www.sciencemag.org/cgi/content/full/science.1219274/DC1

Supplementary Materials for

Enantioselective C-H Crotylation of Primary Alcohols via Hydrohydroxyalkylation of Butadiene

Jason R. Zbieg, Eiji Yamaguchi, Emma L. McInturff, Michael J. Krische*

*To whom correspondence should be addressed. E-mail: mkrische@mail.utexas.edu

Published 22 March 2012 on *Science* Express
DOI: 10.1126/science.1219274

This PDF file includes:

- Materials and Methods
- Fig. S1
- Tables S1 to S4
- References (*34–41*)

Materials and Methods

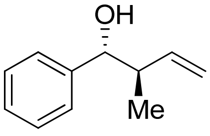
General Information

All reactions were run under an atmosphere of argon. Tetrahydrofuran (THF) and toluene were obtained from Pure-Solv MD-5 Solvent Purification System (Innovative Technology). Anhydrous solvents were transferred by oven-dried syringe. Sealed tubes (13×100 mm^2) were purchased from Fisher Scientific (catalog number 14-959-35C) and were dried in an oven overnight and cooled under a stream of argon prior to use. $RuH_2(CO)(PPh_3)_3$ were prepared according to literature procedure *(34)*. All ligands were used as received from Strem Chemicals Inc. Alcohols and aldehydes were purified by distillation or recrystallization immediately prior to use. Preparative column chromatography employing silica gel was performed according to the method of Still *(35)*. Analytical thin-layer chromatography (TLC) was carried out using 0.25 mm commercial silica gel plates (Dynamic Adsorbents F_{254}). Visualization was accomplished with UV light followed by dipping in a *p*-anisaldehyde solution and heating. Purification of reaction products was carried out by flash column chromatography using Silicycle silica gel (40-63 μm).

Spectroscopy and Spectrometry

Infrared spectra were recorded on a Thermo Nicolet 380 spectrometer. Low-resolution mass spectra (LRMS) were obtained on a Karatos MS9 and are reported as m/z (relative intensity). Accurate masses are reported for the molecular ion (M+H, M or M-H) or a suitable fragment ion. ^1H NMR spectra were recorded on a Varian Gemini (400 MHz) spectrometer at ambient temperature unless otherwise noted. Chemical shifts are reported in delta (δ) units, parts per million (ppm) downfield from trimethylsilane or ppm relative to the center of the singlet at 7.26 ppm for deuteriochloroform. Data are reported as: multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration and coupling constant(s) in Hz. ^{13}C NMR spectra were recorded on a Varian Gemini (100 MHz) spectrometer and were routinely run with broadband decoupling. Chemical shifts are reported in ppm from tetramethylsilane, with the residual solvent resonance employed as the internal standard ($CDCl_3$ at 77.0 ppm).

Experimental Details and Characterization Data



(1R,2R)-2-methyl-1-phenylbut-3-en-1-ol (3a)

From Alcohol Oxidation Level: To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stir bar was added $RuH_2(CO)(PPh_3)_3$ (13.8 mg, 0.015 mmol, 5 mol%), dppf (8.3 mg, 0.015 mmol, 5 mol%), (*R*)-phosphoric acid $\mathbf{A_9}$ (15.1 mg, 0.03 mmol, 10 mol%). The tube was sealed with a rubber septum and purged with nitrogen. Alcohol **1a** (0.031 mL, 0.30 mmol, 100 mol%) and tetrahydrofuran (0.15 mL, 2.0 M concentration with respect to alcohol) were added and the solution was cooled to -78°C. Butadiene (0.10 mL, 1.20 mmol, 400 mol%) was quickly added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 95°C (oil bath temperature) for 48 hrs, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO_2; 0-10% EtOAc/hexanes) to furnish the title compound (41.8 mg, 0.26 mmol, *anti*:*syn* = 8:1, 95:5 er) as a colorless oil in 86% yield.

From Aldehyde Oxidation Level: To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stir bar was added $RuH_2(CO)(PPh_3)_3$ (13.8 mg, 0.015 mmol, 5 mol%), dppf (8.3 mg, 0.015 mmol, 5 mol%), (*R*)-phosphoric acid $\mathbf{A_9}$ (15.1 mg, 0.03 mmol, 10 mol%). The tube was sealed with a rubber septum and purged with nitrogen. Aldehyde **2a** (0.031 mL, 0.30 mmol, 100 mol%), tetrahydrofuran (0.15 mL, 2.0 M concentration with respect to alcohol) and 1,4-butanediol (0.053 mL, 0.60 mmol, 200 mol%) were added and the solution was cooled to -78°C. Butadiene (0.10 mL, 1.20 mmol, 400 mol%) was quickly added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 95°C (oil bath temperature) for 48 hrs, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO_2; 0-10% EtOAc/hexanes) to furnish the title compound (36.2 mg, 0.22 mmol, *anti*:*syn* = 8:1, 94:6 er) as a colorless oil in 74% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26-7.38 (m, 5H), 5.86-5.76 (m, 1H), 5.24-5.17 (m, 2H), 4.35 (d, J = 8.0 Hz, 1H), 2.52-2.45 (m, 1H), 2.07 (br s, 1H), 0.87 (d, J = 6.8 Hz, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): δ 142.6, 140.9, 128.5, 127.9, 127.1, 117.1, 78.1, 46.6, 16.8.

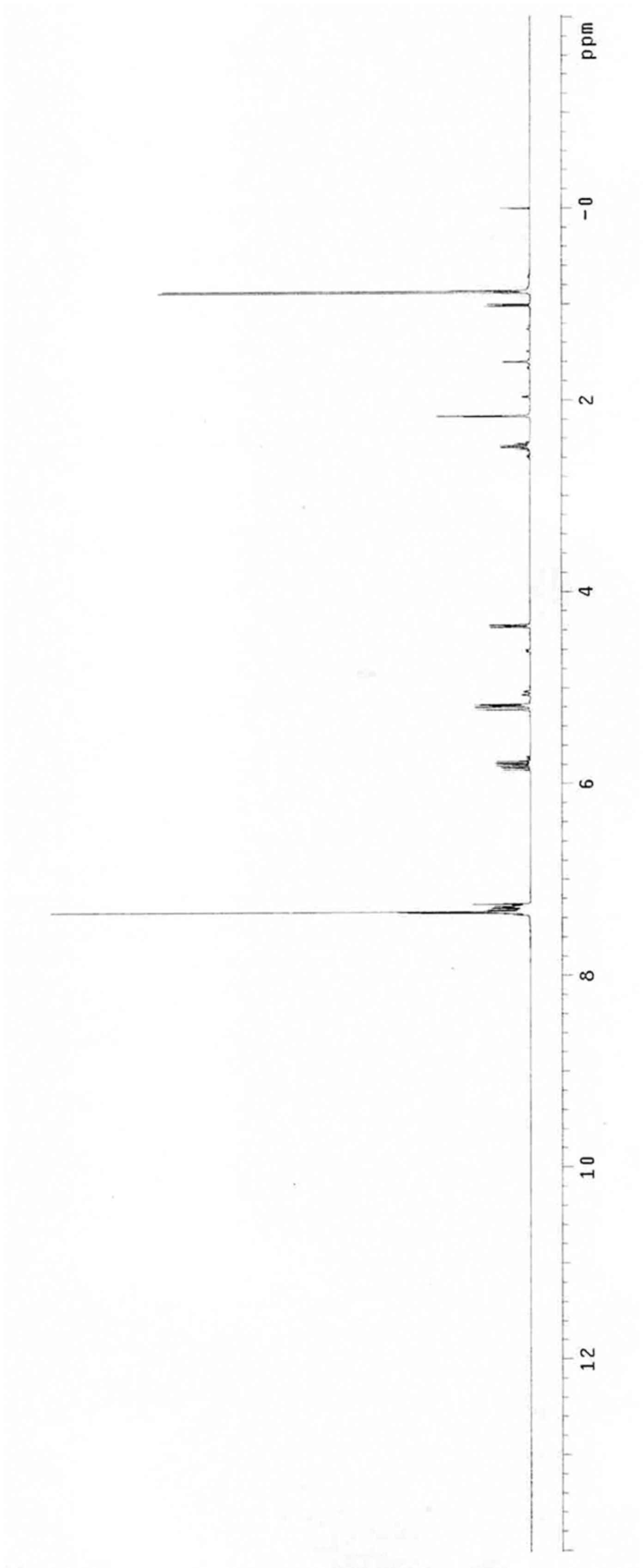
LRMS (CI+) *m/z* 145 $[M-OH]^+$

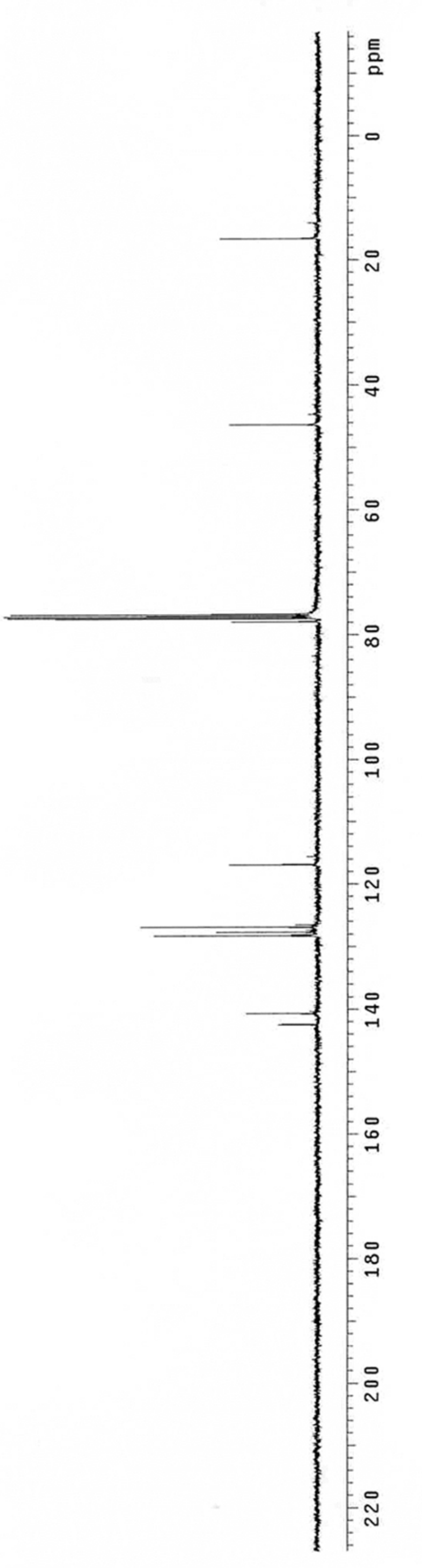
$[\alpha]_D^{25}$ = +51 (c =1.0, CH_2Cl_2).

FTIR (neat): 3411, 3064, 3029, 2964, 2927, 2356, 1940, 1638, 1493, 1453, 1416, 1372, 1261, 1195, 1075, 1018, 912, 800, 759, 700, 680 cm^{-1}.

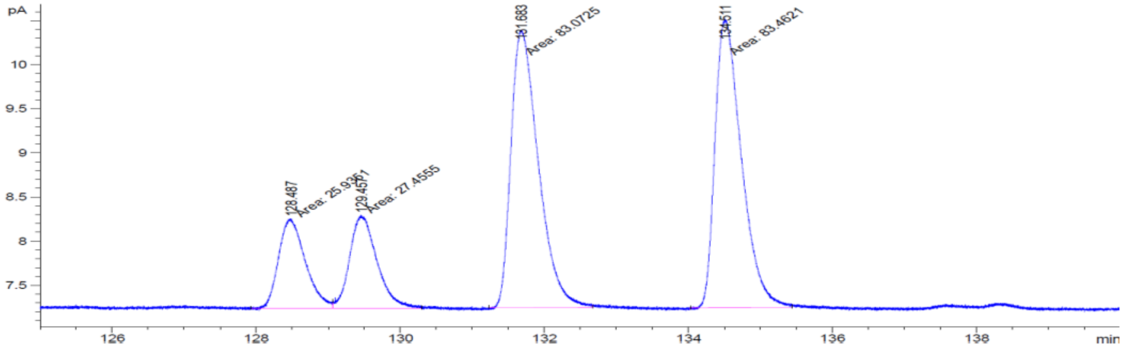
GC: Cyclosil-B: Initial temperature: 50 °C (5 min hold); 50-100 °C, rate: 0.5 °C/min (20 min hold); 100-135 °C, rate: 0.5 °C/min) t_{major} = 128.5 min, t_{minor}=129.5 min.

The spectroscopic properties of this compound were consistent with the data available in the literature *(36)*.


ppm
0
2
4
6
8
10
12

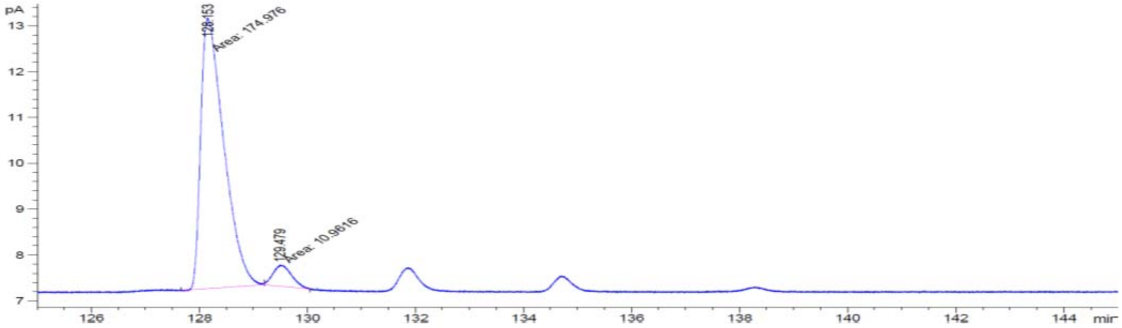

ppm
0
20
40
60
80
100
120
140
160
180
200
220

Racemic:



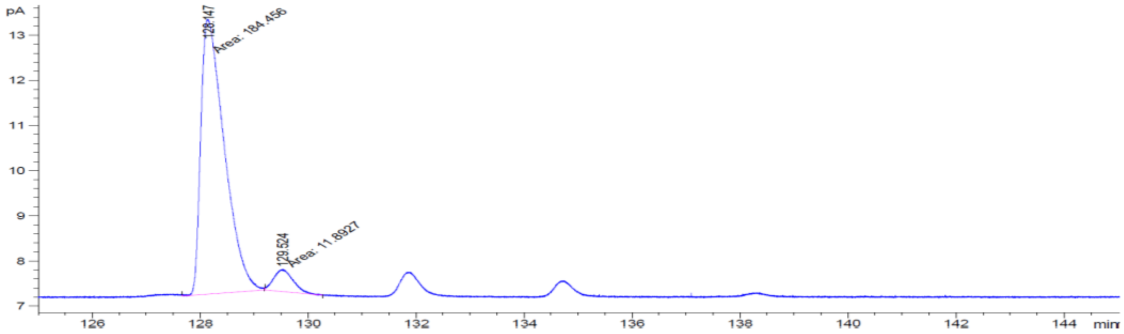
```
Signal 1: FID1 A, Front Signal

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [pA*s]      [pA]        %
----|-------|----|-------|----------|----------|--------|
   1 128.487 MM    0.4274   25.93510    1.01129 11.79269
   2 129.457 MM    0.4346   27.45553    1.05302 12.48403
   3 131.683 MM    0.4412   83.07246    3.13815 37.77306
   4 134.511 MM    0.4255   83.46207    3.26915 37.95022
```

Alcohol:

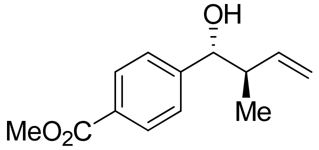


```
Peak RetTime Type  Width     Area      Height      Area
  #   [min]        [min]   [pA*s]      [pA]         %
----|-------|----|-------|----------|----------|---------|
   1 128.150 MM    0.4959  175.98094    5.91434 94.67967
   2 129.534 MM    0.3749    9.88889 4.39651e-1  5.32033
```

Aldehyde:



```
Signal 1: FID1 A, Front Signal

Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]    [pA*s]       [pA]         %
----|-------|----|-------|----------|----------|--------|
   1 128.147 MM     0.5053  184.45619    6.08412 93.94308
   2 129.524 MM     0.4021   11.89270 4.92998e-1  6.05692
```



Methyl 4-((1R,2R)-1-hydroxy-2-methylbut-3-en-1-yl)benzoate (3b)

From Alcohol Oxidation Level: To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stir bar was added $RuH_2(CO)(PPh_3)_3$ (13.8 mg, 0.015 mmol, 5 mol%), dppf (8.3 mg, 0.015 mmol, 5 mol%), (*R*)-phosphoric acid $\mathbf{A_9}$ (15.1 mg, 0.03 mmol, 10 mol%) and alcohol **1b** (49.9 mg, 0.30 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. Tetrahydrofuran (0.15 mL, 2.0 M concentration with respect to alcohol) was added and the solution was cooled to -78°C. Butadiene (0.10 mL, 1.20 mmol, 400 mol%) was quickly added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 95°C (oil bath temperature) for 48 hrs, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO_2; 0-20% EtOAc/hexanes) to furnish the title compound (52.9 mg, 0.24 mmol, *anti*:*syn* = 7:1, 94:6 er) as a colorless oil in 80% yield.

From Aldehyde Oxidation Level: To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stir bar was added $RuH_2(CO)(PPh_3)_3$ (13.8 mg, 0.015 mmol, 5 mol%), dppf (8.3 mg, 0.015 mmol, 5 mol%), (*R*)-phosphoric acid $\mathbf{A_9}$ (15.1 mg, 0.03 mmol, 10 mol%) and aldehyde **2b** (49.2 mg, 0.30 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. Tetrahydrofuran (0.15 mL, 2.0 M concentration with respect to alcohol) and 1,4-butanediol (0.053 mL, 0.60 mmol, 200 mol%) were added and the solution was cooled to -78°C. Butadiene (0.10 mL, 1.20 mmol, 400 mol%) was quickly added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 95°C (oil bath temperature) for 48 hrs, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO_2; 0-20% EtOAc/hexanes) to furnish the title compound (52.9 mg, 0.24 mmol, *anti*:*syn* = 6:1, 93:7 er) as a colorless oil in 80% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, *J* = 8.0 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 5.79-5.69 (m, 1H), 5.17-5.12 (m, 2H), 4.40 (d, *J* = 7.2 Hz, 1H), 3.88 (s, 3H), 2.49-2.36 (m, 2H), 0.86 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 147.9, 140.1, 129.7, 129.6, 127.0, 117.5, 77.3, 52.3, 46.5,16.6.

