Electronic Supporting Information

Synthesis of α-Fluoro-β-hydroxy Esters by an Enantioselective Reformatsky-type Reaction

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Table 4. Selected NMR data for α-fluoro-β-hydroxy esters.

Product	Ar	R	(2*S*,3*S*)/(2*R*,3*R*)	(2*R*,3*S*)/(2*S*,3*R*)
1	Ph	Me	δ_F -194.5 δ_C 92.9 (d, $^1J_{CF}$ 194.2 Hz)	δ_F -192.0 δ_C 93.5 (d, $^1J_{CF}$ 199.2 Hz)
2	Ph	Et	δ_F -196.4 δ_C 93.0 (d, $^1J_{CF}$ 193.2 Hz)	δ_F -193.4 δ_C 92.3 (d, $^1J_{CF}$ 201.2 Hz)
3	Ph	Pr	δ_F -196.2 δ_C 93.0 (d, $^1J_{CF}$ 193.3 Hz)	δ_F -193.1 δ_C 92.5 (d, $^1J_{CF}$ 201.2 Hz)
4	Ph	*iso*-Bu	δ_F -195.4 δ_C 93.4 (d, $^1J_{CF}$ 193.2 Hz)	δ_F -192.1 δ_C 92.8 (d, $^1J_{CF}$ 198.1 Hz)
5	2-MeOC$_6$H$_4$	Me	δ_F -197.0 δ_C 91.2 (d, $^1J_{CF}$ 188.1 Hz)	δ_F -195.1 δ_C 92.5 (d, $^1J_{CF}$ 189.2 Hz)
6	4-MeOC$_6$H$_4$	Me	δ_F -193.9 δ_C 92.9 (d, $^1J_{CF}$ 194.2 Hz)	δ_F -191.9 δ_C 92.5 (d, $^1J_{CF}$ 198.1 Hz)
7	4-ClC$_6$H$_4$	Me	δ_F -194.5 δ_C 91.6 (d, $^1J_{CF}$ 194.2 Hz)	δ_F -191.9 δ_C 93.1 (d, $^1J_{CF}$ 199.2 Hz)
8	1-indanone		δ_F -196.4 δ_C 92.3 (d, $^1J_{CF}$ 192.2 Hz)	δ_F -193.5 δ_C 90.7 (d, $^1J_{CF}$ 193.2 Hz)
9	1-tetralone		δ_F -198.0 δ_C 93.6 (d, $^1J_{CF}$ 191.2 Hz)	δ_F -191.4 δ_C 91.8 (d, $^1J_{CF}$ 196.2 Hz)

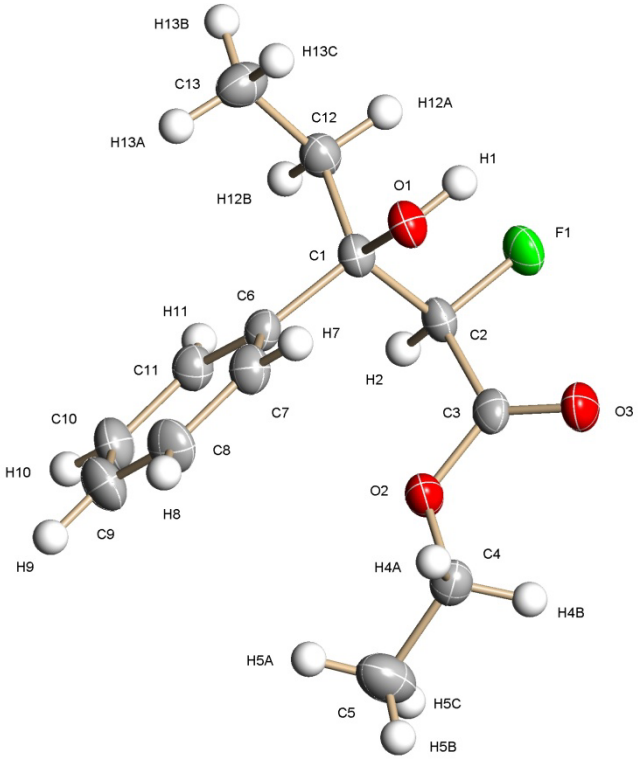


Figure 1. Molecular structure of ethyl 2-fluoro-3-hydroxy-3-phenylpentanoate **2a** showing 50% displacement ellipsoids.

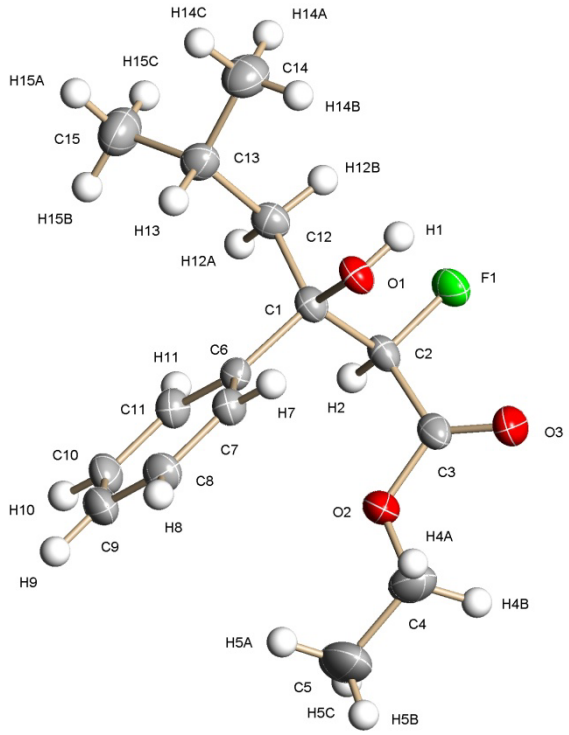


Figure 2. Molecular structure of ethyl-2-fluoro-3-hydroxy-5-methyl-3-phenylhexanoate **4a** showing 50% displacement ellipsoids.

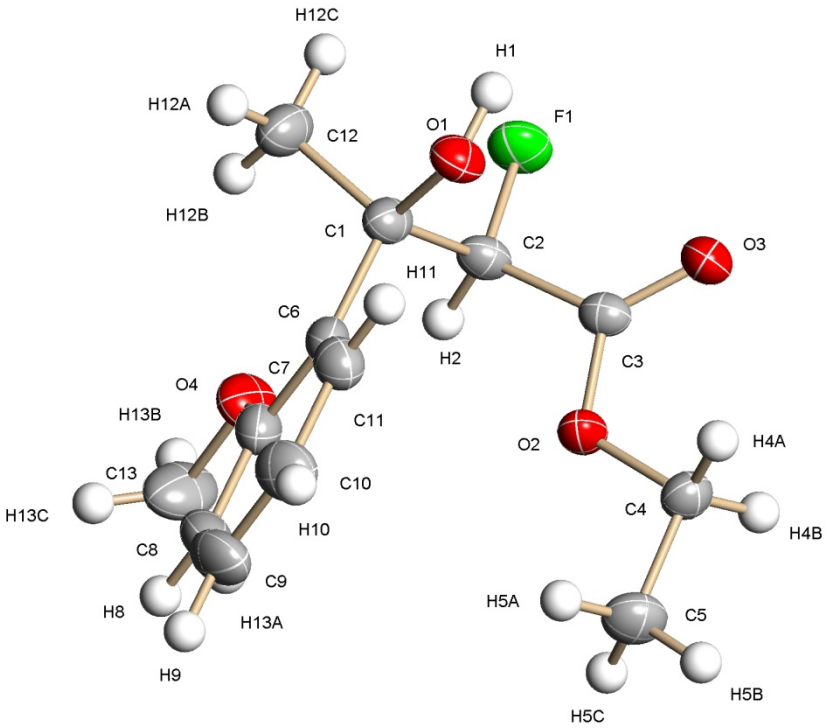


Figure 3. Molecular structure of ethyl-2-fluoro-3-hydroxy-3-(2-methoxyphenyl)butanoate **5a** showing 50% displacement ellipsoids.

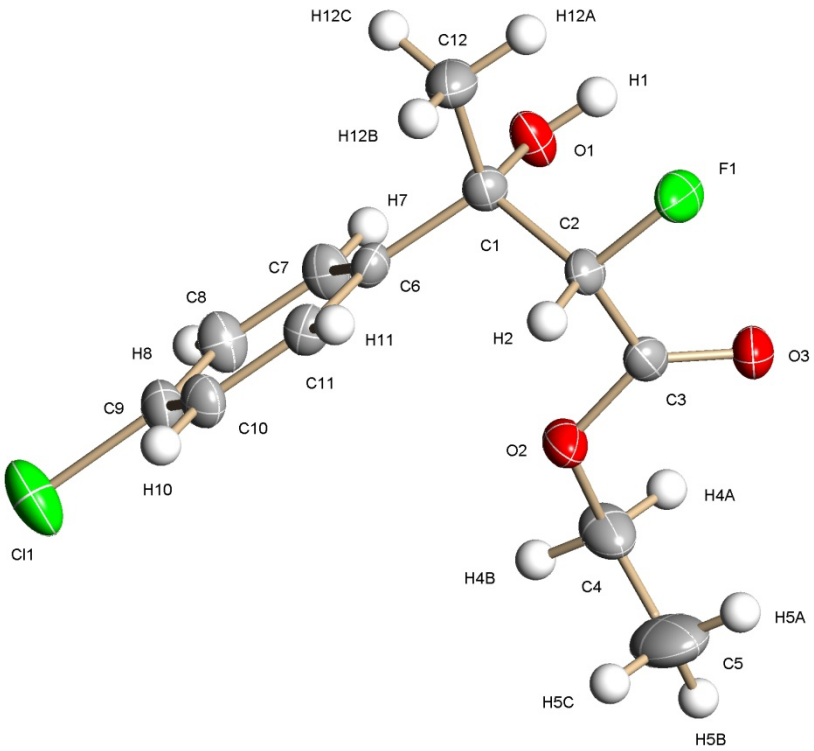


Figure 4. Molecular structure of ethyl-3-(4-chlorophenyl)-2-fluoro-3-hydroxy-butanoate **7a** showing 50% displacement ellipsoids.

Table 5. Selected bond lengths (Å) and bond angles (°) with estimated standard deviations (e.s.d.s.) in parenthesis for compounds **1a** (R= Me), **2a** (R = Et), **4a** (R = ^{i}Bu), **5a** (Ar = 2-MeOC$_6$H$_4$) and **7a** (Ar = 4-ClC$_6$H$_4$).

	1a (R = Me)	**2a** (R = Et)	**4a** (R = ^{i}Bu)	**5a** (Ar = 2-MeOC$_6$H$_4$)	**7a** (Ar = 4-ClC$_6$H$_4$)
C(1)-O(1)	1.417(3)	1.417(2)	1.4188(19)	1.419(2)	1.424(4)
C(1)-C(6)	1.521(3)	1.523(2)	1.529(2)	1.529(2)	1.527(4)
C(1)-C(12)	1.522(3)	1.538(2)	1.533(2)	1.530(2)	1.517(4)
C(1)-C(2)	1.556(3)	1.551(2)	1.549(2)	1.548(2)	1.539(4)
C(2)-F(1)	1.386(2)	1.3920(18)	1.3937(17)	1.3927(19)	1.393(3)
C(2)-H(2)	1.0000	1.0000	1.0000	1.0000	1.0000
C(2)-C(3)	1.520(3)	1.517(2)	1.509(2)	1.511(2)	1.511(4)
C(3)-O(3)	1.202(3)	1.208(2)	1.201(2)	1.2048(19)	1.207(4)
C(3)-O(2)	1.322(3)	1.3261(19)	1.3345(19)	1.326(2)	1.324(4)
O(2)-C(4)	1.465(3)	1.454(2)	1.446(2)	1.4569(19)	1.451(4)
O(1)-C(1)-C(12)	110.8(2)	110.50(14)	110.98(12)	109.37(13)	110.1(3)
O(1)-C(1)-C(6)	107.79(19)	107.91(13)	107.16(12)	107.09(12)	107.4(2)
O(1)-C(1)-C(2)	108.4(2)	108.48(13)	109.05(13)	107.66(12)	108.5(2)
C(12)-C(1)-C(6)	111.6(2)	112.86(13)	111.90(13)	110.81(14)	110.8(2)
C(12)-C(1)-C(2)	109.4(2)	108.83(14)	108.42(13)	111.26(13)	109.9(3)
C(6)-C(1)-C(2)	108.8(2)	108.14(13)	109.29(12)	110.51(12)	110.1(2)
C(1)-C(2)-F(1)	108.70(19)	108.41(13)	107.69(12)	108.46(12)	108.5(2)
C(1)-C(2)-H(2)	109.8	110.0	109.9	110.1	109.5
C(1)-C(2)-C(3)	112.0(2)	112.14(14)	112.33(13)	111.46(12)	113.1(3)
F(1)-C(2)-H(2)	109.8	110.0	109.9	110.1	109.5
F(1)-C(2)-C(3)	106.57(19)	106.33(12)	107.03(13)	106.66(13)	106.8(2)
H(2)-C(2)-C(3)	109.8	110.0	109.9	110.1	109.5
C(2)-C(3)-O(3)	124.5(2)	124.27(16)	125.80(15)	125.16(14)	124.6(3)
C(2)-C(3)-O(2)	110.6(2)	110.11(14)	109.79(14)	109.96(13)	110.5(3)
O(3)-C(3)-O(2)	124.9(2)	125.62(16)	124.38(16)	124.89(14)	124.9(3)
C(3)-O(2)-C(4)	116.13(19)	117.70(13)	116.31(14)	116.60(12)	117.3(2)
O(1)-C(1)-C(2)-F(1)	71.9(2)	-65.29(16)	-63.88(16)	-73.25(14)	72.6(3)
C(6)-C(1)-C(2)-F(1)	-171.07(18)	177.92(12)	179.28(12)	170.12(12)	-170.2(2)
C(12)-C(1)-C(2)-F(1)	-48.9(3)	54.98(17)	57.07(16)	46.58(17)	-47.9(3)
F(1)-C(2)-C(3)-O(3)	-12.3(3)	18.2(2)	20.2(2)	12.8(2)	-6.8(4)
F(1)-C(2)-C(3)-O(2)	165.89(18)	-161.94(13)	-161.38(12)	-167.31(12)	172.9(2)

Table 6. Intermolecular hydrogen bond distances and angles as well as intermolecular H···F bond distances and angles with symmetry codes for compounds **1a** (R= Me), **2a** (R = Et), **4a** (R = ^{i}Bu), **5a** (Ar = 2-MeOC$_6$H$_4$) and **7a** (Ar = 4-ClC$_6$H$_4$).

Product	D-H···A[a]	*d*(D-H) (Å)	*d*(H···A) (Å)	*d*(D···A) (Å)	<DHA (°)
1a	O(1)H(1)···O(3)^{i}	0.84	2.04	2.865(2)	168.3
2a	O(1)H(1)···O(3)^{ii}	0.84	2.11	2.9378(18)	166.6
4a	O(1)H(1)···O(3)^{iii}	0.84	2.01	2.847(2)	172.1
5a	O(1)H(1)···O(3)^{ii}	0.84	2.07	2.855(2)	155.0
7a	O(1)H(1)···O(3)^{iv}	0.84	2.08	2.889(3)	162.5
1a	O(1)H(1)···F(1)^{i}	0.84	2.62	3.122(2)	119.5
2a	O(1)H(1)···F(1)^{ii}	0.84	2.46	2.9250(16)	115.9
4a	O(1)H(1)···F(1)^{iii}	0.84	2.60	3.010(2)	111.2
5a	O(1)H(1)···F(1)^{ii}	0.84	2.53	3.029(2)	119.5
7a	O(1)H(1)···F(1)^{iv}	0.84	2.42	2.979(3)	124.3

[a] Symmetry transformations used to generate equivalent atoms: (i) –x+1, -y+2, -z+2; (ii) –x+1, -y, -z+1; (iii) –x, -y+1, -z; (iv) –x+2, y+½, -z+$^{3}/_{2}$.

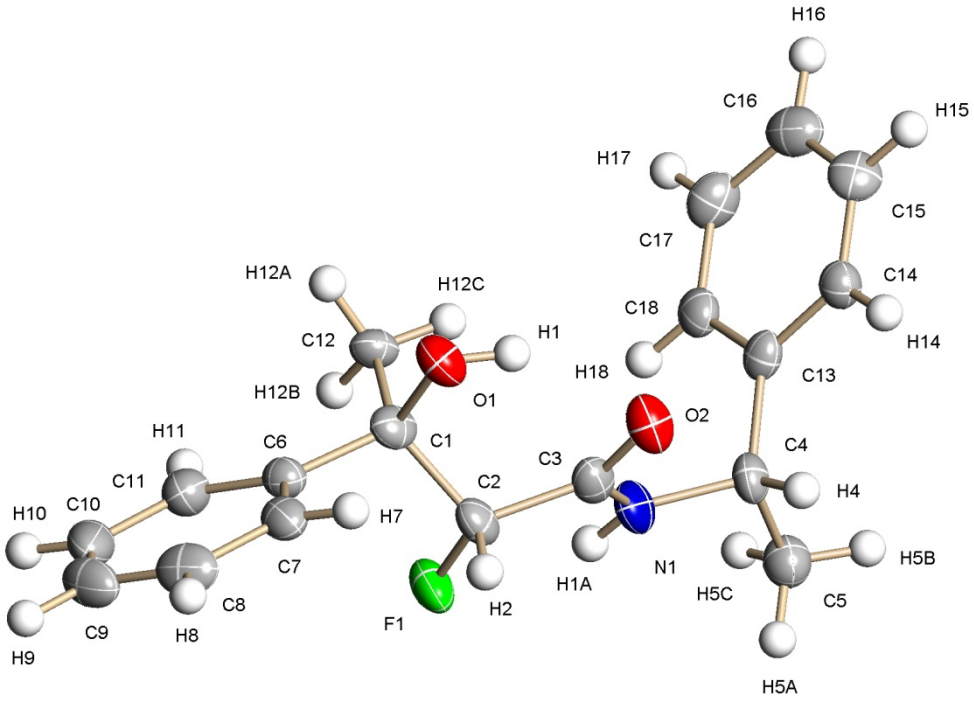


Figure 5. Molecular structure of 2(*R*)-fluoro-3(*R*)-hydroxy-3-phenyl-*N*-((*S*)-1-phenylethyl)-butanamide **10b** showing 50% displacement ellipsoids.

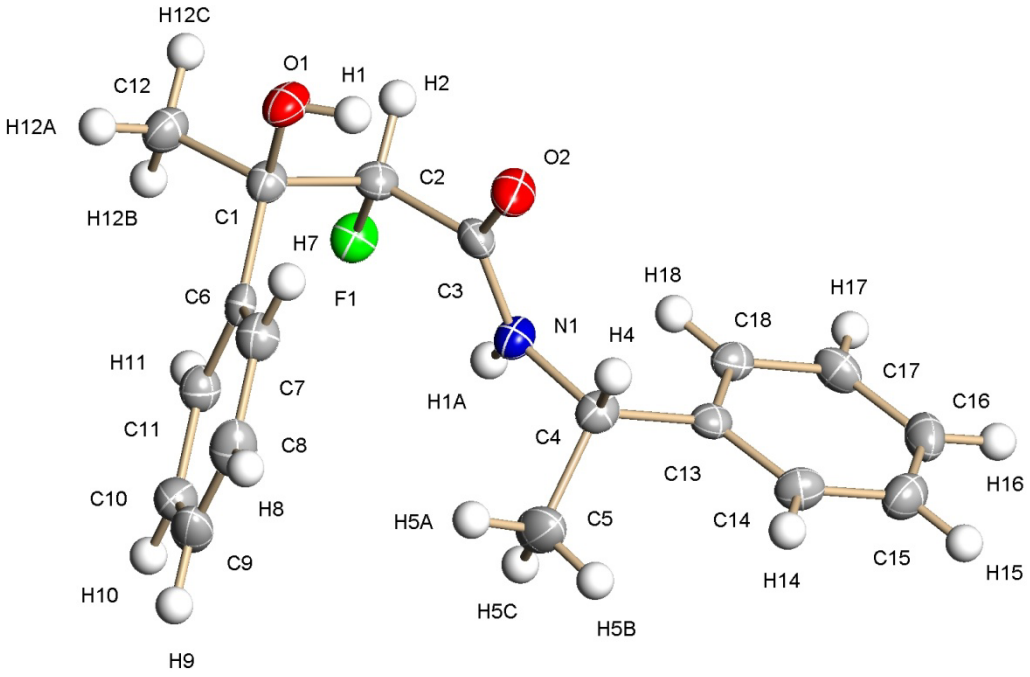


Figure 6. Molecular structure of 2(*S*)-fluoro-3(*R*)-hydroxy-3-phenyl-*N*-((*S*)-1-phenylethyl)-butanamide **10d** showing 50% displacement ellipsoids.

