SUPPORTING INFORMATION

The "factory in a lab": Telescoping the Matteson and Matteson-Hoppe-Aggarwal boronate chemistry under flow conditions

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1. General information

Reactions were monitored by GC-MS or GC-FID. Chemicals were purchased from Abcr, Sigma Aldrich, Fisher Scientific or TCI and were used without purification unless stated otherwise. B_2pin_2 was obtained from AllyChem and was recrystallised from pentane prior to use. HBpin was purchased from fluorochem. nBuLi was acquired from Acros (Fisher Scientific) and titrated against biphenylacetic acid three times prior to use. Bromochloromethane was purchased from Sigma Aldrich, purity > 99.5%, and after distillation stored at 4°C under light exclusion. (+)-Sparteine (97 %) was purchased from abcr and distilled over CaH_2. ^{1}H NMR spectra were recorded with a Bruker Avance-400 (400 MHz). ^{13}C NMR spectra were recorded at 101 MHz with a Bruker Avance-400. ^{1}H NMR chemical shifts are reported relative to TMS and were referenced via residual proton resonances of the corresponding deuterated solvent ($CDCl_3$: 7.26 ppm), whereas ^{13}C NMR spectra are reported relative to TMS using the carbon signals of the deuterated solvent ($CDCl_3$: 77.16 ppm). ^{1}H-NMR data are reported as following: chemical shift (δ in ppm) (multiplicitiy, coupling constant (*J*) where applicable, number of hydrogens, assigned hydrogen). Splittings for ^{1}H-NMR signals are reported with the following symbols: bs = broad singlet, s = singlet, d = doublet, t = triplet, q =quartet, qi = quintet, sxt = sextet, h = heptet, dd = doublet of doublets, dt = doublet of triplets, m = multiplet. ^{13}CNMR data are reported as follows: chemical shift, assigned carbon. COSY, HMBC and HSQC (and NOESY if necessary) experiments were conducted for full characterization. Numbering of the protons/carbons is arbitrary and does not correspond to IUPAC, whereas the naming of compounds corresponds to IUPAC.

GC/MS GC/MS analyses were carried out on with an Agilent 7890B GC with 5977B GC/MSD and Gerstel MPS Robotic XL with KAS 4C injector. Samples were analysed on an Optima 5HT column, 30 m x 250 µm i.d. x film thickness 0.25 µm). Carrier gas, He; injector temp., 60°C to 300°C at 12°C/min, splitless; temp. program: 50°C (isothermal 1 min) to 300°C, at 20 °C/min and held isothermal for 6.5 min at 300°C; FID: 300°C , H2: 30 mL/min, N2: 25 mL/min, MSD: ion source: EI 70 eV, 230 °C; detector: quadrupole, EI mass spectra were acquired over the mass range of 30 –650 amu.

HR-GC/MS analyses were carried out on a Waters GCT Premier mass spectrometer coupled with an Agilent 6890n GC with CTC CombiPAL sampler. Samples were analysed on an Optima 5HT column, 30

m x 250 µm i.d. x film thickness 0.25 µm). Carrier gas, He; injector temp. 300°C, split ratio 1:40; temp. program: 50°C (isothermal 1 min) to 300°C, at 20 °C/min and held isothermal for 6.5 min at 300°C; FID: 300°C, H2: 30 mL/min, N2: 25 mL/min, GCT-Premier: ion source: EI 70 eV, 250 °C; detector-voltage: 2500 V, EI mass spectra were acquired over the mass range of 20 –800 amu.

HR-ESI-MS analysis was performed on Waters LCT Premier mass spectrometer coupled with a Waters Alliance 2695 HPLC. The sample was dissolved in a suitable solvent (approx.. 1 mg/mL) and diluted in methanol (1:100). An aliquot of 5 µL was injected in constant flow of methanol without any HPLC column installed and data were recorded in positive or negative ion mode.

GC-O analyses were carried out with an Agilent GC 7890B chromatograph with Gerstel CIS4 Cold Injector, coupled to a Gerstel OPD 3 sniffer. Samples were analyzed on a Zebron ZB-FFAP (7KG-G009-11) column (60 m x 0.25 mm i.d. x film thickness 0.25 µm). Carrier gas, He; flow 1.4 mL/min; injector temp.: 50°C to 260 °C at 12 °C/s; split ratio 1:5; temp. program: 50 °C to 230 °C at 8 °C/min held isothermal for 22.5 min. Transfer to Gerstel ODP 3 is made through 1 m x 150 µm column without stationary phase at 280 °C.
For screening and optimization of the reactions, samples were analysed by a HP 6890 Series GC System coupled to a FID with a 7683 Series injector from Agilent Technologies with a Restek MXT®-1 column (15 m x 250 µm i.d. x film thickness 0.1 µm).
Optical rotations [α]TD were measured on Polarimeter 241 (Perkin Elmer) at a wavelength of 589 nm (sodium D line) and the concentration c is given in x 10 mg • mL^{-1} and the temperature in °C. Melting points were measured with OptiMelt (Stanford Research Systems).

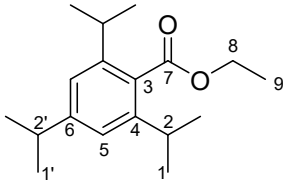
Single crystal X-ray analysis was carried out on a Rigaku XtaLab with a Dectris Pilatus3 R 200K-A detector.

Flow Equpiment

The technical drawings for the prototype development of the static mixer can be found in reference S1. Steel capillaries with an outer diameter of 1/16“ and an inner diameter of 1.0 mm consisting of stainless steel 1.4404 (316L/V4A) were purchased from TECHLAB. PTFE tubing with an outer diameter of 1/16“ and an inner diameter of 1.0 mm was purchased from Bohlender. Solutions were pumped with Fusion 4000 pumps from CHEMYX and high-pressure glass syringes from SETonic in volumes of 10, 25 and 50 mL. The reactor capillaries were placed in individual cooling/heating baths for temperature control.

2. Chemical synthesis

Ethyl 2,4,6-tri*iso*propylbenzoate (10)



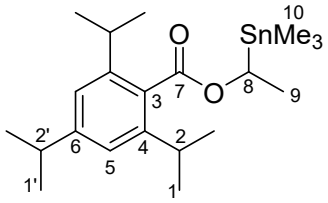
10

2,4,6-Tri*iso*propylbenzoic acid (50.6 g, 204 mmol, 1 eq), tetra-n-butylammonium hydrogen sulfate (5.53 g, 16.3 mmol, 0.08 eq) and bromoethane (111 g, 75.5 mL, 1.02 mol, 5 eq) were dissolved in $CHCl_3$ (1 L). A solution of sodium hydroxide (25.3 g, 632 mmol, 3.1 eq) in water (0.8 L) was added and the biphasic mixture was stirred vigorously (large magnetic stir bar; 1400 rpm) at rt (20°C) for 20 h. Then, layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 150 mL). The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was dissolved in *n*-pentane and the insoluble salts were filtered off. The solvent was removed under reduced pressure and remaining solvent and bromoethane were removed by stirring the residue under high vacuum to afford ethyl 2,4,6-tri*iso*propylbenzoate **10** (55.66 g, 201.4 mmol; 98.8 %) as a colourless yellowish oil.

R_f = 0.50 (PE/EtOAc = 9:1)**; ^{1}H-NMR** ($CDCl_3$, 400 MHz): δ = 7.01 (s, 2H, H_5), 4.38 (q, ^2J = 7.1 Hz, 2H, H_8), 2.89 (hept, ^2J = 6.9 Hz, 1H, $H_{2'}$), 2.87 (hept, ^2J = 6.9 Hz, 2H, H_2), 1.37 (t, ^2J = 7.1 Hz, 3H, H_9), 1.25 (d, ^2J = 6.8 Hz, 12H, H_1), 1.24 (d, ^2J = 6.9 Hz, 6H, $H_{1'}$) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): δ = 171.0 (C_7), 150.2 (C_6), 144.9 (C_4), 130.8 (C_3), 121.0 (C_5), 60.9 (C_8), 34.6 ($C_{2'}$), 31.6 (C_2), 24.3 (C_1), 24.1 ($C_{1'}$), 14.4 (C_9) ppm.

Spectral data are in accordance with those reported in the literature.[S1]

1-(Trimethylstannyl)ethyl 2,4,6-tri*iso*propylbenzoate (*rac*)-6



(*rac*)-**6**

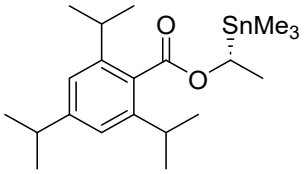
In a flame dried 1 L Schlenk flask flushed with argon, ethyl 2,4,6-tri*iso*propylbenzoate **S1** (35.0 g, 36.7 mL, 127 mmol, 1 eq) and freshly distilled TMEDA (19.1 g, 24.7 mL, 165 mmol, 1.3 eq) were dissolved in dry Et_2O (350 mL). The solution was cooled to -78 °C (slightly yellow solution) and *sec*-BuLi (127 mL, 1.3 M, 165 mmol, 1.3 eq) was added dropwise at a rate of 1 mL/min (colour change to deep purple/brown) and the reaction mixture was stirred for 2 h at this temperature. Then a freshly prepared solution of Me_3SnCl (32.8 g, 165 mmol, 1.3 eq) in dry Et_2O (100 mL) was added dropwise over a period of 1 h (colour change to colourless/pale yellow). After the addition the solution was stirred for 1 h at -78 °C and then slowly warmed up to rt. After 30 min at rt, H_3PO_4 (aq. 5 %, 250 mL) was added and the mixture was stirred for 30 min. The aqueous layer was extracted with Et_2O (3 × 200 mL). The organic extracts were combined, dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield a colourless, slightly yellow oil. The crude material was recrystallised as follows: a round bottom flask containing the crude material in MeOH (4 mL/g) with an attached condenser was brought to reflux and

the solution was allowed to slowly cool to room temperature. Since no crystallisation was observed at rt, the flask was cooled to 4 °C for a couple of hours and then kept at -20 °C overnight after which time crystrallization had occurred. The solid was then filtered and washed with MeOH (-20 °C) to remove yellow impurities and recrystallised a second time by slowly cooling the refluxing methanolic solution to rt. 1-(Trimethylstannyl)ethyl 2,4,6-tri*iso*propylbenzoate (*rac*)-**6** (41.9 g, 95.4 mmol; 75 %) was collected as a colourless solid.

R_f = 0.58 (PE/EtOAc = 9:1)**; ^{1}H-NMR** ($CDCl_3$, 400 MHz): 6.99 (s, 2H, H_5), 5.08 – 5.00 (m, 1H, H_8)), 2.93 – 2.80 (m, 3H, $H_{2,2'}$), 1.59 (d, *J* = 7.6 Hz, 3H, H_9), 1.24 (d, *J* = 6.9 Hz, 18H, $H_{1,1'}$), 0.18 (s, d, *J* = 54.1 Hz, 51.7 Hz, 9H, H_{10}) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): 171.4 (C_7), 150.1 (C_6), 145.0 (C_4), 130.9 (C_3), 120.9 (C_5), 67.2 (C_8), 34.5 ($C_{2'}$), 31.5 (C_2), 24.5 ($C_{1'}$), 24.2 (C_1), 24.1 (C_1), 19.4 (C_9), -9.8 (C_{10}) ppm.

Spectroscopic data are in accordance with those reported in the literature.[S1]

(*R*)-1-(Trimethylstannyl)ethyl 2,4,6-tri*iso*propylbenzoate [(*R*)-6]



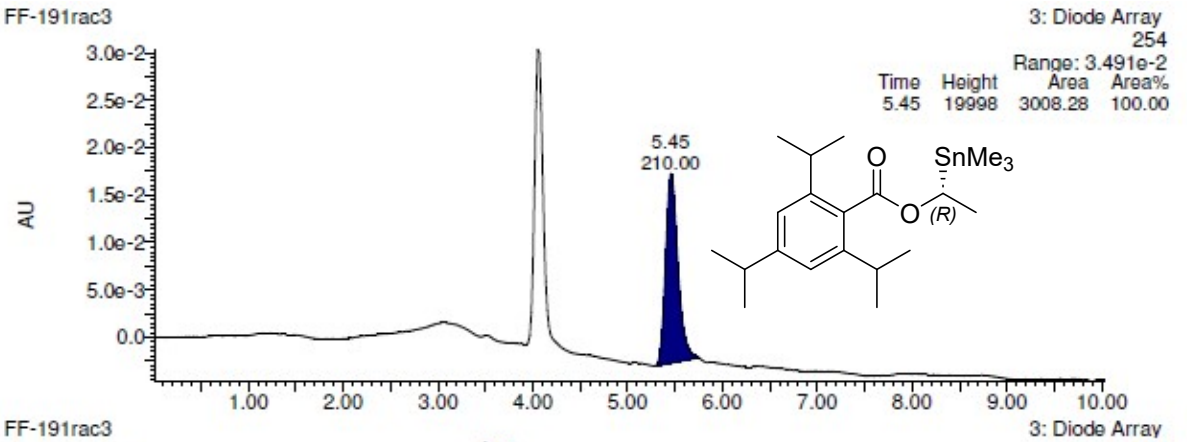
(*R*)-**6**

In a flame dried 500 mL Schlenk flask filled with argon, ethyl 2,4,6-triisopropylbenzoate **S1** (8.80 g, 9.23 mL, 31.8 mmol, 1 eq) and (+)-sparteine (9.5 mL, 41.4 mmol, 1.3 eq) were dissolved in dry Et_2O (175 mL). The solution was cooled to -78 °C (slightly yellow solution) and *sec*-BuLi (31.8 mL, 1.3 M, 41.4 mmol, 1.3 eq) was added dropwise at a rate of 0.5 mL/min (colour change to red/brown). The solution was then stirred for 3.5 h at this temperature. A freshly prepared solution of Me_3SnCl (8.25 g, 41.4 mmol, 1.3 eq) in dry Et_2O (41 mL) was added dropwise at a rate of 1 mL/min (colour change to colourless/pale yellow). After addition, the solution was stirred for 1 h at -78 °C and then slowly warmed up to rt. After 30 min at rt, H_3PO_4 (aq. 5 %, 100 mL) was added and the mixture was stirred for 30 min. The layers were separated and the organic layer was washed with H_3PO_4 (aq. 5 %, 3 × 100 mL). The combined aqueous layers were extracted with Et_2O (3 × 100 mL). The organic phases were combined, dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield a pale yellow oil. After cooling crystals formed. The crude material was then recrystallised as follows: a round bottom flask containing the crude material in MeOH (3.5 mL/g) with an attached condenser was brought to reflux and the solution was allowed to slowly cool to room temperature. After the first crystals had formed, the flask was cooled at 4 °C for a couple of hours and at -20 °C overnight. Then, the crystals were filtered and washed with MeOH (-20 °C) to yield (*R*)-1-(trimethylstannyl)ethyl 2,4,6-triisopropylbenzoate (*R*)-**6** (11.7 g, 26.6 mmol, 84 %) as colourless needles. A second recrystallisation step yielded the product (*R*)-**6** (9.34 g, 21.3 mmol;. 67 %, e.r = 99.9 : 0.1) as colourless needles.

R_f = 0.58 (PE/EtOAc = 9:1)**;** $[\alpha]_D^{24} = -36.8^\circ$ (c = 1.00, $CHCl_3$); **^{1}H-NMR** ($CDCl_3$, 400 MHz): 6.99 (s, 2H), 5.08 – 5.00 (m, 1H), 2.93 – 2.81, 1.59 (d, *J* = 7.6 Hz, 3H), 1.24 (d, *J* = 6.9 Hz, 18H), 0.18 (s, d, *J* = 54.1 Hz, *J* = 51.8 Hz, 3H) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): 171.4, 150.1, 145.0, 130.9, 120.9, 67.2, 34.5, 31.5, 24.5, 24.2, 24.1, 19.4,- 9.8 ppm.

Spectral data are in accordance with those reported in the literature.[S1]

Chiral HPLC: Daicel Chiralpak-IB column (25 cm), hexane, 0.9 mL/min, 30 °C, 254 nm, t_R = 4.05 min (*S*), 5.45 min (*R*), e.e. = 99.9 %.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2.0e-2
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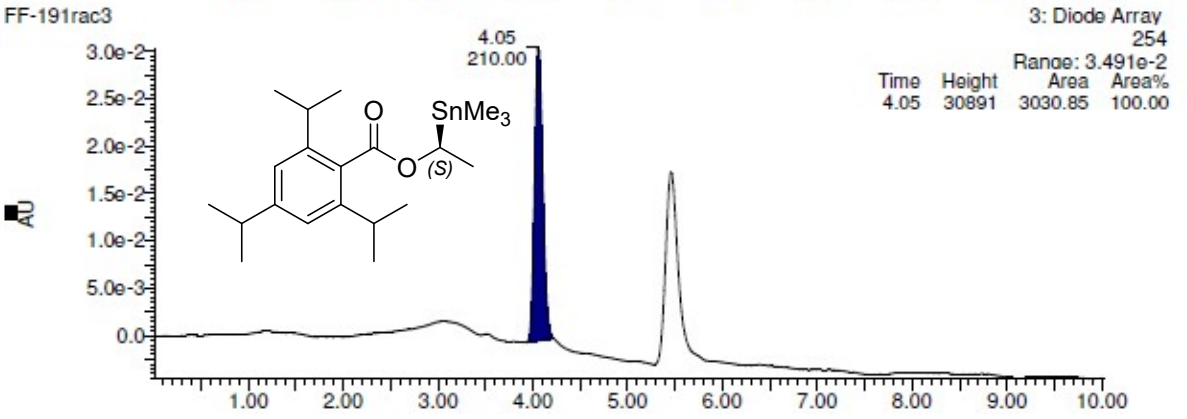
SnMe3
O (R)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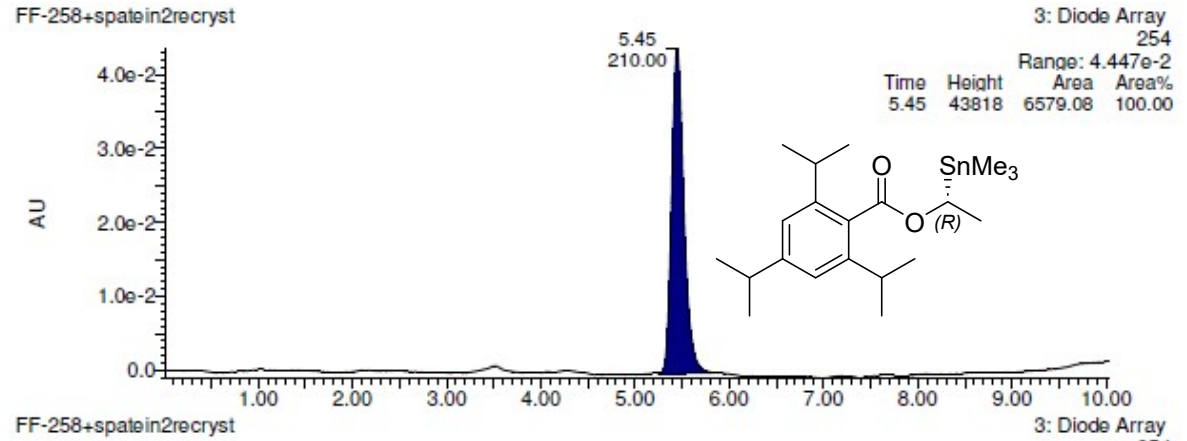
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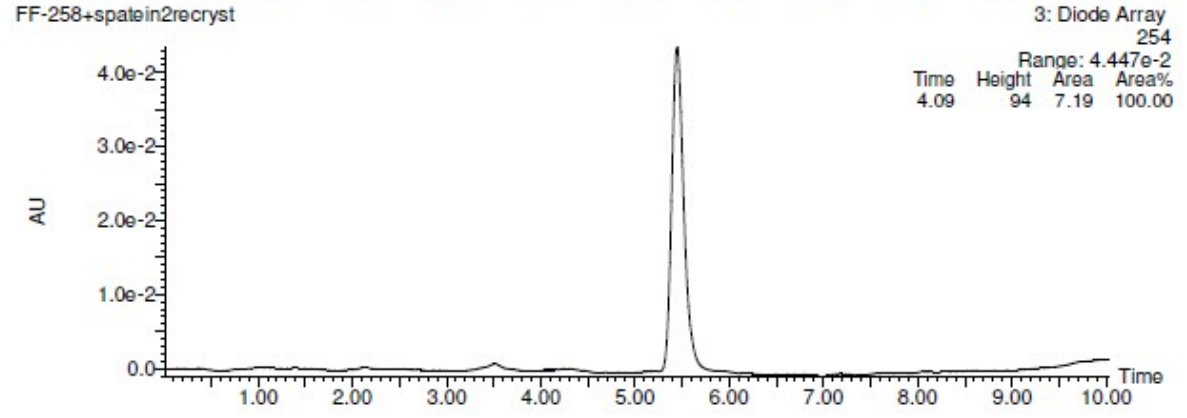
O (R)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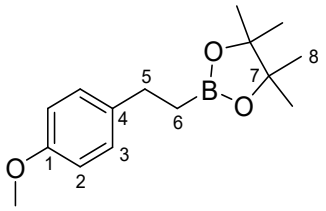
1.00 2.00 3.00 4.00 5.00 6.00 7.00 8.00 9.00 10.00
Time

2-(4-Methoxyphenethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3a)



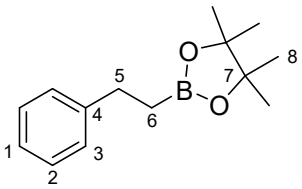
3a

To a flame dried flask filled with argon was added dichloro(p-cymene)ruthenium(II) dimer (57.1 mg, 0.093 mmol, 0.05 mol%). 4-Methoxystyrene (25.0 g, 186.3 mmol, 1 eq) and 4,4,5,5,-tetramethyl-1,3,2-dioxaborolane (27.1 mL, 186.3 mmol, 1 eq) were added to the flask at 0 °C. The reaction mixture was then stirred at rt for 72 h. The mixture was then filtered through a pad of Celite® with Et_2O. The organic phase was washed with a sat. $NaHCO_3$ solution, water and brine, dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by flash column chromatography (silica, PE/EtOAc = 20:1) afforded 2-(4-methoxyphenethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**3a**) as a colourless liquid (42.4 g, 162 mmol; 87 %).

R_f: 0.29 (PE/EtOAc = 10:1); **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.13 (d, *J* = 8.6 Hz, 2H, H_3), 6.81 (d, *J* = 8.6 Hz, 2H, H_2), 3.78 (s, 3H, H_{OMe}), 2.69 (t, *J* = 8.1 Hz, 2H, H_5), 1.22(s, 12H, H_8), 1.11 (t, *J* = 8.2 Hz, 2H, H_6) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): 157.7 (C_1), 136.7 (C_4), 129.0 (C_3), 113.7 (C_2), 83.2 (C_7), 55.4 (C_{OMe}), 29.2 (C_8), 25.0 (C_5) ppm (the carbon attached to the boron atom was not observed due to quadrupolar relaxation).

Spectroscopic data are in accordance with those reported in the literature.[S2]

4,4,5,5-Tetramethyl-2-phenethyl-1,3,2-dioxaborolane (3b)



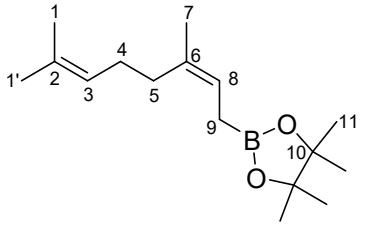
3b

To a flame dried flask filled with argon was added Dichloro(p-cymene)ruthenium(II) dimer (26.7 mg, 0.044 mmol, 0.05 mol%). Styrene (10 mL, 87.3 mmol, 1 eq) and 4,4,5,5,-tetramethyl-1,3,2-dioxaborolane (13.1 mL, 87.3 mmol, 1 eq) were added to the flask at 0 °C. The reaction mixture was then stirred at rt for 24 h. The mixture was then filtered through a pad of Celite® and washed with Et_2O. The organic phase was washed with bicarbonate, water and brine, dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by flash column chromatography (silica gel, PE/EtOAc = 50:1) afforded the 4,4,5,5-tetramethyl-2-phenethyl-1,3,2-dioxaborolane (**3b**) (16.2 g, 69.8 mmol; 80 %) as a colourless solid.

R_f: 0.45 (PE/EtOAc = 9:1); **m.p.** = 32-33 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.23 – 7.20 (m, 4H, $H_{2,3}$), 7.17 – 7.13 (m, 1H, H_1), 2.75 (t, *J* = 8.2 Hz, 2H, H_5), 1.22 (s, 12H, H_8), 1.14 (t, *J* = 8.2 Hz, 2H, H_6) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): 144.6 (C_4), 128.3 (C_2), 128.1 (C_3), 125.6 (C_1), 83.2 (C_7), 30.1 (C_5), 25.0 (C_8) ppm (the carbon attached to the boron was not observed due to quadrupolar relaxation).

Spectral data are in accordance with those reported in the literature.[S2]

(*Z*)-2-(3,7-Dimethylocta-2,6-dien-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3c)



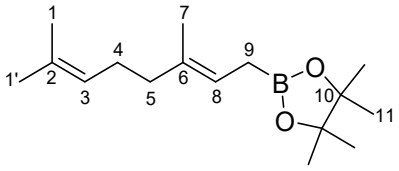
3c

In a flame dried Schlenk flask, $Ni(COD)_2$ (420 mg, 1.53 mmol, 5 mol%) and tricyclohexylphosphine (429 mg, 1.53 mmol, 5 mol%) were weighed in a glove box followed by addition of neryl acetate (6.60 mL, 30.6 mmol, 1 eq), bis(pinacolato)diborane (7.76 g, 30.6 mmol, 1 eq) and and dry EtOAc (57 mL). The mixture was stirred at 60 °C for 18 h under inert atmosphere. The crude mixture was filtered through a short pad of Celite® (10 mm) and silica gel (10 mm) (eluating with PE/EtOAc 10:1), and the solvent was evaporated under reduced pressure to yield a slightly green liquid. Purification by flash column chromatography (silica gel, PE/EtOAc = 50:1) afforded (Z)-2-(3,7-dimethylocta-2,6-dien-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**3c**) as a colourless liquid (5.60 g, 21.2 mmol; 69 %).

R_f: 0.50 (PE/EtOAc = 10:1); **^{1}H-NMR** ($CDCl_3$, 400 MHz): 5.24 (dt, *J* = 7.7, 1.2 Hz, 1H, H_8), 5.15 – 5.10 (m, 1H, H_3), 2.06 – 1.99 (m, 4H, $H_{4,5}$), 1.69 (d, *J* = 1.3 Hz, 3H, H_7), 1.68 (s, 3H, $H_{1'}$) 1.62 – 1.61 (m, 5H, $H_{1,9}$), 1.24 (s, 12H, H_{11}) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz):135.4 (C_6), 131.5 (C_2), 124.7 (C_3), 119.2 (C_8), 83.2 (C_{10}), 32.0 (C_5), 26.6 (C_4), 25.8 ($C_{1'}$), 24.9 (C_{11}), 23.6 (C_7), 17.8 (C_1) ppm (the carbon attached to the boron atom was not observed due to quadrupolar relaxation).

Spectroscopic data are in accordance with those reported in the literature.[S3]

(*E*)-2-(3,7-dimethylocta-2,6-dien-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3d)



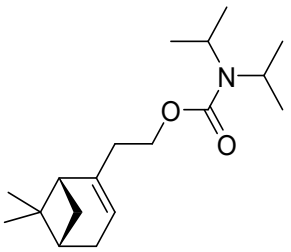
3d

In a Schlenk flask, $Ni(COD)_2$ (281 mg, 1.02 mmol, 5 mol%) and tricyclohexylphosphine (286 mg, 1.02 mmol, 5 mol%) were weighed in a glove box followed by addition of geranyl acetate (4.37 mL, 20.4 mmol, 1 eq), bis(pinacolato)diborane (5.44 g, 21.4 mmol, 1 eq) and and dry EtOAc (40 mL). The mixture was stirred at 60 °C for 18 h under inert atmosphere. The crude mixture was filtered through a short pad of Celite® (10 mm) and silica gel (10 mm) (eluating with PE/EtOAc 10:1), and the solvent was evaporated under reduced pressure to yield a slightly green liquid. Purification by flash column chromatography (silica gel, PE/EtOAc = 50:1) afforded (*E*)-2-(3,7-dimethylocta-2,6-dien-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**3d**) as a colourless liquid (2.27 g, 8.59 mmol; 42 %).

R_f: 0.49 (PE/EtOAc = 10:1); **^{1}H-NMR** ($CDCl_3$, 400 MHz): 5.27 – 5.23 (m, 1H, H_8), 5.12 – 5.08 (m, 1H, H_3), 2.07 – 1.99 (m, 4H, $H_{4,5}$), 1.67 (d, *J* = 1.0 Hz, 3H, $H_{1'}$), 1.61 – 1.58 (m, 8H, $H_{1,7,9}$), 1.24 (s, 12H, H_{11}) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): 135.3 (C_6), 131.3 (C_2), 124.6 (C_3), 118.7 (C_8), 83.2 (C_{10}), 39.9 (C_5), 27.0 (C_4), 25.9 ($C_{1'}$), 24.9 (C_{11}), 17.8 (C_1), 16.0 (C_7) ppm (the carbon attached to the boron atom was not observed due to quadrupolar relaxation).

