

Remote Ester Group Leads to Efficient Kinetic Resolution of Racemic Aliphatic Alcohols via Asymmetric Hydrogenation

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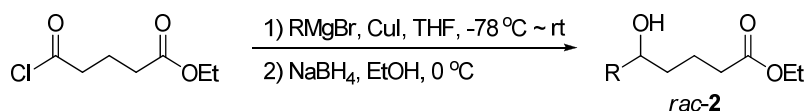
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General: All reactions and manipulations which are sensitive to moisture or air were performed under an inert atmosphere of nitrogen. All chemicals were purchased from J & K, Acros and Aldrich and were used as received. Hydrogen gas (99.999%) was purchased from Boc Gas Inc., Tianjin. 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. Melting points were measured on a RY-I apparatus and uncorrected. ^1H NMR spectra were recorded at 400 MHz on Bruker AV 400 spectrometer. ^{13}C NMR spectra were recorded at 100 MHz on Bruker AV 400 spectrometer. NMR spectra were recorded in deuterated chloroform (CDCl_3) as a solvent, with residual chloroform (δ 7.26 ppm. for ^1H NMR and δ 77.00 ppm. for ^{13}C NMR) or tetramethylsilane (TMS, δ 0.00 ppm. for ^1H NMR) taken as the inert standard, and were reported in ppm. Abbreviations for signal coupling are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Coupling constants were taken from the spectra directly and are uncorrected. Optical rotations were determined using a Perkin Elmer 341 polarimeter. HRMS were recorded on APEXII and ZAB-HS spectrometer. HPLC analyses were performed using Hewlett Packard Model HP1100 instruments with Chiralcel OJ-H, OD-H, AD-H column.

(A) Preparation of racemic δ -alkyl δ -hydroxy esters

The δ -alkyl δ -hydroxy esters were prepared according to the literature method illustrated below.

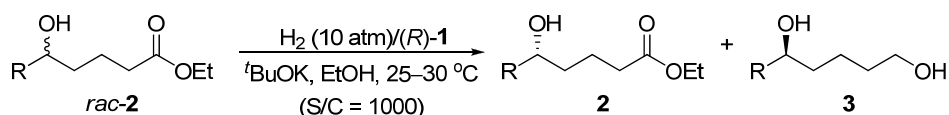


To a stirred solution of ethyl 5-chloro-5-oxopentanoate (4.5 g, 25 mmol) and CuI (476 mg, 2.5 mmol) in THF (75 mL) was added alkyl magnesium bromide (22.5 mmol) in situ generated from magnesium turnings and alkyl bromide at $-78\text{ }^{\circ}\text{C}$ under N_2 atmosphere. The resulting mixture was allowed to slowly warm up to room temperature overnight and then quenched with saturated NH_4Cl (50 mL). The layers were separated and the aqueous layer was extracted with EtOAc (50 mL \times 3). The combined organic layers were washed with brine, dried over anhydrous MgSO_4 , and concentrated in vacuo to yield the desired δ -alkyl δ -ketoesters as a crude product.

To a solution of the crude δ -alkyl δ -ketoesters in EtOH (50 mL) was added NaBH_4 (22.5 mmol) at $0\text{ }^{\circ}\text{C}$ and the resulting mixture was stirred for 7 min at this temperature. The reaction mixture was then quenched with H_2O at the same temperature and concentrated in vacuo to remove EtOH. The residue was extracted with EtOAc (50 mL \times 3). The combined organic layers were washed with brine, dried over anhydrous MgSO_4 and concentrated in vacuo. The residue was chromatographed on silica gel column with EtOAc/petroleum ether as an eluent to offer the corresponding racemic δ -alkyl δ -hydroxy esters.

(B) Kinetic resolution of racemic δ -hydroxy esters via catalytic ester hydrogenation

Kinetic resolution of *rac*-**2**



To a 20 mL hydrogenation vessel in an autoclave was added racemic δ -hydroxy esters *rac*-**2** (1.0 mmol), a solution of iridium catalyst (*R*)-**1** in EtOH (0.002 mmol/mL, 0.5 mL, 0.001 mmol), a solution of *t*-BuOK in EtOH (0.08 mmol/mL, 0.5 mL, 0.04 mmol), and 1.0 mL of anhydrous EtOH. The autoclave was purged with hydrogen by pressurizing to 5 atm and releasing the pressure. This procedure was repeated three times and then pressurized to 10 atm of H_2 . The reaction mixture was stirred at room temperature ($25\text{--}30\text{ }^{\circ}\text{C}$) until the hydrogen pressure bled down to 9.5 atm. The solvent was removed in vacuo and the residue was purified by flash column chromatography on silica gel with petroleum ether/ethyl acetate as an eluent to afford the chiral δ -hydroxy esters **2** and diols **3**.

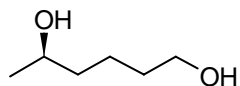
The ee values of the chiral δ -hydroxy esters **2** and diols **3** were determined by transformation of them into the corresponding benzoyl esters. The general procedure was shown as follows: The chiral δ -hydroxy esters **2** and diols **3** (0.2 mmol) was reacted with benzoyl chloride (70 mg, 0.5 mmol) in the presence of pyridine (47 mg, 0.6 mmol) in DCM (5 mL) for 2 h. The reaction mixture was then quenched with saturated NH_4Cl (5 mL) and extracted with DCM (5 mL \times 3). The combined extracts were washed with brine, dried over anhydrous MgSO_4 and concentrated in vacuo. After a flash chromatography on silica gel (petroleum ether/ethyl acetate = 10:1), the desired benzoyl esters were obtained in nearly quantitative yields.

(*S*)-Ethyl 5-hydroxyhexanoate (**2a**)¹

Colorless oil, 1 h, 47% yield, 93.7% ee, $[\alpha]_{\text{D}}^{20} +8.4$ (*c* 1.0, MeOH). ^1H NMR (400 MHz, CDCl_3) δ 4.13 (q, $J = 7.2\text{ Hz}$, 2H), 3.85–3.75 (m, 1H), 2.33 (t, $J = 7.2\text{ Hz}$, 2H), 1.82–1.61 (m, 2H), 1.58–1.43 (m, 3H), 1.25 (t, $J = 7.2\text{ Hz}$, 3H), 1.20 (d, $J = 6.4\text{ Hz}$, 3H).

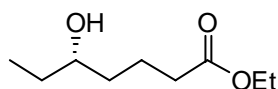
^{13}C NMR (100 MHz, CDCl_3) δ 173.75, 67.54, 60.33, 38.56, 34.08, 23.49, 21.02, 14.23. HPLC conditions: Chiralcel OJ-H column (25 cm \times 0.46 cm ID); *n*-hexane/2-propanol = 98:2; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; t_{R} (*S*) = 9.72 min and t_{R} (*R*) = 10.37 min.

(*R*)-Hexane-1,5-diol (3a)²



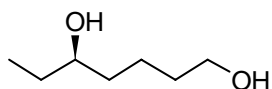
Colorless oil, 1 h, 46% yield, 94% ee, $[\alpha]_{\text{D}}^{20} -7.4$ (*c* 1.0, MeOH). [lit.² $[\alpha]_{\text{D}}^{24} -6.3$ (*c* 1.0, MeOH)]. ^1H NMR (400 MHz, CDCl_3) δ 3.87–3.76 (m, 1H), 3.65 (t, *J* = 6.4 Hz, 2H), 1.70–1.54 (m, 4H), 1.53–1.36 (m, 4H), 1.19 (d, *J* = 6.0 Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 67.97, 62.72, 38.81, 32.50, 23.54, 21.88. HPLC conditions: Chiralcel OD-H column (25 cm \times 0.46 cm ID); *n*-hexane/2-propanol = 90:10; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; t_{R} (*S*) = 5.95 min and t_{R} (*R*) = 7.13 min.

(*S*)-Ethyl 5-hydroxyheptanoate (2b)



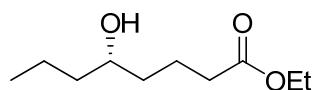
Colorless oil, 2 h, 44% yield, 95% ee, $[\alpha]_{\text{D}}^{20} +6.2$ (*c* 2.0, MeOH). ^1H NMR (400 MHz, CDCl_3) δ 4.11 (q, *J* = 7.2 Hz, 2H), 3.54–3.48 (m, 1H), 2.32 (t, *J* = 7.2 Hz, 2H), 1.83–1.61 (m, 3H), 1.55–1.36 (m, 4H), 1.24 (t, *J* = 7.2 Hz, 3H), 0.92 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 173.81, 72.66, 60.28, 36.15, 34.11, 30.10, 20.93, 14.19, 9.83. HPLC conditions: Chiralcel OJ-H column (25 cm \times 0.46 cm ID); *n*-hexane/2-propanol = 99:1; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; t_{R} (*S*) = 19.76 min and t_{R} (*R*) = 20.81 min. HRMS (ESI) Calcd for $\text{C}_{11}\text{H}_{23}\text{O}_3$ ($[\text{M} + \text{H}]^+$): 175.1329, Found: 175.1329.

(*R*)-Heptane-1,5-diol (3b)³



Colorless oil, 2 h, 47% yield, 94% ee, $[\alpha]_{\text{D}}^{20} -9.0$ (*c* 2.0, MeOH). [lit.² $[\alpha]_{\text{D}}^{24} +2.1$ (*c* 1.0, MeOH), *S* enantiomer]. ^1H NMR (300 MHz, CDCl_3) δ 3.66 (t, *J* = 6.4 Hz, 2H), 3.60–3.49 (m, 1H), 1.68–1.38 (m, 10H), 0.94 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 73.13, 62.63, 36.37, 32.51, 30.18, 21.77, 9.87. HPLC conditions: Chiralcel OD-H column (25 cm \times 0.46 cm ID); *n*-hexane/2-propanol = 90:10; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; t_{R} (*S*) = 5.49 min and t_{R} (*R*) = 6.42 min.

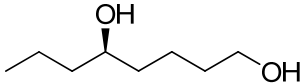
(*S*)-Ethyl 5-hydroxyoctanoate (2c)



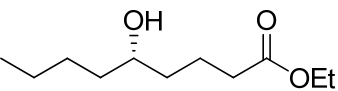
Colorless oil, 2 h, 43% yield, 96% ee, $[\alpha]_{\text{D}}^{20} +2.0$ (*c* 1.0, MeOH). ^1H NMR (400 MHz, CDCl_3) δ 4.11 (q, *J* = 7.2 Hz, 2H), 3.65–3.53 (m, 1H), 2.32 (t, *J* = 7.2 Hz, 2H), 1.83–1.61 (m, 3H), 1.53–1.32 (m, 6H), 1.24 (t, *J* = 7.2 Hz, 3H), 0.91 (t, *J* = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 173.78, 71.04, 60.27, 39.58, 36.70, 34.12, 20.93, 18.76, 14.19,

14.03. HPLC conditions: Chiralcel AD-H column (25 cm × 0.46 cm ID); *n*-hexane/2-propanol = 98:2; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; t_R (*S*) = 7.06 min and t_R (*R*) = 7.57 min. HRMS (ESI) Calcd for C₁₁H₂₃O₃ ([M + H]⁺): 189.1486, Found: 189.1483.

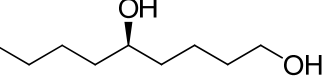
(*R*)-Octane-1,5-diol (3c)²

 Colorless oil, 2 h, 47% yield, 96% ee, $[\alpha]^{20}_D -1.4$ (*c* 1.0, MeOH). [lit.² $[\alpha]^{26}_D -1.0$ (*c* 1.0, MeOH)]. ¹H NMR (400 MHz, CDCl₃) δ 3.70–3.55 (m, 3H), 2.33 (br s, 2H), 1.72–1.23 (m, 10H), 0.91 (t, *J* = 6.8 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 71.43, 62.48, 39.66, 36.84, 32.43, 21.72, 18.80, 14.07. HPLC conditions: Chiralcel OD-H column (25 cm × 0.46 cm ID); *n*-hexane/2-propanol = 90:10; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; t_R (*S*) = 5.13 min and t_R (*R*) = 5.78 min.

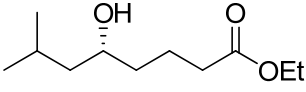
(*S*)-Ethyl 5-hydroxynonanoate (2d)⁴

 Colorless oil, 2 h, 45% yield, 95% ee, $[\alpha]^{20}_D +1.8$ (*c* 1.0, MeOH). ¹H NMR (400 MHz, CDCl₃) δ 4.11 (q, *J* = 7.2 Hz, 2H), 3.62–3.52 (m, 1H), 2.31 (t, *J* = 7.2 Hz, 2H), 1.84–1.61 (m, 3H), 1.54–1.36 (m, 5H), 1.35–1.27 (m, 3H), 1.24 (t, *J* = 7.2 Hz, 3H), 0.88 (t, *J* = 6.8 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 173.78, 71.31, 60.26, 37.11, 36.68, 34.12, 27.76, 22.67, 20.93, 14.19, 14.01. HPLC conditions: Chiralcel AD-H column (25 cm × 0.46 cm ID); *n*-hexane/2-propanol = 95:5; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; t_R (*S*) = 5.28 min and t_R (*R*) = 5.69 min.

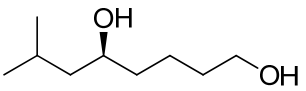
(*R*)-Nonane-1,5-diol (3d)²

 Colorless oil, 2 h, 48% yield, 96% ee, $[\alpha]^{20}_D -0.4$ (*c* 1.0, MeOH). [lit.² $[\alpha]^{24}_D +0.5$ (*c* 1.0, MeOH), *S* enantiomer]. ¹H NMR (400 MHz, CDCl₃) δ 3.67 (t, *J* = 6.0 Hz, 2H), 3.64–3.57 (m, 1H), 1.65–1.25 (m, 14H), 0.91 (t, *J* = 6.8 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 71.70, 62.46, 37.18, 36.81, 32.43, 27.82, 22.71, 21.73, 14.04. HPLC conditions: Chiralcel OD-H column (25 cm × 0.46 cm ID); *n*-hexane/2-propanol = 90:10; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; t_R (*S*) = 4.90 min and t_R (*R*) = 5.47 min.

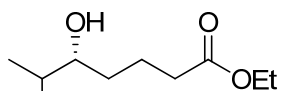
(*R*)-Ethyl 5-hydroxy-7-methyloctanoate (2e)


 Colorless oil, 3 h, 49% yield, 90% ee, $[\alpha]^{20}_{\text{D}} -24.0$ (*c* 2.0, MeOH). ^1H NMR (400 MHz, CDCl_3) δ 4.11 (q, $J = 7.2$ Hz, 2H), 3.70–3.61 (m, 1H), 2.31 (t, $J = 7.2$ Hz, 2H), 1.80–1.60 (m, 4H), 1.52–1.31 (m, 3H), 1.27–1.16 (m, 4H), 0.93–0.86 (m, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ 173.78, 69.29, 60.26, 46.69, 37.26, 34.11, 24.53, 23.40, 21.99, 20.90, 14.19. HPLC conditions: Chiralcel AD-H column (25 cm \times 0.46 cm ID); *n*-hexane/2-propanol = 99:1; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; t_{R} (*R*) = 6.56 min and t_{R} (*S*) = 6.97 min. HRMS (ESI) Calcd for $\text{C}_{11}\text{H}_{23}\text{O}_3$ ($[\text{M} + \text{H}]^+$): 203.1642, Found: 203.1642.

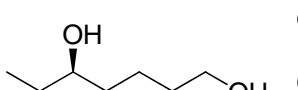
(S)-7-Methyloctane-1,5-diol (3e)


 Colorless oil, 3 h, 44% yield, 96% ee, $[\alpha]^{20}_{\text{D}} +10.3$ (*c* 2.0, MeOH). ^1H NMR (400 MHz, CDCl_3) δ 3.71–3.59 (m, 3H), 2.16 (br s, 2H), 1.82–1.68 (m, 1H), 1.67–1.31 (m, 7H), 1.26–1.16 (m, 1H), 0.98–0.84 (m, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ 69.65, 62.50, 46.76, 37.43, 32.45, 24.54, 23.43, 22.02, 21.70. HPLC conditions: Chiralcel OD-H column (25 cm \times 0.46 cm ID); *n*-hexane/2-propanol = 90:10; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; t_{R} (*R*) = 4.71 min and t_{R} (*S*) = 5.26 min. HRMS (ESI) Calcd for $\text{C}_9\text{H}_{21}\text{O}_2$ ($[\text{M} + \text{H}]^+$): 161.1536, Found: 161.1539.

(R)-Ethyl 5-hydroxy-6-methylheptanoate (2f)

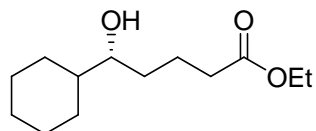

 Colorless oil, 6 h, 43% yield, 98% ee, $[\alpha]^{20}_{\text{D}} +16.2$ (*c* 1.0, MeOH). ^1H NMR (400 MHz, CDCl_3) δ 4.11 (q, $J = 7.2$ Hz, 2H), 3.34 (s, 1H), 2.32 (t, $J = 7.2$ Hz, 2H), 1.86–1.76 (m, 1H), 1.71–1.58 (m, 3H), 1.52–1.34 (m, 2H), 1.24 (t, $J = 7.2$ Hz, 3H), 0.90 (d, $J = 2.4$ Hz, 3H), 0.88 (d, $J = 2.4$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 173.80, 76.14, 60.25, 34.14, 33.47, 33.40, 21.32, 18.75, 17.12, 14.19. HPLC conditions: Chiralcel OD-H column (25 cm \times 0.46 cm ID); *n*-hexane/2-propanol = 98:2; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; t_{R} (*R*) = 9.41 min and t_{R} (*S*) = 9.85 min. HRMS (ESI) Calcd for $\text{C}_{10}\text{H}_{20}\text{O}_3$ ($[\text{M} + \text{H}]^+$): 189.1486, Found: 189.1487.

(S)-6-Methylheptane-1,5-diol (3f)⁵


 Colorless oil, 6 h, 49% yield, 97% ee, $[\alpha]^{20}_{\text{D}} -25.4$ (*c* 1.0, MeOH). ^1H NMR (400 MHz, CDCl_3) δ 3.61 (t, $J = 6.4$ Hz, 2H), 3.36–3.29 (m, 1H), 2.70 (br s, 1H), 2.36 (br s, 1H), 1.70–1.32 (m, 7H), 0.88 (d, $J = 6.8$ Hz, 6H). ^{13}C

NMR (100 MHz, CDCl₃) δ 76.48, 62.36, 33.57, 33.42, 32.41, 22.14, 18.75, 17.28. HPLC conditions: Chiralcel OD-H column (25 cm \times 0.46 cm ID); *n*-hexane/2-propanol = 90:10; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; t_R (*R*) = 4.99 min and t_R (*S*) = 5.75 min.

(*R*)-Ethyl 5-cyclohexyl-5-hydroxypentanoate (2g)



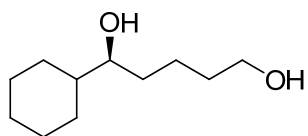
Colorless oil, 5 h, 44% yield, 99% ee, $[\alpha]_D^{20} +10.4$ (*c* 1.0, MeOH). ¹H

NMR (400 MHz, CDCl₃) δ 4.11 (q, *J* = 7.2 Hz, 2H), 3.38–3.29 (m, 1H),

2.32 (t, *J* = 7.2 Hz, 2H), 1.84–1.69 (m, 4H), 1.69–1.56 (m, 4H), 1.56–

1.46 (m, 1H), 1.45–1.35 (m, 1H), 1.34–0.93 (m, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 173.78, 75.61, 60.23, 43.53, 34.17, 33.41, 29.16, 27.72, 26.47, 26.27, 26.12, 21.25, 14.20. HPLC conditions: Chiralcel AD-H column (25 cm \times 0.46 cm ID); *n*-hexane/2-propanol = 95:5; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; t_R (*R*) = 6.16 min and t_R (*S*) = 6.76 min. HRMS (ESI) Calcd for C₁₃H₂₅O₃ ([M + H]⁺): 229.1798, Found: 229.1799.

(*S*)-1-Cyclohexylpentane-1,5-diol (3g)⁶



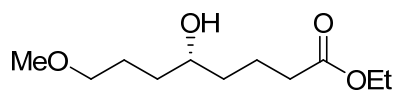
White solid, m.p. 62–64 °C, 5 h, 50% yield, 94% ee, $[\alpha]_D^{20} -16.8$ (*c* 1.0,

MeOH). ¹H NMR (400 MHz, CDCl₃) δ 3.66 (t, *J* = 6.0 Hz, 2H), 3.41–

3.33 (m, 1H), 1.85–1.71 (m, 3H), 1.63–1.93 (m, 16H). ¹³C NMR (100

MHz, CDCl₃) δ 75.86, 62.24, 43.64, 33.41, 32.40, 29.13, 27.88, 26.48, 26.28, 26.14, 22.04. HPLC conditions: Chiralcel OD-H column (25 cm \times 0.46 cm ID); *n*-hexane/2-propanol = 95:5; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; t_R (*R*) = 6.04 min and t_R (*S*) = 6.85 min.

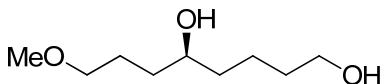
(*R*)-Ethyl 5-hydroxy-8-methoxyoctanoate (2h)



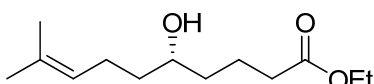
Colorless oil, 1 h, 45% yield, 97% ee, $[\alpha]_D^{20} -4.2$ (*c* 1.0, MeOH).

¹H NMR (400 MHz, CDCl₃) δ 4.10 (q, *J* = 7.2 Hz, 2H), 3.61–3.51 (m, 1H), 3.39 (t, *J* = 5.2 Hz, 2H), 3.32 (s, 3H), 2.76 (s, 1H), 2.31 (t, *J* = 7.2 Hz, 2H), 1.80–1.55 (m, 5H), 1.49–1.37 (m, 3H), 1.23 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 173.75, 72.98, 70.94, 60.21, 58.53, 36.74, 34.83, 34.15, 26.19, 21.11, 14.19. HPLC conditions: Chiralcel AD-H column (25 cm \times 0.46 cm ID); *n*-hexane/2-propanol = 98:2; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; t_R (*R*) = 17.46 min and t_R (*S*) = 18.43 min. HRMS (ESI) Calcd for C₁₁H₂₃O₄ ([M + H]⁺): 219.1596, Found: 219.1590.

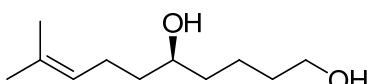
(S)-8-Methoxyoctane-1,5-diol (3h)

 Colorless oil, 1 h, 46% yield, 91% ee, $[\alpha]_D^{20} +1.0$ (*c* 1.0, MeOH). ^1H NMR (400 MHz, CDCl_3) δ 3.64–3.54 (m, 3H), 3.39 (t, *J* = 5.6 Hz, 2H), 3.32 (s, 3H), 3.11 (br s, 1H), 2.47 (br s, 1H), 1.73–1.63 (m, 2H), 1.63–1.48 (m, 4H), 1.47–1.36 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 73.02, 71.29, 62.46, 58.53, 36.88, 34.78, 32.46, 26.18, 21.83. HPLC conditions: Chiralcel OD-H column (25 cm \times 0.46 cm ID); *n*-hexane/2-propanol = 97:3; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; t_R (*R*) = 27.22 min and t_R (*S*) = 28.78 min. HRMS (ESI) Calcd for $\text{C}_9\text{H}_{21}\text{O}_4$ ($[\text{M} + \text{H}]^+$): 177.1486, Found: 177.1488.

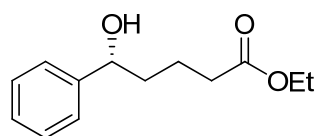
(R)-Ethyl 5-hydroxy-9-methyldec-8-enoate (2i)

 Colorless oil, 2 h, 44% yield, 94% ee, $[\alpha]_D^{20} -1.8$ (*c* 1.0, MeOH). ^1H NMR (400 MHz, CDCl_3) δ 5.16–5.09 (m, 1H), 4.13 (q, *J* = 7.2 Hz, 2H), 3.64–3.56 (m, 1H), 2.33 (t, *J* = 7.2 Hz, 2H), 2.18–1.99 (m, 2H), 1.84–1.65 (m, 5H), 1.62 (s, 3H), 1.57 (br s, 1H), 1.54–1.40 (m, 4H), 1.26 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 173.76, 132.04, 124.00, 71.07, 60.25, 37.27, 36.71, 34.11, 25.66, 24.30, 20.93, 17.62, 14.18. HPLC conditions: Chiralcel OJ-H column (25 cm \times 0.46 cm ID); *n*-hexane/2-propanol = 98:2; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; t_R (*R*) = 7.30 min and t_R (*S*) = 7.70 min. HRMS (ESI) Calcd for $\text{C}_{13}\text{H}_{25}\text{O}_3$ ($[\text{M} + \text{H}]^+$): 229.1799, Found: 229.1801.

(S)-9-Methyldec-8-ene-1,5-diol (3i)

 Colorless oil, 2 h, 48% yield, 93% ee, $[\alpha]_D^{20} +4.0$ (*c* 1.0, MeOH). ^1H NMR (400 MHz, CDCl_3) δ 5.17–5.09 (m, 1H), 3.70–3.58 (m, 3H), 2.18–1.99 (m, 2H), 1.69 (s, 3H), 1.66–1.36 (m, 13H). ^{13}C NMR (100 MHz, CDCl_3) δ 132.01, 124.07, 71.50, 62.47, 37.36, 36.84, 32.43, 25.67, 24.35, 21.73, 17.64. HPLC conditions: Chiralcel OD-H column (25 cm \times 0.46 cm ID); *n*-hexane/2-propanol = 90:10; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; t_R (*R*) = 6.89 min and t_R (*S*) = 7.60 min. HRMS (ESI) Calcd for $\text{C}_{11}\text{H}_{23}\text{O}_2$ ($[\text{M} + \text{H}]^+$): 187.1693, Found: 187.1695.

(R)-Ethyl 5-hydroxy-5-phenylpentanoate (2j)⁷



Colorless oil, 0.4 h, 49% yield, 94% ee, $[\alpha]^{20}_D +30.6$ (c 1.0, CHCl_3). [lit.⁷

$[\alpha]^{23}_D -31.7$ (c 1.2, CHCl_3), *S* enantiomer]. ^1H NMR (400 MHz, CDCl_3)

δ 7.37–7.30 (m, 4H), 7.29–7.23 (m, 1H), 4.69–4.59 (m, 1H), 4.09 (q, J =

7.2 Hz, 2H), 2.40 (s, 1H), 2.30 (t, J = 7.2 Hz, 2H), 1.84–1.69 (m, 3H), 1.68–1.52 (m, 1H), 1.23 (t, J = 7.2

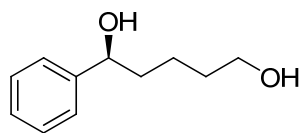
Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 173.62, 144.49, 128.37, 127.46, 125.77, 73.96, 60.26, 38.28,

33.92, 21.11, 14.14. HPLC conditions: Chiralcel OD-H column (25 cm \times 0.46 cm ID); *n*-hexane/2-

propanol = 95:5; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; t_R (*R*) = 16.07 min and t_R (*S*) =

17.39 min.

(*S*)-1-Phenylpentane-1,5-diol (**3j**)⁸



Colorless oil, 0.4 h, 47% yield, 95% ee, $[\alpha]^{20}_D -41.2$ (c 1.0, CHCl_3). [lit.⁸

$[\alpha]^{20}_D -41.9$ (c 1.0, benzene)]. HPLC conditions: Chiralcel OD-H column

(25 cm \times 0.46 cm ID); *n*-hexane/2-propanol = 90:10; temp, rt; flow rate

= 1.0 mL/min; 220 nm UV detector; t_R (*S*) = 12.45 min and t_R (*R*) = 13.44 min.

Kinetic study of the kinetic resolution of *rac*-**2a**.

Kinetic study of the kinetic resolution of *rac*-**2a** was performed according to the general procedure for the asymmetric hydrogenation of *rac*-**2**. The hydrogenations were performed in parallel and stopped after 15, 30, 45, 60, 90, 120 min and the conversions or yields and ee values were determined by ^1H NMR and HPLC, respectively. The data and the plot are outlined in Table 1 and Figure 1, respectively.

Table 1 The data of asymmetric hydrogenation of *rac*-**2a**^a.

Time (min)	2a		3a	
	yield (%)	ee (%)	yield (%)	ee (%)
0	100	0	0	
15	74	31.7	26	97.3
30	54	77.3	46	95.5
45	51	91.7	49	94.6
60	50	93.7	50	94.2
90	46	100	54	90.6
120	45	100	55	85.4

^a ^1H NMR showed that the reaction mixture contained less than 2% δ -lactone, which was calculated to the yield of **2a** in this table.

