Supporting Information

Cooperative Hydrogen-Bond-Donor Catalysis with Hydrogen Chloride Enables Highly Enantioselective Prins Cyclization Reactions

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Table of Contents

1. General Information

All reactions were performed in flame dried vials or round bottom flasks unless otherwise noted. Vials and flasks were fitted with rubber septa, and reactions were conducted under an atmosphere of nitrogen except where noted. Stainless steel syringes and cannulas were used to transfer air and moisture sensitive liquids. Column chromatography was performed on a Biotage Isolera automated purification system using silica gel 60 (230-400 mesh) from EM Science. Commercial chemical reagents were purchased from Sigma Aldrich, Alfa Aesar, Strem, or TCI, and used as received. Anhydrous solvents (benzene, dichloromethane, diethyl ether, N,N-dimethylformamide, tetrahydrofuran, and toluene) were dried by passage through activated alumina columns using a solvent purification system. Proton nuclear magnetic resonance (^{1}H NMR), fluorine nuclear magnetic resonance (^{19}F NMR), and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Bruker Avance Neo 400 spectrometer. Proton, fluorine, and carbon chemical shifts are reported in parts per million downfield from tetramethylsilane and are referenced to residual proton in the NMR solvent ($CHCl_3$ = δ 7.27), the fluorine resonances of trifluorotoluene (F_3CPh = δ -63.72) or fluorobenzene (FPh = δ -113.15), or the carbon resonances of the NMR solvent ($CDCl_3$ = δ 77.00) respectively. NMR data are represented as follows: chemical shift, multiplicity (br = broad signal, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, td= triplet of doublets, dd = doublet of doublets), coupling constants (J) in Hertz (Hz), integration. Note that some ^{13}C NMR spectra were obtained without ^{19}F decoupling.

Optical rotations were measured using a 1.0 mL cell with a 5 cm path length on a Jasco DIP 370 digital polarimeter. Gas chromatography (GC) analysis was performed on an Agilent 7890A series GC system outfitted with commercially available Cyclosil-B (30m) and CP-Chirasil Dex CB (25m) columns. High-performance liquid chromatography (HPLC) analysis was performed using an Agilent 1200 series quaternary HPLC system with commercially available ChiralPak and ChiralCel columns. High-resolution mass spectrometry was measured at the Small Molecule Mass Spectrometry Facility at Harvard University within the Faculty of Arts and Sciences using an Agilent 6210 TOF LC/MS spectrometer or a Waters Quattro micro GC/MS/MS spectrometer. NMR spectra were processed with the MestReNova (Mestrelab Research). Solutions of hydrochloric acid (in Et_2O) were titrated prior to use. Ethanol used for catalytic reactions was stored over activated molecular sieves.

Abbreviations used:
Aq. – aqueous, Boc – tert–butyloxycarbonyl, n-BuLi – n-butyllithium, DCM – dichloromethane, DMF – N,N-dimethylformamide, DMP – Dess Martin Periodinane, d.r. – diastereomeric ratio, ee – enantiomeric excess, Et_2O – diethyl ether, EtOAc – ethyl acetate, HBD – hydrogen-bond donor, HCl – hydrochloric acid, HR-MS – high resolution mass spectrometry, IPA – isopropanol, THF – tetrahydrofuran, TLC – thin layer chromatography

2. Synthesis and Characterization of Catalysts 6,7, 9-11, and Intermediates

Catalysts **4** and **5** were synthesized according to previously reported procedures.[1,2]

Synthesis of HBD catalysts—chiral pyrrole synthesis

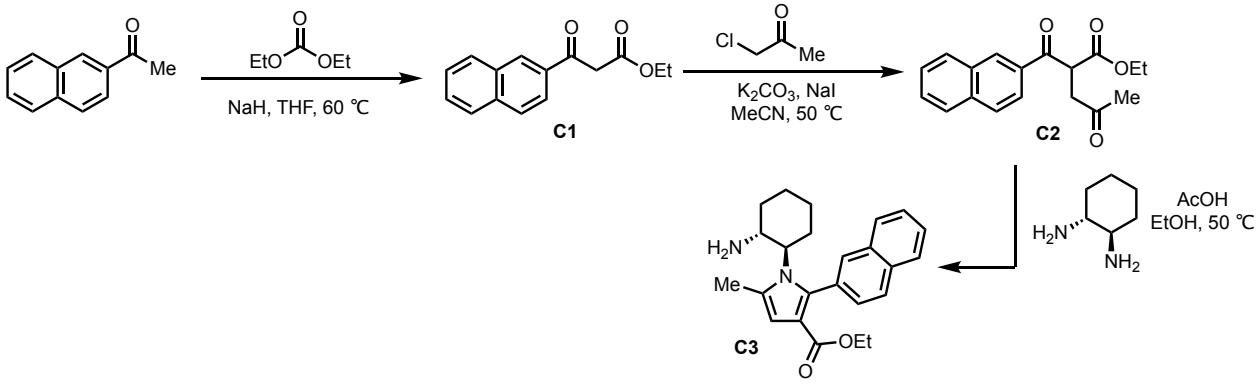
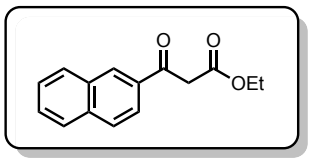


Figure S1. Synthesis of chiral pyrrole moiety

ethyl 3-(naphthalen-2-yl)-3-oxopropanoate (C1)



To a stirring slurry of sodium hydride (60% dispersion in mineral oil, 1.12 g, 28.0 mmol, 2.8 eq.) and diethyl carbonate (2.42 mL, 10.0 mmol, 2.0 eq.) in anhydrous THF (10 mL) was added a solution (THF, 6 mL) of 2-acetonaphthone (1.70 g, 10.0 mmol, 1.0 eq.) dropwise over ten minutes. Following addition of the ketone, the reaction mixture was brought to reflux (60 °C) for 2 hours. After this period, the reaction was quenched by the addition of NH_4Cl (sat. aq.) and diluted in Et_2O. The

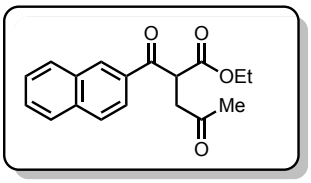
reaction was transferred to a separatory funnel and the aqueous layer was extracted (3X) with Et_2O. The organic layers were combined, filtered over $MgSO_4$, and concentrated *in vacuo*. The resulting residue was purified via flash column chromatography using a gradient of 0 to 60% DCM in hexanes (v/v) to provide product **C1** in 90% yield (2.18 g) as a clear yellow oil that solidifies upon cooling to 4 °C. Note that compound **C1** exists as a 5:1 mixture of keto-enol tautomers.

^{1}H NMR: (400 MHz, $CDCl_3$) δ (keto tautomer) 8.45 (s, 1H), 7.99 (m, 2H), 7.89 (m, 2H), 7.61 (m, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 4.12 (s, 2H), 1.26 (t, *J* = 7.1 Hz, 3H). (enol tautomer) δ 12.68 (s, 1H), 8.36 (s, 1H), 7.85 (m, 2H), 7.78 (m, 1H), 7.53 (m, 3H), 5.81 (s, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 1.36 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ (keto tautomer) 192.41, 167.56, 135.80, 133.39, 132.40, 130.57, 129.66, 128.85, 128.69, 127.80, 126.95, 123.80, 61.50, 46.08, 14.07. δ (enol tautomer) 173.20, 171.22, 134.65, 132.81, 130.59, 129.03, 128.23, 127.65, 127.52, 126.68, 126.63, 122.54, 87.84, 60.35, 14.30.

HR-MS: (ESI) calcd. for $C_{15}H_{14}O_3$ 243.1016 [M + H^+], found 243.1018

ethyl 2-(2-naphthoyl)-4-oxopentanoate (C2)



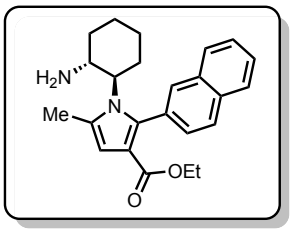
A flame-dried round bottom flask was charged with β-keto ester **C1** (2.18 g, 8.99 mmol, 1.0 eq.), potassium carbonate (1.50 g, 10.80 mmol, 1.2 eq.), and sodium iodide (1.48 g, 9.90 mmol, 1.1 eq.) in 40 mL of dry MeCN. Chloroacetone (796 μL, 9.90 mmol, 1.1 eq.) was added in a single portion and the reaction mixture was heated to 50 °C for 24 hours with vigorous stirring. After this period, the reaction was quenched by the addition of NH_4Cl (sat. aq.) and diluted in Et_2O. The reaction was transferred to a separatory funnel and the aqueous layer was extracted (3X) with Et_2O. The organic layers were combined, filtered over $MgSO_4$, and concentrated *in vacuo*. The resulting residue was purified via flash column chromatography using a gradient of 0 to 15% EtOAc in hexanes (v/v) to provide product **C2** in 80% yield (2.15 g) as a clear yellow oil.

^{1}H NMR: (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.06 (dd, *J* = 8.6, 1.8 Hz, 1H), 8.00 (m, 1H), 7.90 (dd, *J* = 9.8, 7.9 Hz, 2H), 7.60 (m, 2H), 5.08 (t, *J* = 6.9 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.25 (m, 2H), 2.26 (s, 3H), 1.16 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 205.45, 194.46, 169.23, 135.77, 133.24, 132.43, 130.94, 129.76, 128.79, 128.55, 127.73, 126.86, 124.20, 61.74, 48.83, 42.31, 29.82, 13.89.

HR-MS: (ESI) calcd. for $C_{18}H_{18}O_4$ 299.1278 [M + H^+], found 299.1280

ethyl 1-((1*R*,2*R*)-2-aminocyclohexyl)-5-methyl-2-(naphthalen-2-yl)-1*H*-pyrrole-3-carboxylate (C3)



A flame dried round bottom flask was charged with intermediate **C2** (0.834 g, 2.80 mmol, 1.0 eq.) and R,R-trans-1,2-diaminocyclohexane (0.415 g, 3.63 mmol, 1.3 eq.) in 14 mL of anhydrous ethanol. Acetic acid (207 μL, 3.63 mmol, 1.3 eq.) was added and the reaction mixture was heated to 50 °C for 24 hours. After this period, the reaction was quenched by the slow addition of $NaHCO_3$ (sat. aq.) and diluted in DCM. The reaction was transferred to a separatory funnel and the aqueous layer was extracted (3X) with DCM. The organic layers were combined, filtered over $MgSO_4$, and concentrated *in vacuo*. The resulting orange residue was purified via flash column chromatography using a gradient of 0 to 2% MeOH in DCM (v/v) to provide product **C3** in 54% yield (0.563 g) as an orange solid. Note that compound **C3** exists as a 4:1 mixture of rotomers about the CN bond of the pyrrole moiety. Reported NMR data below correspond to the major rotomer.

^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.88 (m, 4H), 7.51 (m, 3H), 6.49 (s, 1H), 4.03 (q, *J* = 7.1 Hz, 2H), 3.56 (m, 1H), 3.20 (td, *J* = 10.6, 3.9 Hz, 1H), 2.46 (s, 3H), 1.96 (m, 2H), 1.69 (m, 2H), 1.26 (m, 5H), 1.00 (m, 4H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 164.62, 140.31, 132.88, 131.02, 129.32, 128.31, 128.13, 128.01, 127.68, 127.45, 126.29, 126.06, 112.66, 111.23, 108.24, 64.84, 59.06, 52.53, 35.20, 31.68, 25.61, 24.93, 15.01, 14.04.

HR-MS: (ESI) calcd. for $C_{24}H_{28}N_2O_2$ 377.2224 [M + H^+], found 377.2222

$[a]_D^{22} = +3.0°$ (c =1.0, CH_2Cl_2)

Synthesis of HBD catalysts 6-11—final assembly

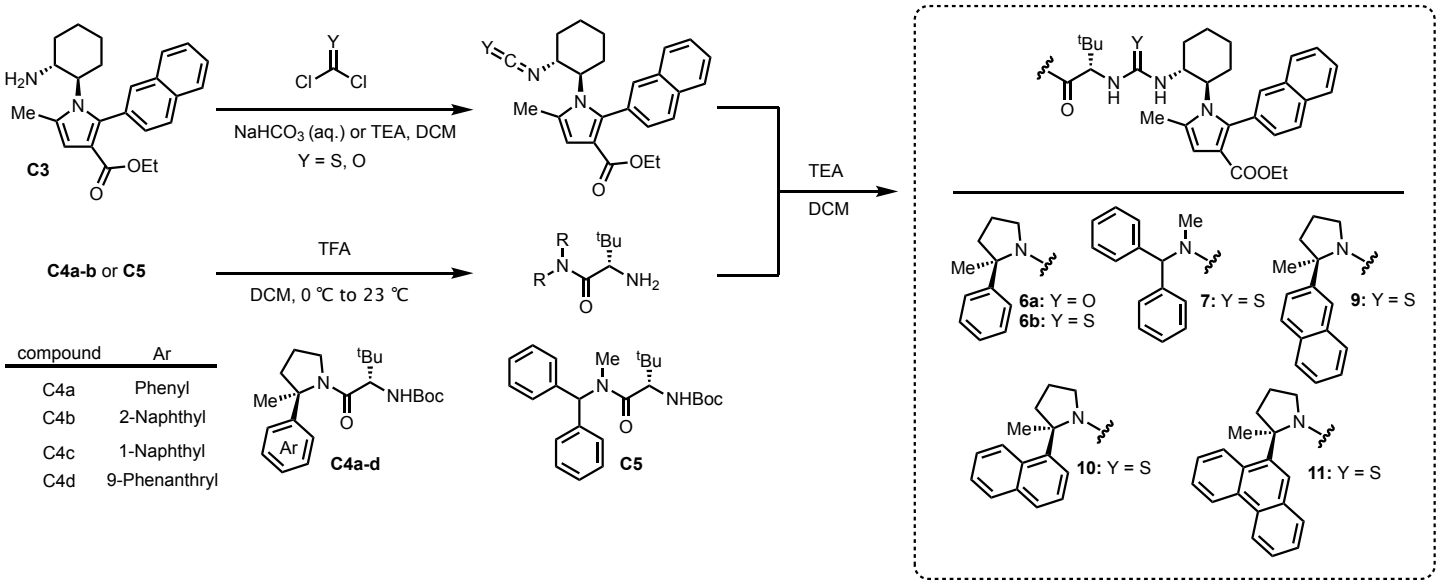


Figure S2. Synthesis of chiral pyrrole-based HBD catalysts

Compounds **C4a-d** and **C5** were synthesized according to previously reported routes.[1,3] Characterization data were consistent with these previous reports. Characterization data for **C4b** are provided below.

General procedure for final catalyst assembly:

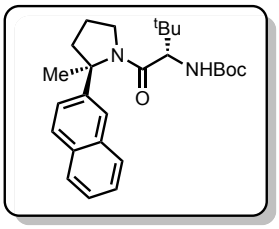
*Synthesis of iso(thio)cyanates derived from **C3**:*

To a flame-dried around bottom flask was added amine **C3** (1.0 eq.), DCM (0.1 M with respect to **C3**), and a saturated aqueous solution of sodium bicarbonate (0.1 M with respect to **C3**). (Thio)phosgene (1.0 eq.) was added directly to the DCM layer and following addition, the reaction mixture was stirred vigorously for 1 hour. After this period, the reaction mixture was transferred to a separatory funnel and the aqueous layer was extracted (2X) with DCM. The organic layers were combined, filtered over $MgSO_4$, and concentrated *in vacuo* for at least 30 minutes (note: concentration was performed using a rotovap unit installed in a well-ventilated hood in the event that any unreacted (thio)phosgene remained). The resulting orange residue was purified via flash column chromatography using a gradient of 0 to 30% Et_2O in hexanes (v/v) to provide the iso(thio)cyanate derivative of **C3** as a white solid that was used immediately in the next step. Note: for synthesis of isocyanate derivatives, the above procedure was used with the following modification: triethylamine (1.5 eq.) was used instead of aqueous sodium bicarbonate.

Synthesis of (thio)urea catalysts:

Chiral amino acid derived fragments **C4** or **C5** (1.0 eq.) were subjected to treatment with 25% trifluoroacetic acid in DCM (v/v) (overall concentration 0.15 M with respect to **C4** or **C5**) at 0 °C for 30 min followed by warming to room temperature for an additional hour. After this period, reactions were cooled back to 0 °C and carefully quenched with sat. aq. $NaHCO_3$. The reaction mixture was transferred to a separatory funnel and the aqueous layer was extracted with DCM (2X). The organic layers were combined, filtered over $MgSO_4$, and concentrated *in vacuo*. Finally, a solution of **C3** (1.0 eq.) and triethylamine (1.0 eq.) in DCM (0.2 M with respect to **C3**) was added to the vial containing the free amine and the ensuing reaction was allowed to take place for 12 hours. Reactions were quenched by the addition of sat. aq. NH_4Cl and were extracted with DCM (2X). The resulting residue was purified via flash column chromatography using a gradient of 0 to 50% Et_2O in hexanes (v/v) to provide products **6, 7,** and **9-11** in 68-92% yields as white solids.

***tert*-butyl ((*S*)-3,3-dimethyl-1-((*R*)-2-methyl-2-(naphthalen-2-yl)pyrrolidin-1-yl)-1-oxobutan-2-yl)carbamate (C4b)**



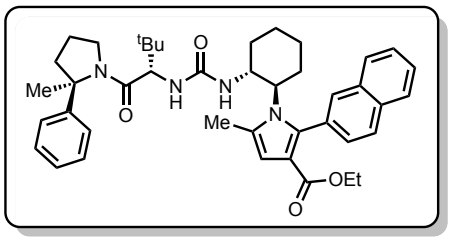
^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.75 (m, 3H), 7.62 (s, 1H), 7.40 (qd, *J* = 6.9, 3.4 Hz, 2H), 7.30 (dd, *J* = 8.6, 2.0 Hz, 1H), 5.16 (d, *J* = 10.0 Hz, 1H), 4.40 (d, *J* = 10.1 Hz, 1H), 4.28 (dt, *J* = 10.0, 6.4 Hz, 1H), 3.89 (dt, *J* = 10.0, 7.4 Hz, 1H), 2.10 (td, *J* = 6.8, 3.1 Hz, 2H), 2.01 (s, 3H), 1.93 (m, 2H), 1.52 (s, 9H), 1.05 (s, 9H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 170.01, 156.37, 143.67, 133.26, 132.04, 128.07, 127.88, 127.33, 125.67, 125.28, 123.46, 123.12, 79.44, 67.26, 58.76, 50.06, 44.36, 34.82, 28.43, 26.42, 24.94, 22.63.

HR-MS: (ESI) calcd. for $C_{26}H_{36}N_2O_3$ 425.2799 [M + H^+], found 425.2802

$[a]_D^{22} = +9.0°$ (c = 1.0, CH_2Cl_2)

ethyl 1-((1*R*,2*R*)-2-(3-((*S*)-3,3-dimethyl-1-((*R*)-2-methyl-2-phenylpyrrolidin-1-yl)-1-oxobutan-2-yl)ureido)cyclohexyl)-5-methyl-2-(naphthalen-2-yl)-1*H*-pyrrole-3-carboxylate (6a)



Synthesized according to the general procedure on 0.69 mmol scale. 69% yield, 0.132 g, white solid.

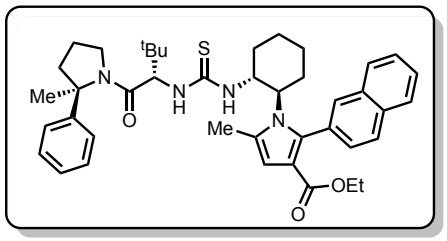
^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.88 (m, 4H), 7.50 (m, 3H), 7.20 (t, *J* = 7.7 Hz, 2H), 7.08 (m, 3H), 6.47 (s, 1H), 4.92 (s, 1H), 4.57 (s, 1H), 4.19 (s, 1H), 4.07 (s, 1H), 3.97 (m, 2H), 3.81 (m, 2H), 3.68 (m, 1H), 2.54 (s, 3H), 2.03 (m, 5H), 1.88 (m, 6H), 1.76 (s, 1H), 1.61 (s, 1H), 1.32 (m, 1H), 0.99 (s, 9H), 0.95 (m, 3H), 0.85 (m, 1H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 170.12, 164.55, 156.71, 145.75, 139.44, 132.97, 130.82, 130.51, 129.30, 129.14, 128.79, 128.50, 128.22, 127.78, 127.58, 126.41, 126.26, 125.95, 124.43, 112.87, 110.96, 67.12, 60.41, 58.99, 57.87, 51.79, 50.00, 44.37, 35.49, 34.43, 32.61, 26.39, 25.32, 25.09, 24.67, 22.38, 14.95, 14.02.

HR-MS: (ESI) calcd. for $C_{42}H_{52}N_4O_4$ 677.4061 [M + H^+], found 677.4061

$[a]_D^{22} = +120.0°$ (c = 0.5, CH_2Cl_2)

ethyl 1-((1*R*,2*R*)-2-(3-((*S*)-3,3-dimethyl-1-((*R*)-2-methyl-2-phenylpyrrolidin-1-yl)-1-oxobutan-2-yl)thioureido)cyclohexyl)-5-methyl-2-(naphthalen-2-yl)-1*H*-pyrrole-3-carboxylate (6b)



Synthesized according to the general procedure on 2.0 mmol scale. 72% yield, 1.0 g, white solid.

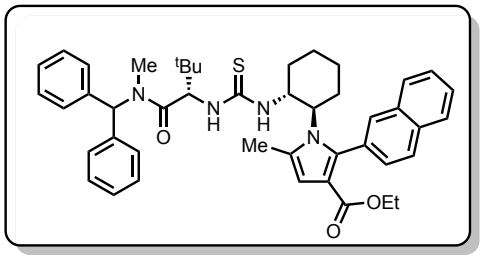
^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.94 (m, 4H), 7.56 (m, 3H), 7.19 (t, *J* = 7.6 Hz, 2H), 7.10 (d, *J* = 8.3 Hz, 3H), 6.49 (s, 1H), 6.02 (m, 1H), 5.44 (d, *J* = 9.6 Hz, 1H), 4.44 (m, 1H), 4.24 (s, 1H), 3.99 (m, 2H), 3.84 (m, 1H), 3.78 (m, 1H), 2.51 (s, 3H), 2.05 (m, 5H), 1.87 (m, 5H), 1.77 (m, 2H), 1.58 (m, 1H), 1.25 (m, 1H), 1.03 (s, 9H), 0.94 (m, 3H), 0.88 (m, 1H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 181.70, 169.68, 164.43, 145.54, 139.51, 133.00, 131.32, 130.58, 130.21, 129.43, 129.03, 128.78, 128.09, 127.80, 127.52, 127.26, 126.47, 126.24, 125.93, 124.65, 113.26, 111.77, 67.34, 62.88, 59.73, 59.06, 54.94, 50.21, 44.43, 35.83, 33.49, 32.23, 26.51, 25.08, 24.27, 22.42, 15.21, 13.99.

HR-MS: (ESI) calcd. for $C_{42}H_{52}N_4O_3S$ 693.3833 [M + H^+], found 693.3836

$[a]_D^{22} = +98.0°$ (c = 0.5, CH_2Cl_2)

ethyl 1-((1*R*,2*R*)-2-(3-((*S*)-1-(benzhydryl(methyl)amino)-3,3-dimethyl-1-oxobutan-2-yl)thioureido)cyclohexyl)-5-methyl-2-(naphthalen-2-yl)-1*H*-pyrrole-3-carboxylate (7)



Synthesized according to the general procedure on 0.6 mmol scale. 92% yield, 0.363 g, white solid.

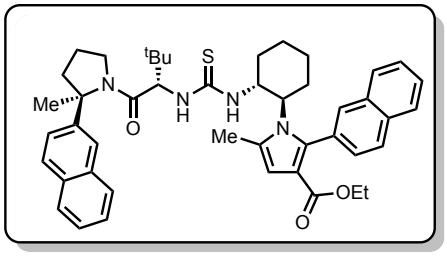
^{1}H NMR: (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.90 (m, 2H), 7.68 (m, 1H), 7.55 (m, 2H), 7.35 (m, 7H), 7.24 (m, 2H), 7.13 (m, 3H), 6.41 (s, 1H), 6.16 (s, 1H), 5.55 (d, *J* = 9.4 Hz, 1H), 5.37 (bs, 1H), 4.46 (bs, 1H), 3.99 (q, *J* = 14.3 Hz, 2H), 3.92 (s, 1H), 3.82 (bs, 1H), 3.05 (s, 3H), 2.52 (s, 3H), 2.22 (d, *J* = 13.0 Hz, 1H), 2.11 (m, 2H), 1.81 (d, *J* = 13.8 Hz, 1H), 1.64 (s, 1H), 1.34 (m, 2H), 1.01 (s, 9H), 0.91 (m, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 182.12, 172.69, 164.45, 139.36, 139.24, 138.03, 133.01, 131.39, 130.59, 130.27, 129.40, 129.08, 128.67, 128.48, 128.41, 128.08, 127.84, 127.65, 127.29, 127.08, 126.55, 126.40, 113.21, 111.68, 64.14, 61.03, 60.73, 59.82, 59.06, 55.26, 36.04, 33.54, 33.27, 32.22, 26.68, 25.28, 24.35, 15.14, 13.98.

HR-MS: (ESI) calcd. for $C_{45}H_{52}N_4O_3S$ 729.3833 [M + H^+], found 729.3832

$[a]_D^{22} = +127.6°$ (c = 0.5, CH_2Cl_2)

ethyl 1-((1*R*,2*R*)-2-(3-((*S*)-3,3-dimethyl-1-((*R*)-2-methyl-2-(naphthalen-2-yl)pyrrolidin-1-yl)-1-oxobutan-2-yl)thioureido)cyclohexyl)-5-methyl-2-(naphthalen-2-yl)-1*H*-pyrrole-3-carboxylate (9)



Synthesized according to the general procedure on 0.71 mmol scale. 68% yield, 0.352 g, white solid.

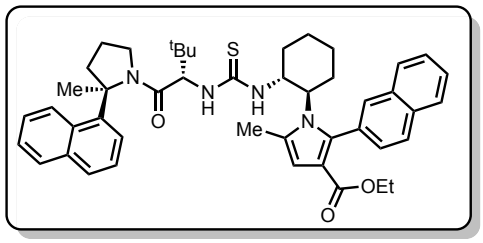
^{1}H NMR: (400 MHz, $CDCl_3$) δ 8.04 (m, 1H), 7.90 (m, 2H), 7.62 (m, 8H), 7.31 (s, 2H), 7.24 (m, 1H), 6.49 (s, 1H), 5.87 (bs, 1H), 5.46 (d, *J* = 9.5 Hz, 2H), 4.54 (m, 1H), 4.00 (m, 3H), 3.90 (m, 1H), 3.71 (m, 1H), 2.46 (s, 3H), 2.10 (td, *J* = 6.8, 1.9 Hz, 2H), 1.99 (s, 4H), 1.93 (m, 2H), 1.67 (m, 2H), 1.35 (m, 1H), 1.05 (s, 9H), 0.92 (m, 6H), 0.67 (q, *J* = 12.4 Hz, 1H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 181.79, 169.80, 164.41, 143.05, 139.60, 133.16, 132.88, 131.93, 131.34, 130.53, 130.16, 129.45, 129.06, 128.79, 128.08, 127.81, 127.52, 127.30, 127.14, 126.56, 126.35, 125.85, 125.62, 125.23, 123.36, 113.26, 111.82, 67.49, 63.13, 59.74, 59.06, 54.84, 50.27, 44.25, 35.59, 33.44, 32.14, 26.54, 25.08, 24.84, 24.15, 22.62, 15.20, 13.97.

HR-MS: (ESI) calcd. for $C_{46}H_{54}N_4O_3S$ 743.3989 [M + H^+], found 743.3985

$[a]_D^{22} = +88.4°$ (c = 0.5, CH_2Cl_2)

ethyl 1-((1*R*,2*R*)-2-(3-((*S*)-3,3-dimethyl-1-((*R*)-2-methyl-2-(naphthalen-1-yl)pyrrolidin-1-yl)-1-oxobutan-2-yl)thioureido)cyclohexyl)-5-methyl-2-(naphthalen-2-yl)-1*H*-pyrrole-3-carboxylate (10)



Synthesized according to the general procedure on 0.70 mmol scale. 84% yield, 0.439 g, white solid.

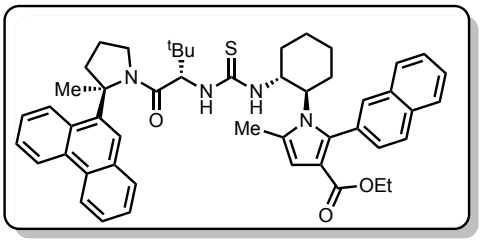
^{1}H NMR: (400 MHz, $CDCl_3$) δ 8.12 (m, 1H), 7.93 (m, 3H), 7.64 (m, 5H), 7.35 (m, 4H), 7.08 (m, 1H), 6.45 (s, 1H), 5.67 (bs, 1H), 5.49 (d, *J* = 9.5 Hz, 1H), 5.28 (m, 1H), 4.57 (bs, 1H), 4.03 (m, 3H), 3.79 (m, 1H), 3.64 (m, 1H), 2.65 (s, 1H), 2.39 (s, 3H), 2.19 (bs, 2H), 2.05 (s, 3H), 1.96 (s, 4H), 1.67 (m, 2H), 1.28 (m, 2H), 1.02 (s, 9H), 0.95 (m, 4H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 181.51, 169.45, 164.41, 139.49, 134.58, 133.19, 132.97, 131.37, 130.55, 130.18, 129.44, 129.16, 129.01, 128.81, 128.12, 127.87, 127.50, 127.28, 126.56, 126.35, 126.17, 125.57, 125.00, 124.80, 124.38, 124.10, 113.24, 111.80, 67.96, 62.71, 59.59, 59.02, 54.43, 48.92, 40.96, 35.77, 32.82, 32.00, 26.49, 25.06, 24.06, 23.18, 15.13, 13.97.

HR-MS: (ESI) calcd. for $C_{46}H_{54}N_4O_3S$ 743.3989 [M + H^+], found 743.3988

$[a]_D^{22} = +91.2°$ (c = 0.5, CH_2Cl_2)

ethyl 1-((1*R*,2*R*)-2-(3-((*S*)-3,3-dimethyl-1-((*R*)-2-methyl-2-(phenanthren-9-yl)pyrrolidin-1-yl)-1-oxobutan-2-yl)thioureido)cyclohexyl)-5-methyl-2-(naphthalen-2-yl)-1*H*-pyrrole-3-carboxylate (11)



Synthesized according to the general procedure on 0.27 mmol scale. 84% yield, 0.179 g, white solid.

^{1}H NMR: (400 MHz, $CDCl_3$) δ 8.56 (m, 2H), 8.02 (m, 4H), 7.66 (m, 10H), 6.44 (s, 1H), 5.51 (d, *J* = 9.3 Hz, 3H), 4.67 (m, 1H), 4.11 (bs, 1H), 3.99 (m, 2H), 3.72 (m, 2H), 2.71 (s, 1H), 2.37 (s, 3H), 2.12 (m, 5H), 1.93 (s, 3H), 1.64 (m, 2H), 1.27 (m, 1H), 1.03 (s, 9H), 0.92 (m, 6H).

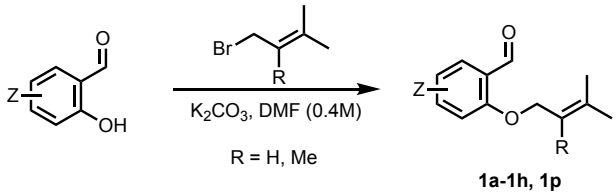
^{13}C NMR: (101 MHz, $CDCl_3$) δ ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.57, 169.64, 164.40, 139.52, 133.22, 133.13, 133.01, 131.44, 131.29, 130.57, 130.17, 129.90, 129.52, 129.13, 128.99, 128.87, 128.15, 127.87, 127.77, 127.52, 127.30, 126.59, 126.45, 126.34, 125.58, 125.14, 123.28, 121.90, 113.28, 111.94, 67.81, 62.96, 59.65, 59.04, 54.41, 48.91, 40.35, 35.76, 35.66, 33.09, 32.02, 31.88, 26.52, 24.99, 24.01, 23.11, 15.21, 13.99.

HR-MS: (ESI) calcd. for $C_{50}H_{56}N_4O_3S$ 793.4146 [M + H^+], found 793.4147

$[a]_D^{22} = +70.0°$ (c = 0.5, CH_2Cl_2)

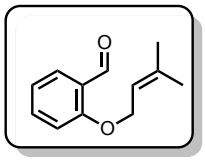
3. Synthesis and Characterization of Substrates 1a-1t, and Intermediates

General procedure for the synthesis of substrates 1a-1h, 1p



To a stirring suspension of K_2CO_3 (12.3 mmol, 1.5 eq.) in anhydrous DMF (20 mL) was added salicylaldehyde (8.2 mmol, 1.0 eq.) followed immediately by allylic bromide (10.6 mmol, 1.3 eq.). Reactions were stirred vigorously at room temperature for 24-48 h after which brine (50 mL) was added and reactions were extracted (2X 50 mL) with Et_2O. The organic layers were combined, filtered over $MgSO_4$, and concentrated *in vacuo*. The resulting residue was purified via flash column chromatography using a gradient of 0 to 5% Et_2O in hexanes (v/v) to provide products **1a-1h, 1p** in 65-98% yield.

2-((3-methylbut-2-en-1-yl)oxy)benzaldehyde (1a)



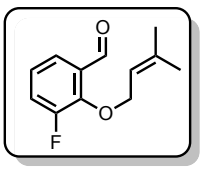
Synthesized according to the general procedure on 8.2 mmol scale. 65% yield (1.02 g, clear colorless oil)

^{1}H NMR: (400 MHz, $CDCl_3$) δ 10.50 (s, 1H), 7.83 (dd, *J* = 7.7, 1.9 Hz, 1H), 7.53 (ddd, *J* = 8.7, 7.4, 1.9 Hz, 1H), 7.00 (m, 2H), 5.51 (t, *J* = 6.7, 1H), 4.64 (d, *J* = 6.6 Hz, 2H), 1.81 (s, 3H), 1.76 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 189.96, 161.32, 138.67, 135.75, 128.24, 125.10, 120.51, 118.94, 112.92, 65.44, 25.73, 18.25.

HR-MS: (APCI) calcd. for $C_{12}H_{14}O_2$ 191.1067 [M + H^+], found 191.1069

3-fluoro-2-((3-methylbut-2-en-1-yl)oxy)benzaldehyde (1b)



Synthesized according to the general procedure on 5.0 mmol scale. 83% yield (0.87 g, clear colorless oil)

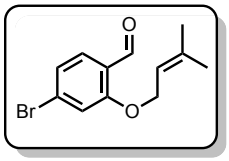
^{1}H NMR: (400 MHz, $CDCl_3$) δ 10.38 (s, 1H), 7.60 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.33 (ddd, *J* = 11.5, 8.1, 1.7 Hz, 1H), 7.10 (td, *J* = 8.0, 4.5 Hz, 1H), 5.50 (tq, *J* = 7.5, 1.4 Hz, 1H), 4.75 (d, *J* = 7.5 Hz, 2H), 1.76 (s, 2H), 1.65 (d, *J* = 1.4 Hz, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 189.27 (d, *J* = 3.3 Hz), 155.60 (d, *J* = 249.0 Hz), 149.29 (d, *J* = 11.2 Hz), 141.00, 131.00 (d, *J* = 2.1 Hz), 123.55 (d, *J* = 7.3 Hz), 123.01 (d, *J* = 3.3 Hz), 122.49 (d, *J* = 19.3 Hz), 118.73, 71.11 (d, *J* = 6.2 Hz), 25.75, 17.91.

^{19}F NMR: (376 MHz, $CDCl_3$) δ -129.70 (s, 1F).

HR-MS: (APCI) calcd. for $C_{12}H_{13}FO_2$ 209.0972 [M + H^+], found 209.0974

4-bromo-2-((3-methylbut-2-en-1-yl)oxy)benzaldehyde (1c)



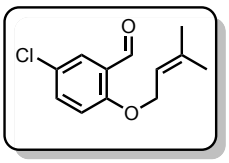
Synthesized according to the general procedure on 1.3 mmol scale. 98% yield (0.33 g, white solid)

^{1}H NMR: (400 MHz, $CDCl_3$) δ 10.42 (s, 1H), 7.69 (d, *J* = 8.6 Hz, 1H), 7.16 (m, 2H), 5.49 (ddq, *J* = 8.1, 5.6, 1.4 Hz, 1H), 4.63 (d, *J* = 6.7 Hz, 2H), 1.83 (s, 3H), 1.78 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 188.97, 161.43, 139.52, 130.35, 129.45, 124.01, 123.94, 118.25, 116.53, 65.85, 25.78, 18.31.

HR-MS: (APCI) calcd. for $C_{12}H_{13}BrO_2$ 269.0172 [M + H^+], found 269.0176

5-chloro-2-((3-methylbut-2-en-1-yl)oxy)benzaldehyde (1d)



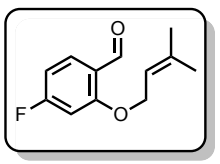
Synthesized according to the general procedure on 2.5 mmol scale. 93% yield (0.520 g, clear colorless oil)

^{1}H NMR: (400 MHz, $CDCl_3$) δ 10.42 (s, 1H), 7.77 (d, *J* = 2.8 Hz, 1H), 7.46 (dd, *J* = 8.9, 2.8 Hz, 1H), 6.94 (d, *J* = 8.9 Hz, 1H), 5.47 (tdt, *J* = 5.6, 2.8, 1.4 Hz, 1H), 4.63 (d, *J* = 6.7 Hz, 2H), 1.81 (s, 3H), 1.76 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 188.64, 159.73, 139.23, 135.22, 127.78, 126.19, 125.97, 118.52, 114.63, 65.87, 25.74, 18.28.

HR-MS: (APCI) calcd. for $C_{12}H_{13}ClO_2$ 225.0677 [M + H^+], found 225.0680

4-fluoro-2-((3-methylbut-2-en-1-yl)oxy)benzaldehyde (1e)



Synthesized according to the general procedure on 4.0 mmol scale. 72% yield (0.60 g, clear colorless oil)

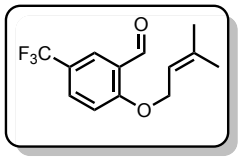
^{1}H NMR: (400 MHz, $CDCl_3$) δ 10.38 (s, 1H), 7.85 (dd, *J* = 8.6, 6.9 Hz, 1H), 6.69 (m, 2H), 5.49 (tdd, *J* = 6.5, 2.9, 1.4 Hz, 1H), 4.62 (d, *J* = 6.7 Hz, 2H), 1.82 (s, 3H), 1.77 (d, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 188.40, 167.59 (d, *J* = 255.7 Hz), 163.02 (d, *J* = 11.2 Hz), 139.40, 130.61 (d, *J* = 11.7 Hz), 121.88 (d, *J* = 2.6 Hz), 118.28, 107.97 (d, *J* = 22.2 Hz), 100.72 (d, *J* = 25.7 Hz), 65.83, 25.75, 18.29.

^{19}F NMR: (376 MHz, $CDCl_3$) δ -100.85 (s, 1F).

HR-MS: (APCI) calcd. for $C_{12}H_{13}FO_2$ 209.0972 [M + H^+], found 209.0974

2-((3-methylbut-2-en-1-yl)oxy)-5-(trifluoromethyl)benzaldehyde (1f)



Synthesized according to the general procedure on 2.0 mmol scale. 81% yield (0.414 g, clear colorless oil)

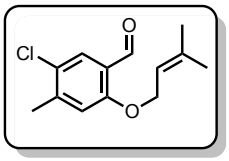
^{1}H NMR: (400 MHz, $CDCl_3$) δ 10.49 (s, 1H), 8.11 (d, *J* = 2.4 Hz, 1H), 7.77 (d, *J* = 8.9 Hz, 1H), 7.09 (d, *J* = 8.8 Hz, 1H), 5.50 (tdd, *J* = 8.1, 6.6, 1.4 Hz, 1H), 4.72 (d, *J* = 6.7 Hz, 2H), 1.83 (ds, 3H), 1.79 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 188.69, 163.15, 139.74, 132.32 (q, *J* = 3.5 Hz), 125.91 (q, *J* = 3.8 Hz), 124.25 (d, *J* = 199.4 Hz), 123.19, 122.62 (d, *J* = 38.8 Hz), 118.15, 113.21, 65.89, 25.79, 18.35.

^{19}F NMR: (470 MHz, $CDCl_3$) δ -62.08 (s, 3F).

HR-MS: (ESI) calcd. for $C_{13}H_{13}F_3O_2$ 282.0793 [M + Na^+], found 282.0790

5-chloro-4-methyl-2-((3-methylbut-2-en-1-yl)oxy)benzaldehyde (1g)



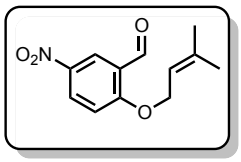
Synthesized according to the general procedure on 1.5 mmol scale. 85% yield (0.299 g, white solid)

^{1}H NMR: (400 MHz, $CDCl_3$) δ 10.37 (s, 1H), 7.78 (s, 1H), 6.87 (s, 1H), 5.49 (ddt, *J* = 6.6, 5.0, 1.4 Hz, 1H), 4.62 (d, *J* = 6.7 Hz, 2H), 2.42 (s, 3H), 1.82 (s, 3H), 1.77 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 188.47, 159.59, 144.38, 139.10, 128.26, 126.65, 124.25, 118.66, 115.56, 65.79, 25.78, 21.21, 18.30.

HR-MS: (APCI) calcd. for $C_{13}H_{15}ClO_2$ 239.0833 [M + H^+], found 239.0837

2-((3-methylbut-2-en-1-yl)oxy)-5-nitrobenzaldehyde (1h)



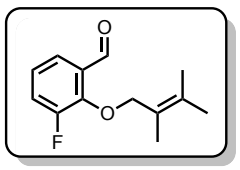
Synthesized according to the general procedure on 1.5 mmol scale. 76% yield (0.264 g, clear colorless oil)

^{1}H NMR: (400 MHz, $CDCl_3$) δ 10.46 (s, 1H), 8.69 (m, 1H), 8.40 (ddt, *J* = 9.2, 2.8, 1.3 Hz, 1H), 7.11 (d, *J* = 9.2 Hz, 1H), 5.50 (tdd, *J* = 6.8, 2.8, 1.5 Hz, 1H), 4.78 (d, *J* = 6.7 Hz, 2H), 1.83 (s, 3H), 1.80 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 187.74, 165.07, 141.33, 140.52, 130.46, 124.73, 124.49, 117.55, 113.25, 66.55, 25.76, 18.37.

HR-MS: (APCI) calcd. for $C_{12}H_{13}NO_4$ 236.0917 [M + H^+], found 236.0921

2-((2,3-dimethylbut-2-en-1-yl)oxy)-3-fluorobenzaldehyde (1p)



Synthesized according to the general procedure on 1.7 mmol scale using 1-bromo-2,3-dimethylbut-2-ene. The allyl bromide electrophile was synthesized according to the literature.[4] 84% yield (0.312 g, white solid)

^{1}H NMR: (400 MHz, $CDCl_3$) δ 10.38 (s, 1H), 7.61 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.34 (ddd, *J* = 11.5, 8.1, 1.7 Hz, 1H), 7.11 (td, *J* = 8.0, 4.4 Hz, 1H), 4.75 (s, 2H), 1.83 (s, 3H), 1.71 (m, 6H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 189.19 (d, *J* = 3.3 Hz), 155.67 (d, *J* = 249.3 Hz), 149.84 (d, *J* = 11.1 Hz), 133.72, 130.99 (d, *J* = 2.2 Hz), 123.53 (d, *J* = 7.3 Hz), 123.34, 123.08 (d, *J* = 3.4 Hz), 122.56 (d, *J* = 19.4 Hz), 76.24 (d, *J* = 6.2 Hz), 20.90, 20.21, 17.48.

^{19}F NMR: (376 MHz, $CDCl_3$) δ -129.45 (s, 1F).

HR-MS: (APCI) calcd. for $C_{13}H_{15}FO_2$ 223.1129 [M + H^+], found 223.1132

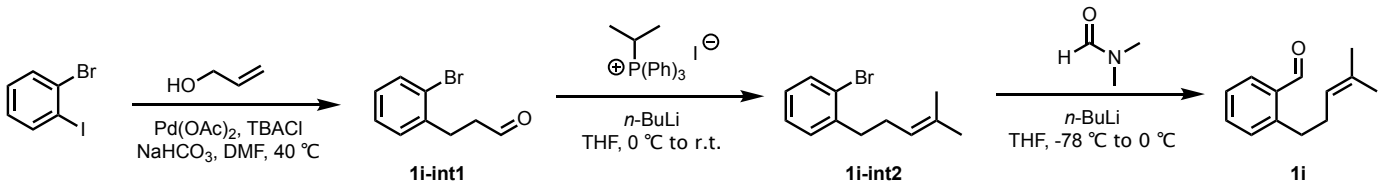
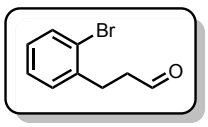


Figure S3. Synthesis of substrate **1i**

3-(2-bromophenyl)propanal (1i-int1)



2-bromoiodobenzene (1.54 mL, 12.0 mmol, 1.0 eq.), allyl alcohol (1.23 mL, 18.0 mmol, 1.5 eq.), tetrabutyl ammonium chloride (3.33 g, 12.0 mmol, 1.0 eq.), sodium bicarbonate (2.52 g, 30.0 mmol, 2.5 eq.), and palladium acetate (0.053 g, 0.24 mmol, 0.02 eq.) were dissolved in anhydrous DMF (13 mL). The reaction mixture was brought to 40 °C for 48 hours, and after this time, was quenched by the addition of brine (30 mL) and diluted in Et_2O (50 mL). The reaction was transferred to a separatory funnel and the aqueous layer was extracted (3X 50 mL) with Et_2O. The organic layers were combined, filtered over $MgSO_4$, and concentrated *in vacuo*. The resulting residue was purified

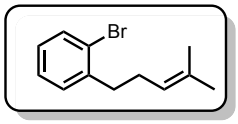
via flash column chromatography using a gradient of 0 to 10% Et_2O in hexanes (v/v) to provide product **1i-int1** in 69% yield (1.77 g) as a clear colorless oil.

^{1}H NMR: (400 MHz, $CDCl_3$) δ 9.85 (t, *J* = 1.3 Hz, 1H), 7.55 (m, 1H), 7.26 (m, 3H), 7.10 (m, 1H), 3.09 (dd, *J* = 8.1, 7.1 Hz, 3H), 2.82 (td, *J* = 7.6, 1.3 Hz, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 201.07, 139.66, 132.95, 130.51, 128.12, 127.65, 124.26, 43.66, 28.68.

HR-MS: (APCI) calcd. for C_9H_9BrO 212.9910 [M + H^+], found 212.9912

1-bromo-2-(4-methylpent-3-en-1-yl)benzene (1i-int2)



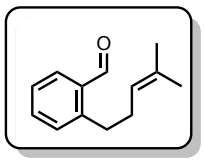
A stirring suspension of isopropyltriphenylphosphonium iodide (4.56 g, 10.6 mmol, 1.5 eq.) in anhydrous THF (15 mL) was cooled to 0 °C before *n*-butyllithium (3.1 mL, 7.74 mmol, 1.1 eq.) was added dropwise over 5 minutes. Upon addition of the organolithium, an immediate dark orange color was observed. After 30 minutes, a solution of aldehyde **1i-int1** (1.50 g, 7.04 mmol, 1.0 eq.) in THF (5 mL) was added slowly and the reaction was allowed to proceed for 24 hours, gradually warming to room temperature. The reaction mixture was quenched by the addition of sat. aq. NH_4Cl (30 mL) and extracted (3X 50 mL) with Et_2O. The organic layers were combined, filtered over $MgSO_4$, and concentrated *in vacuo*. The resulting residue was purified via flash column chromatography using hexanes as the eluent to provide product **1i-int2** in 66% yield (1.11 g) as a clear colorless oil.

^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.53 (m, 1H), 7.22 (m, 2H), 7.05 (ddd, *J* = 8.0, 6.2, 2.9 Hz, 1H), 5.20 (ddq, *J* = 8.7, 5.8, 1.5 Hz, 1H), 2.75 (m, 2H), 2.31 (m, 2H), 1.70 (s, 3H), 1.58 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 141.50, 132.68, 132.63, 130.44, 127.41, 127.24, 124.46, 123.21, 36.39, 28.41, 25.67, 17.60.

HR-MS: (APCI) calcd. for $C_{12}H_{15}Br$ 239.0430 [M + H^+], found 239.0435

2-(4-methylpent-3-en-1-yl)benzaldehyde (1i)



A stirring solution of aryl bromide **1i-int2** (0.50 g, 2.09 mmol, 1.0 eq.) in anhydrous THF (8 mL) was cooled to -78 °C before *n*-butyllithium (1.62 mL, 2.30 mmol, 1.1 eq.) was added dropwise over 5 minutes. After 5 minutes, the reaction was warmed to 0 °C and anhydrous DMF (193 μL, 2.57 mmol, 1.2 eq.) was added. Following 30 minutes of reaction at 0 °C, the reaction mixture was quenched by the addition of sat. aq. NH_4Cl (10 mL) and extracted (3X 20 mL) with Et_2O. The organic layers were combined, filtered over $MgSO_4$, and concentrated *in vacuo*. The resulting residue was purified via flash column chromatography using a gradient of 0 to 3% Et_2O in hexanes (v/v) to provide product **1i** in 46% yield (0.18 g) as a clear colorless oil.

^{1}H NMR: (400 MHz, $CDCl_3$) δ 10.28 (s, 1H), 7.84 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.51 (td, *J* = 7.5, 1.5 Hz, 1H), 7.37 (td, *J* = 7.5, 1.2 Hz, 1H), 7.28 (d, *J* = 8.2 Hz, 1H), 5.19 (tp, *J* = 7.4, 1.5 Hz, 1H), 3.06 (m, 2H), 2.31 (q, *J* = 7.5 Hz, 2H), 1.67 (s, 3H), 1.46 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 191.96, 145.05, 133.83, 133.70, 133.21, 131.11, 130.97, 126.44, 122.79, 32.36, 30.54, 25.62, 17.48.

HR-MS: (APCI) calcd. for $C_{13}H_{16}O$ 189.1274 [M + H^+], found 189.1274

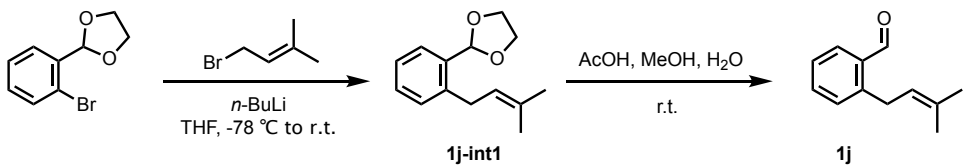
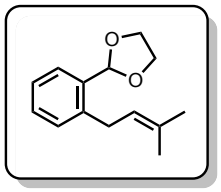


Figure S4. Synthesis of substrate **1j**

2-(2-(3-methylbut-2-en-1-yl)phenyl)-1,3-dioxolane (1j-int1)



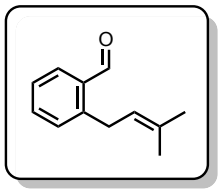
A stirring solution of aryl bromide (297 µL, 2.0 mmol, 1.0 eq.) in anhydrous THF (10 mL) was cooled to -78 °C before *n*-butyllithium solution (840 µL, 2.1 mmol, 1.05 eq.) was added dropwise over ten minutes. After the reaction was maintained at -78 °C for 30 minutes, prenyl bromide (242 µL, 2.1 mmol, 1.05 eq.) were added in a single motion. Following addition, the reaction was allowed to proceed at -78 °C for 30 minutes, after which the ice bath was removed and the reaction slowly warmed to room temperature. After one hour, the reaction was quenched with sat. aq. NH_4Cl (10 mL) and extracted (3X 40 mL) with Et_2O. The organic layers were combined, filtered over $MgSO_4$, and concentrated *in vacuo*. The resulting residue was purified via flash column chromatography using a gradient of 0 to 5% Et_2O in hexanes (v/v) to provide product **1j-int1** in 75% yield (0.327 g) as a clear colorless oil.

^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.57 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.30 (td, *J* = 7.4, 1.6 Hz, 1H), 7.22 (ddd, *J* = 12.4, 7.2, 1.6 Hz, 2H), 6.01 (s, 1H), 5.29 (ddp, *J* = 7.2, 5.9, 1.5 Hz, 1H), 4.16 (m, 2H), 4.05 (m, 2H), 3.49 (d, *J* = 7.2 Hz, 2H), 1.75 (s, 3H), 1.74 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 140.24, 135.02, 132.40, 129.38, 129.11, 125.91, 125.88, 122.91, 101.58, 65.23, 30.88, 25.73, 17.85.

HR-MS: (APCI) calcd. for $C_{14}H_{18}O_2$ 219.1380 [M + H$^+$], found 219.1382

2-(3-methylbut-2-en-1-yl)benzaldehyde (1j)



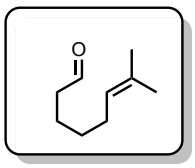
Acetal **1j-int1** (0.327g, 1.5 mmol, 1.0 eq.) was dissolved in a mixture of THF (5 mL) and water (5 mL). Glacial acetic acid (5 mL) was added, and the reaction was allowed to stir at room temperature for 1 hour, before TLC analysis indicated full consumption of the starting material. The crude reaction was then diluted in Et_2O (30 mL) and cooled to 0 °C before sat. aq. $NaHCO_3$ (30 mL) was added slowly. After bubbling had ceased, the reaction was transferred to a separatory funnel and the aqueous layer was extracted (3X 40 mL) with Et_2O. The organic layers were combined, filtered over $MgSO_4$, and concentrated *in vacuo*. The resulting residue was purified via flash column chromatography using a gradient of 0 to 15% DCM in hexanes (v/v) to provide product **1j** in 76% yield (0.197 g) as a clear colorless oil.

^{1}H NMR: (400 MHz, $CDCl_3$) δ 10.30 (s, 1H), 7.84 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.52 (td, *J* = 7.5, 1.5 Hz, 1H), 7.37 (td, *J* = 7.6, 1.2 Hz, 1H), 7.31 (d, *J* = 7.6 Hz, 1H), 5.28 (tp, *J* = 7.1, 1.3 Hz, 1H), 3.77 (d, *J* = 7.0 Hz, 2H), 1.75 (s, 6H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 192.49, 144.46, 133.92, 133.75, 133.07, 131.17, 130.49, 126.47, 122.62, 31.19, 25.69, 17.97.

HR-MS: (APCI) calcd. for $C_{12}H_{14}O$ 175.1117 [M + H$^+$], found 175.1119

7-methyloct-6-enal (1k)



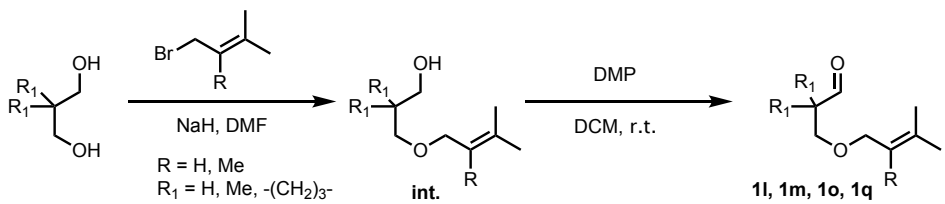
Synthesized according to the literature[5] on 12.0 mmol scale. NMR spectra were in agreement with those reported. 20% yield over 5 steps (0.288 g, clear colorless oil).

^{1}H NMR: (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 5.11 (td, *J* = 7.1, 3.6 Hz, 1H), 2.43 (td, *J* = 7.4, 1.9 Hz, 2H), 2.01 (q, *J* = 7.3 Hz, 2H), 1.69 (s, 3H), 1.64 (m, 2H), 1.61 (s, 3H), 1.38 (tt, *J* = 10.0, 6.5 Hz, 2H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 202.83, 131.90, 123.98, 43.84, 29.33, 27.67, 25.69, 21.69, 17.67.

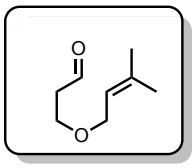
HR-MS: (APCI) calcd. for $C_9H_{16}O$ 141.1274 [M + H$^+$], found 141.1275

General procedure for the synthesis of substrates 1l, 1m, 1o, and 1q



Substrates **1l**, **1m**, **1o**, and **1q** were synthesized according to the following general procedure. *Step 1:* To a slurry of NaH (1.5 eq.) in dry DMF (1.0 M with respect to the diol) was added the appropriate diol (5.0 eq.) and the reaction mixture was allowed to stir for 15 min. Then, allylic bromide (1.0 eq.) was added and the reaction was allowed to stir at room temperature for 24 hours. After this period, the reaction was diluted in NH_4Cl (sat. aq.) and extracted (2X) with Et_2O. The organic layers were combined, filtered over $MgSO_4$, and was concentrated under reduced pressure. The resulting crude alkylated intermediate (**int**. in the scheme above) was then purified via silica gel chromatography using Et_2O/hexanes. *Step 2:* Alcohol intermediates (**int.**) were taken in anhydrous DCM (0.2 M) and subjected to treatment with DMP (1.2 eq.) for 1 hour. After this time, the crude reactions were passed through a short pad of silica gel eluting with 50% Et_2O/hexanes (v/v). The eluent was concentrated under reduced pressure and the resulting residue was purified via flash column chromatography using a gradient of 0 to 5% Et_2O in hexanes (v/v) to provide products **1l**, **1m**, **1o**, and **1q**.

3-((3-methylbut-2-en-1-yl)oxy)propanal (1l)



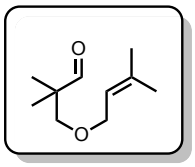
Synthesized according to the general procedure on 3.5 mmol scale. 82% yield (0.402 g, clear colorless oil)

^{1}H NMR: (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 5.33 (ddq, *J* = 8.4, 7.0, 1.4 Hz, 1H), 3.99 (d, *J* = 7.0 Hz, 2H), 3.76 (t, *J* = 6.1 Hz, 2H), 2.68 (td, *J* = 6.1, 1.8 Hz, 2H), 1.75 (s, 3H), 1.68 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 201.31, 137.53, 120.61, 67.53, 63.52, 43.93, 25.76, 17.98.

HR-MS: (APCI) calcd. for $C_8H_{14}O_2$ 143.1067 [M + H^+], found 143.1068

2,2-dimethyl-3-((3-methylbut-2-en-1-yl)oxy)propanal (1m)



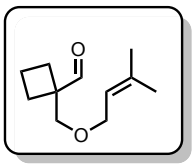
Synthesized according to the general procedure on 1.6 mmol scale. 76% yield (0.202 g, clear colorless oil)

^{1}H NMR: (400 MHz, $CDCl_3$) δ 9.57 (s, 1H), 5.29 (tt, *J* = 6.7, 1.4 Hz, 1H), 3.95 (d, *J* = 6.8 Hz, 2H), 3.41 (s, 2H), 1.75 (s, 3H), 1.66 (s, 3H), 1.08 (s, 6H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 205.61, 136.93, 120.95, 74.94, 67.98, 47.08, 25.75, 19.09, 18.05.

HR-MS: (APCI) calcd. for $C_{10}H_{18}O_2$ 171.1380 [M + H^+], found 171.1382

2,2-dimethyl-3-((3-methylbut-2-en-1-yl)oxy)propanal (1o)



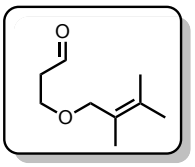
Synthesized according to the general procedure on 1.25 mmol scale. 69% yield (0.158 g, clear colorless oil)

^{1}H NMR: (400 MHz, $CDCl_3$) δ 9.69 (s, 1H), 5.32 (dddd, *J* = 8.3, 5.6, 2.9, 1.5 Hz, 1H), 3.98 (d, *J* = 6.9 Hz, 2H), 3.68 (s, 2H), 2.31 (m, 2H), 1.94 (m, 4H), 1.75 (s, 3H), 1.67 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 203.24, 137.20, 120.88, 72.35, 67.89, 52.42, 25.78, 24.49, 18.06, 15.56.

HR-MS: (APCI) calcd. for $C_{11}H_{18}O_2$ 183.1380 [M + H^+], found 183.1382

3-((2,3-dimethylbut-2-en-1-yl)oxy)propanal (1q)



Synthesized according to the general procedure on 1.15 mmol scale. 74% yield (0.132 g, clear colorless oil)

^{1}H NMR: (400 MHz, $CDCl_3$) δ 9.81 (t, *J* = 2.1 Hz, 1H), 3.99 (s, 2H), 3.72 (t, *J* = 6.1 Hz, 2H), 2.68 (td, *J* = 6.1, 1.9 Hz, 2H), 1.74 (s, 3H), 1.70 (s, 6H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 201.42, 130.47, 124.58, 71.77, 63.28, 43.92, 20.84, 20.12, 16.71, 16.66.

HR-MS: (APCI) calcd. for $C_9H_{16}O_2$ 157.1223 [M + H^+], found 157.1225

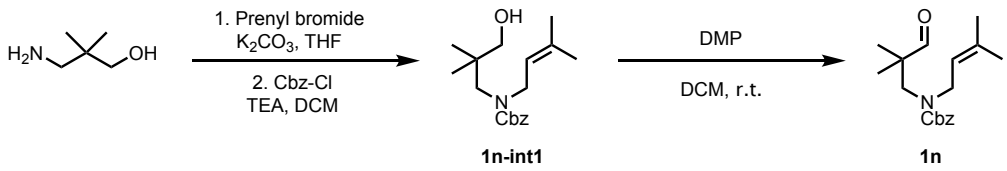
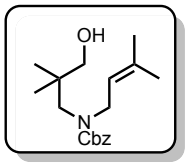


Figure S5. Synthesis of substrate **1n**

benzyl (3-hydroxy-2,2-dimethylpropyl)(3-methylbut-2-en-1-yl)carbamate (1n-int1)



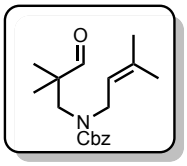
To a stirring solution of 3-amino-2,2-dimethyl-1-propanol (0.516 g, 5.0 mmol, 2.0 eq.) and K_2CO_3 (0.518 g, 3.75 mmol, 1.5 eq.) in THF (13 mL) was added prenyl bromide (288 µL, 1.5 mmol, 1.0 eq.) dropwise over two minutes. The allylation reaction was allowed to proceed for 2 hours at room temperature before being diluted in Et_2O and washed with brine (2X). The organic layer was filtered over $MgSO_4$, concentrated *in vacuo*, and the resulting residue was resuspended in DCM (13 mL) and cooled to 0 °C before TEA (3.46 mL, 25 mmol, 5.0 eq.) and CbzCl (2.15 mL, 15 mmol, 3.0 eq) were added in succession. After one hour, the reaction was quenched by the addition of sat. aq. $NaHCO_3$ and extracted with Et_2O (3X). The organic layers were combined, filtered over $MgSO_4$, and concentrated *in vacuo*. The resulting residue was purified via flash column chromatography using a gradient of 0 to 30% Et_2O in hexanes (v/v) to provide product **1n-int1** in 63% yield (0.48 g) as a clear light yellow oil.

^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.37 (m, 5H), 7.31 (dt, *J* = 7.2, 2.9 Hz, 1H), 5.16 (s, 3H), 4.71 (d, *J* = 5.2 Hz, 1H), 4.35 (t, *J* = 7.5 Hz, 1H), 3.86 (d, *J* = 6.8 Hz, 2H), 3.18 (d, *J* = 7.5 Hz, 2H), 3.08 (s, 1H), 1.71 (s, 3H), 1.59 (s, 3H), 0.91 (s, 6H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 158.38, 140.89, 136.48, 135.24, 128.55, 128.47, 128.04, 127.83, 127.64, 126.97, 120.11, 67.94, 67.59, 65.38, 53.56, 47.64, 37.92, 25.67, 23.33, 17.83.

HR-MS: (APCI) calcd. for $C_{18}H_{27}NO_3$ 306.2064 [M + H^+], found 306.2070

benzyl (2,2-dimethyl-3-oxopropyl)(3-methylbut-2-en-1-yl)carbamate (1n)



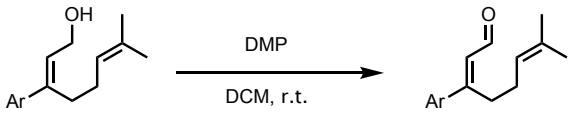
Alcohol intermediate **1n-int1** (0.188 g, 0.62 mmol, 1.0 eq.) was taken in anhydrous DCM (3.1 mL) and subjected to treatment with DMP (0.284 g, 0.67 mmol, 1.1 eq.) for 1 hour. After this time, the crude reaction was passed through a short pad of silica gel eluting with 50% Et_2O/hexanes (v/v). The eluent was concentrated under reduced pressure and the resulting residue was purified via flash column chromatography using a gradient of 0 to 5% Et_2O in hexanes (v/v) to provide product **1n** as a clear colorless oil in 85% yield (0.160 g). Note: **1n** exists as a 1.5 : 1 mixture of rotomers about the CN bond of the Cbz group.

^{1}H NMR: (400 MHz, $CDCl_3$) δ 9.48 (s, 1H), 7.35 (m, 5H), 5.10 (m, 3H), 3.84 (m, 2H), 3.35 (m, 2H), 1.64 (m, 6H), 1.07 (m, 6H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 204.42, 156.89, 136.62, 135.46, 128.43, 127.92, 127.79, 120.04, 67.29, 53.34, 52.02, 48.03, 46.78, 25.68, 20.03, 17.82.

HR-MS: (APCI) calcd. for $C_{18}H_{25}NO_3$ 304.1907 [M + H^+], found 304.1913

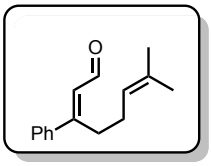
General procedure for the synthesis of substrates 1s-1u



1r-1t

Enal substrates were generated from the corresponding allylic alcohols via Dess-Martin periodinane mediated oxidation. The corresponding allylic alcohol[1] (1.0 eq.) was taken in DCM (0.2 M) and DMP (1.2 eq.) was added in a single portion. The reaction mixture was stirred vigorously for 30 min after which point it was filtered over a short pad of silica gel eluting with 25% Et_2O/hexanes (v/v). The eluent was concentrated under reduced pressure and the resulting residue was purified via flash column chromatography using a gradient of 0 to 5% Et_2O in hexanes (v/v) to provide products **1r-1t**.

(*E*)-7-methyl-3-phenylocta-2,6-dienal (1r)



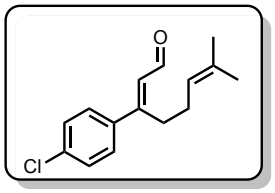
Synthesized according to the general procedure on 0.69 mmol scale. 78% yield (0.116 g, clear colorless oil)

^{1}H NMR: (400 MHz, $CDCl_3$) δ 10.08 (d, *J* = 8.0 Hz, 1H), 7.51 (m, 2H), 7.43 (m, 3H), 6.30 (d, *J* = 8.0 Hz, 1H), 5.12 (ddt, *J* = 8.9, 7.4, 1.5 Hz, 1H), 3.06 (t, *J* = 7.4 Hz, 2H), 2.20 (q, *J* = 7.5 Hz, 2H), 1.67 (s, 3H), 1.50 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 191.05, 162.13, 139.76, 133.95, 129.83, 128.76, 128.05, 126.70, 122.10, 29.94, 27.98, 25.62, 17.75.

HR-MS: (APCI) calcd. for $C_{15}H_{18}O$ 215.1430 [M + H^+], found 215.1430

(*E*)-3-(4-chlorophenyl)-7-methylocta-2,6-dienal (1s)



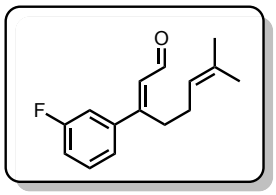
Synthesized according to the general procedure on 2.70 mmol scale. 72% yield (0.483 g, clear yellow oil)

^{1}H NMR: (400 MHz, $CDCl_3$) δ 10.07 (d, *J* = 7.9 Hz, 1H), 7.41 (m, 4H), 6.26 (d, *J* = 7.9 Hz, 1H), 5.09 (tdd, *J* = 6.0, 2.9, 1.5 Hz, 1H), 3.03 (t, *J* = 7.4 Hz, 2H), 2.18 (q, *J* = 7.4 Hz, 2H), 1.66 (s, 3H), 1.49 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 190.80, 160.52, 138.17, 135.90, 134.17, 129.03, 128.20, 128.00, 121.85, 29.83, 27.85, 25.61, 17.77.

HR-MS: (APCI) calcd. for $C_{15}H_{17}ClO$ 250.1074 [M + H^+], found 250.1076

(*E*)-3-(3-fluorophenyl)-7-methylocta-2,6-dienal (1t)



Synthesized according to the general procedure on 1.80 mmol scale. 93% yield (0.389 g, clear yellow oil)

^{1}H NMR: (400 MHz, $CDCl_3$) δ 10.08 (d, *J* = 7.9 Hz, 1H), 7.39 (td, *J* = 8.0, 5.8 Hz, 1H), 7.29 (m, 1H), 7.19 (dt, *J* = 10.1, 2.2 Hz, 1H), 7.12 (m, 1H), 6.28 (d, *J* = 7.9 Hz, 1H), 5.10 (ddt, *J* = 9.0, 7.3, 1.5 Hz, 1H), 3.03 (t, *J* = 7.4 Hz, 2H), 2.20 (q, *J* = 7.4 Hz, 2H), 1.67 (s, 3H), 1.50 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 190.82, 162.93 (d, *J* = 247.0 Hz), 160.40 (d, *J* = 2.3 Hz), 142.16 (d, *J* = 7.3 Hz), 134.21, 130.34 (d, *J* = 8.3 Hz), 128.60, 122.41 (d, *J* = 2.9 Hz), 121.84, 116.61 (d, *J* = 21.2 Hz), 113.69 (d, *J* = 22.4 Hz), 29.95, 27.83, 25.61, 17.76.

^{19}F NMR: (376 MHz, $CDCl_3$) δ -113.23 (s, 1F).

HR-MS: (APCI) calcd. for $C_{15}H_{17}FO$ 223.1336 [M + H^+], found 223.1338

4. Procedures for Catalytic Enantioselective Prins Cyclization Reactions

4.1 Optimization experiments:

General procedure A for optimization experiments using various Brønsted Acids:

Hydrogen-bond donor catalyst (10 mol%) and substrate **1a** (0.08 mmol, 1.0 eq.) were weighed directly into a flame-dried 1 dram vial charged with a magnetic stir bar. Anhydrous C_6D_6 (800 μL) was added, followed by mesitylene internal standard (6 μL). Reactions were initiated by the addition of stock solutions of Brønsted acid (3 μL of 2M solutions in Et_2O) added through the vial septum cap and were carried out at 23 °C for 24 hours. Following addition of the acid, the punctured septum was replaced immediately and the vial top was wrapped in electrical tape to prevent any volume changes. After 24 hours, a 550 μL aliquot of the reaction mixture was removed for analysis by ^{1}H NMR. The remaining portion of the reaction was diluted in Et_2O (500 μL), quenched with triethylamine (0.16 mmol, 2 eq.), passed through a short plug of silica gel eluting with Et_2O, and concentrated under reduced pressure before determination of enantiomeric excess following TMS derivatization as described below.

General procedure B for optimization experiments using AcCl/EtOH:

Hydrogen-bond donor catalyst (2-10 mol%) and substrate (0.08 mmol, 1.0 eq.) were weighed directly into a flame-dried 1 dram vial charged with a magnetic stir bar. Anhydrous C_6D_6 (800 μL) was added, followed by mesitylene internal standard (6 μL) and a solution of ethanol in anhydrous diethyl ether (12 μL of a 2.0 M solution, 0.024 mmol, 0.3 eq.). Reactions were initiated by the addition of acetyl chloride (12 μL of a 2 M solution, 0.024 mmol, 0.3 eq.) through the septum cap and were carried out at 23 °C for 24 hours. Following addition of AcCl, the punctured septum was replaced immediately and the vial top was wrapped in electrical tape to prevent any volume changes. After the specified period of time, a 550 μL aliquot of the reaction mixture was removed for analysis by ^{1}H NMR. The remaining portion of the reaction was diluted in Et_2O (500 μL), quenched with triethylamine (0.16 mmol, 2 eq.), passed through a short plug of silica gel eluting with Et_2O, and concentrated under reduced pressure before determination of enantiomeric excess following TMS derivatization as described below.

4.2 Scope-scale experiments:

General procedure C for enantioselective Prins reactions:

Hydrogen-bond donor catalyst **9** (0.0111 g, 0.015 mmol, 5 mol%) and substrate **1** (0.3 mmol, 1.0 eq.) were weighed directly into a flame-dried 20 mL scintillation vial charged with a magnetic stir bar. Anhydrous toluene (3 mL) was added, followed by a solution of anhydrous ethanol in anhydrous diethyl ether (45 μL of a 2 M solution, 0.1 mmol, 0.3 eq.). Reactions were initiated by the addition of an ethereal solution of acetyl chloride (45 μL of a 2 M solution, 0.1 mmol, 0.3 eq.) and were carried out at 23 °C. After completion of the reaction (as indicated by TLC analysis), a solution of KHMDS in THF (180 μL of a 1 M solution, 0.180 mmol, 0.6 eq.) was added and a dark yellow color was seen to develop. After 10 minutes, the reaction mixture was passed through a plug of silica gel eluting with Et_2O and concentrated *in vacuo*. The resulting residue was purified via flash column chromatography using Et_2O and hexanes as the eluents to provide homoallylic alcohol products. Enantiomeric excess of cyclized products was evaluated following TMS derivatization as described below.

General procedure D for enantioselective Prins reactions of volatile substrates:

Hydrogen-bond donor catalyst **9** (0.0037 g, 0.01 mmol 5 mol%) and substrate **1** (0.1 mmol, 1.0 eq.) were weighed directly into a flame-dried 1 dram vial charged with a magnetic stir bar. C_6D_6 (1 mL) and mesitylene internal standard (6 μL) were added, followed by a solution of ethanol in anhydrous diethyl ether (15 μL of a 2 M solution, 0.1 mmol, 0.3 eq.). Reactions were initiated by the addition of an ethereal solution of acetyl chloride (15 μL of a 2 M solution, 0.1 mmol, 0.3 eq.) through the septum cap and were carried out at 23 °C. Following addition of AcCl, 600 μL of the reaction were removed and transferred to an oven-dried 5 mm NMR tube fitted with a rubber septum. After completion of the reaction (5 h), a solution of KHMDS in THF (36 μL of a 1 M solution, 0.036 mmol, 0.6 eq.) was added and a dark yellow color was seen to develop immediately. After 10 minutes, the reaction mixture was analyzed by ^{1}H NMR to determine the yield of cyclized products against the mesitylene internal standard. The reaction mixture was then passed through a plug of silica gel eluting with Et_2O and concentrated *in vacuo*. Enantiomeric excess values were evaluated by chiral GC following the TMS derivatization as described below.

4.3 Gram-scale synthesis of 2b:

Hydrogen-bond donor catalyst **9** (0.0371 g, 0.05 mmol, 1 mol%) and substrate **1b** (1.04 g, 5.0 mmol, 1.0 eq.) were weighed directly into a flame-dried 20 mL vial and then transferred (using 5 mL of anhydrous toluene) to a flame-dried 200 mL round bottom flask charged with a magnetic stir bar. Anhydrous toluene (45 mL) was added, followed by a solution of HCl in Et_2O (2 M, 1.5 mol, 0.3 eq.), which was added dropwise over a 5 minute period. After one hour at 23 °C, the reaction was observed to have proceeded to full conversion by TLC (30% Et_2O in hexanes, v/v) and a solution of KHMDS in THF (2.25 mL of a 1 M solution, 2.25 mmol, 0.45 eq.) was added. After 10 minutes, 50 mL of sat. aq. NH_4Cl were added, followed by 100 mL of Et_2O, and the biphasic mixture was transferred to a separatory funnel. The organic layer was washed with sat. aq. NH_4Cl (2X), filtered over $MgSO_4$, and concentrated *in vacuo*. The resulting residue was purified via flash column chromatography using a gradient of 0 to 30% Et_2O in hexanes (v/v) to provide product **2b** in 71% yield (0.744 g) as a white solid. 0.023 g of catalyst **9** were recovered from the reaction (62% recovery). Enantiomeric excess of **2b** was evaluated following TMS derivatization as described below and was found to be 96% ee. **2b** could be recrystallized from 2:1 (v/v) hexanes/DCM to provide product in 99% ee.

General procedure for racemic Prins reactions:

Substrate **1** (0.05 mmol) was weighed directly into a flame-dried 1-dram vial charged with a magnetic stir bar. Anhydrous toluene (500 μL) was added, followed by HCl (12.5 μL of a 2 M solution in Et_2O, 0.025 mmol, 0.5 eq.) and reactions were allowed to stir at 23 °C for 24-72 hours. After this time, the solvent was evaporated under reduced pressure and the crude reaction mixture was analyzed by chiral GC or HPLC following the TMS derivatization as described below.

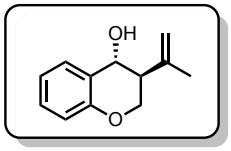
General procedure for silylation of compounds 2 for determination of enantiomeric excess:

Chiral homoallylic alcohol products **2** were in some cases derivatized to the corresponding TMS protected ethers prior to evaluation of ee using the following procedure. TMS protection was used to achieve superior separation using chiral GC as well as enhanced volatility. To a flame-dried vial charged with homoallylic alcohol (0.05 mmol, 1 eq.) was added DCM (500 μL) and TEA (0.35 mmol, 7 eq.). TMSCl (0.15 mmol, 3 eq.) was added and the reaction was allowed to proceed at 23 °C for 5 minutes. After this period, the reaction was concentrated under reduced pressure and the resulting solid white residue was taken in Et_2O (1.5 mL) and filtered through a 0.2 μM filter directly into a GC vial. Enantioselectivity values were determined for products **2h, 2n,** and **2p** as the free alcohols without derivatization. Product **2m** was protected as the acetate using the above procedure with Ac_2O in place of TMSCl.

