Supplementary information

MANGANESE CATALYZED HYDROGENATION OF ENANTIOMERICALLY PURE ESTERS

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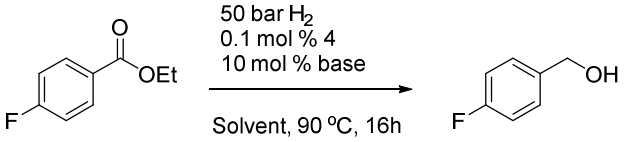
1. Tables and graphs

Table S1. Hydrogenation of ethyl para-fluorobenzoate - base study[a]



Base	Solvent	Conversion (%)[b]	Product (%)[b]
None	Isopropanol	0 %	0 %
KO^{t}Bu[c]	Isopropanol	>99 %	>99 %
K_2CO_3	Isopropanol	>99 %	>99 %
K_2CO_3	Ethanol	>99 %	>99 %
$KHCO_3$	Isopropanol	1.8 %	1.8 %
K_3PO_4	Isopropanol	>99 %	>99 %
KOH	Isopropanol	>99 %	>99 %
Na_2CO_3	Isopropanol	27 %	27 %
$NaHCO_3$	Isopropanol	1.3 %	1.3 %
$NaHCO_3$	Ethanol	0 %	0 %
NaOMe	Isopropanol	54 %	11 %
NaOEt	Isopropanol	9 %	9 %

a. 1.49 mmol substrate, 0.0015 mmol catalyst, 0.15 mmol base, 50 bar hydrogen pressure, solvent (0.5 M), at 90 °C, 16 h; b. assessed by ^{1}H-NMR using 1-methylnaphthalene as internal standard; c. Reaction run using 1 mol % **4** at 75 °C.

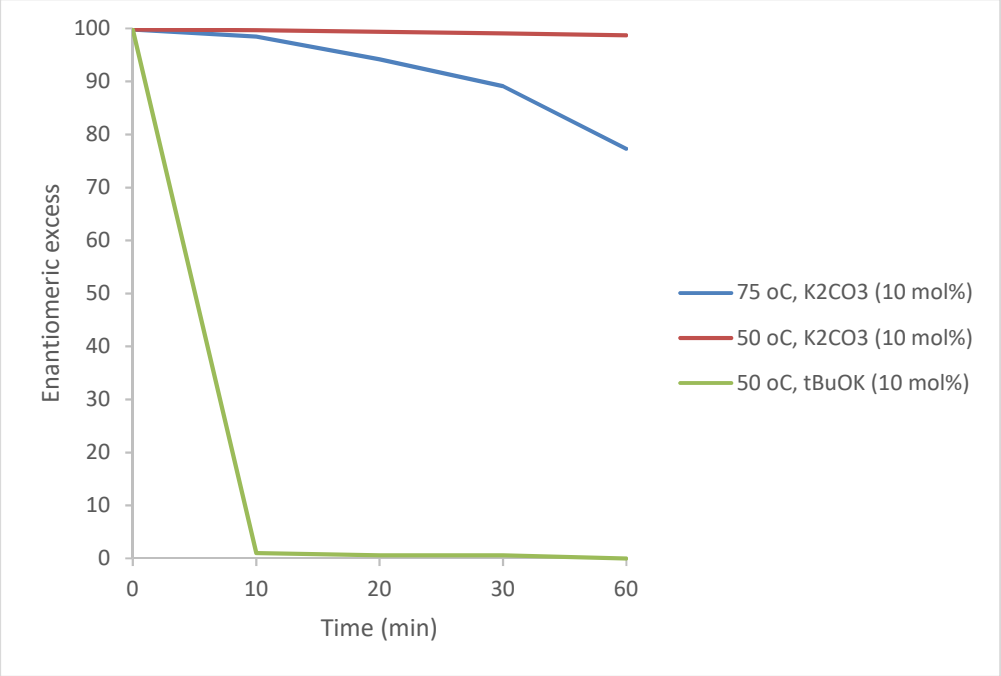


Figure S1. Racemization of (*S*)-ethyl naproxen using either potassium *tert*-butoxide (10 mol %) or potassium carbonate (10 mol %) at different temperatures. The enantiomeric excess was monitored using chiral HPLC (Chiralcel ODH using *n*-hexane / isopropanol (99/1) at 1 mL/min).

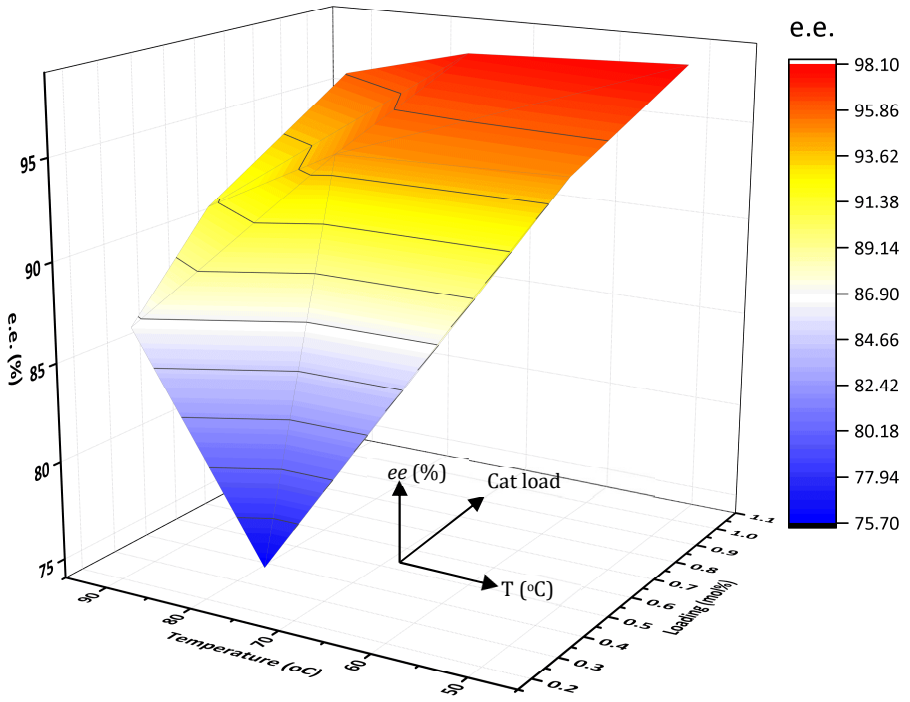


Figure S2. Combined representation of the effect on temperature and catalyst loading on the enantiomeric excess of (*S*)-naproxol using 10 mol % potassium carbonate and 50 bar hydrogen pressure.

Table S2. Impact of catalyst loading and solvent on the enantiomeric purity of (*S*)-naproxol[a]

Solvent	Catalyst load (mol%)	Conversion (%)[b]	*ee* (%)[c]
Ethanol	0.25	>99	13
Ethanol	0.5	>99	35
Isopropanol	0.25	>99	76
Isopropanol	0.5	>99	95

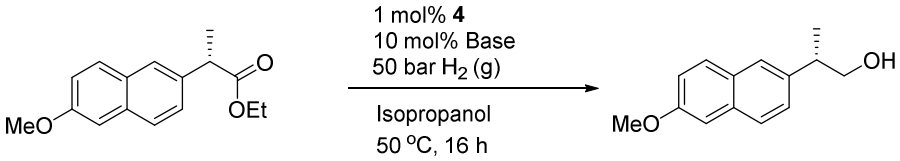
a. 1.00 mmol substrate, 0.0025 – 0.005 mmol catalyst, 0.10 mmol K_2CO_3, 50 bar hydrogen pressure, solvent (0.4 M), at 75 °C, 16 h; b. assessed by ^{1}H-NMR using 1-methylnaphthalene as internal standard; c. determined by chiral HPLC using a Chiralcel ODH column and *n*-hexane / isopropanol (96/4) as mobile phase with a flow of 1 mL/min.

Table S3. Base dependency on conversion and enantiomeric excess of (*S*)-naproxol[a]

Base (mol%)	Conversion (%)[b]	*ee* (%)[c]
1.25	44	96
2.5	65	93
5.0	66	93
10.0	>99	92

a. 0.8 mmol substrate, 0.002 mmol catalyst, x mol % K_2CO_3, 50 bar hydrogen pressure, solvent (0.4 M), at 50 °C, 16 h; b. assessed by ^{1}H-NMR using 1-methylnaphthalene as internal standard; c. determined by chiral HPLC using a Chiralcel ODH column and n-hexane / isopropanol (96/4) as mobile phase with a flow of 1 mL/min.

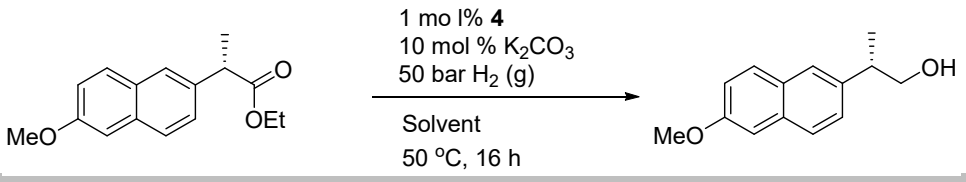
Table S4. Base study on the hydrogenation of (*S*) – ethyl naproxen[a]



Base	Conversion (%)[b]	$ee_{product}$ (%)[c]	ee_{SM} (%)[c]
K_2CO_3	>99	98	N/A
$KHCO_3$	0	N/A	>99
K_3PO_4	>99	96	N/A
KBH_4[d]	>99	88	N/A
Na_2CO_3	0	N/A	>99
$NaHCO_3$	0	N/A	>99
$NaBH_4$	>99	50	N/A

a. 1.00 mmol substrate, 0.01 mmol catalyst, 0.10 mmol base, 50 bar hydrogen pressure, isopropanol (0.4 M), at 75 °C, 16 h; b. assessed by ^{1}H-NMR using 1-methylnaphthalene as internal standard; c. determined by chiral HPLC using a Chiralcel ODH column and n-hexane / isopropanol (96/4) as mobile phase with a flow of 1 mL/min; d. reaction run at 75 °C as no conversion was observed at 50 °C.

Table S5. Co-solvent study on the hydrogenation of (*S*)-ethyl naproxen[a]



Co-solvent	Amount	Solvent	Conversion (%)[b]	ee_{SM} (%)[c]	ee-$_{product}$(%)[c]
None	N/A	Toluene	0	>99	N/A
Isopropanol	2 vol %	Toluene	2	>99	N/A
Isopropanol	5 vol %	Toluene	27	>99	99
Isopropanol	10 vol %	Toluene	28	>99	99
Isopropanol	20 vol %	Toluene	81	98	99
Isopropanol	40 vol %	Toluene	95	93	99
None	N/A	Isopropanol	>99	N/A	98

a. conditions: 0.97 mmol (*S*)-ethyl naproxen, 0.00097 mmol Mn catalyst, 0.097 mmol K_2CO_3, 50 bar hydrogen gas, isopropanol (0.4 M) at 50 °C for 16 h; b. assessed by ^{1}H-NMR using 1-methylnaphthalene as internal standard; c. determined by chiral HPLC using a Chiralcel ODH column and n-hexane / isopropanol (96/4) as mobile phase with a flow of 1 mL/min.

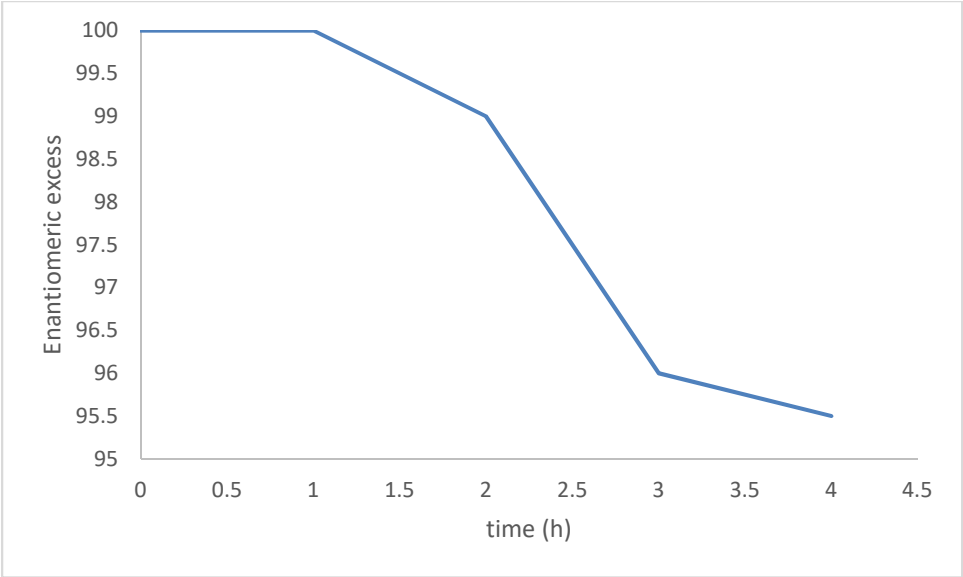


Figure S3. Racemization of (*S*)-ethyl 1,2,3,4-tetrahydronaphthalene-1-carboxylate using 10 mol % potassium carbonate in isopropanol at 50 °C. The enantiomeric excess was monitored by chiral HPLC (Chiralcel OD-H column, mobile phase: *n-h*exane / IPA (99/1), flow 1 mL/min.

2. Experimental

The preparation of solutions for the use in catalytic reactions were carried out under either argon or nitrogen atmospheres. All glassware was used oven dried or flame dried and cooled under vacuum before use. Solvents were degassed either by bubbling argon or nitrogen through the solvent for at least 1 h prior to use or freeze-pumped-thawed before use. Unless otherwise noted all chemicals were purchased from Sigma-Aldrich, Acros, Alfa Aesar, Strem or TCI and used as received (excepts when further degassed as stated above). Room temperature or ambient temperature refers to the temperature range 15-25 °C. Heating the reaction mixtures were affected by either an oil bath or a Drysyn heating block. Reported temperature is the oil bath or heating block temperature and not internal temperature unless stated and was measured using a contact thermometer (PT-1000). *In vacuo* refers to either the use of a Heidolph Laborota 4001 rotary evaporator or the use of a high-vacuum line. Analytical thin layer chromatography (TLC) was carried out on pre-coated plastic plates (Kieselgel 60 F254 silica). TLC visualization was carried out using a UV lamp (254nm) or using a 1% potassium permanganate aqueous solution. Flash silica chromatography was performed using Kieselgel 60 silica. ^{1}H, ^{13}C, ^{31}P, ^{19}F NMR was carried out using either a Bruker Avance 300 (300 MHz for ^{1}H, 75 MHz for ^{13}C, 121 MHz for ^{31}P and 282 MHz for

^{19}F), a Bruker Avance II 400 (400 MHz ^{1}H, 100 MHz ^{13}C, 161 MHz ^{31}P and 376 MHz for ^{19}F) or a Bruker Ultrashield 500 (500 MHz ^{1}H, 125 MHz ^{13}C, 201 MHz ^{31}P and 470 MHz for ^{19}F). NMR analyses were carried out at room temperature in the deuterated. The chemical shifts are quoted as parts per million (ppm). Coupling constants, *J*, are quoted in Hz. Multiplicities are indicated by: s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). The abbreviation "br" is used to denote broad peak shape. Infrared spectra were recorded on a Shimadzu IRAffinity-1 using Pike attenuated total reflectance (ATR) accessory. Peaks are reported as weak (w), medium (m) or strong (s). The abbreviation "br" denote a broad peak shape and "sh" denote a sharp peak shape. All units are reported in cm^{-1}. Mass spectrometric (m/z) data were acquired by electrospray ionisation (ESI) or electron impact (EI) either at the University of St Andrews Mass Spectrometry facility (using Micromass LCT spectrometer or Micromass GCT spectrometer) or at the EPRSC National Mass Spectrometry Service Centre, Swansea (using Orbitrap nano-ESI, Finnigan MAT 900 XLT or Finnigan MAT 95 XP). Values are reported as a ratio of mass to charge in Daltons. Optical rotations were measured on a Perkin Elmer 341 polarimeter using a 1 ml cell with a 1 dm path length at room temperature using the sodium D-line, and a suitable solvent that is reported along with the concentration (c = g/100ml). HPLC analysis has been determined using a Varian Prostar operated by Galaxie workstation PC software. For chromatograms where peak baselines were not fully resolved the lowest point between the two peaks were chosen as the cut-off point.

General procedure for hydrogenation of achiral esters and lactones

Substrate (1.60 mmol) was added to a Schlenk flask together with 1-methylnaphthalene (56 µL, 0.40 mmol, 0.25 equiv.) and ethanol (3.2 mL) and degassed by bubbling argon gas through the solution for at least 30 min. To a microwave vial containing a magnetic bead was added catalyst (1.2-12 mg, 0.0016-0.016 mmol, 0.001-0.001 depending on substrate) and base (22 g, 0.16 mmol, 0.10 equiv.). The vial was capped and put under an inert atmosphere using vacuum / argon cycles (3). The degassed substrate solution was added to the vial under argon. The vial was pierced by two 18G needles and placed in a stainless-steel autoclave under argon atmosphere. The vessel was sealed and pressurized with hydrogen gas to 50 bar. The pressure was released, and the procedure repeated twice. Finally, the vessel was pressurized with hydrogen gas (50 bar), sealed and placed in a pre-heated oil-bath at the designated reaction temperature (90 °C) for 16 h. The vessel was cooled to ambient temperature and the pressure slowly released. The vial was uncapped, and an aliquot was taken, diluted with deuterated chloroform and analyzed by ^{1}H-NMR to assess the conversion using 1-methylnaphthalene as internal standard. The crude products were purified by column chromatography.

Large scale hydrogenation of Sclareolide

Degassed (by argon sparging) ethanol (40 mL) was added to an opem stainless-steel autoclave fitted with a glass insert and a cross-shaped stir bar, followed by manganese catalyst (14 mg, 0.02 mmol, 0.001 equiv.), potassium carbonate (276 mg, 2.00 mmol, 0.10 equiv.) and finally (R)-Sclareolide (5.0 g, 20.0 mmol, 1.0 equiv.). The material was washed in with degassed ethanol (10 mL). The vessel was sealed and pressurized with hydrogen gas (50 bar) and vented to the atmosphere. This was repeated 4 times. The vessel as pressurized to 50 bar with hydrogen gas and placed in an oil-bath pre-heated to 90 °C for 16 h, then cooled to ambient temperature and the pressure carefully vented to the atmosphere. The yellow solution was transferred to a round-bottom flask and concentrated to about 20 mL volume *in vacuo* and left to cool to ambient temperature under gentle stirring and filtered to remove residual inorganic material and washed with ethanol (5 mL). Water (75 mL) was added which resulted in the formation of a white slurry which was aged for 1 h, then filtered and washed with water (30 mL) and hexanes (50 mL) to give sclareodiol as a white solid (3.8 g, 14.9 mmol, 75 % isolated yield). For characterization see section 3.

General procedure for the hydrogenation of α-chiral esters

Substrate (1.00 mmol, 1.0 equiv.) was added to a Schlenk flask together with 1-methylnaphthalene (50 µL, 0.35 mmol, 0.35 equiv.) and isopropanol (2.8 mL) and degassed by bubbling argon gas through the solution for at least 30 min. To a microwave vial, containing a magnetic bead, was added catalyst (7.3 mg, 0.01 mmol, 0.01 equiv.) and potassium carbonate (14 mg, 0.10 mmol, 0.10 equiv.). The vial was capped and put under an inert atmosphere using vacuum / argon cycles (3). The degassed substrate solution was added to the vial under argon. The vial was pierced by two 18G needles and placed in a stainless-steel autoclave under argon atmosphere. The vessel was sealed and pressurized with hydrogen gas to 50 bar. The pressure was released, and the procedure repeated twice. Finally, the vessel was pressurized with hydrogen gas (50 bar), sealed and placed in a pre-heated oil-bath at the designated reaction temperature (50 °C to 110 °C) for 16 h. The vessel was cooled to ambient temperature and the pressure slowly released. The vial was uncapped, and an aliquot was taken, diluted with deuterated chloroform and analyzed by ^{1}H-NMR to assess the conversion using 1-methylnaphthalene as internal standard. The crude products were purified by column chromatography and analyzed by chiral HPLC and NMR.

Racemization of (*S*)-ethyl naproxen

(*S*)-ethyl naproxen (0.5 g, 1.94 mmol, 1.0 equiv.) was dissolved in anhydrous isopropanol (6.5 mL) in a round-bottom flask containing a magnetic stir bar at room temperature. The mixture was heated to the desired temperature (50 – 90 °C) under an inert atmosphere. Potassium carbonate (27 mg, 0.19 mmol, 0.10 equiv.) or potassium *t*butoxide (190 µL, 0.10 equiv., 1M solution in *t*butanol) was added. The mixture was samples continuously and the aliquots were analyzed by chiral HPLC (Chiralcel ODH, *n*-hexane/isopropanol (99/1), flow 1 mL/min) for 1-2 h.

Racemization of (*S*)-ethyl 1,2,3,4-tetrahydronaphthalene

(*S*)-ethyl 1,2,3,4-tetrahydronaphthalene (50 mg, 0.245 mmol, 1.0 equiv.) was dissolved in anhydrous isopropanol (0.8 mL) in a round-bottom flask containing a magnetic stir bar at room temperature. The mixture was heated to the desired temperature (50 °C)

under an inert atmosphere. Potassium carbonate (3.4 mg, 0.025 mmol, 0.10 equiv.) was added. The mixture was samples continuously and the aliquots were analyzed by chiral HPLC (Chiralcel ODH, *n*-hexane/isopropanol (99/1), flow 1 mL/min) for 4 h.

3. Synthesis and characterization data

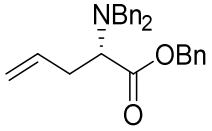
Catalyst synthesis

Catalyst *rac*-**4** was synthesised according to previously reported procedure[1] but starting from racemic starting material.

Substrate synthesis and characterization data

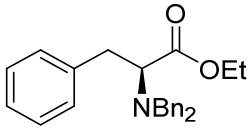
Substrates **5a-5h**, **7a** and **9j** were bought either from Sigma Aldrich or Alfa Aesar and used without any further purification.

(*S*)-Benzyl *N*, *N*-dibenzyl allylglycinate, 9a



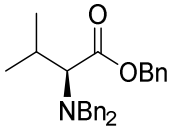
(*S*)-allylglycine (1.0g, 8.68 mmol, 1.0 equiv.), sodium hydroxide (0.70g, 17.36 mmol, 2.0 equiv.) and sodium carbonate (1.84g, 17.36 mmol, 2.0 equiv.) was dissolved in water (20 mL) in a 100 mL 2-neck round-bottom flask at room temperature. The mixture was heated to reflux and benzyl bromide (3.1 mL, 26.0 mmol, 3.0 equiv.) was slowly added over 20 min. The opaque milky mixture was refluxed for another 1.5 h, then cooled to room temperature and extracted with diethyl ether (2x50 mL). The combined organic layers were extracted with 4N HCl (aq, 2x 25mL). The aqueous layers were combined, and the pH adjusted to 10-11 using potassium carbonate, extracted with diethyl ether (3x50 mL). The organic layers were dried over magnesium sulfate, filtered and concentrated to dryness. The crude product was purified by column chromatography using a gradient of 100% petroleum ether (60-40) to petroleum ether / ethyl acetate (30/1) to isolate the product as a colorless oil (1.6g, 4.2 mmol, 48 %). ^{1}H-NMR ($CDCl_3$) δ: 7.45-7.22 (15H, m, Ph-H), 5.75 (1H, m, C<u>H</u>=CH_2), 5.28 (1H, d, J = 12.2 Hz, PhC<u>H</u>$_2$O), 5.18 (1H, d, J = 12.2 Hz, PhC<u>H</u>$_2$O-), 5.06 (2H, m, -CH=C<u>H</u>$_2$), 3.93 (2H, d, J = 13.5 Hz PhC<u>H</u>$_2$N), 3.54 (2H, d, J = 13.5 Hz PhC<u>H</u>$_2$N), 3.50 (1H, d, J = 7.4 Hz, C<u>H</u>CO_2R), 2.56 (2H, m, -C<u>H</u>$_2$-); ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 172.2 (-<u>C</u>O_2R), 139.46 (<u>C</u>$_{Ar}CH_2$N), 136.0 (<u>C</u>$_{Ar}CH_2$O), 134.93 (CH_2=<u>C</u>HCH_2-), 128.83 (<u>C</u>$_{Ar}$), 128.59 (<u>C</u>$_{Ar}$), 128.48 (<u>C</u>$_{Ar}$), 128.34 (<u>C</u>$_{Ar}$), 128.19 (<u>C</u>$_{Ar}$), 128.19 (<u>C</u>$_{Ar}$), 126.98 (<u>C</u>$_{Ar}$), 117.01 (<u>C</u>H_2=CHCH_2-), 66.03 (<u>C</u>HCO_2R), 60.73 (Ph<u>C</u>H_2O), 54.40 (Ph<u>C</u>H_2N), 33.98 (-<u>C</u>H_2-); HRMS (ES+): calculated for [$C_{26}H_{28}NO_2^+$]: 386.2115 found: 386.2111; Chiral analysis was performed using serial linked Chiralcel AD-H and OD-H column using *n*-hexane as the mobile phase, flow 0.5 mL/min; t_R (*R*-enantiomer, minor): 39.7 min; t_R (*S*-enantiomer, major): 45.5 min, *ee* >99 %. Fits with previously published data.[2]

***L*-Ethyl *N*, *N*-dibenzylphenylalaninate, 9b**



L-ethyl phenylalanine hydrochloride (1.5g, 6.53 mmol, 1.0 equiv.) was stirred in acetonitrile (30 mL) at room temperature in a 100 mL round-bottom flask. Benzyl bromide (2.4 mL, 20.6 mmol, 3.2 equiv.) and ethyldiisopropylamine (6 mL, 34.4 mmol, 5.3 equiv.) was added to the flask and the formed slurry was heated to reflux for 5 h, then cooled to ambient temperature and volatiles removed *in vacuo*. The crude material was dissolved in ethyl acetate and washed with water (3 x 20 mL), dried over magnesium sulfate, filtered and concentrated to a brown oil. The product was purified by column chromatography using a gradient of hexanes / ethyl acetate (9/1 – 1/1) to give the title compound as a colorless oil (1.3 g, 3.5 mmol, 53 %); $[\alpha]_D^{20}$: -77.2 (*c.* 1.00, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 7.31-7.22 (12H, m, Ph-H), 7.06 (2H, m, Ph-H), 4.33 (2H, m, -OC<u>H</u>$_2$CH$_3$), 4.00 (2H, d, J = 13.8 Hz, -NC<u>H</u>$_2$Ph), 3.69 (1H, t, J = 8.50 Hz PhCH_2C<u>H</u>N-), 3.61 (2H, d, J = 13.8 Hz, -NC<u>H</u>$_2$Ph), 3.08 (2H, m, PhC<u>H</u>$_2$-), 1.34 (3H, t, J = 7.62 Hz, C<u>H</u>$_3$CH$_2$O); ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 172.28 (-<u>C</u>O_2R), 139.34 (-<u>C</u>$_{Ar}CH_2$-), 138.24 (-<u>C</u>$_{Ar}CH_2$-), 129.47 (<u>C</u>$_{Ar}$), 128.73 (<u>C</u>$_{Ar}$), 128.17 (<u>C</u>$_{Ar}$), 126.92 (<u>C</u>$_{Ar}$), 126.24 (<u>C</u>$_{Ar}$), 62.28 (<u>C</u>HCO_2R), 60.23 (<u>C</u>H_3CO), 54.45 (-<u>C</u>H_2Ph-), 35.79 (-<u>C</u>H_2-), 14.59 (-<u>C</u>H_3); HRMS (ES+): calculated for [$C_{25}H_{28}NO_2$+]: 374.2115 found: 374.2111. Fits with previously published data.[14]

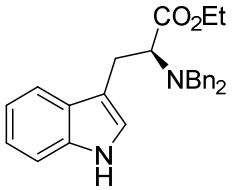
***L*-Benzyl *N, N,* dibenzylvalinate, 9c**



L-valine (2.0 g, 17.1 mmol, 1.0 equiv.), sodium hydroxide (1.4 g, 34.2 mmol, 2.0 equiv.) and sodium carbonate (3.6 g, 34.2 mmol, 2.0 equiv.) were dissolved in water (40 mL) and heated to 50 °C. Benzyl bromide (6.0 mL, 51.2 mmol, 3.0 equiv.) was added and the mixture stirred at 50 °C for 17 h, then at reflux for 1.5 h, cooled to room temperature and extracted with diethyl ether (2x 30 mL). The combined organic layers were dried over magnesium sulfate, filtered and concentrated to dryness. The product as purified by column chromatography (hexanes / diethyl ether 90/10) to give the title compound as a colorless oil (4.2 g, 10.8 mmol, 63 %). $[\alpha]_D^{20}$:

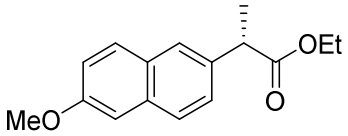
-115.1 (*c.* 1.00, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 7.39 (15H, m, Ph-H), 5.36 (1H, d, J = 12.0 Hz PhC<u>H</u>$_2$O), 5.22 (1H, d, J = 12.0 Hz PhC<u>H</u>$_2$O), 4.03 (2H, d, J = 13.6 Hz PhC<u>H</u>$_2$N), 3.34 (2H, d, J = 13.6 Hz PhC<u>H</u>$_2$N), 2.97 (1H, d, J = 12 Hz, C<u>H</u>CO$_2$R), 2.24 (1H, m, -C<u>H</u>(CH$_3$)$_2$), 1.08 (3H, d, J = 8.5 Hz, -C<u>H</u>$_3$), 0.84 (3H, d, J = 8.5 Hz, -C<u>H</u>$_3$); ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 171.90 (-<u>C</u>O$_2$R), 139.53 (<u>C</u>$_{Ar}$CH$_2$N), 136.16 (<u>C</u>$_{Ar}$CH$_2$O), 128.82 (<u>C</u>$_{Ar}$), 128.69 (<u>C</u>$_{Ar}$), 128.60 (<u>C</u>$_{Ar}$), 128.36 (<u>C</u>$_{Ar}$), 128.24 (<u>C</u>$_{Ar}$), 126.94 (<u>C</u>$_{Ar}$), 68.16 (<u>C</u>HCO$_2$R), 65.74 (Ph<u>C</u>H$_2$O), 54.64 (Ph<u>C</u>H$_2$N), 27.32 (-<u>C</u>H-), 20.00 (-<u>C</u>H$_3$), 19.58 (-<u>C</u>H$_3$); HRMS (ES+): calculated for [$C_{26}H_{30}NO_2^+$]: 388.2271 found: 388.2267. Fits with previously published data.[15]

_L_-Ethyl _N, N_-dibenzyltryptophan, 9d



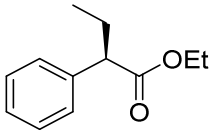
Tryptophan ethyl ester hydrochloride salt (5.0 g, 18.6 mmol, 1.0 equiv.) and sodium iodide (0.30 g, 0.19 mmol, 0.10 equiv.) was stirred in acetonitrile (50 mL) at room temperature under an argon atmosphere. Ethyldiisopropylamine (16.5 mL, 94.4 mmol, 5.1 equiv.) and benzyl bromide (7.5 mL, 63.4 mmol, 3.4 equiv.) was added and the formed slurry was heated to reflux 4 h. The slurry was cooled to room temperature and concentrated to dryness. The crude was dissolved in water (30 mL) and extracted with diethyl ether (2x 25 mL). The combined organic layers were washed with 1N HCl (aq, 25 mL) and dried over magnesium sulfate, filtered and concentrated to dryness. The product was purified by column chromatography using a hexane / diethyl ether gradient (9/1 – 0/1) to give the title compound as an orange solid (3.3 g, 8.0 mmol, 43 %). The product was found to contain trace amounts of DCM as an impurity. $[\alpha]_D^{20}$: -91.8 (*c.* 1.00, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 7.94 (1H, s, NH), 7.32 (12H, m, Ar-H), 7.17 (2H, m, Ar-H), 6.99 (1H, m, Ar-H), 6.92 (1H, m, Ar-H), 5.33 (DCM), 4.27 (1H, m, CH$_3$C<u>H</u>$_2$O-), 4.14 (1H, m, CH$_3$C<u>H</u>$_2$O-), 4.06 (2H, d, J = 13.9 Hz, PhC<u>H</u>$_2$N-), 3.82 (1H, m, -C<u>H</u>-), 3.61 (2H, d, J = 13.9 Hz PhC<u>H</u>$_2$N), 3.42 (1H, m, ArC<u>H</u>$_2$-), 3.12 (1H, m, ArC<u>H</u>$_2$), 2.21 (Acetone), 1.31 (3H, t, J = 9.5 Hz, C<u>H</u>$_3$CH$_2$O); ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 172.42 (-<u>C</u>O$_2$R), 139.62 (<u>C</u>$_{Ar}$CH$_2$N), 136.11 (<u>C</u>$_{Ar}$), 128.83 (<u>C</u>$_{Ar}$), 128.22 (<u>C</u>$_{Ar}$), 127.50 (<u>C</u>$_{Ar}$), 126.94 (<u>C</u>$_{Ar}$), 122.76 (<u>C</u>$_{Ar}$), 121.77 (<u>C</u>$_{Ar}$), 119.18 (<u>C</u>$_{Ar}$), 118.79 (<u>C</u>$_{Ar}$), 112.23 (<u>C</u>$_{Ar}$), 110.90 (<u>C</u>$_{Ar}$), 61.27 (<u>C</u>HCO$_2$R), 60.08 (CH$_3$<u>C</u>H$_2$O), 54.68 (Ph<u>C</u>H$_2$N), 26.19 (-<u>C</u>H$_2$-), 14.61 (CH$_2$<u>C</u>H$_3$); HRMS (ES+): calculated for [$C_{27}H_{29}N_2O_2$+]: 413.2224 found: 413.2211

***(S)*-Ethyl naproxen, 9e**



(*S*)-naproxen (5 g, 21.7 mmol, 1.0 equivalents) and sulfuric acid (1 mL) were heated in ethanol (50 mL) at 50 °C for 18 h then cooled to room temperature and volatiles removed *in vacuo*. The crude was dissolved in ethyl acetate (50 mL) and washed with saturated aqueous sodium bicarbonate (40 mL) followed by water (50 mL). The organic solution was dried over magnesium sulfate, filtered and concentrated to give the title compound as a white solid (4.7 g, 18.2 mmol, 84 %). $[\alpha]_D^{20}$: +39.3 (*c.* 1.00, $CHCl_3$), Lit.:+42 (*c.* 1.00, $CHCl_3$)[16]; ^{1}H-NMR ($CDCl_3$) δ: 7.72 (3H, m, Ar-H), 7.45 (1H, dd, J = 8.5 / 1.8 Hz, Ar-H), 7.17 (2H, m, Ar-H), 4.17 (2H, m, CH$_3$C<u>H</u>$_2$O), 3.94 (3H, s, CH$_3$O-), 3.88 (1H, q, J = 7.3 Hz, ArC<u>H</u>(CH$_3$)CO$_2$R), 1.61 (3H, d, J = 7.3 Hz, -CH$_3$), 1.24 (3H, t, J = 7.5 Hz, -OCH$_2$C<u>H</u>$_3$) ; ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 174.72 (-<u>C</u>O$_2$R), 157.62 (C$_{Ar}$OMe), 135.86 (<u>C</u>$_{Ar}$), 133.67 (<u>C</u>$_{Ar}$), 129.30 (<u>C</u>$_{Ar}$), 128.95 (<u>C</u>$_{Ar}$), 127.12 (<u>C</u>$_{Ar}$), 126.27 (<u>C</u>$_{Ar}$), 125.93 (<u>C</u>$_{Ar}$), 118.96 (<u>C</u>$_{Ar}$), 105.58 (<u>C</u>$_{Ar}$), 60.78 (<u>C</u>H$_3$O), 55.32 (Ar<u>C</u>H), 45.51 (-<u>C</u>H$_2$O), 18.66 (-<u>C</u>H$_3$), 14.17 (-<u>C</u>H$_3$); HRMS (EI+): calculated for [$C_{16}H_{18}O_3$]: 258.1256 found: 258.1260; Chiral analysis was performed using a Chiralcel OD-H column using *n*-hexane / isopropanol (99/1) mobile phase, flow 1.0 mL/min; t_R (*R*-enantiomer, minor): 8.9 min; t_R (*S*-enantiomer, major): 10.5 min, *ee* 99 %. Fits with previously published data.[17]

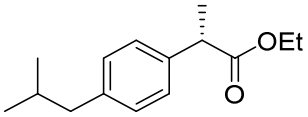
***(R)*-Ethyl 2-phenylbutyrate, 9f**



(*R*)-2-phenylbutyric acid (800 mg, 4.88 mmol, 1.0 equiv.) was dissolved in dichloromethane (20 mL) at room temperature. DMF (0.1 mL) was added followed by thionyl chloride (0.44 mL, 5.64 mmol, 1.2 equiv.). The solution was stirred at room temperature for 2 h then concentrated to dryness. The crude mixture was dissolved in ethanol (20 mL) and DMAP (10 mg) added and heated to reflux for 2 h. After cooling the mixture to room temperature volatiles were removed *in vacuo*. The crude product was dissolved in diethyl ether (25 mL) and washed with water (2 x 15 mL), dried over magnesium sulfate, filtered and concentrated to dryness and dissolved in hexanes / diethyl ether (80/20), filtered over silica and concentrated to give the title compound as a colorless oil (760 mg, 3.42 mmol, 70 %). $[\alpha]_D^{20}$: -45.5 (*c.* 1.5, $CHCl_3$), Lit.: -65.7 (*c.* 1.508, Et_2O)[18]; ^{1}H-NMR ($CDCl_3$) δ: 7.34 (4H, m, Ph-H), 7.28 (1H, m, Ph-H), 4.14 (2H, m, CH$_3$C<u>H</u>$_2$O), 3.46 (1H, t, J = 8.0 Hz PhC<u>H</u>(C$_2$H$_5$)CO$_2$R), 2.12 (1H, m, -C<u>H</u>$_2$-), 1.82 (1H, m, -C<u>H</u>$_2$-), 1.24 (3H, t, J = 7.1 Hz, C<u>H</u>$_3$CH$_2$O), 0.92 (3H, t, J = 7.4 Hz, -C<u>H</u>$_3$); ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 174.08 (-<u>C</u>O$_2$R), 139.26 (<u>C</u>$_{Ar}$CH$_2$), 128.51 (<u>C</u>$_{Ar}$), 127.95 (<u>C</u>$_{Ar}$), 127.10 (<u>C</u>$_{Ar}$), 60.62 (<u>C</u>H$_2$O), 53.56 (Ph<u>C</u>H$_2$), 31.61 (-<u>C</u>H$_2$-), 14.17 (-<u>C</u>H$_3$), 12.20 (-<u>C</u>H$_3$); HRMS (EI+): calculated for [$C_{12}H_{16}O_2$]: 192.1150 found: 180.1146;

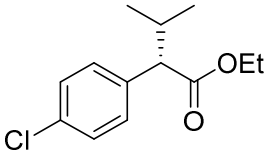
Chiral analysis was performed using a Chiralcel OD-H column using *n*-hexane / isopropanol (99.5/0.5) mobile phase, flow 0.5 mL/min; t_R (*R*-enantiomer, major): 10.7 min; t_R (*S*-enantiomer, minor): 11.3 min, *ee* >99 %. Fits with previously published data.[19]

***(S)*-Ethyl ibuprofen, 9g**



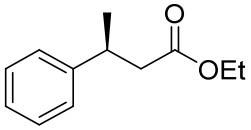
(*S*)-ibuprofen (1.0 g, 4.85 mmol, 1.0 equiv.) was dissolved in ethanol (20 mL) and sulfuric acid (0.1 mL) was added. The mixture was heated to 60 °C for 20 h and concentrated to dryness. The crude was dissolved in diethyl ether (30 mL), washed with aqueous saturated sodium bicarbonate (20 mL) and water (2 x 20 mL), dried over magnesium sulfate, filtered and concentrated to dryness to give the title compound as a colorless oil (0.94 g, 4.00 mmol, 83 %). $[\alpha]_D^{20}$: +45.6 (*c.* 1.00, $CHCl_3$), Lit.: +33.9 (*c.* 1.1, $CHCl_3$, 76 % *ee*)[20]; ^{1}H-NMR ($CDCl_3$) δ: 7.23 (2H, d, J = 7.77 Hz, Ar-H), 7.12 (2H, d, J = 7.77 Hz, Ar-H), 4.15 (2H, m, $CH_3C\underline{H}_2O$), 3.71 (1H, q, J = 6.50 Hz -CH-), 2.47 (2H, d, J = 7.02, $ArC\underline{H}_2$-), 1.86 (1H, m, -CH-), 1.51 (3H, d, J = 7.4 Hz, -$C\underline{H}_3$), 1.24 (3H, t, J = 7.65 Hz, -$OCH_2C\underline{H}_3$), 0.92 (3H, d, J = 5.6 Hz, -CH_3); ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 174.91 (-$\underline{C}O_2R$), 140.65 (C_{Ar}), 137.89 ($\underline{C}_{Ar}$), 129.30 ($\underline{C}_{Ar}$), 127.13 ($\underline{C}_{Ar}$), 60.67 ($CH_3\underline{C}H_2O$), 45.18 ($Ar\underline{C}H$), 30.21 (-$\underline{C}H$-), 22.14 (-CH_2-), 18.64 (-$\underline{C}H_3$), 14.15 (-$\underline{C}H_3$); HRMS (EI+): calculated for [$C_{15}H_{22}O_2$]: 234.1620 found: 234.1622. Fits with previously published data.[20]

***(S)*-Ethyl 2-(4-chlorophenyl)-3-methylbutyrate, 9h**



Based on a previously published procedure[3] Racemic 2-(4-chlorophenyl)-3-methylbutyric acid (5.0 g, 23.5 mmol, 1.0 equiv.) was treated with (*S*)-phenylethylamine (1.8 g, 14.8 mmol, 0.63 equiv.) in n-butanol (15.0 g) / water (7.0 g) mixture at 60 °C and a white suspension formed. The mixture was heated to reflux for 1 h then cooled to 35 °C, held for 40 min and the product was filtered off. The wet cake was added back to the vessel and fresh n-butanol (19 mL) and water (7 mL) as added and the mixture heated to reflux for 1 h, then cooled to 50 °C and filtered. The wet cake was again returned to the flask and fresh n-butanol (5.3 mL) and water (1.9 mL) added. The mixture was heated to reflux for 1 h then cooled to ambient and left to age for 16 h. The salt was filtered off and washed with n-butanol (10 mL) and then returned to the vessel and 20 mL conc. HCl (aq) added. The mixture was extracted with toluene (15 mL) and the combined organic layers were pooled, dried over magnesium sulfate, filtered and concentrated to give the (*S*)-2-(4-chlorophenyl)-3-methylbutyric acid as a white solid (1.6 g, 7.52 mmol, 51 % (based on charge of amine)).
(*S*)-2-(4-chlorophenyl)-3-methylbutyric acid (1.6 g, 7.52 mmol, 1.0 equiv.) was treated with thionyl chloride (0.8 mL, 11.3 mmol, 1.5 equiv.) and DMF (0.1 mL) in dichloromethane (20 mL) for 3 h at room temperature under an atmosphere of argon. The mixture was concentrated, and the crude was dissolved in ethanol (20 mL) and DMAP (10 mg) added. The solution was stirred at room temperature for 18 h, then concentrated to dryness. The crude material was dissolved in dichloromethane (25 mL) and washed with saturated aqueous sodium carbonate (20 mL), 15 v/v % sulfuric acid (10 mL), saturated aqueous sodium bicarbonate (15 mL) and water (15 mL), dried over magnesium sulfate, filtered and concentrated to give the title compound as a yellow oil (1.2 g, 5.00 mmol, 66 %). $[\alpha]_D^{20}$: +32.7 (*c.* 1.00, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 7.30 (4H, m, Ar-H), 4.13 (2H, m, $CH_3C\underline{H}_2O$), 3.13 (1H, d, J = 8.4 Hz, -CH-), 2.31 (1H, m, -$C\underline{H}(CH_3)_2$), 1.24 (3H, t, J = 8.4 Hz, -$OCH_2C\underline{H}_3$), 1.06 (3H, d, J = 7.8 Hz, -$C\underline{H}_3$), 0.72 (3H, d, J = 7.8 Hz, -$C\underline{H}_3$); ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 173.63 (-$\underline{C}O_2R$), 136.96 ($\underline{C}_{Ar}$), 133.02 ($\underline{C}_{Ar}$), 129.83 ($\underline{C}_{Ar}$), 128.58 ($\underline{C}_{Ar}$), 60.70 ($CH_3\underline{C}H_2O$), 59.59 ($Ar\underline{C}H$), 32.04 (-$\underline{C}H$-), 21.36 (-$\underline{C}H$-), 20.17 (-$\underline{C}H_3$), 14.17 (-$\underline{C}H_3$); HRMS (EI+): calculated for [$C_{13}H_{17}ClO_2$]: 240.0917 found: 240.0919; Chiral analysis was performed using a Chiralcel OJ column using 100% *n*-hexane mobile phase, flow 0.5 mL/min; t_R (*R*-enantiomer, minor): 8.9 min; t_R (*S*-enantiomer, major): 9.6 min, *ee* 96 %.

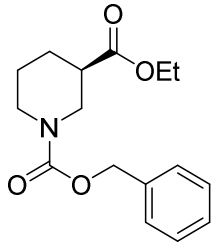
***(R)*-Ethyl 3-phenylbutyrate, 9i**



(R)-3-phenylbutyric acid (1.0 g, 6.1 mmol, 1.0 equiv.) was dissolved in dichloromethane (15 mL) at room temperature. DMF (0.1 mL) was added followed by thionyl chloride (0.70 mL, 9.1 mmol, 1.5 equiv.). The solution was stirred at room temperature for 4 h then concentrated to dryness. The crude mixture was dissolved in ethanol (10 mL) and DMAP (10 mg) added and stirred at room temperature for 16 h and volatiles were removed *in vacuo*. The crude product was dissolved in diethyl ether (25 mL) and washed with saturated aqueous sodium bicarbonate (15 mL) and water (15 mL), dried over magnesium sulfate, filtered over silica and concentrated to give the title compound as a colorless oil (1.0 g, 5.2 mmol, 85 %). $[\alpha]_D^{20}$: +31.5 (*c.* 1.60, Et_2O), Lit.: +21.4 (*c.* 1.508, Et_2O)[18]; ^{1}H-NMR ($CDCl_3$) δ: 7.35-7.22 (5H, m, Ph-H), 4.11 (2H, q, J = 7.8 Hz, $CH_3C\underline{H}_2O$), 3.31 (1H, m, $PhC\underline{H}(C\underline{H}_3)CO_2R$), 2.60 (2H, m, -$C\underline{H}_2$-), 1.34 (3H, d, J = 7.3 Hz, -$C\underline{H}_3$), 1.22 (3H, t, J = 7.8 Hz, $C\underline{H}_3CH_2O$),

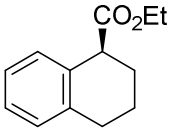
^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 172.42 (-$\underline{C}O_2R$), 145.75 ($\underline{C}_{Ar}CH_2$), 128.49 ($\underline{C}_{Ar}$), 126.78 ($\underline{C}_{Ar}$), 126.39 ($\underline{C}_{Ar}$), 60.28 ($\underline{C}H_2O$), 43.02 (Ph$\underline{C}H_2$), 36.54 (-$\underline{C}H_2$-), 21.84 (-$\underline{C}H_3$), 14.20 (-$\underline{C}H_3$); HRMS (EI+): calculated for [$C_{12}H_{16}O_2$]: 192.1150 found: 192.1151. Fits with previously published data.[21]

***(R)-N-Cbz*-Ethyl nipecotate, 9k**



(*R*)-ethyl nipecotate (310 mg, 1.97 mmol, 1.0 equiv., *ee* 88 %) was dissolved in dichloromethane (10 mL) at room temperature under an argon atmosphere. Benzyl chloroformate (0.28 mL, 1.97 mmol, 1.0 equiv.) and triethyl amine (0.33 mL, 2.37 mmol, 1.2 equiv.) was added and the formed mixture stirred at room temperature for 16 h. The organic solution was washed with water (10 mL), 20 v/v% Aqueous acetic acid (10 mL) and aqueous sodium bicarbonate (10 mL) and finally water (10 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated to dryness. The product was purified using column chromatography (hexane / ethyl acetate 4/1) to give the title compound as a colorless viscous oil (313 mg, 1.15 mmol, 58 %). $[\alpha]_D^{20}$: -42.5 (*c.* 1.00, $CHCl_3$, 88 % *ee*); The isolated product showed rotamers on the NMR timescale. Assignment was made using 2D-NMR. ^{1}H-NMR ($CDCl_3$) (major rotamer) δ: 7.72 (3H, m, Ar-H), 7.45 (1H, dd, J = 8.5 / 1.8 Hz, Ar-H), 7.17 (2H, m, Ar-H), 4.17 (2H, m, $CH_3C\underline{H}_2O$), 3.94 (3H, s, CH_3O-), 3.88 (1H, q, J = 7.3 Hz, ArC$\underline{H}(CH_3)CO_2R$), 1.61 (3H, d, J = 7.3 Hz, -CH_3), 1.24 (3H, t, J = 7.5 Hz, -$OCH_2C\underline{H}_3$); ^{1}H-NMR ($CDCl_3$) (minor rotamer) δ: 7.72 (3H, m, Ar-H), 7.45 (1H, dd, J = 8.5 / 1.8 Hz, Ar-H), 7.17 (2H, m, Ar-H), 4.17 (2H, m, $CH_3C\underline{H}_2O$), 3.94 (3H, s, CH_3O-), 3.88 (1H, q, J = 7.3 Hz, ArC$\underline{H}(CH_3)CO_2R$), 1.61 (3H, d, J = 7.3 Hz, -CH_3), 1.24 (3H, t, J = 7.5 Hz, -$OCH_2C\underline{H}_3$); ^{13}C -{^{1}H}-NMR ($CDCl_3$) (major) δ: 174.72 (-$\underline{C}O_2R$), 157.62 (C_{Ar}OMe), 135.86 ($\underline{C}_{Ar}$), 133.67 ($\underline{C}_{Ar}$), 129.30 ($\underline{C}_{Ar}$), 128.95 ($\underline{C}_{Ar}$), 127.12 ($\underline{C}_{Ar}$), 126.27 ($\underline{C}_{Ar}$), 125.93 ($\underline{C}_{Ar}$), 118.96 ($\underline{C}_{Ar}$), 105.58 ($\underline{C}_{Ar}$), 60.78 ($\underline{C}H_3O$), 55.32 (Ar$\underline{C}H$), 45.51 (-$\underline{C}H_2O$), 18.66 (-$\underline{C}H_3$), 14.17 (-$\underline{C}H_3$); ^{13}C -{^{1}H}-NMR ($CDCl_3$) (minor) δ: 174.72 (-$\underline{C}O_2R$), 157.62 (C_{Ar}OMe), 135.86 ($\underline{C}_{Ar}$), 133.67 ($\underline{C}_{Ar}$), 129.30 ($\underline{C}_{Ar}$), 128.95 ($\underline{C}_{Ar}$), 127.12 ($\underline{C}_{Ar}$), 126.27 ($\underline{C}_{Ar}$), 125.93 ($\underline{C}_{Ar}$), 118.96 ($\underline{C}_{Ar}$), 105.58 ($\underline{C}_{Ar}$), 60.78 ($\underline{C}H_3O$), 55.32 (Ar$\underline{C}H$), 45.51 (-$\underline{C}H_2O$), 18.66 (-$\underline{C}H_3$), 14.17 (-$\underline{C}H_3$); HRMS (EI+): calculated for [$C_{16}H_{21}NO_4$ – CO_2]: 247.1572 found: 247.1653; Chiral analysis was performed using a Chiralcel AD-H column using *n*-hexane / isopropanol (95/5) mobile phase, flow 1.0 mL/min; t_R (*S*-enantiomer, minor): 15.0 min; t_R (*R*-enantiomer, major): 16.1 min, *ee* 87 %.

