CHEMISTRY
A EUROPEAN JOURNAL

Supporting Information

The First Enantioselective Addition of Diethylzinc to Aldehydes in Ionic Liquids Catalysed by a Recyclable Ion-Tagged Diphenylprolinol

Marco Lombardo,* Michel Chiarucci and Claudio Trombini

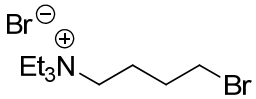
Department of Chemistry "G. Ciamician", University of Bologna, via Selmi 2, 40126, Bologna, Italy

General information

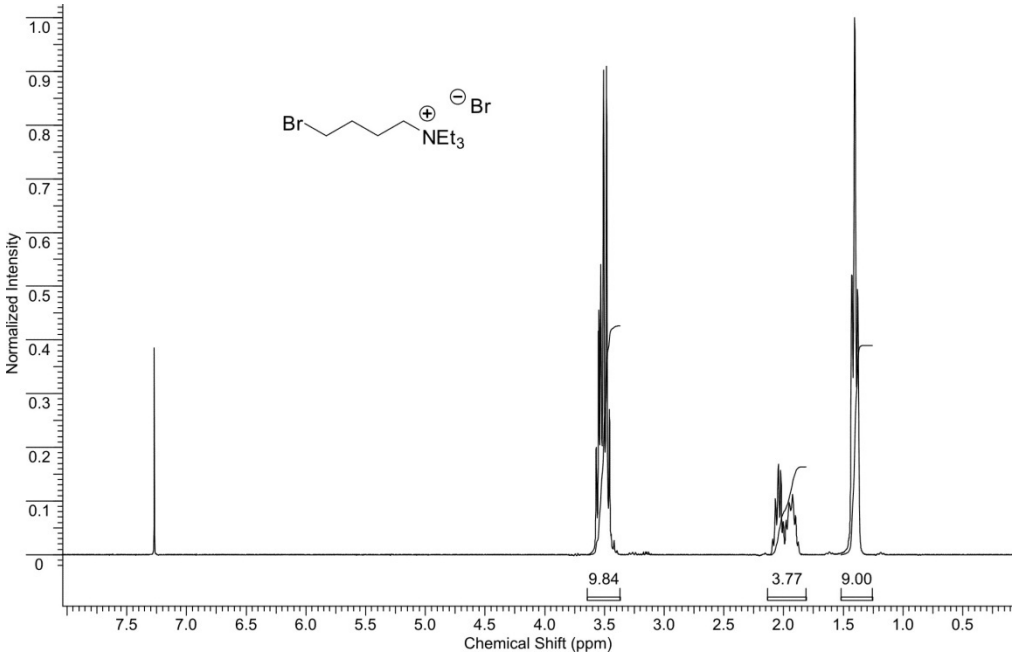
^{1}H and ^{13}C NMR were recorded on a Varian Inova 300 and on a Varian Gemini 200; chemical shifts (δ) are reported in ppm relative to TMS. Gas chromatographic analyses were performed with a Agilent 6850 GC-system coupled to a Agilent 5975 mass selective detector (50 ° C, 2 min → 280 ° C, 10 ° C / min → 280 ° C, 10 min). Chiral GC analyses were performed on a HP 5890 II instrument using a chiral Megadex cyclodextrin column (5.25 m). Chiral HPLC studies were carried out on a Hewlett-Packard series 1090 instrument. Optical rotations were measured with a Perkin-Elmer 343 polarimeter. Reactions were monitored by TLC and GC-MS. Flash-chromatography was carried out using Merck silica gel 60 (230-400 mesh particle size). All reagents were commercially available and were used without further purification, unless otherwise stated.

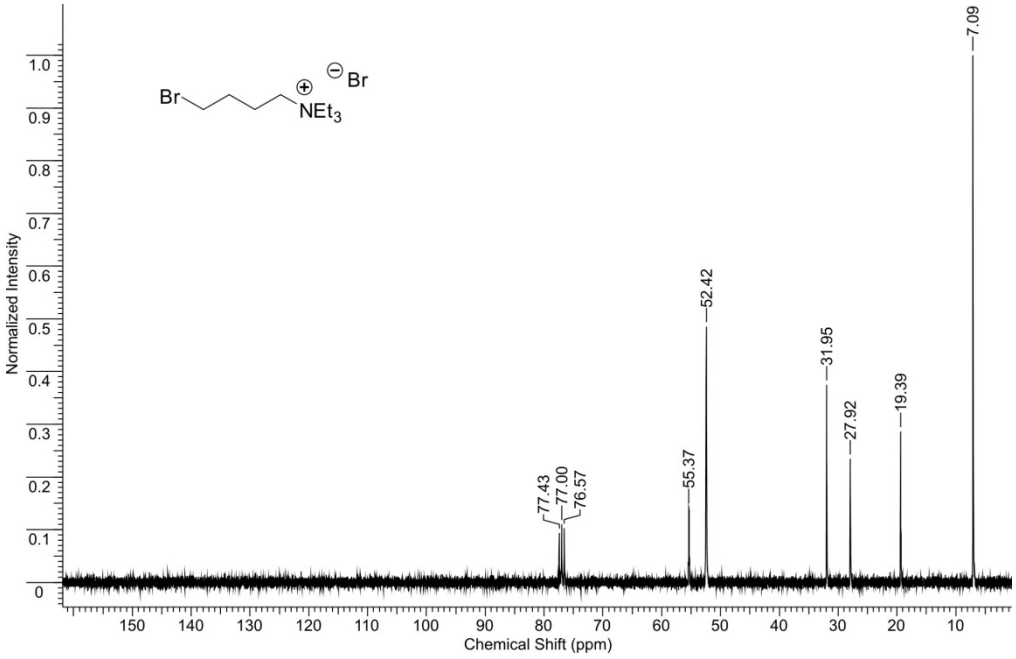
Synthesis of the catalyst

N,N,N,N-(4-Bromo-buthyl)-triethyl-ammonium bromide

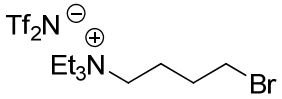


Triethylamine (1.39 mL, 10 mmol) is added to 1,4-dibromoethane (3,58 mL, 30 mmol) and the solution is stirred at 80 °C for 3 h. The resulting suspension is cooled to 0 °C, EtOAc is added and the title product is isolated by filtration as a white solid in 96% yield (3.05 g, 9.26 mmol). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.40 (t, *J* = 7.2 Hz, 9 H), 1.86-1.99 (m, 2 H), 1.99-2.11 (m, 2 H), 3.43-3.60 (m, 10 H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 7.1, 19.4, 27.9, 32.0, 52.4, 55.4. Anal. Calcd for $C_{10}H_{23}Br_2N$ (317.10): C, 37.88; H, 7.31; N, 4.42. Found: C, 37.76; H, 7.33; N, 4.41.

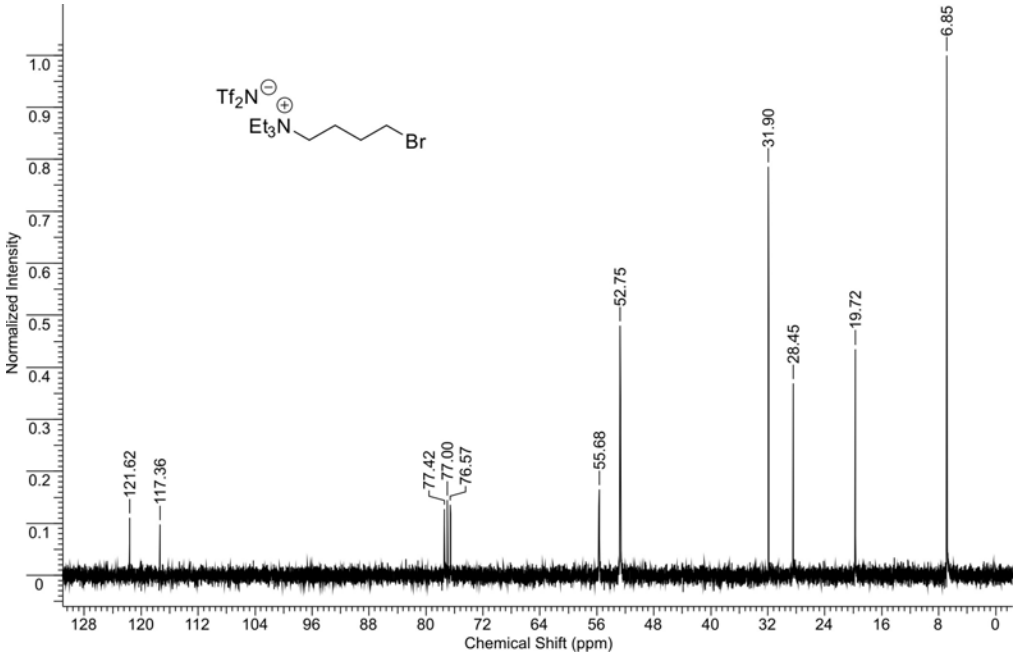




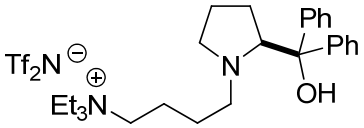
***N*,*N*,*N*,*N*-(4-Bromo-buthyl)-triethyl-ammonium bis(trifluoromethylsulfonyl)imide**



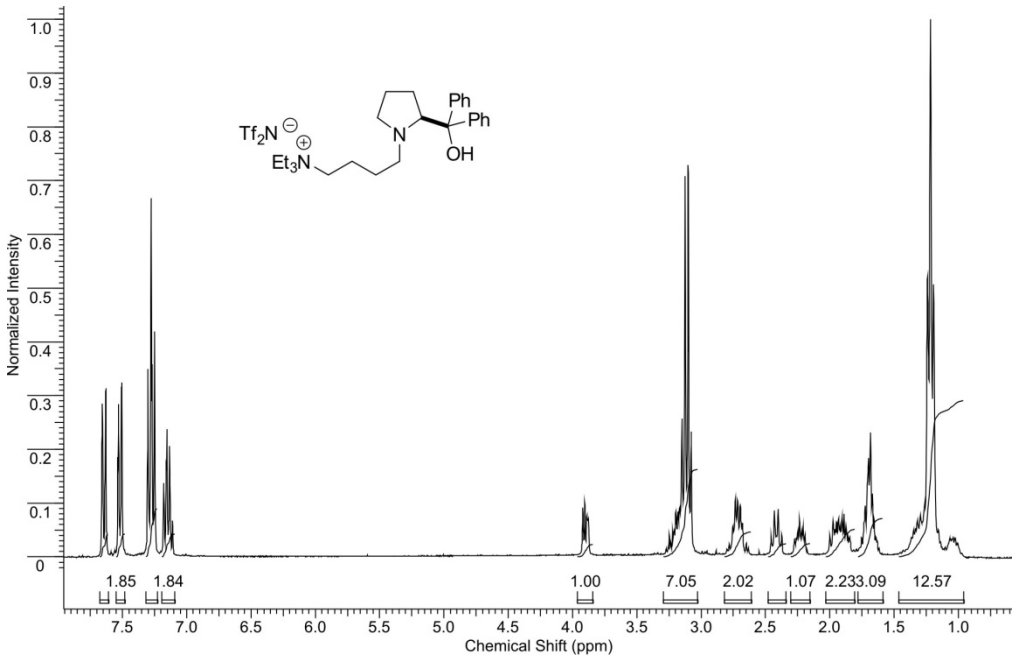
Lithium bis(trifluoromethylsulfonyl)imide (0.6 g, 2.1 mmol) is added at rt to a solution of *N*,*N*,*N*,*N*-(4-bromo-buthyl)-triethyl-ammonium bromide (0.63 g, 2 mmol) in water (1 mL) and the solution is stirred for at rt for 12 h. The title product is extracted with CH_2Cl_2 (2 × 5 mL) and the combined organic phases are washed with water until a negative $AgNO_3$ test was obtained. The organic phase is dried (Na_2SO_4) and evaporated at reduced pressure to give 0.96 g (1.86 mmol, 93%) of the title compound as a clear dense oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.36 (t, *J* = 7.3 Hz, 9 H), 1.79 - 1.93 (m, 2 H), 1.93 - 2.05 (m, 2 H), 3.16 - 3.25 (m, 2 H), 3.31 (q, *J* = 7.5 Hz, 6 H), 3.50 (t, 2 H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 6.9, 19.7, 28.4, 31.9, 52.7, 55.7, 117.4, 121.6; Anal. Calcd for $C_{12}H_{23}BrF_6N_2O_4S_2$ (517.35): C, 27.86; H, 4.48; N, 5.41. Found: C, 27.95; H, 4.49; N, 5.40.

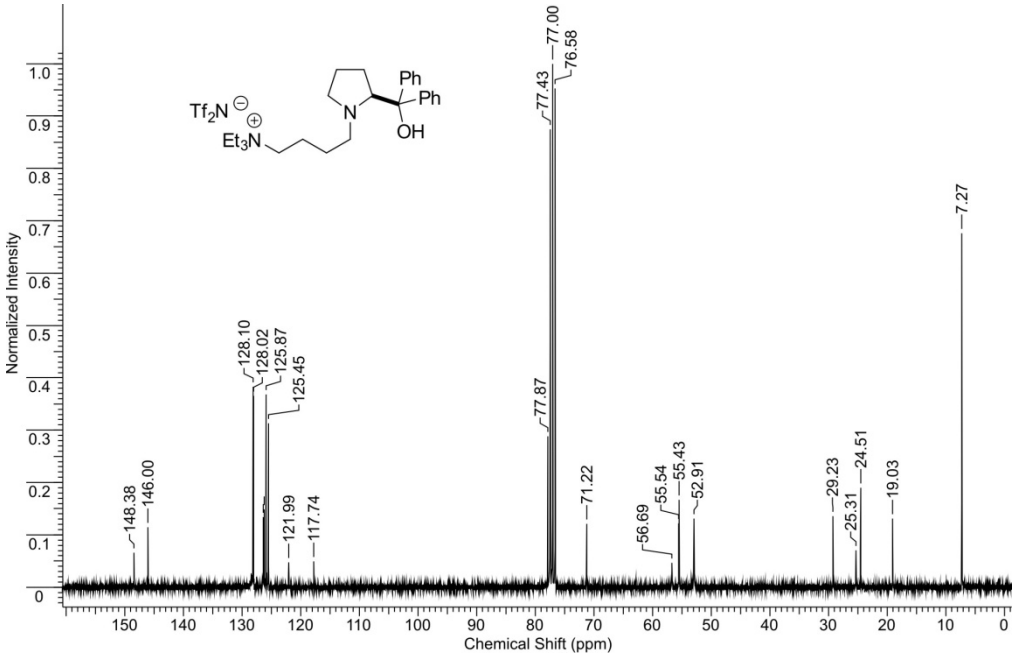


Ligand 1b



N,*N*,*N*,*N*-(4-bromo-buthyl)-triethyl-ammonium bis(trifluoromethylsulfonyl)imide (0.78 g, 1.5 mmol) is added a solution of diphenylprolinol (0.4 g, 1.58 mmol) and NaI (0.224 g, 1.5 mmol) in CH_3CN and the solution is stirred at 80 °C for 24 h. After cooling to rt the organic solvent is evaporated at reduced pressure, CH_2Cl_2 is added (5 mL) and the organic layer is washed with NaOH water solution (1 mL, 2 M). The organic phase is dried (Na_2SO_4) and evaporated at reduced pressure to afford a dense oil that is further purified by flash-chromatography on silica eluting with CH_2Cl_2/MeOH 95:5. The title product is obtained as a clear dense oil in 98% yield (1.01 g, 1.47 mmol). $[\alpha]^{D}_{20}$ (c = 4.7, $CHCl_3$) = +8.9; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.96 - 1.12 (m, 1 H), 1.22 (t, *J* = 7.1 Hz, 9 H), 1.26 - 1.46 (m, 3 H), 1.60 - 1.77 (m, 3 H), 1.93 (ddd, *J* = 16.8, 8.6, 4.6 Hz, 1 H), 2.23 (ddd, *J* = 12.2, 7.8, 4.4 Hz, 1 H), 2.36 - 2.47 (m, 2 H), 2.62 - 2.81 (m, 2 H), 3.11 (q, *J* = 7.2 Hz, 6 H), 3.16 - 3.29 (m, 1 H), 3.90 (dd, *J* = 9.0, 4.2 Hz, 1 H), 7.10 - 7.19 (m, 2 H), 7.28 (t, *J* = 7.7 Hz, 3 H), 7.52 (dd, *J* = 8.3, 1.2 Hz, 2 H), 7.64 (dd, *J* = 8.3, 1.2 Hz, 2 H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 7.3, 19.0, 24.5, 25.3, 29.2, 52.9, 55.4, 55.5, 56.7, 71.2, 77.9, 117.7, 122.0, 125.5, 125.9, 126.2, 126.4, 128.0, 128.1, 146.0, 148.4; Anal. Calcd for $C_{29}H_{41}F_6N_3O_5S_2$ (689.77): C, 50.50; H, 5.99; N, 6.09. Found: C, 50.56; H, 6.01; N, 6.10.