5. Synthesis and Characterization of Products 2a-2t

5.1 Tabulated characterization data

(3*S*,4*R*)-3-(prop-1-en-2-yl)chroman-4-ol (2a)



Synthesized from **1a** according to general procedure C on 0.3 mmol scale using 5 mol% of catalyst **9**. 24 h reaction time. 79% yield (0.045 g, white solid), d.r. = 35 : 1 (crude material), d.r. = 39 : 1 (purified material).

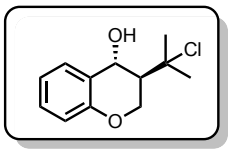
^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.47 (dt, *J* = 7.7, 1.2 Hz, 1H), 7.20 (ddd, *J* = 8.6, 7.5, 1.7 Hz, 1H), 6.96 (td, *J* = 7.5, 1.2 Hz, 1H), 6.83 (dd, *J* = 8.3, 1.2 Hz, 1H), 5.02 (s, 1H), 4.87 (s, 1H), 4.83 (d, *J* = 7.7 Hz, 1H), 4.28 (dd, *J* = 11.2, 3.5 Hz, 1H), 4.10 (dd, *J* = 11.2, 8.8 Hz, 1H), 2.60 (td, *J* = 8.2, 3.5 Hz, 1H), 2.00 (s, 1H), 1.85 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 153.98, 142.00, 129.18, 128.18, 124.51, 120.81, 116.42, 113.77, 67.05, 66.55, 47.78, 21.49.

HR-MS: (ESI) calcd. for $C_{12}H_{14}O_2$ 191.1067 [M + H^+], found 191.1067

$[a]_D^{22} = +17.0°$ (c = 1.0, CH_2Cl_2)

(3*S*,4*R*)-3-(2-chloropropan-2-yl)chroman-4-ol (3a)



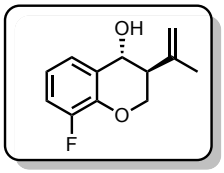
Synthesized from **1a**. **3a** was found to be Inseparable from **2a** using conventional silica gel chromatography. Characterization was performed on a 3:1 mixture of **3a** and **2a**. The data presented below correspond to **3a**.

^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.41 (m, 1H), 7.23 (m, 1H), 6.99 (m, 1H), 6.85 (m, 1H), 4.99 (m, 1H), 4.35 (m, 2H), 2.30 (dt, *J* = 5.4, 4.0 Hz, 1H), 1.73 (s, 3H), 1.59 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 154.61, 129.61, 129.56, 124.80, 121.45, 116.82, 71.54, 65.47, 64.60, 52.43, 31.50, 31.27.

HR-MS: (APCI) calcd. for $C_{12}H_{15}ClO_2$ 261.0455 [M + Cl^-], found 261.0455

(3*S*,4*R*)-8-fluoro-3-(prop-1-en-2-yl)chroman-4-ol (2b)



Synthesized from **1b** according to general procedure C on 0.3 mmol scale using 5 mol% of catalyst **9**. 3 h reaction time. 80% yield (0.050 g, white solid), d.r. = 31 : 1 (crude material), d.r. = 33 : 1 (purified material).

^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 7.8 Hz, 1H), 7.01 (ddd, *J* = 10.6, 8.2, 1.6 Hz, 1H), 6.88 (td, *J* = 7.9, 4.8 Hz, 1H), 5.04 (s, 1H), 4.89 (s, 1H), 4.85 (dd, *J* = 7.9, 4.9 Hz, 1H), 4.38 (dd, *J* = 11.3, 3.6 Hz, 1H), 4.17 (dd, *J* = 11.2, 8.9 Hz, 1H), 2.63 (td, *J* = 8.4, 3.6 Hz, 1H), 2.04 (m, 1H), 1.85 (s, 3H).

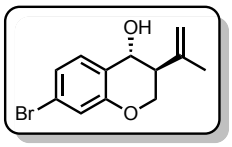
^{13}C NMR: (101 MHz, $CDCl_3$) δ 151.08 (d, *J* = 245.0 Hz), 142.37 (d, *J* = 11.3 Hz), 141.47, 126.97 (d, *J* = 1.4 Hz), 123.03 (d, *J* = 3.6 Hz), 120.22 (d, *J* = 7.0 Hz), 115.40 (d, *J* = 17.8 Hz), 114.18, 67.00, 66.65 (d, *J* = 3.0 Hz), 47.48, 21.43.

^{19}F NMR: (376 MHz, $CDCl_3$) δ -138.01 (s, 1F)

HR-MS: (APCI) calcd. for $C_{12}H_{13}FO_2$ 209.0972 [M + H^+], found 209.0974

$[a]_D^{22} = +22.2°$ (c = 1.0, CH_2Cl_2)

(3*S*,4*R*)-7-bromo-3-(prop-1-en-2-yl)chroman-4-ol (2c)



Synthesized from **1c** according to general procedure C on 0.3 mmol scale using 5 mol% of catalyst **9**. 24 h reaction time. 77% yield (0.062 g, white solid), d.r. = 26 : 1 (crude material), d.r. = 34 : 1 (purified material).

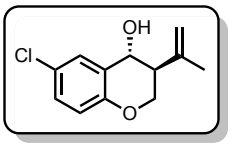
^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.2 Hz, 1H), 7.08 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.00 (d, *J* = 2.0 Hz, 1H), 5.03 (s, 1H), 4.87 (s, 1H), 4.76 (dd, *J* = 7.9, 4.6 Hz, 1H), 4.27 (dd, *J* = 11.2, 3.6 Hz, 1H), 4.09 (dd, *J* = 11.3, 8.9 Hz, 1H), 2.57 (td, *J* = 8.4, 3.6 Hz, 1H), 2.02 (m, 1H) 1.84 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 154.76, 141.54, 129.50, 123.92, 123.55, 122.18, 119.51, 114.11, 66.81, 66.66, 47.49, 21.41.

HR-MS: (APCI) calcd. for $C_{12}H_{13}BrO_2$ 269.0172 [M + H^+], found 269.0171

$[a]_D^{22} = +2.2°$ (c = 1.0, CH_2Cl_2)

(3*S*,4*R*)-6-chloro-3-(prop-1-en-2-yl)chroman-4-ol (2d)



Synthesized from **1d** according to general procedure C on 0.3 mmol scale using 5 mol% of catalyst **9**. 24 h reaction time. 84% yield (0.056 g, white solid), d.r. = 22 : 1 (crude material), d.r. = 26 : 1 (purified material).

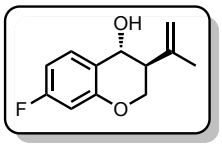
^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.46 (dd, *J* = 2.6, 0.9 Hz, 1H), 7.13 (m, 1H), 6.75 (d, *J* = 8.7 Hz, 1H), 5.04 (s, 1H), 4.88 (s, 1H), 4.78 (dd, *J* = 8.1, 4.9 Hz, 1H), 4.26 (dd, *J* = 11.3, 3.6 Hz, 1H), 4.07 (dd, *J* = 11.3, 9.2 Hz, 1H), 2.57 (td, *J* = 8.7, 3.6 Hz, 1H), 2.06 (s, 1H), 1.83 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 152.57, 141.55, 129.11, 127.82, 125.97, 125.59, 117.80, 114.16, 66.84, 66.80, 47.53, 21.36.

HR-MS: (APCI) calcd. for $C_{12}H_{13}ClO_2$ 225.0677 [M + H^+], found 225.0677

$[a]_D^{22} = -7.0°$ (c = 1.0, CH_2Cl_2)

(3*S*,4*R*)-7-fluoro-3-(prop-1-en-2-yl)chroman-4-ol (2e)



Synthesized from **1e** according to general procedure C on 0.3 mmol scale using 5 mol% of catalyst **9**. 24 h reaction time. 72% yield (0.045 g, white solid), d.r. = 30 : 1 (crude material), d.r. = 31 : 1 (purified material).

^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.41 (dd, *J* = 8.6, 6.6 Hz, 1H), 6.68 (m, 1H), 6.54 (dd, *J* = 10.2, 2.5 Hz, 1H), 5.02 (s, 1H), 4.86 (s, 1H), 4.79 (dd, *J* = 7.7, 4.0 Hz, 1H), 4.28 (dd, *J* = 11.2, 3.5 Hz, 1H), 4.11 (dd, *J* = 11.2, 8.6 Hz, 1H), 2.57 (td, *J* = 8.2, 3.6 Hz, 1H), 1.99 (s, 1H), 1.83 (s, 3H).

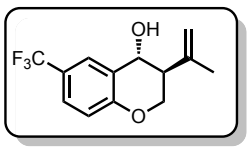
^{13}C NMR: (101 MHz, $CDCl_3$) δ 163.05 (d, *J* = 245.6 Hz), 155.16 (d, *J* = 12.3 Hz), 141.66, 129.51 (d, *J* = 10.1 Hz), 120.42 (d, *J* = 3.1 Hz), 113.98, 108.10 (d, *J* = 21.8 Hz), 103.46 (d, *J* = 24.6 Hz), 66.74, 66.60, 47.58, 21.48.

^{19}F NMR: (376 MHz, $CDCl_3$) δ -113.58 (s, 1F)

HR-MS: (APCI) calcd. for $C_{12}H_{13}FO_2$ 209.0972 [M + H^+], found 209.0975

$[a]_D^{22} = +10.0°$ (c = 1.0, CH_2Cl_2)

(3*S*,4*R*)-3-(prop-1-en-2-yl)-6-(trifluoromethyl)chroman-4-ol (2f)



Synthesized from **1f** according to general procedure C on 0.3 mmol scale using 5 mol% of catalyst **9**. 15 h reaction time. 81% yield (0.063 g, white solid), d.r. = 22 : 1 (crude material), d.r. = 24 : 1 (purified material).

^{1}H NMR: (500 MHz, $CDCl_3$) 7.78 (s, 1H), 7.44 (d, *J* = 8.6 Hz, 1H), 6.89 (d, *J* = 8.6 Hz, 1H), 5.07 (s, 1H), 4.91 (s, 1H), 4.84 (d, *J* = 8.3 Hz, 1H), 4.33 (dd, *J* = 11.3, 3.6 Hz, 1H), 4.13 (dd, *J* = 11.3, 9.4 Hz, 1H), 2.61 (td, *J* = 8.8, 3.6 Hz, 1H), 2.09 (br, 1H), 1.85 (s, 3H).

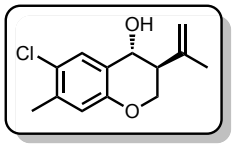
^{13}C NMR: (101 MHz, $CDCl_3$) δ 156.53, 141.29, 126.21 (q, *J* = 3.6 Hz), 125.69 (q, *J* = 3.9 Hz), 124.78, 123.07 (d, *J* = 14.1 Hz), 122.82, 116.82, 114.41, 67.06, 66.64, 47.39, 21.32.

^{19}F NMR: (470 MHz, $CDCl_3$) δ -61.58 (s, 3F)

HR-MS: (ESI) calcd. for $C_{13}H_{13}F_3O_2$ 258.0828 [M + H^+], found 258.0826

$[a]_D^{22} = +2.2°$ (c = 1.0, $CDCl_3$)

(3*S*,4*R*)-6-chloro-7-methyl-3-(prop-1-en-2-yl)chroman-4-ol (2g)



Synthesized from **1g** according to general procedure C on 0.3 mmol scale using 5 mol% of catalyst **9**. 24 h reaction time. 77% yield (0.055 g, white solid), d.r. = 23 : 1 (crude material), d.r. = 28 : 1 (purified material).

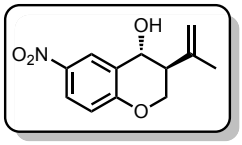
^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.42 (s, 1H), 6.69 (s, 1H), 5.02 (s, 1H), 4.86 (s, 1H), 4.76 (dd, *J* = 7.8, 4.6 Hz, 1H), 4.25 (ddd, *J* = 11.3, 3.5, 1.1 Hz, 1H), 4.06 (dd, *J* = 11.2, 8.8 Hz, 1H), 2.54 (td, *J* = 8.3, 3.5 Hz, 1H), 2.31 (s, 3H), 2.00 (m, 1H), 1.83 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 152.41, 141.70, 137.00, 128.21, 125.98, 123.47, 118.50, 113.95, 66.64, 66.62, 47.63, 21.47, 19.91.

HR-MS: (APCI) calcd. for $C_{13}H_{15}ClO_2$ 239.0833 [M + H^+], found 239.0834

$[a]_D^{22} = -5.0°$ (c = 1.0, CH_2Cl_2)

(3*S*,4*R*)-6-nitro-3-(prop-1-en-2-yl)chroman-4-ol (2h)



Synthesized from **1h** according to general procedure C on 0.3 mmol scale using 5 mol% of catalyst **9**. 24 h reaction time. 79% yield (0.056 g, light yellow solid), d.r. = 17 : 1 (crude material), d.r. = 20 : 1 (purified material).

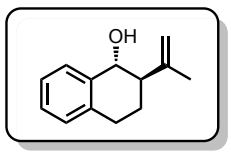
^{1}H NMR: (400 MHz, $CDCl_3$) δ 8.43 (s, 1H), 8.08 (d, *J* = 9.1 Hz, 1H), 6.89 (d, *J* = 9.1 Hz, 1H), 5.09 (s, 1H), 4.92 (s, 1H), 4.86 (dd, *J* = 8.5, 3.6 Hz, 1H), 4.40 (dd, *J* = 11.4, 3.8 Hz, 1H), 4.18 (dd, *J* = 11.5, 9.5 Hz, 1H), 2.62 (td, *J* = 9.0, 3.8 Hz, 1H), 2.32 (m, 1H), 1.85 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 159.29, 141.49, 140.78, 125.12, 125.02, 124.72, 117.04, 114.78, 67.55, 66.39, 46.97, 21.29.

HR-MS: (APCI) calcd. for $C_{12}H_{13}NO_4$ 236.0917 [M + H^+], found 236.0920

$[a]_D^{22} = -29.2°$ (c = 1.0, CH_2Cl_2)

(1*R*,2*R*)-2-(prop-1-en-2-yl)-1,2,3,4-tetrahydronaphthalen-1-ol (2i)



Synthesized from **1i** according to general procedure C on 0.3 mmol scale using 5 mol% of catalyst **9**. 4 h reaction time. 73% yield (0.041 g, white solid), d.r. = 16 : 1 (crude material), d.r. = 16 : 1 (purified material).

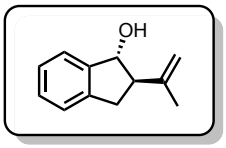
^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.7 Hz, 1H), 7.22 (dtd, *J* = 18.0, 7.3, 1.6 Hz, 2H), 7.10 (d, *J* = 7.1 Hz, 1H), 4.97 (s, 1H), 4.90 (s, 1H), 4.71 (dd, *J* = 9.5, 4.1 Hz, 1H), 2.86 (m, 2H), 2.39 (ddd, *J* = 12.1, 9.4, 3.1 Hz, 1H), 2.07 (m, 1H), 1.91 (m, 2H), 1.82 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 146.16, 138.54, 136.08, 128.39, 127.15, 127.03, 126.18, 112.96, 70.04, 51.27, 28.99, 26.18, 19.29.

HR-MS: (APCI) calcd. for $C_{13}H_{16}O$ 188.1162 [M + H^+], found 188.1155

$[a]_D^{22} = -38.6°$ (c = 1.0, CH_2Cl_2)

(1*R*,2*R*)-2-(prop-1-en-2-yl)-2,3-dihydro-1*H*-inden-1-ol (2j)



Synthesized from **1j** according to general procedure C on 0.3 mmol scale using 5 mol% of catalyst **9**. 24 h reaction time. 55% yield (0.029 g, white solid), d.r. = 12 : 1 (crude material), d.r. = 13 : 1 (purified material).

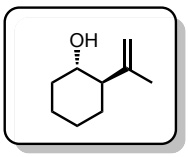
^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.41 (m, 1H), 7.25 (m, 3H), 5.12 (m, 1H), 4.96 (s, 1H), 4.91 (s, 1H), 3.08 (m, 1H), 2.85 (m, 2H), 1.92 (m,, 1H), 1.86 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 144.92, 144.32, 141.10, 128.09, 126.84, 124.61, 123.80, 111.67, 78.90, 58.37, 34.69, 20.68.

HR-MS: (APCI) calcd. for $C_{12}H_{14}O$ 175.1117 [M + H^+], found 175.1119

$[a]_D^{22} = +19.0°$ (c = 1.0, CH_2Cl_2)

(1*S*,2*R*)-2-(prop-1-en-2-yl)cyclohexan-1-ol (2k)



Synthesized from **1k** according to general procedure D for volatile substrates on 0.1 mmol scale using 5 mol% of catalyst **9**. 5 h reaction time. 54% yield of the trans diastereomer by ^{1}H NMR. Yield assessed from crude reaction mixture using mesitylene as an internal quantitative standard. d.r. = 2 : 1 (crude material).

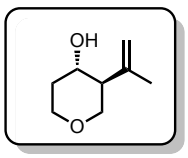
^{1}H NMR: (600 MHz, $CDCl_3$) δ 4.91 (s, 1H), 4.87 (s, 1H), 3.44 (td, *J* = 9.9, 4.2 Hz, 1H), 2.08 (m, 1H), 1.94 (m, 1H), 1.87 (s, 1H), 1.79 (m, 1H), 1.73 (s, 3H), 1.69 (m, 2H), 1.27 (m, 4H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 146.65, 112.80, 70.70, 54.59, 34.07, 30.17, 25.65, 24.86, 19.17.

HR-MS: (APCI) calcd. for $C_9H_{16}O$ 141.1274 [M + H^+], found 141.1273

$[a]_D^{22} = -4.8°$ (c = 0.25, CH_2Cl_2)

(3*S*,4*S*)-3-(prop-1-en-2-yl)tetrahydro-2*H*-pyran-4-ol (2l)



Synthesized from **1l** according to general procedure D for volatile substrates on 0.1 mmol scale using 5 mol% of catalyst **9**. 5 h reaction time. 50% yield of the trans diastereomer by ^{1}H NMR, d.r. = 2 : 1 (crude material). Yield and d.r. assessed from crude reaction mixture using mesitylene as an internal quantitative standard.

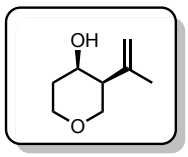
^{1}H NMR: (400 MHz, $CDCl_3$) δ 5.00 (s, 1H), 4.92 (s, 1H), 3.87 (ddd, *J* = 11.4, 4.8, 1.4 Hz, 1H), 3.49 (dd, *J* = 11.4, 1.4 Hz, 1H), 3.39 (dd, *J* = 10.6, 3.1 Hz, 1H), 3.24 (t, *J* = 11.4 Hz, 1H), 3.13 (d, *J* = 11.5 Hz, 1H), 2.44 (td, *J* = 11.0, 4.7 Hz, 1H), 1.74 (s, 3H), 1.63 (d, *J* = 3.2 Hz, 1H), 1.05 (s, 3H), 0.95 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 142.35, 114.40, 77.92, 76.05, 71.14, 48.34, 35.86, 23.55, 20.52, 17.49.

HR-MS: (APCI) calcd. for $C_8H_{14}O_2$ 143.1067 [M + H^+], found 143.1068

$[a]_D^{22} = +7.6°$ (c = 0.5, CH_2Cl_2)

(3*S*,4*R*)-3-(prop-1-en-2-yl)tetrahydro-2*H*-pyran-4-ol (2l-cis)



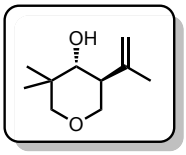
Synthesized from **1l** according to general procedure D for volatile substrates on 0.1 mmol scale using 5 mol% of catalyst **9**. 24 h reaction time. 23% yield of the cis diastereomer by ^{1}H NMR. Yield assessed from crude reaction mixture using mesitylene as an internal quantitative standard. Absolute configuration unknown.

^{1}H NMR: (400 MHz, $CDCl_3$) δ 5.00 (s, 1H), 4.64 (s, 1H), 4.11 (s, 1H), 3.75 (m, 4H), 2.38 (m, 1H), 1.86 (m, 2H), 1.80 (s, 3H), 1.65 (s, 1H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 143.81, 112.22, 65.01, 63.33, 62.37, 47.08, 32.13, 22.89.

HR-MS: (APCI) calcd. for $C_8H_{14}O_2$ 143.1067 [M + H^+], found 143.1068

(4*R*,5*S*)-3,3-dimethyl-5-(prop-1-en-2-yl)tetrahydro-2*H*-pyran-4-ol (2m)



Synthesized from **1m** according to general procedure C on 0.3 mmol scale using 5 mol% of catalyst **9**. 24 h reaction time. Isolated as an inseparable mixture of diastereomers in 84% combined yield (0.043 g, white solid), d.r. = 8 : 1 (crude material), d.r. = 8 : 1 (purified material).

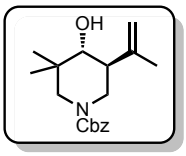
^{1}H NMR: (400 MHz, $CDCl_3$) δ 5.00 (s, 1H), 4.92 (s, 1H), 3.87 (ddd, *J* = 11.4, 4.8, 1.4 Hz, 1H), 3.49 (dd, *J* = 11.4, 1.4 Hz, 1H), 3.39 (dd, *J* = 10.6, 3.1 Hz, 1H), 3.24 (t, *J* = 11.4 Hz, 1H), 3.13 (d, *J* = 11.5 Hz, 1H), 2.44 (td, *J* = 11.0, 4.7 Hz, 1H), 1.74 (s, 3H), 1.63 (d, *J* = 3.2 Hz, 1H), 1.05 (s, 3H), 0.95 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 142.35, 114.40, 77.92, 76.05, 71.14, 48.34, 35.86, 23.55, 20.52, 17.49.

HR-MS: (APCI) calcd. for $C_{10}H_{18}O_2$ 171.1380 [M + H^+], found 171.1381

$[a]_D^{22} = +28.6°$ (c = 1.0, CH_2Cl_2)

benzyl (4*R*,5*S*)-4-hydroxy-3,3-dimethyl-5-(prop-1-en-2-yl)piperidine-1-carboxylate (2n)



Synthesized from **1n** according to general procedure C on 0.3 mmol scale using 5 mol% of catalyst **9**. 1 h reaction time. Isolated as an inseparable mixture of diastereomers in 78% combined yield (0.071 g, light yellow oil), d.r. = 8 : 1 (crude material), d.r. = 8 : 1 (purified material).

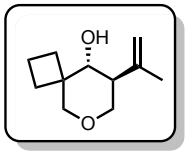
^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.37 (m, 5H), 5.14 (m, 2H), 5.02 (s, 1H), 4.93 (s, 1H), 4.25 (d, *J* = 13.6 Hz, 1H), 3.89 (d, *J* = 13.4 Hz, 1H), 3.30 (dd, *J* = 10.6, 2.9 Hz, 1H), 2.60 (m, 2H), 2.31 (m, 1H), 1.76 (s, 3H), 1.66 (s, 1H), 1.04 (s, 3H), 0.91 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 155.44, 142.94, 136.77, 128.47, 127.98, 127.84, 114.72, 76.50, 67.16, 54.65, 47.32, 41.10, 35.79, 25.14, 19.99, 17.05.

HR-MS: (APCI) calcd. for $C_{18}H_{25}NO_3$ 304.1907 [M + H^+], found 304.1908

$[a]_D^{22} = +12.6°$ (c = 1.0, CH_2Cl_2)

(8*S*,9*R*)-8-(prop-1-en-2-yl)-6-oxaspiro[3.5]nonan-9-ol (2o)



Synthesized from **1o** according to general procedure C on 0.3 mmol scale using 5 mol% of catalyst **9**. 24 h reaction time, d.r. = 3 : 1 (crude material). The diastereomers of **2o** were found to be separable by conventional silica gel chromatography. The data below correspond to the major trans diastereomer, isolated in 53% yield (0.029 g, white solid).

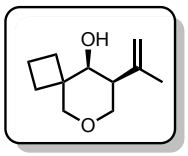
^{1}H NMR: (400 MHz, $CDCl_3$) δ 5.00 (s, 1H), 4.91 (s, 1H), 3.98 (d, *J* = 11.5 Hz, 1H), 3.79 (ddd, *J* = 11.3, 4.5, 1.4 Hz, 1H), 3.38 (dd, *J* = 10.4, 3.0 Hz, 1H), 3.24 (ddd, *J* = 11.2, 6.4, 4.6 Hz, 2H), 2.26 (m, 2H), 2.17 (td, *J* = 10.8, 4.5 Hz, 1H), 1.86 (m, 4H), 1.74 (s, 3H), 1.41 (m, 1H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 142.11, 114.35, 75.29, 73.23, 70.54, 48.96, 43.13, 23.81, 23.08, 20.62, 15.33.

HR-MS: (APCI) calcd. for $C_{11}H_{18}O_2$ 183.1380 [M + H^+], found 183.1382

$[a]_D^{22} = +37.8°$ (c = 1.0, CH_2Cl_2)

(8*S*,9*S*)-8-(prop-1-en-2-yl)-6-oxaspiro[3.5]nonan-9-ol (2o-cis)



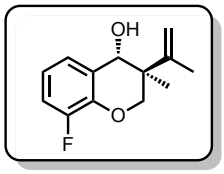
Synthesized from **1o** according to general procedure C on 0.3 mmol scale using 5 mol% of catalyst **9**. 24 h reaction time. The diastereomers of **2o** were found to be separable by conventional silica gel chromatography. The data below correspond to the minor cis diastereomer, isolated in 20% yield (0.011 g, white solid). Absolute configuration unknown.

^{1}H NMR: (400 MHz, $CDCl_3$) δ 4.98 (s, 1H), 4.62 (s, 1H), 3.85 (s, 1H), 3.65 (m, 4H), 2.32 (dd, *J* = 11.2, 4.8 Hz, 1H), 2.06 (tdd, *J* = 8.7, 4.8, 2.1 Hz, 1H), 1.94 (m, 4H), 1.80 (s, 3H), 1.62 (m, 1H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 143.61, 112.11, 71.36, 69.78, 64.34, 43.19, 41.62, 29.16, 26.39, 22.70, 15.18.

HR-MS: (APCI) calcd. for $C_{11}H_{18}O_2$ 183.1380 [M + H^+], found 183.1383

(3*S*,4*R*)-8-fluoro-3-methyl-3-(prop-1-en-2-yl)chroman-4-ol (2p)



Synthesized from **1p** according to general procedure C on 0.3 mmol scale using 5 mol% of catalyst **9**. 2 h reaction time. 94% yield (0.063 g, white solid), d.r. > 50 : 1 (crude material), d.r. > 50 : 1 (purified material).

^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.15 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.00 (ddd, *J* = 11.0, 8.1, 1.6 Hz, 1H), 6.86 (td, *J* = 7.9, 4.8 Hz, 1H), 4.95 (m, 2H), 4.85 (d, *J* = 4.2 Hz, 1H), 4.22 (d, *J* = 11.3 Hz, 1H), 4.14 (d, *J* = 11.2 Hz, 1H), 1.82 (m, 4H), 1.18 (s, 3H).

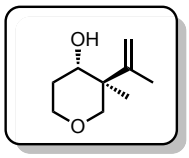
^{13}C NMR: (101 MHz, $CDCl_3$) δ 151.00 (d, *J* = 245.0 Hz), 145.31, 141.82 (d, *J* = 11.1 Hz), 126.60 (d, *J* = 1.7 Hz), 123.79 (d, *J* = 3.6 Hz), 120.17 (d, *J* = 7.0 Hz), 115.57 (d, *J* = 17.8 Hz), 113.09, 69.88, 68.78 (d, *J* = 2.9 Hz), 41.45, 19.71, 16.67.

^{19}F NMR: (376 MHz, $CDCl_3$) δ -137.93 (s, 1F)

HR-MS: (APCI) calcd. for $C_{13}H_{15}FO_2$ 223.1129 [M + H^+], found 223.1131

$[a]_D^{22} = +58.2°$ (c = 1.0, CH_2Cl_2)

(3*S*,4*S*)-3-methyl-3-(prop-1-en-2-yl)tetrahydro-2*H*-pyran-4-ol (2q)



Synthesized from **1q** according to general procedure C on 0.3 mmol scale using 5 mol% of catalyst **9** with the following modification: 15 mol% AcCl and 15 mol% EtOH were used. 24 h reaction time. Isolated as an inseparable mixture of diastereomers in 65% combined yield (0.031 g, clear colorless oil), d.r. = 5 : 1 (crude material), d.r. = 5 : 1 (purified material).

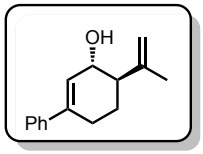
^{1}H NMR: (400 MHz, $CDCl_3$) δ 5.05 (s, 1H), 5.01 (s, 1H), 4.02 (m, 1H), 3.92 (m, 1H), 3.54 (dd, *J* = 11.4, 1.2 Hz, 1H), 3.47 (dq, *J* = 11.4, 3.7 Hz, 1H), 3.38 (d, *J* = 11.4 Hz, 1H), 1.79 (m, 5H), 1.62 (s, 1H), 1.17 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 147.21, 113.49, 73.95, 70.06, 66.68, 45.24, 29.76, 19.93, 14.66.

HR-MS: (APCI) calcd. for $C_9H_{16}O_2$ 157.1223 [M + H^+], found 157.1225

$[a]_D^{22} = -15.6°$ (c = 1.0, CH_2Cl_2)

(3*S*,4*R*)-4-(prop-1-en-2-yl)-3,4,5,6-tetrahydro-[1,1'-biphenyl]-3-ol (2r)



Synthesized from **1r** according to general procedure C on 0.3 mmol scale using 10 mol% of catalyst **9**. 24 h reaction time. 49% yield (0.031 g, light yellow oil), d.r. = 9 : 1 (crude material), d.r. = 9 : 1 (purified material).

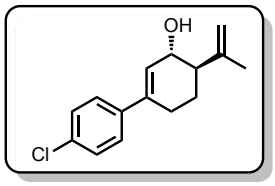
^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.43 (m, 2H), 7.33 (m, 2H), 7.28 (m, 1H), 6.13 (dt, *J* = 2.3, 1.3 Hz, 1H), 4.96 (s, 1H), 4.93 (s, 1H), 4.34 (dt, *J* = 9.5, 3.0 Hz, 1H), 2.54 (m, 2H), 2.24 (ddd, *J* = 12.3, 9.1, 2.9 Hz, 1H), 1.91 (m, 2H), 1.77 (m, 4H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 146.16, 140.82, 138.37, 128.29, 127.37, 126.62, 125.33, 112.65, 69.20, 50.65, 27.60, 26.39, 19.33.

HR-MS: (APCI) calcd. for $C_{15}H_{18}O$ 215.1430 [M + H^+], found 215.1432

$[a]_D^{22} = -16.2°$ (c = 1.0, CH_2Cl_2)

(3*S*,4*R*)-4'-chloro-4-(prop-1-en-2-yl)-3,4,5,6-tetrahydro-[1,1'-biphenyl]-3-ol (2s)



Synthesized from **1s** according to general procedure C on 0.3 mmol scale using 5 mol% of catalyst **9**. 3 h reaction time. 64% yield (0.048 g, light yellow oil), d.r. = 13 : 1 (crude material), d.r. = 13 : 1 (purified material).

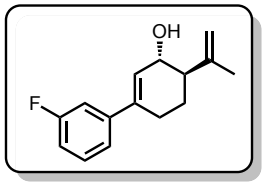
^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.36 (m, 2H), 7.30 (m, 2H), 6.12 (s, 1H), 4.96 (s, 1H), 4.92 (s, 1H), 4.32 (m, 1H), 2.49 (m, 2H), 2.23 (ddd, *J* = 12.3, 9.1, 2.9 Hz, 1H), 1.92 (m, 3H), 1.79 (s, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 145.95, 139.22, 137.24, 133.12, 128.41, 127.15, 126.59, 112.80, 69.08, 50.53, 27.53, 26.26, 19.28.

HR-MS: (APCI) calcd. for $C_{15}H_{17}ClO$ 249.0866 [M + H^+], found 249.0685

$[a]_D^{22} = -7.0°$ (c = 1.0, CH_2Cl_2)

(3*S*,4*R*)-3'-fluoro-4-(prop-1-en-2-yl)-3,4,5,6-tetrahydro-[1,1'-biphenyl]-3-ol (2t)



Synthesized from **1t** according to general procedure C on 0.3 mmol scale using 5 mol% of catalyst **9**. 2 h reaction time. 66% yield (0.046 g, light yellow oil), d.r. = 18 : 1 (crude material), d.r. = 20 : 1 (purified material).

^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.29 (td, *J* = 8.0, 6.0 Hz, 1H), 7.21 (dt, *J* = 7.8, 1.3 Hz, 1H), 7.11 (dt, *J* = 10.7, 2.2 Hz, 1H), 6.96 (td, *J* = 8.2, 2.5 Hz, 1H), 6.16 (s, 1H), 4.96 (s, 1H), 4.92 (s, 1H), 4.33 (dt, *J* = 9.4, 3.0 Hz, 1H), 2.49 (m, 2H), 2.23 (ddd, *J* = 12.3, 9.2, 2.9 Hz, 1H), 1.93 (m, 2H), 1.79 (s, 3H), 1.76 (m, 1H).

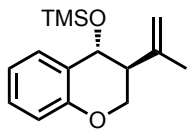
^{13}C NMR: (101 MHz, $CDCl_3$) δ 162.91 (d, *J* = 244.9 Hz), 145.94, 143.15 (d, *J* = 7.5 Hz), 137.25 (d, *J* = 2.3 Hz), 129.67 (d, *J* = 8.4 Hz), 127.70, 120.92 (d, *J* = 2.8 Hz), 114.10 (d, *J* = 21.4 Hz), 112.81, 112.27 (d, *J* = 22.0 Hz), 69.06, 50.53, 27.51, 26.25, 19.29.

^{19}F NMR: (376 MHz, $CDCl_3$) δ -114.53 (s, 1F)

HR-MS: (APCI) calcd. for $C_{15}H_{17}FO$ 231.1191 [M + H^+], found 231.1186

$[a]_D^{22} = +5.0°$ (c = 1.0, CH_2Cl_2)

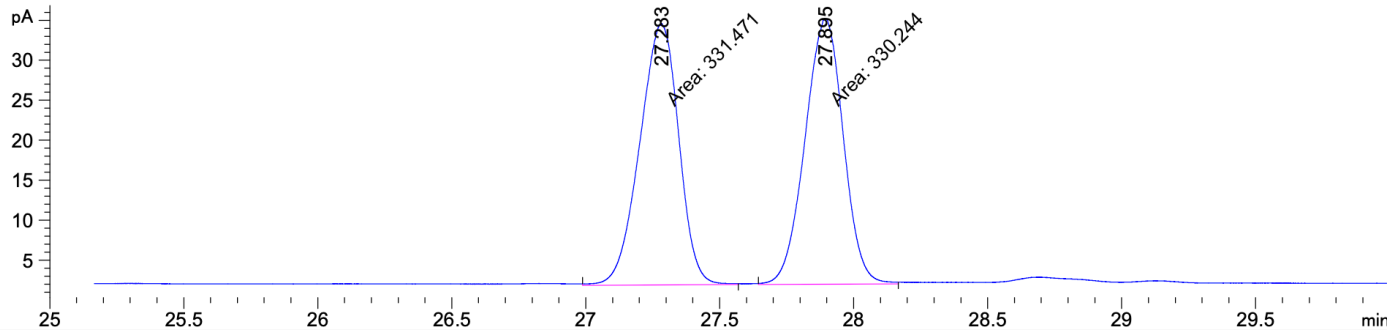
5.2 GC and HPLC traces of enantioenriched products



2a, 96% ee
(ee evaluated using OTMS derivative)

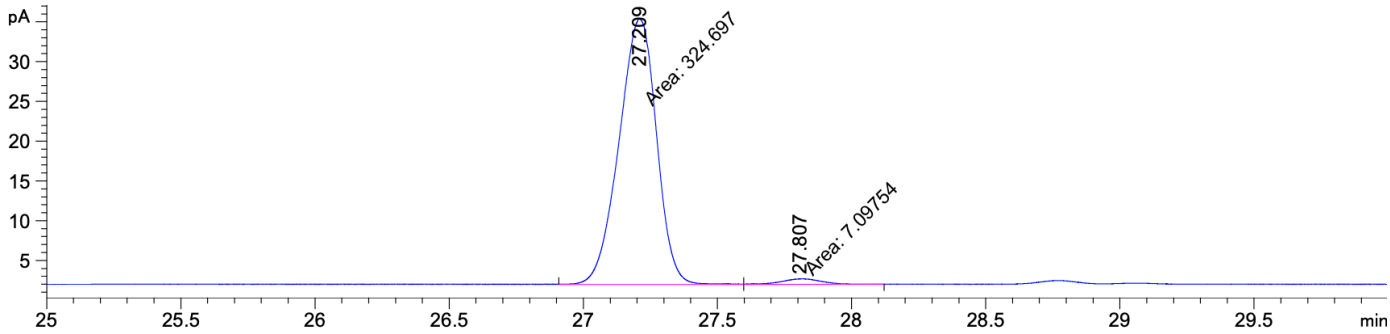
GC (CP-Chirasil Dex CB, 25 m)
125 ℃ - 145 ℃, 0.5 ℃/min, 7 psi

racemic sample



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	27.283	MM	0.1689	331.47098	32.71778	50.09274
2	27.895	MM	0.1657	330.24359	33.21354	49.90726

enantioenriched sample



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
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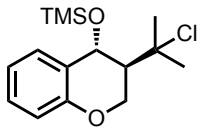
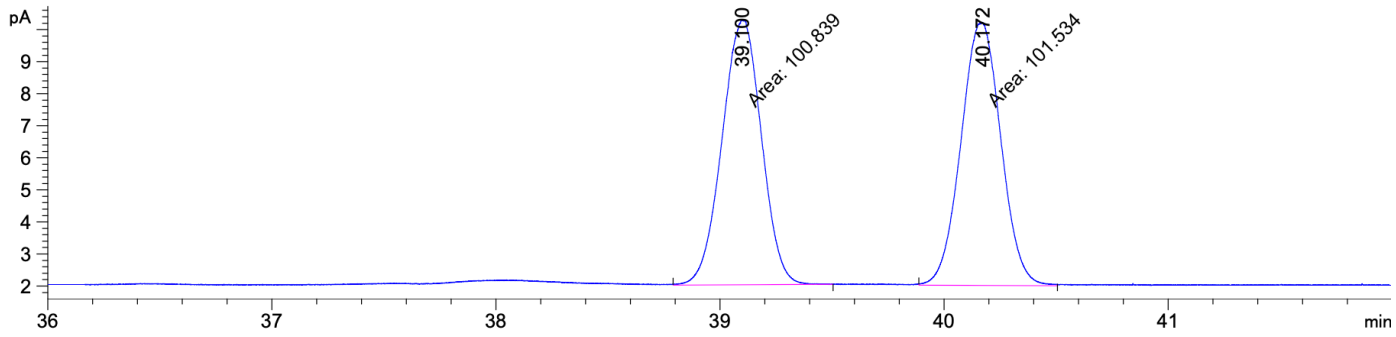
2	27.807	FM	0.1697	7.09754	6.97255e-1	2.13914



3a, 98% ee
(ee evaluated using OTMS derivative)

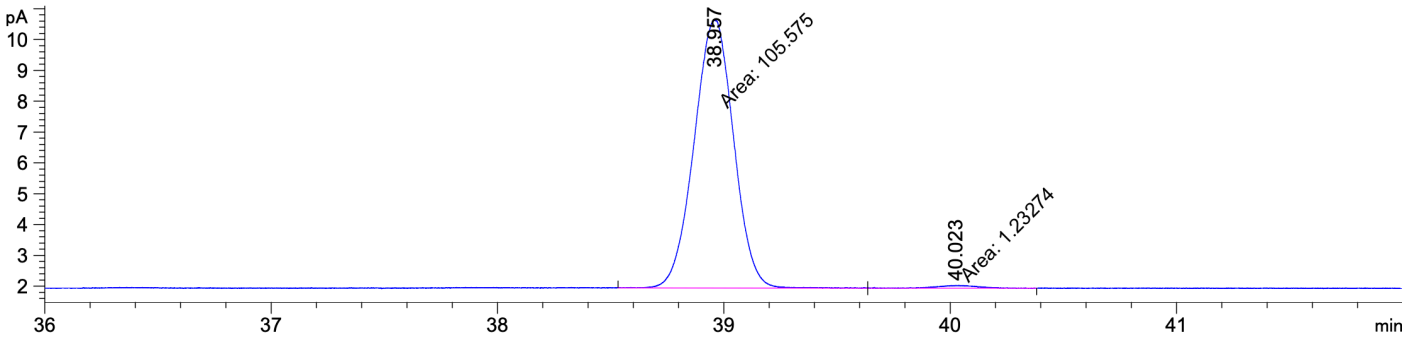
GC (CP-Chirasil Dex CB, 25 m)
125 ℃ - 145 ℃, 0.5 ℃/min, 7 psi

racemic sample

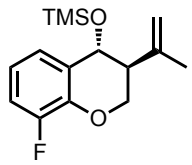


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	39.100	MM	0.2032	100.83939	8.26988	49.82839
2	40.172	MM	0.2062	101.53397	8.20612	50.17161

enantioenriched sample



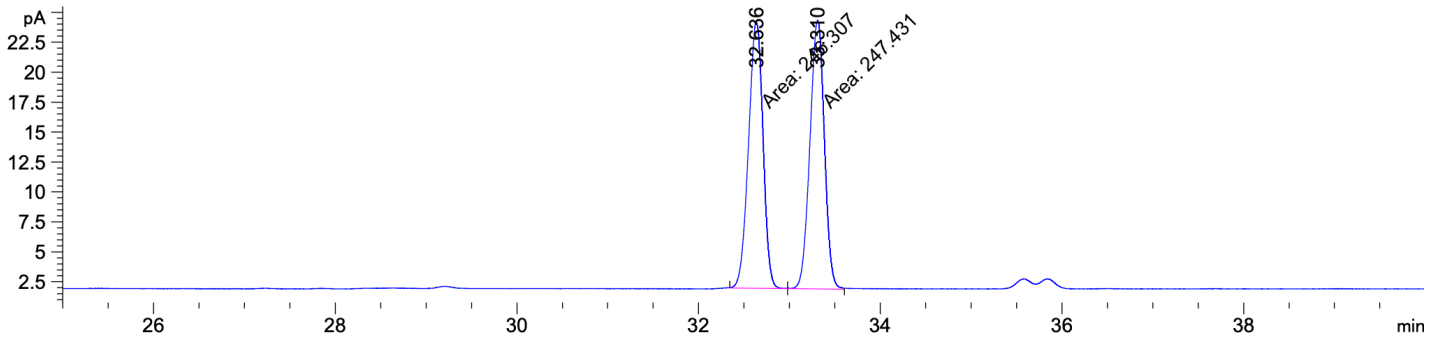
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	38.957	MF	0.2020	105.57536	8.71163	98.84583
2	40.023	FM	0.2233	1.23274	9.20271e-2	1.15417



GC (CP-Chirasil Dex CB, 25 m)
125 ℃ - 145 ℃, 0.5 ℃/min, 7 psi

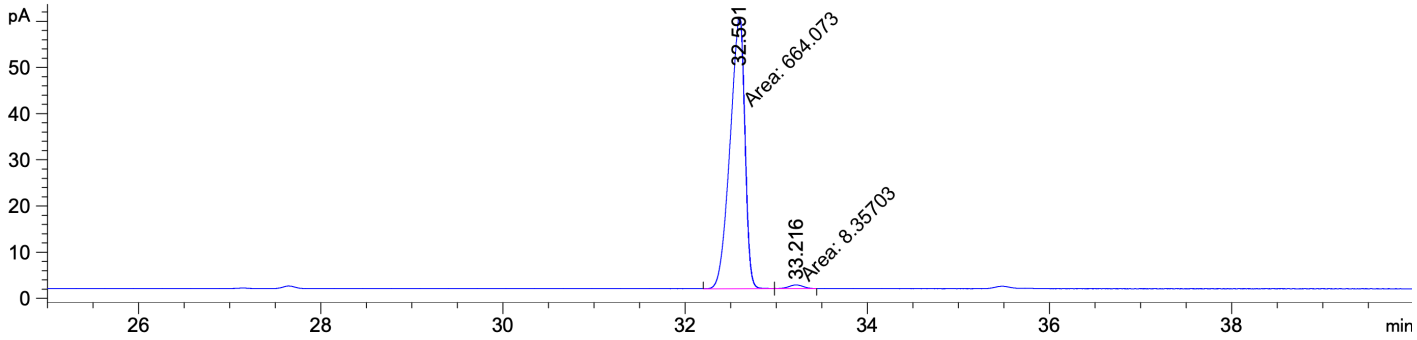
2b, 98% ee
(ee evaluated using OTMS derivative)

racemic sample

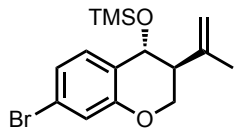


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	32.636	MF	0.1841	246.30708	22.30269	49.88619
2	33.310	FM	0.1839	247.43092	22.42530	50.11381

enantioenriched sample



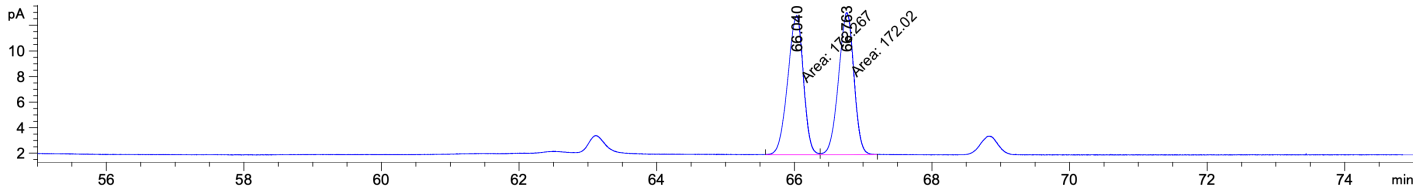
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	32.591	MM	0.1886	664.07269	58.67761	98.75719
2	33.216	MM	0.1748	8.35703	7.96933e-1	1.24281



2c, 96% ee
(ee evaluated using OTMS derivative**)**

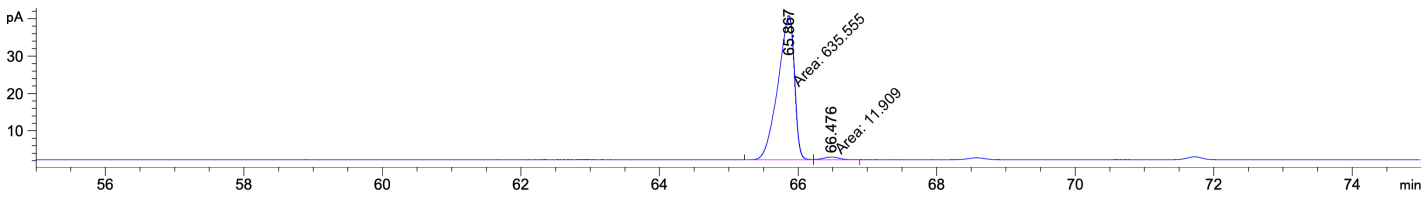
GC (CP-Chirasil Dex CB, 25 m)
120 ℃ - 180 ℃, 0.5 ℃/min, 7 psi

racemic sample

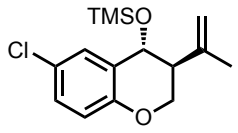


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	66.040	MF	0.2640	172.26672	10.87363	50.03589
2	66.763	FM	0.2578	172.01961	11.12067	49.96411

enantioenriched sample



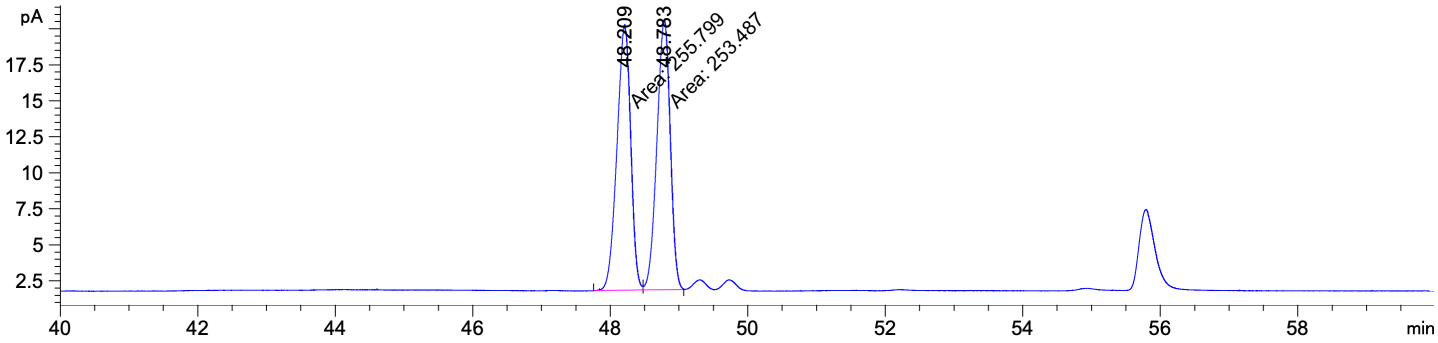
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	65.867	MF	0.2746	635.55548	38.57752	98.16067
2	66.476	FM	0.2644	11.90901	7.50578e-1	1.83933



GC (CP-Chirasil Dex CB, 25 m)
120 ℃ - 170 ℃, 0.5 ℃/min, 7 psi

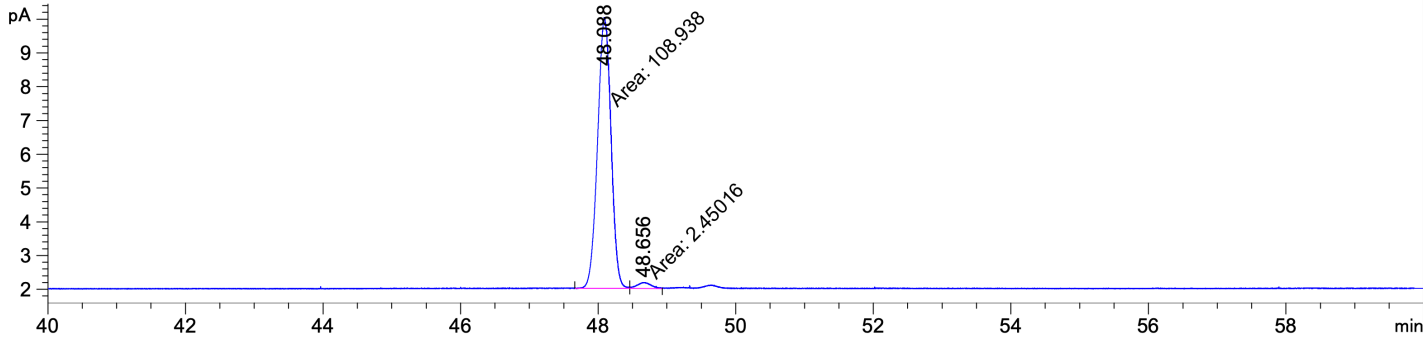
2d, 96% ee
(ee evaluated using OTMS derivative)

racemic sample

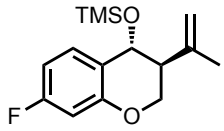


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	48.209	MF	0.2311	255.79863	18.45101	50.22697
2	48.783	FM	0.2254	253.48680	18.74529	49.77303

enantioenriched sample



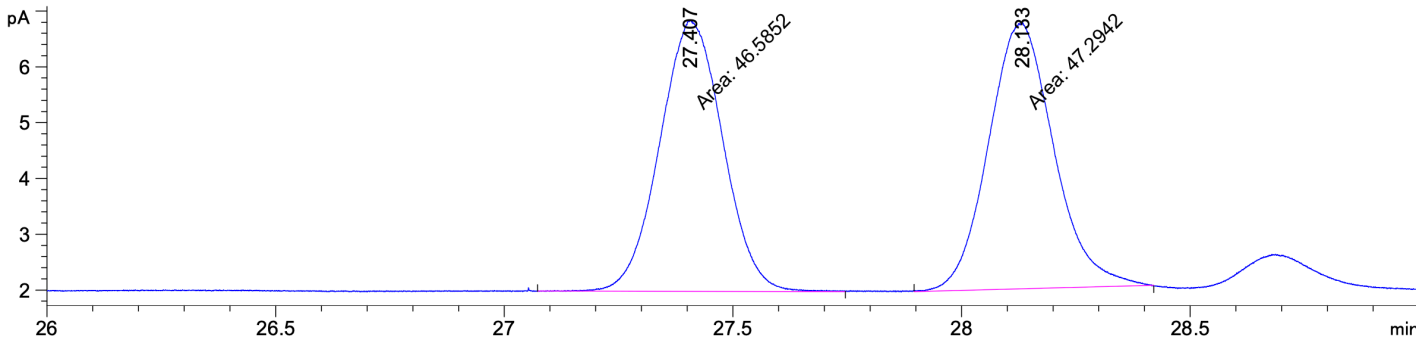
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	48.088	MF	0.2262	108.93795	8.02712	97.80034
2	48.656	FM	0.2281	2.45016	1.79046e-1	2.19966



GC (CP-Chirasil Dex CB, 25 m)
120 ℃ - 145 ℃, 0.5 ℃/min, 7 psi

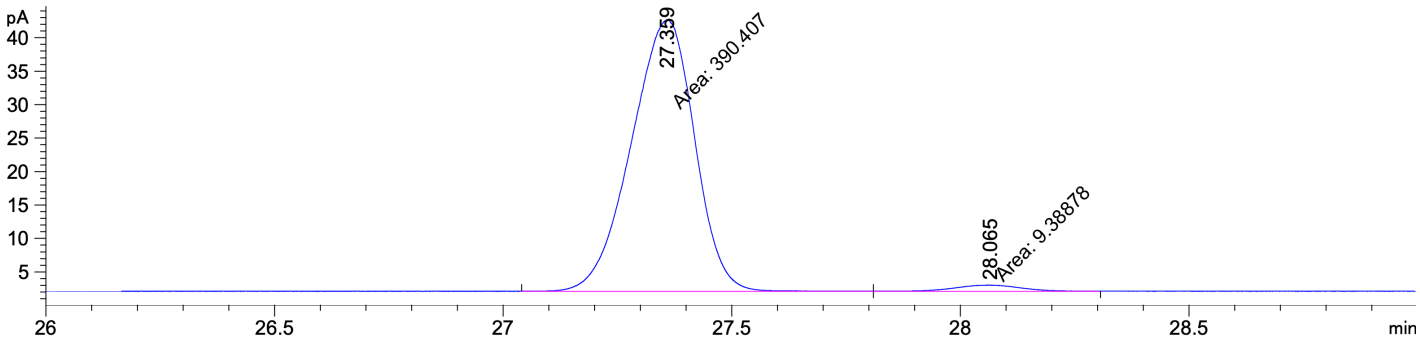
2e, 95% ee
(ee evaluated using OTMS derivative)

racemic sample

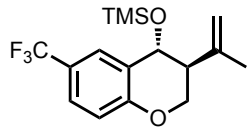


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	27.407	MM	0.1595	46.58520	4.86742	49.62240
2	28.133	MM	0.1651	47.29418	4.77371	50.37760

enantioenriched sample



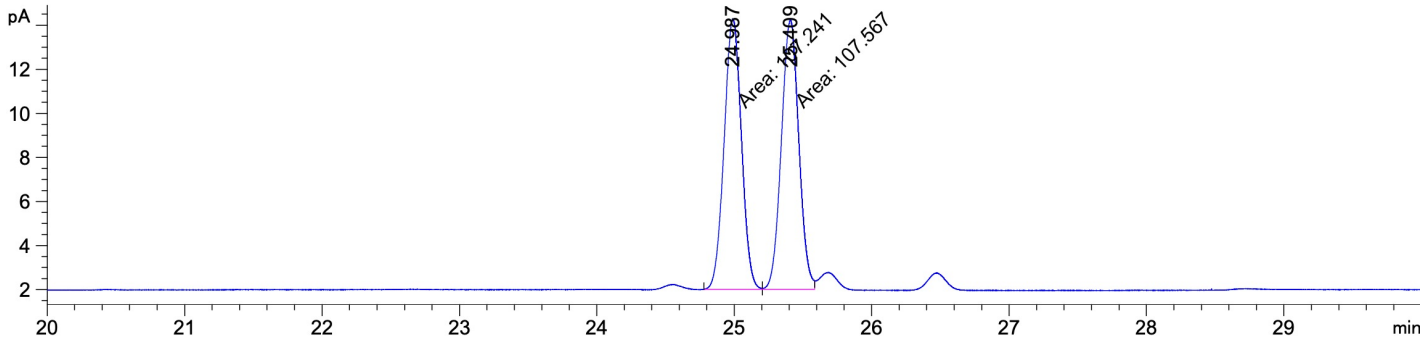
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	27.359	MF	0.1603	390.40741	40.58126	97.65161
2	28.065	FM	0.1682	9.38878	9.30305e-1	2.34839



GC (CP-Chirasil Dex CB, 25 m)
120 ℃ - 145 ℃, 0.5 ℃/min, 7 psi

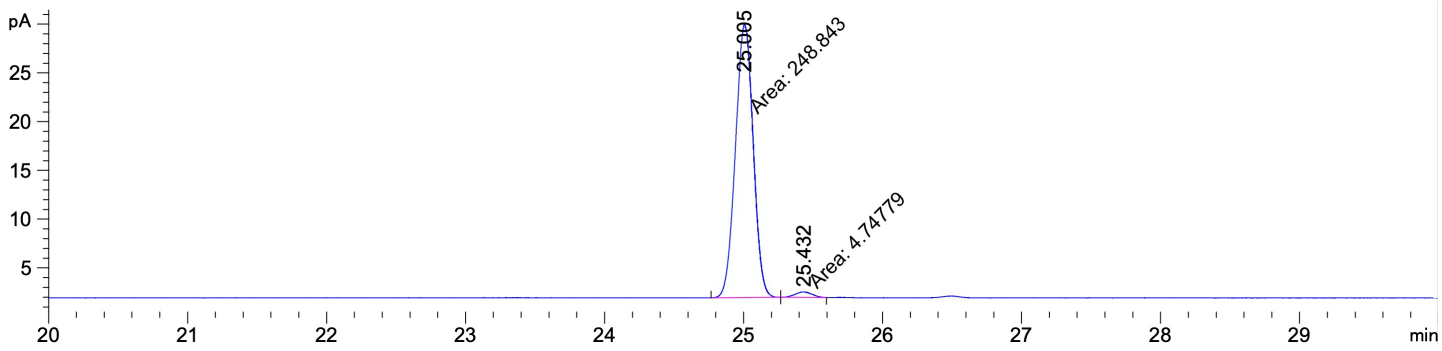
2f, 96% ee
(ee evaluated using OTMS derivative)

racemic sample

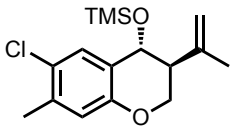


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	24.987	MF	0.1457	107.24072	12.26632	49.92395
2	25.409	FM	0.1469	107.56744	12.20798	50.07605

enantioenriched sample



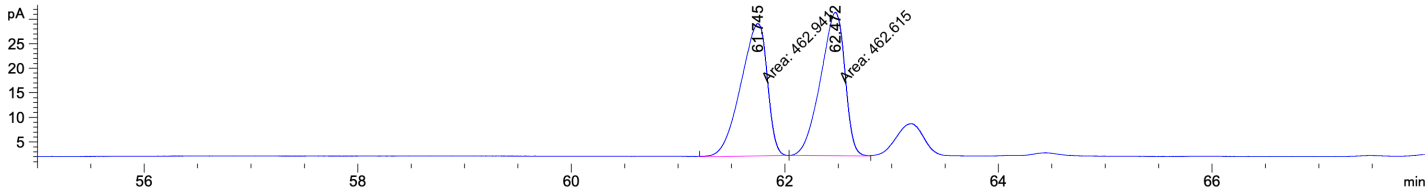
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	25.005	MM	0.1476	248.84320	28.09731	98.12778
2	25.432	MM	0.1422	4.74779	5.56521e-1	1.87222



2g, 96% ee
(ee evaluated using OTMS derivative)

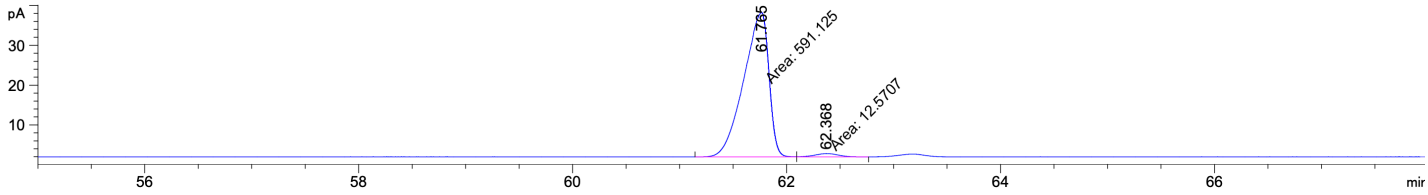
GC (CP-Chirasil Dex CB, 25 m)
120 ℃ - 180 ℃, 0.5 ℃/min, 7 psi

racemic sample



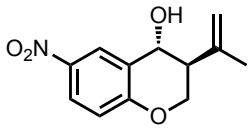
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	61.745	MM	0.2860	462.94058	26.97376	50.01761
2	62.472	MM	0.2638	462.61469	29.22861	49.98239

enantioenriched sample



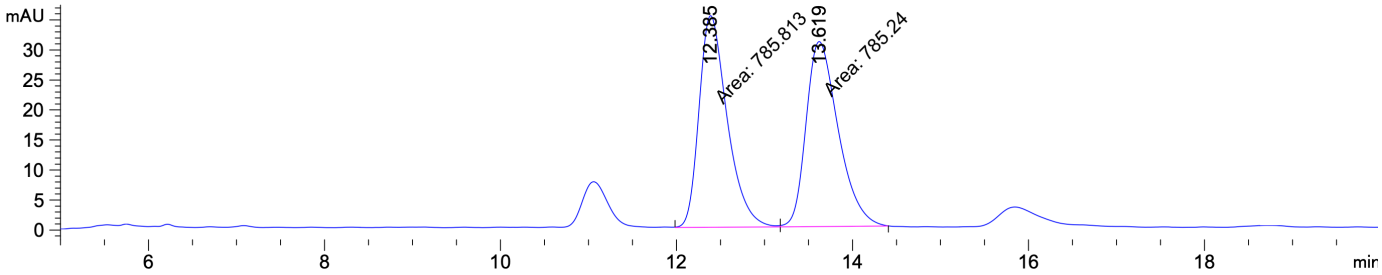
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	61.765	MF	0.2709	591.12482	36.36334	97.91770
2	62.368	FM	0.2513	12.57074	8.33590e-1	2.08230

HPLC (AS-H)
10% IPA/Hexanes, 1 mL/min, 254 nm



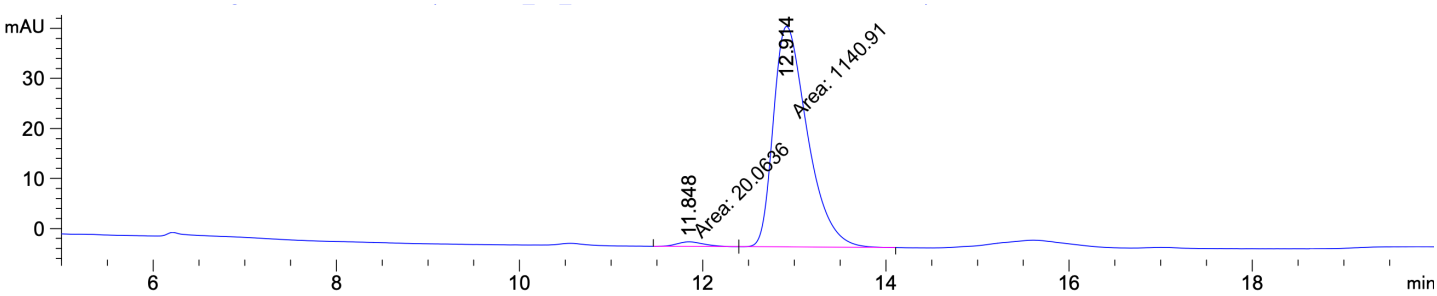
2h, 97% ee

racemic sample



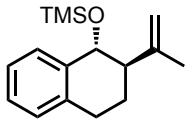
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.385	MF	0.3711	785.81342	35.28750	50.0183
2	13.619	FM	0.4242	785.23993	30.85104	49.9817

enantioenriched sample



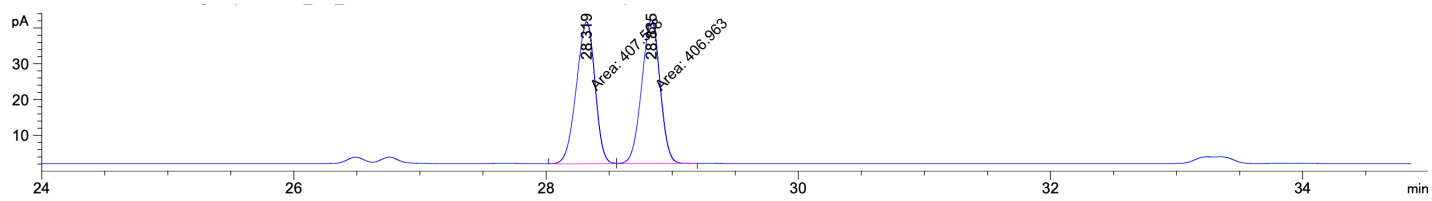
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.848	MF	0.3538	20.06356	9.45258e-1	1.7282
2	12.914	FM	0.4311	1140.90942	44.10820	98.2718

GC (CP-Chirasil Dex CB, 25 m)
120 ℃ - 145 ℃, 0.5 ℃/min, 7 psi



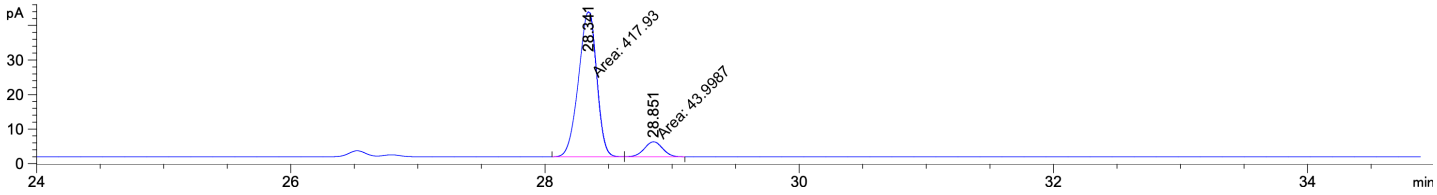
2i, 81% ee
(ee evaluated using OTMS derivative)

racemic sample



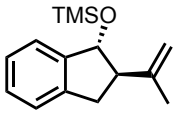
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	28.319	MF	0.1710	407.56750	39.71247	50.03708
2	28.835	FM	0.1689	406.96338	40.15838	49.96292

enantioenriched sample



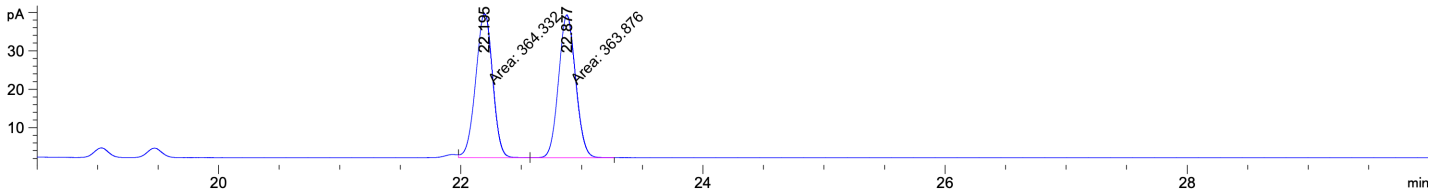
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	28.341	MF	0.1657	417.92990	42.04565	90.47499
2	28.851	FM	0.1683	43.99873	4.35766	9.52501

GC (CP-Chirasil Dex CB, 25 m)
120 ℃ - 135 ℃, 0.2 ℃/min, 7 psi



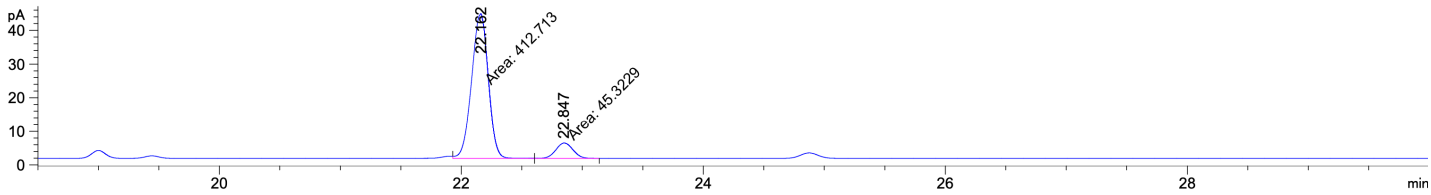
2j, 80% ee
(ee evaluated using OTMS derivative)

racemic sample

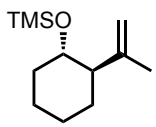


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	22.195	FM	0.1616	364.33215	37.58689	50.03134
2	22.877	FM	0.1631	363.87570	37.17232	49.96866

enantioenriched sample



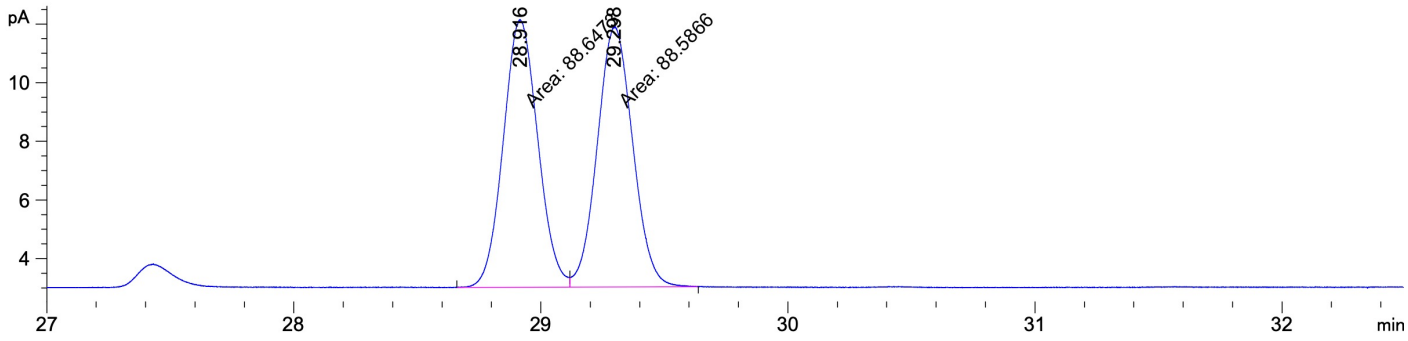
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	22.162	FM	0.1598	412.71304	43.03346	90.10495
2	22.847	FM	0.1646	45.32290	4.58843	9.89505



2k, 89% ee
(ee evaluated using
OTMS derivative)

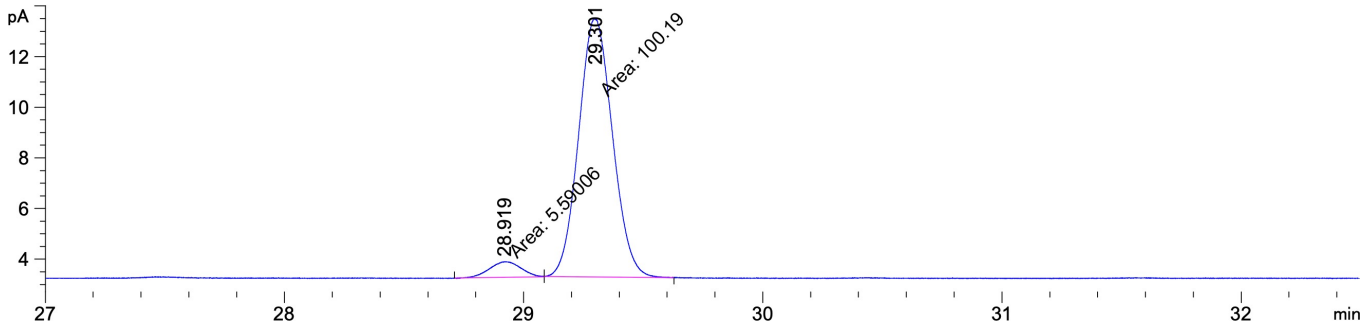
GC (Cyclosil-B, 30 m)
70 ℃ - 100 ℃, 0.5 ℃/min, 7 psi

racemic sample

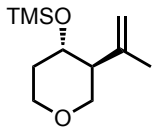


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	28.916	MF	0.1619	88.64730	9.12300	50.01713
2	29.298	FM	0.1665	88.58659	8.86935	49.98287

enantioenriched sample



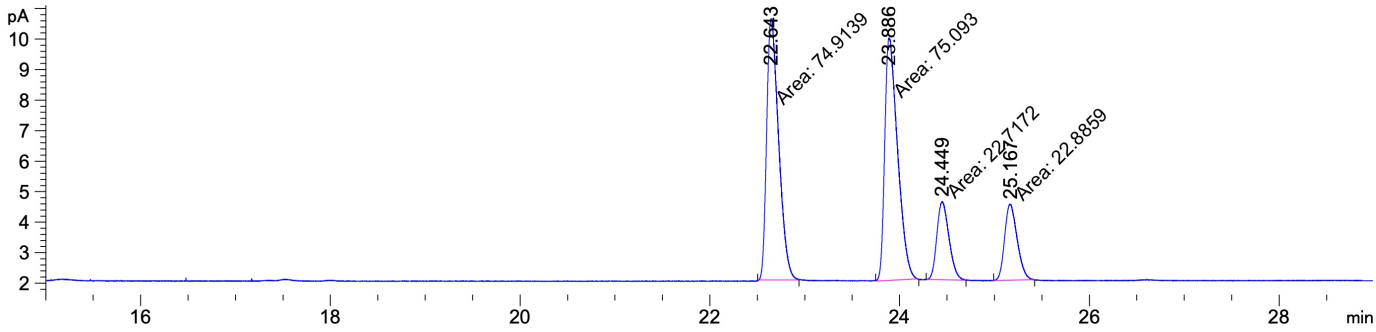
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	28.919	MM	0.1507	5.59006	6.18342e-1	5.28461
2	29.301	MM	0.1637	100.18998	10.19746	94.71539



2l, 91% ee *trans*, 67% ee *cis*
(ee evaluated using OTMS derivative)

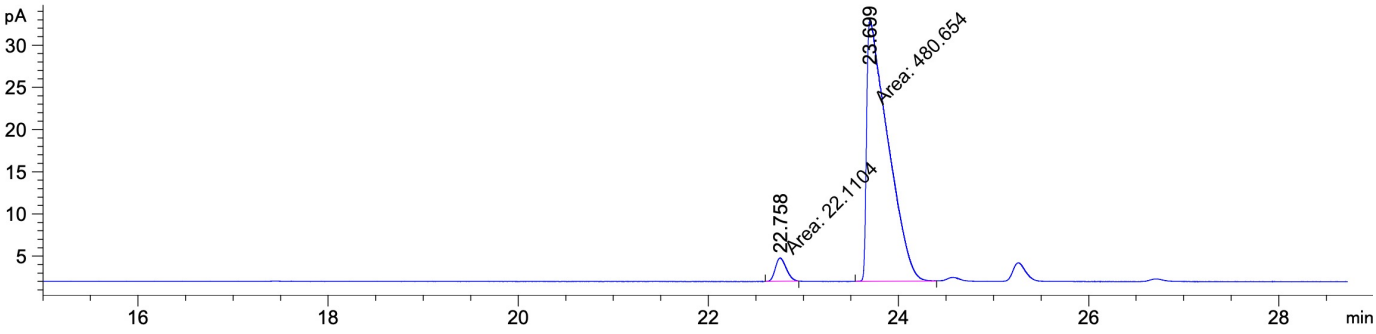
GC (CP-Chirasil Dex CB, 25 m)
80 °C - 100 °C, 0.5 °C/min, 7 psi

racemic sample



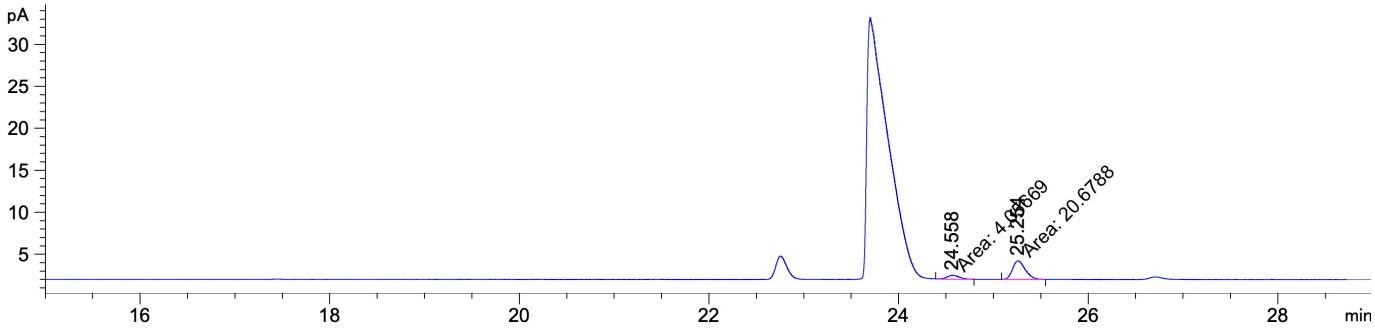
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	22.643	MM	0.1458	74.91386	8.56313	38.29756
2	23.886	MM	0.1575	75.09303	7.94540	38.38915
3	24.449	MM	0.1483	22.71725	2.55361	11.61354
4	25.167	MM	0.1532	22.88588	2.48974	11.69975

enantioenriched sample (trans)

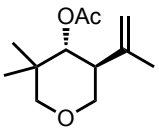


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	22.758	MM	0.1334	22.11038	2.76336	4.39776
2	23.699	MM	0.2571	480.65439	31.15800	95.60224

enantioenriched sample (cis)