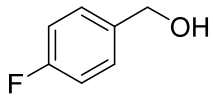
***(S)*-Ethyl-1,2,3,4-tetrahydronaphthalene-1-carboxylate, 9l**



(S)-1,2,3,4-tetrahydronaphthalene-1-carboxylic acid (1.0 g, 5.67 mmol, 1.0 equiv.) was dissolved in ethanol (20 mL) at room temperature. Sulfuric acid (0.1 mL) was added followed and the solution was stirred at 60 °C for 16 h then concentrated to dryness. The crude mixture was dissolved in ethyl acetate (25 mL) and washed with saturated aqueous sodium bicarbonate (15 mL) and water (15 mL), dried over magnesium sulfate, filtered over silica and concentrated. The product was further purified by column chromatography using hexanes / diethyl ether (9/1) to give the title compound as a colorless oil (0.6 g, 2.94 mmol, 52 %). $[\alpha]_D^{20}$: -3.4 (*c.* 1.00, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 7.21-7.12 (4H, m, Ar-H), 4.21 (2H, q, J = 7.0 Hz, $CH_3C\underline{H}_2O$), 3.84 (1H, t, J = 5.9 Hz, -C$\underline{H}$-), 2.82 (2H, m, -C$\underline{H}_2$-), 2.17 (1H, m, -C$\underline{H}_2$-), 2.02 (2H, m,-C$\underline{H}_2$-), 1.80 (1H, m, -C$\underline{H}_2$-), 1.30 (3H, t, J = 7.0 Hz, -$OCH_2C\underline{H}_3$); ^{13}C -{^{1}H}-{DEPT}-NMR ($CDCl_3$) δ: 174.97 (-$\underline{C}O_2R$), 137.23 (C_{Ar}), 133.41 ($\underline{C}_{Ar}$), 129.42 ($\underline{C}_{Ar}$), 126.76 ($\underline{C}_{Ar}$), 125.73 ($\underline{C}_{Ar}$), 60.73 ($CH_3\underline{C}H_2O$), 44.87 (-$\underline{C}$H-), 29,19 (-$\underline{C}H_2$-), 26.66 (-$\underline{C}H_2$-), 20.65 (-$\underline{C}H_2$-), 14.90 (-$\underline{C}H_3$); HRMS (EI+): calculated for [$C_{13}H_{16}O_2$]: 204.1150 found: 204.1152; Chiral analysis was performed using a Chiralcel OD-H column using *n*-hexane / isopropanol (99/1) mobile phase, flow 1 mL/min; t_R (*R*-enantiomer, minor): 6.1 min; t_R (*S*-enantiomer, major): 7.2 min, *ee* >99 %. Fits with previously published data.[22]

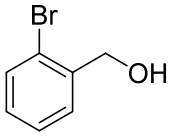
Product characterization data

4-fluorobenzyl alcohol, 6a



The product was purified by column chromatography using 100 % hexane followed by dichloromethane / methanol (95/5) to give the title compound as a colorless oil. 250 mg (1.49 mmol) ethyl *p*-fluorobenzoate gave 170 mg (1.35 mmol) *p*-fluorobenzyl alcohol (90 %); ^{1}H-NMR ($CDCl_3$) δ: 7.39 (2H, m, Ar-H), 7.10 (2H, m, Hz, Ar-H), 4.70 (2H, s, Ar-C$\underline{H}_2$OH); ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 163.30 ($\underline{C}_{Ar}$-F), 136.59 ($\underline{C}_{Ar}$-CH_2OH 128.81 ($\underline{C}_{Ar}$-H), 115.50 ($\underline{C}_{Ar}$-H), 64.72 (Ar-$\underline{C}H_2$OH); ^{19}F-{^{1}H}-NMR ($CDCl_3$): δ: -114.89; HRMS (EI+): calculated for [C_7H_7FO]: 126.0481, found: 126.0477. Fits with previously published data.[4]

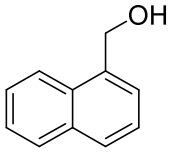
2-bromobenzyl alcohol, 6b



The product was purified by column chromatography using 100 % hexane followed by dichloromethane / methanol (95/5) to give the title compound as a white solid. 353 mg (1.64 mmol) methyl *o*-bromobenzoate gave 250 mg (1.34 mmol) *o*-bromobenzyl alcohol (82 %).

^{1}H-NMR ($CDCl_3$) δ: 7.57 (1H, d, J = 8.2 Hz, Ar-H), 7.51 (1H, d, J = 8.2 Hz, Ar-H), 7.36 (1H, t, J = 7.3 Hz, Ar-H), 7.19 (1H, t, J = 7.3 Hz, Ar-H), 4.78 (2H, s, Ar-C$\underline{H}_2$OH); ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 139.71 ($\underline{C}_{Ar}$ –CH_2OH), 132.61 ($\underline{C}_{Ar}$-H), 129.15 ($\underline{C}_{Ar}$-H), 128.93 ($\underline{C}_{Ar}$-H), 127.67 ($\underline{C}_{Ar}$-H), 122.59 ($\underline{C}_{Ar}$-Br), 65.13 (-$\underline{C}H_2$OH); HRMS (EI): calculated for [C_7H_7BrO]: 185.9680 / 187.9660; found 185.9678 / 187.9670 Fits with previously published data.[5]

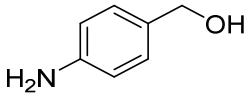
1-hydroxymethylnaphthalene, 6c



The product was purified by column chromatography using 100 % hexane followed by dichloromethane / methanol (95/5) to give the title compound as a white solid. 320 mg (1.60 mmol) ethyl 1-naphthanoate gave 240 mg (1.52 mmol) 1-hydroxymethylnaphthalene (95 %).

^{1}H-NMR ($CDCl_3$) δ: 8.15 (1H, d, J = 7.5 Hz, Ar-H), 7.91 (1H, d, J = 7.9 Hz, Ar-H), 7.85 (1H, d, J = 8.4 Hz, Ar-H), 7.56 (3H, m, Ar-H), 7.48 (1H, m, Ar-H), 5.17 (2H, d, J = 3.9 Hz, Ar-C$\underline{H}_2$OH), 1.91 (1H, m, Ar-CH_2O$\underline{H}$); ^{13}C -{^{1}H}-DEPT NMR ($CDCl_3$) δ: 136.26 ($\underline{C}_{Ar}$-CH_2-), 133.80 (C_{Ar}), 131.23 ($\underline{C}_{Ar}$), 128.69 ($\underline{C}_{Ar}$), 128.61 ($\underline{C}_{Ar}$) 126.37 ($\underline{C}_{Ar}$), 125.91 ($\underline{C}_{Ar}$), 125.91 ($\underline{C}_{Ar}$), 125.36 ($\underline{C}_{Ar}$), 123.66 ($\underline{C}_{Ar}$), 63.72 (-$\underline{C}H_2$OH) HRMS (EI+): calculated for [$C_{11}H_{10}O$]: 158.0732 found 158.0729. Fits with previously published data.[6]

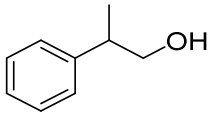
4-aminobenzyl alcohol, 6d



The product was purified by column chromatography using 100 % hexane followed by dichloromethane / methanol (90/10) to give the title compound as a colorless oil. 225 mg (1.49 mmol) methyl *p*-aminobenzoate gave 160 mg (1.30 mmol) *p*-aminobenzyl alcohol (88 %).

^{1}H-NMR ($CDCl_3$) δ: 7.19 (2H, d, J =9.0 Hz, Ar-H), 6.70 (2H, d, J = 8.9 Hz, Ar-H), 4.58 (2H, s, Ar-C$\underline{H}_2$OH), 3.70 (2H, br s, -N$\underline{H}_2$); ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 146.09 ($\underline{C}_{Ar}$-CH_2OH), 131.01 ($\underline{C}_{Ar}$ –NH_2), 128.82 (Ar-C), 115.12 (Ar-C), 65.36 (-$\underline{C}H_2$OH); HRMS (EI+): calculated for [C_7H_9NO]: 123.0684, found: 123.0681. Fits with previously published data.[1]

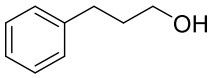
***Rac*-2-phenylpropan-1-ol, 6e**



The product was purified by column chromatography using 100 % hexane followed by dichloromethane / methanol (95/5) to give the title compound as a pale-yellow oil. 293 mg (1.64 mmol) ethyl 2-phenylpropionate gave 153 mg (1.12 mmol) 2-phenylpropan-1-ol (70 %).

^{1}H-NMR ($CDCl_3$) δ: 7.36 (2H, m, Ph-H), 7.28 (3H, m, Ph-H), 3.74 (2H, t, J =6.9 Hz, -C$\underline{H}_2$OH), 2.98 (1H, m, -C$\underline{H}$(CH_3)-), 1.31 (3H, d, J = 7.2 Hz, -CH_3); ^{13}C -{^{1}H}-DEPT NMR ($CDCl_3$) δ: 143.63 ($\underline{C}_{Ar}$), 128.67 ($\underline{C}_{Ar}$), 127.50 ($\underline{C}_{Ar}$), 126.71 ($\underline{C}_{Ar}$), 68.74 (-$\underline{C}H_2$OH), 42.46 (-$\underline{C}$H(CH_3)-), 17.60 ($\underline{C}H_3$); HRMS (EI+): calculated for [$C_9H_{12}O$]: 136.0888 found 136.0894. Fits with previously published data.[7]

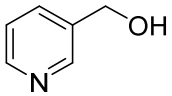
3-phenylpropan-1-ol, 6f



The product was purified by column chromatography using hexanes / diethyl ether (3/2) to give the title compound as a colorless oil. 220 mg (1.23 mmol) ethyl 3-phenylpropionate gave 150 mg (1.10 mmol) 3-phenylpropan-1-ol (90 %).

^{1}H-NMR ($CDCl_3$) δ: 7.32 (2H, m, Ph-H), 7.22 (3H, m, Ph-H), 3.71 (2H, t, J = 6.4 Hz, -C$\underline{H}_2$OH), 2.74 (2H, t, J = 7.4 Hz, Ph-C$\underline{H}_2$-), 1.93 (2H, m, -C$\underline{H}_2$$CH_2$OH); ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 141.81 ($\underline{C}_{Ar}$-CH_2-), 141.43 (C_{Ar}), 128.44 ($\underline{C}_{Ar}$), 128.41 ($\underline{C}_{Ar}$), 125.88 ($\underline{C}_{Ar}$) 62.33 (-$\underline{C}H_2$OH), 34.24 (Ph$\underline{C}H_2$-), 32.09 (-$\underline{C}H_2$-); HRMS (EI+): calculated for [$C_9H_{12}O$]: 136.0888 found 136.0884. Fits with previously published data.[1]

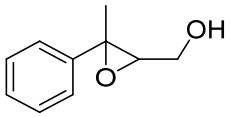
3-hydroxymethylpyridine, 6g



The product was purified by column chromatography using 100 % hexane followed by dichloromethane / methanol (9/1) to give the title compound as a white solid. 225 mg (1.64 mmol) methyl nicotinate gave 150 mg (1.37 mmol) 3-hydroxymethylpyridine (85 %).

^{1}H-NMR ($CDCl_3$) δ: 8.55 (1H, s, Ar-H), 8.50 (1H, d, J = 3.3 Hz Ar-H), 7.75 (1H, d, J = 8.4 Hz, Ar-H), 7.30 (1H, m, Ar-H), 4.74 (2H, s, -C$\underline{H}_2$OH), 3.30 (1H, s, -OH); ^{13}C -{^{1}H}-DEPT NMR ($CDCl_3$) δ: 148.69 ($\underline{C}_{Ar}$), 148.34 ($\underline{C}_{Ar}$), 136.54 ($\underline{C}_{Ar}$), 135.00 ($\underline{C}_{Ar}$), 123.58 ($\underline{C}_{Ar}$), 127.29 ($\underline{C}_{Ar}$), 62.51 (-$\underline{C}$H$_2$OH); HRMS (ES+): calculated for [$C_6H_8NO^+$]: 110.0600 found 110.0599. Fits with previously published data.[8]

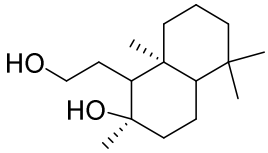
***Rac*-(3-methyl-3-phenyloxiran-2-yl)methanol, 50:50 mixture of cis and trans, 6h**



The product was purified by column chromatography using 100 % hexane followed by 100 % ethyl acetate to give the title compound as a colorless oil. 500 mg (2.42 mmol) ethyl 3-methyl-3-phenylglycidate gave 280 mg (1.70 mmol) (3-methyl-3-phenyloxiran-2-yl)methanol (71 %). ^{1}H-NMR ($CDCl_3$) δ: *diastereomer 1:* 7.37 (4H, m, Ph-H), 7.31 (1H, m, Ph-H), 4.00 (1H, m, -C$\underline{H}_2$OH), 3.87 (1H, m, -C$\underline{H}_2$OH), 3.12 (1H, m, -CH(O)-), 1.88 (1H, m, -OH), 1.73 (3H, s, -C$\underline{H}_3$); *Diastereomer 2:* 7.37 (4H, m, Ph-H), 7.31 (1H, m, Ph-H), 3.47 (1H, m, -C$\underline{H}_2$OH), 3.31 (2H, m, -C$\underline{H}_2$OH and -CH(O)-), 1.70 (3H, s, -C$\underline{H}_3$), 1.58 (1H, m, -OH); ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: *Diastereomer 1* 142.02 ($\underline{C}_{Ar}$), 128.42 ($\underline{C}_{Ar}$), 127.56 ($\underline{C}_{Ar}$), 126.12 ($\underline{C}_{Ar}$), 125.06 ($\underline{C}_{Ar}$), 66.02 (-$\underline{C}$H(O)-), 61.35 ($\underline{C}$H$_2$OH), 60.89 (-$\underline{C}$(CH$_3$)-O-), 24.68 (-CH$_3$); *Diastereomer 2:* 138.92 ($\underline{C}_{Ar}$), 128.34 ($\underline{C}_{Ar}$), 127.56 ($\underline{C}_{Ar}$), 126.12 ($\underline{C}_{Ar}$), 125.06 ($\underline{C}_{Ar}$), 64.46 (-$\underline{C}$H(O)-, 61.84 ($\underline{C}$H$_2$OH), 62.87 (-$\underline{C}$(CH$_3$)-O-), 17.83 (-CH$_3$)

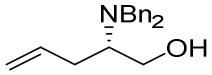
HRMS (EI+): calculated for [$C_{10}H_{12}O_2$-OH]: 148.0804 found: 148.0888. Fits with previously published data.[9]

(*R*)-Sclareodiol, 8a



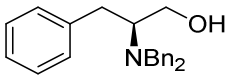
[α]$_D^{20}$: -17.2 (*c.* 1.00, $CHCl_3$) Lit.: -16.9 (*c.* 0.99, $CHCl_3$)[23]; ^{1}H-NMR ($CDCl_3$) δ: 3.81 (1H, m, -C$\underline{H}_2$OH), 3.49 (1H, m, -C$\underline{H}_2$OH), 1.90 (1H, d, J = 12.9 Hz, -C$\underline{H}$-), 1.66 (8H, m, Aliphatic-H), 1.45 (5H, m, Aliphatic-H), 1.22 (3H, s, -C$\underline{H}_3$), 1.16 (1H, m, Aliphatic-H), 0.98 (1H, m, Aliphatic-H), 0.95 (1H, m, Aliphatic-H), 0.91 (3H, s,-C$\underline{H}_3$), 0.81 (6H, s,-C$\underline{H}_3$); ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 73.16 (-C(CH$_3$)OH), 64.22 (-CH$_2$OH), 59.07, 56.01, 44.32, 41.88, 39.32, 33.42, 33.29, 27.88, 24.70, 21.49, 20.49, 18.41, 15.32 (Aliphatic-C); HRMS (EI+): calculated for [$C_{16}H_{30}O_2$-H_2O]: 236.2140 found: 236.2179. Fits with previously published data.[24]

(*S*)-2-(dibenzylamino)pent-4-en-1-ol, 10a



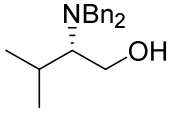
(*S*)-Benzyl *N*, *N*-dibenzylallylglycine (400 mg, 1.04 mmol, 1 equiv., 98 % ee), manganese catalyst (7.5 mg, 0.01 mmol, 0.01 equiv.), potassium carbonate (14 mg, 0.10 mmol, 0.1 equivalents) and 1-methylnaphthalene (~50 µL, internal standard) was added to a glass insert containing a stirring bar and the insert put in an autoclave fitted with a vacuum / gas inlet and a charging port. The autoclave was sealed and evacuated and refilled with argon. This was repeated twice. Degassed isopropanol (6.0 mL) was added via the charging port and the vessel was pressurized with hydrogen gas (50 bar) and vented to the atmosphere. This was repeated twice. The pressure was set to 50 bar using hydrogen gas and the autoclave sealed and placed in a pre-heated oil bath (50 °C) and the stirring as set to 1200 rpm and left for 16 h. After the reaction, the vessel was cooled to ambient temperature and vented to the atmosphere, the reaction was analyzed by ^{1}H-NMR and conversion was estimated using the internal standard (1-methylnaphthalene). The reaction mixture was evaporated to dryness and the crude product was purified by column chromatography using 100% hexane followed by hexane / diethyl ether (90/10) to give the (*S*)-N, N-dibenzylallyl glycinol as a colorless oil (212 mg, 76 %). [α]$_D^{20}$: +63.1° (*c.* 1.20, $CHCl_3$); Lit. [α]$_D^{20}$: +60.1° (*c.* 0.5, $CHCl_3$)[2]; ^{1}H-NMR ($CDCl_3$) δ: 7.36-7.26 (10H, m, Ph-H), 5.77 (1H, m, -C$\underline{H}$=CH$_2$), 5.14-5.06 (2H, m, -CH=C$\underline{H}_2$), 3.88 (2H, d, J = 13.9 Hz, PhC$\underline{H}_2$N), 3.47 (4H, m, PhC$\underline{H}_2$N and -C$\underline{H}_2$OH), 3.07 (1H, s, -OH), 2.92 (1H, m, -C$\underline{H}$(NBn$_2$)-), 2.56 (1H, m, -C$\underline{H}_2$-), 2.00 (1H, m, -C$\underline{H}_2$-); ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 139.12 ($\underline{C}_{Ar}$CH$_2$N), 135.38 ($\underline{C}_{Ar}$), 129.05 ($\underline{C}_{Ar}$), 128.53 ($\underline{C}_{Ar}$), 127.29 ($\underline{C}_{Ar}$), 117.05 ($\underline{C}_{Ar}$), 60.69 (-$\underline{C}$H$_2$OH), 55.68 (-CH=$\underline{C}$H$_2$), 53.22 (-$\underline{C}$H=CH$_2$), 29.66 (-$\underline{C}$H$_2$-); HRMS (ES+): calculated for [$C_{19}H_{24}NO^+$]: 282.1852 found: 282.1844; Chiral analysis was performed using a Chiralcel OD-H column using *n*-hexane / isopropanol (90/10) mobile phase, flow 0.5 mL/min; t_R (*R*-enantiomer, minor): 11.8 min; t_R (*S*-enantiomer, major): 16.1 min, *ee* >99 %. Fits with previously published data.[2]

(*S*)-*N, N*-dibenzylphenylalaninol, 10b



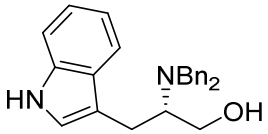
(*S*)-Ethyl *N*, *N*-dibenzylphenylalanine (670 mg, 1.76 mmol, 1 equiv., 99.8 % ee) and 1-methylnaphthalene (~50 µL, internal standard) was dissolved in degassed isopropanol (7.0 mL). Manganese catalyst (13.0 mg, 0.018 mmol, 0.01 equiv.) and potassium carbonate (24.8 mg, 0.10 mmol, 0.1 equiv.) was added to a glass insert containing a stirring bar and the insert put in an autoclave fitted with a vacuum / gas inlet and a charging port. The autoclave was sealed and evacuated and refilled with argon. This was repeated twice. The substrate solution was added via the charging port, and the vessel pressurized with hydrogen gas (50 bar) and vented to the atmosphere. This was repeated twice. The pressure was set to 50 bar using hydrogen gas and the autoclave sealed and placed in a pre-heated oil bath (110 ^{o}C) and the stirring as set to 1200 rpm and left for 16 h. After the reaction, the vessel was cooled to ambient temperature and vented to the atmosphere, the reaction was analyzed by ^{1}H-NMR and conversion was estimated using the internal standard (1-methylnaphthalene). The reaction mixture was evaporated to dryness and the crude product was purified by column chromatography using 100% hexane followed by hexane / diethyl ether (90/10) to give the (*S*)-N, N-dibenzylphenylalaninol as a white solid (400 mg, 66 %). [α_D^{20}]: -4.8^{o} (*c.* 1.20, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 7.38-7.27 (12H, m, Ph-H), 7.22 (1H, m, Ph-H), 7.14 (2H, d, J = 7.7 Hz, Ph-H), 3.96 (2H, d, J = 13.8 Hz, PhC$\underline{H}_2$N), 3.54 (3H, m, PhC$\underline{H}_2$N and -C$\underline{H}$-), 3.37 (1H, s, -OH), 3.13 (2H, m, -C$\underline{H}_2$OH), 3.05 (1H, m, -C$\underline{H}_2$-), 2.47 (1H, m, -C$\underline{H}_2$-); ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 139.16 ($\underline{C}_{Ar}CH_2N$), 139.08 ($\underline{C}_{Ar}CH_2$-), 129.04 ($\underline{C}_{Ar}$), 129.04 ($\underline{C}_{Ar}$), 127.35 ($\underline{C}_{Ar}$), 126.27 ($\underline{C}_{Ar}$), 60.88 (-$\underline{C}H_2$OH), 60.32 (Ph$\underline{C}H_2$-), 53.25 (Ph$\underline{C}H_2$N), 31.74 (-$\underline{C}$H-); HRMS (ES+): calculated for [$C_{23}H_{25}NO^{+}$]: 332.2009 found: 332.2002; Chiral analysis was performed using a Chiralcel OD-H column using *n*-hexane / isopropanol (90/10) mobile phase, flow 1.0 mL/min; t_R (*R*-enantiomer, minor): 9.8 min; t_R (*S*-enantiomer, major): 12.8 min, *ee* >99 %. Fits with previously published data.[10]

(*S*)-*N, N*-dibenzylvalinol, 10c



(*S*)-Benzyl *N*, *N*-dibenzylvaline (289 mg, 0.75 mmol, 1 equiv., 99.8 % ee), manganese catalyst (5.4 mg, 0.0075 mmol, 0.01 equiv.), potassium carbonate (10 mg, 0.075 mmol, 0.1 equivalents) and 1-methylnaphthalene (~50 µL, internal standard) was added to a microwave vial containing a stirring bead. The vial was sealed and evacuated and refilled with argon. This was repeated twice. De-gassed isopropanol (2.5 mL) was added and the vial septum as pierced with 2x18G needles and placed in a stainless-steel autoclave under argon atmosphere. The vessel was pressurized with hydrogen gas (50 bar) and vented to the atmosphere. This was repeated twice. The pressure was set to 50 bar using hydrogen gas and the autoclave sealed and placed in a pre-heated oil bath (110 ^{o}C) and the stirring as set to 1200 rpm and left for 16 h. After the reaction, the vessel was cooled to ambient temperature and vented to the atmosphere, the reaction was analyzed by ^{1}H-NMR and conversion was estimated using the internal standard (1-methylnaphthalene). The reaction mixture was evaporated to dryness and the crude product was purified by column chromatography using 100% hexane followed by hexane / diethyl ether (4/1) to give the (*S*)-N, N-dibenzylvalinol as a colorless oil (160 mg, 75 %). [$\alpha]_D^{20}$: +28.6^{o} (*c.* 1.2, $CHCl_3$), Lit. [$\alpha]_D^{20}$: +24.5^{o}, (*c.* 0.8, $CHCl_3$)[11]; ^{1}H-NMR ($CDCl_3$) δ: 7.33 (4H, m, Ph-H), 7.27 (6H, m, Ph-H), 3.91 (2H, d, J = 13.5 Hz, PhC$\underline{H}_2$N), 3.60 (2H, d, J = 13.5 Hz, PhC$\underline{H}_2$N), 3.68 (1H, dd, J = 11.0 Hz / 3.6 Hz C$\underline{H}_2$OH), 3.46 (1H, dd, J = 10.7 Hz / 4.7 Hz, C$\underline{H}_2$OH), 2.56 (1H, m, -C$\underline{H}$-), 2.09 (1H, m, -C$\underline{H}$-), 1.17 (3H, d, J = 6.6 Hz, -CH_3), 0.91 (3H, d, J = 6.6 Hz, -CH_3); ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 139.68 ($\underline{C}_{Ar}CH_2N$), 129.22 ($\underline{C}_{Ar}$), 128.46 ($\underline{C}_{Ar}$), 127.16 ($\underline{C}_{Ar}$), 64.66 (-$\underline{C}H_2$OH), 59.24 (Ph$\underline{C}H_2$N), 54.20 (-$\underline{C}$H-), 27.63 (-$\underline{C}$H-), 22.80 (-CH_3), 20.14 (-CH_3); HRMS (ES+): calculated for [$C_{19}H_{25}NO^{+}$]: 284.2009 found: 284.2002; Chiral analysis was performed using a Chiralcel OD-H column using *n*-hexane / isopropanol (98/2) mobile phase, flow 0.5 mL/min; t_R (*R*-enantiomer, minor): 23.6 min; t_R (*S*-enantiomer, major): 25.8 min, *ee* >99 %. Fits with previous published data.[11]

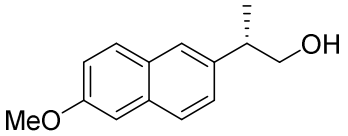
(*2S*)-2-[Bis(phenylmethyl)amino]-1*H*-indole-3-propan-1-ol, 10d



(*S*)-Ethyl *N*, *N*-dibenzyltryptophan (1000 mg, 2.42 mmol, 1 equiv., 99.8 % ee) and 1-methylnaphthalene (~50 µL, internal standard) was dissolved in degassed isopropanol (7.0 mL). Manganese catalyst (17.5 mg, 0.024 mmol, 0.01 equiv.) and potassium carbonate (33.5 mg, 0.24 mmol, 0.1 equiv.) was added to a glass insert containing a stirring bar and the insert put in an autoclave fitted with a vacuum / gas inlet and a charging port. The autoclave was sealed and evacuated and refilled with argon. This was repeated twice. The substrate solution was added via the charging port, and the vessel pressurized with hydrogen gas (50 bar) and vented to the atmosphere. This was repeated twice. The pressure was set to 50 bar using hydrogen gas and the autoclave sealed and placed in a pre-heated oil bath (110 ^{o}C) and the stirring as set to 1200 rpm and left for 16 h. After the reaction, the vessel was cooled to ambient temperature and vented to the atmosphere, the reaction was analyzed by ^{1}H-NMR and conversion was estimated using the internal standard (1-methylnaphthalene). The reaction mixture was evaporated to dryness and the crude product was purified by column chromatography using 100% hexane followed by ethyl acetate to give the (*S*)-N,N-dibenzyltryptphanol as a white solid (830 mg, 92 %).[$\alpha]_D^{20}$: +44.5 (*c.* 1.00, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 8.09 (1H, s, NH), 7.85-7.25 (12H, m, Ar-H), 7.22 (1H, t, J = 8.2 Hz, Ar-H), 7.13 (1H, t, J = 8.1 Hz, Ar-H), 6.93 (1H, s, Ar-H), 4.02 (2H, d, J = 12.9 Hz, PhC$\underline{H}_2$N), 3.63 (2H, d, J = 12.9 Hz, PhC$\underline{H}_2$N), 3.57 (1H, d, J = 10.2 Hz,

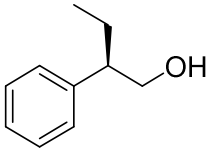
C<u>H</u>$_2$OH), 3.47 (1H, dd, J = 10.5 Hz / 4.3 Hz, C<u>H</u>$_2$OH), 3.30 (2H, m, -C<u>H</u>$_2$-), 2.70 (1H, m, -C<u>H</u>-); ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 139.31 (<u>C</u>$_{Ar}$CH$_2$N), 136.29 (<u>C</u>$_{Ar}$), 129.05 (<u>C</u>$_{Ar}$), 128.54 (<u>C</u>$_{Ar}$), 127.30 (<u>C</u>$_{Ar}$), 122.13 (<u>C</u>$_{Ar}$), 121.96 (<u>C</u>$_{Ar}$), 119.31 (<u>C</u>$_{Ar}$), 118.70 (<u>C</u>$_{Ar}$), 112.93 (<u>C</u>$_{Ar}$), 111.21 (<u>C</u>$_{Ar}$), 61.00 (-<u>C</u>H$_2$OH), 59.47 (Ph<u>C</u>H$_2$N), 53.28 (-<u>C</u>H-), 20.79 (-<u>C</u>H$_2$-); HRMS (ES+): calculated for [$C_{25}H_{27}ON_2^+$]: 371.2118 found: 371.2110; Chiral analysis was performed using a Chiralcel AD-H column using *n*-hexane / isopropanol (90/10) mobile phase, flow 1.0 mL/min; t_R (*R*-enantiomer, minor): 26.8 min; t_R (*S*-enantiomer, major): 30.6 min, *ee* >99 %.

(*S*)-Naproxol, 10e



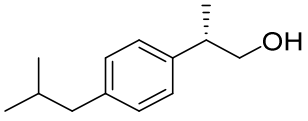
(*S*)-Ethyl naproxen (500 mg, 1.94 mmol, 1 equiv., 99.8 % ee) and 1-methylnaphthalene (~50 µL, internal standard), manganese catalyst (14 mg, 0.019 mmol, 0.01 equiv.) and potassium carbonate (27 mg, 0.19 mmol, 0.1 equiv.) was added to a glass insert containing a stirring bar and the insert put in an autoclave fitted with a vacuum / gas inlet and a charging port. The vessel was sealed and evacuated and refilled with argon. This was repeated twice. Degassed isopropanol (6.3 mL) was added through the charging port and the autoclave was pressurized with hydrogen gas (50 bar) and vented to the atmosphere. This was repeated twice. The pressure was set to 50 bar using hydrogen gas and the autoclave sealed and placed in a pre-heated oil bath (50 °C) and the stirring as set to 1200 rpm and left for 16 h. After the reaction, the vessel was cooled to ambient temperature and vented to the atmosphere, the reaction was analyzed by ^{1}H-NMR and conversion was estimated using the internal standard (1-methylnaphthalene). The reaction mixture was evaporated to dryness and the crude product was purified by column chromatography using 100% hexane followed by hexane / ethyl acetate (1/1) to give the (*S*)-2-(6-methoxynaphthalene-2-yl)propan-1-ol as a white solid (450 mg, 90 %). $[\alpha]_D^{20}$: -19.1 (*c.* 1.00, $CHCl_3$) Lit.: -17.9 (*c.*0.8, $CHCl_3$)[25]; ^{1}H-NMR ($CDCl_3$) δ: 7.74 (2H, t, J = 8.9 Hz, Ar-H), 7.64 (1H, s, Ar-H), 7.37 (1H, d, J = 7.7 Hz, Ar-H), 7.16 (2H, m, Ar-H), 3.94 (3H, s, -OCH$_3$), 3.80 (2H, d, J = 7.1 Hz, -C<u>H</u>$_2$OH), 3.12 (1H, m, C<u>H</u>(CH$_3$)-), 1.38 (3H, d, J = 7.2 Hz, -C<u>H</u>$_3$); ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 157.23 (<u>C</u>$_{Ar}$-OCH$_3$), 138.63 (<u>C</u>$_{Ar}$), 133.55 (<u>C</u>$_{Ar}$), 129.11(<u>C</u>$_{Ar}$), 129.03 (<u>C</u>$_{Ar}$), 127.24 (<u>C</u>$_{Ar}$), 126.27 (<u>C</u>$_{Ar}$), 125.93 (<u>C</u>$_{Ar}$), 118.93 (<u>C</u>$_{Ar}$), 105.58 (<u>C</u>$_{Ar}$), 68.66 (-O<u>C</u>H$_3$), 55.33 (-<u>C</u>H$_2$OH), 42.39 (Ar<u>C</u>H(CH$_3$)), 17.66 (-<u>C</u>H$_3$); HRMS (ES+): calculated for [$C_{41}H_{16}NaO_2^+$]: 239.1043 found: 239.1038; Chiral analysis was performed using a Chiralcel OD-H column using *n*-hexane / isopropanol (96/4) mobile phase, flow 1.0 mL/min; t_R (*S*-enantiomer, major): 18.1 min; t_R (*R*-enantiomer, minor): 19.2 min, *ee* 98.5 %. Fits with previously published data[12]

(*R*)-2-phenyl-1-butanol, 10f



(*R*)-Ethyl 2-phenylbutyrate (200 mg, 1.04 mmol, 1 equiv., 99.0 % ee), manganese catalyst (7.5 mg, 0.001 mmol, 0.01 equiv.), potassium carbonate (14 mg, 0.10 mmol, 0.1 equivalents) and 1-methylnaphthalene (~50 µL, internal standard) was added to a microwave vial containing a stirring bead. The vial was sealed and evacuated and refilled with argon. This was repeated twice. Degassed isopropanol (2.4 mL) was added and the vial septum as pierced with 2x18G needles and placed in a stainless-steel autoclave under argon atmosphere. The vessel was pressurized with hydrogen gas (50 bar) and vented to the atmosphere. This was repeated twice. The pressure was set to 50 bar using hydrogen gas and the autoclave sealed and placed in a pre-heated oil bath (50 °C) and the stirring as set to 1200 rpm and left for 16 h. After the reaction, the vessel was cooled to ambient temperature and vented to the atmosphere, the reaction was analyzed by ^{1}H-NMR and conversion was estimated using the internal standard (1-methylnaphthalene). The reaction mixture was evaporated to dryness and the crude product was purified by column chromatography using 100% hexane followed by hexane / ethyl acetate (1/1) to give the (*S*)-2-phenylbutan-1-ol as a colorless oil (140 mg, 90 %). $[\alpha]_D^{20}$: -22.3 (*c.* 1.4, $CHCl_3$) Lit. $[\alpha]_D^{20}$: -15.1 (*c.* 0.95, $CHCl_3$)[13]; ^{1}H-NMR ($CDCl_3$) δ: 7.36 (2H, m, Ph-H), 7.24 (3H, m, Ph-H), 3.78 (2H, m, C<u>H</u>$_2$OH), 2.72 (1H, m, PhC<u>H</u>(C$_2$H$_5$)CH$_2$OH), 1.78 (1H, m, C<u>H</u>$_2$CH$_3$), 1.61 (1H, m, C<u>H</u>$_2$CH$_3$), 0.86 (3H, t, J = 7.5 Hz, -C<u>H</u>$_3$); ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 142.25 (<u>C</u>$_{Ar}$), 128.64 (<u>C</u>$_{Ar}$), 128.12 (<u>C</u>$_{Ar}$), 126.73 (<u>C</u>$_{Ar}$), 67.36 (-<u>C</u>H$_2$OH), 50.52 (Ph<u>C</u>H(C$_2$H$_5$)-), 25.01 (<u>C</u>H$_2$CH$_3$), 12.00 (-<u>C</u>H$_3$); HRMS (EI+): calculated for [$C_{10}H_{14}O$]: 150.1045 found: 150.1044; Chiral analysis was performed using a Chiralcel AD-H column using *n*-hexane / isopropanol (98/2) mobile phase, flow 1.0 mL/min; t_R (*R*-enantiomer, major): 14.9 min; t_R (*S*-enantiomer, minor): 16.3 min, *ee* 98 %. Fits with previously published data.[13]

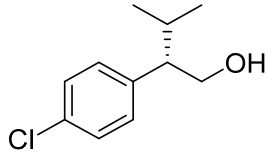
***(S)*-2-(4-isobutylphenyl)propan-1-ol, 10g**



(*S*)-Ethyl ibuprofen (235 mg, 1.00 mmol, 1 equiv., 99.0 % ee), manganese catalyst (7.3 mg, 0.001 mmol, 0.01 equiv.), potassium carbonate (14 mg, 0.10 mmol, 0.1 equivalents) and 1-methylnaphthalene (~50 µL, internal standard) was added to a microwave vial containing a stirring bead. The vial was sealed and evacuated and refilled with argon. This was repeated twice. Degassed isopropanol (2.8 mL) was added and the vial septum as pierced with 2x18G needles and placed in a stainless-steel autoclave under argon

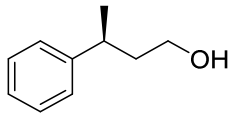
atmosphere. The vessel was pressurized with hydrogen gas (50 bar) and vented to the atmosphere. This was repeated twice. The pressure was set to 50 bar using hydrogen gas and the autoclave sealed and placed in a pre-heated oil bath (50 °C) and the stirring as set to 1200 rpm and left for 16 h. After the reaction, the vessel was cooled to ambient temperature and vented to the atmosphere, the reaction was analyzed by ^{1}H-NMR and conversion was estimated using the internal standard (1-methylnaphthalene). The reaction mixture was evaporated to dryness and the crude product was purified by column chromatography using 100% hexane followed by dichloromethane / methanol (95/5) to give the (*S*)-2-(4-isobutylphenyl)propan-1-ol as a colorless oil (185 mg, 96 %). $[\alpha]_D^{20}$: -36 (*c.* 1.00, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 7.17 (2H, d, J = 8.4 Hz, Ar-H), 7.13 (2H, d, J = 8.4 Hz, Ar-H), 3.71 (2H, d, J = 7.6 Hz, -C<u>H</u>$_2$OH), 2.95 (1H, m, ArC<u>H</u>-), 2.48 (2H, d, J = 7.8 Hz,-C<u>H</u>$_2$Ar), 1.88 (1H, m, -C<u>H</u>-), 1.29 (3H, d, J = 6.9 Hz, -C<u>H</u>$_3$), 0.93 (6H, d, J = 6.3 Hz, -(C<u>H</u>$_3$)$_2$); ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 140.68 (<u>C</u>$_{Ar}$), 140.09 (<u>C</u>$_{Ar}$), 129.48 (<u>C</u>$_{Ar}$), 127.17 (<u>C</u>$_{Ar}$), 68.81 (-<u>C</u>H$_2$OH), 45.04 (-<u>C</u>H-), 42.04 (Ar<u>C</u>H$_2$-), 30.24 (-CH-), 22.43 (-<u>C</u>H$_3$), 17.63 (-<u>C</u>H$_3$); HRMS (EI+): calculated for [$C_{13}H_{20}O$]: 192.1514 found: 192.1517; Chiral analysis was performed using a Chiralcel AD-H column using *n*-hexane / isopropanol (90/10) mobile phase, flow 1.0 mL/min; t_R (*R*-enantiomer, minor): 19.2 min; t_R (*S*-enantiomer, major): 20.2 min, *ee* 98.8 %.

(*S*)-2-(4-chlorophenyl)-3-methylbutanol, 10h



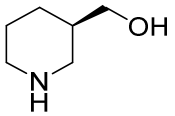
(*S*)-Ethyl 3-methyl-(4-chlorophenyl)-butyrate (241 mg, 1.00 mmol, 1 equiv., 96 % ee), manganese catalyst (7.3 mg, 0.001 mmol, 0.01 equiv.), potassium carbonate (14 mg, 0.10 mmol, 0.1 equivalents) and 1-methylnaphthalene (~50 µL, internal standard) was added to a microwave vial containing a stirring bead. The vial was sealed and evacuated and refilled with argon. This was repeated twice. Degassed isopropanol (2.8 mL) was added and the vial septum as pierced with 2x18G needles and placed in a stainless-steel autoclave under argon atmosphere. The vessel was pressurized with hydrogen gas (50 bar) and vented to the atmosphere. This was repeated twice. The pressure was set to 50 bar using hydrogen gas and the autoclave sealed and placed in a pre-heated oil bath (50 °C) and the stirring as set to 1200 rpm and left for 16 h. After the reaction, the vessel was cooled to ambient temperature and vented to the atmosphere, the reaction was analyzed by ^{1}H-NMR and conversion was estimated using the internal standard (1-methylnaphthalene). The reaction mixture was evaporated to dryness and the crude product was purified by column chromatography using 100% hexane followed by dichloromethane / methanol (95/5) to give the (*S*)-2-(4-chlorophenyl)-2-methylbutan-1-ol as a colorless oil (181 mg, 91 %). $[\alpha]_D^{20}$: +6.7 (*c.* 1.00, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 7.32 (2H, d, J = 8.6 Hz, Ar-H), 7.26 (2H, d, J = 8.6 Hz, Ar-H), 3.95 (1H, dd, J = 10.8 /4.8 Hz, -C<u>H</u>$_2$OH), 3.83 (1H, dd, J = 10.8/4.8 Hz, -C<u>H</u>$_2$OH), 2.52 (1H, m, ArC<u>H</u>-), 1.93 (1H, m,-C<u>H</u>-), 1.02 (3H, d, J = 6.6 Hz, -(C<u>H</u>$_3$)$_2$), 0.75 (3H, d, J = 6.6 Hz, -(C<u>H</u>$_3$)$_2$); ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 140.33 (<u>C</u>$_{Ar}$-Cl), 132.37 (<u>C</u>$_{Ar}$), 130.06 (<u>C</u>$_{Ar}$), 128.70 (<u>C</u>$_{Ar}$), 65.06 (-<u>C</u>H$_2$OH), 55.16 (-<u>C</u>H-), 29.99 (-<u>C</u>H$_3$), 20.86 (-<u>C</u>H$_3$); HRMS (EI+): calculated for [$C_{11}H_{15}ClO$]: 198.0811/200.0872 found: 198.0809 / 200.0810; Chiral analysis was performed using a Chiralcel AD-H column using *n*-hexane / isopropanol (99/1) mobile phase, flow 1.0 mL/min; t_R (*R*-enantiomer, minor): 27.1 min; t_R (*S*-enantiomer, major): 34.1 min, *ee* 96 %.

(*R*)-3-phenyl-1-butanol, 10i



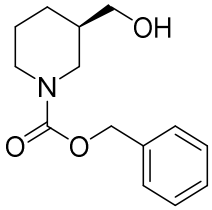
(*R*)-Ethyl 3-phenylbutyrate (200 mg, 1.04 mmol, 1 equiv., 99.0 % ee), manganese catalyst (7.5 mg, 0.001 mmol, 0.01 equiv.), potassium carbonate (14 mg, 0.10 mmol, 0.1 equivalents) and 1-methylnaphthalene (~50 µL, internal standard) was added to a microwave vial containing a stirring bead. The vial was sealed and evacuated and refilled with argon. This was repeated twice. Degassed isopropanol (2.4 mL) was added and the vial septum as pierced with 2x18G needles and placed in a stainless-steel autoclave under argon atmosphere. The vessel was pressurized with hydrogen gas (50 bar) and vented to the atmosphere. This was repeated twice. The pressure was set to 50 bar using hydrogen gas and the autoclave sealed and placed in a pre-heated oil bath (50 °C) and the stirring as set to 1200 rpm and left for 16 h. After the reaction, the vessel was cooled to ambient temperature and vented to the atmosphere, the reaction was analyzed by ^{1}H-NMR and conversion was estimated using the internal standard (1-methylnaphthalene). The reaction mixture was evaporated to dryness and the crude product was purified by column chromatography using 100% hexane followed by hexane / ethyl acetate (1/1) to give the (*S*)-3-phenylbutan-1-ol as a colorless oil (150 mg, 96 %). $[\alpha]_D^{20}$: +26.9 (*c.* 1.1, $CHCl_3$); Lit. $[\alpha]_D^{20}$: 25.5 (*c.*1.52, $CHCl_3$)[13]; ^{1}H-NMR ($CDCl_3$) δ: 7.33 (2H, m, Ph-H), 7.23 (3H, m, Ph-H), 3.58 (2H, m, C<u>H</u>$_2$OH), 2.91 (1H, m, PhC<u>H</u>(CH_3)), 1.88 (2H, m, -C<u>H</u>$_2$-), 1.30 (2H, d, J = 7.8 Hz, -CH_3); ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 146.82 (<u>C</u>$_{Ar}$), 128.50 (<u>C</u>$_{Ar}$), 126.97 (<u>C</u>$_{Ar}$), 126.14 (<u>C</u>$_{Ar}$), 61.23 (-<u>C</u>H$_2$OH), 40.99 (Ph<u>C</u>H(CH_3)-), 36.46 (<u>C</u>H$_2$), 22.44 (-<u>C</u>H$_3$); HRMS (EI+): calculated for [$C_{10}H_{14}O$]: 150.1045 found: 150.1043; Chiral analysis was performed using a Chiralcel OD-H column using *n*-hexane / isopropanol (98/2) mobile phase, flow 1.0 mL/min; t_R (*S*-enantiomer, minor): 20.3 min; t_R (*R*-enantiomer, major): 24.2 min, *ee* >99 %.
Fits with previously published data.[13]

(*R*)-3-hydroxymethylpiperidine, 10j



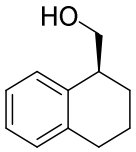
(R)-Ethyl nipecotate (180 mg, 1.00 mmol, 1 equiv., 88 % ee), manganese catalyst (7.2 mg, 0.001 mmol, 0.01 equiv.), potassium carbonate (14 mg, 0.10 mmol, 0.1 equivalents) and 1-methylnaphthalene (~30 µL, internal standard) was added to a microwave vial containing a stirring bead. The vial was sealed and evacuated and refilled with argon. This was repeated twice. Degassed isopropanol (2.3 mL) was added and the vial septum as pierced with 2x18G needles and placed in a stainless-steel autoclave under argon atmosphere. The vessel was pressurized with hydrogen gas (50 bar) and vented to the atmosphere. This was repeated twice. The pressure was set to 50 bar using hydrogen gas and the autoclave sealed and placed in a pre-heated oil bath (50 ^{o}C) and the stirring as set to 1200 rpm and left for 16 h. After the reaction, the vessel was cooled to ambient temperature and vented to the atmosphere, the reaction was analyzed by ^{1}H-NMR and conversion was estimated using the internal standard (1-methylnaphthalene). The reaction mixture was evaporated to dryness and the crude product was purified by column chromatography using 100% hexane followed by dichloromethane / methanol (95/5) to give the (*R*)-3-hydroxymethylpiperidine as a colorless oil (140 mg, 90 %); ^{1}H-NMR ($CDCl_3$) δ: 3.53 (1H, m, -C<u>H</u>$_2$OH), 3.45 (1H, m, -C<u>H</u>$_2$OH), 3.15 (1H, br dd, J = 12.0 / 3.9 Hz, -NH), 2.98 (1H, d, J =12.0 Hz, -C<u>H</u>$_2$-), 2.59 (1H, m, -C<u>H</u>-), 2.41 (2H, m, -C<u>H</u>$_2$-), 1.80 (1H, m, -C<u>H</u>$_2$-), 1.69 (2H, m, -C<u>H</u>$_2$-), 1.49 (1H, m, -C<u>H</u>$_2$-), 1.17 (1H, m, -C<u>H</u>$_2$-); ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 66.03 (-<u>C</u>H$_2$OH), 50.12 (<u>C</u>H$_2$-N), 47.00, 39.43, 27.92, 25.87 (<u>C</u>H$_2$); HRMS (ES+): calculated for [$C_6H_{14}NO^+$]: 116.1070 found: 116.1069; Chiral analysis was performed as the *cbz* protected species using a Chiralcel AD-H column using *n*-hexane / isopropanol (95/5) mobile phase, flow 1.0 mL/min; t_R (*S*-enantiomer, minor): 27.2 min; t_R (*R*-enantiomer, major): 29.5 min, *ee* 87 %. Fits with previously published data.[26]

(*R*)-*N*-Cbz-3-hydroxymethylpiperidine, 10k



(R)-Ethyl-*N*-cbz-nipecotate (273 mg, 1.00 mmol, 1 equiv., 88 % ee), manganese catalyst (7.2 mg, 0.001 mmol, 0.01 equiv.), potassium carbonate (14 mg, 0.10 mmol, 0.1 equivalents) and 1-methylnaphthalene (~30 µL, internal standard) was added to a microwave vial containing a stirring bead. The vial was sealed and evacuated and refilled with argon. This was repeated twice. Degassed isopropanol (2.3 mL) was added and the vial septum as pierced with 2x18G needles and placed in a stainless-steel autoclave under argon atmosphere. The vessel was pressurized with hydrogen gas (50 bar) and vented to the atmosphere. This was repeated twice. The pressure was set to 50 bar using hydrogen gas and the autoclave sealed and placed in a pre-heated oil bath (50 ^{o}C) and the stirring as set to 1200 rpm and left for 16 h. After the reaction, the vessel was cooled to ambient temperature and vented to the atmosphere, the reaction was analyzed by ^{1}H-NMR and conversion was estimated using the internal standard (1-methylnaphthalene). The reaction mixture was evaporated to dryness and the crude product was purified by column chromatography using 100% hexane followed by ethyl acetate to give the (*R*)-*N*-Cbz-3-hydroxymethylpiperidine as a colorless oil (188 mg, 0.75 mmol, 75 %). $[\alpha]_D^{20}$: -19.5 (*c.* 1.00, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 7.38 (4H, m, Ph-H), 7.33 (1H, m, Ph-H), 5.16 (2H, br s, PhC<u>H</u>$_2$N), 4.01-3.88 (2H, br m, -C<u>H</u>$_2$-), 3.54 (2H, br m, -C<u>H</u>$_2$OH), 3.18-2.87 (2H, m, -C<u>H</u>$_2$-), 1.84 (2H, m, -C<u>H</u>$_2$-), 1.66 (2H, m, -C<u>H</u>$_2$-), 1.49 (1H, m, -C<u>H</u>$_2$-), 1.31 (1H, m, -C<u>H</u>$_2$-); ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 136.87 (-<u>C</u>(=O)OBn), 128.51 (<u>C</u>$_{Ar}$), 127.99 (<u>C</u>$_{Ar}$), 127.86 (<u>C</u>$_{Ar}$), 67.09 (Ph<u>C</u>H$_2$O), 65.00 / 64.29 (<u>C</u>H$_2$-O), 46.58 (<u>C</u>H$_2$-N), 44.94, 38.42, 37.83, 26.72, 24.00 (<u>C</u>H$_2$); HRMS (EI+): calculated for [$C_{14}H_{19}NO_3$]: 249.1365 found: 249.1368; Chiral analysis was performed using a Chiralcel AD-H column using *n*-hexane / isopropanol (95/5) mobile phase, flow 1.0 mL/min; t_R (*S*-enantiomer, minor): 27.2 min; t_R (*R*-enantiomer, major): 29.5 min, *ee* 87 %.