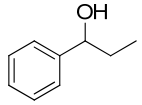




HPLC and GC Data

Racemic samples of alkylation products were prepared by addition of EtMgBr to the corresponding aldehyde.

Table 1. HPLC data

Product	Column	*n*-Hexane / *i*-PrOH	Flow rate [mL/min]	t_R [min]
	OD	99:1	0.8	28.4 (*R*), 31.2 (*S*)

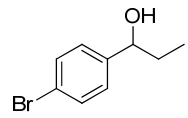
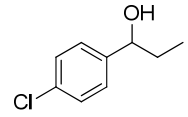
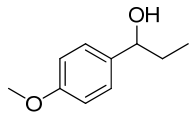
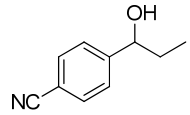
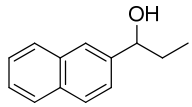
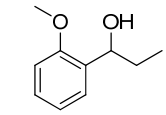
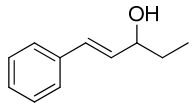
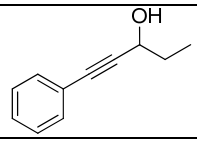
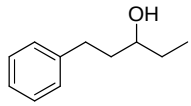
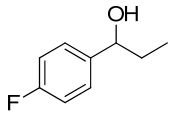
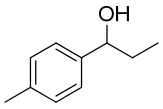
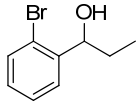
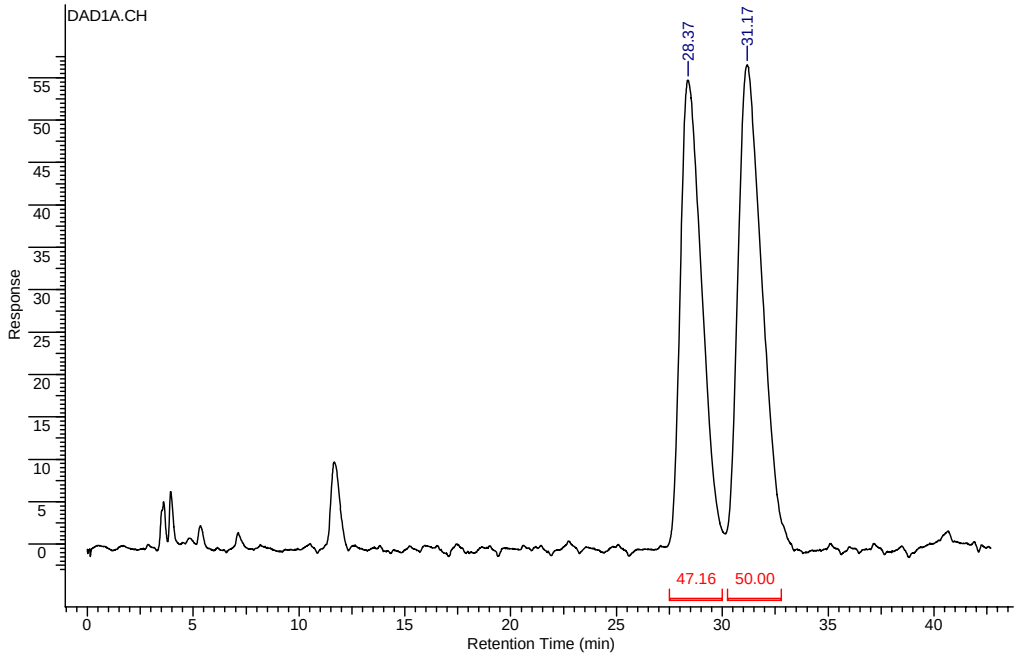
	OJ	97:3	0.8	17.9 (*S*), 19.4 (*R*)
	OD	99:1	0.8	25.2 (*S*), 27.6 (*R*)
	OD	99:1	1.0	35.5 (*R*), 42.4 (*S*)
	AD	97:3	0.8	31.6 (*R*), 34.2 (*S*)
	OD	95:5	1.0	15.2 (*S*), 17.0 (*R*)
	OD	98:2	1.0	16.9 (*S*), 18.8 (*R*)
	OD	95:5	1.0	11.9 (*R*), 19.6 (*S*)
	OJ	90:10	1.0	7.9 (*R*), 9.2 (S)
	OD	90:10	1.0	6.1 (*R*), 7.7 (S)

Table 2. GC data

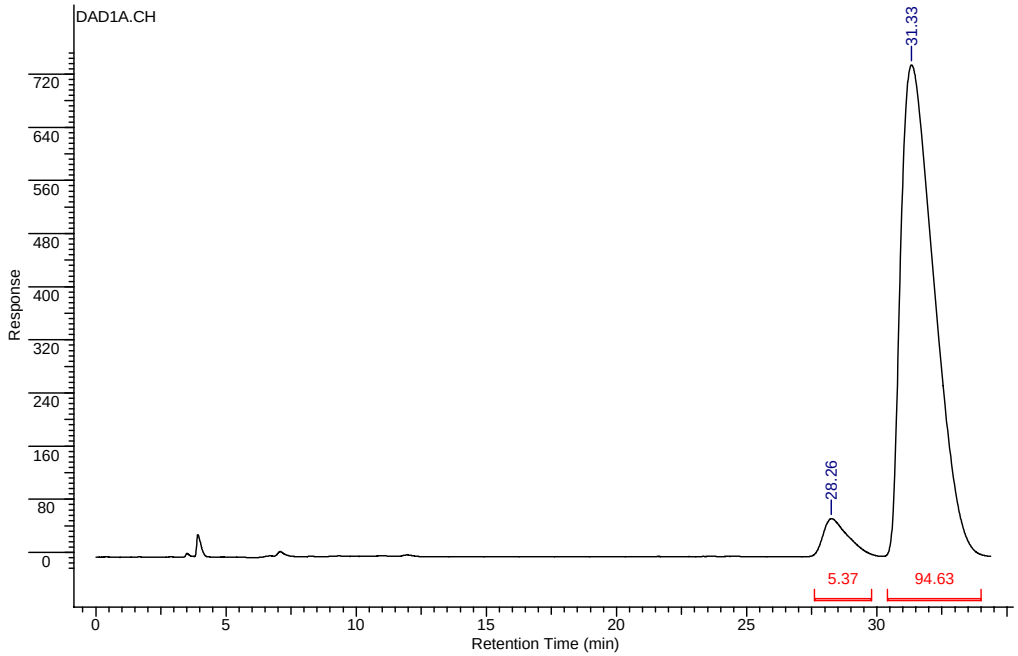
Product	**Column**	**T [°C]**	**Flow rate [mL/min]**	**t_R [min]**
	Megadex-5	110	3.13	15.1 (*R*), 17.8 (*S*)
	Megadex-5	120	3.13	11.2 (*R*), 13.0 (*S*)
	Megadex-5	130	3.13	22.5 (*R*), 25.2 (*S*)

1-Phenylpropan-1-ol (Table 2, Entry 1)

Racemic mixture

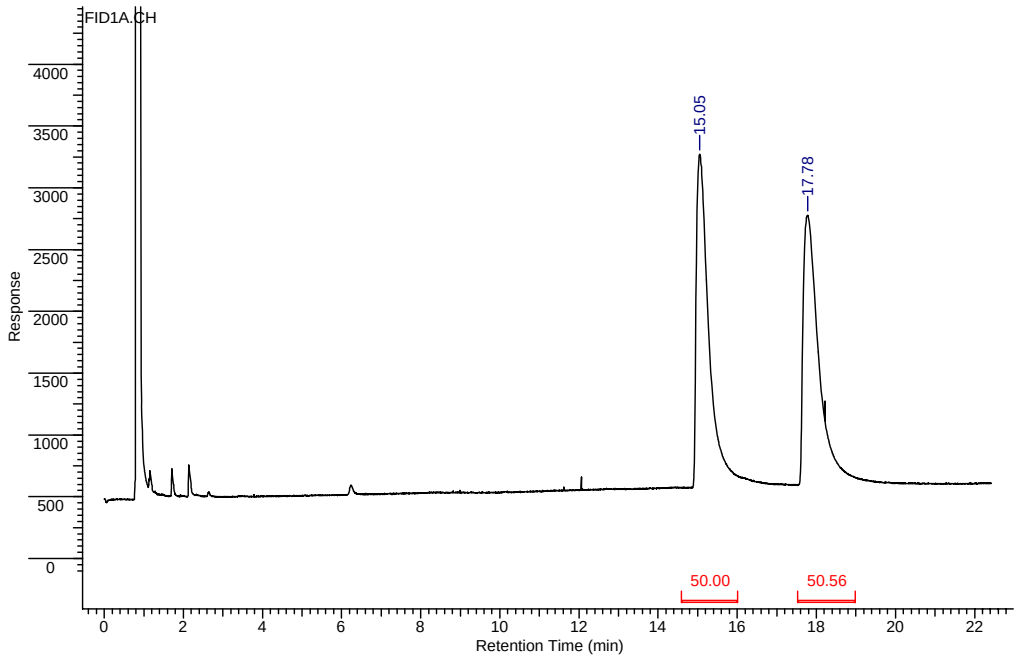


Crude reaction mixture

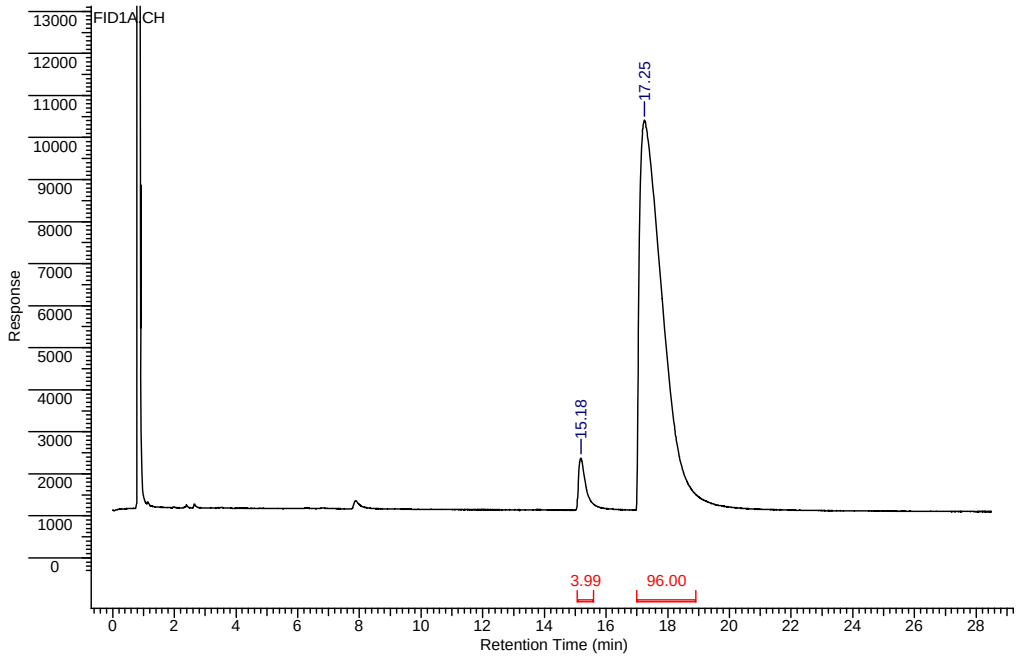


1-(4-Fluorophenyl)propan-1-ol (Table 3, Entry 1)

Racemic mixture

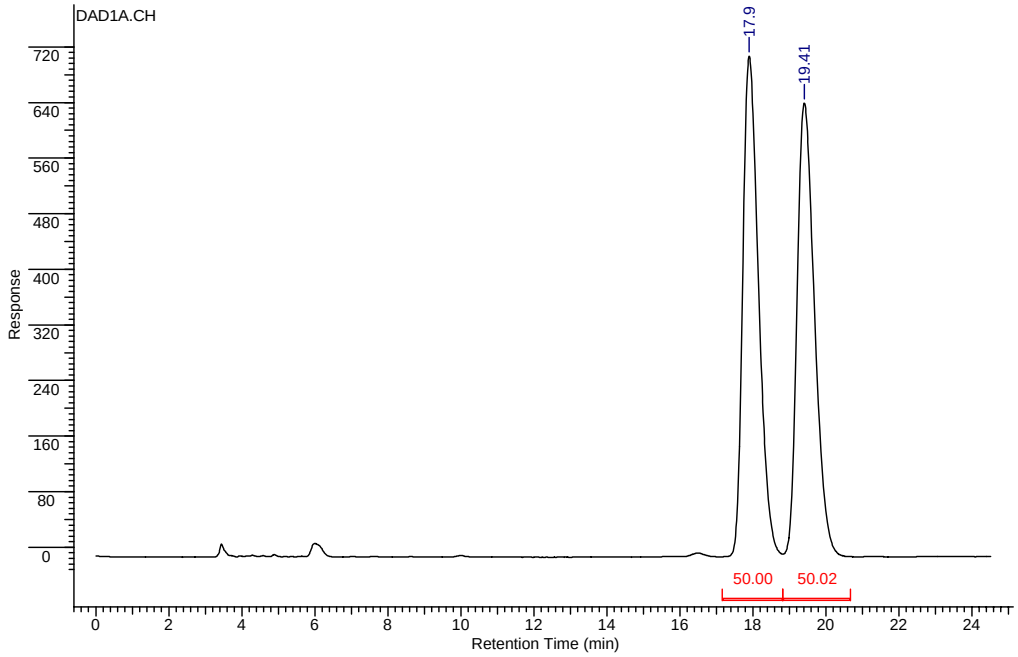


Crude reaction mixture

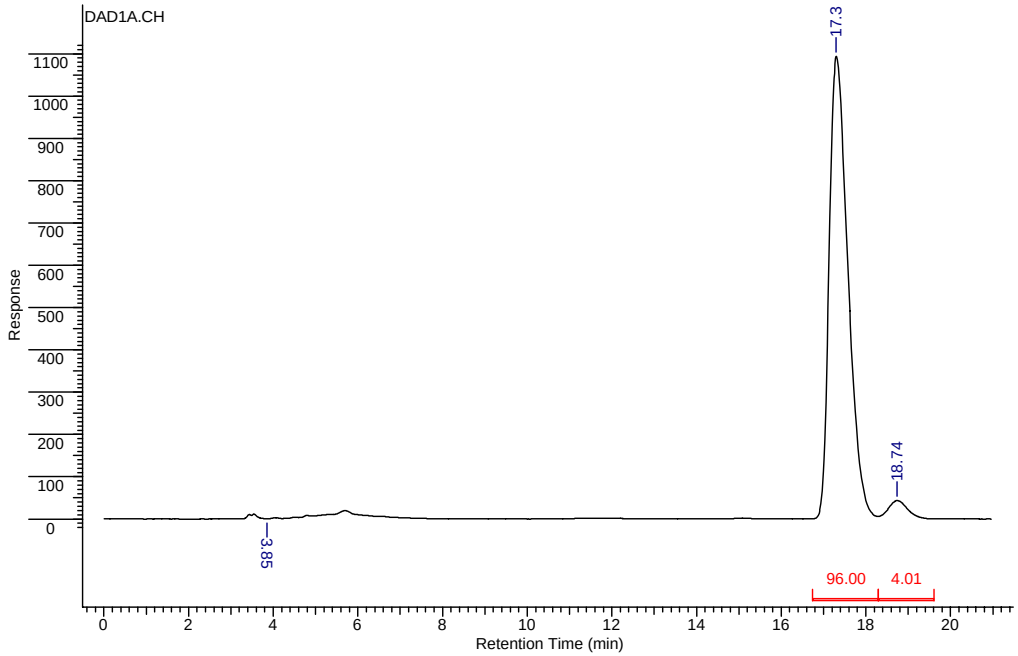


1-(4-Bromophenyl)propan-1-ol (Table 3, Entry 2)