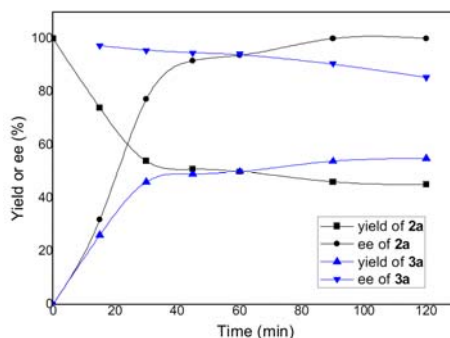
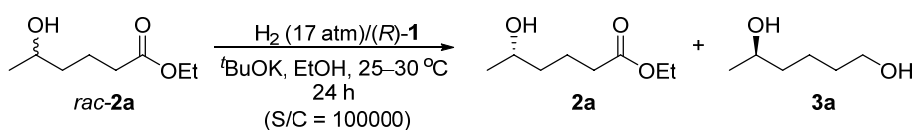


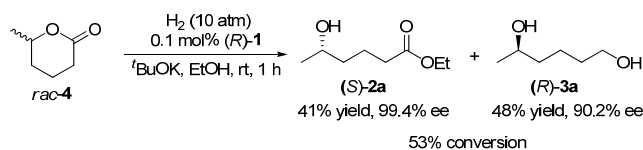
Figure 1. The plots of hydrogenation of *rac*-**2a** with (*R*)-**1**.

Kinetic resolution of *rac*-2a** at S/C = 100000.**



To a 100 mL hydrogenation vessel in an autoclave was added *rac*-**2** (8.0 g, 50 mmol), a solution of iridium catalyst (*R*)-**1** in EtOH (0.0005 mmol/mL, 1.0 mL, 0.0005 mmol), a solution of *t*-BuOK in EtOH (0.2 mmol/mL, 9 mL, 1.8 mmol), and 20 mL of anhydrous EtOH under N₂ atmosphere. The autoclave was purged with hydrogen by pressurizing to 10 atm and releasing the pressure. This procedure was repeated three times and then pressurized to 17 atm of H₂. After the reaction mixture was stirred at room temperature (25 °C) for 24 h, saturated NH₄Cl (20 mL) was added. EtOH was removed in vacuo and the residue was extracted with EtOAc (20 mL × 3). The combined extracts were washed with brine, dried over MgSO₄ and concentrated in vacuo to afford a crude product, which was purified by flash column chromatography on silical gel with petroleum ether/ethyl acetate (3:1 to 1:3) as the eluent to afford 3.52 g (44% yield) (*S*)-**2a** with 97% ee and 2.71 g (46% yield) (*R*)-**3a** with 93% ee. The analytic data and HPLC conditions see above.

Kinetic resolution of δ -methyl- δ -valerolactone (*rac*-4**) at S/C = 1000.**

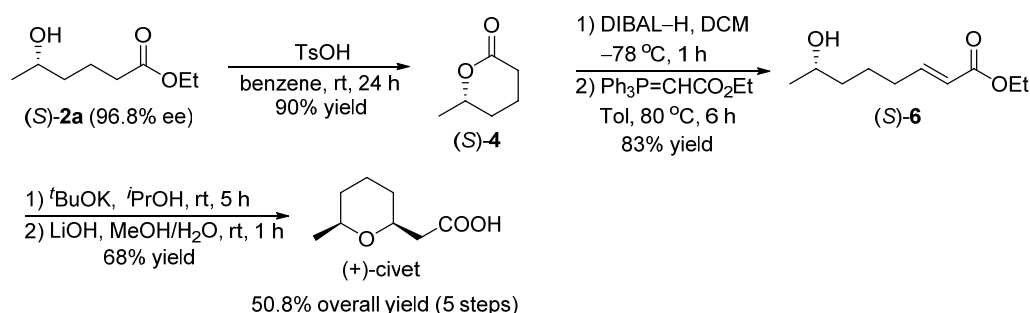


To a 20 mL hydrogenation vessel in an autoclave was added racemic δ -methyl- δ -valerolactone (*rac*-**2**, 114 mg, 1.0 mmol), a solution of iridium catalyst (*R*)-**1** in EtOH (0.002 mmol/mL, 0.5 mL, 0.001 mmol), a solution of *t*-BuOK in EtOH (0.08 mmol/mL, 0.5 mL, 0.04 mmol), and 1.0 mL of anhydrous EtOH. The autoclave was purged with hydrogen by pressurizing to 5 atm and releasing the pressure. This procedure was repeated three times and then pressurized to 10 atm of H₂. The reaction mixture was stirred at room temperature (25–30 °C) until the hydrogen pressure bled down to 9.5 atm (1 h). The solvent was removed in vacuo and the residue was purified by flash column chromatography on silical gel with petroleum ether/ethyl acetate as an eluent to afford (*S*)-**2a** in 41% yield with 99.4% ee and (*R*)-**3a** in 48%

yield with 90% ee (53% conversion, determined by ^1H NMR). The analytic data and HPLC conditions see above.

(C) Asymmetric synthesis of (+)-civet and (*R*)-lisofylline.

The asymmetric synthesis of (+)-civet was outlined below.



Synthesis of (*S*)-4

To a solution of (*S*)-**2a** (528 mg, 3 mmol) in benzene (10 mL) was added TsOH (114 mg, 0.6 mmol) at room temperature. After the reaction mixture was stirred for 24 h, saturated NaHCO_3 (5 mL) was added. The layers were separated and the aqueous layer was extracted with EtOAc (5 mL \times 3). The combined organic layers were washed with brine, dried over MgSO_4 and concentrated in vacuo to afford a crude product, which was purified by chromatography on silica gel column (petroleum ether/ethyl acetate = 3:1) to provide the desired product (*S*)-**4** (308 mg, 90% yield) as a colorless oil. $[\alpha]_{\text{D}}^{20}$ -31.1 (c 1.0, EtOH). [lit.⁹ $[\alpha]_{\text{D}}^{20}$ -30.2 (c 1.3, EtOH)]. ^1H NMR (400 MHz, CDCl_3) δ 4.48–4.37 (m, 1H), 2.64–2.51 (m, 1H), 2.50–2.37 (m, 1H), 1.99–1.77 (m, 3H), 1.60–1.43 (m, 1H), 1.36 (d, J = 6.4 Hz, 3H).

Synthesis of (*S*)-6¹⁰

To a solution of (*S*)-**4** (228 mg, 2 mmol) in DCM (5 mL) was added dropwise DIBAL-H (1.0 M in hexane, 2 mL, 2 mmol) at -78 $^\circ\text{C}$ over 30 min. After the reaction mixture was stirred for 0.5 h at this temperature, saturated sodium potassium tartrate (Rochelle salt, 5 mL) was added. The mixture was allowed to warm to room temperature and vigorously stirred for 1 h. The layers were separated and the aqueous layer was extracted with DCM (5 mL \times 3). The combined organic layers were washed with brine, dried over MgSO_4 and concentrated in vacuo to afford (*S*)-**5** (215 mg, 93% yield) as a crude product.

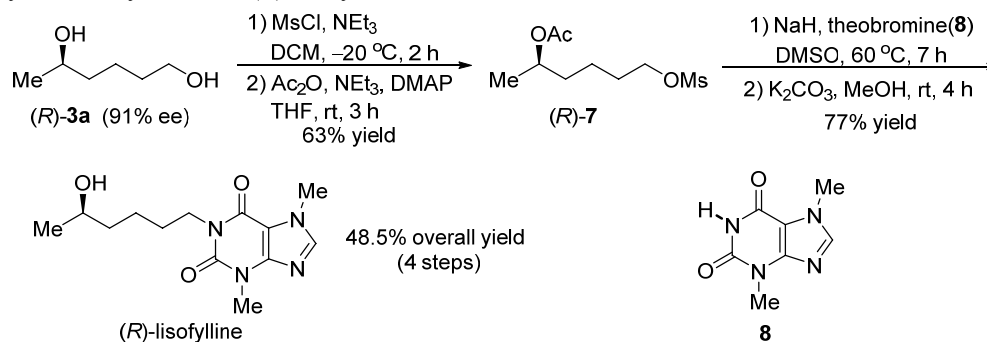
To a solution of the crude lactol in Tol (10 mL) was added (carbethoxymethylene)-triphenylphosphorane (1.04 g, 3 mmol), and the mixture was stirred at 80 $^\circ\text{C}$ for 6 h. The solvent was

evaporated and the remaining crude product was purified by chromatography on silica gel column (petroleum ether/ethyl acetate = 3:1) to provide the desired product (*S*)-**6** (308 mg, 83% yield over two steps) as a colorless oil. $[\alpha]_D^{20} +9.1$ (c 1.0, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 6.95 (dt, *J* = 15.6, 6.8 Hz, 1H), 5.81 (dt, *J* = 15.6, 1.6 Hz, 1H), 4.17 (q, *J* = 7.2 Hz, 2H), 3.85–3.74 (m, 1H), 2.26–2.17 (m, 2H), 1.66–1.39 (m, 5H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.18 (d, *J* = 6.4 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 166.69, 148.87, 121.51, 67.74, 60.16, 38.54, 32.02, 24.15, 23.54, 14.22. HRMS (ESI) Calcd for C₁₀H₁₈O₃ ([M + H]⁺): 187.1329, Found: 187.1327.

Synthesis of (+)-civet

To a solution of (*S*)-**6** (186 mg, 1 mmol) in *i*PrOH (5 mL) was added *t*BuOK (22.4 mg, 0.2 mmol) at room temperature. After the reaction mixture was stirred for 5 h, the solvent of the reaction mixture was slowly removed under reduce pressure and the residue was dissolved with methanol (5 mL). 1 N LiOH (5 mL, 5 mmol) was added to the mixture and the reaction mixture was stirred for 1 h. After acidified with 2 N HCl to pH 1, the solution was extracted with EtOAc (5 mL × 3), dried over anhydrous MgSO₄, and concentrated in vacuo to yield a crude product, which was purified by flash chromatography on silica gel column (petroleum ether/ethyl acetate = 1:1) to provide the desired product (+)-civet (107 mg, 68% yield over two steps) as a colorless oil. $[\alpha]_D^{20} +22.0$ (c 1.0, CHCl₃). [lit. ¹¹ $[\alpha]_D^{20} +22.4$ (c 0.25, CHCl₃)]. ¹H NMR (400 MHz, CDCl₃) δ 9.40 (s, 1H), 3.81–3.71 (m, 1H), 3.56–3.45 (m, 1H), 2.56 (dd, *J* = 15.6, 7.6 Hz, 1H), 2.46 (dd, *J* = 15.6, 5.2 Hz, 1H), 1.86–1.77 (m, 1H), 1.67–1.46 (m, 3H), 1.30–1.19 (m, 2H), 1.16 (d, *J* = 6.4 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 175.72, 74.41, 73.93, 41.23, 32.71, 30.72, 23.16, 21.94.

The asymmetric synthesis of (*R*)-lisofylline was outlined below.



Synthesis of (*R*)-7

To a solution of (*R*)-**3a** (730 mg, 5 mmol) in DCM (10 mL) was added Et₃N (555 mg, 5.5 mmol) and MsCl (570 mg, 5 mmol) at –20 °C under N₂ atmosphere. The reaction mixture was stirred at the same temperature for 2 h and quenched with saturated NH₄Cl (15 mL). The layers were separated and the aqueous layer was extracted with DCM (15 mL × 3). The combined extractes were washed with saturated NaHCO₃ (20 mL) and brine, dried over anhydrous MgSO₄ and concentrated in vacuo to afford a crude product, which was purified by flash chromatography on silica gel column (petroleum ether/ethyl acetate = 3:1) to provide the desired product (*R*)-5-hydroxyhexyl methanesulfonate (672 mg, 69% yield) as a colorless oil. [α]_D²⁰ –9.6 (*c* 1.0, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 4.24 (t, *J* = 6.4 Hz, 2H), 3.87–3.77 (m, 1H), 3.01 (s, 3H), 1.83–1.73 (m, 2H), 1.68 (s, 1H), 1.58–1.42 (m, 4H), 1.20 (d, *J* = 6.0 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 69.92, 67.63, 38.37, 37.31, 29.03, 23.56, 21.64. HRMS (ESI) Calcd for C₇H₁₇O₄S ([M + H]⁺): 197.0843, Found: 197.0841.

A mixture of (*R*)-5-hydroxyhexyl methanesulfonate (390 mg, 1.74 mmol), Ac₂O (673 mg, 6.6 mmol), NEt₃ (707 mg, 7.0 mmol), DMAP (61 mg, 0.5 mmol) and THF (10 mL) were stirred at room temperature for 4 h. After removing of THF in vacuo, the residue was diluted with EtOAc (10 mL). The solution was washed with saturated NaHCO₃ (10 mL) and brine, dried over anhydrous MgSO₄ and concentrated in vacuo to afford a crude product, which was purified by flash chromatography on silica gelcolumn (petroleum ether/ethyl acetate = 3:1) to provide the desired product (*R*)-**7** (426 mg, 92% yield) as a colorless oil. [α]_D²⁰ –1.8 (*c* 1.0, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 4.94–4.83 (m, 1H), 4.21 (t, *J* = 6.4 Hz, 2H), 3.00 (s, 3H), 2.02 (s, 3H), 1.81–1.70 (m, 2H), 1.66–1.39 (m, 4H), 1.20 (d, *J* = 6.4 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 170.71, 70.39, 69.67, 37.32, 35.15, 28.85, 21.33, 21.31, 19.87. HRMS (ESI) Calcd for C₉H₁₉O₅S ([M + H]⁺): 239.0948, Found: 239.0950.

Synthesis of (*R*)-lisofylline

To a solution of NaH (38.4 mg, 1.6 mmol) in DMSO (10 mL) was slowly added the theobromine **8** (288 mg, 1.6 mmol) under N₂ atmosphere. The reaction mixture was heated to 60 °C and added slowly a solution of (*R*)-**7** (288 mg, 1.6 mmol) in DMSO (2 mL). After stirring 20 h and cooling to room temperature, H₂O (10 mL) was added to the reaction mixture. The solution was extracted with EtOAc (10 mL × 3), and the combined extractes were washed with brine, dried over anhydrous MgSO₄ and concentrated in vacuo to afford a crude product.

The obtained crude product was dissolved in MeOH (20 mL) and K₂CO₃ (1.1 g, 8 mmol) was added

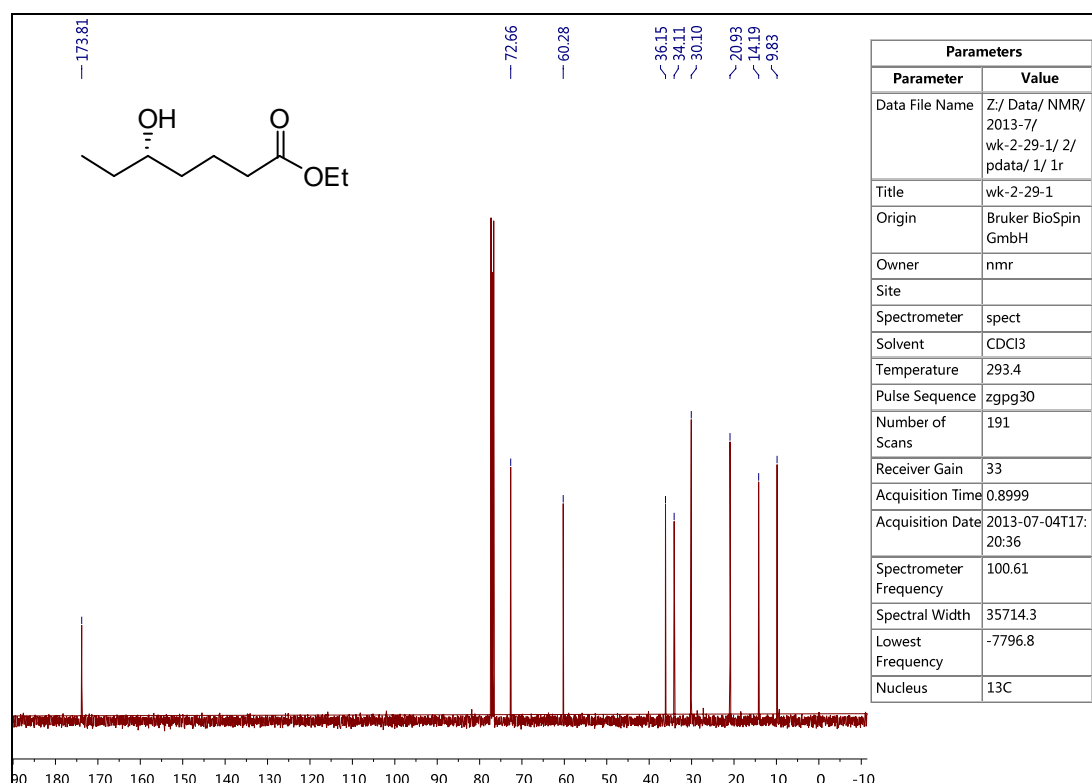
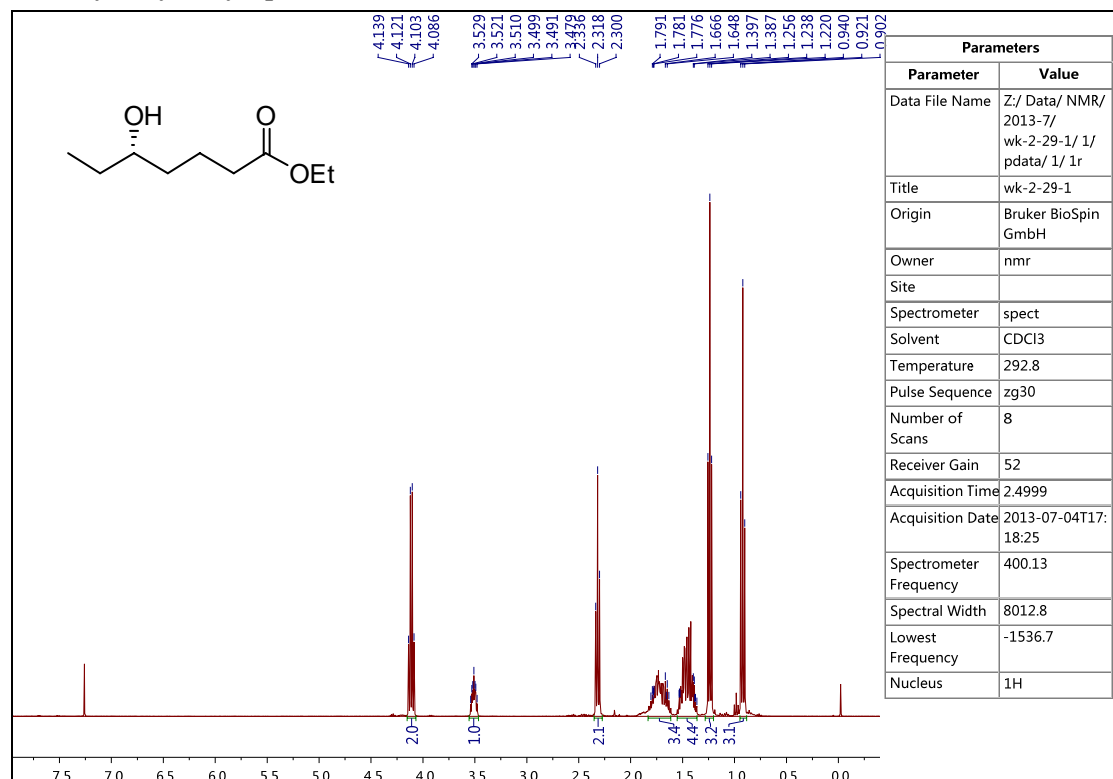
to the solution at room temperature. After stirring 10 h, H₂O (10 mL) was added to the reaction mixture. The solution was extracted with EtOAc (10 mL × 3), and the combined extractes were washed with brine, dried over anhydrous MgSO₄ and concentrated in vacuo to afford a crude product, which was purified by flash chromatography on silica gel column with ethyl acetate as the eluent to provide the desired product (*R*)-lisofylline (375 mg, 77% yield) as white solid. m.p. 123–125 °C, $[\alpha]_D^{20}$ –5.0 (*c* 1.0, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.50 (s, 1H), 4.00 (t, *J* = 7.6 Hz, 2H), 3.97 (s, 3H), 3.83–3.75 (m, 1H), 3.55 (s, 3H), 1.73–1.62 (m, 2H), 1.56–1.35 (m, 5H), 1.17 (d, *J* = 6.0 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 155.33, 151.47, 148.71, 141.39, 107.64, 67.79, 41.10, 38.73, 33.55, 29.66, 27.86, 23.46, 22.87. HRMS (ESI) Calcd for C₁₃H₂₁N₄O₃ ([M + H]⁺): 281.1609, Found: 281.1613.

References

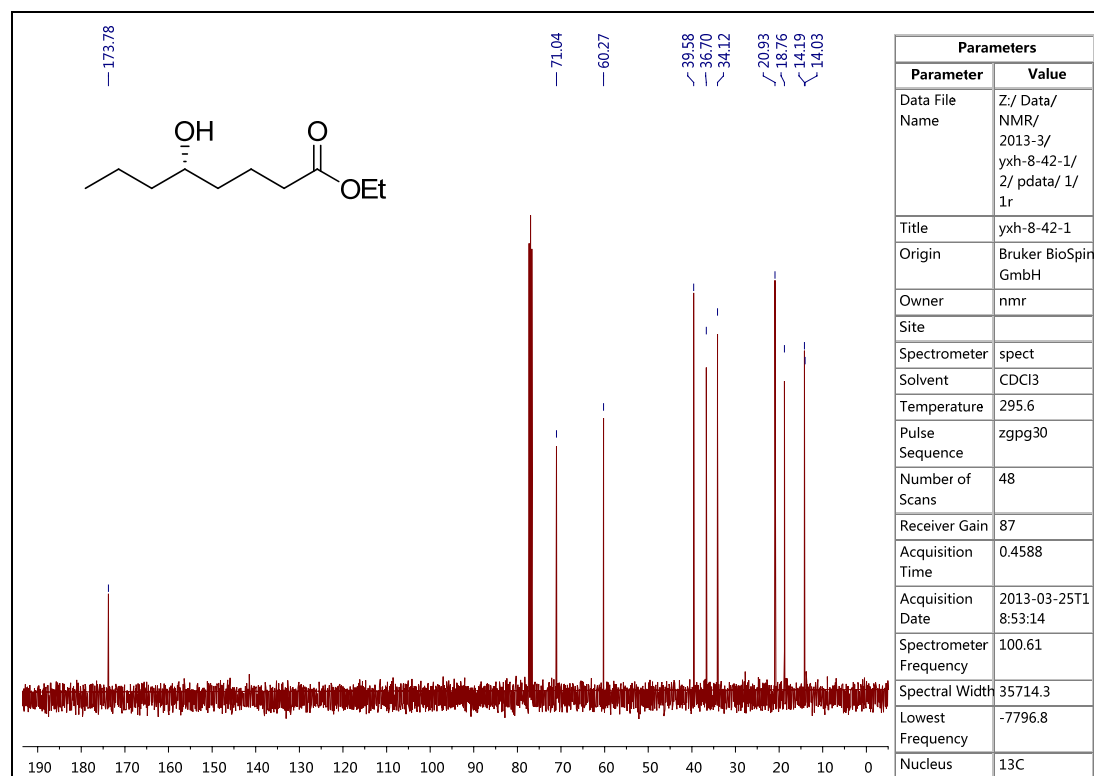
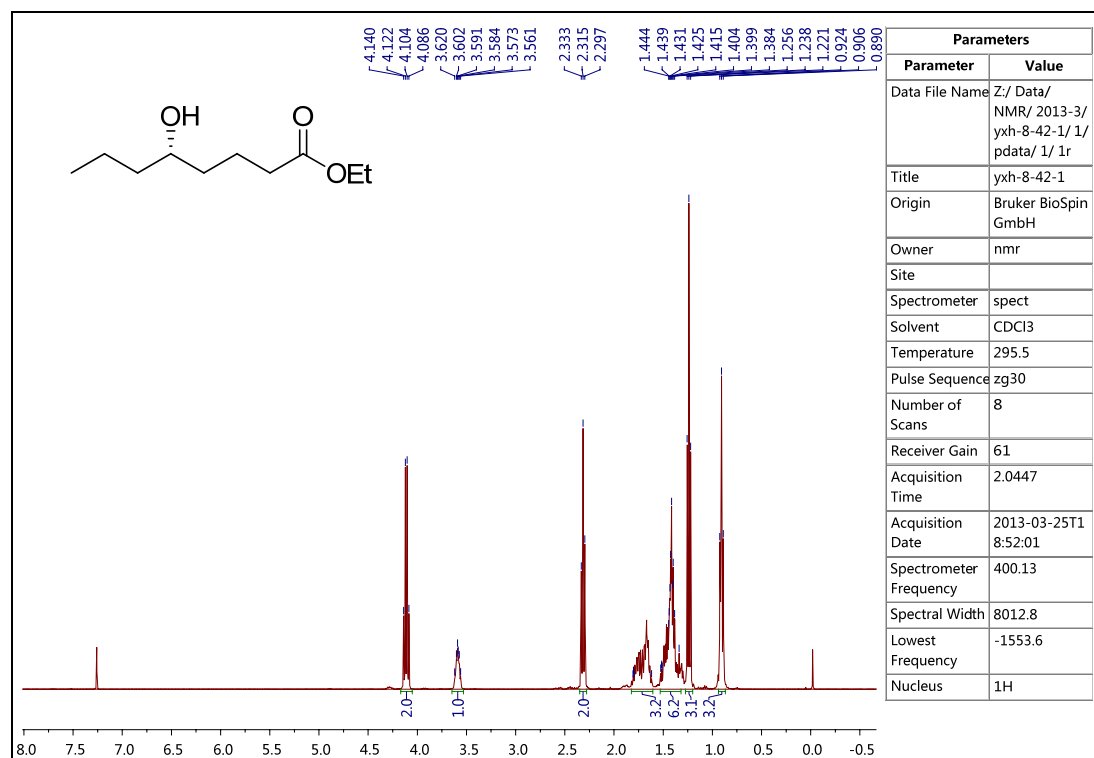
1. Sugai, T.; Hamada, K.; Akeboshi, T.; Ikeda, H.; Hatay, H. *Synlett* **1997**, 983.
2. Riswoko, A.; Aoki, Y.; Hirose, T.; Nohira, H. *Enantiomer* **2002**, 7, 33.
3. Seehafer, K.; Rominger, F.; Helmchen, G.; Langhans, M.; Robinson, D. G.; Özata, B.; Brügger, B.; Strating, J. R. P. M.; Kuppeveld, F. J. M.; Klein, C. D. *J. Med. Chem.* **2013**, 56, 5872.
4. Rieke, R. D.; Hanson, M. V.; Brown, J. D. *J. Org. Chem.* **1996**, 61, 2726.
5. Ramón, D. J.; Yus, M. *Tetrahedron* **1992**, 48, 3585.
6. Jiang, X.; London, E. K.; Morris, D. J.; Clarkson, G. J.; Wills, M. *Tetrahedron* **2010**, 66, 9828.
7. Fujii, A.; Hashiguchi, S.; Uematsu, N.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1996**, 118, 2521.
8. Yang, X.-H.; Xie, J.-H.; Liu, W.-P.; Zhou, Q.-L. *Angew. Chem., Int. Ed.* **2013**, 52, 7833.
9. Arai, K.; Rawlings, B. J.; Yoshizawa, Y.; Vederas, J. C. *J. Am. Chem. Soc.* **1989**, 111, 3391.
10. Valot, G.; Regens, C. S.; O'Malley, D. P.; Godineau, E.; Takikawa, H.; Fürstner, A. *Angew. Chem., Int. Ed.* **2013**, 52, 9534.
11. Sultana, S.; Indukuri, K.; Deka, M. J.; Saikia, A. K. *J. Org. Chem.* **2013**, 78, 12182.