Spectroscopic data are in accordance with those reported in the literature.[S4]

2-[(1*R*,5*S*)-6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-yl]ethyl di*iso*propylcarbamate (S1)

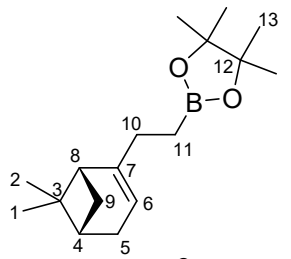


S1

To a flame-dried round-bottomed flask attached with a reflux condenser and filled with argon was added diisopropylcarbamic chloride (8.27 g, 50.5 mmol, 1.2 eq), triethylamine (5.54 g, 54.7 mmol, 1.3 eq), 2-((1R,5S)-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)ethan-1-ol (7.00 g , 42.1 mmol, 1 eq) and Toluol (40 mL). The reaction mixture was heated at reflux for 18h (the colour of the reaction mixture was yellow to orange with a gel-like precipitate). After allowing to cool to room temperature, water was added and the mixture was extracted three times with EtOAc. The combined organic layers were washed with aq HCl (1 M), brine, dried over anhydrous magnesium sulfate, filtered and concentrated *in vacuo* to yield a yellow oil. Column chromatography (PE/EtOAc = 25:1) yielded 2-((1R,5S)-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)ethyl diisopropylcarbamate (**S1**) as a colourless pale yellow oil (11.9 g, 40.5 mmol; 96 %).

R_f = 0.42 (PE/EtOAc 10:1); **^{1}H-NMR** ($CDCl_3$, 400 MHz): 5.30 – 5.27 (m, 1H), 4.08 (t, *J* = 6.9 Hz, 2H), 3.89 (bs,2H), 2.35 (dt, *J* = 8.5 Hz, 5.6 Hz, 1H), 2.31 – 2.14 (m, 4H), 2.08 – 2.04 (m, 2H), 1.26 (s, 3H), 1.88 (dd, *J* = 6.8 Hz, 0.8 Hz, 12H), 1.14 (d, *J* = 8.5 Hz, 1H), 0.82 (s, 3H) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): 155.8, 144.6, 118.6, 62.8, 45.8 (bs 45.9), 40.9, 38.1, 36.7, 31.7, 31.5, 26.4, 21.2 (bs 21.1) ppm.

2-{2-[(1*R*,5*S*)-6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-yl]ethyl]}-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3e)



3e

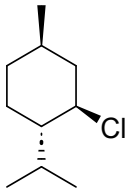
To a flame dried 500 mL Schlenk flask filled with argon was added 2-((1*R*,5*S*)-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)ethyl di*iso*propylcarbamate (11.50 g, 39.2 mmol, 1 eq), freshly distilled TMEDA (5.92 g, 7.68 mL, 51.0 mmol, 1.3 eq) and dry Et_2O (100 mL). The solution was cooled to -78 °C and *sec*-butyllithium (39.19 mL, 1.3 molar, 50.95 mmol, 1.3 eq) was added dropwise (1mL/min) (the solution turns yellow upon addition of *sec*-BuLi). Stirring was continued at this temperature for 2 h and a solution of 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (10.03 g, 11.4 mL, 78.38 mmol, 2.0 eq) in dry Et_2O (24 mL) was added dropwise (1 mL/min). The solution was added until the yellow coulor had disappeared and the solution was stirred for 2.5 h at -78 °C before warming up to rt with a water bath. Stirring was continued for 18 h at rt and a white precipitate appeared. The mixture was cooled to 0°C and 100 mL of a 1 M solution of KH_2PO_4 was added carefully (gas evolution). The organic layer was cut off and the aqueous layer was extracted with MTBE (3x), dried over $MgSO_4$,

filtrated and concentrated *in vacuo*. Purification by flash column chromatography (silica gel, PE/EtOAc = 50:1) afforded 2-(2-((1R,5S)-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)ethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**3e**) as a colourless liquid (3.50 g, 12.7 mmol; 32 %).

R_f = 0.25 (PE/EtOAc 25:1); $[\alpha]_D^{28} =$ -23.9° (c = 1.00, CH_2Cl_2); **^{1}H-NMR** ($CDCl_3$, 400 MHz): 5.17 – 5.14 (m, 1H, H_6), 2.32 (dt, *J* = 8.4 Hz, 5.6 Hz, 1H, H_9), 2.26 – 2.11 (m, 2H, H_5), 2.10 – 1.97 (m, 4H, $H_{4,8,10}$), 1.25 (s, 3H, H_2), 1.23 (s, 12H, H_{13}), 1.14 (d, *J* = 8.4 Hz, 1H, H_9), 0.88 – 0.82 (m, 2H, H_{11}), 0.81 (s, 3H, H_1) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): 150.3 (C_7), 114.4 (C_6), 83.1 (C_{12}), 46.1 (C_8), 41.1 (C_4), 38.1 (C_3), 31.7 (C_9), 31.3 (C_5), 30.9 (C_{10}), 26.5 (C_2), 25.0 (C_{13}), 24.9 (C_{13}), 21.3 (C_1) ppm (the carbon attached to the boron atom was not observed due to quadrupolar relaxation).

Spectroscopic data are in accordance with those reported in the literature.[S5]

(1*S*,2*R*,4*R*)-2-Chloro-1-isopropyl-4-methylcyclohexane (S2)



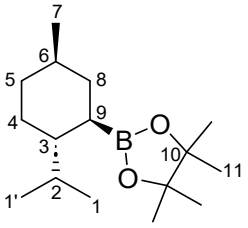
S2

"Lucas reagent" was prepared by dissolving anhydrous $ZnCl_2$ (497 g, 3.64 mol, 3.3 eq) in 340 mL of 37% aqueous HCl acid with cooling. Then (-)-menthol (172.6 g, 1.1 mol, 1 eq.) was added to the "Lucas reagent". The mixture was stirred vigorously at 35-40 °C for 5h. The mixture was then cooled and extracted with 1.5 L of petroleum ether. The organic layer was washed with water and then with concentrated sulfuric acid. The petroleum ether solution was then washed five times with water and was dried with magnesium sulfate. Vacuum distillation (85°C, 12 mbar) yielded the title compound **S2** as a coulourless liquid (160.4 g, 0.92 mol, dr >99:1; 83 %, 91 % GC-purity).

$[\alpha]_D^{20} = -46.8°$ (c = 1.00, EtOH); **^{1}H-NMR** ($CDCl_3$, 400 MHz): 3.78 (dt, *J* = 11.1 Hz, *J* = 4.1 Hz, 1H), 2.35 (dsept, *J* = 7.0 Hz, ^2J = 2.9 Hz, 1H), 2.25 – 2.20 (m, 1H), 1.75 – 1.68 (m, 2H), 1.48 – 1.34 (m, 3H), 1.08 – 0.96 (m,2H), 0.93 – 0.90 (m, 6H), 0.77 (d, *J* = 7.0 Hz,3H), ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): 64.1, 50.6, 46.9, 34.4, 33.5, 27.2, 24.4, 22.1, 21.1, 15.3 ppm.

Spectroscopic data are in accordance with those reported in the literature.[S6]

2-[(1*R*,2*R*,5*R*)-2-Isopropyl-5-methylcyclohexyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3f)



3f

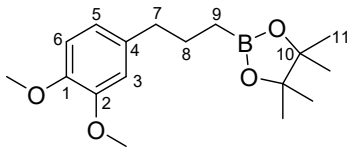
A flame-dried 500 mL Schlenk flask was flushed with argon and filled with CuCl (346 mg, 3.49 mmol, 0.1 eq) and XantPhos (2.02 g, 3.49 mmol, 0.1 rq). Subsequently, dry THF (30 mL) and B_2pin_2 (17.8 g,

69.9 mmol, 2 eq) were added. The flask was put into an ice bath and 70 mL of a 1 M KO*t*Bu solution (7.84 g, 69.9 mmol in THF, 2 eq) was added quickly via syringe (reaction turned from slightly milky/yellow to dark brown) at 0°C. All the reagents were allowed to mix up at room temperature within 5 min, the flask was then put back into the ice bath and (1*S*,2*R*,4*R*)-2-chloro-1-isopropyl-4-methylcyclohexane (6.71 g, 7.17 mL, 91% Wt, 34.9 mmol, 1 eq) was added dropwise via syringe over 10 min. The brown suspension was vigorously stirred at room temperature for 48 h. The suspension was diluted with pentane and filtered through a plug of celite followed by a second filtration through silica gel eluating with pentane/Et_2O (10:1). Evaporation of the solvent yielded a colourless oil. Column chromatography (pentane/Et_2O 50:1 to 35:1) yielded 2-((1*R*,2*R*,5*R*)-2-isopropyl-5-methylcyclohexyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**3f**) (6.60 g, 24.8 mmol; 71 %) as a colourless oil (single diastereomer).

R_f: 0.57 (PE/EtOAc = 10:1); $[\alpha]_D^{28} =$ -23.1° (c = 1.00, CH_2Cl_2); **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ = 1.74 – 1.57 (m, 4H, $H_{2,4,5,8}$), 1.33 – 1.19 (m, 14 H, $H_{4,6,11}$), 1.00 -0.87 (m overlapping with d, 0.89, ^2J = 6.9 Hz, 7H, $H_{1(d),4,5,8,9}$), 0.84 (d, ^2J = 6.5 Hz, 3H, H_7), 0.76 (d, ^2J = 6.9 Hz, 3H, $H_{1'}$) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): δ = 82.8 (C_{10}), 43.9 (C_3), 37.3 (C_5), 35.5 (C_8), 33.6 (C_6), 32.2 (C_2), 26.1 (C_4), 24.9 (C_{11}), 24.8 (C_{11}), 22.9 (C_7), 21.8 (C_1), 16.6 ($C_{1'}$) ppm (the carbon attached to the boron atom was not observed due to quadrupolar relaxation).

Spectral data are in accordance with those reported in the literature.[S4]

2-(3-(3,4-Dimethoxyphenyl)propyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3g)



3g

To a flame dried flask filled with argon was added dichloro(p-cymene)ruthenium(II) dimer (8.6 mg, 14.0 µmol, 0.05 mol%). 4-allyl-1,2-dimethoxybenzene (5.00 g, 28.1 mmol, 1 eq), 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.1 mL, 28.1 mmol, 1 eq) and were added to the flask at 0 °C. The solution was stirred for 96 h at rt, filtered through a plug of Celite® (ca. 10 mm) and silicagel (ca. 20 mm), eluated with PE/EtOAc 4:1 to yield a reddish liquid. Column chromatography (PE/EtOAc 10:1 to 4:1 yielded 2-(3-(3,4-dimethoxyphenyl)propyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**3g**) (5.56 g, 18.2 mmol; 65 %) as a colourless oil (ratio linear:branched = 93:7).

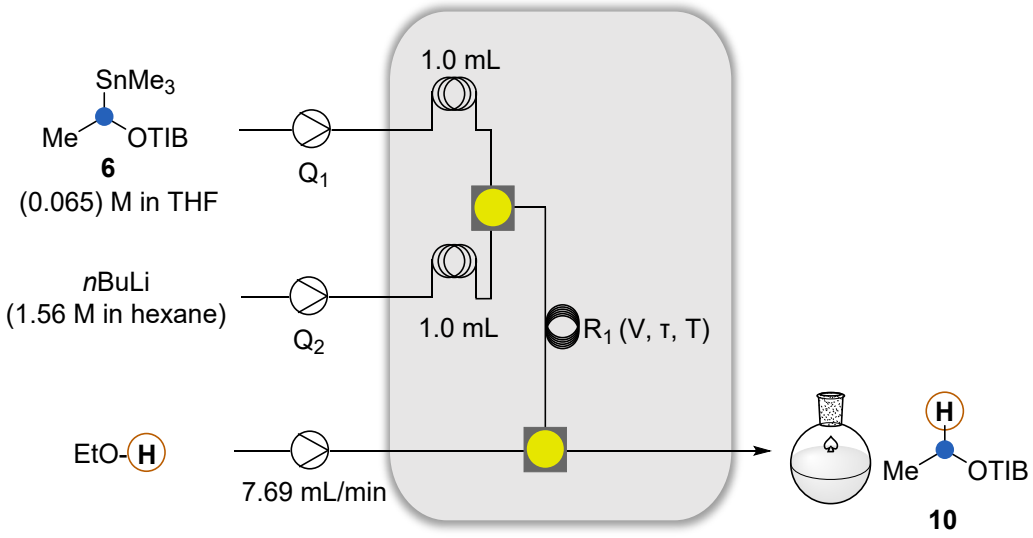
R_f: 0.28 (PE/EtOAc = 4:1); **^{1}H-NMR** ($CDCl_3$, 400 MHz): 6.79 – 6.70 (m, 3H, $H_{3,5,6}$), 3.87 (s, 3H, H_{OMe}), 3.85 (s, 3H, H_{OMe}), 2.55 (t, *J* = 7.6 Hz, 2H, H_7), 1.71 (quint, *J* = 7.8 Hz, 2H, H_8), 1.24 (s, 12H, H_{11}), 0.82 (t, *J* = 7.9 Hz, 2H, H_9) ppm. Doublet at 0.96 ppm (*J* = 7.2 Hz, 3H, CH_3) and two singlets at 1.19 (12H, Bpin) belong to the branched boronic ester; **^{13}C-NMR** ($CDCl_3$, 101 MHz): 148.8 (C_2), 147.1(C_1), 135.6 (C_4), 120.5 (C_5), 112.0 (C_6), 111.3 (C_3), 83.1 (C_{10}), 56.1 (C_{OMe}), 55.9 (C_{OMe}), 38.4 (C_7), 26.4 (C_8), 25.0 (C_{11}) ppm (the carbon attached to the boron atom was not observed due to quadrupolar relaxation).

Spectroscopic data are in accordance with those reported in the literature.[S7]

3. Flow Setup and Synthesis

The generation of the carbanion from the Sn-species was investigated by mixing a stream of *n*BuLi (approx. 1.6 M in hexanes) and a stream of **6** (as a THF solution) in the static mixer and quenching the

reaction by adding a stream of ethanol through a T-piece. An optimisation was conducted varying the reaction parameters. Yields were determined via GC-FID.



Scheme S1: Designed flow system to investigate the Sn-Li exchange

Table S1: Temperature -residence time screening of the Sn-Li exchange

V (R_1): **0.16 mL**

Entry	T (R1) [°C]	Eq. **6**/nBuLi	Q_1 [mL/min]	Q_2 [mL/min]	τ [s]	Yield [%]
1	**-42**	**1**	**12,3**	**0,51**	**0,75**	**82**
2	**-42**	**1**	**9,22**	**0,38**	**1**	**77**
3	-42	1	6,15	0,25	1,5	n.d.
4	**-42**	**1**	**3,07**	**0,13**	**3**	**82**
5	-42	1	1,54	0,06	6	72
6	-42	1	0,77	0,03	12	57
7	-60	1	12,3	0,51	0,75	62
8	-60	1	6,15	0,25	1,5	64
9	-78	1	12,3	0,51	0,75	36
10	-78	1	6,15	0,25	1,5	54

n.d.: not determined, reactor clogging

Prolonged reaction times achieved through lowering the flow rate led to a decrease in yield, which is caused by decreased mixing, especially when the concentration difference of the reacting species is high. As it can be seen, the conversion at -42°C is good at higher flow rates, but not full so the reactor volume was increased (see **table S2**). Lower temperatures resulted in decreased conversion.

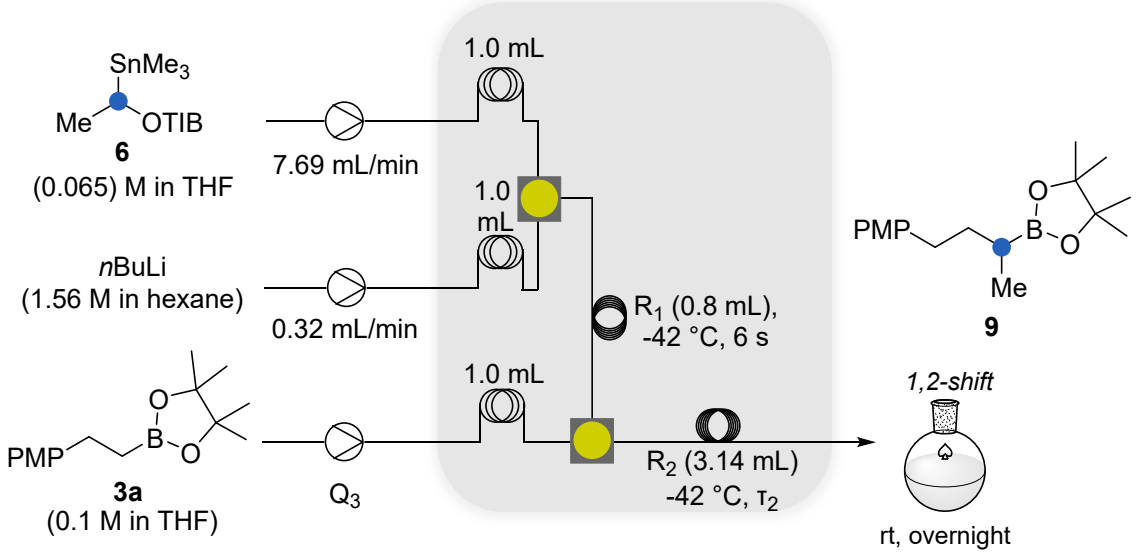
Table S2: Temperature -residence time screening of the Sn-Li exchange with increased reactor volume

V (R_1): **0.8 mL**

Entry	T (R_1) in °C	Eq. **6**/*n*BuLi	Q_1 [mL/min]	Q_2 [mL/min]	τ in s	Yield %
11	-42	1	11,52	0,49	4	96
12	**-42**	**1**	7,68	0,32	**6**	**98**
13	-42	1	5,12	0,22	9	87

14	-42	1	3,84	0,16	12	73
15	-42	1	3,07	0,13	15	79
16	-42	1	2,30	0,10	20	79

To optimise the overall reaction, parameters for the carbanion generation (Table **S2**, Entry **12**) were maintained and only the parameter for the addition boronic ester were changed. The results are shown in table **S3**.



Scheme S2: Flow setup for the investigation of the mono homologisation of boronic esters.

Table S3: Optimisation of reagent equivalents by adjusting the flow rate.

V (R_2): **3.14 mL**

Entry	T (R1,R2) in °C	Eq. **6**/nBuLi	Q_3 [mL/min]	τ_1 in s	τ_2 in s	Yield (GC) %
17	-42	1.3	3,84	6	15,9	95
18	-42	1.4	3,56	6	16,3	97
19	**-42**	**1.5**	3,33	**6**	**16,6**	**99**
20	-42	1.6	3,12	6	16,9	98

With the optimal conditions in hand reaching almost full converion to the elongated boronic ester, we decided to increase the residence time in R_2 to 20 s (ID = 1mm, l = 5000 mm, V= 3.9 mL) in anticipation that sterically more demanding boronic esters might react slower than the model substrate.

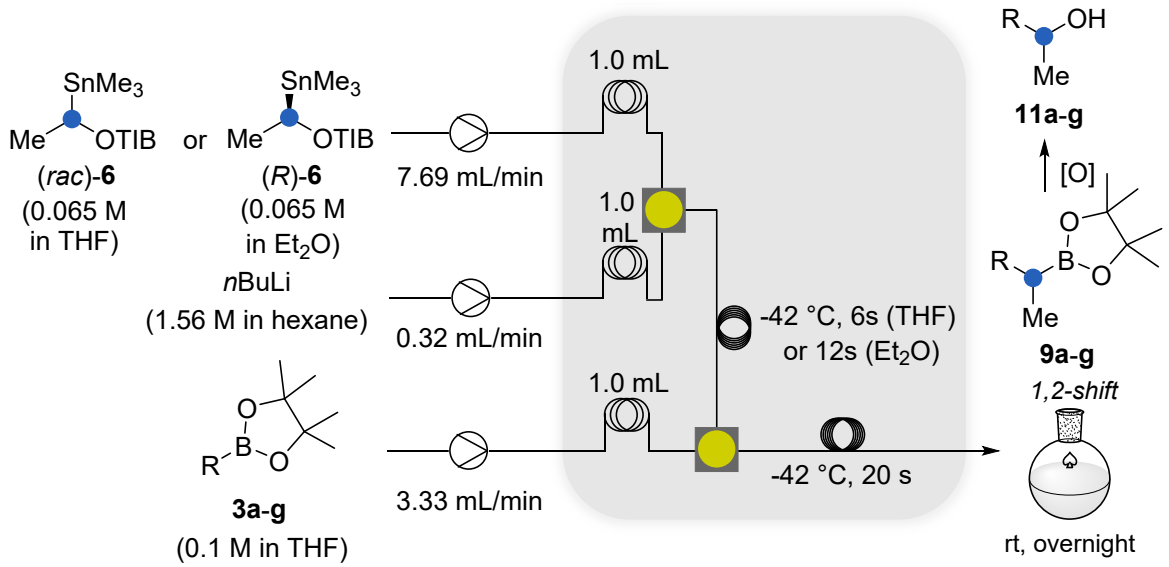
General procedure 1 (GP 1): Oxidation

The crude boronic ester was dissolved in THF (5 mL) and an aqueous solution of NaOH (2 M, 3 mL) was added. After cooling to 0 °C, H_2O_2 (35 % in H_2O, 1.5 mL) was added dropwise. After the addition, the solution was stirred at this temperature for 30 mins, then warmed to rt and stirred for 1-4 h. $Na_2S_2O_3$ (aq.) was carefully added dropwise at 0 °C to quench the reaction, then EtOAc was added. The aqueous layer was extracted with EtOAc (3x), the combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*.

4. Mono homologisation

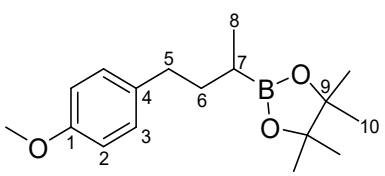
General Procedure A

The cooling bath temperature was set at -42 °C and all reaction streams entering the cooling bath were precooled with a coiled cooling loop (ID = 1mm, l = 1275 mm, V = 1 mL). The organotin species **6** (0.065 M in THF, 7.69 mL/min, 1.5 eq.) was mixed with *n*BuLi (1.56 M, 0.32 mL/min, 1.5 eq.) in the static mixer and reacted for 6 s (ID = 1mm, l = 1019 mm, V = 0.8 mL) or 12s (ID = 1mm, l =2038 mm, 1.6 mL) for Et_2O (flow rates were kept constant) in the coil to generate the organolithium species which was then mixed with a precooled stream of boronic ester (0.1 M in THF, 3.33 mL/min, 1.0 eq.) in a second static mixer and reacted for 20 s (ID = 1mm, l = 5000 mm, V = 3.9 mL) before leaving the cooling bath and being collected in a flask immersed in a water bath set at 20°C. To ensure steady state, the reactor system was flushed for approximately 60 s before the sample was collected. The collected sample was allowed to sit for 18 h at rt (20 °C) before the solvent was evaporated *in vacuo* and water and Et_2O were added. The aqueous layer was extracted with Et_2O (2x), the combined organic layers were washed with brine, dried over $MgSO_4$ and the solvent was evaporated *in vacuo* to yield the crude product.



Scheme S3: Flow setup for the mono homologisation of selected boronic esters **3a-3g.**

2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (9a)



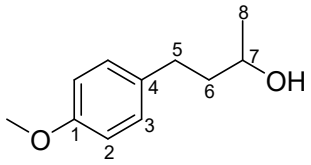
9a

The title compound was synthesised according to general procedure A using boronic ester **3a**. The crude product was purified by flash column chromatography (silica gel, PE/EtOAc 20:1) to yield boronic ester **9a** (191 mg, 0.658 mmol, 99 %) as a colourless oil.

R_f: 0.33 (PE/EtOAc = 10:1); **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.10 (d, *J* = 8.6 Hz, 2H, H_3), 6.81 (d, *J* = 8.6 Hz, 2H, H_2), 3.78 (s, 3H, H_{OMe}), 2.62 – 2.50 (m, 2H, H_5), 1.80 – 1.70 (m, 1H, H_6), 1.60 - 1.50 (m, 1H, H_6), 1.25 (s, 12H, H_{10}), 1.10 – 1.03 (m, 1H, H_7), 1.01 (m, 3H, H_8) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): 157.7 (C_1), 135.4 (C_4), 129.4 (C_3), 113.8 (C_2), 83.0 (C_9), 55.4 (C_{OMe}), 35.7 (C_5), 34.5 (C_6), 24.9 (C_{10}), 24.9 (C_{10}), 15.6 (C_8) ppm. (the carbon attached to the boron was not observed due to quadrupolar relaxation); **HRMS** (ESI) *m/z* calc. for $C_{17}H_{27}BO_3Na$ $[M+Na]^+$: 313.1951 ; found 313.1953

Spectral data are in accordance with those reported in the literature.[S8]

4-(4-Methoxyphenyl)butan-2-ol (11a)



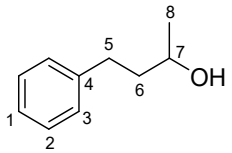
11a

The title compound was synthesised according to **general procedure A** followed by oxidation (**GP 1**) using boronic ester **3a**. The crude product was purified by flash column chromatography (silica gel, PE/EtOAc 5:1) to yield alcohol **11a** (118 mg, 0.655 mmol, 98 %) as a colourless oil.

R_f: 0.18 (PE/EtOAc = 3:1); **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.14 – 7.10 (m, 2H, H_3), 6.85 – 6.81 (m, 2H, H_2), 3.82 (sxt, *J* = 6.2 Hz, 1H, H_7), 3.79 (s, 3H, H_{OMe}), 2.74 – 2.58 (m, 2H, H_5), 1.81 – 1.67 (m, 2H, H_6), 1.37 (bs, 1H, OH), 1.22 (d, *J* = 6.2 Hz, 3H, H_8) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): 157.9 (C_1), 134.2 (C_4), 129.4 (C_3), 114.0 (C_2), 67.7 (C_7), 55.4 (C_{OMe}), 41.2 (C_5), 31.3 (C_6), 23.8 (C_8) ppm; **HRMS** (GCMS-CI) *m/z* calc. for $C_{11}H_{16}O$ $[M]^{\bullet+}$ 180.1150, found 180.1150.

Spectral data are in accordance with those reported in the literature.[S8]

4-Phenylbutan-2-ol (11b)



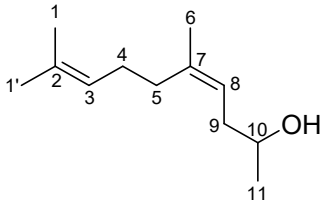
11b

The title compound was synthesised according to **general procedure A** followed by oxidation (**GP1**) using boronic ester **3b**. The crude product was purified by flash column chromatography (silica gel, PE/EtOAc 10:1) to yield alcohol **11b** (98 mg, 0.652 mmol, 98 %) as a colourless oil.

R_f: 0.27 (PE/EtOAc = 3:1); **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.31 – 7.27 (m, 2H, H_{Ar}), 7.22 – 7.17 (m, 3H, H_{Ar}), 3.84 (sxt, *J* = 6.2 Hz, 1H, H_7), 2.80 – 2.64 (m, 2H, H_5), 1.85 – 1.71 (m, 2H, H_6), 1.36 (bs, 1H, OH), 1.24 (d, *J* = 6.2 Hz, 3H, H_8) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): 142.2 (C_4), 128.5 (C_2), 128.5 (C_3), 126.0 (C_1), 67.7 (C_7), 41.0 (C_5), 32.3 (C_6), 23.8 (C_8) ppm; **HRMS** (GCMS-CI) *m/z* calc. for $C_{10}H_{14}O$ $[M]^{\bullet+}$ 150.1045, found 150.1048.

Spectral data are in accordance with those reported in the literature.[S9]

(*Z*)-5,9-Dimethyldeca-4,8-dien-2-ol (11c)

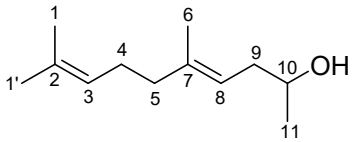


11c

The title compound was synthesised according to **general procedure A** followed by oxidation (**GP 1**) using boronic ester **3c**. The crude product was purified by flash column chromatography (silica gel, PE/EtOAc 10:1) to yield alcohol **11c** (114 mg, 0.625 mmol, 94 %) as a colourless oil.

R_f: = 0.33 (PE/EtOAc = 3:1); **^{1}H-NMR** ($CDCl_3$, 400 MHz): 5.19 – 5.15 (m, 1H, H_8), 5.13 – 5.08 (m, 1H, H_3), 3.78 (sxt, *J* = 6.2 Hz, 1H, H_{10}), 2.23 – 2.11 (m, 2H, H_9), 2.10 – 2.03 (m, 4H, $H_{4,5}$), 1.74 (d, *J* = 1.1 Hz, 3H, H_6), 1.68 (s, 3H, $H_{1'}$), 1.61 (s, 3H, H_1), 1.54 (bs, 1H, OH), 1.19 (d, *J* = 6.2 Hz, 3H, H_{11}) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): 139.0 (C_7), 132.0 (C_2), 124.2 (C_3), 121.0 (C_8), 68.1 (C_{10}), 37.9 (C_9), 32.2 (C_5), 26.7 (C_4), 25.8 ($C_{1'}$), 23.7 (C_6), 23.0 (C_{11}), 17.8 (C_1) ppm; **HRMS** (GCMS-CI) *m/z* calc. for $C_{12}H_{23}O$ $[M+H]^+$: 183.1749, found 183.1750.

(*E*)-5,9-Dimethyldeca-4,8-dien-2-ol (11d)

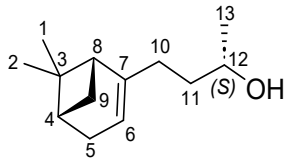


11d

The title compound was synthesised according to **general procedure A** followed by oxidation (**GP 1**) using boronic ester **3d**. The crude product was purified by flash column chromatography (silica gel, PE/EtOAc 10:1) to yield alcohol **11d** (114 mg, 0.625 mmol, 94 %) as a colourless oil.

R_f: 0.33 (PE/EtOAc = 3:1); **^{1}H-NMR** ($CDCl_3$, 400 MHz): 5.18 – 5.14 (m, 1H, H_8), 5.09 – 5.05 (m, 1H, H_3), 3.79 (sxt, *J* = 6.2 Hz, 1H, H_{10}), 2.23 – 2.02 (m, 6H, $H_{4,5,9}$), 1.68 (d, *J* = 0.8 Hz, 3H, $H_{1'}$), 1.63 (s, 3H, H_6), 1.60 (s, 3H, H_1) 1.58 (bs, OH), 1.19 (d, *J* = 6.2 Hz, 3H, H_{11}) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): 139.0 (C_7), 131.9 (C_2), 124.3 (C_3), 120.3 (C_8), 67.9 (C_{10}), 40.0 (C_5), 38.1 (C_9), 26.6 (C_4), 25.8 ($C_{1'}$), 22.7 (C_{11}), 17.8 (C_1), 16.4 (C_6) ppm; **HRMS** (GCMS-CI) *m/z* calc. for $C_{12}H_{23}O$ $[M+H]^+$: 183.1749, found 183.1742.

