# Enantioselective cascade formal reductive insertion of allylic alcohols into C(O)-C bond of 1,3-diketones: ready access to synthetically valuable 3-alkylpentanol units

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# General informations

NMR spectra were recorded on a Bruker AC 300 (300 MHz) or a Bruker AC 400 (400 MHz) spectrometer in $CDCl_3$ in general. Chemical shifts are given in ppm, using as internal standards the residual $CHCl_3$ signal for $^1H$ NMR ($\delta$ = 7.26) and the deuterated solvent signal for $^{13}C$ NMR ($\delta$ = 77.0). Data for $^{13}C$ NMR are reported as follows: chemical shift (multiplicity). Data for $^1H$ NMR are reported as follows: chemical shift (multiplicity [s = singulet, d = doublet, t = triplet, q = quadruplet, m = multiplet, br = broad], coupling constants *J* in Hertz (Hz), integration).

Anhydrous toluene (PhMe), tetrahydrofuran (THF), diethylether ($Et_2O$) and dichloromethane ($CH_2Cl_2$) were obtained from on a Solvent Purification System M Braun SPS-800. Unless specified, the other solvents were used in their commercial form without further purification. Xylene was used in its commercial form and conserved over activated molecular sieves (4Å).

Thin-Layer Chromatography (TLC) were developed on silica Merck 60F254 and revealed under UV lamp ($\lambda$ = 254 nm) and with universal stain: p-Anisaldehyde (prepared with 30g of ice, 60 mL of EtOH, 5 mL of $H_2SO_4$, 5 mL of p-anisaldehyde and 0.5 mL of AcOH). Flash Chromatography was performed following the method of Still on 40 – 63 μm silica gel eluted with the specified eluent.

High resolution mass spectra (HRMS) were performed on a QStar Elite (Applied Biosystems SCIEX) spectrometer equipped with atmospheric pression ionization source (API) pneumaticly assisted. Samples were ionized by positive electrospray mode as follows: electrospray tension (ISV): 5500 V; opening tension (OR): 50 V; nebulization gas pression (air): 20 psi.

Chiral HPLC analyses were performed at the Chiral Chromatography Laboratory of Aix Marseille University (ISM2, Laboratoire de Stéréochimie Dynamique et Chiralité).The screening of chiral stationary phases was performed on two chromatographic units:

1) Merck-Lachrom unit : Merck D-7000 system manager, Merck-Lachrom L-7100 pump, Merck-Lachrom L-7200 autosampler, Merck-Lachrom L-7360 oven, Merck-Lachrom L-7400 UV-detector, with EZChrom Elite software.

2) Lachrom-Elite unit : L-2130 pump, L-2200 autosampler, L-2350 oven and DAD L-2455 detector.

- The samples were also detected by detectors of chirality : Jasco OR-1590 polarimeter or Jasco CD-1595 detector. The sign given by the on-line polarimeter is the sign of the enantiomers in the solvent used for the chromatographic separation. The sign given by the on-line circular dichroism detector is the sign of the enantiomers in the solvent used for the chromatographic separation, at the chosen wavelength.
- Hexane, 2-PrOH and ethanol, HPLC grade, from Hipersolv Chromanorm (VWR), were degassed and filtered on a 0.45 μm millipore membrane before use. Retention times Rt in minutes, retention factors ki = (Rti-Rt0)/Rt0 and enantioselectivity factor $\alpha$ = k2/k1 are given. Rt0 was determined by injection of tri-tertio-butyl benzene.
- The different analytical columns (250x46 mm)® tested are Chiralcel OD-3, OJ-H, Chiralpak® AS-H, AD-H, AZ-H, IA, IB and IC columns from Chiral Technology Europa (Illkirch, France), Lux-Amylose-2, Lux-Cellulose-2 and Lux-Cellulose-4, from Phenomenex and Whelk-O1 (S,S) and Ulmo (S,S) from Regis Technologies (Morton Grove, USA).

Chiral GC analysis were preformed on a HP 4890 using 6 bar argon as vector. Column: 25m/0,25 mm. Chromatogram analyzed with ChromNav software.

Optical rotations were measured at 20 °C in $CHCl_3$ with a Anton Paar MCP 200 polarimeter with a 0.2 cm length.

All commercially available reagents were used as received except cinnamyl alcohol, distilled prior to use.

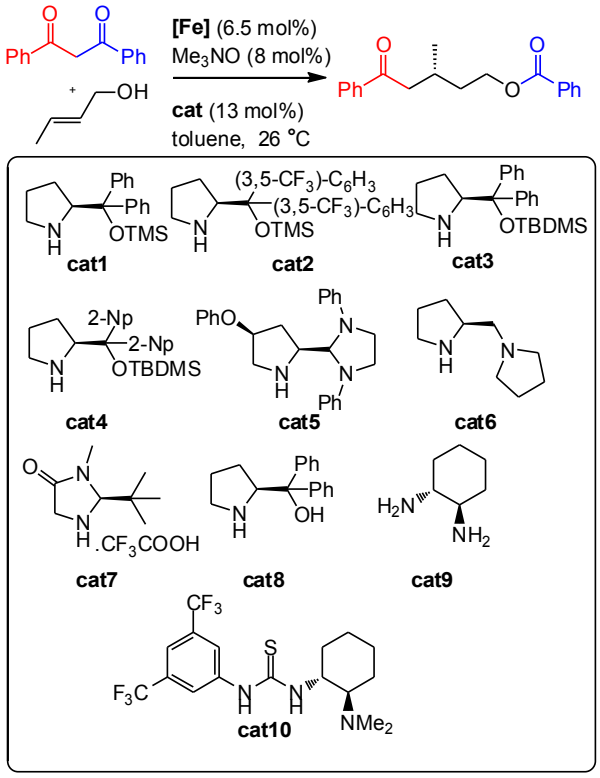
Knolker complex **[Fe]**,[1] was prepared according to known literature procedure. 2-acetyl-3,4-dihydronaphthalen-1(2H)-one and 2-acetyl-2,3-dihydro-1H-inden-1-one (from ethyl acetate as acylating reagent),[2] 4-hydroxybut-2-en-1-yl benzoate,[3] 5-phenylpent-2-en-1-ol,[4] 1,3-bis(4-fluorophenyl)propane-1,3-dione,[5] were prepared according to known literature procedures.

HPLC/GC racemates were prepared by using a *R* and *S* mixture of aminocatalyst **cat1**.

[1] T. N. Plank, J. L. Drake, D. K. Kim, T. W. Funk, *Adv. Synth. Catal.* **2012**, *354*, 597.
[2] A. J. Grenning, J. A. Tunge, *J. Am. Chem. Soc.* **2011**, *133*, 14785.
[3] M. Takeda, R. Shintani, T. Hayashi, *J. Org. Chem.* **2013**, *78*, 5007.
[4] B. Tessie, D. Jakob, M. Maziar, R. Per, S. Peter, *Adv. Synth. Catal*, **2011**, 353, 2022.
[5] T. Choshi, S. Horimoto, C. Y. Wang, H. Nagase, M. Ichikawa, E. Sugino, S. Hibino, *Chem. Pharm. Bull.* **1992**, *40*, 1047.

## Optimization of the cascade:

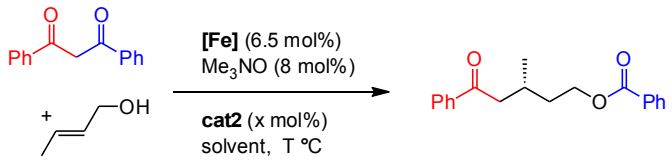
**Table 1.** Catalyst screening




| Entry | Catalyst | Yield | *er* |
|---|---|---|---|
| 1 | **cat1** | 59% | 78:22 |
| 2 | **cat2** | **51%** | **85.5:14.5** |
| 3 | **cat3** | 74% | 83.5:16.5 |
| 4 | **cat4** | **58%** | **86:14** |
| 5 | **cat5** | 59% | 78.5:21.5 |
| 6 | **cat6** | 48% conv | nd |
| 7 | **cat7** | <10% | nd |
| 8 | **cat8** | 57% | 53:47 |
| 9 | **cat9** | 15% | 55:45 |
| 10 | **cat10** | <10% | nd |

Reactions run using 0.2 mmol of diketone and 0.4 mmol of crotyl alcohol. Reaction time = 62-66h nd = not determined. conv = conversion.

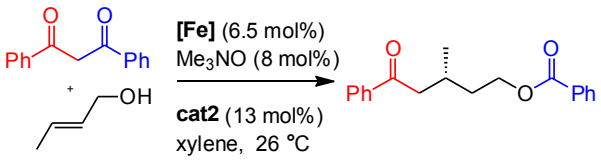
**Table 2.** Reaction optimization




| Entry | Solvent | T°C | x mol% | **Crotyl alcohol** eq | Yield | *er* |
|---|---|---|---|---|---|---|
| 1 | toluene | 26 | 13% | 2 | 51% | 85.5:14.5 |
| 2 | $CH_2Cl_2$ | 26 | 13% | 2 | 29% | 81:19 |
| 3 | *n*-hexane | 26 | 13% | 2 | 65% | 79:21 |
| 4 | 1,4-dioxane | 26 | 13% | 2 | 57% | 88.5:11.5 |
| 5 | xylene | 26 | 13% | 2 | 71% | 89:11 |
| 6 | Cl-$C_6H_5$ | 26 | 13% | 2 | 60% | 83:17 |
| 7 | $CF_3$-$C_6H_5$ | 26 | 13% | 2 | 67% | 84:16 |
| 8 | $CH_3CN$ | 26 | 13% | 2 | <10% | nd |
| 9 | xylene | 26 | 8% | 2 | 65% | 89:11 |
| 10 | xylene | 26 | 5% | 2 | 59% | 87.5:12.5 |
| 11 | xylene | 26 | 13% | 1.1 | 44% | 86.5:13.5 |
| 12[a] | xylene | 10 | 13% | 2 | 27% | 86:14 |
| 13[b] | xylene | 20 | 13% | 2 | 81% | 89:11 |
| **14[b,c]** | **xylene** | **20** | **13%** | **2** | **96%** | **90:10** |

Reactions run using 0.2 mmol of diketone. Reaction time = 66h**.** nd = not determined. Xylene refers to an isomer mixture of xylene. [a] reaction time = 96h. [b] Use of $Me_3NO.2H_2O$ (10 mol%) instead of $Me_3NO$. [c] Aqueous $NH_4Cl$ treatment instead of direct filtration over silica gel.

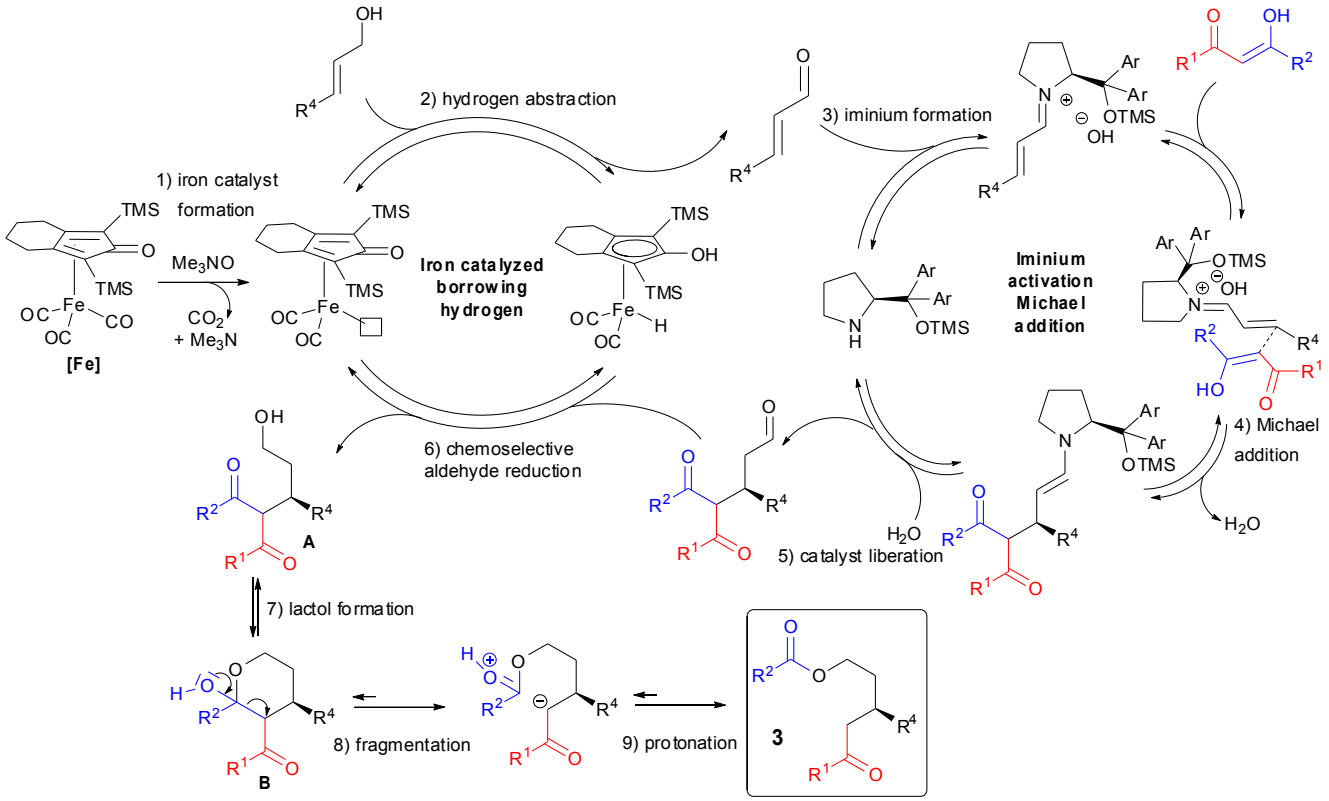
## Use of additives in the cascade:




**additives:** -MS 4Å: 9% yield
-LiOAc (2 eq): 31% yield, 85.5: 14.5 *er*
-PhCOOH (13 mol%): 42% conversion

# Mechanism of the cascade:

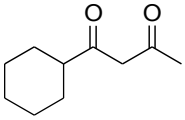
The proposed mechanism of the reaction is depicted in scheme 1. The reaction is initiated by decoordination of one CO from the iron complex by the oxidative addition of $Me_3NO$ (step 1). The active iron complex is then able to abstract hydrogen from the allylic alcohol (step 2) leading to the α,β-unsaturated aldehyde. This aldehyde is then activated by the organocatalyst leading to the iminium ion (step 3) that can then react with the enol. Addition occurs from the less hindered face giving as the major product the depicted enantiomer (step 4). Catalyst liberation (step 5) provides the aliphatic aldehyde that is chemoselectively reduced in the presence of two ketones by the iron hydride in step 6 to give hydroxy 1,3-diketone A precursor of the key lactol intermediate B (step 7). The presence of the second ketone as electron-withdrawing group on this lactol is crucial to favor the next ring opening (step 8) that gives after final reprotonation the expected products 3. The fragmentation occurs spontaneously at temperature ranging from 20 to 40°C and does not require any external reagents (no base). The differences in reactivity observed between the different ketones make it hard for now to determine the rate determining step of this complex system that can also be substrate dependent.