Table 7. Intramolecular and intermolecular hydrogen bond distances (Å) and angles (°) with symmetry codes for amides **10b** and **10d**.

Product	D-H···A	*d*(D-H) (Å)	*d*(H···A) (Å)	*d*(D···A) (Å)	<DHA (°)
10b	O(1)H(1)···O(2)[a]	0.84	2.00	2.727(5)	144.3
10d	O(1)H(1)···O(2)[a]	0.84	2.13	2.831(2)	140.8
10b	N(1)H(1A)···O(2)[bi]	0.88	2.58	3.347(6)	146.0
10d	N(1)H(1A)···O(2)[bii]	0.88	2.19	2.985(3)	150.8

[a] Intramolecular hydrogen bonding; [b]Symmetry transformations used to generate equivalent atoms: (i) x, y-1, z; (ii) –x+1, y–$^1/_2$, -z +$^1/_2$.

Table 8. Selected bond lengths (Å) and bond angles (°) with estimated standard deviations (e.s.d.s.) in parenthesis for amides **10b** and **10d**.

	10b	**10d**
C(1)-O(1)	1.441(6)	1.419(3)
C(1)-C(6)	1.516(7)	1.531(3)
C(1)-C(12)	1.521(6)	1.531(3)
C(1)-C(2)	1.523(7)	1.551(3)
C(2)-F(1)	1.389(6)	1.392(2)
C(2)-H(2)	1.0000	1.0000
C(2)-C(3)	1.485(7)	1.515(3)
C(3)-O(2)	1.249(6)	1.238(3)
C(3)-N(1)	1.341(7)	1.329(3)
N(1)-C(4)	1.463(6)	1.460(3)
O(1)-C(1)-C(12)	108.3(4)	105.43(19)
O(1)-C(1)-C(6)	105.7(5)	111.85(19)
O(1)-C(1)-C(2)	108.0(4)	107.49(19)
C(12)-C(1)-C(6)	113.4(5)	111.8(2)
C(12)-C(1)-C(2)	111.1(4)	109.6(2)
C(6)-C(1)-C(2)	110.0(4)	110.51(17)
C(1)-C(2)-F(1)	108.4(4)	109.75(18)
C(1)-C(2)-H(2)	107.9	108.8
C(1)-C(2)-C(3)	114.0(4)	110.78(19)
F(1)-C(2)-H(2)	107.9	108.8
F(1)-C(2)-C(3)	110.5(5)	110.02(18)
H(2)-C(2)-C(3)	107.9	108.8
C(2)-C(3)-N(1)	118.1(6)	117.3(2)
C(2)-C(3)-O(2)	120.0(6)	118.2(2)
N(1)-C(3)-O(2)	121.9(5)	124.4(2)
C(3)-N(1)-C(4)	122.2(5)	123.2(2)
O(1)-C(1)-C(2)-F(1)	179.8(4)	-168.85(18)
C(6)-C(1)-C(2)-F(1)	65.0(6)	68.8(2)
C(12)-C(1)-C(2)-F(1)	-61.5(5)	-54.8(2)
F(1)-C(2)-C(3)-N(1)	1.1(7)	-8.8(3)
F(1)-C(2)-C(3)-O(2)	-177.4(5)	174.2(2)

Experimental

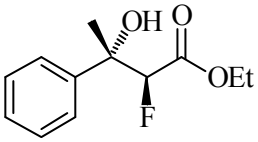
Proton, ^{19}F and ^{13}C NMR spectra were recorded on a Bruker DRX 400 spectrometer at 400.13, 376.46 and 100.62 MHz respectively and were referenced to external $SiMe_4$ (^{1}H), external $CFCl_3$ (^{19}F) and to external $SiMe_4$ (^{13}C) using the high frequency positive convention. Electron impact (EI) and fast atom bombardment (FAB) mass spectra were recorded on a Kratos concept 1 H, double focussing, forward geometry mass spectrometer. 3-Nitrobenzyl alcohol was used as the matrix for the FAB spectra. Electrospray mass spectra were obtained on a Micromass Quatro LC. High performance liquid chromatography was carried out on a Perkin Elmer HPLC Liquid Chromatograph supported with either an OD-H (Daicel) or an AS (Daicel) column and a UV-VIS detector. X-ray crystallography data were collected on a Bruker Apex SMART 2000 diffractometer using graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å). Preparative, centrifugally accelerated, radial thin-layer chromatography was carried out on a Harrison Research Chromatotron Model 79240.

THF was obtained dry from a distillation machine model Puresolve^{TM}, and was stored in sealed ampoules over 4Å molecular sieves under an atmosphere of dry nitrogen. (1*R*,2*S*)-1-Phenyl-2-(1-pyrrolidinyl)propan-1-ol was dried using the Kugelröhr oven at 100 ^{o}C under oil pump vacuum for 30 min. After cooling, the crystals of the chiral aminoalcohol were dissolved in dry diethyl ether and the solvent was removed under vacuum. The second step was not a purification process and the only aim was to obtain small crystals that were convenient to use. The dry aminoalcohol was stored in a flushbox under nitrogen.

General Procedure for Table 1.

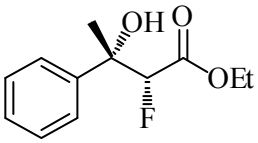
Under an argon atmosphere a dry three neck flask was charged with THF (8 mL), the required ketone (1.0 mmol) and ethyl iodofluoroacetate (0.20 mL, 0.35 g, 1.5 mmol). After 30 min of stirring the reaction mixture at 0 ^{o}C, diethylzinc (1.5 mL, 1.0 M solution in hexane, 1.5 mmol) was added and the reaction mixture was stirred for another 4.5 h at 0 ^{o}C. After quenching the reaction mixture with 1 M HCl (10 mL), it was extracted with ethyl acetate (3 x 10 mL). The organic layer was washed with 1 M HCl (10 mL), brine (10 mL) and water (10 ml) before being dried over magnesium sulphate. The product was purified by column chromatography on silica gel.

Preparation of ethyl-2-fluoro-3-hydroxy-3-phenylbutanoate 1



(2*S*,3*S*)

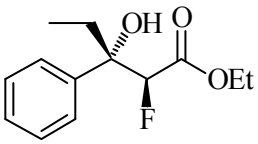
The title compound was prepared using acetophenone (0.12 mL, 0.12 g, 1.0 mmol). After purification by column chromatography (10 % EtOAc in hexane) on silica gel, the pure product was obtained as a colourless oil (0.22 g, 98 %). Crystals were formed from the pure product and were recrystallised from hexane to give the pure (2*S*,3*S*)/(2*R*,3*R*)-diastereoisomer **1a** as colourless crystals (0.12 g, 53 %). M.p. 76-78 ^{o}C (lit.,[10a] 76.5-78 ^{o}C). The characterisation data was in agreement with the literature.[10a] δ_H ($CDCl_3$) 1.00 (3H, t, $^3J_{HH}$ 7.0 Hz, OCH_2CH_3), 1.65 (3H, d, $^4J_{HF}$ 2.0 Hz, CH_3), 3.15 (1H, br s, O*H*), 4.02 (2H, q, $^3J_{HH}$ 7.0 Hz, OCH_2CH_3), 4.84 (1H, d, $^2J_{HF}$ 47.7 Hz, C*H*F), 7.22 (1H, tt, $^3J_{HH}$ 7.4 Hz, $^4J_{HH}$ 1.6 Hz, ArH), 7.29 (2H, tt, $^3J_{HH}$ 7.4, $^4J_{HH}$ 1.6 Hz, ArH), 7.40 (2H, dt, $^3J_{HH}$ 7.4 Hz, $^4J_{HH}$ 1.6 Hz); δ_F ($CDCl_3$) -194.54 (d, $^2J_{FH}$ 48.2 Hz, C*F*H); δ_C ($CDCl_3$) 13.8 (CH_3), 25.4 (d, $^3J_{CF}$ 2.1 Hz, CH_3), 61.6 (CH_2), 74.7 (d, $^2J_{CF}$ 20.1 Hz, C), 92.9 (d, $^1J_{CF}$ 194.2 Hz, CH), 125.4 (CH), 127.7 (CH), 128.2 (CH), 142.1 (C), 168.0 (d, $^2J_{CF}$ 24.1 Hz, CO); *m/z* (FAB) 227.10787 (MH^+. $C_{12}H_{16}FO_3$ requires 227.10795). The enantiomers were separated on a chiralcel OD-H column eluted with 1 % IPA in hexane. The flow rate of the mobile phase was set at 1.0 mL/min. R_t = 12.68 min (ethyl-2(*S*)-fluoro-3(*S*)-hydroxy-3-phenylbutanoate), 14.90 min (ethyl-2(*R*)-fluoro-3(*R*)-hydroxy-3-phenyl-butanoate).



(2*R*,3*S*)

The pure sample of (2*R*,3*S*)/(2*S*,3*R*)-ethyl-2-fluoro-3-hydroxy-3-phenylbutanoate **1b** was obtained as a colourless oil after purification on the chromatotron with 5 % Et_2O in hexane (0.012 g, 5 %). The characterisation data was in agreement with the literature.[10a] δ_H ($CDCl_3$) 0.99 (3H, t, $^3J_{HH}$ 7.0 Hz, OCH_2CH_3), 1.60 (3H, d, $^4J_{HF}$ 2.7 Hz, CH_3), 3.40 (1H, br s, O*H*), 4.00 (1H, dq, $^2J_{HH}$ 10.6 Hz, $^3J_{HH}$ 7.0 Hz, OCH_AH_B), 4.05 (1H, dq, $^2J_{HH}$ 10.6 Hz, $^3J_{HH}$ 7.0 Hz, OCH_AH_B), 4.93 (1H, d, $^2J_{HF}$ 47.7 Hz, C*H*F), 7.21 (1H, tt, $^3J_{HH}$ 7.4 Hz, $^4J_{HH}$ 2.3 Hz, ArH), 7.27 (2H, dt, $^3J_{HH}$ 7.0 Hz, $^4J_{HH}$ 2.3 Hz, ArH), 7.41 (2H, dt, $^3J_{HH}$ 8.2 Hz, $^4J_{HH}$ 1.2 Hz, ArH); δ_F ($CDCl_3$) -192.00 (d, $^2J_{FH}$ 47.6 Hz, C*F*H); δ_C ($CDCl_3$) 13.8 (CH_3), 26.1 (d, $^3J_{CF}$ 2.1 Hz, CH_3), 61.8 (CH_2), 75.0 (d, $^2J_{CF}$ 20.1 Hz, C), 93.5 (d, $^1J_{CF}$ 199.2 Hz, CH), 125.1 (CH), 127.7 (CH), 128.3 (CH), 142.8 (C), 168.5 (d, $^2J_{CF}$ 23.1 Hz, CO). The enantiomers were separated on a chiralcel OD-H column eluted with 1 % IPA in hexane. The flow rate of the mobile phase was set at 1.0 mL/min. R_t = 9.65 min (ethyl-2(*S*)-fluoro-3(*R*)-hydroxy-3-phenylbutanoate), 11.27 min (ethyl-2(*R*)-fluoro-3(*S*)-hydroxy-3-phenylbutanoate).

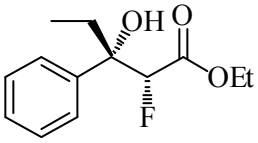
Preparation of (2*S*,3*S*)/(2*R*,3*R*)-ethyl 2-fluoro-3-hydroxy-3-phenylpentanoate 2a



(2*S*,3*S*)

The title compound was prepared using propiophenone (0.13 mL, 0.13 g, 1.0 mmol). After initial purification by column chromatography (10 % EtOAc in hexane) on silica gel, the sample was purified using the chromatotron (5 % Et_2O in hexane) to give colourless crystals (0.101 g, 40 %). M.p. 60-61 ^oC. δ_H ($CDCl_3$) 0.69 (3H, t, $^3J_{HH}$ 7.4 Hz, CH_2CH_3), 0.93 (3H, t, $^3J_{HH}$ 7.4 Hz, OCH_2CH_3), 1.93 (2H, qd, $^3J_{HH}$ 7.4 Hz, $^4J_{HF}$ 2.0 Hz, CH_2CH_3), 2.94 (1H, br s, O*H*), 3.97 (2H, q, $^3J_{HH}$ 7.0 Hz, OCH_2CH_3), 4.88 (1H, d, $^2J_{HF}$ 47.7 Hz, C*H*F), 7.21 (1H, tm, $^3J_{HH}$ 7.4 Hz, ArH), 7.28 (2H, tm, $^3J_{HH}$ 7.4, ArH), 7.35 (2H, dt, $^3J_{HH}$ 7.0 Hz, $^4J_{HH}$ 2.0 Hz, ArH); δ_F ($CDCl_3$) -196.37 (d, $^2J_{FH}$ 47.6 Hz, C*F*H); δ_C ($CDCl_3$) 7.0 (CH_3), 13.6 (CH_3), 30.4 (CH_2), 61.5 (CH_2), 77.4 (d, $^2J_{CF}$ 20.1 Hz, C), 93.0 (d, $^1J_{CF}$ 193.2 Hz, CH), 125.9 (CH), 127.5 (CH), 128.1 (CH), 139.7 (d, $^3J_{CF}$ 2.0 Hz, C), 167.9 (d, $^2J_{CF}$ 26.2 Hz, CO); *m/z* (FAB) 239.1084 ($(M-H)^+$. $C_{13}H_{16}FO_3$ requires 239.1083). Crystals of **2a**, suitable for X-ray diffraction, were grown by slow evaporation from hexane. The enantiomers were separated on a chiralcel OD-H column eluted with 0.5 % IPA in hexane. The flow rate of the mobile phase was set at 1.0 mL/min. R_t= 20.60 min (major enantiomer), 23.18 min (minor enantiomer).

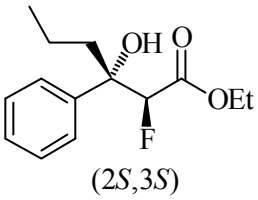
Preparation of (2*R*,3*S*)/(2*S*,3*R*)-ethyl-2-fluoro-3-hydroxy-3-phenylpentanoate 2b



(2*R*,3*S*)

The product was purified by column chromatography (10 % EtOAc in hexane) on silica gel to give a colourless oil (0.097 g, 40 %). δ_H ($CDCl_3$) 0.80 (3H, t, $^3J_{HH}$ 7.4 Hz, CH_2CH_3), 0.95 (3H, t, $^3J_{HH}$ 7.4 Hz, OCH_2CH_3), 1.94 (2H, 2x qd, $^3J_{HH}$ 7.4 Hz, $^4J_{HF}$ 1.6 Hz, $CH_AH_BCH_3$), 3.48 (1H, br s, O*H*), 3.97 (1H, dq, $^2J_{HH}$ 11.0 Hz, $^3J_{HH}$ 7.4 Hz, OCH_AH_B), 4.02 (1H, dq, $^2J_{HH}$ 11.0 Hz, $^3J_{HH}$ 7.4 Hz, OCH_AH_B), 4.97 (1H, d, $^2J_{HF}$ 47.7 Hz, C*H*F), 7.19 (1H, tt, $^3J_{HH}$ 7.4 Hz, $^4J_{HH}$ 1.2 Hz, ArH), 7.26 (2H, td, $^3J_{HH}$ 7.4, $^4J_{HH}$ 1.6 Hz, ArH), 7.38 (2H, dt, $^3J_{HH}$ 7.4 Hz, $^4J_{HH}$ 1.6 Hz, ArH); δ_F ($CDCl_3$) -193.36 (d, $^2J_{FH}$ 47.6 Hz, C*F*H); δ_C ($CDCl_3$) 7.2 (CH_3), 13.8 (CH_3), 31.4 (d, $^3J_{CF}$ 3.0 Hz, CH_2), 61.8 (CH_2), 77.0 (d, $^2J_{CF}$ 19.2 Hz, C), 92.3 (d, $^1J_{CF}$ 201.2 Hz, CH), 125.5 (CH), 127.5 (CH), 128.1 (CH), 141.5 (C), 169.2 (d, $^2J_{CF}$ 22.1 Hz, CO); *m/z* (FAB) 239.1076 ($(M-H)^+$. $C_{13}H_{16}FO_3$ requires 239.1083). The enantiomers were separated on a chiralcel OD-H column eluted with 0.5 % IPA in hexane. The flow rate of the mobile phase was set at 1.0 mL/min. R_t= 9.77 min (minor enantiomer), 10.86 min (major enantiomer).

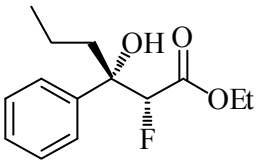
Preparation of (2*S*,3*S*)/(2*R*,3*R*)-ethyl 2-fluoro-3-hydroxy-3-phenylhexanoate 3a



(2*S*,3*S*)

The title compound was prepared using 1-phenylbutan-1-one (0.15 mL, 0.15 g, 1.0 mmol). The product was purified by column chromatography (10 % EtOAc in hexane) on silica gel to give colourless crystals (0.14 g, 57 %) which contained < 3 % of the (2*R*,3*S*)/(2*S*,3*R*)-diastereomer. δ_H ($CDCl_3$) 0.79 (3H, t, $^3J_{HH}$ 7.4 Hz, CH_2CH_3), 0.87-1.00 (1H, m, $CH_AH_BCH_3$), 0.93 (3H, t, $^3J_{HH}$ 7.4 Hz, OCH_2CH_3), 1.24-1.36 (1H, m, $CH_AH_BCH_3$), 1.86-1.98 (2H, m, $CH_2CH_2CH_3$), 2.98 (1H, br s, O*H*), 3.95 (2H, q, $^3J_{HH}$ 7.0 Hz, OCH_2CH_3), 4.87 (1H, d, $^2J_{HF}$ 48.1 Hz, C*H*F), 7.20 (1H, tm, $^3J_{HH}$ 7.0 Hz, ArH), 7.28 (2H, tt, $^3J_{HH}$ 7.0, $^4J_{HH}$ 2.0 Hz, ArH), 7.35 (2H, dt, $^3J_{HH}$ 7.0 Hz, $^4J_{HH}$ 2.0 Hz, ArH); δ_F ($CDCl_3$) -196.15 (d, $^2J_{FH}$ 47.6 Hz, C*F*H); δ_C ($CDCl_3$) 13.6 (CH_3), 14.3 (CH_3), 16.1 (CH_2), 39.9 (CH_2), 61.5 (CH_2), 77.3 (d, $^2J_{CF}$ 19.2 Hz, C), 93.0 (d, $^1J_{CF}$ 193.3 Hz, CH), 125.8 (CH), 127.4 (CH), 128.1 (CH), 140.1 (C), 167.9 (d, $^2J_{CF}$ 25.6 Hz, CO); *m/z* (FAB) 277.1216 (MNa^+. $C_{14}H_{19}FO_3Na$ requires 277.1216). The enantiomers were separated on a chiralcel OD-H column eluted with 0.5 % IPA in hexane. The flow rate of the mobile phase was set at 1.0 mL/min. R_t= 17.52 min (minor enantiomer), 21.90 min (major enantiomer).