Racemic mixture

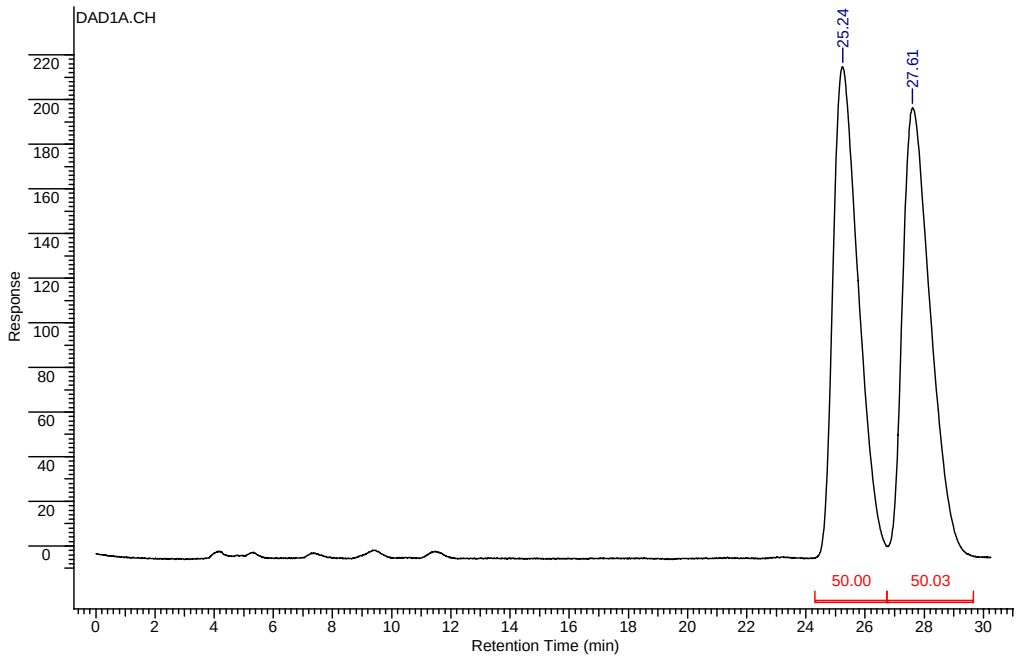


Crude reaction mixture

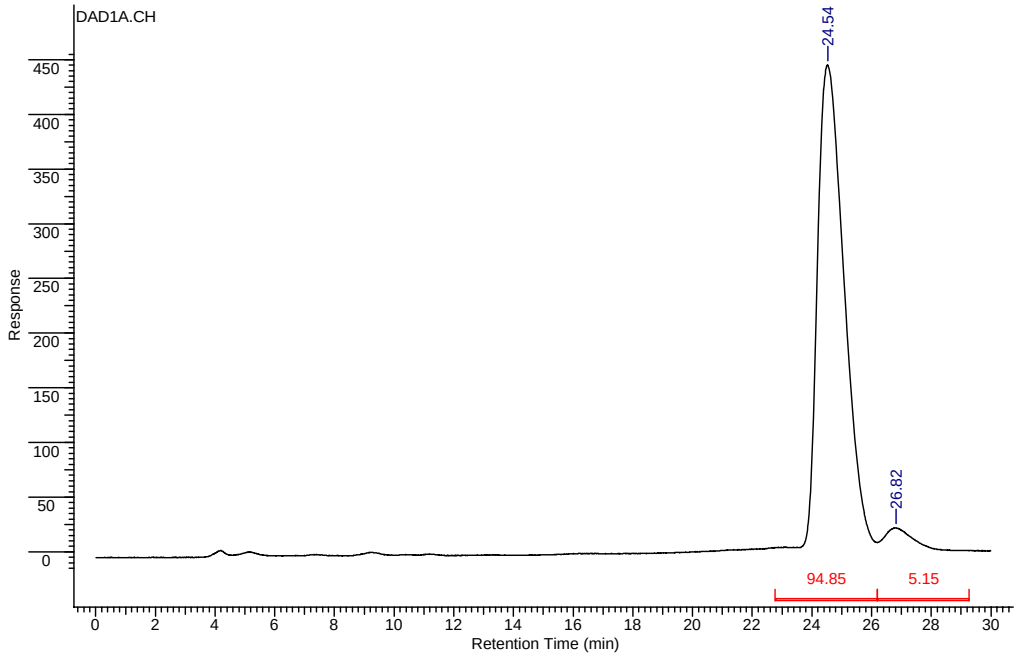


1-(4-Chlorophenyl)propan-1-ol (Table 3, Entry 3)

Racemic mixture

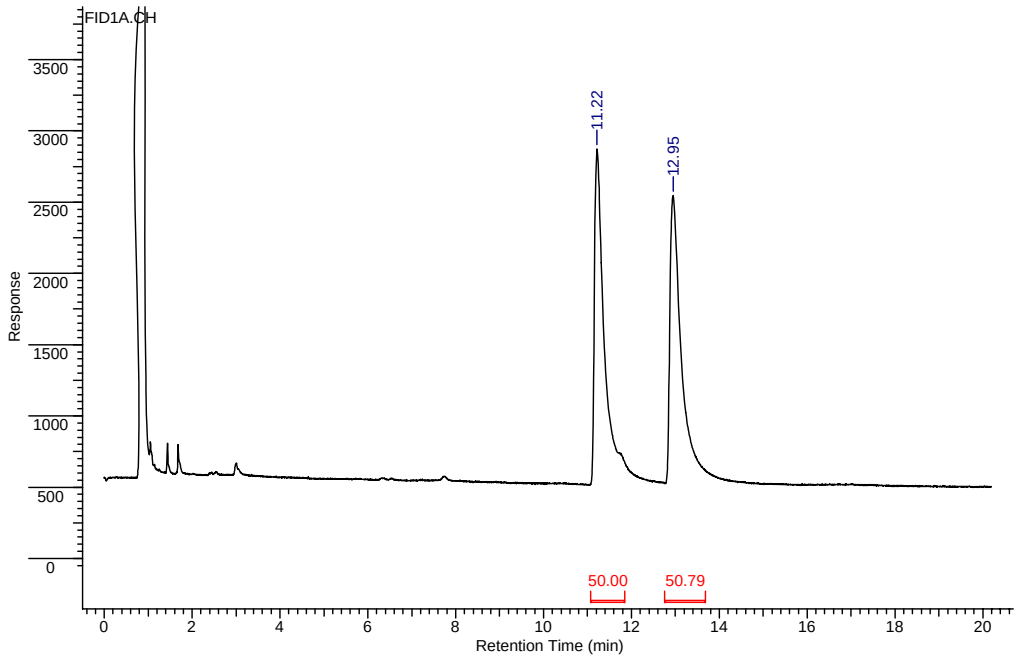


Crude reaction mixture

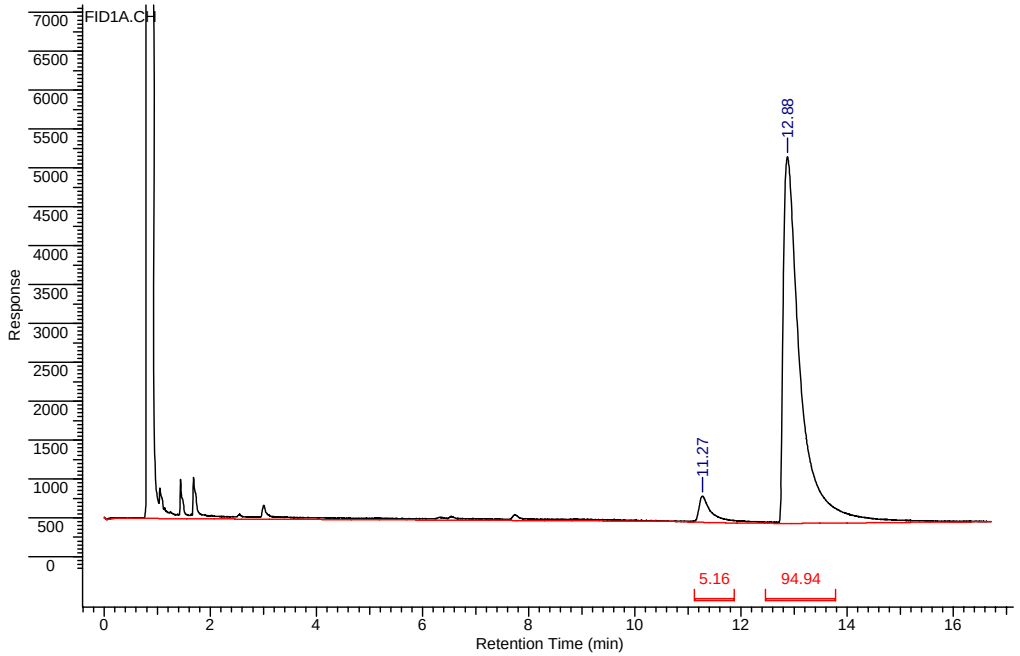


1-*p*-Tolylpropan-1-ol (Table 3, Entry 4)

Racemic mixture

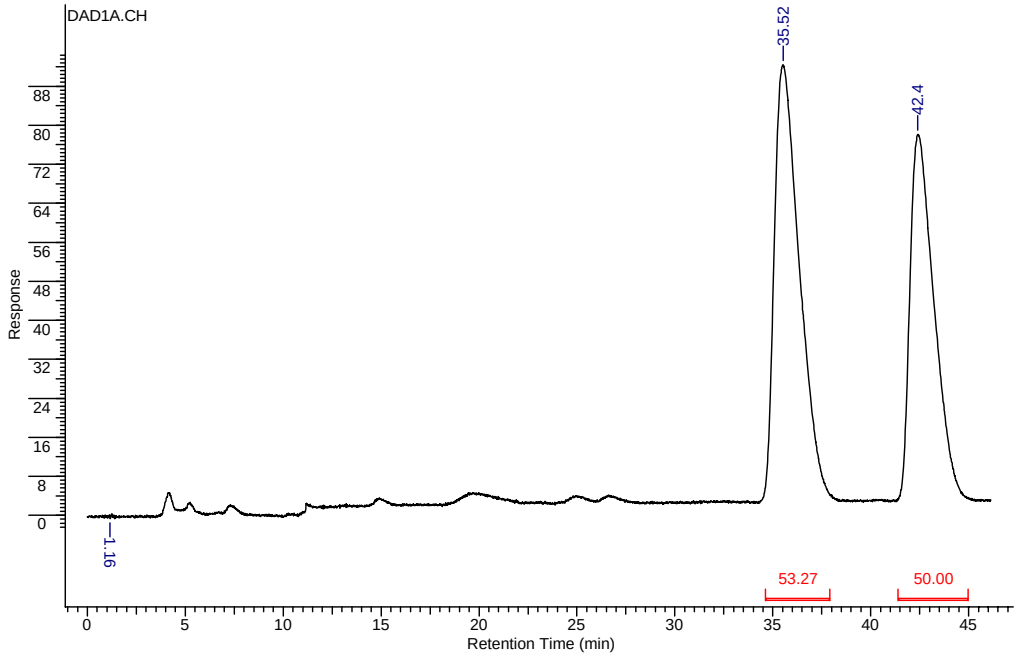


Crude reaction mixture

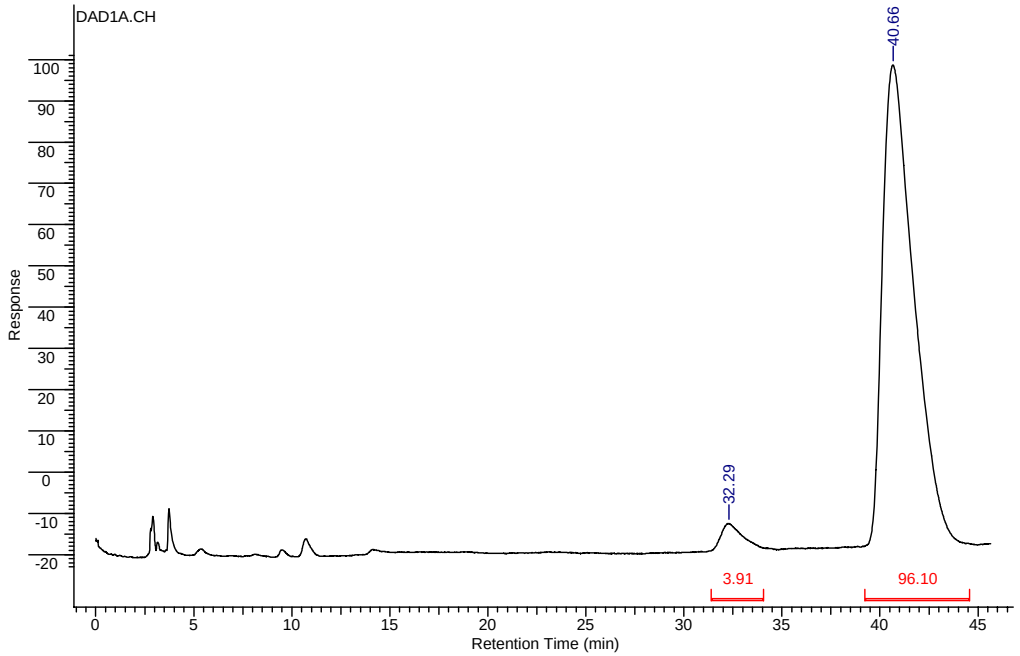


1-(4-Methoxyphenyl)propan-1-ol (Table 3, Entry 5)

Racemic mixture

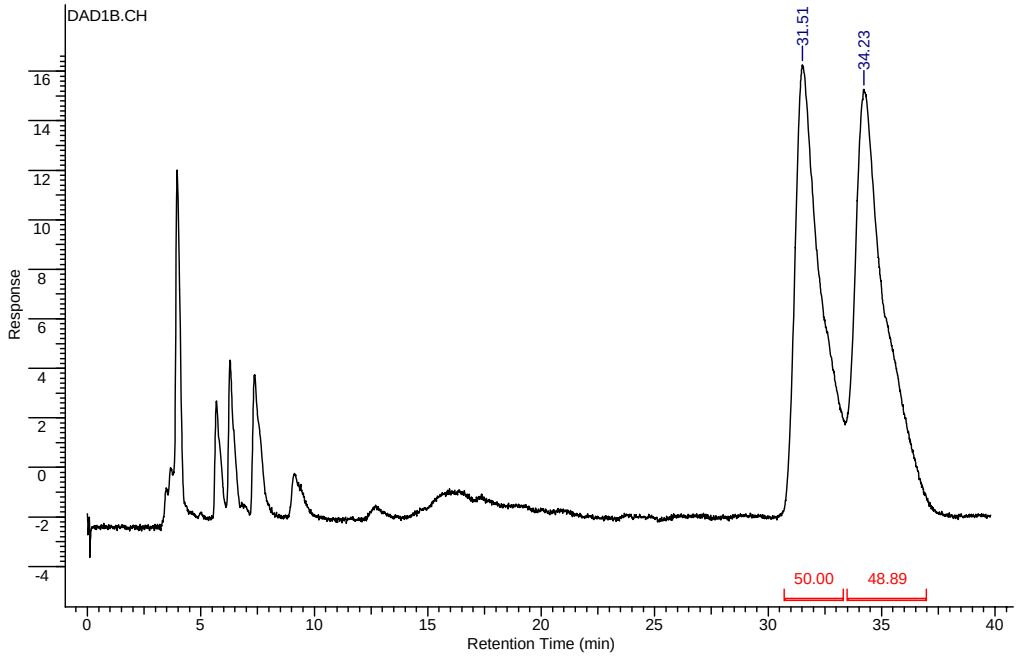


Crude reaction mixture

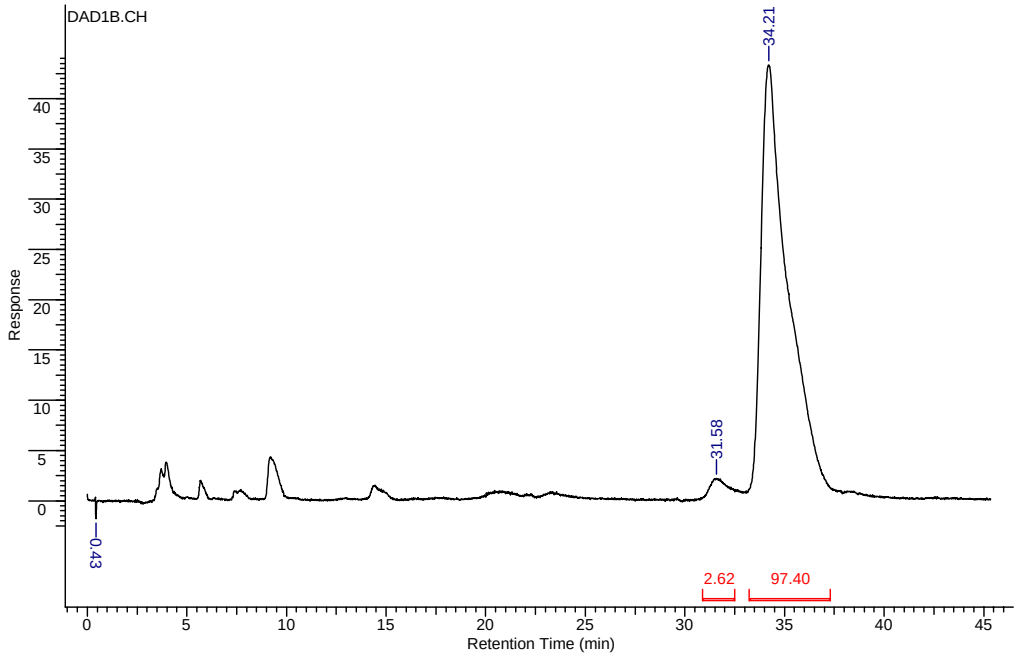


1-(4-Cyanophenyl)propan-1-ol (Table 3, Entry 6)