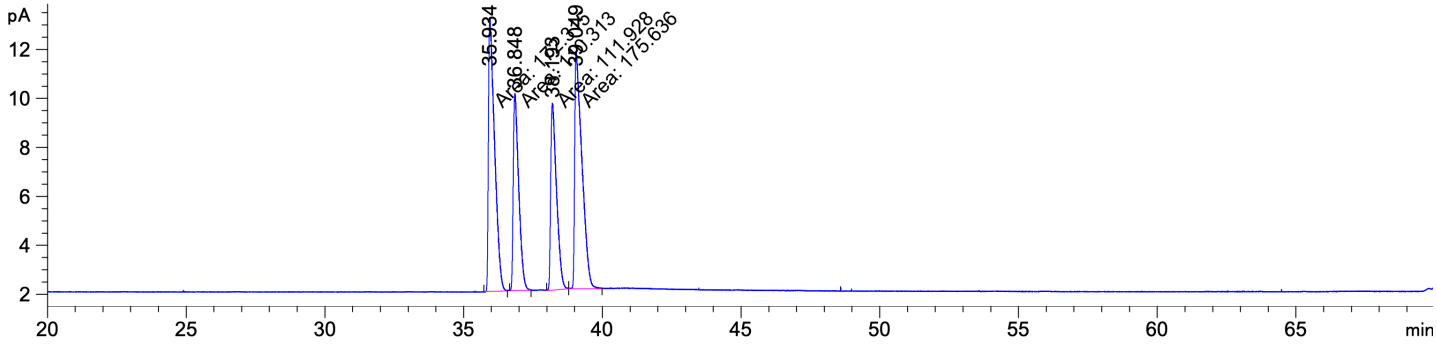
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	24.558	MM	0.1479	4.05669	4.57234e-1	16.40028
2	25.254	MM	0.1559	20.67879	2.21013	83.59972



GC (CP-Chirasil Dex CB, 25 m)
80 ℃ - 130 ℃, 0.5 ℃/min, 7 psi

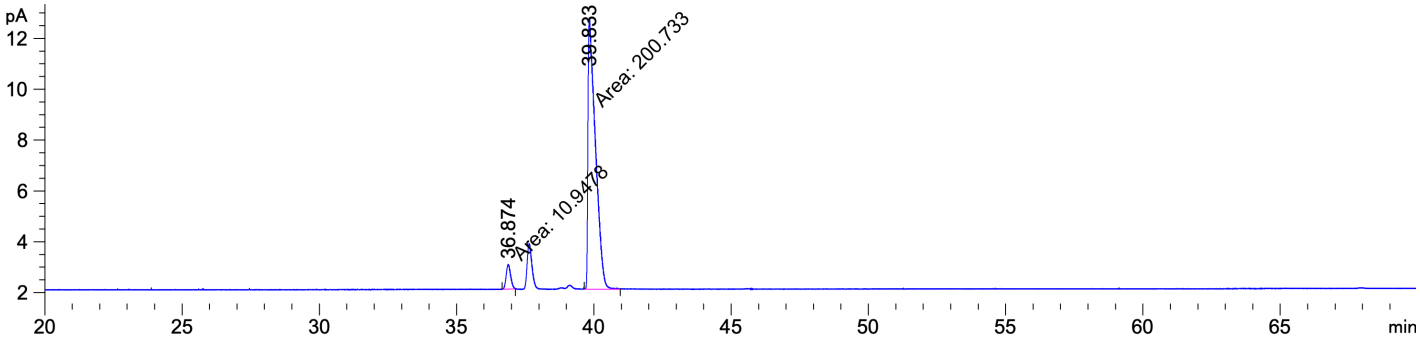
2m, 90% ee *trans*, 84% ee *cis*
(ee evaluated using OAc derivative)

racemic sample



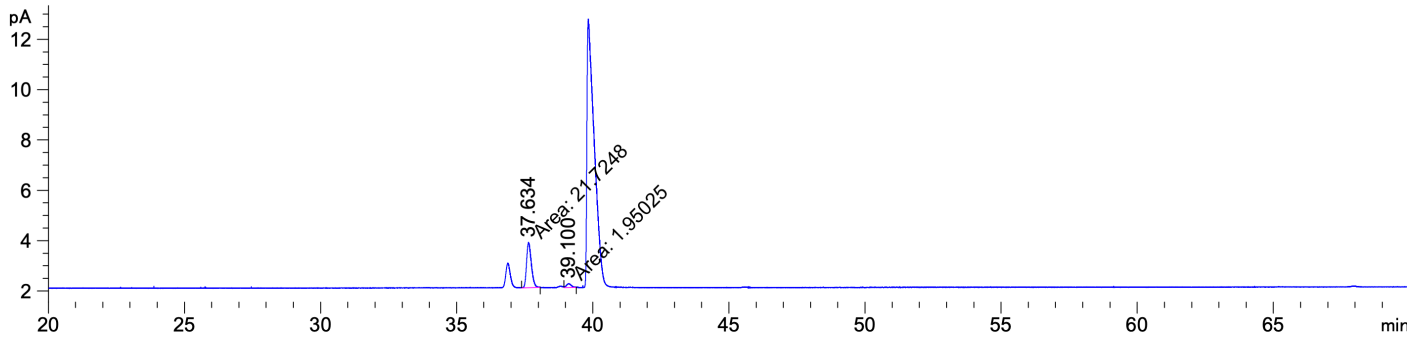
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	35.934	MM	0.2567	172.31531	11.18616	30.22056
2	36.848	MM	0.2289	110.31258	8.03231	19.34656
3	38.193	MM	0.2445	111.92847	7.63130	19.62995
4	39.049	MM	0.3030	175.63593	9.66214	30.80293

enantioenriched sample (trans)

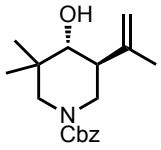


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	36.874	MM	0.1874	10.94784	9.73827e-1	5.17187
2	39.833	MM	0.3141	200.73259	10.65262	94.82813

enantioenriched sample (cis)



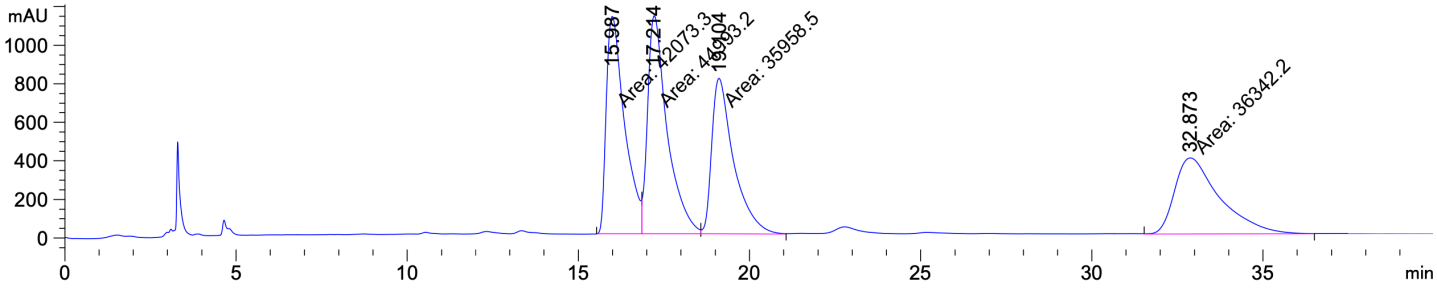
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	37.634	MM	0.2021	21.72478	1.79115	91.76243
2	39.100	MM	0.2085	1.95025	1.55931e-1	8.23757



2n, 90% ee *trans*, 70% ee *cis*

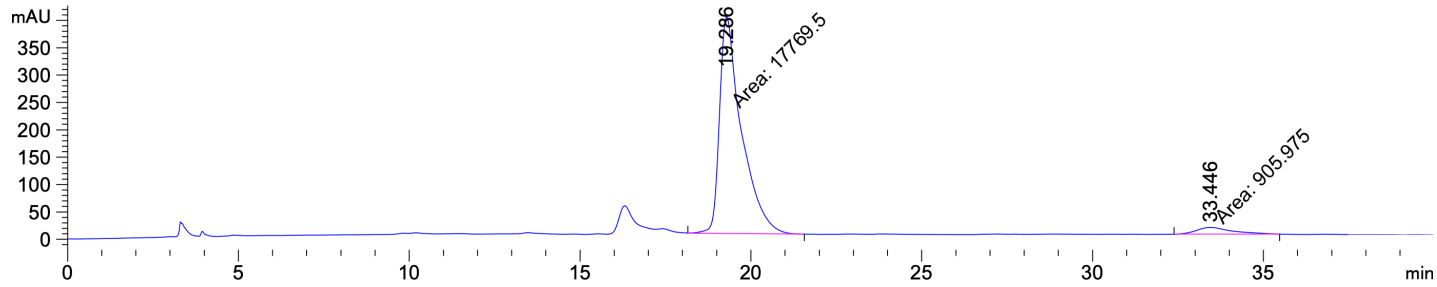
HPLC (AD-H)
4% IPA/Hexanes, 1 mL/min, 210 nm

racemic sample



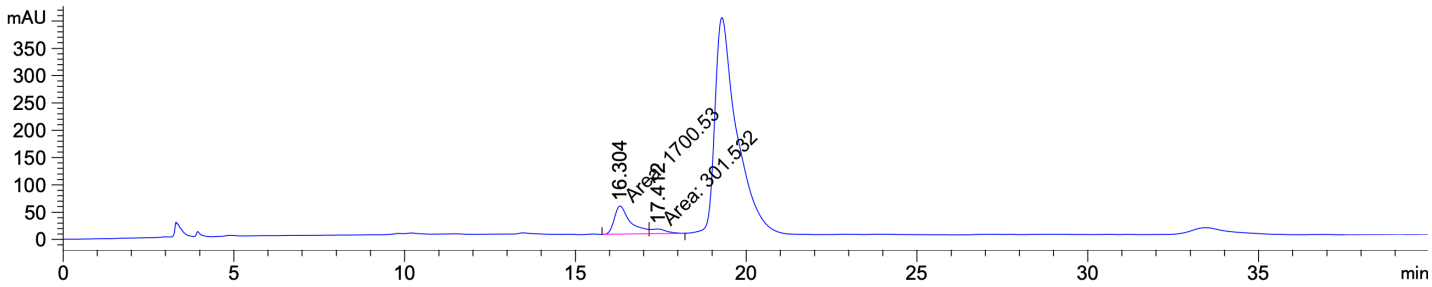
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.987	MF	0.6216	4.20733e4	1128.03796	26.4002
2	17.214	FM	0.6628	4.49932e4	1131.37769	28.2324
3	19.104	FM	0.7420	3.59585e4	807.73743	22.5633
4	32.873	MM	1.5317	3.63422e4	395.45508	22.8041

enantioenriched sample (trans)

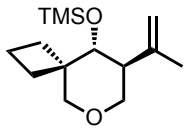


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.286	MM	0.7481	1.77695e4	395.89987	95.1488
2	33.446	MM	1.2215	905.97540	12.36198	4.8512

enantioenriched sample (cis)



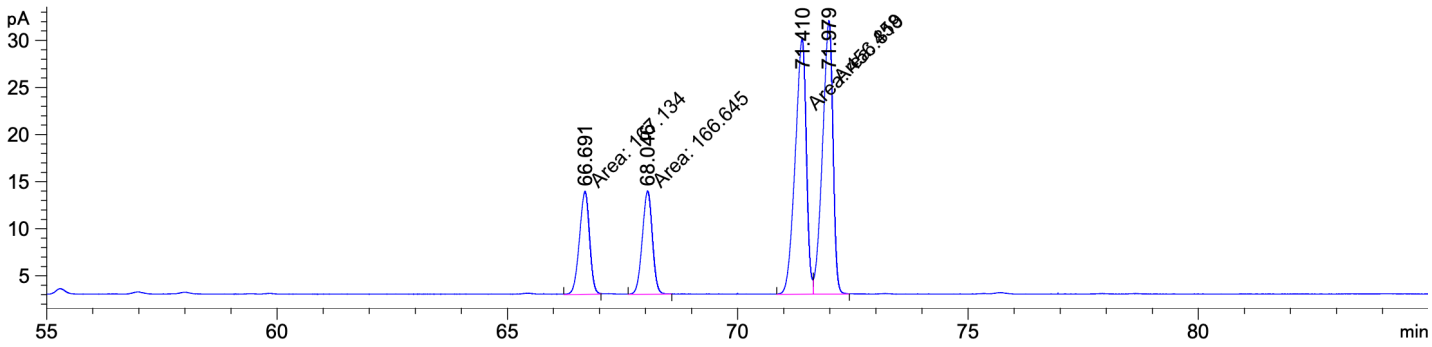
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.304	MF	0.5494	1700.53308	51.58600	84.9389
2	17.412	FM	0.5630	301.53235	8.92564	15.0611



2o, 94% ee *trans*, 83% ee *cis*
(ee evaluated using OTMS derivative)

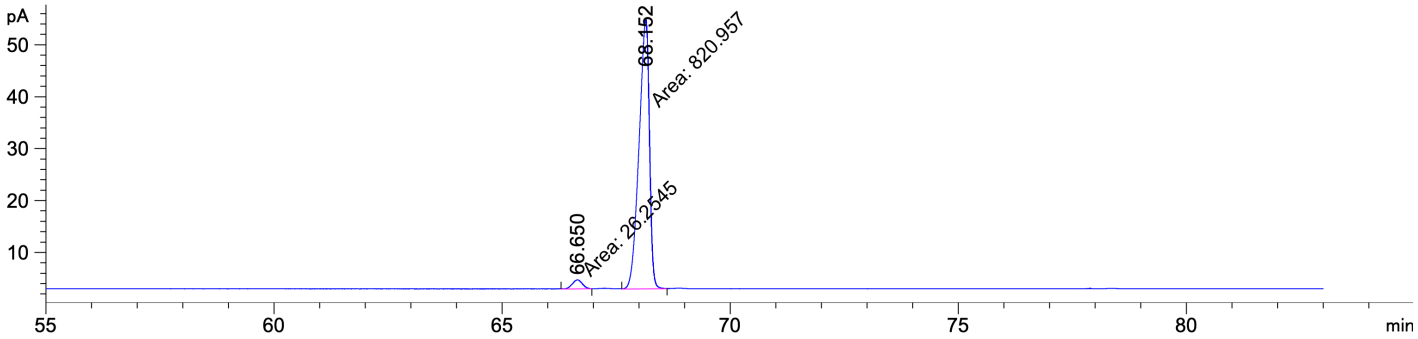
GC (CP-Chirasil Dex CB, 25 m)
80 ℃ - 120 ℃, 0.5 ℃/min, 7 psi

racemic sample



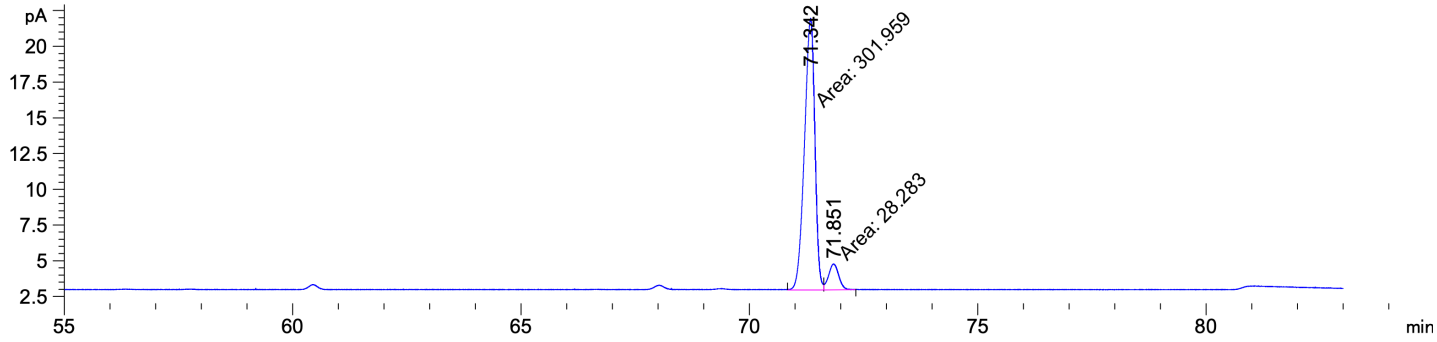
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	66.691	MM	0.2542	167.13368	10.95740	13.38571
2	68.046	MM	0.2534	166.64456	10.96129	13.34654
3	71.410	MF	0.2794	456.81900	27.24578	36.58656
4	71.979	FM	0.2630	458.00046	29.02702	36.68119

enantioenriched sample (trans)

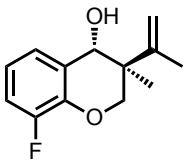


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	66.650	MM	0.2527	26.25447	1.73186	3.09893
2	68.152	MM	0.2630	820.95673	52.01600	96.90107

enantioenriched sample (cis)



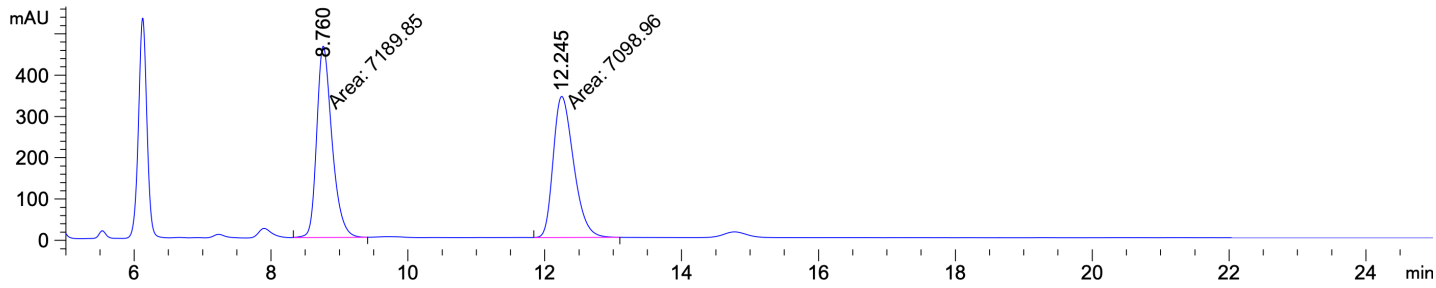
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	71.342	MF	0.2654	301.95911	18.96229	91.43569
2	71.851	FM	0.2602	28.28296	1.81187	8.56431



HPLC (AS-H)
5% IPA/Hexanes, 1 mL/min, 210 nm

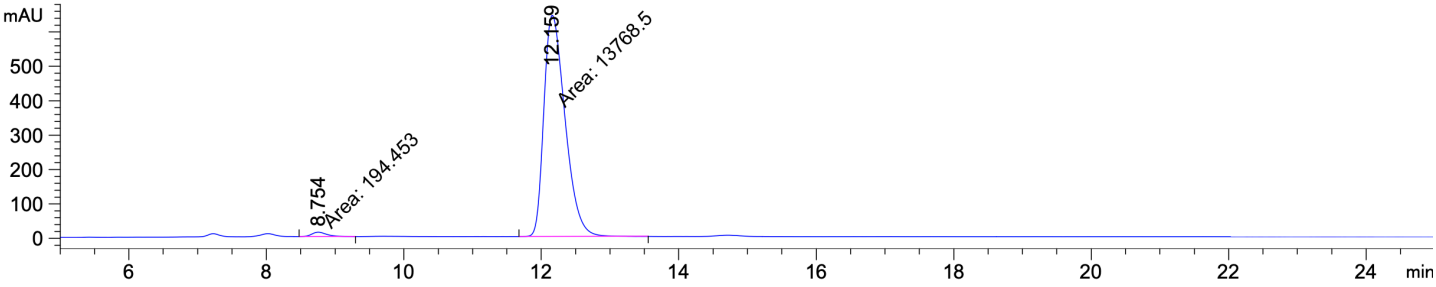
2p, 96% ee

racemic sample

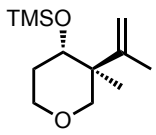


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.760	MM	0.2586	7189.84717	463.45813	50.3180
2	12.245	MM	0.3460	7098.96338	341.93777	49.6820

enantioenriched sample



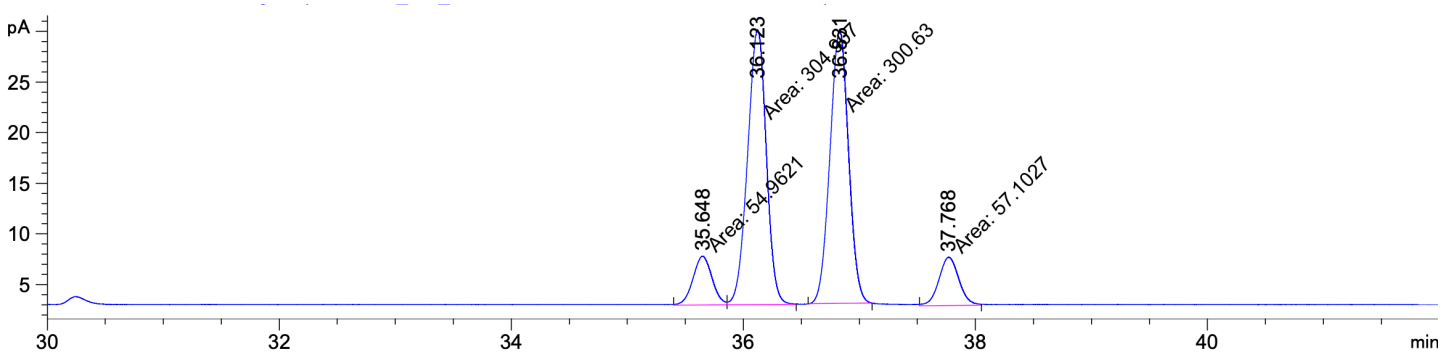
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.362	VB	0.1234	8.36266	1.04426	1.7544
2	12.159	BB	0.3271	468.31775	22.47377	98.2456



GC (Cyclosil-B, 30 m)
80 ℃ - 120 ℃, 0.5 ℃/min, 7 psi

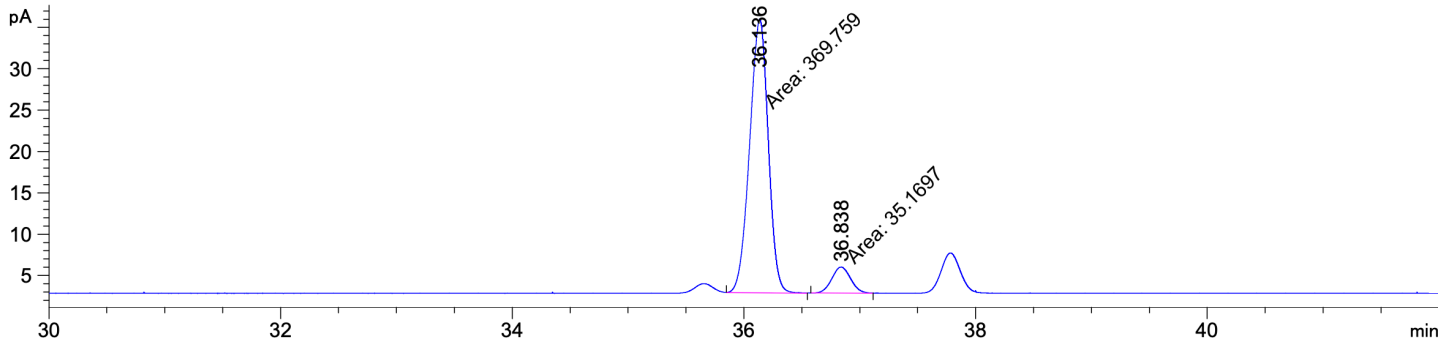
2q, 83% ee *trans*, 62% ee *cis*
(ee evaluated using OTMS derivative)

racemic sample



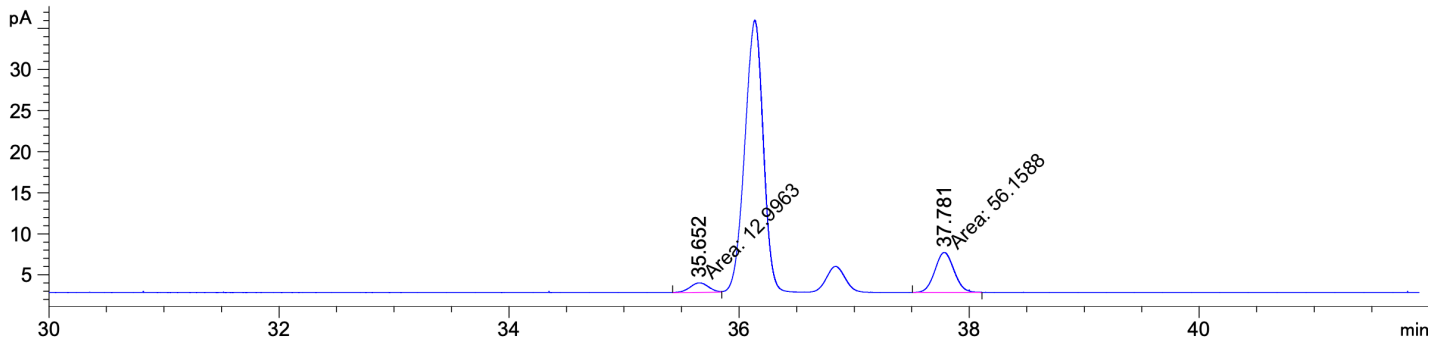
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	35.648	MF	0.1897	54.96210	4.82862	7.65913
2	36.123	FM	0.1870	304.90744	27.17875	42.48974
3	36.831	MM	0.1858	300.63022	26.97410	41.89370
4	37.768	MM	0.1991	57.10271	4.78124	7.95743

enantioenriched sample (trans)

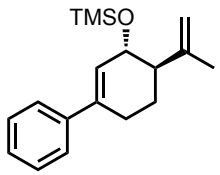


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	36.136	MM	0.1860	369.75946	33.13818	91.31461
2	36.838	MM	0.1868	35.16969	3.13776	8.68539

enantioenriched sample (cis)



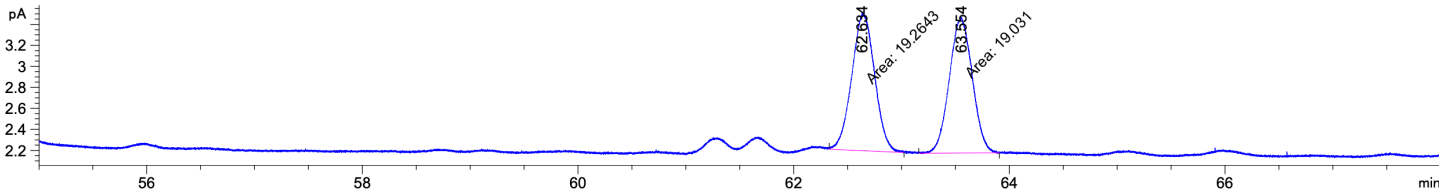
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	35.652	MM	0.1863	12.99626	1.16268	18.79292
2	37.781	MM	0.1926	56.15882	4.86080	81.20708



2r, 90% ee
(ee evaluated using OTMS derivative)

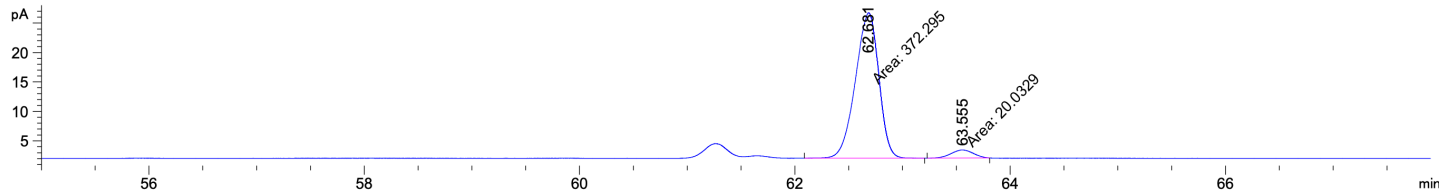
GC (CP-Chirasil Dex CB, 25 m)
120 ℃ - 160 ℃, 0.5 ℃/min, 7 psi

racemic sample

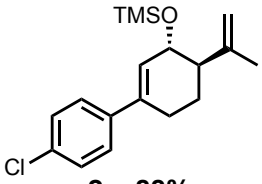


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	62.634	MM	0.2436	19.26432	1.31811	50.30457
2	63.554	MM	0.2456	19.03105	1.29166	49.69543

enantioenriched sample



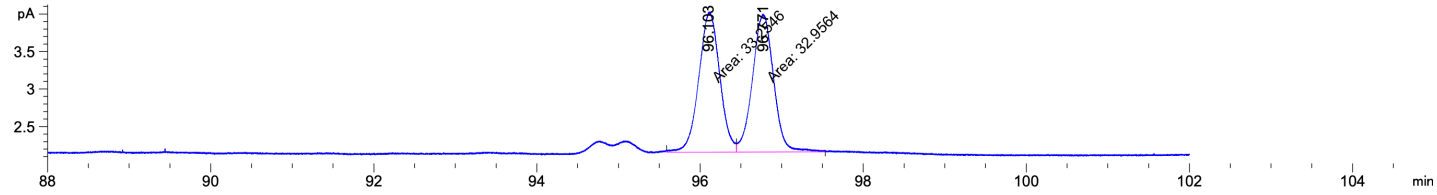
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	62.681	MM	0.2515	372.29523	24.67207	94.89385
2	63.555	MM	0.2402	20.03287	1.38978	5.10615



2s, 88% ee
(ee evaluated using OTMS derivative)

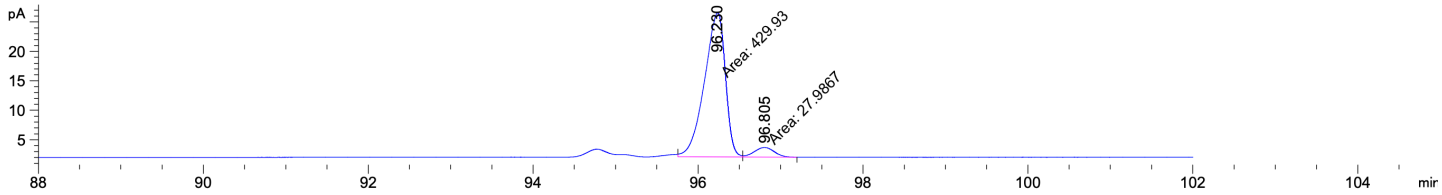
GC (CP-Chirasil Dex CB, 25 m)
120 ℃ - 170 ℃, 0.5 ℃/min, 7 psi

racemic sample

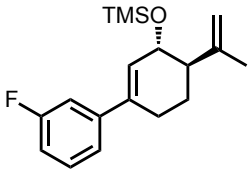


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	96.103	MF	0.2970	33.25460	1.86588	50.22518
2	96.771	FM	0.3007	32.95641	1.82650	49.77482

enantioenriched sample



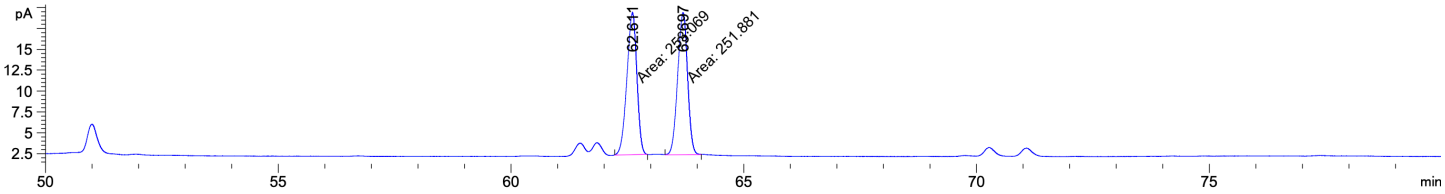
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	96.230	MF	0.2920	429.93018	24.54067	93.88826
2	96.805	FM	0.2826	27.98669	1.65031	6.11174



2t, 90% ee
(ee evaluated using OTMS derivative)

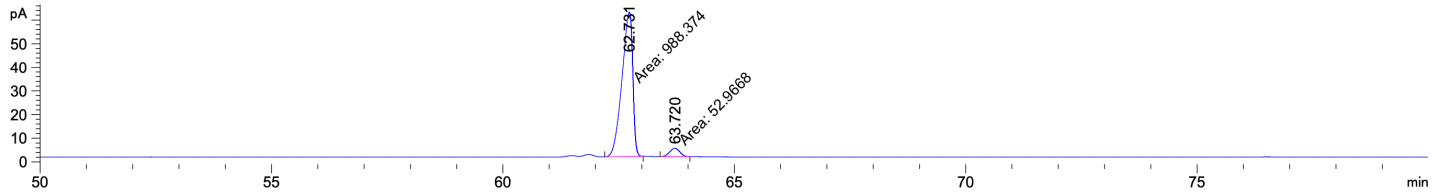
GC (CP-Chirasil Dex CB, 25 m)
120 ℃ - 170 ℃, 0.5 ℃/min, 7 psi

racemic sample



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	62.611	MM	0.2471	253.06856	17.07188	50.11761
2	63.697	MM	0.2462	251.88086	17.04796	49.88239

enantioenriched sample



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	62.731	MM	0.2693	988.37372	61.16815	94.91359
2	63.720	MM	0.2486	52.96683	3.55066	5.08641

6. Kinetics Experiments

6.1 Rates of Edman degradation

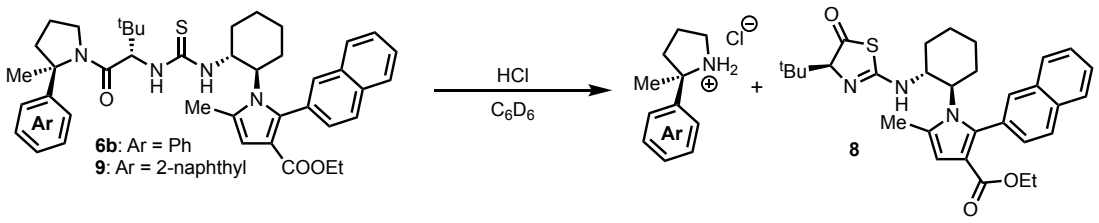


Figure S6. Kinetic analysis of Edman degradation.

Kinetics experiments measuring the rates of Edman degradation of catalysts **6b** and **9** were carried out using ^{1}H NMR spectroscopy with reactions conducted in oven-dried 5 mm diameter NMR tubes. Data collection was performed on an INOVA-600 NMR spectrometer (600 MHz). Experiments were conducted at 21.3 ± 0.2 ºC over a period of 20 minutes, with spectra collected at fixed 10 second intervals with 1.5 second acquisition times and 8.5 second relaxation delays. ^{1}H NMR spectra were analyzed in MestReNova (Mestrelab Research) using phase and baseline corrections. Data extracted from these spectra were analyzed and plotted using Microsoft Excel. Concentration versus time data were fitted to linear functions using a least-squares algorithm in Microsoft Excel.

Sample procedure for kinetics experiments:

A 1000 µL stock solution of HCl in C_6D_6 was prepared by the addition of 240 µL of 2.11 M HCl in Et_2O to 760 µL of C_6D_6 in a flame-dried vial. Separately, an HBD stock solution was prepared by weighing **6b** or **9** (0.0119 g or 0.0126 g respectively) into a flame-dried vial followed by addition of 1700 µL of C_6D_6. To the HBD stock solution was added 5 µL of 1,1,2,2-tetrachloroethane as a quantitative internal standard. 500 µL of this stock solution were distributed between three identical oven-dried NMR tubes, which were then capped with rubber septa and sealed with parafilm. A single NMR spectrum was obtained for the purposes of determining the appropriate acquisition parameters (shim, gain, etc.). The NMR tube was removed from the spectrometer and 10 µL of the HCl stock solution (0.005 mmol, 1 eq.) were added to initiate reactions. The NMR tube was inverted several times and then returned to the NMR probe. The time delay between addition of the HCl stock solution and the beginning of data acquisition was recorded and factored into kinetic models. Experiments were conducted in triplicate. All reactions were found to be homogeneous over the entire reaction course.

HBD concentration was determined by integration of the signal corresponding to the pyrrole methyl group (δ = 2.65 ppm) against the tetrachloroethane internal standard (δ = 4.88 ppm). For all reactions, it was found that no significant side products were formed and the only observable reaction was clean Edman degradation. The first 10% conversion of [HBD] versus time data were fitted to linear functions using a minimization of squares algorithm in Microsoft Excel. Initial rates were taken to be the slopes of fitted concentration vs time data. Reported error values in relative rate measurements were derived by standard error propagation using standard deviations of individual kinetics runs.

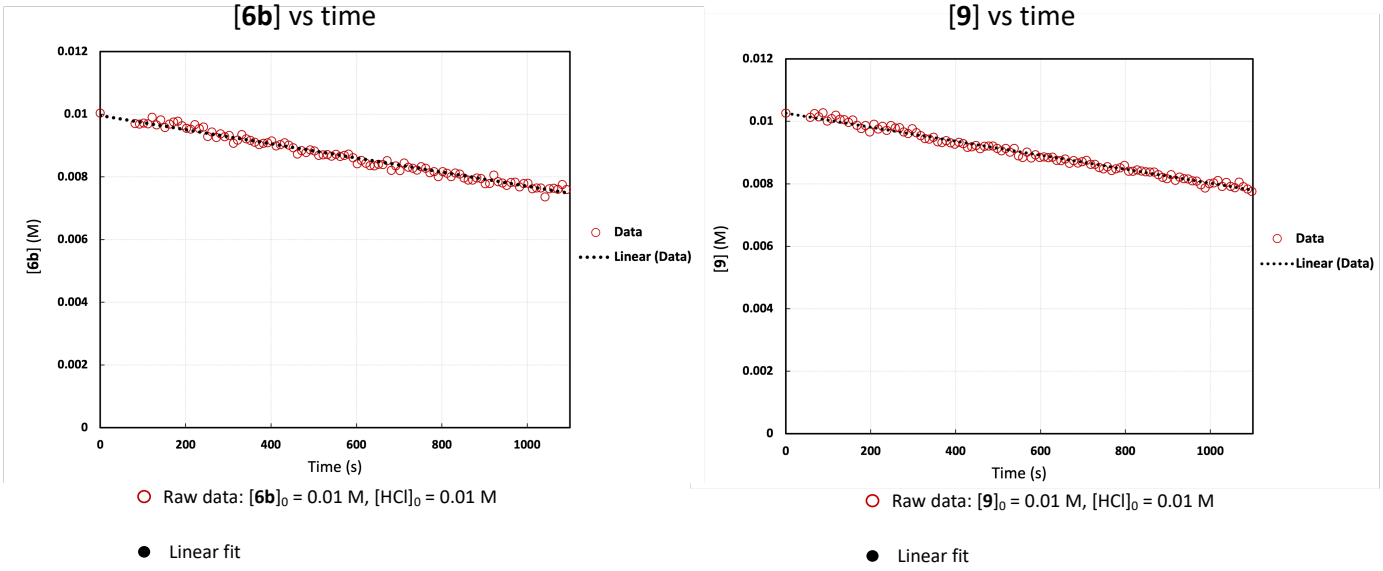


Figure S7. Representative concentration vs time data set for HBD Edman degradation experiments with linear curve fits.

*Representative datasets for the degradation reactions of **6b** and **9** are provided below:*

Time (s)	[6b] (M)	Time (s)	[9] (M)
0	0.0100355	0	0.01025982
82	0.00970044	58	0.01012308
92	0.00968178	68	0.01023925
102	0.00971506	78	0.0101398
112	0.00969143	88	0.01026513
122	0.00990195	98	0.0100031
132	0.0096547	108	0.01007839
142	0.00981825	118	0.01018821
152	0.00957605	128	0.01006183
162	0.00968121	138	0.01005084
172	0.00975043	148	0.00996399
182	0.00977306	158	0.0100347
192	0.00963169	168	0.00986579
202	0.0095498	178	0.00976624
212	0.00952029	188	0.00985888
222	0.00966238	198	0.00965893
232	0.00954204	208	0.00989823
242	0.00958534	218	0.00974771
252	0.00928834	228	0.00983043
262	0.00942607	238	0.00970567
272	0.00925692	248	0.00986384
282	0.00937327	258	0.00978377
292	0.00927583	268	0.00978885
302	0.00932084	278	0.00965258
312	0.00907049	288	0.00960851
322	0.00917332	298	0.0097607
332	0.00934771	308	0.0096312
342	0.00920944	318	0.00953763
352	0.0091625	328	0.00944641
362	0.00910051	338	0.00942285
372	0.00902683	348	0.00948735
382	0.00906956	358	0.00934149
392	0.00908875	368	0.00931219
402	0.00914613	378	0.00937848
412	0.00898861	388	0.00931036
422	0.00902488	398	0.00926459
432	0.00908667	408	0.00932118
442	0.00900978	418	0.00927927
452	0.00892439	428	0.00916397

462	0.00872586	438	0.00917865
472	0.00883631	448	0.00922116
482	0.00877739	458	0.00912311
492	0.00885806	468	0.00920021
502	0.00882901	478	0.00920482
512	0.00868733	488	0.00920202
522	0.00870213	498	0.0091305
532	0.00870427	508	0.00905516
542	0.00865763	518	0.00912527
552	0.00871876	528	0.00901276
562	0.00865197	538	0.0091279
572	0.00868216	548	0.00888738
582	0.00872921	558	0.00883721
592	0.00860929	568	0.00900981
602	0.00841107	578	0.00882468
612	0.00852373	588	0.00892465
622	0.0084344	598	0.00883621
632	0.00836	608	0.00885921
642	0.00835069	618	0.00883188
652	0.00840077	628	0.00884564
662	0.00839392	638	0.00874946
672	0.00851844	648	0.00873732
682	0.00820784	658	0.00879037
692	0.0083492	668	0.00865454
702	0.00819895	678	0.00873551
712	0.00843728	688	0.00866448
722	0.00830742	698	0.00870653
732	0.00827052	708	0.00874277
742	0.00821408	718	0.00862098
752	0.00832096	728	0.00861512
762	0.00827537	738	0.00851648
772	0.00813058	748	0.00847247
782	0.00816368	758	0.00854401
792	0.00800509	768	0.00842532
802	0.00816243	778	0.00847522
812	0.0081143	788	0.00850595
822	0.00800188	798	0.00858556
832	0.00812294	808	0.00840123
842	0.00808582	818	0.0083945
852	0.00796279	828	0.0084404
862	0.00789284	838	0.00840626
872	0.00789462	848	0.00838079

882	0.00796623	858	0.00837193
892	0.00794293	868	0.00837151
902	0.00778131	878	0.00828388
912	0.00778312	888	0.00820007
922	0.00805051	898	0.00816193
932	0.00784594	908	0.0082839
942	0.00780151	918	0.00810843
952	0.00772685	928	0.00820844
962	0.00781965	938	0.00815799
972	0.00782533	948	0.00814811
982	0.00767983	958	0.00809326
992	0.00778608	968	0.00808575
1002	0.00779489	978	0.00796392
1012	0.00762059	988	0.00786187
1022	0.00764202	998	0.00799783
1032	0.00763958	1008	0.00802631
1042	0.00736006	1018	0.00809677
1052	0.00761474	1028	0.00791044
1062	0.00763593	1038	0.00803837
1072	0.00759793	1048	0.00791431
1082	0.00774933	1058	0.00787399
1092	0.00759673	1068	0.00805185
1102	0.00739726	1078	0.00790813
1112	0.00755048	1088	0.0078249
1122	0.00746073	1098	0.00775319
1132	0.00742107	1108	0.00784539
1142	0.00758448	1118	0.00780482
1152	0.00739268	1128	0.00782117
1162	0.00748862	1138	0.00782673
1172	0.0072283	1148	0.00773178
1182	0.00732908	1158	0.00766357
1192	0.00714757	1168	0.00765839
1202	0.00728532	1178	0.00773477
1212	0.00729081	1188	0.0076346
1222	0.00720839	1198	0.00764826
1232	0.00741996	1208	0.00765988
1242	0.00716423	1218	0.00753618
1252	0.00730219	1228	0.00760887
1262	0.0071737	1238	0.00741832
1272	0.00711233	1248	0.00745556

trial	Initial rate (k_{obs}) (M/s)	trial	Initial rate (k_{obs}) (M/s)
6b-Run 1	2.74 E-06	**9**-Run 1	2.64 E-06
6b-Run 2	2.71 E-06	**9**-Run 2	2.79 E-06
6b-Run 3	2.52 E-06	**9**-Run 3	2.50 E-06
Average k_{obs}:	2.65 E-06	**Average k_{obs}:**	2.64 E-06
Stdev.:	1.20 E-07	**Stdev.:**	1.42 E-07
$k_{rel} = k_{6b} / k_9 =$	1.01 ± 0.07	$k_{rel} = k_9 / k_{6b} =$	0.99 ± 0.07

Figure S8. Results of Edman degradation kinetics experiments.

6.2 Rates of Prins cyclization reactions

Kinetic experiments measuring the rates of Prins cyclization reactions were performed using in situ attenuated total reflectance Fourier-transform infrared (ATR FTIR) spectroscopy to track the consumption of aldehyde **1b**. Measurements were performed using a Mettler Toledo ReactIR™ iC 10 ATR FTIR spectrometer and a 9 mm probe with a SiComp (silicon-based) window and a two-neck reaction vessel equipped with air-tight valves. Reactions were performed with the reaction vessel submerged in a temperature-equilibrated oil bath at 23.1 ± 0.2 ºC. Data for the relative rate measurements were acquired over multiple runs.

Time-dependent absorbance data were converted to time-dependent concentration data using the experimentally determined response factor and response constant at the infinity point (the slope and vertical axis intercept respectively in the plot below). Absorbance data were acquired using the aldehyde stretching frequency (with the maximum absorbance value in in range 1715-1685 cm^{-1}) with a two point baseline (defined from 1750-1630 cm^{-1}); here absorbance is measured as the height of the aldehyde peak extending from the two point baseline.

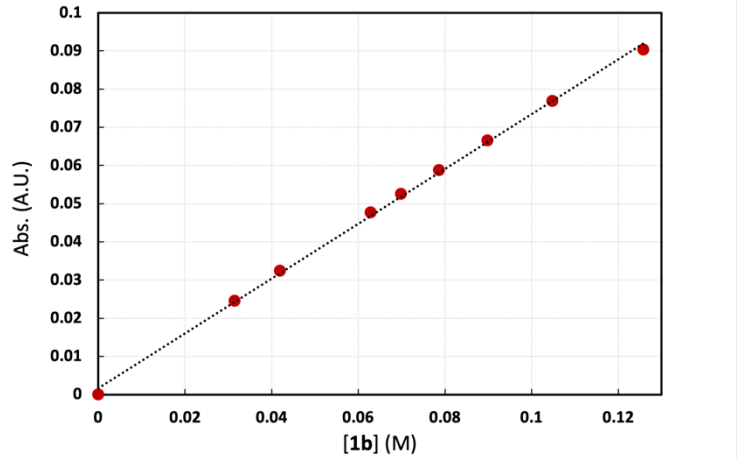


Figure S9. Beer's law plot for determination of the absorbance response factor for **1b** at 1705 cm^{-1}.

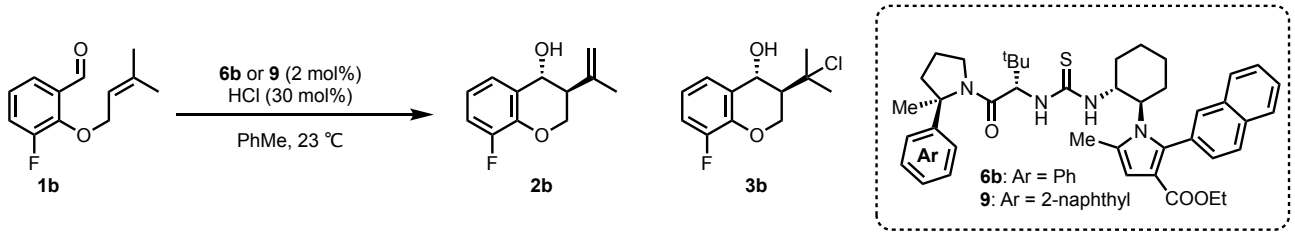


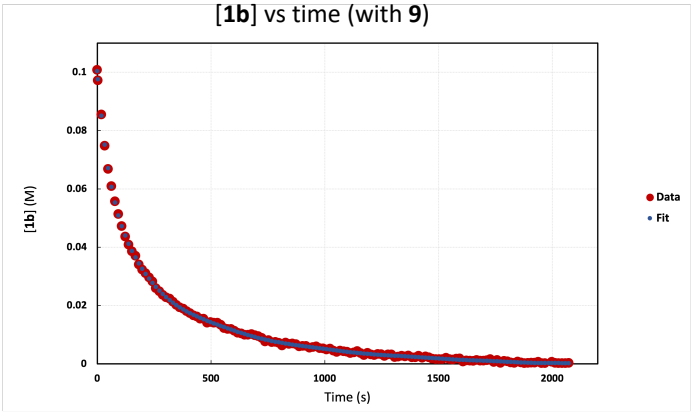
Figure S10. Model reaction for kinetic analysis.

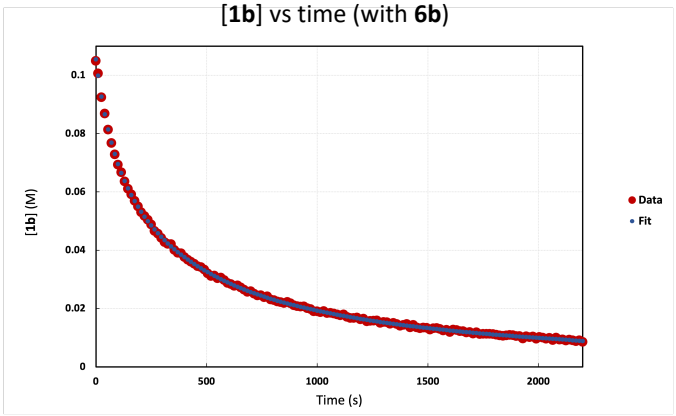
Sample procedure for kinetics experiments:

A 9.0 mL stock solution of substrate **1b** (0.2007g, 1 eq.) and **9** (0.0143g, 2 mol%) in dry toluene was prepared and 2800 µL of this stock solution were transferred to the oven-dried reaction vessel charged with a magnetic stir bar. The vessel was then submerged in

an oil bath (23.1 ± 0.2 °C) and allowed to equilibrate for several minutes prior to initiation of the reaction. A separate stock solution of HCl was generated (500 μL of a 2.17 M solution in Et_2O added to 1900 μL of toluene) and 200 μL of this solution were added to the reaction vessel to initiate reactions. The time delay between addition of HCl and acquisition of the first spectrum following addition was noted and factored into kinetics data. The effect of dilution upon addition of the HCl stock solution was also factored into kinetics data. Data were collected in 15 second intervals. All reactions catalyzed by **9** were observed to proceed to >98% conversion (as determined by ^{19}F NMR analysis of the crude reaction mixtures). Reactions were quenched by the addition of 100 μL of triethylamine prior to analysis by ^{19}F NMR. The above procedure was followed in recording the rate of the Prins reaction catalyzed by **6b**. Both **9** and **6b** were found to be fully stable over the entire reaction course, with no detectable Edman degradation taking place using substrate **1b**. In recording the rate of the background process catalyzed by HCl alone, the above procedure was followed omitting HBD catalyst and using a 60 second data collection interval. All reactions were found to be homogeneous over the entire reaction course.

In order to increase the accuracy of initial rates measurements for reactions catalyzed by **9**, concentration vs. time data were first fit to 15th order polynomial functions. Initial rates were taken to be the slopes of linear least-squares fits of the polynomial-fitted conversion vs time data over the first 5% conversion. A good curve-fit was necessary to obtain reliable initial rates measurements since reactions typically proceed to >25% conversion within the first 4 data points. Initial rates measurements on the background reaction catalyzed by HCl alone were obtained using linear least-squares fits of the first 5% of conversion vs. time data. The slopes of these linear fits were taken to be the initial rates. The first time derivative of the polynomial fits of [**1b**] vs time data were used to extract instantaneous rates. The rate comparison between **9** and **6b** was performed using instantaneous rates at [**1b**] = 0.09 M. Reported error values in relative rate measurements were derived by standard error propagation using standard deviations of individual kinetics runs.





Raw data: $[\mathbf{1b}]_0$ = 0.1 M, $[\mathbf{9}]_T$ = 0.002 M, [HCl] = 0.030 M

Polynomial fit of the following form:

$$[\mathbf{1b}] = A*(t\wedge15)+B*(t\wedge14)+C*(t\wedge13)+D*(t\wedge12)+E*(t\wedge11)+F*(t\wedge10)+G*(t\wedge9)+H*(t\wedge8)$$
$$I*(t\wedge7)+J*(t\wedge6)+K*(t\wedge5)+L*(t\wedge4)+M*(t\wedge3)+N*(t\wedge2)+O*(t)+P$$

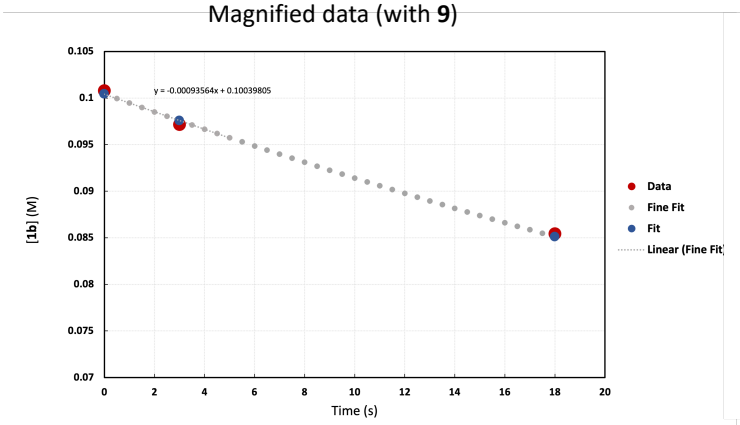
$$[\mathbf{1b}]_{fit} = (4.51E\text{-}46)*(t\wedge15)+(-6.87E\text{-}42)*(t\wedge14)+(4.65E\text{-}38)*(t\wedge13)+(-1.84E\text{-}34)*(t\wedge12)+(4.68E\text{-}31)*(t\wedge11)+(-7.93E\text{-}28)*(t\wedge10)+(8.77E\text{-}25)*(t\wedge9)+(-5.58E\text{-}22)*(t\wedge8)+(6.02E\text{-}20)*(t\wedge7)+ (2.39E\text{-}16)*(t\wedge6)+(-2.41E\text{-}13)*(t\wedge5)+(1.22E\text{-}10)*(t\wedge4)+(-3.76E\text{-}8)*(t\wedge3)+(7.33E\text{-}6)*(t\wedge2)+(9.71E\text{-}4)*(t)+0.100$$

Raw data: $[\mathbf{1b}]_0$ = 0.1 M, $[\mathbf{6b}]_T$ = 0.002 M, [HCl] = 0.030 M

Polynomial fit of the following form:

$$[\mathbf{1b}] = A*(t\wedge15)+B*(t\wedge14)+C*(t\wedge13)+D*(t\wedge12)+E*(t\wedge11)+F*(t\wedge10)+G*(t\wedge9)+H*(t\wedge8)$$
$$I*(t\wedge7)+J*(t\wedge6)+K*(t\wedge5)+L*(t\wedge4)+M*(t\wedge3)+N*(t\wedge2)+O*(t)+P$$

$$[\mathbf{1b}]_{fit} = (-7.93E\text{-}48)*(t\wedge15)+(1.70E\text{-}43)*(t\wedge14)+(-1.65E\text{-}39)*(t\wedge13)+(9.57E\text{-}36)*(t\wedge12)+(-3.70E\text{-}32)*(t\wedge11)+(1.01E\text{-}28)*(t\wedge10)+(-1.98E\text{-}25)*(t\wedge9)+(2.86E\text{-}22)*(t\wedge8)+(-3.04E\text{-}19)*(t\wedge7)+ (2.38E\text{-}16)*(t\wedge6)+(-1.35E\text{-}13)*(t\wedge5)+(5.55E\text{-}11)*(t\wedge4)+(-1.62E\text{-}8)*(t\wedge3)+(3.45E\text{-}6)*(t\wedge2)+(-5.85E\text{-}4)*(t)+0.105$$



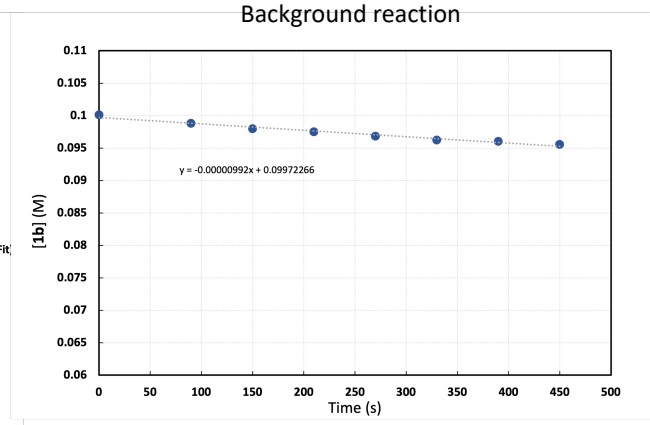


Figure S11. Representative concentration vs time data set for HBD kinetics experiments with polynomial curve fits (top). The first ~15% conversion for the reaction catalyzed by **9** are magnified on the bottom left, with the polynomial fit in blue and grey. The background reaction catalyzed by HCl alone is shown in the bottom right. In both cases, the first 5% conversion are fit by linear least squares approach.

*A representative dataset for the reaction catalyzed by **9** is provided below:*

Time (s)	[1b] (M)	Polynomial fit (M)	Rate (M/s)
0.00	0.10125653	0.101274503	0.001031658
9.00	0.09313623	0.092700024	0.000878377
24.00	0.08033292	0.081108478	0.000677369
39.00	0.07222747	0.072113301	0.000529622
54.00	0.0651471	0.065022219	0.0004215
69.00	0.0592056	0.059323049	0.000342512
84.00	0.054676	0.054641425	0.000284677
99.00	0.05136746	0.050707212	0.000241999
114.00	0.04729921	0.047328053	0.00021004
129.00	0.04445563	0.044368761	0.000185563
144.00	0.0416285	0.041735444	0.000166255
159.00	0.03925742	0.039363443	0.000150499
174.00	0.03644226	0.03720831	0.00013719
189.00	0.0353247	0.035239189	0.0001256
204.00	0.03320323	0.033434052	0.000115266
219.00	0.03190152	0.031776377	0.000105903
234.00	0.03025101	0.030252913	9.73513E-05
249.00	0.02917788	0.028852232	8.95218E-05
264.00	0.0278061	0.027563877	8.23692E-05
279.00	0.0265934	0.026377901	7.58679E-05
294.00	0.02494456	0.025284679	6.99986E-05
309.00	0.02432219	0.024274893	6.47391E-05
324.00	0.02367656	0.023339599	6.00607E-05
339.00	0.02281947	0.02247035	5.59263E-05
354.00	0.02118874	0.021659312	5.22913E-05
369.00	0.02115267	0.020899366	4.91053E-05
384.00	0.0197111	0.02018418	4.63141E-05
399.00	0.01964034	0.019508243	4.38627E-05
414.00	0.01880527	0.018866869	4.16971E-05
429.00	0.01812119	0.018256155	3.97666E-05
444.00	0.01791447	0.017672928	3.80251E-05
459.00	0.01674453	0.017114659	3.64326E-05
474.00	0.01659521	0.016579374	3.49556E-05
489.00	0.01608706	0.016065548	3.35675E-05
504.00	0.01557125	0.015572006	3.22481E-05
519.00	0.01465427	0.015097832	3.09834E-05

534.00	0.0144984	0.014642274	2.97649E-05
549.00	0.01444254	0.014204676	2.85884E-05
564.00	0.01403872	0.013784413	2.74536E-05
579.00	0.01306324	0.013380848	2.63625E-05
594.00	0.01324795	0.0129933	2.53188E-05
609.00	0.01295334	0.012621027	2.43267E-05
624.00	0.01269285	0.012263218	2.33907E-05
639.00	0.01179746	0.011919009	2.25141E-05
654.00	0.01202814	0.011587486	2.16993E-05
669.00	0.0113775	0.011267717	2.09469E-05
684.00	0.01141018	0.010958771	2.02559E-05
699.00	0.01025548	0.010659749	1.96232E-05
714.00	0.00998894	0.010369808	1.90441E-05
729.00	0.00932165	0.010088188	1.85125E-05
744.00	0.00977477	0.009814234	1.80207E-05
759.00	0.00943432	0.00954741	1.75604E-05
774.00	0.00872177	0.009287308	1.71228E-05
789.00	0.00978961	0.009033659	1.66987E-05
804.00	0.00874009	0.008786324	1.62795E-05
819.00	0.00861957	0.008545289	1.58574E-05
834.00	0.00805871	0.008310651	1.54254E-05
849.00	0.00791245	0.008082602	1.49782E-05
864.00	0.00815015	0.0078614	1.45119E-05
879.00	0.00761399	0.00764735	1.40244E-05
894.00	0.00765764	0.007440775	1.35154E-05
909.00	0.00682585	0.007241987	1.29865E-05
924.00	0.00763531	0.007051263	1.24409E-05
939.00	0.00692975	0.00686882	1.18834E-05
954.00	0.00672466	0.006694791	1.13202E-05
969.00	0.0065279	0.006529208	1.07584E-05
984.00	0.0064184	0.006371992	1.0206E-05
999.00	0.00663374	0.006222941	9.67115E-06
1014.00	0.00578693	0.006081728	9.16224E-06
1029.00	0.00630017	0.005947905	8.68715E-06
1044.00	0.00560865	0.005820908	8.2531E-06
1059.00	0.00575232	0.005700075	7.86631E-06
1074.00	0.00489298	0.005584658	7.53171E-06
1089.00	0.00541375	0.005473845	7.25273E-06
1104.00	0.00530592	0.005366789	7.03112E-06
1119.00	0.00549785	0.005262624	6.86692E-06
1134.00	0.00515807	0.005160503	6.75837E-06
1149.00	0.00548881	0.005059612	6.702E-06

1164.00	0.00463304	0.004959207	6.69276E-06
1179.00	0.00471234	0.004858626	6.72419E-06
1194.00	0.00466894	0.004757315	6.78867E-06
1209.00	0.00470149	0.004654843	6.87771E-06
1224.00	0.00462995	0.004550906	6.9823E-06
1239.00	0.0045043	0.004445342	7.09326E-06
1254.00	0.00361057	0.004338122	7.20159E-06
1269.00	0.0042253	0.00422935	7.29885E-06
1284.00	0.00473058	0.00411925	7.37751E-06
1299.00	0.00378507	0.00400815	7.43121E-06
1314.00	0.00395832	0.003896463	7.45508E-06
1329.00	0.00413576	0.003784663	7.4459E-06
1344.00	0.00457859	0.003673258	7.40223E-06
1359.00	0.00325403	0.003562767	7.32445E-06
1374.00	0.00249471	0.003453685	7.21472E-06
1389.00	0.00378769	0.003346466	7.07687E-06
1404.00	0.00354119	0.003241493	6.91617E-06
1419.00	0.00342106	0.003139063	6.73903E-06
1434.00	0.00304804	0.003039369	6.55265E-06
1449.00	0.00237562	0.002942492	6.3646E-06
1464.00	0.00253563	0.002848401	6.18237E-06
1479.00	0.00257657	0.002756957	6.01285E-06
1494.00	0.00324729	0.002667923	5.86191E-06
1509.00	0.00241653	0.002580985	5.73391E-06
1524.00	0.00187639	0.002495778	5.63133E-06
1539.00	0.0020403	0.002411916	5.55443E-06
1554.00	0.00275282	0.002329027	5.50105E-06
1569.00	0.0022426	0.00224679	5.46657E-06
1584.00	0.0023951	0.002164971	5.44391E-06
1599.00	0.00241339	0.00208346	5.42379E-06
1614.00	0.00209994	0.002002299	5.39518E-06
1629.00	0.00205448	0.001921708	5.3458E-06
1644.00	0.00207805	0.001842093	5.26293E-06
1659.00	0.00172528	0.001764049	5.13425E-06
1674.00	0.00168231	0.001688349	4.94889E-06
1689.00	0.00138327	0.001615908	4.69849E-06
1704.00	0.0012274	0.001547744	4.3783E-06
1719.00	0.00127072	0.00148491	3.98823E-06
1734.00	0.00141165	0.00142842	3.53381E-06
1749.00	0.00157472	0.001379159	3.02688E-06
1764.00	0.00117958	0.001337784	2.48601E-06
1779.00	0.0011426	0.001304623	1.93649E-06

1794.00	0.00167898	0.001279576	1.40982E-06
1809.00	0.00162021	0.001262032	9.42622E-07
1824.00	0.00117512	0.001250801	5.74841E-07
1839.00	0.00111876	0.001244085	3.47239E-07
1854.00	0.00102922	0.00123949	2.98156E-07
1869.00	0.00143925	0.001234087	4.5956E-07
1884.00	0.00138019	0.001224543	8.52518E-07
1899.00	0.00060613	0.001207323	1.48229E-06
1914.00	0.0013201	0.001178964	2.33332E-06
1929.00	0.00132212	0.001136417	3.36468E-06
1944.00	0.00083293	0.001077466	4.5065E-06

*A representative dataset for the reaction catalyzed by **6b** is provided below:*

Time (s)	[1b] (M)	Polynomial fit (M)	Rate (M/s)
0.00	0.10489338	0.105383009	0.000585397
10.00	0.10060566	0.09985822	0.000521078
25.00	0.09243488	0.092670173	0.000440201
40.00	0.0867795	0.086574579	0.000374868
55.00	0.08133612	0.081361502	0.000322079
70.00	0.07674258	0.076861913	0.000279365
85.00	0.07276919	0.072940327	0.000244709
100.00	0.06927803	0.069488605	0.000216471
115.00	0.06667085	0.06642078	0.000193325
130.00	0.0635225	0.063668733	0.000174209
145.00	0.06104555	0.061178636	0.000158273
160.00	0.05911924	0.058908008	0.000144847
175.00	0.05684956	0.056823321	0.000133404
190.00	0.05500878	0.054898055	0.000123531
205.00	0.05297409	0.053111132	0.000114912
220.00	0.05166959	0.051445674	0.000107301
235.00	0.05035437	0.04988801	0.000100512
250.00	0.04878618	0.048426917	9.44042E-05
265.00	0.04657724	0.047053017	8.88706E-05
280.00	0.04563031	0.045758338	8.383E-05
295.00	0.04416938	0.044535964	7.92207E-05
310.00	0.04274398	0.043379799	7.49952E-05
325.00	0.04214278	0.042284381	7.11155E-05
340.00	0.04202605	0.041244759	6.75509E-05
355.00	0.04003315	0.040256411	6.4275E-05
370.00	0.03903956	0.039315184	6.12644E-05
385.00	0.03892394	0.038417258	5.84979E-05
400.00	0.03757097	0.037559127	5.59552E-05

415.00	0.03670539	0.036737582	5.36167E-05
430.00	0.03602479	0.035949701	5.14635E-05
445.00	0.03529656	0.035192844	4.94772E-05
460.00	0.03445382	0.03446464	4.764E-05
475.00	0.03416883	0.033762984	4.59348E-05
490.00	0.03333069	0.033086018	4.43454E-05
505.00	0.03199011	0.03243212	4.28566E-05
520.00	0.0310677	0.031799888	4.14545E-05
535.00	0.03127567	0.031188116	4.01264E-05
550.00	0.03031606	0.030595781	3.88612E-05
565.00	0.03056317	0.030022014	3.76492E-05
580.00	0.029687	0.029466081	3.6482E-05
595.00	0.02873311	0.028927361	3.53532E-05
610.00	0.02830924	0.028405322	3.42572E-05
625.00	0.02769689	0.027899501	3.31902E-05
640.00	0.02791015	0.027409484	3.21496E-05
655.00	0.0271861	0.026934889	3.11337E-05
670.00	0.02641928	0.026475352	3.01419E-05
685.00	0.02568881	0.02603051	2.91745E-05
700.00	0.0258536	0.025599992	2.82321E-05
715.00	0.02504722	0.025183413	2.73163E-05
730.00	0.02443014	0.024780363	2.64286E-05
745.00	0.0244867	0.024390406	2.55708E-05
760.00	0.0238412	0.02401308	2.47448E-05
775.00	0.02414598	0.023647894	2.39524E-05
790.00	0.02305864	0.023294331	2.31952E-05
805.00	0.02282978	0.022951854	2.24745E-05
820.00	0.02236788	0.022619908	2.17913E-05
835.00	0.02216465	0.022297925	2.11461E-05
850.00	0.02183048	0.021985334	2.0539E-05
865.00	0.02221744	0.021681565	1.99698E-05
880.00	0.02175331	0.021386056	1.94375E-05
895.00	0.02109138	0.021098261	1.8941E-05
910.00	0.02072169	0.020817655	1.84786E-05
925.00	0.02063407	0.020543741	1.80484E-05
940.00	0.02066778	0.020276055	1.76479E-05
955.00	0.02002772	0.020014169	1.72746E-05
970.00	0.01979551	0.019757696	1.69256E-05
985.00	0.01896587	0.019506293	1.65981E-05
1000.00	0.01899833	0.01925966	1.62891E-05
1015.00	0.01866806	0.019017544	1.59954E-05
1030.00	0.01908692	0.018779735	1.57143E-05

1045.00	0.0183527	0.018546066	1.54429E-05
1060.00	0.01846664	0.018316411	1.51787E-05
1075.00	0.018218	0.018090681	1.49192E-05
1090.00	0.01792269	0.017868821	1.46624E-05
1105.00	0.0176044	0.017650804	1.44065E-05
1120.00	0.01792241	0.017436629	1.415E-05
1135.00	0.01708971	0.017226312	1.38919E-05
1150.00	0.01673395	0.017019883	1.36314E-05
1165.00	0.01672531	0.016817382	1.33682E-05
1180.00	0.0168777	0.016618851	1.31022E-05
1195.00	0.01626466	0.016424328	1.28337E-05
1210.00	0.01648809	0.016233849	1.25633E-05
1225.00	0.01557278	0.016047435	1.22918E-05
1240.00	0.01573743	0.015865094	1.20203E-05
1255.00	0.01577796	0.01568682	1.175E-05
1270.00	0.0158178	0.015512582	1.14822E-05
1285.00	0.01503023	0.015342332	1.12185E-05
1300.00	0.01533835	0.015175999	1.09603E-05
1315.00	0.01524516	0.01501349	1.07089E-05
1330.00	0.01468979	0.01485469	1.04659E-05
1345.00	0.01503803	0.014699466	1.02324E-05
1360.00	0.01459256	0.014547666	1.00095E-05
1375.00	0.01405251	0.014399123	9.7982E-06
1390.00	0.01432484	0.014253659	9.59914E-06
1405.00	0.01461178	0.014111086	9.41276E-06
1420.00	0.0134899	0.013971212	9.23924E-06
1435.00	0.01430826	0.013833844	9.07848E-06
1450.00	0.01347388	0.013698795	8.93011E-06
1465.00	0.01319432	0.013565882	8.7935E-06
1480.00	0.01343056	0.013434936	8.66776E-06
1495.00	0.01332957	0.013305801	8.55176E-06
1510.00	0.01269285	0.013178341	8.44419E-06
1525.00	0.01320825	0.01305244	8.34354E-06
1540.00	0.01323806	0.012928008	8.24821E-06
1555.00	0.0129727	0.012804976	8.15649E-06
1570.00	0.01237373	0.012683304	8.06663E-06
1585.00	0.01266736	0.012562976	7.97692E-06
1600.00	0.01186725	0.012444004	7.88569E-06
1615.00	0.01268784	0.012326421	7.7914E-06
1630.00	0.01256025	0.012210284	7.69268E-06
1645.00	0.01219738	0.012095668	7.58835E-06
1660.00	0.01216841	0.011982666	7.47751E-06

1675.00	0.01172225	0.011871379	7.35953E-06
1690.00	0.0118621	0.011761917	7.23411E-06
1705.00	0.01136858	0.011654393	7.10129E-06
1720.00	0.01180429	0.011548913	6.96146E-06
1735.00	0.01115862	0.01144558	6.81537E-06
1750.00	0.01123828	0.011344478	6.66413E-06
1765.00	0.0112922	0.011245675	6.50916E-06
1780.00	0.01129104	0.011149213	6.35221E-06
1795.00	0.01114874	0.011055109	6.19528E-06
1810.00	0.01097349	0.010963344	6.04061E-06
1825.00	0.01069831	0.010873867	5.89059E-06
1840.00	0.01055875	0.01078659	5.74771E-06
1855.00	0.01069018	0.010701387	5.61447E-06
1870.00	0.01084648	0.010618095	5.49334E-06
1885.00	0.01082615	0.010536515	5.38663E-06
1900.00	0.01046851	0.010456414	5.29642E-06
1915.00	0.0105212	0.010377531	5.22451E-06
1930.00	0.00962674	0.01029958	5.17228E-06
1945.00	0.01042605	0.010222259	5.14065E-06
1960.00	0.01012165	0.010145256	5.13001E-06
1975.00	0.01032707	0.010068255	5.14013E-06
1990.00	0.00959096	0.009990952	5.17014E-06
2005.00	0.01019159	0.009913059	5.21849E-06
2020.00	0.00997349	0.009834317	5.28294E-06
2035.00	0.00955949	0.009754505	5.36054E-06
2050.00	0.0098576	0.009673453	5.44771E-06
2065.00	0.0091403	0.009591047	5.54021E-06
2080.00	0.00997309	0.009507244	5.63331E-06
2095.00	0.00924233	0.009422071	5.72179E-06
2110.00	0.00937007	0.00933564	5.80015E-06
2125.00	0.00895387	0.009248146	5.8627E-06
2140.00	0.00927183	0.009159867	5.90375E-06
2155.00	0.00903517	0.009071168	5.9178E-06
2170.00	0.00876961	0.008982494	5.89974E-06
2185.00	0.00900768	0.008894359	5.84508E-06
2200.00	0.00850539	0.008807343	5.75015E-06
2215.00	0.00880138	0.008722069	5.61235E-06
2230.00	0.00933835	0.008639193	5.43036E-06
2245.00	0.00887422	0.008559379	5.20433E-06
2260.00	0.00850476	0.008483275	4.93609E-06
2275.00	0.00852669	0.008411489	4.62927E-06
2290.00	0.00775657	0.008344562	4.28939E-06

2305.00	0.00862332	0.008282936	3.92394E-06
2320.00	0.00853335	0.008226925	3.54233E-06
2335.00	0.00760453	0.008176691	3.15578E-06
2350.00	0.00792464	0.008132212	2.77715E-06
2365.00	0.00792967	0.008093266	2.42063E-06
2380.00	0.0081581	0.008059408	2.10131E-06
2395.00	0.00777278	0.008029964	1.83469E-06
2410.00	0.007665	0.008004027	1.636E-06
2425.00	0.00813034	0.007980472	1.51943E-06
2440.00	0.00829171	0.007957972	1.49721E-06
2455.00	0.00831684	0.007935038	1.57859E-06
2470.00	0.00754524	0.00791007	1.76872E-06
2485.00	0.00823039	0.007881432	2.06736E-06
2500.00	0.00811511	0.007847539	2.4677E-06
2515.00	0.00784393	0.007806965	2.95494E-06
2530.00	0.00723194	0.007758575	3.50507E-06

*A representative dataset for the reaction catalyzed by HCl in the absence of **9** is provided below:*

Time (s)	**[1b] (M)**
0.00	0.10011083
90.00	0.0988022
150.00	0.09798301
210.00	0.09748475
270.00	0.09683466
330.00	0.09624613
390.00	0.09601783
450.00	0.09555189
510.00	0.09476668
570.00	0.09442583
630.00	0.09375233
690.00	0.09350717
750.00	0.09278131
810.00	0.09264508
870.00	0.09234726
930.00	0.09185667
990.00	0.09135172
1050.00	0.09128695
1110.00	0.09052988
1170.00	0.09044602
1230.00	0.08998217
1290.00	0.08981293

1350.00	0.0894867
1410.00	0.08929545
1470.00	0.08853475
1530.00	0.0885133
1590.00	0.08825045
1650.00	0.08732191
1710.00	0.08758824
1770.00	0.08750662
1830.00	0.08697618
1890.00	0.08646371
1950.00	0.08650634
2010.00	0.08599359
2070.00	0.08567586
2130.00	0.08547012
2190.00	0.08529433
2250.00	0.0849915
2310.00	0.08471249
2370.00	0.0844268
2430.00	0.08416548
2490.00	0.08403733
2550.00	0.08380666
2610.00	0.08321201
2670.00	0.08351149
2730.00	0.08326187
2790.00	0.08279802
2850.00	0.08272238
2910.00	0.08250146
2970.00	0.08208511
3030.00	0.08229071
3090.00	0.08181919
3150.00	0.08158783
3210.00	0.0813194
3270.00	0.08095556
3330.00	0.08093996

trial	initial rate (M/s)	rate at [1b] = 0.09 M (M/s)	2b : 3b	d.r. (2b)	d.r. (3b)	ee (2b)	ee (3b)
2 mol% 9-Run 1	9.36 E-04	8.13 E-04	3.1 : 1	28 : 1	> 50 : 1	96%	98%
2 mol% 9-Run 2	9.80 E-04	8.38 E-04	3.1 : 1	29 : 1	> 50 : 1	96%	98%
2 mol% 9-Run 3	9.87 E-04	8.33 E-04	3.1 : 1	28 : 1	> 50 : 1	96%	98%
Average k_{obs} :	9.67 E-04	8.28 E-04					
Stdev.:	2.76 E-05	1.30 E-05					

k_{rel} :	9 vs background	9 vs 6b
	93 ± 5	2.01 ± 0.03

trial	initial rate (M/s)	2b : 3b	d.r. (2b)	d.r. (3b)	ee (2b)	ee (3b)
0 mol% HBD-Run 1	1.05 E-05	3.3 : 1	4.1 : 1	8.3 : 1	—	—
0 mol% HBD-Run 2	9.92 E-06	3.2 : 1	4.1 : 1	9.1 : 1	—	—
0 mol% HBD-Run 3	1.08 E-05	3.2 : 1	4.1 : 1	9.6 : 1	—	—
Average k_{obs} :	1.04 E-05					
Stdev.:	4.28 E-07					

trial	rate at [1b] = 0.09 M (M/s)	2b : 3b	d.r. (2b)	d.r. (3b)	ee (2b)	ee (3b)
2 mol% 6b-Run 1	4.14 E-04	3.7 : 1	34 : 1	> 50 : 1	96%	96%
2 mol% 6b-Run 2	4.10 E-04	3.7 : 1	30 : 1	> 50 : 1	96%	96%
Average k_{obs} :	4.12 E-04					
Stdev.:	2.93 E-06					

Figure S12. Results of kinetics experiments measuring rates of cyclization of **1b**.