(D) NMR spectra of new compounds

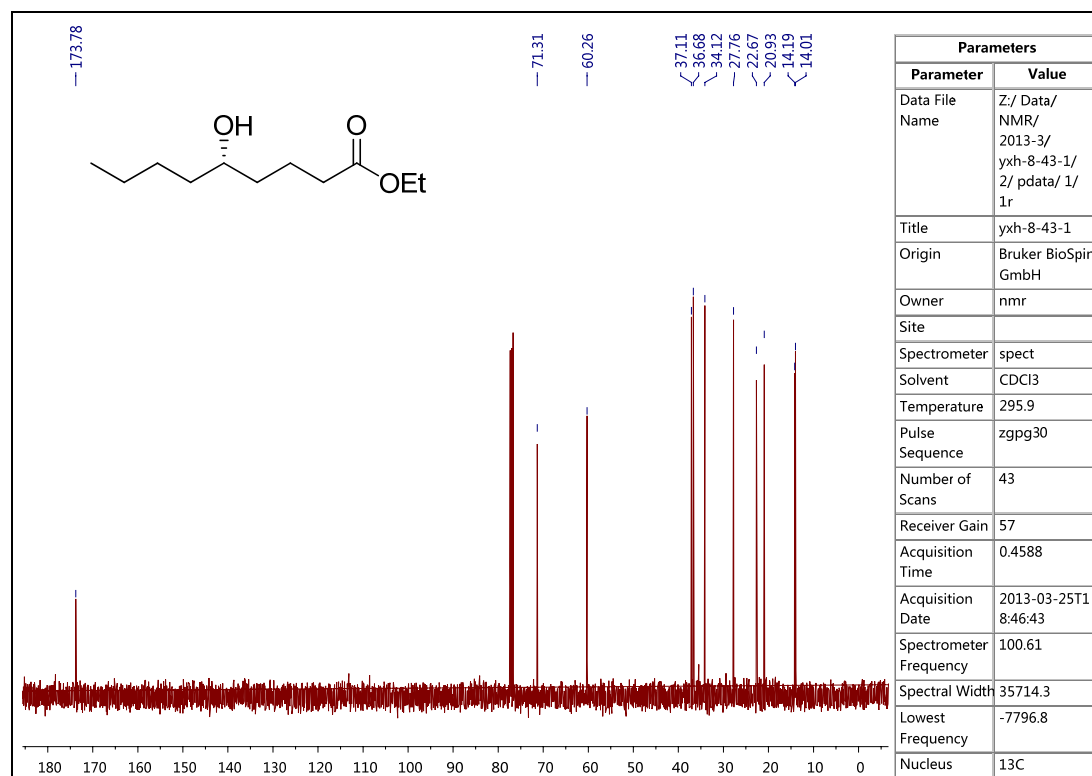
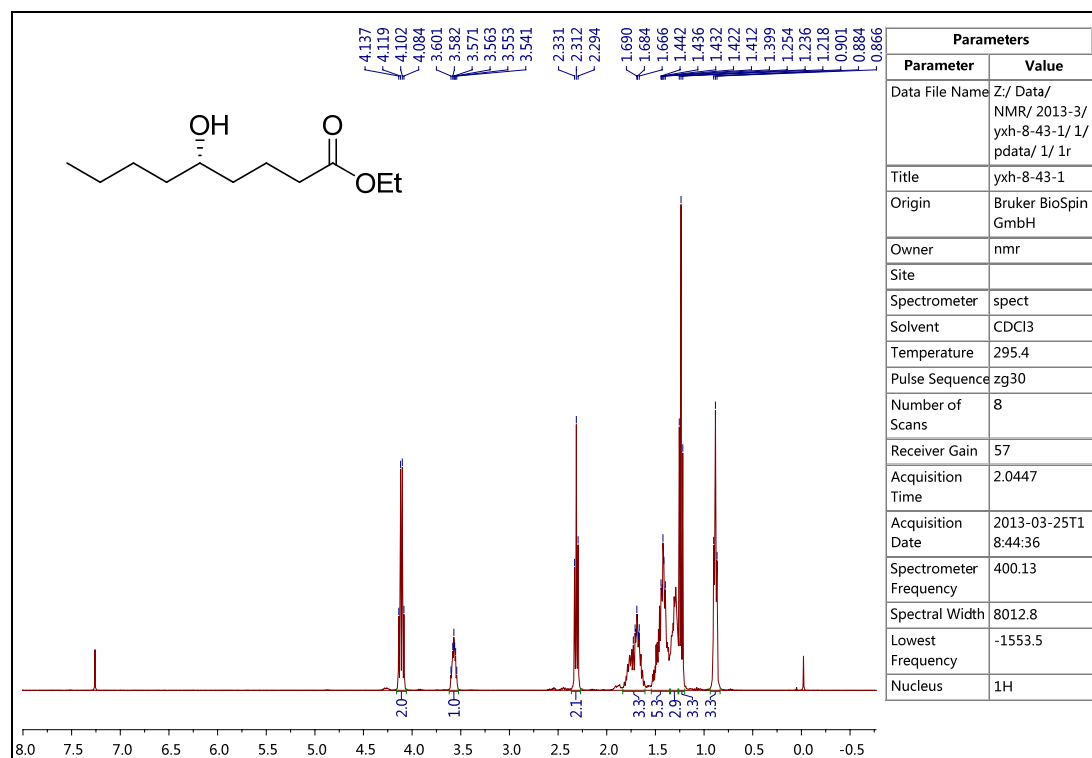
(S)-Ethyl 5-hydroxyheptanoate (2b)



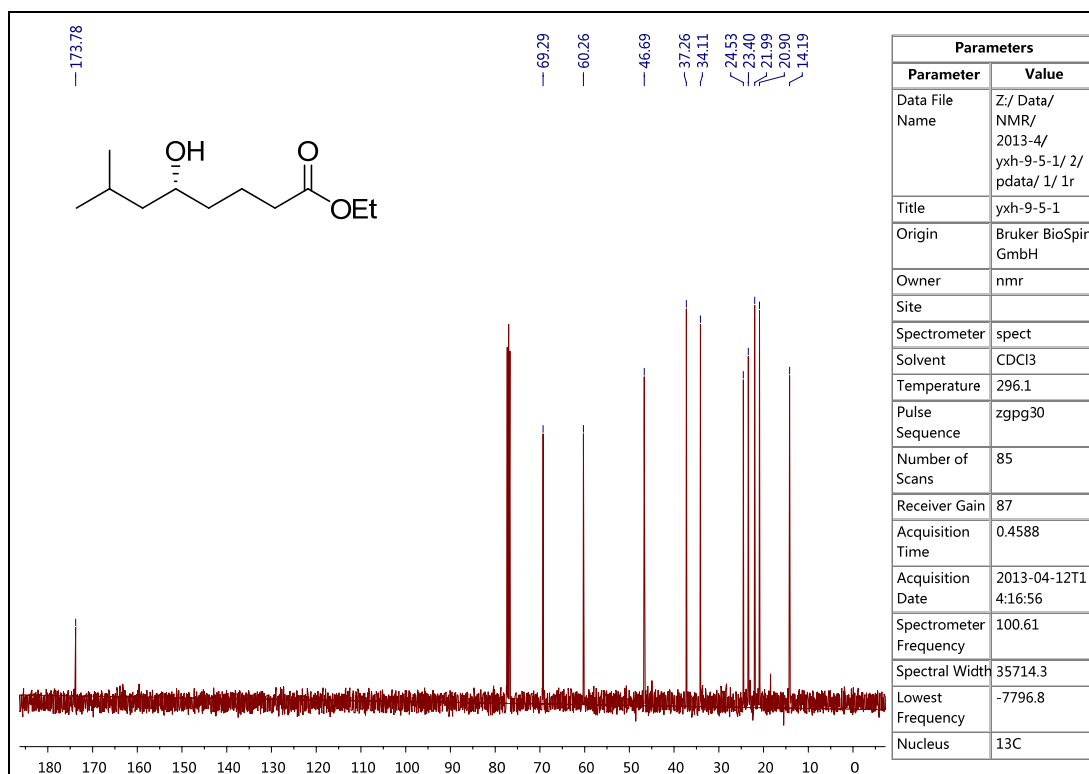
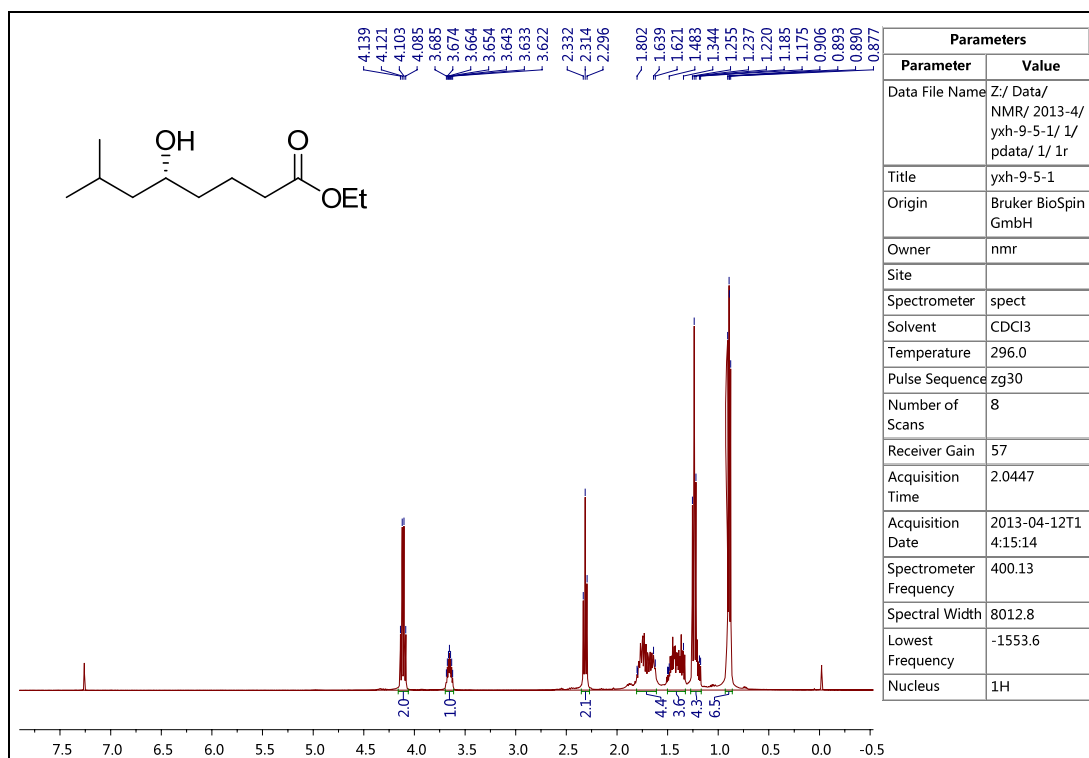
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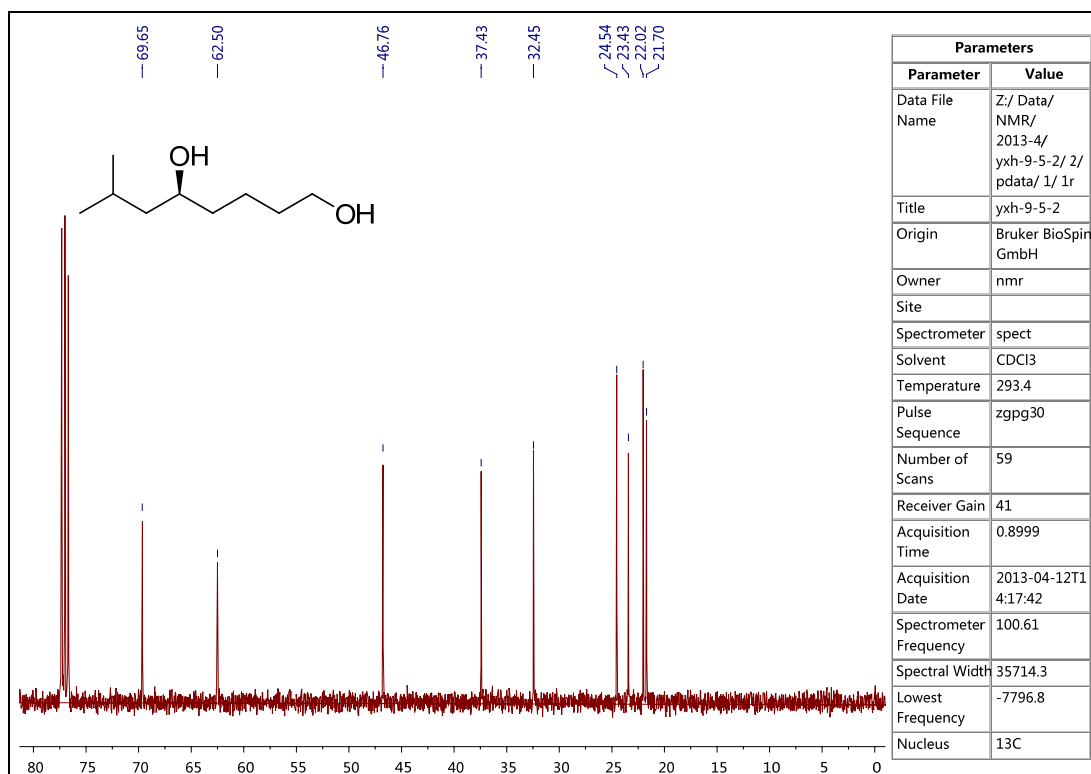
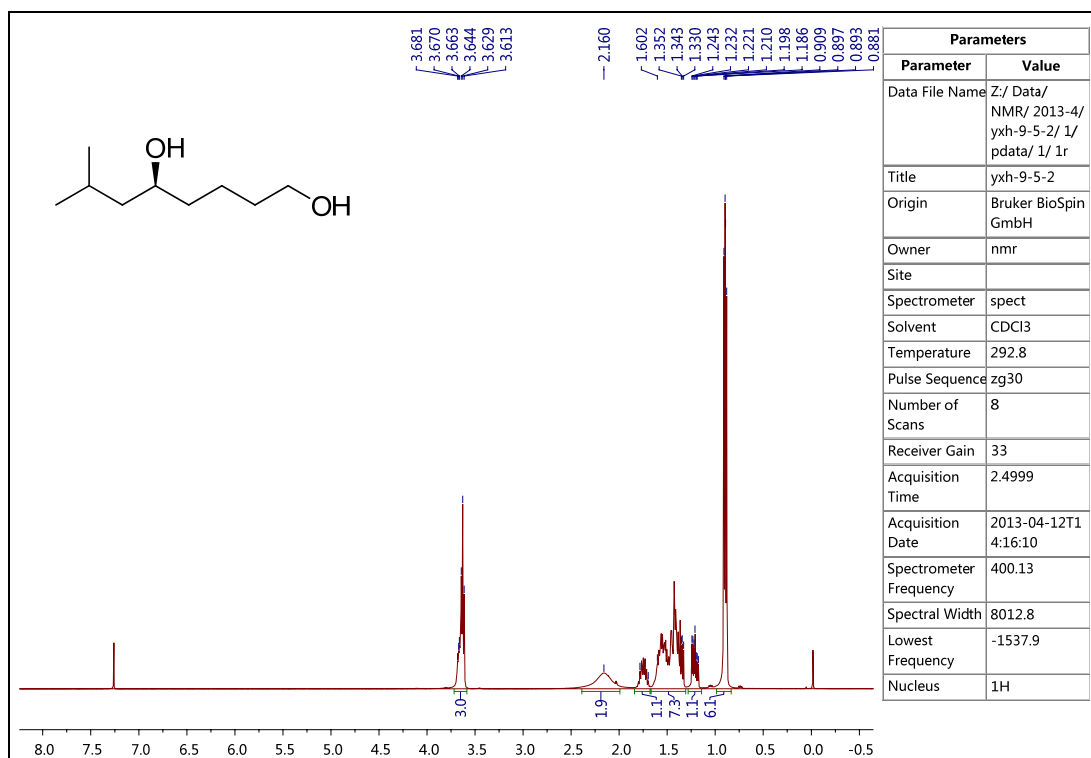
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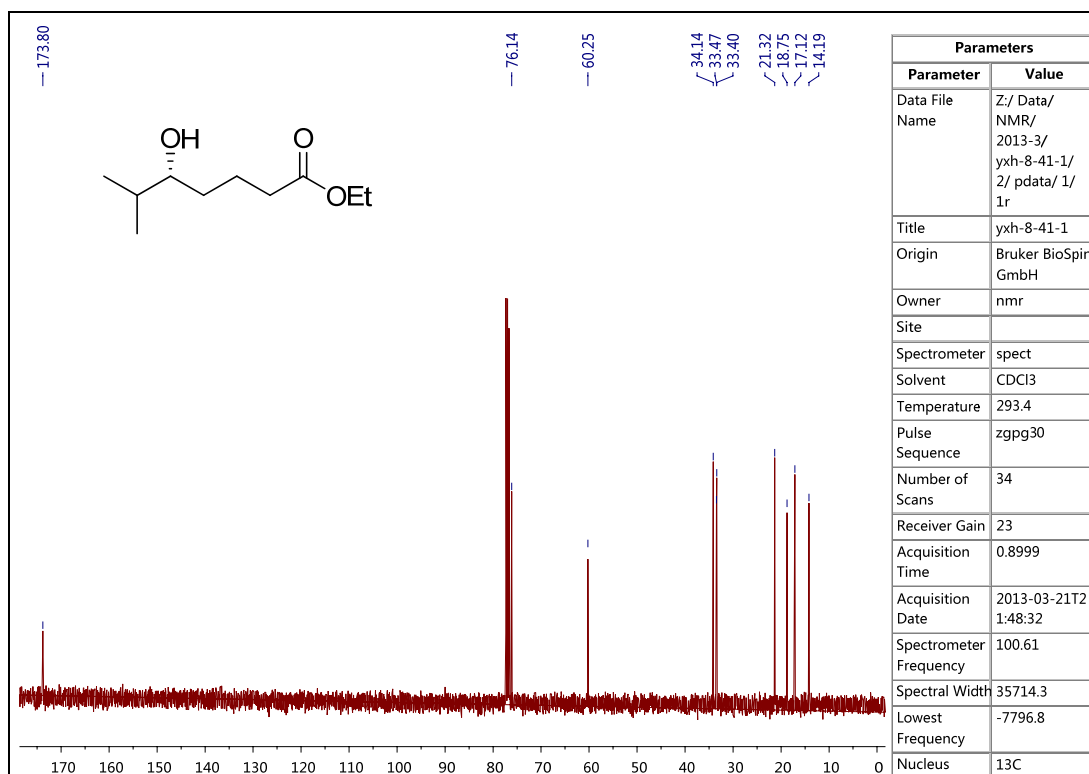
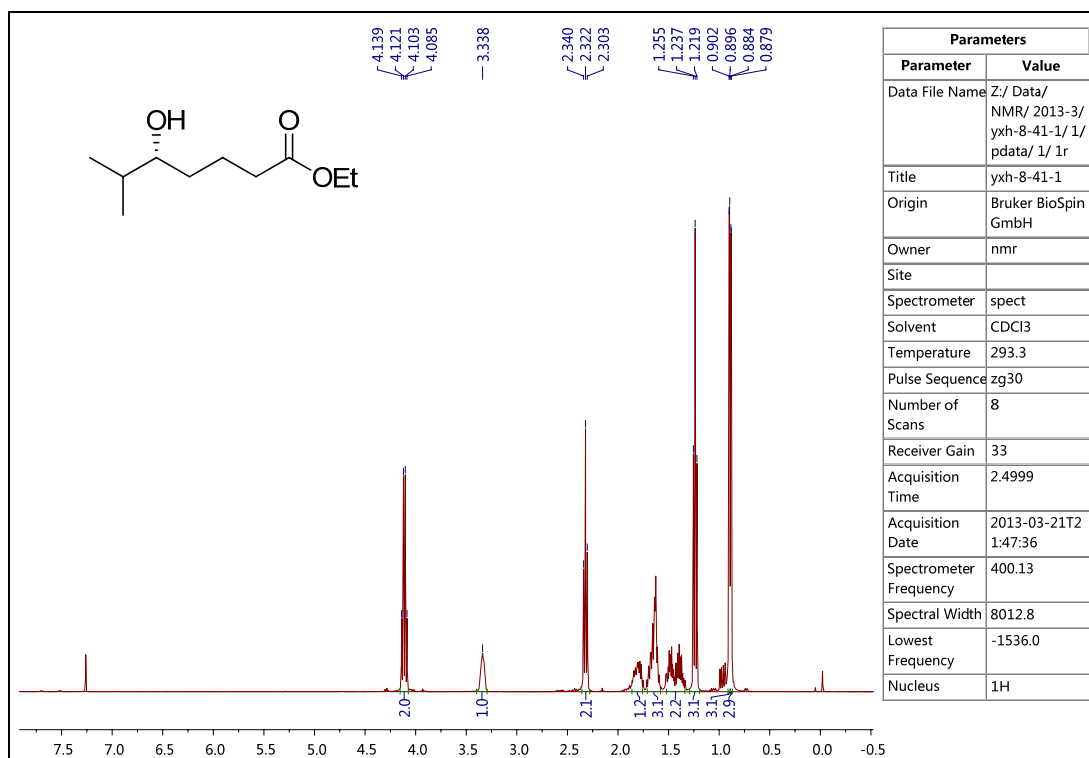
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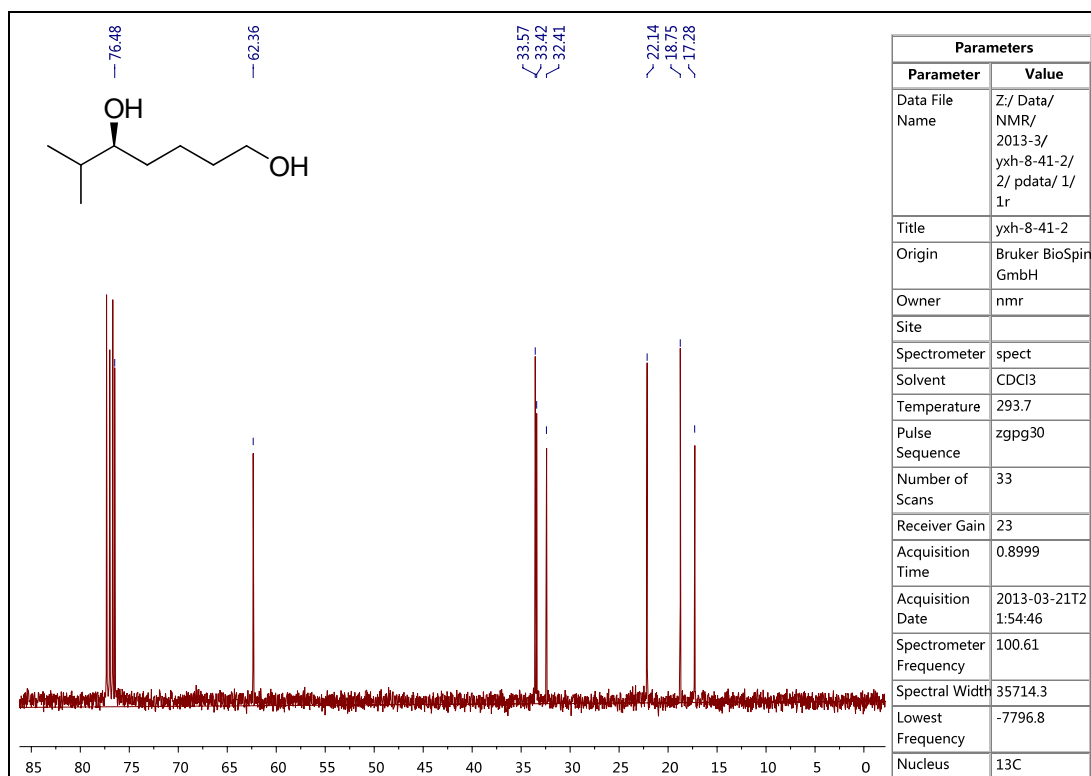
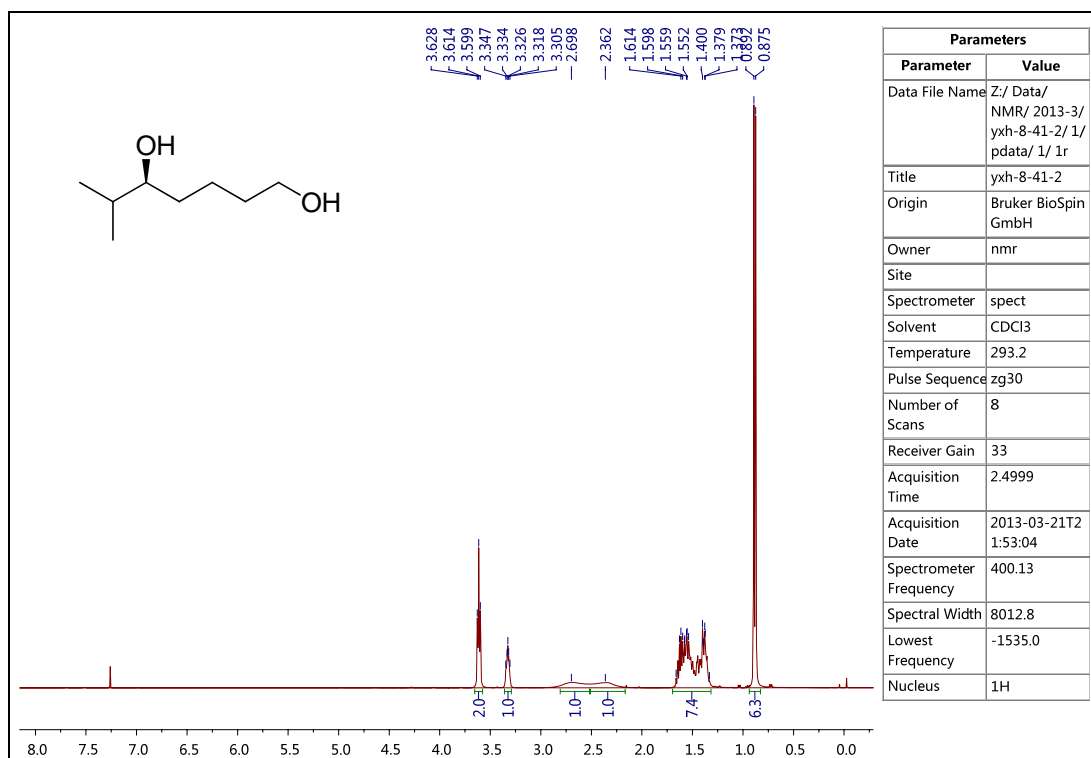
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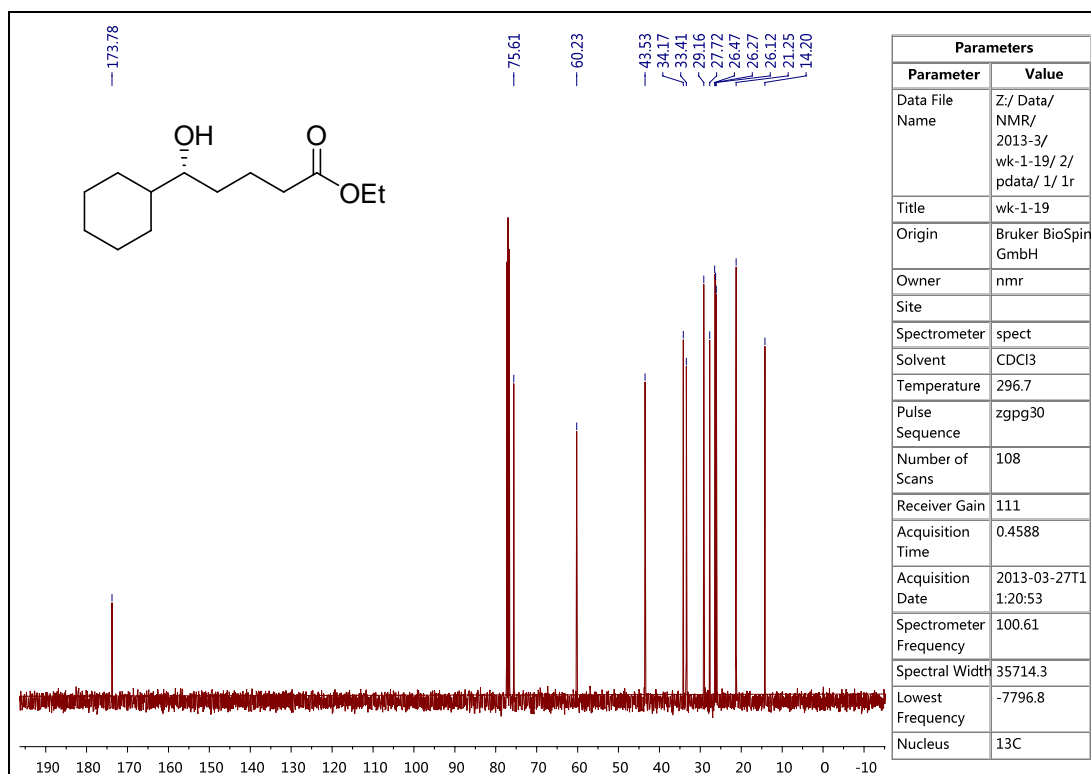
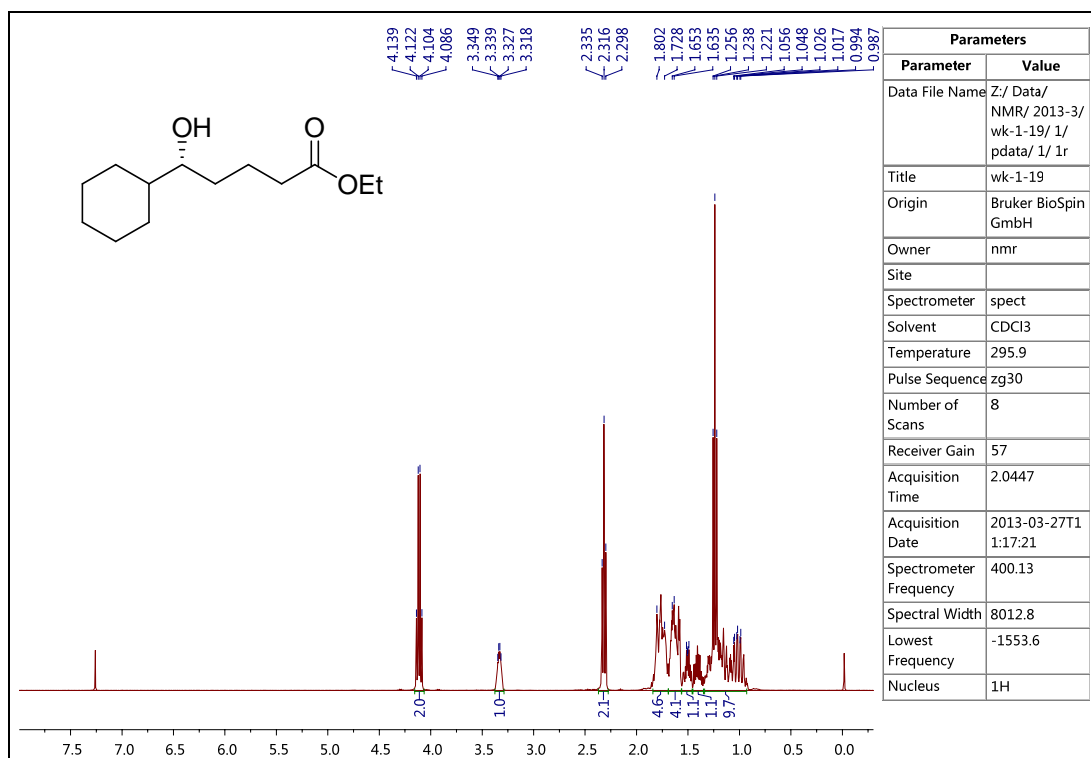
(R)-Ethyl 5-hydroxy-6-methylheptanoate (2f)