**Scheme 1.** Mechanism of the cascade transformation

# Experimental section:

Preparation of 1-cyclohexylbutane-1,3-dione **1l**:



To a solution of 683 mg of NaH (60% in oil, 23.83 mmol, 3 eq) in 6 ml of dry THF at room temperature under argon was slowly added 1.024 g of 1-cyclohexylethan-1-one (8.1 mmol, 1 eq) and the mixture stirred at room temperature under argon for 20 minutes. 1.4 ml of dry EtOAc was then added, the schlenck tube sealed ans stirred at 60°C for one hour. 8 ml of saturated aqueous $NH_4Cl$ were then carefully added, the aqueous phase extracted by 3 times 10 ml diethyl ether, the organic layer washed by 10 ml brine, dried over $Na_2SO_4$, filtered and the solvent evaporated. Purification over silica gel (petroleum ether/ethyl acetate (9/1) gave 849 mg of the diketone as a pale yellow oil. 5,04 mml, 62% yield.

$R_f$ = 0.39 (petroleum ether / ethyl acetate (7/3)).

NMR of the product indicated a 0,27/1 ratio between diketone and enol form.

$^1$H NMR (300 MHz, $CDCl_3$): δ (ppm) = 1.12-1.83 (m, 10H $CH_2$ of cyclohexyl), 2.04 (s, $CH_3$), 2.09-2.15 (m, CH of cyclohexyl), 2.19 ($CH_3$ of diketone form), 3.57 ($CH_2$ of diketone form), 5.46 (s, CH of enol), 15.59 (s, OH). $^{13}$C NMR (75 MHz, $CDCl_3$) (only the enol form is described): δ (ppm) = 25.1 ($CH_3$), 25.4 ($CH_2$), 25.7 ($CH_2$), 28.0 ($CH_2$), 46.2 (CH), 97.9 (CH), 192.3 (CO), 196.9 ((OH)*C*=C). Datas are in agreement with the literature.[6]

# General method:

## General procedure for the redox neutral alcohol fonctionalization acyl transfer cascade :

To a solution of 1,3-diketone (0.2 mmol, 1 eq) in 0.6 ml of xylene is successively added 15,5 mg of (*S*)-diaryl prolinol TMS-ether **cat2** (0.026 mmol, 13 mol%) and 0.4 mmol of allyl alcohol (2.0 eq). 5.4 mg of Knölker complex **[Fe]** (0.013 mmol, 6.5 mol%) and 2.4 mg of $Me_3NO.2H_2O$ (0.02 mmol, 10 mol%) are then added all at once. Argon is immediately passed through the vial for 20 secondes, the vial closed and stirred at room temperature (20-23ºC) for the indicated time. 1.5 ml of saturated aqueous $NH_4Cl$ are then added, the aqueous layer extracted by three times 2 ml diethyl ether, the combined organic layers dried over $Na_2SO_4$, and filtered. The resulting solution is placed at 40°C on the rota-vapor for 5-15 minutes and the solvent evaporated. Purification over silica gel (petroleum ether/ethyl acetate unless specified) directly yields the corresponding rearranged products.

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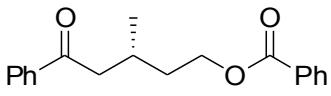


**Compound 3a.** According to the general procedure using **cat2** and starting from 44.9 mg (0.2 mmol) of 1,3 di-ketone. Reaction time = 66 h. The product was isolated as a pale yellow oil. 57.1 mg (0.192 mmol). 96% yield.

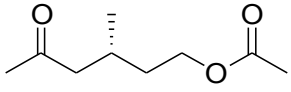
$R_f$ = 0.48 (petroleum ether / ethyl acetate (7/3)). $[\alpha]^{20}_D$ = -67.4º ($CHCl_3$, c = 3.0), 90:10 *er*).

$^1$H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.07 (d, *J* = 6.8 Hz, $CH_3$), 1.71-1.79 (m, 1H of $CH_2$), 1.87-1.94 (m, 1H of $CH_2$), 2.87 (dd (AB), *J* = 16.2; 7.7 Hz, 1H of $CH_2$), 3.04 (dd (AB), *J* = 16.2; 5.9 Hz, 1H of $CH_2$), 4.36-4.45 (m, $CH_2$), 7.40-7.96 (m, 6H arom), 7.92-8.02 (m, 4H arom). $^{13}$C NMR (100 MHz, $CDCl_3$): δ (ppm) = 19.9 ($CH_3$), 26.9 (CH), 35.5 ($CH_2$), 45.6 ($CH_2$), 63.0 ($CH_2$), 128.0 (CH arom), 128.3 (CH arom), 128.5 (CH arom), 129.5 (CH arom), 130.3 (C arom), 132.8 (CH arom), 132.9 (CH arom), 137.2 (C arom), 166.6 (COO), 199.5 (CO).

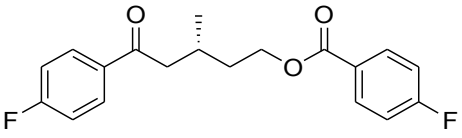
HPLC determination: Chiralpak ID, Heptane/Ethanol 90/10, 1 ml/min, DAD and polarimeter: rt (maj) = 7.5 min;

[6] V. Fargeas, M. Baalouch, E. Metay, J. Baffreau, D. Ménard, P. Gosselin, J-P. Bergé, C. Barthomeuf, J. Lebreton, *Tetrahedron* **2004**, *60*, 10359.

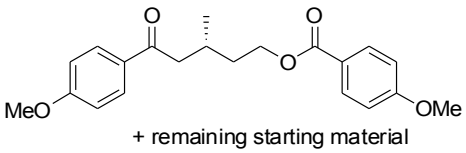
rt (min) = 9.9 min.
HRMS ESI $[M+H]^+$ calcd for $C_{19}H_{20}O_3$: 297.1485. Observed: 297.1486.



**Compound 3b.** According to the general procedure using **cat2** and starting from 20.1 mg (0.2 mmol) of 1,3 di-ketone. Reaction time = 66 h. The product was isolated as a pale yellow oil. 32.4 mg (0.188 mmol). 94% yield.
$R_f$ = 0.32 (petroleum ether / ethyl acetate (8/2)). $[\alpha]^{20}_D$ = -41.6 ($CHCl_3$, c = 0.92, 90:10 *er*).
$^1$H NMR (400 MHz, $CDCl_3$): δ (ppm) = 0.92 (d, *J* = 6.8 Hz, $CH_3$), 1.44-1.52 (m, 1H of $CH_2$), 1.59-1.68 (m, 1H of $CH_2$), 2.03 (s, $CH_3$), 2.07-2.17 (m, $CH_3$ and CH), 2.29 (dd (AB), *J* = 16.4; 7.9 Hz, 1H of $CH_2$), 2.44 (dd (AB), *J* = 16.4; 5.7 Hz, 1H of $CH_2$), 4.02-4.14 (m, $CH_2$). $^{13}$C NMR (100 MHz, $CDCl_3$): δ (ppm) = 19.6 ($CH_3$), 21.0 ($CH_3$), 26.1 (CH), 30.4 ($CH_3$), 35.2 ($CH_2$), 50.7 ($CH_2$), 62.4 ($CH_2$), 171.1 (COO), 208.1 (CO).
Chiral GC analysis: Hydrodex-β-3P, 70°C-60min-1°C/min-150°C. rt (min)= 88.8 min; rt (maj) = 91.2 min.
HRMS ESI $[M+H]^+$ calcd for $C_9H_{17}O_3$: 173.1172. Observed: 173.1172.

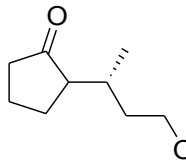


**Compound 3c.** According to the general procedure using **cat2** and starting from 52.6 mg (0.2 mmol) of 1,3 di-ketone. Reaction time = 47 h. The product was isolated as a pale yellow oil. 47.1 mg (0.141 mmol). 75% yield.
$R_f$ = 0.59 (petroleum ether / ethyl acetate (9/1)). $[\alpha]^{20}_D$ = -34.8° ($CHCl_3$, c= 0.030, 86:14 *er*).
$^1$H NMR (400 MHz, $CDCl_3$) δ (ppm) = 1.07 (d, *J* = 6.8 Hz; $CH_3$) 1.72 (td, *J* = 14.0; 6.4 Hz, 1H of $CH_2$), 1.90 (td, (AB) *J* = 13.6; 7.2 Hz, 1H of $CH_2$), 2.38-2.45 (m, CH), 2.86 (dd, (AB) *J* = 7.6; 16.4 Hz, 1H of $CH_2$), 3.00 (dd, (AB) *J* = 6.4; 16.4 Hz, 1H of $CH_2$), 4.29-4.47 (m, $CH_2$), 7.10 (dd, *J* = 8.4, 16.3 Hz, 4H arom), 7.97 (dd, *J* = 5.5, 8.7 Hz, 2H arom), 8.02 (dd, *J* = 5.5, 8.7 Hz, 2H arom), $^{13}$C NMR (75 MHz, $CDCl_3$) *δ* 19.9 ($CH_3$), 26.8 (CH), 35.4 ($CH_2$), 45.5 ($CH_2$), 63.1 ($CH_2$), 115.5 (CH arom, d, *J* = 15 Hz), 115.8 (CH arom, d, *J* = 14 Hz), 126.5 (C arom, d, *J* = 3 Hz), 130.7 (CH arom, d, *J* = 10 Hz), 132.1 (CH arom, d, *J* = 9 Hz), 133.6 (C arom, d, *J* = 3 Hz), 165.8 (COO), 165.7 (C arom-F, d, *J* = 253 Hz), 165.8 (C arom-F, d, *J* = 253 Hz), 197.9 (CO). $^{19}$F NMR (376 MHz, $CDCl_3$) δ (ppm) = -105.72 (tt, *J* = 5.5, 13.7 Hz), -105.30 (tt, *J* = 5.5, 13.6 Hz).
HPLC determination : Lux-Amylose-2, Heptane/Isopropanol 90/10, 1 mL.min$^{-1}$, UV 254 nm et polarimetre, rt (maj) = 12.3 min, rt (min) = 17.7 min.
HRMS (ESI) Found $[M+H]^+$ m/z 333.1297, $[C_{19}H_{19}O_3F_2]^+$ calculated 333.1297.

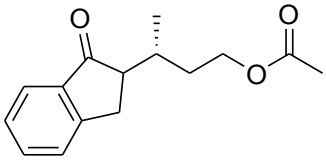


+ remaining starting material

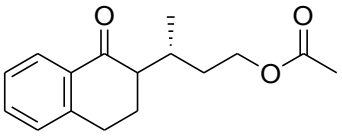
**Compound 3d.** According to the general procedure using **cat2** and starting from 55.9 mg (0.2 mmol) of 1,3 di-ketone. Reaction time = 66 h. Conversion was not total and the remaining diketone could not be separated from the product.
$R_f$ = 0.29 (petroleum ether / ethyl acetate (8/2)). $[\alpha]^{20}_D$ = -22.5º ($CHCl_3$, c = 0.95, 90:10 *er*).
NMR of a mixture of the product with around 30% of remaining starting material. $^1$H NMR (300 MHz, $CDCl_3$): δ (ppm) = 1.07 (d, *J* = 6.6 Hz, $CH_3$), 1.71-1.88 (m, 2 $CH_2$), 2.39-2.44 (m, CH), 2.80 (dd (AB), *J* = 15.8; 7.7 Hz, 1H of $CH_2$), 2.98 (dd (AB), *J* = 15.8; 6.0 Hz, 1H of $CH_2$), 3.85 (s, 2 CH3), 4.35-4.39 (m, $CH_2$), 6.88-6.99 (m, 4 CH arom), 7.91-7.99 (m, 4 CH arom). $^{13}$C NMR (75 MHz, $CDCl_3$): δ (ppm) = 20.0 ($CH_3$), 27.1 (CH), 35.5 ($CH_2$), 45.3 ($CH_2$), 55.4 ($CH_3$), 55.5 ($CH_3$), 62.7 ($CH_2$), 113.5 (CH arom), 113.7 (CH arom), 122.7 (C arom), 129.0 (C arom), 130.3 (CH arom), 130.4 (CH arom), 131.5 (CH arom), 163.4 (COO), 198.2 (CO).
HPLC determination: Chiralpak ID, Heptane/Ethanol 90/10, 1 ml/min, DAD: rt (maj) = 7.8 min; rt (min) = 10.3 min.