Racemic mixture

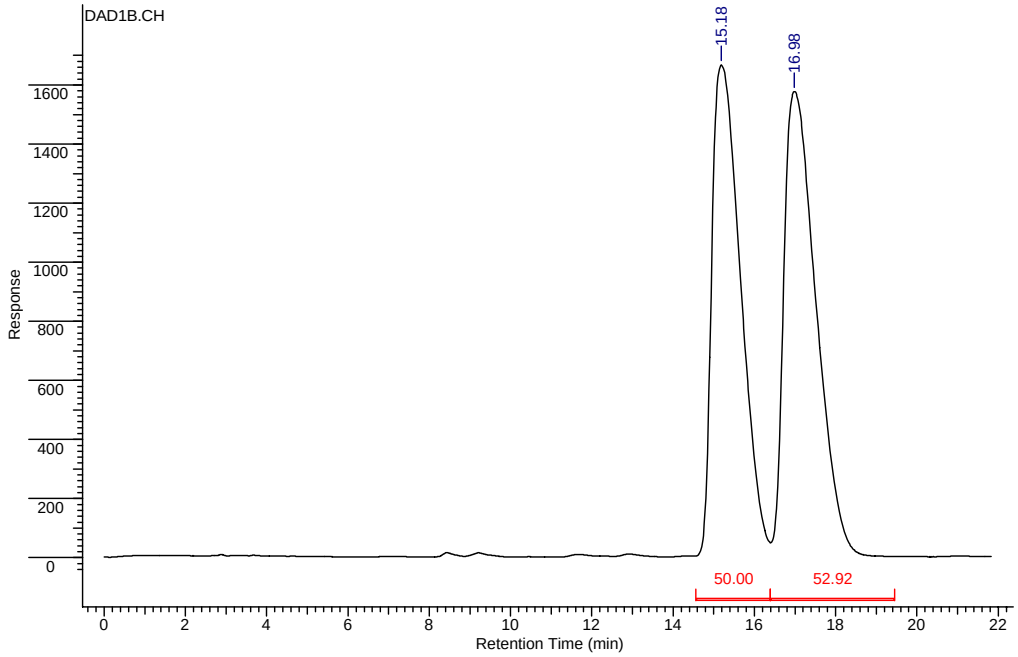


Crude reaction mixture

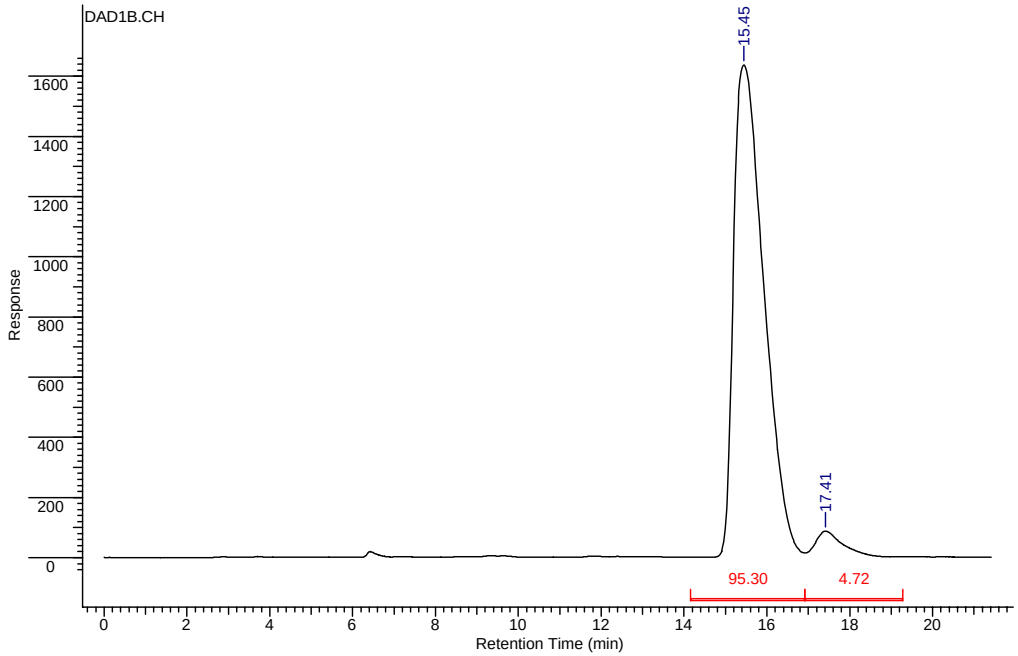


1-(Naphthalen-2-yl)propan-1-ol (Table 3, Entry 7)

Racemic mixture

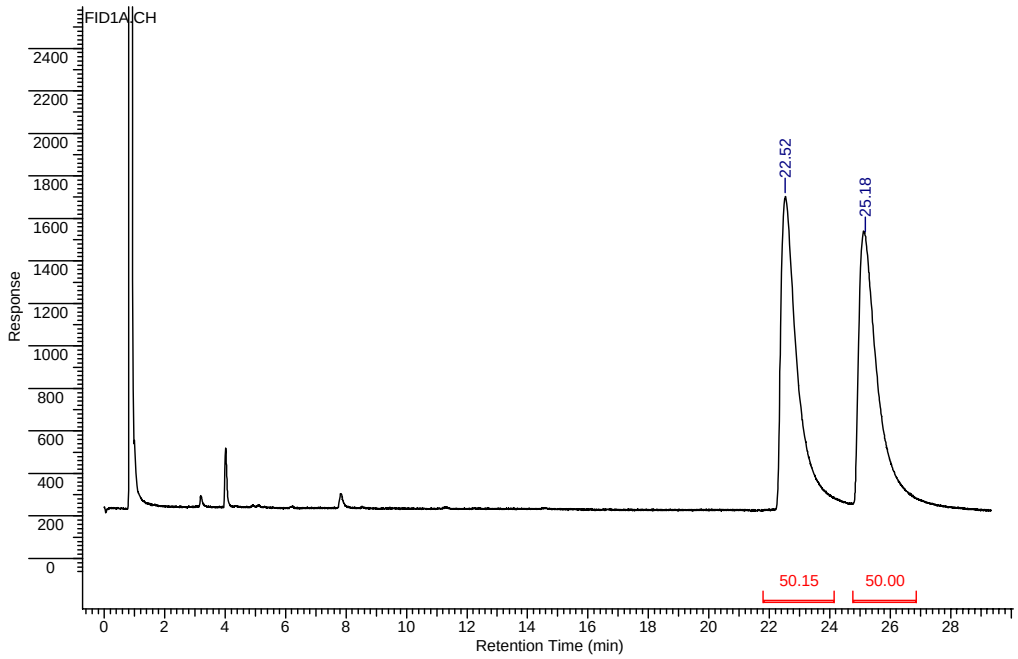


Crude reaction mixture

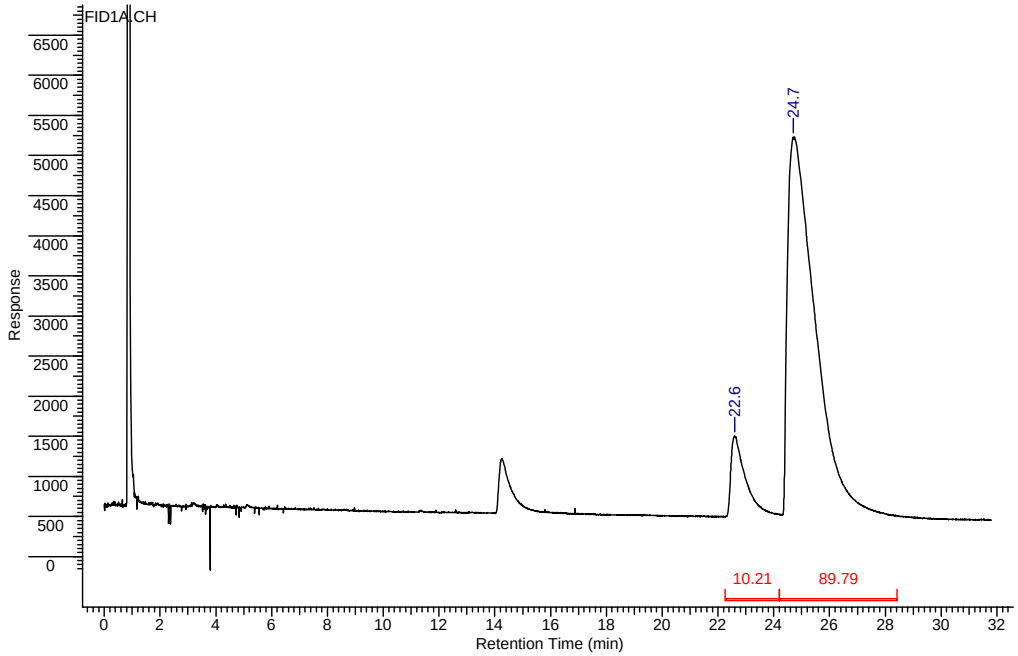


1-(2-Bromophenyl)propan-1-ol (Table 3, Entry 8)

Racemic mixture

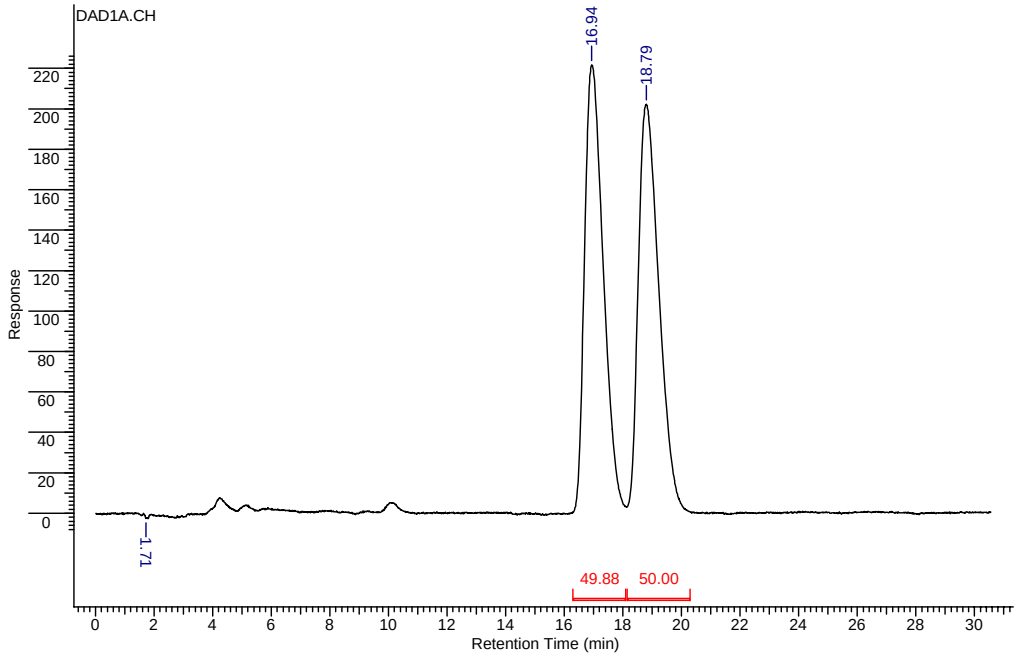


Crude reaction mixture

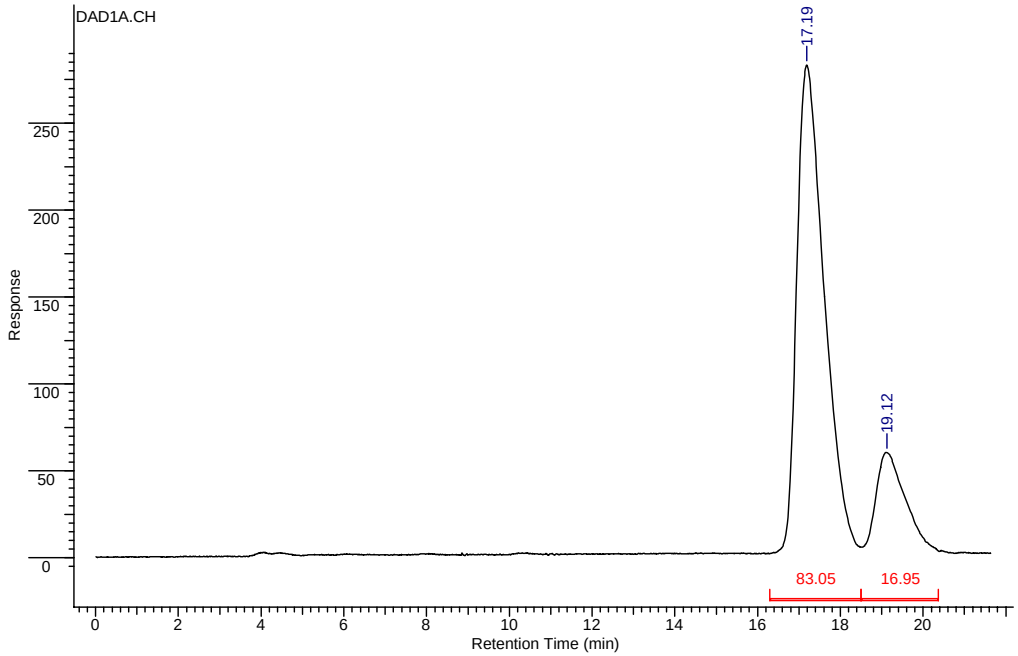


1-(2- Methoxyphenyl)propan-1-ol (Table 3, Entry 9)

