Supporting Information

Selection between Diastereomeric Kinetic *vs* Thermodynamic Carbonyl Binding Modes Enables Enantioselective Iridium-Catalyzed *anti*-(α-Aryl)allylation of Aqueous Fluoral Hydrate and Difluoroacetaldehyde Ethyl Hemiacetal

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General Information

All reactions were performed under an argon atmosphere using oven dried glassware. Iridium catalyzed reactions were run in sealed tubes (13x100 mm) which were purchased from Fischer Scientific (catalog number 14-959-35C). Tetrahydrofuran was dried with sodium-benzophenone and distilled immediately prior to use. Reaction control was performed by analytical thin-layer chromatography (TLC) using 0.25 mm commercial silica gel plates (Dynanmic Absorbents F_{254}). Visualization was carried out with UV light followed by staining with potassium permanganate or p-anisaldehyde stain solution and heating. Products were purified by flash chromatography using Silacycle silica gel (40–63 μm) or Fischer Chemical aluminum oxide (basic, Brockman I, 60-325 mesh).

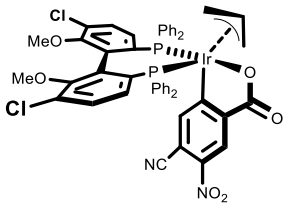
Fluoral hydrate (75% in water) was purchased through Oakwood Chemical, difluoroacetaldehyde ethyl hemiacetal (90% in ethanol) through AstaTech, and potassium carbonate through Fisher Chemicals and used without further purification.

Allylic acetates 2a[1] 2b–2c,[2] 2d,[3] 2e,[4] 2f–2l[2] were prepared according to previous literature.

Spectrometry, Spectroscopy, and Data Collection

Nuclear magnetic resonance spectra (^{1}H, ^{13}C, ^{19}F, ^{31}P) were recorded on a Varian MR-400 or an Avance III 500 spectrometer. The chemical shifts are given as parts per million (ppm) and were referenced to the residual solvent signal ($CDCl_3$: δ_H = 7.26 ppm, δ_C = 77.16 ppm, Acetone-d_6: δ_H = 2.05 ppm, δ_C = 29.84 ppm). Infrared spectra were recorded on a Perkin-Elmer 1600 spectrometer using a diamond ATR unit. High-resolution mass spectra (HRMS) were obtained on a Karatos MS9 and are reported for the molecular ion (M-H, M, M+H, or M+Na) as m/z (relative intensity). Melting points were taken on a Stuart SMP3 melting point apparatus. Specific optical rotations were recorded on an Atago AP-300 automatic polarimeter at the sodium line (589 nm) in $CHCl_3$. Solution concentrations are given in the units of 10^{-2} g mL^{-1}.

Detailed Procedure for Preparation of Preformed Iridium Catalyst



To a sealed tube equipped with a magnetic stir bar was added Cs_2CO_3 (501.8 mg, 1.54 mmol, 200 mol%), 4-cyano-3-nitrobenzoic acid (296.8 mg, 1.54 mmol, 200 mol%), (*S*)-Cl,MeO-BIPHEP (503.0 mg, 0.772 mmol, 100 mol%) and $[Ir(cod)Cl]_2$ (259.3 mg, 0.386 mmol, 50 mol%). The reaction vessel was purged with argon and THF (7.7 mL, 0.1 M) was added followed by allyl acetate (0.208 mL, 1.93 mmol, 250 mol%). The resulting mixture was stirred at room temperature for 30 min, and for another 90 min at 80 ˚C. After cooling to ambient temperature, the mixture was filtered through a celite plug with the aid of DCM (45 mL). The combined filtrate was concentrated *in vacuo* and subjected to flash column chromatography (DCM:THF = 10:1). The resulting gum-like residue was dissolved in THF (2.0 mL). Addition of HPLC grade hexanes (20 mL) led to formation of a precipitate. The product was filtered and washed with HPLC grade hexanes, followed by removal of trace amount of solvent *in vacuo,* to provide a light yellow powder (620.0 mg, 0.577 mmol) in 75% yield as a mixture of stereoisomers.

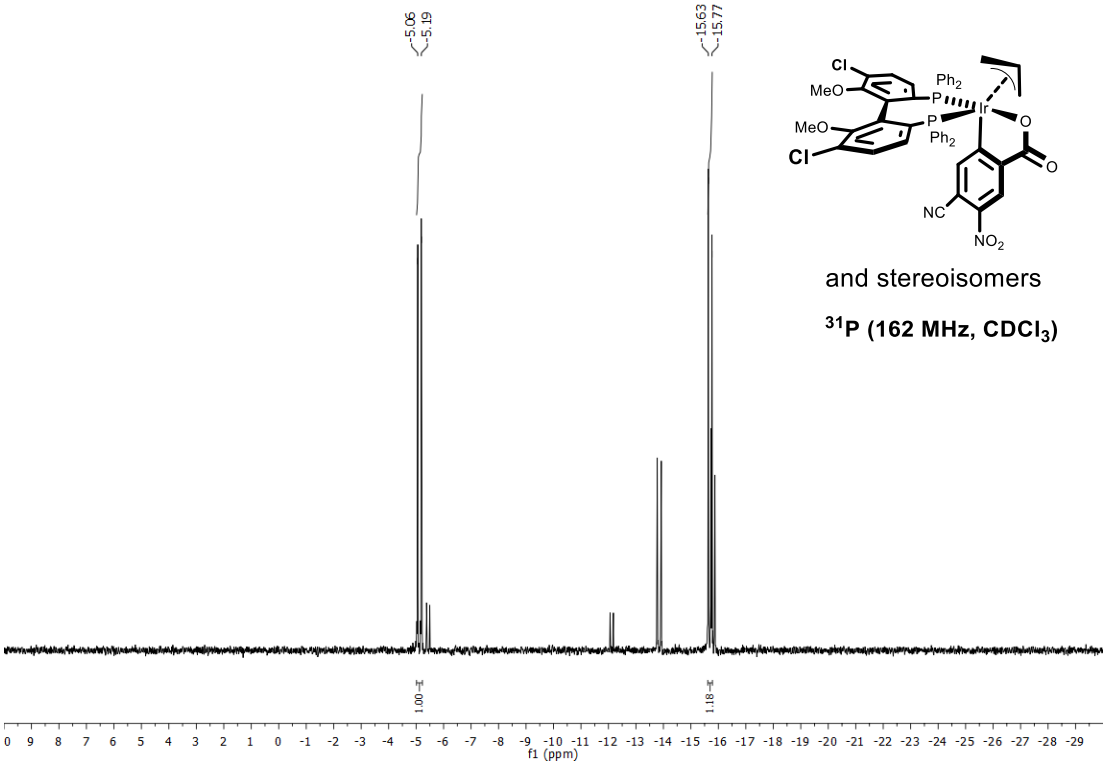
Spectral data is reported for the major isomer.

^{31}P NMR (162 MHz, $CDCl_3$): δ = -5.12 (d, *J* = 21.3 Hz), -15.70 (d, *J* = 21.4 Hz).

HRMS (ESI) Calculated for $C_{49}H_{37}Cl_2IrN_2O_6P_2$ $[M+H]^+$ = 1075.1195, Found 1075.1197.

$[\alpha]_D^{28}$: –4.0 (*c* = 1.0, $CHCl_3$)

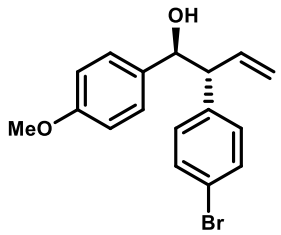
MP: 231-236 ˚C (decomposition)



General Procedure for Iridium Catalyzed Aryl Allylation of Aromatic Aldehydes

A pressure tube was equipped with a magnetic stir bar and charged with preformed iridium catalyst (10.7 mg, 10 μmol, 5 mol%), aldehyde (0.20 mmol, 100 mol%), K_2CO_3 (27.6 mg, 0.20 mmol, 100 mol%), 1-(4-bromophenyl)allyl acetate (0.40 mmol, 200 mol%). The pressure tube was purged with argon. Anhydrous THF (1.0 mL, 0.2 M) and 2-propanol (31 μL, 0.40 mmol, 200 mol%) were added via syringe. The sealed reaction vessel was stirred at 100 °C. After 24 h the solvent was removed *in vacuo* and the residue was subjected to flash column chromatography on silica.

(1S,2R)-2-(4-bromophenyl)-1-(4-methoxyphenyl)but-3-en-1-ol (3b)



The title compound was prepared according to the general procedure using 4-methoxybenzaldehyde (27.2 mg, 200 μmol) and 1-(4-bromophenyl)allyl acetate (102 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 6:1 → 3:1) provided the title compound (35.6 mg, 107 μmol, *anti:syn* = 9:1) in 54% yield as a yellow oil.

TLC (SiO_2) R_f = 0.37 (hexanes/ethyl acetate = 3:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34 – 7.29 (m, 2H), 7.08 – 7.01 (m, 2H), 6.94 – 6.88 (m, 2H), 6.78 – 6.72 (m, 2H), 6.19 (ddd, *J* = 17.0, 10.2, 8.7 Hz, 1H), 5.28 (d, *J* = 10.1 Hz, 1H), 5.22 (dt, *J* = 17.2, 1.3 Hz, 1H), 4.76 (dd, *J* = 8.0, 1.7 Hz, 1H), 3.76 (s, 3H), 3.51 (t, *J* = 8.3 Hz, 1H), 2.22 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.1, 139.9, 137.8, 133.8, 131.5, 130.2, 128.0, 120.5, 118.7, 113.6, 76.8, 58.7, 55.3.

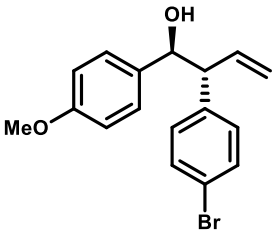
HRMS (ESI) Calculated for $C_{17}H_{17}{}^{79}BrO_2$ $[M+Na]^+$ = 355.0304, Found 355.0299.

FTIR (neat) 3430, 2999, 2907, 2836, 1612, 1513, 1248, 1175, 1034, 1010, 921, 830 cm^{-1}.

$[\alpha]_D^{34}$: –9.0 (*c* = 1.0, $CHCl_3$)

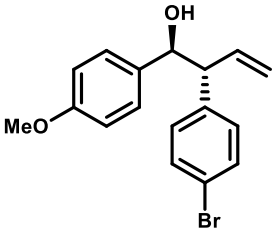
HPLC: (Chiralcel AD-H column, hexanes:*i*-PrOH = 95:5, 1.0 mL/min, 210 nm), *ee* = 5%.

3b

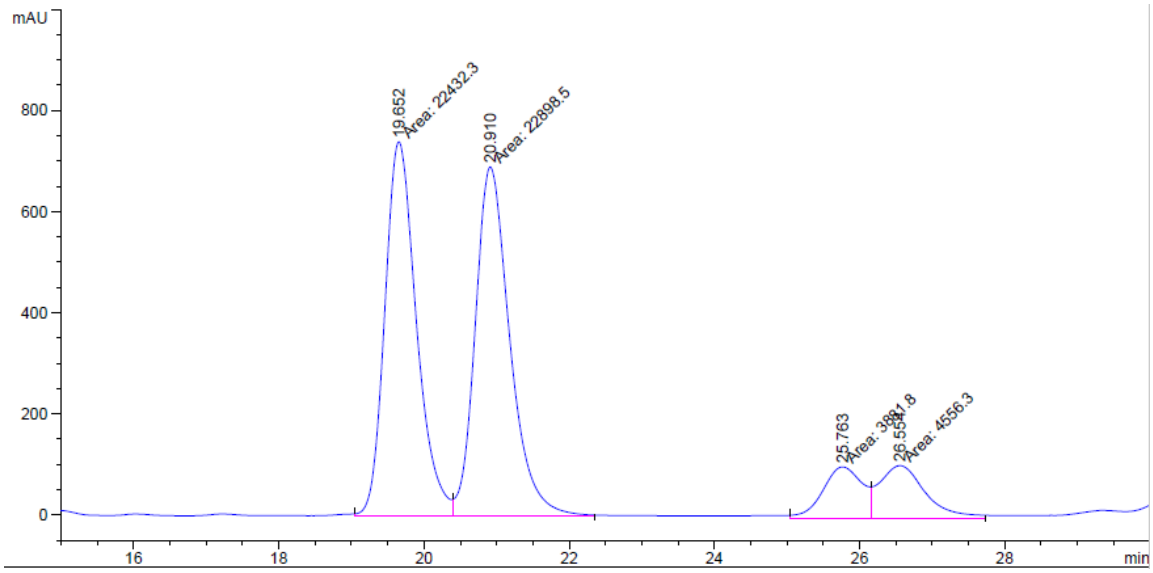


^{1}H (500 MHz, $CDCl_3$)

3b



^{13}C (125 MHz, $CDCl_3$)



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1	19.652	MF	0.5049	2.24323e4	740.49207	41.7198
2	20.910	FM	0.5525	2.28985e4	690.73303	42.5869
3	25.763	MF	0.6353	3881.79907	101.82919	7.2194
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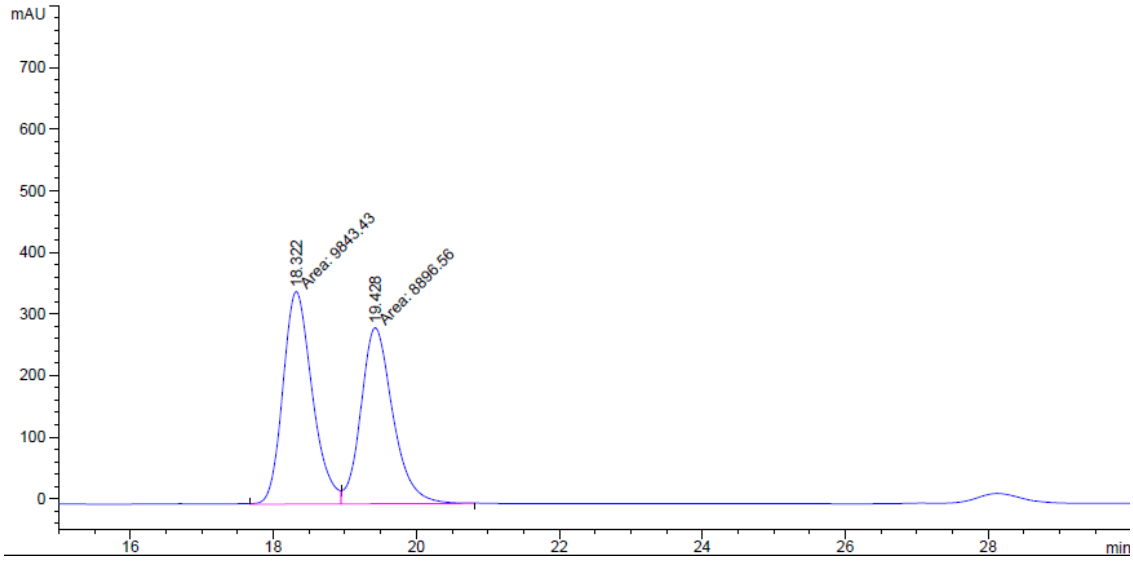

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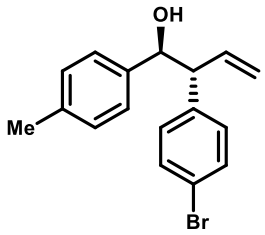
1	18.322	MF	0.4757	9843.43359	344.85089	52.5264
2	19.428	FM	0.5187	8896.55762	285.84869	47.4736

(1S,2R)-2-(4-bromophenyl)-1-(p-tolyl)but-3-en-1-ol (3c)



The title compound was prepared according to the general procedure using 4-methylbenzaldehyde (24.1 mg, 201 μmol) and 1-(4-bromophenyl)allyl acetate (102 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 10:1 → 5:1) provided the title compound (43.7 mg, 138 μmol, *anti:syn* = 4:1) in 69% yield as a yellow oil.

TLC (SiO_2) R_f = 0.43 (hexanes/ethyl acetate = 3:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.36 – 7.29 (m, 2H), 7.03 (s, 4H), 6.97 – 6.90 (m, 2H), 6.19 (ddd, *J* = 17.1, 10.3, 8.6 Hz, 1H), 5.27 (dd, *J* = 10.3, 1.6 Hz, 1H), 5.20 (dt, *J* = 17.1, 1.3 Hz, 1H), 4.78 (d, *J* = 7.8 Hz, 1H), 3.53 (t, *J* = 8.2 Hz, 1H), 2.29 (s, 3H), 2.25 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.0, 138.7, 137.7, 137.4, 131.5, 130.2, 128.9, 126.7, 120.5, 118.7, 77.0, 58.4, 21.2.

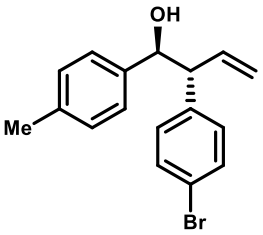
HRMS (CI) Calculated for $C_{17}H_{17}{}^{79}BrO$ $[M-H]^+$ = 315.0385, Found 315.0373.

FTIR (neat) 3439, 2918, 2861, 1487, 1402, 1179, 1073, 1010, 919, 816, 743 cm^{-1}.

$[\alpha]_D^{32}$: –6.3 (*c* = 1.0, $CHCl_3$)

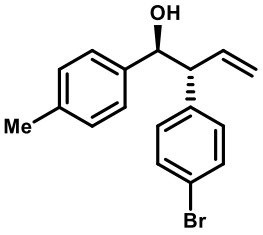
HPLC: (Chiralcel AD-H column, hexanes:*i*-PrOH = 95:5, 1.0 mL/min, 210 nm), *ee* = 12%.

3c

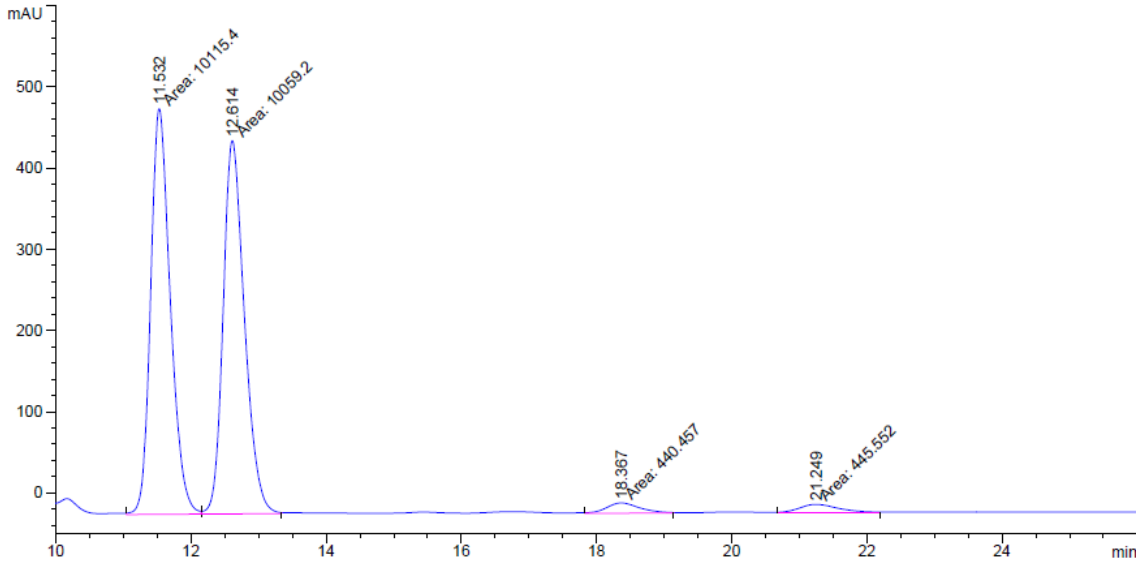


^{1}H (500 MHz, $CDCl_3$)

3c



^{13}C (125 MHz, $CDCl_3$)



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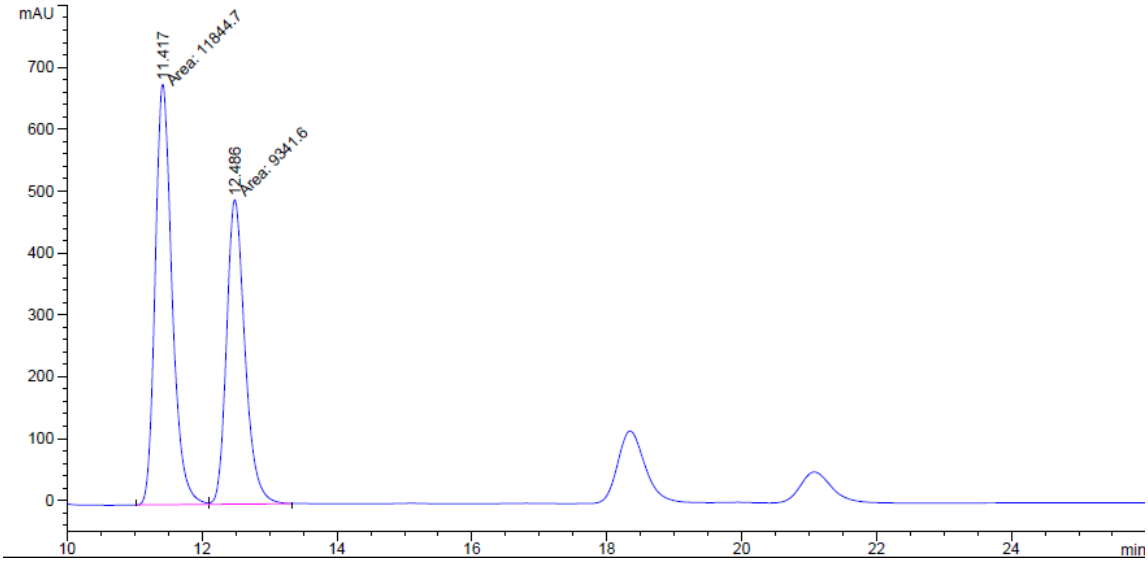
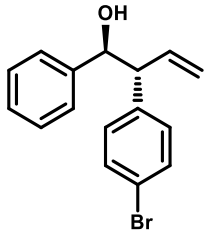
1	11.532	MF	0.3375	1.01154e4	499.51868	48.0300
2	12.614	FM	0.3648	1.00592e4	459.53488	47.7631
3	18.367	MM	0.5765	440.45721	12.73298	2.0914
4	21.249	MM	0.7047	445.55240	10.53725	2.1156



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.417	MF	0.2903	1.18447e4	680.00964	55.9073
2	12.486	FM	0.3163	9341.59961	492.20648	44.0927

(1*S*,2*R*)-2-(4-Bromophenyl)-1-phenylbut-3-en-1-ol (3d)



The title compound was prepared according to the general procedure using benzaldehyde (22.1 mg, 208 µmol) and 1-(4-bromophenyl)allyl acetate (102 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 6:1) provided the title compound (46.6 mg, 154 µmol, *anti:syn* = 4:1) in 74% yield as a yellow oil.

TLC (SiO_2) R_f = 0.36 (hexanes/ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.30 (m, 2H), 7.27–7.19 (m, 3H), 7.16–7.12 (m, 2H), 6.95–6.90 (m, 2H), 6.20 (ddd, *J* = 17.1, 10.3, 8.4 Hz, 1H), 5.28 (dd, *J* = 10.3, 1.5 Hz, 1H), 5.21 (d, *J* = 17.1 Hz, 1H), 4.80 (d, *J* = 7.7 Hz, 1H), 3.53 (t, *J* = 8.4 Hz, 1H), 2.29 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.7, 139.8, 137.5, 131.5, 130.2, 128.2, 127.8, 126.8, 120.6, 118.9, 77.2, 58.6.

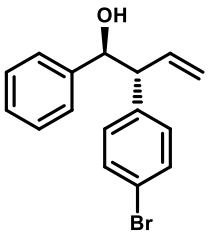
HRMS (CI) Calculated for $C_{16}H_{14}{}^{79}BrO$ $[M–H]^+$ = 301.0228, Found 301.0222.

FTIR (neat) 3434, 3062, 3029, 2920, 1487, 1074, 1010, 920, 814, 762, 726, 700 cm^{-1}.

$[\alpha]_D^{34}$: –3.8 (*c* = 1.0, $CHCl_3$)

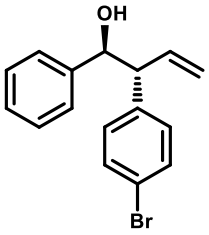
HPLC: (Chiralcel AD-H column, hexanes:*i*-PrOH = 95:5, 1.0 mL/min, 210 nm), *ee* = 15%.

3d

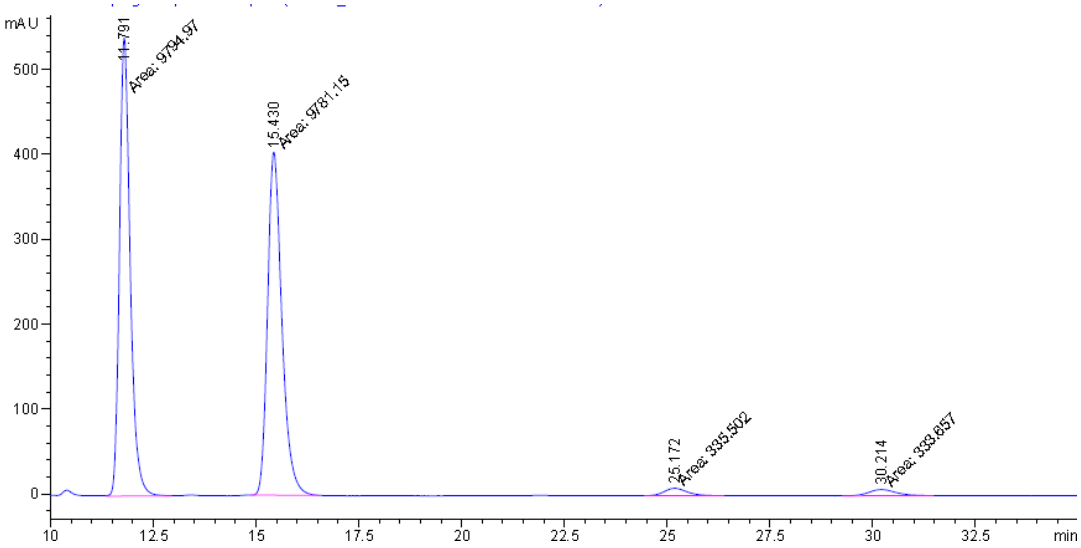


^{1}H (500 MHz, $CDCl_3$)

3d



^{13}C (125 MHz, $CDCl_3$)



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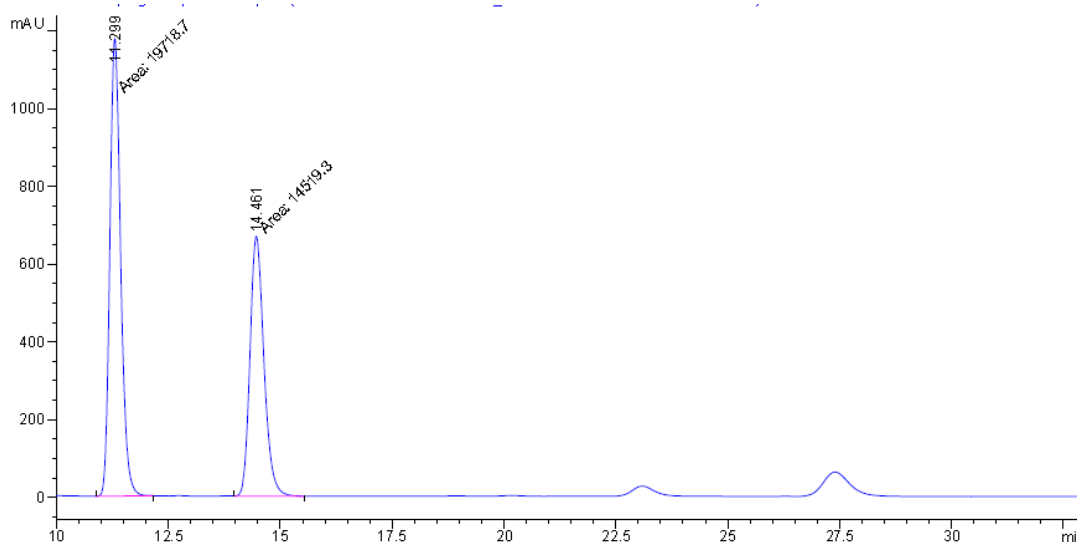
2	15.430	MM	0.4034	9781.14648	404.14508	48.3132
3	25.172	MM	0.6432	335.50162	8.69356	1.6572
4	30.214	MM	0.7663	333.65698	7.25710	1.6481



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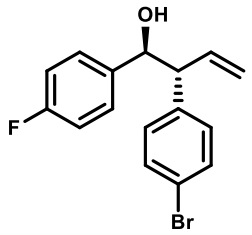
1	11.299	MM	0.2793	1.97187e4	1176.70996	57.5931
2	14.461	MM	0.3619	1.45193e4	668.66504	42.4069

(1S,2R)-2-(4-bromophenyl)-1-(4-fluorophenyl)but-3-en-1-ol (3e)



The title compound was prepared according to the general procedure using 4-fluorobenzaldehyde (24.8 mg, 200 µmol) and 1-(4-bromophenyl)allyl acetate (102 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 8:1 → 5:1) provided the title compound (56.5 mg, 176 µmol, *anti:syn* = 3:1) in 88% yield as a yellow oil.

TLC (SiO_2) R_f = 0.37 (hexanes/ethyl acetate = 3:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.37 – 7.29 (m, 2H), 7.12 – 7.06 (m, 2H), 6.94 – 6.87 (m, 4H), 6.18 (ddd, *J* = 17.0, 10.2, 8.8 Hz, 1H), 5.29 (d, *J* = 10.2 Hz, 1H), 5.23 (dt, *J* = 17.1, 1.2 Hz, 1H), 4.76 (d, *J* = 7.9 Hz, 1H), 3.46 (t, *J* = 8.4 Hz, 1H), 2.37 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.2 (d, *J* = 245.7 Hz), 139.5, 137.4 (d, *J* = 3.1 Hz), 137.3, 131.6, 130.1, 128.4 (d, *J* = 8.1 Hz), 120.7, 119.1, 115.0 (d, *J* = 21.4 Hz), 76.6, 58.9.

^{19}F NMR (471 MHz, $CDCl_3$): δ = -114.61 – -114.69 (m).

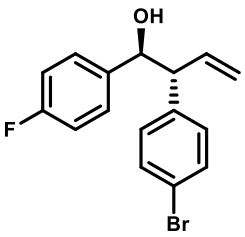
HRMS (CI) Calculated for $C_{16}H_{14}{}^{79}BrFO$ $[M-H]^+$ = 319.0134, Found 319.0133.

FTIR (neat) 3433, 3072, 2915, 1604, 1509, 1488, 1402, 1223, 1157, 1011, 924, 834 cm^{-1}.

$[\alpha]_D^{33}$: –6.5 (*c* = 1.0, $CHCl_3$)

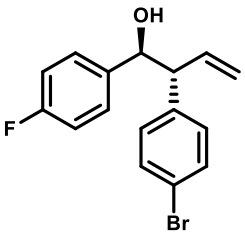
HPLC: (Chiralcel AD-H column, hexanes:*i*-PrOH = 95:5, 1.0 mL/min, 230 nm), *ee* = 16%.

3e



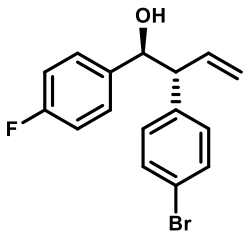
^{1}H (500 MHz, $CDCl_3$)

3e

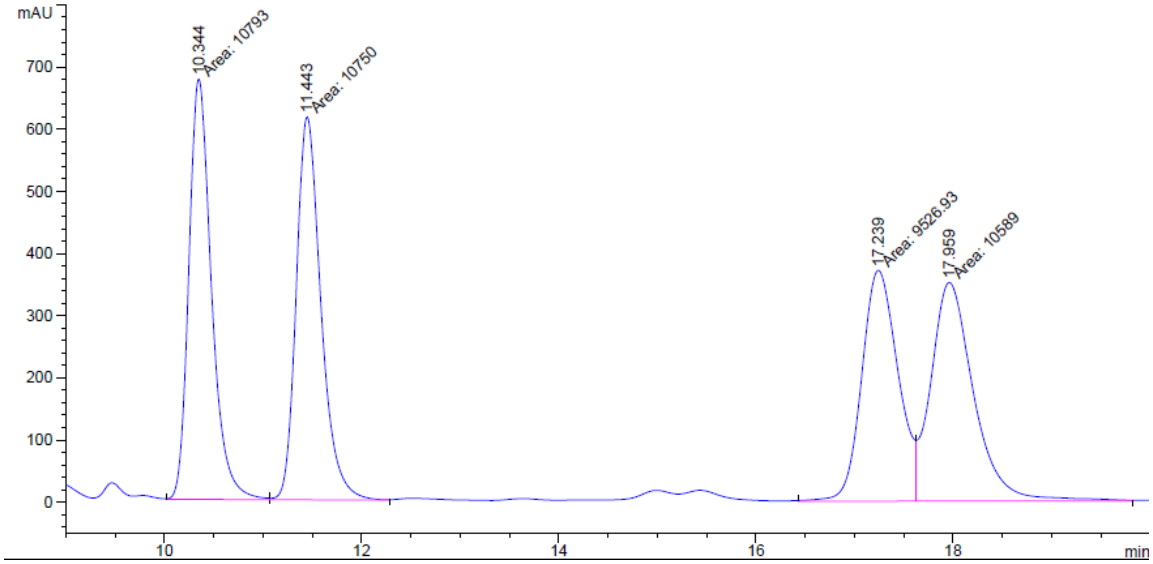


^{13}C (125 MHz, $CDCl_3$)

3e



^{19}F (471 MHz, $CDCl_3$)



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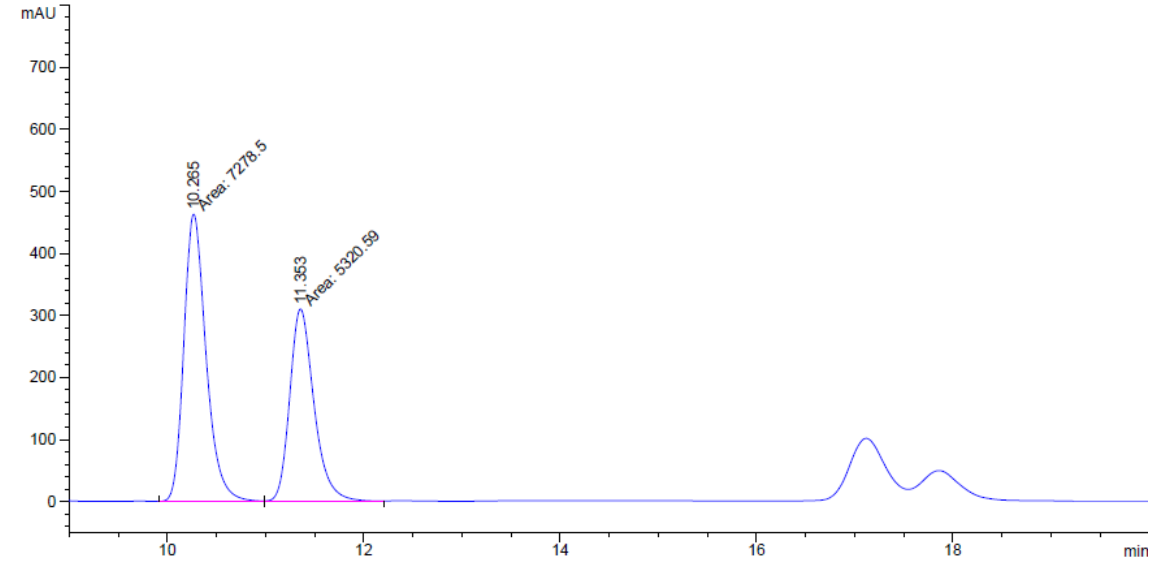
1	10.344	MF	0.2659	1.07930e4	676.44989	25.9080
2	11.443	FM	0.2908	1.07500e4	616.21399	25.8048
3	17.239	MF	0.4276	9526.93359	371.34500	22.8689
4	17.959	FM	0.5016	1.05890e4	351.85855	25.4183



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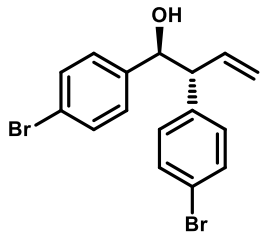
1	10.265	MF	0.2619	7278.50488	463.13281	57.7701
2	11.353	FM	0.2861	5320.58691	309.96762	42.2299

(1*S*,2*R*)-1,2-Bis(4-bromophenyl)but-3-en-1-ol (3f)



The title compound was prepared according to the general procedure using 4-bromobenzaldehyde (37.1 mg, 201 µmol) and 1-(4-bromophenyl)allyl acetate (102 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 6:1) provided the title compound (67.5 mg, 177 µmol, *anti:syn* = 4:1) in 88% yield as a yellow oil.

TLC (SiO_2) R_f = 0.28 + 0.22 (hexanes/ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.37–7.31 (m, 4H), 7.02–6.96 (m, 2H), 6.94–6.88 (m, 2H), 6.16 (dt, *J* = 17.1, 9.9 Hz, 1H), 5.29 (d, *J* = 9.9 Hz, 1H), 5.22 (d, *J* = 17.1 Hz, 1H), 4.74 (d, *J* = 8.0 Hz, 1H), 3.45 (t, *J* = 8.0 Hz, 1H), 2.35 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.6, 139.3, 137.1, 131.7, 131.3, 130.1, 128.5, 121.6, 120.8, 119.3, 76.6, 58.6.

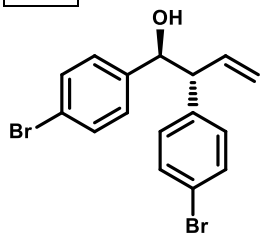
HRMS (CI) Calculated for $C_{16}H_{16}{}^{79}Br_2O$ $[M–H]^+$ = 378.9333, Found 378.9330.

FTIR (neat) 3434, 3078, 2919, 1487, 1403, 1072, 1010, 925, 819, 745 cm^{-1}.

$[\alpha]_D^{34}$: +6.0 (*c* = 1.0, $CHCl_3$)

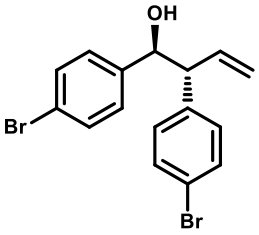
HPLC: (Chiralcel OJ-H column, hexanes:*i*-PrOH = 92:8, 1.0 mL/min, 210 nm), *ee* = 23%.

3f

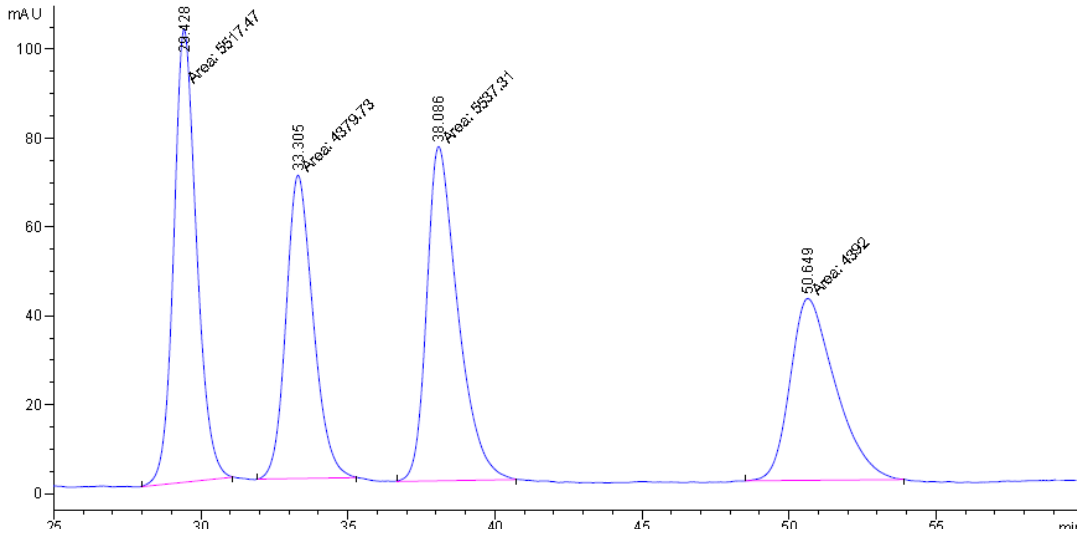


^{1}H (500 MHz, $CDCl_3$)

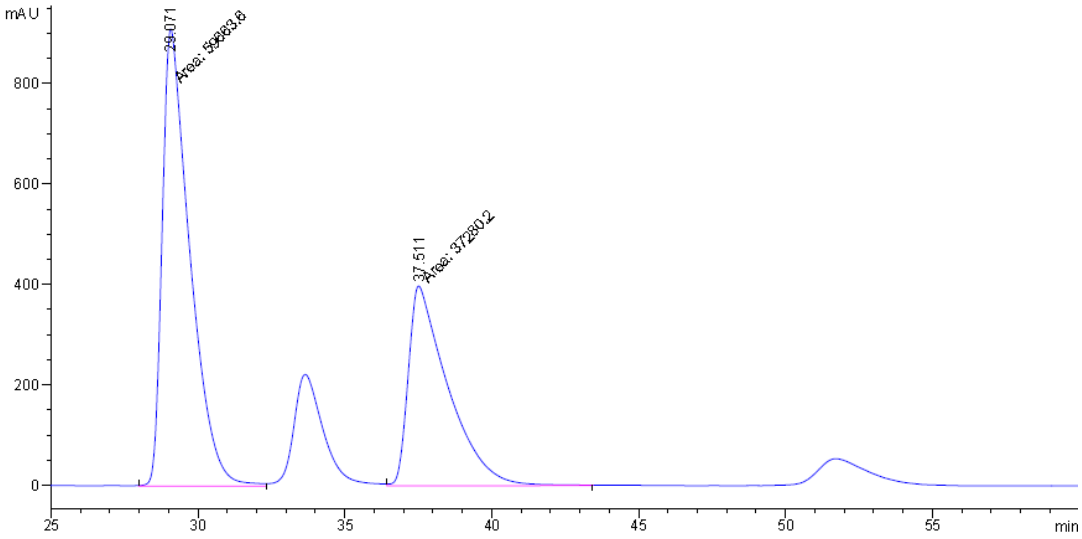
3f



^{13}C (125 MHz, $CDCl_3$)

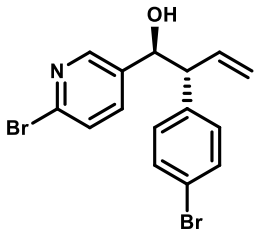


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.428	MM	0.9020	5517.47168	101.95429	27.8288
2	33.305	MM	1.0698	4379.72510	68.23000	22.0903
3	38.086	MM	1.2271	5537.31055	75.21107	27.9288
4	50.649	MM	1.7890	4391.99707	40.91771	22.1522



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.071	MF	1.0923	5.96636e4	910.36182	61.5445
2	37.511	FM	1.5622	3.72802e4	397.73111	38.4555

(1S,2R)-2-(4-bromophenyl)-1-(6-bromopyridin-3-yl)but-3-en-1-ol (3g)



The title compound was prepared according to the general procedure using 6-bromopyridine-3-carbaldehyde (37.1 mg, 199 µmol) and 1-(4-bromophenyl)allyl acetate (102 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 4:1) provided the title compound (62.5 mg, 163 µmol, *anti:syn* 5:1) in 82% yield as a yellow oil.

TLC (SiO_2) R_f = 0.21 (hexanes/ethyl acetate = 3:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.05 (s, 1H), 7.39 – 7.31 (m, 4H), 6.95 – 6.90 (m, 2H), 6.14 (ddd, *J* = 17.0, 10.3, 8.9 Hz, 1H), 5.32 (dd, *J* = 10.2, 1.4 Hz, 1H), 5.24 (dt, *J* = 17.0, 1.1 Hz, 1H), 4.81 (dd, *J* = 7.8, 2.2 Hz, 1H), 3.43 (t, *J* = 8.3 Hz, 1H), 2.60 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.8, 141.3, 138.6, 137.0, 136.5, 136.4, 132.0, 130.0, 127.6, 121.3, 120.0, 74.3, 58.7.

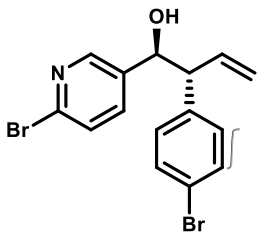
HRMS (ESI) Calculated for $C_{15}H_{13}{}^{79}Br_2NO$ $[M+Na]^+$ = 403.9256, Found 403.9260.

FTIR (neat) 3315, 3082, 2909, 1581, 1564, 1488, 1455, 1402, 1087, 1074, 101, 924, 831, 750 cm^{-1}.

$[\alpha]_D^{30}$: +8.3 (*c* = 1.0, $CHCl_3$)

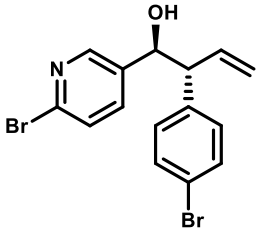
HPLC: (Chiralcel AD-H column, hexanes:*i*-PrOH = 95:5, 1.0 mL/min, 230 nm), *ee* = 37%.

3g

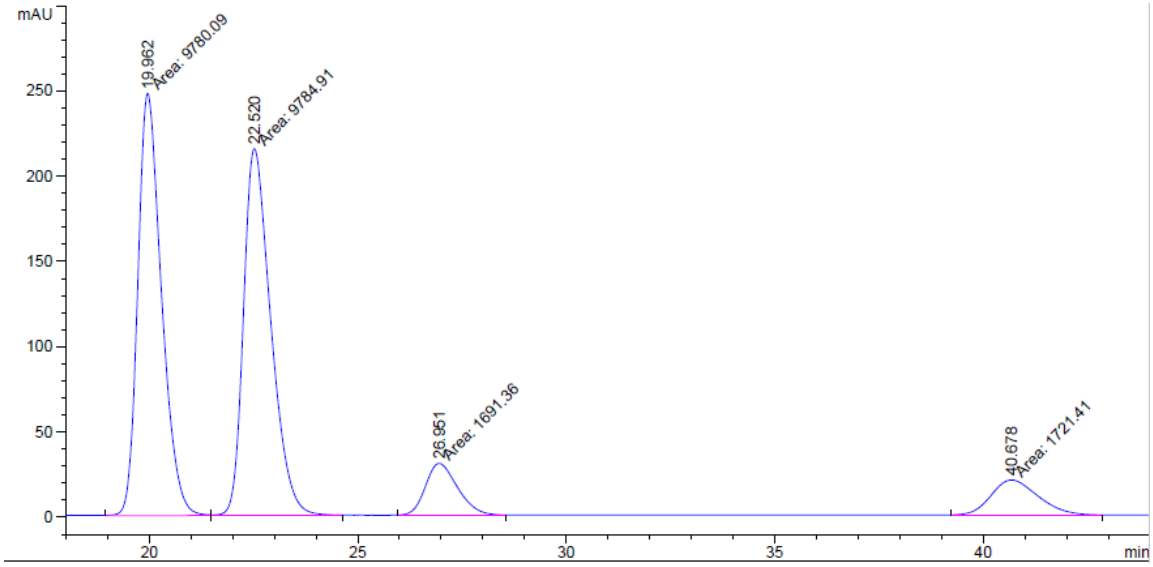


^{1}H (500 MHz, $CDCl_3$)

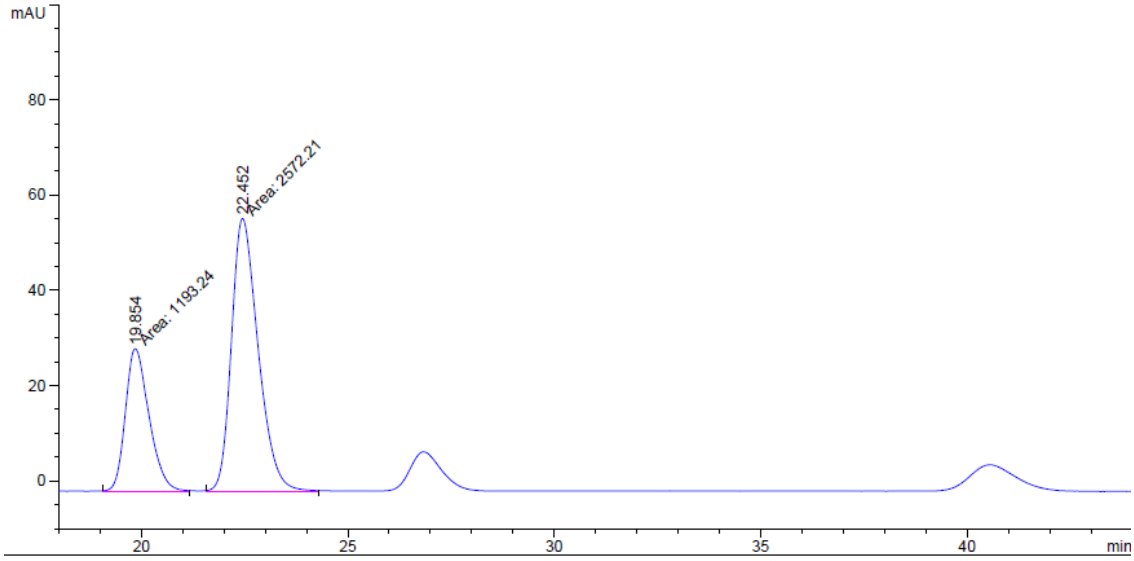
3g



^{13}C (125 MHz, $CDCl_3$)

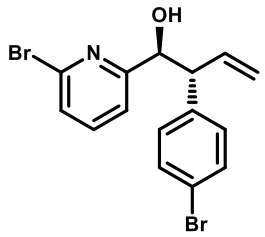


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.962	MF	0.6583	9780.09277	247.61111	42.5633
2	22.520	FM	0.7581	9784.91113	215.10538	42.5842
3	26.951	MM	0.9147	1691.35913	30.81730	7.3608
4	40.678	MM	1.3607	1721.40955	21.08541	7.4916



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.854	MM	0.6640	1193.23975	29.94984	31.6891
2	22.452	MM	0.7487	2572.21289	57.25787	68.3109

(1*S*,2*R*)-2-(4-Bromophenyl)-1-(6-bromopyridin-2-yl)but-3-en-1-ol (3h)



The title compound was prepared according to the general procedure using 6-bromopyridine-2-carbaldehyde (37.2 mg, 200 μmol) and 1-(4-bromophenyl)allyl acetate (102 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 6:1) provided the title compound (57.8 mg, 151 μmol, *anti:syn* 4:1) in 75% yield as a yellow oil.

TLC (SiO_2) R_f = 0.25 (hexanes/ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.41–7.37 (m, 3H), 7.33 (d, *J* = 7.8 Hz, 1H), 7.07 (d, *J* = 8.3 Hz, 2H), 6.96 (d, *J* = 7.5 Hz, 1H), 6.14 (ddd, *J* = 17.2, 10.5, 8.2 Hz, 1H), 5.16 (d, *J* = 10.5 Hz, 1H), 5.01 (d, *J* = 17.2 Hz, 1H), 4.88 (t, *J* = 6.2 Hz, 1H), 3.69 (t, *J* = 7.2 Hz, 1H), 3.45 (d, *J* = 6.5 Hz, 1H).

