Rhodium-Catalyzed Regioselective Ring-Opening of Vinyl Epoxides with $Et_3N{\cdot}3HF$ Reagent - Formation of Allylic Fluorohydrins

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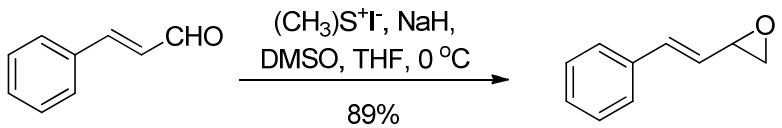
Methods and Reagents. $Et_3N{\cdot}3HF$ was stored in a glove box and fresh aliquots were removed 2 weeks for use in the fluorination reaction. All fluorination reactions were conducted in 2 mL disposable polypropylene centrifuge vials under ambient atmosphere. Other reactions were performed in oven-dried Schlenk flasks fitted with glass stoppers under positive argon pressure. All dry solvents were obtained from a SG Waters solvent system utilizing activated alumina columns under an argon pressure. The rhodium and iridium catalysts were handled and transferred to polypropylene vials within a glove box under a N_2 atmosphere. All chemicals and reagents were obtained from commercial vendors and used without further purification. All iridium and rhodium catalysts were purchased from Strem. Vinyl epoxides **1**,**11**, and **12** were purchased from Sigma-Aldrich Company. Analytical thin-layer chromatography (TLC) was used to monitor the progress of the reactions and performed using pre-coated glass plates with 230-400 mesh silica gel impregnated with a fluorescent indicator (250 nm). Visualization was achieved using UV light, potassium permanganate. Crude NMR yields of all fluorohydrins were determined by using α,α,α-trifluorotoluene ($PhCF_3$) as an internal standard and by integration of crude ^{19}F NMR. Organic solutions were concentrated by rotary evaporation below 40 ^oC at 25 torr. Flash chromatography was performed on silica gel flash chromatography columns or a Teledyne Isco CombiFlash R_f system utilizing normal phase pre-column cartridges and gold high performance columns. The *ee*'s were determined by HPLC using a Diacel Chiralcel OJ-3 4.6 x 150 mm column with flow rates and mobile phases as indicated.

Instrumentation. All proton (^1H) nuclear magnetic resonance spectra were recorded on a 400 MHz or 500 MHz spectrometer. All carbon (^{13}C) nuclear magnetic resonance spectra were recorded on a 100 MHz or 125 MHz NMR spectrometer. All fluorine (^{19}F) nuclear magnetic resonance spectra were recorded on a 282 MHz, 377 MHz or 470MHz spectrometer with proton decoupling. All deuterated solvents were used as received from Cambridge Isotope Laboratories. ^1H NMR, ^{13}C NMR, and ^{19}F NMR chemical shifts are expressed in parts per million (δ scale) relative to the chemical shift of residual solvent. Reference peaks for $CDCl_3$ in ^1H NMR and ^{13}C NMR spectra were set at 7.26 ppm and 77.16 ppm respectively. ^{19}F reference peak was set at -63 ppm for α,α,α-trifluorotoluene in $CDCl_3$ as an internal standard. Data are presented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and bs = broad singlet), integration, and coupling constant in hertz (Hz). Infrared (IR) spectra were reported in cm^{-1}. High resolution TOF mass spectrometry utilizing electrospray ionization in positive mode was performed to confirm the identity of the compounds. Enantiomeric excess was measured by chiral HPLC using Diacel Chiralcel OJ-3 (4.6 x 150mm) column. Specific rotations were obtained using a Jasco DIP-1000 polarimeter with CH_2Cl_2 as the solvent.

General Procedure for the Preparation of Vinyl Epoxides 3 - 10.[i]



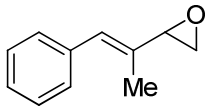
8A **8**

A 25 mL oven-dried Schlenk flask was charged with NaH (60% dispersion in oil, washed hexanes (5 x 5 mL) and dried under vacuum, 0.25 g, 6.3 mmol, 3.1 equiv). Dry THF (3 mL) and DMSO (3 mL) were added to the flask and the resulting slurry solution was cooled to 0 ^oC. Trimethylsulfonium iodide (1.22g, 6 mmol, 3 equiv) and DMSO (5 mL) were added to a separate

oven-dried Schlenk flask. The solution was transferred slowly to the NaH solution via cannula. After the transfer was complete, cinnamaldehyde **8A** (0.26 g, 2 mmol) was then added to the reaction mixture in one portion. The resulting mixture was stirred at 0 °C for 1 h, then at room temperature for another 1 h and quenched with distilled water (1 mL). The resulting mixture was then diluted with diethyl ether (40 mL) and brine (30 mL). The two layers were separated, and the aqueous layer was back extracted with diethyl ether (2 x 20 mL). The combined organic layer was dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by silica gel flash column chromatography (7% ethyl acetate in hexane + 3% triethylamine) afforded **8** (0.25 g, 89%) as a yellow oil.

^{1}H and ^{13}C NMR spectra match with the literature report.[ii]

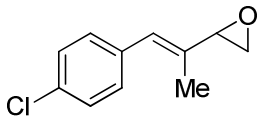
(*E*)-2-Styryloxirane
Yield: 89%
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39-7.38 (m, 2H), 7.34-7.31 (m, 2H), 7.28-7.25 (m, 1H), 6.82 (d, *J* = 16.0 Hz, 1H), 5.88 (dd, *J* = 16.0, 8.0 Hz, 1H), 3.60-3.49 (m, 1H), 3.06 (dd, *J* = 5.2, 4.1 Hz, 1H), 2.78 (dd, *J* = 5.2, 2.6 Hz, 1H).
^{13}C NMR (126 MHz, $CDCl_3$): δ 136.3 , 134.7 , 128.8 , 128.2 , 127.1 , 126.6 , 52.8 , 49.4.
IR (film, cm^{-1}): ν = 2982, 1729, 1644, 1450, 1368, 1243, 1187, 1141, 1038, 969.



3

^{1}H and ^{13}C NMR spectra match with the literature report.[iii]

(*E*)-2-(1-Phenylprop-1-en-2-yl)oxirane
Yield: 99%
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43 – 7.15 (m, 6H), 6.68 (s, 1H), 3.54 – 3.45 (m, 1H), 2.95 (dd, *J* = 5.2, 4.2 Hz, 1H), 2.82 (dd, *J* = 5.2, 2.7 Hz, 1H), 1.75 (d, *J* = 1.4 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$): δ 137.2 , 134.2 , 129.0, 128.9, 128.3, 126.9, 56.3, 46.99, 12.0.
IR (film, cm^{-1}): ν = 3053, 2987, 2919, 1733, 1600, 1490, 1444, 1376, 1313, 1256, 1029, 895.



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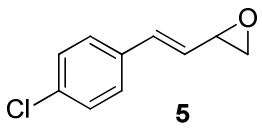
(*E*)-2-(1-(4-chlorophenyl)prop-1-en-2-yl)oxirane
Yield: 39%
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 – 7.28 (m, 2H), 7.24 – 7.19 (m, 2H), 6.60 (s, 1H), 3.51 – 3.46 (m, 1H), 2.95 (dd, *J* = 5.2, 4.2 Hz, 1H), 2.80 (dd, *J* = 5.2, 2.7 Hz, 1H), 1.73 (d, *J* = 1.4 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 135.63 , 135.04 , 132.61 , 130.31 , 128.53 , 127.52 , 56.06 , 47.09 , 12.11 .
IR (film, cm^{-1}): ν = 3050, 2989, 1492, 1374, 1254, 1092, 1039, 1013, 879, 817.
HRMS (TOF EI+): calc. for $C_{11}H_{11}ClO$ $(M)^+$: 194.0498; found: 194.0503.



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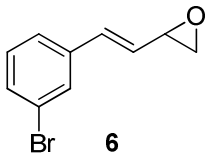
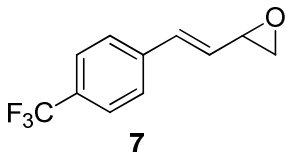
(*E*)-2-(4-Chlorostyryl)oxirane
Yield: 50%
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 (m, *J* = 0.6 Hz, 4H), 6.76 (d, *J* = 16.0 Hz, 1H), 5.85 (dd, *J* = 16.0, 8.0 Hz, 1H), 3.55- 3.46 (m, 1H), 3.06 (dd, *J* = 5.2, 4.1 Hz, 1H), 2.77 (dd, *J* = 5.2, 2.6 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 134.68 , 133.82 , 133.36 , 128.94 , 127.78 , 127.74 , 52.59, 49.40 .
IR (film, cm^{-1}): ν = 3047, 2987, 2914, 1592, 1492, 1386, 1243, 1088, 965, 930, 825.
HRMS (TOF EI+): calc. for $C_{10}H_9ClO$ $(M)^+$: 180.0342; found: 180.0339.



6

(*E*)-2-(3-Bromostyryl)oxirane
Yield: 51%
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53-7.52 (m, 1H), 7.40-7.37 (m, 1H), 7.30-7.27 (m, 1H), 7.21-7.17 (m, 1H), 6.73 (d, *J* = 16.0 Hz, 1H), 5.89 (dd, *J* = 16.0, 7.8 Hz, 1H), 3.56 – 3.47 (m, 1H), 3.06 (dd, *J* = 5.2, 4.1 Hz, 1H), 2.76 (dd, *J* = 5.2, 2.6 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 138.4 , 133.0 , 131.0 , 130.3 , 129.5 , 128.8 , 125.2 , 123.0, 77.5, 77.2 , 76.8 , 52.4 , 49.4.
IR (film, cm^{-1}): ν = 3049, 2985, 2915, 1727, 1588, 1562, 1473, 1244, 1070, 961, 930, 830.
HRMS (TOF EI+): calc. for $C_{10}H_9BrO$ $(M)^+$: 223.9837; found: 223.9836.