(*S*)-1-hydroxymethyl-1,2,3,4-tetrahydronaphthalene, 10l

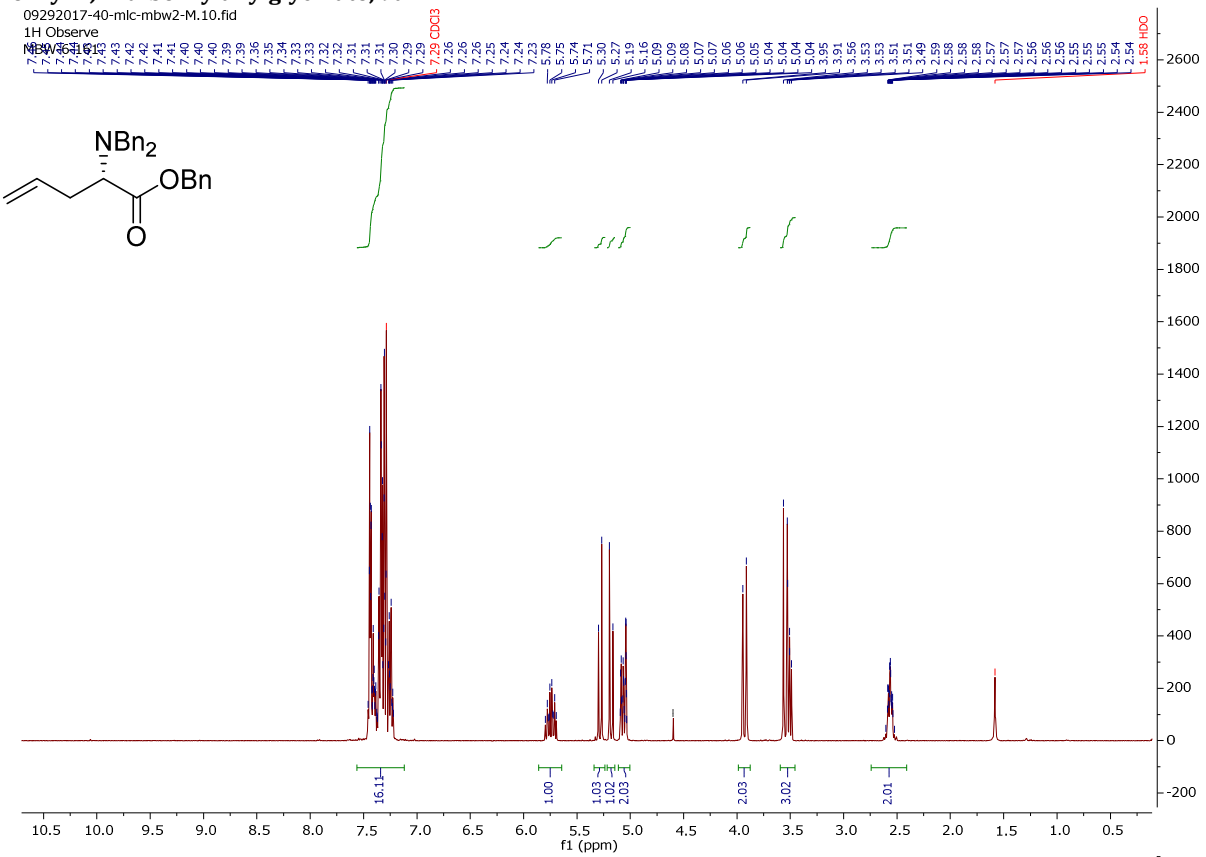


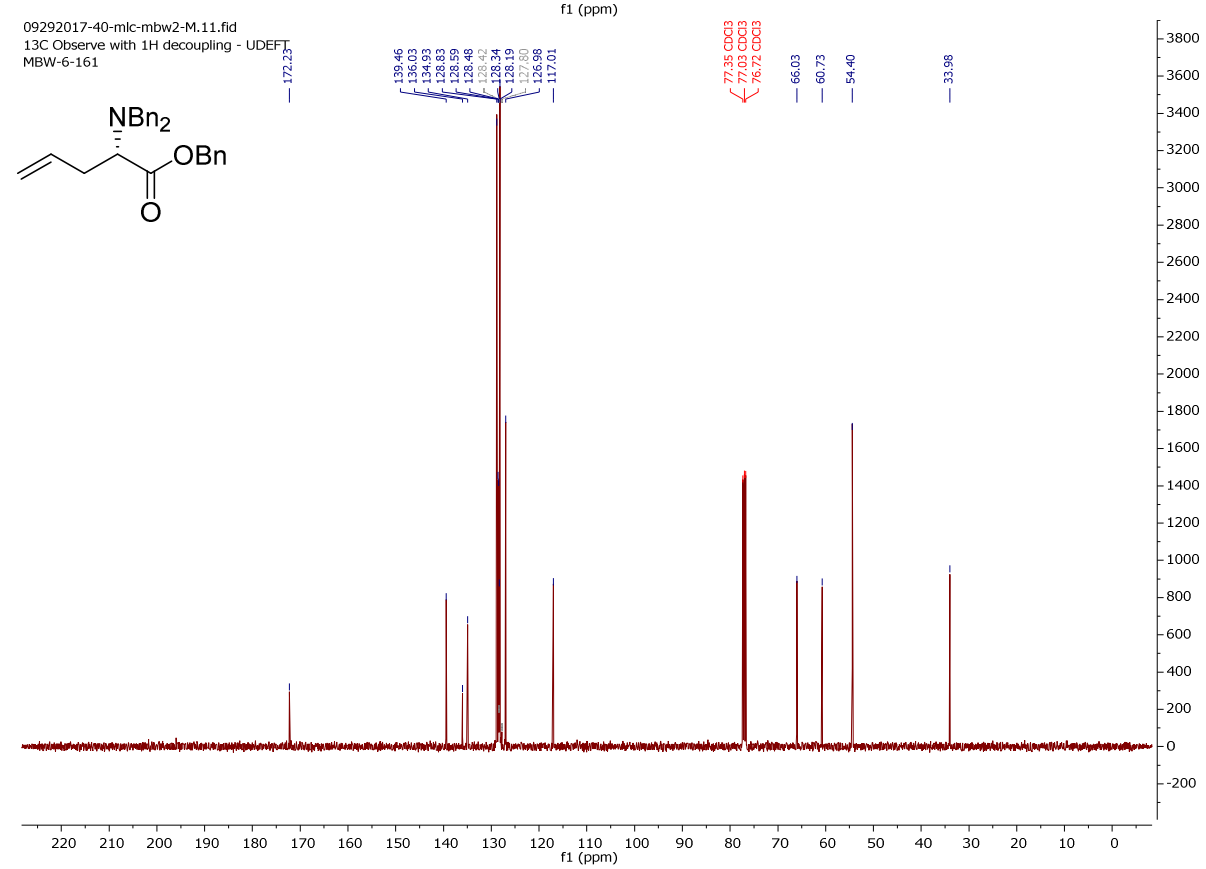
(S)-Ethyl 1,2,3,4-tetrahydronaphthalene-1-carboxylate (500 mg, 2.45 mmol, 1.0 equiv.) and 1-methylnaphthalene (internal standard) (100 µL, 0.73 mmol, 0.30 equiv.) was dissolved in isopropanol (6 mL) and degassed with argon. Mn catalyst (17.7 mg, 0.024 mmol, 0.01 equiv.) and potassium carbonate (33.8 mg, 0.245 mmol, 0.1 equiv.) was charged to an autoclave fitted with a Teflon insert and a cross shaped stir bar, an injection port, a sampling port, pressure gauge and a pressure inlet. The vessel as sealed and evacuated and refilled with argon three times. The degassed substrate solution was added to the injection port and the vessel was pressurized with hydrogen gas (43 bar) and vented three times. The vessel was pressurized with hydrogen gas to 43 bar and inserted in a Drysyn heating block pre-heated to 50 ^{o}C. After 21 h the vessel was cooled to room temperature and vented. The solution was concentrated to dryness and analyzed by ^{1}H NMR showing >95 % conversion. The product as purified by column chromatography using 100 % hexane followed by dichloromethane / methanol (95/5) to give the title compound as a pale-yellow oil (300 mg, 1.85 mmol, 75 %).

$[\alpha]_D^{20}$: +82.8 (*c.* 1.10, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 7.27 (1H, m, Ar-H), 7.20-7.12 (3H, m, Ar-H), 3.84 (2H, d, J = 6.1 Hz, -C<u>H</u>$_2$OH), 3.02 (1H, m, -C<u>H</u>-), 2.79 (2H, m, -C<u>H</u>$_2$-), 1.97 (3H, m, -C<u>H</u>$_2$-), 1.78 (1H, m, -C<u>H</u>$_2$-); ^{13}C -{^{1}H}-NMR ($CDCl_3$) δ: 138.20 (<u>C</u>$_{Ar}$Cl), 136.70 (<u>C</u>$_{Ar}$-CH), 129.39 (<u>C</u>$_{Ar}$), 128.75 (<u>C</u>$_{Ar}$), 126.15 (<u>C</u>$_{Ar}$), 125.72 (<u>C</u>$_{Ar}$), 67.17 (-<u>C</u>H$_2$OH), 40.33 (-<u>C</u>H-), 29.14(-<u>C</u>H$_2$-), 25.21 (-<u>C</u>H$_2$-), 19.80 (-<u>C</u>H$_2$-); HRMS (EI+): calculated for [$C_{11}H_{14}O$]: 162.1045 found: 162.1048; Chiral analysis was performed using a Chiralcel OD-H column using *n*-hexane / isopropanol (98/2) mobile phase, flow 0.5 mL/min; t_R (*S*-enantiomer, major): 32.1 min; t_R (*R*-enantiomer, minor): 33.4 min, *ee* 88 %. Fits with previously published data.[27]

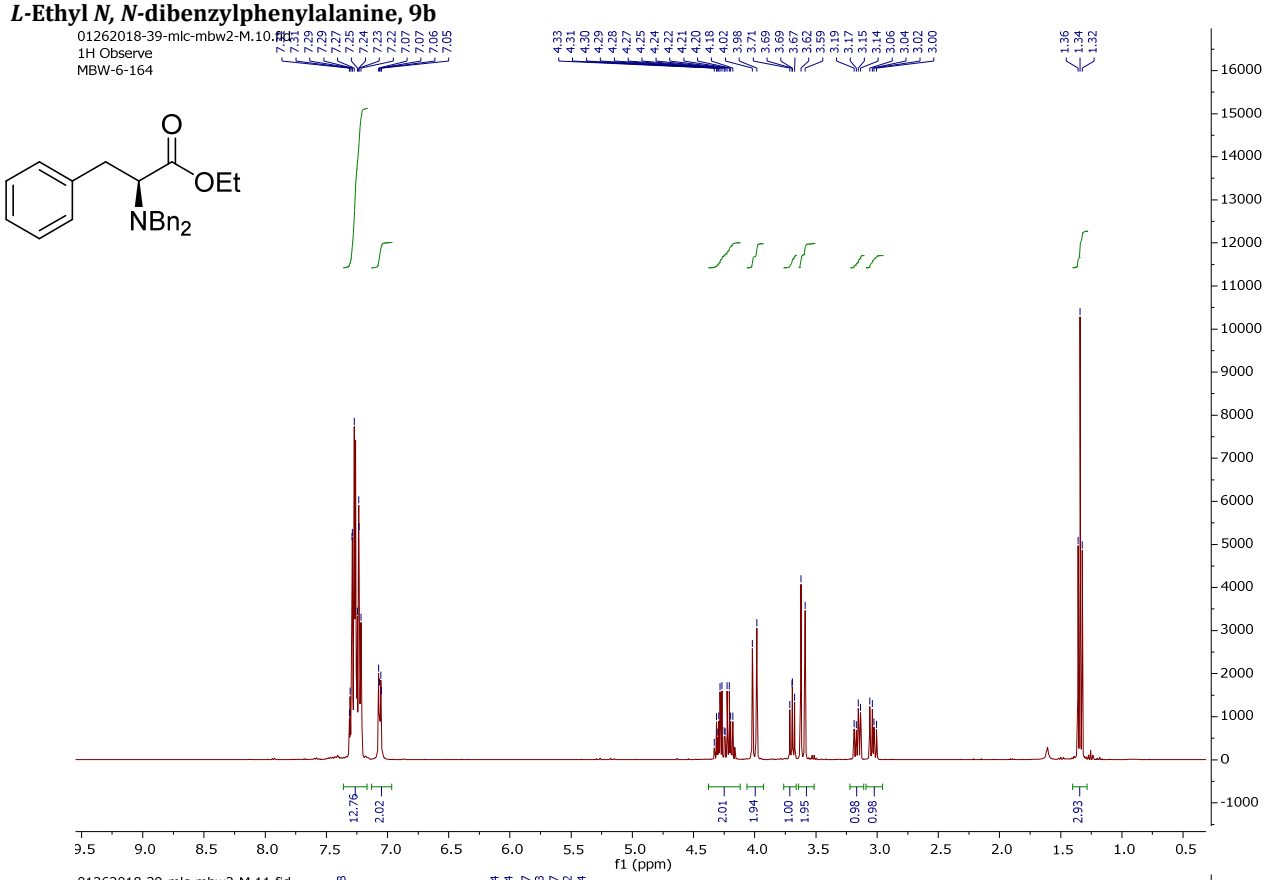
4. Spectra

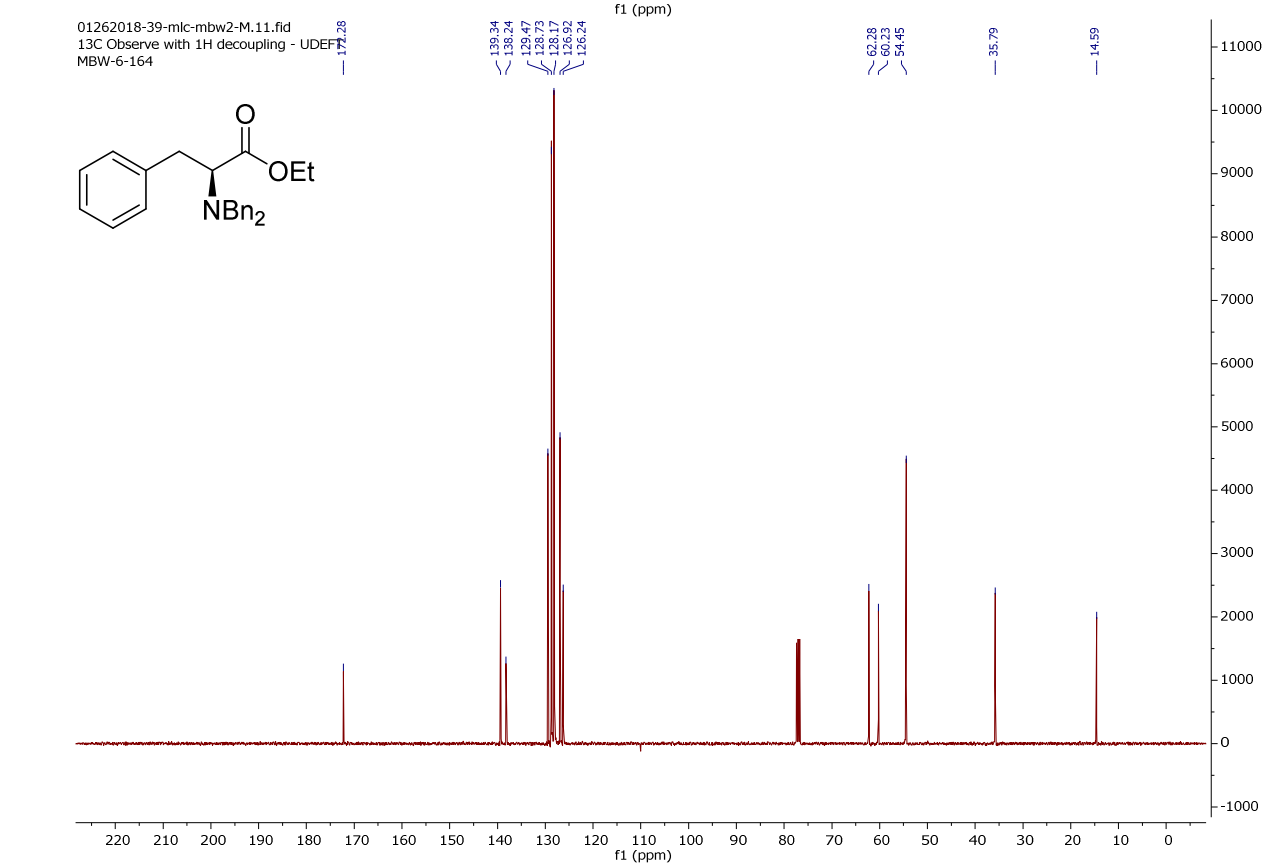
(S)-Benzyl *N, N*-dibenzylallylglycinate, 9a



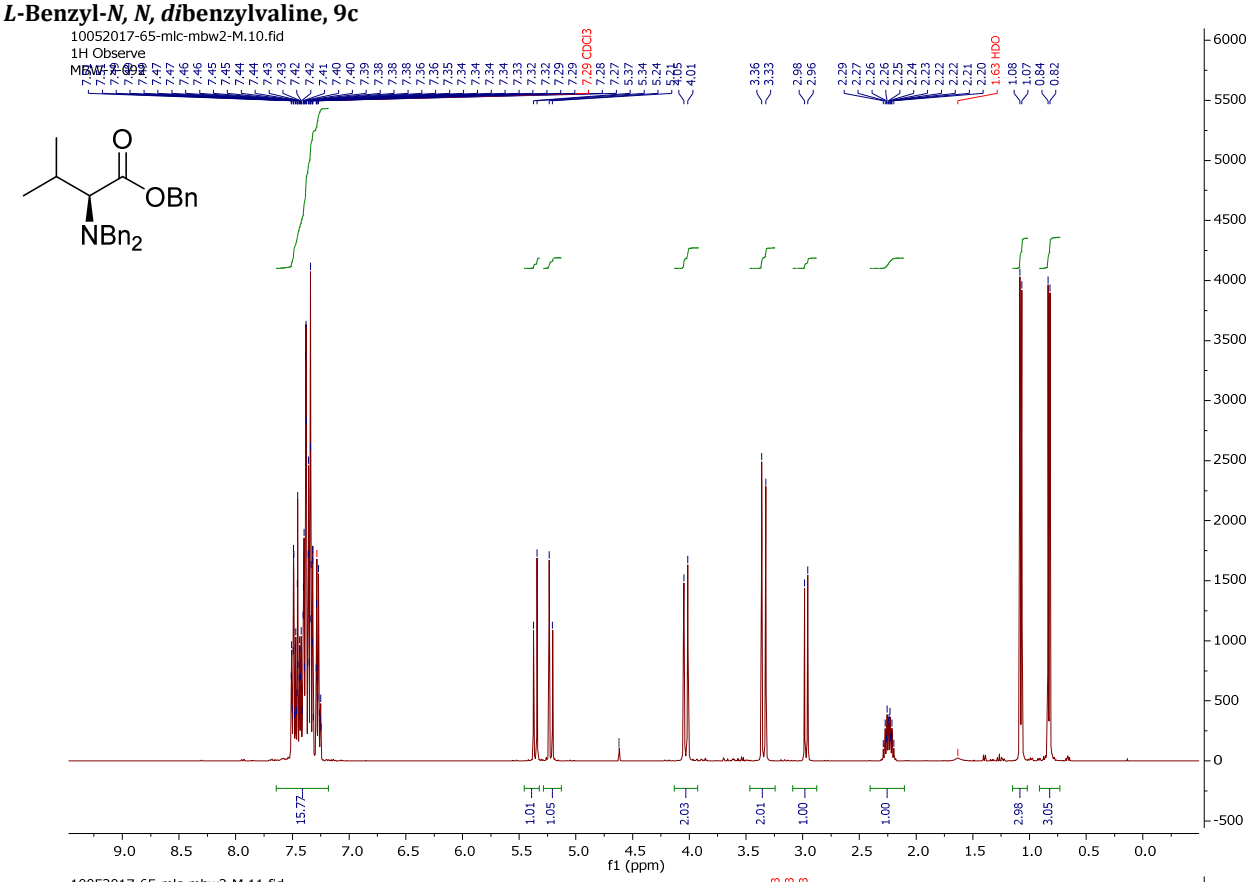


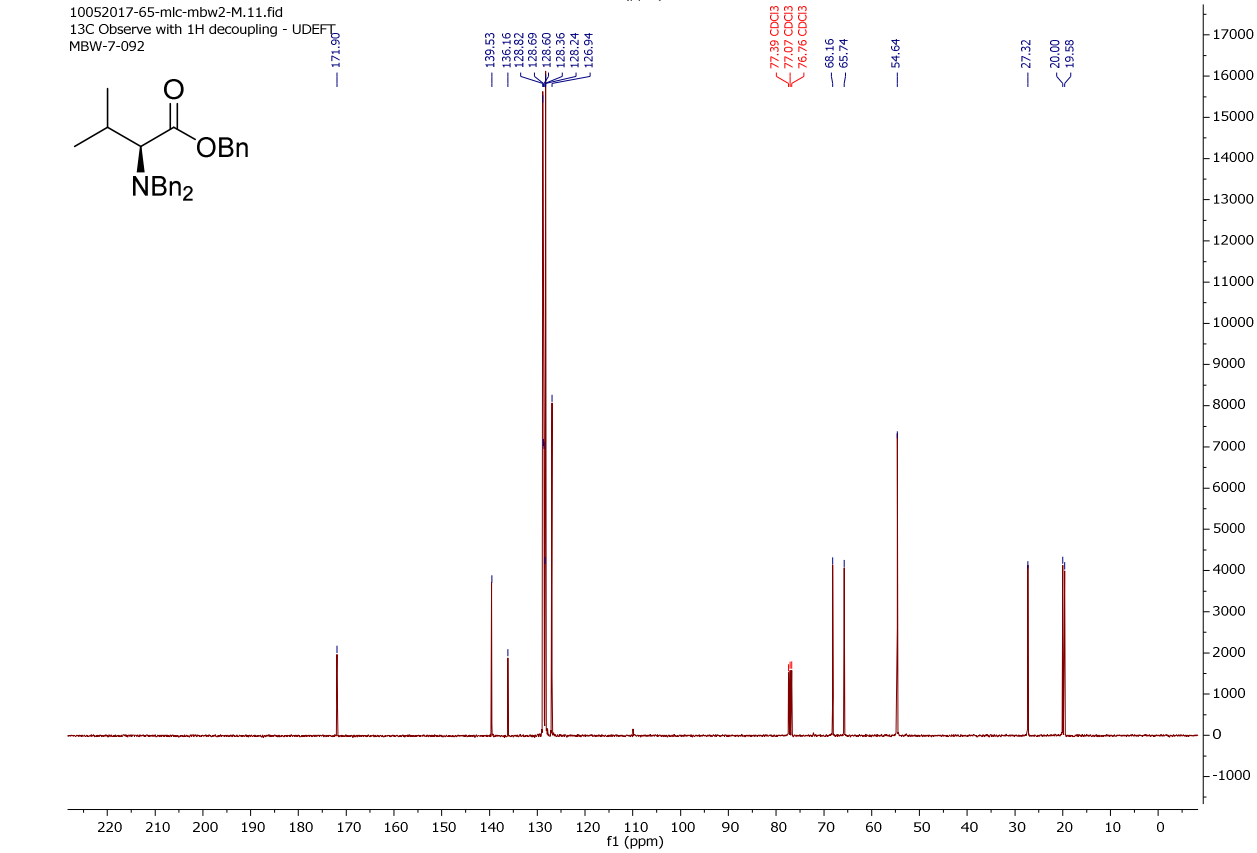
***L*-Ethyl *N, N*-dibenzylphenylalanine, 9b**



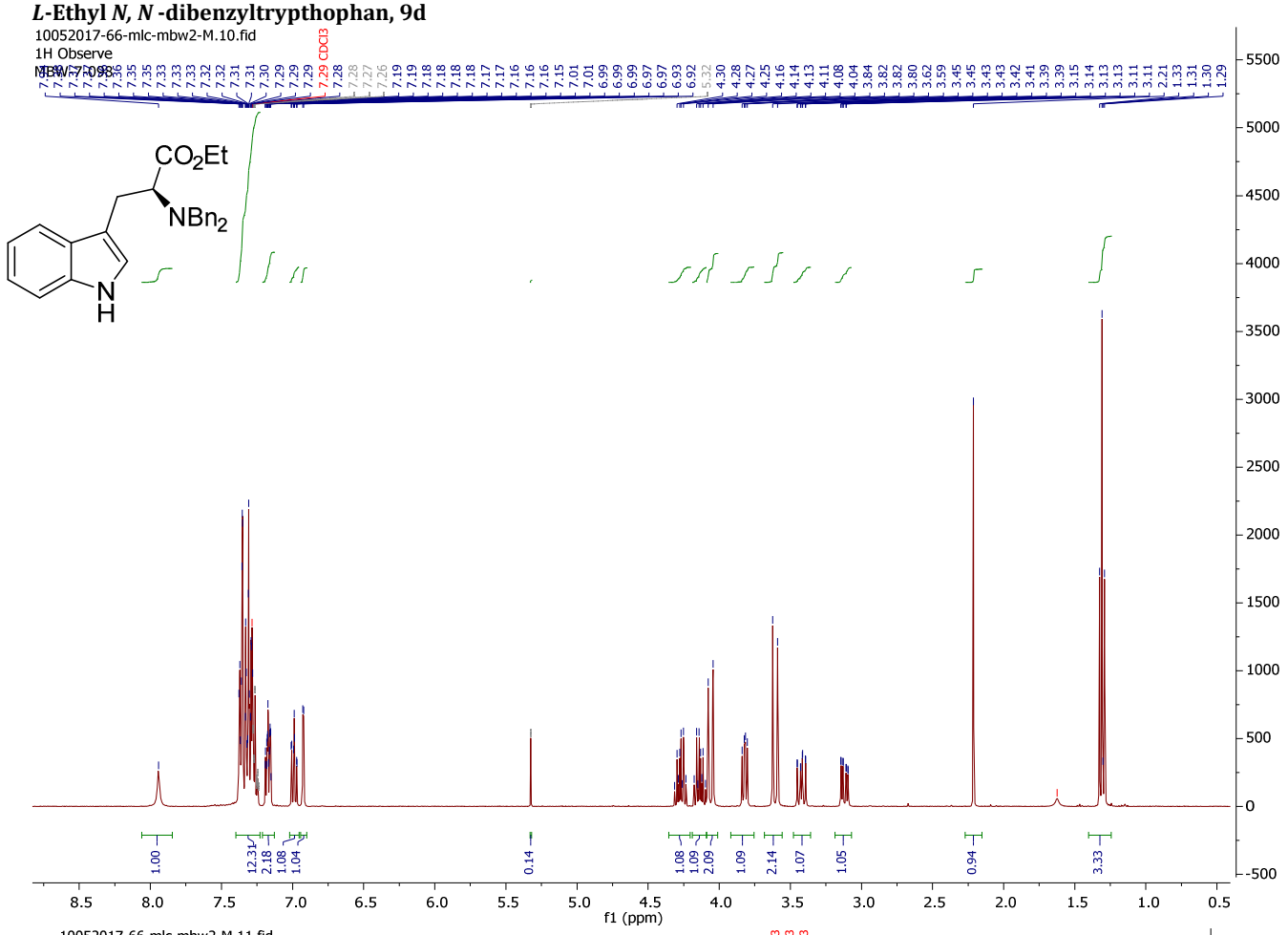


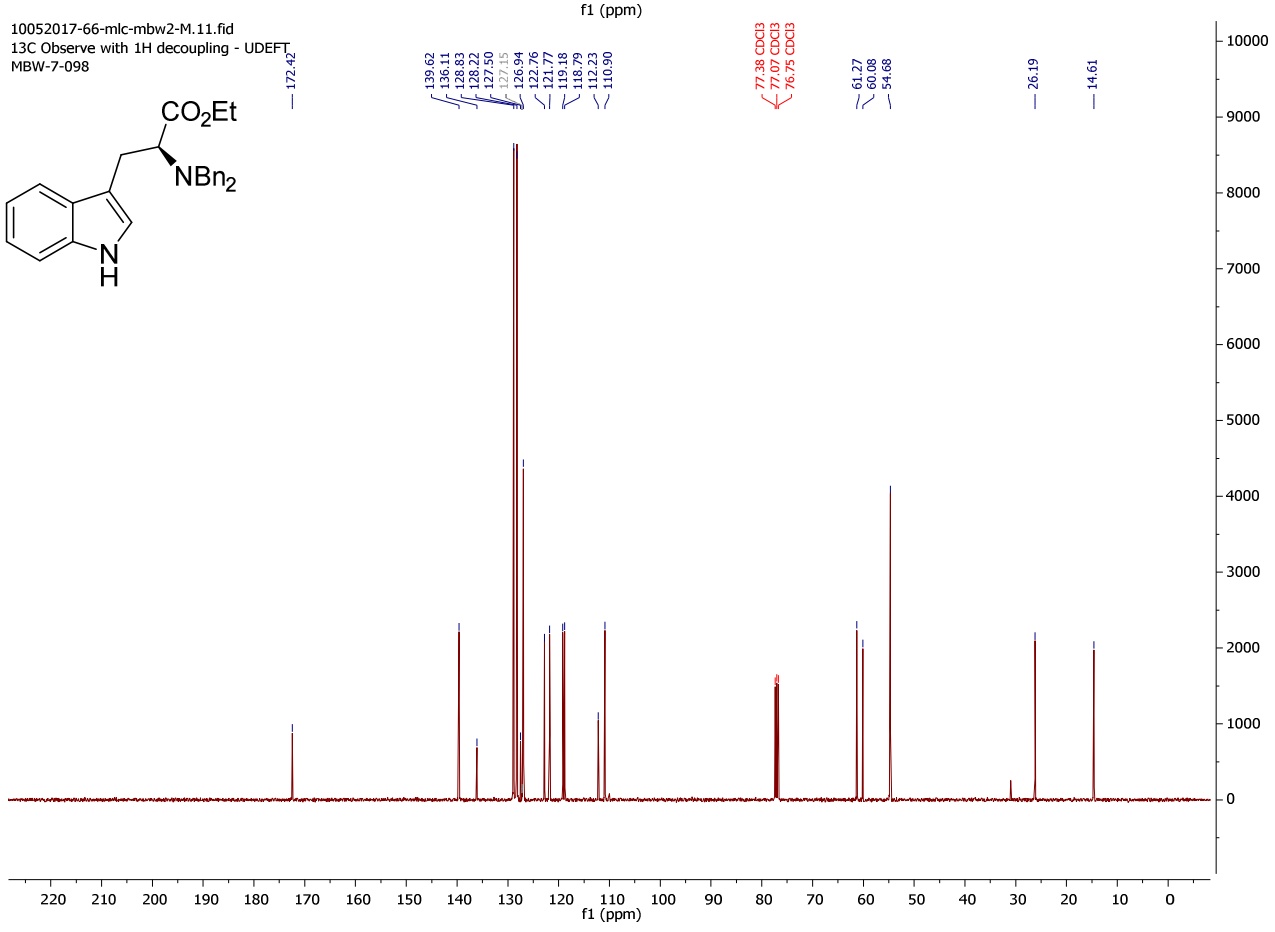
***L*-Benzyl-*N, N, di*benzylvaline, 9c**



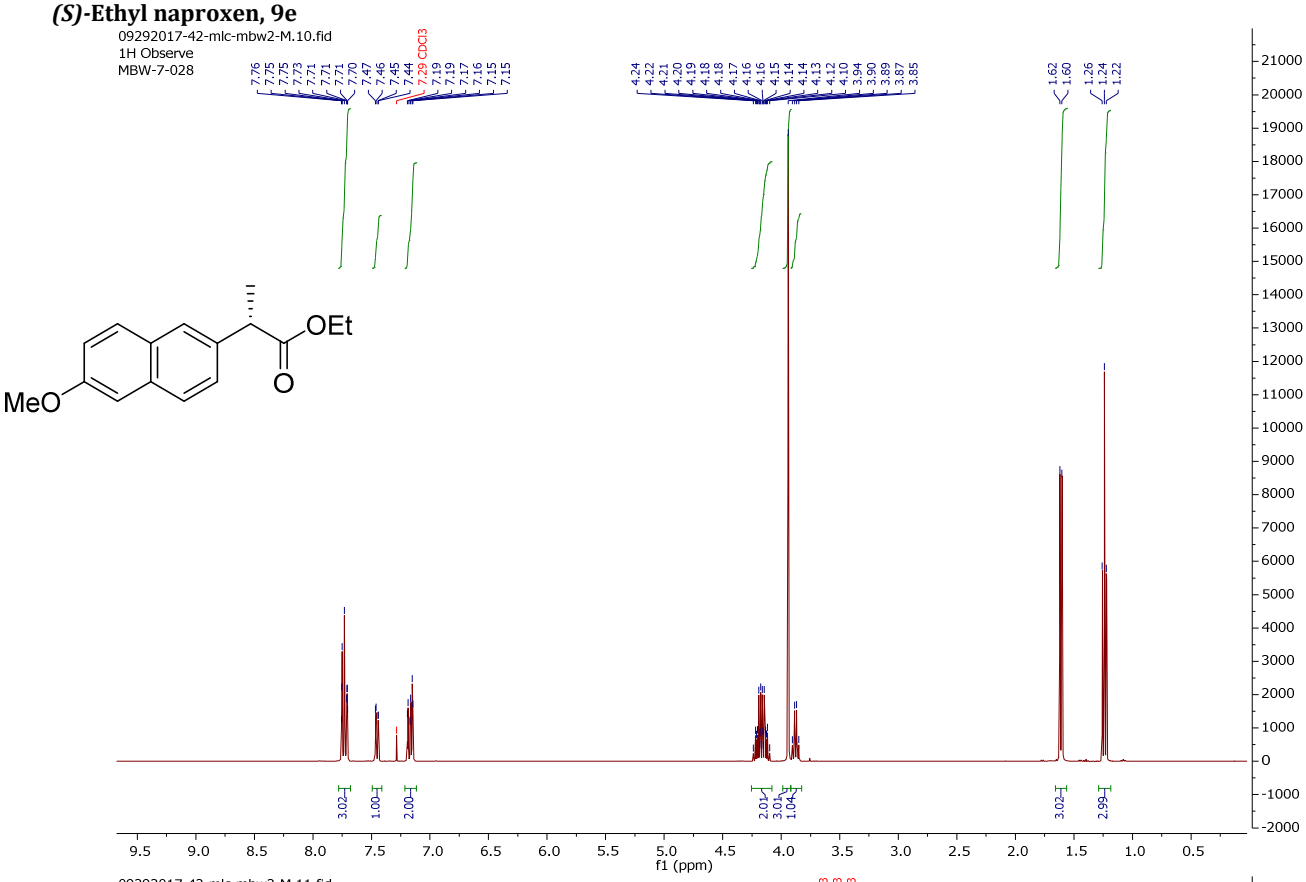


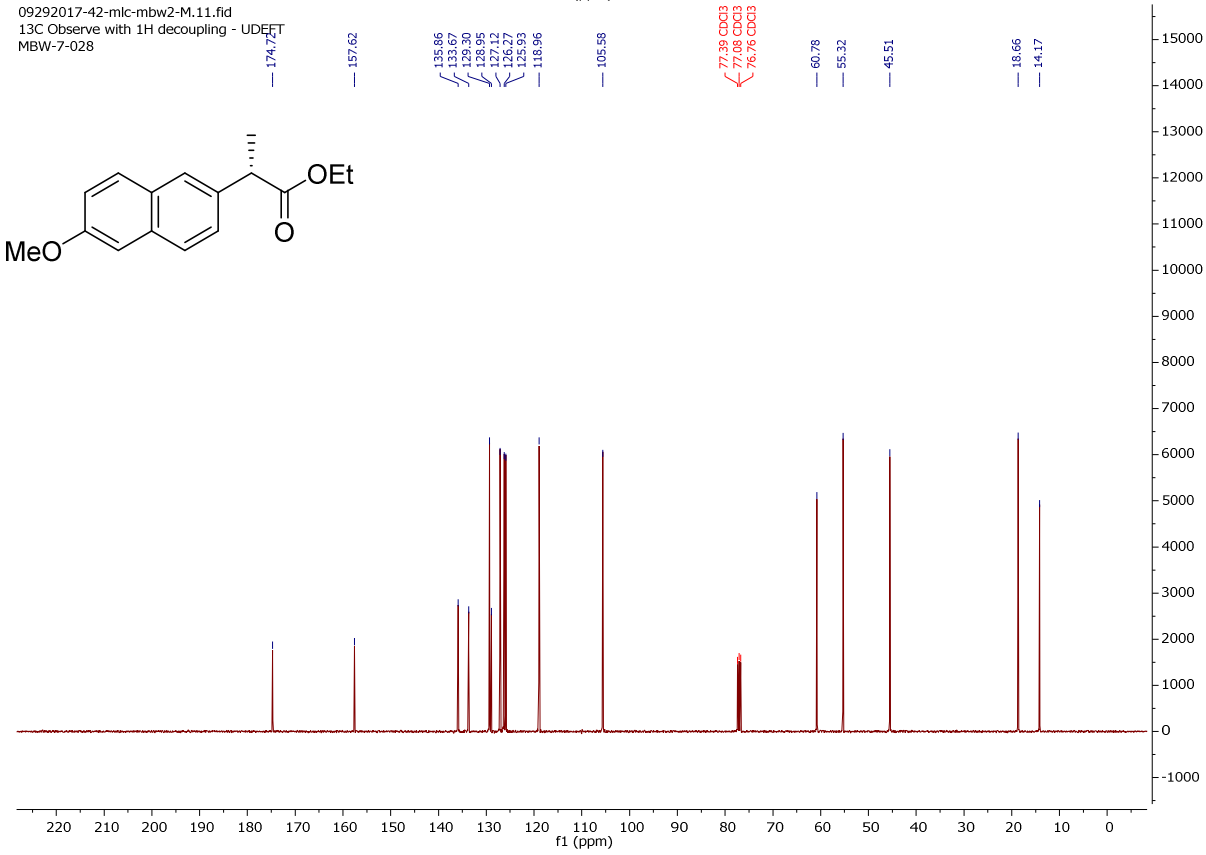
***L*-Ethyl *N, N* -dibenzyltrypthophan, 9d**



