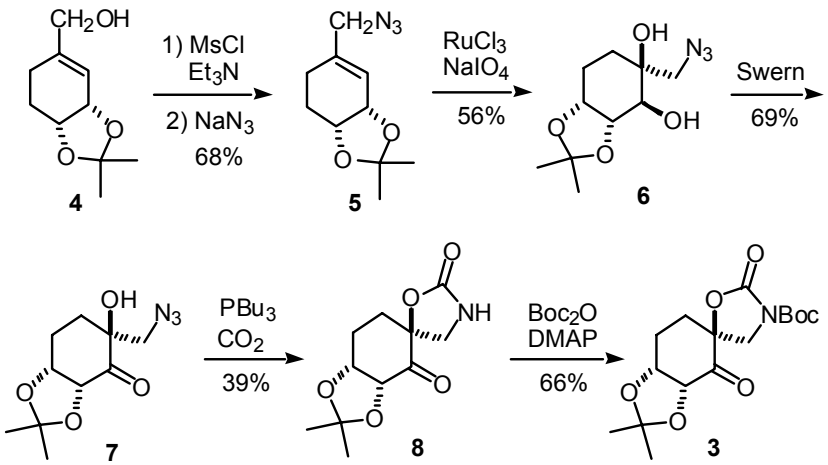
Supporting Methods and Materials

Synthesis of Ketone 3 from Alcohol 4



Alcohol **4** was prepared based on the reported procedure (1, 2).

Preparation of Diol 6. To a solution of alcohol **4** (3.43 g, 18.6 mmol) in CH_2Cl_2 (10 ml) at 0°C were added Et_3N (7.77 ml, 55.8 mmol) and MsCl (2.16 ml, 27.9 mmol). After stirring for 2 h, the solvent was removed by rotary evaporation. To the resulting residue was added acetone (20 ml) followed by a solution of NaN_3 (1.57 g, 24.2 mmol) in water (10.1 ml). After stirring at room temperature for an additional 16 h, the acetone was removed by rotary evaporation, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried (Na_2SO_4), filtered, and concentrated to give azide **5** as an orange solid (2.65 g, 68%). An analytic sample was purified by flash chromatography (1:1 EtOAc/hexanes). The remainder of the material was used for the next step without additional purification. IR (film) 2,100 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 5.69 (br s, 1H), 4.49 (m, 1H), 4.29 (m, 1H), 3.70 (s, 2H), 2.15 (m, 1H), 2.00–1.76 (m, 3H), 1.37 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 136.8, 124.1, 108.7, 72.5, 71.8, 56.9, 28.2, 26.6, 25.6, 22.3.

To a solution of compound **5** (2.0 g, 9.56 mmol) in CH_3CN (37 ml) and EtOAc (37 ml) at 0°C was added dropwise an aqueous solution containing $RuCl_3$ (0.14 g, 0.67 mmol) and $NaIO_4$ (2.66 g, 12.4 mmol) (11.8 ml) over 5 min. After an additional 15 min, the reaction was quenched with saturated $Na_2S_2O_3$ (15 ml). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (silica gel was buffered with 1% Et_3N) (1:1 EtOAc/hexanes) to give diol **6** as a clear oil (1.30 g, 56%) (some amount of ketone **7** was isolated also) (0.57 g, 25%). $[\alpha]_D^{20}$ = –44.2 (*c* = 0.095, $CHCl_3$); IR (film) 3,430, 2,104 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 4.31 (m, 1H), 4.00 (dd, *J* = 7.2, 5.1 Hz, 1H), 3.57 (dd, *J* = 7.2, 3.0 Hz, 1H), 3.45 (d, *J* = 12.3 Hz, 1H), 3.36

(d, J = 12.3 Hz, 1H), 2.72 (br s, 1H), 2.37 (br s, 1H), 2.18–2.01 (m, 1H), 2.01–1.90 (m, 1H), 1.71–1.60 (m, 2H), 1.50 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 109.1, 80.2, 74.3, 74.1, 74.0, 58.4, 28.7, 27.5, 26.6, 21.6. High-resolution MS calcd for $C_{10}H_{18}N_3O_4$ (M + 1): 244.1297. Found: 244.1299.

