Supporting information for

Efficient Asymmetric Transfer Hydrogenation of Ketones in Ethanol with Chiral Iridium Complexes of SpiroPAP Ligands as Catalysts

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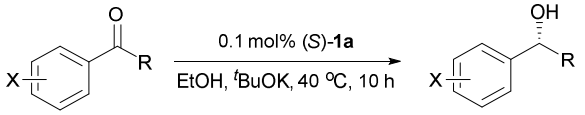
General: All reactions and manipulations which are sensitive to moisture or air were performed in an argon-filled glovebox (VAC DRI-LAB HE 493) or using standard Schlenk techniques. Anhydrous THF was distilled from sodium benzophenone ketyl. Anhydrous CH_2Cl_2 and Et_3N were freshly distilled from calcium hydride. Anhydrous EtOH was freshly distilled from magnesium. $[Ir(COD)Cl]_2$ was purchased from J&K Chemical Company. ^{t}BuOK, and other chemical reagents were purchased from Acros and Aldrich Chemical Company. Melting points were measured on a RY-I apparatus and uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AMX-400 spectrometers. Chemical shifts were reported in ppm downfield from internal $Si(CH_3)_4$ and external 85% H_3PO_4, respectively. Optical rotations were determined using a Perkin Elmer 341 polarimeter. GC analyses were performed using a Hewlett Packard Model HP 6890 Series. HPLC analyses were performed using Hewlett Packard Model HP 1100 instruments. For the ReactIR stepwise stoichiometric reaction experiments, the reaction spectra were recorded using an IC 15 from Mettler-Toledo AutoChem. Data manipulation was carried out using the iC IR software, version 4.2 and 4.3.

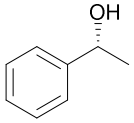
A. Asymmetric transfer hydrogenation of simple ketones.



2 (*R*)-**3**

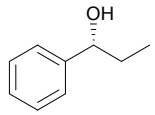
General procedure for S/C = 1000: To a dry 25 mL Schlenk tube flushed with nitrogen was added (*S*)-**1a** (2.0 mg, 2.0 μmol) and 1 mL EtOH. Then, ketones **1** (2.0 mmol) in 1 mL EtOH and ^{t}BuOK (22.4 mg, 0.2 mmol) in 3 mL EtOH were added via a syringe successively. The reaction solution was stirred at 40 °C stirred for 4–10 h (monitored by GC). The solvent was removed in vacuo and the residue was purified by flash column chromatography on silical gel with petroleum ether/ethyl acetate (5:1) as the eluent to afford the chiral alcohols **3**. The enantioselectivity was determined by HPLC or GC with chiral column.

(*R*)-1-Phenylethanol ((*R*)-3a)[1]



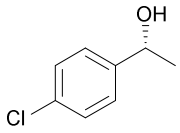
4 h, 99% yield, 98% ee (*R*). $[\alpha]_D^{20}$ + 44.5 (*c* 1.0, CH_2Cl_2). GC conditions: Supelco β-DEX™225, df = 0.25 μm, 0.25 mm i.d. × 25 m, carrier gas, N_2 (flow 2 mL/min); injection temp, 230 °C; initial column temperature, 100 °C; progress rate, 1 °C/min; final column temperature, 120 °C; progress rate, 10 °C/min; final column temperature, 200 °C; detector temperature, 250 °C); t_R (*R*) = 9.32 min; t_R (*S*) = 10.01 min.

(*R*)-1-Phenylpropanol ((*R*)-3b)[1]



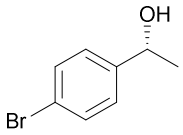
10 h, 95% yield, 97% ee (*R*). $[\alpha]_D^{20}$ + 44.5 (*c* 1.0, $CHCl_3$). SFC conditions:, Chiralcel OJ-H column; eluent, *i*-propanol/CO_2 = 1:99, temp, r.t.; flow rate, 2.0 mL/min; detection, 220 nm light); t_R(*S*) = 7.45 min; t_R (*R*) = 8.14 min.

(*R*)-1-(4-Chlorophenyl)ethanol ((*R*)-3c)[1]



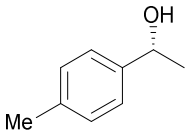
10 h, 95% yield, 96% ee (*R*). $[\alpha]_D^{20}$ + 43.5 (*c* 1.0, $CHCl_3$). HPLC conditions: Chiralcel OD-H column; eluent, *i*-propanol/hexane = 2:98; temp, r.t.; flow rate, 1.0 mL/min; detection, 220 nm light); t_R (*S*) = 15.08 min; t_R (*R*) = 16.91 min.

(*R*)-1-(4-Bromophenyl)ethanol ((*R*)-3d)[1]



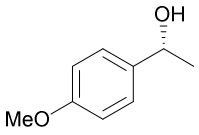
10 h, 95% yield, 91% ee (*R*). $[\alpha]_D^{20}$ + 36.5 (*c* 1.0, $CHCl_3$). GC conditions: Supelco β-DEX™ 225, df = 0.25 μm, 0.25 mm i.d. x 25 m, carrier gas, N_2 (flow 2 mL/min); injection temp, 230 °C; initial column temperature, 100 °C; progress rate, 1 °C/min; final column temperature, 160 °C; progress rate, 10 °C/min; final column temperature, 200 °C; detector temperature, 250 °C); t_R (*R*) = 35.43 min; t_R (*S*) = 36.98 min.

(*R*)-1-(4-Methylphenyl)ethanol ((*R*)-3e)[1]



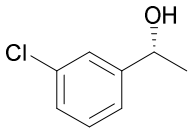
10 h, 98% yield, 90% ee (*R*). $[\alpha]_D^{20}$ + 53.8 (*c* 1.0, $CHCl_3$). HPLC conditions: Chiralcel OJ-H column; eluent, *i*-propanol/hexane = 5:95; temp, r.t.; flow rate, 1.0 mL/min; detection, 220 nm light); t_R (*S*) = 10.51 min; t_R (*R*) = 11.95 min.

(*R*)-1-(4-Methoxylphenyl)ethanol ((*R*)-3f)[1]



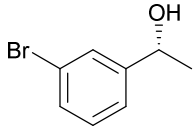
10 h, 93% yield, 95% ee (*R*). $[\alpha]_D^{20}$ + 56.8 (*c* 1.0, $CHCl_3$). HPLC conditions: Chiralcel OJ-H column; eluent, *i*-propanol/hexane = 10:90; temp, r.t.; flow rate, 1.0 mL/min; detection, 220 nm light);; t_R (*S*) = 15.11 min; t_R (*R*) = 16.54 min.

(*R*)-1-(3-Chlorophenyl)ethanol ((*R*)-3g)[2]



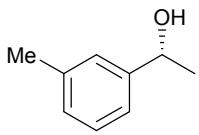
10 h, 93% yield, 96% ee (*R*). $[\alpha]_D^{20}$ + 56.8 (*c* 1.0, $CHCl_3$). HPLC conditions: Chiralcel OJ-H column; eluent, *i*-propanol/hexane = 5:95; temp, r.t.; flow rate, 1.0 mL/min; detection, 220 nm light); t_R (*S*) = 15.92 min; t_R (*R*) = 16.74 min.

(*R*)-1-(3-Bromophenyl)ethanol ((*R*)-3h)[1]



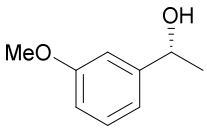
10 h, 96% yield, 93% ee (*R*). $[\alpha]_D^{20}$ + 33.3 (*c* 1.0, $CHCl_3$). HPLC conditions: Chiralcel OJ-H column; eluent, *i*-propanol/hexane = 2:98; temp, r.t.; flow rate, 1.0 mL/min; detection, 220 nm light; t_R (*S*) = 7.45 min; t_R (*R*) = 8.47 min.

(*R*)-1-(3-Methylphenyl)ethanol ((*R*)-3i)[1]



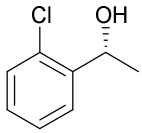
10 h, 98% yield, 96% ee (*R*). $[\alpha]_D^{20}$ + 47.8 (*c* 1.0, $CHCl_3$). HPLC conditions: Chiralcel OJ-H column; eluent, *i*-propanol/hexane = 5:95; temp, r.t.; flow rate, 1.0 mL/min; detection, 220 nm light; t_R (*S*) = 8.64 min; t_R (*R*) = 9.25 min.

(*R*)-1-(3-Methoxylphenyl)ethanol ((*R*)-3j)[1]



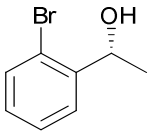
10 h, 95% yield, 97% ee (*R*). $[\alpha]_D^{20}$ +42.7 (*c* 1.0, $CHCl_3$). SFC conditions: Chiralcel OJ-H column; eluent, *i*-propanol / CO_2 = 1:99; temp, r.t.; flow rate, 2.0 mL/min; detection, 220 nm light; t_R (*S*) = 11.01 min; t_R (*R*) = 12.76 min.

(*R*)-1-(2-Chlorophenyl)ethanol ((*R*)-3k)[1]



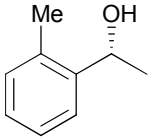
10 h, 99% yield, 98% ee (*R*). $[\alpha]_D^{20}$ + 66.8 (*c* 1.0, $CHCl_3$). HPLC conditions: Chiralcel OD-H column; eluent, *i*-propanol/hexane = 2:98; temp, r.t.; flow rate, 1.0 mL/min; detection, 220 nm light; t_R (*R*) = 15.25 min; t_R (*S*) = 16.3 min.

(*R*)-1-(2-Bromophenyl)ethanol ((*R*)-3l)[1]



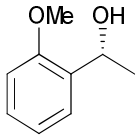
10 h, 94% yield, 96% ee (*R*). $[\alpha]_D^{20}$ + 54.3 (*c* 1.0, $CHCl_3$). HPLC conditions: Chiralcel OD-H column; eluent, *i*-propanol/hexane = 2:98; temp, r.t.; flow rate, 1.0 mL/min; detection, 220 nm light); t_R (*S*) = 13.51 min; t_R (*R*) = 14.92 min.

(*R*)-1-(2-Methylphenyl)ethanol ((*R*)-3m)[1]



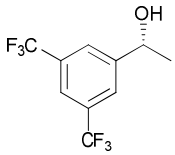
10 h, 96% yield, 98% ee (*R*). $[\alpha]_D^{20}$ + 79.8 (*c* 1.0, $CHCl_3$). GC conditions: Coating CP Chirasil-DEX CB, CP7502, df = 0.25 μm, 0.25 mm i.d. x 25 m; carrier gas, N_2 (flow 2.0 mL/min); injection temp, 250 °C; initial column temperature, 100 °C; progress rate, 1.0 °C/min; final column temperature, 160 °C; t_R (*R*) = 19.00 min; t_R (*S*) = 22.91 min].

(*R*)-1-(2-Methoxylphenyl)ethanol ((*R*)-3n)[1]



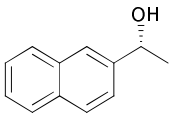
10 h, 99% yield, 96% ee (*R*). $[\alpha]_D^{20}$ +23.7 (*c* 1.0, $CHCl_3$). HPLC conditions: Chiralcel OD-H column; eluent, *i*-propanol/hexane = 2:98; temp, r.t.; flow rate, 1.0 mL/min; detection, 220 nm light; t_R (*S*) = 20.89 min; t_R (*R*) = 21.9 min.

(*R*)-1-(3,5-bis(trifluoromethyl)phenyl)ethanol ((*R*)-3o)[1]



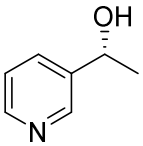
10 h, 98% yield, 93% ee (*R*). $[\alpha]_D^{20}$ +22.7 (*c* 1.0, $CHCl_3$). HPLC conditions: Chiralcel OD-H column; eluent, *i*-propanol/hexane = 2:98; temp, r.t.; flow rate, 1.0 mL/min; detection, 220 nm light; t_R (*S*) = 12.43 min; t_R (*R*) = 14.74 min.

(*R*)-1-(2-Naphtyl)ethanol ((*R*)-3p)[1]



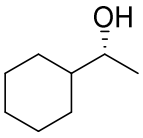
10 h, 99% yield, 95% ee (*R*). $[\alpha]_D^{20}$ +48.9 (*c* 1.0, $CHCl_3$). HPLC conditions: Chiralcel OD-H column; eluent, *i*-propanol /hexane = 2:98; temp, r.t.; flow rate, 1.0 mL/min; detection, 220 nm light); t_R (*S*) = 50.52 min; t_R (*R*) = 52.98 min.

(*R*)-1-(Pyridin-3-yl)ethan-1-ol ((*R*)-3q)



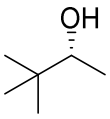
10 h, 87% yield, 93% ee (*R*). $[\alpha]_D^{20}$ +19.6 (*c* 1.0, $CHCl_3$). HPLC conditions: Chiralcel OJ-H column; eluent, *i*-propanol/hexane = 25:75; temp, r.t.; flow rate, 1.0 mL/min; detection, 220 nm light); t_R (*R*) = 3.97 min; t_R (*S*) = 4.56 min.

(*R*)-1-Cyclohexylethan-1-ol ((*R*)-3r)



10 h, 97% yield, 83% ee (*R*). $[\alpha]_D^{20}$ −25.2 (*c* 1.2, $CHCl_3$). HPLC conditions (To the corresponding benzylacelated derivatives): Chiralcel OD-H column; eluent, *i*-propanol/hexane = 2:98; temp, r.t.; flow rate, 1.0 mL/min; detection, 220 nm light); t_R (*S*) = 6.17 min; t_R (*R*) = 6.79 min.