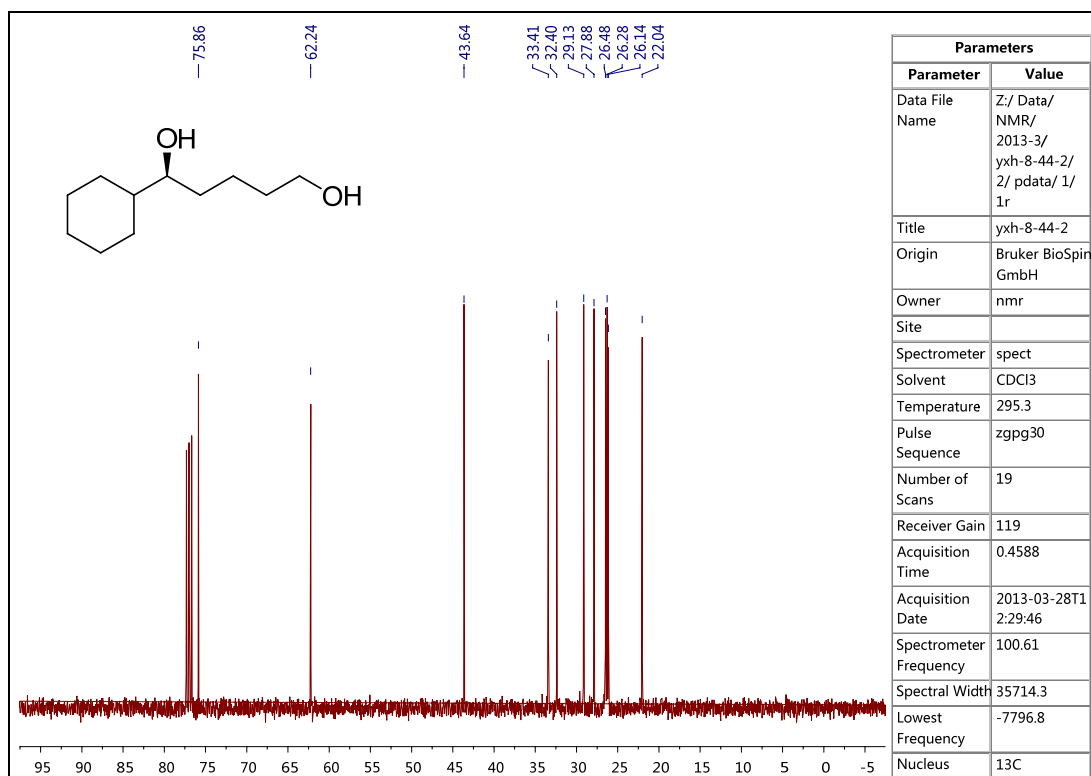
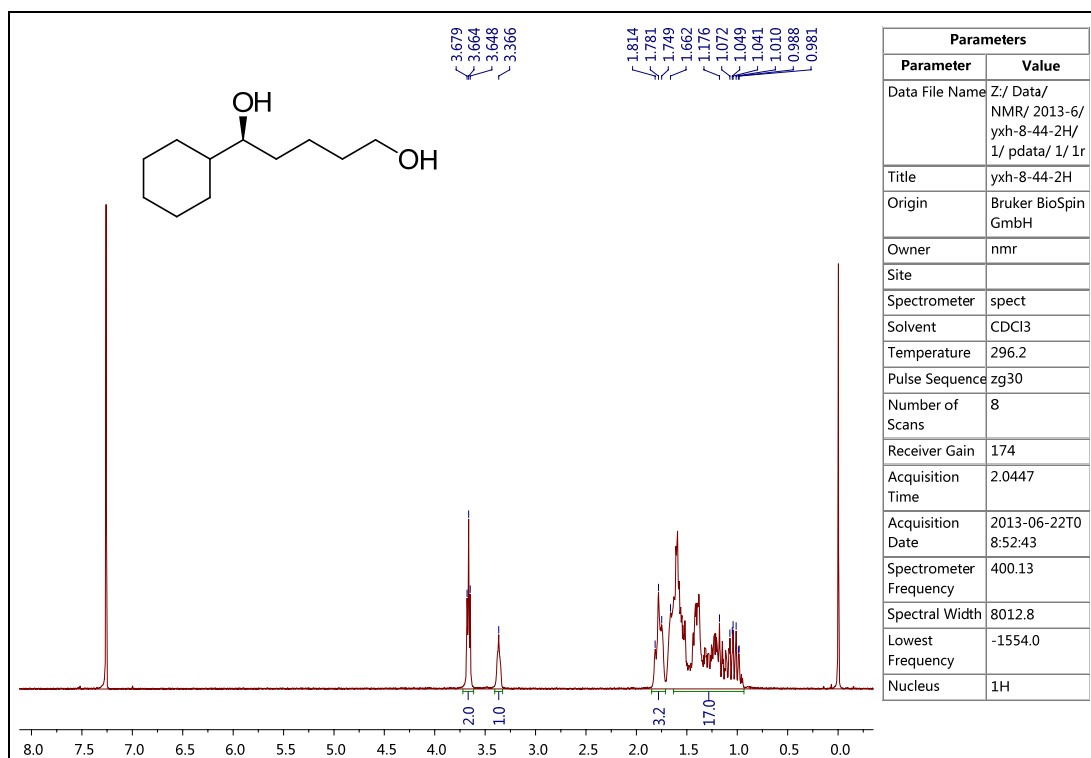
(S)-6-Methylheptane-1,5-diol (3f)



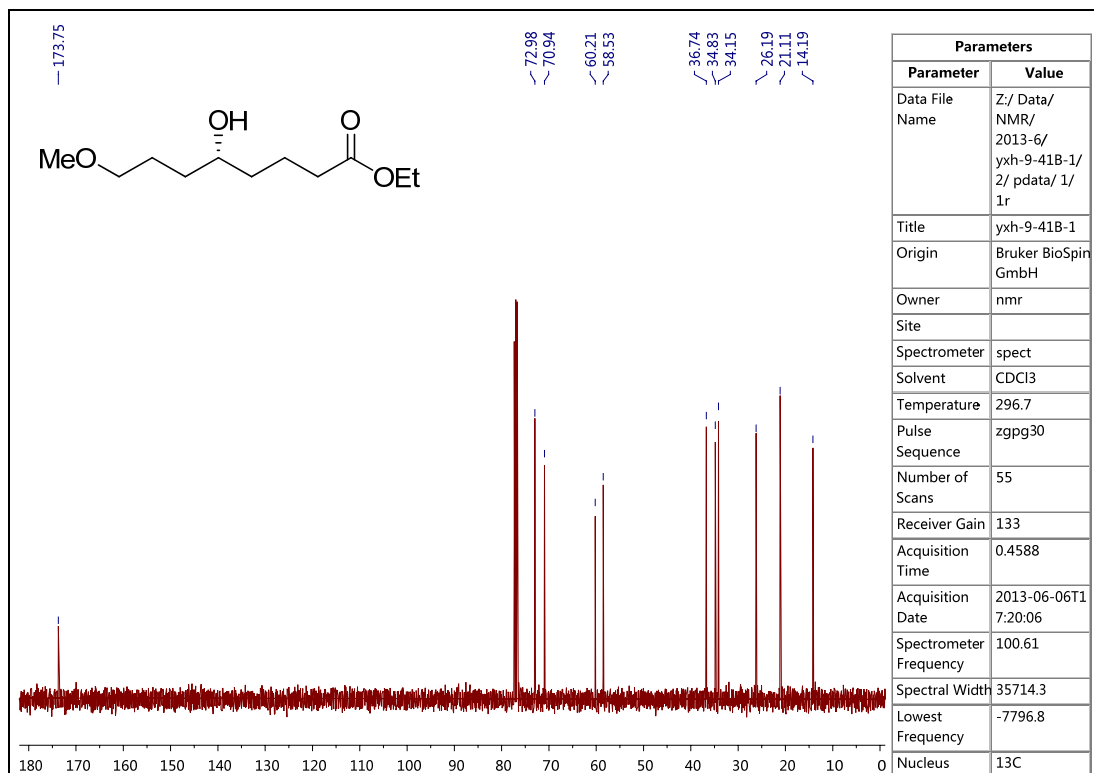
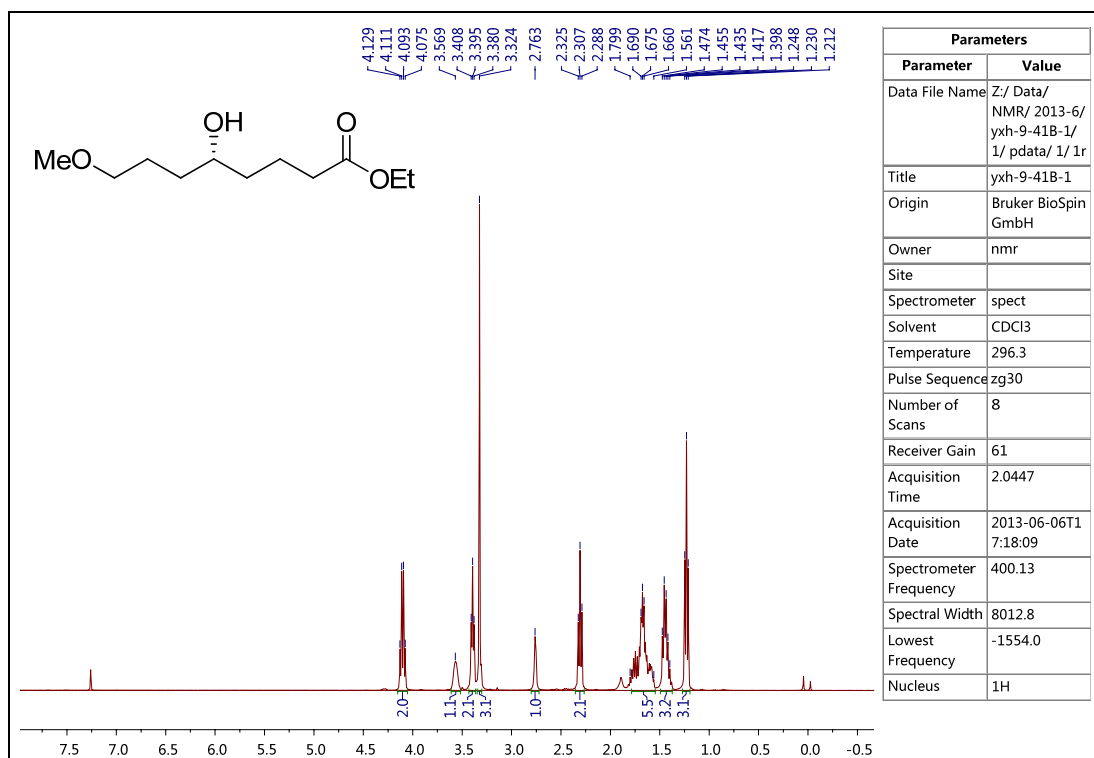
(R)-Ethyl 5-cyclohexyl-5-hydroxypentanoate (2g)



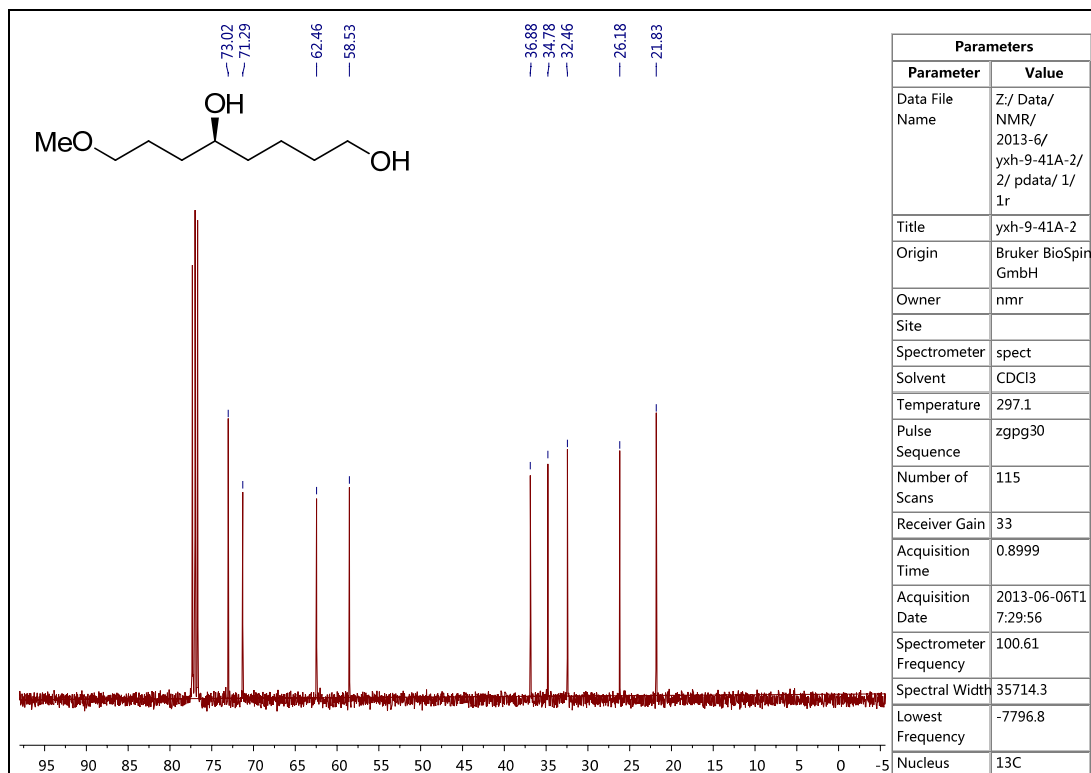
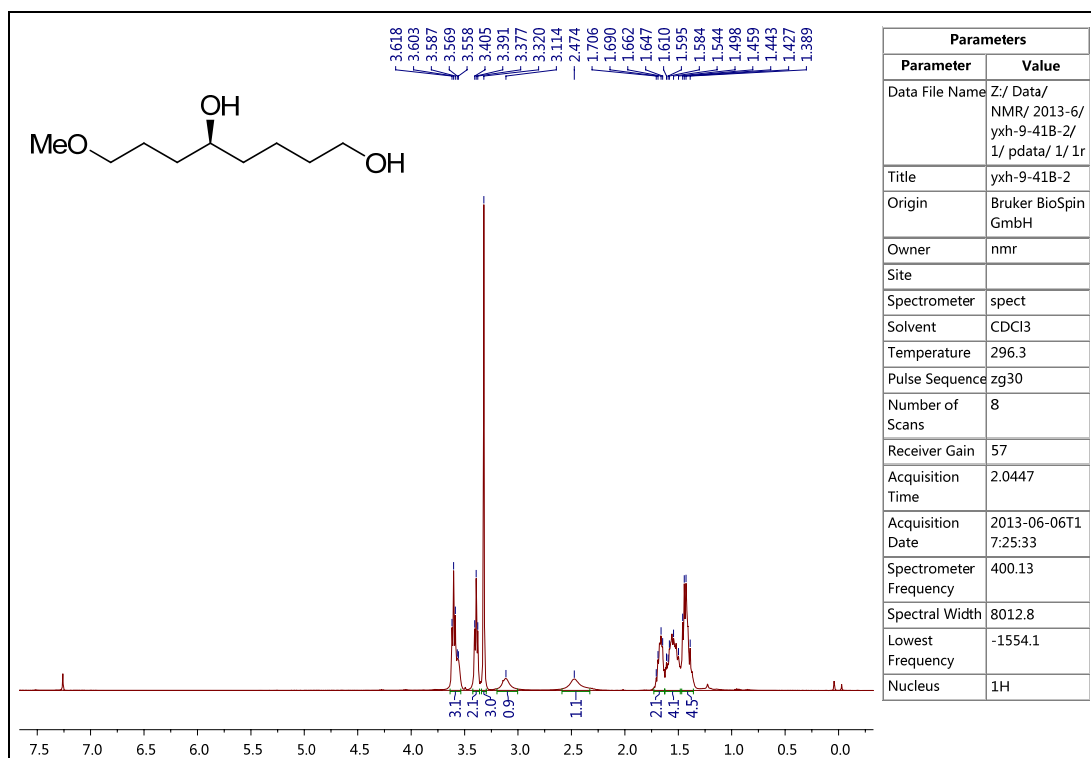
(S)-1-Cyclohexylpentane-1,5-diol (3g)



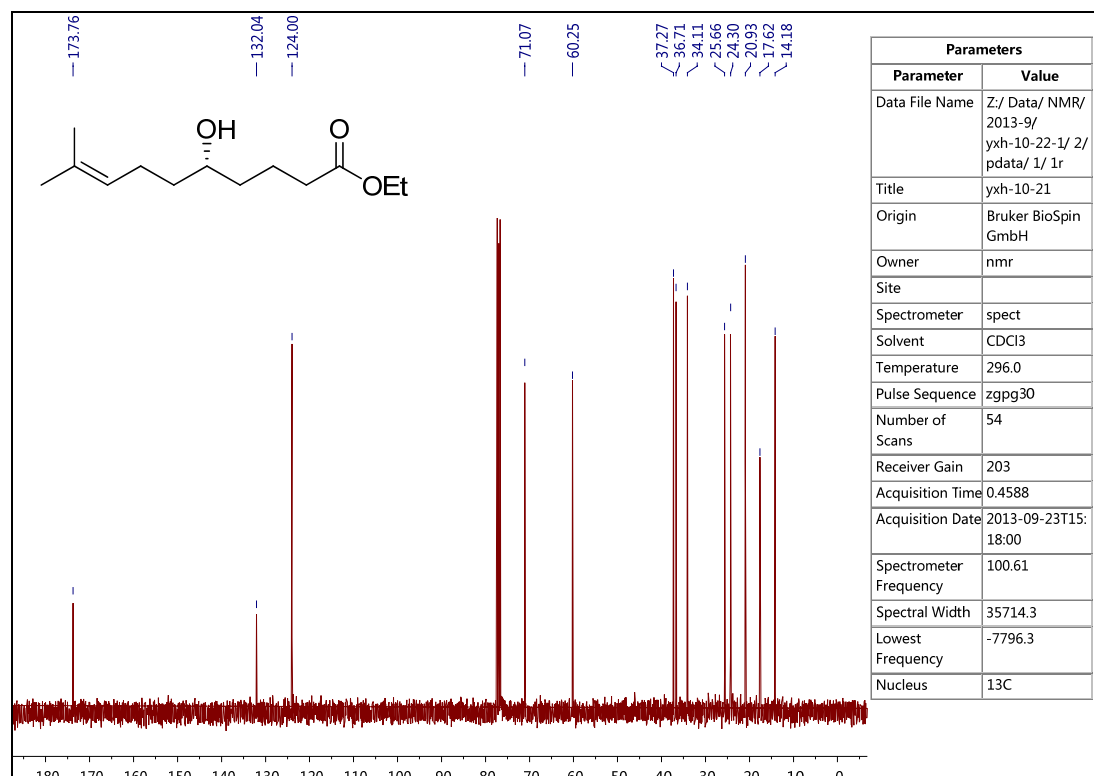
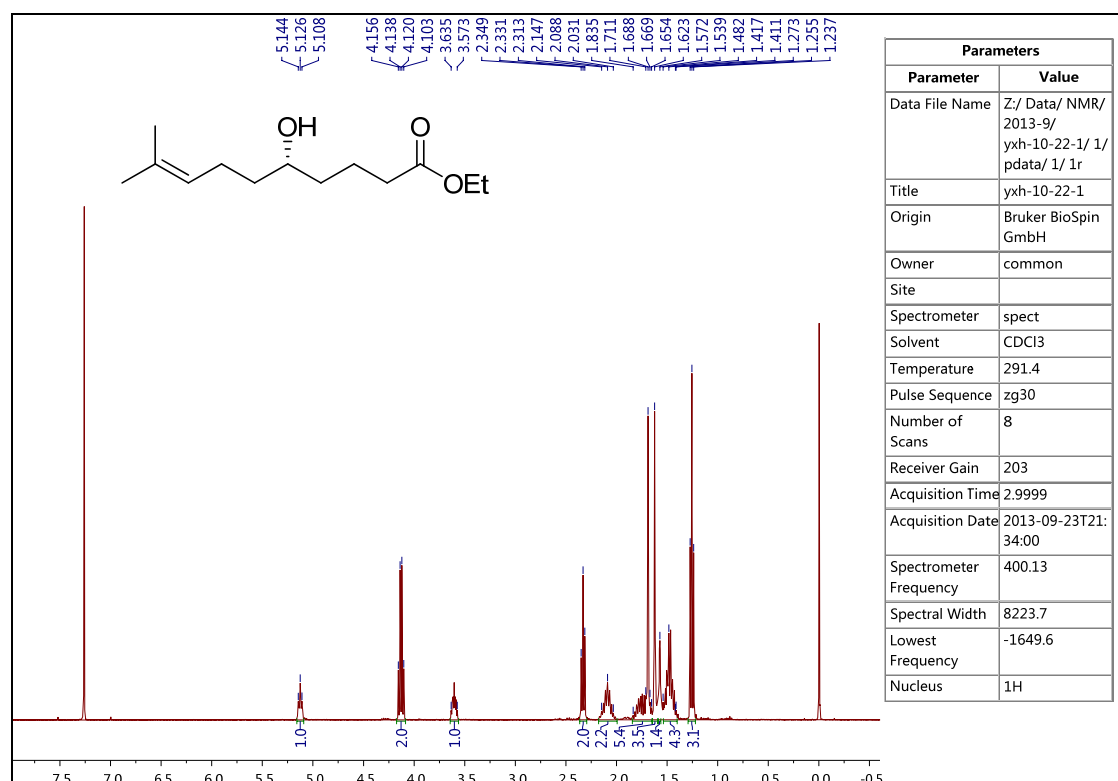
(R)-Ethyl 5-hydroxy-8-methoxyoctanoate (2h)



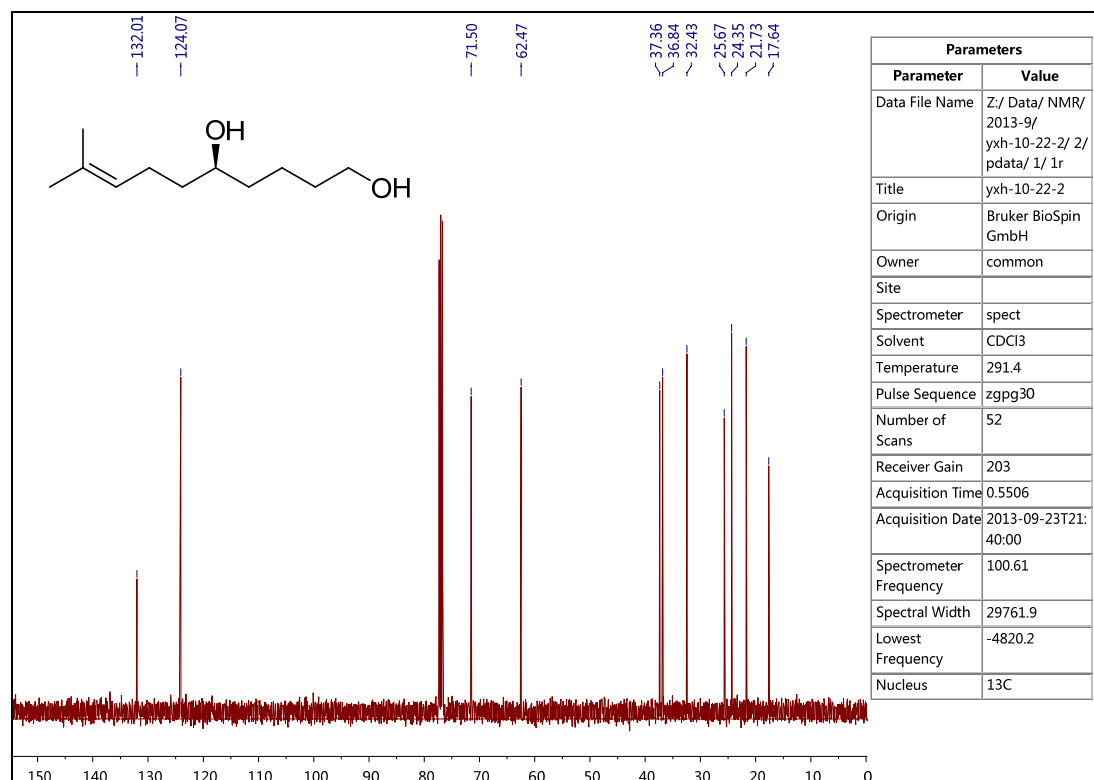
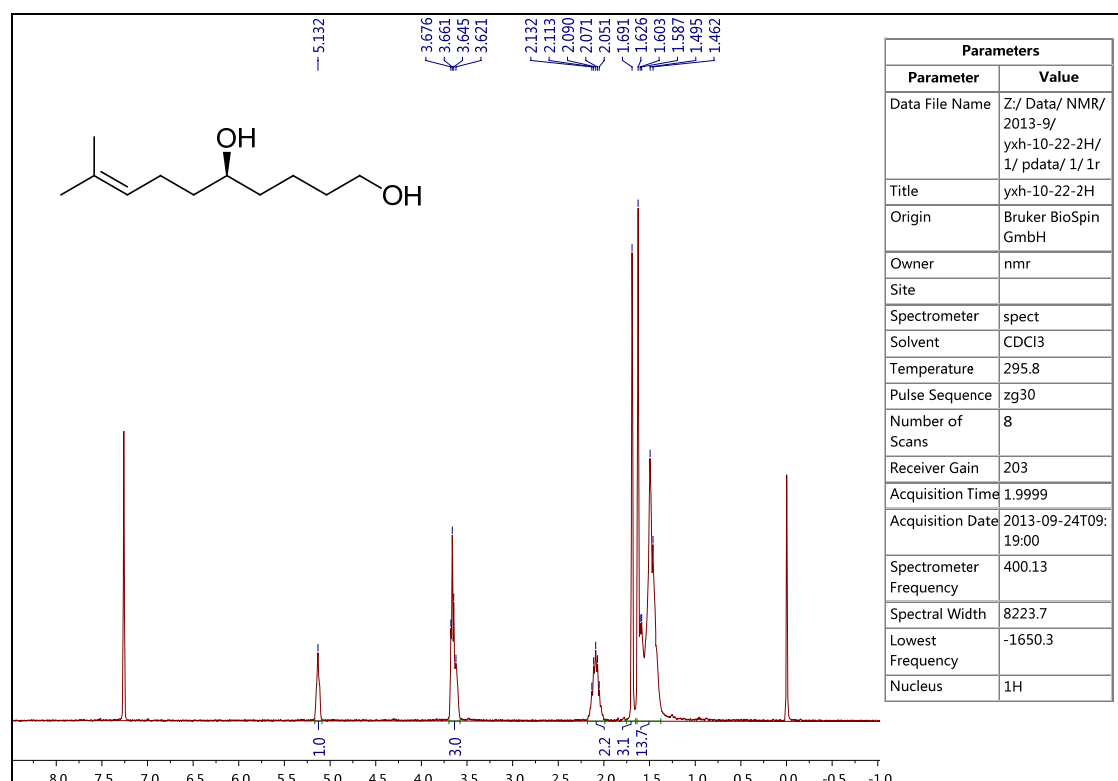
(S)-8-Methoxyoctane-1,5-diol (3h)