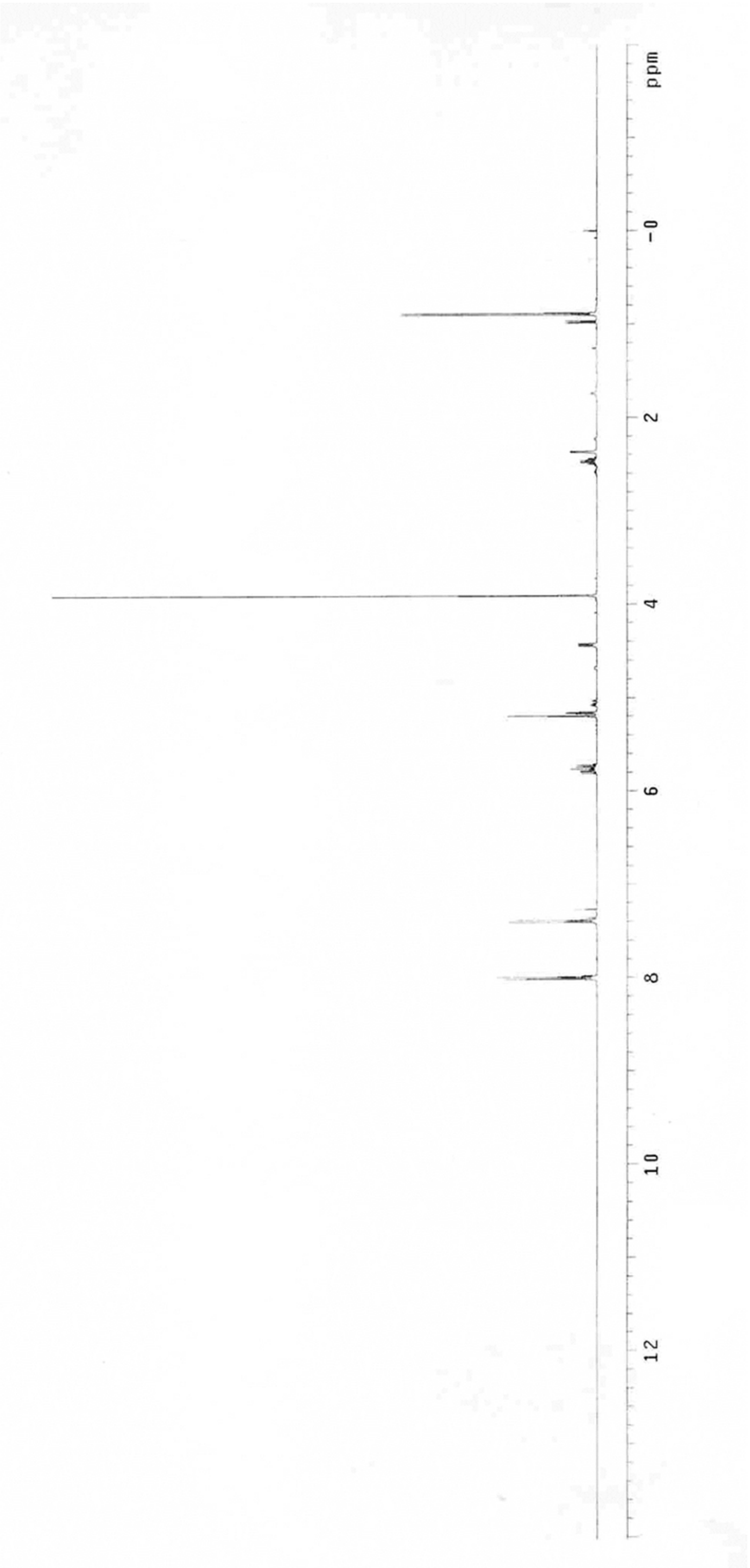
LRMS (CI+) *m/z* 221 $[M+H]^+$

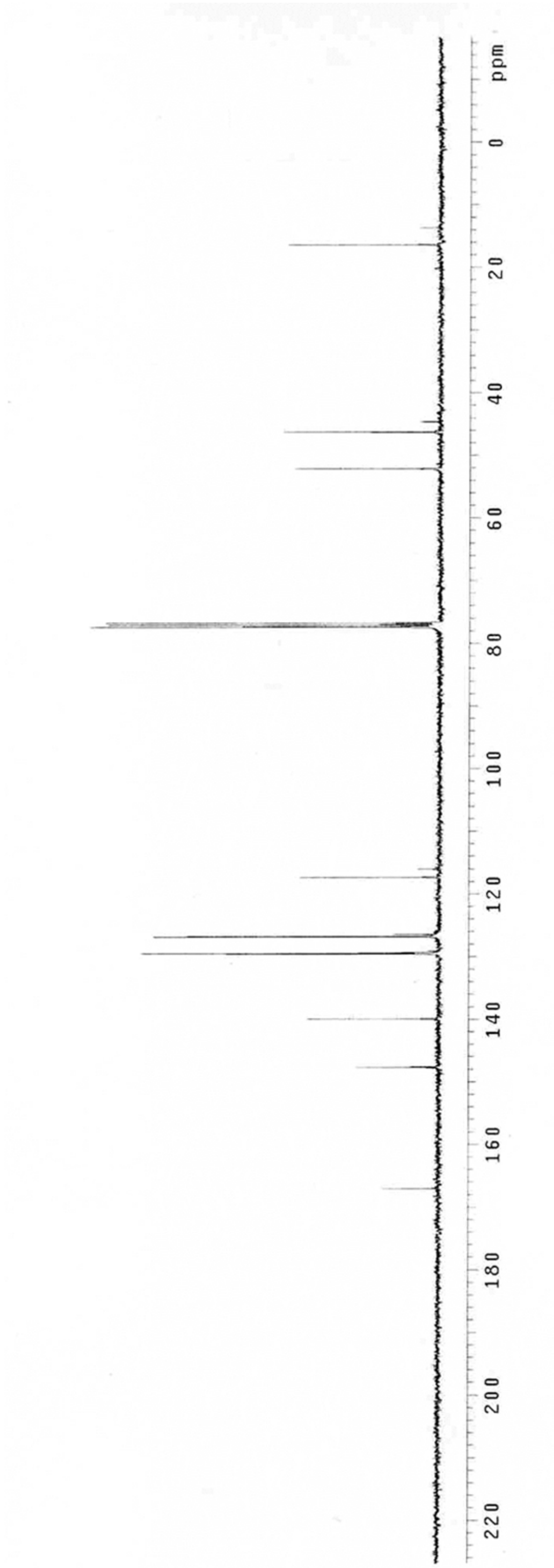
$[\alpha]_D^{25}$ = +41.4 (c =1.0, $CHCl_3$).

FTIR (neat): 3467, 2953, 1719, 1435, 1276, 1177, 1110, 1017, 915, 810, 709 cm^{-1}.

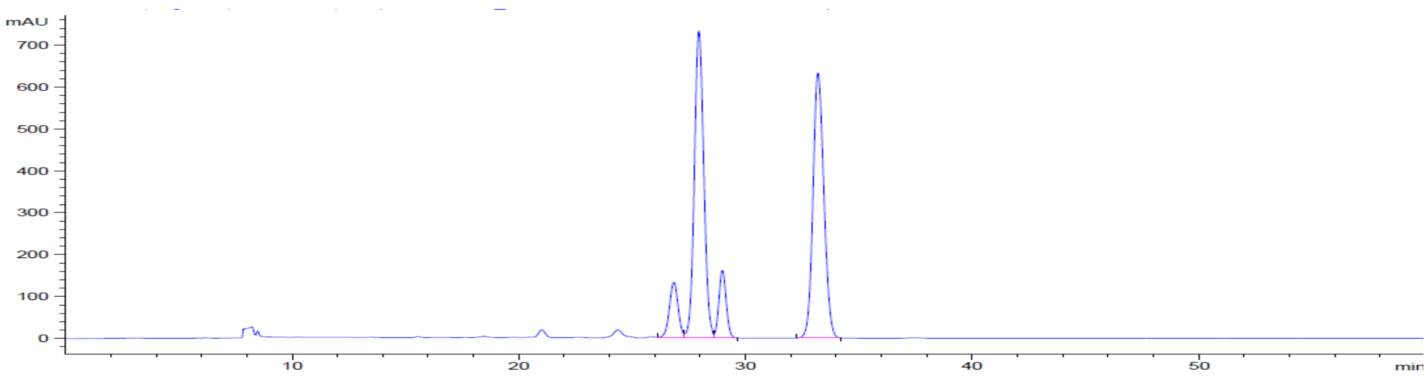
HPLC (Chiralcel AD-H column, hexanes:*i*-PrOH = 95:5, 0.5 mL/min, 230 nm), t_{major} = 27.9 min, t_{minor} = 33.2 min.

The spectroscopic properties of this compound were consistent with the data available in the literature *(37)*.


ppm
0
2
4
6
8
10
12

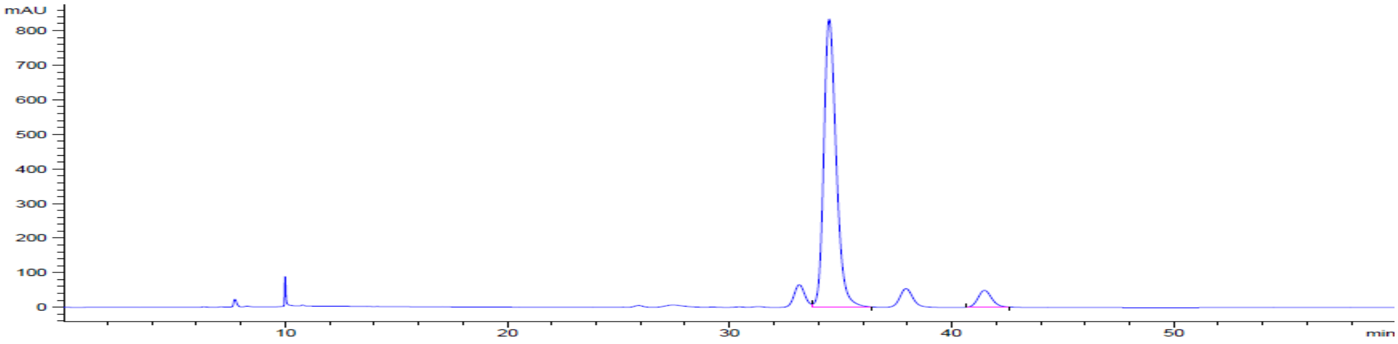

ppm
0
20
40
60
80
100
120
140
160
180
200
220

Racemic:



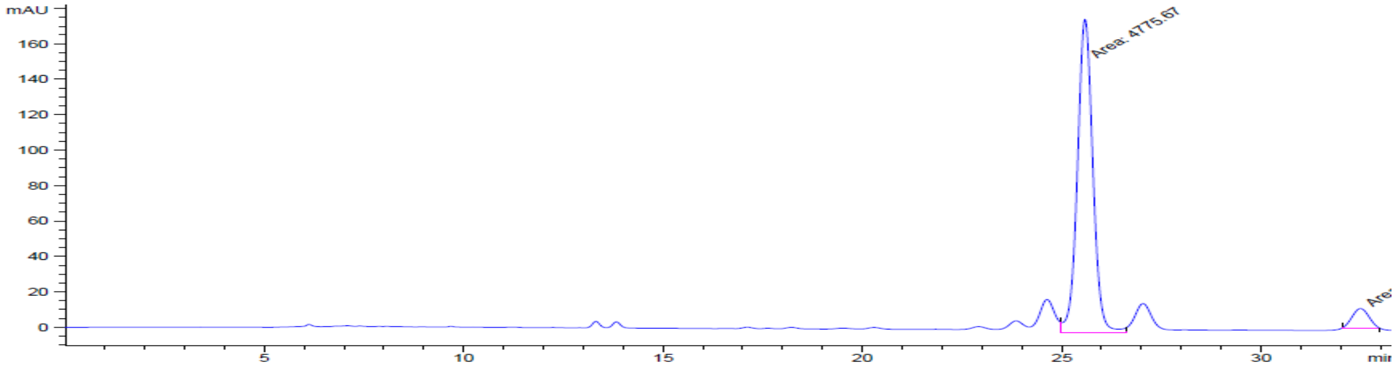
```
Signal 1: DAD1 D, Sig=230,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  26.829 VV    0.4213 3614.49023  132.89398   7.2899
   2  27.934 VV    0.4491 2.11800e4   732.98383  42.7168
   3  28.972 VB    0.3489 3641.41187  161.56358   7.3441
   4  33.189 BB    0.5157 2.11465e4   633.12537  42.6492
```

Alcohol:

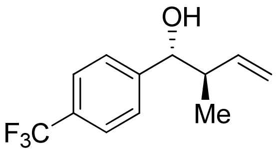


```
Signal 1: DAD1 D, Sig=230,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  34.472 VB    0.5980 3.24260e4   833.27014  93.8669
   2  41.461 BB    0.6686 2118.67383   49.17524   6.1331
```

Aldehyde:



```
Signal 1: DAD1 D, Sig=230,16 Ref=360,100

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  25.578 MM    0.4504 4775.66992  176.73450  93.3899
   2  32.485 MM    0.4940  338.02231   11.40450   6.6101
```



(1R,2R)-2-methyl-1-(4-(trifluoromethyl)phenyl)but-3-en-1-ol (3c)

From Alcohol Oxidation Level: To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stir bar was added $RuH_2(CO)(PPh_3)_3$ (13.8 mg, 0.015 mmol, 5 mol%), dppf (8.3 mg, 0.015 mmol, 5 mol%), (*R*)-phosphoric acid **A_9** (15.1 mg, 0.03 mmol, 10 mol%). The tube was sealed with a rubber septum and purged with nitrogen. Alcohol **1c** (0.041 mL, 0.30 mmol, 100 mol%) and tetrahydrofuran (0.15 mL, 2.0 M concentration with respect to alcohol) were added and the solution was cooled to -78°C. Butadiene (0.10 mL, 1.20 mmol, 400 mol%) was quickly added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 95°C (oil bath temperature) for 48 hrs, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO_2; 0-20% EtOAc/hexanes) to furnish the title compound (57.3 mg, 0.25 mmol, *anti*:*syn* = 7:1, 96:4 er) as a colorless oil in 83% yield.

From Aldehyde Oxidation Level: To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stir bar was added $RuH_2(CO)(PPh_3)_3$ (13.8 mg, 0.015 mmol, 5 mol%), dppf (8.3 mg, 0.015 mmol, 5 mol%), (*R*)-phosphoric acid **A_9** (15.1 mg, 0.03 mmol, 10 mol%). The tube was sealed with a rubber septum and purged with nitrogen. Aldehyde **3a** (0.041 mL, 0.30 mmol, 100 mol%), tetrahydrofuran (0.15 mL, 2.0 M concentration with respect to alcohol) and 1,4-butanediol (0.053 mL, 0.60 mmol, 200 mol%) were added and the solution was cooled to -78°C. Butadiene (0.10 mL, 1.20 mmol, 400 mol%) was quickly added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 95°C (oil bath temperature) for 48 hrs, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO_2; 0-10% EtOAc/hexanes) to furnish the title compound (43.6 mg, 0.19 mmol, *anti*:*syn* = 6:1, 94:6 er) as a colorless oil in 63% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, *J* = 8.0 Hz, 2H), 7.44 (d, *J* = 8.0 Hz, 2H), 5.81-5.72 (m, 1H), 5.23-5.18 (m, 2H), 4.43 (dd, *J* = 7.2 Hz, 2.6Hz, 1H), 2.51-2.42 (m, 1H), 2.26 (d, *J* = 2.6Hz, 1H) 0.89 (d, *J* = 6.8 Hz, 3H).

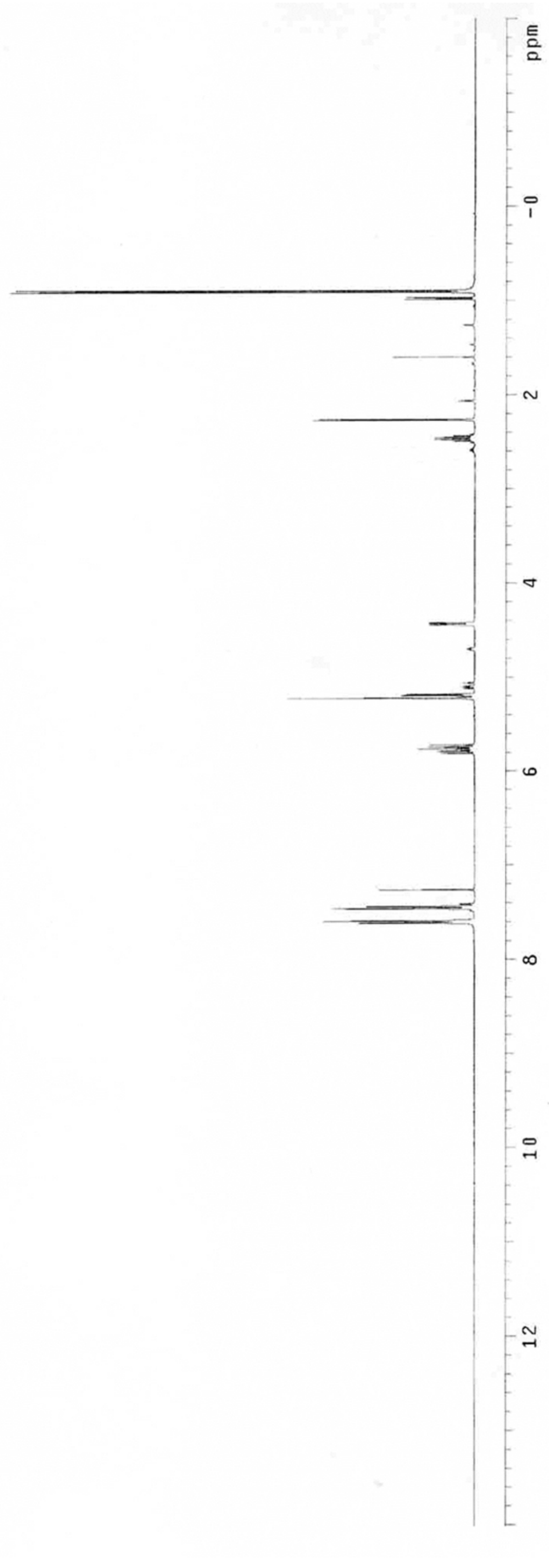
^{13}C NMR (100 MHz, $CDCl_3$): δ 146.3, 139.8, 129.7 (q, J = 32 Hz), 127.1, 125.2 (q, J = 3.7 Hz), 124.0 (q, J = 271 Hz), 117.6, 77.2, 46.4, 16.4 ppm.

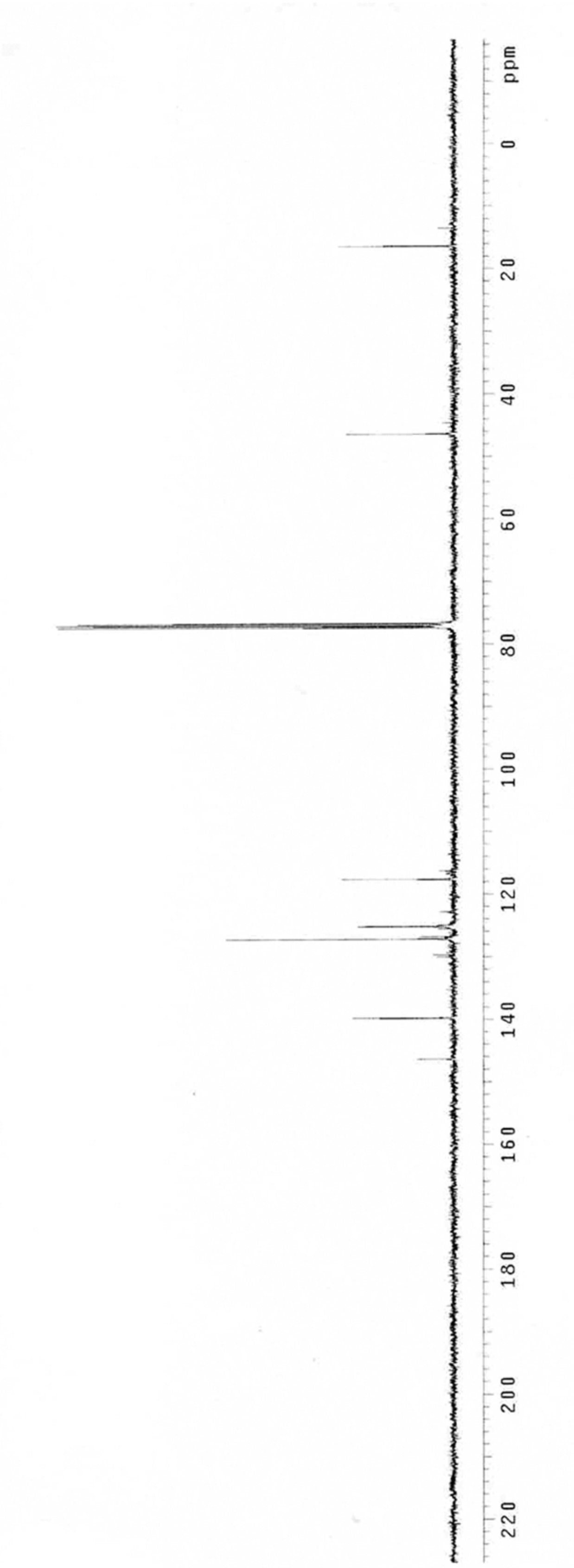
LRMS (CI+) *m/z* 213 $[M\text{-}OH]^+$

$[\alpha]_D^{25}$ = +52 (c =1.0, $CHCl_3$) reported for 92% ee of the *(R,R)* compound $[\alpha]_D^{25}$ = +55 (c =1.0, $CHCl_3$).