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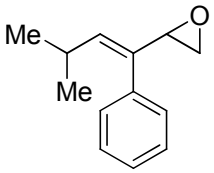
^{1}H and ^{13}C NMR spectra match with the literature report.[iv]

(*E*)-2-(4-(trifluoromethyl)styryl)oxirane
Yield: 10 %
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, *J* = 8.3 Hz, 2H), 7.47 (d, *J* = 8.2 Hz, 2H), 6.84 (d, *J* = 16.0 Hz, 1H), 5.99 (dd, *J* = 16.0, 7.8 Hz, 1H), 3.58 – 3.49 (m, 1H), 3.09 (dd, *J* = 5.2, 4.1 Hz, 1H), 2.79 (dd, *J* = 5.2, 2.6 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 139.54, δ 133.03 , 129.89 , 126.71 , 126.22 , 126.03 , 125.77 , 125.73 , 52.37 , 49.43 .
IR (film, cm^{-1}): ν =2997, 1703, 1619, 1325, 1166, 1120, 1068, 913, 832, 745.



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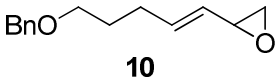
(*E*)-2-(3-Methyl-1-phenylbut-1-enyl)oxirane
Yield: 72%
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 – 7.27 (m, 3H), 7.14 (m, 2H), 5.69 (d, *J* = 10.1 Hz, 1H), 3.50 (ddd, *J* = 4.0, 2.7, 0.5 Hz, 1H), 2.82 (dd, *J* = 5.4, 4.0 Hz, 1H), 2.39 (dd, *J* = 5.4, 2.7 Hz, 1H), 2.34 (dq, *J* = 10.1, 6.6 Hz, 1H), 0.97 (d, *J* = 6.6 Hz, 3H), 0.90 (d, *J* = 6.6 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$): δ 140.0, 136.4, 135.1, 129.3, 128.1, 127.3, 55.2, 47.6, 28.0, 23.1, 23.0.
IR (film, cm^{-1}): ν = 3054, 2959, 2867, 1726, 1466, 1362, 1254, 1073, 966, 869.
HRMS (TOF EI+): calc. for $C_{13}H_{16}O$ $(M)^+$: 188.1201; found: 188.1213.



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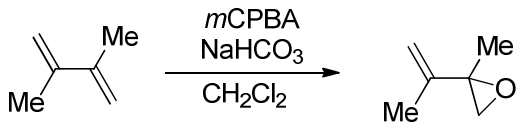
(*E*)-2-(5-(benzyloxy)pent-1-enyl)oxirane
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.27 (m, 5H), 5.96 (dt, *J* = 15.4, 6.8 Hz, 1H), 5.15 (ddt, *J* = 15.5, 8.2, 1.5 Hz, 1H), 4.50 (s, 2H), 3.48 (t, *J* = 6.4 Hz, 2H), 3.31 (ddd, *J* = 7.9, 3.8, 2.8 Hz, 1H), 2.94 (dd, *J* = 5.1, 4.1 Hz, 1H), 2.63 (dd, *J* = 5.1, 2.7 Hz, 1H), 2.24 – 2.10 (m, 2H), 1.77 – 1.66 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 138.65 , 136.59 , 128.51 , 128.15 , 127.78 , 127.69 , 73.05 , 69.63 , 52.59 , 48.98 , 29.13 , 29.10 .
IR (film, cm^{-1}): ν = 2936, 2856, 1469, 1454, 1365, 1104, 968, 840, 739, 698.
HRMS (TOF EI+): calc. for $C_{14}H_{18}O_2$ $(M)^+$: 218.1307; found: 218.1307

Procedure for the Preparation of Vinyl Epoxide 13



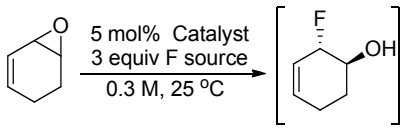
13A **13**

A 500 mL round-bottom flask was charged with 2,3-dimethyl-1,3-butyldiene **13A** (1.23 g, 15 mmol, 1 equiv) and CH_2Cl_2 (150 mL). *meta*-Chloroperoxybenzoic acid (2.85g, 16.5 mmol, 1.1 equiv, 77% purity) was then added to the solution. The reaction mixture was stirred at 0 °C for 3 h and quenched with aqueous Na_2SO_3 solution (30 mL). The aqueous layer was back extracted with CH_2Cl_2 (2 x 50 mL). Vinyl epoxide **13** (0.155 g, 16%) was isolated by reduced-pressure distillation as a colorless oil.

^{1}H and ^{13}C NMR spectra match with the literature report. [v]

2-Methyl-2-(prop-1-en-2-yl)oxirane
Yield: 16%
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.06 (s, 1H), 4.95 – 4.92 (m, 1H), 2.77 (d, *J* = 5.3 Hz, 1H), 2.71 (d, *J* = 5.3 Hz, 1H), 1.74 – 1.70 (m, 5H), 1.46 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 144.8, 112.7, 58.1, 54.2, 20.7, 18.6.
IR (film, cm^{-1}): ν = 2917, 2851, 1752, 1492, 1370, 1315, 1229, 1028, 913.

General Procedure for Ring-Opening of Vinyl Epoxide in Table 1

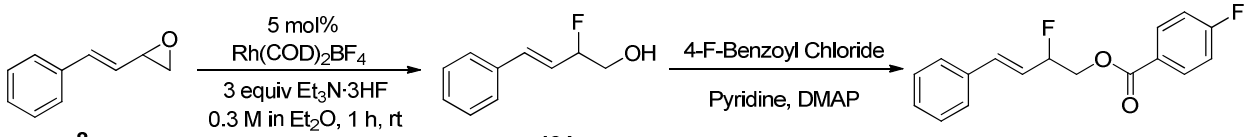


1 **2A**

Entry	Catalyst	Loading (mol%)	F source	Solvent	Time (h)	NMR Yield **2A** (%)[b]
1	$[IrClCOD_2]_2$	2.5	$Et_3N{\cdot}3HF$	Et_2O	2	37
2	$[RhClCOD_2]_2$	2.5	$Et_3N{\cdot}3HF$	Et_2O	2	55
3	$RhCOD_2OTf$	5	$Et_3N{\cdot}3HF$	Et_2O	0.5	70
4	$RhCOD_2BF_4$	5	$Et_3N{\cdot}3HF$	Et_2O	0.5	88
5	$RhCOD_2BF_4$	5	$Et_3N{\cdot}3HF$	MTBE	0.5	71
6	$RhCOD_2BF_4$	5	$Et_3N{\cdot}3HF$	CH_2Cl_2	0.5	79
7	$RhCOD_2BF_4$	5	$Et_3N{\cdot}3HF$	THF	0.5	92
8	None	0	$Et_3N{\cdot}3HF$	THF	18	23
9	$RhCOD_2BF_4$	5	CsF	THF	18	0
10	$RhCOD_2BF_4$	5	TBAT	THF	18	0
11	$RhCOD_2BF_4$	5	AgF	THF	18	0
12	$RhCOD_2BF_4$	5	KF	THF	18	0

A 2-mL polypropylene vial was charged with rhodium or iridium catalyst (5 or 10 μmol, 2.5 or 5 mol%) in the glove box. The vial was sealed and removed from the glove box. To this vial, solvent (0.2 mL) and $Et_3N{\cdot}3HF$ (0.1 mL, 0.63 mmol, 3 equiv) were sequentially added under an ambient atmosphere. A separate 2-mL polypropylene vial was charged with vinyl epoxide **1** (30.7 mg, 0.21 mmol, 1 equiv) and α,α,α-trifluorotoluene (8.5 μL, 0.07 mmol, 0.33 equiv) and solvent (0.5 mL). The solution of vinyl epoxide and α,α,α-trifluorotoluene was then added to the stirring solution of catalyst by glass pipette in one portion. The resulting mixture was sealed under ambient air and allowed to stir at room temperature. An aliquot of the reaction mixture was diluted with 1.5 mL $CDCl_3$ and analyzed by crude ^{1}H and ^{19}F after 30 min.

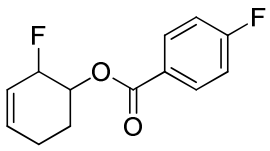
General Procedure for Rhodium-Catalyzed Ring-Opening of Vinyl Epoxides Followed by Derivatization of Allylic Fluorohydrins (Tables 1 and 2)



8 **19A** **19**

A 2 mL polypropylene vial was charged with bis(cycloocta-1,5-diene)rhodium(I) tetrafluoroborate (4.2 mg, 10 μmol, 5 mol%) in a glove box. The vial was sealed and removed from the glove box. To this vial, diethyl ether (0.2 mL) and $Et_3N{\cdot}3HF$ (0.1 mL, 0.63 mmol, 3 equiv) were sequentially added under an ambient atmosphere. A separate 2 mL polypropylene vial was charged with vinyl epoxide **8** (30.7 mg, 0.21 mmol, 1 equiv) and α,α,α-trifluorotoluene (8.5 μL, 0.07 mmol, 0.33 equiv) and diethyl ether (0.5 mL). The solution of vinyl epoxide **8** and α,α,α-trifluorotoluene in diethyl ether was then added to the stirring solution of catalyst by glass pipette in one portion. The resulting mixture was allowed to stir at room temperature under ambient air. After 1 h, the organic layer was transferred to a glass vial and the aqueous layer from the reaction mixture was further extracted with Et_2O (3 x 0.5 mL). Pyridine (1 mL), 4-fluorobenzoyl chloride (0.2 mL) and 4-dimethylaminopyridine (1 crystal) were sequentially added to the combined organic layer containing crude allylic fluorohydrin **19A**. The reaction mixture was stirred at room temperature for 18 h. The mixture was then diluted with Et_2O (20 mL) and brine (20 mL). The two layers were separated and the aqueous layer was back extracted with Et_2O (2 × 20 mL). The combined organic layer was washed with 1 M HCl (20 mL) and saturated $NaHCO_3$ solution (20 mL) and dried with anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. Purification by silica gel flash chromatography column (hexane → 3 % ethyl acetate in hexane) provided **19** (35 mg, 58% isolated yield) as a colorless oil.