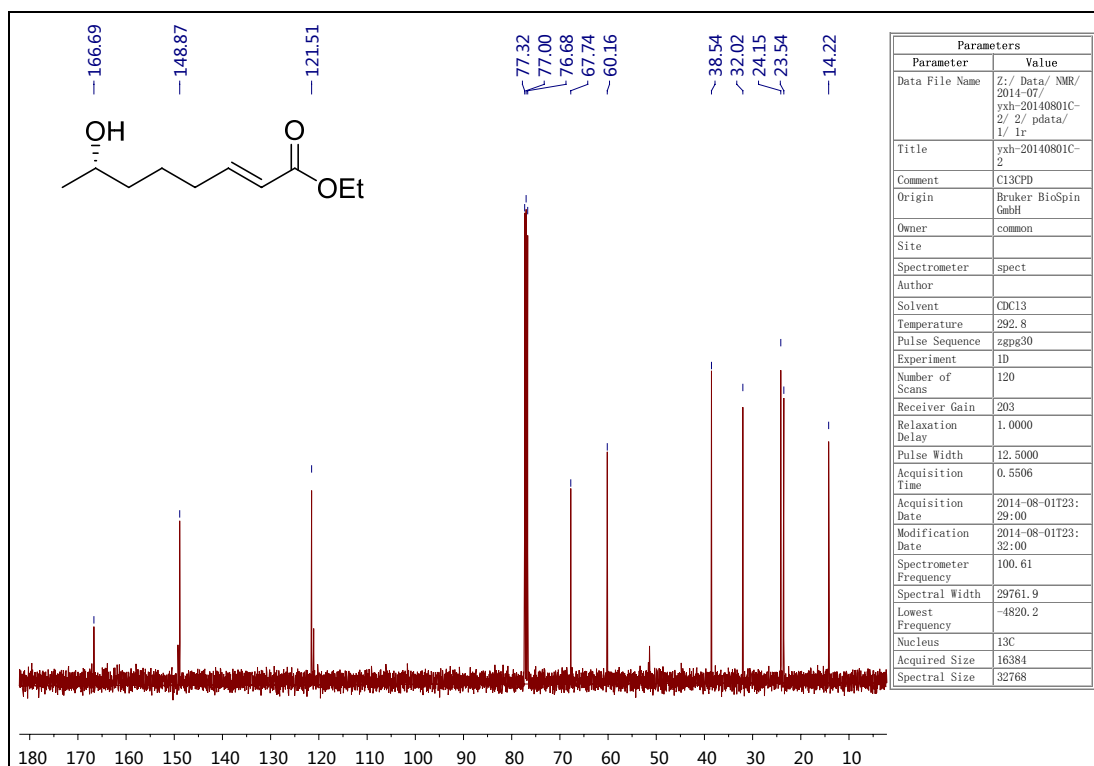
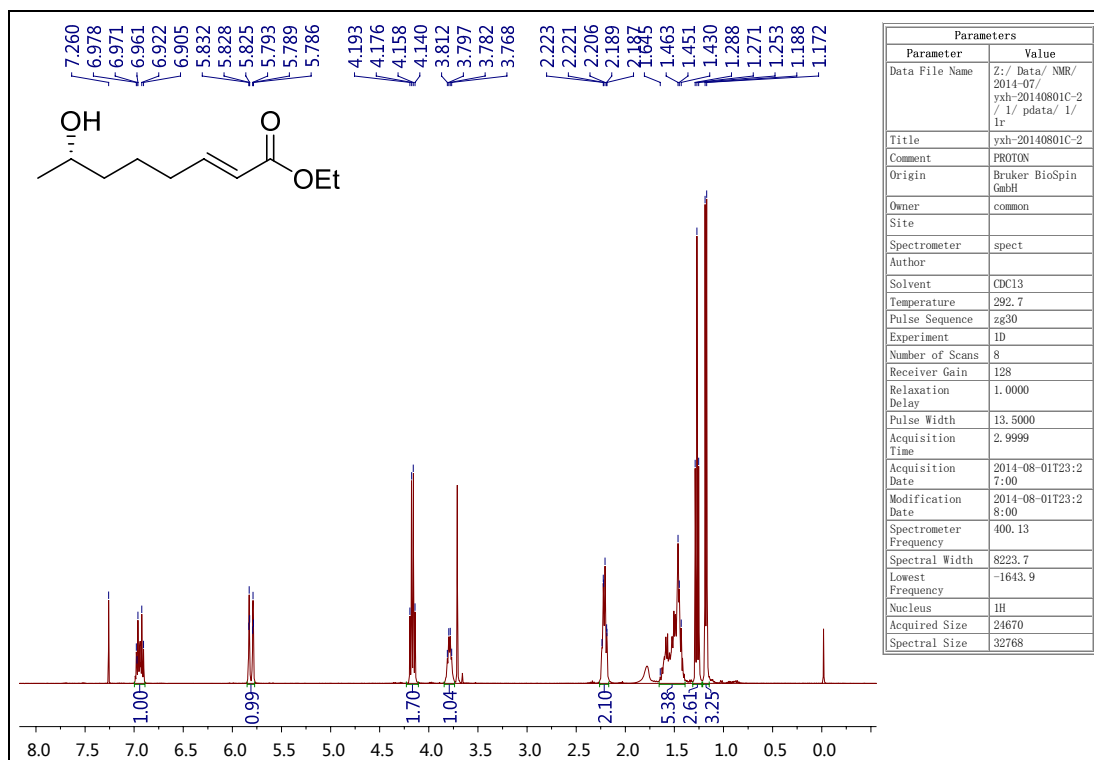
(R)-Ethyl 5-hydroxy-9-methyldec-8-enoate (2i)



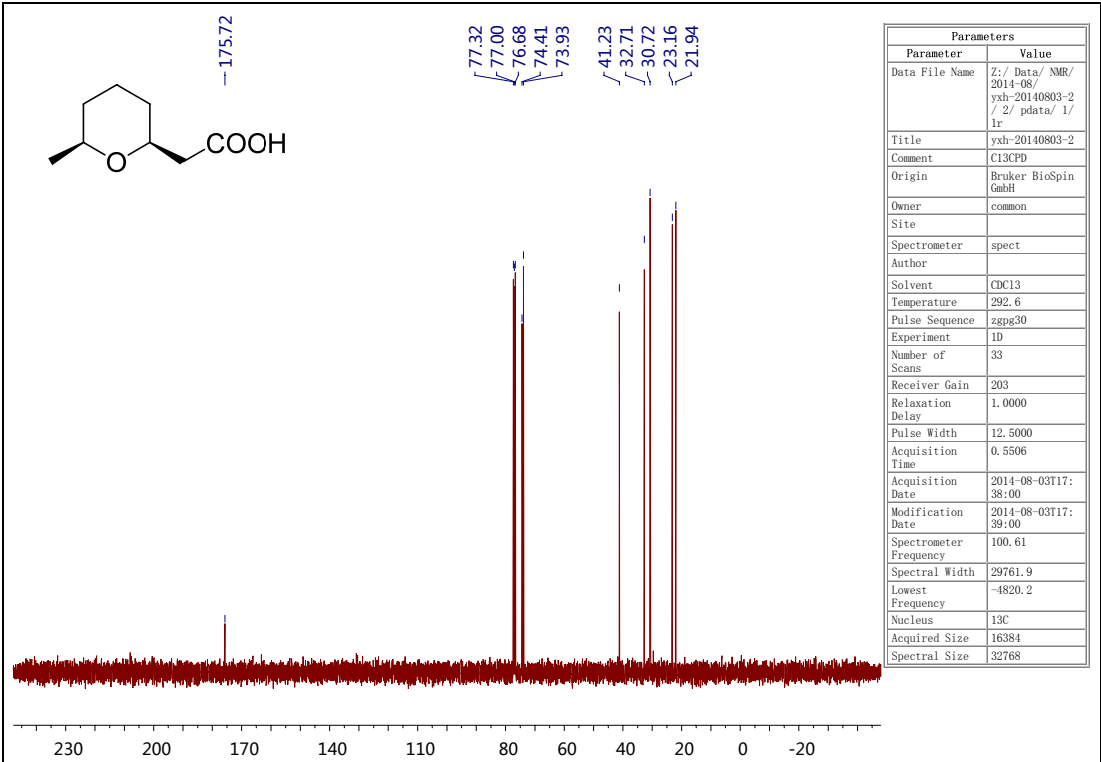
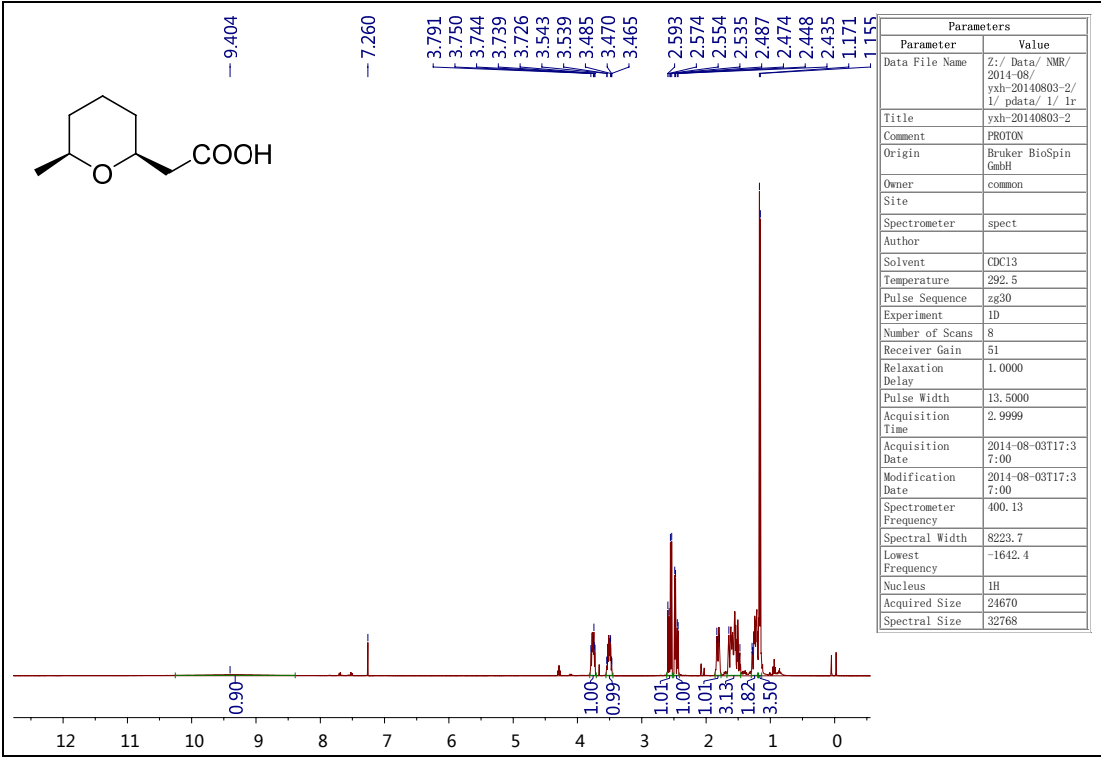
(S)-9-Methyldec-8-ene-1,5-diol (3i)



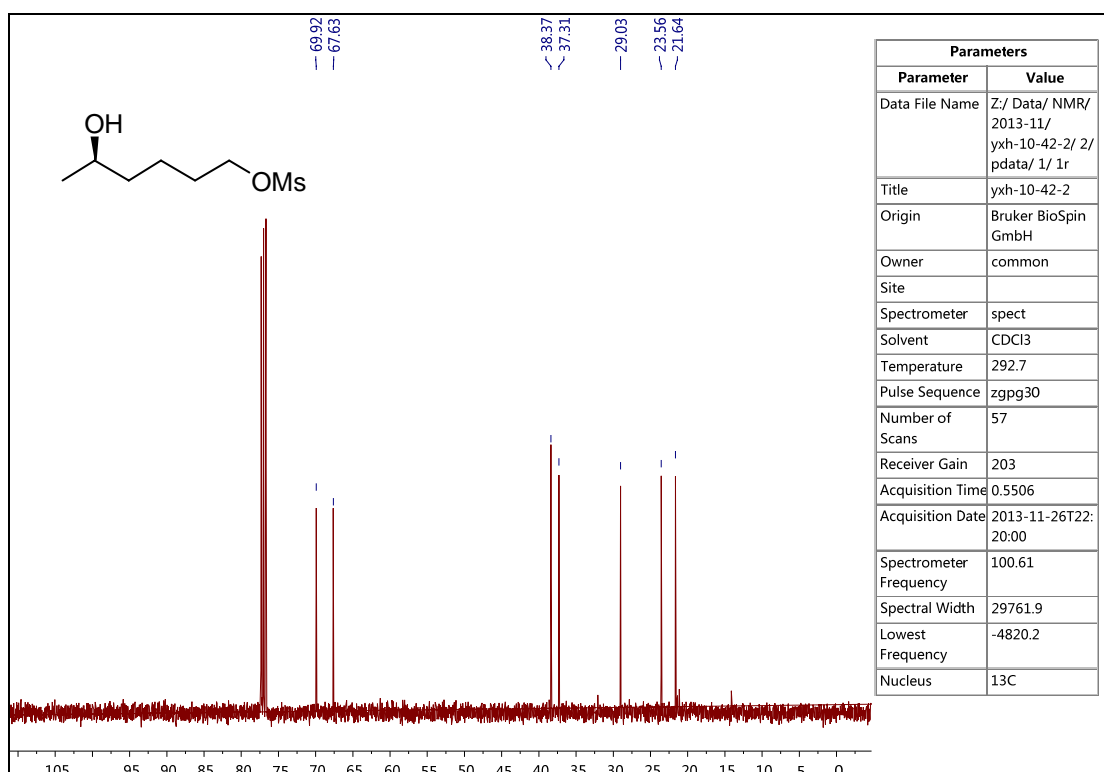
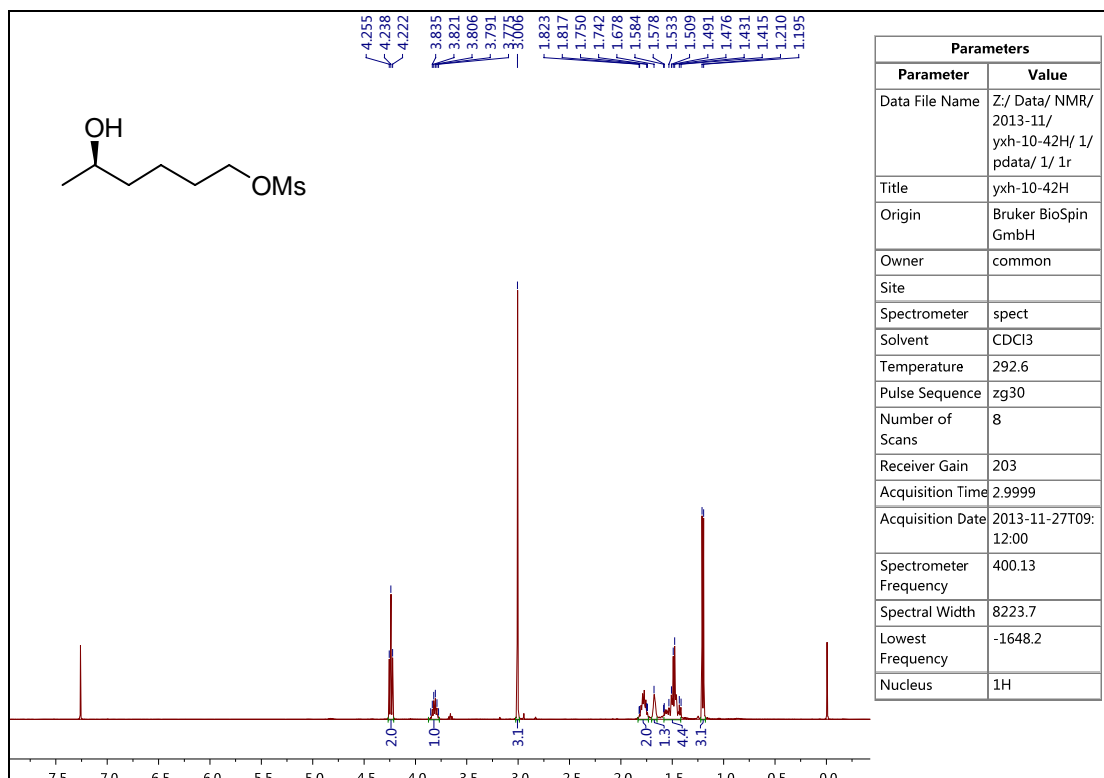
Compound (S)-6



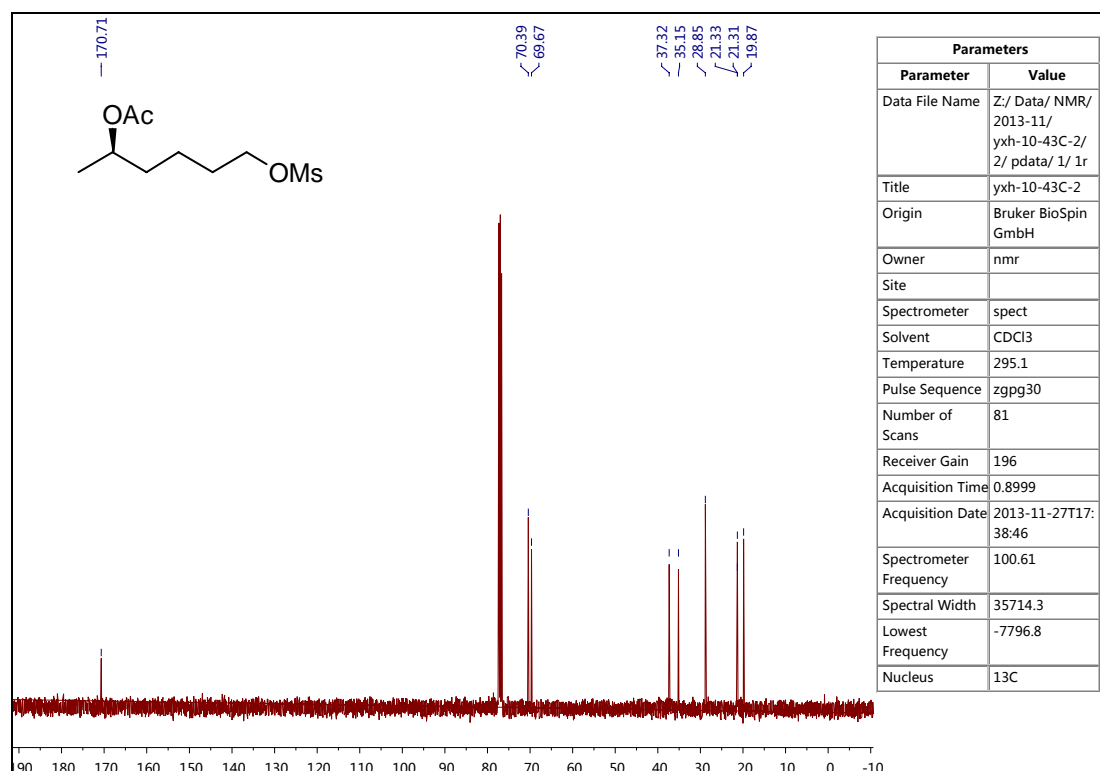
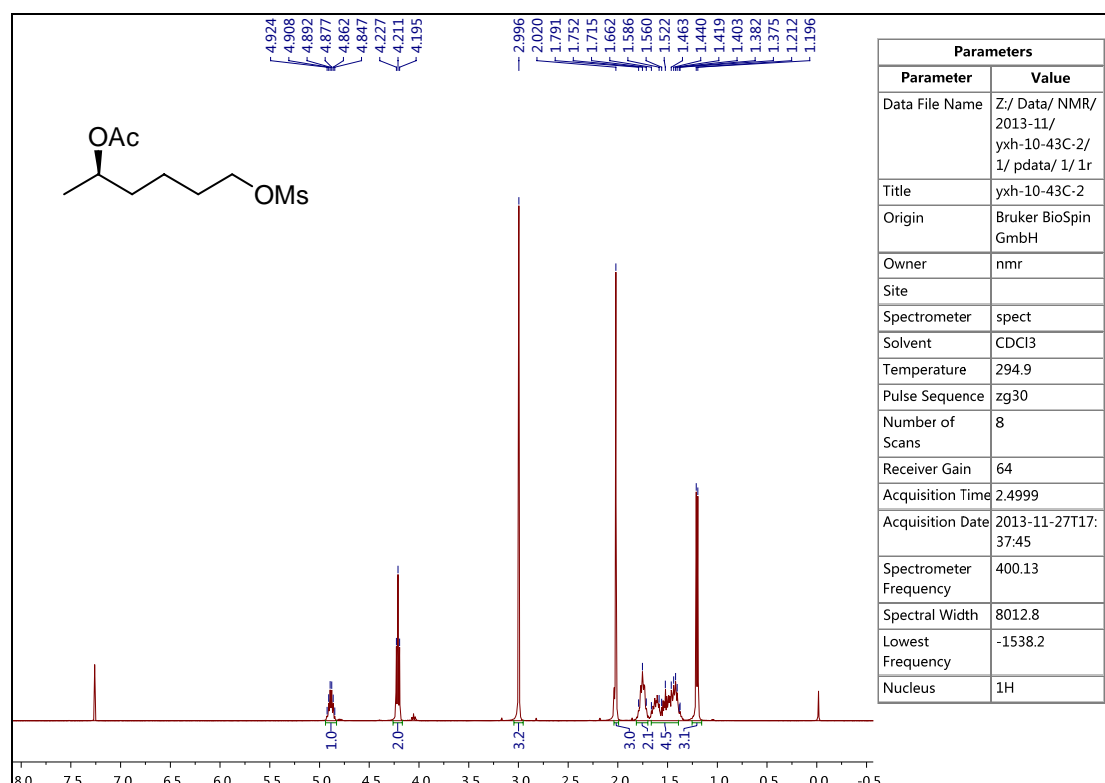
(+)-civet



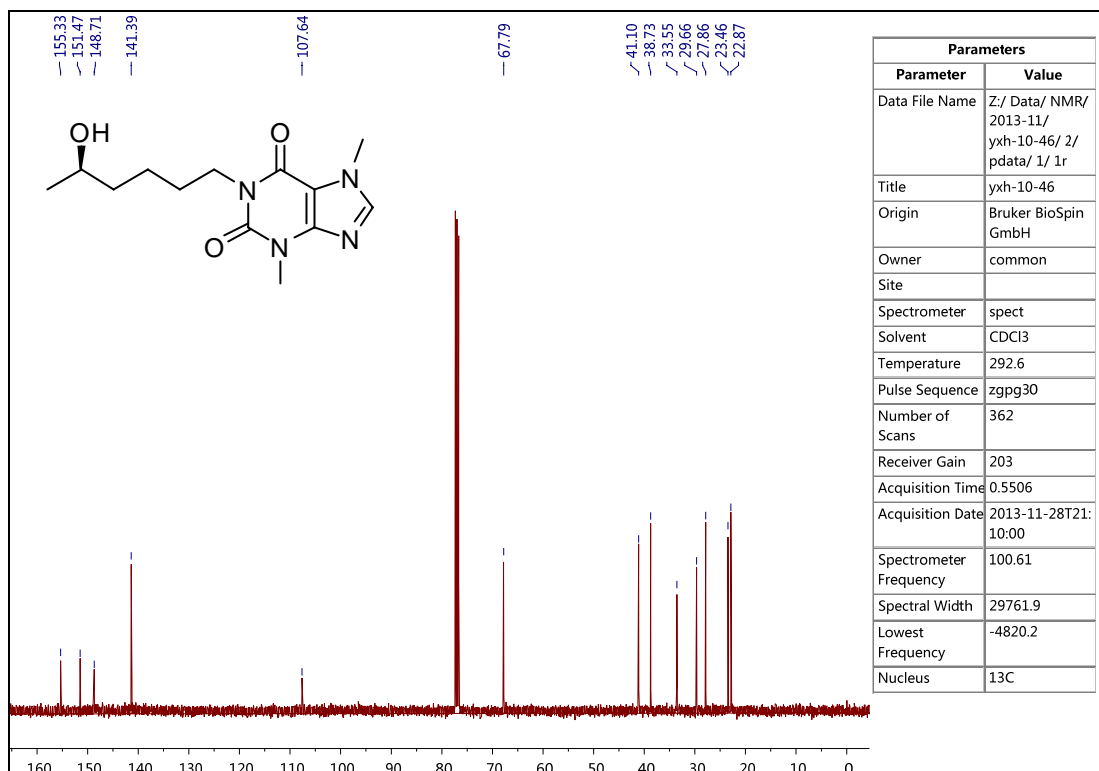
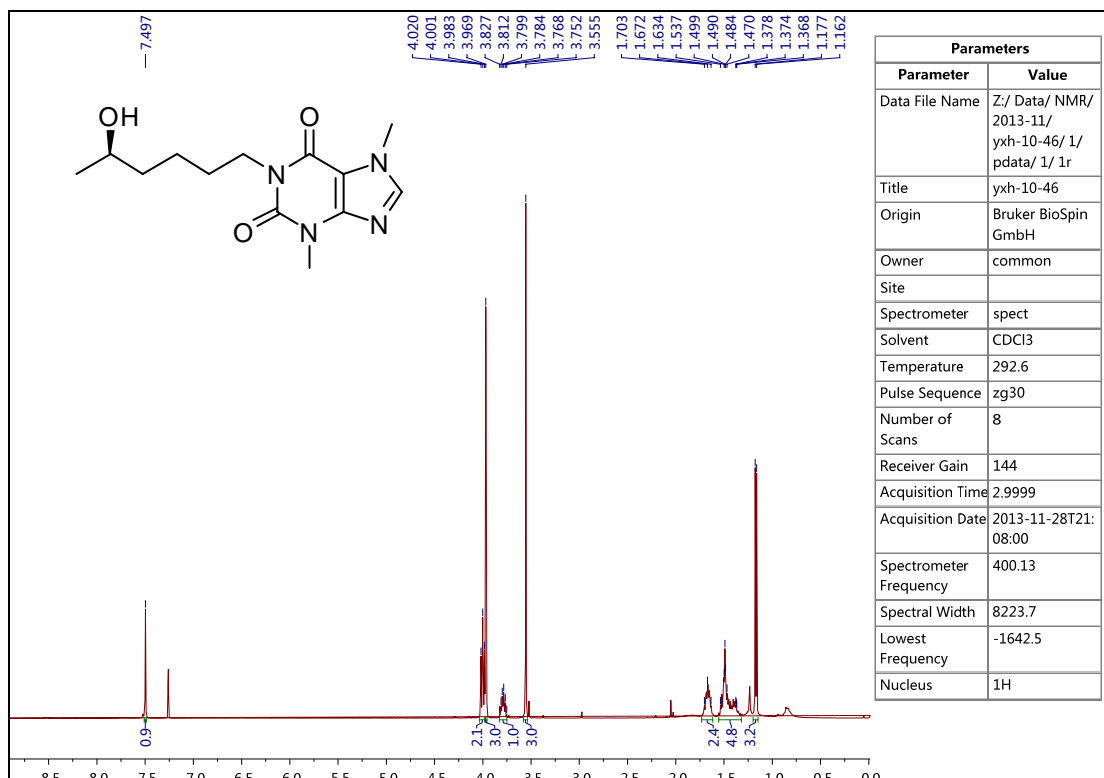
(R)-5-Hydroxyhexyl methanesulfonate



Compound (R)-7

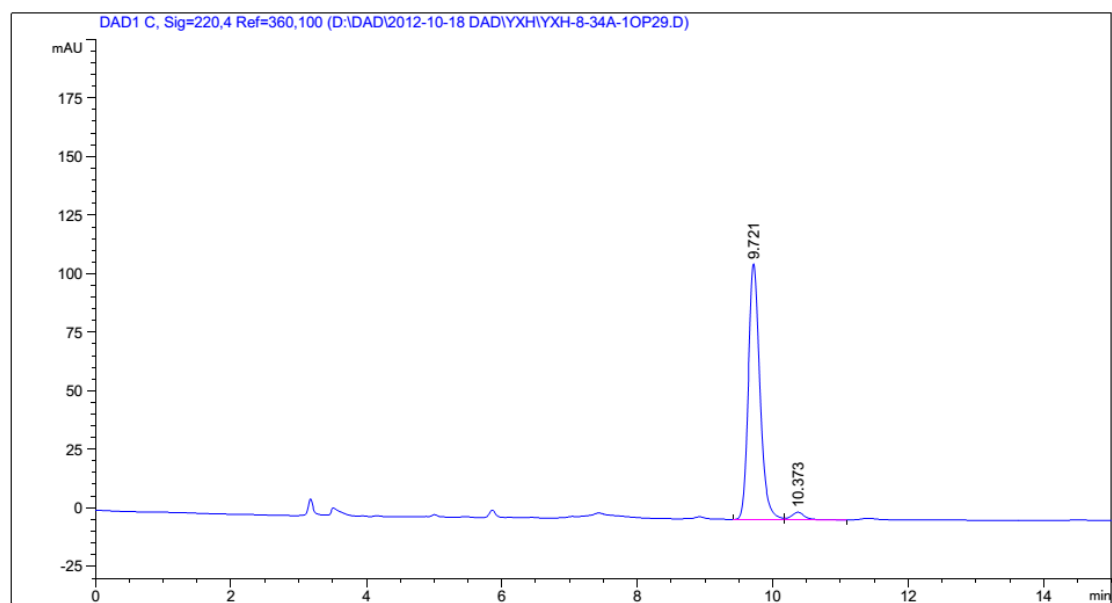
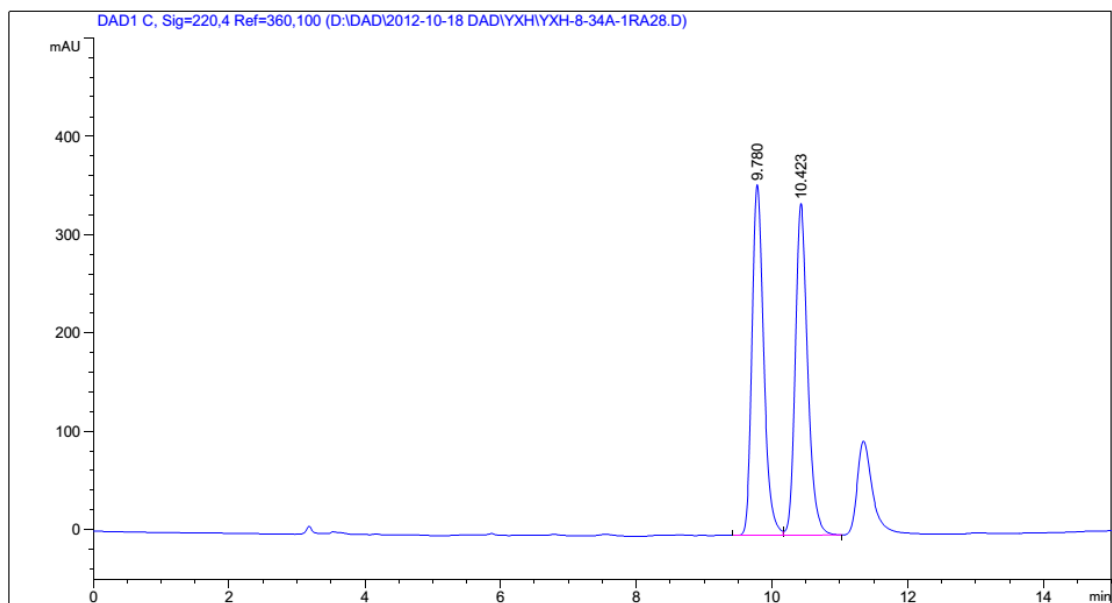