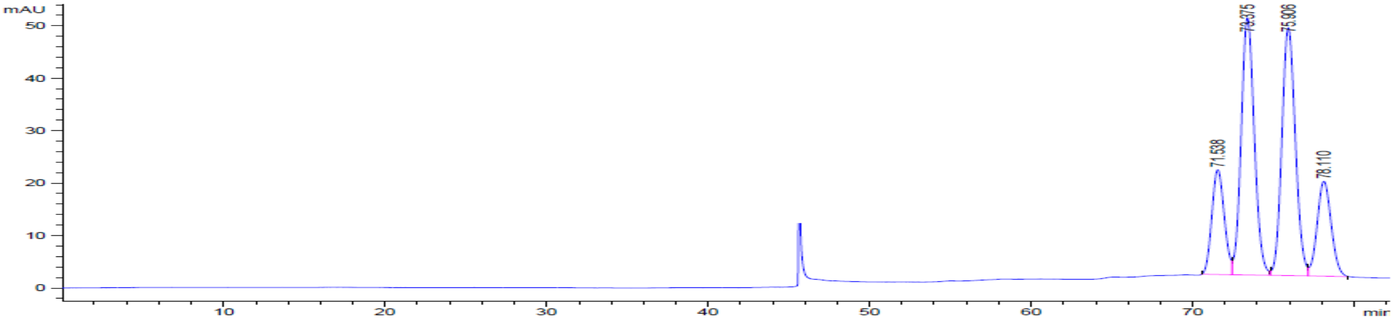
FTIR (neat): 3380, 2976, 1620, 1458, 1418, 1323, 1162, 1120, 1066, 1016, 917, 831, 763, 741, 684 cm^{-}

HPLC (Compound **3c** was converted to the 4-nitro-benzoate for analysis, Chiralcel OD-H/OD-H/OD-H column, hexanes:*i*-PrOH = 97:3, 0.3 mL/min, 254 nm), t_{major} = 71.5 min, t_{minor} = 75.9 min
The spectroscopic properties of this compound were consistent with the data available in the literature *(38).*


12
10
8
6
4
2
0
ppm

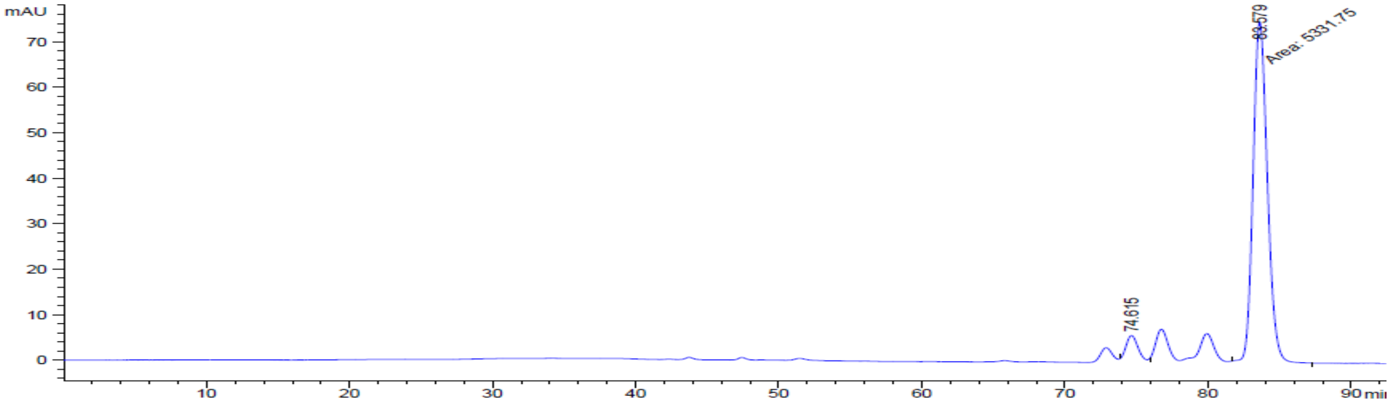

ppm
0
20
40
60
80
100
120
140
160
180
200
220

Racemic:



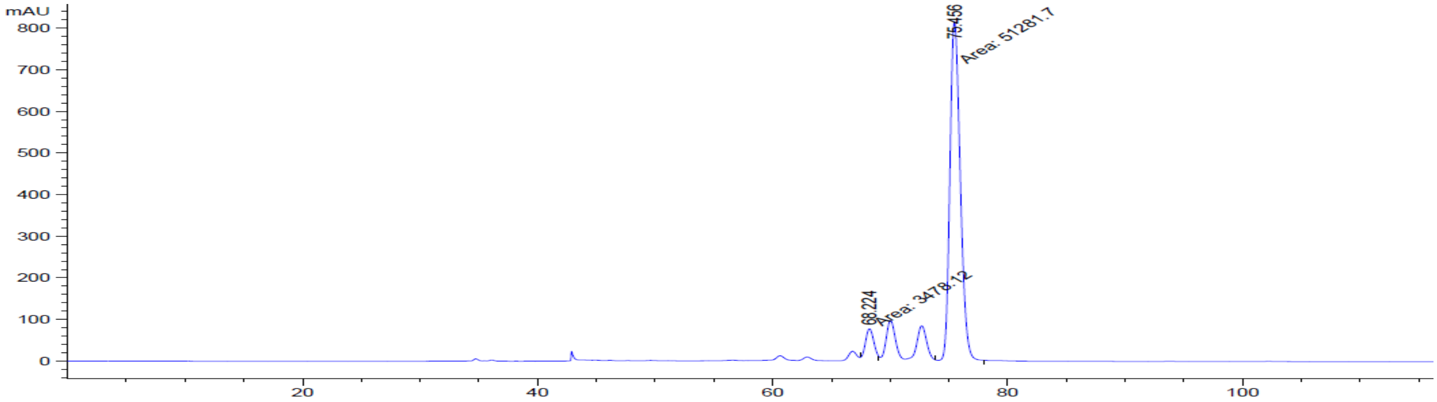
```
Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak RetTime Type  Width     Area       Height      Area
  #    [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  71.538 BV    0.8227 1070.34790   19.99071  13.8908
   2  73.375 VB    0.8762 2782.27124   49.01735  36.1078
   3  75.906 BV    0.9000 2755.28467   47.27272  35.7575
   4  78.110 VB    0.9231 1097.55933   18.10957  14.2439
```

Alcohol:

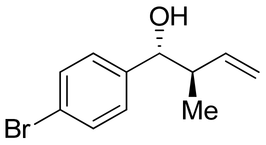


```
Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak RetTime Type  Width     Area       Height      Area
  #    [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  74.615 BB    0.6295  251.10977    5.02046   4.4979
   2  83.579 MM    1.1806 5331.75098   75.27206  95.5021
```

Aldehyde:



```
Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  68.224 MM     0.8067 3478.12378   71.85876   6.3516
   2  75.456 MM     1.0425 5.12817e4   819.85419  93.6484
```



(1R,2R)-1-(4-bromophenyl)-2-methylbut-3-en-1-ol (3d)

From Alcohol Oxidation Level: To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stir bar was added $RuH_2(CO)(PPh_3)_3$ (13.8 mg, 0.015 mmol, 5 mol%), dppf (8.3 mg, 0.015 mmol, 5 mol%), (*R*)-phosphoric acid $\mathbf{A_9}$ (15.1 mg, 0.03 mmol, 10 mol%) and alcohol **1d** (56.1 mg, 0.30 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. Tetrahydrofuran (0.15 mL, 2.0 M concentration with respect to alcohol) was added and the solution was cooled to -78°C. Butadiene (0.10 mL, 1.20 mmol, 400 mol%) was quickly added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 95°C (oil bath temperature) for 48 hrs, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO_2; 0-20% EtOAc/hexanes) to furnish the title compound (70.2 mg, 0.29 mmol, *anti*:*syn* = 5:1, 93:7 er) as a colorless oil in 83% yield.

From Aldehyde Oxidation Level: To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stir bar was added $RuH_2(CO)(PPh_3)_3$ (13.8 mg, 0.015 mmol, 5 mol%), dppf (8.3 mg, 0.015 mmol, 5 mol%), (*R*)-phosphoric acid $\mathbf{A_9}$ (15.1 mg, 0.03 mmol, 10 mol%) and aldehyde **2d** (55.5 mg, 0.30 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. Tetrahydrofuran (0.15 mL, 2.0 M concentration with respect to alcohol) and 1,4-butanediol (0.053 mL, 0.60 mmol, 200 mol%) were added and the solution was cooled to -78°C. Butadiene (0.10 mL, 1.20 mmol, 400 mol%) was quickly added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 95°C (oil bath temperature) for 48 hrs, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO_2; 0-20% EtOAc/hexanes) to furnish the title compound (58.7 mg, 0.24 mmol, *anti*:*syn* = 5:1, 93:7 er) as a colorless oil in 81% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 5.81-5.71 (m,1H), 5.22-5.16 (m, 2H), 4.32 (d, *J* = 7.6 Hz, 1H), 2.45-2.37 (m, 1H), 2.20 (s, 1H), 0.87 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 141.4, 140.1, 131.3, 128.6, 121.4, 117.3, 77.1, 46.4, 16.4 ppm.

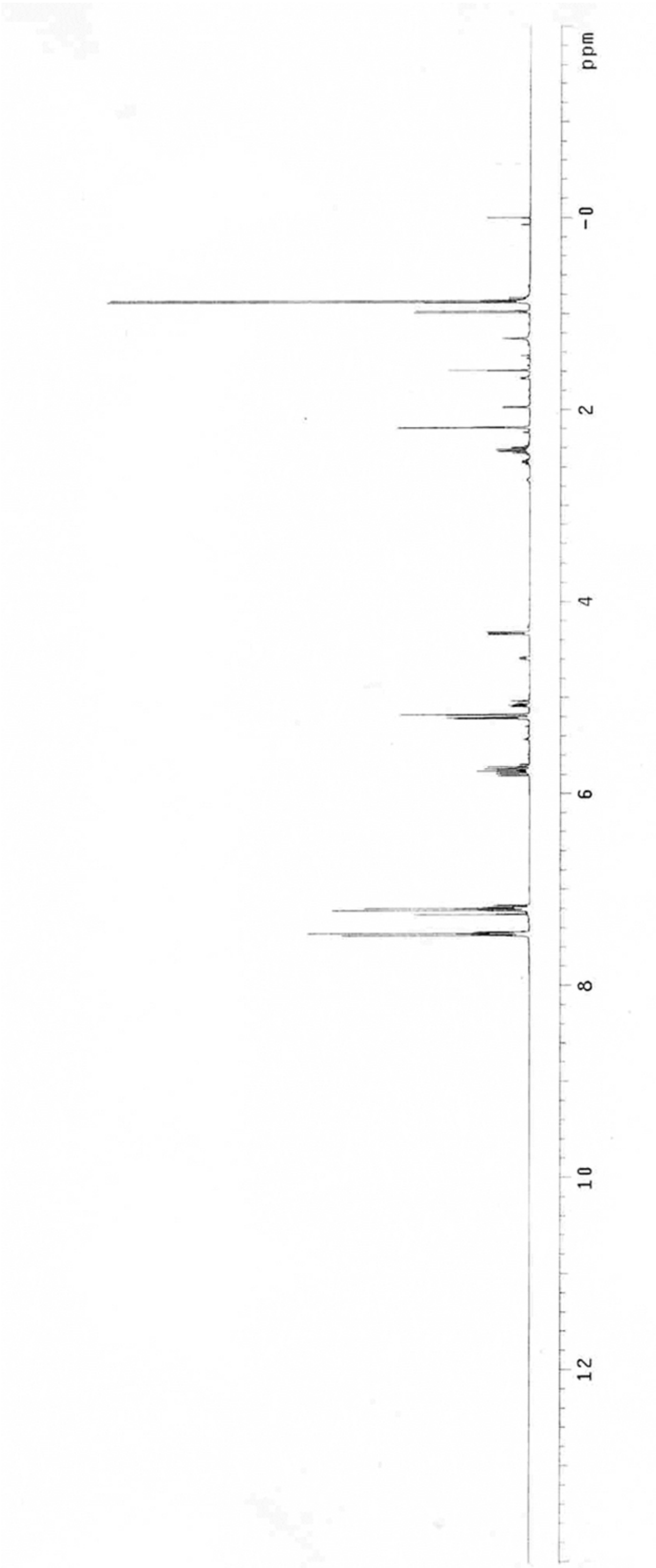
LRMS (CI+). *m/z* 223 $[M\text{-}OH]^+$

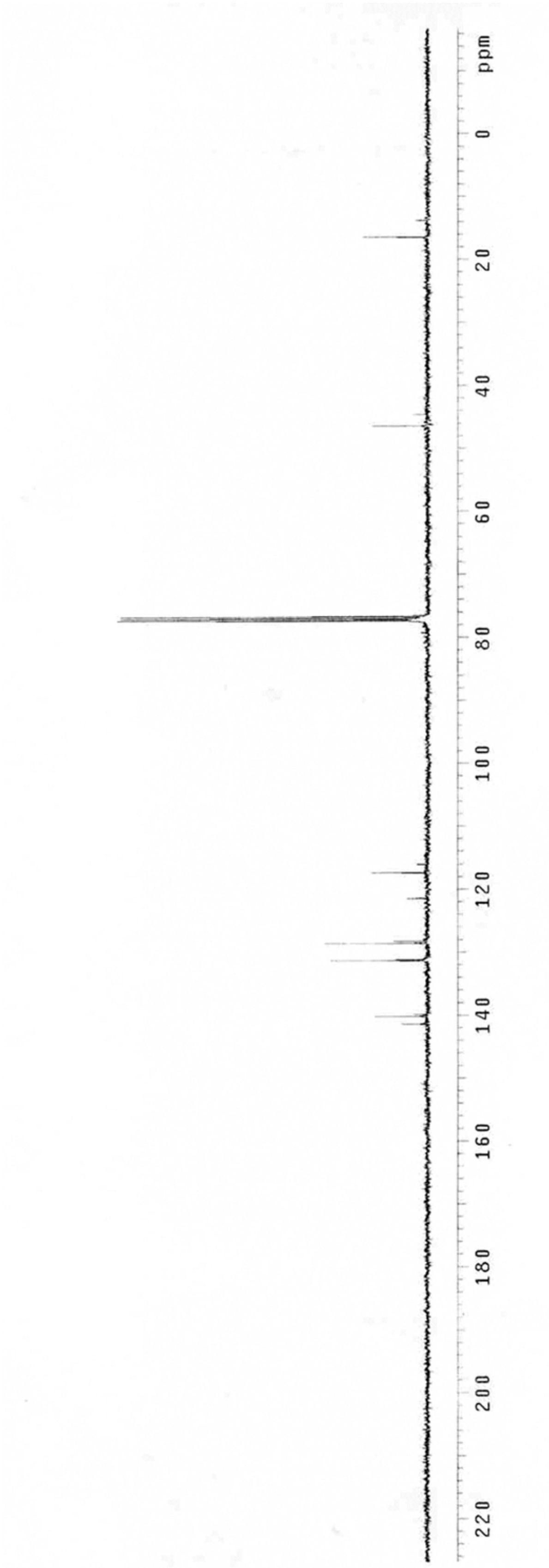
$[\alpha]_D^{25}$ = +53 (c =1.0, $CHCl_3$).

FTIR (neat): 3404, 2972, 2928, 1486, 1070, 1009, 916, 817, 755, 666 cm^{-1}.

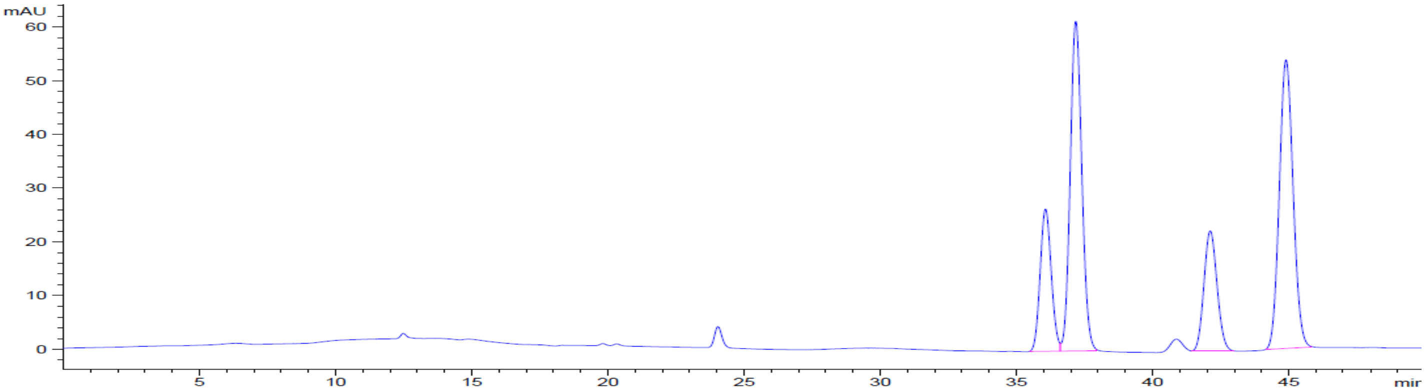
HPLC (Chiralcel AS-H/AS-H column, hexanes:*i*-PrOH = 98.5:1.5, 0.5 mL/min, 230 nm), t_{major} = 36.1 min, t_{minor} = 42.1 min.