7. X-Ray Crystallographic Information

Crystals suitable for X-ray crystallographic analysis were obtained from a nearly saturated solution of enantioenriched **2c** in 50% DCM, 50% hexanes (v/v) which was allowed to slowly evaporate at ambient temperature over a two day period. A crystal mounted on a diffractometer was collected data at 100 K. The intensities of the reflections were collected by means of a Bruker APEX II CCD diffractometer ($Mo_{K\alpha}$ radiation, λ=0.71073 Å), and equipped with an Oxford Cryosystems nitrogen flow apparatus. The collection method involved 0.5° scans in ω at 28° in 2θ. Data integration down to 0.78 Å resolution was carried out using SAINT V8.37A (Bruker diffractometer, 2016) with reflection spot size optimization. Absorption corrections were made with the program SADABS (Bruker diffractometer, 2016). The structure was solved by the Intrinsic Phasing methods and refined by least-squares methods again F^2 using SHELXT-2014 (Sheldrick, 2015) and SHELXL-2014 (Sheldrick, 2015) with OLEX 2 interface (Dolomanov, et al., 2009). Non-hydrogen atoms were refined anisotropically, and hydrogen atoms were allowed to ride on the respective atoms. Crystal data as well as details of data collection and refinement are summarized in Table 1, geometric parameters are shown in Table 2, and hydrogen-bond parameters are listed in Table 3. The Ortep plots produced with SHELXL-2014 program, and the three-dimensional supramolecular architecture drawing was produced with Accelrys DS Visualizer 2.0 (Accelrys, 2007).

Table 1. Experimental details

	DAK-5-III
Crystal data	
Chemical formula	$C_{12}H_{13}BrO_2$
M_r	269.13
Crystal system, space group	Trigonal, $P3_1$
Temperature (K)	100
a, c (Å)	12.0964 (6), 6.6179 (3)
V (Å^3)	838.62 (9)
Z	3
Radiation type	Mo $K\alpha$
μ (mm^{-1})	3.65
Crystal size (mm)	0.08 × 0.01 × 0.01
Data collection	

Diffractometer	Bruker D8 goniometer with CCD area detector
Absorption correction	Multi-scan *SADABS*
T_{min}, T_{max}	0.526, 0.694
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	19872, 2472, 2327
R_{int}	0.031
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.640
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.028, 0.068, 1.05
No. of reflections	2472
No. of parameters	141
No. of restraints	1
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	1.03, -0.49
Absolute structure	Flack x determined using 1102 quotients [(I+)-(I-)]/[(I+)+(I-)] (Parsons, Flack and Wagner, Acta Cryst. B69 (2013) 249-259).
Absolute structure parameter	-0.012 (3)

Computer programs: *SAINT* 8.37A (Bruker-AXS, 2015), *SHELXT2014* (Sheldrick, 2015), *SHELXL2014* (Sheldrick, 2015), Bruker *SHELXTL* (Sheldrick, 2015).

Table 2. Geometric parameters (Å, º)

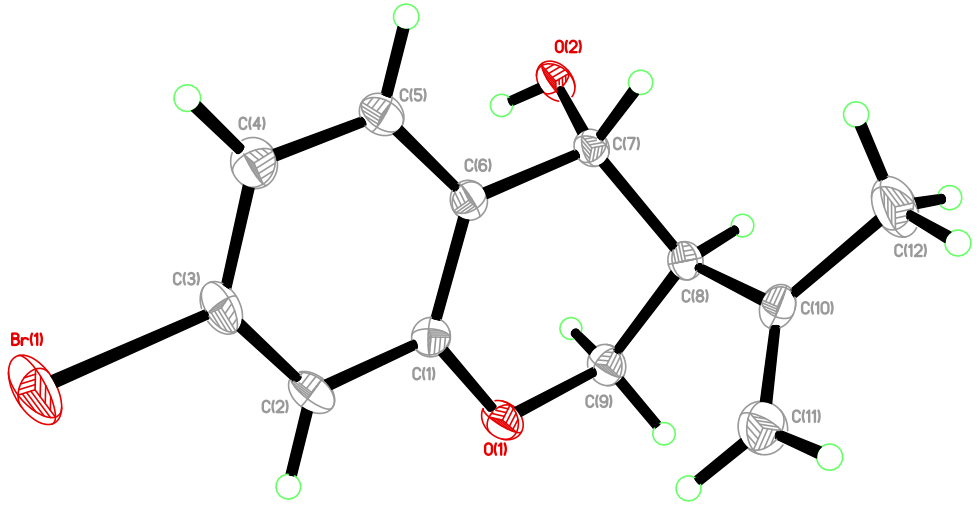
Br1—C3	1.899 (4)	C7—C8	1.539 (6)
O1—C1	1.361 (5)	C7—H7	1.0000
O1—C9	1.444 (5)	C8—C10	1.518 (6)
O2—C7	1.438 (5)	C8—C9	1.523 (6)
O2—H2	0.69 (6)	C8—H8	1.0000
C1—C2	1.390 (6)	C9—H9A	0.9900
C1—C6	1.411 (6)	C9—H9B	0.9900
C2—C3	1.374 (6)	C10—C11	1.331 (7)
C2—H2A	0.9500	C10—C12	1.506 (6)
C3—C4	1.389 (6)	C11—H11A	0.9500
C4—C5	1.386 (6)	C11—H11B	0.9500
C4—H4	0.9500	C12—H12A	0.9800
C5—C6	1.394 (6)	C12—H12B	0.9800
C5—H5	0.9500	C12—H12C	0.9800
C6—C7	1.502 (6)		
C1—O1—C9	117.6 (3)	C8—C7—H7	108.1

C7—O2—H2	112 (5)	C10—C8—C9	115.6 (4)
O1—C1—C2	116.2 (4)	C10—C8—C7	111.8 (3)
O1—C1—C6	123.3 (3)	C9—C8—C7	108.5 (3)
C2—C1—C6	120.5 (4)	C10—C8—H8	106.8
C3—C2—C1	119.5 (4)	C9—C8—H8	106.8
C3—C2—H2A	120.2	C7—C8—H8	106.8
C1—C2—H2A	120.2	O1—C9—C8	113.6 (3)
C2—C3—C4	122.1 (4)	O1—C9—H9A	108.8
C2—C3—Br1	118.3 (3)	C8—C9—H9A	108.8
C4—C3—Br1	119.6 (3)	O1—C9—H9B	108.8
C5—C4—C3	117.6 (4)	C8—C9—H9B	108.8
C5—C4—H4	121.2	H9A—C9—H9B	107.7
C3—C4—H4	121.2	C11—C10—C12	120.9 (4)
C4—C5—C6	122.7 (4)	C11—C10—C8	124.1 (4)
C4—C5—H5	118.6	C12—C10—C8	115.0 (4)
C6—C5—H5	118.6	C10—C11—H11A	120.0
C5—C6—C1	117.6 (4)	C10—C11—H11B	120.0
C5—C6—C7	122.0 (4)	H11A—C11—H11B	120.0
C1—C6—C7	120.4 (4)	C10—C12—H12A	109.5
O2—C7—C6	111.2 (3)	C10—C12—H12B	109.5
O2—C7—C8	110.8 (3)	H12A—C12—H12B	109.5
C6—C7—C8	110.5 (3)	C10—C12—H12C	109.5
O2—C7—H7	108.1	H12A—C12—H12C	109.5
C6—C7—H7	108.1	H12B—C12—H12C	109.5
C9—O1—C1—C2	174.0 (4)	C5—C6—C7—O2	-78.7 (5)
C9—O1—C1—C6	-7.0 (6)	C1—C6—C7—O2	100.8 (4)
O1—C1—C2—C3	-178.9 (4)	C5—C6—C7—C8	157.8 (4)
C6—C1—C2—C3	2.2 (6)	C1—C6—C7—C8	-22.7 (5)
C1—C2—C3—C4	-1.8 (7)	O2—C7—C8—C10	156.6 (3)
C1—C2—C3—Br1	177.6 (3)	C6—C7—C8—C10	-79.6 (4)
C2—C3—C4—C5	0.6 (7)	O2—C7—C8—C9	-74.8 (4)
Br1—C3—C4—C5	-178.8 (3)	C6—C7—C8—C9	49.0 (4)
C3—C4—C5—C6	0.2 (7)	C1—O1—C9—C8	36.9 (5)
C4—C5—C6—C1	0.2 (6)	C10—C8—C9—O1	68.5 (5)
C4—C5—C6—C7	179.7 (4)	C7—C8—C9—O1	-58.0 (4)
O1—C1—C6—C5	179.8 (4)	C9—C8—C10—C11	-19.3 (6)
C2—C1—C6—C5	-1.4 (6)	C7—C8—C10—C11	105.4 (5)
O1—C1—C6—C7	0.2 (6)	C9—C8—C10—C12	162.1 (4)
C2—C1—C6—C7	179.1 (4)	C7—C8—C10—C12	-73.1 (5)

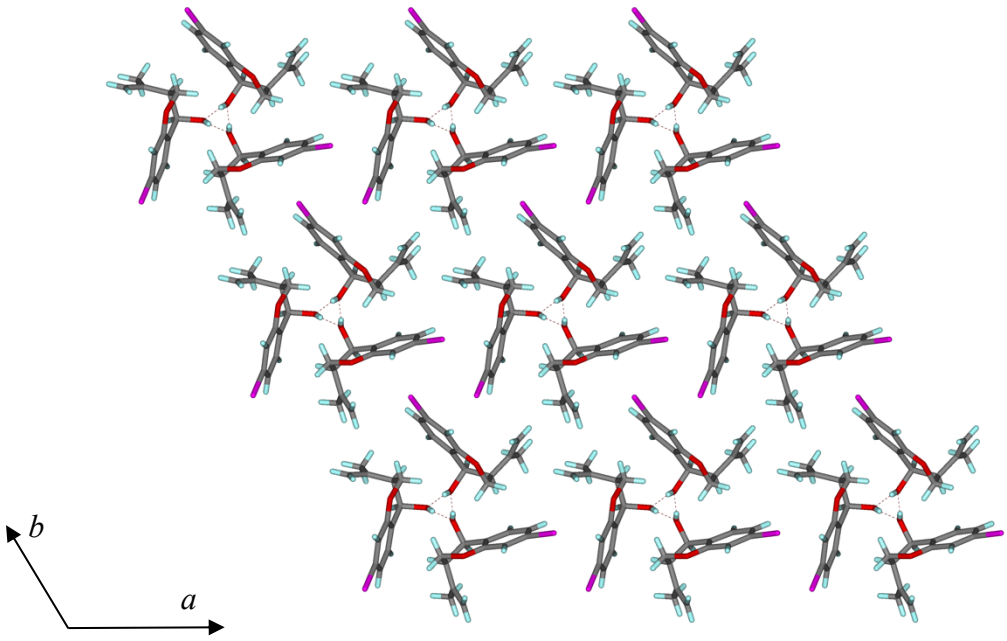
Table 3. Hydrogen-bond parameters

D—H···*A*	*D*—H (Å)	H···*A* (Å)	*D*···*A* (Å)	*D*—H···*A* (°)
O2—H2···O2^{i}	0.69 (6)	2.01 (6)	2.689 (3)	169 (6)

Symmetry code(s): (i) -*y*+1, *x*-*y*, *z*+1/3.



Perspective views showing 50% probability displacement



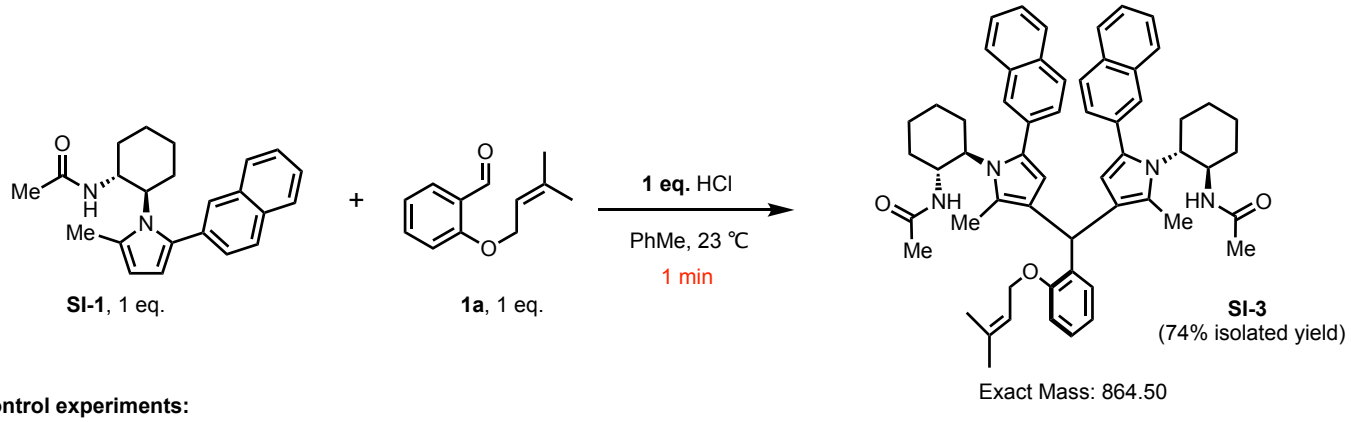
Three-dimensional supramolecular architecture viewed along the *c*-axis direction.

Crystallographic References:

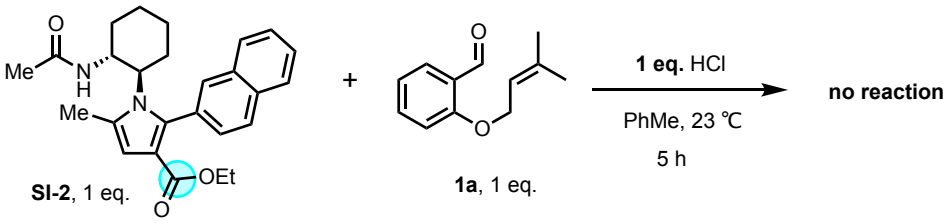
[1] Bruker AXS APEX3, Bruker AXS, Madison, Wisconsin, 2016.
[2] O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann J. Appl. Cryst. 2009, 42, 339-341
[3] G. M. Sheldrick, *Acta Cryst*. 2015. A**71**, 3-8.
[4] G. M. Sheldrick, *Acta Cryst*. 2015, C**71**, 3-8.
[5] Accelrys DS Visualizer v2.0.1, Accelrys Software. Inc., 2007.

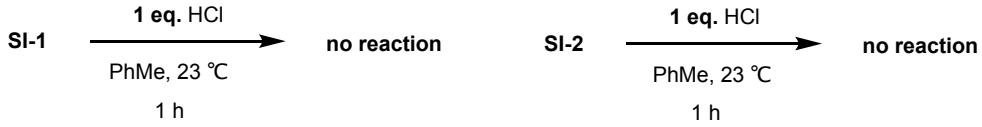
8. Additional Reaction Optimization Data

8.1 Pyrrole degradation studies



Control experiments:





Pyrrole-bearing catalysts such as **5** were found to be unstable under the reaction conditions used in the HCl-promoted Prins reaction of **1a**. To more directly probe the origin of this instability, we synthesized simplified acetylated analogs **SI-1** and **SI-2**, and subjected them to treatment with combinations of HCl and **1a**. Reaction conditions: 0.015 mmol **SI-1** and 0.015 mmol **1a** were weighed into a flame dried 1-dram vial charged with a magnetic stir bar. 1.5 mL of anhydrous toluene were added, followed by 0.015 mmol of HCl (2.17 M in Et_2O). Upon addition of HCl, an immediate color change from faint yellow to dark orange was noted. TLC analysis (80% EtOAc/Hexanes, v/v) indicated full consumption of **SI-1** after 1 minute, and after this period 0.03 mmol triethylamine were added. The crude reaction was loaded directly onto a silica gel column eluting with 90% EtOAc/10% Hexanes (v/v) to purify dimeric adduct **SI-3** (0.048 g, light red solid, 74% yield) which was characterized by a combination of NMR spectroscopy and HR-MS (data shown below). Control experiments conducted using the same conditions established that ester derivative **SI-2** does not undergo the analogous addition reaction or engage in any other promiscuous behavior. Finally, **SI-1** and **SI-2** were each found to be stable to HCl alone.

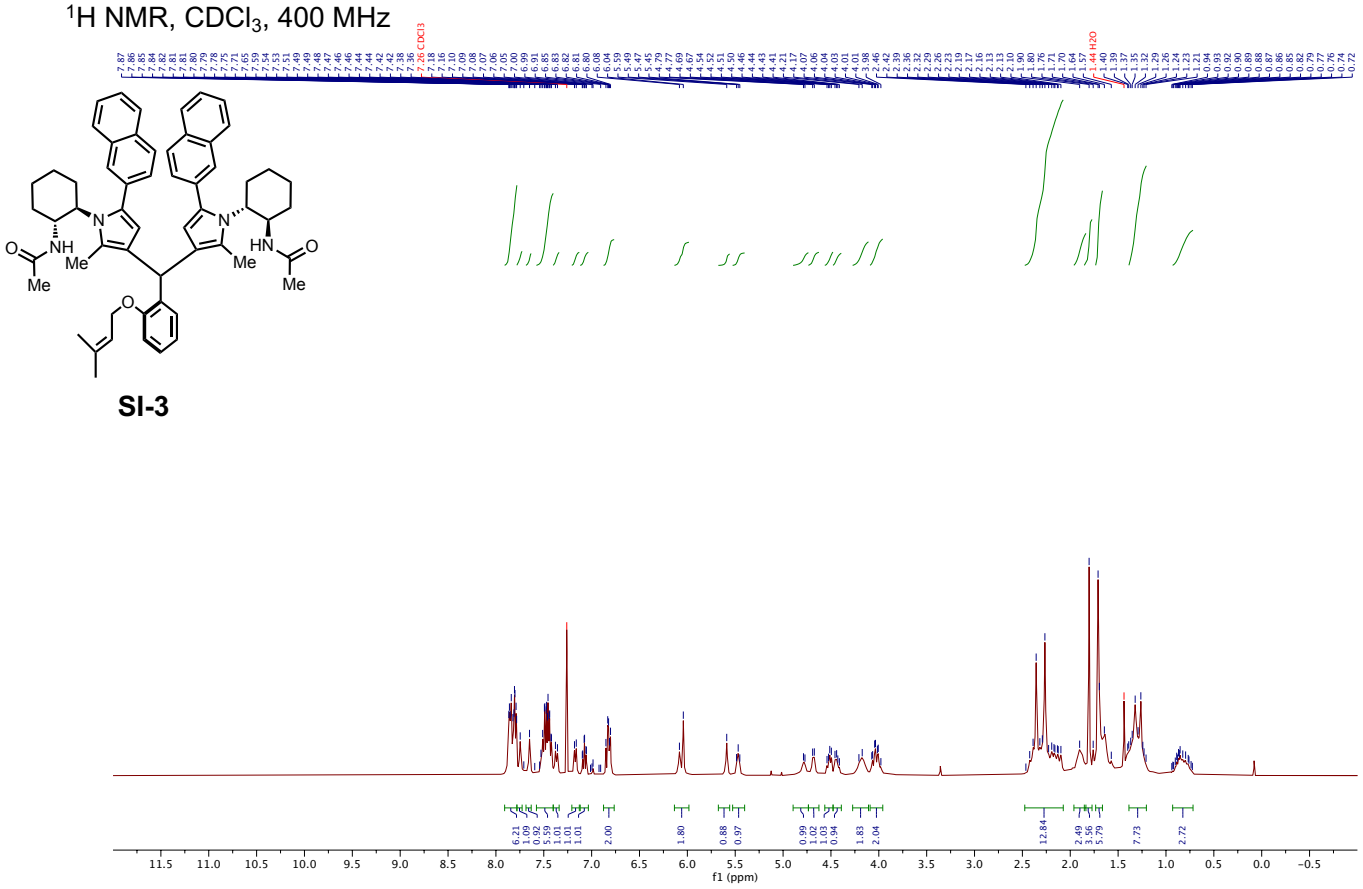
Characterization data for **SI-3**:

^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.83 (m, 6H), 7.76 (s, 1H), 7.66 (s, 1H), 7.48 (m, 6H), 7.38 (d, J = 8.5 Hz, 1H), 7.18 (d, J = 7.5 Hz, 1H), 7.09 (td, J = 7.7, 1.7 Hz, 1H), 6.83 (m, 2H), 6.07 (m, 2H), 5.60 (s, 1H), 5.49 (m, 1H), 4.79 (m, 1H), 4.69 (m, 1H), 4.53 (m, 1H), 4.44 (m, 1H), 4.20 (m, 2H), 4.04 (m, 2H), 2.34 (m, 13H), 1.91 (bs, 2H), 1.81 (s, 4H), 1.71 (m, 6H), 1.29 (m, 8H), 0.84 (m, 3H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 169.39, 169.07, 155.84, 136.84, 135.53, 133.93, 133.57, 132.03, 131.90, 129.04, 128.05, 127.76, 127.69, 127.63, 127.32, 126.95, 126.65, 126.42, 126.37, 126.28, 125.74, 125.66, 120.73, 120.24, 112.12, 111.24, 110.82, 65.35, 60.06, 59.98, 52.01, 33.59, 32.59, 25.95, 25.79, 24.61, 23.19, 22.90, 18.17, 12.24.

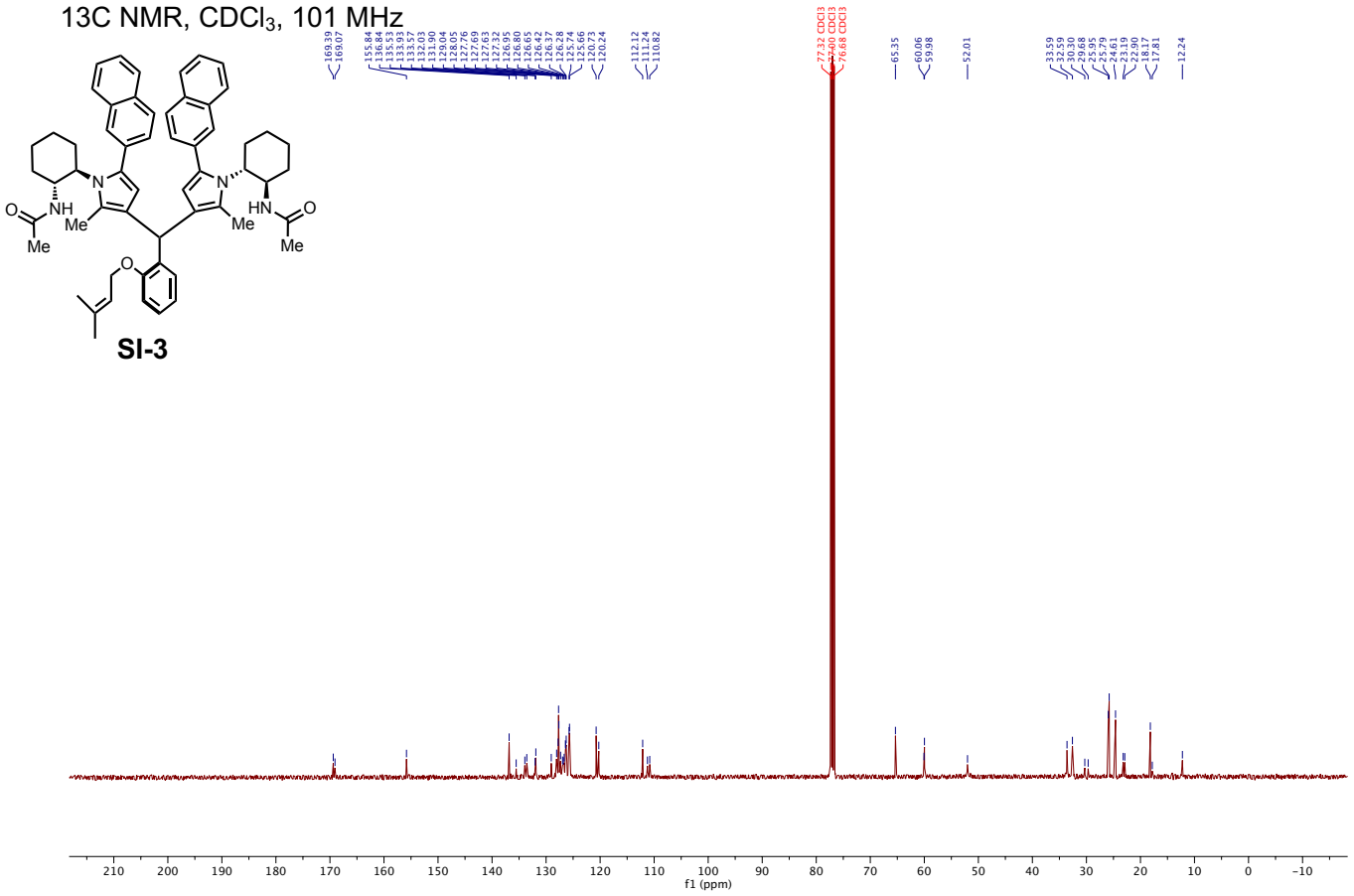
HR-MS: (ESI) calcd. for $C_{58}H_{64}N_4O_3$ 865.5051 [M + H^+], found 865.5046

^{1}H NMR, $CDCl_3$, 400 MHz



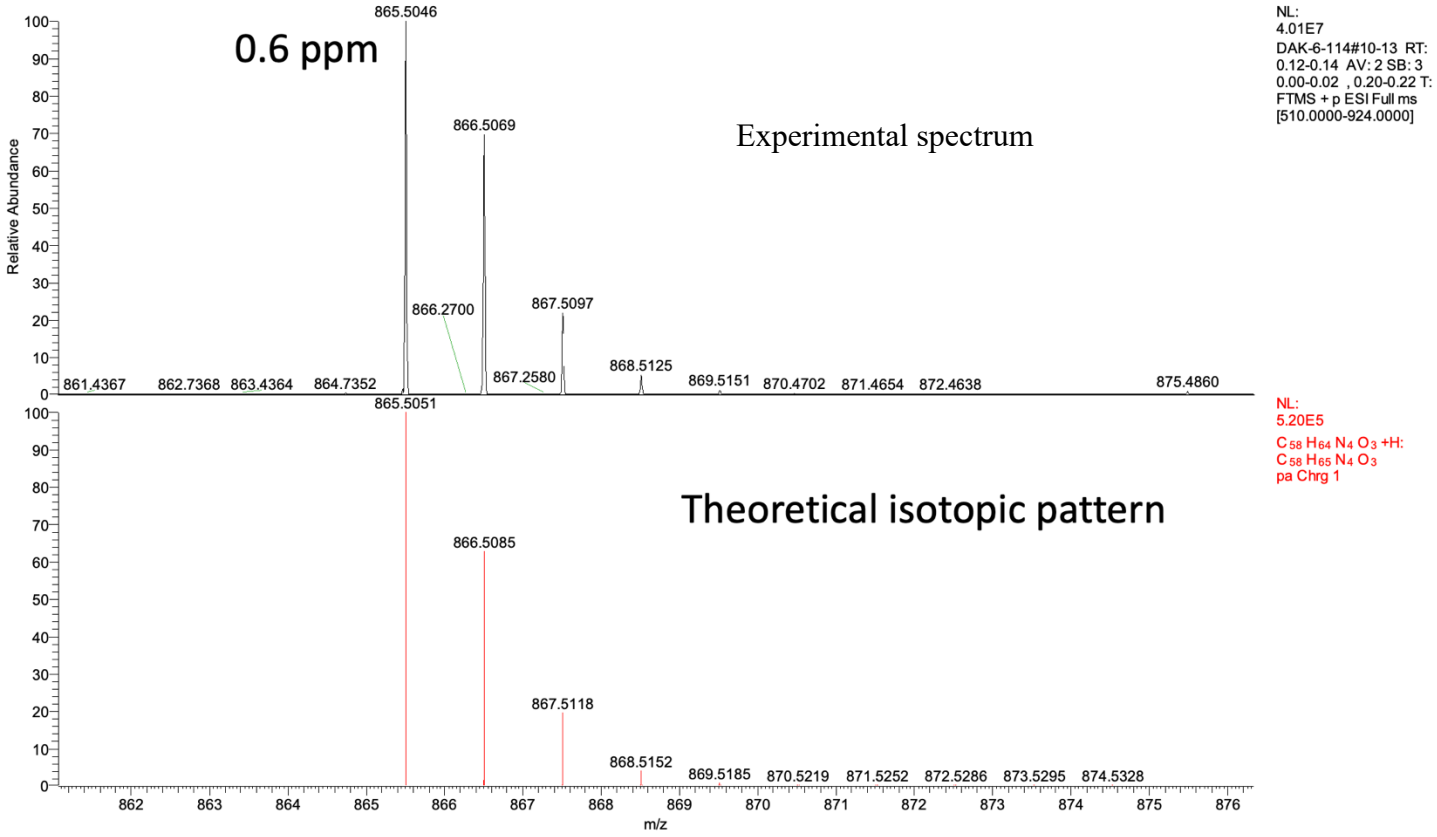
SI-3

13C NMR, $CDCl_3$, 101 MHz

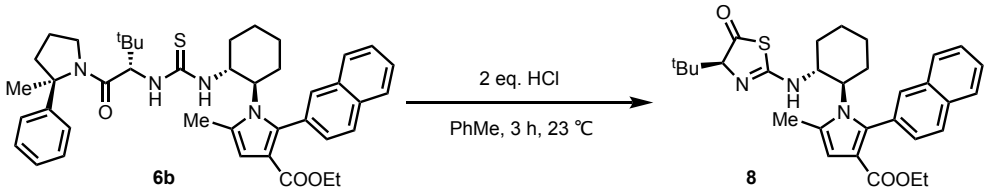


SI-3

SI-3 HR-MS data:



8.2 Edman degradation studies



Hydrogen-bond donor catalysts **6**-**11** were observed to undergo Edman degradation in the presence of HCl to cleanly afford heterocycle **8** and the corresponding aryl pyrrolidine. For the purposes of isolation and characterization of the Edman product **8**, we subjected **6b** (0.050 mmol, 0.035 g) to treatment with HCl (0.010 mmol of a 2.17 M solution in Et_2O, 2.0 eq.) in toluene (1.7 mL). After 3 hours at 23 °C, the reaction was observed to have proceeded to approximately 50% conversion as judged by TLC analysis (35% Et_2O/Hexanes, v/v). The solvent was vaporized *in vacuo* and the resulting residue was purified by silica gel chromatography (35% Et_2O in hexanes) to afford heterocycle **8** as a white solid in 32% yield (0.0086 g).

On the basis of the diagnostic carbon resonance at 207 ppm in the ^{13}C NMR corresponding to the carbon of the thioester, the structure of **8** is assigned as pictured and not as the corresponding thiohydantoin (which is the final product in certain Edman degradation protocols). It is not possible at this time to definitively assign the position of the unsaturation in the iosthiourea motif, but our tentative prediction is pictured.

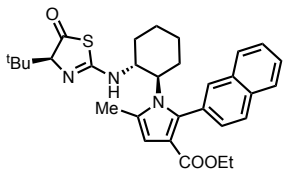
Characterization data for **8**:

^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.89 (m, 4H), 7.56 (m, 3H), 6.41 (s, 1H), 4.29 (s, 1H), 4.03 (s, 3H), 3.75 (s, 1H), 2.50 (s, 3H), 2.17 (m, 2H), 1.83 (m, 1H), 1.70 (m, 1H), 1.35 (m, 2H), 0.99 (m, 12H), 0.87 (m, 2H).

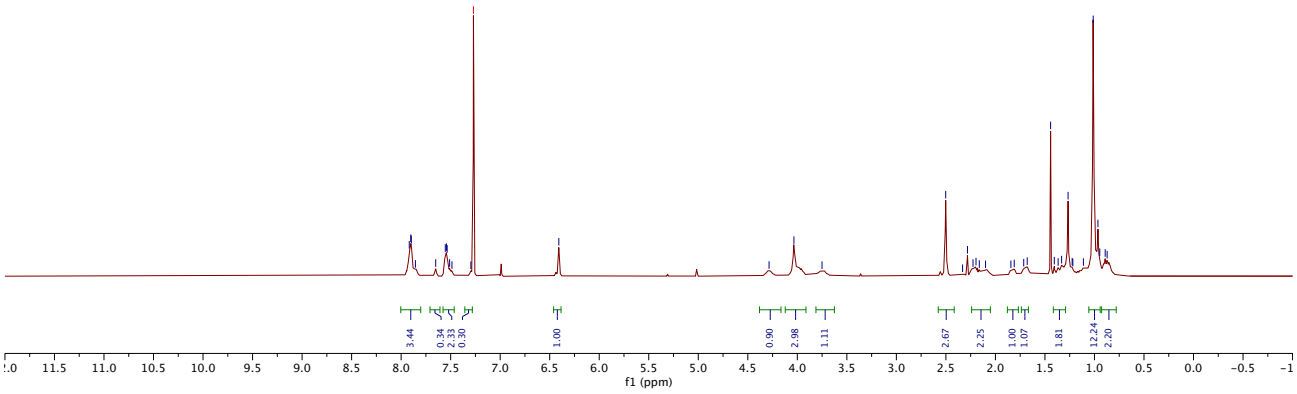
^{13}C NMR: (101 MHz, $CDCl_3$) δ 207.01, 164.56, 152.23, 139.44, 139.14, 132.99, 131.00, 130.79, 130.44, 129.24, 129.11, 128.32, 128.17, 127.90, 127.80, 127.71, 127.39, 126.53, 126.40, 126.28, 125.49, 112.95, 111.09, 89.33, 88.70, 61.08, 60.90, 59.05, 53.91, 52.79, 37.14, 37.02, 34.04, 33.63, 33.52, 31.90, 31.68, 30.89, 30.29, 29.67, 26.65, 26.48, 25.40, 24.72, 24.64, 22.66, 15.24, 14.09, 14.03.

HR-MS: (ESI) calcd. for $C_{31}H_{37}N_3O_3S$ 532.2628 [$M + H^+$], found 532.2618

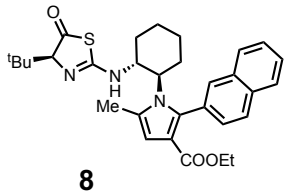
^{1}H NMR, $CDCl_3$, 400 MHz



8



13C NMR, $CDCl_3$, 101 MHz



8

8 HR-MS data:

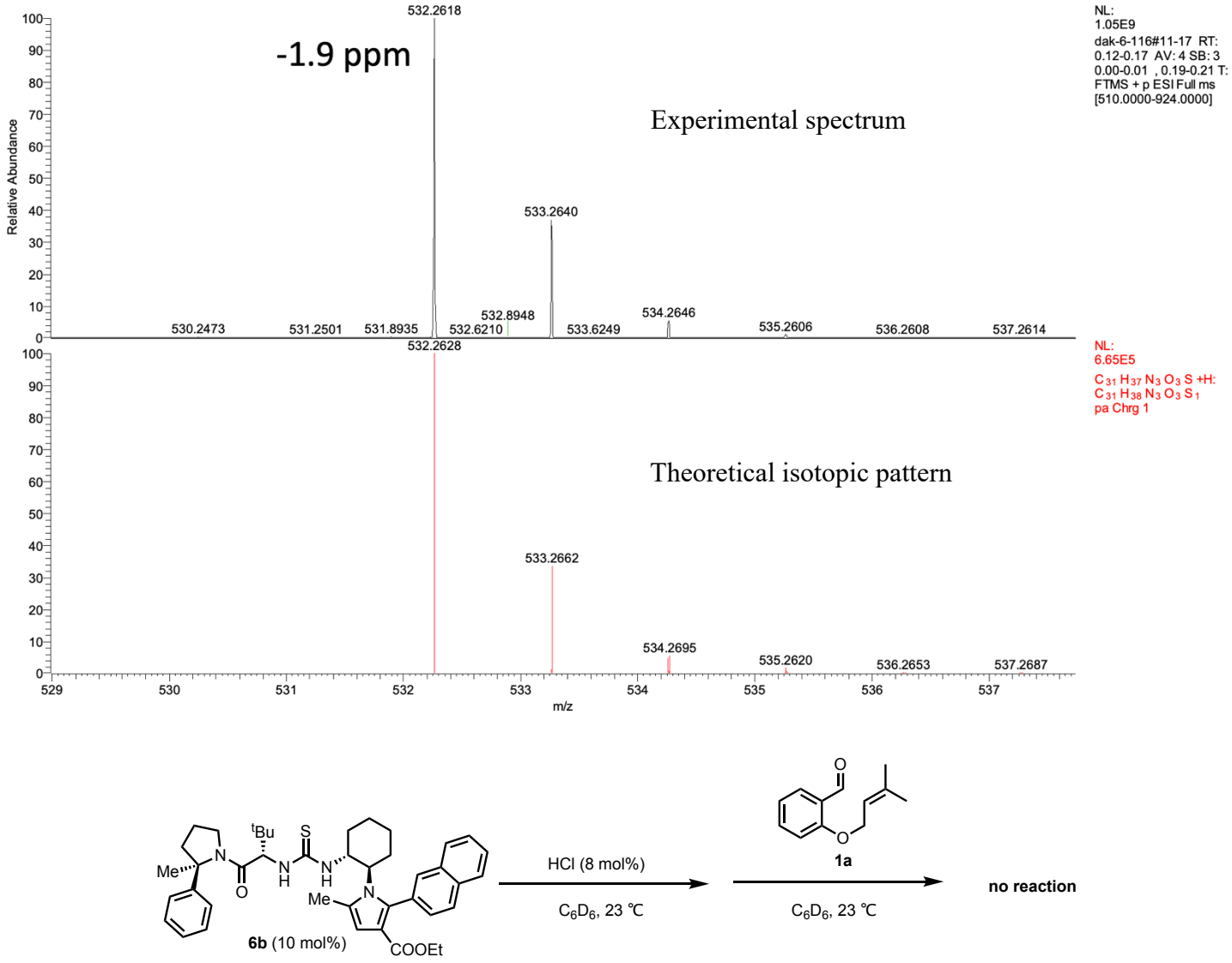
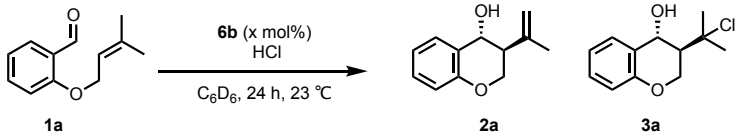


Figure S13. Assessing potential catalytic activity of Edman decomposition products

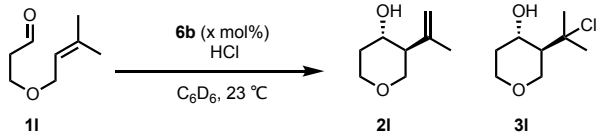
The possibility that the products of Edman degradation (heterocycle **8** or the aryl pyrrolidine) could be catalytically active in the Prins reaction was tested by first incubating HBD catalyst **6b** (0.006 mmol, 10 mol%) with HCl (0.0048 mol, 8 mol%) in 300 µL of C_6D_6 for 15 hours at 23 °C. Incubation was carried out in a vial sealed with electrical tape to prevent any volume changes. After this time, **6b** was observed to have degraded to the corresponding Edman product as judged by TLC analysis (35% Et_2O/Hexanes, v/v). Then, a 300 µL stock solution of substrate **1a** (0.06 mmol) in C_6D_6 was added, along with mesitylene internal standard (6 µL). After 1 hour, no reaction of **1a** was observed to have taken place by ^1H NMR analysis of the crude reaction mixture. Only unreacted starting material **1a** was observed. By comparison, the analogous experiment in which HCl is added last proceeds to 33% conversion in 1 hour. This result indicates that the Edman decomposition products are not catalytically active in the Prins reaction.

8.3 Optimization of HCl slow release methods



entry	"HCl" (mol%)	6b (mol%)	conversion (%)	2a : 3a	ee 2a (%)	ee 3a (%)
1	HCl (15)	10	65	3.1 : 1	97	98
2	HCl (20)	10	80	3.0 : 1	97	98
3	HCl (30)	10	96	3.1 : 1	96	98
4	HCl (30)	5	88	3.1 : 1	92	94
5*	AcCl + EtOH (30)	10	95	3.0 : 1	97	98
6	AcCl + EtOH (30)	5	93	3.0 : 1	95	97

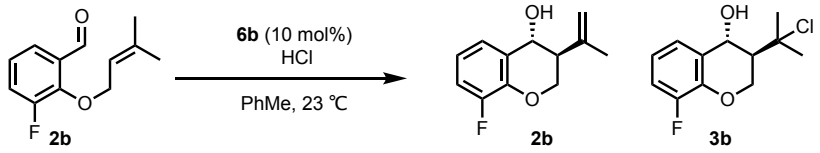
*4h reaction time



entry	"HCl" (mol%)	6b (mol%)	time (hr.)	conversion (%)	ee 2l (%)
1	HCl (30)	10	1	>95	89
2	HCl (30)	5	1	>95	85
3	AcCl + EtOH (30)	10	1	>95	91
4	AcCl + EtOH (30)	5	4	>95	89

Figure S14. Comparison of HCl and AcCl-based HCl slow-release methods.

While the use of 30 mol% HCl loadings with substrates **1a** and **1l** were found to result in highly enantioenriched products, we found that 1:1 combinations of AcCl and EtOH produced cyclized products in higher ee.

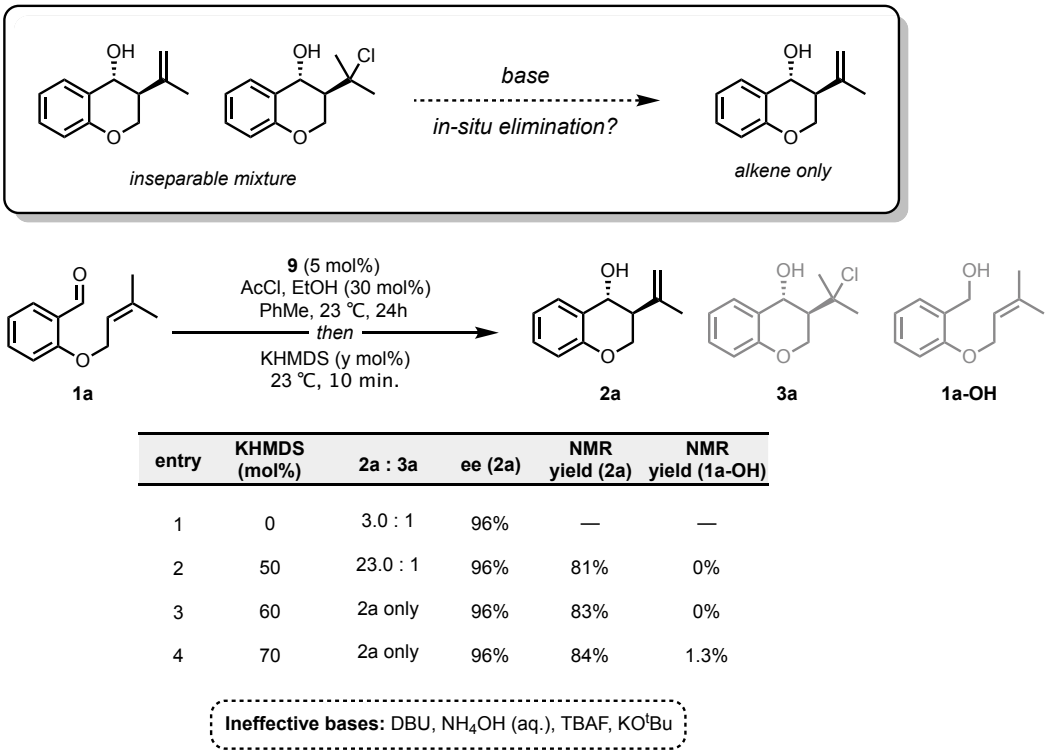


entry	"HCl" (mol%)	6b (mol%)	time (hr.)	conversion (%)	2a : 3a	ee 2a (%)	ee 3a (%)
1	4-$MeOC_6H_4C(O)Cl$ + MeOH (30)	10	22	25	3.8 : 1	98	99
2	$C_6H_5C(O)Cl$ + MeOH (30)	10	22	42	3.7 : 1	98	99
3	4-Cl-$C_6H_4C(O)Cl$ + MeOH (30)	10	22	63	3.7 : 1	98	99

Figure S15. Comparison of HCl slow-release methods

Although the use of various benzoyl chloride derivatives lead to the formation of highly enantioenriched products, these reactions were found to be inconveniently slow compared to the reaction performed with AcCl and EtOH.

8.4 Optimization of KHMDS quench



entry	KHMDS (mol%)	2a : 3a	ee (2a)	NMR yield (2a)	NMR yield (1a-OH)
1	0	3.0 : 1	96%	—	—
2	50	23.0 : 1	96%	81%	0%
3	60	2a only	96%	83%	0%
4	70	2a only	96%	84%	1.3%

Ineffective bases: DBU, NH_4OH (aq.), TBAF, KO^tBu

Figure S16. Screen of KHMDS loadings.

A series of bases were surveyed for a quench to promote elimination of **3a** to the corresponding alkene product, **2a**, with KHMDS (as a 1 M solution in THF) proving optimal. Importantly, compounds **2** and **3** were found to be inseparable by conventional column chromatography, which necessitated the development of conditions that would work for mixtures of the two compounds. In control experiments, subjecting purified mixtures of **2a** and **3a** to treatment with KHMDS resulted in full conversion of **3a** within 10 minutes as observed by ^{1}H NMR. The appropriate amount of KHMDS to use as a quench at the end of the reaction involving HBD catalyst, AcCl, and EtOH was determined empirically as there are a number of acidic species in solution that could undergo deprotonation in the presence of strong base. Note: all reactions in the above figure were taken to >95% conversion of **1a** before addition of KHMDS. Reactions were carried out using 0.05 mmol of **1a** according to general procedure B (section 4.1) with reactions quenched by the addition of KHMDS (1 M solution in THF) and subsequently passed through a short plug of SiO_2 eluting with Et_2O prior to analysis.

For a 5 mol% loading of catalyst **9**, the optimal quench was determined to be 60 mol% KHMDS which resulted in full conversion of **3a** to form a mixture of **2a** and **1a**. Using the lowest loadings of KHMDS possible is desirable, as excess KHMDS leads to the formation of small amounts of Cannizzaro product (**1a-OH**) derived from reduction of the reformed **1a** starting material (see below). **1a-OH** was found to be separable from **2a** using 10% silver nitrate on silica gel eluting with 50% (Et_2O/Hexanes) (v/v). The Cannizzaro reaction was found to be relevant only for aromatic substrates **1a**-**1j**.

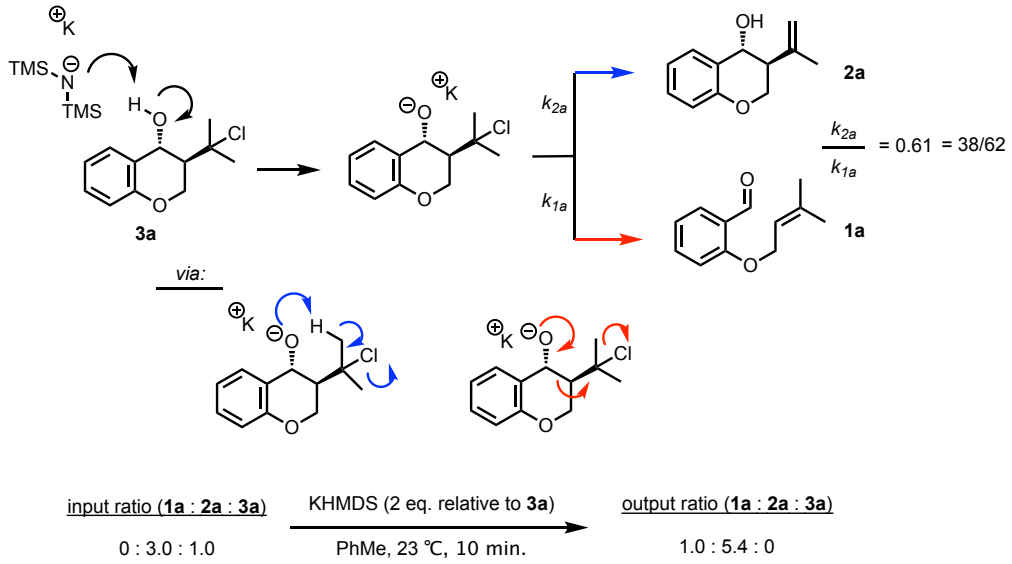


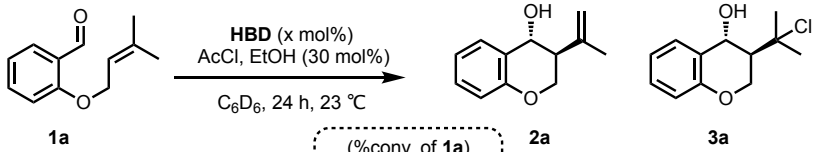
Figure S17. Partitioning of **3a** upon exposure to KHMDS.

It was found that KHMDS promotes elimination of **3a** to form **2a**, but also induces substantial intramolecular elimination of **3a** to reform starting material **1a**. To determine the partitioning ratio of **3a**, a 3.0 : 1.0 mixture of **2a** and **3a** (0.05 mmol total) was treated with KHMDS (2.0 eq. with respect to **3a**, 25 μL of a 1 M solution in THF) for 10 min at 23 °C in PhMe (500 μL). After this time, the reaction was passed through a short pad of silica gel eluting with Et_2O and concentrated under reduced pressure. The resulting residue was analyzed by ^1H NMR. No residual **3a** was observed, and the ratio **2a** : **1a** was observed to be 5.40 : 1. These data indicate that 38% of **3a** undergoes elimination to form **2a** while the remaining 62% reverts to starting material **1a**.

This ratio of products was found to be invariant with changes to the loading of base, as well as the identity of the solvent and temperature of the reaction. Hence, although full consumption of **3a** is observed, upon exposure to KHMDS, the yield of **2a** in catalytic reactions is lowered due to reformation of the starting material. Importantly, this accounts for the moderate-to-good yields of the Prins reaction (Figure 2 in the main text) even though most reactions provide near quantitative yields of the combination of homoallylic alcohol **2** and the corresponding tertiary chloride **3** products prior to KHMDS treatment.

8.5 Optimization of arylpyrrolidine structure

Variable HBD loading experiments:



Ar	HBD	x =	1%	2%	5%	10%
Ph	**6b**		(56) 63/65	(68) 82/84	(93) 95/97	(95) 97/98
2-Nap	**9**		(65) 80/85	(83) 92/95	(98) 96/98	(96) 96/98
1-Nap	**10**		(79) 78/80	(93) 86/89	(100) 93/95	(100) 94/97
9-Phen	**11**		(84) 82/88	(96) 89/95	(100) 91/96	(100) 92/97

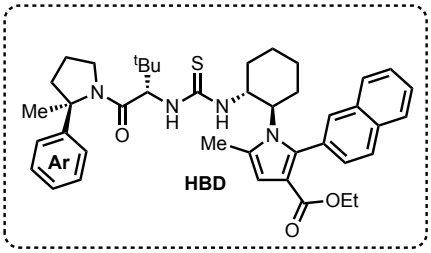


Figure S18. Variable HBD loading experiments. All experiments were conducted according to general procedure B (section 4.1) for 24 h except the 10 mol% experiment with **6b** which was carried out for 4 h. Although catalysts **10** and **11** provide higher conversions at low loadings compared to **9**, the 2-naphthyl substituted catalyst is the only HBD that results in highly enantioselective outcomes with loadings < 5 mol%.

8.6 Additional substrates

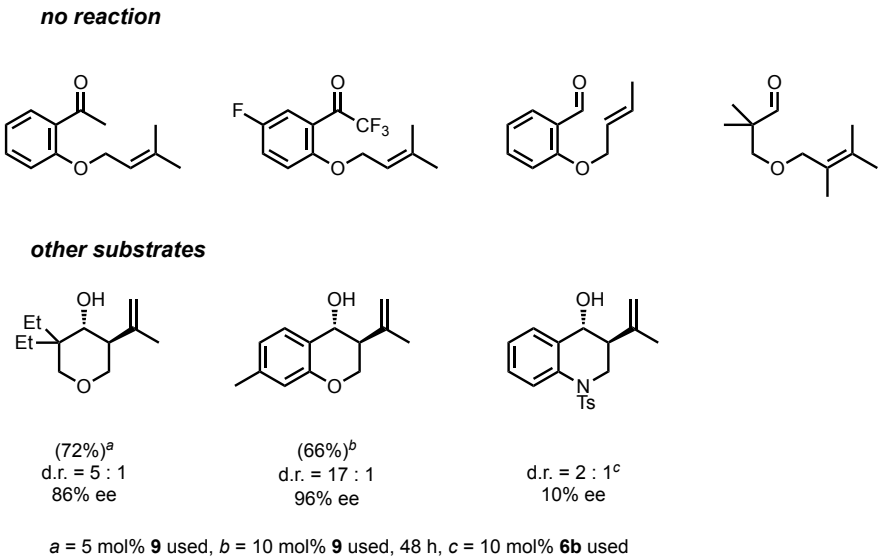
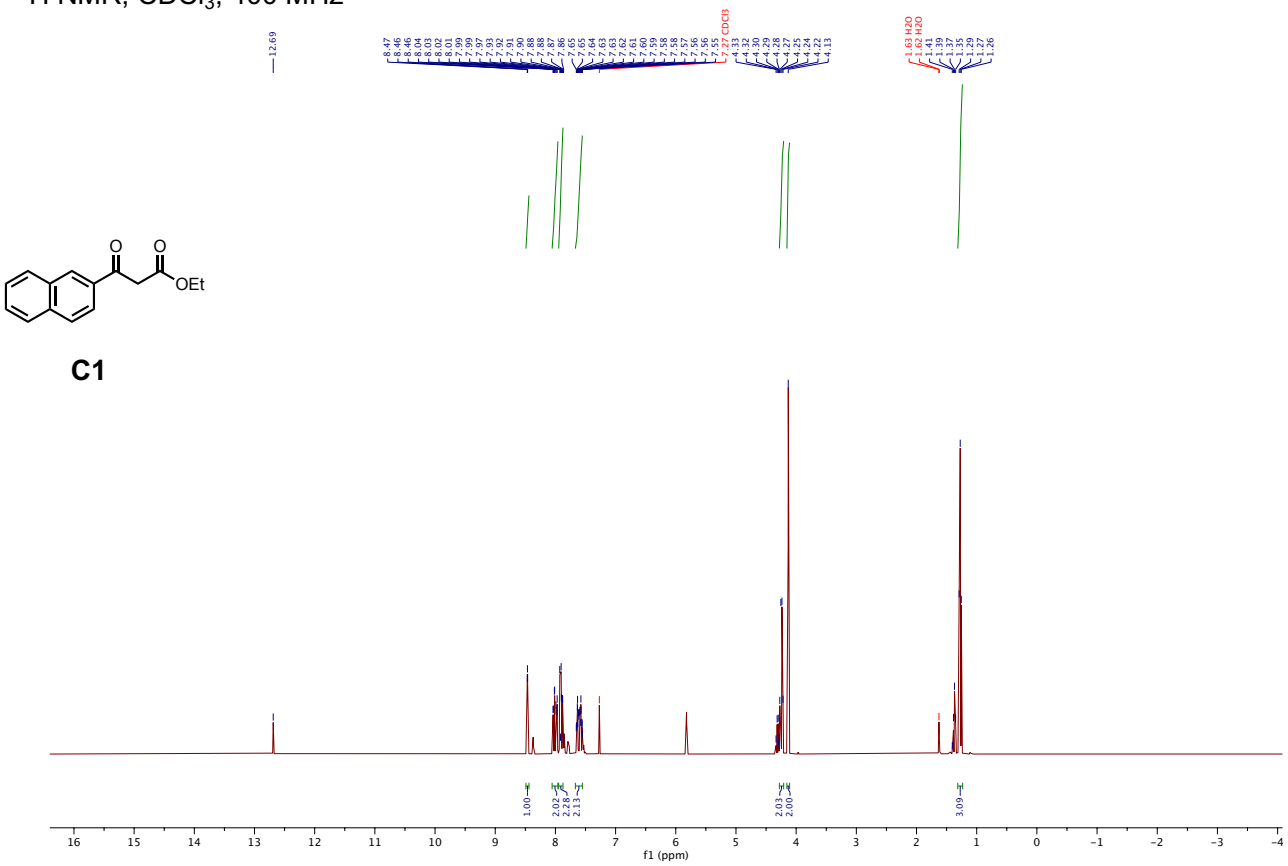


Figure S19. Alternative substrates. Reactions were conducted using the above substrates according to general procedures in section 4. The use of tetrasubstituted alkene nucleophiles and aldehyde electrophiles was found to be necessary for reactivity. Electron-rich arylaldehyde substrates were observed to react very slowly and although high ee could be achieved, higher HBD loadings and reaction times were required.

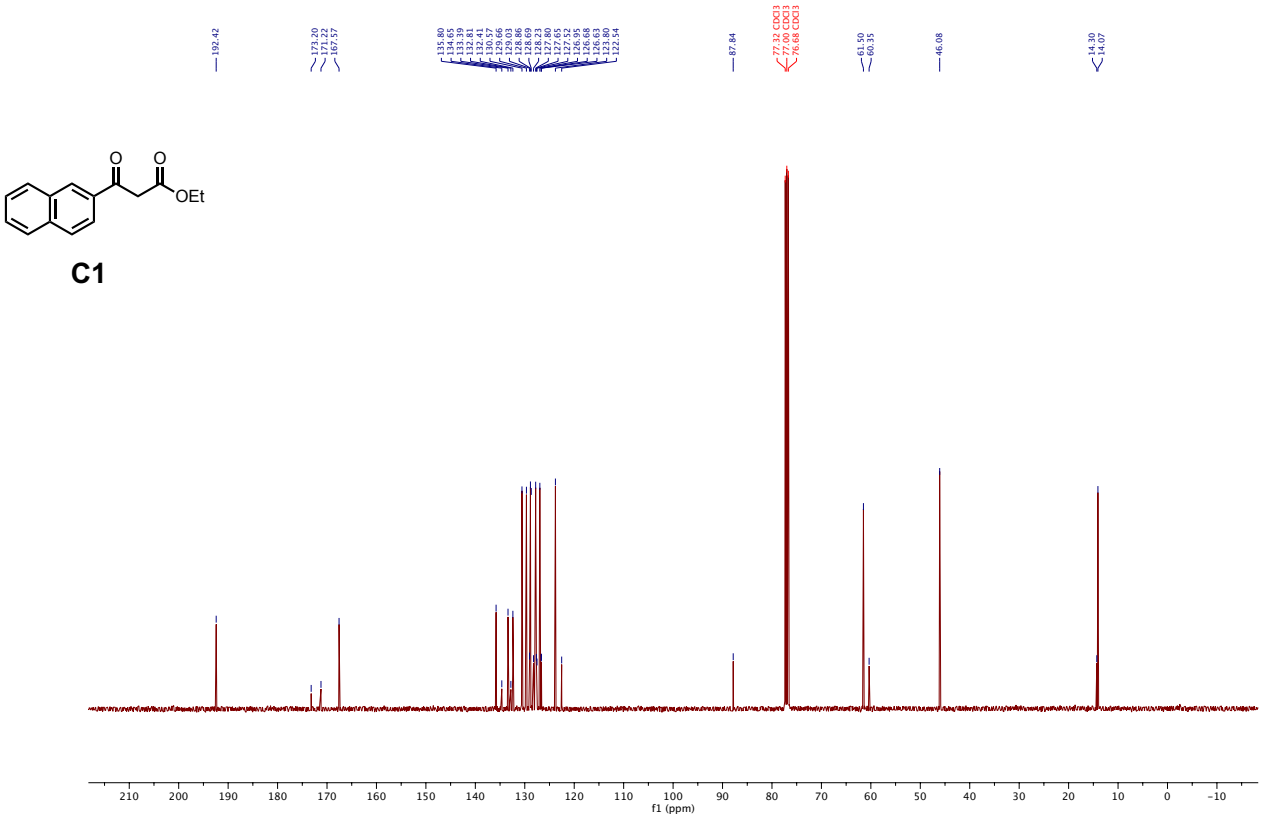
9. ^{1}H, ^{13}C, and ^{19}F NMR spectra