(*S*)-4-((1*R*,5*S*)-6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-yl)butan-2-ol (11e)

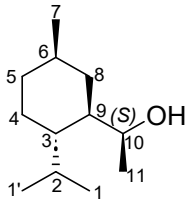


11e

The title compound was synthesised according to **general procedure A** followed by oxidation (**GP 1**) using boronic ester **3e**. The crude product was purified by flash column chromatography (silica gel, PE/EtOAc 10:1) to yield alcohol **13e** (92.0 mg, 0.47 mmol, 71 %) as a colourless oil.

R_f: 0.49 (PE/EtOAc = 7:3); $[\alpha]_D^{20} = -29.1°$ (c = 1.00, CH_2Cl_2); **^{1}H-NMR** (C_6D_6, 400 MHz): 5.22 – 5.19 (m, 1H, H_6), 3.54 (sxt, *J* = 6.2 Hz, 1H, H_{12}), 2.34 (dt, *J* = 8.5, 5.6 Hz, 1H, H_9), 2.28 – 2.14 (m, 2H, H_5), 2.10 – 1.91 (m, 4H, $H_{4,8,10}$), 1.46 – 1.34, m, 2H, H_{11}), 1.25 (s, 3H, H_1), 1.24 (d, *J* = 8.5 Hz, 3H, H_9), 1.13 (d, *J* = 6.2 Hz, H_{13}), 0.91 (s, 3H, H_2) ppm; **^{13}C-NMR** (C_6D_6, 101 MHz): 148.5 (C_7), 116.2 (C_6), 67.5 (C_{12}), 46.2 (C_8), 41.3 (C_4), 38.1 (C_3), 37.2 (C_{11}), 33.6 (C_{10}), 32.0 (C_9), 31.6 (C_5), 26.5 (C_1), 23.8 (C_{13}), 21.4 (C_2) ppm; **HRMS** (GCMS-EI) *m/z* calc. for $C_{13}H_{22}O$ $[M]^{\bullet+}$: 194.1662, found 194.1671.

(*S*)-1-((1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl)ethan-1-ol (11f)

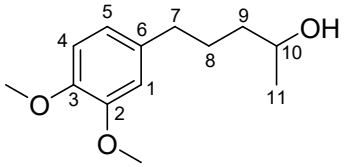


11f

The title compound was synthesised according to **general procedure A** followed by oxidation (**GP 1**) using boronic ester **3f**. The crude product was purified by flash column chromatography (silica gel, PE/EtOAc 10:1) to yield alcohol **11f** (111 mg, 0.60 mmol, 90 %) as a colourless oil. To prove the configuration of the newly formed alcohol, an exemplary esterification with 4-nitro benzoic acid was conducted (see compound **12**)

R_{f2}: 0.50 (PE/EtOAc = 7:3); $[\alpha]_D^{20} = -57.8°$ (c = 1.00, $CHCl_3$); **^{1}H-NMR** ($CDCl_3$, 400 MHz): 4.14 – 4.08 (m, 1H, H_{10}), 1.87 – 1.77 (m, 2H, $H_{2,8}$), 1.76 – 1.70 (m, 1H, H_5), 1.67 – 1.63 (m, 1H, H_4), 1.56 – 1.49 (m, 1H, H_9), 1.37 – 1.26 (m, 2H, $H_{6,OH}$), 1.05 (d, *J* = 6.6 Hz, 3H, H_{11}), 1.01 – 0.94 (m, 2H, $H_{3,4}$), 0.91 (d, *J* = 6.6 Hz, 3H, H_7), 0.88 (d, *J* = 6.9 Hz, 3H, H_1), 0.85 – 0.81 (m, 1H, H_5), 0.78 (d, *J* = 6.9 Hz, 3H, $H_{1'}$), 0.70 (q, *J* = 12.1 Hz, 3H, H_8) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): 67.1 (C_{10}), 45.4 (C_9), 44.8 (C_3), 35.5 (C_5), 33.0 (C_8), 32.7 (C_6), 26.3 (C_2), 24.6 (C_4), 23.0 (C_7), 21.6 ($C_{1'}$), 16.8 (C_{11}), 15.4 (C_1) ppm; **HRMS** (GCMS-EI) *m/z* calc. for $C_{12}H_{22}$ [M-H_2O]: 166.1722, found 166.1723.

5-(3,4-Dimethoxyphenyl)pentan-2-ol (11g)

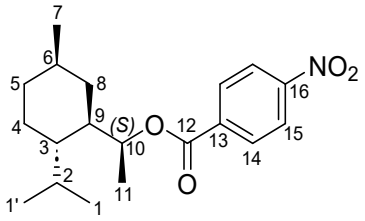


11g

The title compound was synthesised according to **general procedure A** followed by oxidation (**GP 1**) using boronic ester **3g**. The crude product was purified by flash column chromatography (silica gel, PE/EtOAc 3:1 to 2:1) to yield alcohol **11g** (142 mg, 0.633 mmol, 95 %) as a colourless oil.

R_f: 0.31 (PE/EtOAc = 1:1); **^{1}H-NMR** ($CDCl_3$, 400 MHz): 6.80 – 6.78 (m, 1H,), 6.73 – 6.67 (m, 2H), 3.87 (s, 3H, H_{OMe}), 3.85 (s, 3H, H_{OMe}), 3.82 (sxt, *J* = 6.2 Hz, 1H, H_{10}), 2.58 (t, *J* = 7.6 Hz, 2H, H_7), 1.78 – 1.69 (m, 1H, H_9), 1.67 – 1.58 (m, 1H, H_9), 1.52 – 1.45 (m, 2H, H_8), 1.19 (d, *J* = 6.2 Hz, 3H, H_{11}) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): 148.9, 147.3, 135.2, 120.3, 111.9, 111.3, 68.2 (C_{11}), 56.1, 56.0, 39.0, 35.6, 27.9, 23.7 ppm; **HRMS** (ESI) *m/z* calc. for $C_{13}H_{20}O_3Na$ $[M+Na]^+$: 247.1310, found 247.1299.

(*S*)-1-((1*R*,2,5*R*)-2-Isopropyl-5-methylcyclohexyl)ethyl 4-nitrobenzoate (12)



12

(*S*)-1-((1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl)ethan-1-ol (22.1 mg, 120 µmol, 1 eq), p-nitrobenzoic acid (24.0 mg, 144 µmol, 1.2 eq), Dicyclohexylcarbodiimide (29.7 mg, 25.7 µL, 144 µmol, 1.2 eq) and DCM (1 mL) were added to a flask flushed with nitrogen, then 4-Dimethylaminopyridine (1.46 mg, 12.0 µmol, 0.1 eq) was added. The mixture was stirred at rt for 18 h. The suspension was filtered and the solids were washed with 2 mL of DCM. The solvent was evaporated until a white solid appeared again. The crude product was dissolved in a minimal amount of a mixture of PE/EtOAc (20:1, solids still remained) and purified by column chromatography (PE/EtOAc = 20:1). Evaporation of the solvent yielded (*S*)-1-((1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl)ethyl 4-nitrobenzoate **12** (35.0 mg, 105 µmol, 87.5 %) as a colourless solid. Recrystallisation from MeOH with drop of water yielded colourless crystals suitable for x-ray analysis.

R_f: 0.49 (PE/EtOAc = 10:1); m.p. 78 – 82 °C; **^{1}H-NMR** ($CDCl_3$, 400 MHz): 8.29 (d, *J* = 9.0 Hz, 2H, H_{15}), 8.21 (d, *J* = 9.0 Hz, 2H, H_{14}), 5.52 – 5.47 (m, 1H, H_{10}), 1.94 (dsept, *J* = 6.9 Hz, *J* = 2.8 Hz, 1H, H_2), 1.84 – 1.68 (m 4H, $H_{4,5,8,9}$), 1.38 – 1.32 (m, 1H, H_6), 1.26 (d, *J* = 6.6 Hz, 3H, H_{11}), 1.15 – 1.00 (m, 2H, $H_{3,4}$), 0.94 – 0.86 (m, 11H, $H_{1,1',5,7,8}$) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): 164.2 (C_{12}), 150.6 (C_{16}), 136.6 (C_{13}), 130.8 (C_{14}), 123.7 (C_{15}), 73.1 (C_{10}), 44.6 (C_3), 42.6 (C_9), 35.4 (C_8), 34.2 (C_5), 32.5 (C_6), 26.8 (C_2), 24.4 (C_4), 23.0 (C_7), 21.6 (C_1), 15.4 ($C_{1'}$), 13.6 (C_{11}) ppm.

Xray-analysis: Single colourless plate-shaped crystals of (*S*)-1-((1*R*,2,5*R*)-2-Isopropyl-5-methylcyclohexyl)ethyl 4-nitrobenzoate (12) were crystallized from methanol/water at room temperature. A suitable crystal 0.43×0.23×0.09 mm^3 was selected and mounted on a 18 mm mounted CryoLoop (20 micron, 0.2 - 0.3 mm, Hampton Research) on an XtaLAB AFC12 (RINC): Kappa single diffractometer. The crystal was kept at a steady *T* = 100.00(10) K during data collection. The structure was solved with the ShelXT 2018/2[S10] structure solution program using the Intrinsic Phasing solution method and by using **Olex2**[S11] as the graphical interface. The model was refined with version 2019/3 of ShelXL 2019/3[S12] using Least Squares minimisation.

Crystal Data. $C_{19}H_{27}NO_4$, M_r = 333.41, triclinic, *P*1 (No. 1), a = 7.7793(3) Å, b = 7.8250(3) Å, c = 17.2242(5) Å, α = 100.816(3)°, β = 90.891(3)°, γ = 117.488(4)°, *V* = 907.30(6) $Å^3$, *T* = 100.00(10) K, *Z* = 2, *Z'* = 2, μ(Cu K_α) = 0.687, 36244 reflections measured, 7321 unique (R_{int} = 0.0695) which were used in all calculations. The final wR_2 was 0.1329 (all data) and R_1 was 0.0456 (I > 2(I)). Absolute structure determination: Flack parameter: -0.09(16); Hooft parameter: -0.11(11).

CDCC 2357370 contain the supplementary crystallographic data for this structure. These data can be obtained free of charge via www.ccdc.cam.ac.uk/structures/

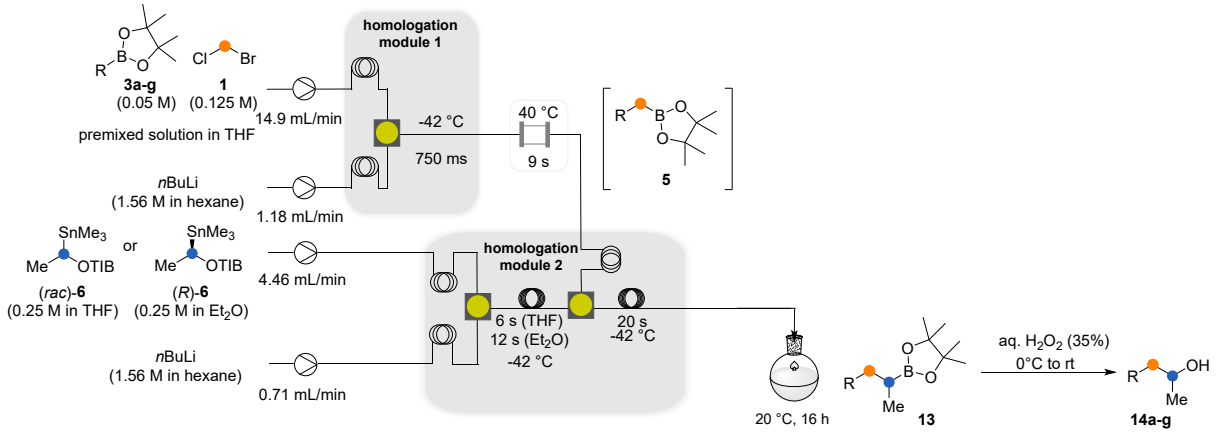
5. Bishomologisation

With these results in hand, we moved on to combine the previously published method of the Matteson reaction in flow with the Matteson-Hoppe-Aggarwal homologation protocol. Changes to the original

protocol were made to suit the reaction times and material consumption for subsequent reaction steps. An equimolar ratio of bromochloromethane and *n*BuLi was used to ensure that the carbanion generated in the subsequent step was only coming from the Sn species and not from remaining bromochloromethane.

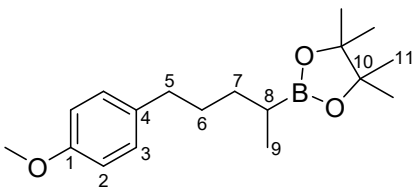
General Procedure B

The cooling bath temperature was set at -42 °C and all reaction streams entering the cooling bath were precooled with a coiled cooling loop (ID = 1mm, L = 1275 mm, V = 1 mL). The boronic ester (0.05 M in THF, 1 eq) was premixed with $ClCH_2Br$ (0.125 M, 2.5 eq) and fed (14.9 mL/min) into the static mixer together with *n*BuLi (1.56 M, 1.18 mL/min, 2.5 eq) for 750 ms (ID = 1 mm, l = 255 mm, V = 0.2 mL) in the subsequent reactor followed by directing the stream into a coil immersed in an electrically heated water bath (40°C) for 9 s (ID = 1 mm, l = 3200 mm, V = 2.5 mL). The stream was then again cooled in a coiled loop and fed into a second static mixer. In parallel, the organotin species **6** or (*R*)-**6a** (0.25 M in THF or Et_2O, 4.46 mL/min, 1.5 eq.) was mixed with nBuLi (1.56 M, 0.71 mL/min, 1.5 eq.) in another static mixer and reacted for 6 s (ID = 1 mm, l = 660 mm, V = 0.52 mL) or 12 s (ID = 1 mm, l = 1320 mm, V = 1.04 mL) in case of Et_2O as solvent and enantiopure (*R*)-1-(trimethylstannyl)ethyl 2,4,6-triisopropylbenzoate (flow rates were kept constant) in the coil to generate the organolithium species **7** which was then reacted with the aforementioned precooled stream of boronic ester for 20 s (ID = 1 mm, l = 9000 mm, V = 7.07 mL) before leaving the cooling bath and being collected in a flask immersed in a water bath set at 20°C. To ensure steady state, the reactor system was flushed for approximately 120 s before the sample was collected. The collected sample was allowed to sit for 18 h at rt (20 °C) before the solvent was evaporated *in vacuo* and water and Et_2O were added. The aqueous layer was extracted with Et_2O (2x), the combined organic layers were washed with brine, dried over $MgSO_4$ and the solvent was evaporated *in vacuo* to yield the crude boronic ester.



Scheme S4: Flow setup for the double homologisation of selected boronic esters **3a-g.**

2-[5-(4-Methoxyphenyl)pentan-2-yl)]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (13a)



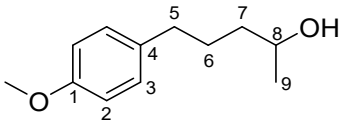
13a

The title compound was synthesised according to the **general procedure B** using boronic ester **3a**. The crude product was purified by flash column chromatography (silica gel, PE/EtOAc 20:1) to yield boronic ester **13a** (210 mg, 0.69 mmol; 93 %) as a colourless oil.

R_f: 0.35 (PE/EtOAc = 10:1); **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.09 (d, *J* = 8.5 Hz, 2H, H_3), 6.81 (d, *J* = 8.6 Hz, 2H, H_2), 3.78 (s, 3H, H_{OMe}), 2.54 (t, *J* = 7.7 Hz, 2H, H_5), 1.66 – 1.56 (m, 2H, H_6), 1.54 – 1.45 (m, 1H, H_7), 1.39 - 1.28 (m, 1H, H_7), 1.23 (s, 12H), 1.07 – 1.00 (m, 1H, H_8), 0.96 (m, 3H, H_9) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): 157.7 (C_1), 135.2 (C_4), 129.3 (C_3), 113.8 (C_2), 83.0 (C_{10}), 55.4 (C_{OMe}), 35.4 (C_5), 33.0 (C_7), 31.2 (C_6), 24.9 (C_{11}), 24.9 (C_{11}), 15.6 (C_9) (the carbon attached to the boron was not observed due to quadrupolar relaxation) ppm; **HRMS** (ESI) *m/z* calc. for $C_{18}H_{29}BO_3Na$ $[M+Na]^+$: 327.2107 ; found 327.2108.

Spectral data are in accordance with those reported in the literature.[S13]

45**-(4-Methoxyphenyl)pentan-2-ol (14a)**



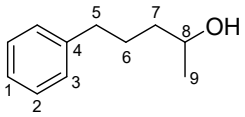
14a

The title compound was synthesised according to the **general procedure B** followed by oxidation (**GP 1**) using boronic ester **3a**. The crude product was purified by flash column chromatography (silica gel, PE/EtOAc 5:1) to yield alcohol **14a** (134 mg, 0.69 mmol; 93 %) as a colourless oil.

R_f: 0.18 (PE/EtOAc = 3:1); **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.11 – 7.08 (m, 2H, H_3), 6.84 – 6.81 (m, 2H, H_2), 3.81 (sxt, *J* = 6.2 Hz, 1H, H_8), 3.79 (s, 3H, H_{OMe}) 2.58 (t, *J* = 7.6 Hz, 2H, H_5), 1.77 – 1.56 (m, 2H, H_7), 1.54 – 1.42 (m, 2H, H_6), 1.32 (bs, 1H, OH), 1.18 (d, *J* = 6.2 Hz, 3H, H_9) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): 157.9 (C_1), 134.6 (C_4), 129.4 (C_3), 113.9 (C_2), 68.2 (C_8), 55.4 (C_{OMe}), 39.0 (C_7), 35.1 (C_5), 27.9 (C_6), 23.7 (C_9) ppm; **HRMS** (GCMS-CI) *m/z* calc. for $C_{12}H_{18}O_2$ $[M]^{+\bullet}$: 194.1307; found 194.1302.

Spectral data are in accordance with those reported in the literature.[S14]

5-Phenylpentan-2-ol (14b)



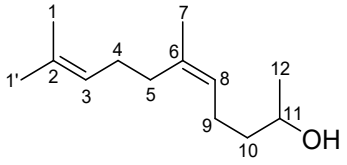
14b

The title compound was synthesised according to the **general procedure B** followed by oxidation (**GP 1**) using boronic ester **3b**. The crude product was purified by flash column chromatography (silica gel, PE/EtOAc 10:1) to yield alcohol **14b** (111 mg, 0.68 mmol; 91 %) as a colourless oil.

R_f: 0.27 (PE/EtOAc = 3:1); **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.31 -7.16 (m, 5H, $H_{1,2,3}$), 3.82 (sxt, *J* = 6.2 Hz, 1H, H_8), 2.64 (t, *J* = 7.7 Hz, 2H, H_5), 1.81 – 1.60 (m, 2H, H_7), 1.56 – 1.44 (m, 2H, H_6), 1.30 (bs, 1H, OH), 1.19 (d, *J* = 6.2 Hz, 3H, H_9) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): 142.5 (C_4), 128.5 (C_2), 128.4 (C_3), 125.9 (C_1), 68.2 (C_8), 39.0 (C_7), 36.0 (C_5), 27.7 (C_7), 23.7 (C_9) ppm; **HRMS** (GCMS-CI) *m/z* calc. for $C_{11}H_{16}O$ $[M]^{+\bullet}$: 164.1193; found 164.1201.

Spectral data are in accordance with those reported in the literature.[S15]

(Z)-6,10-Dimethylundeca-5,9-dien-2-ol (14c)

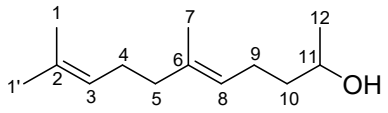


14c

The title compound was synthesised according to the **general procedure B** followed by oxidation (**GP 1**) using boronic ester **3c**. The crude product was purified by flash column chromatography (silica gel, PE/EtOAc 10:1) to yield alcohol **14c** (123 mg, 0.63 mmol; 84 %) as a colourless oil.

R_f: 0.38 (PE/EtOAc = 3:1); **^{1}H-NMR** ($CDCl_3$, 400 MHz): 5.16 – 5.10 (m, 2H, $H_{3,8}$), 3.80 (sxt, *J* = 6.2 Hz, 1H, H_{11}), 2.15 – 2.01 (m, 6H, $H_{4,5,9}$), 1.70 – 1.68 (m, 6H, $H_{1',7}$), 1.61 (bs, 3H, H_1), 1.53 – 1.45 (m, 2H, H_{10}), 1.40 (bs, 1H, OH), 1.19 (d, *J* = 6.2 Hz, 3H, H_{12}) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): 136.0 (C_6), 131.8 (C_2), 124.9 (C_8), 124.4 (C_3), 68.1 (C_{11}), 39.6 (C_{10}), 32.1 (C_5), 26.7 (C_4), 25.9 ($C_{1'}$), 24.4 (C_9), 23.6 (C_{12}), 23.5 (C_7), 17.8 (C_1) ppm; **HRMS** (GCMS-CI) *m/z* calc. for $C_{13}H_{25}O$ $[M+H]^+$: 197.1905; found 197.1896.

(*E*)-6,10-Dimethylundeca-5,9-dien-2-ol (14d)



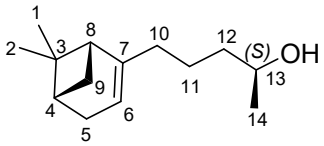
14d

The title compound was synthesised according to the **general procedure B** followed by oxidation (**GP 1**) using boronic ester **4d**. The crude product was purified by flash column chromatography (silica gel, PE/EtOAc 10:1) to yield alcohol **14d** (124 mg, 0.63 mmol; 85 %) as a colourless oil.

R_f: 0.36 (PE/EtOAc = 3:1); **^{1}H-NMR** ($CDCl_3$, 400 MHz): 5.14 (dt, *J* = 7.2 Hz, 1.2 Hz, 1H, H_8), 5.08 (tt, *J* = 6.8 Hz, 1.4 Hz, H_3), 3.81 (sxt, *J* = 6.2 Hz, 1H, H_{11}), 2.12 – 2.04 (m, 4H, $H_{4,9}$), 2.00 – 1.97 (m, 2H, H_{10}), 1.68 (d, *J* = 1.0 Hz, 3H, $H_{1'}$), 1.62 (s, 3H, H_7), 1.60 (s, 3H, H_1), 1.53 – 1.46 (m, 2H, H_{10}), 1.41 (bs, 1H, OH), 1.19 (d, *J* = 6.2 Hz, 3H, H_{12}) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): 135.8 (C_6), 131.6 (C_2), 124.4 (C_3), 124.1 (C_8), 68.1 (C_{11}), 39.9 (C_5), 39.3 (C_{10}), 26.8 (C_4), 25.8 ($C_{1'}$), 24.5 (C_9), 23.6 (C_{12}), 17.8 (C_1), 16.1 (C_7) ppm; **HRMS** (GCMS-CI) *m/z* calc. for $C_{13}H_{25}O$ $[M+H]^+$: 197.1905; found 197.1906.

Spectral data are in accordance with those reported in the literature.[S16]

(*S*)-5-[(1*R*,5*S*)-6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-yl]pentan-2-ol (14e)

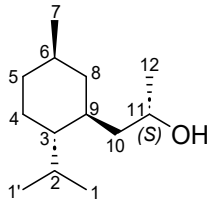


14e

The title compound was synthesised according to the **general procedure B** followed by oxidation (**GP 1**) using boronic ester **3e**. The crude product was purified by flash column chromatography (silica gel, PE/EtOAc 10:1) to yield alcohol **14e** (90 mg, 0.43 mmol; 58 %) as a colourless oil.

R_f: 0.40 (PE/EtOAc = 3:1); $[\alpha]_D^{20} = -26.7°$ (c = 1.00); **^{1}H-NMR** ($CDCl_3$, 400 MHz): 5.19 – 5.16 (m, 1H, H_6), 3.83 – 3.76 (m, 1H, H_{13}), 2.35 (dt, *J* = 8.5 Hz, *J* = 5.6 Hz, H_9), 2.27 – 2.14 (m, 2H, H_5), 2.10 – 2.05 (m, 1H, H_4), 2.00 (dt, *J* = 1.4 Hz, 5.6 Hz, H_8), 1.98 – 1.92 (m, 2H, H_{10}), 1.52 – 1.31 (m, 5H, $H_{11,12,\ OH}$), 1.26 (s, 3H, H_2), 1.18 (d, *J* = 6.2 Hz, H_{14}), 1.13 (d, *J* = 8.5 Hz, H_9), 0.82 (s, 3H, H_1) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): 148.4 (C_7), 116.1 (C_6), 68.3 (C_{13}), 45.9 (C_8), 41.0 (C_4), 39.3 (C_{11}), 38.1 (C_{10}), 37.0 (C_{10}), 31.8 (C_9), 31.4 (C_5), 26.5 (C_2), 23.7 (C_{14}), 23.5 (C_{12}), 21.4 (C_1) ppm; **HRMS** (GCMS-EI) *m/z* calc. for $C_{14}H_{24}O$ $[M]^{\bullet+}$: 208.1827, found 208.1823

(*S*)-1-[(1*S*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl]propan-2-ol (14f)

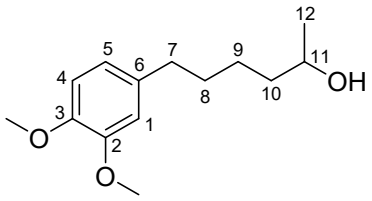


14f

The title compound was synthesised according to the **general procedure B** followed by oxidation (**GP 1**) using boronic ester **3f**. The crude product was purified by flash column chromatography (silica gel, PE/EtOAc 10:1) to yield alcohol **14f** (120 mg, 0.60 mmol; 81 %) as a colourless oil.

R_f: 0.42 (PE/EtOAc = 3:1); $[\alpha]_D^{20} = -69.5°$ (c = 1.00, $CHCl_3$); **^{1}H-NMR** ($CDCl_3$, 400 MHz): 3.96 – 3.88 (m, 1H, H_{11}), 2.05 – 1.97 (dsept, *J* = 6.9 Hz, 2.9 Hz, 1H, H_2), 1.78 – 1.67 (m, 2H, $H_{5,8}$), 1.66 – 1.60 (m, 2H, $H_{4,10}$), 1.36 – 1.27 (m, 1H, H_6), 1.23 – 1.19 (m, 2H, H_9), 1.17 (d, *J* = 6.1 Hz, 3H, H_{12}), 1.02 – 0.95 (m, 1H, H_4), 0.92 – 0.87 (m, 1H, H_3) 0.89 (d, *J* = 6.9 Hz, 3H, H_1), 0.86 (d, *J* = 6.6 Hz, 3H, H_7), 0.84 – 0.78 (m, 1H, H_5), 0.72 (d, *J* = 6.9 Hz, 3H, $H_{1'}$), 0.64 (q, *J* = 11.9 Hz, 1H, H_8) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): 67.0 (C_{11}), 47.9 (C_3), 43.4 (C_{10}), 42.1 (C_8), 36.9 (C_9), 35.3 (C_5), 32.9 (C_6), 26.5 (C_2), 24.4 (C_4), 23.3 (C_{12}), 22.9 (C_7), 21.8 (C_1), 15.3 ($C_{1'}$) ppm; **HRMS** (GCMS-CI) *m/z* calc. for $C_{13}H_{25}$ $[M\text{-}H_2O+H]^+$: 181.1956, found 181.1954.

6-(3,4-Dimethoxyphenyl)hexan-2-ol (14g)



14g

The title compound was synthesised according to the **general procedure B** followed by oxidation (**GP 1**) using boronic ester **3g**. The crude product was purified by flash column chromatography (silica gel, PE/EtOAc 3:1) to yield alcohol **14g** (158 mg, 0.66 mmol; 89 %) as a colourless oil.

R_f: 0.33 (PE/EtOAc = 1:1); **^{1}H-NMR** ($CDCl_3$, 400 MHz): 6.79 -6.77 (m, 1H, H_4), 6-71 – 6.67 (m, 2H, $H_{1,5}$), 3.87 (s, 3H, H_{OMe}), 3.85 (s, 3H, H_{OMe}), 3.83 – 3.75 (m, 1H, H_{11}), 2.56 (t, *J* = 7.7 Hz, 2H, H_7), 1.53 – 1.40 (m, 6H, $H_{8,9,10}$), 1.18 (d, *J* = 6.2 Hz, 3H, H_{12}) ppm; **^{13}C-NMR** ($CDCl_3$, 101 MHz): 148.9 (C_2), 147.2 (C_3), 135.4 (C_6), 120.2 (C_5), 111.9 (C_4), 111.3 (C_1), 68.2 (C_{11}), 56.1 (C_{OMe}), 55.9 (C_{OMe}), 39.3 (C_{10}), 35.6 (C_7), 31.8 (C_8), 25.5 (C_9), 23.7 (C_{12}) ppm; **HRMS** (ESI) *m/z* calc. for $C_{14}H_{22}O_3Na$ $[M+Na]^+$: 261.1467; found 261.1464.

The NMR spectrum reveals approx. 7-8 % of branched product (2 doublets at 0.89).