Racemic mixture

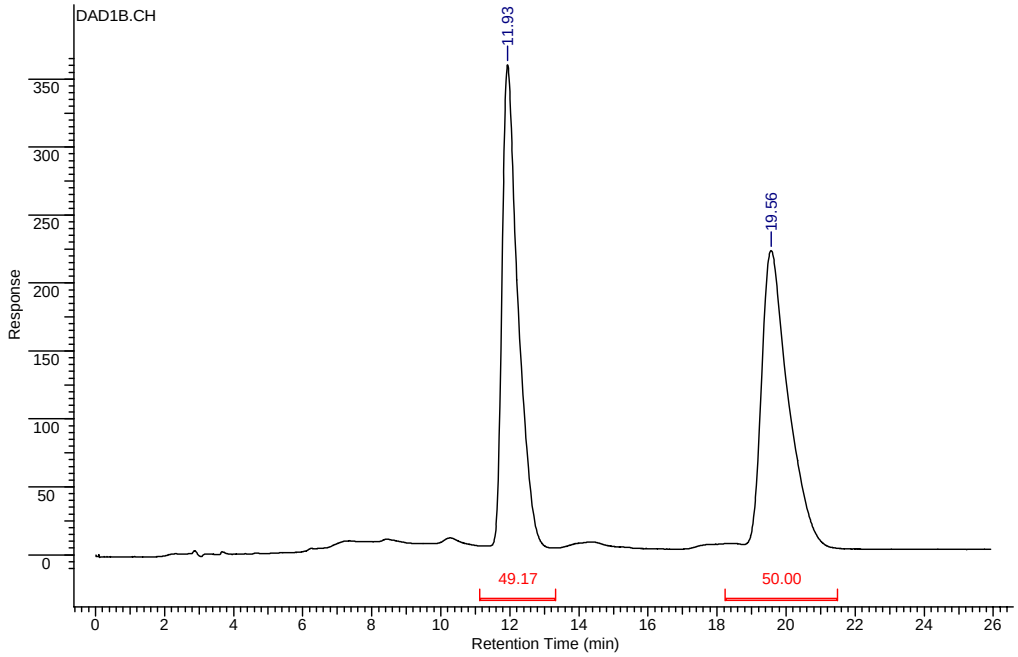


Crude reaction mixture

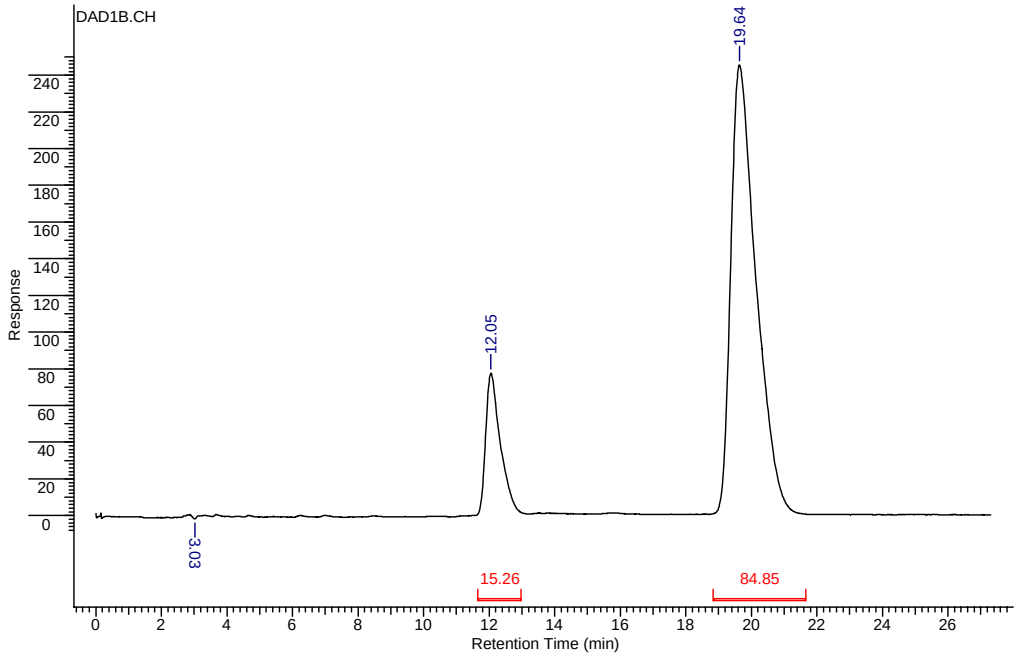


(*E*)-1-Phenylpent-1-en-3-ol (Table 3, Entry 10)

Racemic mixture

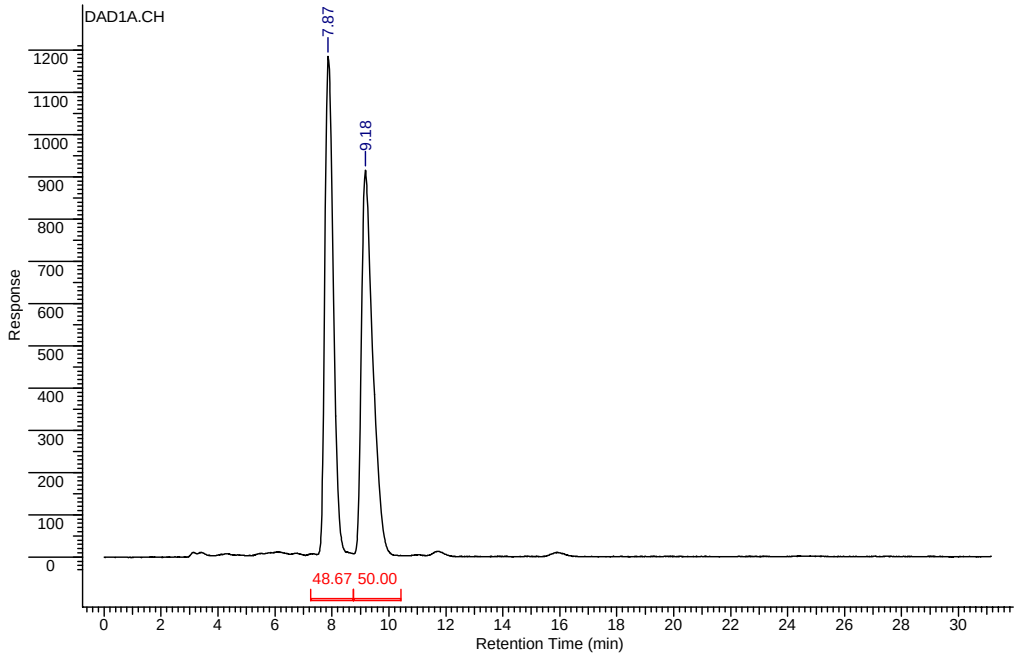


Crude reaction mixture

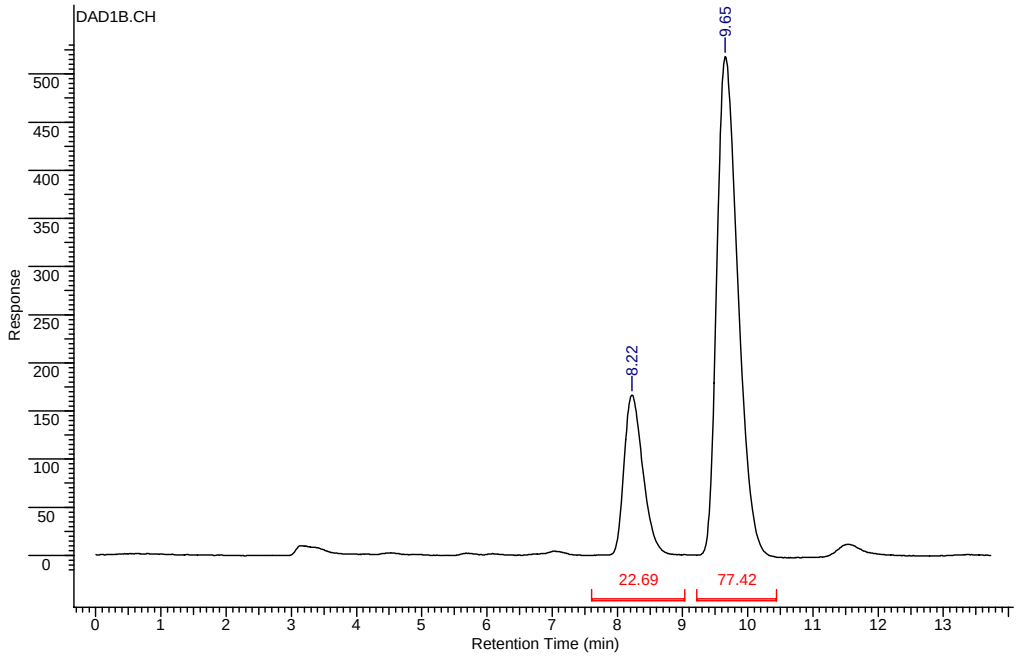


1-Phenylpent-1-yn-3-ol (Table 3, Entry 11)

Racemic mixture

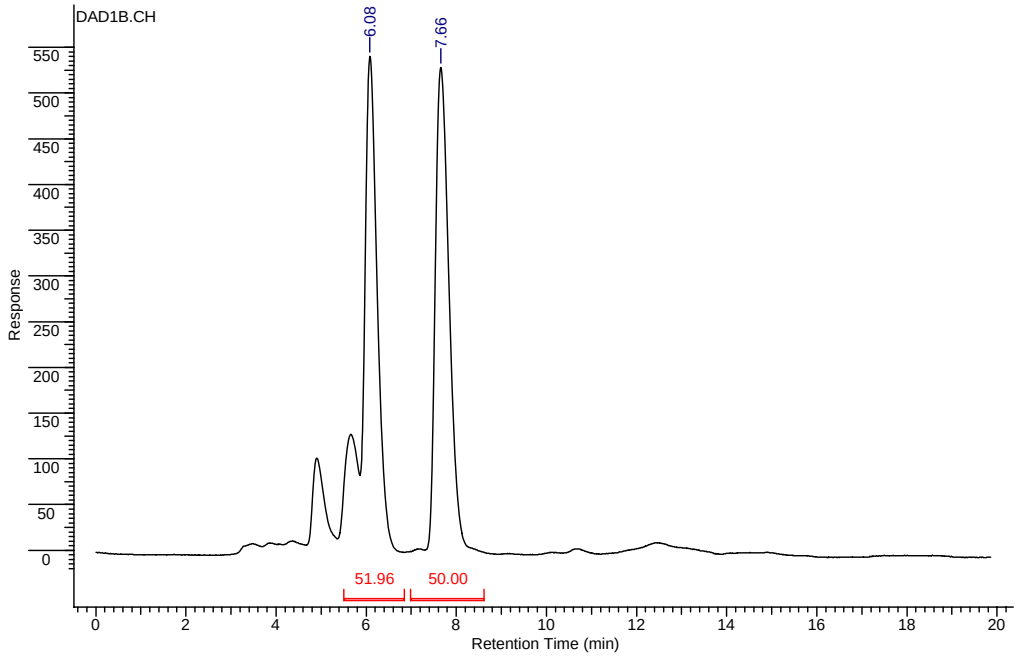


Crude reaction mixture

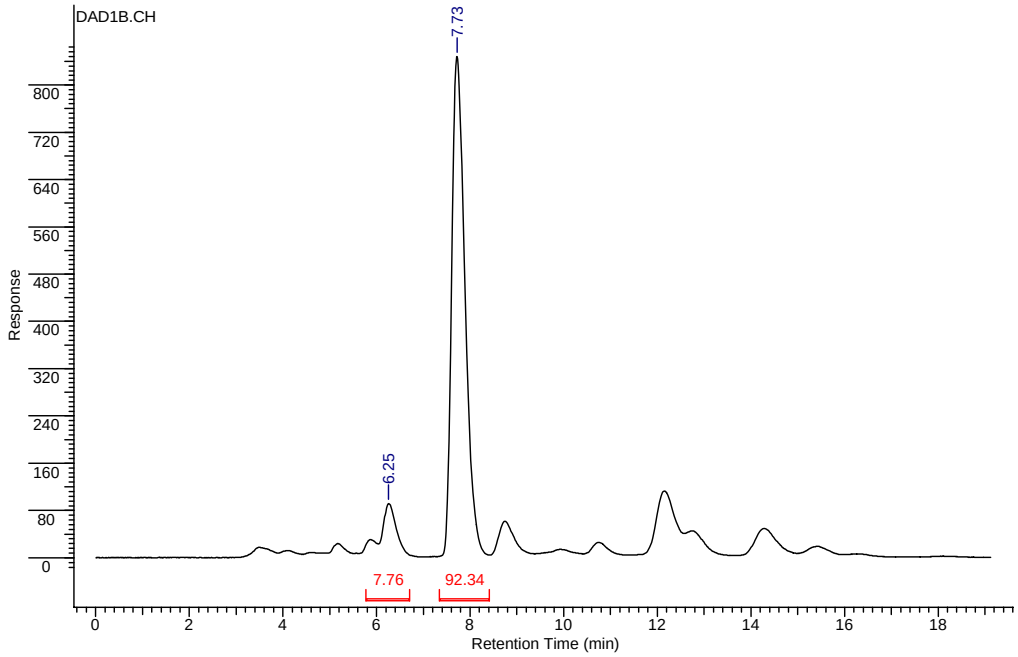


1-Phenylpentan-3-ol (Table 3, Entry 12)