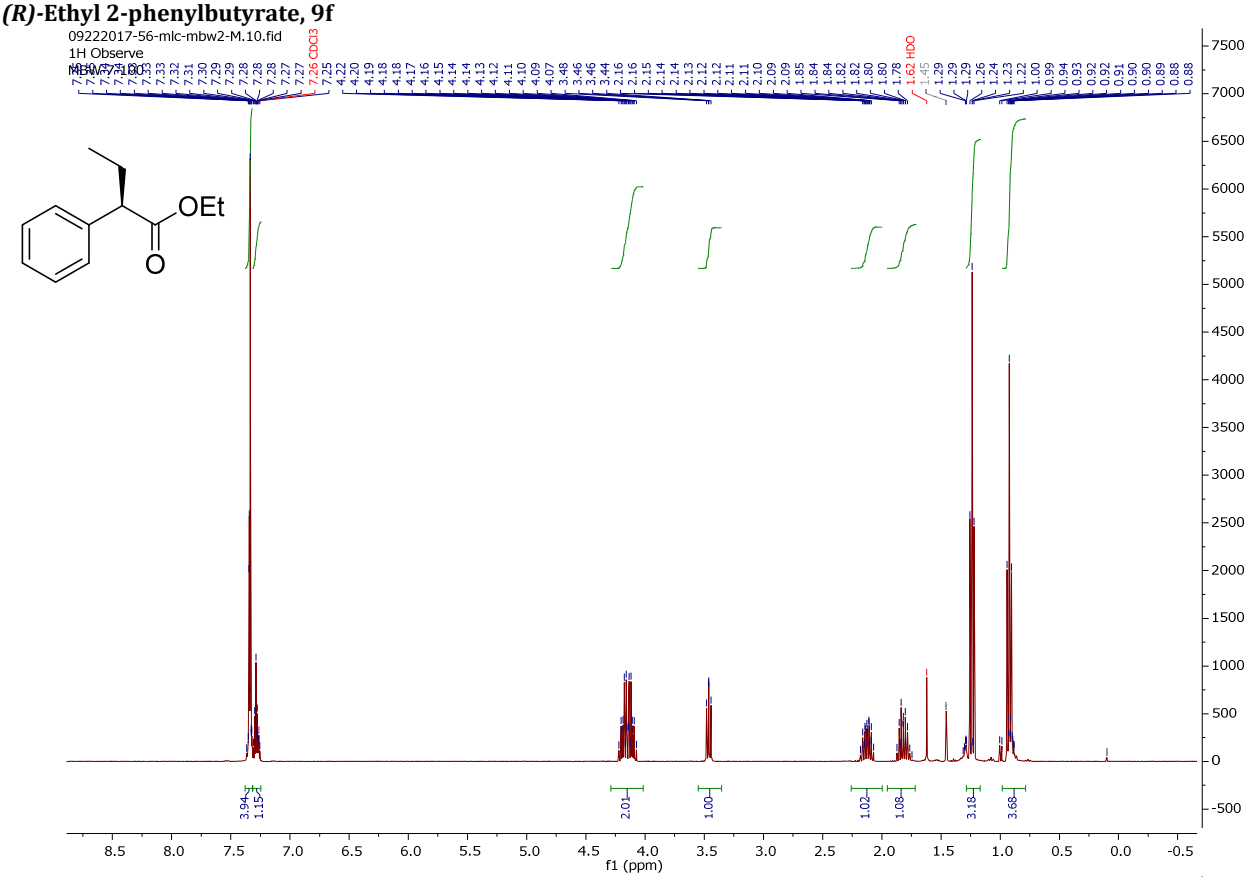


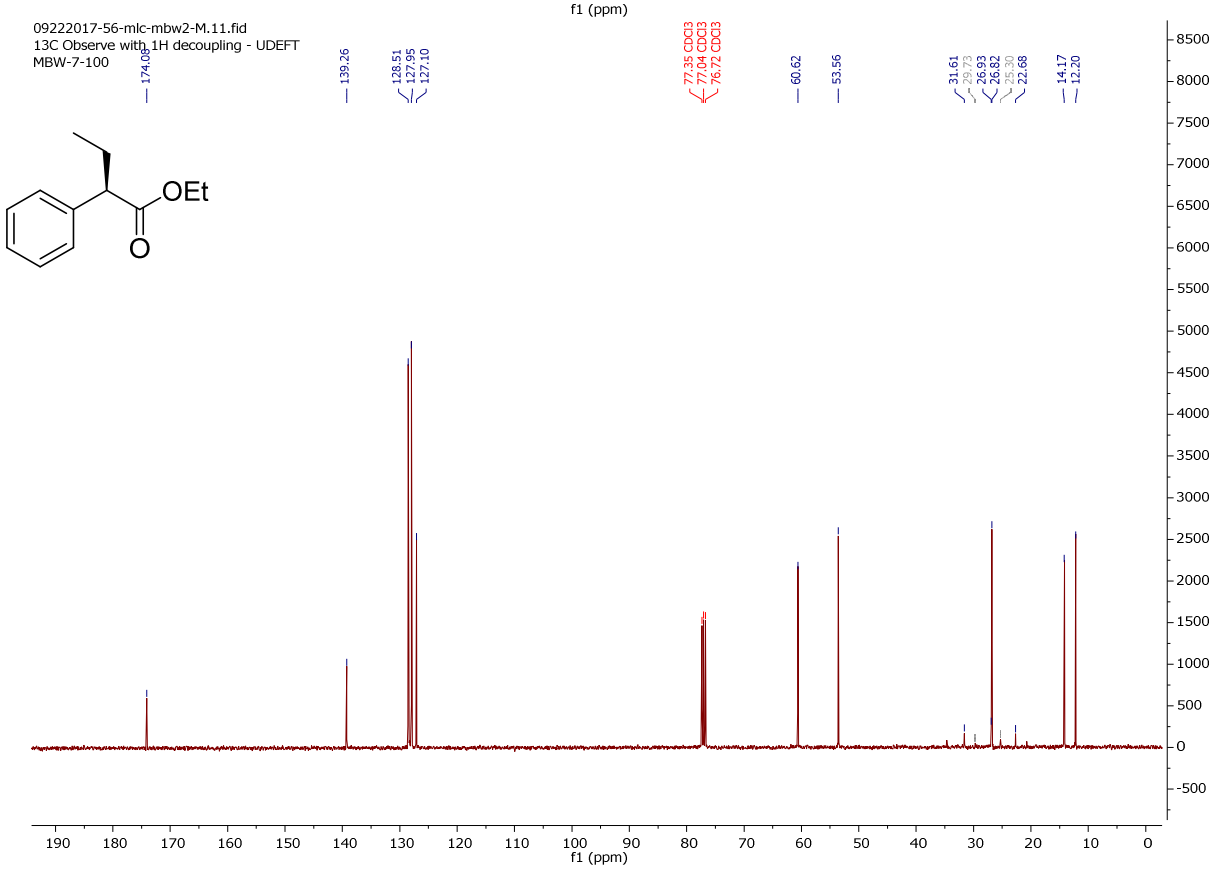
***(S)*-Ethyl naproxen, 9e**



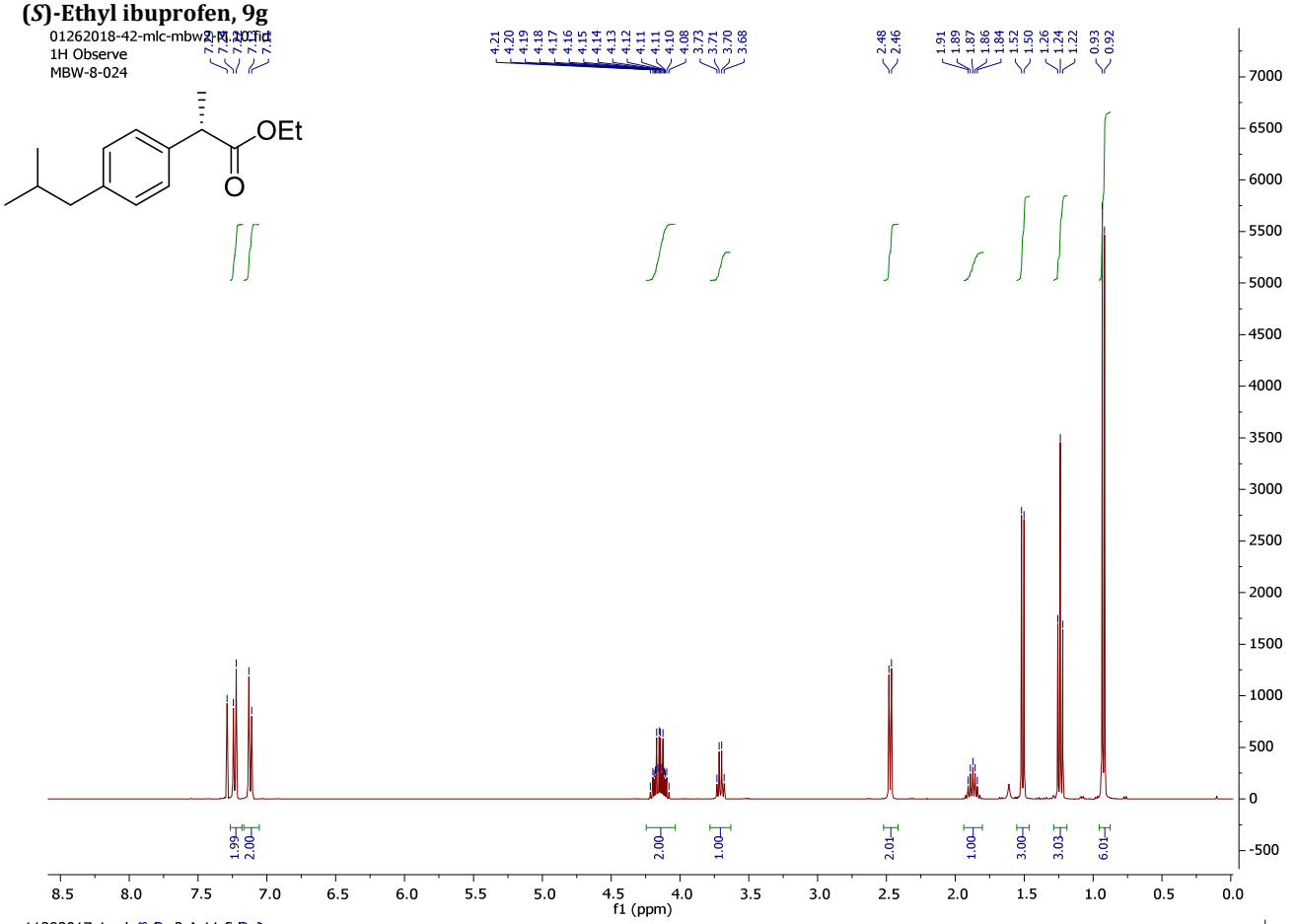


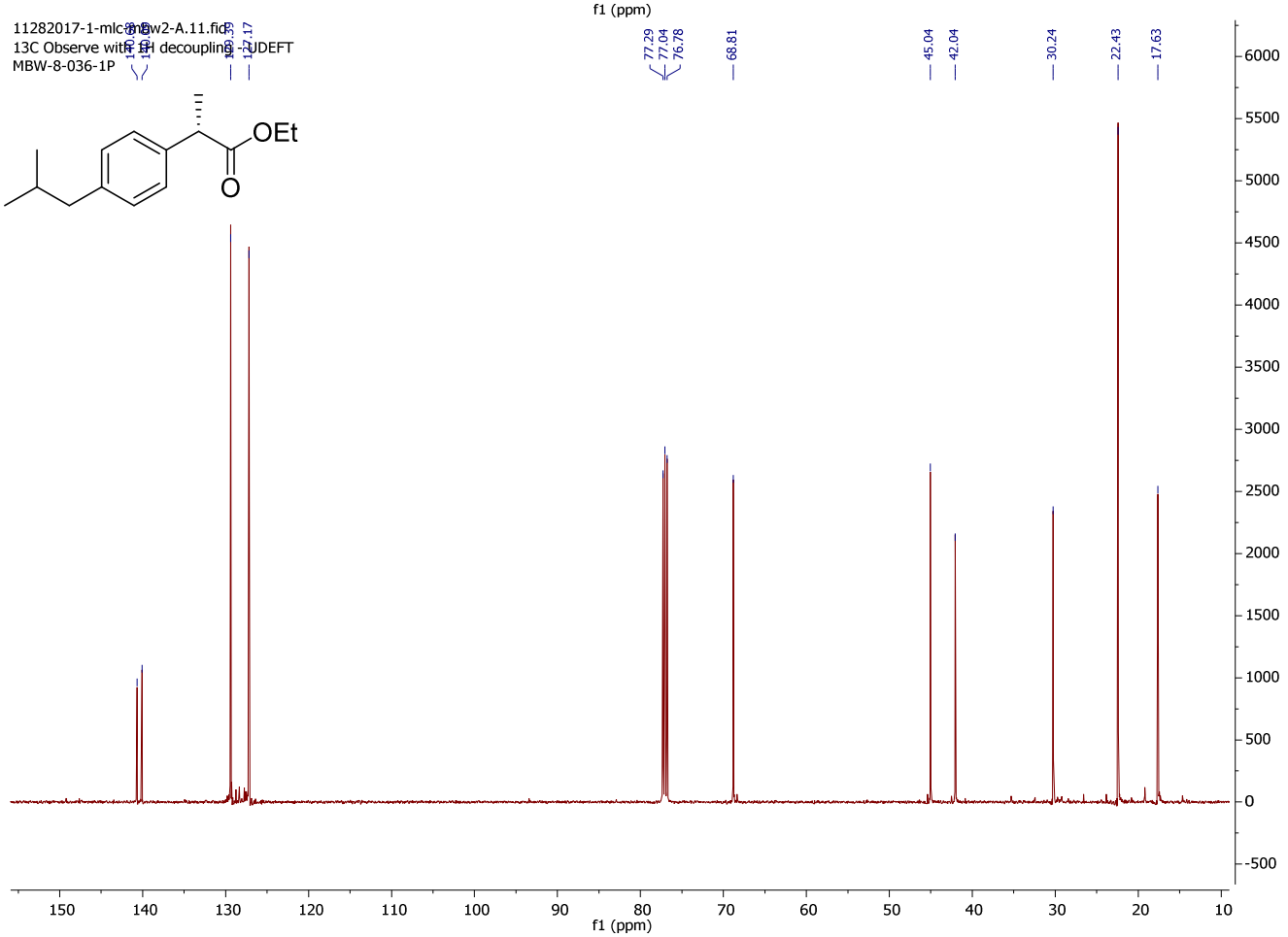
***(R)*-Ethyl 2-phenylbutyrate, 9f**



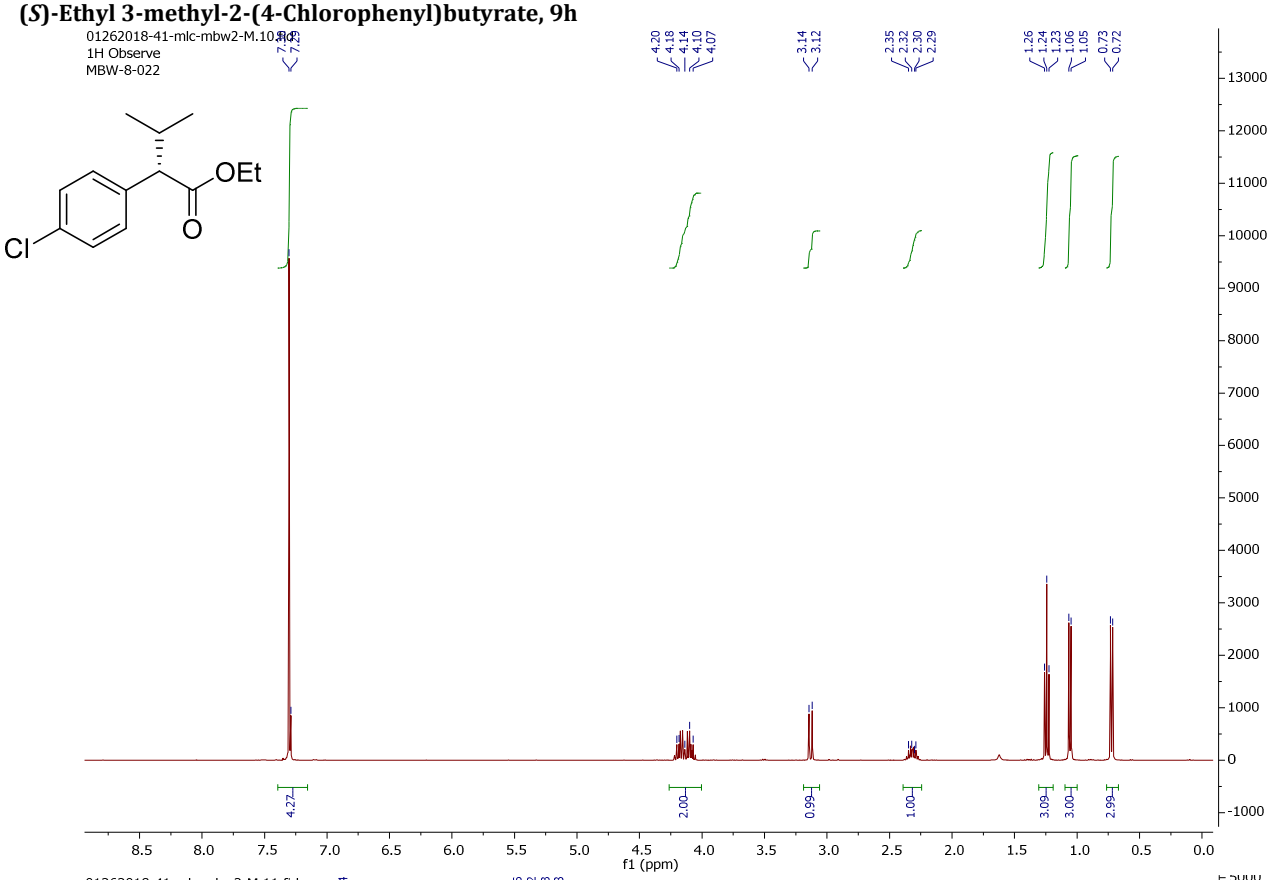


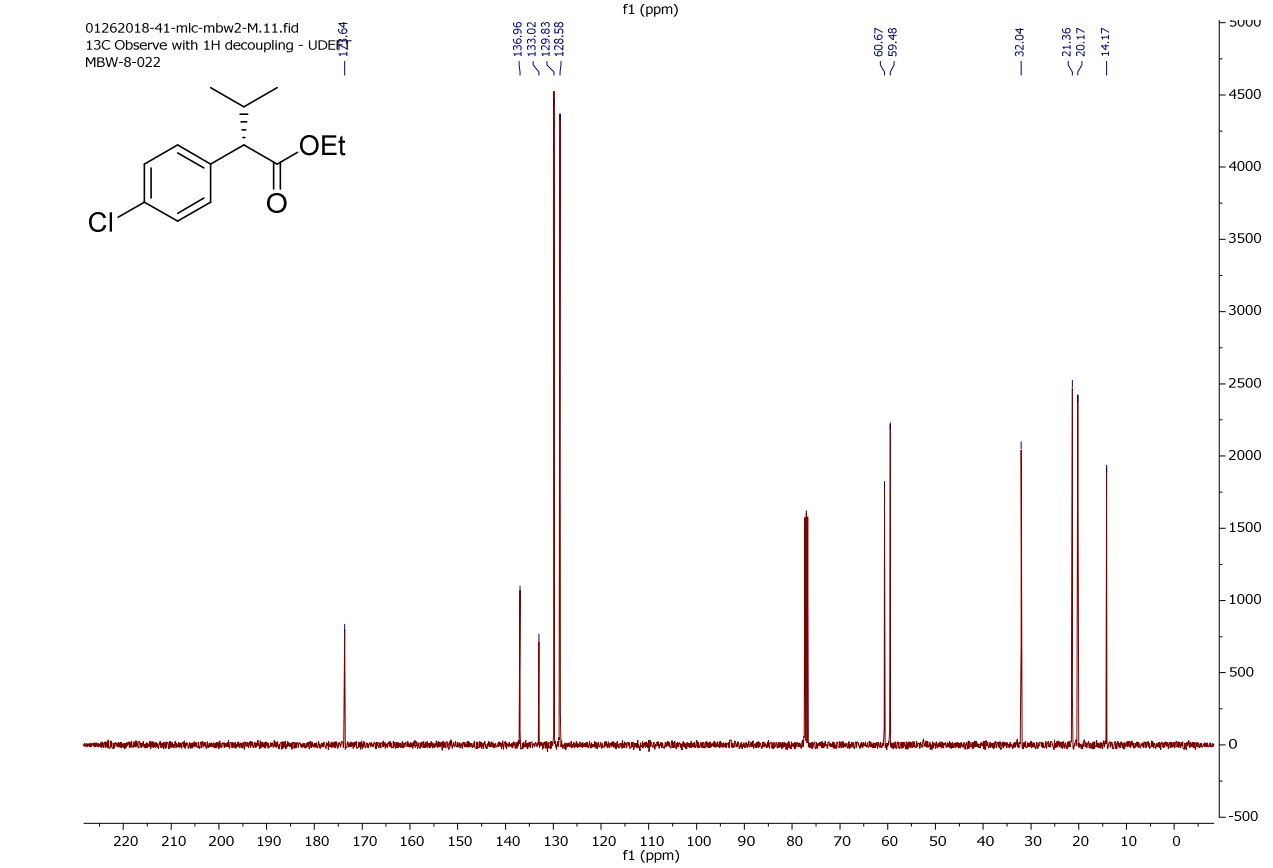
(*S*)-Ethyl ibuprofen, 9g



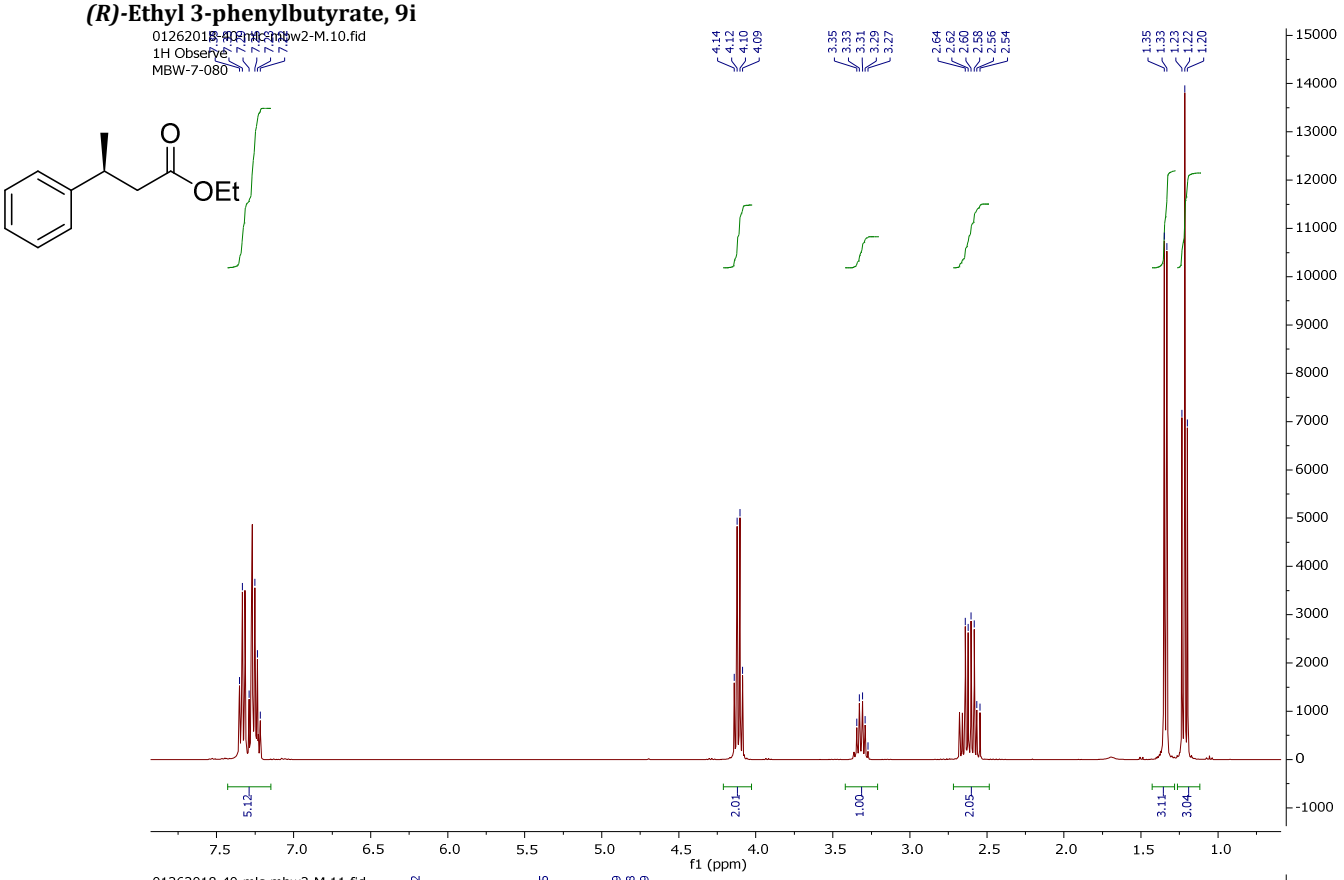


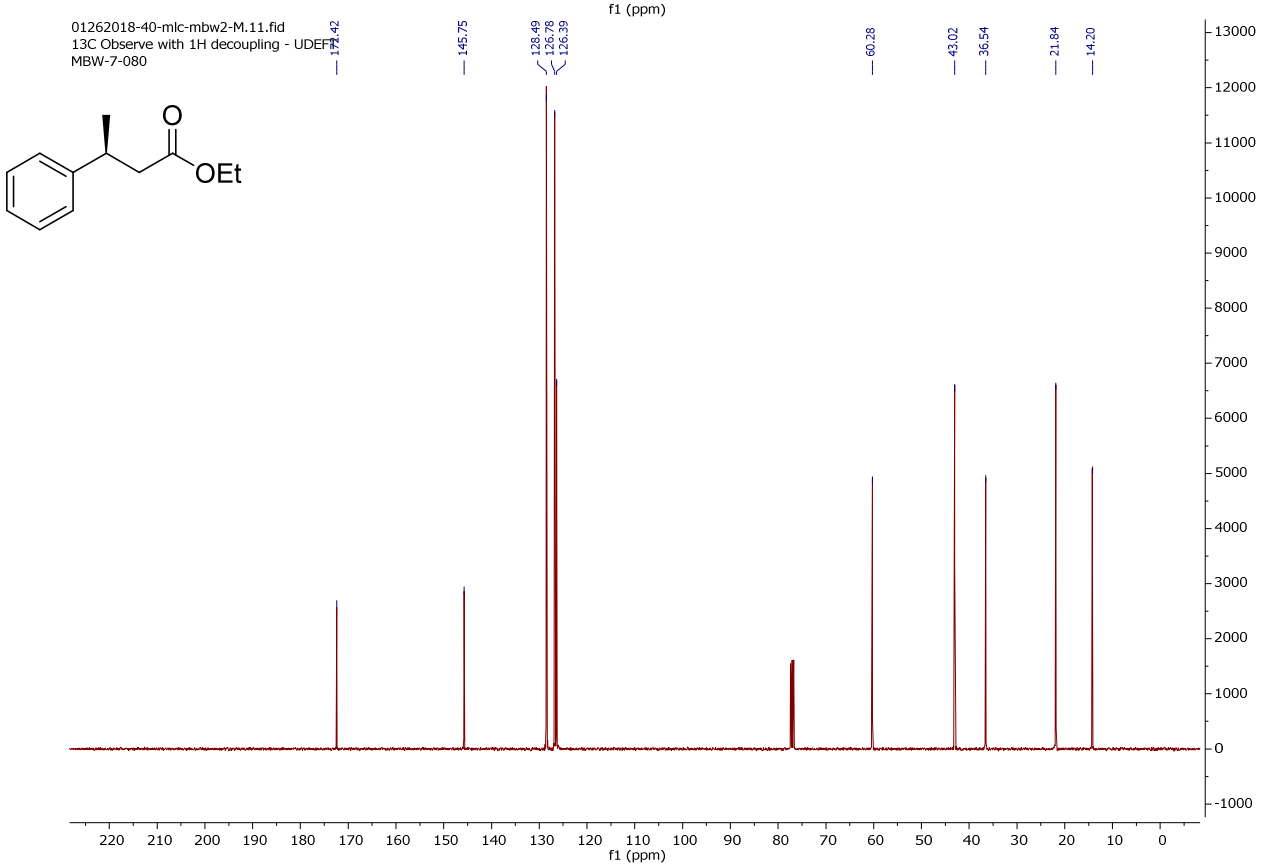
(*S*)-Ethyl 3-methyl-2-(4-Chlorophenyl)butyrate, 9h



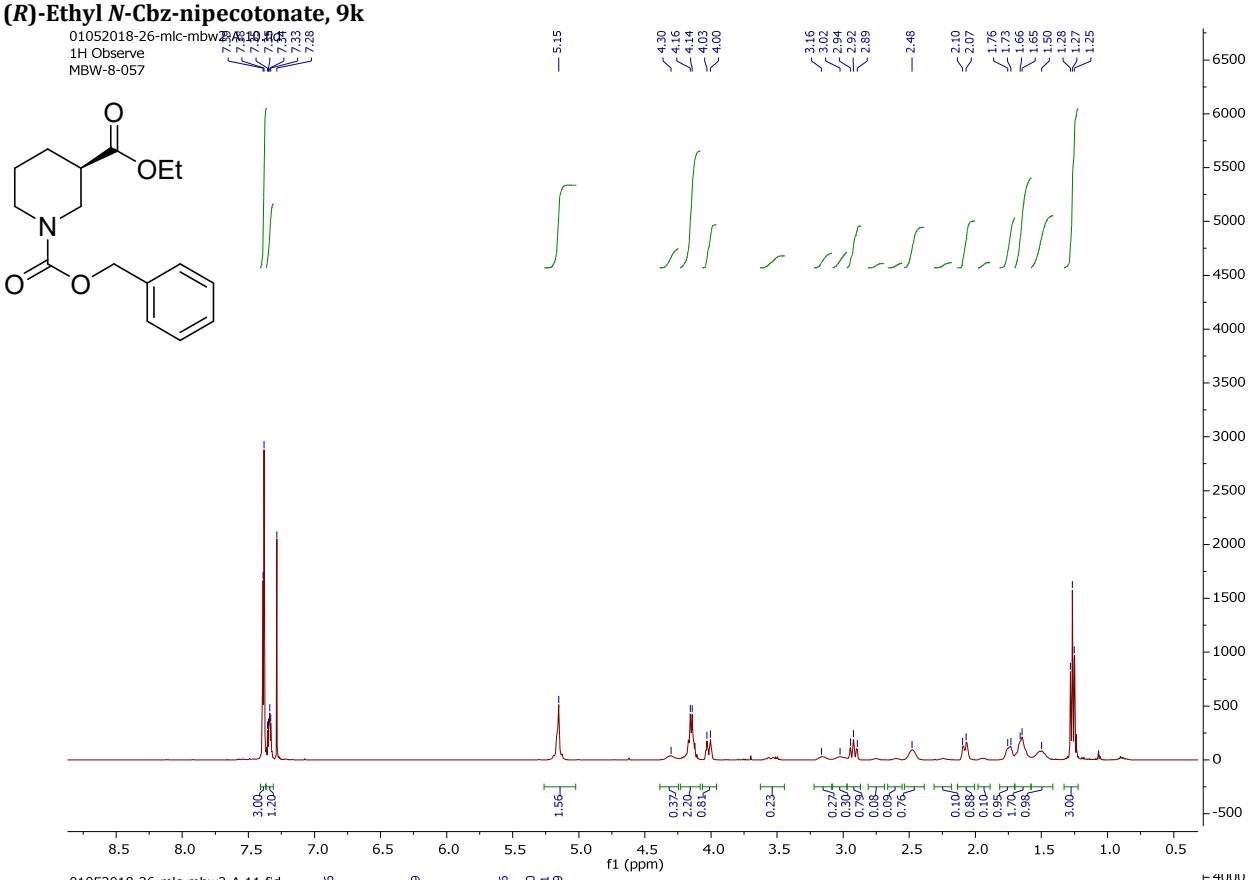


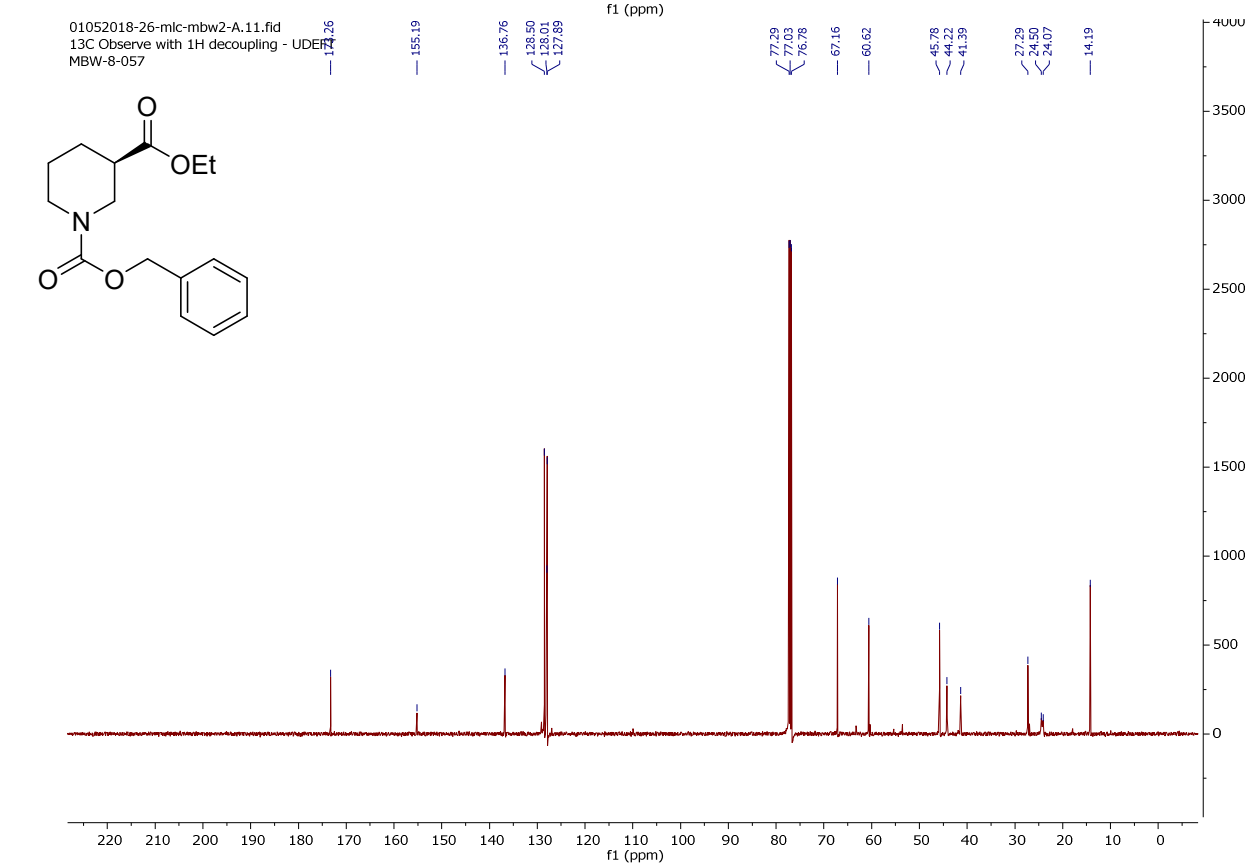
***(R)*-Ethyl 3-phenylbutyrate, 9i**



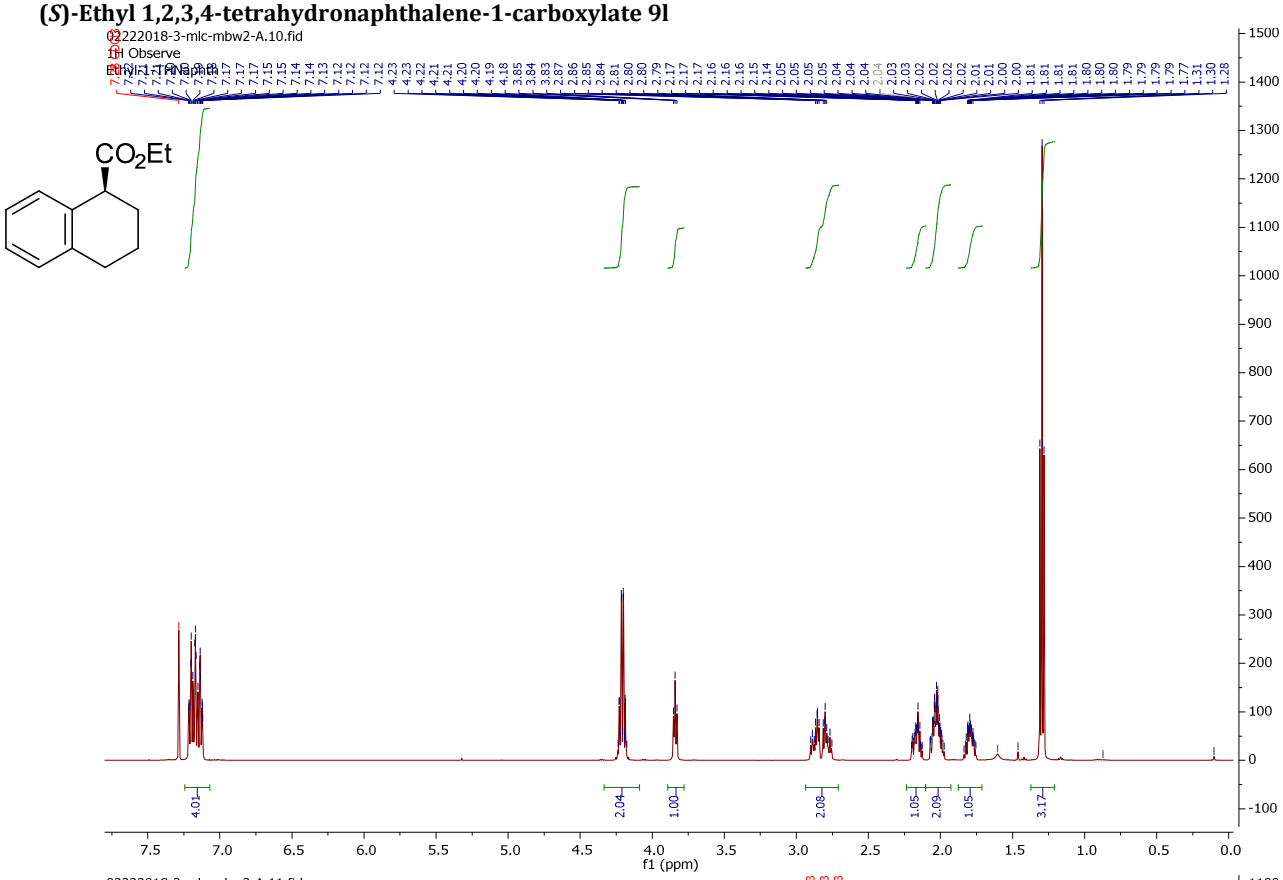


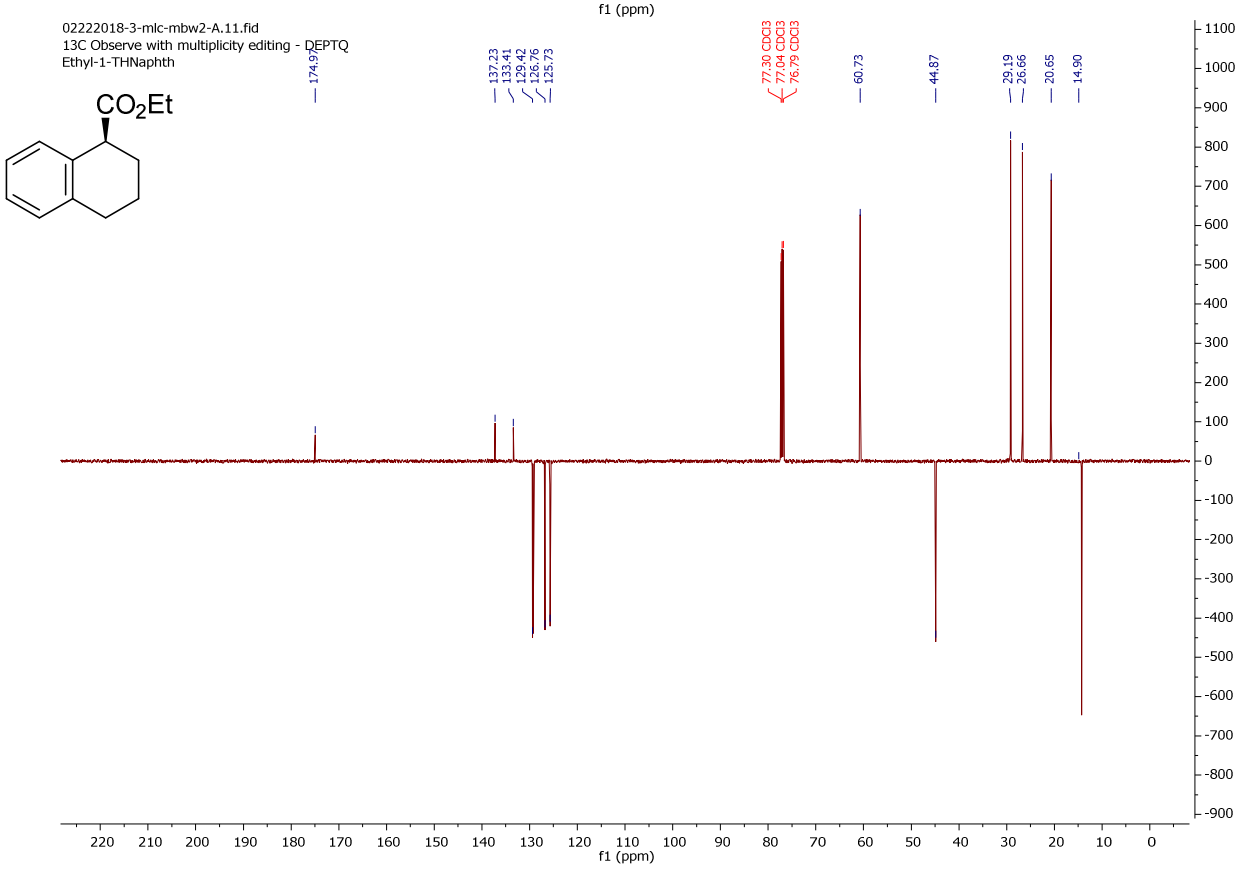
(*R*)-Ethyl *N*-Cbz-nipecotonate, 9k



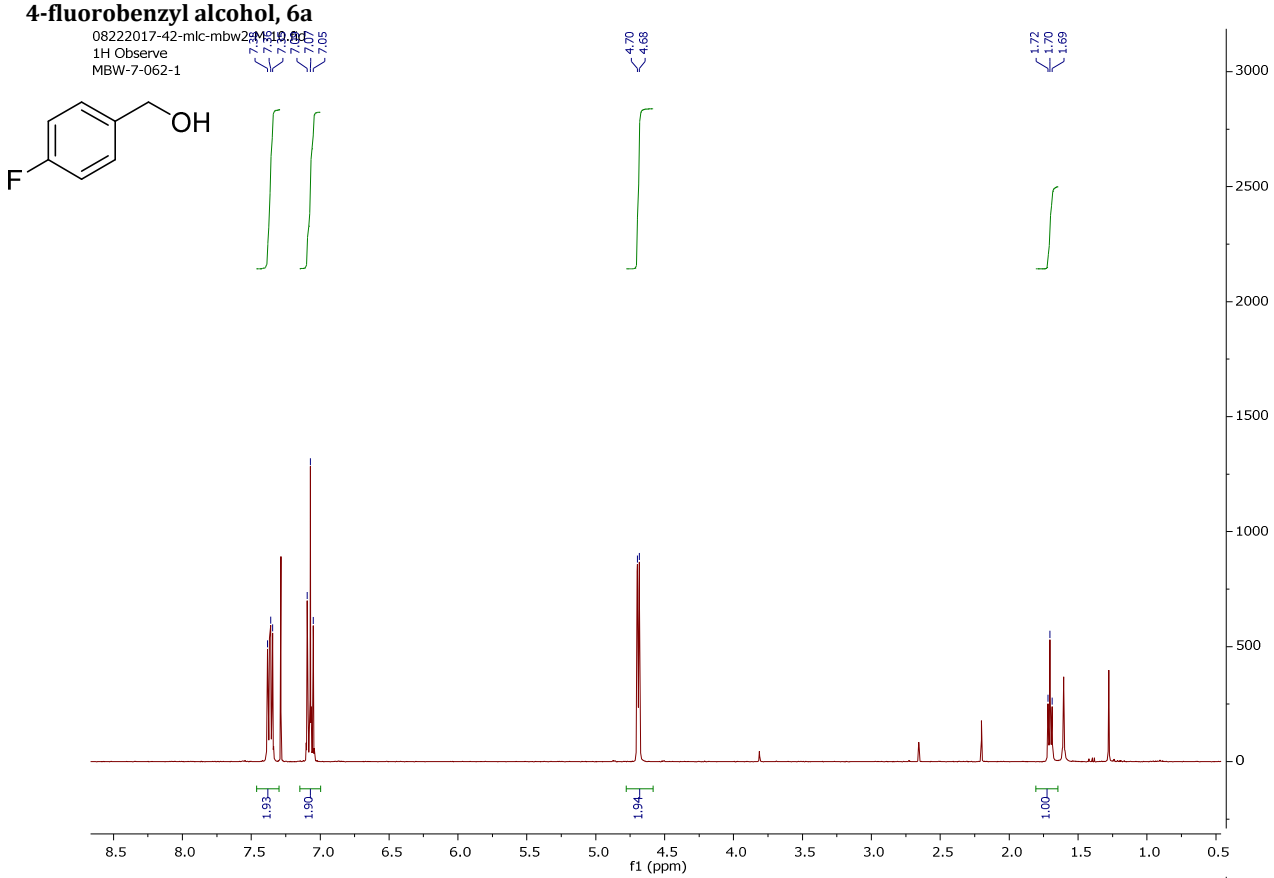


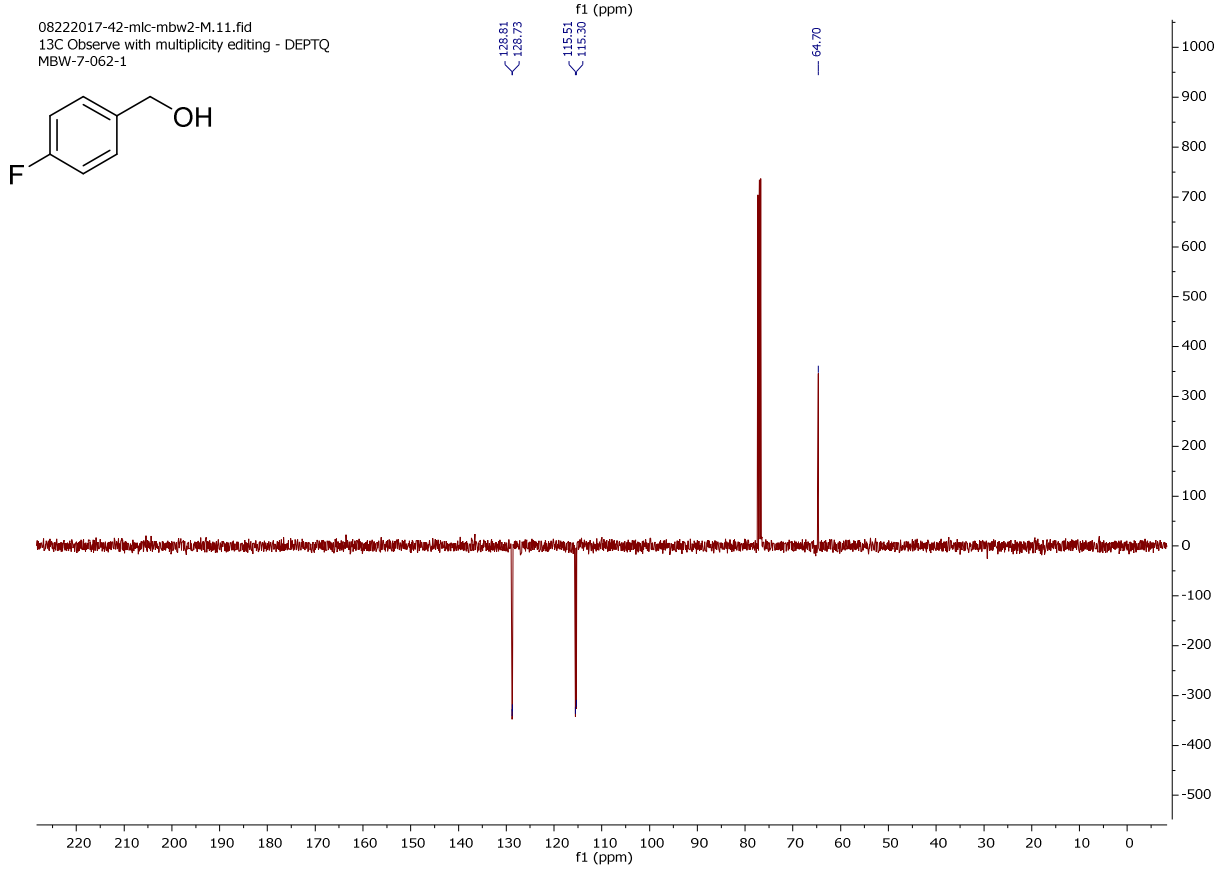
(*S*)-Ethyl 1,2,3,4-tetrahydronaphthalene-1-carboxylate 9l

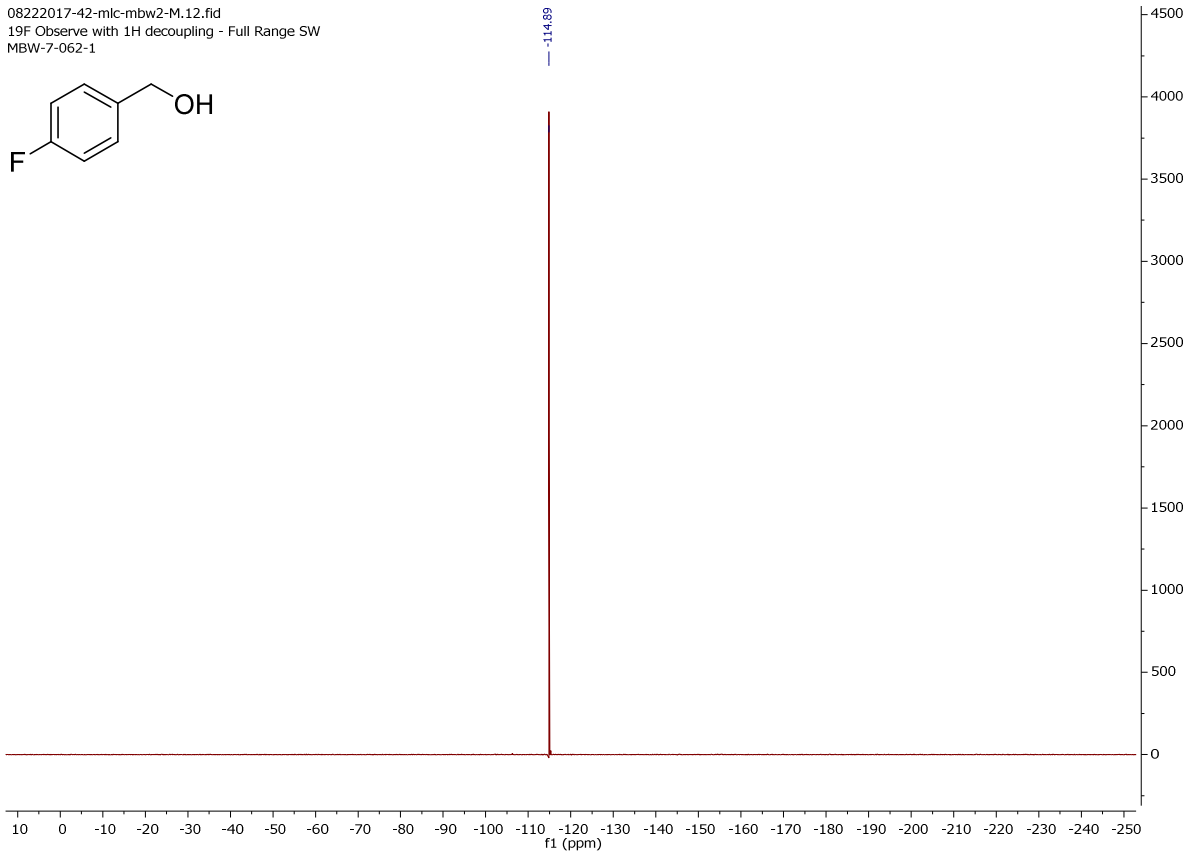




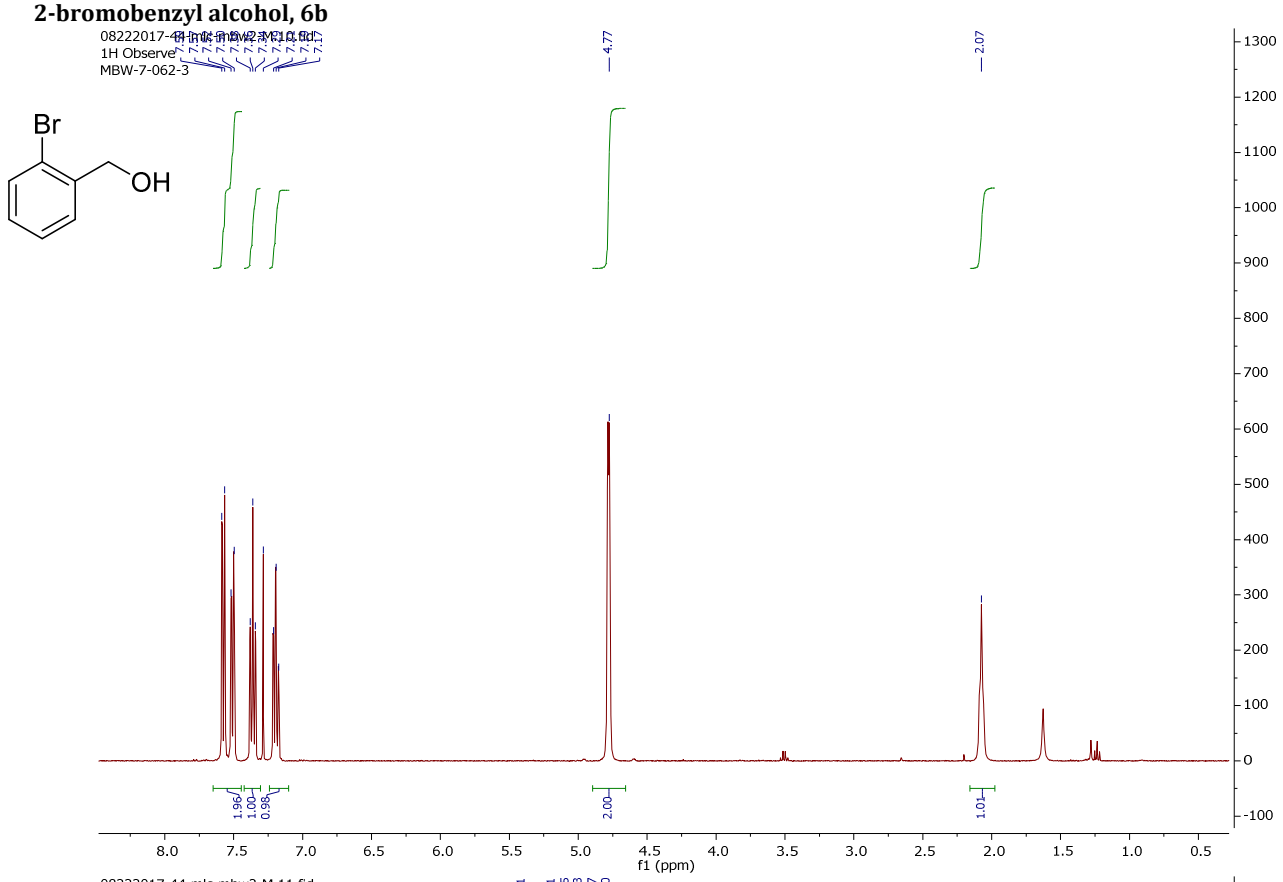
4-fluorobenzyl alcohol, 6a

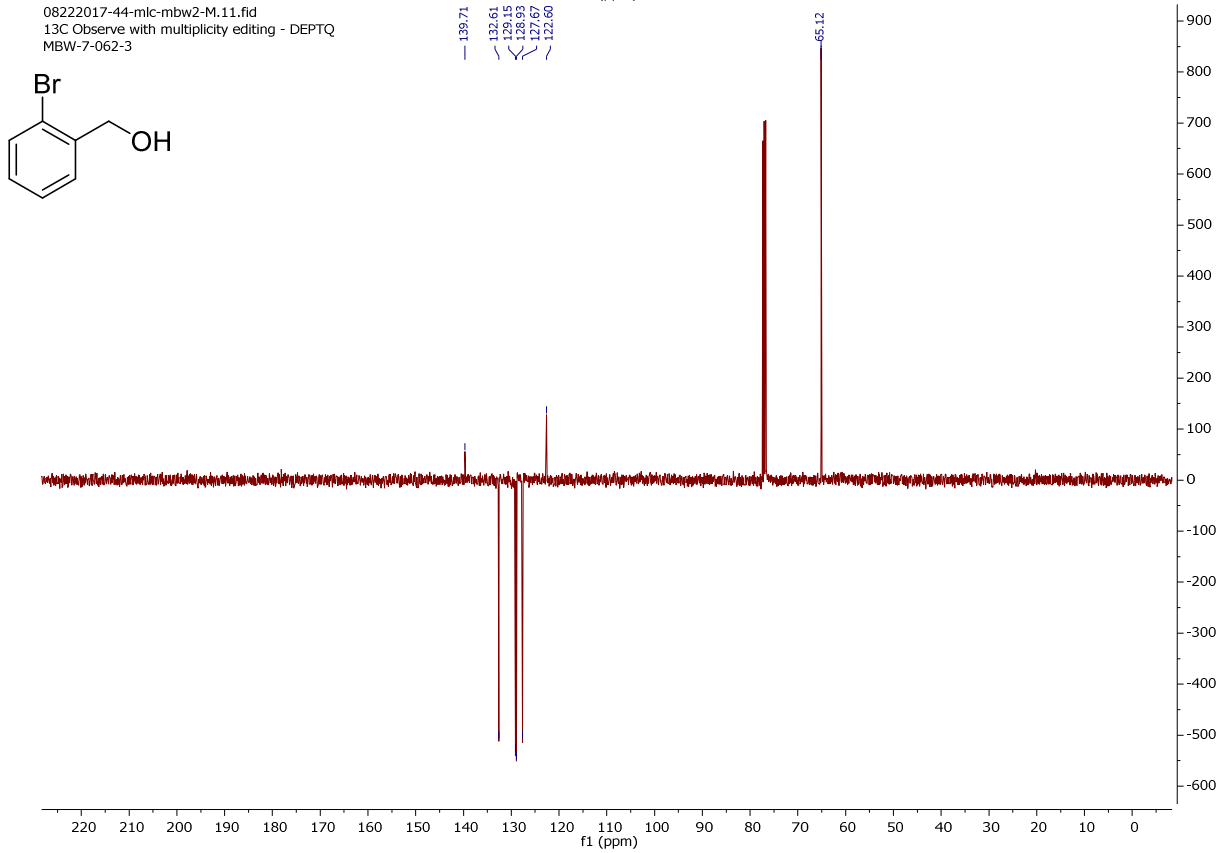




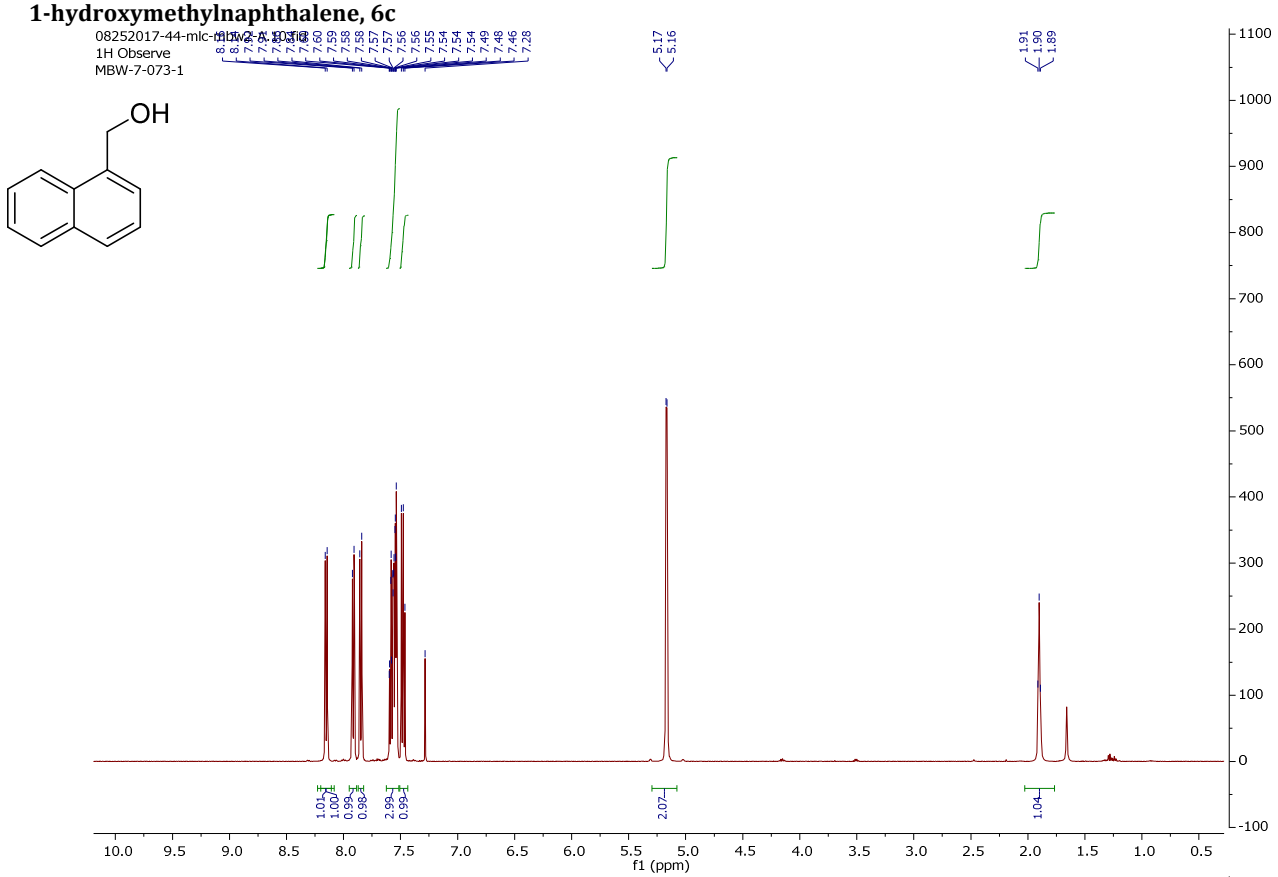

08222017-42-mlc-mbw2-M.12.fid
19F Observe with 1H decoupling - Full Range SW
MBW-7-062-1
-114.89
OH
F
4500
4000
3500
3000
2500
2000
1500
1000
500
0
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240 -250
f1 (ppm)

