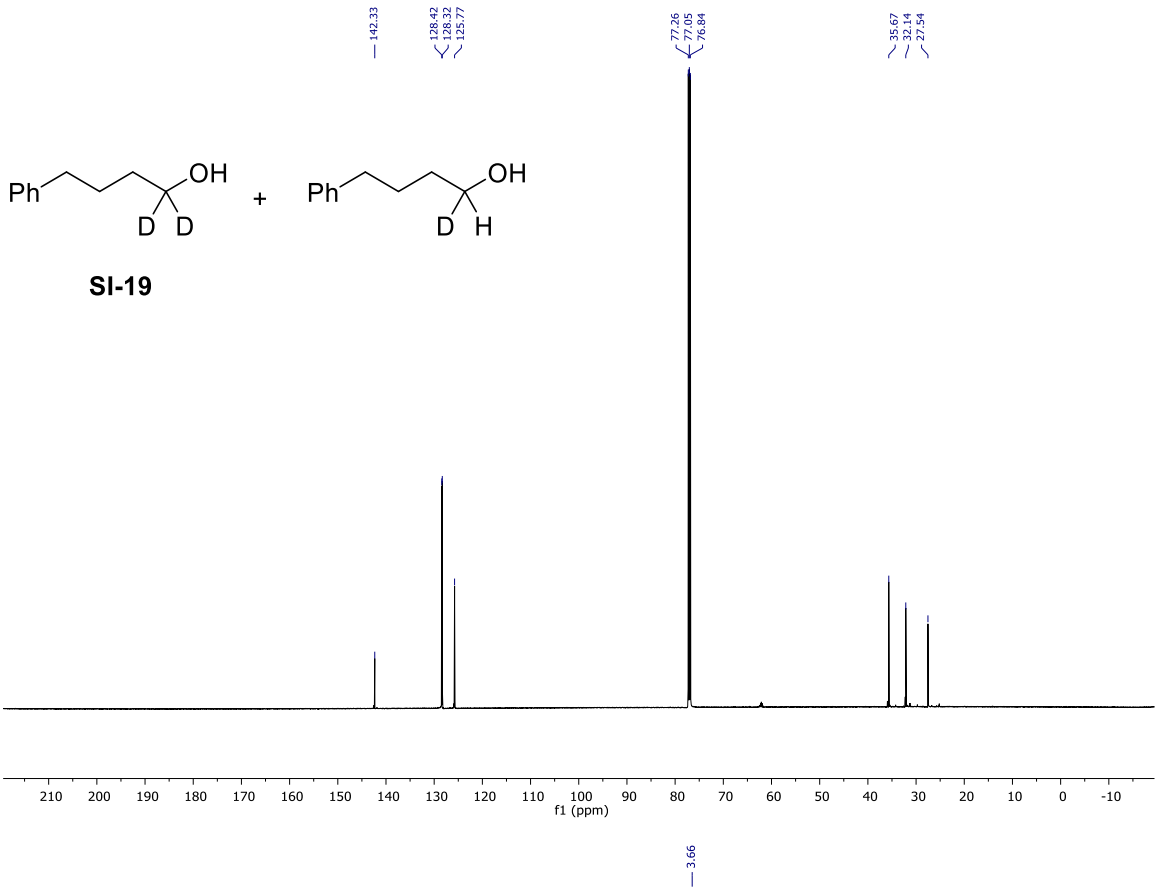
24

68.44
35.77
33.15
31.87
29.61
26.95
22.67
16.59
14.11
f1 (ppm)


Ph
OH
D D
+
Ph
OH
D H

SI-19

7.32
7.31
7.30
7.28
7.22
7.21
7.21
7.20
7.20
2.69
2.67
2.66
1.75
1.74
1.74
1.73
1.73
1.72
1.72
1.71
1.71
1.70
1.64
1.62
1.61
2.55
3.20
0.04
0.15
2.00
2.01
2.13
0.94
f1 (ppm)



SI-19

3.66

^{2}H NMR Spectrum for **SI-19**