^{1}H NMR, $CDCl_3$, 400 MHz



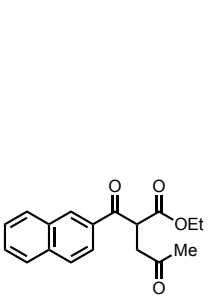
C1

13C NMR, $CDCl_3$, 101 MHz



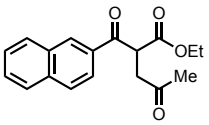
C1

^{1}H NMR, $CDCl_3$, 400 MHz



C2

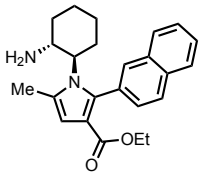
13C NMR, $CDCl_3$, 101 MHz



C2

^{1}H NMR, $CDCl_3$, 400 MHz

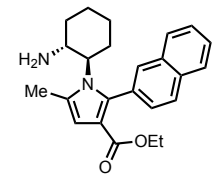
4:1 rotameric ratio



C3

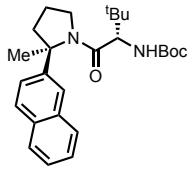
13C NMR, $CDCl_3$, 101 MHz

4:1 rotameric ratio



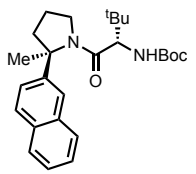
C3

^{1}H NMR, $CDCl_3$, 400 MHz



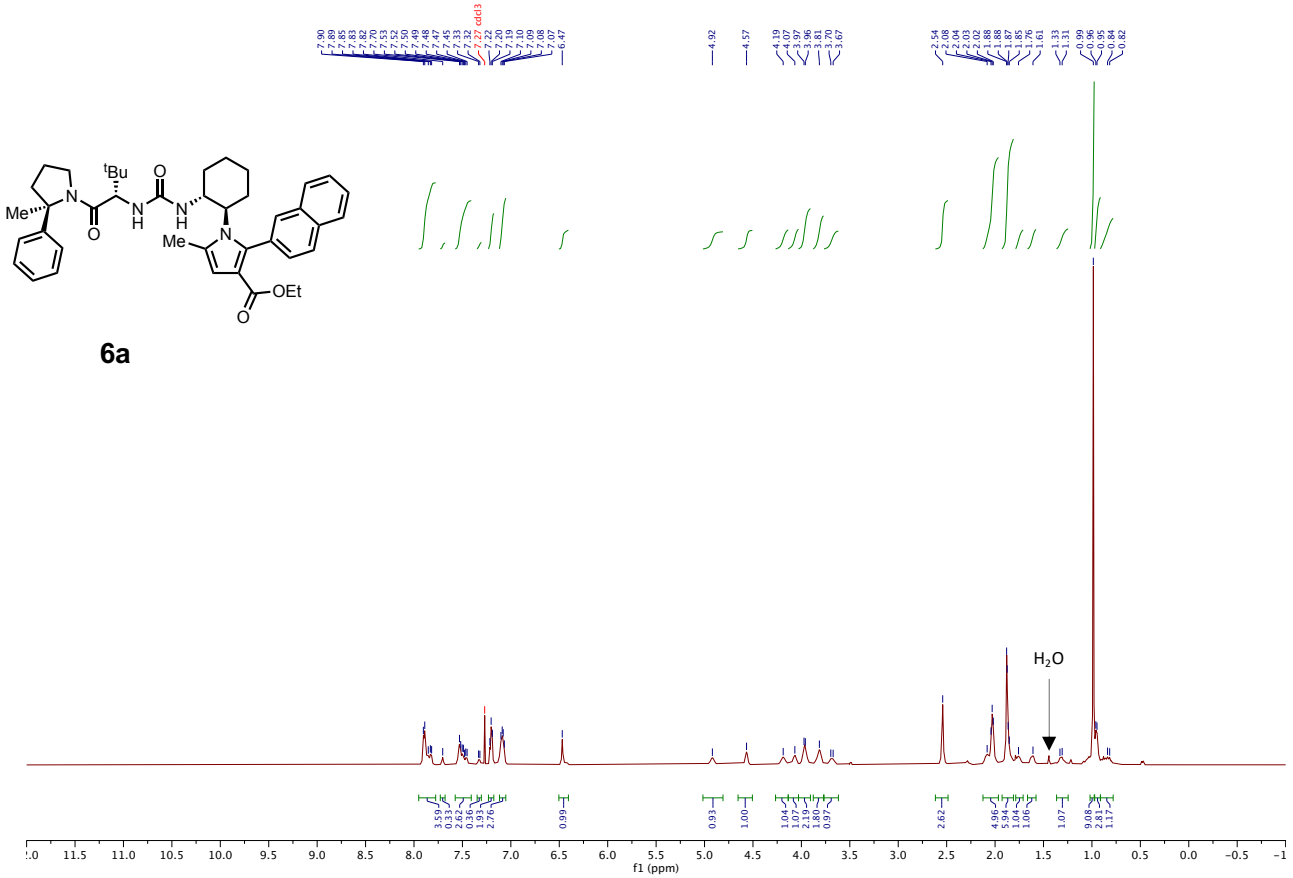
C4b

13C NMR, $CDCl_3$, 101 MHz



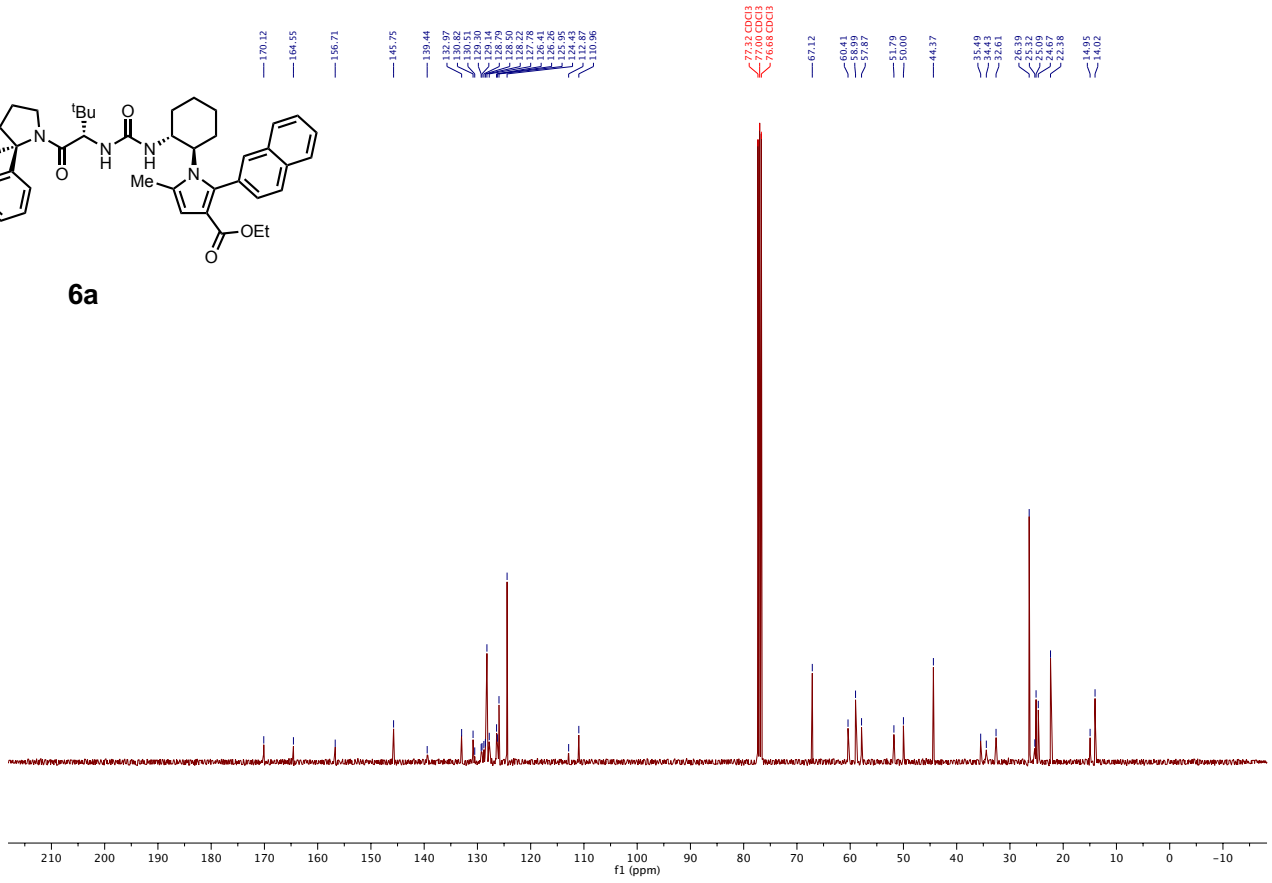
C4b

^{1}H NMR, $CDCl_3$, 400 MHz



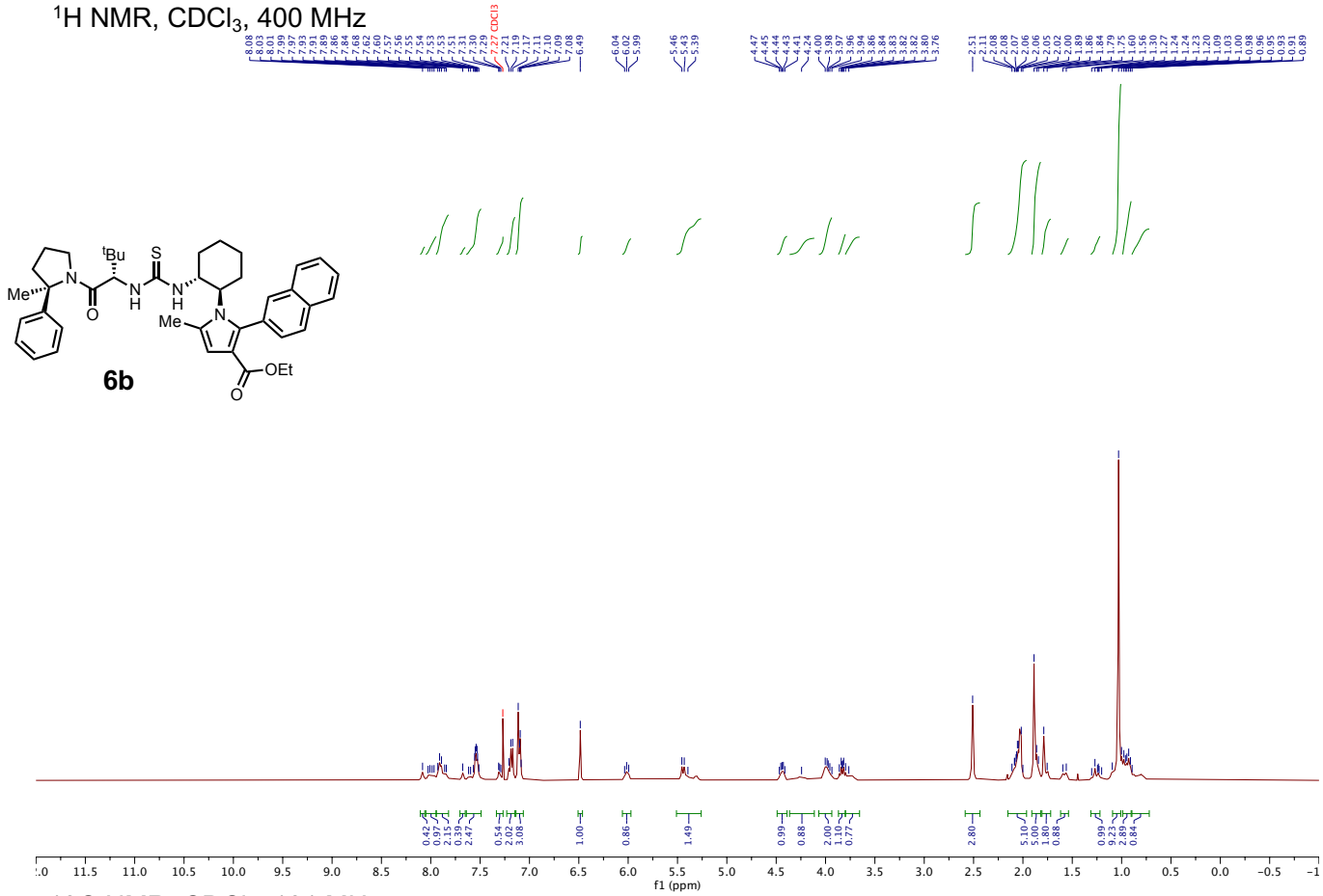
6a

13C NMR, $CDCl_3$, 101 MHz



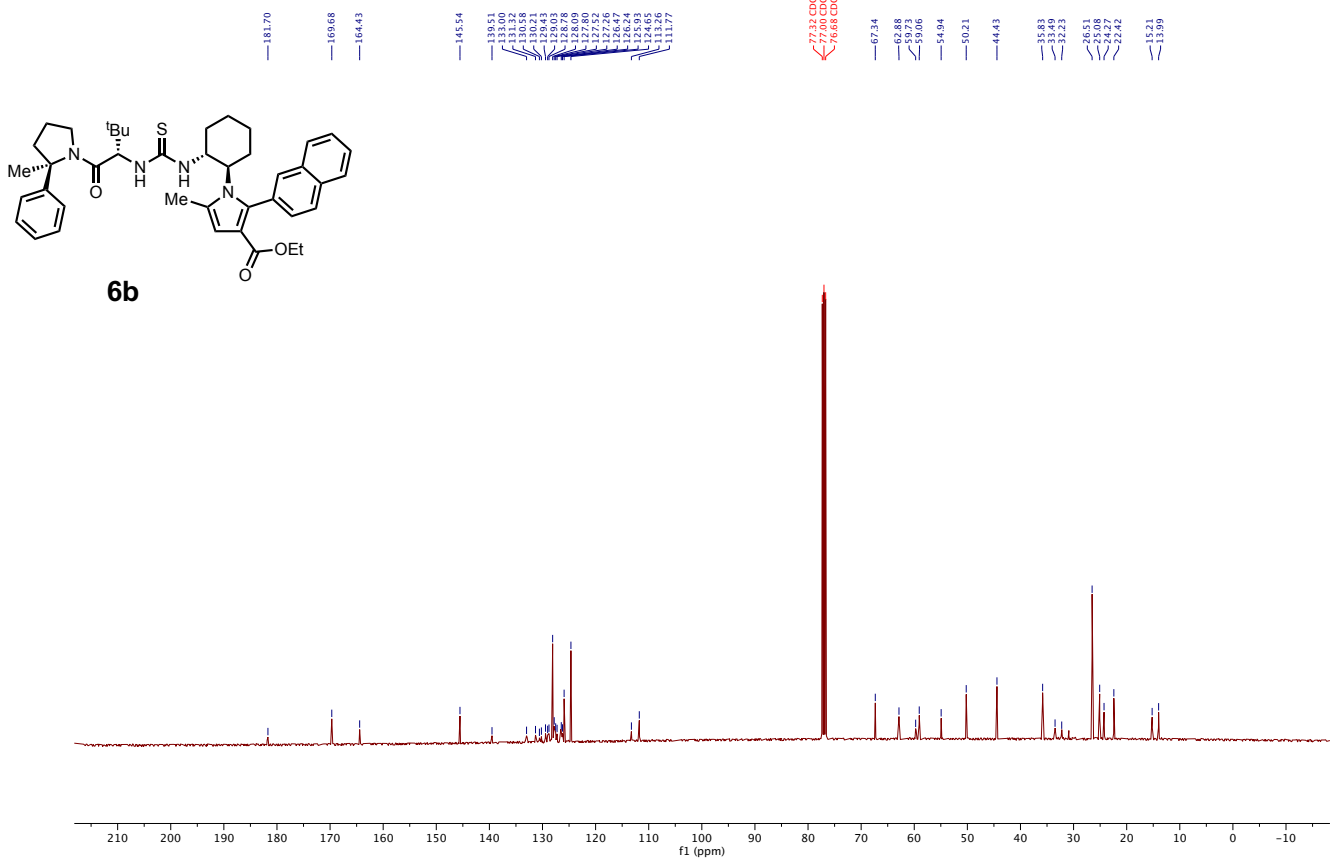
6a

^{1}H NMR, $CDCl_3$, 400 MHz



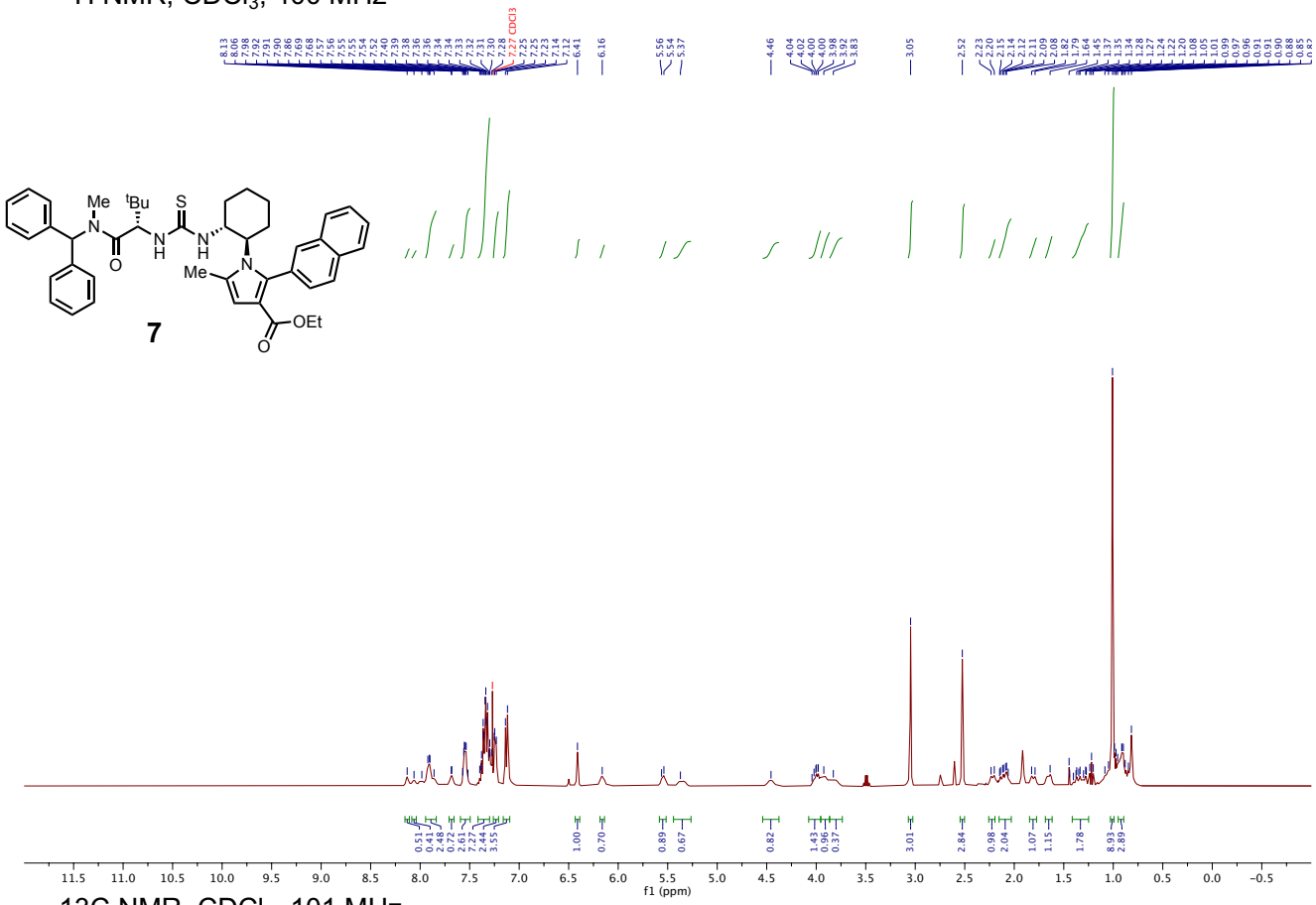
6b

13C NMR, $CDCl_3$, 101 MHz

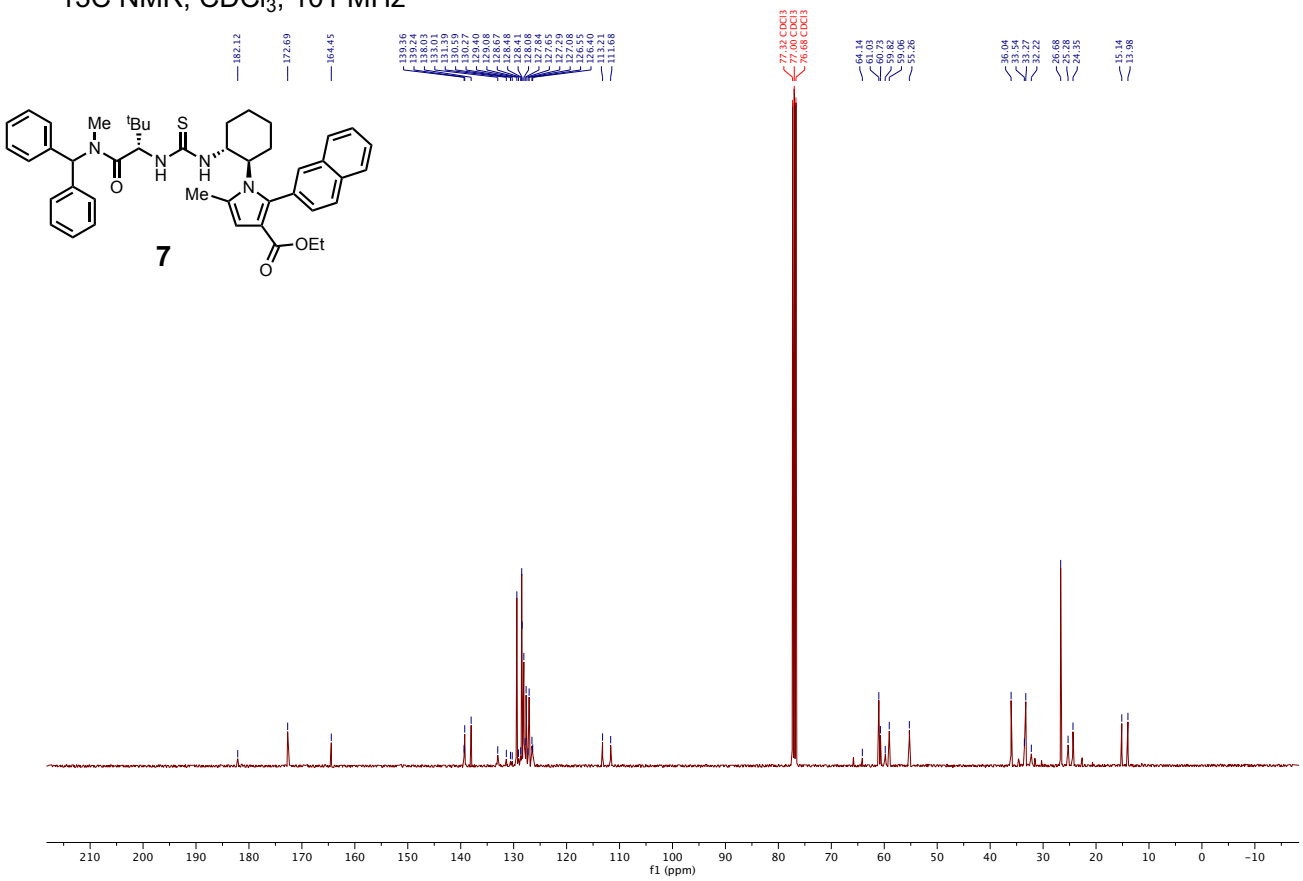


6b

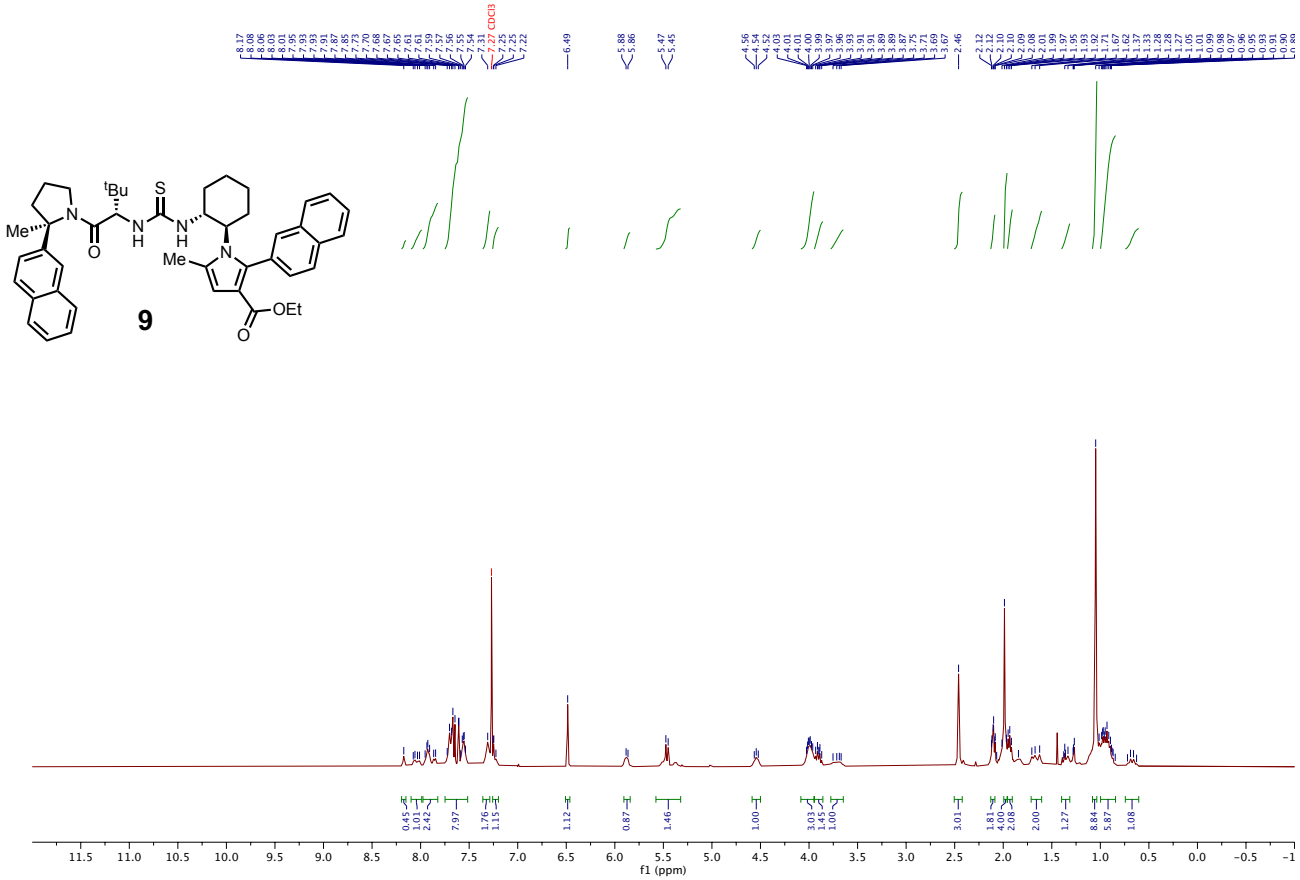
^{1}H NMR, $CDCl_3$, 400 MHz



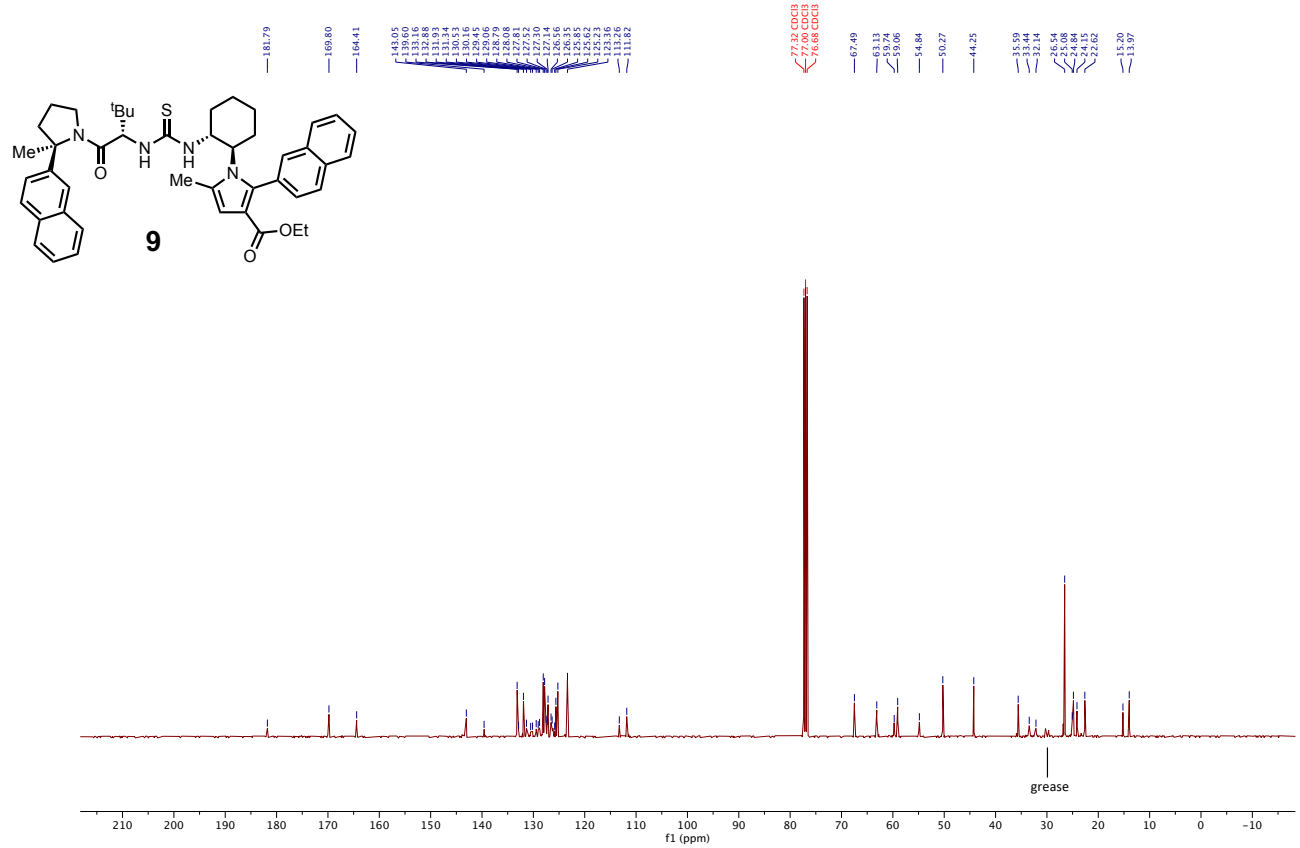
13C NMR, $CDCl_3$, 101 MHz



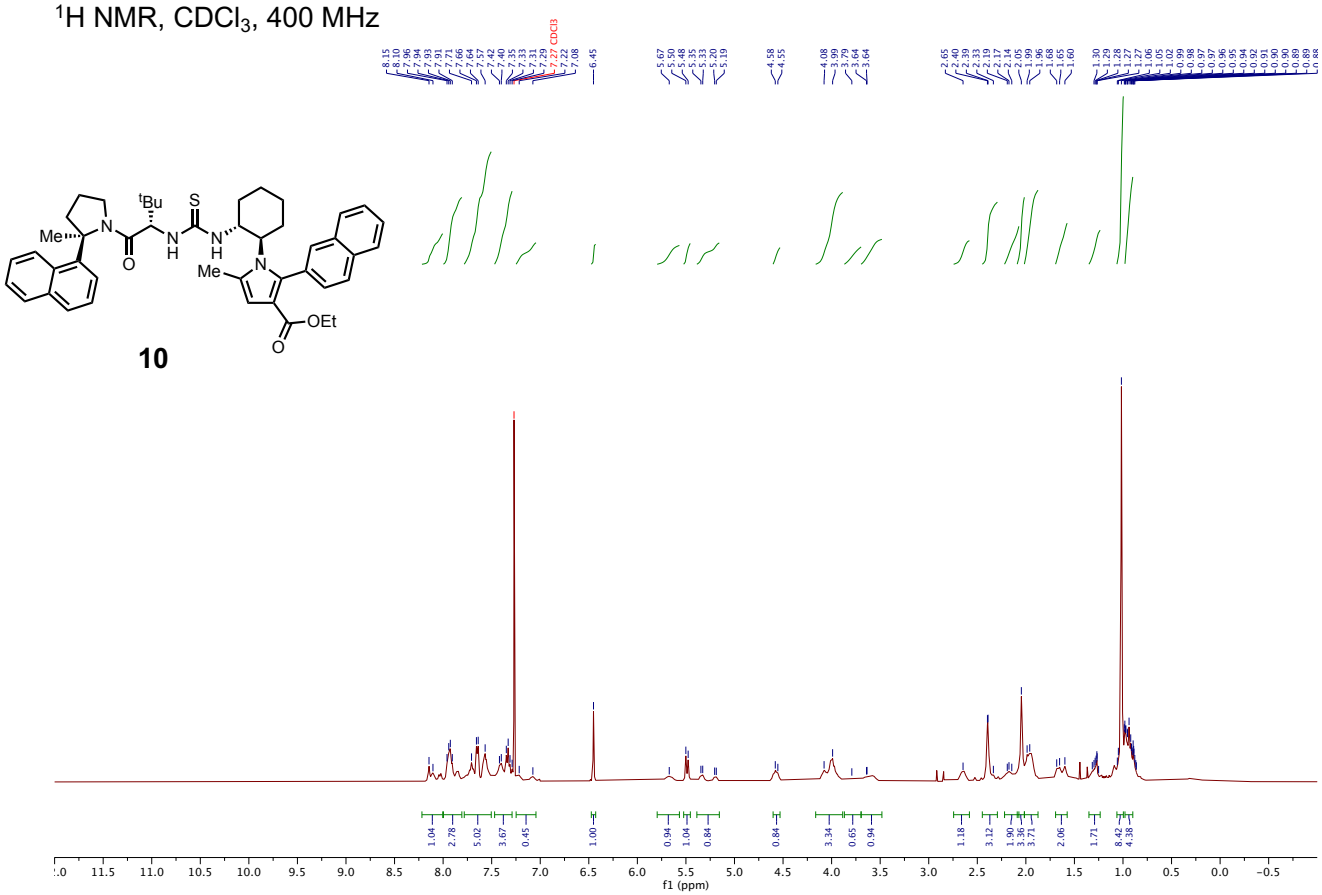
^{1}H NMR, $CDCl_3$, 400 MHz



13C NMR, $CDCl_3$, 101 MHz

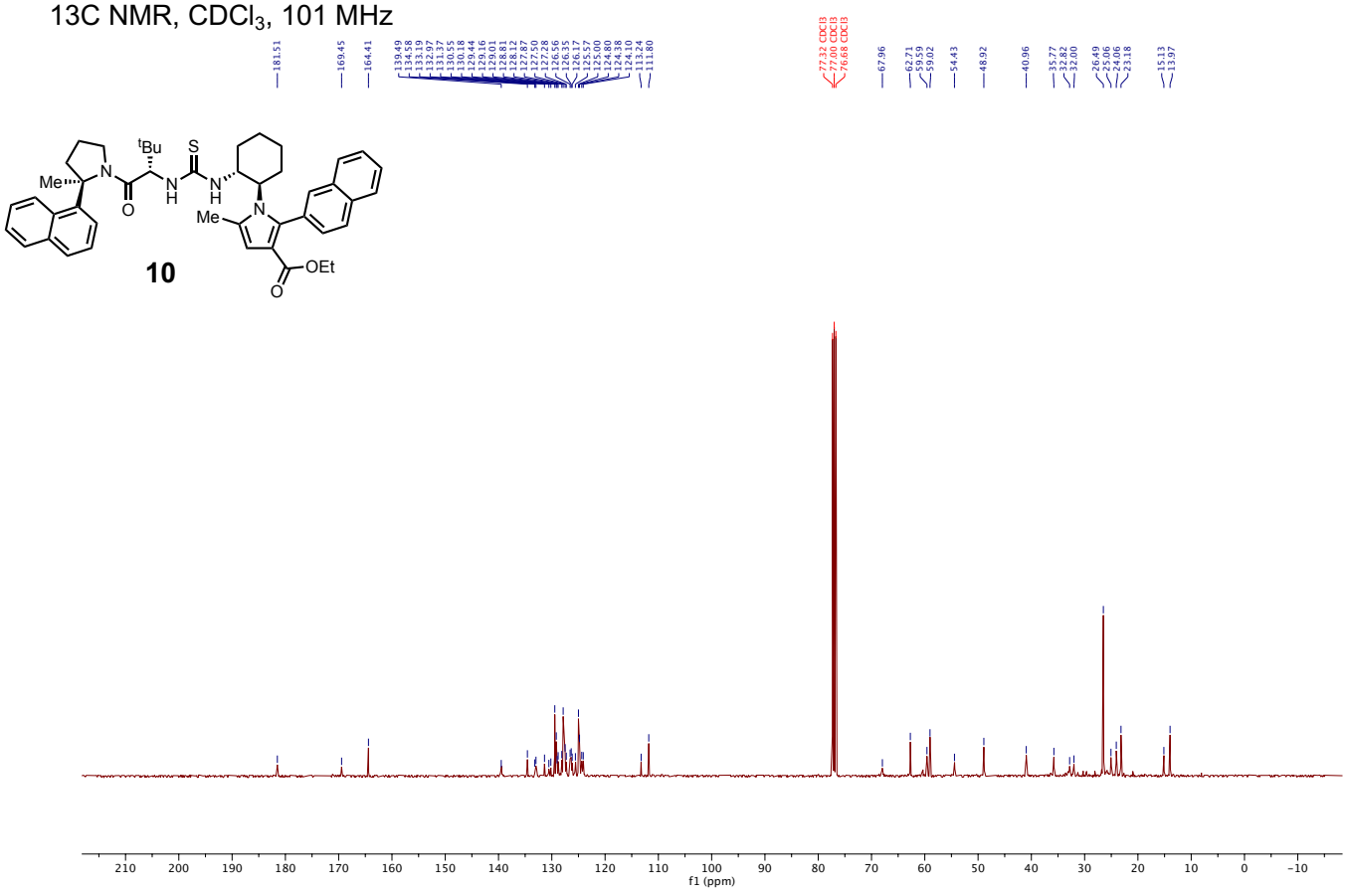


^{1}H NMR, $CDCl_3$, 400 MHz



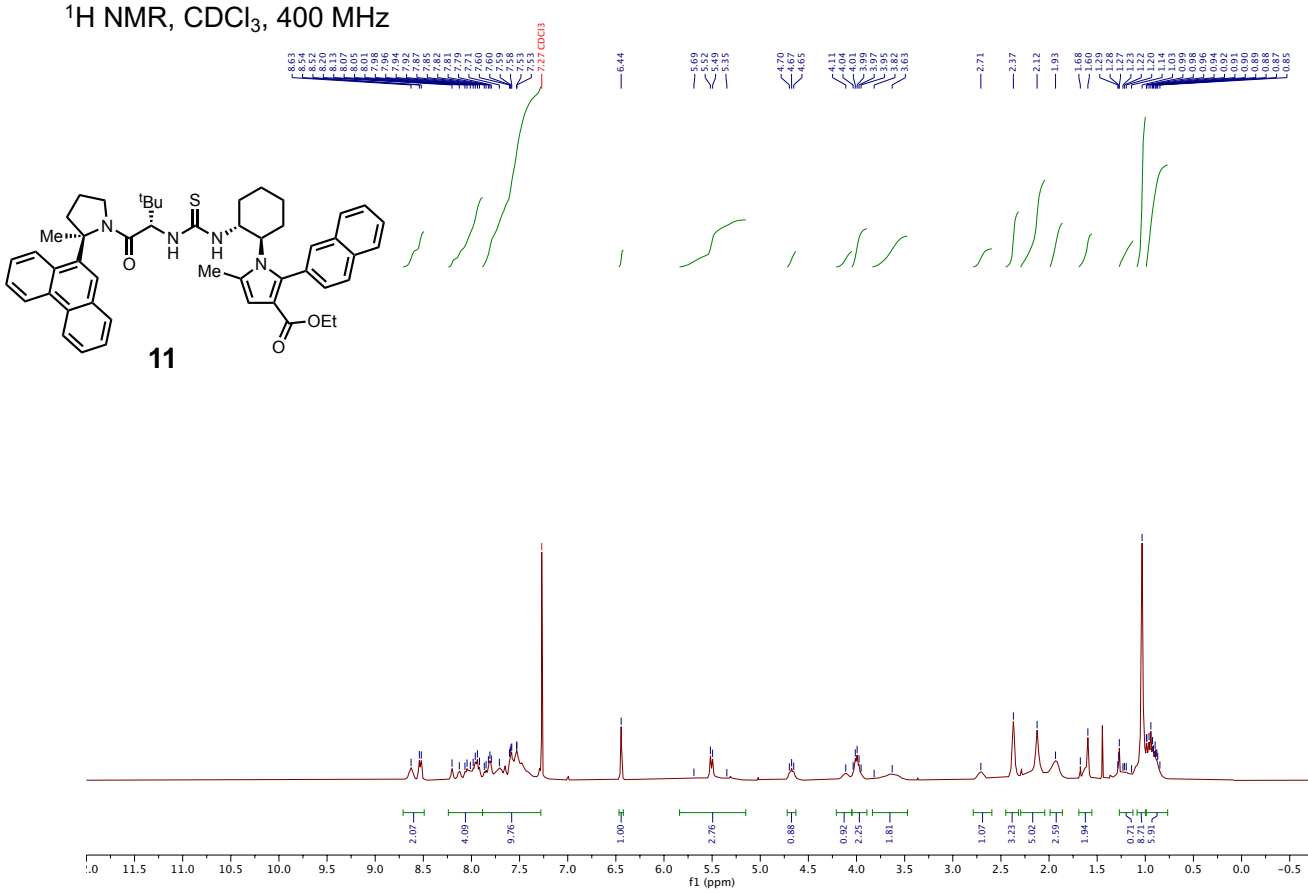
10

13C NMR, $CDCl_3$, 101 MHz

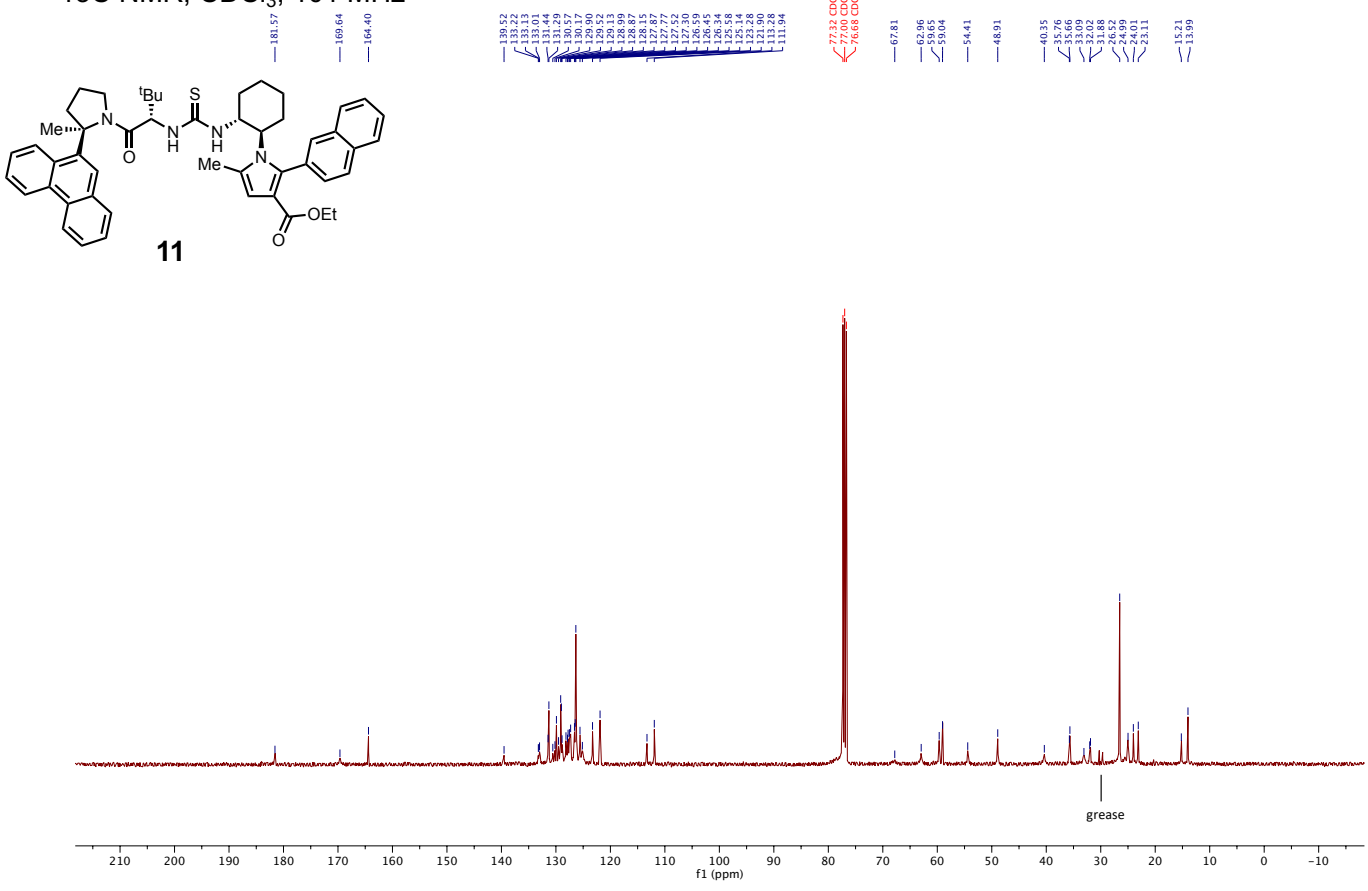


10

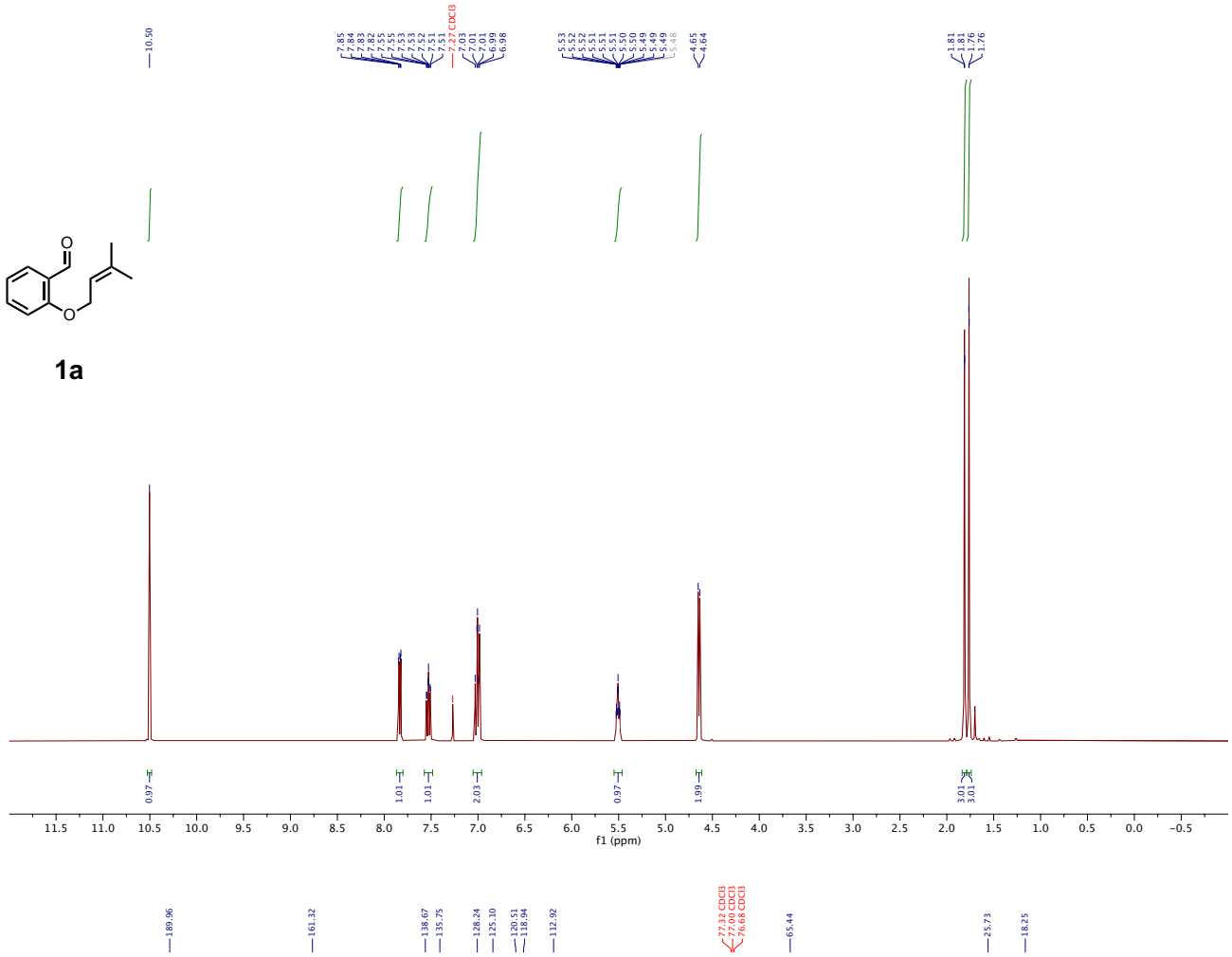
^{1}H NMR, $CDCl_3$, 400 MHz



13C NMR, $CDCl_3$, 101 MHz

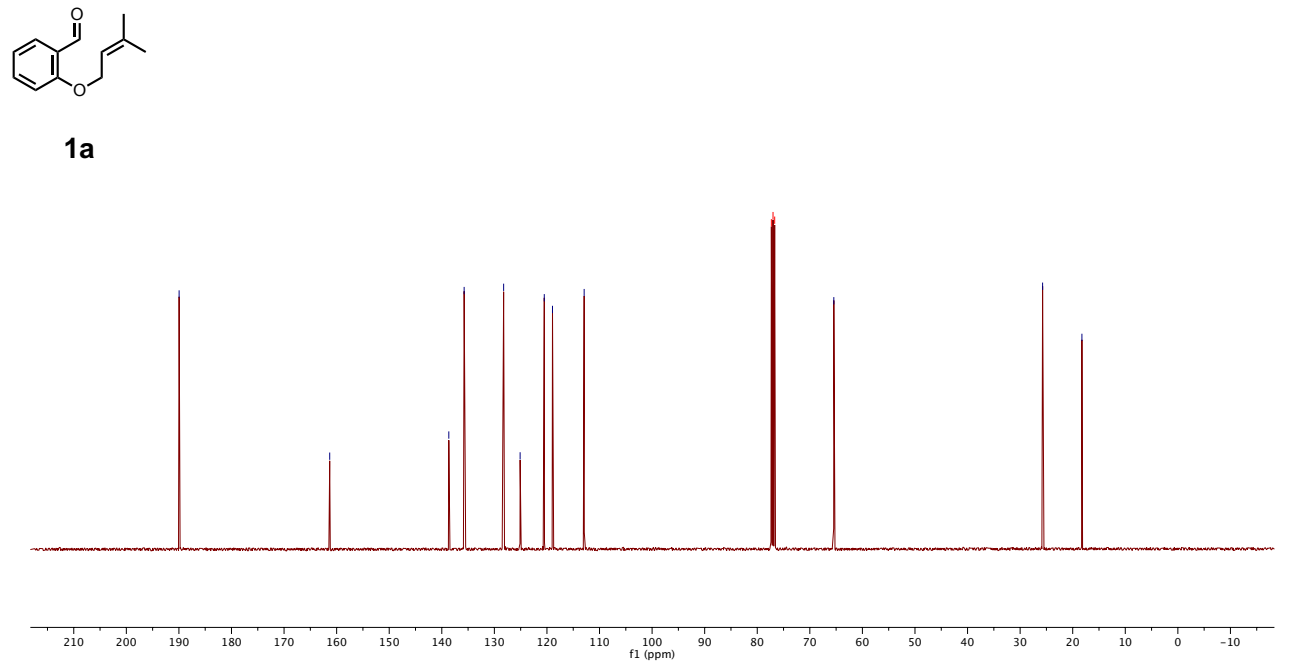


^{1}H NMR, $CDCl_3$, 400 MHz



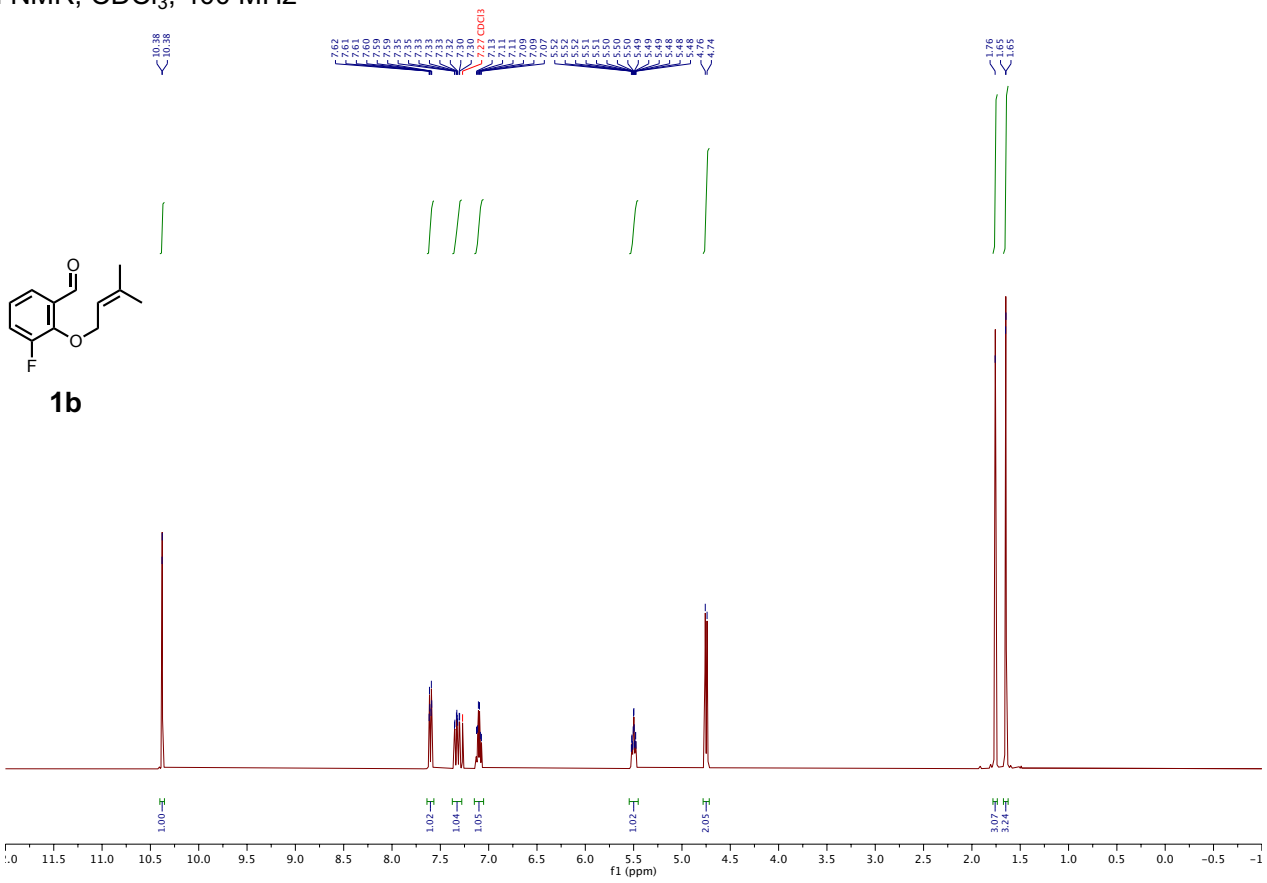
1a

13C NMR, $CDCl_3$, 101 MHz