Preparation of Ketone 8. To a solution of DMSO (0.10 ml, 1.44 mmol) in CH_2Cl_2 (0.97 ml) at –78°C was added dropwise oxalyl chloride (0.0664 ml, 0.77 mmol). After warming to room temperature for exactly 3 min, the reaction mixture was cooled to –78°C again. A solution of alcohol **6** (0.14 g, 0.58 mmol) in CH_2Cl_2 (5.3 ml) then was added dropwise. After the mixture was stirred at –78°C for an additional 1.5 h, Et_3N (0.289 ml, 2.07 mmol) was added. The reaction mixture was allowed to warm to room temperature for 15 min. Saturated aqueous NH_4Cl was added, followed by water. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried (Na_2SO_4) , filtered, concentrated, and purified by flash chromatography (1:1 EtOAc/hexanes buffered with 1% Et_3N) to give ketone **7** as a white solid (0.097 g, 69%) (note that the solvent used for packing the silica gel column and the eluent must be buffered with Et_3N; otherwise, a large amount of ketal will be removed on the silica gel column). mp 73–75°C; $[\alpha]_D^{20}$ = –18.2 (c = 0.055, $CHCl_3$); IR (film) 3,438, 2,107, 1,734 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 4.78 (d, J = 5.7 Hz, 1H), 4.60 (m, 1H), 3.74 (d, J = 12.6 Hz, 1H), 3.30 (d, J = 12.6 Hz, 1H), 3.23 (s, 1H), 2.21 (m, 1H), 2.00–1.85 (m, 3H), 1.44 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 207.6, 110.3, 78.7, 78.0, 77.9, 56.4, 31.0, 27.0, 25.9, 21.8.

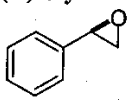
A solution of **7** (0.19 g, 0.79 mmol) in anhydrous CH_3CN (60 ml) (note that it is essential to use dry CH_3CN, because any incidental water in the reaction will give low yield) was sparged with CO_2 in a three-necked round-bottomed flask equipped with a reflux condenser for ≈2 h. To this clear colorless solution was added dropwise PBu_3 (0.20 g, 1.0 mmol) at room temperature. After stirring under CO_2 to completion as monitored by TLC (2:1 EtOAc/hexanes), the clear yellow solution was concentrated and purified by flash chromatography (silica gel buffered with 2% Et_3N) (2:1 EtOAc/hexanes) to give ketone **8** as an off-white solid (0.075 g, 39%) (note that this compound is typically isolated containing some tributylphosphine oxide; it is important to remove tributylphosphine oxide as much as possible, because the following reaction is tolerant of <5% of tributylphosphine oxide). $[\alpha]_D^{20}$ = –32.8 (c = 0.5, $CHCl_3$); IR (film) 3,337, 1,771, 1,746 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.71 (br s, 1H), 4.85 (d, J = 5.1 Hz, 1H), 4.63 (m, 1H), 4.34 (d, J = 8.9 Hz, 1H), 3.16 (J = 8.9 Hz, 1H), 2.50 (m, 1H), 2.30–2.00 (m, 3H), 1.43 (s, 3H), 1.40 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 201.4, 156.7, 110.0, 85.2, 78.8, 77.4, 44.4, 32.9, 27.1, 26.1, 21.1. High-resolution MS calcd for $C_{11}H_{16}NO_5$ (M + 1): 242.1028. Found: 242.1029.

Preparation of Ketone 3. To a solution of **8** (0.075 g, 0.31 mmol) in tetrahydrofuran (2 ml) at room temperature was added di-*tert*-butyldicarbonate (0.088 g, 0.40 mmol) followed by a solution of 4-(dimethylamino)pyridine in tetrahydrofuran (0.1 M, 0.01 ml, 0.001 mmol). After stirring to completion as monitored by TLC (2:1 EtOAc/hexanes) (≈30 min), the mixture was filtered immediately through a prepacked silica gel plug (buffered with 2% Et_3N) and washed with EtOAc/hexanes (1:1). The combined filtrate