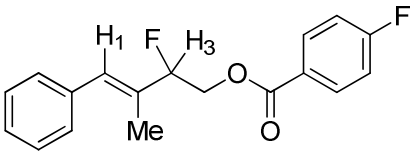
(*E*)-2-Fluoro-4-phenylbut-3-enyl 4-fluorobenzoate
Yield: 58% (0.2 mmol reaction)
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 – 8.00 (m, 2H), 7.44 – 7.40 (m, 2H), 7.38 – 7.28 (m, 3H), 7.18 – 7.08 (m, 2H), 6.89 – 6.72 (m, 1H), 6.27 (ddd, *J* = 16.0, 13.2, 6.6 Hz, 1H), 5.64 – 5.16 (m, 1H), 4.80 – 4.18 (m, 2H).
^{13}C NMR (126 MHz, $CDCl_3$): δ 166.1 (d, *J*= 254.5 Hz), 165.4 , 135.7 (d, *J* = 1.5 Hz), 135.1 (d, *J* = 11.5 Hz), 132.5 (d, *J* = 9.4 Hz), 128.9, 128.8 (d, *J*= 13.9 Hz), 127.0 (d, *J* = 1.4 Hz), 126.4 (d, *J* = 3.0 Hz), 122.6 (d, *J* = 18.7 Hz), 115.8 (d, *J* = 22.0 Hz), 909 (d, *J* = 172.9 Hz), 66.3 (d, *J* = 24.0 Hz).
^{19}F NMR (376 MHz, $CDCl_3$): δ -105.08 , -181.35.
IR (film, cm^{-1}): ν = 1725, 1604, 1508, 1271, 1154, 1128, 1092, 970, 913, 854.
HRMS (TOF EI+): calc. for $C_{17}H_{14}F_2O_2$ $(M)^+$: 288.0962; found: 288.0981.



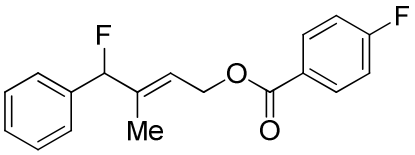
2

2-Fluorocyclohex-3-enyl 4-fluorobenzoate
Yield: 79 % (0.2 mmol reaction)
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.17 – 7.90 (m, 2H), 7.12 (t, *J* = 8.7 Hz, 2H), 6.05 – 5.97 (m, 1H), 5.83 – 5.75 (m, 1H), 5.32 (dddd, *J* = 13.8, 10.2, 6.3, 3.7 Hz, 1H), 5.24 – 5.08 (m, 1H), 2.37 – 2.21 (m, 1H), 2.17 – 2.10 (m, 1H), 1.89 – 1.80 (m, 1H).
^{13}C NMR (126 MHz, CDCl3): δ 166.2 (d, *J* = 254.4 Hz), 165.2, 132.8 (d, *J* = 9.4 Hz), 132.6 (d, *J* = 9.4 Hz), 126.7 (d, *J* = 3.0 Hz), 124.3 (d, *J* = 20.2 Hz), 115.9 (d, *J* = 22.0 Hz), 88.6 (d, *J* = 169.7 Hz), 72.9 (d, *J* = 21.7 Hz), δ 25.29 (d, *J* = 4.5 Hz), 23.85 (d, *J* = 3.1 Hz).
^{19}F NMR (471 MHz, CDCl3): δ -105.43 , -177.35.
IR (film, cm^{-1}): ν = 2932, 1720, 1604, 1508, 1268, 1239, 1154, 1115, 1014, 853.

HRMS (TOF EI+): calc. for $C_{13}H_{12}O_2F_2$ $(M)^+$: 238.0805; found: 238.0822.



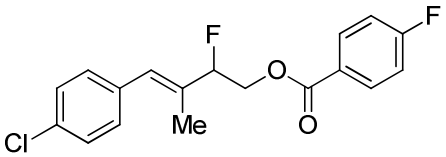
14



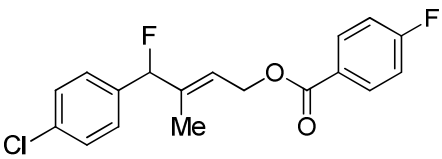
14B

Compound **14** is the major isolated product. (**14:14B** = 11:1).
(*See Spectral Data File for Complete Assignment of Compounds **14** and **14B**).*

(*E*)-2-Fluoro-3-methyl-4-phenylbut-3-enyl 4-fluorobenzoate (14)
Yield: 60 % (0.2 mmol reaction)
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.16 – 8.10 (m, 2H), 7.41 – 7.35 (m, 2H), 7.33 – 7.28 (m, 3H), 7.17 – 7.11 (m, 2H), 6.70 (s, 1H, **H-1**), 5.29 (ddd, *J* = 48.6, 7.1, 3.5 Hz, 1H, **H-3**), 4.73 – 4.51 (m, 2H), 2.00 (d, *J* = 1.5 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 165.9 (d, *J*= 255.5 Hz), 165.3, 136.4 , 132.3 (d, *J* = 9.1 Hz), 132.2 (d, *J* = 16.5 Hz), 129.0 (d, *J*= 11.1 Hz), 128.97, 128.3, 127.2, 125.9 (d, *J* = 2.9 Hz), 115.6 (d, *J* = 22.0 Hz)., 94.4 (d, *J* = 177.1 Hz), 65.4 (d, *J* = 25.6 Hz), 13.7 (d, *J* = 3.4 Hz).
^{19}F NMR (282 MHz, $CDCl_3$): δ -105.14 , -184.46 .
IR (film, cm^{-1}): ν = 2950, 1722, 1603, 1508, 1267, 1240, 1154, 1119, 1090, 854.
HRMS (TOF EI+): calc. for $C_{18}H_{16}F_2O_2$ $(M)^+$: 302.1118; found: 302.1139.



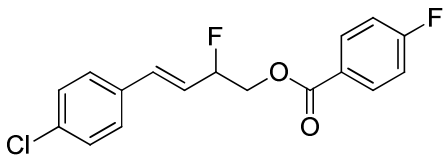
15



15B

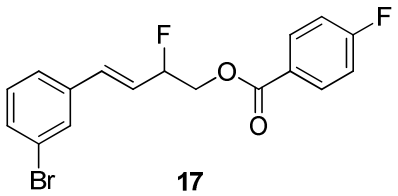
*Compound **15** is the major product (**15**:**15B** = 11:1). See Spectral Data File*

(*E*)-4-(4-chlorophenyl)-2-fluoro-3-methylbut-3-enyl 4-fluorobenzoate (15)
Yield: 62% (0.5 mmol reaction)
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 – 8.06 (m, 2H), 7.36 – 7.29 (m, 2H), 7.22 – 7.17 (m, 2H), 7.16 – 7.09 (m, 2H), 6.61 (s, 1H), 5.24 (ddd, *J* = 48.5, 6.7, 3.1 Hz, 1H), 4.66 – 4.48 (m, 2H), 1.94 (d, *J* = 1.4 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 165.95 (d, *J* = 254.3 Hz), 165.29 , 134.75 , 132.97 , 132.92 (d, *J* = 16.2 Hz), 132.32 (d, *J* = 9.5 Hz), 130.24 , 128.46 , 127.64 (d, *J* = 11.0 Hz), 125.87 (d, *J* = 2.9 Hz), 115.66 (d, *J* = 22.1 Hz), 94.15 (d, *J* = 177.8 Hz), 65.27 (d, *J* = 25.4 Hz), 13.78 (d, *J* = 3.6 Hz).
^{19}F NMR (376 MHz, $CDCl_3$): δ -104.97, -184.59.
IR (film, cm^{-1}): ν = 2956, 1721, 1602, 1508, 1490, 1266, 1239, 1154, 1118, 1090, 1013, 853.
HRMS (TOF EI+): calc. for $C_{18}H_{15}ClF_2O_2$ $(M)^+$: 336.0729; found: 336.0748.



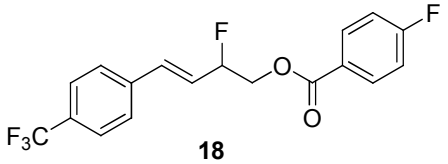
16

(*E*)-4-(4-Chlorophenyl)-2-fluorobut-3-enyl 4-fluorobenzoate
Yield: 46% (0.2 mmol reaction)
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.12 – 8.07 (m, 2H), 7.36 – 7.30 (m, 4H), 7.13 (t, *J* = 8.6 Hz, 2H), 6.77 (ddd, *J* = 16.1, 3.5, 1.3 Hz, 1H), 6.24 (ddd, *J* = 16.0, 13.6, 6.4 Hz, 1H), 5.40 (dtdd, *J* = 48.8, 6.8, 3.0, 1.4 Hz, 1H), 4.63 – 4.43 (m, 2H).
^{13}C NMR (126 MHz, $CDCl_3$): δ 166.1 (d, J= 254.5 Hz), 165.40, 134.50 , 134.18 , 133.66 (d, *J* = 11.5 Hz), 132.49 (d, *J* = 9.3 Hz), 129.07, 128.17, 125.99 (d, *J* = 2.9 Hz), 123.25 (d, *J* = 18.6 Hz), 115.80 (d, *J* = 22.0 Hz), 90.72 (d, *J* = 173.5 Hz), 66.18 (d, *J* = 23.9 Hz).
^{19}F NMR (471 MHz, $CDCl_3$): δ -104.97 , -182.16.
IR (film, cm^{-1}): ν = 1720, 1603, 1508, 1493, 1413, 1272, 1134, 1091, 973, 855.
HRMS (TOF EI+): calc. for $C_{17}H_{13}ClF_2O_2$ $(M)^+$: 322.0572; found: 322.0588