6. References (supporting information)

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7. Attachments: Copies of NMR Spectra

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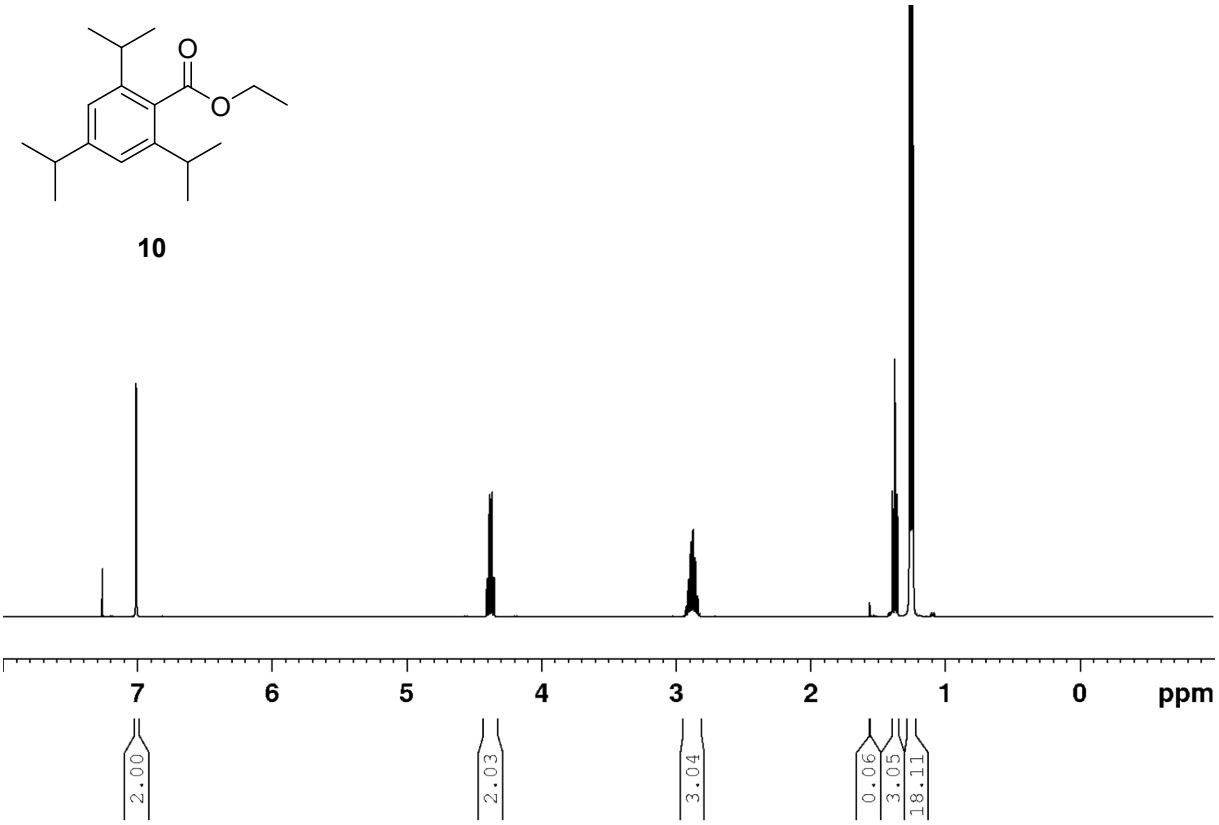

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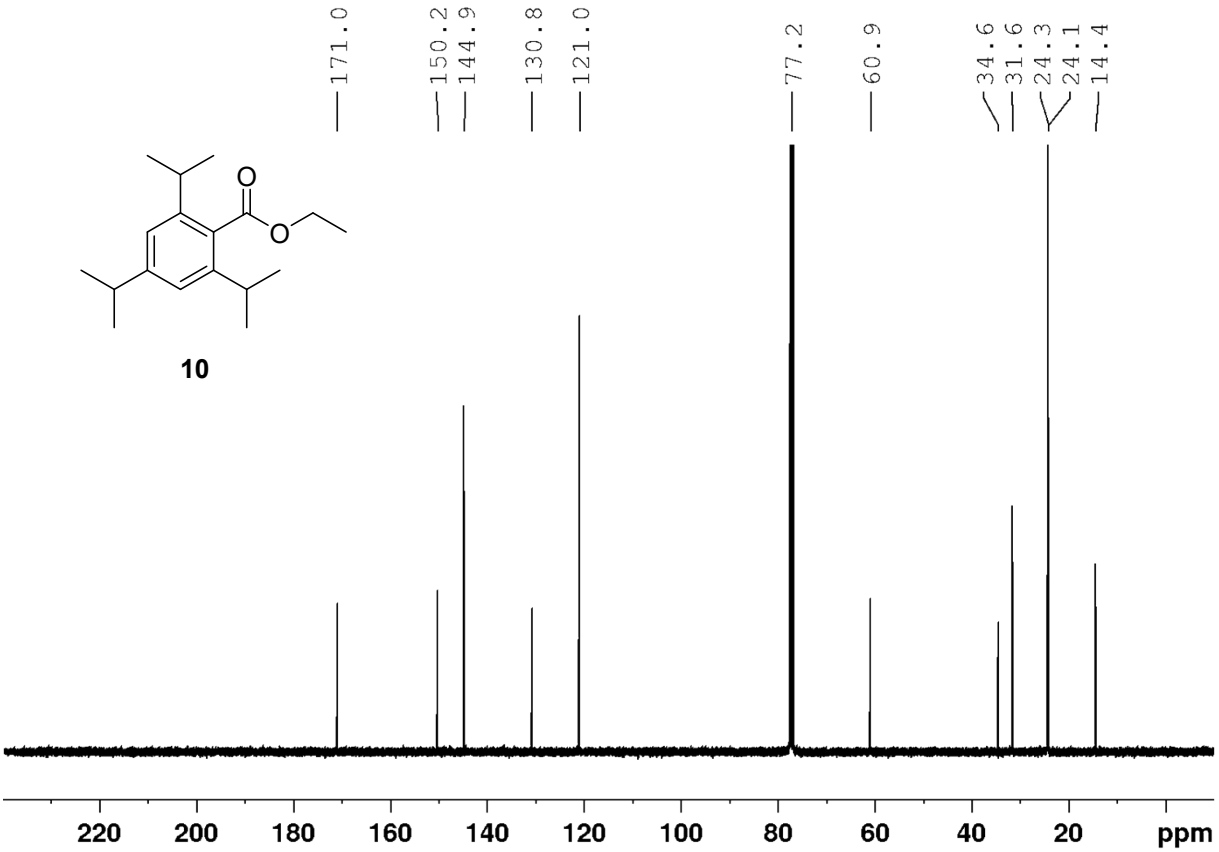

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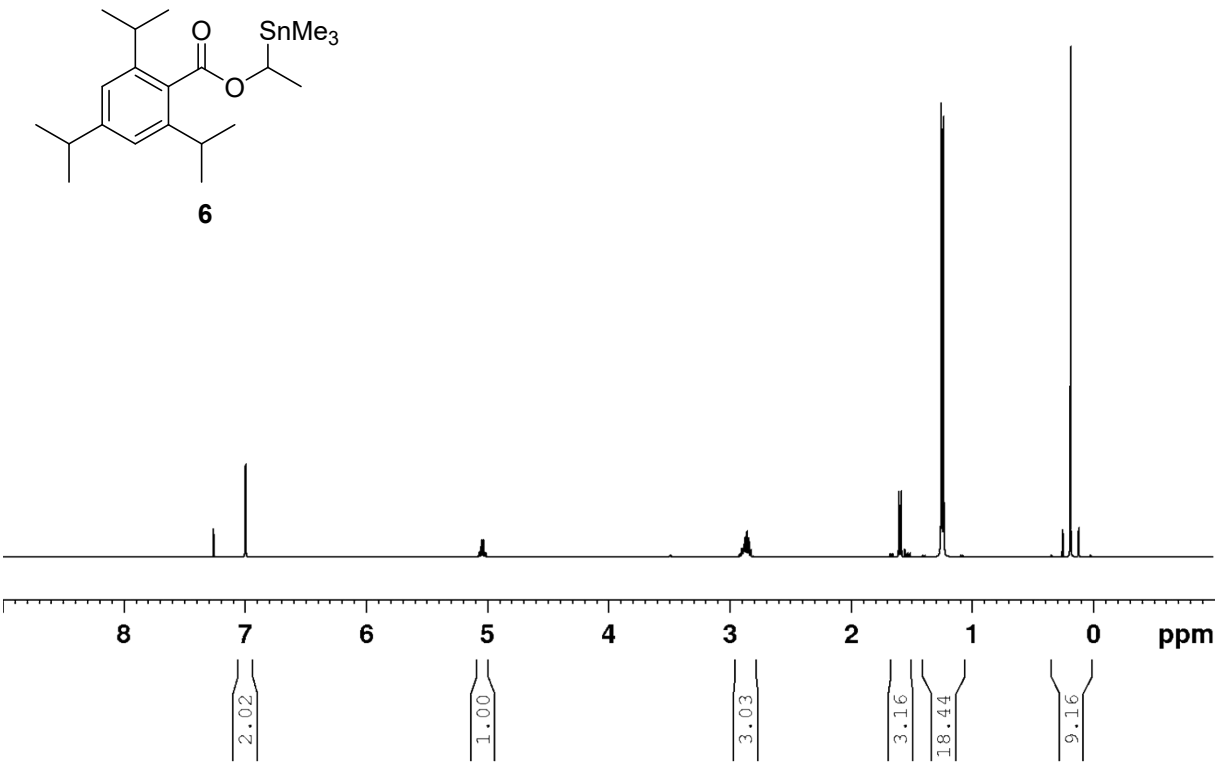

6

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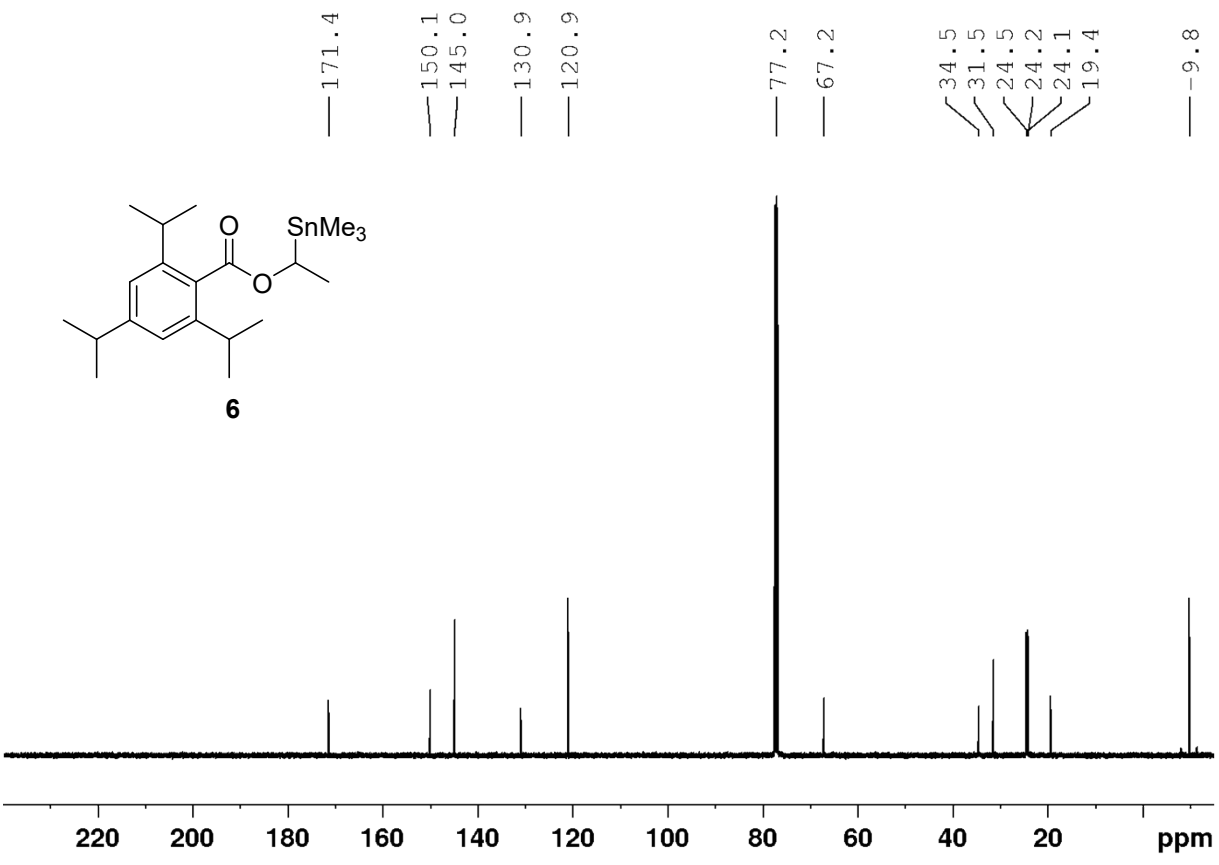

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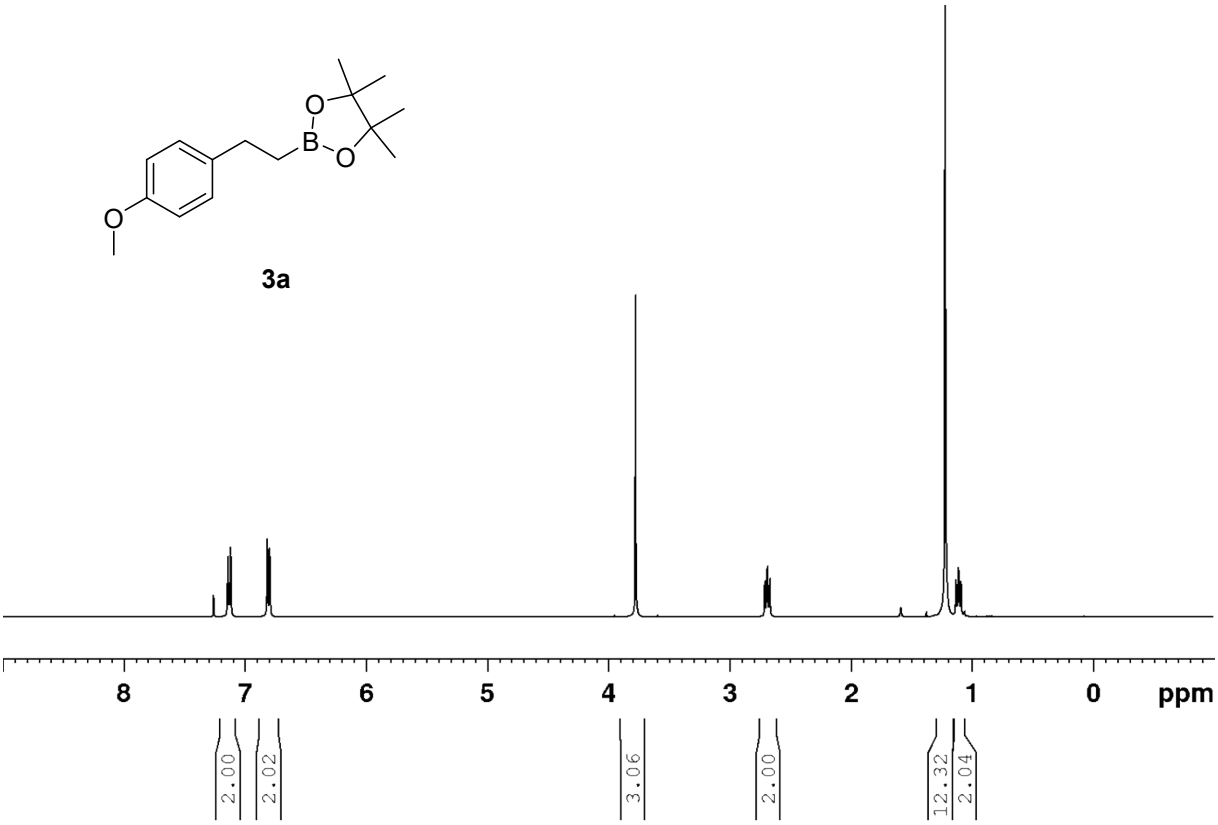

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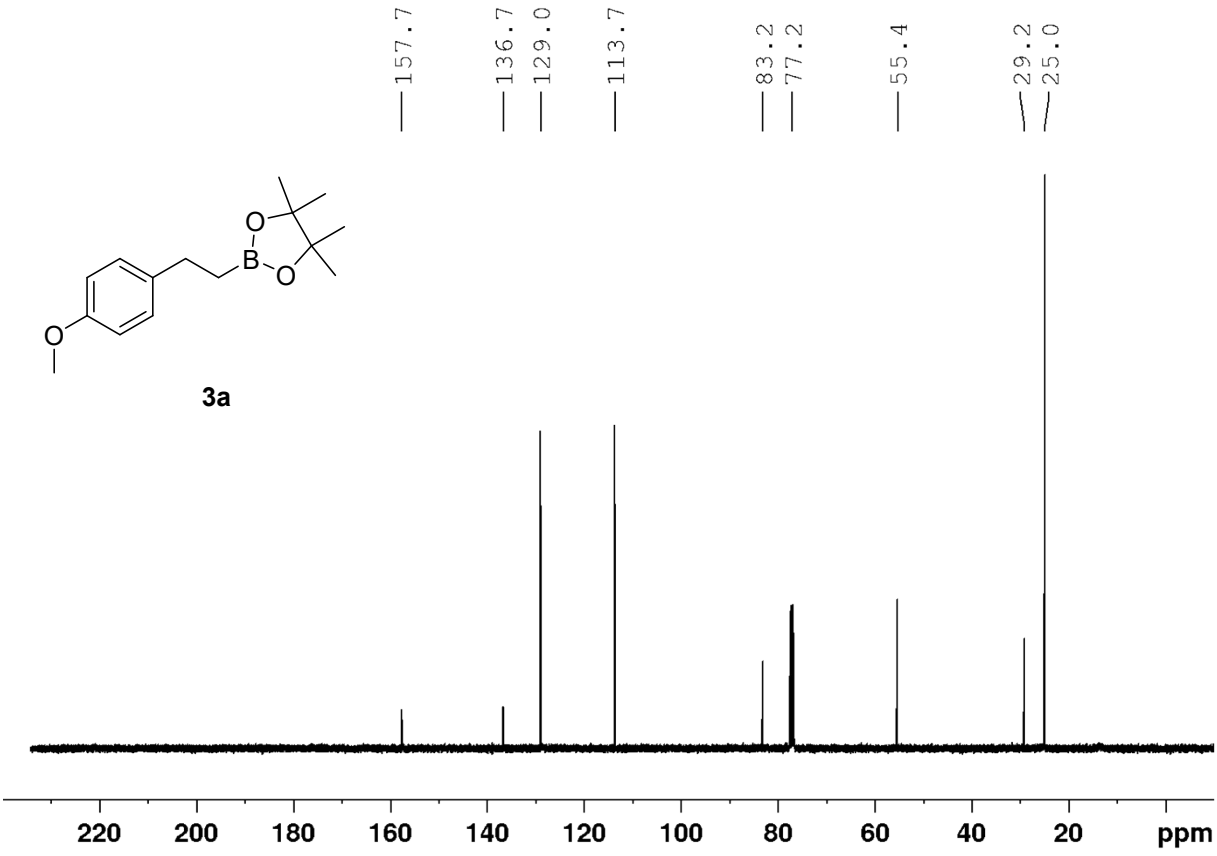

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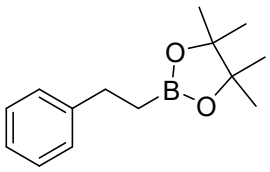

3b

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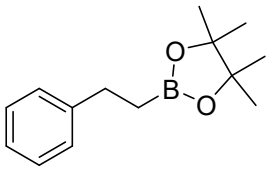

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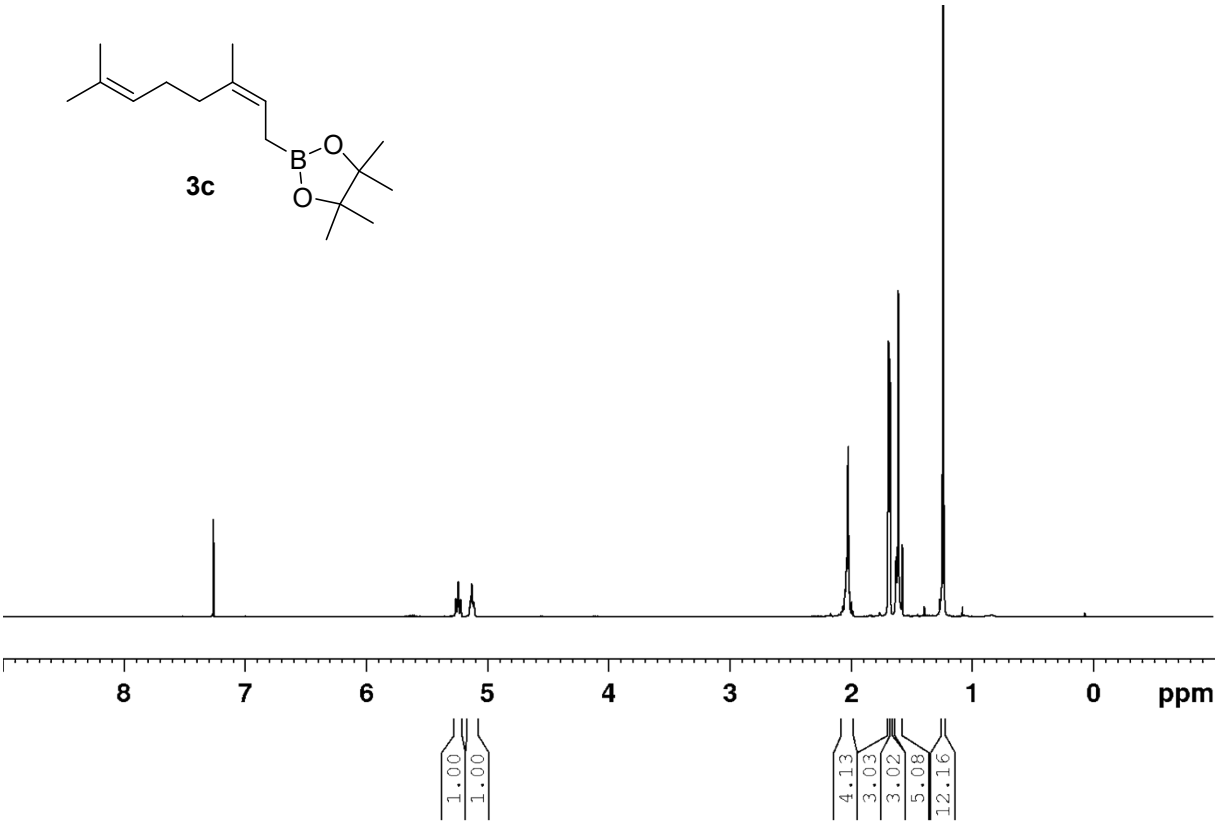

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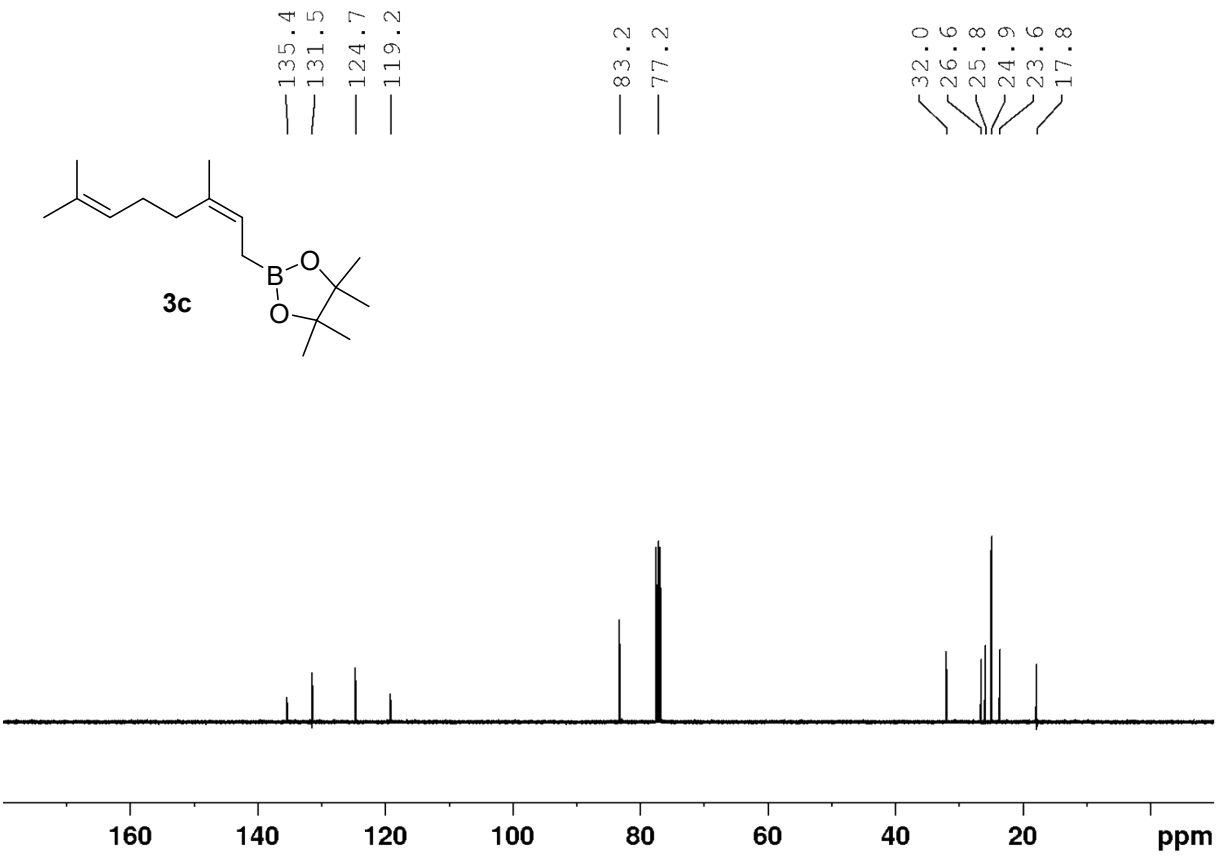

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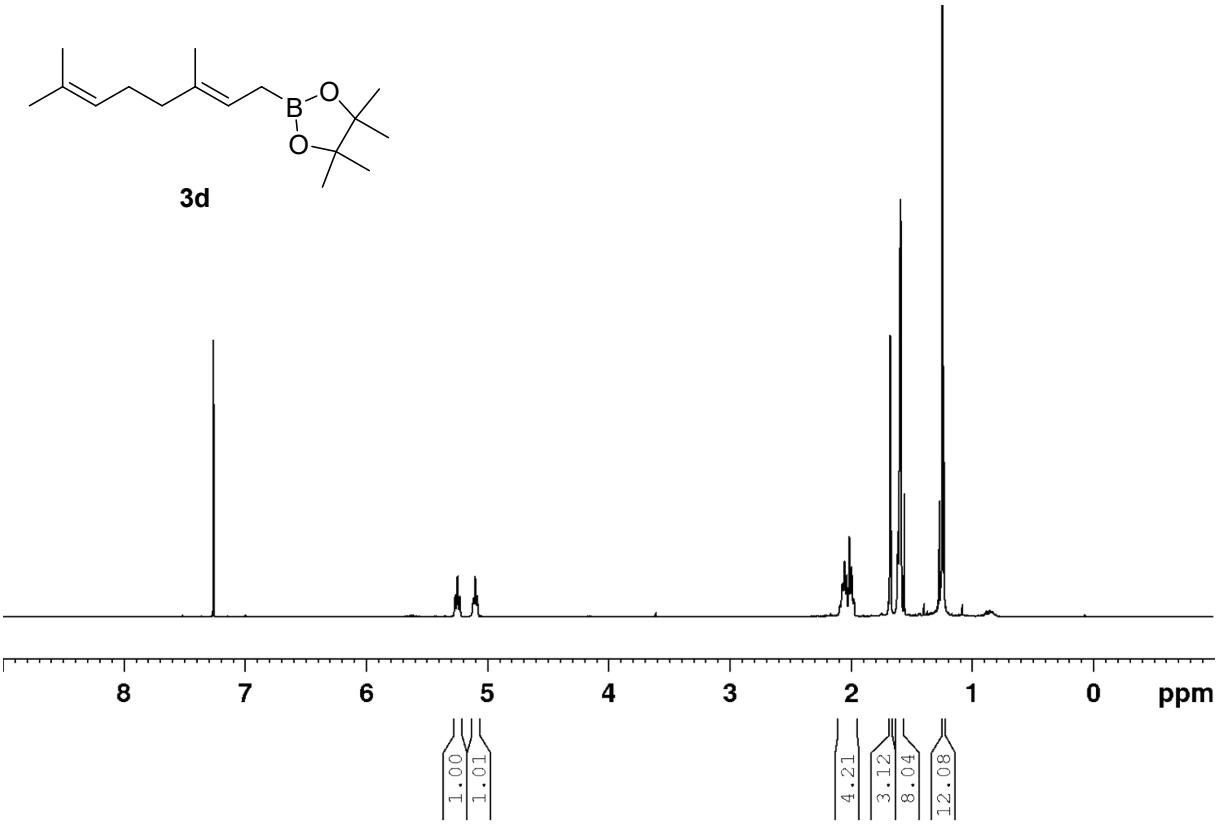