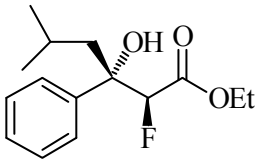
Preparation of (2*R*,3*S*)/(2*S*,3*R*)-ethyl-2-fluoro-3-hydroxy-3-phenylhexanoate 3b



(2*R*,3*S*)

The product was purified using 5 % diethyl ether in hexane on the chromatotron to give a colourless oil (0.054g, 20 %). δ_H ($CDCl_3$) 0.81 (3H, t, $^3J_{HH}$ 7.4 Hz, CH_2CH_3), 0.94 (3H, t, $^3J_{HH}$ 7.0 Hz, OCH_2CH_3), 1.04-1.17 (1H, m, $CH_AH_BCH_3$), 1.31-1.45 (1H, m, $CH_AH_BCH_3$), 1.79-1.93 (2H, m, $CH_2CH_2CH_3$), 3.50 (1H, br s, O*H*), 3.95 (2H, m, $OCH_AH_BCH_3$), 4.96 (1H, d, $^2J_{HF}$ 47.7 Hz, C*H*F), 7.18 (1H, tt, $^3J_{HH}$ 7.2 Hz, $^4J_{HH}$ 2.3 Hz, ArH), 7.25 (2H, tm, $^3J_{HH}$ 7.0, ArH), 7.35 (2H, dt, $^3J_{HH}$ 7.2 Hz, $^4J_{HH}$ 1.2 Hz); δ_F ($CDCl_3$) -193.06 (d, $^2J_{FH}$ 47.6 Hz, C*F*H); δ_C ($CDCl_3$) 13.7 (CH_3), 14.2 (CH_3), 16.2 (CH_2), 40.8 (CH_2), 61.8 (CH_2), 76.9 (d, $^2J_{CF}$ 20.1 Hz, C), 92.5 (d, $^1J_{CF}$ 201.2 Hz, CH), 125.4 (CH), 127.5 (CH), 128.1 (CH), 141.8 (C), 169.1 (d, $^2J_{CF}$ 23.1 Hz, CO). The enantiomers were separated on a chiralcel OD-H column eluted with 0.5 % IPA in hexane. The flow rate of the mobile phase was set at 1.0 mL/min. R_t= 9.57 min (minor enantiomer), 10.46 min (major enantiomer).

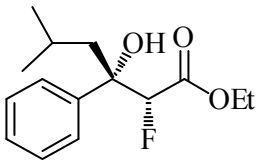
Preparation of (2*S*,3*S*)/(2*R*,3*R*)-ethyl-2-fluoro-3-hydroxy-5-methyl-3-phenylhexanoate 4a



(2*S*,3*S*)

The title compound was prepared using 3-methyl-1-phenylbutan-1-one (0.17 mL, 0.16 g, 1.0 mmol). The product was purified by column chromatography (5 % EtOAc in hexane) on silica gel to give colourless crystals (0.11 g, 46 %). M.p. 70-72 ^{o}C. δ_H ($CDCl_3$) 0.62 (3H, d, $^3J_{HH}$ 6.6 Hz, CHCH_3), 0.85 (3H, d, $^3J_{HH}$ 6.6 Hz, CHCH_3), 0.91 (3H, t, $^3J_{HH}$ 7.0 Hz, OCH$_2$CH_3), 1.42-1.55 (1H, m, CH(CH$_3$)$_2$), 1.81 (1H, ddd, $^2J_{HH}$ 14.5 Hz, $^3J_{HH}$ 7.4 Hz, $^4J_{HF}$ 2.3 Hz, CH_AH$_B$CH(CH$_3$)$_2$), 1.95 (1H, ddd, $^2J_{HH}$ 14.5 Hz, $^3J_{HH}$ 4.7 Hz, $^4J_{HF}$ 1.2 Hz, CH$_A$$H_B$CH(CH$_3$)$_2$), 2.99 (1H, s, O$H$), 3.93 (2H, q, $^3J_{HH}$ 7.4 Hz, OCH_2CH$_3$), 4.80 (1H, d, $^2J_{HF}$ 48.1 Hz, CHF), 7.21 (1H, tt, $^3J_{HH}$ 7.4 Hz, $^4J_{HH}$ 2.3 Hz, ArH), 7.28 (2H, tm, $^3J_{HH}$ 7.4, ArH), 7.36 (2H, dm, $^3J_{HH}$ 7.4 Hz, ArH); δ_F ($CDCl_3$) -195.35 (d, $^2J_{FH}$ 47.6 Hz, CFH); δ_C ($CDCl_3$) 13.6 (CH$_3$), 23.8 (CH$_3$), 23.9 (CH$_3$), 24.5 (CH), 45.6 (CH$_2$), 61.4 (CH$_2$), 77.8 (d, $^2J_{CF}$ 19.1 Hz, C), 93.4 (d, $^1J_{CF}$ 193.2 Hz, CH), 126.0 (CH), 127.4 (CH), 128.1 (CH), 140.2 (C), 167.8 (d, $^2J_{CF}$ 24.1 Hz, CO); *m/z* (FAB) 267.1389 ((M-H)$^+$. $C_{15}H_{20}FO_3$ requires 267.1396). Crystals of **4a**, suitable for X-ray diffraction, were grown by slow evaporation from a solution of 5 % diethyl ether in hexane. The enantiomers were separated on a chiralcel OD-H column eluted with 0.5 % IPA in hexane. The flow rate of the mobile phase was set at 1.0 mL/min. R_t= 12.84 min (minor enantiomer), 14.75 min (major enantiomer).

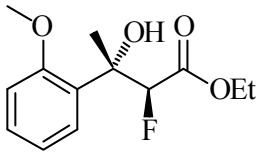
Preparation of (2*R*,3*S*)/(2*S*,3*R*)-ethyl-2-fluoro-3-hydroxy-5-methyl-3-phenylhexanoate 4b



(2*R*,3*S*)

The product was purified by column chromatography (5 % EtOAc in hexane) on silica gel to give a colourless oil (0.058 g, 22 %). δ_H ($CDCl_3$) 0.66 (3H, d, $^3J_{HH}$ 6.6 Hz, CHCH_3), 0.88 (3H, d, $^3J_{HH}$ 6.6 Hz, CHCH_3), 0.93 (3H, t, $^3J_{HH}$ 7.0 Hz, OCH$_2$CH_3), 1.56-1.66 (1H, m, CH(CH$_3$)$_2$), 1.74 (1H, ddd, $^2J_{HH}$ 14.5 Hz, $^3J_{HH}$ 7.4 Hz, $^4J_{HF}$ 1.2 Hz, CH_AH$_B$CH(CH$_3$)$_2$), 1.93 (1H, ddd, $^2J_{HH}$ 14.5 Hz, $^3J_{HH}$ 5.1 Hz, $^4J_{HF}$ 2.7 Hz, CH$_A$$H_B$ CH(CH$_3$)$_2$), 3.55 (1H, br s, OH), 3.91-4.07 (2H, m, OC$H_A$$H_BCH_3$), 4.92 (1H, d, $^2J_{HF}$ 47.7 Hz, CHF), 7.16 (1H, m, ArH), 7.25 (2H, tm, $^3J_{HH}$ 7.8 Hz, ArH), 7.39 (2H, dt, $^3J_{HH}$ 8.2 Hz, $^4J_{HH}$ 1.2 Hz, ArH); δ_F ($CDCl_3$) -192.14 (d, $^2J_{FH}$ 47.6 Hz, CFH); δ_C ($CDCl_3$) 13.7 (CH$_3$), 23.8 (CH), 24.2 (CH$_3$), 24.4 (CH$_3$), 46.4 (CH$_2$), 61.8 (CH$_2$), 77.4 (d, $^2J_{CF}$ 17.1 Hz, C), 92.8 (d, $^1J_{CF}$ 201.2 Hz, CH), 125.5 (d, $^4J_{CF}$ 3.0 Hz, CH), 127.5 (CH), 128.1 (CH), 141.8 (C), 169.1 (d, $^2J_{CF}$ 23.1 Hz, CO); *m/z* (FAB) 267.1396 ((M-H)$^+$. $C_{15}H_{20}FO_3$ requires 267.1396). The enantiomers were separated on a chiralcel OD-H column eluted with 0.5 % IPA in hexane. The flow rate of the mobile phase was set at 1.0 mL/min. R_t= 7.88 min (minor enantiomer), 8.64 min (major enantiomer).

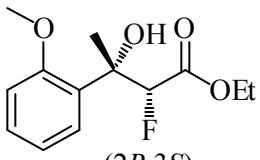
Preparation of (2*S*,3*S*)/(2*R*,3*R*)-ethyl-2-fluoro-3-hydroxy-3-(2-methoxyphenyl)butanoate 5a



(2*S*,3*S*)

The title compound was prepared using 2-methoxyacetophenone (0.14 mL, 0.15 g, 1.0 mmol). The product was purified by column chromatography (10 % EtOAc in hexane) on silica gel to give colourless crystals (0.15 g, 58 %). M.p. 62 °C. δ_H ($CDCl_3$) 0.92 (3H, t, $^3J_{HH}$ 7.0 Hz, OCH_2CH_3), 1.65 (3H, d, $^4J_{HF}$ 2.0 Hz, CH_3), 3.60 (1H, br s, O*H*), 3.82 (3H, s, OCH_3), 3.92 (1H, dq, $^2J_{HH}$ 10.6 Hz, $^3J_{HH}$ 7.0 Hz, $OCH_AH_BCH_3$), 3.97 (1H, dq, $^2J_{HH}$ 10.6 Hz, $^3J_{HH}$ 7.0 Hz, $OCH_AH_BCH_3$), 5.43 (1H, d, $^2J_{HF}$ 48.5 Hz, C*H*F), 6.84 (1H, dd, $^3J_{HH}$ 8.2 Hz, $^4J_{HH}$ 1.2 Hz, ArH), 6.90 (1H, td, $^3J_{HH}$ 7.4, $^4J_{HH}$ 1.2 Hz, ArH), 7.22 (1H, ddd, $^3J_{HH}$ 8.2 Hz, $^3J_{HH}$ 7.4 Hz, $^4J_{HH}$ 1.6 Hz, ArH), 7.43 (1H, dd, $^3J_{HH}$ 7.8, $^4J_{HH}$ 1.6 Hz, ArH); δ_F ($CDCl_3$) -196.95 (d, $^2J_{FH}$ 47.6 Hz, C*F*H); δ_C ($CDCl_3$) 13.7 (CH_3), 25.7 (d, $^3J_{CF}$ 4.0 Hz, CH_3), 55.42 (CH_3), 61.0 (CH_2), 75.1 (d, $^2J_{CF}$ 21.1 Hz, C), 91.2 (d, $^1J_{CF}$ 188.1 Hz, CH), 111.1 (CH), 121.0 (CH), 127.2 (CH), 129.2 (CH), 130.2 (C), 156.3 (C), 168.0 (d, $^2J_{CF}$ 25.2 Hz, CO); *m/z* (FAB) 255.1032 ($(M-H)^+$. $C_{13}H_{16}FO_4$ requires 255.1033). Crystals of **5a**, suitable for X-ray diffraction, were grown by slow evaporation from cold hexane (5 °C). The enantiomers were separated on a chiralcel OD-H column eluted with 1 % IPA in hexane. The flow rate of the mobile phase was set at 1.0 mL/min. R_t = 12.57 min (major enantiomer), 15.33 min (minor enantiomer).

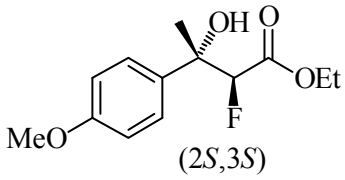
Preparation of (2*R*,3*S*)/(2*S*,3*R*)-ethyl-2-fluoro-3-hydroxy-3-(2-methoxyphenyl)-butanoate 5b



(2*R*,3*S*)

After initial purification by column chromatography (10 % EtOAc in hexane) on silica gel, the sample was purified using the chromatotron (5 % Et_2O in hexane) to give a colourless oil (0.051 g, 20 %). δ_H ($CDCl_3$) 1.07 (3H, t, $^3J_{HH}$ 7.0 Hz, OCH_2CH_3), 1.61 (3H, d, $^4J_{HF}$ 2.0 Hz, CH_3), 3.82 (3H, s OCH_3), 3.95 (1H, br s, O*H*), 3.90-4.11 (2H, m, OCH_2CH_3), 5.40 (1H, d, $^2J_{HF}$ 48.5 Hz, C*H*F), 6.85 (1H, d, $^3J_{HH}$ 7.4 Hz, ArH), 6.94 (1H, td, $^3J_{HH}$ 7.4, $^4J_{HH}$ 1.2 Hz, ArH), 7.22 (1H, td, $^3J_{HH}$ 8.0 Hz, $^4J_{HH}$ 1.6 Hz, ArH), 7.37 (1H, dd, $^3J_{HH}$ 7.8, $^4J_{HH}$ 1.6 Hz, ArH); δ_F ($CDCl_3$) -195.08 (d, $^2J_{FH}$ 47.6 Hz, C*F*H); δ_C ($CDCl_3$) 13.9 (CH_3), 22.3 (d, $^3J_{CF}$ 5.0 Hz, CH_3), 55.5 (CH_3), 61.2 (CH_2), 75.9 (d, $^2J_{CF}$ 21.1 Hz, C), 92.5 (d, $^1J_{CF}$ 189.2 Hz, CH), 111.3 (CH), 121.2 (CH), 127.3 (CH), 129.4 (CH), 130.2 (C), 156.6 (C), 167.9 (d, $^2J_{CF}$ 24.1 Hz, CO); *m/z* (FAB) 255.1042 ($(M-H)^+$. $C_{13}H_{16}FO_4$ requires 255.1033). The enantiomers were separated on a chiralcel OD-H column eluted with 1 % IPA in hexane. The flow rate of the mobile phase was set at 1.0 mL/min. R_t = 22.08 min (major enantiomer), 36.74 min (minor enantiomer).

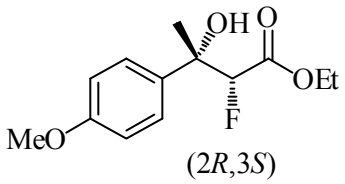
Preparation of (2*S*,3*S*)/(2*R*,3*R*)-ethyl-2-fluoro-3-hydroxy-3-(4-methoxyphenyl)-butanoate 6a



(2*S*,3*S*)

The title compound was prepared using 4-methoxyacetophenone (0.12 mL, 0.15 g, 1.0 mmol). After initial purification by column chromatography (10 % EtOAc in hexane) on silica gel, the sample was purified using the chromatotron (Et_2O:hexane = 1:5) to give a colourless oil (0.154 g, 60 %) containing 11 % of (2*R*,3*S*)/(2*S*,3*R*)-diastereoisomer. δ_H ($CDCl_3$) 1.15 (3H, t, $^3J_{HH}$ 7.0 Hz, OCH_2CH_3), 1.69 (3H, d, $^4J_{HF}$ 2.0 Hz, CH_3), 3.21 (1H, s, O*H*), 3.83 (3H, s, OCH_3), 4.15 (2H, qd, $^3J_{HH}$ 7.0 Hz, $^5J_{HF}$ 1.2 Hz, OCH_2CH_3), 4.89 (1H, d, $^2J_{HF}$ 47.7 Hz, C*H*F), 6.89 (2H, d, $^3J_{HH}$ 9.0 Hz, ArH), 7.41 (2H, d, $^3J_{HH}$ 9.0, ArH); δ_F ($CDCl_3$) -193.89 (d, $^2J_{FH}$ 47.6 Hz, C*F*H); δ_C ($CDCl_3$) 13.9 (CH_3), 25.3 (CH_3), 55.3 (CH_3), 61.7 (CH_2), 74.4 (d, $^2J_{CF}$ 21.1 Hz, C), 92.9 (d, $^1J_{CF}$ 194.2 Hz, CH), 113.6 (CH), 126.7 (CH), 134.3 (C), 159.1 (C), 168.2 (d, $^2J_{CF}$ 24.1 Hz, CO). The enantiomers were separated on a chiralcel OD-H column eluted with 0.5 % IPA in hexane. The flow rate of the mobile phase was set at 1.0 mL/min. R_t = 46.93 min (major enantiomer), 67.96 min (minor enantiomer).

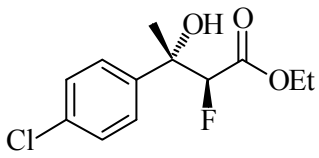
Preparation of (2*R*,3*S*)/(2*S*,3*R*)-ethyl-2-fluoro-3-hydroxy-3-(4-methoxyphenyl)-butanoate 6b



(2*R*,3*S*)

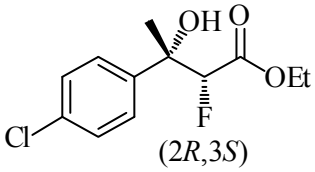
After initial purification by column chromatography (10 % EtOAc in hexane) on silica gel, the sample was purified using the chromatotron (Et_2O:hexane = 1:5) to give a colourless oil (0.064 g, 25 %). δ_H ($CDCl_3$) 1.12 (3H, t, $^3J_{HH}$ 7.0 Hz, OCH_2CH_3), 1.67 (3H, d, $^4J_{HF}$ 2.7 Hz, CH_3), 3.43 (1H, br s, O*H*), 3.82 (3H, s, OCH_3), 4.09-4.17 (2H, m, $OCH_AH_BCH_3$), 4.98 (1H, d, $^3J_{HF}$ 48.1 Hz, C*H*F), 6.89 (2H, d, $^3J_{HH}$ 9.0 Hz, ArH), 7.42 (2H, d, $^3J_{HH}$ 9.0, ArH); δ_F ($CDCl_3$) -191.86 (d, $^2J_{FH}$ 47.6 Hz, C*F*H); δ_C ($CDCl_3$) 13.9 (CH_3), 26.1 (CH_3), 55.2 (CH_3), 61.8 (CH_2), 74.7 (d, $^2J_{CF}$ 20.8 Hz, C), 92.5 (d, $^1J_{CF}$ 198.1 Hz, CH), 113.6 (CH), 126.4 (CH), 134.8 (C), 159.1 (C), 168.6 (d, $^2J_{CF}$ 24.0 Hz, CO); *m/z* (FAB) 256.11060 (M^+. $C_{13}H_{17}FO_4$ requires 256.11066). The enantiomers were separated on a chiralcel OD-H column eluted with 0.5 % IPA in hexane. The flow rate of the mobile phase was set at 1.0 mL/min. R_t = 32.32 min (major enantiomer), 37.30 min (minor enantiomer).