was concentrated and purified by flash chromatography (silica gel buffered with 2% Et_3N) (1:2 ether/hexanes) to give ketone **3** as a white solid (0.070 g, 66%): mp 130–132°C; $[\alpha]_D^{20} = -20$ (*c* = 0.1, $CHCl_3$); IR (film) 1,824, 1,747, 1,728 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 4.82 (d, *J* = 5.1 Hz, 1H), 4.64 (d, *J* = 10.6 Hz, 1H), 4.62 (m, 1H), 3.48 (d, *J* = 10.6 Hz, 1H), 2.45 (m, 1H), 2.20 (m, 3H), 1.54 (s, 9H), 1.44 (s, 3H), 1.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 201.1, 150.0, 148.9, 110.4, 84.7, 81.4, 78.9, 77.3, 47.5, 32.8, 28.0, 27.2, 26.1, 21.0. High-resolution MS calcd for $C_{16}H_{24}NO_7$ (M + 1): 342.1553. Found: 342.1545.

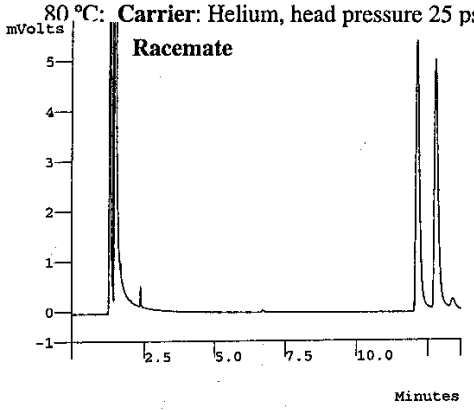
The chromatograms for the determination of enantiomeric excess of the epoxides.

(R)-Styrene oxide (Table 1, Entry 1)



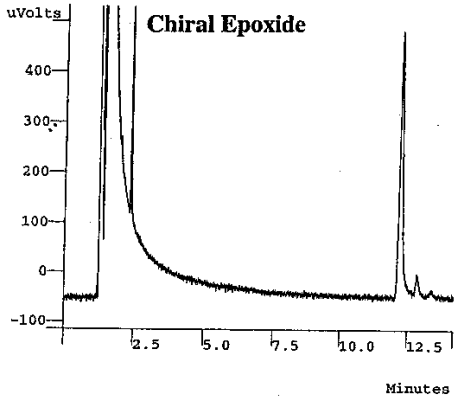
GC Conditions: Column: Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc. **Oven**: 80 °C; **Carrier**: Helium, head pressure 25 psi; **Detection**: FID 250 °C

Racemate



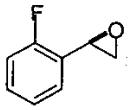
Peak No	Peak Name	Result ()	Ret. Time (min)
1		50.0995	12.099
2		49.9005	12.743
	Totals	100.0000	

Chiral Epoxide



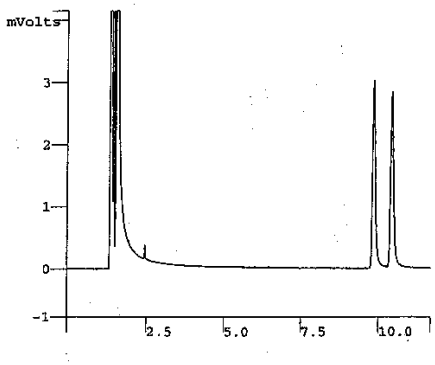
Peak No	Peak Name	Result ()	Ret. Time (min)
1		95.0540	12.182
2		4.9460	12.849
	Totals	100.0000	

2-Fluorostyrene oxide (Table 1, Entry 2)



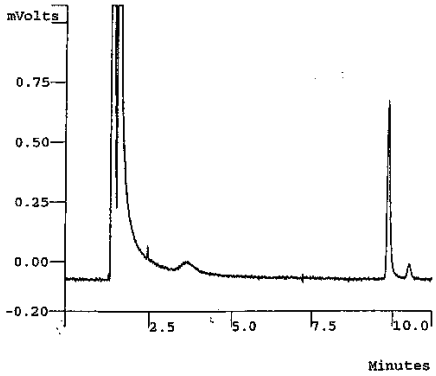
GC Conditions: Column: Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc. **Oven**: 80 °C; **Carrier**: Helium, head pressure 25 psi; **Detection**: FID 250 °C

