

## Supporting Information

### **Cyclometallated Iridium-PhanePhos Complexes Are Active Catalysts in Enantioselective Allene-Fluoral Reductive Coupling and Related Alcohol-Mediated Carbonyl Additions that Form Acyclic Quaternary Carbon Stereocenters**

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## **General Information**

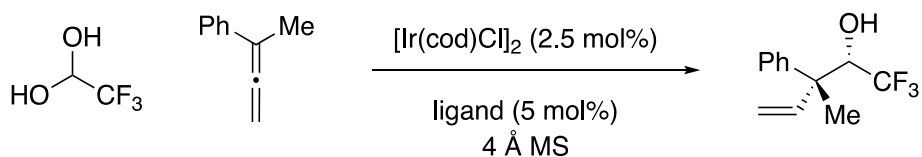
All reactions were run under an atmosphere of argon, unless otherwise indicated. Resealable pressure tubes (13x100 mm) were purchased from Fischer Scientific (catalog number 14-959-35C) and were flame dried followed by cooling in a desiccator or under a stream of argon prior to use. [Ir(cod)Cl]<sub>2</sub> and (*R*)-PhanePhos ligand were used as received from Strem Chemicals Inc. Preparative column chromatography employing Silicycle silica gel (40-63  $\mu$ m) was performed according to the method of Still.<sup>1</sup> Analytical thin-layer chromatography (TLC) was carried out using 0.25 mm commercial silica gel plates (Dynamic Absorbents F<sub>254</sub>). Visualization was accomplished with UV light followed by dipping in CAM, *p*-Anisaldehyde (PAA), or KMnO<sub>4</sub> stain solution followed by heating. Specific optical rotations were recorded on an Atago AP-300 automatic polarimeter at the sodium line (589.3 nm) in CHCl<sub>3</sub>. Solution concentrations are given in the units of 10<sup>-2</sup> g mL<sup>-1</sup>. 4Å molecular sieves (Sigma Aldrich, powder, 325 mesh particle size) were dried prior to each use by heating with a propane torch *in vacuo* and cooling to room temperature under Ar. 1,1-Disubstituted allenes **1a-1e**<sup>2</sup>, **1g**<sup>3</sup>, **1h**<sup>3</sup>, **1i**<sup>3</sup>, **1p**<sup>2</sup>, **1q**<sup>4</sup>, **1s**<sup>4</sup> and **1u**<sup>5</sup> were prepared according to literature procedures. 1,1-Disubstituted allenes were stable for several months at -20 °C, but some degradation can be observed at higher temperatures. Racemic reactions were conducted using a 1:1 ratio of (*R*)- and (*S*)-PhanePhos.

## **Spectroscopy, Spectrometry, and Data Collection**

Infrared spectra were recorded on a Perkin-Elmer 1600 spectrometer. High-resolution mass spectra (HRMS) were obtained on a Karatos MS9 and are reported as *m/z* (relative intensity). Accurate masses are reported for the molecular ion (M+H, M+Na), or a suitable fragment ion. Proton nuclear magnetic resonance (<sup>1</sup>H NMR) spectra were recorded with a Varian INOVA (500 MHz) spectrometer equipped with a Bruker AVANCE III cryoprobe. Chemical shifts are reported in delta ( $\delta$ ) units, parts per million (ppm) downfield from tetramethylsilane or ppm relative to the center of the singlet at 7.26 ppm for deuteriochloroform. Data reported as multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). Integration and coupling constants were reported in Hertz (Hz). Carbon-13 nuclear magnetic resonance (<sup>13</sup>C NMR) spectra were recorded with a Varian INOVA (125 MHz) spectrometer and were routinely run with broadband decoupling. Chemical shifts are reported in delta ( $\delta$ ) units, ppm relative to the center of the triplet at 77.16 ppm for deuteriochloroform. Fluorine-19 nuclear magnetic resonance (<sup>19</sup>F NMR) spectra were recorded with a Varian INOVA (470 MHz) spectrometer. Deuterium nuclear magnetic resonance (<sup>2</sup>H NMR) spectra were recorded in CHCl<sub>3</sub> solution with a Varian Gemini 500 (77 MHz) spectrometer (relaxation delay 2.00s).

## Experimental Details and Spectral Data

### Selected Optimization Experiments



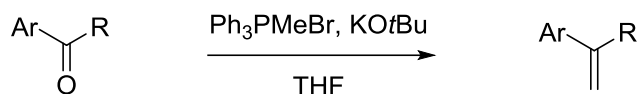
Ligand	Solvent (M)	Additive	Temp. (°C)	Yield (%)	ee (%)	dr
( <i>R</i> )-SEGPPOS*	THF (0.2 M)	-	100	89	28	8:1
( <i>R</i> )-DM-SEGPPOS*	THF (0.2 M)	-	100	41	80	7:1
( <i>R</i> )-PhanePhos	THF (0.2 M)	-	100	45	96	7:1
( <i>R</i> )-PhanePhos	Dioxane (0.2 M)	-	100	74	97	6:1
( <i>R</i> )-PhanePhos	PhMe (0.2 M)	-	100	53	96	5:1
( <i>R</i> )-PhanePhos	DMF (0.2 M)	-	100	54	96	9:1
( <i>R</i> )-PhanePhos	<sup>t</sup> AmylOH (0.2 M)	-	100	24	96	7:1
( <i>R</i> )-PhanePhos	<sup>t</sup> BuOH (0.2 M)	-	100	67	96	6:1
( <i>R</i> )-PhanePhos	<sup>t</sup> BuOH (0.2 M)	TBAI (10 mol%)	100	N/D	N/D	6:1
( <i>R</i> )-PhanePhos	<sup>t</sup> BuOH (0.2 M)	TBAC (10 mol%)	100	N/D	N/D	10:1
( <i>R</i> )-PhanePhos	<sup>t</sup> BuOH (0.2 M)	TBAC (25 mol%)	100	N/D	N/D	13:1
( <i>R</i> )-PhanePhos	<sup>t</sup> BuOH (0.2 M)	TBAC (50 mol%)	100	N/D	N/D	15:1
( <i>R</i> )-PhanePhos	<sup>t</sup> BuOH (0.2 M)	TBAC (100 mol%)	100	78	96	17:1
( <i>R</i> )-PhanePhos	<sup>t</sup> BuOH (0.2 M)	LiCl (100 mol%)	100	51**	N/D	18:1
( <i>R</i> )-PhanePhos	<sup>t</sup> BuOH (0.2 M)	NaCl (100 mol%)	100	53**	N/D	18:1
( <i>R</i> )-PhanePhos	<sup>t</sup> BuOH (0.2 M)	TBAC (100 mol%)	90	N/D	N/D	17:1
( <i>R</i> )-PhanePhos	<sup>t</sup> BuOH (0.2 M)	TBAC (100 mol%)	80	N/D	N/D	17:1

\* Cyclometallated *C,O*-benzoate Krische catalyst

\*\* Inseparable over reduction of product observed

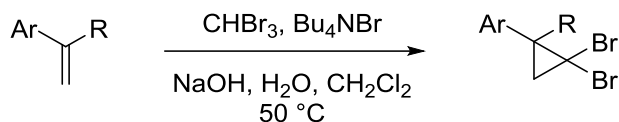
## General Procedures

### General Procedure A



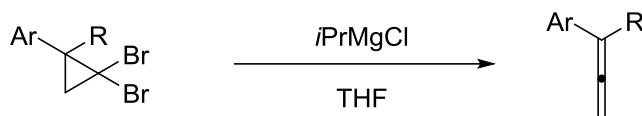
To a round-bottomed flask equipped with a magnetic stir bar under an argon atmosphere charged with methyltriphenylphosphonium bromide (110 mol%) in THF (0.25M) at 0 °C was added potassium *tert*-butoxide (120 mol%). The reaction mixture was allowed to stir at room temperature for 1 hour. Acetophenone (100 mol%) was added and the reaction mixture was allowed to stir at room temperature for 16 hours. To the reaction mixture was added H<sub>2</sub>O. The reaction mixture was transferred to a separatory funnel and the aqueous layer was extracted with Et<sub>2</sub>O (3x). The combined organic extracts were washed with brine, dried (MgSO<sub>4</sub>), filtered, and the solvent was removed *in vacuo*. The residue was subjected to flash column chromatography (SiO<sub>2</sub>) under the conditions noted to afford the styrenes.

### General Procedure B



To a round-bottomed flask equipped with a magnetic stir bar under an argon atmosphere charged with styrene (100 mol%), bromoform (200 mol%) and tetrabutylammonium bromide (10 mol %) in CH<sub>2</sub>Cl<sub>2</sub> (3M) was added dropwise sodium hydroxide (50% in H<sub>2</sub>O, 500 mol%). The reaction mixture was allowed to stir for 24 hours at 50 °C. The reaction mixture was cooled to room temperature, diluted with EtOAc, and H<sub>2</sub>O was added. The reaction mixture was transferred to a separatory funnel and the aqueous layer was extracted with EtOAc (3x). The combined organic extracts were washed with aqueous HCl (1N), H<sub>2</sub>O and brine. The solution was dried (MgSO<sub>4</sub>), filtered and the solvent was removed *in vacuo*. The residue was subjected to flash column chromatography (SiO<sub>2</sub>) under the conditions noted to afford the 1,1-dibromo-cyclopropanes.

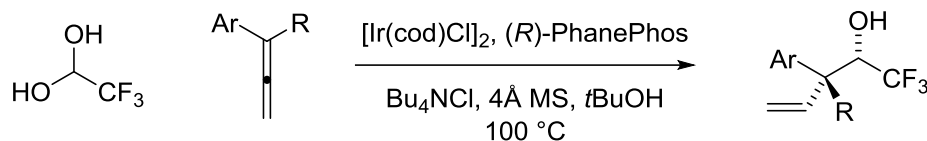
### General Procedure C



To a round-bottomed flask equipped with a magnetic stir bar under an argon atmosphere charged with cyclopropane (100 mol%) in THF (0.5 M) was added dropwise isopropylmagnesium chloride (2M in THF, 180 mol%). The reaction mixture was allowed to stir for 1 hour at room temperature. Aqueous HCl (1N) was added to the reaction mixture and the mixture was

transferred to a separatory funnel. The aqueous layer was extracted with Et<sub>2</sub>O (3x) and the combined organic extracts were washed with brine. The solution was dried (MgSO<sub>4</sub>), filtered, and the solvent was removed *in vacuo*. The residue was subjected to flash column chromatography (SiO<sub>2</sub>) under the conditions noted to afford the 1,1-disubstituted allenes.

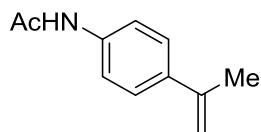
#### General Procedure D



To a dried pressure tube under an argon atmosphere charged with [Ir(cod)Cl]<sub>2</sub> (2.5 mol%), (*R*)-PhanePhos (5 mol%), tetrabutylammonium chloride (100 mol%) and dried 4 Å molecular sieves (300 wt%) was added 1,1-disubstituted allene (200 mol%), isopropanol (200 mol%) and tert-butanol (0.2M) followed by fluoral hydrate (100 mol%). The reaction mixture was allowed to stir for 16 hours at 100 °C. The solvent was removed *in vacuo* and the residue was subjected to flash column chromatography (SiO<sub>2</sub>) under the noted conditions to furnish the fluoral adducts.

## Procedures and Spectral Data for 1,1-Disubstituted Allenes 1a-1r

### *N*-(4-(prop-1-en-2-yl)phenyl)acetamide (**S1f**)

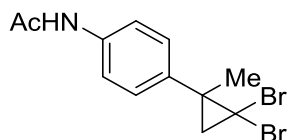


**S1f**

4'-acetamidoacetophenone (2.51 g, 14.20 mmol) was subjected to general procedure A. Upon flash column chromatography (SiO<sub>2</sub>, 1:2 EtOAc/hexanes), the title compound **S1f** (1.99 g, 11.35 mmol) was obtained as a light yellow solid in 80% yield

The spectral data recorded for this compound was in complete agreement with the literature.<sup>6</sup>

***N*-(4-(2,2-dibromo-1-methylcyclopropyl)phenyl)acetamide (**S2f**)**



**S2f**

Styrene **S1f** (1.99 g, 11.35 mmol) was subjected to general procedure B. Upon flash column chromatography (SiO<sub>2</sub>, 1:1 EtOAc/hexanes), the title compound **S2f** (2.33 g, 6.72 mmol) was obtained as a clear oil in 59% yield.

R<sub>f</sub> = 0.3 (10:1 CH<sub>2</sub>Cl<sub>2</sub> : MeOH)

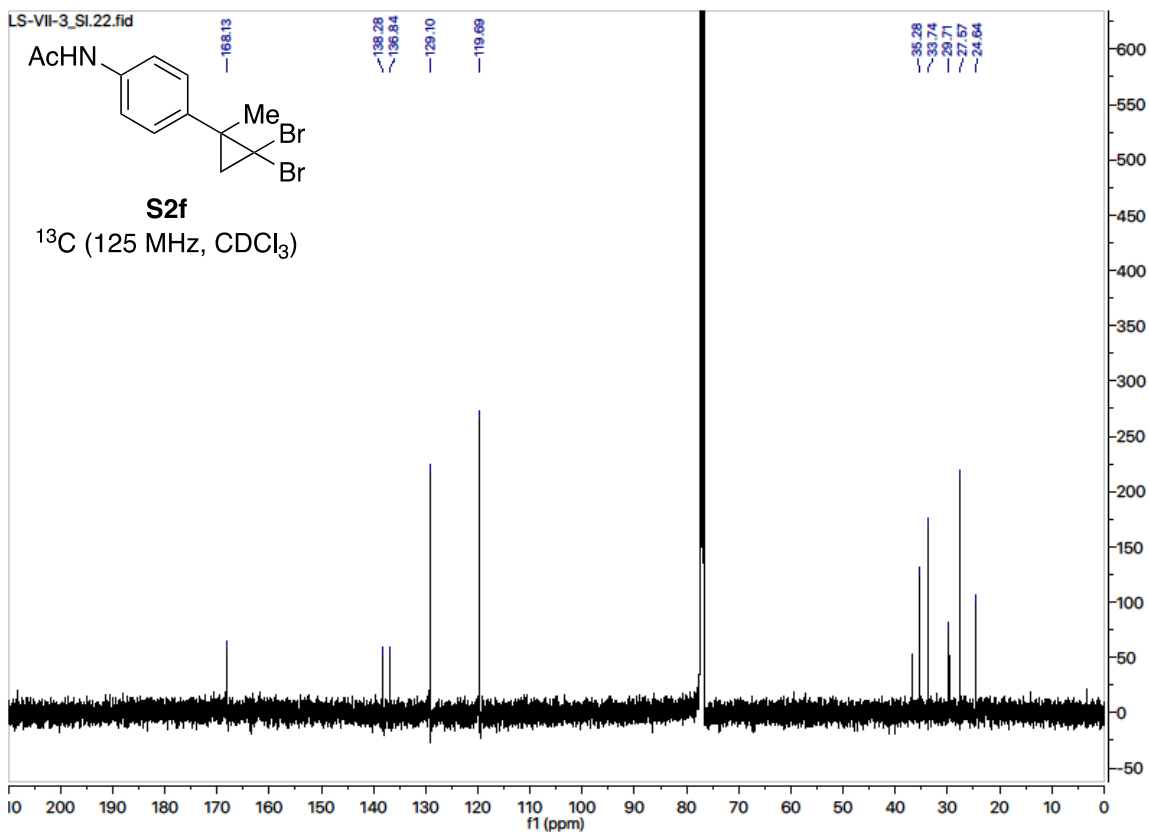
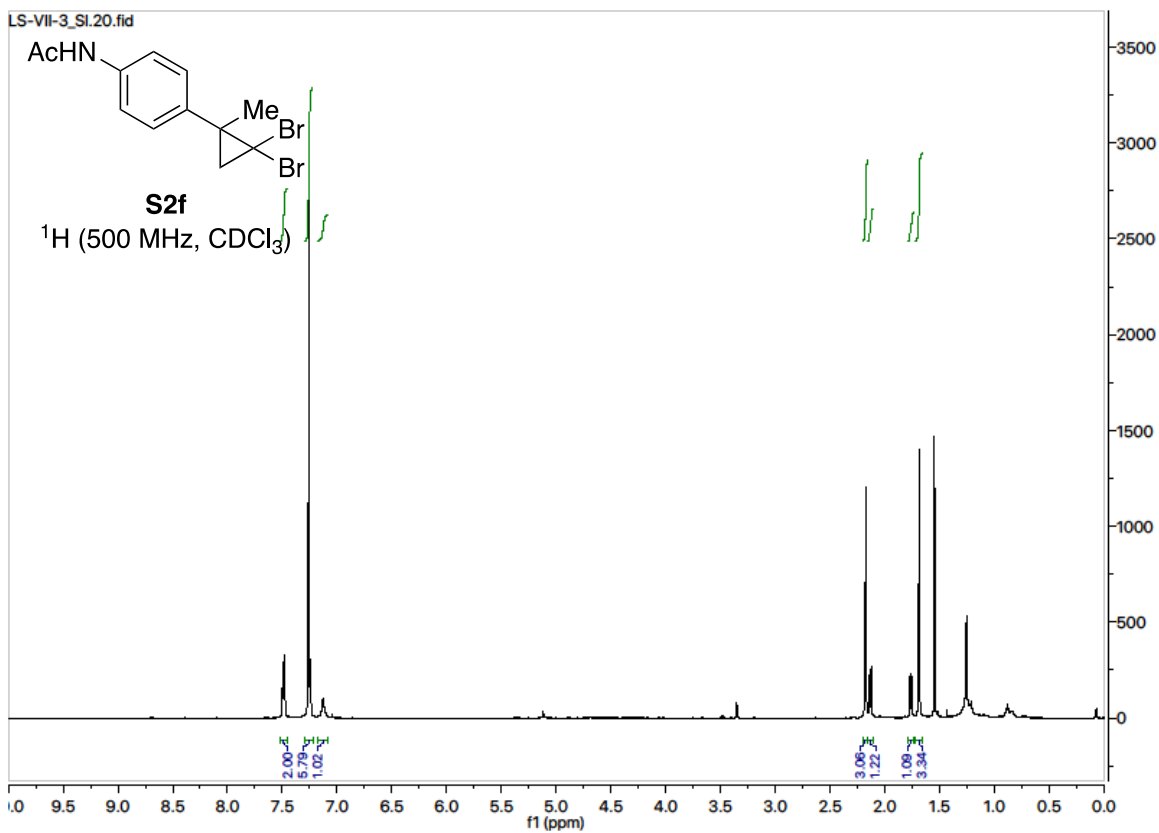
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.49 (d, *J* = 8.4 Hz, 2H), 7.25 (d, *J* = 8.2 Hz, 2H), 7.13 (bs, 1H), 2.18 (s, 3H), 2.13 (d, *J* = 7.4 Hz, 1H), 1.76, (d, *J* = 7.6 Hz, 1H), 1.69 (s, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 168.1, 138.3, 136.8, 129.1, 119.7, 35.3, 33.7, 29.7, 27.6, 24.6.

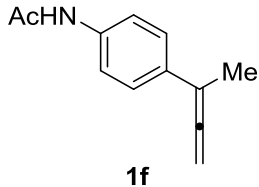
HRMS (ESI+H, *m/z*) for C<sub>12</sub>H<sub>13</sub>Br<sub>2</sub>NO: calcd. = 345.9437; found = 345.9434.

FTIR (neat): 3300, 2900, 2400, 1700, 1600, 1500, 1350, 800 cm<sup>-1</sup>.





***N*-(4-(buta-2,3-dien-2-yl)phenyl)acetamide (**1f**)**



1,1-disubstituted cyclopropane **S2f** (2.33 g, 6.72 mmol) was subjected to general procedure C. Upon flash column chromatography (SiO<sub>2</sub>, 1:2 EtOAc:hexanes), the title compound **1f** (968.8 mg, 5.17 mmol) was obtained as a light yellow solid in 79% yield.

R<sub>f</sub> = 0.3 (1:1 hexanes : EtOAc)

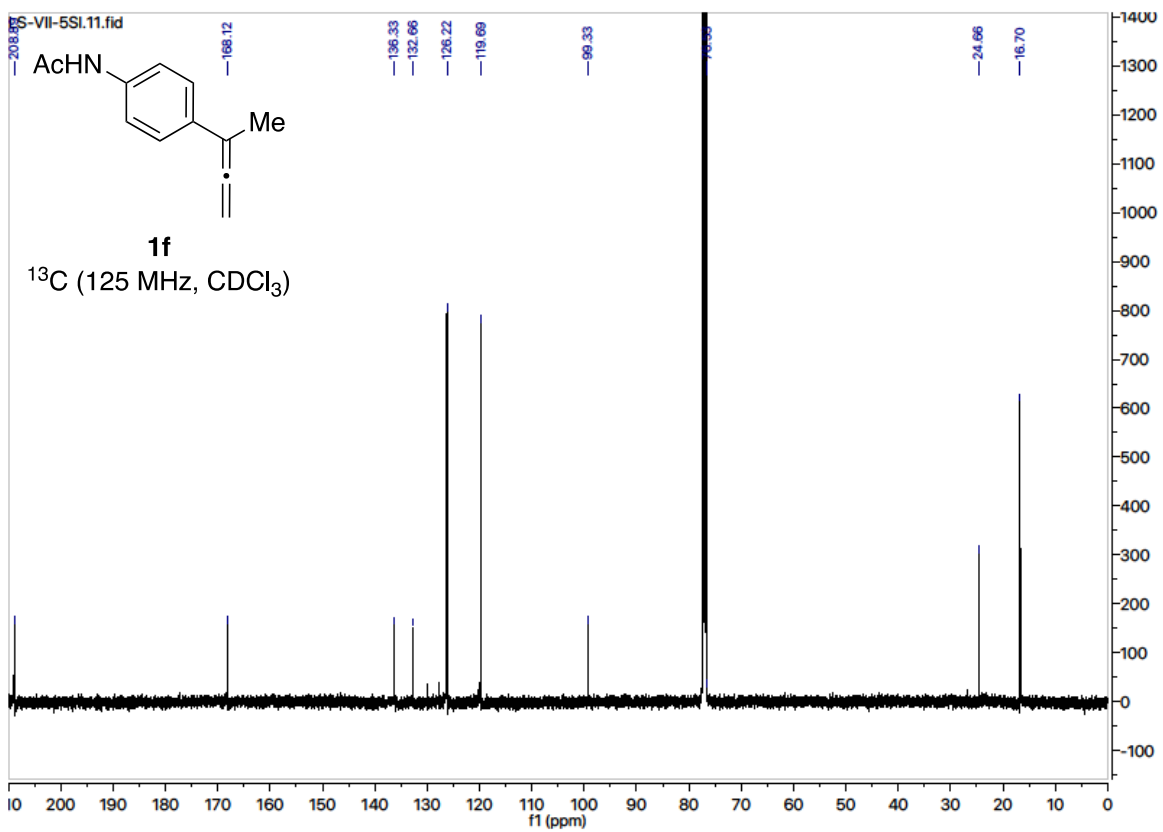
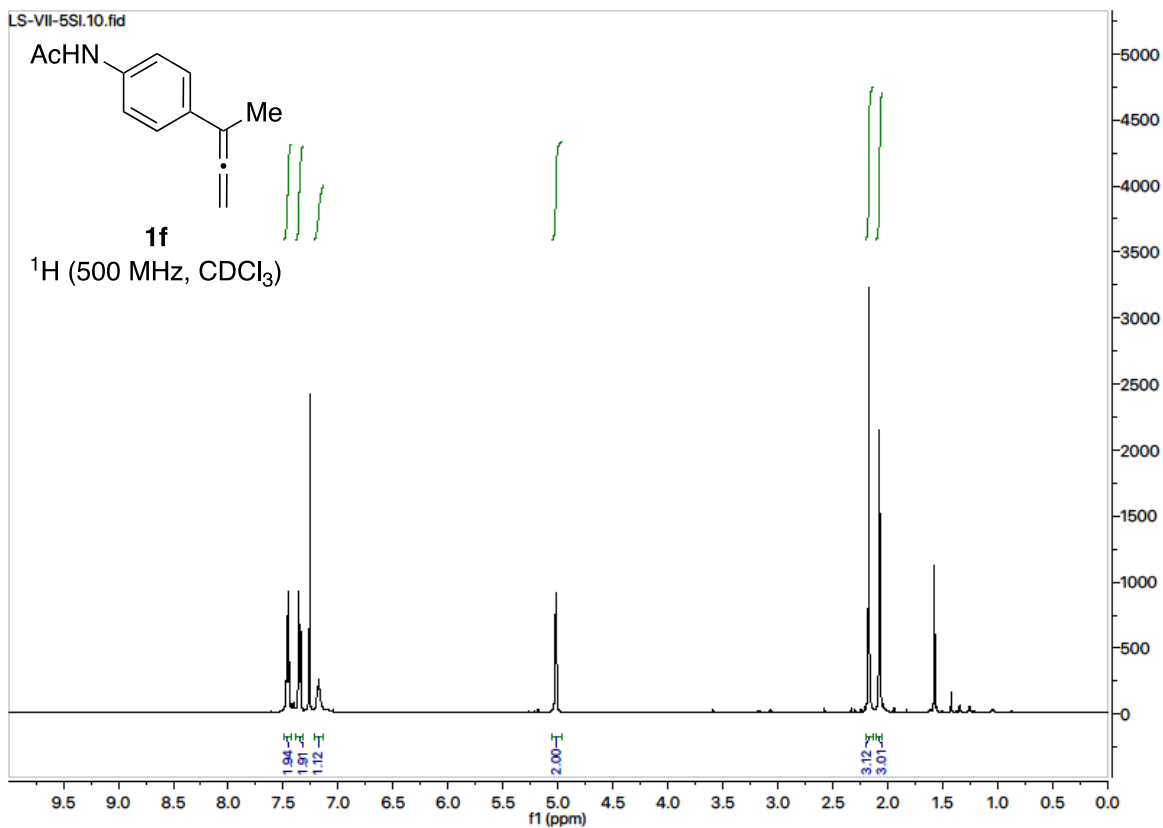
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.46 (d, *J* = 8.7 Hz, 2H), 7.35 (d, *J* = 8.4 Hz, 2H), 7.18 (bs, 1H), 5.02 (q, *J* = 3.1 Hz, 2H), 2.17 (s, 3H), 2.07 (t, *J* = 3.1 Hz, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 208.9, 168.1, 136.3, 132.7, 126.2, 119.7, 99.3, 76.6, 24.7, 16.7.

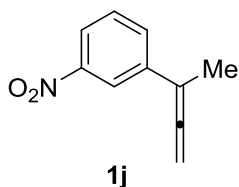
HRMS (ESI+H, *m/z*) for C<sub>12</sub>H<sub>13</sub>NO: calcd. = 188.1070; found = 188.1073.

FTIR (neat): 3300, 3000, 2350, 1650, 1600, 1550, 1500, 1400, 1350, 1300, 800 cm<sup>-1</sup>.

MP: 66-68 °C



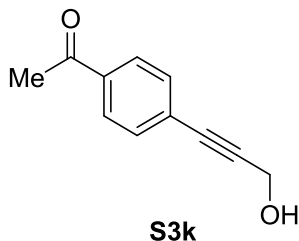
**1-(buta-2,3-dien-2-yl)-3-nitrobenzene (1j)**



In a dry rounded bottom flask with indium (0.92 g, 8 mmol), was added anhydrous DMF (8 mL) and 1-bromo-2-butyne (1.05 mL, 12 mmol, 150 mol %) under nitrogen atmosphere. After 1 hour, the resulting homogenous solution was added to a suspension of 3-nitroiodobenzene (2.00 g, 8.00 mmol, 100 mol %), Pd(PPh<sub>3</sub>)<sub>4</sub> (0.37 g, 0.32 mmol, 4 mol %) and lithium iodide (3.21 g, 24 mmol, 300 mol %) in anhydrous DMF (8 mL). This mixture was stirred at 100 °C for 1 h, cooled to room temperature and quenched with saturated aqueous NaHCO<sub>3</sub> (15 mL). The aqueous layer was extracted with diethyl ether (3 x 30 mL), and the combined organic solvents were washed with water (20 mL) and brine (2 x 20 mL), dried with Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using hexanes/EtOAc 20:1 to give the desired allene **1j** (0.49 g, 2.80 mmol) as a yellow oil in 35 % yield.<sup>7</sup>

The spectral data recorded for this compound was in complete agreement with the literature.<sup>8</sup>

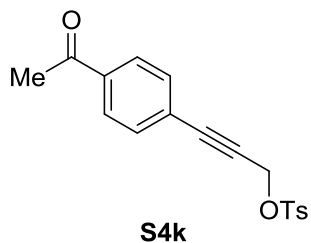
**1-(4-(3-hydroxyprop-1-yn-1-yl)phenyl)ethan-1-one (S3k)**



In a dry pressure tube with 4-bromoacetophenone (2.0 g, 10 mmol),  $\text{PdCl}_2(\text{PPh}_3)_2$  (0.14 g, 0.2 mmol, 2 mol %), copper (I) iodide (0.19 g, 1 mmol, 10 mol %) was purged with argon and propargyl alcohol (0.71 mL, 12 mmol, 120 mol %) and triethylamine (20 mL) were added. The resulting mixture was heated to 80 °C for 12 h, cooled to room temperature and quenched with saturated aqueous  $\text{NaHCO}_3$  (15 mL). The aqueous layer was extracted with dichloromethane (3 x 30 mL), and the combined organic solvents were dried with  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using *n*-hexane/EtOAc 3:1 to give the desired alcohol (1.74 g, 10 mmol) as white solid in 99 % yield.

The spectral data recorded for this compound was in complete agreement with the literature.<sup>9</sup>

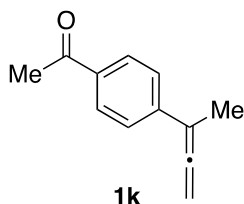
### 3-(4-acetylphenyl)prop-2-yn-1-yl 4-methylbenzenesulfonate (S4k)



In a dry rounded bottom flask with 1-(4-(3-hydroxyprop-1-yn-1-yl)phenyl)ethan-1-one (1.0 g, 5.74 mmol) and tosyl chloride (1.20 g, 6.31 mmol, 110 mol %), was added diethyl ether (8 mL) and then potassium hydroxide (1.61 g, 28.7 mmol, 500 mol %) at 0 °C. The mixture was allowed to warm to room temperature and after 1 h was quenched with water (30 mL) and extracted with diethyl ether (3 x 30 mL). The combined organic solvents were dried with Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using *n*-hexane/EtOAc 2:1 to give the desired tosylate (1.40 g, 4.26 mmol) as white solid in 74 % yield.

The spectral data recorded for this compound was in complete agreement with the literature.<sup>10</sup>

**1-(4-(buta-2,3-dien-2-yl)phenyl)ethan-1-one (1k)**



In a dry rounded bottom flask with copper (I) bromide (0.48 g, 3.33 mmol, 100 mol %) purged with nitrogen atmosphere in THF (10 mL) was added methylmagnesium bromide (1.1 mL, 100 mol %, 3 M) dropwise. After 1 h, a THF (10 mL) solution of 3-(4-acetylphenyl)prop-2-yn-1-yl 4-methylbenzenesulfonate (1.04 g, 3.17 mmol) was added dropwise and the solution was allowed to stir at room temperature for 1 h. After 1 h, reaction was quenched with water (30 mL) and extracted with dichloromethane (3 x 30 mL). The combined organic solvents were dried with Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using *n*-hexane/EtOAc 10:1 to give the desired allene (0.21 g, 1.21 mmol) as clear oil in 38 % yield.

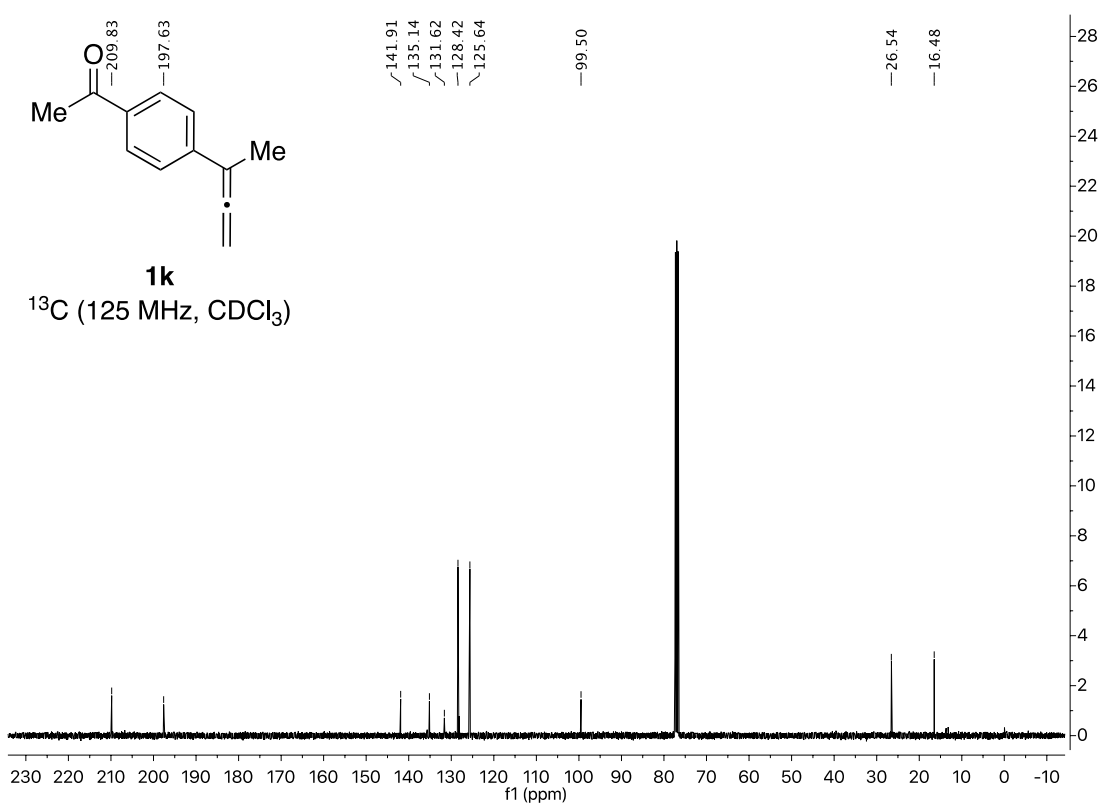
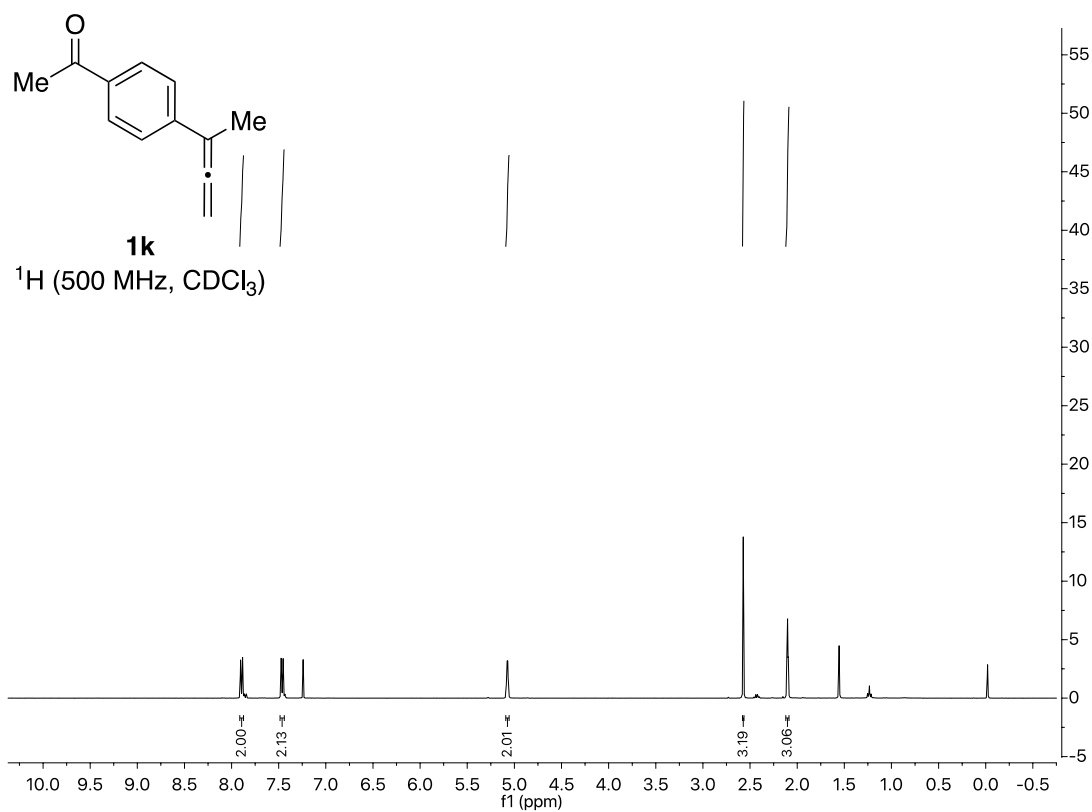
R<sub>f</sub> = 0.51 (5:1 hexanes : EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.89 (dd, *J* = 8.5, 1.4 Hz, 2H), 7.46 (d, *J* = 8.1 Hz, 2H), 5.07 (q, *J* = 3.2 Hz, 2H), 2.57 (s, 3H), 2.12 – 2.09 (m, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 209.8, 197.6, 141.9, 135.1, 131.6, 128.4, 125.6, 99.5, 26.5, 16.5.

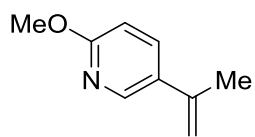
HRMS (ESI + H, *m/z*) for C<sub>12</sub>H<sub>13</sub>O: calcd. = 173.0963; found = 173.0961.

FTIR (neat): 2944, 2866, 1682, 1462, 1356, 1192, 996, 976, 882, 826, 678, 662 cm<sup>-1</sup>.





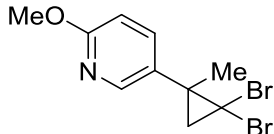
**2-Methoxy-5-(prop-1-en-2-yl)pyridine (S1m)**



**S1m**

5-Acetyl-2-methoxypyridine (1.51 g, 10 mmol) was subjected to general procedure A. The product was passed through a short silica plug (EtOAc) and used in the next step without further purification.

**5-(2,2-Dibromo-1-methylcyclopropyl)-2-methoxypyridine (S2m)**



**S2m**

Styrene **S1m** (10 mmol) was subjected to general procedure B. Upon flash column chromatography (SiO<sub>2</sub>, 3:97 EtOAc:hexanes), the title compound **S2m** (1.63 g, 5.5 mmol) was obtained as a light yellow solid in 55% yield over two steps.

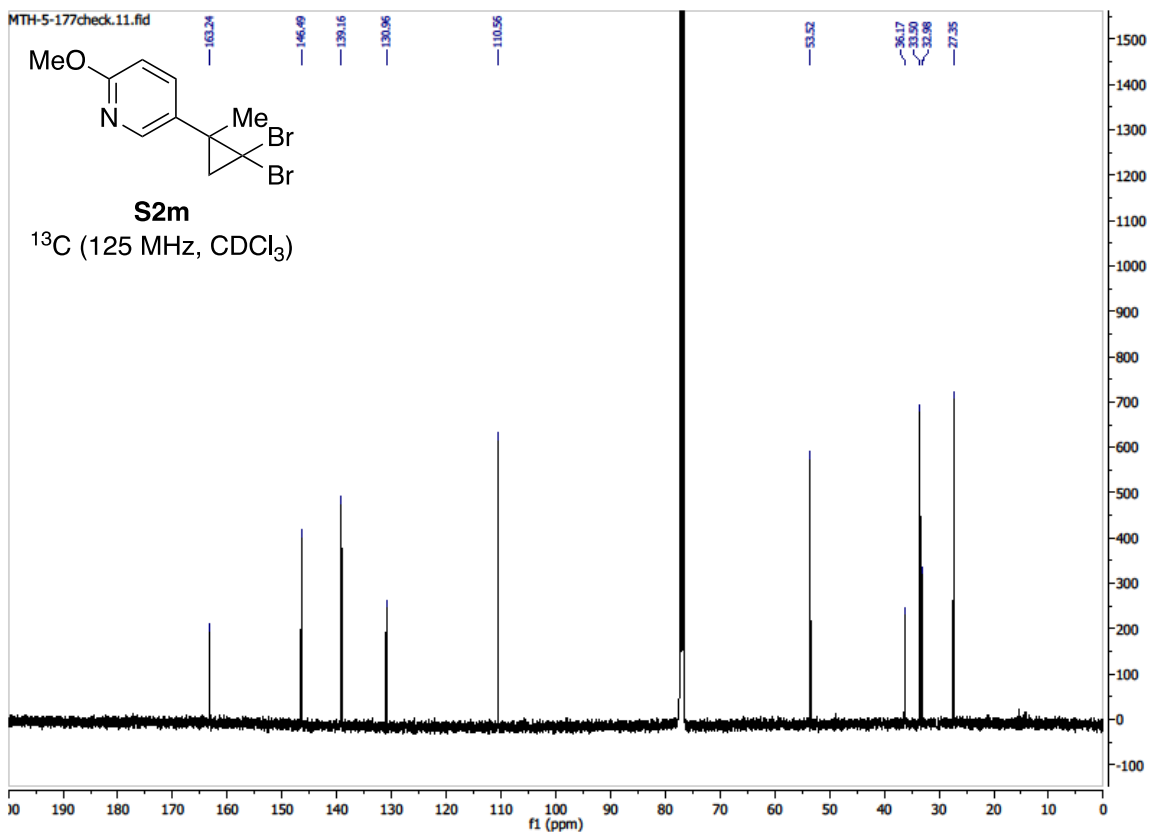
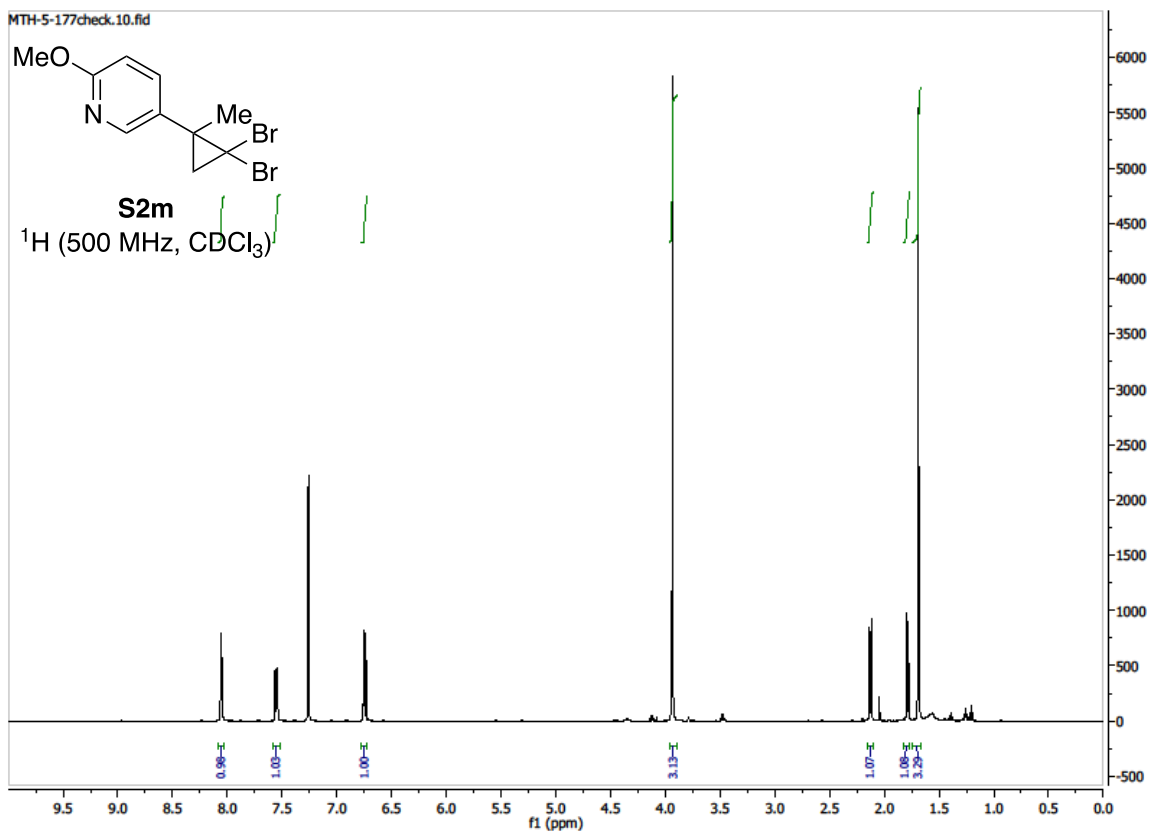
R<sub>f</sub> = 0.32 (95:5 hexanes:EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 8.05 (d, *J* = 2.5 Hz, 1H), 7.55 (dd, *J* = 2.5, 8.3 Hz, 1H), 6.74 (d, *J* = 8.3 Hz, 1H), 3.94 (s, 3H), 2.13 (d, *J* = 7.3 Hz, 1H), 1.79 (d, *J* = 7.3 Hz, 1H), 1.69 (s, 3H).

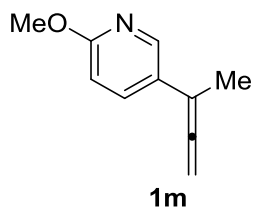
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 163.2, 146.5, 139.2, 131.0, 110.6, 53.5, 36.2, 33.5, 33.0, 27.4.

HRMS (ESI+H, *m/z*) for C<sub>10</sub>H<sub>11</sub>Br<sub>2</sub>NO: calcd. = 319.9280; found = 319.9277.

FTIR (neat): 2982, 1608, 1495, 1375, 1309, 1063, 1023, 832 cm<sup>-1</sup>.



**5-(Buta-2,3-dien-2-yl)-2-methoxypyridine (**1m**)**



1,1-Disubstituted cyclopropane **S2m** (1.63 g, 5.5 mmol) was subjected to general procedure C. Upon flash column chromatography (SiO<sub>2</sub>, 3:97 EtOAc:hexanes), the title compound **1m** (640 mg, 4.0 mmol) was obtained as a colorless oil in 73% yield.

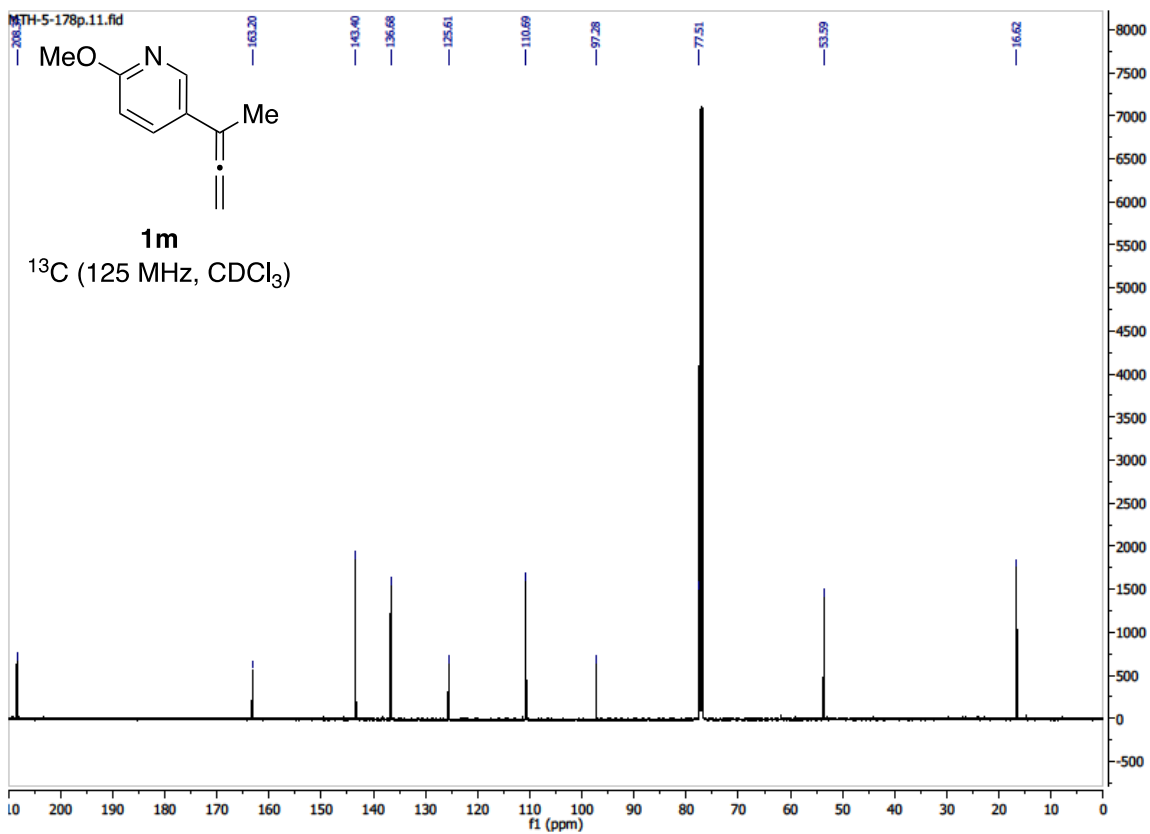
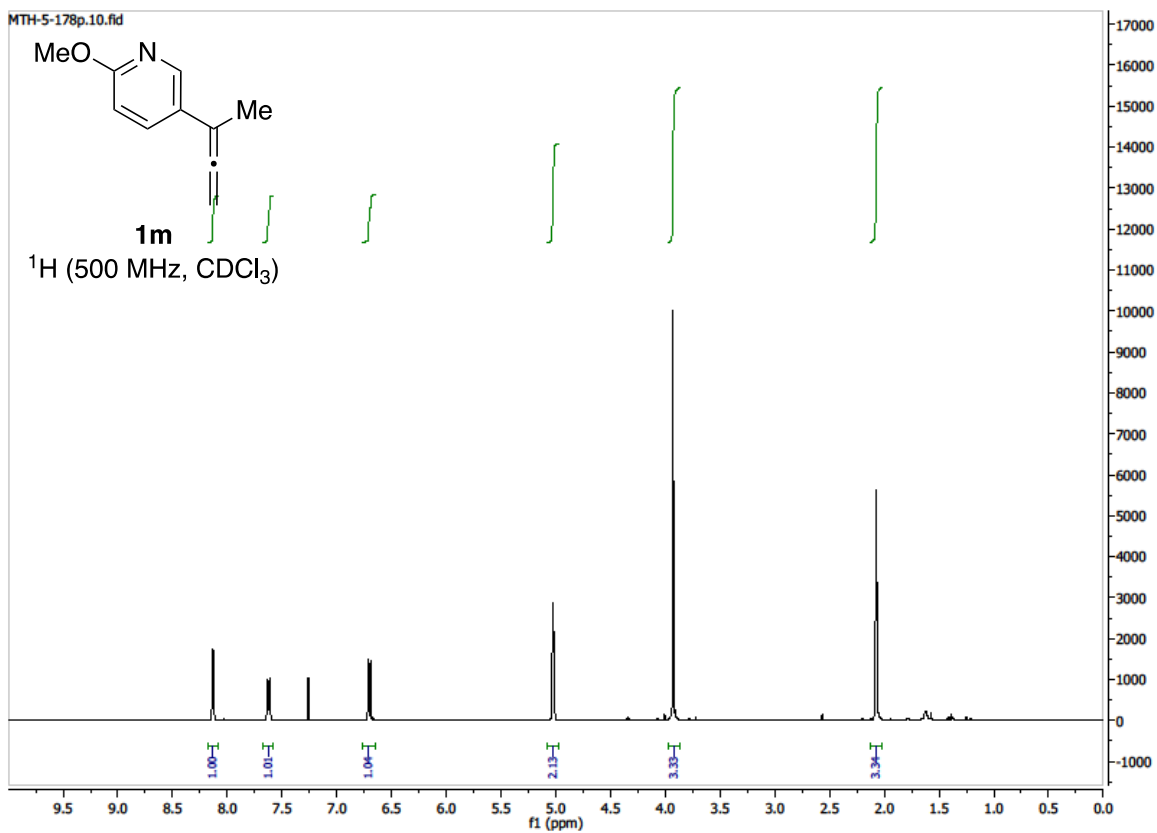
R<sub>f</sub> = 0.41 (95:5 hexanes:EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 8.13 (s, 1H), 7.62 (d, *J* = 9.3 Hz, 1H), 6.70 (d, *J* = 9.3 Hz, 1H), 5.03 (q, *J* = 2.8 Hz, 2H), 3.93 (s, 3H), 2.08 (t, *J* = 2.8 Hz, 3H).

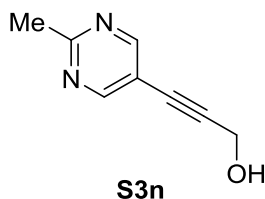
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 208.4, 163.2, 143.4, 136.7, 125.6, 110.7, 97.3, 77.5, 53.6, 16.6.

HRMS (CI<sup>+</sup>, *m/z*) for C<sub>10</sub>H<sub>11</sub>NO: calcd. = 162.0913; found = 162.0916.

FTIR (neat): 2950, 1725, 1661, 1602, 1493, 1263, 1022 cm<sup>-1</sup>.



### 3-(2-Methylpyrimidin-5-yl)prop-2-yn-1-ol (S3n)



To a stirred solution of 5-bromo-2-methylpyrimidine (2.60 g, 15 mmol) in DMF (15 mL) was added triethylamine (4.2 mL, 30 mmol) and propargyl alcohol (0.97 mL, 16.5 mmol). The solution was sparged for 10 minutes with Ar. Copper iodide (114 mg, 0.6 mmol) and bis(triphenylphosphine)palladium (II) dichloride (211 mg, 0.3 mmol) were added and the reaction mixture was stirred at 100 °C for 36 h. H<sub>2</sub>O (100 mL) and ethyl acetate (100 mL) were added and the reaction mixture was filtered. The phases were separated and the aqueous layer washed with ethyl acetate (3 x 100 mL). The combined organic phases were washed with brine (100 mL), dried (MgSO<sub>4</sub>), filtered and the solvent removed *in vacuo*. The residue was subjected to flash column chromatography (SiO<sub>2</sub>, 2:1 hexanes:EtOAc) to afford the title compound (0.79 g, 5.3 mmol) as a light yellow solid in 36% yield.

R<sub>f</sub> = 0.1 (1:1 hexanes:EtOAc)

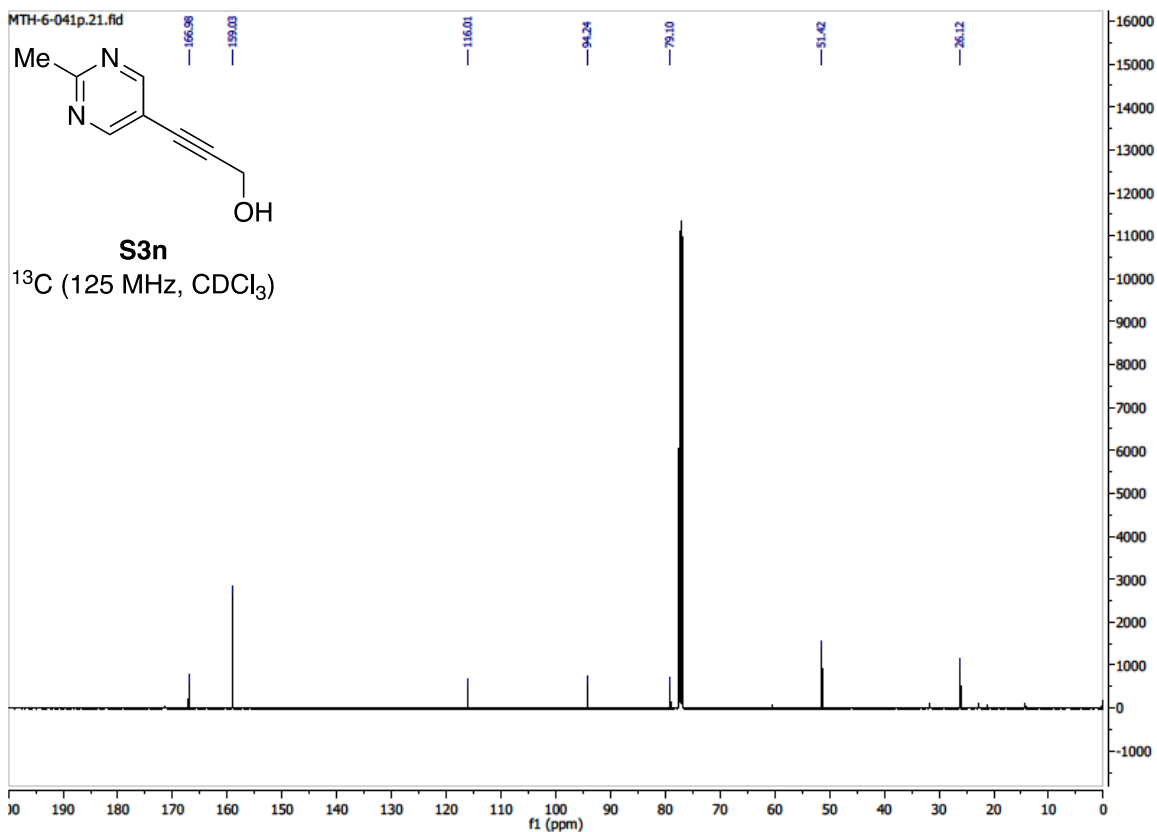
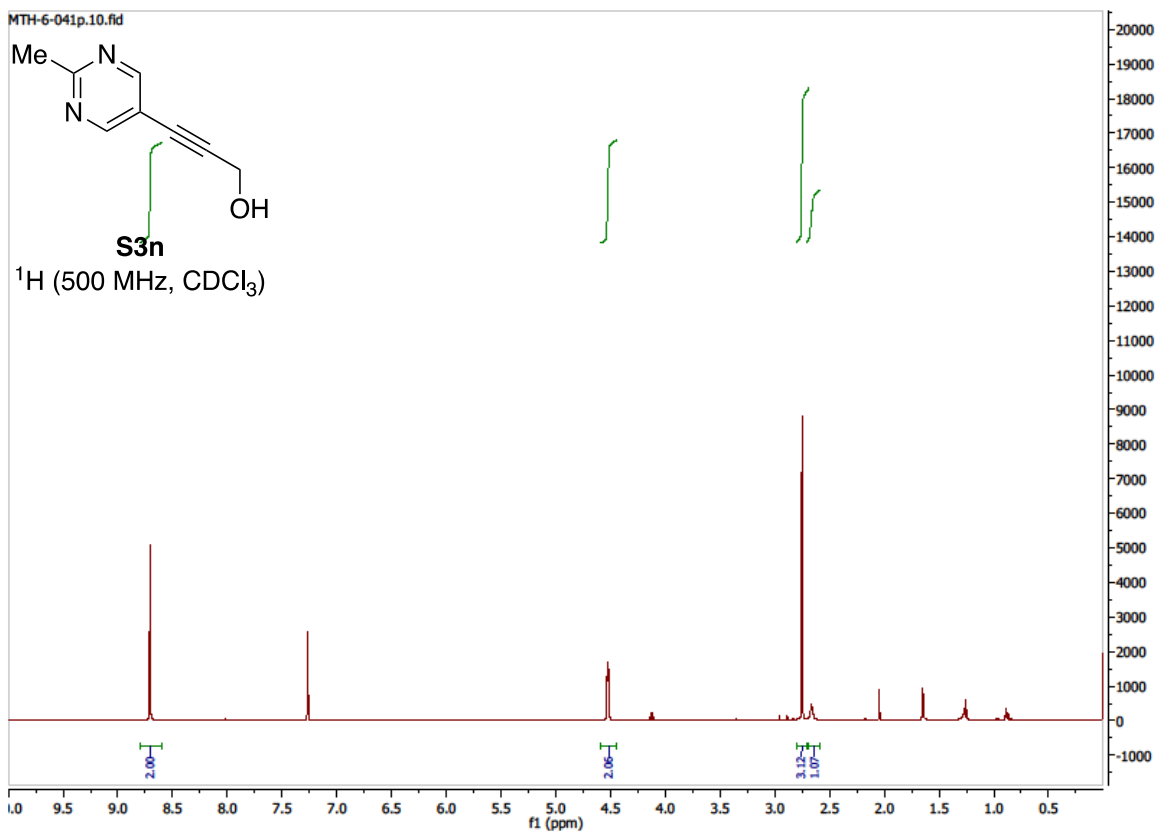
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 8.71 (s, 2H), 4.52 (d, *J* = 5.6 Hz, 2H), 2.75 (s, 3H), 2.67 (t, *J* = 5.6 Hz, 1H, OH).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 167.0, 159.0, 116.0, 94.2, 79.1, 51.4, 26.1.

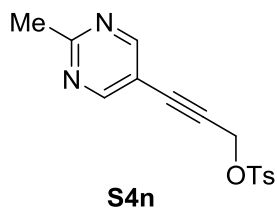
HRMS (ESI+H, *m/z*) for C<sub>8</sub>H<sub>8</sub>N<sub>2</sub>O: calcd. = 149.0709; found = 149.0710.

FTIR (neat): 3708, 3258, 2938, 2864, 2360, 1589, 1447, 1032, 744 cm<sup>-1</sup>.

MP = 120-123 °C.



### 3-(2-methylpyrimidin-5-yl)prop-2-yn-1-yl 4-methylbenzenesulfonate (**S4n**)



To a stirred solution of propargyl alcohol **S3n** (0.74 g, 5.0 mmol) in Et<sub>2</sub>O (7 mL) at 0 °C was added tosyl chloride (1.05 g, 5.5 mmol) followed by crushed potassium hydroxide (1.40 g, 25 mmol). The reaction mixture was stirred at 0 °C for 1 hour. The reaction mixture was poured onto ice water (30 mL) and diluted with Et<sub>2</sub>O (30 mL). The phases were separated and the organic phase was washed with H<sub>2</sub>O (2 x 30 mL). The combined aqueous phases were washed with Et<sub>2</sub>O (2 x 30 mL). The combined organic phases were washed with brine (20 mL), dried (MgSO<sub>4</sub>), filtered and the solvent removed *in vacuo*. The residue was subjected to flash column chromatography (SiO<sub>2</sub>, 1:1 hexanes:EtOAc) to afford the title compound (1.22 g, 4.1 mmol) as a light yellow solid in 81% yield.

R<sub>f</sub> = 0.16 (1:1 hexanes : EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 8.50 (s, 2H), 7.85 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 4.96 (s, 2H), 2.73 (s, 3H), 2.42 (s, 3H).

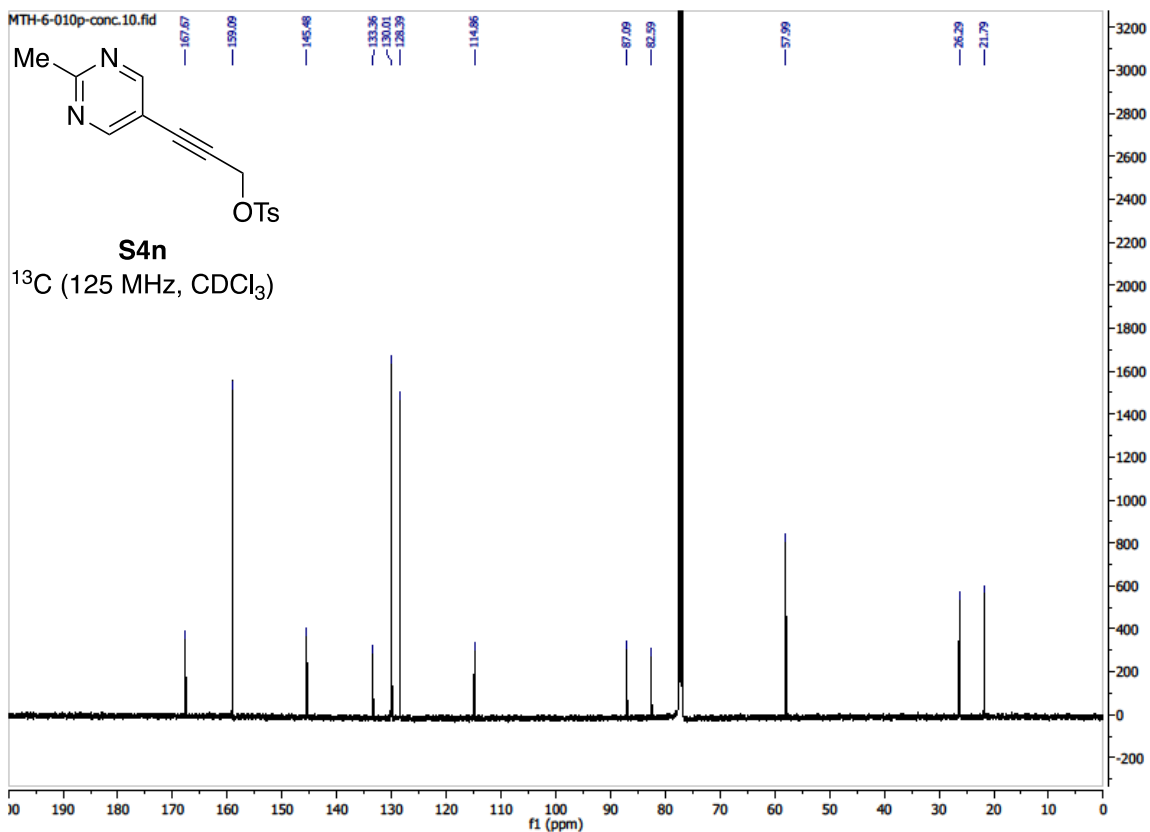
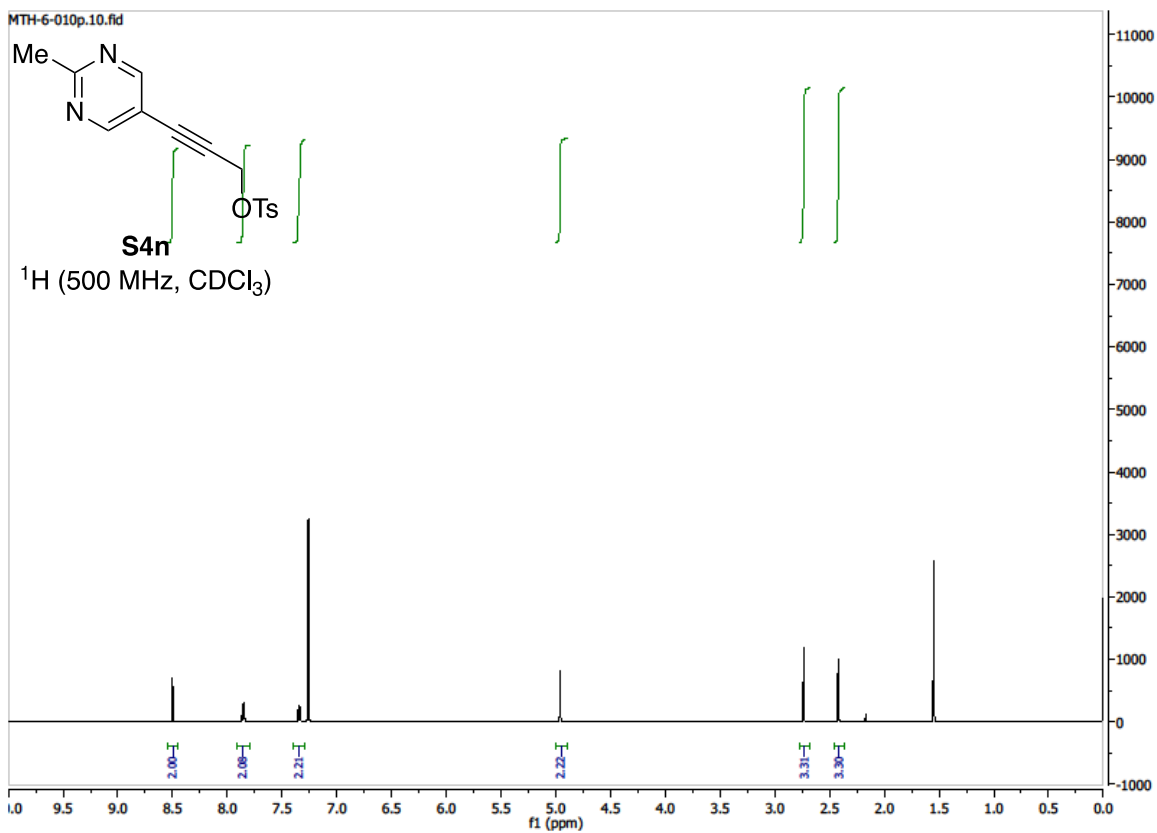
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 167.7, 159.1, 145.5, 133.4, 130.0, 128.4, 114.9, 87.1, 82.6, 58.0, 26.3, 21.8.

HRMS (Cl<sup>+</sup>, *m/z*) for C<sub>15</sub>H<sub>14</sub>N<sub>2</sub>O<sub>3</sub>S: calcd. = 303.0798; found = 303.0796.

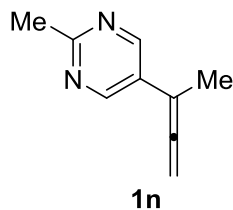
FTIR (neat): 3709, 2981, 2362, 1584, 1446, 1369, 1176, 939, 746 cm<sup>-1</sup>.

MP = 105-107 °C.





### 5-(Buta-2,3-dien-2-yl)-2-methylpyrimidine (**1n**)



To a stirred solution of propargyl tosylate **S4n** (0.40 g, 1.3 mmol) and copper (I) bromide (37 mg, 0.3 mmol) in THF (2 mL) was added MeMgBr (3 M in Et<sub>2</sub>O, 0.5 mL, 1.6 mmol) dropwise over 10 minutes. The reaction mixture was stirred for 1 hour at 25 °C. Saturated aqueous NH<sub>4</sub>Cl solution (2 mL) and EtOAc (3 mL) were added and the phases were separated. The aqueous phase was washed with EtOAc (3 x 3 mL) and the combined organic phases were washed with brine (5 mL), dried (MgSO<sub>4</sub>), filtered and the solvent removed *in vacuo*. The residue was subjected to flash column chromatography (SiO<sub>2</sub>, 2:1 hexanes:EtOAc) to afford the title compound **1n** (113 mg, 0.78 mmol) as a light yellow solid in 65% yield.

R<sub>f</sub> = 0.27 (2:1 hexanes : EtOAc)

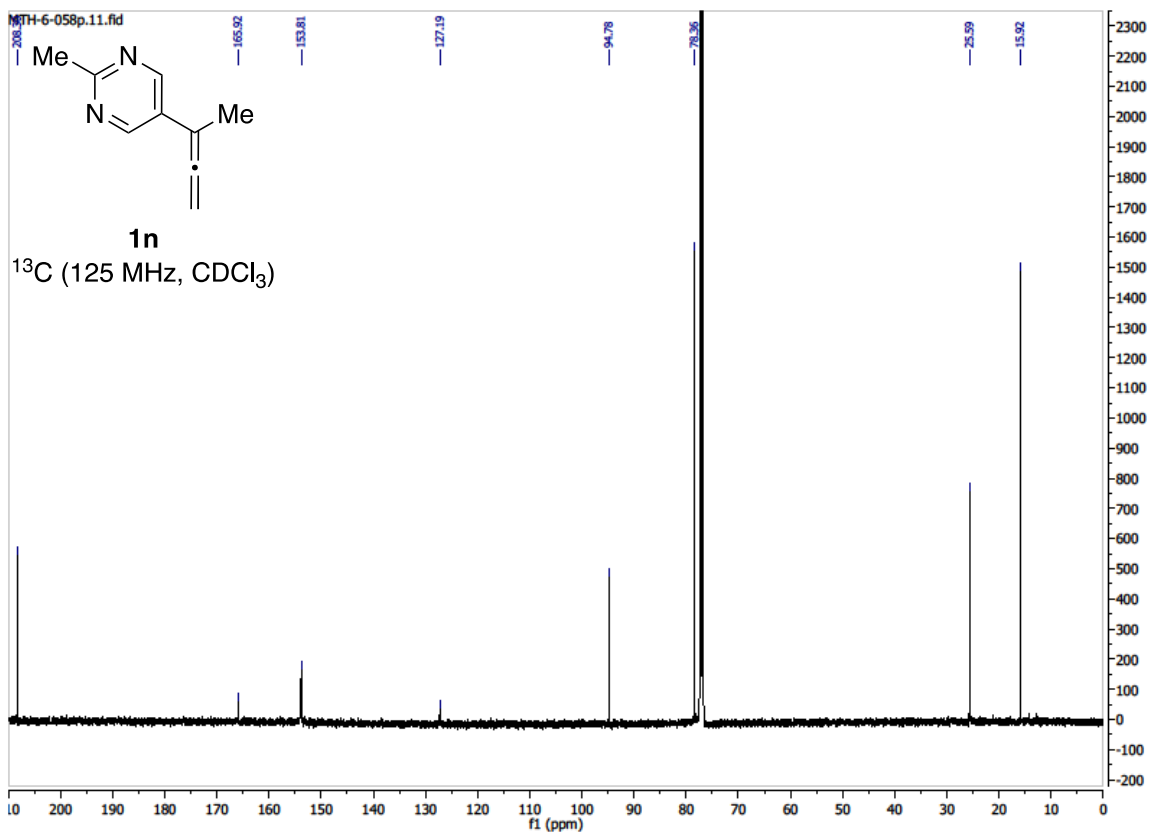
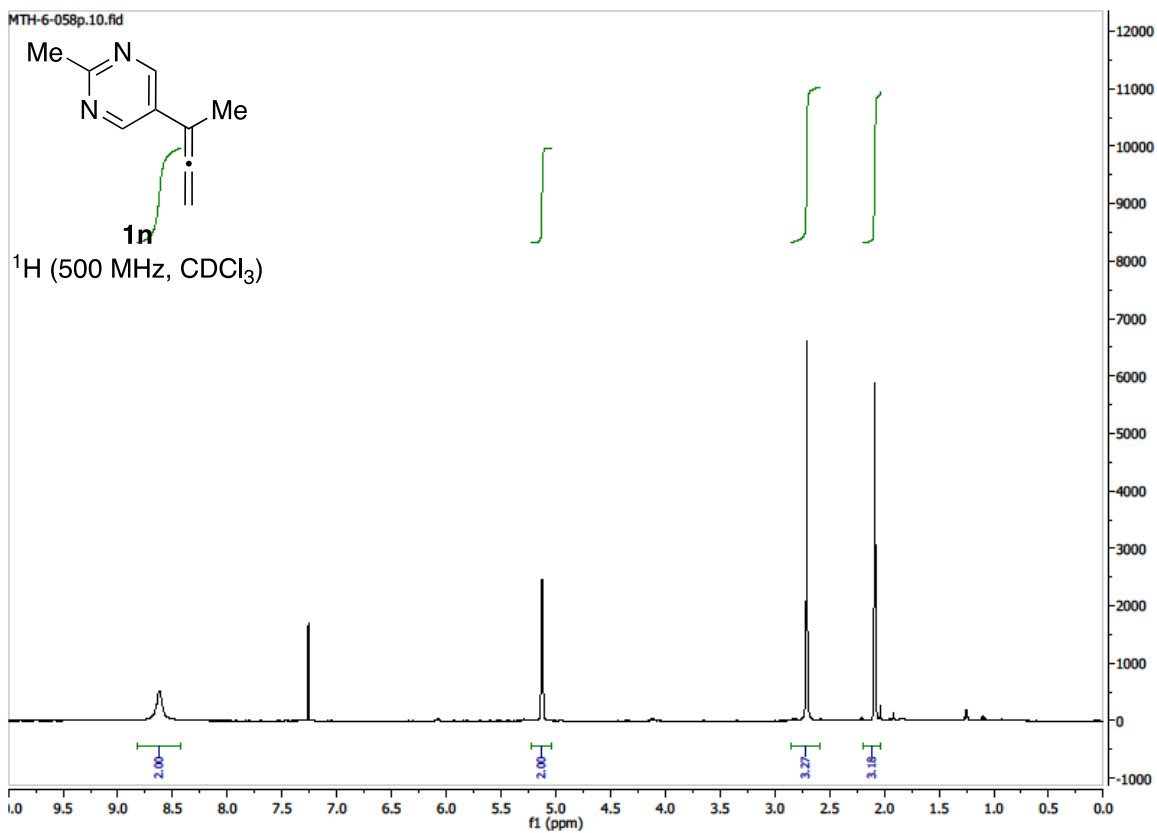
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 8.62 (s, 2H), 5.13 (q, *J* = 3.3 Hz, 2H), 2.71 (s, 3H), 2.09 (t, *J* = 3.3 Hz, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 208.3, 165.9, 153.8, 127.2, 94.8, 78.4, 25.6, 15.9.

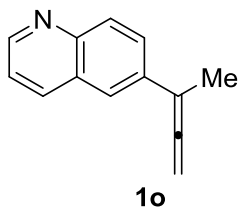
HRMS (ESI<sup>+</sup>, *m/z*) for C<sub>9</sub>H<sub>10</sub>N<sub>2</sub>: calcd. = 147.0917; found = 147.0917.

FTIR (neat): 2986, 1944, 1584, 1546, 1412, 1034, 858 cm<sup>-1</sup>.

MP = 57-60 °C.



**6-(Buta-2,3-dien-2-yl)quinoline (1o)**



6-Bromoquinoline (1.08 mL, 8.0 mmol) was subjected to general described in **lj**.<sup>7</sup> Upon flash column chromatography (SiO<sub>2</sub>, 1:3 EtOAc/hexanes), the title compound **1o** (0.65 g, 3.6 mmol) was obtained as a light yellow oil in 45 % yield.

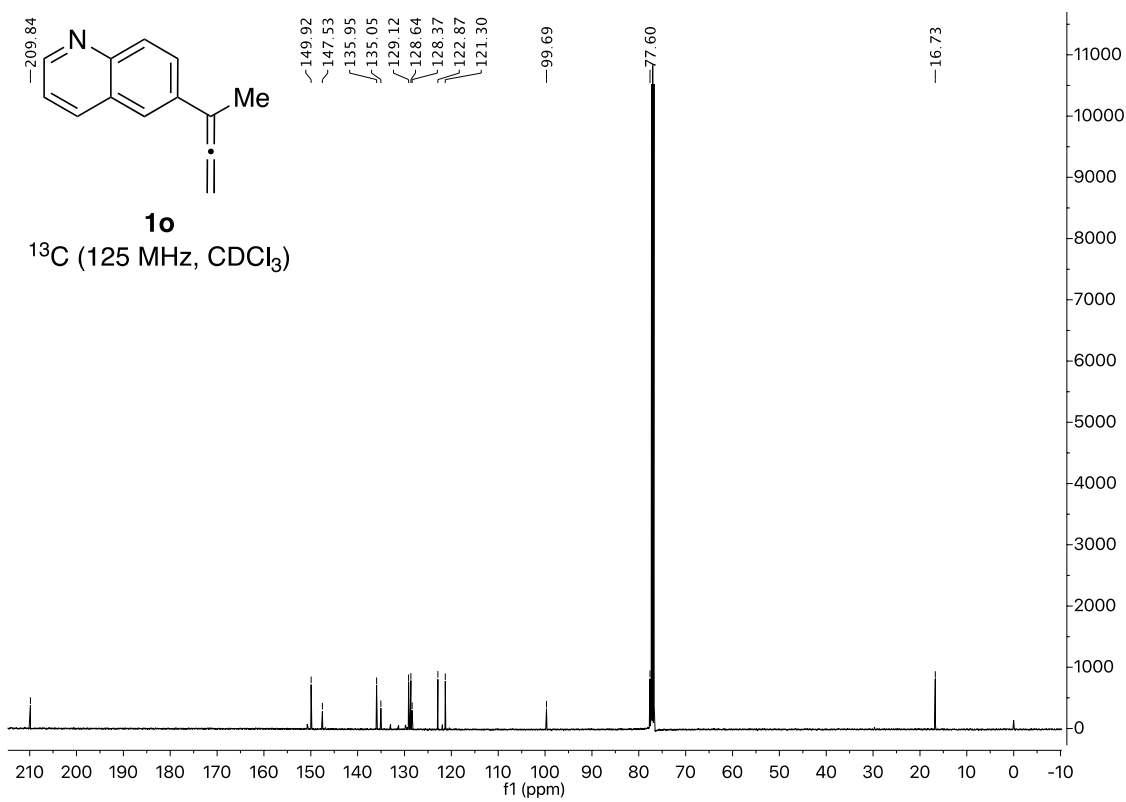
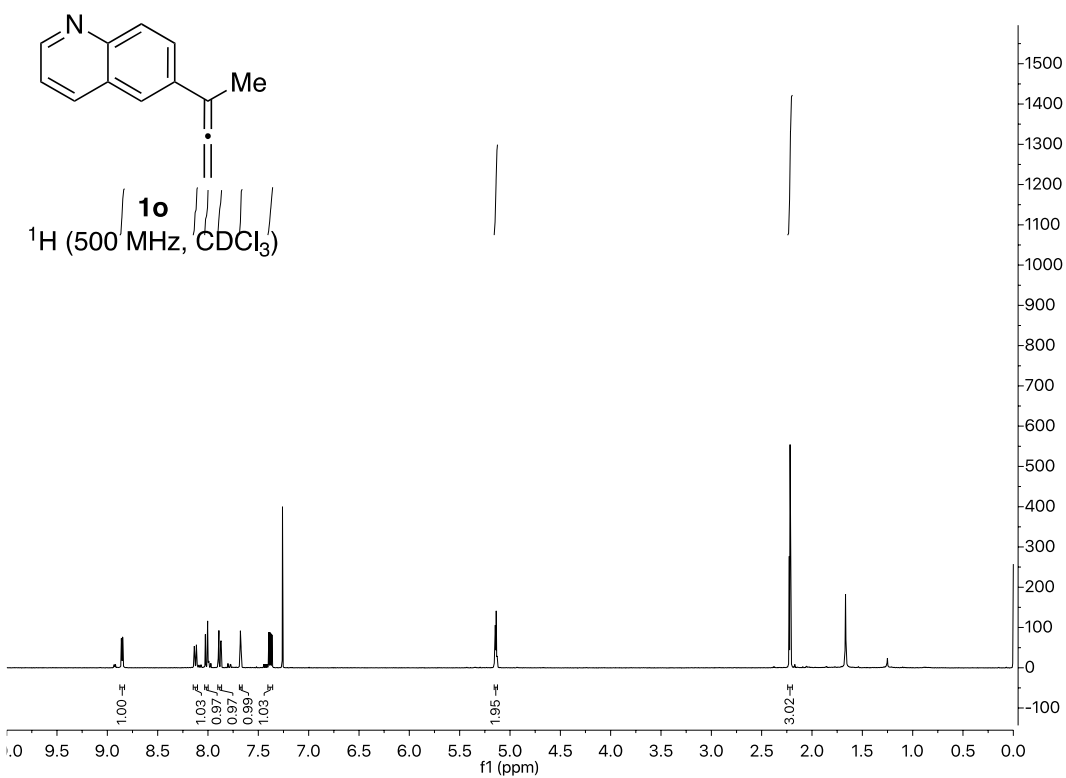
R<sub>f</sub> = 0.29 (3:1 hexanes : EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 8.85 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.12 (dd, *J* = 8.3, 1.8 Hz, 1H), 8.02 (d, *J* = 8.8 Hz, 1H), 7.88 (dd, *J* = 8.9, 2.1 Hz, 1H), 7.68 (d, *J* = 2.0 Hz, 1H), 7.38 (dd, *J* = 8.3, 4.3 Hz, 1H), 5.14 (q, *J* = 3.1 Hz, 2H), 2.22 (t, *J* = 3.1 Hz, 3H).

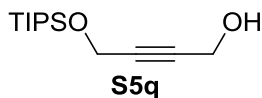
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 209.8, 149.9, 147.5, 136.0, 135.1, 129.1, 128.6, 128.4, 122.9, 121.3, 99.7, 77.6, 16.7.

HRMS (ESI + H, *m/z*) for C<sub>13</sub>H<sub>11</sub>N: calcd. = 182.0964; found = 182.0968.

FTIR (neat): 2981, 1933, 1572, 1488, 1371, 1317, 953, 876, 830, 793, 771 cm<sup>-1</sup>.

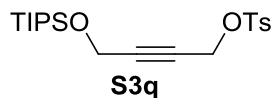


#### 4-((Triisopropylsilyl)oxy)but-2-yn-1-ol (**S5q**)



To a stirred solution of propargyl alcohol (2.4 mL, 40 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (130 mL) at 0 °C was added imidazole (3.3 g, 48 mmol) followed by triisopropylchloride (9.4 mL, 44 mmol). The reaction mixture was stirred for 14 hours. Water (100 mL) was added and the phases were separated. The organic phase was washed with water (100 mL), brine (100 mL), dried (MgSO<sub>4</sub>), filtered and the solvent removed *in vacuo*. The silyl propargyl ether was dissolved in THF (40 mL) and cooled to -78 °C. *n*BuLi (2.5M in hexane, 19.2 mL, 48 mmol) was added and the reaction mixture was stirred at -78 °C for 10 minutes. The reaction mixture was warmed to 0 °C and stirred for 1 hour. The reaction mixture was cooled to -78 °C and paraformaldehyde (1.44 g, 48 mmol) was added in a single portion. The reaction mixture was allowed to warm to room temperature and stirred for 14 hours. Saturated aqueous NH<sub>4</sub>Cl solution (50 mL) was added followed by EtOAc (100 mL). The phases were separated and the organic phase was washed with water (2 x 100 mL). The combined aqueous phases were washed with EtOAc (2 x 100 mL). The combined organic phases were washed with brine (200 mL), dried (MgSO<sub>4</sub>), filtered and the solvent removed *in vacuo*. The crude material **S5q** was used in the following step without purification.