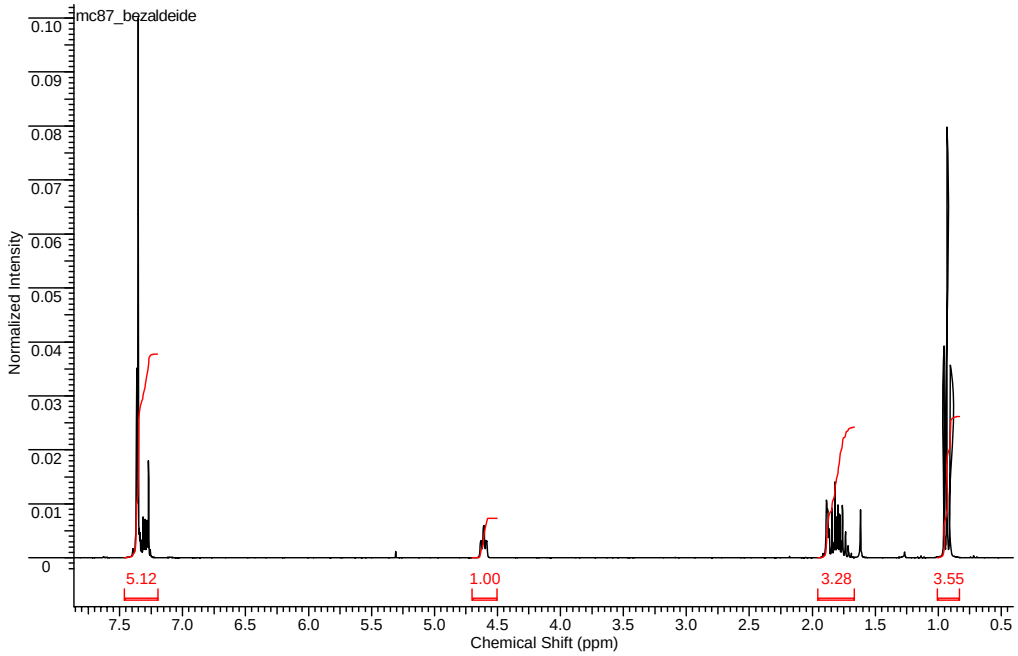
Racemic mixture

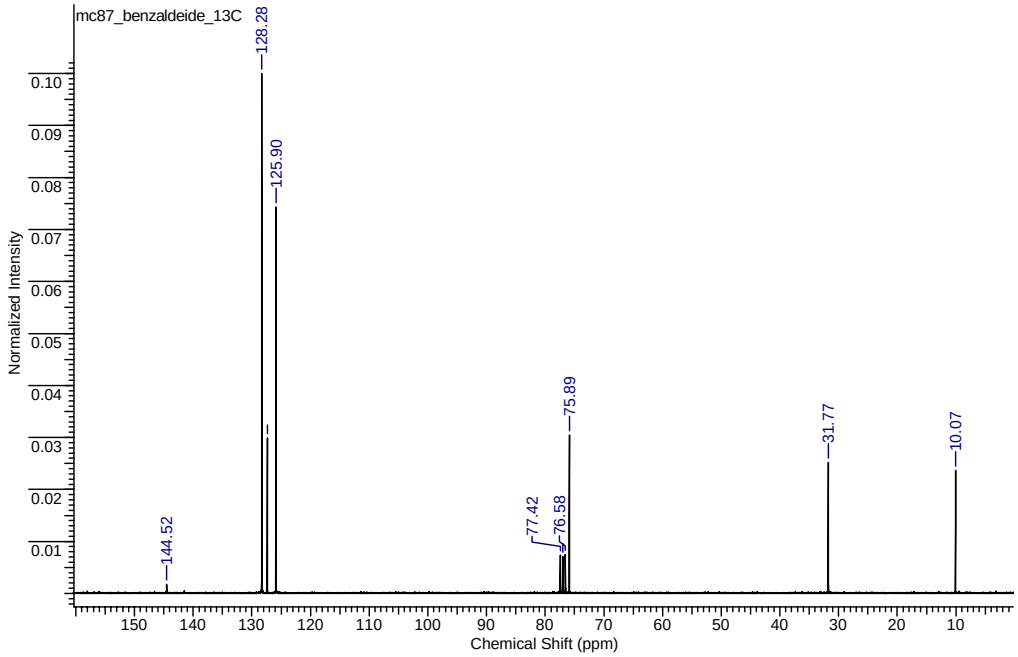


Crude reaction mixture

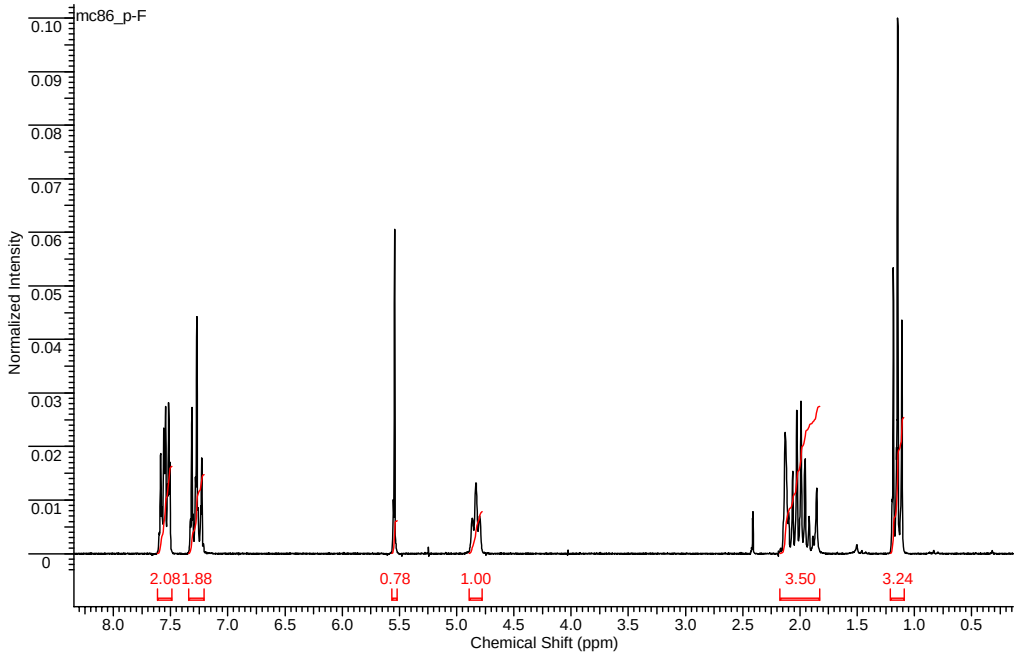


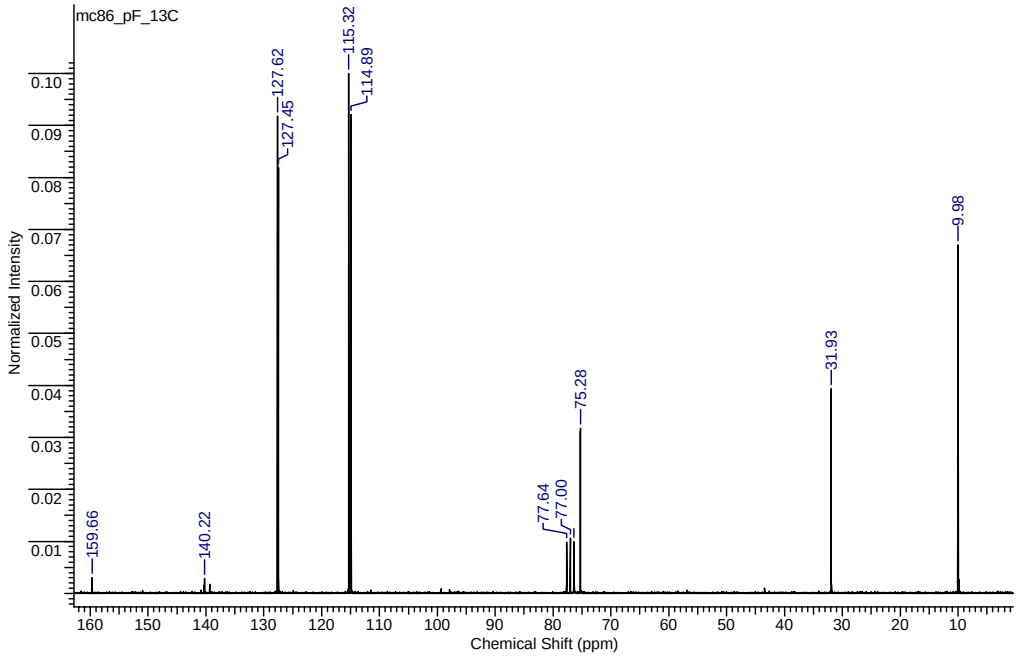
NMR Data
1-Phenylpropan-1-ol (Table 2, Entry 1)



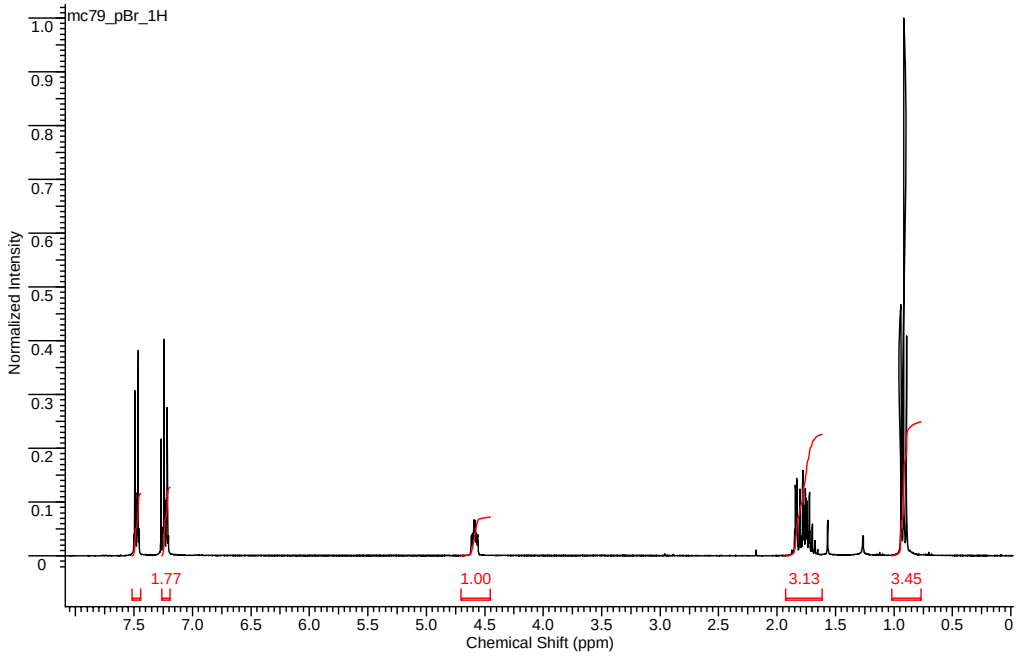


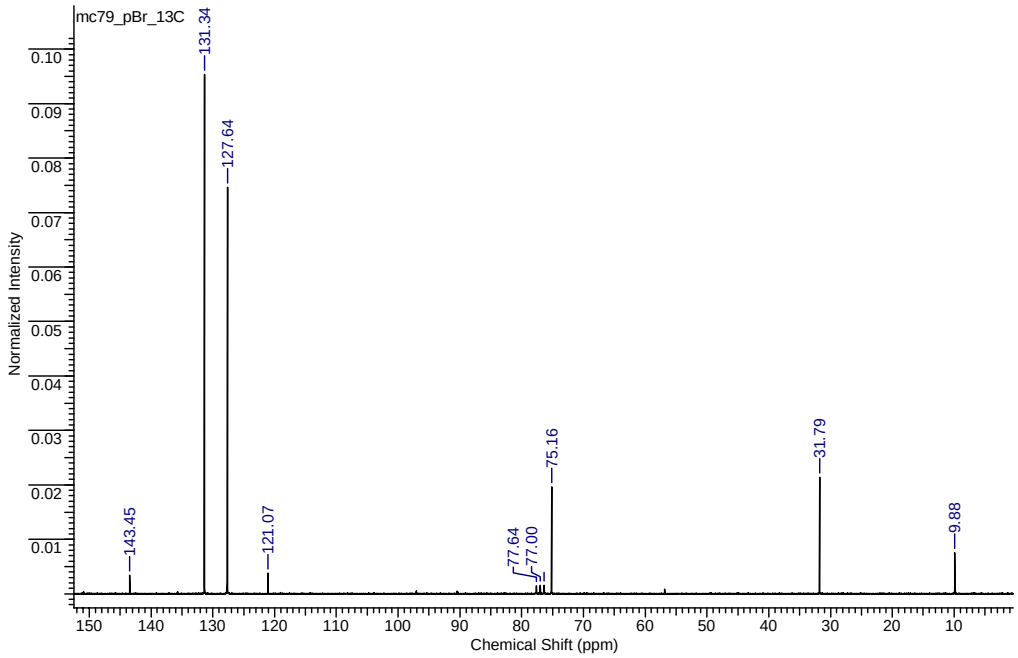
1-(4-Fluorophenyl)propan-1-ol (Table 3, Entry 1)



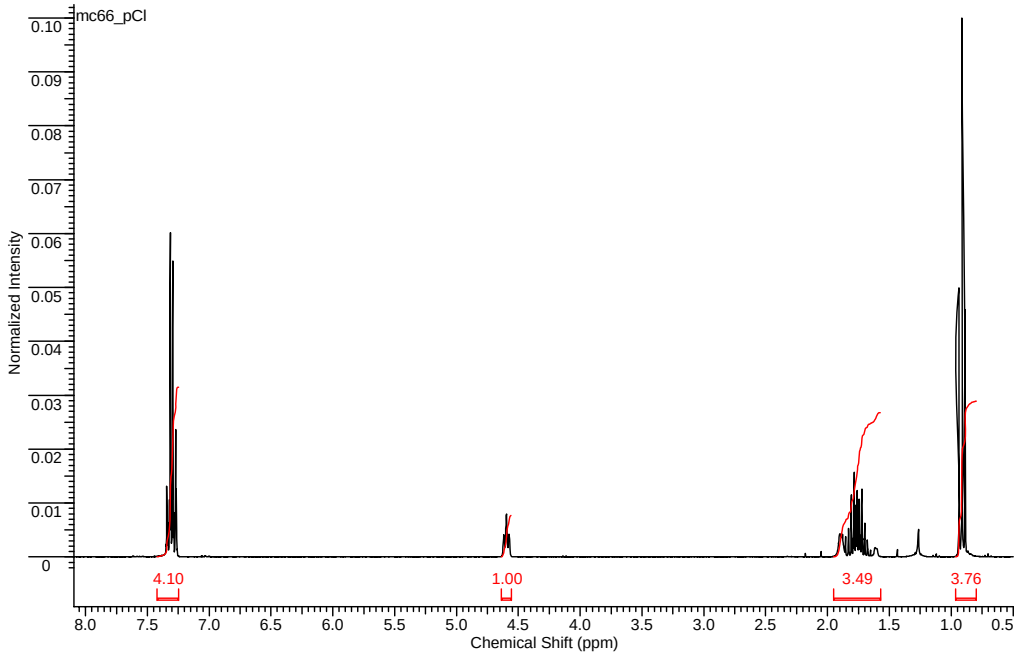


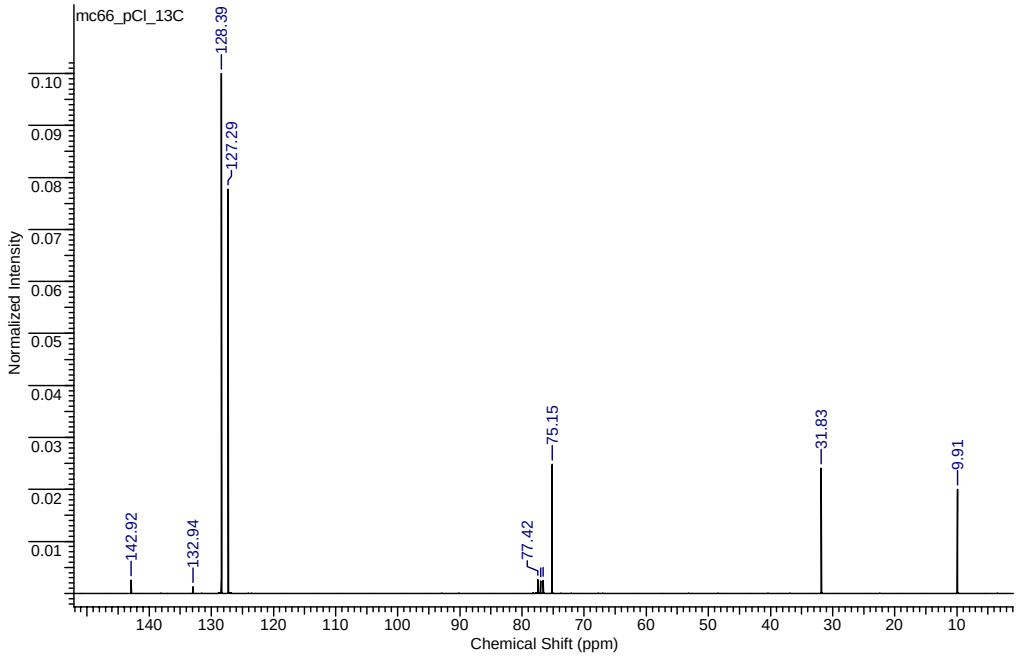
1-(4-Bromophenyl)propan-1-ol (Table 3, Entry 2)



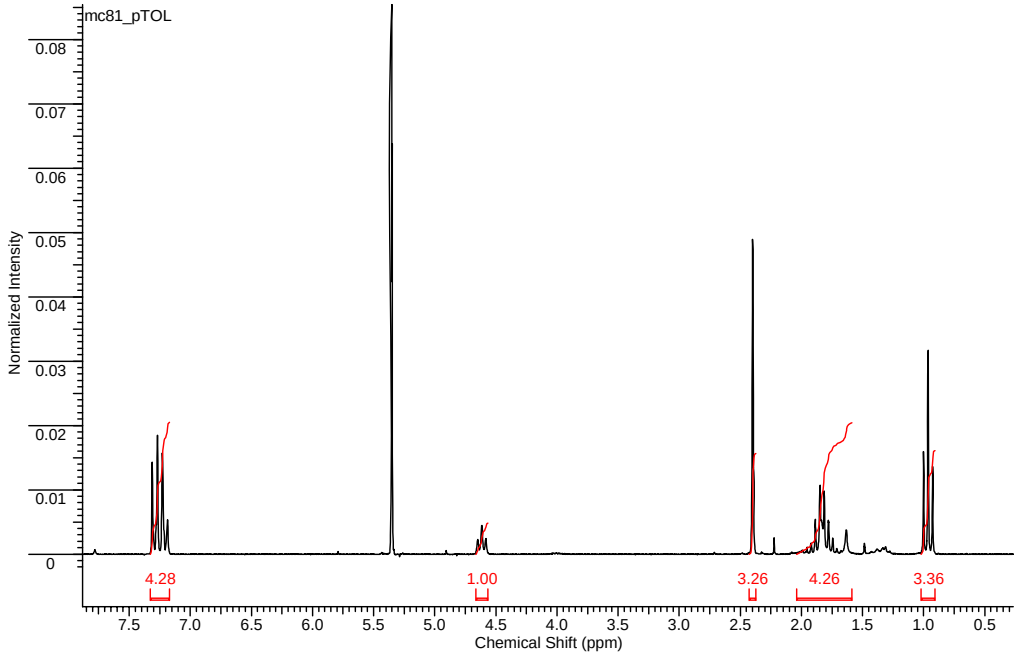


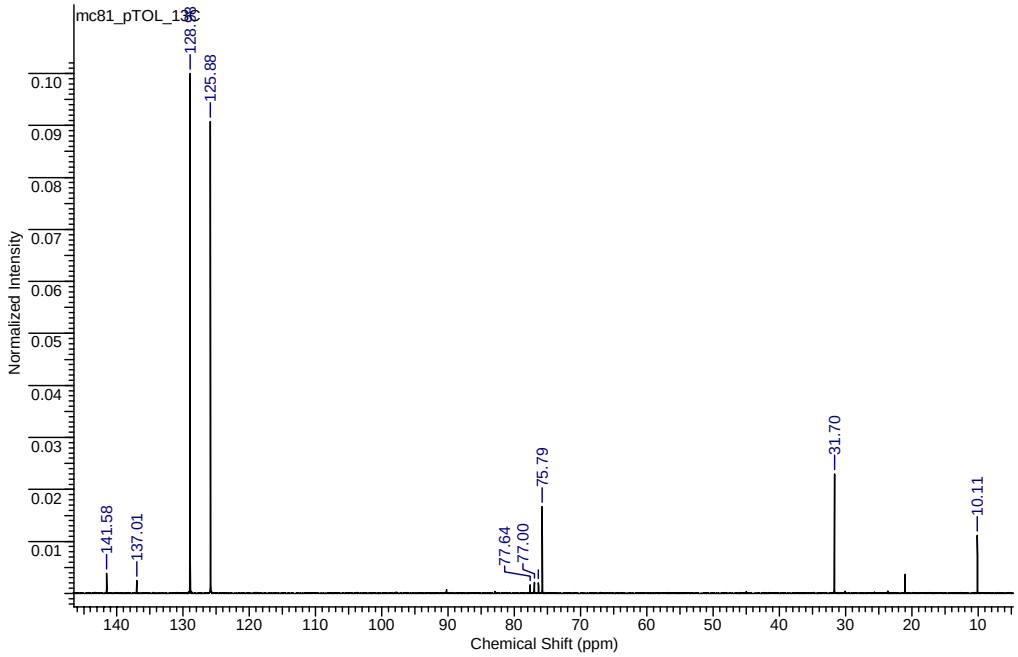
1-(4-Chlorophenyl)propan-1-ol (Table 3, Entry 3)