**Compound 3e.** According to the general procedure using **cat2** and starting from 25.1 mg (0.2 mmol) of 1,3 di-ketone. Reaction time = 68 h. The product was isolated as a pale yellow oil in a 55:45 *dr*. 30.9 mg (0.156 mmol). 78% yield, 55:45 *dr* and 86:14 *er* on both dias).
$R_f$= 0.27 (petroleum ether / ethyl acetate (8/2)).
NMR mixture of the two diastereoisomers. $^1$H NMR (400 MHz, $CDCl_3$): δ (ppm) = 0.79 (d, *J* = 6.8 Hz, $CH_3$, minor dia), 0.99 (d, *J* = 6.8 Hz, $CH_3$, major dia), 1.49-1.77 (m, 4H), 1,99-2,34 (9H), 3.98-4.17 (m, CH2). $^{13}$C NMR (75 MHz, $CDCl_3$): δ (ppm) = 15.3 ($CH_3$, minor dia), 17.5 ($CH_3$, minor dia), 20.6 ($CH_2$, both dia), 20.9 ($CH_3$, both dia), 23.8 ($CH_2$, minor dia), 25.5 ($CH_2$, minor dia), 28.7 (CH, minor dia), 29.3 (CH, major dia), 32.1 ($CH_2$, major dia), 33.9 ($CH_2$, minor dia), 39.1 ($CH_2$, both dia), 53.4 (CH, minor dia), 54.4 (CH, minor dia), 62.5 ($CH_2$, minor dia), 62.8 ($CH_2$, major dia), 171.1 (COO, both dia), CO > 210 ppm.
GC determination: Lipodex-e, 70 °C-0 min-1 °C/min-150 °C : major dia: rt (maj) = 50.9 min; rt (min) = 54.1 min; minor dia: rt (maj) = 52.5 min; rt (min) = 52.9 min.
HRMS ESI $[M+H]^+$ calcd for $C_{11}H_{19}O_3$: 199.1329. Observed: 199.1327.

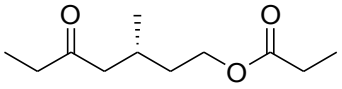


**Compound 3f.** According to the general procedure using **cat2** and starting from 34.8 mg (0.2 mmol) of 1,3 di-ketone. Reaction time = 83 h. The product was isolated as a pale yellow oil. 37.2 mg (0.150 mmol). 75% yield.
$R_f$= 0.26 (petroleum ether / ethyl acetate (9/1)). (80:20 *er*, 59:41 *dr*).
$^1$H NMR (300 MHz, $CDCl_3$) δ 0.78 (d, *J* = 7.2 Hz, $CH_3$ dia 1), 1.02 (d, *J* = 6.9 Hz, $CH_3$ dia 2), 1.47 – 1.84 (m, 2x$CH_2$ dia 1 and 2), 2.00 (s, $CH_3$ dia 2), 2.07 (s, $CH_3$ dia 1), 2.23-2.40 (m, CH dia 2), 2.41-2.57 (m, CH dia 1), 2.75 (m, 2x1H of $CH_2$ dia 1 and 2), 2.85-3.02 (m, 2x1H of $CH_2$ dia 1 and 2), 3.06 – 3.33 (m, 2xCH dia 1 and 2), 3.94-4.28 (m, 2x$CH_2$ dia 1 and 2), 7.36 (m, 2x1H arom dia 1 and 2), 7.45 – 7.50 (m, 2x1H arom dia 1 and 2), 7.55-7.62 (m, 2x1H arom dia 1 and 2), 7.74 (m, 2x1H arom dia 1 and 2). $^{13}$C NMR (75 MHz, ) δ (ppm) = 14.5 ($CH_3$ dia 1), 17.2 ($CH_3$ dia 2), 20.9 ($CH_3$ dia 1), 21.0 ($CH_3$ dia 2), 27.7 ($CH_2$ dia 1), 29.4 ($CH_2$ dia 2), 29.7 ($CH_2$ dia 1), 30.5 (CH dia 1), 31.3 (CH dia 2), 33.8 (CH dia 2), 51.3 (CH dia 1), 52.1 (CH dia 2), 62.6 ($CH_2$ dia 1), 62.8 ($CH_2$ dia 2), 123.7 (CH arom dia 1), 123.7 (CH arom dia 2), 126.5 (CH arom dia 1), 126.5 (CH arom dia 2), 127.4 (2xCH arom dia 1 and 2), 134.7 (CH arom dia 1), 134.7 (CH arom dia 2), 137.5 (C arom dia 1), 137.6 (C arom dia 2), 153.8 (C arom dia 1), 153.9 (C arom dia 2), 171.1 (COO dia 1), 171.2 (COO dia 2), 208.1 (CO dia 1), 208.4 (CO dia 2).
HPLC determination : Lux-cellulose-2, Heptane/Isopropanol 95/5, 1mL.min$^{-1}$, UV 254 nm and polarimeter, rt (min, dia1) = 19.4 min, rt (maj, dia1) = 22.1 min, rt (min, dia2) = 23.8 min, rt (maj, dia2) = 29.6 min.
HRMS (ESI) Found $[M+H]^+$ m/z 247.1326, $[C_{15}H_{19}O_3]^+$ calculated 247.1329.



**Compound 3g.** According to the general procedure using **cat2** and starting from 37.5 mg (0.2 mmol) of 1,3 di-ketone. Reaction time = 108 h. The product was isolated as a pale yellow oil. 44.5 mg (0.141 mmol). 85% yield.
$R_f$= 0.42 (petroleum ether / ethyl acetate (9/1)). (87.5:12.5 *er*, 55:45 *dr*).
$^1$H NMR (300 MHz, $CDCl_3$) δ (ppm) = 0.70 (d, *J* = 6.8 Hz, $CH_3$ dia 1), 0.84 (d, *J* = 6.9 Hz, $CH_3$ dia 2), 1.33 (m, 1H of $CH_2$ dia 1 and 2), 1.43-1.64 (m, 1H of $CH_2$ dia 1 and 2), 1.63-1.79 (m, 1H of $CH_2$ dia 1 and 2), 1.82 (s, $CH_3$ dia 2), 1.84 (s, $CH_3$ dia 1), 1.87–2.01 (m, 1H of $CH_2$ dia 1 and 2), 2.15–2.34 (m, 2xCH dia1 and 2), 2.43 (m, 2xCH dia 1 and 2), 2.75–2.88 (m, 2x$CH_2$ dia 1 and 2), 3.84-4.05 (m, 2x$CH_2$ dia 1 and 2), 7.03 (m, 2H arom dia 1 and 2), 7.11 (m, 2H arom dia 1 and 2), 7.22–7.29 (m, 2H arom dia 1 and 2), 7.79–7.86 (m, 2H arom dia 1 and 2).$^{13}$C NMR (75 MHz, $CDCl_3$) *δ* (ppm) = 15.7 ($CH_3$ dia 1), 17.4 ($CH_3$ dia 2), 20.9 ($CH_3$ dia 1), 21.0 ($CH_3$ dia 2), 23.2 ($CH_2$ dia 1), 24.2 ($CH_2$ dia 2), 28.3 ($CH_2$ dia 1), 28.9 ($CH_2$ dia 2), 29.1 (CH dia 1), 29.1 (CH dia 2), 32.0 ($CH_2$ dia 1), 33.2 ($CH_2$ dia 2), 52.1 (CH dia 1), 53.3 (CH dia 2), 62.9 ($CH_2$ dia 1), 63.3 ($CH_2$ dia 2), 126.6 (CH arom dia 1 and 2), 127.4 (CH arom dia 1 and 2), 128.6 (CH arom dia 1 and 2), 132.9 (CH arom dia 1), 132.9 (CH arom dia 2), 133.1 (C arom dia 1), 133.2 (C arom dia 2), 143.8 (C arom dia 1), 143.9 (C arom dia 2), 171.1 (COO dia 1), 171.2 (COO dia 2), 199.1 (CO dia 1), 199.2 (CO dia 2).
HPLC determination : (S,S)-Whelk-O1, Heptane/isopropanol 70/30, 1 mL.min$^{-1}$, UV 254 nm et CD254nm, rt (maj, dia1) = 12.1 min, rt (min, dia1) = 15.2 min, rt (min, dia2) = 14.2, rt (maj, dia2) = 17.3 min.

HRMS (ESI) Found $[M+H]^+$ m/z 261.1478, $[C_{16}H_{21}O_3]^+$ calculated 261.1485.



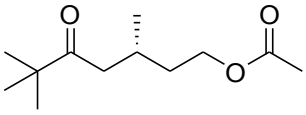
**Compound 3h.** According to the general procedure using **cat1** and starting from 25.5 mg (0.2 mmol) of 1,3 di-ketone. Reaction time = 47 h. The product was isolated as an orange oil. 28.1 mg (0.185 mmol). 70% yield.

$R_f$= 0.56 (petroleum ether / ethyl acetate (9/1)). $[\alpha]^{20}_D$ = -17.6° ($CHCl_3$, c= 0.050, 90:10 *er*).

$^1$H NMR (400 MHz, $CDCl_3$) δ 0.94 (d, *J* = 9.6 Hz, $CH_3$), 1.06 (t, *J* = 7.5 Hz, $CH_3$), 1.15 (t, *J* = 7.2 Hz, $CH_3$), 1.44-1.55 (m, 1H of $CH_2$), 1.61-1.71 (m, 1H of $CH_2$), 2.10-2.23 (m, CH), 2.24-2.47 (m, 3x$CH_2$), 4.11 (m, $CH_2$). $^{13}$C NMR (75 MHz, $CDCl_3$) δ (ppm) = 7.7 ($CH_3$) 9.1 ($CH_3$), 19.7 ($CH_3$), 26.2 (CH), 27.6 ($CH_2$), 35.3 ($CH_2$), 36.6 ($CH_2$), 49.4 ($CH_2$), 62.3 ($CH_2$), 174.5 (COO), 210.8 (CO).

GC determination : Hydrodex, method 120 min at 90 °C then 1 °C.min$^{-1}$ to 150 °C, rt (min) = 119.4 min, rt (maj) = 122.0 min.

HRMS (ESI) Found $[M+H]^+$ m/z 201.1486, $[C_{11}H_{21}O_3]^+$ calculated 201.1485.



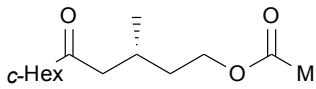
**Compound 3i.** According to the general procedure using **cat1** and starting from 142.3 mg (1.0 mmol) of 1,3 di-ketone. Reaction time = 63 h. The product was isolated as a red oil. 105.2 mg (0.491 mmol). 49% yield.

$R_f$ = 0.56 (petroleum ether / ethyl acetate (9/1)). $[\alpha]^{20}_D$ = -13.2° ($CHCl_3$, c= 0.047, 93.5:6.5 *er*).

$^1$H NMR (300 MHz, $CDCl_3$) δ (ppm) = 0.90 (d, *J* = 6.6 Hz, $CH_3$), 1.12 (s, 3x$CH_3$), 1.46 (m, 1H of $CH_2$), 1.65 (m, 1H of $CH_2$), 2.04 (s, $CH_3$), 2.26-2.12 (m, CH), 2.38 (dd, (AB) *J* = 6.3; 17.4 Hz, 1H of $CH_2$), 2.45 (dd, (AB) *J* = 7.2; 17.4 Hz, 1H of $CH_2$), 4.00-4.17 (m, $CH_2$). $^{13}$C NMR (75 MHz, $CDCl_3$) δ (ppm) = 19.7 ($CH_3$), 21.0 ($CH_3$), 25.7 (CH), 26.4 ($CH_3$), 35.2 ($CH_2$), 43.6 (Cquat), 44.2 ($CH_2$), 62.6 ($CH_2$), 171.2 (COO), 214.9 (CO).

GC determination : Lipodex E, method 60 min at 80 °C, then 1 °C.min$^{-1}$ to 150 °C, rt (min) = 70.9 min, rt (maj) = 71.7 min.

HRMS (ESI) Found $[M+NH_4]^+$ m/z 232.1906, $[C_{12}H_{26}NO_3]^+$ calculated232.1907.



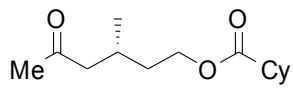
**Compound 3j.** According to the general procedure using **cat1** and starting from 33,9 mg (0.2 mmol) of 1,3 di-ketone. Reaction time = 48 h. The product was isolated as a pale yellow oil. 24.9 mg (0.103 mmol). 52% yield.

$R_f$= 0.42 (petroleum ether / ethyl acetate (7/3)). $[\alpha]^{20}_D$ = -8,6º ($CHCl_3$, c = 0.72, 92.5:7.5 *er*).

$^1$H NMR (300 MHz, $CDCl_3$): δ (ppm) = 0,91 (d, *J* = 6.6 Hz, $CH_3$), 1.21-1.84 (m, 6 $CH_2$), 2.04 (s, $CH_3$), 2.09-2.44 (m, $CH_2$ and 2CH), 4.03-4.13 (m, $CH_2$). $^{13}$C NMR (75 MHz, $CDCl_3$): δ (ppm) = 19.7 ($CH_3$), 21.0 ($CH_3$), 25.6 ($CH_2$), 25.7 ($CH_2$), 25.8 ($CH_2$), 25.9 (CH), 28.3 ($CH_2$), 28.4 ($CH_2$), 35.2 ($CH_2$), 47.7 ($CH_2$), 51.2 (CH), 62.5 ($CH_2$), 171.1 (COO), 213.3 (CO).

Chiral GC analysis on the corresponding diol obtained trough $LiAlH_4$ reduction: Lipodex-E, 130°C-60min-1°C/min-150°C. rt (maj)= 63.9 min; rt (min) = 95.7 min

HRMS ESI $[M+H]^+$ calcd for $C_{14}H_{25}O_3$: 241.1798. Observed: 241.1797.



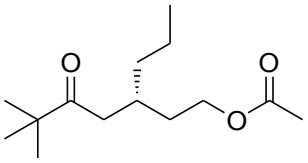
**Compound 3k.** According to the general procedure using **cat1** and starting from 33,9 mg (0.2 mmol) of 1,3 di-ketone. Reaction time = 48 h. The product was isolated as a pale yellow oil. 16.4 mg (0.0682 mmol). 34% yield.

$R_f$= 0.37 (petroleum ether / ethyl acetate (7/3)). $[\alpha]^{20}_D$ = -10.4º ($CHCl_3$, c = 1.04, 96:4 *er*).