#### 4-((Triisopropylsilyl)oxy)but-2-yn-1-yl 4-methylbenzenesulfonate (S3q)



To a stirred solution of propargyl alcohol **S5q** (~40 mmol) in Et<sub>2</sub>O (40 mL) at 0 °C was added tosyl chloride (6.1 g, 32 mmol) followed by crushed potassium hydroxide (11.2 g, 200 mmol). The reaction mixture was stirred at 0 °C for 1 hour. The reaction mixture was poured onto ice water (100 mL) and diluted with Et<sub>2</sub>O (100 mL). The phases were separated and the organic phase was washed with H<sub>2</sub>O (2 x 100 mL). The combined aqueous phases were washed with Et<sub>2</sub>O (2 x 100 mL). The combined organic phases were washed with brine (100 mL), dried (MgSO<sub>4</sub>), filtered and the solvent removed *in vacuo*. The residue was subjected to flash column chromatography (SiO<sub>2</sub>, 5:95 ethyl acetate:hexanes) to afford the title compound (10.3 g, 26 mmol) as a colorless oil in 65% yield over 3 steps.

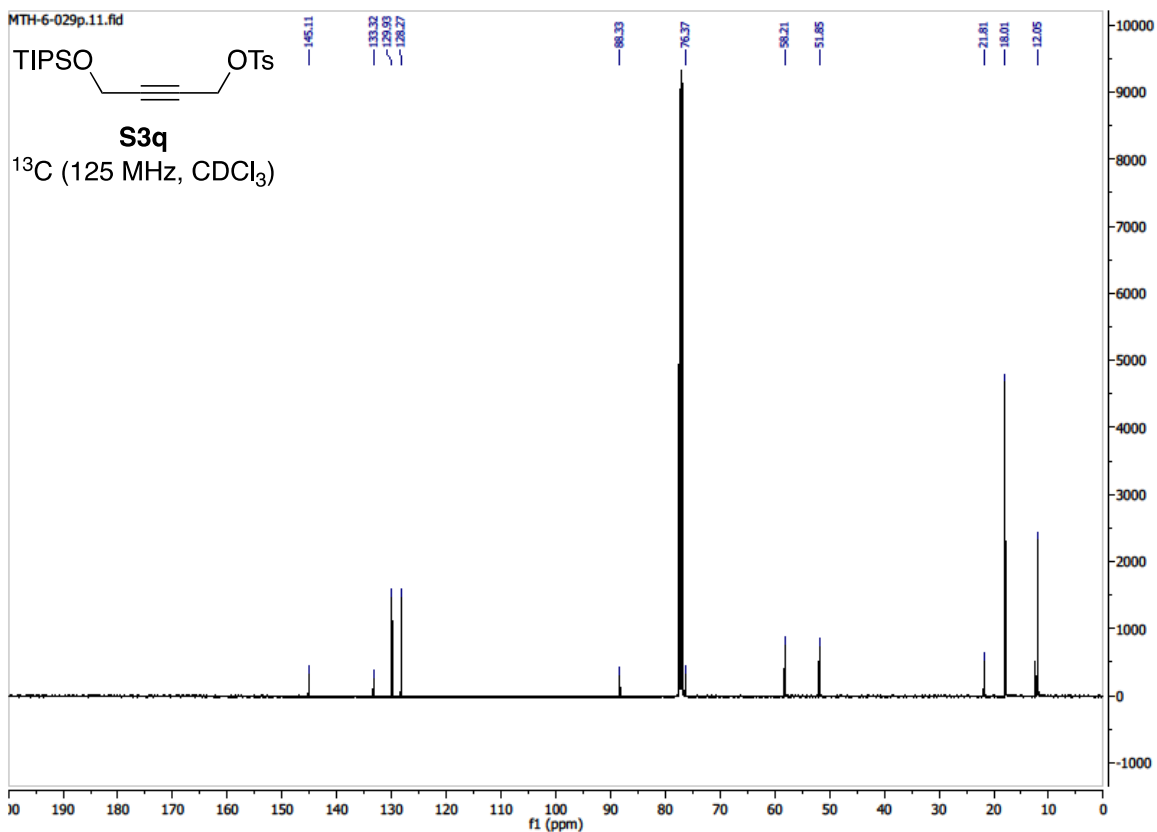
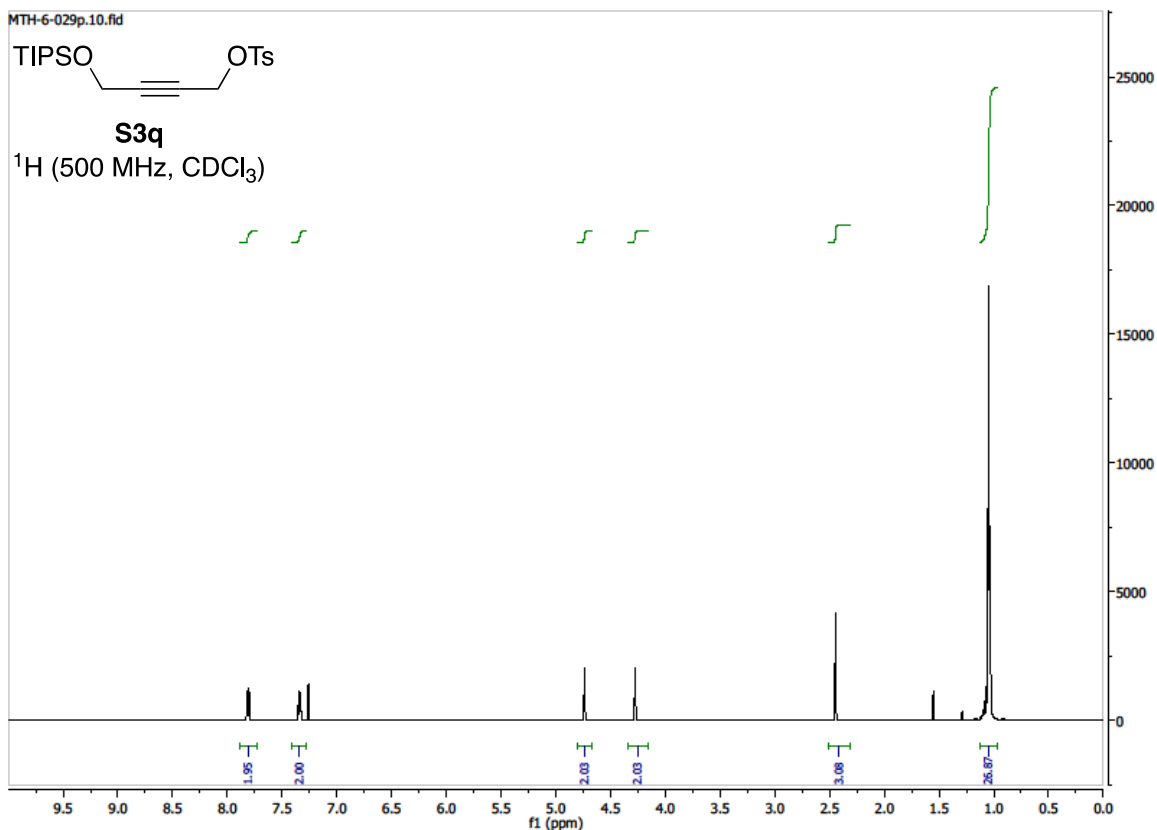
R<sub>f</sub> = 0.41 (9:1 hexanes:EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.81 (d, *J* = 7.9 Hz, 2H), 7.34 (d, *J* = 7.9 Hz, 2H), 4.74 (s, 2H), 4.28 (s, 2H), 2.45 (s, 3H), 1.05 (m, 21H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 145.1, 133.3, 129.9, 128.3, 88.3, 76.4, 48.2, 51.9, 21.8, 18.0, 12.1.

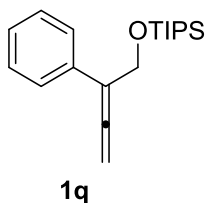
HRMS (ESI+NH<sub>4</sub>, *m/z*) for C<sub>20</sub>H<sub>32</sub>O<sub>4</sub>SSi: calcd. = 414.2129; found = 414.2135.

FTIR (neat): 3708, 2942, 2866, 2360, 1464, 1367, 1176, 1057, 946, 755, 665 cm<sup>-1</sup>.





**Triisopropyl((2-phenyl-buta-2,3-dien-1-yl)oxy)silane (1q)**



To a stirred solution of copper (I) bromide (1.43 g, 10 mmol) in THF (20 mL) was added PhMgBr (3M in Et<sub>2</sub>O, 4 mL, 12 mmol) over 5 minutes. The reaction mixture was stirred for 5 minutes. In a separate flask propargyl tosylate **S3q** (3.97 g, 10 mmol) was dissolved in THF (20 mL). The prepared nucleophile was added to this second flask dropwise over 10 minutes and the reaction mixture was stirred for 1 hour. Saturated aqueous NH<sub>4</sub>Cl solution (50 mL) was added followed by EtOAc (50 mL). The phases were separated and the organic phase was washed with water (2 x 50 mL). The combined aqueous phases were washed with EtOAc (2 x 50 mL). The combined organic phases were washed with brine (100 mL), dried (MgSO<sub>4</sub>), filtered and the solvent removed *in vacuo*. The residue was subjected to flash column chromatography (SiO<sub>2</sub>, hexanes) to afford the title compound (2.36 g, 7.9 mmol) as a colorless oil in 79% yield. Note: The use of stoichiometric copper (I) bromide was essential to minimize the formation of the inseparable isomeric alkyne through S<sub>N</sub>2 attack.

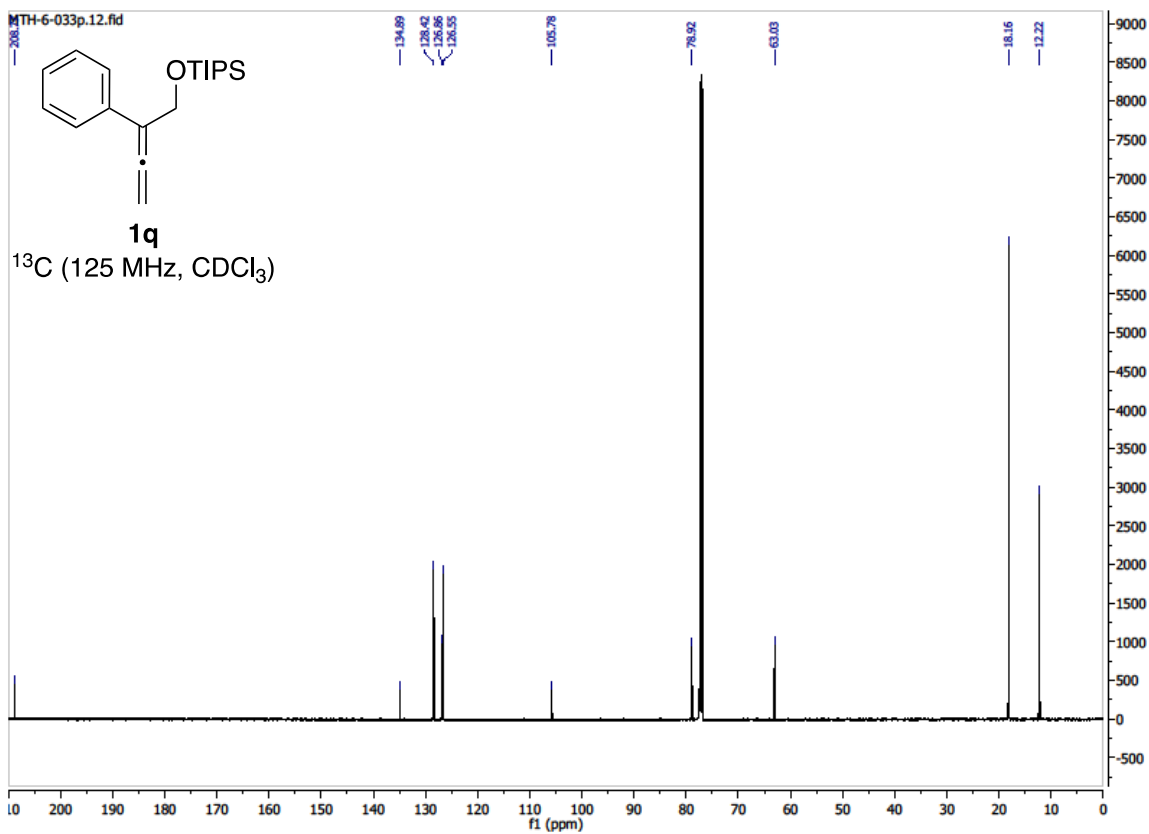
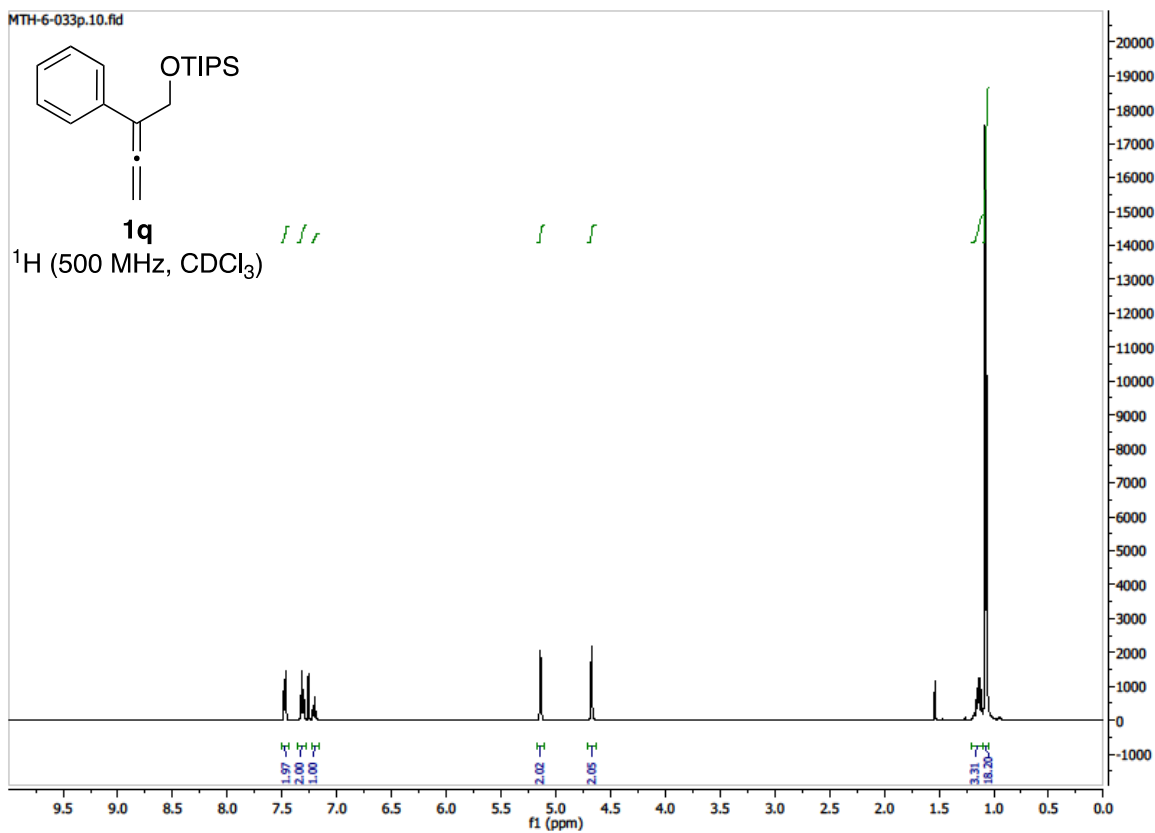
R<sub>f</sub> = 0.29 (hexanes)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.47 (d, *J* = 7.8 Hz, 2H), 7.32 (t, *J* = 7.8 Hz, 2H), 7.20 (t, *J* = 7.8 Hz, 1H), 5.14 (t, *J* = 2.8 Hz, 2H), 4.68 (t, *J* = 2.8 Hz, 2H), 1.13 (m, 3H), 1.07 (d, *J* = 6.5 Hz, 18H).

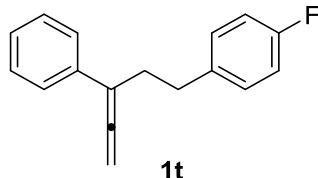
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 208.7, 134.9, 128.4, 126.9, 126.6, 105.8, 78.9, 63.0, 18.2, 12.2.

HRMS (ESI+H, *m/z*) for C<sub>19</sub>H<sub>30</sub>OSi: calcd. = 303.2139; found = 303.2140.

FTIR (neat): 2943, 2867, 1707, 1494, 1247, 10098, 1026, 883, 688 cm<sup>-1</sup>.



### 1-Fluoro-4-(3-phenyl-415-penta-3,4-dien-1-yl)benzene (1t)



Magnesium turnings (108 mg, 4.5 mmol) were placed into a 3-necked flask equipped with a reflux condenser. THF (6 mL) was added followed by a single crystal of iodine and the reaction mixture was stirred until the solution decolorized. 4-Fluorophenethyl bromide (910 mg, 4.5 mmol) was added and the reaction mixture was heated until it began to reflux. The heat was removed and the reaction mixture was stirred until the reflux ended. In a separate flask, 3-phenyl-2-propyn-1-ol tosylate<sup>4</sup> (860 mg, 3 mmol) and copper (I) bromide (43 mg, 0.3 mmol) were dissolved in THF (6 mL). The Grignard reagent was transferred to this flask through a cannula and the reaction mixture was stirred at room temperature for 1 hour. Saturated aqueous NH<sub>4</sub>Cl solution (10 mL) was added followed by EtOAc (10 mL). The phases were separated and the organic phase was washed with water (2 x 10 mL). The combined aqueous phases were washed with EtOAc (2 x 10 mL). The combined organic phases were washed with brine (20 mL), dried (MgSO<sub>4</sub>), filtered and the solvent removed *in vacuo*. The residue was subjected to flash column chromatography (SiO<sub>2</sub>, hexanes) to afford the title compound (0.48 g, 2.0 mmol) as a colorless oil in 67% yield as a 4:1 mixture of allene:alkyne.

R<sub>f</sub> = 0.37 (hexanes)

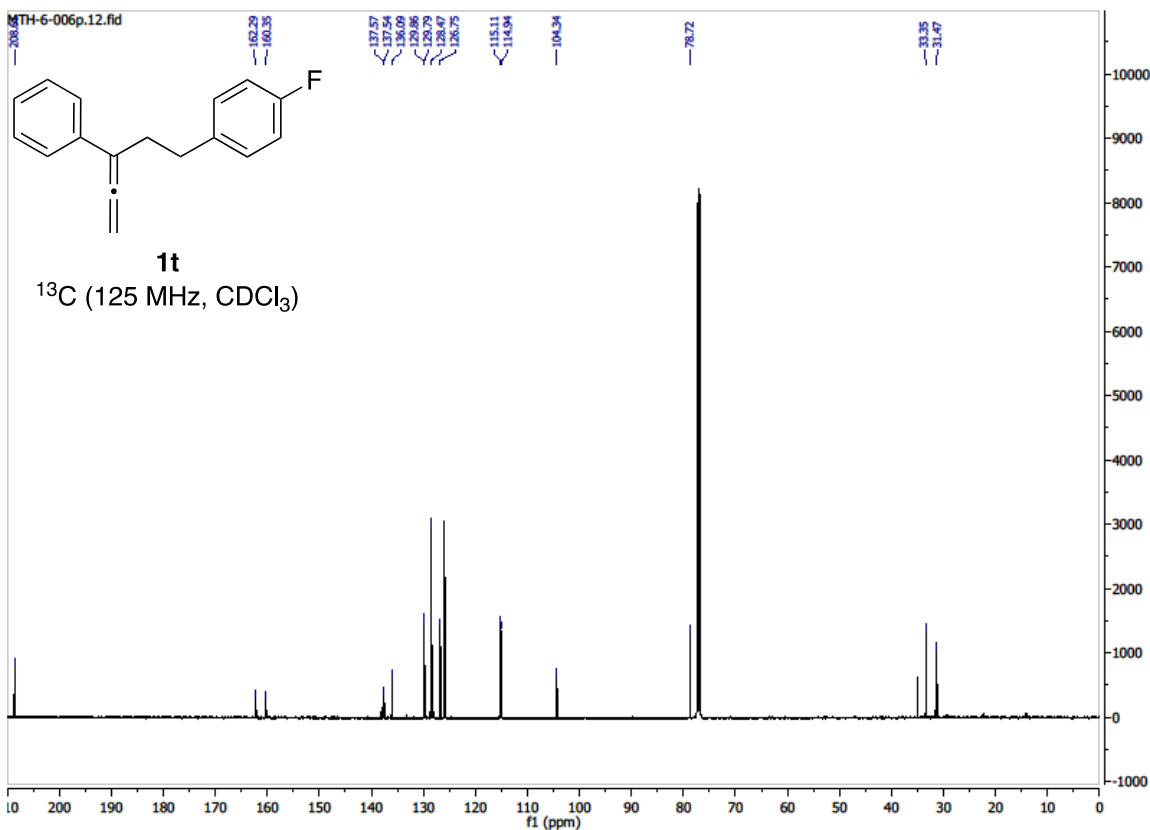
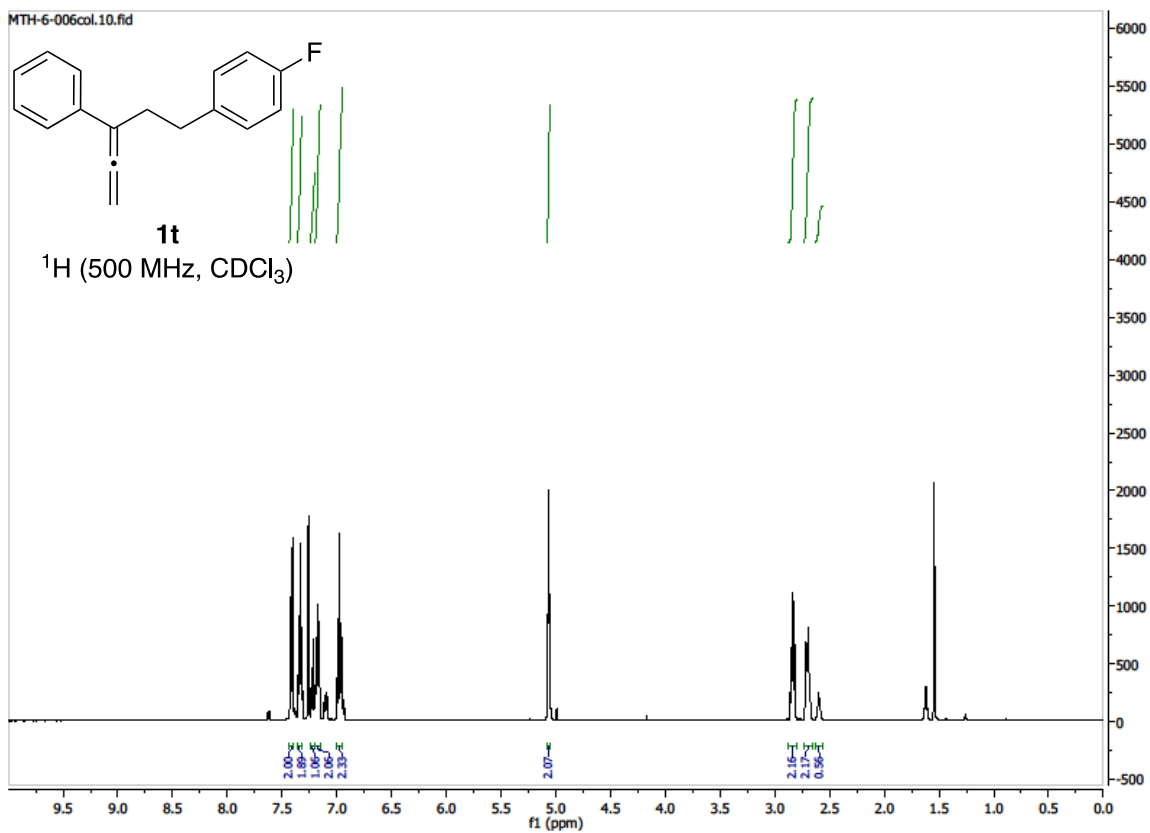
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.40 (d, *J* = 7.6 Hz, 2H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.22 (t, *J* = 7.6 Hz, 1H), 7.17 (dd, *J* = 5.8, 8.5 Hz, 2H), 6.98 (dd, *J* = 8.5, 8.5 Hz, 2H), 5.07 (t, *J* = 3.2 Hz, 2H), 2.84 (m, 2H), 2.70 (m, 2H).

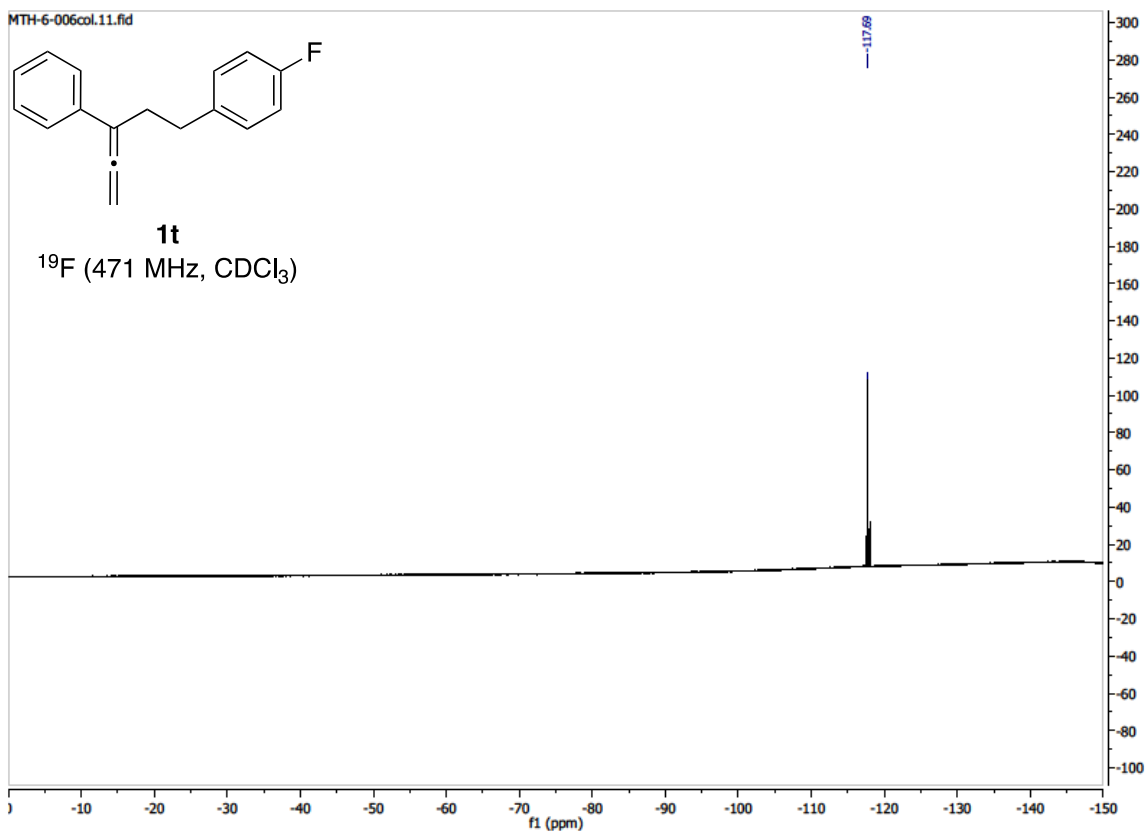
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 208.6, 161.4 (d, *J* = 240 Hz), 137.6 (d, *J* = 3 Hz), 136.1, 129.8 (d, *J* = 8 Hz), 128.5, 126.8, 125.9, 115.0 (d, *J* = 21 Hz), 104.3, 78.7, 33.4, 31.5.

<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -117.7 (tt, *J* = 5.7, 8.5 Hz).

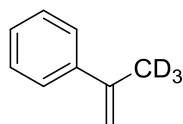
HRMS (CI<sup>+</sup>, *m/z*) for C<sub>17</sub>H<sub>14</sub>F: calcd. = 237.1080; found = 237.1083.

FTIR (neat): 2928, 1940, 1723, 1509, 1220, 1157, 824, 759 cm<sup>-1</sup>.





**(Prop-1-en-2-yl-3,3,3-d<sub>3</sub>)benzene (*deuterio-S1a*)**

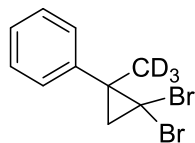


*deuterio-S1a*

Acetophenone- $\beta,\beta,\beta$ -d<sub>3</sub> (1.17 mL, 10 mmol) was subjected to general procedure A. Upon flash column chromatography (SiO<sub>2</sub>, hexanes), the title compound *deuterio-S1a* (0.98 g, 8.1 mmol) was obtained as a clear oil in 81% yield. Note: Keeping the reaction mixture at 0 °C throughout this reaction was essential to avoid H-D exchange.

The data reported was consistent with literature data.<sup>11</sup>

**(2,2-dibromo-1-(methyl-d<sub>3</sub>)cyclopropyl)benzene (*deuterio*-S2a)**



*deuterio*-S2a

Styrene *deuterio*-S1a (0.98 g, 8.1 mmol) was subjected to general procedure B. Upon flash column chromatography (SiO<sub>2</sub>, hexanes), the title compound *deuterio*-S2a (1.79 g, 6.1 mmol) was obtained as a clear oil in 75% yield.

R<sub>f</sub> = 0.44 (hexanes)

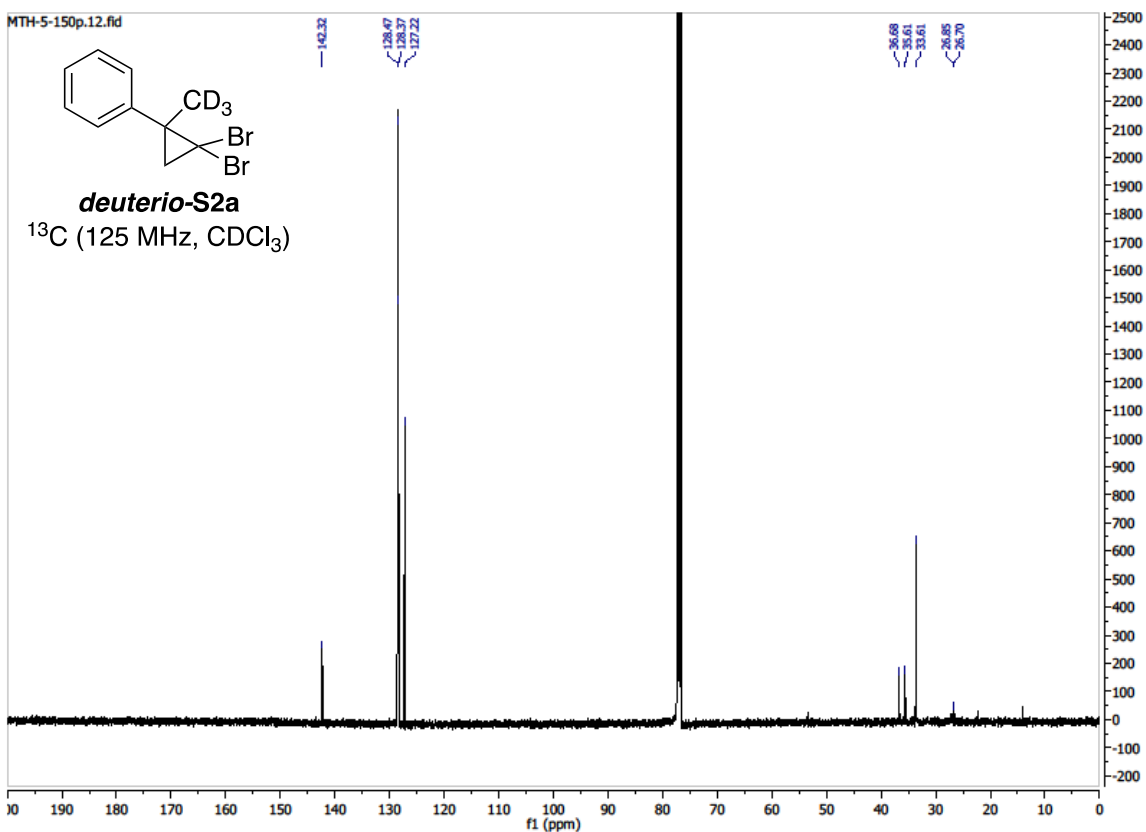
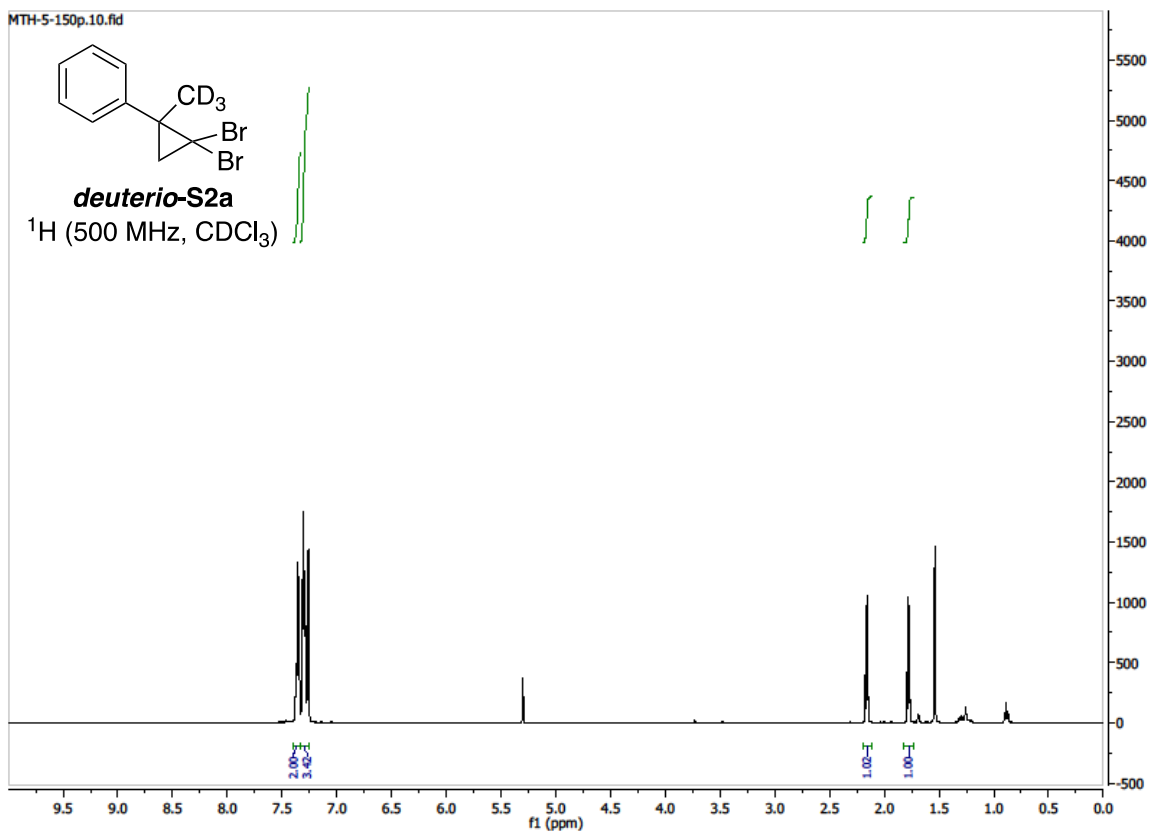
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.36 (m, 2H), 7.30 (m, 3H), 2.16 (d, *J* = 8.6 Hz, 1H), 1.78 (d, *J* = 8.6 Hz, 1H).

<sup>2</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 1.63

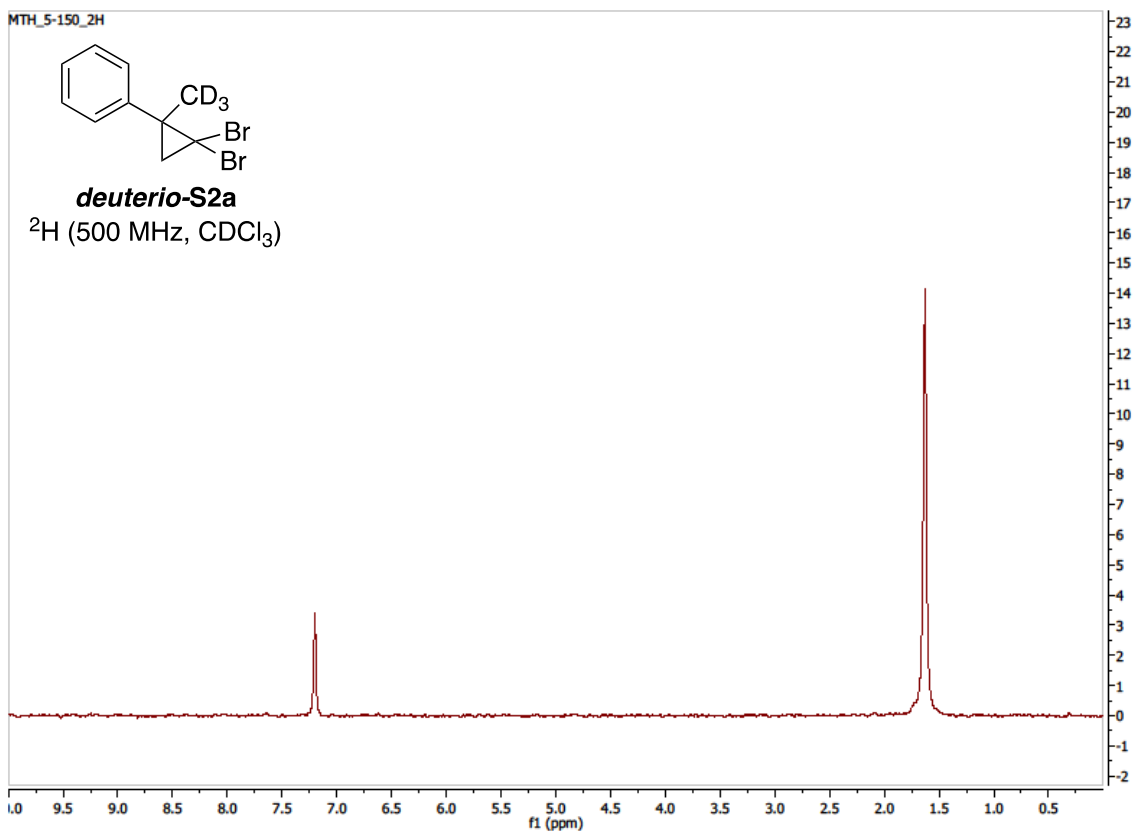
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 142.3, 128.5, 128.4, 127.2, 36.7, 35.6, 33.6, 26.8 (m).

HRMS (Cl<sup>+</sup>, *m/z*) for C<sub>10</sub>H<sub>8</sub>D<sub>3</sub>Br<sub>2</sub>: calcd. = 291.9416; found = 291.9416.

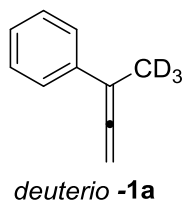
FTIR (neat): 3058, 3027, 2925, 2360, 1495, 1446, 1427, 1067, 1017, 749 cm<sup>-1</sup>.







**(Buta-2,3-dien-2-yl-1,1,1-d<sub>3</sub>)benzene (*deuterio-1a*)**



1,1-disubstituted cyclopropane *deuterio-S1a* (1.36 g, 4.6 mmol) was subjected to general procedure C. Upon flash column chromatography (SiO<sub>2</sub>, pentane), the title compound *deuterio-1a* (0.53 g, 4.0 mmol) was obtained as a clear oil in 87% yield.

R<sub>f</sub> = 0.47 (hexanes)

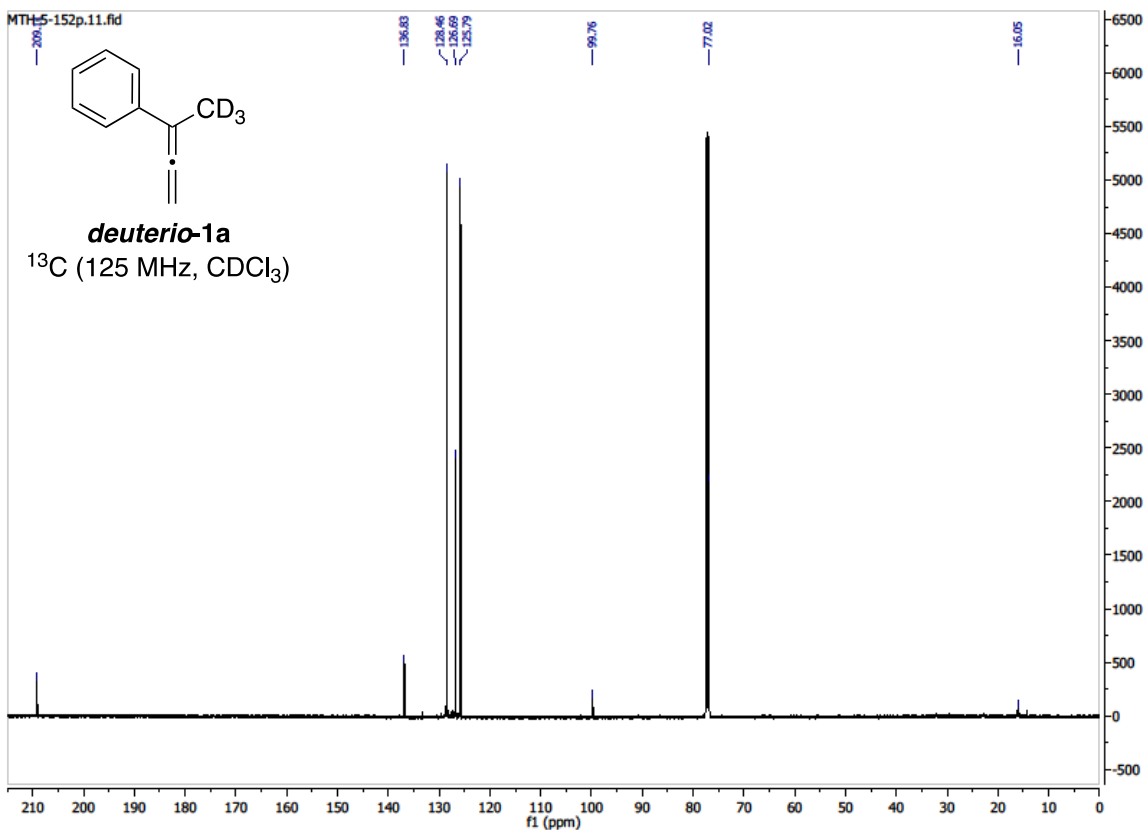
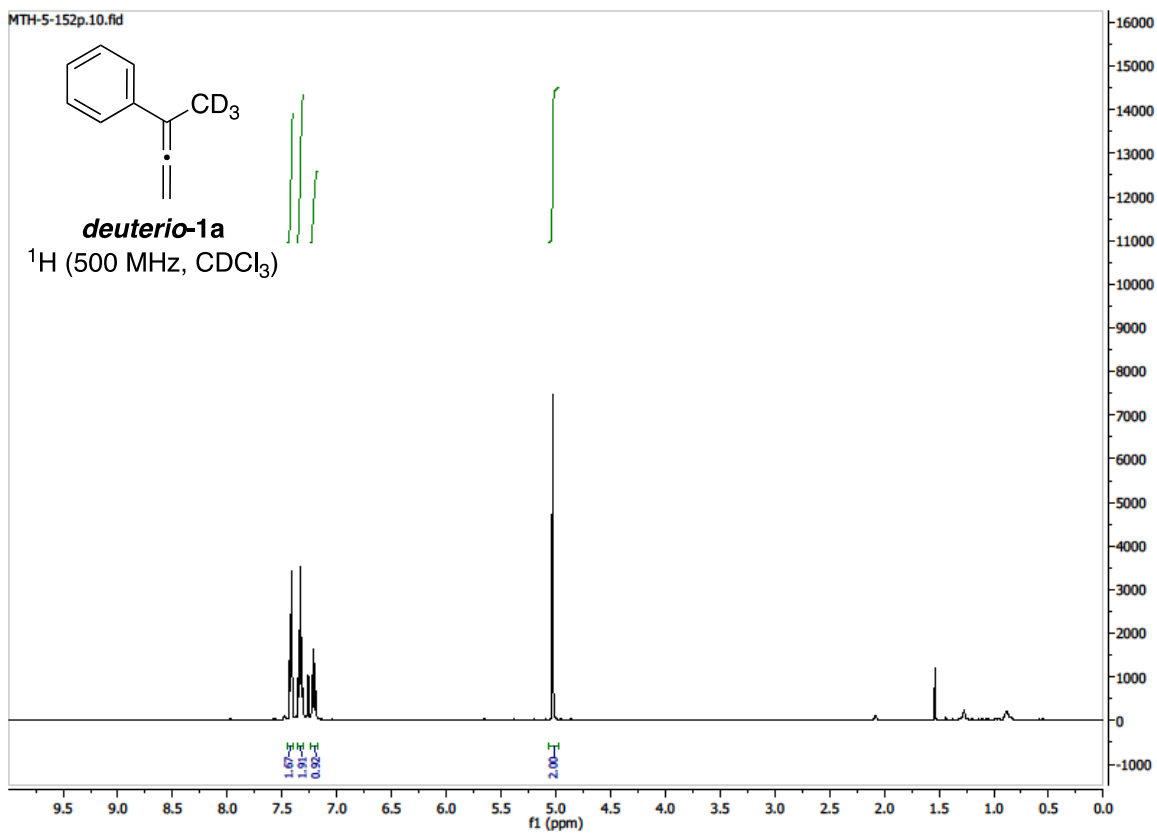
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.42 (d, *J* = 8.4 Hz, 2H), 7.33 (t, *J* = 8.4 Hz, 2H), 7.21 (t, *J* = 8.4 Hz, 1H), 5.03 (s, 2H).

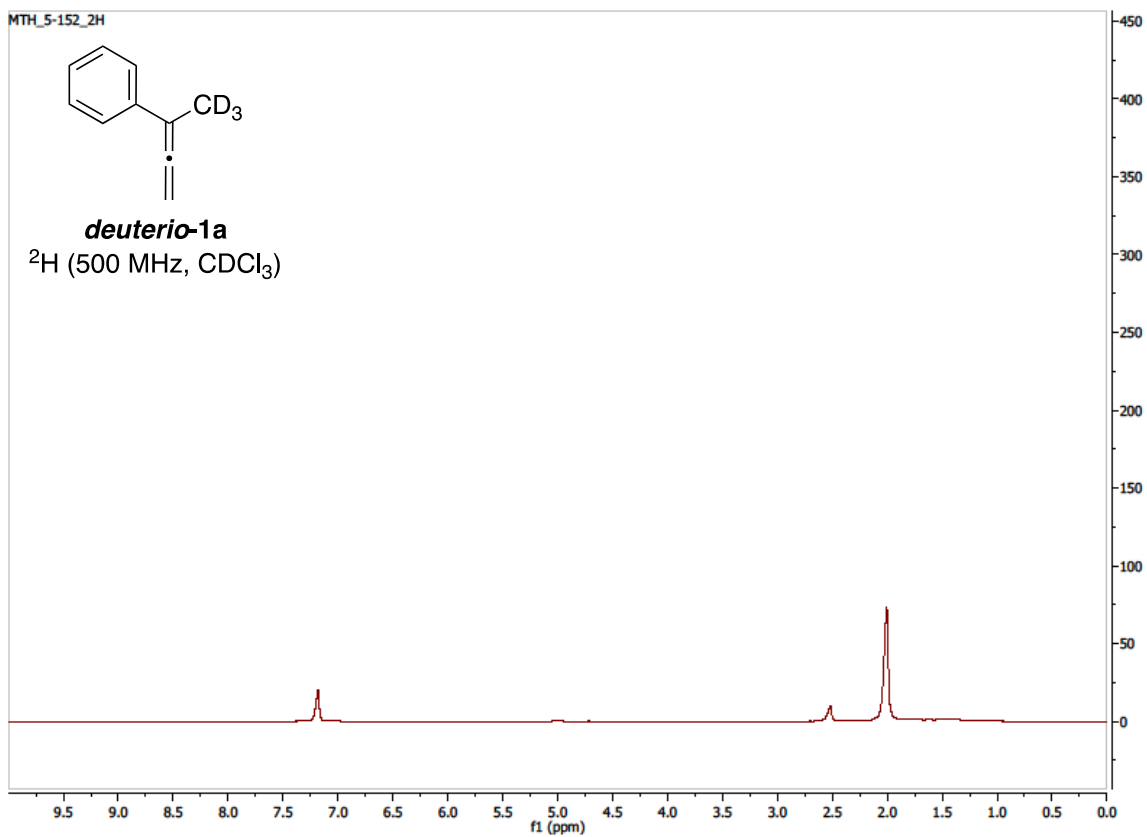
<sup>2</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 2.01.

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 209.1, 136.8, 128.5, 126.7, 125.8, 99.8, 77.0, 16.1 (m).

HRMS (CI<sup>+</sup>, *m/z*) for C<sub>10</sub>H<sub>6</sub>D<sub>3</sub>: calcd. = 132.0893; found = 132.888.

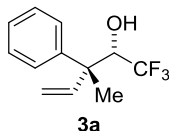
FTIR (neat): 3029, 2973, 1938, 1724, 1680, 1494, 1449, 1267, 1033, 758, 695 cm<sup>-1</sup>.





## Procedure and Spectral Data for Coupling Products of Fluoral and 1,1-Disubstituted Allenes 3a-3u

### **(2*S*,3*R*)-1,1,1-trifluoro-3-methyl-3-phenylpent-4-en-2-ol (3a)**



1,1-Disubstituted allene **1a** (52 mg, 0.4 mmol) was subjected to general procedure D. Upon flash column chromatography (SiO<sub>2</sub>, 4:96 EtOAc:hexanes), the title compound **3a** (35.7 mg, 0.16 mmol, 17:1 dr) was obtained as a yellow oil in 78% yield. Note: This reaction was repeated on 2 mmol scale using [Ir(cod)Cl]<sub>2</sub> (1 mol%) and (*R*)-PhanePhos (2 mol%) to afford the product in 71% yield and 17:1 dr.

R<sub>f</sub> = 0.41 (90:10 hexanes : EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.40-7.34 (m, 4H), 7.26 (m, 1H), 6.39 (dd, *J* = 11.1, 17.8 Hz, 1H), 5.36 (d, *J* = 11.1 Hz, 1H), 5.20 (d, *J* = 17.8 Hz, 1H), 4.39 (dq, *J* = 6.0, 7.9 Hz, 1H), 2.19 (d, *J* = 6.0 Hz, 1H, OH), 1.57 (s, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 143.8, 140.8, 128.7, 127.1, 127.0, 126.2 (q, *J* = 285 Hz), 124.0, 76.0 (q, *J* = 26.0 Hz), 47.5, 21.1 (q, *J* = 2.7 Hz).

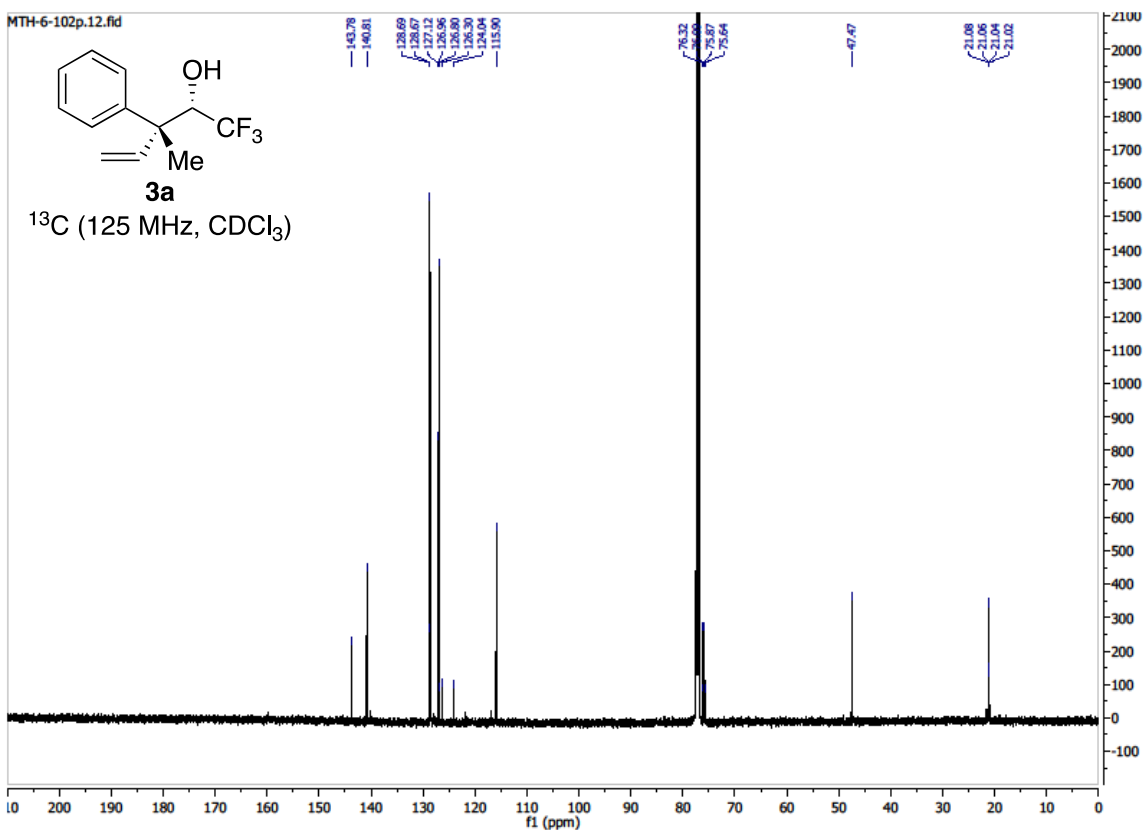
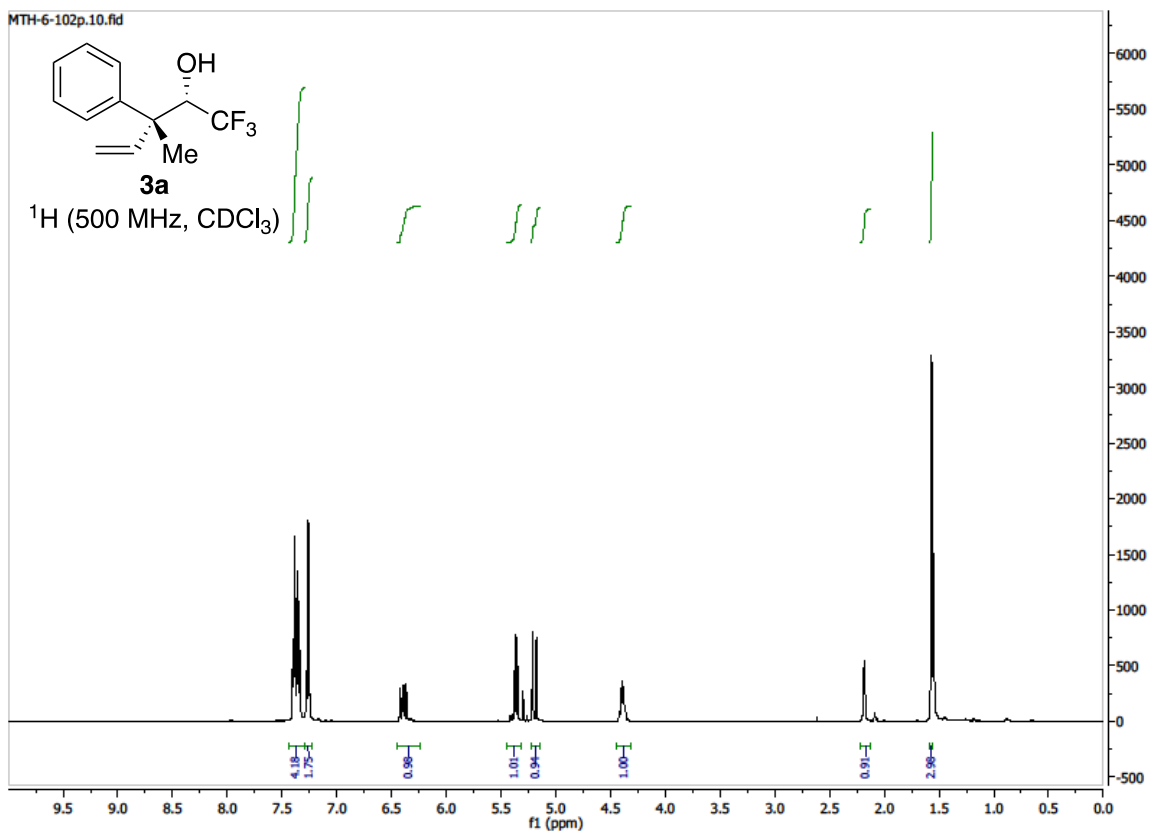
<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -70.7 (d, *J* = 7.4 Hz).

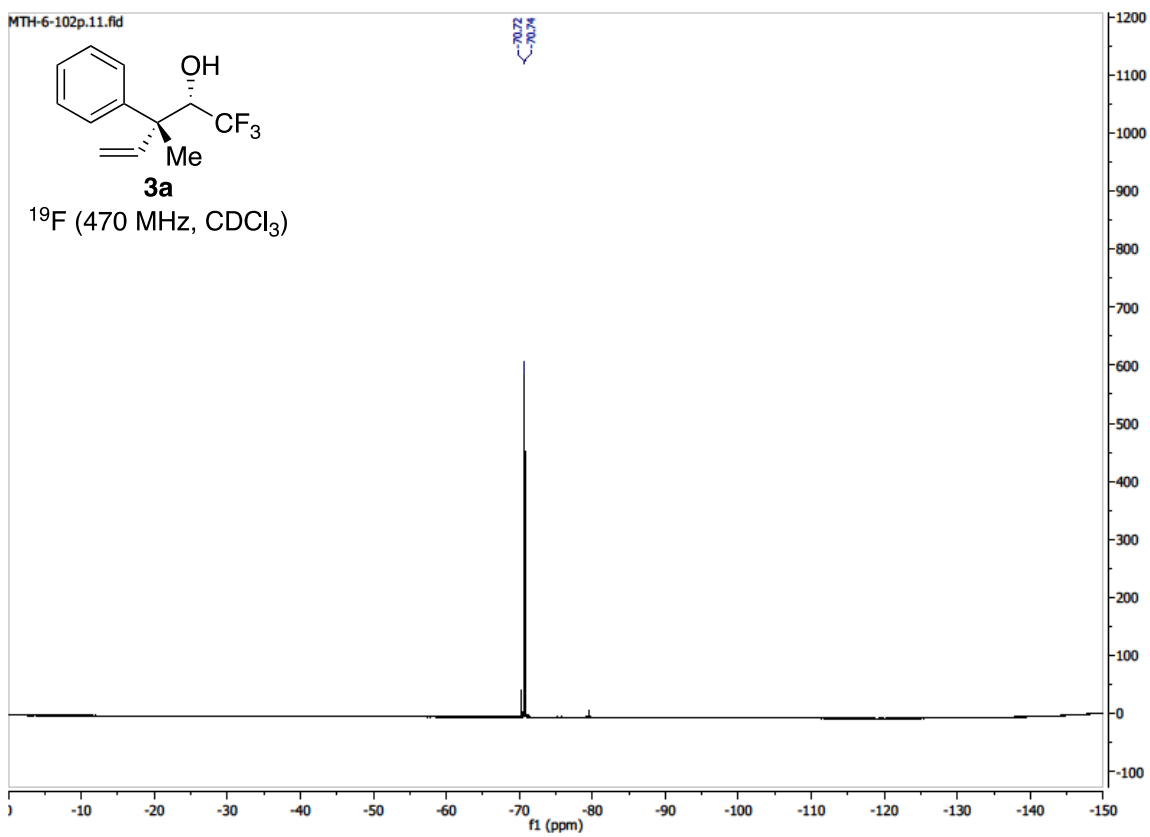
HRMS (CI<sup>+</sup>, *m/z*) for C<sub>12</sub>H<sub>13</sub>OF<sub>3</sub>: calcd. = 230.0918; found = 230.0922.

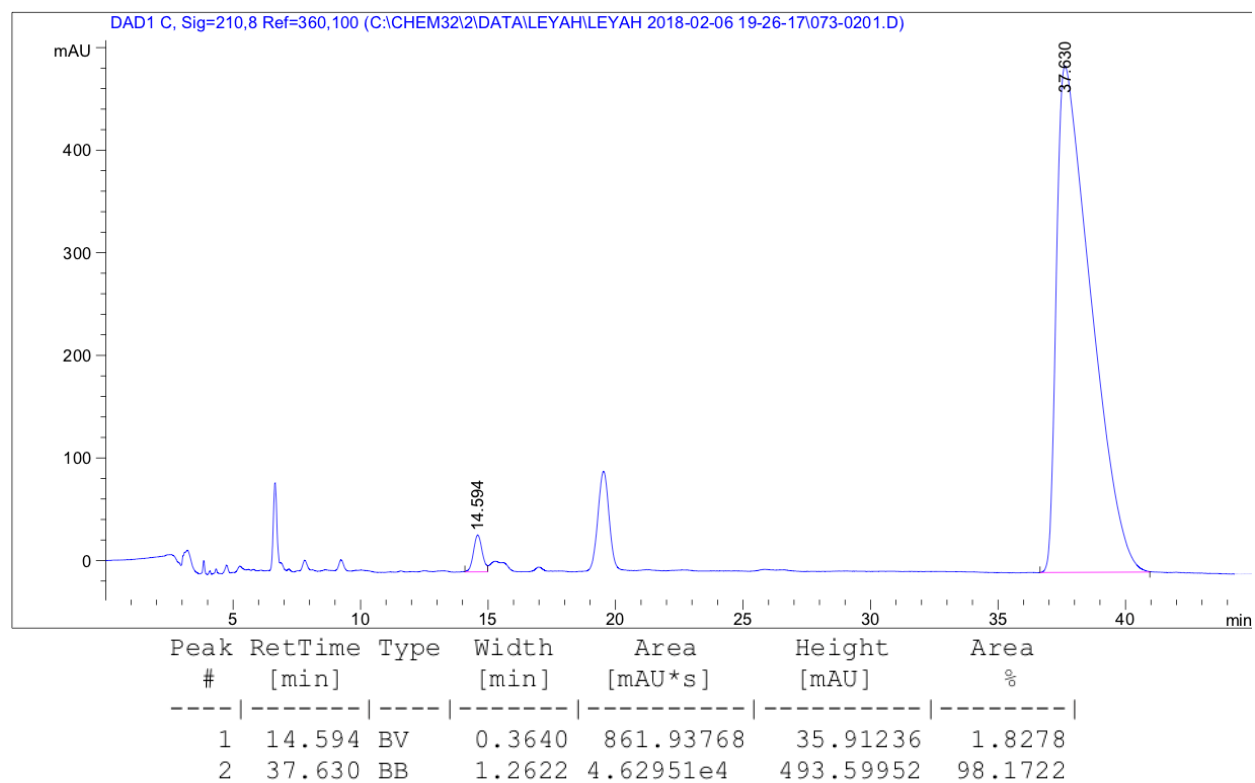
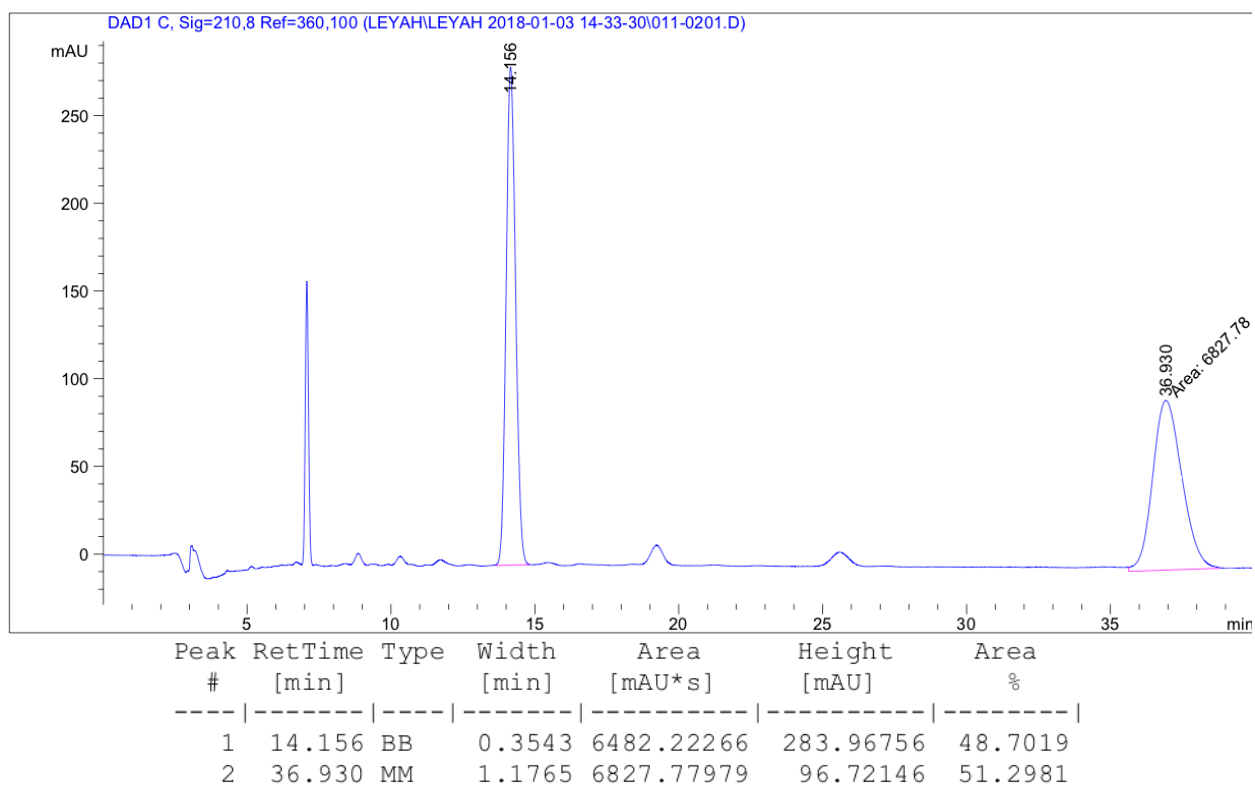
FTIR (neat): 3459, 2993, 2363, 1496, 1446, 1271, 1156, 1122, 926, 762, 701 cm<sup>-1</sup>.

HPLC: (Chiralcel column OJ-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 210 nm) ee = 96%.

[α]<sub>D</sub><sup>24</sup> = -4.5 (c = 1.0, CHCl<sub>3</sub>).

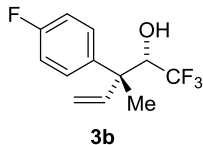








**(2*S*,3*R*)-1,1,1-trifluoro-3-(4-fluorophenyl)-3-methylpent-4-en-2-ol (3b)**



1,1-Disubstituted allene **1b** (59.3 mg, 0.4 mmol) was subjected to general procedure D. Upon flash column chromatography (SiO<sub>2</sub>, 1:10 EtOAc/hexanes), the title compound **3b** (40.2 mg, 0.16 mmol, 19:1 dr) was obtained as a light yellow oil in 81% yield.

R<sub>f</sub> = 0.4 (4:1 hexanes : EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.36 (m, 2H), 7.03 (m, 2H), 6.35 (dd, *J* = 10.9, 17.7 Hz, 1H), 5.35 (d, *J* = 10.9 Hz, 1H), 5.17 (d, *J* = 17.6 Hz, 1H), 4.33 (dq, *J* = 5.3, 1.8 Hz, 1H), 2.22 (d, *J* = 5.4 Hz, 1H), 1.56 (q, *J* = 1.1 Hz, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 161.6 (d, *J* = 246.5 Hz), 140.8, 139.2 (d, *J* = 3.2 Hz), 128.6 (d, *J* = 7.9 Hz), 125.0 (q, *J* = 283.5 Hz), 115.8, 115.2 (d, *J* = 21.2 Hz), 75.7 (q, *J* = 28.1 Hz), 46.9, 21.0 (q, *J* = 2.6 Hz).

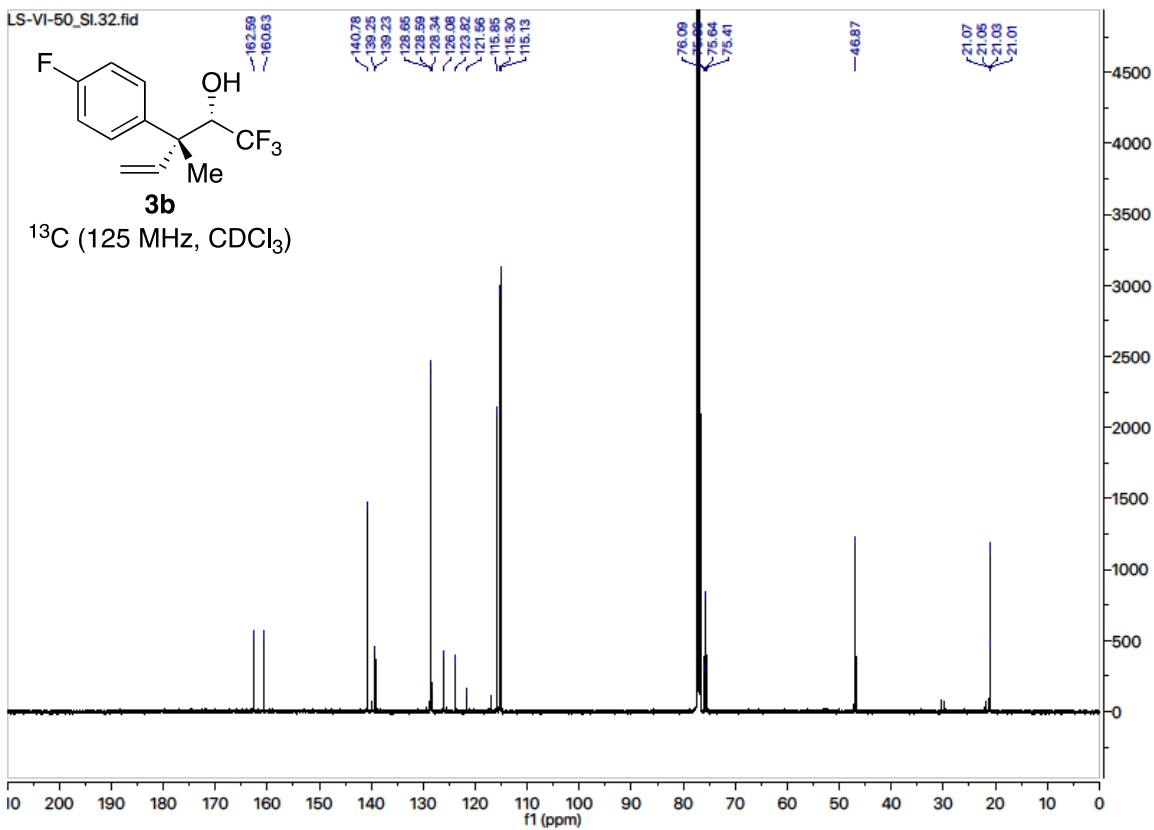
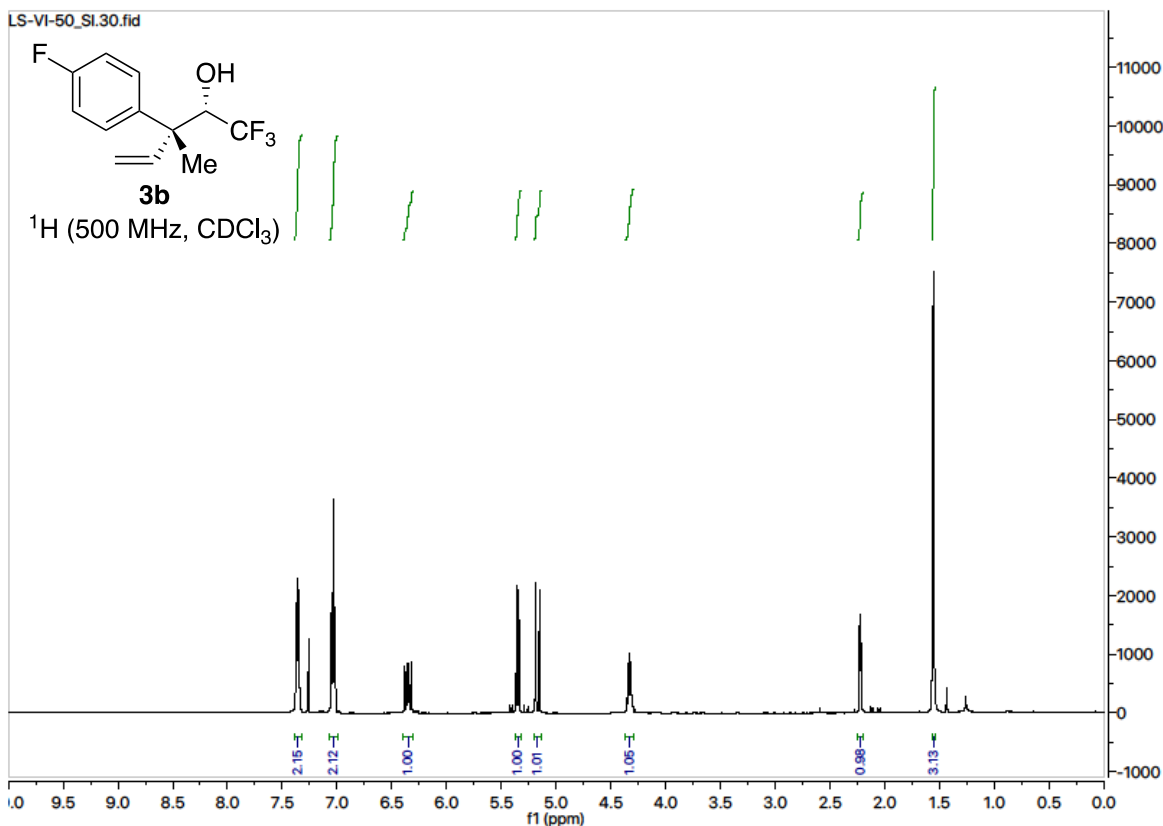
<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -70.8 (d, *J* = 7.2 Hz), -116.0 (m).

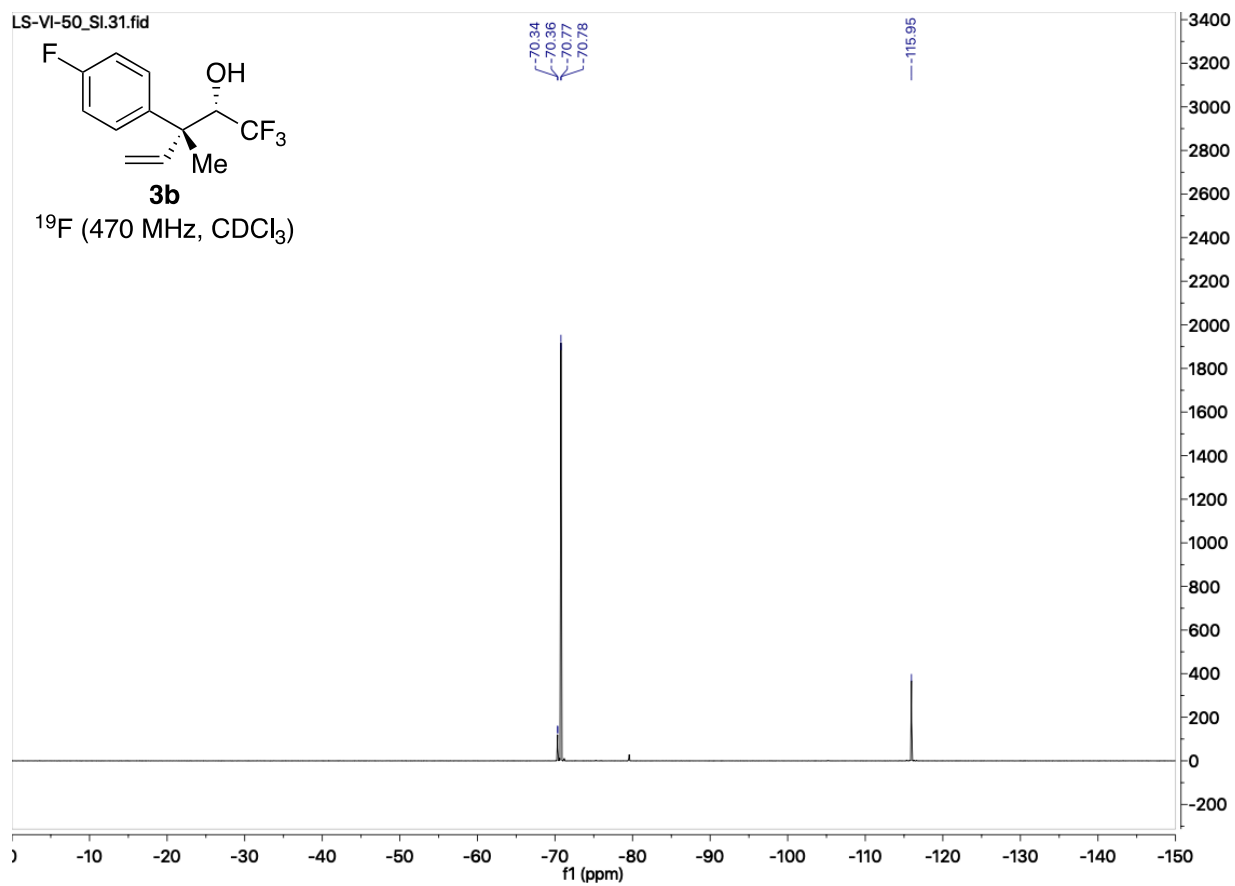
HRMS (CI+, *m/z*) for C<sub>12</sub>H<sub>12</sub>F<sub>4</sub>O: calcd. = 248.0824; found = 248.0821.

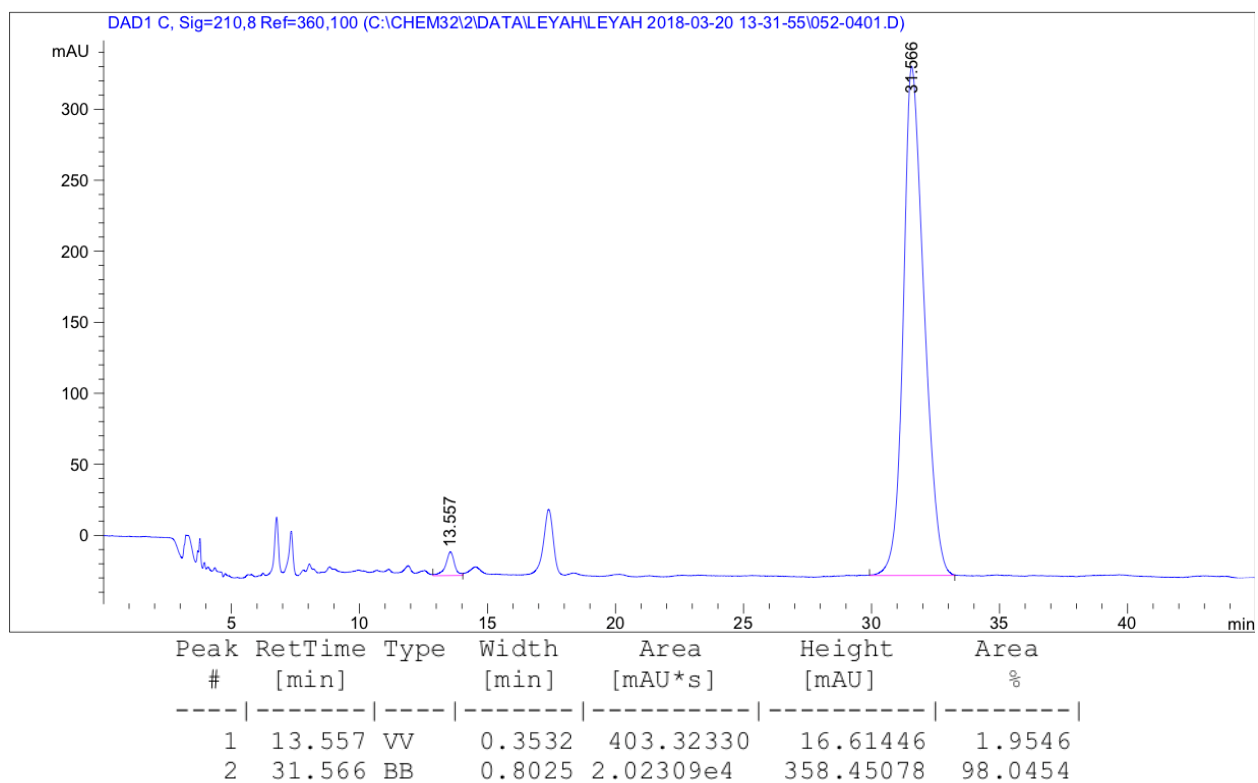
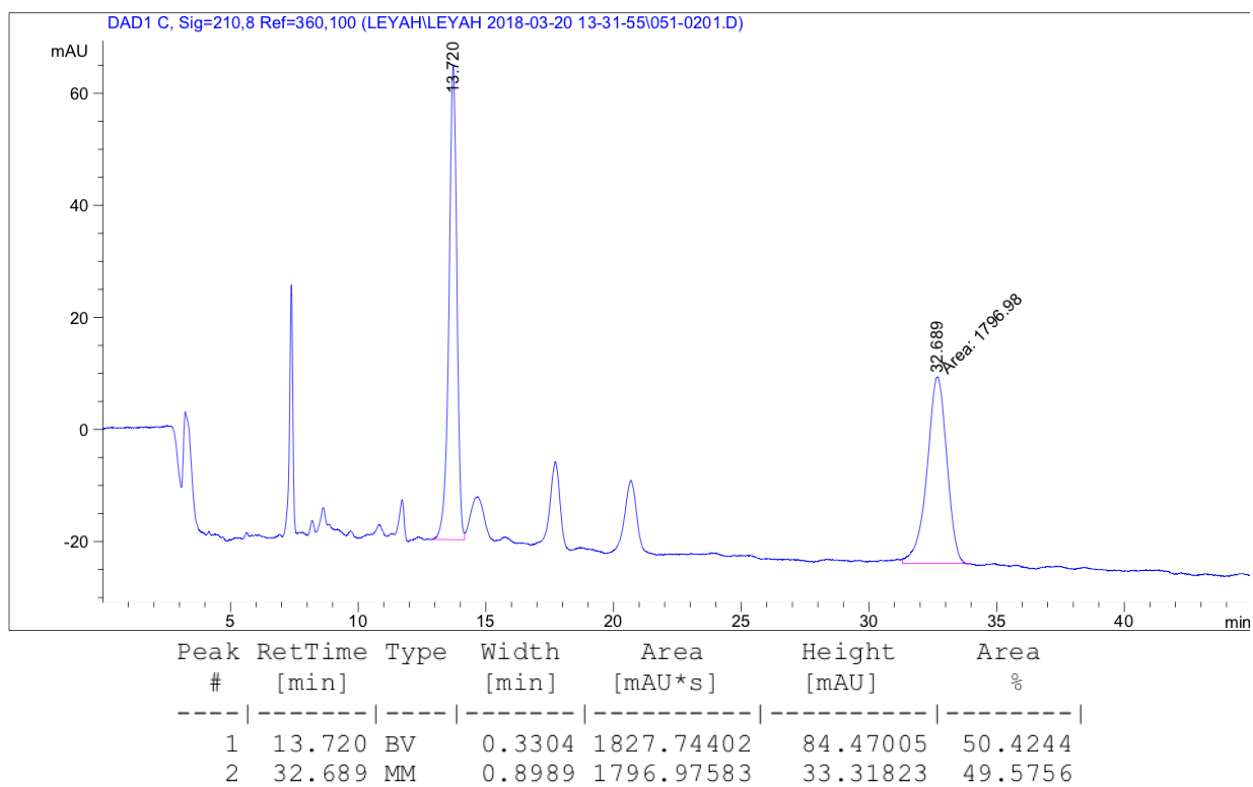
FTIR (neat): 3500, 2950, 2900, 1600, 1500, 1200, 1150, 1100, 900, 800, 600 cm<sup>-1</sup>.

HPLC: (Chiralcel column OJ-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 210 nm) ee = 96%.

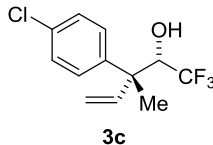
[α]<sub>D</sub><sup>24</sup> = -15.8 (c = 1.1, CHCl<sub>3</sub>).







**(2*S*,3*R*)-1,1,1-trifluoro-3-(4-chlorophenyl)-3-methylpent-4-en-2-ol (3c)**



1,1-Disubstituted allene **1c** (65.9 mg, 0.4 mmol) was subjected to general procedure D. Upon flash column chromatography (SiO<sub>2</sub>, 5:95 EtOAc/hexanes), the title compound **3c** (38.3 mg, 0.14 mmol, 18:1 dr) was obtained as a light yellow oil in 72% yield.

R<sub>f</sub> = 0.4 (4:1 hexanes : EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.32 (m, 4H), 6.34 (dd, *J* = 10.7, 17.7 Hz, 1H), 5.36 (d, *J* = 10.9 Hz, 1H), 5.17 (d, *J* = 17.6 Hz, 1H), 4.33 (dq, *J* = 7.2, 5.7 Hz, 1H), 2.25 (d, *J* = 5.4 Hz, 1H), 1.55 (q, *J* = 1.5 Hz, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 142.2, 140.5, 132.9, 128.5, 128.4, 125.0 (q, *J* = 284.0 Hz), 116.1, 75.6 (q, *J* = 28.3 Hz), 47.0, 20.9 (q, *J* = 2.5 Hz).