The spectroscopic properties of this compound were consistent with the data available in the literature *(37)*.


ppm
0
2
4
6
8
10
12

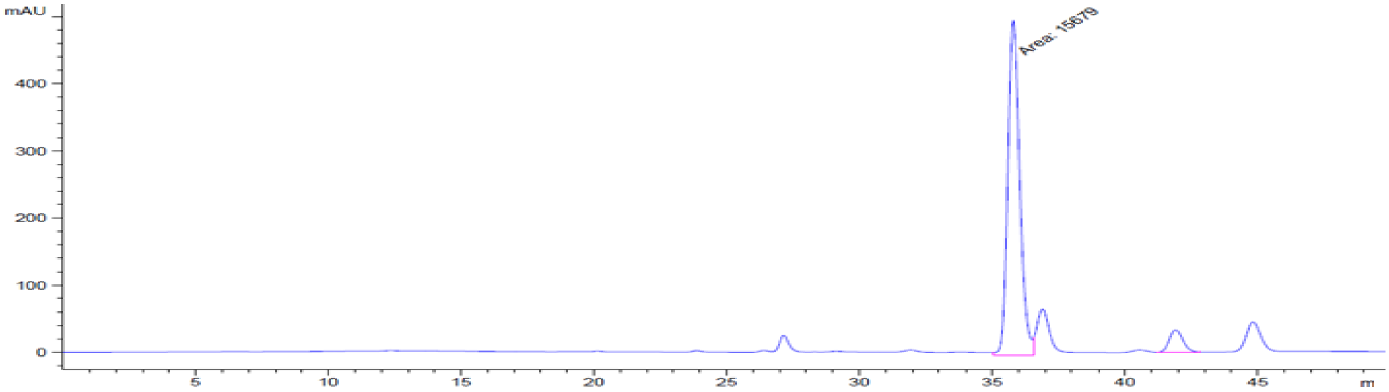

220
200
180
160
140
120
100
80
60
40
20
0
ppm

Racemic:



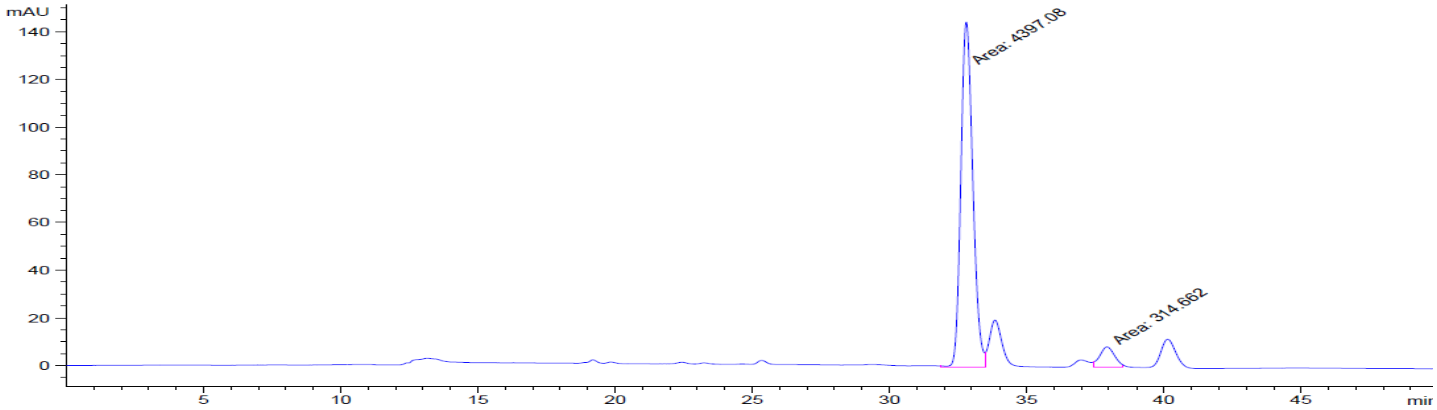
```
Signal 1: DAD1 D, Sig=230,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]         [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  36.059 BV    0.4445  755.69861   26.51514  14.4623
   2  37.171 VB    0.4590 1816.62524   61.43822  34.7659
   3  42.107 VB    0.5178  753.44275   22.43484  14.4191
   4  44.890 BB    0.5520 1899.53650   53.78403  36.3527
```

Alcohol:

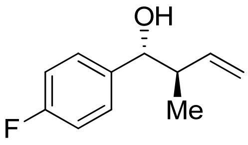


```
Signal 1: DAD1 D, Sig=230,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]         [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  35.784 MM    0.5248 1.56790e4  497.92374  92.9868
   2  41.902 VB    0.5521 1182.53137   33.47377   7.0132
```

Aldehyde:



```
Signal 1: DAD1 D, Sig=230,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  32.791 MM     0.5067 4397.08496  144.62340  93.3218
   2  37.920 MM     0.6218  314.66193    8.43464   6.6782
```



(1R,2R)-1-(4-fluorophenyl)-2-methylbut-3-en-1-ol (3e)

From Alcohol Oxidation Level: To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stir bar was added $RuH_2(CO)(PPh_3)_3$ (13.8 mg, 0.015 mmol, 5 mol%), dppf (8.3 mg, 0.015 mmol, 5 mol%), (*R*)-phosphoric acid $\mathbf{A_9}$ (15.1 mg, 0.03 mmol, 10 mol%). The tube was sealed with a rubber septum and purged with nitrogen. Alcohol **1e** (0.033 mL, 0.30 mmol, 100 mol%) and tetrahydrofuran (0.15 mL, 2.0 M concentration with respect to alcohol) were added and the solution was cooled to -78°C. Butadiene (0.10 mL, 1.20 mmol, 400 mol%) was quickly added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 95°C (oil bath temperature) for 48 hrs, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO_2; 0-20% EtOAc/hexanes) to furnish the title compound (45.8 mg, 0.26 mmol, *anti*:*syn* = 6:1, 93:7 er) as a colorless oil in 85% yield.

From Aldehyde Oxidation Level: To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stir bar was added $RuH_2(CO)(PPh_3)_3$ (13.8 mg, 0.015 mmol, 5 mol%), dppf (8.3 mg, 0.015 mmol, 5 mol%), (*R*)-phosphoric acid $\mathbf{A_9}$ (15.1 mg, 0.03 mmol, 10 mol%). The tube was sealed with a rubber septum and purged with nitrogen. Aldehyde **2e** (0.032 mL, 0.30 mmol, 100 mol%), tetrahydrofuran (0.15 mL, 2.0 M concentration with respect to alcohol) and 1,4-butanediol (0.053 mL, 0.60 mmol, 200 mol%) were added and the solution was cooled to -78°C. Butadiene (0.10 mL, 1.20 mmol, 400 mol%) was quickly added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 95°C (oil bath temperature) for 48 hrs, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO_2; 0-20% EtOAc/hexanes) to furnish the title compound (43.2 mg, 0.24 mmol, *anti*:*syn* = 5:1, 94:6 er) as a colorless oil in 80% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31-7.26 (m, 2H), 7.05-7.00 (m, 2H), 5.82-5.73 (m,1H), 5.22-5.17 (m, 2H), 4.33 (dd, *J* = 7.6 Hz, 2.4 Hz, 1H), 2.47-2.38 (m, 1H), 2.24 (d, *J* = 2.4 Hz, 1H), 0.85 (d, *J* = 6.8 Hz, 3H).

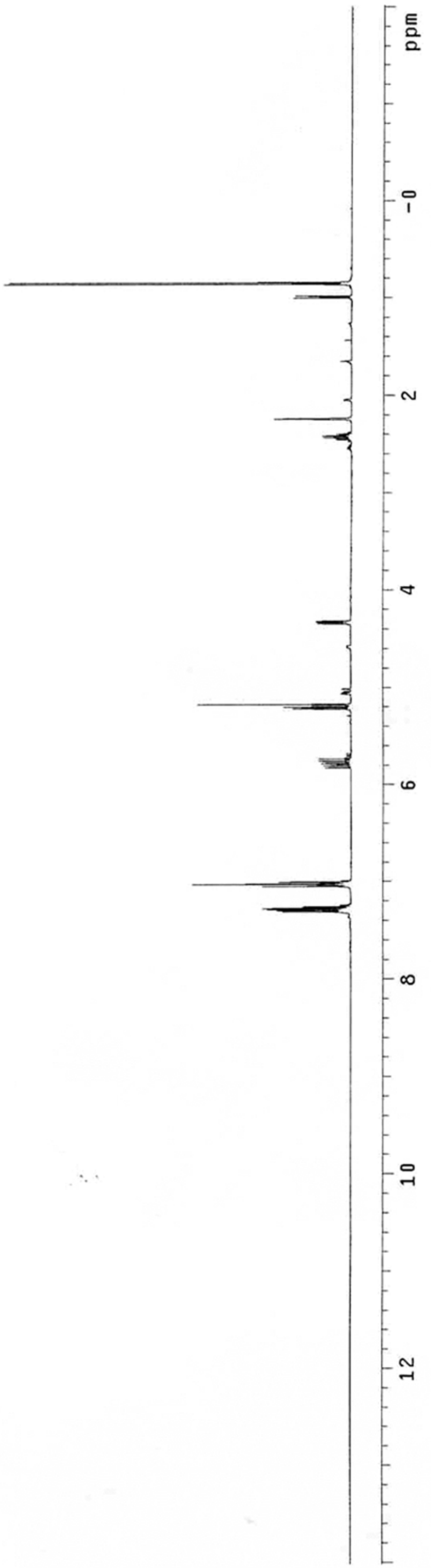
^{13}C NMR (100 MHz, $CDCl_3$): δ 162.3 (d, 244.0 Hz), 140.4, 138.1 (d, 3.0 Hz), 128.4 (d, 8.2 Hz), 117.1, 115.0 (d, 21.6 Hz), 77.1, 46.5, 16.5 ppm.

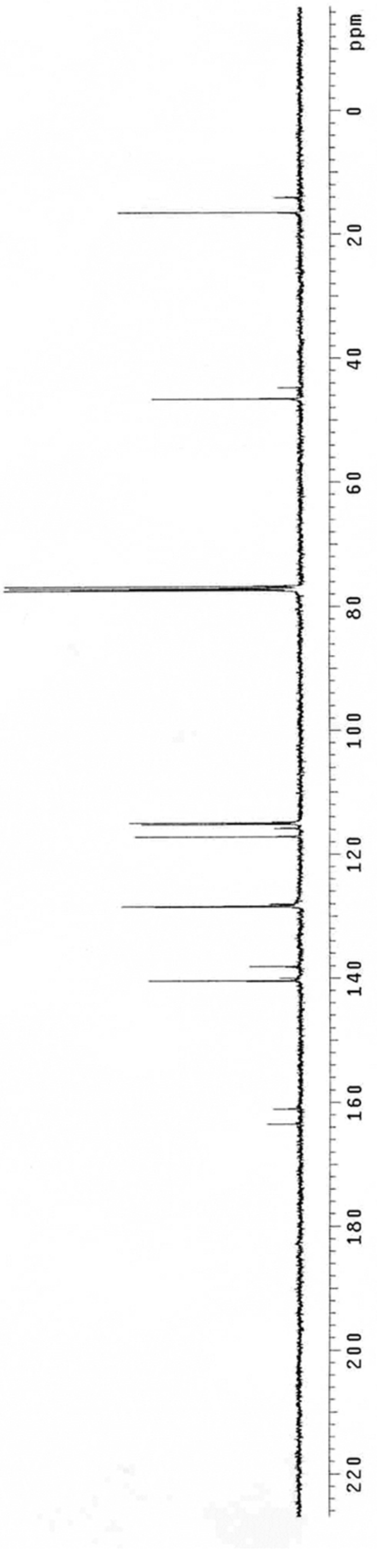
LRMS (CI+). *m/z* 181 $[M+H]^+$

$[\alpha]_D^{25}$ = +56.6 (c =1.0, $CHCl_3$).

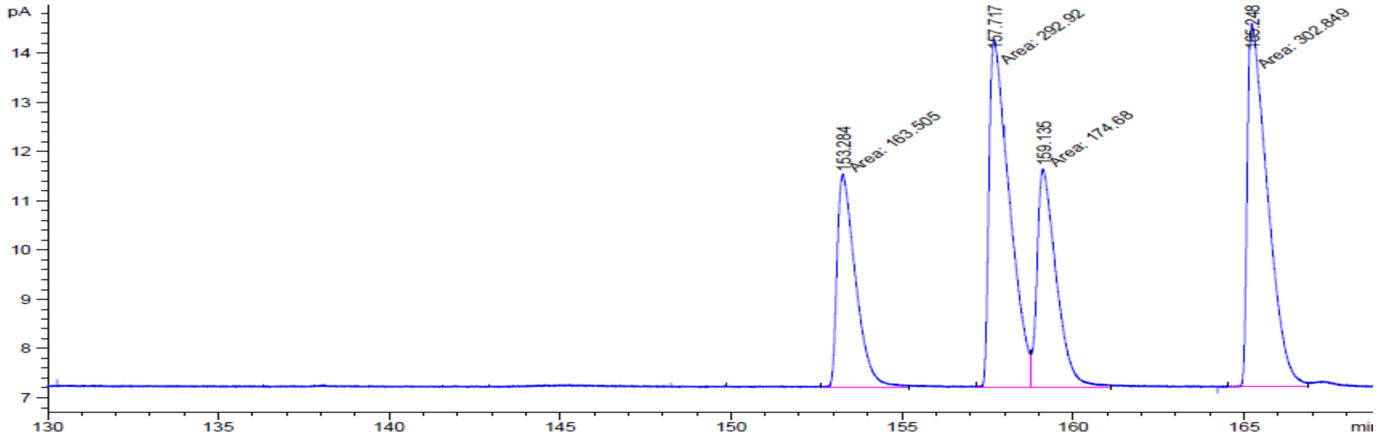
FTIR (neat): 3411 3412, 2975, 1634, 1603, 1509, 1417, 1220, 1157, 1012, 829, 676 cm^{-1}.

GC: Cyclosil-B: Initial temperature: 50 °C (5 min hold); 50-100 °C, rate: 0.4 °C/min (25 min hold); 100-150 °C, rate: 0.4 °C/min) t_{major} = 153.2 min, t_{minor}=159.1 min.


12
10
8
6
4
2
0
ppm

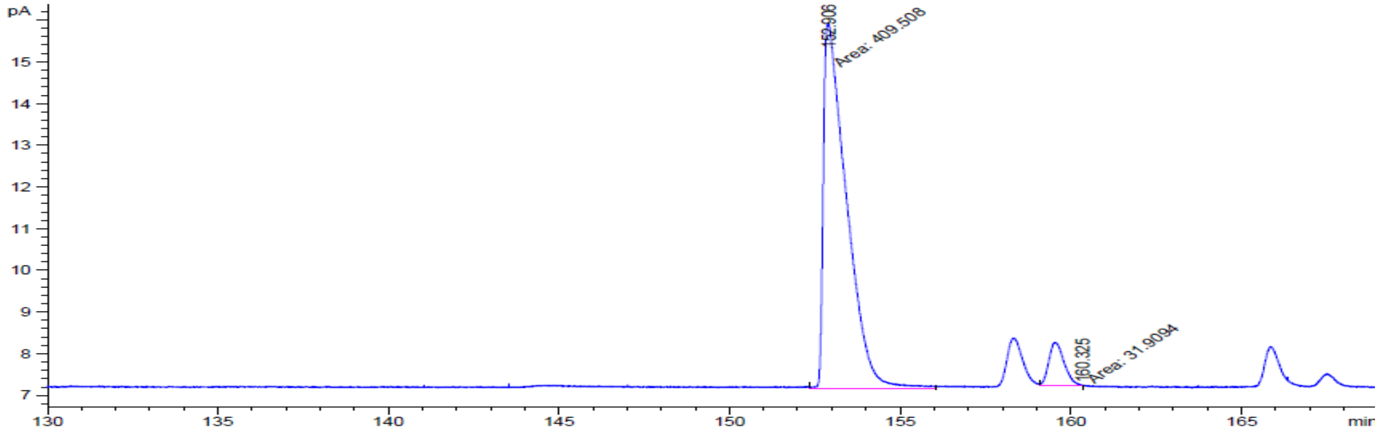

ppm
0
20
40
60
80
100
120
140
160
180
200
220

Racemic:



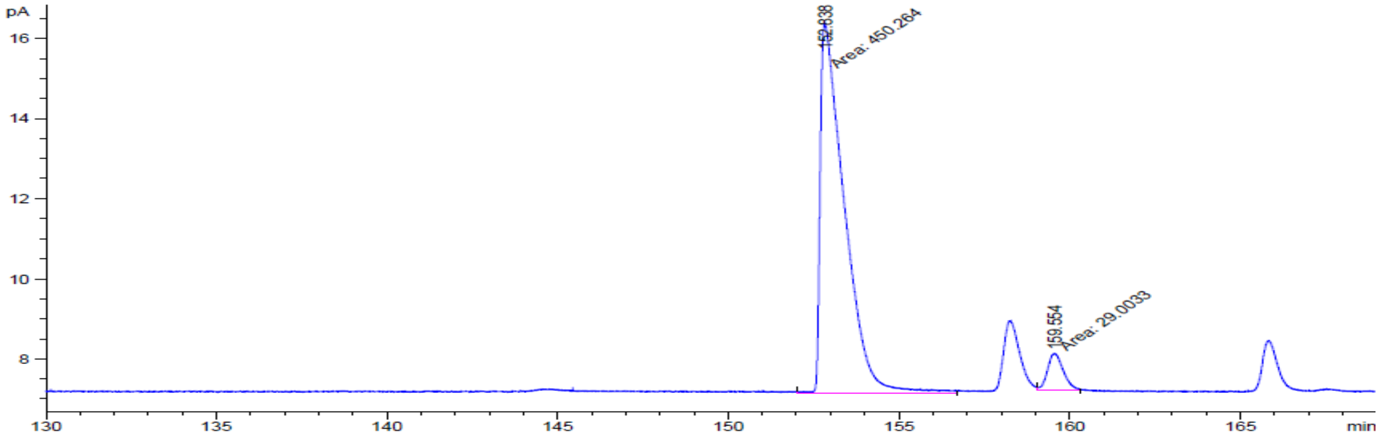
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]         [min]   [pA*s]     [pA]         %
----|-------|----|-------|----------|----------|--------|
   1 153.284 MM    0.6296  163.50467    4.32844 17.50671
   2 157.717 MM    0.6907  292.92029    7.06814 31.36345
   3 159.135 MM    0.6552  174.67986    4.44339 18.70326
   4 165.248 MM    0.6844  302.84937    7.37467 32.42658
```

Alcohol:

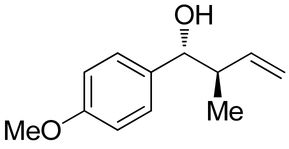


```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]         [min]   [pA*s]     [pA]         %
----|-------|----|-------|----------|----------|--------|
   1 152.906 MM    0.7791  409.50766    8.75974 92.77114
   2 160.325 MM N  0.0000   31.90941 5.93895e-3  7.22886
```

Aldehyde:



```
Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [pA*s]       [pA]         %
----|-------|----|-------|----------|----------|--------|
   1 152.838 MM    0.8133  450.26407    9.22715 93.94842
   2 159.554 MM    0.5249   29.00325 9.20927e-1  6.05158
```



(1R,2R)-1-(4-methoxyphenyl)-2-methylbut-3-en-1-ol

From Alcohol Oxidation Level: To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stir bar was added $RuH_2(CO)(PPh_3)_3$ (13.8 mg, 0.015 mmol, 5 mol%), dppf (8.3 mg, 0.015 mmol, 5 mol%), (*R*)-phosphoric acid $\mathbf{A_9}$ (15.1 mg, 0.03 mmol, 10 mol%) and alcohol **1f** (37.2 µL, 0.30 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. Tetrahydrofuran (0.15 mL, 2.0 M concentration with respect to alcohol) was added and the solution was cooled to -78°C. Butadiene (0.10 mL, 1.20 mmol, 400 mol%) was quickly added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 95°C (oil bath temperature) for 48 hrs, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO_2; 0-20% EtOAc/hexanes) to furnish the title compound (41.7 mg, 0.22 mmol, *anti*:*syn* = 6:1, 93:7 er) as a colorless oil in 72% yield.

From Aldehyde Oxidation Level: To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stir bar was added $RuH_2(CO)(PPh_3)_3$ (13.8 mg, 0.015 mmol, 5 mol%), dppf (8.3 mg, 0.015 mmol, 5 mol%), (*R*)-phosphoric acid $\mathbf{A_9}$ (15.1 mg, 0.03 mmol, 10 mol%) and aldehyde **2f** (36.5 µL, 0.30 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. Tetrahydrofuran (0.15 mL, 2.0 M concentration with respect to alcohol) and 1,4-butanediol (0.053 mL, 0.60 mmol, 200 mol%) were added and the solution was cooled to -78°C. Butadiene (0.10 mL, 1.20 mmol, 400 mol%) was quickly added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 95°C (oil bath temperature) for 48 hrs, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO_2; 0-20% EtOAc/hexanes) to furnish the title compound (38.1 mg, 0.20 mmol, *anti*:*syn* = 6:1, 94:6 er) as a colorless oil in 66% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 (d, J = 7.8 Hz, 2H), 6.88 (d, J = 7.8 Hz, 2H), 5.86-5.77 (m, 1H), 5.29-5.16 (m, 2H), 4.30 (d, J = 8.0 Hz, 1H), 3.80 (s, 3H), 2.50-2.41 (m, 1H), 2.15 (s, 1H), 0.85 (d, J = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 159.1, 141.0, 134.6, 128.0, 116.7, 113.6, 77.5, 55.3, 46.4, 16.6 ppm.

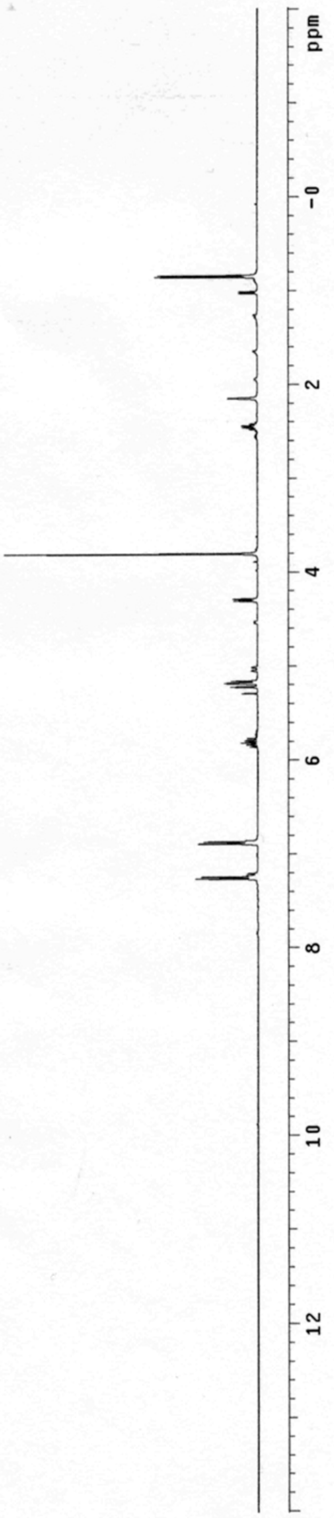
LRMS (CI+). *m/z* 193 $[M+H]^+$

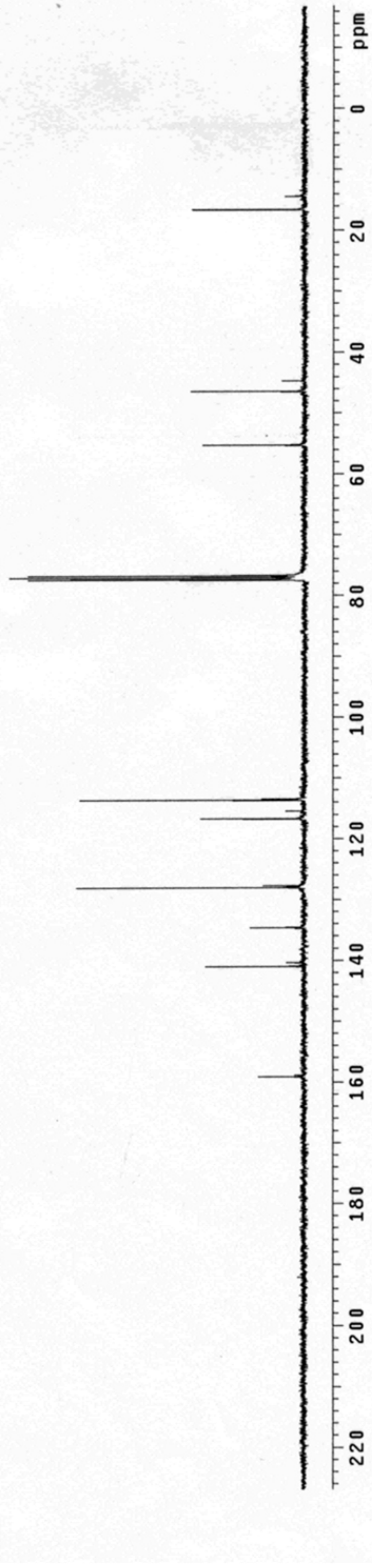
$[\alpha]_D^{25}$ = +51.8 (c =1.0, $CHCl_3$).

FTIR (neat): 2961, 1611, 1510, 1458, 1302, 1260, 1173, 1032, 911, 731 cm^{-1}.

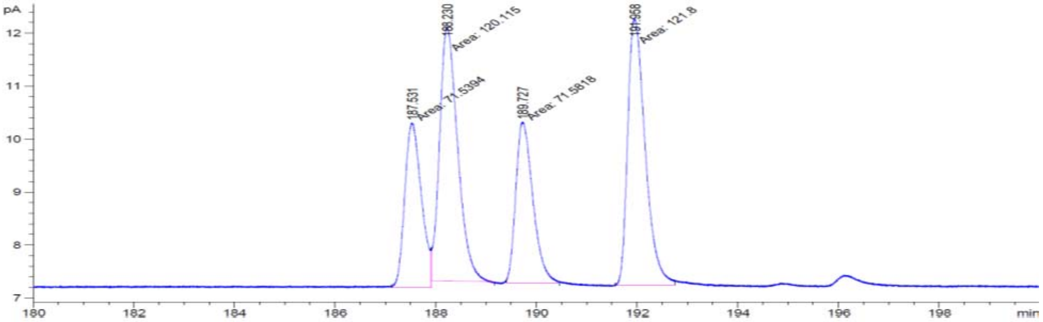
GC Cyclosil-B: Initial temperature: 50 °C (5 min hold); 50-115 °C rate: 0.5 C/min (20 min hold); 115-165°C, rate: 0.475 C/min t_{major} = 184.9 min, t_{minor} = 187.3 min.

The spectroscopic properties of this compound were consistent with the data available in the literature *(39).*


ppm
-0
2
4
6
8
10
12

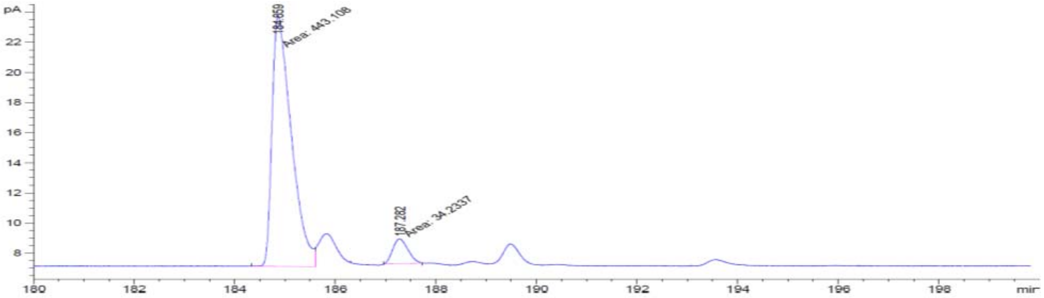

ppm
0
20
40
60
80
100
120
140
160
180
200
220

Racemic:



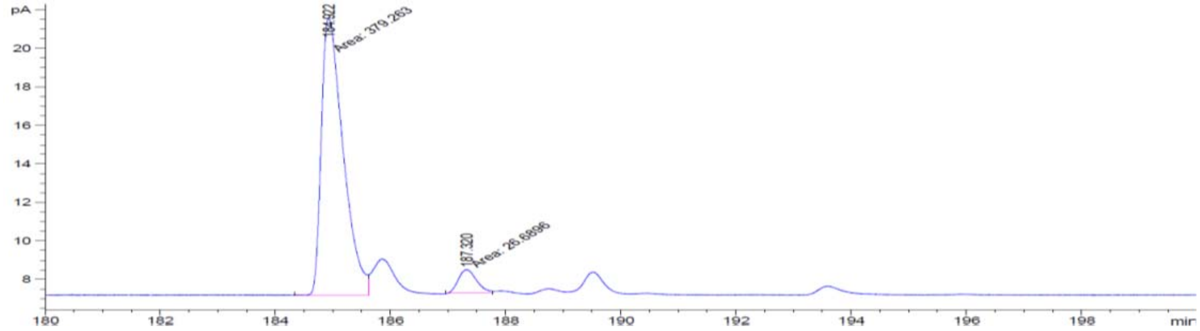
```
Signal 1: FID1 A, Front Signal

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]    [pA*s]      [pA]         %
----|-------|----|-------|----------|----------|--------|
   1 187.531 MM     0.3824   71.53935    3.11795 18.57991
   2 188.230 MM     0.4184  120.11469    4.78511 31.19569
   3 189.727 MM     0.3924   71.58181    3.03999 18.59093
   4 191.958 MM     0.4030  121.80028    5.03745 31.63347
```

Alcohol:

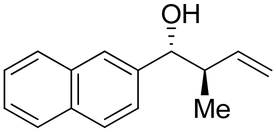


```
Signal 1: FID1 A, Front Signal

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]    [pA*s]      [pA]         %
----|-------|----|-------|----------|----------|--------|
   1 184.859 MM     0.4458  443.10831   16.56563 92.82827
   2 187.282 MM     0.3435   34.23370    1.66111  7.17173
```

Aldehyde:



```
Signal 1: FID1 A, Front Signal

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]    [pA*s]      [pA]        %
----|-------|----|-------|----------|----------|--------|
   1 184.922 MM    0.4388  379.26254   14.40639 93.42543
   2 187.320 MM    0.3610   26.68959    1.23206  6.57457
```



(1R,2R)-2-methyl-1-(naphthalen-2-yl)but-3-en-1-ol (3g)

From Alcohol Oxidation Level: To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stir bar was added $RuH_2(CO)(PPh_3)_3$ (13.8 mg, 0.015 mmol, 5 mol%), dppf (8.3 mg, 0.015 mmol, 5 mol%), (*R*)-phosphoric acid $\mathbf{A_9}$ (15.1 mg, 0.03 mmol, 10 mol%) and alcohol **1f** (47.2 mg, 0.30 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. Tetrahydrofuran (0.15 mL, 2.0 M concentration with respect to alcohol) was added and the solution was cooled to -78°C. Butadiene (0.10 mL, 1.20 mmol, 400 mol%) was quickly added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 95°C (oil bath temperature) for 48 hrs, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO_2; 0-20% EtOAc/hexanes) to furnish the title compound (60.4 mg, 0.29 mmol, *anti*:*syn* = 9:1, 94:6 er) as a colorless oil in 95% yield.

From Aldehyde Oxidation Level: To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stir bar was added $RuH_2(CO)(PPh_3)_3$ (13.8 mg, 0.015 mmol, 5 mol%), dppf (8.3 mg, 0.015 mmol, 5 mol%), (*R*)-phosphoric acid $\mathbf{A_9}$ (15.1 mg, 0.03 mmol, 10 mol%) and aldehyde **2f** (46.8 mg, 0.30 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. Tetrahydrofuran (0.15 mL, 2.0 M concentration with respect to alcohol) and 1,4-butanediol (0.053 mL, 0.60 mmol, 200 mol%) were added and the solution was cooled to -78°C. Butadiene (0.10 mL, 1.20 mmol, 400 mol%) was quickly added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 95°C (oil bath temperature) for 48 hrs, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO_2; 0-20% EtOAc/hexanes) to furnish the title compound (50.0 mg, 0.24 mmol, *anti*:*syn* = 4:1, 93:7 er) as a colorless oil in 79% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85-7.83 (m, 3H), 7.78 (s, 1H), 7.51-7.46 (m, 3H), 5.91-5.82 (m,1H), 5.27-5.20 (m, 2H), 4.53 (dd, *J* = 8.0 Hz, 2.0 Hz, 1H), 2.65-2.56 (m, 1H), 2.32 (d, *J* = 2.0 Hz, 1H), 0.92 (d, *J* = 6.8 Hz, 3H).

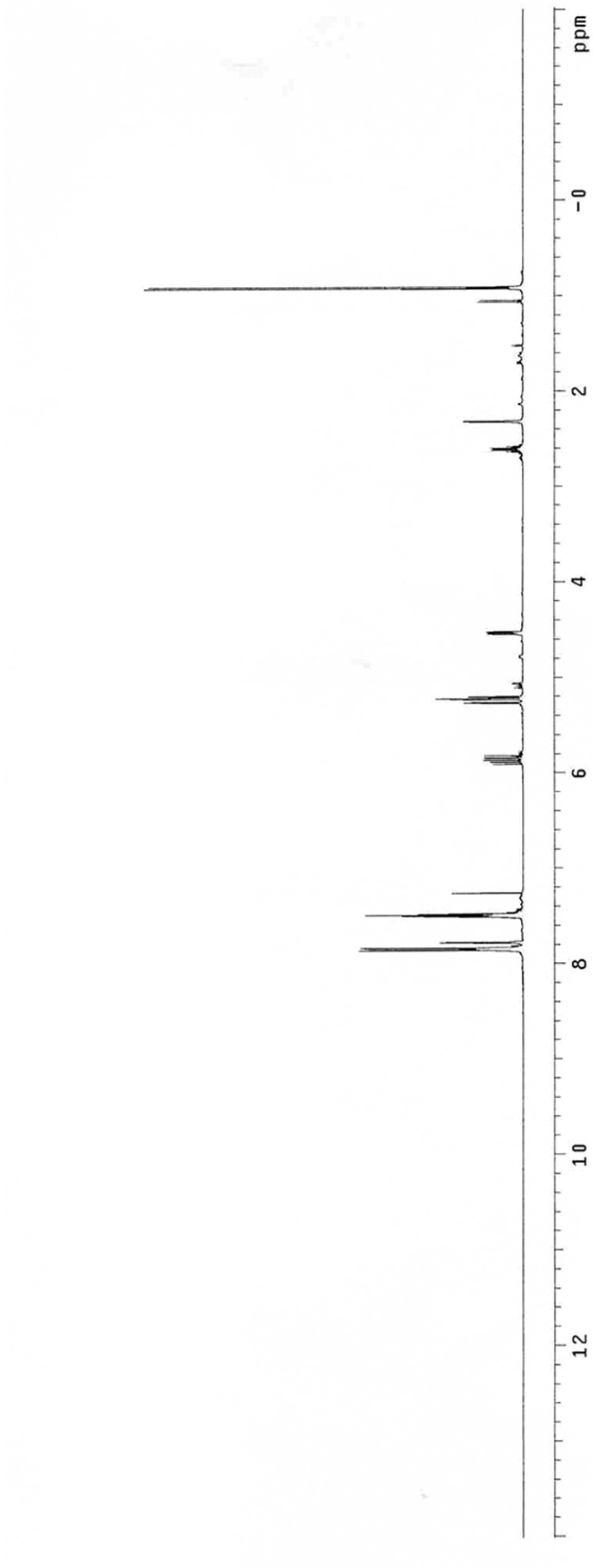
^{13}C NMR (100 MHz, $CDCl_3$): δ 140.6, 139.9, 133.2, 133.1, 128.1, 128.0, 127.7, 126.1, 126.0, 125.8, 124.7, 117.0, 78.0, 46.2, 16.6 ppm.

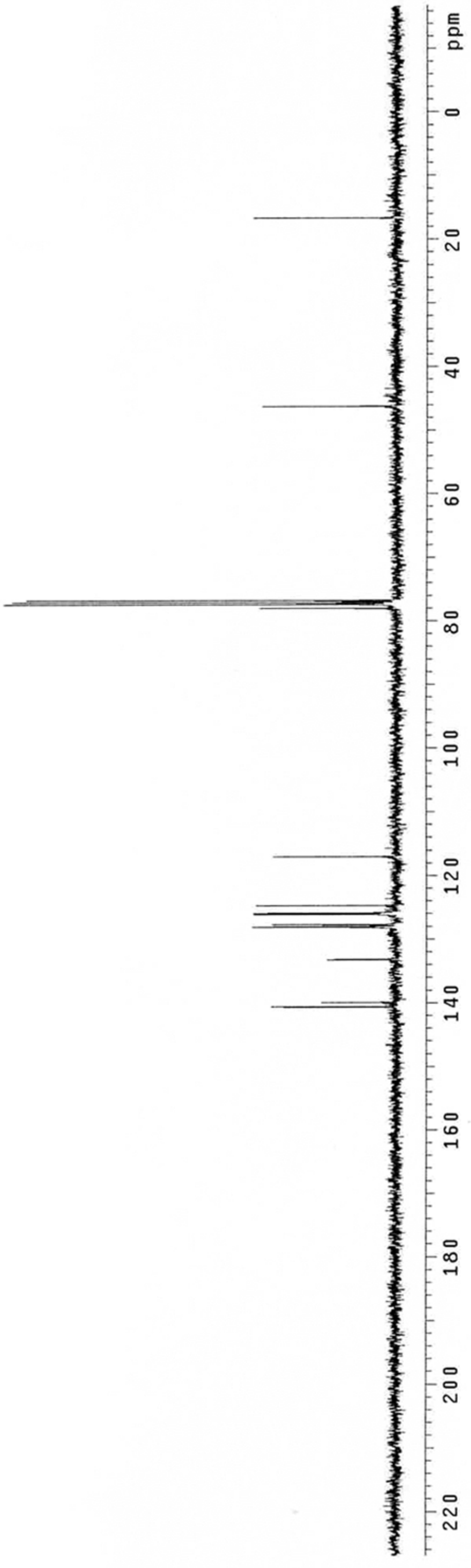
LRMS (CI+). *m/z* 213 $[M+H]^+$

$[\alpha]_D^{25}$ = +57(c =1.0, $CHCl_3$).

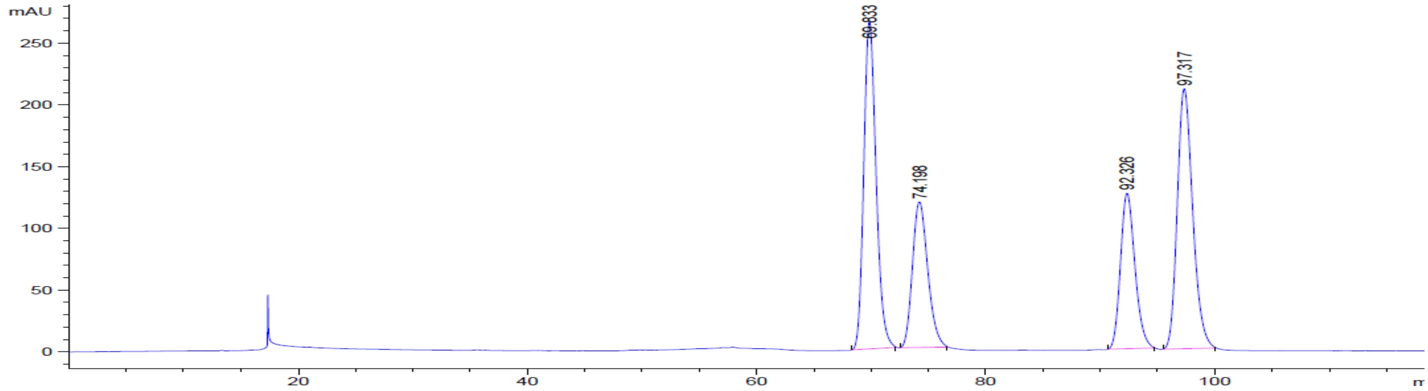
FTIR (neat): 3411, 3056, 2972, 2869, 2359, 1932, 1636, 1507, 1371, 1270, 1159, 1123, 1018, 908, 817, 731 cm^{-1}

HPLC (Chiralcel AS-H/AS-H column, hexanes:*i*-PrOH = 95:5, 0.5 mL/min, 230 nm), t_{major} = 74.2 min, t_{minor} = 92.3 min.
The spectroscopic properties of this compound were consistent with the data available in the literature *(40)*.


ppm
0
2
4
6
8
10
12

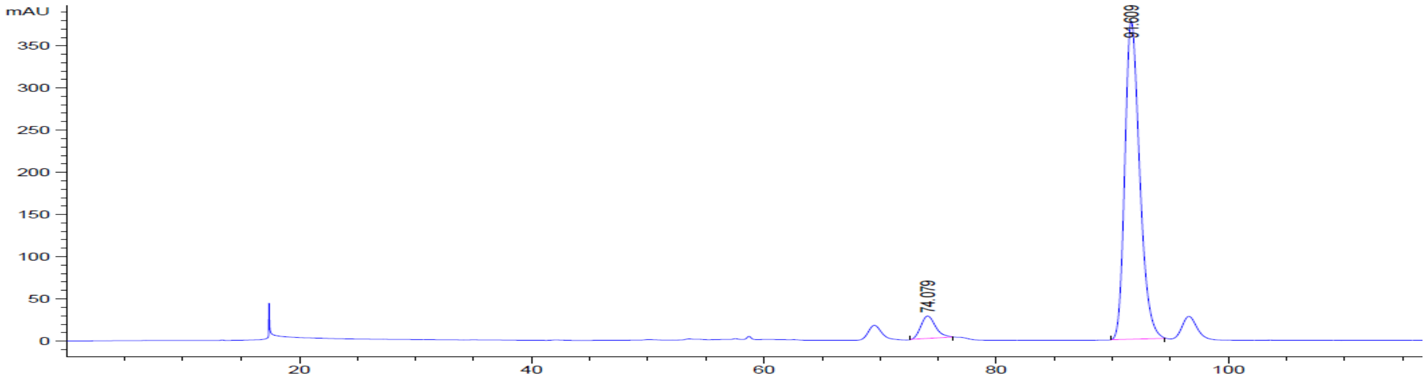

ppm
0
20
40
60
80
100
120
140
160
180
200
220

Racemic:



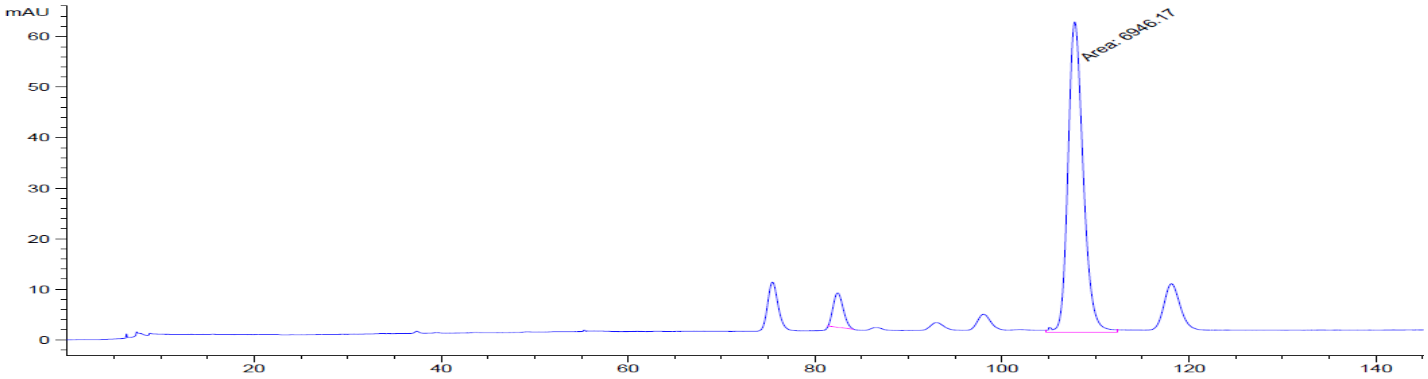
```
Peak RetTime Type  Width     Area       Height      Area
  #   [min]         [min]  [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1  69.833 BB    1.1523 1.98477e4  265.46753  32.1878
  2  74.198 BB    1.4103 1.09874e4  118.00423  17.8187
  3  92.326 BB    1.3431 1.10806e4  126.10297  17.9699
  4  97.317 BB    1.4340 1.97466e4  210.59084  32.0237
```

Alcohol:



```
Peak RetTime Type  Width     Area       Height      Area
  #   [min]         [min]  [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1  74.079 BB    1.2793 2362.48633   26.83085   6.5819
  2  91.609 BB    1.3594 3.35310e4  377.10840  93.4181
```

Aldehyde:



```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  82.392 BB     0.9000  515.88885    6.83912   6.9135
   2 107.752 MM     1.8871 6946.17285   61.34930  93.0865
```

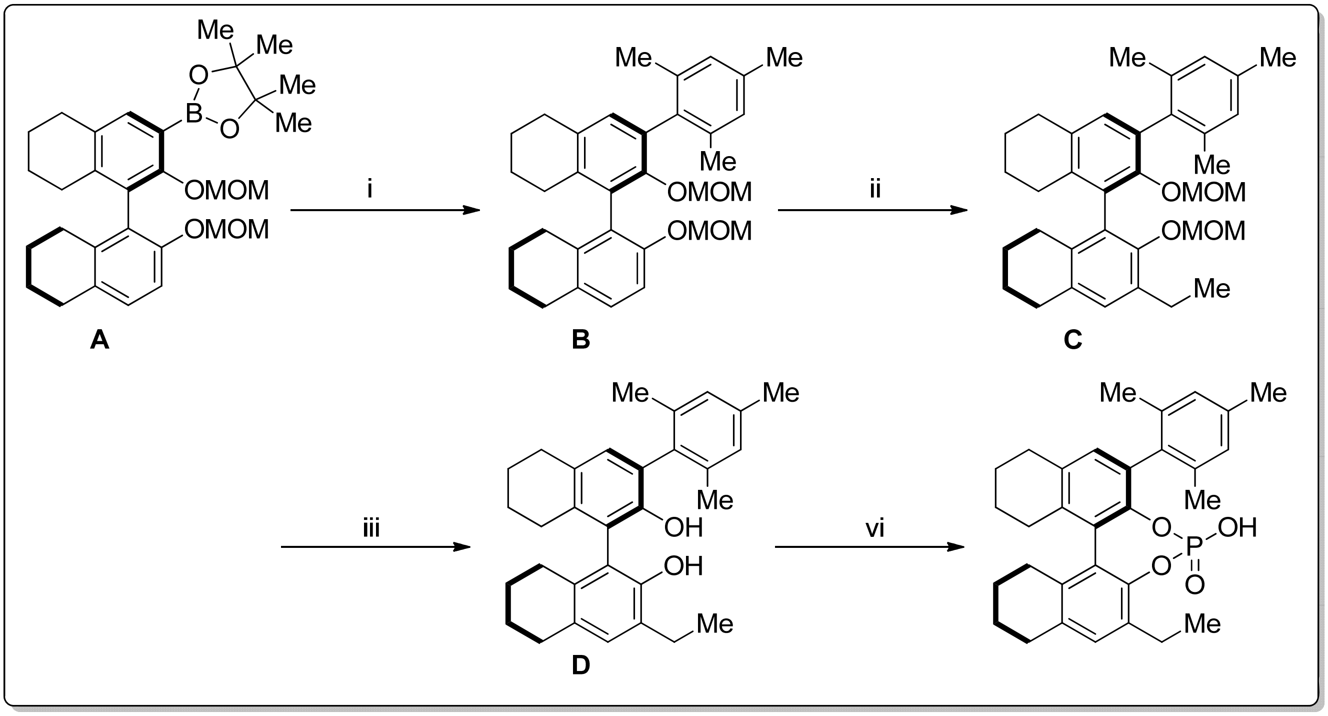
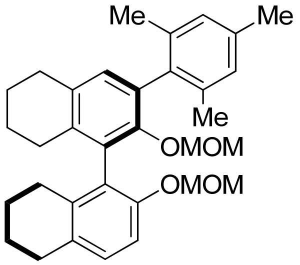


Figure S1: Chiral Phosphoric Acid A_9 Synthetic Approach
(i) $Pd(PPh_3)_4$ (5 mol%), 2-bromomesitylene (300 mol%), NaOH (350 mol%), THF, H_2O, 95 ºC, 18hr. (ii) *n*-BuLi (150 mol%), iodoethane (150 mol%), THF, 18 hr. (iii) *conc.* HCl, EtOH, 18 hr. (vi) $POCl_3$ (130 mol%), pyridine, 115 ºC, 18 hr then H_2O, 115 ºC, 3h.

(R)-3-mesityl-2,2'-bis(methoxymethoxy)-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthalene (B)



To a flame dried resealable pressure tube equipped with a magnetic stir bar was added compound **A** (3.72 g, 9.2 mmol, 100 mol%), $Pd(PPh_3)_4$ (0.53 g, 0.46 mmol, 5 mol%), and NaOH (1.3 g, 32.2 mmol, 350 mol%). The tube was sealed with a rubber septum and purged with nitrogen. Tetrahydrofuran (46 mL, 0.2 M concentration with respect to compound **A**), water (18.4 mL, 0.5 M concentration with respect to compound **A**) and bromomesitylene (4.2 mL, 27.6 mmol, 300 mol%) were added. The solution was then vigourously degassed and the rubber septum quickly replaced with a screw cap. The mixture was heated at 95°C (oil bath temperature) for 18 hr, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was transferred to separatory funnel and extracted with CH_2Cl_2 (3x100 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2; ethyl acetate:hexanes, 1:15) to furnish the title compound (3.50 g, 7.2 mmol) as a white solid in 78% yield *(41).*

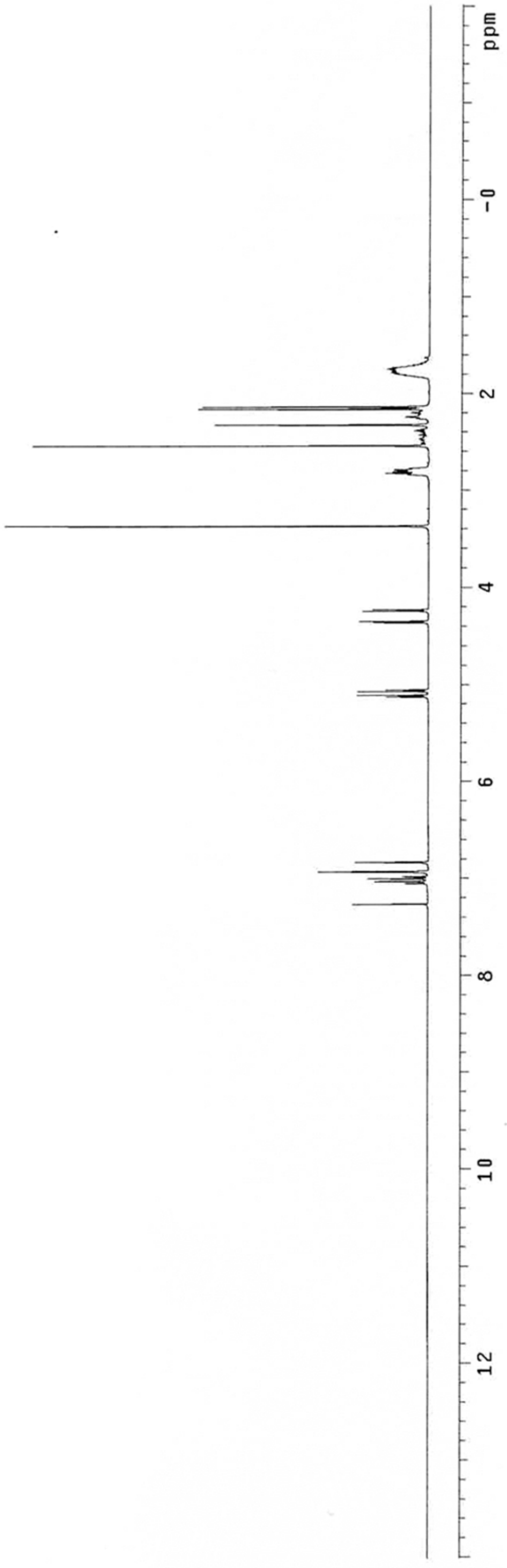
m.p.: 64-65 ºC

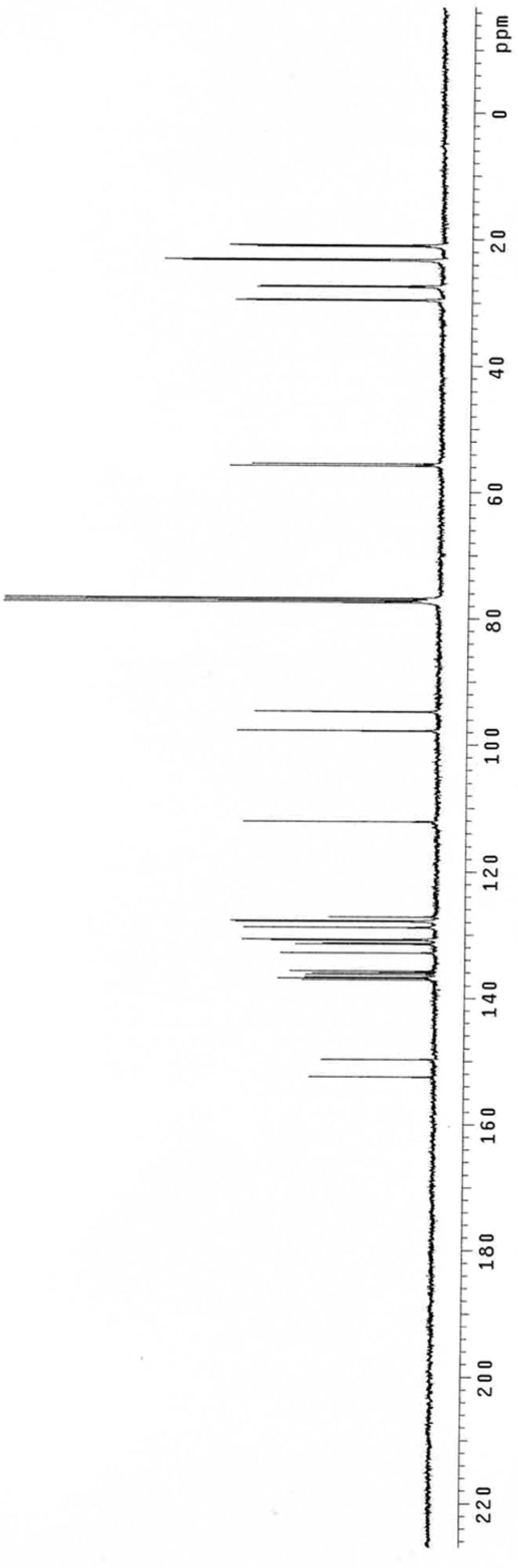
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.04 (d, *J* = 8.6 Hz, 1H), 6.99 (d, *J* = 8.6 Hz, 1H), 6.93 (s, 2H), 6.83 (s, 1H), 5.12 (d, *J* = 6.7 Hz, 1H), 5.06 (d, *J* = 6.7 Hz, 1H), 4.36 (d, *J* = 5.5 Hz, 1H), 4.24 (d, *J* = 5.5 Hz, 1H), 3.37 (s, 3H), 2.84-2.78 (m, 4H), 2.54 (s, 3H), 2.47-2.38 (m, 2H), 2.33 (s, 3H), 2.26-2.20 (m, 2H), 2.16 (s, 3H), 2.14 (s, 3H), 1.81-1.63 (m, 8H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 152.5, 149.7, 137.1, 136.8, 136.7, 136.2, 136.0, 135.7, 132.9, 131.5, 131.3, 130.8, 130.7, 128.8, 127.9, 127.8, 127.1, 112.1, 97.7, 94.7, 55.6, 55.6, 29.6, 29.4, 27.5, 27.3, 23.3, 23.2, 23.1, 23.1, 21.1, 20.9, 20.8 ppm.

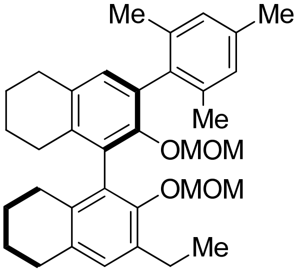
LRMS (CI+) *m/z* 500 $[M]^+$.

FTIR (neat): 2922, 1478, 1244, 1206, 1060, 1016, 984, 922, 849, 807 cm^{-1}.


12
10
8
6
4
2
0
ppm


ppm
0
20
40
60
80
100
120
140
160
180
200
220

(R)-3-ethyl-3'-mesityl-2,2'-bis(methoxymethoxy)-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthalene (C)



To a flame dried 100 mL round bottom flask compound **B** (1.70g, 3.4 mmol, 100 mol%) is added. The flask is sealed with a rubber septum and purged with nitrogen. Tetrahydrofuran (11 mL, 0.3 M concentration with respect to compound **B**) is added and the solution is cooled to 0°C. A solution of 2.5M *n*-BuLi in hexanes (2.0 mL, 5.1 mmol, 150 mol%) is added dropwise and stirred for 10 minutes. The reaction mixture is then allowed to warm to RT and stir for an additional 3 hrs. Iodoethane (0.4 mL, 5.1mmol, 150 mol%) is added dropwise and the mixture is stirred for 18 hrs. Upon complete consumption of starting material, as determined by TLC analysis, ammonium chloride (15 mL, sat. aq. sol.) was added. The organic layer was extracted with CH_2Cl_2 (3x50 mL) and the combined organic extracts were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (SiO_2; diethylether:hexanes, 1:20) to provide the title compound (1.12 g, 2.1 mmol) as a white solid in 63% yield.

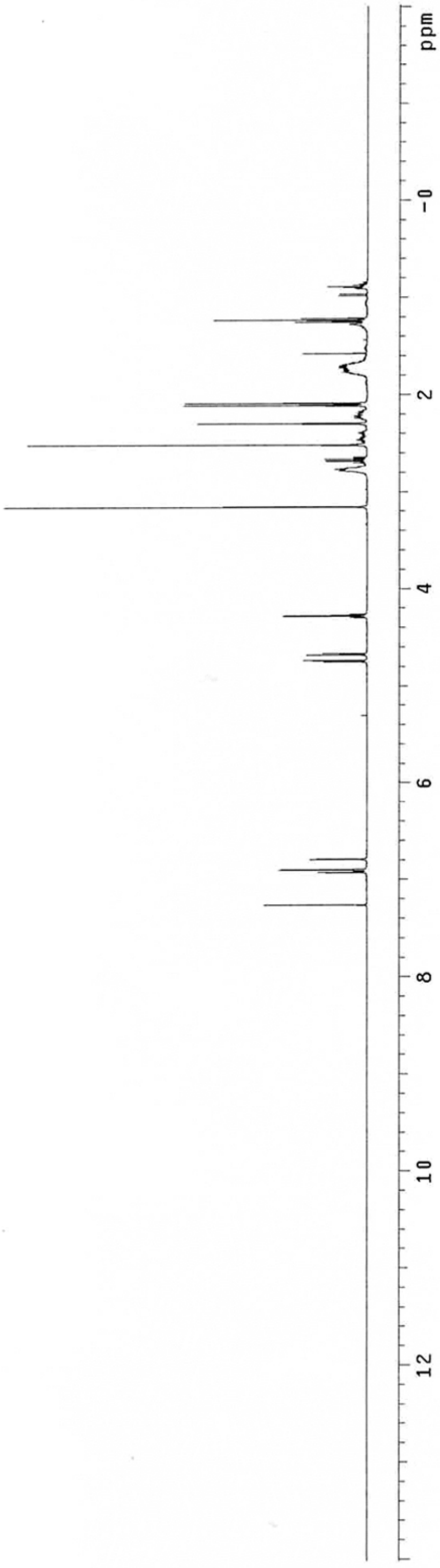
m.p.: 63-66 ºC

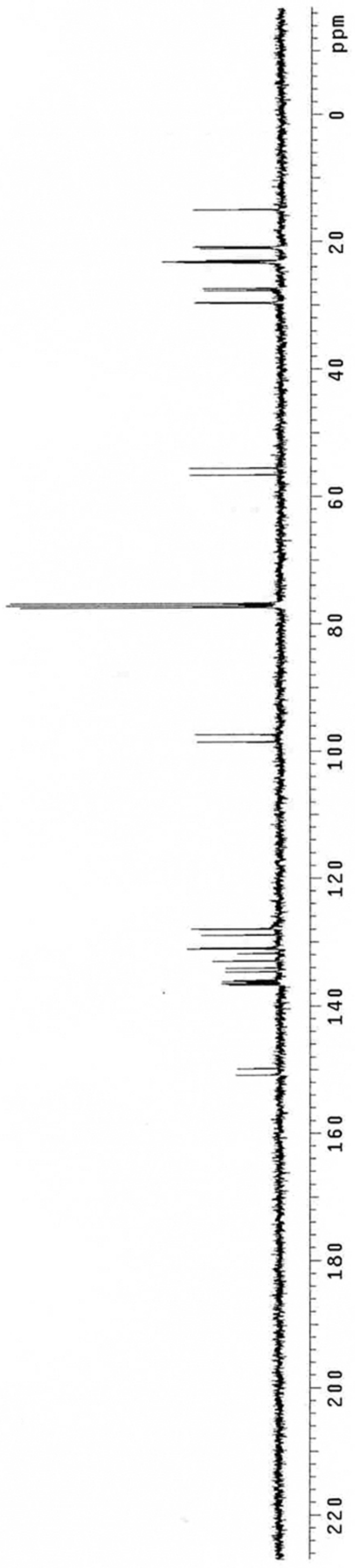
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.93 (s, 3H), 6.90 (s, 3H), 6.79 (s, 3H), 4.75 (d, *J* = 5.5 Hz, 1H), 4.67 (d, *J* = 5.5 Hz, 1H), 4.29 (d, *J* = 5.7 Hz, 1H), 4.27 (d, *J* = 5.7 Hz, 1H), 3.15 (s, 3H), 2.78-2.75 (m, 2H), 2.67 (q, *J* = 7.5 Hz, 2H), 2.52 (s, 3H), 2.48-2.39 (m, 2H), 2.30 (s, 3H), 2.30-2.18 (m, 2H), 2.11 (s, 3H), 2.09 (s, 3H), 1.78-1.69 (m, 8H), 1.23 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 150.8, 149.8, 136.7, 136.5, 136.4, 136.1, 135.9, 134.6, 134.0, 132.9, 131.1, 131.0, 130.9, 128.9, 128.0, 127.9, 98.5, 97.3, 56.5, 55.5, 31.6, 29.6, 29.6, 27.7, 27.4, 23.3, 23.2, 23.1, 22.9, 21.1, 20.9, 20.8, 14.9 ppm.

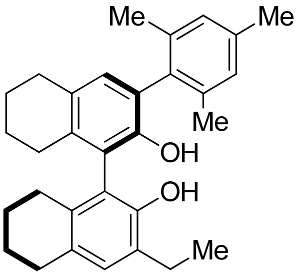
LRMS (CI+) *m/z* 528 $[M]^+$.

FTIR (neat): 2926, 1711, 1437, 1359, 1280, 1095, 909 cm^{-1}.


ppm
0
2
4
6
8
10
12


ppm
0
20
40
60
80
100
120
140
160
180
200
220

(*R*)-3-ethyl-3'-mesityl-5,5',6,6',7,7',8,8'-octahydro-[1,1'-binaphthalene]-2,2'-diol (D)



To a 250 mL round bottom flask compound **C** (1.12 g, 2.1 mmol, 100 mol%) is added. Ethanol (70 mL, 0.03 M concentration with respect to compound **C**) and *conc*. hydrochloric acid (7 mL, 0.3 M concentration with respect to compound **C**) were added sequentially. The reaction mixture is stirred at room temperature overnight. Upon complete consumption of starting material, as determined by TLC analysis, the reaction mixture is concentrated *in vacuo*. The residue was purified by column chromatography (SiO_2; DCM:hexanes, 1:1) to provide the title compound (0.88 g, 2.0 mmol) as a white solid in 95% yield.

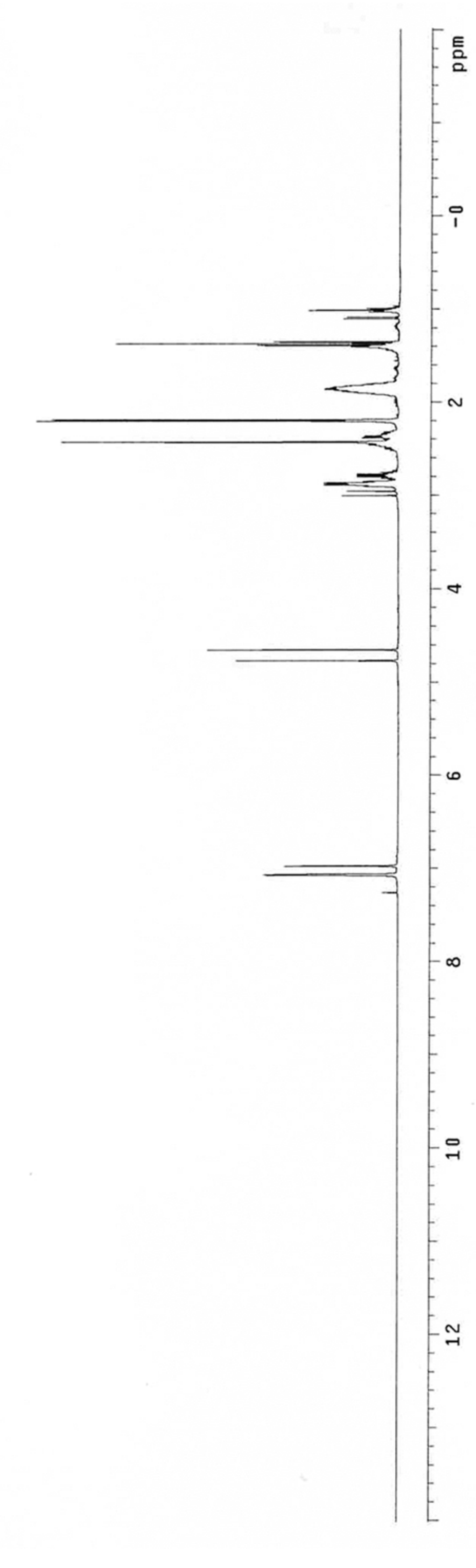
m.p.: 89-92 ºC

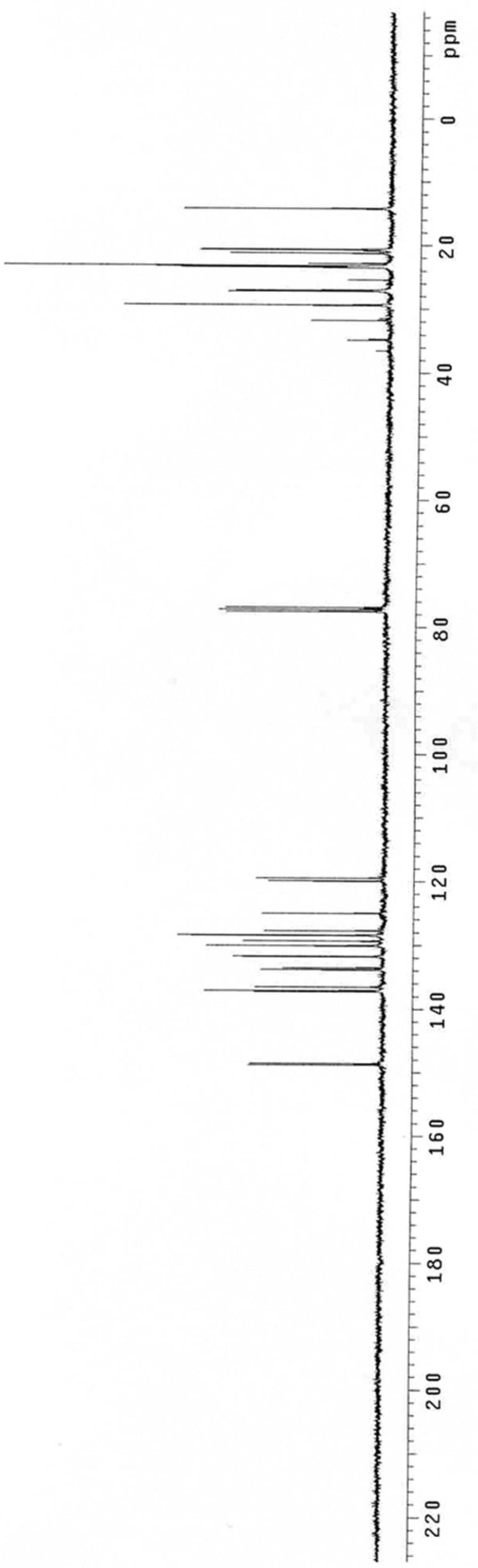
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.07 (s, 2H), 7.06 (s, 1H), 6.97 (s, 1H), 4.77 (s, 1H), 4.65 (s, 1H), 2.88 (q, *J* = 7.4 Hz, 2H), 2.81-2.75 (m, 4H), 2.52-2.31 (m, 7H), 2.20 (s, 3H), 2.19 (s, 3H), 1.91-1.73 (m, 8H), 1.37 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 148.8, 148.6, 137.2, 137.1, 137.0, 136.5, 133.8, 133.5, 131.7, 130.1, 130.0, 129.3, 128.5, 128.4, 127.7, 125.0, 119.9, 119.5, 31.7, 29.4, 27.2, 27.0, 23.4, 23.3, 23.2, 23.2, 22.8, 21.2, 20.7, 20.6, 14.2 ppm.

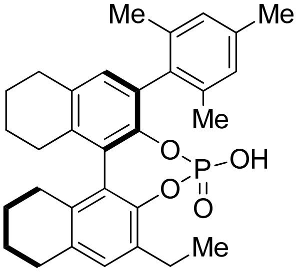
LRMS (CI+) *m/z* 440 $[M]^+$.

FTIR (neat): 2926, 1450, 1264, 1154, 982, 736 cm^{-1}.


ppm
0
2
4
6
8
10
12


ppm
0
20
40
60
80
100
120
140
160
180
200
220

(*R*)-2-ethyl-4-hydroxy-6-mesityl-8,9,10,11,12,13,14,15-octahydrodinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepine 4-oxide (A_9)