(R)-Lisofylline



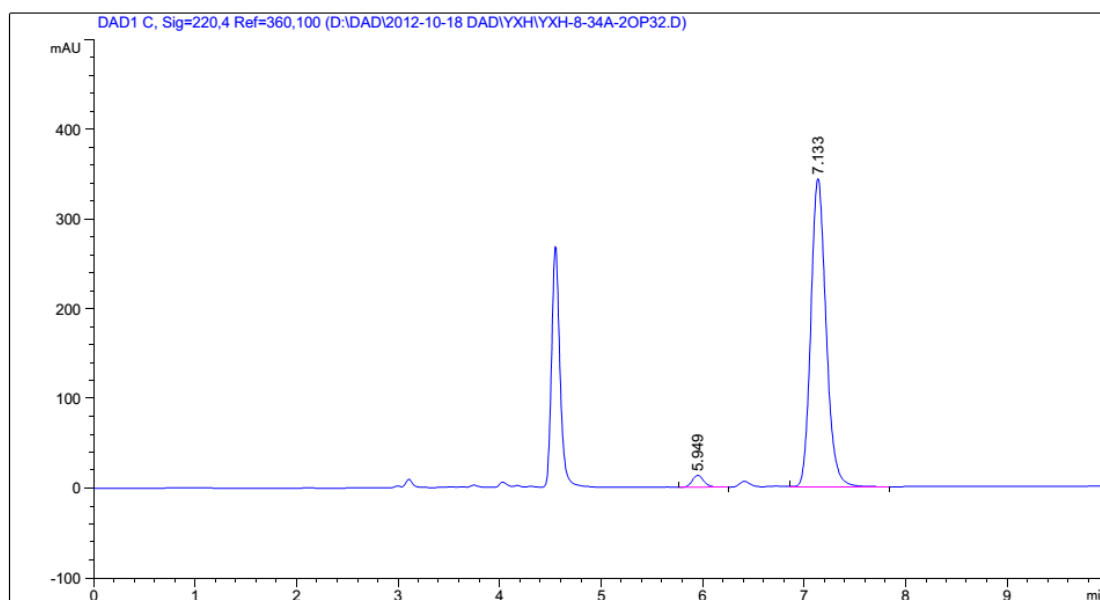
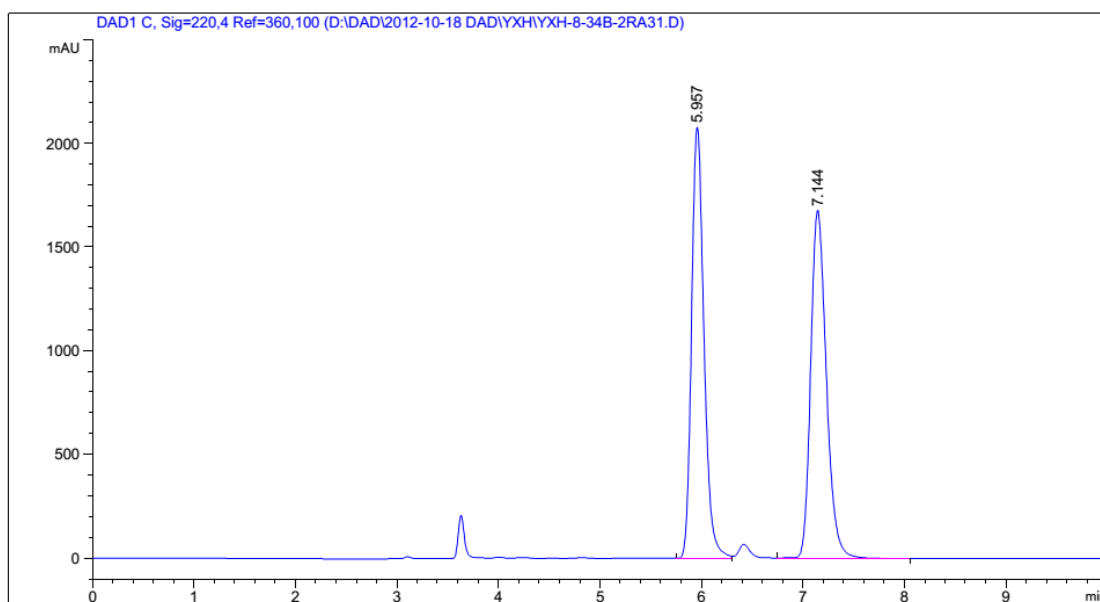
(E) HPLC charts for hydrogenation products

(S)-Ethyl 5-hydroxyhexanoate (2a)



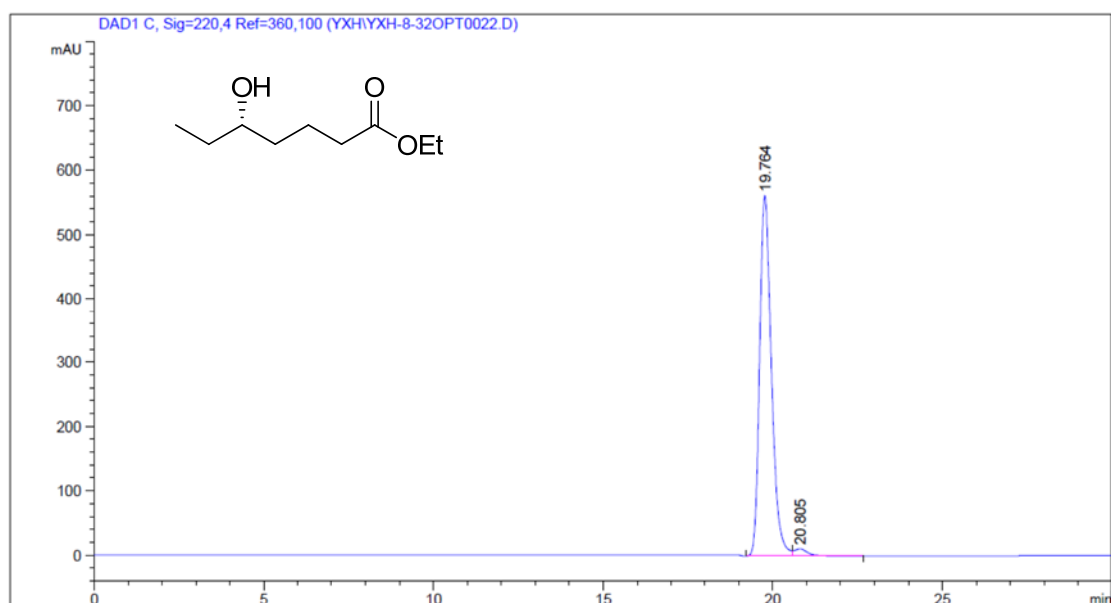
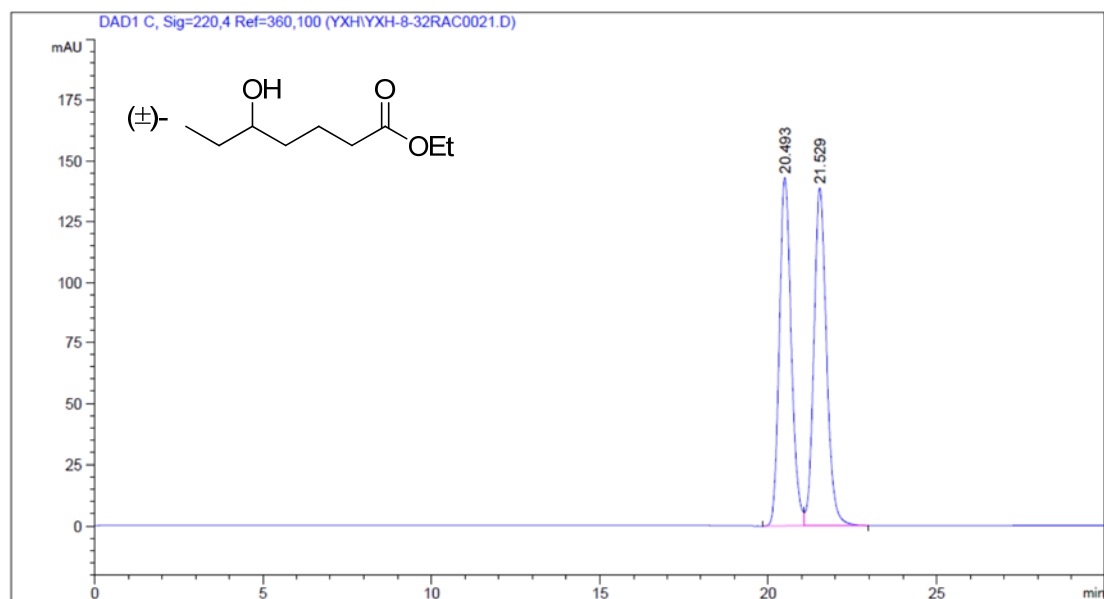
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.721	BV	0.1865	1294.39648	109.01040	96.8620
2	10.373	VB	0.2032	41.93449	3.15144	3.1380

(R)-Hexane-1,5-diol (3a)



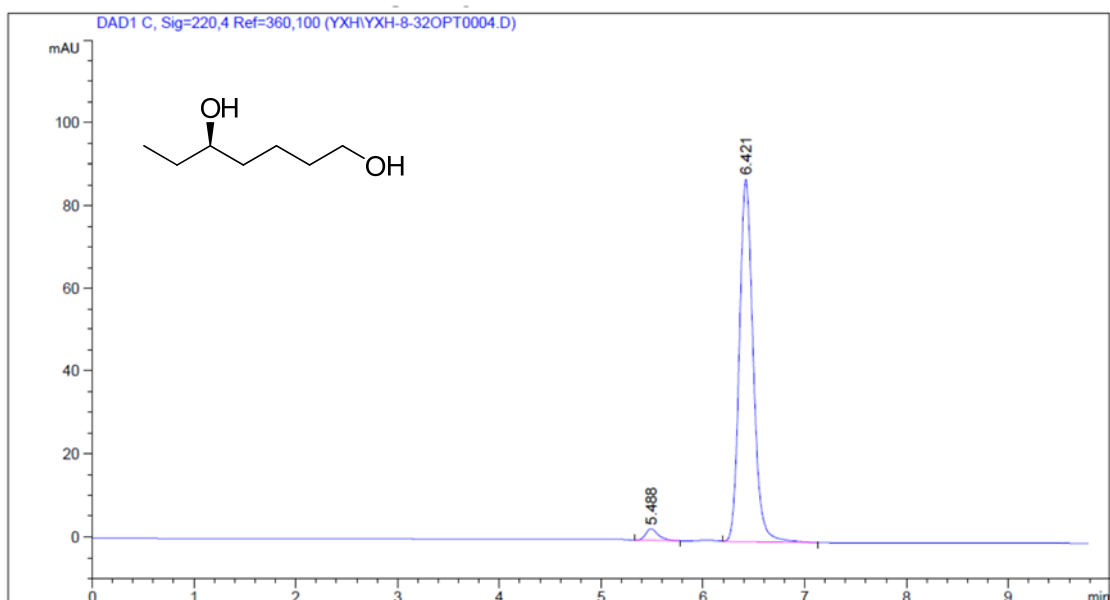
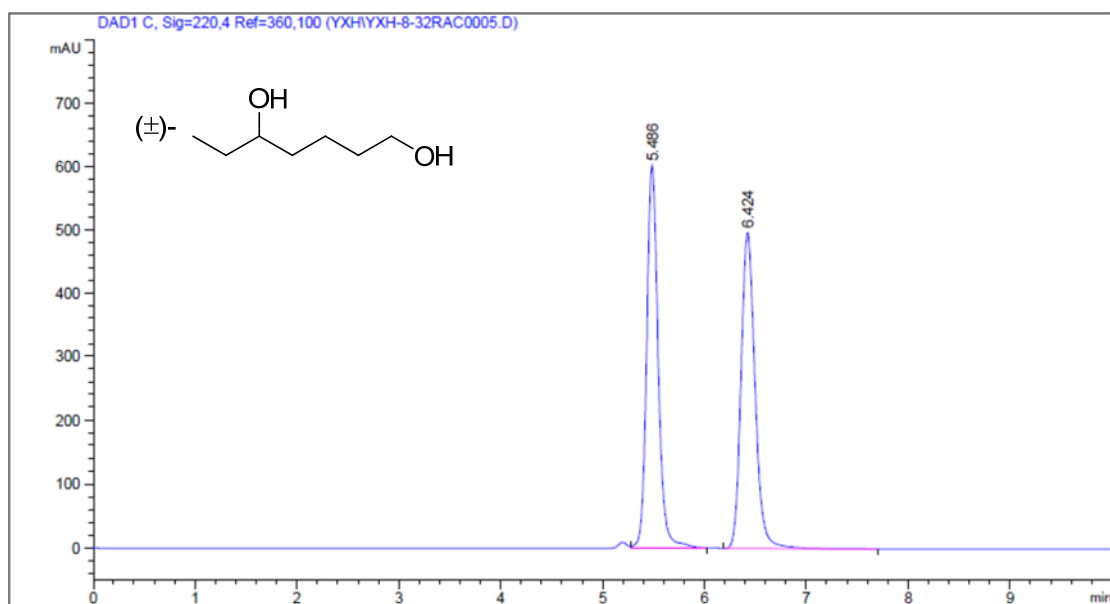
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.949	BB	0.1266	106.81757	13.17145	2.8980
2	7.133	VB	0.1614	3579.13965	343.96564	97.1020

(S)-Ethyl 5-hydroxyheptanoate (2b)



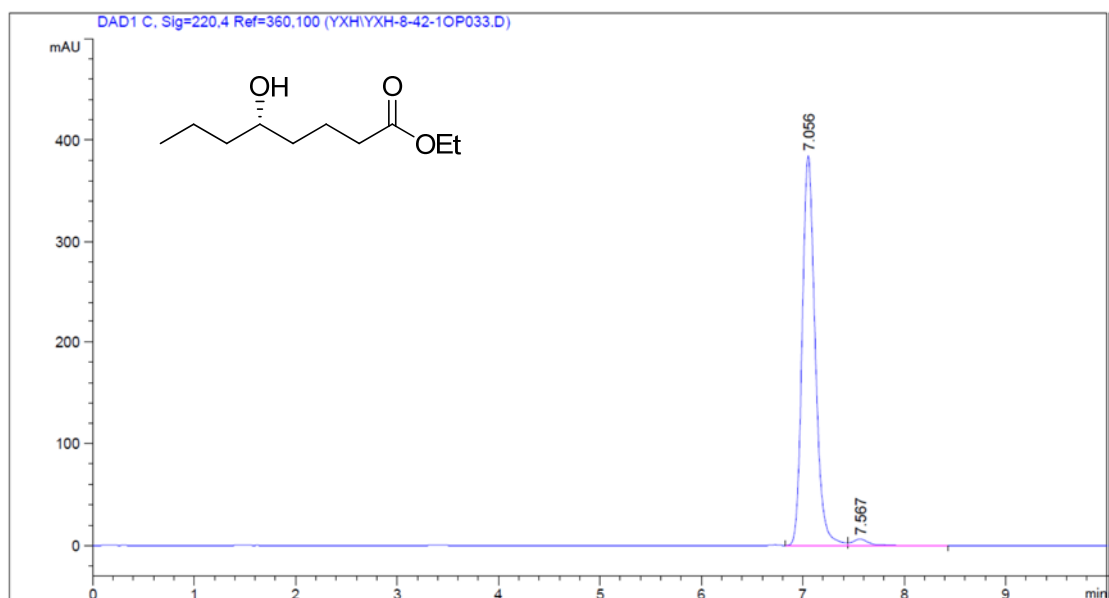
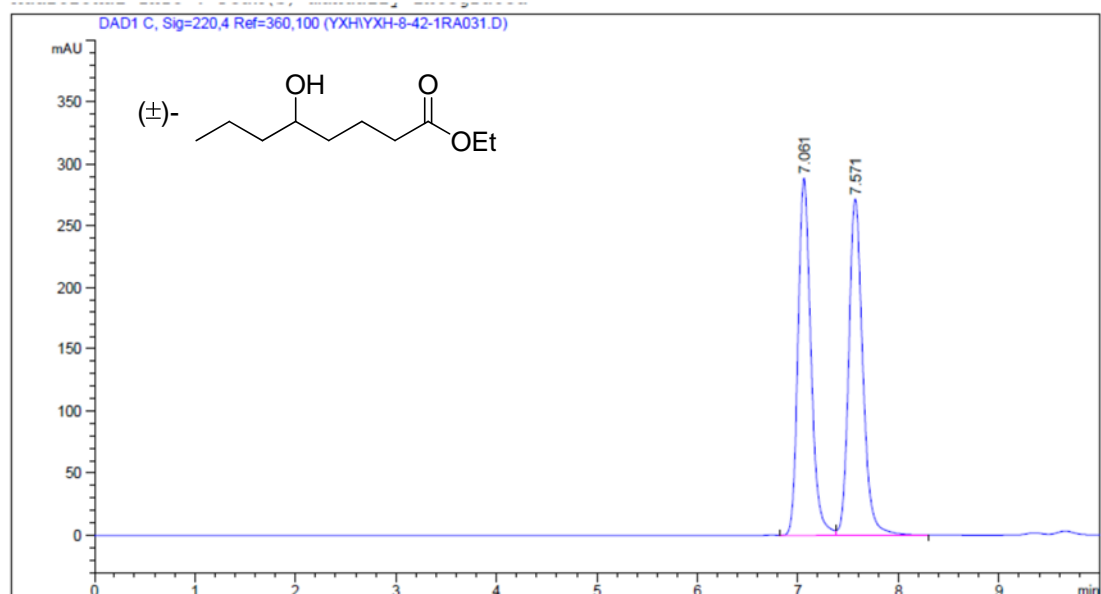
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.764	BV	0.3696	1.35525e4	561.50873	97.6858
2	20.805	VB	0.4243	321.06604	11.07391	2.3142

(R)-Heptane-1,5-diol (3b)



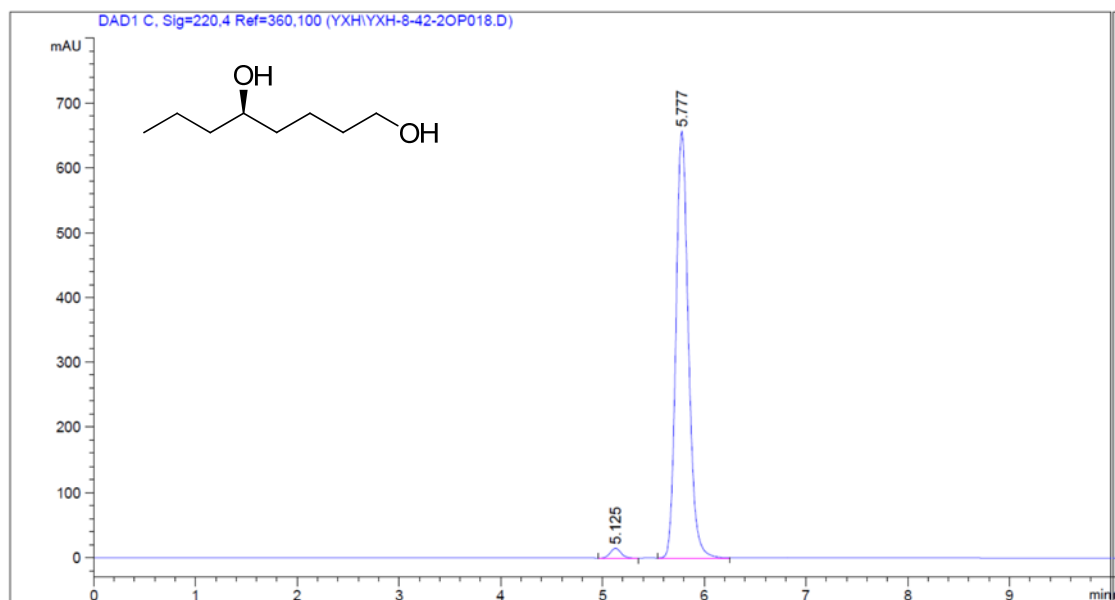
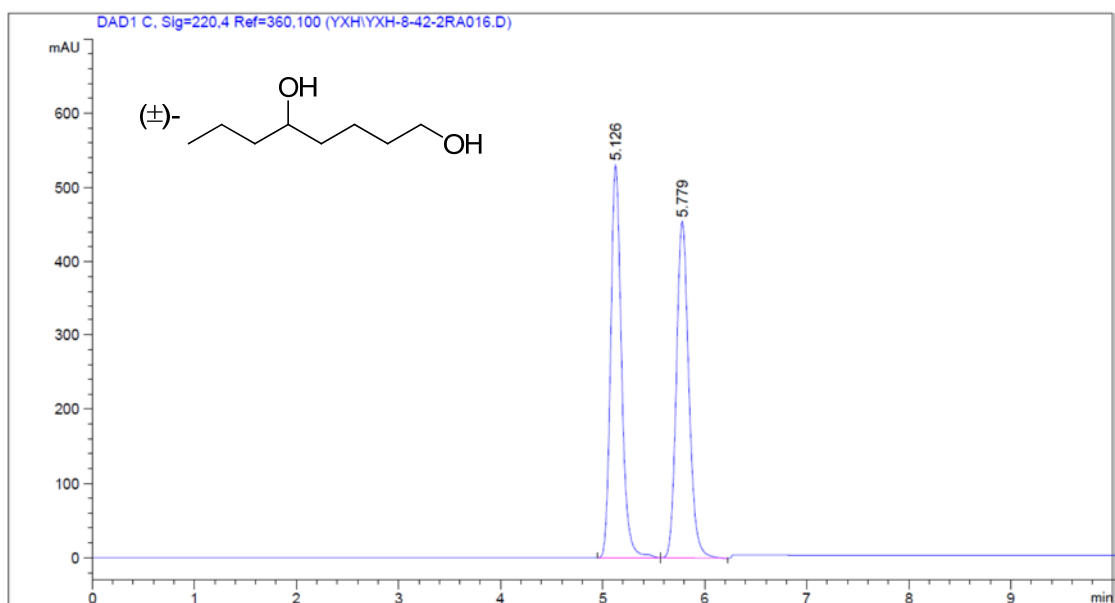
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.488	BB	0.1303	23.60989	2.74646	2.7928
2	6.421	VB	0.1434	821.76239	87.60590	97.2072

(S)-Ethyl 5-hydroxyoctanoate (2c)



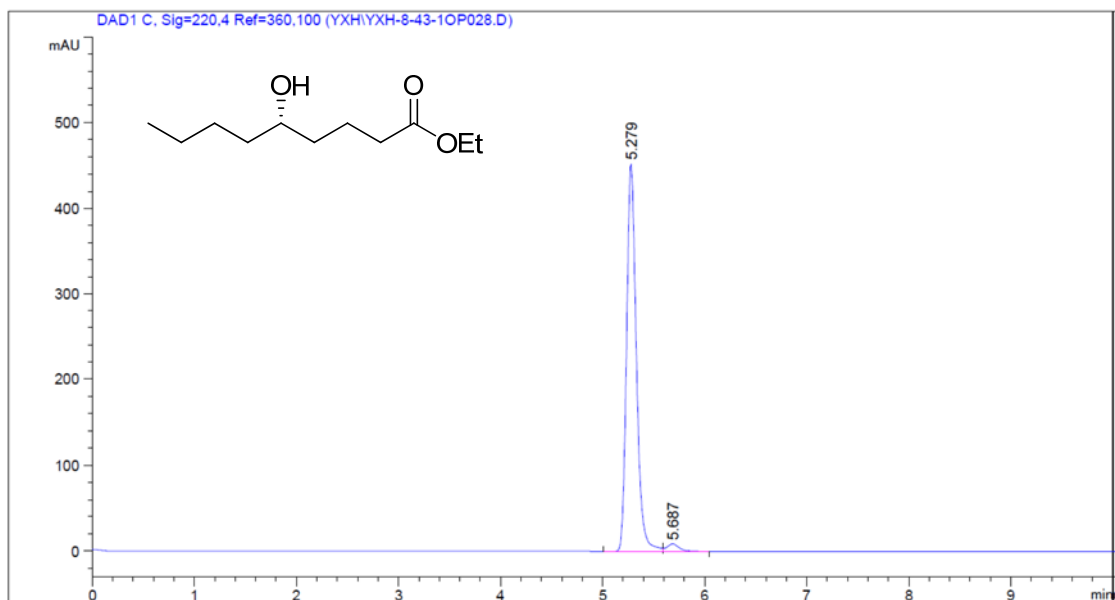
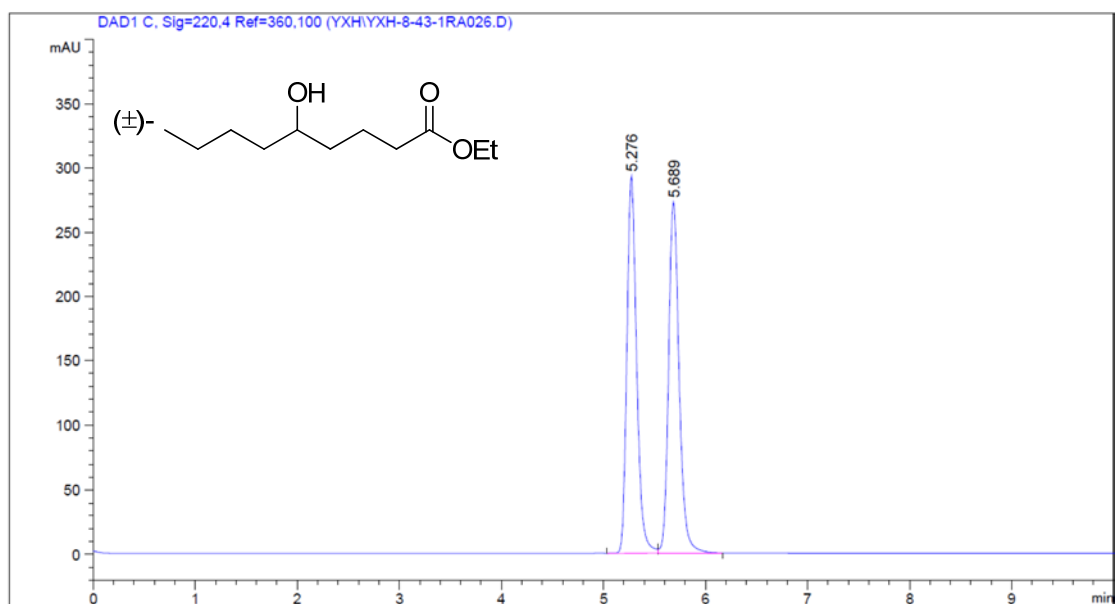
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.056	VV	0.1378	3422.46973	384.66495	97.8780
2	7.567	VB	0.1686	74.19841	6.43255	2.1220

(R)-Octane-1,5-diol (3c)