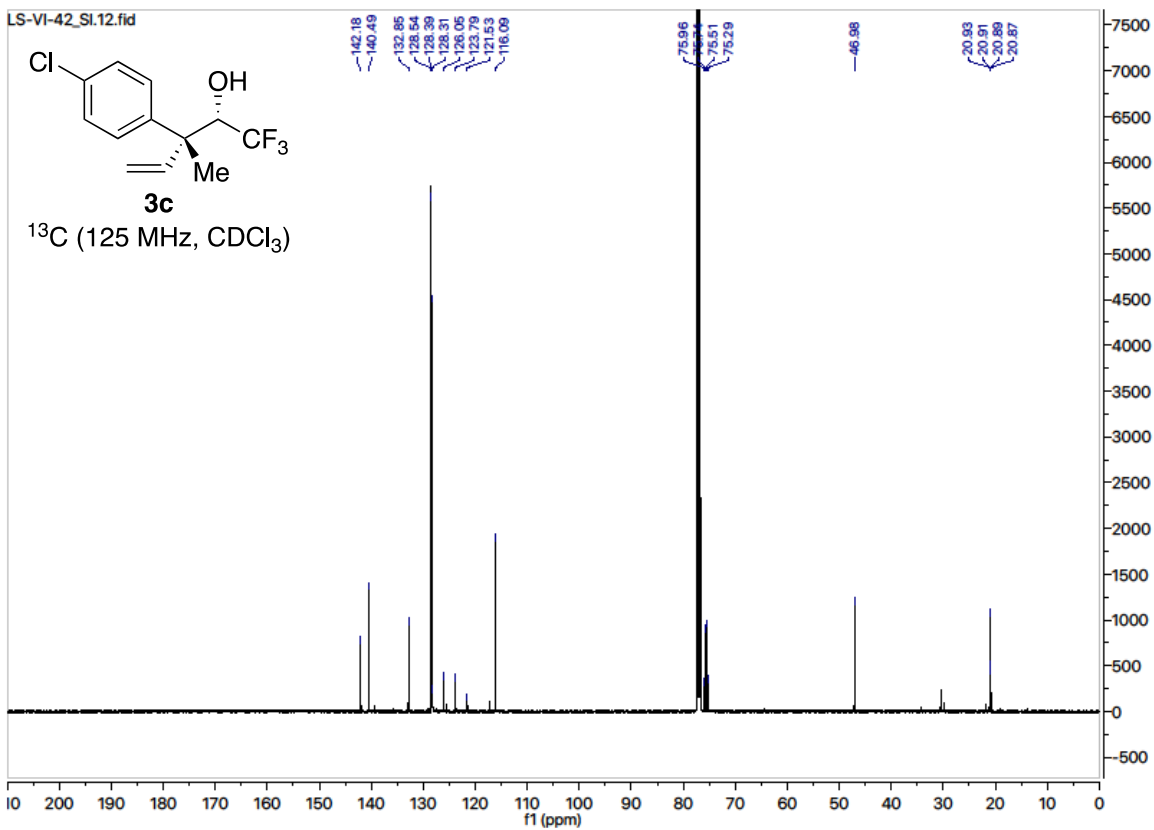
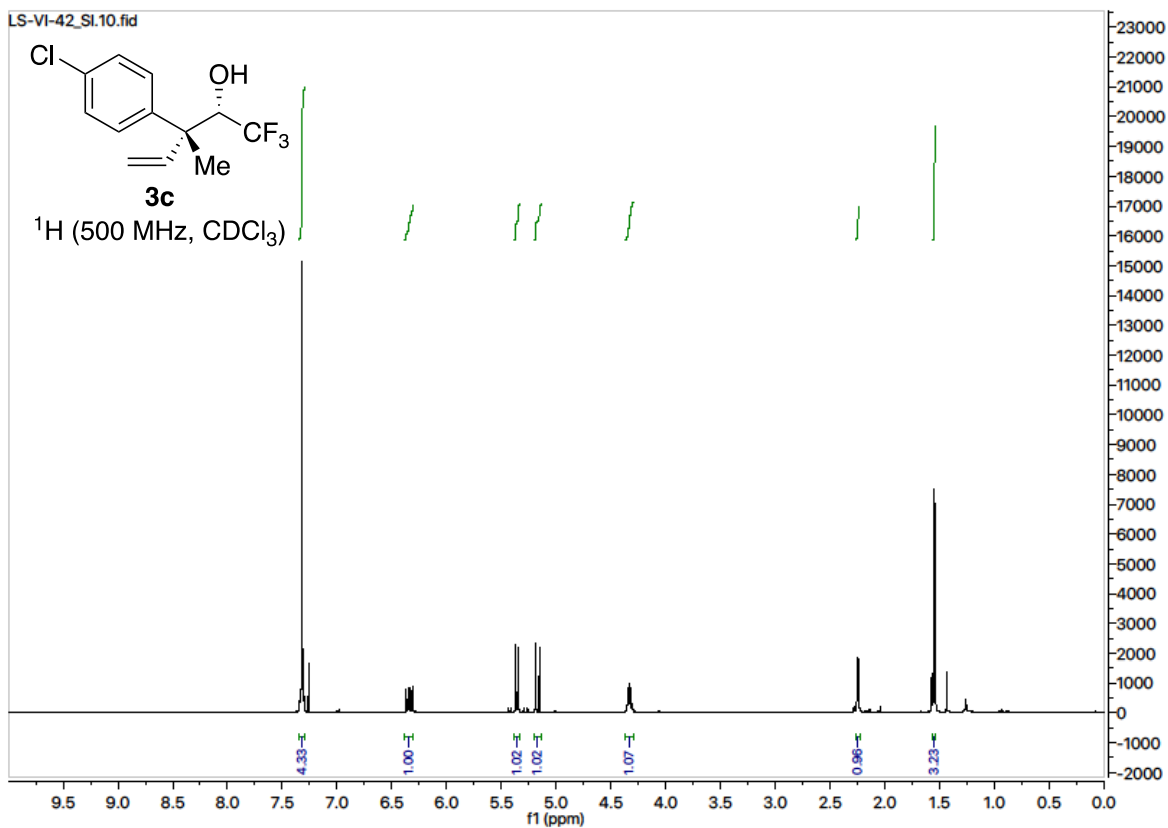
<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -70.8 (d, *J* = 7.2 Hz).

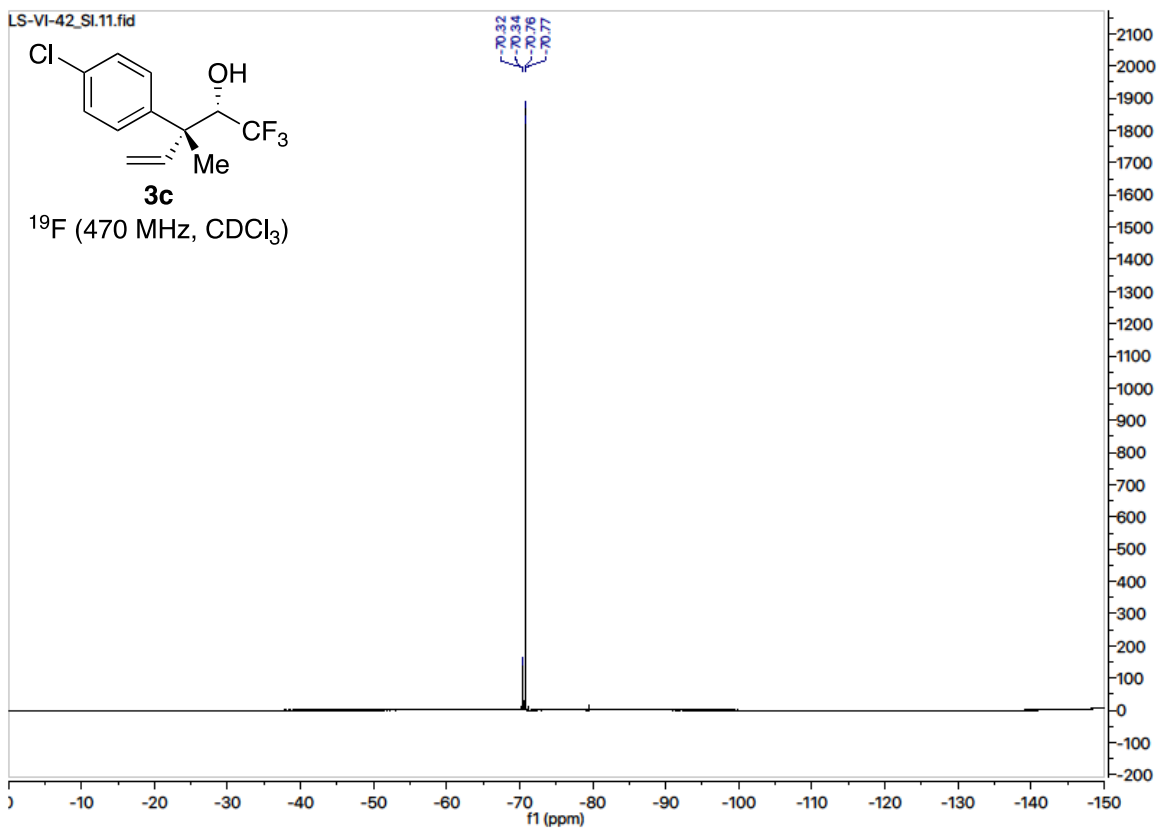
HRMS (CI+, *m/z*) for C<sub>12</sub>H<sub>12</sub>ClF<sub>3</sub>O: calcd. = 264.0529; found = 264.0532.

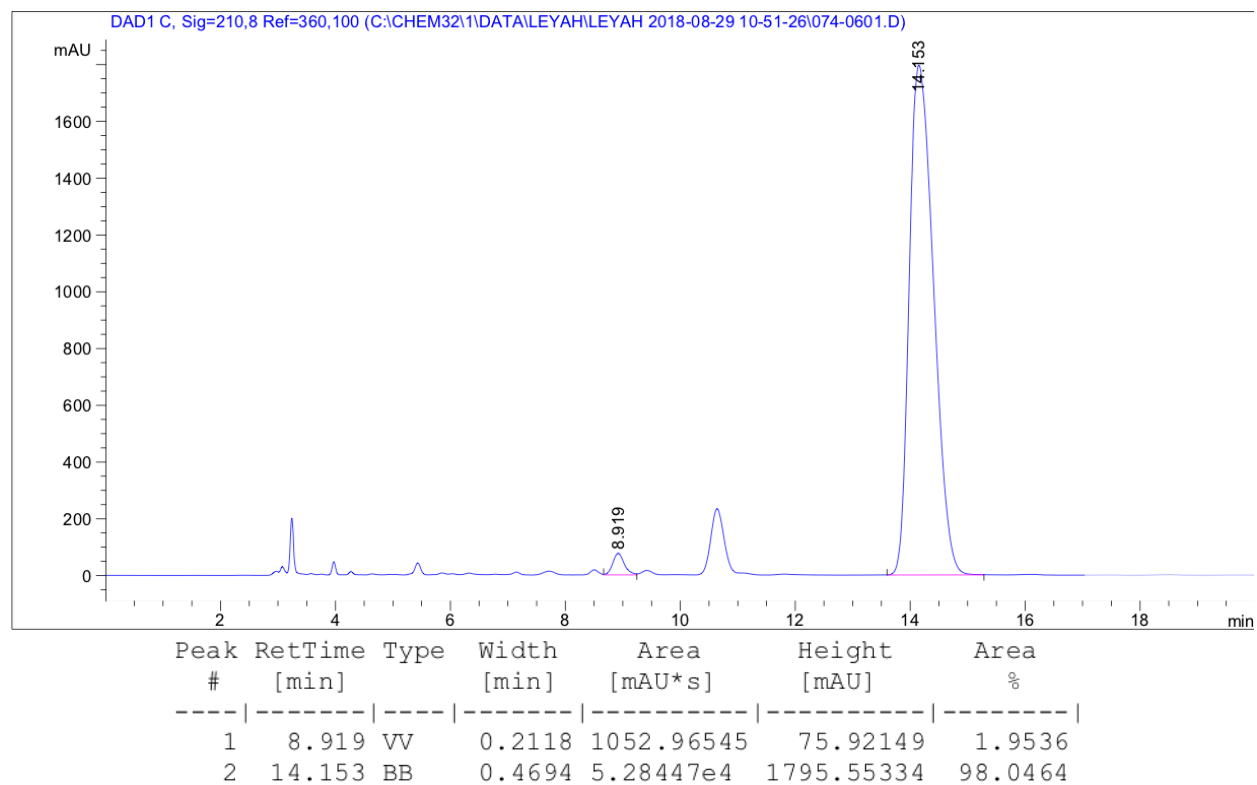
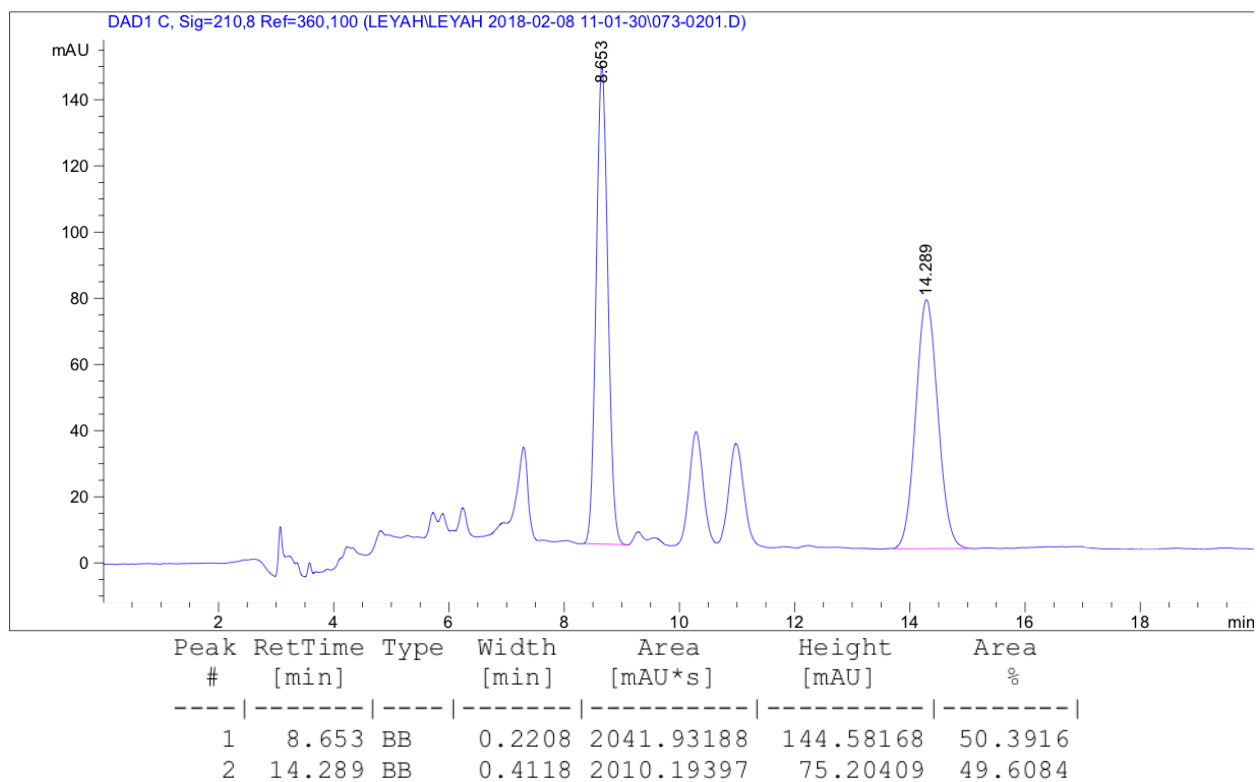
FTIR (neat): 3450, 3000, 1500, 1300, 1150, 1100, 1050, 1000, 900, 800, 350, 300 cm<sup>-1</sup>.

HPLC: (Chiralcel column OJ-H, Hexane:2-PrOH = 93:7, 1.0 mL/min, 210 nm) ee = 96%.

[α]<sub>D</sub><sup>24</sup> = -37.7 (c = 1.1, CHCl<sub>3</sub>).

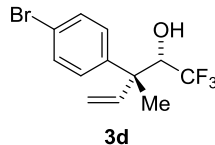








**(2*S*,3*R*)-3-(4-bromophenyl)-1,1,1-trifluoro-3-methylpent-4-en-2-ol (3d)**



1,1-Disubstituted allene **1d** (836.4 mg, 4 mmol) was subjected to general procedure D. Upon flash column chromatography (SiO<sub>2</sub>, 1:9 EtOAc/hexanes), the title compound **3d** (528.5 mg, 1.71 mmol, 19:1 dr) was obtained as a light yellow oil in 85% yield.

R<sub>f</sub> = 0.4 (4:1 hexanes : EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.49 (d, *J* = 8.9, 2H), 7.29 (d, *J* = 8.5 Hz, 2H), 6.36 (dd, *J* = 10.9, 17.7 Hz, 1H), 5.38 (d, *J* = 10.9 Hz, 1H), 5.19 (d, *J* = 17.5 Hz, 1H), 4.35 (dq, *J* = 7.2, 5.8 Hz, 1H), 2.29 (d, *J* = 5.5 Hz, 1H), 1.56 (q, *J* = 1.3 Hz, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 142.8, 140.4, 131.5, 128.8, 125.0 (q, *J* = 284.8 Hz), 121.0, 116.1, 75.6 (q, *J* = 28.3 Hz), 47.0, 20.9 (q, *J* = 2.4 Hz).

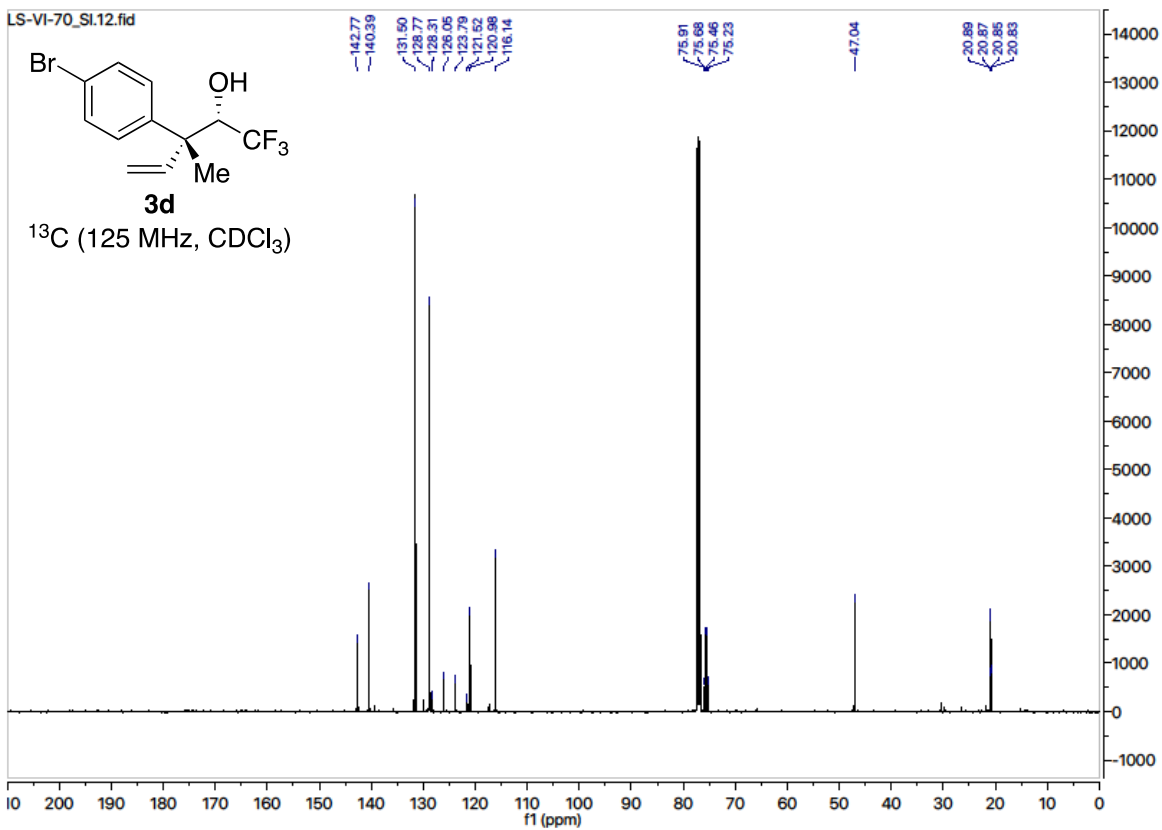
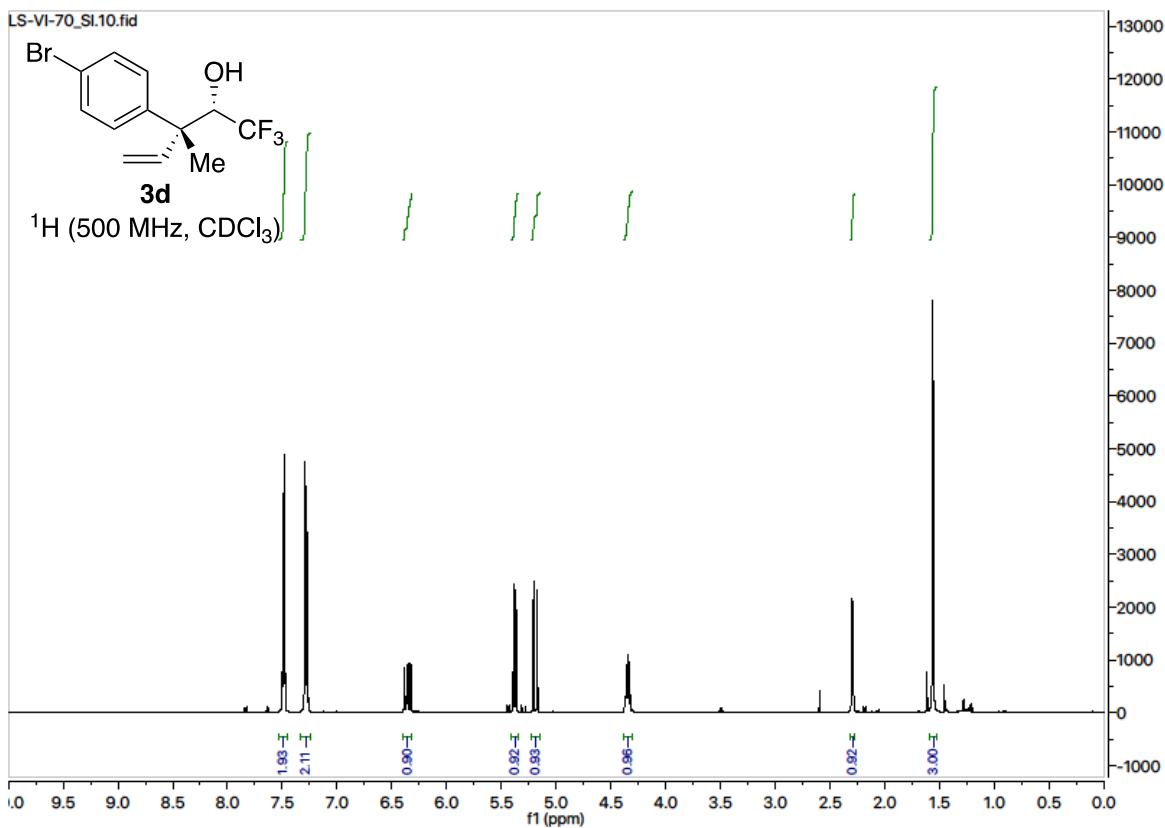
<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -70.75 (d, *J* = 7.2 Hz).

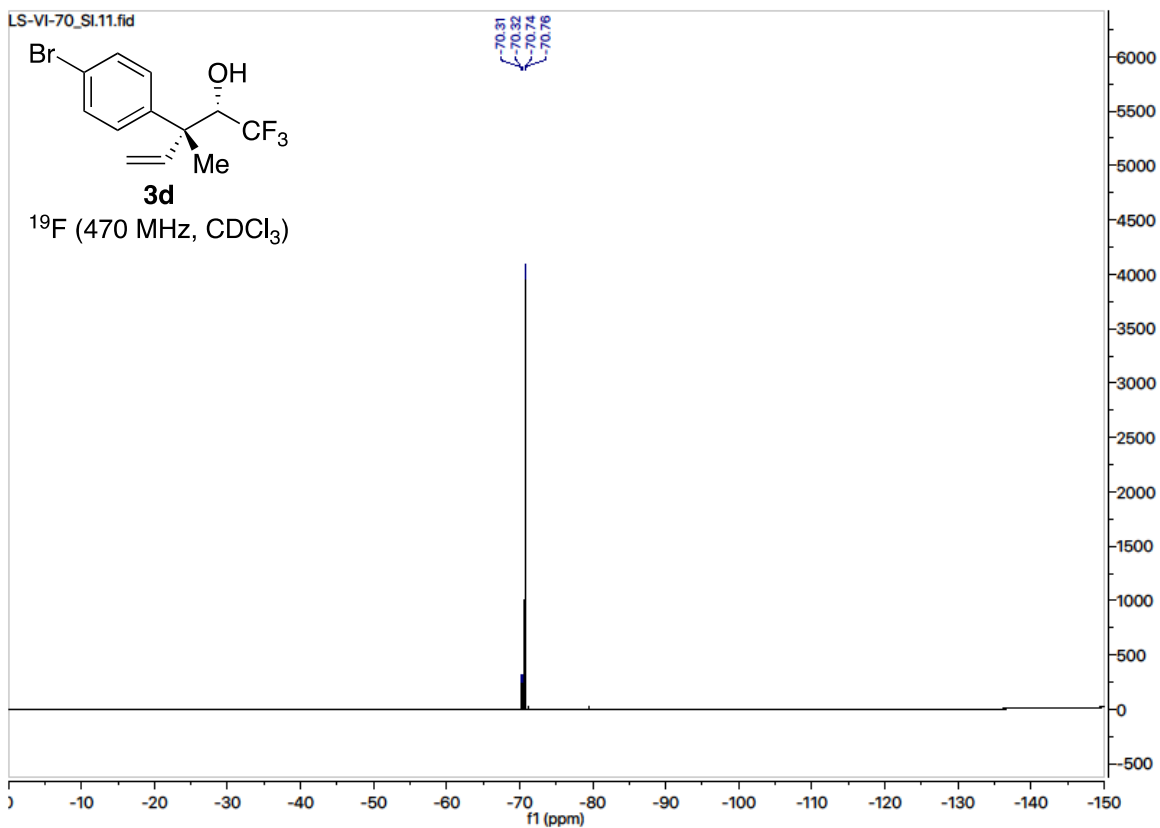
HRMS (CI+,  $m/z$ ) for C<sub>12</sub>H<sub>12</sub>BrF<sub>3</sub>O: calcd. = 308.0024; found = 308.0023.

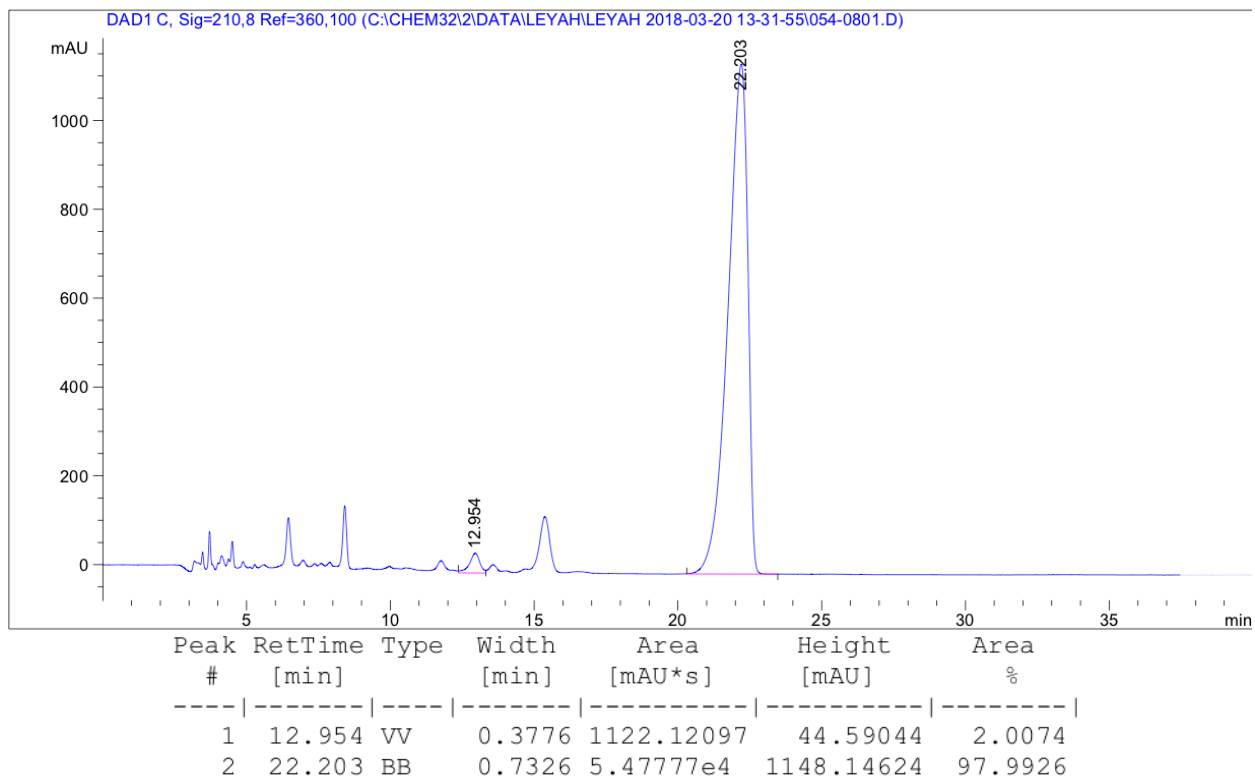
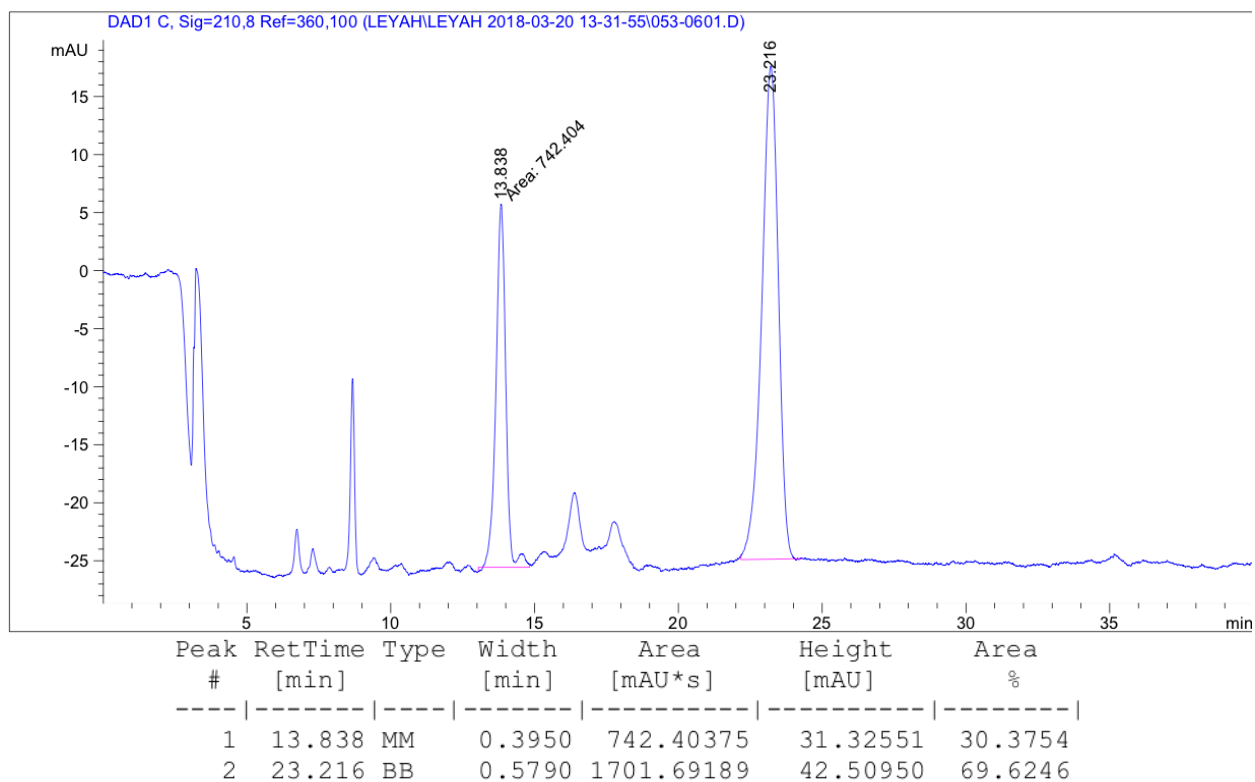
FTIR (neat): 3500, 2950, 1500, 1300, 1150, 110, 1050, 1000, 900, 800, 700, 600 cm<sup>-1</sup>.

HPLC: (Chiralcel column OJ-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 210 nm) ee = 96%.

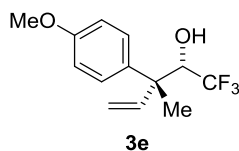
$$[\alpha]_D^{24} = -46.4 \text{ (c = 1.1, CHCl}_3\text{)}.$$







**(2*S*,3*R*)-1,1,1-trifluoro-3-(4-methoxyphenyl)-3-methylpent-4-en-2-ol (3e)**



1,1-Disubstituted allene **1e** (64.9 mg, 0.4 mmol) was subjected to general procedure D. Upon flash column chromatography (SiO<sub>2</sub>, 5:95 EtOAc/hexanes), the title compound **3e** (39.6 mg, 0.16 mmol, 14:1 dr) was obtained as a light yellow oil in 79% yield.

R<sub>f</sub> = 0.3 (4:1 hexanes : EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.3 (m, 2H), 6.88 (m, 2H), 6.37 (dd, *J* = 10.9, 17.7 Hz, 1H), 5.34 (d, *J* = 11.0 Hz, 1H), 5.17 (d, *J* = 17.7 Hz, 1H), 4.32 (dq, *J* = 5.4, 1.9 Hz, 1H), 3.80 (s, 3H), 2.17 (d, *J* = 5.1 Hz, 1H), 1.54 (q, *J* = 1.4 Hz, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 158.4, 140.9, 135.4, 128.0, 125.1 (q, *J* = 282.9 Hz), 115.4, 113.8, 75.9 (q, *J* = 27.9 Hz), 55.3, 46.7, 21.1 (q, *J* = 2.4 Hz).

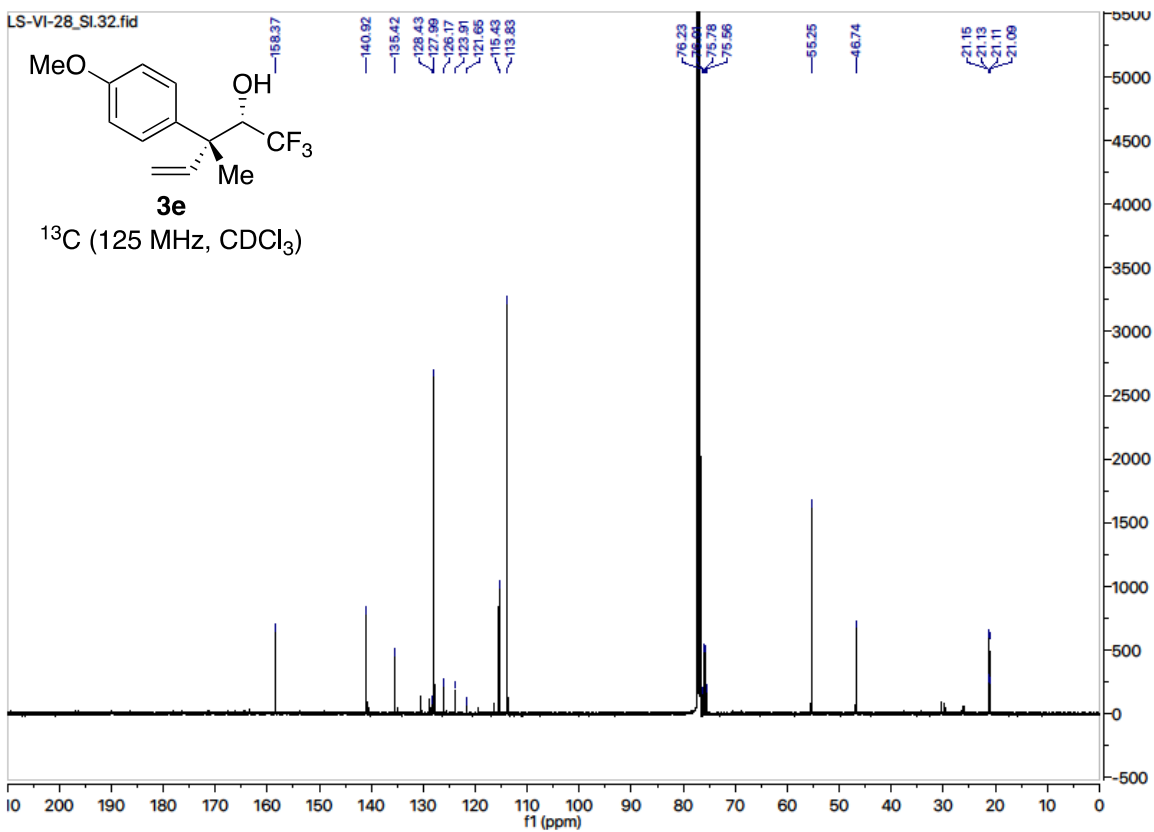
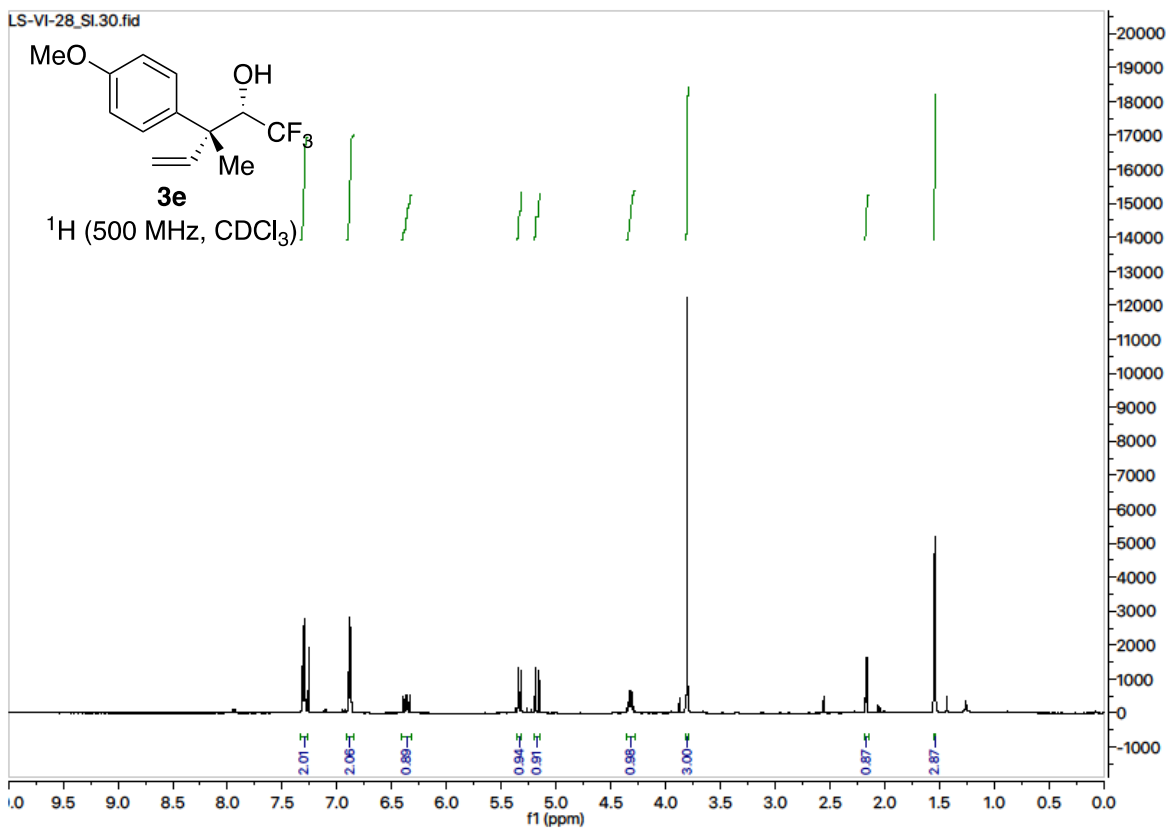
<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -70.7 (d, *J* = 7.2 Hz).

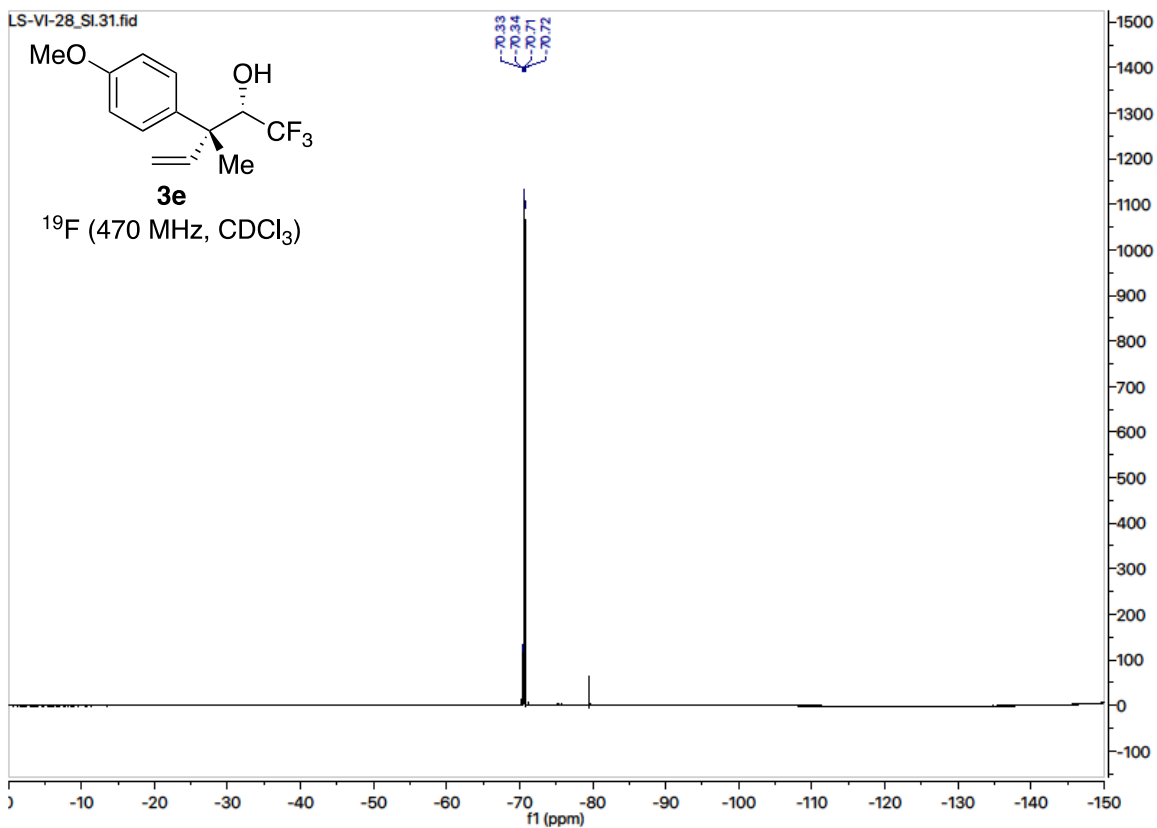
HRMS (APPI, *m/z*) for C<sub>13</sub>H<sub>15</sub>F<sub>3</sub>O<sub>2</sub>: calcd. = 261.1097; found = 261.1096.

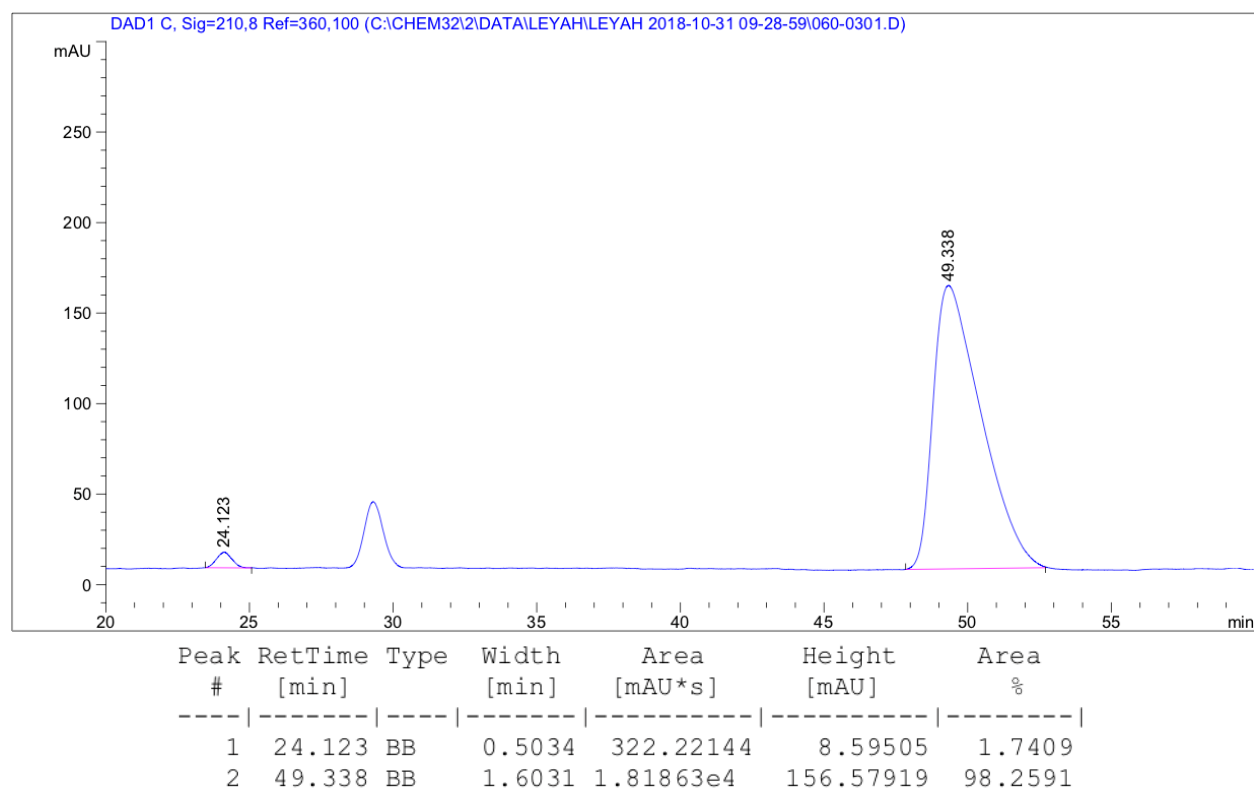
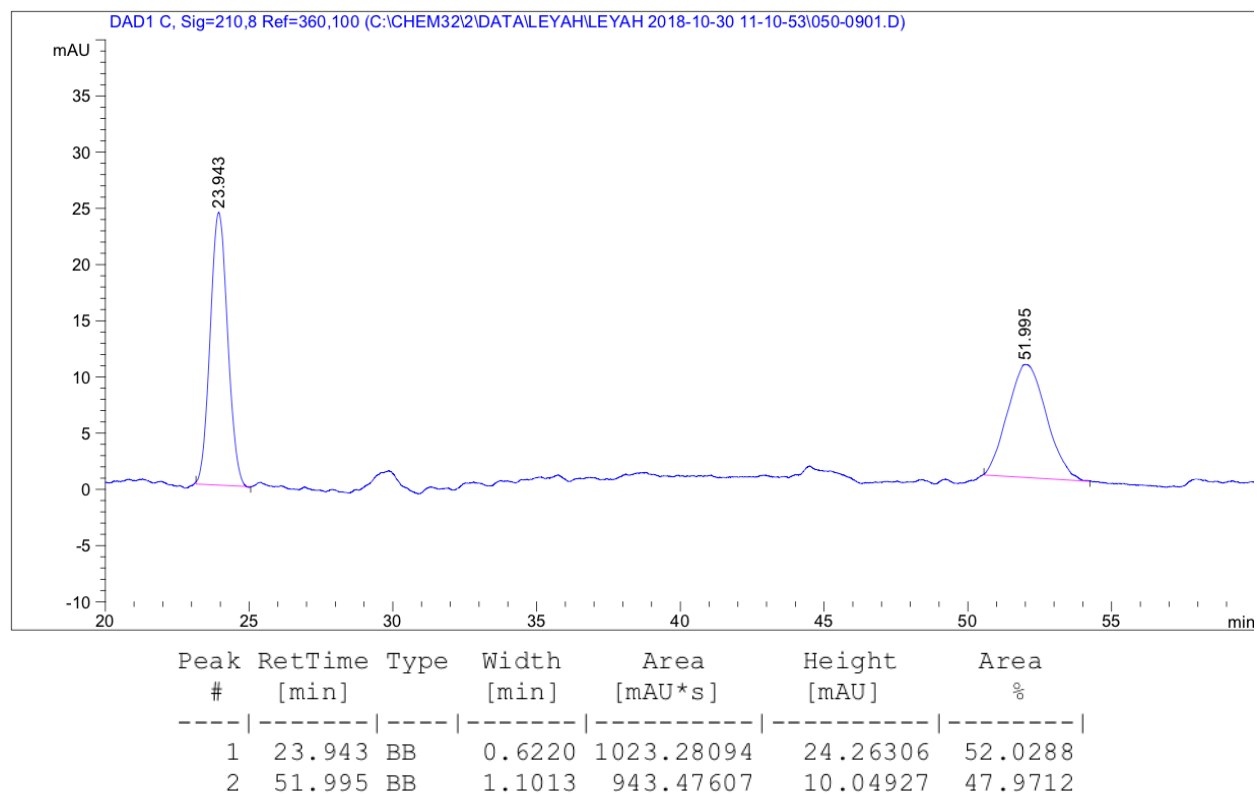
FTIR (neat): 3500, 2950, 2800, 1510, 1250, 1150, 1050, 1000, 900, 800 cm<sup>-1</sup>.

HPLC: (Chiralcel column OJ-H, Hexane:2-PrOH = 92:8, 1.0 mL/min, 210 nm) ee = 96%.

[α]<sub>D</sub><sup>24</sup> = -22.8 (c = 1.1, CHCl<sub>3</sub>).

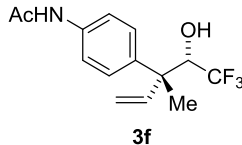








***N*-(4-((3*R*,4*S*)-5,5,5-trifluoro-4-hydroxy-3-methylpent-1-en-3-yl)phenyl)acetamide (**3f**)**



1,1-Disubstituted allene **1f** (74.9 mg, 0.4 mmol) was subjected to general procedure D. Upon flash column chromatography (SiO<sub>2</sub>, 1:1 EtOAc/hexanes), the title compound **3f** (36.7 mg, 0.13 mmol, 11:1 dr) was obtained as a light yellow oil in 64% yield.

R<sub>f</sub> = 0.2 (10:1 CH<sub>2</sub>Cl<sub>2</sub> : MeOH)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.49 (s, 1H), 7.43 (d, *J* = 8.6 Hz, 2 H), 7.31 (d, *J* = 8.6 Hz, 2H), 6.37 (dd, *J* = 11.0, 17.6 Hz, 1H), 5.32 (d, *J* = 10.9 Hz, 1H), 5.16 (d, *J* = 17.7 Hz, 1H), 4.32 (dq, *J* = 5.2, 2.0 Hz, 1H), 3.04 (d, *J* = 5.6 Hz, 1H), 2.11 (s, 3H), 1.52 (bs, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 168.9, 140.7, 140.1, 136.4, 127.5, 125.2 (q, *J* = 284.3 Hz), 119.9, 115.5, 75.6 (q, *J* = 28.2 Hz), 47.0, 24.4, 21.1 (q, *J* = 1.9 Hz).

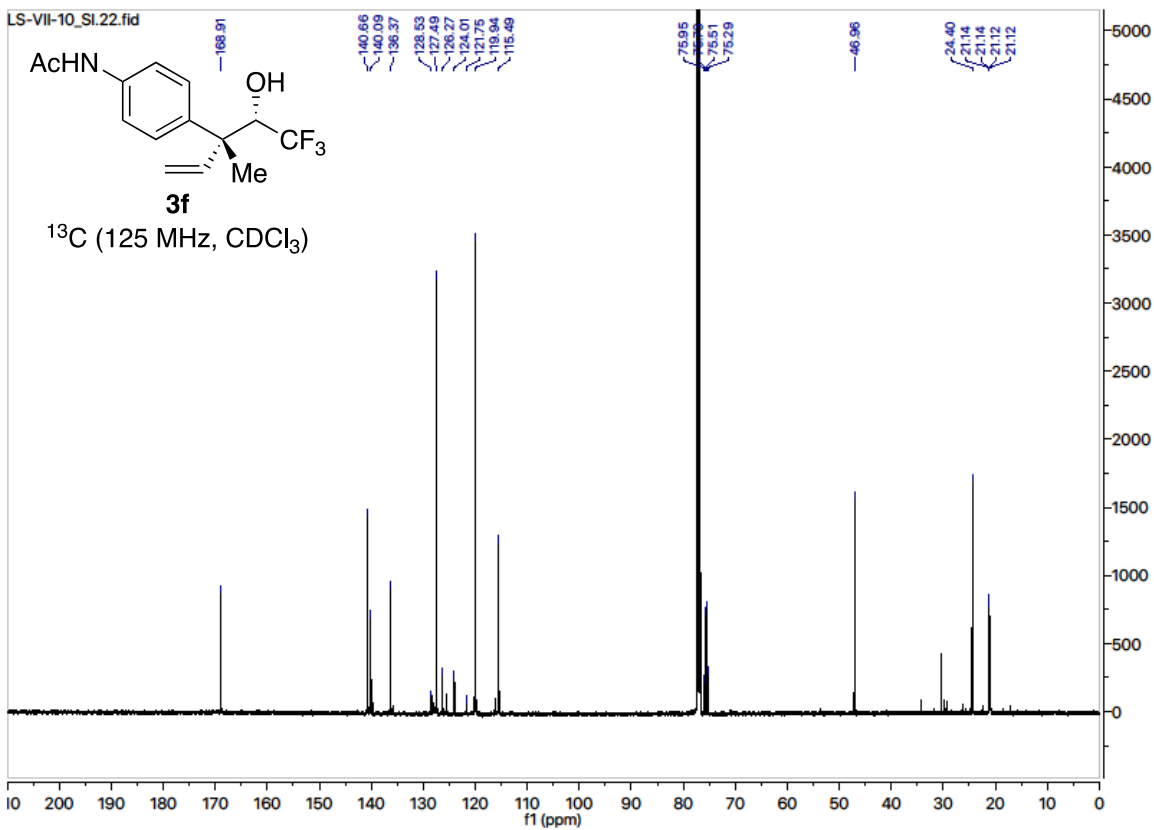
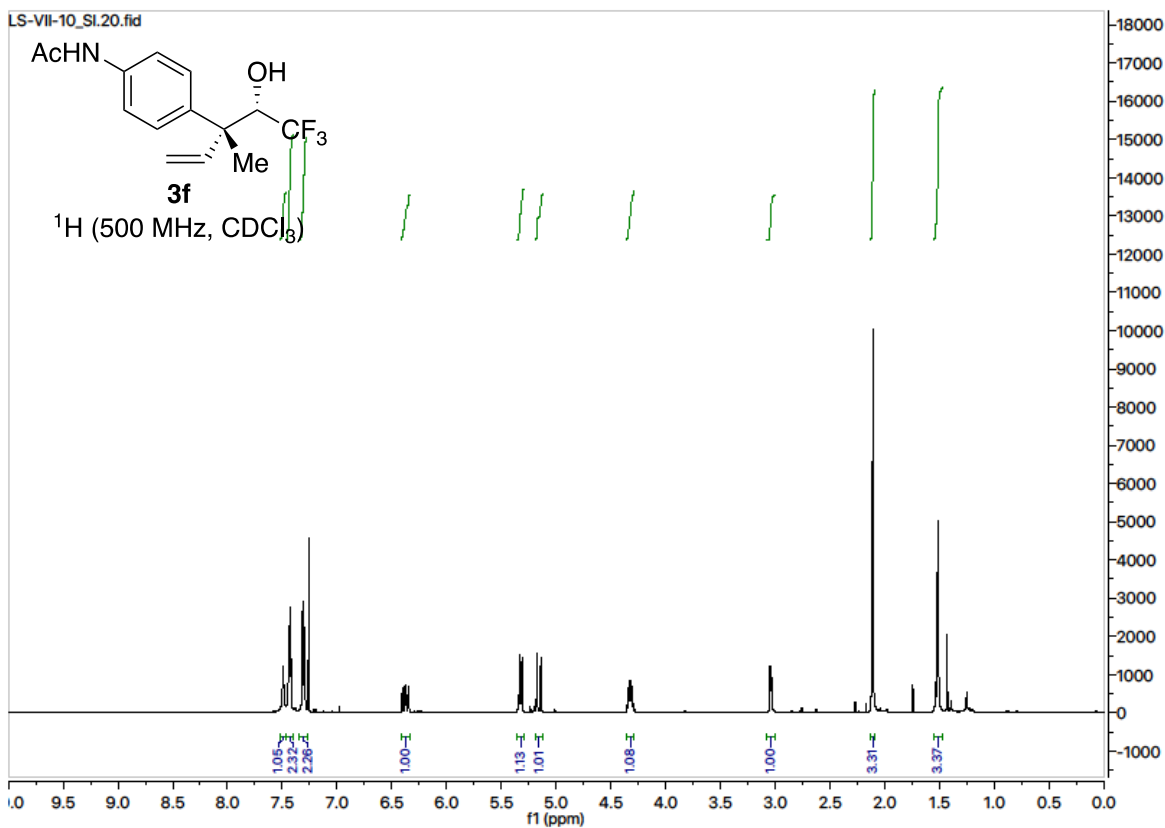
<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -70.7 (d, *J* = 7.1 Hz).

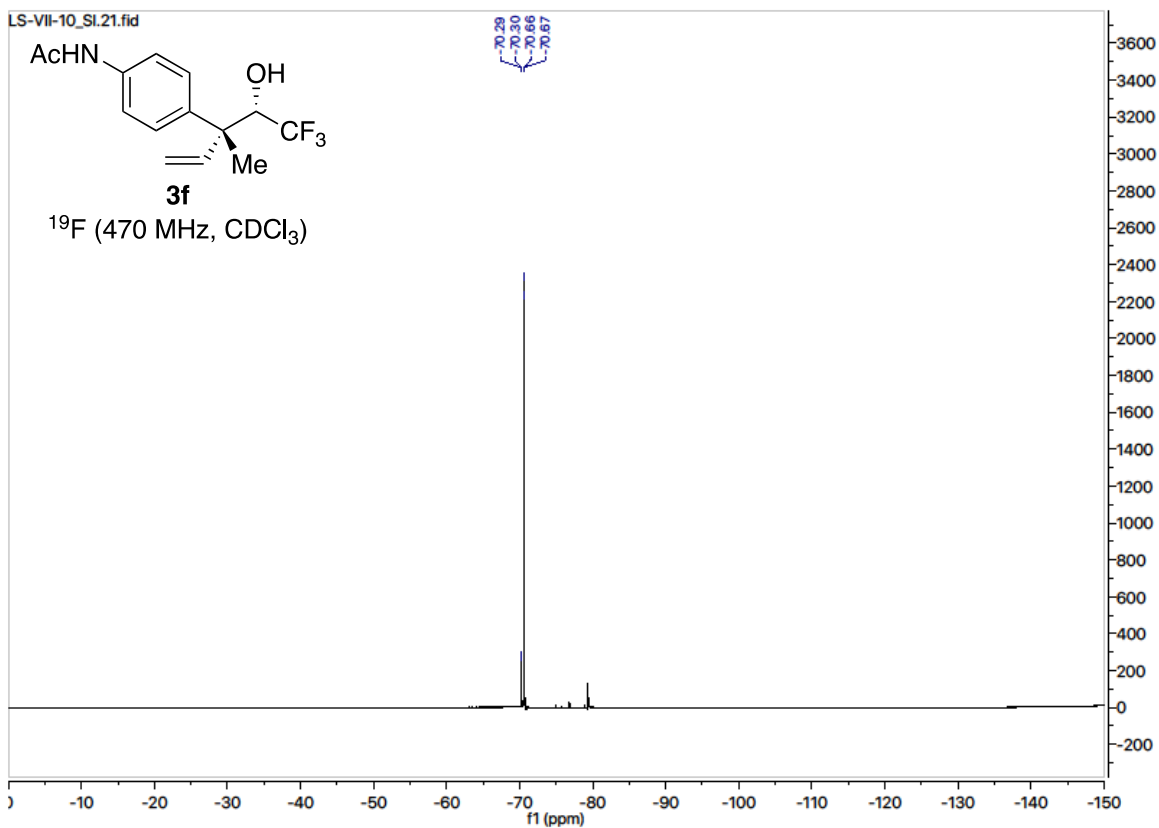
HRMS (ESI+H, *m/z*) for C<sub>14</sub>H<sub>16</sub>F<sub>3</sub>NO<sub>2</sub>: calcd. = 288.1206; found = 288.1211.

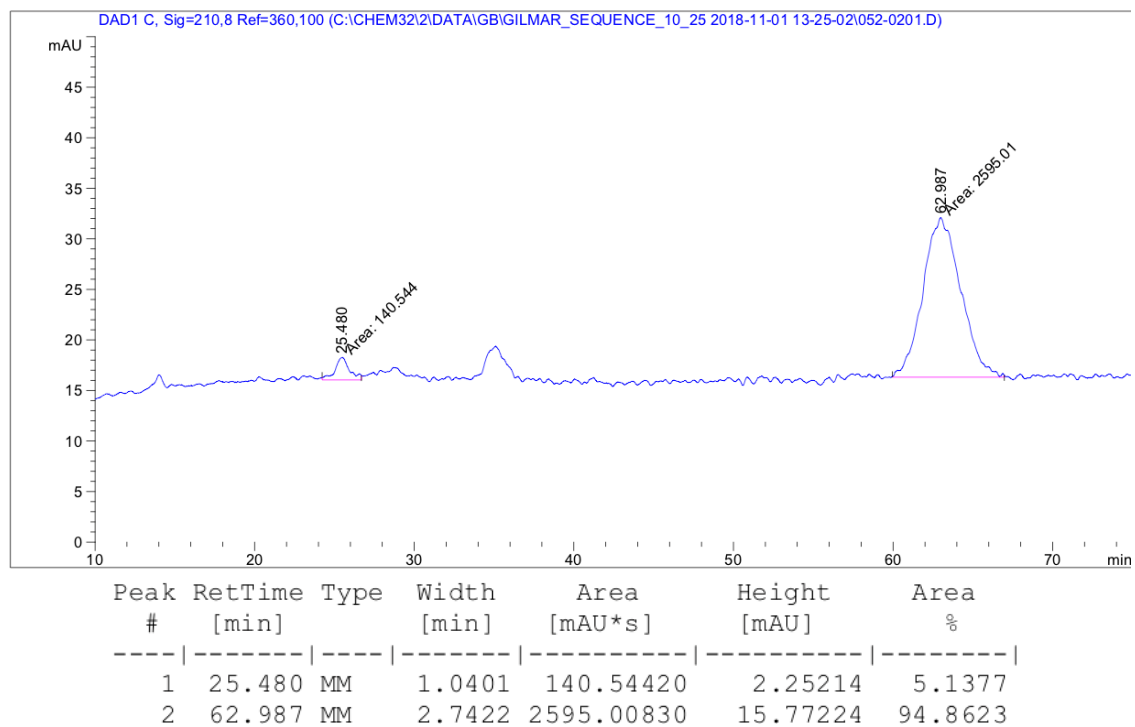
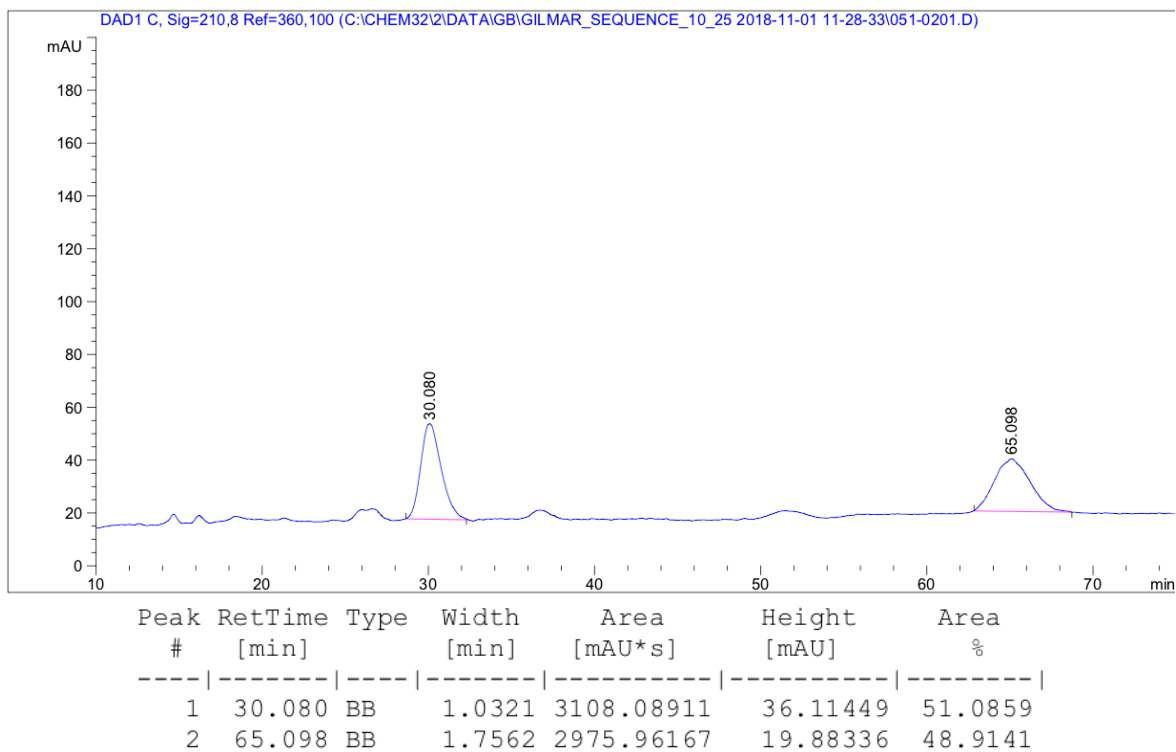
FTIR (neat): 3300, 2300, 1700, 1600, 1500, 1350, 1250, 1150, 1100, 650 cm<sup>-1</sup>.

HPLC: (Chiralcel column OJ-H, Hexane:2-PrOH = 90:10, 1.0 mL/min, 210 nm) ee = 90%.

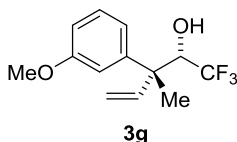
[α]<sub>D</sub><sup>24</sup> = -29.5 (c = 1.1, CHCl<sub>3</sub>).







**(2*S*,3*R*)-1,1,1-trifluoro-3-(3-methoxyphenyl)-3-methylpent-4-en-2-ol (3g)**



1,1-Disubstituted allene **1g** (64.1 mg, 0.4 mmol) was subjected to general procedure D. Upon flash column chromatography (SiO<sub>2</sub>, 1:10 EtOAc/hexanes), the title compound **3g** (39.6 mg, 0.15 mmol, 18:1 dr) was obtained as a light yellow oil in 76% yield.

R<sub>f</sub> = 0.3 (4:1 hexanes : EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.28 (t, *J* = 8.0 Hz, 1H), 6.98 (m, 1H), 6.94 (m, 1H), 6.80 (m, 1H), 6.38 (dd, *J* = 11.1, 17.7 Hz, 1H), 5.36 (d, *J* = 11.0 Hz, 1H), 5.21 (d, *J* = 17.7 Hz, 1H), 4.37 (dq, *J* = 5.3, 2.0 Hz, 1H), 3.81 (s, 3H), 2.21 (d, *J* = 5.1 Hz, 1H), 1.55 (q, *J* = 1.4 Hz, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 159.7, 145.5, 140.3, 129.5, 125.0 (q, *J* = 283.8 Hz), 119.0, 115.8, 113.7, 111.5, 75.9 (q, *J* = 28.3 Hz), 55.2, 47.4, 21.0 (q, *J* = 2.6 Hz).

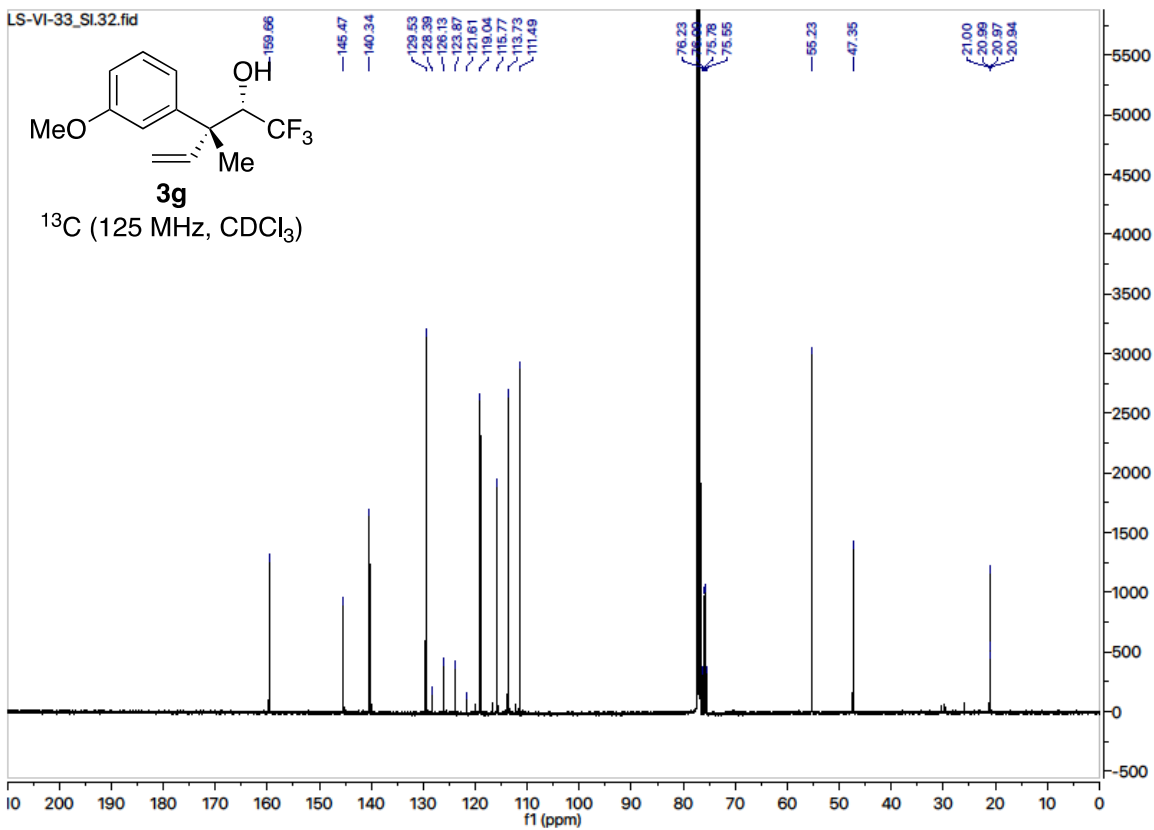
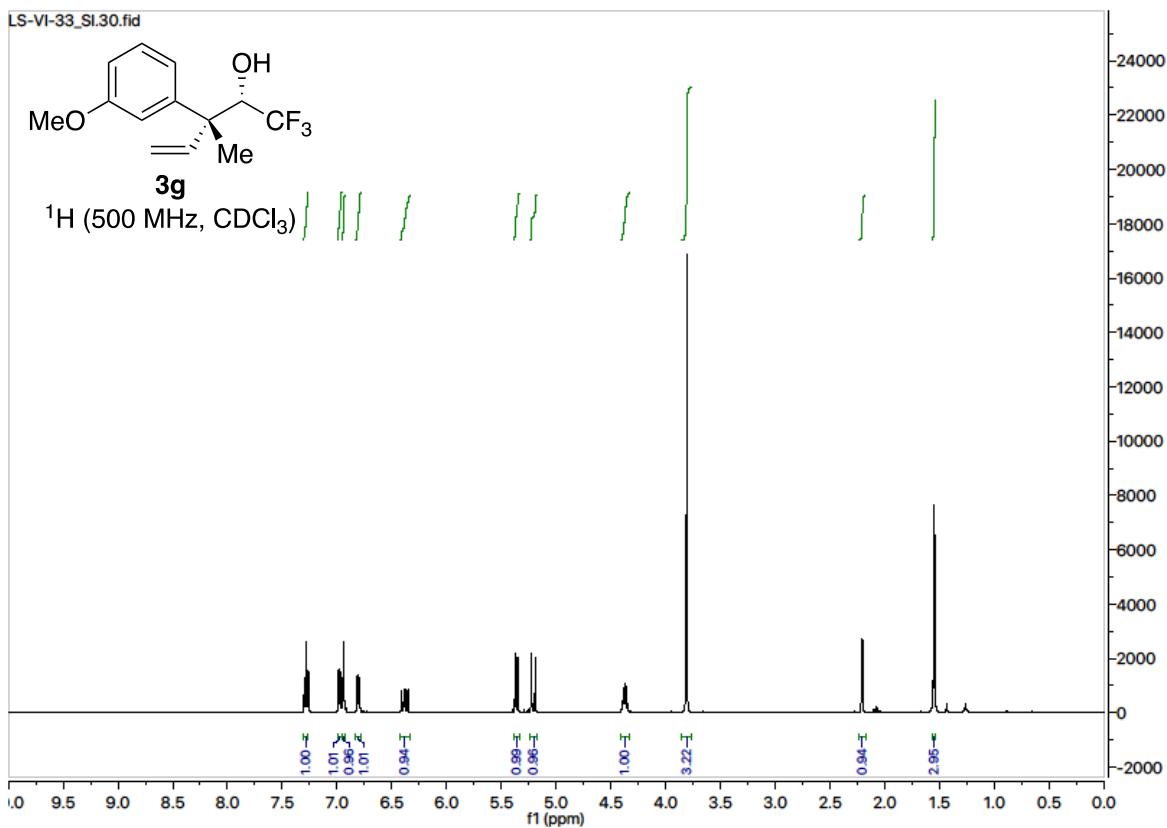
<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -70.7 (d, *J* = 7.2 Hz).

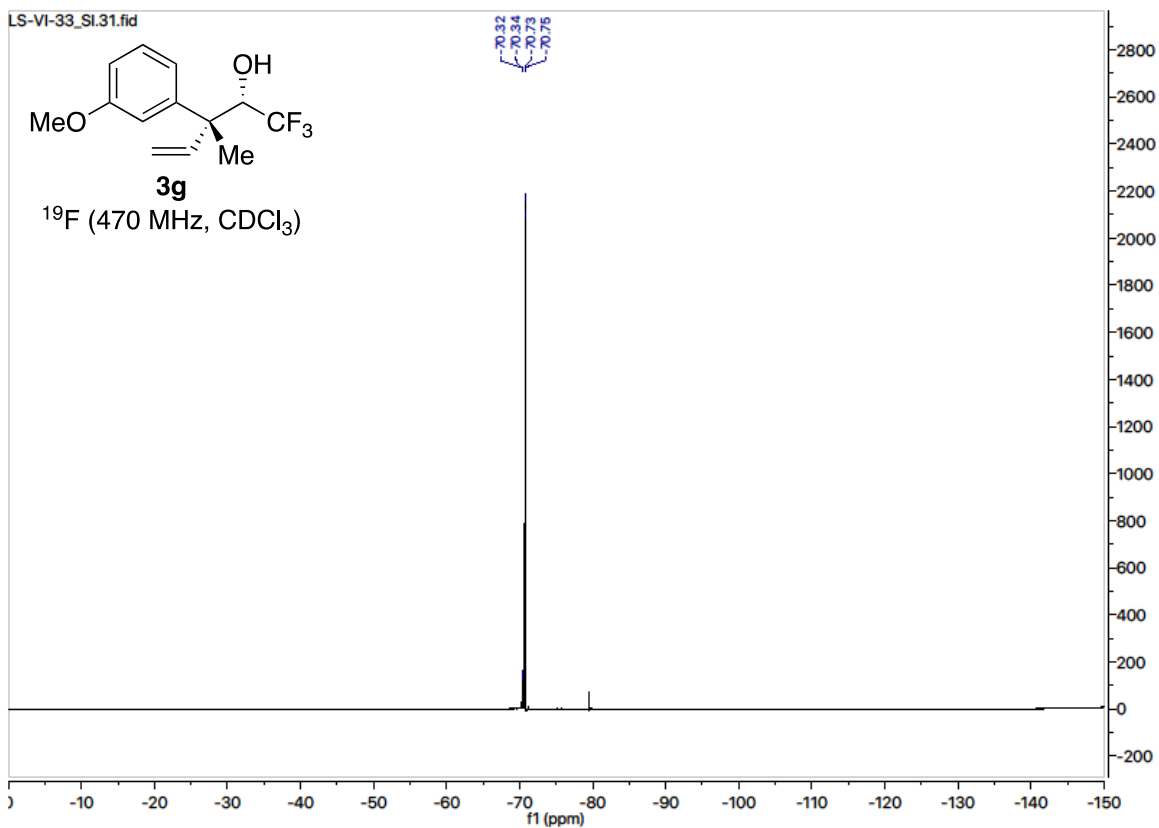
HRMS (APPI, *m/z*) for C<sub>13</sub>H<sub>15</sub>F<sub>3</sub>O<sub>2</sub>: calcd. = 261.1097; found = 261.1091.

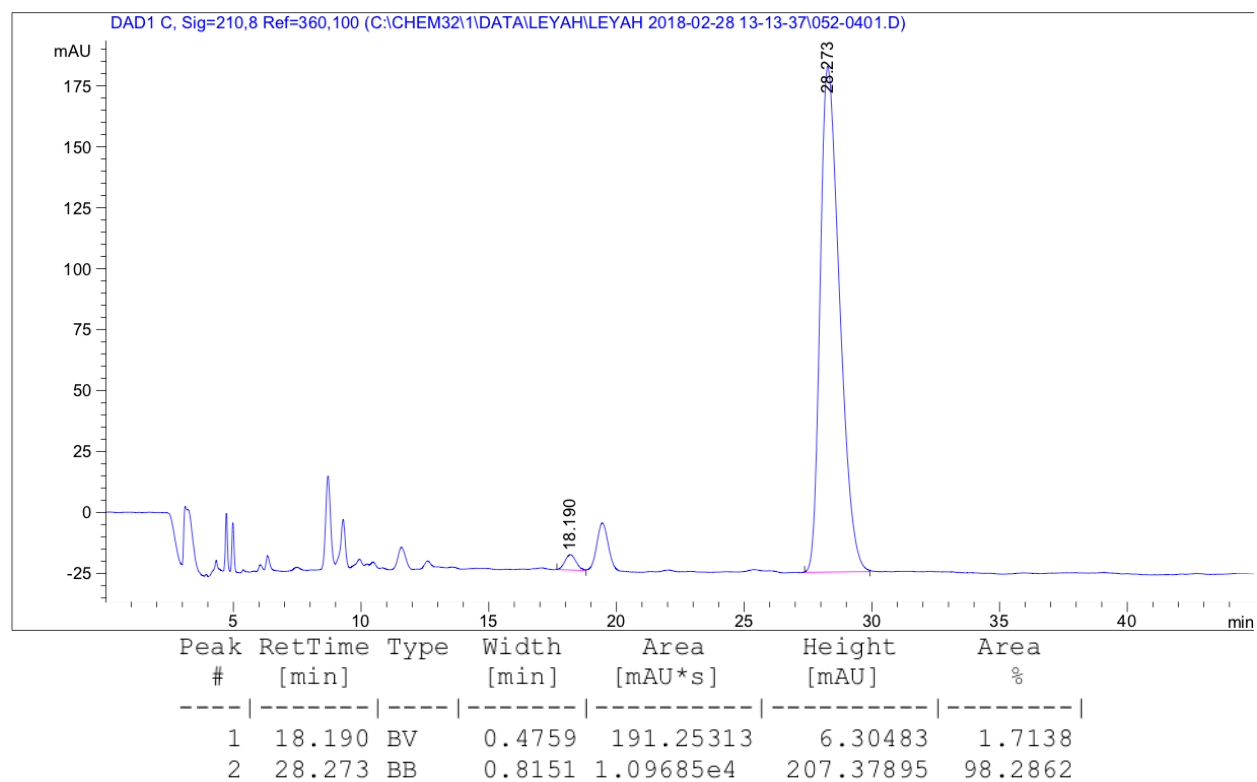
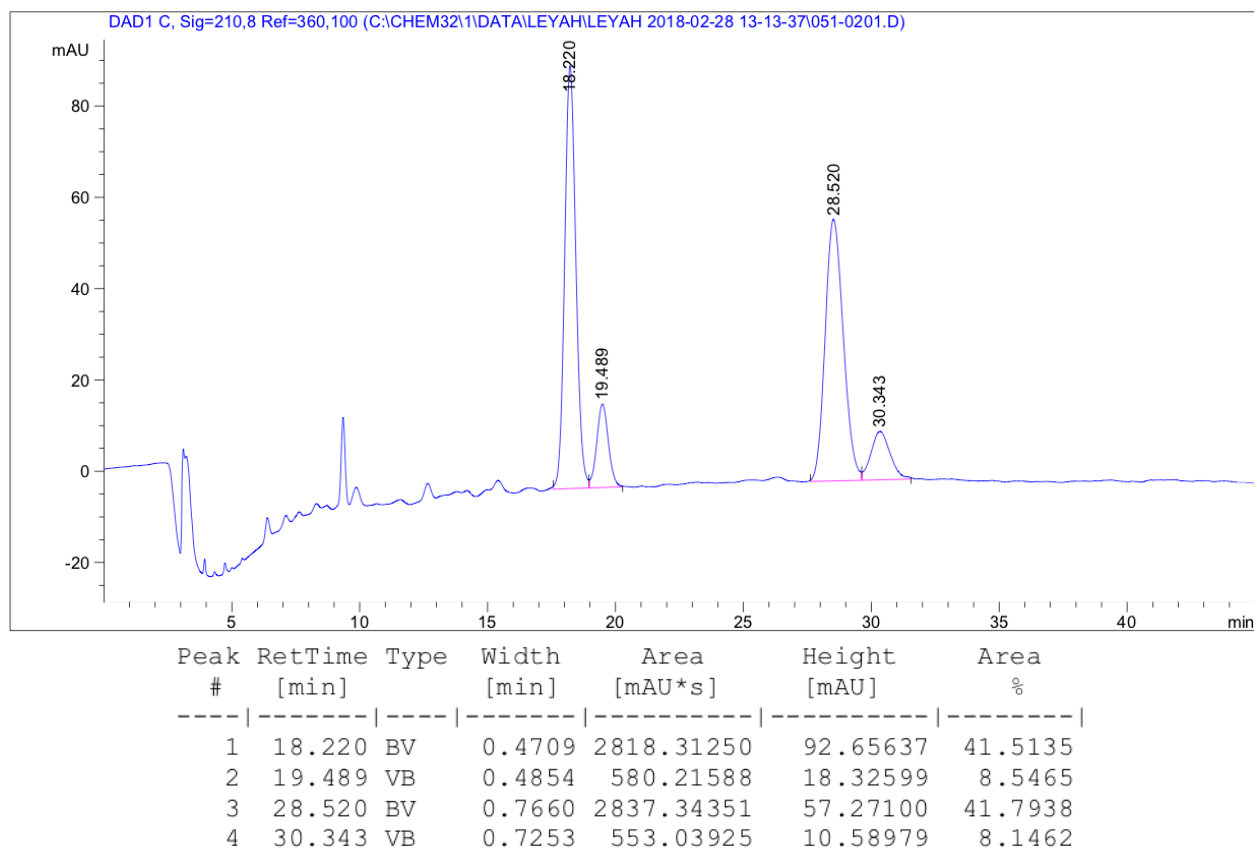
FTIR (neat): 3450, 3000, 2850, 1550, 1450, 1250, 1150, 1100, 1000, 900, 800, 700 cm<sup>-1</sup>.

HPLC: (Chiralcel column OJ-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 210 nm) ee = 96%.

[α]<sub>D</sub><sup>24</sup> = -28.0 (c = 1.1, CHCl<sub>3</sub>).

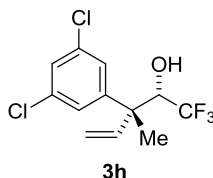








**(2*S*,3*R*)-3-(3,5-dichlorophenyl)-1,1,1-trifluoro-3-methylpent-4-en-2-ol (3h)**



1,1-Disubstituted allene **1h** (80 mg, 0.4 mmol) was subjected to general procedure D. Upon flash column chromatography (SiO<sub>2</sub>, 4:96 EtOAc/hexanes), the title compound **3h** (42.5 mg, 0.14 mmol, 19:1 dr) was obtained as a yellow oil in 71% yield.

R<sub>f</sub> = 0.38 (9:1 hexanes : EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.26 (s, 3H), 6.31 (dd, *J* = 9.7, 15.4 Hz, 1H), 5.41 (d, *J* = 9.7 Hz, 1H), 5.20 (d, *J* = 15.4 Hz, 1H), 4.30 (dq, *J* = 6.3 Hz, 1H), 2.30 (d, *J* = 6.3 Hz, 1H, OH), 1.53 (s, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 147.6, 139.4, 135.0, 127.1, 125.8, 124.9 (q, *J* = 285 Hz), 116.8, 75.4 (q, *J* = 30 Hz), 47.2, 21.0.