Racemate



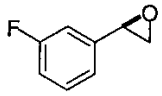
Peak No	Peak Name	Result ()	Ret. Time (min)
1		50.3680	9.824
2		49.6320	10.394
	Totals	100.0000	

Chiral Epoxide



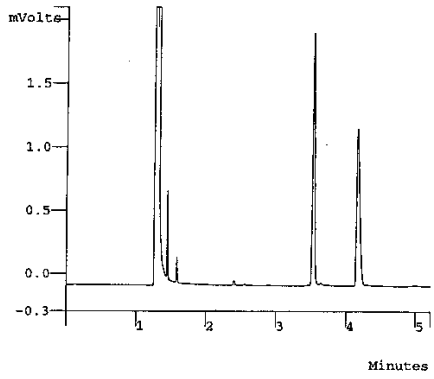
Peak No	Peak Name	Result ()	Ret. Time (min)
1		94.3897	9.849
2		5.6103	10.441
	Totals	100.0000	

3-Fluorostyrene oxide (Table 1, Entry 3)



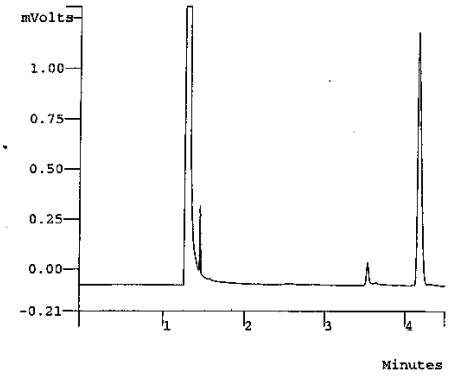
GC Conditions: Column: Chiraldex G-TA (Cat. No. 73033), Adv. Separation Technologies, Inc. **Oven**: 100 °C; **Carrier**: Helium, head pressure 25 psi; **Detection**: FID 250 °C

Racemate



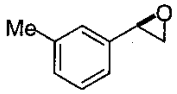
Peak No	Peak Name	Result ()	Ret. Time (min)
1		50.4681	3.516
2		49.5319	4.151
	Totals	100.0000	

Chiral Epoxide



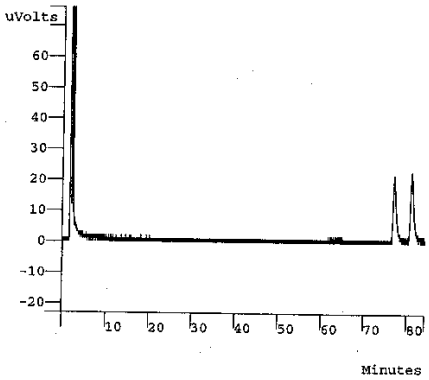
Peak No	Peak Name	Result ()	Ret. Time (min)
1		5.1969	3.531
2		94.8031	4.154
	Totals	100.0000	

3-Methylstyrene oxide (Table 1, Entry 4)



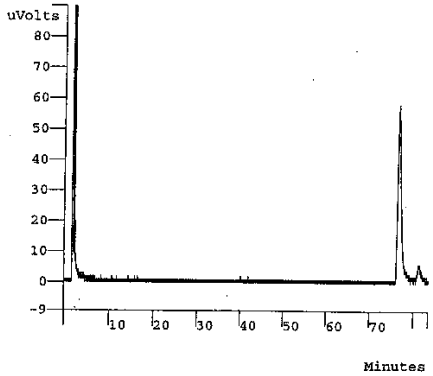
GC Conditions: Column: Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc. **Oven**: 60 °C; **Carrier**: Helium, head pressure 20 psi; **Detection**: FID 250 °C

Racemate



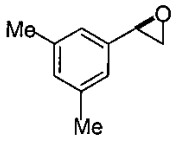
Peak No	Peak Name	Result ()	Ret. Time (min)
1		50.1996	76.842
2		49.8004	80.891
	Totals	100.0000	