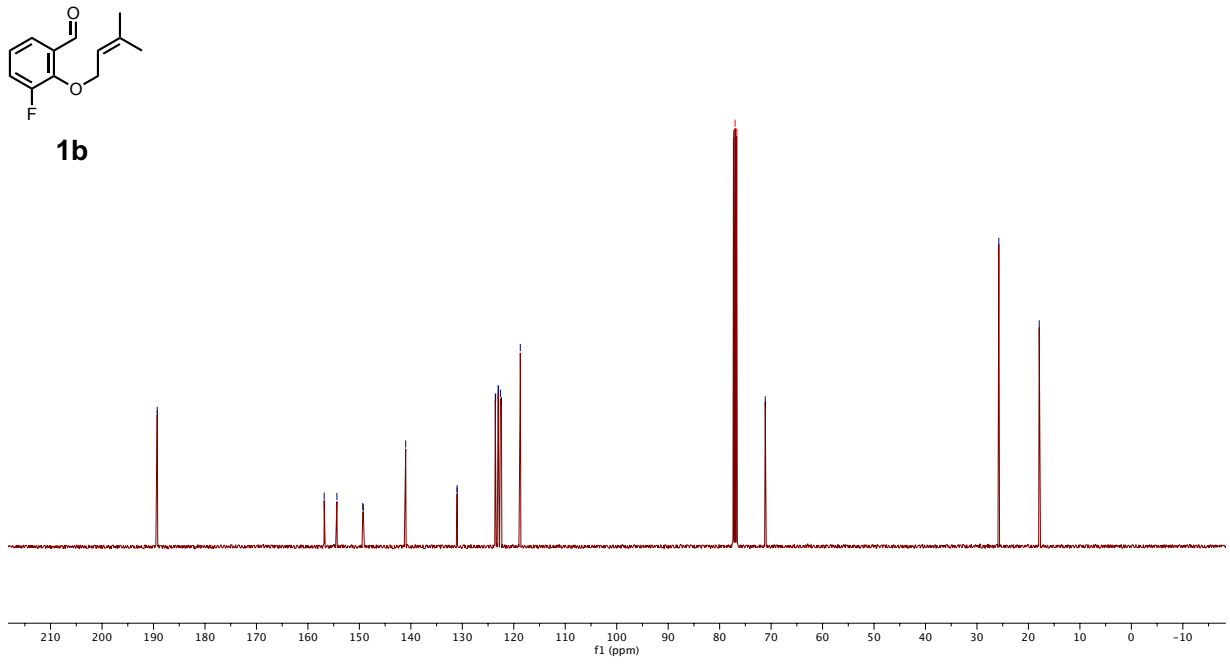
1a

^{1}H NMR, $CDCl_3$, 400 MHz



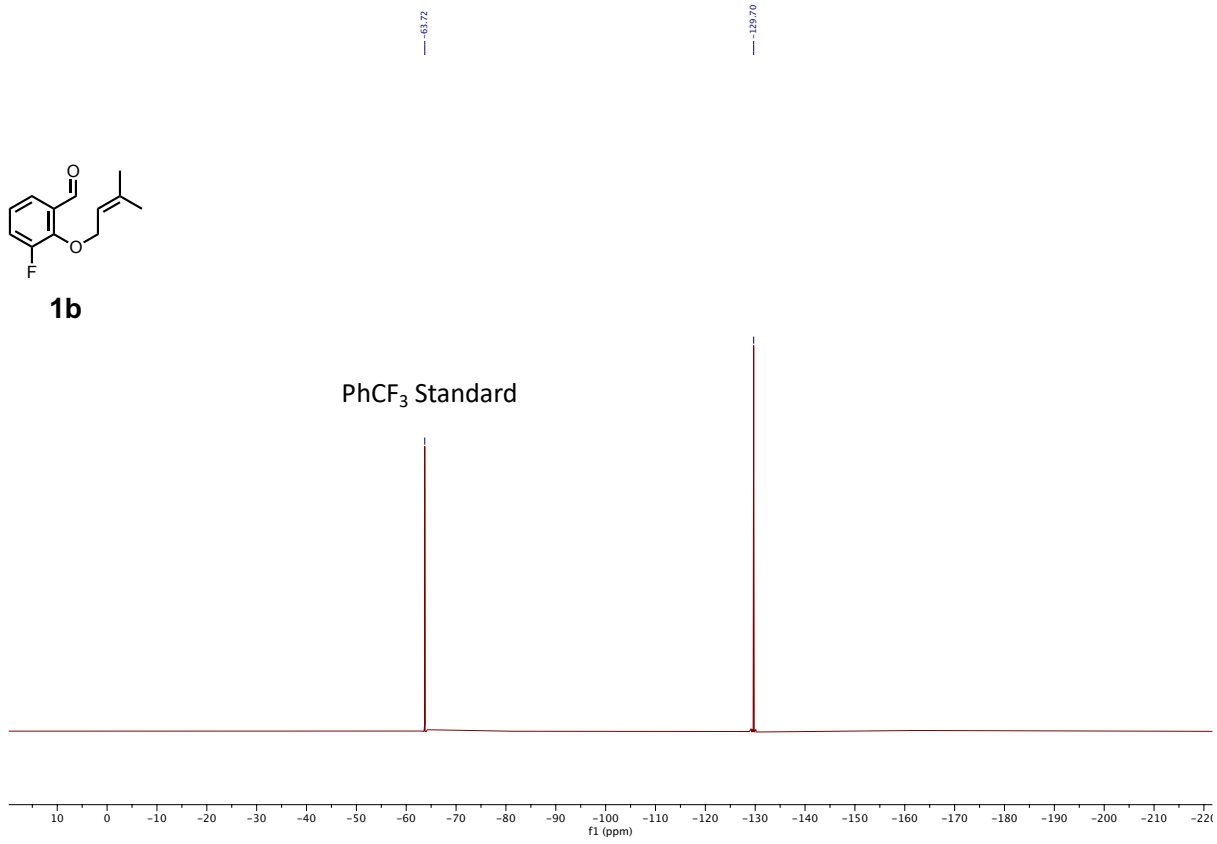
1b

13C NMR, $CDCl_3$, 101 MHz

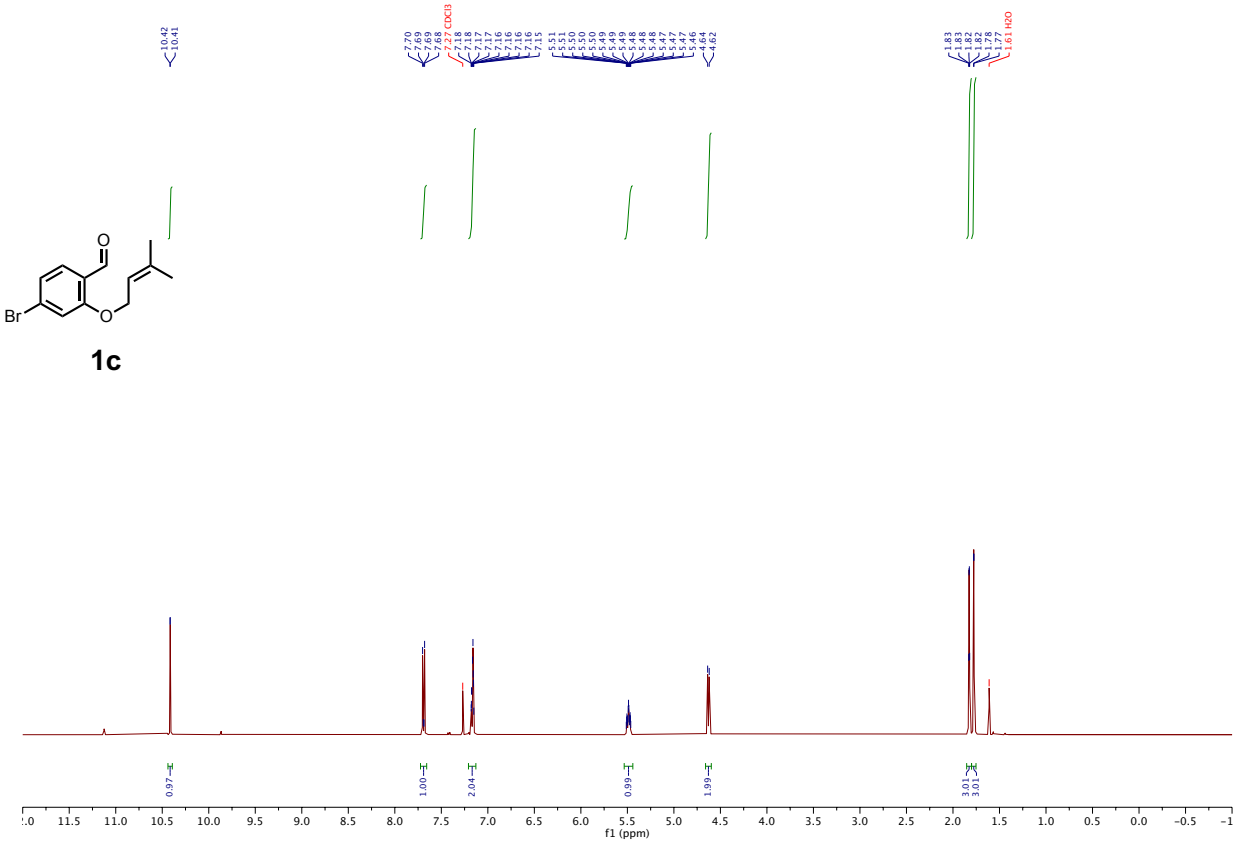


1b

^{19}F NMR, $CDCl_3$, 376 MHz

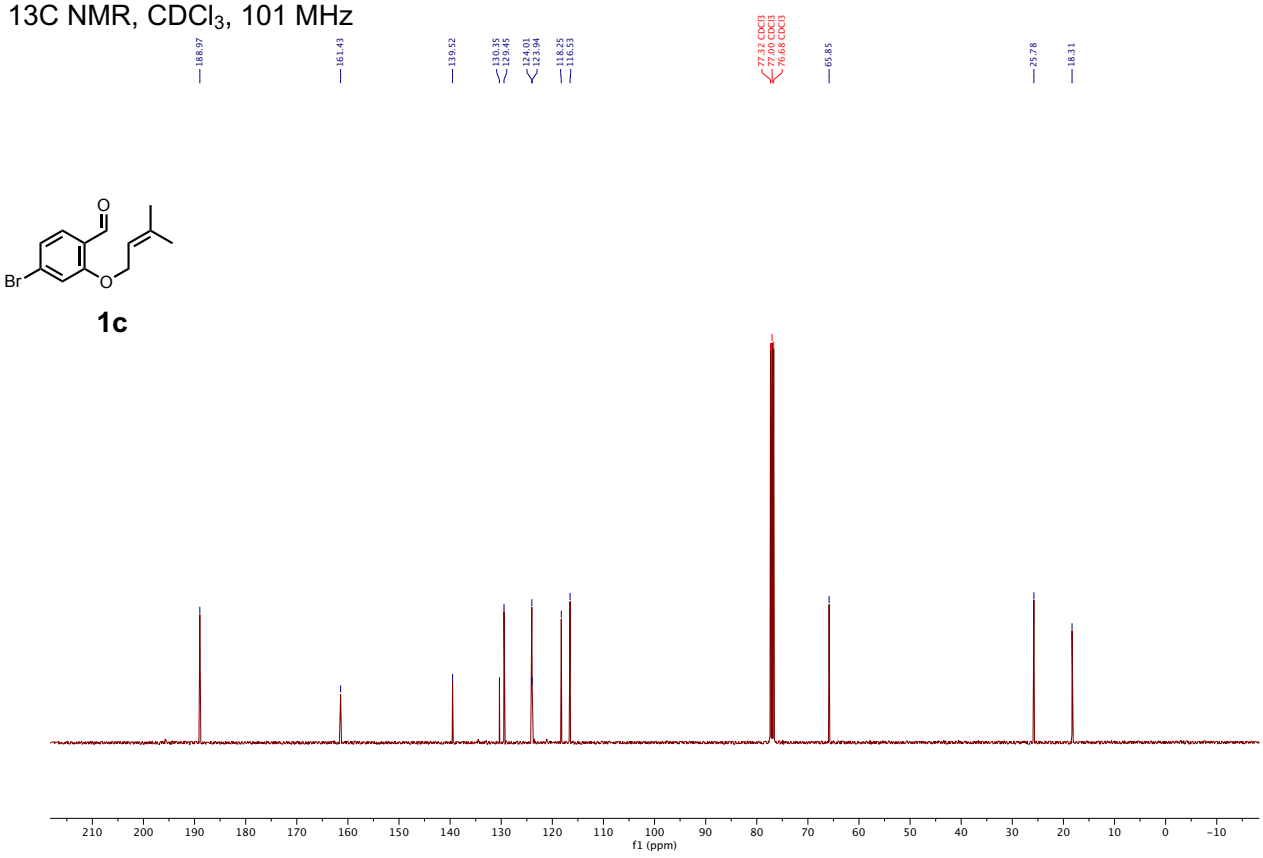


^{1}H NMR, $CDCl_3$, 400 MHz



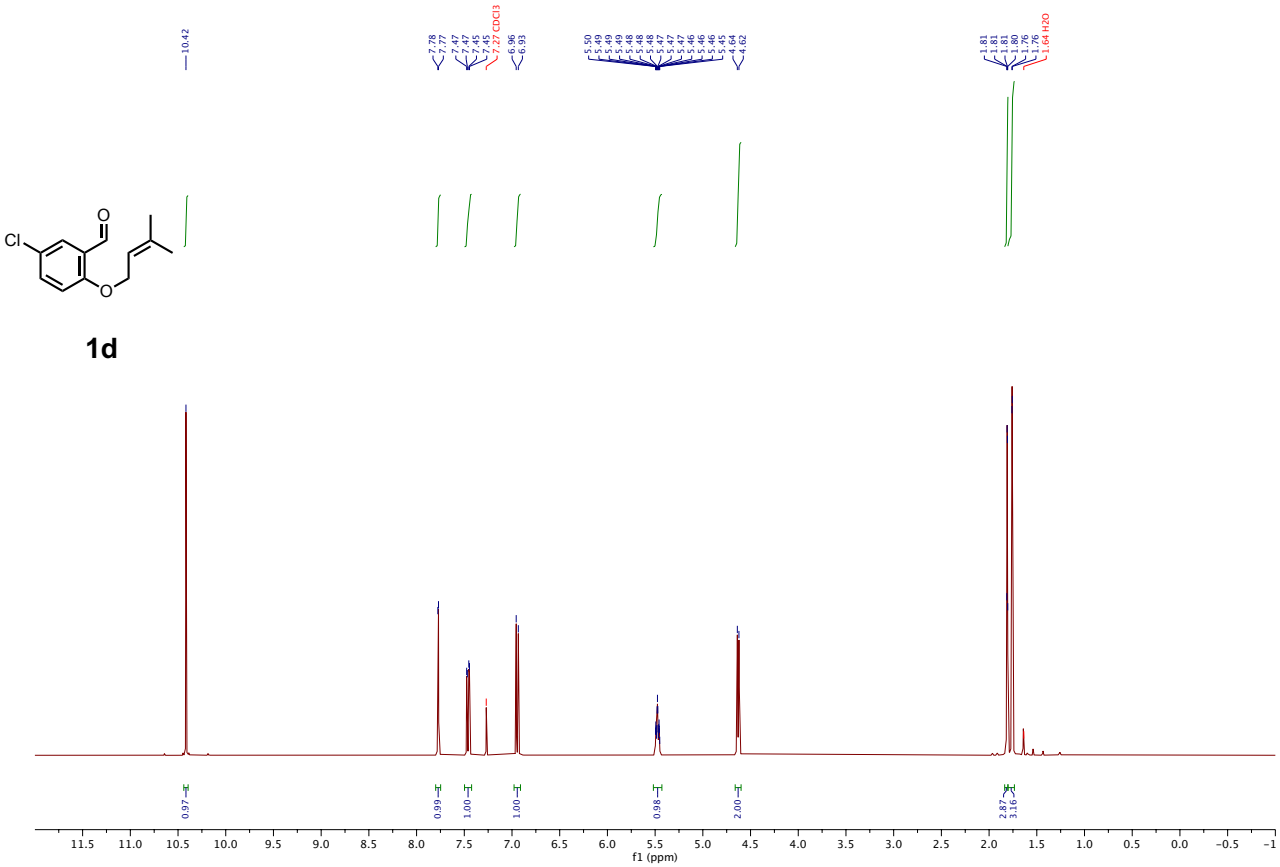
1c

13C NMR, $CDCl_3$, 101 MHz



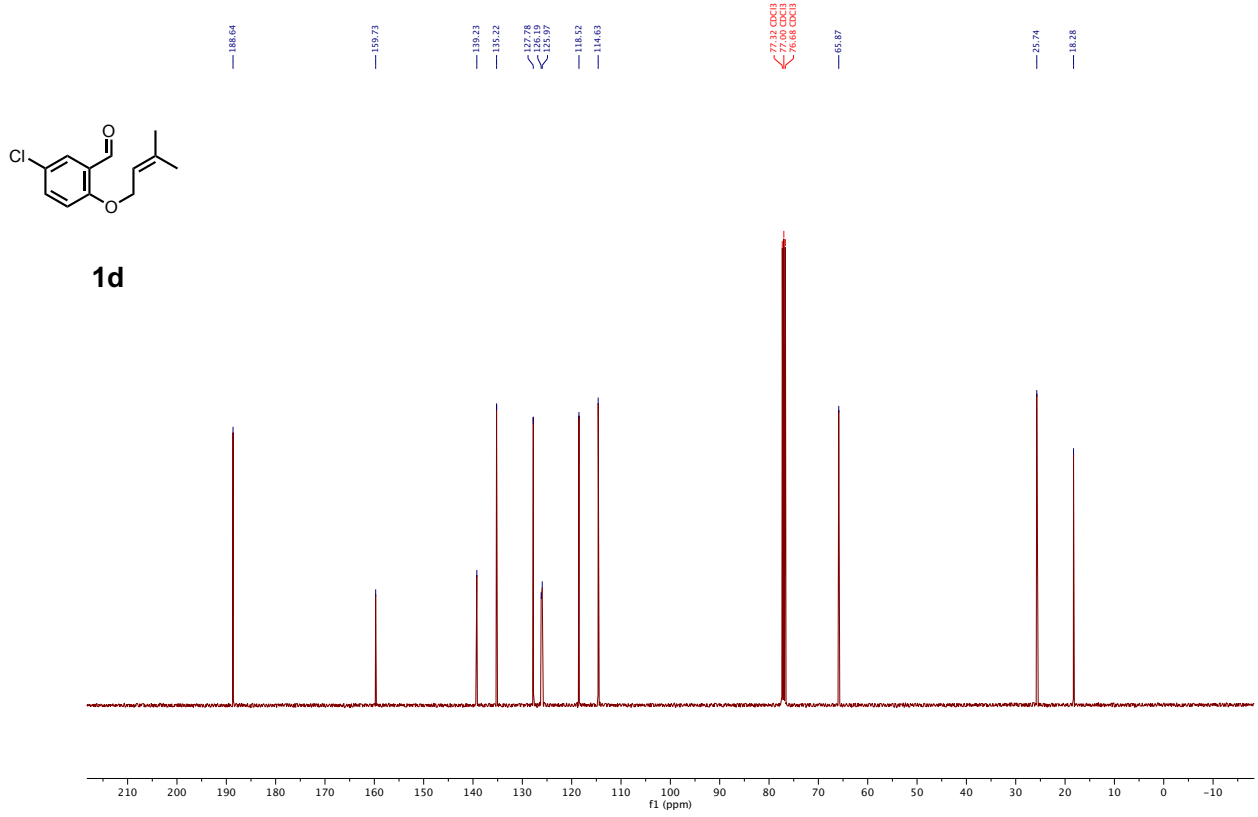
1c

^{1}H NMR, $CDCl_3$, 400 MHz



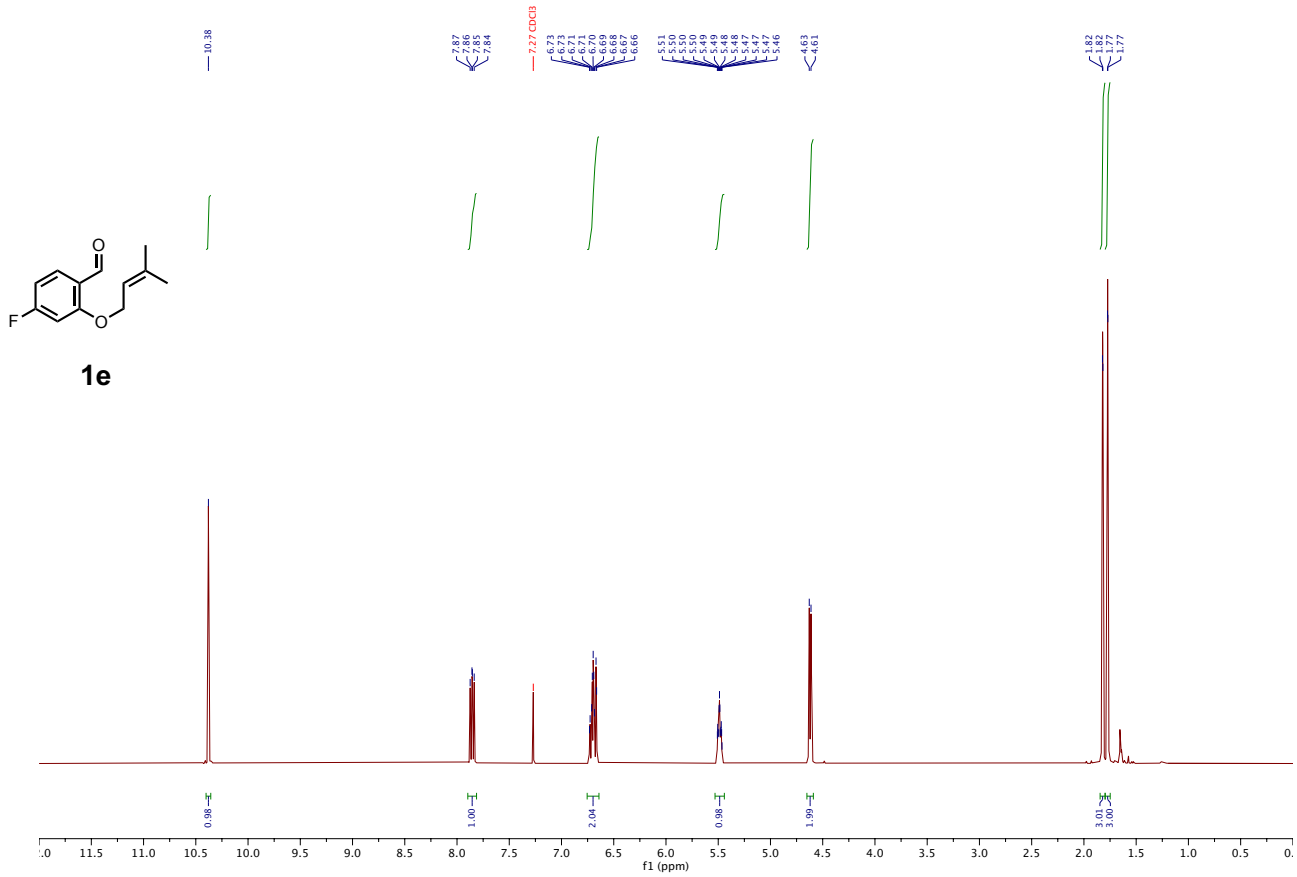
1d

13C NMR, $CDCl_3$, 101 MHz



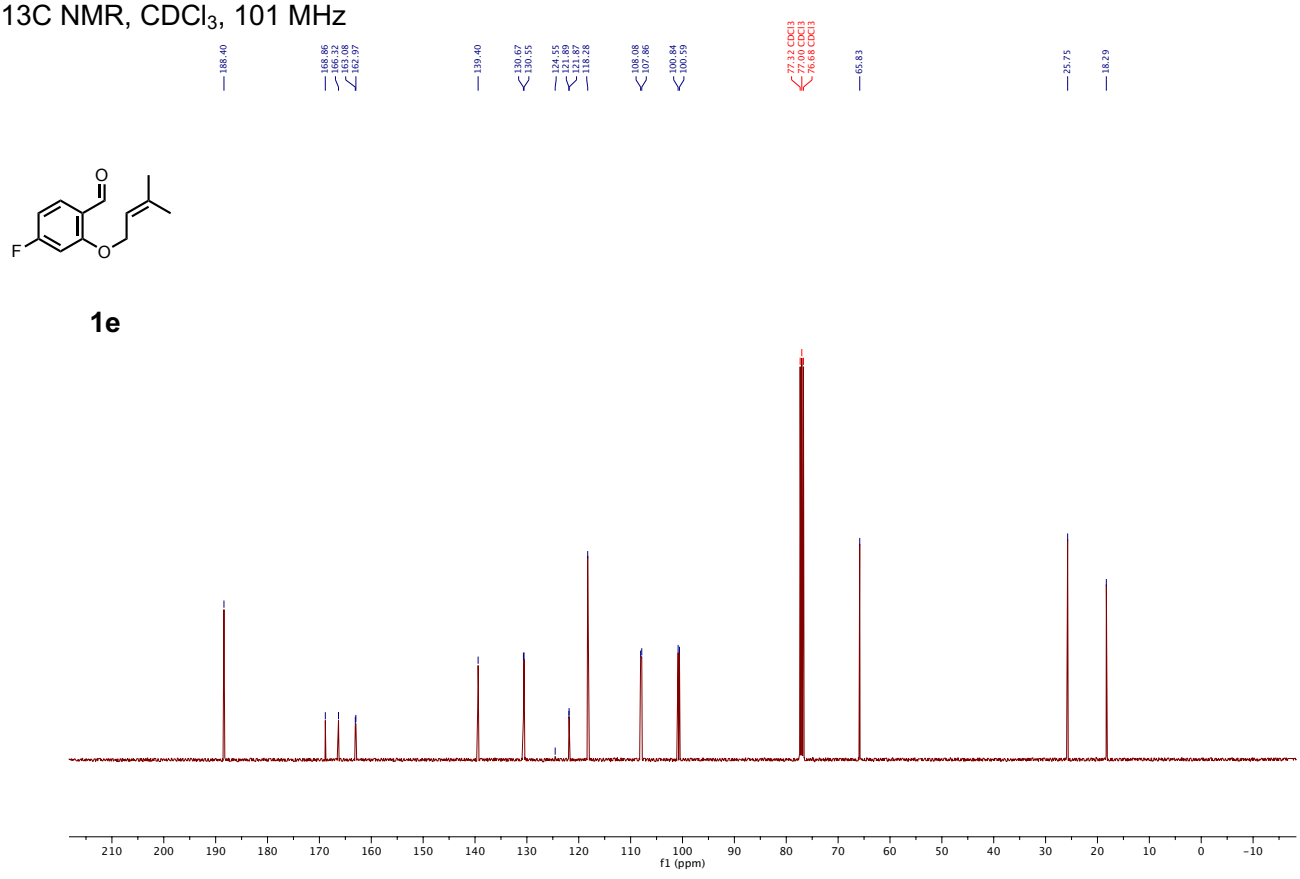
1d

^{1}H NMR, $CDCl_3$, 400 MHz



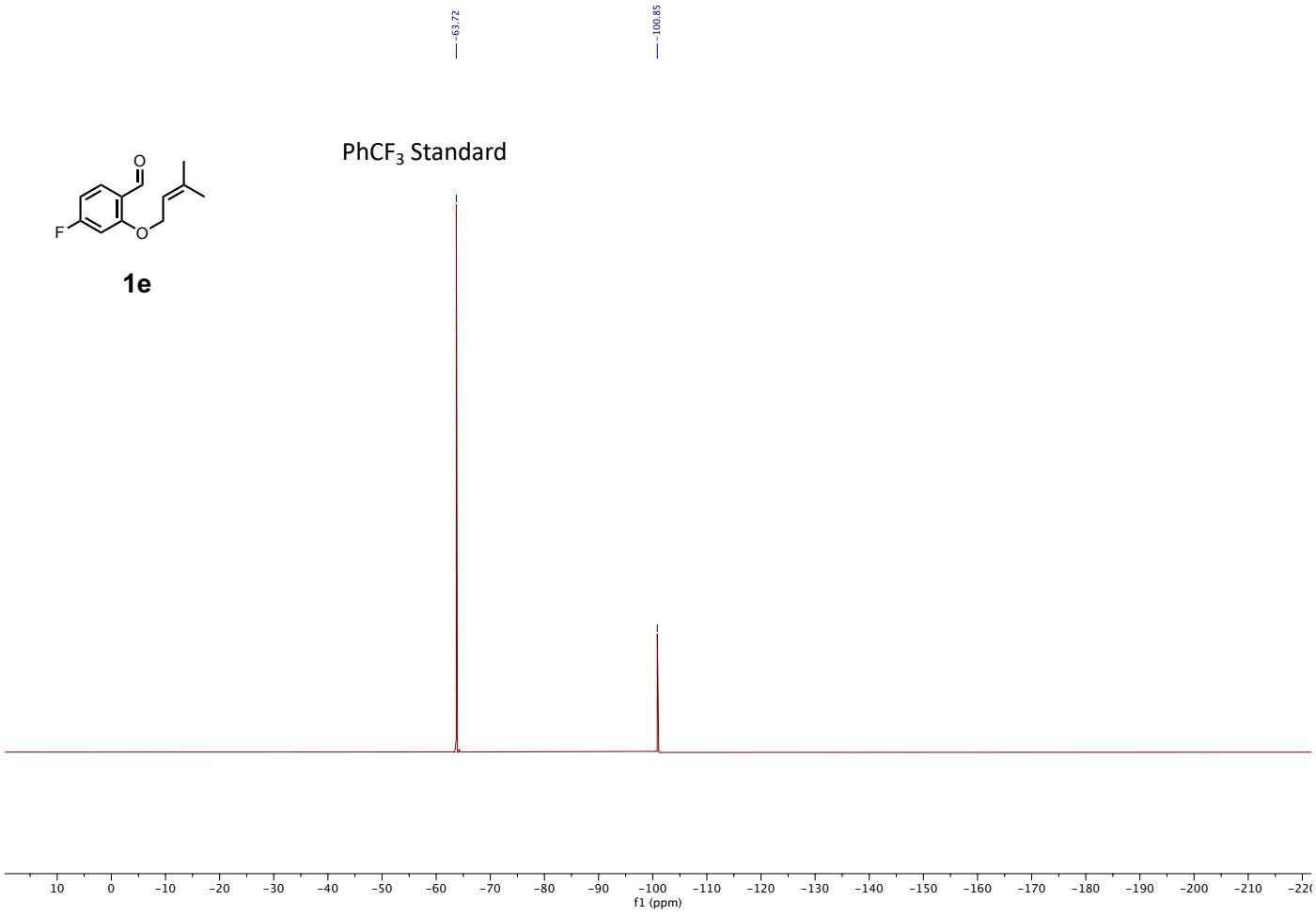
1e

13C NMR, $CDCl_3$, 101 MHz

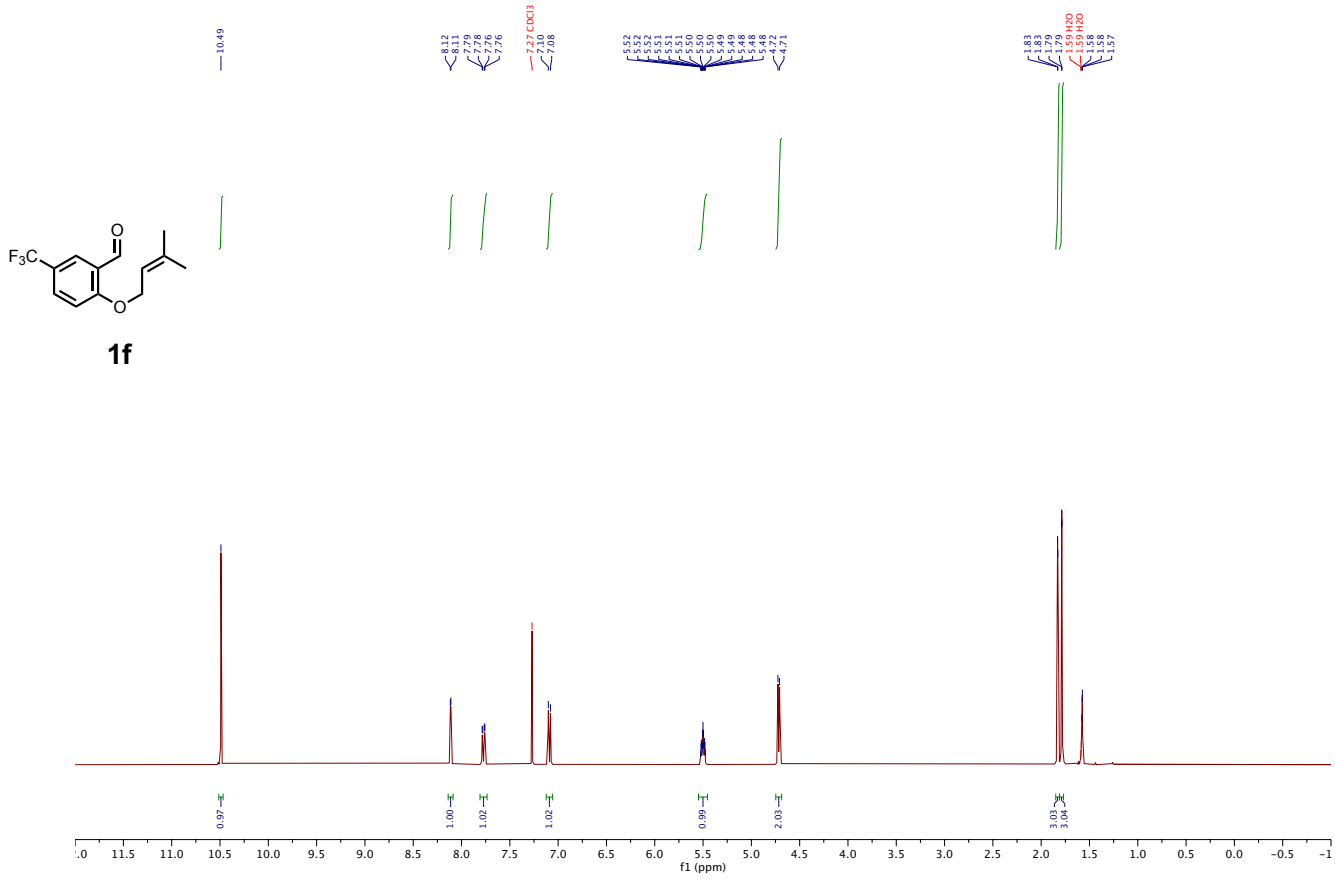


1e

^{19}F NMR, $CDCl_3$, 376 MHz

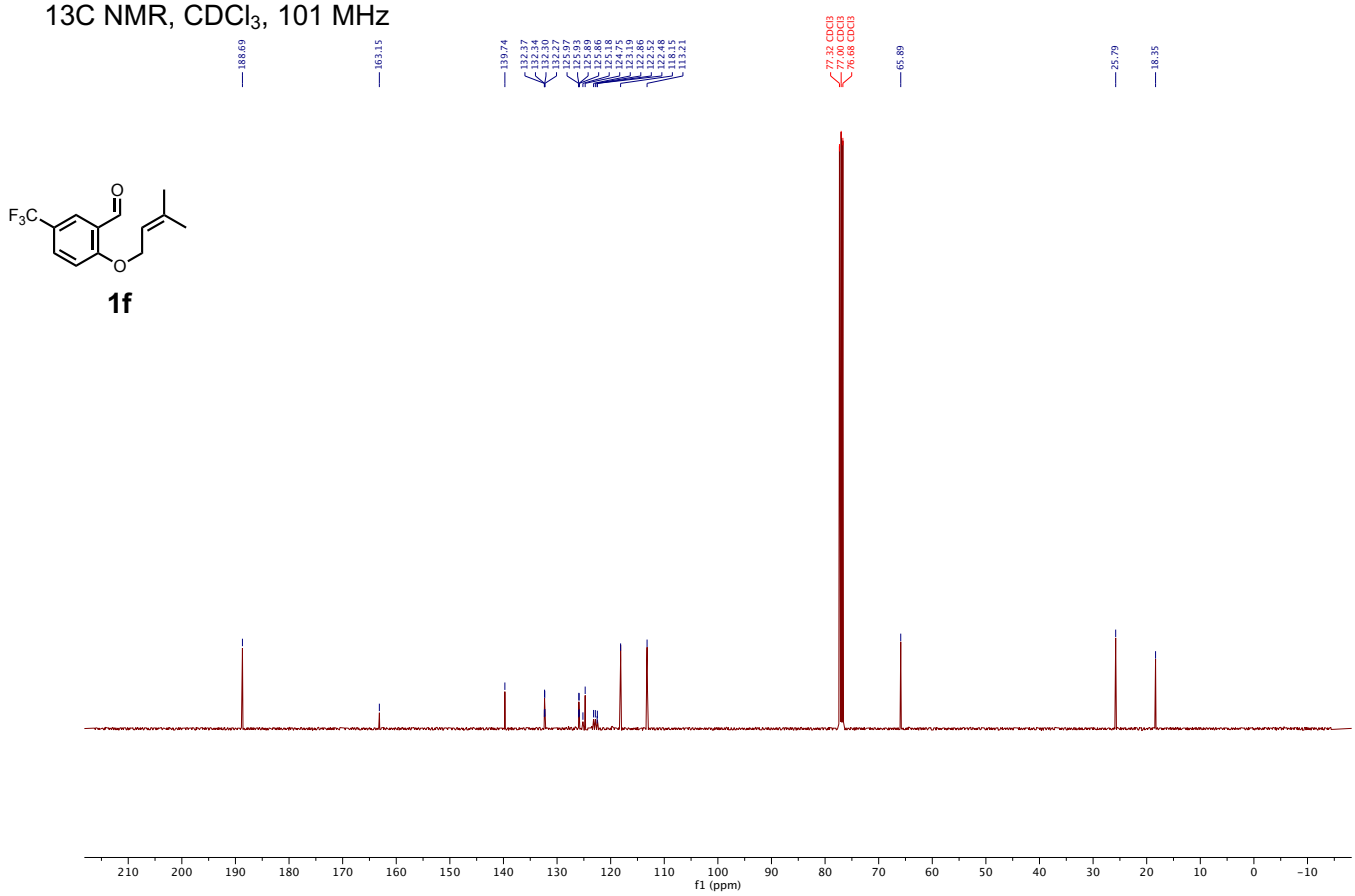


^{1}H NMR, $CDCl_3$, 400 MHz



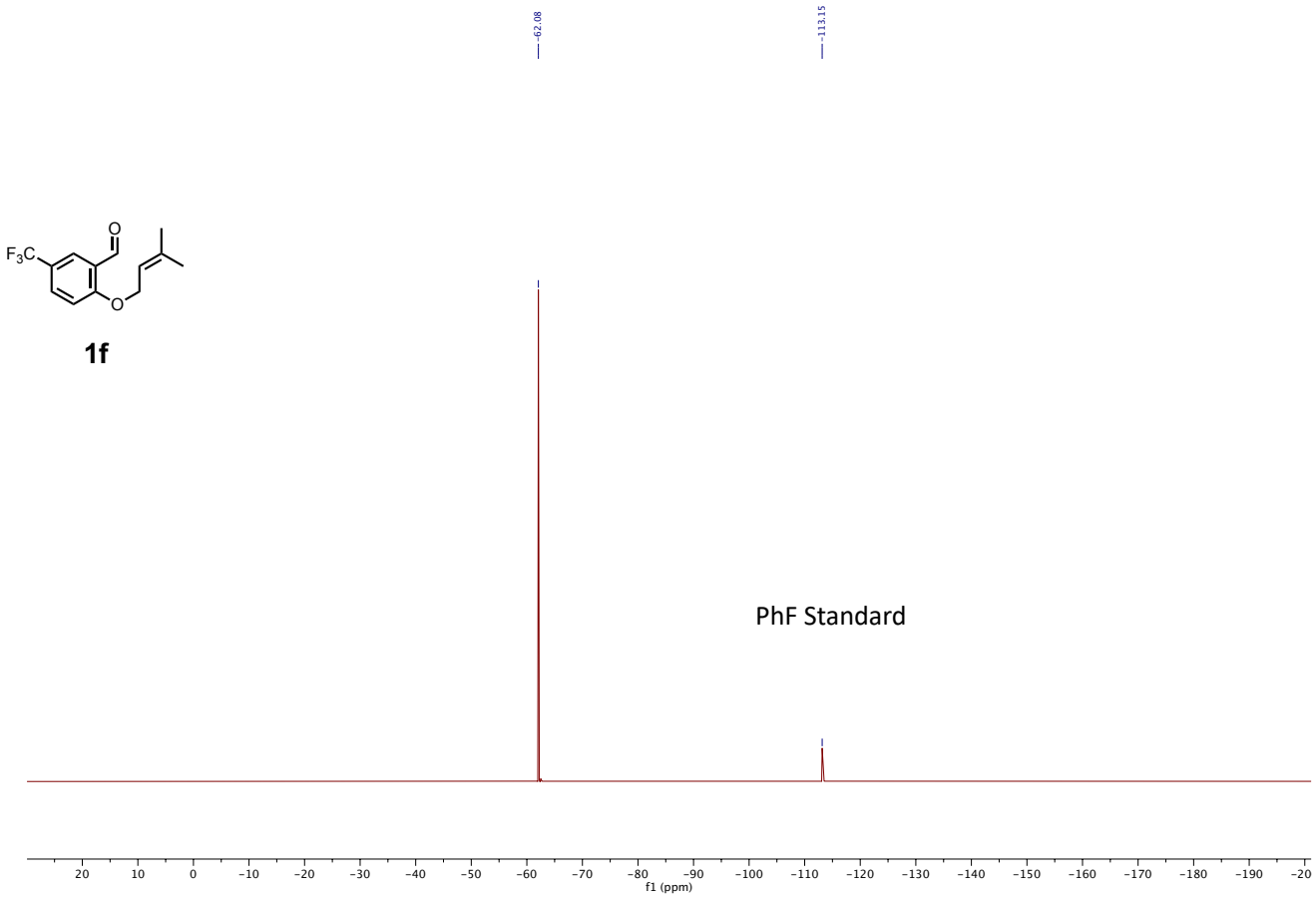
1f

13C NMR, $CDCl_3$, 101 MHz

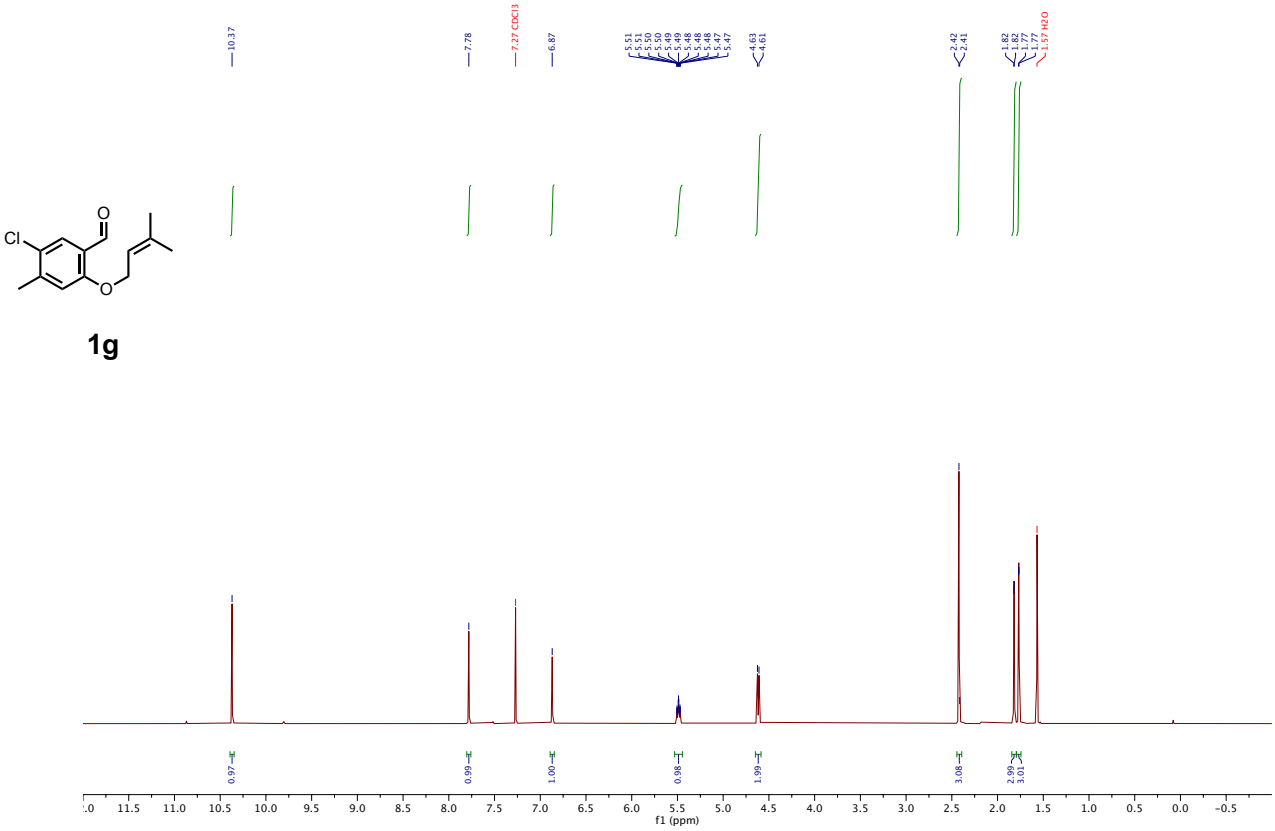


1f

^{19}F NMR, $CDCl_3$, 470 MHz

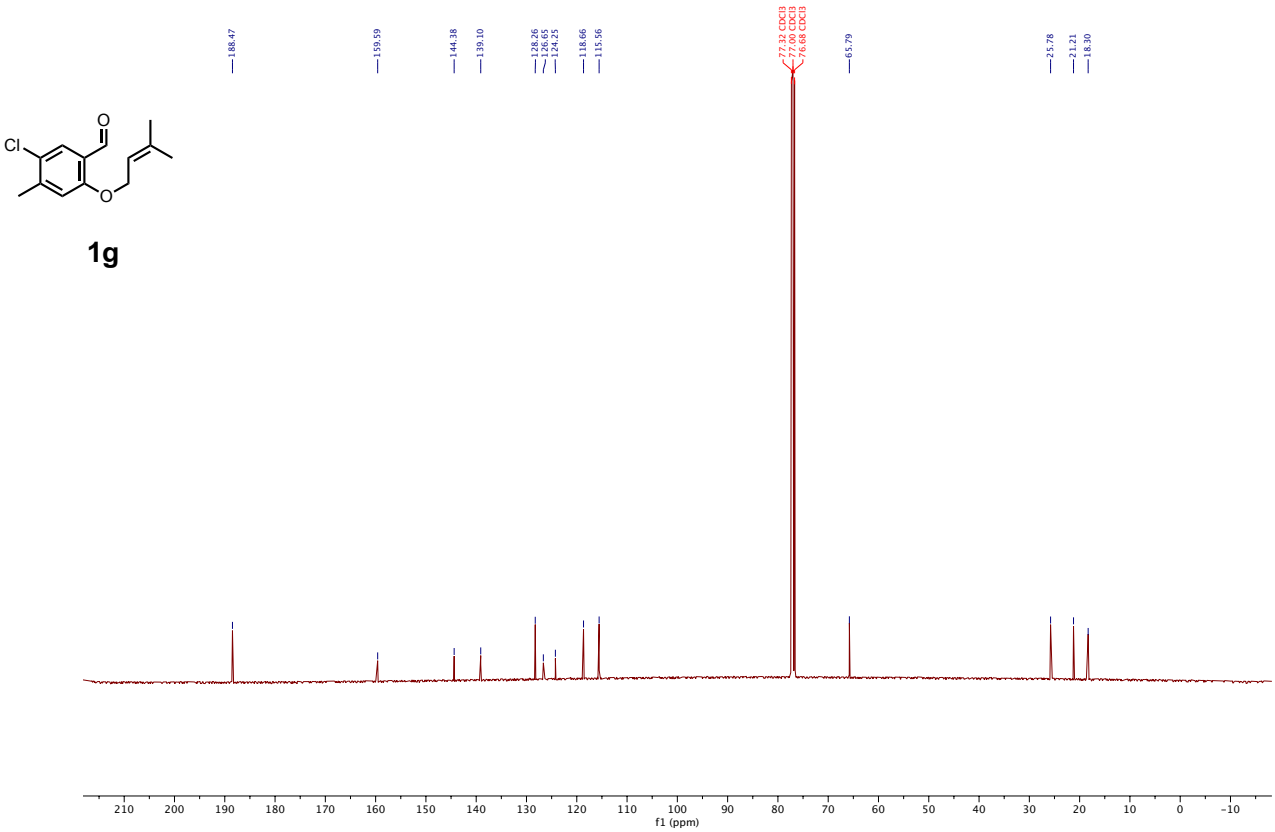


^{1}H NMR, $CDCl_3$, 400 MHz



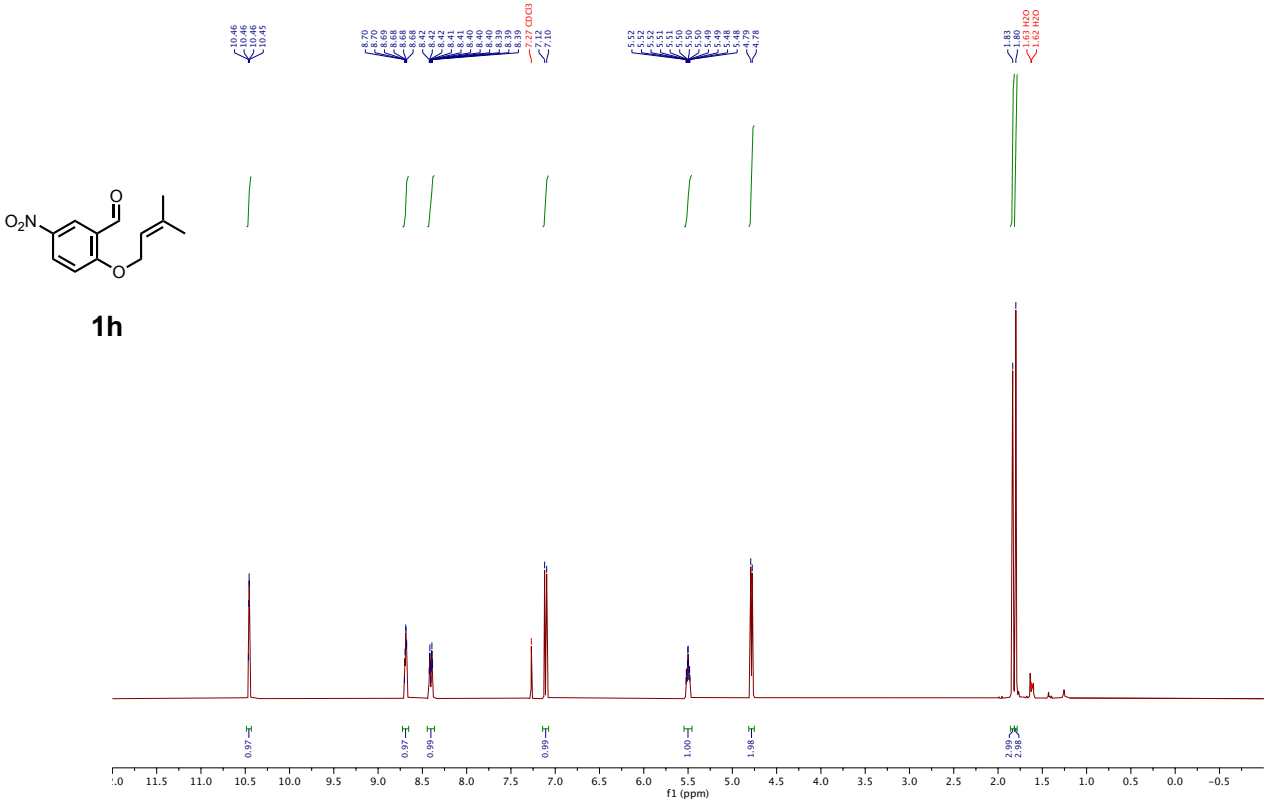
1g

13C NMR, $CDCl_3$, 101 MHz



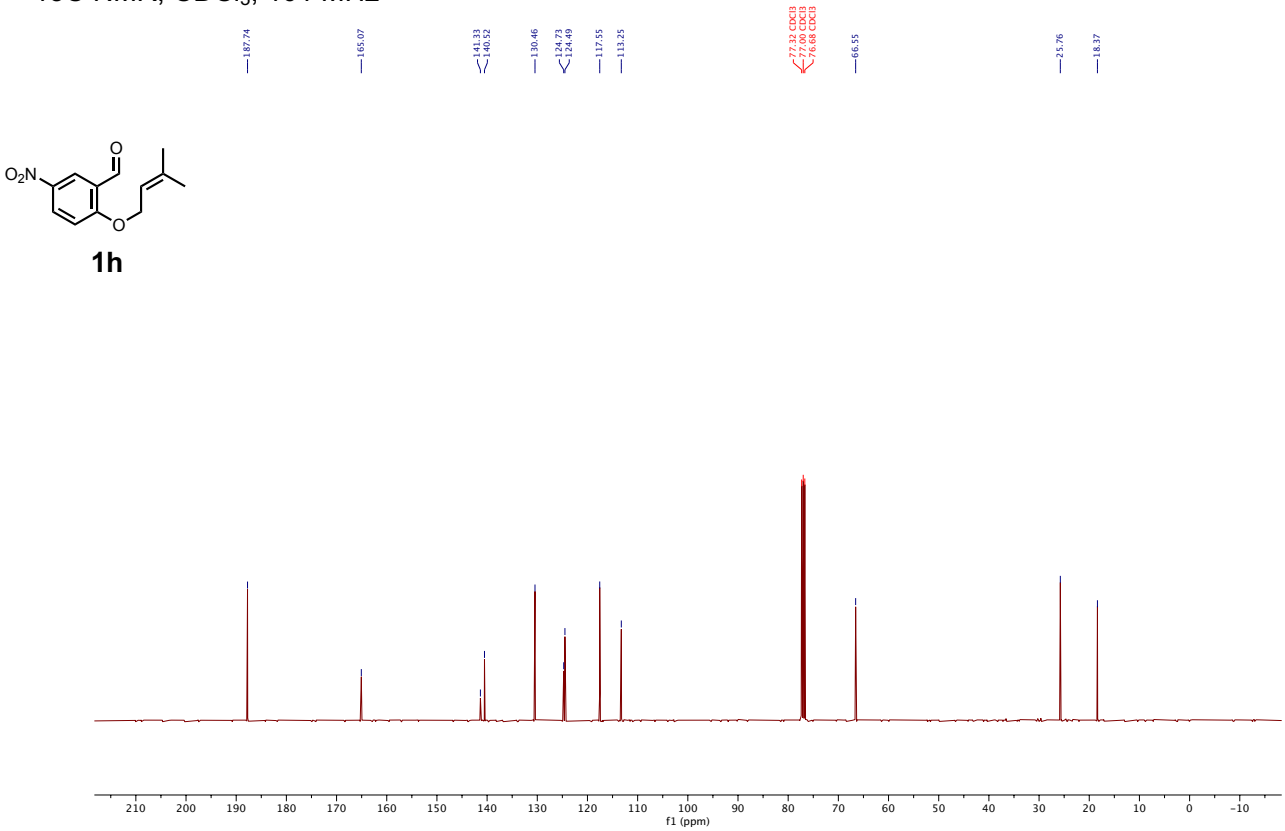
1g

^{1}H NMR, $CDCl_3$, 400 MHz



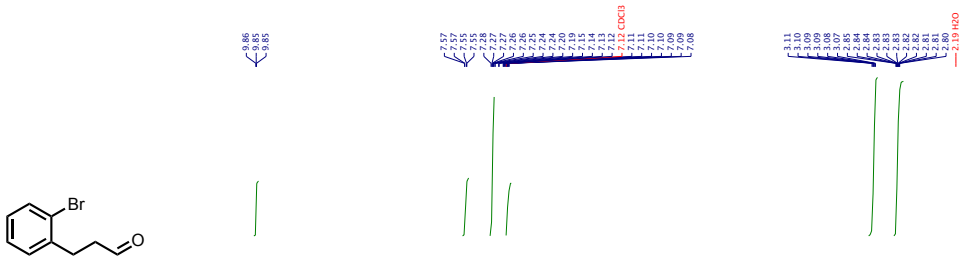
1h

13C NMR, $CDCl_3$, 101 MHz

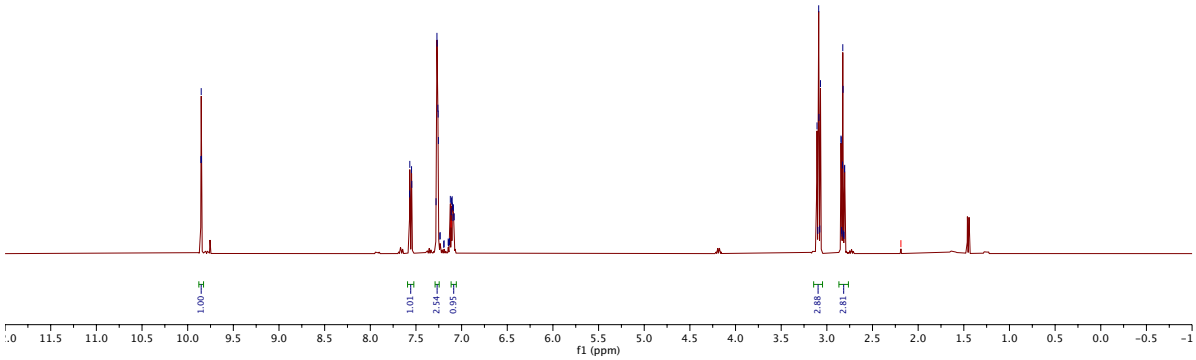


1h

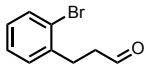
^{1}H NMR, $CDCl_3$, 400 MHz



1i-int1



13C NMR, $CDCl_3$, 101 MHz



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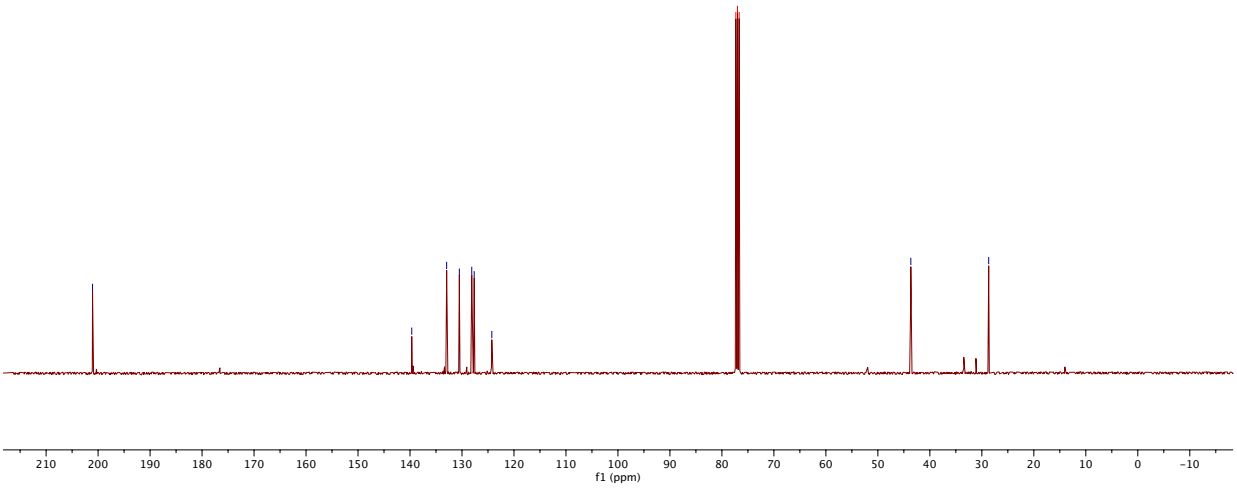
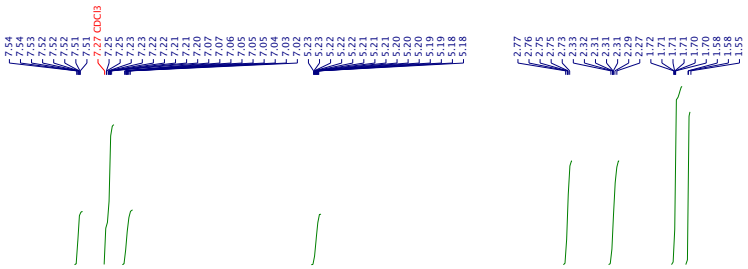
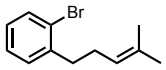
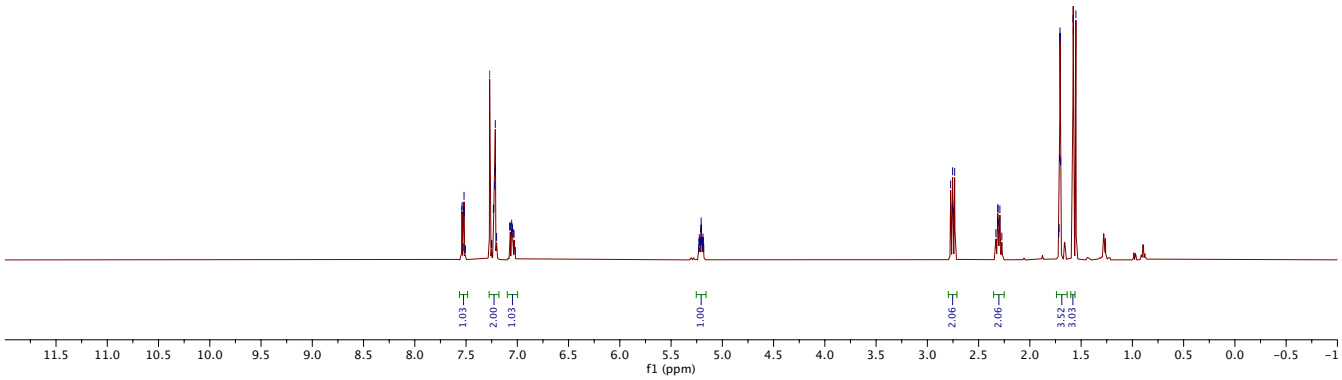