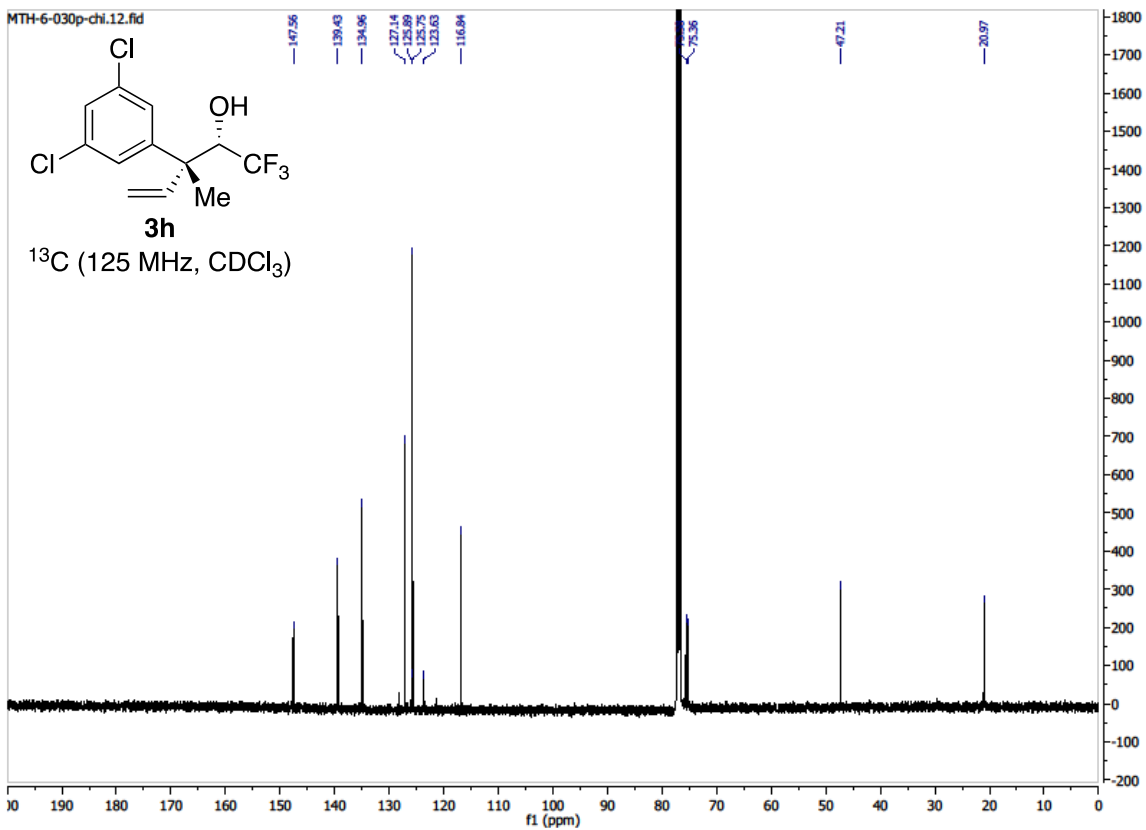
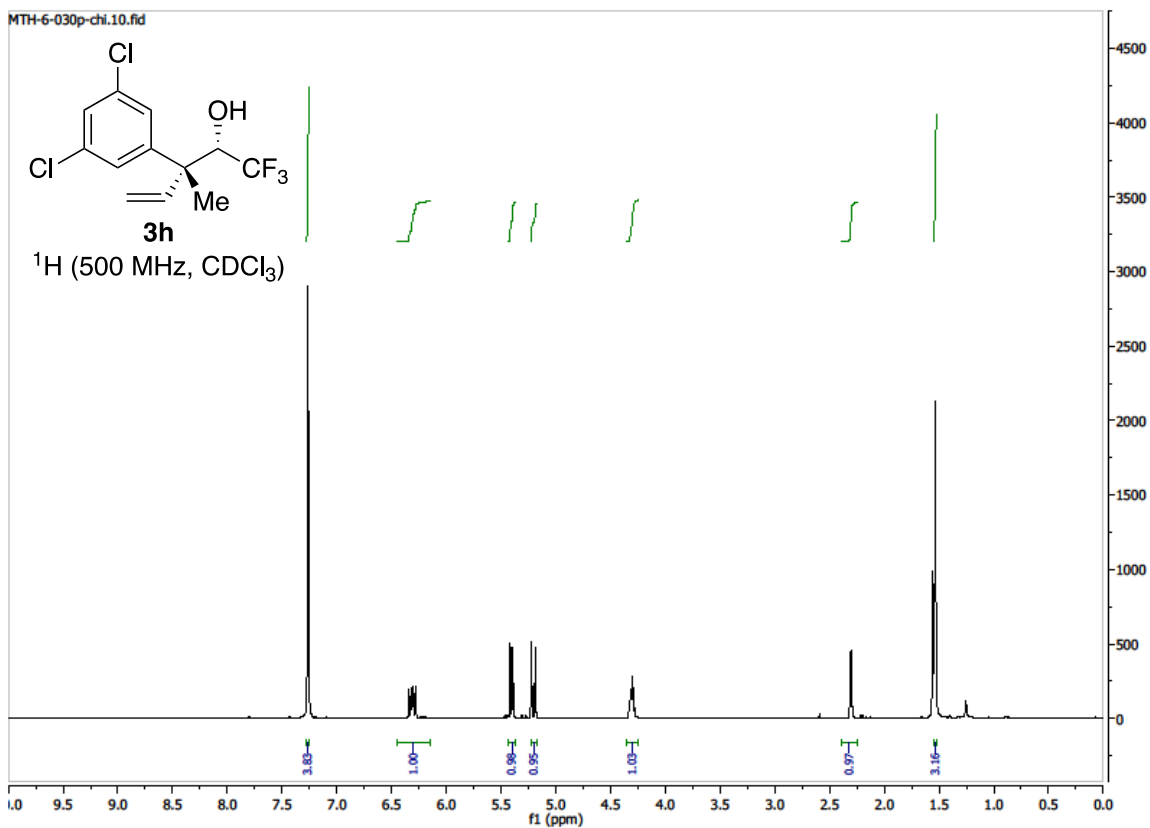
<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -70.9 (d, *J* = 6.3 Hz).

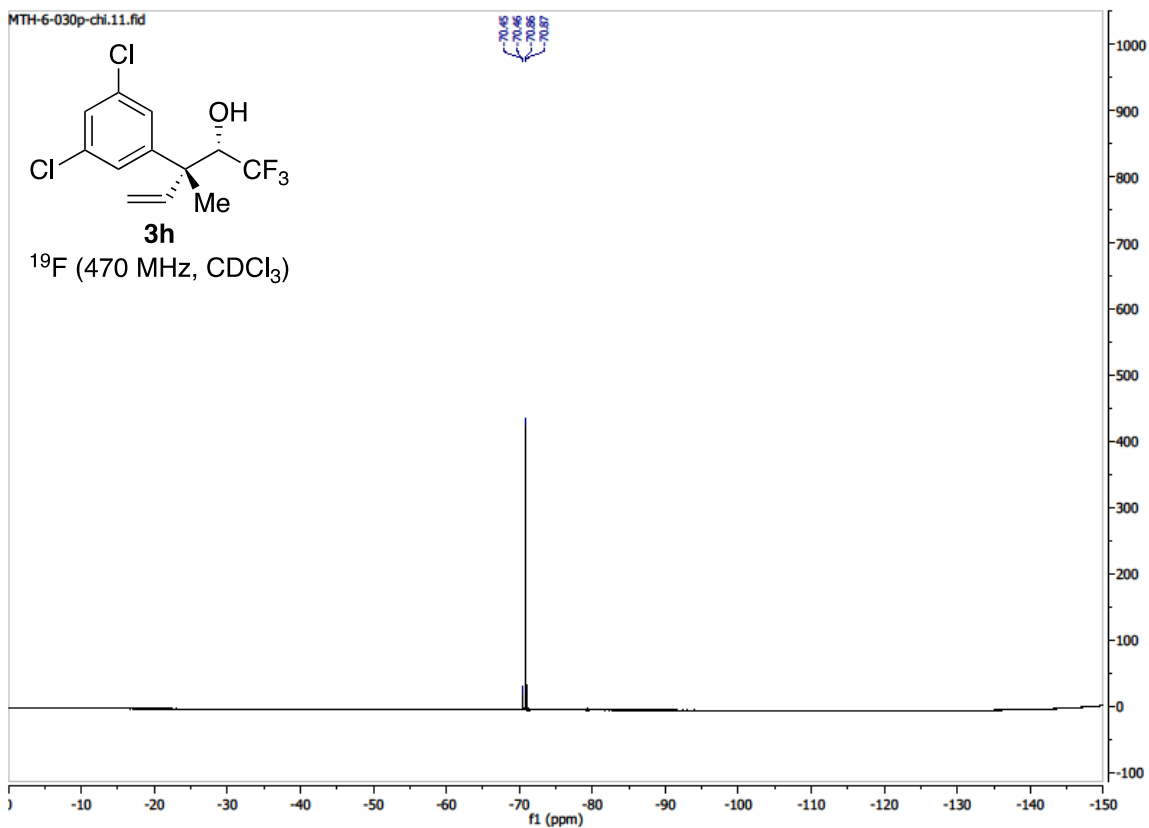
HRMS (Cl<sup>+</sup>, *m/z*) for C<sub>12</sub>H<sub>11</sub>F<sub>3</sub>Cl<sub>2</sub>: calcd. = 298.0139; found = 298.0136.

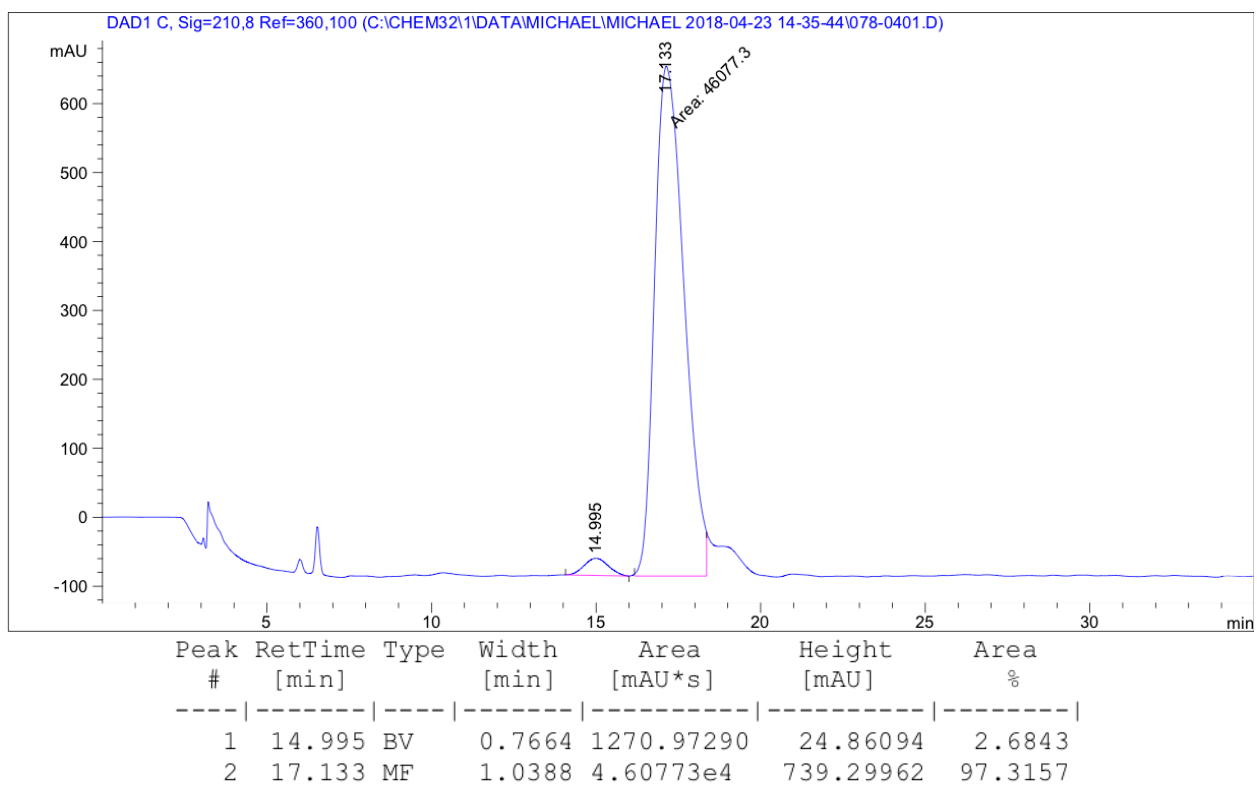
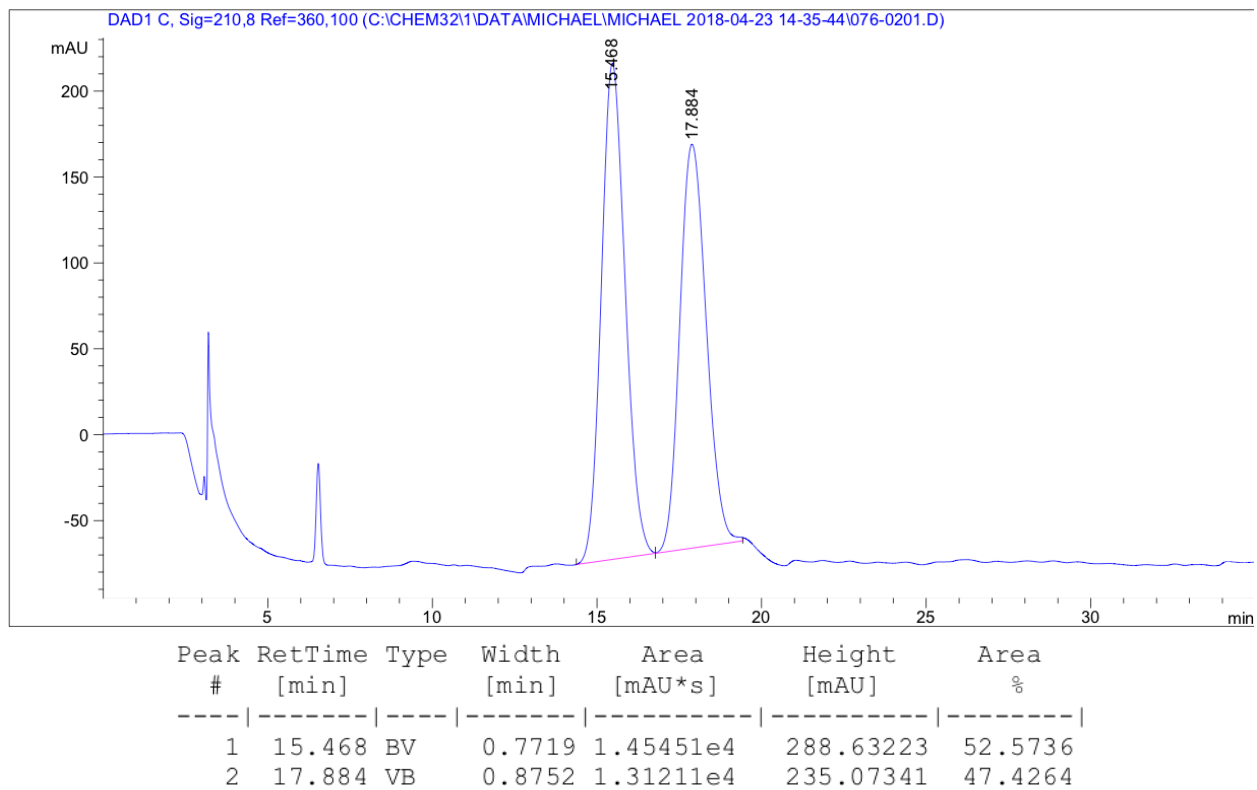
FTIR (neat): 3442, 2981, 1586, 1564, 1417, 1271, 1165, 1131, 1033, 932, 801, 699 cm<sup>-1</sup>.

HPLC: (Chiralcel column OJ-H, Hexane:2-PrOH = 99:1, 1.0 mL/min, 210 nm) ee = 95%.

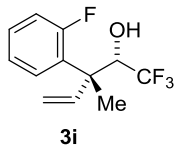
[α]<sub>D</sub><sup>24</sup> = -31.3 (c = 1.0, CHCl<sub>3</sub>).







**(2*S*,3*R*)-1,1,1-trifluoro-3-(2-fluorophenyl)-3-methylpent-4-en-2-ol (3i)**



1,1-Disubstituted allene **1i** (59.2 mg, 0.4 mmol) was subjected to general procedure D. Upon flash column chromatography (SiO<sub>2</sub>, 4:96 EtOAc/hexanes), the title compound **3i** (28.8 mg, 0.12 mmol, 13:1) was obtained as a yellow oil in 58% yield.

R<sub>f</sub> = 0.39 (9:1 hexanes : EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.35 (t, *J* = 10 Hz, 1H), 7.27 (m, 1H), 7.13 (t, *J* = 8.7 Hz, 1H), 7.03 (dd, *J* = 8.7, 10.0 Hz, 1H), 6.45 (dd, *J* = 9.9, 17.6 Hz, 1H), 5.30 (d, *J* = 9.9 Hz, 1H), 5.13 (d, *J* = 17.6 Hz, 1H), 4.81 (dq, *J* = 6.6 Hz, 1H), 2.32 (d, *J* = 6.6 Hz, 1H, OH), 1.62 (s, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 160.9 (d, *J* = 242 Hz), 140.3, 130.1 (d, *J* = 12 Hz), 129.1 (d, *J* = 9 Hz), 128.9 (d, *J* = 5 Hz), 125.1 (q, *J* = 285 Hz), 124.3 (d, *J* = 3 Hz), 116.3 (d, *J* = 24 Hz), 115.5, 72.9 (dq, *J* = 8, 28 Hz), 46.8, 18.4.

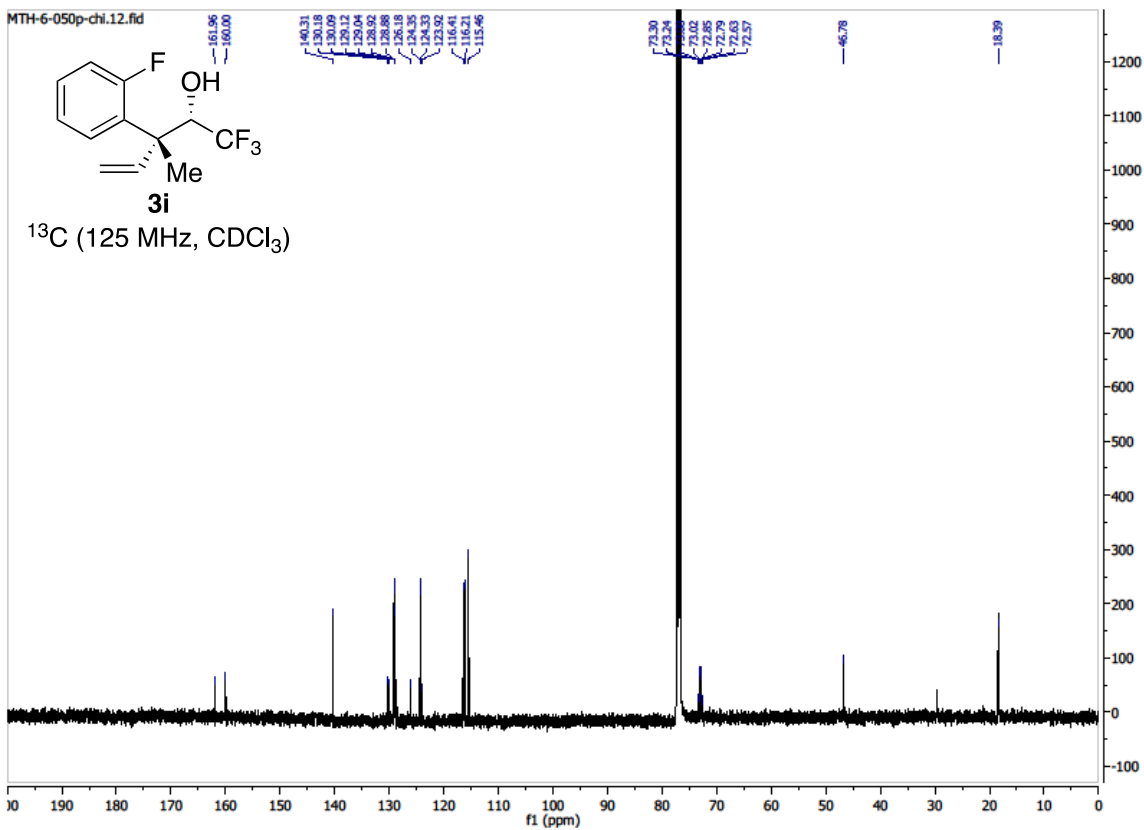
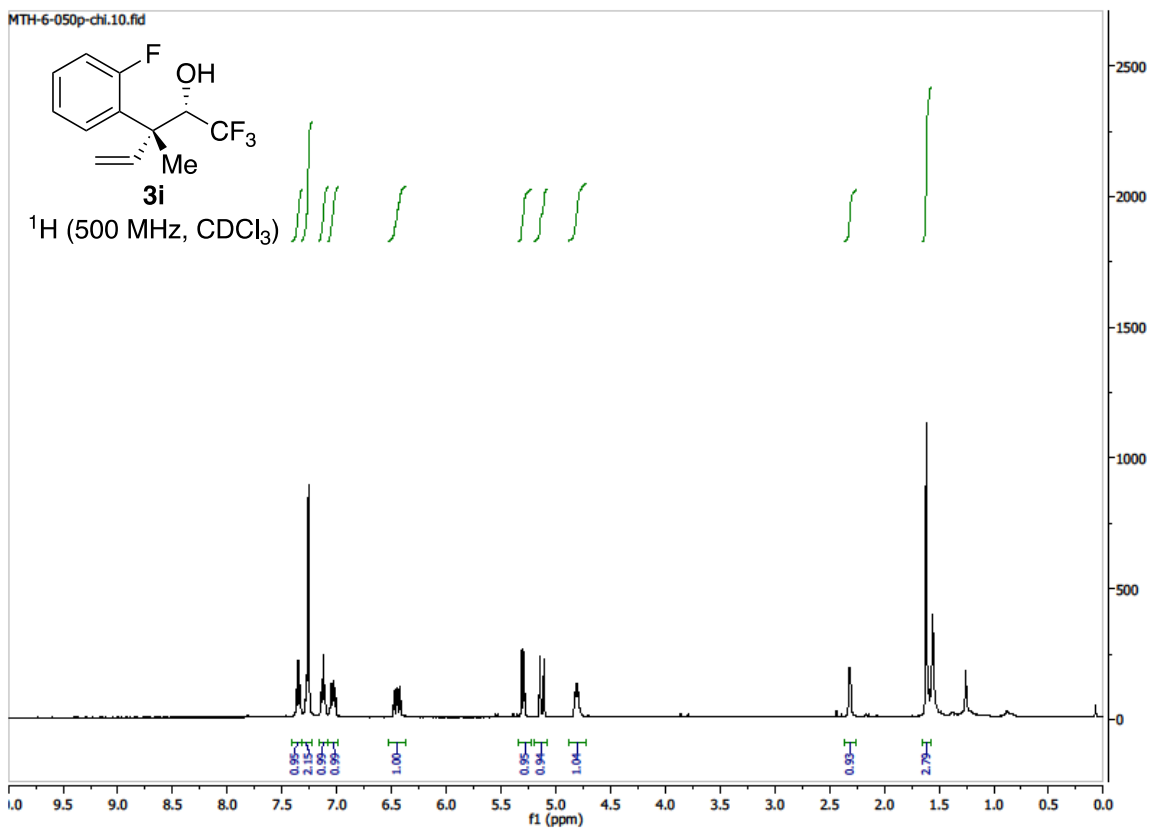
<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -71.4 (d, *J* = 6.6 Hz), -108.6 (m).

HRMS (CI+, *m/z*) for C<sub>12</sub>H<sub>12</sub>OF<sub>4</sub>: calcd. = 248.0824; found = 248.0827.

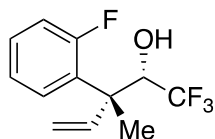
FTIR (neat): 3430, 2931, 2368, 1489, 1451, 1276, 1166, 1103, 929, 810, 757 cm<sup>-1</sup>.

HPLC: (Chiralcel column OJ-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 210 nm) ee = 96%.

[α]<sub>D</sub><sup>24</sup> = +16.3 (c = 0.61, CHCl<sub>3</sub>).

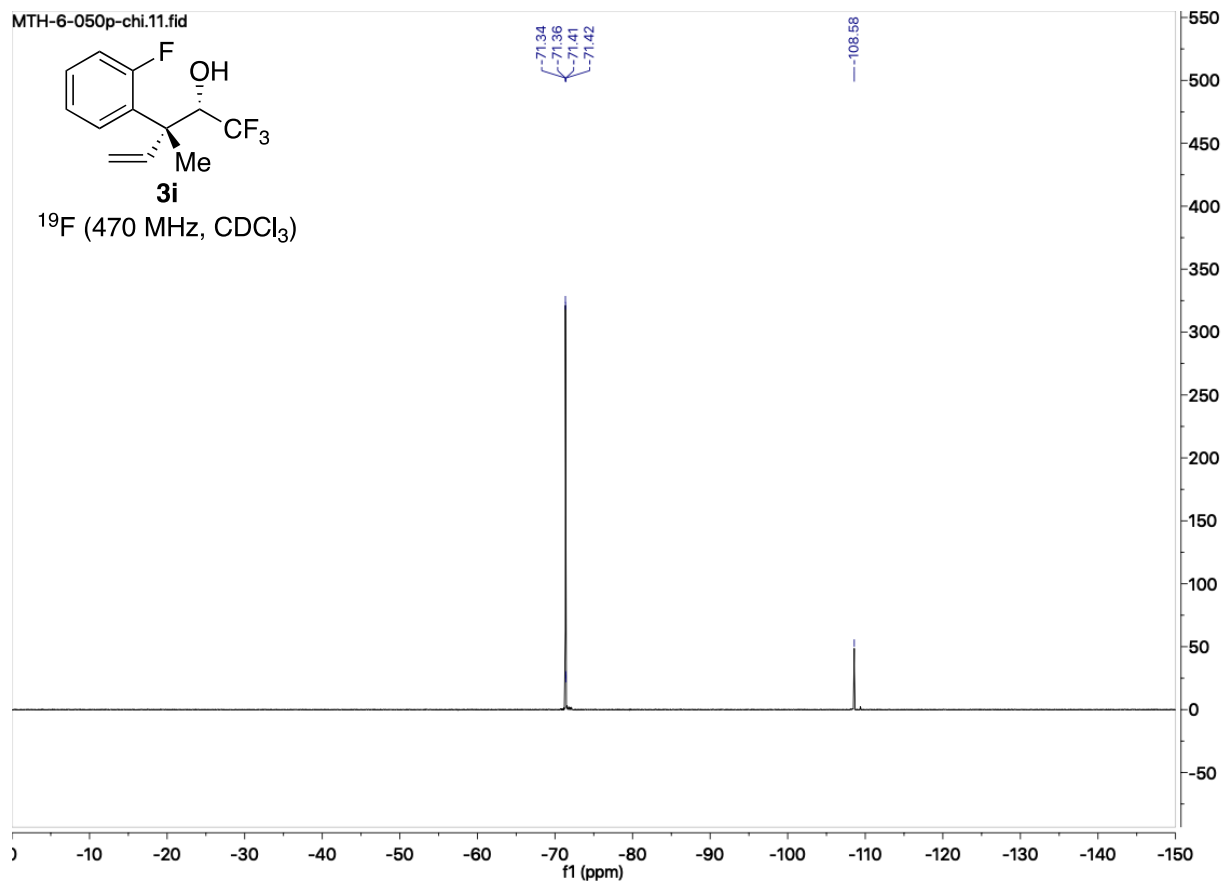


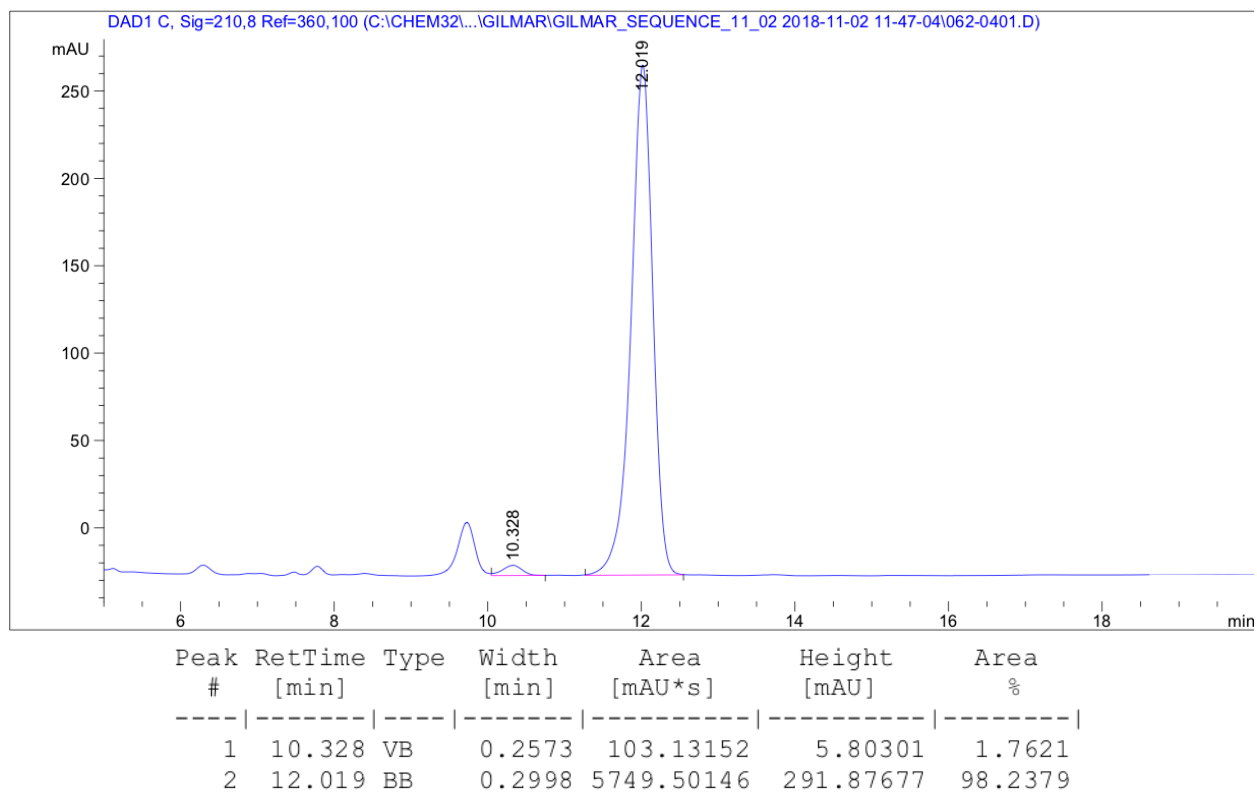
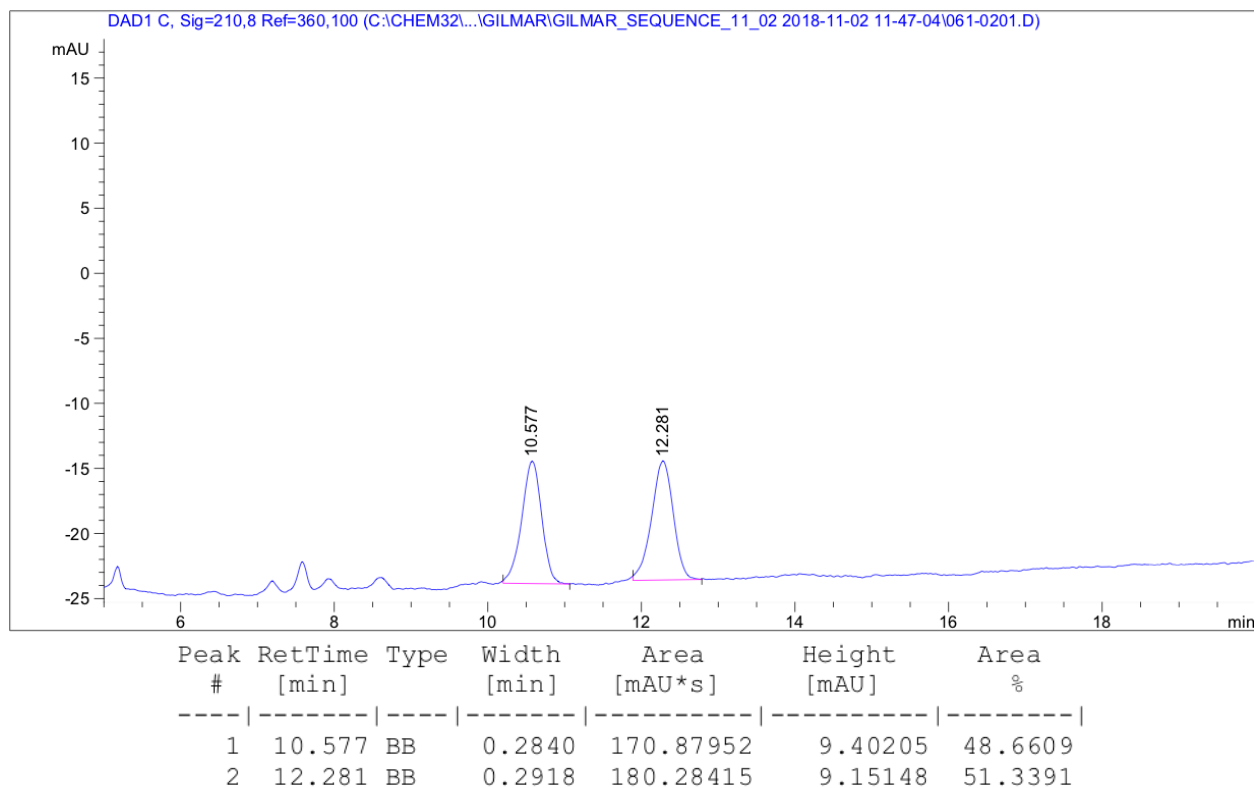
MTH-6-050p-chi.11.fid



**3i**

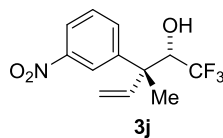
<sup>19</sup>F (470 MHz, CDCl<sub>3</sub>)







**(2*S*,3*R*)-1,1,1-trifluoro-3-methyl-3-(3-nitrophenyl)pent-4-en-2-ol (3j)**



1,1-Disubstituted allene **1j** (70.1 mg, 0.4 mmol) was subjected to general procedure D. Upon flash column chromatography (SiO<sub>2</sub>, 1:9 EtOAc/hexanes), the title compound **3j** (40.7 mg, 0.15 mmol, > 20:1 dr) was obtained as a light yellow oil in 74% yield.

R<sub>f</sub> = 0.2 (9:1 Hexanes : EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 8.29 (t, *J* = 2.1 Hz, 1H), 8.13 (dd, *J* = 8.3, 2.3 Hz, 1H), 7.80 – 7.72 (m, 1H), 7.52 (t, *J* = 8.0 Hz, 1H), 6.40 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.43 (d, *J* = 10.9 Hz, 1H), 5.21 (d, *J* = 17.6 Hz, 1H), 4.45 – 4.35 (m, 1H), 2.51 (d, *J* = 5.5 Hz, 1H), 1.63 (s, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 148.3, 146.2, 139.9, 133.3, 129.2, 124.8 (q, *J* = 285 Hz), 122.2, 122.0, 116.9, 75.5 (q, *J* = 28.5 Hz), 47.3, 29.7, 21.1 (q, *J* = 2.46 Hz).

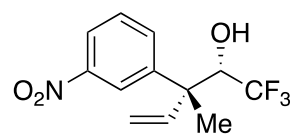
<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -70.8 (d, *J* = 7.27 Hz),

HRMS (CI+H, *m/z*) for C<sub>12</sub>H<sub>13</sub>NO<sub>2</sub>F<sub>3</sub>: calcd. = 276.0848; found = 276.0843.

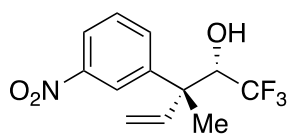
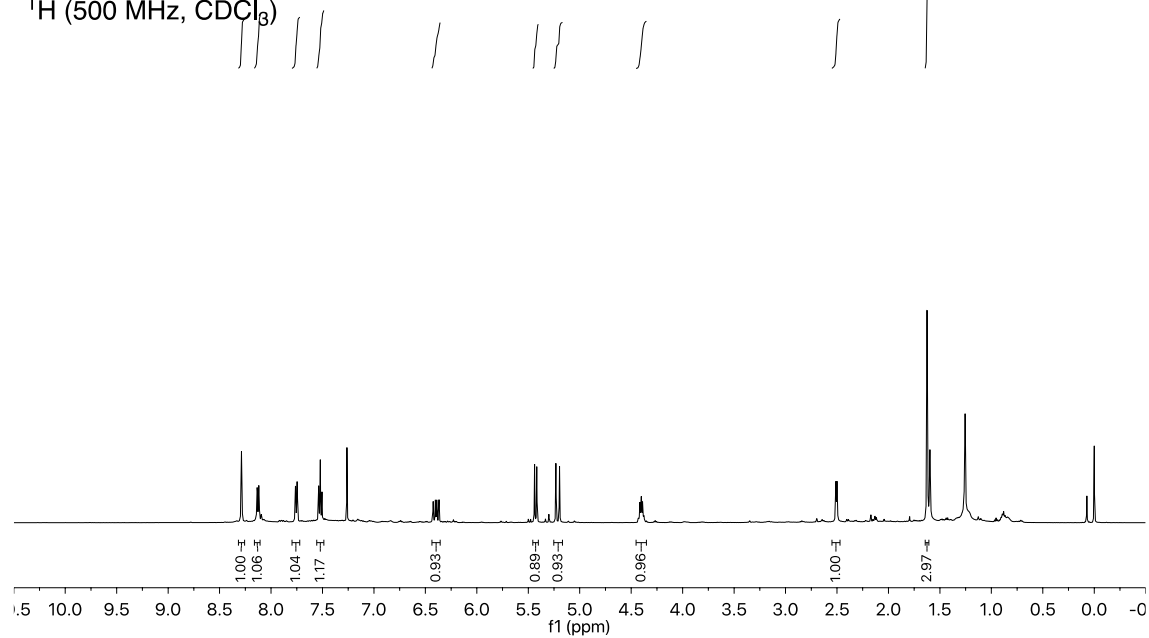
FTIR (neat): 3473, 2922, 2852, 1528, 1349, 1217, 1156, 1091, 928, 693 cm<sup>-1</sup>.

HPLC: (Chiralcel column AD-H, Hexane:2-PrOH = 97:3, 1.0 mL/min, 210 nm) ee = 96%.

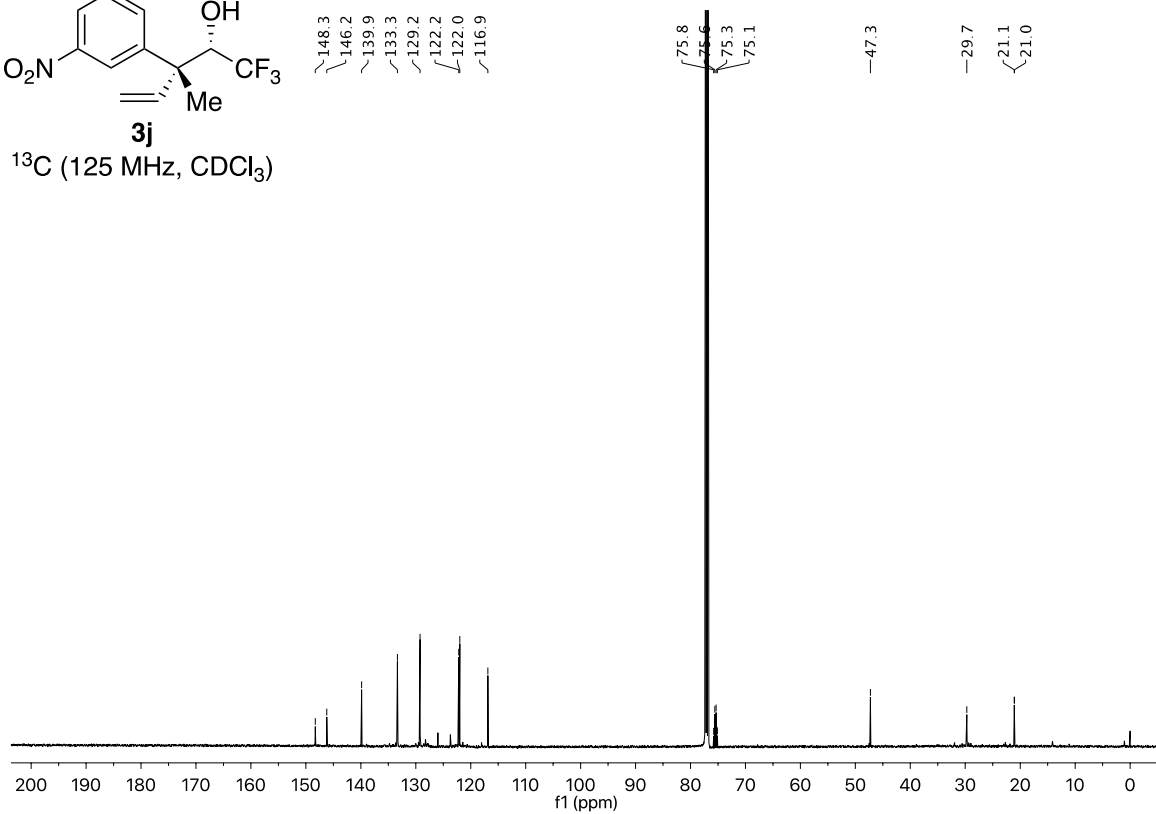
[α]<sub>D</sub><sup>24</sup> = +5.8 (c = 0.5, CHCl<sub>3</sub>).



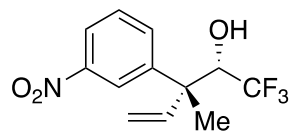
**3j**  
<sup>1</sup>H (500 MHz, CDCl<sub>3</sub>)



**3j**  
<sup>13</sup>C (125 MHz, CDCl<sub>3</sub>)

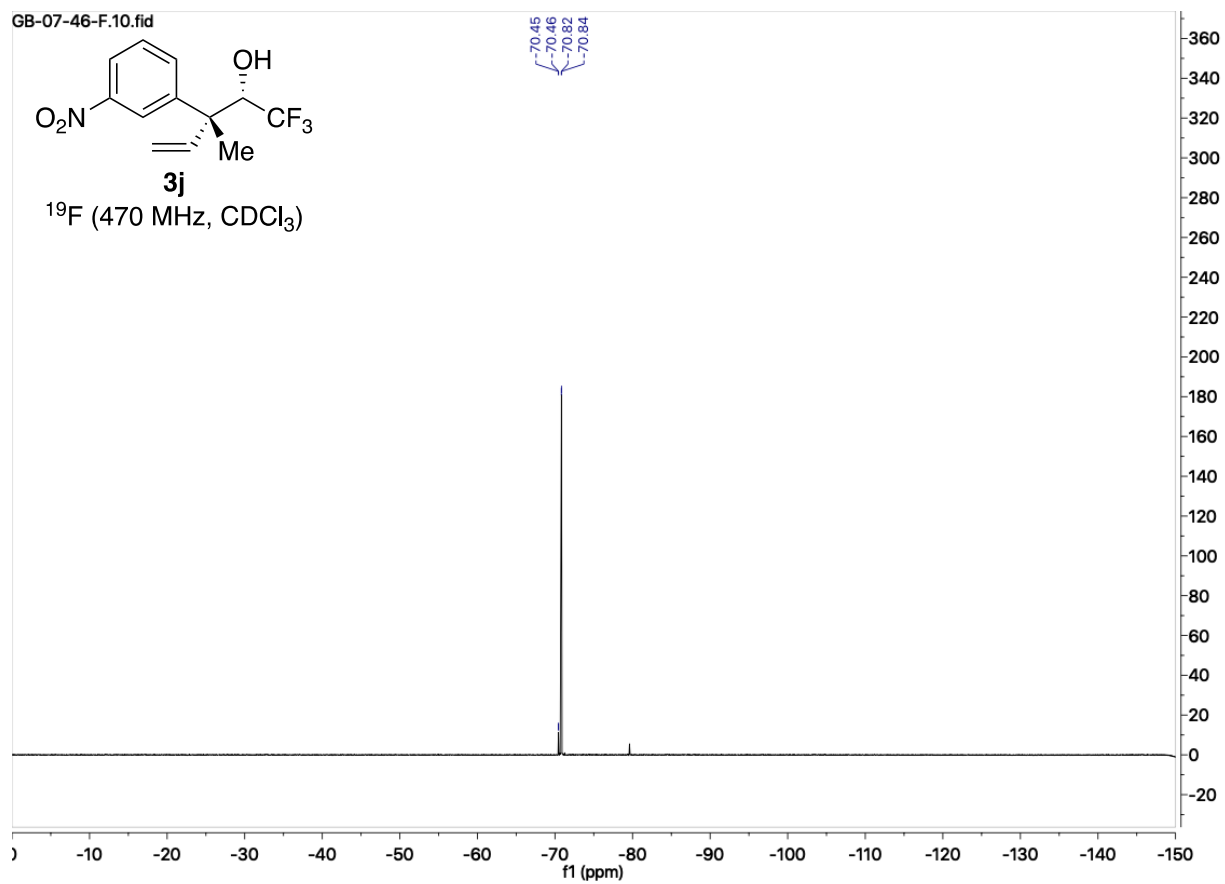


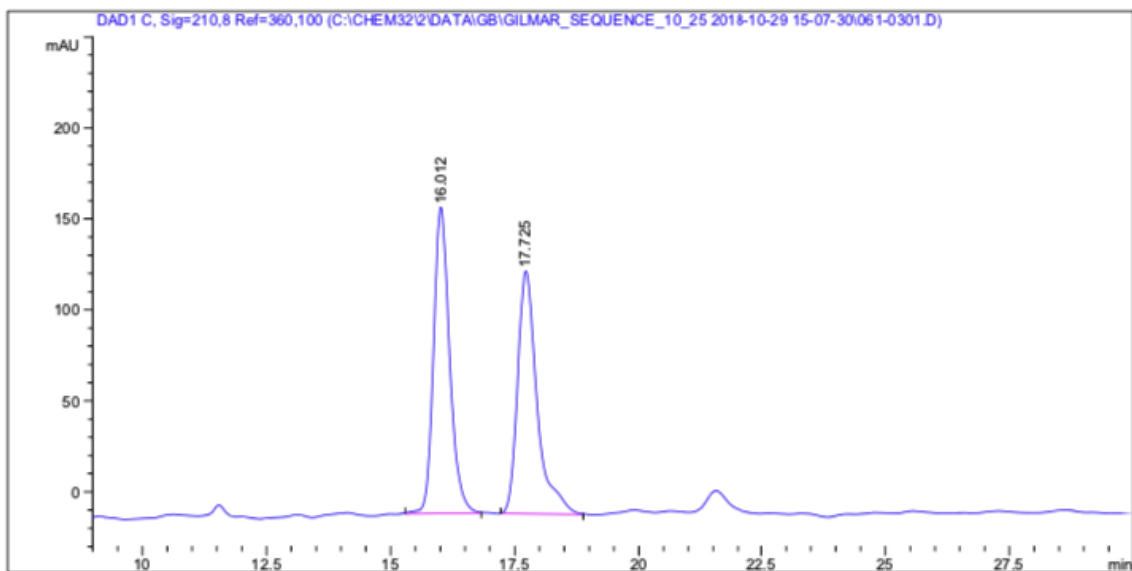
GB-07-46-F.10.fid



**3j**

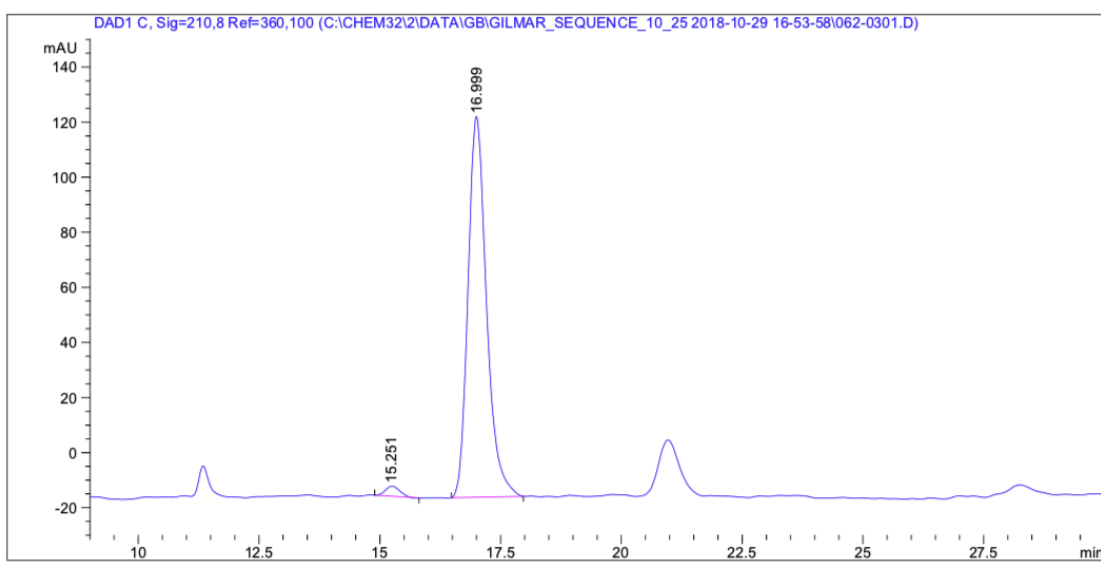
$^{19}\text{F}$  (470 MHz,  $\text{CDCl}_3$ )





Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.012	BB	0.3429	3790.50903	168.21773	50.9917
2	17.725	BB	0.4109	3643.07642	133.26028	49.0083

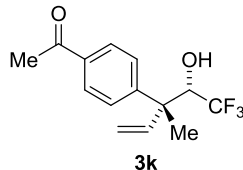
Totals : 7433.58545 301.47801



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.251	BB	0.2966	74.57161	3.64580	1.9835
2	16.999	BB	0.4051	3684.99146	138.21021	98.0165

Totals : 3759.56306 141.85601

**1-(4-((3*R*,4*S*)-5,5,5-trifluoro-4-hydroxy-3-methylpent-1-en-3-yl)phenyl)ethan-1-one (3k)**



1,1-Disubstituted allene **1k** (69 mg, 0.4 mmol) was subjected to general procedure D. Upon flash column chromatography (SiO<sub>2</sub>, 1:5 EtOAc/hexanes), the title compound **3k** (46.8 mg, 0.17 mmol, 20:1 dr) was obtained as a light yellow solid in 86% yield.

R<sub>f</sub> = 0.14 (5:1 Hexanes : Ethyl acetate)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.95 – 7.91 (m, 2H), 7.51 – 7.48 (m, 2H), 6.38 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.39 (d, *J* = 10.8 Hz, 1H), 5.19 (d, *J* = 17.5 Hz, 1H), 4.42 (qd, *J* = 7.2, 5.5 Hz, 1H), 2.59 (s, 3H), 2.35 (d, *J* = 5.7 Hz, 1H), 1.59 (d, *J* = 1.6 Hz, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 197.7, 149.2, 140.3, 135.7, 128.5, 127.2, 124.9 (q, *J* = 282 Hz), 116.4, 75.5 (q, *J* = 28 Hz), 47.5, 26.6, 20.7 (q, 2.6 Hz).

<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -70.8 (d, *J* = 7.1 Hz).

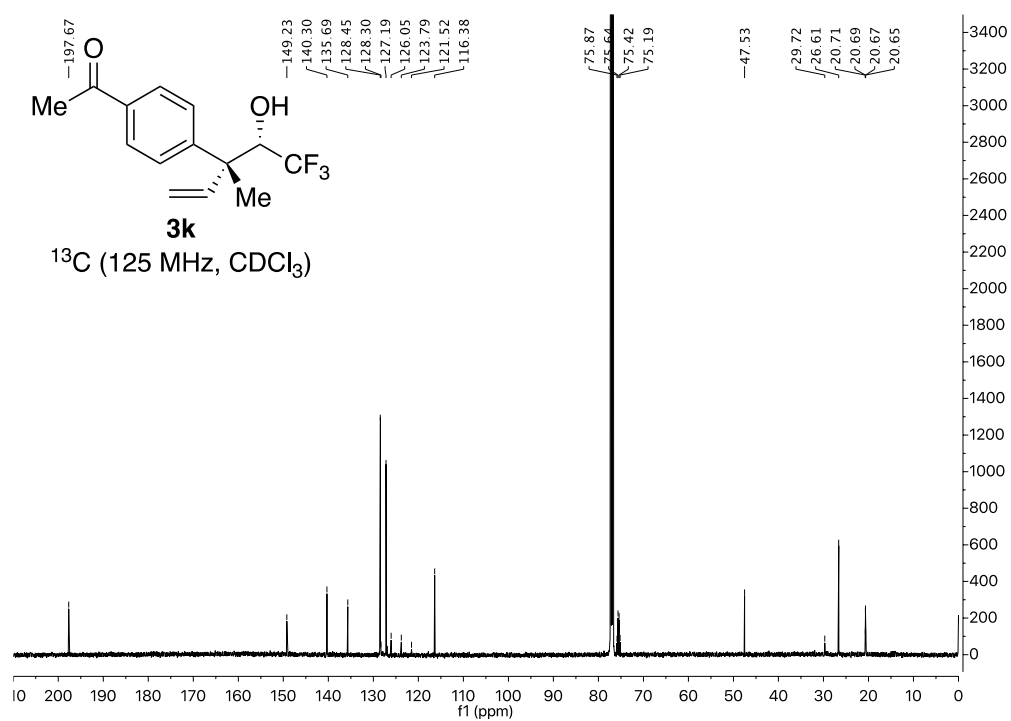
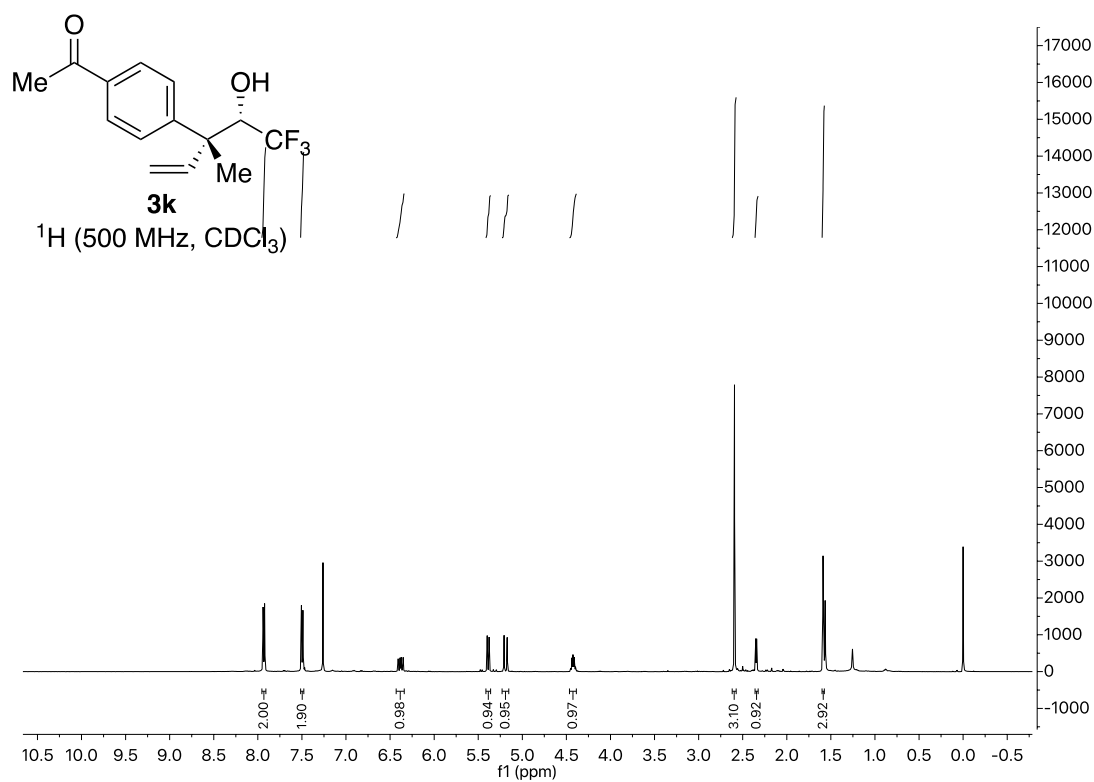
HRMS (ESI + H, *m/z*) for C<sub>14</sub>H<sub>16</sub>F<sub>3</sub>O<sub>2</sub>: calcd. = 273.1097; found = 273.100.

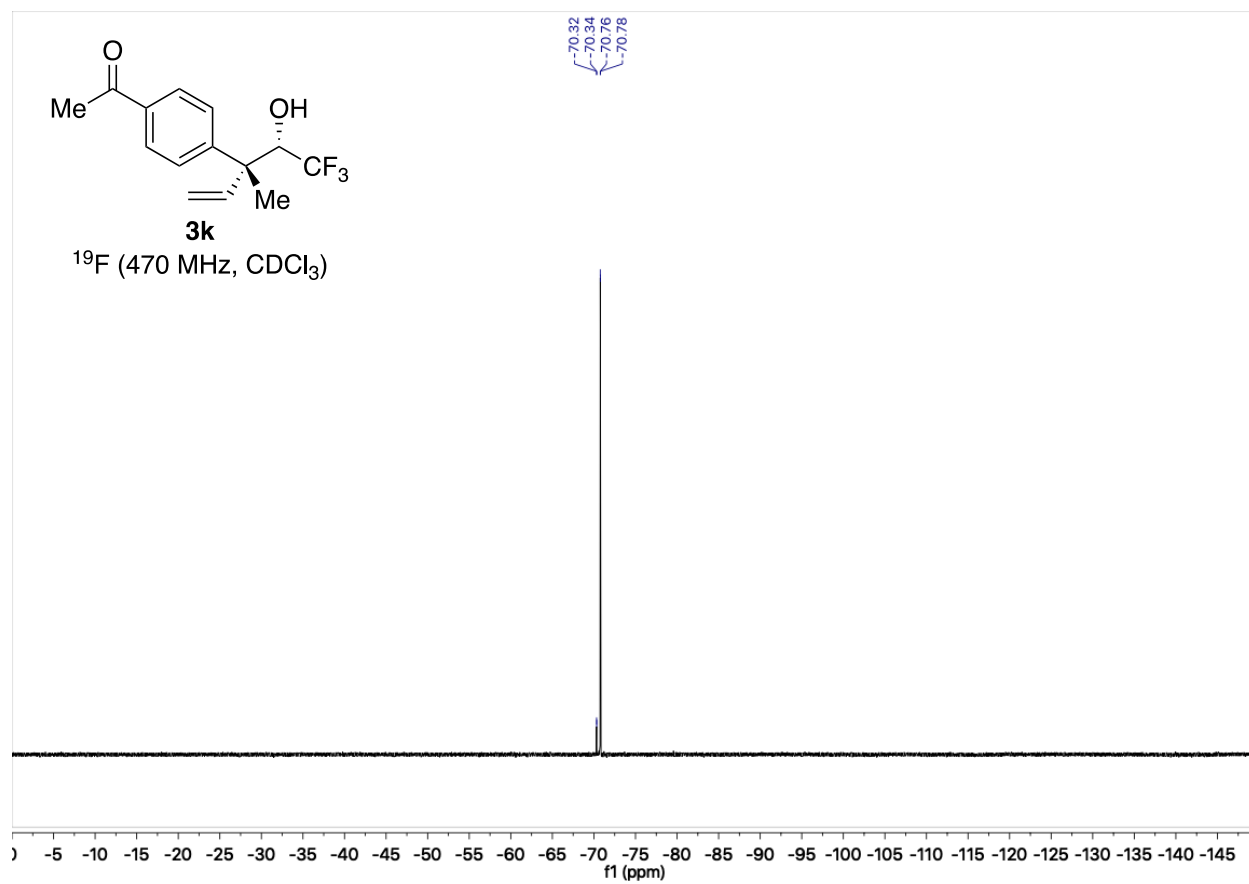
FTIR (neat): 3427, 2922, 2853, 1674, 1605, 1407, 1360, 1271, 1154, 1121, 1095, 1014, 960, 822, 692 cm<sup>-1</sup>.

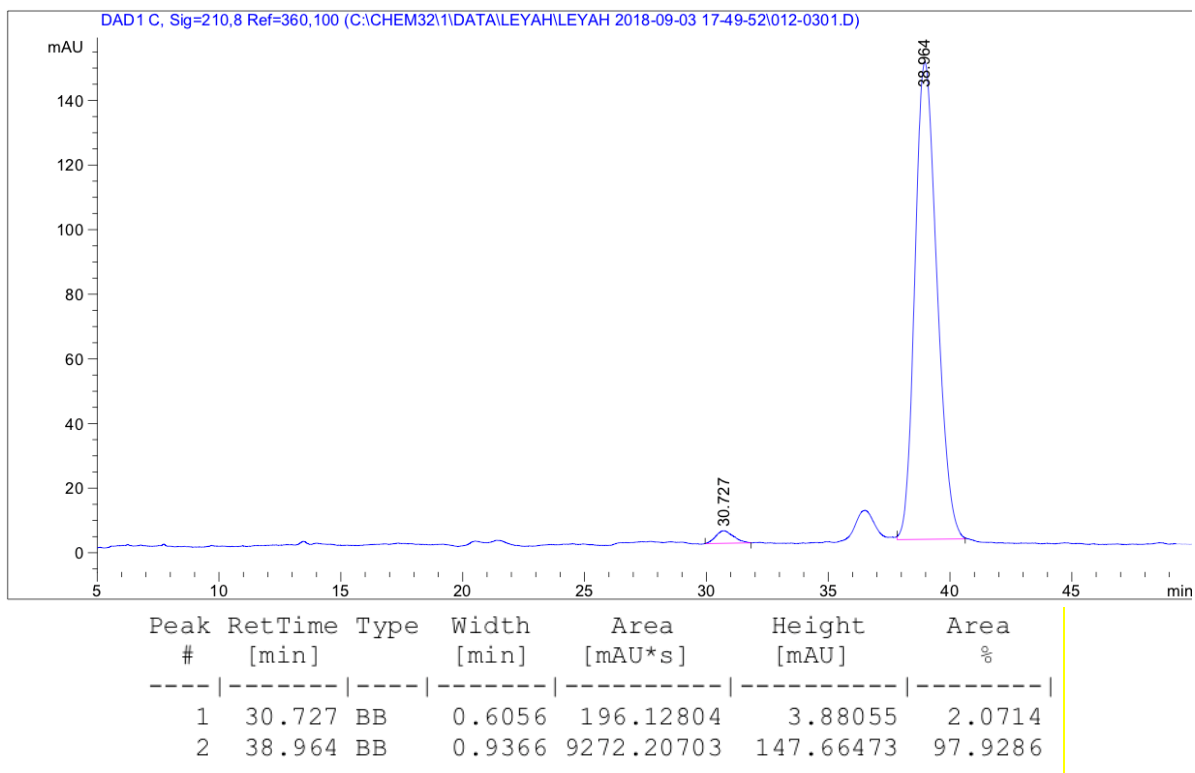
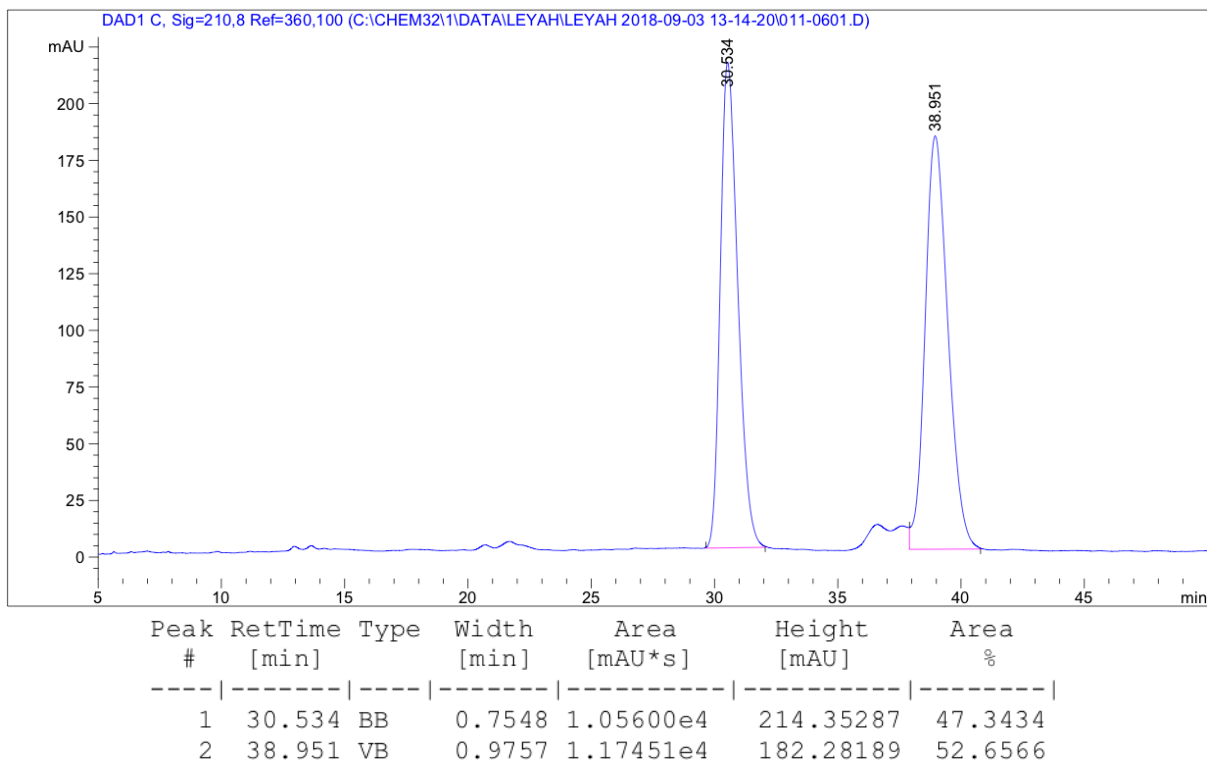
HPLC: (Chiralcel column OJ-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 210 nm) ee = 96%.

[α]<sub>D</sub><sup>24</sup> = -16 (c = 0.5, CHCl<sub>3</sub>).

MP = 62-65 °C

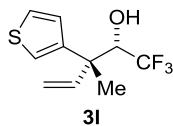








**(2*S*,3*R*)-1,1,1-trifluoro-3-methyl-3-(thiophen-3-yl)pent-4-en-2-ol (3l)**



1,1-Disubstituted allene **1l** (54.5 mg, 0.4 mmol) was subjected to general procedure D using a reaction time of 8 hours. Upon flash column chromatography (SiO<sub>2</sub>, 5:95 EtOAc/hexanes), the title compound **3l** (32.3 mg, 0.14 mmol, 13:1 dr) was obtained as a clear oil in 68% yield. Note: the shorter reaction time was required due to the formation of overreduced product under standard reaction times. Additionally instability on chiral column was observed.

R<sub>f</sub> = 0.3 (4:1 hexanes : EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.33 (m, 1H), 7.15 (m, 1H), 7.08 (m, 1H), 6.35 (dd, *J* = 6.4, 17.6 Hz, 1H), 5.31 (d, *J* = 10.9 Hz, 1H), 5.15 (d, *J* = 17.6 Hz, 1H), 4.23 (dq, *J* = 7.3, 6.2 Hz, 1H), 2.23 (d, *J* = 5.8 Hz, 1H), 1.58 (q, *J* = 1.4 Hz, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 144.5, 140.2, 126.5, 126.0, 124.9 (q, *J* = 283.5 Hz), 121.8, 115.8, 75.8 (q, *J* = 28.3 Hz), 45.9, 21.4 (q, *J* = 2.4 Hz).

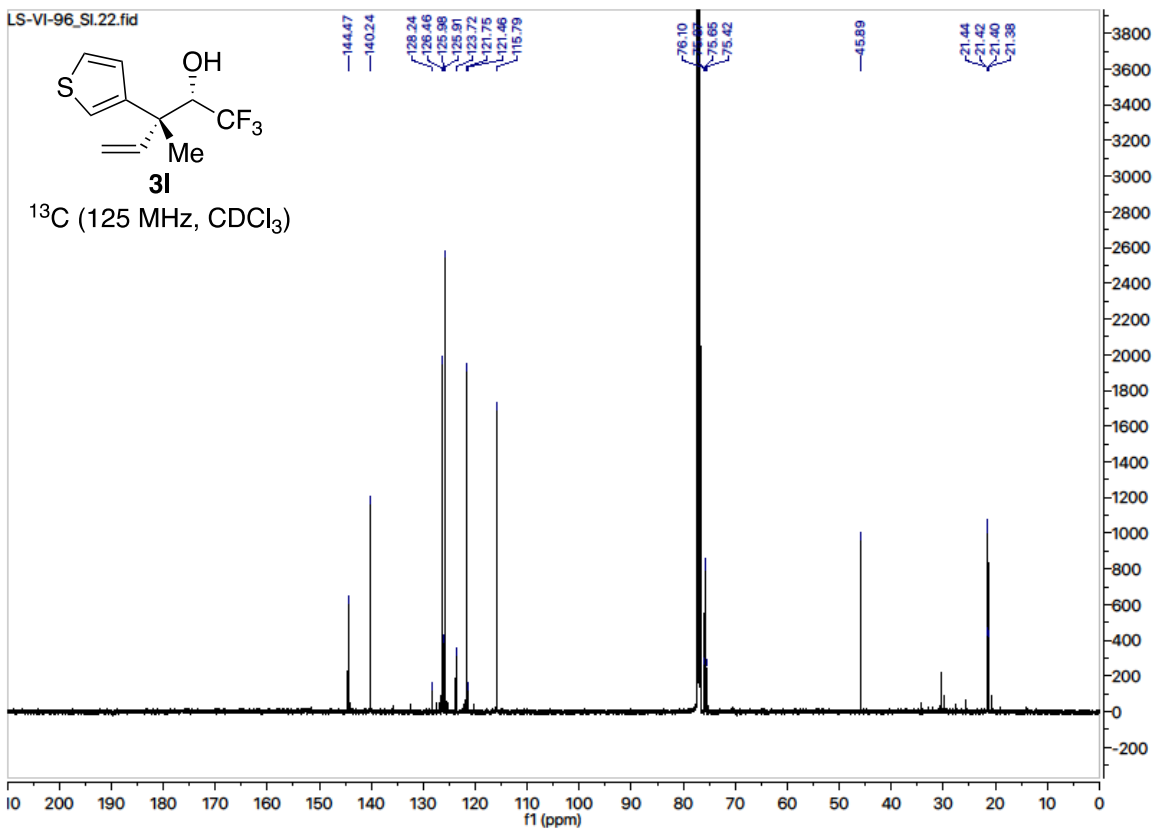
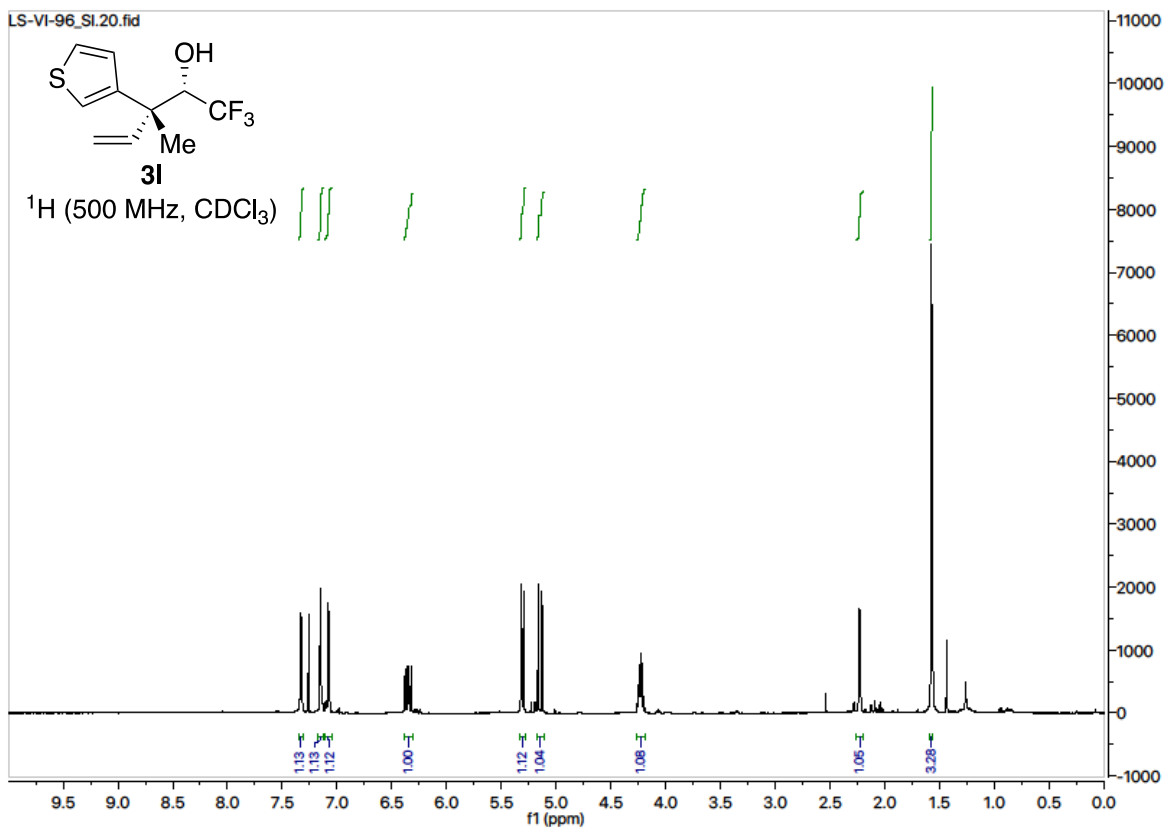
<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -71.1 (d, *J* = 7.3 Hz).

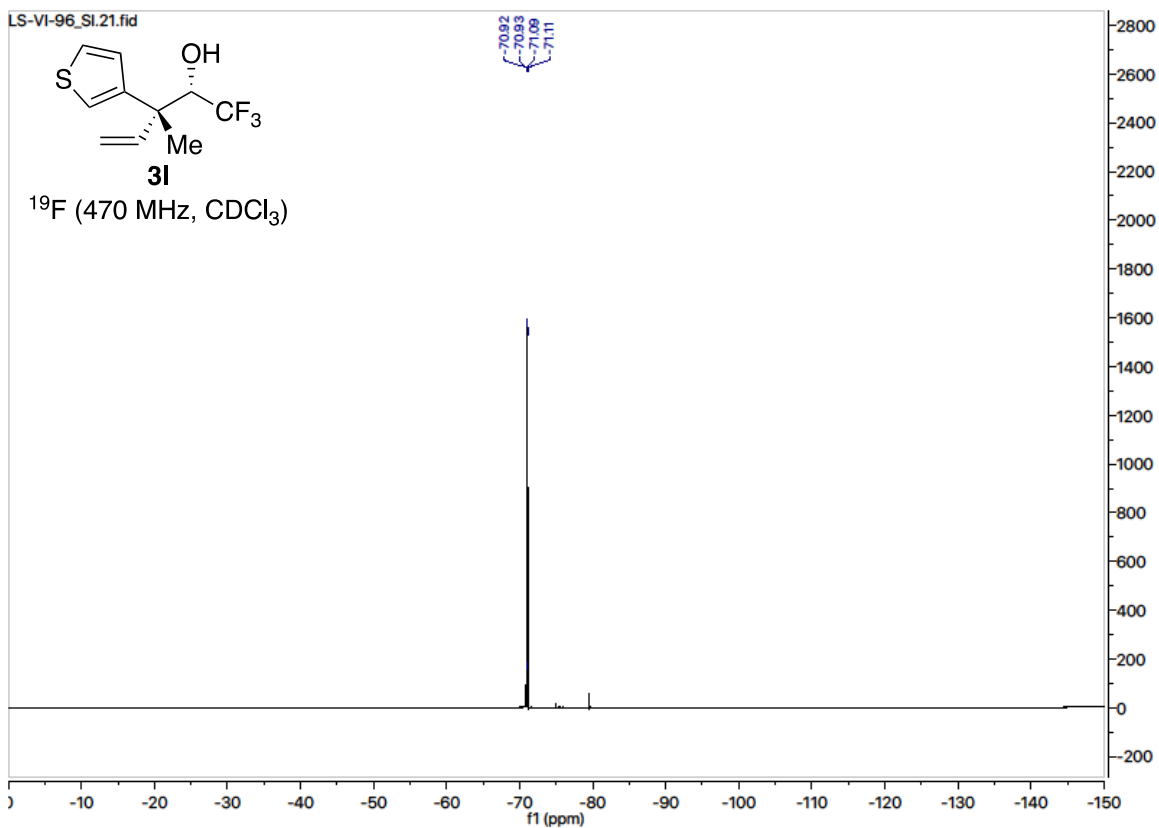
HRMS (CI<sup>+</sup>, *m/z*) for C<sub>10</sub>H<sub>11</sub>F<sub>3</sub>OS: calcd. = 236.0483; found = 236.0479.

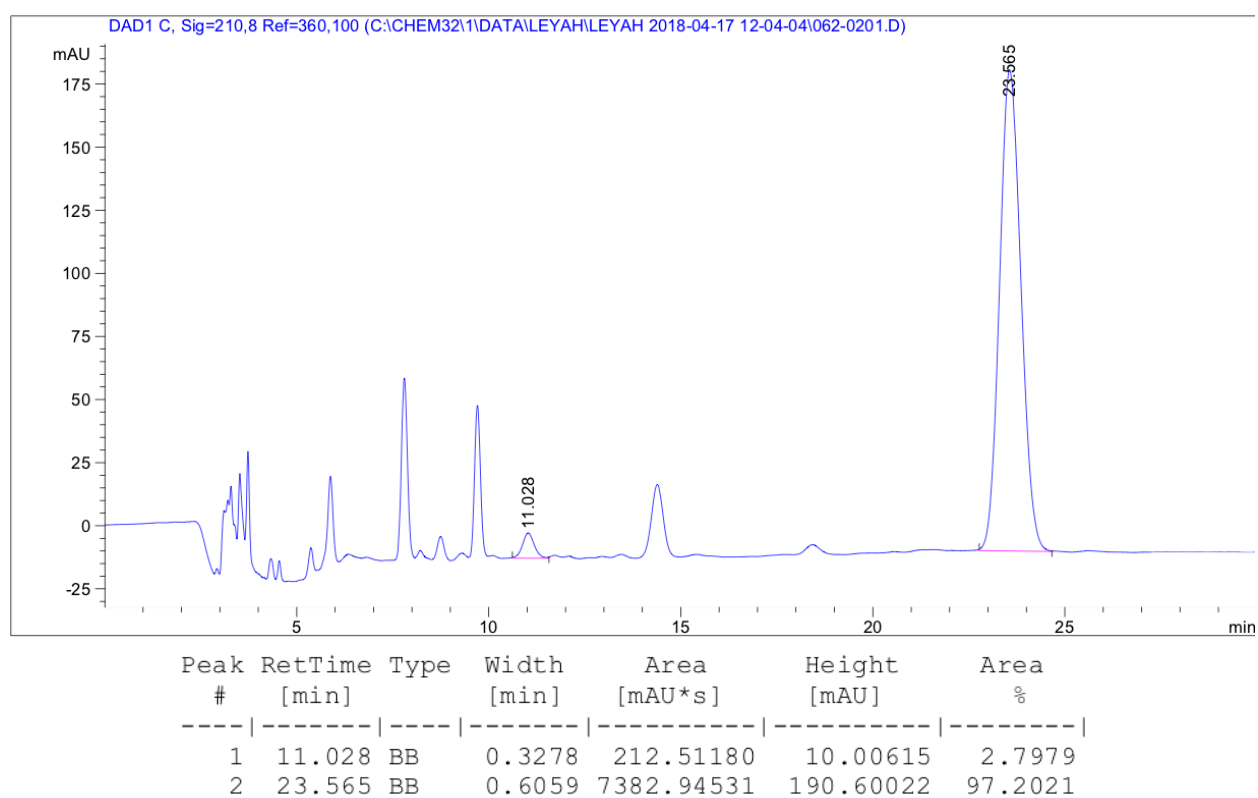
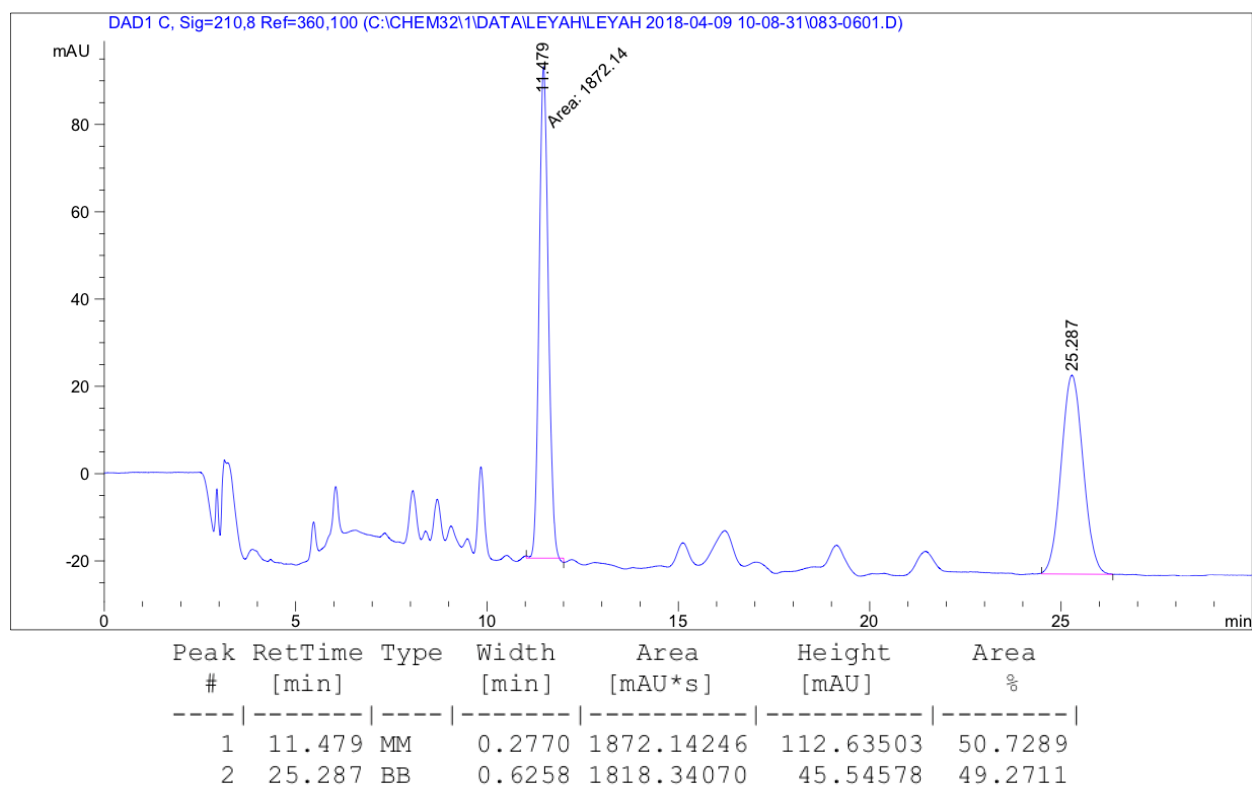
FTIR (neat): 3500, 2950, 2900, 1450, 1400, 1300, 1150, 1100, 1000, 900, 800, 700, 650 cm<sup>-1</sup>.

HPLC: (Chiralcel column OJ-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 210 nm) ee = 94%.

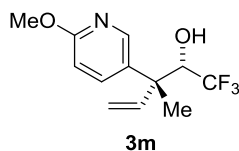
[α]<sub>D</sub><sup>24</sup> = -17.5 (c = 1.1, CHCl<sub>3</sub>).







**(2*S*,3*R*)-1,1,1-trifluoro-3-(6-methoxypyridin-3-yl)-3-methylpent-4-en-2-ol (3*m*)**



1,1-Disubstituted allene **1m** (64 mg, 0.4 mmol) was subjected to general procedure D. Upon flash column chromatography (SiO<sub>2</sub>, 1:9 EtOAc/hexanes), the title compound **3m** (35.5 mg, 0.14 mmol, 19:1 dr) was obtained as a yellow oil in 68% yield.

R<sub>f</sub> = 0.19 (9:1 hexanes : EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 8.18 (d, *J* = 2.7 Hz, 1H), 7.60 (dd, *J* = 2.7, 9.5 Hz, 1H), 6.72 (d, *J* = 9.5 Hz, 1H), 6.34 (dd, *J* = 10.9, 17.7 Hz, 1H), 5.34 (d, *J* = 10.9 Hz, 1H), 5.15 (d, *J* = 17.7 Hz, 1H), 4.27 (dq, *J* = 6.5 Hz, 1H), 3.92 (s, 3H), 2.41 (d, *J* = 6.5 Hz, 1H, *OH*), 1.56 (s, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 163.0, 145.5, 140.5, 137.8, 131.6, 124.9 (q, *J* = 277 Hz), 116.0, 110.4, 75.5 (q, *J* = 30 Hz), 53.5, 45.5, 20.9.