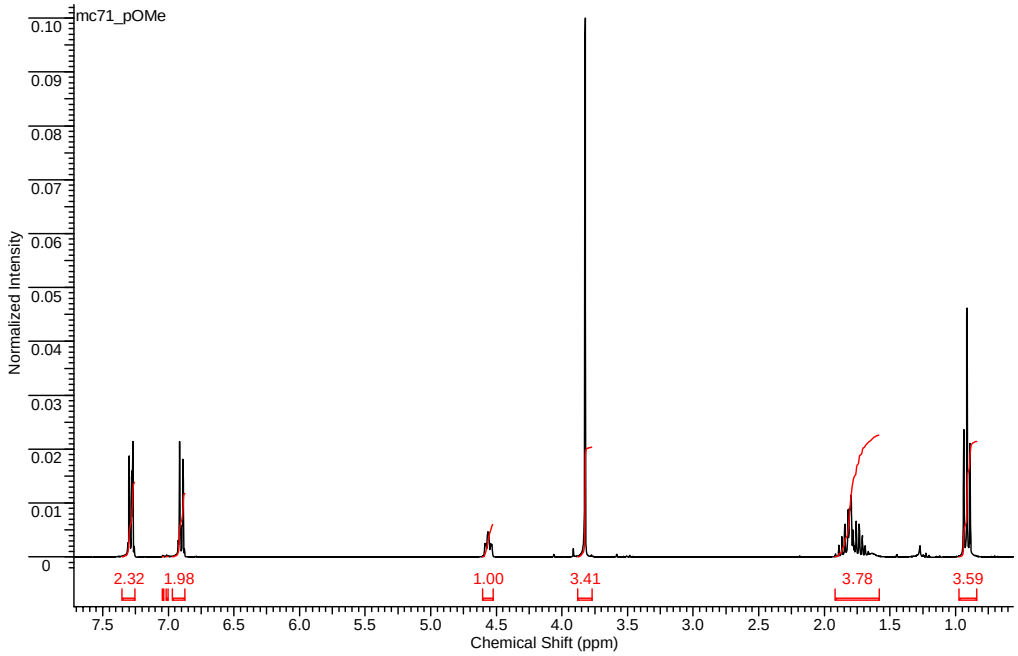


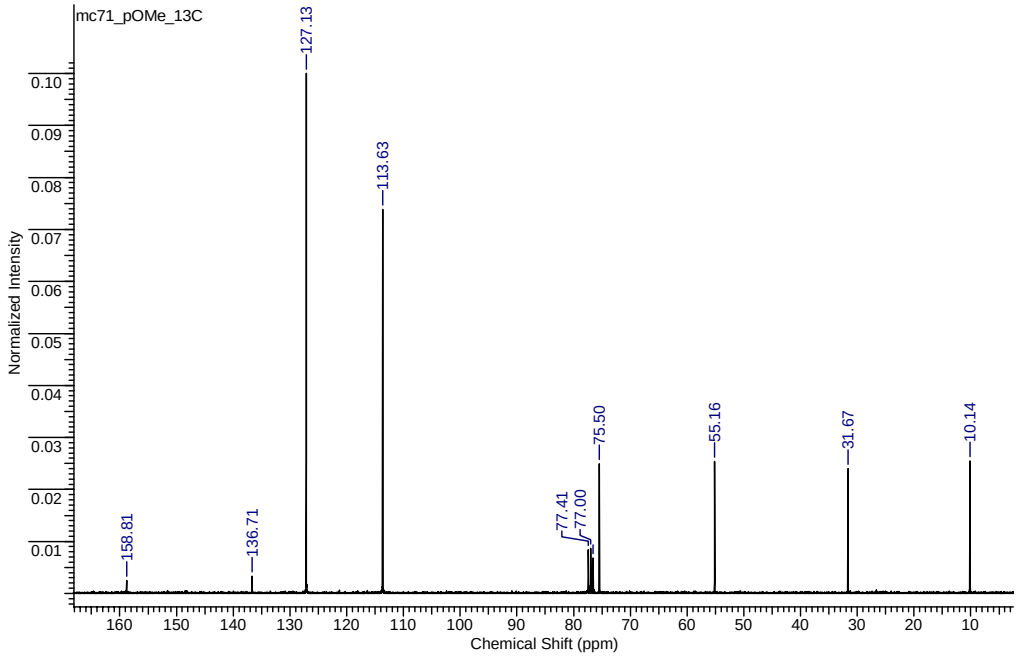
1-*p*-Tolylpropan-1-ol (Table 3, Entry 4)



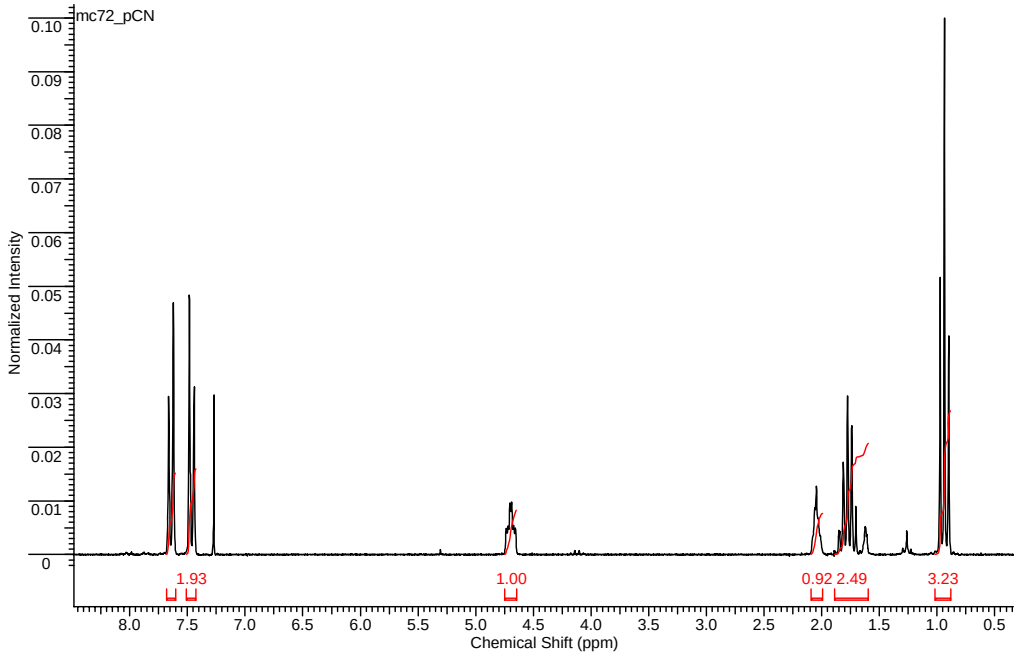


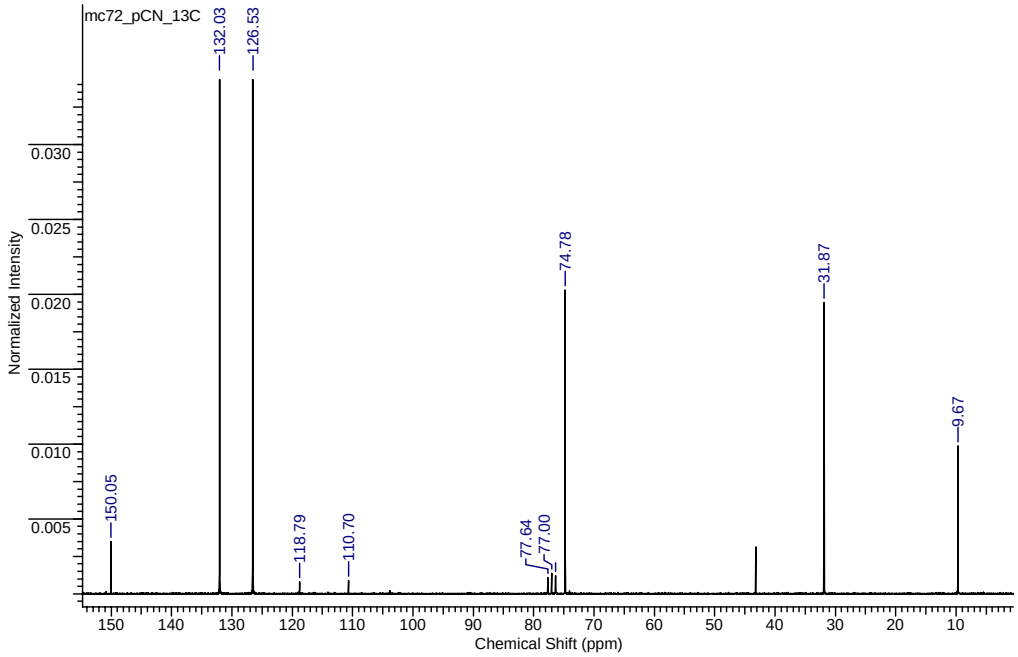
1-(4-Methoxyphenyl)propan-1-ol (Table 3, Entry 5)



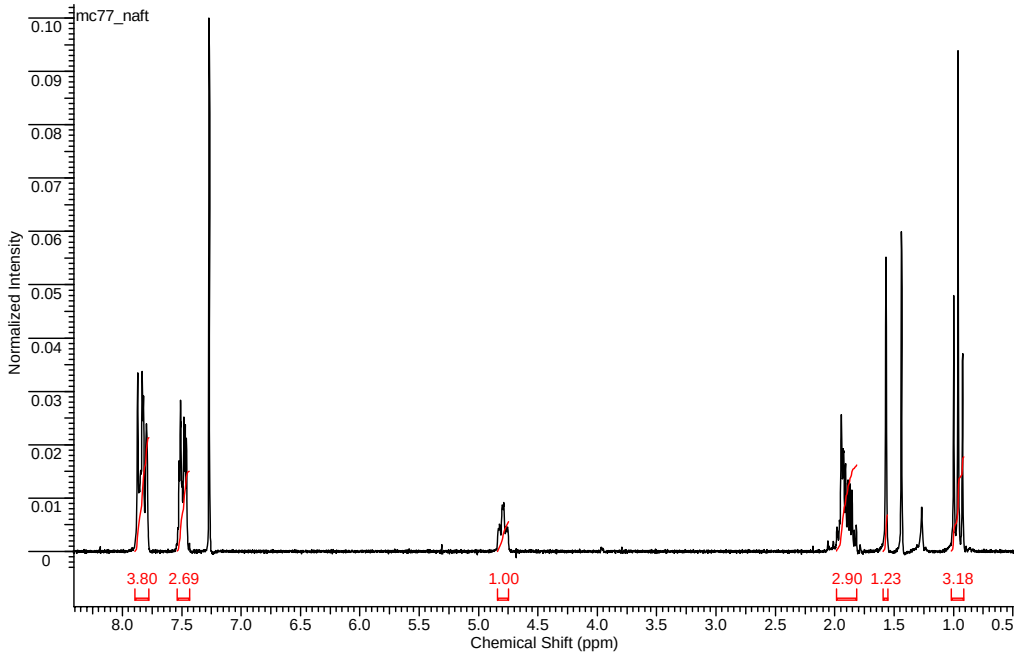


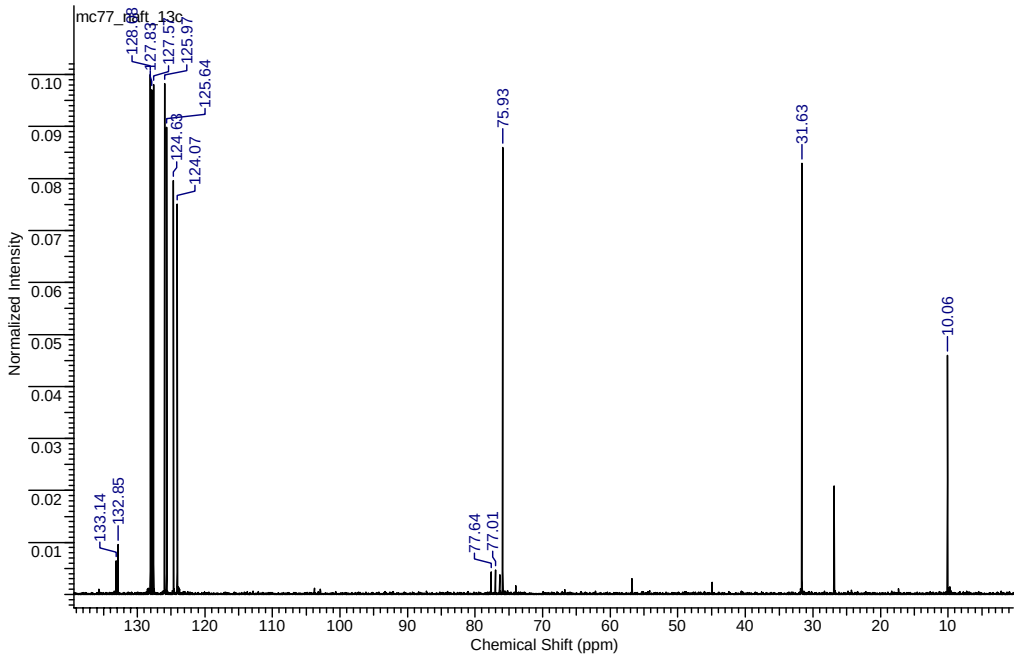
1-(4-Cyanophenyl)propan-1-ol (Table 3, Entry 6)