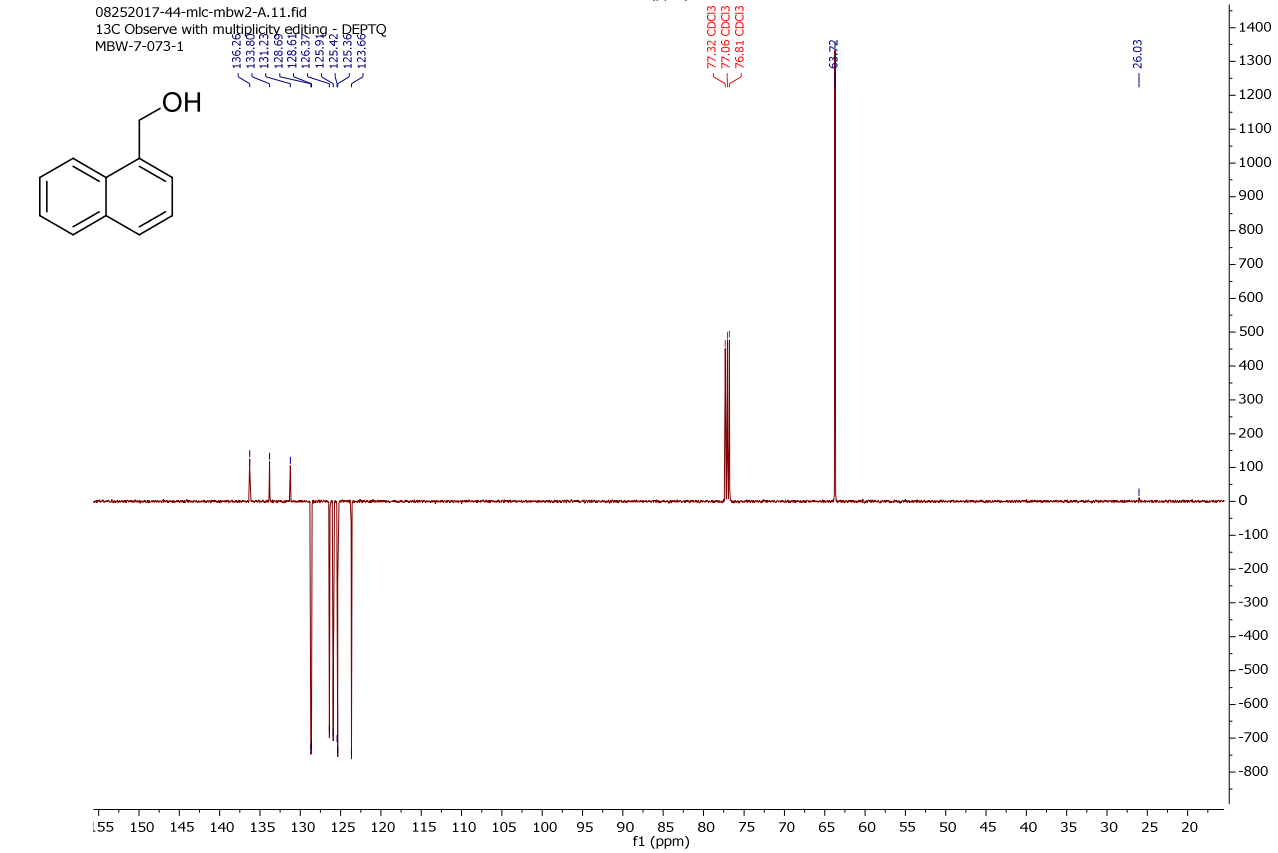
2-bromobenzyl alcohol, 6b



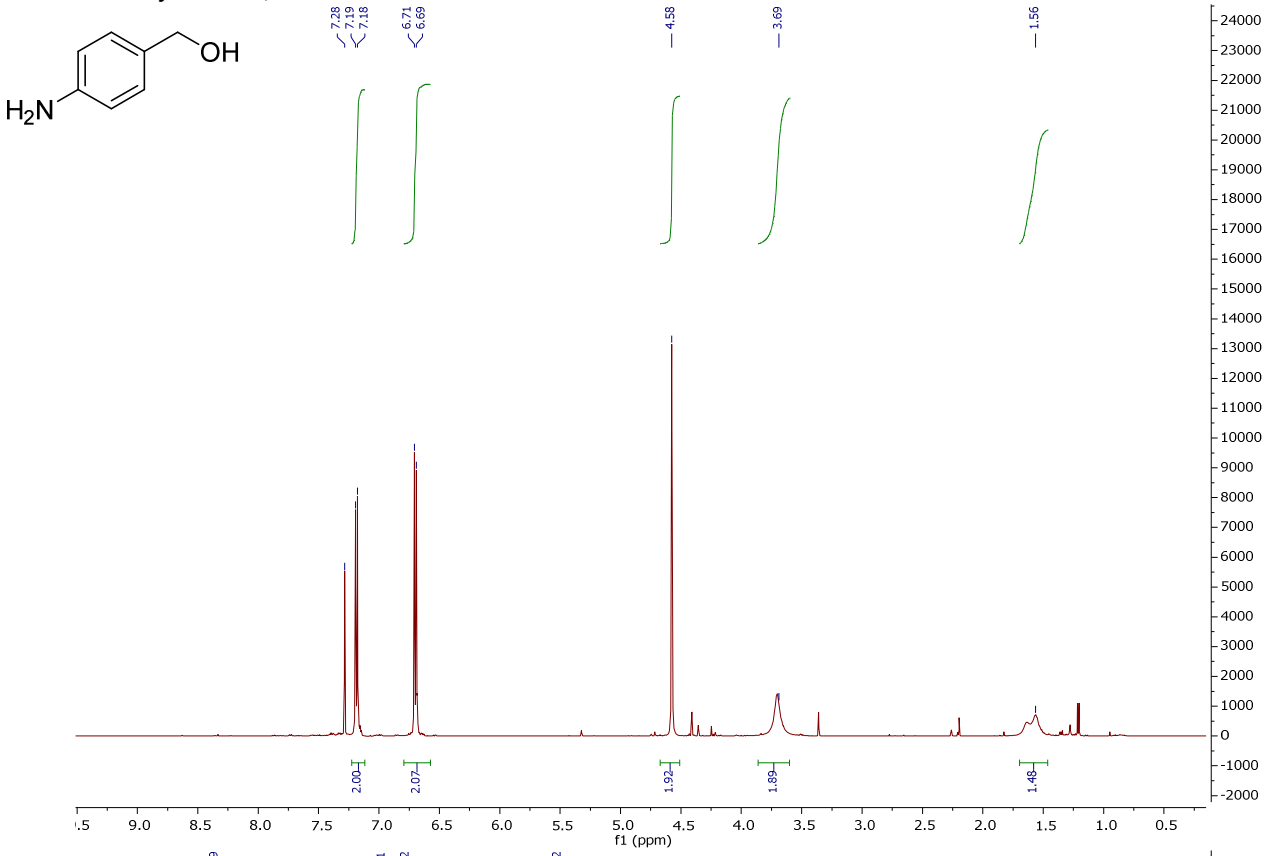


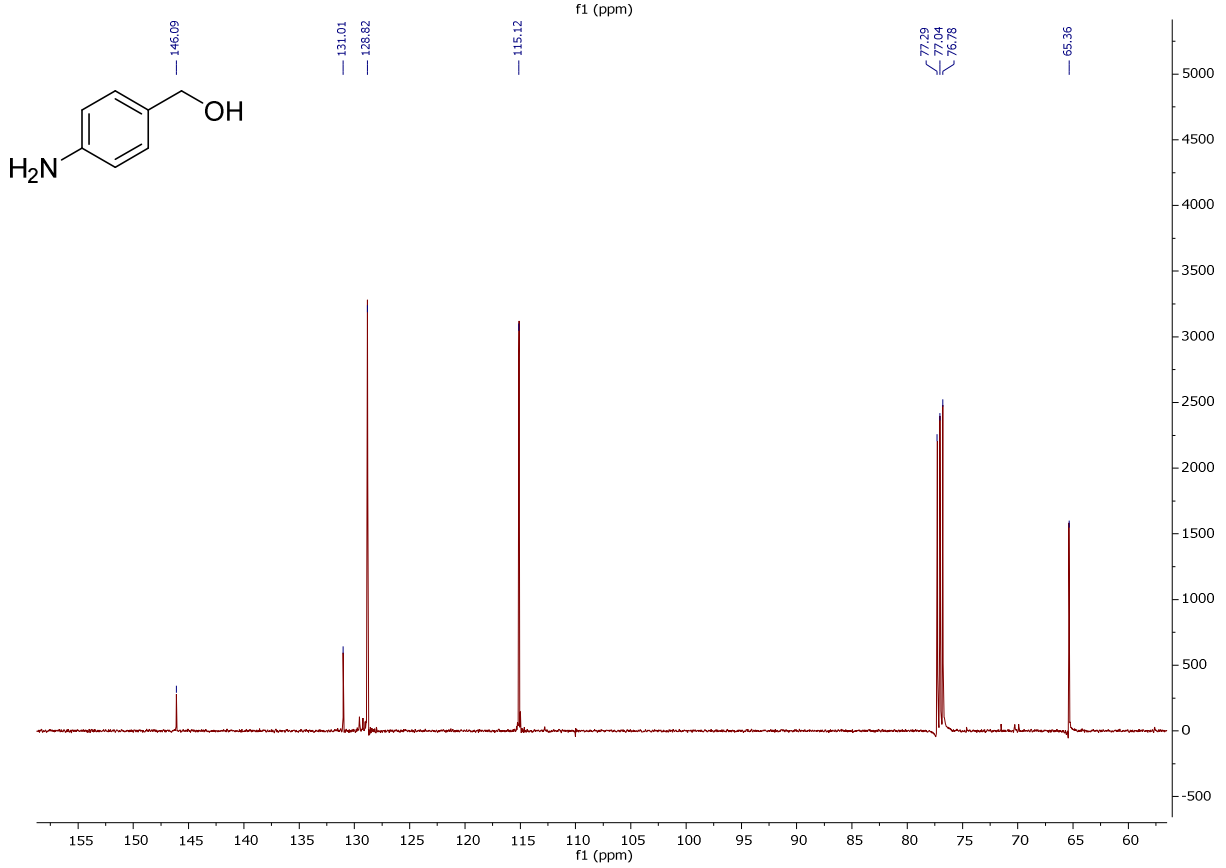
1-hydroxymethylnaphthalene, 6c



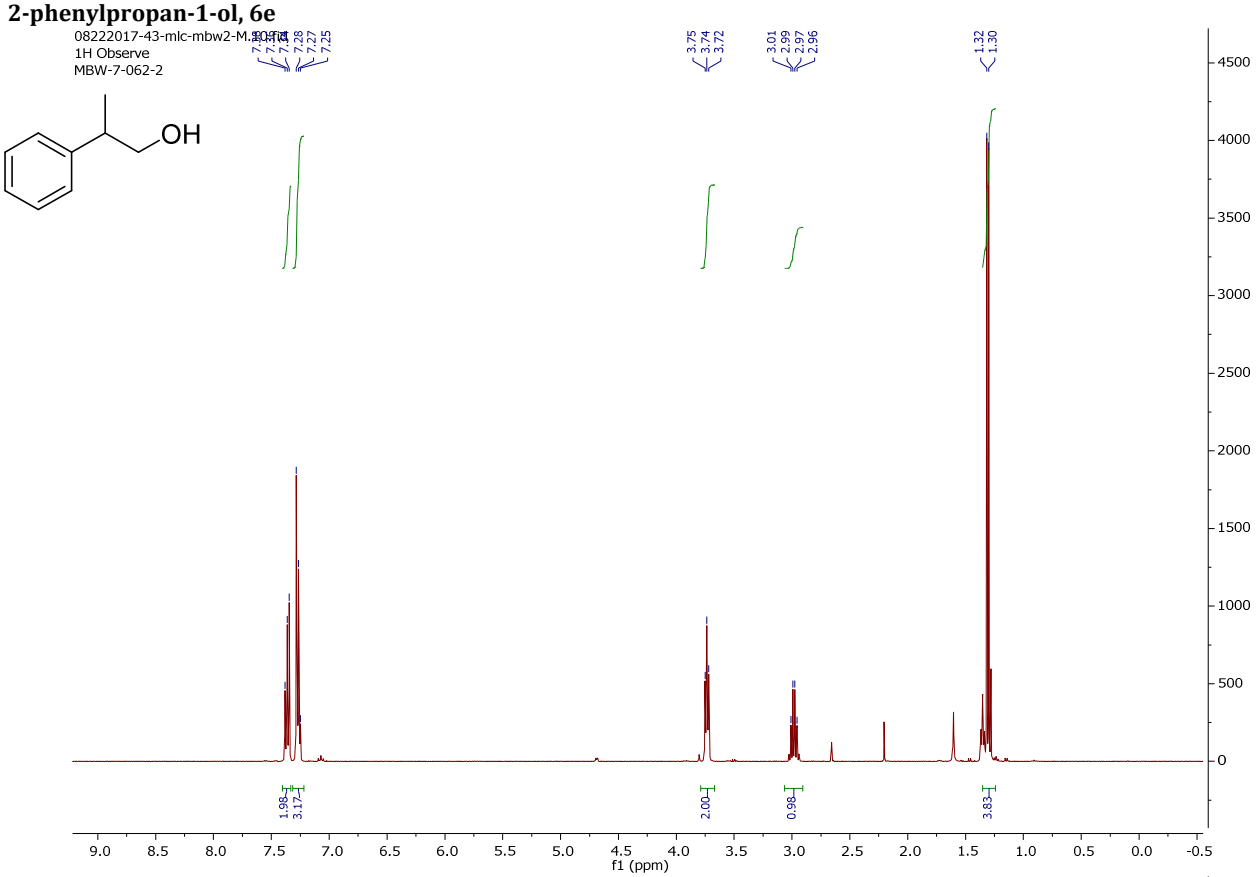


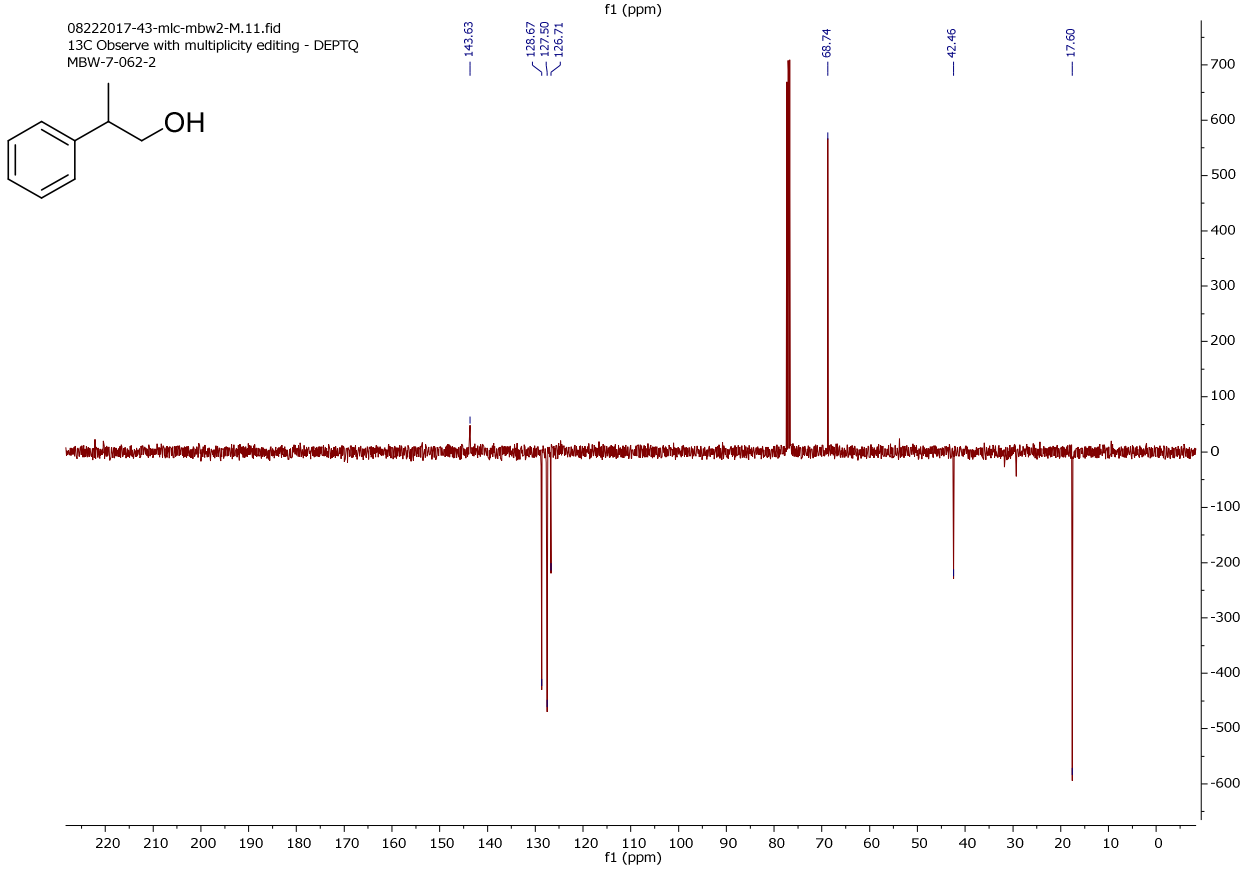
4-Aminobenzyl alcohol, 6d



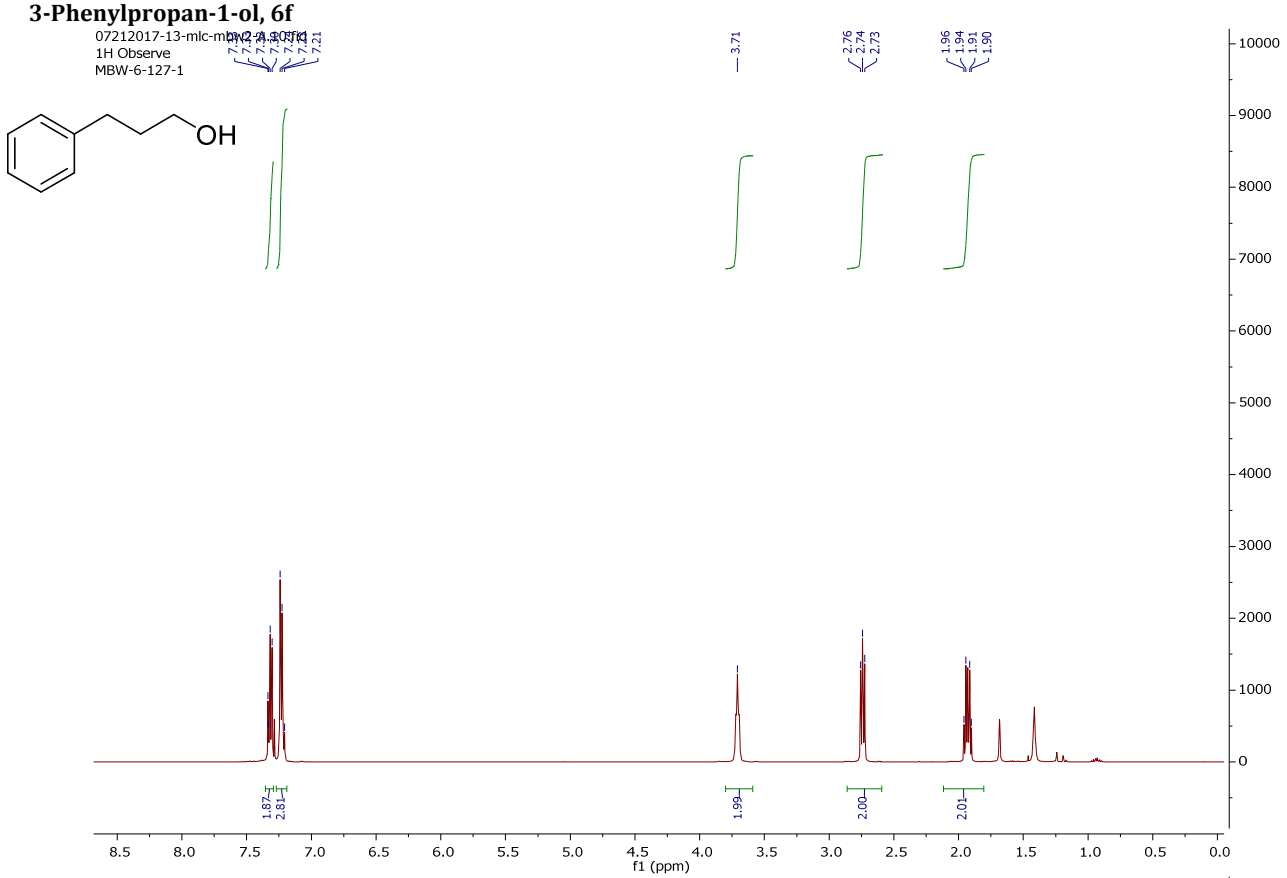


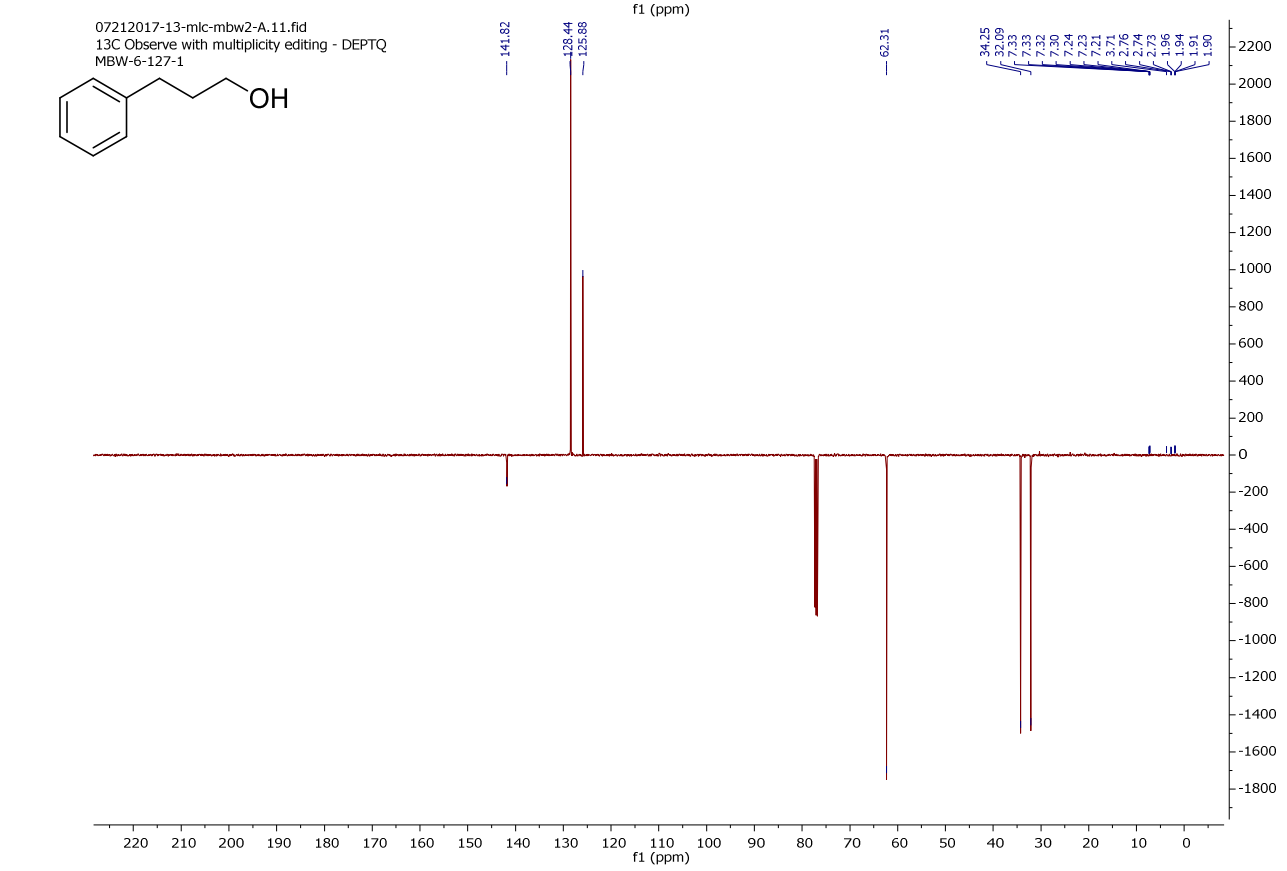
2-phenylpropan-1-ol, 6e



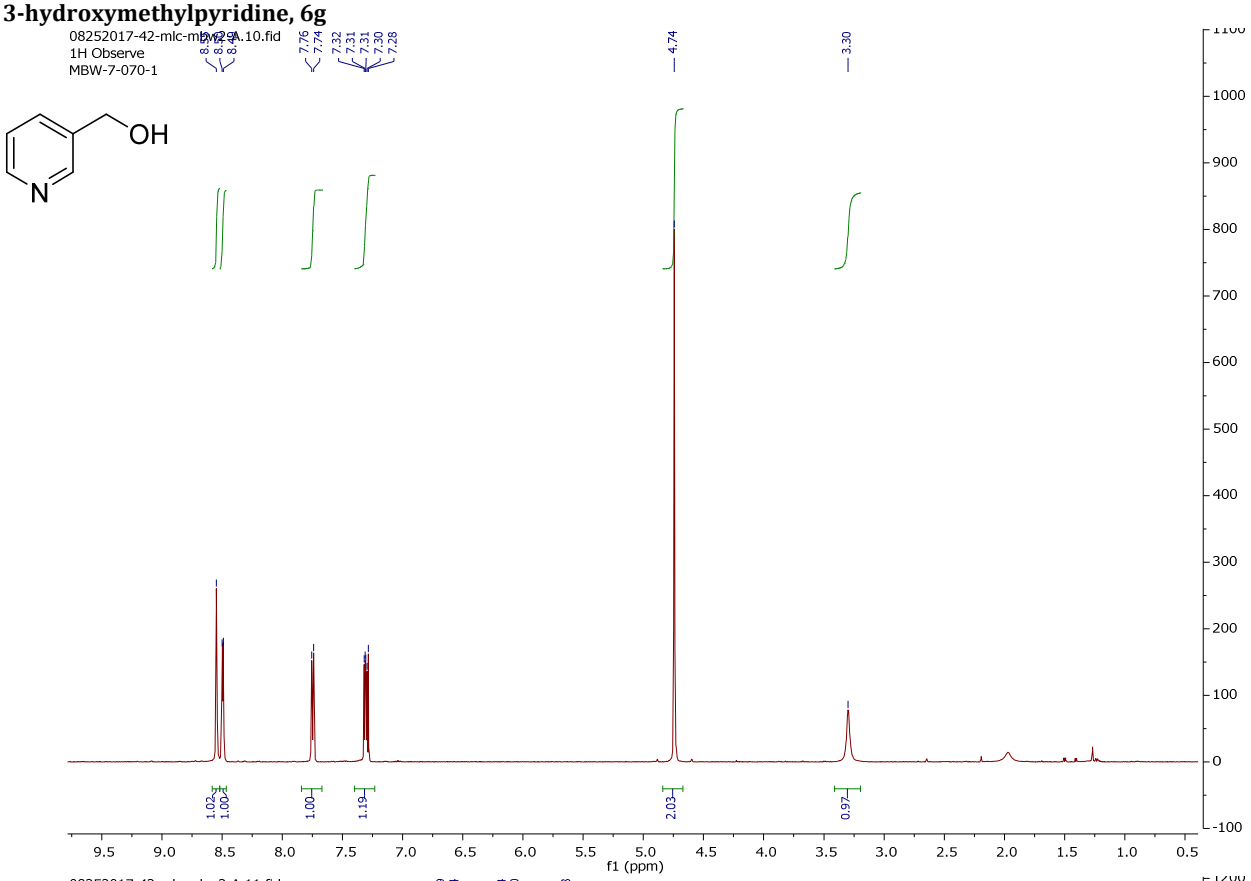


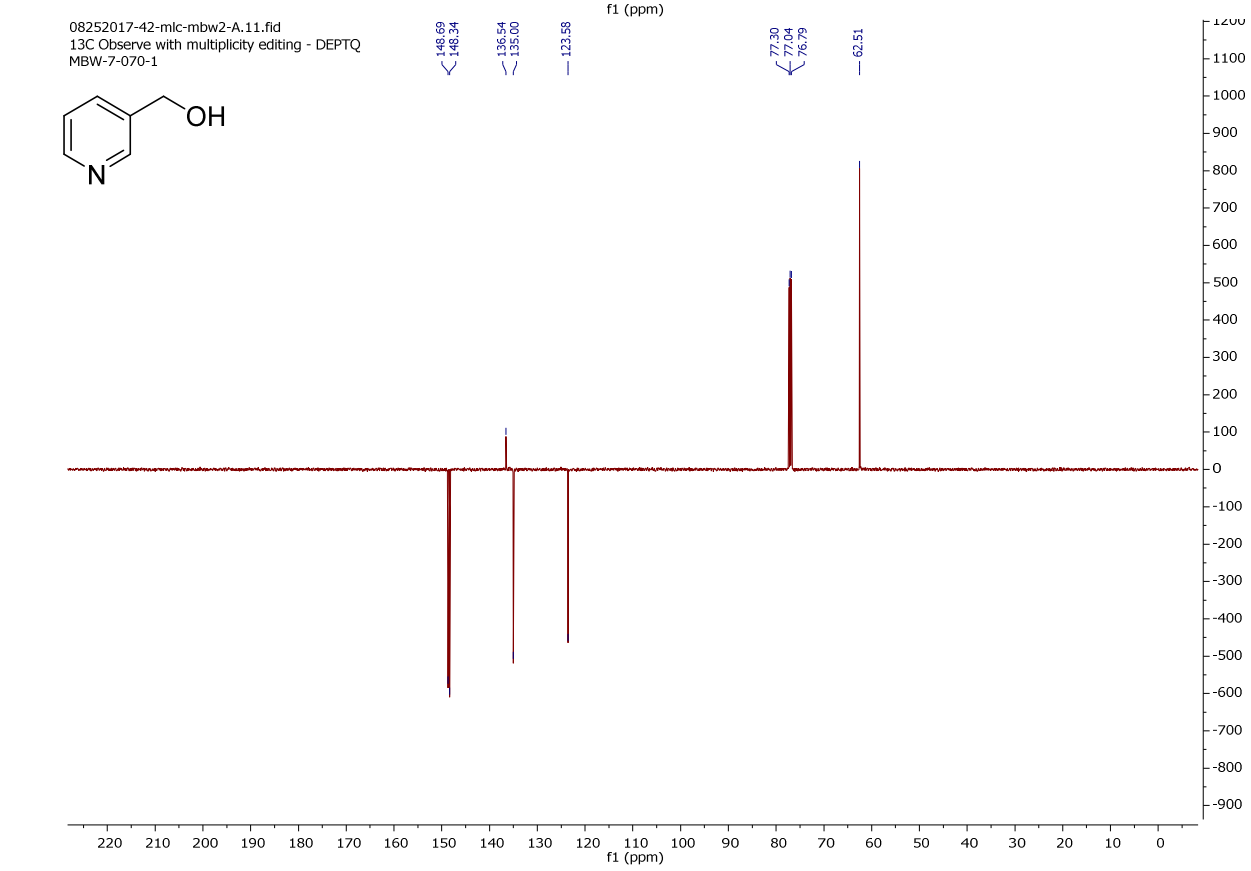
3-Phenylpropan-1-ol, 6f



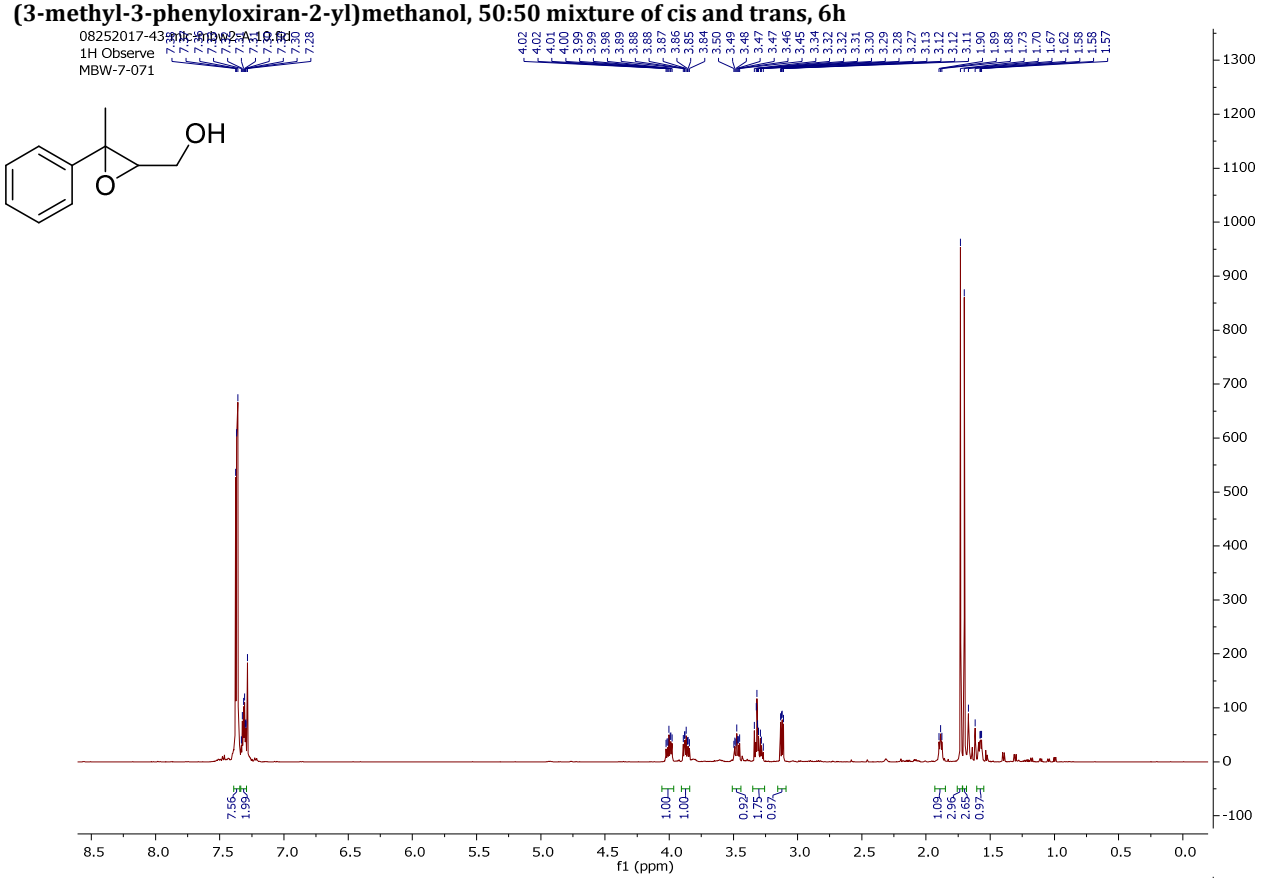


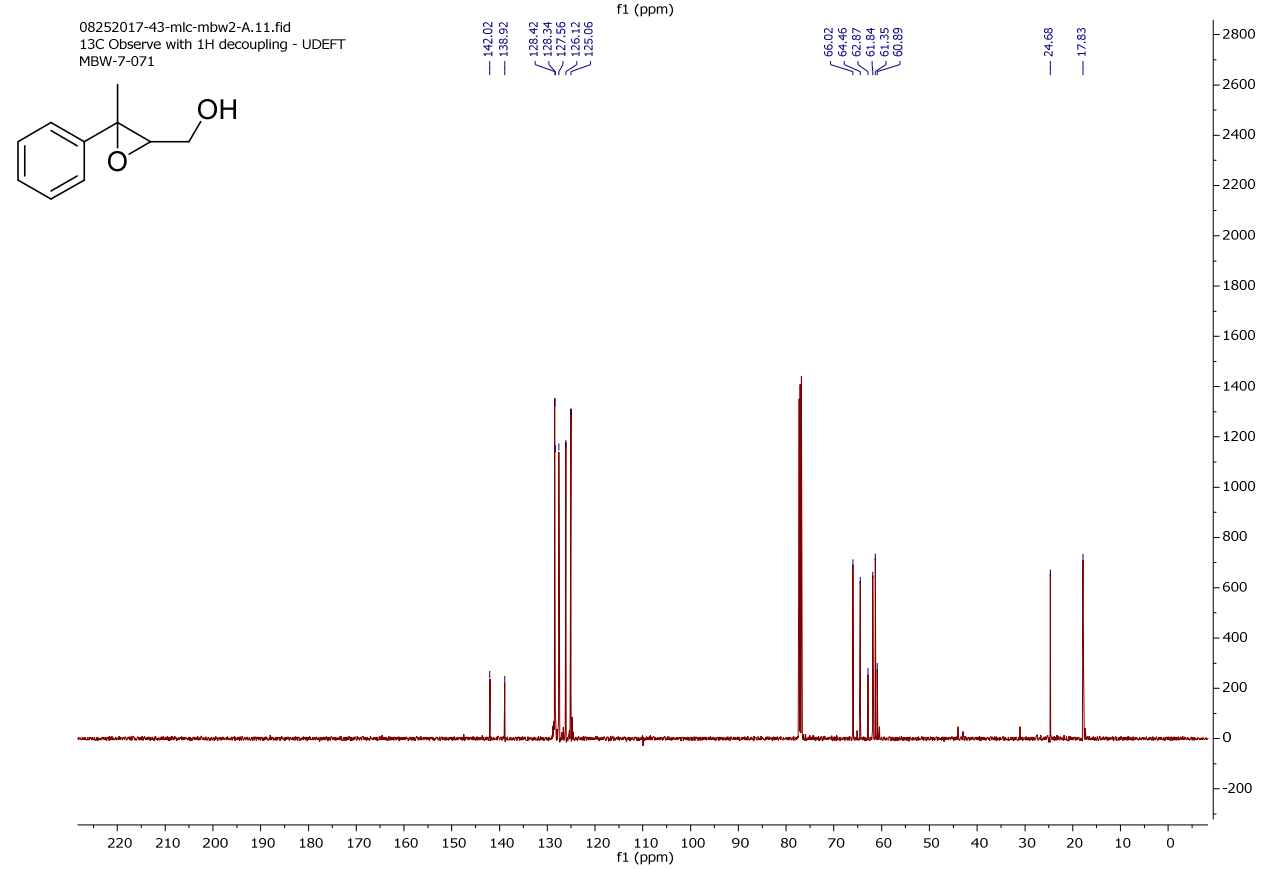
3-hydroxymethylpyridine, 6g



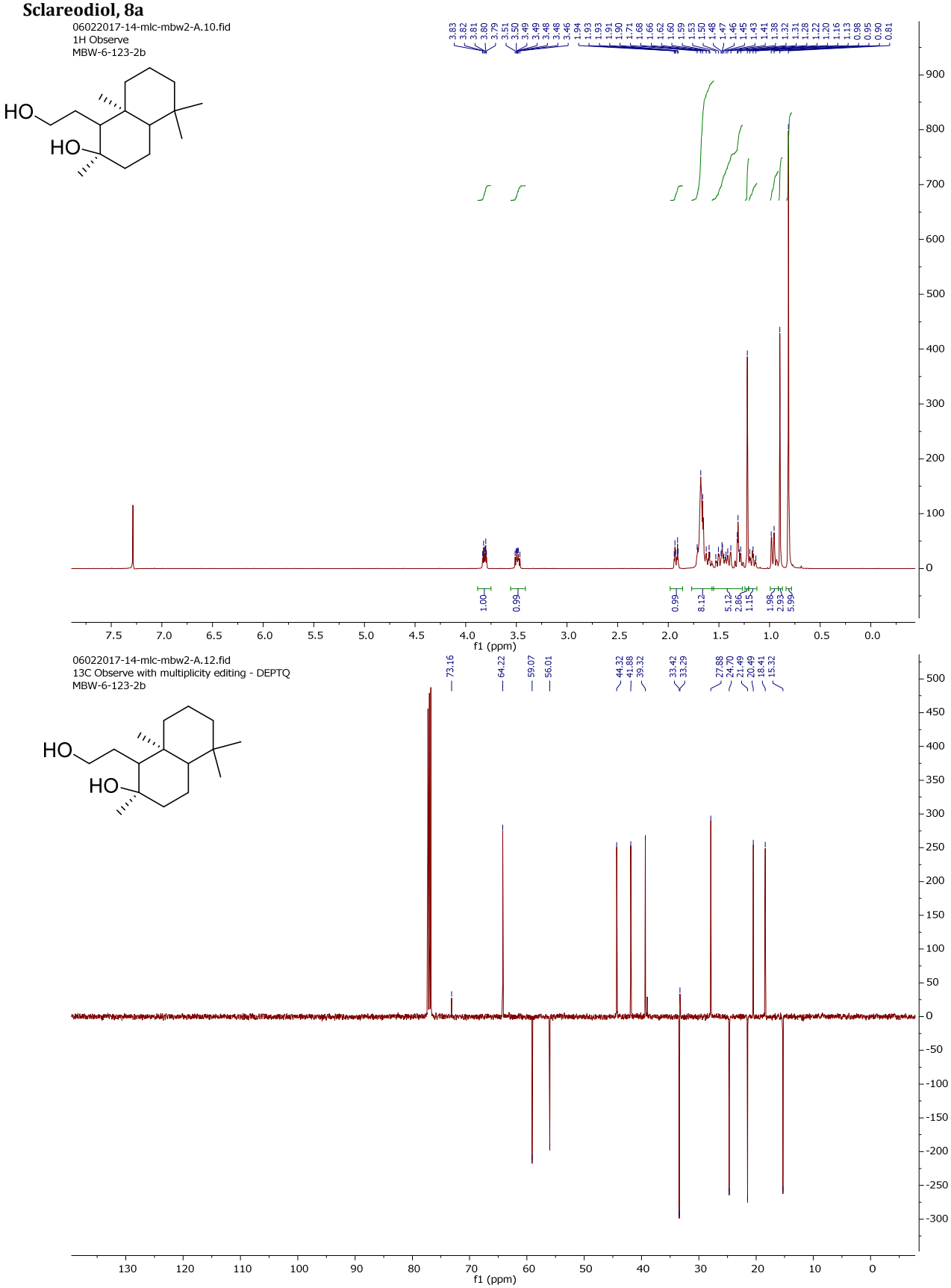


(3-methyl-3-phenyloxiran-2-yl)methanol, 50:50 mixture of cis and trans, 6h

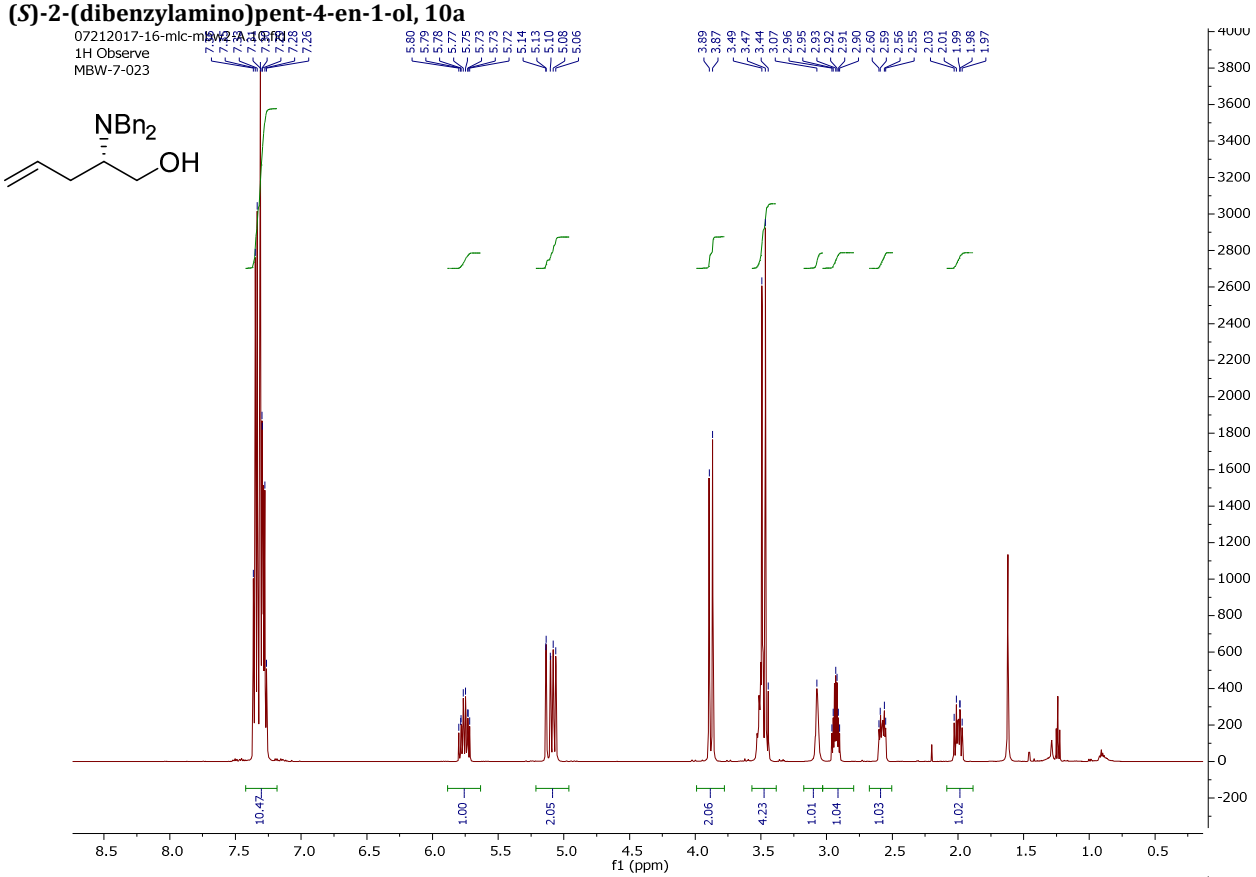


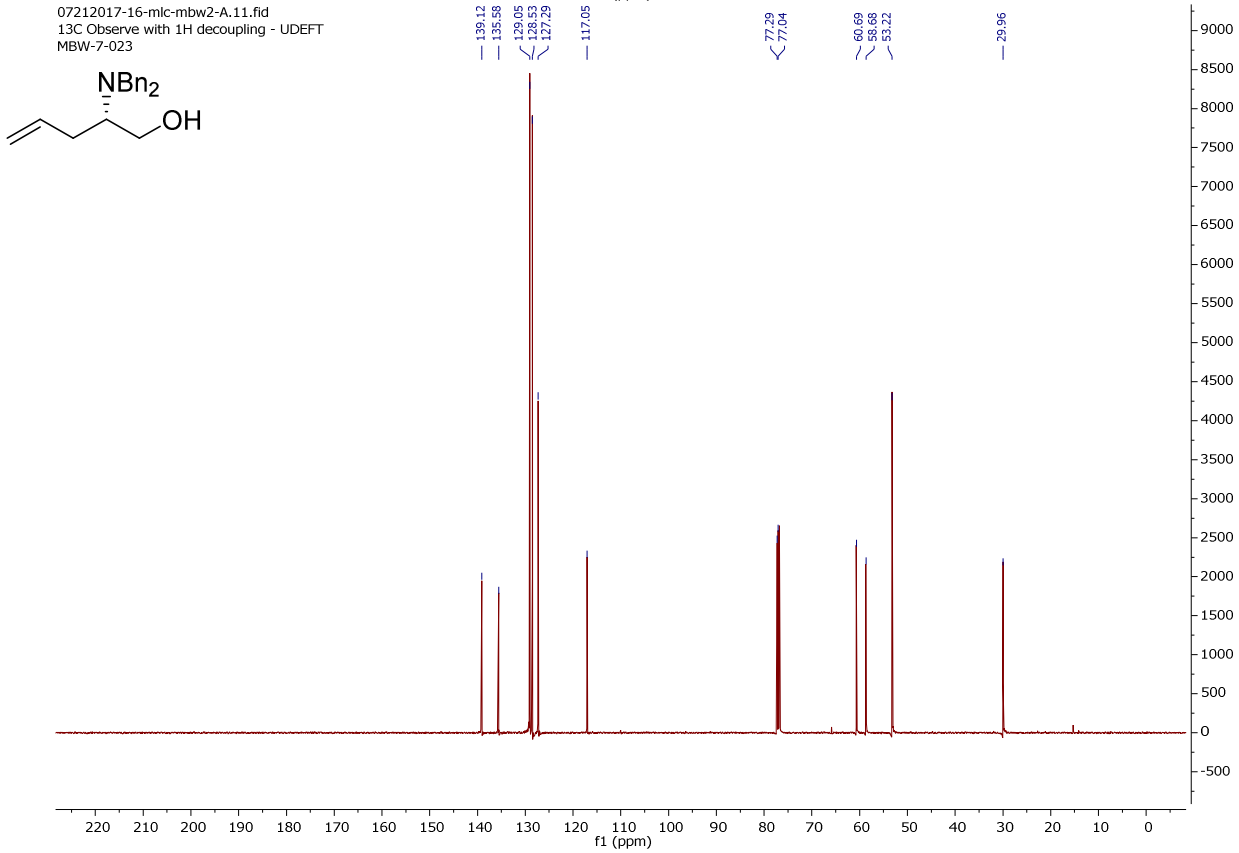


Sclareodiol, 8a