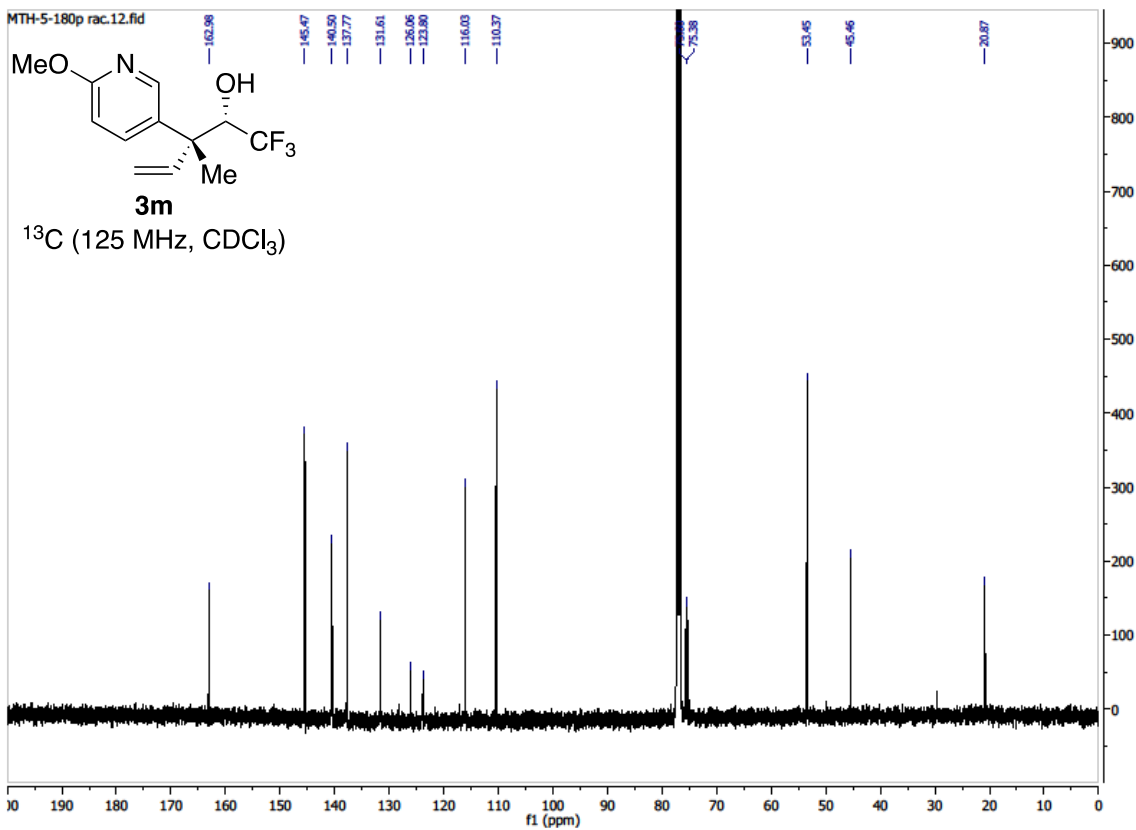
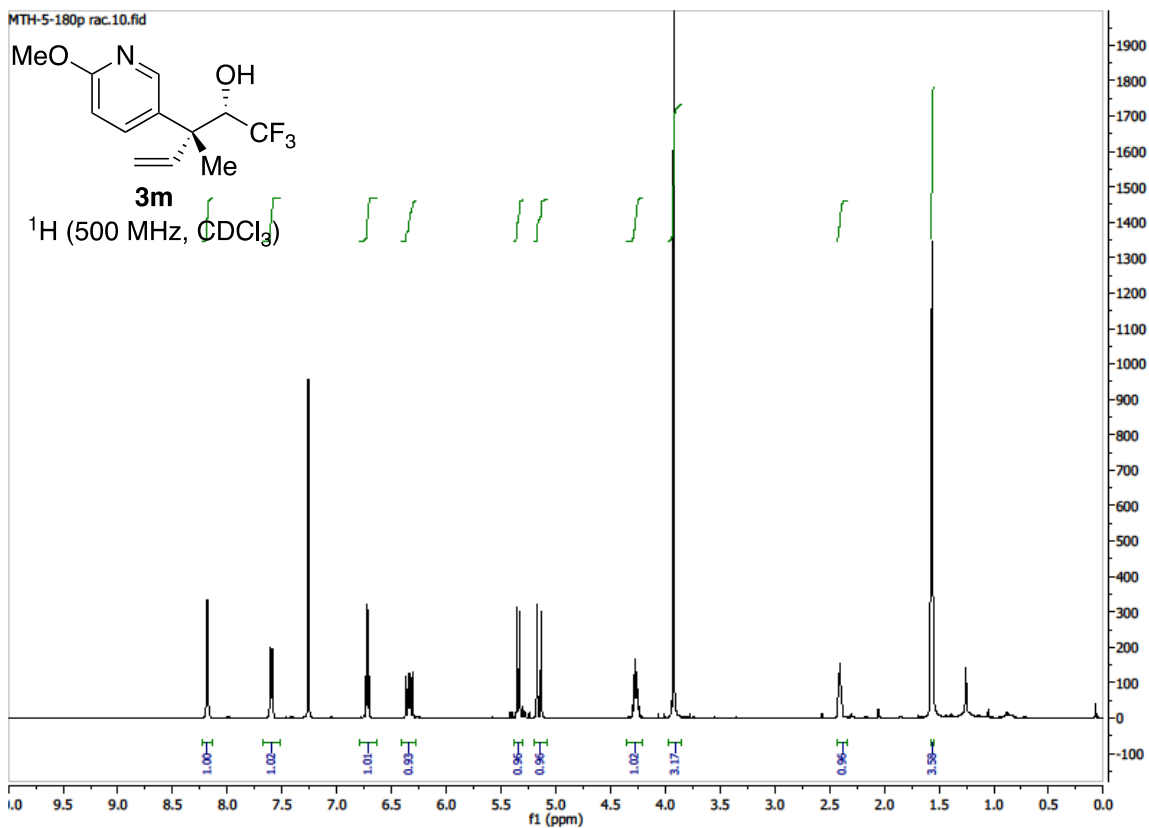
<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -70.8 (d, *J* = 6.8 Hz).

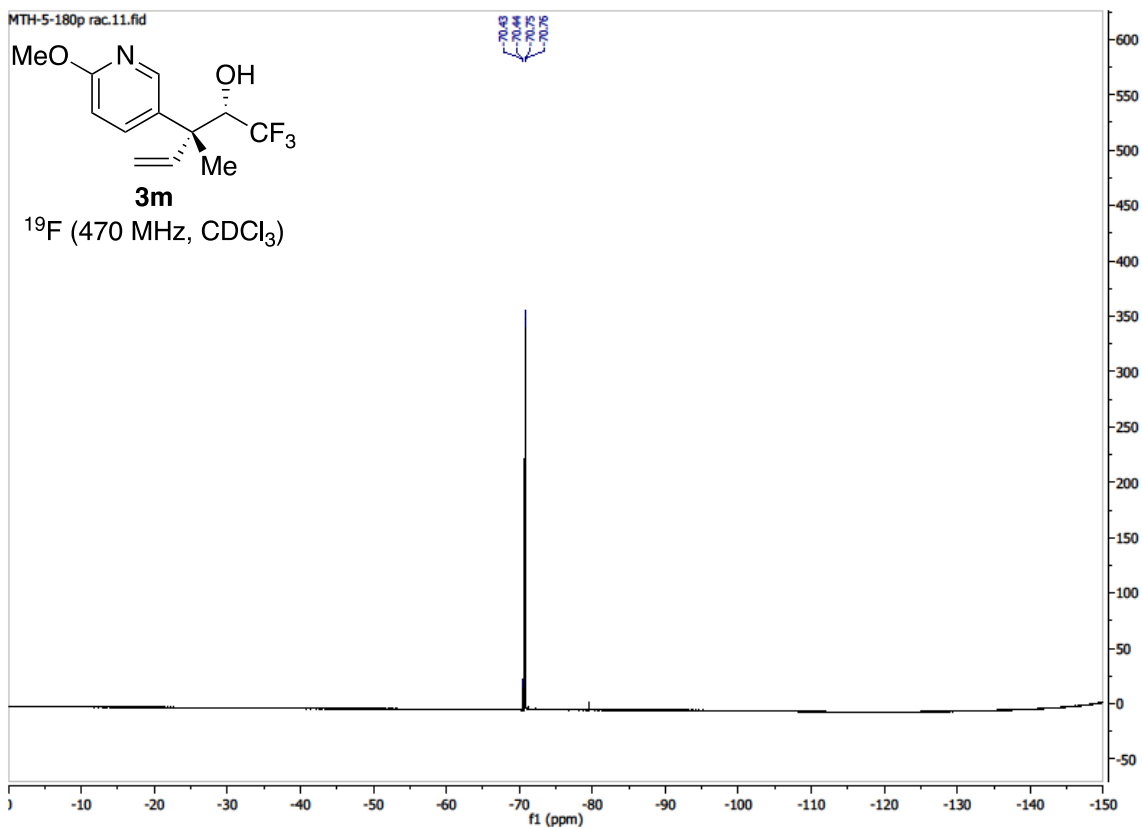
HRMS (ESI+H, *m/z*) for C<sub>12</sub>H<sub>14</sub>F<sub>3</sub>NO<sub>2</sub>: calcd. = 262.1049; found = 262.1051.

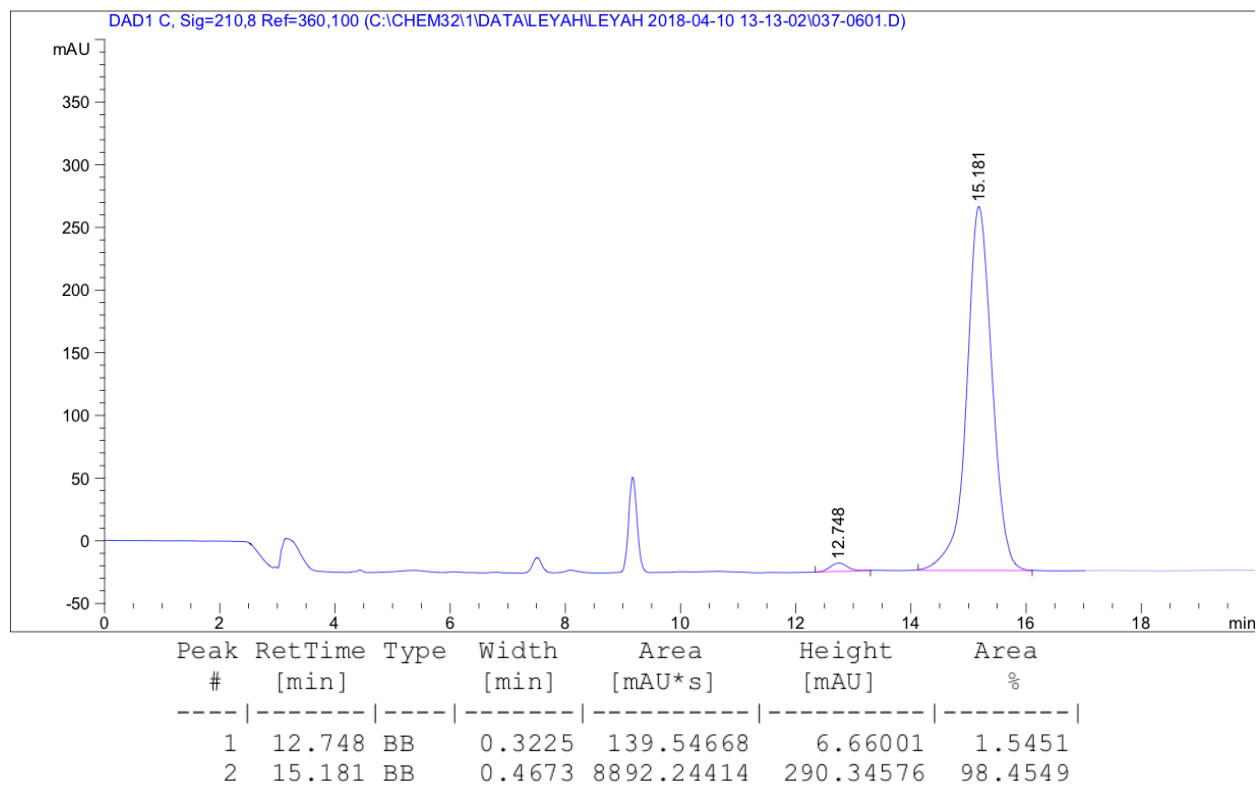
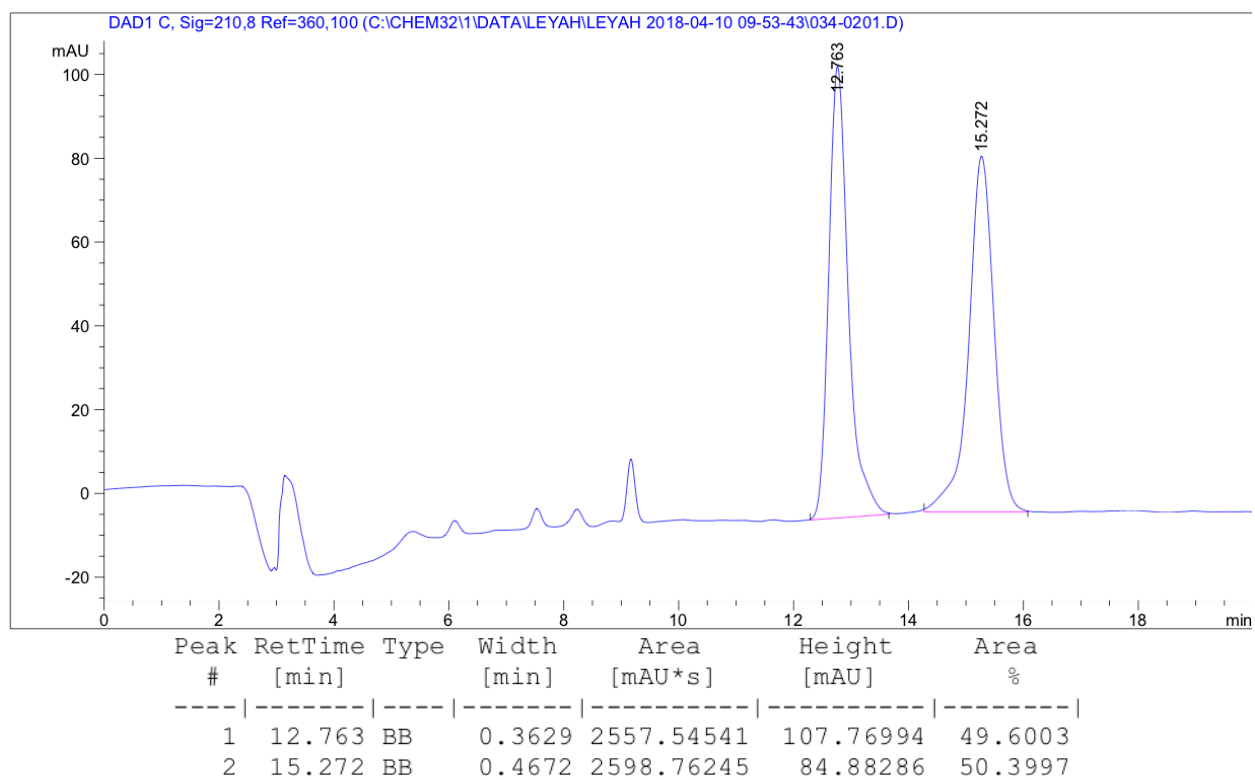
FTIR (neat): 3375, 2981, 2359, 1606, 1498, 1385, 1272, 1158, 1026, 927, 828 cm<sup>-1</sup>.

HPLC: (Chiralcel column OJ-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 210 nm) ee = 97%.

[α]<sub>D</sub><sup>24</sup> = -60 (c = 0.25, CHCl<sub>3</sub>).

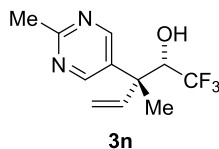








**(2*S*,3*R*)-1,1,1-trifluoro-3-methyl-3-(2-methylpyrimidin-5-yl)pent-4-en-2-ol (3n)**



1,1-Disubstituted allene **1n** (58 mg, 0.4 mmol) was subjected to general procedure D. Upon flash column chromatography (SiO<sub>2</sub>, 2:1 EtOAc:hexanes), the title compound **3n** (33.8 mg, 0.14 mmol, 15:1 dr) was obtained as a yellow solid in 69% yield.

R<sub>f</sub> = 0.31 (1:2 hexanes : EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 8.59 (s, 2H), 6.34 (dd, *J* = 11.8, 17.8 Hz, 1H), 5.35 (d, *J* = 11.8 Hz, 1H), 5.13 (d, *J* = 17.8 Hz, 1H), 4.19 (q, *J* = 7.6 Hz, 1H), 2.63 (s, 3H), 1.54 (s, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 166.2, 156.0, 138.9, 134.1, 124.9 (q, *J* = 286.7 Hz), 117.3, 75.1 (q, *J* = 29.0 Hz), 44.6, 25.3, 21.2.

<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -70.8 (d, *J* = 7.6 Hz).

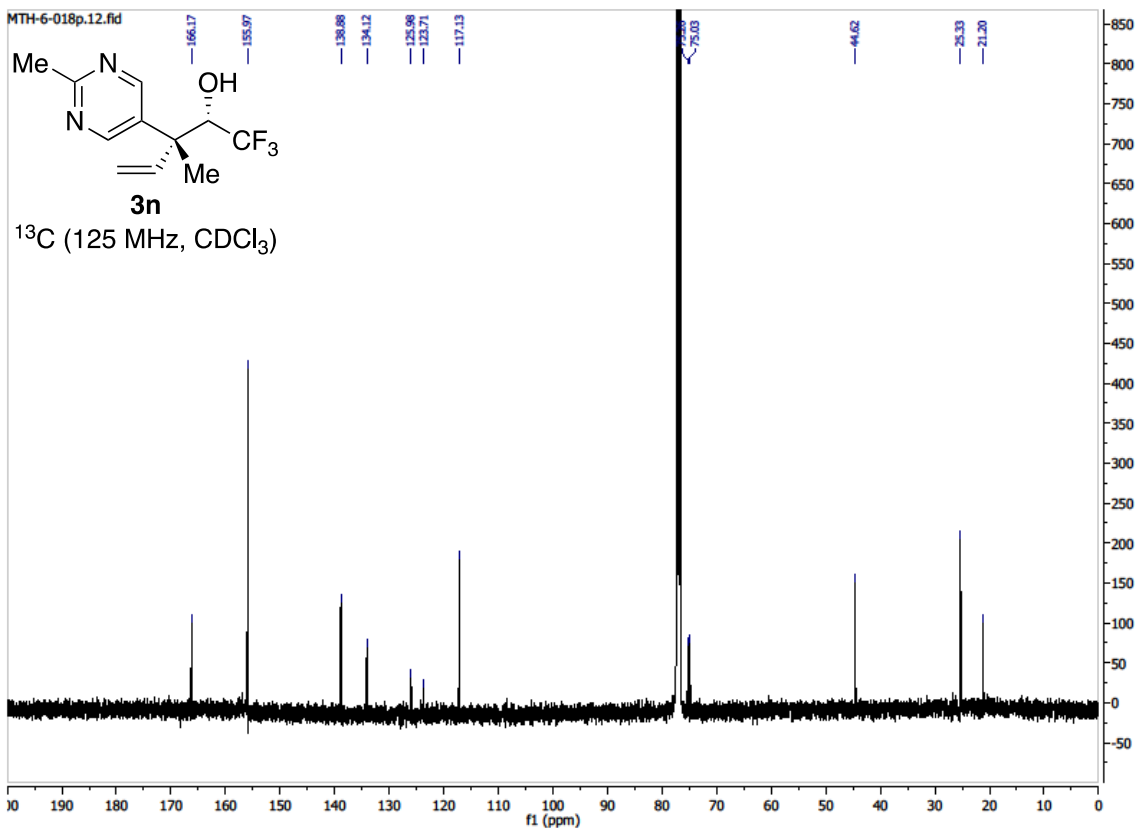
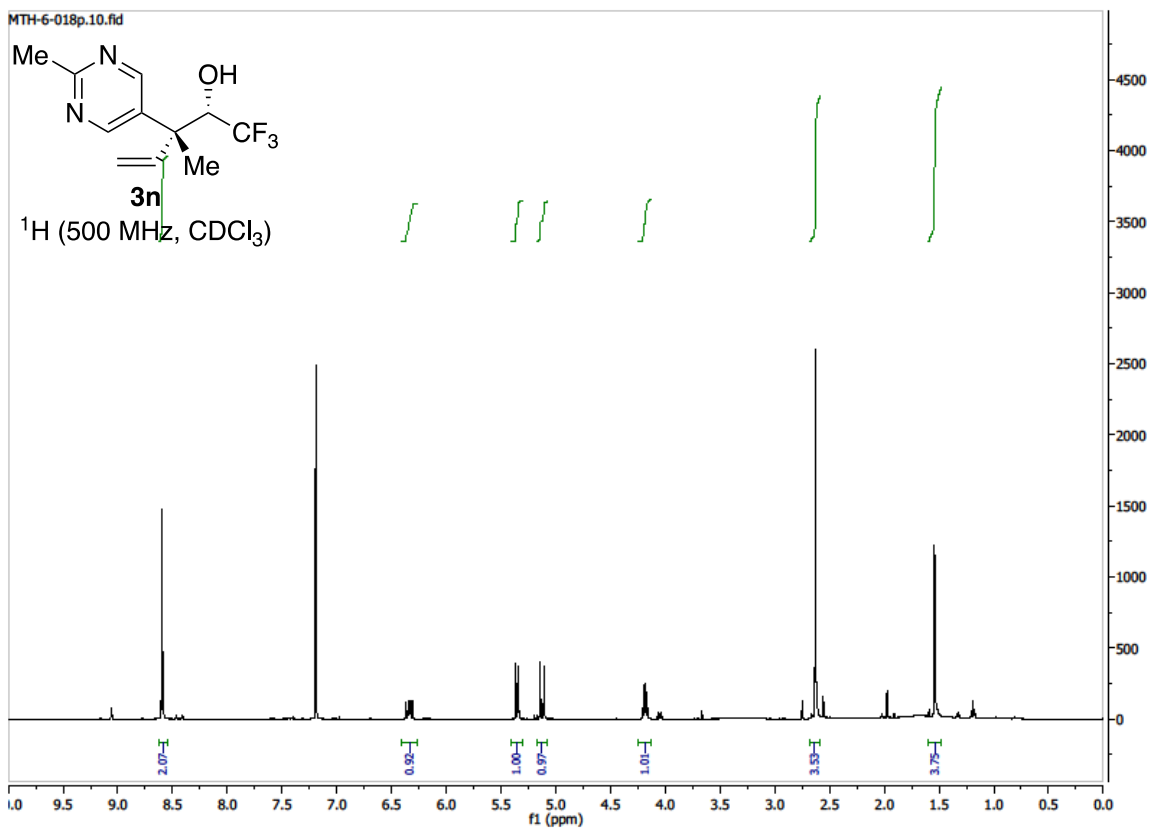
HRMS (CI+, *m/z*) for C<sub>11</sub>H<sub>13</sub>F<sub>3</sub>N<sub>2</sub>O: calcd. = 247.1053; found = 247.1052.

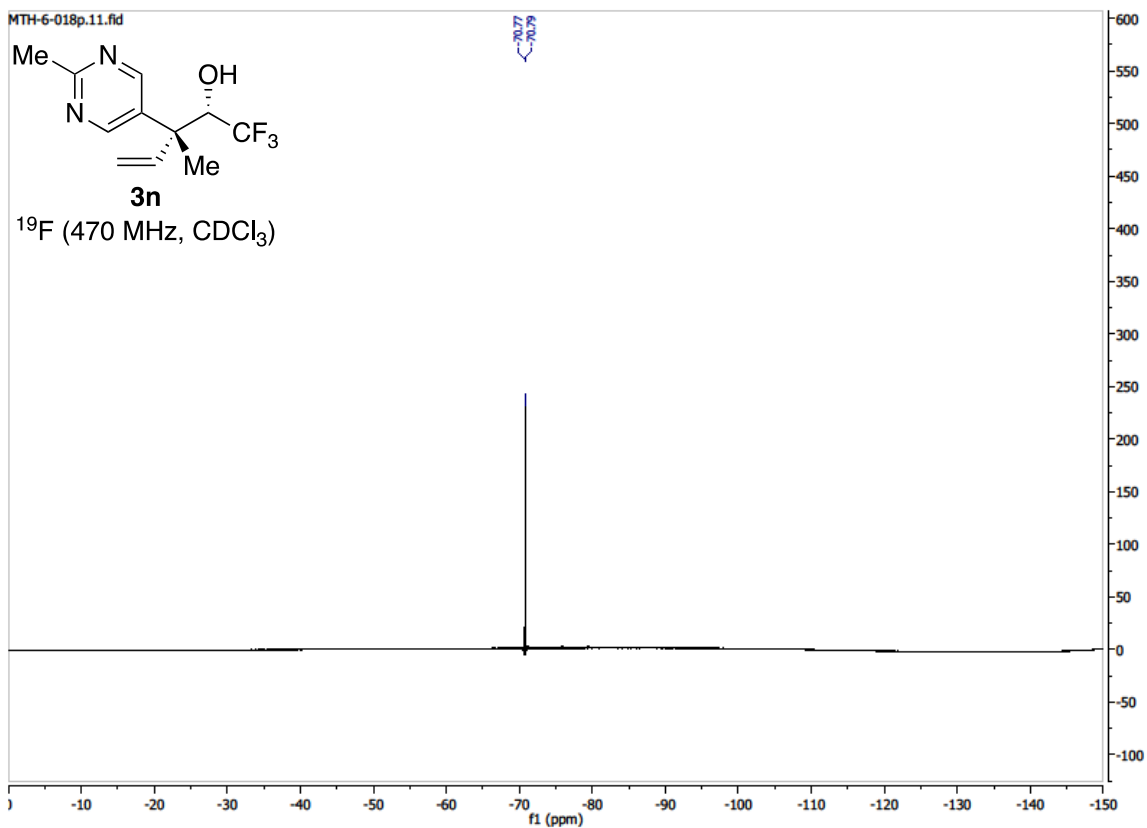
FTIR (neat): 3158, 2937, 2364, 1589, 1451, 1271, 1156, 1127, 931, 753, 698 cm<sup>-1</sup>.

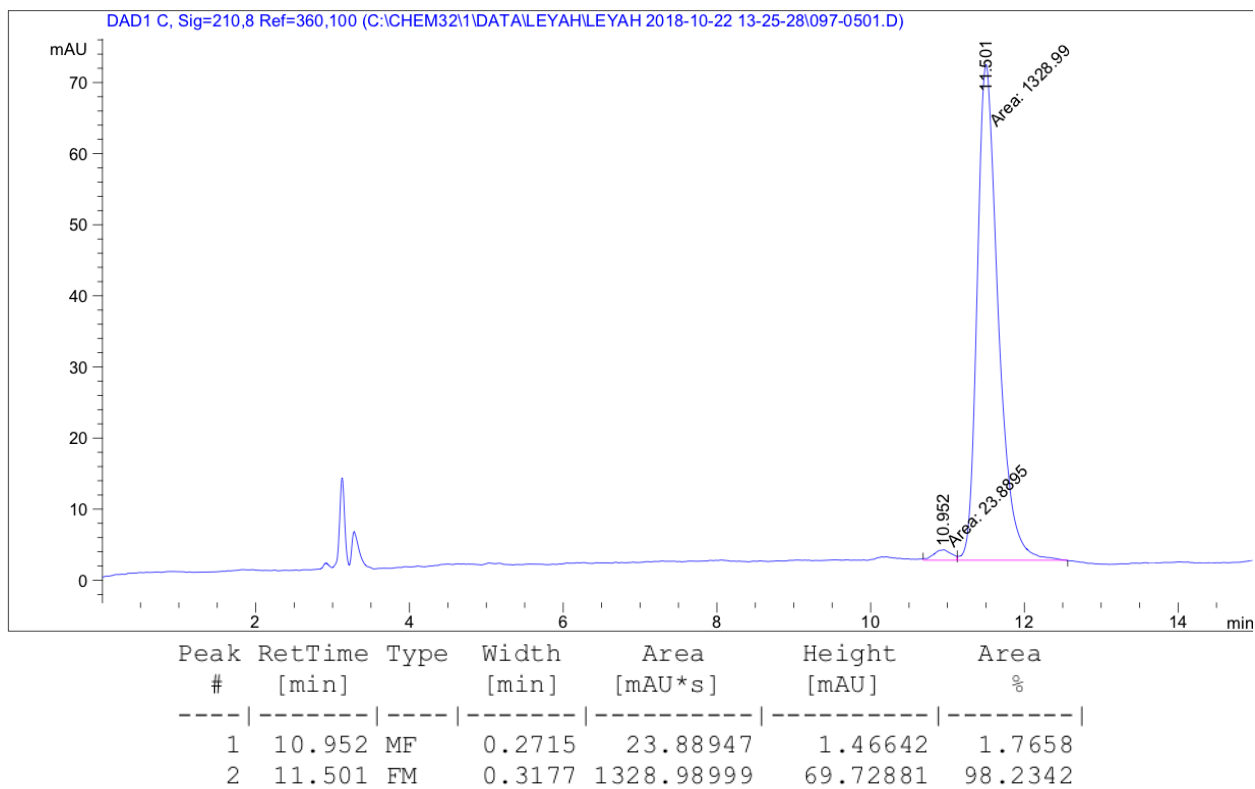
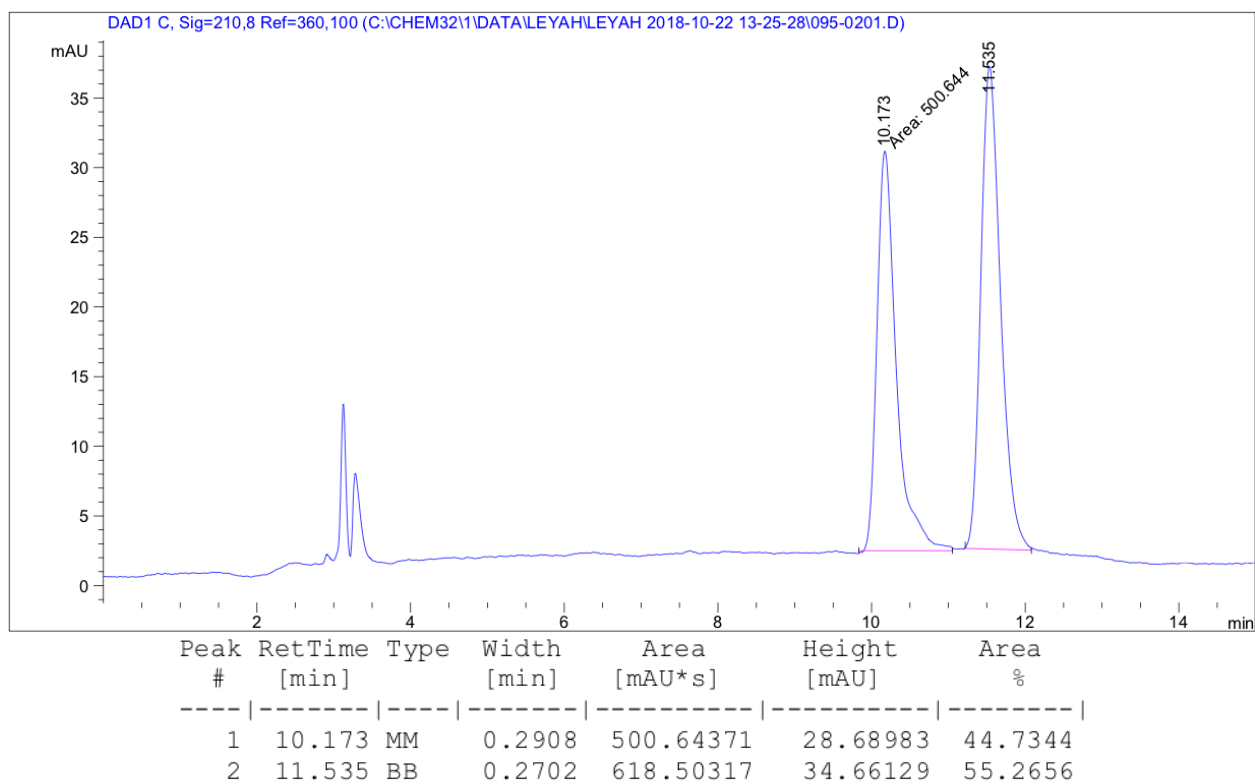
HPLC: (Chiralcel column OD-3, Hexane:2-PrOH = 97:3, 1.0 mL/min, 210 nm) ee = 96%.

[α]<sub>D</sub><sup>24</sup> = -41 (c = 0.25, CHCl<sub>3</sub>).

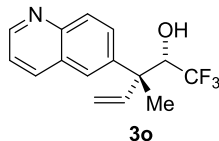
MP = 74-77 °C







**(2*S*,3*R*)-1,1,1-trifluoro-3-methyl-3-(quinolin-6-yl)pent-4-en-2-ol (3o)**



1,1-Disubstituted allene **1o** (72 mg, 0.4 mmol) was subjected to general procedure D. Upon flash column chromatography (SiO<sub>2</sub>, 1:2 EtOAc/hexanes), the title compound **3o** (39.2 mg, 0.14 mmol, >20:1 dr) was obtained as a light yellow solid in 70% yield.

R<sub>f</sub> = 0.11 (2:1 Hexanes : Ethyl acetate)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 8.29 (t, *J* = 2.1 Hz, 1H), 8.13 (dd, *J* = 8.3, 2.3 Hz, 1H), 7.80 – 7.72 (m, 1H), 7.52 (t, *J* = 8.0 Hz, 1H), 6.40 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.43 (d, *J* = 10.9 Hz, 1H), 5.21 (d, *J* = 17.6 Hz, 1H), 4.45 – 4.35 (m, 1H), 2.51 (d, *J* = 5.5 Hz, 1H), 1.63 (s, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 150.3, 146.8, 142.9, 140.5, 136.6, 129.0, 128.9, 127.9, 125.8, 124.2 (q, *J* = 285 Hz), 121.3, 116.2, 75.5 (q, *J* = 28 Hz), 47.5, 21.3 (q, *J* = 2.37 Hz).

<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -70.7 (d, *J* = 6.97 Hz).

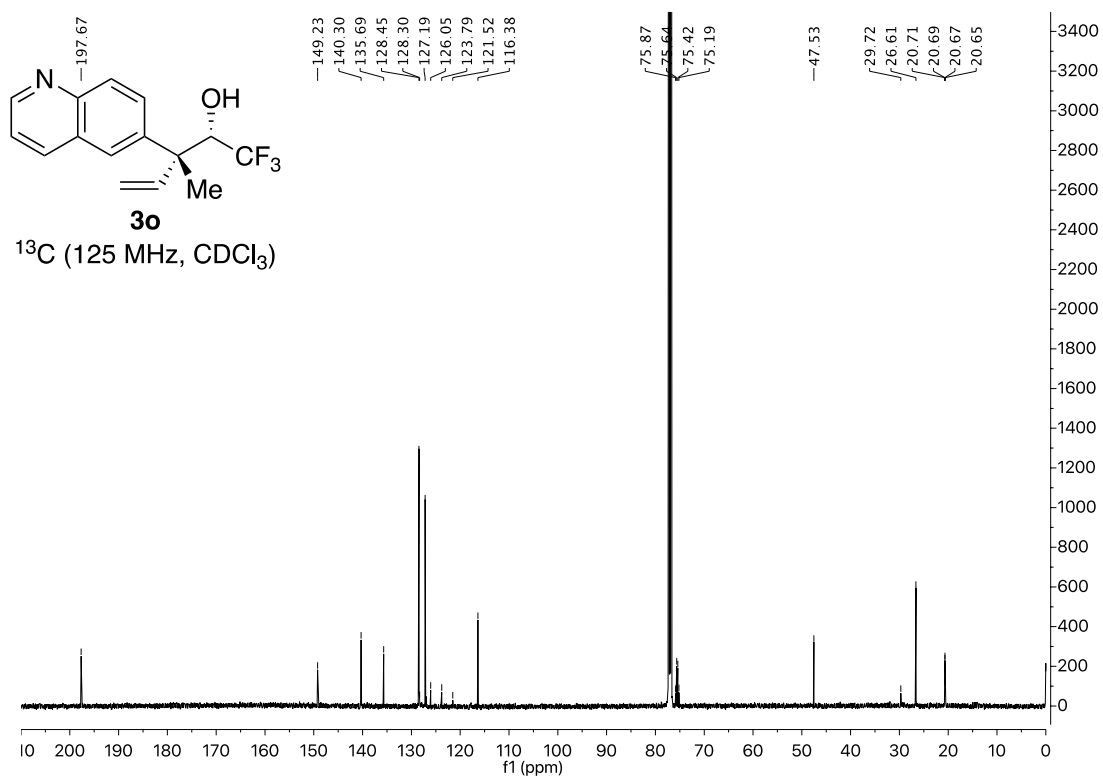
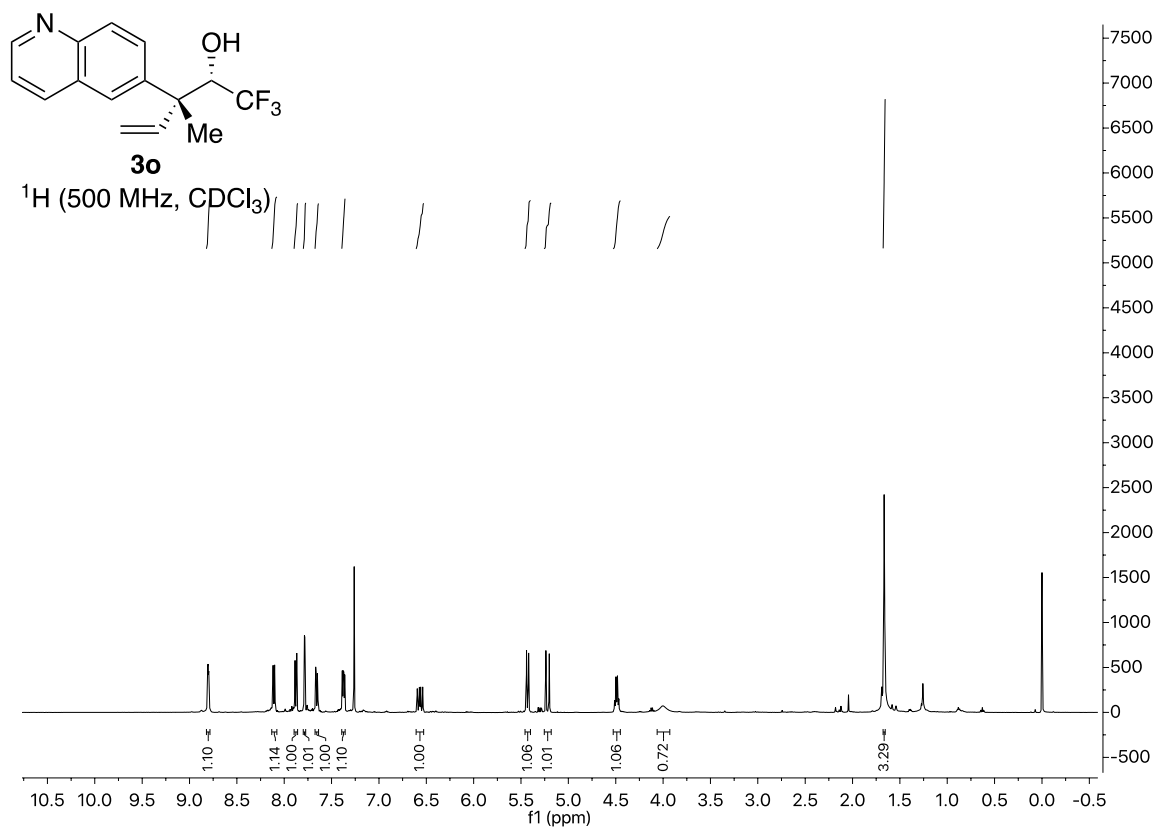
HRMS (ESI + H, *m/z*) for C<sub>15</sub>H<sub>14</sub>F<sub>3</sub>NO: calcd. = 282.1100; found = 282.1008.

FTIR (neat): 3161, 2923, 2853, 1500, 1378, 1271, 1152, 1129, 1112, 1098, 937, 834 cm<sup>-1</sup>.

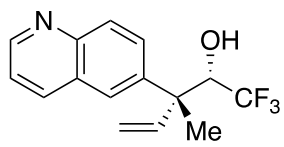
HPLC: (Chiralcel column AD-H, Hexane:2-PrOH = 97:3, 1.0 mL/min, 210 nm) ee = 95%.

[α]<sub>D</sub><sup>24</sup> = -11.8 (c = 1.0, CHCl<sub>3</sub>).

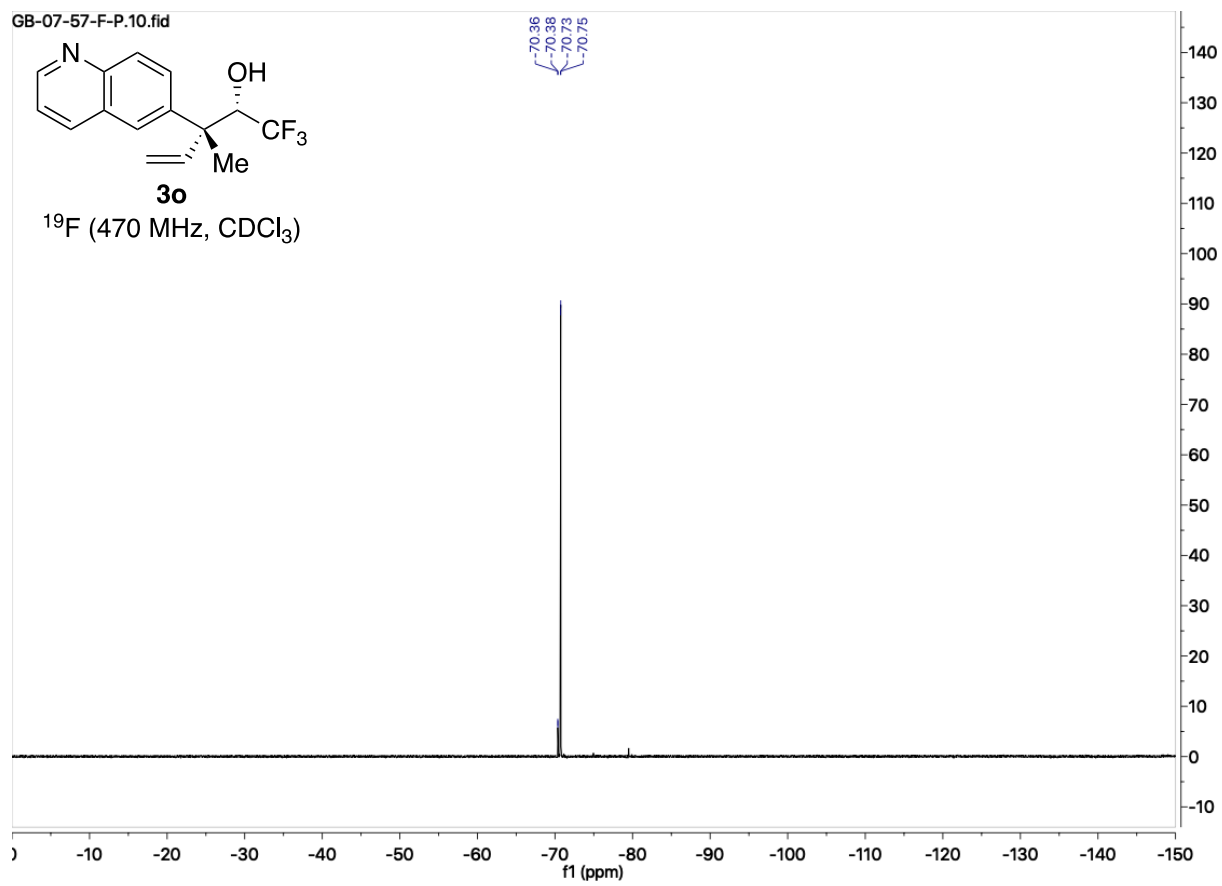
MP = 139-140 °C

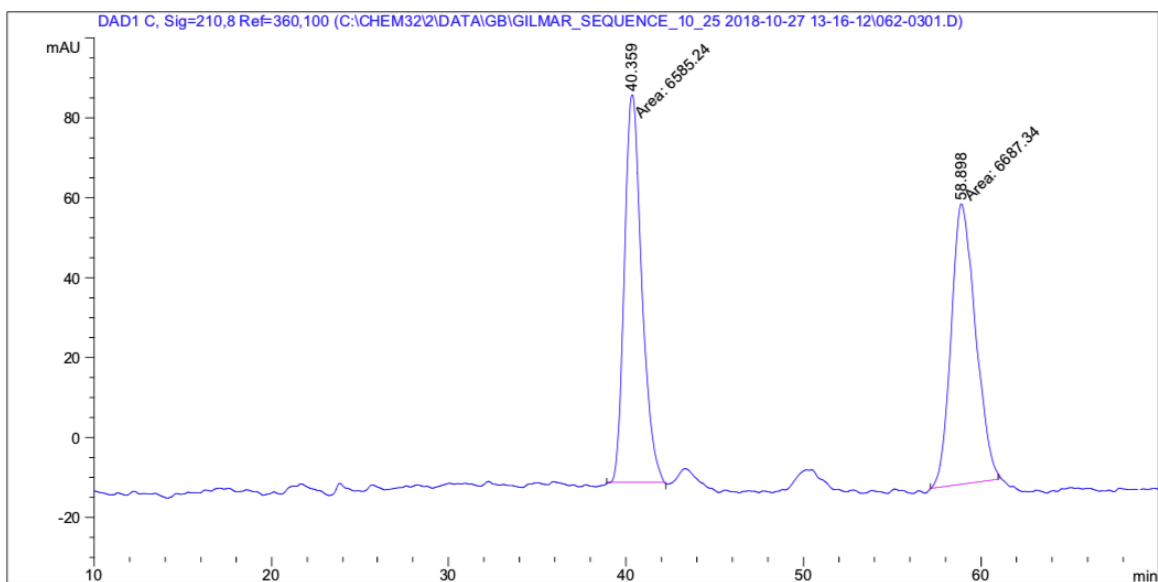


GB-07-57-F-P.10.fid



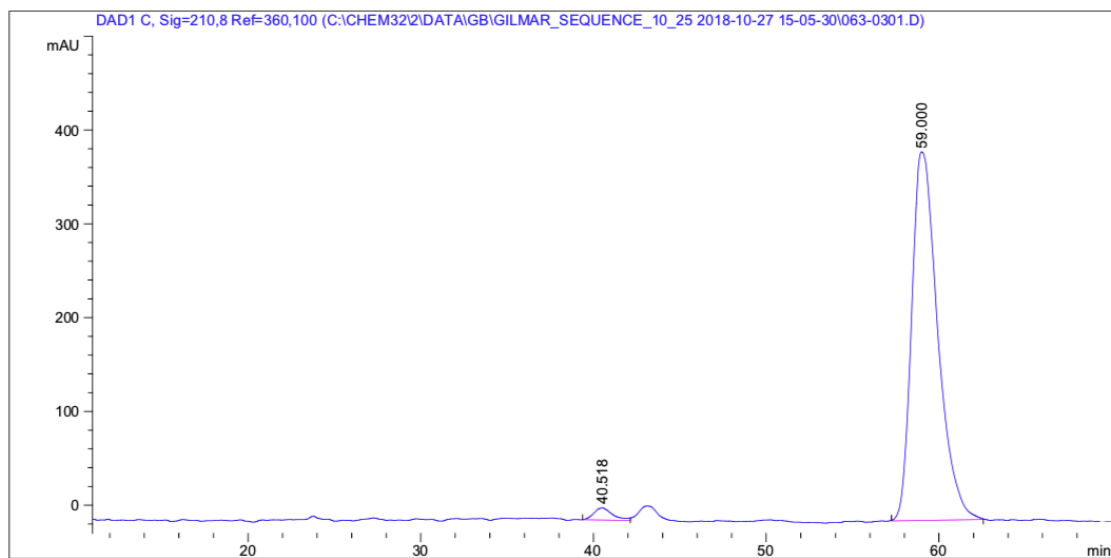
$^{19}\text{F}$  (470 MHz,  $\text{CDCl}_3$ )





Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	40.359	MM	1.1315	6585.24463	97.00160	49.6154
2	58.898	MM	1.5873	6687.34277	70.21903	50.3846

Totals : 1.32726e4 167.22063

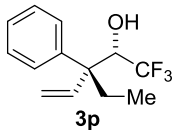


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	40.518	BB	0.9239	982.01605	12.90356	2.3299
2	59.000	BB	1.5343	4.11656e4	392.91953	97.6701

Totals : 4.21476e4 405.82309



**(2*S*,3*R*)-3-ethyl-1,1,1-trifluoro-3-phenylpent-4-en-2-ol (3p)**



1,1-Disubstituted allene **1p** (58 mg, 0.4 mmol) was subjected to general procedure D. Upon flash column chromatography (SiO<sub>2</sub>, 4:96 EtOAc/hexanes), the title compound **3p** (37 mg, 0.15 mmol, 12:1 dr) was obtained as a yellow oil in 76% yield.

R<sub>f</sub> = 0.41 (9:1 hexanes : EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.37 (m, 4H), 7.27 (m, 1H), 6.23 (dd, *J* = 10.6, 18.0 Hz, 1H), 5.47 (d, *J* = 10.6 Hz, 1H), 5.17 (d, *J* = 18.0 Hz, 1H), 4.49 (dq, *J* = 7.1, 7.1 Hz, 1H), 2.20 (d, *J* = 7.1 Hz, 1H, OH), 2.04 (m, 2H), 0.68 (t, *J* = 7.5 Hz, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 140.6, 138.8, 128.4, 128.2, 126.9, 125.2 (q, *J* = 279 Hz), 117.6, 74.2 (q, *J* = 31 Hz), 51.9, 28.3, 8.6.

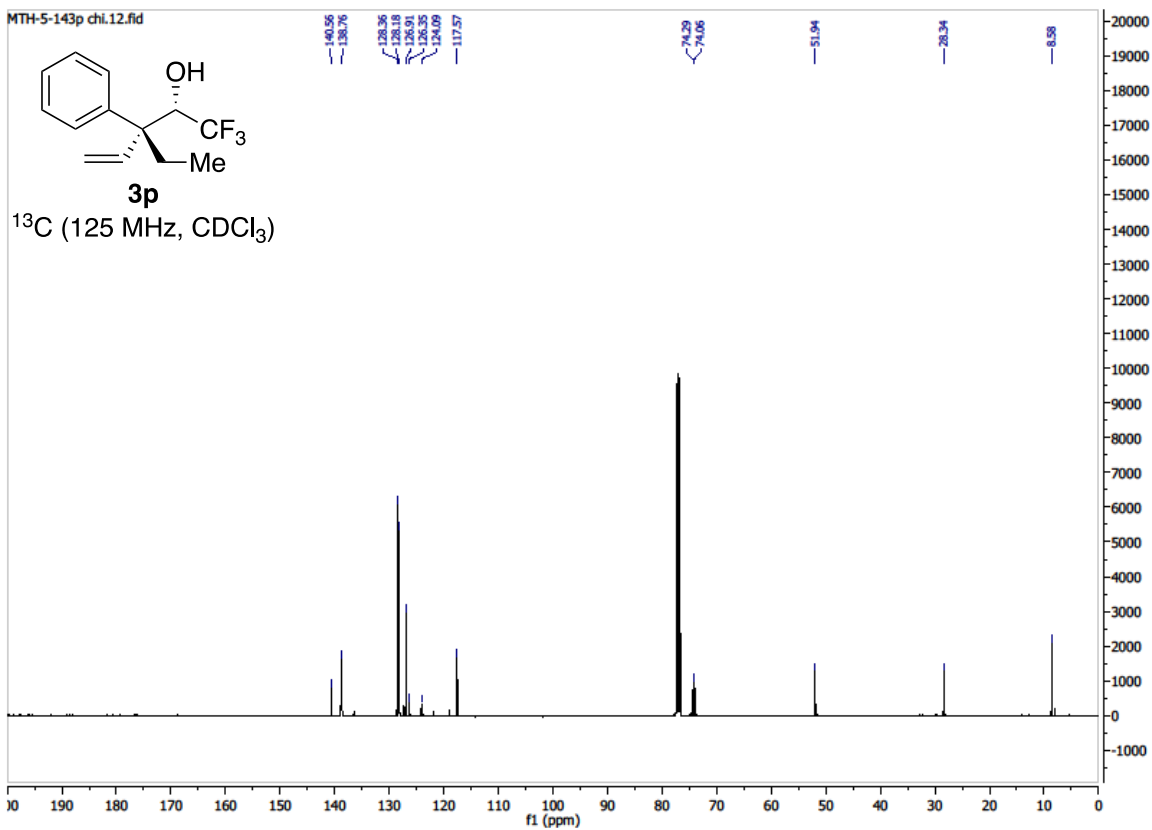
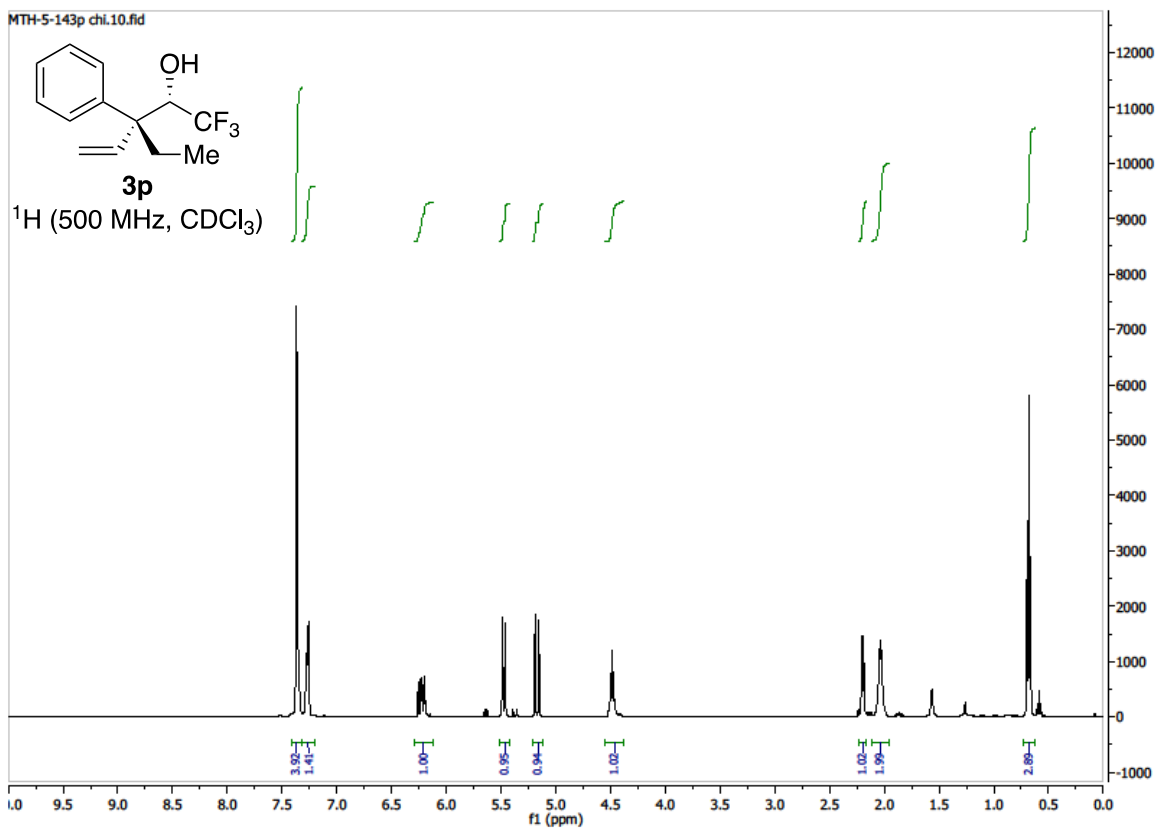
<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -70.4 (d, *J* = 7.1 Hz).

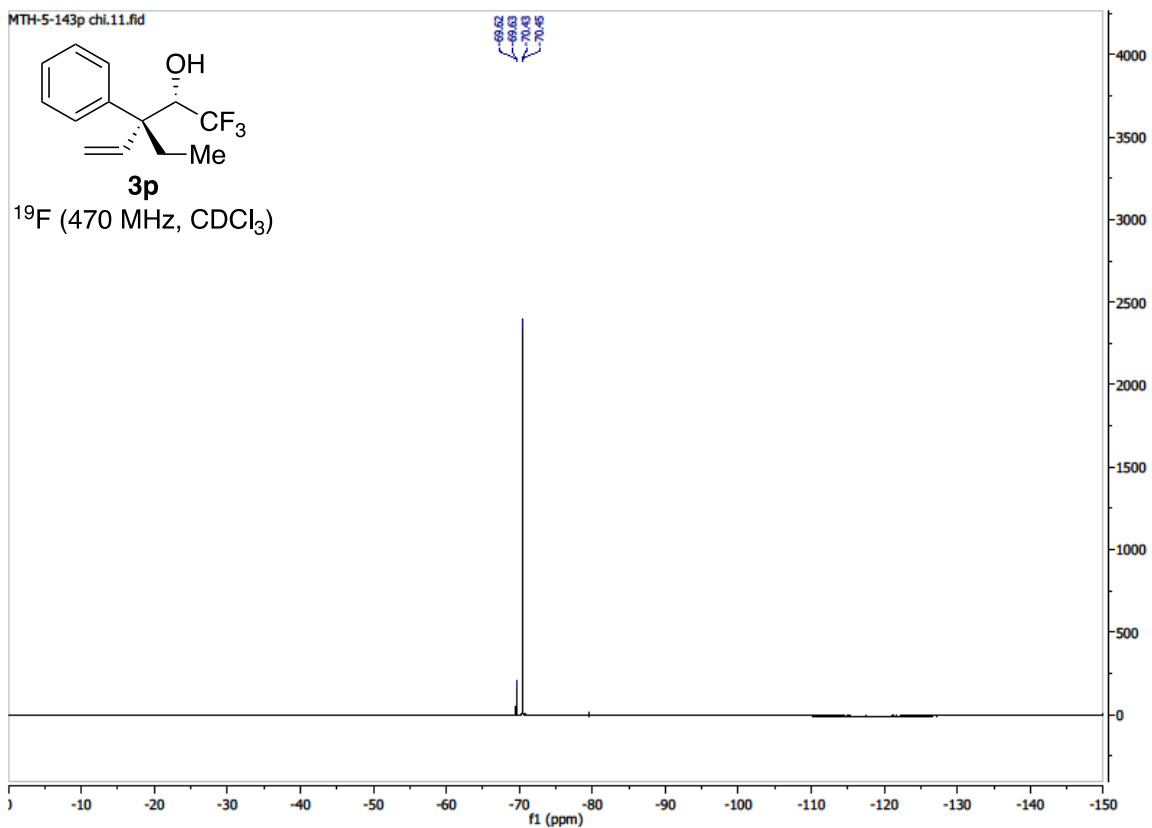
HRMS (CI<sup>+</sup>, *m/z*) for C<sub>13</sub>H<sub>15</sub>OF<sub>3</sub>: calcd. = 244.1075; found = 244.1071.

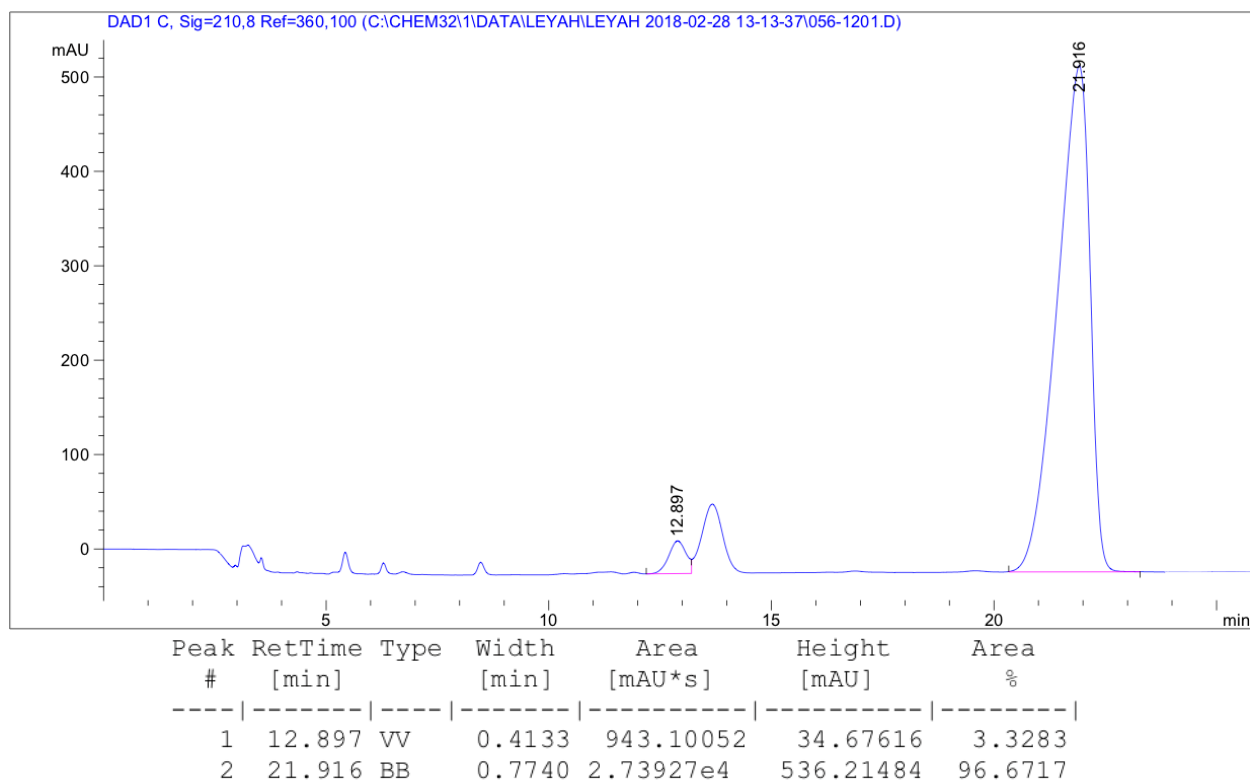
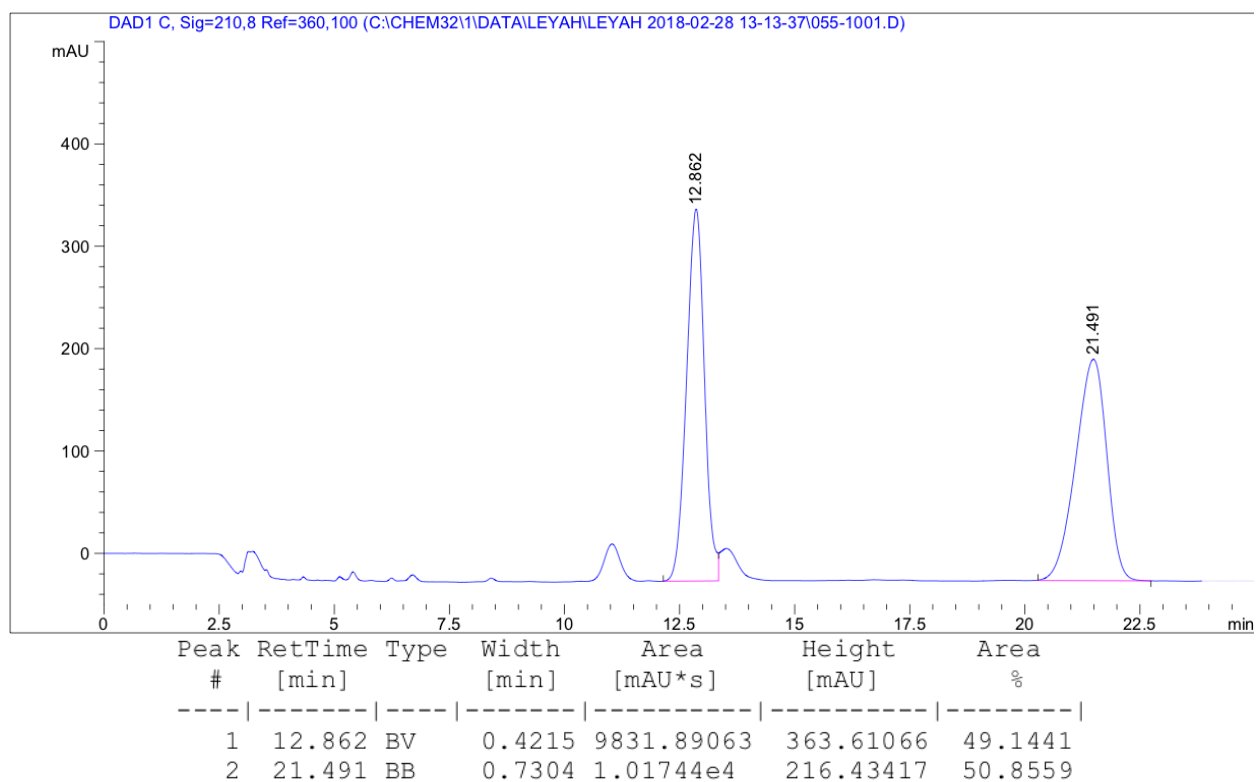
FTIR (neat): 3473, 2980, 2367, 1497, 1447, 1271, 1155, 1121, 1088, 926, 752, 701 cm<sup>-1</sup>.

HPLC: (Chiralcel column OJ-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 210 nm) ee = 93%.

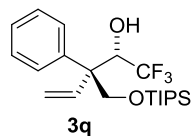
[α]<sub>D</sub><sup>24</sup> = -5.3 (c = 1.0, CHCl<sub>3</sub>).







**(2*S*,3*R*)-1,1,1-trifluoro-3-phenyl-3-(((triisopropylsilyl)oxy)methyl)pent-4-en-2-ol (3q)**



1,1-Disubstituted allene **1q** (121 mg, 0.4 mmol) was subjected to general procedure D. Upon flash column chromatography (SiO<sub>2</sub>, 3:97 EtOAc/hexanes), the title compound **3q** (46.3 mg, 0.12 mmol, 20:1 dr) was obtained as a yellow oil in 58% yield. Note: HPLC traces were run on the silyl deprotected material.

R<sub>f</sub> = 0.44 (9:1 hexanes : EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.32 (dd, *J* = 7.3, 7.3 Hz, 2H), 7.25 (m, 3H), 6.21 (dd, *J* = 10.9, 17.0 Hz, 1H), 5.41 (d, *J* = 10.9 Hz, 1H), 5.27 (d, *J* = 17.0 Hz, 1H), 4.79 (d, *J* = 8.5 Hz, 1H), 4.75 (d, *J* = 9.5 Hz, 1H), 4.63 (dq, *J* = 7.8, 8.5 Hz, 1H), 4.23 (d, *J* = 9.5 Hz, 1H), 1.14 (m, 3H), 1.06 (d, *J* = 6.8 Hz, 18H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 140.6, 139.5, 128.3, 127.5, 127.3, 125.6 (q, *J* = 286 Hz), 117.1, 75.8 (q, *J* = 23 Hz), 69.2 (q, *J* = 2 Hz), 50.1, 18.0, 11.9.

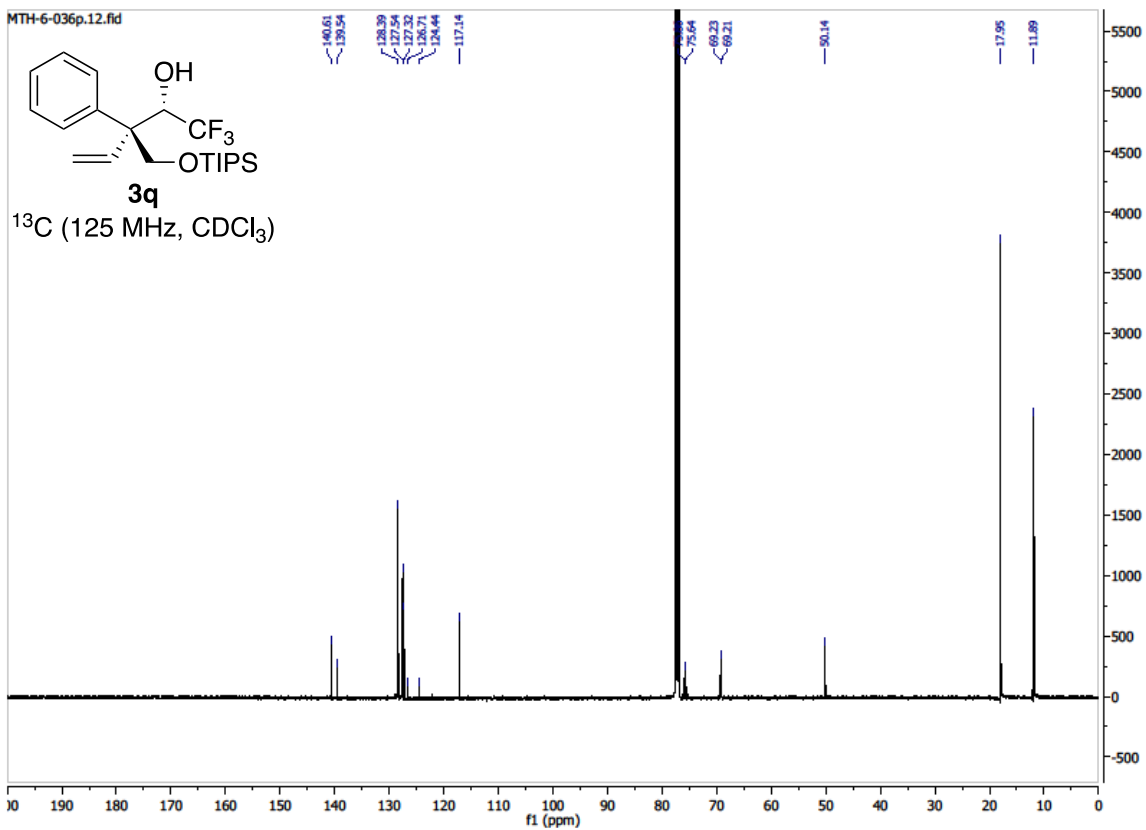
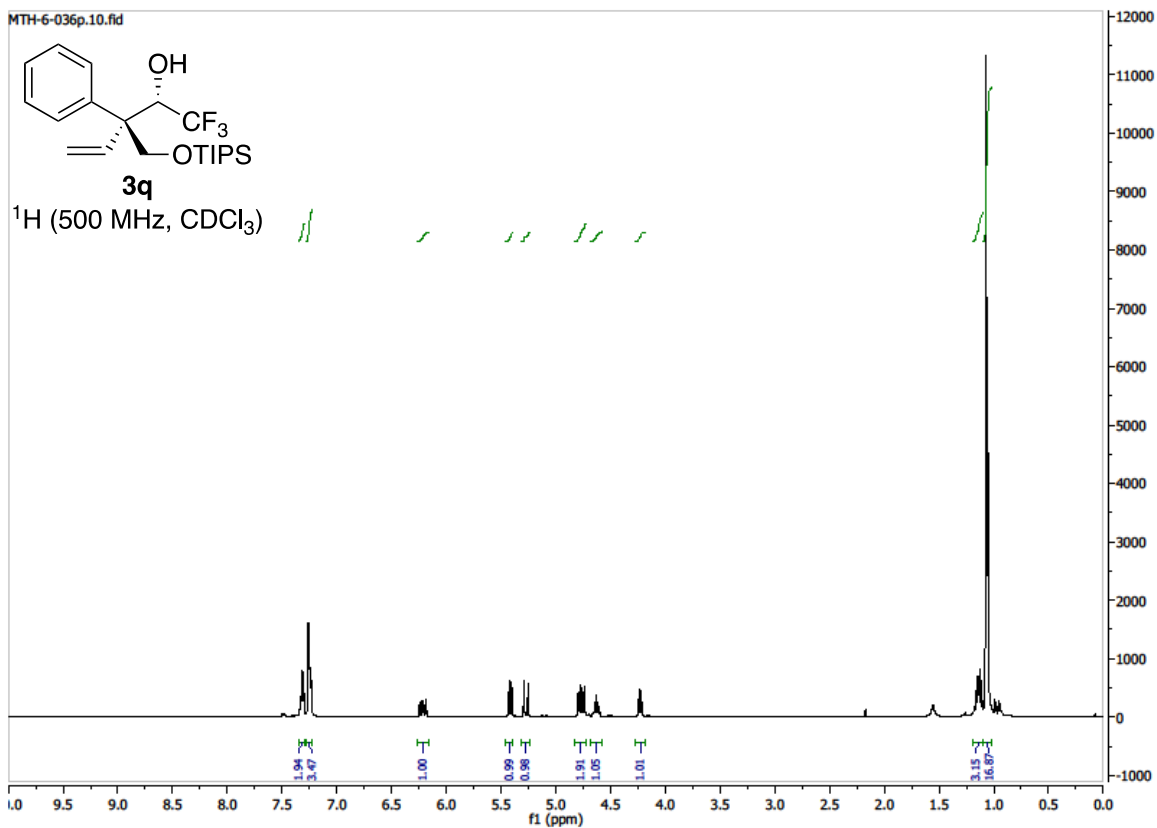
<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -71.2 (d, *J* = 8.0 Hz).

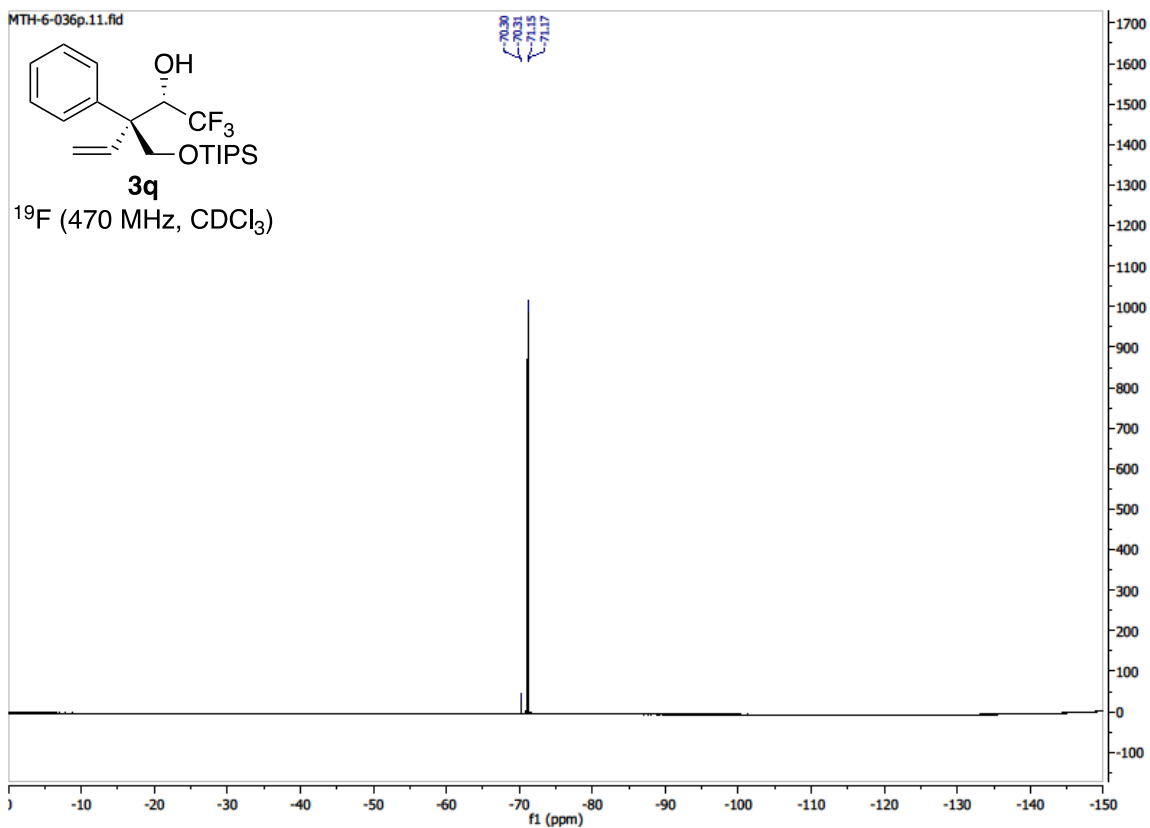
HRMS (ESI+Na, *m/z*) for C<sub>21</sub>H<sub>33</sub>F<sub>3</sub>O<sub>2</sub>Si: calcd. = 425.2094; found = 425.2091.

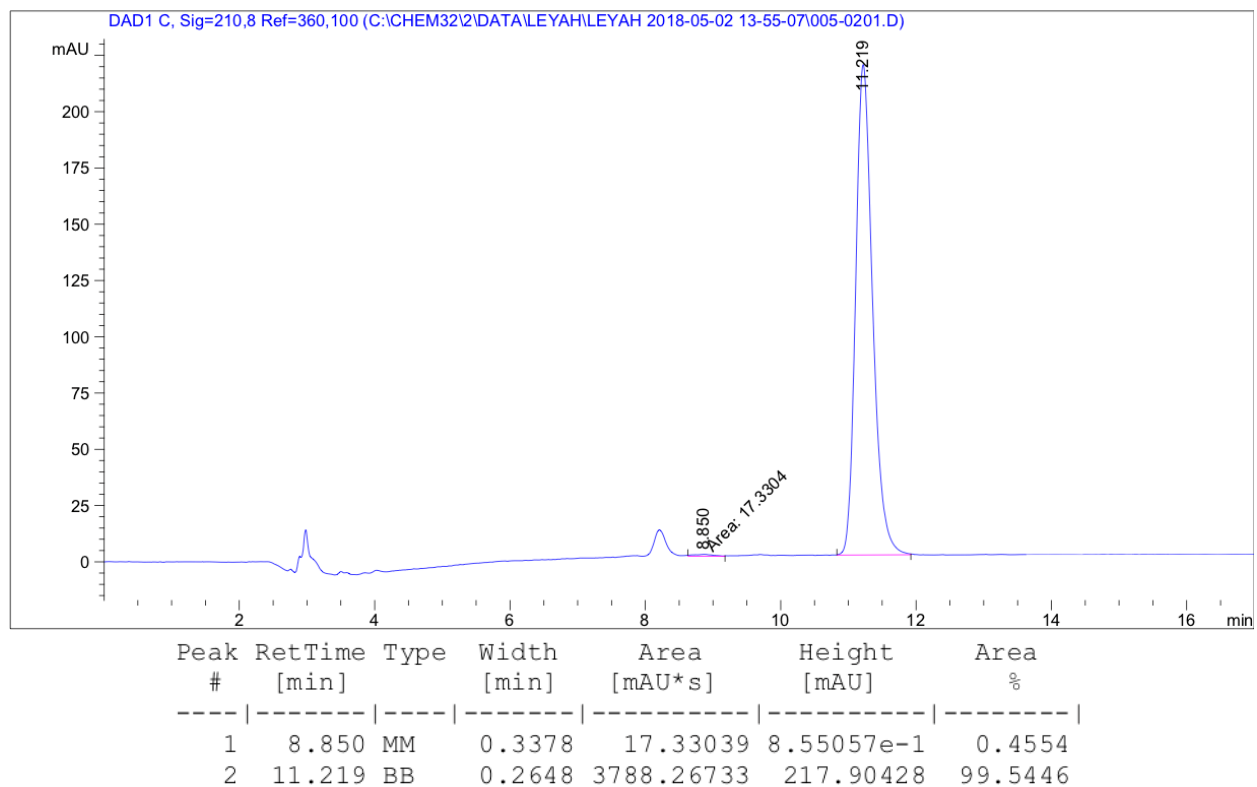
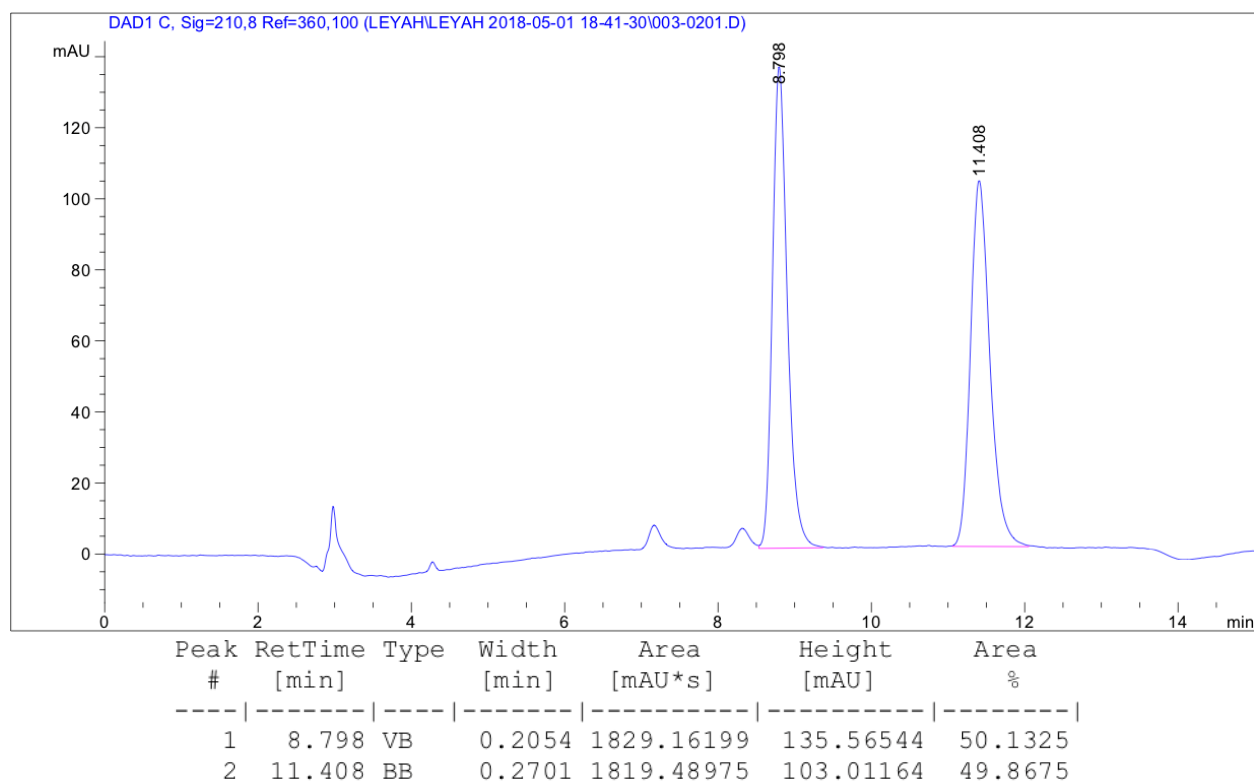
FTIR (neat): 3421, 2944, 2867, 2361, 1464, 1386, 1262, 1173, 1092, 882, 768 cm<sup>-1</sup>.

HPLC: (Chiralcel column AD-H, Hexane:2-PrOH = 92:8, 1.0 mL/min, 210 nm) ee = 99%.

[α]<sub>D</sub><sup>24</sup> = +9.0 (c = 1.0, CHCl<sub>3</sub>).

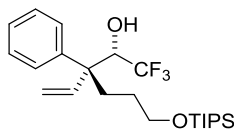








**(2*S*,3*R*)-1,1,1-trifluoro-3-phenyl-6-((triisopropylsilyl)oxy)-3vinylhexan-2-ol (3r)**



1,1-Disubstituted allene **1r** (132 mg, 0.4 mmol) was subjected to general procedure D. Upon flash column chromatography (SiO<sub>2</sub>, 3:97 EtOAc/hexanes), the title compound **3r** (72.2 mg, 0.17 mmol, 10:1 dr) was obtained as a yellow oil in 84% yield. Note: HPLC traces were run on the silyl deprotected material.

R<sub>f</sub> = 0.47 (9:1 hexanes : EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.40-7.33 (m, 4H), 7.26 (m, 1H), 6.24 (dd, *J* = 11.6, 18.3 Hz, 1H), 5.46 (d, *J* = 11.6 Hz, 1H), 5.23 (d, *J* = 18.3 Hz, 1H), 4.47 (dq, *J* = 7.0, 7.0 Hz, 1H), 3.59 (m, 2H), 2.34 (d, *J* = 7.0 Hz, 1H, OH), 2.17-2.02 (m, 2H), 1.32 (m, 1H), 1.23 (m, 1H), 1.07-1.01 (m, 21H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 140.9, 138.7, 128.4, 128.1, 126.9, 125.2 (q, *J* = 285 Hz), 117.5, 74.8 (q, *J* = 29 Hz), 63.4, 51.2, 31.8, 27.6, 18.0, 11.9.