17

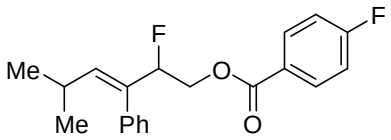
(*E*)-4-(3-Bromophenyl)-2-fluorobut-3-enyl 4-fluorobenzoate
Yield: 43% (0.5 mmol reaction)
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 – 8.05 (m, 2H), 7.56 (s, 1H), 7.43 (d, *J* = 7.8 Hz, 1H), 7.32 (d, *J* = 7.8 Hz, 1H), 7.22 (t, *J* = 7.8 Hz, 1H), 7.18 – 7.09 (m, 2H), 6.75 (dd, *J* = 16.0, 3.1 Hz, 1H), 6.27 (ddd, *J* = 16.0, 14.1, 6.2 Hz, 1H), 5.57 – 5.22 (m, 1H), 4.69 – 4.37 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 166.10(d, *J*= 254.3), 165.37 , 137.77 , 133.30 (d, *J* = 13.8 Hz), 132.50 (d, *J* = 9.4 Hz), 131.54, 130.38, 129.78, 125.92 (d, *J* = 2.1 Hz), 125.67, 124.17 (d, *J* = 16.1 Hz), 123.04 , 115.60 (d, *J* = 50.3 Hz), 90.59 (d, *J* = 173.3 Hz), 66.09 (d, *J* = 26.8 Hz).
^{19}F NMR (282 MHz, $CDCl_3$): δ -104.97, -183.06 .
IR (film, cm^{-1}): ν = 2949, 1719, 1602, 1507, 1268, 1239, 1118, 1089, 967, 853.
HRMS (TOF EI+): calc. for $C_{17}H_{13}BrF_2O_2$ $(M)^+$: 366.0067; found: 366.0064.



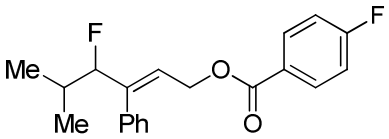
18

(*E*)-2-fluoro-4-(4-(trifluoromethyl)phenyl)but-3-enyl 4-fluorobenzoate
Yield: 46 % (0.2 mmol reaction)
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 – 8.05 (m, 2H), 7.60 (d, *J* = 8.2 Hz, 2H), 7.51 (d, *J* = 8.3 Hz, 2H), 7.20 – 7.05 (m, 2H), 6.85 (dd, *J* = 16.1, 2.1 Hz, 1H), 6.36 (ddd, *J* = 16.0, 14.5, 6.1 Hz, 1H), 5.57 – 5.32 (m, 1H), 4.70 – 4.39 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 166.10 (d, *J* = 254.3 Hz), 165.39, 139.08, 133.09 (d, *J* = 12.2 Hz), 132.50 (d, *J* = 9.4 Hz), 127.13 , 125.86 , 125.25 (d, *J* = 18.7 Hz), 115.83 (d, *J* = 22.1 Hz), 90.50 (d, *J* = 174.5 Hz), 65.82 (d, *J* = 53.9 Hz).
^{19}F NMR (282 MHz, $CDCl_3$): δ -62.73, -104.93 , -183.86 .
IR (film, cm^{-1}): ν = 1724, 1603, 1508, 1325, 1269, 1123, 1067, 854, 767.
HRMS (TOF EI+): calc. for $C_{18}H_{13}O_2F_5$ $(M)^+$: 356.0836; found: 356.0827.



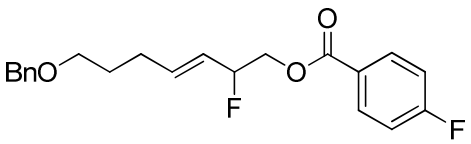
20



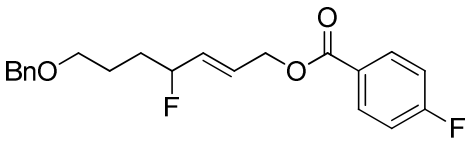
20B

*Compound **20** is the major product (**20**:**20B** = 6:1). See Spectral Data File*

(*E*)-2-Fluoro-5-methyl-3-phenylhex-3-enyl 4-fluorobenzoate (20)
Yield: 59 % (0.2 mmol reaction)
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.09 – 8.00 (m, 2H), 7.41 – 7.29 (m, 3H), 7.24 – 7.16 (m, 2H), 7.14 – 7.06 (m, 2H), 5.75 (d, *J* = 9.9 Hz, 1H), 5.34 (dd, *J* = 48.3, 7.1 Hz, 1H), 4.53 – 4.18 (m, 2H), 2.33 (s, 1H), 1.03 – 0.83 (m, 6H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 166.04 (d, *J* = 255.7 Hz), 165.23 , 136.60, 133.72 (d, *J* = 15.8 Hz), 132.42 (d, *J* =9.4 Hz), 129.21, 128.89, 128.61, 127.73, 115.55 (d, *J* = 33.7 Hz), 93.01 (d, *J* = 148.0 Hz), 65.45 (d, *J* = 32.5 Hz), 27.55 , 22.44.
^{19}F NMR (471 MHz, $CDCl_3$): δ -105.31 , -180.83.
IR (film, cm^{-1}): ν = 2960, 2868, 1725, 1603, 1508, 1269, 1240, 1154, 1123, 1091, 855.
HRMS (TOF EI+): calc. for $C_{20}H_{20}O_2F_2$ $(M)^+$: 330.1431; found: 330.1439

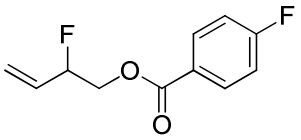


21



21B

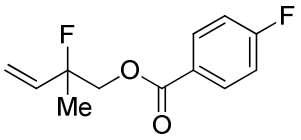
7-(benzyloxy)-2-fluorohept-3-enyl 4-fluorobenzoate (21)
Yield: 48 % (0.2 mmol reaction, mixture of **21** and **21B**)
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 – 8.02 (m, 2H), 7.38 – 7.26 (m, 5H), 7.20 – 7.03 (m, 2H), 6.02 – 5.85 (m, 2H), 5.66 – 5.51 (m, 1H), 5.16 (dtd, *J* = 49.5, 7.2, 3.2 Hz, 1H), 4.53 – 4.44 (m, 2H), 4.48 – 4.30 (m, 2H), 3.55 – 3.43 (m, 2H), 2.27 – 2.16 (m, 2H), 1.91 – 1.60 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 165.84 (d, *J* = 260.7 Hz), 165.23 , 138.45 , 137.14 (d, *J* = 11.0 Hz), 132.36 , 132.27 , 128.38 , 127.63 , 127.58 , 124.12 (d, *J* = 19.0 Hz), 115.59 (d, *J* = 22.0 Hz), 90.75 (d, *J* = 170.9 Hz), 72.93 , 69.31 , 66.26 (d, *J* = 24.2 Hz), 32.20 , 28.95 .
^{19}F NMR (376 MHz, $CDCl_3$): δ -105.26, -179.45.
IR (film, cm^{-1}): ν = 2941, 2858, 1722, 1604, 1508, 1268, 1107, 972, 855, 767.
HRMS (TOF EI+): calc. for $C_{21}H_{22}O_3F_2$ $(M)^+$: 360.1537; found: 360.1545.



22

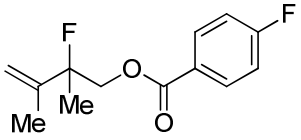
^{1}H and ^{13}C NMR spectra match with the literature report. [vi]

2-Fluorobut-3-enyl 4-fluorobenzoate
Yield: 49% (0.2 mmol reaction) and 44 % (0.5 mmol reaction)
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.12 – 8.04 (m, 2H), 7.15 – 7.08 (m, 2H), 5.94 (dddd, *J* = 17.4, 15.3, 10.8, 5.7 Hz, 1H), 5.55 – 5.48 (m, 1H), 5.39 (d, *J* = 10.8 Hz, 1H), 5.23 (dd, *J* = 48.8, 1.5 Hz, 1H), 4.55 – 4.34 (m, 2H).
^{13}C NMR (126 MHz, $CDCl_3$): δ 166.1 (d, *J*= 254.5 Hz), 165.4, 132.8 (d, *J* = 9.4 Hz), 132.0 (d, *J* = 19.4 Hz), 126.0 (d, *J* = 3.1 Hz), 119.6 (d, *J* = 11.4 Hz), 115.8 (d, *J* = 22.1 Hz), 90.8 (d, *J* = 173.5 Hz), 66.1 (d, *J* = 23.3 Hz).
^{19}F NMR (471 MHz, $CDCl_3$): δ -105.11, -186.11.
IR (film, cm^{-1}): ν = 1724, 1604, 1508, 1431, 1266, 1238, 1155, 1118, 854.
HRMS (TOF EI+): calc. for $C_{12}H_{12}O_2F_2$ $(M)^+$: 226.0805; found: 226.0834.



23

2-Fluoro-2-methylbut-3-enyl 4-fluorobenzoate
Yield: 70 % (0.2 mmol reaction)
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 – 8.04 (m, 2H), 7.16 – 7.08 (m, 2H), 5.96 (td, *J* = 17.5, 11.0 Hz, 1H), 5.45 (d, *J* = 17.5 Hz, 1H), 5.28 (d, *J* = 11.0 Hz, 1H), 4.37 (dd, *J* = 20.5, 1.5 Hz, 2H), 1.53 (d, *J* = 21.4 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 166.3 (d, *J*= 255.5 Hz), 165.5, 137.3 (d, *J* = 22.2 Hz), 132.6 (d, *J* = 9.4 Hz), 126.3 , 116.4 (d, *J* = 11.0 Hz), 116.0 (d, *J* = 22.0 Hz), 95.6 (d, *J*= 135.2 Hz), 68.8 (d, *J* = 24.9 Hz), 22.4 (d, *J* = 24.2 Hz).
^{19}F NMR (471 MHz, $CDCl_3$): δ -105.23 , -154.44.
IR (film, cm^{-1}): ν = 2917, 1675, 1444, 1380, 1195, 1121.
HRMS (TOF EI+): calc. for $C_{12}H_{12}O_2F_2$ $(M)^+$: 226.0805; found: 226.0834.