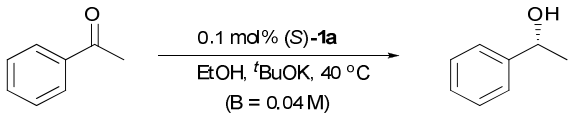
(*R*)-3,3-Dimethylbutan-2-ol ((*R*)-3s)



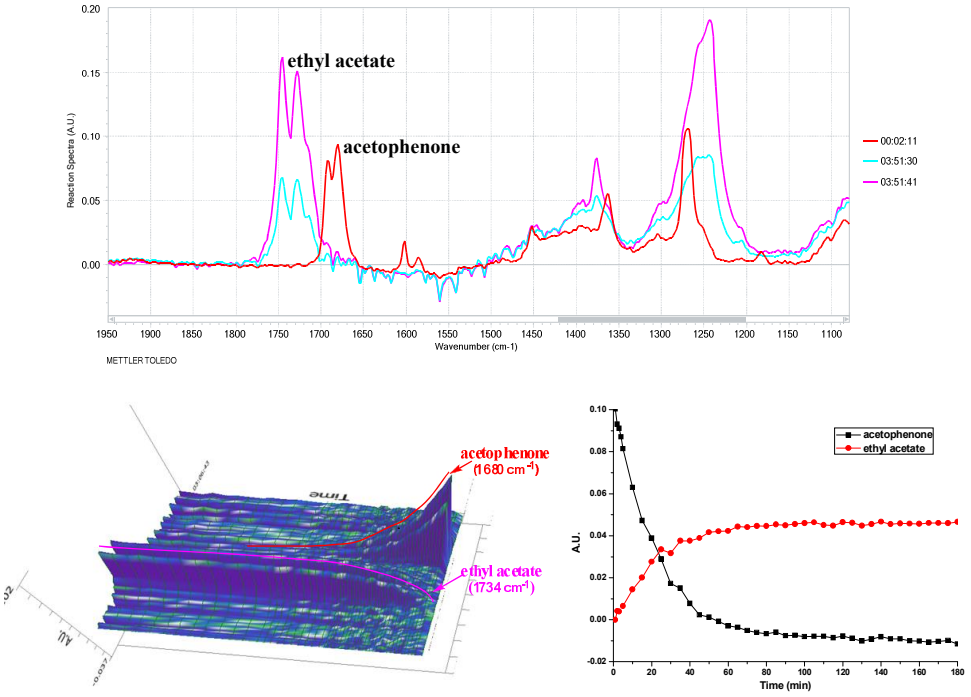
10 h, 90% yield, 80% ee (*R*). $[\alpha]_D^{20}$ −3.7 (*c* 1.0, $CHCl_3$). GC condition (Supelco beta-DEX™ 225, df = 0.25 μm, 0.25 mm i.d. x 25 m, fused silica capillary column); carrier gas, N_2 (flow 1 mL/min); injection temp, 250 °C; initial column temperature, 70 °C; progress rate, hold for 40 min then 0.5 °C /min; final column temperature, 180 °C); t_R (*R*) = 24.27 min; t_R (*S*) = 27.97 min.

Asymmetric transfer hydrogenation of 2a on a gram scale (S/C = 2000): To a dry 500 mL three-necked round flask flushed with nitrogen was added (*S*)-**1a** (50 mg, 0.1 mmol) in 10 mL EtOH. Then, **2a** (12.0 g, 0.1 mol) in 200 mL EtOH and ^{t}BuOK (22.4 mg, 0.2 mmol) in 40 mL EtOH were added via a syringe successively. The reaction solution was stirred at 40 °C stirred for 16 h (monitored by GC, 99% conversion). The solvent was removed in vacuo and the residue was purified by flash column chromatography on silical gel with petroleum ether/ethyl acetate (5:1) as the eluent to afford (*R*)-**3a** (11.7 g, 96% yield, 98% ee) as a colorless oil.

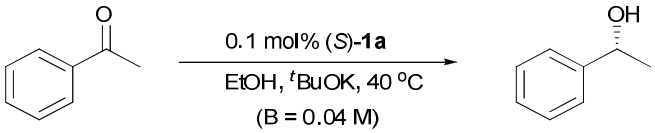
B. Monitored the asymmetric transfer hydrogenation using online IR techniques



The IR probe was inserted through an adapter into the middle neck of a 25 mL three-necked reaction flask which contained a befitting magnetic stirring bar, another neck were capped by rubber plug for injections and the last neck was connected to a nitrogen line. Following evacuation under vacuum and flushing with nitrogen for three times. Then, (*S*)-**1a** (2.0 mg, 2.0 μmol) in 1 mL EtOH and ^{t}BuOK (22.4 mg, 0.2 mmol) in 3 mL EtOH was injected to the reaction flask, followed by additions of acetophenone (240 mg, 2.0 mmol) in 1 mL EtOH. The resulting mixture was allowed to stir at 40 °C and the whole process was monitored by operando IR though the probe.

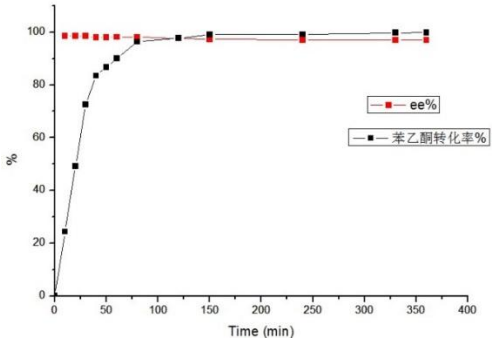


Monitored the asymmetric transfer hydrogenation using GC



The ^{t}BuOK (22.4 mg, 0.2 mmol), (*S*)-**1a** (2.0 mg, 2.0 μmol) were introduced into 15 mL anoven-dried Schlenk tube in an argon-filled glove box. EtOH (5 mL) was injected and the solution was stirred at 50 °C under the argon atmosphere for 5 min, followed by additions of acetophenone (240 mg, 2.0 mmol). The resulting mixture was stirred for 10 h at 50 °C. The conversion and enantioselectivity was determined by GC with chiral column every 10 min. GC [(Supelco β-DEX™ 225, df = 0.25 μm, 0.25 mm i.d. × 25 m, N_2 (2 mL/min); injection temp, 230 °C; initial column temperature, 100 °C; progress rate, 1.0 °C /min; final column temperature, 120 °C; progress rate, 10.0 °C /min; final column temperature, 200 °C； detector temperature, 250 °C); t_1 (*R*) = 9.21 min; t_2 (*S*) = 9.94 min].

Time (min)	Conv. (%)	ee (%)	Time (min)	Conv. (%)	ee (%)
10	24.3	98.5	80	96.4	98.1
20	49.2	98.6	120	97.7	97.7
30	72.5	98.5	150	99.1	97.3
40	83.5	98.1	240	99.2	97.1
50	86.7	98.0	330	99.8	97.1
60	90.1	98.2	360	99.9	97.1

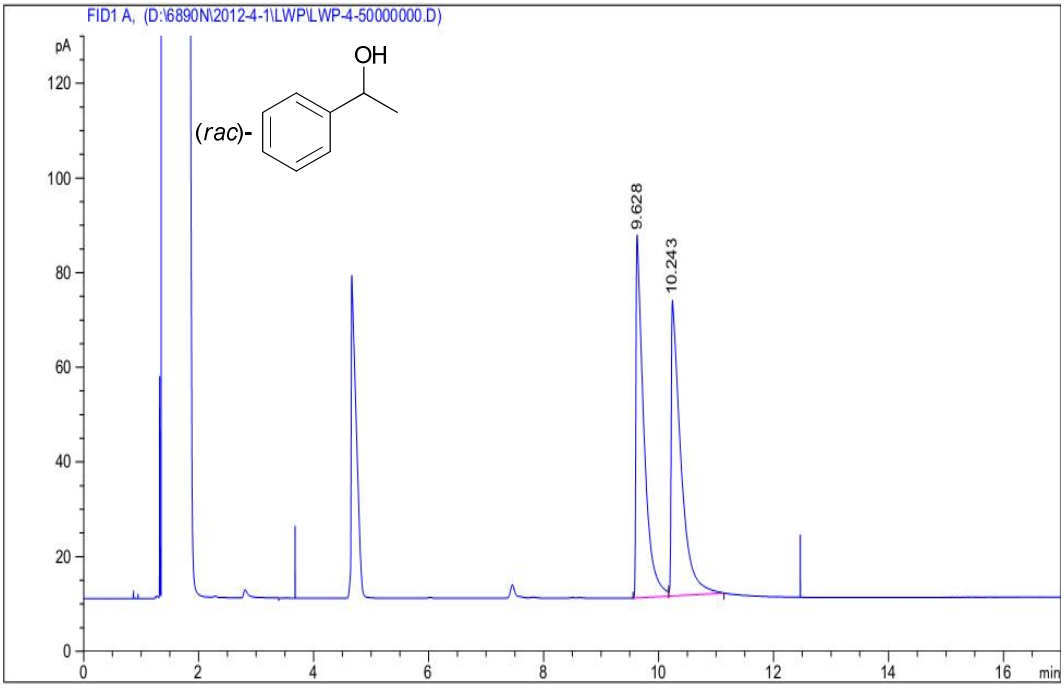


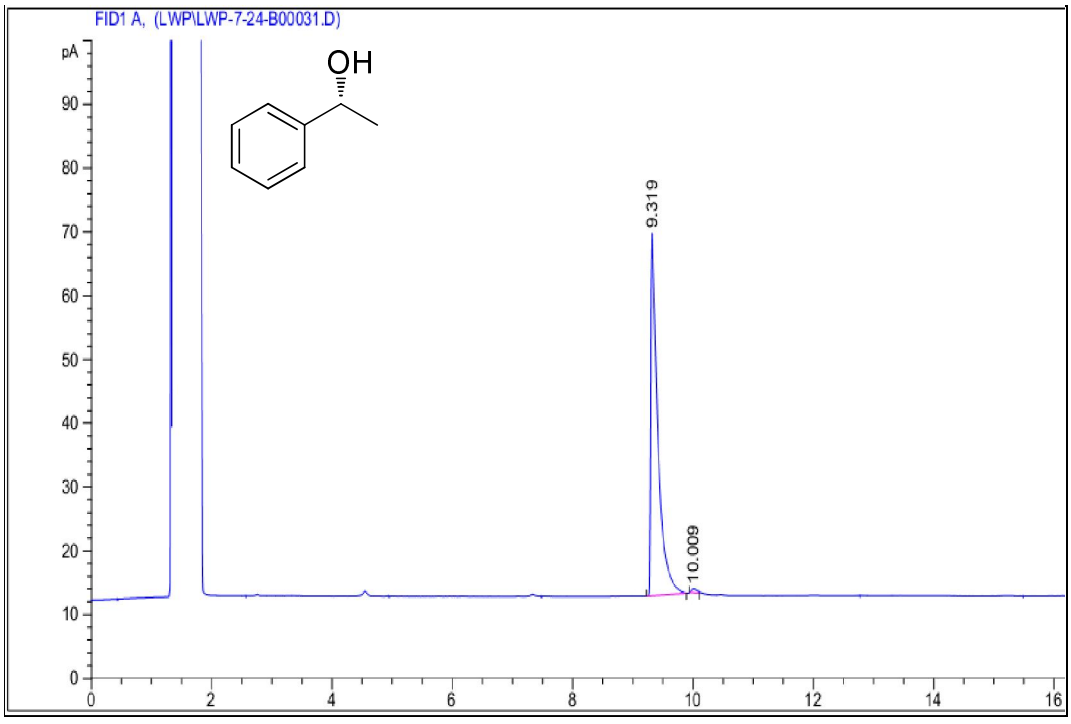
References

1. J.-H. Xie, X.-Y. Liu, J.-B. Xie, L.-X. Wang and Q.-L. Zhou, *Angew. Chem. Int. Ed.* **2011**, *50*, 7329.
2. J.-B. Xie, J.-H. Xie, X.-Y. Liu, Q.-Q. Zhang and Q.-L. Zhou, *Chem. –Asian J.* **2011**, *6*, 899.

C) GC and HPLC charts for hydrogenation products

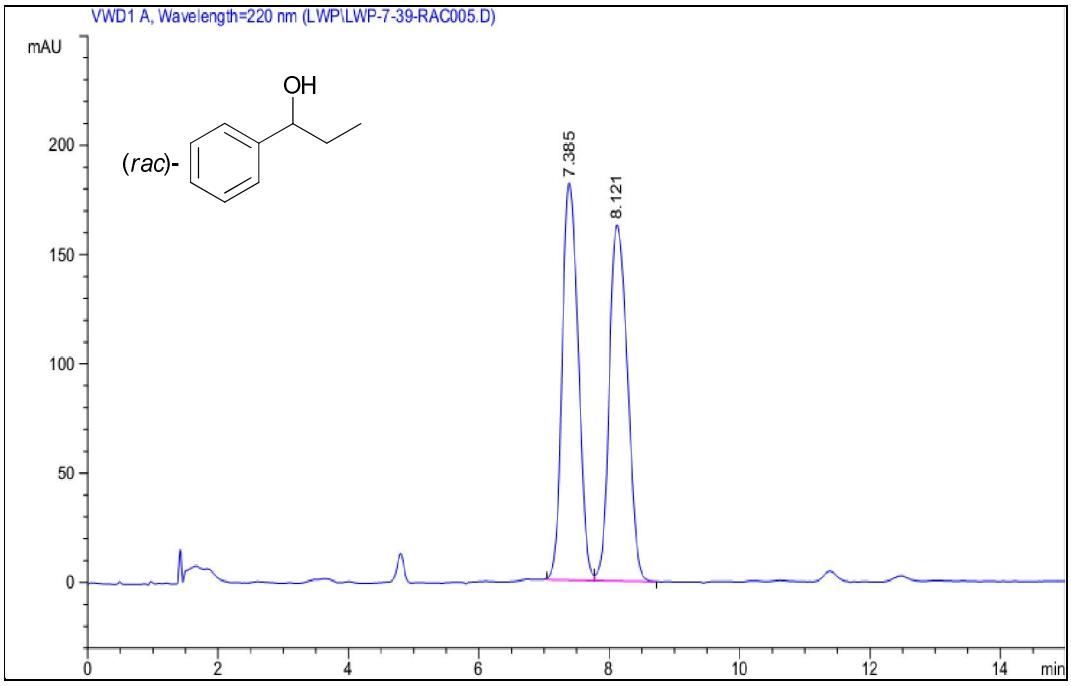
(*R*)-1-Phenylethanol ((*R*)-3a)