Preparation of (2*S*,3*S*)/(2*R*,3*R*)-ethyl-3-(4-chlorophenyl)-2-fluoro-3-hydroxy-butanoate 7a



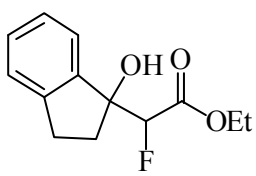
The title compound was prepared using 4-chloroacetophenone (0.13 mL, 0.15 g, 1.0 mmol). The product was purified by column chromatography (10 % EtOAc in hexane) on silica gel to give the product as colourless crystals (0.004 g, 5 %). M.p. 62-63 °C. δ_H ($CDCl_3$) 1.06 (3H, t, $^3J_{HH}$ 7.0 Hz, OCH_2CH_3), 1.60 (3H, d, $^4J_{HF}$ 2.3 Hz, CH_3), 3.20 (1H, br s, O*H*), 4.07 (2H, q, $^3J_{HH}$ 7.0 Hz, OCH_2CH_3), 4.79 (1H, d, $^2J_{HF}$ 47.3 Hz, C*H*F), 7.26 (2H, d, $^3J_{HH}$ 9.0 Hz, ArH), 7.35 (2H, d, $^3J_{HH}$ 9.0, ArH); δ_F ($CDCl_3$) -194.45 (d, $^2J_{FH}$ 47.6 Hz, C*F*H); δ_C ($CDCl_3$) 12.8 (CH_3), 24.3 (CH_3), 60.8 (CH_2), 73.4 (d, $^2J_{CF}$ 20.1 Hz, C), 91.6 (d, $^1J_{CF}$ 194.2 Hz, CH), 126.0 (CH), 127.3 (CH), 132.7 (C), 139.7 (C), 166.9 (d, $^2J_{CF}$ 24.1 Hz, CO); *m/z* (FAB) 259.0538 ($(M-H)^+$. $C_{12}H_{13}ClFO_3$ requires 259.0537). Crystals of **7a**, suitable for X-ray diffraction, were grown by slow evaporation from a solution of 5 % diethyl ether in hexane. The enantiomers were separated on a chiralcel AS column eluted with 10 % IPA in hexane. The flow rate of the mobile phase was set at 1.0 mL/min. R_t= 6.66 min (minor enantiomer), 13.71 min (major enantiomer).

Preparation of (2*R*,3*S*)/(2*S*,3*R*)-ethyl-3-(4-chlorophenyl)-2-fluoro-3-hydroxy-butanoate 7b



The product was purified by column chromatography (10 % EtOAc in hexane) on silica gel to give the product as a colourless oil (0.05 g, 20 %). δ_H ($CDCl_3$) 1.03 (3H, t, $^3J_{HH}$ 7.0 Hz, OCH_2CH_3), 1.57 (3H, d, $^4J_{HF}$ 2.3 Hz, CH_3), 3.49 (1H, br s, O*H*), 3.99-4.10 (2H, m, $^3J_{HH}$ 7.0 Hz, $OCH_AH_BCH_3$), 4.89 (1H, d, $^2J_{HF}$ 47.7 Hz, C*H*F), 7.24 (2H, d, $^3J_{HH}$ 9.0 Hz, ArH), 7.35 (2H, d, $^3J_{HH}$ 9.0, ArH); δ_F ($CDCl_3$) -191.88 (d, $^2J_{FH}$ 47.6 Hz, C*F*H); δ_C ($CDCl_3$) 13.8 (CH_3), 26.3 (d, $^3J_{CF}$ 3.0 Hz, CH_3), 62.0 (CH_2), 74.7 (d, $^2J_{CF}$ 19.1 Hz, C), 93.1 (d, $^1J_{CF}$ 199.2 Hz, CH), 126.7 (CH), 128.4 (CH), 133.7 (C), 141.4 (C), 168.5 (d, $^2J_{CF}$ 22.1 Hz, CO); *m/z* (FAB) 259.0539 ($(M-H)^+$. $C_{12}H_{13}ClFO_3$ requires 259.0537). The enantiomers were separated on a chiralcel AD column eluted with 2 % IPA in hexane. The flow rate of the mobile phase was set at 1.0 mL/min. R_t= 12.86 min (major enantiomer), 15.53 min (minor enantiomer).

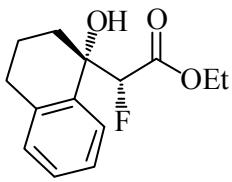
Preparation of ethyl-2-fluoro-2-(1-hydroxy-2,3-dihydro-1H-inden-1-yl)acetate 8



The title compound was prepared using indanone (0.13 g, 1.0 mmol). The product was purified by column chromatography (10 % EtOAc in hexane) on silica gel gave the pure product containing a 54:46 mixture of (2*S*,3*S*)/(2*R*,3*R*):(2*R*,3*S*)/(2*S*,3*R*)-diastereoisomers as a colourless oil (0.20 g, 84 %). δ_H ($CDCl_3$) 1.14 (3H, t, $^3J_{HH}$ 7.0 Hz, OCH_2CH_3) and 1.18 (3H, t, $^3J_{HH}$ 7.0 Hz, OCH_2CH_3),

2.04-2.14 (2H, m, CH*H*), 2.51-2.66 (2H, m, CH*H*), 2.75-2.87 (2H, m, C*H*H), 2.93-3.03 (3H, m, CH*H* and O*H*), 3.15 (1H, br s, O*H*), 4.11 (4H, m, OCH_AH_BCH$_3$), 4.91 (1H, d, $^2J_{HF}$ 47.7 Hz, C*H*F) and 5.03 (1H, d, $^2J_{HF}$ 47.7 Hz, C*H*F), 7.15-7.26 (6H, m, ArH), 7.32 (1H, d, $^3J_{HH}$ 7.8 Hz, ArH), 7.36 (1H, d, $^3J_{HH}$ 7.8 Hz, ArH); δ_F ($CDCl_3$) -193.48 (1F, d, $^2J_{FH}$ 47.6 Hz, C*F*H) and -196.39 (1F, d, $^2J_{FH}$ 47.6 Hz, C*F*H); δ_C ($CDCl_3$) 13.9 and 14.0 (CH_3), 29.5 and 29.7 (CH_2), 35.9 (CH_2) and 36.5 (d, $^3J_{CF}$ 3.0 Hz, CH_2), 61.8 and 61.9 (CH_2), 83.4 (d, $^2J_{CF}$ 21.1 Hz, C) and 83.7 (d, $^2J_{CF}$ 20.1 Hz, C), 90.7 (d, $^1J_{CF}$ 193.2 Hz, CH) and 92.3 (d, $^1J_{CF}$ 192.2 Hz, CH), 123.7 (CH), 124.37 (CH), 124.40 (CH), 125.0 (CH), 126.8 (CH), 129.3 (CH), 141.9 (C), 142.5 (C), 143.8 (C), 144.1 (C), 167.9 (d, $^2J_{CF}$ 24.1 Hz, CO) and 168.5 (d, $^2J_{CF}$ 24.1 Hz, CO); *m/z* (ES^+) 221.0982 ($(M\text{-}OH)^+$. $C_{13}H_{14}FO_2$ requires 221.0978). The enantiomers were separated on a chiralcel OD-H column eluted with 1 % IPA in hexane. The flow rate of the mobile phase was set at 1.0 mL/min. R_t for (2*R*,3*S*)/(2*S*,3*R*)-diastereomer = 17.56 min (major enantiomer), 24.70 min (minor enantiomer); R_t for (2*S*,3*S*)/(2*R*,3*R*)-diastereomer = 19.09 min (major enantiomer), 22.14 min (minor enantiomer).

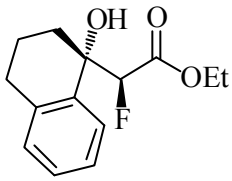
Preparation of (2*R*,3*S*)/(2*S*,3*R*)-ethyl-2-fluoro-2-(1-hydroxy-1,2,3,4-tetrahydronaphthalen-1-yl)acetate 9b



(2*R*,3*S*)

The title compound was prepared using tetralone (0.13 mL, 0.15 g, 1.0 mmol). The product was purified by column chromatography (10 % EtOAc in hexane) on silica gel to give the pure product as a 54:46 mixture of diastereoisomers (0.24 g, 96 %). The pure sample of the (2*R*,3*S*)/(2*S*,3*R*)-diastereoisomer was separated by chromatotron (20 % Et_2O in hexane) to give a colourless oil (0.055 g, 22 %). δ_H ($CDCl_3$) 1.21 (3H, t, $^3J_{HH}$ 7.0 Hz, OCH_2CH_3), 1.75-1.89 (3H, m, CH_2C*H*H), 2.09-2.17 (1H, m, CH*H*), 2.65-2.80 (2H, m, CH_2), 3.08 (1H, br s, O*H*), 4.18 (1H, dq, $^2J_{HH}$ 13.7 Hz, $^3J_{HH}$ 7.0 Hz, OCH_AH$_B$CH$_3$), 4.25 (1H, dq, $^2J_{HH}$ 13.7 Hz, $^3J_{HH}$ 7.0 Hz, OCH$_A$$H_BCH_3$), 5.07 (1H, d, $^2J_{HF}$ 47.3 Hz, C*H*F), 7.03-7.07 (1H, m, ArH), 7.14-7.18 (2H, m, ArH), 7.44-7.49 (1H, m, ArH); δ_F ($CDCl_3$) -191.36 (d, $^2J_{FH}$ 47.6 Hz, C*F*H); δ_C ($CDCl_3$) 14.1 (CH_3), 18.9 (CH_2), 29.4 (CH_2), 33.1 (CH_2), 62.0 (CH_2), 72.4 (d, $^2J_{CF}$ 21.1 Hz, C), 91.8 (d, $^1J_{CF}$ 196.2 Hz, CH), 126.3 (CH), 126.6 (CH), 128.1 (CH), 129.1 (CH), 136.1 (C), 138.4 (C), 169.0 (d, $^2J_{CF}$ 24.1 Hz, CO); *m/z* (ES^+) 275.1067 (MNa^+. $C_{14}H_{17}FO_3Na$ requires 275.1059). The enantiomers were separated on a chiralcel OD-H column eluted with 0.5 % IPA in hexane. The flow rate of the mobile phase was set at 1.0 mL/min. R_t = 35.82 min (major enantiomer), 44.38 min (minor enantiomer).

Preparation of (2*S*,3*S*)/(2*R*,3*R*)-ethyl-2-fluoro-2-(1-hydroxy-1,2,3,4-tetrahydronaphthalen-1-yl)acetate 9a



(2*S*,3*S*)

The spectral properties of the (2*S*,3*S*)/(2*R*,3*R*)-diastereoisomer were assigned from the sample still containing 40 % of the (2*S*,3*R*)/(2*R*,3*S*)-diastereoisomer. δ_H ($CDCl_3$) 1.08 (3H, t, $^3J_{HH}$ 7.0 Hz, CH_2CH_3), 1.84-2.04 (3H, m, $CH_2CH_AH_B$), 2.19-2.29 (1H, m, CH_AH_B), 2.68-2.90 (3H, m, CH_2 and O*H*), 4.08 (1H, dq, $^2J_{HH}$ 17.2 Hz, $^3J_{HH}$ 7.0 Hz, $OCH_AH_BCH_3$), 4.15 (1H, dq, $^2J_{HH}$ 17.2 Hz, $^3J_{HH}$ 7.0 Hz, $OCH_AH_BCH_3$), 5.19 (1H, d, $^2J_{HF}$ 48.1 Hz, C*H*F), 7.12-7.16 (1H, m, ArH), 7.24-7.27 (2H, m, ArH), 7.54-7.60 (1H, m, ArH); δ_F ($CDCl_3$) -198.13 (d, $^2J_{FH}$ 47.6 Hz, C*F*H); δ_C ($CDCl_3$) 13.7 (CH_3), 19.3 (CH_2), 29.6 (CH_2), 33.0 (d, $^3J_{CF}$ 4.0 Hz, CH_2), 61.4 (CH_2), 73.2 (d, $^2J_{CF}$ 21.1 Hz, C), 93.6 (d, $^1J_{CF}$ 191.2 Hz, CH), 126.1 (CH), 127.8 (CH), 128.2 (CH), 129.0 (CH), 135.9 (C), 137.7 (C), 167.5 (d, $^2J_{CF}$ 25.2 Hz, CO); *m/z* (FAB) 235 $(M\text{-}OH)^+$, 215 $(M\text{-}OH\text{-}HF)^+$. The enantiomers were separated on a chiralcel OD-H column eluted with 0.5 % IPA in hexane. The flow rate of the mobile phase was set at 1.0 mL/min. R_t = 68.02 min (major enantiomer), 78.87 min (minor enantiomer).

General Procedure for Table 2

Each reaction was run in duplicate and the average yield and enantiomeric excess is reported. Under an argon atmosphere a dry three neck flask was charged with THF (8 mL), acetophenone (0.12 mL, 0.12 g, 1.0 mmol), the required amount of ethyl iodofluoroacetate and (1*R*,2*S*)-1-phenyl-2-(1-pyrrolidinyl)propan-1-ol (0.205g, 1.0 mmol). After 30 min of stirring at the stated temperature, the required amount of a 1.0 M solution of diethylzinc was added and the reaction mixture was left to stir for another 4.5 h. After quenching the reaction mixture with 1 M HCl (10 mL), it was extracted with ethyl acetate (3 x 10 mL). The organic layer was washed with 1 M HCl (30 mL), brine (30 mL) and water (30 ml) before being dried over magnesium sulphate. The solvent was removed and the pure product was purified by column chromatography on silica gel.

General Procedure for Table 3

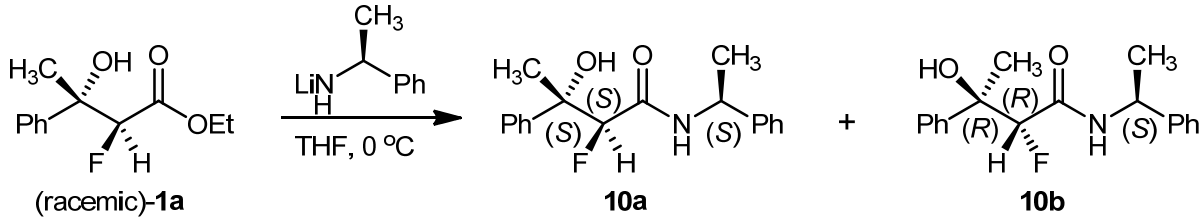
Each reaction was run in duplicate and the average yield and enantiomeric excess is reported. Under an argon atmosphere a dry three neck flask was charged with THF (8 mL), (1*R*,2*S*)-1-phenyl-2-(1-pyrrolidinyl)propan-1-ol (0.205g, 1.0 mmol), the required ketone (1.0 mmol) and ethyl iodofluoroacetate (0.29 mL, 0.47 g, 2.0 mmol). After 30 min of stirring the reaction mixture at -40 ^oC, diethylzinc (3.5 mL, 1.0 M solution in hexane, 3.5 mmol) was added and the reaction mixture was stirred at -40 ^oC for another 4.5 h. After quenching the reaction mixture with 1 M HCl (10 mL), it was extracted with ethyl acetate (3 x 10 mL). The organic layer was washed with 1 M HCl

(30 mL), brine (30 mL) and water (30 ml) before being dried over magnesium sulphate. The solvent was removed and the product was purified by column chromatography on silica gel.

Determination of the absolute configuration of the new chiral centres in ethyl-2-fluoro-3-hydroxy-3-phenylbutanoate 1

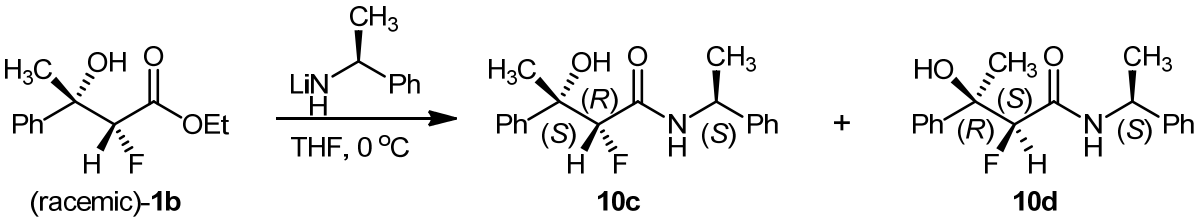
The two diastereoisomers of ethyl-2-fluoro-3-hydroxy-3-phenylbutanoate (**1a** and **1b**) were separated and for each reaction the pure racemic diastereoisomer was used. A dry 25 mL two neck round-bottomed flask was cooled to 0 °C and charged with the required amount of THF, (*S*)-(1-phenylethyl)amine and *n*-butyllithium (1.6 M solution in hexane). After 30 minutes of stirring at 0 °C, the solution of ester in THF (1 mL) was added and the reaction mixture was stirred at 0 °C for 16 hours. The reaction mixture was then quenched with water (5 mL), acidified to pH 5 with 1 M HCl and extracted with diethyl ether (3 x 5 mL). The organic fractions were combined and dried over $MgSO_4$ before the solvent was removed. The crude product was purified by column chromatography on silica gel.

Preparation of 2(*R*)-fluoro-3(*R*)-hydroxy-3-phenyl-N-((*S*)-1-phenylethyl)-butanamide 10b



The title compound was prepared by a modification of Braun's method[9b] using racemic (2*S*,3*S*)/(2*R*,3*R*)-ethyl-2-fluoro-3-hydroxy-3-phenylbutanoate **1a** (0.05 g, 0.22 mmol), THF (3 mL), (*S*)-(1-phenylethyl)amine (0.07 mL, 0.07 g, 0.55 mmol) and *n*-butyllithium (0.5 mL, 1.6 M solution in hexane, 0.8 mmol). The crude product was purified by column chromatography (5 % EtOAc in hexane) on silica gel to give colourless crystals **10b** (0.023 g, 8 %). M.p. 114-116 °C. δ_H ($CDCl_3$) 1.46 (3H, s, C*H*$_3$), 1.47 (3H, d, $^3J_{HH}$ 7.6 Hz, C*H*$_3$), 4.68 (1H, d, $^2J_{HF}$ 47.7 Hz, C*H*F), 4.70 (1H, br s, O*H*), 5.11 (1H, quintet, $^3J_{HH}$ 7.0 Hz, C*H*CH$_3$), 6.60 (1H, br s, N*H*), 7.22-733 (8H, m, ArH), 7.45 (2H, dt, $^3J_{HH}$ 8.2 Hz, $^4J_{HH}$ 1.6 Hz, ArH); δ_F ($CDCl_3$) -191.67 (d, $^2J_{FH}$ 47.6 Hz, C*F*H); δ_C ($CDCl_3$) 21.6 (CH_3), 22.8 (CH_3), 48.8 (CH), 73.9 (d, $^2J_{CF}$ 19.2 Hz, C), 93.1 (d, $^1J_{CF}$ 196.5 Hz, CH), 126.0 (CH), 126.1 (CH), 127.7 (CH), 127.8 (CH), 128.1 (CH), 128.9 (CH), 142.2 (C), 143.0 (C), 168.8 (CO); *m/z* (FAB) 302.1558 (MH^+. $C_{18}H_{21}FNO_2$ requires 302.1556). Crystals suitable for X-ray crystallography were grown by slow recrystallisation from hexane.