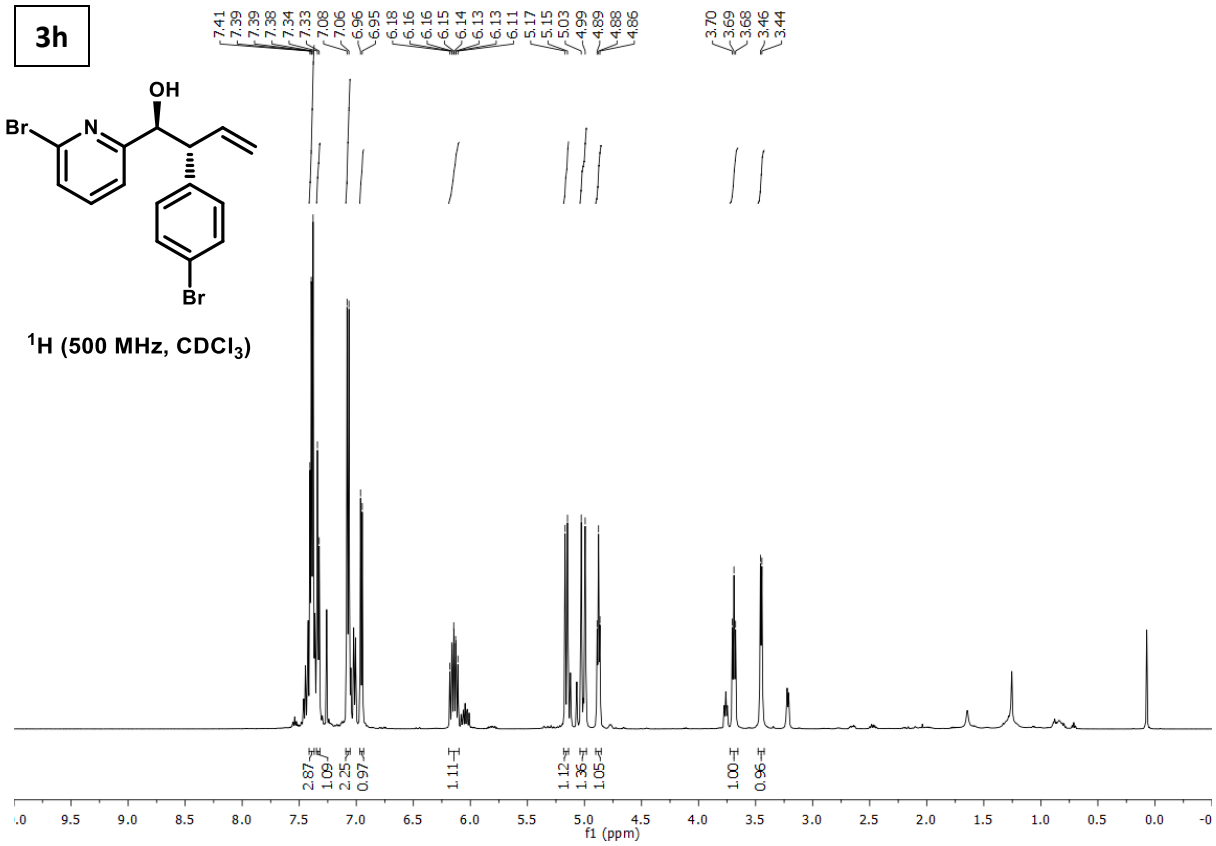
^{13}C NMR (125 MHz, $CDCl_3$): δ = 161.9, 141.2, 139.9, 138.7, 136.2, 131.7, 130.3, 127.0, 120.8, 120.5, 118.6, 76.2, 56.6.

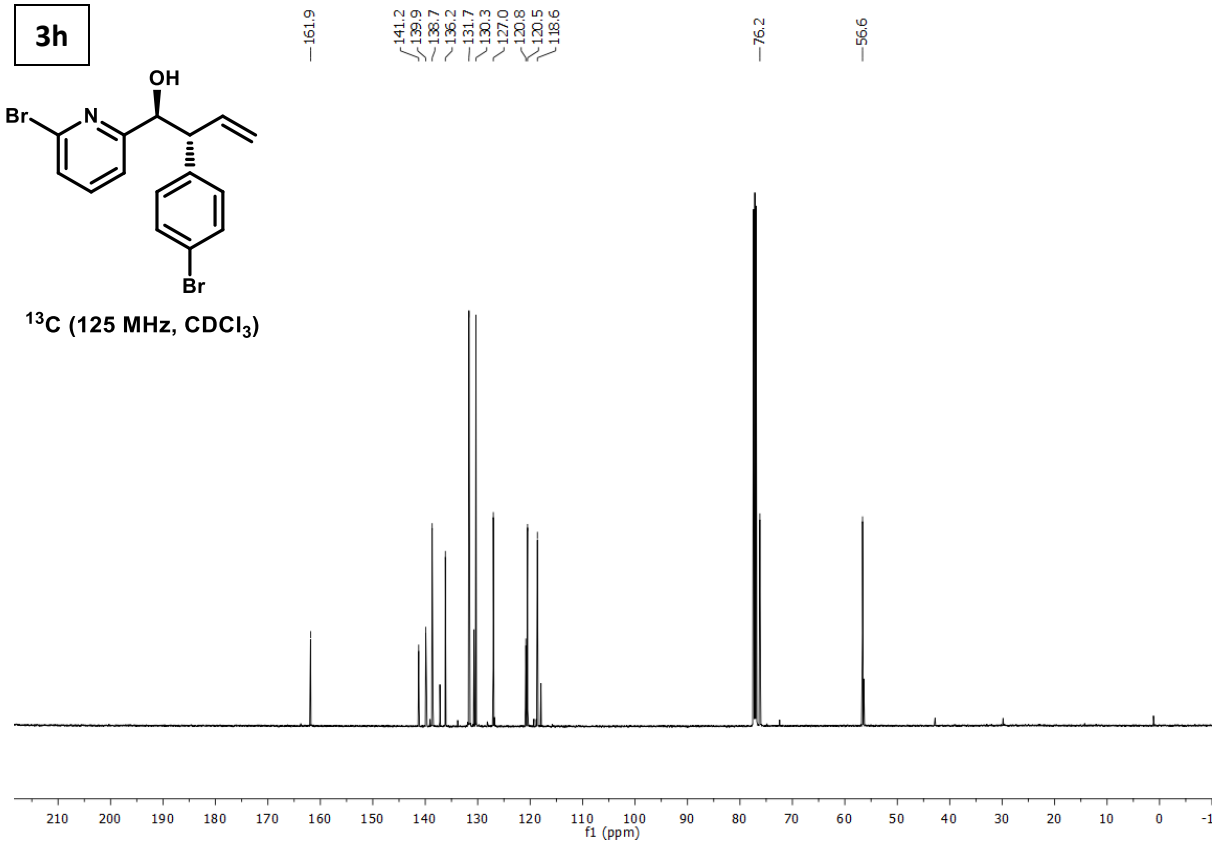
HRMS (APPI) Calculated for $C_{15}H_{14}{}^{79}Br_2NO$ $[M+H]^+$ = 381.9437, Found 381.9447.

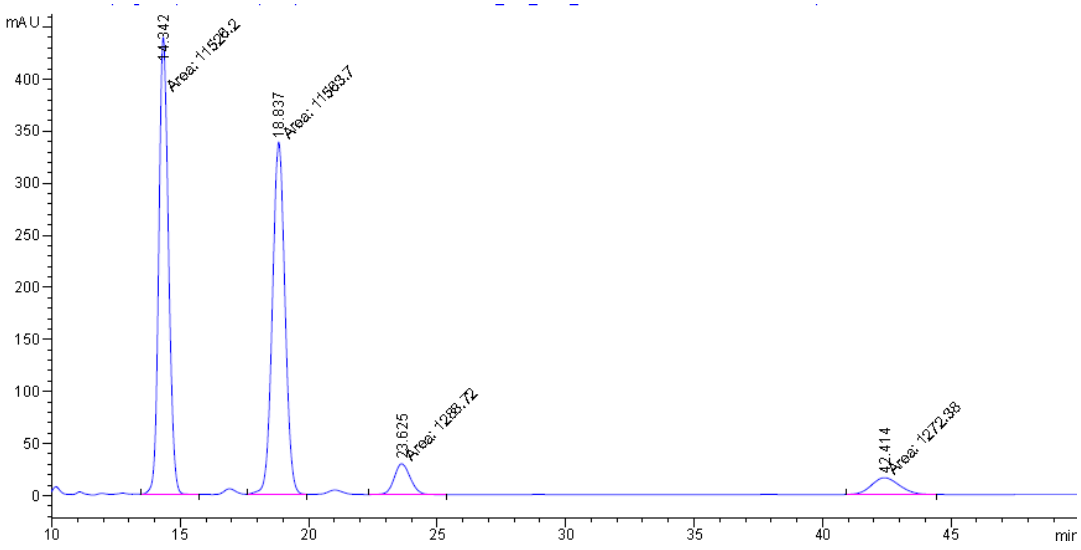
FTIR (neat) 3411, 2923, 1582, 1556, 1488, 1437, 1406, 1125, 1072, 1011 cm^{-1}.

$[\alpha]_D^{33}$: –71.5 (*c* = 1.0, $CHCl_3$)

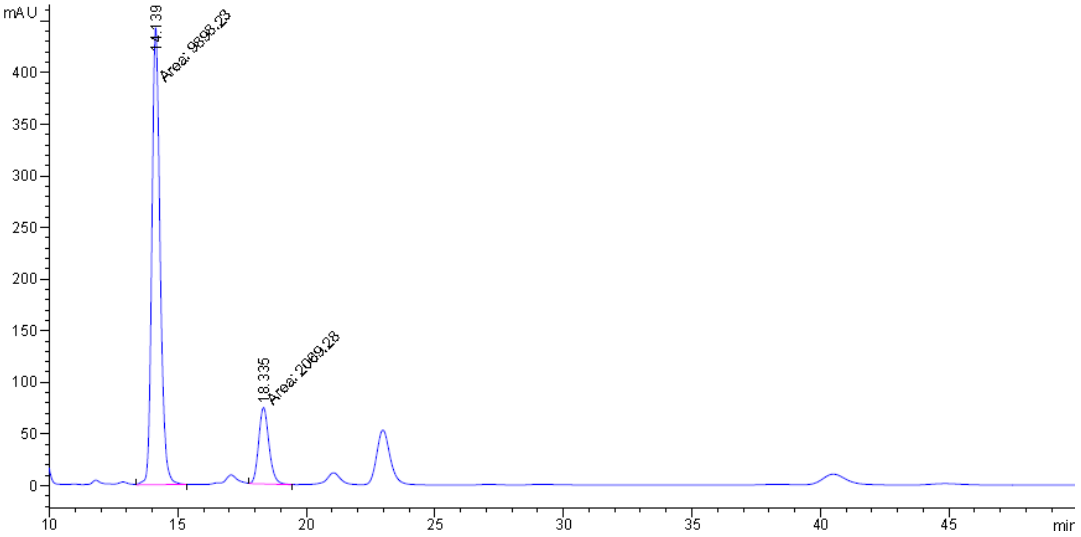
HPLC: (Chiralcel AD-H column, hexanes:*i*-PrOH = 95:5, 1.0 mL/min, 254 nm), *ee* = 65%.


3h
OH
Br
N
Br
^{1}H (500 MHz, CDCl$_3$)
7.41
7.39
7.39
7.38
7.34
7.33
7.08
7.06
6.96
6.95
6.18
6.16
6.16
6.15
6.14
6.13
6.13
6.11
5.17
5.15
5.03
4.99
4.89
4.88
4.86
3.70
3.69
3.68
3.46
3.44
2.87
1.09
2.25
0.97
1.11
1.12
1.36
1.05
1.00
0.96
f1 (ppm)


3h
OH
Br
N
Br
^{13}C (125 MHz, CDCl$_3$)
161.9
141.2
139.9
138.7
136.2
131.7
130.3
127.0
120.8
120.5
118.6
76.2
56.6
f1 (ppm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.342	MM	0.4376	1.15262e4	438.95636	44.9348
2	18.837	MM	0.5693	1.15637e4	338.50641	45.0808
3	23.625	MM	0.7249	1288.72083	29.62928	5.0241
4	42.414	MM	1.2950	1272.38135	16.37522	4.9604

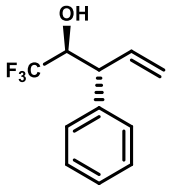


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.139	MM	0.3728	9898.23242	442.54211	82.7092
2	18.335	MM	0.4658	2069.27808	74.04234	17.2908

General Procedure and Spectral Data for Iridium Catalyzed *anti*-(α-Aryl)Allylation of Fluoral Hydrate 1i to form Products 4a-4l

A pressure tube was equipped with a magnetic stir bar and charged with preformed iridium catalyst (10.7 mg, 10 μmol, 5 mol%), K_2CO_3 (27.6 mg, 0.20 mmol, 100 mol%), allyl donor (0.40 mmol, 200 mol%) and 4A molecular sieves (90 mg, 300 wt%). The pressure tube was purged with argon. Anhydrous THF (1.0 mL, 0.2 M), 2-propanol (31 μL, 0.40 mmol, 200 mol%), and fluoral hydrate (75% in H_2O, 22 μL, 0.20 mmol, 100 mol%) were added via syringe. The sealed reaction vessel was stirred at 100 °C. After 24 h the solvent was removed *in vacuo* and the residue was subjected to flash column chromatography on silica.

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



The title compound was prepared according to the general procedure using fluoral hydrate (75% in H_2O, 22 μL, 200 μmol) and 1-phenylallyl acetate (71 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 20:1 → 8:1) provided the title compound (36.7 mg, 170 μmol, *anti:syn* = >20:1) in 85% yield as a yellow oil.

TLC (SiO_2) R_f = 0.60 (hexanes/ethyl acetate = 3:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35 – 7.17 (m, 5H), 6.15 (ddd, *J* = 17.0, 10.1, 8.5 Hz, 1H), 5.27 (dt, *J* = 10.2, 0.9 Hz, 1H), 5.15 (dt, *J* = 17.1, 1.2 Hz, 1H), 4.20 (h, *J* = 6.4 Hz, 1H), 3.69 (dd, *J* = 8.5, 5.1 Hz, 1H), 2.35 (d, *J* = 5.6 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 139.8, 135.0, 128.9, 128.2, 127.4, 124.8 (d, *J* = 283.2 Hz), 119.9, 73.1 (q, *J* = 29.5 Hz), 50.2.

^{19}F NMR (471 MHz, $CDCl_3$): δ = –76.0 (d, *J* = 6.9 Hz).

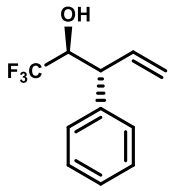
HRMS (CI) Calculated for $C_{11}H_{11}F_3O$ $[M]^+$ = 216.0762, Found 216.0766.

FTIR (neat) 3443, 2927, 1266, 1165, 1109, 925, 852, 761, 735, 701 cm^{-1}.

$[\alpha]_D^{34}$: –65.0 (*c* = 0.5, $CHCl_3$)

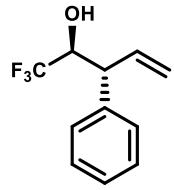
HPLC: (Chiralcel AS-H column, hexanes:*i*-PrOH = 99:1, 1.0 mL/min, 210 nm), *ee* = 93%.

4a



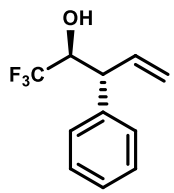
^{1}H (500 MHz, $CDCl_3$)

4a

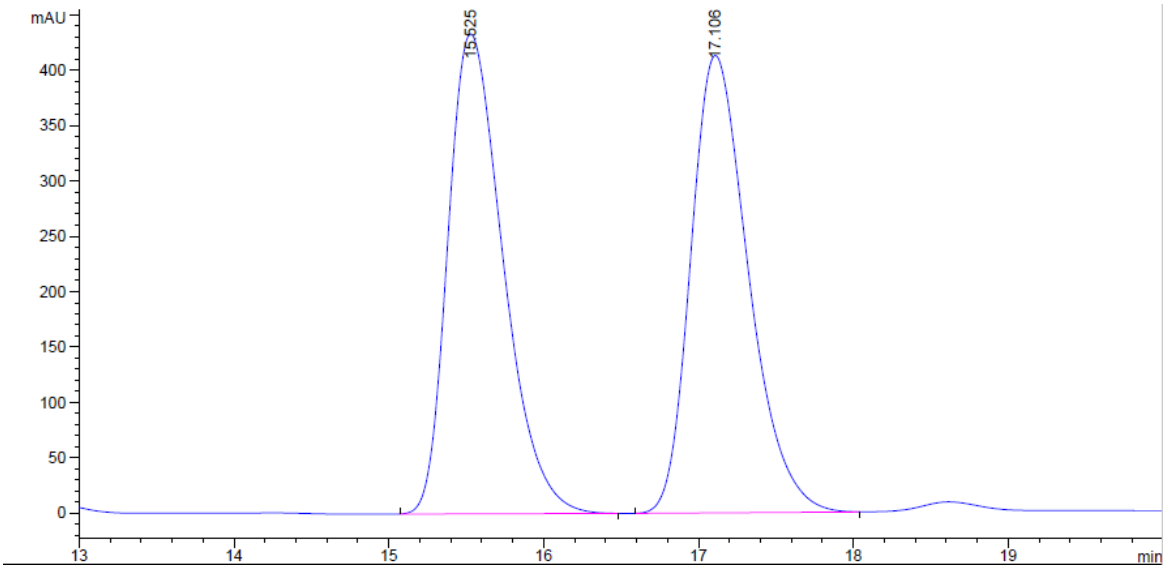


^{13}C (125 MHz, $CDCl_3$)

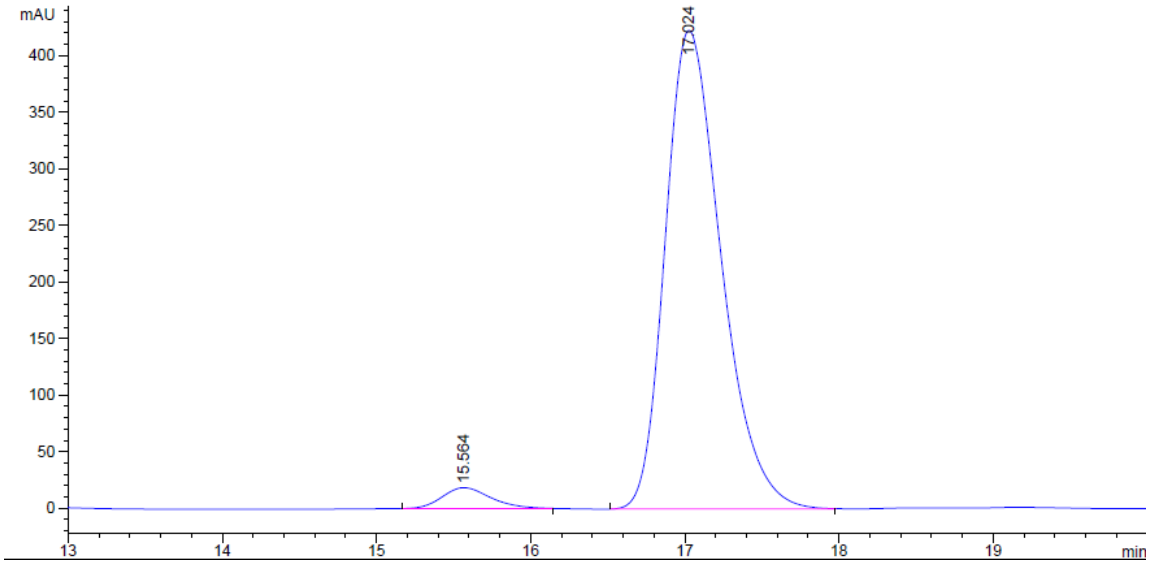
4a



^{19}F (471 MHz, $CDCl_3$)

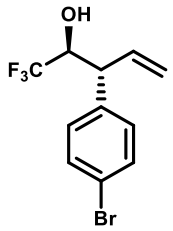


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.525	BB	0.3846	1.07149e4	433.17065	50.0908
2	17.106	BB	0.3998	1.06761e4	412.67371	49.9092



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.564	BB	0.3368	412.85068	18.60910	3.7250
2	17.024	BB	0.3904	1.06704e4	422.83902	96.2750

(2S,3R)-3-(4-bromophenyl)-1,1,1-trifluoropent-4-en-2-ol (4b)



The title compound was prepared according to the general procedure using fluoral hydrate (75% in H_2O, 22 µL, 200 µmol) and 1-(4-bromophenyl)allyl acetate (102 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 20:1 → 8:1) provided the title compound (51.8 mg, 176 µmol, *anti:syn* = >20:1) in 88% yield as a yellow oil.

TLC (SiO_2) R_f = 0.60 (hexanes/ethyl acetate = 3:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.51 – 7.41 (m, 2H), 7.21 – 7.13 (m, 2H), 6.22 – 6.08 (m, 1H), 5.32 (dt, *J* = 10.3, 1.0 Hz, 1H), 5.17 (dt, *J* = 17.1, 1.2 Hz, 1H), 4.20 (h, *J* = 6.5 Hz, 1H), 3.69 (dd, *J* = 8.3, 5.0 Hz, 1H), 2.43 (d, *J* = 5.9 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.9, 134.5, 132.0, 129.9, 124.7 (d, *J* = 283.3 Hz), 121.4, 120.3, 72.9 (q, *J* = 29.6 Hz), 49.5.

^{19}F NMR (471 MHz, $CDCl_3$): δ = –76.0 (d, *J* = 6.8 Hz)

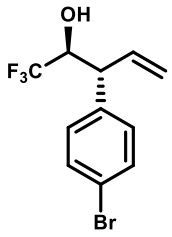
HRMS (CI) Calculated for $C_{11}H_{10}BrF_3O$ $[M]^+$ = 293.9867, Found 293.9868.

FTIR (neat) 3460, 2923, 1489, 1405, 1270, 1168, 1108, 1075, 1011, 928, 817, 720 cm^{-1}.

$[\alpha]_D^{27}$: –87.3 (*c* = 1.0, $CHCl_3$)

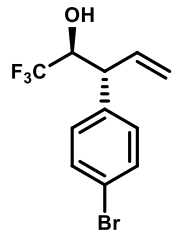
HPLC: (Chiralcel AS-H column, hexanes:*i*-PrOH = 99:1, 1.0 mL/min, 230 nm), *ee* = 94%.

4b



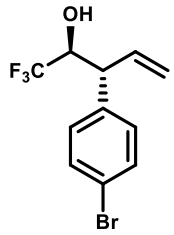
^{1}H (500 MHz, $CDCl_3$)

4b

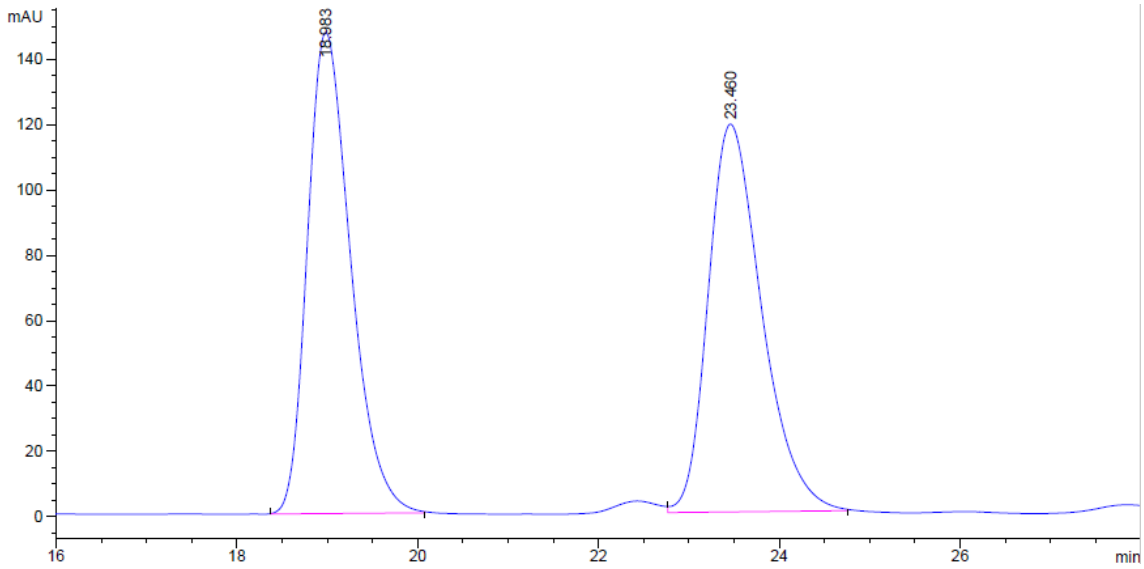


^{13}C (125 MHz, $CDCl_3$)

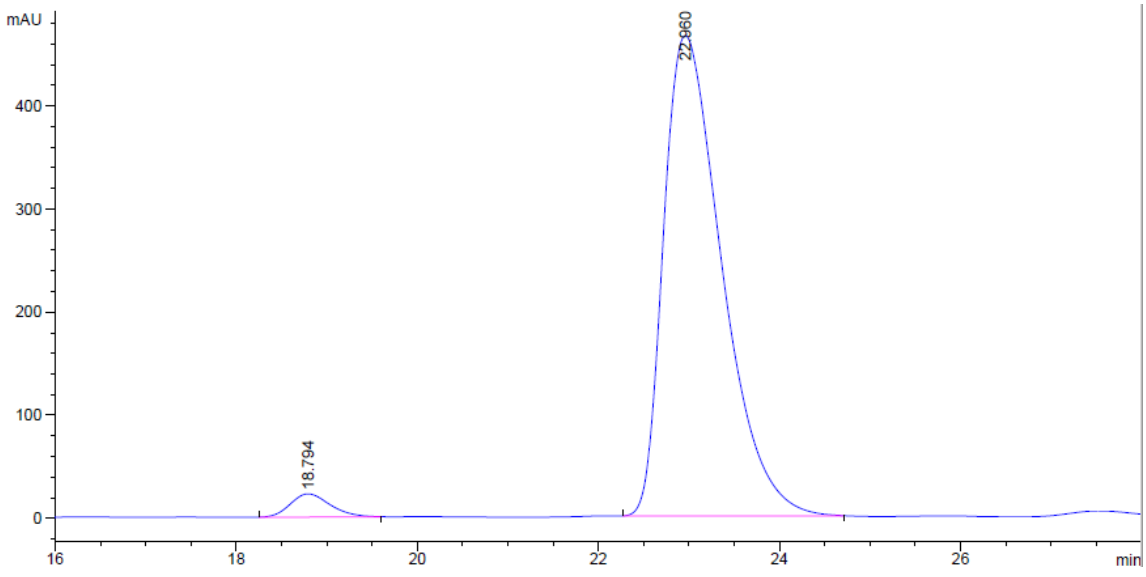
4b



^{19}F (471 MHz, $CDCl_3$)

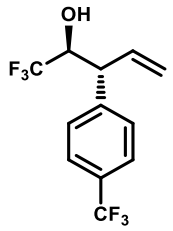


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.983	BB	0.5165	4904.00586	147.26453	50.0566
2	23.460	VB	0.6348	4892.91162	118.72536	49.9434



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.794	BB	0.4733	689.50726	22.51617	3.2090
2	22.960	BB	0.6906	2.07968e4	466.09949	96.7910

(2*S*,3*R*)-1,1,1-Trifluoro-3-(4-(trifluoromethyl)phenyl)pent-4-en-2-ol (4c)



The title compound was prepared according to the general procedure using fluoral hydrate (75% in H_2O, 22 μL, 200 μmol) and 1-(4-(trifluoromethyl)phenyl)allyl acetate (98 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 20:1 → 8:1) provided the title compound (36.3 mg, 128 μmol, *anti:syn* = >20:1) in 64% yield as a yellow oil.

TLC (SiO_2) R_f = 0.18 (hexanes/ethyl acetate = 10:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.63–7.58 (m, 2H), 7.46–7.41 (m, 2H), 6.19 (ddd, *J* = 17.6, 10.2, 8.4 Hz, 1H), 5.35 (d, *J* = 10.2 Hz, 1H), 5.18 (dt, *J* = 17.6, 1.0 Hz, 1H), 4.25 (pd, *J* = 6.5, 4.9 Hz, 1H), 3.80 (dd, *J* = 8.4, 4.9 Hz, 1H), 2.42 (d, *J* = 6.5 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.9, 134.2, 129.8 (q, *J* = 32.6 Hz), 128.6, 125.9 (q, *J* = 3.8 Hz), 124.6 (q, *J* = 284.0 Hz), 124.2 (q, *J* = 272.0 Hz), 120.6, 72.9 (q, *J* = 29.8 Hz), 49.9.

^{19}F NMR (471 MHz, $CDCl_3$): δ = –62.6, –76.1 (d, *J* = 6.5 Hz)

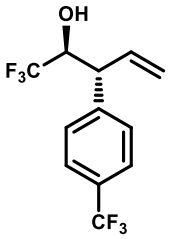
HRMS (CI) Calculated for $C_{12}H_{10}F_6O$ $[M]^+$ = 284.0636, Found 284.0636.

FTIR (neat) 3434, 2923, 1325, 1266, 1164, 1110, 1067, 1019, 832, 700 cm^{-1}.

$[\alpha]_D^{33}$: –59.3 (*c* = 1.0, $CHCl_3$)

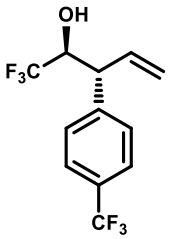
HPLC: (Chiralcel AS-H column, hexanes:*i*-PrOH = 99:1, 1.0 mL/min, 210 nm), *ee* = 93%.

4c



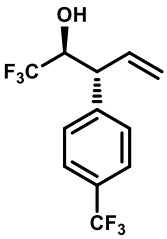
^{1}H (500 MHz, $CDCl_3$)

4c

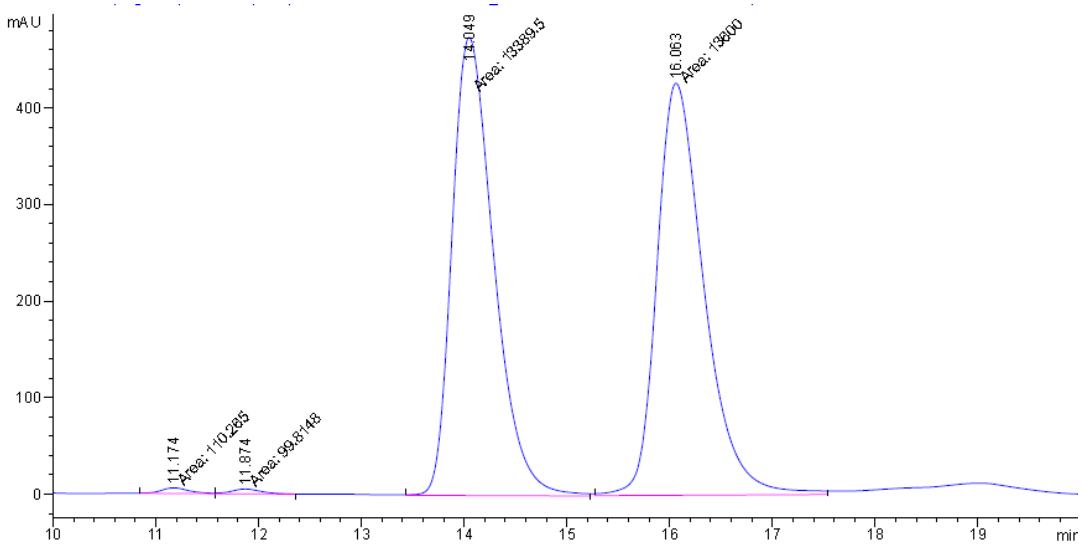


^{13}C (125 MHz, $CDCl_3$)

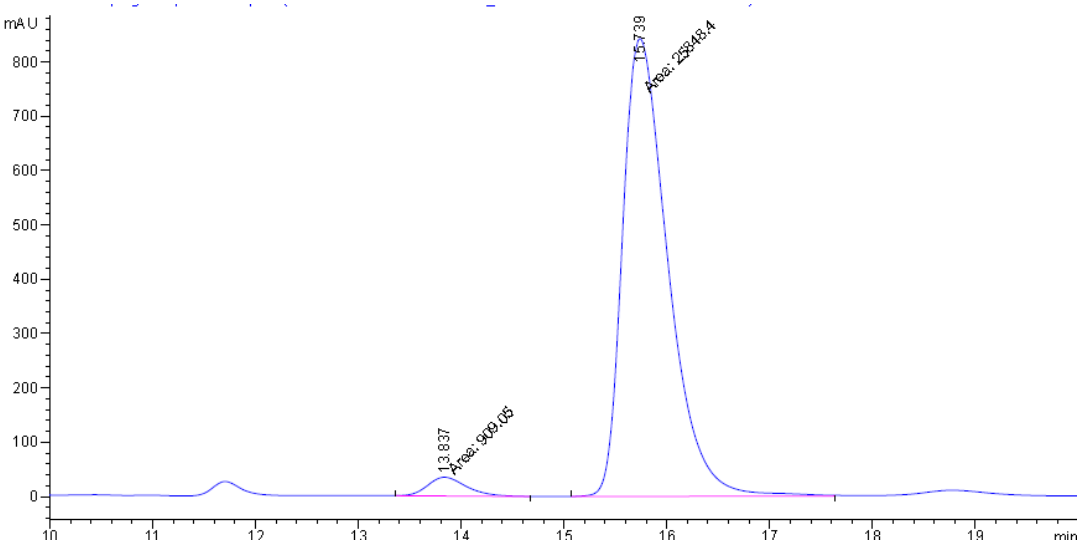
4c



^{19}F (471 MHz, $CDCl_3$)

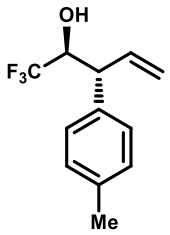


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.174	MF	0.3123	110.26528	5.88381	0.4054
2	11.874	FM	0.3321	99.81478	5.00884	0.3670
3	14.049	MM	0.4704	1.33895e4	474.37296	49.2268
4	16.063	MM	0.5313	1.36000e4	426.59085	50.0008



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.837	MM	0.4389	909.05029	34.52143	3.3974
2	15.739	MM	0.5114	2.58484e4	842.32935	96.6026

(2*S*,3*R*)-1,1,1-Trifluoro-3-(*p*-tolyl)pent-4-en-2-ol (4d)



The title compound was prepared according to the general procedure using fluoral hydrate (75% in H_2O, 22 µL, 200 µmol) and 1-(*p*-tolyl)allyl acetate (76 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 20:1 → 8:1) provided the title compound (35.5 mg, 154 µmol, *anti:syn* = >20:1) in 77% yield as a yellow oil.

TLC (SiO_2) R_f = 0.18 (hexanes/ethyl acetate = 10:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.23–7.12 (m, 4H), 6.18 (ddd, *J* = 17.6, 10.2, 8.6 Hz, 1H), 5.30 (dd, *J* = 10.2, 1.3 Hz, 1H), 5.19 (dt, *J* = 17.6, 1.3 Hz, 1H), 4.28–4.17 (m, 1H), 3.70 (dd, *J* = 8.6, 5.2 Hz, 1H), 2.35 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.1, 136.8, 135.2, 129.6, 128.0, 123.7 (d, *J* = 283.5 Hz), 119.7, 73.2 (q, *J* = 29.3 Hz), 49.9, 21.2.

^{19}F NMR (471 MHz, $CDCl_3$): δ = –75.9 (d, *J* = 6.9 Hz)

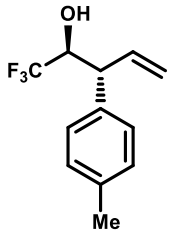
HRMS (CI) Calculated for $C_{12}H_{14}F_3O$ $[M+H]^+$ = 231.0997, Found 231.0999.

FTIR (neat) 3459, 2924, 1267, 1166, 1115, 924, 811, 783, 685, 669 cm^{-1}.

$[\alpha]_D^{33}$: –77.8 (*c* = 1.0, $CHCl_3$)

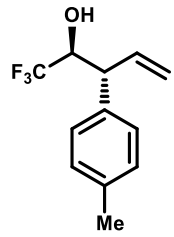
HPLC: (Chiralcel AS-H column, hexanes:*i*-PrOH = 99:1, 1.0 mL/min, 210 nm), *ee* = 92%.

4d



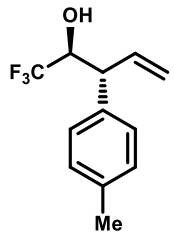
^{1}H (500 MHz, $CDCl_3$)

4d

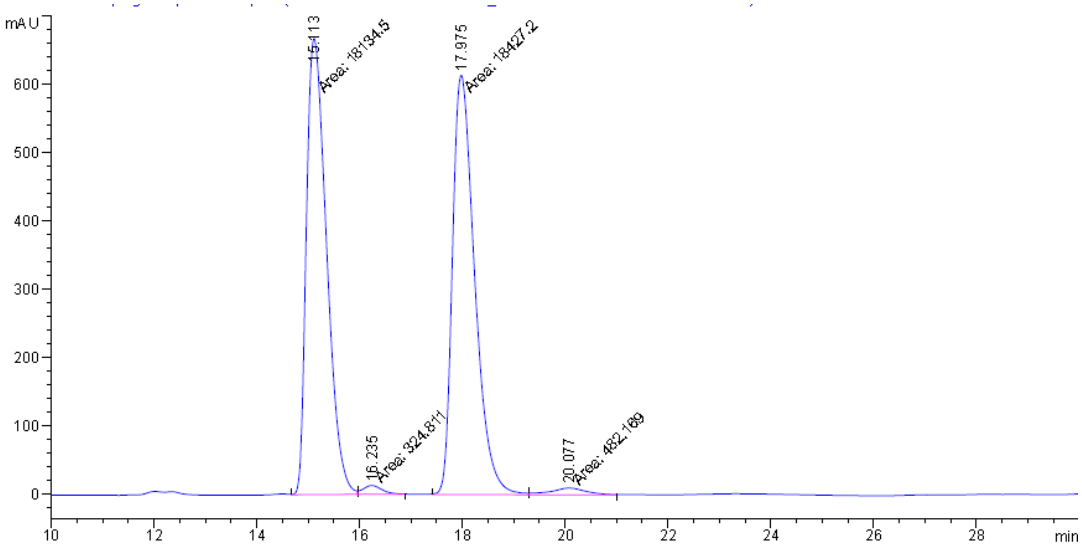


^{13}C (125 MHz, $CDCl_3$)

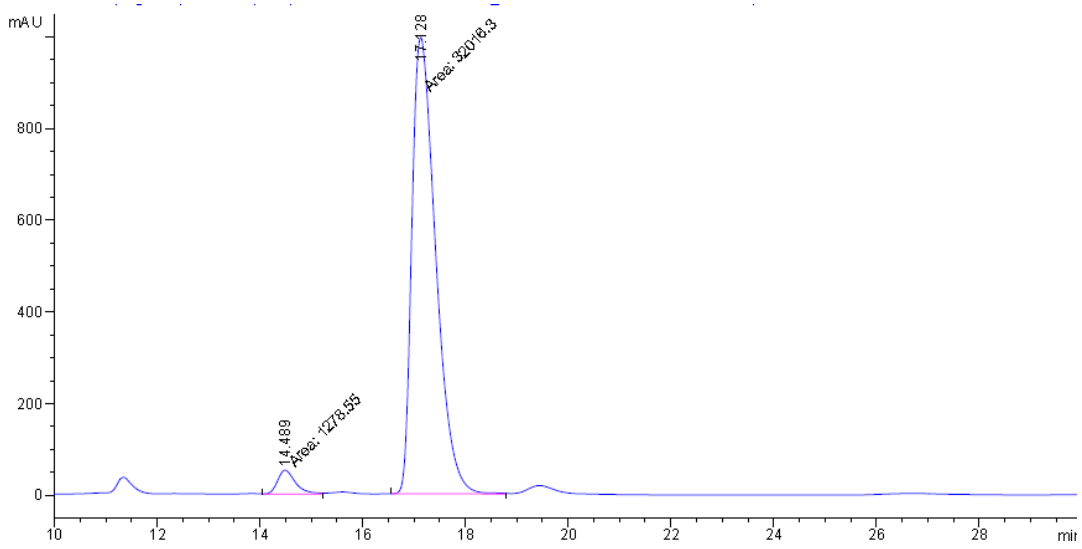
4d



^{19}F (471 MHz, $CDCl_3$)

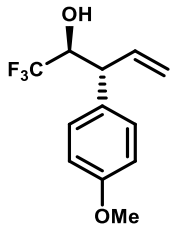


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.113	MF	0.4531	1.81345e4	667.04077	48.5286
2	16.235	FM	0.4216	324.81085	12.84072	0.8692
3	17.975	MF	0.5008	1.84272e4	613.20197	49.3119
4	20.077	FM	0.8083	482.16904	9.94247	1.2903



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.489	MF	0.4079	1278.54797	52.24576	3.8401
2	17.128	MF	0.5362	3.20163e4	995.22772	96.1599

(2*S*,3*R*)-1,1,1-Trifluoro-3-(4-methoxyphenyl)pent-4-en-2-ol (4e)



The title compound was prepared according to the general procedure using fluoral hydrate (75% in H_2O, 22 µL, 200 µmol) and 1-(4-methoxyphenyl)allyl acetate (82 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 20:1 → 8:1) provided the title compound (34.9 mg, 142 µmol, *anti:syn* = >20:1) in 71% yield as a yellow oil.

TLC (SiO_2) R_f = 0.36 (hexanes/ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.21 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 6.22 – 6.11 (m, 1H), 5.29 (dt, *J* = 10.2, 1.0 Hz, 1H), 5.17 (dt, *J* = 17.2, 1.3 Hz, 1H), 4.24 – 4.15 (m, 1H), 3.80 (s, 3H), 3.69 (dd, *J* = 8.4, 5.2 Hz, 1H), 2.42 (d, *J* = 6.2 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.8, 135.3, 131.8, 129.2, 124.8 (q, *J* = 283.3 Hz), 119.5, 114.3, 73.2 (q, *J* = 29.2 Hz), 55.4, 49.4.

^{19}F NMR (471 MHz, $CDCl_3$): δ = -75.89 (d, *J* = 6.9 Hz).

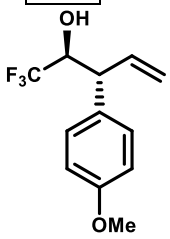
HRMS (CI) Calculated for $C_{12}H_{13}F_3O_2$ $[M]^+$ = 246.0868, Found 246.0866.

FTIR (neat) 3458, 3007, 2360, 1738, 1512, 1366, 1232, 1111, 1032, 826 cm^{-1}.

$[\alpha]_D^{33}$: –73.5 (*c* = 1.0, $CHCl_3$)

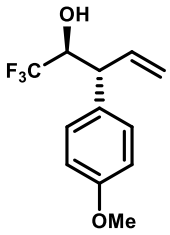
HPLC: (Chiralcel OD-H column, hexanes:*i*-PrOH = 99:1, 1.0 mL/min, 230 nm), *ee* = 92%.

4e



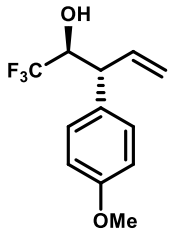
^{1}H (500 MHz, $CDCl_3$)

4e

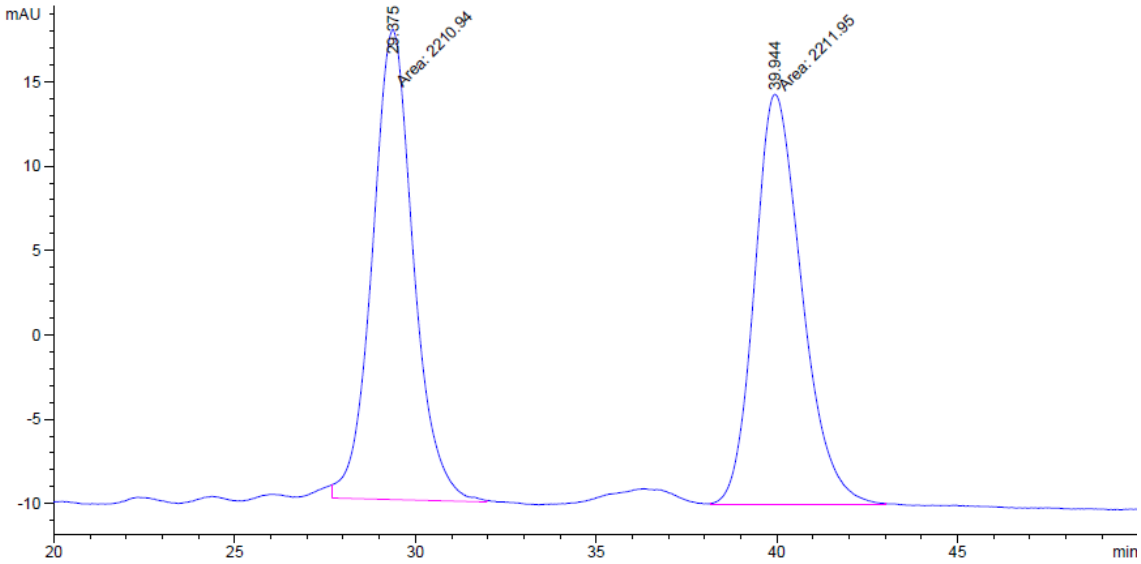


^{13}C (125 MHz, $CDCl_3$)

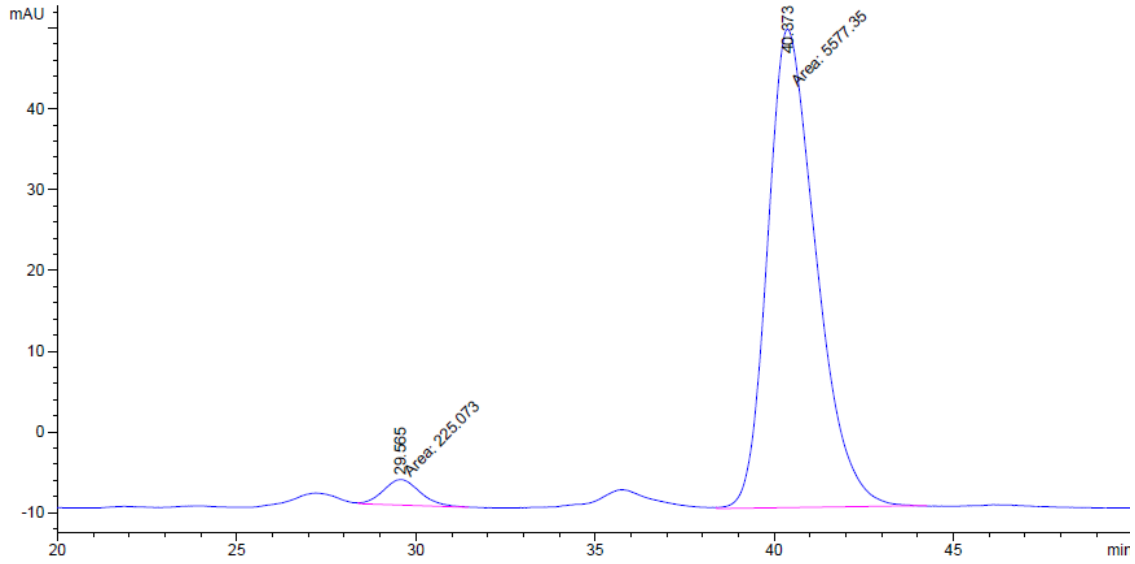
4e



^{19}F (471 MHz, $CDCl_3$)

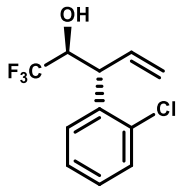


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.375	FM	1.3222	2210.93848	27.86860	49.9886
2	39.944	MM	1.5162	2211.94775	24.31518	50.0114



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.565	MM	1.1884	225.07312	3.15641	3.8790
2	40.373	MM	1.5699	5577.34863	59.21095	96.1210

(2S,3R)-3-(2-chlorophenyl)-1,1,1-trifluoropent-4-en-2-ol (4f)



The title compound was prepared according to the general procedure using fluoral hydrate (75% in H_2O, 22 µL, 200 µmol) and 1-(2-chlorophenyl)allyl acetate (84 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 20:1 → 8:1) provided the title compound (30.1 mg, 120 µmol, *anti:syn* = >20:1) in 60% yield as a yellow oil.

TLC (SiO_2) R_f = 0.57 (hexanes/ethyl acetate = 3:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.46 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.40 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.27 (td, *J* = 7.5, 1.4 Hz, 1H), 7.22 (td, *J* = 7.6, 1.7 Hz, 1H), 6.24 (dddt, *J* = 17.2, 10.1, 8.2, 1.0 Hz, 1H), 5.36 – 5.33 (m, 1H), 5.18 (dt, *J* = 17.2, 1.2 Hz, 1H), 4.40 – 4.22 (m, 2H), 2.40 (d, *J* = 6.6 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.7, 133.4, 133.3, 130.1, 129.8, 128.6, 127.2, 124.7 (d, *J* = 283.3 Hz), 120.7, 71.9 (q, *J* = 30.0 Hz), 45.6.

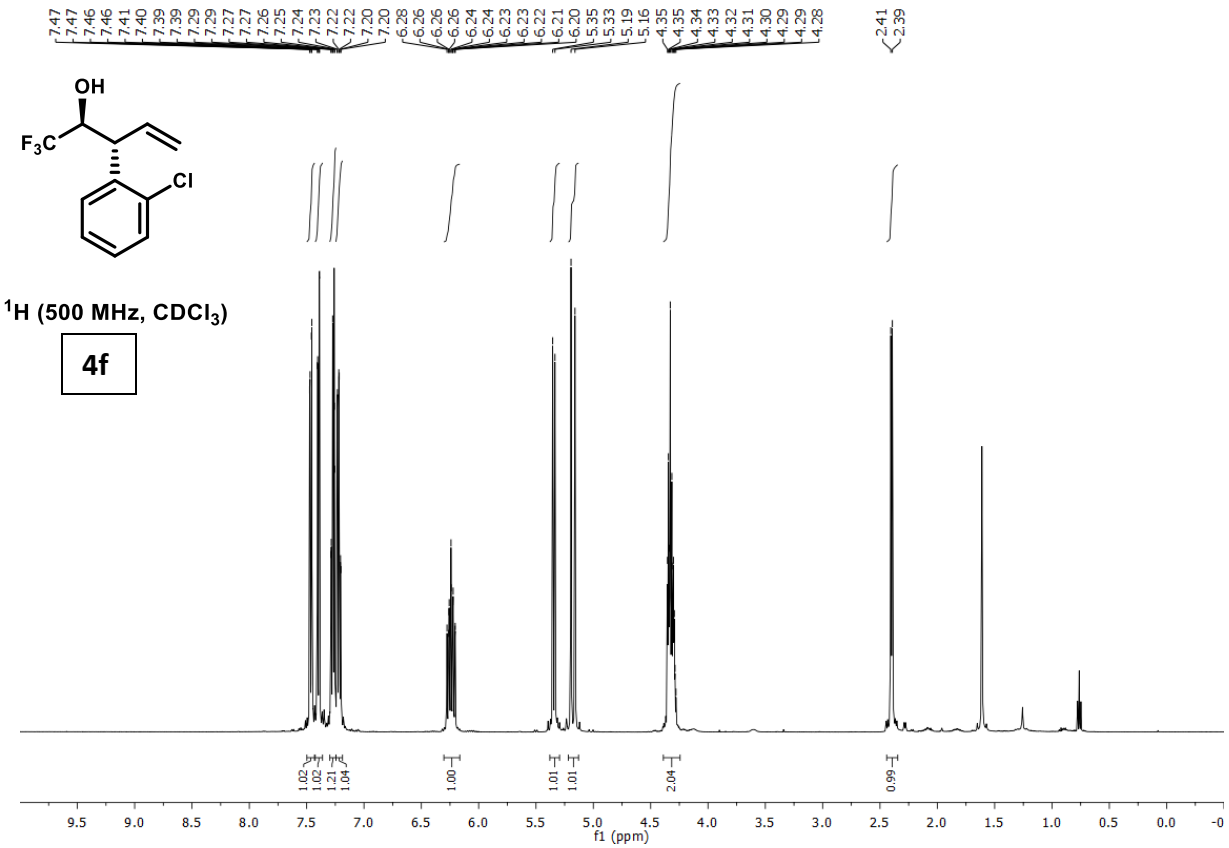
^{19}F NMR (471 MHz, $CDCl_3$): δ = –76.5 (d, *J* = 6.9 Hz).