Chiral Epoxide



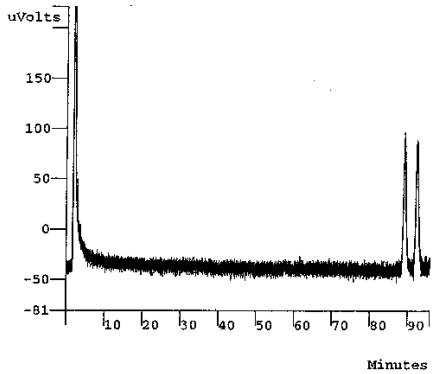
Peak No	Peak Name	Result ()	Ret. Time (min)
1		96.2861	76.427
2		3.7139	81.033
	Totals	100.0000	

3,5-Dimethylstyrene oxide (Table 1, Entry 5)



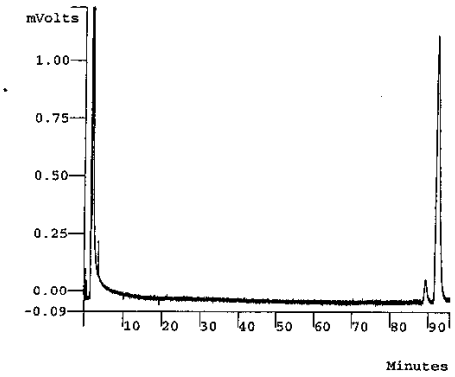
GC Conditions: Column: Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc. **Oven**: 70 °C; **Carrier**: Helium, head pressure 20 psi; **Detection**: FID 250 °C

Racemate



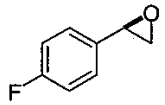
Peak No	Peak Name	Result ()	Ret. Time (min)
1		49.2782	89.007
2		50.7218	92.313
	Totals	100.0000	

Chiral Epoxide



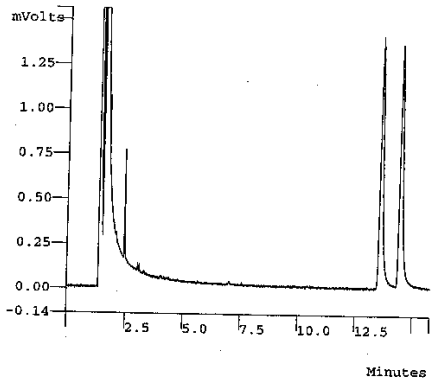
Peak No	Peak Name	Result ()	Ret. Time (min)
1		5.2812	89.283
2		94.7188	91.923
	Totals	100.0000	

(R)-4-Fluorostyrene oxide (Table 1, Entry 6)



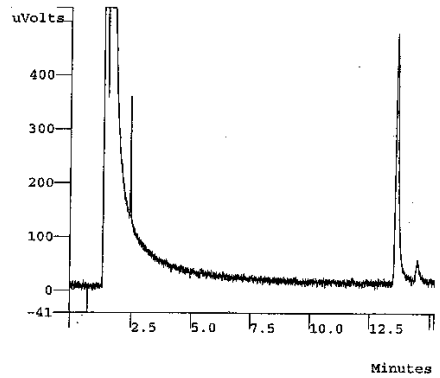
GC Conditions: Column: Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc. **Oven**: 80 °C; **Carrier**: Helium, head pressure 25 psi; **Detection**: FID 250 °C

Racemate



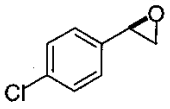
Peak No	Peak Name	Result ()	Ret. Time (min)
1		49.6178	13.568
2		50.3822	14.424
	Totals	100.0000	

Chiral Epoxide



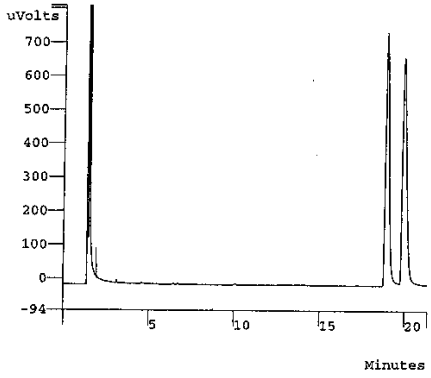
Peak No	Peak Name	Result ()	Ret. Time (min)
1		95.1250	13.601
2		4.8750	14.481
	Totals	100.0000	

(R)-4-Chlorostyrene oxide (Table 1, Entry 7)