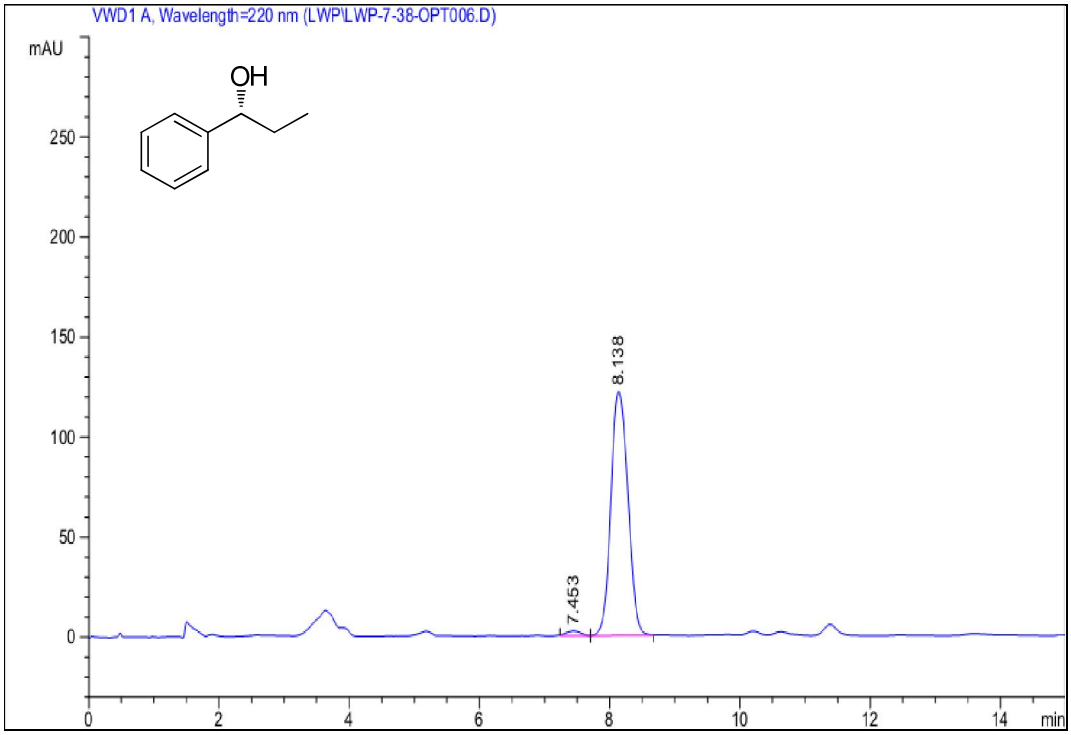




Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	9.319	BBA	0.1104	454.80872	56.82066	99.14006
2	10.009	BBA	0.0795	3.94501	6.25782e-1	0.85994

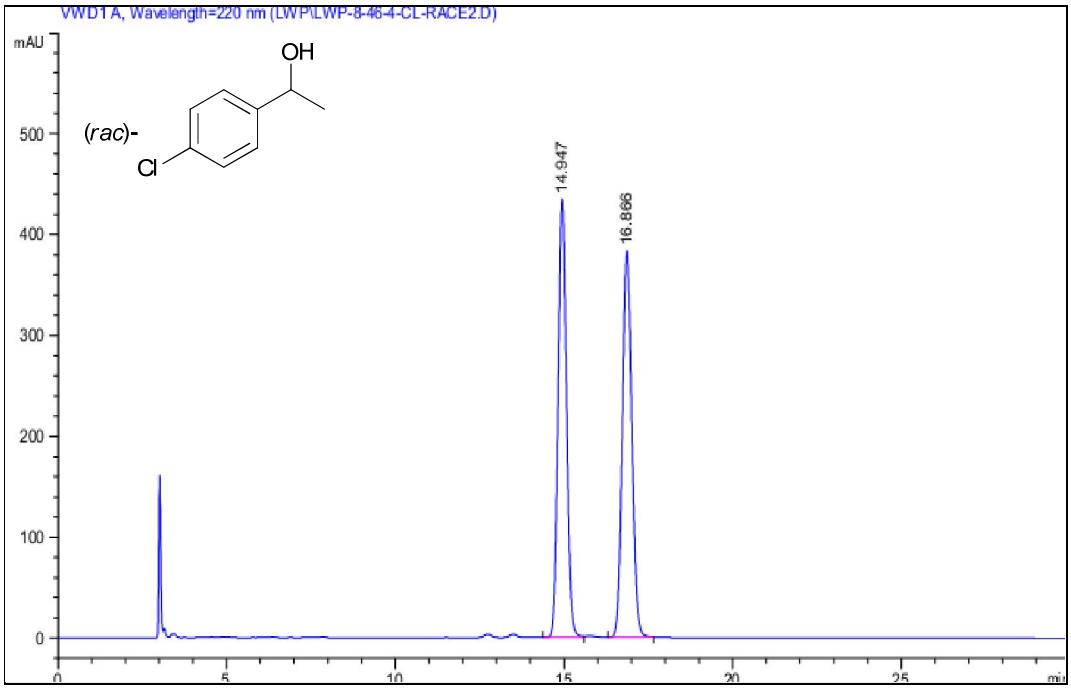
(*R*)-Phenylpropanol ((*R*)-3b)

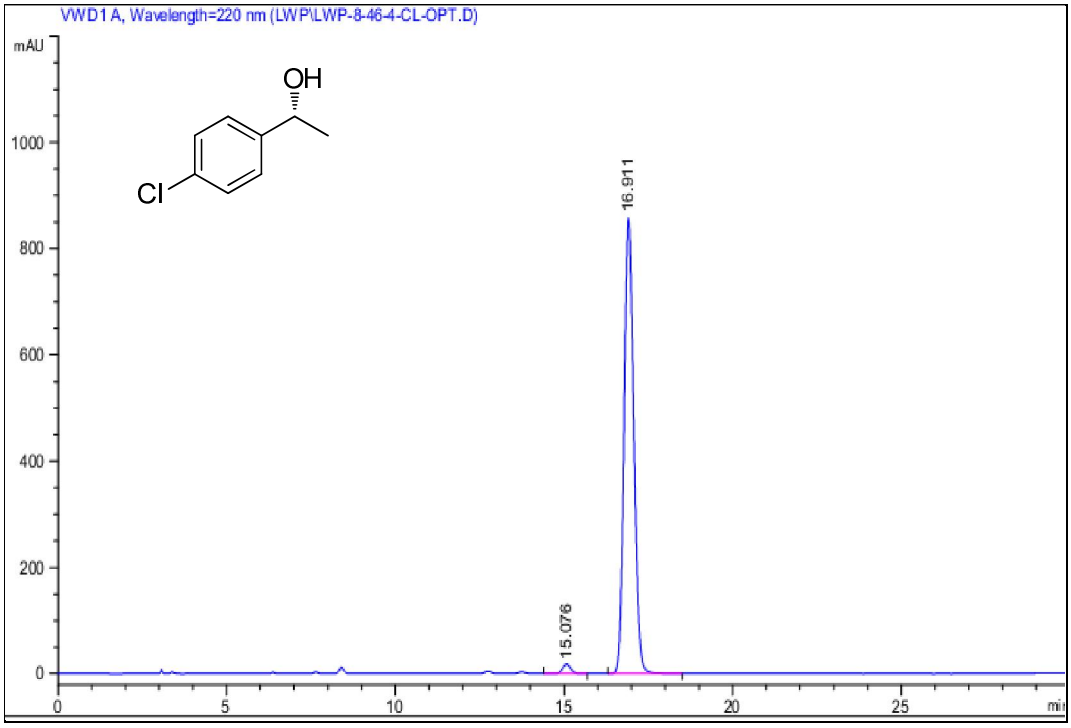




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Area %
1	7.453	BV	0.2437	35.73774	1.5853
2	8.138	VB	0.2922	2218.61719	98.4147

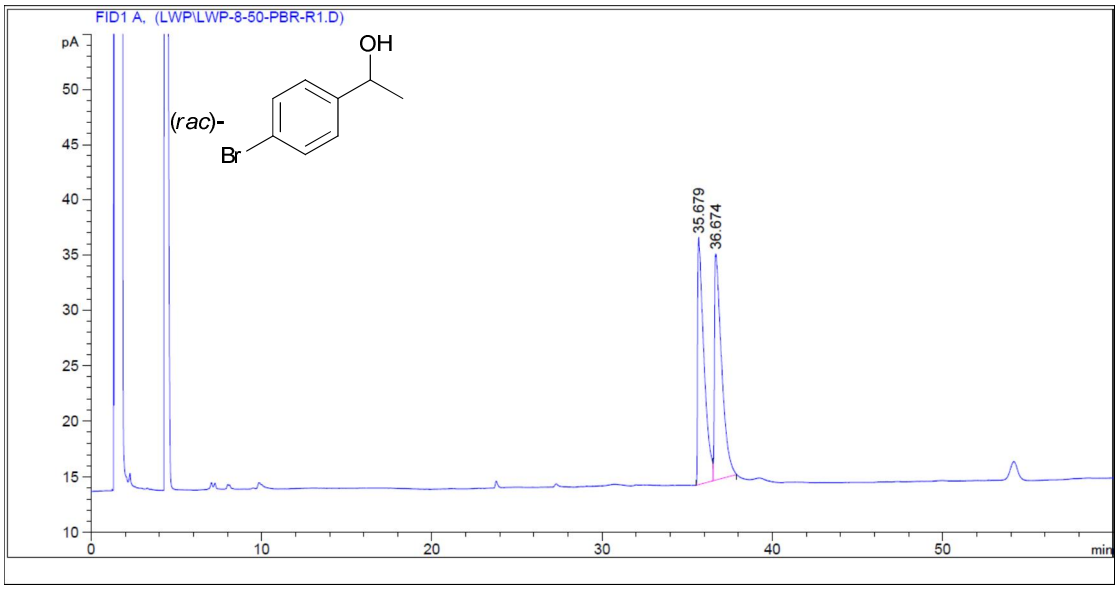
(*R*)-1-(4-Chlorophenyl)ethanol ((*R*)-3c)

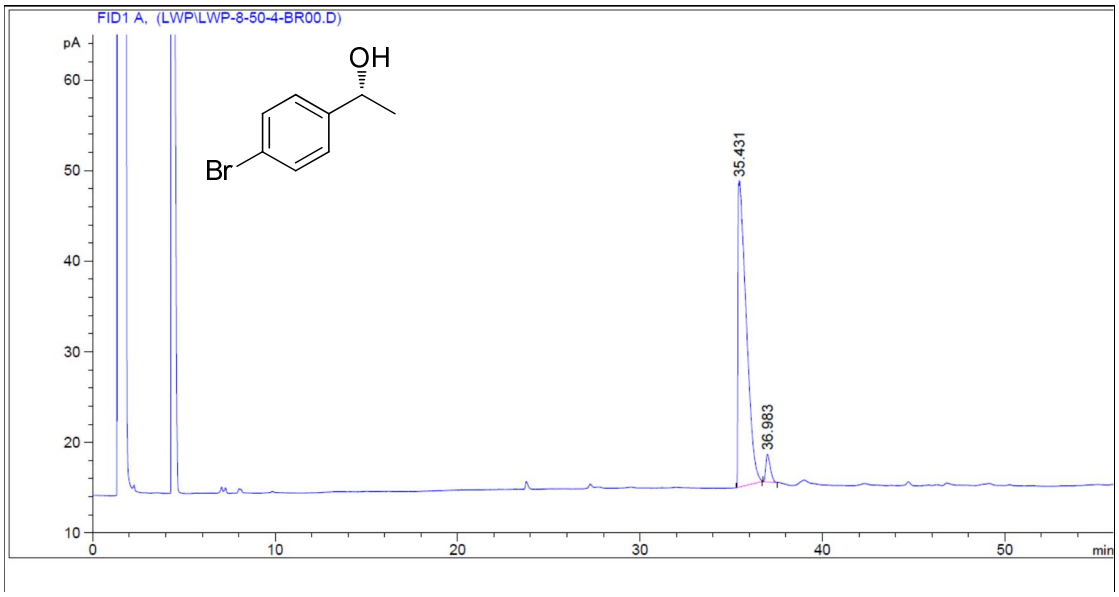




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.076	BB	0.2769	319.21994	17.91408	1.8136
2	16.911	BB	0.3130	1.72824e4	858.07178	98.1864

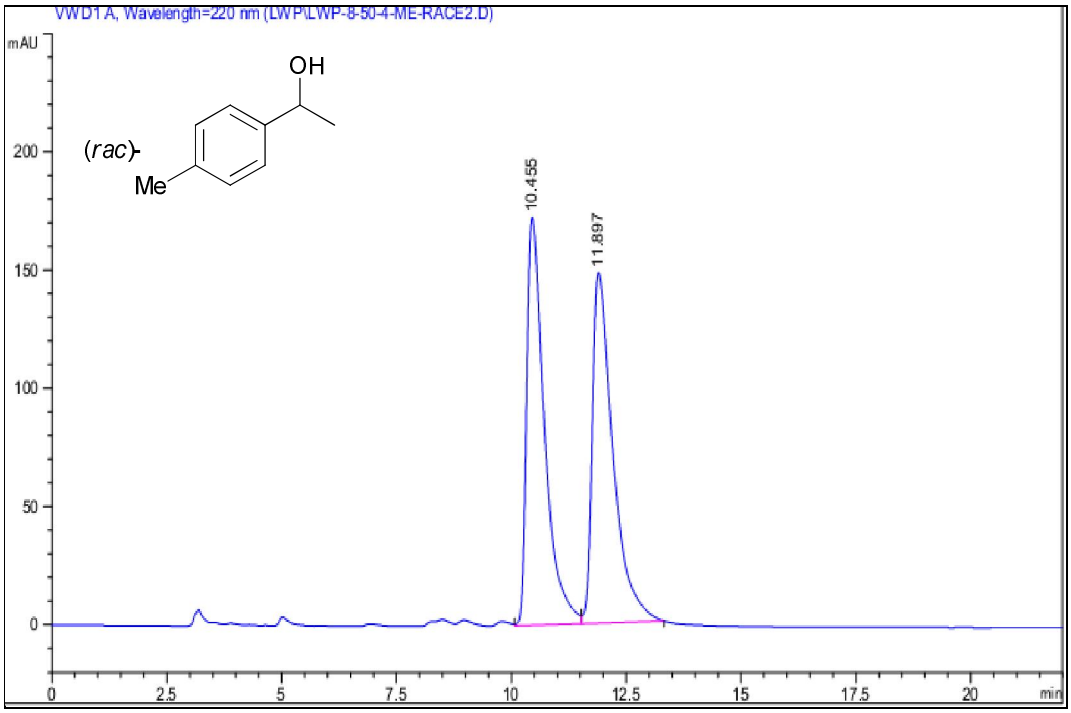
(*R*)-1-(4-Bromophenyl)ethanol ((*R*)-3d)