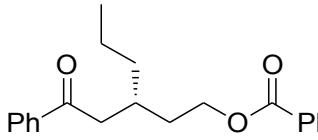
$^1$H NMR (300 MHz, $CDCl_3$): δ (ppm) = 0,94 (d, *J* = 6.6 Hz, $CH_3$), 1.21-1.88 (m, 6 $CH_2$), 2.04-2.12 (CH), 2.13 (s, $CH_3$), 2.20-2.43 (m, $CH_2$ and 1CH), 4.03-4.13 (m, $CH_2$). $^{13}$C NMR (75 MHz, $CDCl_3$): δ (ppm) = 19.6 ($CH_3$), 25.4 ($CH_2$), 25.7 ($CH_2$), 26.2 ($CH_3$), 29.0 ($CH_2$), 30.4 (CH), 35.3 ($CH_2$), 43.2 (CH), 50.7 ($CH_2$), 62.0 ($CH_2$), 176.1 (COO), 208.2 (CO).

GC determination: Lipodex-E, 140°C-35 min: rt (min) = 25.3 min; rt (maj) = 29.2 min.

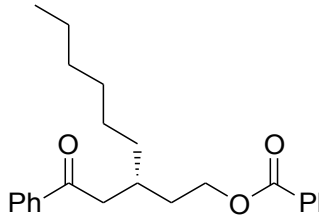
HRMS ESI $[M+H]^+$ calcd for $C_{14}H_{25}O_3$: 241.1798. Observed: 241.1797.



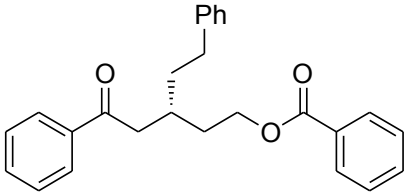
**Compound 3l.** According to the general procedure using **cat1** and starting from 28.7 mg (0.2 mmol) of 1,3 di-ketone. Reaction time = 38 h. The product was isolated as a yellow oil 21.1 mg (0.087 mmol). 43% yield.
$R_f$ = 0.57 (petroleum ether / ethyl acetate (95/5)). $[\alpha]^{20}_D$ = -30.0° ($CHCl_3$, c= 0.041, > 92% ee).
$^1$H NMR (300 MHz, $CDCl_3$) δ (ppm) = 0.88 (t, *J* = 6.6 Hz, $CH_3$), 1.13 (s, 3x$CH_3$), 1.18 – 1.32 (m, 2x$CH_2$), 1.51-1.67 (m, $CH_2$), 2.04 (s, $CH_3$), 2.10 (m, CH), 2.41 (dd, (AB) *J* = 17.7, 6.3 Hz, 1H of $CH_2$), 2.49 (dd, (AB) *J* = 17.7; 6.6 Hz, 1H of $CH_2$), 3.99-4.13 (m, $CH_2$).$^{13}$C NMR (75 MHz, $CDCl_3$) δ (ppm) = 14.2 ($CH_3$), 19.7 ($CH_2$), 21.0 ($CH_3$), 26.4 ($CH_3$), 29.9 (CH), 32.5 ($CH_2$), 36.2 ($CH_2$), 41.1 ($CH_2$), 44.2 (Cquat), 62.7 ($CH_2$), 171.2 (COO), 215.2 (CO).
HPLC determination on two different columns: Chiralpak AZ-H, Heptane/Ethanol 95/5, 1 ml/min, UV 310 nm: rt (maj) = 5.1 min; rt (min) = 5.5 min. Lux amylose-2, Heptane/Ethanol 95/5, 1 ml/min, UV 310 nm: rt (maj) = 5.8 min; rt (min) = 7.5 min.
HRMS (ESI) Found $[M+H]^+$ m/z 243.1955 $[C_{14}H_{27}O_3]^+$ calculated 243.1956, found $[M+NH_4]^+$ m/z 260.2221 $[C_{14}H_{30}NO_3]^+$ calculated 260.2220.



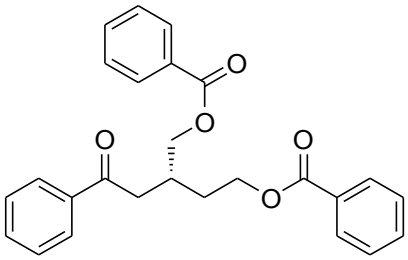
**Compound 3m.** According to the general procedure using **cat2** and starting from 44.3 mg (0.2 mmol) of 1,3 di-ketone. Reaction time = 68 h. The product was isolated as a pale yellow oil. 47.5 mg (0.146 mmol). 73% yield.
$R_f$ = 0.47 (petroleum ether / ethyl acetate (8/2)). $[\alpha]^{20}_D$ = -21.0º ($CHCl_3$, c = 2.1, 82:18 *er*).
$^1$H NMR (300 MHz, $CDCl_3$): δ (ppm) = 0.90 (t, *J* = 6.8 Hz, $CH_3$), 1.38-1.44 (m, 2 $CH_2$), 1.80-1.92 (m, $CH_2$), 2.34-2.39 (m, CH), 3.00 (d, *J* = 6.6 Hz, $CH_2$), 4.38 (t, *J* = 6.8 Hz, $CH_2$), 7.39-7.60 (m, 6H arom), 7.92-8.00 (m, 4H arom). $^{13}$C NMR (75 MHz, $CDCl_3$): δ (ppm) = 14.2 ($CH_3$), 19.8 ($CH_2$), 31.3 (CH), 32.7 ($CH_2$), 36.4 ($CH_2$), 43.2 ($CH_2$), 63.1 ($CH_2$), 35.5 ($CH_2$), 45.6 ($CH_2$), 63.0 ($CH_2$), 128.0 (CH arom), 128.3 (CH arom), 128.5 (CH arom), 129.5 (CH arom), 130.3 (C arom), 132.8 (CH arom), 132.9 (CH arom), 137.2 (C arom), 166.6 (COO), 199.8 (CO).
HPLC determination: Chiralcel OD-3, Heptane/Ethanol 90/10, 1 ml/min, UV 254nm and polarimeter: rt (min) = 5.1 min; rt (maj) = 6.3 min.
HRMS ESI $[M+H]^+$ calcd for $C_{21}H_{25}O_3$: 325.1798. Observed: 325.1797.



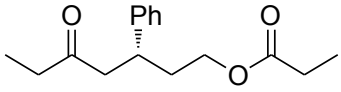
**Compound 3n.** According to the general procedure using **cat2** and starting from 44.6 mg (0.2 mmol) of 1,3 di-ketone. Reaction time = 68 h. The product was isolated as a pale yellow oil. 57.2 mg (0.156 mmol). 78% yield.
$R_f$ = 0.49 (petroleum ether / ethyl acetate (8/2)). $[\alpha]^{20}_D$ = -23.9º ($CHCl_3$, c = 1.14, 83.5:6.5 *er*).
$^1$H NMR (300 MHz, $CDCl_3$): δ (ppm) = 0.94 (t, *J* = 6.6 Hz, $CH_3$), 1.31-1.55 (m, 5 $CH_2$), 1.91-1.96 (m, $CH_2$), 2.39-2.46 (m, CH), 3.07 (d, *J* = 6.6 Hz, $CH_2$), 4.46 (t, *J* = 6.6 Hz, $CH2)_2$ 7.34-7.62 (m, 6H arom), 8.01-8.09 (m, 4H arom). $^{13}$C NMR (75 MHz, $CDCl_3$): δ (ppm) = 14.3 ($CH_3$), 22.8 ($CH_2$), 26.9 ($CH_2$), 29.7 ($CH_2$), 31.7 (CH), 32.0 ($CH_2$), 33.0 ($CH_2$), 34.3 ($CH_2$), 43.4 ($CH_2$), 63.4 ($CH_2$), 128.3 (CH arom), 128.5 (CH arom), 128.8 (CH arom), 129.7 (CH arom), 130.5 (C arom), 133.0 (CH arom), 133.2 (CH arom), 137.5 (C arom), 166.8 (COO), 200.1 (CO).
HPLC determination: Chiralpak Az-H, Heptane/Ethanol 90/10, 1 ml/min, UV 254nm and polarimeter: rt (maj) = 7.4 min; rt (min) = 8.2 min.
HRMS ESI $[M+H]^+$ calcd for $C_{24}H_{31}O_3$: 367.2268. Observed: 367.2266.



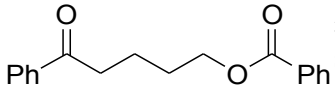

**Compound 3o.** According to the general procedure using **cat2** and starting from 45.1 mg (0.2 mmol) of 1,3 di-ketone. Reaction time = 43 h. The product was isolated as a red oil. 32.0 mg (0.065 mmol). 32% yield.
$R_f$ = 0.54 (petroleum ether / ethyl acetate (9/1)). $[\alpha]^{20}_D$ = -14.0° ($CHCl_3$, c= 0.026, 85:15 *er*).
$^1$H NMR (300 MHz, $CDCl_3$) δ (ppm) = 1.79 (m, $CH_2$), 1.91 (m, $CH_2$), 2.43 (m, CH), 2.70 (m, $CH_2$), 3.06 (d, *J* = 6.7 Hz, $CH_2$), 4.41 (t, *J* = 6.7 Hz, $CH_2$), 7.13-7.19 (m, 2H arom), 7.19-7.27 (m, 2H arom), 7.41 (m, 5H arom), 7.49-7.59 (m, 2H arom), 7.94 (m, 4H arom.). $^{13}$C NMR (75 MHz, $CDCl_3$) δ (ppm) = 31.3 (CH), 32.7 ($CH_2$), 33.1 ($CH_2$), 35.9 ($CH_2$), 43.1 ($CH_2$), 62.9 ($CH_2$), 125.8 (CH arom), 128.0 (CH arom), 128.3 (2xCH arom), 128.4 (CH arom), 128.6 (CH arom), 129.5 (CH arom), 130.2 (C arom), 132.8 (CH arom), 133.0 (CH arom), 137.1 (C arom), 141.9 (C arom), 166.6 (COO),199.6 (CO).
HPLC determination : Lux-Cellulose-4, Heptane/Isopropanol 95/5, 1 mL.min$^{-1}$, UV 254 nm et polarimetre, rt (min) = 12.7 min, rt (maj) = 13.9 min.
HRMS (ESI) Found $[M+H]^+$ m/z 387.1954, $[C_{26}H_{27}O_3]^+$ calculated 387.1955




**Compound 3p.** According to the general procedure using **cat2** and starting from 45.0 mg (0.2 mmol) of 1,3 di-ketone. Reaction time = 43 h. The product was isolated as a pale yellow oil 63.9 mg (0.166 mmol). 83% yield.
$R_f$ = 0.24 (petroleum ether / ethyl acetate (9/1)). $[\alpha]^{20}_D$ = -13.5° ($CHCl_3$, c= 0.025, 70:30 *er*).
$^1$H NMR (300 MHz, $CDCl_3$) δ (ppm) = 1.95 - 2.15 (m, $CH_2$), 2.90 (m, CH), 3.13 (dd, (AB) *J* = 6.3; 17.4 Hz, 1H of $CH_2$), 3.26 (dd, (AB) *J* = 6.6; 17.1 Hz, 1H of $CH_2$), 4.38-4.53 (m, 2x$CH_2$), 7.35-7.47 (m, 6H arom), 7.50-7.59 (m, 3H arom), 7.92-8.03 (m, 6H arom). $^{13}$C NMR (75 MHz, $CDCl_3$) δ (ppm) = 30.7 (CH), 31.6 ($CH_2$), 40.3 ($CH_2$), 62.8 ($CH_2$), 67.0 ($CH_2$), 128.1 (CH arom), 128.3 (CH arom), 128.4 (CH arom), 128.6 (CH arom), 129.6 (CH arom), 129.6 (CH arom), 129.9 (C arom), 130.1 (C arom), 132.9 (CH arom), 133.0 (CH arom), 133.2 (CH arom), 136.9 (C arom), 166.4 (COO), 166.5 (COO), 198.4 (CO).
HPLC determination : Chiralcel OD-3, Heptane/Ethanol 50/50, 1 mL.min$^{-1}$, UV 254 nm et polarimetre, rt (min) = 6.2 min, rt (maj) = 7.3 min.
HRMS (ESI) Found $[M+H]^+$ m/z 417.1697, $[C_{26}H_{25}O_5]^+$ calculated 417.1697.




**Compound 3q.** According to the general procedure using **cat2** and starting from 25.5 mg (0.2 mmol) of 1,3 di-ketone. Reaction time = 47 h. The product was isolated as a pale yellow oil. 39.3 mg (0.149 mmol). 75% yield.
$R_f$ = 0.42 (petroleum ether / ethyl acetate (9/1)). $[\alpha]^{20}_D$ = -28.1° ($CHCl_3$, c= 0.038, 86:14 *er*).
$^1$H NMR (300 MHz, $CDCl_3$) δ (ppm) = 0.95 (t, *J* = 7.3 Hz, $CH_3$), 1.10 (t, *J* = 7.6 Hz, $CH_3$), 1.80 - 2.07 (m, $CH_2$), 2.14 – 2.41 (m, 2x$CH_2$), 2.69 (dd, (AB) *J* = 6.9; 16.2 Hz, 1H of $CH_2$), 2.77 (dd, (AB) *J* = 7.2; 16.2 Hz, 1H of $CH_2$), 3.22 – 3.36 (m, CH), 3.84 (m, 1H of $CH_2$), 3.98 (m, 1H of $CH_2$), 7.13 – 7.23 (m, 3H arom), 7.26 – 7.34 (m, 2H arom). $^{13}$C NMR (75 MHz, $CDCl_3$) δ (ppm) = 7.5 ($CH_3$), 9.1 ($CH_3$), 27.5 ($CH_2$), 34.9 ($CH_2$), 36.7 (CH), 37.9 ($CH_2$), 49.3 ($CH_2$), 62.3 ($CH_2$), 126.7 (CH arom), 127.4 (2xCH arom), 128.6 (2xCH arom), 143.3 (C arom), 174.4 (COO), 209.8 (CO).
HPLC determination : Chiralpak IF, Hexane/Ethanol 95/5, 1 mL.min$^{-1}$, DAD and CD 254nm, rt (min) = 9.3 min, rt (maj) = 11.4 min.
HRMS (ESI) Found $[M+H]^+$ m/z 263.1642, $[C_{16}H_{23}O_3]^+$ calculated 263.1642.