^{1}H NMR, $CDCl_3$, 400 MHz

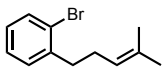




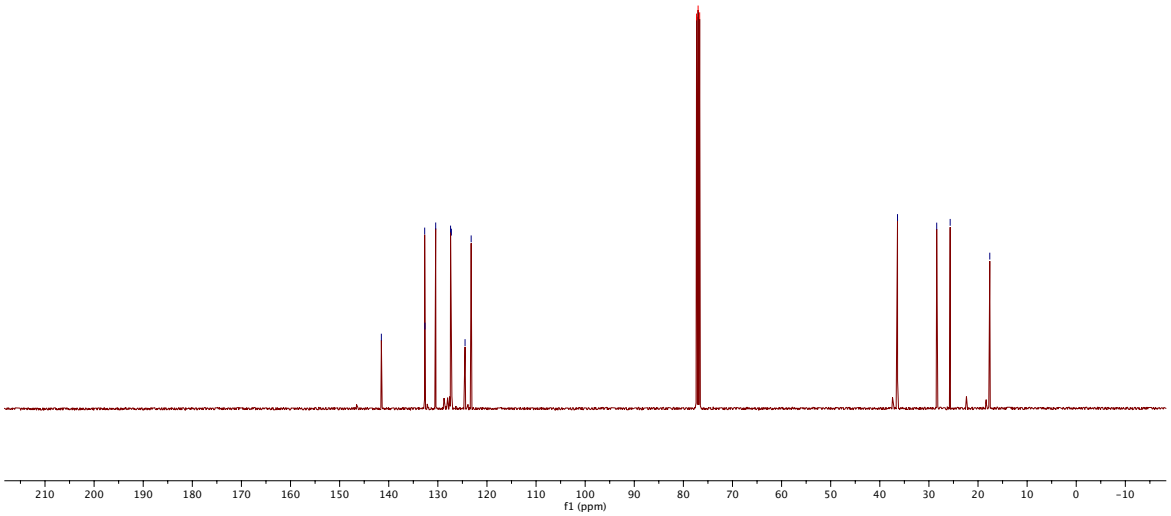
1i-int2



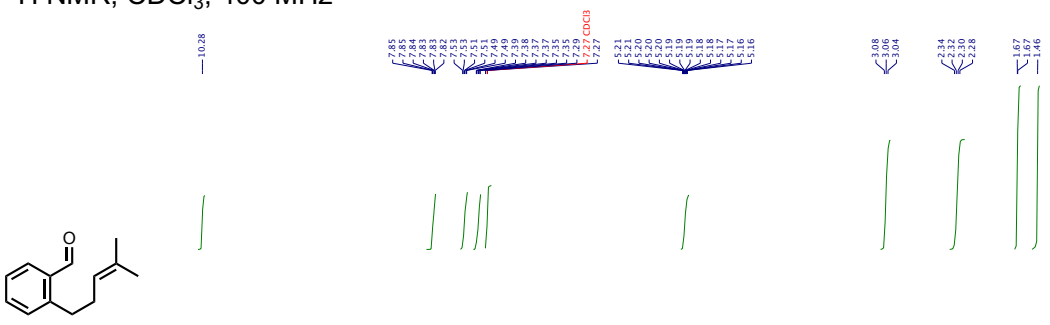
13C NMR, $CDCl_3$, 101 MHz



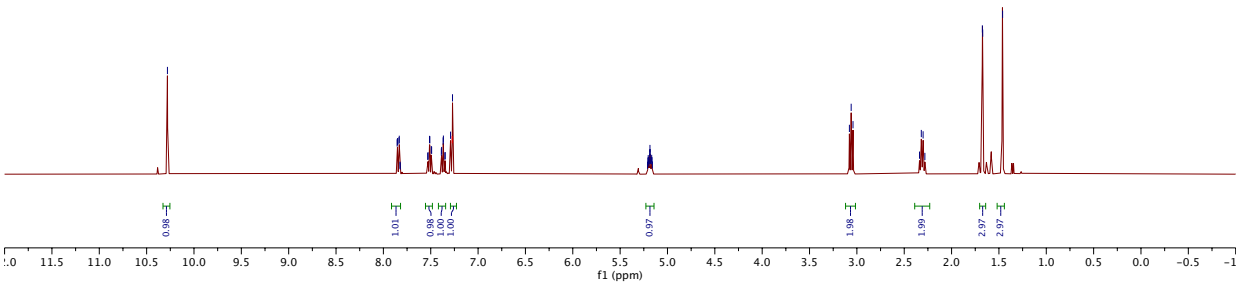
1i-int2



^{1}H NMR, $CDCl_3$, 400 MHz

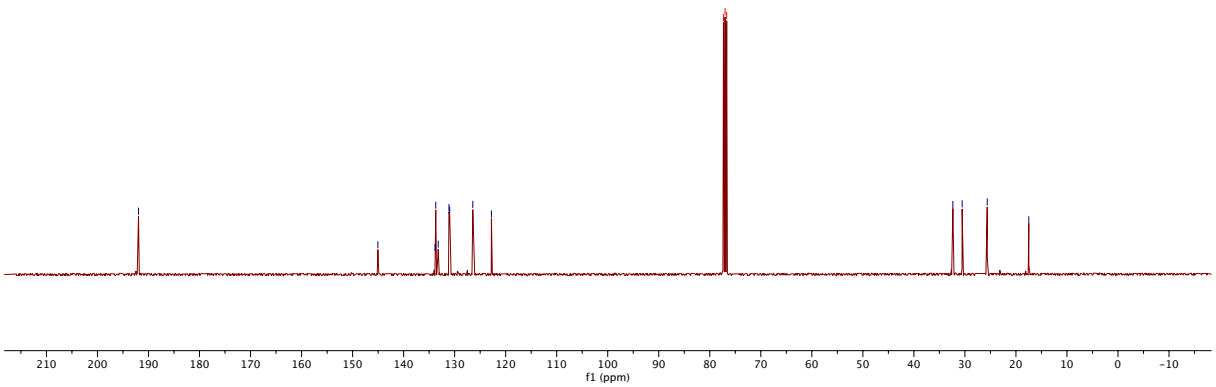


1i

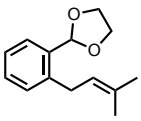


13C NMR, $CDCl_3$, 101 MHz

1i

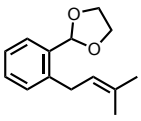


^{1}H NMR, $CDCl_3$, 400 MHz



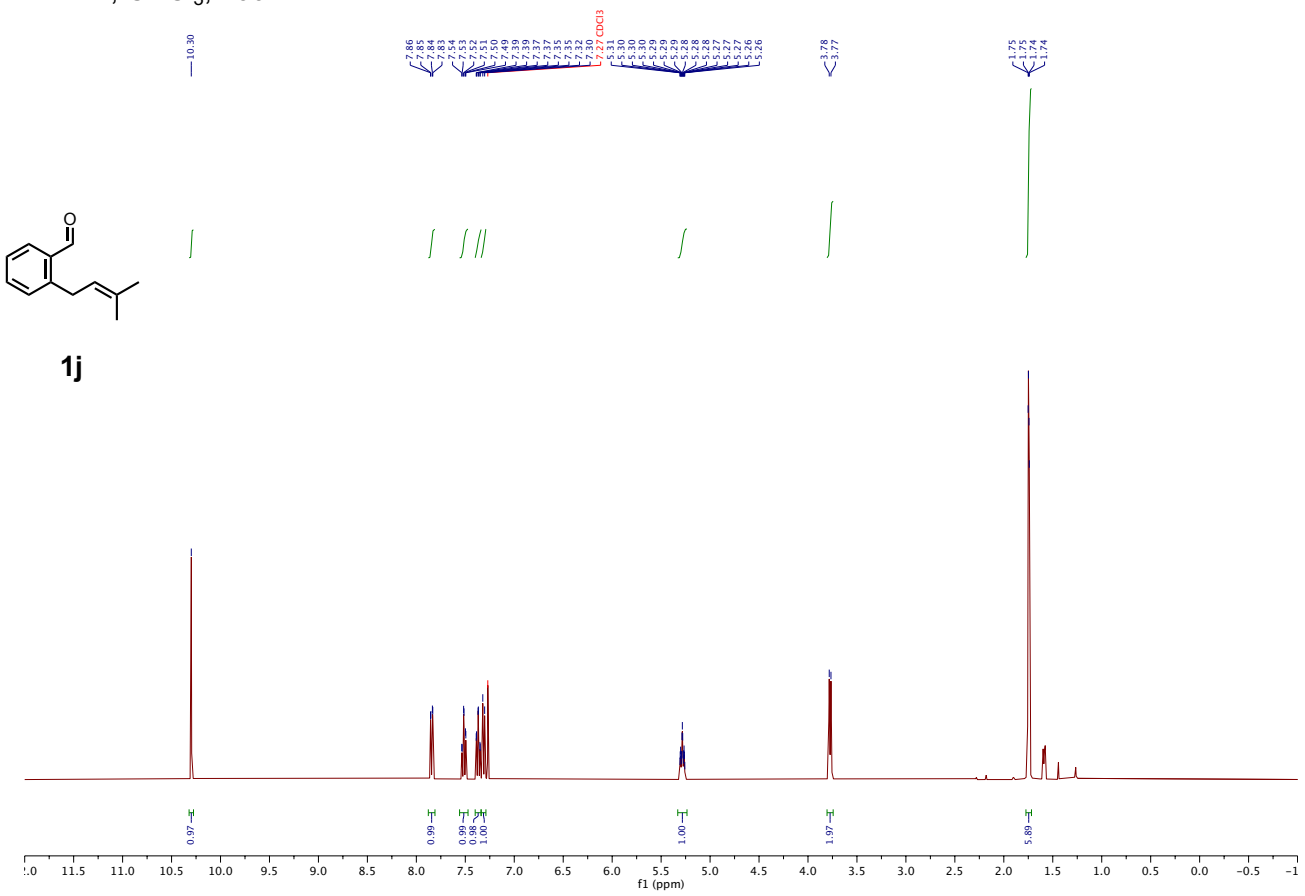
1j-int1

13C NMR, $CDCl_3$, 101 MHz



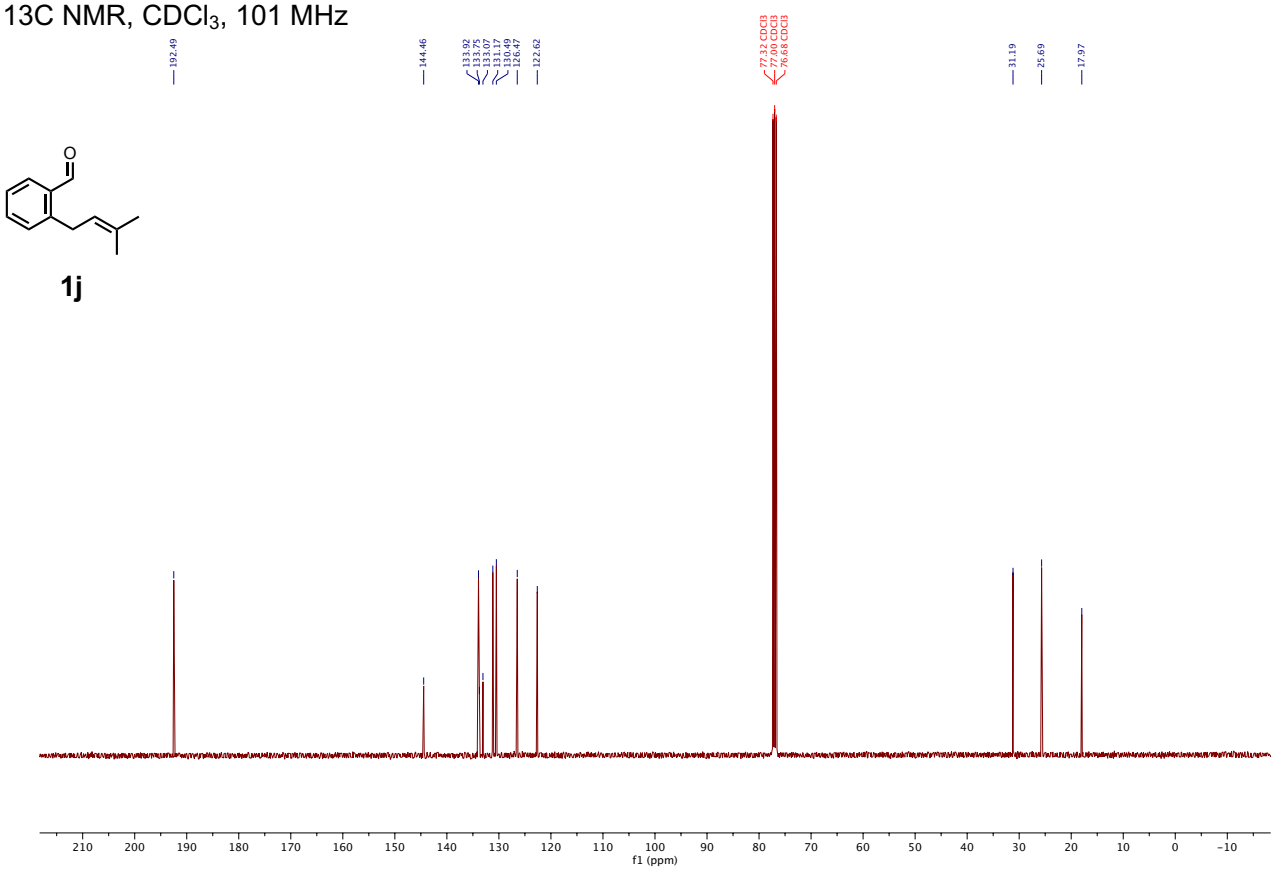
1j-int1

^{1}H NMR, $CDCl_3$, 400 MHz



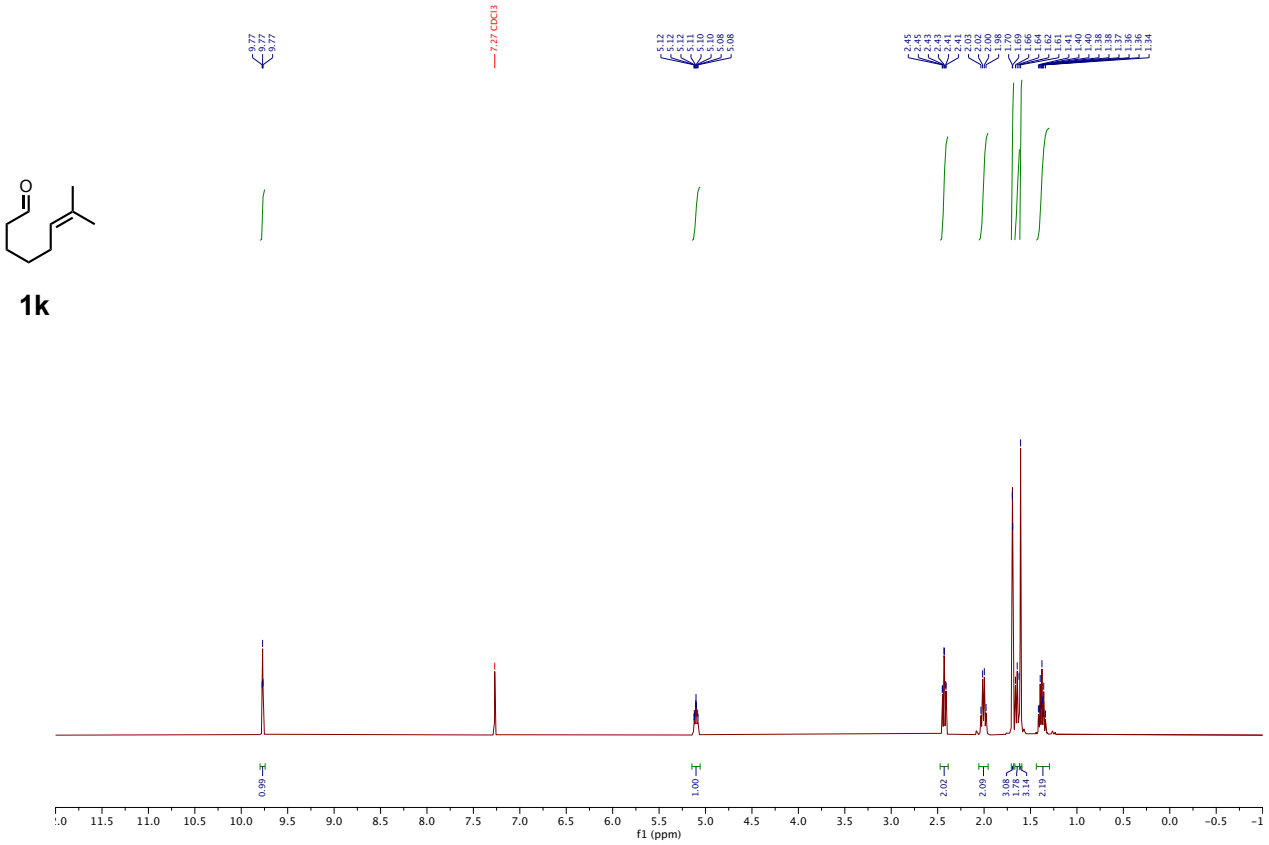
1j

13C NMR, $CDCl_3$, 101 MHz



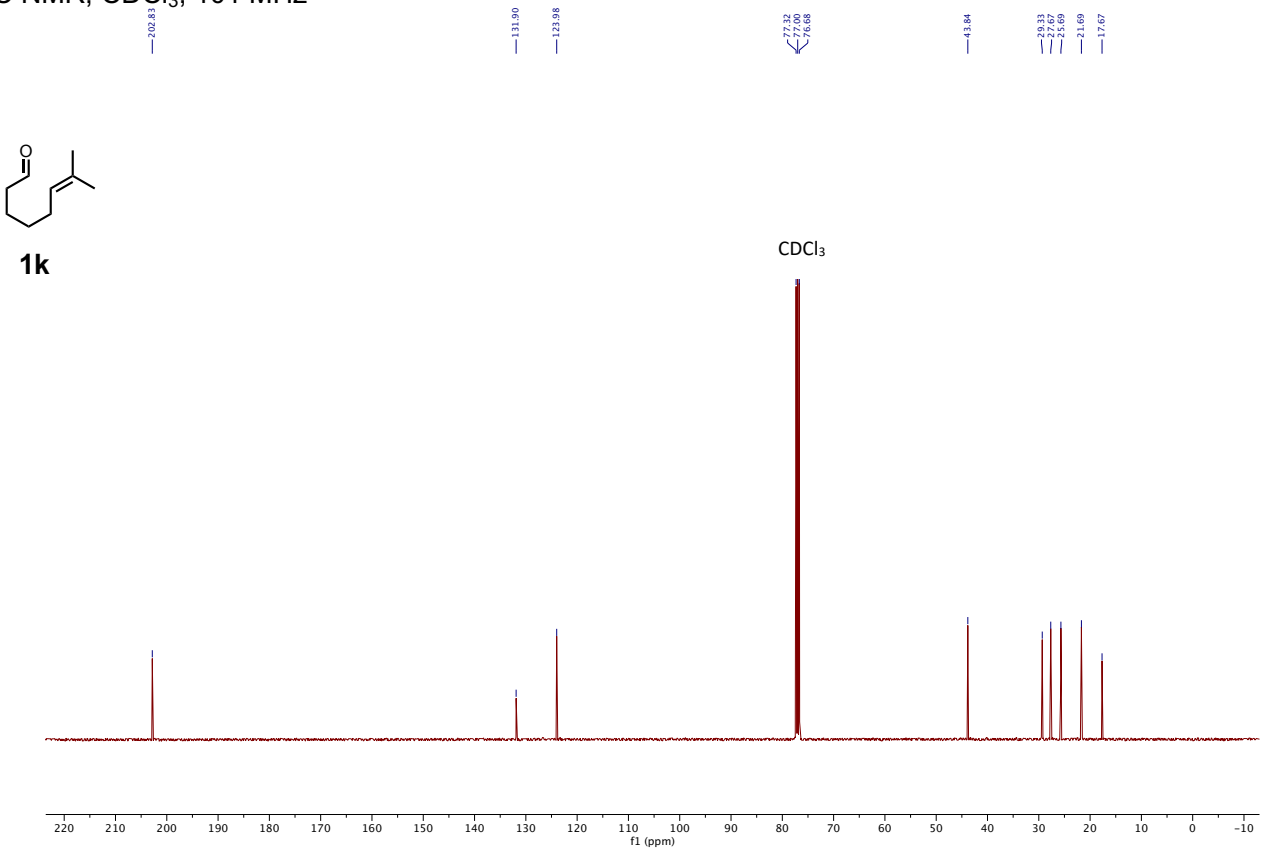
1j

^{1}H NMR, $CDCl_3$, 400 MHz



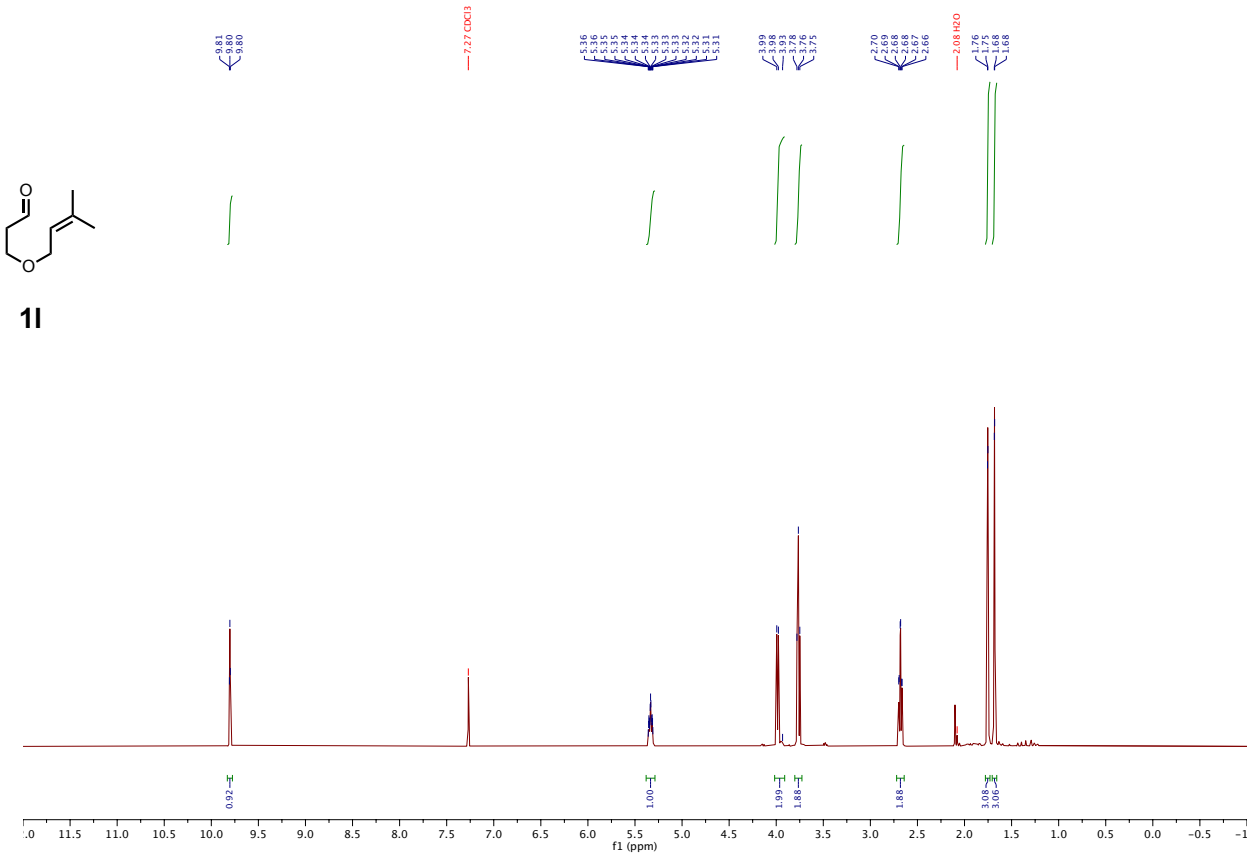
1k

13C NMR, $CDCl_3$, 101 MHz



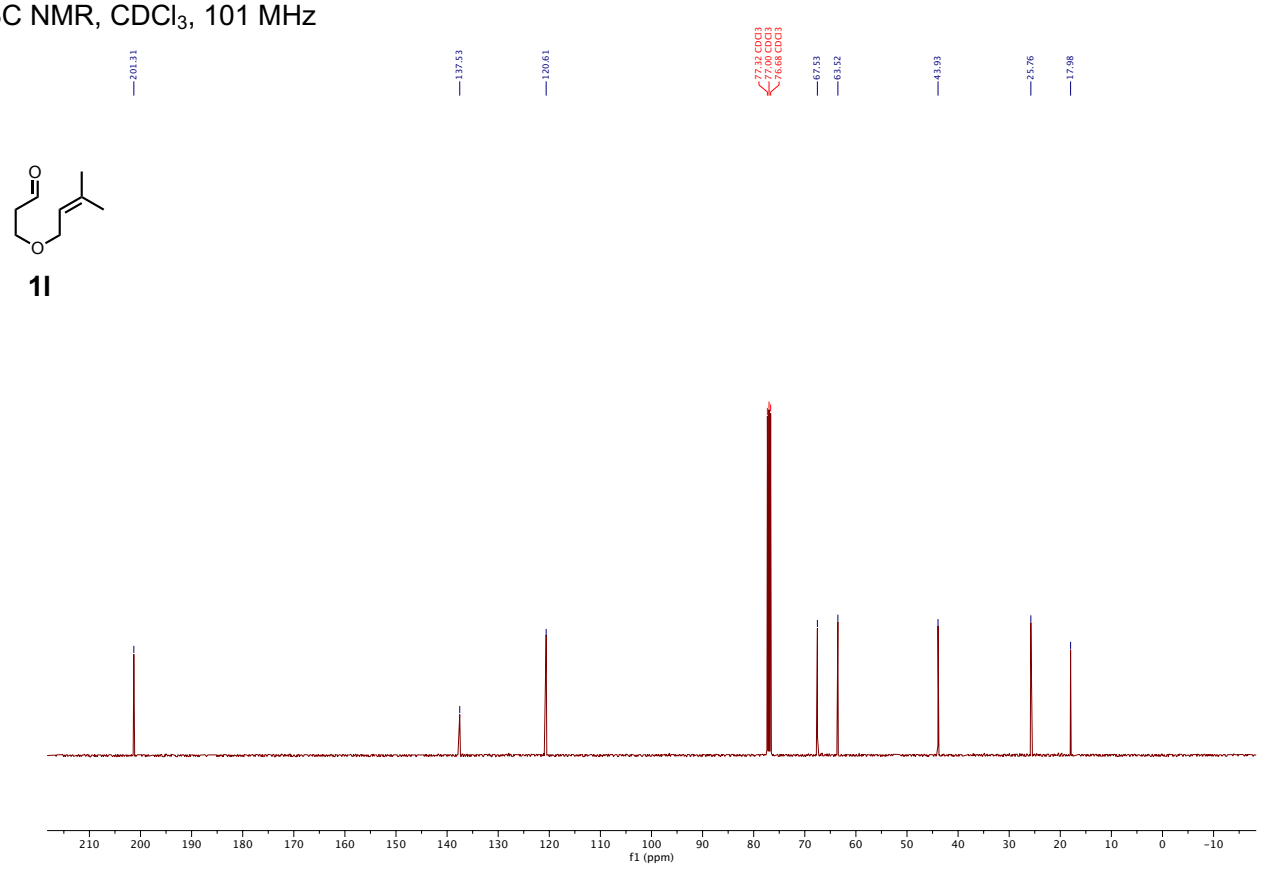
1k

^{1}H NMR, $CDCl_3$, 400 MHz



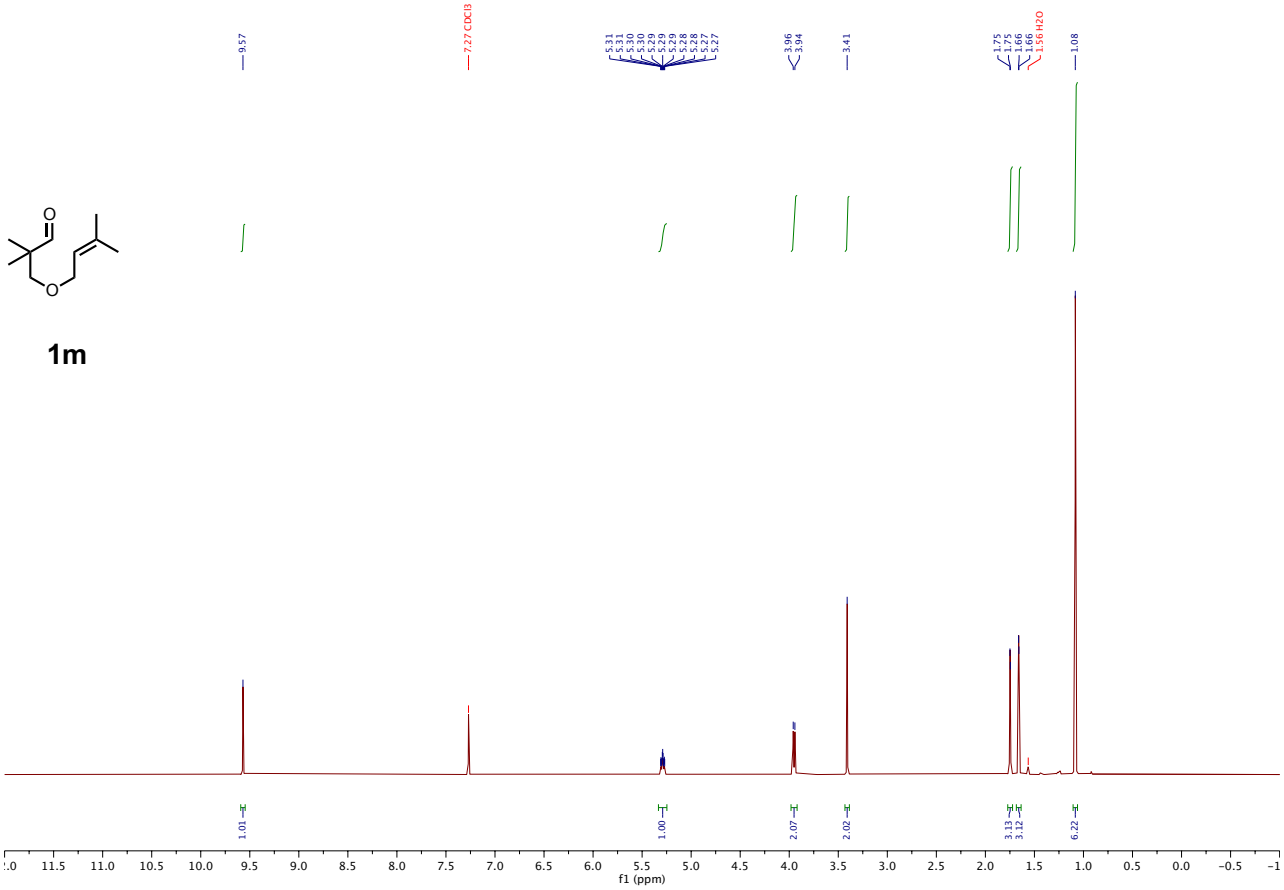
1l

13C NMR, $CDCl_3$, 101 MHz



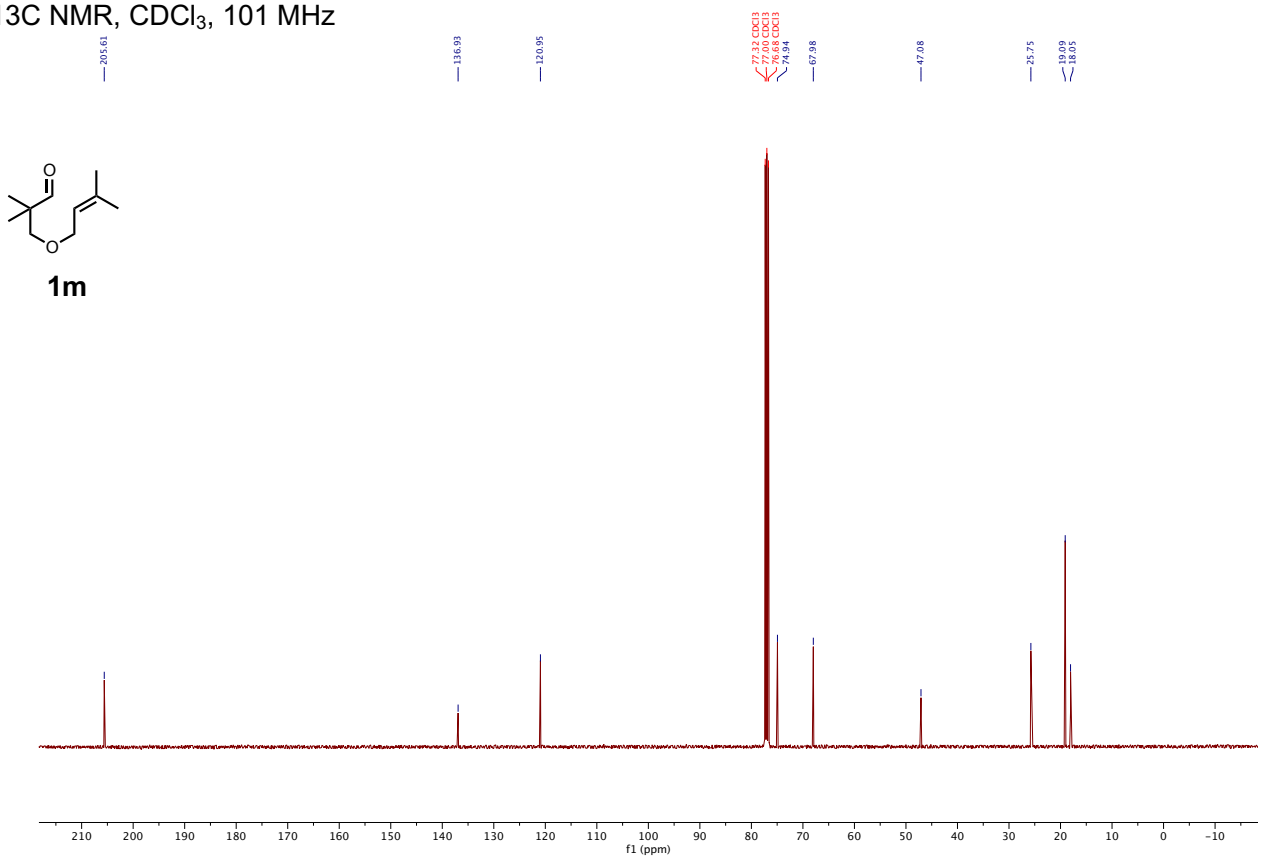
1l

^{1}H NMR, $CDCl_3$, 400 MHz



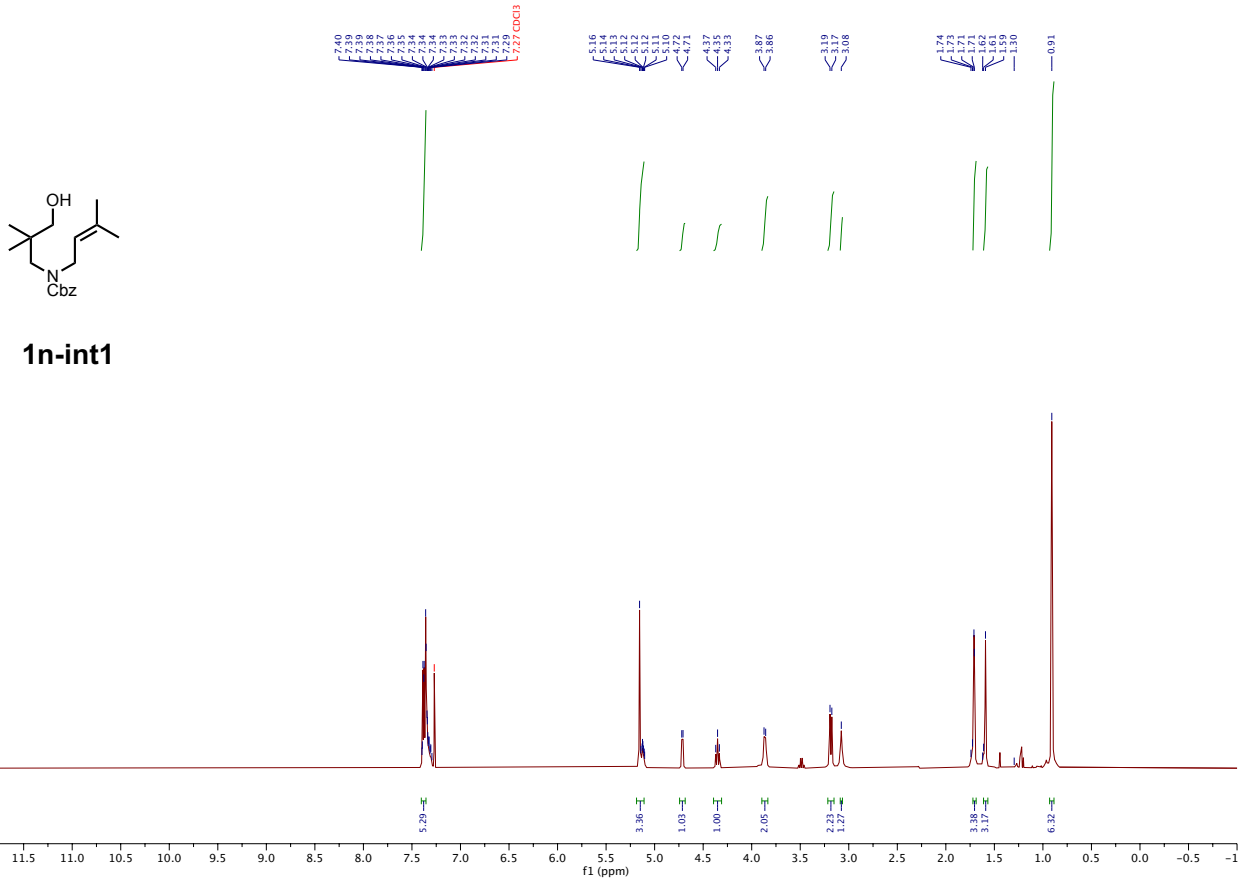
1m

13C NMR, $CDCl_3$, 101 MHz



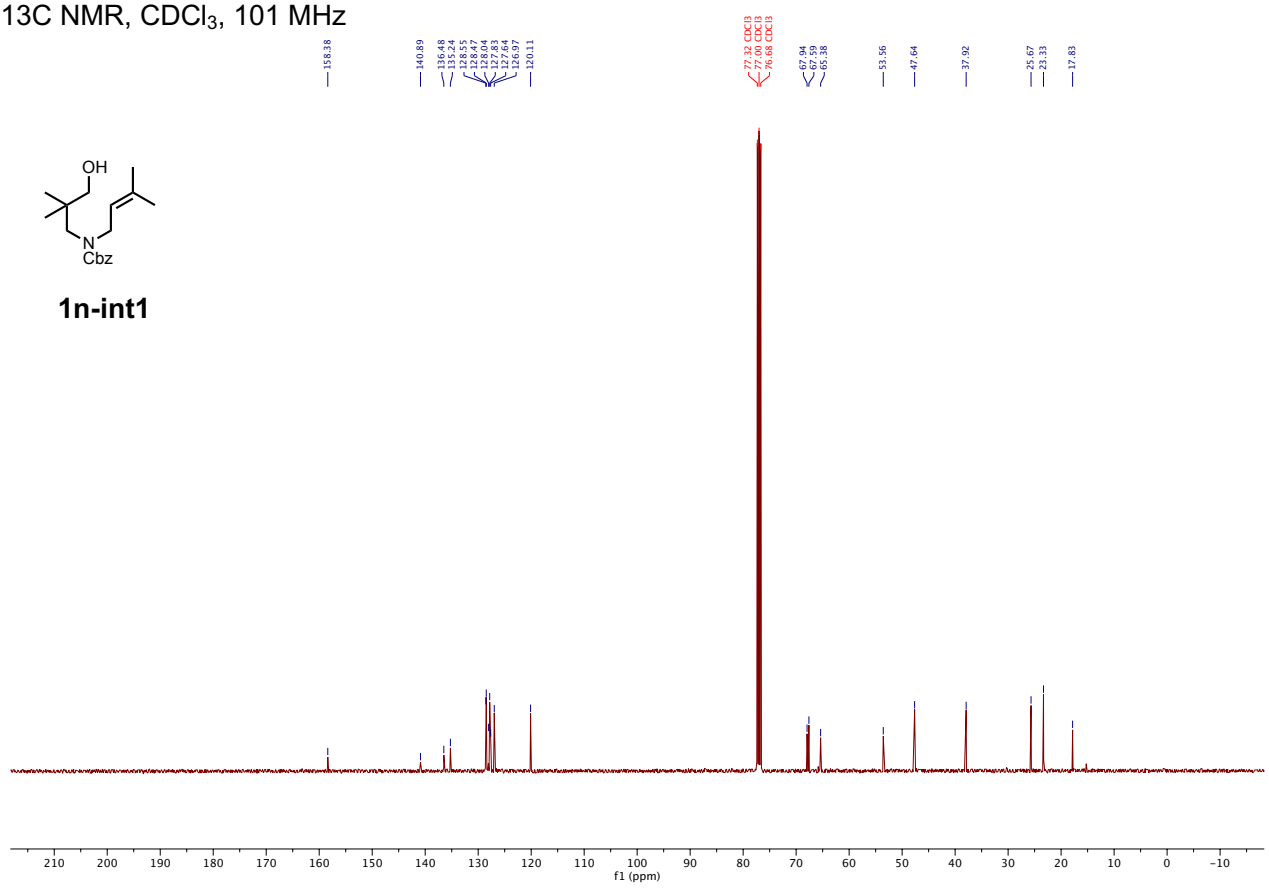
1m

^{1}H NMR, $CDCl_3$, 400 MHz



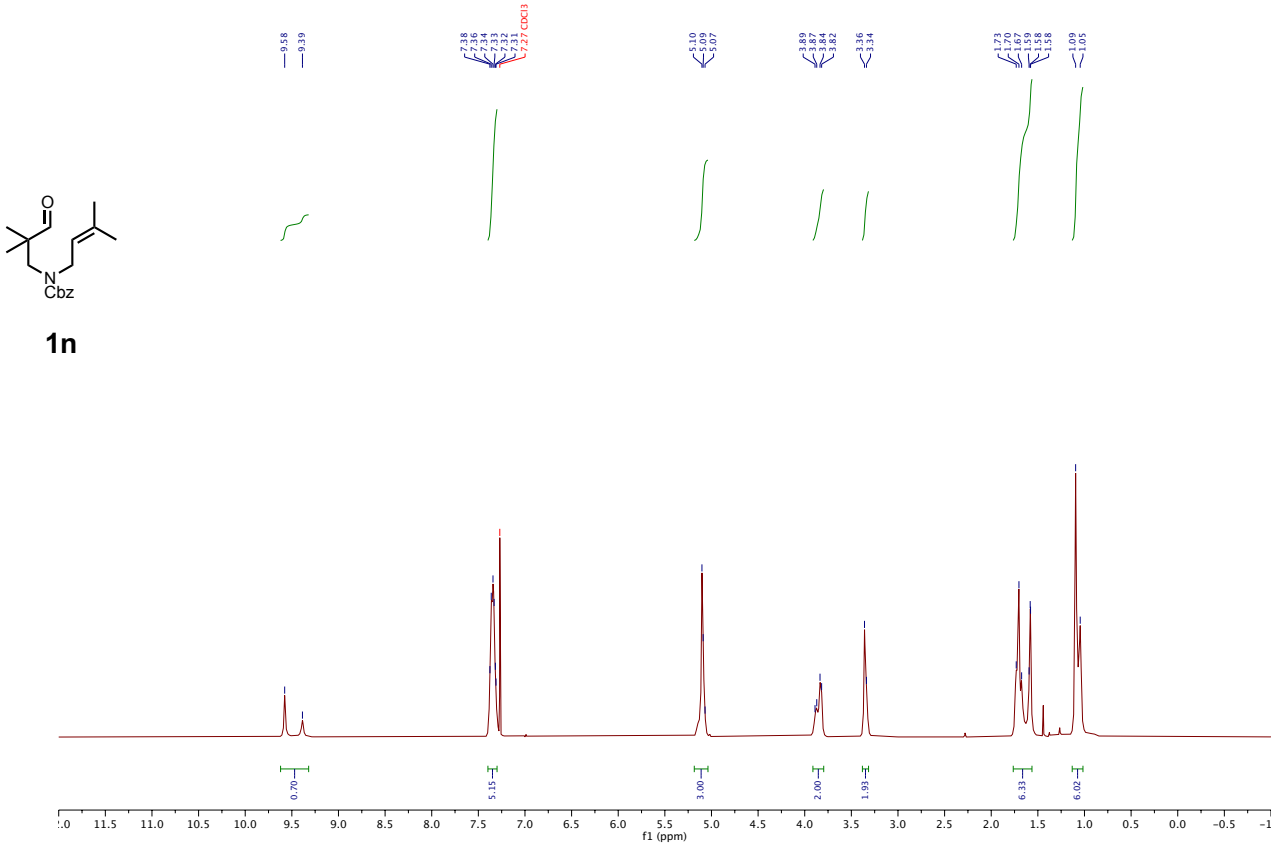
1n-int1

13C NMR, $CDCl_3$, 101 MHz



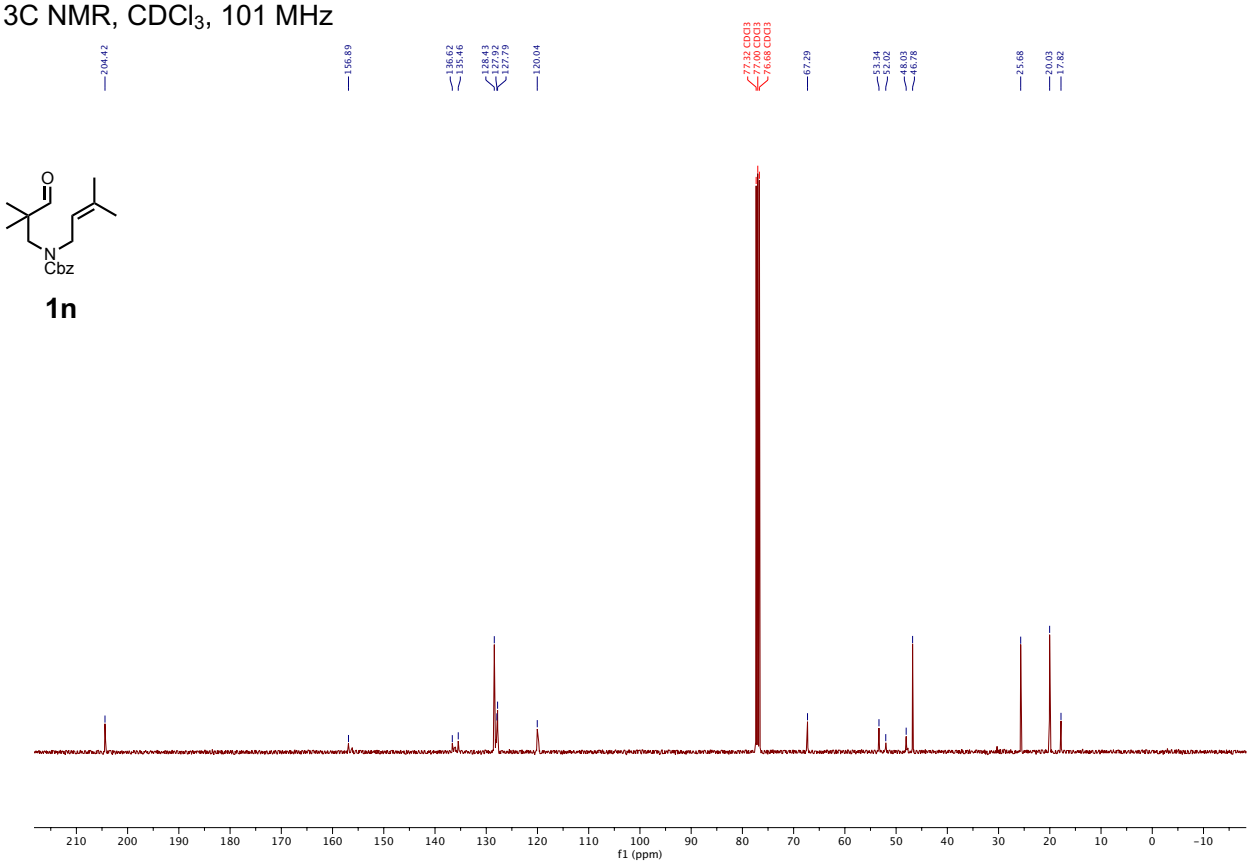
1n-int1

^{1}H NMR, $CDCl_3$, 400 MHz



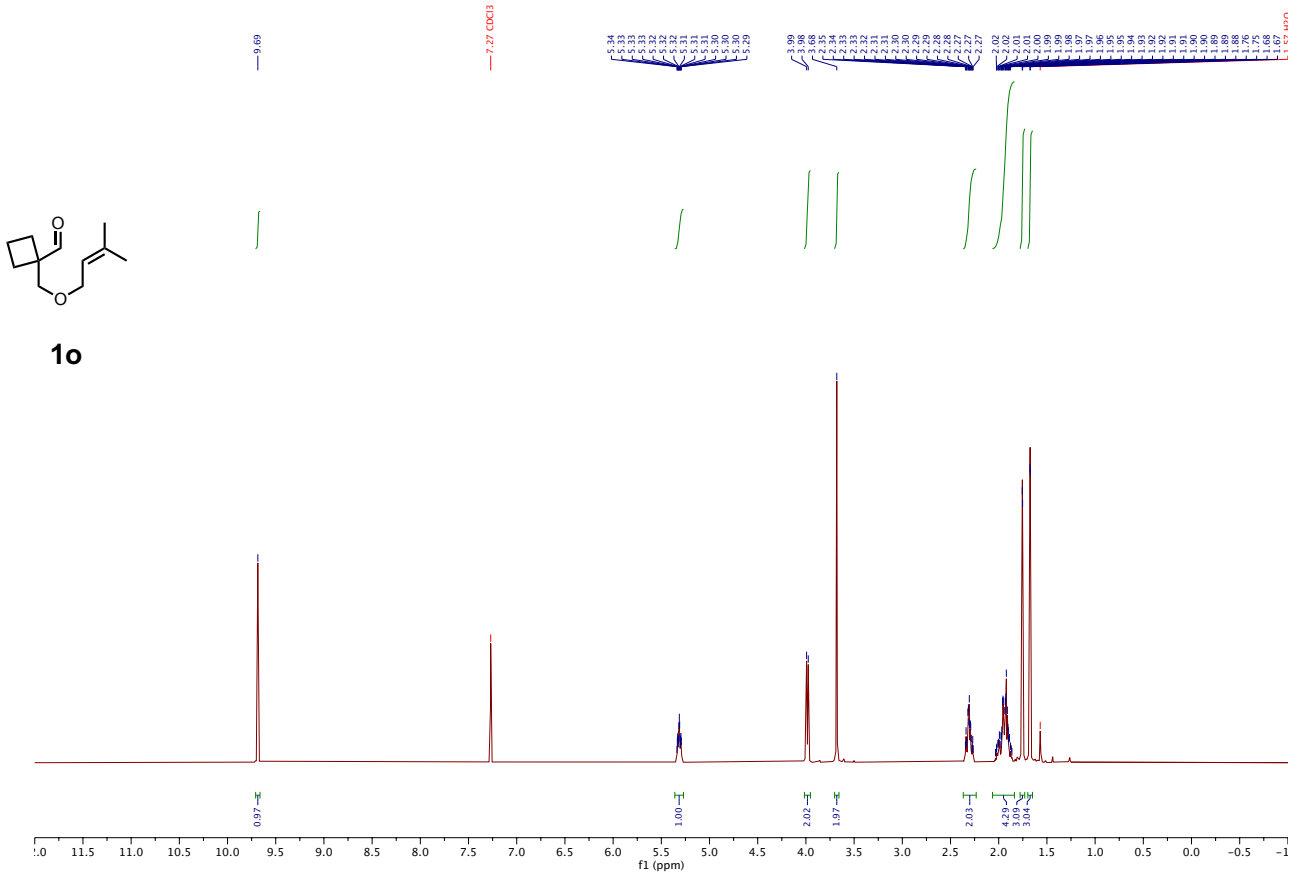
1n

13C NMR, $CDCl_3$, 101 MHz



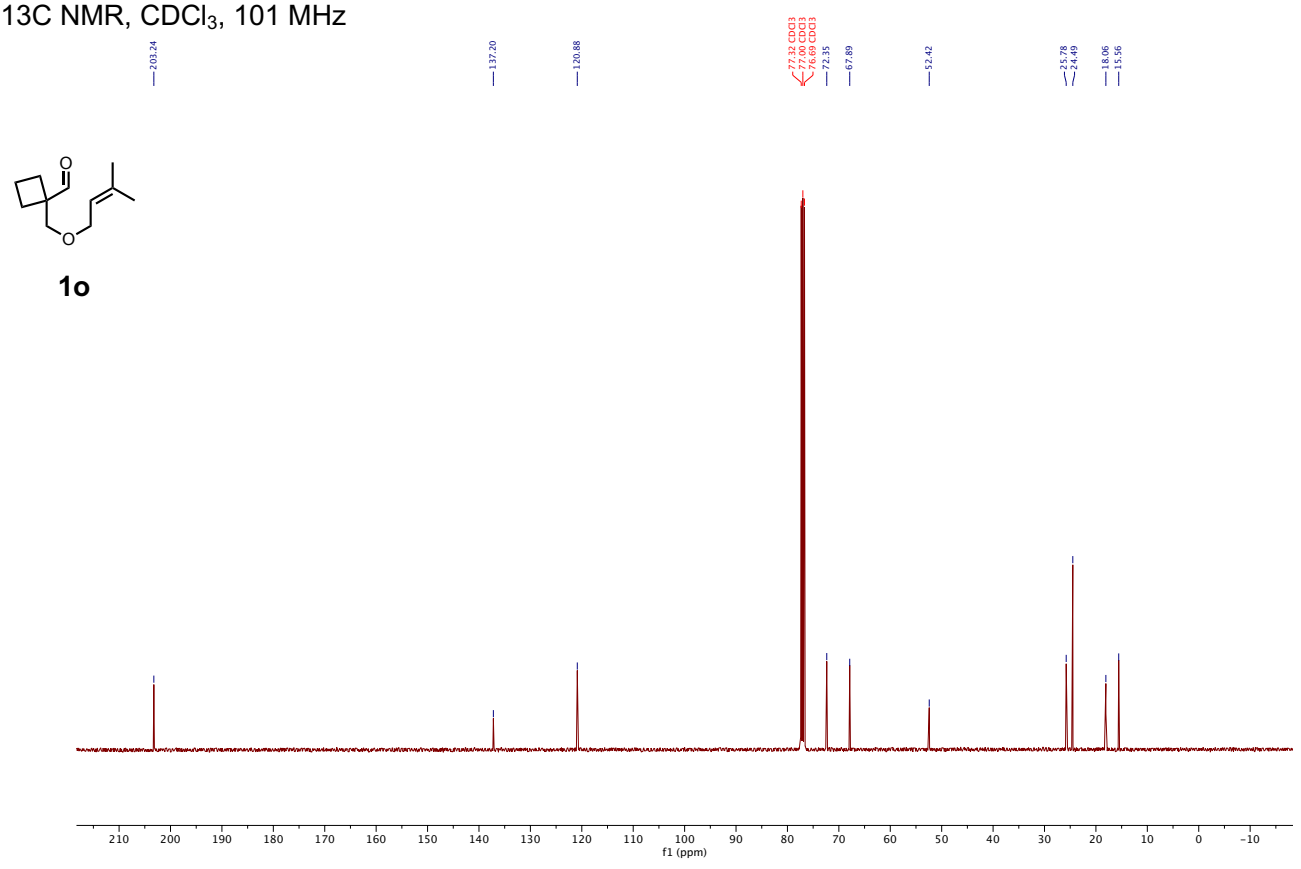
1n

^{1}H NMR, $CDCl_3$, 400 MHz



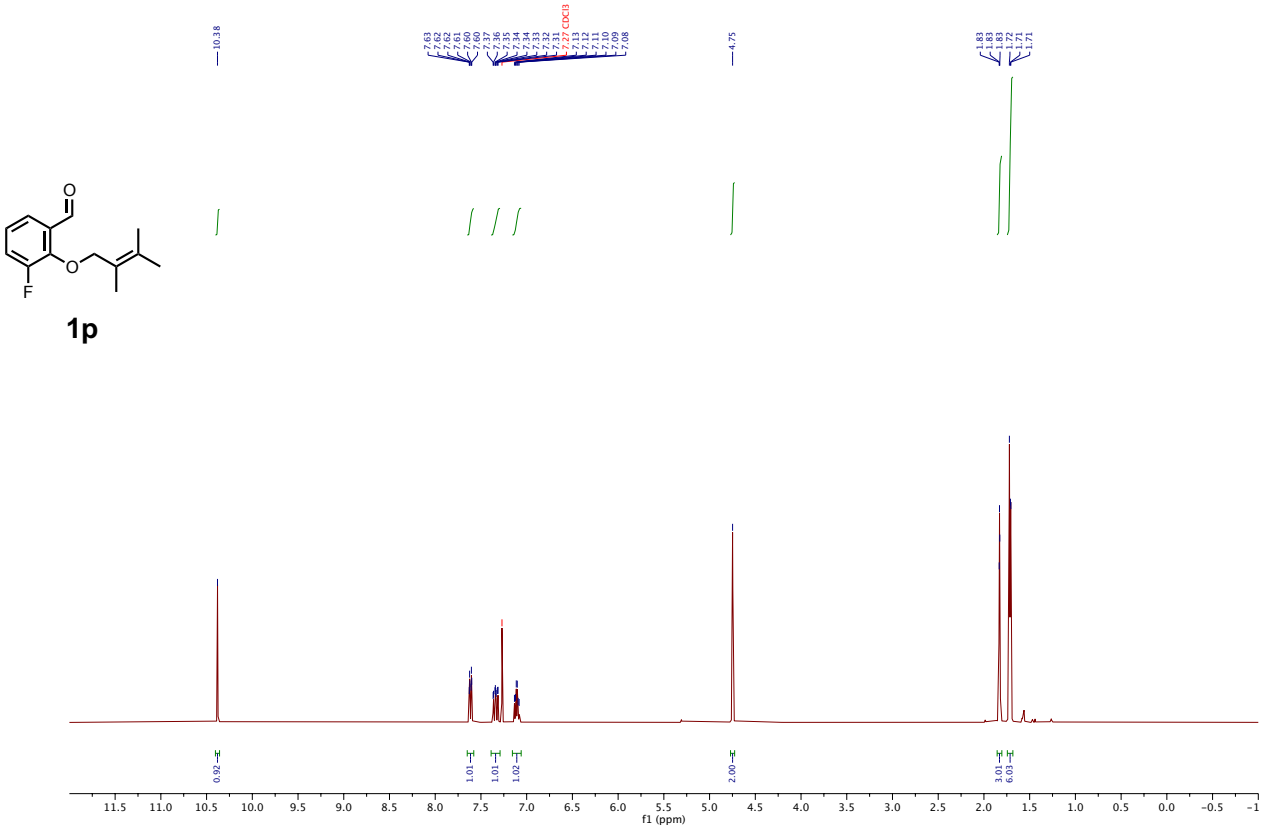
1o

13C NMR, $CDCl_3$, 101 MHz



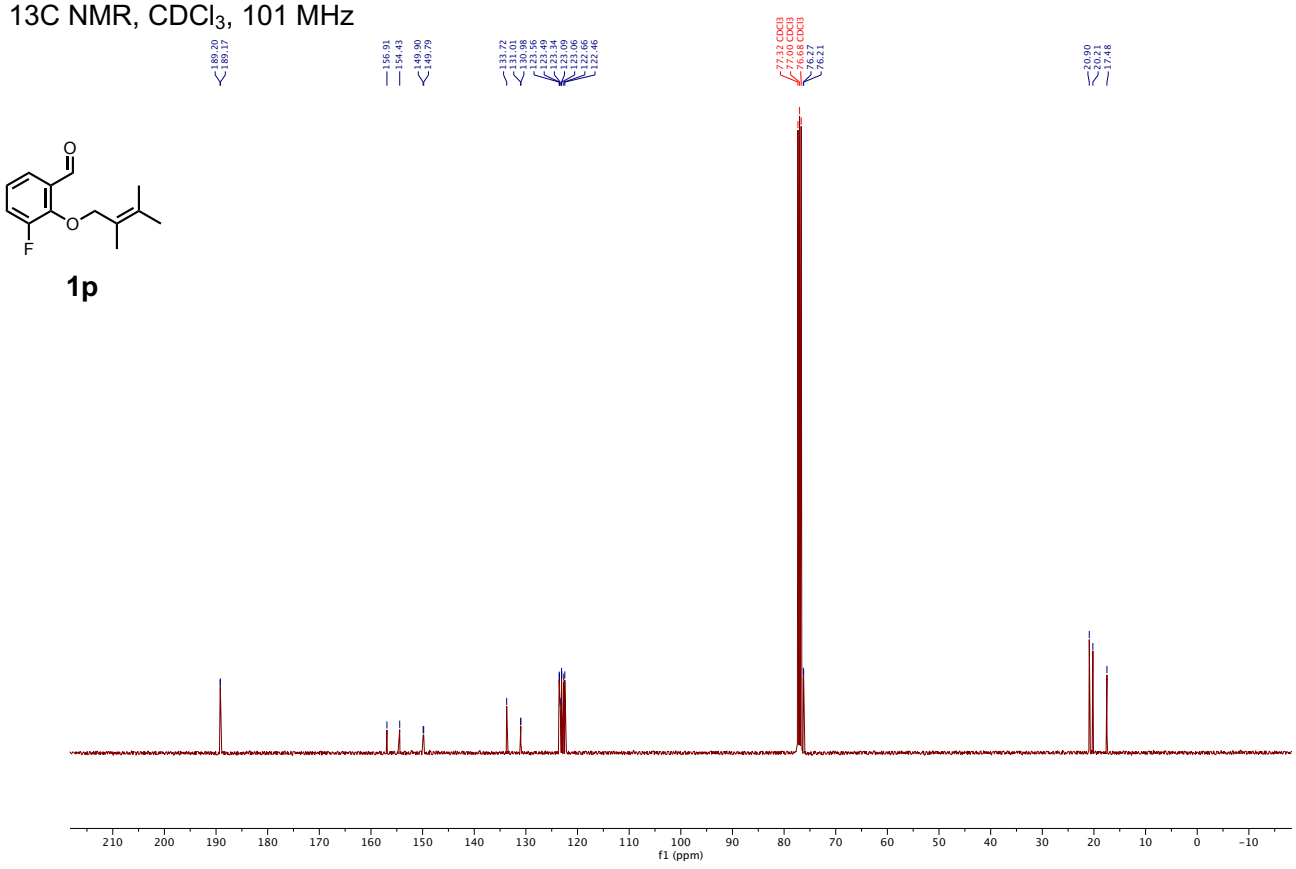
1o

^{1}H NMR, $CDCl_3$, 400 MHz



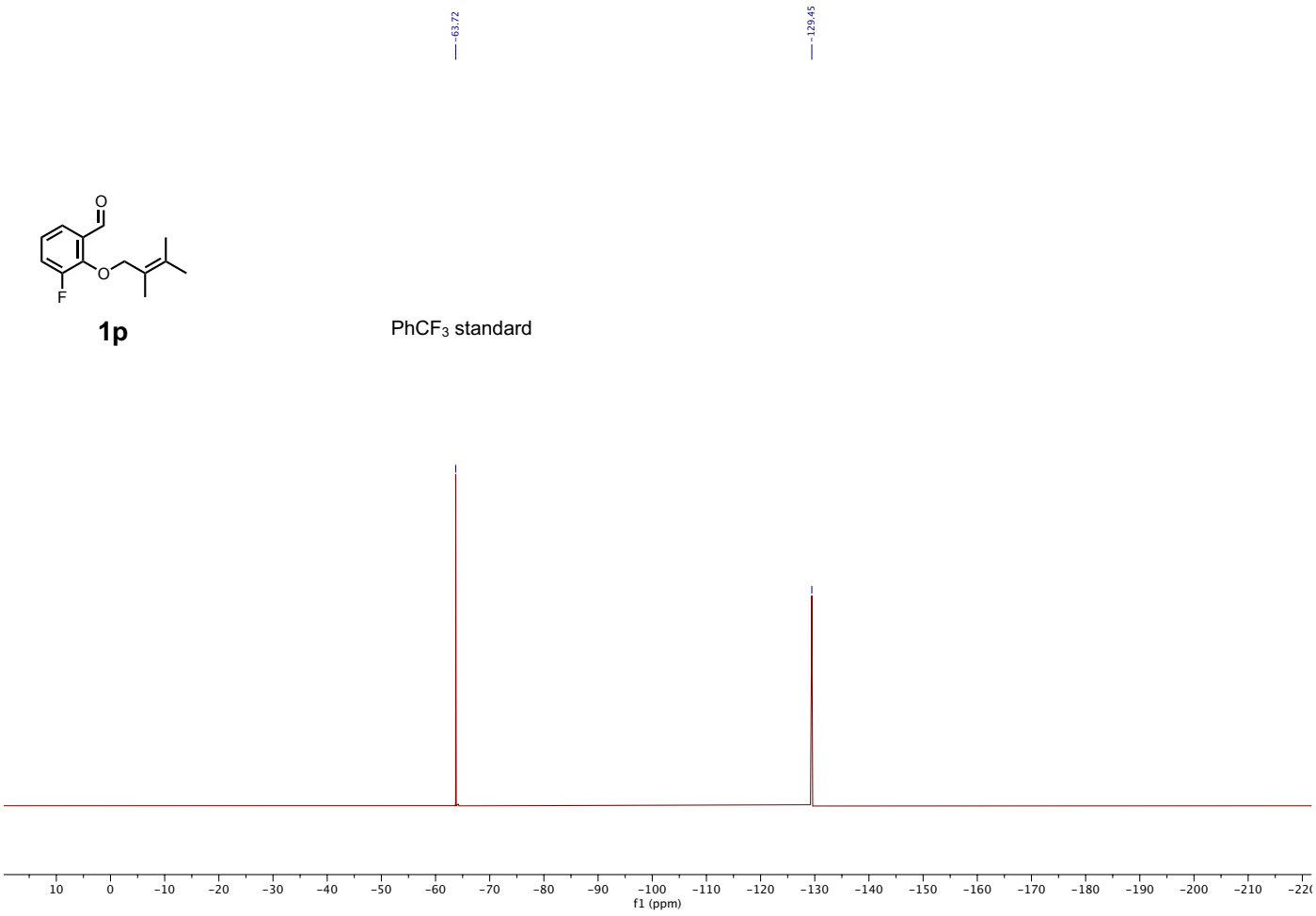
1p

13C NMR, $CDCl_3$, 101 MHz



1p

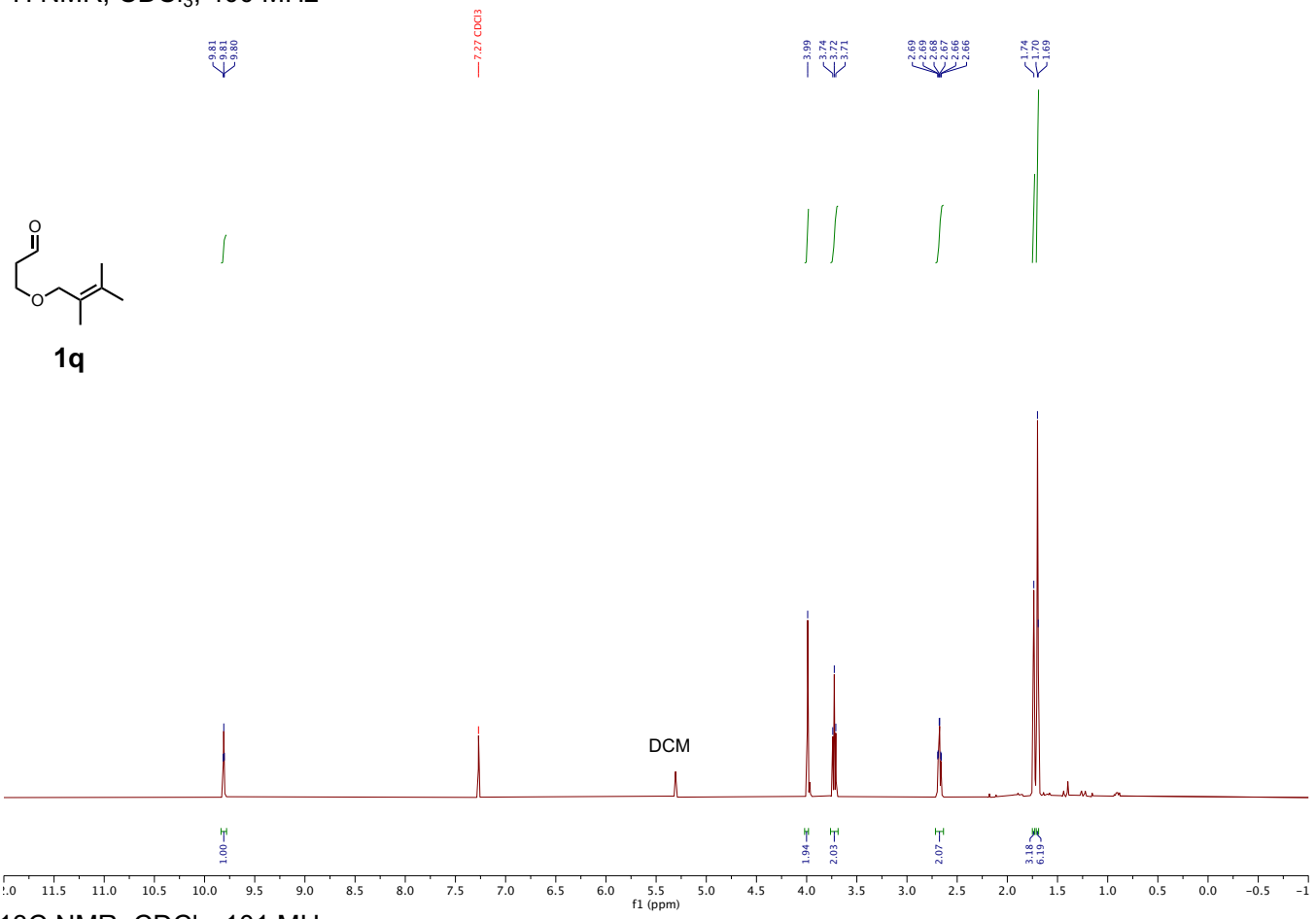
^{19}F NMR, $CDCl_3$, 376 MHz



1p

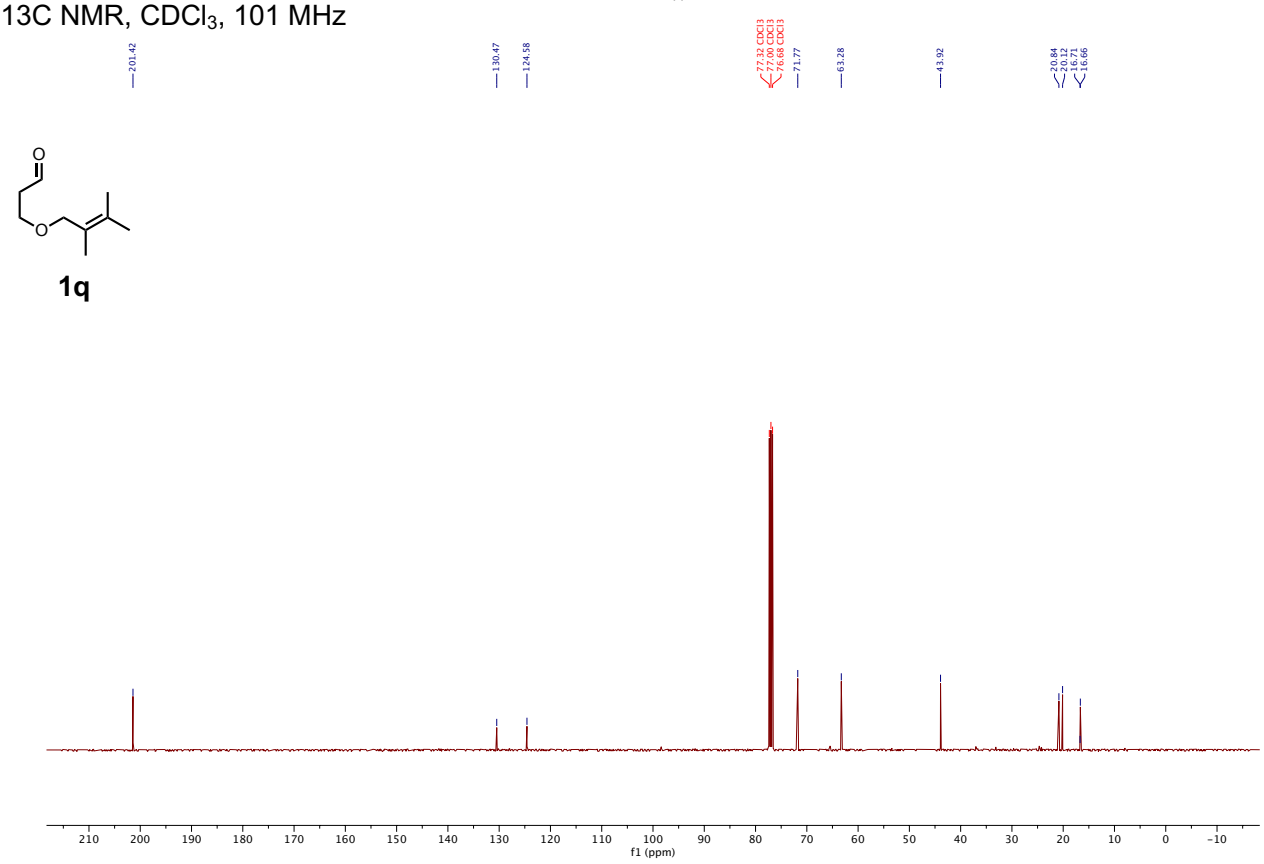
$PhCF_3$ standard

^{1}H NMR, $CDCl_3$, 400 MHz



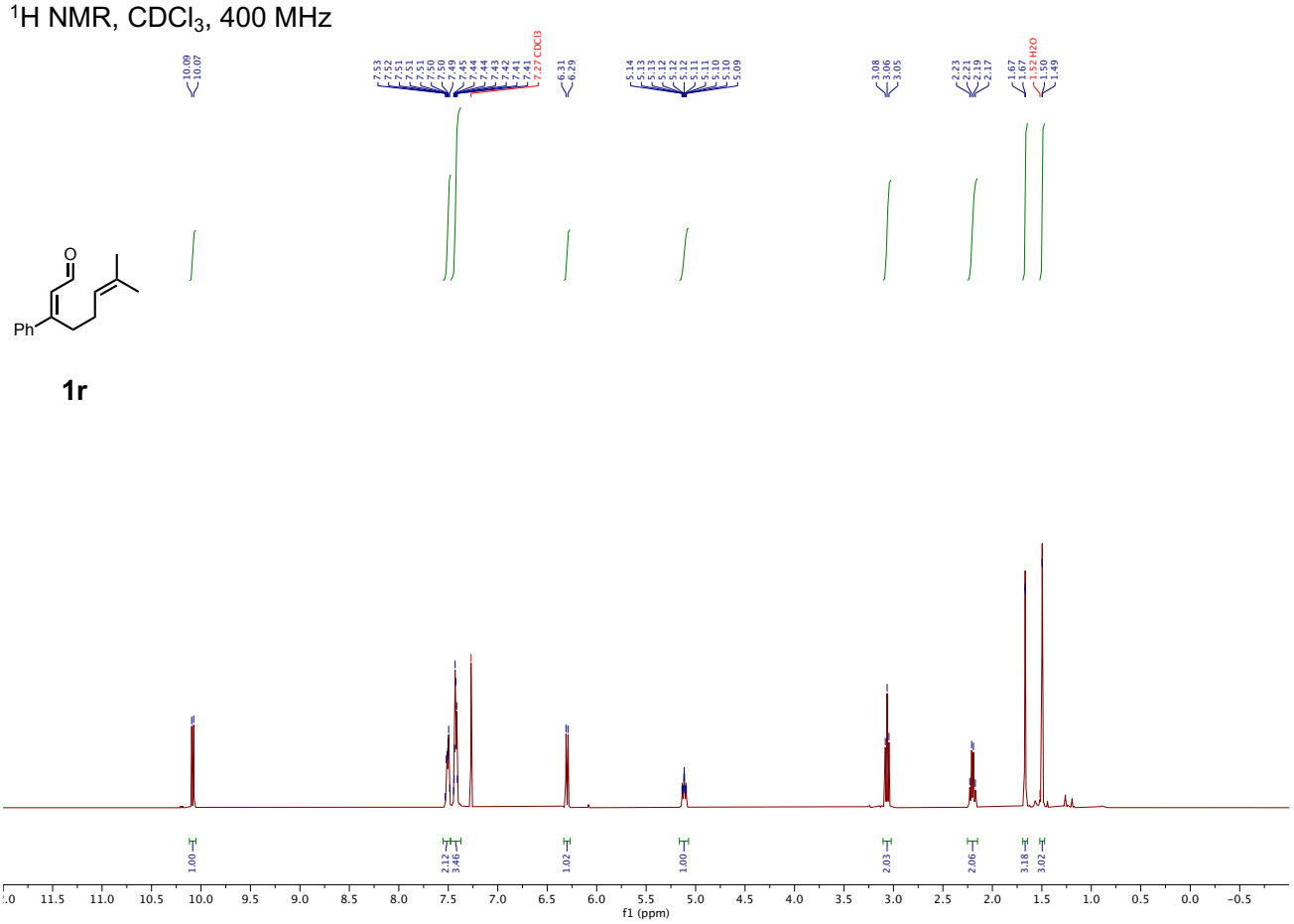
1q

13C NMR, $CDCl_3$, 101 MHz



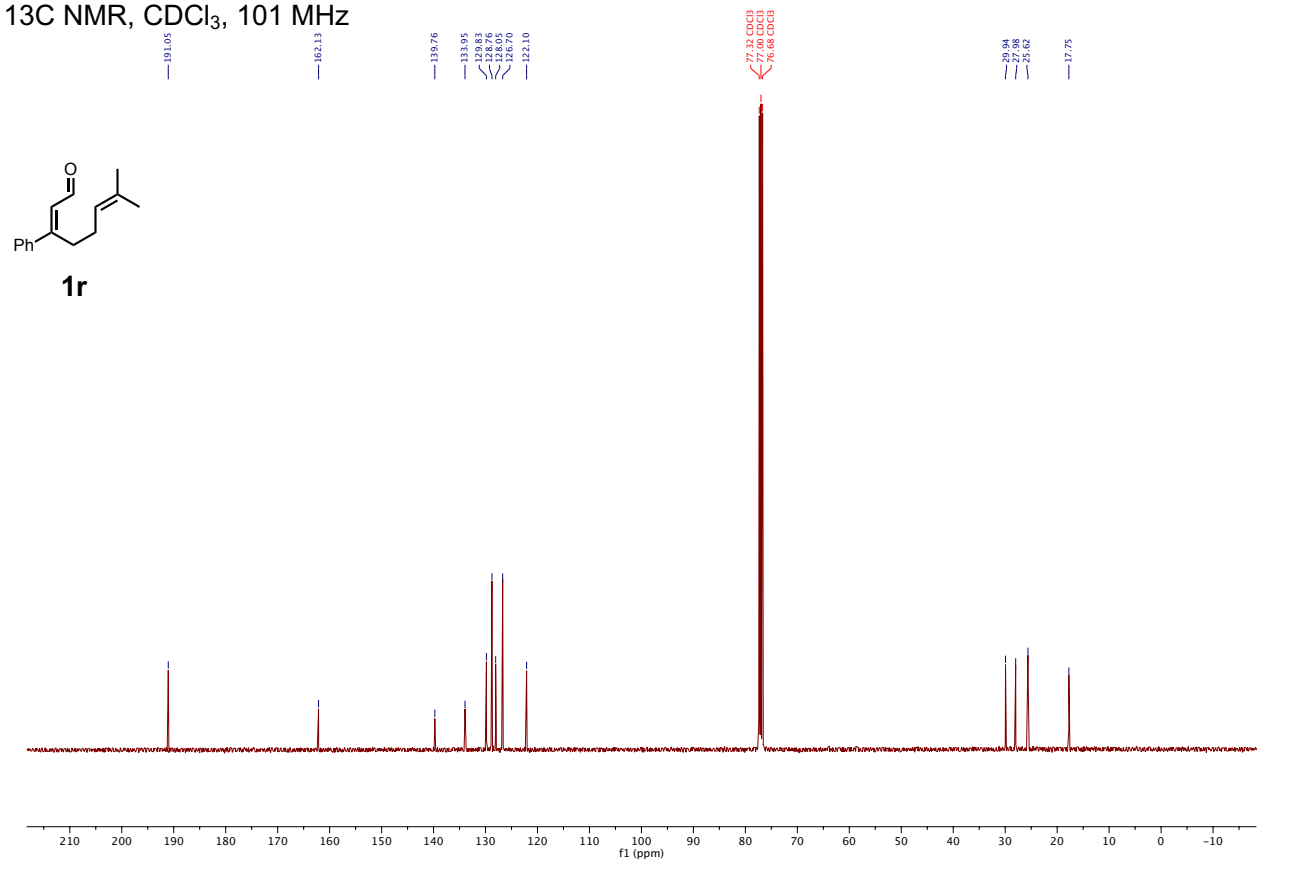
1q

^{1}H NMR, $CDCl_3$, 400 MHz



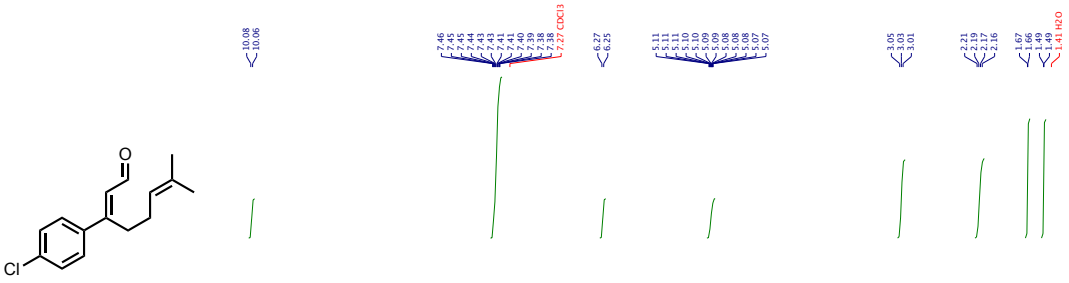
1r

13C NMR, $CDCl_3$, 101 MHz

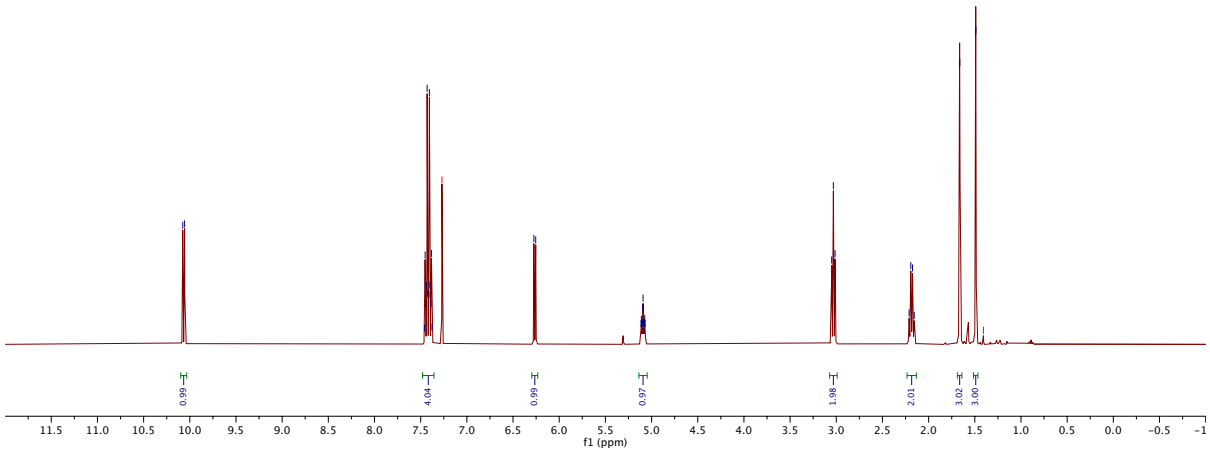


1r

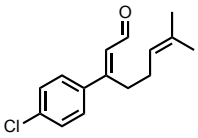
^{1}H NMR, $CDCl_3$, 400 MHz



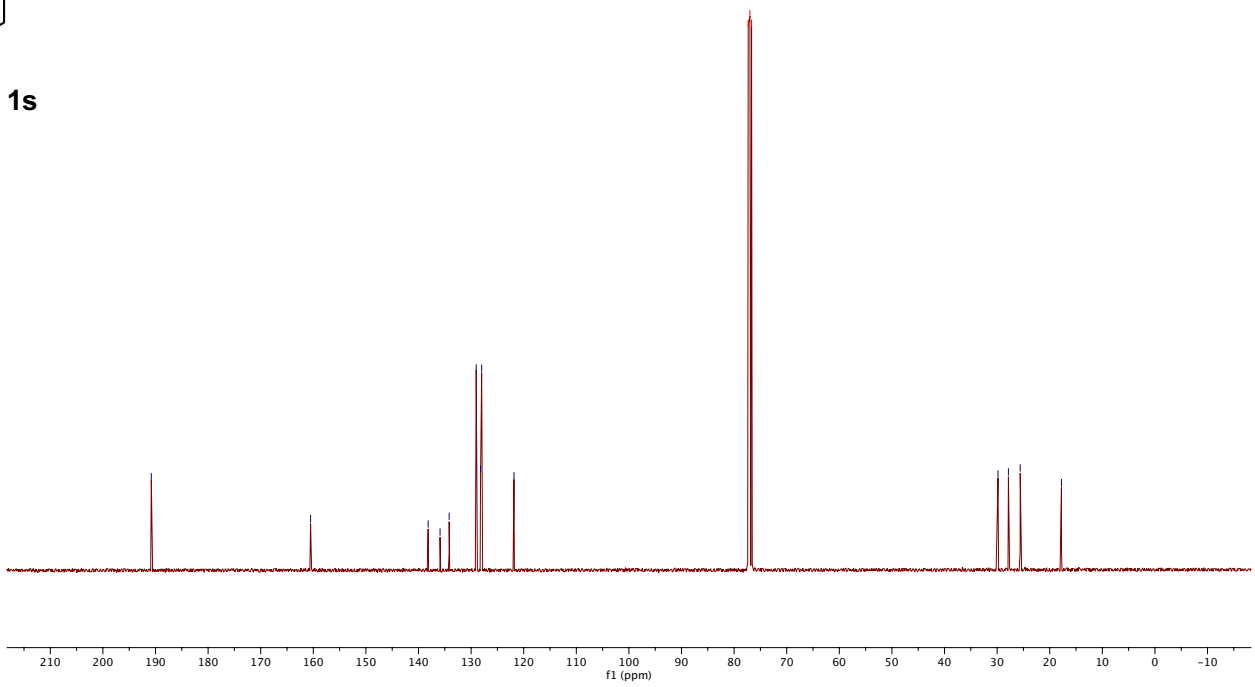
1s



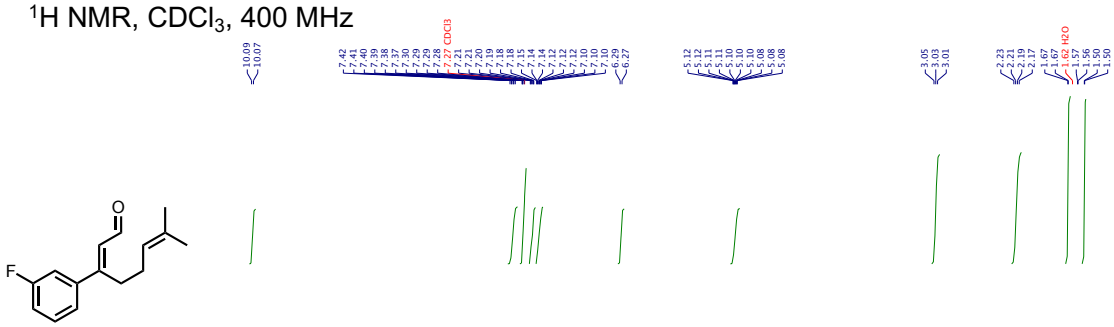
13C NMR, $CDCl_3$, 101 MHz



1s



^{1}H NMR, $CDCl_3$, 400 MHz



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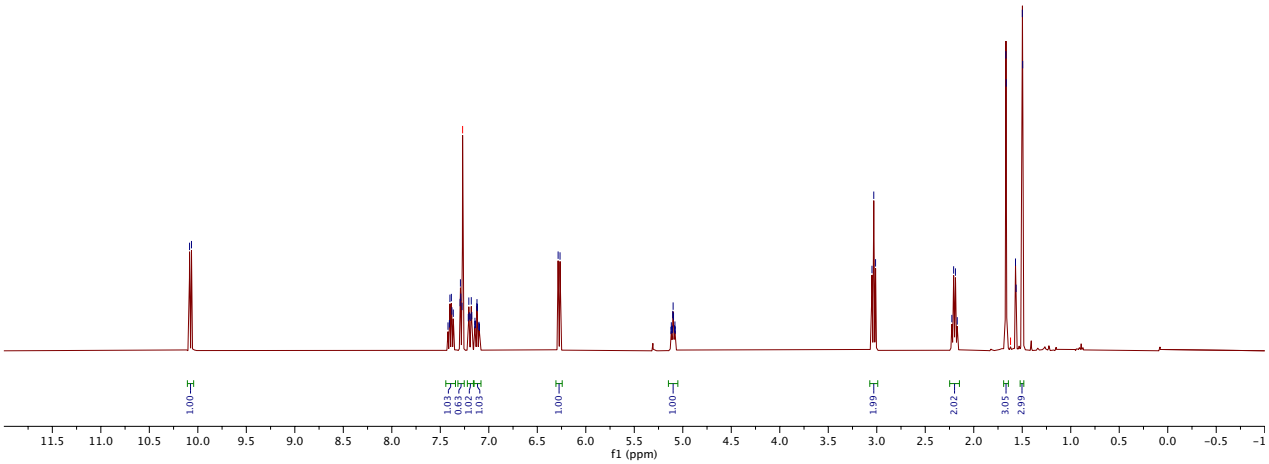
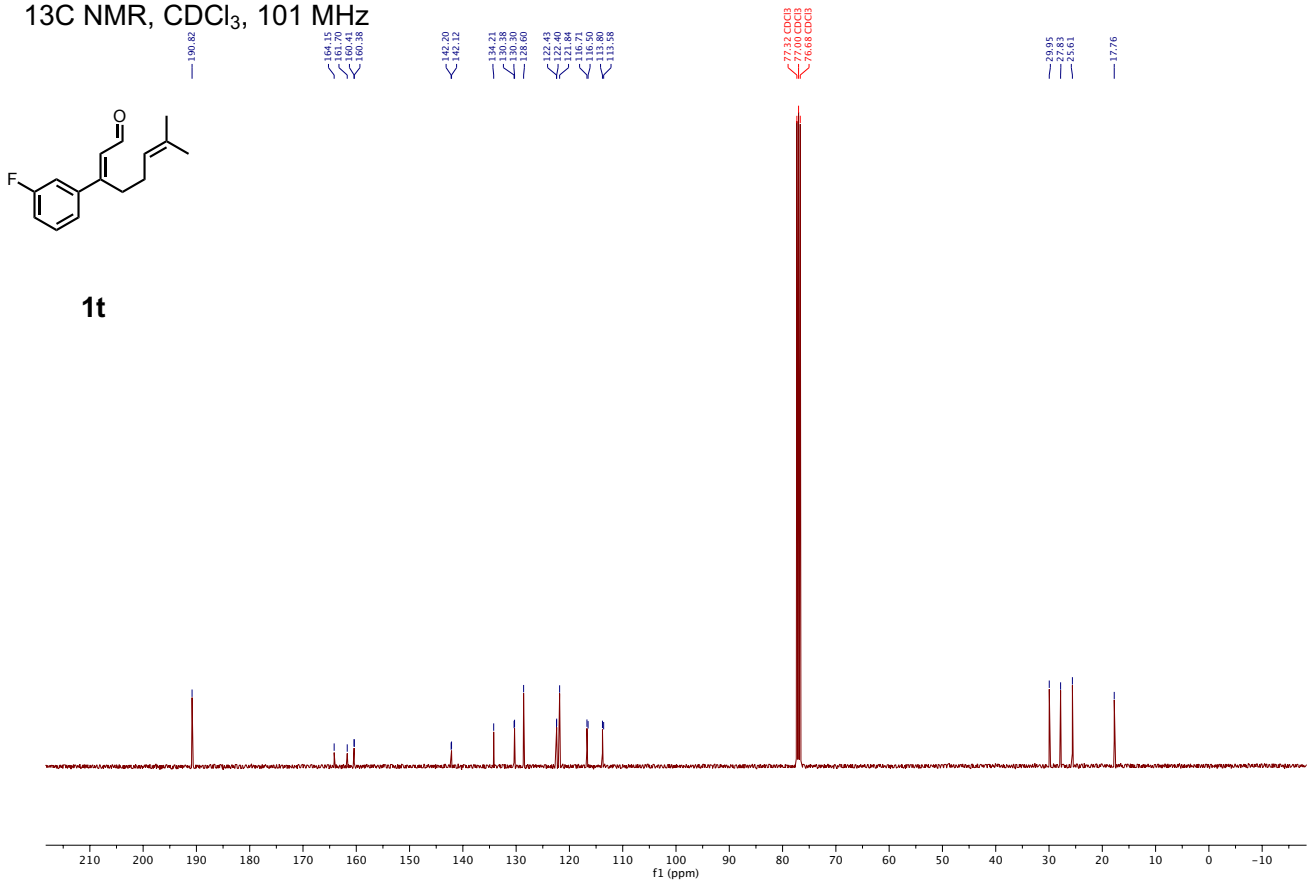
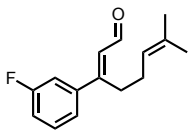