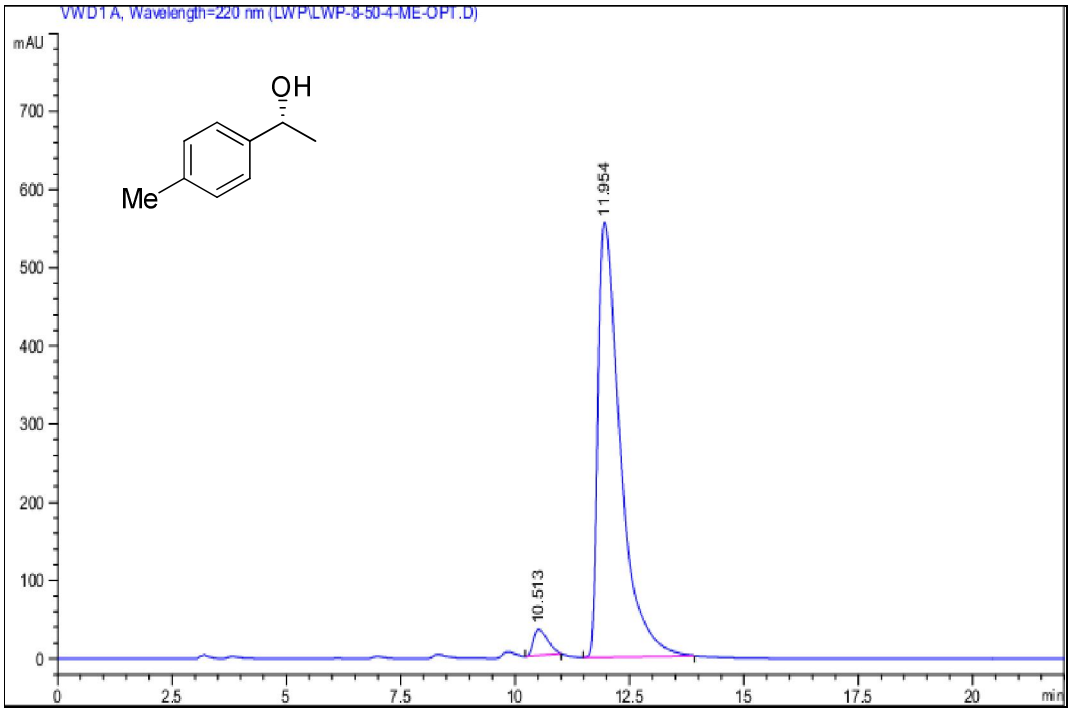




Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	35.432	BBA	0.3956	1070.23914	33.78563	95.47440
2	36.984	BBA	0.2457	50.73057	3.02416	4.52560

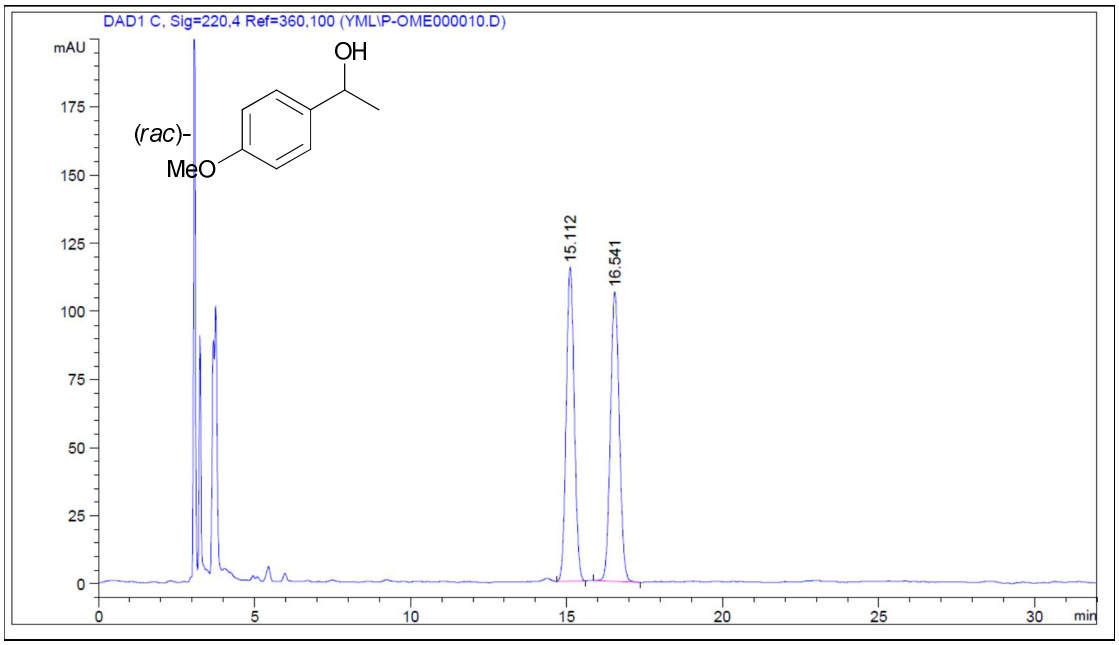
(*R*)-1-(4-Methylphenyl)ethanol ((*R*)-3e)

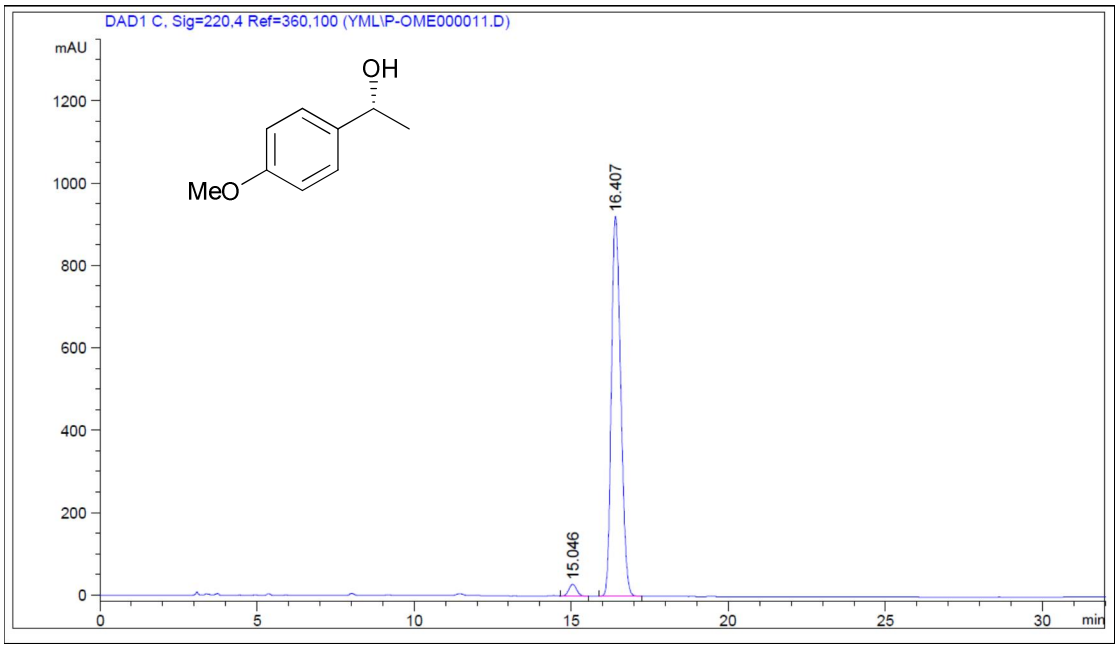




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.513	VV	0.4059	1010.70502	36.97809	4.9450
2	11.954	VB	0.5112	1.94280e4	557.99689	95.0550

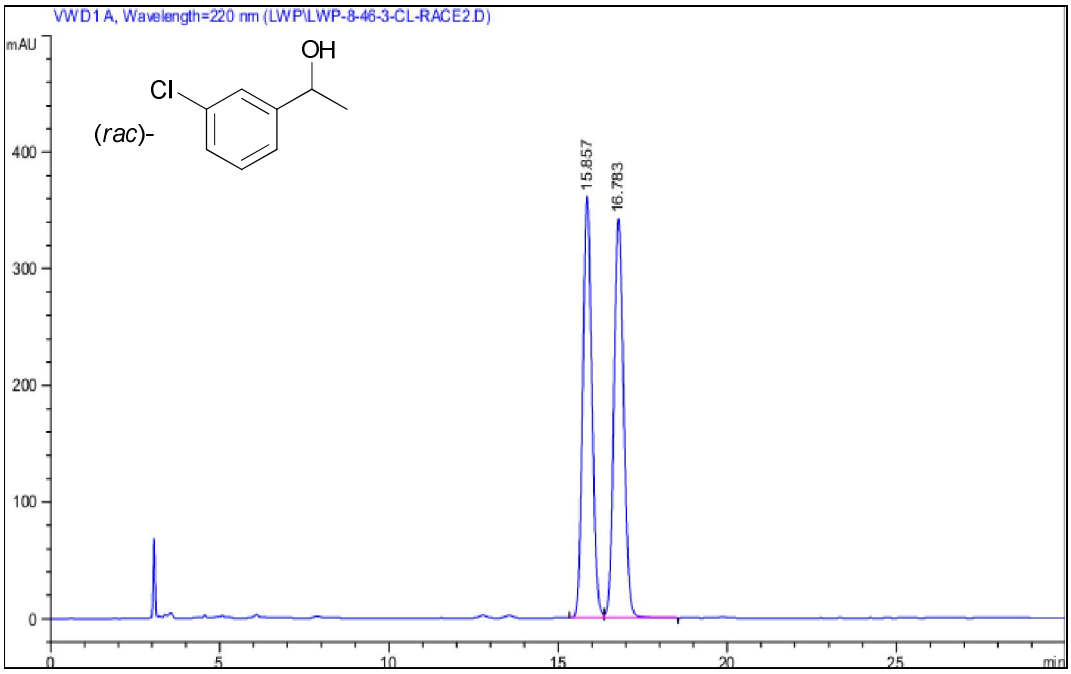
(*R*)-1-(4-Methoxylphenyl)ethanol ((*R*)-3f)

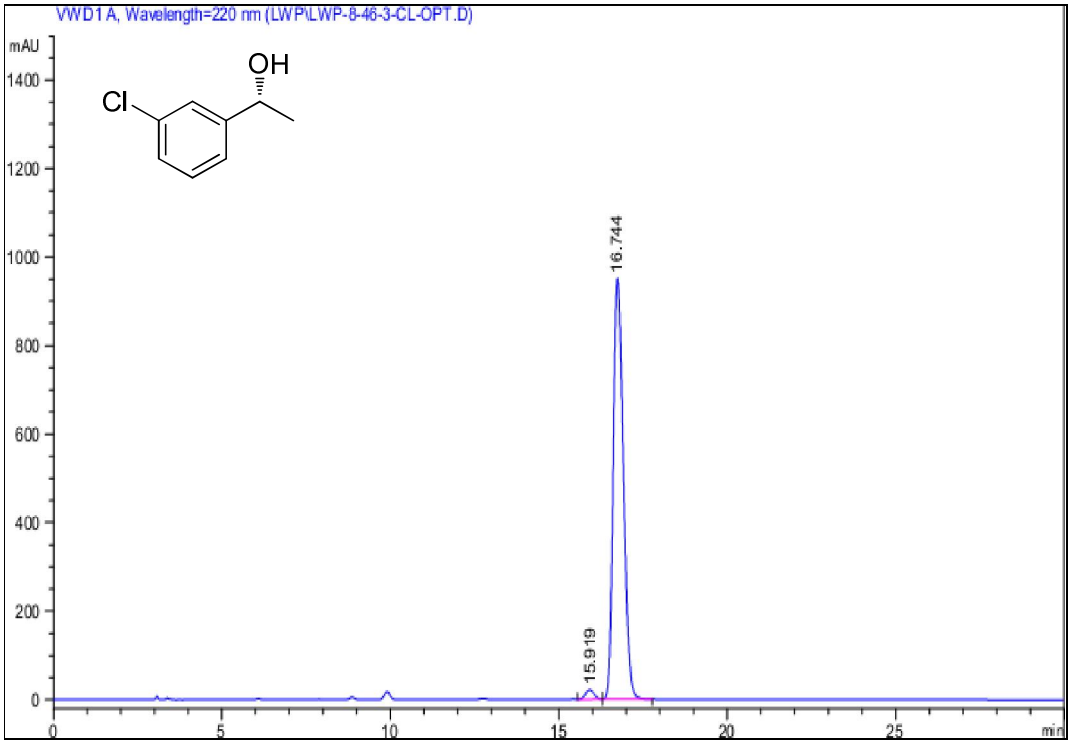




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.046	VB	0.2757	510.72522	28.96727	2.6000
2	16.407	BB	0.3260	1.91324e4	922.29346	97.4000

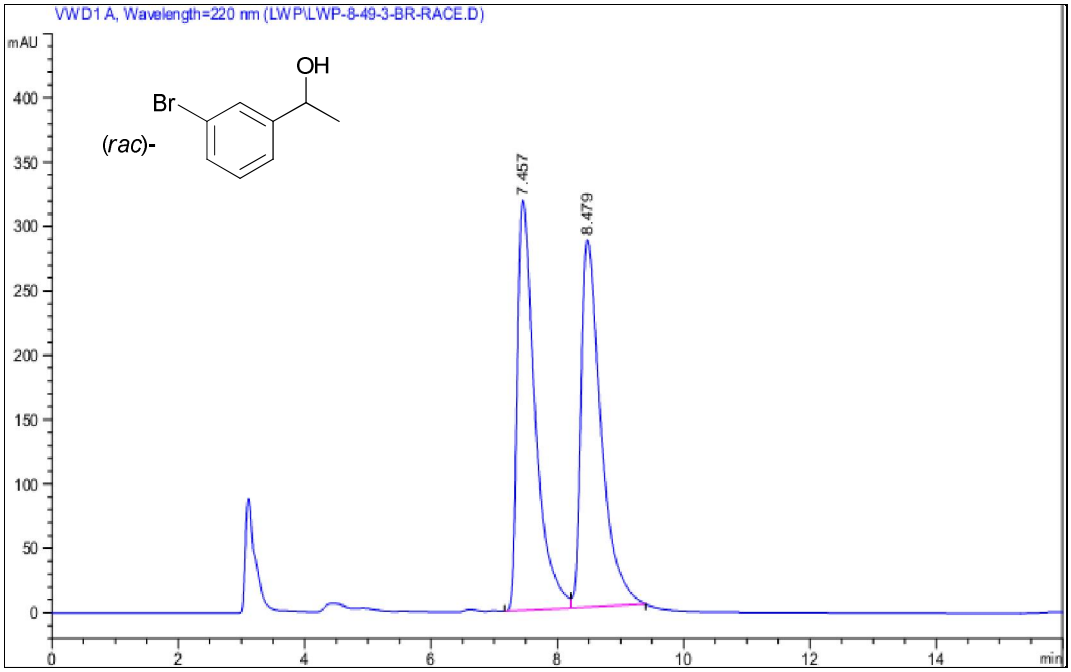
(*R*)-1-(3-Chlorophenyl)ethanol ((*R*)-3g)