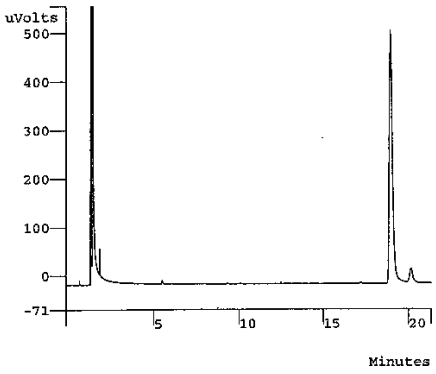
GC Conditions: Column: Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc. **Oven**: 100 °C; **Carrier**: Helium, head pressure 25 psi; **Detection**: FID 250 °C

Racemate



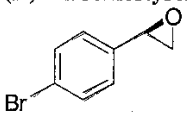
Peak No	Peak Name	Result ()	Ret. Time (min)
1		49.4743	18.849
2		50.5257	19.868
	Totals	100.0000	

Chiral Epoxide



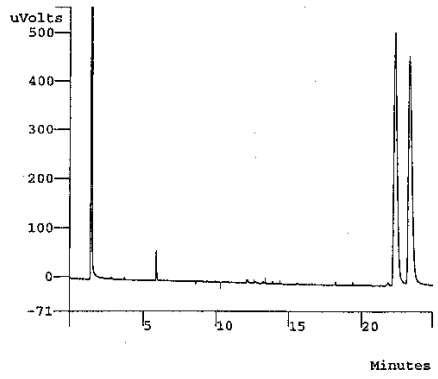
Peak No	Peak Name	Result ()	Ret. Time (min)
1		95.3065	18.954
2		4.6935	20.134
	Totals	100.0000	

(R)-4-Bromostyrene oxide (Table 1, Entry 8)



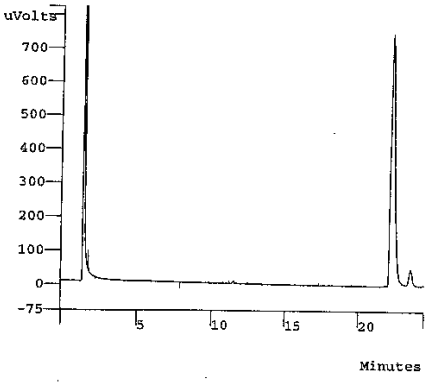
GC Conditions: Column: Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc. **Oven**: 110 °C; **Carrier**: Helium, head pressure 25 psi; **Detection**: FID 250 °C

Racemate



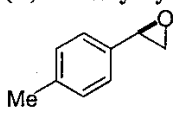
Peak No	Peak Name	Result ()	Ret. Time (min)
1		49.4556	22.192
2		50.5444	23.179
	Totals	100.0000	

Chiral Epoxide



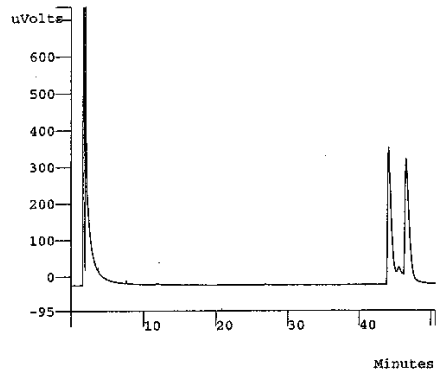
Peak No	Peak Name	Result ()	Ret. Time (min)
1		95.2081	22.126
2		4.7919	23.397
	Totals	100.0000	

(R)-4-Methylstyrene oxide (Table 1, Entry 9)



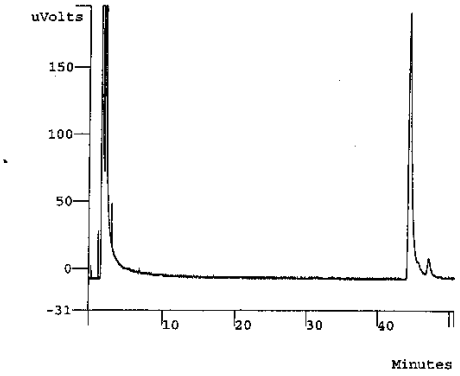
GC Conditions: Column: Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc. **Oven**: 70 °C; **Carrier**: Helium, head pressure 20 psi; **Detection**: FID 250 °C