Preparation of 2(*S*)-fluoro-3(*R*)-hydroxy-3-phenyl-N-((*S*)-1-phenylethyl)butanamide 10d



The title compound was prepared using racemic (2*R*,3*S*)/(2*S*,3*R*)-ethyl-2-fluoro-3-hydroxy-3-phenyl-butanoate **1b** (0.09 g, 0.4 mmol), THF (5 mL), (*S*)-(1-phenylethyl)amine (0.13 mL, 0.12 g, 1.0 mmol) and *n*-butyllithium (1.0 mL, 1.0 M solution in hexane, 1.6 mmol). The crude product was purified by column chromatography (40 % Et_2O in hexane) on silica gel to give 2(*S*)-fluoro-3(*R*)-hydroxy-3-phenyl-N-((*S*)-1-phenylethyl)-butanamide **10d** as colourless crystals (0.016 g, 13 %). M.p. 140-142 °C. δ_H ($CDCl_3$) 0.87 (3H, d, $^3J_{HH}$ 7.2 Hz, C*H*$_3$), 1.63 (3H, d, $^4J_{HF}$ 2.3 Hz, C*H*$_3$), 4.75 (1H, quintet, $^3J_{HH}$ 7.4 Hz, C*H*CH$_3$), 4.81 (1H, d, $^2J_{HF}$ 48.5 Hz, C*H*F), 4.99 (1H, s, O*H*), 6.13 (1H, br s, N*H*), 7.09 (2H, d, $^3J_{HH}$ 6.4 Hz, ArH), 7.15-7.31 (6H, m, ArH), 7.41 (2H, d, $^3J_{HH}$ 8.2 Hz, ArH); δ_F ($CDCl_3$) -191.28 (d, $^2J_{FH}$ 47.6 Hz, C*F*H); δ_C ($CDCl_3$) 20.6 (CH_3), 26.6 (d, $^3J_{CF}$ 3.0 Hz, CH_3), 48.1 (CH), 74.4 (d, $^2J_{CF}$ 18.0 Hz, C), 93.8 (d, $^1J_{CF}$ 201.2 Hz, CH), 125.5 (d, $^4J_{CF}$ 3.0 Hz, CH), 126.1 (CH), 127.5 (CH), 127.8 (CH), 128.0 (CH), 128.8 (CH), 141.6 (C), 142.5 (C), 168.4 (d, $^2J_{CF}$ 19.1 Hz, CO); *m/z* (FAB) 302.1552 (MH^+. $C_{18}H_{21}FNO_2$ requires 302.1556). Crystals suitable for X-ray crystallography were grown by recrystallisation from Et_2O/hexane solution (40/60).

Determination of the absolute configuration of the new chiral centres in ethyl-2-fluoro-3-hydroxy-3-phenylbutanoate 1

The diastereoisomers of enantiomeric ethyl-2-fluoro-3-hydroxy-3-phenylbutanoate **1** were isolated by column chromatography (20 % Et_2O in hexane) on silica gel. The procedure above was repeated separately with (2*S*,3*S*)/(2*R*,3*R*)-diastereoisomer **1a** (86 % ee) and (2*R*,3*S*)/(2*S*,3*R*)-diastereoisomer **1b** (73 % ee) using (*S*)-(1-phenylethyl)amine (0.2 mL, 0.19 g, 1.5 mmol), *n*-butyllithium (1.4 mL, 1.6 M in hexane, 2.2 mmol), THF (6 mL) and the ester **1** (0.11 g, 0.5 mmol). The crude product obtained in the reaction with (2*S*,3*S*)/(2*R*,3*R*)-diastereoisomer **1a** consisted of a 91:9 mixture of (2*S*,3*S*)-**(10a)**:(2*R*,3*R*)-**(10b)** diastereoisomers according to the ^{19}F NMR spectrum. The crude product obtained in the reaction with (2*R*,3*S*)/(2*S*,3*R*)-diastereoisomer **1b** consisted of a 88:12 mixture of (2*R*,3*S*)-**(10c)**:(2*S*,3*R*)-**(10d)** diastereoisomers according to the ^{19}F NMR spectrum.

Structure solution and refinement

Tables 9 & 10 summarise the crystallographic data for (2*S*,3*S*)/(2*R*,3*R*)-ethyl 2-fluoro-3-hydroxy-3-phenylpentanoate **2a**, (2*S*,3*S*)/(2*R*,3*R*)-ethyl-2-fluoro-3-hydroxy-5-methyl-3-phenylhexanoate **4a,** (2*S*,3*S*)/(2*R*,3*R*)-ethyl-2-fluoro-3-hydroxy-3-(2-methoxyphenyl)butanoate **5a**, (2*S*,3*S*)/(2*R*,3*R*)-ethyl-3-(4-chlorophenyl)-2-fluoro-3-hydroxy-butanoate **7a**, 2(*R*)-fluoro-3(*R*)-hydroxy-3-phenyl-N-((*S*)-1-phenylethyl)-butanamide **10b** and 2(*S*)-fluoro-3(*R*)-hydroxy-3-phenyl-N-((*S*)-1-phenylethyl)-butanamide **10d** respectively. The data for all of the compounds were collected on a Bruker APEX 2000 CCD diffractometer using graphite monochromated Mo-Kα radiation (λ = 0.71073 Å). The data were corrected for Lorentz and polarization effects, and empirical absorption corrections were applied. The structures were solved by direct methods and refined by full-matrix least squares cycles on F^2 for all data, using SHELXTL version 6.10.[12] All hydrogen atoms were included in calculated positions (C-H = 0.95-1.00 Å) riding on the bonded atom with isotropic displacement parameters set to 1.5 Ueq(C) for methyl H atoms and 1.2 Ueq(C) for all other H atoms. All non hydrogen atoms were refined with anisotropic displacement parameters. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with The Cambridge Crystallographic Data Centre and allocated the deposition numbers CCDC: 859759 - 859764. Copies of the data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

References

12 G. M. Sheldrick, SHELXTL Version 6.10, Bruker AXS, Inc., Maddison, Wisconsin, USA, 2000.

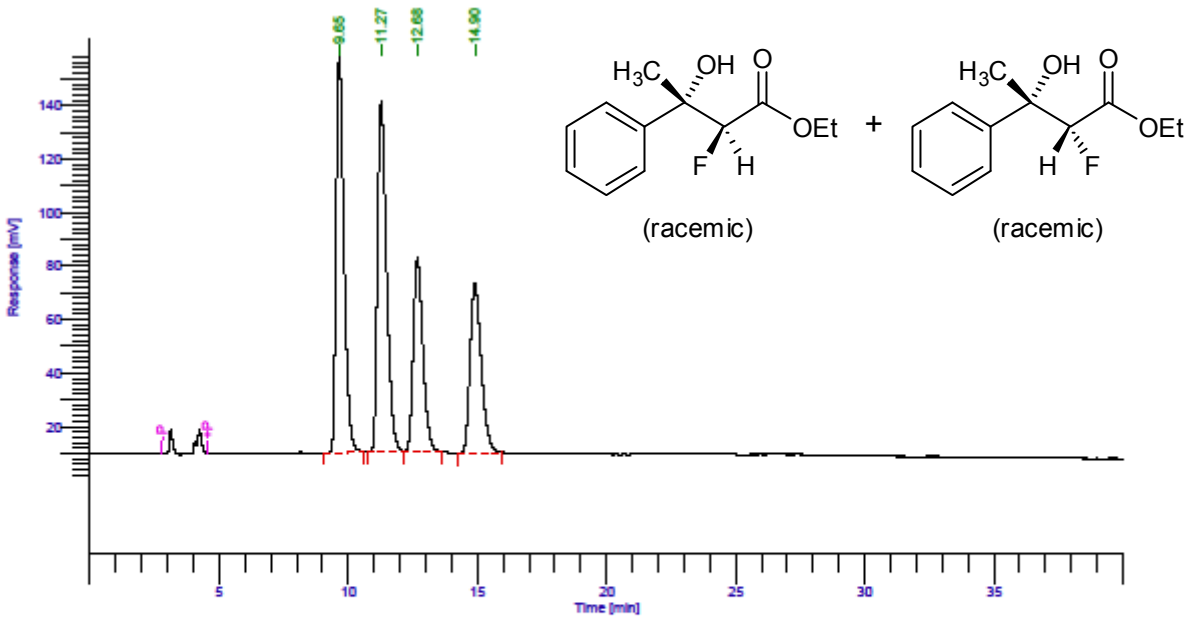
Table 9. Crystallographic data for compounds **2a** (R = Et), **4a** (R = ^{i}Bu), **5a** (Ar = 2-MeOC$_6$H$_4$) and **7a** (Ar = 4-ClC$_6$H$_4$).

	2a (R = Et)	**4a** (R = ^{i}Bu)	**5a** (Ar = 2-MeOC$_6$H$_4$)	**7a** (Ar = 4-ClC$_6$H$_4$)
Formula	$C_{13}H_{17}FO_3$	$C_{15}H_{21}FO_3$	$C_{13}H_{17}FO_4$	$C_{12}H_{14}ClFO_3$
Formula weight	240.27	268.32	256.27	260.68
Crystal system	Monoclinic	Monoclinic	Monoclinic	Monoclinic
Space group	P2(1)/c	P2(1)/n	P2(1)/c	P2(1)/c
Unit cell dimensions				
a (Å)	12.166(4)	9.898(6)	11.620(8)	13.326(4)
b (Å)	8.639(3)	5.655(3)	8.862(6)	5.5683(19)
c (Å)	12.008(4)	26.387(15)	12.963(9)	17.049(6)
α (°)	90	90	90	90
β (°)	101.599(6)	97.357(10)	101.478(12)	92.031(7)
γ (°)	90	90	90	90
U (Å^3)	1236.4(7)	1464.8(15)	1308.1(16)	1264.3(7)
Temperature (K)	150(2)	150(2)	150(2)	150(2)
Z	4	4	4	4
D_c (Mg m^{-3})	1.291	1.217	1.301	1.369
μ(Mo-Kα) (mm^{-1})	0.100	0.091	0.104	0.308
F (000)	512	576	544	544
Dimensions (mm^3)	0.32 x 0.25 x 0.10	0.33 x 0.24 x 0.16	0.32 x 0.29 x 0.16	0.29 x 0.11 x 0.08

Data collection range (°)	1.71 – 25.00	2.12 – 25.00	2.80 – 26.00	1.53 – 25.00
Index ranges	$-14 \le h \le 14$	$-11 \le h \le 11$	$-14 \le h \le 14$	$-15 \le h \le 15$
	$-10 \le k \le 10$	$-6 \le k \le 6$	$-10 \le k \le 10$	$-6 \le k \le 6$
	$-14 \le l \le 14$	$-31 \le l \le 31$	$-15 \le l \le 15$	$-20 \le l \le 20$
Reflections	8620	9931	9707	8734
Unique reflections (R_{int})	2181 (0.0571)	2584 (0.0636)	2555 (0.0541)	2236 (0.0788)
θ_{max} (% complete)	25.00 (100.0)	25.00 (99.9)	26.00 (99.7)	25.00 (99.9)
Absorption correction	Empirical	Empirical	Empirical	Empirical
Max/min transmission	0.969 / 0.706	0.969 / 0.664	0.969 / 0.653	0.969 / 0.617
Data/restraints/parameters	2181 / 0 / 156	2584 / 0 / 175	2555 / 0 / 166	2236 / 0 / 156
Goodness of fit on F^2	1.029	1.019	1.038	0.981
Final R indices [$I > 2\sigma(I)$]				
R_1	0.0465	0.0468	0.0449	0.0675
wR_2	0.1113	0.1118	0.1054	0.1519
R indices (all data)				
R_1	0.0621	0.0609	0.0586	0.0951
wR_2	0.1188	0.1192	0.1128	0.1654
Largest diff. peak, hole ($eÅ^{-3}$)	0.246, -0.188	0.211, -0.178	0.192, -0.192	1.119, -0.327

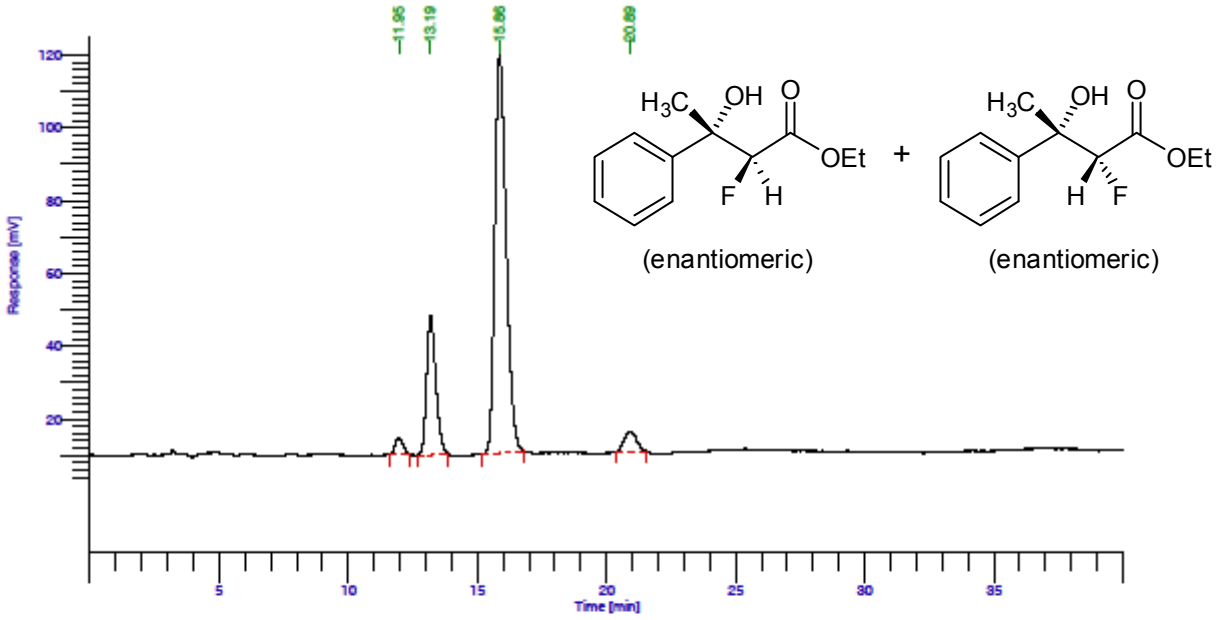
Table 10. Crystallographic data for 2(*R*)-fluoro-3(*R*)-hydroxy-3-phenyl-N-((*S*)-1-phenylethyl)-butanamide **10b** and 2(*S*)-fluoro-3(*R*)-hydroxy-3-phenyl-N-((*S*)-1-phenylethyl)-butanamide **10d**.

	10b	**10d**
Formula	$C_{18}H_{20}FNO_2$	$C_{18}H_{20}FNO_2$
Formula weight	301.35	301.35
Crystal system	Monoclinic	Orthorhombic
Space group	C2	P2(1)2(1)2(1)
Unit cell dimensions		
a (Å)	19.119(6)	8.306(3)
b (Å)	5.5114(16)	9.746(3)
c (Å)	15.207(4)	18.935(6)
α (°)	90	90
β (°)	109.351(6)	90
γ (°)	90	90
U (Å^3)	1511.9(8)	1532.7(8)
Temperature (K)	150(2)	150(2)
Z	4	4
D_c (Mg m^{-3})	1.324	1.306
μ(Mo-Kα) (mm^{-1})	0.094	0.093
F (000)	640	640
Dimensions (mm^3)	0.20 x 0.10 x 0.04	0.26 x 0.14 x 0.07
Data collection range (°)	2.23 – 26.00	2.15 – 25.99
Index ranges	$-23 \le h \le 23$	$-10 \le h \le 10$
	$-6 \le k \le 6$	$-12 \le k \le 11$
	$-18 \le l \le 18$	$-22 \le l \le 23$
Reflections	5986	11981
Unique reflections (R_{int})	1648 (0.1603)	1750 (0.0879)
θ_{max} (% complete)	26.00 (99.8)	25.99 (99.9)
Absorption correction	Empirical	Empirical
Max/min transmission	0.969 / 0.412	0.969 / 0.795
Data/restraints/parameters	1648 / 1 / 203	1750 / 0 / 202
Goodness of fit on F^2	0.826	0.995
Final *R* indices [$I > 2\sigma(I)$]		
R_1	0.0608	0.0417
wR_2	0.0819	0.0774
R indices (all data)		
R_1	0.1326	0.0505
wR_2	0.0972	0.0801
Largest diff. peak, hole (eÅ^{-3})	0.215, -0.220	0.191, -0.210



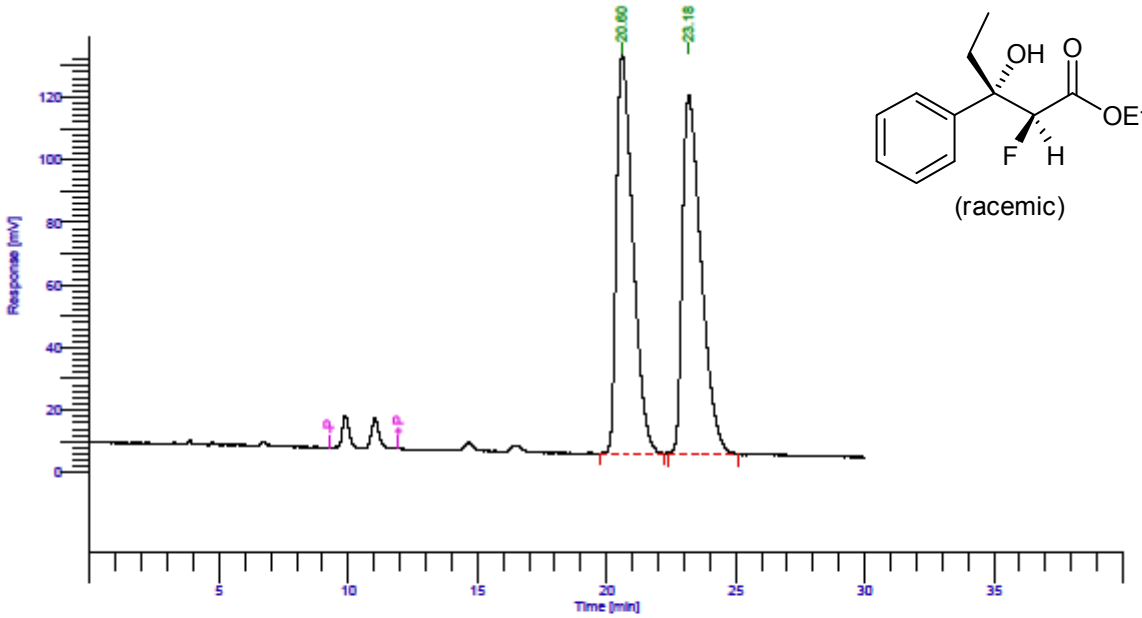
Chiralcel OD-H

Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	9.65	3157591	148481	31.1	BB
2	11.27	3203717	130987	31.5	BV
3	12.68	1891401	72509	18.6	VB
4	14.90	1909831	63519	18.8	BB
		10162541	415497	100.0	



Chiralcel OD-H

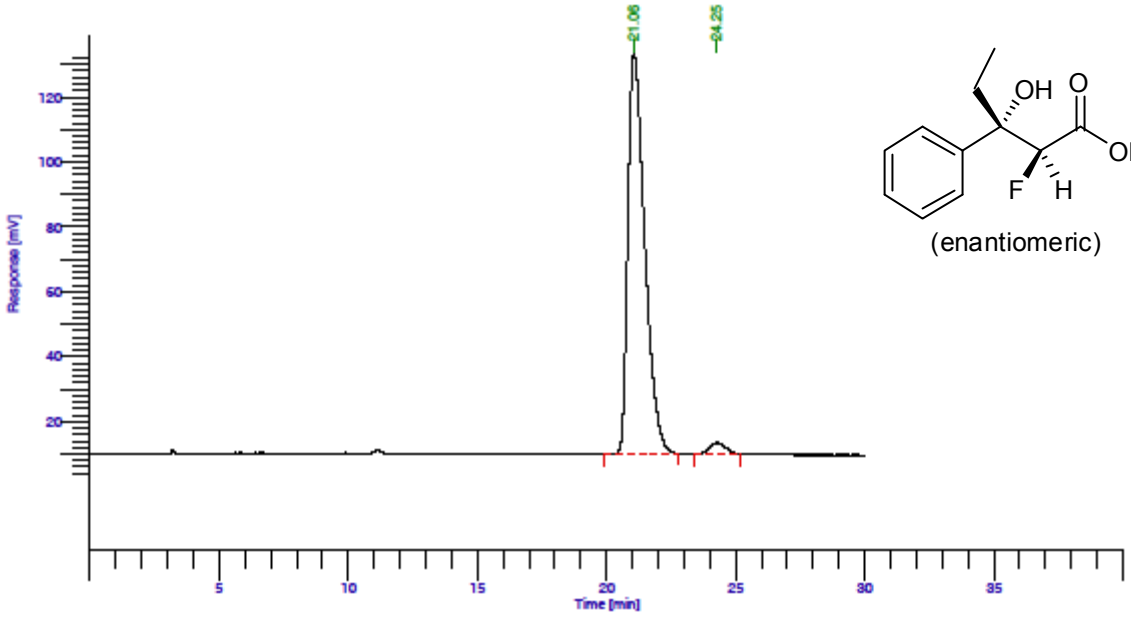
Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	11.95	92638	4529	2.0	BB
2	13.19	955605	38280	20.9	BB
3	15.86	3339659	109697	73.0	BB
4	20.89	185966	5602	4.1	BB
		4573868	158108	100.0	