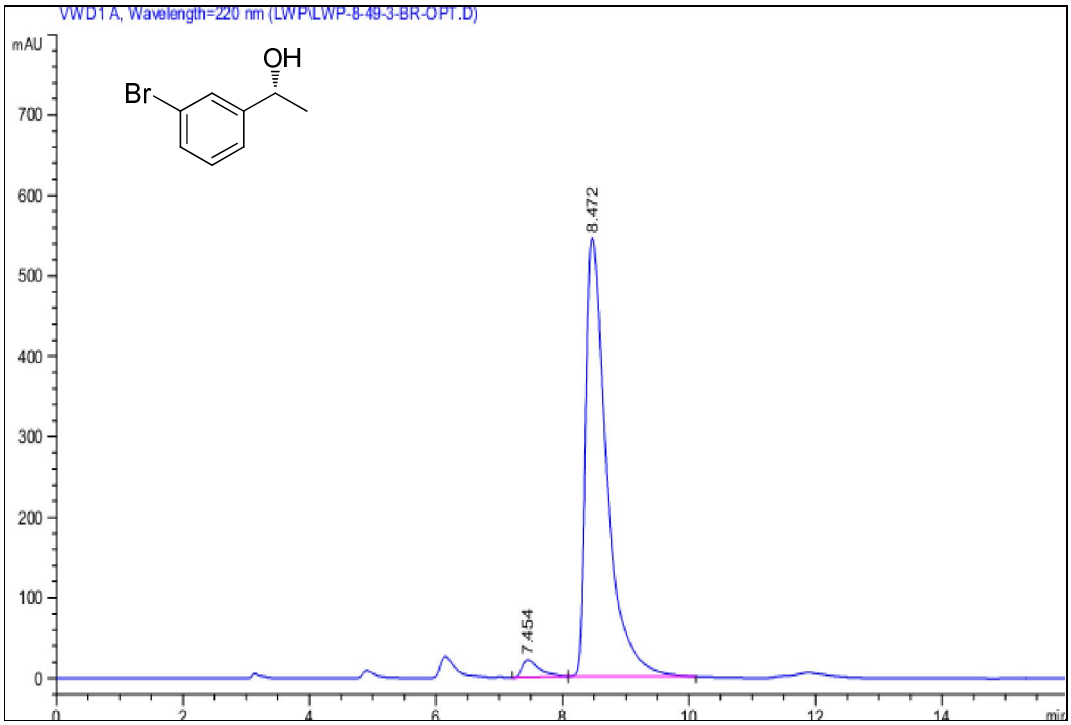




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.919	VV	0.2985	413.53085	21.49445	2.0295
2	16.744	VB	0.3275	1.99624e4	952.42230	97.9705

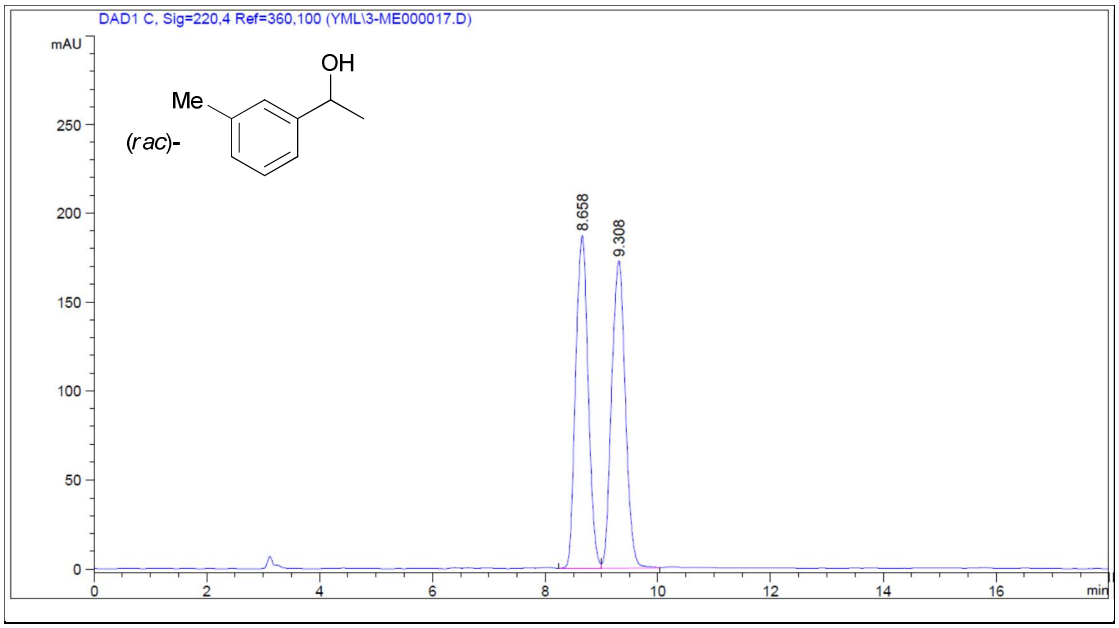
(*R*)-1-(3-Bromophenyl)ethanol ((*R*)-3h)

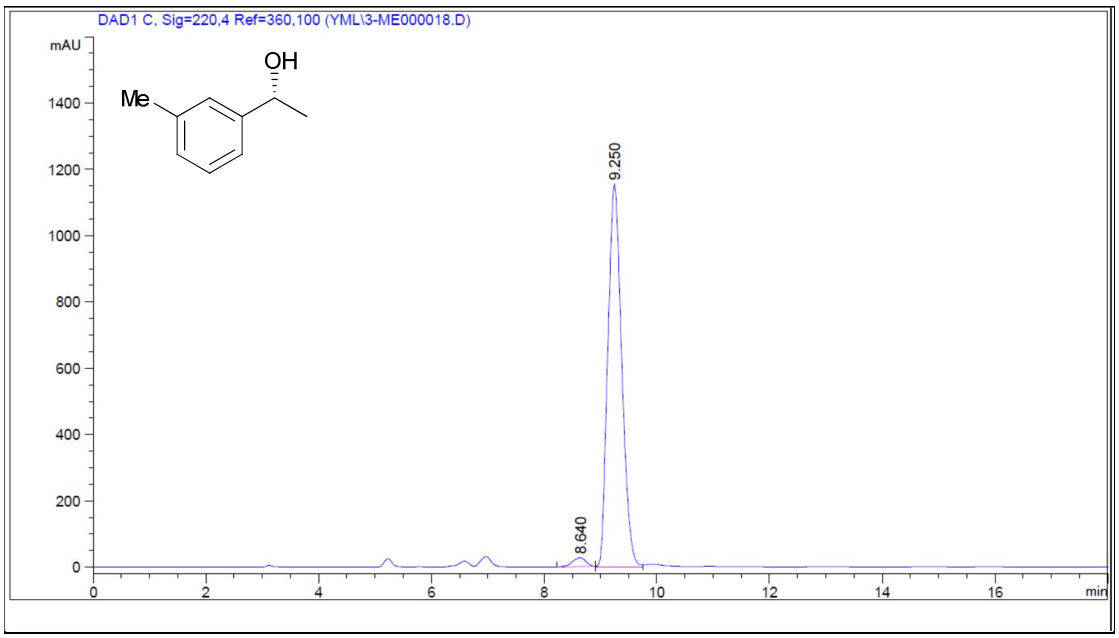




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.454	BV	0.3043	458.48782	21.89795	3.4423
2	8.472	VB	0.3475	1.28608e4	546.53442	96.5577

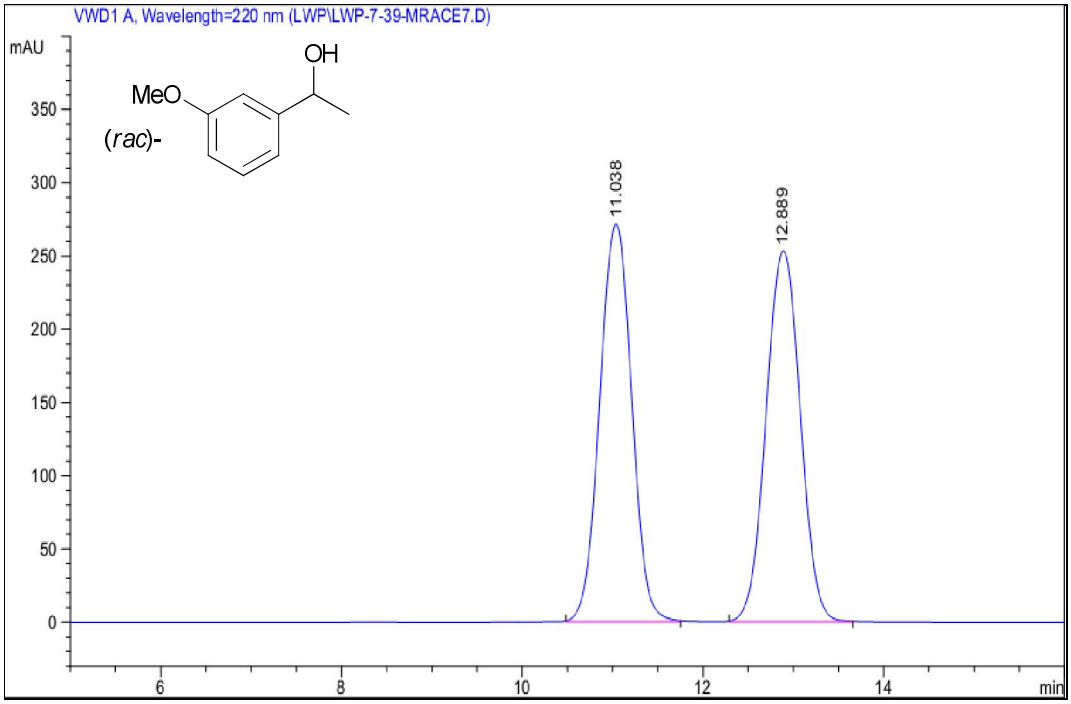
(*R*)-1-(3-Methylphenyl)ethanol ((*R*)-3i)

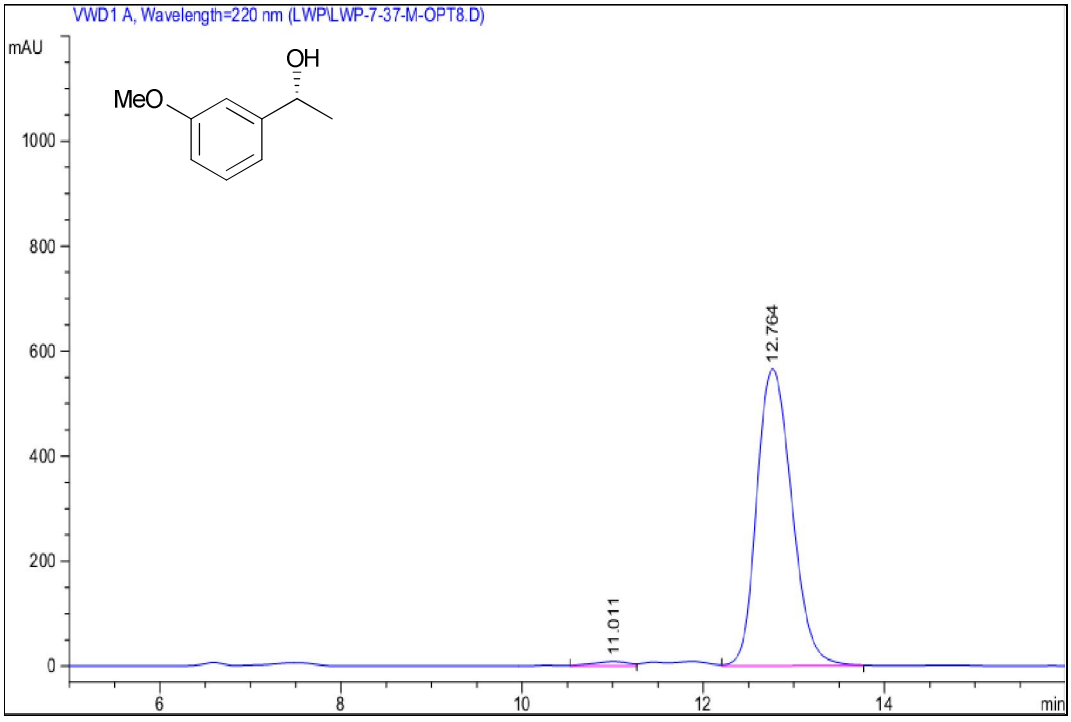




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.640	BB	0.2700	452.47665	26.66003	2.2515
2	9.250	BV	0.2750	1.96440e4	1151.86292	97.7485

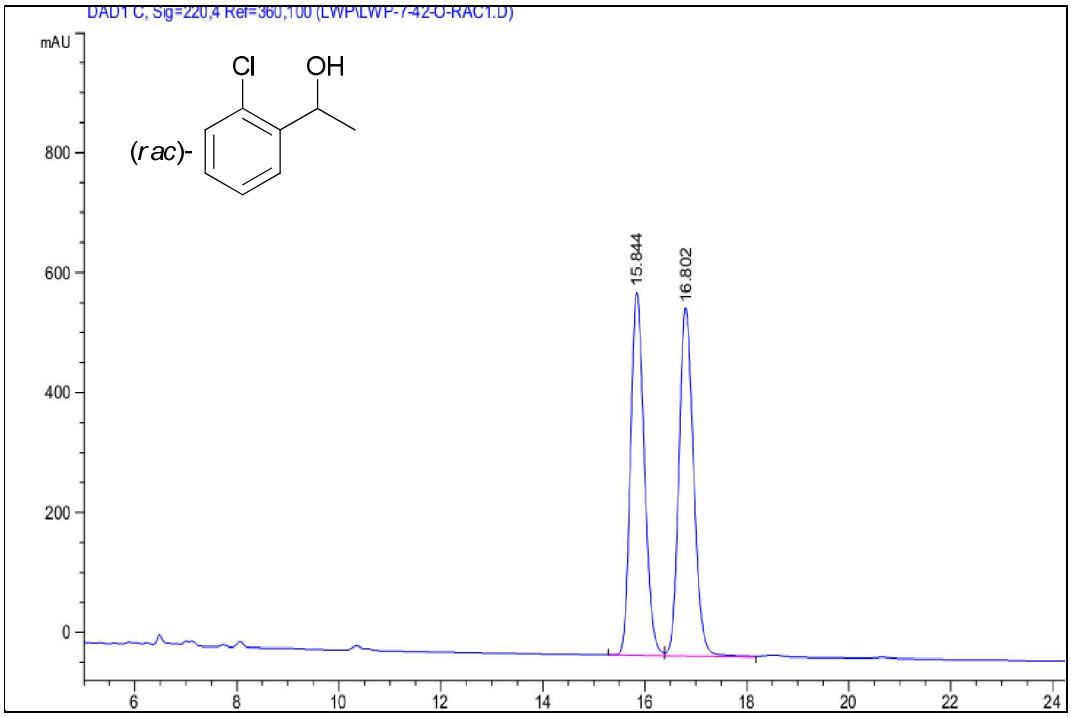
(*R*)-1-(3-Methoxylphenyl)ethanol ((*R*)-3j)