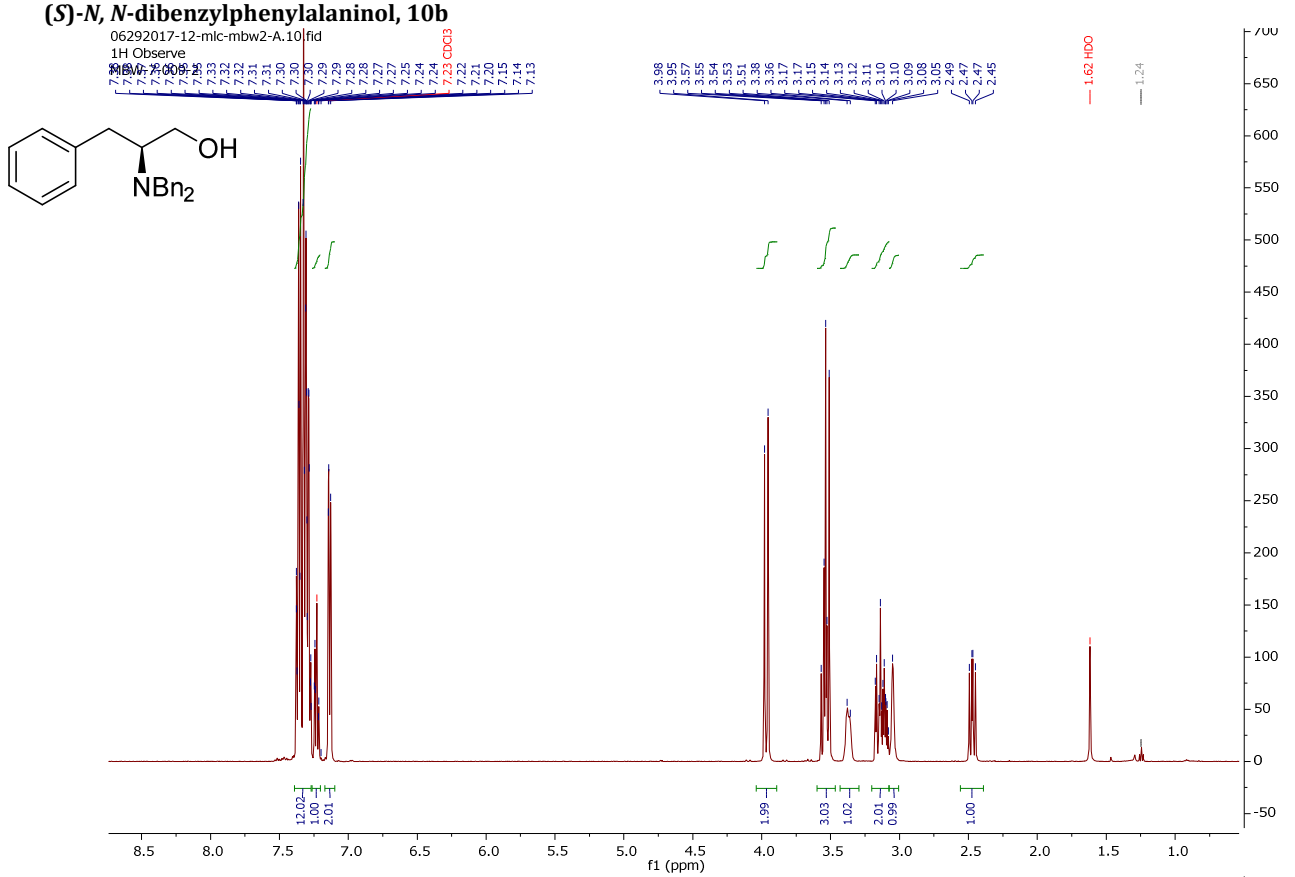


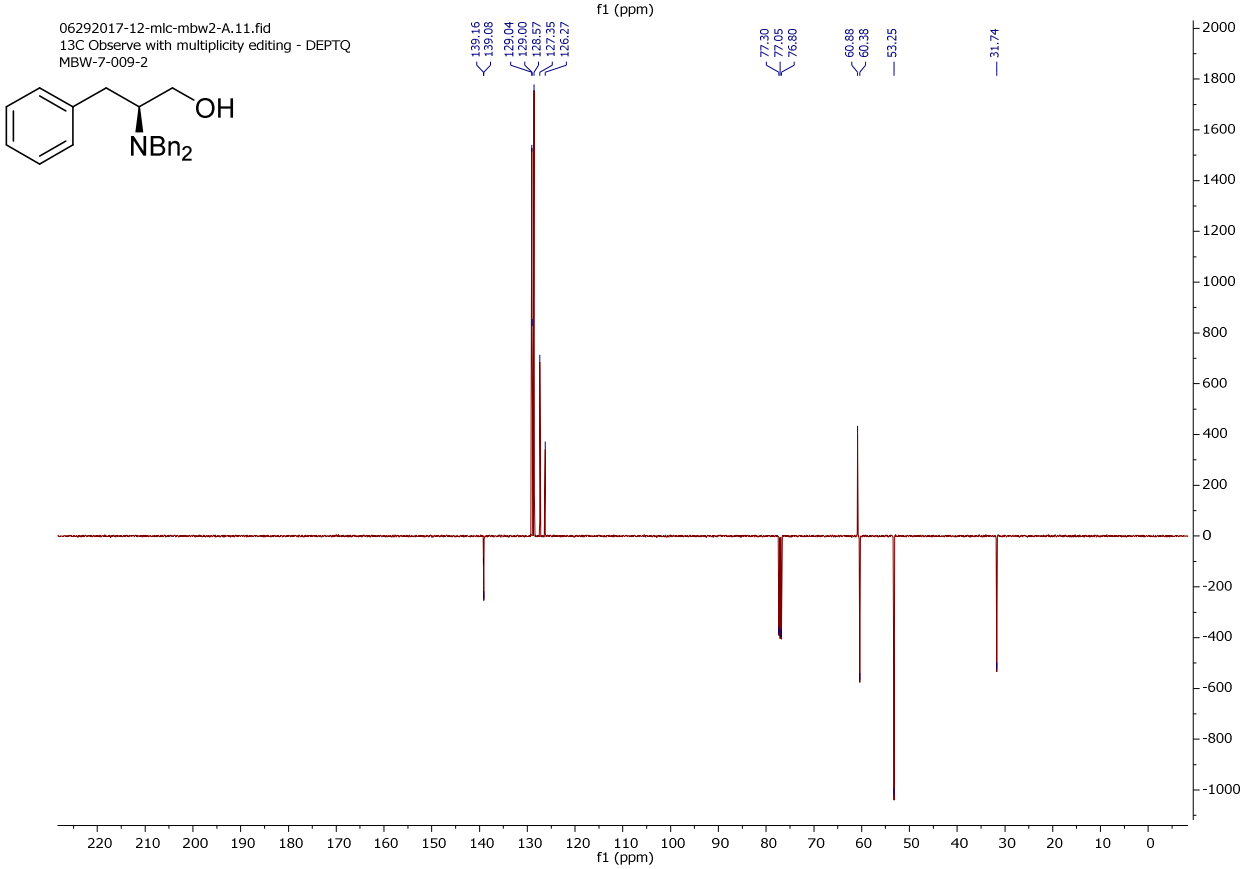
(*S*)-2-(dibenzylamino)pent-4-en-1-ol, 10a



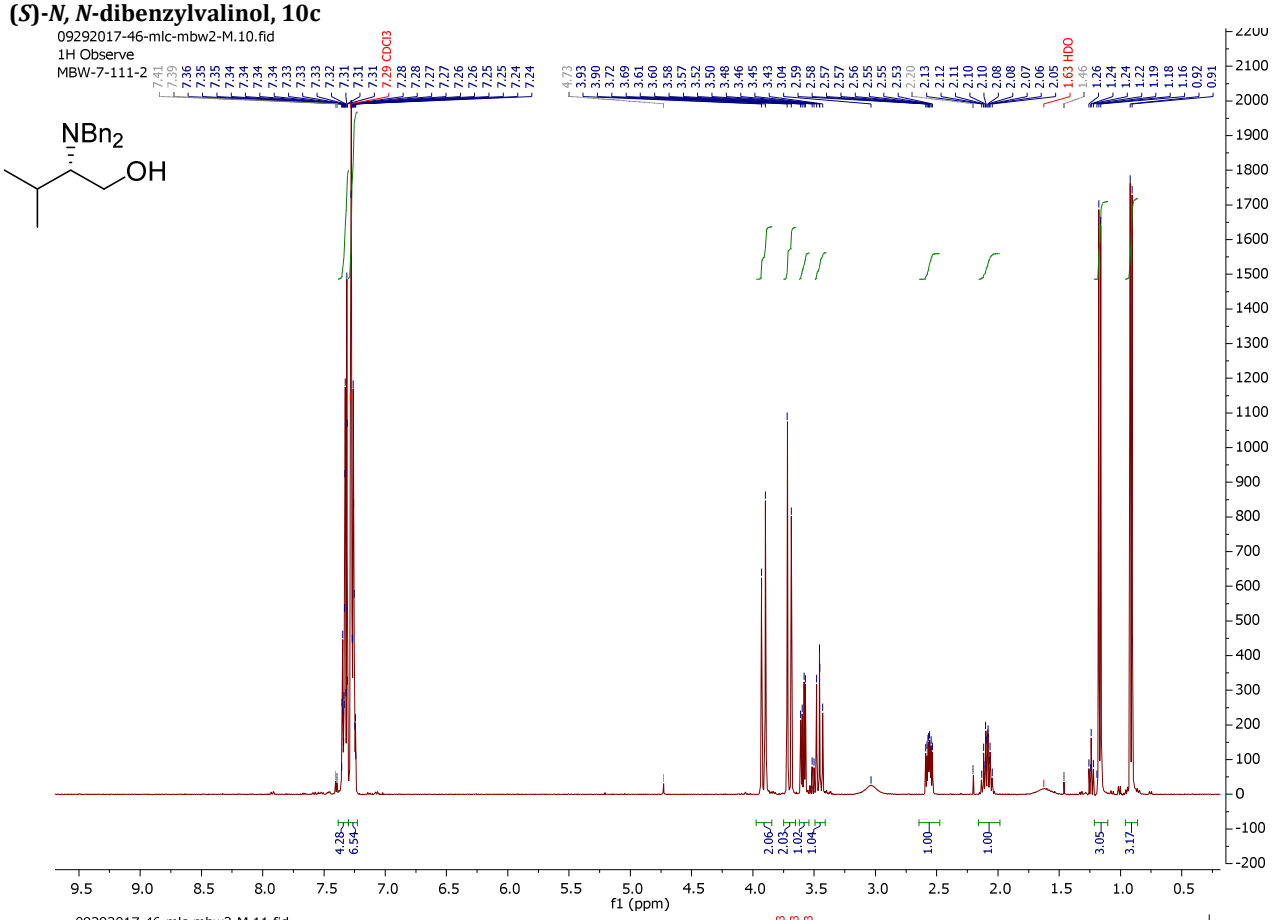


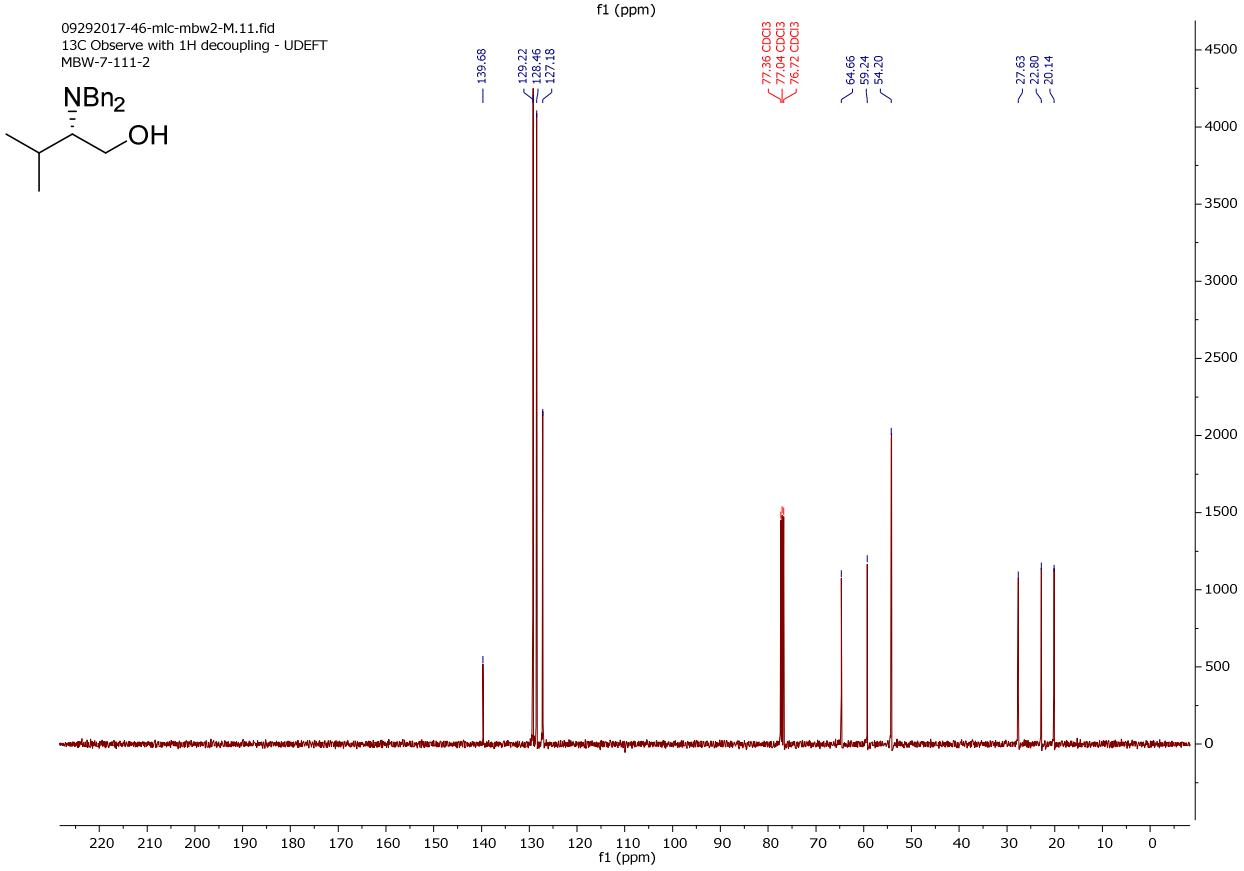
(*S*)-*N*, *N*-dibenzylphenylalaninol, 10b



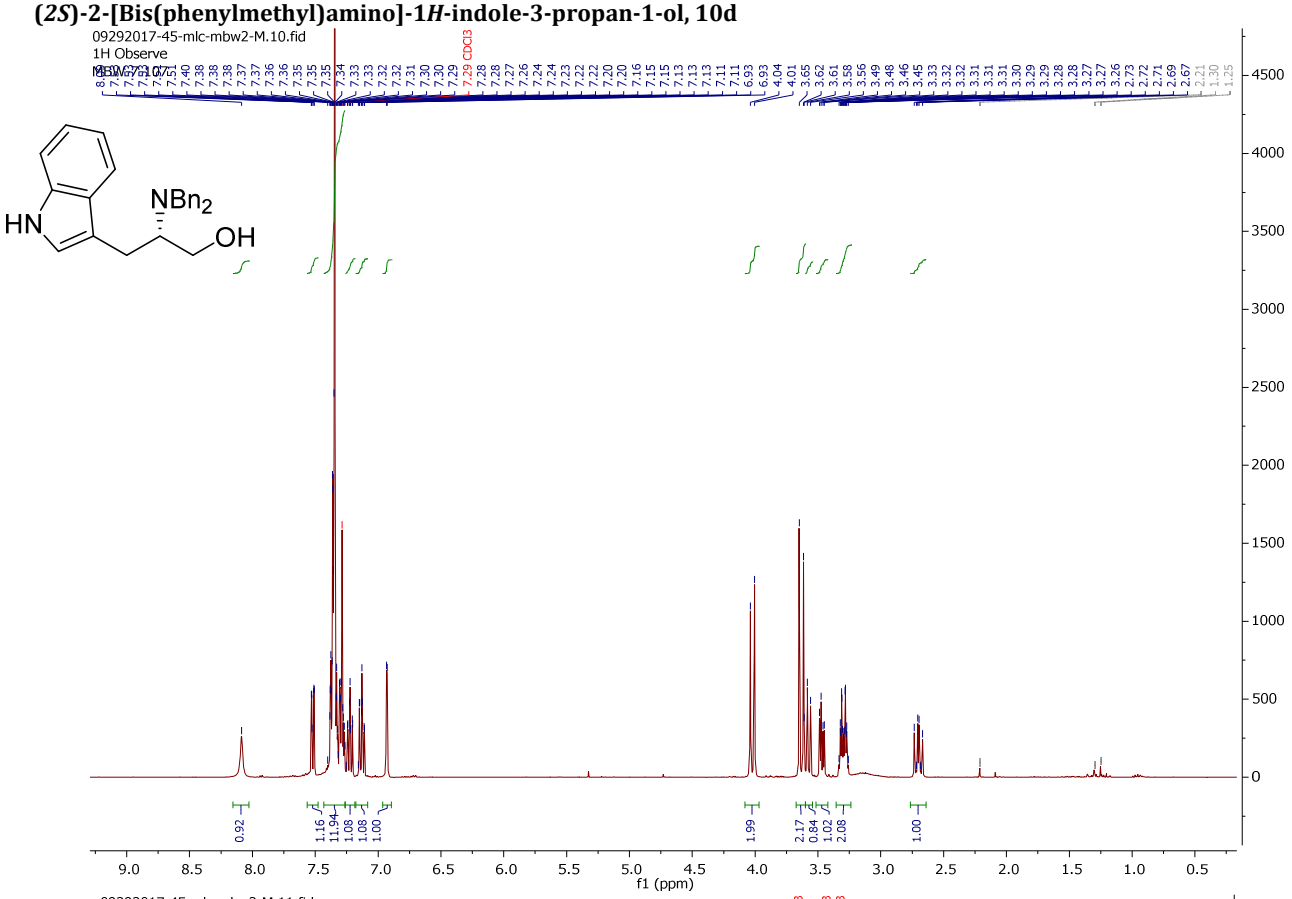


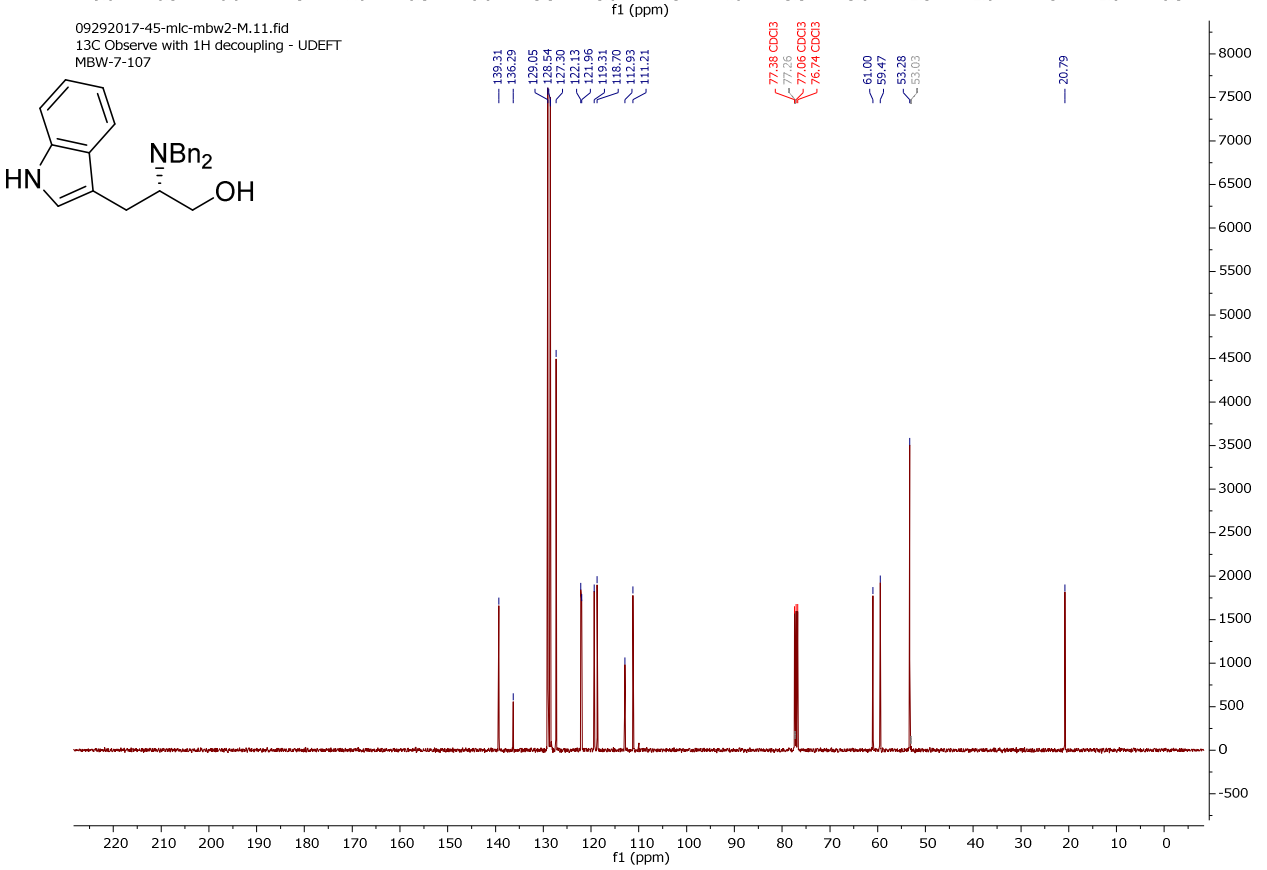
(*S*)-*N*, *N*-dibenzylvalinol, 10c



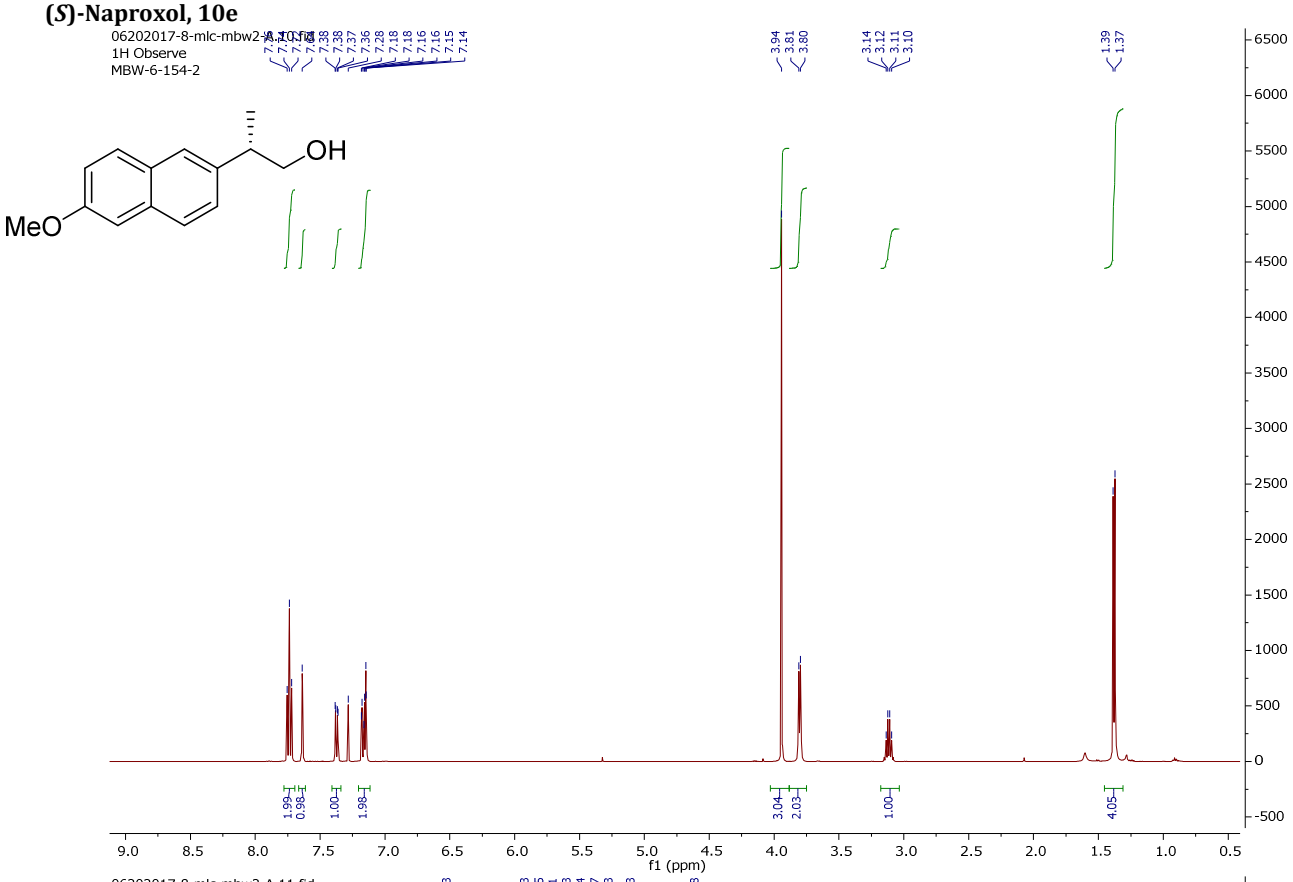


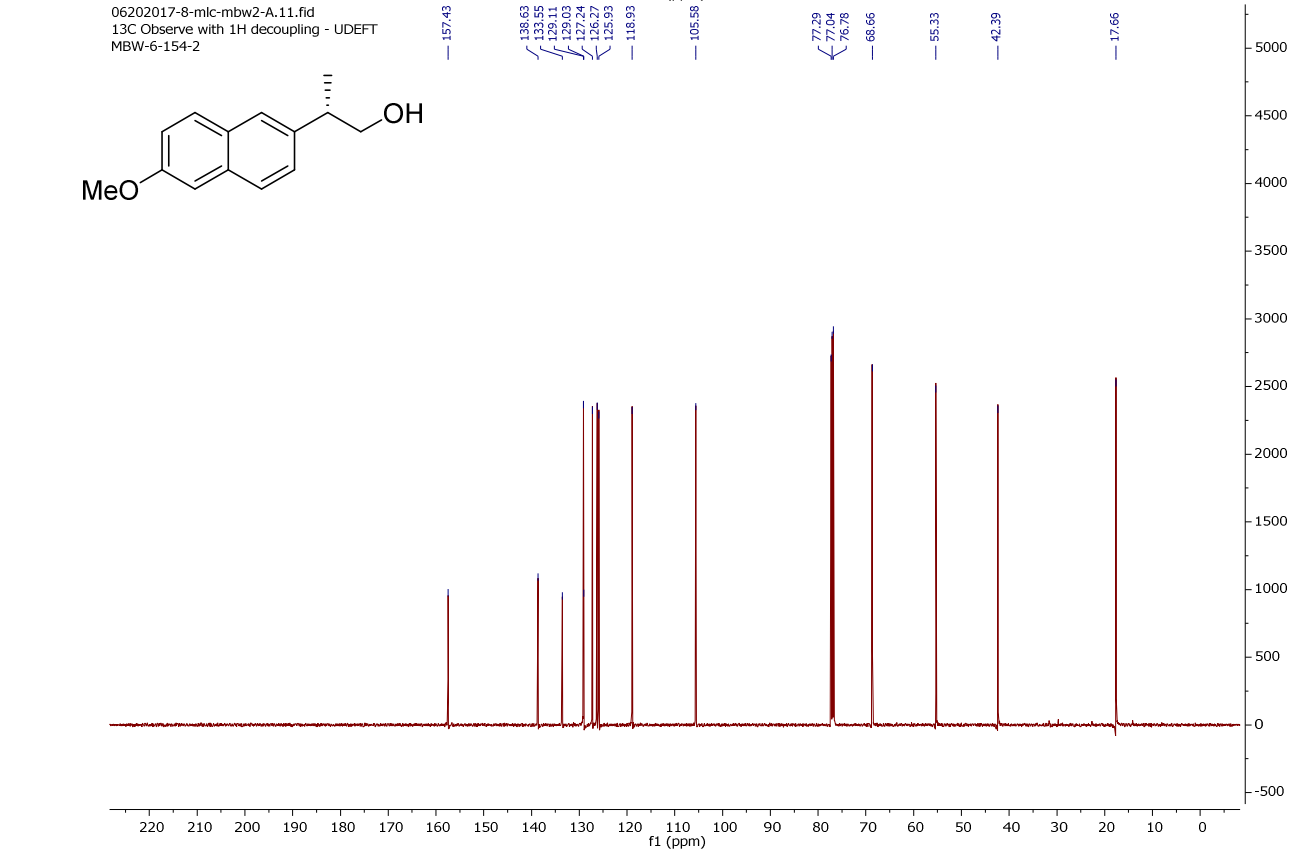
(*2S*)-2-[Bis(phenylmethyl)amino]-1*H*-indole-3-propan-1-ol, 10d



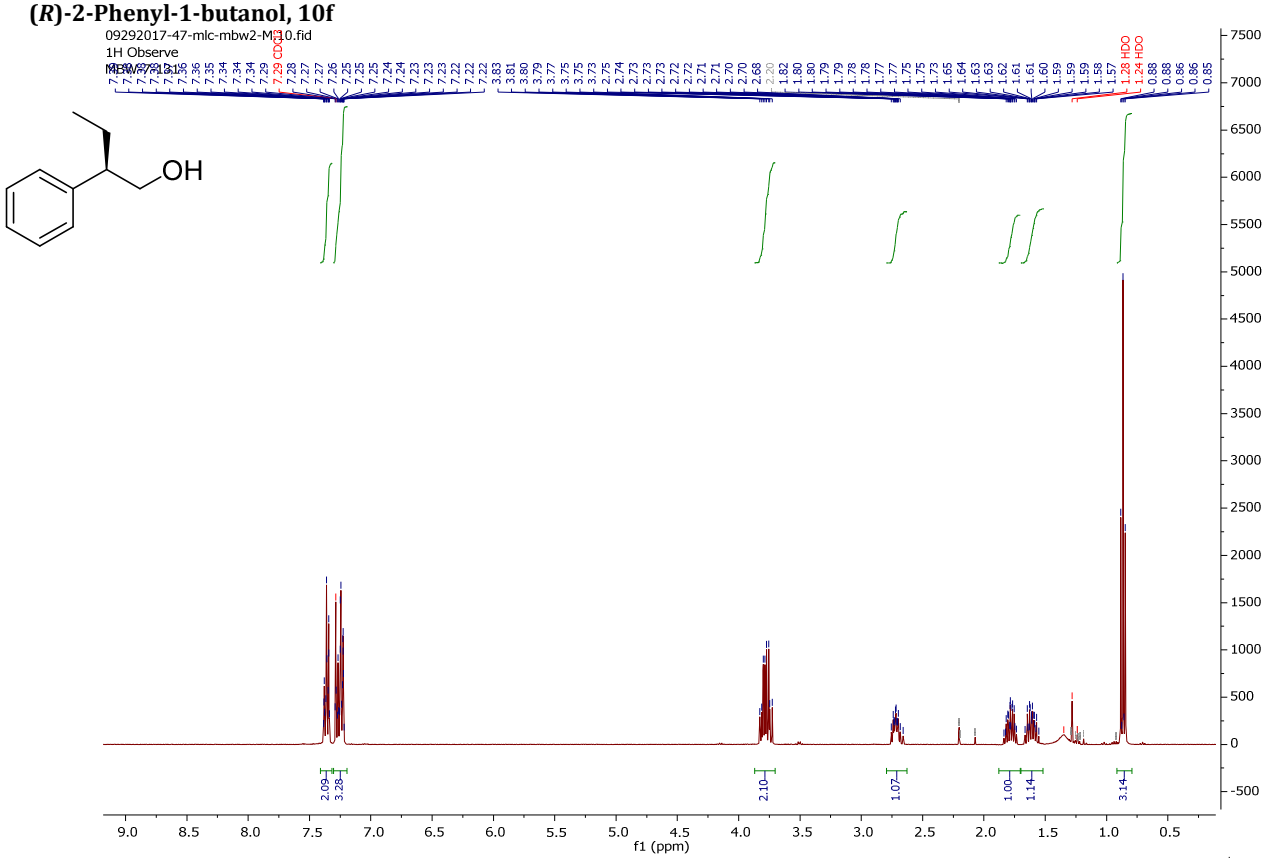


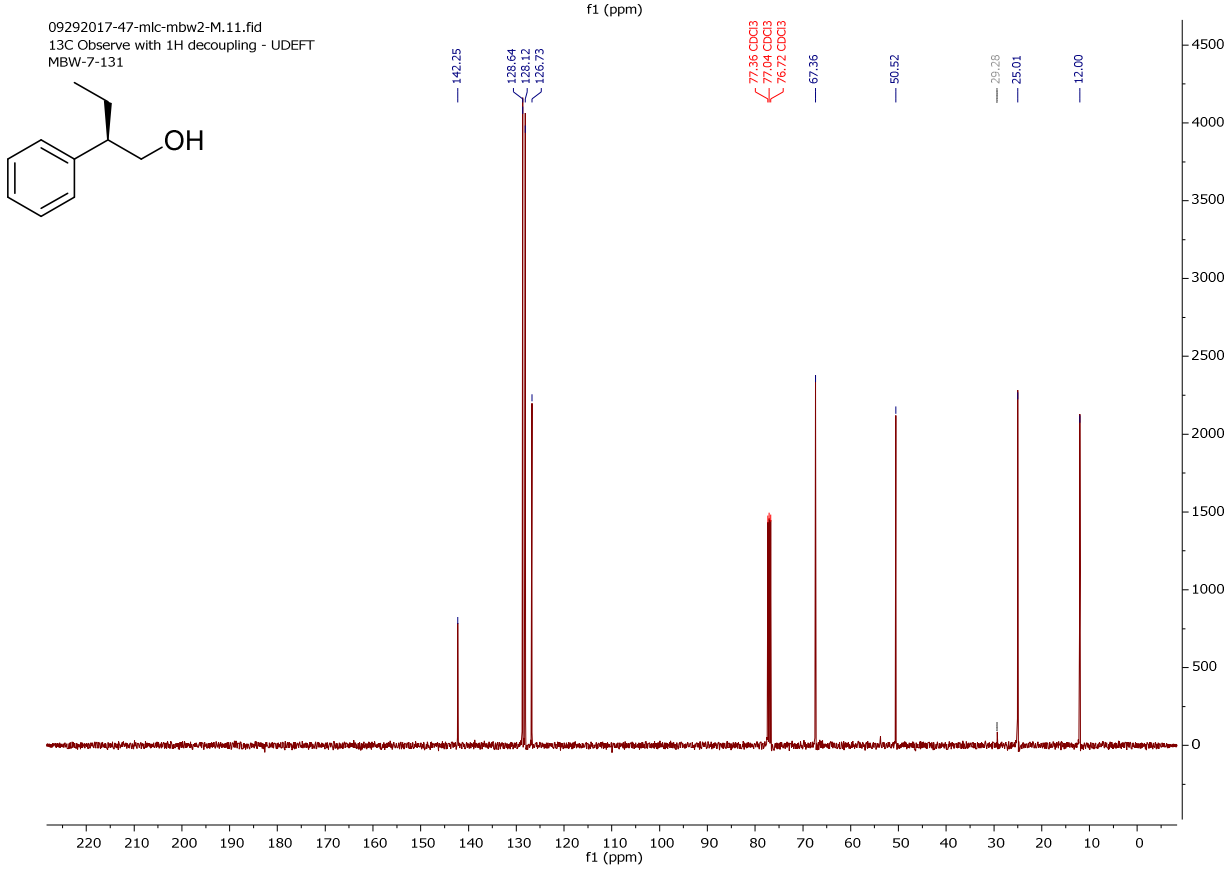
(*S*)-Naproxol, 10e



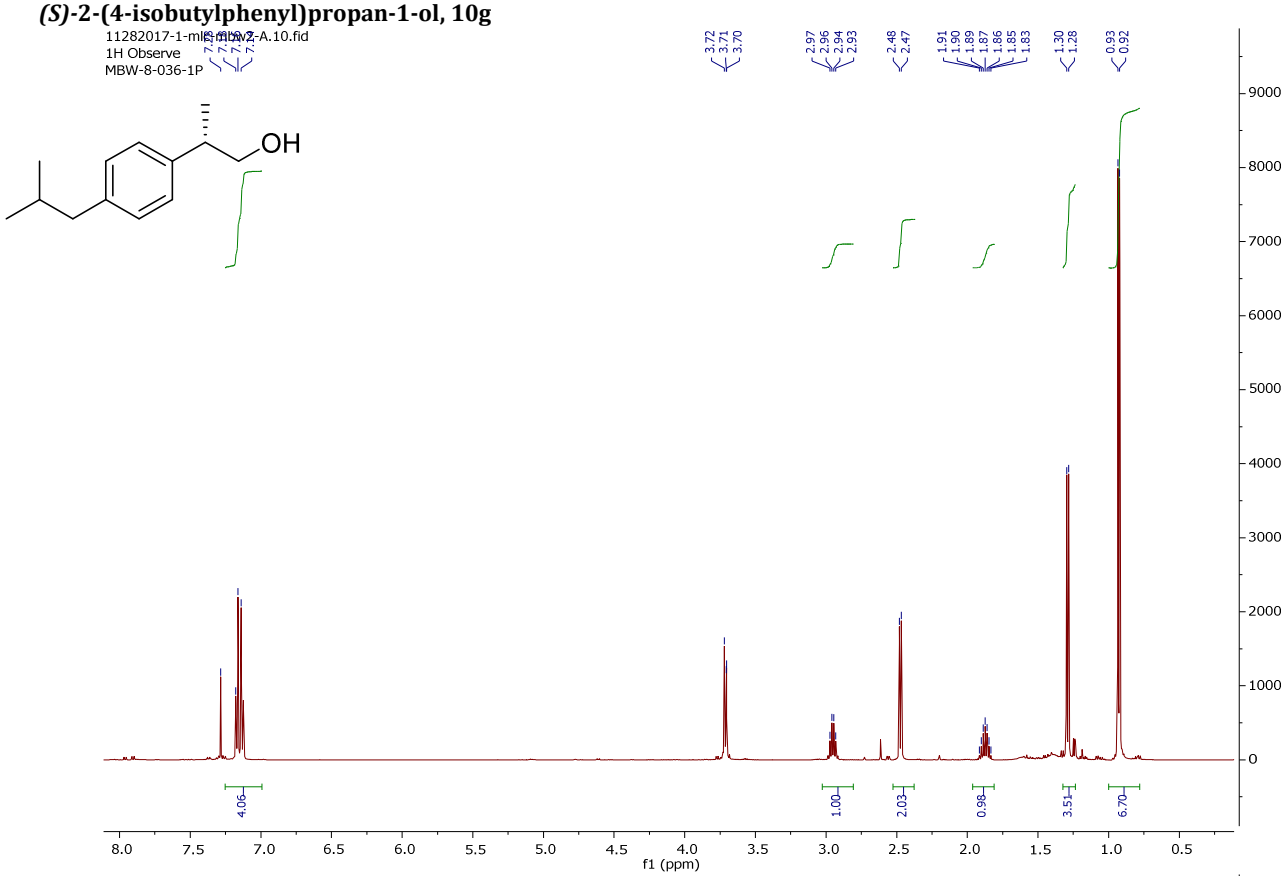


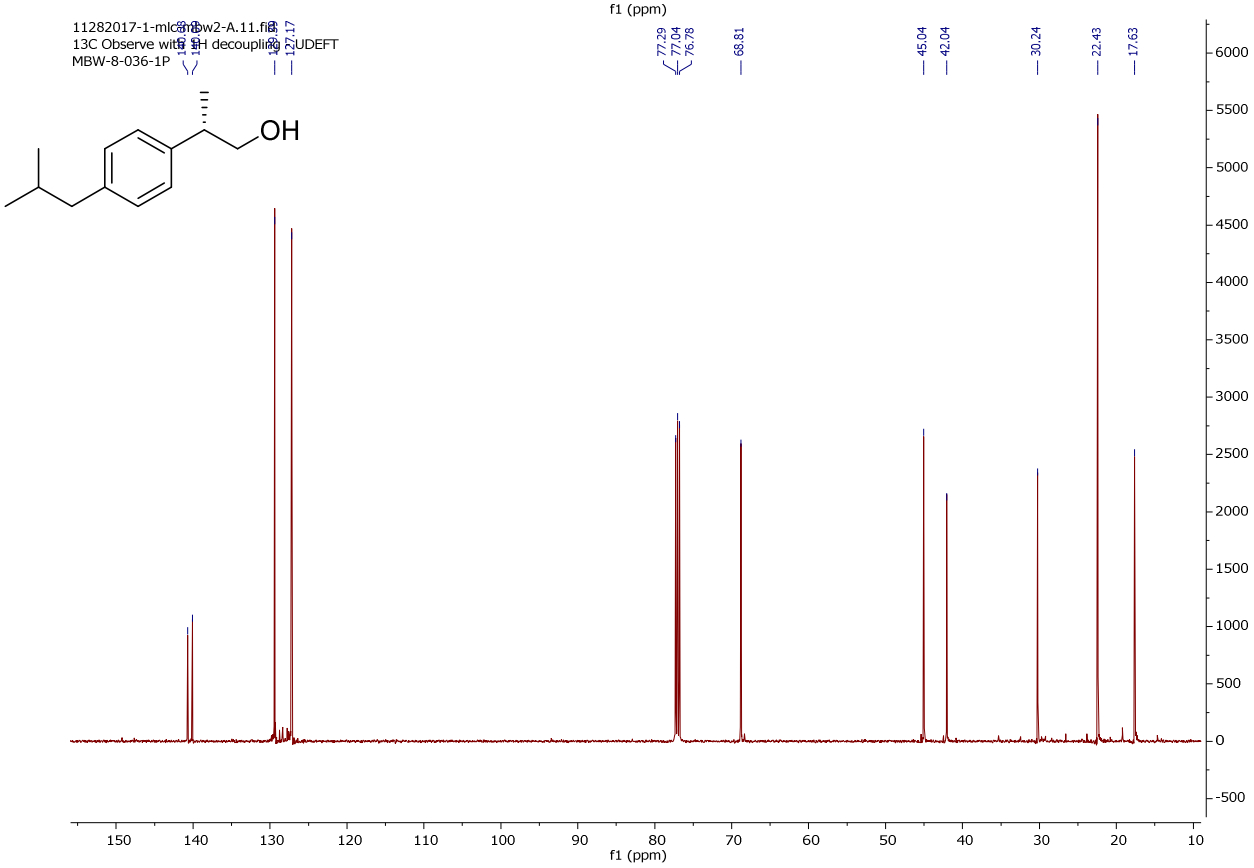
(*R*)-2-Phenyl-1-butanol, 10f



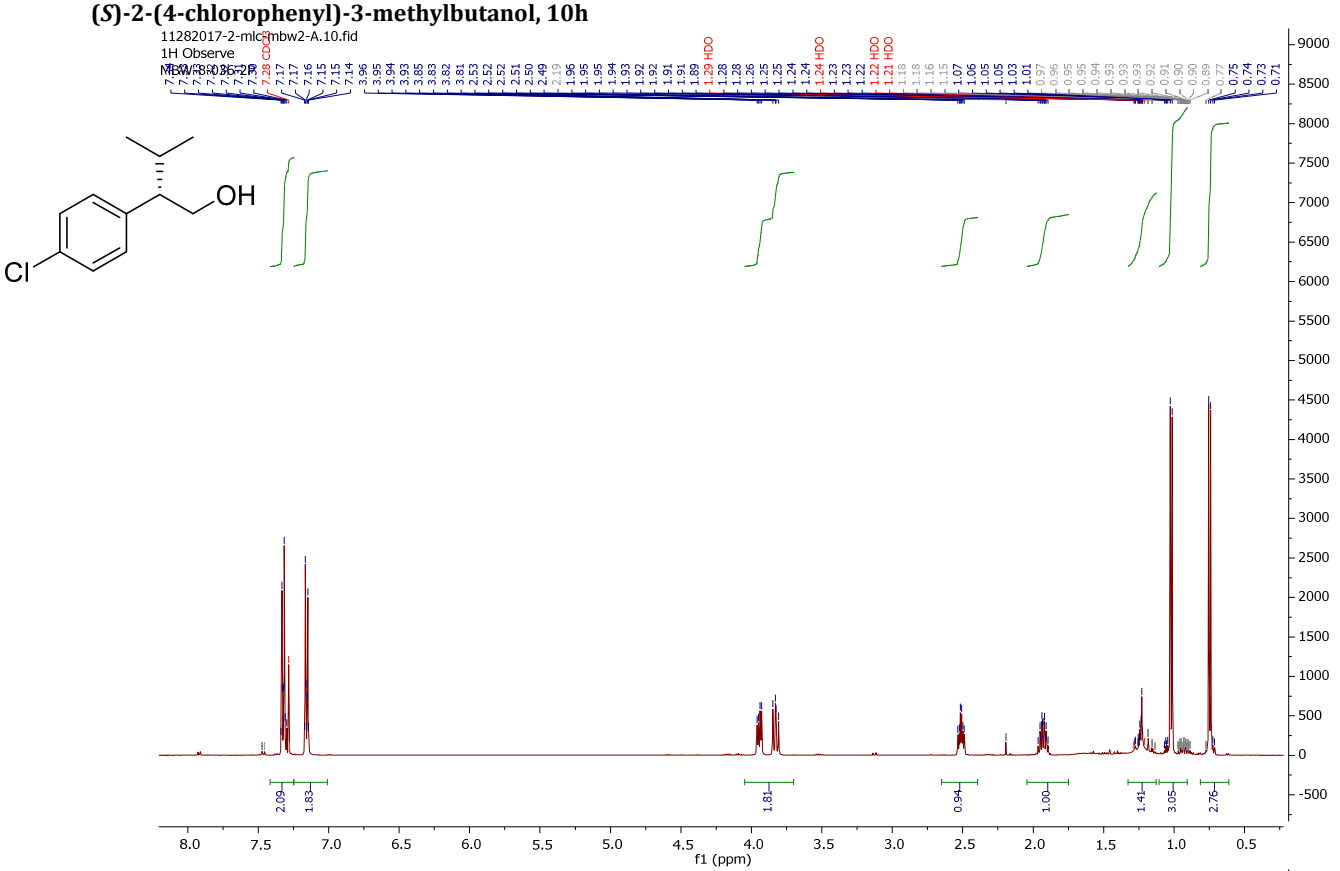


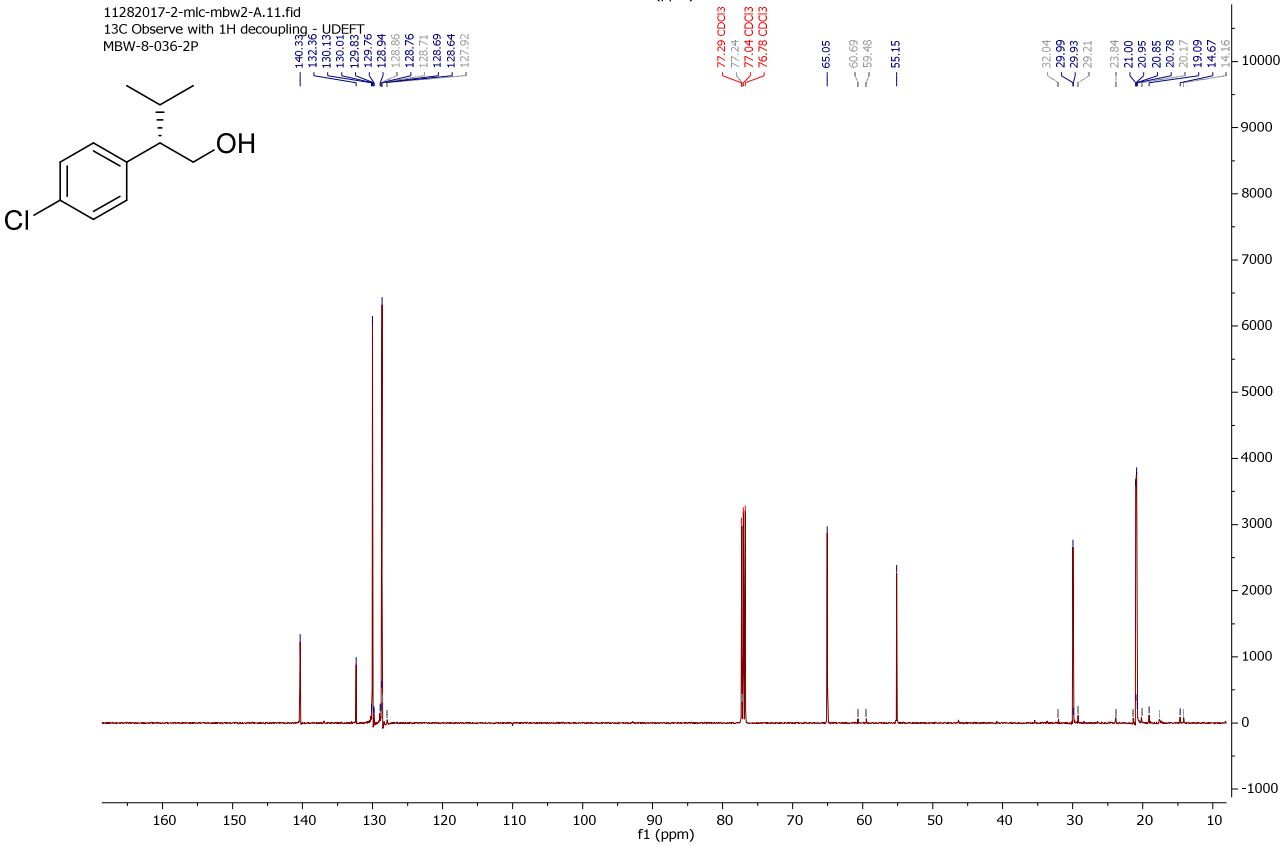
***(S)*-2-(4-isobutylphenyl)propan-1-ol, 10g**