To a 100 mL round bottom flask equipped with a reflux condenser is added compound **D** (0.44g, 1 mmol, 100 mol%). Pyridine (2 mL, 0.5 M concentration with respect to compound **D**) and $POCl_3$ (.170 mL, 1.8 mmol, 180 mol%) were added to the reaction mixture. The mixture was heated at 115°C (oil bath temperature) for 18 hrs, at which point the reaction mixture was allowed to cool to ambient temperature. Water (1 mL, 1.0 M concentration with respect to compound **D**) was added dropwise and then heated to 115°C for an additional 3 hrs. Upon complete consumption of starting material, as determined by TLC analysis, the reaction mixture was cooled to ambient temperature and a solution of hydrochloric acid (10 mL, 3M aq. sol.) was added. The organic layer was extracted with CH_2Cl_2 (3x50 mL) and the combined organic extracts were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (SiO_2; 0-20% IPA:CH_2Cl_2,) and concentrated *in vacuo*. The residue was diluted with CH_2Cl_2 then washed with a solution of hydrochloric acid (10 mL, 3M aq. sol.) and concentrated *in vacuo* to provide the title compound (0.46 g, 0.92 mmol) as a white solid in 92% yield.

m.p.: 228-230 ºC

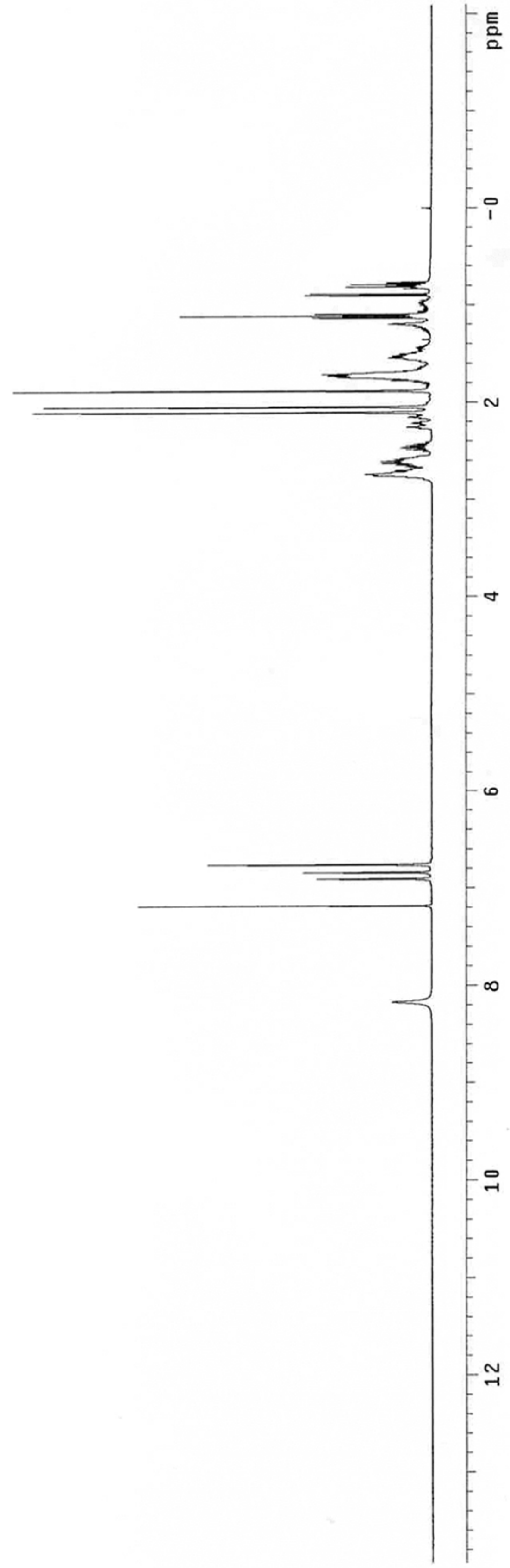
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (brs, 1H), 6.90 (s, 1H), 6.84 (s, 1H), 6.76 (s, 1H), 2.81-2.69 (m, 4H), 2.66-2.55 (m, 3H), 2.49-2.42 (m, 1H), 2.27-2.12 (m, 2H), 2.10 (s, 3H), 2.05 (s, 3H), 1.88 (s, 3H), 1.79-1.66 (m, 8H), 1.11 (t, *J* = 7.5 Hz, 3H).

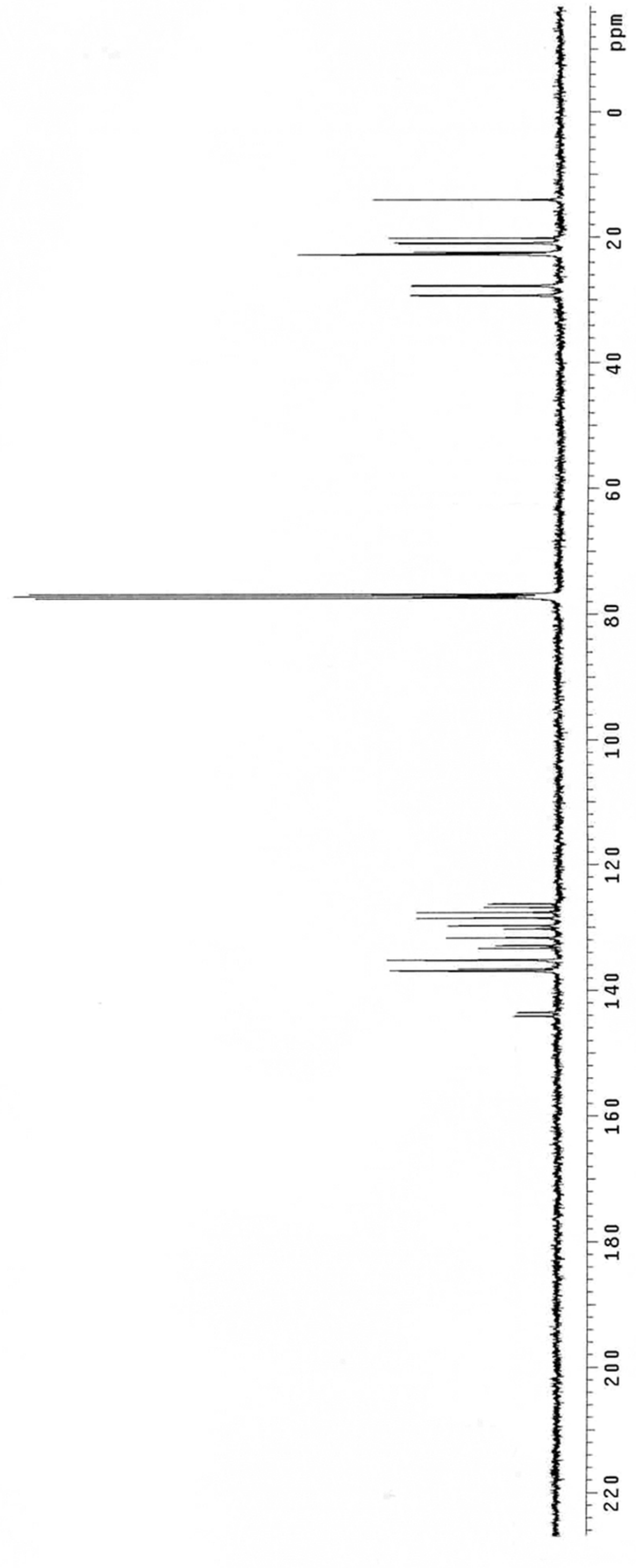
^{13}C NMR (100 MHz, $CDCl_3$): δ 144.1, 144.0, 143.5, 143.4, 136.9, 136.8, 136.5, 135.1, 135.0, 133.3, 132.8, 131.6, 130.2, 129.7, 128.5, 127.6, 126.7, 126.2, 29.3, 29.2, 27.8, 27.7, 22.8, 22.7, 22.7, 22.6, 22.3, 21.0, 20.8, 20.2, 14.0 ppm.

^{31}P NMR (162 MHz, $CDCl_3$): 2.5 ppm.

LRMS (CI+) *m/z* 502 $[M]^+$.

FTIR (neat): 2931, 1612, 1434, 1245, 1202, 1017, 905, 728 cm^{-1}.

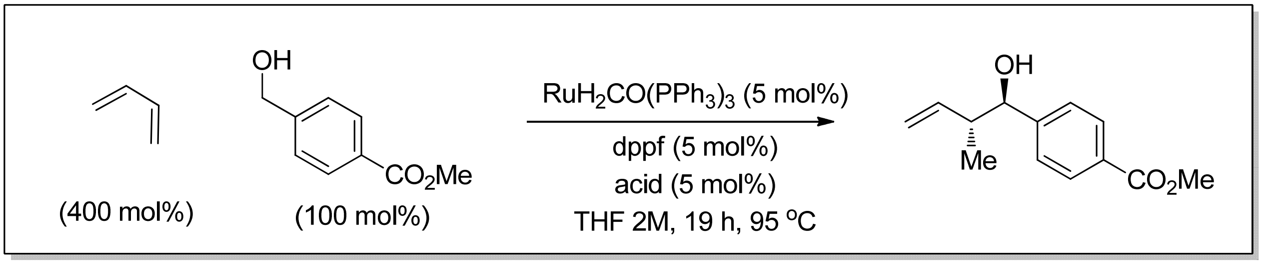

12
10
8
6
4
2
0
ppm

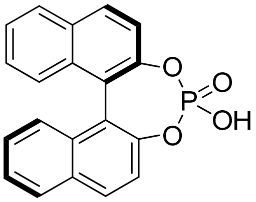

ppm
0
20
40
60
80
100
120
140
160
180
200
220

Optimization of *(R)*-BINOL phosphoric acids.

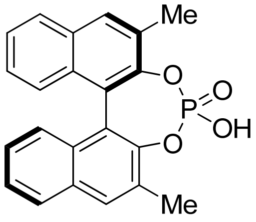
Table S1.

Evaluation of 3,3’-disubstituted *(R)*-BINOL phosphoric acids

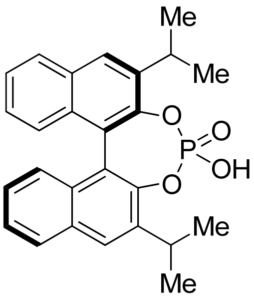




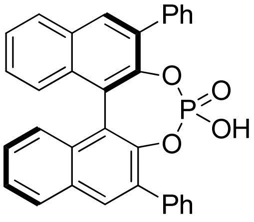
45% Yield
1:1 dr
4% ee



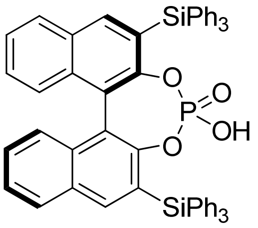
48% Yield
2:1 dr
33% ee



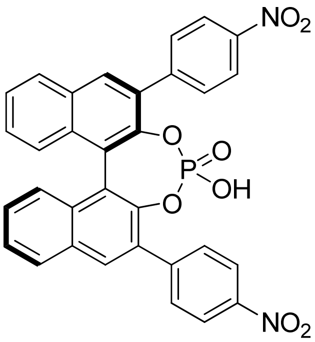
83% Yield
1:2 dr
15% ee



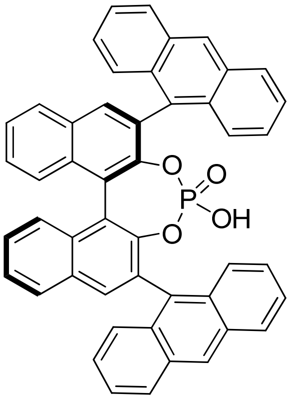
91% Yield
5:1 dr
14% ee



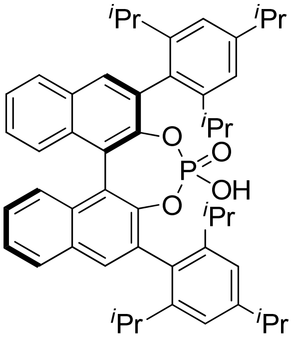
61% Yield
1:1 dr
6% ee



80% Yield
1:1 dr
9% ee



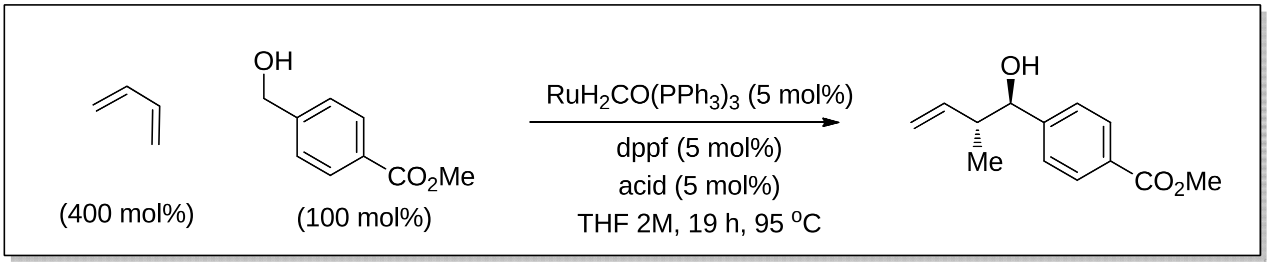
82% Yield
1:1 dr
10% ee

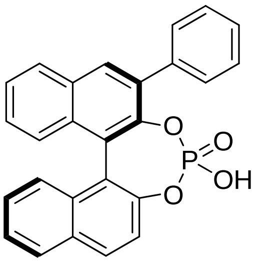


60% Yield
1:1 dr
0% ee

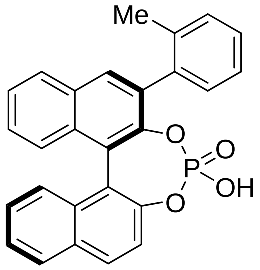
Table S2.

Evaluation of mono-substituted *(R)*-BINOL phosphoric acids

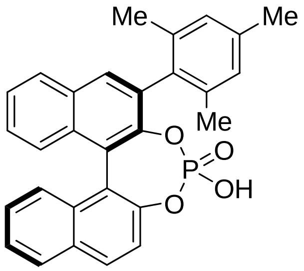




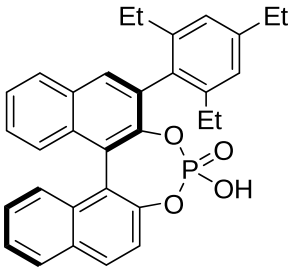
83% Yield
2:1 dr
37% ee



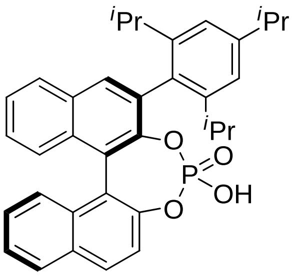
38% Yield
1:1 dr
21% ee



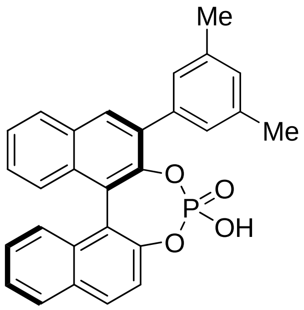
84% Yield
3:1 dr
73% ee



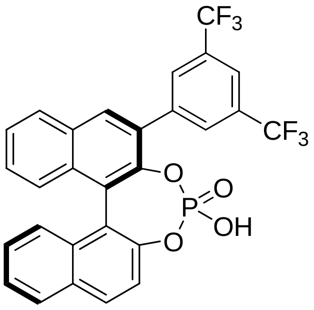
18% Yield
2:1 dr
54% ee



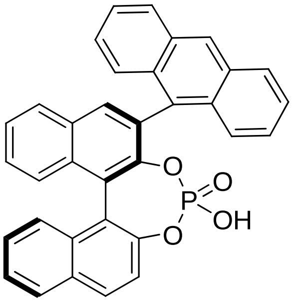
41% Yield
2:1 dr
62% ee



18% Yield
2:1 dr
30% ee



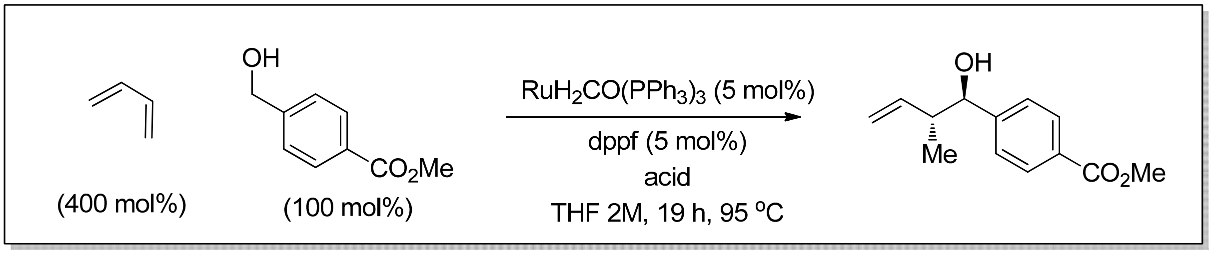
15% Yield
1:1 dr
15% ee



36% Yield
2:1 dr
60% ee

Table S3.

Evaluation of acid loading of various 3’-substituted,3-mesityl-*(R)*-BINOL phosphoric acids



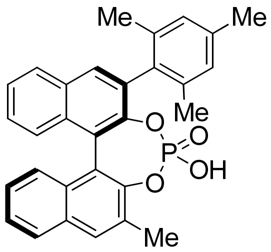
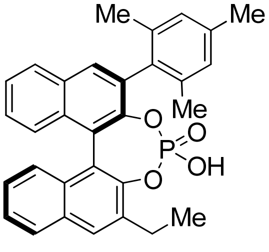
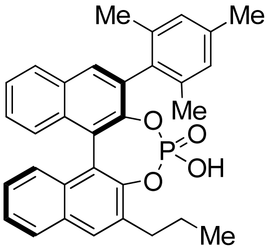
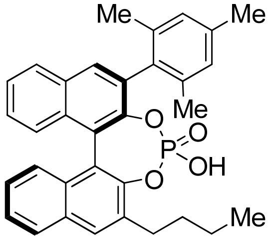
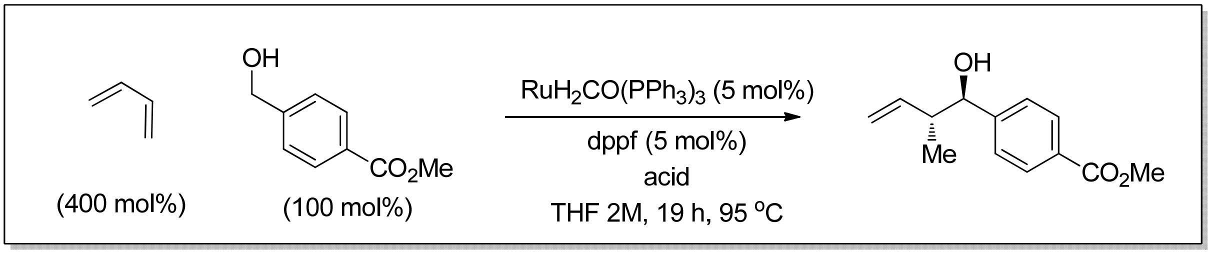
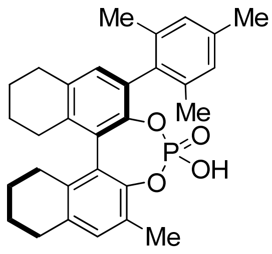
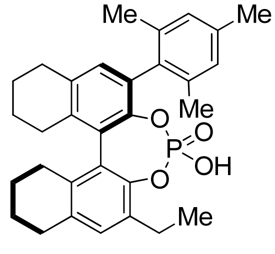
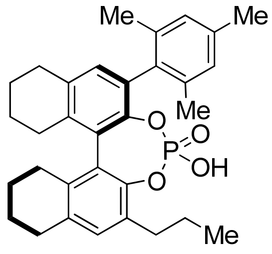
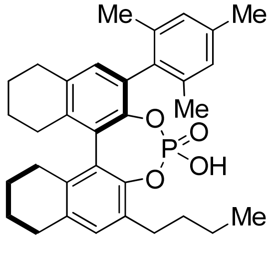
				
5 mol% acid	15% Yield 6 : 1 dr 71% ee	21% Yield 5 : 1 dr 71% ee		
10 mol% acid	23% Yield 6 : 1 dr 78% ee	33% Yield 8 : 1 dr 84% ee	41% Yield 4 : 1 dr 72% ee	33% Yield 7 : 1 dr 76% ee

Table S4.

Evaluation of different substituent of *(R)*-3,3’-disubstituted *(R)*-H$_8$-BINOL phosphoric acids derivatives.



				
5 mol% acid	15% Yield 5 : 1 dr 72% ee	45% Yield 3 : 1 dr 78% ee	45% Yield 5 : 1 dr 71% ee	36% Yield 5 : 1 dr 75% ee
10 mol% acid	53% Yield 8 : 1 dr 84% ee	**50% Yield** **8 : 1 dr** **87% ee**	32% Yield 6 : 1 dr 83% ee	50% Yield 6 : 1 dr 83% ee

References and Notes

1. M. Butters *et al*., Critical assessment of pharmaceutical processes - a rationale for changing the synthetic route. *Chem. Rev.* **106**, 3002 (2006). doi:10.1021/cr050982w

2. R. A. Sheldon, E. The, Factor: Fifteen years on. *Green Chem.* **9**, 1273 (2007). doi:10.1039/b713736m

3. C. A. Busacca, D. R. Fandrick, J. J. Song, C. H. senanayake, the growing impact of catalysis in the pharmaceutical industry. *Adv. Synth. Catal.* **353**, 1825 (2011). doi:10.1002/adsc.201100488

4. J. Magano, J. R. Dunetz, Large-scale applications of transition metal-catalyzed couplings for the synthesis of pharmaceuticals. *Chem. Rev.* **111**, 2177 (2011). doi:10.1021/cr100346g

5. C. D. Frohning, C. W. Kohlpaintner, in *Applied Homogeneous Catalysis with Organometallic Compounds*, B. Cornils, W. A. Herrmann, Eds. (Wiley-VCH, Weinheim, 1996) pp. 29–104.

6. P. W. N. M. van Leeuwen, in *Homogeneous Catalysis: Understanding the Art* (Kluwer, Dordrecht, 2004).

7. J. F. Bower, M. J. Krische, Formation of C–C bonds via iridium-catalyzed hydrogenation and transfer hydrogenation. *Top. Organomet. Chem.* **34**, 107 (2011).

8. A. Hassan, M. J. Krische, Unlocking hydrogenation for C–C bond formation: A brief overview of enantioselective methods. *Org. Process Res. Dev.* **15**, 1236 (2011). doi:10.1021/op200195m

9. I. S. Kim, S. B. Han, M. J. Krische, *anti*-Diastereo- and enantioselective carbonyl crotylation from the alcohol or aldehyde oxidation level employing a cyclometallated iridium catalyst: α-Methyl allyl acetate as a surrogate to preformed crotylmetal reagents. *J. Am. Chem. Soc.* **131**, 2514 (2009). doi:10.1021/ja808857w

10. X. Gao, I. A. Townsend, M. J. Krische, Enhanced anti-diastereo- and enantioselectivity in alcohol-mediated carbonyl crotylation using an isolable single component iridium catalyst. *J. Org. Chem.* **76**, 2350 (2011). doi:10.1021/jo200068q

11. X. Gao, H. Han, M. J. Krische, Direct generation of acyclic polypropionate stereopolyads via double diastereo- and enantioselective iridium-catalyzed crotylation of 1,3-diols: Beyond stepwise carbonyl addition in polyketide construction. *J. Am. Chem. Soc.* **133**, 12795 (2011). doi:10.1021/ja204570w

12. J. R. Zbieg, T. Fukuzumi, M. J. Krische, Iridium-catalyzed hydrohydroxyalkylation of butadiene: Carbonyl crotylation. *Adv. Synth. Catal.* **352**, 2416 (2010). doi:10.1002/adsc.201000599