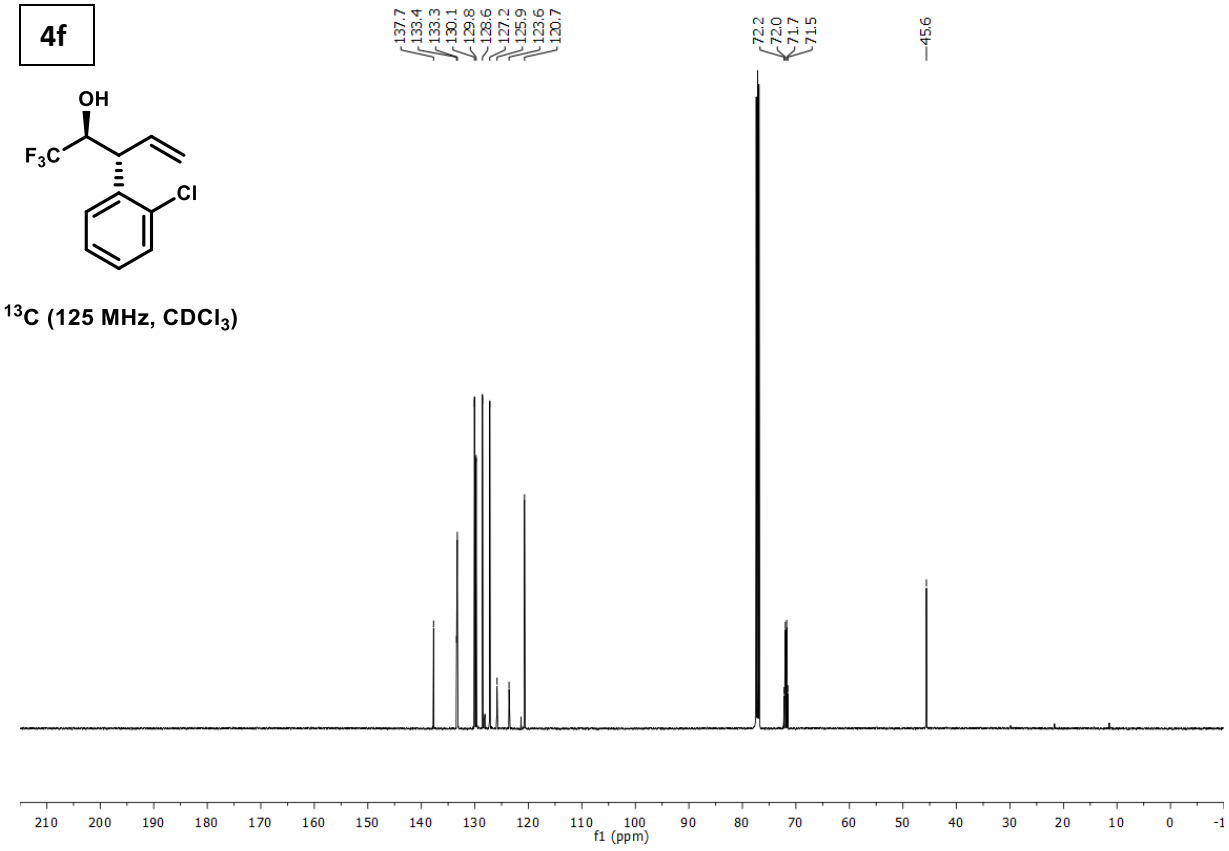
HRMS (CI) Calculated for $C_{11}H_{10}ClF_3O$ $[M]^+$ = 250.0372, Found 250.0367.

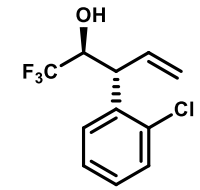
FTIR (neat) 3466, 2926, 1474, 1271, 1170, 1128, 1101, 928, 751, 680 cm^{-1}.

$[\alpha]_D^{30}$: –38.8 (*c* = 1.0, $CHCl_3$)

HPLC: (Chiralcel AS-H column, hexanes:*i*-PrOH = 99:1, 1.0 mL/min, 230 nm), *ee* = 89%.

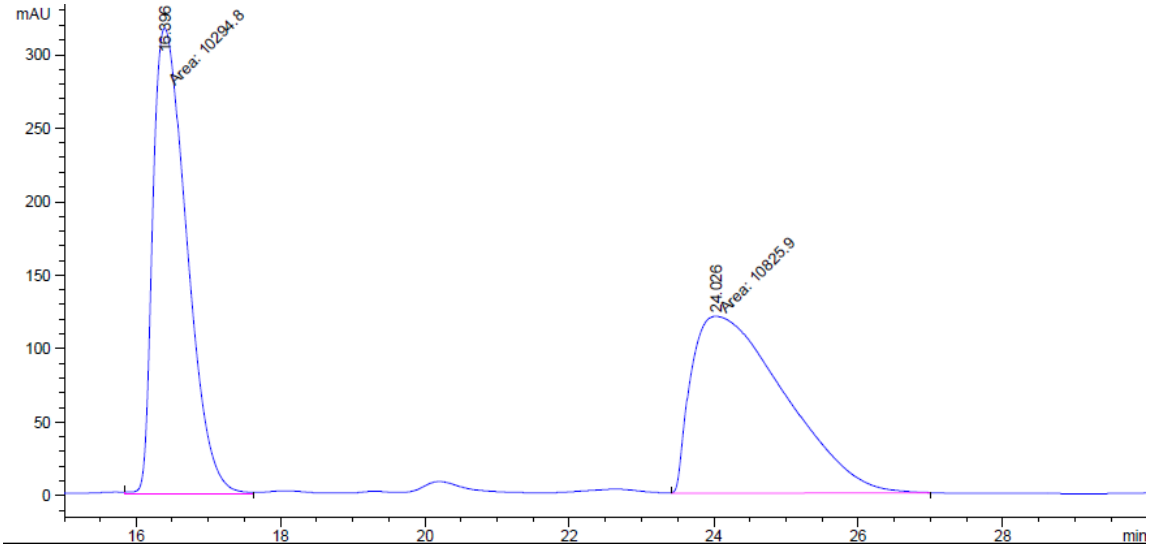

OH
F3C
Cl
1H (500 MHz, CDCl3)
4f
f1 (ppm)


4f
OH
F3C
Cl
13C (125 MHz, CDCl3)
f1 (ppm)

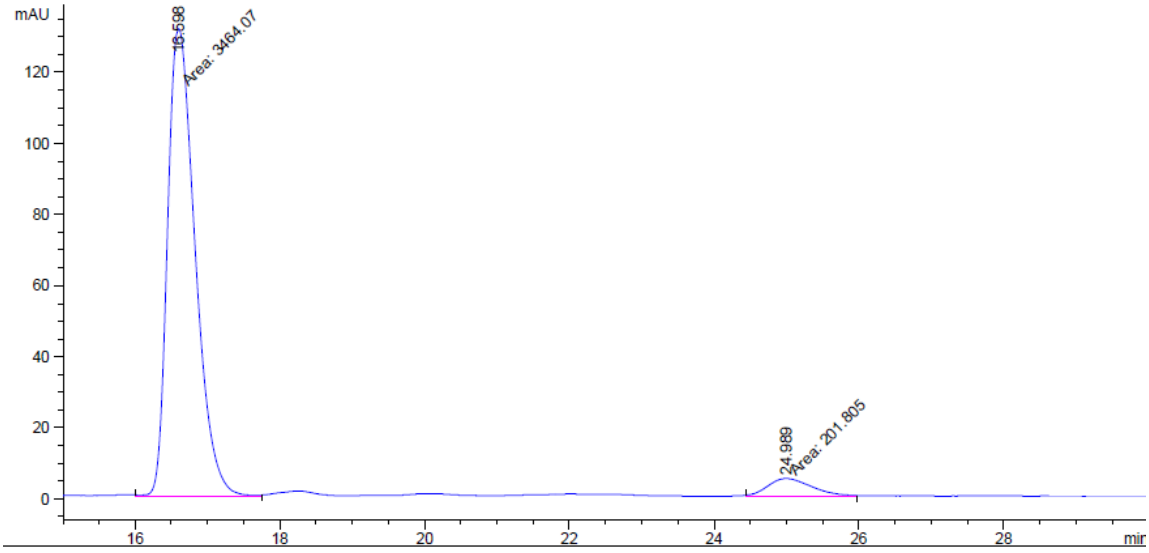


^{19}F (471 MHz, $CDCl_3$)

4f

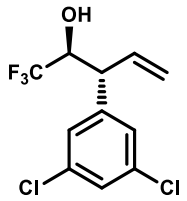


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.396	MM	0.5418	1.02948e4	316.68604	48.7426
2	24.026	MM	1.4987	1.08259e4	120.39088	51.2574



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.598	MM	0.4386	3464.07446	131.63419	94.4950
2	24.989	MM	0.6919	201.80528	4.86140	5.5050

(2S,3R)-3-(3,5-dichlorophenyl)-1,1,1-trifluoropent-4-en-2-ol (4g)



The title compound was prepared according to the general procedure using fluoral hydrate (75% in H_2O, 22 µL, 200 µmol) and 1-(3,5-dichlorophenyl)allyl acetate (98 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 20:1) provided the title compound (52 mg, 182 µmol, *anti:syn* = >20:1) in 91% yield as a yellow oil.

TLC (SiO_2) R_f = 0.34 (hexanes/ethyl acetate = 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): 7.30 – 7.27 (m, 1H), 7.23 – 7.19 (m, 2H), 6.13 (dt, *J* = 17.8, 9.2 Hz, 1H), 5.35 (d, *J* = 10.2 Hz, 1H), 5.19 (d, *J* = 17.1 Hz, 1H), 4.21 (h, *J* = 6.4 Hz, 1H), 3.68 (dd, *J* = 8.1, 4.4 Hz, 1H), 2.43 (d, *J* = 6.1 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.30, 135.34, 133.52, 127.70, 126.83, 125.65, 123.39, 120.84, 72.76 (q, *J* = 30.0 Hz), 49.32.

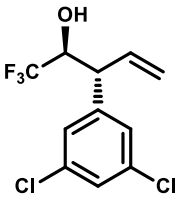
^{19}F NMR (471 MHz, $CDCl_3$): δ = -76.15 (d, *J* = 6.8 Hz).

HRMS (CI) Calculated for $C_{11}H_9Cl_2F_3O$ $[M]^+$ = 283.9983, Found 283.9978.

FTIR (neat) 3548, 2360, 1588, 1568, 1169, 1146, 738, 698 cm^{-1}.

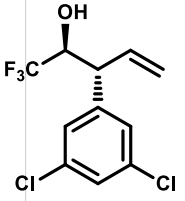
$[\alpha]_D^{33}$: –140.9 (*c* = 1.1, $CHCl_3$)

HPLC: (Chiralcel AS-H column, hexanes:*i*-PrOH = 99:1, 1.0 mL/min, 230 nm), *ee* = 94%.



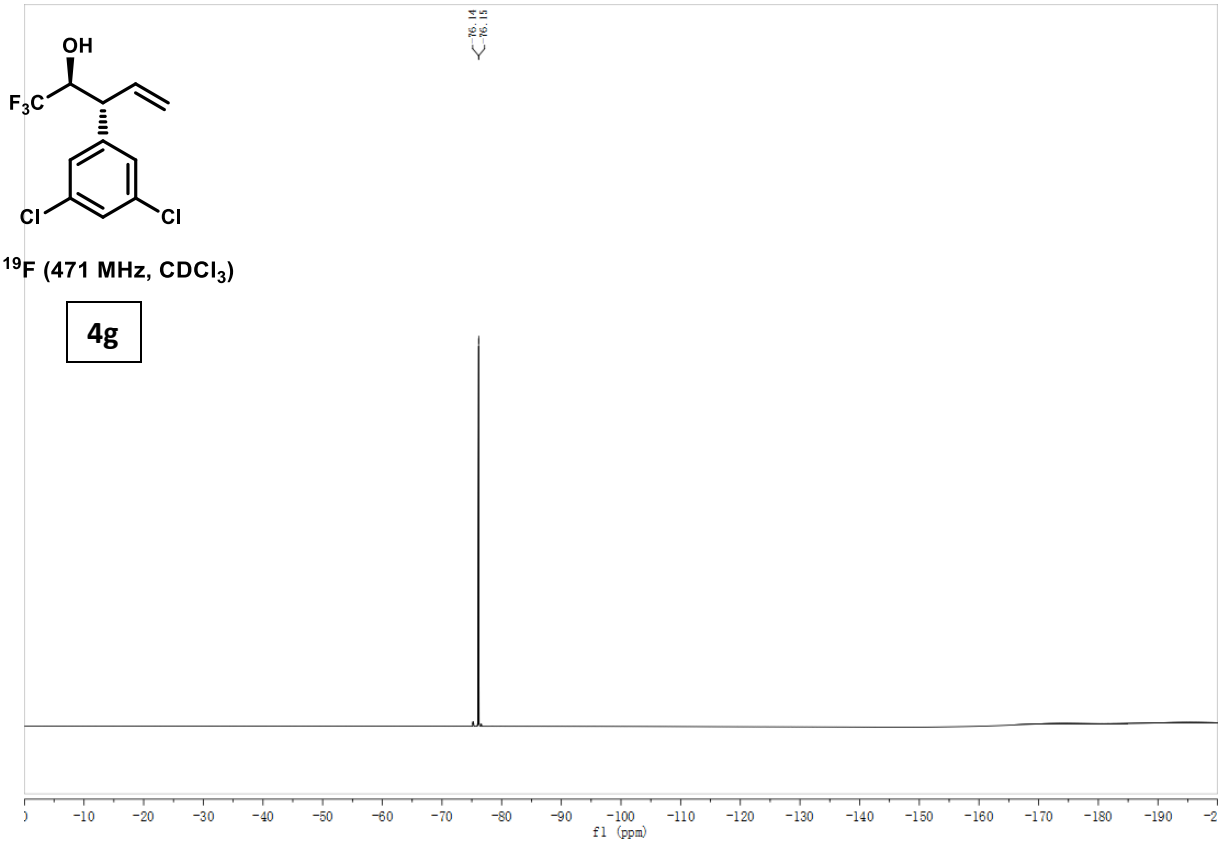
^{1}H (400 MHz, $CDCl_3$)

4g



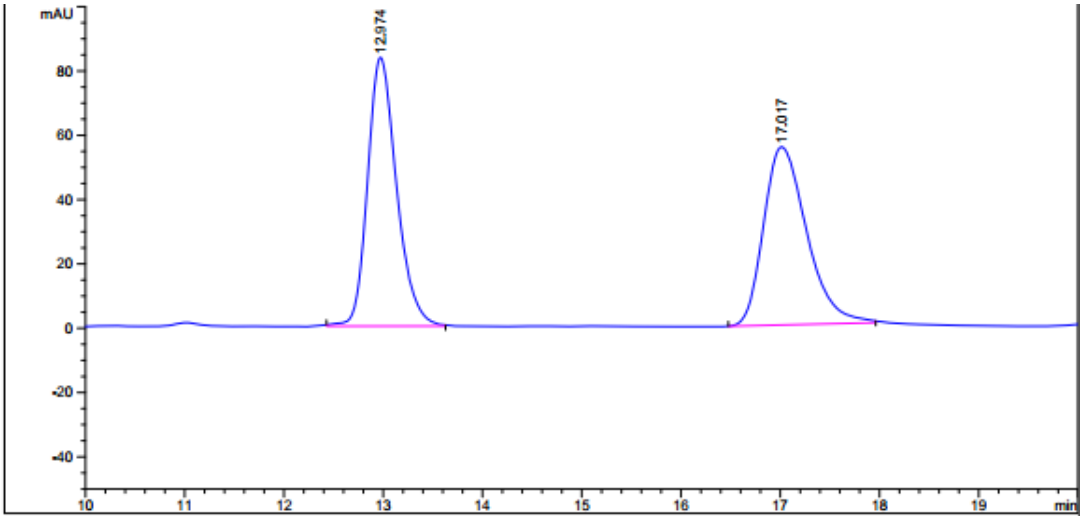
^{13}C (125 MHz, $CDCl_3$)

4g

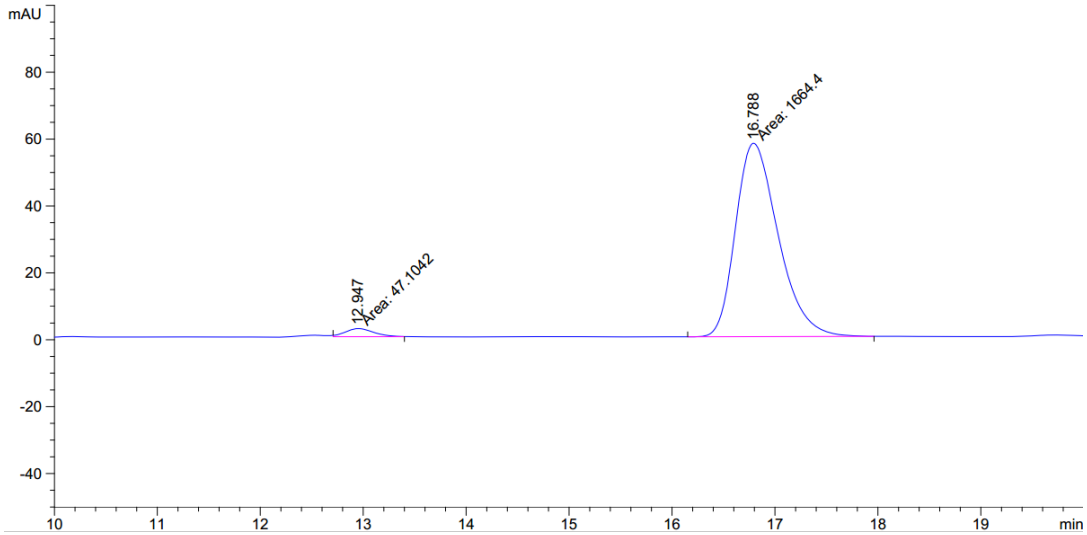


^{19}F (471 MHz, $CDCl_3$)

4g

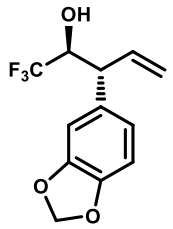


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.974	BB	0.3107	1694.64917	83.54061	50.4033
2	17.017	BB	0.4671	1667.53186	55.40837	49.5967



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.947	FM	0.3225	47.10421	2.43405	2.7522
2	16.788	MM	0.4797	1664.39624	57.82679	97.2478

(2*S*,3*R*)-3-(Benzo[d][1,3]dioxol-5-yl)-1,1,1-trifluoropent-4-en-2-ol (4h)



The title compound was prepared according to the general procedure using fluoral hydrate (75% in H_2O, 22 µL, 200 µmol) and 1-(benzo[d][1,3]dioxol-5-yl)allyl acetate (88 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 20:1 → 8:1) provided the title compound (43.7 mg, 168 µmol, *anti:syn* = >20:1) in 84% yield as a yellow oil.

TLC (SiO_2) R_f = 0.09 (hexanes/ethyl acetate = 10:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.82–6.76 (m, 2H), 6.74 (dd, *J* = 8.0, 1.8 Hz, 1H), 6.14 (ddd, *J* = 17.5, 10.3, 8.4 Hz, 1H), 5.95 (s, 2H), 5.29 (dt, *J* = 10.3, 1.0 Hz, 1H), 5.18 (dt, *J* = 17.5, 1.3 Hz, 1H), 4.22–4.13 (m, 1H), 3.64 (dd, *J* = 8.4, 5.1 Hz, 1H), 2.42 (d, *J* = 6.1 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.0, 146.8, 135.1, 133.6, 124.8 (d, *J* = 283.6 Hz), 121.3, 119.7, 108.6, 108.5, 101.2, 73.2 (q, *J* = 29.4 Hz), 49.8.

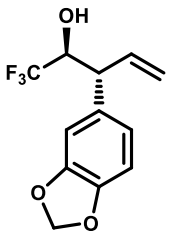
^{19}F NMR (471 MHz, $CDCl_3$): δ = –76.0 (d, *J* = 7.0 Hz)

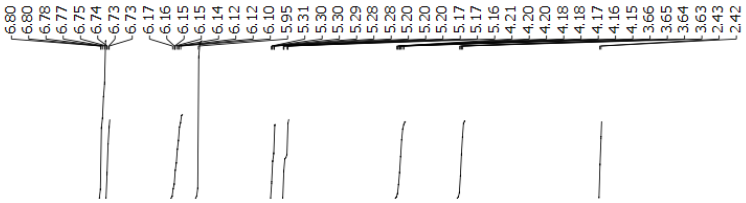
HRMS (CI) Calculated for $C_{12}H_{11}F_3O_3$ $[M]^+$ = 260.0660, Found 260.0658.

FTIR (neat) 3472, 2903, 1490, 1249, 1169, 1102, 1039, 931 cm^{-1}.

$[\alpha]_D^{32}$: –177.8 (*c* = 1.0, $CHCl_3$)

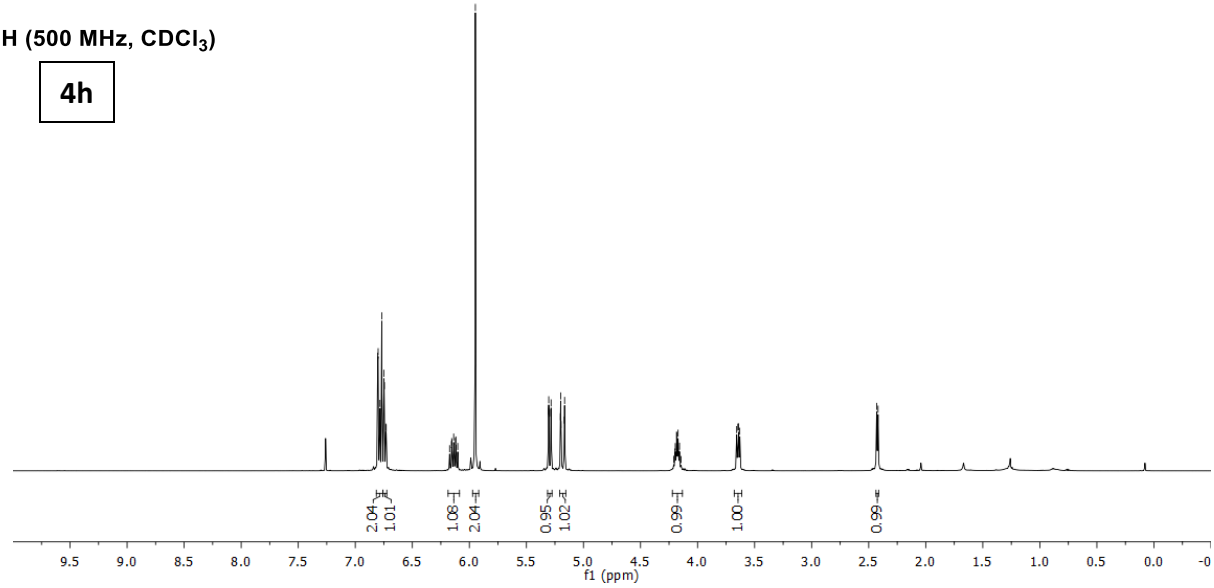
HPLC: (Chiralcel AS-H column, hexanes:*i*-PrOH = 95:5, 1.0 mL/min, 210 nm), *ee* = 92%.

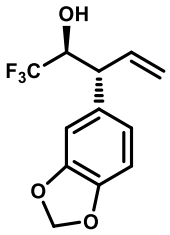


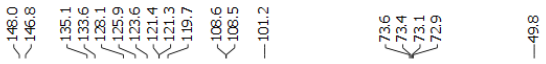


^{1}H (500 MHz, $CDCl_3$)

4h

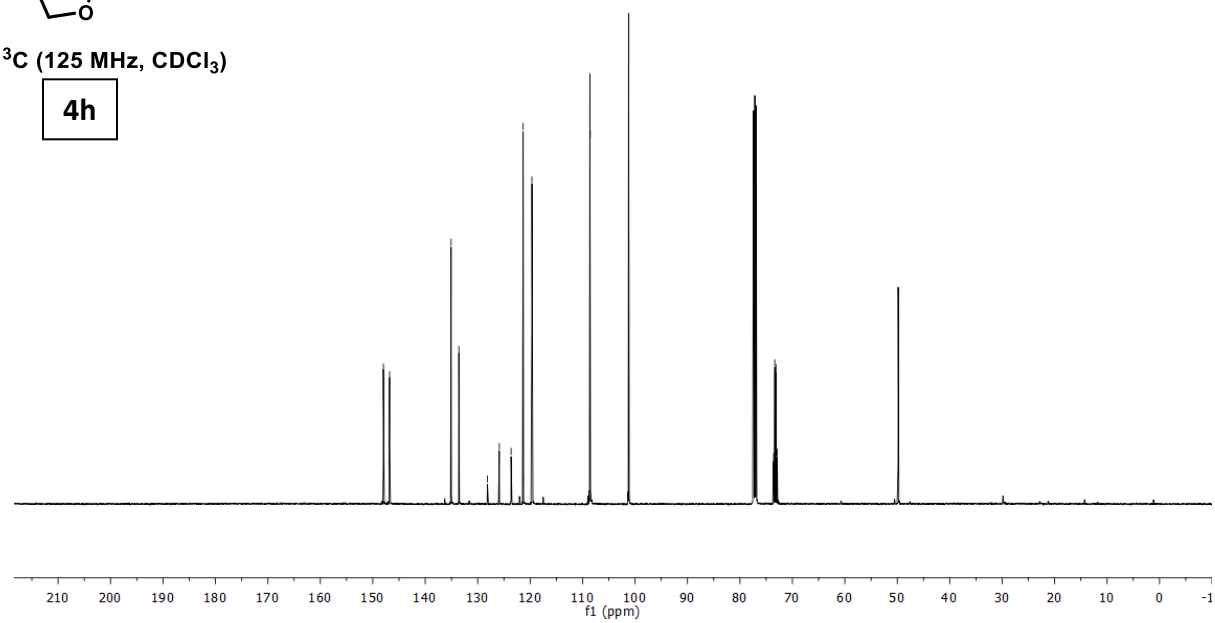


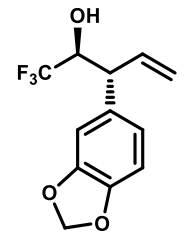




^{13}C (125 MHz, $CDCl_3$)

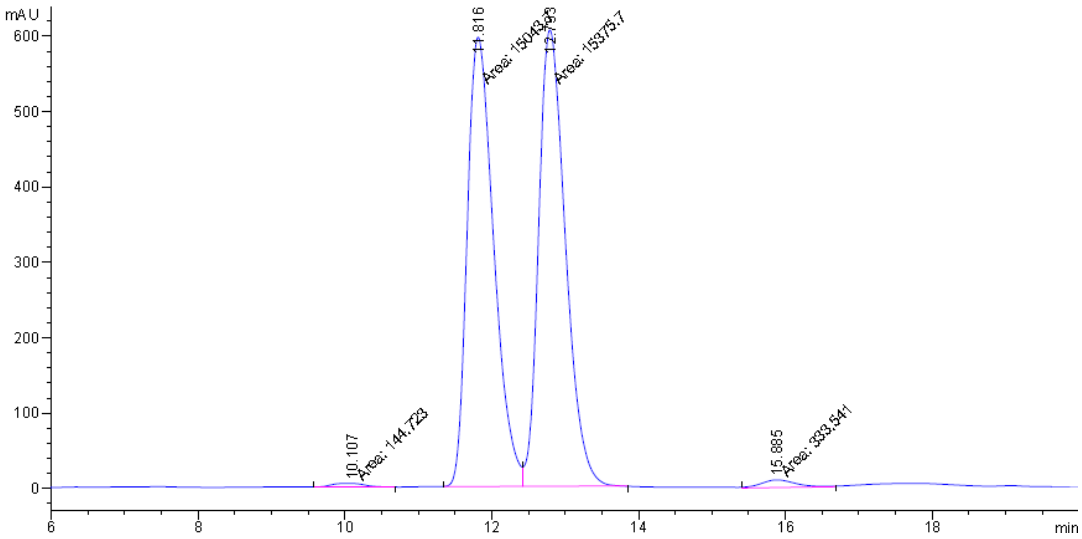
4h



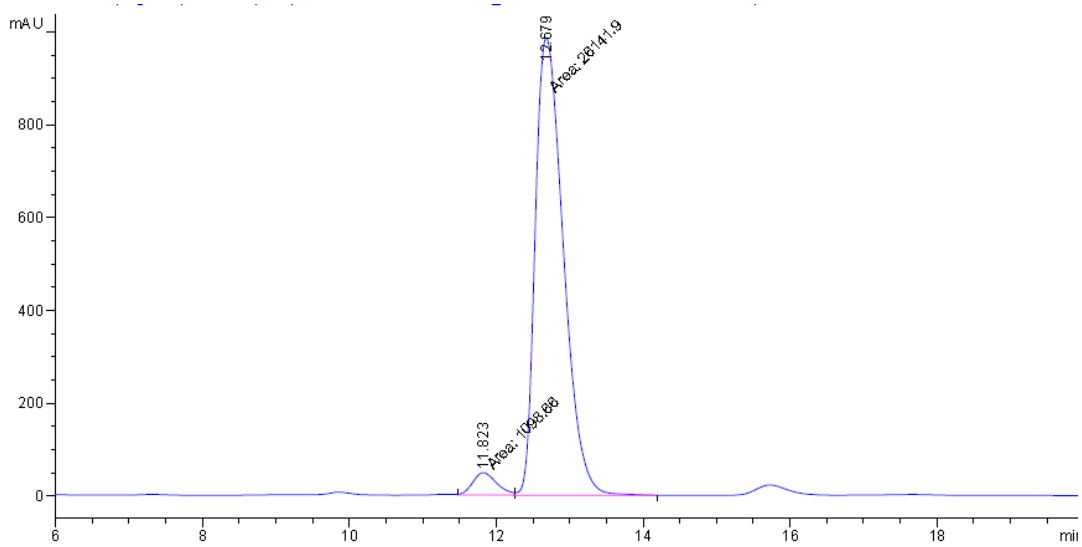


^{19}F (471 MHz, $CDCl_3$)

4h

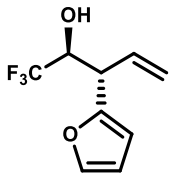


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.107	MM	0.5153	144.72284	4.68052	0.4684
2	11.816	MF	0.4204	1.50437e4	596.34747	48.6887
3	12.793	FM	0.4232	1.53757e4	605.56329	49.7634
4	15.885	MM	0.5463	333.54141	10.17532	1.0795



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.823	MF	0.3788	1098.65637	48.33823	4.0332
2	12.679	FM	0.4426	2.61419e4	984.48370	95.9668

(2S,3S)-1,1,1-trifluoro-3-(furan-2-yl)pent-4-en-2-ol (4i)



The title compound was prepared according to the general procedure using fluoral hydrate (75% in H_2O, 22 μL, 200 μmol) and 1-(furan-2-yl)allyl acetate (66.5 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 20:1) provided the title compound (25 mg, 120 μmol, *anti:syn* = >20:1) in 61% yield as a yellow oil.

TLC (SiO_2) R_f = 0.22 (hexanes/ethyl acetate = 9:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.38 (d, *J* = 1.2 Hz, 1H), 6.36 – 6.32 (m, 1H), 6.21 (d, *J* = 3.2 Hz, 1H), 6.14 – 6.04 (m, 1H), 5.36 (d, *J* = 10.2 Hz, 1H), 5.25 (d, *J* = 17.2 Hz, 1H), 4.40 (d, *J* = 5.4 Hz, 1H), 3.87 (dd, *J* = 8.3, 4.3 Hz, 1H), 2.50 (d, *J* = 5.4 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.30, 135.34, 133.52, 127.70, 126.83, 125.65, 123.39, 120.84, 71.43 (q, *J* = 30.0 Hz), 49.32.

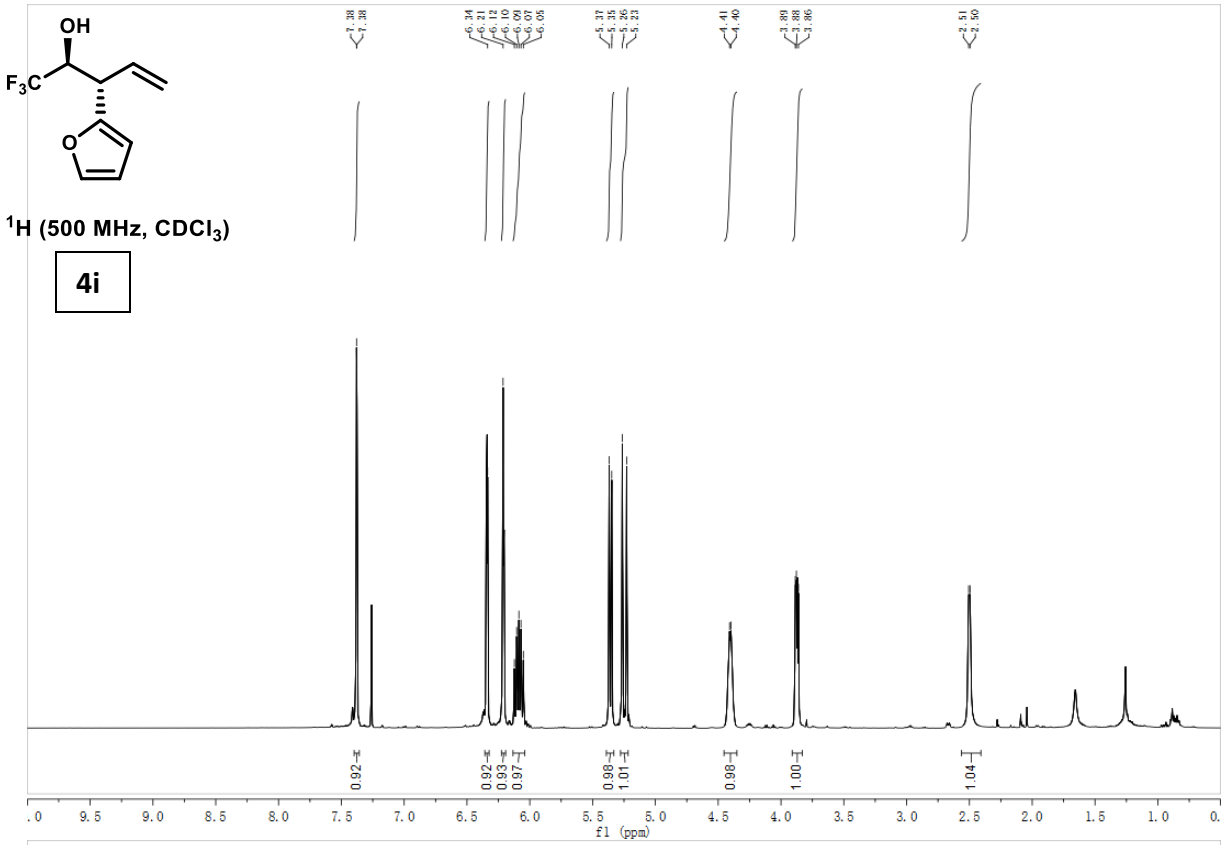
^{19}F NMR (471 MHz, $CDCl_3$): δ = -76.26 (d, *J* = 6.9 Hz).

HRMS (CI) Calculated for $C_9H_9F_5O_2$ $[M]^+$ = 206.0555, Found 206.0554.

FTIR (neat) 3432, 2925, 1264, 1130, 895, 734, 703 cm^{-1}.

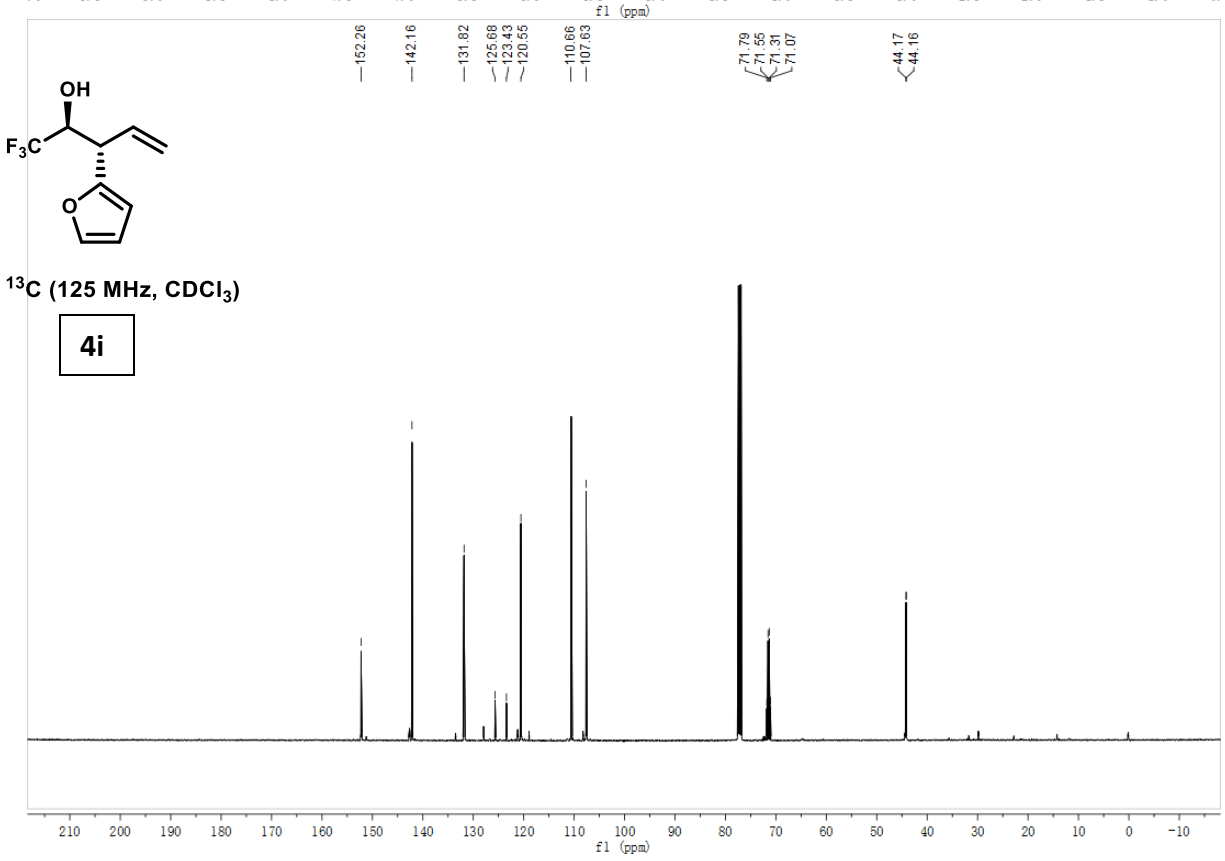
$[\alpha]_D^{33}$: –103 (*c* = 0.1, $CHCl_3$)

HPLC: (Chiralcel AD-H column, hexanes:*i*-PrOH = 99:1, 1.0 mL/min, 230 nm), *ee* = 94%.



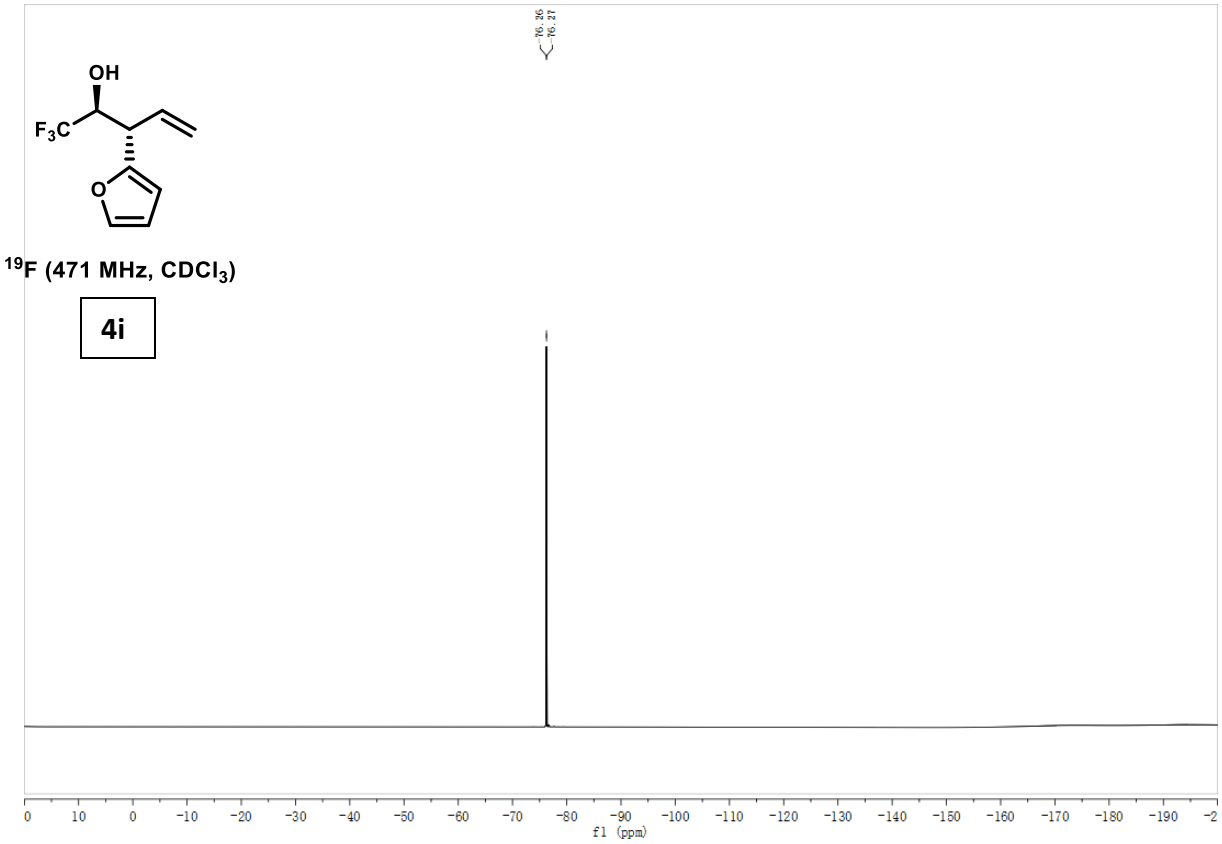
^{1}H (500 MHz, $CDCl_3$)

4i



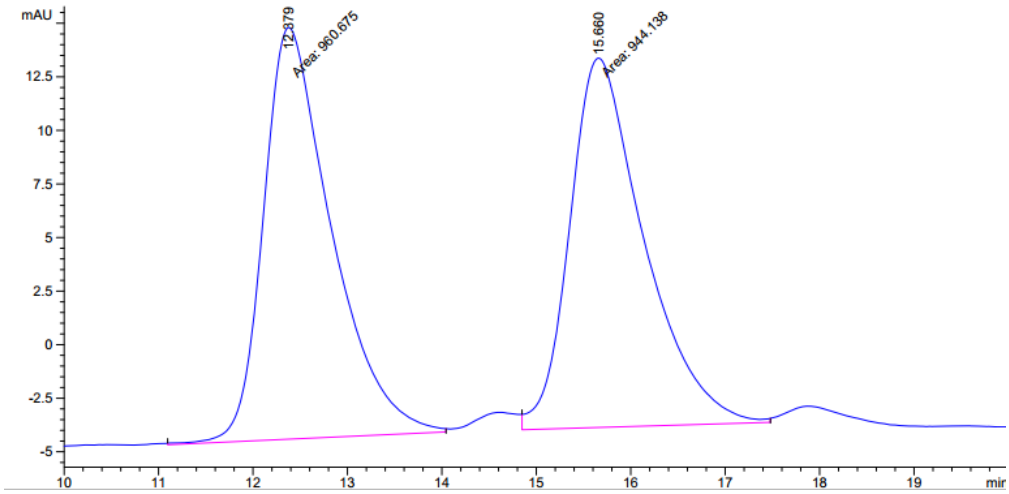
^{13}C (125 MHz, $CDCl_3$)

4i

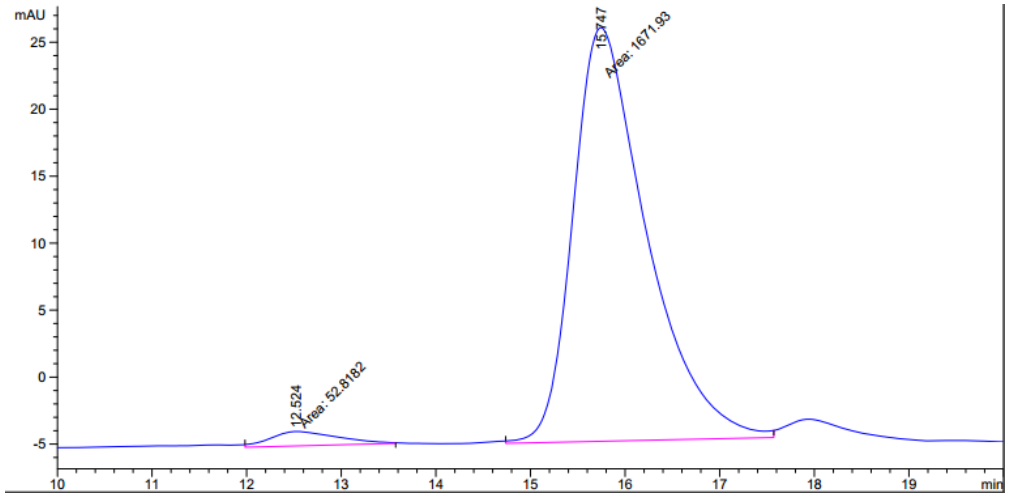


^{19}F (471 MHz, $CDCl_3$)

4i

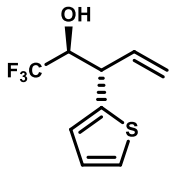


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.379	MM	0.8334	960.67517	19.21226	50.4341
2	15.660	FM	0.9129	944.13849	17.23668	49.5659



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.524	MM	0.8187	52.81821	1.07522	3.0624
2	15.747	MM	0.9024	1671.92981	30.88092	96.9376

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



The title compound was prepared according to the general procedure using fluoral hydrate (75% in H_2O, 22 μL, 200 μmol) and 1-(thiophn-2-yl)allyl acetate (72.8 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 20:1) provided the title compound (36.2 mg, 164 μmol, *anti:syn* = >20:1) in 82% yield as a yellow oil.

TLC (SiO_2) R_f = 0.53 (hexanes/ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.24 (dd, *J* = 4.4, 2.0 Hz, 1H), 6.99 (d, *J* = 4.5 Hz, 2H), 6.21 – 6.09 (m, 1H), 5.34 (dt, *J* = 10.2, 0.9 Hz, 1H), 5.25 (dt, *J* = 17.1, 1.2 Hz, 1H), 4.29 (td, *J* = 6.9, 3.7 Hz, 1H), 4.09 (dd, *J* = 8.4, 3.7 Hz, 1H), 2.46 (d, *J* = 6.6 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.1, 133.9, 127.0, 125.5, 124.8, 124.5 (q, *J* = 283.3 Hz), 120.1, 73.5 (q, *J* = 29.9 Hz), 45.4.

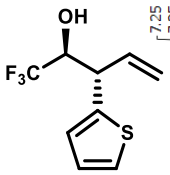
^{19}F NMR (471 MHz, $CDCl_3$): δ = -75.8 (d, *J* = 6.9 Hz).

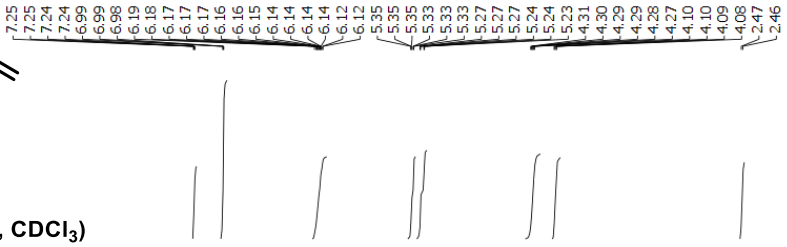
HRMS (CI) Calculated for $C_9H_9F_3OS$ $[M]^+$ = 222.0326, Found 222.0329.

FTIR (neat) 3456, 2970, 2361, 1738, 1366, 1270, 1106, 927, 852, 695 cm^{-1}.

$[\alpha]_D^{33}$: –74.5 (*c* = 1.0, $CHCl_3$)

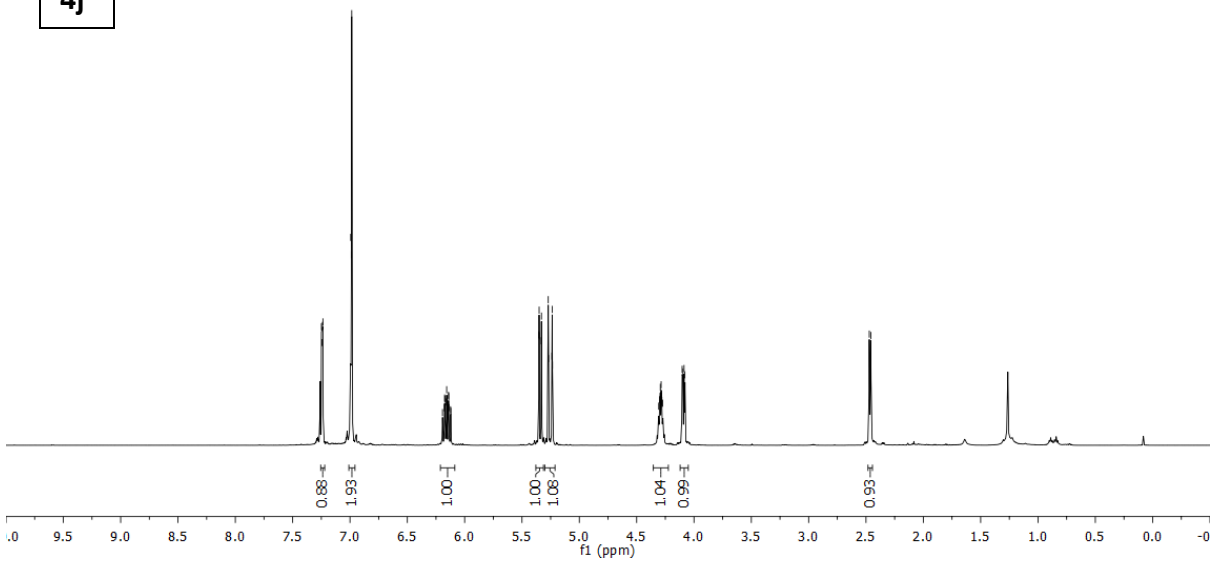
HPLC: (Chiralcel OJ-H column, hexanes:*i*-PrOH = 99:1, 1.0 mL/min, 230 nm), *ee* = 94%.