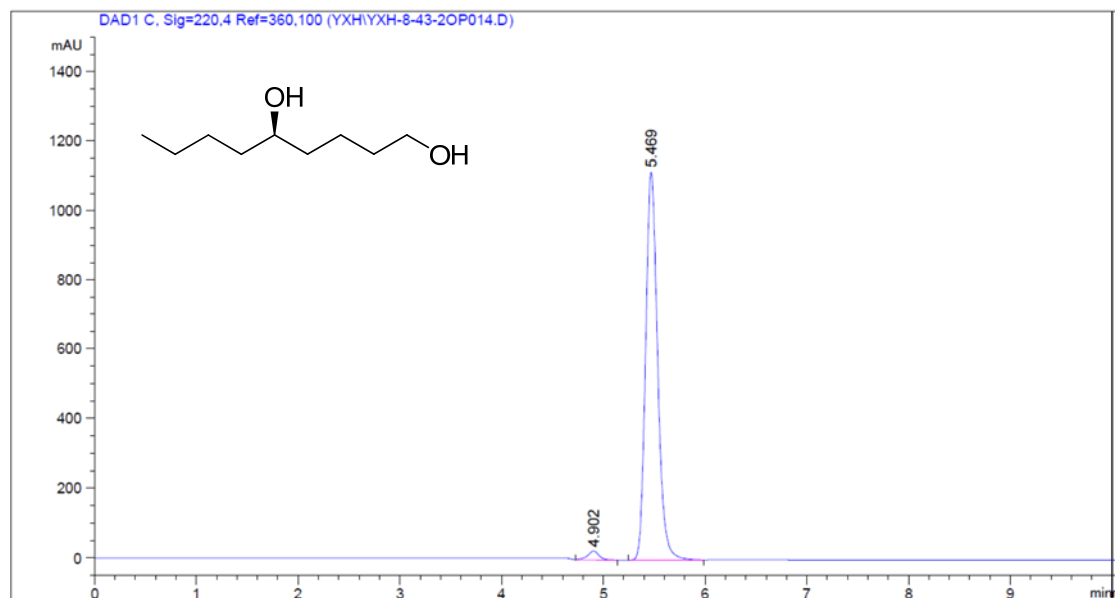
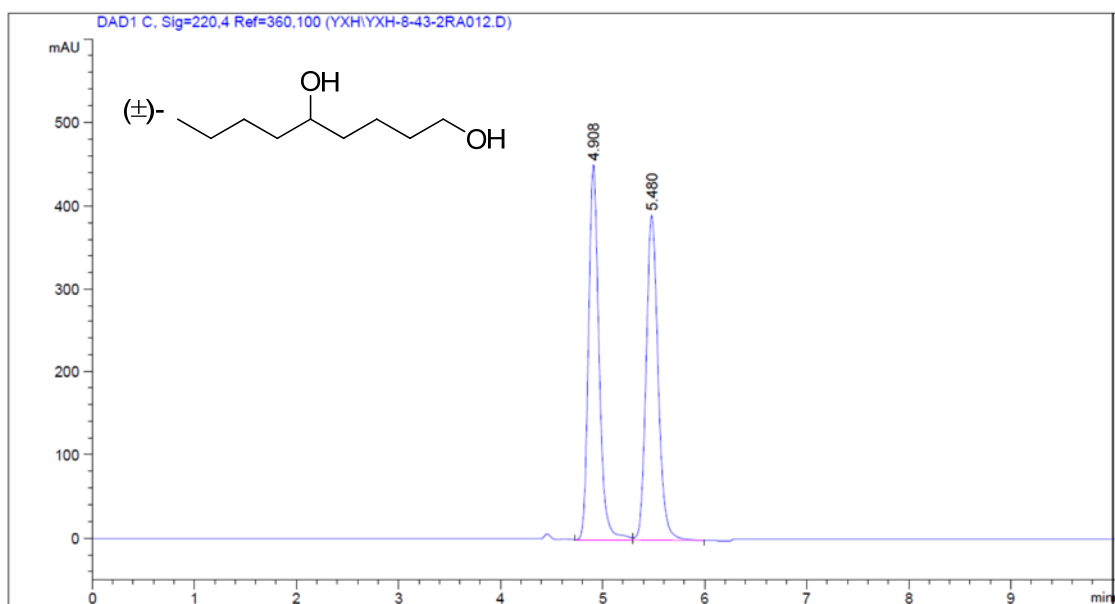
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.125	BB	0.1129	113.29295	15.20423	1.9829
2	5.777	VV	0.1316	5600.14697	656.08356	98.0171

(S)-Ethyl 5-hydroxynonanoate (2d)



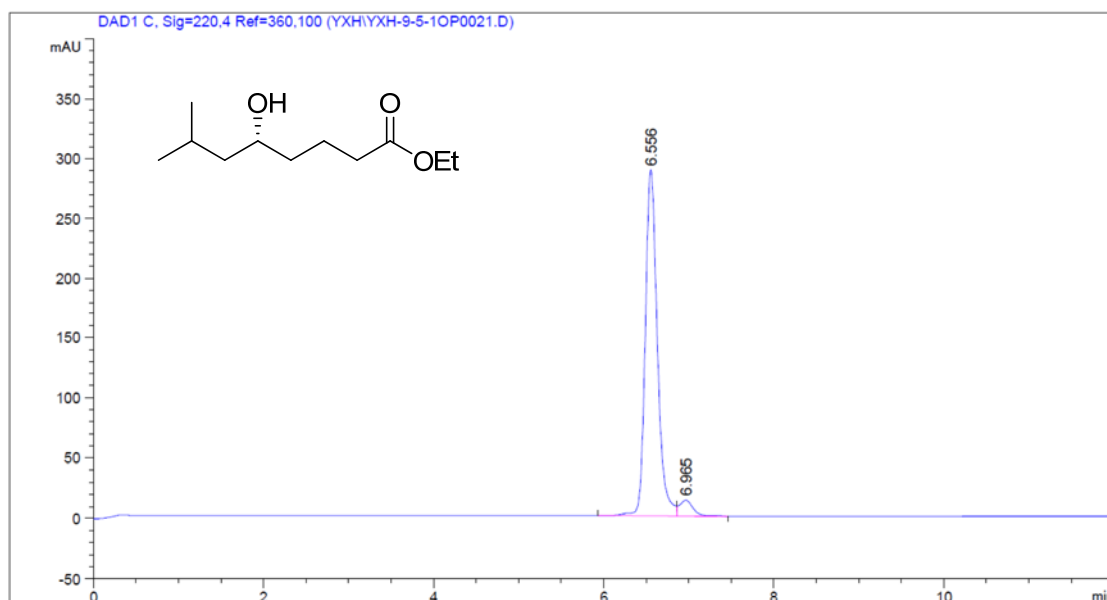
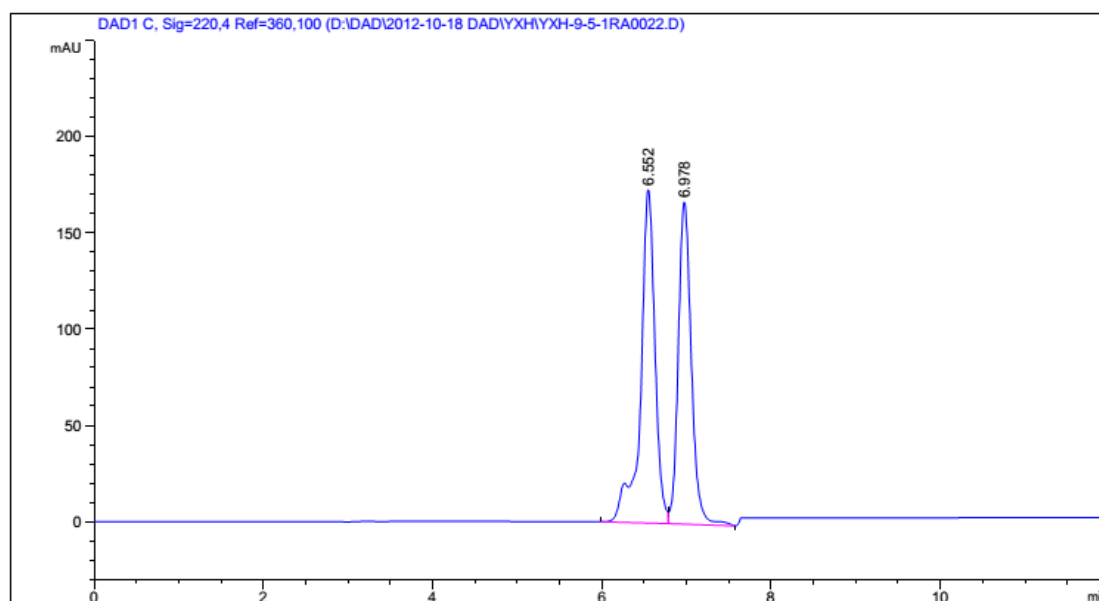
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.279	BV	0.1015	3005.33545	452.35345	97.5633
2	5.687	VB	0.1255	75.06156	8.79686	2.4367

(R)-Nonane-1,5-diol (3d)



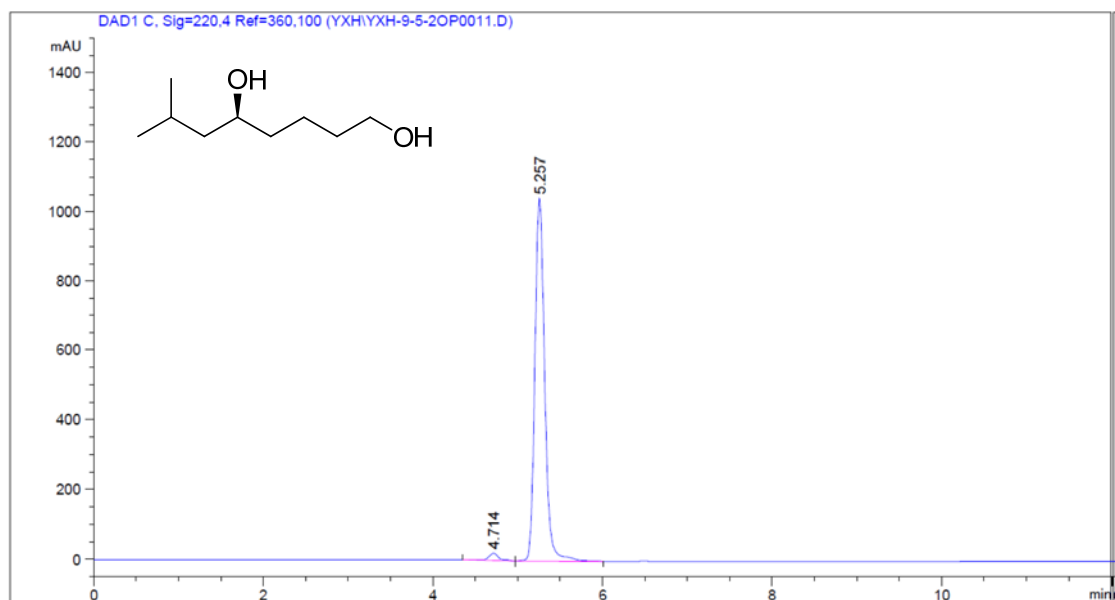
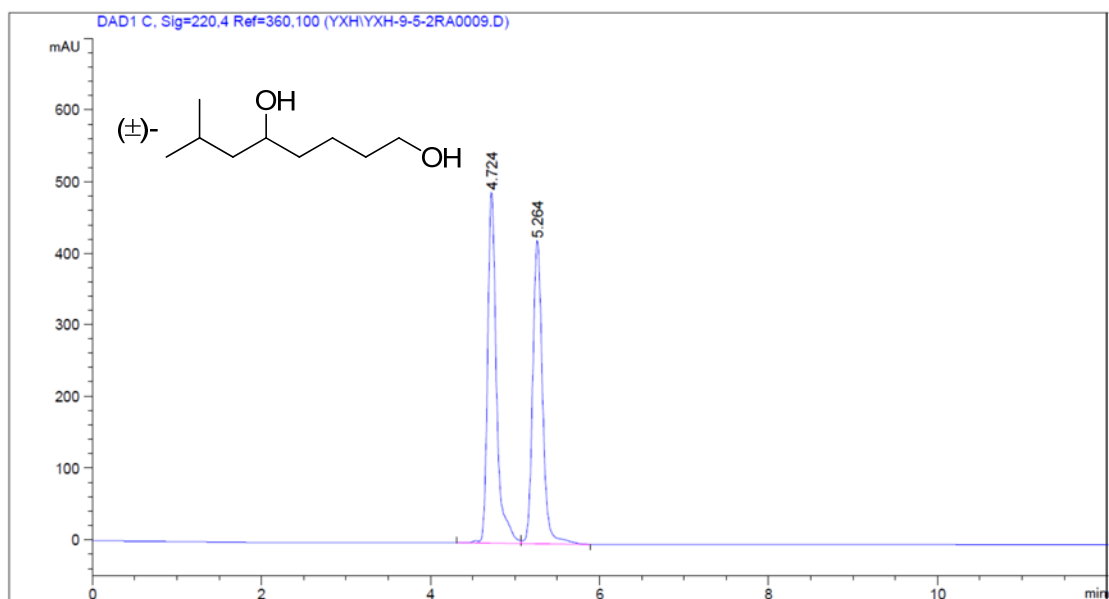
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.902	BB	0.1138	190.20189	25.28094	2.0403
2	5.469	BB	0.1273	9132.16992	1118.46399	97.9597

(R)-Ethyl 5-hydroxy-7-methyloctanoate (2e)



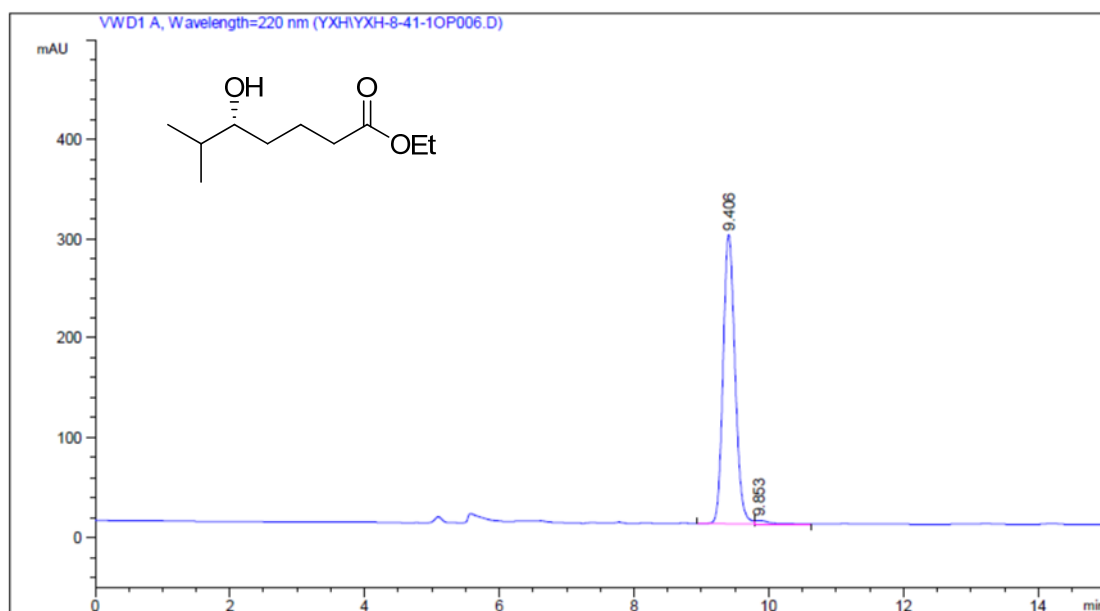
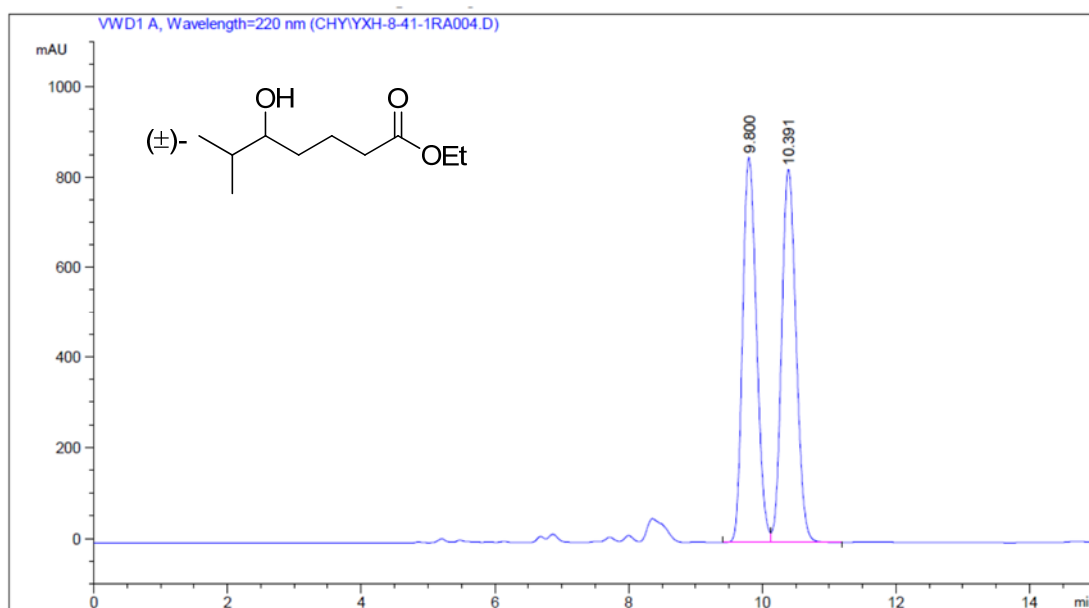
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.556	BV	0.1547	2833.94897	288.37079	94.8235
2	6.965	VB	0.1721	154.70706	13.26401	5.1765

(S)-7-Methyloctane-1,5-diol (3e)



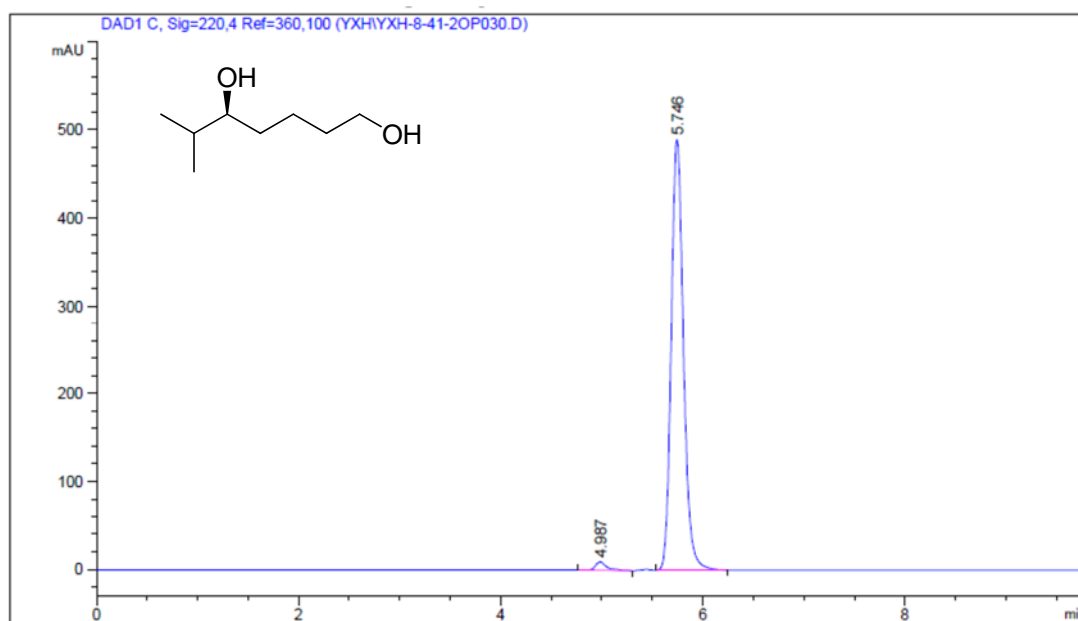
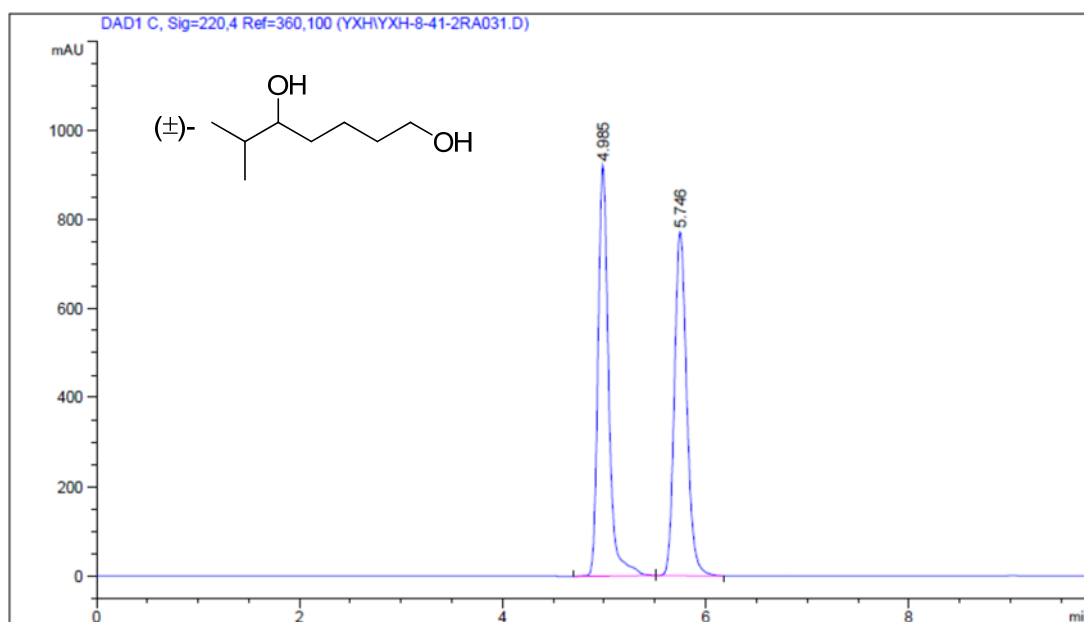
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.714	BB	0.1315	176.74823	20.72272	2.0671
2	5.257	BB	0.1296	8373.62305	1043.19067	97.9329

(R)-Ethyl 5-hydroxy-6-methylheptanoate (2f)



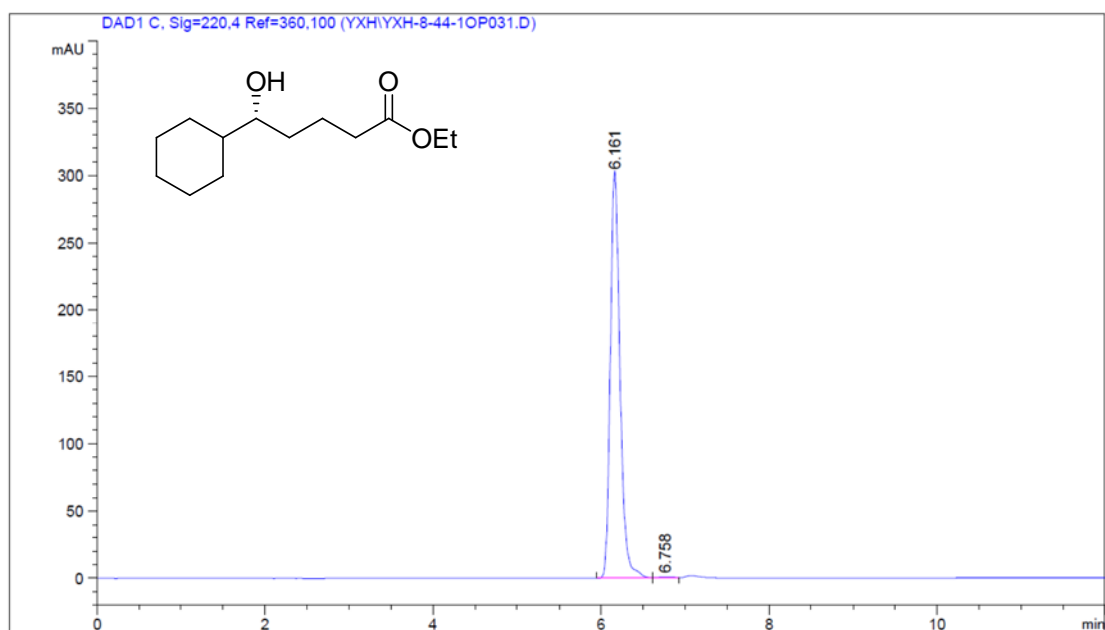
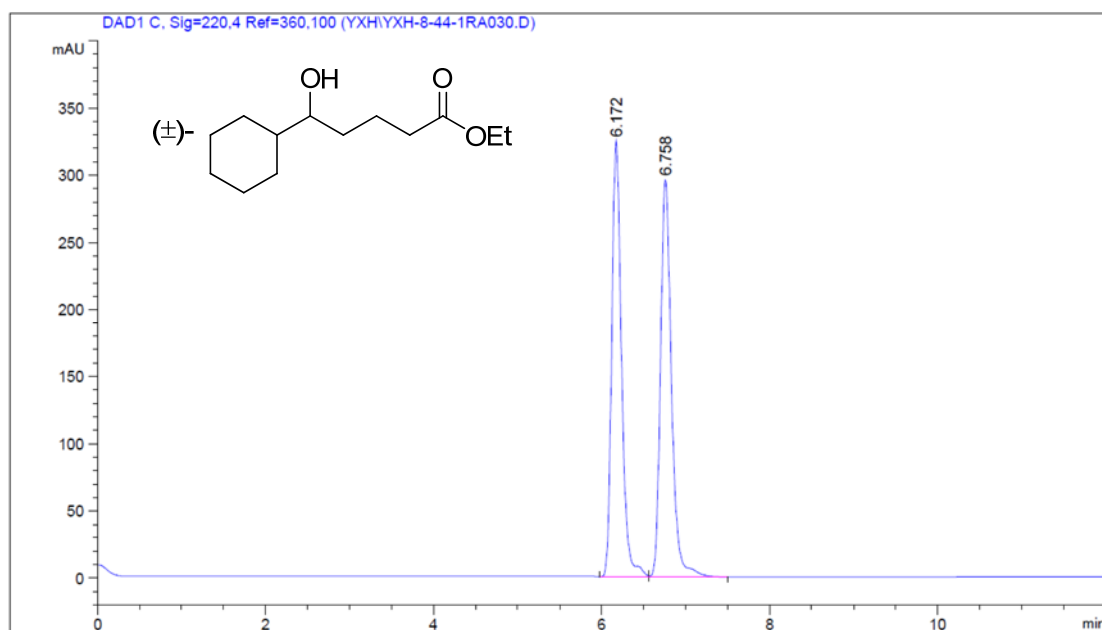
Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height [mAU]	Area %
1	9.406	BV	0.1896	3559.61450	290.33862	98.7224
2	9.853	VB	0.2012	46.06656	3.29123	1.2776

(S)-6-Methylheptane-1,5-diol (3f)



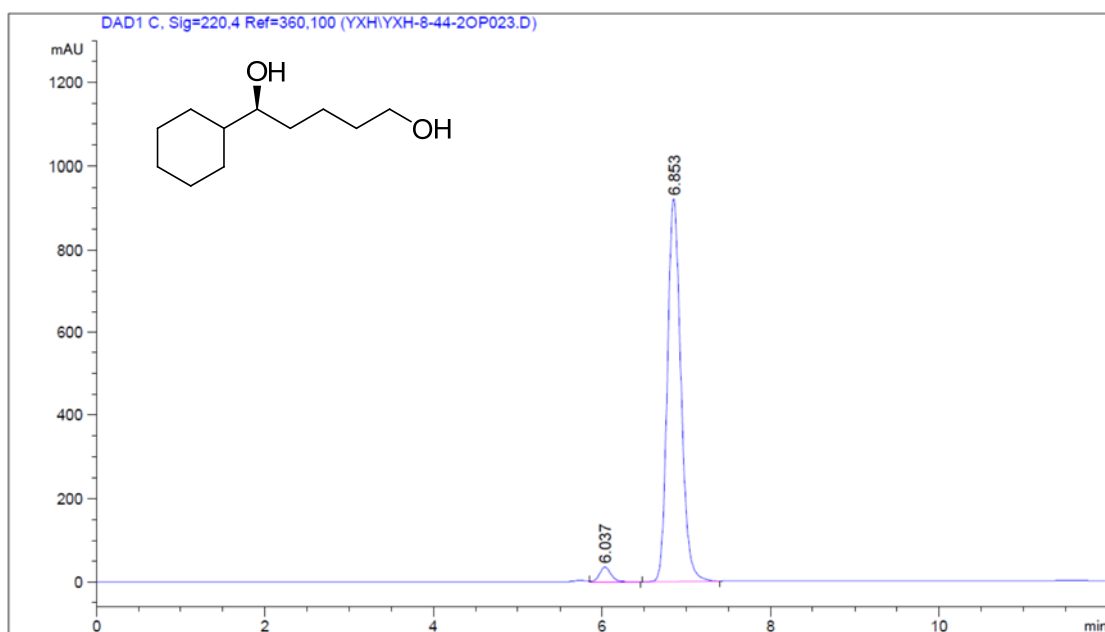
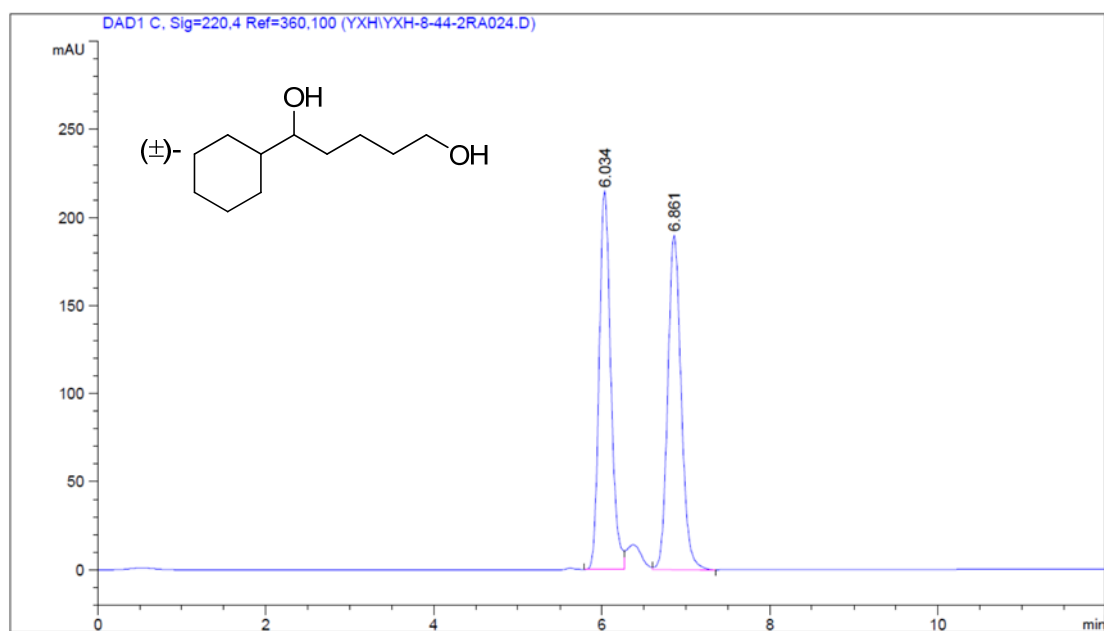
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.987	BB	0.1123	70.71246	9.33830	1.6819
2	5.746	VV	0.1302	4133.60889	490.93378	98.3181