**5-oxo-5-phenylpentyl benzoate:** According to the general procedure using **cat2** and starting from 44.2 mg (0.2 mmol) of 1,3 di-ketone and using 54 µl (0,8 mmol, 4 eq) of allyl alcohol. Reaction time = 66h. The product was isolated as a pale yellow oil after 66h. 38.9 mg (0.124 mmol). 62% yield.
$R_f$ = 0.37 (petroleum ether / ethyl acetate (8/2)).
$^1$H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.88-1.94 (m, 2 $CH_2$), 3.07 (t, J = 6.8 Hz, $CH_2$), 4.40 (t, J = 6.0 Hz, $CH_2$), 7.41-7.57 (m, 6H arom), 7.95-8.04 (m, 4H arom). $^{13}$C NMR (100 MHz, $CDCl_3$): δ (ppm) = 19.0 ($CH_2$), 26.5 ($CH_2$), 36.2 ($CH_2$), 62.9 ($CH_2$), 126.2 (CH arom), 126.6 (CH arom), 126.9 (CH arom), 127.8 (CH arom), 128.6 (C arom), 131.1(CH arom), 131.3 (CH arom), 135.1 (C arom), 164.9 (COO), 198.0 (CO).
HRMS ESI $[M+H]^+$ calcd for $C_{18}H_{19}O_3$: 283.1329. Observed: 283.1329.

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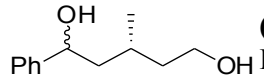
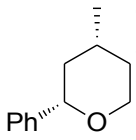
## Synthetic applications of the dual catalysis/cascade:



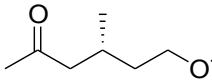
**(3*R*)-5-hydroxy-3-methyl-5-phenylpentyl benzoate:** 88.3 mg (2.33 mmol, 5 eq) of $LiAlH_4$ is dissolved in 8 ml of diethyl ether. A solution of 138.2 mg of **3a** (0.466 mmol, 1 eq) dissolved in 4 ml of dried diethyl ether is subsequently slowly added. The reaction is stirred at room temperature for 2 h 45 before addition of 10 ml of 1M HCl. The mixture is stirred at room temperature for 30 minutes before extraction by three times 10 ml ether, the organic phase are assemble and dried over $Na_2SO_4$, filtered and the solvent evaporated.
Purification by silica gel chromatography (petroleum ether/ ethyl acetate (4/1 to 1/1)) affords 79.2 mg of the deprotected diol (0.408 mmol) as a 1.3:1 mixture of diastereoisomers. Yield = 87%.
$R_f$ = 0.07 (petroleum ether / ethyl acetate (7/3)).
$^1$H NMR (1.3:1 *dr*) (300 MHz, $CDCl_3$): δ (ppm) = 0.88 (d, *J* = 6.4 Hz, $CH_3$ dia syn), 0.93 (d, *J* = 6.2 Hz, $CH_3$ dia anti), 1.29-1.37 (m, $CH_2$ dia syn), 1.47 (q, J = 6.7 Hz, $CH_2$ anti), 1.57-1.82 (m, 3H (both dia)), 2.48 (brs, 2 OH), 3.54-3.67 (m, $CH_2$ both dia). 4.67-4.74 (m, CH both dia), 7.17-7.27 (m, 10 H arom). $^{13}$C NMR (1.3:1 *dr*) (75 MHz, $CDCl_3$): δ (ppm) = 19.9 ($CH_3$, dia anti), 20.5 ($CH_3$, dia syn), 26.3 (CH both dia), 38.9 ($CH_2$, dia syn), 40.1 ($CH_2$, dia anti), 46.2 (CH, dia anti), 46.4 ($CH_2$, dia syn), 60.4, $CH_2$, dia anti), 60.8 ($CH_2$, dia syn), 72.3 (CH, dia syn), 72.4 (CH, dia anti), 125.6 (CH arom, both dia), 125.8 (CH arom, both dia), 127.4 (CH arom, both dia), 127.5 (CH arom, both dia), 128.5 (CH arom, both dia), 144.0 (C arom, both dia), 145.4 (C arom, both dia). Datas for both diastereoisomers are in agreement with the literature.[7]



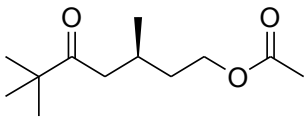
**Compound 4:** 37,9 mg of **(3*R*)-5-hydroxy-3-methyl-5-phenylpentyl benzoate** (0.19 mmol, 1 eq) are dissolved in 2 ml of dried dichloromethane and cooled to 0 °C under argon. 35 µl of $CF_3SO_3H$ (0.4 mmol, 2 eq) are then added and the solution stirred at 0 °C under argon for 1 h 20. 2 ml saturated aqueous $NaHCO_3$ are added, the aqueous layer extracted by three times 2 ml dichloromethane, the combined organic layers dried over $Na_2SO_4$, filtered and the solvent evaporated.
Purification by silica gel chromatography (petroleum ether/ ethyl acetate (6/1 to 3/1)) affords 32.6 mg (0.185 mmol) of **4** in a 10:1 *dr.* Yield = 95%.
$R_f$ = 0.74 (petroleum ether / ethyl acetate (6/4)). $[\alpha]^{20}_D$ = -29.1° ($CHCl_3$, c = 0.83, 90:10 *er*). Lit = -42.0° ($CHCl_3$, c = 1.2).
$^1$H NMR (10:1 *dr*) (300 MHz, $CDCl_3$): δ (ppm) = 1.02 (d, *J* = 6.4 Hz, $CH_3$), 1.18-1.44 (m, $CH_2$), 1.60-1.93 (m, CH and $CH_2$), 3.64 (ddd, *J* = 12.4, 11.5, 2.3 Hz, 1H of $CH_2$), 4.19 (ddd, *J* = 11.5, 4.6, 1.6 Hz, 1H of $CH_2$), 4.35 (dd, *J* = 11.3, 2.0 Hz, CH), 7.25-7.42 (m, 10 H arom). $^{13}$C NMR (10:1 *dr*) (75 MHz, $CDCl_3$): δ (ppm) = 22.3

[7] E. Brenna, C. Fuganti, S. Ronzani, S. Serra, *Can. J. Chem.* **2002**, *80*, 714.

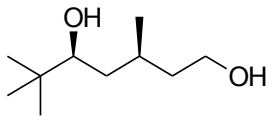
(CH3), 30.8 (CH), 34.4 ($CH_2$), 42.7 ($CH_2$), 68.5 ($CH_2$), 79.8 (CH), 125.8 (CH arom), 126.1 (CH arom), 128.3 (CH arom), 143.2 (C arom). Datas are in agreement with the literature.[8]




**Compound 5:** 48.2 mg of LiOH (2,0 mmol) added to **3b** (85.3 mg, 0.495 mmol) in a mixture of 1 ml of THF and 1 ml of water. After stirring for 1h at room temperature, 3 ml of water are added and the aqueous layer extracted by 3 times 10 ml of diethyl ether, the organic layer assemble, washed with 5 ml brine, dried over $Na_2SO_4$, filtered and the solvent evaporated. The mixture is rapidly filtered over a plug of silica ($Et_2O$), evaporated. The resulting oil is dissolved in 2 ml of dry dichloromethane, 3.5 mg of luditine (0.032 mmol), 0,11 ml of triethylamine (0.79 mmol) and 96.9 mg of TBDMSCl (0.64 mmol) are successively added and the resulting solution stirred at room temperature for 15h. 10 ml saturated aqueous $NH_4Cl$ are then added, the aqueous layer extracted by three times 10 ml of dichloromethane, the organic layer dreied over $Na_2SO_4$, filtered and the solvent evaporated.
Purification by silica gel chromatography (petroleum ether/ ethyl acetate (99/1 to 9/1)) affords 48.4 mg (0.198 mmol) of the protected alcohol. Yield = 40%.
$R_f$ = 0.48 (petroleum ether / ethyl acetate (9/1)). $[\alpha]^{20}_D$ = +2.45º ($CHCl_3$, c = 0.79, 90:10 *er*). Lit = +3.36° ($CHCl_3$, c = 2.05).
$^1$H NMR (400 MHz, $CDCl_3$): δ (ppm) = 0.00 (2 CH3), 0.85 (s, 3 $CH_3$), 0.87 (d, *J* = 6.6 Hz, $CH_3$), 1.36-1.42 (m, 1H of $CH_2$), 1.44-1.51 (m, 1H of $CH_2$), 2.07 (s, $CH_3$), 2.08-2.23 (m, CH and 1H of $CH_2$), 2.43 (dd, *J* = 15.5, 5.5 Hz, 1H of $CH_2$), 3.57-3.62 (m, $CH_2$). $^{13}$C NMR (100 MHz, $CDCl_3$): δ (ppm) = -5.3 ($CH_3$), 18.2 (Cquat), 19.9 ($CH_3$), 25.9 ($CH_3$), 26.3 (CH), 30.2 ($CH_3$), 39.5 ($CH_2$), 51.2 ($CH_2$), 61.0 ($CH_2$), 208.8 (CO).
Datas are in agreement with the literature.[9]




**Compound (+)-3i .** According to the general procedure using **(*R*)-cat1** and starting from 142.7 mg (1.0 mmol) of 1,3 di-ketone. The product was isolated as a red oil. 90 mg (0.42 mmol). 42% yield.
$R_f$ = 0.56 (petroleum ether / ethyl acetate (9/1)) (95:5 *er*).
GC determination : Lipodex, method 60 min at 80 °C then 1 °C.min$^{-1}$ to 150 °C, rt (maj) = 66.4 min, rt (min) = 67.2 min.




**Compound 6.**[10] To a stirred solution of (*R*)-CBS catalyst (1M solution in toluene, 0.5 eq., 17 µL, 0.0571 mmol) in dry toluene (0.4 mL), was added $BH_3.Me_2S$ (0.9 eq., 10 µL, 0.105 mmol) at 0 °C under argon. After stirring for 20 min at 0 °C, a solution of compound **(+)-3i** (1 eq., 25 mg, 0.117 mmol) in dry toluene (0.2 mL) was added and stirring was continued for 48 h at 0 °C ((*R*)-CBS catalyst (0.5 eq., 17 µL, 0.0571 mmol) and $BH_3.Me_2S$ (0.9 eq., 10 µL, 0.105 mmol) were again added after 24 h at 0 °C). After completion, the reaction mixture was quenched carefully drop wise with $H_2O$ (0.8 mL), $K_2CO_3$ (7 eq., 113 mg, 0.817 mmol) was added and the reaction was stirred for 15 min. The organic phase was separated, and the aqueous phase extracted with 20% butanol in EtOAc (4x1 mL). The combined organic extracts were washed with brine (2 mL) and dried over $Na_2SO_4$. The solvent was evaporated and the crude product purified over silica gel petroleum ether/EtOAc gradient 9:1 to 7:3) to give **6** as colorless oil (15 mg, 0.0693 mmol, 59% yield, $[\alpha]^{25}_D$ = -41.0° ($CHCl_3$, c= 0.057, 99:5:0.5 *er*), (lit$[\alpha]^{25}_D$ = -46.6° ($CHCl_3$, c= 1.75)). $^1$H NMR (300 MHz, $CDCl_3$) δ 0.88 (s, 3x$CH_3$), 0.97 (d, *J* = 6.7 Hz, $CH_3$), 1.43 – 1.20 (m, 2x$CH_2$), 1.90 – 1.71 (m, $CH_2$, 2xOH), 3.33 (dd, *J* = 9.8, 2.5 Hz, 1H), 3.81 – 3.61 (m,

[8] See ref 7.
[9] D. C. Beshore, A. B. Smith, III, *J. Am. Chem. Soc.* **2007**, *129*, 4148.
[10] For a related CBS reduction see: G. Sudhakar, K. J. Reddy, J. B. Nanubolu, *Tetrahedron*, **2013**, *69*, 2419.

$CH_2$). $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 21.3 ($CH_3$), 25.6 (CH), 26.9 (3x$CH_3$), 34.9 (Cquat), 38.2 ($CH_2$), 39.1 ($CH_2$), 61.3 ($CH_2$), 77.1 (CH). Datas are in agreement with the literature[11].
GC determination : Hydrodex, method 70 min at 100 °C, then 1 °C.min$^{-1}$ to 150 °C, rt (dia 1, min) = 98.517 min, rt (dia 2, min) = 98.883 min, rt (dia 2, maj) = 99.983 min, rt (dia 1, maj) = 103.217 min.