Racemate



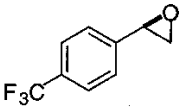
Peak No	Peak Name	Result ()	Ret. Time (min)
1		49.7335	44.049
2		50.2665	46.476
	Totals	**100.0000**	

Chiral Epoxide



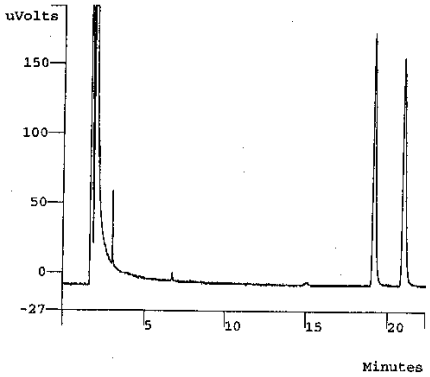
Peak No	Peak Name	Result ()	Ret. Time (min)
1		94.8427	44.322
2		5.1573	47.112
	Totals	**100.0000**	

4-Trifluoromethylstyrene oxide (Table 1, Entry 10)



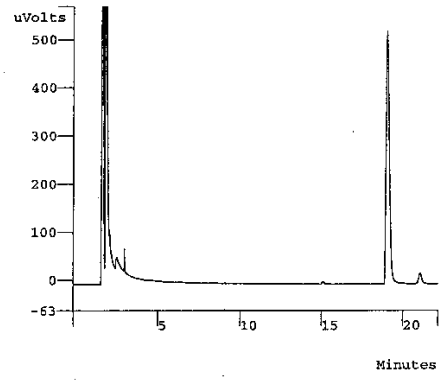
GC Conditions.: Column: Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc. **Oven**: 80 °C; **Carrier**: Helium, head pressure 20 psi; **Detection**: FID 250 °C

Racemate



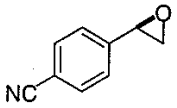
Peak No	Peak Name	Result ()	Ret. Time (min)
1		50.3194	19.104
2		49.6806	20.927
	Totals	**100.0000**	

Chiral Epoxide



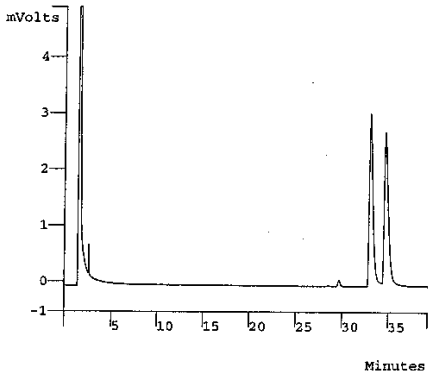
Peak No	Peak Name	Result ()	Ret. Time (min)
1		96.6186	18.981
2		3.3814	21.014
	Totals	**100.0000**	

(R)-4-Cyanostyrene oxide (Table 1, Entry 11)



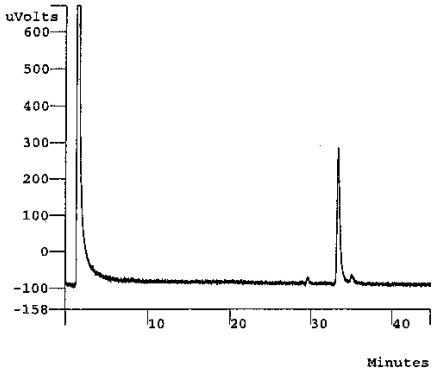
GC Conditions: Column: Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc. **Oven**: 115 °C; **Carrier**: Helium, head pressure 25 psi: **Detection**: FID 250 °C

Racemate



Peak No	Peak Name	Result ()	Ret. Time (min)
1		49.7992	32.951
2		50.2008	34.572
	Totals	**100.0000**	

Chiral Epoxide



Peak No	Peak Name	Result ()	Ret. Time (min)
1		96.2704	33.316
2		3.7296	35.026
	Totals	**100.0000**	

1. McComsey, D. F. & Maryanoff, B. E. (1994) *J. Org. Chem*. **59,** 2652–2654.
2. Wang, Z.-X., Miller, S. M., Anderson, O. P. & Shi, Y. (2001) *J. Org. Chem.* **66,** 521–530.