(racemic)

Chiralcel OD-H

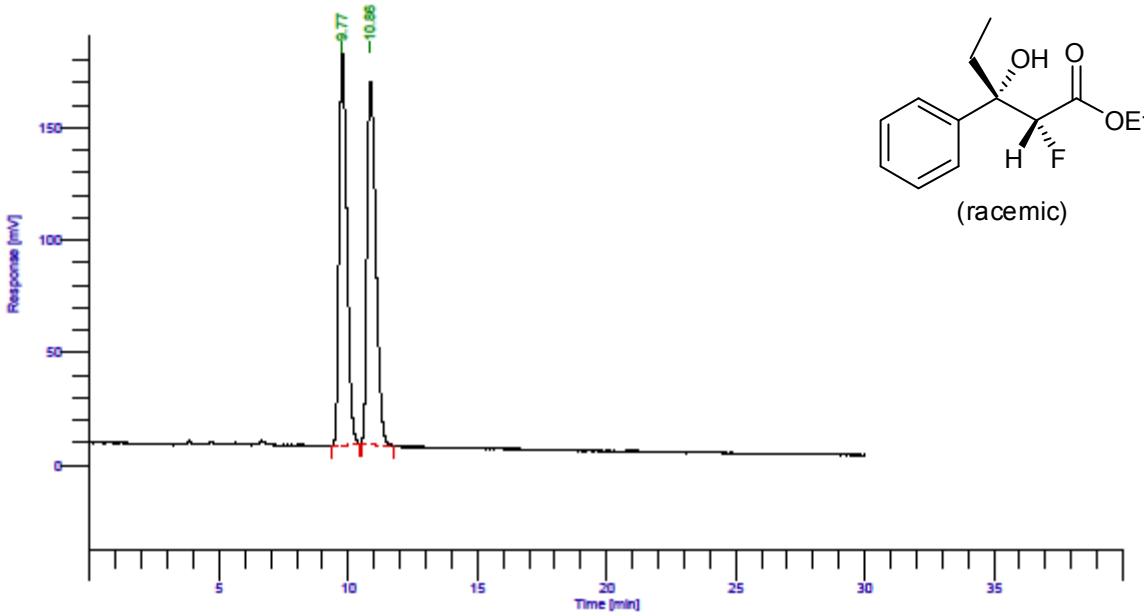
Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	20.60	5694310	127705	49.5	BB
2	23.18	5801309	114713	50.5	BB
		11495619	242419	100.0	



(enantiomeric)

Chiralcel OD-H

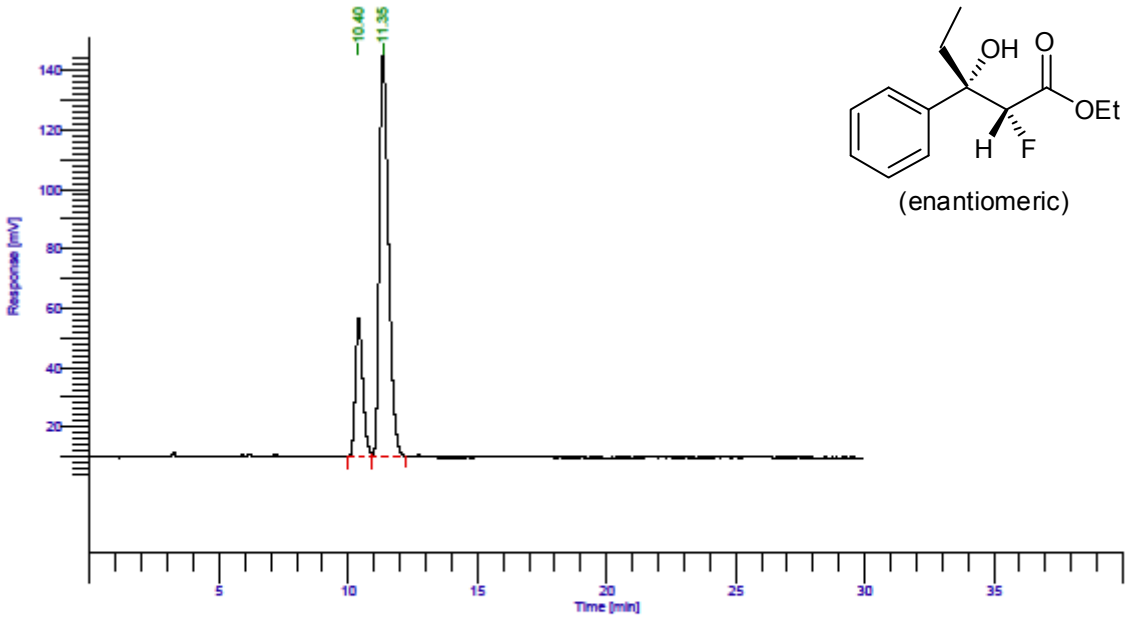
Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	21.06	5604507	123817	97.3	BB
2	24.25	154877	3517	2.7	BB
		5759383	127334	100.0	



(racemic)

Chiralcel OD-H

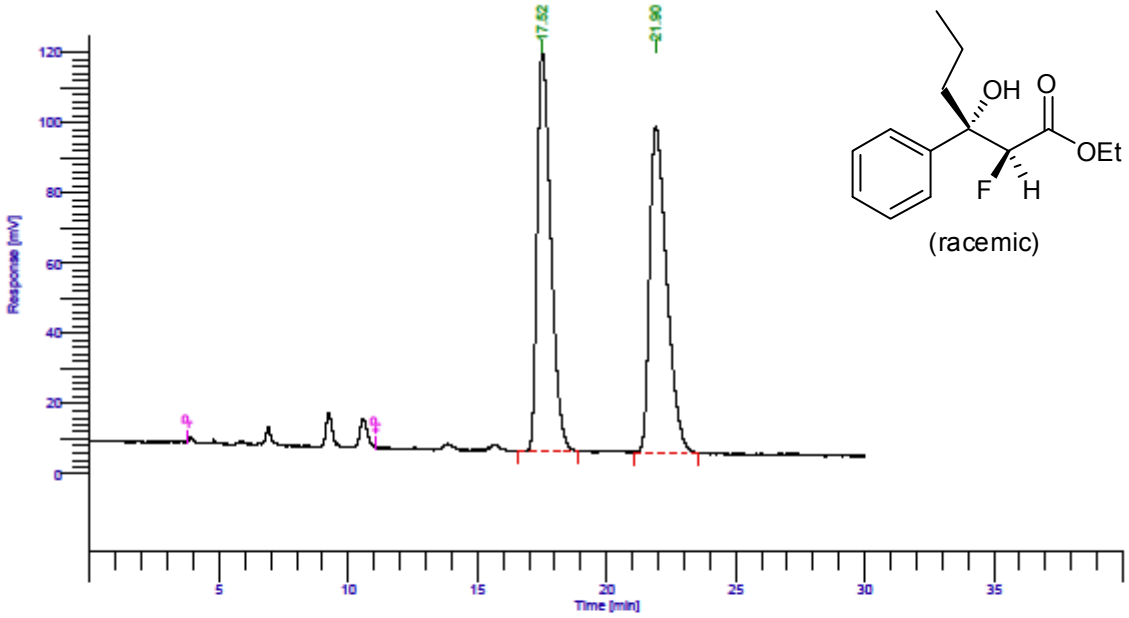
Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	9.77	3699411	174900	49.2	BB
2	10.86	3826152	161208	50.8	BB
		7525562	336108	100.0	



(enantiomeric)

Chiralcel OD-H

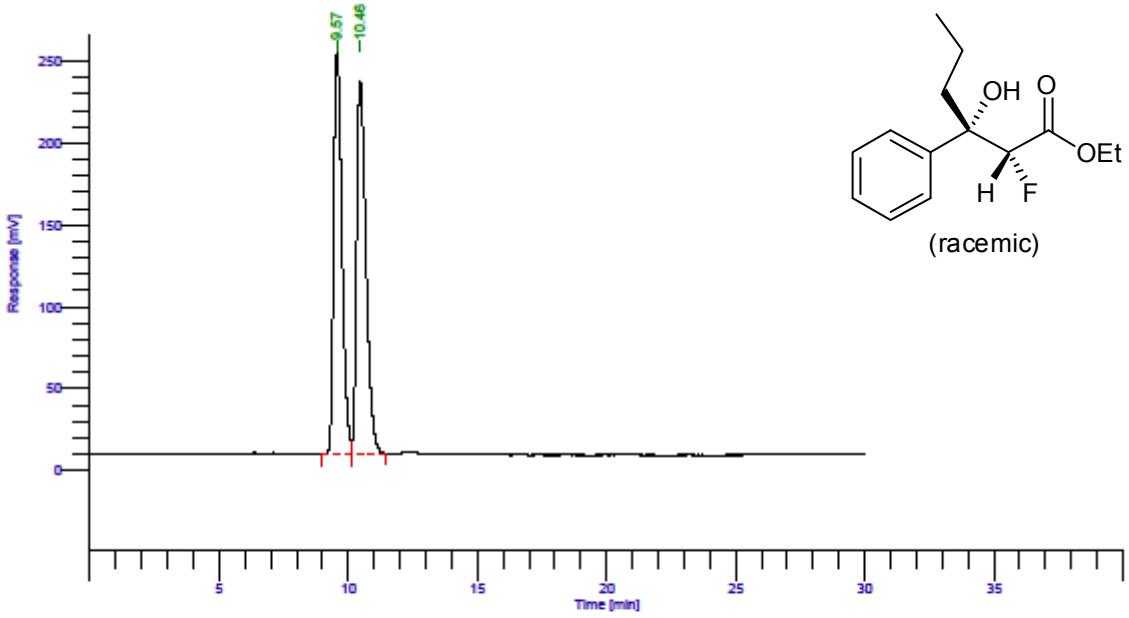
Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	10.40	938974	46240	22.0	BV
2	11.35	3334491	135270	78.0	VB
		4273465	181510	100.0	



(racemic)

Chiralcel OD-H

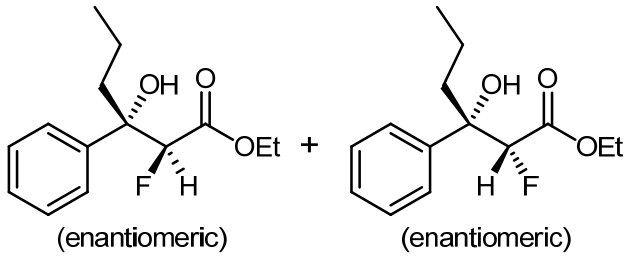
Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	17.52	4216981	113685	49.5	BB
2	21.90	4304819	92855	50.5	BB
		8521800	206540	100.0	



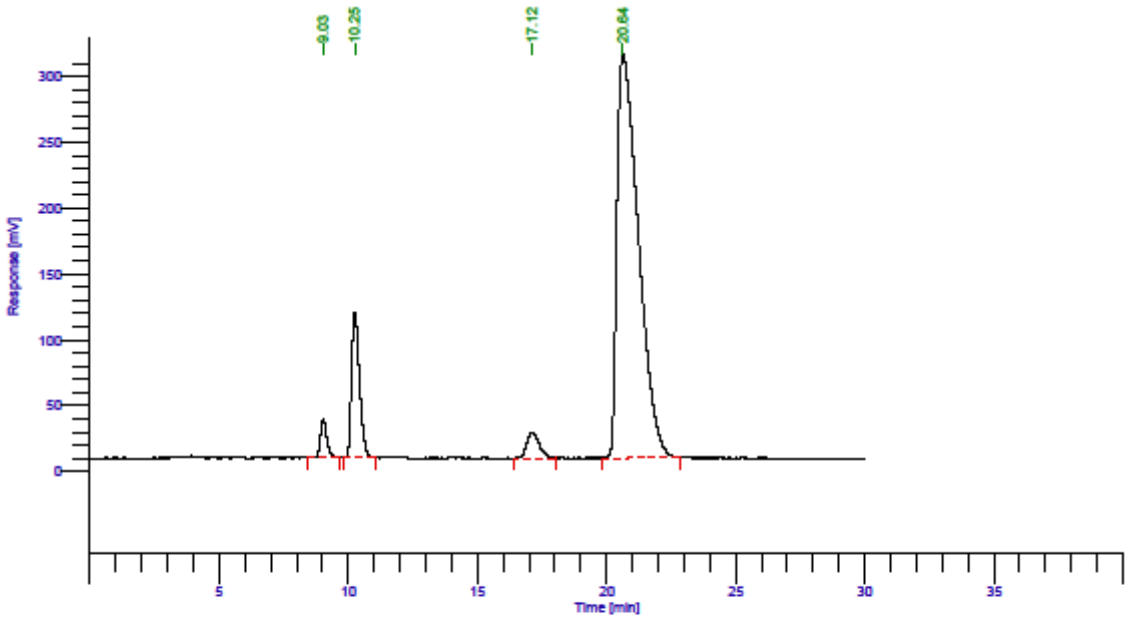
(racemic)

Chiralcel OD-H

Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	9.57	5542228	246250	49.0	BV
2	10.46	5759725	227255	51.0	VB
		11301953	473505	100.0	

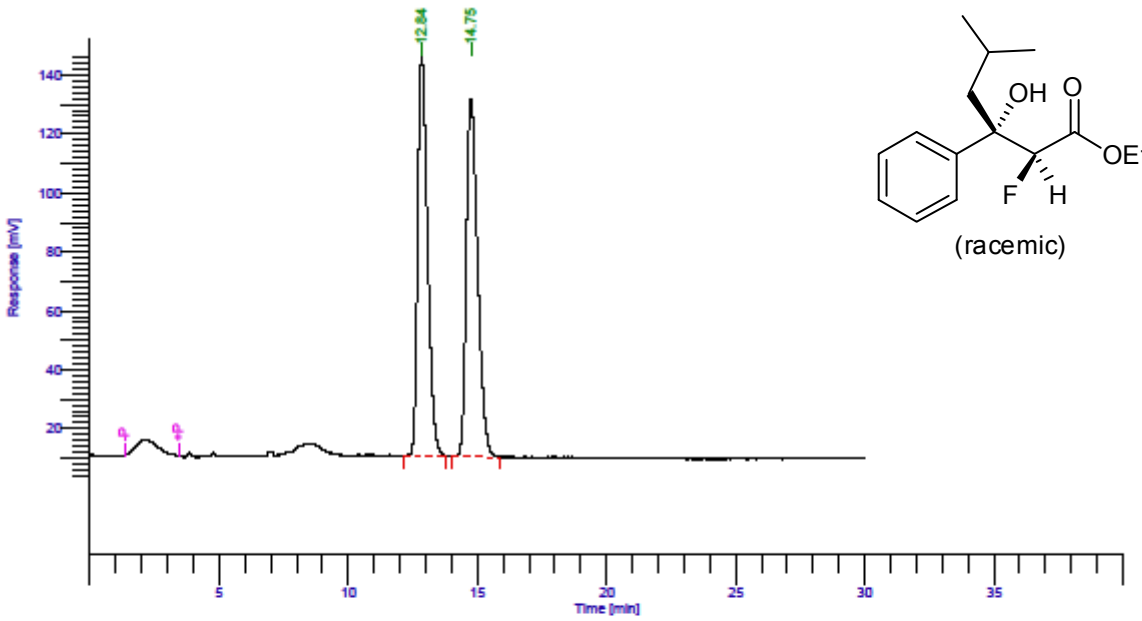


(enantiomeric) (enantiomeric)



Chiralcel OD-H

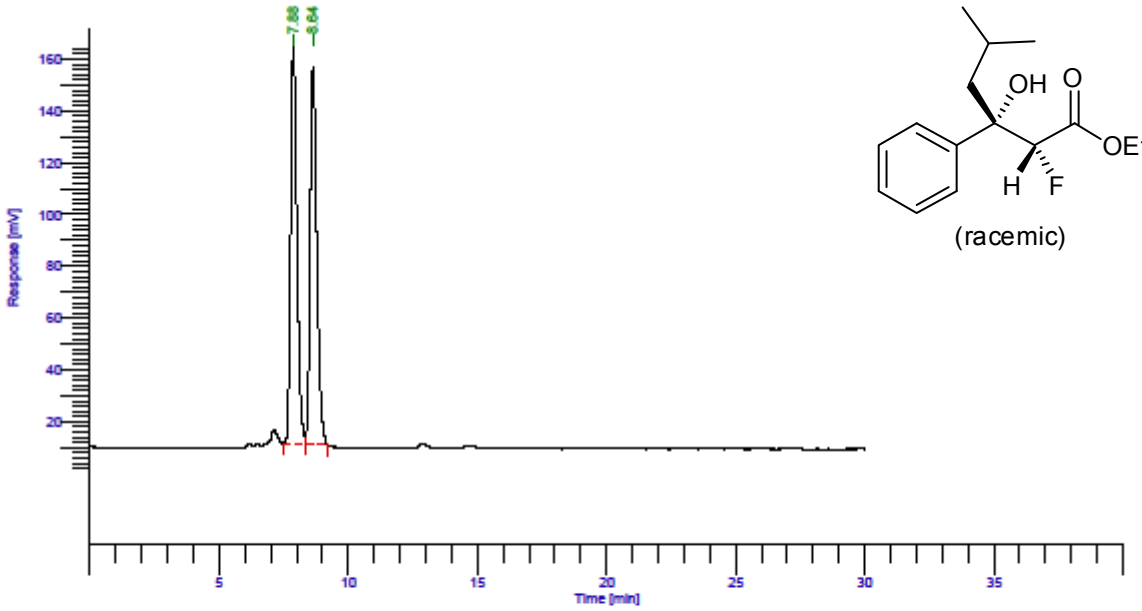
Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	9.03	519141	29192	2.4	BB
2	10.25	2393700	111126	11.3	BB
3	17.12	659031	19672	3.1	BB
4	20.64	17657282	306394	83.2	BB
		21229155	466384	100.0	



(racemic)

Chiralcel OD-H

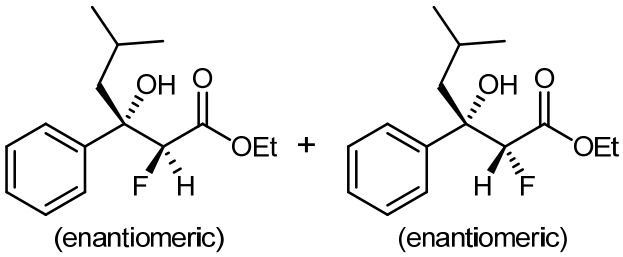
Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	12.84	3639089	135899	49.4	BB
2	14.75	3730374	121505	50.6	BB
		7369463	257404	100.0	