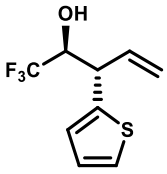




^{1}H (500 MHz, $CDCl_3$)

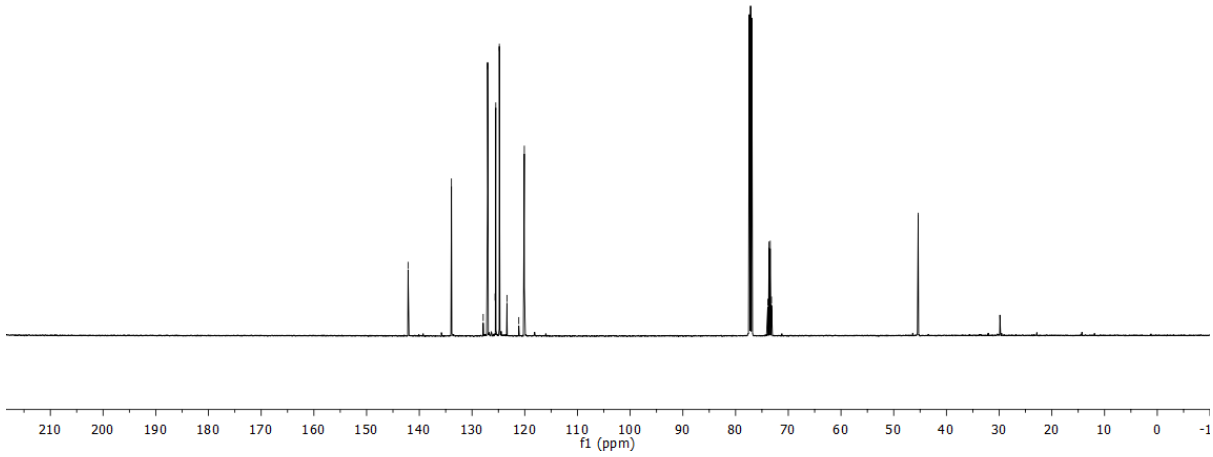
4j

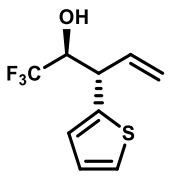




^{13}C (125 MHz, $CDCl_3$)

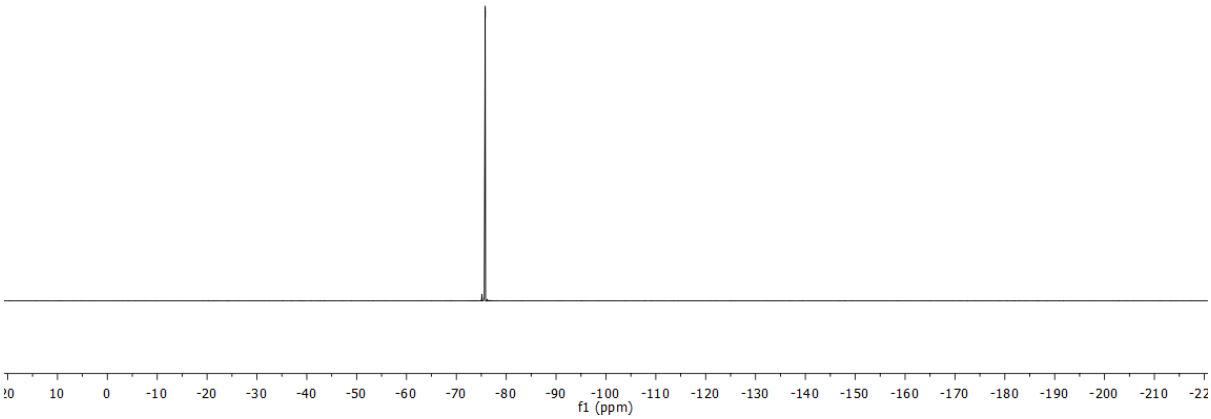
4j

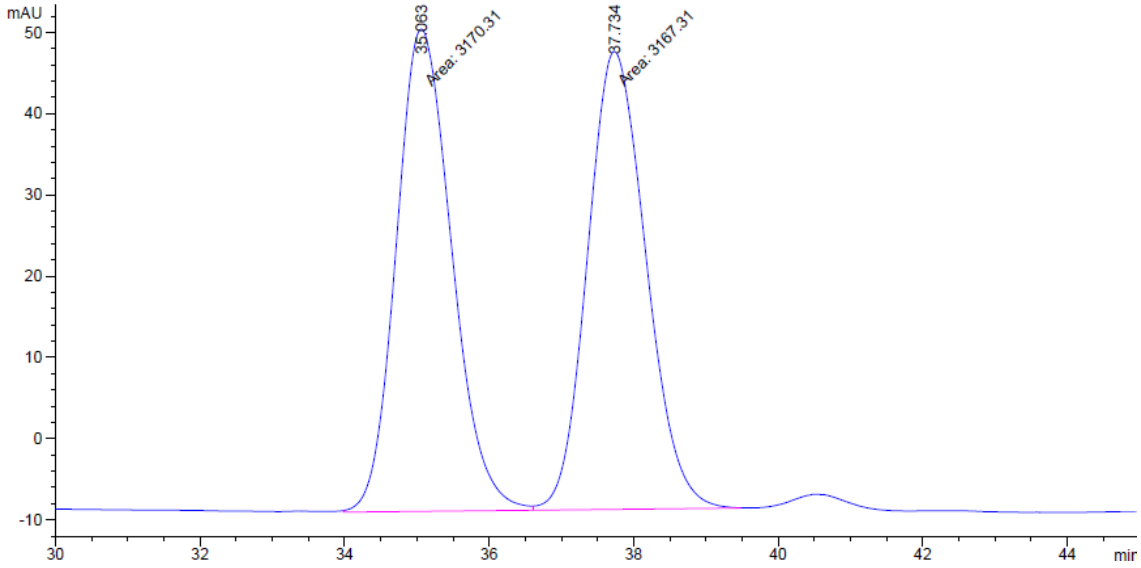




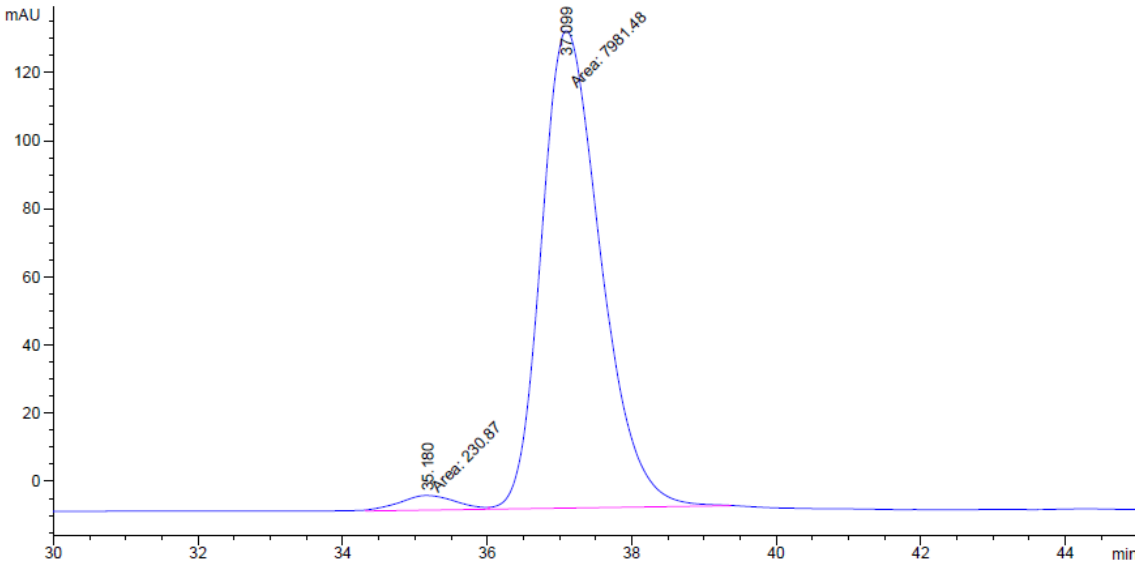
^{19}F (471 MHz, $CDCl_3$)

4j



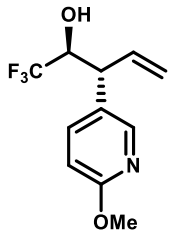


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	35.063	MF	0.8899	3170.31470	59.37821	50.0237
2	37.734	FM	0.9367	3167.30908	56.35373	49.9763



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	35.180	MF	0.6357	230.87035	4.27211	2.8113
2	37.099	FM	0.9494	7981.48096	140.11073	97.1887

(2S,3R)-1,1,1-trifluoro-3-(6-methoxypyridin-3-yl)pent-4-en-2-ol (4k)



The title compound was prepared according to the general procedure using fluoral hydrate (75% in H_2O, 22 μL, 200 μmol) and 1-(6-methoxypyridin-3-yl)allyl acetate (83 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 6:1) provided the title compound (42.8 mg, 173 μmol, *anti:syn* = >20:1) in 87% yield as a yellow oil.

TLC (SiO_2) R_f = 0.37 (hexanes/ethyl acetate = 3:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.04 (dt, *J* = 2.6, 0.6 Hz, 1H), 7.55 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.72 (dd, *J* = 8.5, 0.7 Hz, 1H), 6.18 (dddd, *J* = 17.2, 10.2, 8.1, 0.9 Hz, 1H), 5.29 (dt, *J* = 10.3, 1.0 Hz, 1H), 5.15 (dt, *J* = 17.1, 1.2 Hz, 1H), 4.16 (h, *J* = 6.6 Hz, 1H), 3.89 (s, 3H), 3.68 (dd, *J* = 8.2, 4.8 Hz, 1H), 3.28 (d, *J* = 6.3 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.5, 146.2, 138.8, 134.6, 128.5, 124.8 (d, *J* = 283.5 Hz), 119.8, 111.0, 73.0 (q, *J* = 29.4 Hz), 53.7, 46.8.

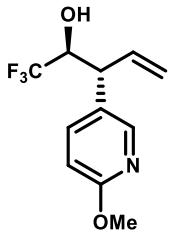
^{19}F NMR (471 MHz, $CDCl_3$): δ = –75.8 (d, *J* = 6.9 Hz)

HRMS (CI) Calculated for $C_{11}H_{13}F_3NO_2$ $[M+H]^+$ = 248.0898, Found 248.0897.

FTIR (neat) 3450, 2951, 1608, 1495, 1395, 1271, 1163, 1128, 1029, 927, 831, 693 cm^{-1}.

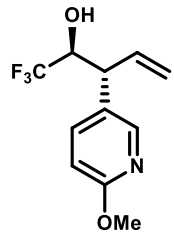
$[\alpha]_D^{33}$: –67.3 (*c* = 1.0, $CHCl_3$)

HPLC: (Chiralcel AS-H column, hexanes:*i*-PrOH = 99:1, 1.0 mL/min, 280 nm), *ee* = 91%.



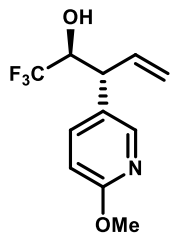
^{1}H (500 MHz, $CDCl_3$)

4k



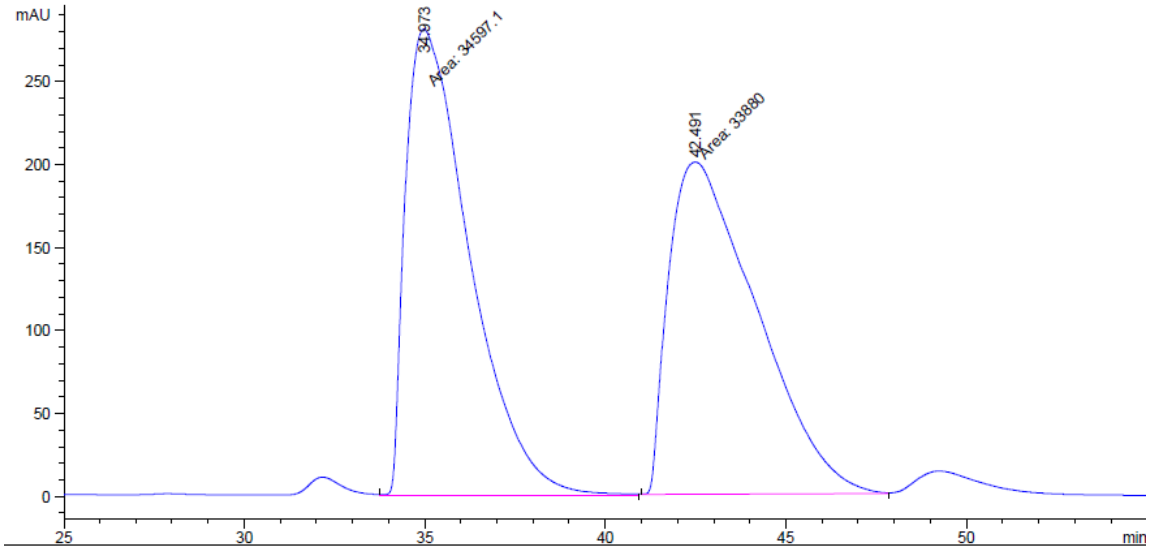
^{13}C (125 MHz, $CDCl_3$)

4k

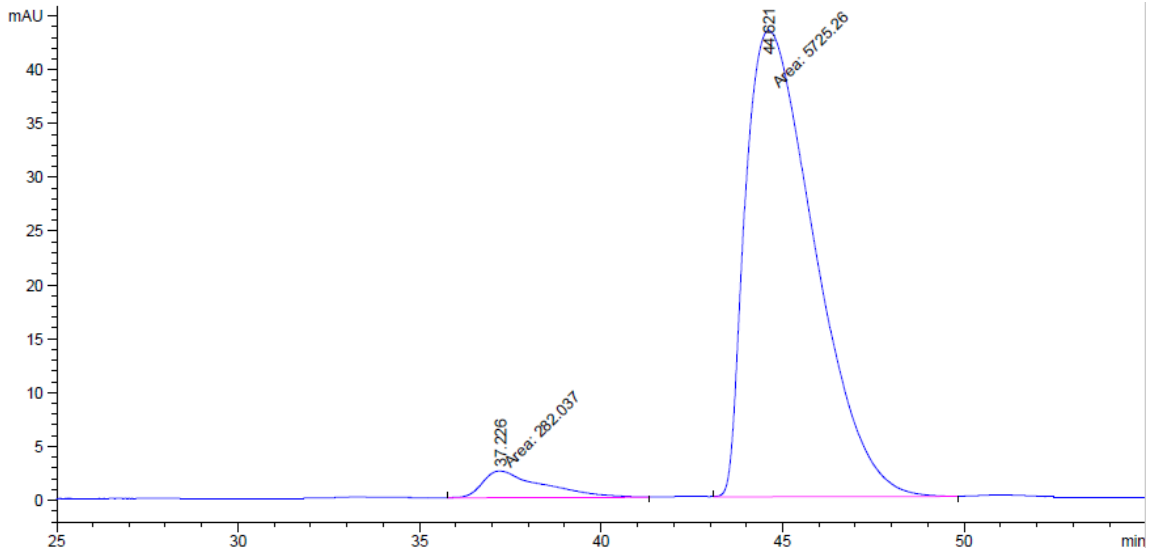


^{19}F (471 MHz, $CDCl_3$)

4k

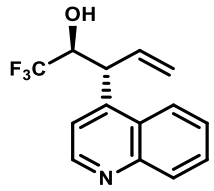


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	34.973	MM	2.0553	3.45971e4	280.54898	50.5236
2	42.491	MM	2.8224	3.38800e4	200.06589	49.4764



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	37.226	MM	1.9009	282.03705	2.47284	4.6949
2	44.621	MM	2.2037	5725.26025	43.30132	95.3051

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



The title compound was prepared according to the general procedure using fluoral hydrate (75% in H_2O, 22 μL, 200 μmol) and 1-(quinolin-4-yl)allyl acetate (91 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 3:1 → 1:1) provided the title compound (44.7 mg, 168 μmol, *anti:syn* = >20:1) in 84% yield as a light yellow solid.

TLC (SiO_2) R_f = 0.21 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.4 (d, *J* = 4.6 Hz, 1H), 7.9 – 7.9 (m, 1H), 7.6 – 7.5 (m, 1H), 7.5 – 7.4 (m, 2H), 7.4 (d, *J* = 4.6 Hz, 1H), 6.8 (s, 1H), 6.6 (dd, *J* = 17.7, 9.1 Hz, 1H), 5.4 (dd, *J* = 10.3, 1.1 Hz, 1H), 5.2 (dt, *J* = 17.3, 1.0 Hz, 1H), 4.6 (dd, *J* = 8.6, 2.4 Hz, 1H), 4.4 (dd, *J* = 7.1, 2.5 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 149.4, 147.9, 147.2, 132.8, 129.7, 129.1, 127.3, 125.8, 125.1 (q, *J* = 283.4 Hz), 122.4, 121.1, 120.3, 71.8 (q, *J* = 29.9 Hz), 44.3.

^{19}F NMR (471 MHz, $CDCl_3$): δ = –75.7 (d, *J* = 7.0 Hz).

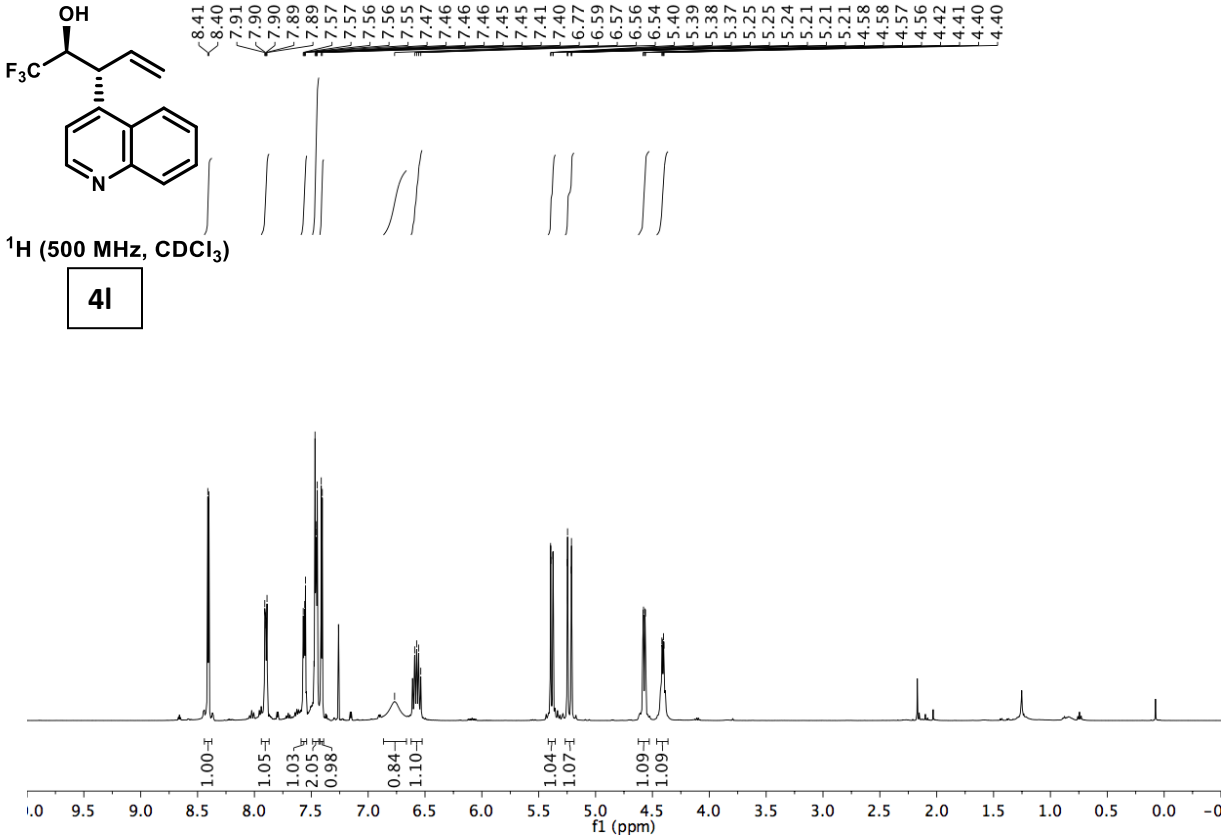
HRMS (ESI) Calculated for $C_{14}H_{12}F_3NO$ $[M+H]^+$ = 268.0944, Found 268.0947.

FTIR (neat) 3083, 2920, 2761, 1592, 1282, 1145, 1108, 980, 773 cm^{-1}.

$[\alpha]_D^{33}$: –14.5 (*c* = 1.0, $CHCl_3$)

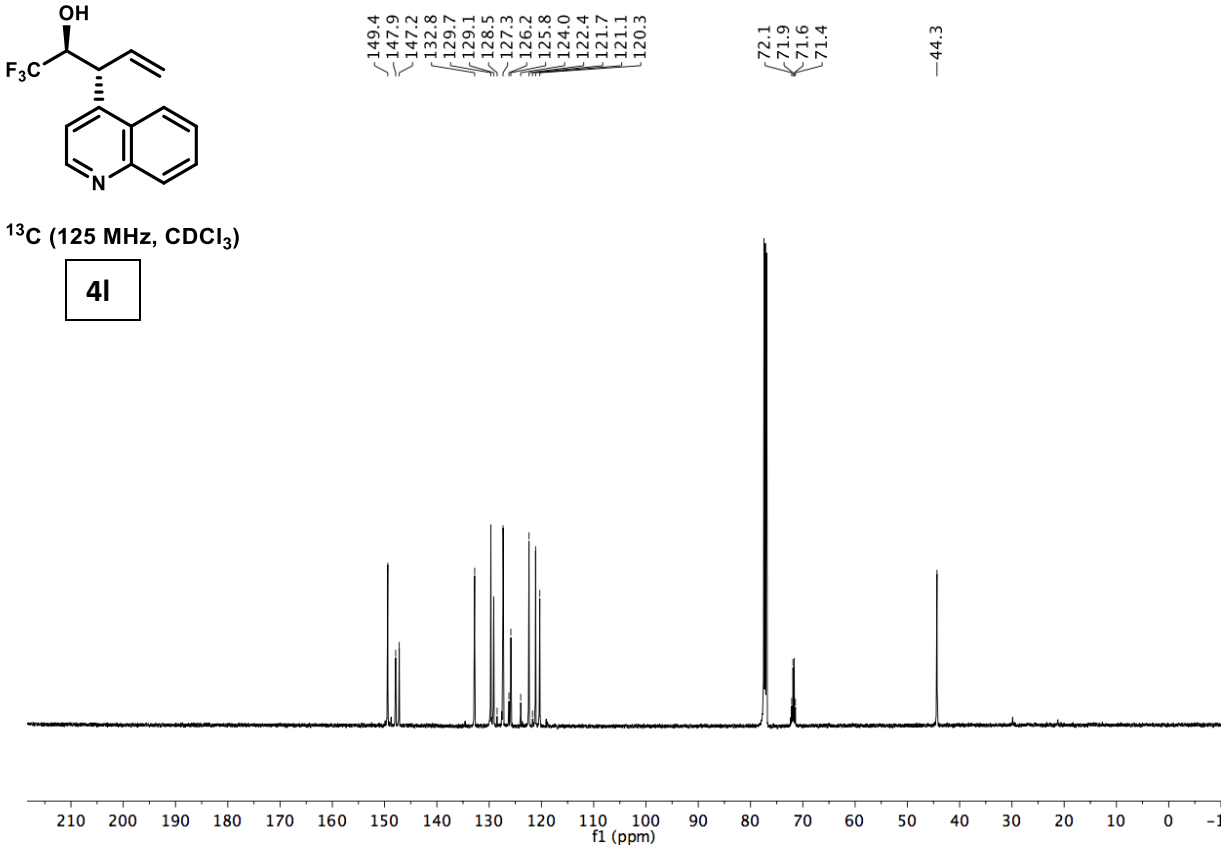
MP: 146˚C.

HPLC: (Chiralcel OD-H column, hexanes:*i*-PrOH = 95:5, 1.0 mL/min, 210 nm), *ee* = 93%.



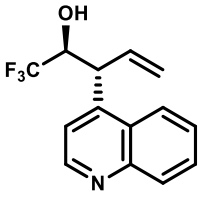
^{1}H (500 MHz, $CDCl_3$)

4l



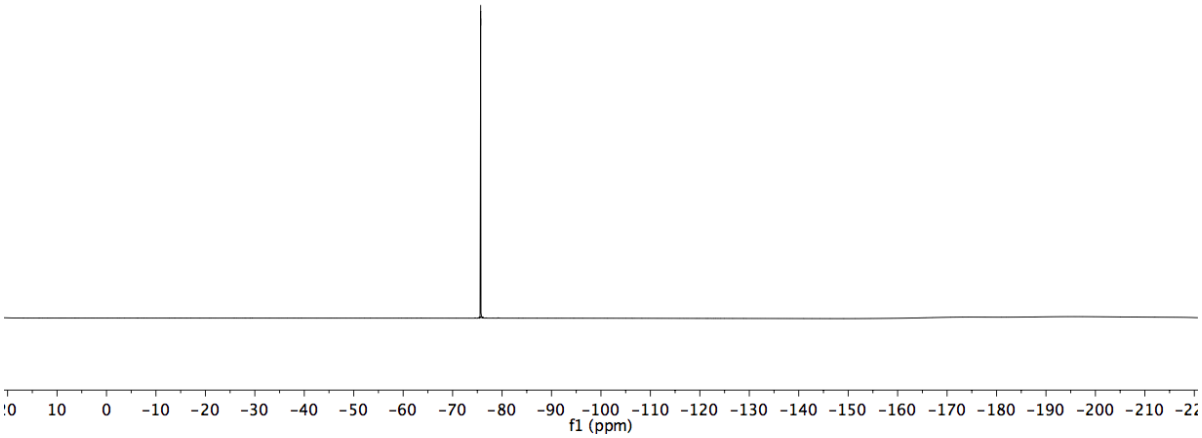
^{13}C (125 MHz, $CDCl_3$)

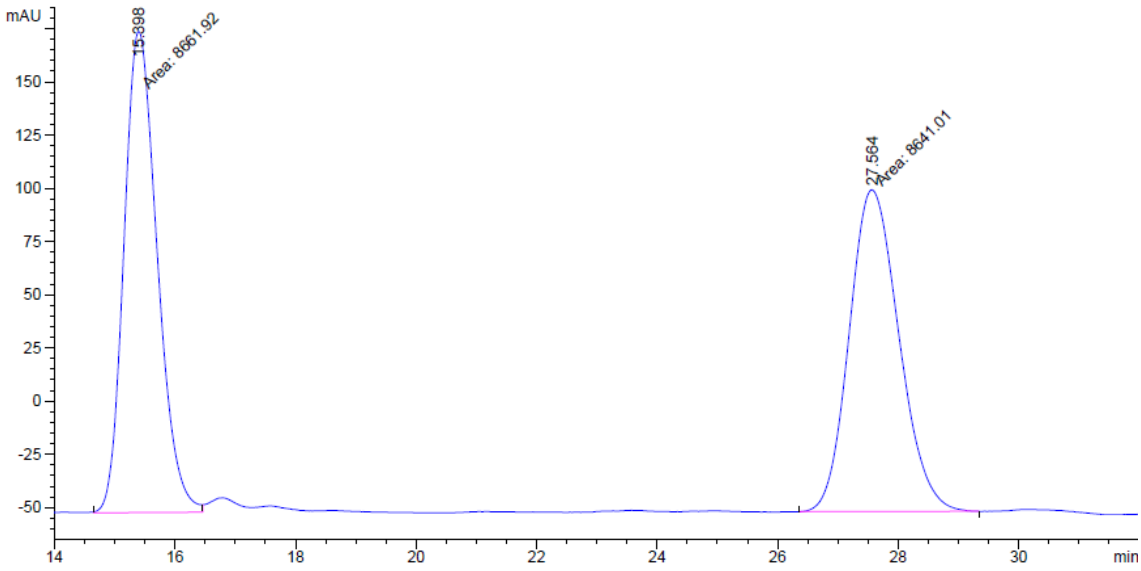
4l



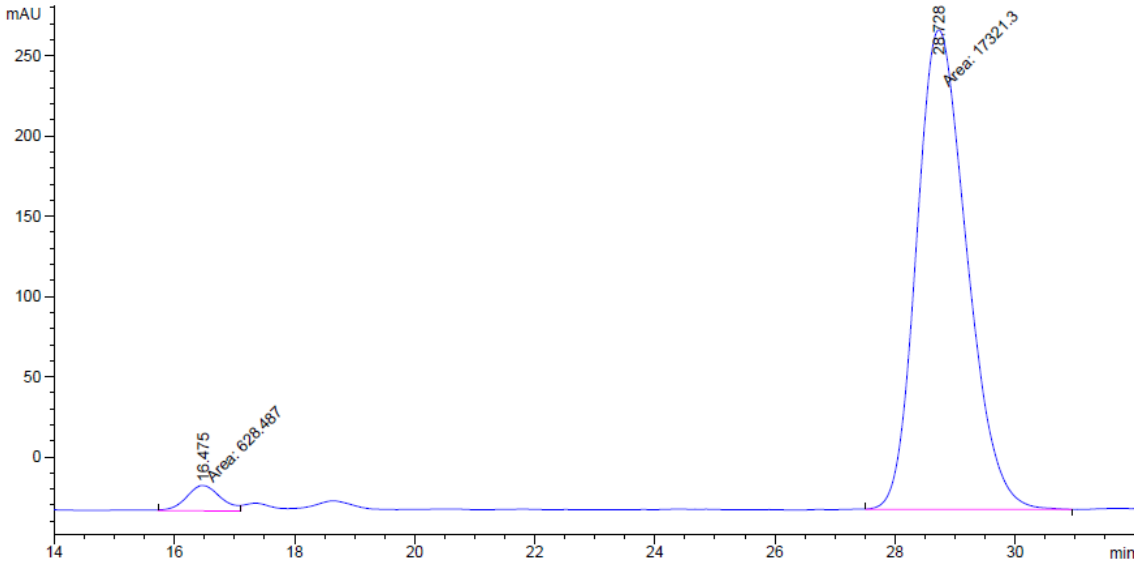
^{19}F (471 MHz, $CDCl_3$)

4l





Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.398	MM	0.6387	8661.92383	226.02888	50.0604
2	27.564	MM	0.9531	8641.00684	151.09846	49.9396

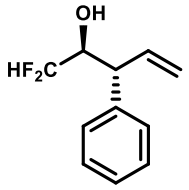


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.475	MM	0.6617	628.48694	15.82979	3.5014
2	28.728	MM	0.9663	1.73213e4	298.74704	96.4986

General Procedure and Spectral Data for Iridium Catalyzed *anti*-(α-Aryl)Allylation of Difluoroacetaldehyde Ethyl Hemiacetal 1j to form Products 5a-5l

A pressure tube was equipped with a magnetic stir bar and charged with preformed iridium catalyst (10.7 mg, 10 μmol, 5 mol%), K_2CO_3 (27.6 mg, 0.20 mmol, 100 mol%), allyl donor (0.40 mmol, 200 mol%) and 5A molecular sieves (28 mg, 100 wt%). The pressure tube was purged with argon. Anhydrous THF (1.0 mL, 0.2 M), 2-propanol (31 μL, 0.40 mmol, 200 mol%), and difluoroacetaldehyde ethyl hemiacetal (90% in EtOH, 28 mg, 200 μmol, 100 mol%) were added via syringe. The sealed reaction vessel was stirred at 100 °C. After 24 h the solvent was removed *in vacuo* and the residue was subjected to flash column chromatography on silica.

(2S,3R)-1,1-difluoro-3-phenylpent-4-en-2-ol (5a)



The title compound was prepared according to the general procedure using difluoroacetaldehyde ethyl hemiacetal (90%, 28 mg, 200 μmol) and 1-phenylallyl acetate (71 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 20:1 → 10:1) provided the title compound (31.5 mg, 159 μmol, *anti:syn* = >20:1) in 80% yield as a yellow oil.

TLC (SiO_2) R_f = 0.53 (hexanes/ethyl acetate = 3:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.37–7.34 (m, 2H), 7.29–7.28 (m, 3H), 6.20 (dt, *J* = 17.8, 9.5 Hz, 1H), 5.54 (td, *J* = 55.6, 3.7 Hz, 1H), 5.29 (d, *J* = 10.2 Hz, 1H), 5.23 (d, *J* = 17.2 Hz, 1H), 4.10 – 3.91 (m, 1H), 3.61 – 3.55 (m, 1H), 2.13 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 139.6, 136.0, 129.1, 128.2, 127.5, 118.9, 115.2 (t, *J* = 243.2 Hz), 73.8 (dd, *J* = 23.1, 20.9 Hz), 51.0 (t, *J* = 3.6 Hz).

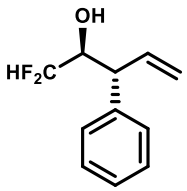
^{19}F NMR (471 MHz, $CDCl_3$): δ = -129.2 (ddd, *J* = 286.4, 54.9, 6.0 Hz), -134.4 (ddd, *J* = 286.4, 56.0, 15.7 Hz).

HRMS (CI) Calculated for $C_{11}H_{12}F_2O$ $[M]^+$ = 198.0856, Found 198.0852.

FTIR (neat) 3442, 3030, 2984, 2926, 1493, 1455, 1150, 1057, 926, 758, 701 cm^{-1}.

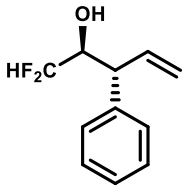
$[\alpha]_D^{33}$: –78.3 (*c* = 1.0, $CHCl_3$)

HPLC: (Chiralcel AS-H column, hexanes:*i*-PrOH = 99:1, 1.0 mL/min, 210 nm), *ee* = 94%.



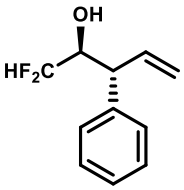
^{1}H (500 MHz, $CDCl_3$)

5a



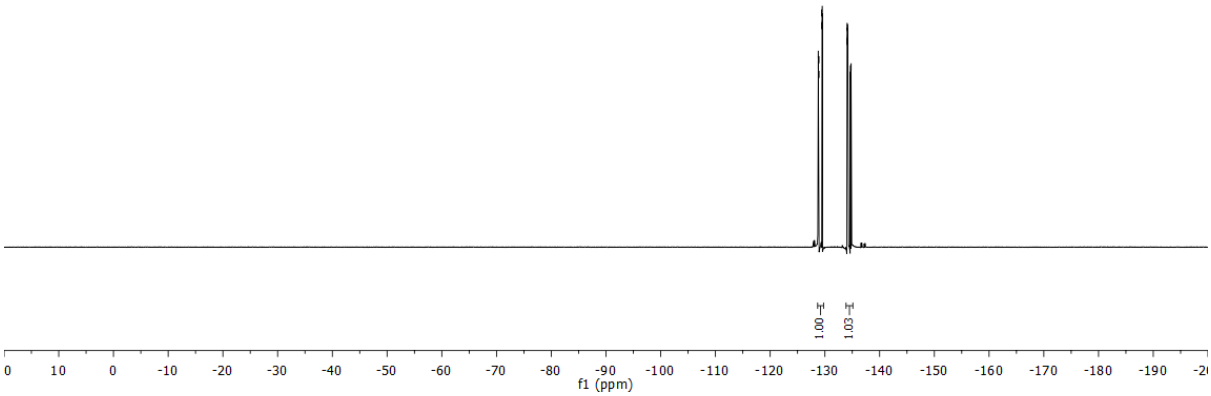
^{13}C (125 MHz, $CDCl_3$)

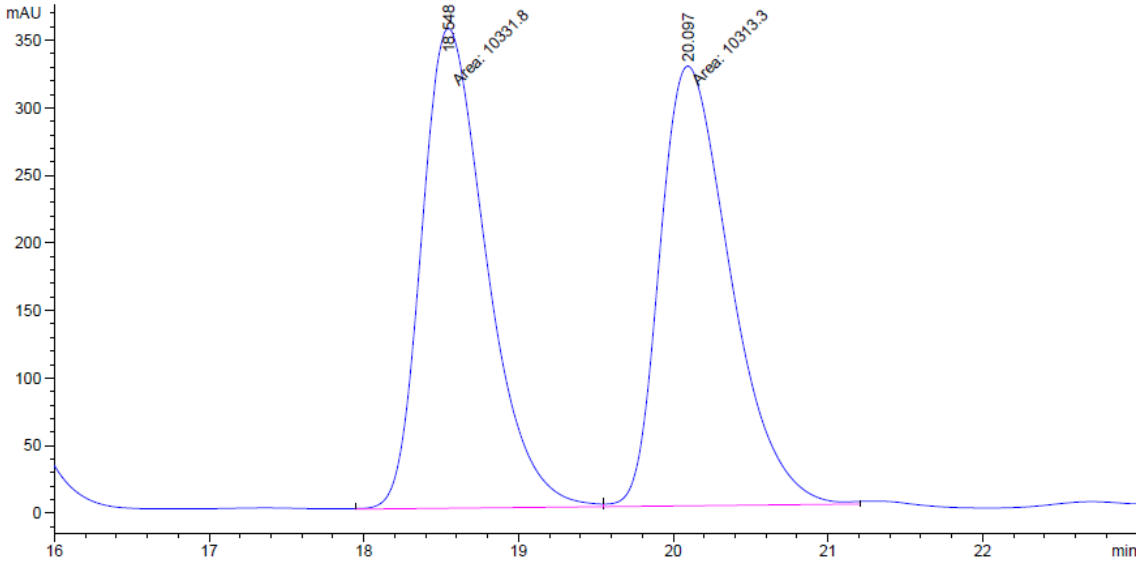
5a



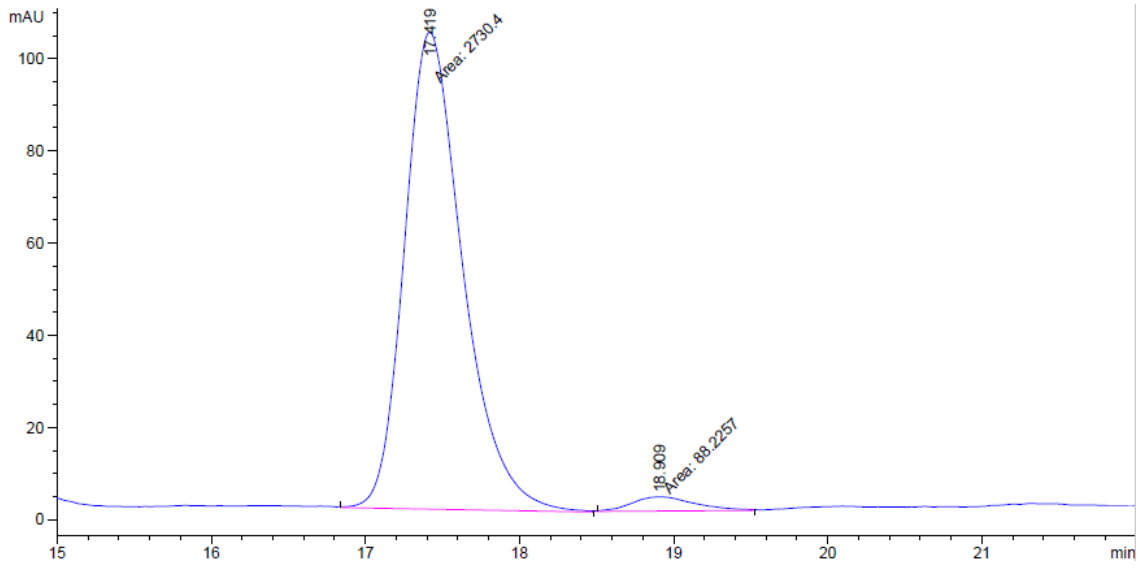
^{19}F (471 MHz, $CDCl_3$)

5a



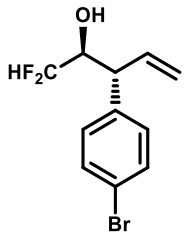


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.548	MF	0.4847	1.03318e4	355.27246	50.0450
2	20.097	FM	0.5282	1.03133e4	325.42999	49.9550



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.419	MM	0.4398	2730.39600	103.46590	96.8699
2	18.909	MM	0.4780	88.22573	3.07628	3.1301

(2*S*,3*R*)-3-(4-Bromophenyl)-1,1-difluoropent-4-en-2-ol (5b)



The title compound was prepared according to the general procedure using difluoroacetaldehyde ethyl hemiacetal (90%, 28 mg, 200 μmol) and 1-(4-bromophenyl)allyl acetate (102 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 20:1) provided the title compound (46.6 mg, 168 μmol, *anti:syn* = >20:1) in 84% yield as a yellow oil.

TLC (SiO_2) R_f = 0.17 (hexanes/ethyl acetate = 10:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.50–7.45 (m, 2H), 7.20–7.16 (m, 2H), 6.16 (ddd, *J* = 17.1, 10.2, 8.7 Hz, 1H), 5.56 (ddd, *J* = 56.2, 54.9, 4.3 Hz, 1H), 5.29 (dd, *J* = 10.2, 1.3 Hz, 1H), 5.22 (dt, *J* = 17.1, 1.3 Hz, 1H), 4.03–3.92 (m, 1H), 3.55 (dd, *J* = 8.7, 5.8 Hz, 1H), 2.20 (d, *J* = 4.5 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.8, 135.2, 132.1, 130.0, 121.3, 119.4, 115.2 (t, *J* = 243.6 Hz), 73.5 (dd, *J* = 23.7, 21.3 Hz), 50.1 (dd, *J* = 4.0, 3.1 Hz).

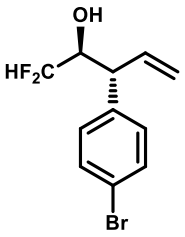
^{19}F NMR (471 MHz, $CDCl_3$): δ = –129.1 (ddd, *J* = 286.5, 55.0, 6.2 Hz), –133.5 (ddd, *J* = 287.6, 56.1, 14.7 Hz).

HRMS (CI) Calculated for $C_{11}H_{11}{}^{79}BrF_2O$ $[M]^+$ = 275.9961, Found 275.9954.

FTIR (neat) 3411, 2982, 2924, 1489, 1150, 1129, 1070, 1011, 929, 821, 760 cm^{-1}.

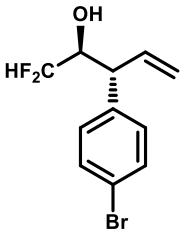
$[\alpha]_D^{33}$: –72.0 (*c* = 1.0, $CHCl_3$)

HPLC: (Chiralcel AD-H column, hexanes:*i*-PrOH = 99:1, 0.5 mL/min, 210 nm), *ee* = 94%.



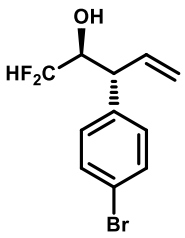
^{1}H (500 MHz, $CDCl_3$)

5b



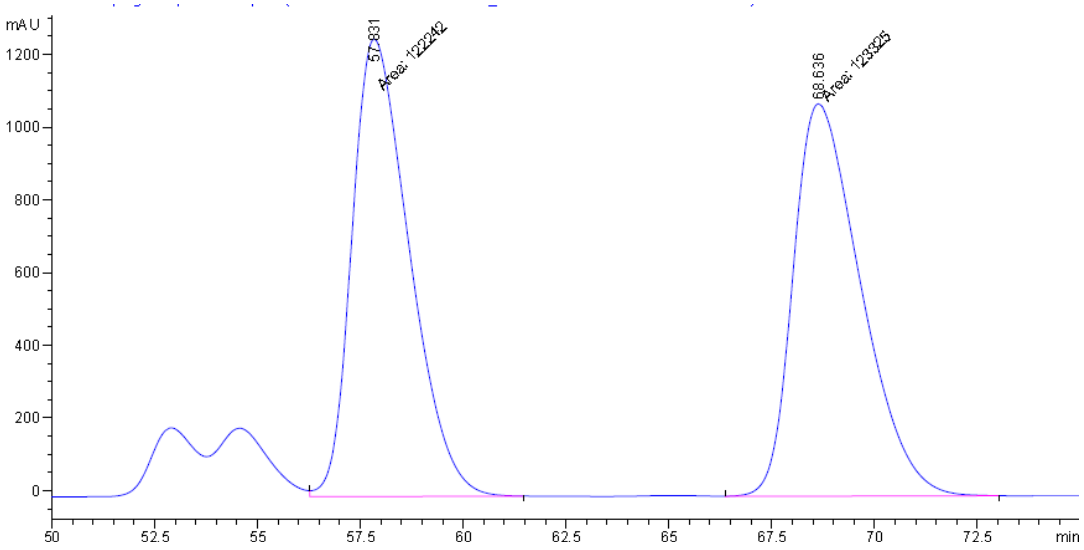
^{13}C (125 MHz, $CDCl_3$)

5b

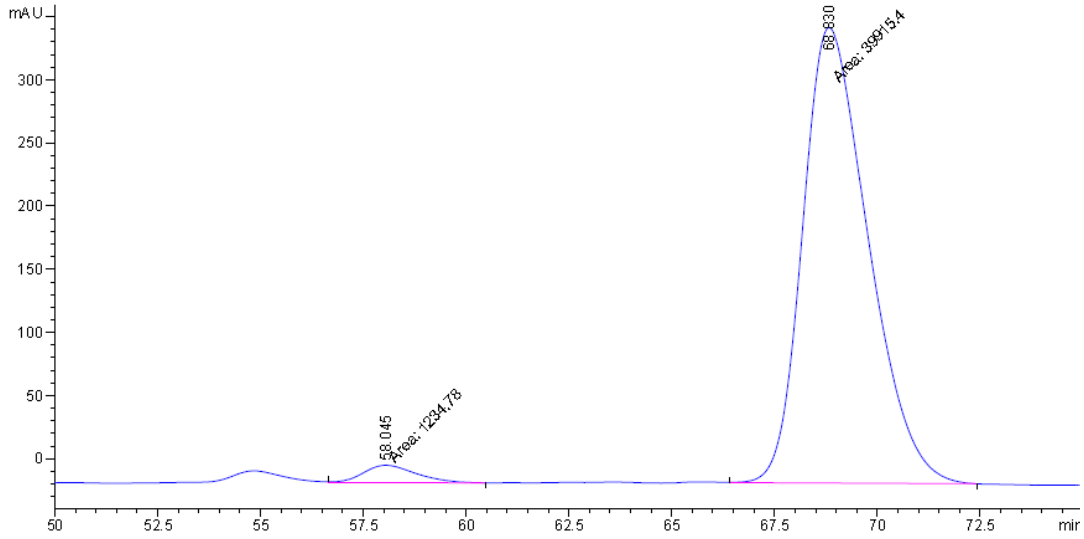


^{19}F (471 MHz, $CDCl_3$)

5b

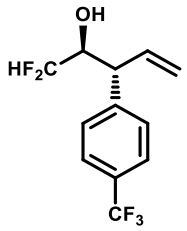


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	57.831	FM	1.6192	1.22242e5	1258.27502	49.7795
2	68.636	MM	1.9040	1.23325e5	1079.52051	50.2205



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	58.045	FM	1.4910	1234.77869	13.80225	3.0007
2	68.830	MM	1.8454	3.99154e4	360.48853	96.9993

(2*S*,3*R*)-1,1-Difluoro-3-(4-(trifluoromethyl)phenyl)pent-4-en-2-ol (5c)



The title compound was prepared according to the general procedure using difluoroacetaldehyde ethyl hemiacetal (90%, 28 mg, 200 μmol) and 1-(4-(trifluoromethyl)phenyl)allyl acetate (98 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 10:1) provided the title compound (43.7 mg, 164 μmol, *anti:syn* = >20:1) in 82% yield as a yellow oil.

TLC (SiO_2) R_f = 0.09 (hexanes/ethyl acetate = 10:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.63–7.59 (m, 2H), 7.46–7.42 (m, 2H), 6.20 (ddd, *J* = 17.1, 10.2, 8.8 Hz, 1H), 5.59 (ddd, *J* = 56.3, 55.0, 4.5 Hz, 1H), 5.33 (dd, *J* = 10.2, 1.2 Hz, 1H), 5.24 (dt, *J* = 17.1, 1.1 Hz, 1H), 4.02 (ddq, *J* = 14.1, 6.2, 4.6 Hz, 1H), 3.67 (dd, *J* = 8.8, 5.3 Hz, 1H), 2.20 (d, *J* = 4.6 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 144.0, 134.8, 129.7 (q, *J* = 32.5 Hz), 128.7, 125.9 (q, *J* = 3.7 Hz), 124.2 (q, *J* = 272.1 Hz), 119.8, 115.2 (t, *J* = 243.7 Hz), 73.5 (dd, *J* = 24.3, 21.6 Hz), 50.4 (dd, *J* = 4.6, 2.6 Hz).

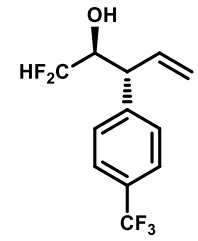
^{19}F NMR (471 MHz, $CDCl_3$): δ = –62.6, –129.0 (ddd, *J* = 288.7, 55.1, 6.4 Hz), –133.0 (ddd, *J* = 288.7, 56.3, 13.9 Hz).

HRMS (CI) Calculated for $C_{12}H_{11}F_5O$ $[M]^+$ = 266.0730, Found 266.0726.

FTIR (neat) 3446, 2924, 1327, 1166, 1125, 1068, 1019, 931, 837, 771 cm^{-1}.

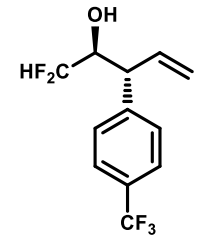
$[\alpha]_D^{33}$: –54.0 (*c* = 1.0, $CHCl_3$)

HPLC: (2× Chiralcel AD-H column, hexanes:*i*-PrOH = 99:1, 0.5 mL/min, 210 nm), *ee* = 94%.