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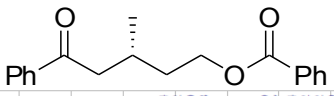
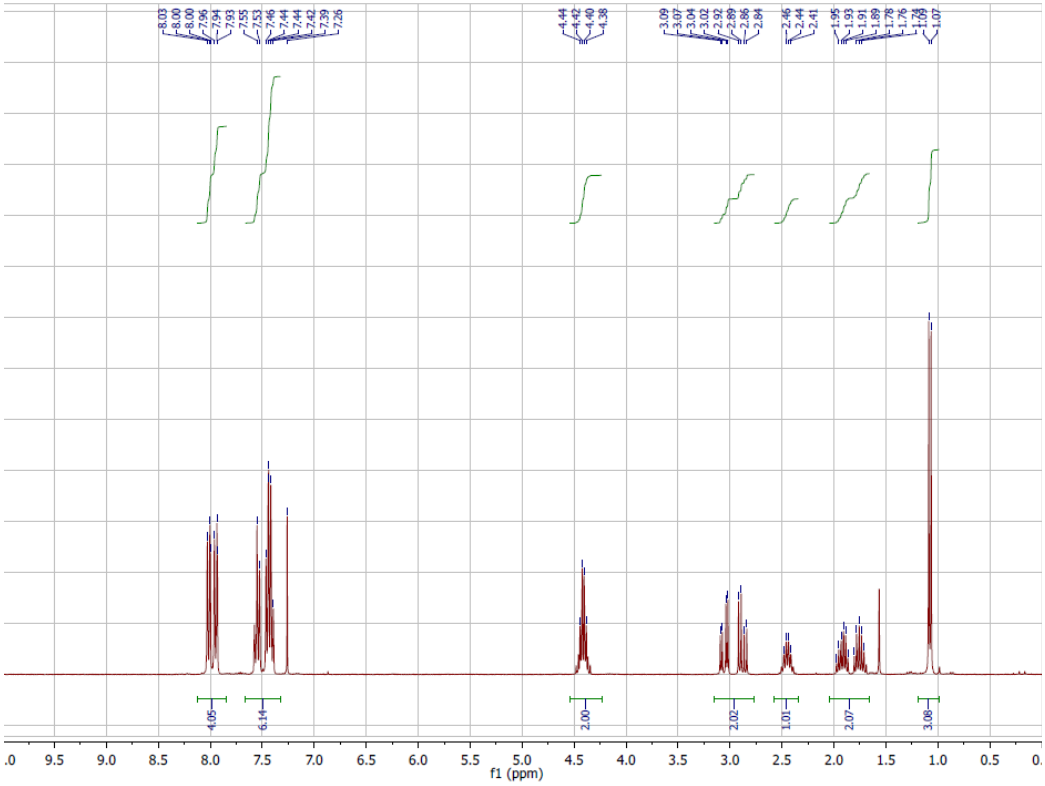
## Spectras:

[11] J. Chen, C. J. Forsyth, *PNAS*, **2004**, *101*, 33, 12067-12072.

**Compound 3a**


O
O
Ph
O
Ph


8.03
8.00
8.00
7.96
7.94
7.93
7.55
7.53
7.46
7.44
7.44
7.42
7.39
7.26
4.44
4.42
4.40
4.38
3.09
3.07
3.04
3.02
2.92
2.89
2.86
2.84
2.46
2.44
2.41
1.95
1.93
1.91
1.89
1.78
1.76
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1.07
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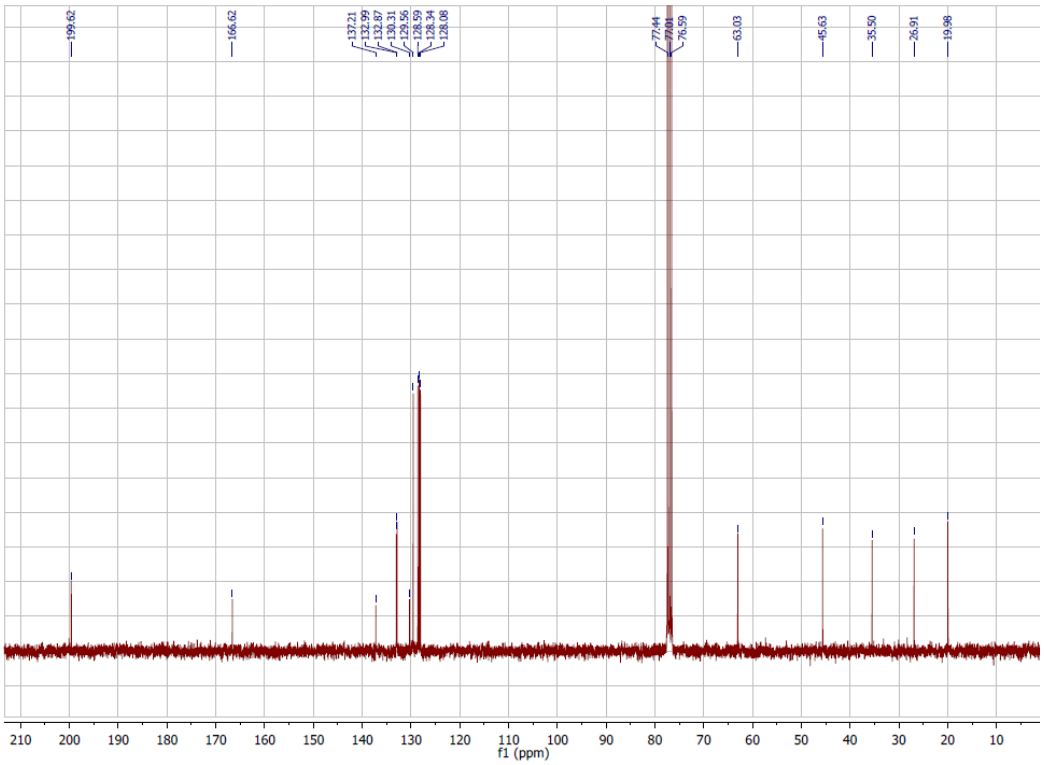
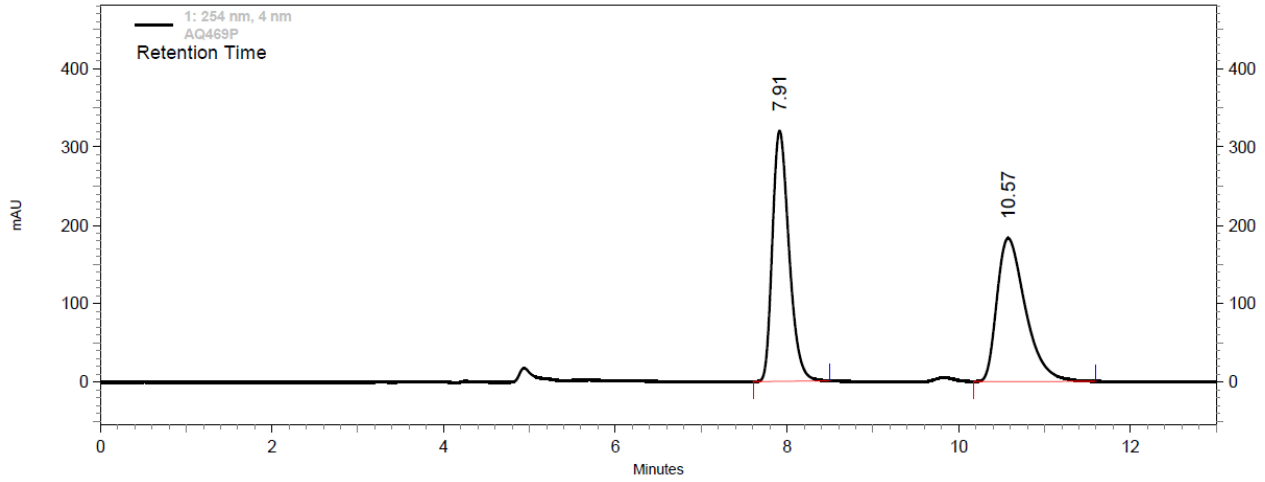
6.14
2.00
2.02
1.01
2.07
3.08
f1 (ppm)


199.62
166.62
137.21
132.99
132.97
128.31
129.56
128.59
128.34
128.08
77.44
77.01
76.59
63.03
45.63
35.50
26.91
19.98
f1 (ppm)

Racemate :

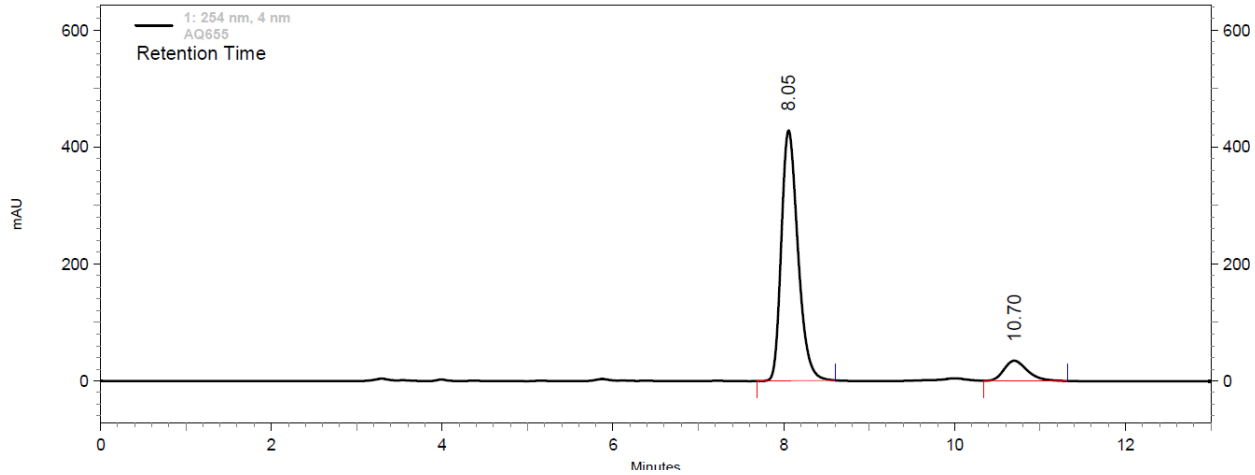
Method description : Chiralpak ID, Hexane/Ethanol 90/10, 1 ml/min, DAD and polarimeter




| Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 7.91 | 17181470 | 50.52 | 1.64 | 1.00 | 0.00 |
| 10.57 | 16826972 | 49.48 | 2.52 | 1.54 | 5.56 |

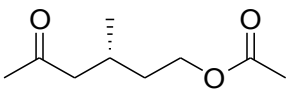
Enantioenriched :

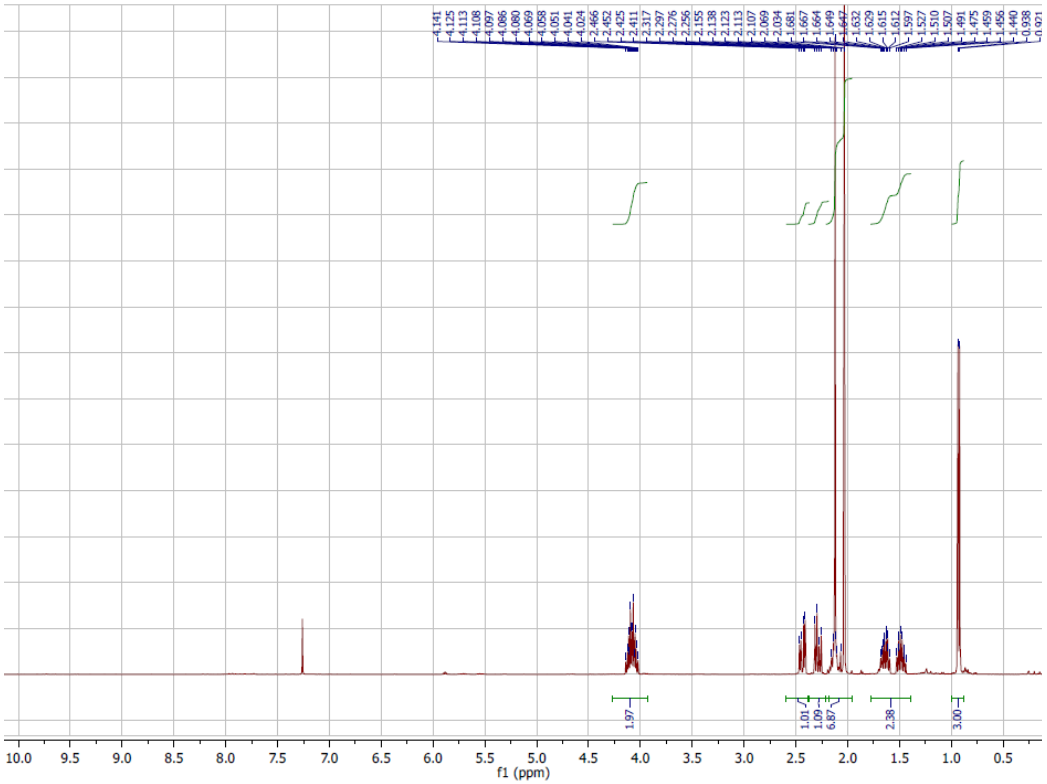
Method description : Chiralpak ID, Heptane/Ethanol 90/10, 1 ml/min, DAD and polarimeter

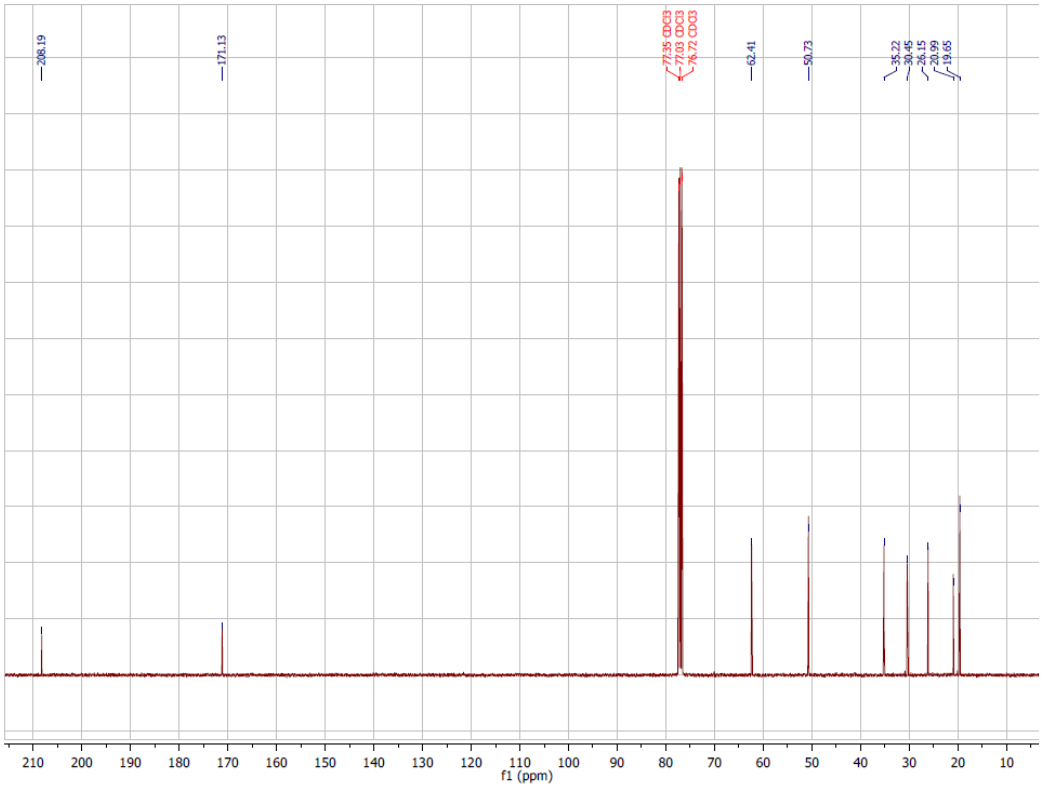



| Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 8.05 | 23011368 | 89.88 | 1.68 | 0.00 | 0.00 |
| 10.70 | 2590786 | 10.12 | 2.57 | 0.00 | 6.22 |