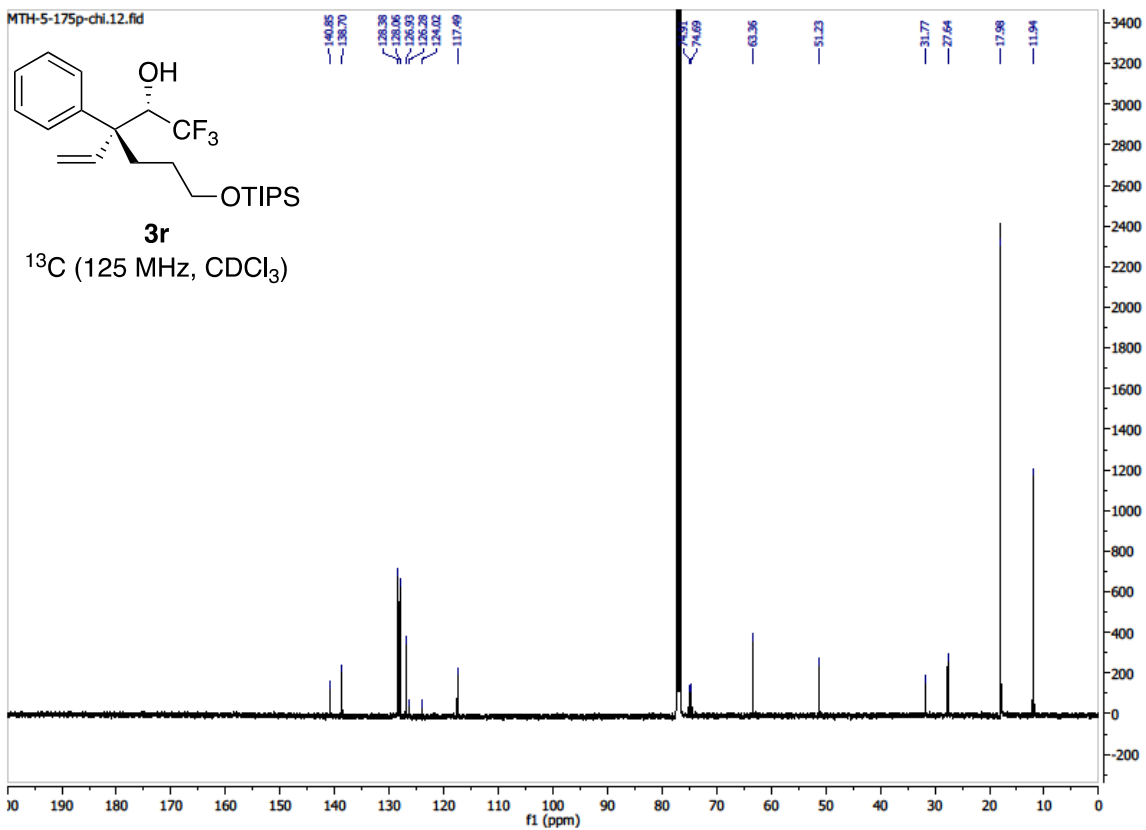
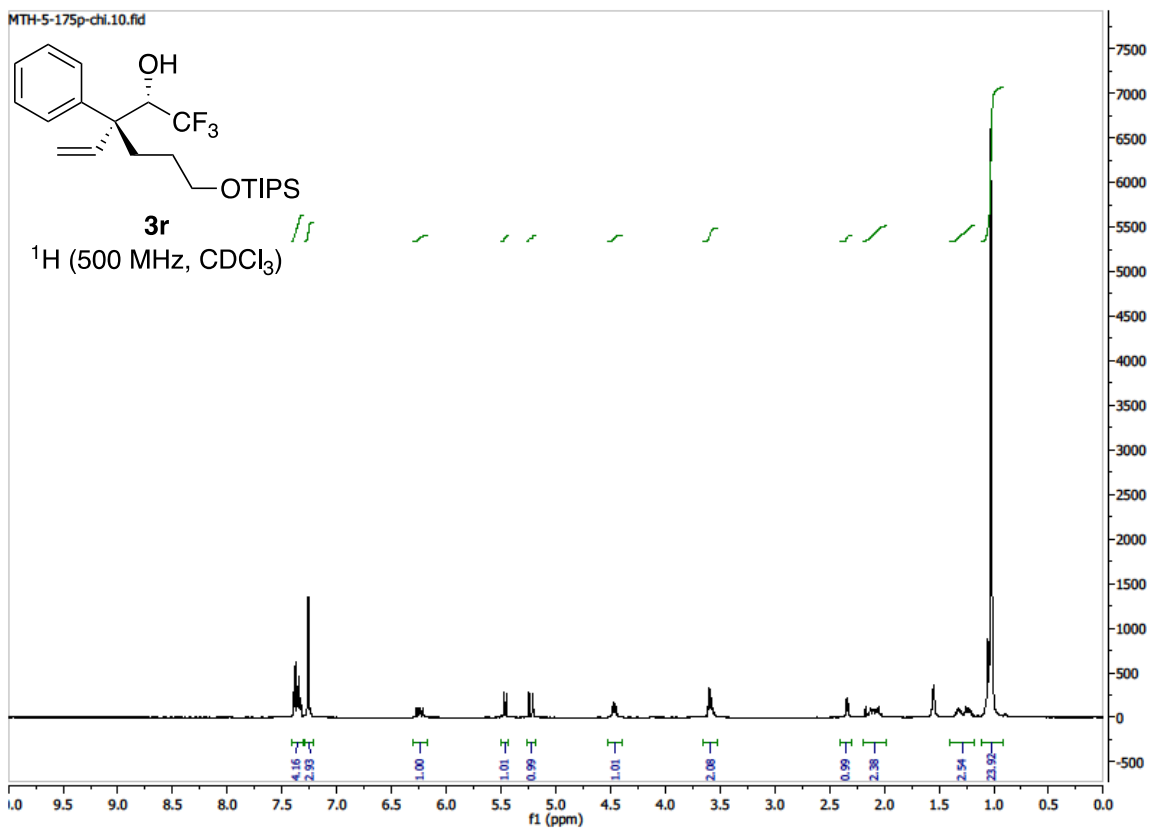
<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -70.4 (d, *J* = 7.0 Hz).

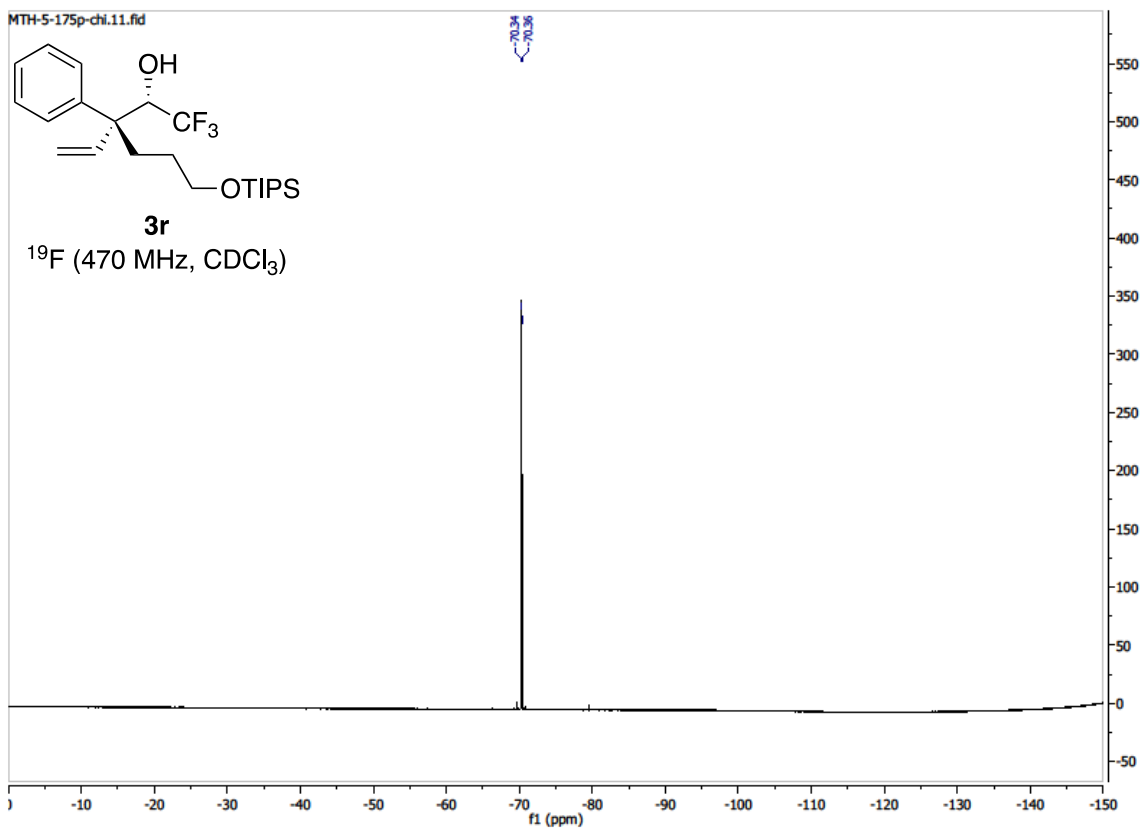
HRMS (ESI+H, *m/z*) for C<sub>23</sub>H<sub>37</sub>F<sub>3</sub>O<sub>2</sub>Si: calcd. = 431.2588; found = 431.2580.

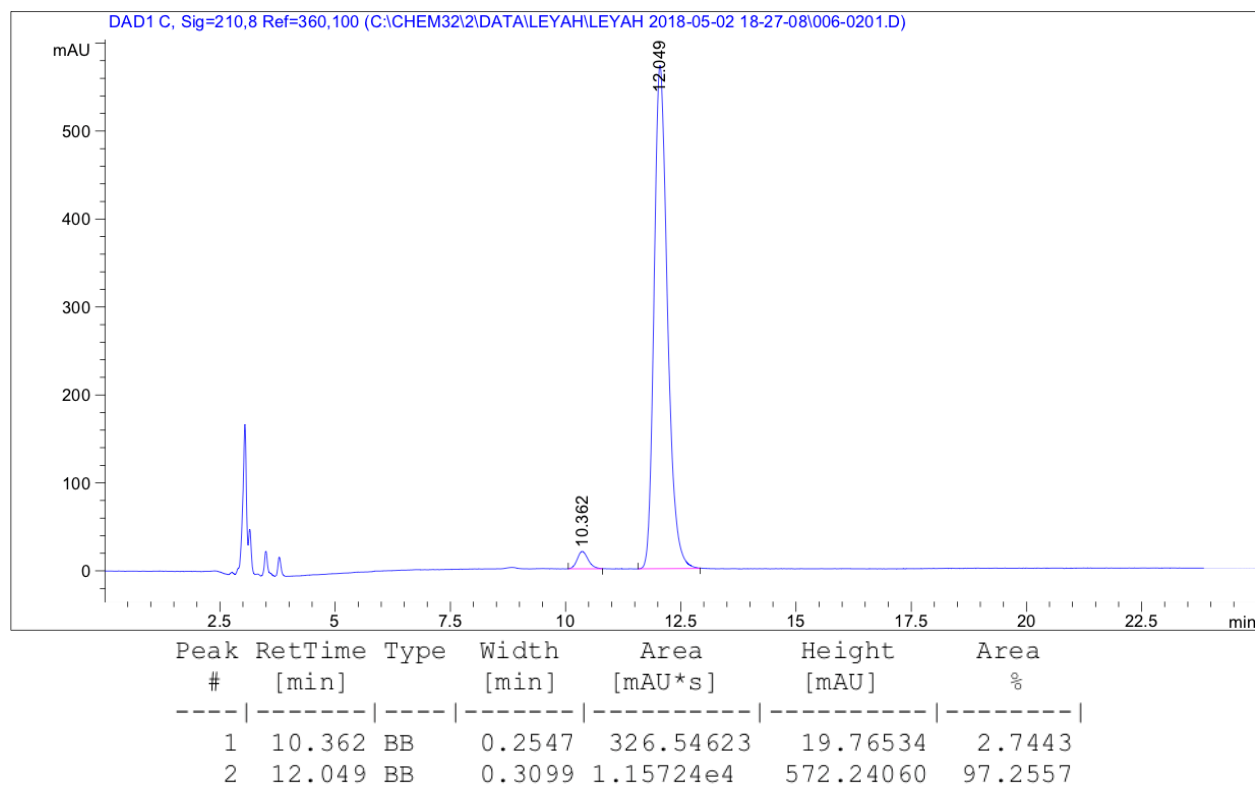
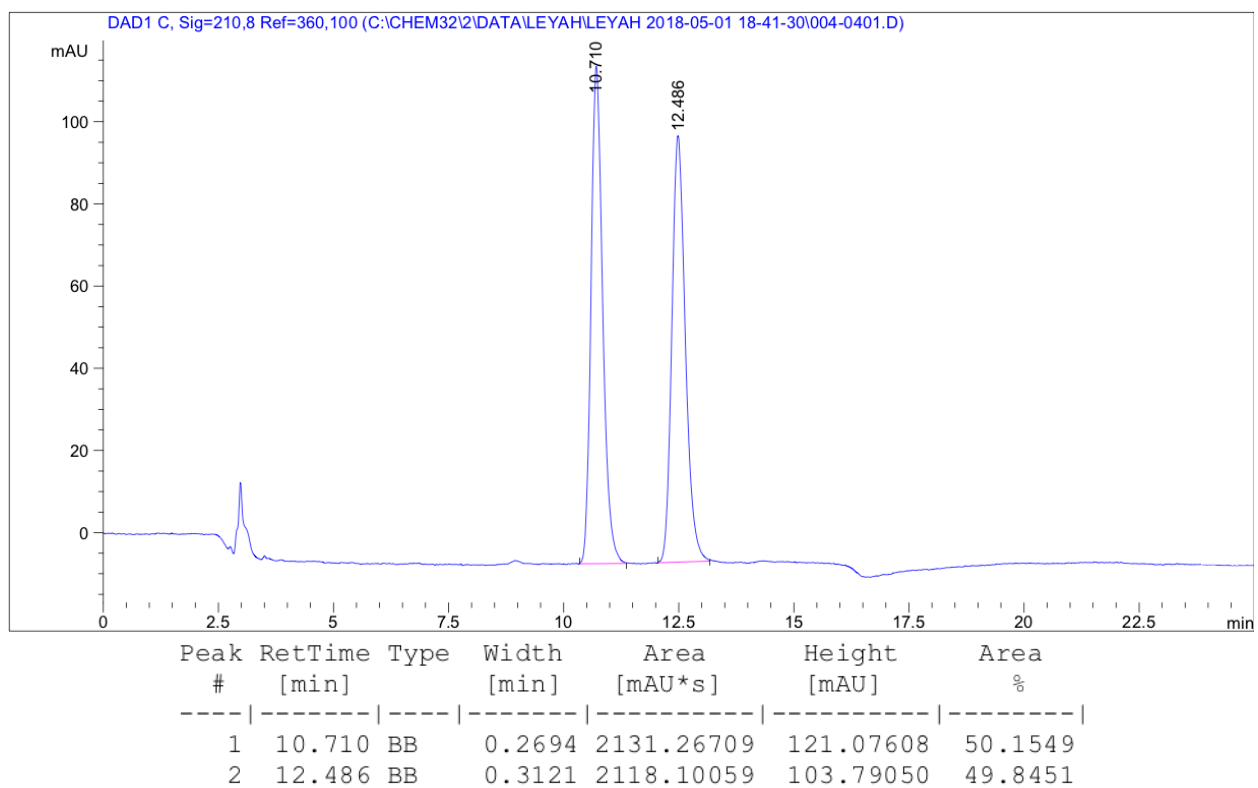
FTIR (neat): 3438, 2943, 2866, 1497, 1463, 1274, 1163, 1115, 1033, 921, 883, 701 cm<sup>-1</sup>.

HPLC: (Chiralcel column AD-H, Hexane:2-PrOH = 92:8, 1.0 mL/min, 210 nm) ee = 95%.

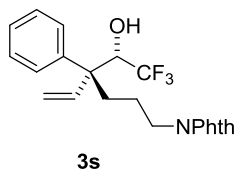
[α]<sub>D</sub><sup>24</sup> = +24.5 (c = 0.51, CHCl<sub>3</sub>).







**2-((*R*)-4-phenyl-4-((*S*)-2,2,2-trifluoro-2-hydroxyethyl)hex-5-en-1-yl)isoindoline-1,3-dione (3s)**



1,1-Disubstituted allene **1s** (121 mg, 0.4 mmol) was subjected to general procedure D. Upon flash column chromatography (SiO<sub>2</sub>, 15:85 EtOAc/hexanes), the title compound **3s** (65.0 mg, 0.16 mmol, 15:1 dr) was obtained as a white solid in 81% yield.

R<sub>f</sub> = 0.37 (75:25 hexanes : EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.75 (m, 2H), 7.64 (m, 2H), 7.28-7.16 (m, 5H), 6.16 (dd, *J* = 11.2, 18.2 Hz, 1H), 5.40 (d, *J* = 11.2 Hz, 1H), 5.09 (d, *J* = 18.2 Hz, 1H), 4.39 (dq, *J* = 7.2 Hz, 1H), 3.52 (t, *J* = 7.30 Hz, 2H), 2.33 (d, *J* = 7.3 Hz, 1H, OH), 1.98 (dd, *J* = 8.2, 9.8 Hz, 2H), 1.40 (m, 1H), 1.34 (m, 1H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 168.5, 140.4, 138.6, 134.1, 132.1, 128.6, 128.0, 127.2, 125.2 (q, *J* = 293 Hz), 123.3, 117.8, 74.5 (q, *J* = 28 Hz), 51.3, 38.2, 32.8, 23.6.

<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -70.5 (d, *J* = 6.8 Hz).

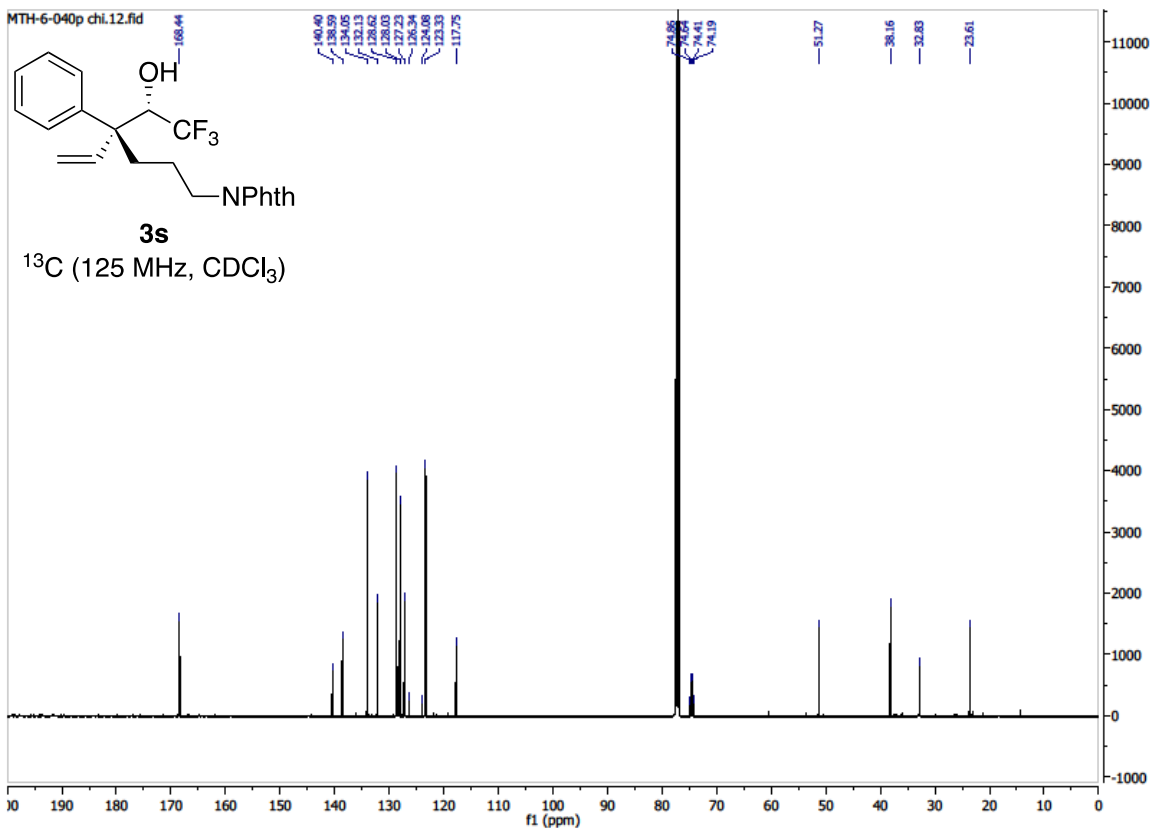
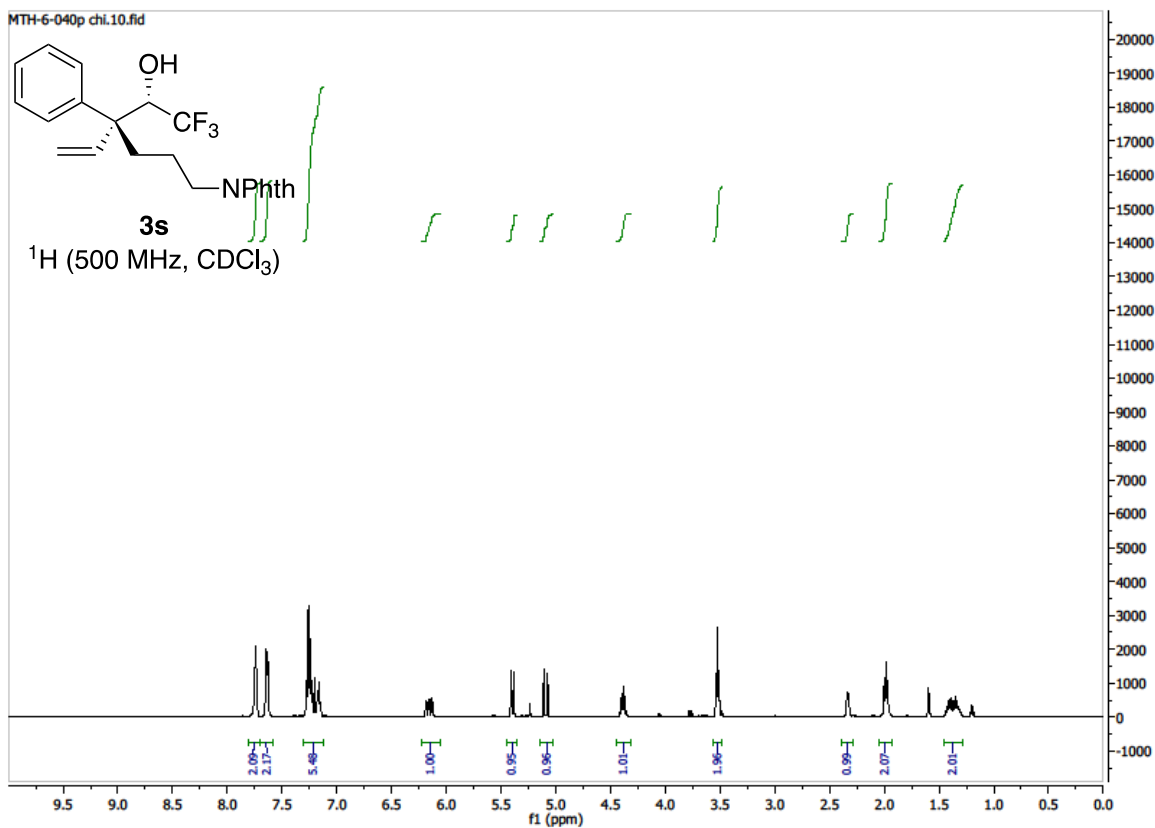
HRMS (ESI+Na, *m/z*) for C<sub>22</sub>H<sub>20</sub>F<sub>3</sub>NO<sub>3</sub>: calcd. = 426.1287; found = 426.1284.

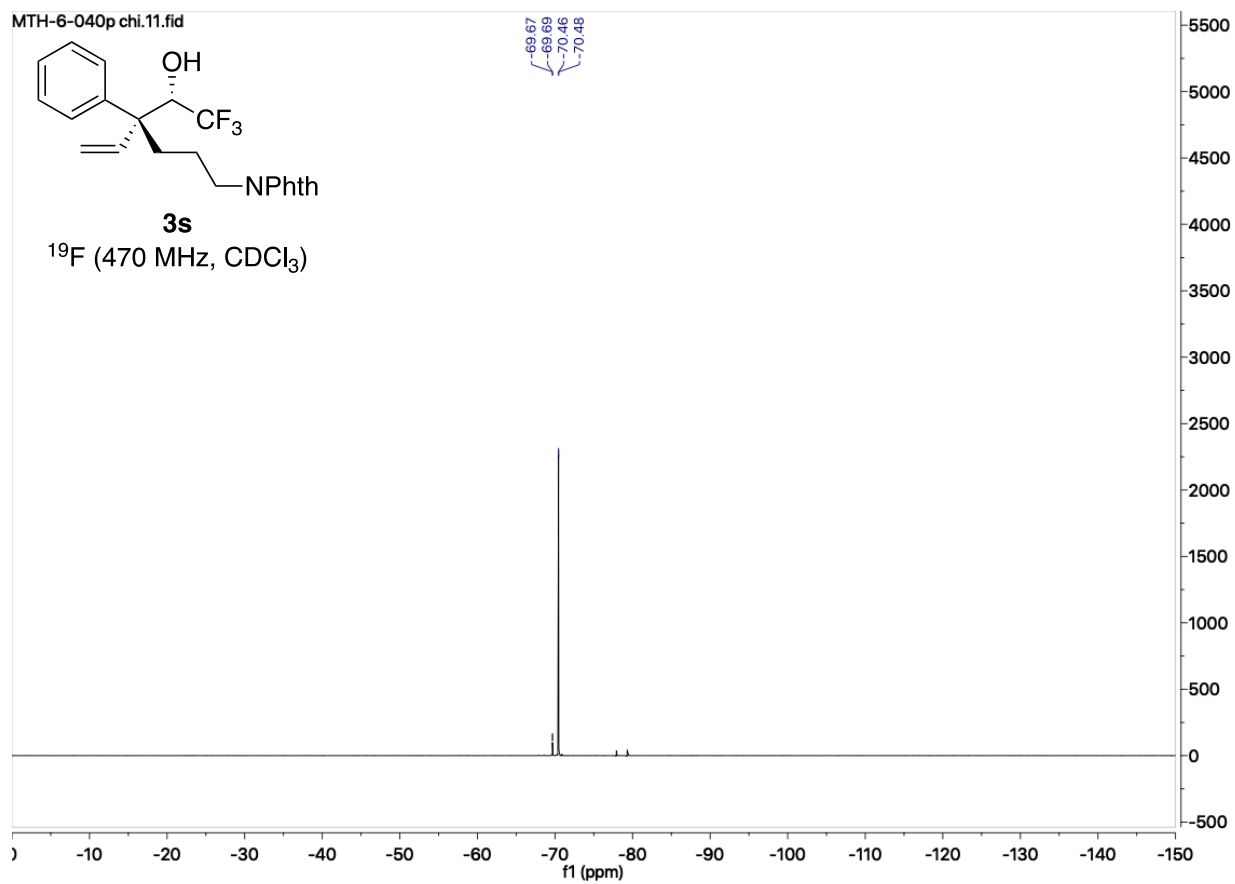
FTIR (neat): 3463, 2939, 2363, 1705, 1439, 1398, 1272, 1156, 1122, 757, 721, 702 cm<sup>-1</sup>.

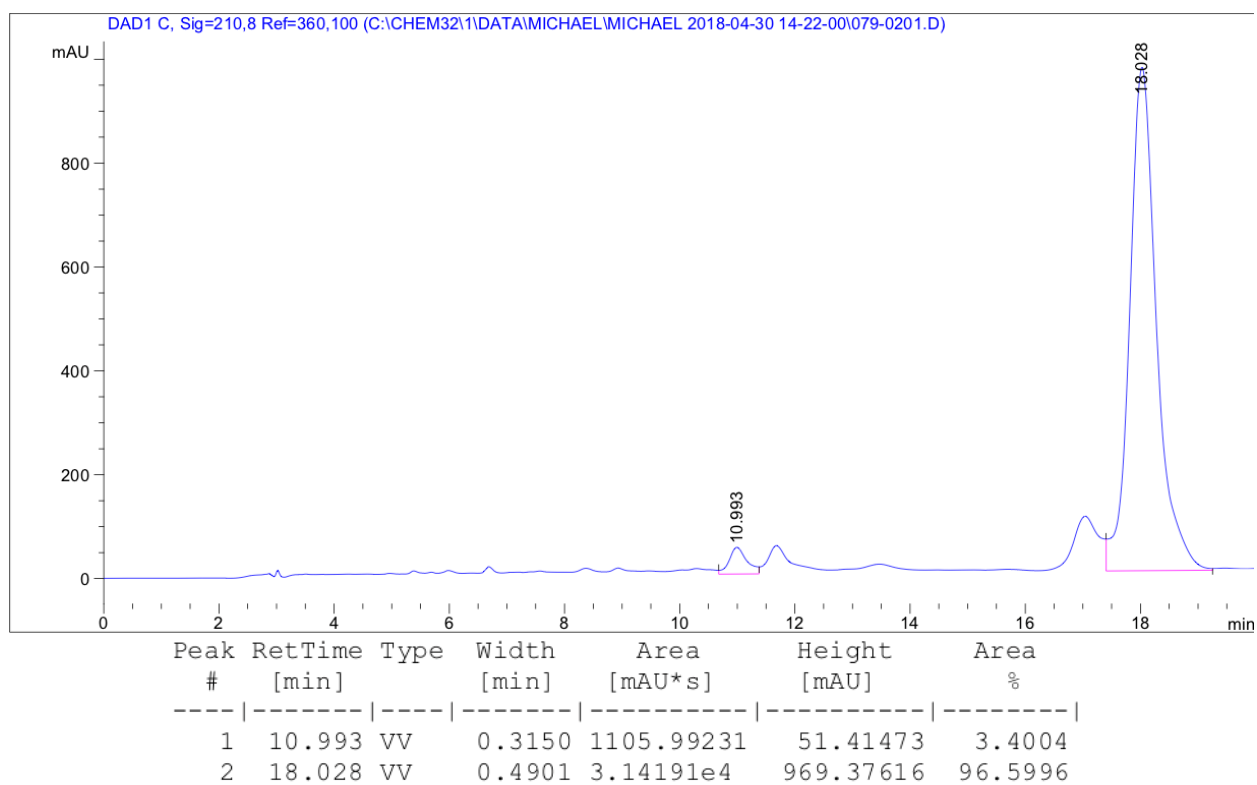
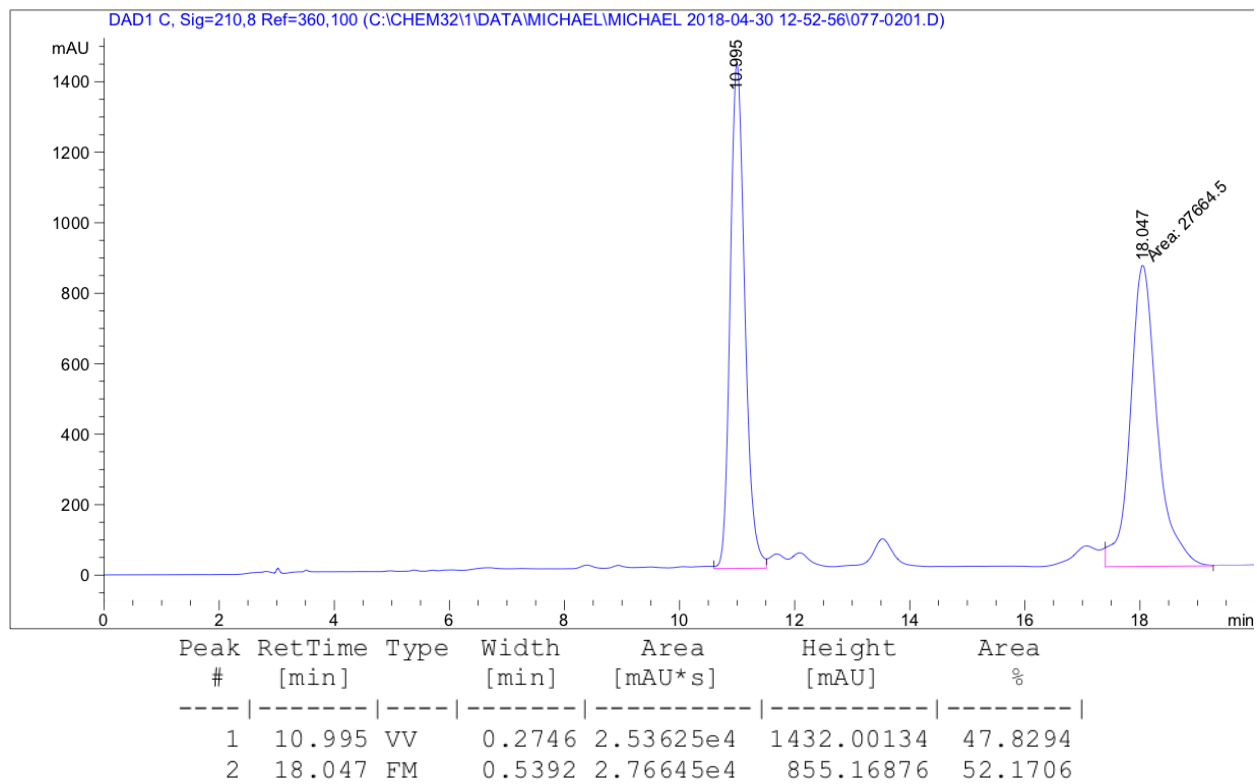
HPLC: (Chiralcel column AD-H, Hexane:2-PrOH = 88:12, 1.0 mL/min, 210 nm) ee = 93%.

[α]<sub>D</sub><sup>24</sup> = -4.5 (c = 1.0, CHCl<sub>3</sub>).

MP = 109-113 °C

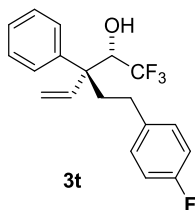








**(2*S*,3*R*)-1,1,1-trifluoro-3-(4-fluorophenethyl)-3-phenylpent-4-en-2-ol (3t)**



1,1-Disubstituted allene **1t** (95 mg, 0.4 mmol) was subjected to general procedure D. Upon flash column chromatography (SiO<sub>2</sub>, 3:97 EtOAc/hexanes), the title compound **3t** (48.6 mg, 14 mmol, 11:1 dr) was obtained as a yellow oil in 72% yield.

R<sub>f</sub> = 0.46 (9:1 hexanes : EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.44-7.39 (m, 4H), 7.31 (t, *J* = 8.0 Hz, 1H), 7.00 (dd, *J* = 5.8, 8.4 Hz, 2H), 6.92 (dd, *J* = 8.4, 8.4 Hz, 2H), 6.30 (dd, *J* = 11.3, 18.3 Hz, 1H), 5.53 (d, *J* = 11.3 Hz, 1H), 5.23 (d, *J* = 18.3 Hz, 1H), 4.56 (dq, *J* = 7.2, 7.2 Hz, 1H), 2.34-2.22 (m, 5H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 161.3 (d, *J* = 245 Hz), 140.5, 138.7, 137.6 (d, *J* = 3 Hz), 129.5 (d, *J* = 8 Hz), 128.6, 128.0, 127.2, 125.1 (q, *J* = 282 Hz), 117.9, 115.1 (d, *J* = 22 Hz), 74.3 (q, *J* = 29 Hz), 51.6, 38.2, 29.7.

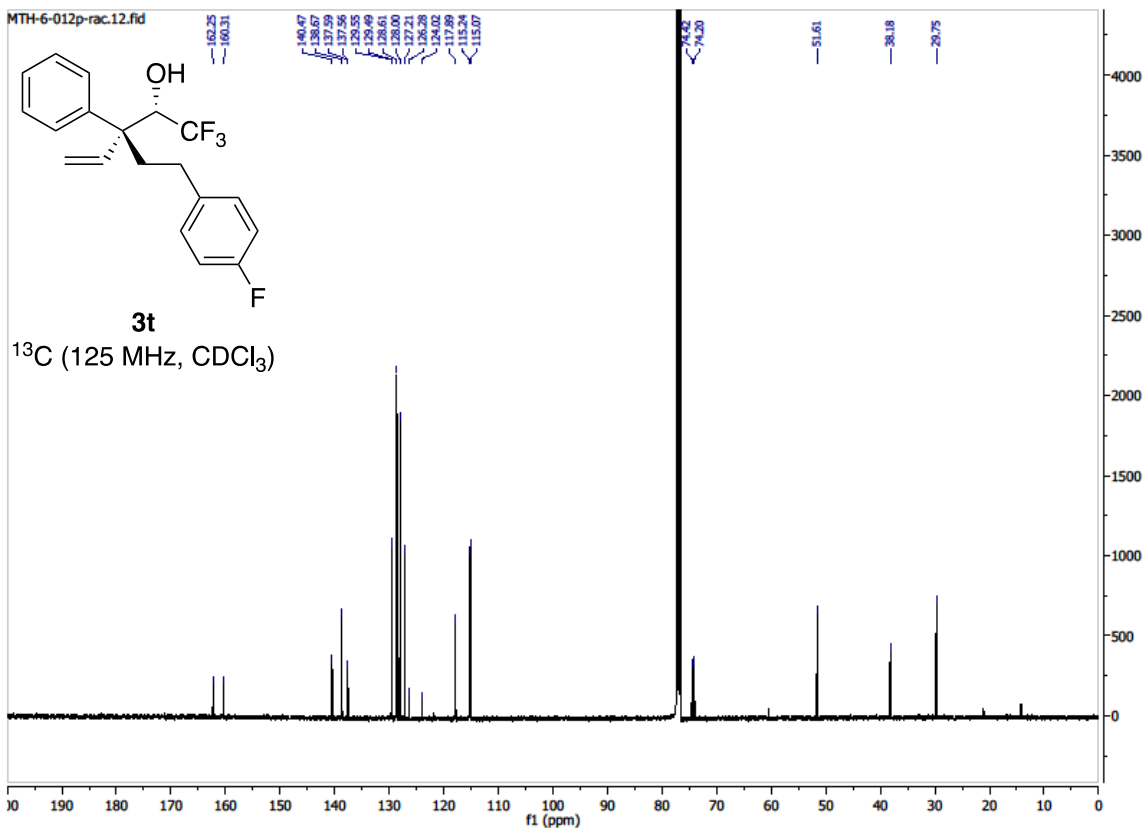
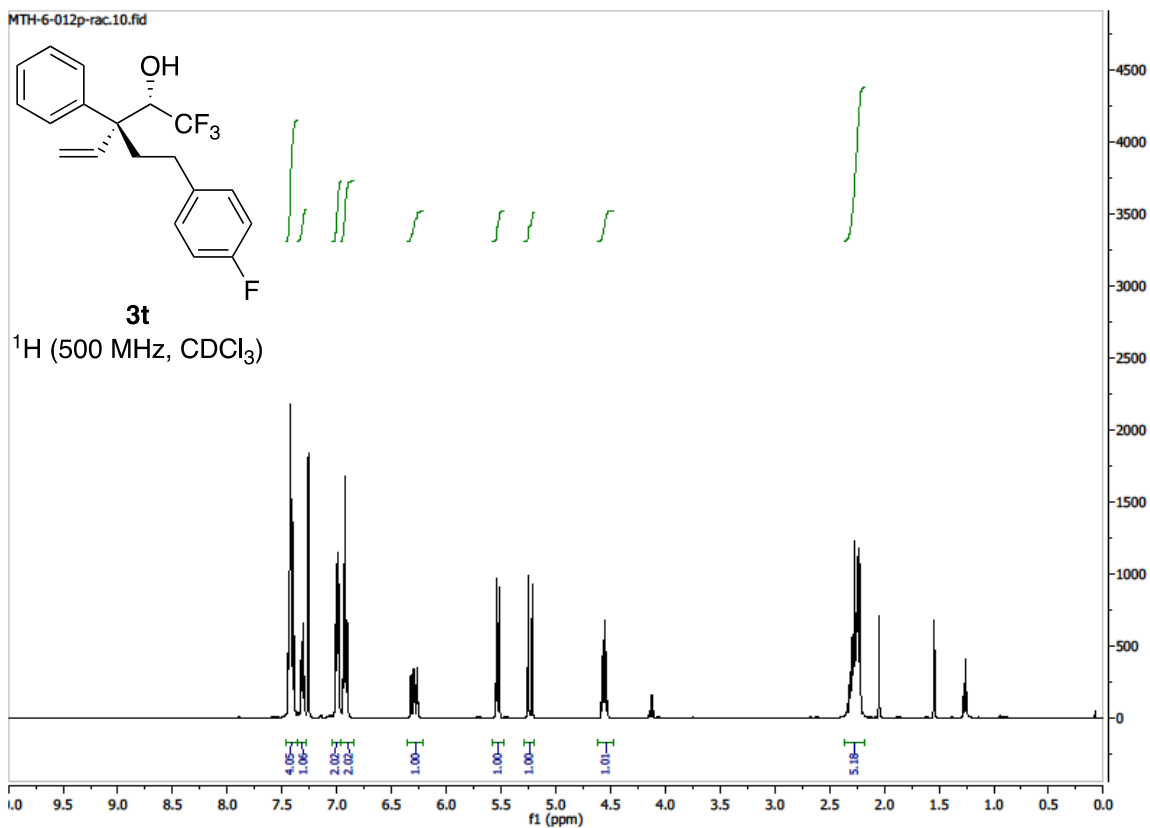
<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -70.4 (d, *J* = 7.2 Hz), -117.5 (tt, *J* = 5.5, 8.2 Hz).

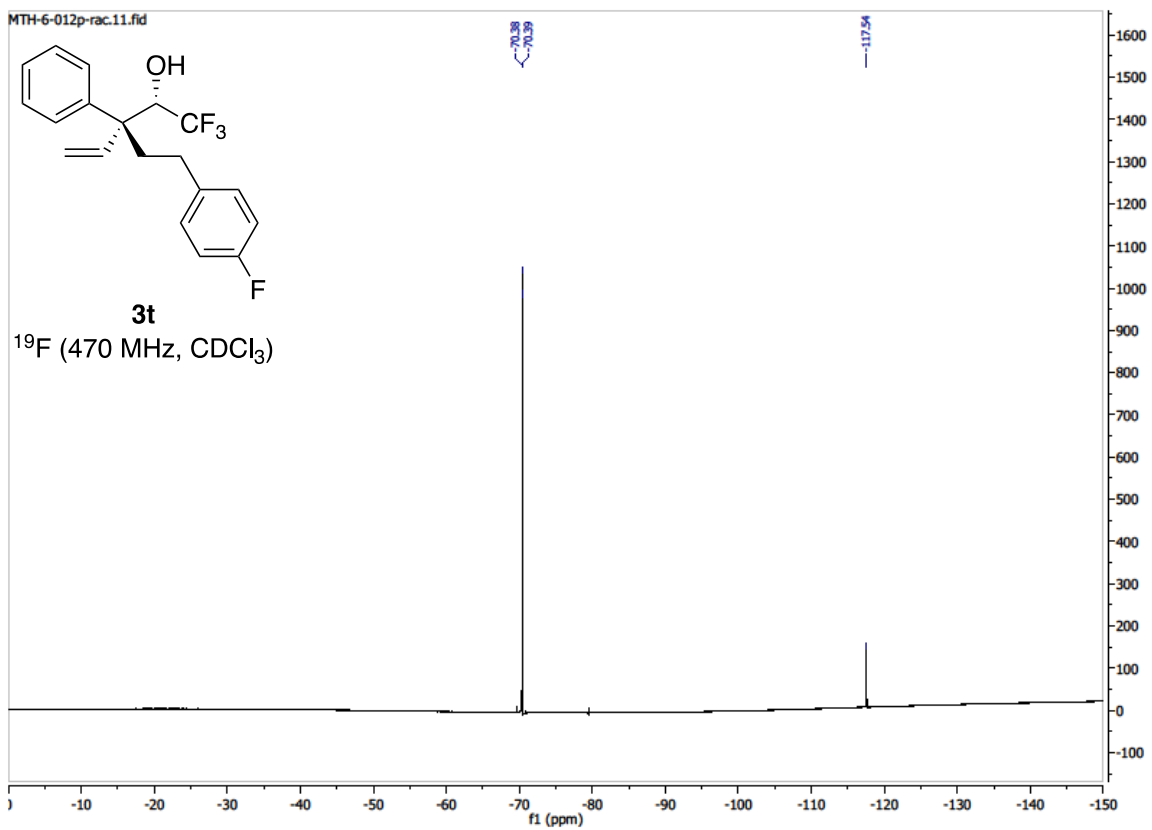
HRMS (CI+, *m/z*) for C<sub>19</sub>H<sub>18</sub>OF<sub>4</sub>: calcd. = 338.1294; found = 338.1297.

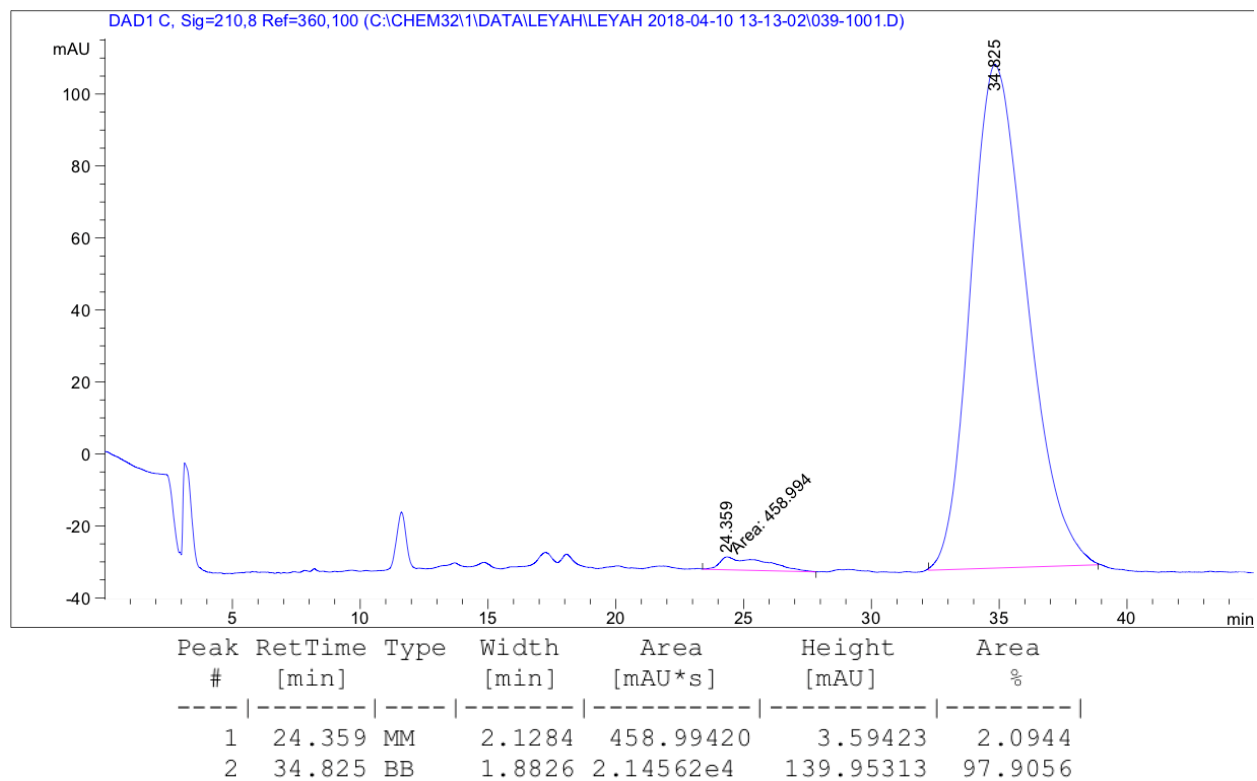
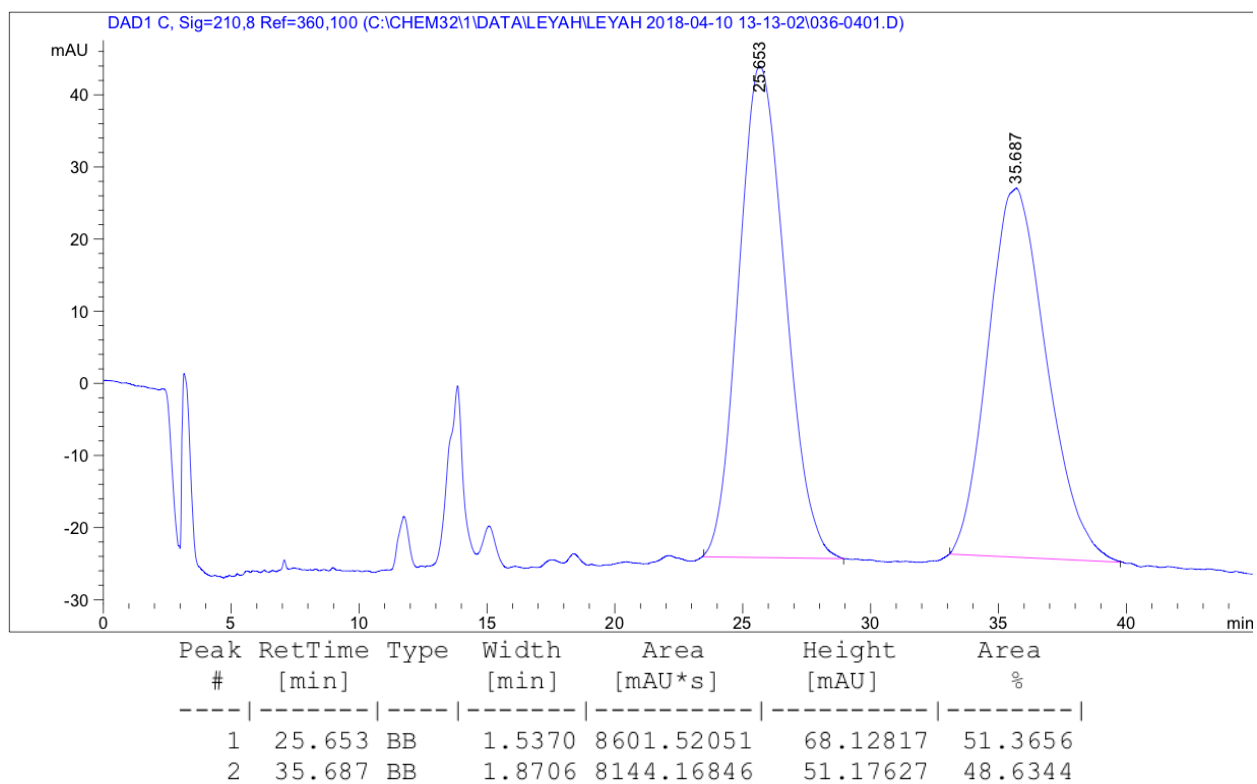
FTIR (neat): 3459, 2993, 2363, 1496, 1416, 1271, 1156, 1122, 1018, 926, 762, 701 cm<sup>-1</sup>.

HPLC: (Chiralcel column OJ-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 210 nm) ee = 96%.

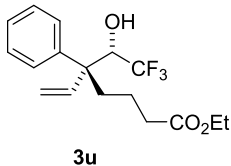
[α]<sub>D</sub><sup>24</sup> = -6.7 (c = 1.0, CHCl<sub>3</sub>).







**Ethyl (R)-5-phenyl-5-((S)-2,2,2-trifluoro-1-hydroxyethyl)hept-6-enoate (**3u**)**



1,1-Disubstituted allene **1u** (92 mg, 0.4 mmol) was subjected to general procedure D. Upon flash column chromatography (SiO<sub>2</sub>, 8:92 EtOAc/hexanes), the title compound **3u** (42.9 mg, 0.13 mmol, 9:1 dr) was obtained as a yellow oil in 65% yield.

R<sub>f</sub> = 0.21 (85:15 hexanes : EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.36 (m, 4H), 7.27 (m, 1H), 6.23 (dd, *J* = 11.3, 18.2 Hz, 1H), 5.48 (d, *J* = 11.3 Hz, 1H), 5.21 (d, *J* = 18.2 Hz, 1H), 4.48 (dq, *J* = 7.3 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 2.40 (d, *J* = 7.3 Hz, 1H, OH), 2.23 (m, 2H), 2.00 (m, 2H), 1.41 (m, 1H), 1.32 (m, 1H), 1.23 (t, *J* = 7.1 Hz, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 173.4, 140.5, 138.6, 128.5, 128.0, 127.1, 125.1 (q, *J* = 282 Hz), 117.5, 74.5 (q, *J* = 29 Hz), 60.4, 51.3, 35.0, 34.3, 19.6, 14.2.

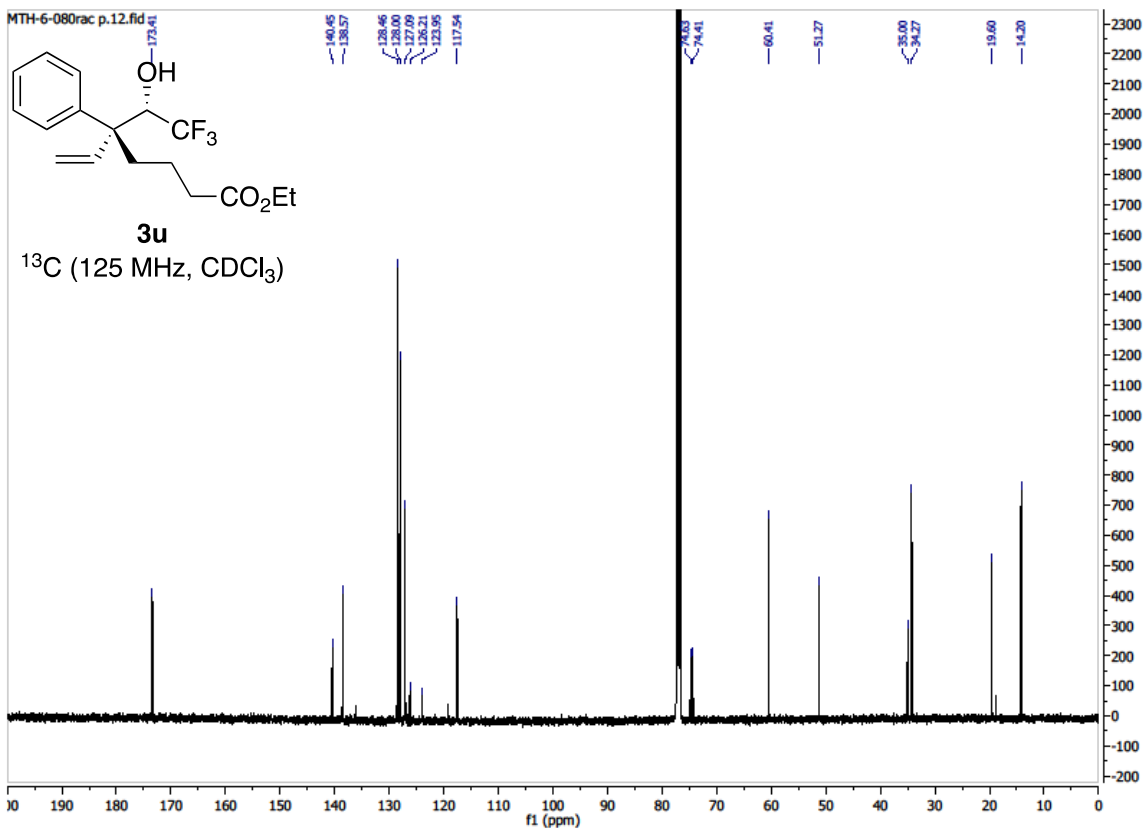
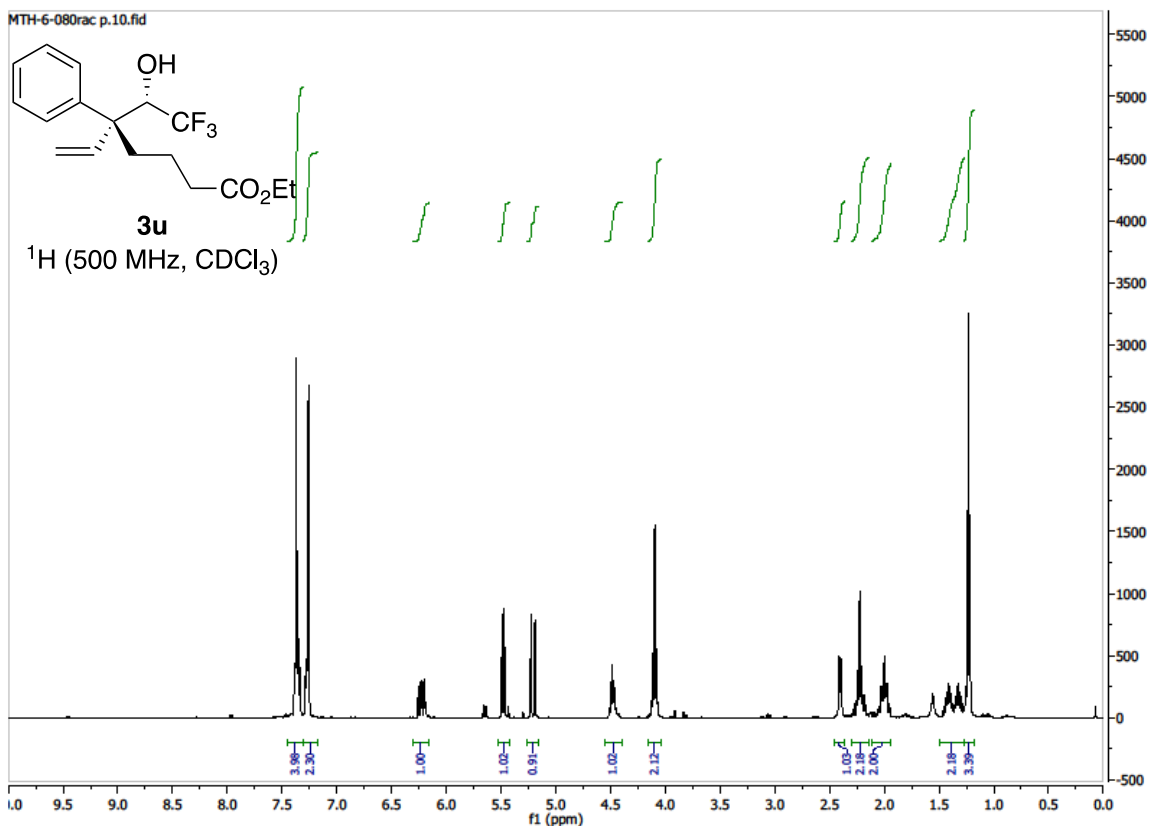
<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -70.4 (d, *J* = 7.3 Hz).

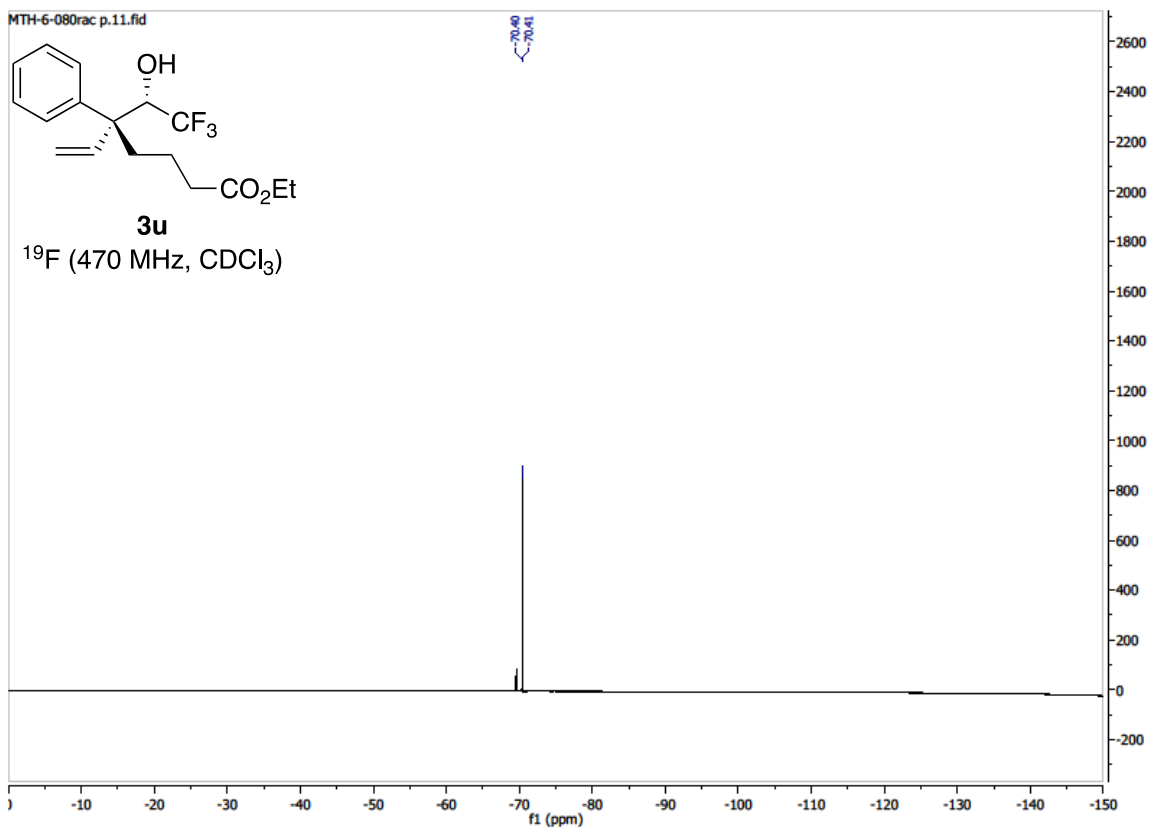
HRMS (ESI+Na, *m/z*) for C<sub>17</sub>H<sub>21</sub>F<sub>3</sub>O<sub>3</sub>: calcd. = 353.1335; found = 353.1336.

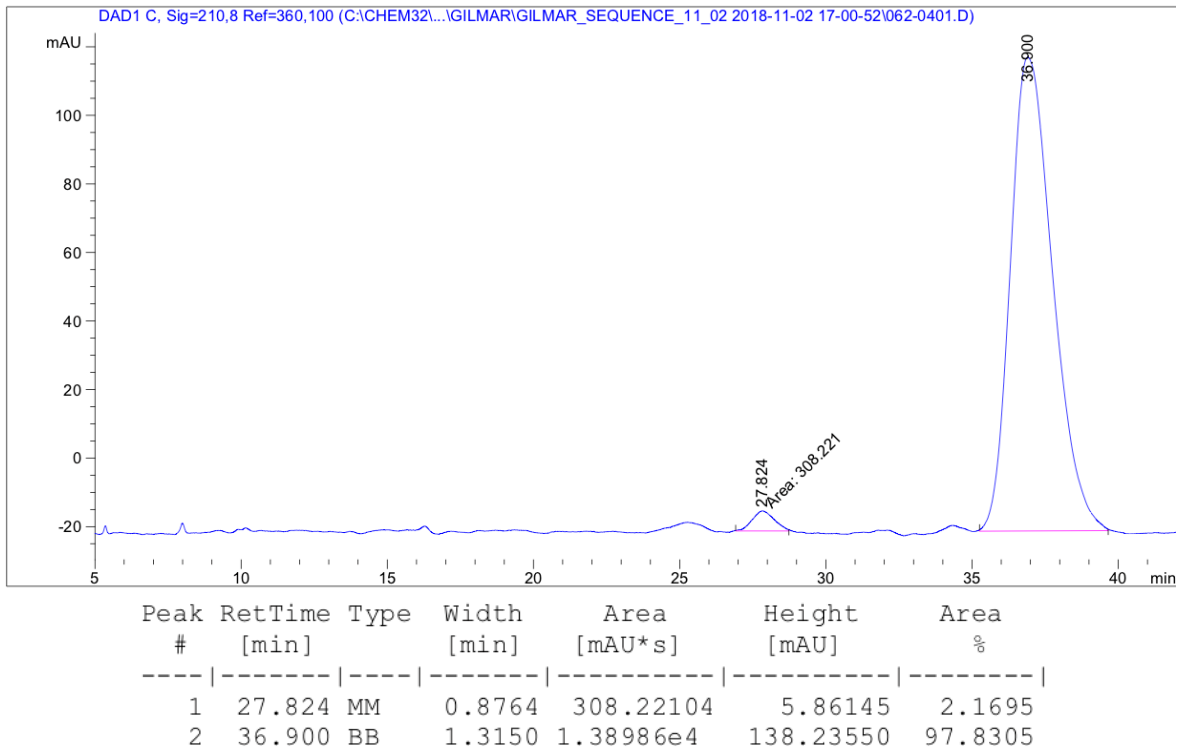
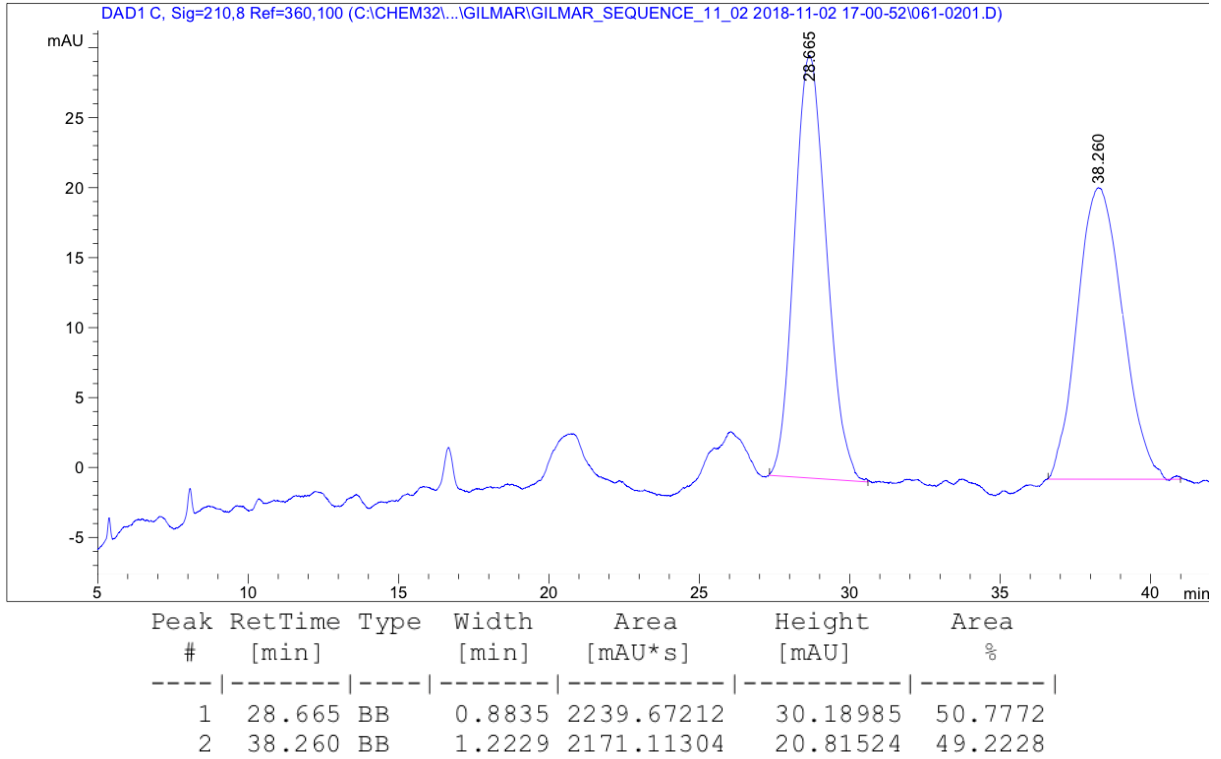
FTIR (neat): 3437, 2981, 2947, 1731, 1600, 1448, 1264, 1156, 1121, 702 cm<sup>-1</sup>.

HPLC: (Chiralcel column OJ-H, Hexane:2-PrOH = 97:3, 1.0 mL/min, 210 nm) ee = 96%.

[α]<sub>D</sub><sup>24</sup> = +10.3 (c = 0.94, CHCl<sub>3</sub>).



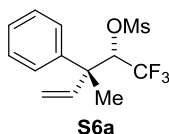






## Procedures and Spectral Data for the Elaboration of Adduct 3a

### **(2*S*,3*R*)-1,1,1-trifluoro-3-methyl-3-phenylpent-4-en-2-yl methanesulfonate (S6a)**



To a stirred solution of alcohol **3a** (236 mg, 1.03 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) was added triethylamine (0.20 mL, 1.55 mmol) followed by methanesulfonyl chloride (0.096 mL, 1.23 mmol). The reaction mixture was stirred for 14 hours at room temperature. Saturated aqueous ammonium chloride (10 mL) was added and the phases were separated. The organic phase was washed with water (2 x 10 mL). The combined aqueous phases were washed with CH<sub>2</sub>Cl<sub>2</sub> (2 x 10 mL). The combined organic phases were washed with brine, dried (MgSO<sub>4</sub>), filtered and the solvent removed *in vacuo*. The residue was subjected to flash column chromatography (SiO<sub>2</sub>, 96:4 hexanes:ethyl acetate) to afford the title compound (276 mg, 0.89 mmol) as a colorless oil in 87% yield. Note: the starting material and product have identical R<sub>f</sub> values so TLC is not an appropriate method for determining reaction completion.

R<sub>f</sub> = 0.41 (9:1 hexanes:EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.41 (d, *J* = 8.9 Hz, 2H), 7.37 (dd, *J* = 8.9, 8.9 Hz, 2H), 7.28 (t, *J* = 8.9 Hz, 1H), 6.42 (dd, *J* = 10.8, 17.4 Hz, 1H), 5.42 (d, *J* = 10.8 Hz, 1H), 5.33 (q, *J* = 6.9 Hz, 1H), 5.25 (d, *J* = 17.4 Hz, 1H), 2.53 (s, 3H), 1.63 (s, 3H).

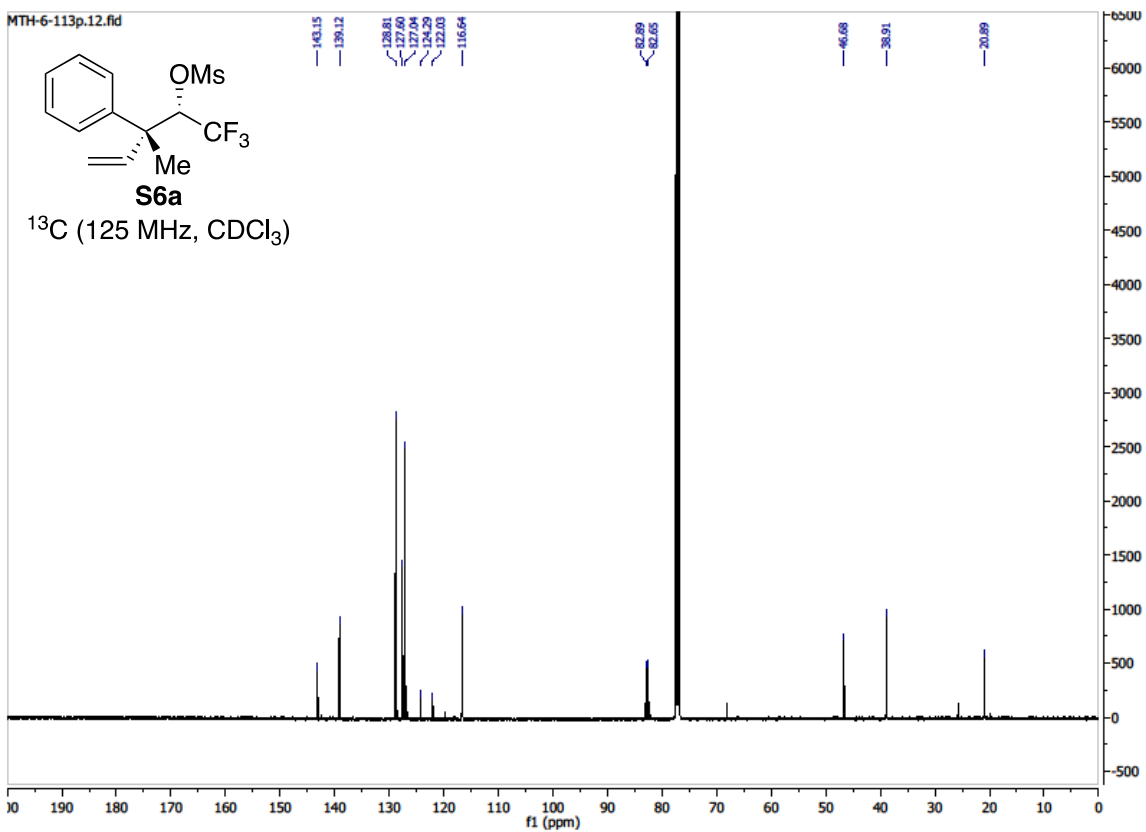
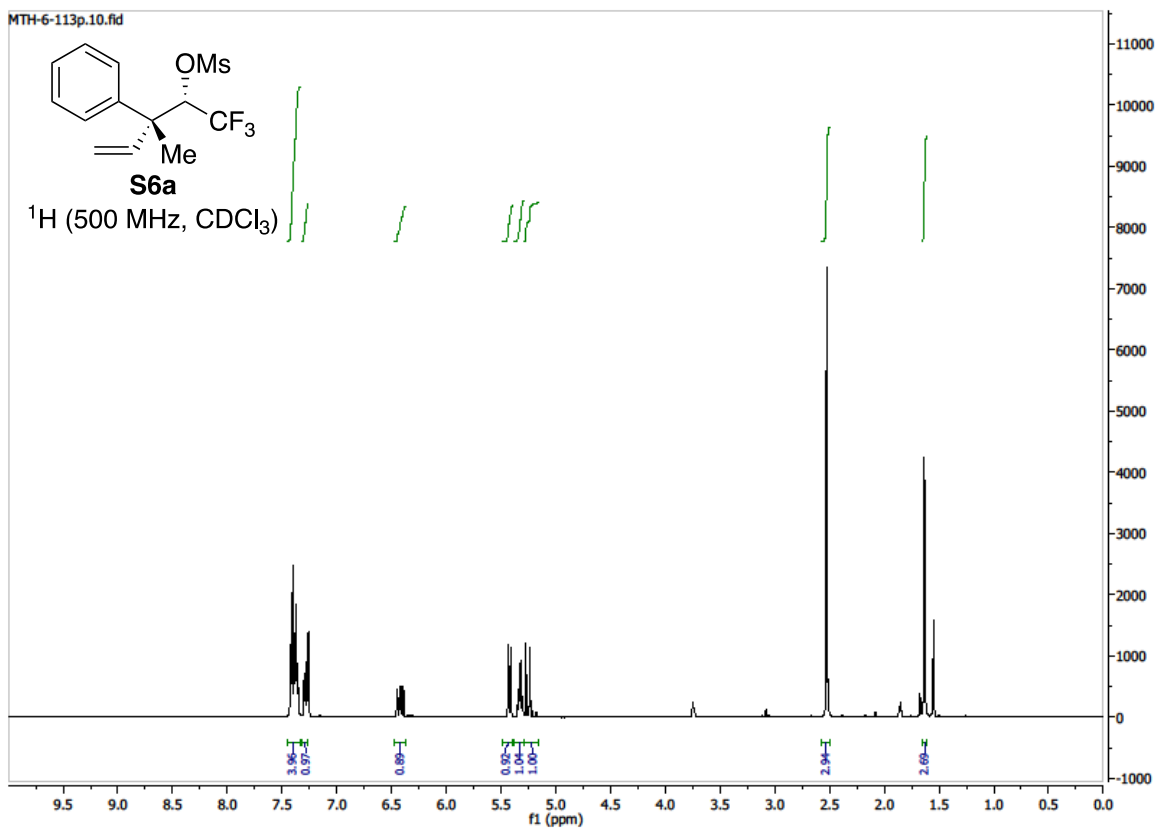
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 143.2, 139.1, 128.8, 127.6, 127.0, 123.3 (q, *J* = 284 Hz), 116.6, 82.8 (q, *J* = 30 Hz), 46.7, 38.9, 20.9.

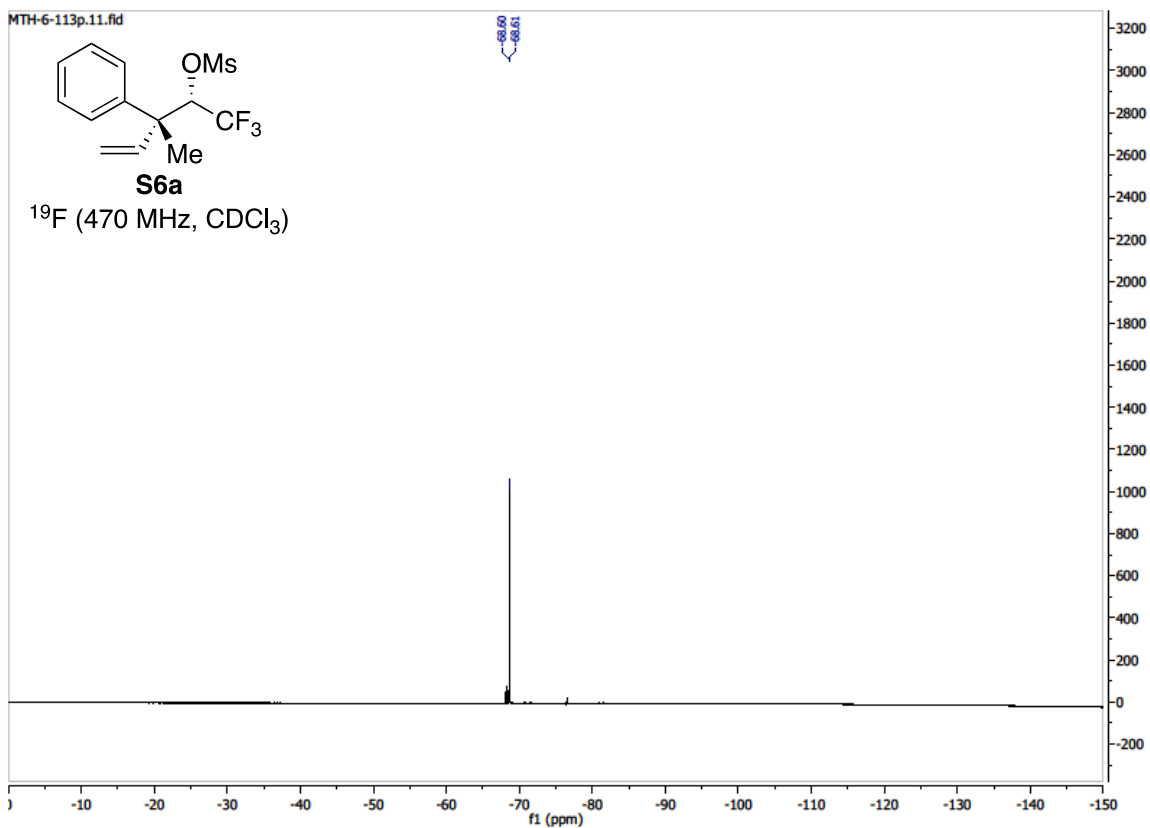
<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -68.6 (d, *J* = 6.9 Hz).

HRMS (ESI+Na, *m/z*) for C<sub>13</sub>H<sub>15</sub>F<sub>3</sub>O<sub>3</sub>S: calcd. = 331.0586; found = 331.0589.

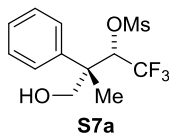
FTIR (neat): 2982, 1497, 1361, 1275, 1176, 1016, 964, 793 cm<sup>-1</sup>.

[α]<sub>D</sub><sup>24</sup> = +8.0 (c = 0.93, CHCl<sub>3</sub>).





**(2*S*,3*S*)-1,1,1-trifluoro-4-hydroxy-3-methyl-3-phenylbutan-2-yl methanesulfonate (S7a)**



To a stirred flask containing mesylate **S6a** (154 mg, 0.5 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) was added MeOH (1 mL) and the reaction mixture was cooled to -78 °C. Ozone was bubbled through the solution until the solution turned blue (~5 mins). N<sub>2</sub> was bubbled through the solution to remove the excess ozone. NaBH<sub>4</sub> (85 mg, 2.5 mmol) was added and the reaction mixture was allowed to warm to room temperature and stirred for 14 hours. Saturated aqueous ammonium chloride (5 mL) was added and the phases were separated. The aqueous phase was washed with CH<sub>2</sub>Cl<sub>2</sub> (2 x 5 mL). The combined organic phases were washed with brine, dried (MgSO<sub>4</sub>), filtered and the solvent removed *in vacuo*. The residue was subjected to flash column chromatography (SiO<sub>2</sub>, 75:25 hexanes:ethyl acetate) to afford the title compound (136 mg, 0.44 mmol) as a colorless oil in 87% yield.

R<sub>f</sub> = 0.23 (80:20 hexanes:EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.49 (d, *J* = 7.8 Hz, 2H), 7.39 (dd, *J* = 7.7, 8.4 Hz, 2H), 7.32 (t, *J* = 7.7 Hz, 1H), 5.61 (q, *J* = 7.4 Hz, 1H), 3.95 (dd, *J* = 6.1, 11.5 Hz, 1H), 3.60 (dd, *J* = 7.1, 11.5 Hz, 1H), 3.17 (s, 3H), 1.96 (t, *J* = 6.5 Hz, 1H, OH), 1.50 (q, *J* = 1.2 Hz, 3H).

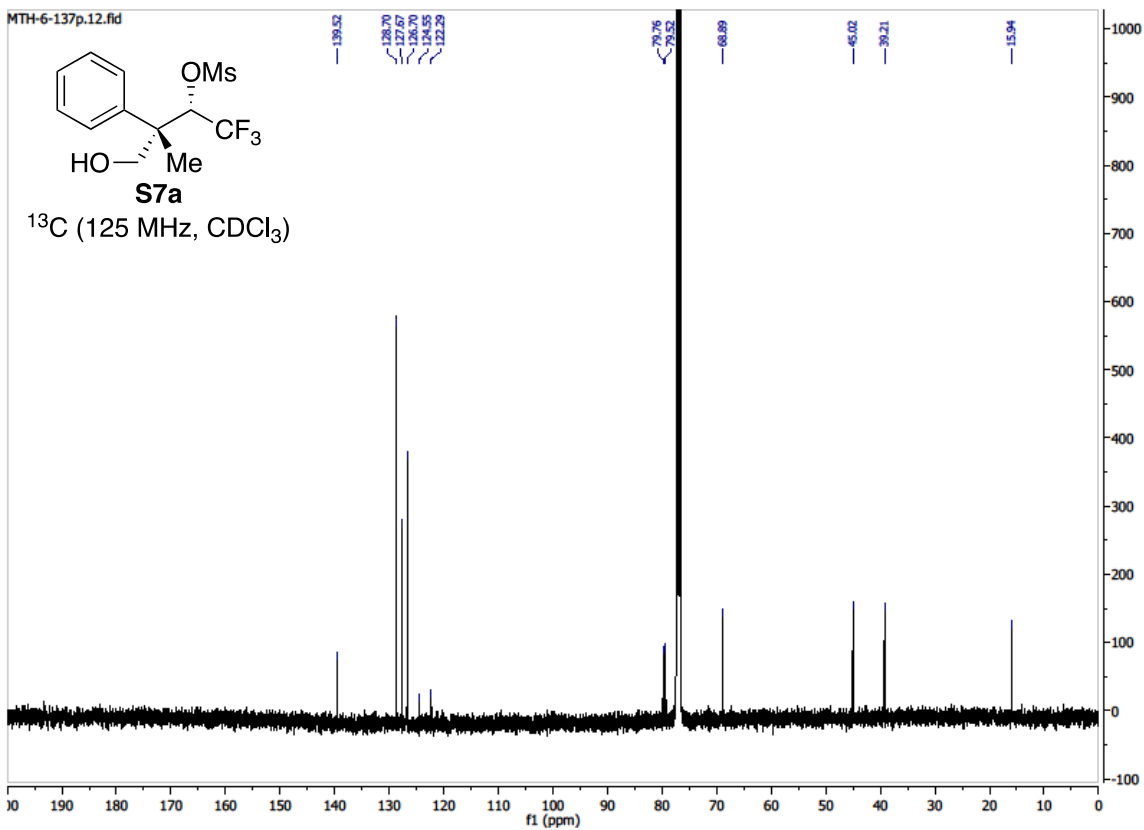
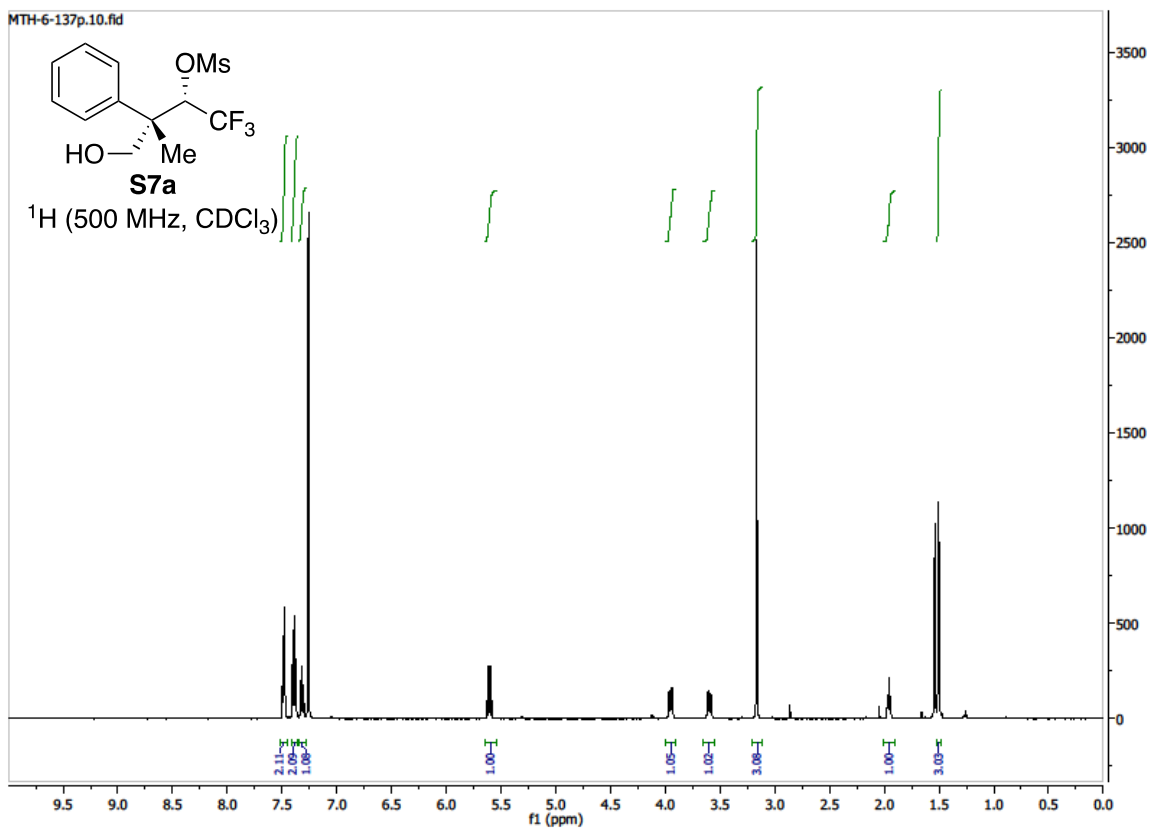
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 139.5, 128.7, 127.7, 126.7, 123.5 (q, *J* = 286 Hz), 79.6 (q, *J* = 29 Hz), 68.9, 45.0, 39.2, 15.9.