13C NMR, $CDCl_3$, 101 MHz



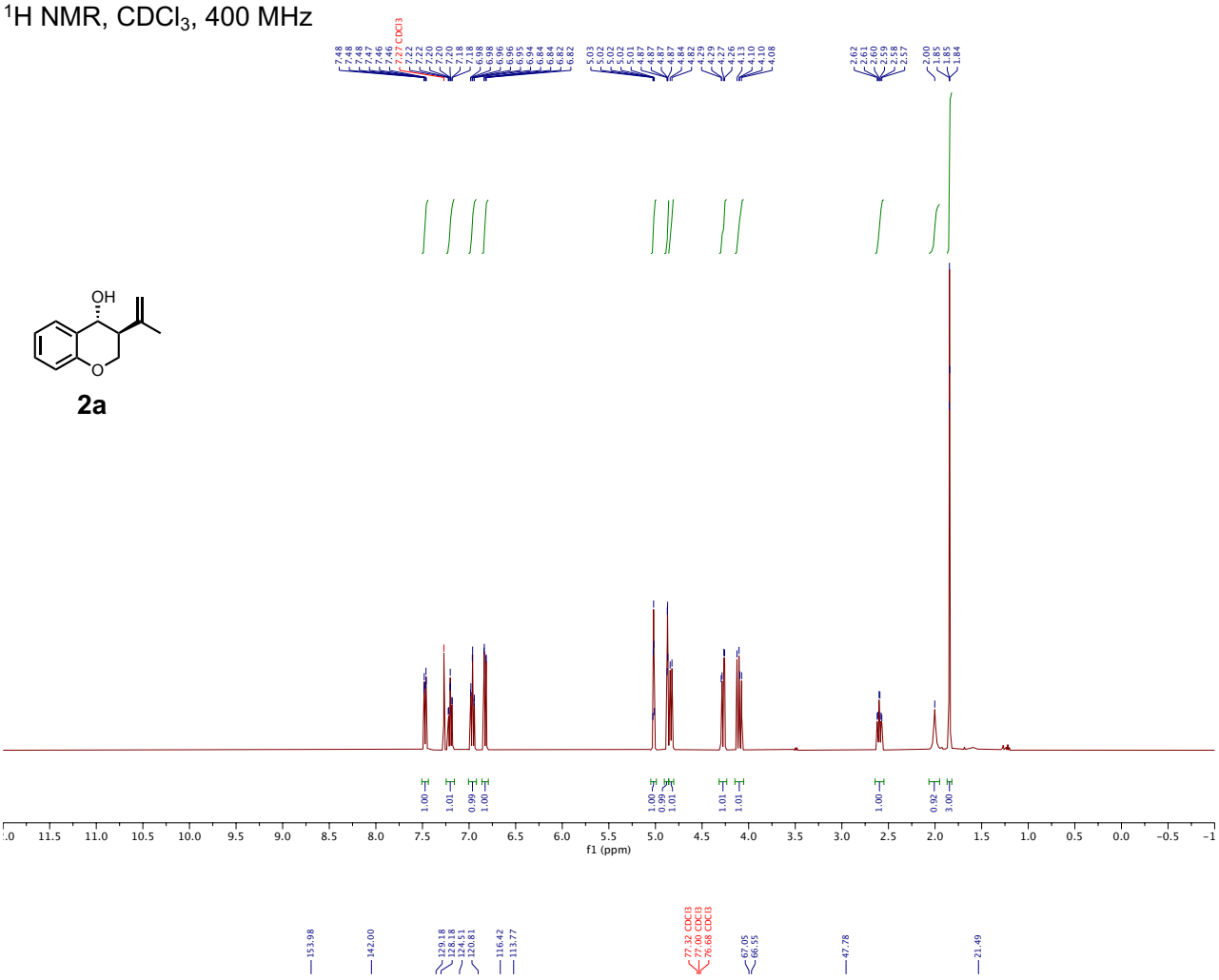
1t

^{19}F NMR, $CDCl_3$, 376 MHz

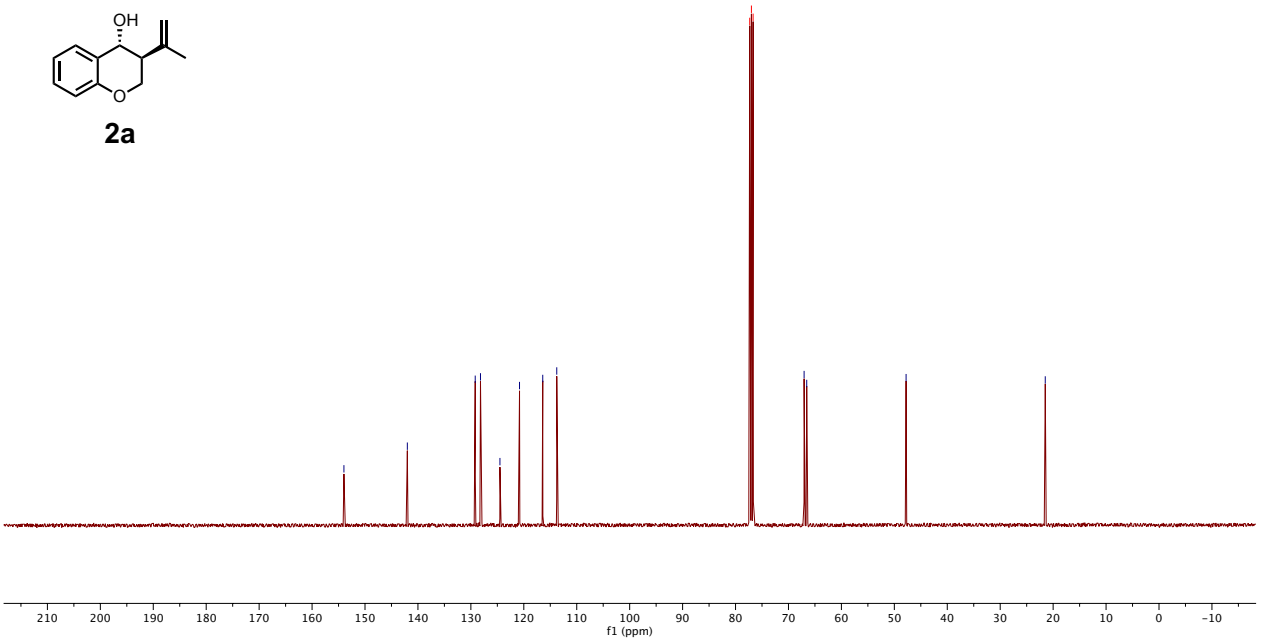


1t

^{1}H NMR, $CDCl_3$, 400 MHz

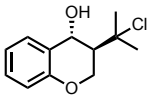


13C NMR, $CDCl_3$, 101 MHz



^{1}H NMR, $CDCl_3$, 400 MHz

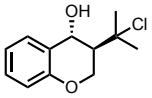
3:1 mixture with **2a**



3a

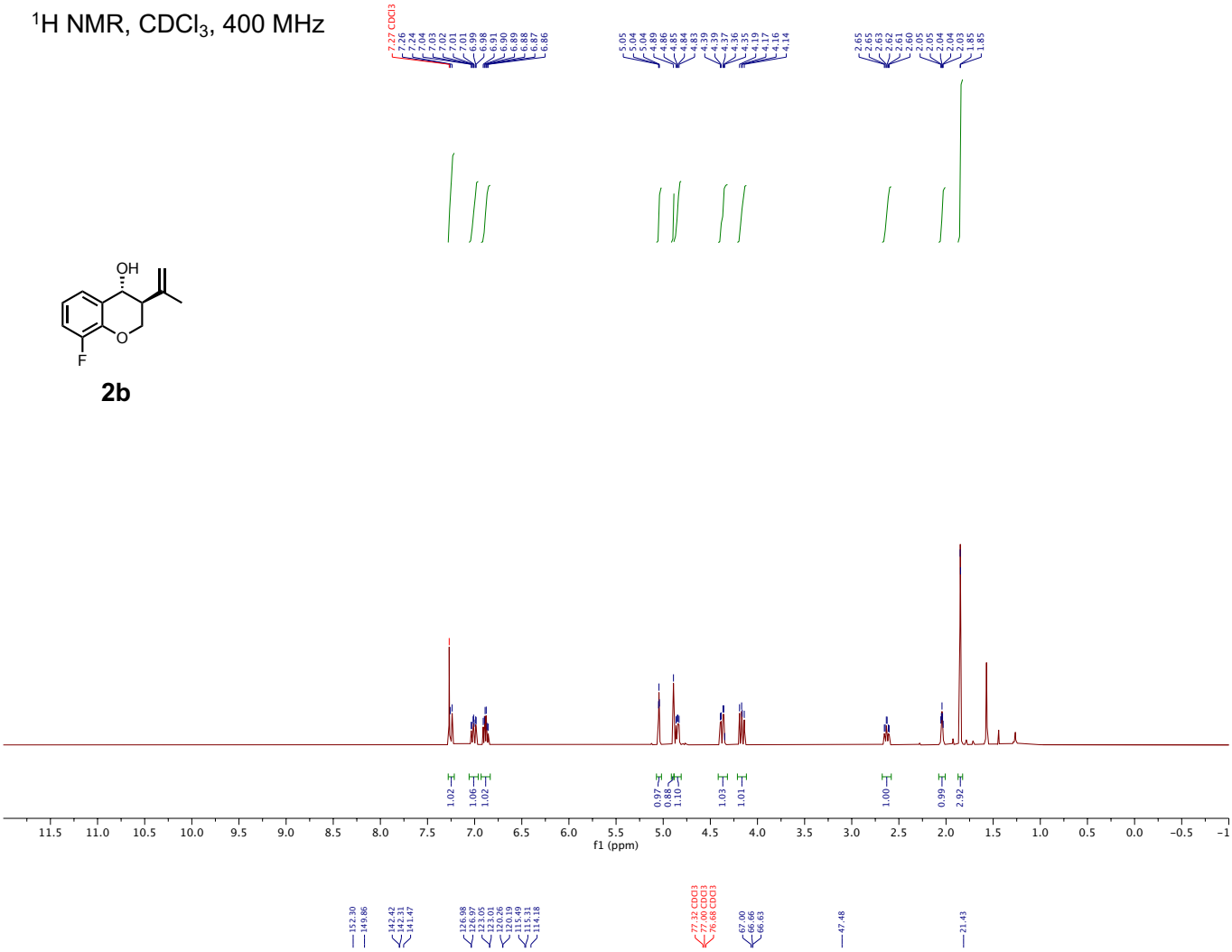
13C NMR, $CDCl_3$, 101 MHz

3:1 mixture with **2a**



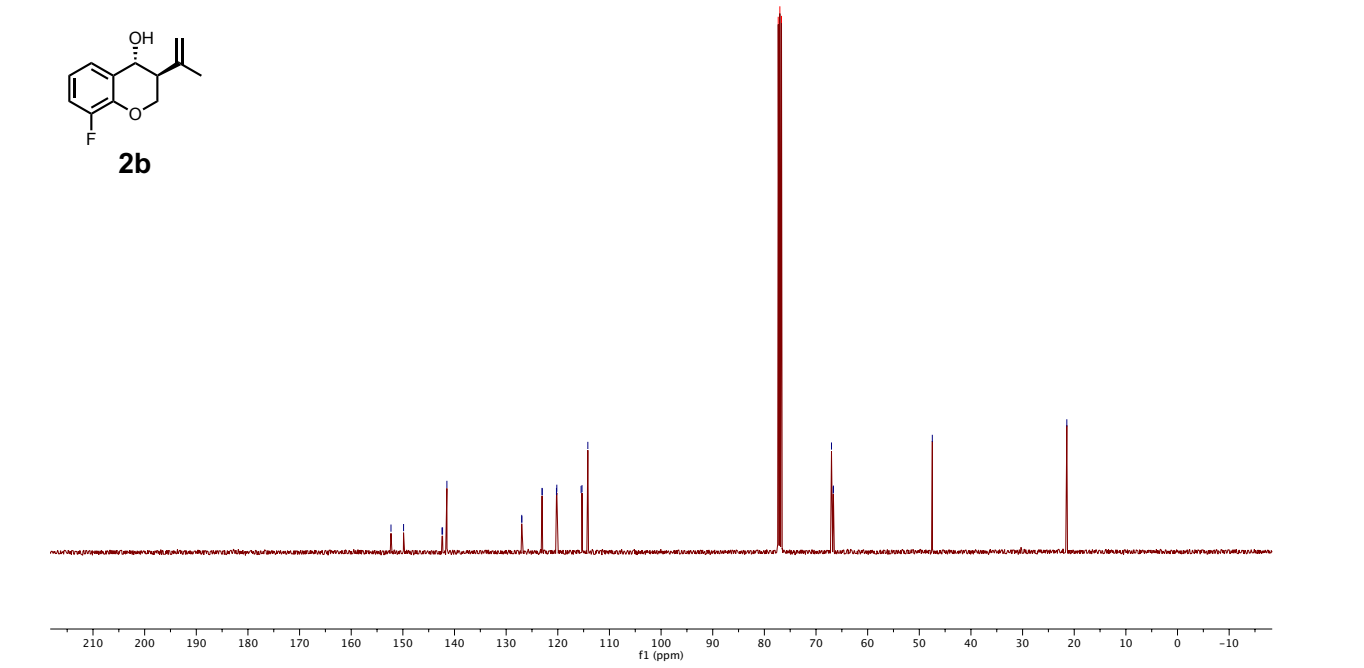
3a

^{1}H NMR, $CDCl_3$, 400 MHz



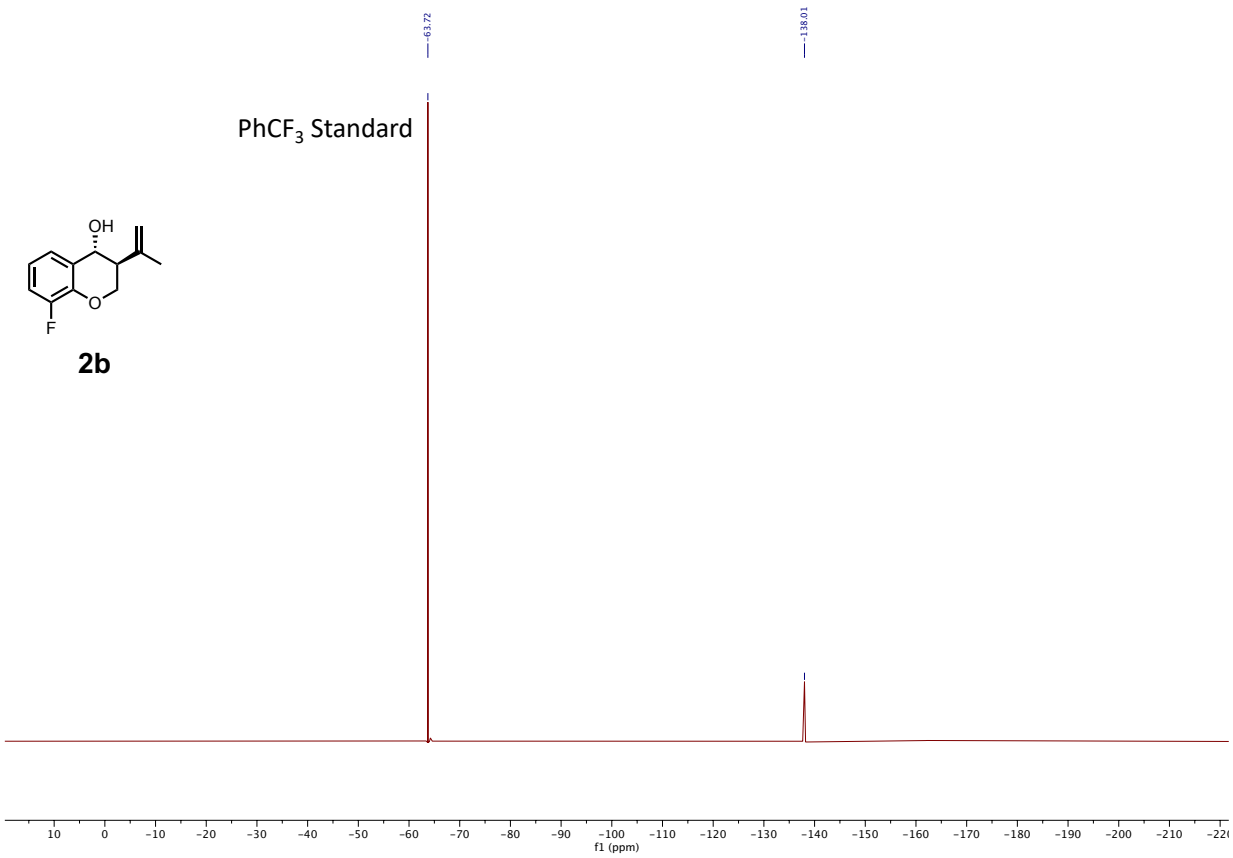
2b

13C NMR, $CDCl_3$, 101 MHz

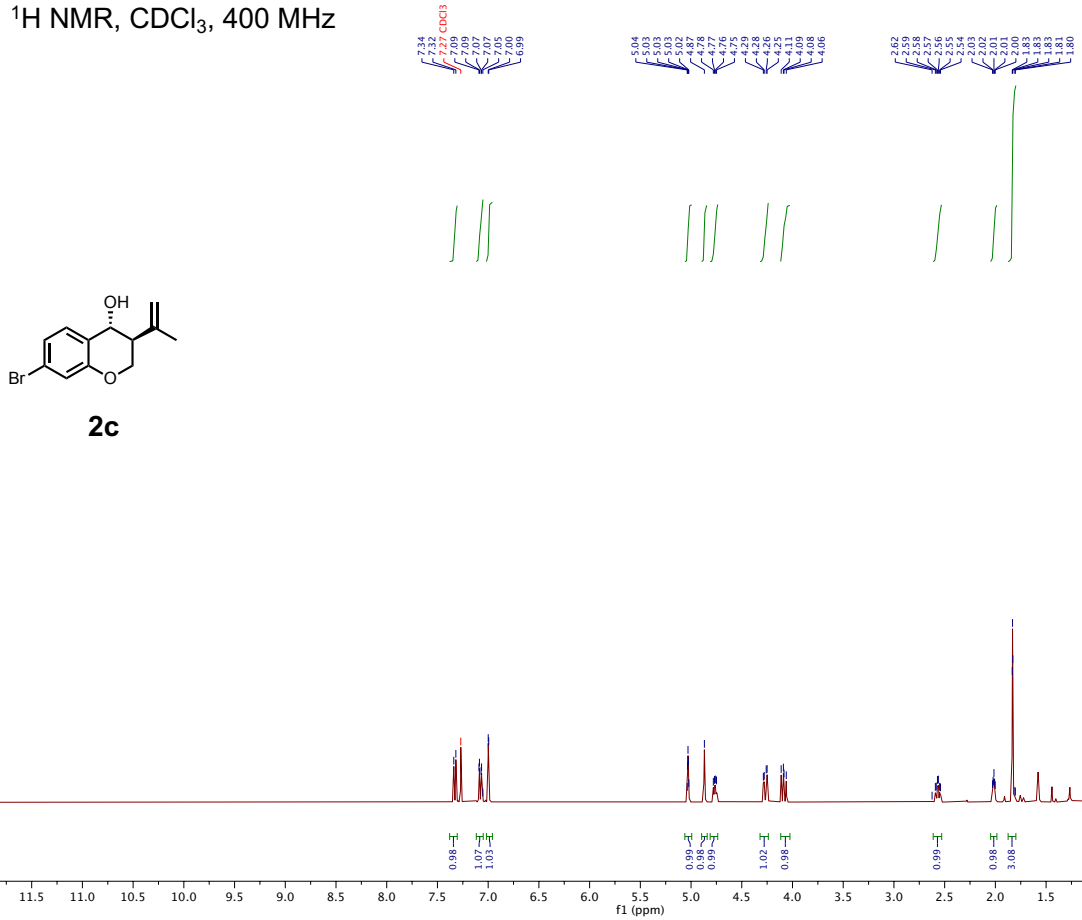


2b

^{19}F NMR, $CDCl_3$, 376 MHz

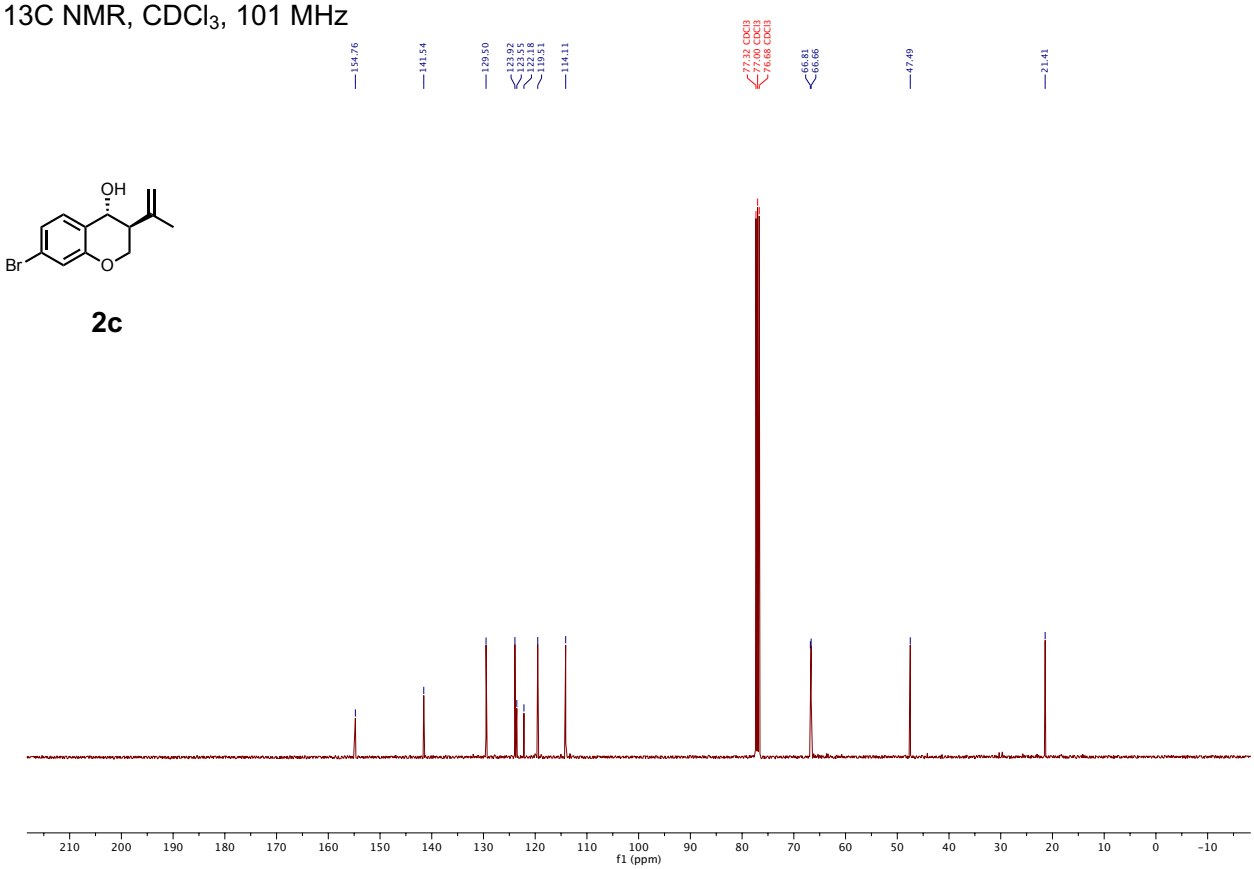


^{1}H NMR, $CDCl_3$, 400 MHz



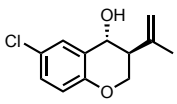
2c

13C NMR, $CDCl_3$, 101 MHz



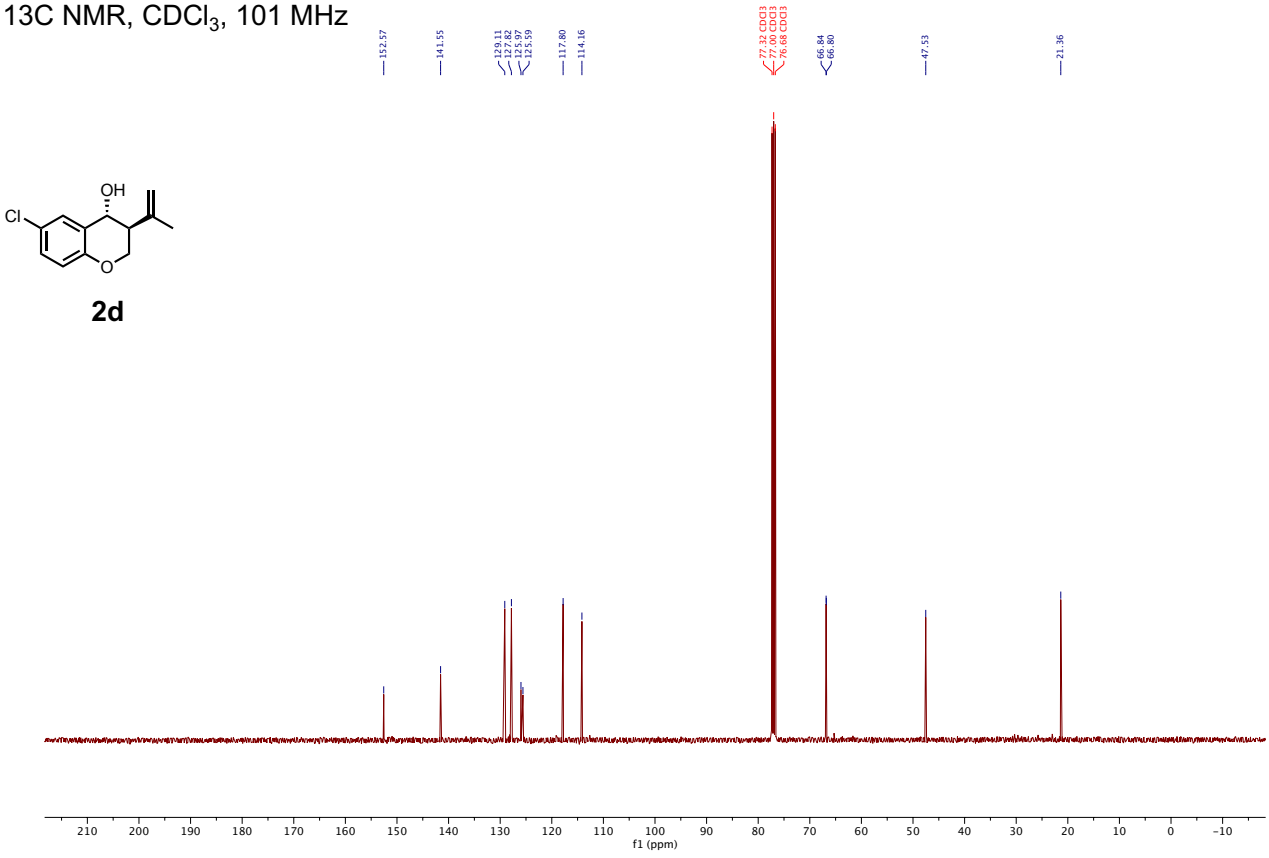
2c

^{1}H NMR, $CDCl_3$, 400 MHz



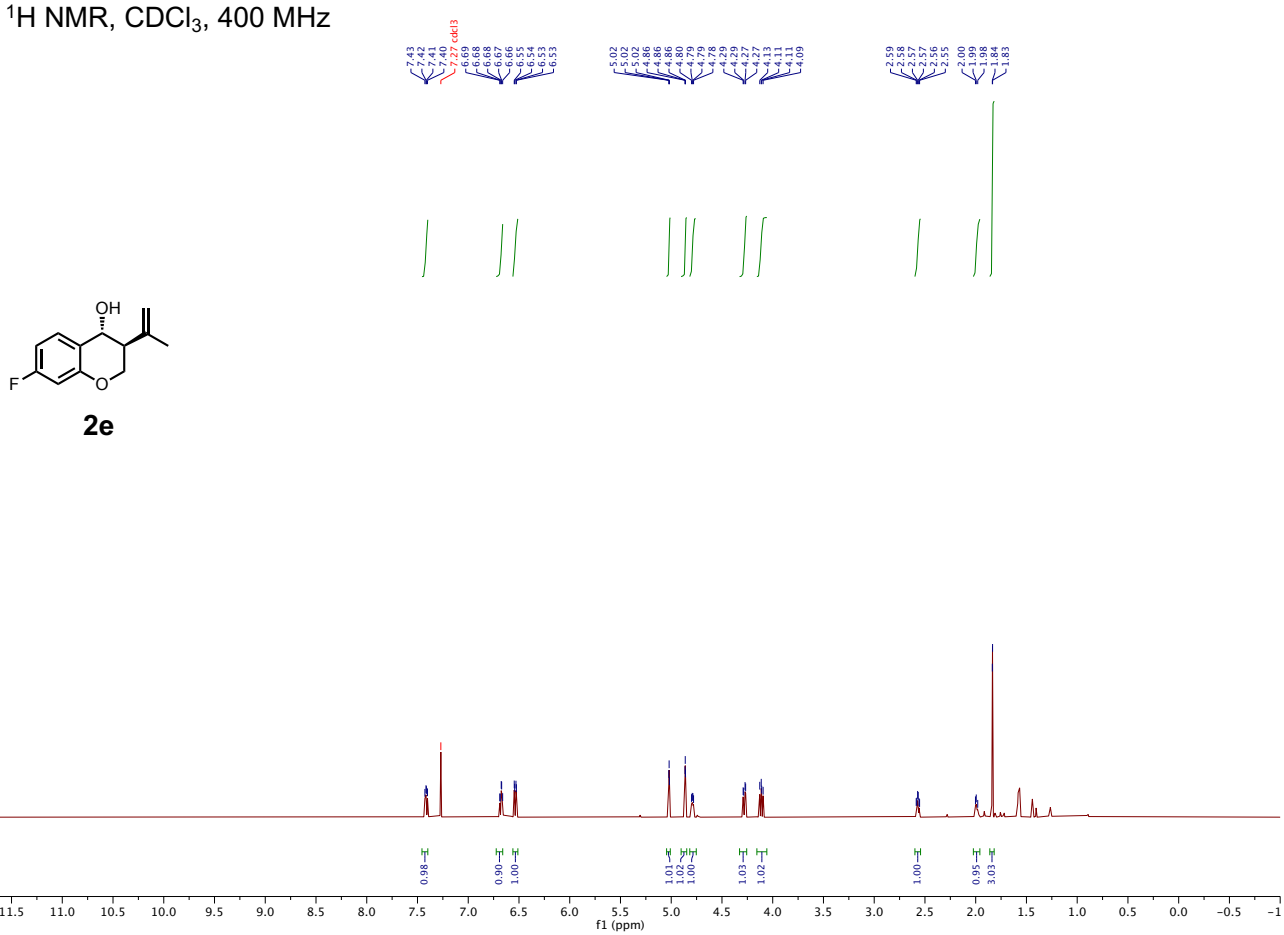
2d

13C NMR, $CDCl_3$, 101 MHz



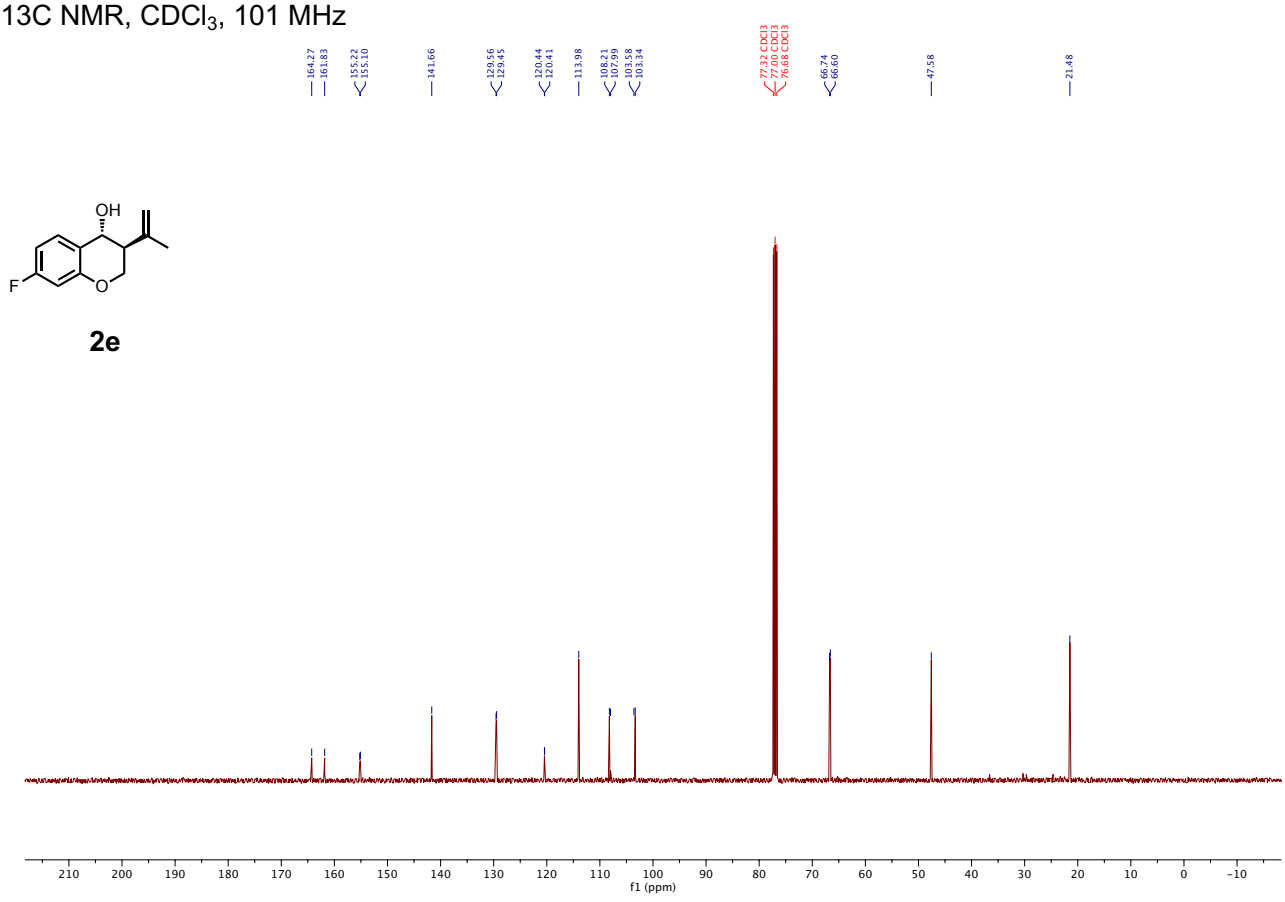
2d

^{1}H NMR, $CDCl_3$, 400 MHz



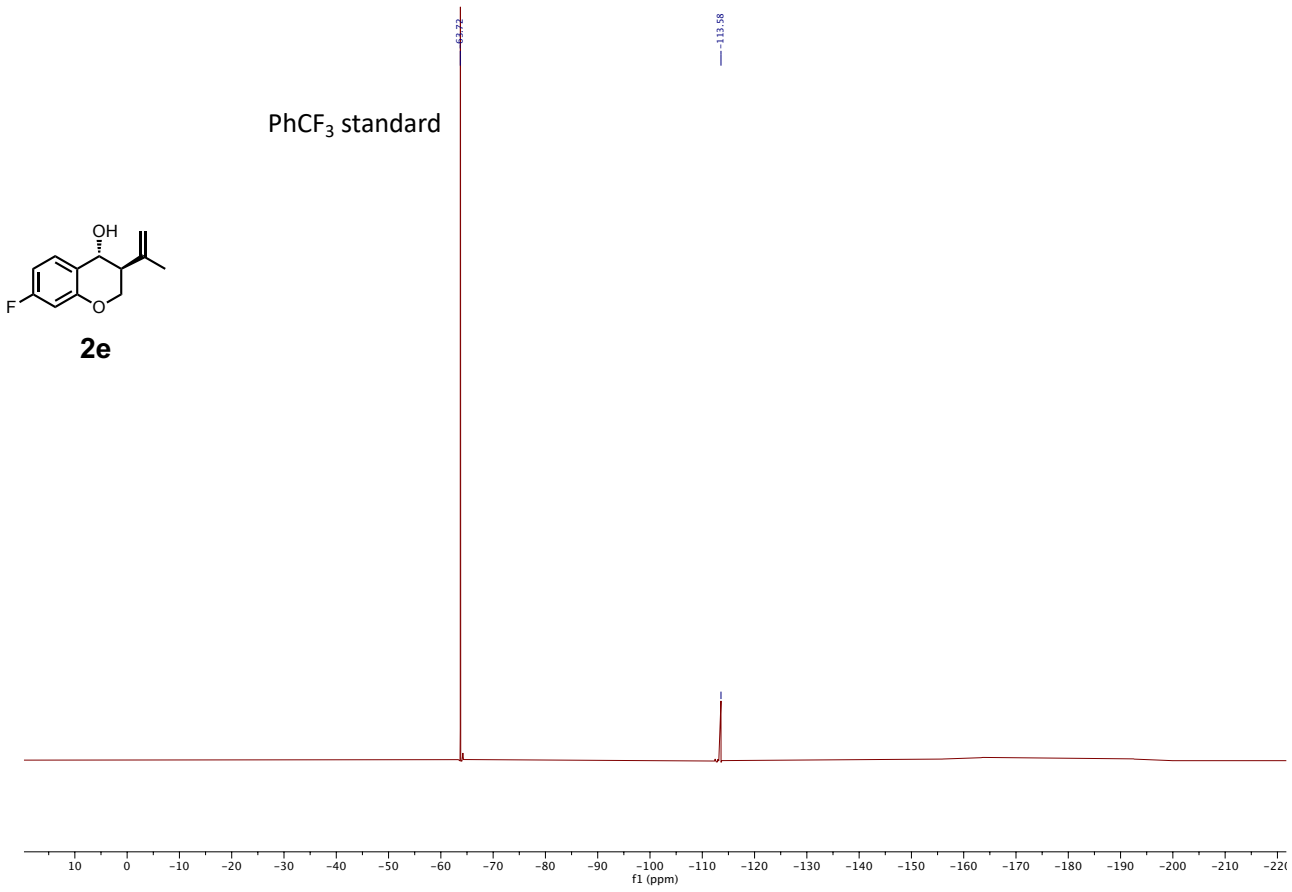
2e

13C NMR, $CDCl_3$, 101 MHz



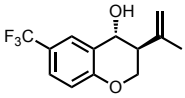
2e

^{19}F NMR, $CDCl_3$, 376 MHz



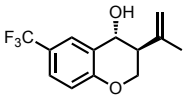
2e

^{1}H NMR, $CDCl_3$, 500 MHz

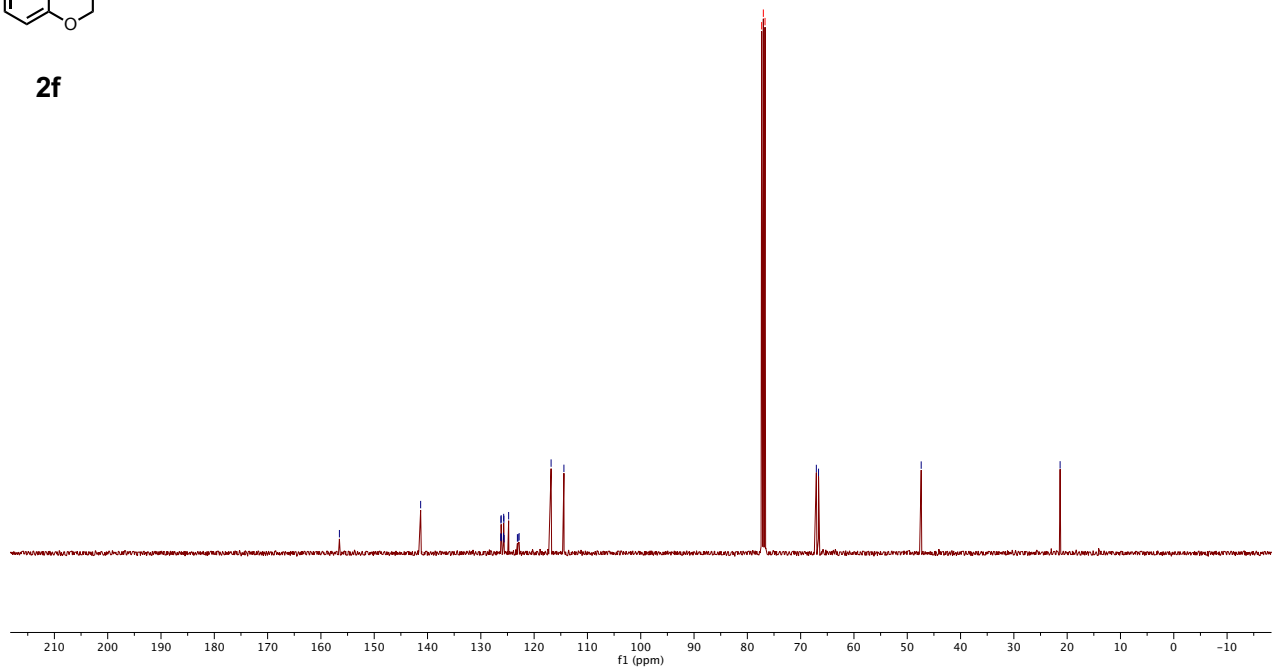


2f

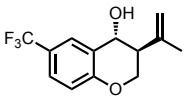
13C NMR, $CDCl_3$, 101 MHz



2f

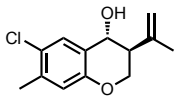


^{19}F NMR, $CDCl_3$, 470 MHz

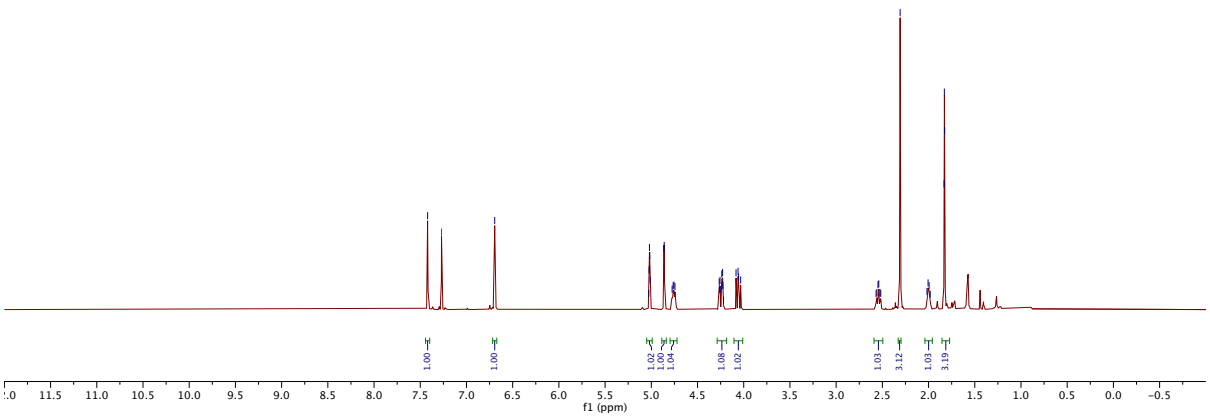


2f

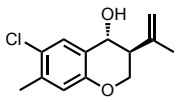
^{1}H NMR, $CDCl_3$, 400 MHz



2g

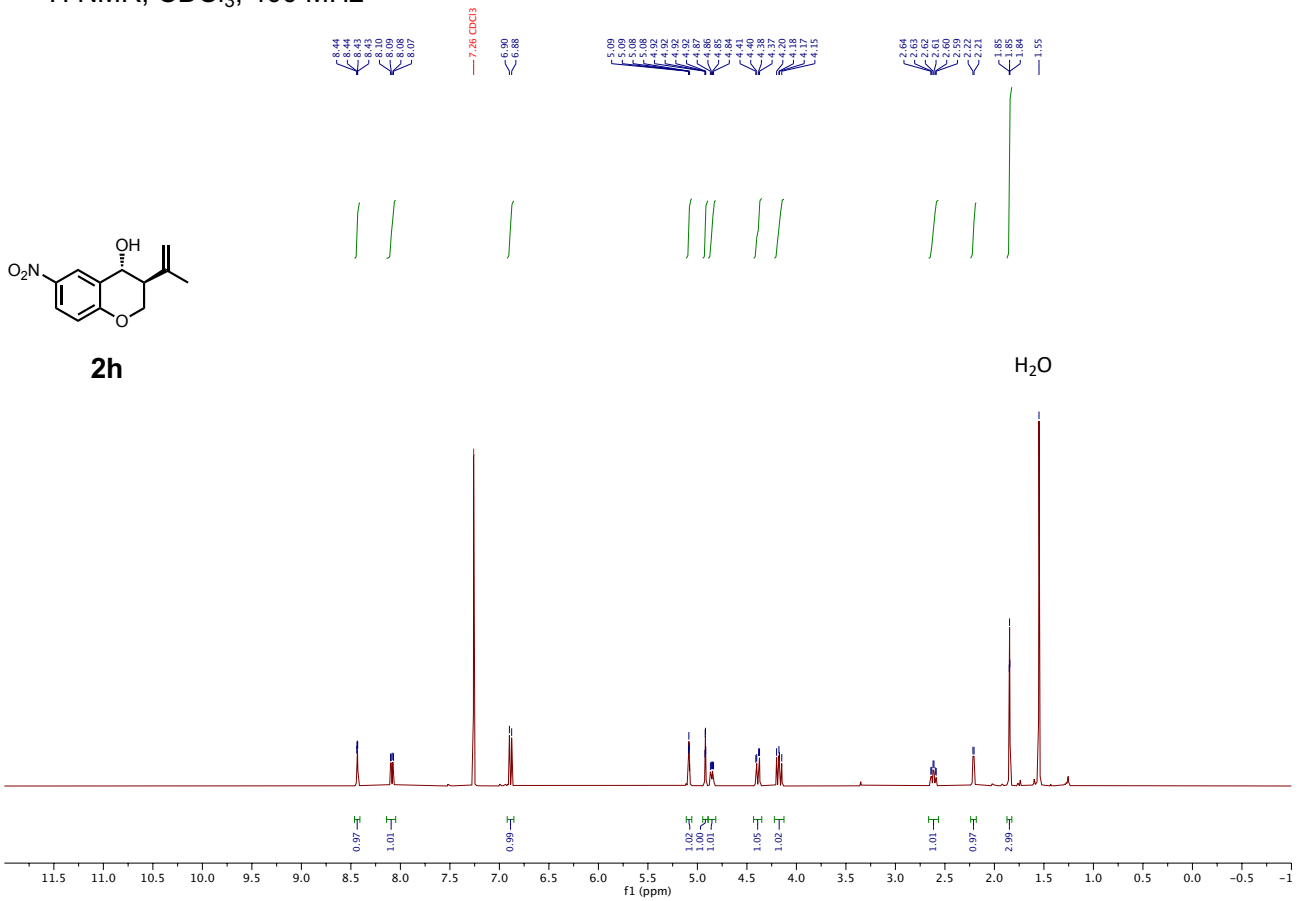


13C NMR, $CDCl_3$, 101 MHz

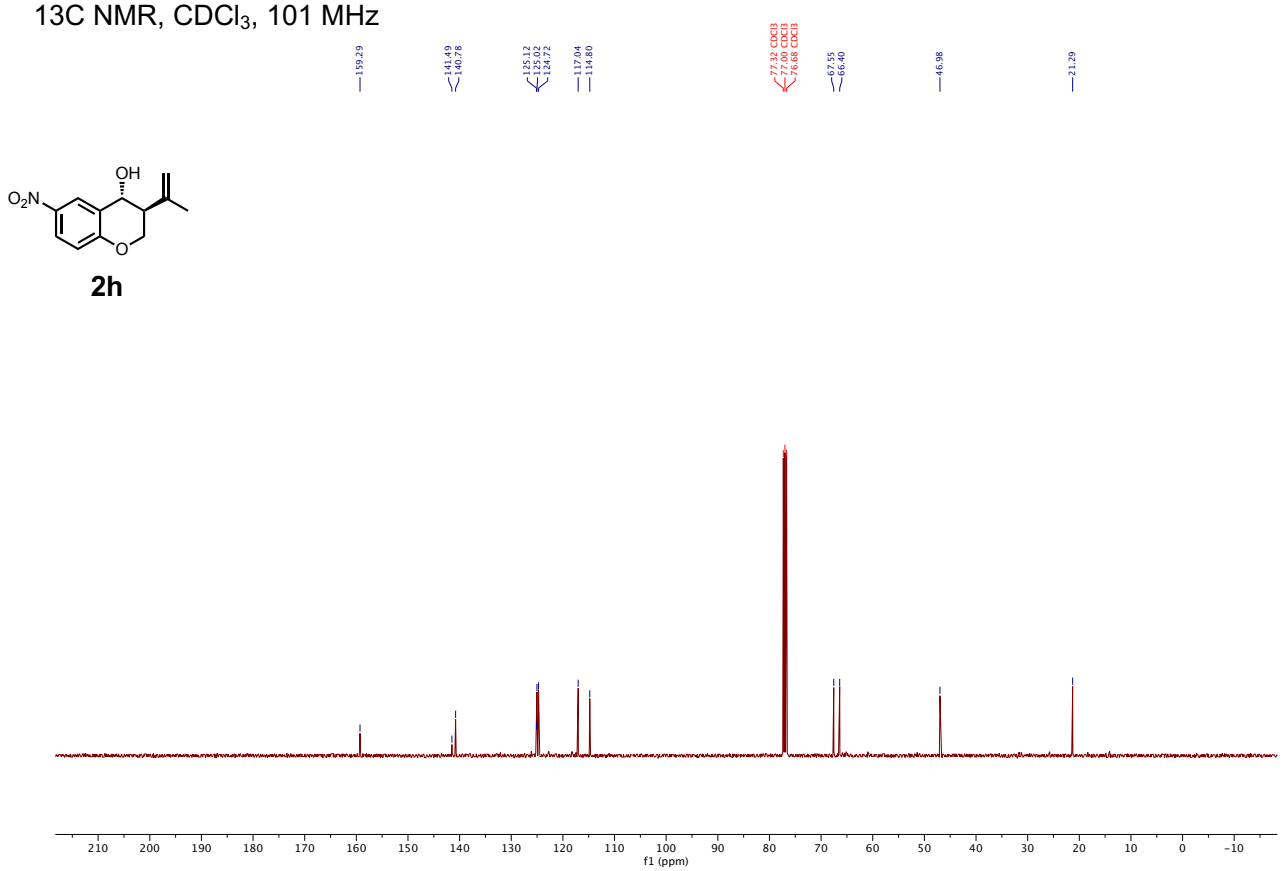


2g

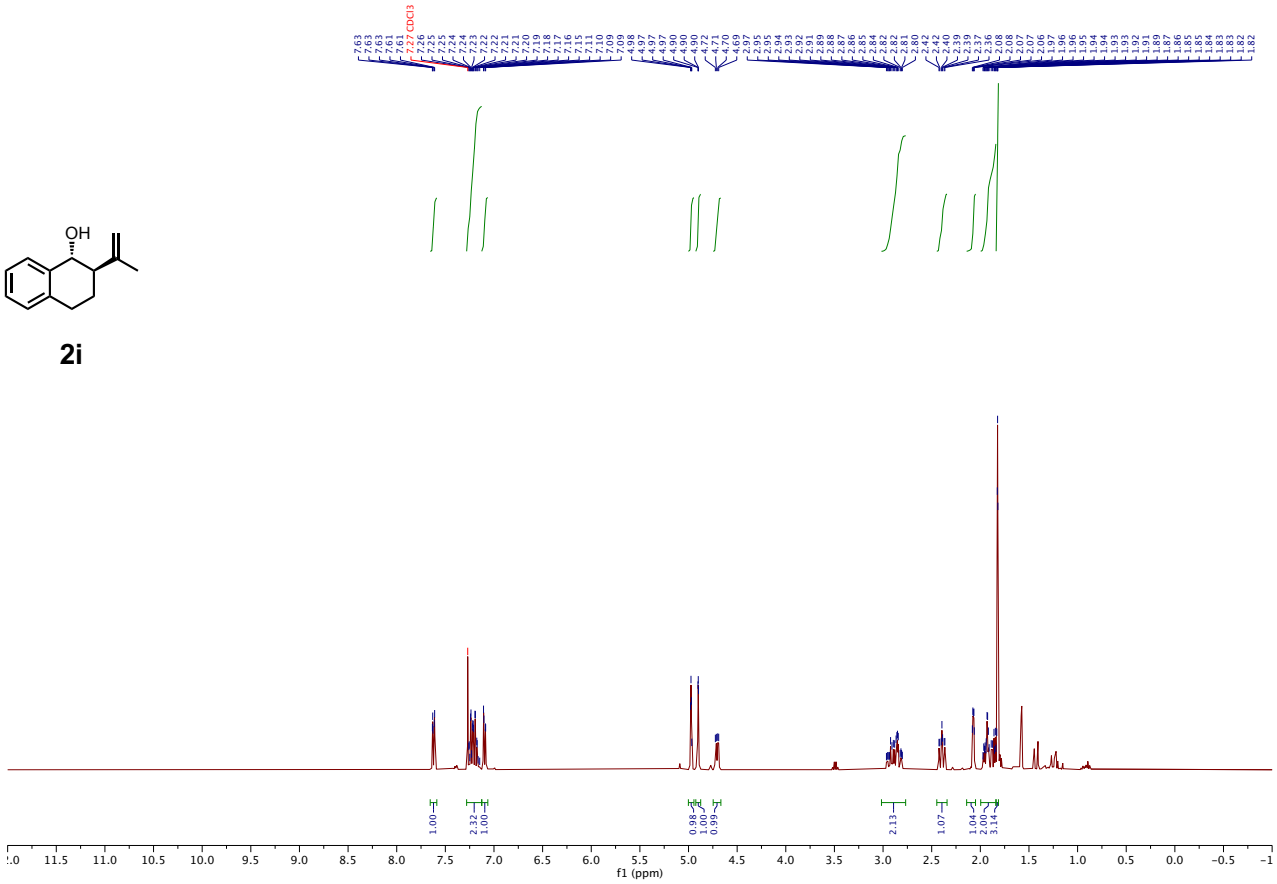
^{1}H NMR, $CDCl_3$, 400 MHz



13C NMR, $CDCl_3$, 101 MHz

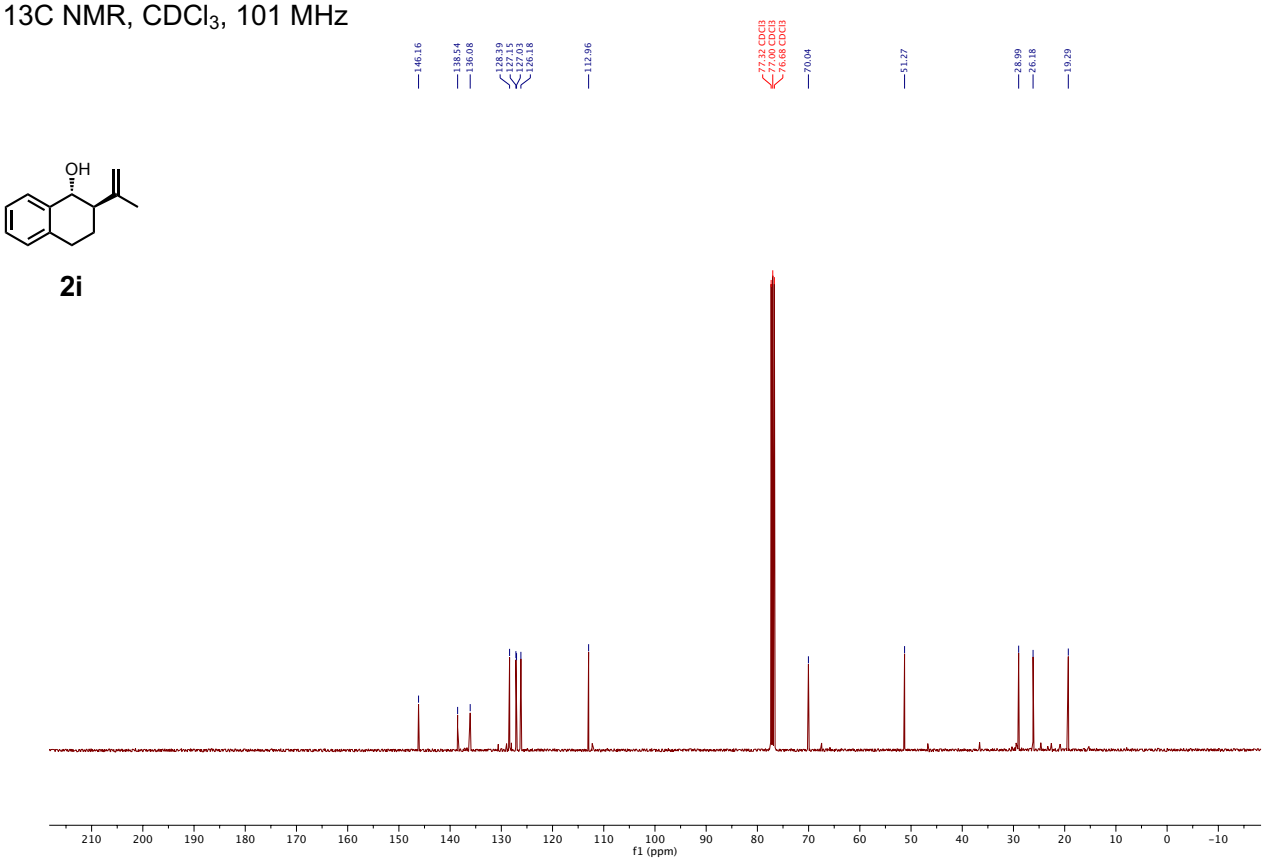


^{1}H NMR, $CDCl_3$, 400 MHz



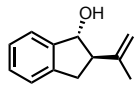
2i

13C NMR, $CDCl_3$, 101 MHz

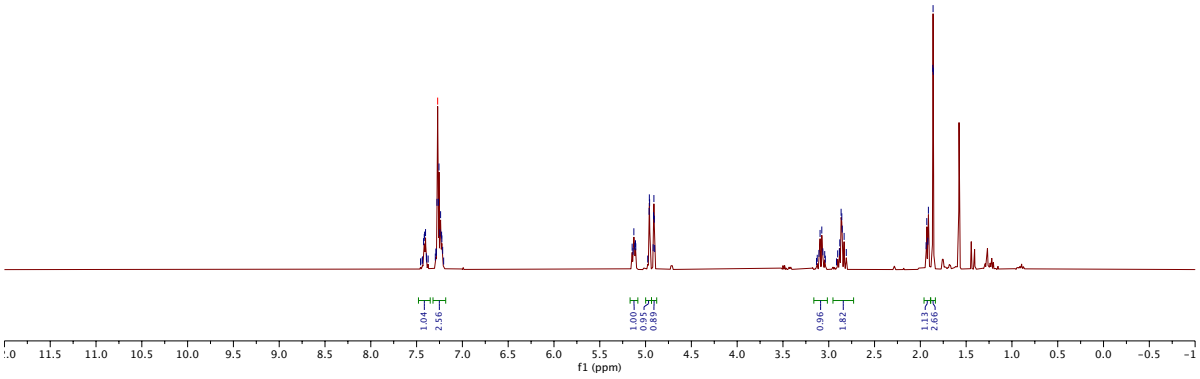


2i

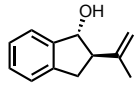
^{1}H NMR, $CDCl_3$, 400 MHz



2j

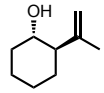


13C NMR, $CDCl_3$, 101 MHz



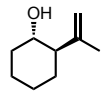
2j

^{1}H NMR, $CDCl_3$, 600 MHz



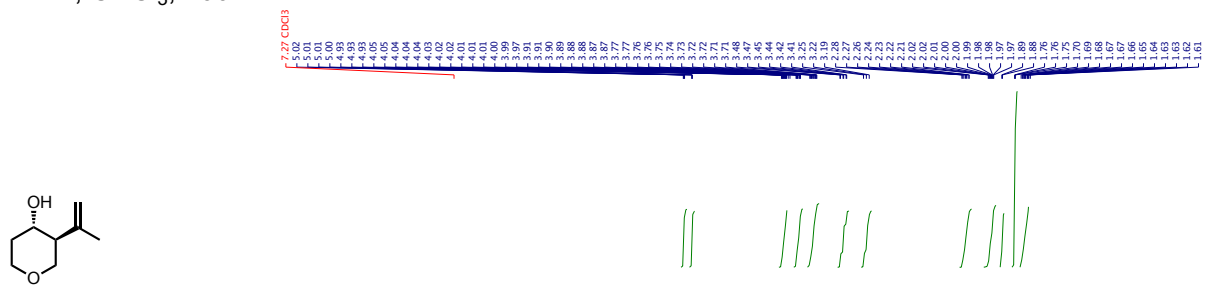
2k

13C NMR, $CDCl_3$, 101 MHz

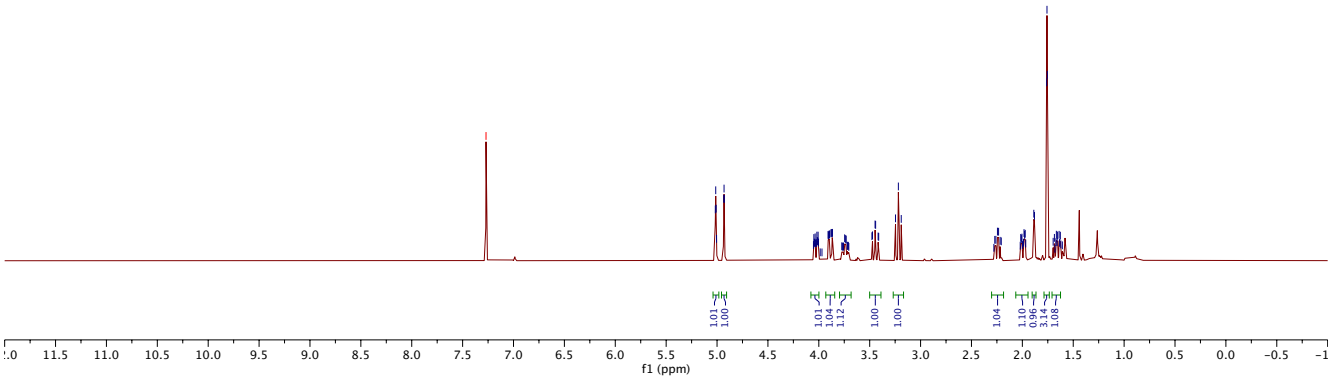


2k

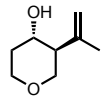
^{1}H NMR, $CDCl_3$, 400 MHz



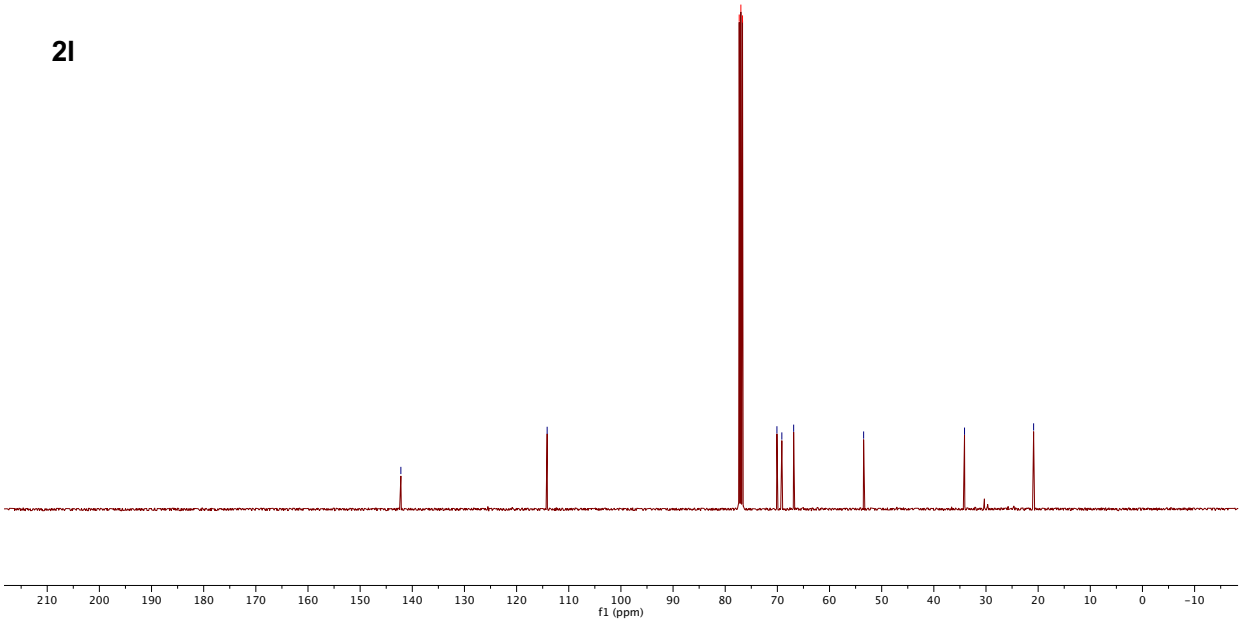
2l



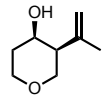
13C NMR, $CDCl_3$, 101 MHz

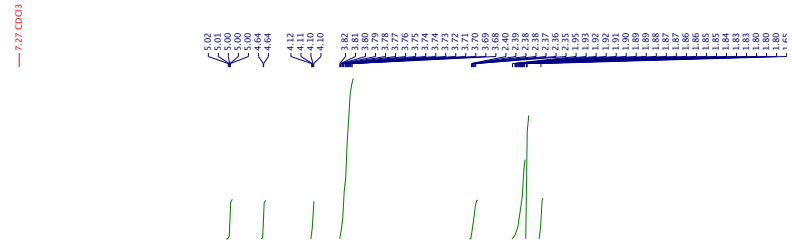


2l

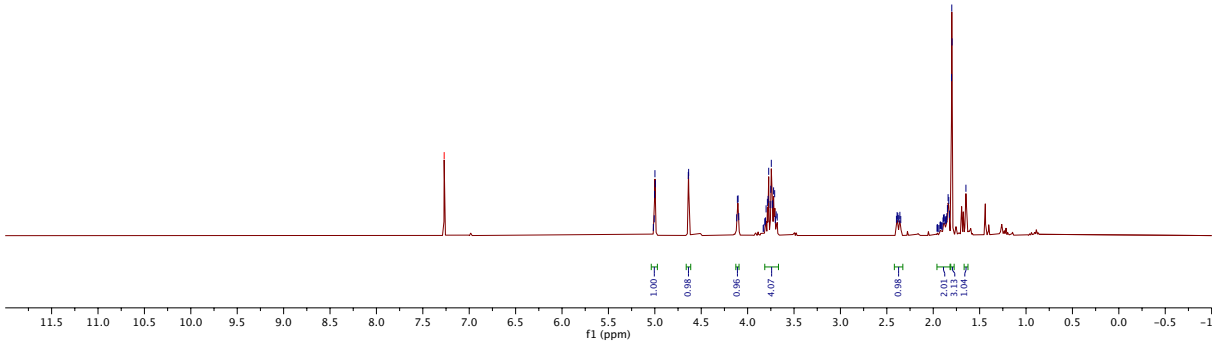


^{1}H NMR, $CDCl_3$, 400 MHz

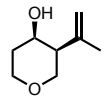




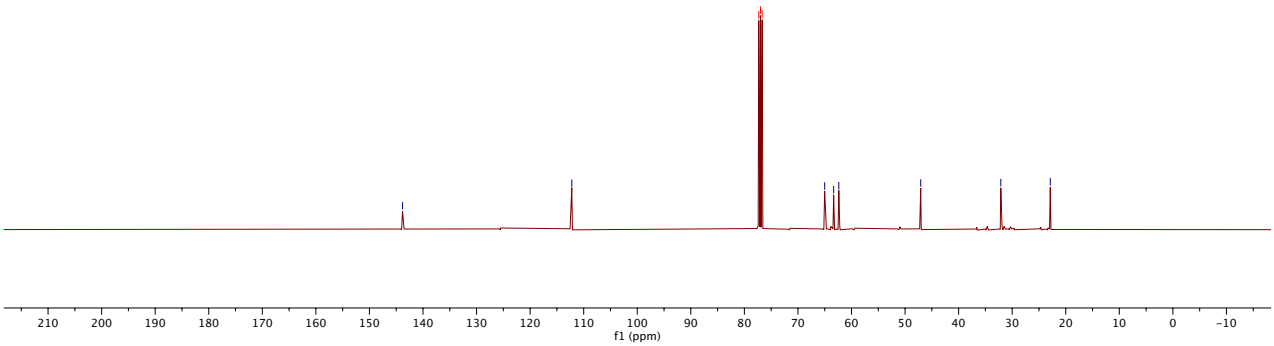
2l-Cis
(absolute configuration unknown)



13C NMR, $CDCl_3$, 101 MHz

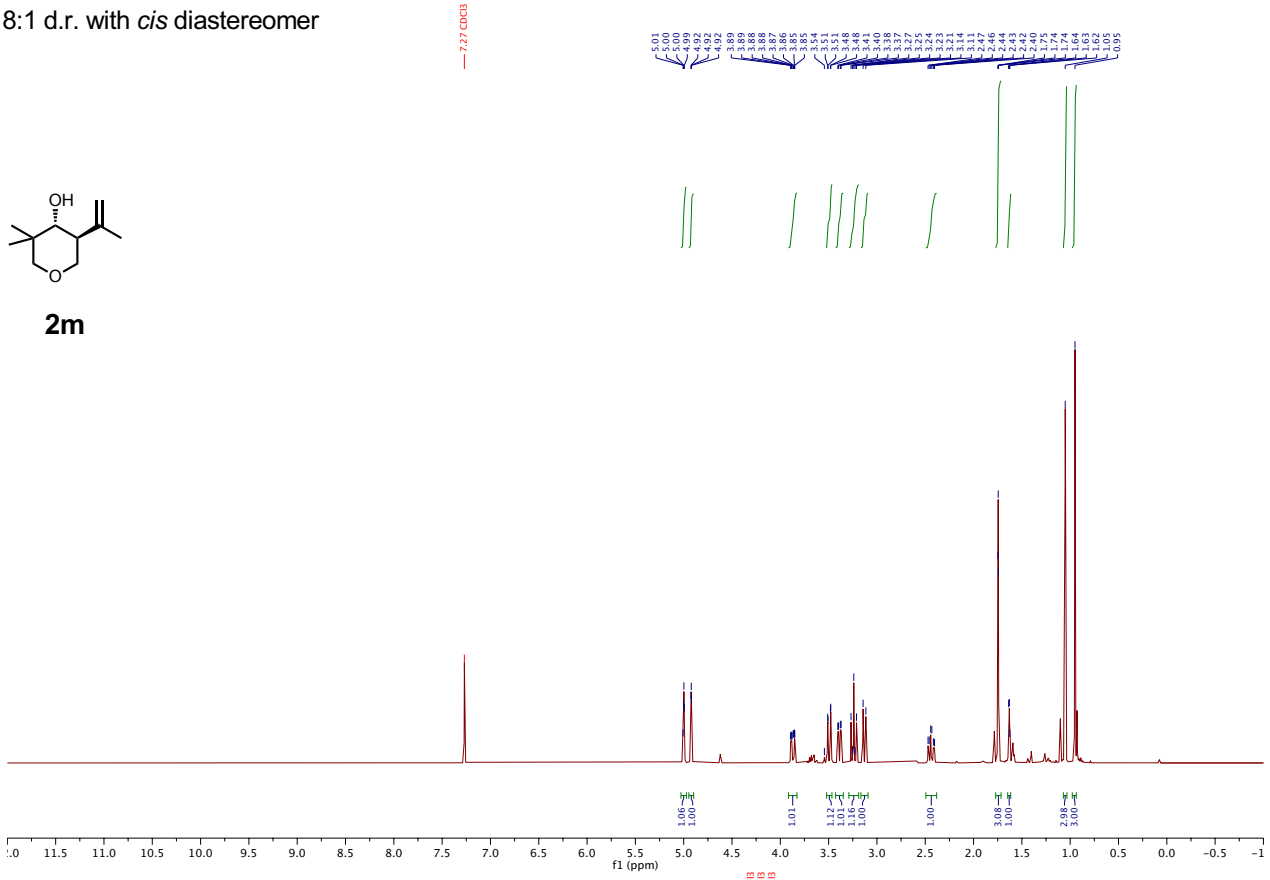


2l-Cis
(absolute configuration unknown)



^{1}H NMR, $CDCl_3$, 400 MHz

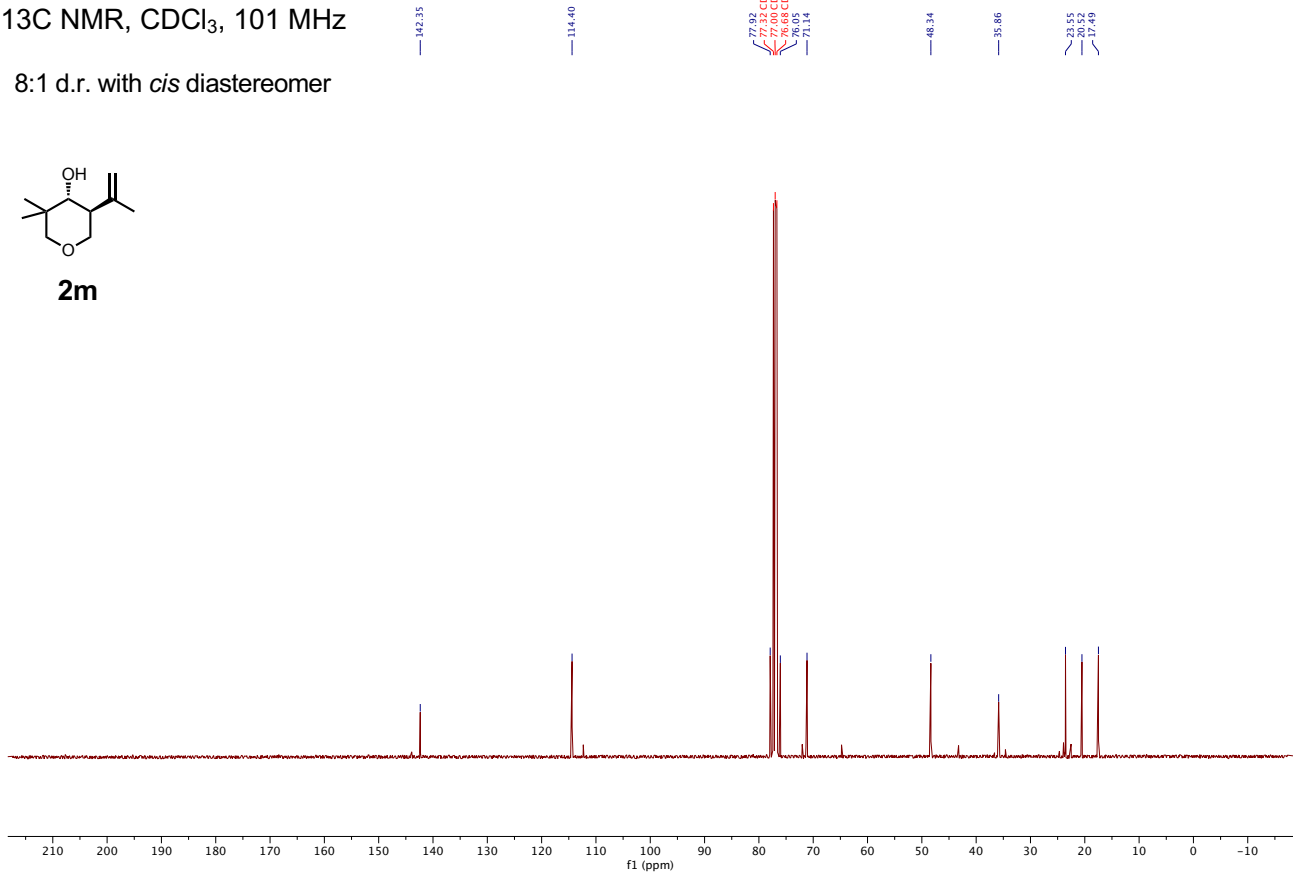
8:1 d.r. with *cis* diastereomer



2m

13C NMR, $CDCl_3$, 101 MHz

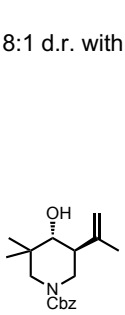
8:1 d.r. with *cis* diastereomer



2m

^{1}H NMR, $CDCl_3$, 400 MHz

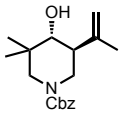
8:1 d.r. with *cis* diastereomer



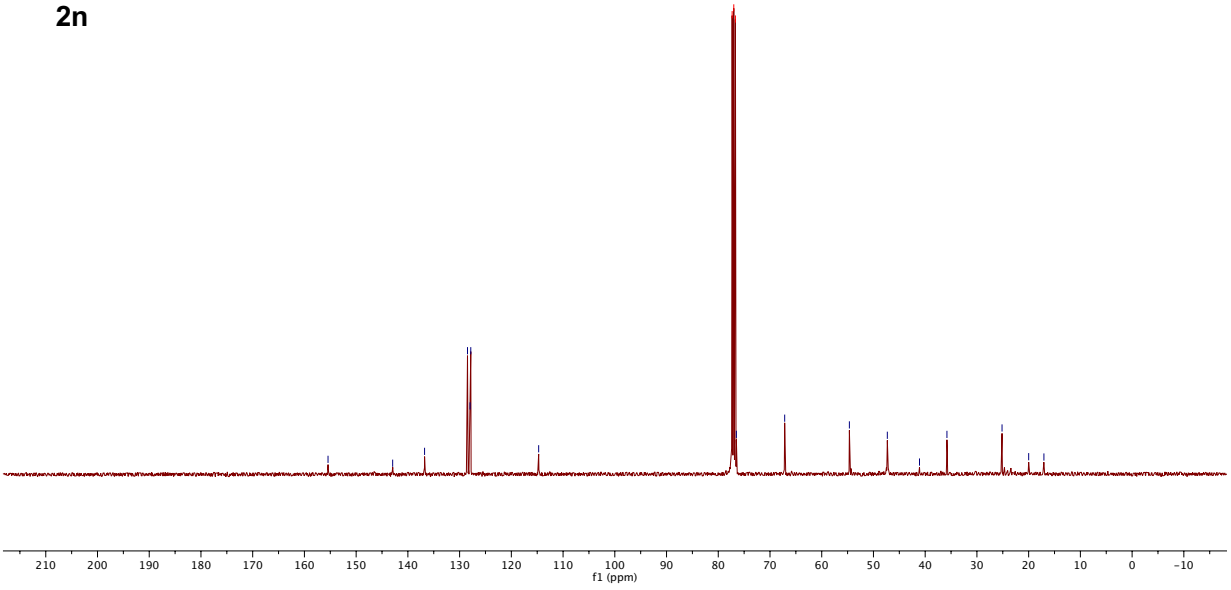
2n

13C NMR, $CDCl_3$, 101 MHz

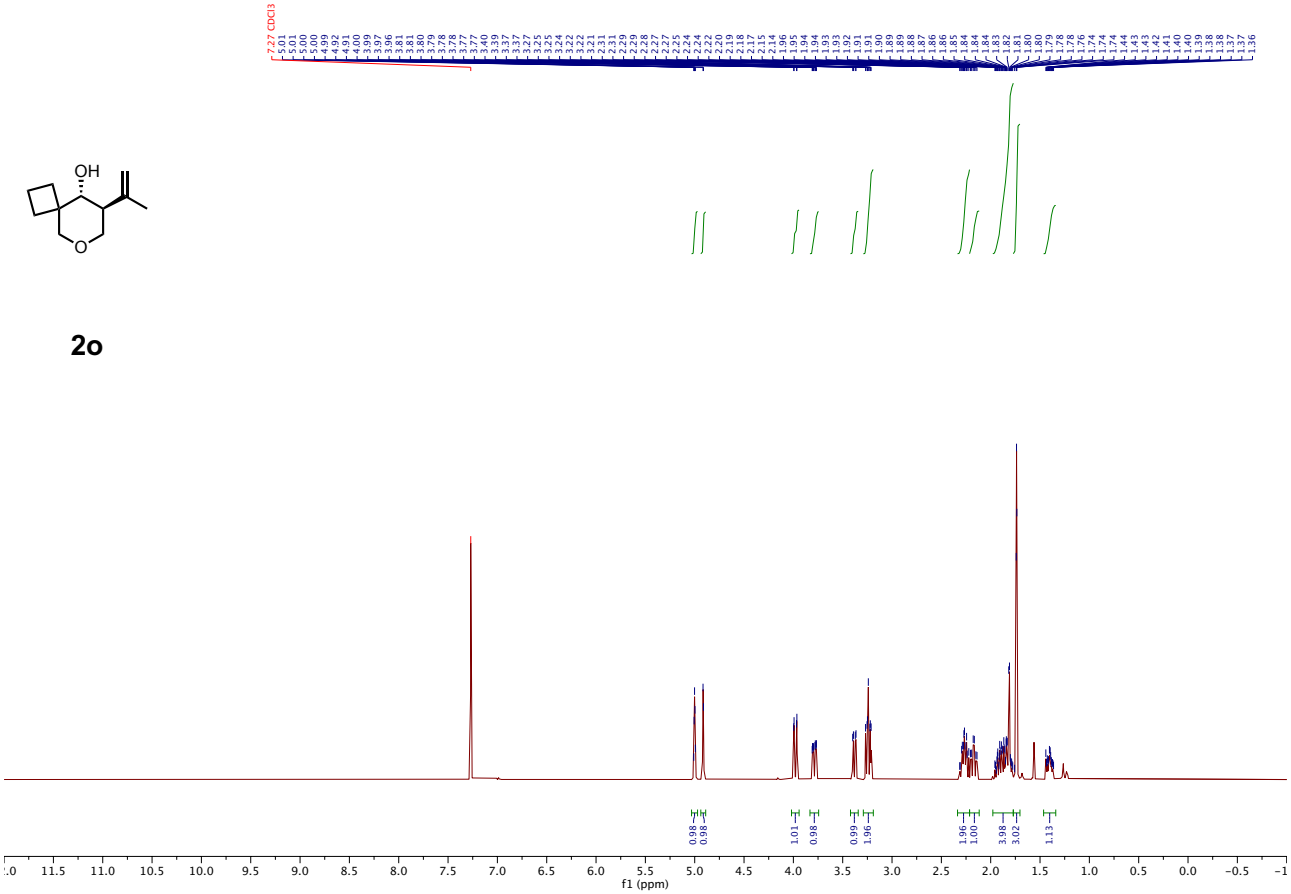
8:1 d.r. with *cis* diastereomer



2n

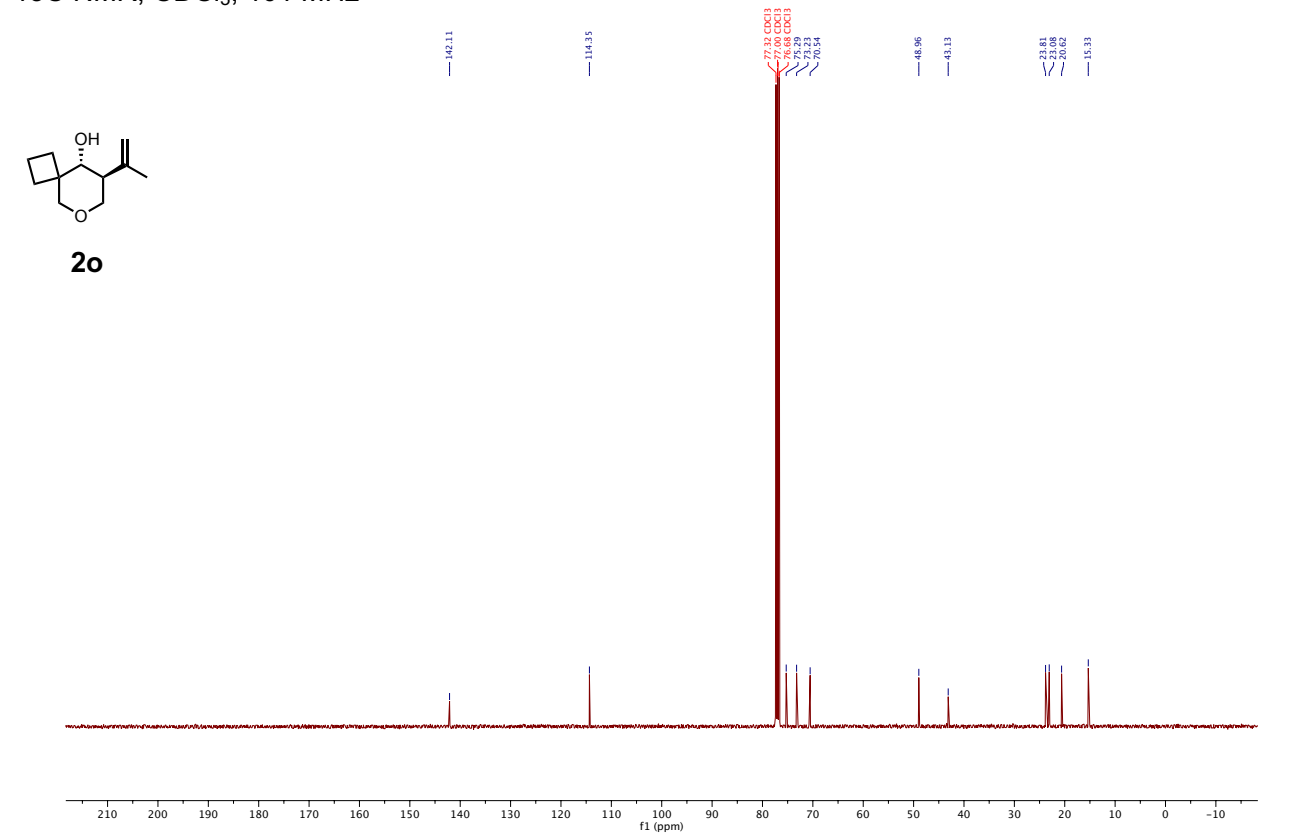


^{1}H NMR, $CDCl_3$, 400 MHz



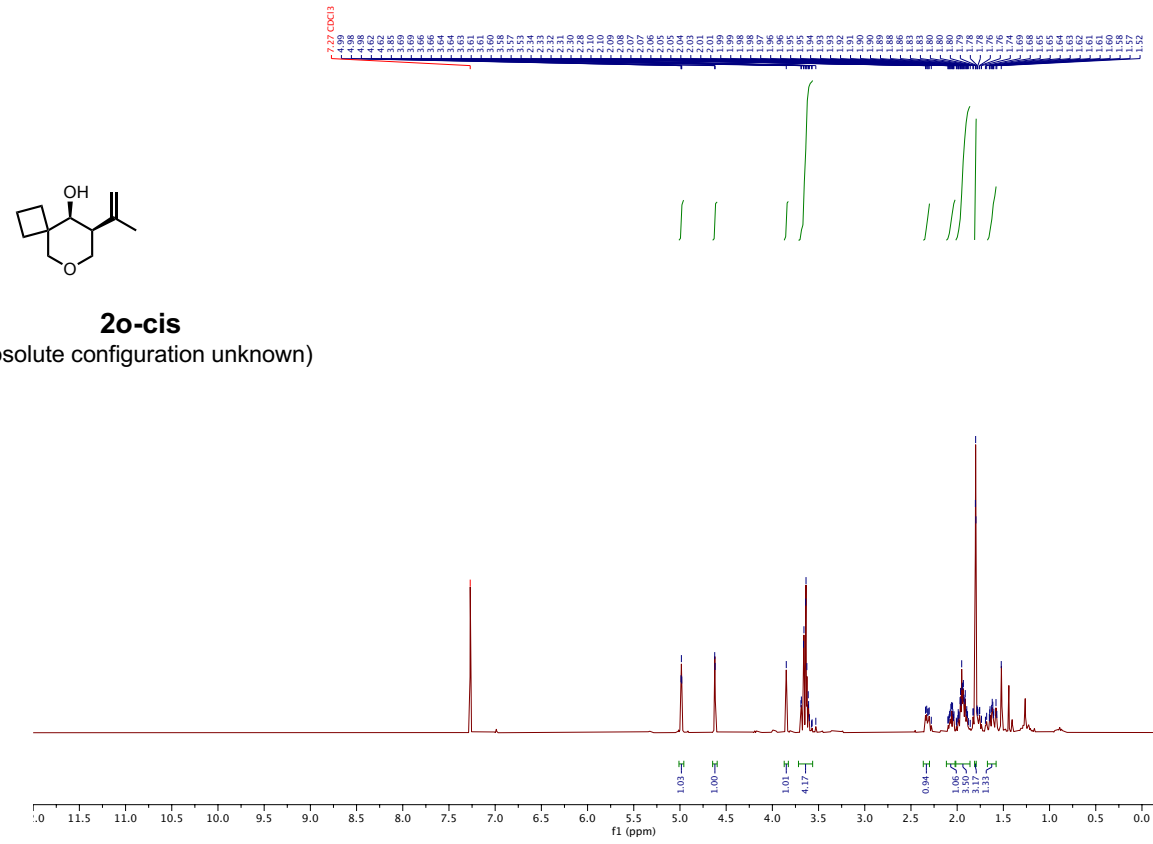
2o

13C NMR, $CDCl_3$, 101 MHz



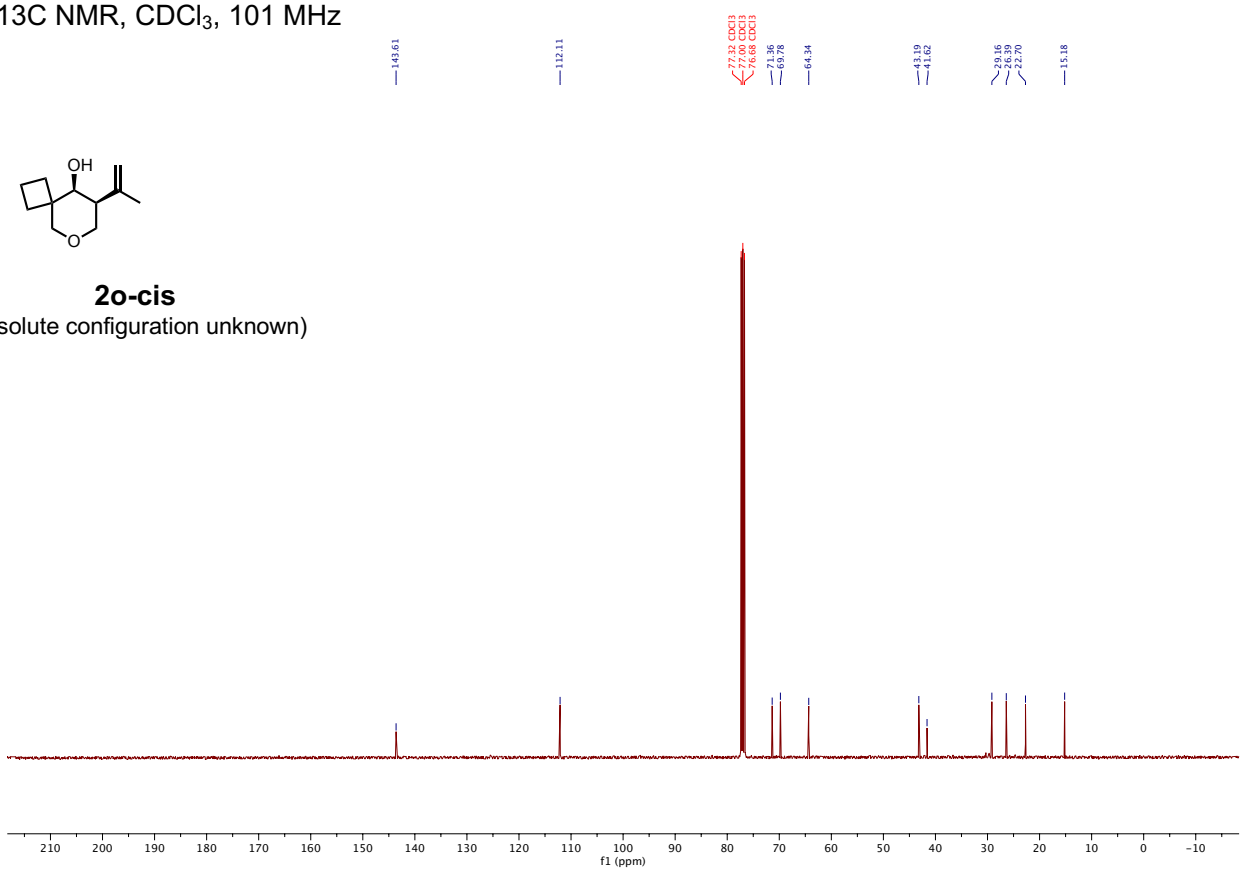
2o

^{1}H NMR, $CDCl_3$, 400 MHz



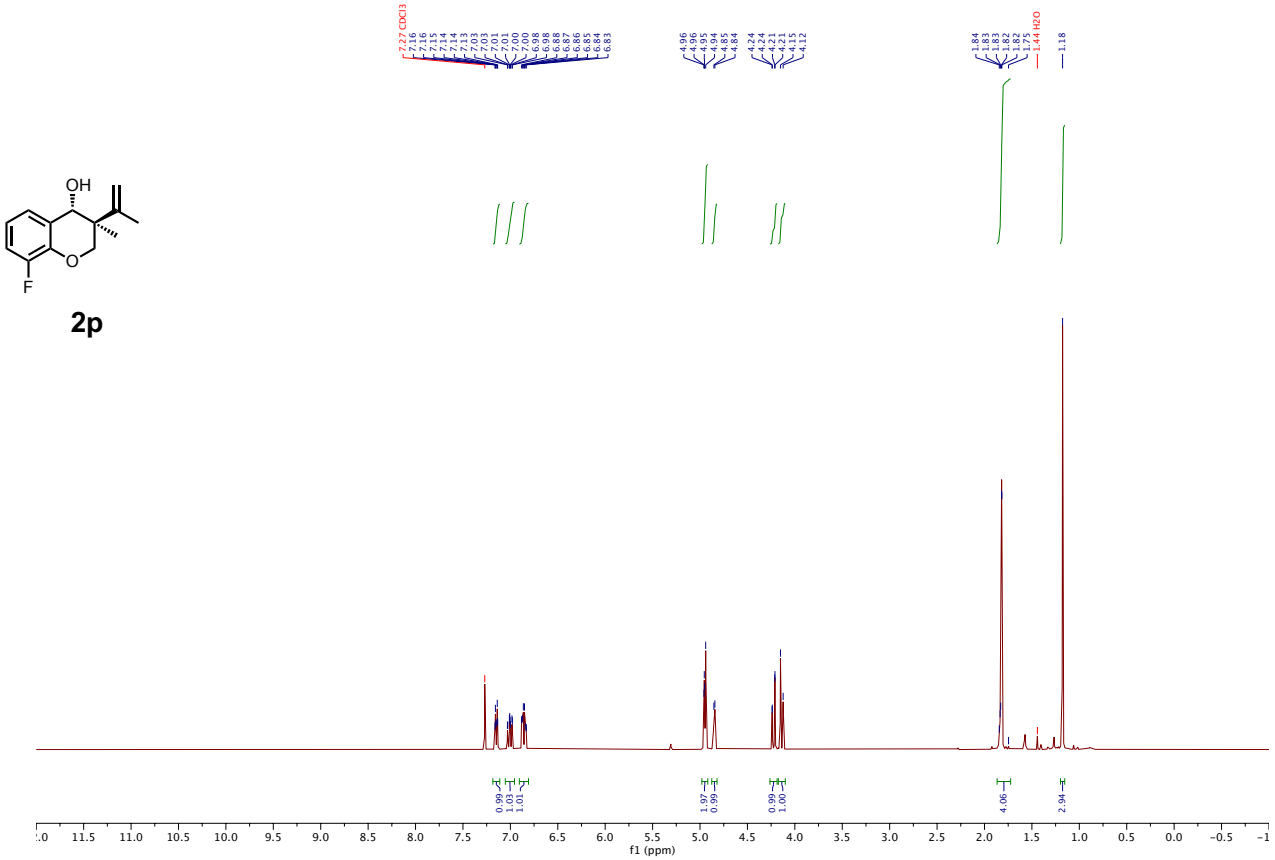
2o-cis
(absolute configuration unknown)

13C NMR, $CDCl_3$, 101 MHz



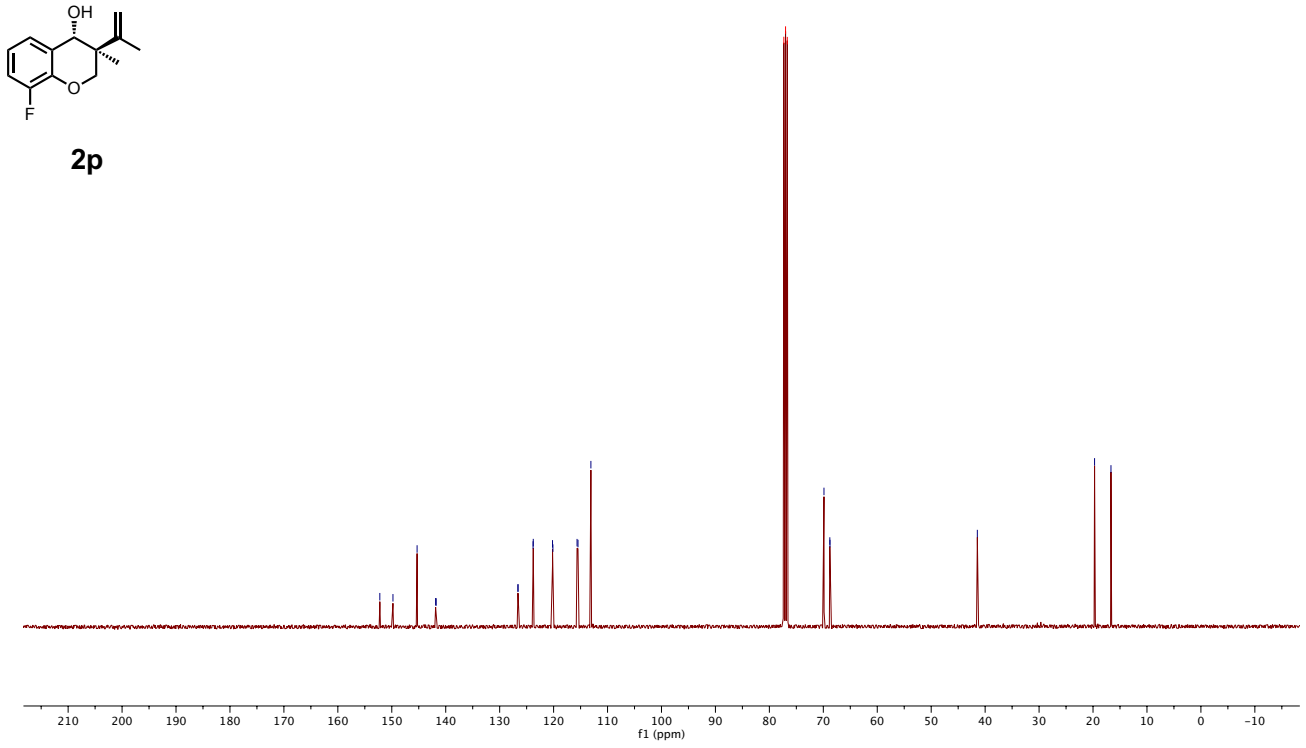
2o-cis
(absolute configuration unknown)

^{1}H NMR, $CDCl_3$, 400 MHz



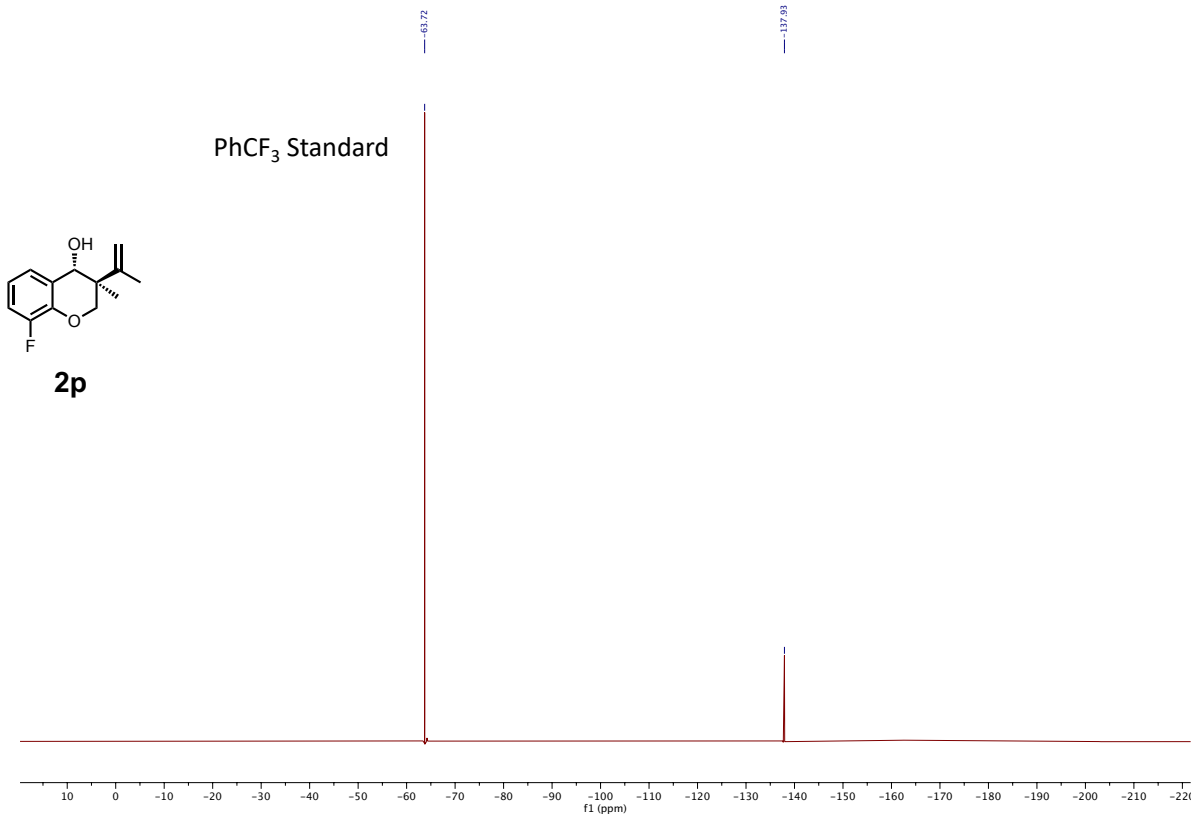
2p

13C NMR, $CDCl_3$, 101 MHz



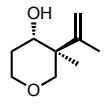
2p

^{19}F NMR, $CDCl_3$, 376 MHz



^{1}H NMR, $CDCl_3$, 400 MHz

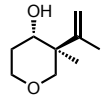
5:1 d.r. with *cis* diastereomer



2q

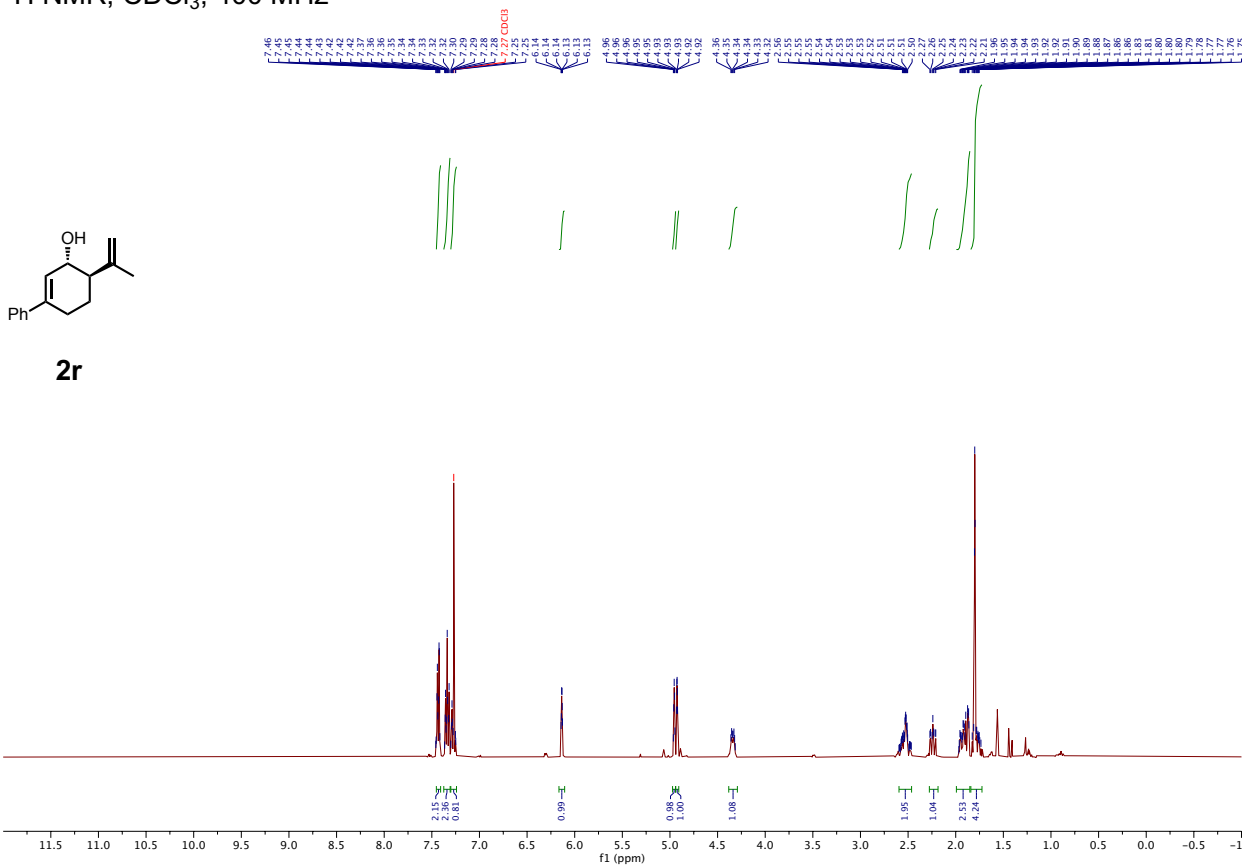
13C NMR, $CDCl_3$, 101 MHz

5:1 d.r. with *cis* diastereomer



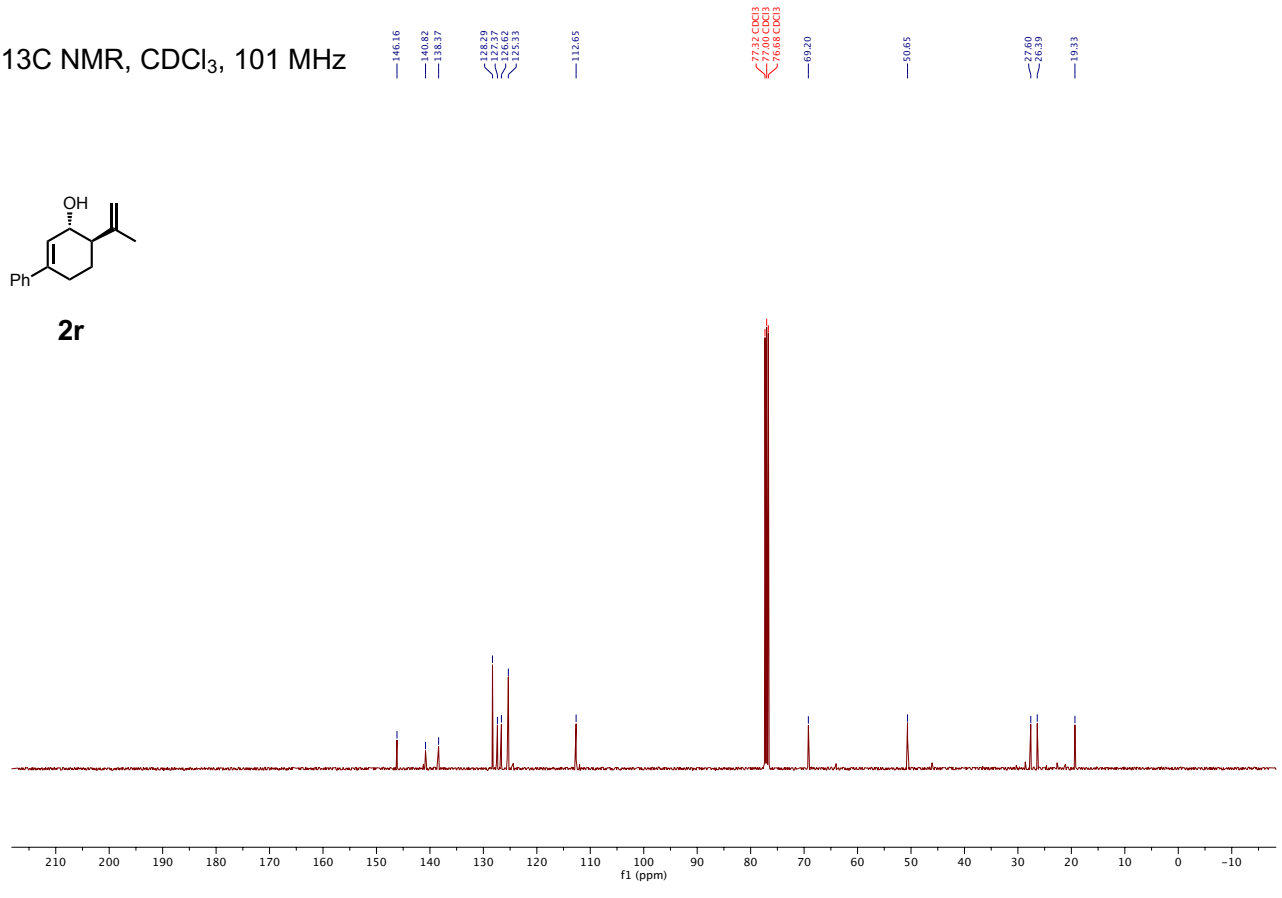
2q

^{1}H NMR, $CDCl_3$, 400 MHz



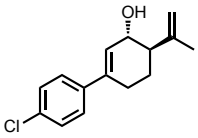
2r

13C NMR, $CDCl_3$, 101 MHz



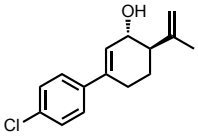
2r

^{1}H NMR, $CDCl_3$, 400 MHz

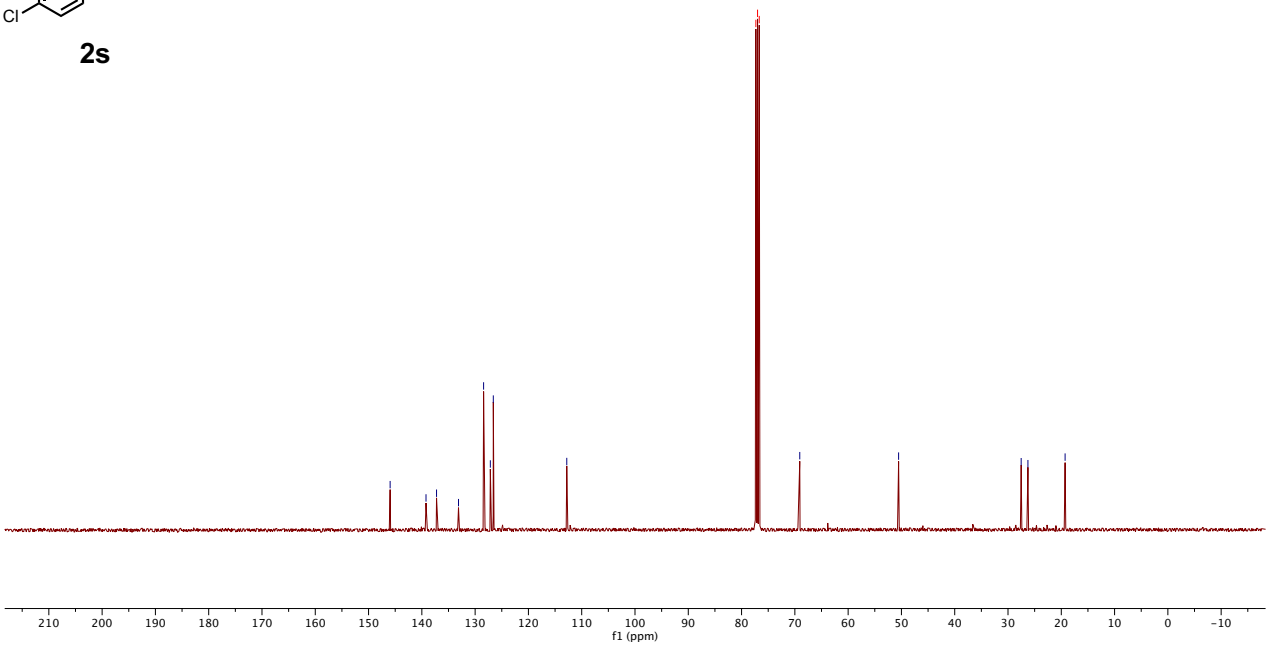


2s

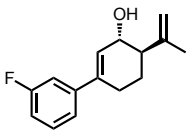
13C NMR, $CDCl_3$, 101 MHz



2s

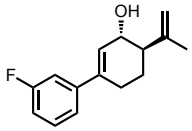


^{1}H NMR, $CDCl_3$, 400 MHz



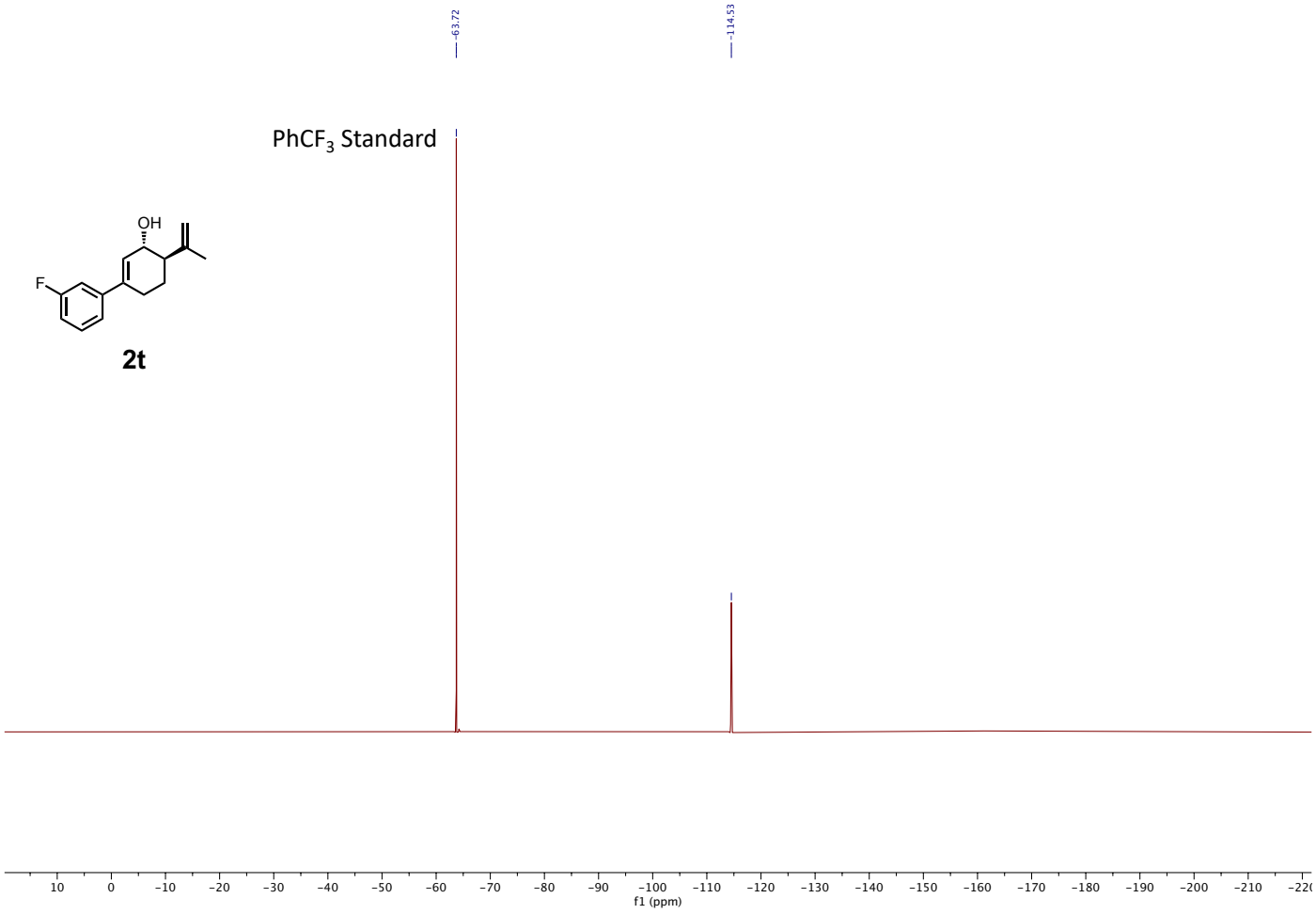
2t

13C NMR, $CDCl_3$, 101 MHz



2t

^{19}F NMR, $CDCl_3$, 376 MHz



10. References

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[2] Kennedy, C. R.; Choi, B. Y.; Reeves, M.; Jacobsen, E. N. *Isr. J. Chem.* **2020**, *60*, 461.

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[4] Kou, X.; Shao, Q.; Ye, C.; Yang, G.; Zhang, W. *J. Am. Chem. Soc*. **2018**, *140*, 7587.

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