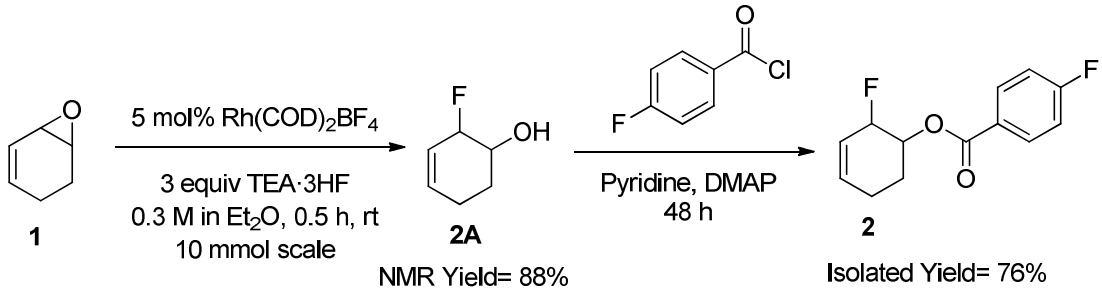


24

2-Fluoro-2,3-dimethylbut-3-enyl 4-fluorobenzoate
Yield: 56 % (0.2 mmol reaction)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 – 8.03 (m, 2H), 7.16 – 7.07 (m, 2H), 5.13 (s, 1H), 5.02 – 4.98 (m, 1H), 4.43 (dd, *J* = 21.1, 1.3 Hz, 2H), 1.84 (dt, *J* = 1.7, 1.0 Hz, 3H), 1.55 (d, *J* = 21.9 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 166.3 (d, *J*= 255.5 Hz), 165.53 , 144.35 (d, *J* = 20.3 Hz), 132.64 (d, *J* = 9.4 Hz), 126.42 , 115.95 (d, *J* = 22.0 Hz), 112.63 (d, *J* = 10.7 Hz), 96.42 (d, *J* = 176.4 Hz), 68.15 (d, *J* = 24.7 Hz), 22.17 (d, *J* = 25.0 Hz), 19.26 (d, *J* = 5.4 Hz).
^{19}F NMR (376 MHz, $CDCl_3$): δ -105.30 , -152.97 .
IR (film, cm^{-1}): ν = 2994, 1726, 1604, 1508, 1270, 1154, 1112, 1091, 854.
HRMS (TOF EI+): calc. for $C_{13}H_{14}O_2F_2$ $(M)^+$: 240.0962; found: 240.0958.

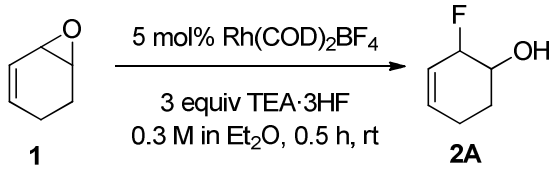
Procedure for the Large Scaled Synthesis of Allylic 4-Fluoro-Benzoate 2



A 50 mL polypropylene vial was charged with bis(cycloocta-1,5-diene)rhodium(I) tetrafluoroborate (203 mg, 0.5 mmol, 5 mol%) in a glove box. The vial was sealed and removed from the glove box. To this vial, diethyl ether (30 mL) and TEA·3HF (4.9 mL, 30 mmol, 3 equiv) were sequentially added under an ambient atmosphere. Vinyl epoxide **1** (0.96 g, 10 mmol, 1 equiv) and α,α,α-trifluorotoluene (0.41 mL, 3.33 mmol, 0.33 equiv) were then added to the stirring solution of catalyst by syringe. The resulting mixture was sealed under ambient air and allowed to stir at room temperature. After 0.5 h, the organic layer was transferred to a glass vial and the aqueous layer from the reaction mixture was extracted with Et_2O (2 × 20 mL). After half of the solvent was removed from the combined organic extract, pyridine (20 mL), 4-fluorobenzoylchloride (2.56 mL, 20 mmol, 2 equiv) and 4-dimethylaminopyridine (0.13 g, 10 mol%) were subsequently added. The reaction mixture was stirred at room temperature for 48 h. The mixture was then diluted with Et_2O (10 mL) and brine (30 mL). The two layers were separated and the aqueous layer was back extracted with Et_2O (2 × 30 mL). The combined organic layer was washed with 1 M HCl (30 mL) and saturated $NaHCO_3$ solution (30 mL) and dried with anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. Purification by silica gel flash chromatography column (hexane/ethyl acetate = 30:1 → 5: 1) resulted in **2** (1.82 g, 76%) as a colorless oil.

Assignment of Regioselectivity for Cyclic Allylic Fluoride

Preparation and Isolation of Allylic Fluorohydrin 2A for Spectroscopic Analysis

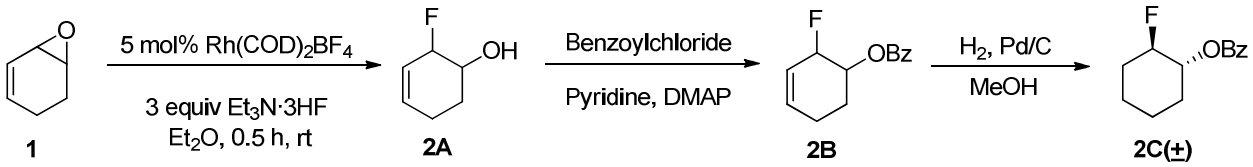


A 2 mL polypropylene vial was charged with bis(cycloocta-1,5-diene)rhodium(I) tetrafluoroborate (8.1 mg, 20 μmol, 5 mol%) in a glove box. The vial was sealed and removed from the glove box. To this vial, diethyl ether (0.3 mL) and $Et_3N{\cdot}3HF$ (0.2 mL, 1.20 mmol, 3 equiv) were sequentially added under an ambient atmosphere. A separate 2 mL polypropylene vial was charged with vinyl epoxide **1** (40.4 mg, 0.42 mmol, 1 equiv) and α,α,α-trifluorotoluene (17 μL, 0.14 mmol, 0.33 equiv) and ether (1 mL). The solution of vinyl epoxide **1** and α,α,α-trifluorotoluene in ether was then added to the stirring solution of catalyst by glass pipette in one portion. The resulting mixture was allowed to stir at room temperature under ambient air. After 0.5 h, the organic layer was transferred to a glass vial and the aqueous layer from the reaction mixture was extracted with Et_2O (3 mL × 3). The combined organic layer was eluting through a mini-column with ethyl acetate and concentrated *in vacuo* to provide volatile allylic fluorohydrin **2A**, which was used immediately for analysis without further purification

^1H and ^{13}C NMR spectra match with the literature report.[vii] COSY spectrum was included in the Spectral Data File.

2-Fluorocyclohex-3-enol
^1H NMR (400 MHz, $CDCl_3$): δ 5.91 – 5.79 (m, 1H), 5.73 – 5.61 (m, 1H), 4.92 (dtd, *J* = 51.6, 4.4, 2.2 Hz, 1H), 3.92 (dddd, *J* = 14.6, 11.5, 6.9, 4.0 Hz, 1H), 3.15 (bs, 1H), 2.26 – 2.14 (m, 2H), 2.02 – 1.93 (m, 1H), 1.77 – 1.60 (m, 1H).
^{13}C NMR (101 MHz, CDCl3): δ 131.53 (d, *J* = 9.1 Hz), 124.38 (d, *J* = 21.3 Hz), 93.49 (d, *J* = 165.8 Hz), 70.66 (d, *J* = 19.0 Hz), 27.49 (d, *J* = 6.1 Hz), 24.27.

Preparation and Isolation of Allylic Benzoate 17C for Spectroscopic Analysis

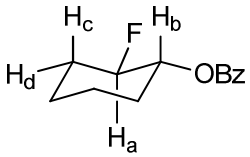


A 2 mL polypropylene vial was charged with bis(cycloocta-1,5-diene)rhodium(I) tetrafluoroborate (4.2 mg, 10 μmol, 5 mol%) in a glove box. The vial was sealed and removed from the glove box. To this vial, diethyl ether (0.2 mL) and $Et_3N{\cdot}3HF$ (0.1 μL, 0.63 mmol, 3 equiv) were sequentially added under an ambient atmosphere. A separate 2 mL polypropylene vial was charged with cyclic vinyl epoxide **1** (20.2 mg, 0.21 mmol, 1 equiv) and α,α,α-trifluorotoluene (8.5 μL, 70 μmol, 0.33 equiv) and diethyl ether (0.5 mL). The solution of vinyl epoxide **1** and α,α,α-trifluorotoluene in diethyl ether was then added to the stirring solution of catalyst by glass pipette in one portion. The resulting mixture was allowed to stir at room temperature under ambient air. After 0.5 h, the organic layer was transferred to a glass vial and the aqueous layer from the reaction mixture was extracted with Et_2O (0.5 mL × 3). Pyridine (1 mL), benzoyl chloride (0.2 mL) and 4-dimethylaminopyridine (1 crystal) were sequentially added. The reaction mixture was stirred at room temperature for 18 h. The mixture was then diluted with Et_2O (20 mL) and brine (20 mL). The two layers were separated and the aqueous layer was back extracted with Et_2O (3 × 20 mL). The combined organic layer was washed with 1 M HCl (20 mL) and saturated $NaHCO_3$ solution (20 mL) and dried with anhydrous $MgSO_4$,

filtered and concentrated *in vacuo*. The crude product of **2B** was dissolved in MeOH (2 mL) and Pd/C (6 mg) was added. The reaction was sealed under an atmosphere of H_2 (1 atm). After 2 h, the reaction was filtered through a pad of Celite and then concentrated *in vacuo*. The resulting residue was loaded onto a silica chromatography column and eluting with a mixture hexane and diethyl ether (15:1) to provide fluoride **2C** as a colorless oil.