13. F. Shibahara, J. F. Bower, M. J. Krische, Ruthenium-catalyzed C−C bond forming transfer hydrogenation: Carbonyl allylation from the alcohol or aldehyde oxidation level employing acyclic 1,3-dienes as surrogates to preformed allyl metal reagents. *J. Am. Chem. Soc.* **130**, 6338 (2008). doi:10.1021/ja801213x

14. J. R. Zbieg, J. Moran, M. J. Krische, Diastereo- and enantioselective ruthenium-catalyzed hydrohydroxy-alkylation of 2-silyl-butadienes: Carbonyl syn-crotylation from the alcohol oxidation level. *J. Am. Chem. Soc.* **133**, 10582 (2011). doi:10.1021/ja2046028

15. H. Alper, N. Hamel, Asymmetric synthesis of acids by the palladium-catalyzed hydrocarboxylation of olefins in the presence of (R)-(-)- or (S)-(+)-1,1'-binaphthyl-2,2'-diyl hydrogen phosphate. *J. Am. Chem. Soc.* **112**, 2803 (1990). doi:10.1021/ja00163a053

16. V. Komanduri, M. J. Krische, Enantioselective reductive coupling of 1,3-enynes to heterocyclic aromatic aldehydes and ketones via rhodium-catalyzed asymmetric hydrogenation: Mechanistic insight into the role of brønsted acid additives. *J. Am. Chem. Soc.* **128**, 16448 (2006). doi:10.1021/ja0673027

17. G. L. Hamilton, E. J. Kang, M. Mba, F. D. Toste, A powerful chiral counterion strategy for asymmetric transition metal catalysis. *Science* **317**, 496 (2007). doi:10.1126/science.1145229

18. M. Rueping, A. P. Antonchick, C. Brinkmann, Dual catalysis: A combined enantioselective brønsted acid and metal-catalyzed reaction—metal catalysis with chiral counterions. *Angew. Chem. Int. Ed.* **46**, 6903 (2007). doi:10.1002/anie.200702439

19. S. Mukherjee, B. List, Chiral counteranions in asymmetric transition-metal catalysis: Highly enantioselective Pd/Brønsted acid-catalyzed direct α-allylation of aldehydes. *J. Am. Chem. Soc.* **129**, 11336 (2007). doi:10.1021/ja074678r

20. S. Liao, B. List, Asymmetric counteranion-directed transition-metal catalysis: Enantioselective epoxidation of alkenes with manganese(III) salen phosphate complexes. *Angew. Chem. Int. Ed.* **49**, 628 (2010). doi:10.1002/anie.200905332

21. G. Jiang, B. List, Enantioselective hydrovinylation via asymmetric counteranion-directed ruthenium catalysis. *Chem. Commun. (Camb.)* **47**, 10022 (2011). doi:10.1039/c1cc12499d

22. B. Xu, S.-F. Zhu, X.-L. Xie, J.-J. Shen, Q.-L. Zhou, Asymmetric N-H insertion reaction cooperatively catalyzed by rhodium and chiral spiro phosphoric acids. *Angew. Chem. Int. Ed.* **50**, 11483 (2011). doi:10.1002/anie.201105485

23. S. E. Denmark, J. Fu, Catalytic enantioselective addition of allylic organometallic reagents to aldehydes and ketones. *Chem. Rev.* **103**, 2763 (2003). doi:10.1021/cr020050h

24. M. Yus, J. C. González-Gómez, F. Foubelo, Catalytic Enantioselective Allylation of Carbonyl Compounds and Imines. *Chem. Rev.* **111**, 7774 (2011). doi:10.1021/cr1004474

25. R. W. Hoffmann, W. Ladner, On the absolute stereochemistry of C-2 and C-3 in stegobinone. *Tetrahedron Lett.* **20**, 4653 (1979). doi:10.1016/S0040-4039(01)86674-0

26. H. C. Brown, K. S. Bhat, Enantiomeric Z- and E-crotyldiisopinocampheylboranes. Synthesis in high optical purity of all four possible stereoisomers of. beta.-methylhomoallyl alcohols. *J. Am. Chem. Soc.* **108**, 293 (1986). doi:10.1021/ja00262a017

27. H. C. Brown, K. S. Bhat, Chiral synthesis via organoboranes. 7. Diastereoselective and enantioselective synthesis of erythro- and threo-.beta.-methylhomoallyl alcohols via enantiomeric (Z)- and (E)-crotylboranes. *J. Am. Chem. Soc.* **108**, 5919 (1986). doi:10.1021/ja00279a042

28. H. Kim, S. Ho, J. L. Leighton, A more comprehensive and highly practical solution to enantioselective aldehyde crotylation. *J. Am. Chem. Soc.* **133**, 6517 (2011). doi:10.1021/ja200712f

29. A. Dobson, S. R. Robinson, M. F. Uttley, Complexes of the Platinum Metals. Part V Perfluorocarboxylato-derivatives. *J. Chem. Soc., Dalton Trans.* (5): 370 (1975). doi:10.1039/dt9750000370

30. J. R. Zbieg, E. L. McInturff, J. C. Leung, M. J. Krische, Amplification of anti-diastereoselectivity via curtin-hammett effects in ruthenium-catalyzed hydrohydroxyalkylation of 1,1-disubstituted allenes: diastereoselectivrs. *J. Am. Chem. Soc.* **133**, 1141 (2011). doi:10.1021/ja1104156

31. H. C. Maytum, B. Tavassoli, J. M. J. Williams, Reduction of aldehydes and ketones by transfer hydrogenation with 1,4-butanediol. *Org. Lett.* **9**, 4387 (2007). doi:10.1021/ol702029n

32. K. Hiraki, N. Ochi, Y. Sasada, H. Hayashida, Y. Fuchita, S. J. Yamanaka, Organoruthenium(II) Complexes formed by Insertion Reactions of Some Vinyl Compounds and Conjugated Dienes into a Hydrido-Ruthenium Bond. *Chem. Soc. Dalton Trans.* 873, 1985.

33. P. Xue *et al*., Isomerism of [Ru(η3-allyl)Cl(CO)(PPh3)2]. *Organometallics* **23**, 4735 (2004). doi:10.1021/om049646g

34. N. Ahmad *et al*., Complexes of ruthenium, osmium, rhodium, and iridium containing hydride carbonyl, or nitrosyl ligands. *Inorg. Synth.* **15**, 45 (1974). doi:10.1002/9780470132463.ch13

35. W. C. Still, M. Kahn, A. Mitra, Rapid chromatographic technique for preparative separations with moderate resolution. *J. Org. Chem.* **43**, 2923 (1978). doi:10.1021/jo00408a041

36. I. Kim, S. B. Han, M. J. Krische, *anti*-Diastereo- and enantioselective carbonyl crotylation from the alcohol or aldehyde oxidation level employing a cyclometallated iridium catalyst: α-Methyl allyl acetate as a surrogate to preformed crotylmetal reagents. *J. Am. Chem. Soc.* **131**, 2514 (2009). doi:10.1021/ja808857w

37. X. Gao, I. Townsend, M. J. Krische, Enhanced *anti*-diastereo- and enantioselectivity in alcohol-mediated carbonyl crotylation using an isolable single component iridium catalyst. *J. Org. Chem.* **76**, 2350 (2011). doi:10.1021/jo200068q

38. A. V. Malkov, L. Dufková, L. Farrugia, P. Kocovsky, Quinox, a quinoline-type N-oxide, as organocatalyst in the asymmetric allylation of aromatic aldehydes with allyltrichlorosilanes: The role of arene–arene interactions. *Angew. Chem. Int. Ed.* **42**, 3674 (2003). doi:10.1002/anie.200351737

39. J. D. Kim, I. S. Kim, C. H. Jin, O. P. Zee, Y. H. Jung, Regioselective and diastereoselective amination with use of chlorosulfonyl isocyanate: A short and efficient synthesis of (−)-cytoxazone. *Org. Lett.* **7**, 4025 (2005). doi:10.1021/ol0515255

40. S. E. Denmark, J. Fu, Catalytic, enantioselective addition of substituted allylic trichlorosilanes using a rationally-designed 2,2‘-bispyrrolidine-based bisphosphoramide. *J. Am. Chem. Soc.* **123**, 9488 (2001). doi:10.1021/ja016552e

41. Starting materials were made in accordance to the procedures in: S. Takizawa, A. Horii, H. Sasai, Acid–Base Organocatalysts for the Aza-Morita–Baylis–Hillman Reaction of Nitroalkenes. *Tetrahedron: Asymmetry* **21**, 891 (2010).