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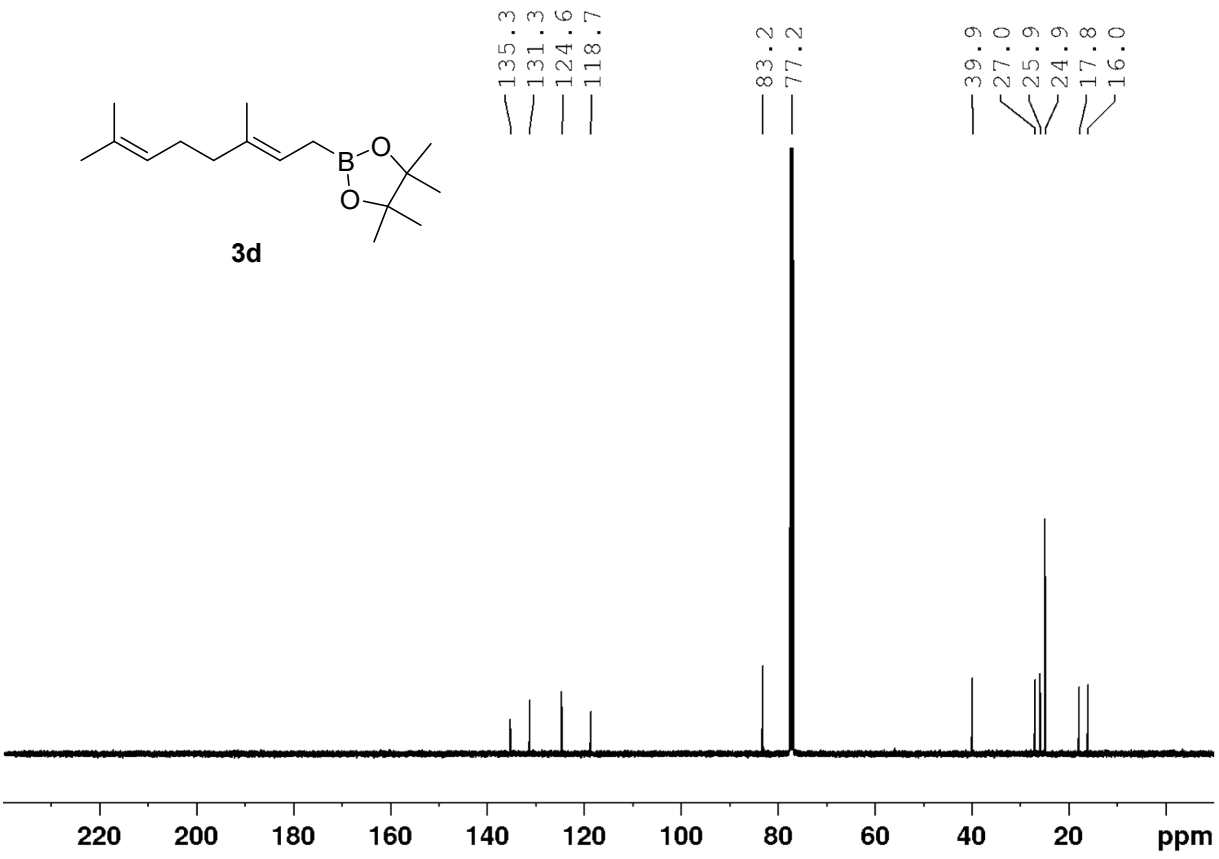

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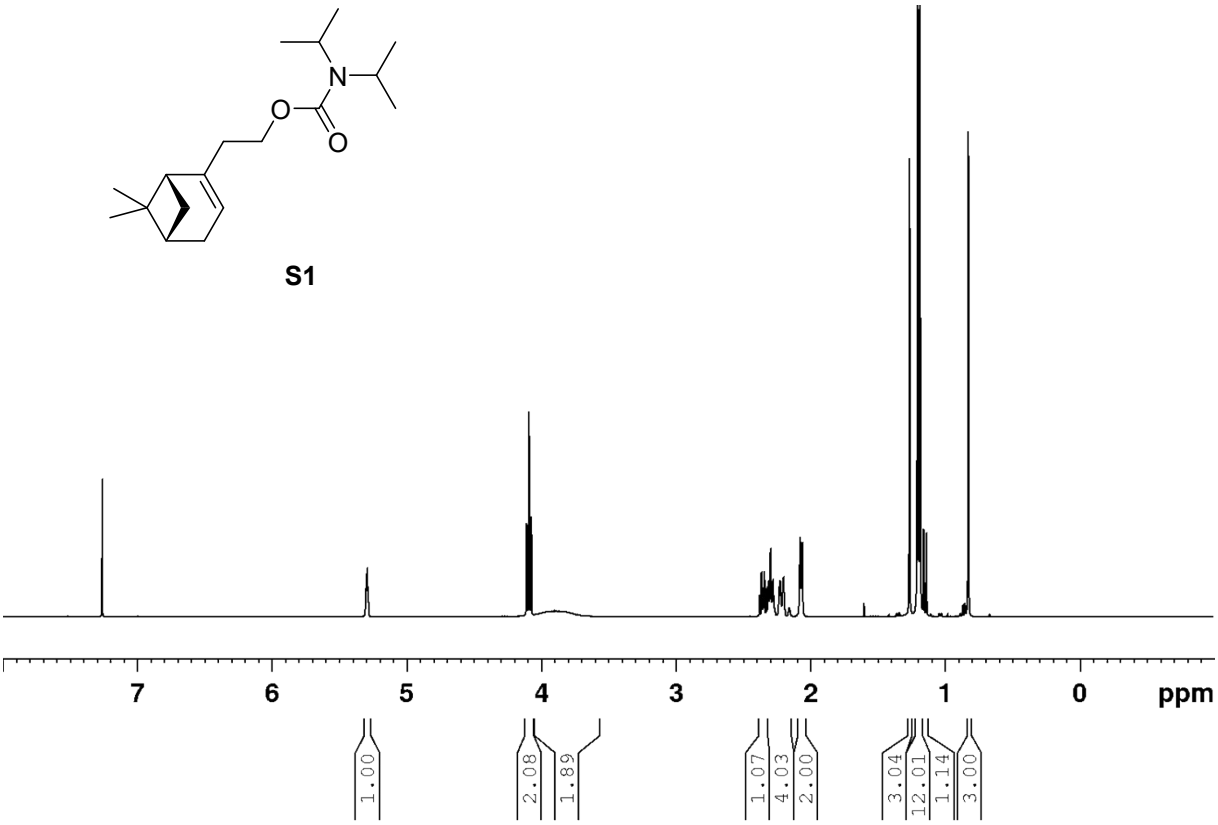

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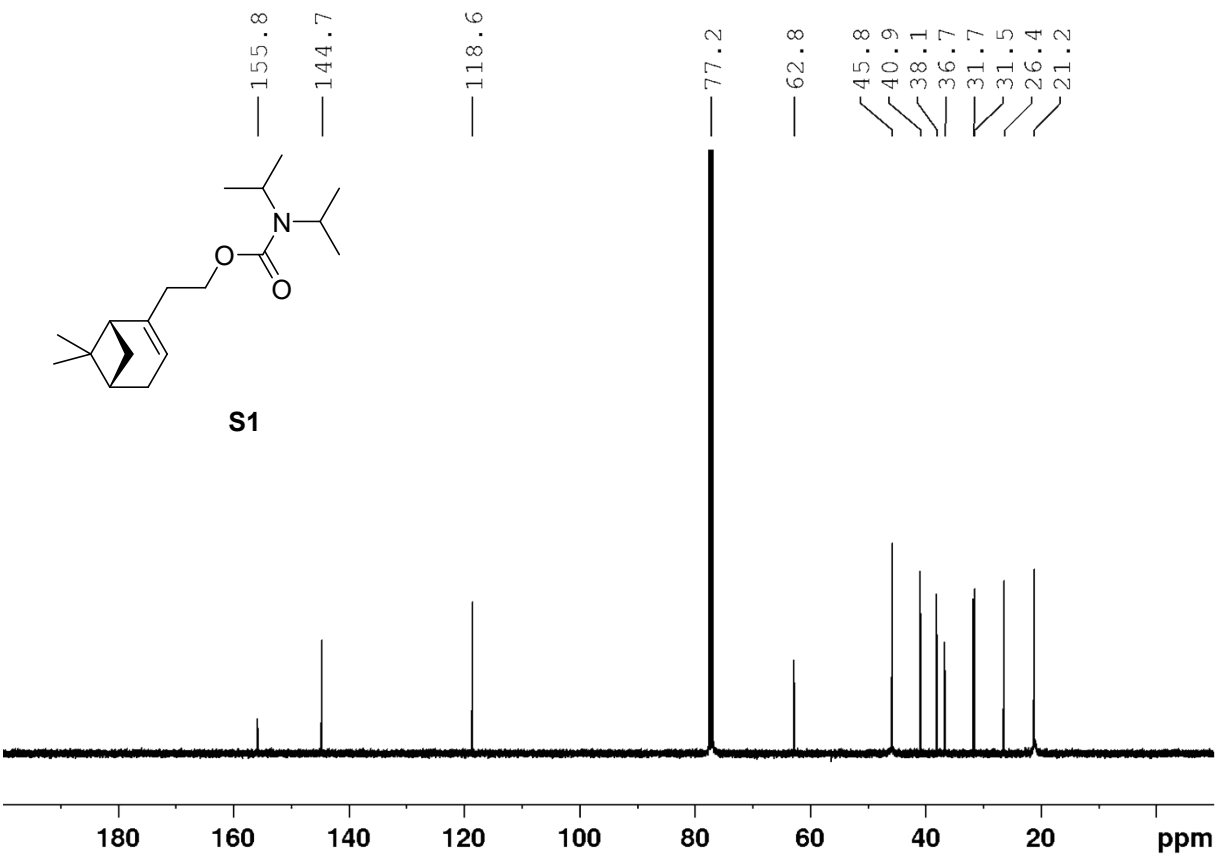

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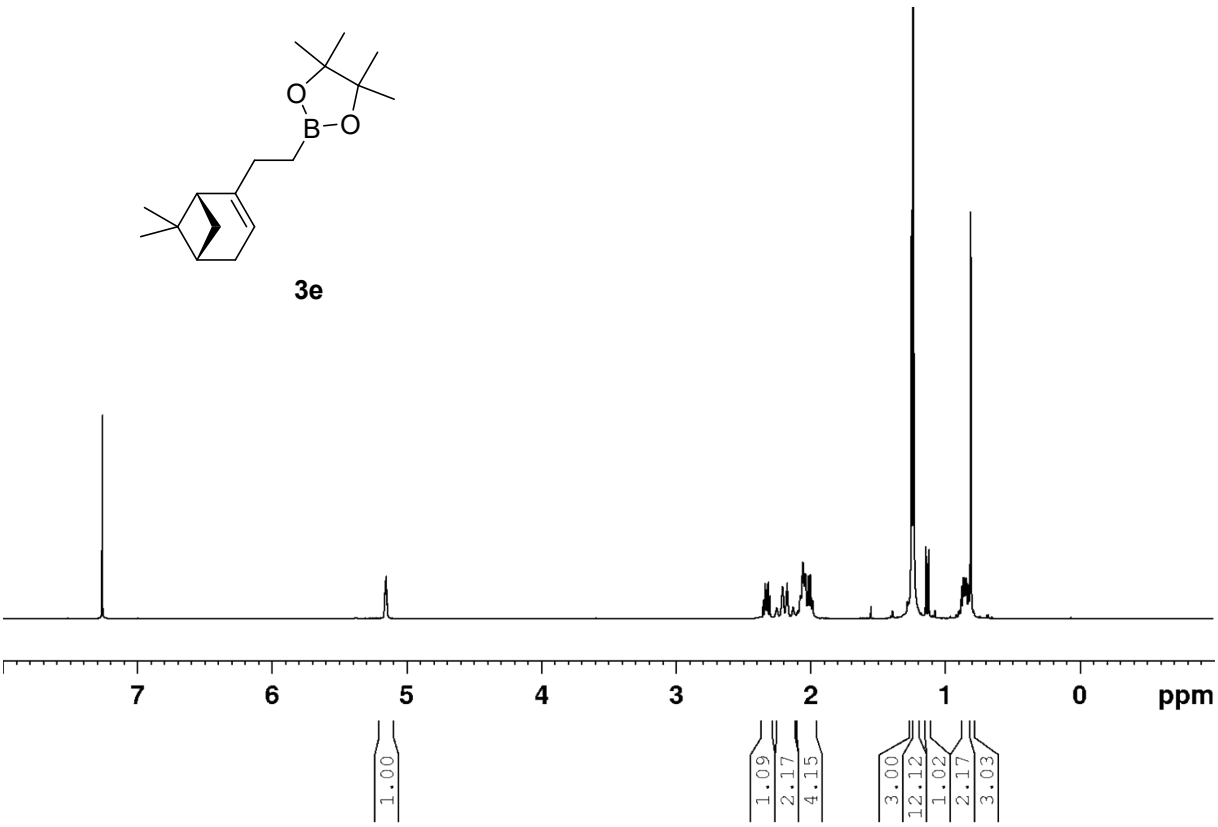

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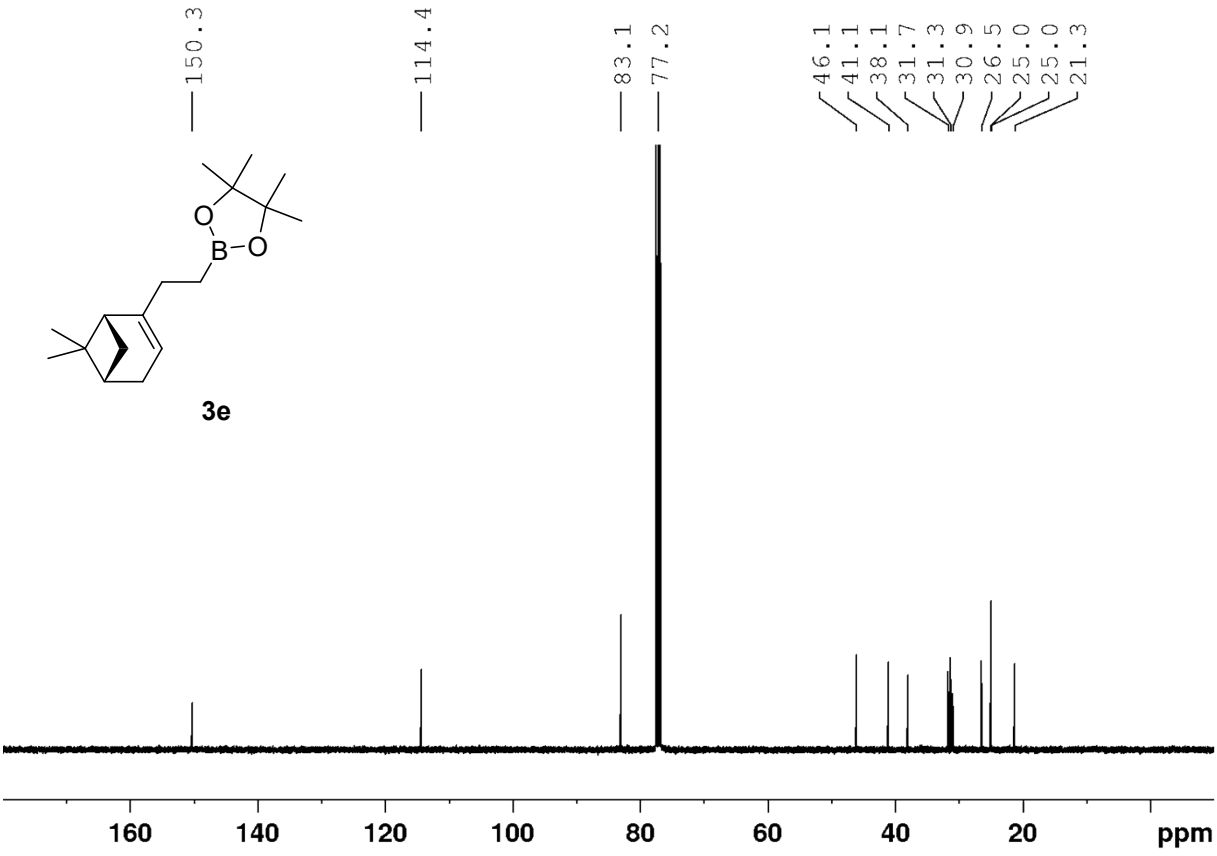

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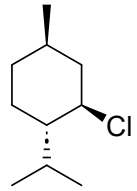

S2

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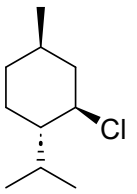

S2

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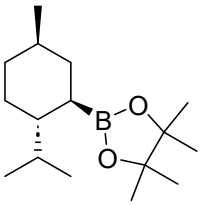

3f

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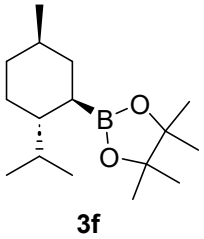

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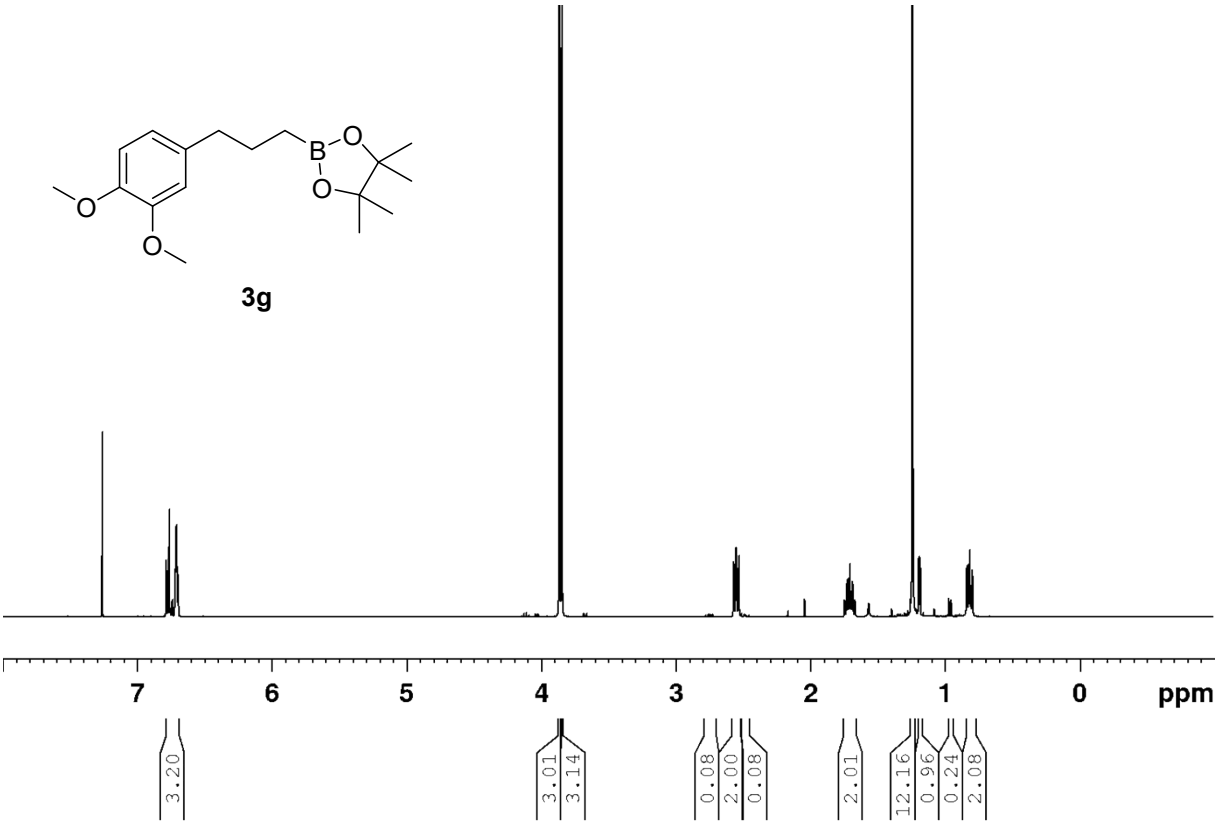

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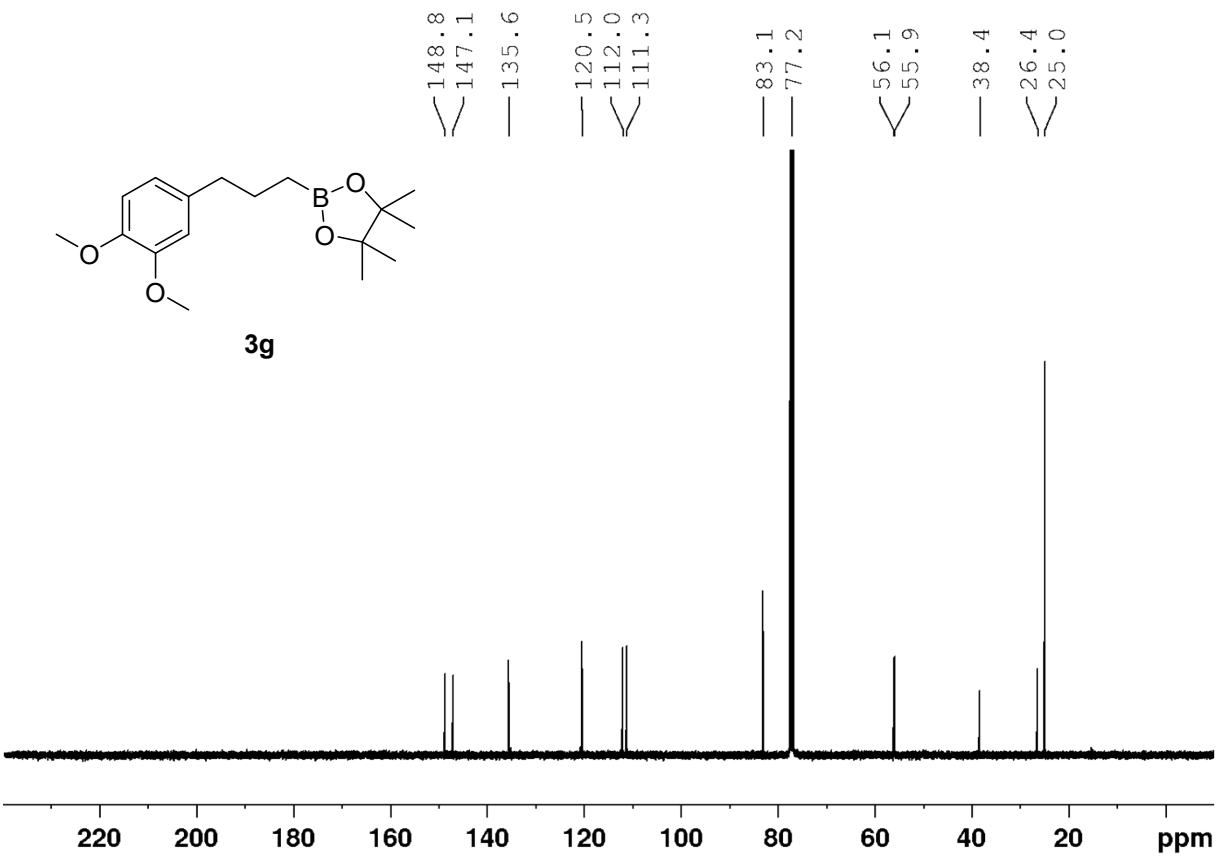

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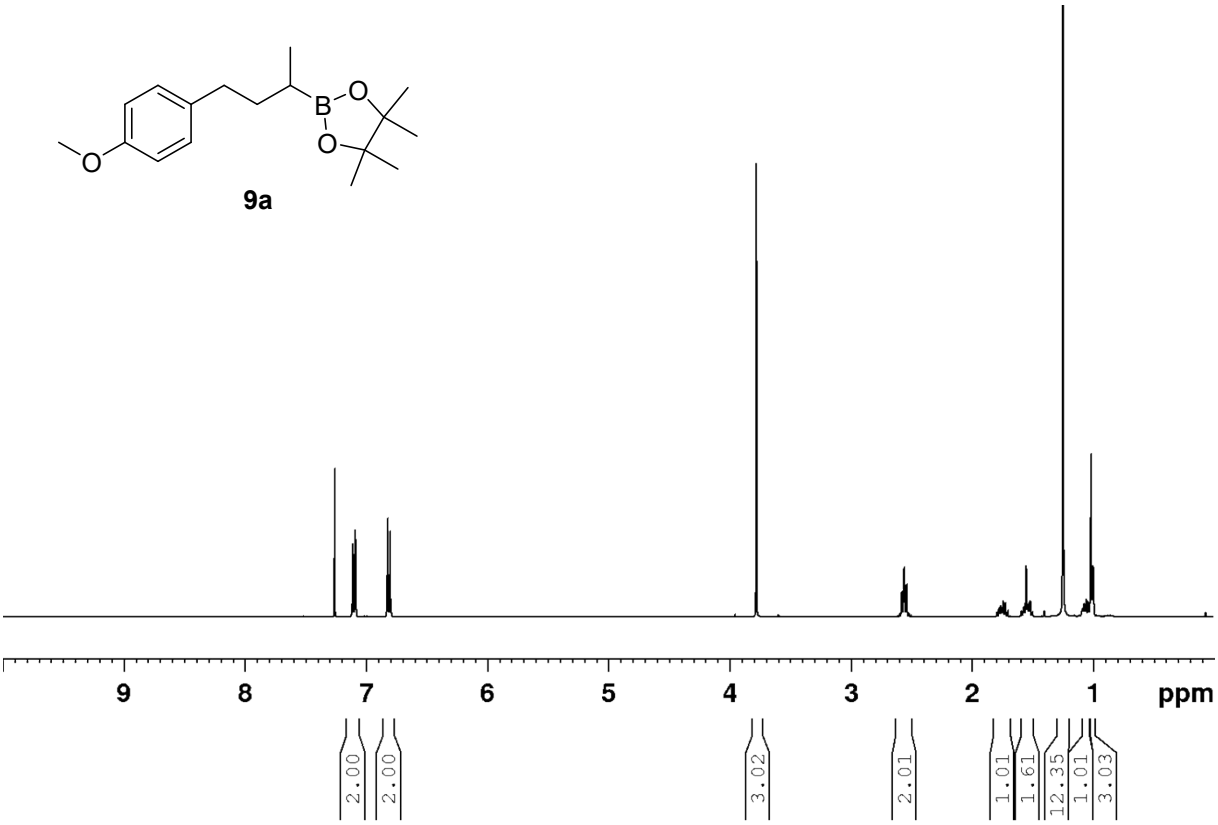

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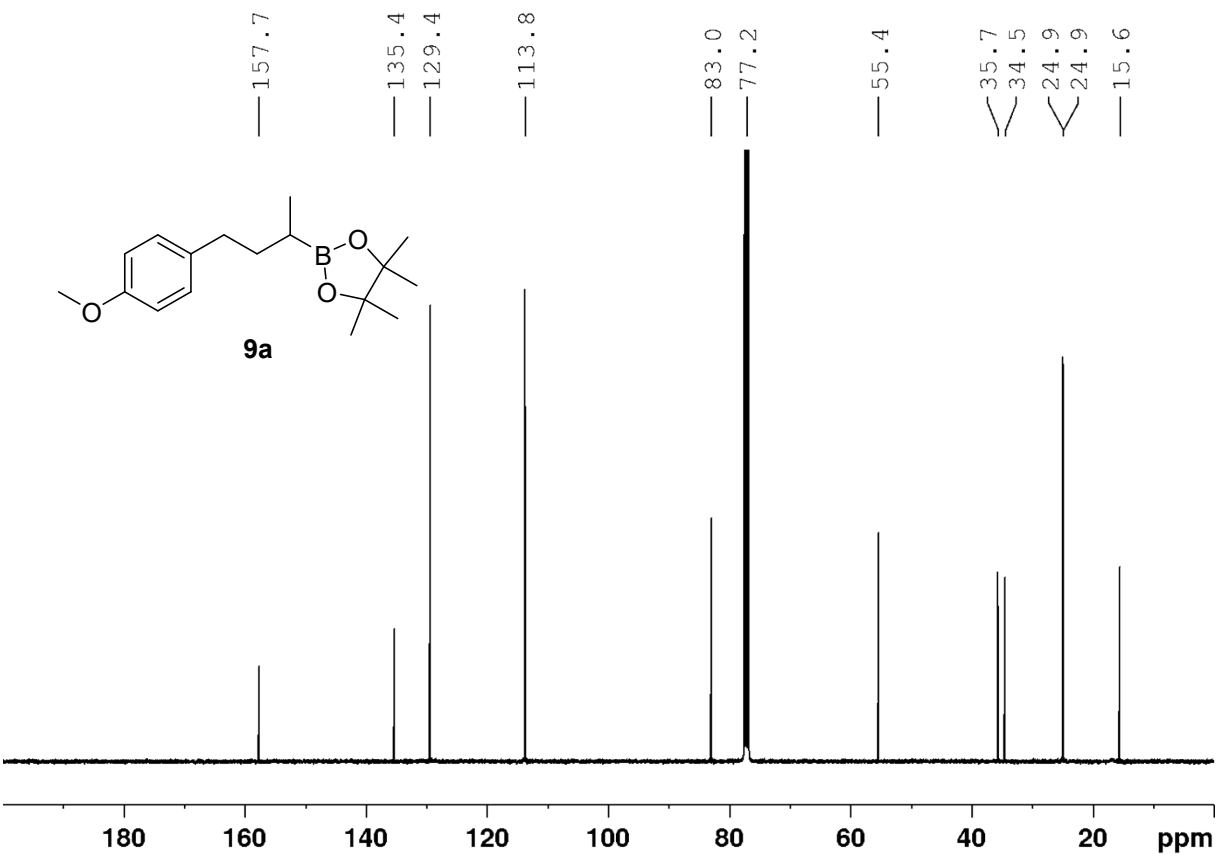