2-Fluorocyclohexyl benzoate

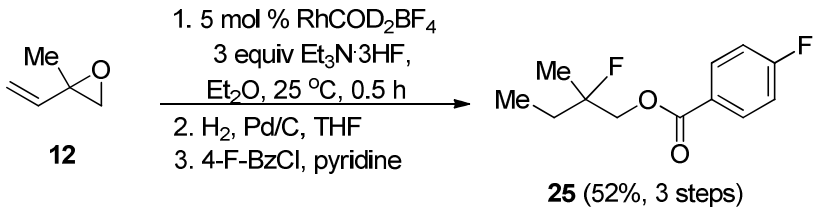
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 – 7.97 (m, 2H), 7.65 – 7.52 (m, 1H), 7.51 – 7.42 (m, 2H), 5.14 (ddt, *J* = 9.9, 8.3, 5.0 Hz, 1H), 4.62 (dddd, *J* = 50.3, 10.0, 8.2, 4.7 Hz, 1H), 2.30 – 2.10 (m, 2H), 1.87 – 1.72 (m, 3H), 1.72 – 1.55 (m, 2H), 1.54 – 1.33 (m, 4H).



2C(±)

δ =4.62 is H_a on the fluorinated carbon. 50.3 Hz is the coupling constant between H_a and F. 10.0, 8.2, 4.7 Hz showed there were two axial-axial coupling and one axial-equatorial coupling. According to this we can determine the relative structure as a 1, 2 trans-addition product.

Procedure for Synthesis of Tertiary Alkyl Fluorides 25 and 26

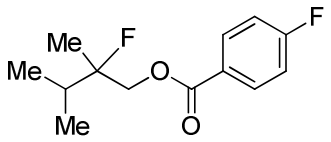


25 (52%, 3 steps)

A 2-mL polypropylene vial was charged with bis(cycloocta-1,5-diene)rhodium(I) tetrafluoroborate (4.2 mg, 10 μmol, 5 mol%) in a glove box. The vial was sealed and removed from the glove box. To this vial, diethyl ether (0.2 mL) and $Et_3N{\cdot}3HF$ (0.1 mL, 0.63 mmol, 3 equiv) were sequentially added under an ambient atmosphere. A separate 2-mL polypropylene vial was sequentially charged with vinyl epoxide **12** (17.7 mg, 0.21 mmol, 1 equiv) and α,α,α-trifluorotoluene (8.5 μL, 70 μmol, 0.33 equiv) and diethyl ether (0.5 mL). The solution of vinyl epoxide **12** and α,α,α-trifluorotoluene in diethyl ether was then added to the stirring solution of catalyst by glass pipette in one portion. The resulting mixture was allowed to stir at room temperature under ambient air. After 0.5 h, the organic layer was transferred to a glass vial and the aqueous layer from the reaction mixture was extracted with Et_2O (0.5 mL × 3). The crude allylic fluorohydrin was dissolved in THF (3 mL) and Pd/C (6 mg) was added. The reaction was sealed under an atmosphere of H_2 (1 atm). After 2 h, the reaction was filtered through a pad of Celite and then concentrated *in vacuo* to remove half of the solvent. Pyridine (1 mL), 4-fluoro-benzoyl chloride (0.2 mL) and 4-dimethylaminopyridine (1 crystal) were sequentially added to the solution. The reaction mixture was stirred at room temperature for 18 h. The mixture was then diluted with Et_2O (10 mL) and brine (10 mL). The two layers were separated and the

aqueous layer was back extracted with Et_2O (3 × 20 mL). The combined organic layer was washed with 1 M HCl (5 mL) and saturated $NaHCO_3$ solution (10 mL) and dried with anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The resulting residue was loaded onto a silica chromatography column and eluting with a mixture hexane and diethyl ether (15:1) to provide fluoride **25** (24.9 mg, 52%) as a colorless oil.

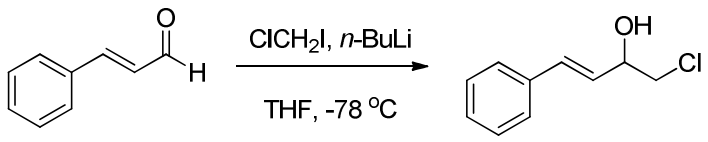
2-Fluoro-2-methylbutyl 4-fluorobenzoate
Yield: 52%
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.13 – 8.05 (m, 2H), 7.13 (t, *J* = 8.6 Hz, 2H), 4.34 (d, *J* = 19.8 Hz, 2H), 1.89 – 1.69 (m, 2H), 1.42 (d, *J* = 21.5 Hz, 3H), 1.01 (t, *J* = 7.6 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$): δ 166.05 (d, *J* = 254.3 Hz), 165.40, 132.42 (d, *J* = 9.4 Hz), 126.21 , 115.77 (d, *J* = 22.0 Hz), 95.61 (d, *J* = 172.0 Hz), 68.58 (d, *J* = 25.3 Hz), 29.80 (d, *J* = 23.1 Hz), 21.15 (d, *J* = 24.4 Hz), 7.79 (d, *J* = 6.6 Hz).
^{19}F NMR (471 MHz, $CDCl_3$): δ -105.25, -153.65.
IR (film, cm^{-1}): ν = 2979, 2946, 1725, 1604, 1508, 1384, 1271, 1154, 1116, 855.
HRMS (TOF EI+): calc. for $C_{12}H_{14}O_2F_2$ $(M)^+$: 228.0962; found: 228.0953.



26

2-Fluoro-2,3-dimethylbutyl 4-fluorobenzoate
Yield : 50% (3 steps)
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 – 8.02 (m, 2H), 7.20 – 7.06 (m, 2H), 4.39 (d, *J* = 21.6 Hz, 2H), 2.22 – 2.09 (m, 1H), 1.35 (d, *J* = 21.8 Hz, 3H), 1.04 (d, *J* = 6.9 Hz, 3H), 0.98 (d, *J* = 7.0 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 166.06 (d, *J* = 254.2 Hz), 165.48 , 132.41 (d, *J* = 9.3 Hz), 126.33 , 115.76 (d, *J* = 22.0 Hz), 97.74 (d, *J* = 172.9 Hz), 67.91 (d, *J* = 23.8 Hz), 33.62 (d, *J* = 27.0 Hz), 17.92 (d, *J* = 25.1 Hz), 17.63 (d, *J* = 6.8 Hz), 16.72 (d, *J* = 6.0 Hz).
^{19}F NMR (376 MHz, $CDCl_3$): δ -105.33, -154.53 .
IR (film, cm^{-1}): ν = 2969, 1721, 1604, 1508, 1385, 1270, 1238, 1153, 1115, 1091, 853.
HRMS (TOF EI+): calc. for $C_{13}H_{16}O_2F_2$ $(M)^+$: 242.1118; found: 242.1126.

Procedure for Synthesis of Chiral Vinyl Epoxide (*R*)-8



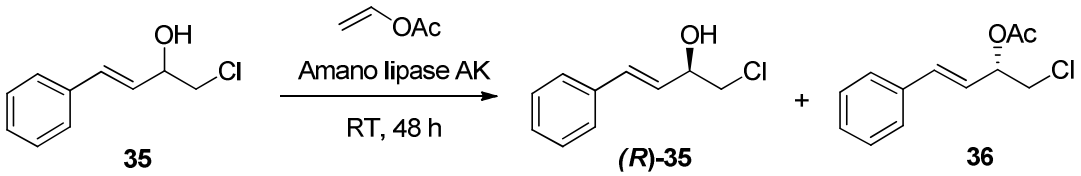
8A **35**

A 25 mL oven-dried Schlenk flask was kept under a stream of nitrogen and then charged with an cinnamaldehyde (0.52 g, 4 mmol) and THF (8 mL, 0.5 M). The resulting solution was cooled to -78 °C and chloroiodomethane (0.452 mL, 6 mmol, 1.5 eq) was added followed by the slow addition of *n*-BuLi (2.4 mL, 1.5 eq, 2.5 M solution in hexanes) over 30 min. The reaction was

maintained at –78 ^{o}C and monitored by TLC. When the starting material had been consumed the reaction mixture was quenched with saturated aqueous NH_4Cl solution and warmed to room temperature. It was transferred to a separatory funnel containing diethyl ether and additional saturated aqueous NH_4Cl solution. The organic layer was separated, and the aqueous layer was back-extracted with ether (2 x 25 mL). The organic layers were combined and dried over magnesium sulfate. The solvent was removed *in vacuo* and the residue purified by silica gel flash chromatography flash chromatography (20% ethyl acetate in hexane) afforded **35** (0.4 g, 56%) as a yellow oil.

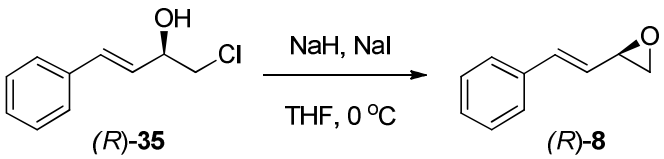
^{1}H and ^{13}C NMR spectra match with the literature report [ii]

(*E*)-1-chloro-4-phenylbut-3-en-2-ol
Yield : 56%
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 – 7.37 (m, 2H), 7.36 – 7.30 (m, 2H), 7.30 – 7.24 (m, 1H), 6.73 (d, *J* = 16.0 Hz, 1H), 6.21 (dd, *J* = 16.0, 6.2 Hz, 1H), 4.59 – 4.49 (m, 1H), 3.72 (dd, *J* = 11.1, 3.7 Hz, 1H), 3.60 (dd, *J* = 11.1, 7.3 Hz, 1H), 2.39 (bs, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 136.20, 132.97 , 128.79 , 128.29 , 127.33 , 126.78 , 72.46 , 49.87 .
IR (film, cm^{-1}): ν = 3405, 3026, 1494, 1449, 1093, 1071, 968.