(R)-Ethyl 5-cyclohexyl-5-hydroxypentanoate (2g)



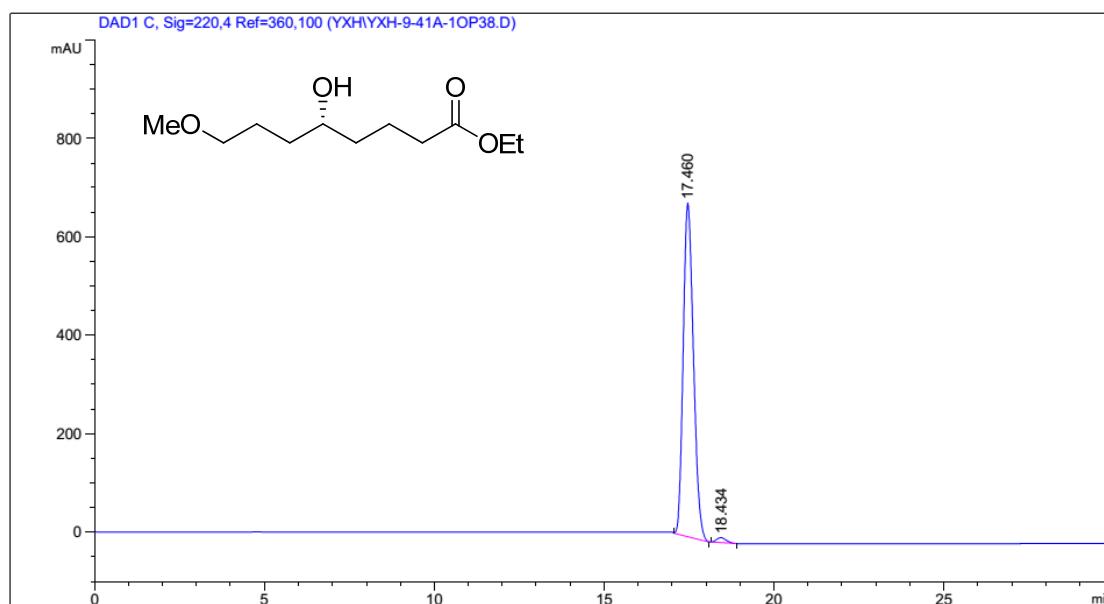
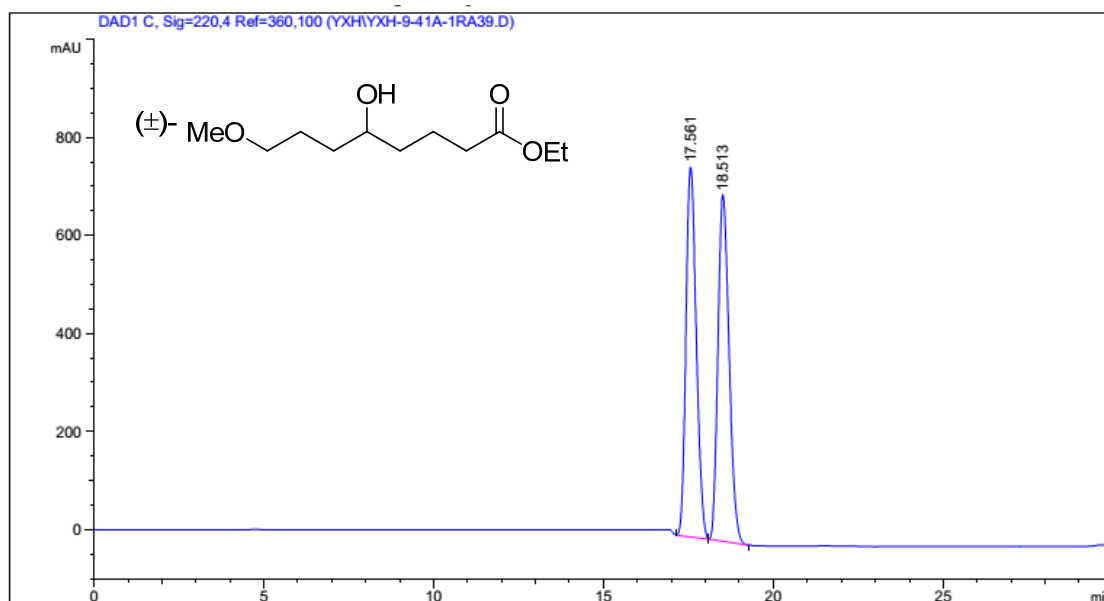
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.161	BV	0.1262	2431.22437	301.16501	99.4909
2	6.758	VV	0.1857	12.44146	9.44103e-1	0.5091

(S)-1-Cyclohexylpentane-1,5-diol (3g)



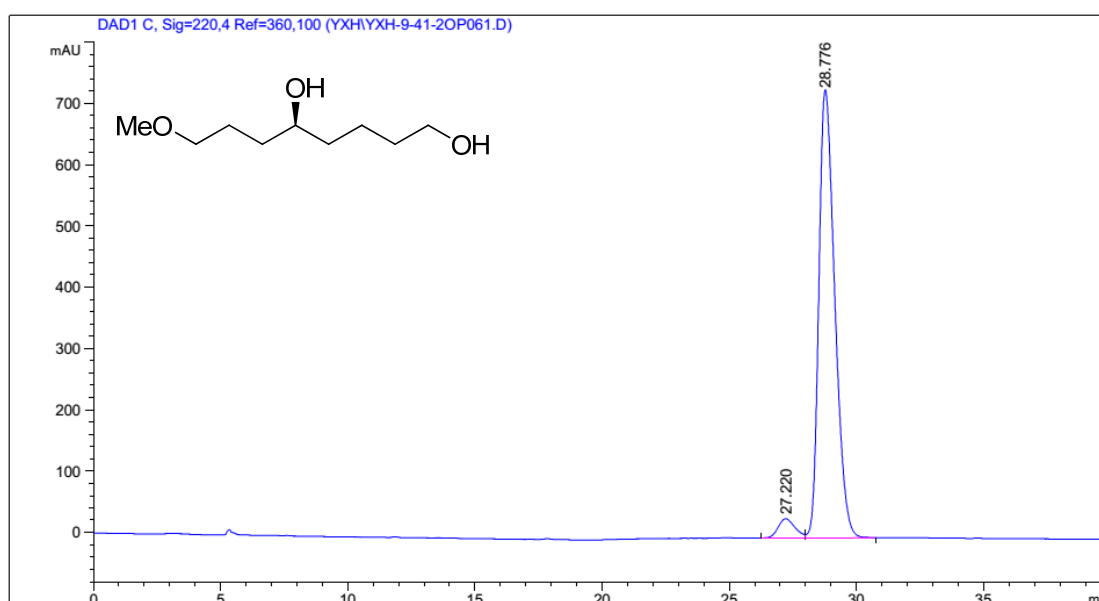
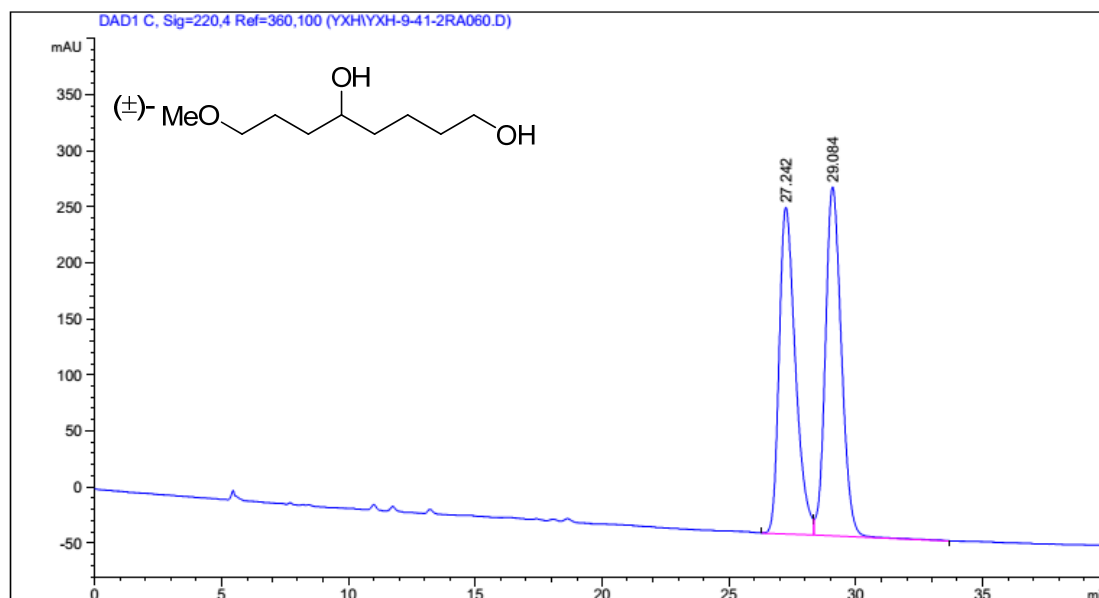
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.037	VB	0.1547	350.45425	35.65987	3.2938
2	6.853	BB	0.1746	1.02894e4	919.31409	96.7062

(R)-Ethyl 5-hydroxy-8-methoxyoctanoate (2h)



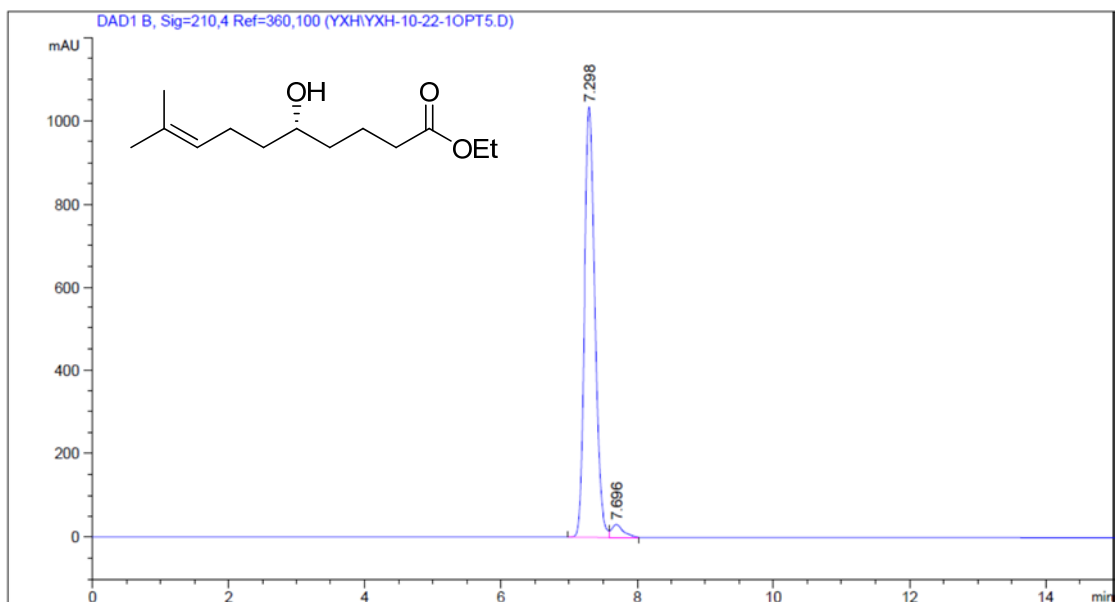
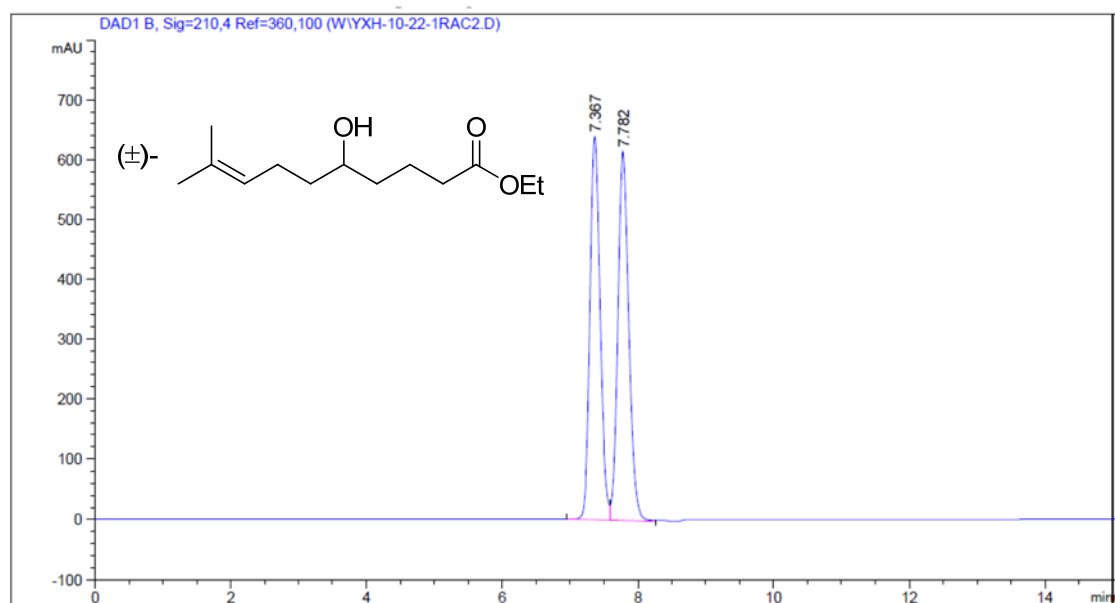
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.460	BB	0.3280	1.41655e4	677.35382	98.6268
2	18.434	BB	0.3148	197.22646	9.96923	1.3732

(S)-8-Methoxyoctane-1,5-diol (3h)



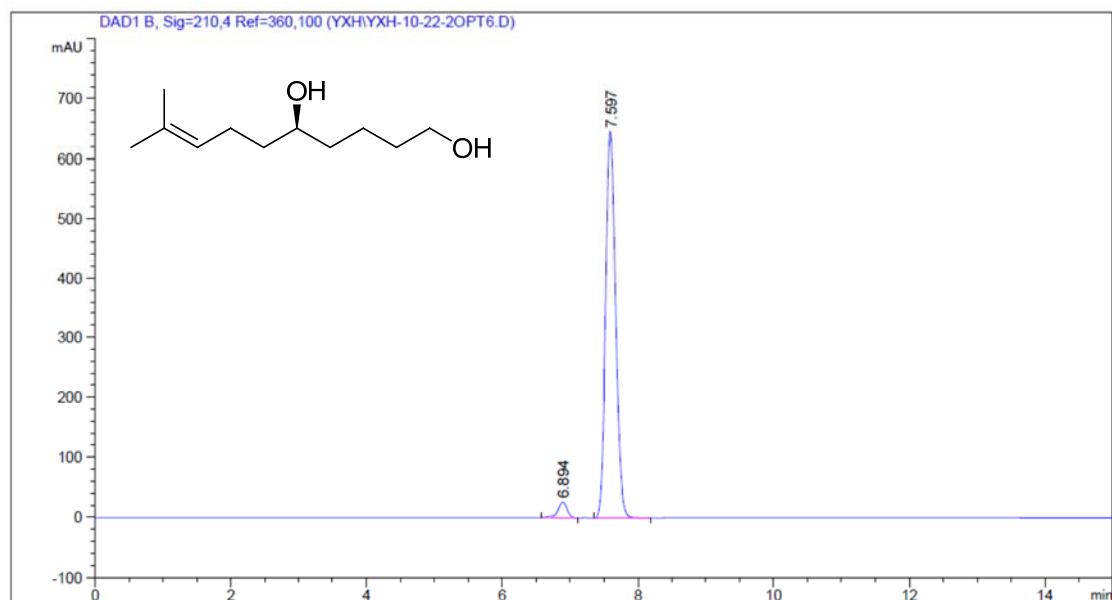
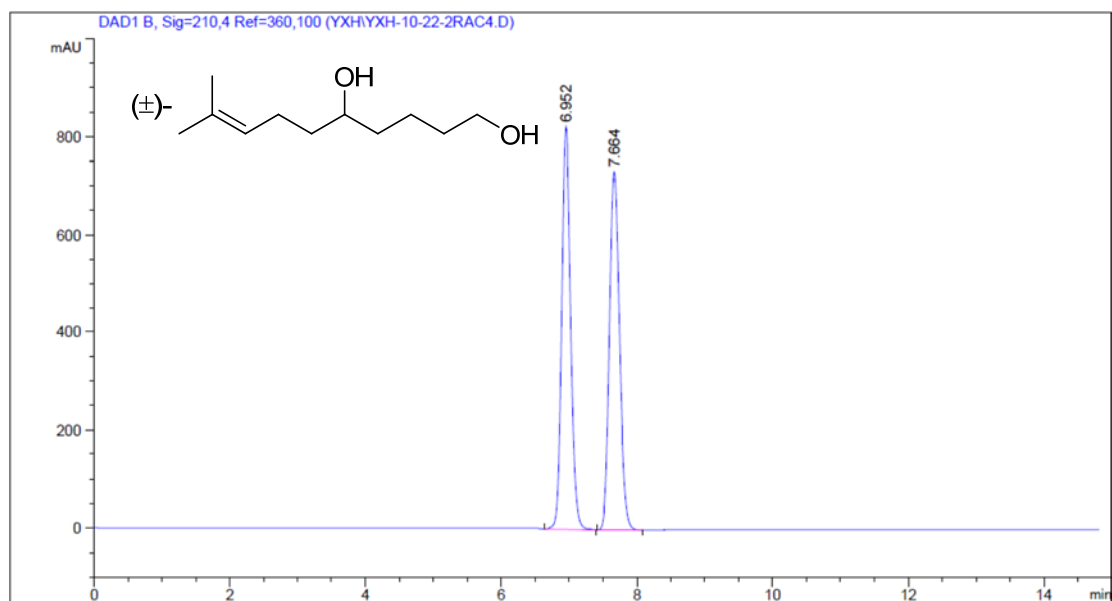
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.220	VV	0.7073	1453.19421	31.43697	4.3716
2	28.776	VB	0.6714	3.17884e4	730.87769	95.6284

(R)-Ethyl 5-hydroxy-9-methyldec-8-enoate (2i)



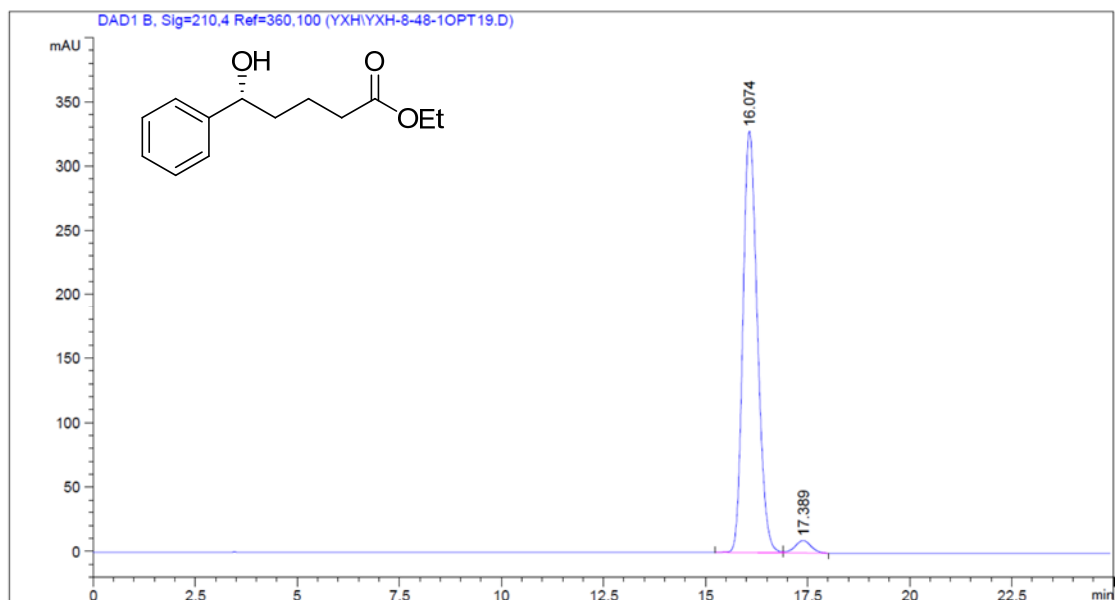
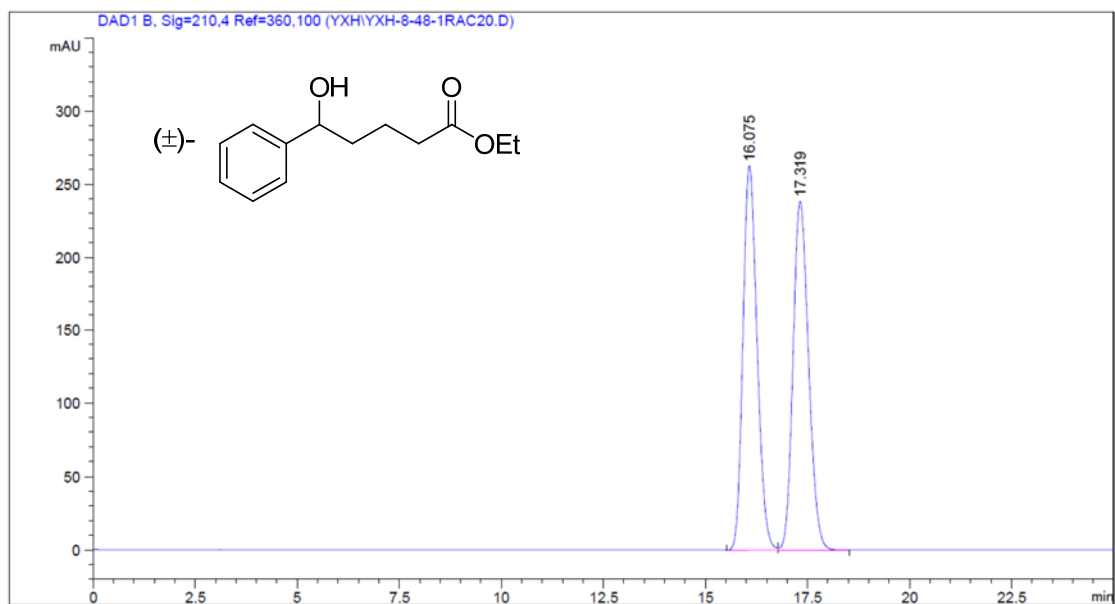
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.298	BV	0.1638	1.09760e4	1034.68091	96.7600
2	7.696	VB	0.1712	367.52780	30.79568	3.2400

(S)-9-Methyldec-8-ene-1,5-diol (3i)



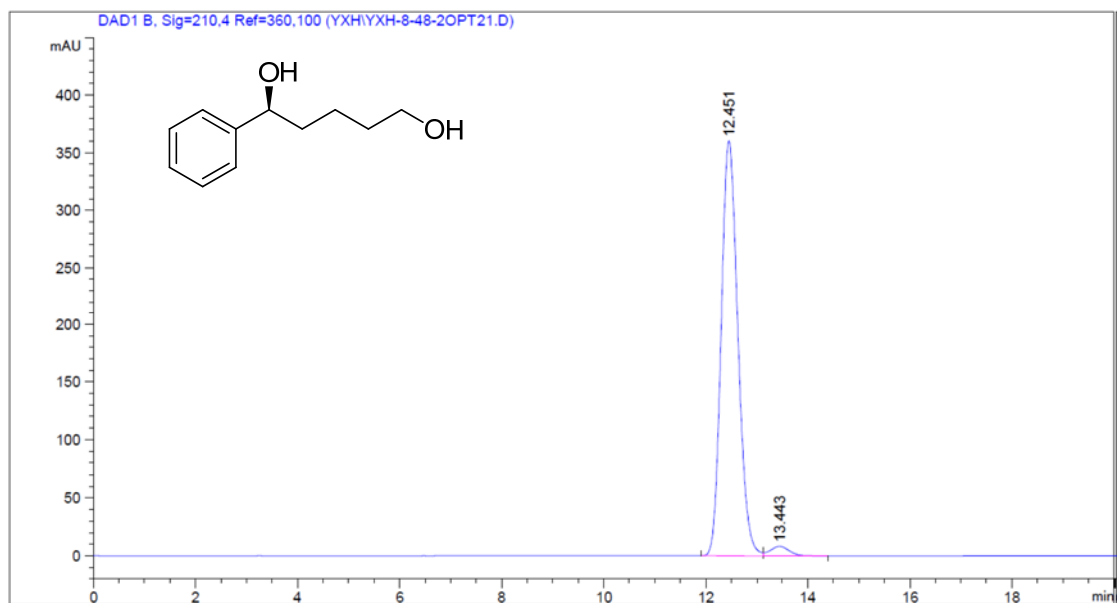
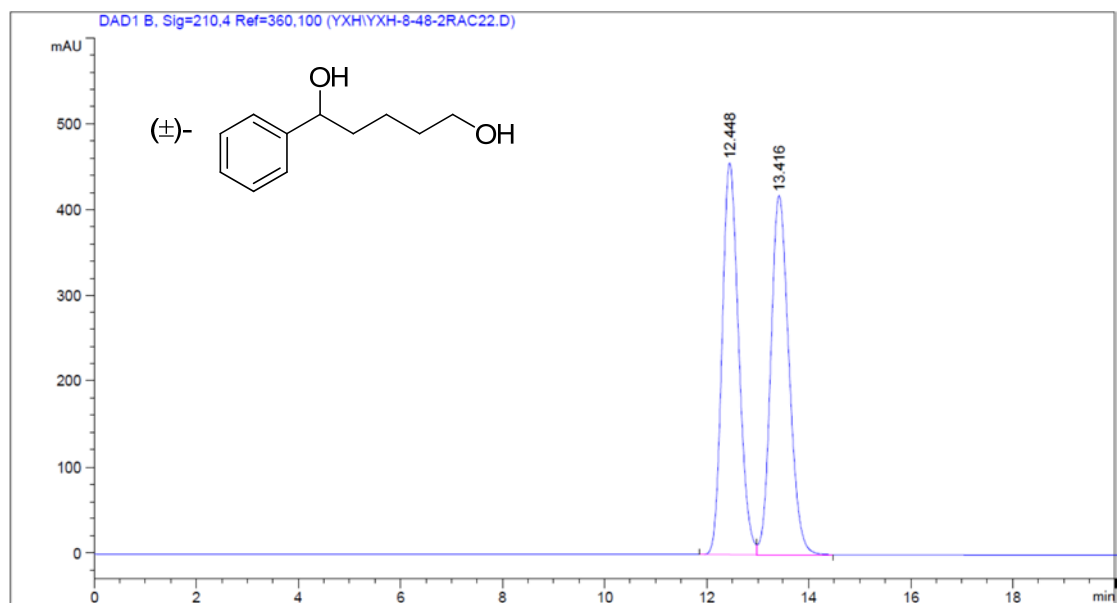
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.894	BB	0.1476	255.36989	26.22133	3.7374
2	7.597	BB	0.1589	6577.53223	645.47601	96.2626

(R)-Ethyl 5-hydroxy-5-phenylpentanoate (2j)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.074	BV	0.3803	8046.26318	327.85928	96.8679
2	17.389	VB	0.4156	260.16528	9.61762	3.1321

(S)-1-Phenylpentane-1,5-diol (3j)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.451	BV	0.3522	8161.90527	360.45322	97.3805
2	13.443	VB	0.3979	219.55640	8.37271	2.6195