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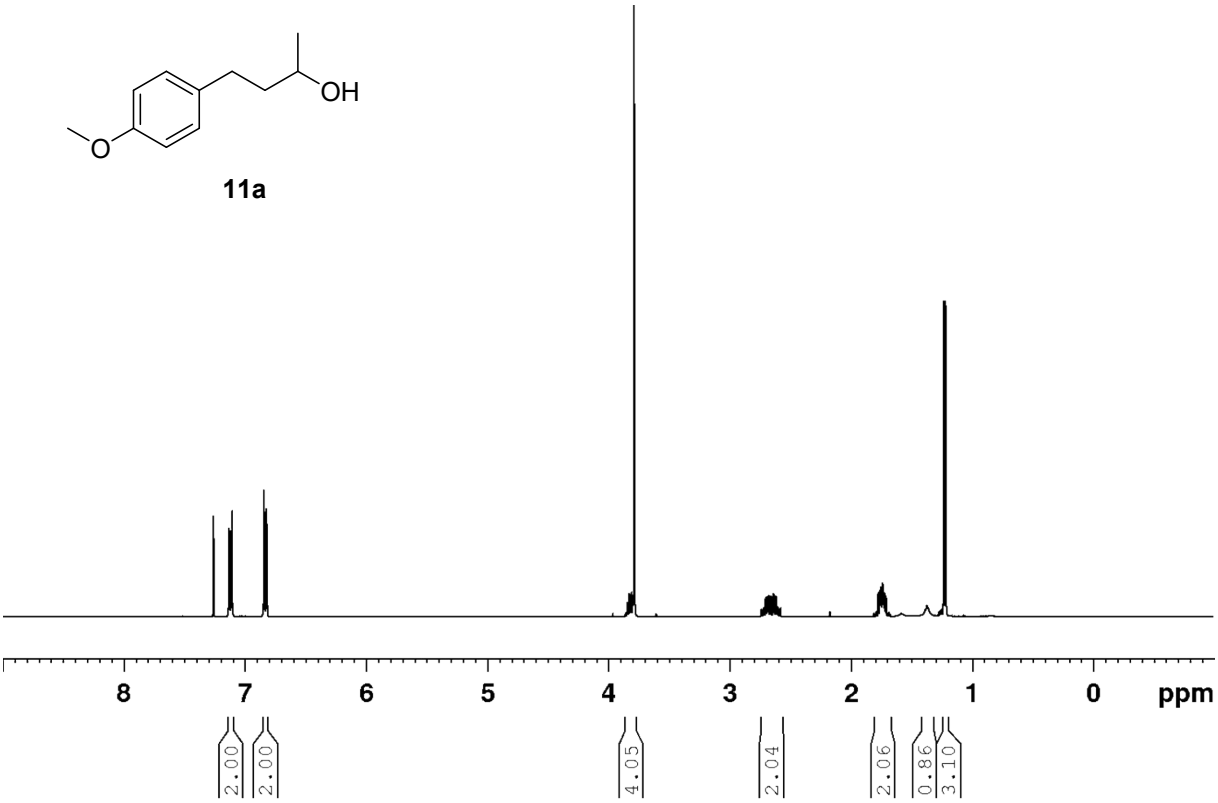
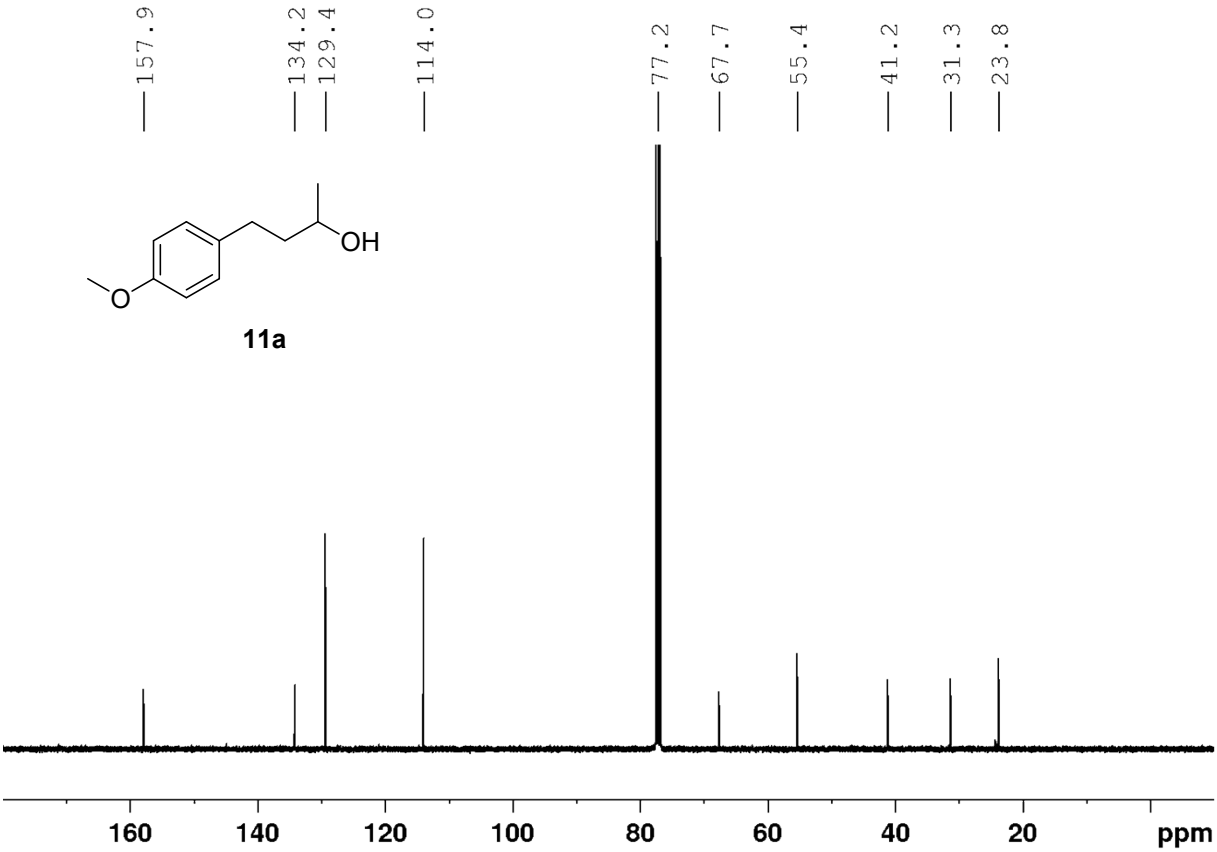
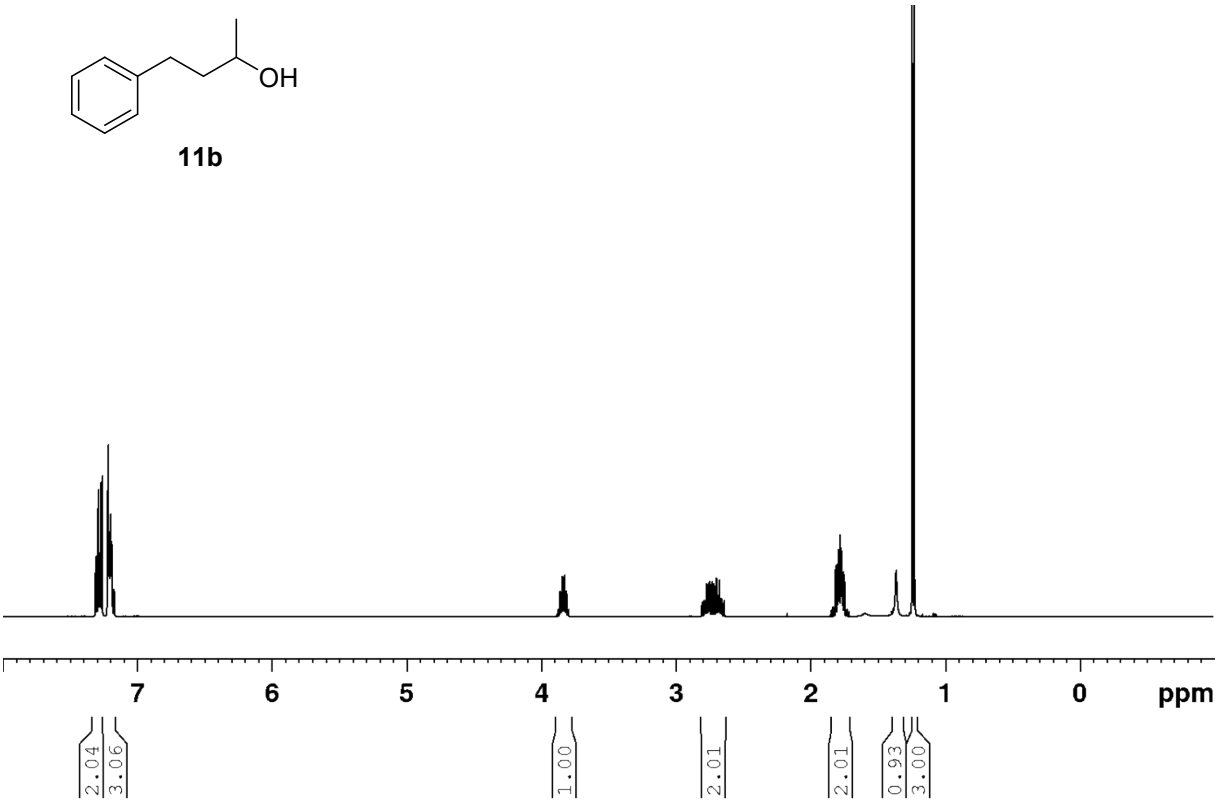


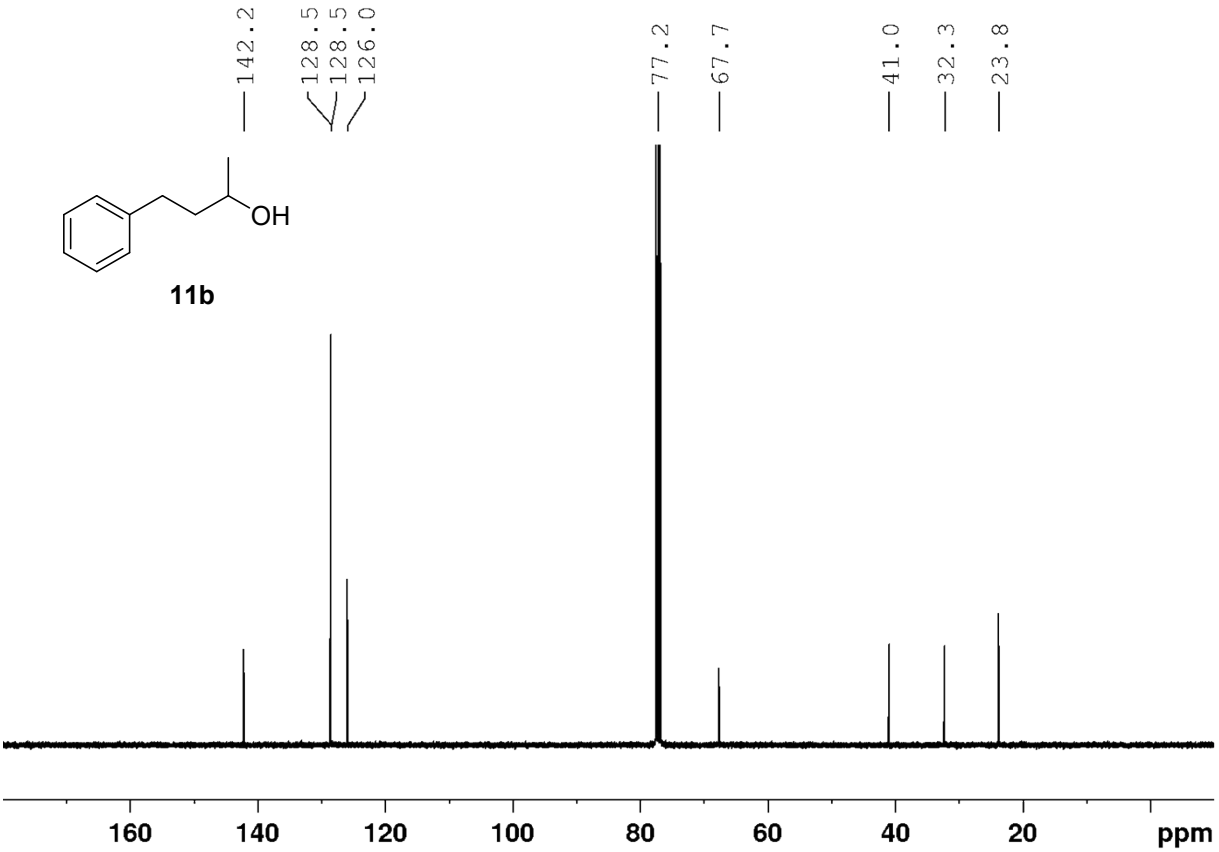
^{13}C-NMR (101 MHz, $CDCl_3$)



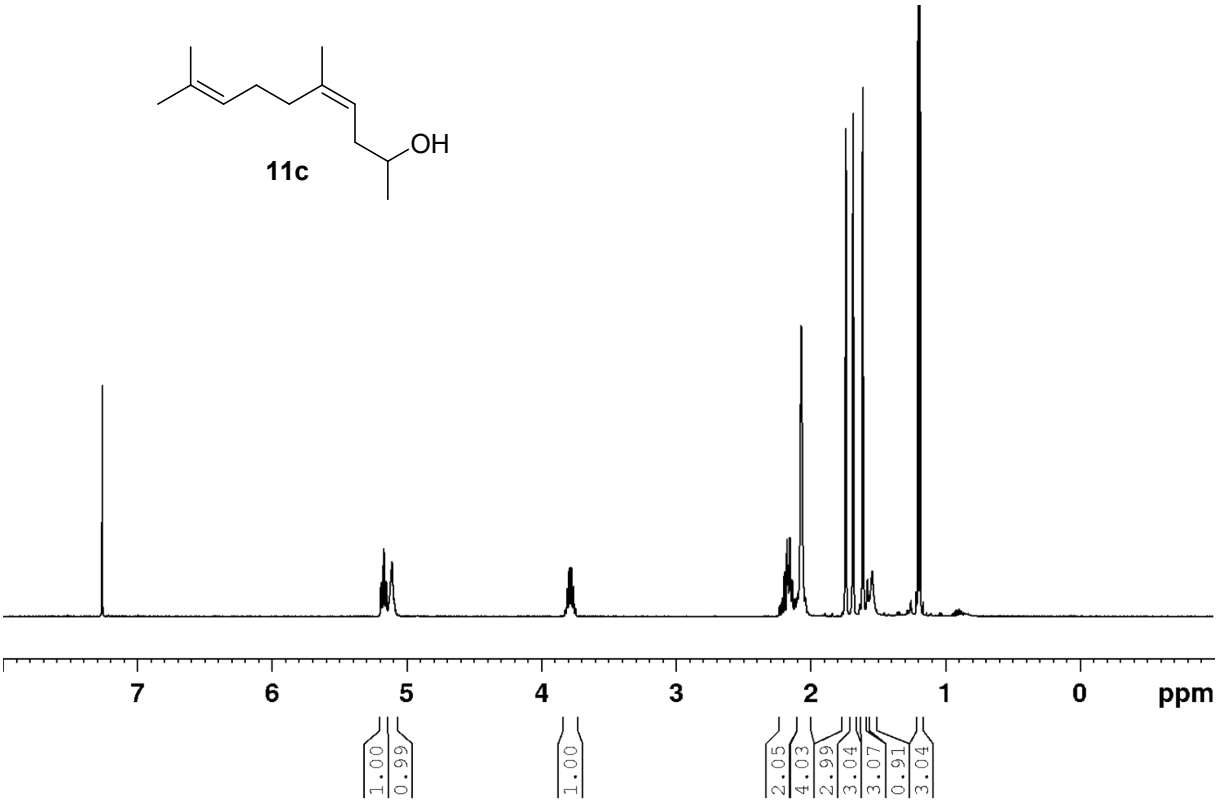
^{1}H-NMR (400 MHz, $CDCl_3$)



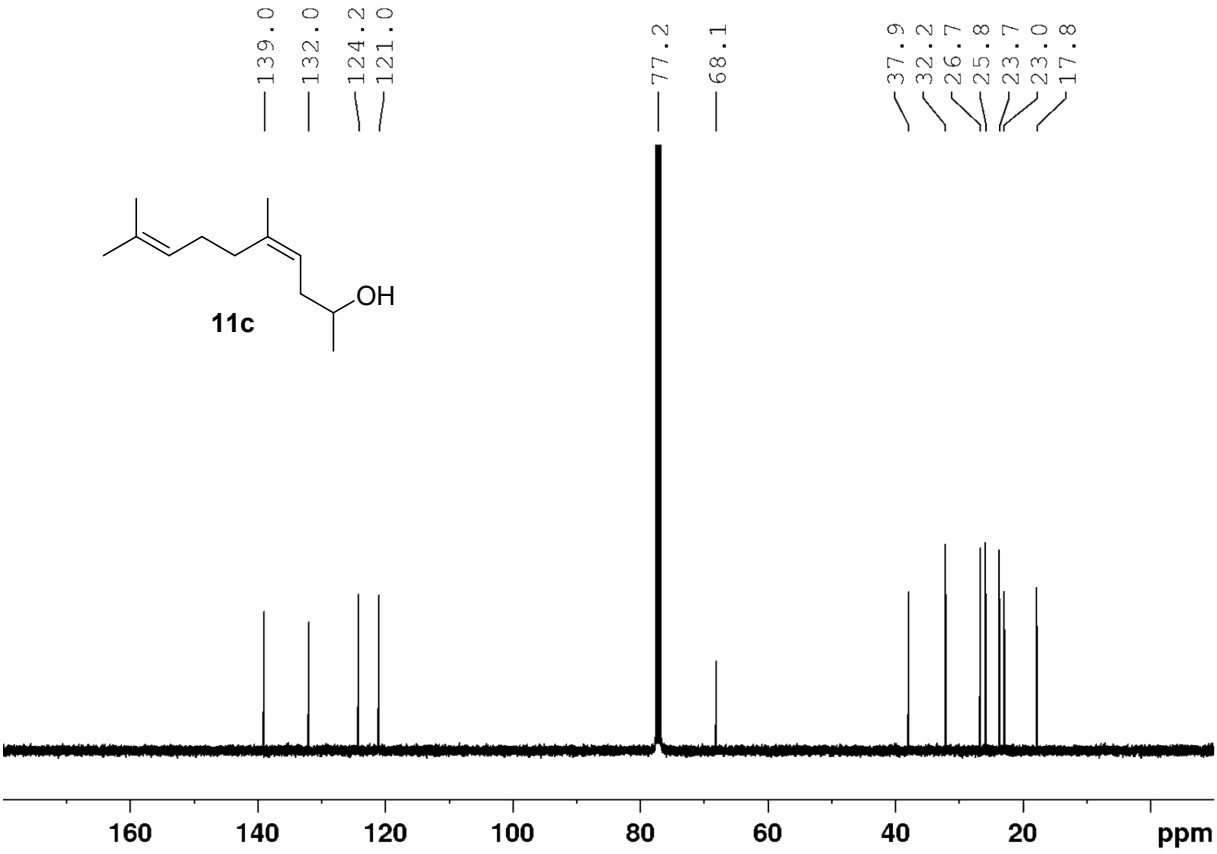
^{13}C-NMR (101 MHz, $CDCl_3$)



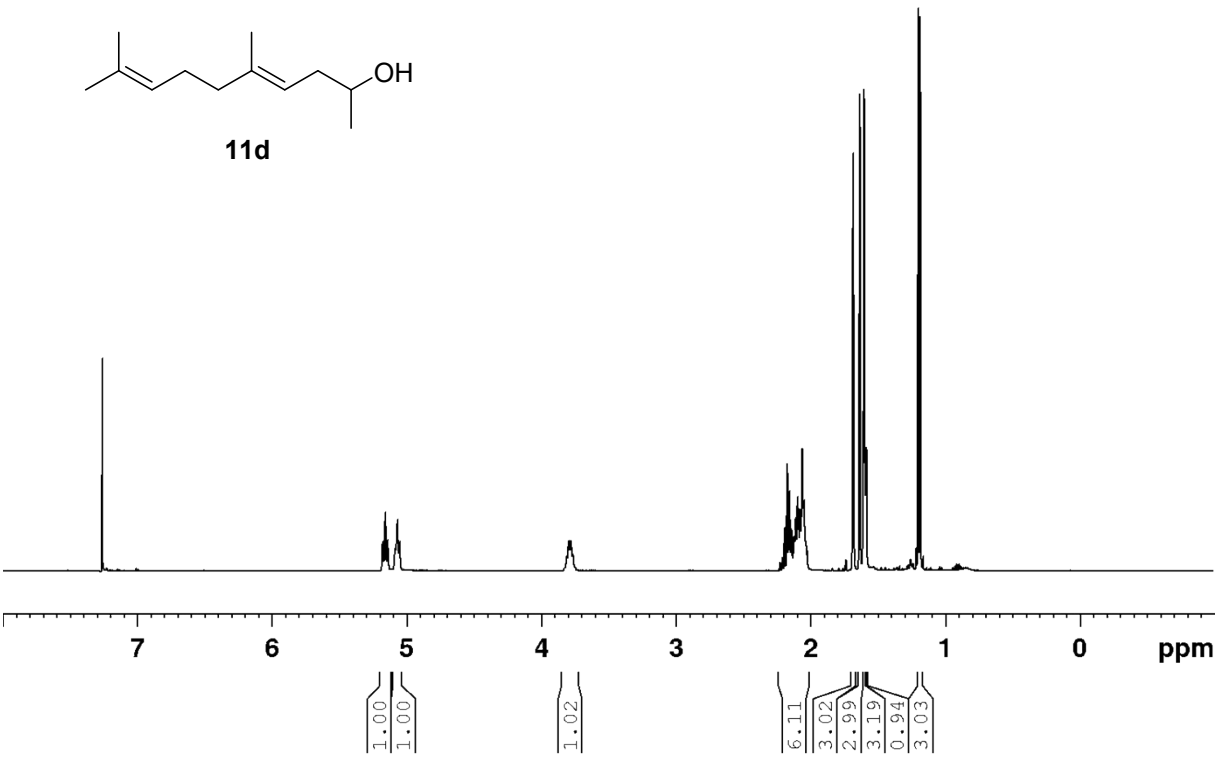
^{1}H-NMR (400 MHz, $CDCl_3$)



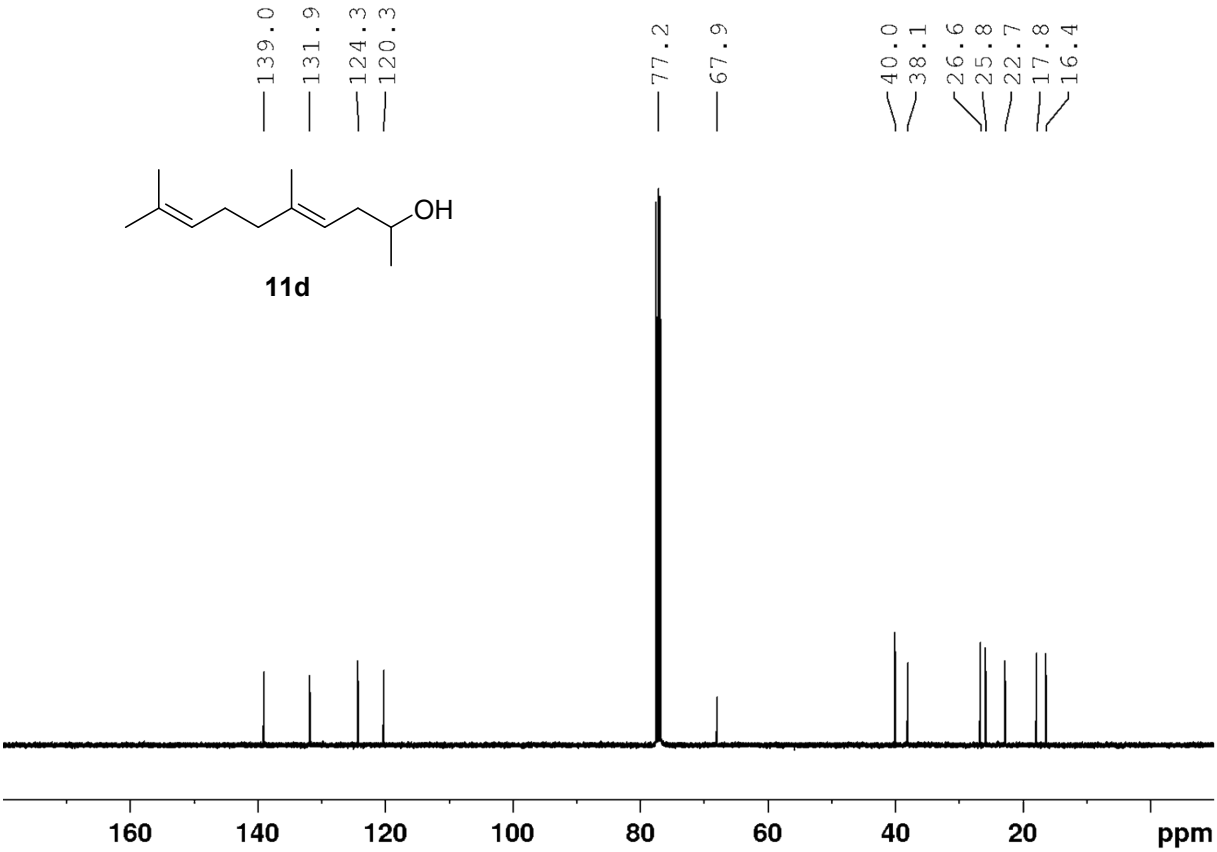
^{13}C-NMR (101 MHz, $CDCl_3$)



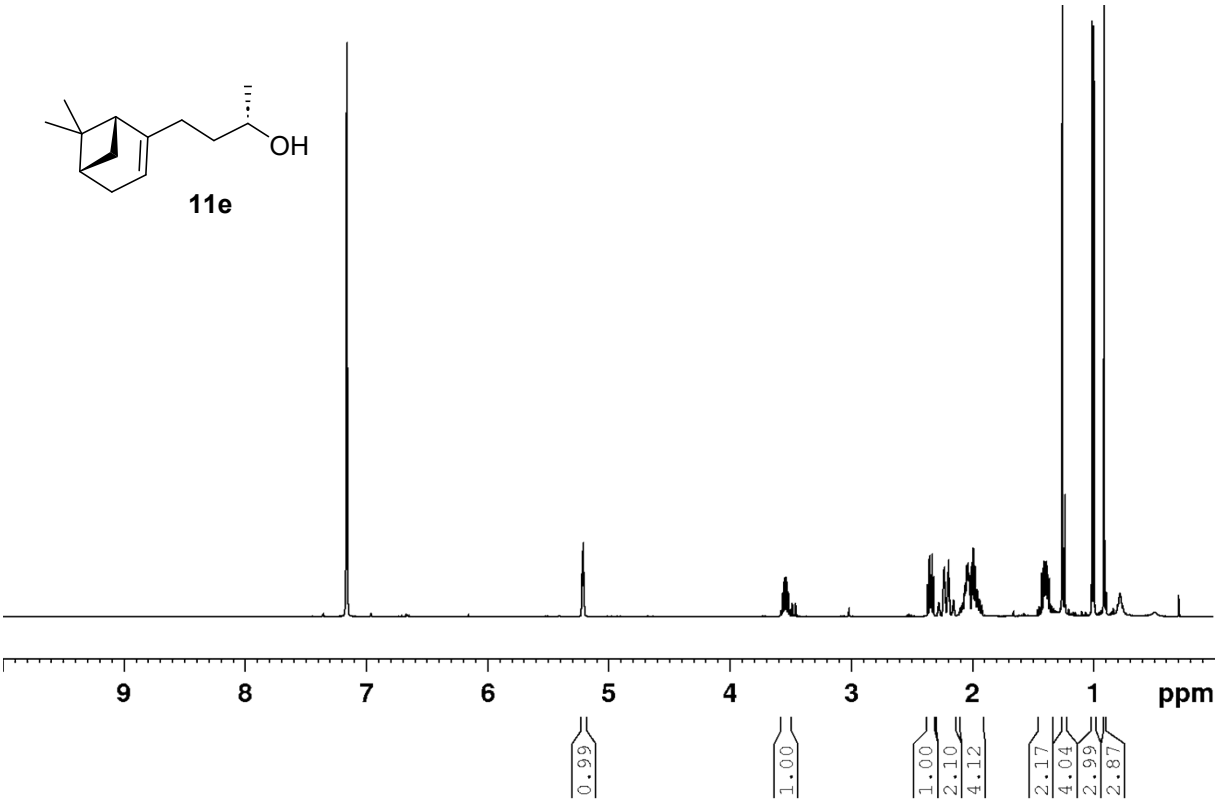
^{1}H-NMR (400 MHz, $CDCl_3$)



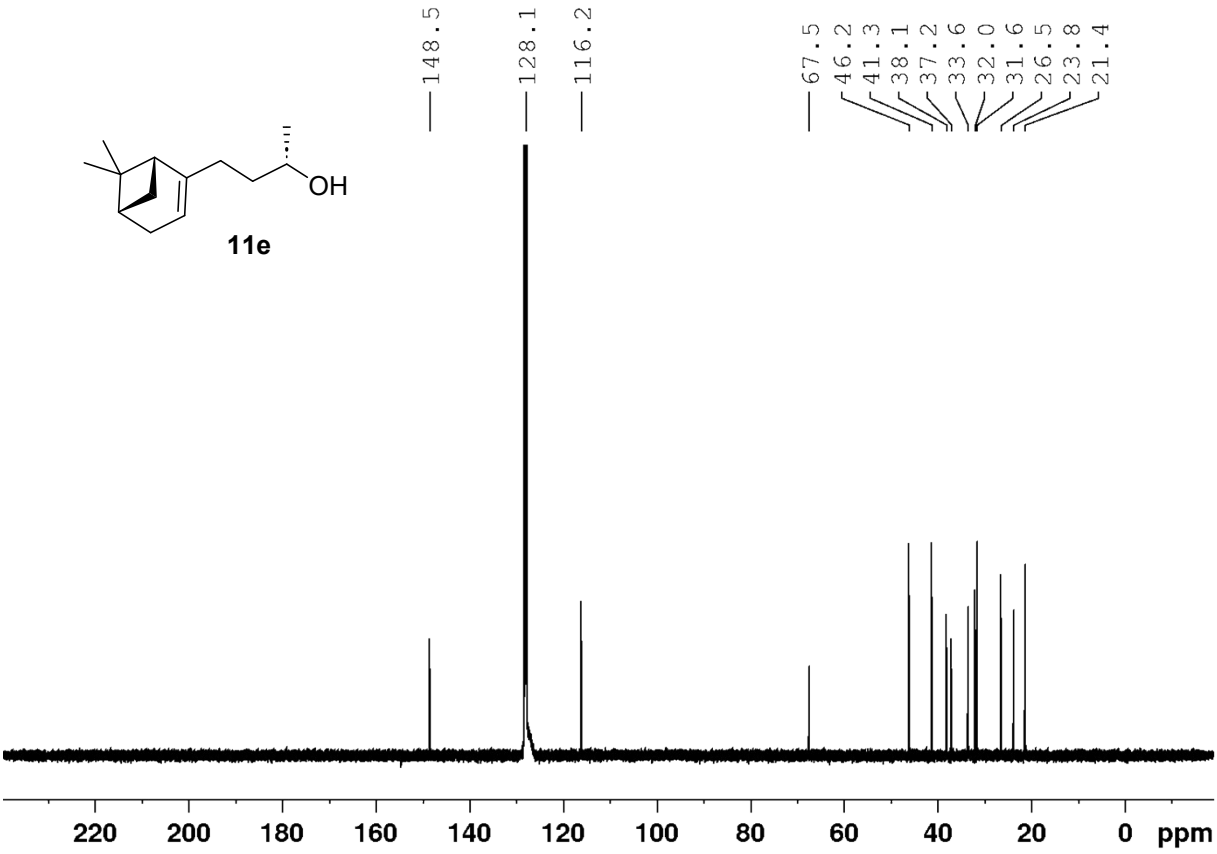
^{13}C-NMR (101 MHz, $CDCl_3$)