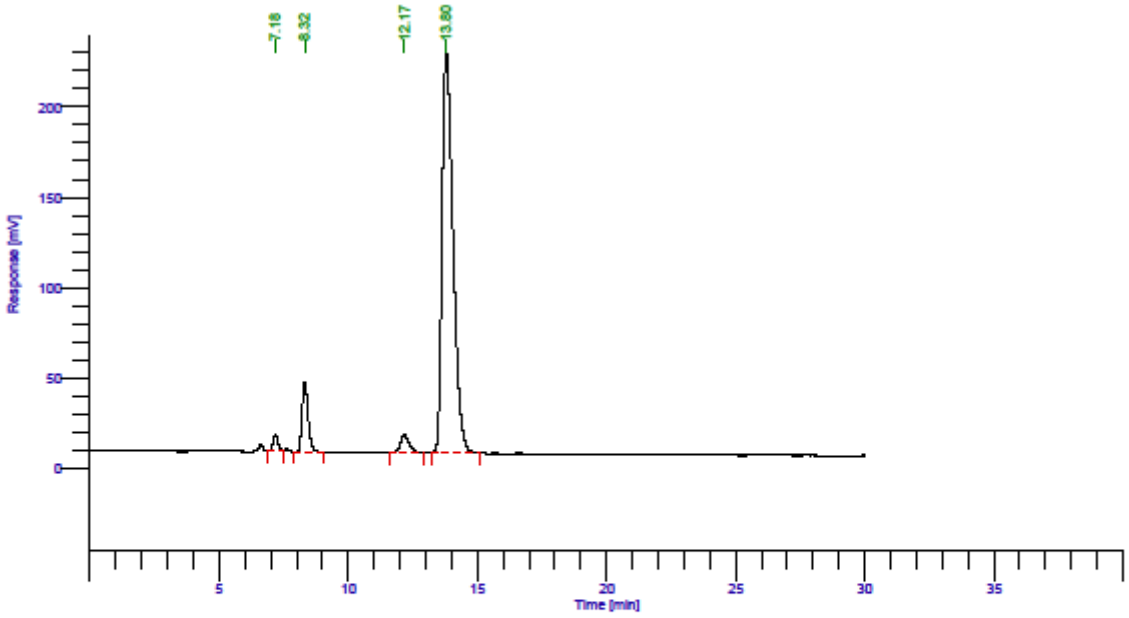
(racemic)

Chiralcel OD-H

Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	7.88	2621812	153638	49.8	BV
2	8.64	2640669	145592	50.2	VB
		5262481	299230	100.0	

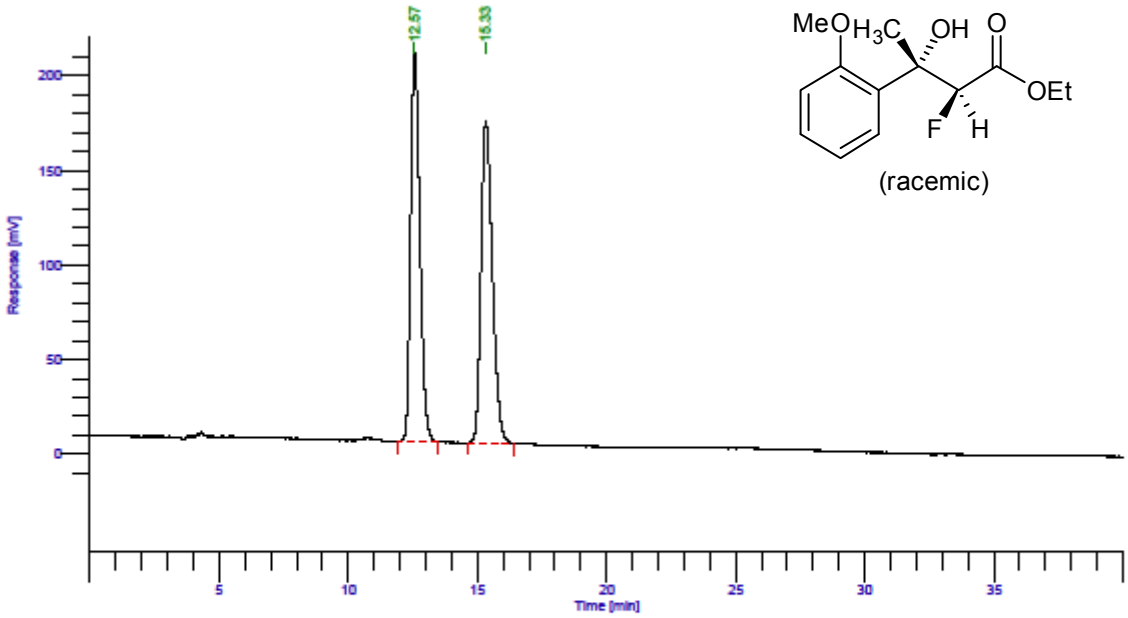


(enantiomeric) (enantiomeric)



Chiralcel OD-H

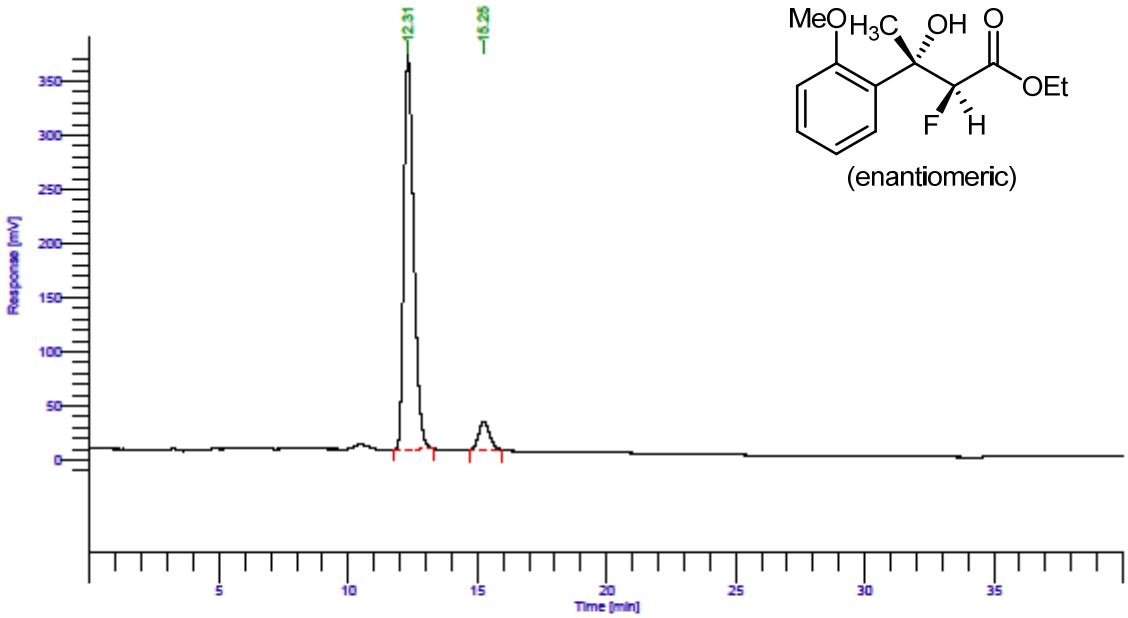
Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	7.18	124230	9181	1.6	BB
2	8.32	624976	38761	8.3	BB
3	12.17	224614	9542	3.0	BB
4	13.80	6577549	221399	87.1	BB
		7551369	278882	100.0	



(racemic)

Chiralcel OD-H

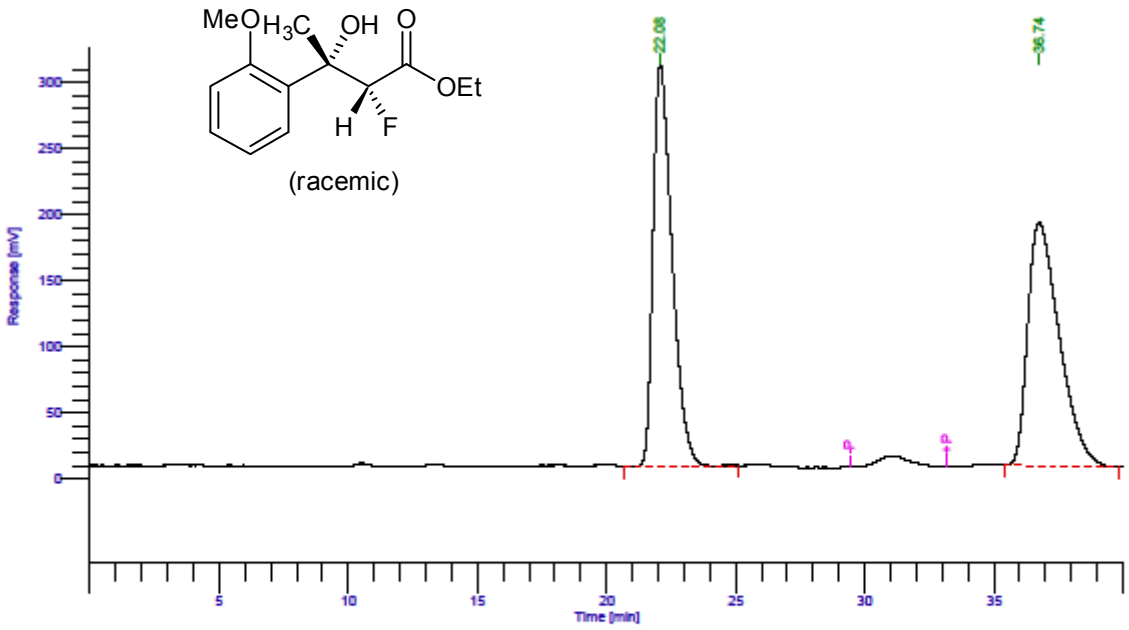
Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	12.57	5125992	205086	49.5	BB
2	15.33	5226647	169837	50.5	BB
		10352640	374923	100.0	



(enantiomeric)

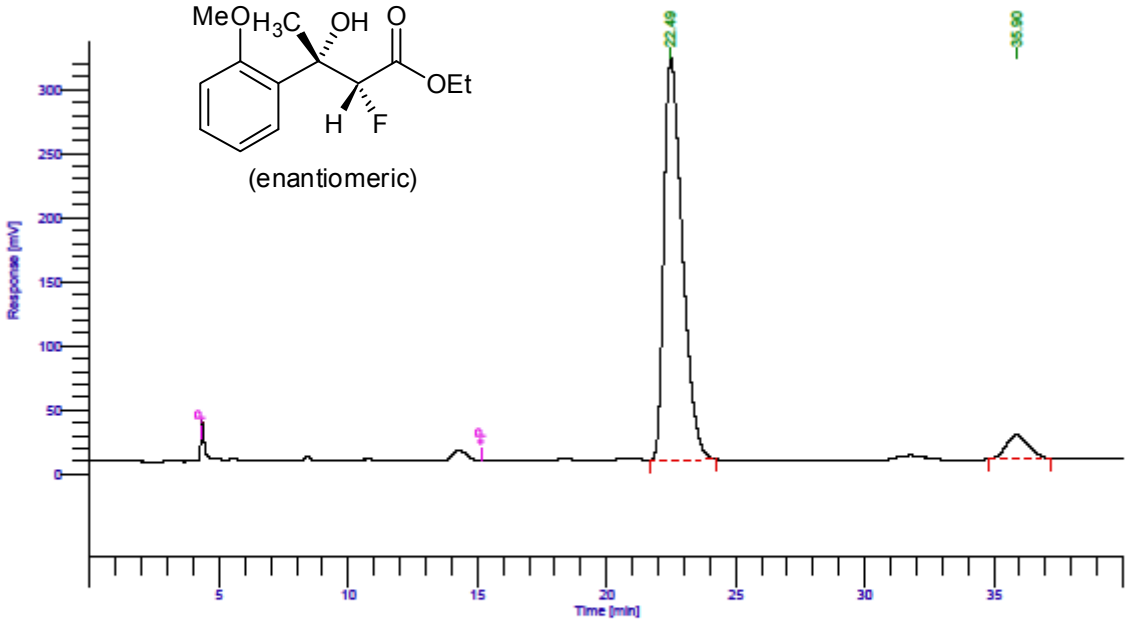
Chiralcel OD-H

Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	12.31	9760862	365250	92.3	BB
2	15.25	815043	26588	7.7	BB
		10575905	391838	100.0	



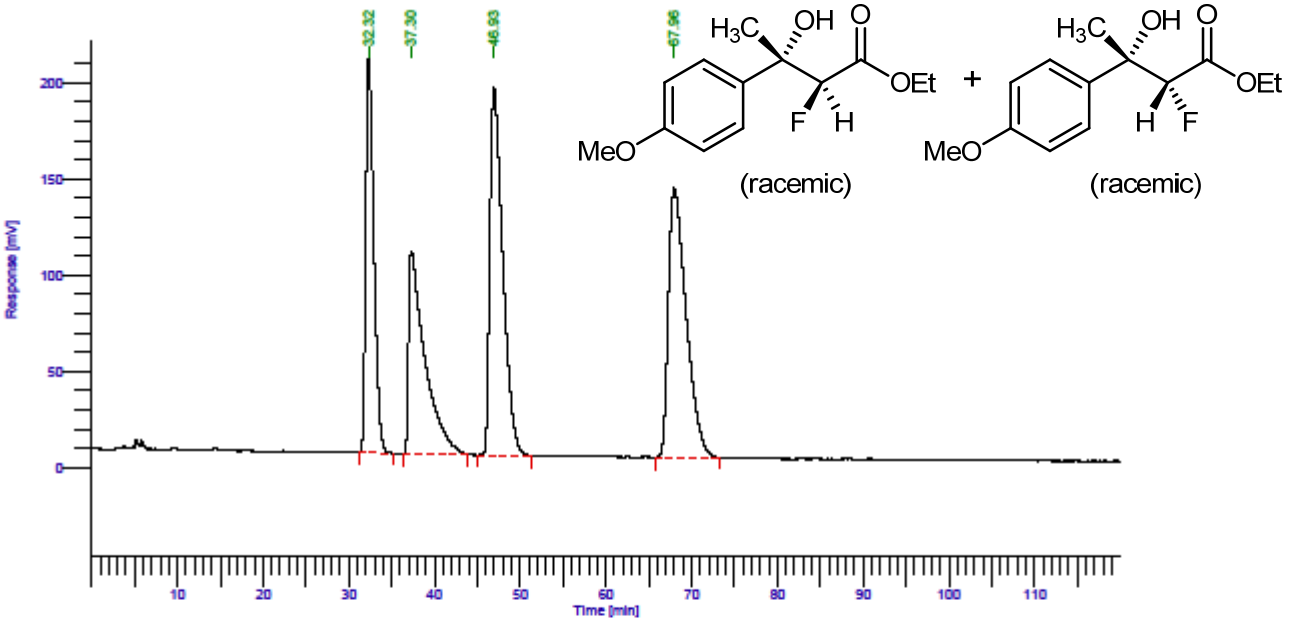
Chiralcel OD-H

Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	22.08	15620167	304025	49.9	BB
2	36.74	15692707	183935	50.1	BB
		31312874	487960	100.0	



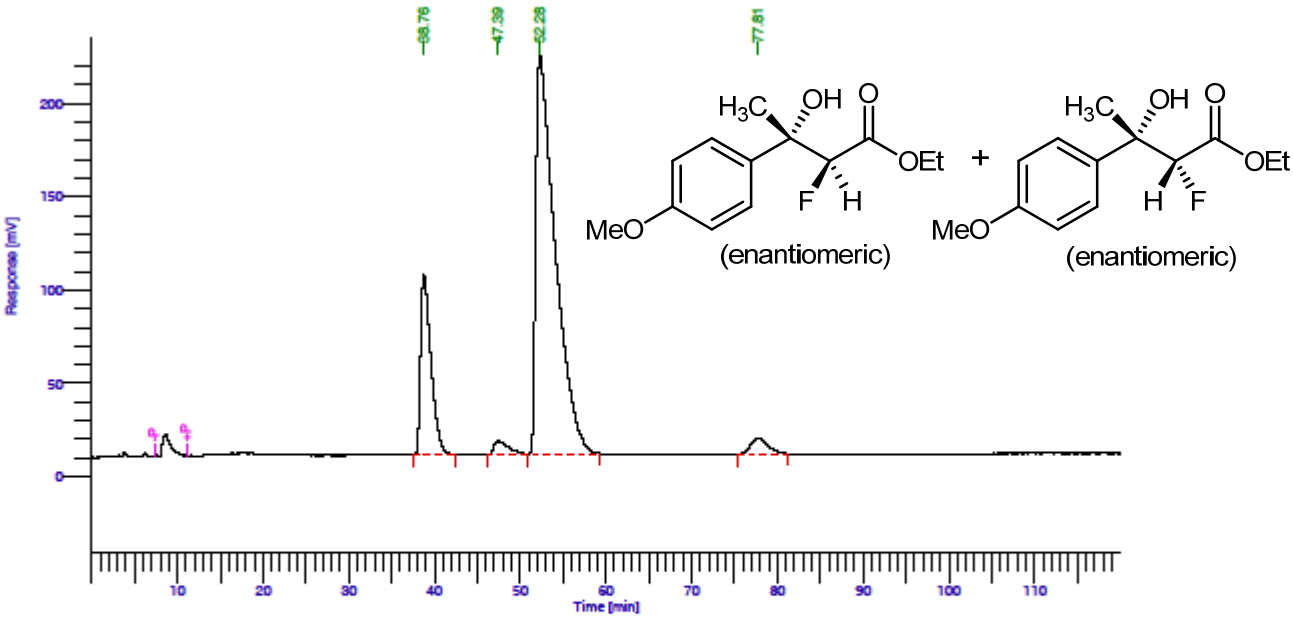
Chiralcel OD-H

Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	22.49	15505303	313274	93.1	BB
2	35.90	1140468	18454	6.9	BB
		16645770	331728	100.0	



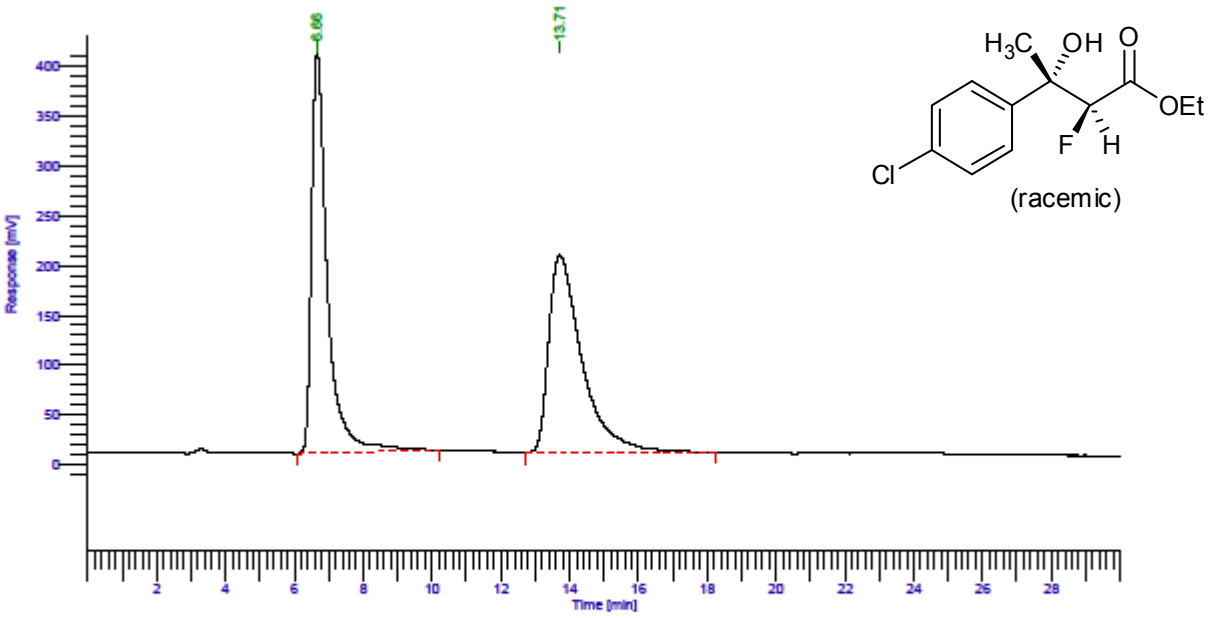
Chiralcel OD-H

Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	32.32	13504919	205099	19.9	BB
2	37.30	13895376	105278	20.5	BB
3	46.93	20097137	191153	29.7	BB
4	67.96	20281852	139991	29.9	BB
		67779284	641522	100.0	