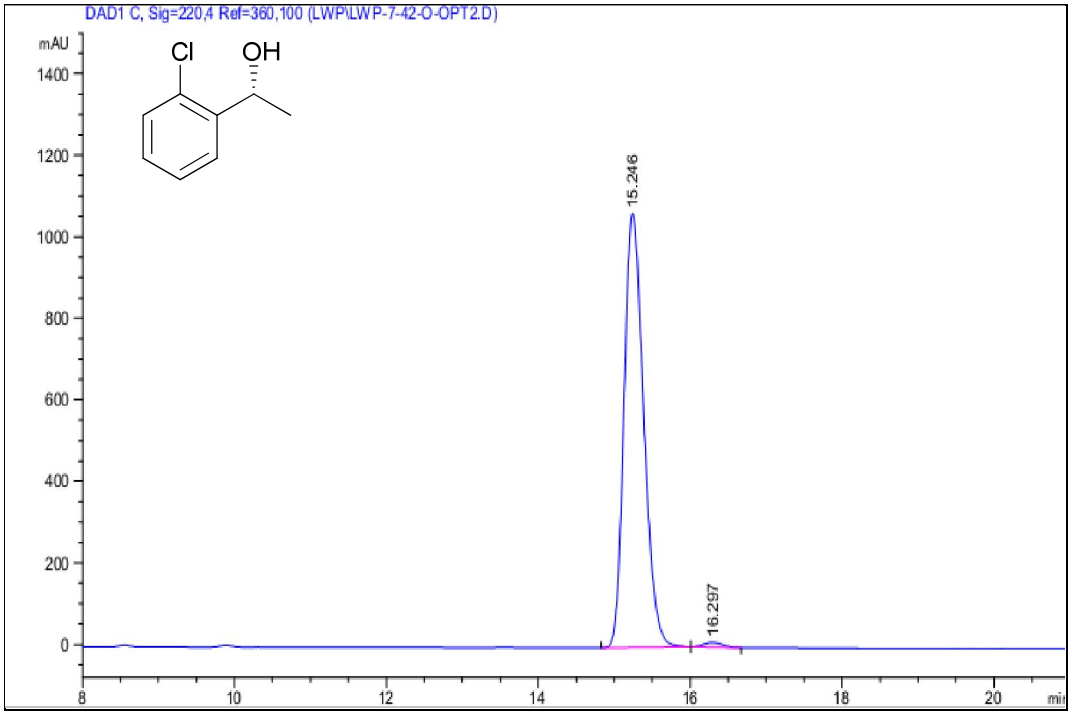




Peak #	RetTime [min]	Type	Width [min]	Area mAU	Area *s	Area %
1	11.011	BV	0.4059	243.99734		1.5760
2	12.764	VB	0.4250	1.52381e4		98.4240

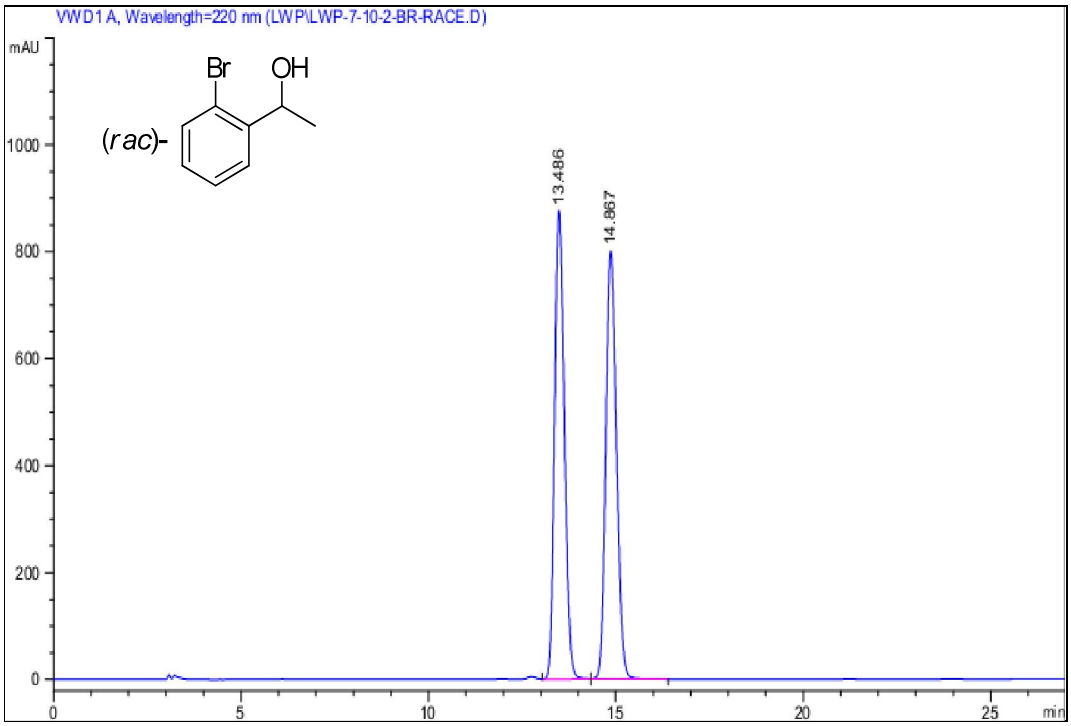
(*R*)-1-(2-Chlorophenyl)ethanol ((*R*)-3k)

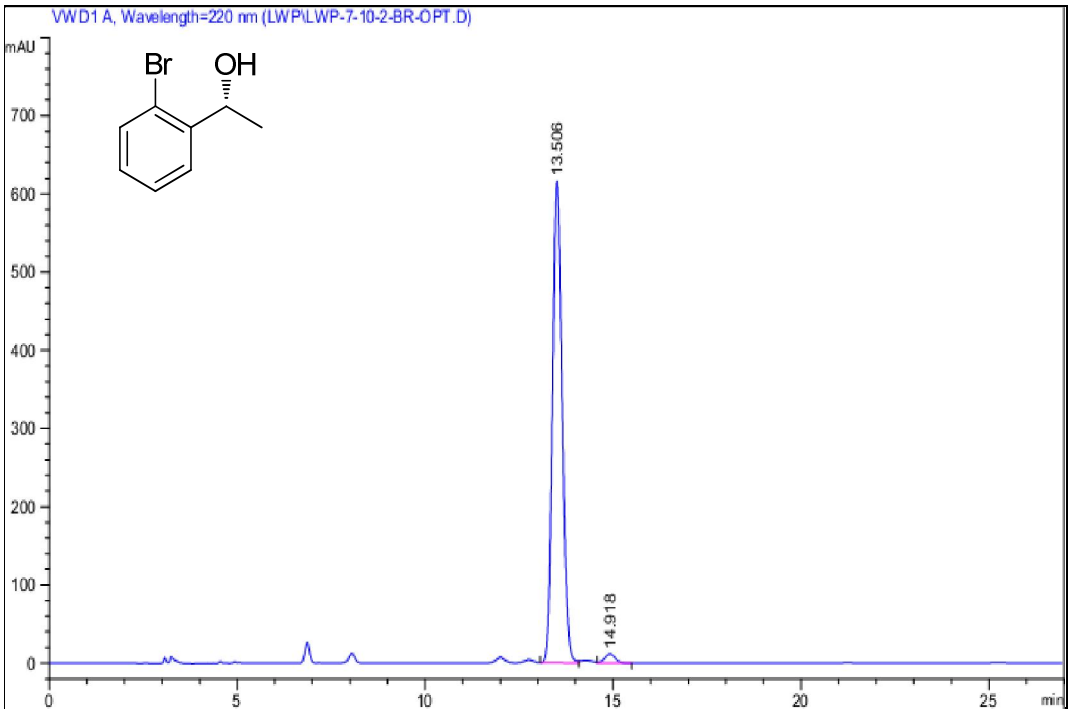




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.246	BBA	0.2820	1.91518e4	1064.10950	98.9372
2	16.297	BBA	0.2712	205.72749	12.04832	1.0628

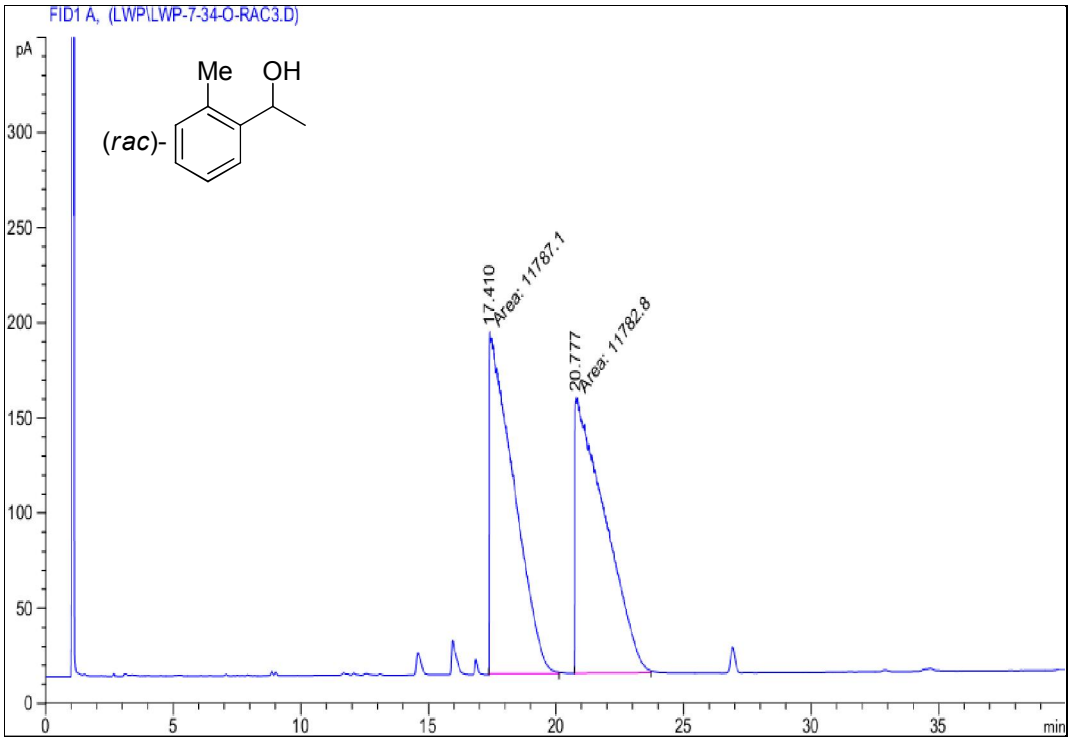
(*R*)-1-(2-Bromophenyl)ethanol ((*R*)-3l)

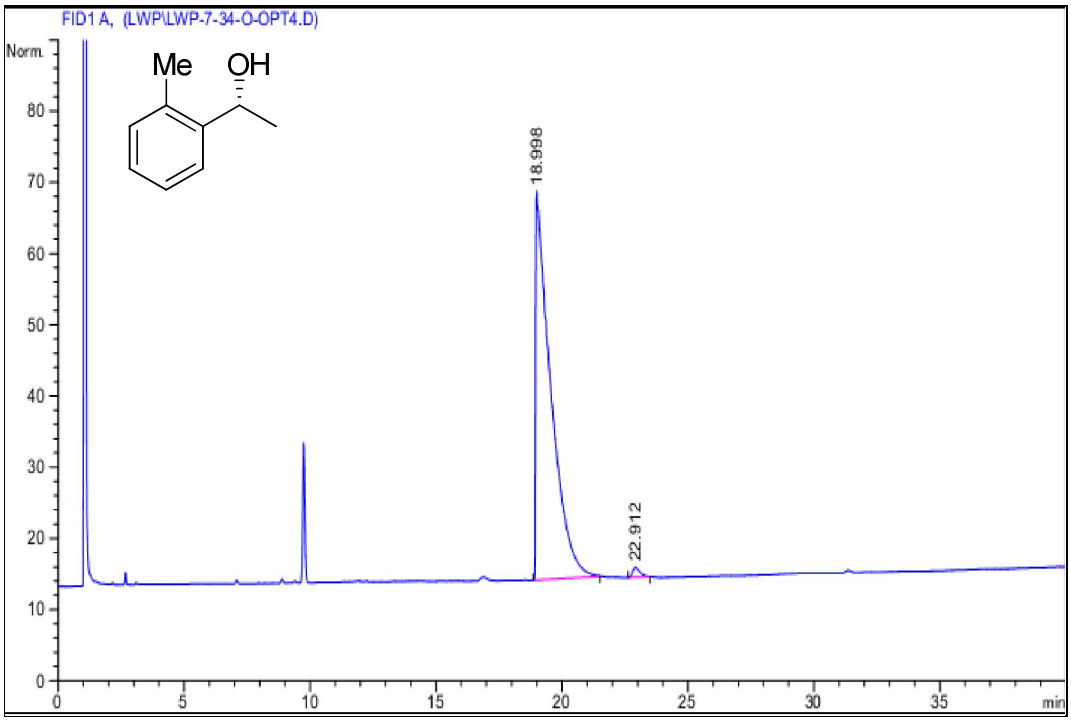




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.506	BV	0.2824	1.11061e4	615.80566	97.9900
2	14.918	VB	0.3060	227.81517	11.60690	2.0100