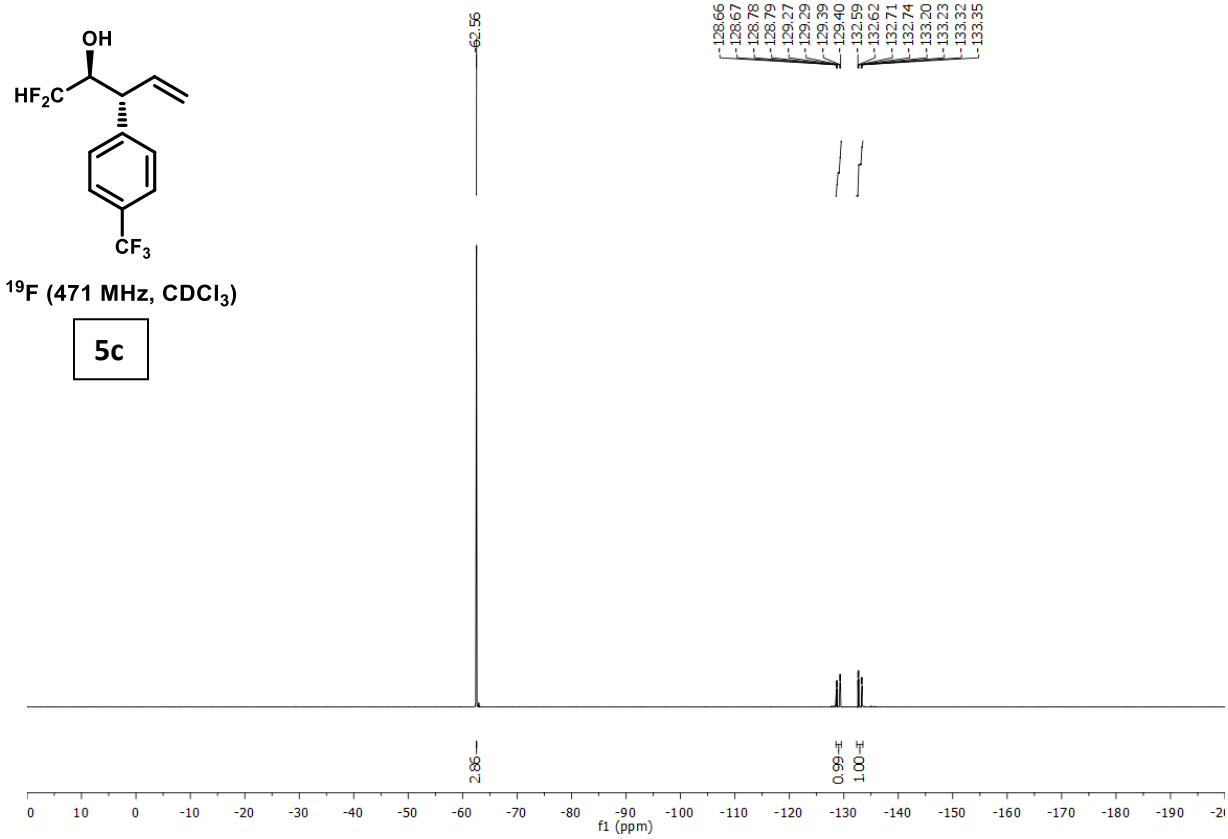
^{1}H (500 MHz, $CDCl_3$)

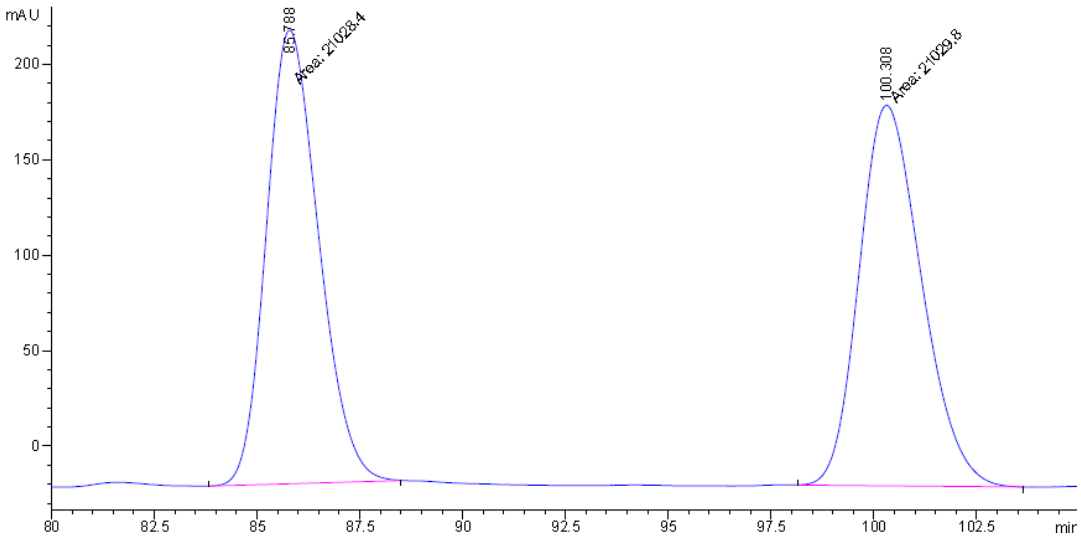
5c



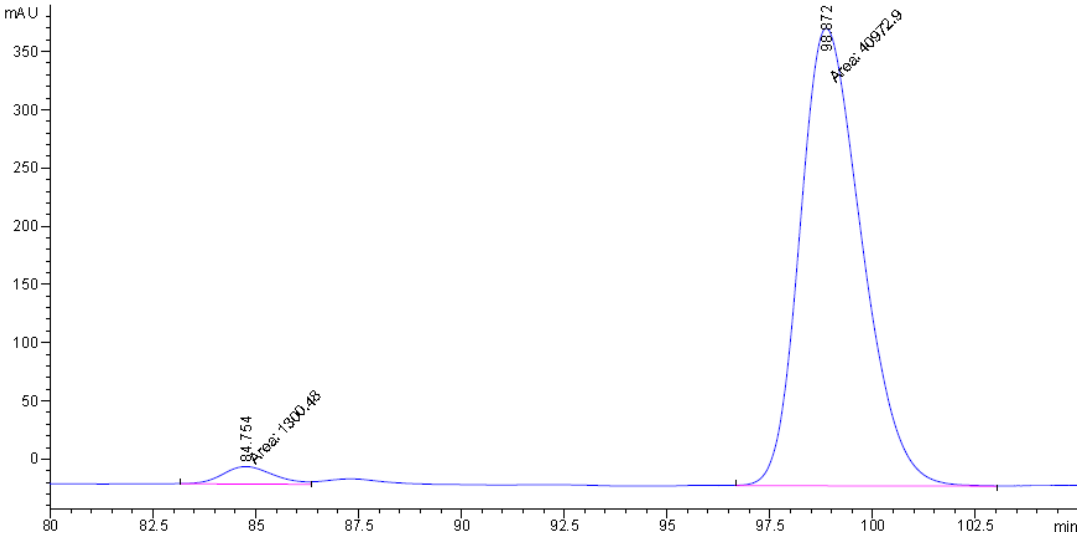
^{13}C (125 MHz, $CDCl_3$)

5c


OH
HF2C
CF3
19F (471 MHz, CDCl3)
5c
-62.56
128.66
128.67
128.78
128.79
129.27
129.29
129.39
129.40
132.59
132.62
132.71
132.74
133.20
133.23
133.32
133.35
2.86
0.99
1.00
f1 (ppm)

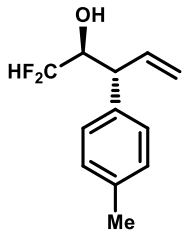


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	85.788	MM	1.4745	2.10284e4	237.68845	49.9984
2	100.308	MM	1.7586	2.10298e4	199.30756	50.0016



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	84.754	MF	1.4389	1300.47583	15.06372	3.0763
2	98.872	MM	1.7377	4.09729e4	392.98737	96.9237

(2*S*,3*R*)-1,1-Difluoro-3-(*p*-tolyl)pent-4-en-2-ol (5d)



The title compound was prepared according to the general procedure using difluoroacetaldehyde ethyl hemiacetal (90%, 28 mg, 200 μmol) and 1-(*p*-tolyl)allyl acetate (76 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 15:1) provided the title compound (31.7 mg, 149 μmol, *anti:syn* = >20:1) in 75% yield as a yellow oil.

TLC (SiO_2) R_f = 0.21 (hexanes/ethyl acetate = 10:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.17 (s, 4H), 6.18 (ddd, *J* = 17.2, 10.3, 8.7 Hz, 1H), 5.54 (ddd, *J* = 56.0, 54.8, 3.7 Hz, 1H), 5.27 (dd, *J* = 10.3, 1.5 Hz, 1H), 5.23 (dt, *J* = 17.2, 1.3 Hz, 1H), 4.05–3.95 (m, 1H), 3.57–3.51 (m, 1H), 2.34 (s, 3H), 2.11 (d, *J* = 4.6 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.2, 136.5, 136.2, 129.8, 128.0, 118.7, 115.2 (t, *J* = 243.1 Hz), 73.7 (dd, *J* = 22.9, 20.7 Hz), 50.7, 21.2.

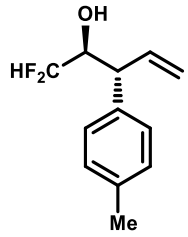
^{19}F NMR (471 MHz, $CDCl_3$): δ = –129.2 (ddd, *J* = 285.9, 54.9, 5.9 Hz), –134.7 (ddd, *J* = 286.0, 56.0, 16.1 Hz).

HRMS (CI) Calculated for $C_{12}H_{14}F_2O$ $[M]^+$ = 212.1013, Found 212.1010.

FTIR (neat) 3411, 2981, 2924, 1514, 1150, 1127, 1057, 1001, 925, 816, 760 cm^{-1}.

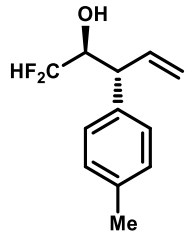
$[\alpha]_D^{33}$: –68.3 (*c* = 1.0, $CHCl_3$)

HPLC: (Chiralcel AD-H column, hexanes:*i*-PrOH = 99:1, 1.0 mL/min, 230 nm), *ee* = 95%.



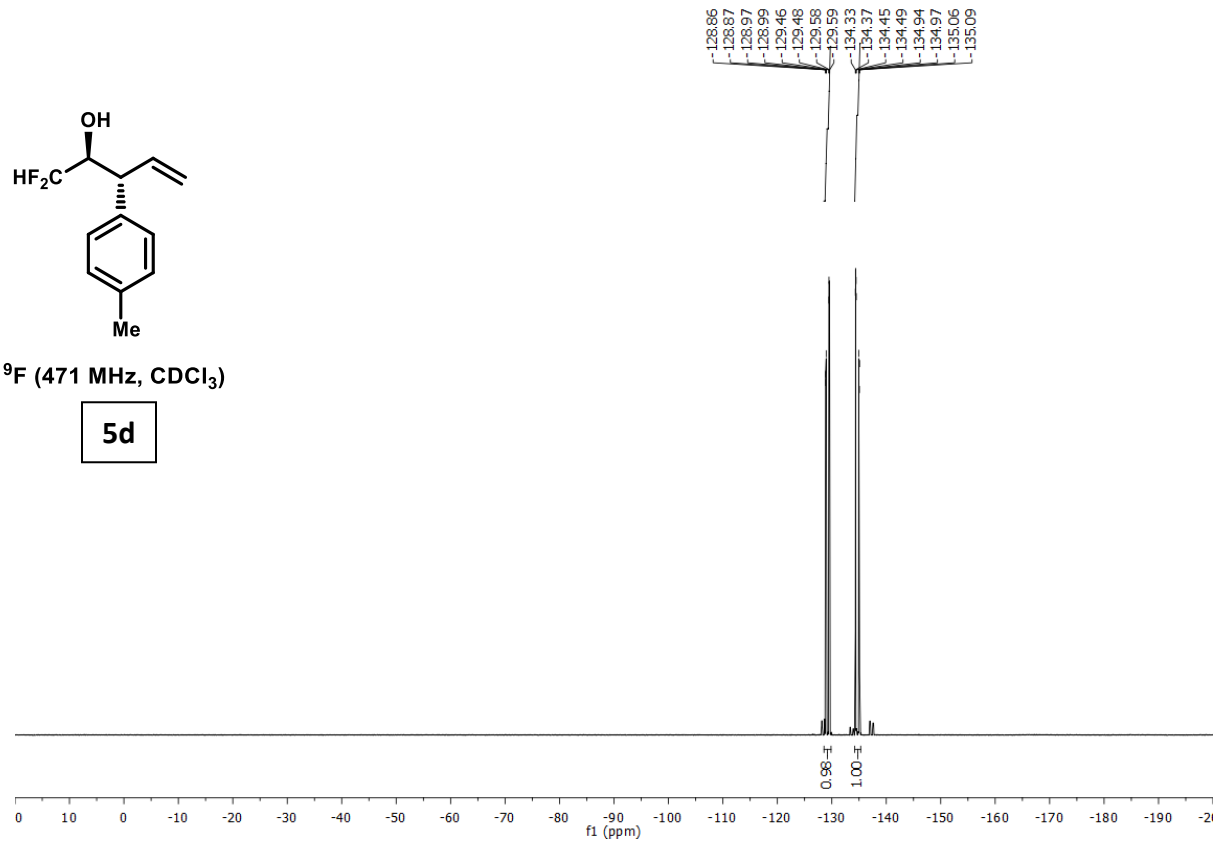
^{1}H (500 MHz, $CDCl_3$)

5d



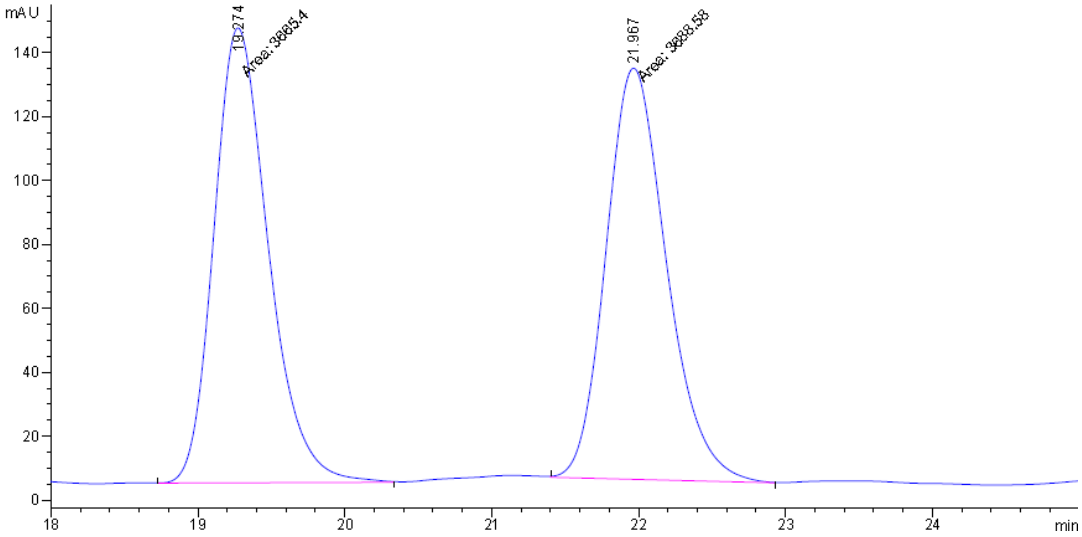
^{13}C (125 MHz, $CDCl_3$)

5d

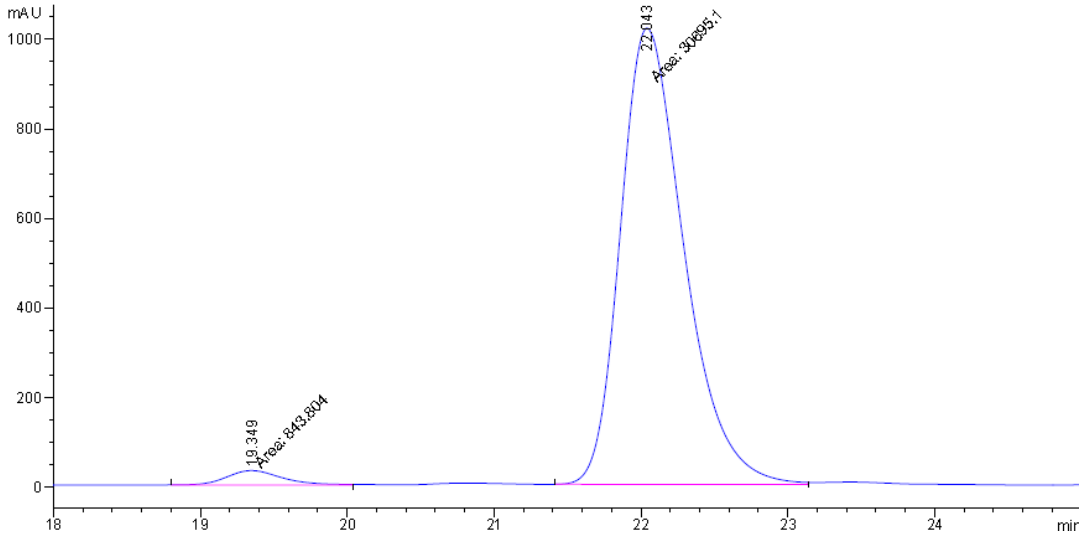


^{19}F (471 MHz, $CDCl_3$)

5d

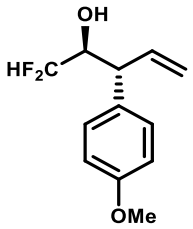


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.274	MM	0.4291	3665.40405	142.37234	49.8424
2	21.967	MM	0.4777	3688.58081	128.68335	50.1576



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.349	MM	0.4376	843.80371	32.13876	2.6754
2	22.043	MM	0.5019	3.06951e4	1019.36761	97.3246

(2*S*,3*R*)-1,1-difluoro-3-(4-methoxyphenyl)pent-4-en-2-ol (5e)



The title compound was prepared according to the general procedure using difluoroacetaldehyde ethyl hemiacetal (90%, 28 mg, 200 μmol) and 1-(4-methoxyphenyl)allyl acetate (82.4 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 20:1-10:1) provided the title compound (37.2 mg, 164 μmol, *anti:syn* = >20:1) in 82% yield as a white solid.

TLC (SiO_2) R_f = 0.26 (hexanes/ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.20 (d, *J* = 8.7 Hz, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 6.17 (ddd, *J* = 17.1, 10.2, 8.6 Hz, 1H), 5.53 (ddd, *J* = 55.9, 54.8, 3.7 Hz, 1H), 5.29 – 5.16 (m, 2H), 3.97 (dddt, *J* = 16.2, 8.3, 6.3, 3.9 Hz, 1H), 3.80 (s, 3H), 3.56 – 3.49 (m, 1H), 2.23 (d, *J* = 4.6 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.8, 136.3, 131.5, 129.2, 118.5 (dd, *J* = 243.5, 25.1 Hz), 115.2 (t, *J* = 243.3 Hz), 114.4, 73.8 (dd, *J* = 22.9, 20.7 Hz), 55.4, 50.2 (t, *J* = 3.7 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ = -129.19 (ddd, *J* = 285.6, 55.0, 5.8 Hz), -134.65 (ddd, *J* = 286.0, 56.0, 16.3 Hz).

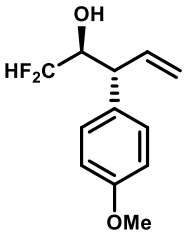
HRMS (CI) Calculated for $C_{12}H_{14}F_2O_2$ $[M]^+$ = 228.0962, Found 228.0960.

FTIR (neat) 3440, 2925, 2363, 1737, 1250, 1155, 1038, 1023, 817, 772 cm^{-1}.

$[\alpha]_D^{33}$: –70.5 (*c* = 1.0, $CHCl_3$)

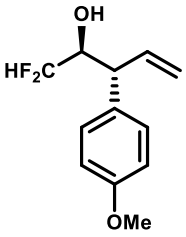
MP: 83-84˚C.

HPLC: (Chiralcel AD-H column, hexanes:*i*-PrOH = 99:1, 1.0 mL/min, 230 nm), *ee* = 93%.



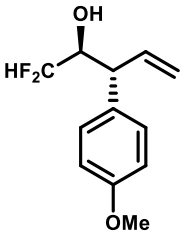
^{1}H (500 MHz, $CDCl_3$)

5e



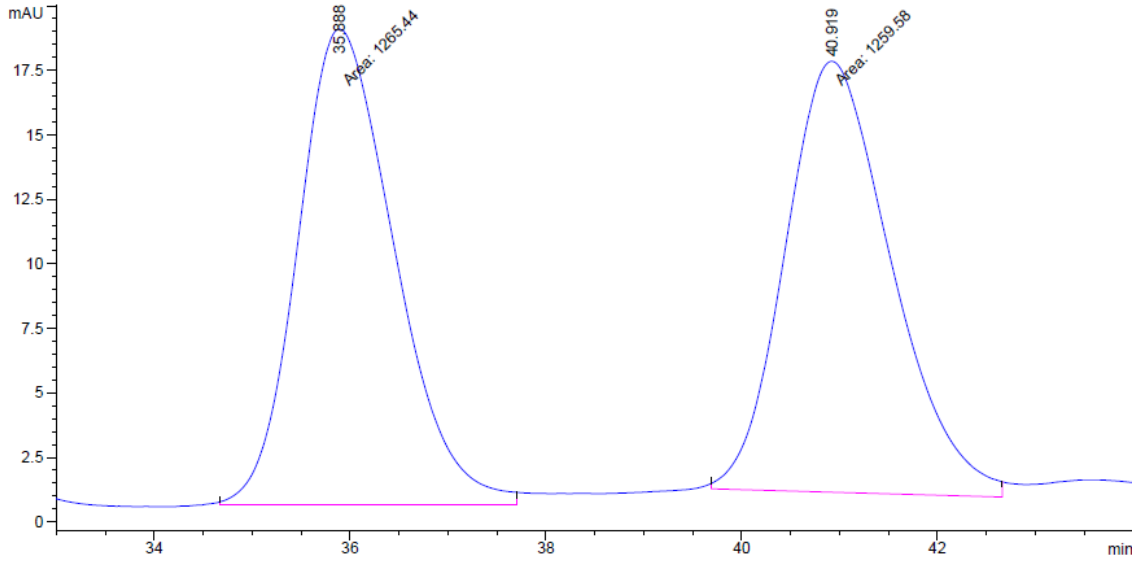
^{13}C (125 MHz, $CDCl_3$)

5e

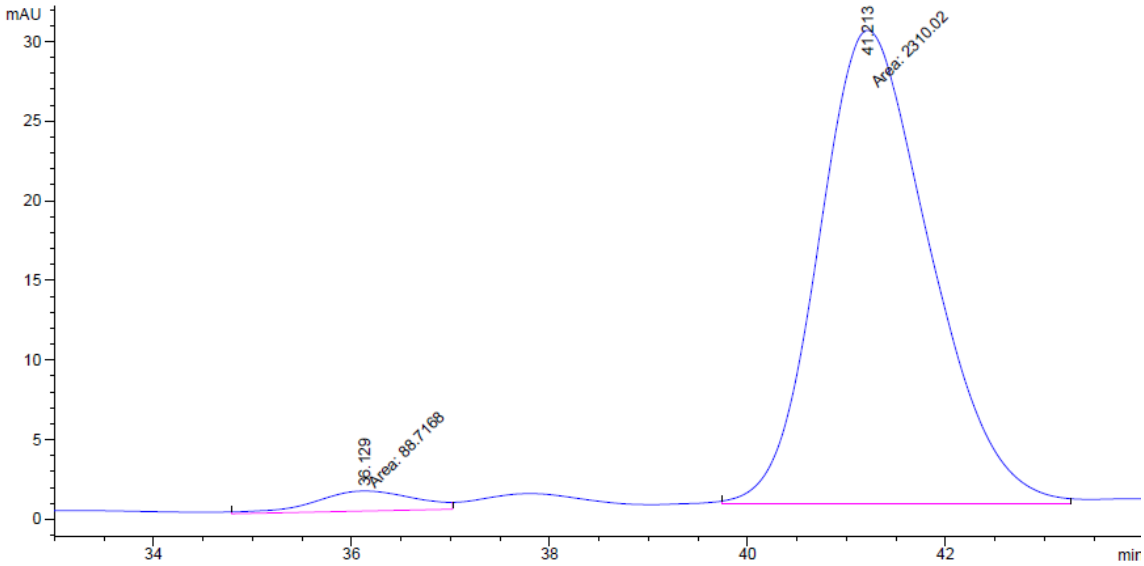


^{19}F (471 MHz, $CDCl_3$)

5e

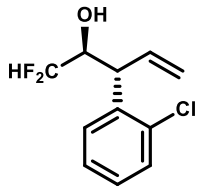


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	35.888	MM	1.1427	1265.43823	18.45711	50.1160
2	40.919	MM	1.2569	1259.57983	16.70190	49.8840



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	36.129	MF	1.1742	88.71684	1.25924	3.6985
2	41.213	MM	1.2962	2310.01831	29.70327	96.3015

(2S,3R)-3-(2-chlorophenyl)-1,1-difluoropent-4-en-2-ol (5f)



The title compound was prepared according to the general procedure using difluoroacetaldehyde ethyl hemiacetal (90%, 27.9 mg, 199 μmol) and 1-(2-chlorophenyl)allyl acetate (84 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 20:1 → 10:1) provided the title compound (35.1 mg, 151 μmol, *anti:syn* = >20:1) in 76% yield as a yellow oil.

TLC (SiO_2) R_f = 0.57 (hexanes/ethyl acetate = 3:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.43 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.40 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.29 – 7.25 (m, 1H), 7.21 (td, *J* = 7.6, 1.7 Hz, 1H), 6.23 (ddd, *J* = 17.1, 10.2, 8.7 Hz, 1H), 5.64 (ddd, *J* = 56.4, 55.0, 4.6 Hz, 1H), 5.32 (dd, *J* = 10.2, 1.4 Hz, 1H), 5.25 (dt, *J* = 17.0, 1.2 Hz, 1H), 4.20 (dd, *J* = 8.8, 4.8 Hz, 1H), 4.08 (ddq, *J* = 14.0, 6.6, 4.8 Hz, 1H), 2.16 (d, *J* = 4.9 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.6, 134.1, 133.5, 130.1, 129.9, 128.5, 127.2, 120.0, 115.4 (t, *J* = 243.8 Hz), 72.6 (dd, *J* = 24.7, 21.5 Hz), 46.3 (dd, *J* = 4.7, 2.7 Hz).

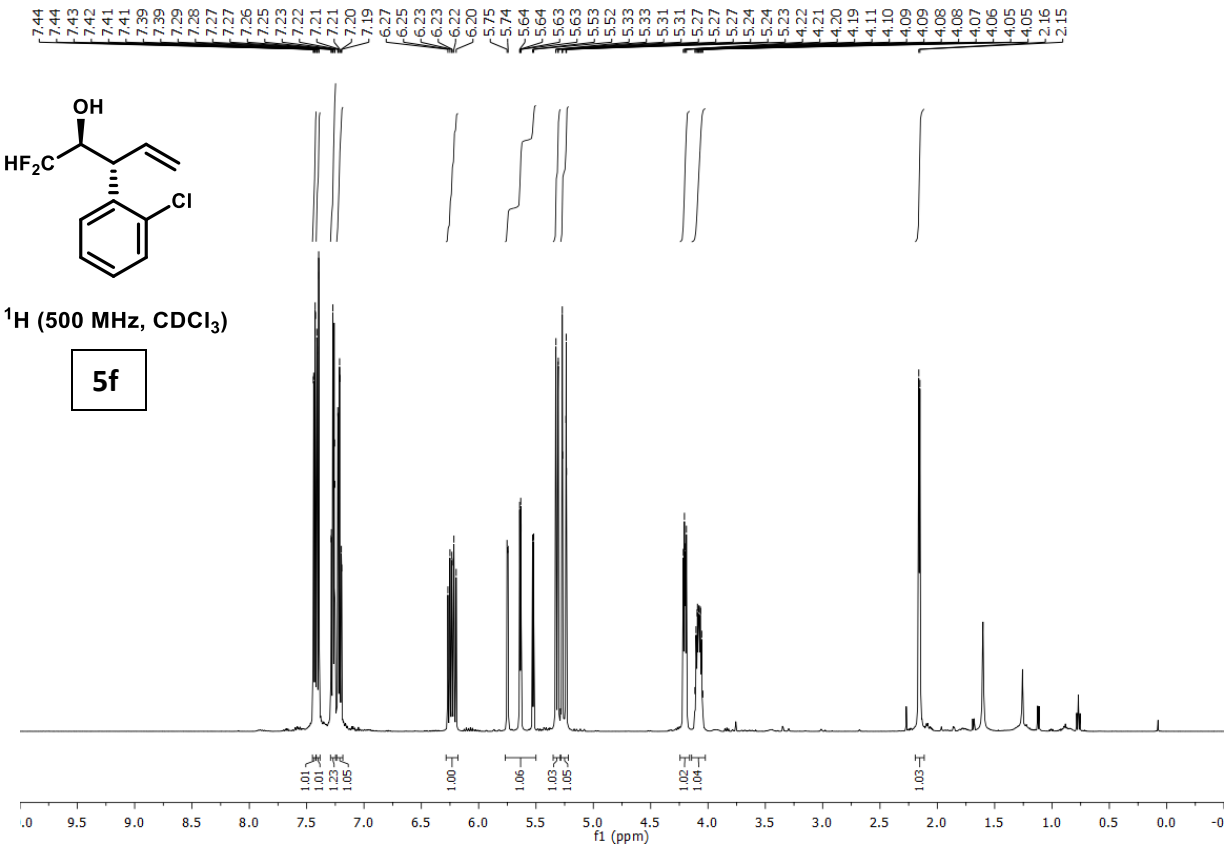
^{19}F NMR (471 MHz, $CDCl_3$): δ = -128.6 (ddd, *J* = 288.0, 55.0, 6.6 Hz), -132.0 (ddd, *J* = 288.0, 56.5, 13.5 Hz).

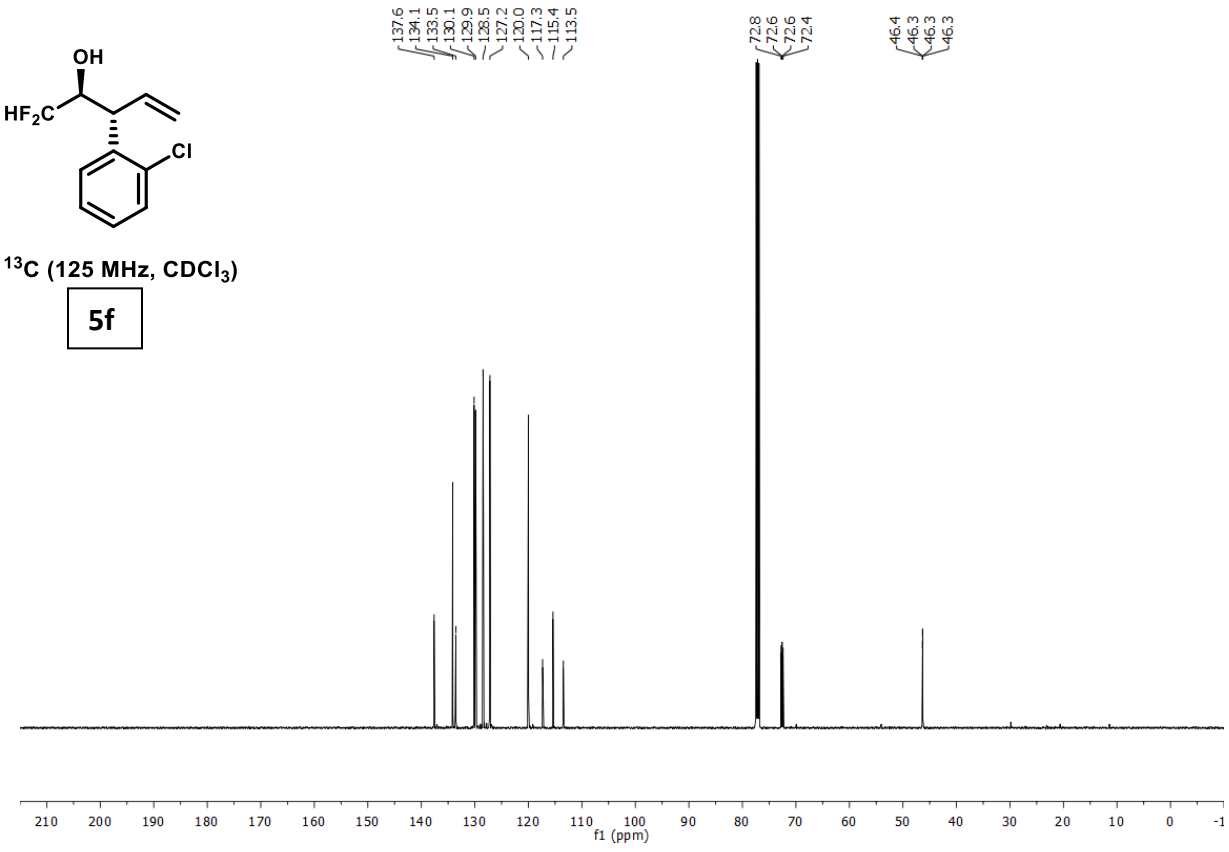
HRMS (CI) Calculated for $C_{11}H_{11}{}^{35}ClF_2O$ $[M]^+$ = 232.0466, Found 232.0465.

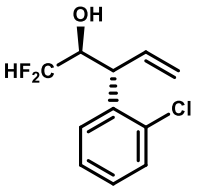
FTIR (neat) 3443, 3074, 2985, 2920, 1474, 1442, 1150, 1066, 1001, 930, 751 cm^{-1}.

$[\alpha]_D^{27}$: –44.3 (*c* = 1.0, $CHCl_3$)

HPLC: (Chiralcel AS-H column, hexanes:*i*-PrOH = 97:3, 1.0 mL/min, 210 nm), *ee* = 92%.

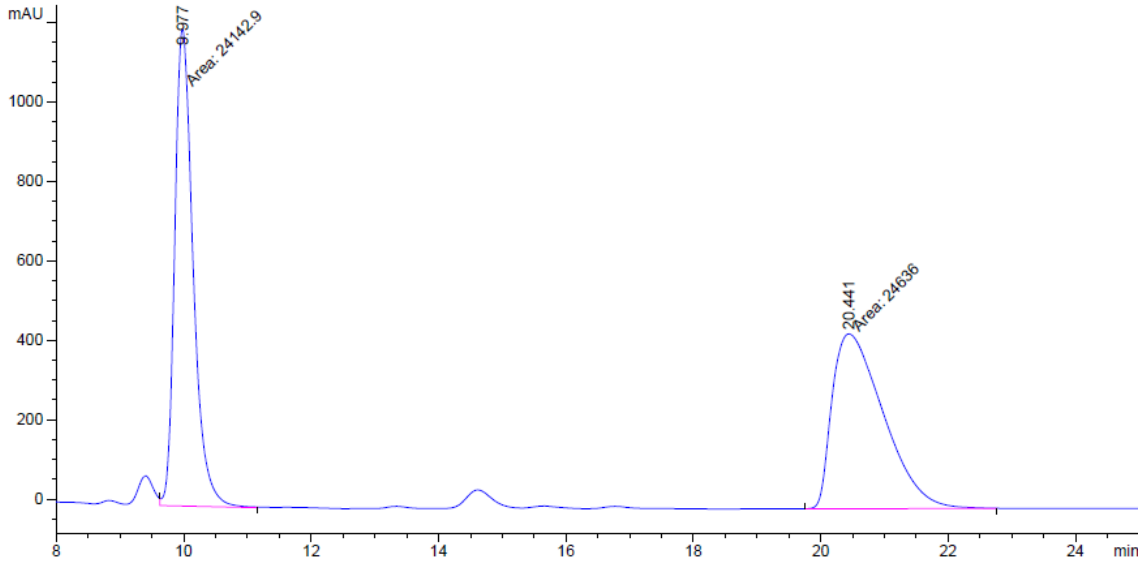

OH
HF2C
Cl
1H (500 MHz, CDCl3)
5f
f1 (ppm)


OH
HF2C
Cl
13C (125 MHz, CDCl3)
5f
f1 (ppm)

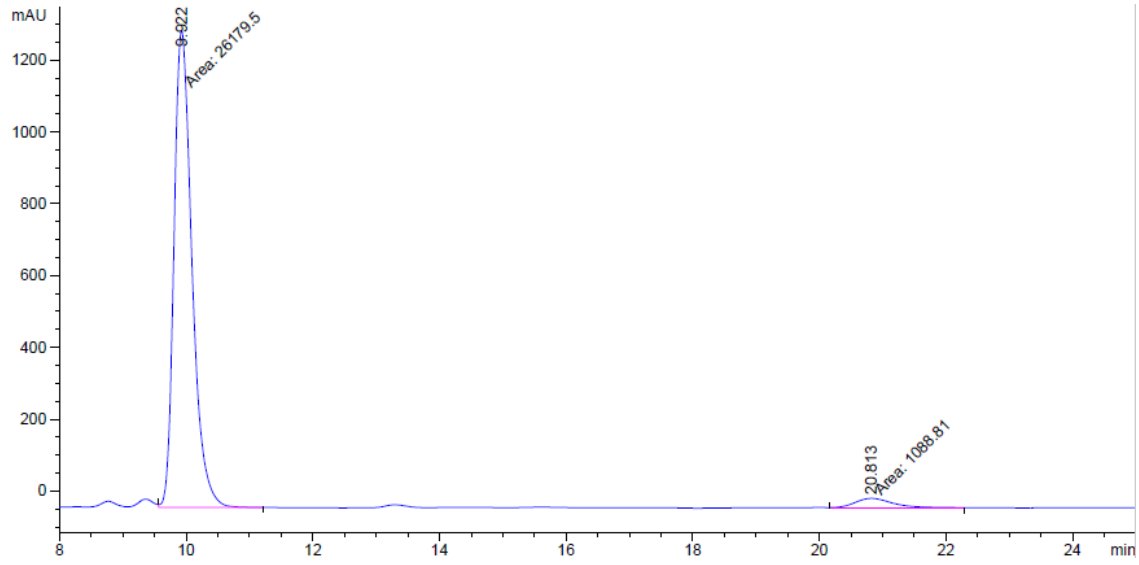


^{19}F (471 MHz, $CDCl_3$)

5f

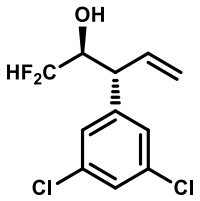


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.977	FM	0.3352	2.41429e4	1200.55249	49.4946
2	20.441	MM	0.9332	2.46360e4	439.98474	50.5054



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.922	FM	0.3286	2.61795e4	1327.65588	96.0070
2	20.813	MM	0.6958	1088.81360	26.08039	3.9930

(2S,3R)-3-(3,5-dichlorophenyl)-1,1-difluoropent-4-en-2-ol (5g)



The title compound was prepared according to the general procedure using difluoroacetaldehyde ethyl hemiacetal (90%, 28 mg, 200 μmol) and 1-(3,5-dichlorophenyl)allyl acetate (98 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 20:1) provided the title compound (43 mg, 160 μmol, *anti:syn* = >20:1) in 77% yield as a yellow oil.

TLC (SiO_2) R_f = 0.38 (hexanes/ethyl acetate = 9:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.28 (t, *J* = 1.7 Hz, 1H), 7.22 (d, *J* = 1.7 Hz, 2H), 6.13 (dt, *J* = 17.3, 9.6 Hz, 1H), 5.61 (ddd, *J* = 56.3, 55.3, 4.9 Hz, 1H), 5.29 (dd, *J* = 43.7, 13.7 Hz, 2H), 4.03 – 3.93 (m, 1H), 3.55 (dd, *J* = 8.8, 4.6 Hz, 1H), 2.21 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.30, 135.34, 133.52, 127.70, 126.83, 125.65, 123.39, 120.84, 73.41 (dd, *J* = 24.8, 22.0 Hz), 49.90 (dd, *J* = 4.9, 2.3 Hz).

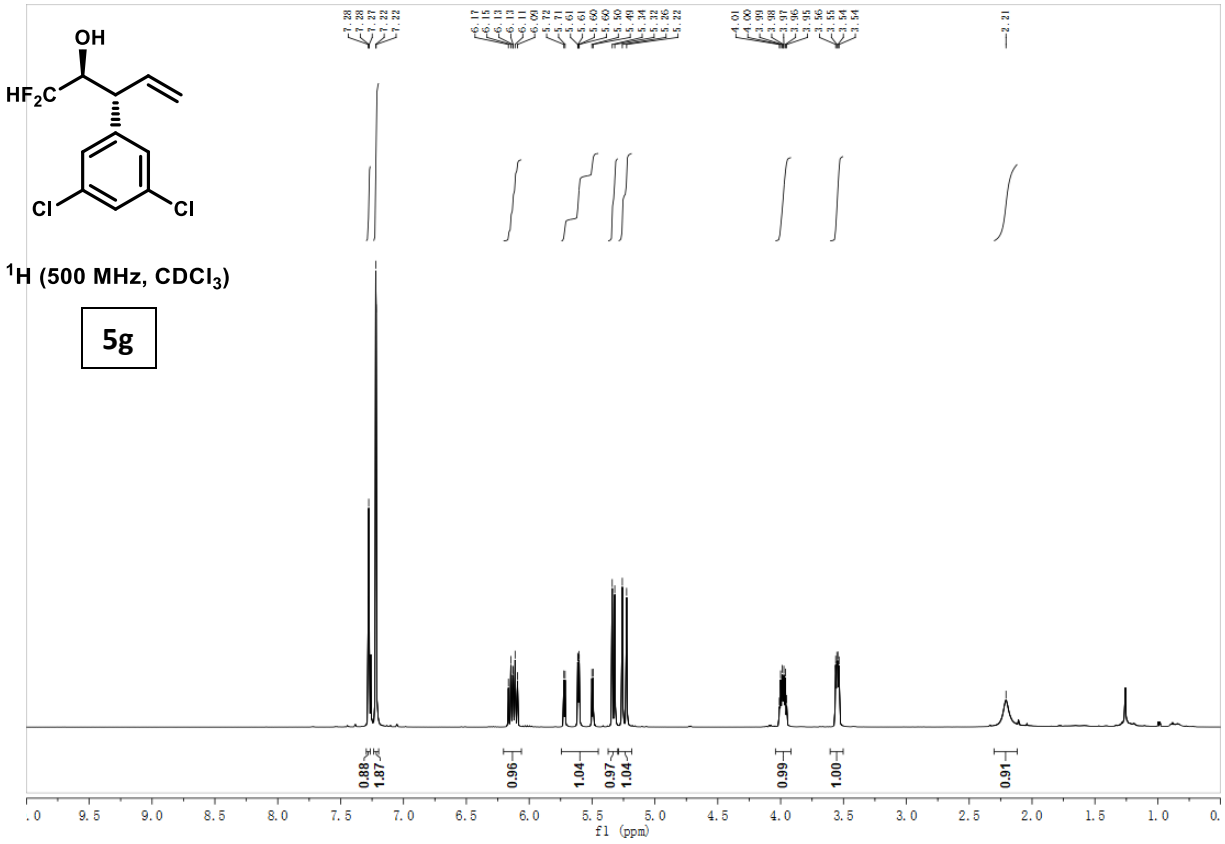
^{19}F NMR (471 MHz, $CDCl_3$): δ = -128.92 (ddd, *J* = 289.4, 55.1, 6.0 Hz), -132.45 (ddd, *J* = 289.4, 56.5, 13.4 Hz).

HRMS (CI) Calculated for $C_{11}H_{10}Cl_2F_2O$ $[M]^+$ = 266.0077, Found 266.0080.

FTIR (neat) 3432, 3083, 2984, 1567, 1433, 1059, 858, 759, 681 cm^{-1}.

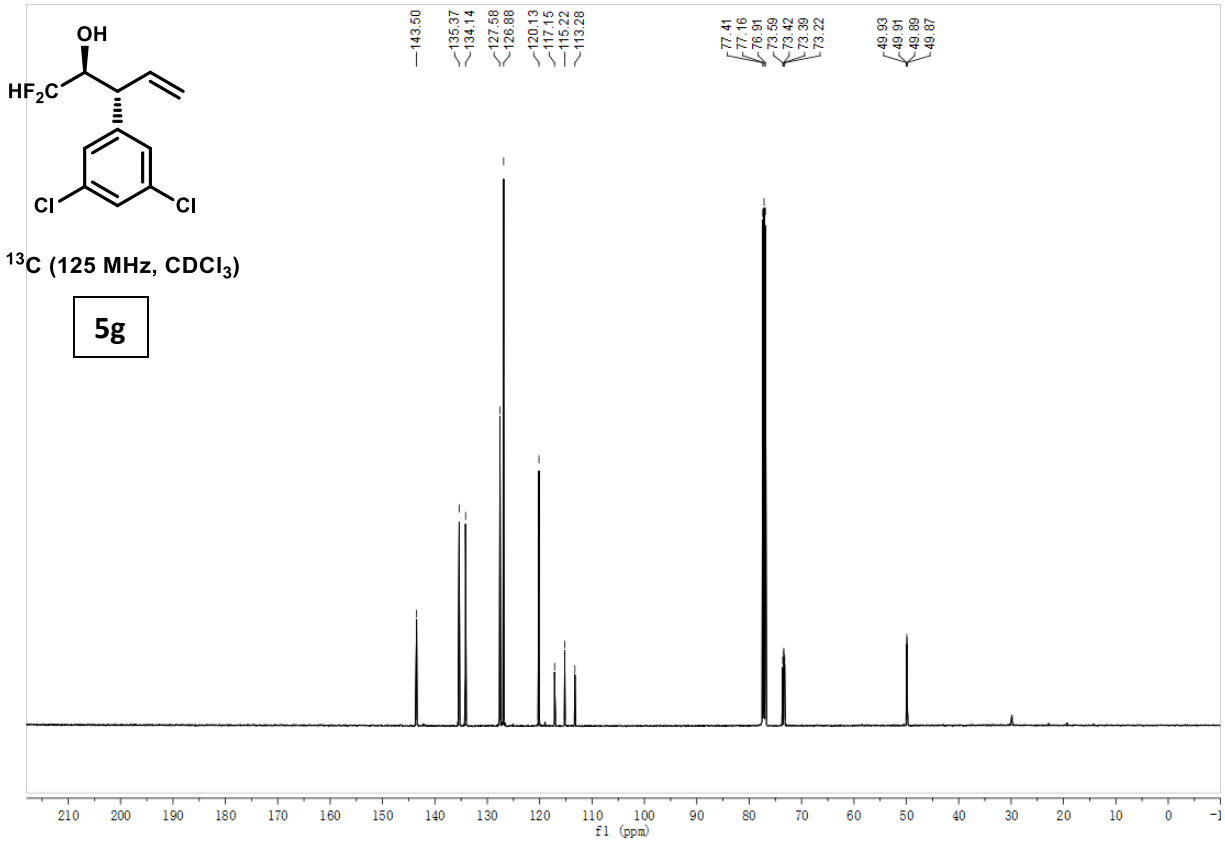
$[\alpha]_D^{33}$: –83.3 (*c* = 1.2, $CHCl_3$)

HPLC: (Chiralcel AS-H column, hexanes:*i*-PrOH = 99:1, 1.0 mL/min, 230 nm), *ee* = 95%.



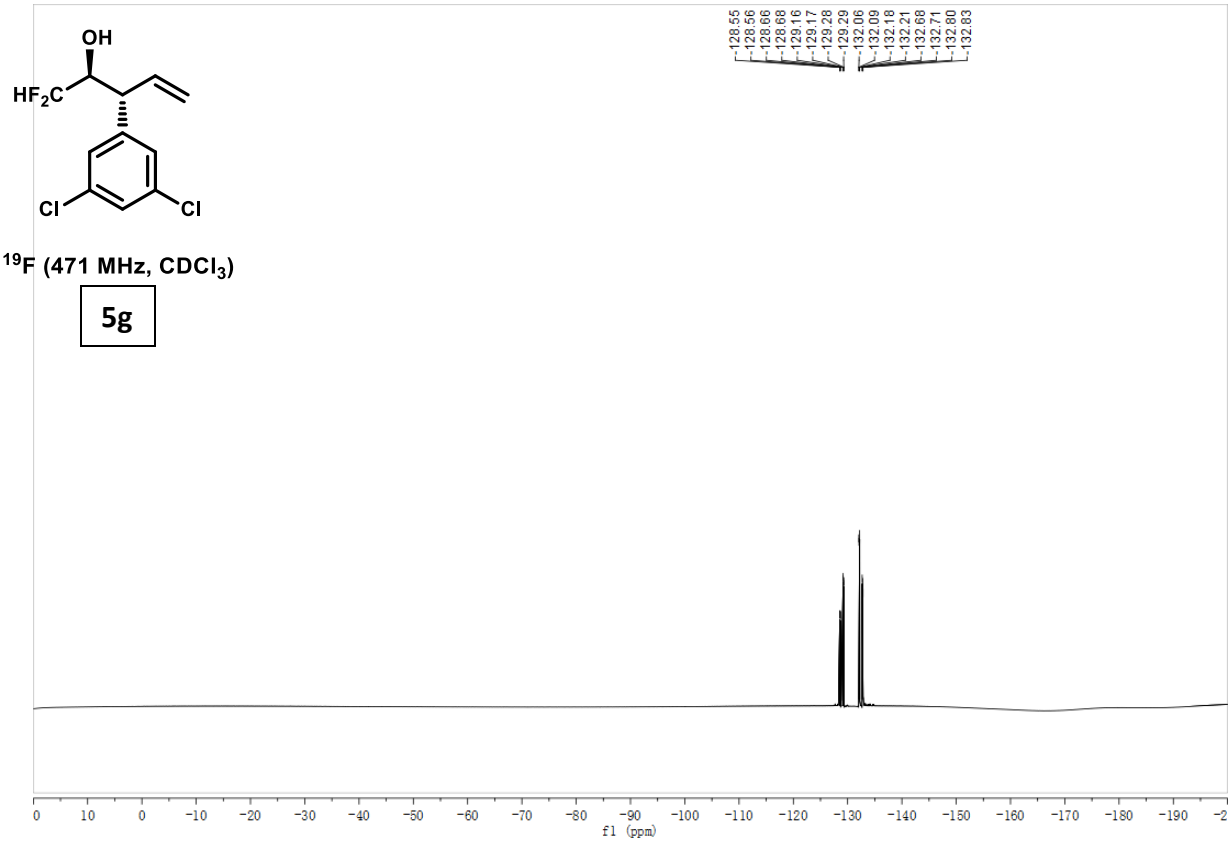
^{1}H (500 MHz, $CDCl_3$)

5g



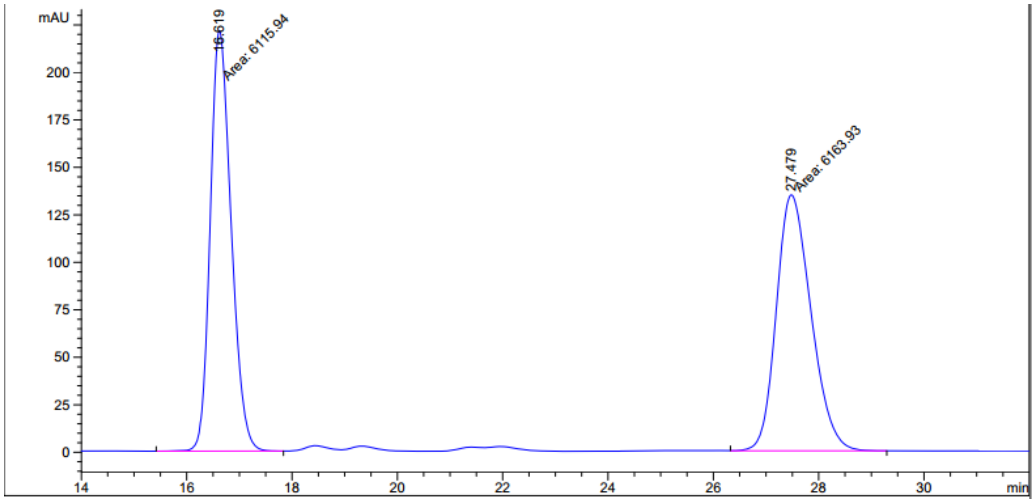
^{13}C (125 MHz, $CDCl_3$)

5g

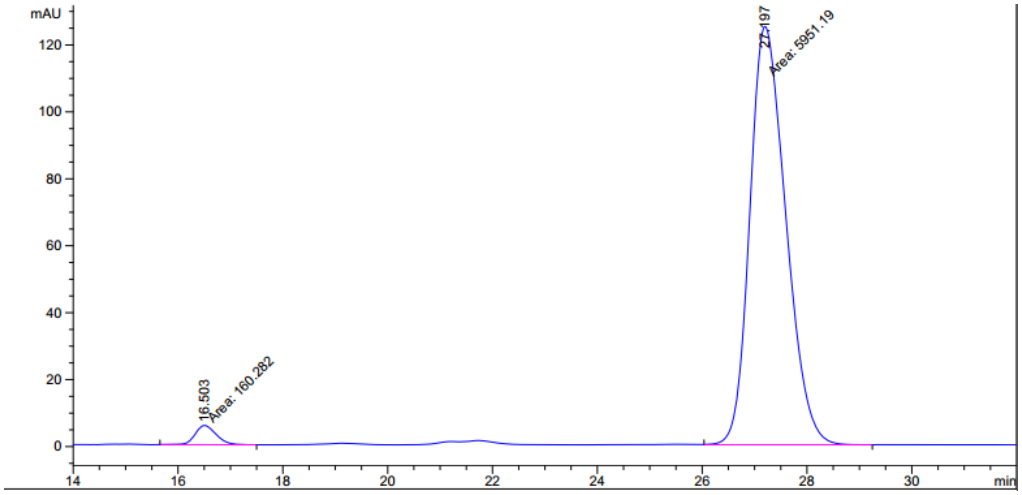


^{19}F (471 MHz, $CDCl_3$)

5g

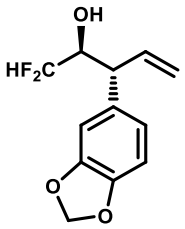


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.619	MM	0.4602	6115.94482	221.49268	49.8046
2	27.479	MM	0.7624	6163.93359	134.74940	50.1954



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.503	MM	0.4642	160.28223	5.75497	2.6226
2	27.197	MM	0.7938	5951.19092	124.95788	97.3774

(2*S*,3*R*)-3-(Benzo[d][1,3]dioxol-5-yl)-1,1-difluoropent-4-en-2-ol (5h)



The title compound was prepared according to the general procedure using difluoroacetaldehyde ethyl hemiacetal (90%, 28 mg, 200 μmol) and 1-(benzo[d][1,3]dioxol-5-yl)allyl acetate (88 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 10:1) provided the title compound (43.0 mg, 178 μmol, *anti:syn* = >20:1) in 89% yield as a yellow oil.