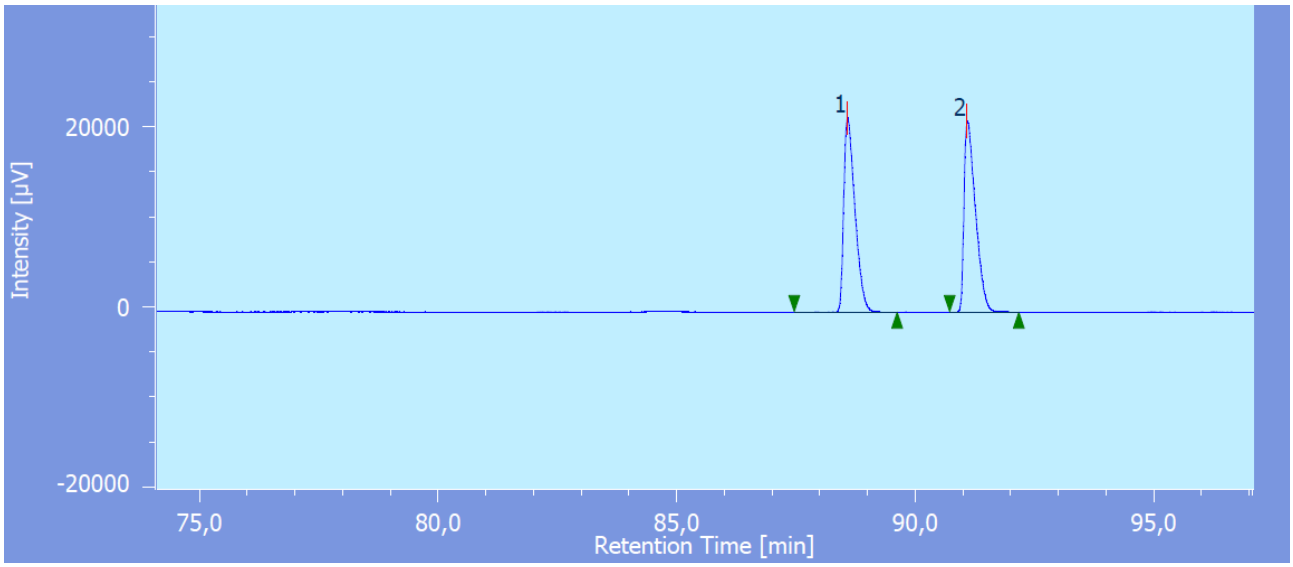
**Compound 3b**





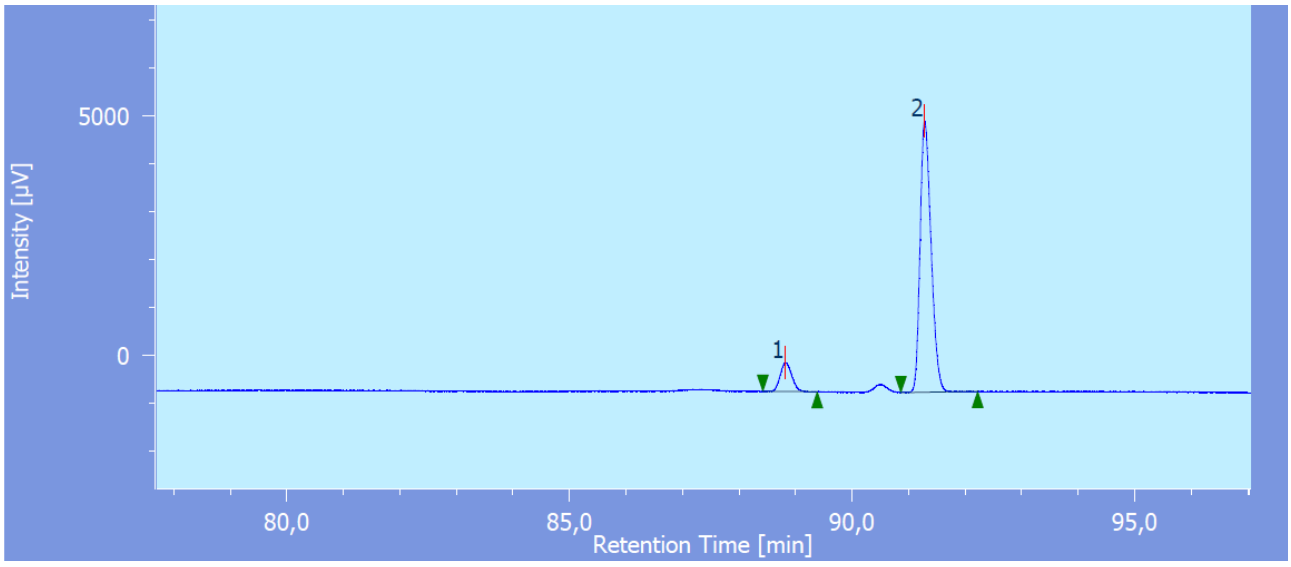



Racemate :



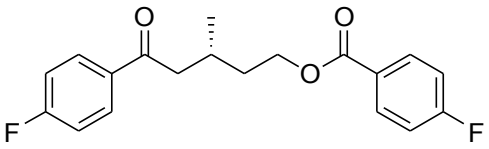

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 1 | 88.583 | 350831 | 21549 | 49.995 | 50.446 | N/A | 684086 | 5.793 | 1.643 | |
| 2 | Unknown | 1 | 91.083 | 350898 | 21169 | 50.005 | 49.554 | N/A | 695245 | N/A | 2.083 | |

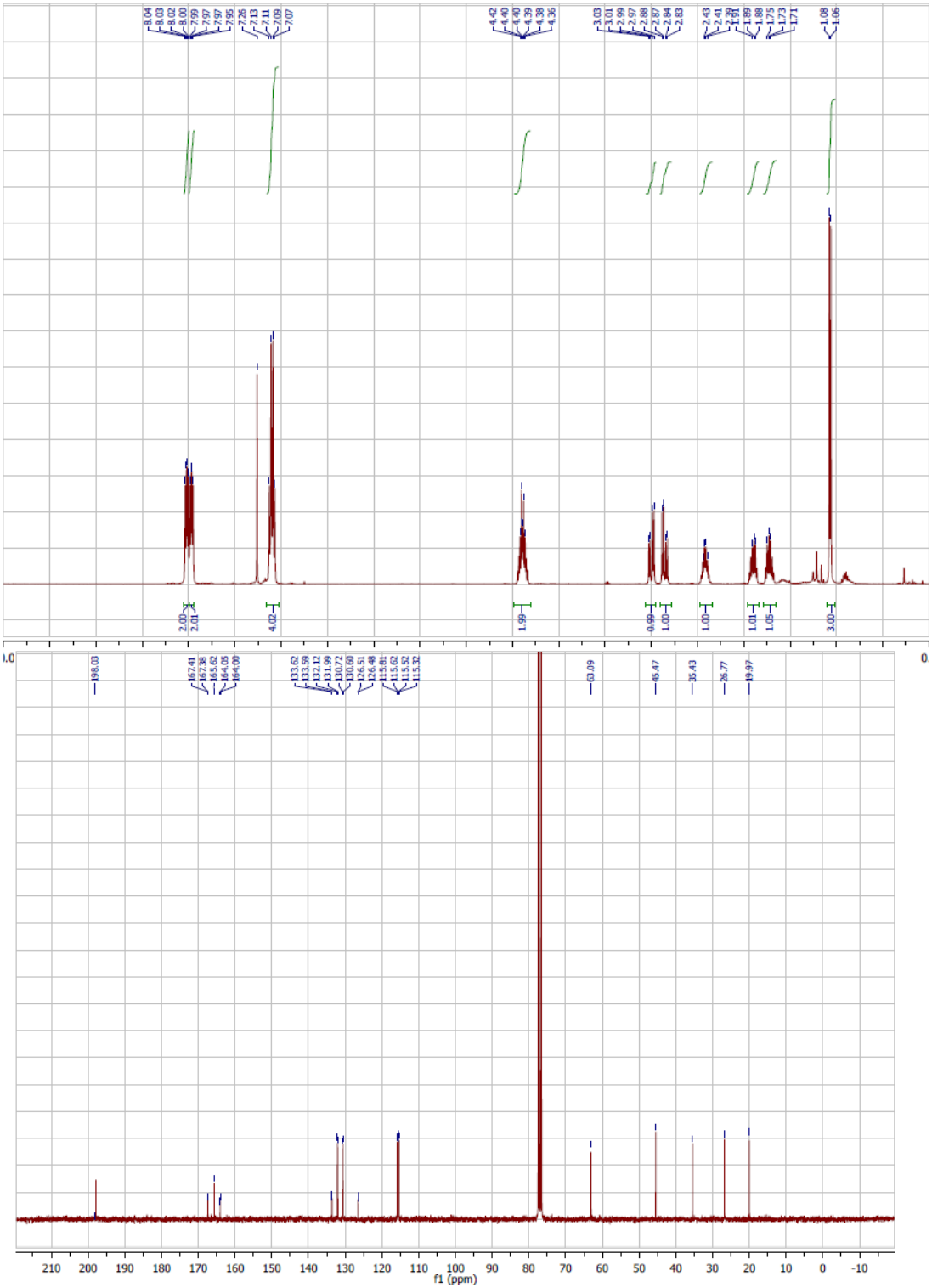
Enantioenriched :



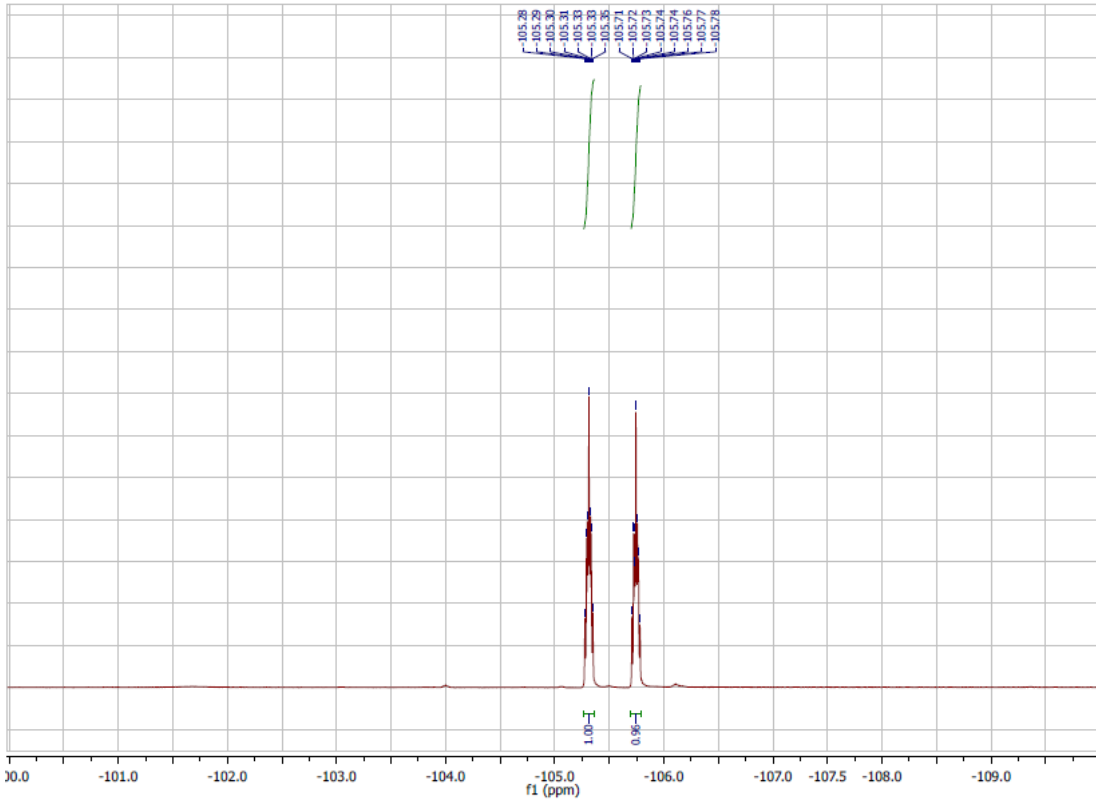

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 1 | 88.817 | 8619 | 603 | 10.157 | 9.645 | N/A | 886661 | 6.722 | 1.136 | |
| 2 | Unknown | 1 | 91.275 | 76238 | 5648 | 89.843 | 90.355 | N/A | 1051327 | N/A | 1.340 | |