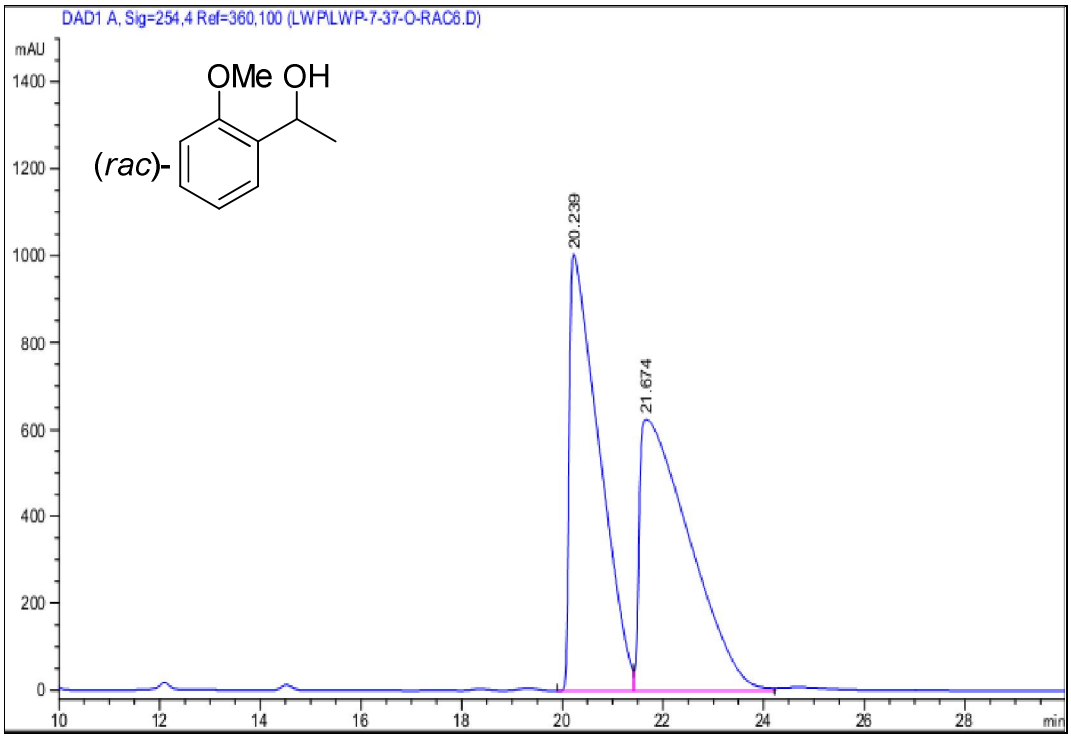
(*R*)-1-(2-Methylphenyl)ethanol ((*R*)-3m)

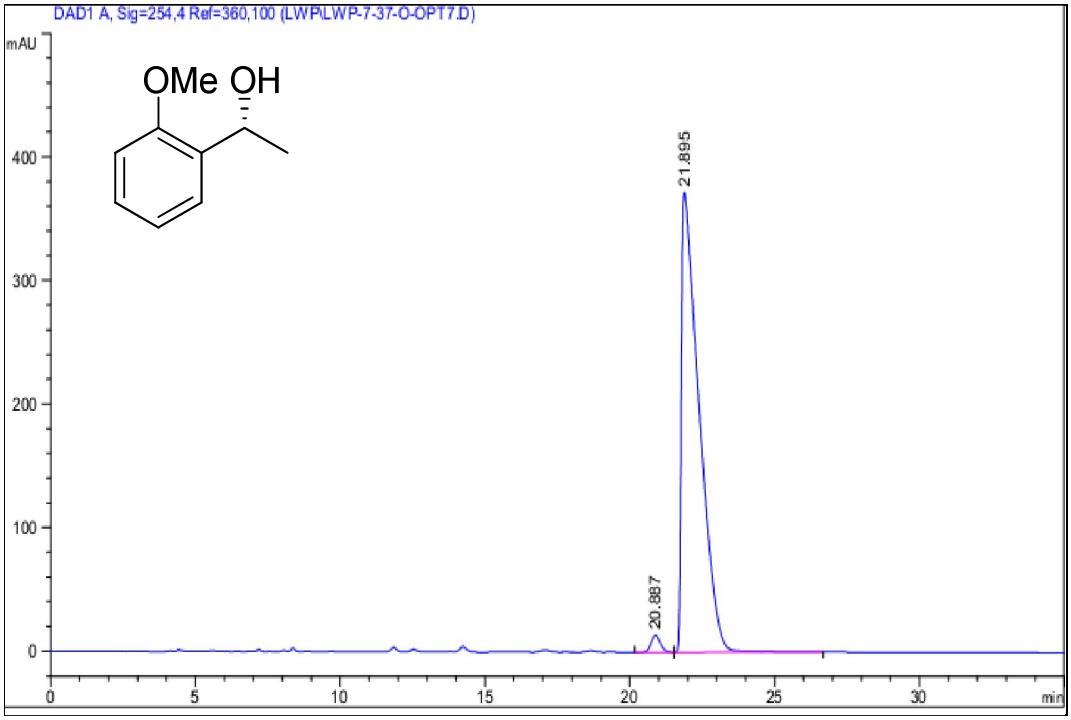




Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	18.998	BB	0.5024	2255.87695	54.55481	98.76598
2	22.912	BB	0.2647	28.18568	1.42521	1.23402

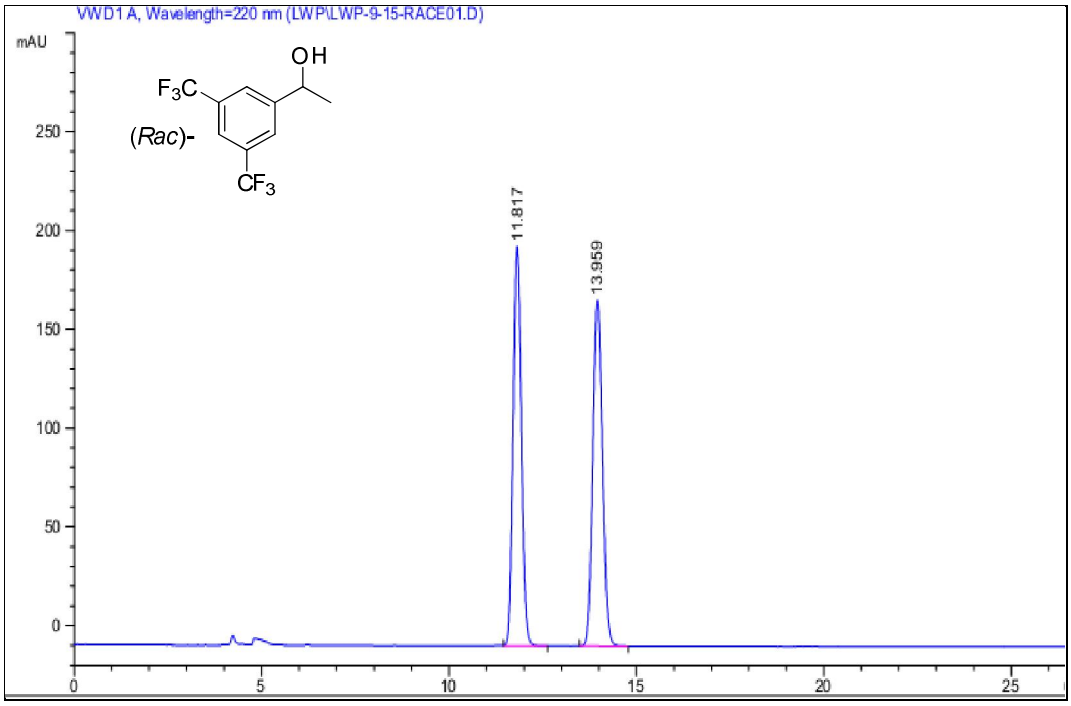
(*R*)-1-(2-Methoxylphenyl)ethanol ((*R*)-3n)

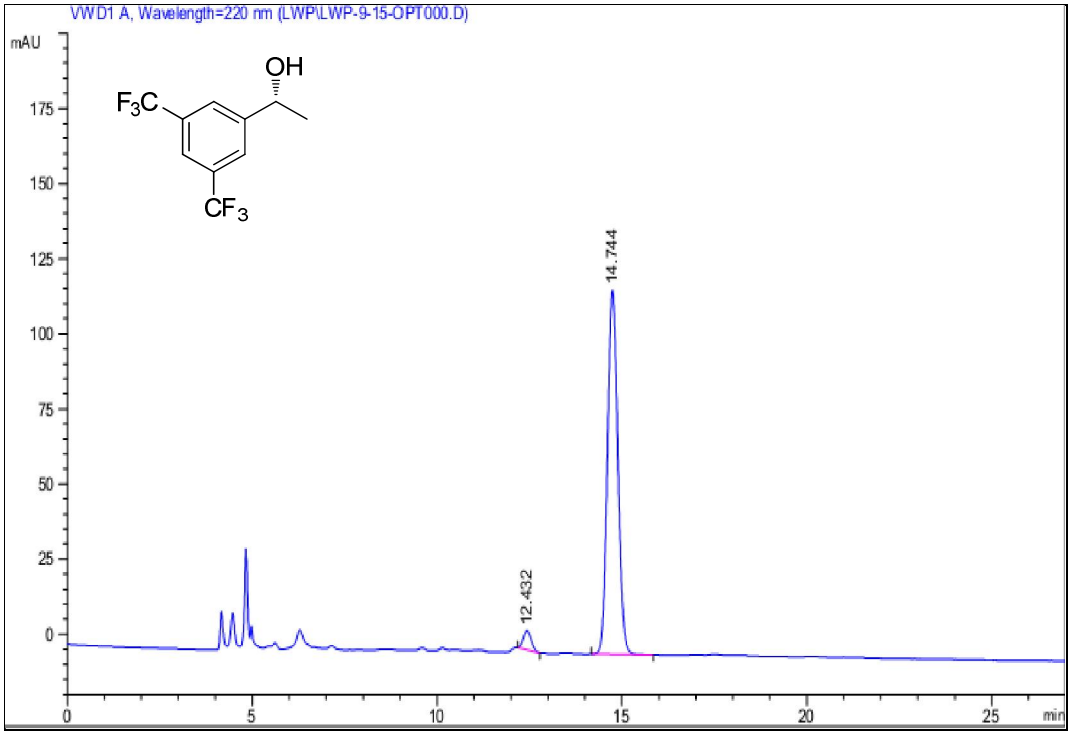




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.887	BV	0.3463	310.80945	13.82665	1.9363
2	21.895	VB	0.6010	1.57412e4	372.52795	98.0637

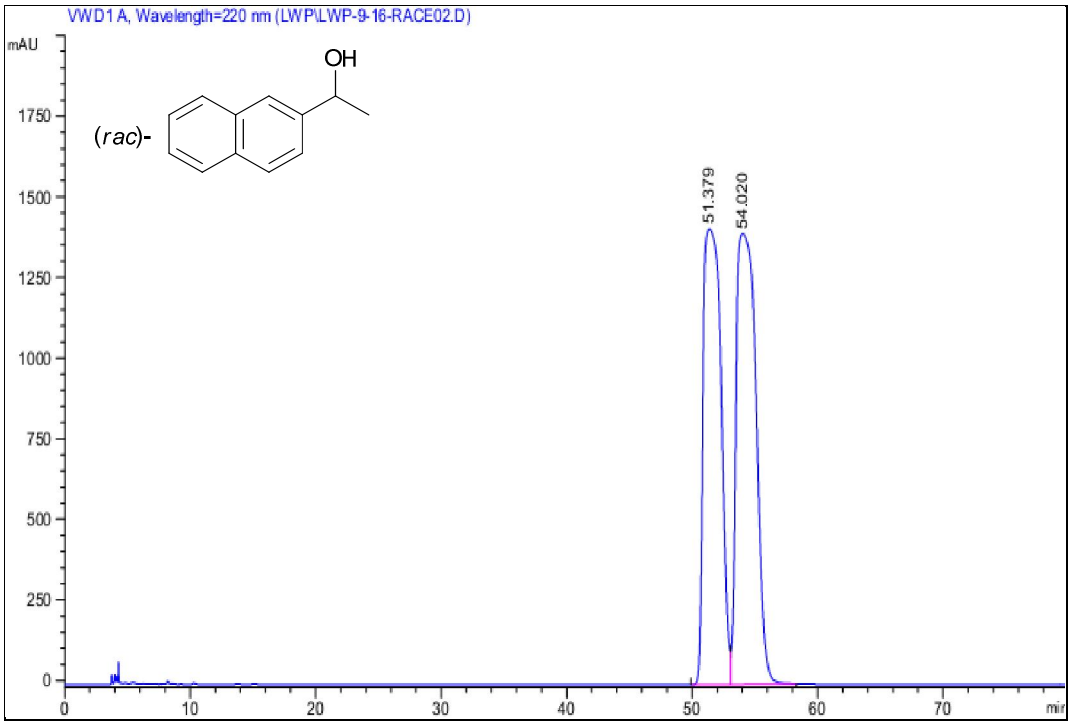
(*R*)-1-(3,5-bis(trifluoromethyl)phenyl)ethanol ((*R*)-3o)

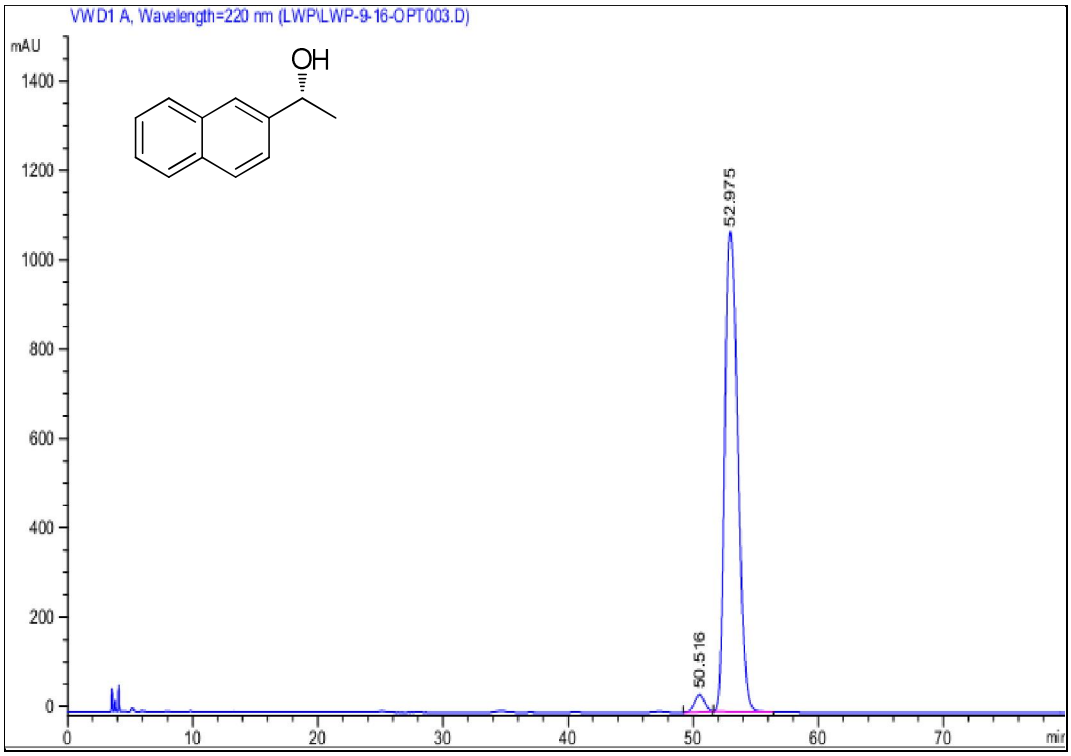




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	12.432	BB	0.2317	91.66946	6.26968	3.7327
2	14.744	BB	0.3049	2364.16284	121.10084	96.2673