<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -68.1 (d, *J* = 7.4 Hz).

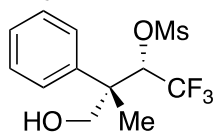
HRMS (ESI+Na, *m/z*) for C<sub>12</sub>H<sub>15</sub>F<sub>3</sub>O<sub>4</sub>S: calcd. = 335.0535; found = 335.0532

FTIR (neat): 3539, 2940, 1498, 1357, 1272, 1176, 1051, 1011, 963, 830, 699 cm<sup>-1</sup>.

[α]<sub>D</sub><sup>24</sup> = +21.3 (c = 0.75, CHCl<sub>3</sub>).

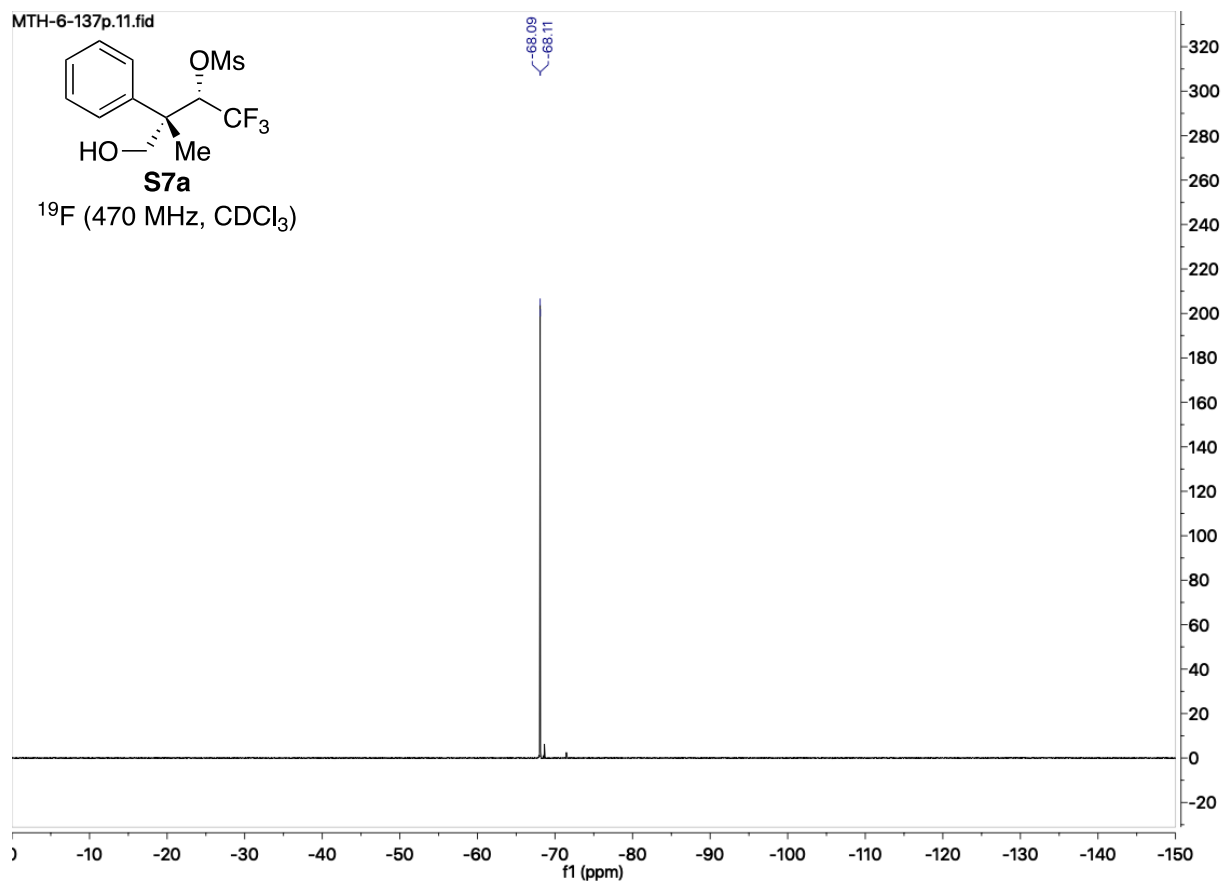


MTH-6-137p.11.fid

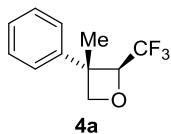


**S7a**

<sup>19</sup>F (470 MHz, CDCl<sub>3</sub>)



**(2*S*,3*S*)-3-methyl-3-phenyl-2-(trifluoromethyl)oxetane (4a)**



To a stirred solution of mesylate **S7a** (130 mg, 0.42 mmol) in THF (4.2 mL) in a pressure tube was added NaH (25 mg, 0.63 mmol, 60% w/w in mineral oil). The reaction mixture was heated to 70 °C for 14 hrs. Water (2 mL) was added followed by Et<sub>2</sub>O (3 mL) and the phases were separated. The organic phase was washed with water (2 x 2 mL) and the combined aqueous phases were washed with Et<sub>2</sub>O (2 x 3 mL). The combined organic phases were washed with brine, dried (MgSO<sub>4</sub>), filtered and the solvent removed *in vacuo*. The residue was subjected to flash column chromatography (SiO<sub>2</sub>, 94:6 hexanes:ethyl acetate) to afford the title compound (69 mg, 0.32 mmol) as a colorless oil in 76% yield.

R<sub>f</sub> = 0.49 (90:10 hexanes:EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.40 (t, *J* = 8.0 Hz, 2H), 7.29 (t, *J* = 8.0 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 5.08 (q, *J* = 7.6 Hz, 1H), 5.03 (d, *J* = 5.3 Hz, 1H), 4.71 (d, *J* = 5.3 Hz, 1H), 1.67 (q, *J* = 1.5 Hz, 3H).

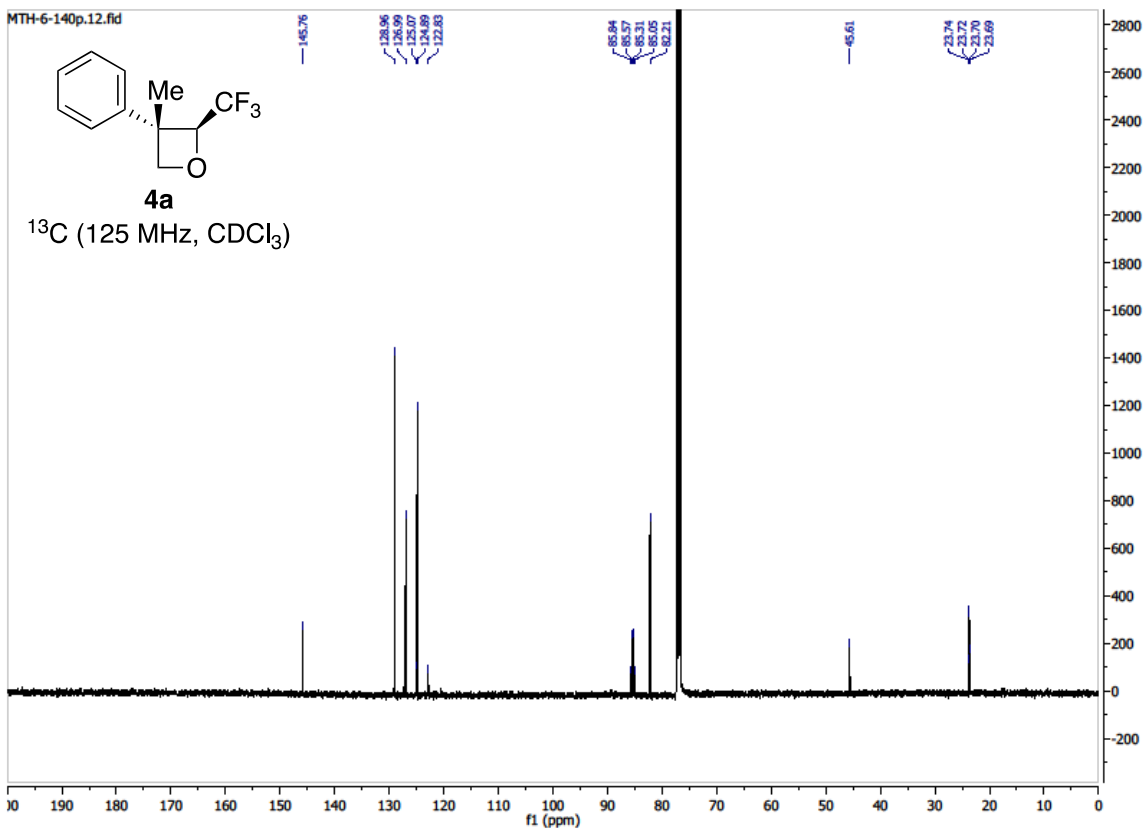
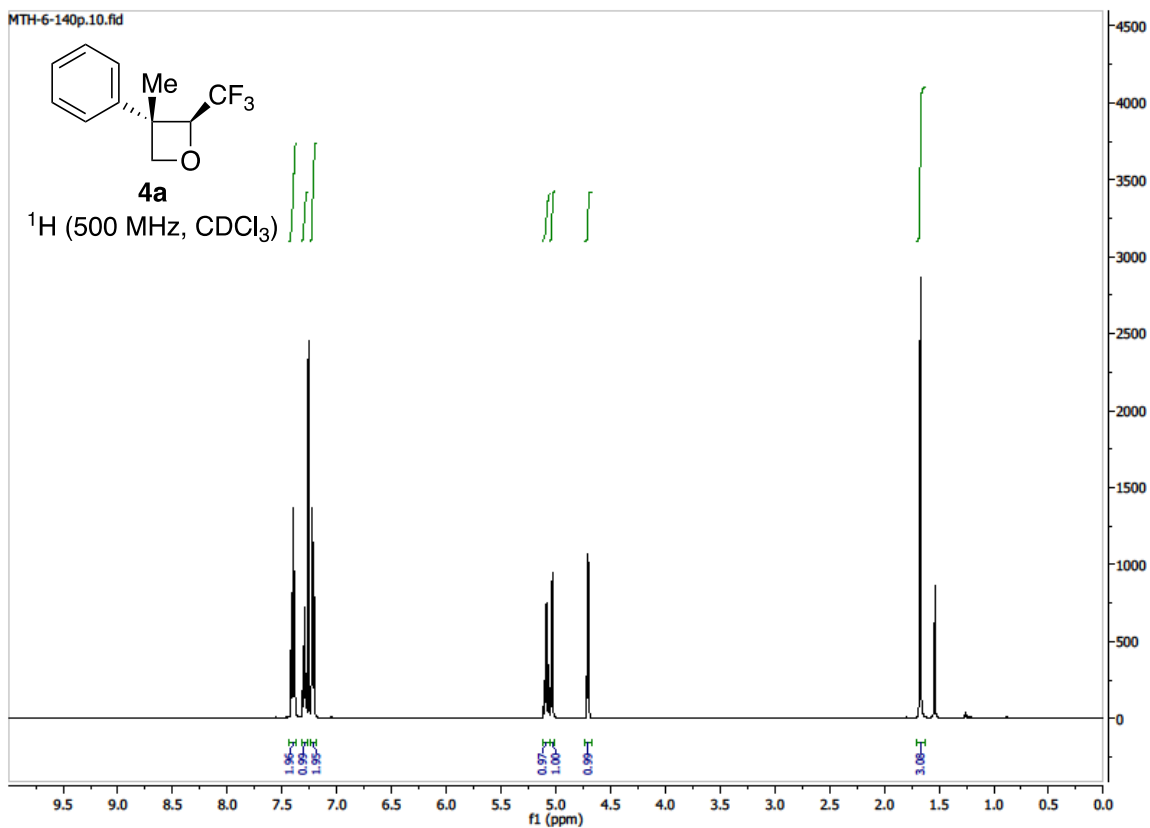
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 145.8, 129.0, 127.0, 124.9, 123.9 (q, *J* = 282 Hz), 85.4 (q, *J* = 32 Hz), 82.2, 45.6, 23.7 (q, *J* = 2.3 Hz).

<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -74.9 (qd, *J* = 1.5, 7.6 Hz).

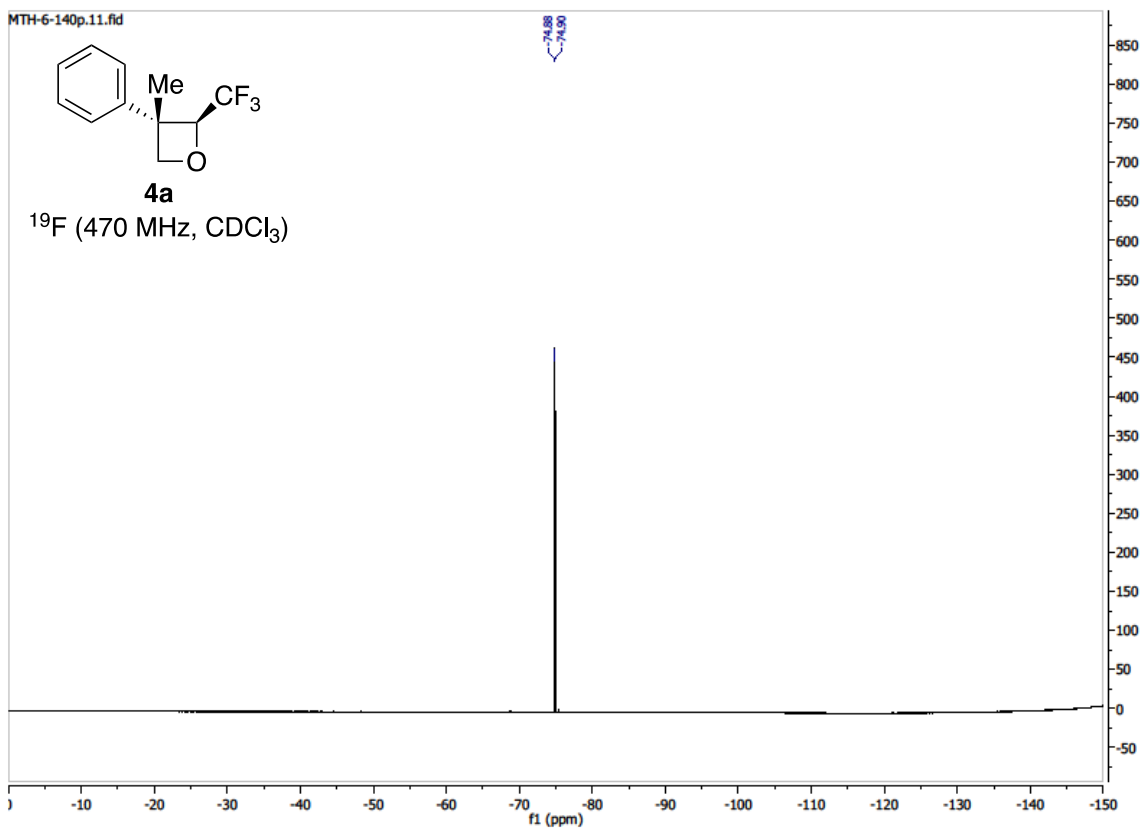
HRMS (CI+, *m/z*) for C<sub>11</sub>H<sub>12</sub>OF<sub>3</sub>: calcd. = 217.0840; found = 217.0842.

FTIR (neat): 2974, 2894, 1498, 1392, 1291, 1153, 1128, 1038, 913, 763, 700 cm<sup>-1</sup>.

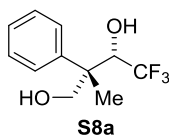
[α]<sub>D</sub><sup>24</sup> = +32.0 (c = 1.0, CHCl<sub>3</sub>).







**(2*S*,3*S*)-4,4,4-trifluoro-2-methyl-2-phenylbutane-1,3-diol (S8a)**



To a stirred flask containing fluoral adduct **3a** (94 mg, 0.41 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (8 mL) was added MeOH (1 mL) and the reaction mixture cooled to -78 °C. Ozone was bubbled through the solution until the solution turned blue (~5 mins). N<sub>2</sub> was bubbled through the solution to remove the excess ozone. NaBH<sub>4</sub> (78 mg, 2.04 mmol) was added and the reaction mixture was allowed to warm to room temperature and stirred for 3 hours. Aqueous 1N HCl (5 mL) and EtOAc (20 mL) were added and the phases were separated. The aqueous phase was washed with EtOAc (2 x 5 mL). The combined organic phases were washed with brine, dried (MgSO<sub>4</sub>), filtered and the solvent removed *in vacuo*. The residue was subjected to flash column chromatography (SiO<sub>2</sub>, 75:25 hexanes:ethyl acetate) to afford the title compound (79 mg, 0.34 mmol) as a colorless oil in 84% yield.

R<sub>f</sub> = 0.23 (70:30 hexanes:EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.44 (d, *J* = 7.7 Hz, 2H), 7.38 (dd, *J* = 7.7, 7.7 Hz, 2H), 7.29 (t, *J* = 7.7 Hz, 1H), 4.61 (q, *J* = 6.5 Hz, 1H), 3.93 (d, *J* = 11.1 Hz, 1H), 3.90 (d, *J* = 11.1 Hz, 1H), 3.75 (br d, *J* = 4.0 Hz, 1H, OH), 2.22 (br s, 1H, OH), 1.47 (q, *J* = 1.4 Hz, 3H).

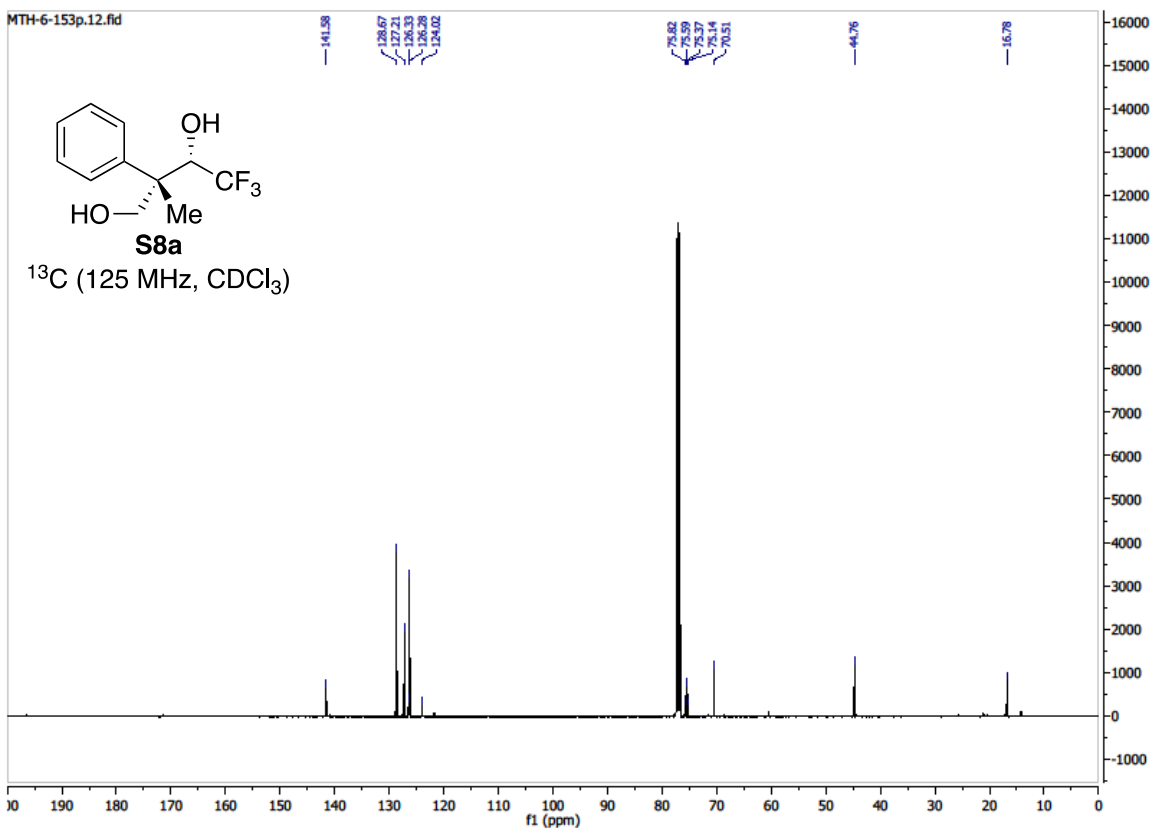
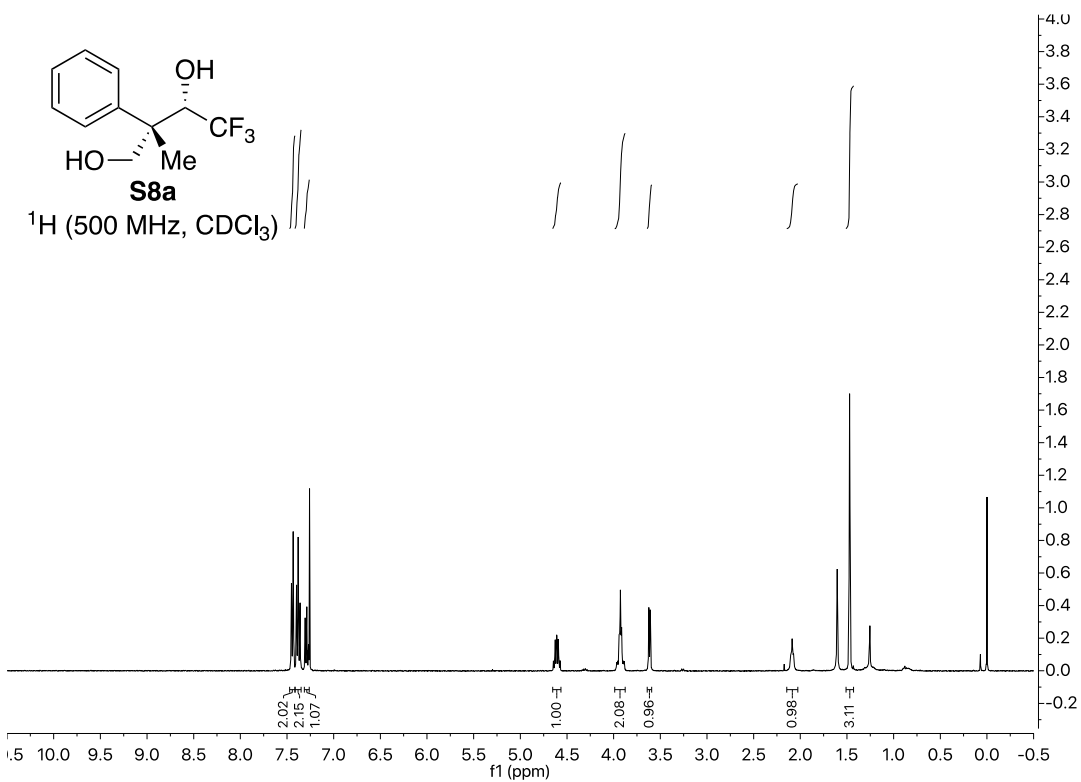
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 141.6, 128.7, 127.2, 126.3, 125.2 (q, *J* = 284 Hz), 75.5 (q, *J* = 28 Hz), 70.5, 44.8, 16.8.

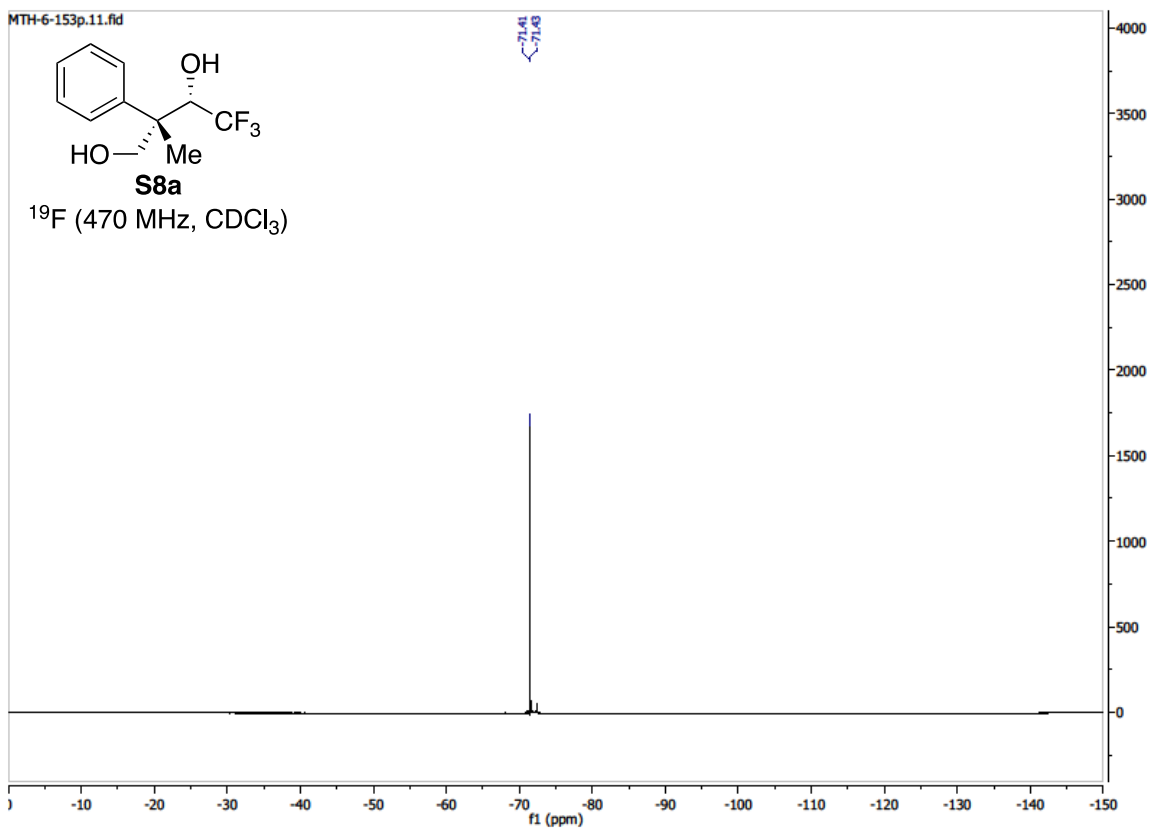
<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -71.42 (d, *J* = 6.7 Hz).

HRMS (EI+, *m/z*) for C<sub>11</sub>H<sub>13</sub>O<sub>2</sub>F<sub>3</sub>: calcd. = 234.0868; found = 234.0872.

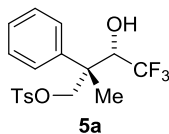
FTIR (neat): 3365, 29991, 1499, 1266, 1166, 1107, 1027, 700 cm<sup>-1</sup>.

[α]<sub>D</sub><sup>24</sup> = -4 (c = 1.0, CHCl<sub>3</sub>).





**(2*S*,3*S*)-4,4,4-trifluoro-3-hydroxy-2-methyl-2-phenylbutyl 4-methylbenzenesulfonate (5a)**



To a stirred solution of diol **S8a** (76 mg, 0.32 mmol) in 2,6-lutidine (0.6 mL, 0.5 M) was added TsCl (124 mg, 0.65 mmol) and the reaction mixture was stirred for 14 hours at room temperature. EtOAc (10 mL) and aqueous 1N HCl (10 mL) were added and the phases separated. The organic phase was washed with aqueous 1N HCl (10 mL). The combined aqueous phases were washed with EtOAc (2 x 10 mL). The combined organic phases were washed with brine, dried (MgSO<sub>4</sub>), filtered and the solvent removed *in vacuo*. The residue was subjected to flash column chromatography (SiO<sub>2</sub>, 80:20 hexanes:EtOAc) to afford the title compound (93 mg, 0.24 mmol) as a white solid in 75% yield.

R<sub>f</sub> = 0.34 (70:30 hexanes:EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.64 (d, *J* = 8.5 Hz, 2H), 7.30-7.22 (m, 7H), 4.52 (dq, *J* = 6.9 Hz, 6.9 Hz, 1H), 4.41 (d, *J* = 9.5 Hz, 1H), 3.88 (d, *J* = 9.5 Hz, 1H), 2.91 (d, *J* = 6.9 Hz, 1H, OH), 2.41 (s, 3H), 1.43 (s, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 145.1, 139.6, 132.2, 129.9, 128.4, 127.9, 127.4, 126.6, 124.9 (q, *J* = 285 Hz), 74.6 (q, *J* = 1 Hz), 72.6 (q, *J* = 29 Hz), 44.2, 21.7, 16.0 (q, *J* = 2 Hz).

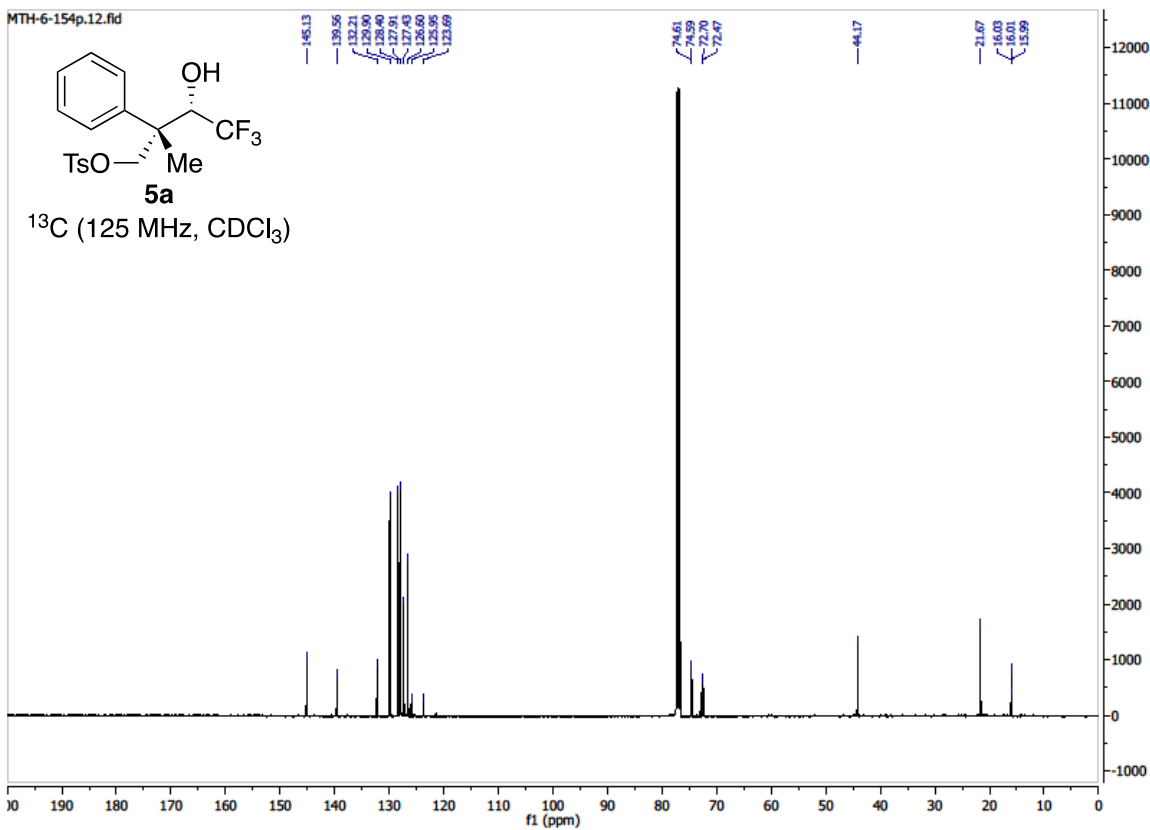
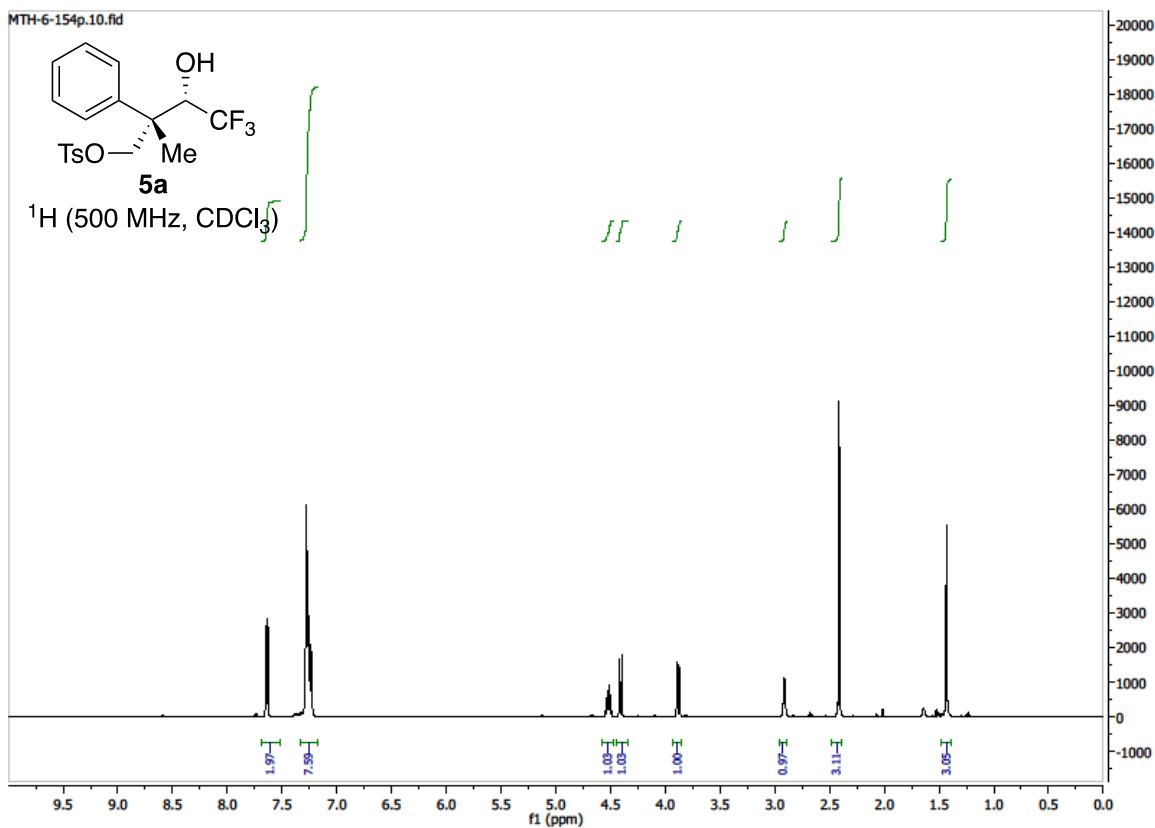
<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -70.6 (d, *J* = 6.9 Hz).

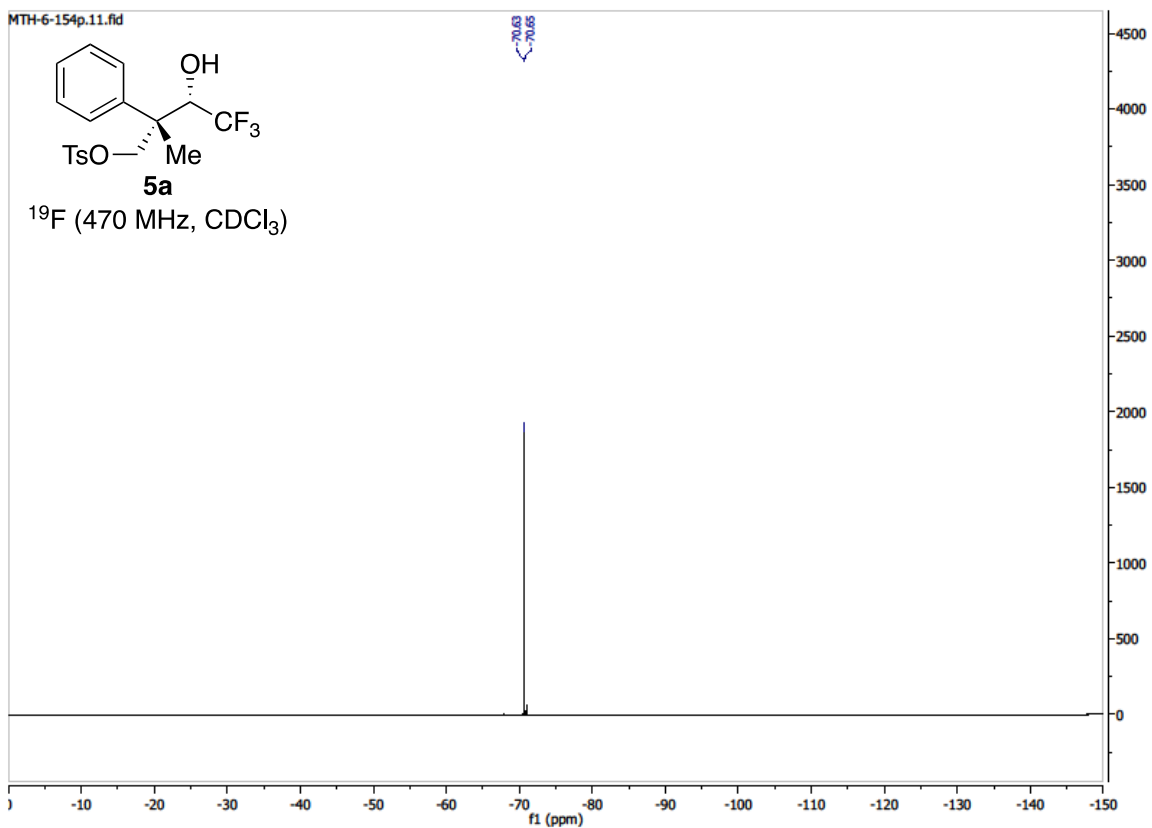
HRMS (ESI+Na, *m/z*) for C<sub>18</sub>H<sub>19</sub>F<sub>3</sub>N<sub>4</sub>S: calcd. = 411.0848; found = 411.0848

FTIR (neat): 3504, 3044, 1599, 1355, 1172, 977, 812 cm<sup>-1</sup>.

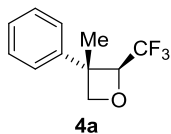
[α]<sub>D</sub><sup>24</sup> = -4 (c = 1.0, CHCl<sub>3</sub>).

MP = 84-87 °C



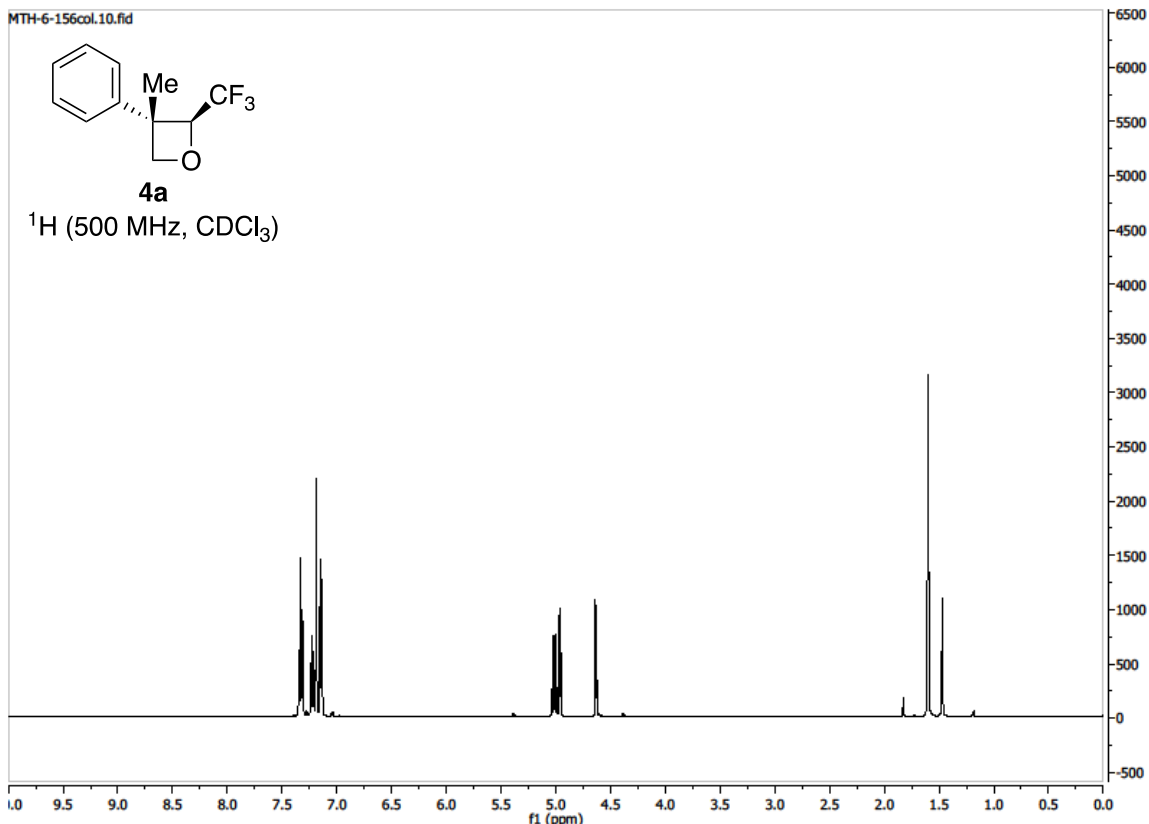


**(2*S*,3*S*)-3-methyl-3-phenyl-2-(trifluoromethyl)oxetane (4a)**



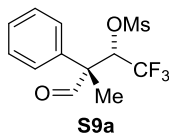
To a stirred solution of tosyl protected alcohol **5a** (71 mg, 0.18 mmol) in THF (1 mL) in a pressure tube was added NaH (11 mg, 0.27 mmol, 60% w/w in mineral oil). The reaction mixture was heated to 25 °C for 14 hrs. Water (2 mL) was added followed by Et<sub>2</sub>O (3 mL) and the phases were separated. The organic phase was washed with water (2 x 2 mL) and the combined aqueous phases were washed with Et<sub>2</sub>O (2 x 3 mL). The combined organic phases were washed with brine, dried (MgSO<sub>4</sub>), filtered and the solvent removed *in vacuo*. The residue was subjected to flash column chromatography (SiO<sub>2</sub>, 93:7 hexanes:ethyl acetate) to afford the title compound (27 mg, 0.12 mmol) as a colorless oil in 68% yield.

The data collected on this sample was in total agreement with the data collected above through the reaction of mesyl protected alcohol **S7a**.





**(2S,3R)-1,1,1-trifluoro-3-methyl-4-oxo-3-phenylbutan-2-yl methanesulfonate (S9a)**



A stirred flask containing mesylate **S6a** (154 mg, 0.5 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) was cooled to -78 °C. Ozone was bubbled through the solution until the solution turned blue (~5 mins). N<sub>2</sub> was bubbled through the solution to remove the excess ozone. PPh<sub>3</sub> (197 mg, 0.75 mmol) was added and the reaction mixture was allowed to warm to room temperature and stirred for 4 hours. The solvent was removed *in vacuo*. The residue was subjected to flash column chromatography (SiO<sub>2</sub>, 85:15 hexanes:EtOAc) to afford the title compound (142 mg, 0.46 mmol) as a light yellow solid in 92% yield.

R<sub>f</sub> = 0.18 (85:15 hexanes:EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 9.34 (s, 1H), 7.44 (dd, *J* = 8.1, 8.1 Hz, 2H), 7.39 (t, *J* = 8.1 Hz, 1H), 7.32 (d, *J* = 8.1 Hz, 2H), 5.76 (q, *J* = 6.5 Hz, 1H), 3.11 (s, 3H), 1.77 (s, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 196.4, 132.4, 129.5, 129.2, 128.0, 123.2 (q, *J* = 282 Hz), 77.8 (q, *J* = 29.9 Hz), 55.4, 39.6, 13.9.

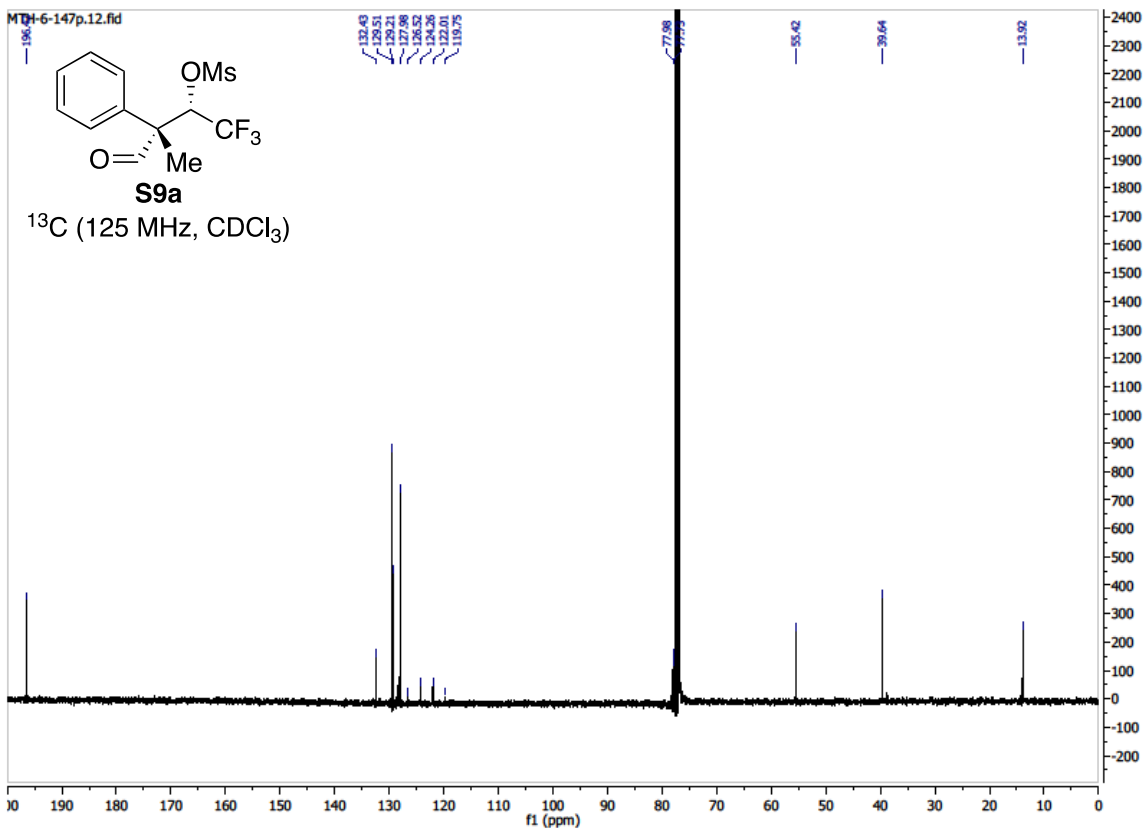
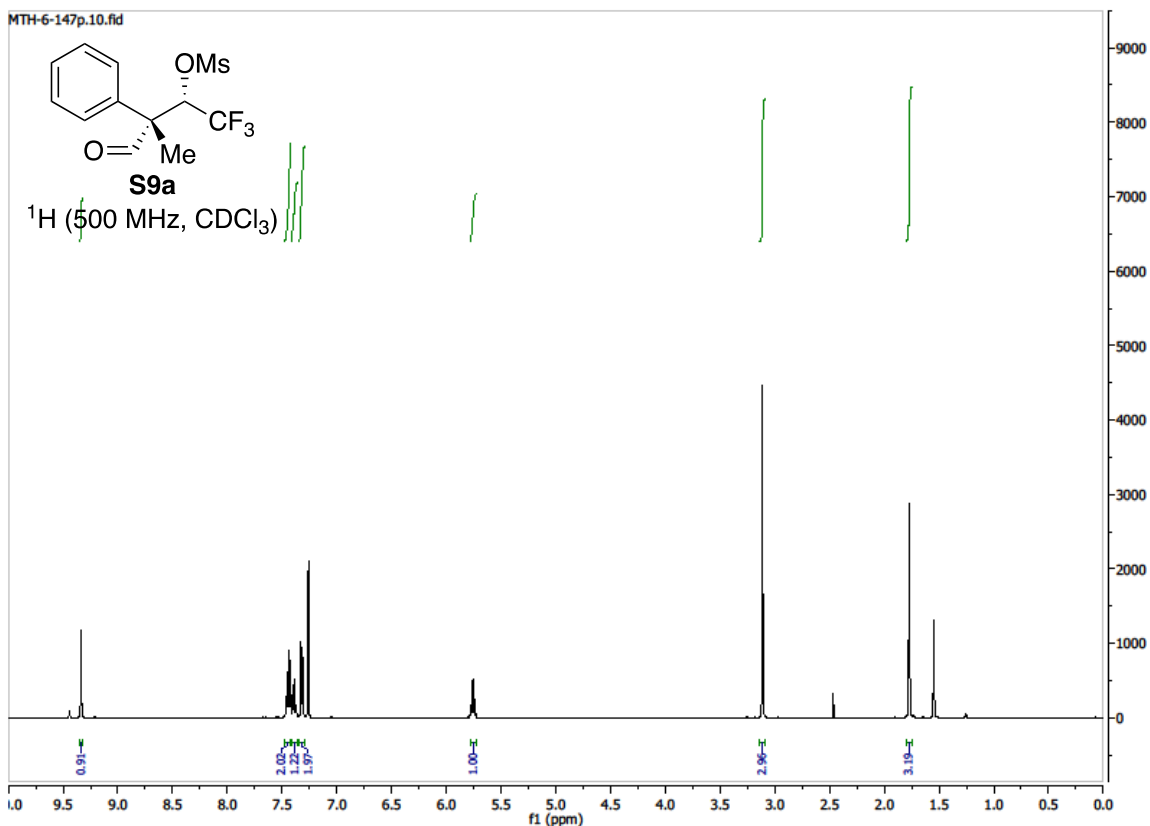
<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -68.7 (d, *J* = 6.5 Hz).

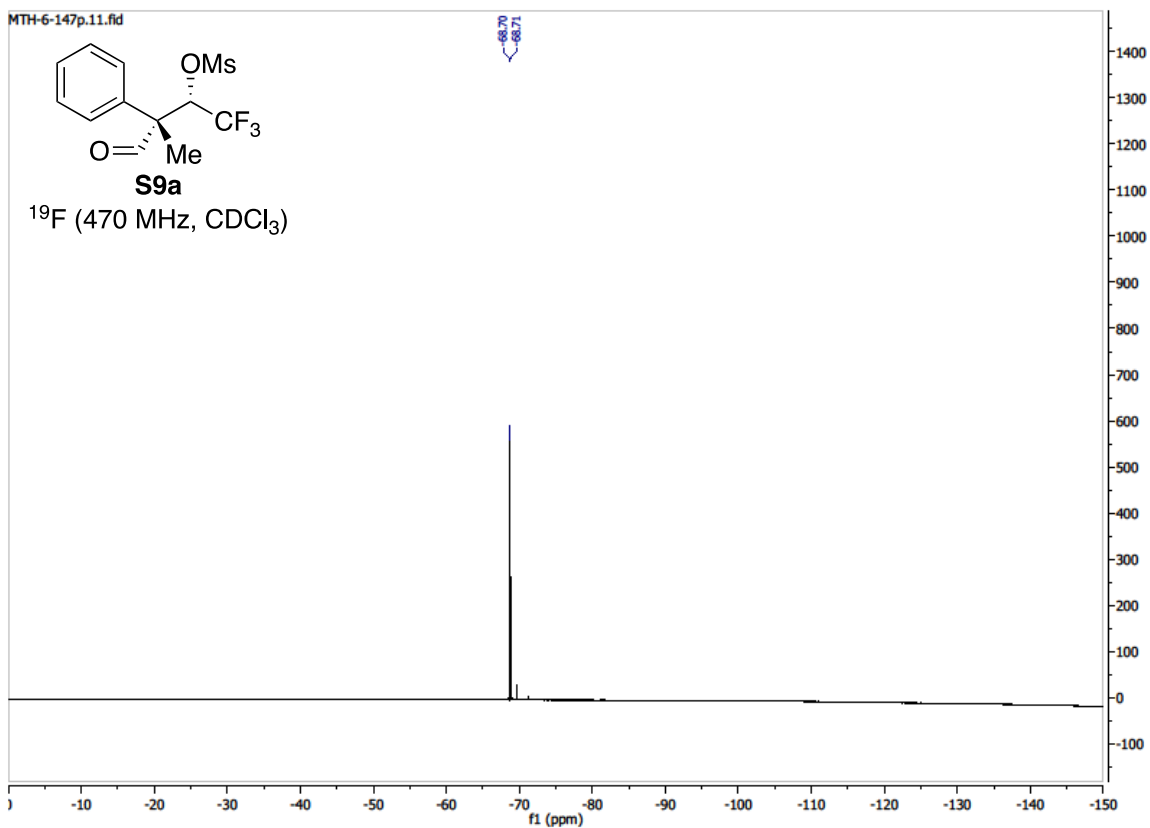
HRMS (ESI+Na, *m/z*) for C<sub>12</sub>H<sub>13</sub>F<sub>3</sub>O<sub>4</sub>S: calcd. = 333.0379; found = 333.0378

FTIR (neat): 3041, 1727, 1497, 1360, 1270, 1179, 1021, 966, 830 cm<sup>-1</sup>.

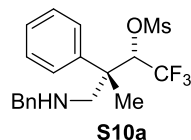
[α]<sub>D</sub><sup>24</sup> = +46 (c = 0.3, CHCl<sub>3</sub>).

MP = 94-97 °C





**(2*S*,3*S*)-4-(benzylamino)-1,1,1-trifluoro-3-methyl-3-phenylbutan-2-yl methanesulfonate (S10a)**



To a stirred solution of aldehyde **S9a** (83 mg, 0.26 mmol) in toluene (0.8 mL) was added AcOH (0.015 mL, 0.26 mmol) followed by benzyl amine (0.057 mL, 0.52 mmol) and 4 Å molecular sieves (80 mg). The reaction mixture was heated to 60 °C for 1 hour. The reaction mixture was cooled to 0 °C and NaBH<sub>3</sub>CN (25 mg, 0.42 mmol) was added in a single portion. The reaction mixture was stirred at 25 °C for 3 hours. Saturated aqueous NaHCO<sub>3</sub> (2 mL) was added followed by EtOAc (3 mL) and the phases were separated. The organic phase was washed with water (2 x 2 mL) and the combined aqueous phases were washed with EtOAc (2 x 2 mL). The combined organic phases were washed with brine, dried (MgSO<sub>4</sub>), filtered and the solvent removed *in vacuo*. The residue was subjected to flash column chromatography (SiO<sub>2</sub>, 88:12 hexanes:EtOAc) to afford the title compound (79 mg, 0.20 mmol) as a light yellow oil in 76% yield.

R<sub>f</sub> = 0.26 (85:15 hexanes:EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.36 (d, *J* = 8.0 Hz, 2H), 7.35 (dd, *J* = 8.0, 8.0 Hz, 2H), 7.27 (m, 3H), 7.22 (m, 3H), 5.59 (q, *J* = 6.5 Hz, 1H), 3.72 (d, *J* = 12.2 Hz, 1H), 3.66 (d, *J* = 12.2 Hz, 1H), 3.11 (d, *J* = 12.2 Hz, 1H), 3.09 (s, 3H), 2.78 (d, *J* = 12.2 Hz, 1H), 1.58 (s, 3H).

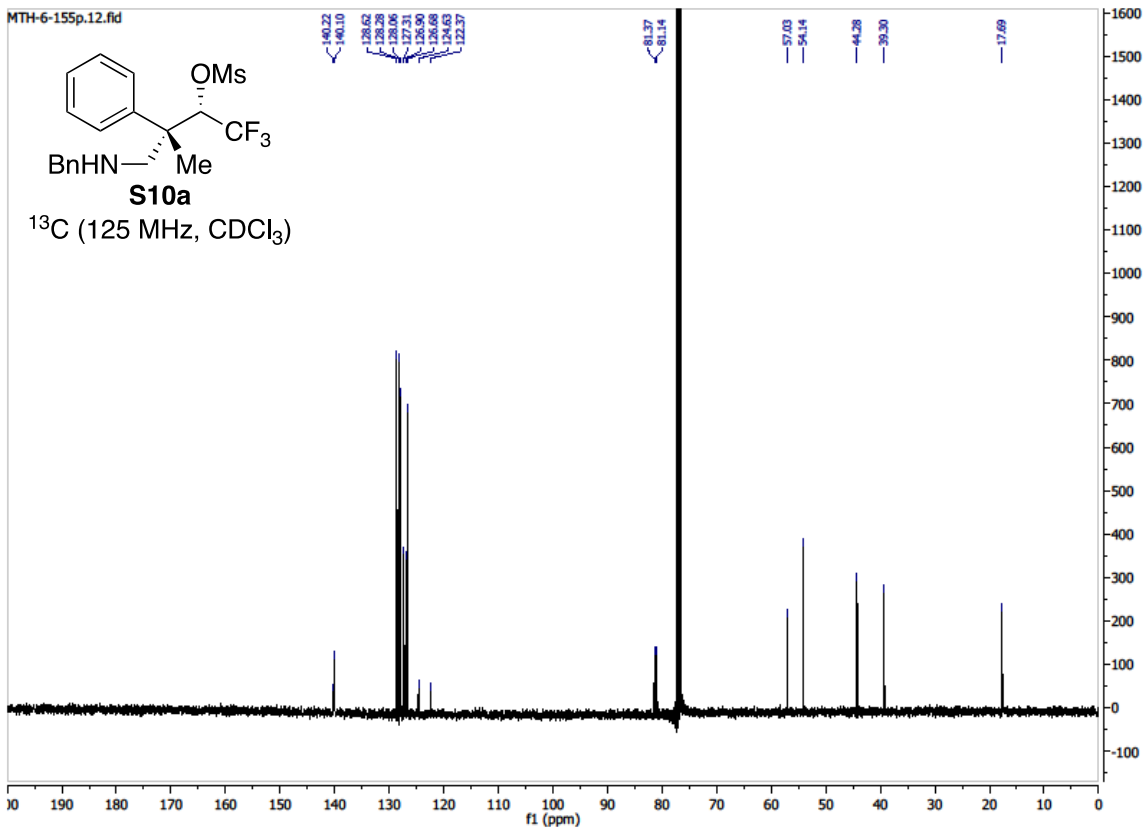
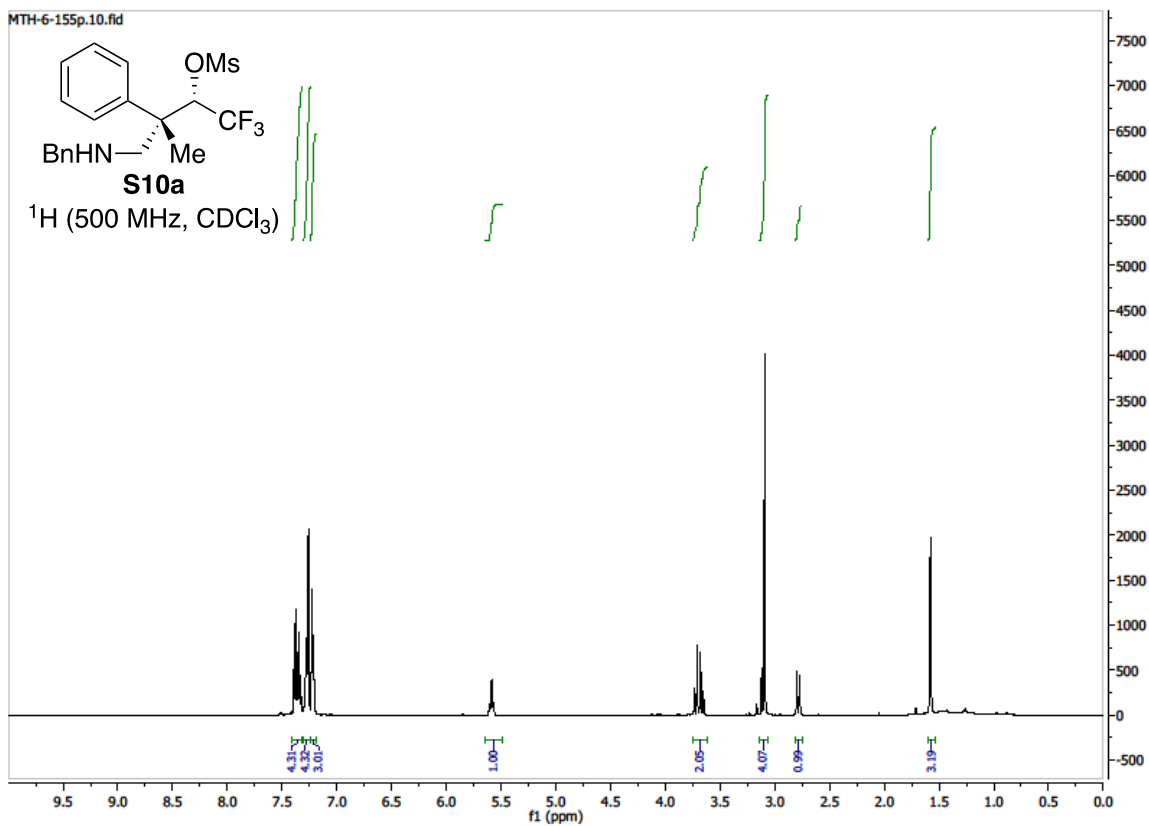
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 140.2, 140.1, 128.6, 128.3, 128.1, 127.3, 126.9, 126.7, 123.5 (q, *J* = 284 Hz), 81.3 (q, *J* = 29 Hz), 57.0, 54.1, 44.3, 39.3, 17.7.

<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -67.8 (d, *J* = 6.5 Hz).

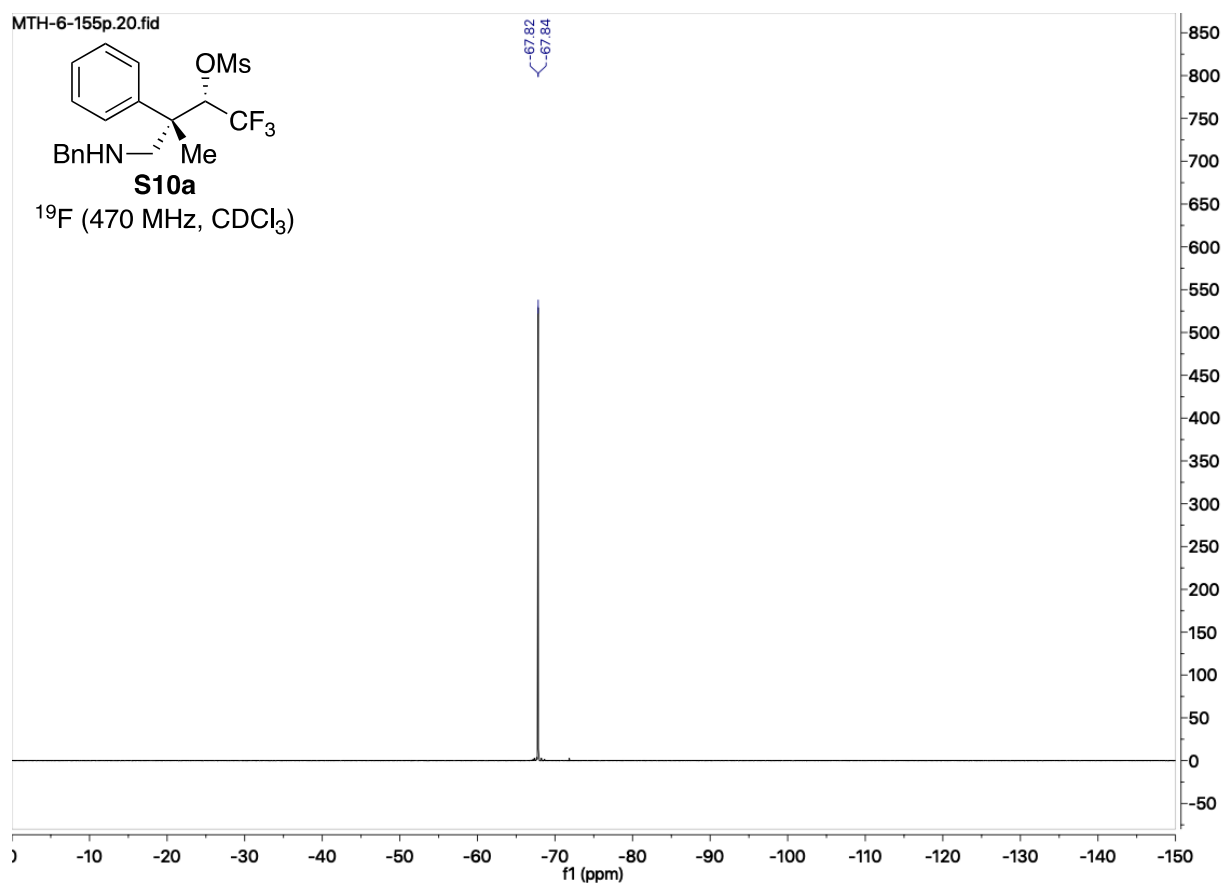
HRMS (ESI+H, *m/z*) for C<sub>19</sub>H<sub>22</sub>F<sub>3</sub>NO<sub>3</sub>S: calcd. = 402.1345; found = 402.1343

FTIR (neat): 3736, 3030, 2924, 1449, 1361, 1179, 963, 832, 699 cm<sup>-1</sup>.

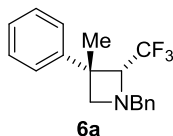
[α]<sub>D</sub><sup>24</sup> = +4 (c = 1.0, CHCl<sub>3</sub>).



MTH-6-155p.20.fid



**(2*R*,3*S*)-1-benzyl-3-methyl-3-phenyl-2-(trifluoromethyl)azetidine (6a)**



To a stirred solution of amine **S10a** (40 mg, 0.1 mmol) in *m*-xylenes (0.5 mL) in a sealable tube was added K<sub>2</sub>CO<sub>3</sub> (28 mg, 0.2 mmol). The reaction mixture was heated to 140 °C for 20 hours in a microwave reactor. The reaction mixture was cooled to 25 °C, filtered and the solvent removed *in vacuo*. The residue was subjected to flash column chromatography (SiO<sub>2</sub>, 95:5 hexanes:EtOAc) to afford the title compound (13.5 mg, 0.045 mmol) as a colorless oil in 45% yield along with recovered starting material (12.8 mg, 0.032 mmol).

R<sub>f</sub> = 0.48 (90:10 hexanes:EtOAc)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.55 (d, *J* = 7.2 Hz, 2H), 7.39-7.25 (m, 8H), 4.07 (d, *J* = 14.0 Hz, 1H), 3.90 (d, *J* = 7.0 Hz, 1H), 3.68 (q, *J* = 7.3 Hz, 1H), 3.61 (d, *J* = 14.0 Hz, 1H), 2.98 (d, *J* = 7.0 Hz, 1H), 1.63 (s, 3H).

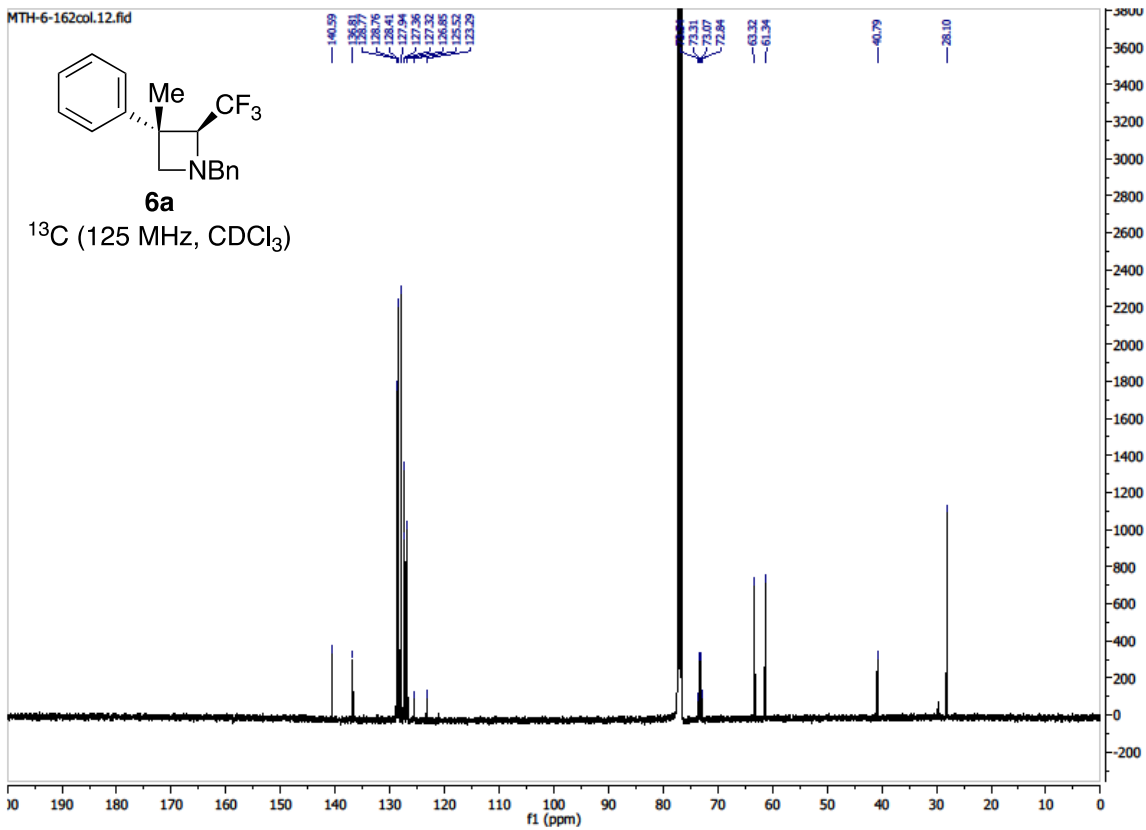
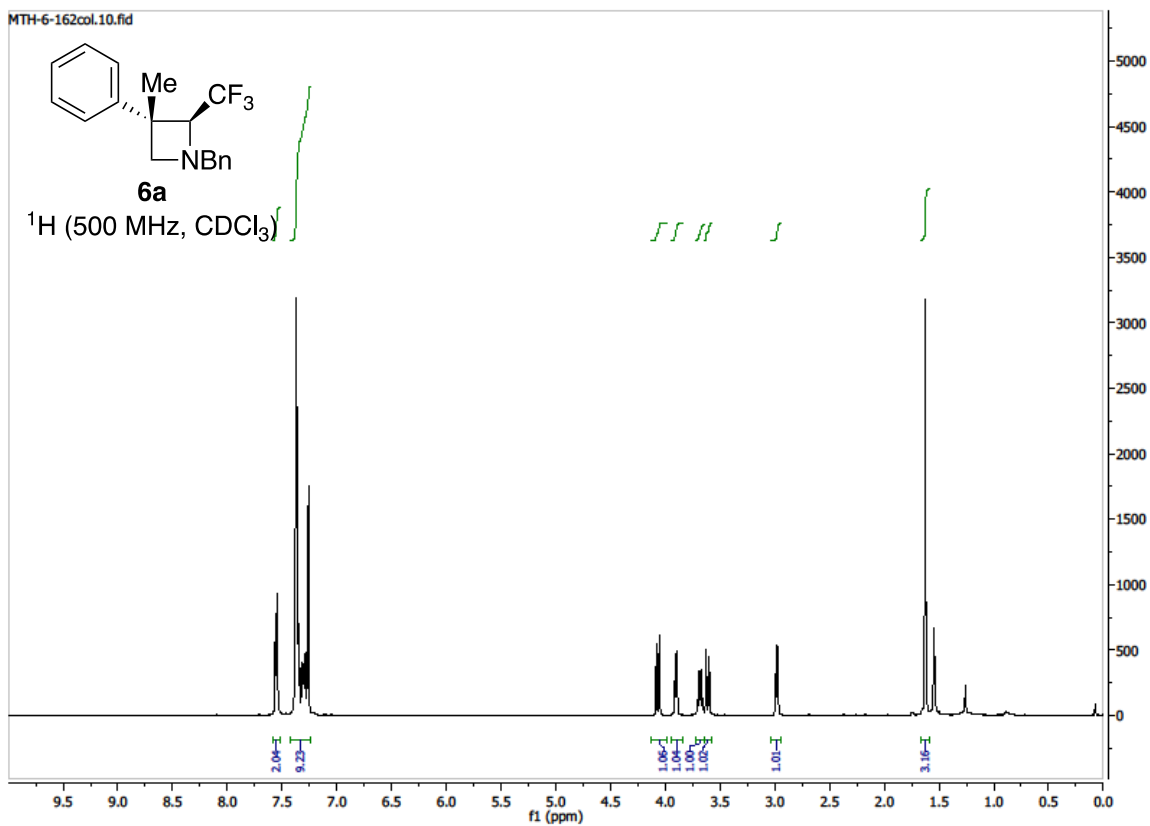
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 140.6, 136.8, 128.8, 128.4, 127.9, 127.4, 127.3, 126.9, 124.4 (q, *J* = 280 Hz), 73.2 (q, *J* = 29 Hz), 63.3, 61.3, 40.8, 28.1.

<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -70.6 (d, *J* = 7.3 Hz).

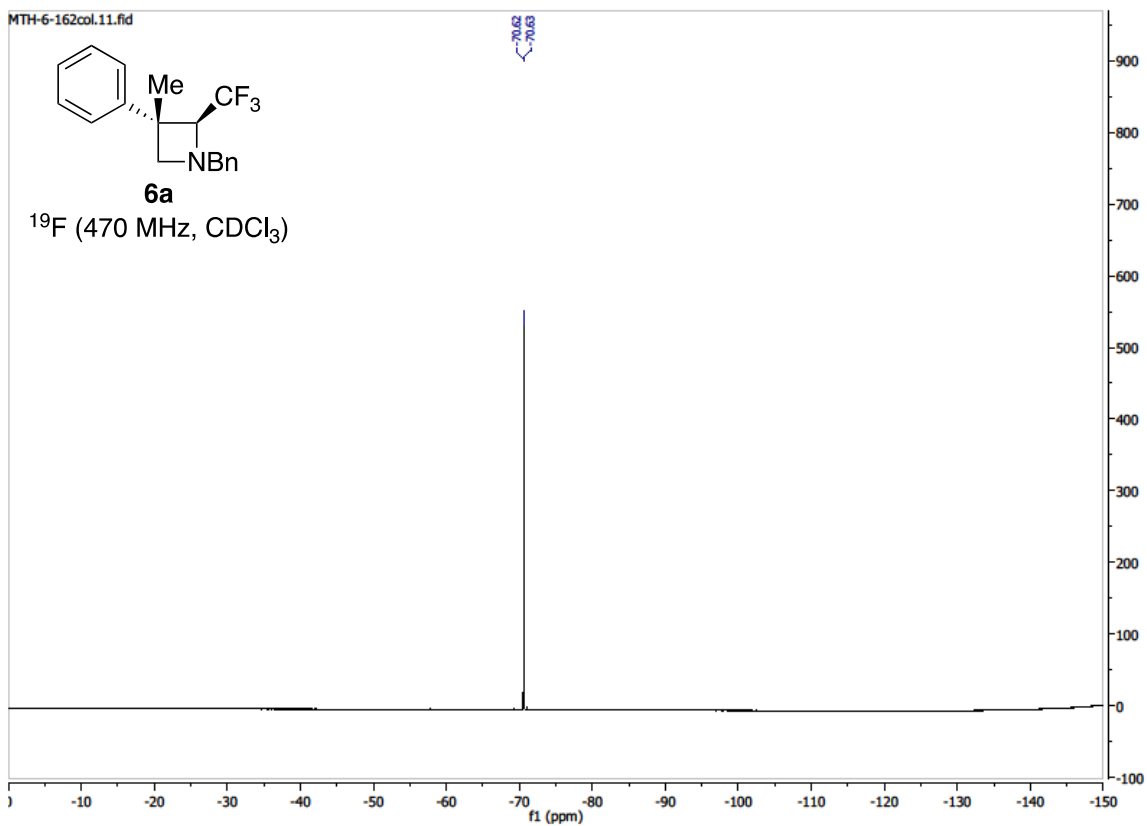
HRMS (ESI+H, *m/z*) for C<sub>18</sub>H<sub>18</sub>F<sub>3</sub>N: calcd. = 306.1464; found = 306.1465

FTIR (neat): 3029, 2927, 2851, 1497, 1294, 1127, 1030, 697 cm<sup>-1</sup>.

[α]<sub>D</sub><sup>24</sup> = -8.8 (c = 0.2, CHCl<sub>3</sub>).

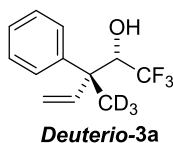






## Isotopic Labeling Studies

### **(2*S*,3*R*)-1,1,1-trifluoro-3-(methyl-d3)-3-phenylpent-4-en-2-ol (*Deuterio-3a*)**



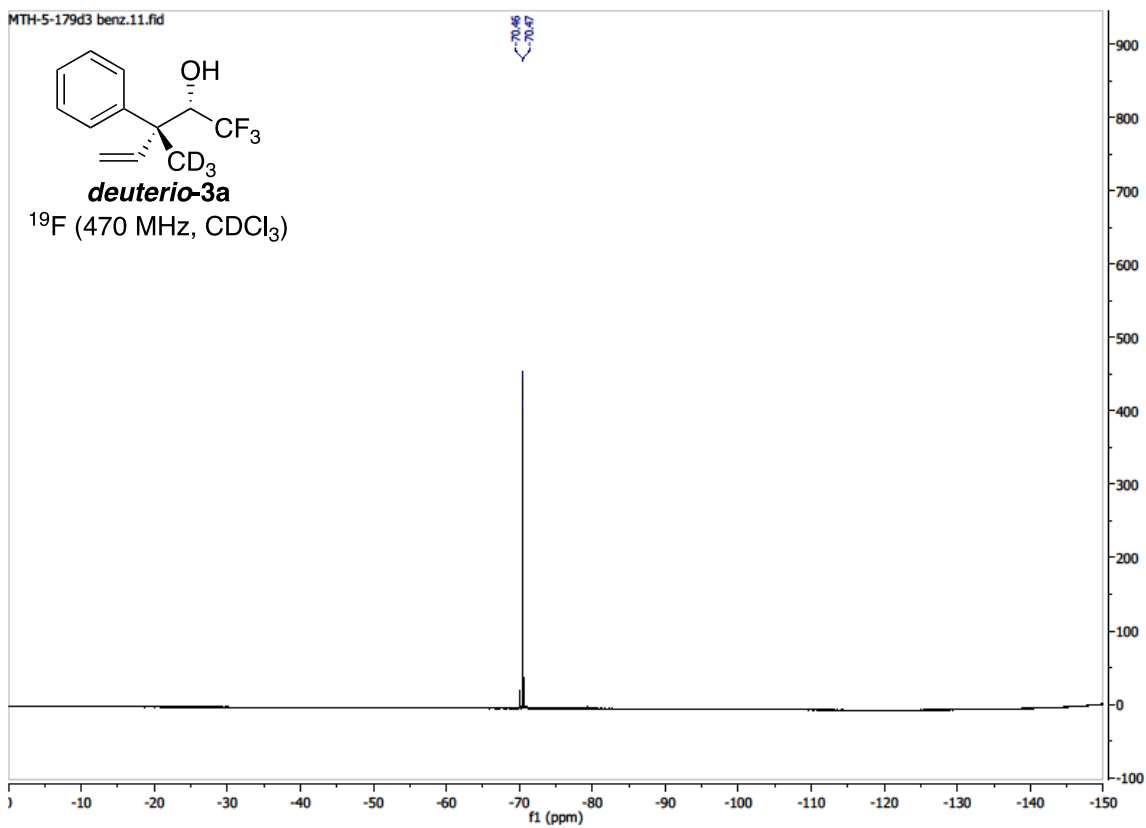
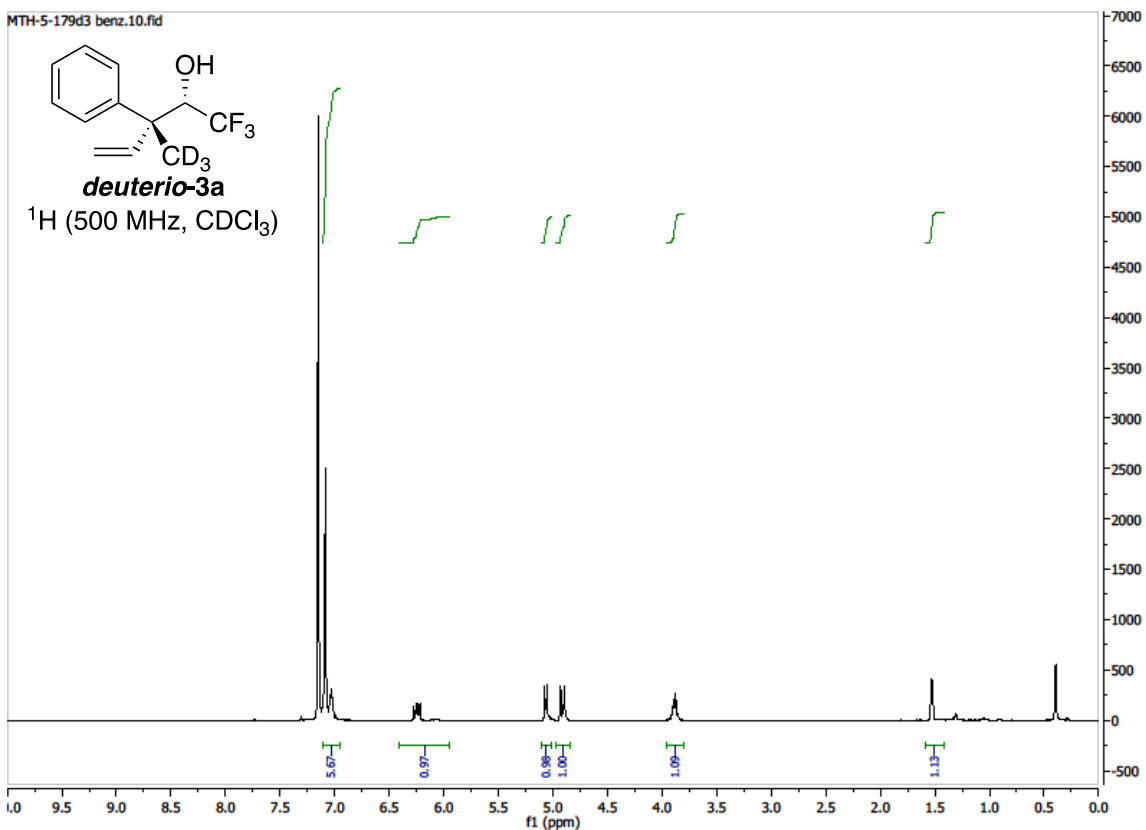
1,1-Disubstituted allene *Deuterio-1a* (52 mg, 0.4 mmol) was subjected to general procedure D. Upon flash column chromatography (SiO<sub>2</sub>, 4:96 EtOAc:hexanes), the title compounds **3a** (33.2 mg, 0.14 mmol, 17:1 dr) was obtained as a yellow oil in 71% yield.

R<sub>f</sub> = 0.41 (90:10 hexanes : EtOAc)

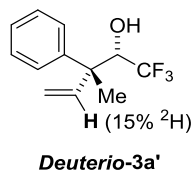
<sup>1</sup>H NMR (500 MHz, C<sub>6</sub>D<sub>6</sub>) δ: 7.12-6.98 (m, 5H), 6.25 (dd, *J* = 10.5, 14.5 Hz, 1H), 5.06 (d, *J* = 10.5 Hz, 1H), 4.91 (d, *J* = 14.5 Hz, 1H), 3.88 (dq, *J* = 7 Hz, 1H), 1.53 (d, *J* = 7 Hz, 1H, OH).