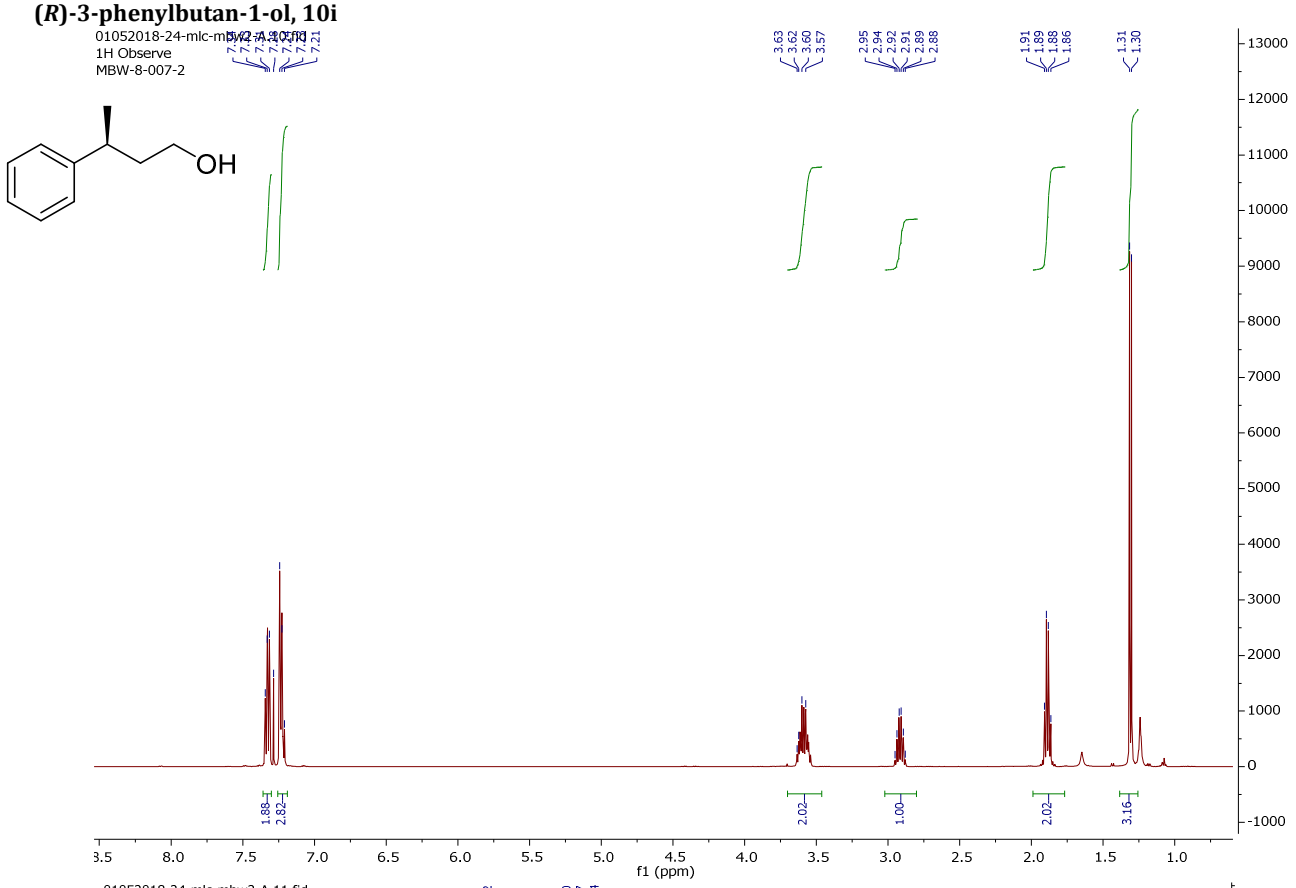


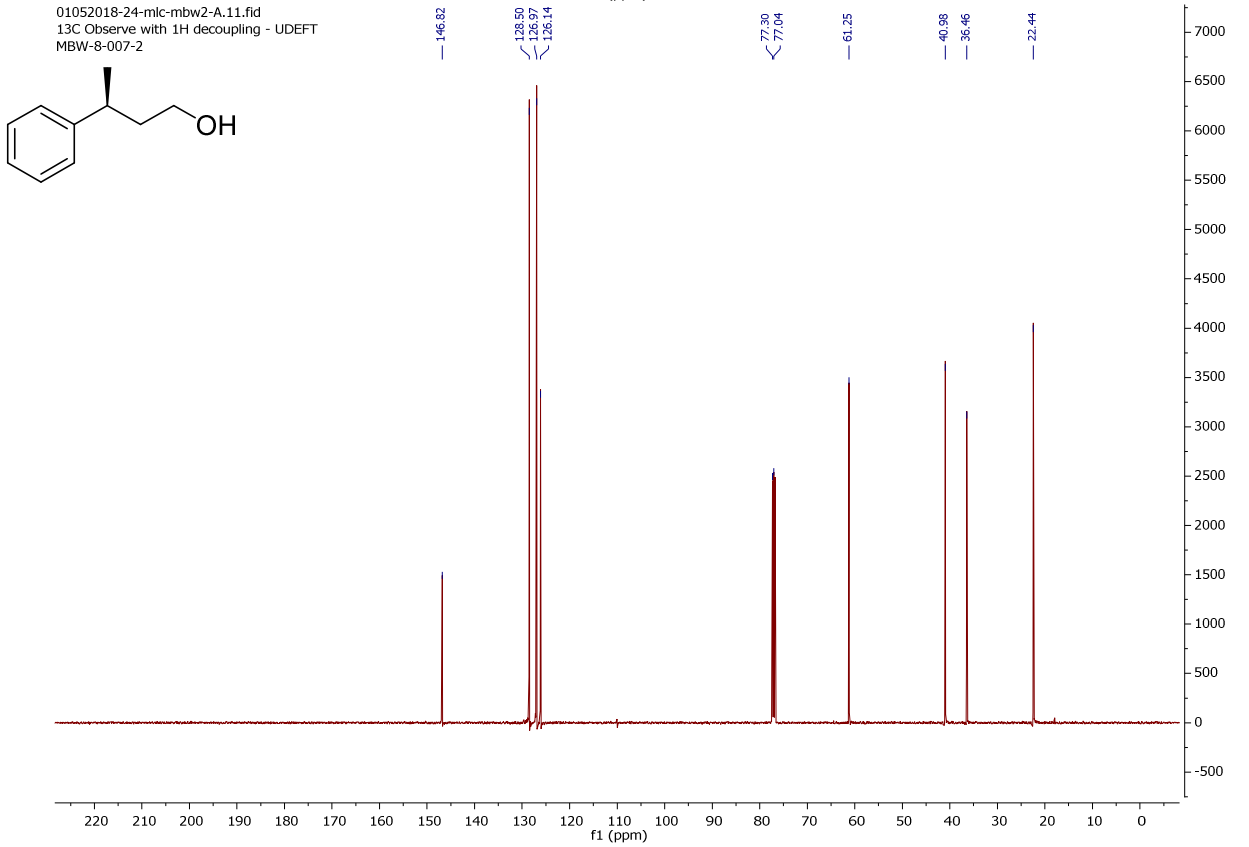
(*S*)-2-(4-chlorophenyl)-3-methylbutanol, 10h



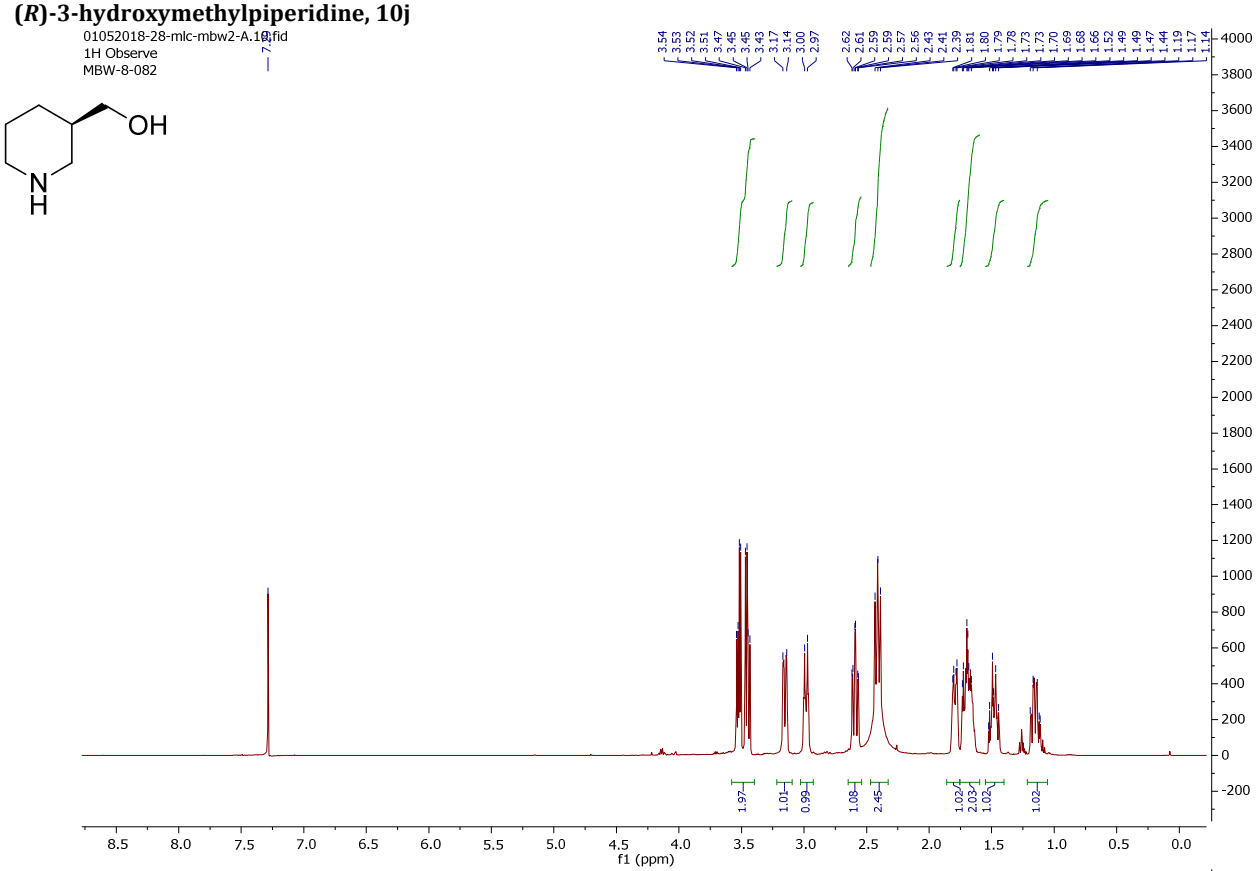


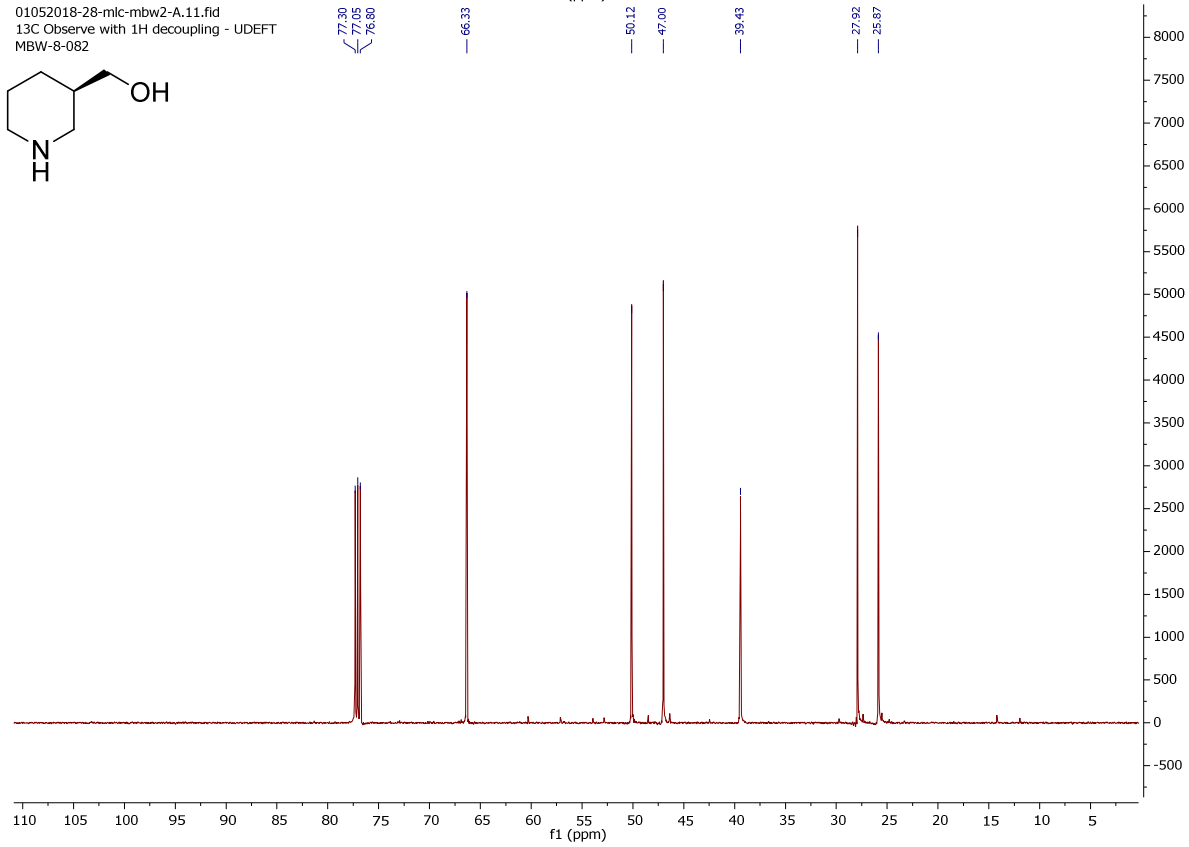
(*R*)-3-phenylbutan-1-ol, 10i



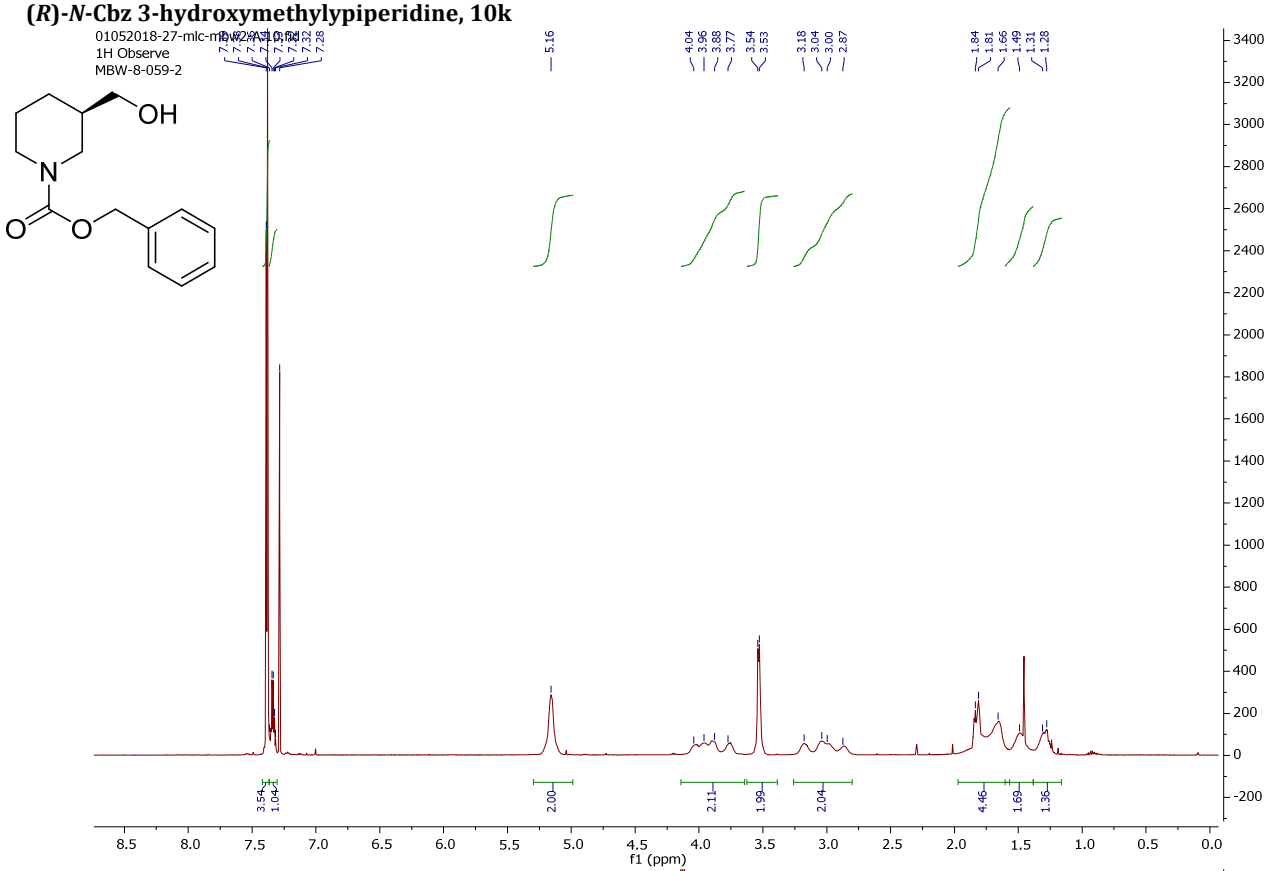


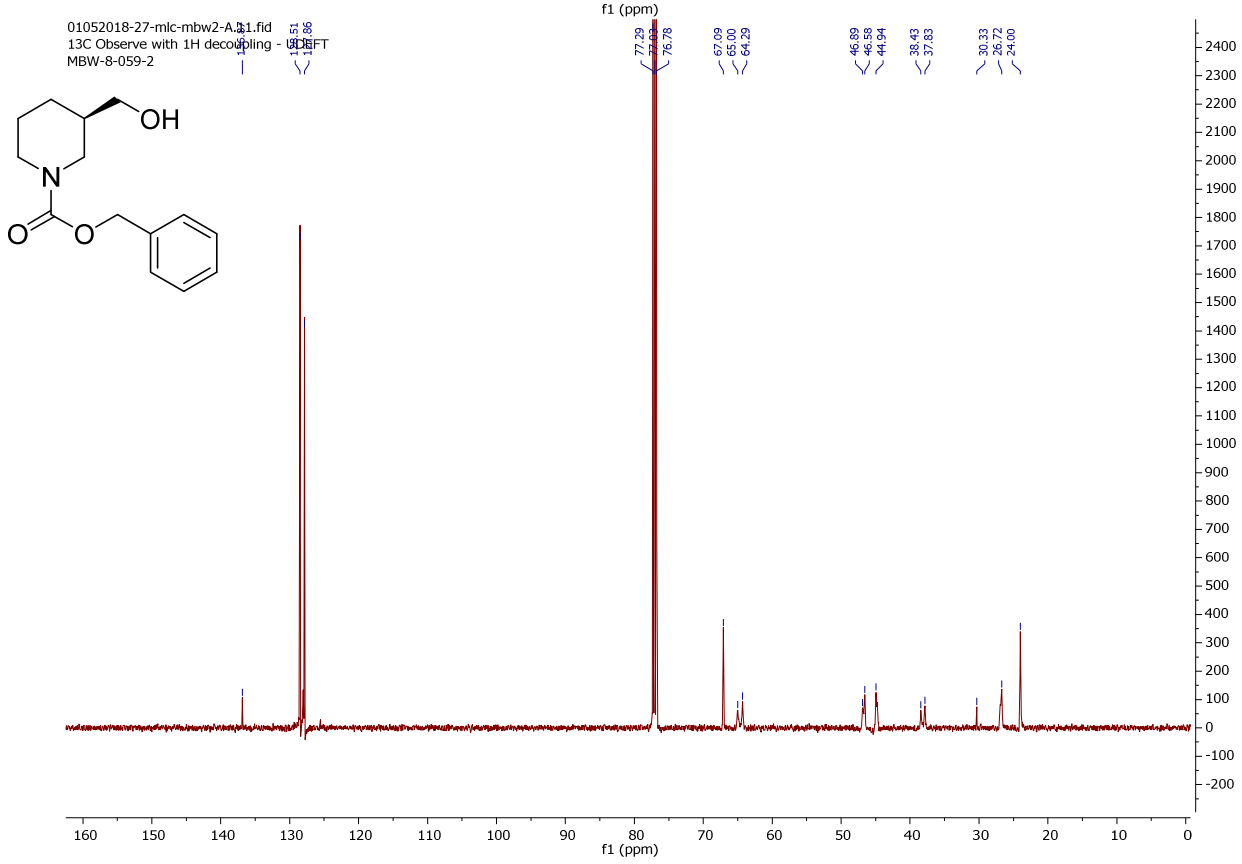
(*R*)-3-hydroxymethylpiperidine, 10j



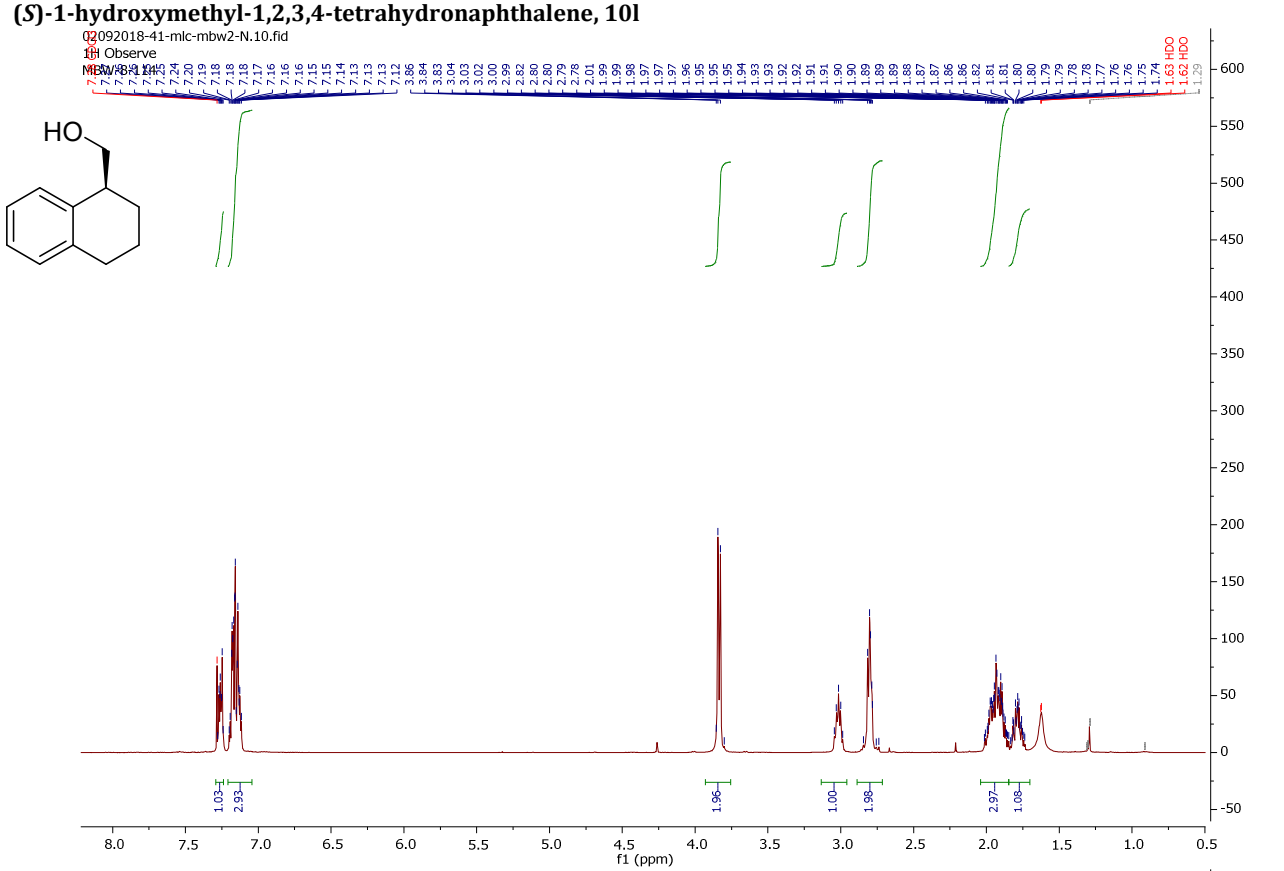


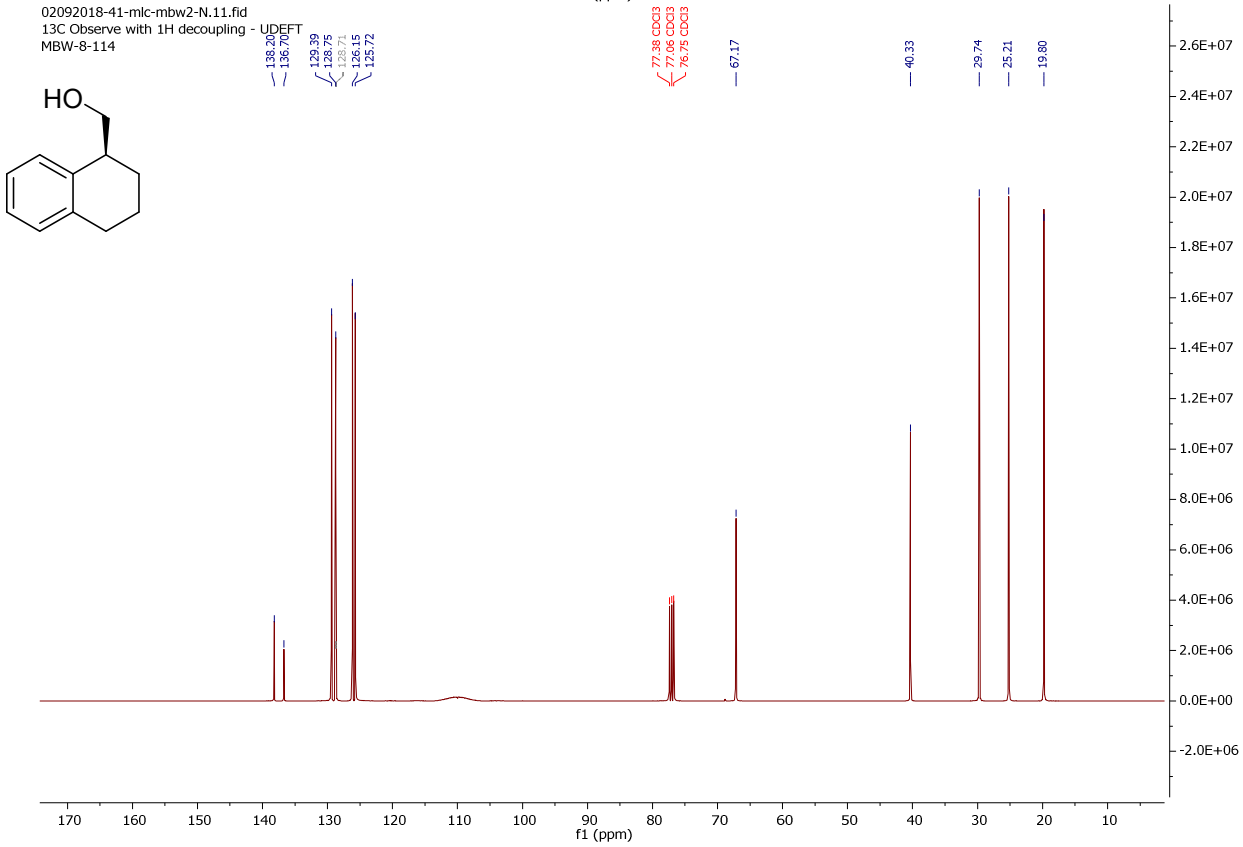
(*R*)-*N*-Cbz 3-hydroxymethylypiperidine, 10k





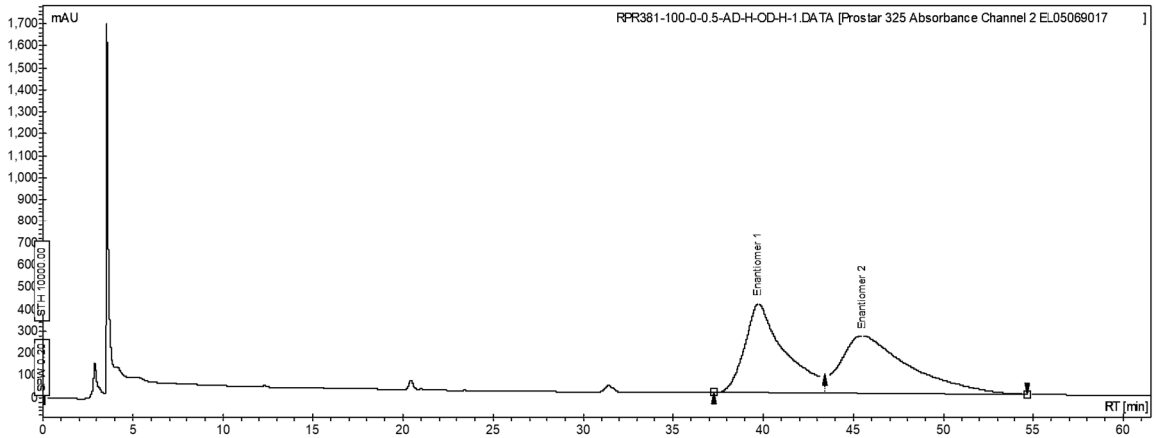
(*S*)-1-hydroxymethyl-1,2,3,4-tetrahydronaphthalene, 10l





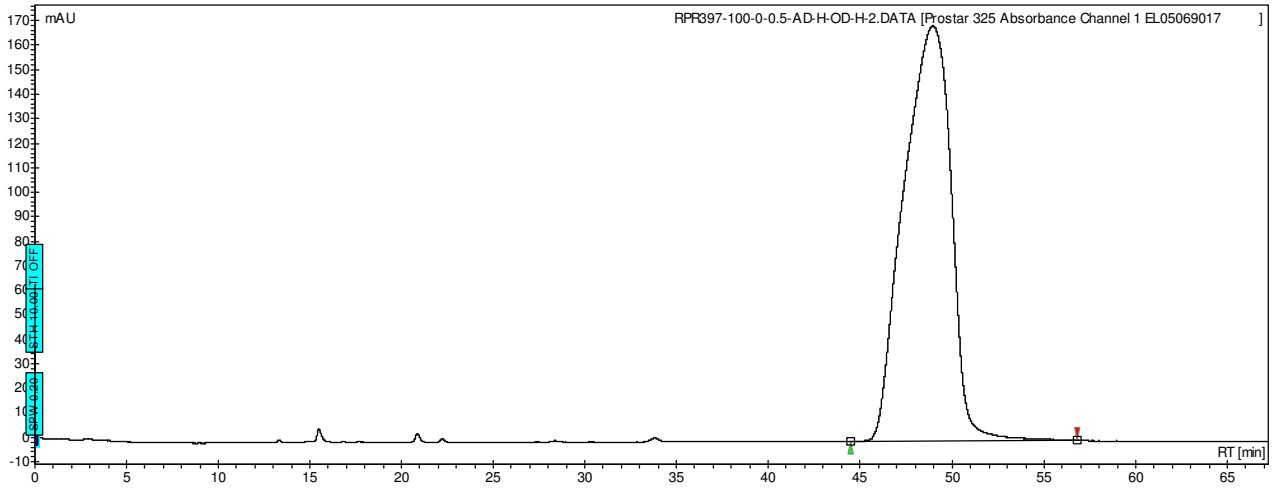
5. Chiral HPLC traces

***rac*-Benzyl-*N, N*-dibenzyl allylglycine, 9a**



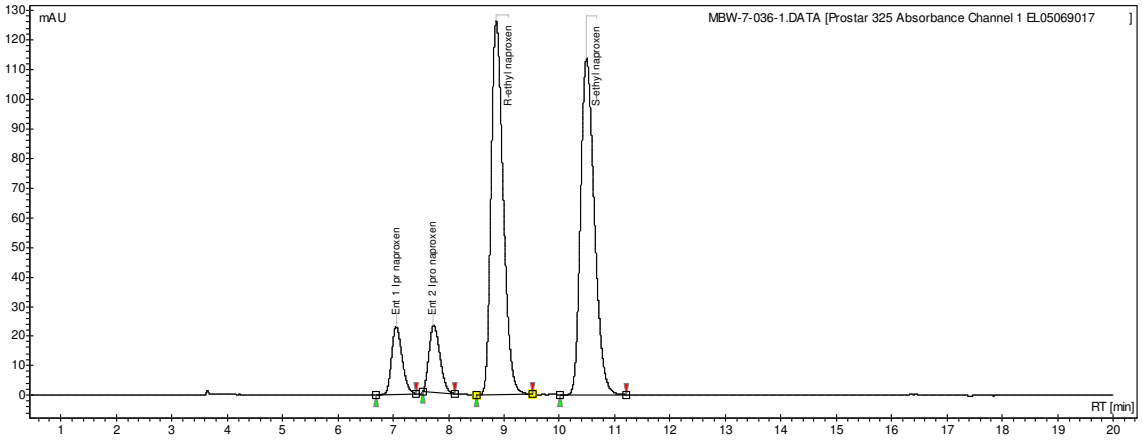
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	Enantiomer 1	39.74	402.2	1028.4	47.663
2	Enantiomer 2	45.49	261.5	1129.2	52.337
Total			663.7	2157.6	100.000

***(S)*-Benzyl-*N, N*-dibenzyl allylglycine, 9a (>99 % *ee*)**



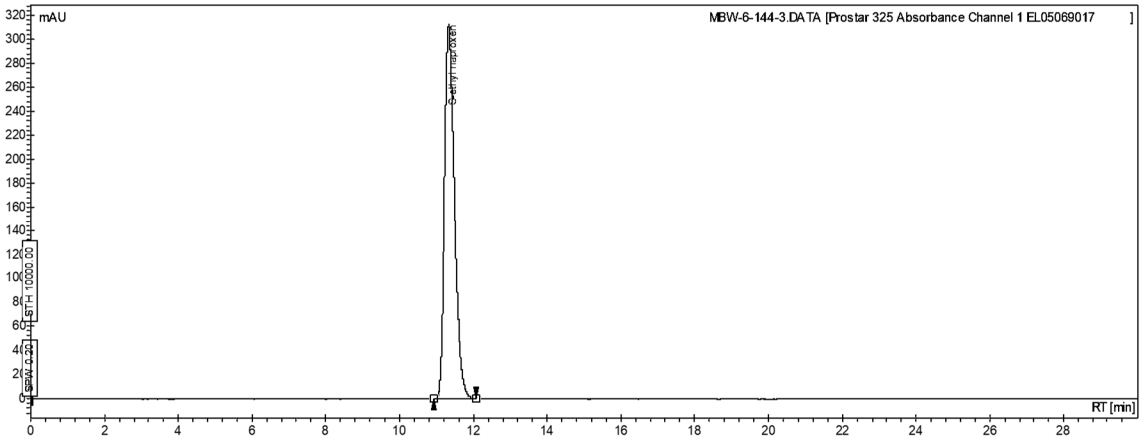
#	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	48.95	100.00	169.3	507.5	100.000
Total			100.00	169.3	507.5	100.000

***rac*-Ethyl naproxen, 9e (made by treating (*S*)-ethyl naproxen with KO^{t}Bu in isopropanol at 50 ^{o}C)**



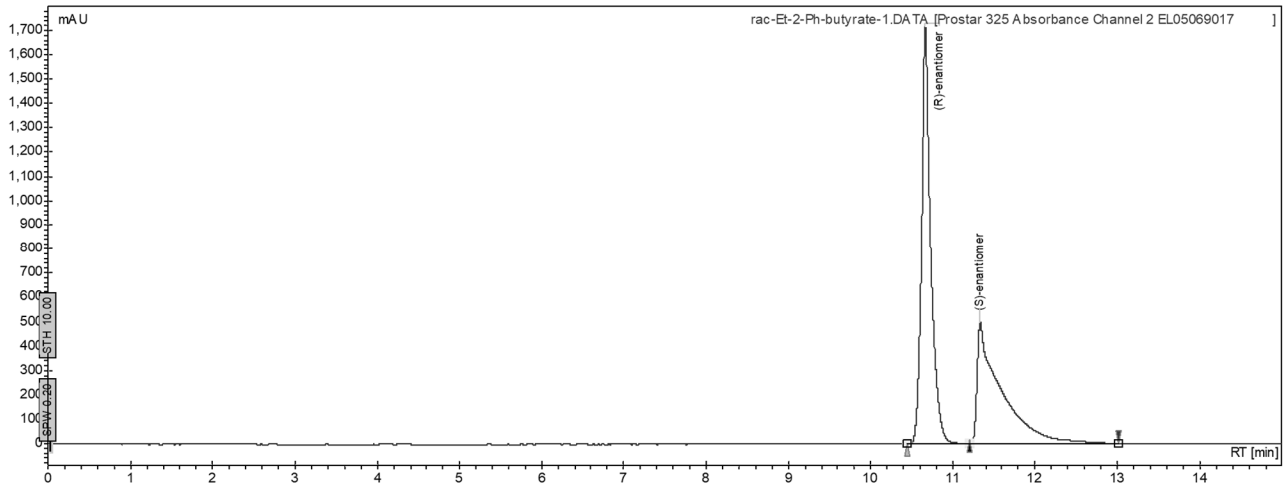
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
3	Ent 1 iPr naproxen	7.05	22.7	5.0	6.693
4	Ent 2 iPr naproxen	7.73	22.7	5.2	6.934
1	R-ethyl naproxen	8.86	126.0	31.9	42.687
2	S-ethyl naproxen	10.49	113.4	32.6	43.686
Total			284.7	74.7	100.000

***(S)*-Ethyl naproxen, 9e (>99 % *ee*)**



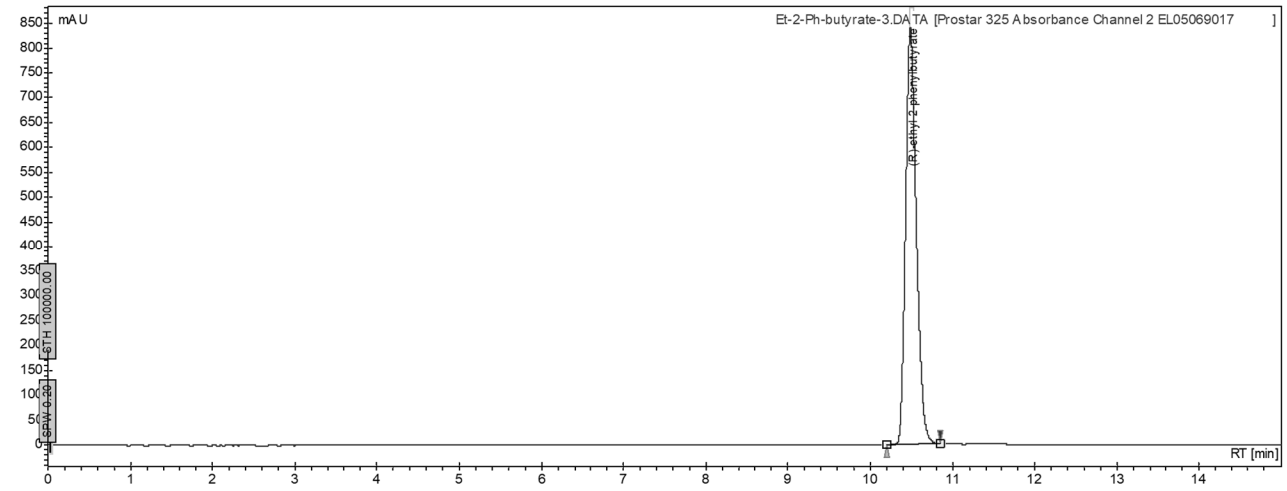
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	S-ethyl naproxen	11.33	313.5	96.9	100.000
Total			313.5	96.9	100.000

***rac*-Ethyl 2-phenylbutyrate, 9f**



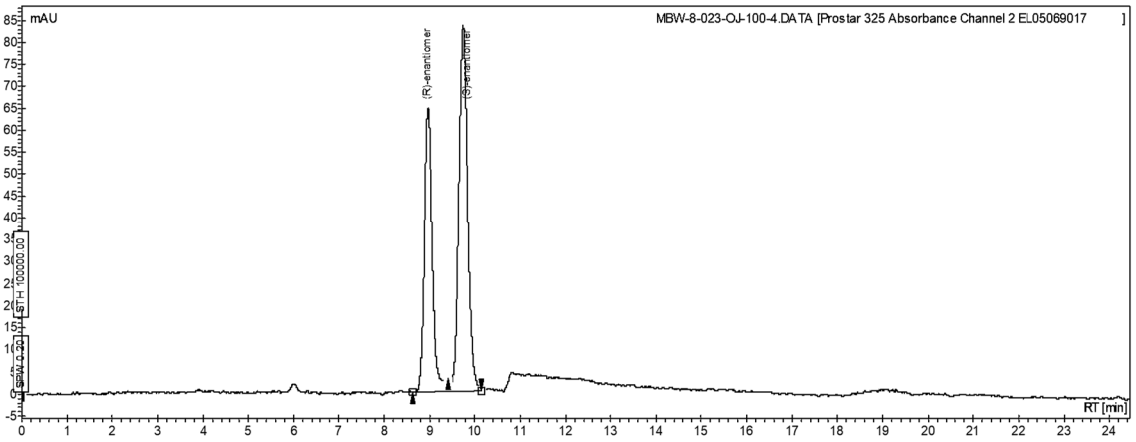
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	(R)-enantiomer	10.67	1710.5	224.3	57.530
2	(S)-enantiomer	11.33	496.5	165.6	42.470
	Total		2207.0	389.9	100.000

***(R)*-Ethyl 2-phenylbutyrate, 9f (>99 % *ee*)**



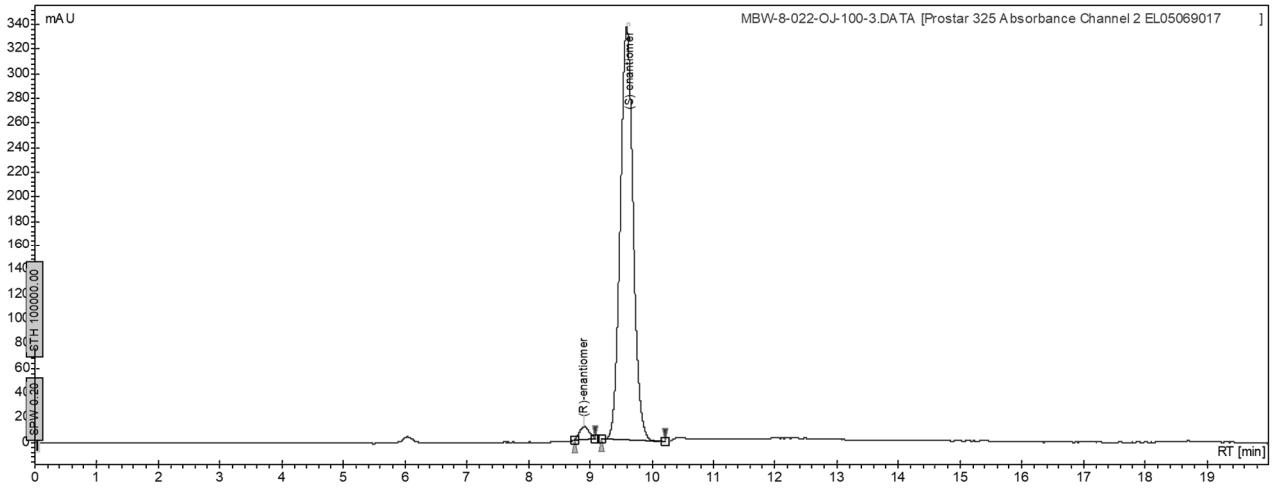
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	(R)-ethyl 2-phenylbutyrate	10.49	839.8	124.0	100.000
	Total		839.8	124.0	100.000

***rac*-Ethyl 2-(4-chlorophenyl)-3-methylbutyrate, 9h**



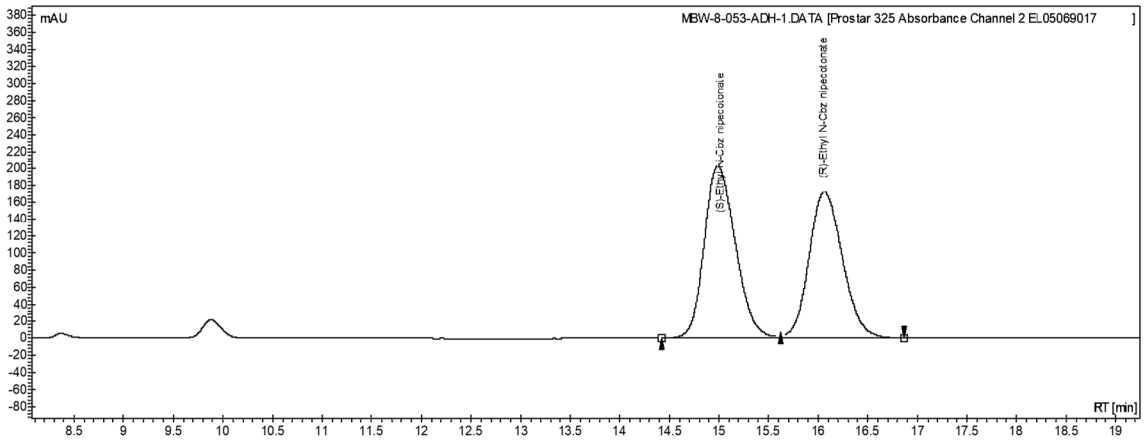
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	(R)-enantiomer	8.97	64.5	13.0	40.842
2	(S)-enantiomer	9.74	83.4	18.8	59.158
Total				31.8	100.000

***(S)*-Ethyl 2-(4-chlorophenyl)-3-methylbutyrate, 9h (96 % *ee*)**



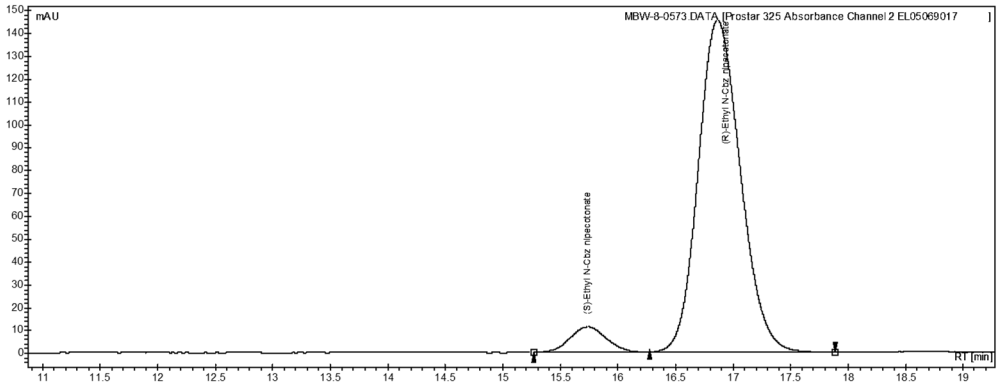
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
2	(R)-enantiomer	8.90	10.0	1.8	2.198
1	(S)-enantiomer	9.59	336.4	80.5	97.802
	Total		346.5	82.3	100.000

***rac-N-Cbz*-Ethyl nipecotate, 9k**



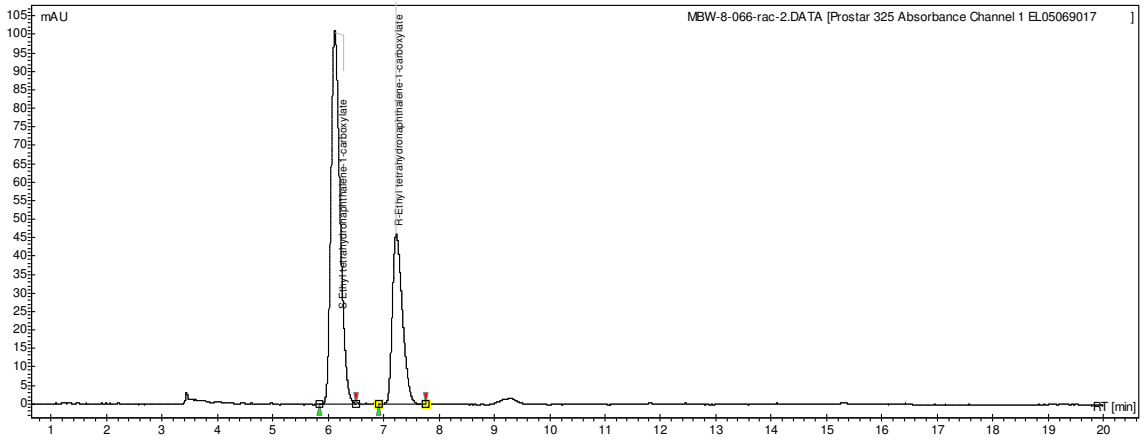
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	(S)-Ethyl N-Cbz nipecotonate	14.99	202.6	73.8	52.334
2	(R)-Ethyl N-Cbz nipecotonate	16.06	172.4	67.2	47.666
Total			375.0	141.0	100.000

***(R)-N-Cbz*-Ethyl nipecotate, 9k (87 % *ee*)**



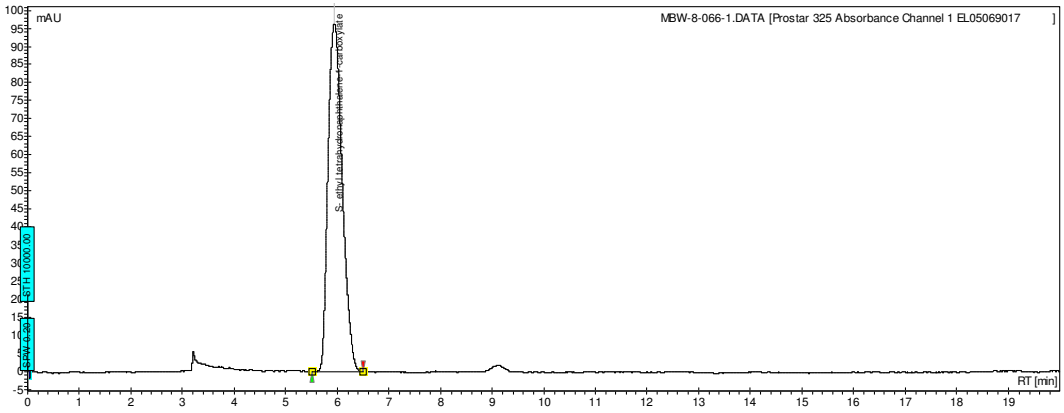
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	(S)-Ethyl N-Cbz nipecotonate	15.74	11.2	4.1	6.206
2	(R)-Ethyl N-Cbz nipecotonate	16.87	145.3	61.6	93.794
Total			156.5	65.6	100.000