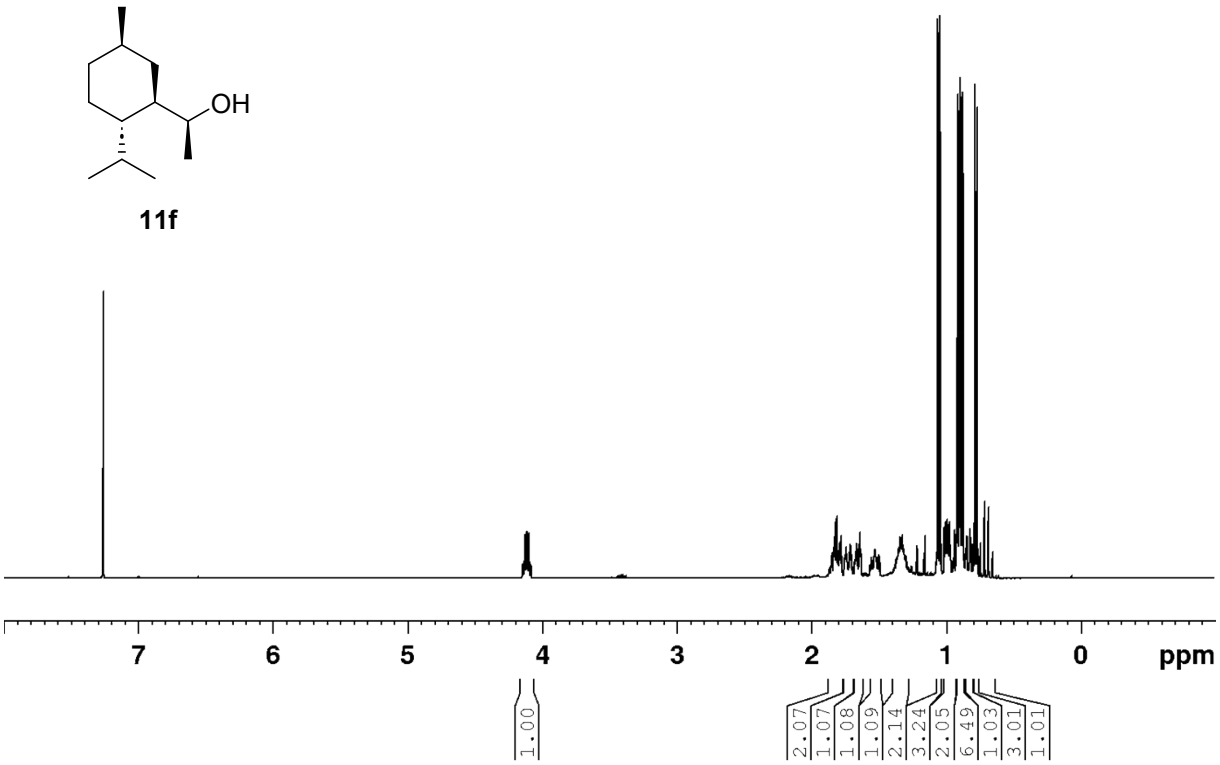
^{1}H-NMR (400 MHz, C_6D_6)



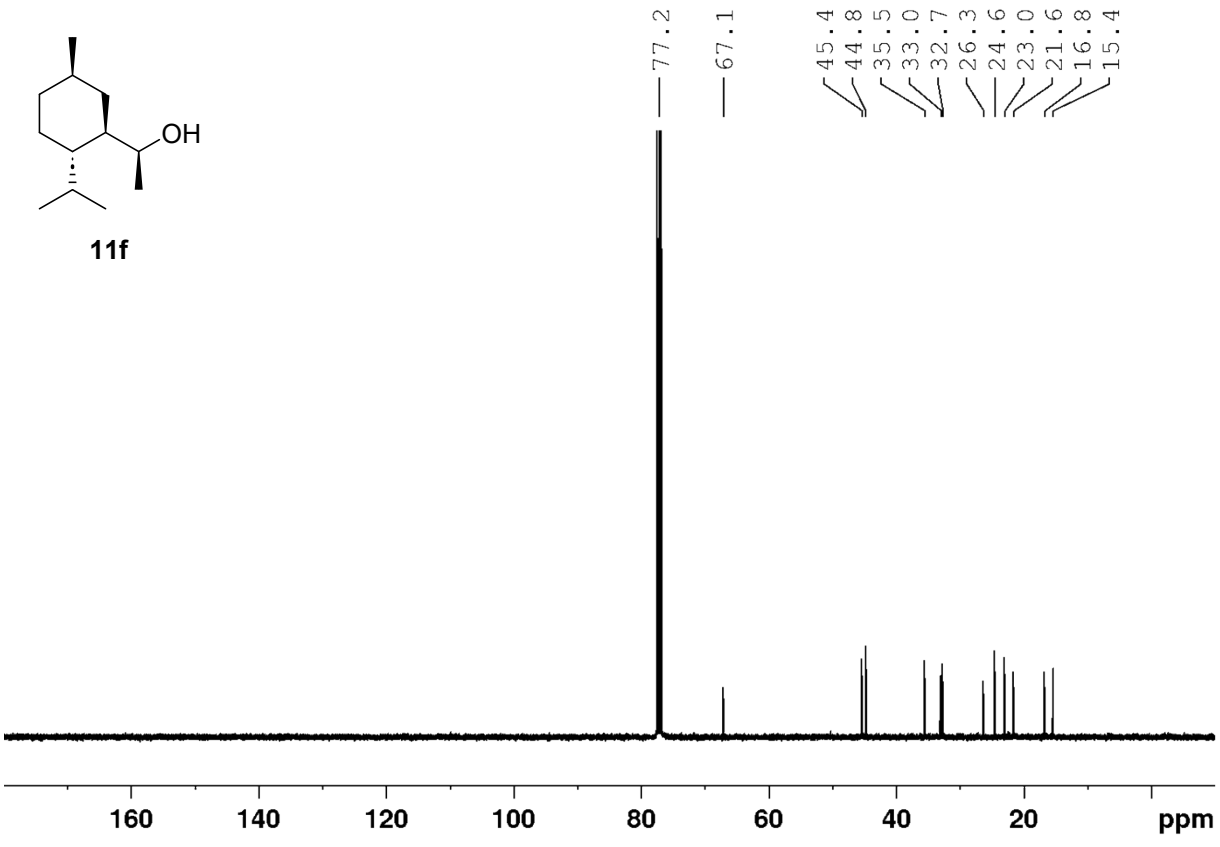
^{13}C-NMR (101 MHz, C_6D_6))



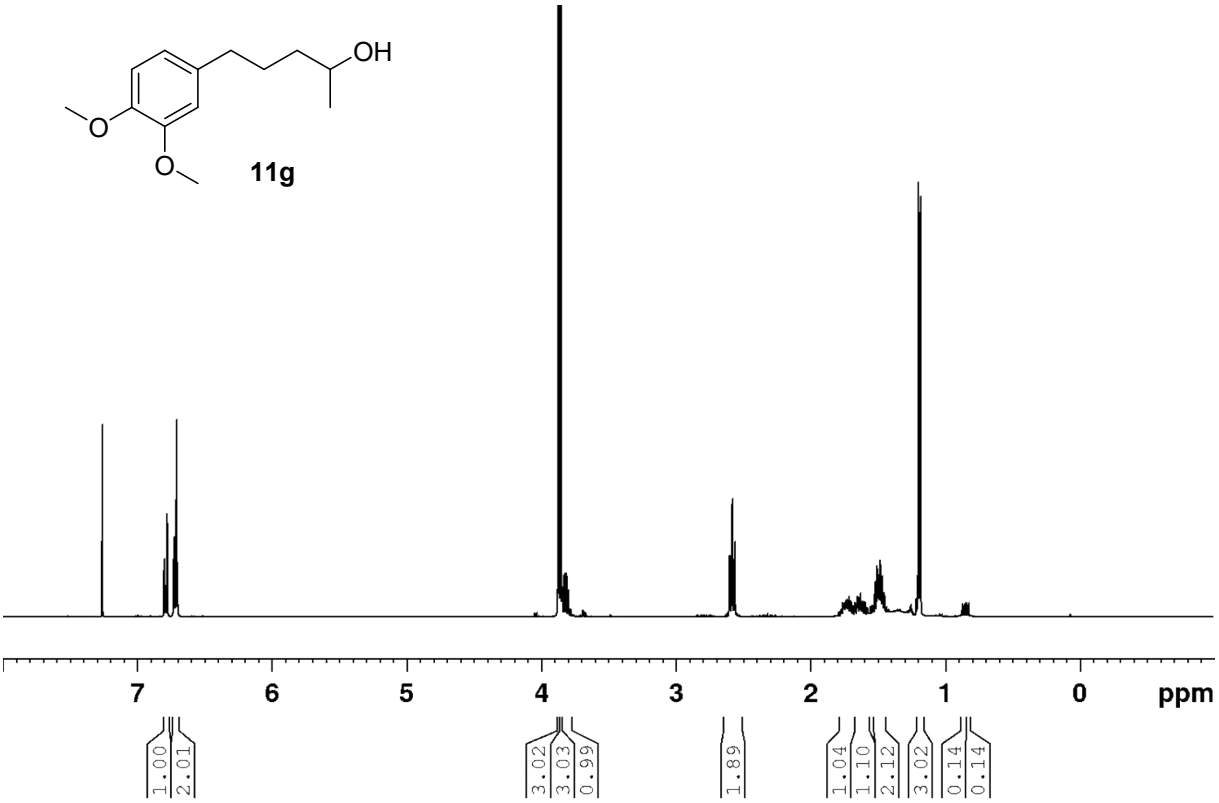
^{1}H-NMR (400 MHz, $CDCl_3$)



^{13}C-NMR (101 MHz, $CDCl_3$)



^{1}H-NMR (400 MHz, $CDCl_3$)



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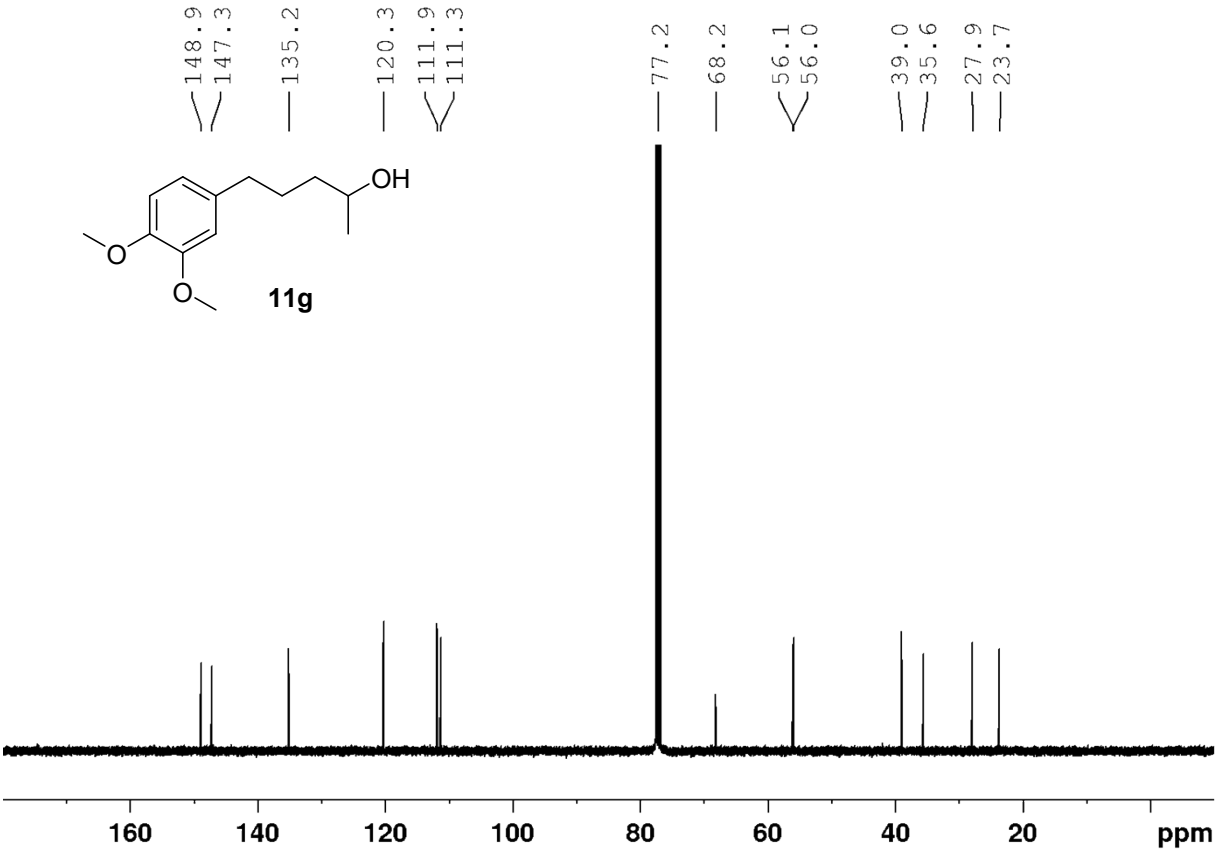
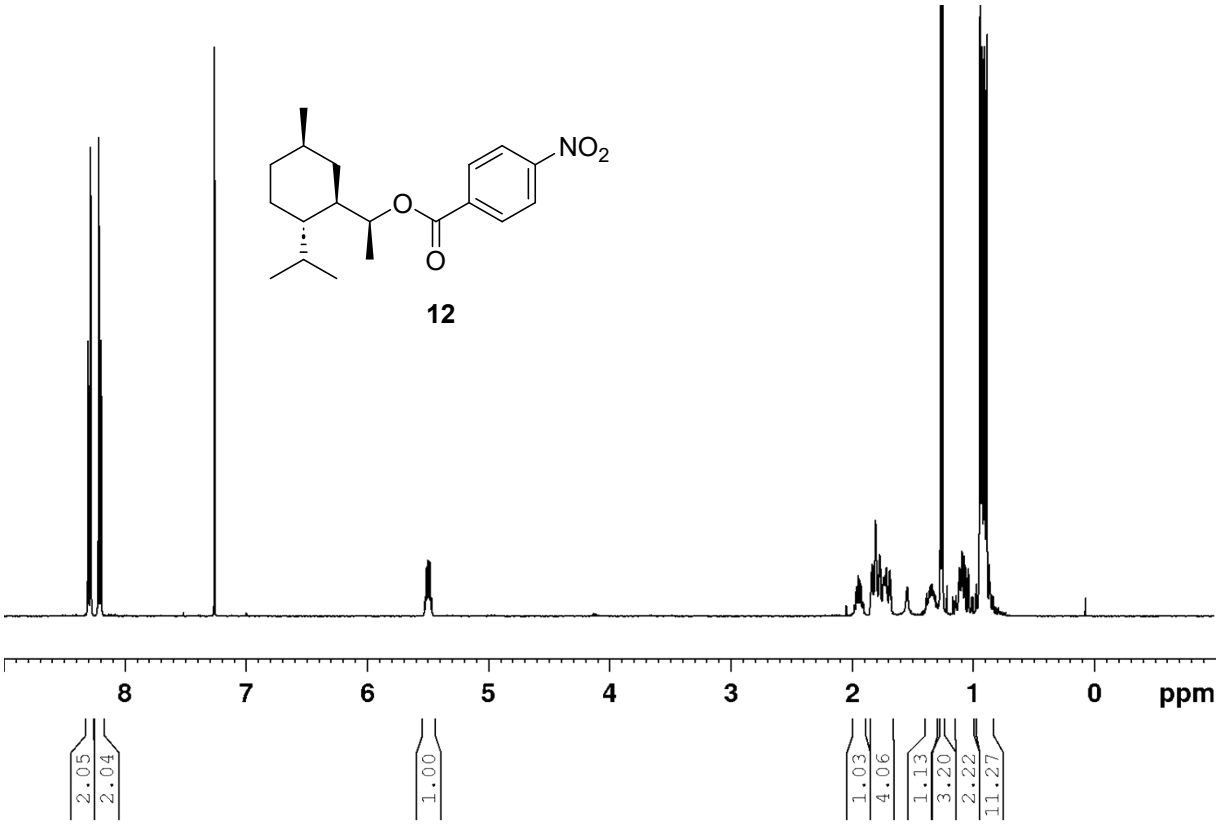
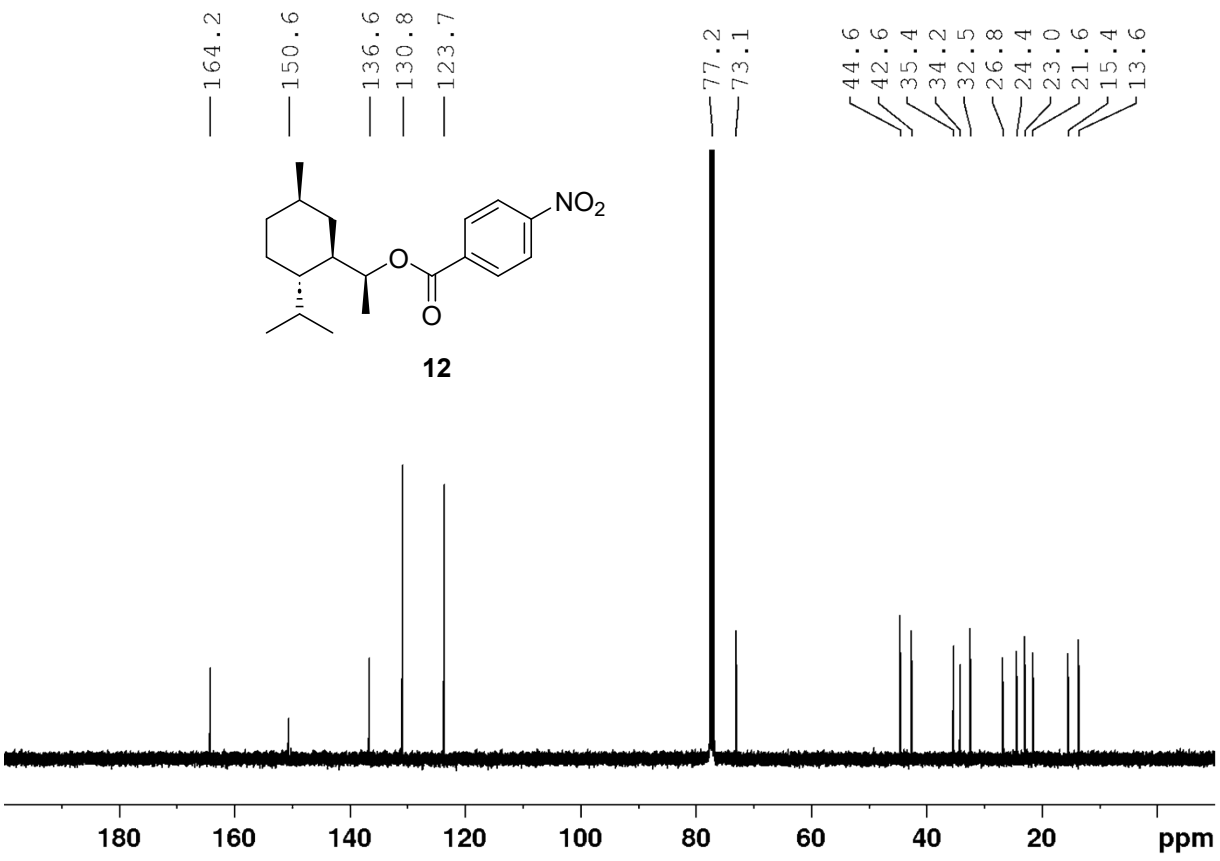


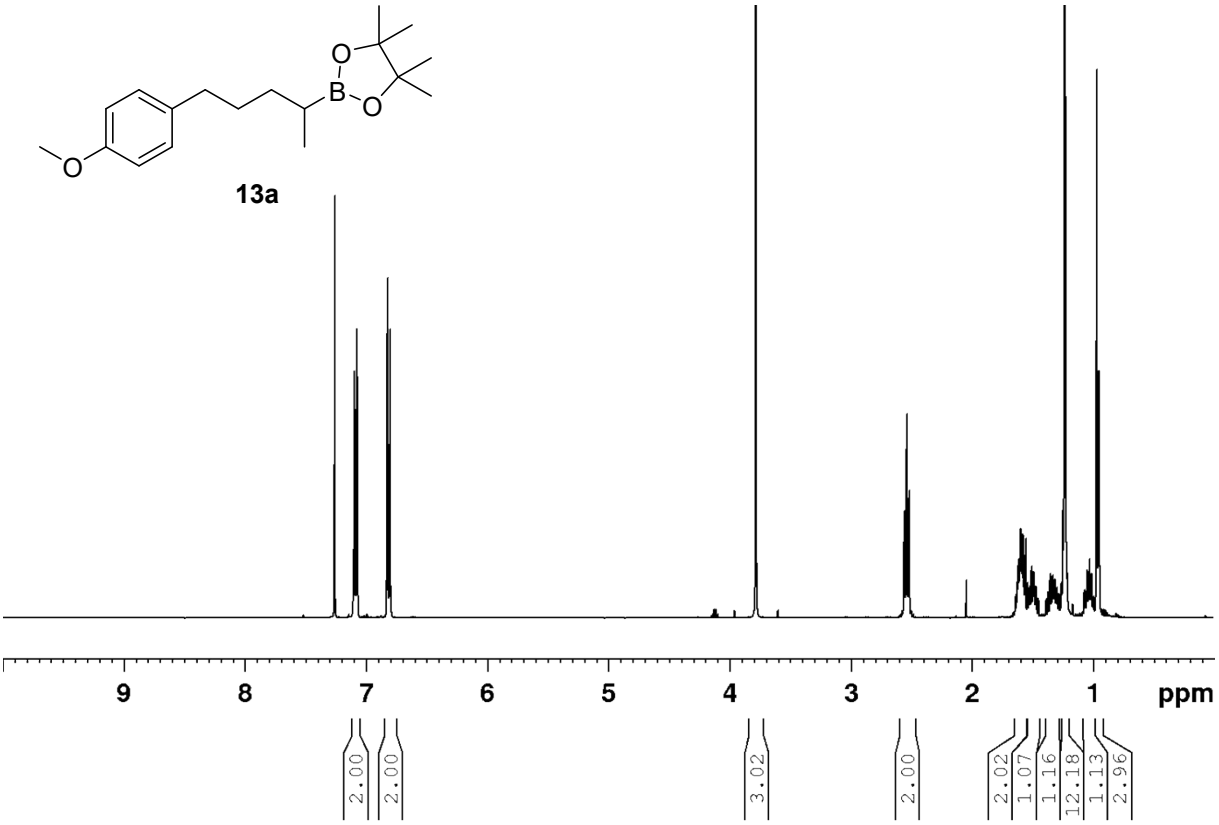
^{1}H-NMR (400 MHz, $CDCl_3$)



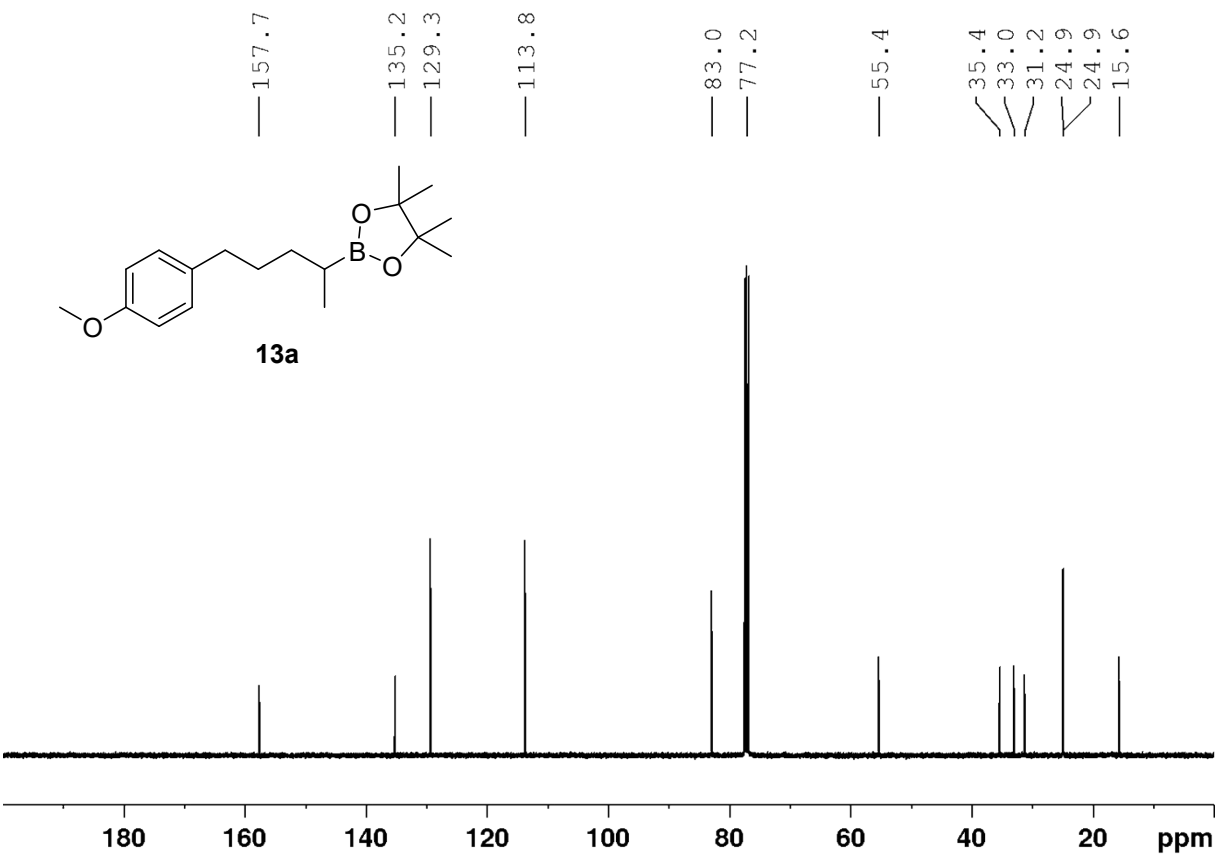
^{13}C-NMR (101 MHz, $CDCl_3$)



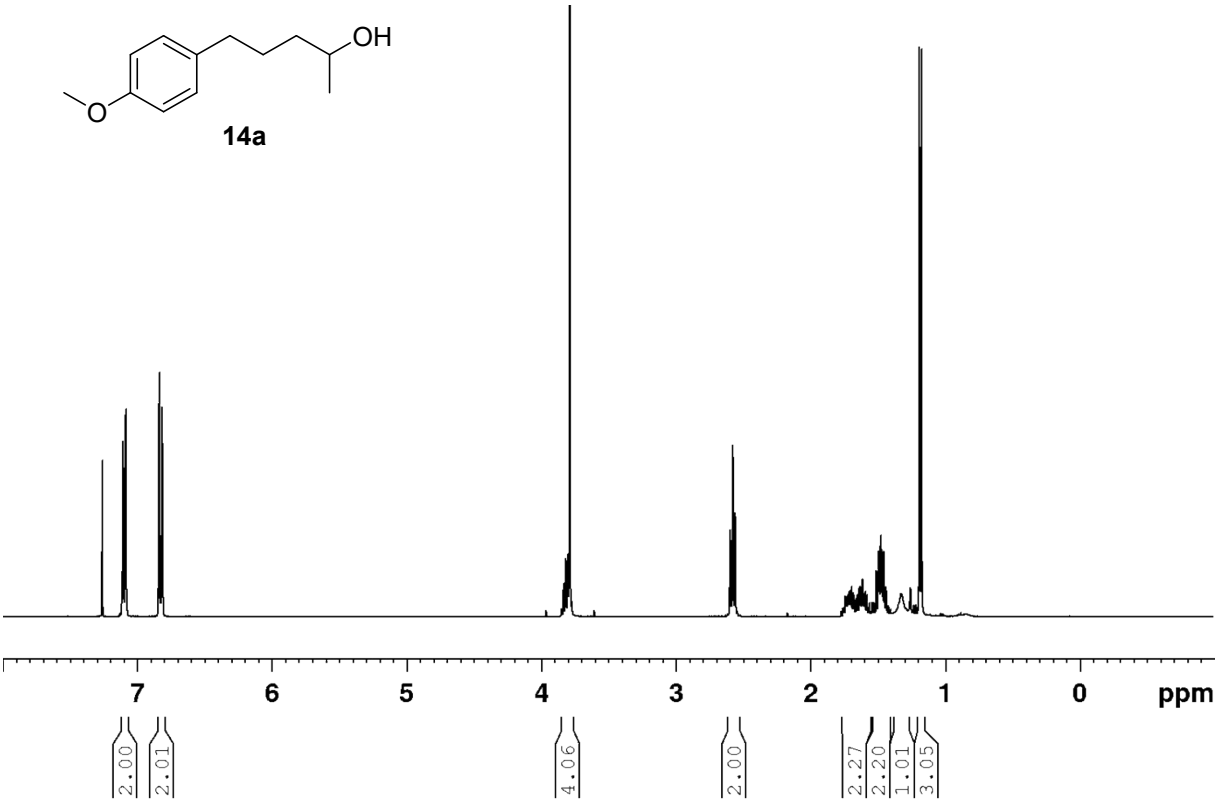
^{1}H-NMR (400 MHz, $CDCl_3$)