TLC (SiO_2) R_f = 0.13 (hexanes/ethyl acetate = 10:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.80–6.77 (m, 2H), 6.73 (dd, *J* = 8.0, 1.8 Hz, 1H), 6.13 (ddd, *J* = 17.1, 10.2, 8.6 Hz, 1H), 5.95 (s, 2H), 5.55 (ddd, *J* = 56.0, 54.8, 3.7 Hz, 1H), 5.28–5.25 (m, 1H), 5.22 (dt, *J* = 17.1, 1.3 Hz, 1H), 4.00–3.91 (m, 1H), 3.52–3.46 (m, 1H), 2.14 (d, *J* = 4.5 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.1, 146.8, 136.0, 133.3, 121.3, 118.7, 115.2 (t, *J* = 243.2 Hz), 108.8, 108.5, 101.3, 73.8 (dd, *J* = 23.1, 20.8 Hz), 50.6 (t, *J* = 3.7 Hz).

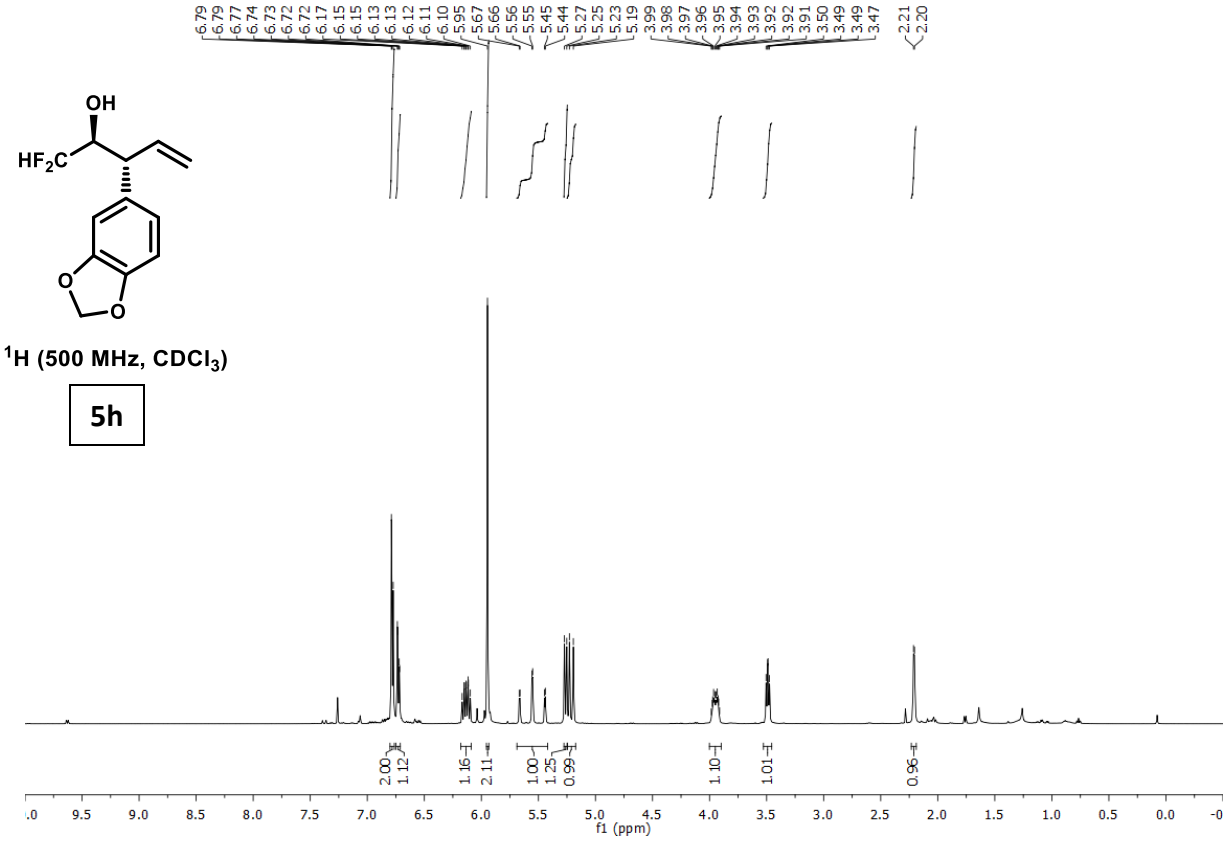
^{19}F NMR (471 MHz, $CDCl_3$): δ = –129.2 (ddd, *J* = 286.1, 54.7, 5.9 Hz), –134.6 (ddd, *J* = 286.2, 56.0, 15.8 Hz).

HRMS (CI) Calculated for $C_{12}H_{12}F_2O_3$ $[M]^+$ = 242.0755, Found 242.0758.

FTIR (neat) 3453, 2982, 2897, 1504, 1488, 1443, 1244, 1134, 1098, 1037, 929 cm^{-1}.

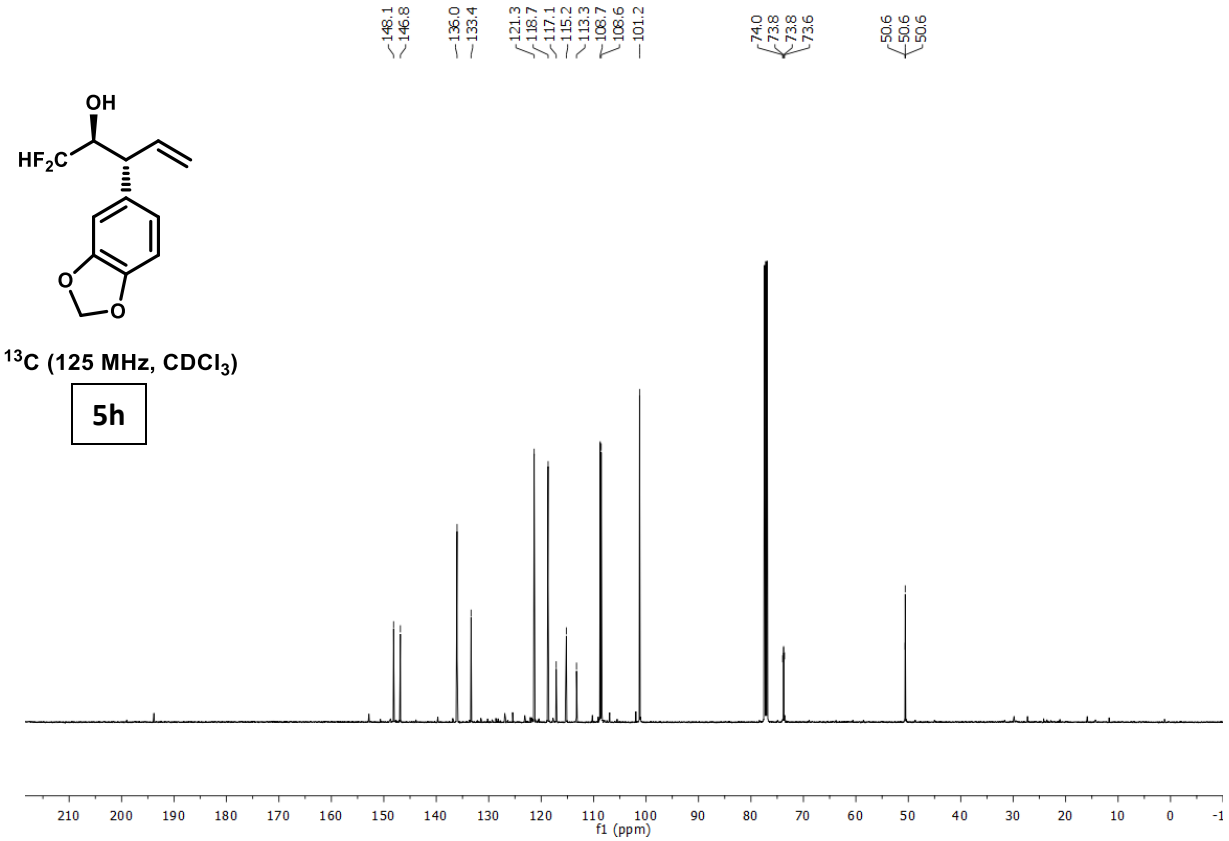
$[\alpha]_D^{32}$: –53.0 (*c* = 1.0, $CHCl_3$)

HPLC: (Chiralcel OJ-H column, hexanes:*i*-PrOH = 97:3, 0.5 mL/min, 210 nm), *ee* = 93%.



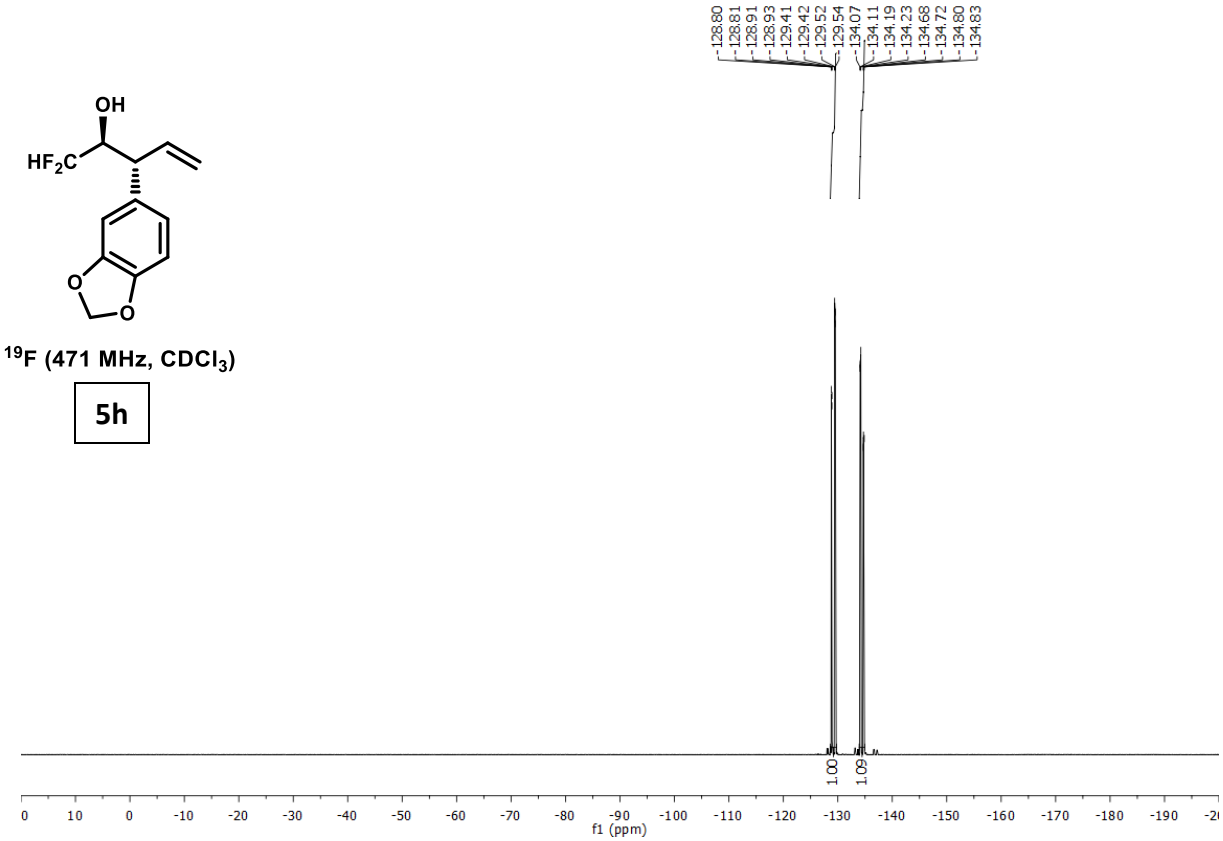
^{1}H (500 MHz, $CDCl_3$)

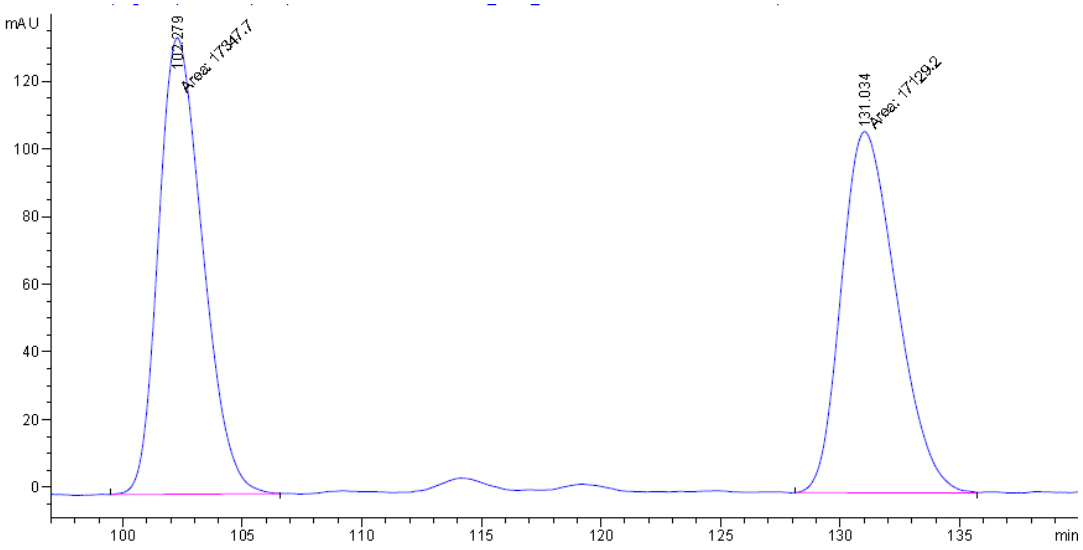
5h



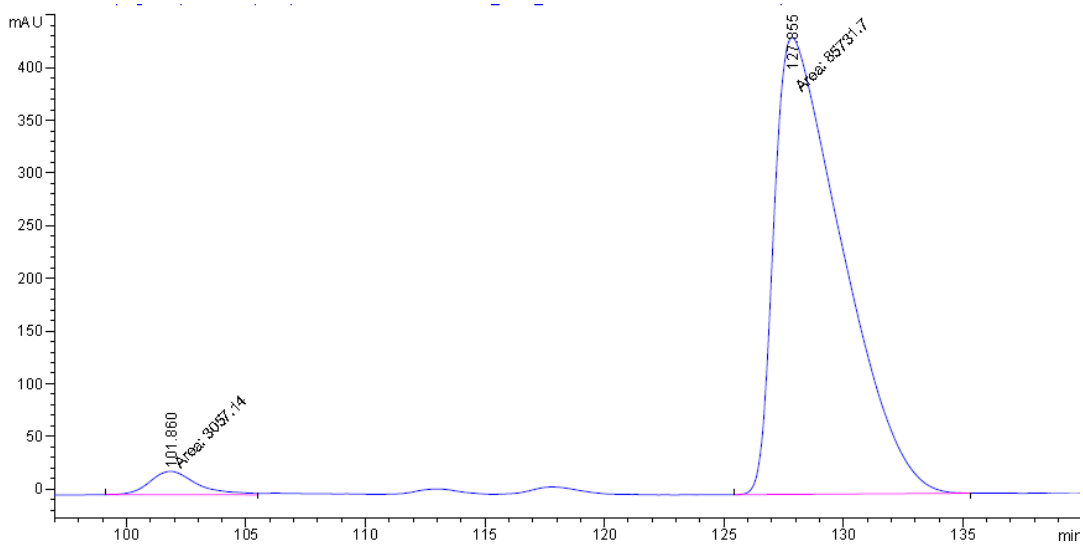
^{13}C (125 MHz, $CDCl_3$)

5h


OH
HF2C
O
O
19F (471 MHz, CDCl3)
5h
128.80
128.81
128.91
128.93
129.41
129.42
129.52
129.54
134.07
134.11
134.19
134.23
134.68
134.72
134.80
134.83
1.00
1.09
0
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

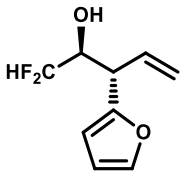


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	102.279	MM	2.1432	1.73477e4	134.90370	50.3169
2	131.034	MM	2.6742	1.71292e4	106.75617	49.6831



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	101.860	MM	2.2946	3057.13696	22.20513	3.4432
2	127.855	MM	3.2946	8.57317e4	433.70004	96.5568

(2S,3S)-1,1-difluoro-3-(furan-2-yl)pent-4-en-2-ol (5i)



The title compound was prepared according to the general procedure using using difluoroacetaldehyde ethyl hemiacetal (90%, 28 mg, 200 μmol) and 1-(furan-2-yl)allyl acetate (66.5 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 20:1) provided the title compound (25 mg, 120 μmol, *anti:syn* = >20:1) in 65% yield as a yellow oil.

TLC (SiO_2) R_f = 0.2 (hexanes/ethyl acetate = 9:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.39 – 7.37 (m, 1H), 6.35 (dd, *J* = 3.2, 1.9 Hz, 1H), 6.19 (d, *J* = 3.2 Hz, 1H), 6.12 – 6.03 (m, 1H), 5.63 (ddd, *J* = 56.3, 54.9, 4.6 Hz, 1H), 5.33 (dd, *J* = 10.1, 0.9 Hz, 1H), 5.27 (d, *J* = 17.2 Hz, 1H), 4.21 – 4.10 (m, 1H), 3.74 (dd, *J* = 8.7, 5.1 Hz, 1H), 2.27 (dd, *J* = 8.9, 3.7 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 152.69, 142.15, 132.73, 119.98, 117.23, 115.29, 113.36, 110.61, 107.44, 72.05 (dd, *J* = 24.6, 21.6 Hz), 44.86 (dd, *J* = 5.1, 2.9 Hz).

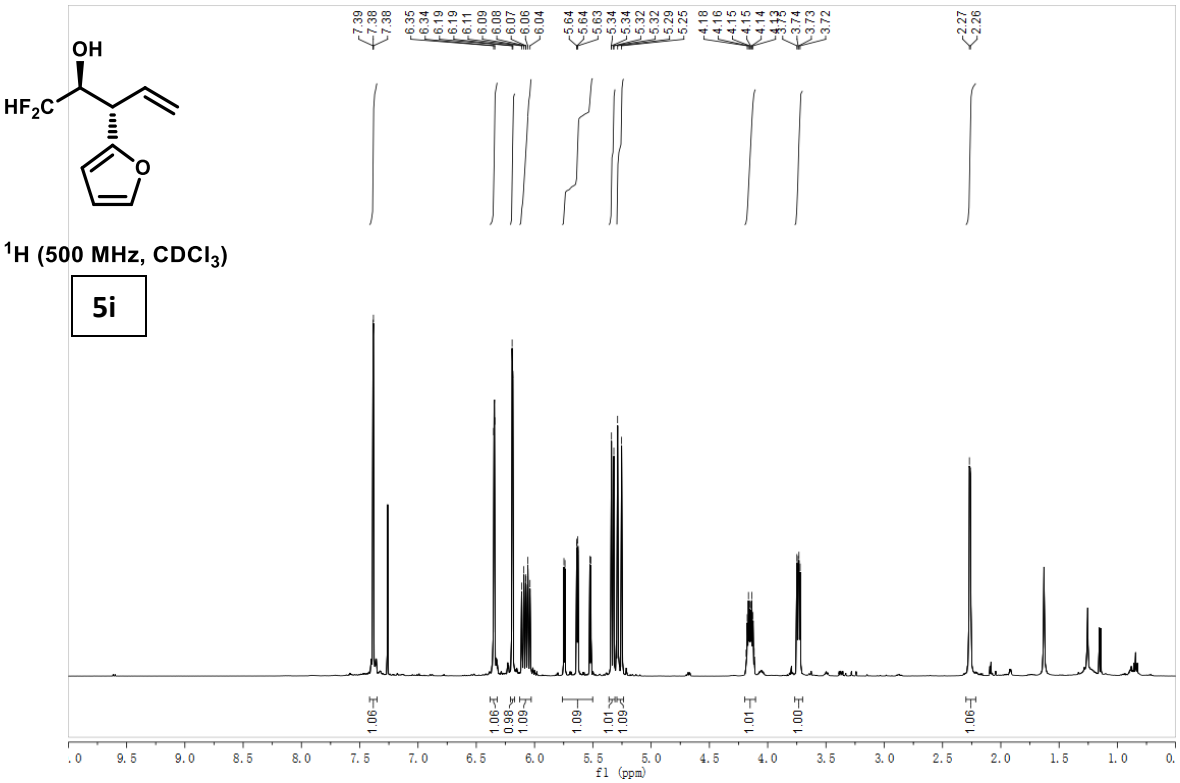
^{19}F NMR (471 MHz, $CDCl_3$): δ = -128.92 (ddd, *J* = 288.8, 54.8, 6.0 Hz), -132.79 (ddd, *J* = 288.8, 56.3, 14.2 Hz).

HRMS (CI) Calculated for $C_9H_{10}F_2O_2$ $[M]^+$ =188.0649, Found 188.0644.

FTIR (neat) 3435, 2926, 1717, 1265, 1062, 935, 734, 703 cm^{-1}.

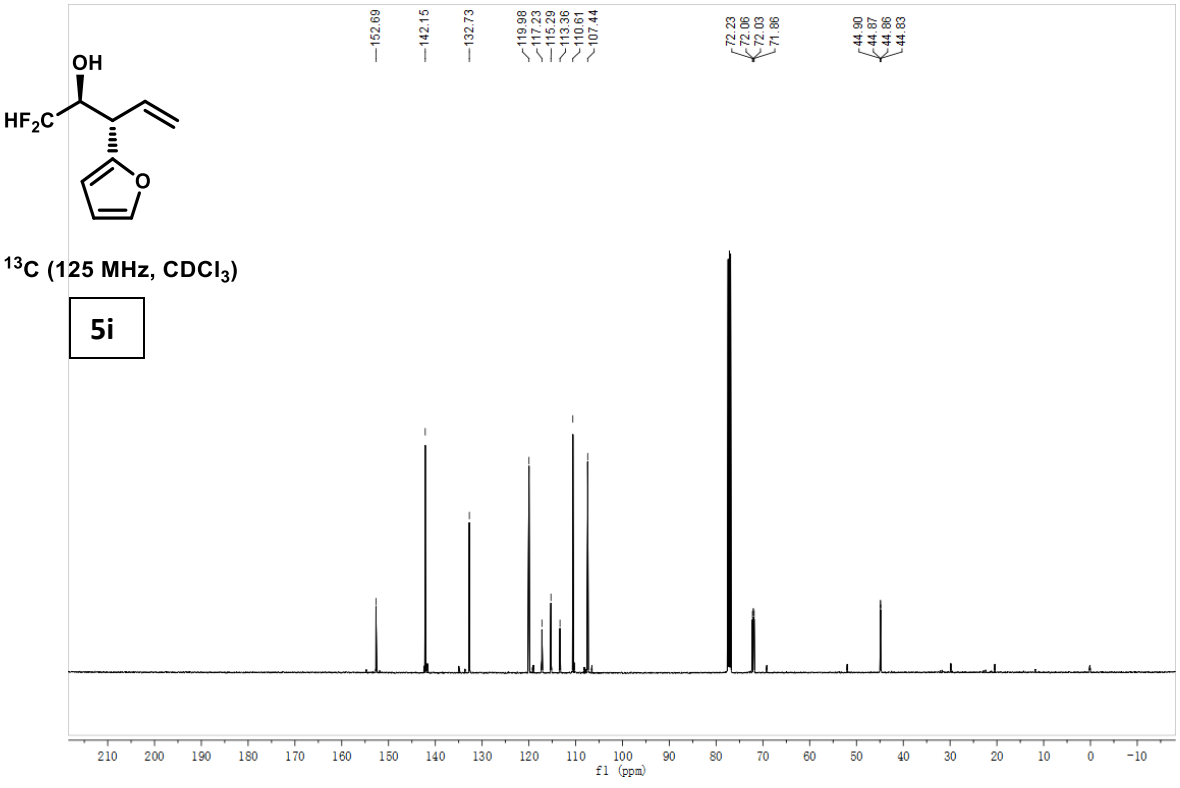
$[\alpha]_D^{33}$: –43.3 (*c* = 0.3, $CHCl_3$)

HPLC: (Chiralcel AD-H column, hexanes:*i*-PrOH = 99:1, 1.0 mL/min, 230 nm), *ee* = 91%.



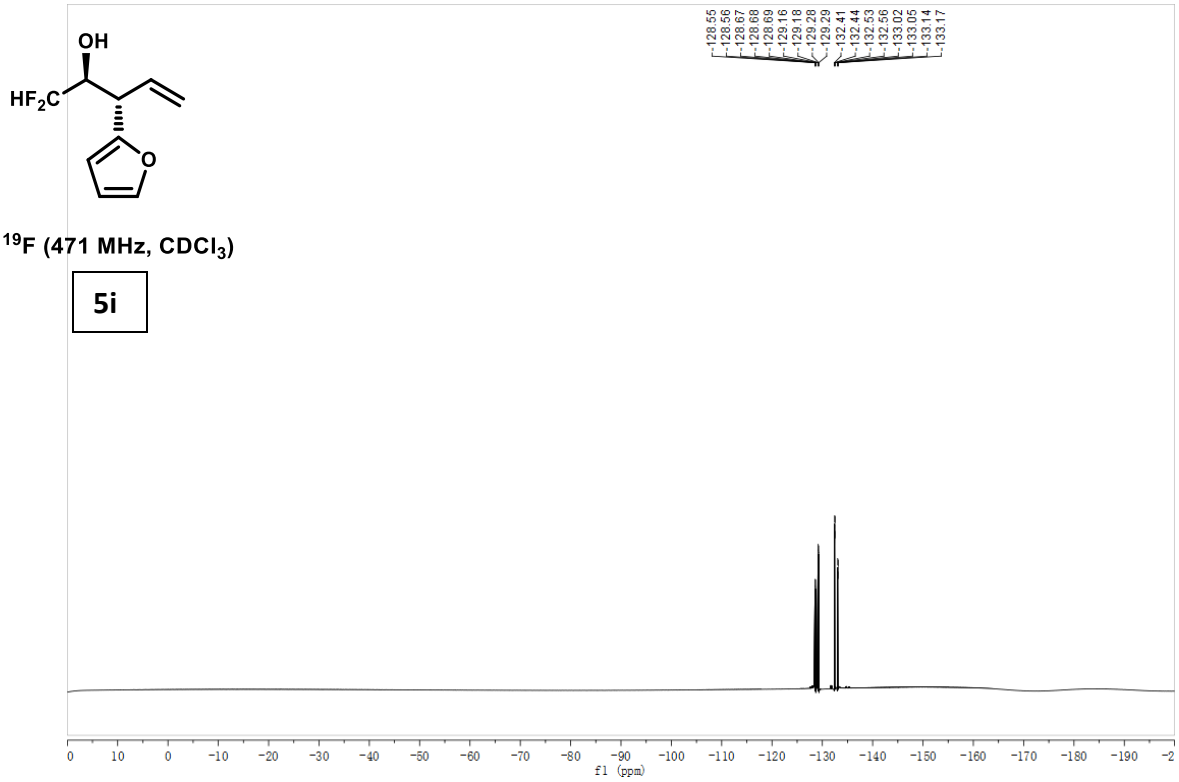
^{1}H (500 MHz, $CDCl_3$)

5i



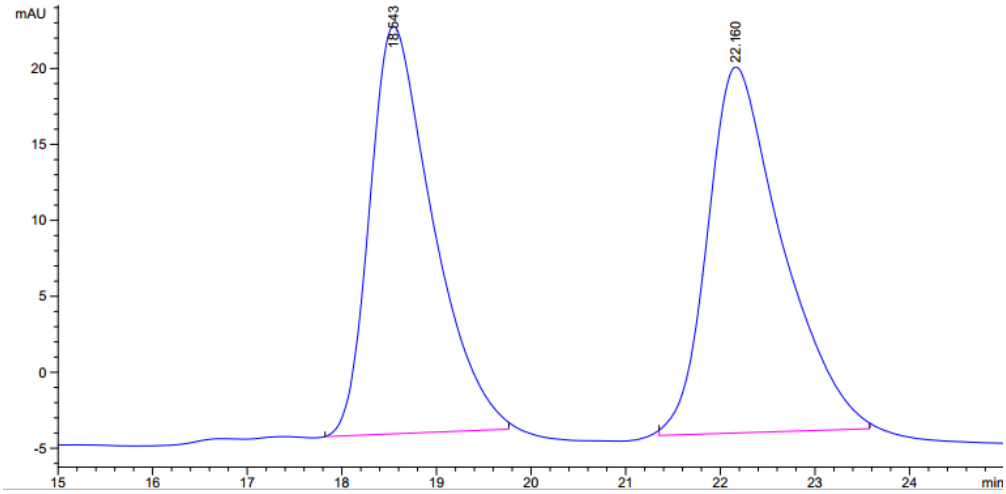
^{13}C (125 MHz, $CDCl_3$)

5i

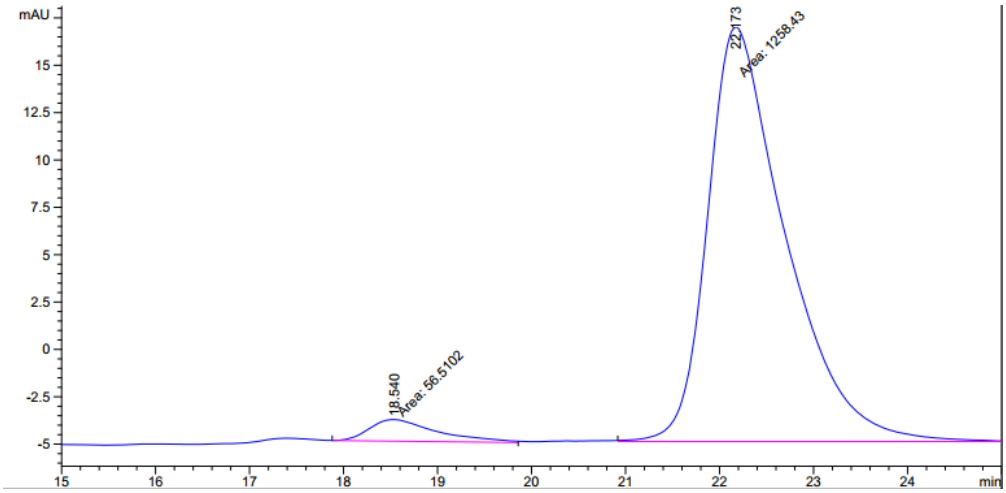


^{19}F (471 MHz, $CDCl_3$)

5i

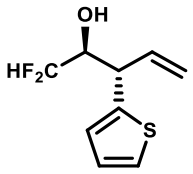


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.543	BB	0.6699	1241.43872	26.82661	48.4237
2	22.160	BB	0.7983	1322.26086	24.09177	51.5763



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.540	MM	0.8269	56.51017	1.13897	4.2975
2	22.173	MM	0.9590	1258.43079	21.87011	95.7025

(2*S*,3*S*)-1,1-difluoro-3-(thiophen-2-yl)pent-4-en-2-ol (5j)



The title compound was prepared according to the general procedure using difluoroacetaldehyde ethyl hemiacetal (90%, 28 mg, 200 μmol) and 1-(thiophen-2-yl)allyl acetate (73 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 20:1) provided the title compound (28.7 mg, 140 μmol, *anti:syn* = >20:1) in 70% yield as a yellow oil.

TLC (SiO_2) R_f = 0.54 (hexanes/ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.24 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.00 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.96 (s, 1H), 6.20 – 6.06 (m, 1H), 5.64 (ddd, *J* = 56.3, 54.9, 4.7 Hz, 1H), 5.34 – 5.24 (m, 2H), 4.03 (dt, *J* = 14.4, 4.8 Hz, 1H), 3.92 (dd, *J* = 8.9, 5.0 Hz, 1H), 2.30 (d, *J* = 4.3 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.3, 135.1, 127.2, 125.3, 124.8, 119.2, 115.3 (t, *J* = 243.3 Hz), 74.0 (dd, *J* = 24.6, 21.4 Hz), 46.3 (dd, *J* = 5.1, 2.7 Hz).

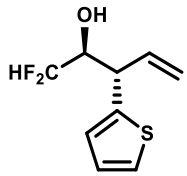
^{19}F NMR (471 MHz, $CDCl_3$): δ = -129.12 (ddd, *J* = 288.7, 54.9, 5.5 Hz), -133.10 (ddd, *J* = 288.6, 56.3, 14.3 Hz).

HRMS (CI) Calculated for $C_9H_{10}OF_2S$ $[M]^+$ = 204.0420, Found 204.0218.

FTIR (neat) 3444, 1420, 1126, 1051, 928, 756, 697 cm^{-1}.

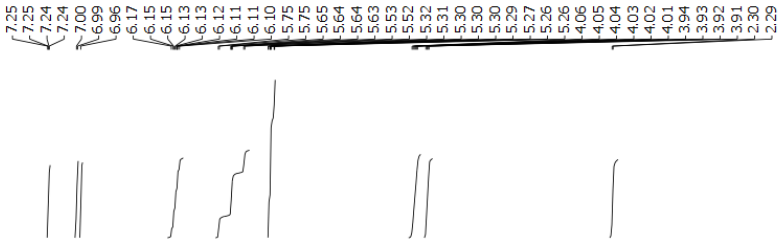
$[\alpha]_D^{33}$: –73.3 (*c* = 1.0, $CHCl_3$)

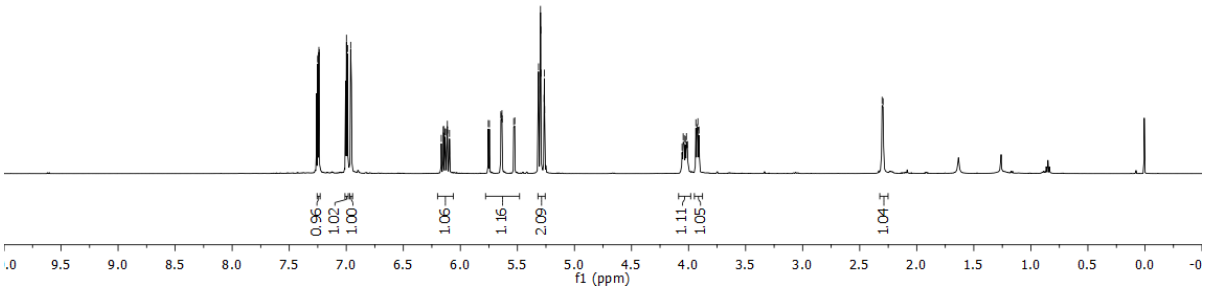
HPLC: (Chiralcel AD-H column, hexanes:*i*-PrOH = 99:1, 1.0 mL/min, 230 nm), *ee* = 88%.

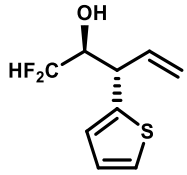


^{1}H (500 MHz, $CDCl_3$)

5j

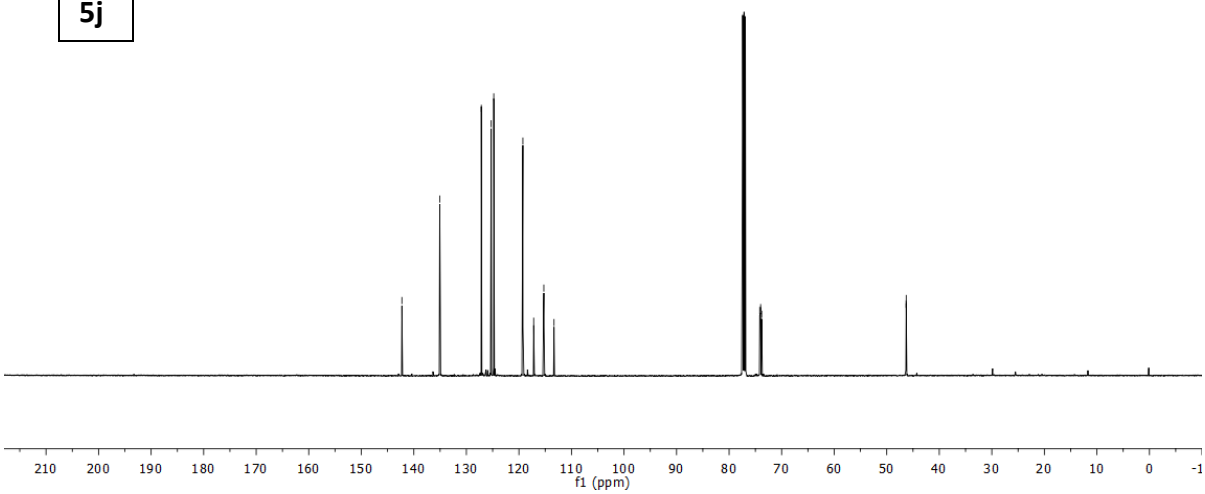


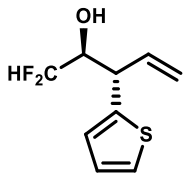




^{13}C (125 MHz, $CDCl_3$)

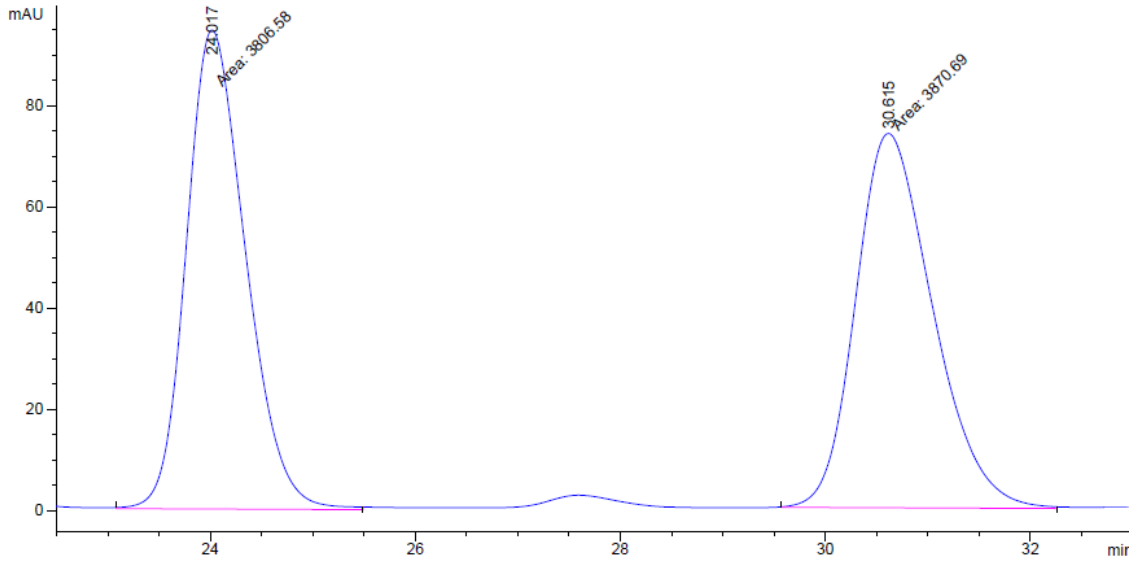
5j



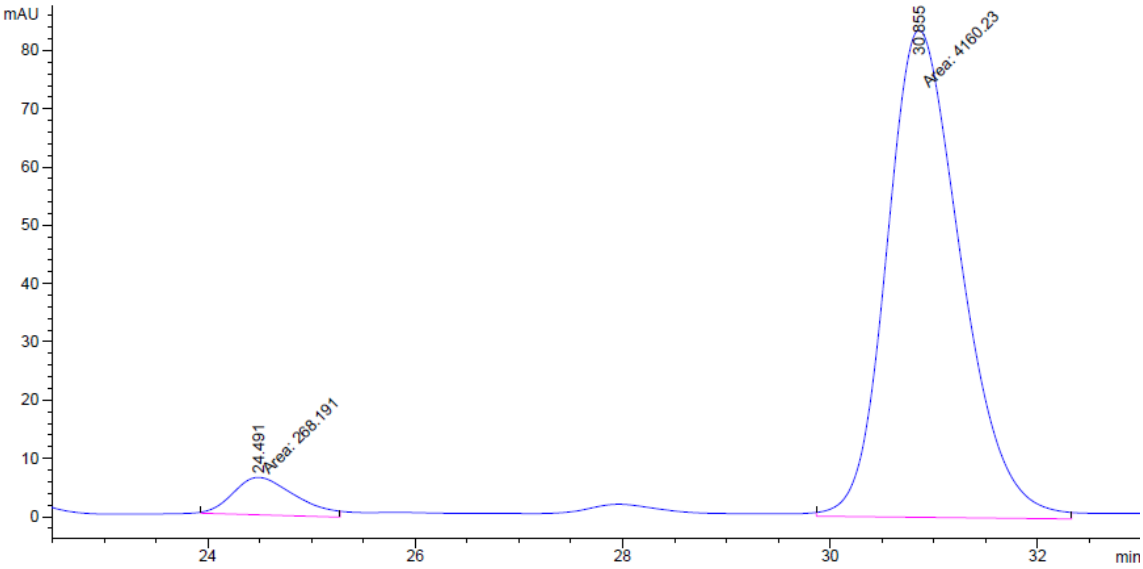


^{19}F (471 MHz, $CDCl_3$)

5j

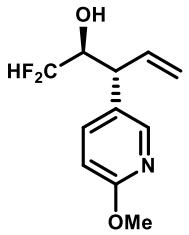


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.017	MM	0.6698	3806.58154	94.72547	49.5825
2	30.615	MM	0.8715	3870.68506	74.02729	50.4175



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.491	MM	0.6966	268.19061	6.41644	6.0561
2	30.855	MM	0.8292	4160.22949	83.61486	93.9439

(2S,3R)-1,1-difluoro-3-(6-methoxypyridin-3-yl)pent-4-en-2-ol (5k)



The title compound was prepared according to the general procedure using difluoroacetaldehyde ethyl hemiacetal (90%, 27.3 mg, 195 µmol) and 1-(6-methoxypyridin-3-yl)allyl acetate (83 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 6:1) provided the title compound (33.5 mg, 146 µmol, *anti:syn* = >20:1) in 75% yield as a yellow oil.

TLC (SiO_2) R_f = 0.37 (hexanes/ethyl acetate = 3:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 2.4 Hz, 1H), 7.54 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.72 (d, *J* = 8.6 Hz, 1H), 6.21 – 6.11 (m, 1H), 5.60 (td, *J* = 55.7, 4.5 Hz, 1H), 5.28 (d, *J* = 10.2 Hz, 1H), 5.21 (d, *J* = 17.1 Hz, 1H), 3.97 – 3.92 (m, 1H), 3.91 (s, 3H), 3.55 (dd, *J* = 8.6, 5.4 Hz, 1H), 2.53 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.5, 146.3, 138.7, 135.2, 128.3, 119.2, 115.4 (t, *J* = 243.6 Hz), 111.1, 73.7 (dd, *J* = 24.2, 21.4 Hz), 53.6, 47.4 (dd, *J* = 4.6, 2.5 Hz).

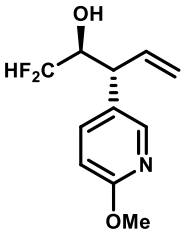
^{19}F NMR (471 MHz, $CDCl_3$): δ = -128.9 (ddd, *J* = 288.4, 55.1, 6.1 Hz), -132.8 (ddd, *J* = 288.5, 56.4, 14.0 Hz).

HRMS (ESI) Calculated for $C_{11}H_{13}F_2NO_2$ $[M+H]^+$ = 230.0987, Found 230.0994.

FTIR (neat) 3235, 2982, 2922, 1607, 1494, 1393, 1291, 1126, 1059, 1029, 928, 833, 774 cm^{-1}.

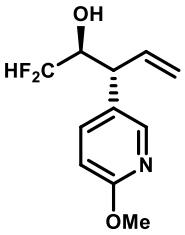
$[\alpha]_D^{29}$: –79.5 (*c* = 1.0, $CHCl_3$)

HPLC: (Chiralcel AS-H column, hexanes:*i*-PrOH = 97:3, 1.0 mL/min, 230 nm), *ee* = 93%.



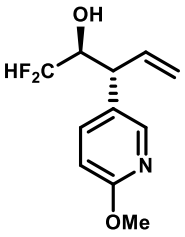
^{1}H (500 MHz, $CDCl_3$)

5k



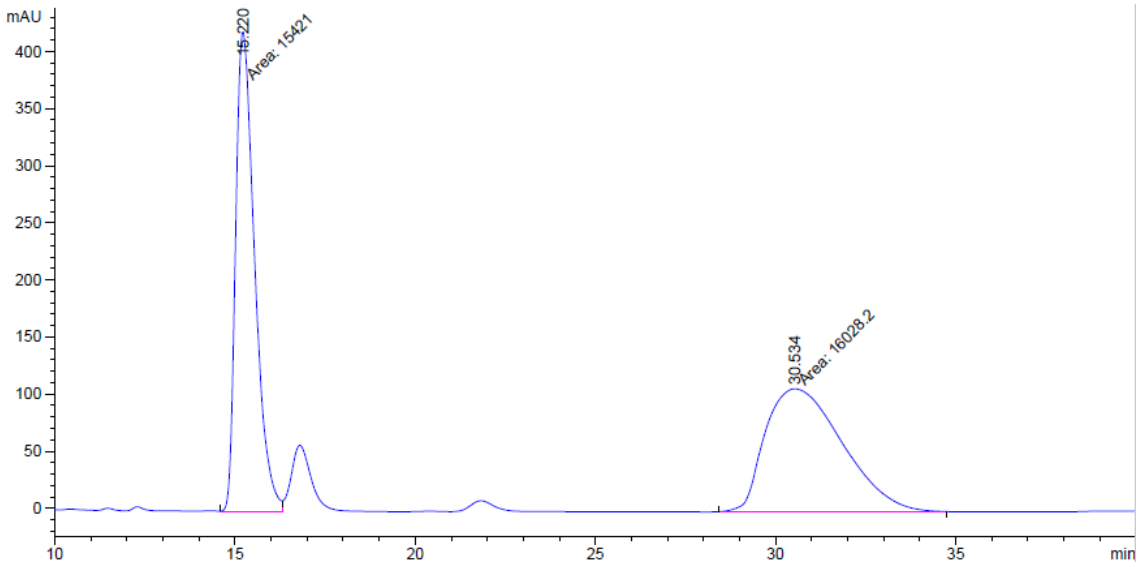
^{13}C (125 MHz, $CDCl_3$)

5k

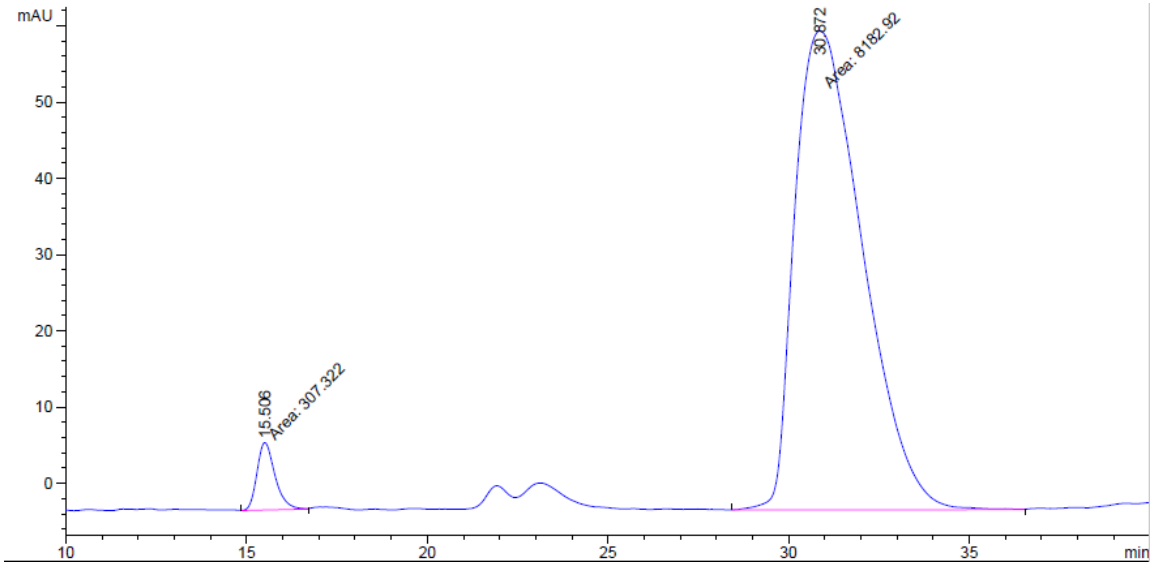


^{19}F (471 MHz, $CDCl_3$)

5k

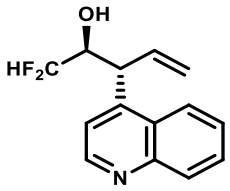


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.220	MF	0.6120	1.54210e4	419.95688	49.0348
2	30.534	MM	2.4809	1.60282e4	107.67802	50.9652



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.506	MM	0.5801	307.32208	8.82987	3.6197
2	30.872	MM	2.1719	8182.91895	62.79467	96.3803

(2*S*,3*R*)-1,1-difluoro-3-(quinolin-4-yl)pent-4-en-2-ol (5l)



The title compound was prepared according to the general procedure using difluoroacetaldehyde ethyl hemiacetal (90%, 28 mg, 200 µmol) and 1-(quinolin-4-yl)allyl acetate (91 mg, 0.40 mmol, 200 mol%). Flash chromatography on silica (Hex/EtOAc 3:1→ 1:1) provided the title compound (42.6 mg, 172 µmol, *anti:syn* = >20:1) in 86% yield as a white solid.