Ethyl-1,2,3,4-tetrahydronaphthalene-1-carboxylate, 9l (scalemic sample prepared by treatment of substrate with KO^{t}Bu in ethanol at room temperature, 33 % *ee*)



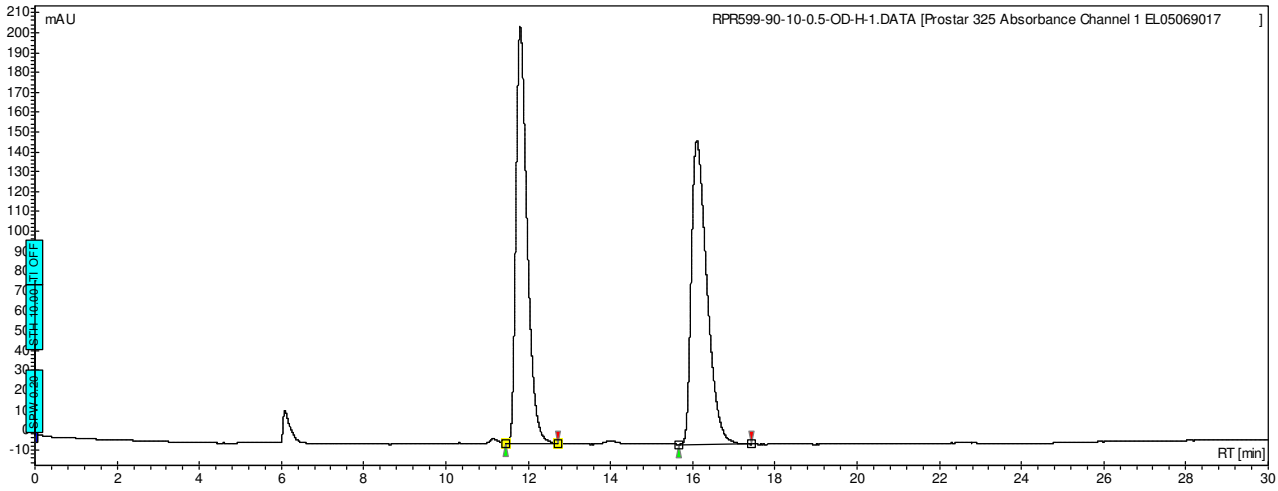
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	S-enantiomer	6.12	101.1	19.3	66.566
2	R-enantiomer	7.23	46.2	9.7	33.434
Total			147.2	28.9	100.000

***(S)*-Ethyl-1,2,3,4-tetrahydronaphthalene-1-carboxylate, 9l (99 % *ee*)**



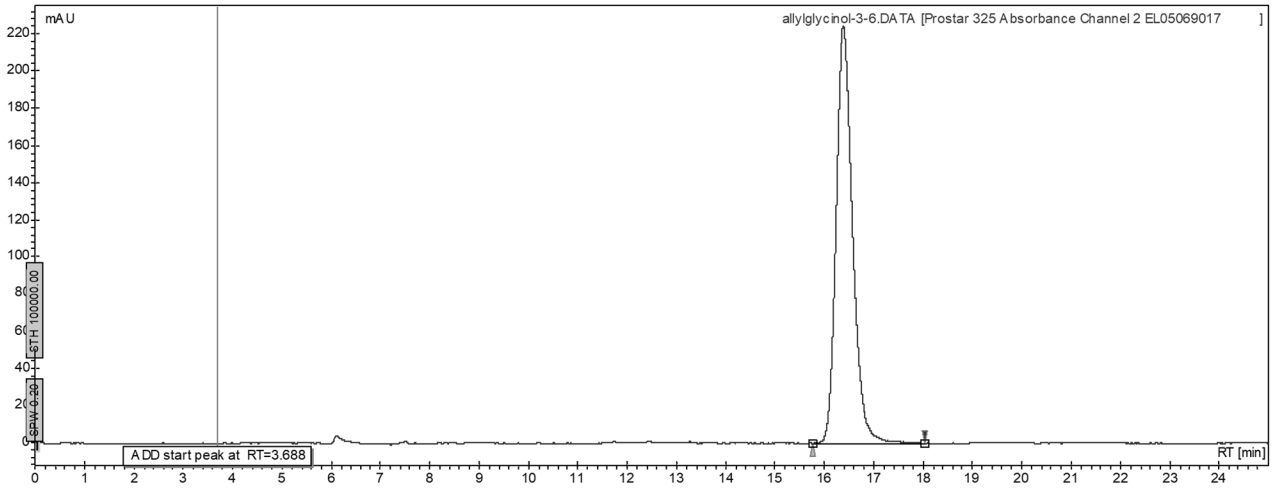
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	S- enantiomer	5.94	96.3	31.0	100.000
Total			96.3	31.0	100.000

***rac*-2-(dibenzylamino)pent-4-en-1-ol, 10a**



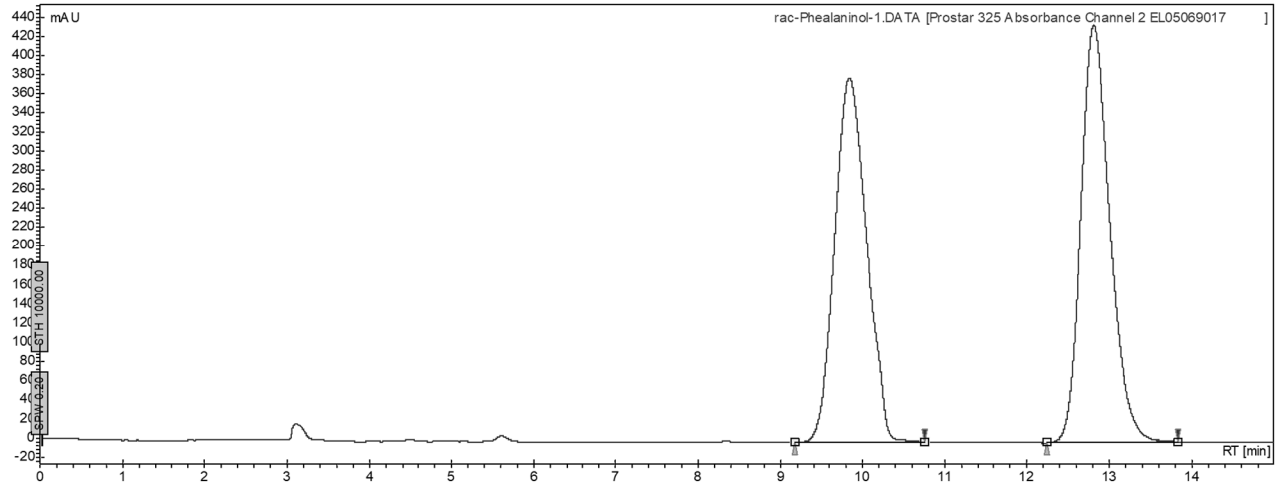
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	11.81	209.8	65.9	49.561
2	UNKNOWN	16.10	153.1	67.0	50.439
Total				132.9	100.000

(*S*)-2-(dibenzylamino)pent-4-en-1-ol, 10a (>99 % *ee*)



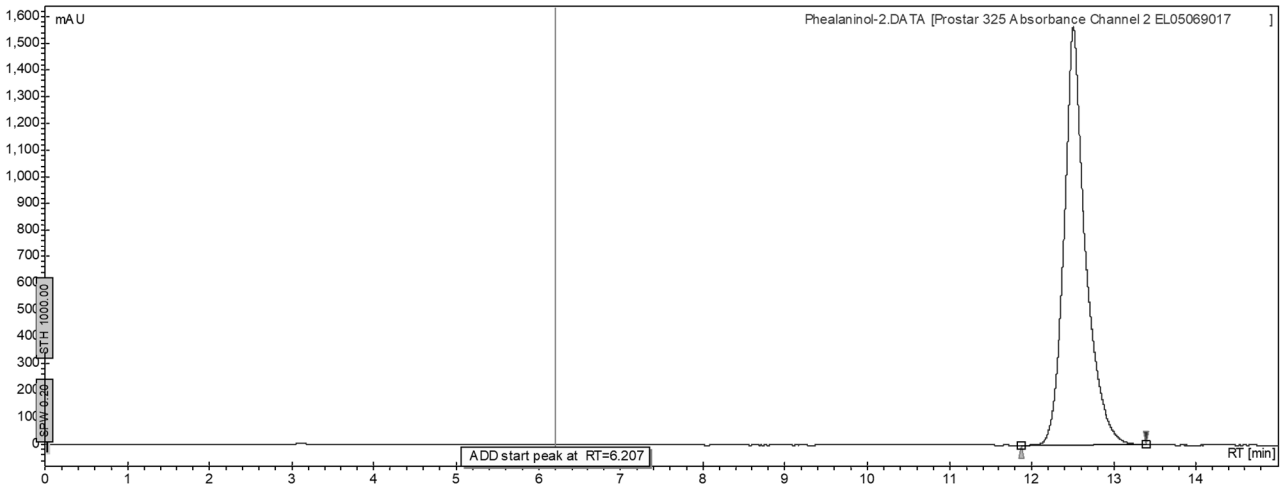
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	16.38	223.9	87.1	100.000
	Total				100.000

***rac-N, N*-dibenzylphenylalaninol, 10b**



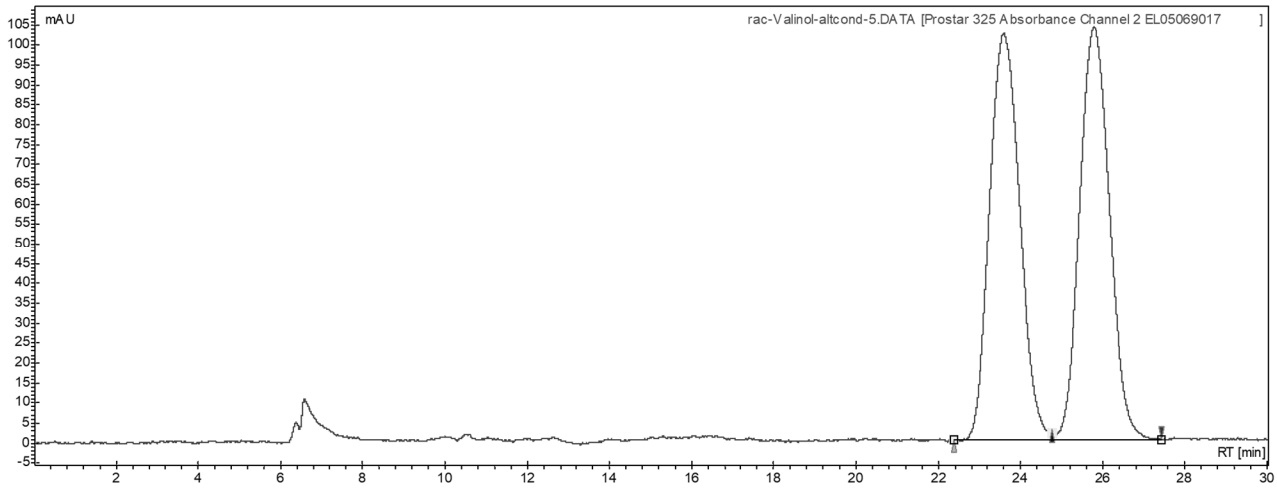
#	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	9.84	49.13	379.6	171.0	49.129
2	UNKNOWN	12.81	50.87	435.1	177.0	50.871
	Total		100.00	814.7	348.0	100.000

(*S*)-*N, N*-dibenzylphenylalaninol, 10b (>99 % *ee*)



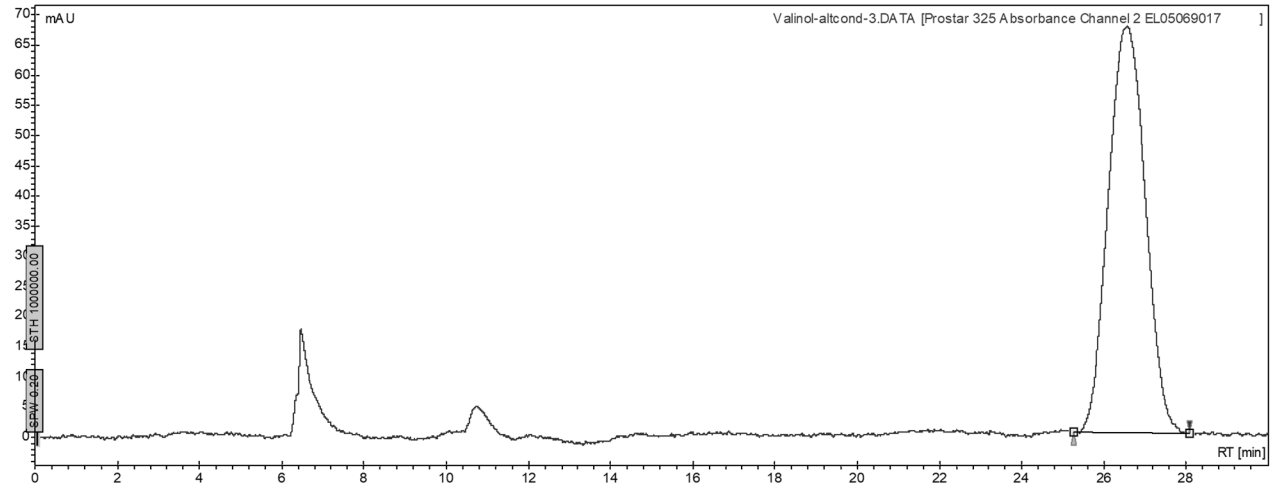
#	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	12.51	100.00	1559.3	466.2	100.000
	Total		100.00	1559.3	466.2	100.000

***rac-N, N*-dibenzylvalinol, 10c**



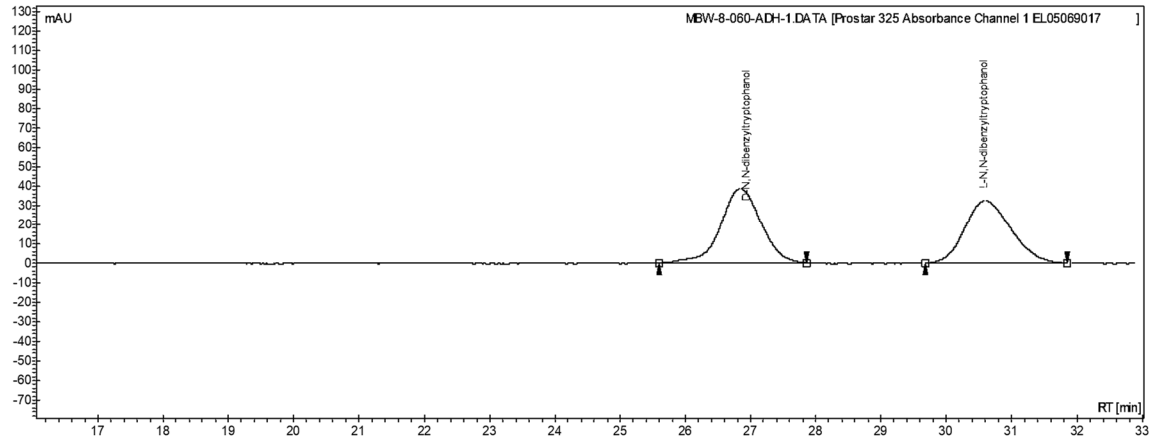
#	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	23.61	49.94	102.1	87.0	49.943
2	UNKNOWN	25.78	50.06	103.6	87.2	50.057
			Total	100.00 205.7	174.2	100.000

(*S*)-*N,N*-dibenzylvalinol, 10c (>99 % *ee*)



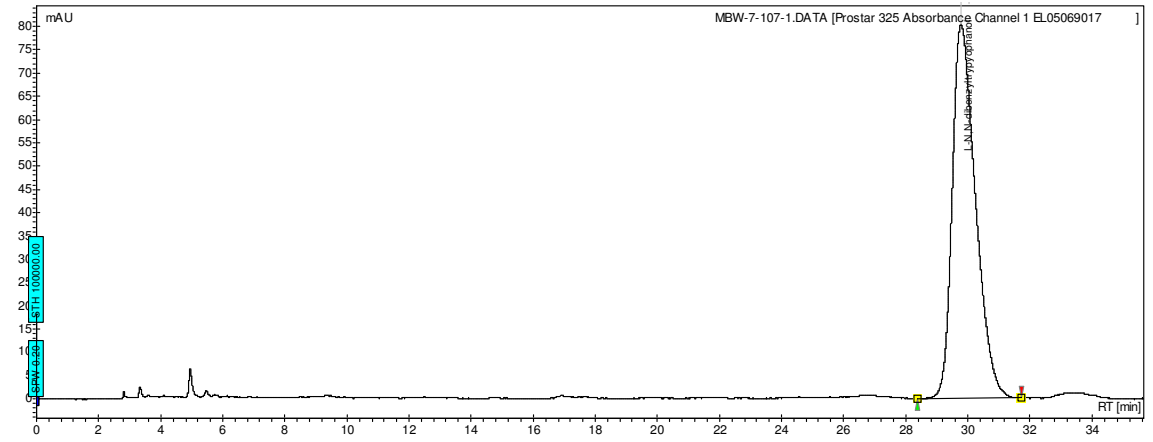
#	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	26.57	100.00	67.3	70.6	100.000
			Total	100.00 67.3	70.6	100.000

***rac*-2-[Bis(phenylmethyl)amino]-1*H*-indole-3-propan-1-ol , 10d**



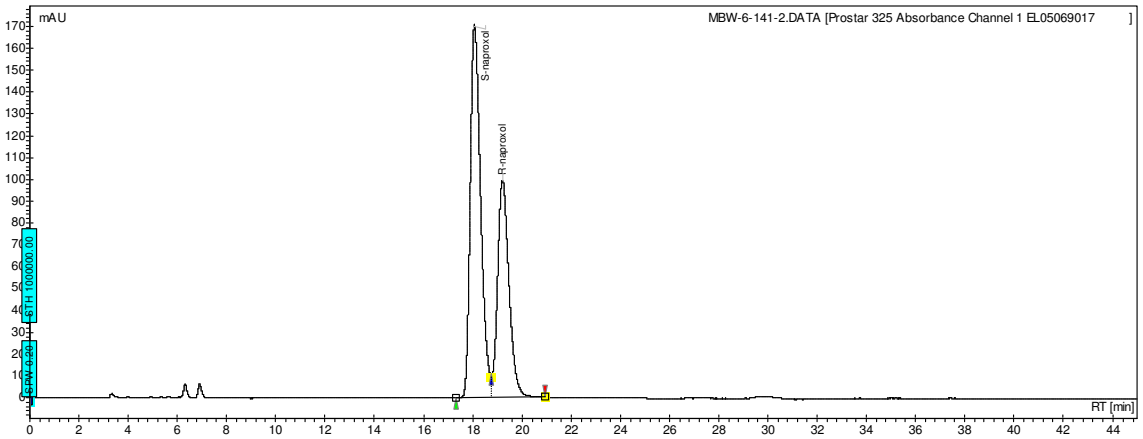
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	D-enantiomer	26.84	38.7	27.6	51.106
2	L-enantiomer	30.59	32.3	26.5	48.894
Total			71.1	54.1	100.000

(*2S*)-2-[Bis(phenylmethyl)amino]-1*H*-indole-3-propan-1-ol , 10d (>99 % *ee*)



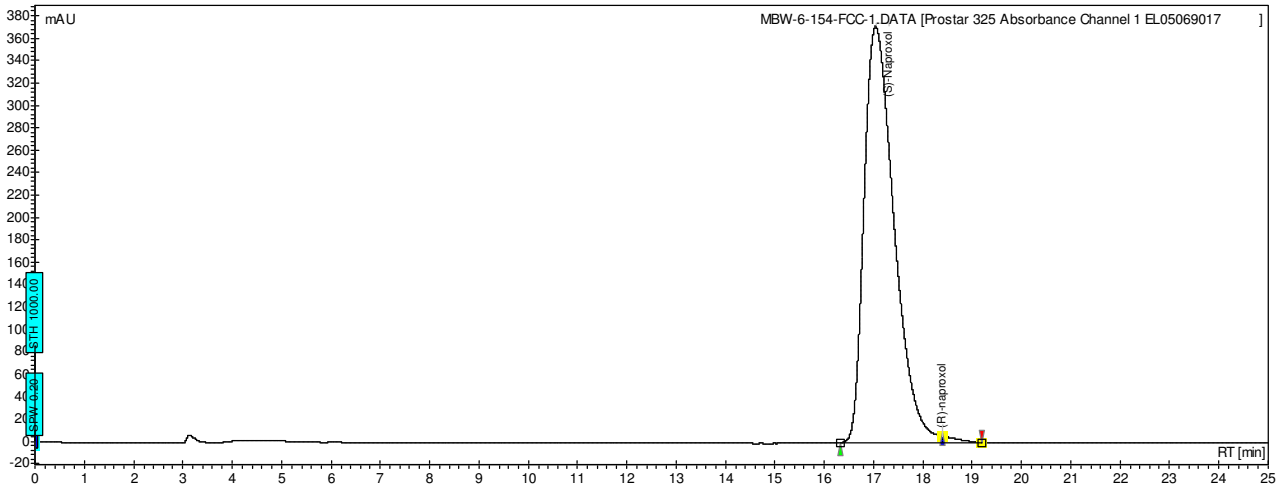
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	L-enantiomer	29.78	80.3	69.7	100.000
Total			80.3	69.7	100.000

Naproxol, 10e (scalemic sample made from reduction of (*S*)-ethyl naproxen in the presence of KO^{t}Bu, 20 % *ee*)



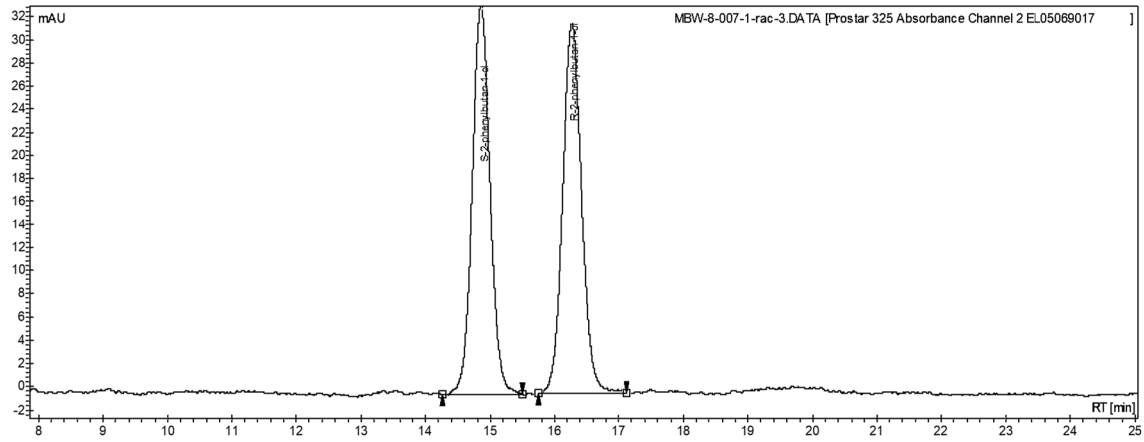
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	S-naproxol	18.07	170.7	83.4	60.931
2	R-naproxol	19.21	99.4	53.5	39.069
Total			270.2	136.9	100.000

(*S*)-naproxol, 10e (98.5 % *ee*)



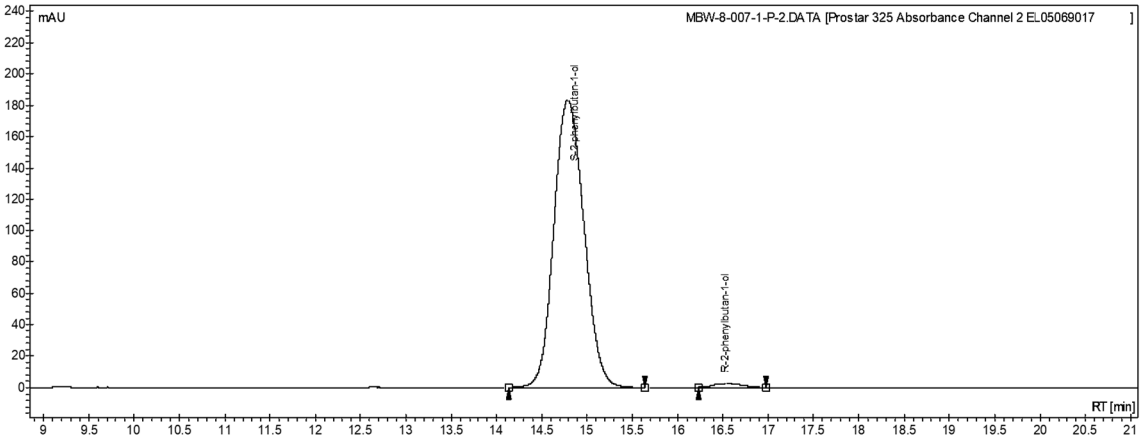
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	(S)-Naproxol	17.04	371.6	262.1	99.263
2	(R)-Naproxol	18.40	5.6	1.9	0.737
		Total		264.1	100.000

***rac*-2-phenyl-1-butanol, 10f**



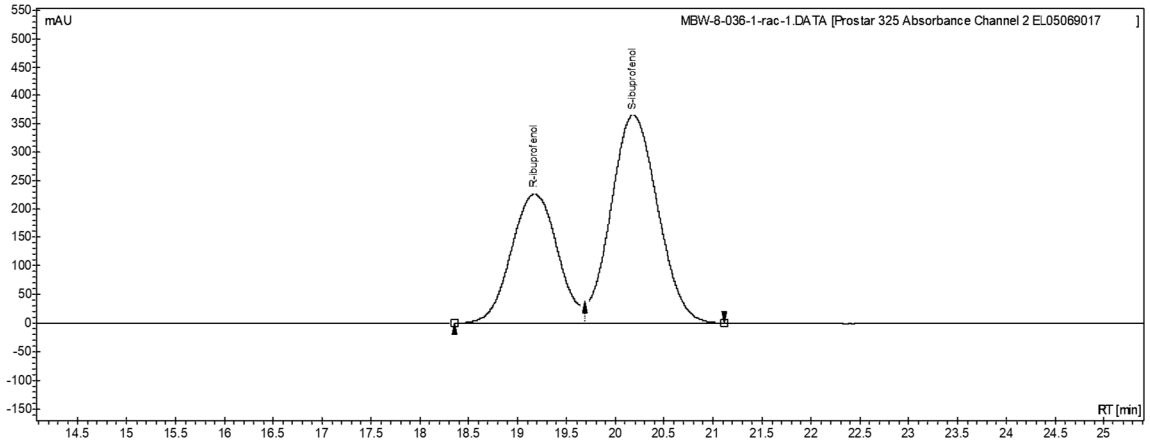
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	S-2-phenylbutan-1-ol	14.86	33.7	10.7	49.831
2	R-2-phenylbutan-1-ol	16.27	32.0	10.8	50.169
Total			65.7	21.5	100.000

(*R*)-2-phenyl-1-butanol, 10f (98 % *ee*)



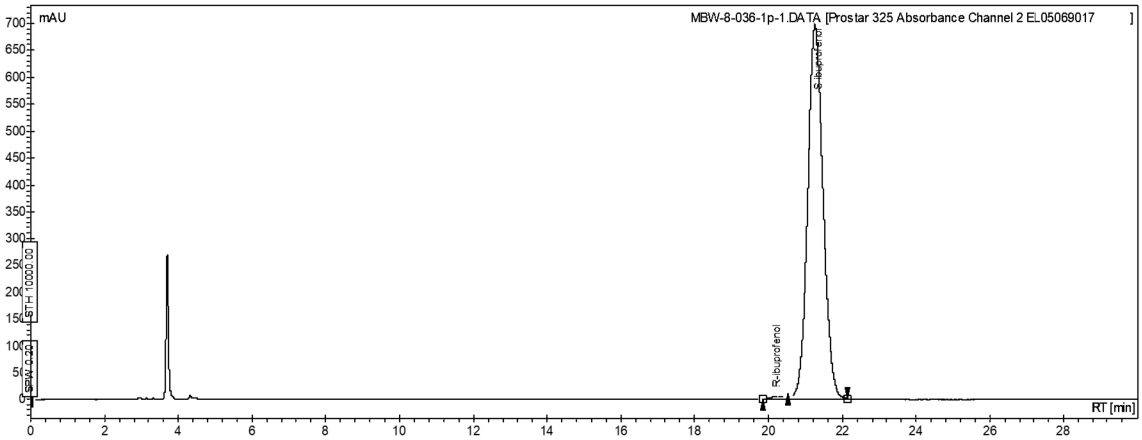
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	S-2-phenylbutan-1-ol	14.79	183.2	70.3	98.840
2	R-2-phenylbutan-1-ol	16.54	2.4	0.8	1.160
Total			185.5	71.1	100.000

***rac*-2-(4-isobutylphenyl)propan-1-ol, 10g (scalemic sample made from reduction of *(S)*-Ethyl ibuprofen using KO^{t}Bu, 24 % *ee*)**



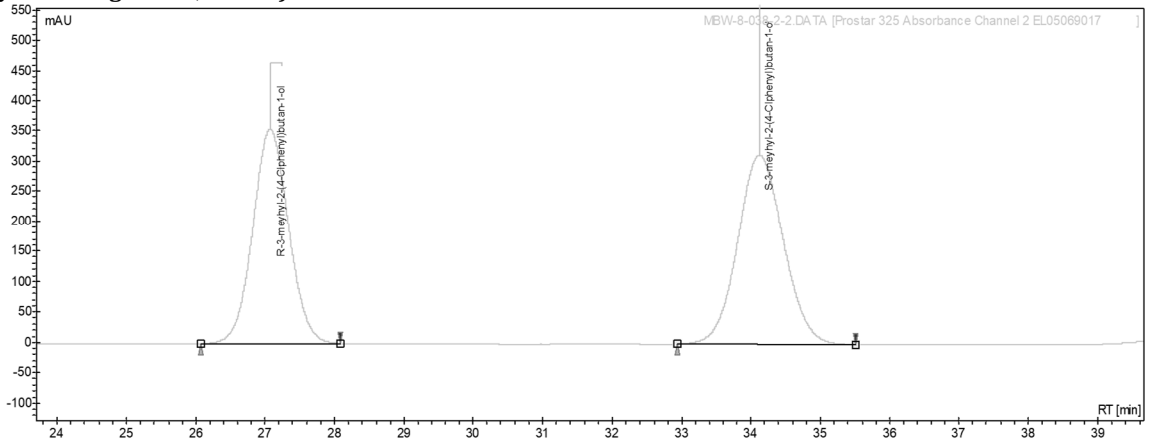
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	R-enantiomer	19.17	226.5	123.9	38.073
2	S-enantiomer	20.18	365.4	201.5	61.927
Total			591.9	325.4	100.000

***(S)*-2-(4-isobutylphenyl)propan-1-ol, 10g (99 % *ee*)**



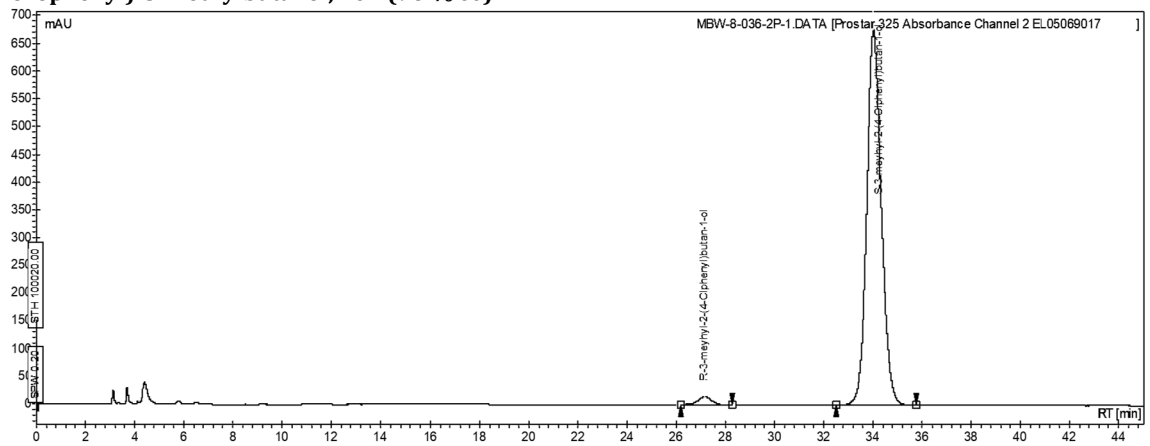
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	R-enantiomer	20.26	4.6	2.0	0.595
2	S-enantiomer	21.26	696.7	335.2	99.405
Total			701.3	337.2	100.000

2-(4-chlorophenyl)-3-methylbutanol, 10h (scalemic sample made from reduction of *(S)*-Ethyl 2-(4-chlorophenyl)-3-methylbutyrate using KO^{t}Bu, 6 % *ee*)



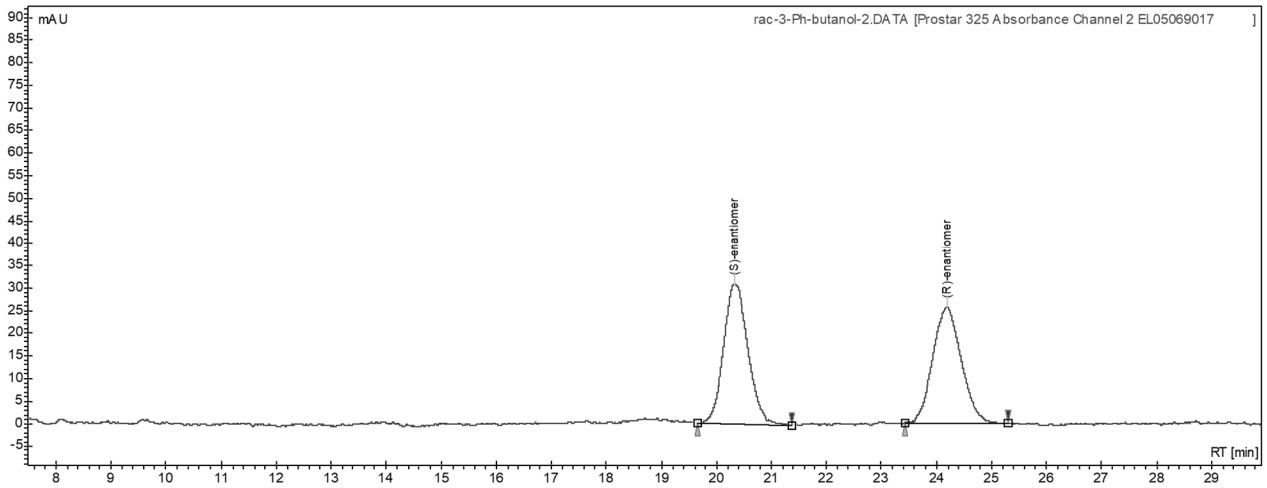
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	R-enantiomer	27.07	355.4	211.6	46.972
2	S-enantiomer	34.12	313.9	238.9	53.028
Total			669.2	450.5	100.000

(*S*)-2-(4-chlorophenyl)-3-methylbutanol, 10h (96 % *ee*)



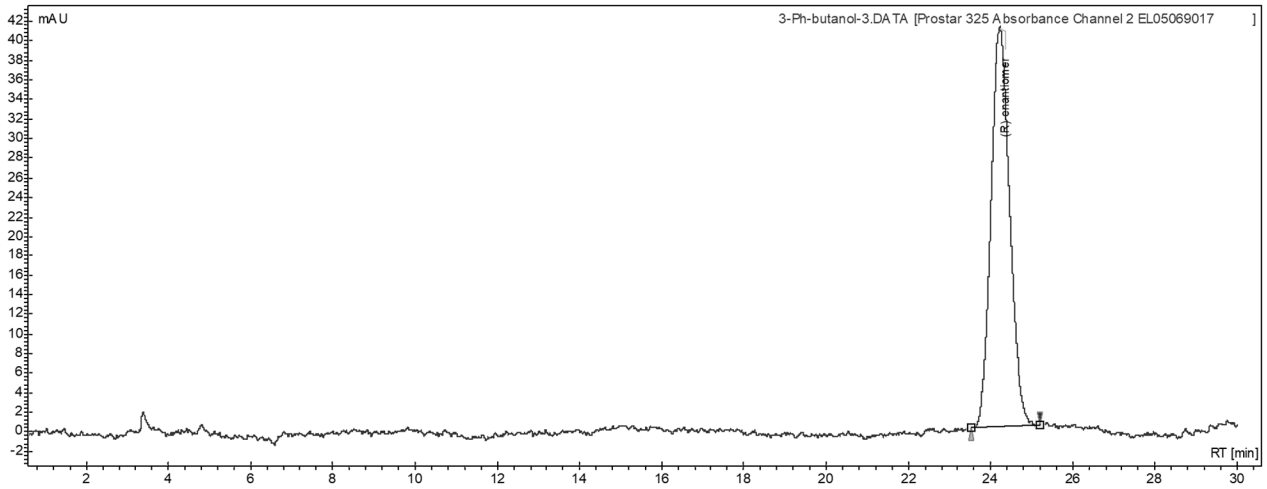
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	R-enantiomer	27.16	13.8	8.7	1.851
2	S-enantiomer	34.02	675.2	461.2	98.149
Total			689.0	469.9	100.000

***rac*-3-phenyl-1-butanol, 10i**



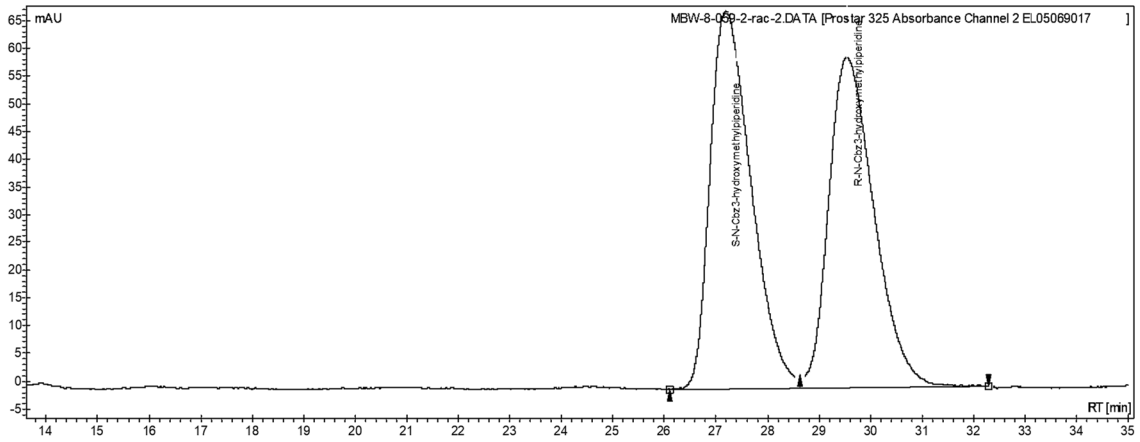
#	Name	Time [Min]		Quantity [% Area]		Height [mAU]	Area [mAU.Min]	Area % [%]
1	(S)-enantiomer	20.32		51.02		30.9	15.8	51.017
2	(R)-enantiomer	24.19		48.98		25.5	15.2	48.983
Total		100.00	56.4	31.0	100.000			

(*R*)-3-phenyl-1-butanol, 10i (>99 % *ee*)



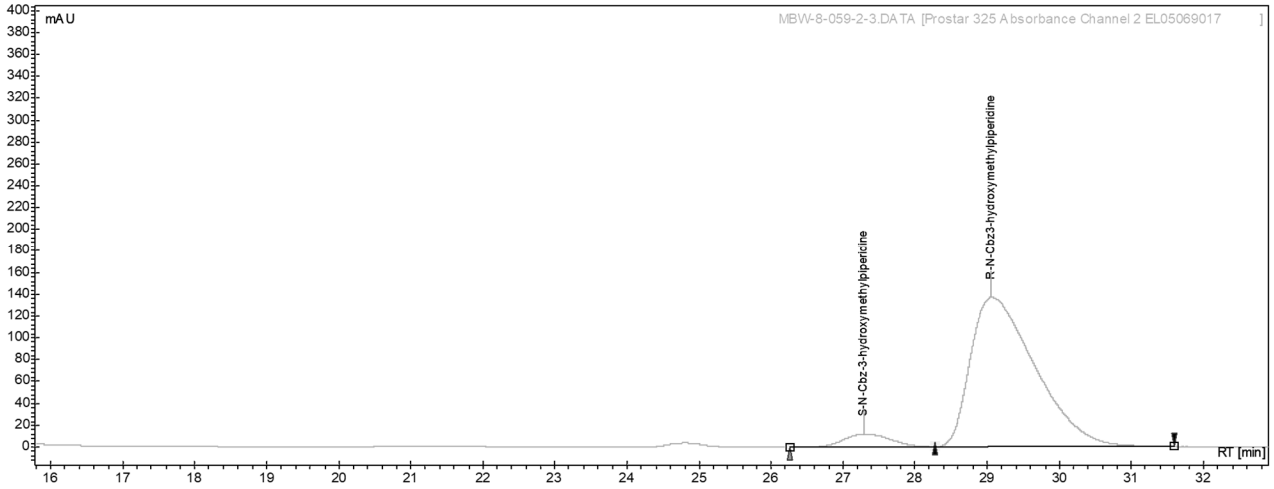
#	Name	Time [Min]		Quantity [% Area]		Height [mAU]	Area [mAU.Min]	Area % [%]
1	(R)-enantiomer	24.23		100.00		40.9	21.5	100.000
Total		100.00	40.9	21.5	100.000			

***rac*-3-hydroxymethylpiperidine (Cbz protected), 10j**



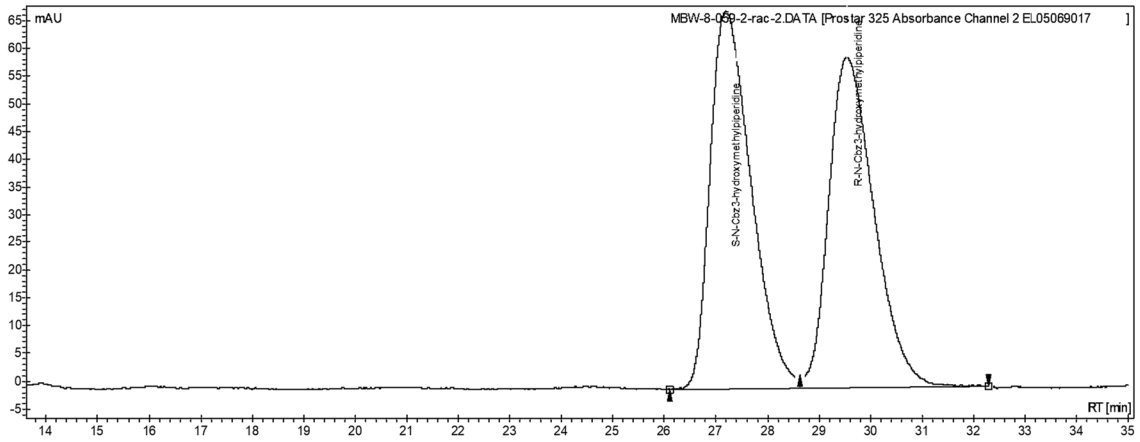
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	S-enantiomer	27.19	68.0	62.7	50.957
2	R-enantiomer	29.54	49.04	60.4	49.043
Total			127.5	123.1	100.000

(*R*)-3-hydroxymethylpiperidine (Cbz protected), 10j (88 % *ee*)



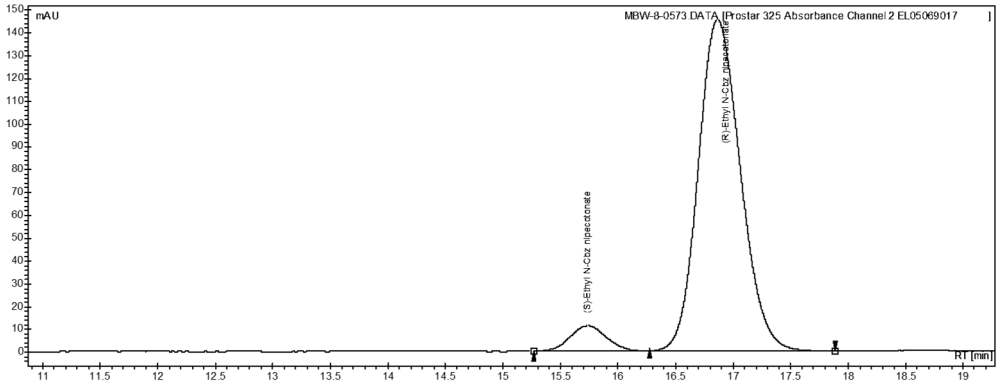
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	S-N-Cbz-3-hydroxymethylpiperidine	27.29	12.4	9.8	6.436
2	R-N-Cbz3-hydroxymethylpiperidine	29.06	137.1	142.7	93.564
Total		100.00 149.5	152.5	100.000	

***rac*-*N*-Cbz-3-hydroxymethylpiperidine, 10k**



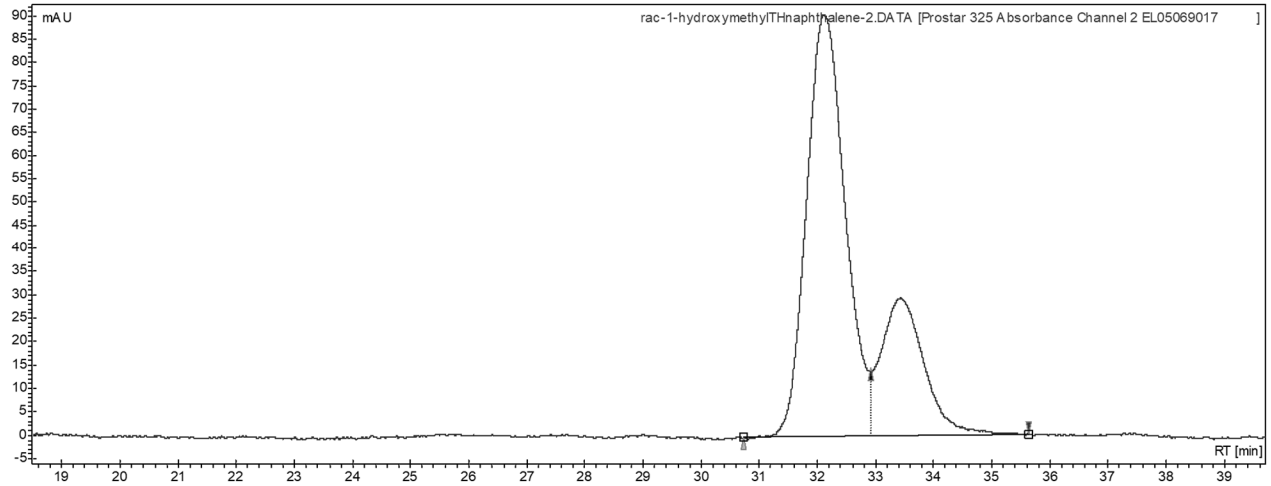
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	S-enantiomer	27.19	68.0	62.7	50.957
2	R-enantiomer	29.54	49.04	60.4	49.043
Total			127.5	123.1	100.000

(*R*)-*N*-Cbz-3-hydroxymethylpiperidine, 10k (87 % *ee*)



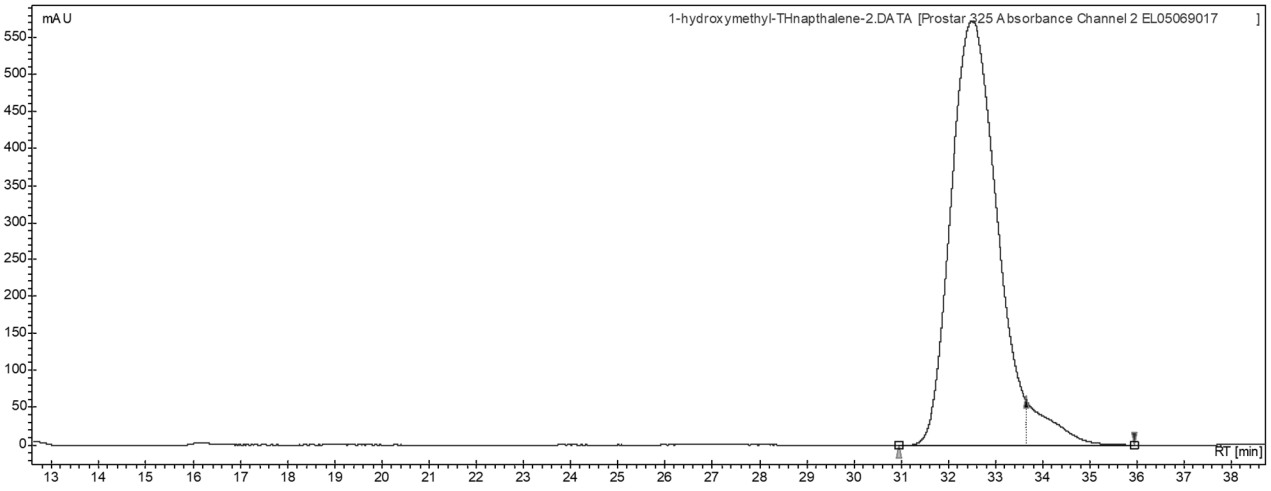
#	Name	Time [Min]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	S-enantiomer	27.29	12.4	9.8	6.436
2	R-enantiomer	29.06	137.1	142.7	93.564
Total			149.5	152.5	100.000

1-hydroxymethyl-1,2,3,4-tetrahydronaphthalene, 10l (scalemic sample made from reduction of *(S)*-Ethyl-1,2,3,4-tetrahydronaphthalene-1-carboxylate at 75 °C, 47 % *ee*)



#	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	32.12	73.47	90.6	69.7	73.471
2	UNKNOWN	33.44	26.53	29.4	25.2	26.529
	Total		100.00	120.0	94.9	100.000

(*S*)-1-hydroxymethyl-1,2,3,4-tetrahydronaphthalene, 10l (88 % *ee*)



#	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	32.49	94.34	573.5	634.7	94.341
2	UNKNOWN	33.64	5.66	60.5	38.1	5.659
	Total		100.00	634.0	672.8	100.000

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