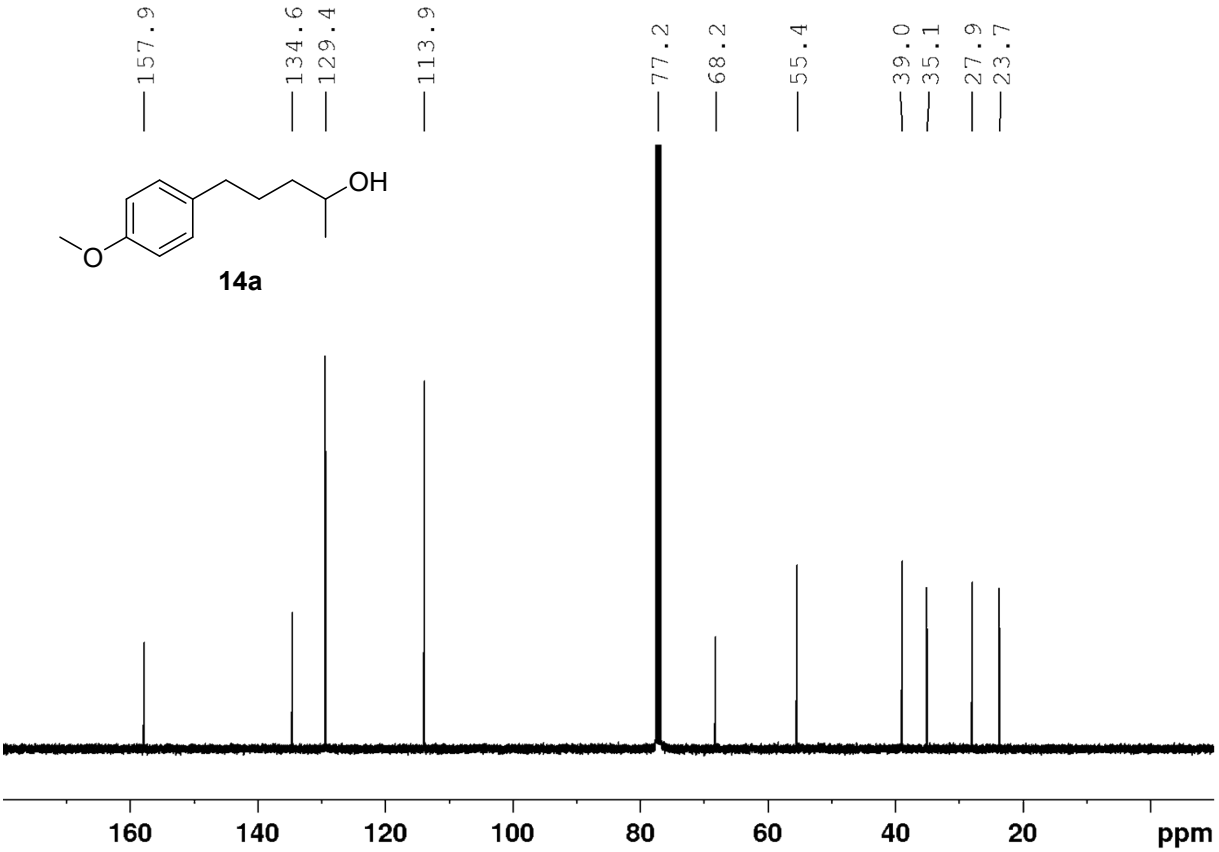
^{13}C-NMR (101 MHz, $CDCl_3$)



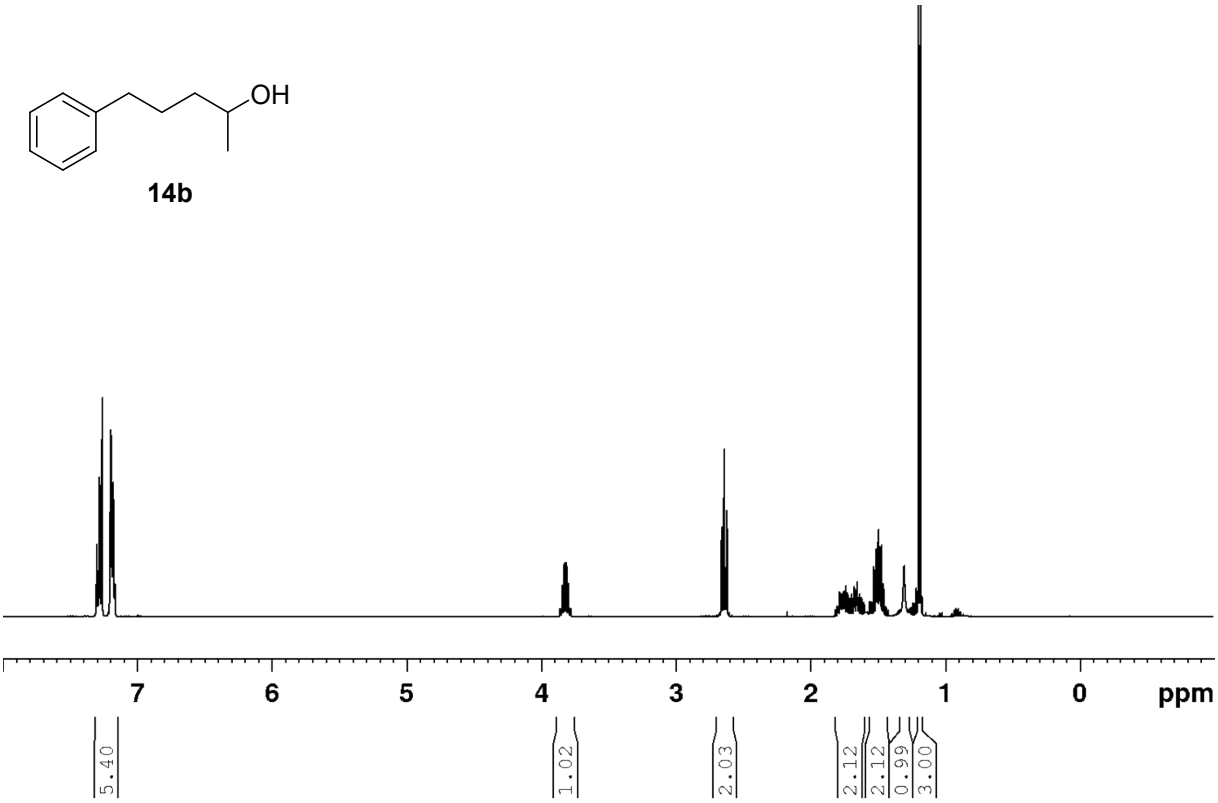
^{1}H-NMR (400 MHz, $CDCl_3$)



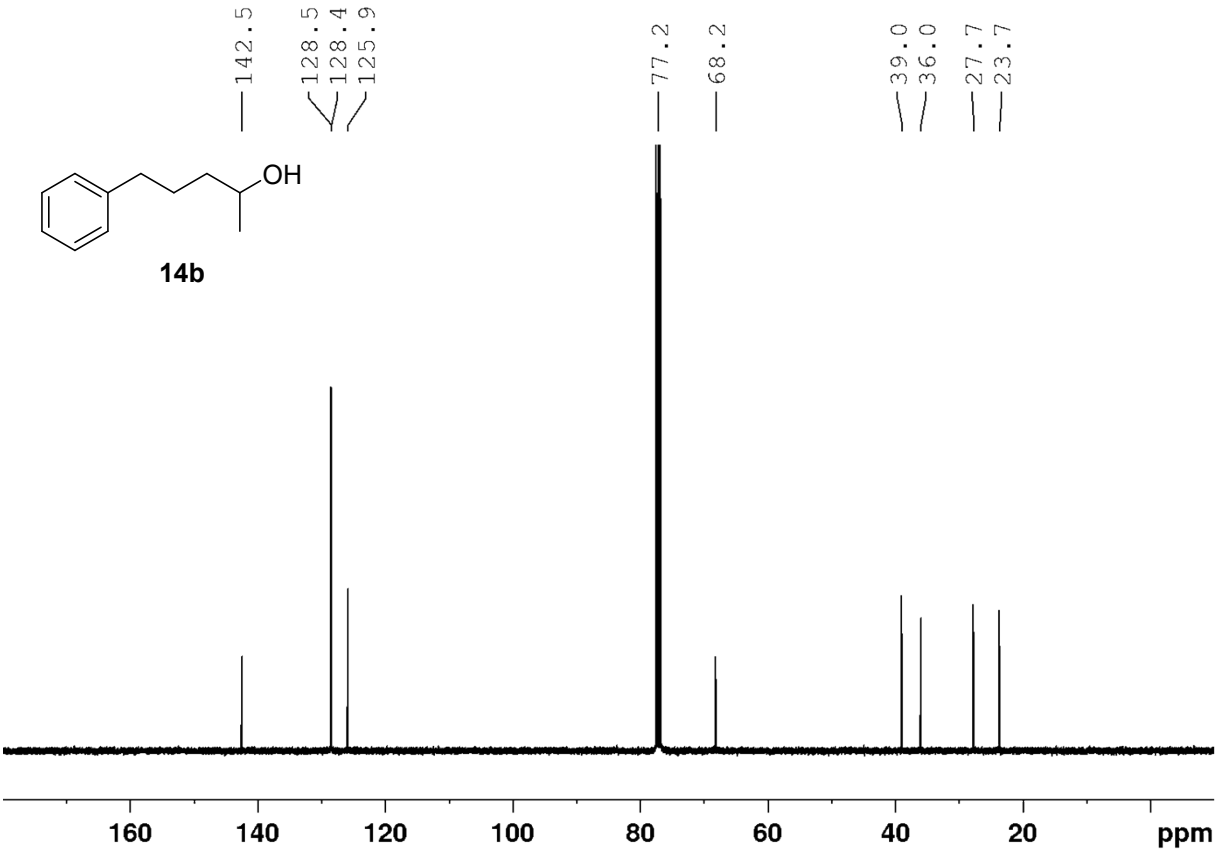
^{13}C-NMR (101 MHz, $CDCl_3$)



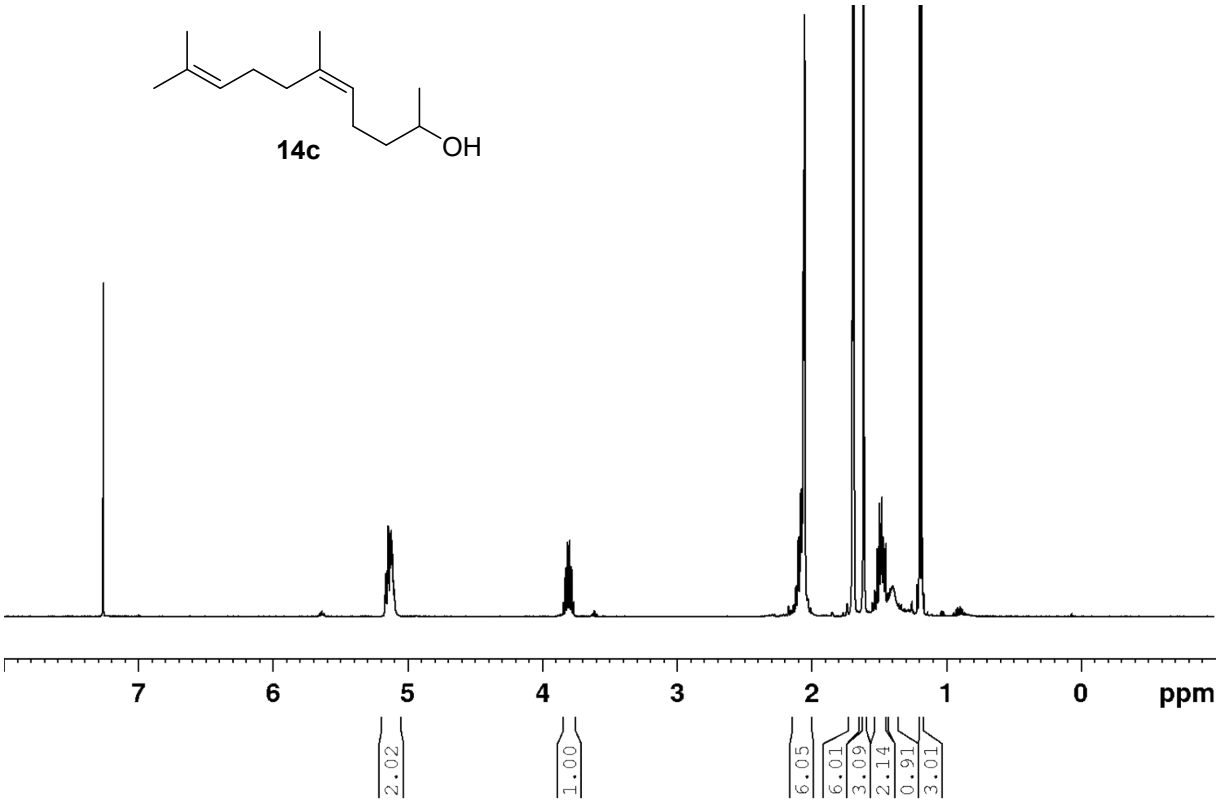
^{1}H-NMR (400 MHz, $CDCl_3$)



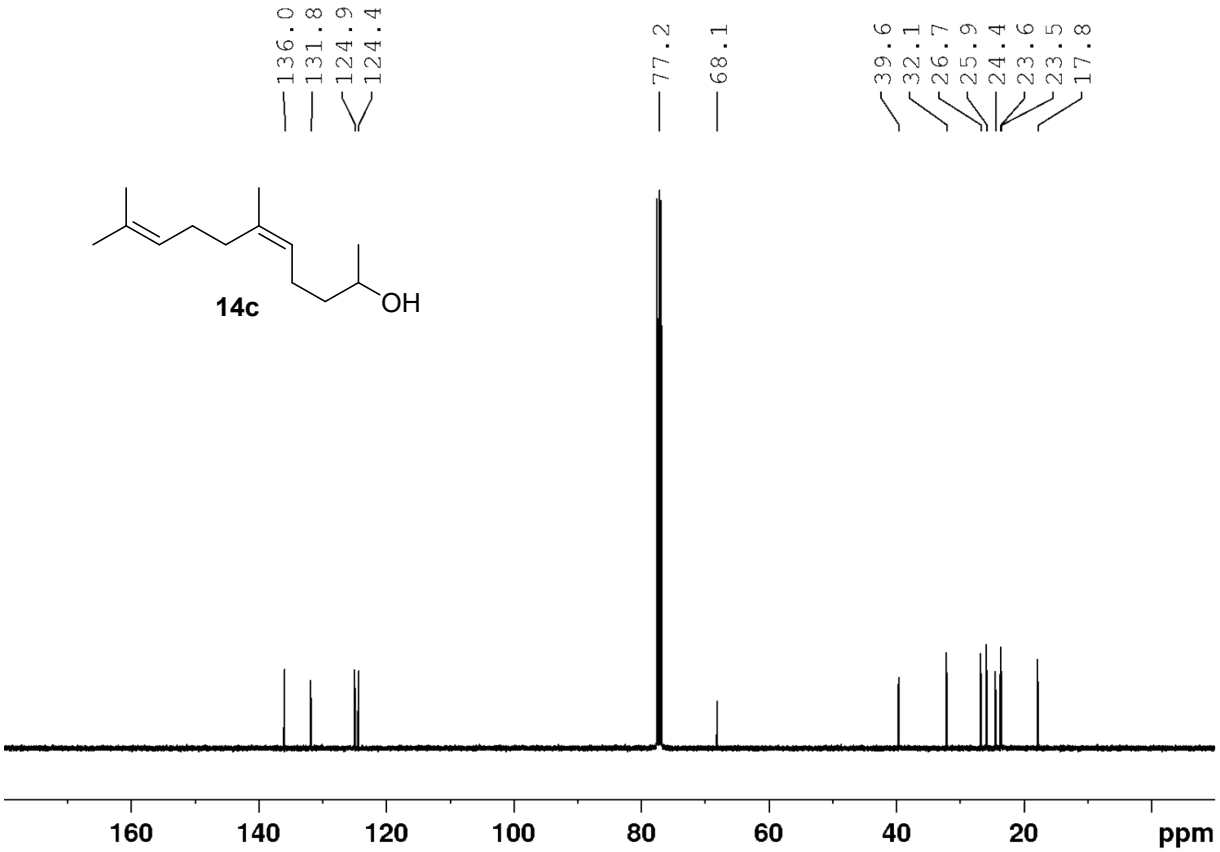
^{13}C-NMR (101 MHz, $CDCl_3$)



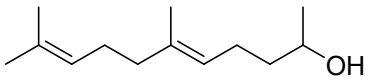
^{1}H-NMR (400 MHz, $CDCl_3$)



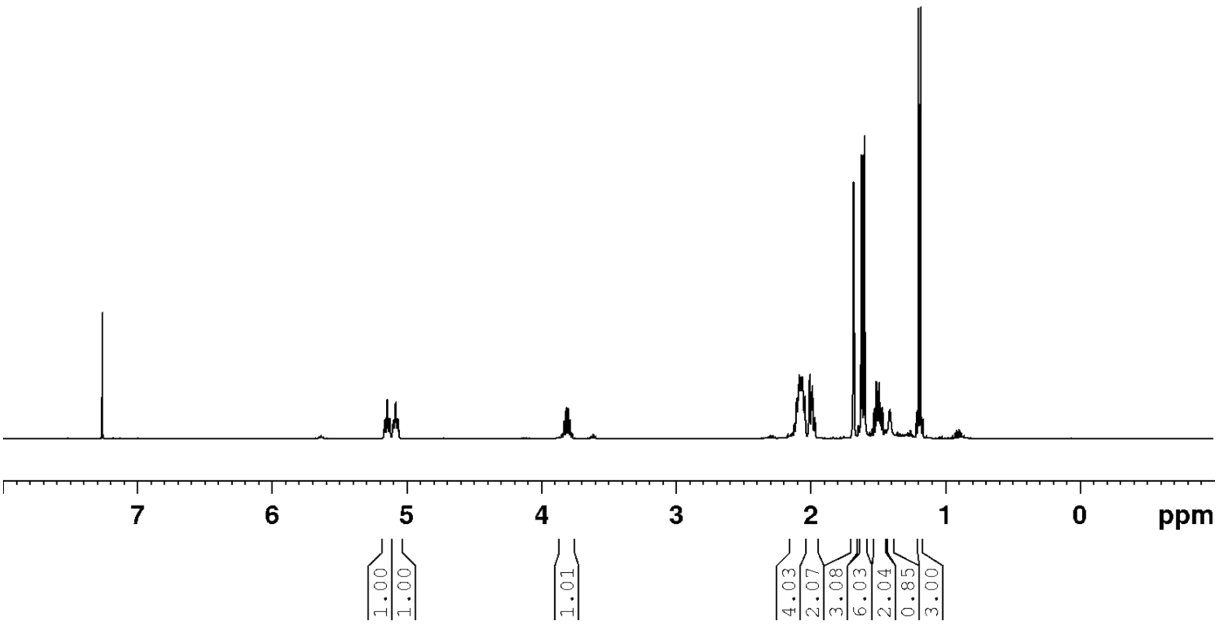
^{13}C-NMR (101 MHz, $CDCl_3$)



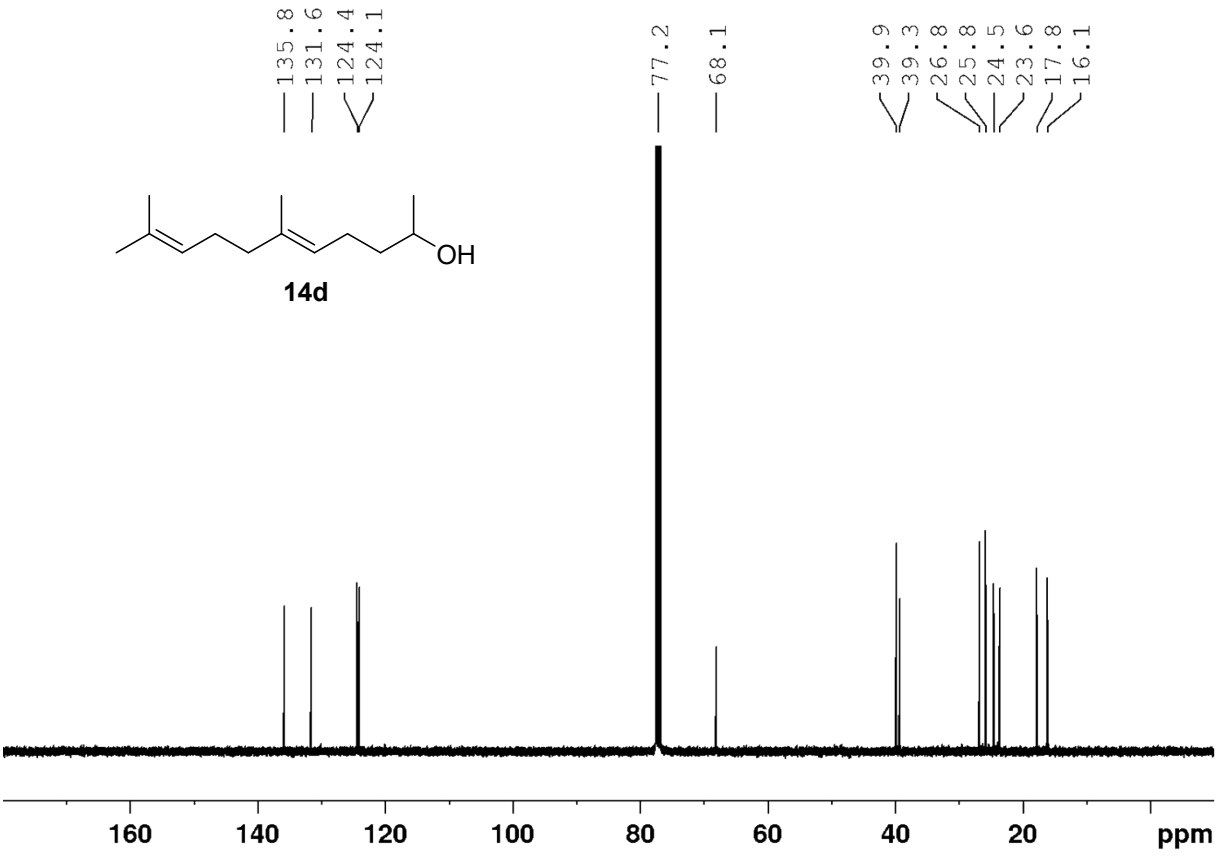
^{1}H-NMR (400 MHz, $CDCl_3$)



14d

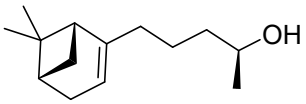


^{13}C-NMR (101 MHz, $CDCl_3$)



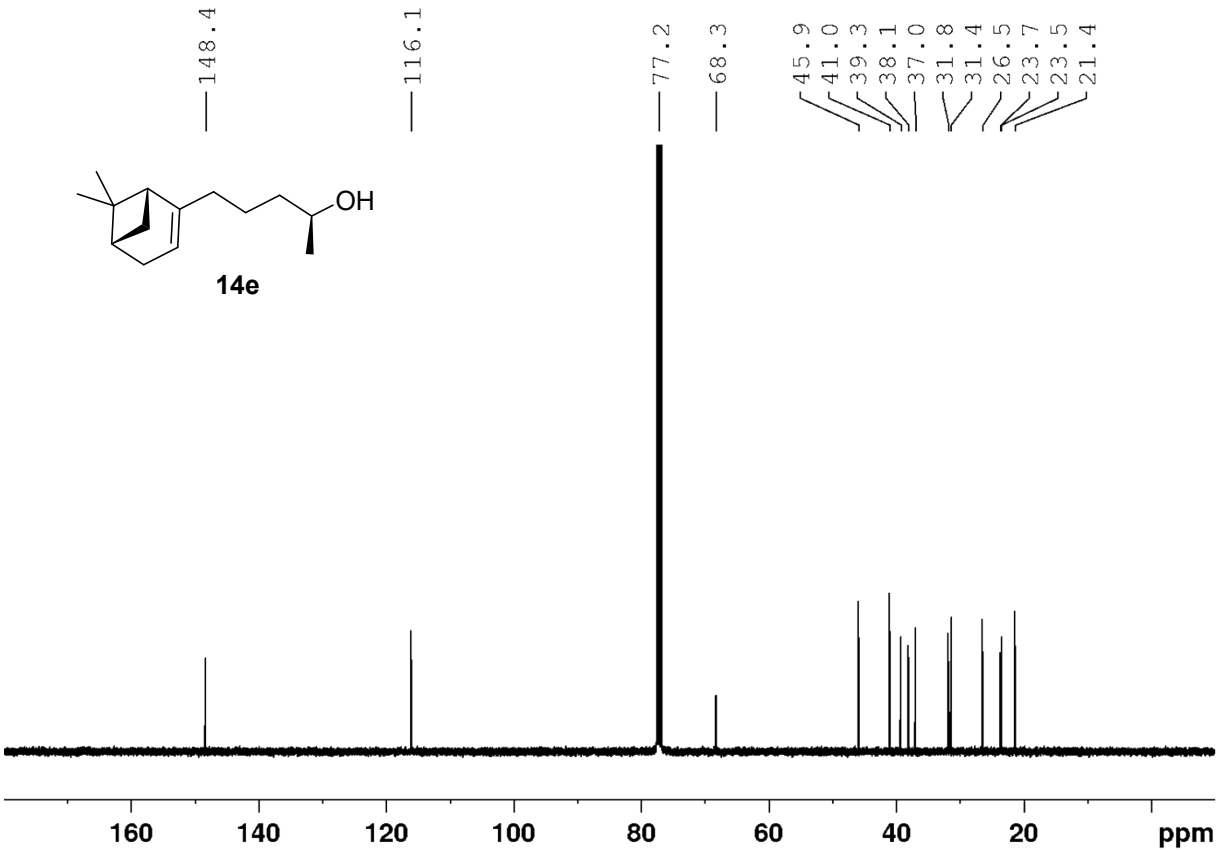
14d

^{1}H-NMR (400 MHz, $CDCl_3$)



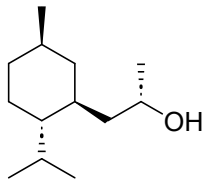
14e

^{13}C-NMR (101 MHz, $CDCl_3$)



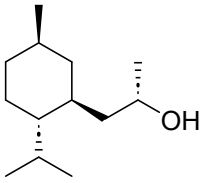
14e

^{1}H-NMR (400 MHz, $CDCl_3$)



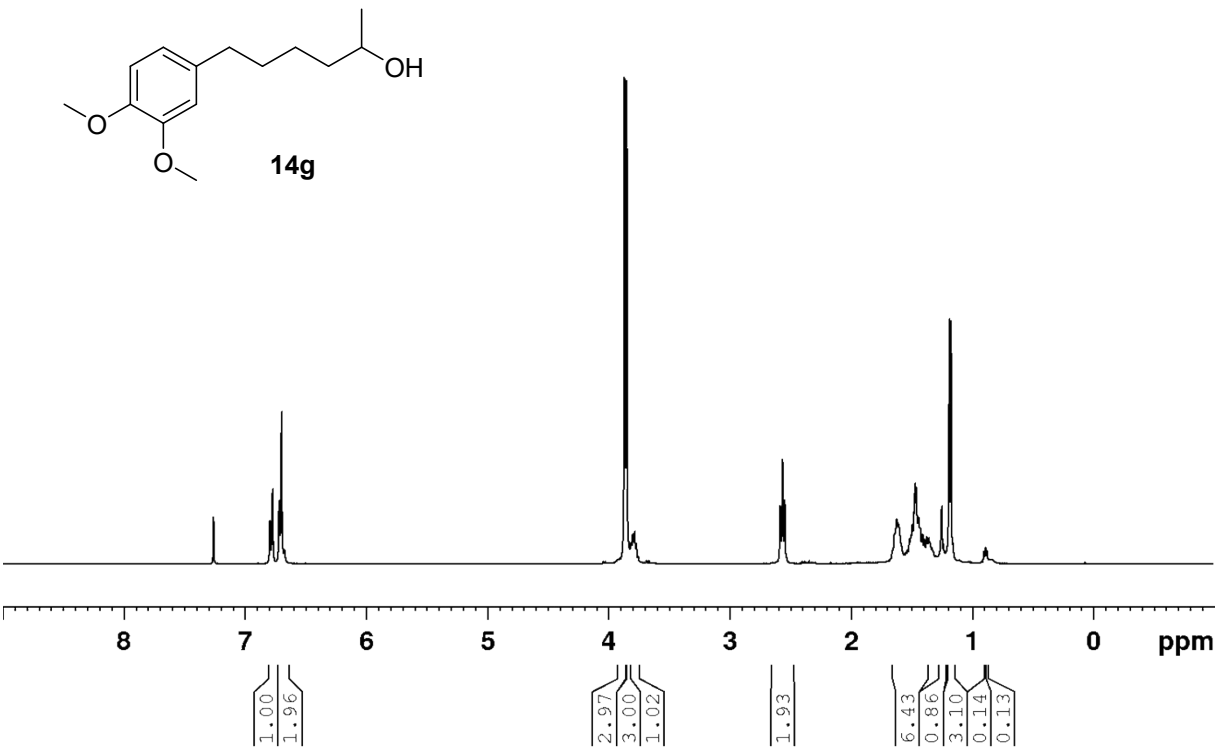
14f

^{13}C-NMR (101 MHz, $CDCl_3$)



14f

^{1}H-NMR (400 MHz, $CDCl_3$)



^{13}C-NMR (101 MHz, $CDCl_3$)