A 10 mL oven-dried Schlenk flask was charged with racemic chlorohydrin **35** and vinyl acetate (1.0 mL/mmol). The resulting solution was stirred at room temperature and amano lipase AK (3.0 mass equiv.) was added as single portion. Reaction progress was monitored by HPLC. At approximately 50% conversion, the suspension was filtered through a pad of Celite, washing with ethyl acetate (100 mL). The solution was concentrated in vacuo and the crude residue was purified by flash chromatography (5-10% ethyl acetate in hexane) to afford (*R*)-**35**

(*R, E*)-1-chloro-4-phenylbut-3-en-2-ol
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 – 7.37 (m, 2H), 7.36 – 7.30 (m, 2H), 7.30 – 7.24 (m, 1H), 6.73 (d, *J* = 16.0 Hz, 1H), 6.21 (dd, *J* = 16.0, 6.2 Hz, 1H), 4.59 – 4.49 (m, 1H), 3.72 (dd, *J* = 11.1, 3.7 Hz, 1H), 3.60 (dd, *J* = 11.1, 7.3 Hz, 1H), 2.39 (bs, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 136.20 , 132.97 , 128.79 , 128.29 , 127.33 , 126.78 , 72.46 , 49.87 .
HPLC: 2.5mg/mL in 50/50 IPA/Hex, 2 µL injection, 4.6 x 150mm Chiralcel OJ-3, 1 mL/min., 5% IPA in hexanes, 254 nm, major 14.63 min., minor 17.49 min , 99 % ee

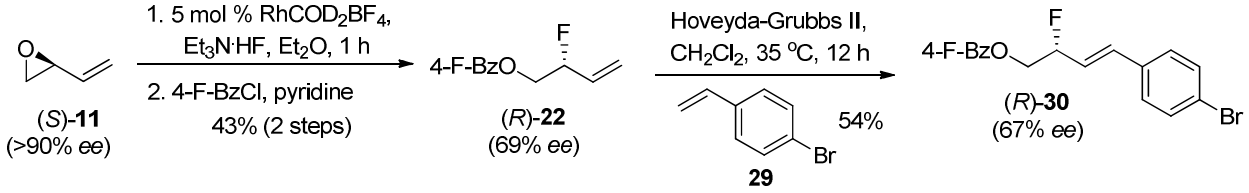


A 10 mL oven-dried Schlenk flask was charged with NaH (60% dispersion in oil, washed hexanes (5 x 5 mL) and dried under vacuum, 42 mg, 1.1 mmol, 1.1 equiv). Dry THF (1 mL) and and NaI (14 mg, 10 mol%)were added to the flask and the resulting slurry solution was cooled to 0 ^{o}C. The heterogenous mixture was stirred for 5 min, a solution of (*R*)-**35** (182 mg, 1 mmol) THF (1 mL) was then added slowly over 30 min. When the addition was complete, the reaction mixture was maintained at 0 ^{o}C, and the reaction progress was followed by TLC. When the starting material was consumed (products usually decompose on TLC), the reaction was quenched with saturated aqueous NH_4Cl solution and transferred to a separatory funnel with ether and additional aqueous NH_4Cl solution. The organic layer was separated, and the aqueous layer back extracted with diethyl ether (2 x 20 mL). The organic layers were combined, dried over magnesium sulfate. The solvent removed *in vacuo*. Vinyl epoxide (*R*)-**8** (125 mg, 86%) was used in fluorination without further purification.

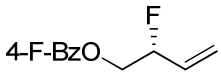
^{1}H and ^{13}C NMR spectra match with the literature report.[ii]

(*E*)-2-Styryloxirane
Yield: 85%
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39-7.38 (m, 2H), 7.34-7.31 (m, 2H), 7.28-7.25 (m, 1H), 6.82 (d, *J* = 16.0 Hz, 1H), 5.88 (dd, *J* = 16.0, 8.0 Hz, 1H), 3.60-3.49 (m, 1H), 3.06 (dd, *J* = 5.2, 4.1 Hz, 1H), 2.78 (dd, *J* = 5.2, 2.6 Hz, 1H).
^{13}C NMR (126 MHz, $CDCl_3$): δ 136.3 , 134.7 , 128.8 , 128.2 , 127.1 , 126.6 , 52.8 , 49.4.
IR (film, cm^{-1}): ν = 2982, 1729, 1644, 1450, 1368, 1243, 1187, 1141, 1038, 969.

Rhodium-Catalyzed Stereospecific Opening of Enantiopure Vinyl Epoxide 11



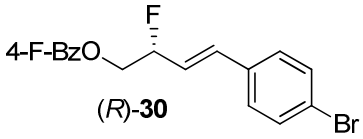
After (*R*)-**22** was isolated from previous procedure for fluorination and benzoylation (see page S-6 and S-7). To an oven-dried 25-mL round-bottom flask was sequentially added (*R*)-**22** (21 mg, 0.1 mmol), 4-bromostyrene (130 μL, 1 mmol, 10 equiv) and dichloromethane (4 mL). Hoveyda-Grubbs II catalyst (3 mg, 5 μmol, 5 mol%) was then added to the solution. The reaction mixture was heated to 35 ^{o}C and refluxed over night. The mixture was directly loaded onto a silica chromatography column, and eluting with hexane to 3 % ethyl acetate in hexane provided (*R*)-**30** (20 mg) as a white solid which was recrystalized from hexane for X-ray crystallographic analysis.



(*R*)-**22**

(*R*)-2-Fluorobut-3-enyl 4-fluorobenzoate
Yield: 43 % (0.5 mmol reaction)

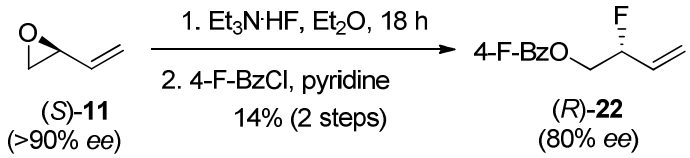
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.12 – 8.04 (m, 2H), 7.15 – 7.08 (m, 2H), 5.94 (dddd, *J* = 17.4, 15.3, 10.8, 5.7 Hz, 1H), 5.55 – 5.48 (m, 1H), 5.39 (d, *J* = 10.8 Hz, 1H), 5.23 (dd, *J* = 48.8, 1.5 Hz, 1H), 4.55 – 4.34 (m, 2H).
^{19}F NMR (471 MHz, $CDCl_3$): δ -105.11, -186.11.
IR (film, cm^{-1}): ν = 1724, 1604, 1508, 1431, 1266, 1238, 1155, 1118, 854.
$[\alpha]^{20}_D$: -0.12, c = 1, $CHCl_3$
HPLC: 2.5mg/mL in 50/50 IPA/Hex, 2 µL injection, 4.6 x 150mm Chiralcel OJ-3, 1 mL/min., 1% IPA in hexanes, 254 nm, major 5.60 min., minor 6.09 min., 69% *ee*



(*R*)-**30**

(*R, E*)-4-(4-Bromophenyl)-2-fluorobut-3-enyl 4-fluorobenzoate
Yield: 54 %
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 – 8.07 (m, 1H), 7.50 – 7.45 (m, 1H), 7.31 – 7.25 (m, 2H), 7.17 – 7.09 (m, 1H), 6.80 – 6.72 (m, 1H), 6.25 (ddd, *J* = 16.1, 13.7, 6.4 Hz, 0H), 5.49 – 5.30 (m, 1H), 4.65 – 4.42 (m, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 166.11(d, *J*= 253.5 Hz), 165.43 , 134.56 , 133.74 (d, *J* = 10.3 Hz), 132.49 (d, *J* = 9.4 Hz), 132.01, 128.48, 125.92, 123.32 (d, *J* = 18.0 Hz), 122.68, 115.81 (d, *J* = 22.0 Hz), 90.76 (d, *J* = 175.3 Hz), 66.17 (d, *J* = 23.4 Hz).
^{19}F NMR (282 MHz, $CDCl_3$): δ -104.99 , -182.35.
IR (film, cm^{-1}): ν = 2952, 1720, 1601, 1506, 1488, 1270, 1133, 1088, 1088, 972, 855.
HRMS (TOF EI+): calc. for $C_{17}H_{13}BrF_2O_2$ $(M)^+$: 366.0067; found: 366.0082
HPLC: 2.5mg/mL in 50/50 IPA/Hex, 2 µL injection, 4.6 x 150mm Chiralcel OJ-3, 1 mL/min., 5% IPA in hexanes, 254 nm, major 16.62 min., minor 23.23 min., 67% *ee*

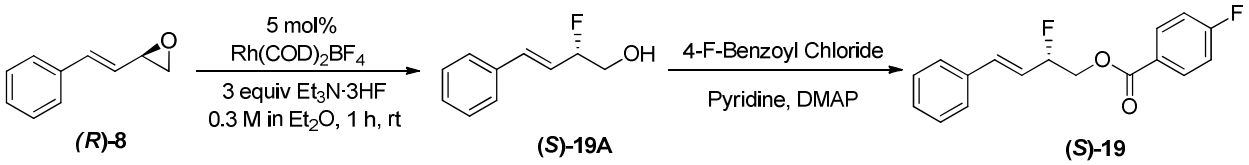
Regioselective Opening of Enantiopure Vinyl Epoxide 11 without the Rhodium Catalyst



(*S*)-**11** (>90% *ee*)
(*R*)-**22** (80% *ee*)

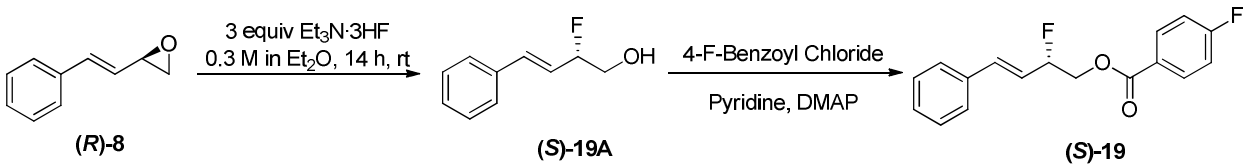
(*R*)-2-Fluorobut-3-enyl 4-fluorobenzoate
Yield: 14 % (0.2 mmol reaction)
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.12 – 8.04 (m, 2H), 7.15 – 7.08 (m, 2H), 5.94 (dddd, *J* = 17.4, 15.3, 10.8, 5.7 Hz, 1H), 5.55 – 5.48 (m, 1H), 5.39 (d, *J* = 10.8 Hz, 1H), 5.23 (dd, *J* = 48.8, 1.5 Hz, 1H), 4.55 – 4.34 (m, 2H).
^{19}F NMR (471 MHz, $CDCl_3$): δ -105.11, -186.11.
HPLC: 2.5mg/mL in 50/50 IPA/Hex, 2 µL injection, 4.6 x 150mm Chiralcel OJ-3, 1 mL/min., 1% IPA in hexanes, 254 nm, major 5.60 min., minor 6.09 min., 80 % *ee*.