TLC (SiO_2) R_f = 0.26 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (500 MHz, Acetone-d_6): δ = 8.81 (d, *J* = 4.5 Hz, 1H), 8.21 (ddt, *J* = 8.5, 1.3, 0.6 Hz, 1H), 8.04 (ddd, *J* = 8.4, 1.4, 0.6 Hz, 1H), 7.74 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.66 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.62 – 7.60 (m, 1H), 6.51 (ddd, *J* = 17.2, 10.3, 8.8 Hz, 1H), 5.82 (ddd, *J* = 56.5, 55.3, 5.1 Hz, 1H), 5.35 – 5.27 (m, 2H), 4.56 (dd, *J* = 9.0, 4.0 Hz, 1H), 4.23 – 4.13 (m, 1H), 2.99 (s, 1H).

^{13}C NMR (125 MHz, Acetone-d_6): δ = 150.7, 149.3, 147.4, 135.8, 131.0, 129.7, 127.5, 127.0, 123.7, 121.7, 119.2, 117.1 (t, *J* = 243.6 Hz), 73.1 (dd, *J* = 24.9, 21.4 Hz), 45.3 (dd, *J* = 5.7, 2.5 Hz).

^{19}F NMR (471 MHz, Acetone-d_6): δ = -128.48 (ddd, *J* = 285.2, 55.3, 6.4 Hz), -131.12 (ddd, *J* = 285.0, 56.7, 14.0 Hz).

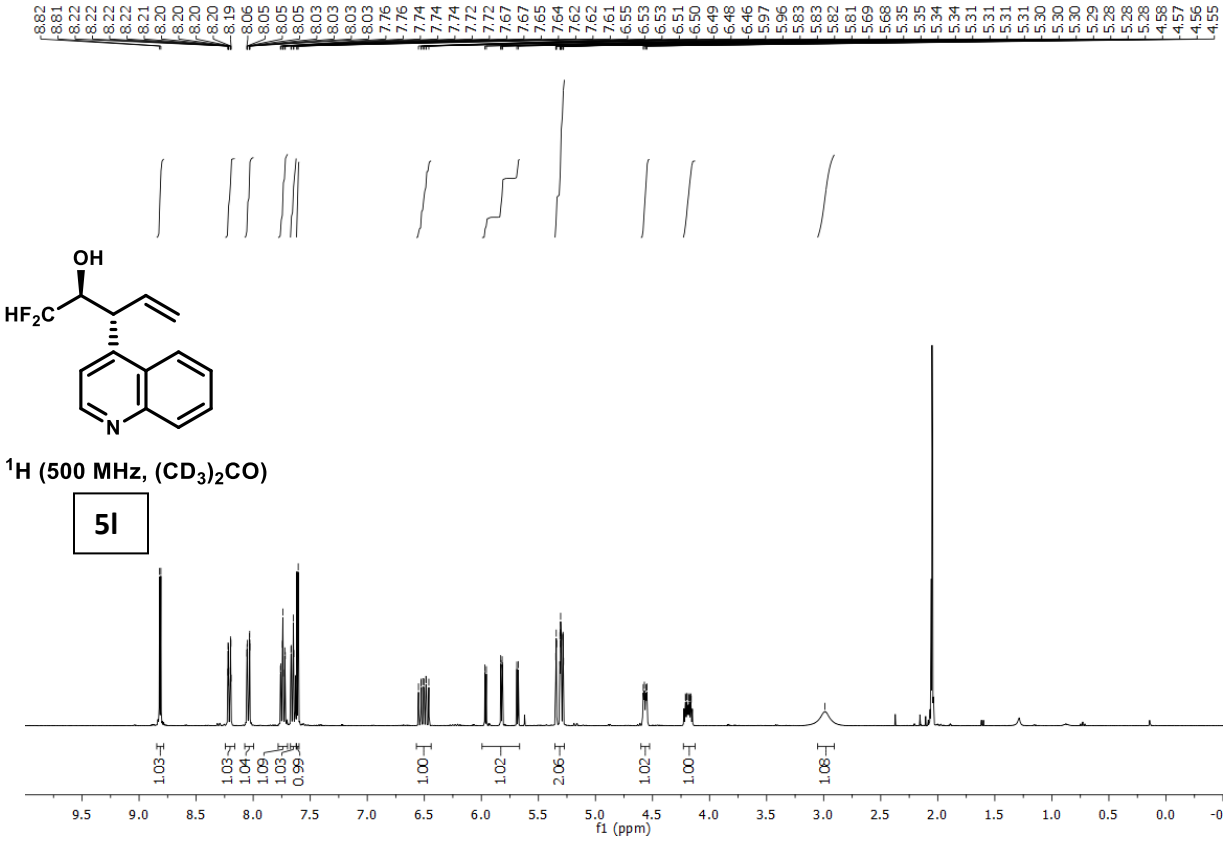
HRMS (ESI) Calculated for $C_{14}H_{13}F_2NO$ $[M+H]^+$ = 250.1038, Found 250.1036.

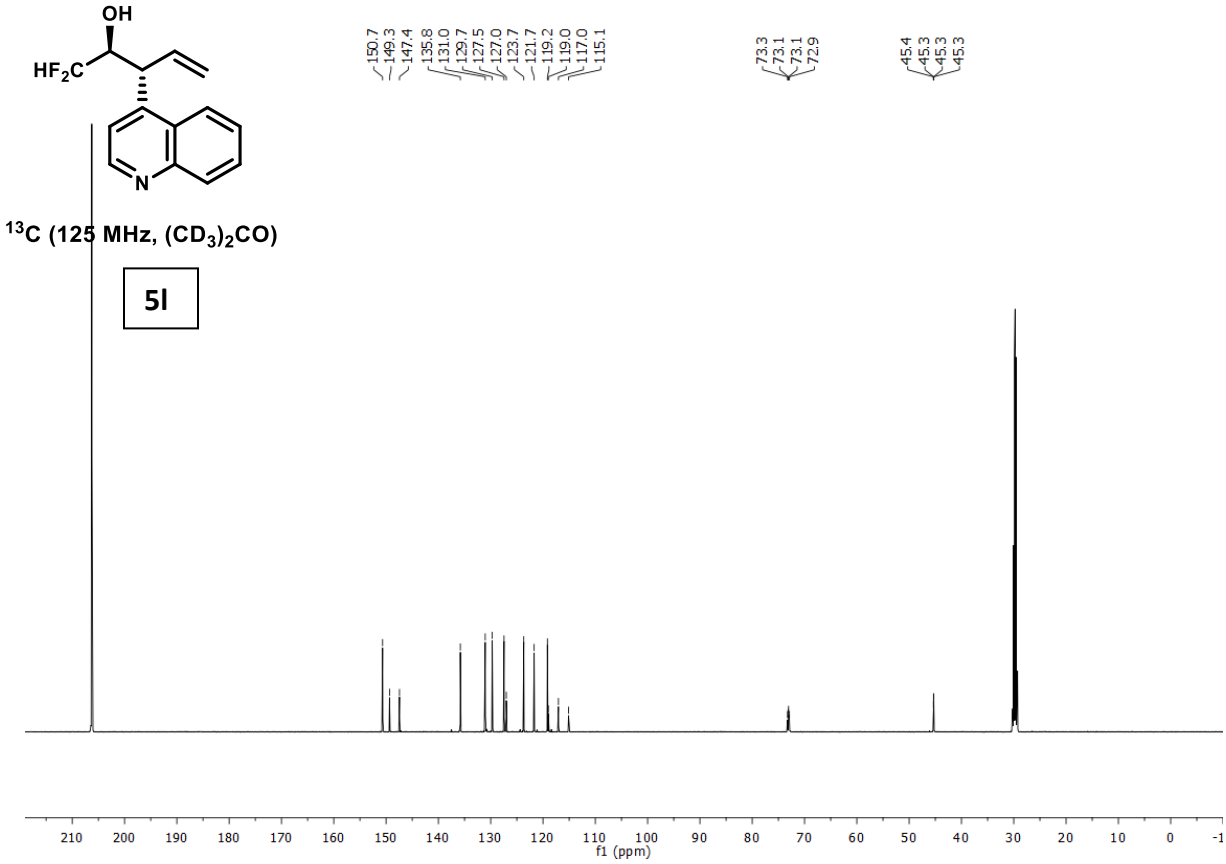
FTIR (neat) 3086, 2361, 1737, 1589, 1280, 1054, 927, 768, 660 cm^{-1}.

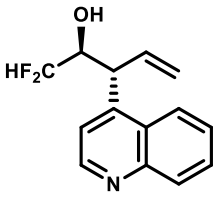
$[\alpha]_D^{33}$: –33.5 (*c* = 1.0, Acetone)

MP: 153-157˚C

HPLC: (Chiralcel AD-H column, hexanes:*i*-PrOH = 95:5, 1.0 mL/min, 210 nm), *ee* = 97%.

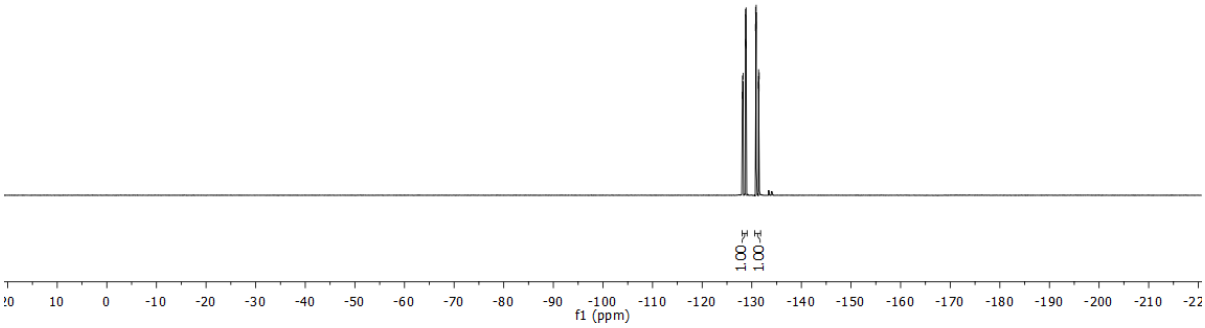

OH
HF2C
N
1H (500 MHz, (CD3)2CO)
5l
f1 (ppm)

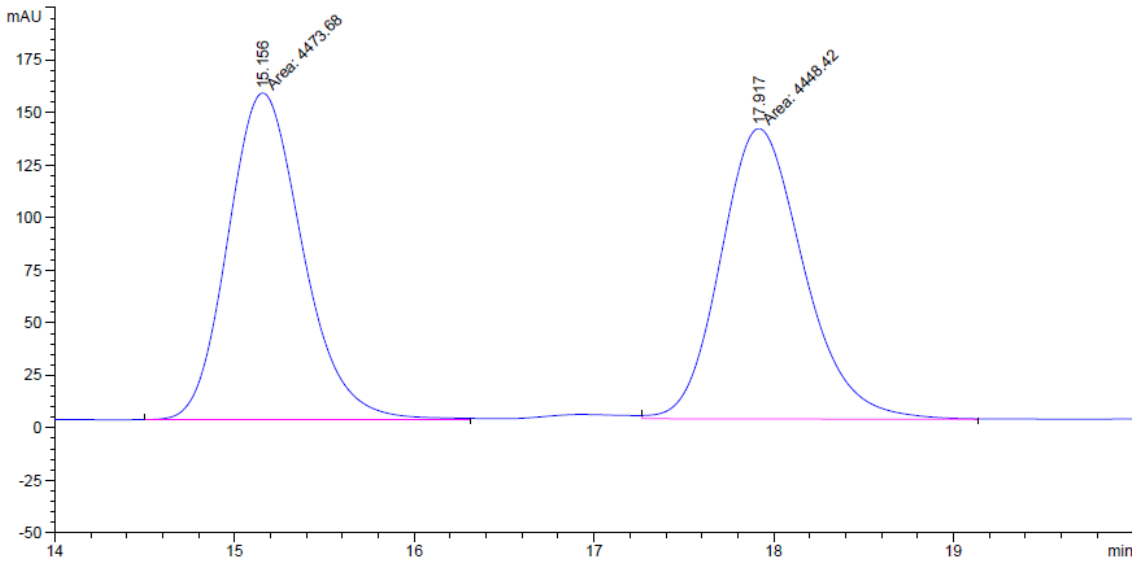

OH
HF2C
N
13C (125 MHz, (CD3)2CO)
5l
f1 (ppm)



^{19}F (471 MHz, $(CD_3)_2CO$)

5l





Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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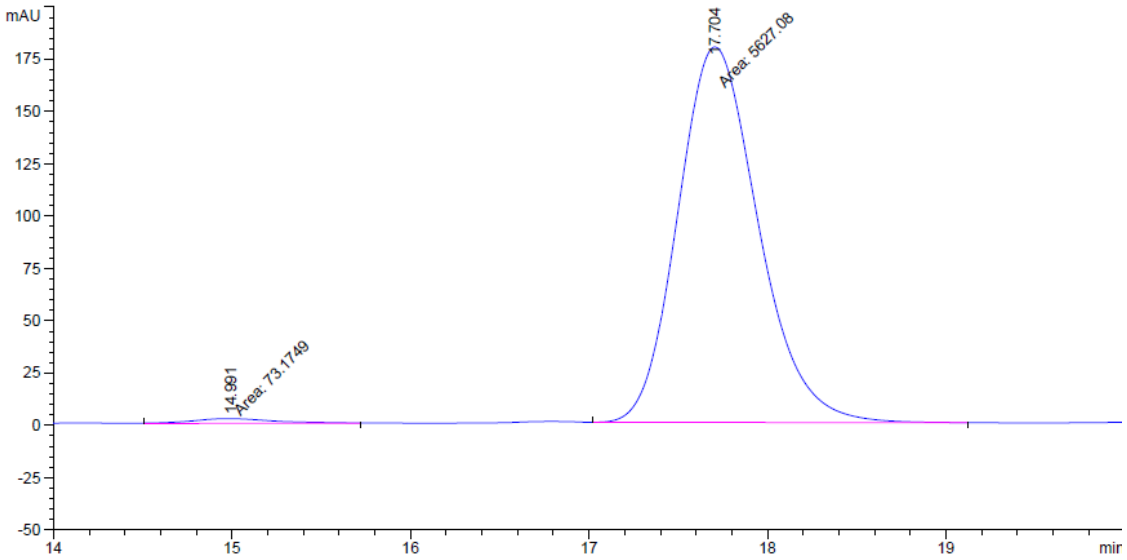
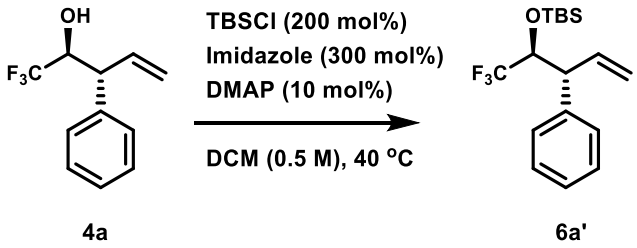
2	17.917	FM	0.5363	4448.41699	138.24548	49.8584



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.991	MM	0.5392	73.17490	2.26182	1.2837
2	17.704	MM	0.5226	5627.07617	179.45941	98.7163

Enantioselective Synthesis of Di- and Trifluoro-methylated Derivatives of *d*-Hyoscyamine 8a and 8b

tert-butyldimethyl(((2S,3R)-1,1,1-trifluoro-3-phenylpent-4-en-2-yl)oxy)silane (6a')



To a solution of alcohol **4a** (216.2 mg, 1.000 mmol, 100 mol%) in CH_2Cl_2 (2 mL) was added imidazole (204.2 mg, 3.000 mmol, 300 mol%), TBSCl (301.5 mg, 2.000 mmol, 200 mol%) and 4-(dimethylamino)pyridine (12.2 mg, 0.100 mmol, 10 mol%). The reaction was heated to 40 °C for 24 h. The contents were diluted with CH_2Cl_2 (2 mL) and washed with H_2O (2 mL). The aqueous layer was extracted with CH_2Cl_2 (2 x 2 mL), and the combined organic phases were washed with brine (2 mL), dried (Na_2SO_4), filtered and the solvent was removed *in vacuo*. The residue was subjected to flash chromatography on silica (Hexanes) to furnish the title compound **6a'** (239.8 mg, 0.726 mmol) in 73% yield as a clear oil.

TLC (SiO_2) R_f = 0.43 (hexanes).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34 – 7.29 (m, 2H), 7.25 – 7.21 (m, 3H), 6.41 – 6.24 (m, 1H), 5.25 (dd, *J* = 10.3, 1.6 Hz, 1H), 5.16 (d, *J* = 17.2 Hz, 1H), 4.23 (qd, *J* = 6.7, 3.7 Hz, 1H), 3.75 (dd, *J* = 9.1, 3.6 Hz, 1H), 0.85 (s, 9H), -0.02 (s, 3H), -0.36 (s, 3H).

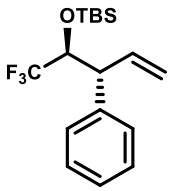
^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.2, 134.9, 128.6, 128.5, 127.0, 124.8 (q, *J* = 284.9 Hz), 118.2, 75.7 (q, *J* = 29.0 Hz), 50.6, 25.8, 18.3, -5.0 (q, *J* = 1.9 Hz), -5.2.

^{19}F NMR (471 MHz, $CDCl_3$): δ = -74.43 (d, *J* = 6.6 Hz).

HRMS (CI) Calculated for $C_{17}H_{25}F_3OSi$ $[M+H]^+$ = 331.1705, Found 331.1706.

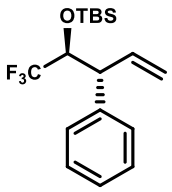
FTIR (neat) 2931, 2860, 1473, 1382, 1260, 1145, 1115, 1002, 927, 876, 829, 779, 700 cm^{-1}.

$[\alpha]_D^{26}$: –140.5 (*c* = 1.0, $CHCl_3$)



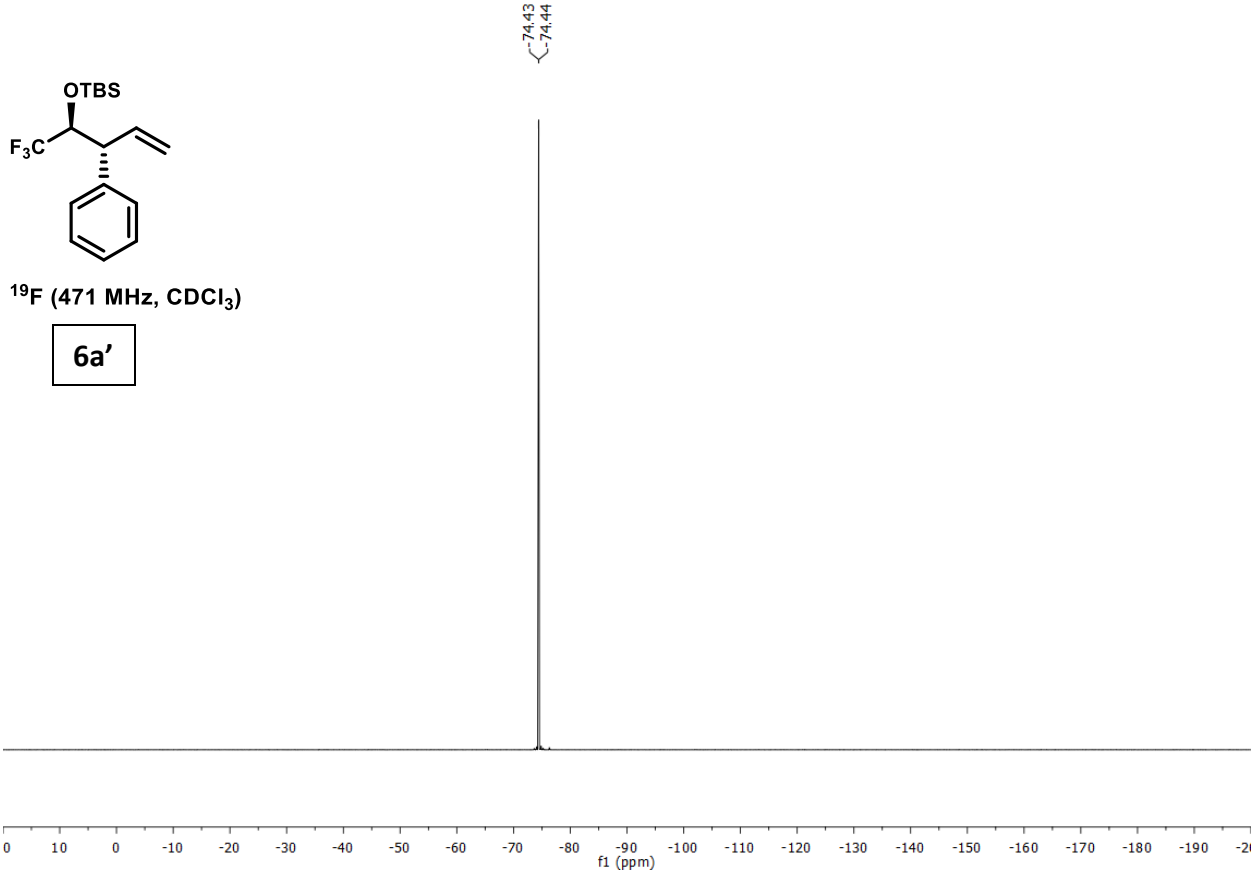
^{1}H (500 MHz, $CDCl_3$)

6a'



^{13}C (125 MHz, $CDCl_3$)

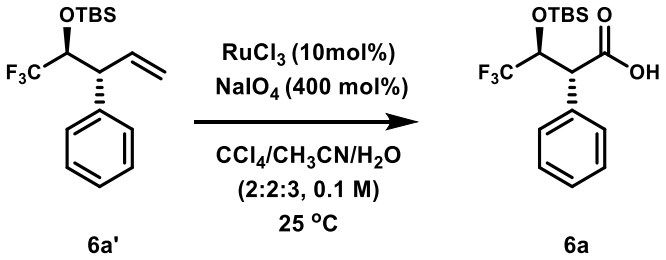
6a'



^{19}F (471 MHz, $CDCl_3$)

6a'

(2R,3S)-3-((tert-butyldimethylsilyl)oxy)-4,4,4-trifluoro-2-phenylbutanoic acid (6a)



6a' 6a

To a stirred solution of **6a'** (195.0 mg, 0.590 mmol, 100 mol%), in 1.7 mL CCl_4, 1.7 mL CH_3CN, and 2.5 mL H_2O was added $NaIO_4$ (504.8 mg, 2.360 mmol, 400 mol%). After all the $NaIO_4$ had dissolved, $RuCl_3.2H_2O$ (14.4 mg, 0.059 mmol, 10 mol%) was added, and the reaction mixture was stirred vigorously for 24 h at 25 °C. The contents were diluted with EtOAc (5 mL) and washed with H_2O (5 mL). The aqueous layer was extracted with EtOAc (2 x 5 mL), and the combined organic phases were washed with brine (5 mL), dried (Na_2SO_4), filtered and the solvent was removed *in vacuo*. The residue was subjected to flash chromatography on silica (Hex/EtOAc 5:1) to furnish the title compound **6a** (145.2 mg, 0.417 mmol) in 71% yield as a white solid.

TLC (SiO_2) R_f = 0.43 (hexanes/ethyl acetate = 3:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.40 – 7.29 (m, 5H), 4.60 (dq, *J* = 9.4, 6.1 Hz, 1H), 3.97 (d, *J* = 9.5 Hz, 1H), 0.85 (s, 9H), 0.14 (s, 3H), 0.08 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.7, 132.7, 128.9, 128.6, 124.3 (q, *J* = 284.1 Hz), 73.1 (q, *J* = 29.7 Hz), 55.1, 25.7, 18.3, -4.8 – -4.9 (m), -5.0.

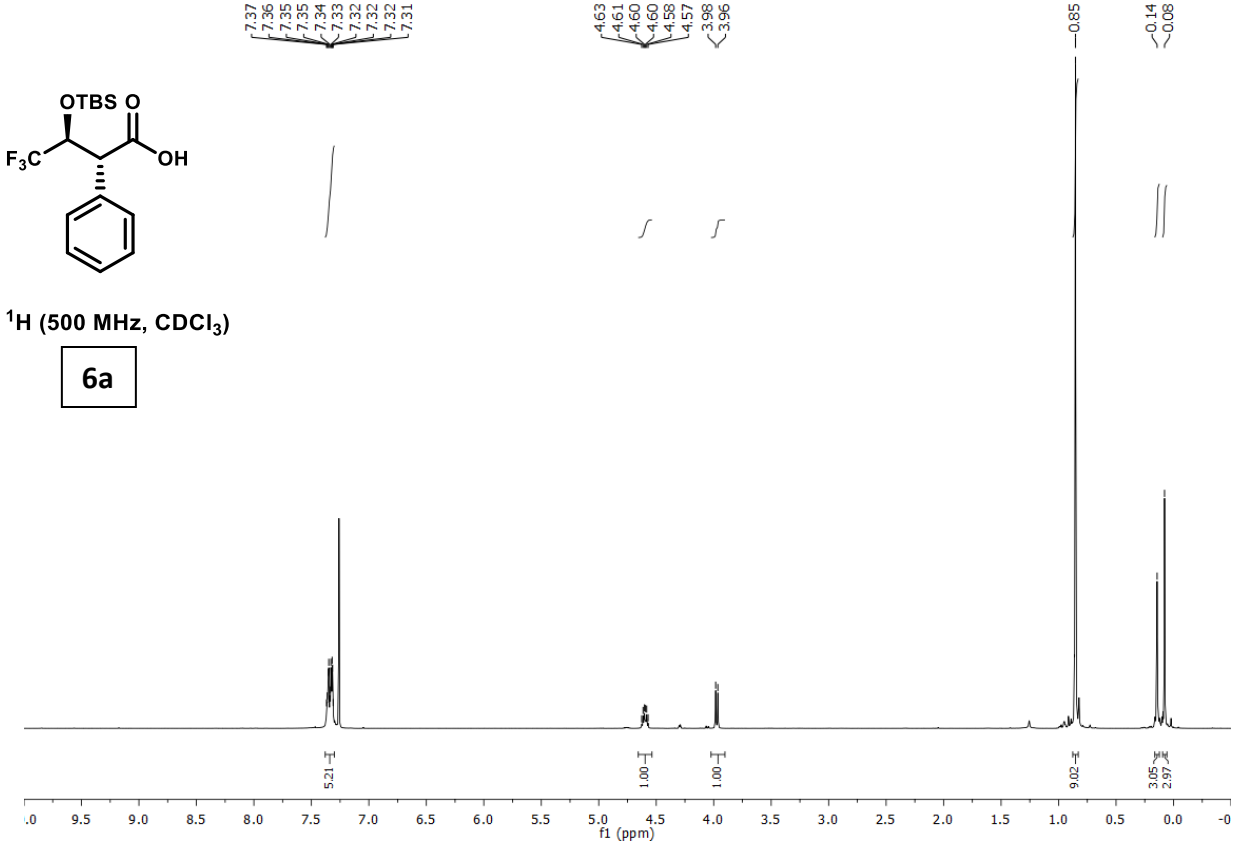
^{19}F NMR (471 MHz, $CDCl_3$): δ = -73.71 (d, *J* = 5.9 Hz).

HRMS (CI) Calculated for $C_{16}H_{23}F_3O_3Si$ $[M+H]^+$ = 349.1447, Found 349.1449.

FTIR (neat) 2932, 2861, 1709, 1363, 1265, 1174, 1131, 892, 834, 784 cm^{-1}.

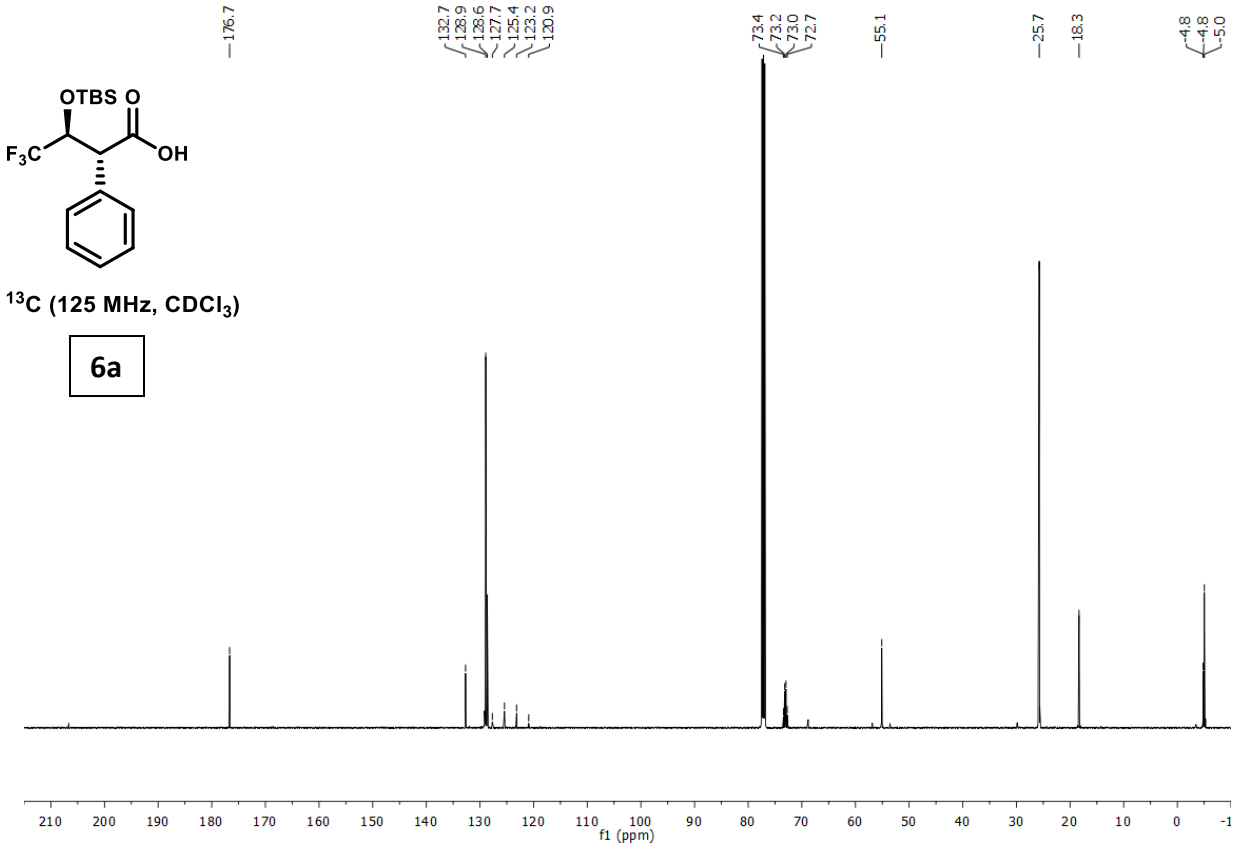
$[\alpha]_D^{28}$: –88.0 (*c* = 1.0, $CHCl_3$)

MP: 100-105˚C



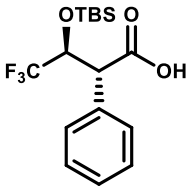
^{1}H (500 MHz, $CDCl_3$)

6a



^{13}C (125 MHz, $CDCl_3$)

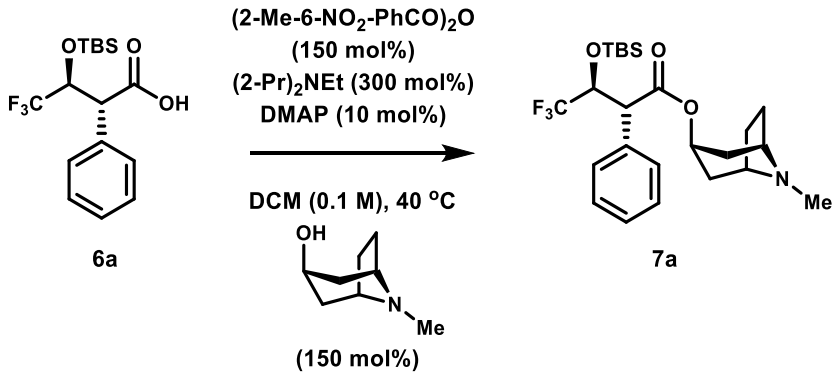
6a



^{19}F (471 MHz, $CDCl_3$)

6a

(1R,3r,5S)-8-methyl-8-azabicyclo[3.2.1]octan-3-yl (2R,3S)-3-((tert-butyldimethylsilyl)oxy)-4,4,4-trifluoro-2-phenylbutanoate (7a)



A vial equipped with a magnetic stir bar was charged with **6a** (19.9 mg, 0.0571 mmol, 100 mol%), 2-methyl-6-nitrobenzoic anhydride (29.5 mg, 0.0857 mmol, 150 mol%), 4-(dimethylamino)pyridine (0.7 mg, 0.0057 mmol, 10 mol%) and purged with argon. Freshly distilled CH_2Cl_2 (570 µL) and *N,N*-diisopropylethylamine (29.3 µL, 0.1713 mmol, 300 mol%), were added sequentially via syringe. The resulting mixture was stirred at 25 °C for 10 minutes. Tropine (12.1 mg, 0.0857 mmol, 150 mol%) was added in a single portion at 25 °C. The reaction was stirred at 40 °C for 20 h. The reaction mixture was concentrated, and the residue was subjected to flash chromatography on basic alumina (DCM/MeOH 98:2) to furnish the title compound **7a** (23.7 mg, 0.0503 mmol, 7:1 dr) in 88% yield as a clear oil.

TLC (Basic Alumina) R_f = 0.50 (DCM/MeOH = 95:5).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.37 – 7.27 (m, 5H), 4.98 (t, *J* = 5.4 Hz, 1H), 4.70 (dq, *J* = 8.3, 5.8 Hz, 1H), 3.81 (d, *J* = 8.5 Hz, 1H), 3.05 (dt, *J* = 6.9, 3.2 Hz, 1H), 2.94 (dt, *J* = 6.8, 3.0 Hz, 1H), 2.21 (s, 3H), 2.10 (dt, *J* = 14.2, 4.2 Hz, 1H), 2.02 (dt, *J* = 15.1, 4.5 Hz, 1H), 1.91 (qdd, *J* = 10.6, 9.0, 7.3, 4.0 Hz, 1H), 1.81 – 1.72 (m, 2H), 1.70 – 1.65 (m, 1H), 1.50 – 1.41 (m, 1H), 1.40 – 1.33 (m, 1H), 0.68 (s, 9H), 0.03 (s, 3H), -0.41 (s, 3H).

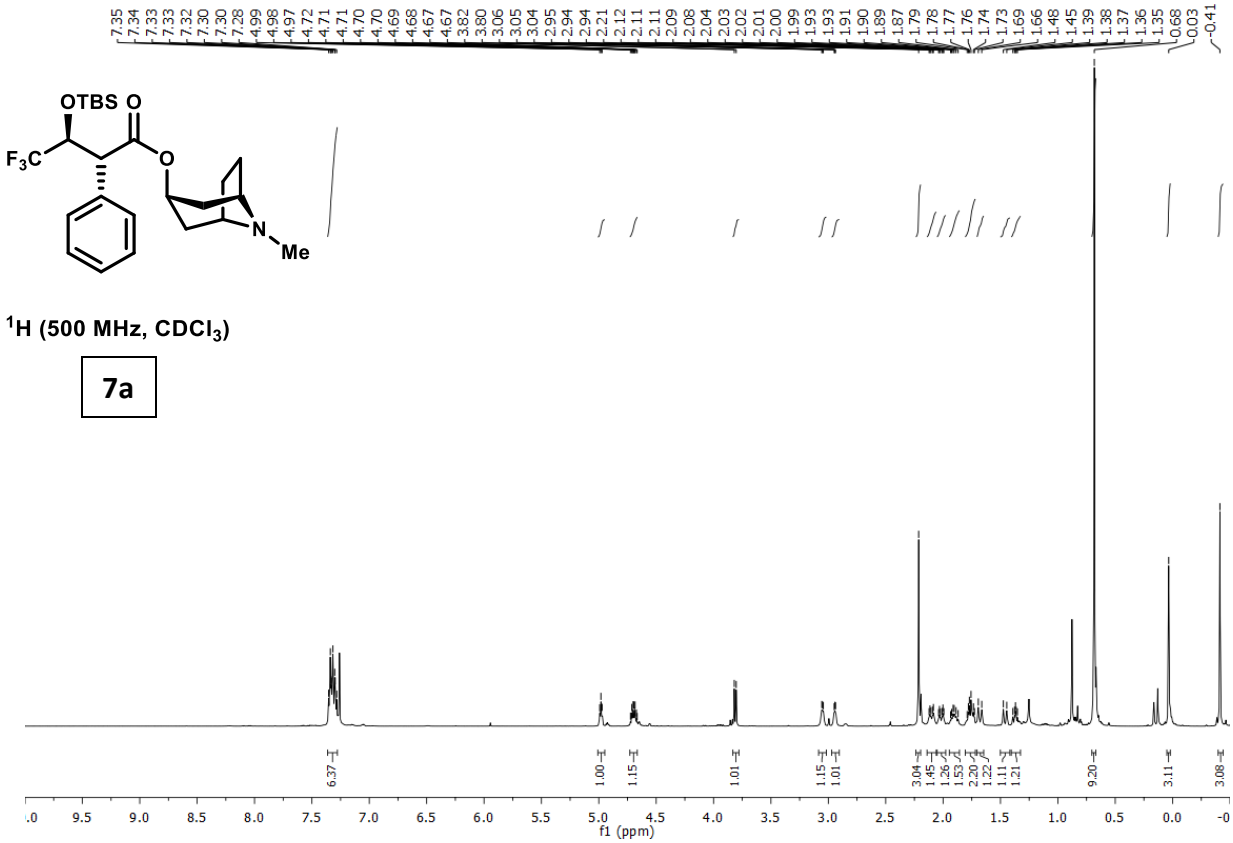
^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.1, 134.1, 129.8, 128.7, 128.2, 124.9 (q, *J* = 284.3 Hz), 72.3 (q, *J* = 30.3 Hz), 68.7, 59.8, 59.7, 53.4, 40.5, 36.4, 36.3, 25.5, 25.4, 25.2, 18.1, -5.2 – -5.4 (m), -5.5.

^{19}F NMR (471 MHz, $CDCl_3$): δ = -76.08 (d, *J* = 5.8 Hz).

HRMS (APPI) Calculated for $C_{24}H_{36}F_3NO_3Si$ $[M+H]^+$ = 472.2489, Found 472.2498.

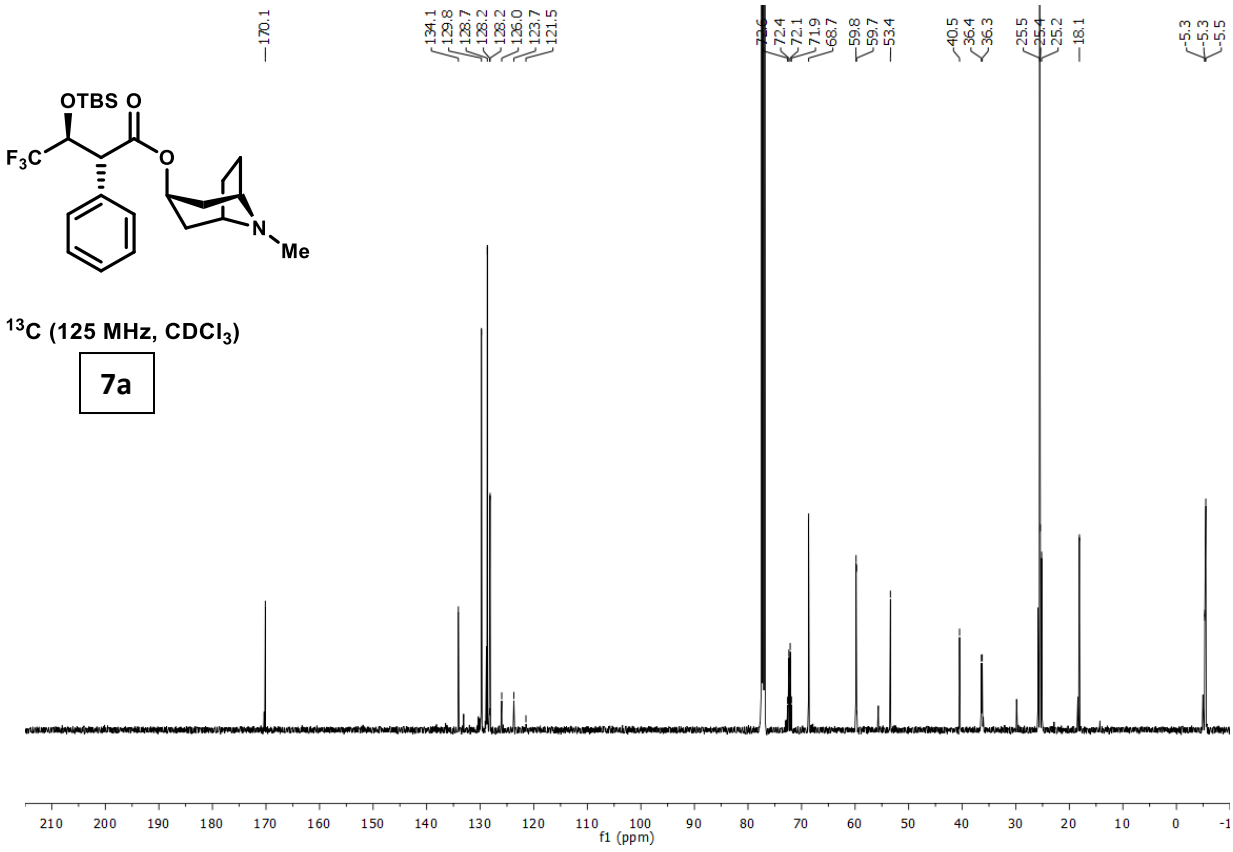
FTIR (neat) 2931, 2859, 1731, 1473, 1269, 1168, 1128, 1034, 840, 782, 700 cm^{-1}.

$[\alpha]_D^{26}$: –31.5 (*c* = 1.0, $CHCl_3$)



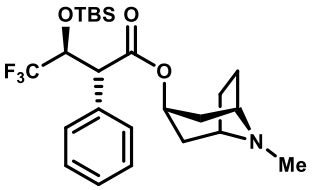
^{1}H (500 MHz, $CDCl_3$)

7a



^{13}C (125 MHz, $CDCl_3$)

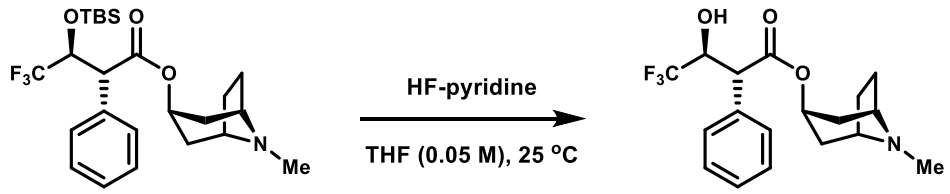
7a



^{19}F (471 MHz, $CDCl_3$)

7a

(1R,3r,5S)-8-methyl-8-azabicyclo[3.2.1]octan-3-yl (2R,3S)-4,4,4-trifluoro-3-hydroxy-2-phenylbutanoate (8a)



7a **8a**

To a polyethylene tube charged with **7a** (10.0 mg, 0.0212 mmol, 100 mol%) in THF (420 µL) was added HF-pyridine (100 µL) dropwise at 25 °C. The resulting mixture was stirred at 25 ºC for 24 h. The reaction was diluted with CH_2Cl_2 (3 mL) and quenched by careful addition of saturated $NaHCO_3$ (2 mL). The reaction mixture was extracted with CH_2Cl_2 (2 x 2 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was subjected to flash chromatography on basic alumina (DCM/MeOH 95:5) to furnish the title compound **8a** (6.7 mg, 0.0188 mmol) in 89% yield as a clear oil.

TLC (Basic Alumina) R_f = 0.30 (DCM/MeOH = 95:5).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.40 – 7.32 (m, 5H), 4.99 (t, *J* = 5.3 Hz, 1H), 4.75 (p, *J* = 6.5 Hz, 1H), 3.87 (d, *J* = 6.9 Hz, 1H), 3.14 – 3.05 (m, 1H), 3.01 – 2.92 (m, 1H), 2.22 (s, 3H), 2.20 – 2.12 (m, 1H), 2.12 – 2.03 (m, 1H), 1.96 – 1.84 (m, 1H), 1.75 (dq, *J* = 10.4, 6.8, 5.0 Hz, 2H), 1.68 (d, *J* = 15.5 Hz, 1H), 1.46 (d, *J* = 15.1 Hz, 1H), 1.24 (ddd, *J* = 13.3, 9.3, 4.6 Hz, 1H).

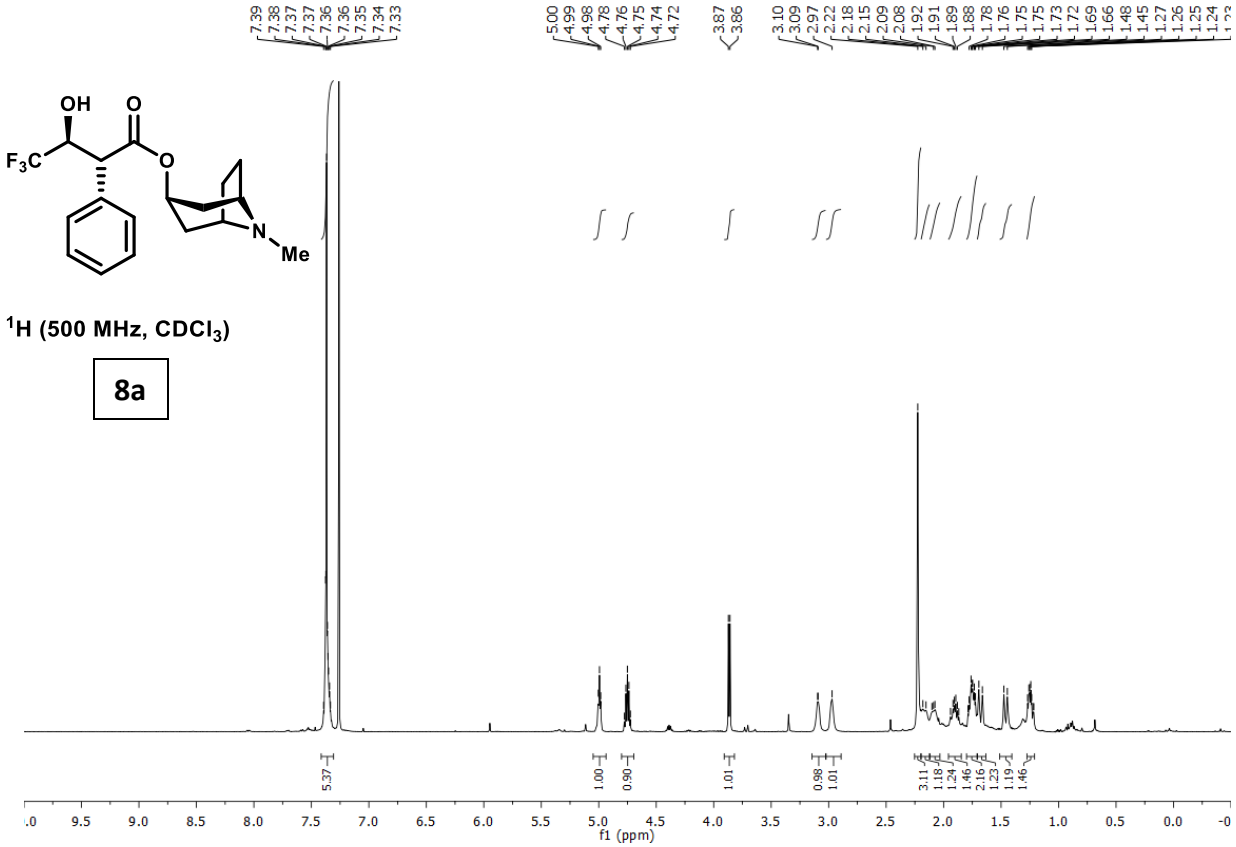
^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.4, 133.0, 129.4, 129.1, 128.5, 124.7 (q, *J* = 282.3 Hz), 70.4 (q, *J* = 30.7 Hz), 68.9, 59.8, 59.7, 52.2, 40.3, 36.2, 36.0, 25.4, 25.0.

^{19}F NMR (471 MHz, $CDCl_3$): δ = -76.92 (d, *J* = 6.4 Hz).

HRMS (ESI) Calculated for $C_{18}H_{22}F_3NO_3$ $[M+H]^+$ = 358.1625, Found 358.1628.