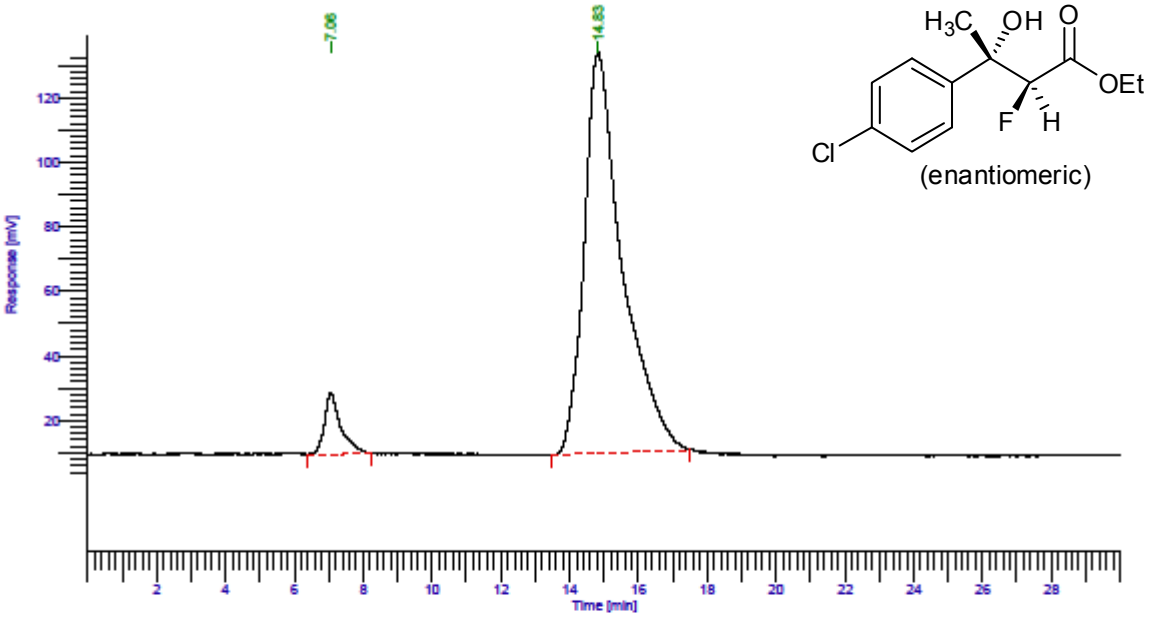
Chiralcel OD-H

Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	38.76	8238545	96943	18.6	BB
2	47.39	893283	7577	2.0	BV
3	52.28	33845564	214605	76.5	VB
4	77.81	1253883	8690	2.8	BB
		44231274	327815	100.0	



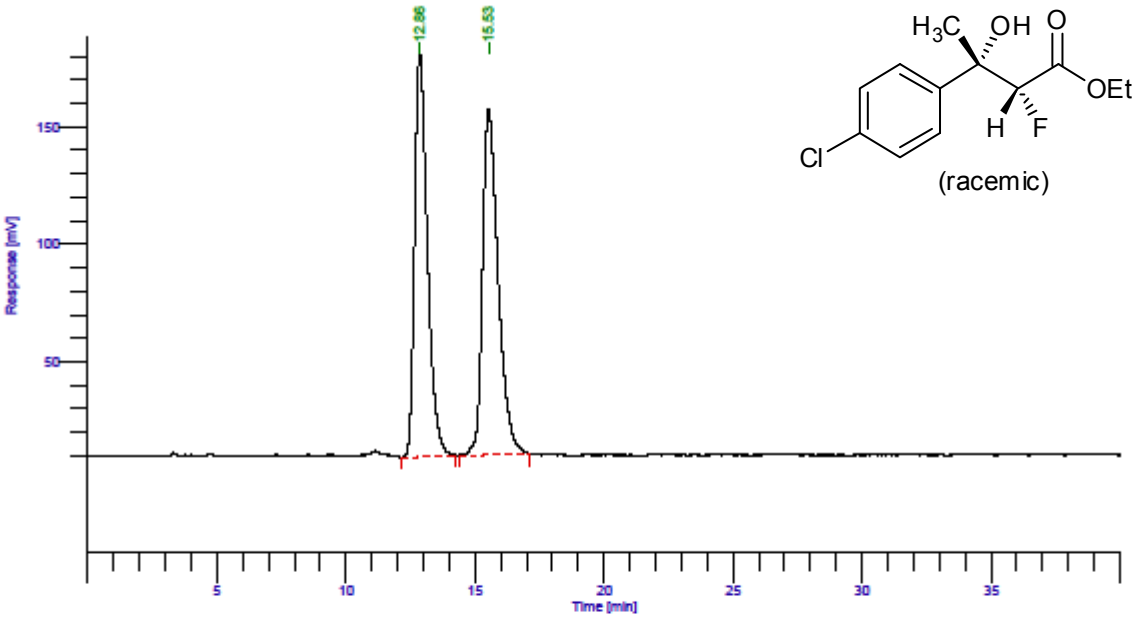
Chiralcel AS

Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	6.66	12904274	403103	49.3	BB
2	13.71	13286935	198366	50.7	BB
		26191209	601469	100.0	



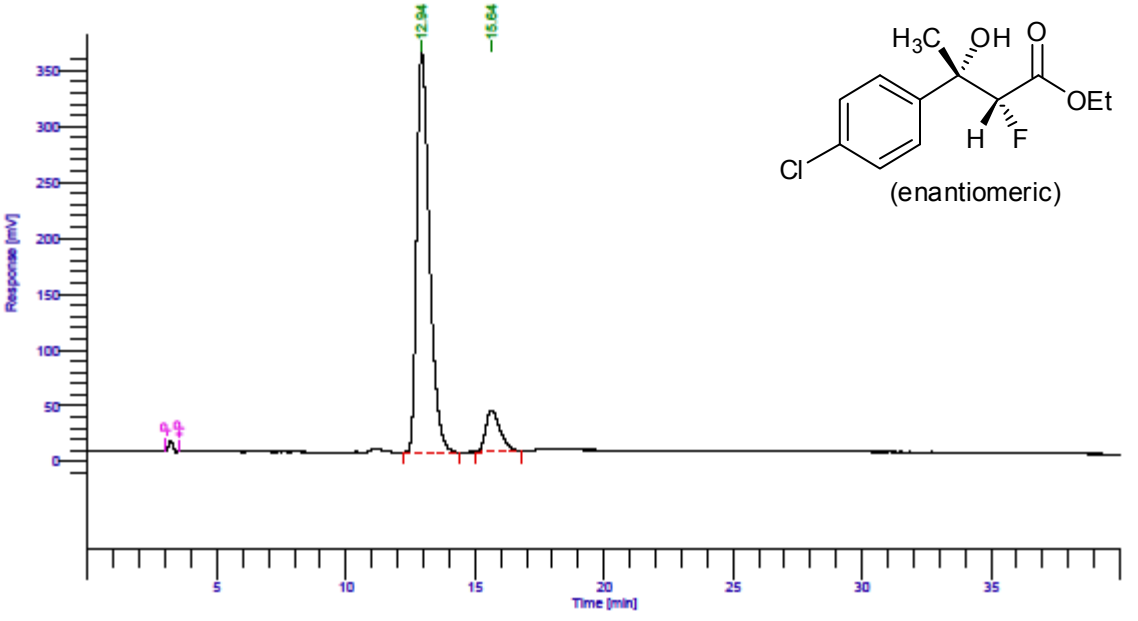
Chiralcel AS

Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	7.06	625956	19130	6.2	BB
2	14.83	9544124	124150	93.8	BB
		10170080	143280	100.0	



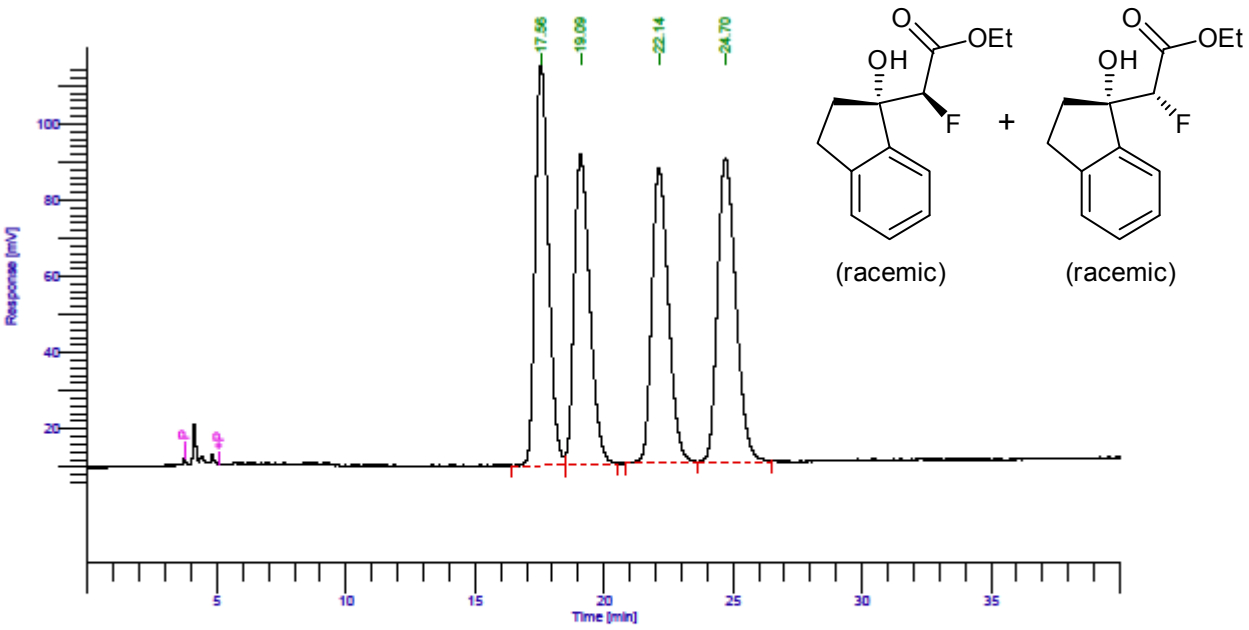
Chiralcel AD

Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	12.86	5923846	171476	48.9	BB
2	15.53	6197011	147101	51.1	BB
		12120857	318577	100.0	



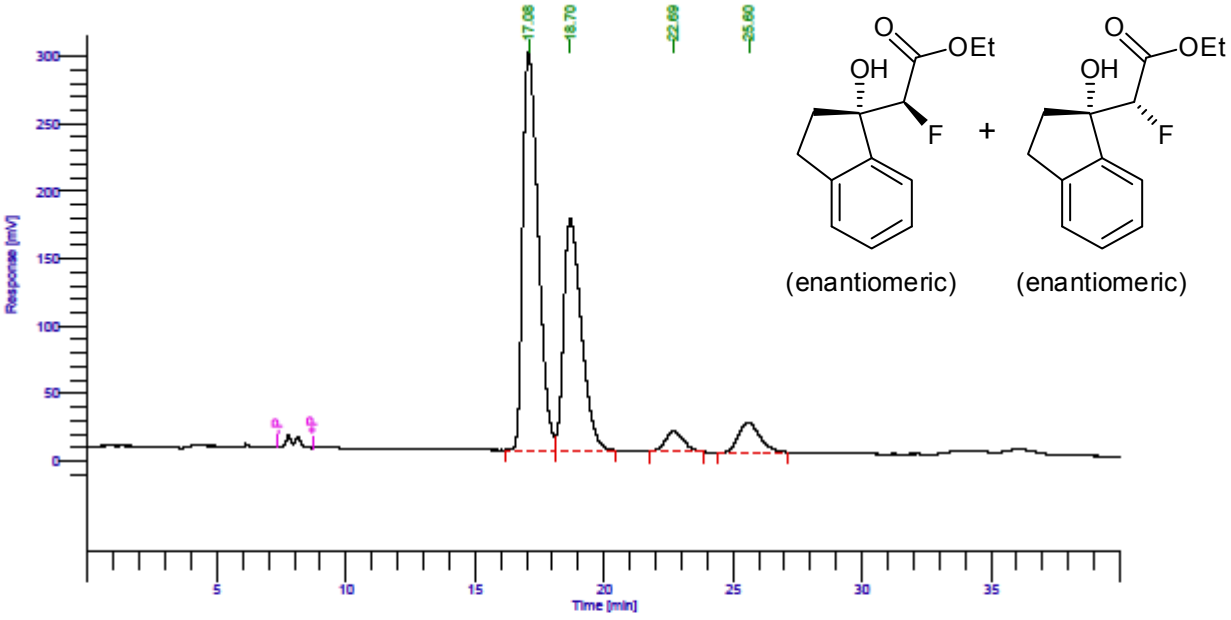
Chiralcel AD

Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	12.94	12352641	358634	89.5	BB
2	15.64	1451320	37098	10.5	BB
		13803961	395732	100.0	



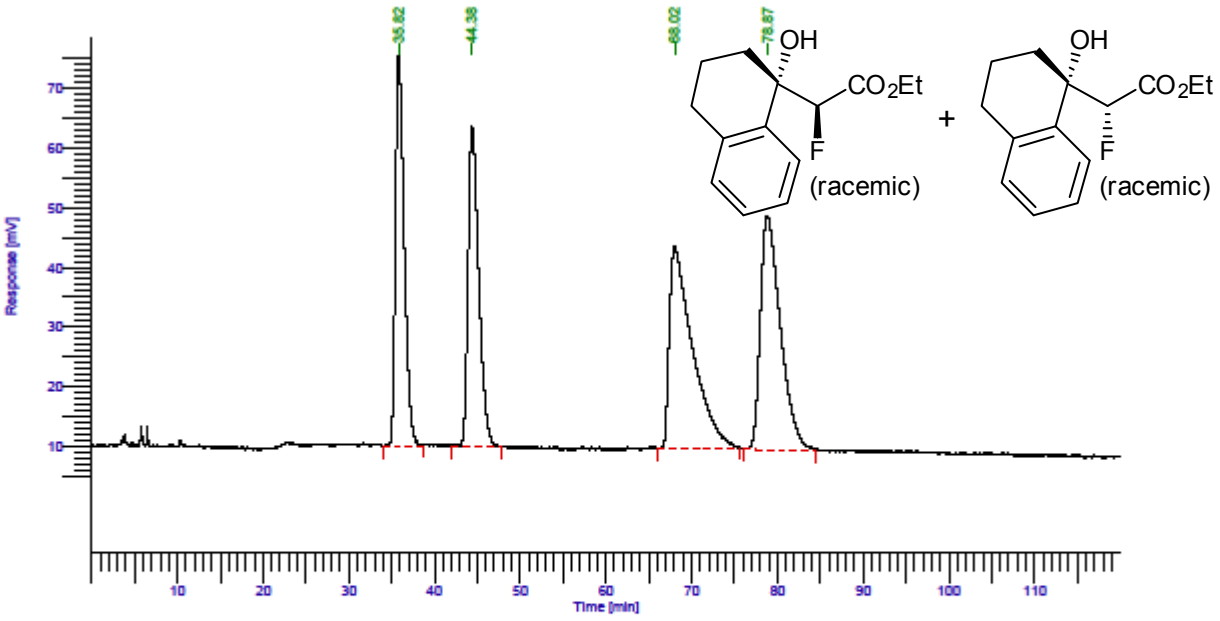
Chiralcel OD-H

Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	17.56	3791377	105186	26.0	BV
2	19.09	3412079	81330	23.4	VB
3	22.14	3453273	77256	23.7	BB
4	24.70	3939850	79795	27.0	BB
		14596580	343567	100.0	



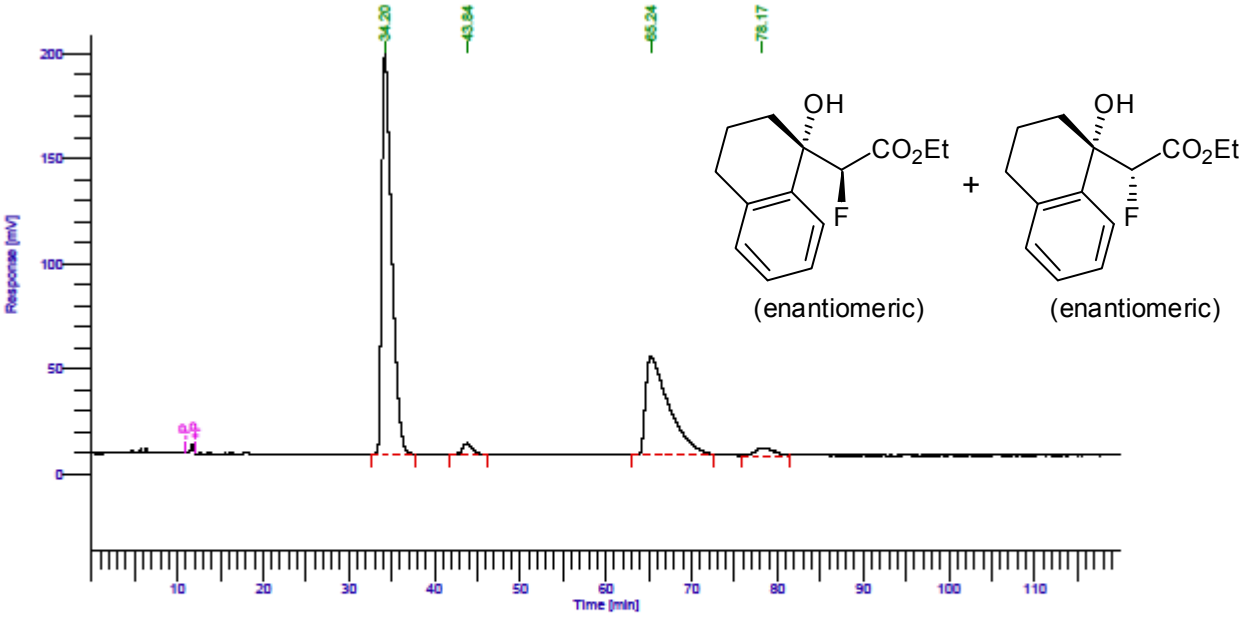
Chiralcel OD-H

Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	17.08	12271607	294992	54.6	BV
2	18.70	8205743	172306	36.5	VB
3	22.69	719610	14889	3.2	BB
4	25.60	1282905	22056	5.7	BB
		22479866	504242	100.0	



Chiralcel OD-H

Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	35.82	4692659	65765	21.2	BB
2	44.38	4711840	53723	21.3	BB
3	68.02	6376086	33864	28.8	BB
4	78.87	6368272	39185	28.8	BB
		22148858	192537	100.0	



Chiralcel OD-H

Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	34.20	15466931	191327	61.1	BB
2	43.84	452389	5460	1.8	BB
3	65.24	8853832	47274	35.0	BB
4	78.17	558177	3653	2.2	BB
		25331329	247714	100.0	