Rhodium-Catalyzed Opening of Enantiopure Vinyl Epoxide 8



(*S*, *E*)-2-Fluoro-4-phenylbut-3-enyl 4-fluorobenzoate
Yield: 51 % (0.2 mmol reaction)
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 – 8.00 (m, 2H), 7.44 – 7.40 (m, 2H), 7.38 – 7.28 (m, 3H), 7.18 – 7.08 (m, 2H), 6.89 – 6.72 (m, 1H), 6.27 (ddd, *J* = 16.0, 13.2, 6.6 Hz, 1H), 5.64 – 5.16 (m, 1H), 4.80 – 4.18 (m, 2H).
^{19}F NMR (376 MHz, $CDCl_3$): δ -105.08 , -181.35.
HPLC: 2.5mg/mL in 50/50 IPA/Hex, 2 µL injection, 4.6 x 150mm Chiralcel OJ-3, 1 mL/min., 1 % IPA in hexanes, 254 nm, major 20.81 min., minor 32.61 min., 10 % *ee*.

Regioselective Opening of Enantiopure Vinyl Epoxide 8 without the Rhodium Catalyst



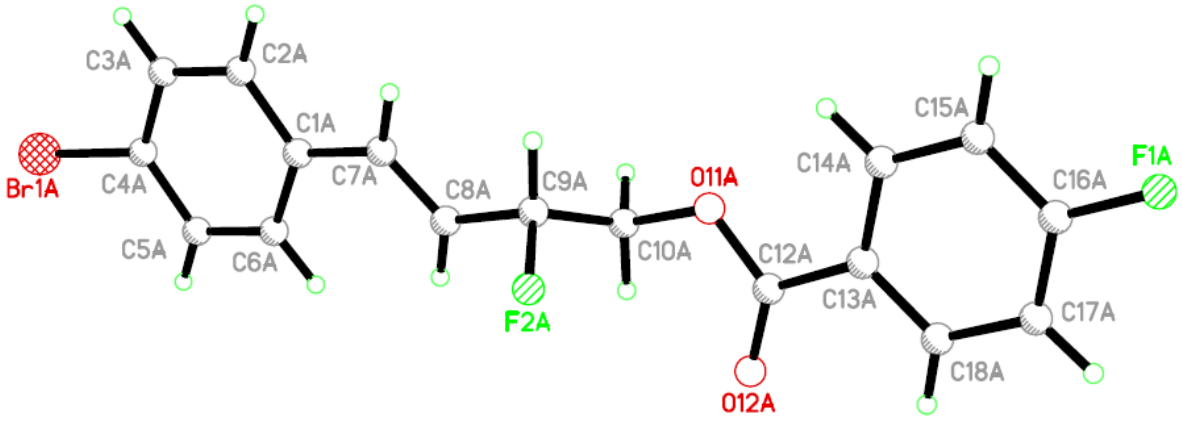
Yield: 30 % (0.2 mmol reaction)
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 – 8.00 (m, 2H), 7.44 – 7.40 (m, 2H), 7.38 – 7.28 (m, 3H), 7.18 – 7.08 (m, 2H), 6.89 – 6.72 (m, 1H), 6.27 (ddd, *J* = 16.0, 13.2, 6.6 Hz, 1H), 5.64 – 5.16 (m, 1H), 4.80 – 4.18 (m, 2H).
^{19}F NMR (376 MHz, $CDCl_3$): δ -105.08 , -181.35.
HPLC: 2.5mg/mL in 50/50 IPA/Hex, 2 µL injection, 4.6 x 150mm Chiralcel OJ-3, 1 mL/min., 1 % IPA in hexanes, 254 nm, major 20.81 min., minor 32.61 min., 13 % *ee*.

The Solid-State Structures of (*R*)-30 (Major Enantiomer) and (*S*)-30 (Minor Enantiomer)

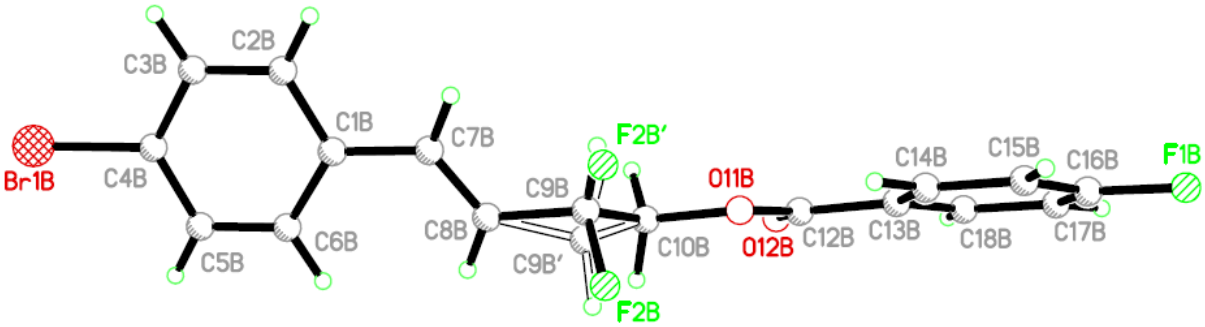
MAJOR ENANTIOMER **MINOR ENANTIOMER**

Crystallographic analysis showed that there are four different conformations for internal allylic fluoride **30**, and three conformations show enantiomeric disorder. The ratio of a major enantiomer to a minor enantiomer is about 19% (major enantiomer) to 1% (minor enantiomer). Conformer I contains only major enantiomer, (*R*)-**30**. Conformers II-IV contained both the major and minor enantiomer of **30**. *Please see Crystallographic Report Document (Word File and Cip File) for Detailed Analysis.*

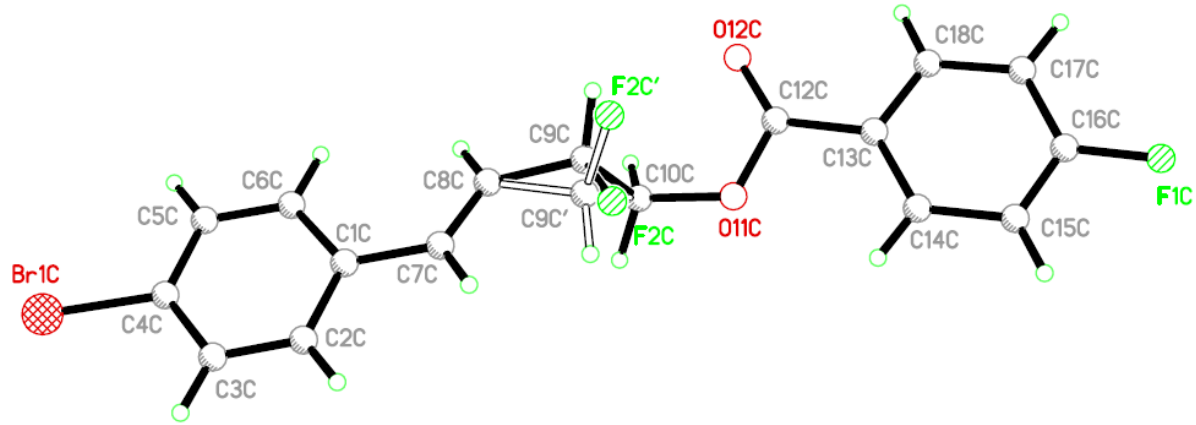
MAJOR ENANTIOMER – CONFORMATION I



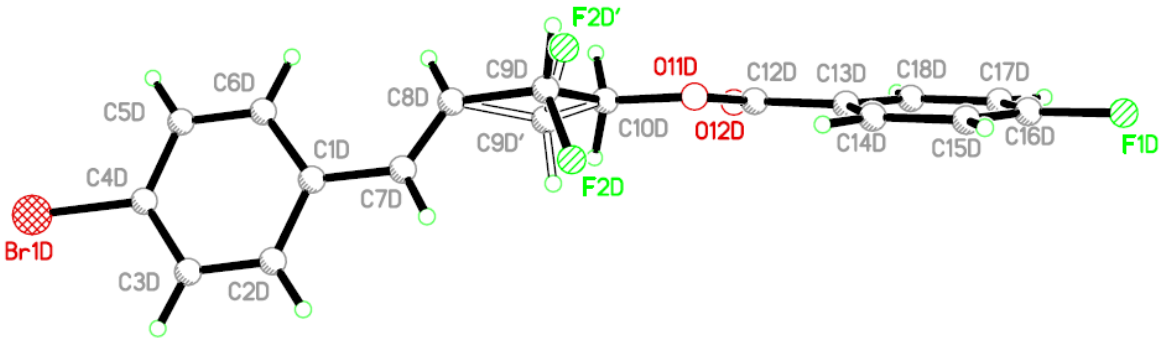
MAJOR AND MINOR ENANTIOMERS – CONFORMATION II



MAJOR AND MINOR ENANTIOMERS – CONFORMATION III



MAJOR AND MINOR ENANTIOMERS – CONFORMATION IV



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