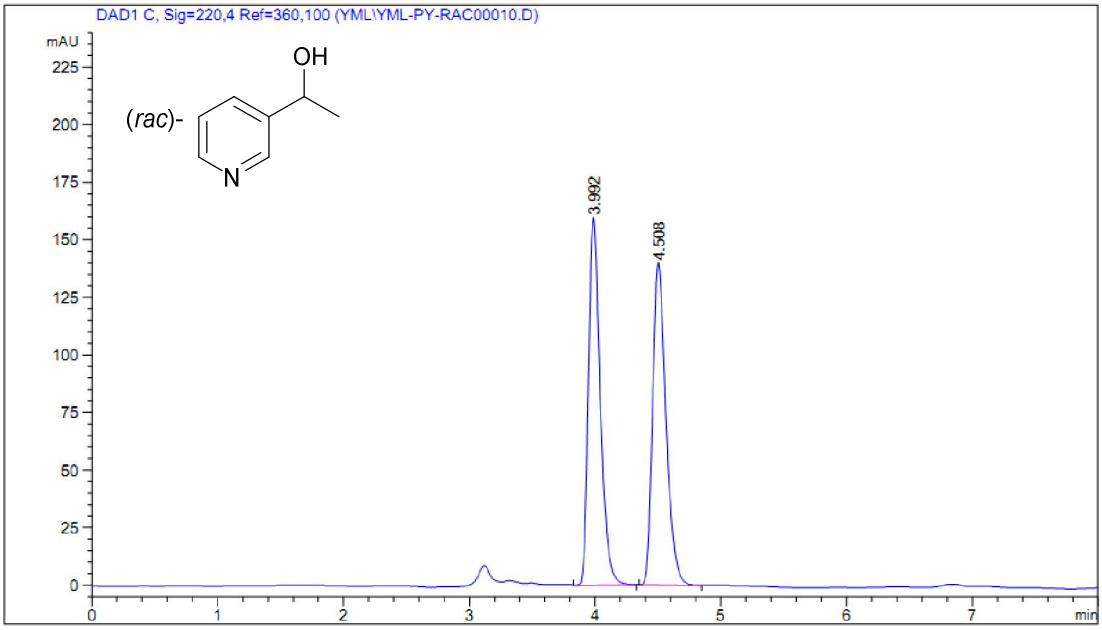
(*R*)-1-(2-Naphtyl)ethanol ((*R*)-3p)

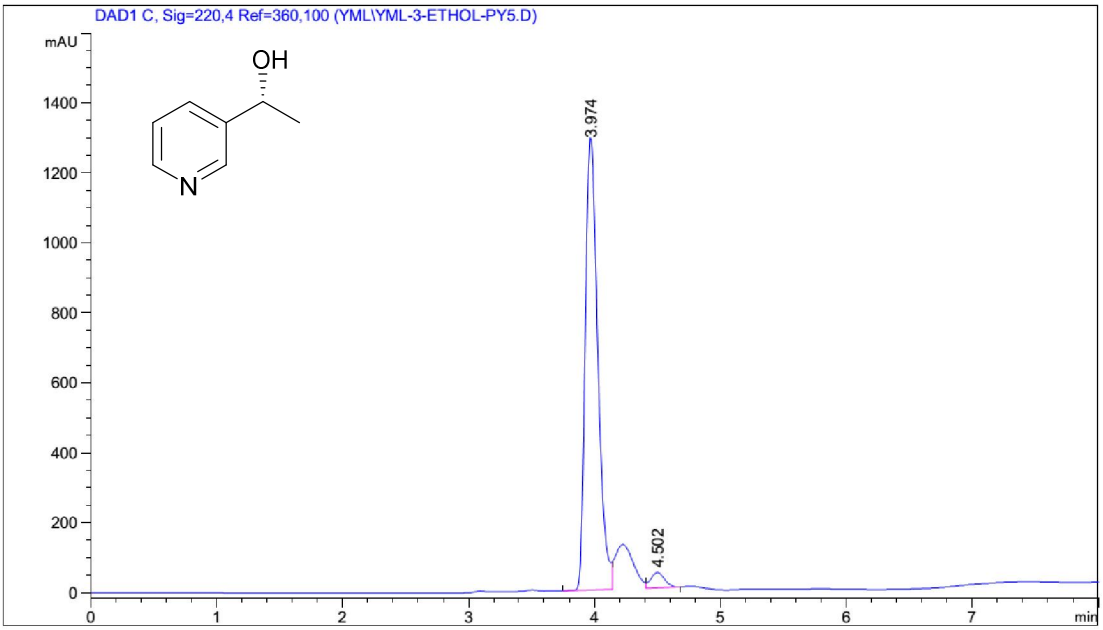




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	50.516	BBA	0.8331	2177.70972	38.84483	2.7315
2	52.975	BB	1.1512	7.75488e4	1073.78894	97.2685

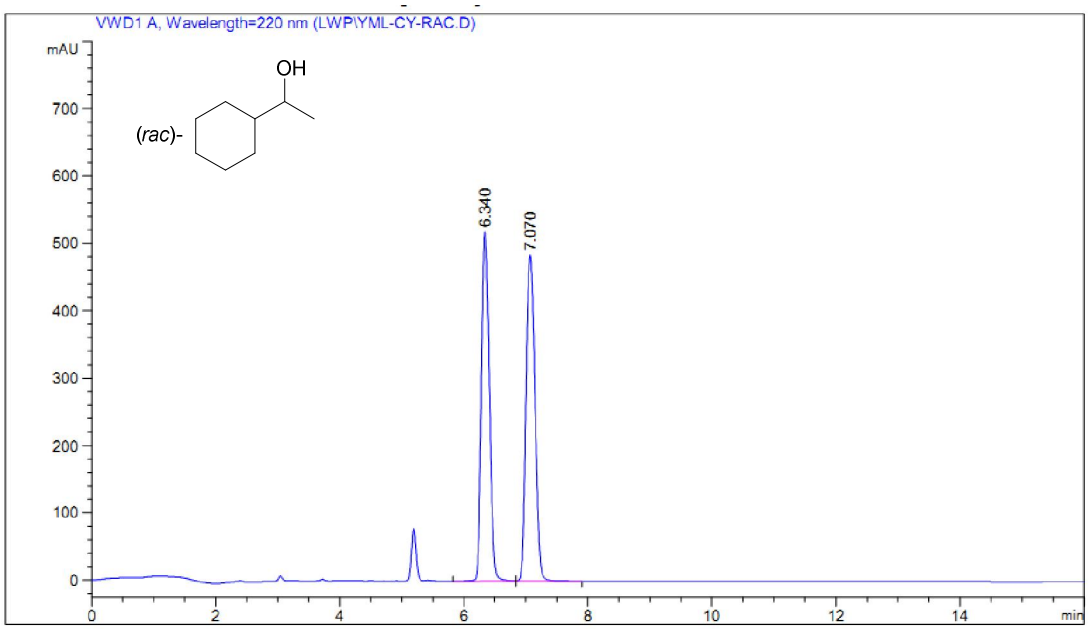
(*R*)-1-(Pyridin-3-yl)ethan-1-ol ((*R*)-3q)

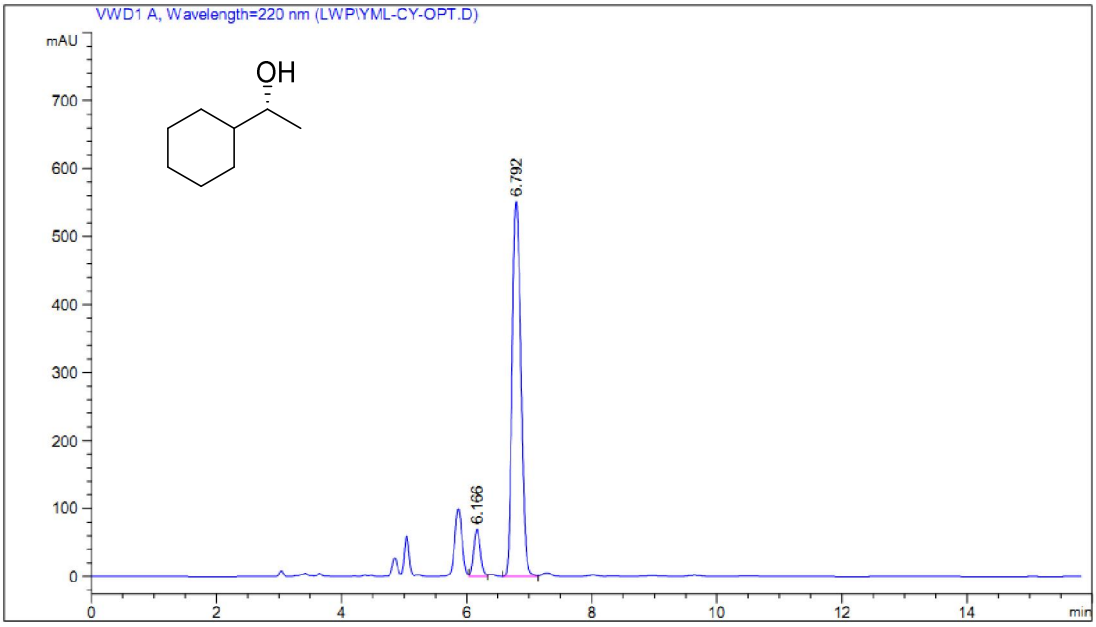




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.974	BV	0.1133	8923.27344	1280.97546	96.3713
2	4.502	VB	0.1214	335.99179	43.85350	3.6287

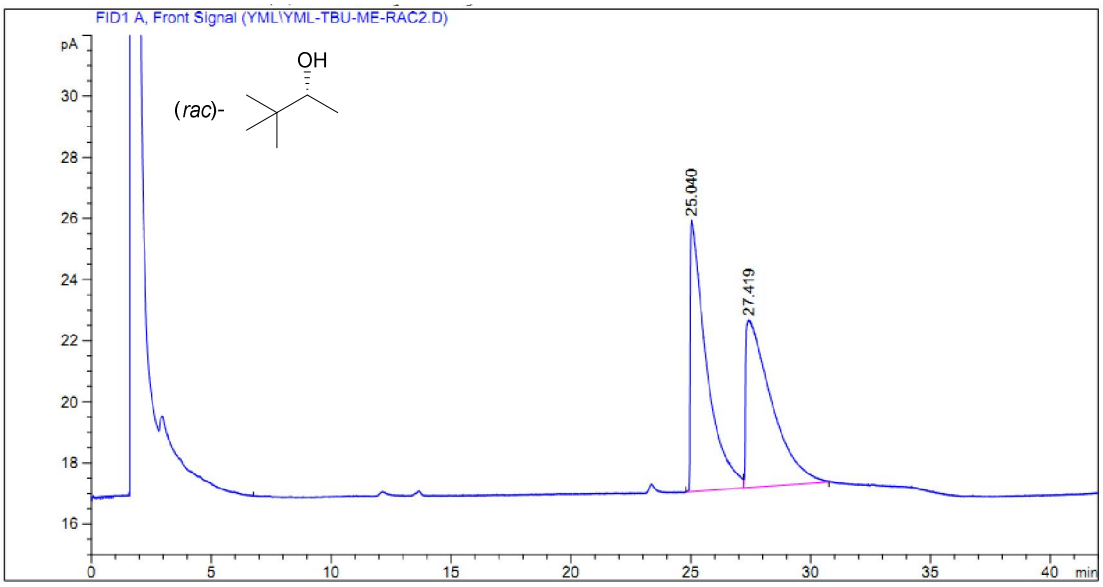
(*R*)-1-Cyclohexylethan-1-ol ((*R*)-3r)

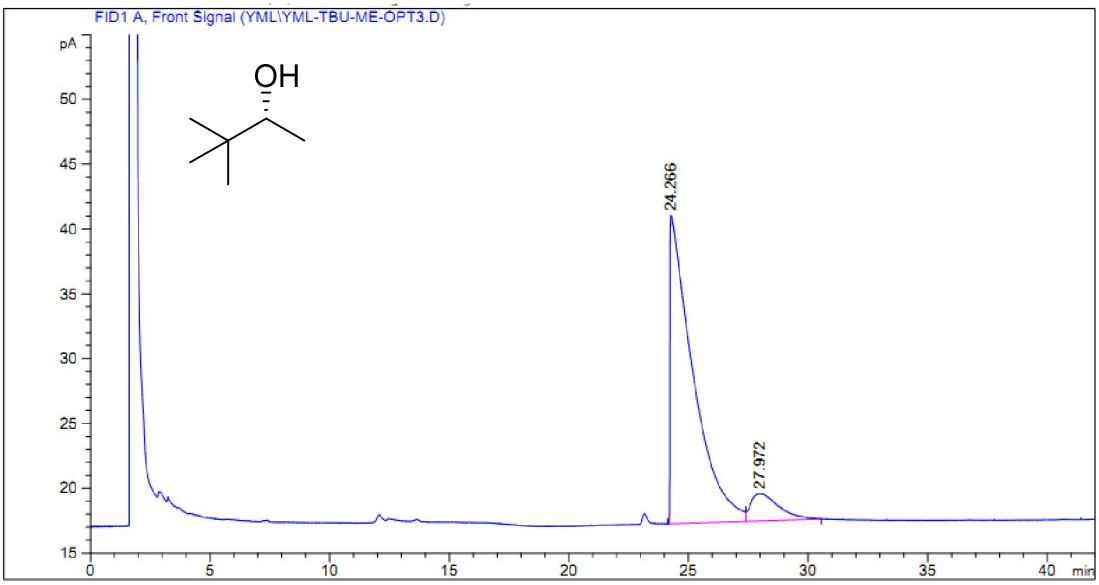




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.166	VV	0.1134	507.50760	69.30202	8.6148
2	6.792	BV	0.1589	5383.60449	551.25592	91.3852

(*R*)-3,3-Dimethylbutan-2-ol ((*R*)-3s)





Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	24.266	BV	0.8084	1581.14014	23.75772	90.12825
2	27.972	VB	0.9659	173.18240	2.12696	9.87175