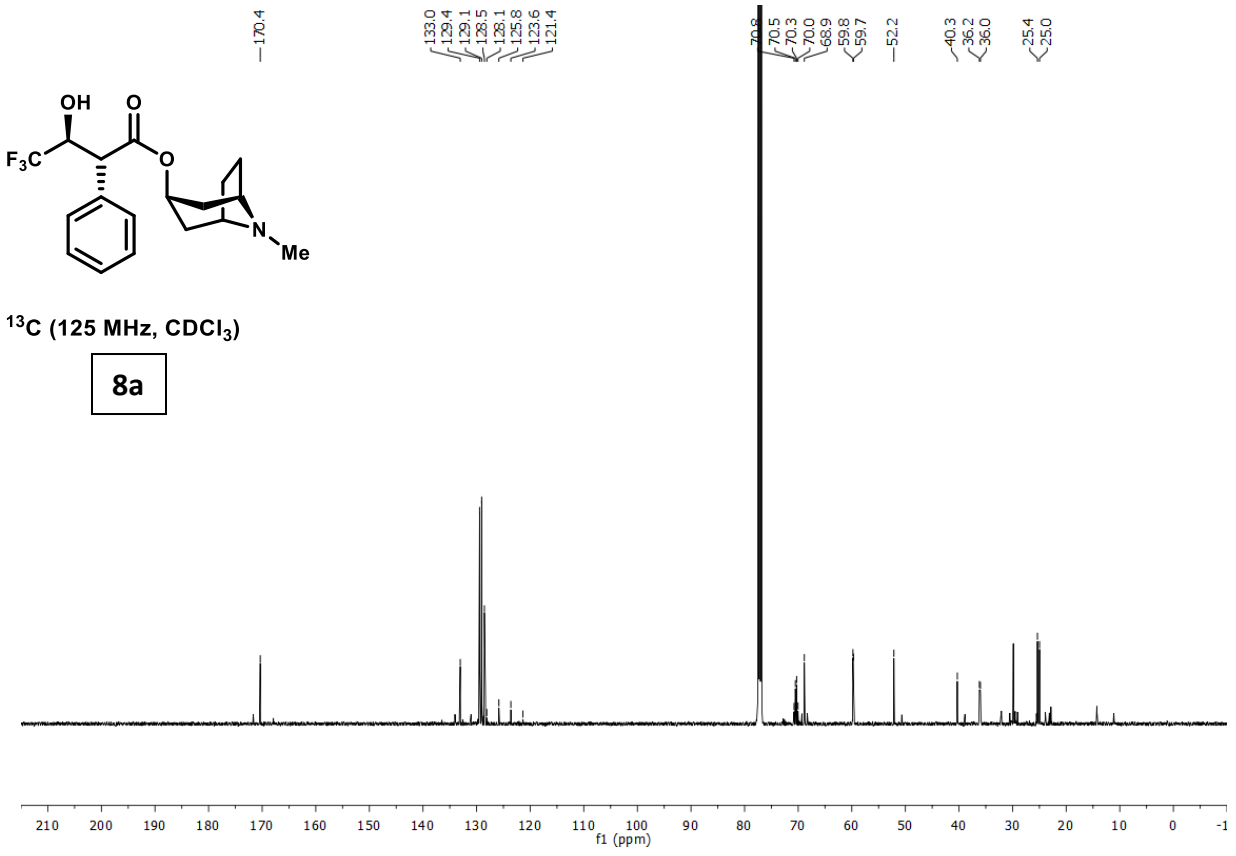
FTIR (neat) 2926, 2853, 1732, 1456, 1269, 1163, 1130, 1032, 700 cm^{-1}.

$[\alpha]_D^{35}$: –20.0 (*c* = 0.5, $CHCl_3$)



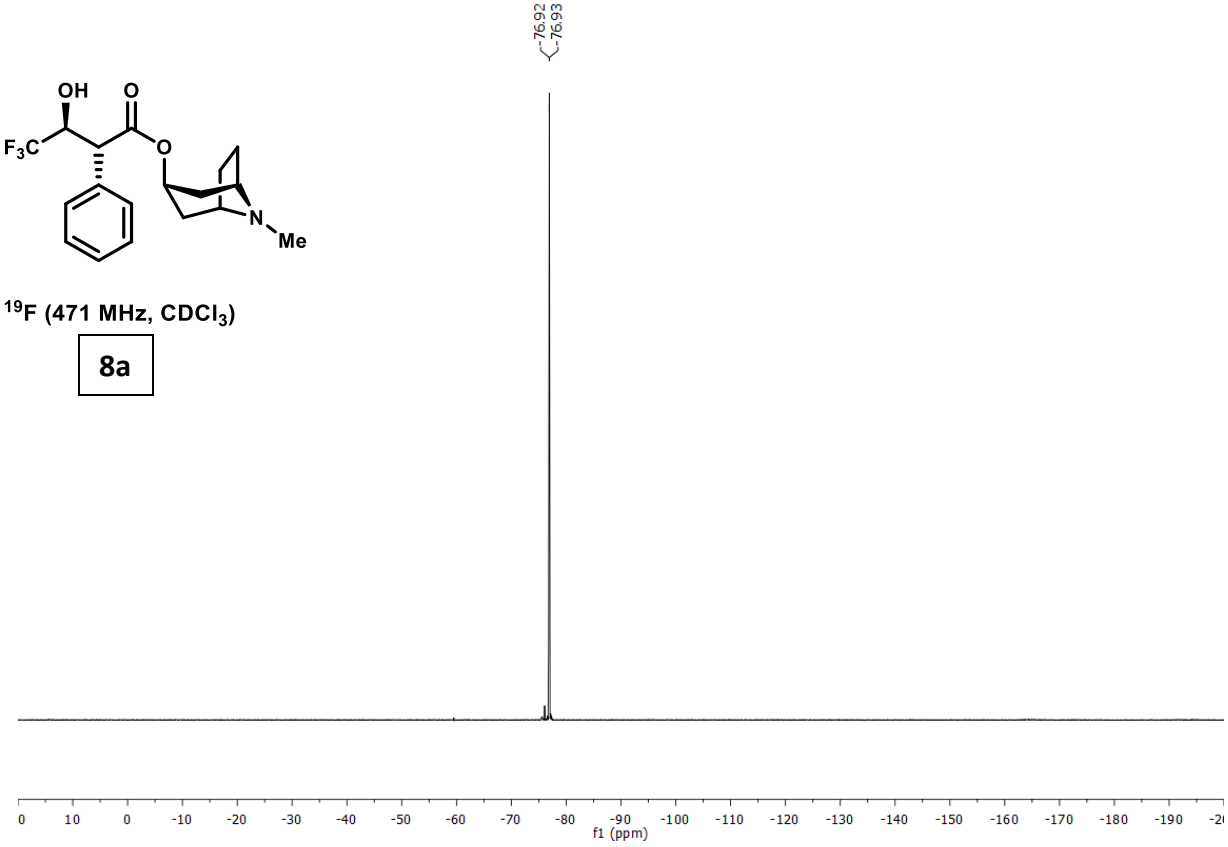
^{1}H (500 MHz, $CDCl_3$)

8a



^{13}C (125 MHz, $CDCl_3$)

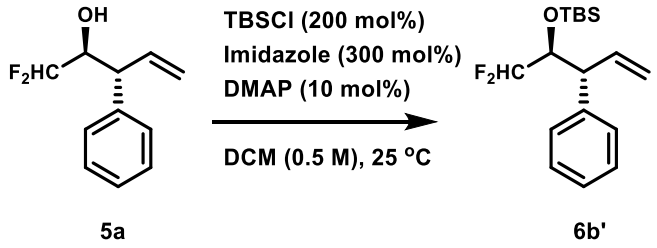
8a



^{19}F (471 MHz, $CDCl_3$)

8a

tert-butyldimethyl(((2S,3R)-1,1,1-trifluoro-3-phenylpent-4-en-2-yl)oxy)silane (6b')



To a solution of alcohol **5a** (99.1 mg, 0.500 mmol, 100 mol%) in CH_2Cl_2 (1 mL) was added imidazole (102.1 mg, 1.500 mmol, 300 mol%), TBSCl (150.7 mg, 1.000 mmol, 200 mol%) and 4-(dimethylamino)pyridine (6.1 mg, 0.050 mmol, 10 mol%). The reaction was allowed to stir at 25 °C for 24 h. The contents were diluted with CH_2Cl_2 (1 mL) and washed with H_2O (1 mL). The aqueous layer was extracted with CH_2Cl_2 (2 x 1 mL), and the combined organic phases were washed with brine (1 mL), dried (Na_2SO_4), filtered and the solvent was removed *in vacuo*. The residue was subjected to flash chromatography on silica (Hexanes) to furnish the title compound **6b'** (137.0 mg, 0.438 mmol) in 88% yield as a clear oil.

TLC (SiO_2) R_f = 0.43 (hexanes).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35 – 7.27 (m, 2H), 7.25 – 7.20 (m, 3H), 6.29 (dt, *J* = 17.2, 9.8 Hz, 1H), 5.49 (ddd, *J* = 56.7, 55.1, 5.3 Hz, 1H), 5.27 (dd, *J* = 10.3, 1.7 Hz, 1H), 5.20 (ddd, *J* = 17.2, 1.8, 0.8 Hz, 1H), 3.98 (dq, *J* = 13.6, 4.6 Hz, 1H), 3.63 (dt, *J* = 9.0, 3.2 Hz, 1H), 0.82 (s, 9H), -0.03 (d, *J* = 1.9 Hz, 3H), -0.36 (s, 3H).

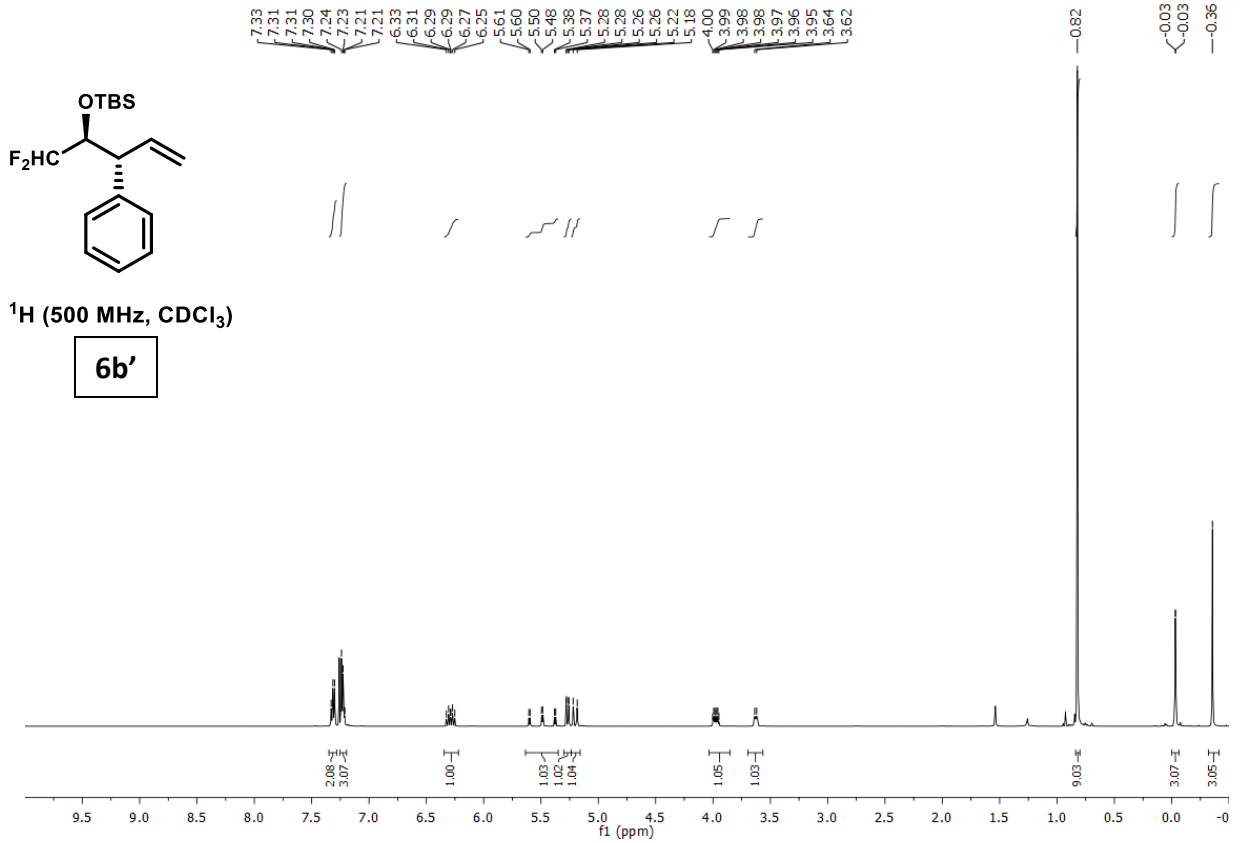
^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.8, 135.4, 128.7, 128.5, 127.0, 118.7, 116.0 (dd, *J* = 245.7, 243.8 Hz), 76.0 (dd, *J* = 25.3, 20.3 Hz), 51.2 (dd, *J* = 5.6, 2.2 Hz), 25.9, 18.3, -4.7 (d, *J* = 3.6 Hz), -5.2.

^{19}F NMR (471 MHz, $CDCl_3$): δ = -127.12 (ddd, *J* = 284.9, 55.5, 5.1 Hz), -129.83 (ddd, *J* = 283.5, 56.7, 13.5 Hz).

HRMS (ESI) Calculated for $C_{17}H_{26}F_2OSi$ $[M+H]^+$ = 313.1799, Found 313.1806.

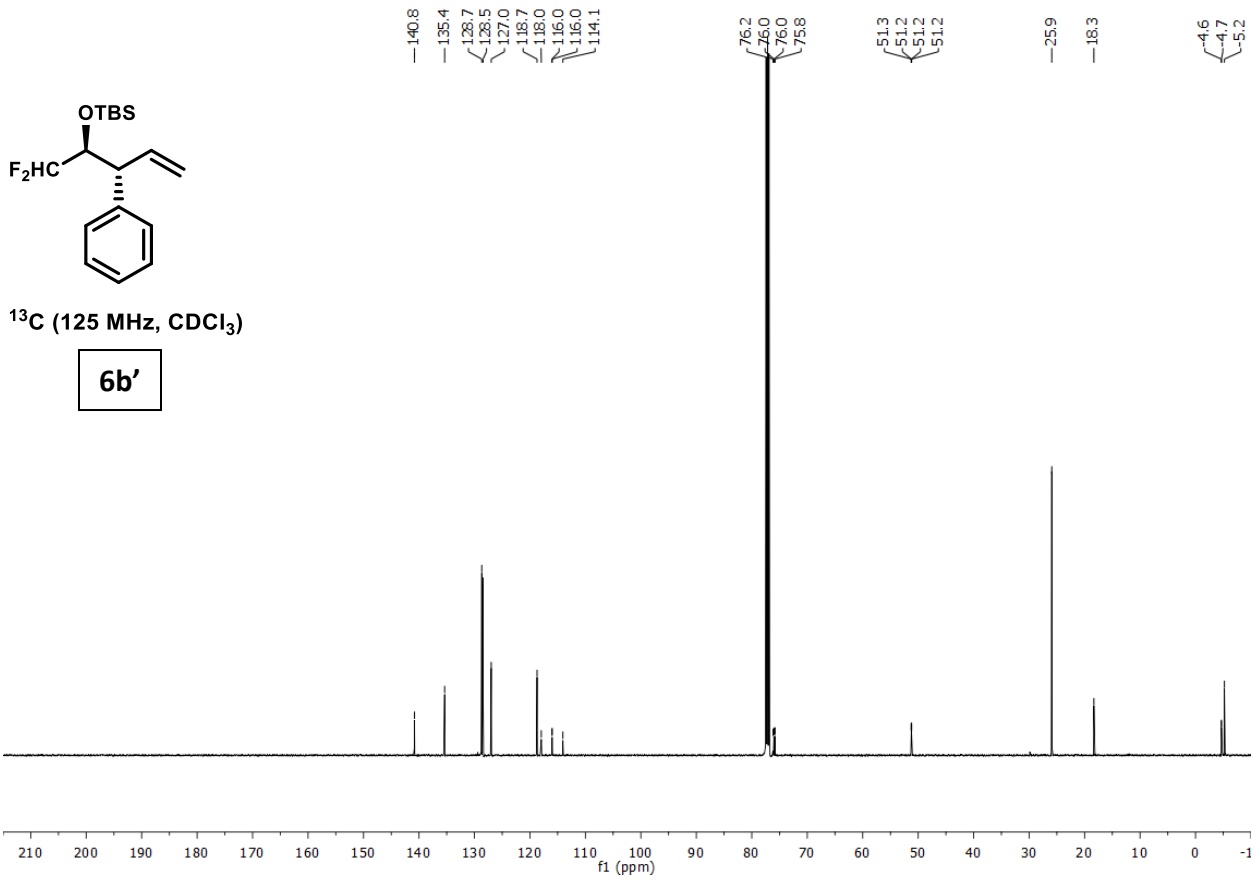
FTIR (neat) 2955, 2930, 2858, 1473, 1256, 1138, 1117, 1069, 1005, 927, 838, 779, 701 cm^{-1}.

$[\alpha]_D^{28}$: –133.3 (*c* = 1.0, $CHCl_3$)



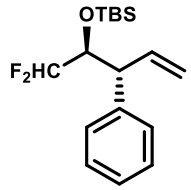
^{1}H (500 MHz, $CDCl_3$)

6b'



^{13}C (125 MHz, $CDCl_3$)

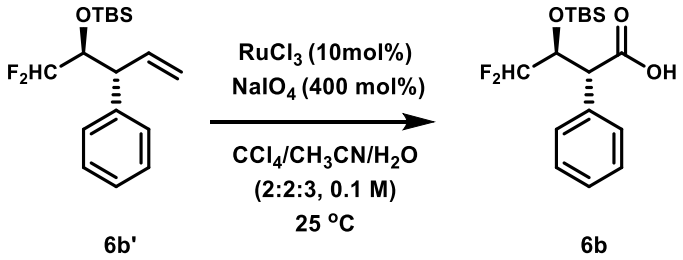
6b'



^{19}F (471 MHz, $CDCl_3$)

6b'

(2R,3S)-3-((tert-butyldimethylsilyl)oxy)-4,4-difluoro-2-phenylbutanoic acid (6b)



To a stirred solution of **6b'** (109.4 mg, 0.350 mmol, 100 mol%), in 1.0 mL CCl_4, 1.0 mL CH_3CN, and 1.5 mL H_2O was added $NaIO_4$ (299.5 mg, 1.400 mmol, 400 mol%). After all the $NaIO_4$ had dissolved, $RuCl_3.2H_2O$ (8.5 mg, 0.035 mmol, 10 mol%) was added, and the reaction mixture was stirred vigorously for 24 h at 25 °C. The contents were diluted with EtOAc (3 mL) and washed with H_2O (3 mL). The aqueous layer was extracted with EtOAc (2 x 3 mL), and the combined organic phases were washed with brine (3 mL), dried (Na_2SO_4), filtered and the solvent was removed *in vacuo*. The residue was subjected to flash chromatography on silica (Hex/EtOAc 5:1) to furnish the title compound **6b** (85.4 mg, 0.258 mmol) in 74% yield as a white solid.

TLC (SiO_2) R_f = 0.43 (hexanes/ethyl acetate = 3:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.40 – 7.28 (m, 5H), 5.30 (td, *J* = 54.4, 1.5 Hz, 1H), 4.43 (dddd, *J* = 19.1, 9.7, 6.0, 1.5 Hz, 1H), 3.88 (d, *J* = 9.6 Hz, 1H), 0.86 (s, 9H), 0.13 (s, 3H), 0.07 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.6, 133.1, 129.3, 128.8, 128.7, 114.2 (dd, *J* = 246.0, 242.6 Hz), 73.7 – 73.3 (m), 54.7, 25.9, 18.4, -4.5 (d, *J* = 3.7 Hz), -5.2.

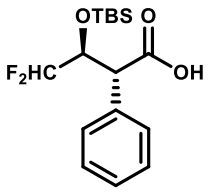
^{19}F NMR (471 MHz, $CDCl_3$): δ = -127.22 (ddd, *J* = 284.4, 54.5, 4.6 Hz), -135.17 (ddd, *J* = 284.2, 54.4, 19.1 Hz).

HRMS (ESI) Calculated for $C_{16}H_{24}F_2O_3Si$ $[M+Na]^+$ = 353.1355, Found 353.1361.

FTIR (neat) 2955, 2930, 2859, 1714, 1254, 1167,1115, 1065, 935, 837, 780, 699 cm^{-1}.

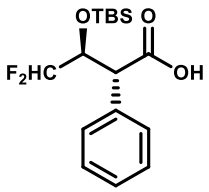
$[\alpha]_D^{29}$: –95.5 (*c* = 1.0, $CHCl_3$)

MP: 98-103˚C



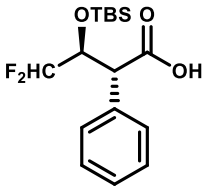
^{1}H (500 MHz, $CDCl_3$)

6b



^{13}C (125 MHz, $CDCl_3$)

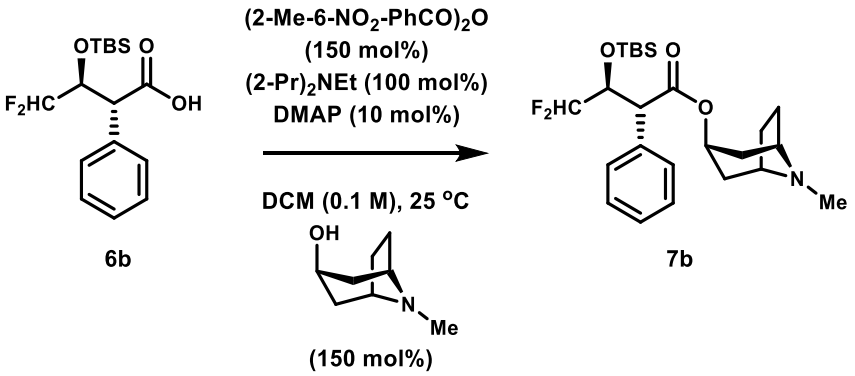
6b



^{19}F (471 MHz, $CDCl_3$)

6b

(1R,3r,5S)-8-methyl-8-azabicyclo[3.2.1]octan-3-yl (2R,3S)-3-((tert-butyldimethylsilyl)oxy)-4,4-difluoro-2-phenylbutanoate (7b)



A vial equipped with a magnetic stir bar was charged with **6b** (10.0 mg, 0.0303 mmol, 100 mol%), 2-methyl-6-nitrobenzoic anhydride (15.7 mg, 0.0455 mmol, 150 mol%), 4-(dimethylamino)pyridine (0.4 mg, 0.0030 mmol, 10 mol%) and purged with argon. Freshly distilled CH_2Cl_2 (300 µL) and *N,N*-diisopropylethylamine (5.2 µL, 0.0303 mmol, 100 mol%), were added sequentially via syringe. The resulting mixture was stirred at 25 °C for 10 minutes. Tropine (6.4 mg, 0.0455 mmol, 150 mol%) was added in a single portion at 25 °C. The reaction was stirred at 25 °C for 20 h. The reaction mixture was concentrated, and the residue was subjected to flash chromatography on basic alumina (DCM/MeOH 98:2) to furnish the title compound **7b** (12.1 mg, 0.0267 mmol, 4:1 dr) in 88% yield as a clear oil.

TLC (Basic Alumina) R_f = 0.50 (DCM/MeOH = 95:5).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.36 – 7.30 (m, 5H), 5.59 (td, *J* = 55.8, 4.0 Hz, 1H), 4.99 (t, *J* = 5.4 Hz, 1H), 4.53 – 4.43 (m, 1H), 3.75 (d, *J* = 7.4 Hz, 1H), 3.08 – 3.02 (m, 1H), 2.98 – 2.92 (m, 1H), 2.22 (s, 3H), 2.14 (d, *J* = 14.5 Hz, 1H), 2.05 (d, *J* = 15.6 Hz, 1H), 1.88 – 1.80 (m, 1H), 1.75 – 1.62 (m, 3H), 1.47 (d, *J* = 15.1 Hz, 1H), 1.23 – 1.17 (m, 1H), 0.73 (s, 9H), 0.03 (s, 3H), -0.29 (s, 3H).

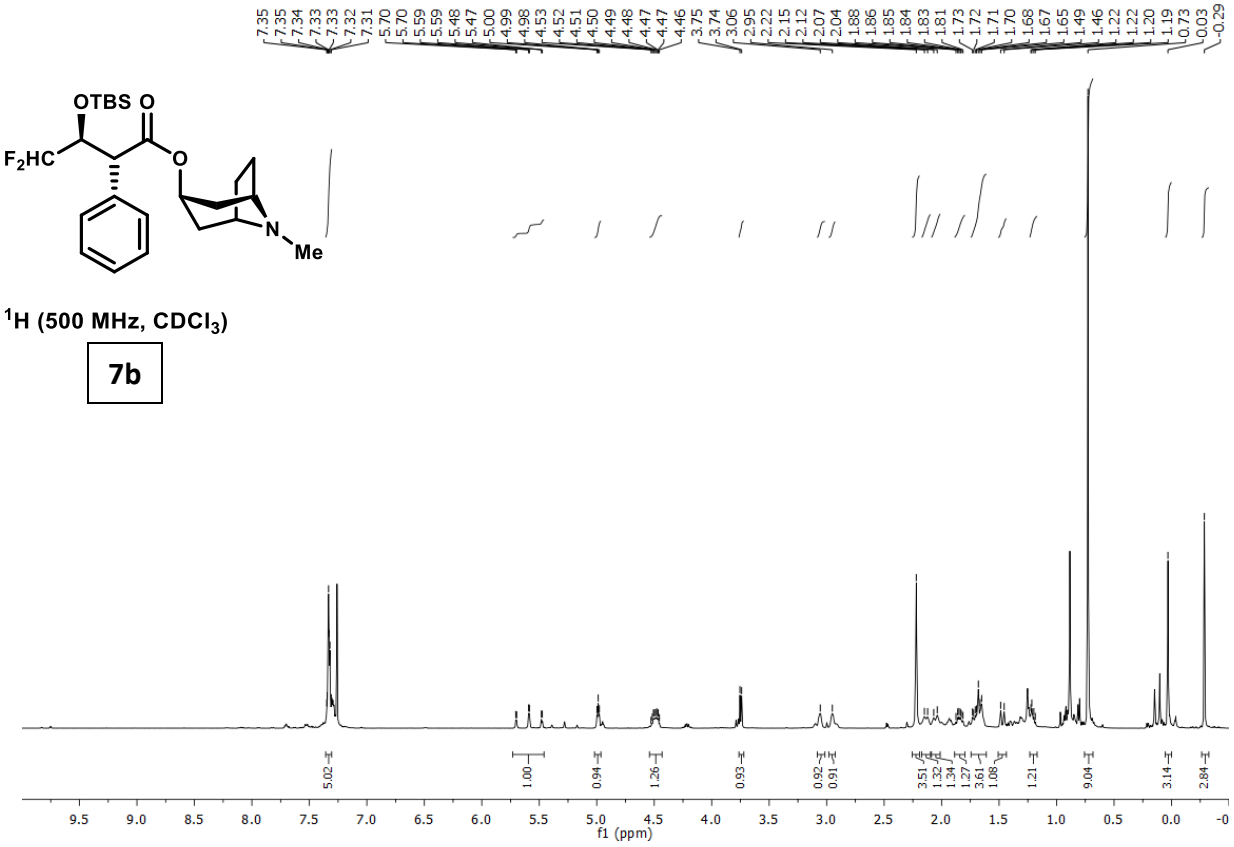
^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.6, 134.7, 129.9, 128.6, 128.0, 115.7 (t, *J* = 245.4 Hz), 73.1 (t, *J* = 22.9 Hz), 68.4, 59.9, 59.8, 53.7 – 53.5 (m), 40.4, 36.4, 36.1, 25.7, 25.4, 25.0, 18.2, -4.9, -5.4.

^{19}F NMR (471 MHz, $CDCl_3$): δ = -126.38 (ddd, *J* = 285.8, 55.2, 4.6 Hz), -130.11 (ddd, *J* = 285.7, 56.3, 14.4 Hz).

HRMS (APPI) Calculated for $C_{24}H_{37}F_2NO_3Si$ $[M+H]^+$ = 454.2584, Found 454.2588.

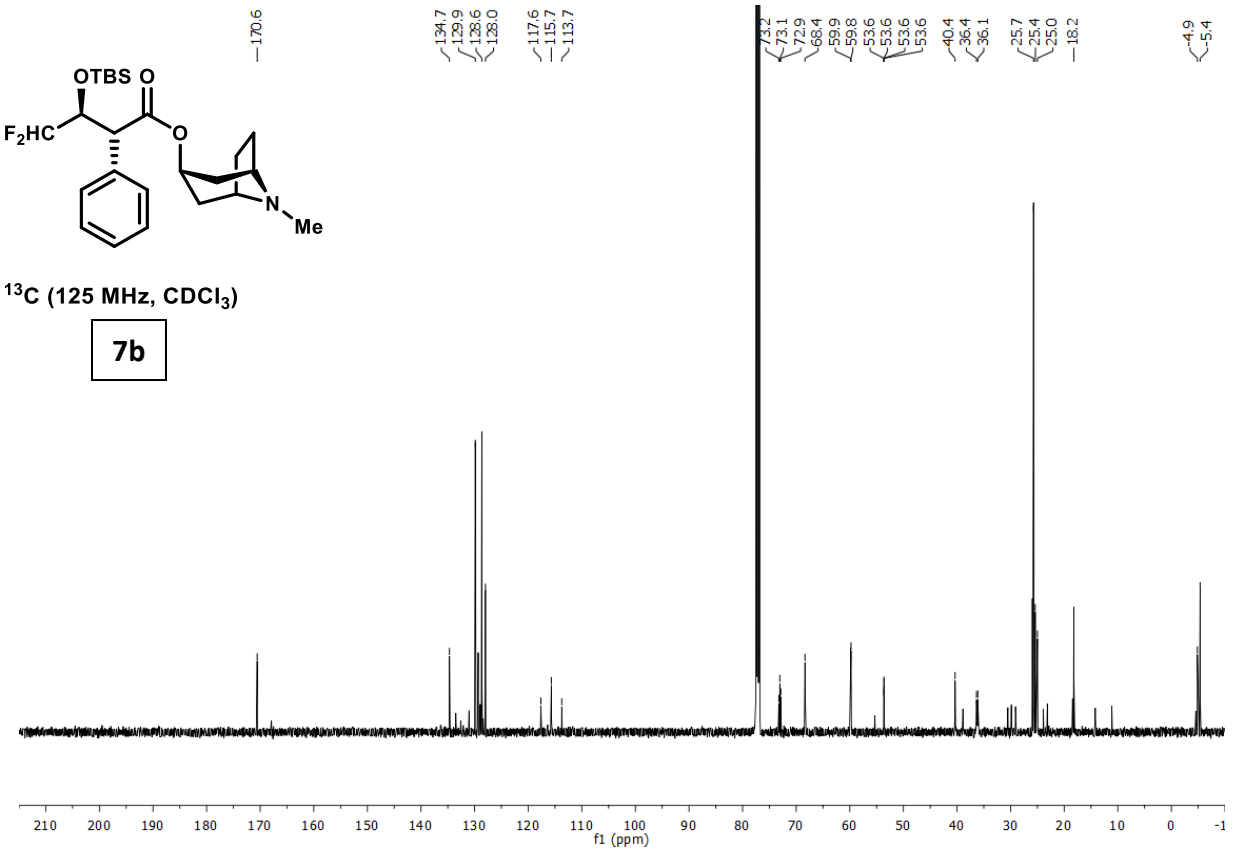
FTIR (neat) 2929, 2856, 1725, 1472, 1254, 1150, 1119, 1064, 1034, 934, 838, 780, 700 cm^{-1}.

$[\alpha]_D^{29}$: –20.5 (*c* = 1.0, $CHCl_3$)



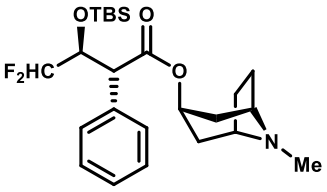
^{1}H (500 MHz, $CDCl_3$)

7b



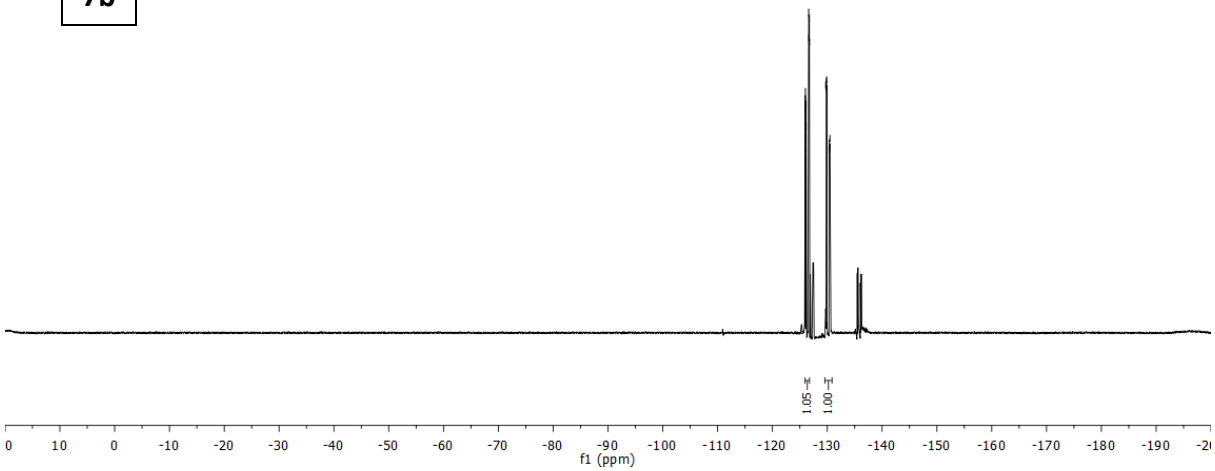
^{13}C (125 MHz, $CDCl_3$)

7b

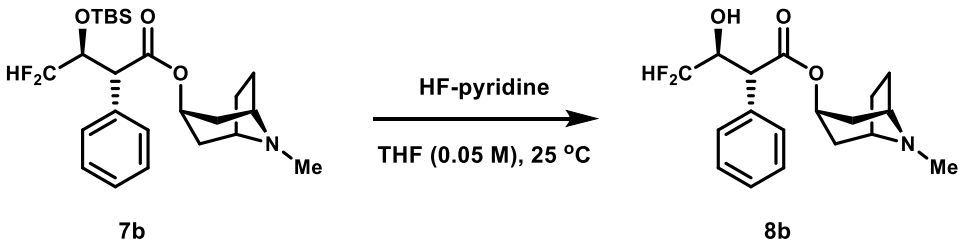


^{19}F (471 MHz, $CDCl_3$)

7b



(1R,3r,5S)-8-methyl-8-azabicyclo[3.2.1]octan-3-yl (2R,3S)-4,4-difluoro-3-hydroxy-2-phenylbutanoate (8b)



7b **8b**

To a polyethylene tube charged with **7b** (10.0 mg, 0.0220 mmol, 100 mol%) in THF (440 μL) was added HF-pyridine (100 μL) dropwise at 25 °C. The resulting mixture was stirred at 25 ºC for 24 h. The reaction was diluted with CH_2Cl_2 (3 mL) and quenched by careful addition of saturated $NaHCO_3$ (2 mL). The reaction mixture was extracted with CH_2Cl_2 (2 x 2 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was subjected to flash chromatography on basic alumina (DCM/MeOH 95:5) to furnish the title compound **8b** (6.0 mg, 0.0177 mmol) in 80% yield as a clear oil.

TLC (Basic Alumina) R_f = 0.40 (DCM/MeOH = 95:5).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.42 – 7.30 (m, 5H), 5.57 (td, *J* = 55.7, 4.9 Hz, 1H), 5.04 (t, *J* = 5.4 Hz, 1H), 4.53 – 4.45 (m, 1H), 3.81 (d, *J* = 6.0 Hz, 1H), 3.17 – 3.09 (m, 1H), 3.05 – 2.96 (m, 1H), 2.26 (s, 3H), 2.22 – 2.14 (m, 1H), 2.31 – 2.23 (m, 1H), 1.93 – 1.84 (m, 1H), 1.78 – 1.63 (m, 3H), 1.49 (d, *J* = 15.2 Hz, 1H), 1.15 – 1.04 (m, 1H).

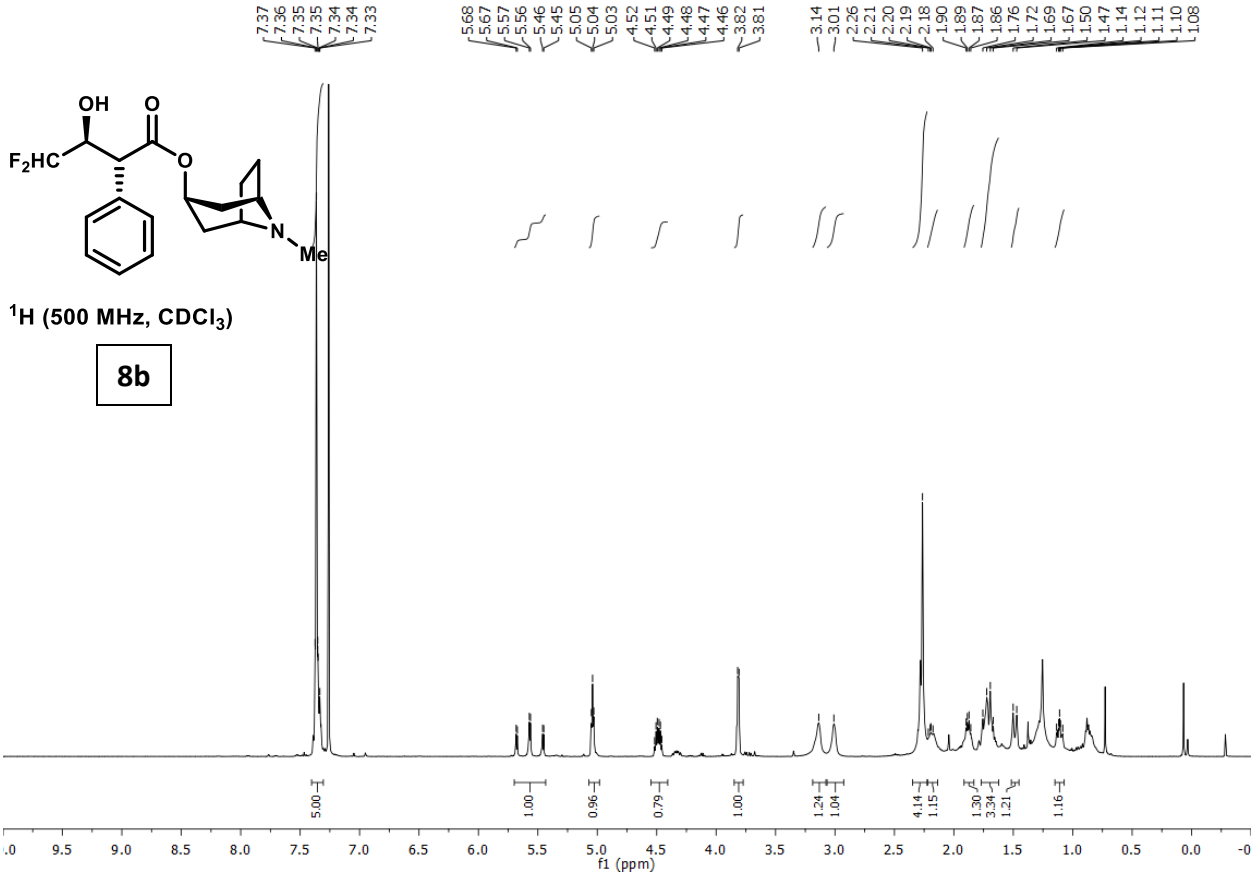
^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.2, 133.4, 129.5, 129.1, 128.4, 115.2 (dd, *J* = 244.8, 241.8 Hz), 71.2 (dd, *J* = 25.0, 23.3 Hz), 68.5, 60.0, 59.9, 51.9 (dd, *J* = 5.2, 1.9 Hz), 40.2, 36.1, 35.9, 25.3, 24.8.

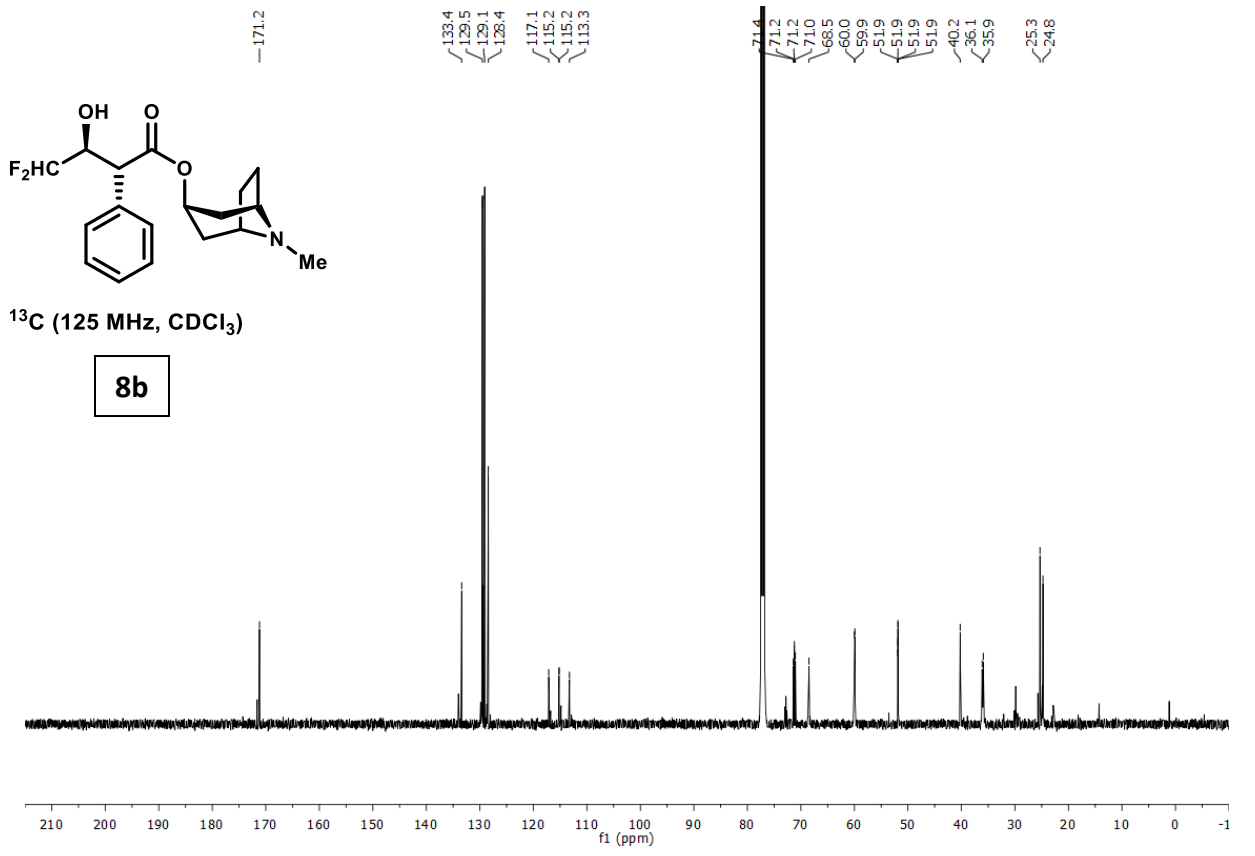
^{19}F NMR (471 MHz, $CDCl_3$): δ = -129.35 (ddd, *J* = 290.7, 54.9, 6.1 Hz), -131.39 (ddd, *J* = 290.6, 56.4, 13.1 Hz).

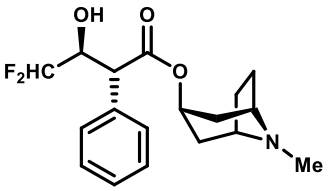
HRMS (ESI) Calculated for $C_{18}H_{23}F_2NO_3$ $[M+H]^+$ = 340.1719, Found 340.1722.

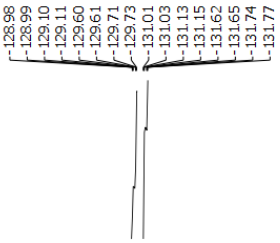
FTIR (neat) 2933, 2856, 1727, 1455, 1276, 1222, 1140, 1065, 1032, 705, 667 cm^{-1}.

$[\alpha]_D^{35}$: –18.5 (*c* = 0.5, $CHCl_3$)


OH
O
F2HC
O
N
Me
1H (500 MHz, CDCl3)
8b

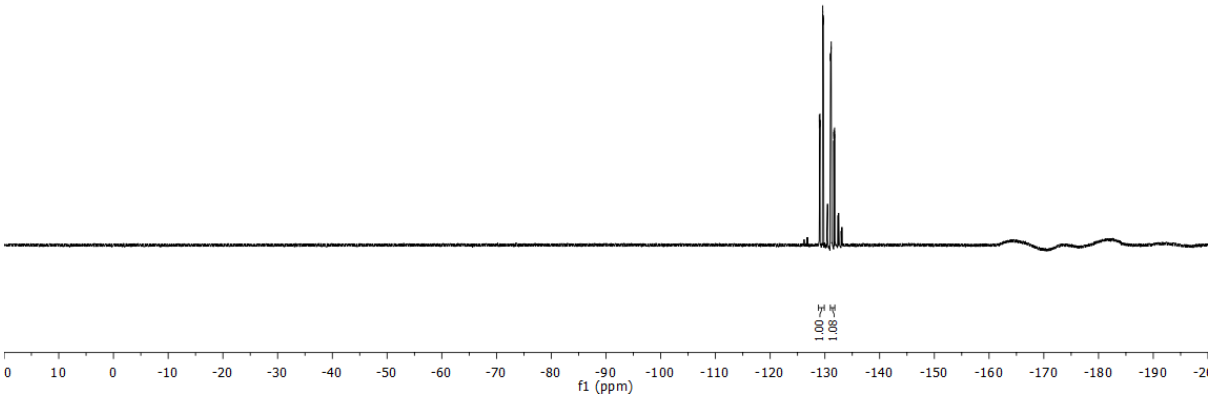

OH
O
F2HC
O
N
Me
13C (125 MHz, CDCl3)
8b





^{19}F (471 MHz, $CDCl_3$)

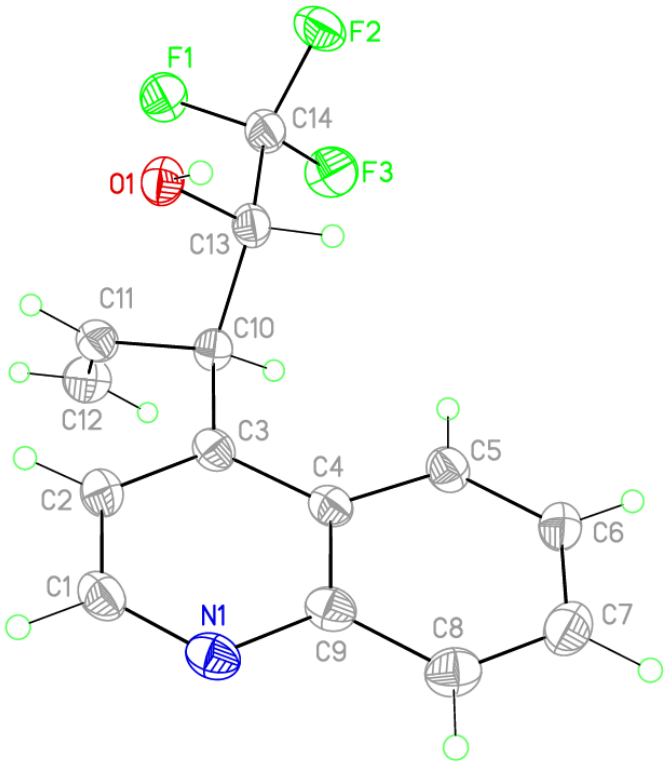
8b



Single Crystal Diffraction Data for 4l

Empirical formula	C14 H12 F3 N O	
Formula weight	267.25	
Temperature	100(2) K	
Wavelength	1.54184 Å	
Crystal system	orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 7.0471(10) Å	α= 90°.
	b = 9.5750(14) Å	β= 90°.
	c = 18.299(3) Å	γ = 90°.
Volume	1234.8(3) $Å^3$	
Z	4	
Density (calculated)	1.438 Mg/m^3	
Absorption coefficient	1.049 mm^{-1}	
F(000)	552	
Crystal size	0.260 x 0.150 x 0.060 mm^3	
Theta range for data collection	4.833 to 75.048°.	
Index ranges	-8<=h<=8, -11<=k<=11, -22<=l<=22	
Reflections collected	9466	
Independent reflections	2495 [R(int) = 0.0467]	
Completeness to theta = 67.684°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00 and 0.651	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2495 / 0 / 176	
Goodness-of-fit on F^2	1.133	
Final R indices [I>2sigma(I)]	R1 = 0.0404, wR2 = 0.1146	
R indices (all data)	R1 = 0.0422, wR2 = 0.1176	
Absolute structure parameter	-0.02(13)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.195 and -0.260 $e.Å^{-3}$	

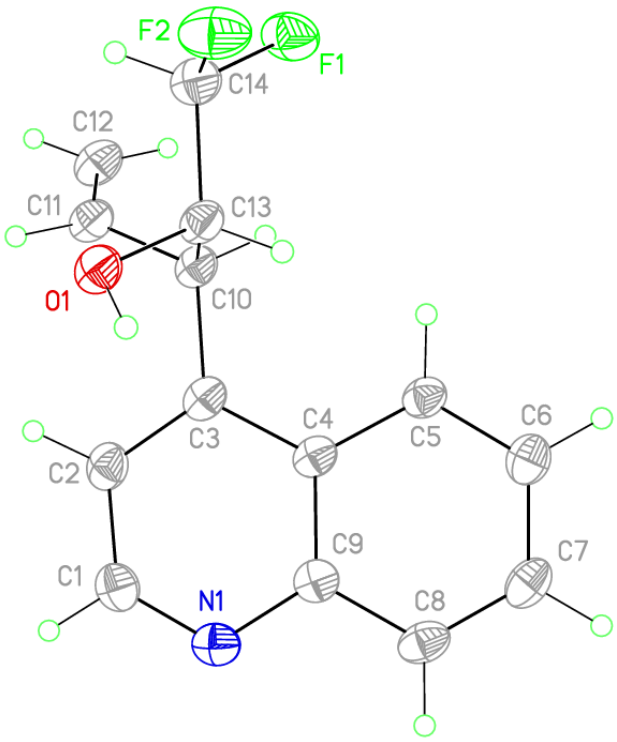
View of **4l** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.



Single Crystal Diffraction Data for 5l

Empirical formula	C14 H13 F2 N O	
Formula weight	249.25	
Temperature	100(2) K	
Wavelength	1.54184 Å	
Crystal system	orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 6.8776(2) Å	α= 90°.
	b = 12.1869(3) Å	β= 90°.
	c = 14.1842(5) Å	γ = 90°.
Volume	1188.87(6) $Å^3$	
Z	4	
Density (calculated)	1.393 Mg/m^3	
Absorption coefficient	0.922 mm^{-1}	
F(000)	520	
Crystal size	0.220 x 0.099 x 0.054 mm^3	
Theta range for data collection	4.784 to 76.030°.	
Index ranges	-8<=h<=8, -15<=k<=15, -17<=l<=16	
Reflections collected	11896	
Independent reflections	2440 [R(int) = 0.0612]	
Completeness to theta = 67.684°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00 and 0.589	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2440 / 108 / 167	
Goodness-of-fit on F^2	1.021	
Final R indices [I>2sigma(I)]	R1 = 0.0410, wR2 = 0.1132	
R indices (all data)	R1 = 0.0434, wR2 = 0.1183	
Absolute structure parameter	0.08(12)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.233 and -0.245 $e.Å^{-3}$	

View of **5l** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.



References

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