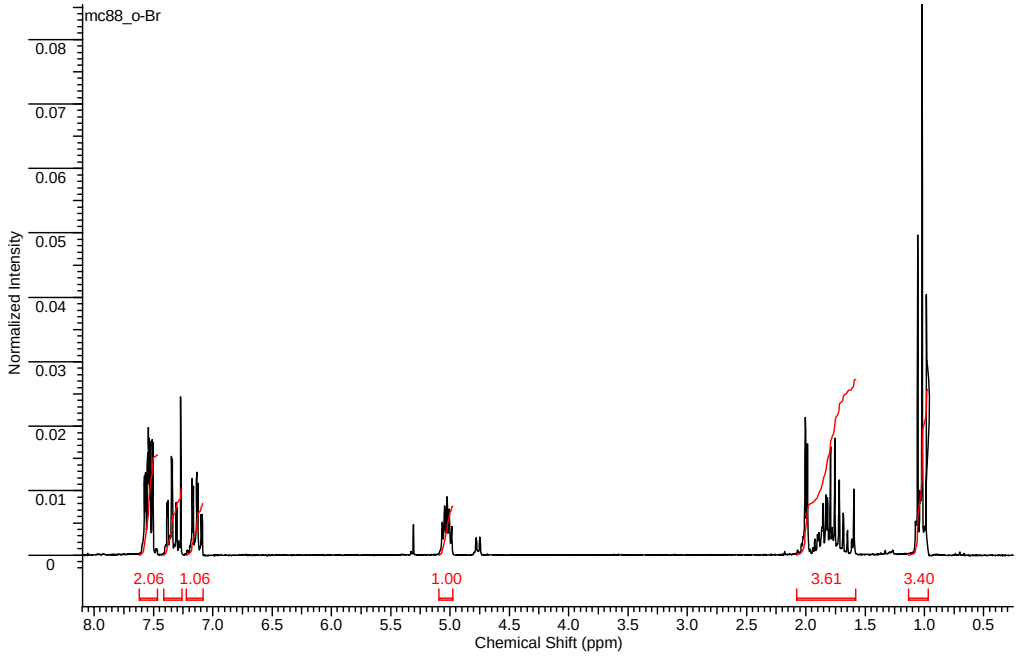


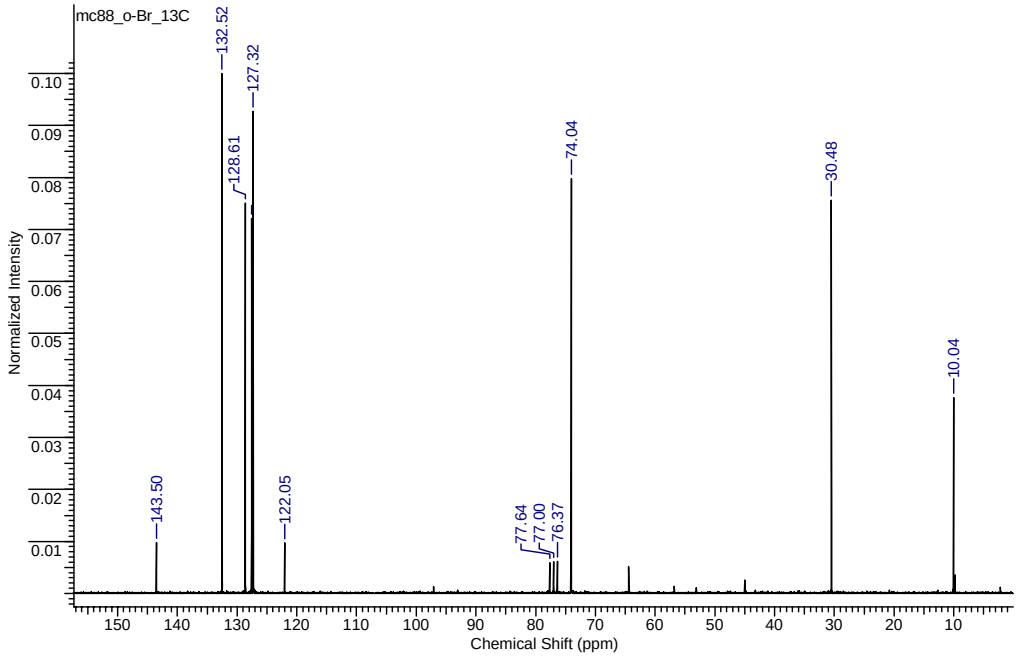
1-(Naphthalen-2-yl)propan-1-ol (Table 3, Entry 7)



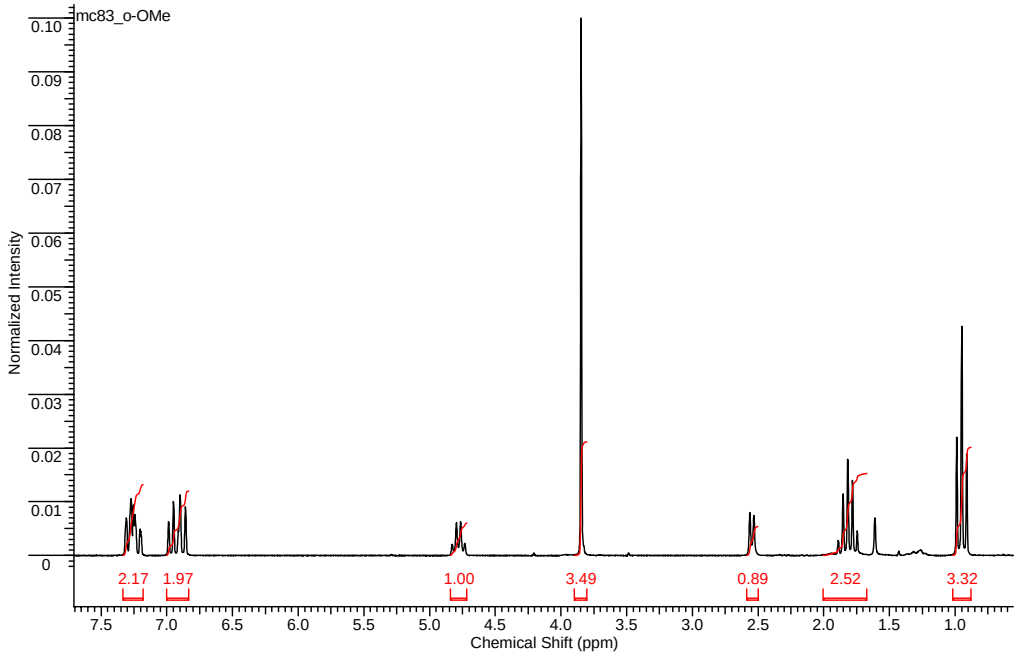


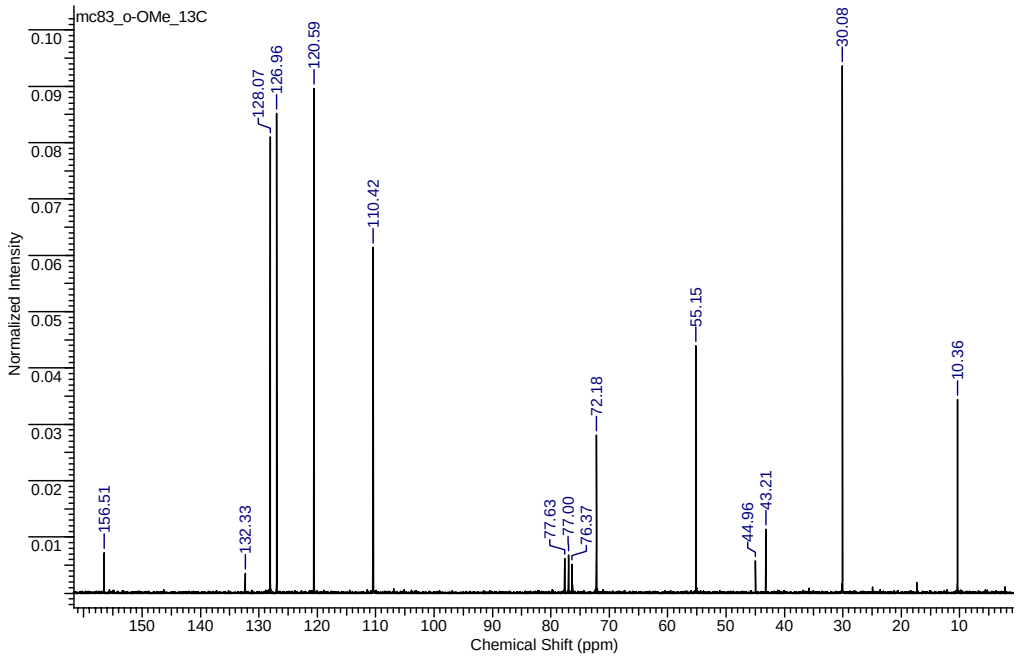
1-(2-Bromophenyl)propan-1-ol (Table 3, Entry 8)



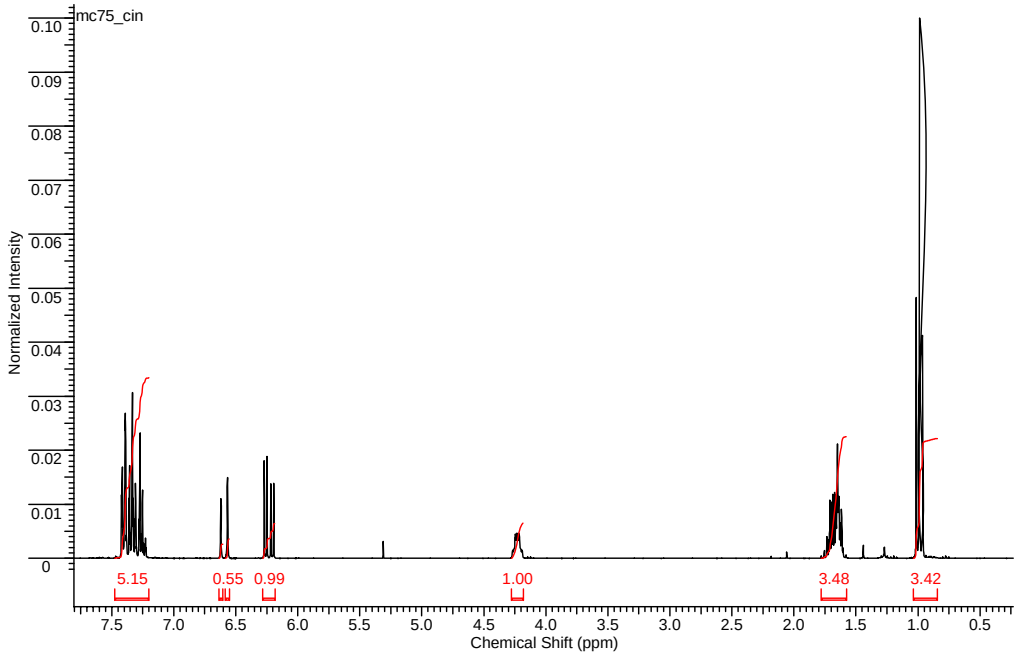


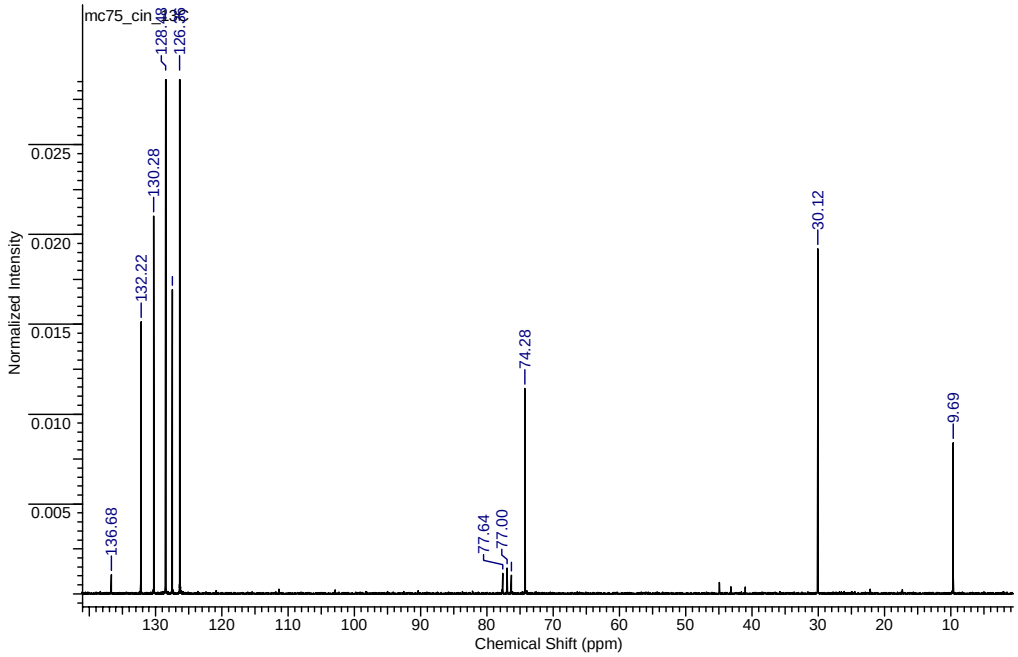
1-(2- Methoxyphenyl)propan-1-ol (Table 3, Entry 9)



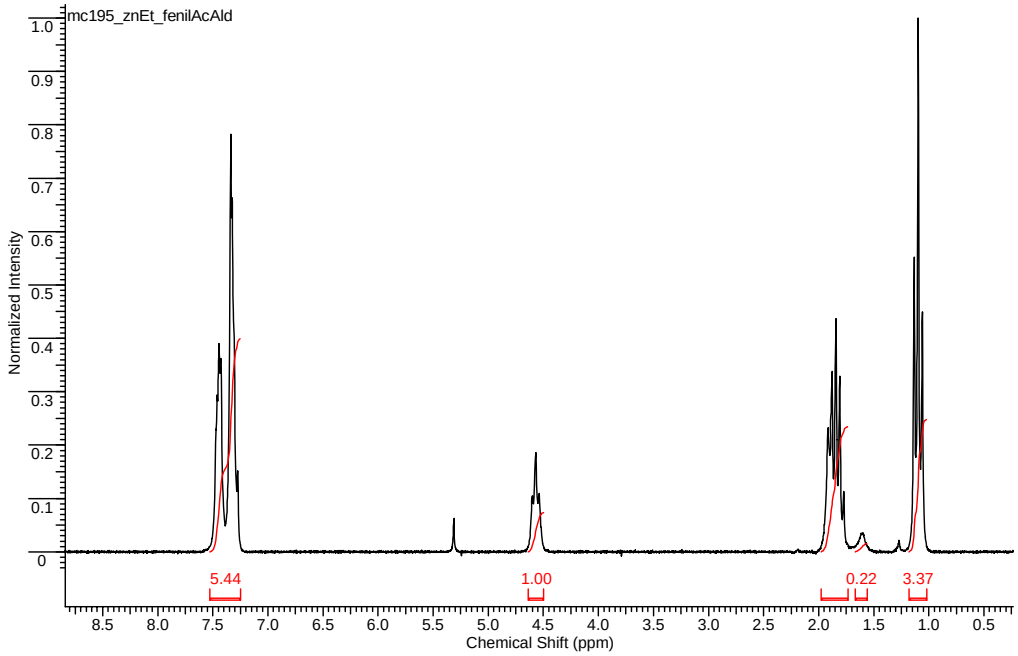


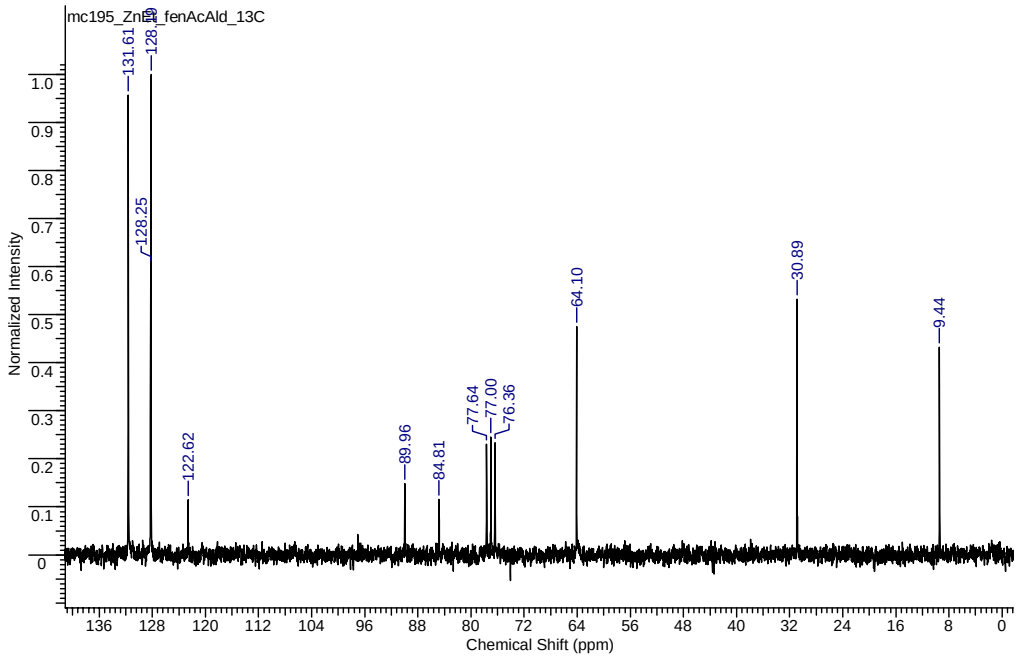
(*E*)-1-Phenylpent-1-en-3-ol (Table 3, Entry 10)





1-Phenylpent-1-yn-3-ol (Table 3, Entry 11)





1-Phenylpentan-3-ol (Table 3, Entry 12)