<sup>19</sup>F NMR (470 MHz, C<sub>6</sub>D<sub>6</sub>) δ: -70.5 (d, *J* = 7 Hz)

HRMS (CI, *m/z*) for C<sub>12</sub>H<sub>9</sub>D<sub>3</sub>OF<sub>3</sub>: calcd. = 232.1029; found = 232.1018



**(2S,3R)-1,1,1-trifluoro-3-methyl-3-phenylpent-4-en-4-d-2-ol (Deuterio-3a')**



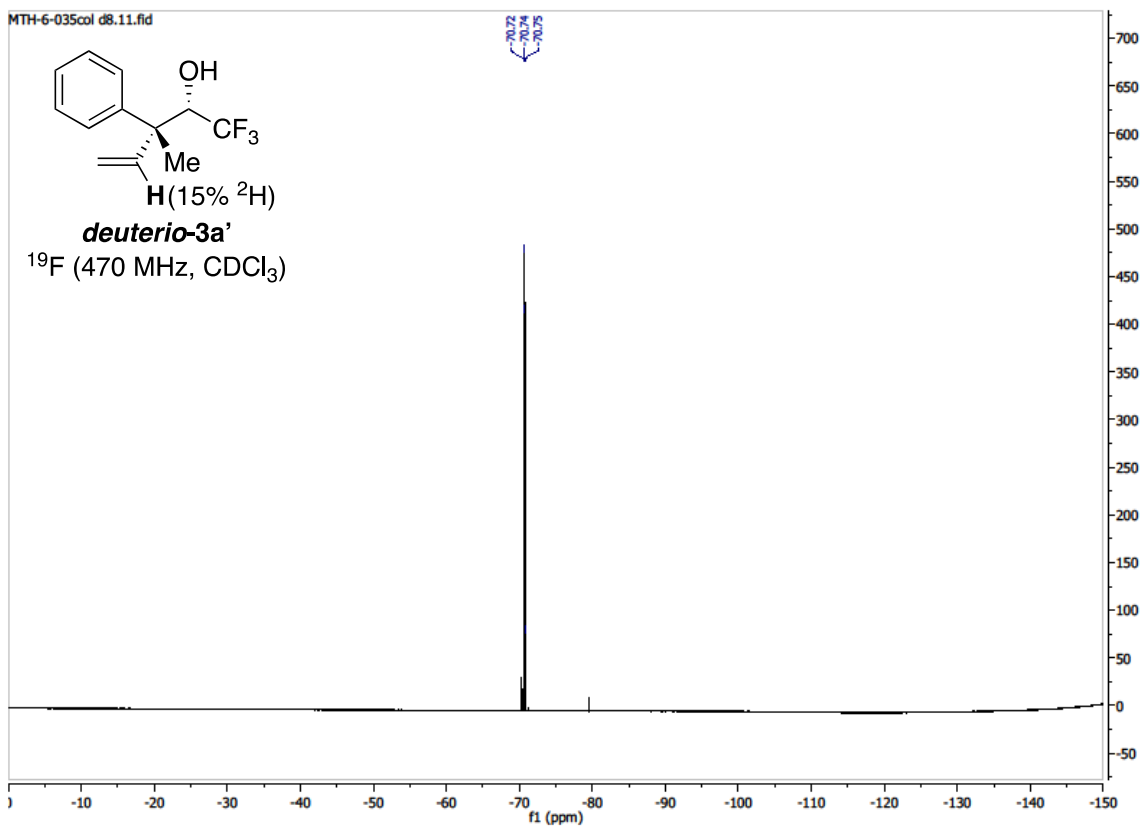
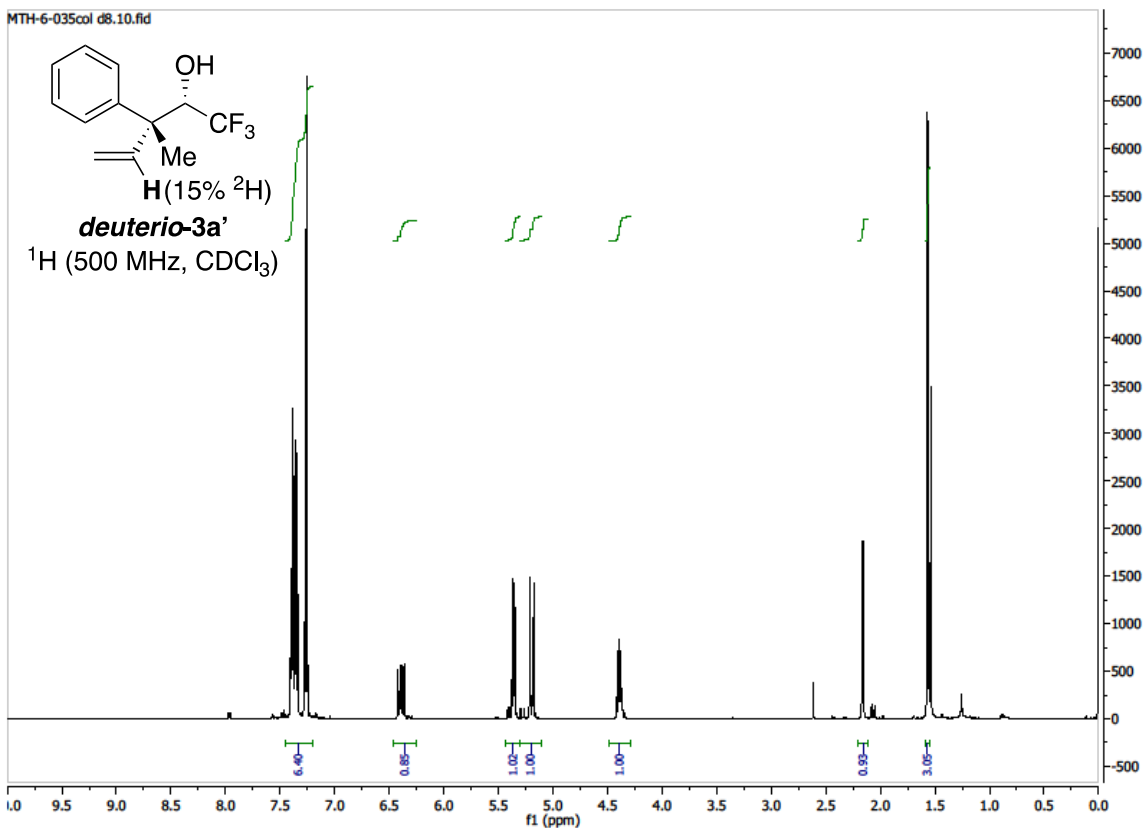
1,1-Disubstituted allene **1a** (52 mg, 0.4 mmol) was subjected to general procedure D using *d*<sub>8</sub>-2-PrOH. Upon flash column chromatography (SiO<sub>2</sub>, 4:96 EtOAc:hexanes), the title compounds **3a** (35.0 mg, 0.16 mmol, 17:1 dr) was obtained as a yellow oil in 75% yield.

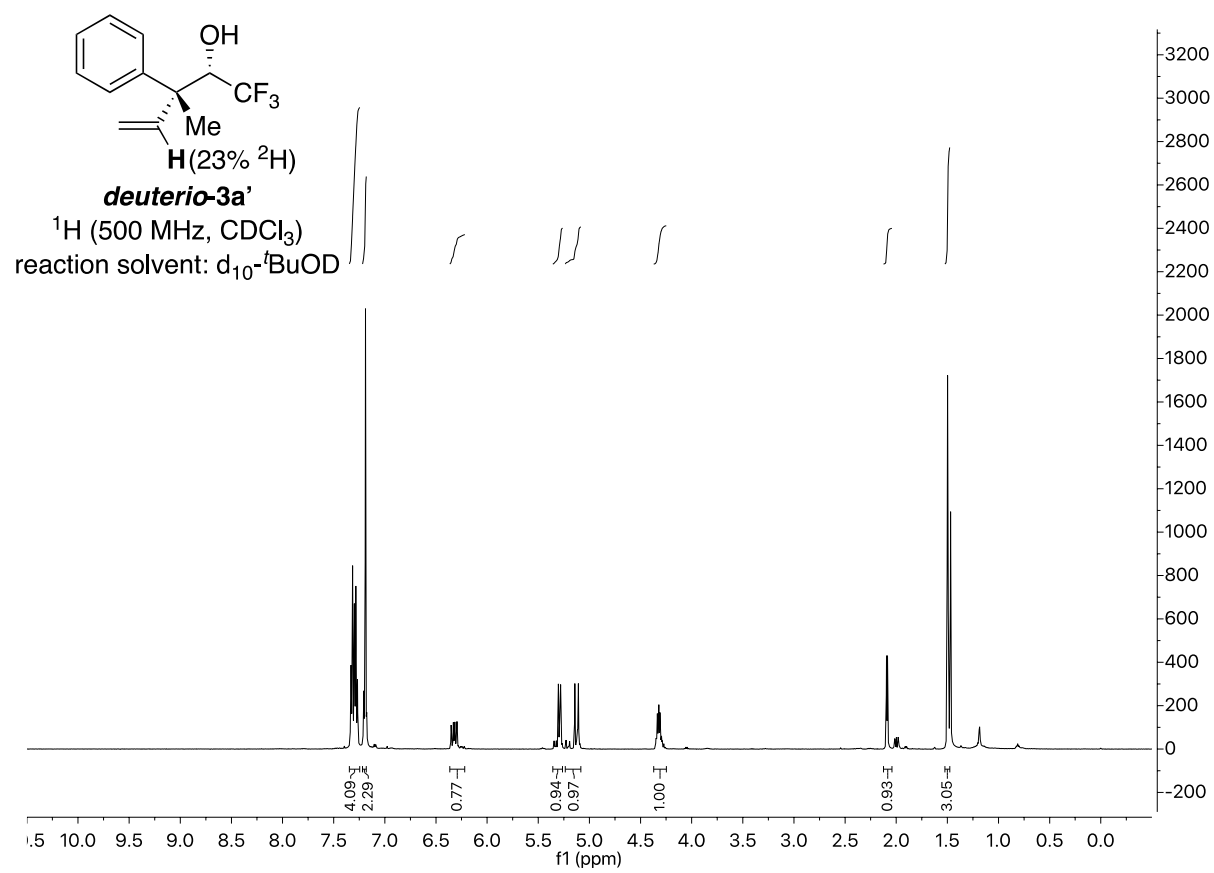
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.40-7.34 (m, 4H), 7.26 (m, 1H), 6.39 (dd, *J* = 11.1, 17.8 Hz, 1H), 5.36 (d, *J* = 11.1 Hz, 1H), 5.20 (d, *J* = 17.8 Hz, 1H), 4.39 (dq, *J* = 6.0, 7.9 Hz, 1H), 2.19 (d, *J* = 6.0 Hz, 1H, OH), 1.57 (s, 3H).

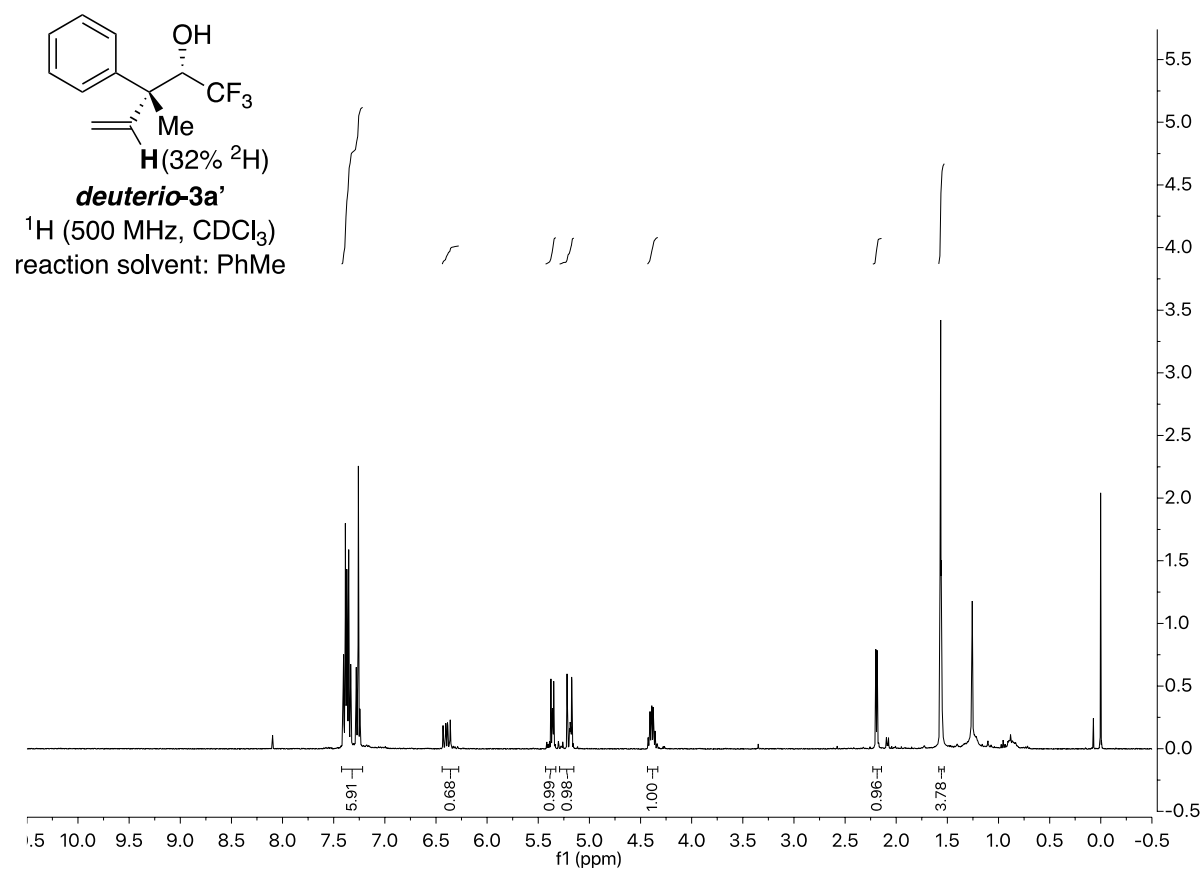
<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ: -70.73 (d, *J* = 7.9 Hz, non-deuterated), -70.75 (d, *J* = 7.9 Hz, deuterated).

HRMS (CI, *m/z*) for C<sub>12</sub>H<sub>11</sub>DOF<sub>3</sub>: calcd. = 230.0903; found = 230.0933.

Reaction was also conducted in *d*<sub>10</sub>-*tert*-butanol and toluene in attempts to increase deuterium incorporation.

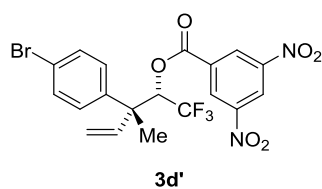
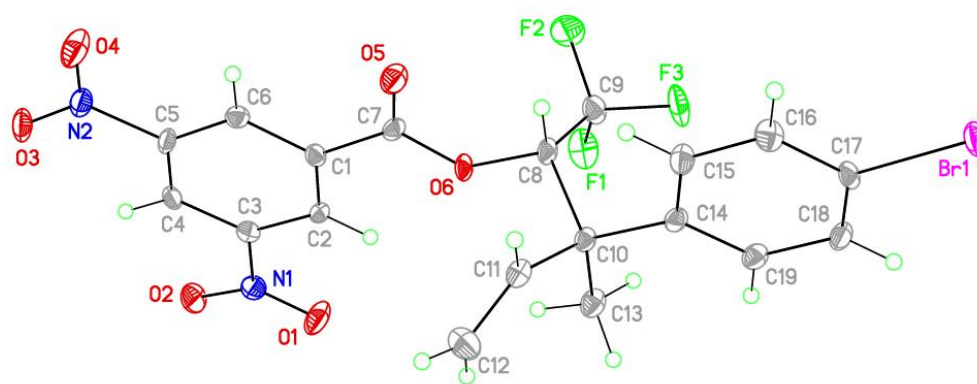






### Single Crystal Diffraction Data for Coupling Product 3d'

**Figure S1.** View of **3d'** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.

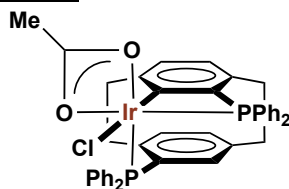




**Table S1. Crystal data and structure refinement for 3d'.**

Empirical formula	C19 H14 Br F3 N2 O6	
Formula weight	503.23	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group	P 21	
Unit cell dimensions	a = 11.4648(11) Å	∠ = 90°.
	b = 7.4731(7) Å	∠ = 94.863(4)°.
	c = 11.5835(11) Å	∠ = 90°.
Volume	988.87(16) Å <sup>3</sup>	
Z	2	
Density (calculated)	1.690 Mg/m <sup>3</sup>	
Absorption coefficient	2.147 mm <sup>-1</sup>	
F(000)	504	
Crystal size	0.34 x 0.22 x 0.18 mm <sup>3</sup>	
Theta range for data collection	2.400 to 30.525°.	
Index ranges	-16<=h<=16, -10<=k<=10, -16<=l<=16	
Reflections collected	30981	
Independent reflections	5960 [R(int) = 0.0407]	
Completeness to theta = 25.242°	99.8 %	
Absorption correction	Numerical	
Max. and min. transmission	0.7386 and 0.6021	
Refinement method	Full-matrix least-squares on F <sup>2</sup>	
Data / restraints / parameters	5960 / 1 / 281	
Goodness-of-fit on F <sup>2</sup>	0.998	
Final R indices [I>2sigma(I)]	R1 = 0.0261, wR2 = 0.0524	
R indices (all data)	R1 = 0.0324, wR2 = 0.0537	
Absolute structure parameter	0.034(3)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.340 and -0.382 e.Å <sup>-3</sup>	

### Procedure and Spectral Data for Ir-PP-I

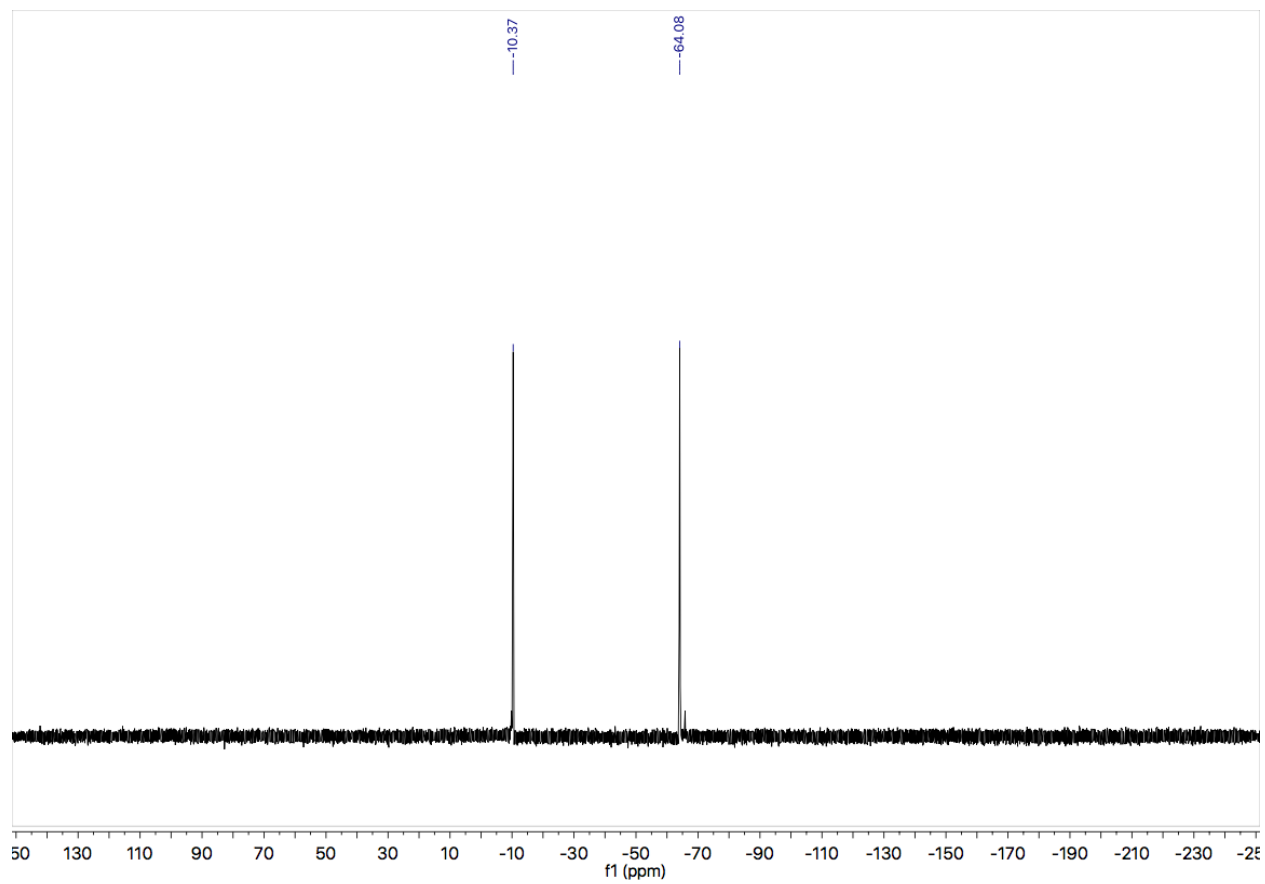


A sealed tube equipped with a magnetic stir bar was charged with  $[\text{Ir}(\text{cod})\text{Cl}]_2$  (10 mg, 0.015 mmol, 100 mol %) and (*R*)-PhanePhos (17.3 mg, 0.03 mmol, 200 mol %). The mixture was purged with argon and THF (0.6 mL, 0.025 M) was added followed by allyl acetate (6.5  $\mu\text{L}$ , 0.06 mmol, 400 mol %). The resulting mixture was stirred at 100  $^\circ\text{C}$  for 1 hour. The reaction mixture was then allowed to cool to ambient temperature. Upon flash column chromatography ( $\text{SiO}_2$ , 30-50%  $\text{Et}_2\text{O}$ :pentane), the title catalyst **Ir-PP-I** (7.8 mg, 0.009 mmol,) was obtained as a yellow powder in 60% yield.

$R_f = 0.45$  (1:1 hexanes : EtOAc)

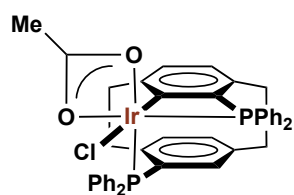
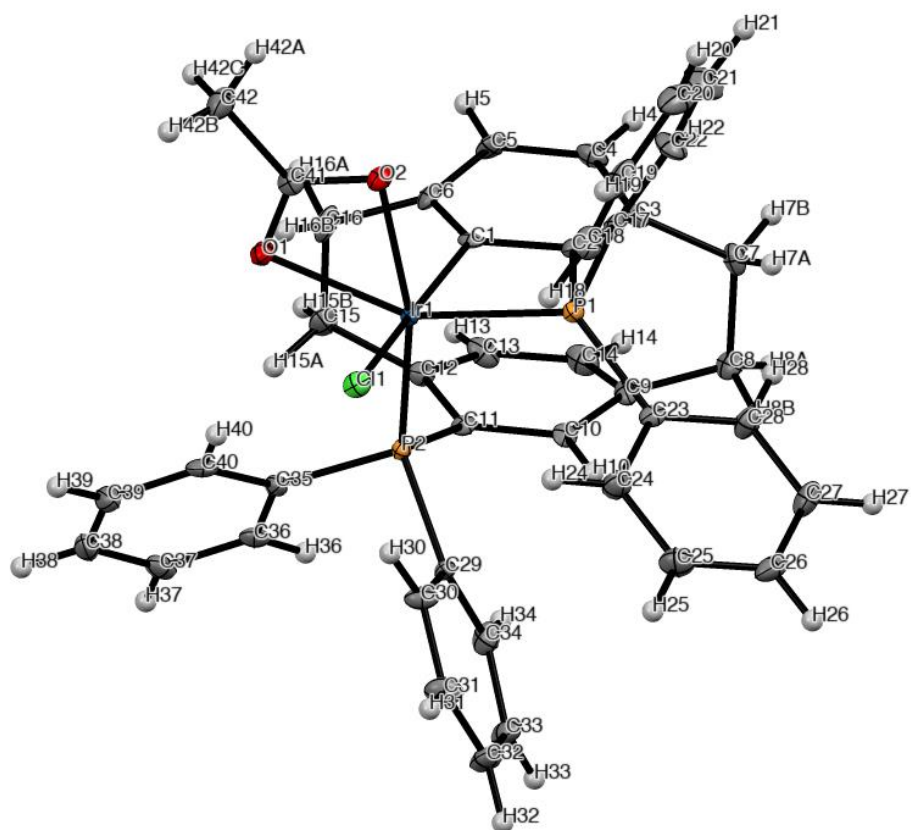
$^{31}\text{P}$  NMR (162 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$ : -64.1, -10.3.

HRMS (ESI  $[\text{M}-\text{Cl}]^+$ ,  $m/z$ ) for  $\text{C}_{42}\text{H}_{36}\text{IrO}_2\text{P}_2$ : calcd. = 827.1817; found = 827.1818.



### Single Crystal Diffraction Data for Ir-PP-I

**Figure S2.** View of Ir-PP-I showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.

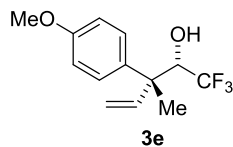


**Table S2. Crystal data and structure refinement for Ir-PP-I.**

Empirical formula	C43 H38 Cl3 Ir O2 P2	
Formula weight	947.22	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 12.012(2) Å	□ = 90°.
	b = 15.314(2) Å	□ = 90°.
	c = 20.235(3) Å	□ = 90°.
Volume	3722.3(10) Å <sup>3</sup>	
Z	4	
Density (calculated)	1.690 Mg/m <sup>3</sup>	
Absorption coefficient	3.926 mm <sup>-1</sup>	
F(000)	1880	
Crystal size	0.170 x 0.060 x 0.050 mm <sup>3</sup>	
Theta range for data collection	2.013 to 28.380°.	
Index ranges	-16<=h<=16, -20<=k<=20, -26<=l<=27	
Reflections collected	77190	
Independent reflections	9295 [R(int) = 0.0796]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Numerical	
Max. and min. transmission	0.8476 and 0.5258	
Refinement method	Full-matrix least-squares on F <sup>2</sup>	
Data / restraints / parameters	9295 / 306 / 461	
Goodness-of-fit on F <sup>2</sup>	1.036	
Final R indices [I>2sigma(I)]	R1 = 0.0266, wR2 = 0.0571	
R indices (all data)	R1 = 0.0319, wR2 = 0.0584	
Absolute structure parameter	-0.008(3)	
Extinction coefficient	n/a	
Largest diff. peak and hole	1.390 and -0.734 e.Å <sup>-3</sup>	

## Procedures and Spectral Data for the Coupling Products Utilizing Ir-PP-I

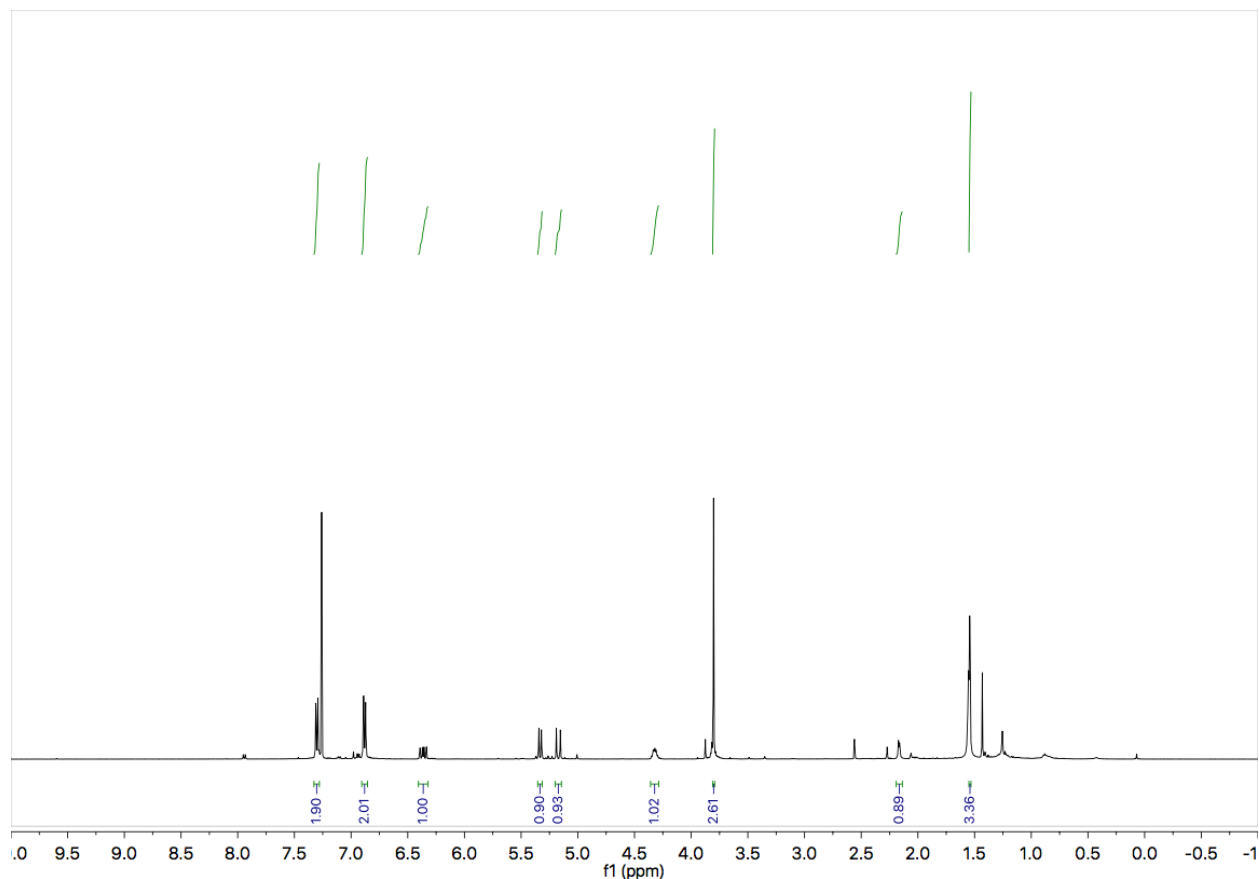
### (2*S*,3*R*)-1,1,1-trifluoro-3-(4-methoxyphenyl)-3-methylpent-4-en-2-ol (**3e**)

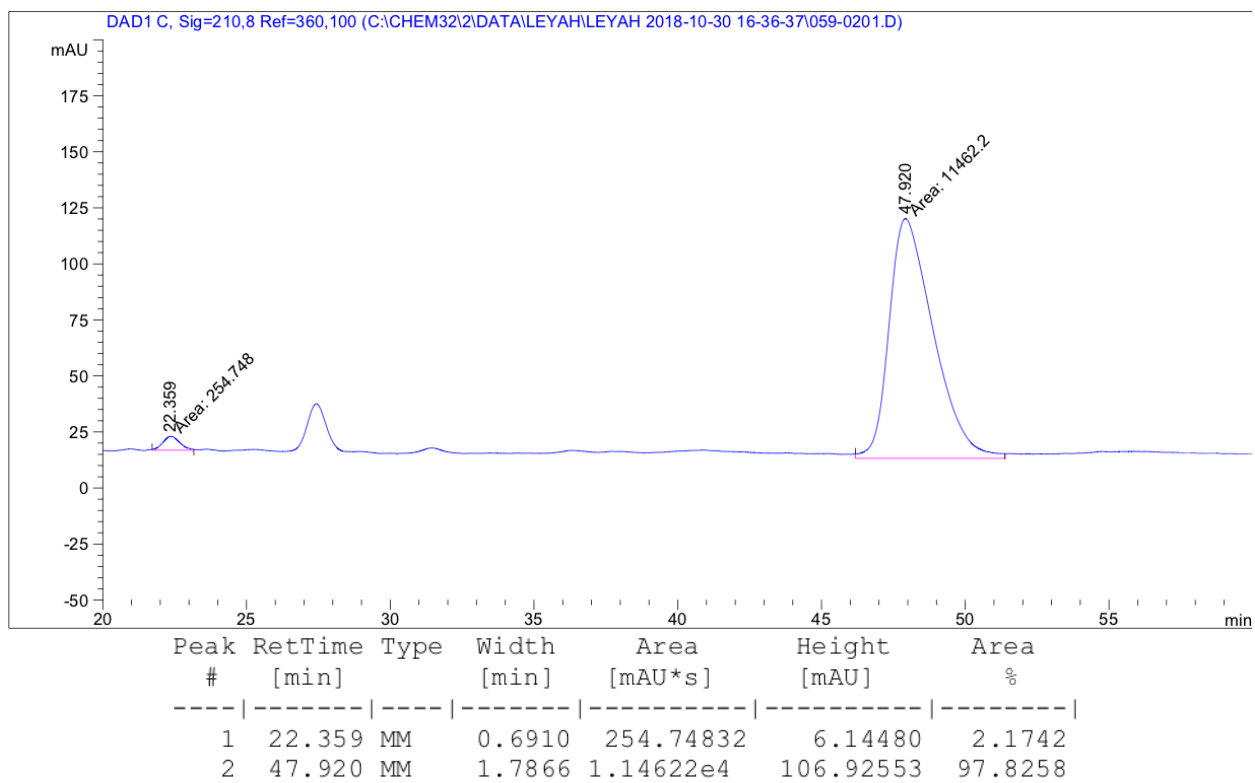
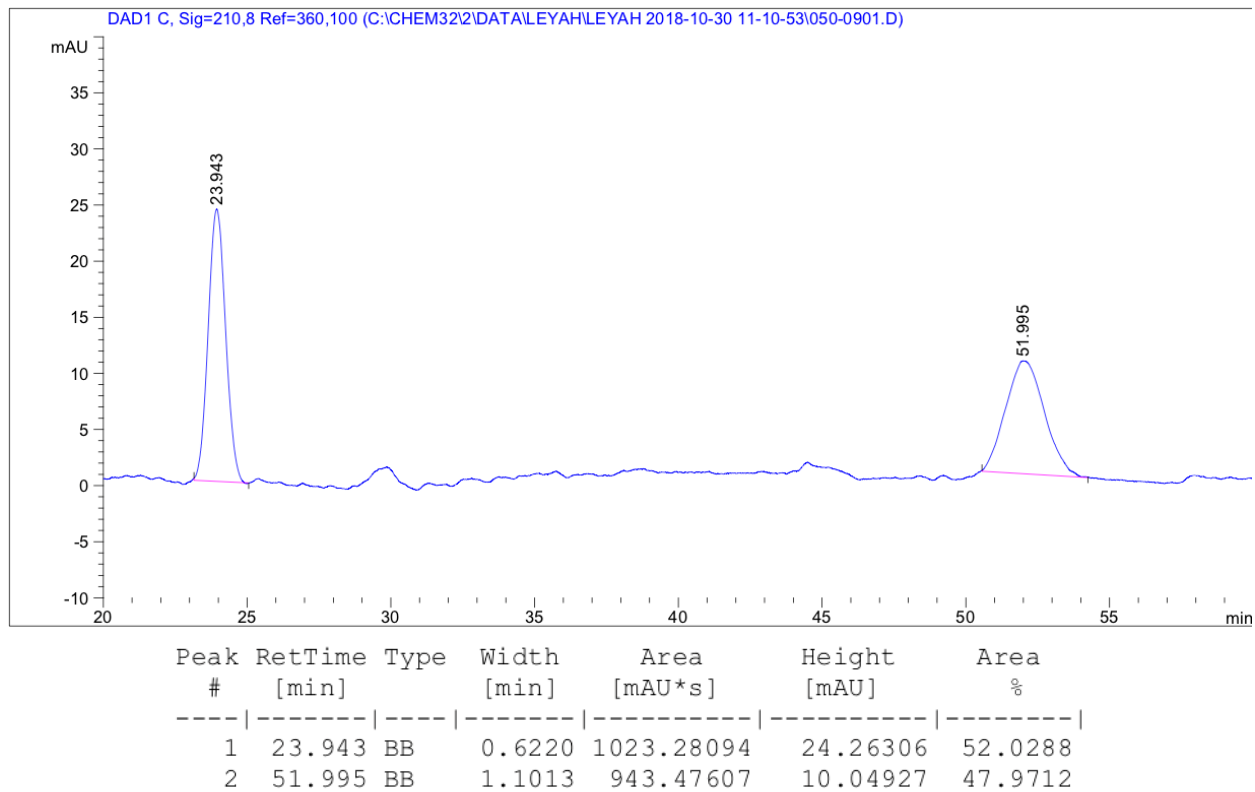


To a dried pressure tube under an argon atmosphere charged with **Ir-PP-I** (8.6 mg, 0.01 mmol, 5 mol%), tetrabutylammonium chloride (56.5 mg, 0.2 mmol, 100 mol%) and dried 4 Å molecular sieves (90 mg, 300 wt%) was added 1,1-disubstituted allene **1e** (64.1 mg, 0.4 mmol, 200 mol%), isopropanol (200 mol%) and tert-butanol (0.2M) followed by fluoral hydrate (30.9 mg, 0.2 mmol, 100 mol%). The reaction mixture was allowed to stir for 16 hours at 100 °C. The solvent was removed *in vacuo*. Upon flash column chromatography (SiO<sub>2</sub>, 5:95 EtOAc:hexanes), the title compound **3e** (37.3 mg, 0.14 mmol, 14:1 dr) was obtained as a light yellow oil in 72% yield.

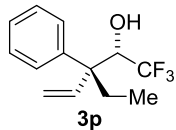
The data collected on this sample was in total agreement with the data collected above with the use of *in situ* generated catalyst to form **3e**.

HPLC: (Chiralcel column OJ-H, Hexane:2-PrOH = 92:8, 1.0 mL/min, 210 nm) ee = 96%.





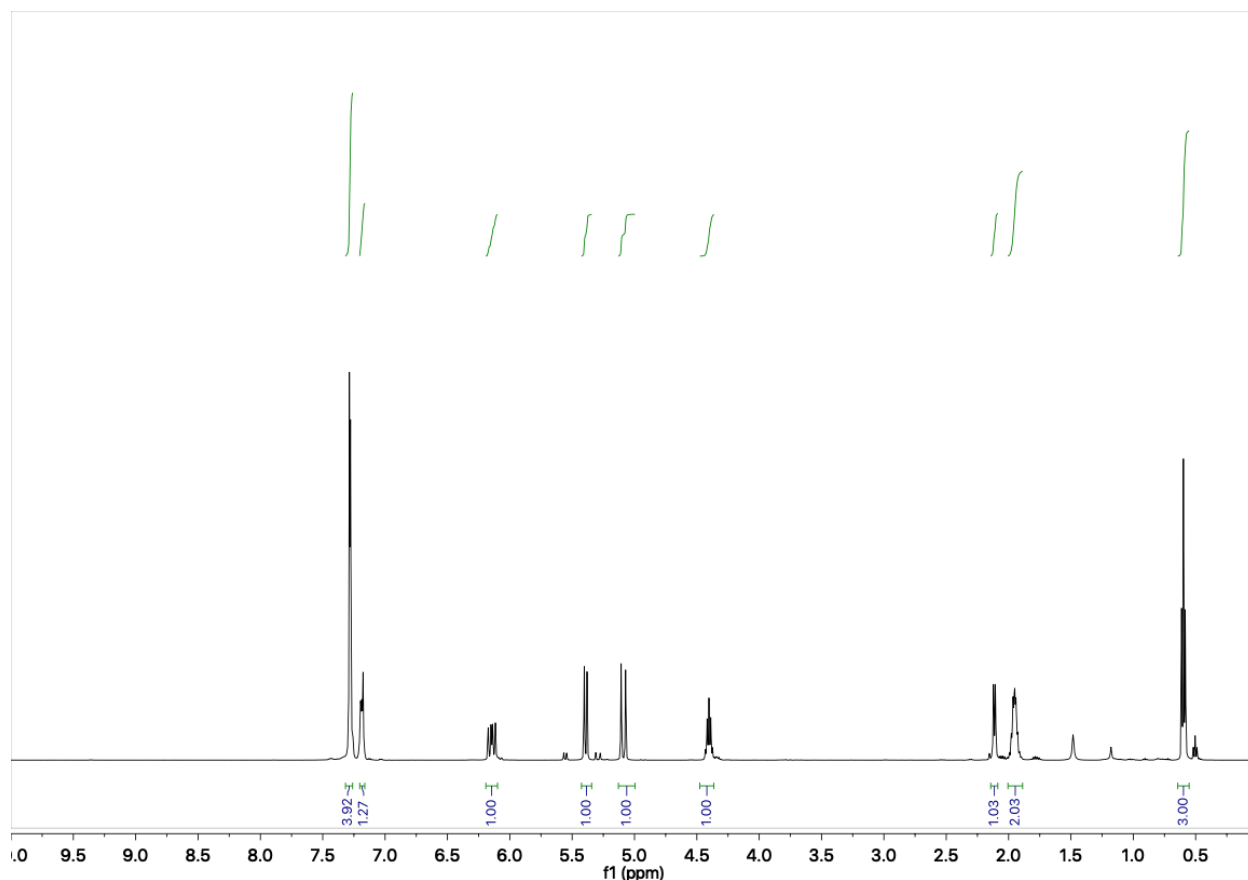
**(2*S*,3*R*)-3-ethyl-1,1,1-trifluoro-3-phenylpent-4-en-2-ol (3p)**



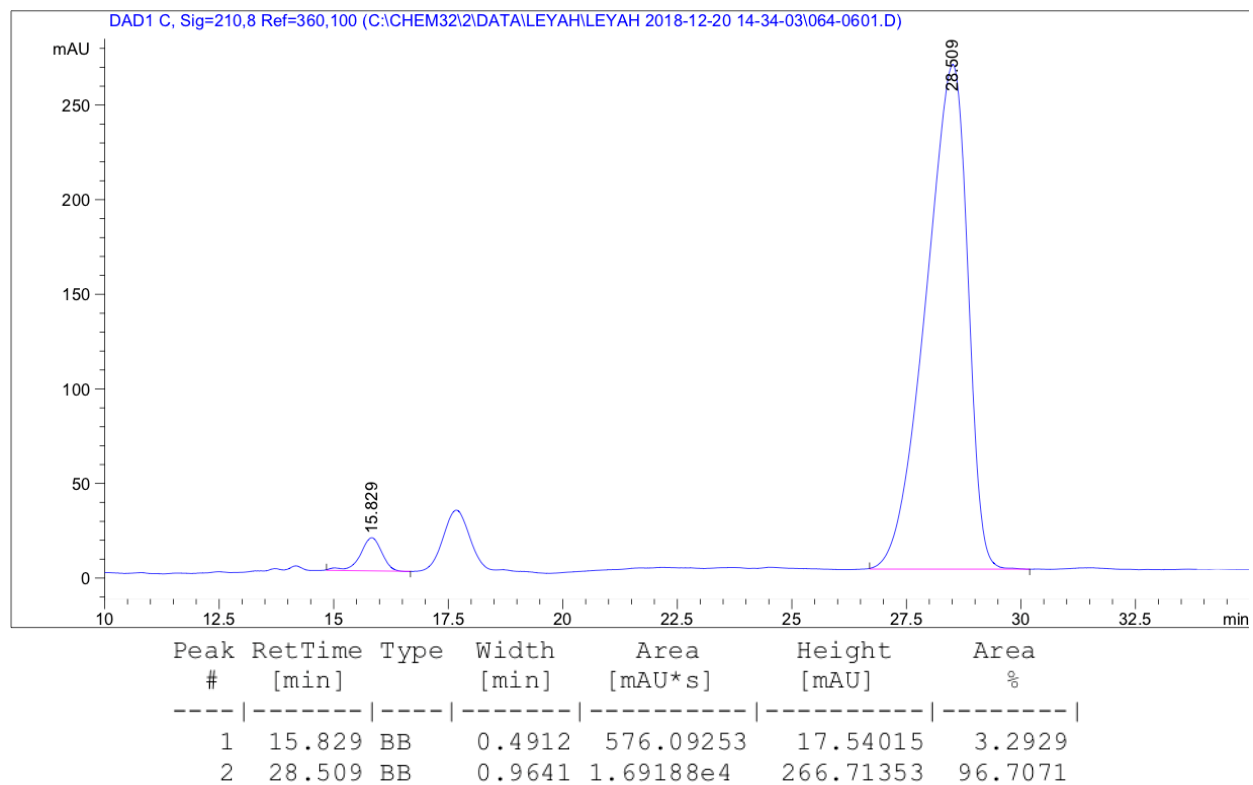
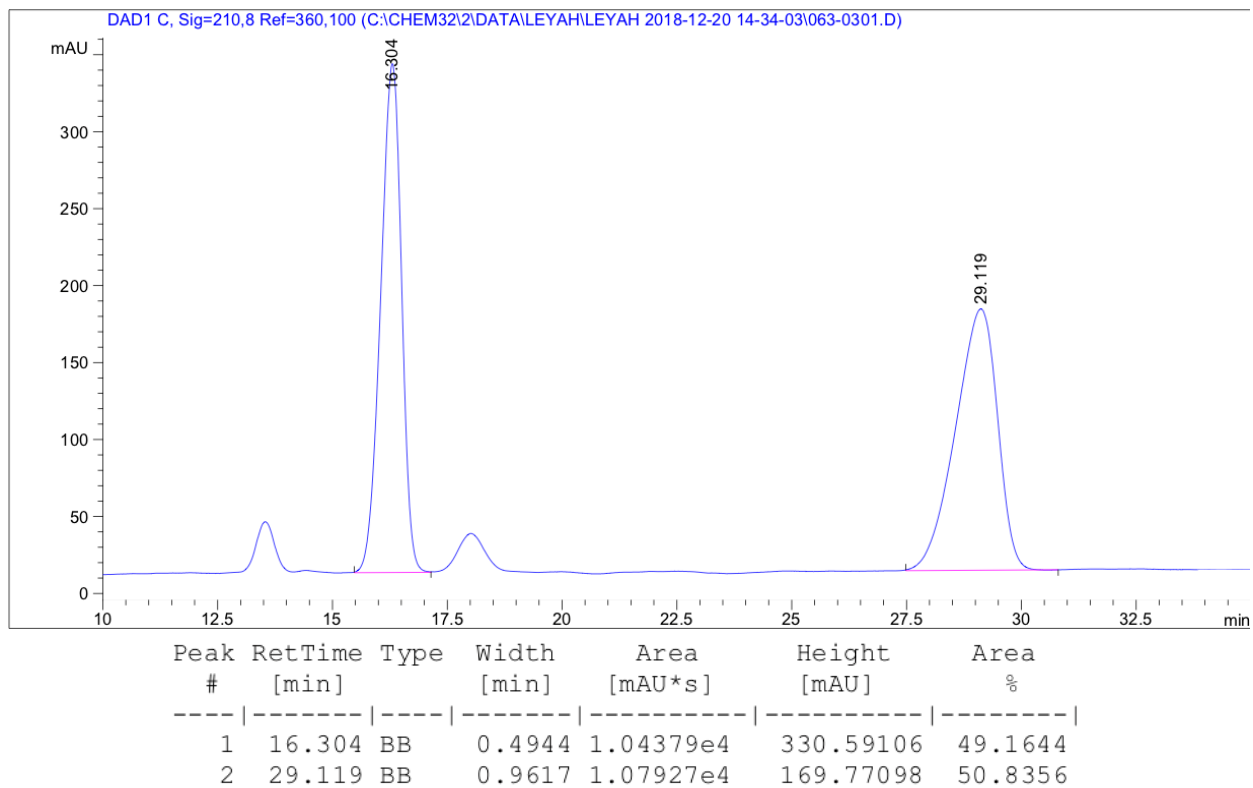
To a dried pressure tube under an argon atmosphere charged with **Ir-PP-I** (8.6 mg, 0.01 mmol, 5 mol%), tetrabutylammonium chloride (56.5 mg, 0.2 mmol, 100 mol%) and dried 4 Å molecular sieves (90 mg, 300 wt%) was added 1,1-disubstituted allene **1p** (57.7 mg, 0.4 mmol, 200 mol%), isopropanol (200 mol%) and tert-butanol (0.2M) followed by fluoral hydrate (30.9 mg, 0.2 mmol, 100 mol%). The reaction mixture was allowed to stir for 16 hours at 100 °C. The solvent was removed *in vacuo*. Upon flash column chromatography (SiO<sub>2</sub>, 4:96 EtOAc:hexanes), the title compound **3p** (30.3 mg, 0.12 mmol, 16:1 dr) was obtained as a yellow oil in 62% yield.

The data collected on this sample was in total agreement with the data collected above with the use of *in situ* generated catalyst to form **3p**.

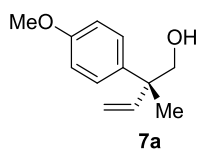
HPLC: (Chiralcel column OJ-H, Hexane:2-PrOH = 95:5, 1.0 mL/min, 210 nm) ee = 93%.







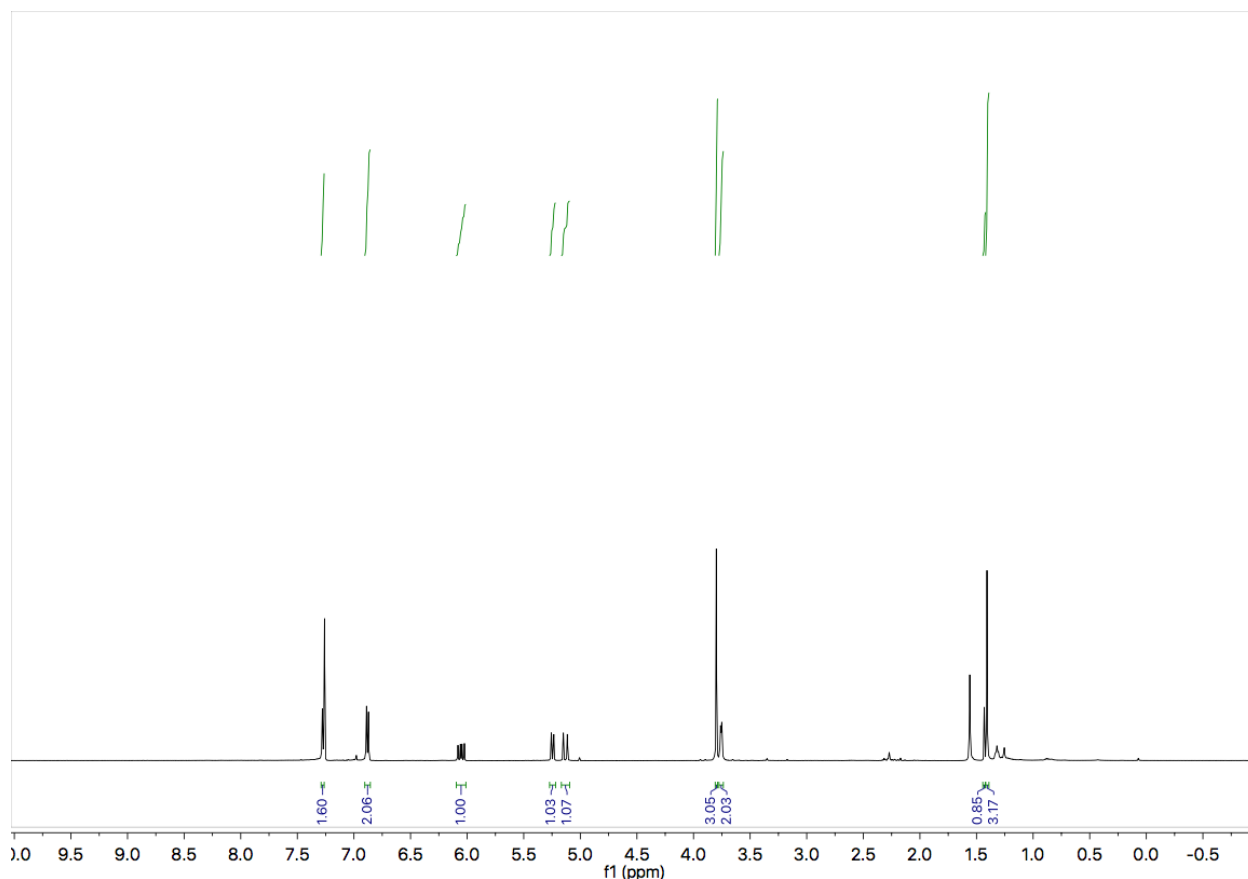
**(R)-2-(4-methoxyphenyl)-2-methylbut-3-en-1-ol (7a)**

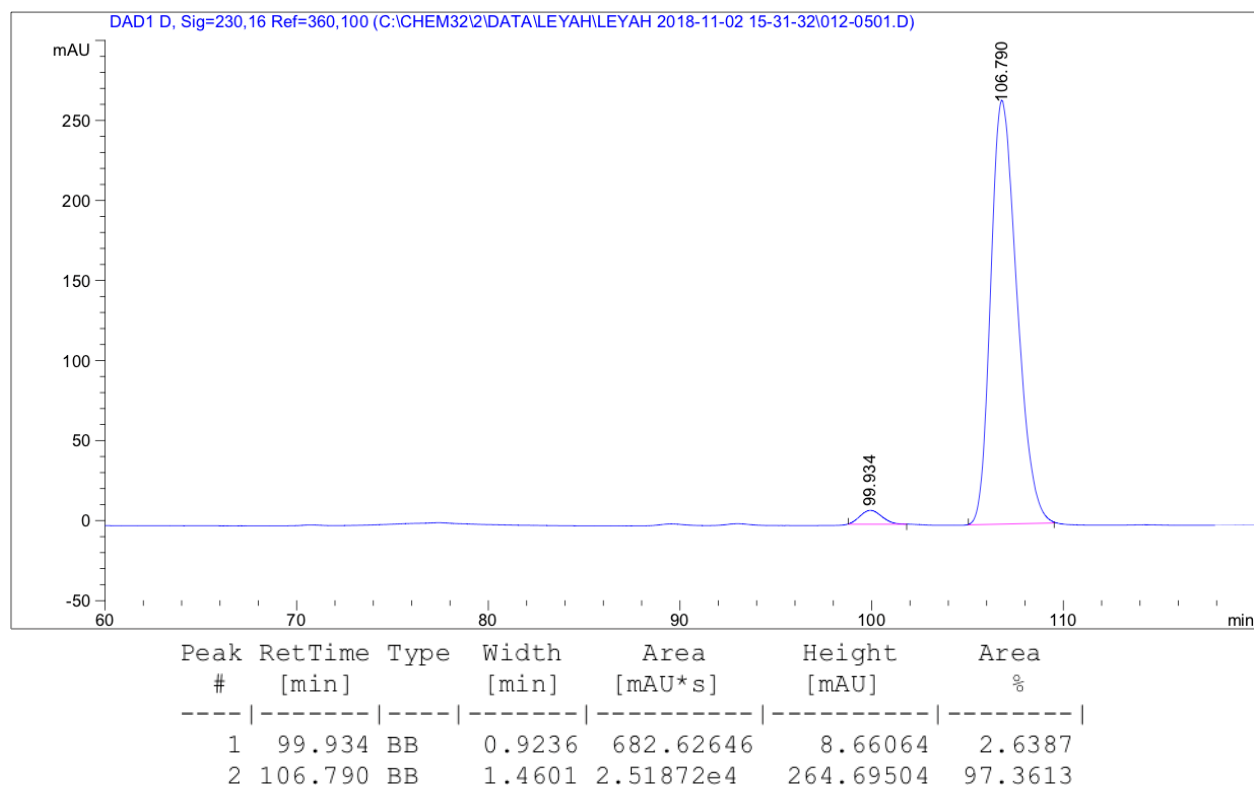
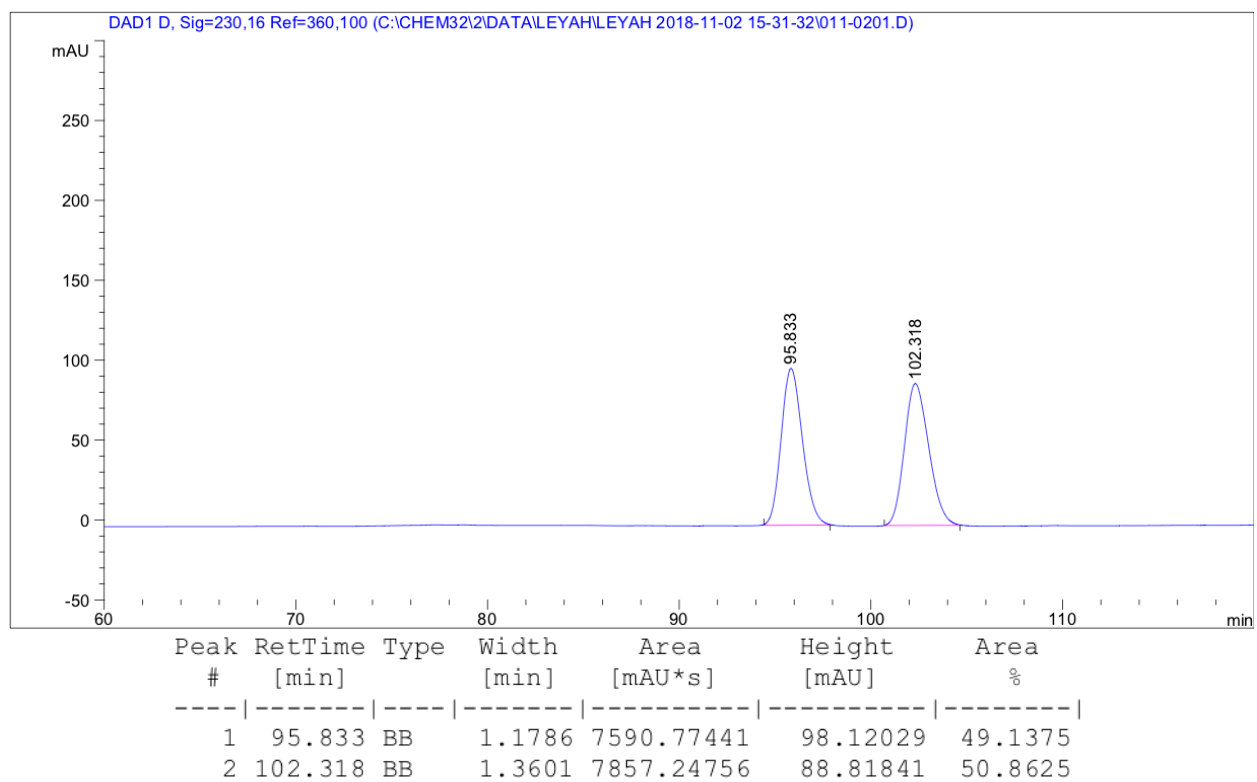


To a dried pressure tube under an argon atmosphere charged with **Ir-PP-I** (8.6 mg, 0.01 mmol, 5 mol%) was added diene *iso-1e* (32.0 mg, 0.2 mmol, 100 mol%), methanol (0.2 mL, 1 M), and acetone (2 mL, 0.1 M). The reaction mixture was allowed to stir for 48 hours at 80 °C. The solvent was removed *in vacuo*. Upon flash column chromatography (SiO<sub>2</sub>, 1:5 EtOAc:hexanes), the title compound **7a** (19.3 mg, 0.10 mmol) was obtained as a clear oil in 50% yield.

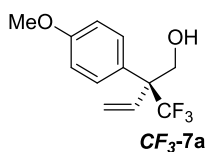
The data collected on this sample was in total agreement with the literature data collected previously with the use of *in situ* generated catalyst.<sup>12</sup>

HPLC: (Chiralcel column AD-H x2, Hexane:2-PrOH = 98:2, 0.5 mL/min, 230 nm) ee = 95%.





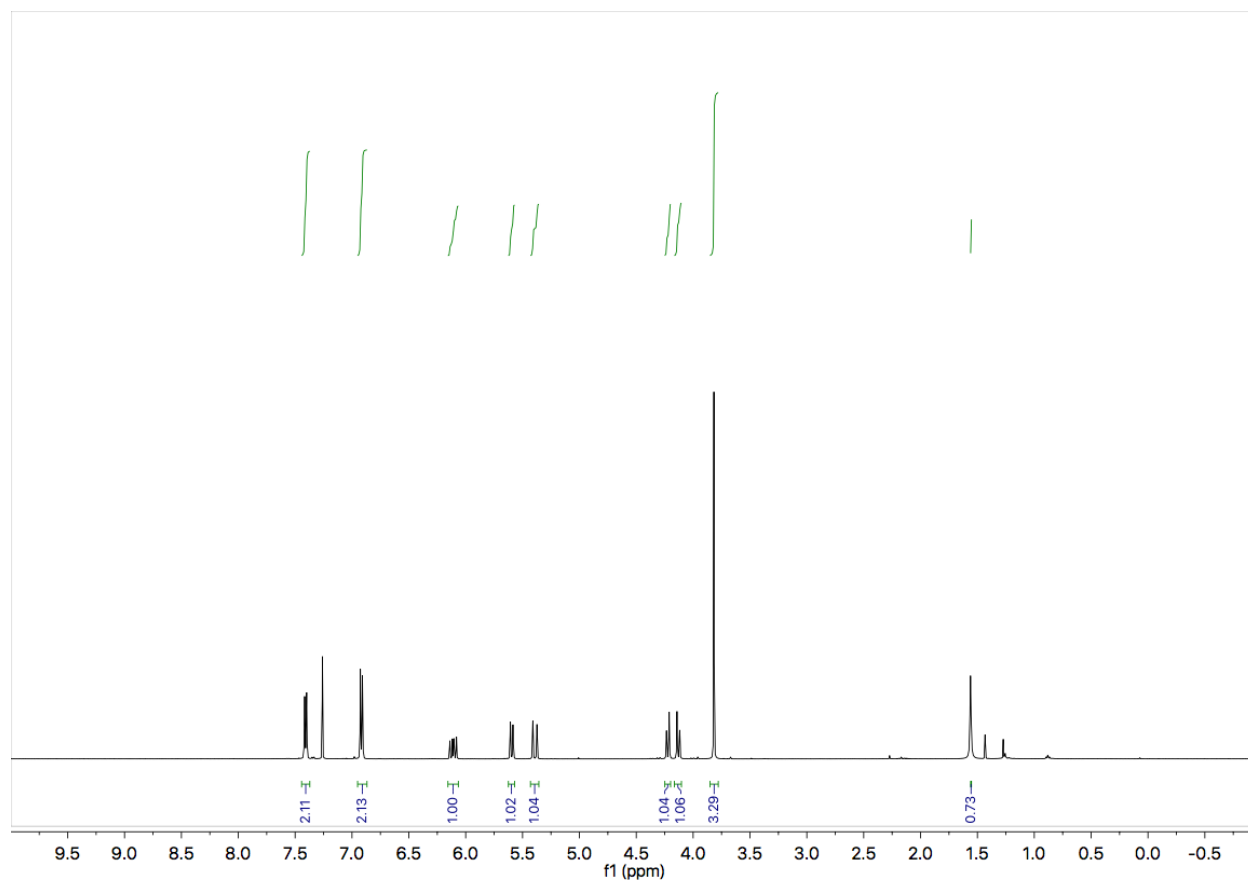
**(S)-2-(4-methoxyphenyl)-2-(trifluoromethyl)but-3-en-1-ol (*CF*<sub>3</sub>-7a)**

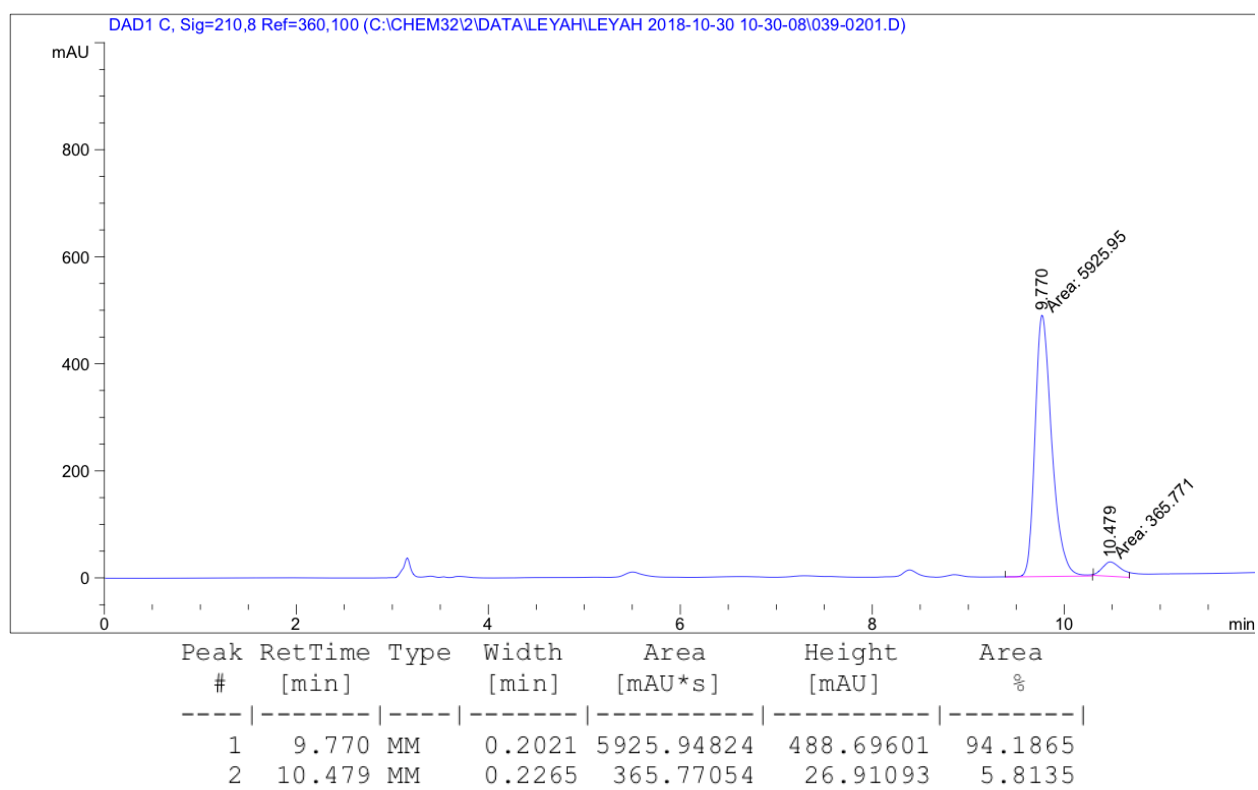
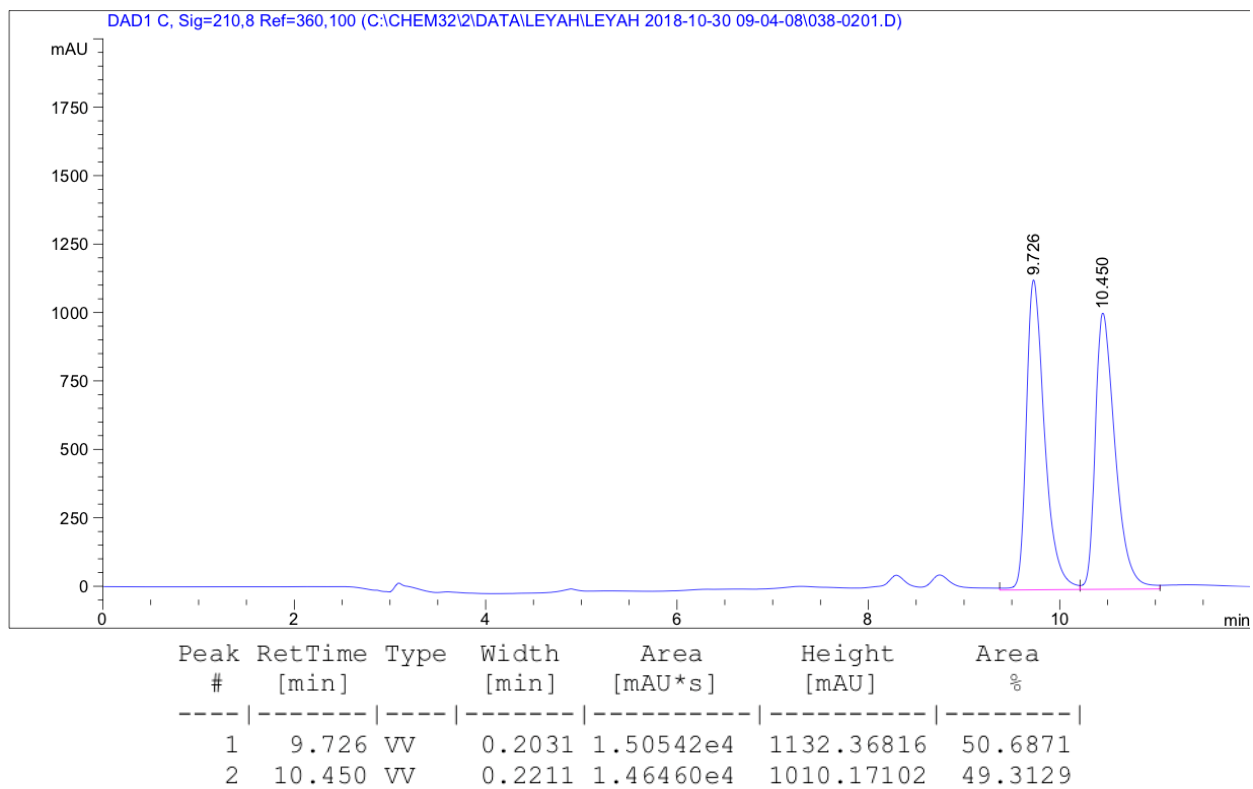


To a dried pressure tube under an argon atmosphere charged with **Ir-PP-I** (8.6 mg, 0.01 mmol, 5 mol%) and tetrabutylammonium iodide (6.4 mg, 0.02 mmol, 10 mol%) was added allene *CF*<sub>3</sub>-**1e** (42.8 mg, 0.2 mmol, 100 mol%), methanol (0.2 mL, 1 M) and acetone (2 mL, 0.1 M). The reaction mixture was allowed to stir for 18 hours at 70 °C. The solvent was removed *in vacuo*. Upon flash column chromatography (SiO<sub>2</sub>, 15:85 EtOAc:hexanes), the title compound *CF*<sub>3</sub>-**7a** (42.5 mg, 0.17 mmol) was obtained as a clear oil in 86% yield.

The data collected on this sample was in total agreement with the literature data collected previously with the use of *in situ* generated catalyst.<sup>13</sup>

HPLC: (Chiralcel column OD-3, Hexane:2-PrOH = 95:5, 1.0 mL/min, 210 nm) ee = 88%.





## Kinetic Studies

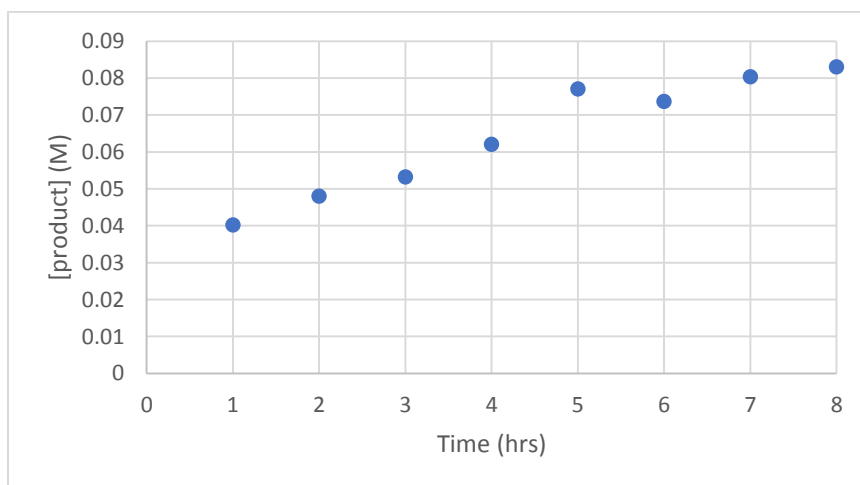
*Standard Conditions:* To a dried 10 mL volumetric flask under an argon atmosphere charged with  $[\text{Ir}(\text{cod})\text{Cl}]_2$  (16.8 mg, 0.025 mmol, 2.5 mol%), (*R*)-PhanePhos (28.8 mg, 0.05 mmol, 5 mol%) and tetrabutylammonium chloride (277.9 mg, 1 mmol, 100 mol%) was added 1,1-disubstituted allene (260.4, 2 mmol, 200 mol%), isopropanol (0.15 mL, 2 mmol, 200 mol%) and fluoral hydrate (154.7 mg, 1 mmol, 100 mol%). The flask was then filled to the mark with tert-butanol and sonicated until full dissolution. To a dried pressure tube under an argon atmosphere charged with dried 4 Å molecular sieves (46 mg) was added 1 mL of the reaction mixture and the tube quickly sealed. Equal number of reaction tubes were assembled per time point monitored. The reaction mixtures were then allowed to stir at 100 °C with a tube removed each hour for analysis.

Reaction progress was monitored by GC analysis. The reaction was cooled to room temperature before 20 µL of cyclodecane (internal standard) was added and then the mixture diluted with dichloromethane (~4 mL). The mixture was then filtered through a small amount of silica gel in a pipette prior to analysis. The concentration of product was determined by GC analysis.

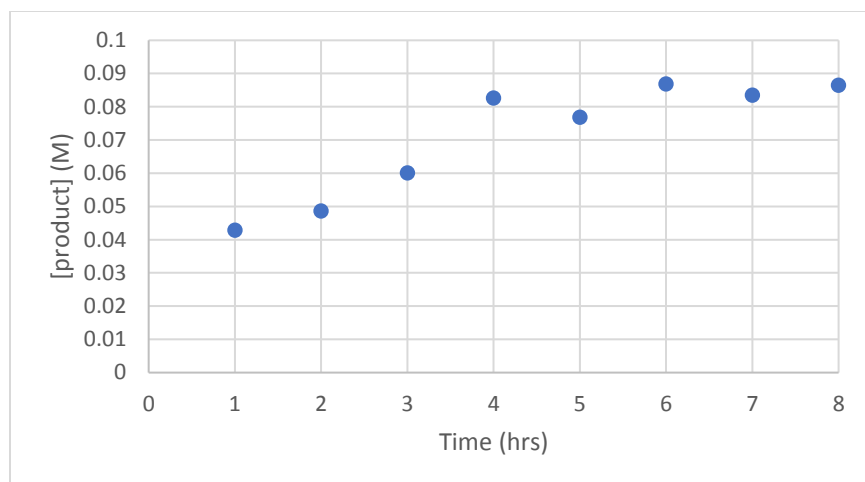
Reaction order determined by submitting data to Bures plot analysis.<sup>14,15</sup>

**Table S1.** Further reaction conditions for the kinetic experiments.

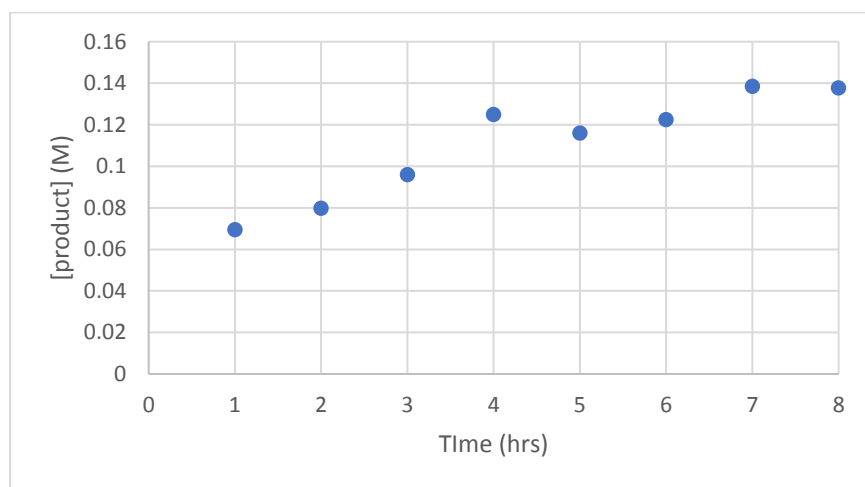
Experiment	[cat] (M)	[allene] (M)	[fluoral] (M)	[excess] [allene]-[fluoral] (M)
Standard	0.005	0.2	0.1	0.1
Different excess 1	0.005	0.4	0.1	0.3
Different excess 2	0.005	0.2	0.2	0.0
Same excess	0.005	0.3	0.2	0.1
Increased catalyst	0.01	0.2	0.1	0.1



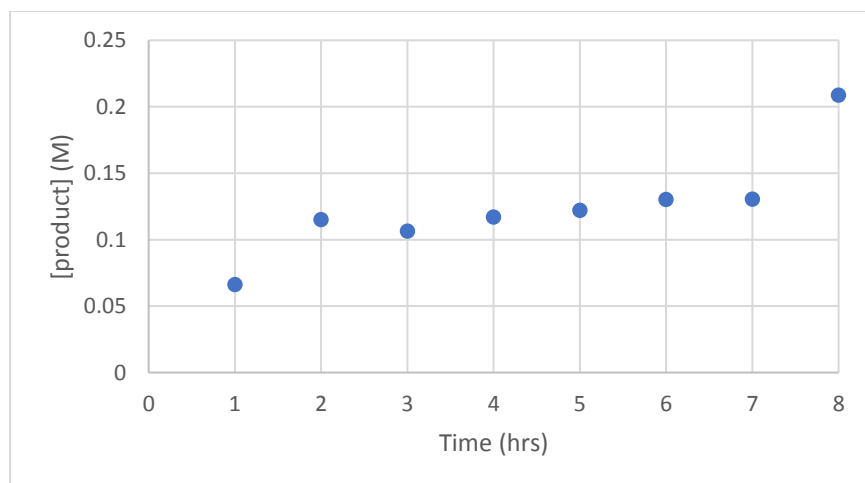
**Figure S3.** Product formation under standard conditions.



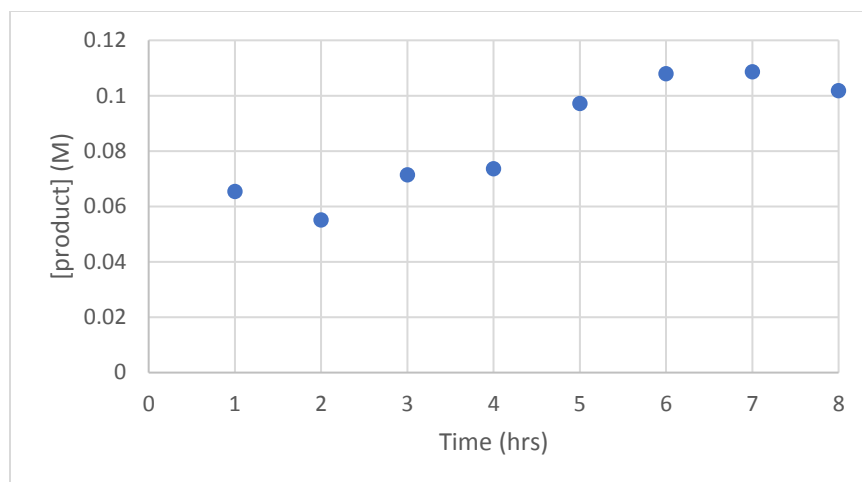
**Figure S4.** Product formation under different excess 1 conditions.



**Figure S5.** Product formation under different excess 2 conditions.

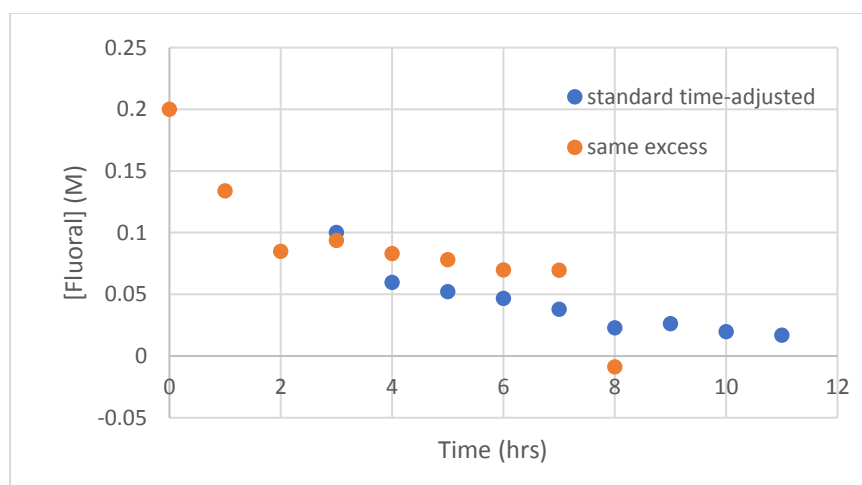


**Figure S6.** Product formation under same excess conditions.



**Figure S7.** Product formation under increased catalyst conditions.

In order to determine if any catalyst deactivation occurred during the reaction the same excess protocol was utilized. The collected product concentration data for both the standard and same excess data sets were converted to fluoral concentration data ( $[\text{Fluoral}]_t = [\text{Fluoral}]_0 - [\text{Product}]_t$ ). Since the standard data set has a starting concentration of fluoral that is half that in the same excess experiment, the standard data was time adjusted to reflect this. This method is representative of starting the reaction from two different starting points. At the point where the same excess data set reaches the starting point of the standard data set they then represent a reaction with the same conditions, with the exception of the first containing product already present and a catalyst that has completed more turnovers.<sup>14</sup> While scattering of the data is apparent due to the nature of the experimental setup, the relative overlap of the two data sets that is observed here indicates that minimal catalyst deactivation occurs throughout the process of the reaction.



**Figure S8.** Evaluation of catalyst performance utilizing same excess protocol.



## HRMS Identification of Catalytic Intermediate

Note: Loss of chloride ion resulting in M<sup>+</sup> ion species

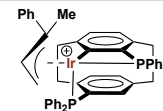
### Target Compound Screening Report

Results Acquired by The University of Texas at Austin Mass Spectrometry Facility

**Data File** MSF18-1462(LS-Ir-PP-allyl)\_hrESIpos1.d  
**Position** P1-C2  
**Acq Method** pos.m

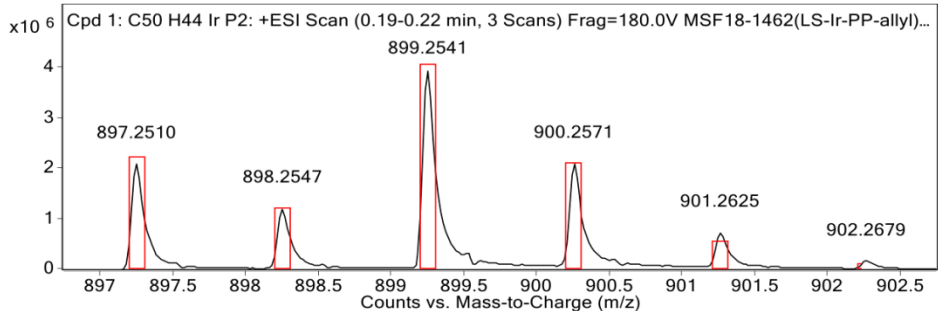
**Sample Name** 1462(LS-Ir-PP-allyl)  
**Instrument Name** Instrument 1  
**Acquired Time** 12/18/2018 1:31:40 PM

**Comment** 1462(LS-Ir-PP-allyl)  
**User Name**  
**DA Method** KS.m



Chemical Formula: C<sub>50</sub>H<sub>44</sub>IrP<sub>2</sub>  
Exact Mass: 899.2547

MS Zoomed Spectrum

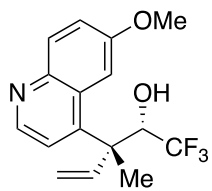
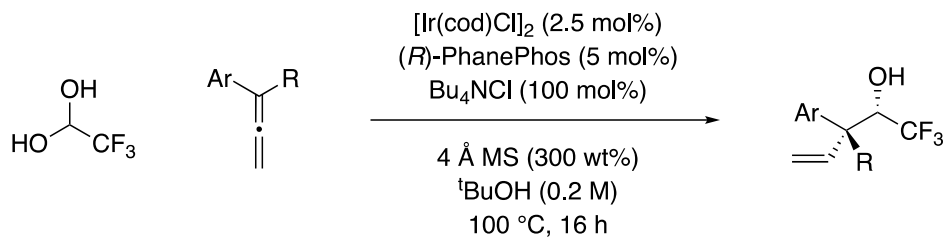


MS Spectrum Peak List

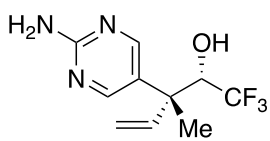
Obs. m/z	Calc. m/z	Charge	Abundance	Formula	Ion Species	Tgt Mass Error (ppm)
897.2510	897.2519	1	2091959	C <sub>50</sub> H <sub>44</sub> IrP <sub>2</sub>	M <sup>+</sup>	0.97
898.2547	898.2552	1	1211029	C <sub>50</sub> H <sub>44</sub> IrP <sub>2</sub>	M <sup>+</sup>	0.62
899.2541	899.2546	1	3946953	C <sub>50</sub> H <sub>44</sub> IrP <sub>2</sub>	M <sup>+</sup>	0.51
900.2571	900.2577	1	2099741	C <sub>50</sub> H <sub>44</sub> IrP <sub>2</sub>	M <sup>+</sup>	0.66
901.2625	901.2610	1	729287	C <sub>50</sub> H <sub>44</sub> IrP <sub>2</sub>	M <sup>+</sup>	-1.61
902.2679	902.2644	1	155926	C <sub>50</sub> H <sub>44</sub> IrP <sub>2</sub>	M <sup>+</sup>	-3.87
903.2714	903.2678	1	26474	C <sub>50</sub> H <sub>44</sub> IrP <sub>2</sub>	M <sup>+</sup>	-3.99
904.2724	904.2711	1	4226	C <sub>50</sub> H <sub>44</sub> IrP <sub>2</sub>	M <sup>+</sup>	-1.43
905.2483	905.2745	1	2875	C <sub>50</sub> H <sub>44</sub> IrP <sub>2</sub>	M <sup>+</sup>	28.97

--- End Of Report ---

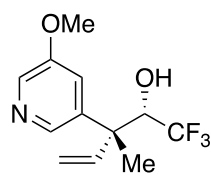
## Additional Substrates



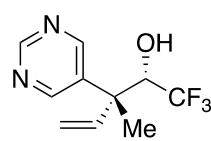
No product observed



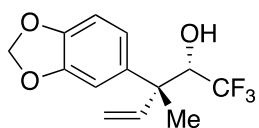
No product observed



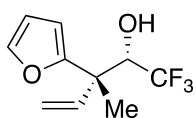
No product observed



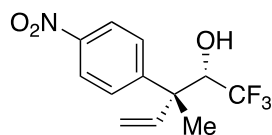
No product observed



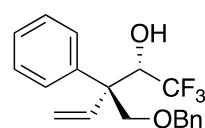
82% yield, 15:1 dr  
88% ee



35% yield, 6:1 dr  
ee N/D



60% yield, 17:1 dr  
96% ee



49% yield, 13:1 dr  
85% ee

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- (15) For the use of Burés plots to determine reaction order, see: (a) Nielsen, C. D.-T.; Burés, J. Visual kinetic analysis. *Chem. Sci.* **2019**, Advance Article. DOI: 10.1039/C8SC04698K.  
(b) Burés, J. Variable Time Normalization Analysis: General Graphical Elucidation of Reaction Orders from Concentration Profiles. *Angew. Chem. Int. Ed.* **2016**, *55*, 16084.  
(c) Burés, J. A Simple Graphical Method to Determine the Order in Catalyst. *Angew. Chem. Int. Ed.* **2016**, *55*, 2028.