**Compound 3c**



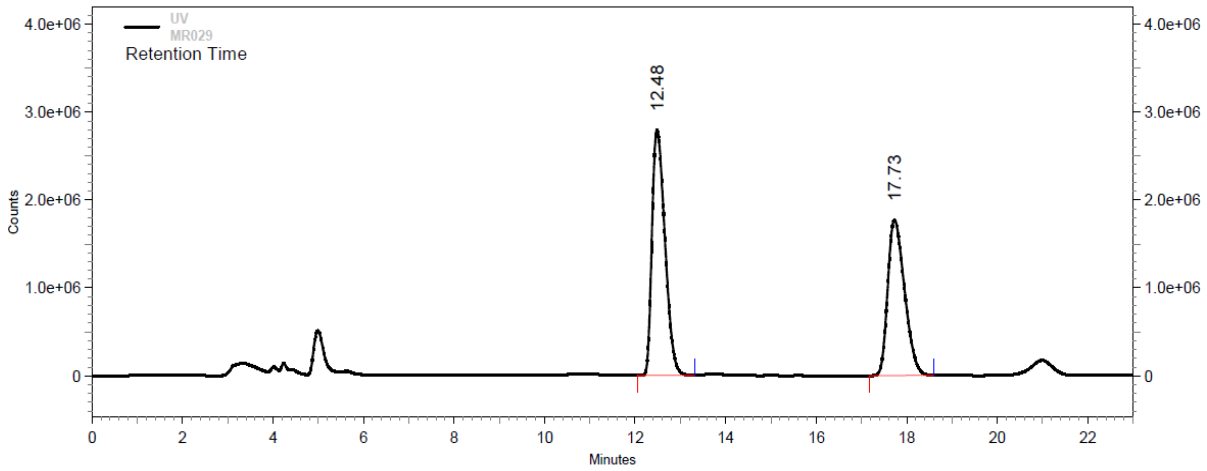



$^{19}F$ NMR:


-105.28
-105.29
-105.30
-105.31
-105.33
-105.33
-105.35
-105.71
-105.72
-105.73
-105.74
-105.74
-105.76
-105.77
-105.78
1.00
0.96
-101.0
-102.0
-103.0
-104.0
-105.0
f1 (ppm)
-106.0
-107.0
-107.5
-108.0
-109.0

Racemate:

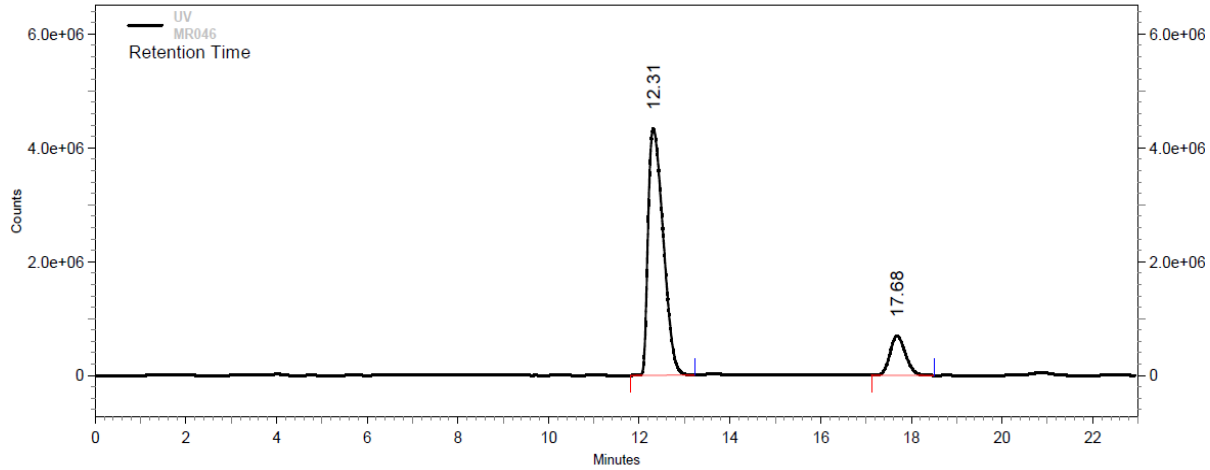
Method description : Lux-Amylose-2, Heptane/Isopropanol 90/10, 1 ml/min, UV 254 nm et polarimetre




| Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 12.48 | 55708708 | 54.90 | 3.16 | 1.00 | 0.00 |
| 17.73 | 45755253 | 45.10 | 4.91 | 1.55 | 8.47 |

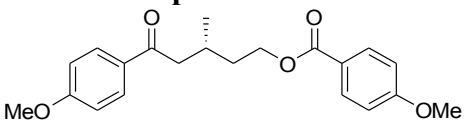
Enantioenriched:

Method description : Lux-Amylose-2, Heptane/Isopropanol 90/10, 1 ml/min, UV 254 nm et polarimetre

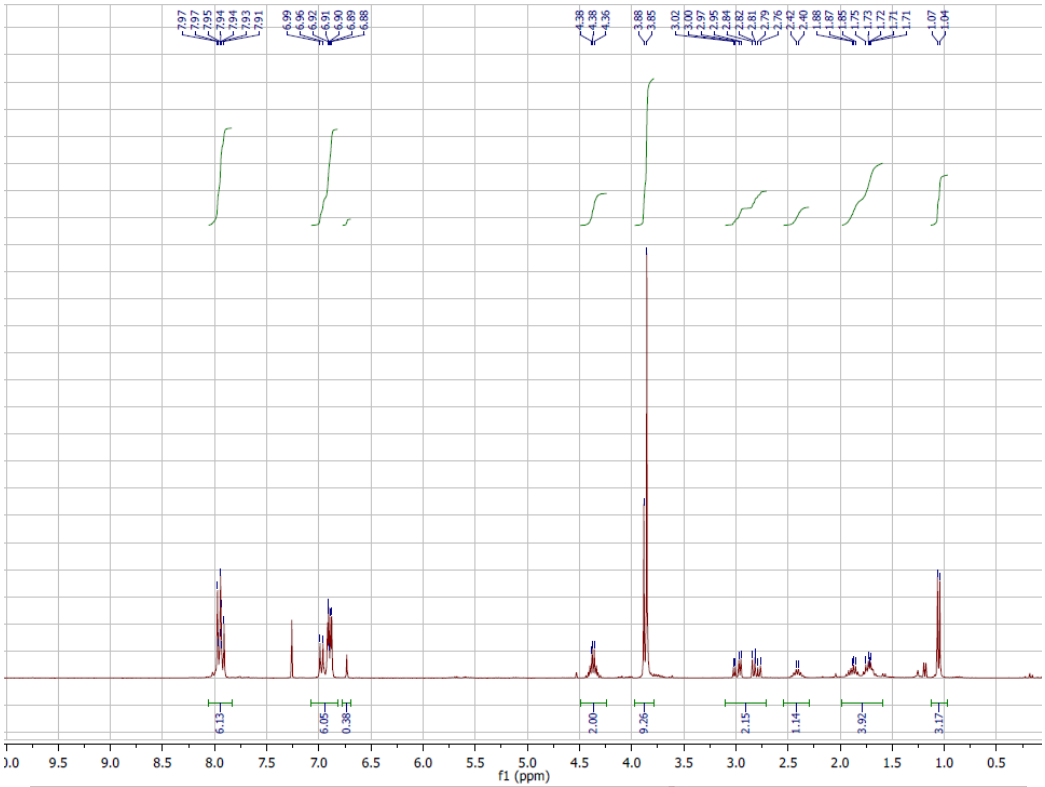


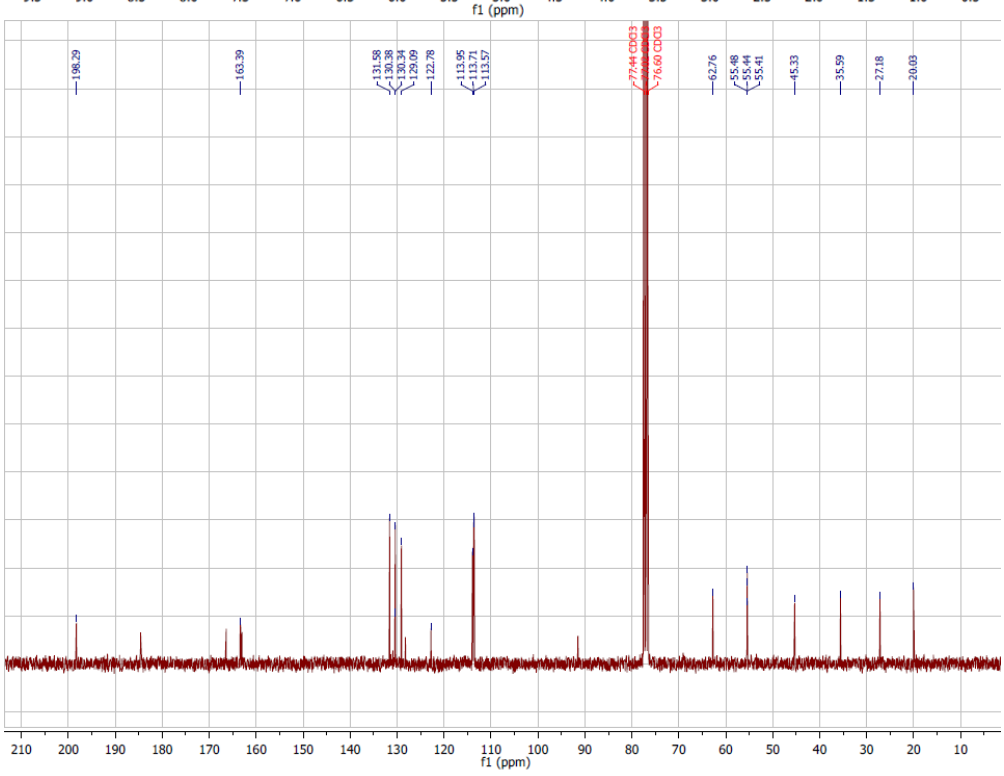

| Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 12.31 | 100165913 | 85.85 | 3.10 | 1.00 | 0.00 |
| 17.68 | 16509561 | 14.15 | 4.89 | 1.58 | 8.47 |

## Compound 3d



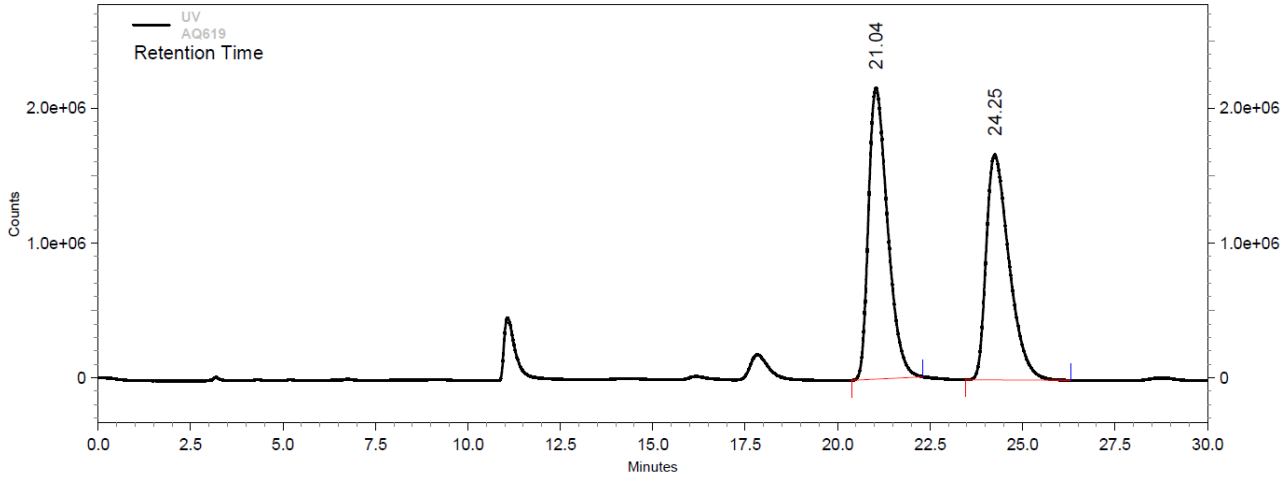

+ remaining starting material



Racemate :

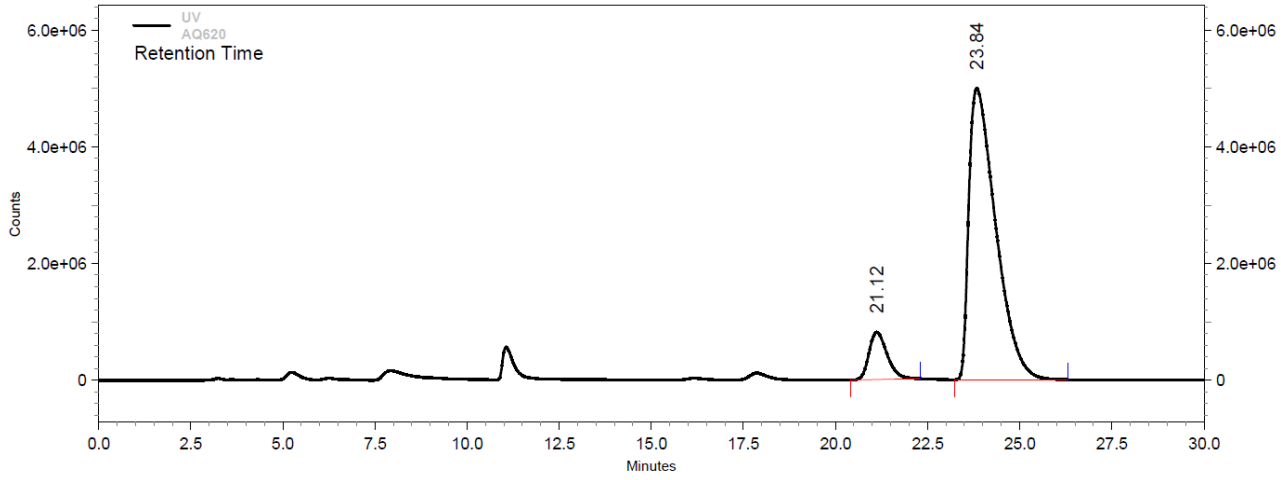
Method description : Chiralcel OD-3, Heptane/isopropanol 90/10, 1 ml/min, UV 254 nm et polarimètre




| Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 21.04 | 77671508 | 51.83 | 6.01 | 1.00 | 0.00 |
| 24.25 | 72174194 | 48.17 | 7.08 | 1.18 | 3.05 |

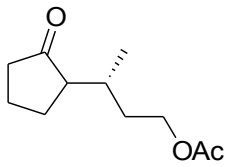
Enantioenriched :

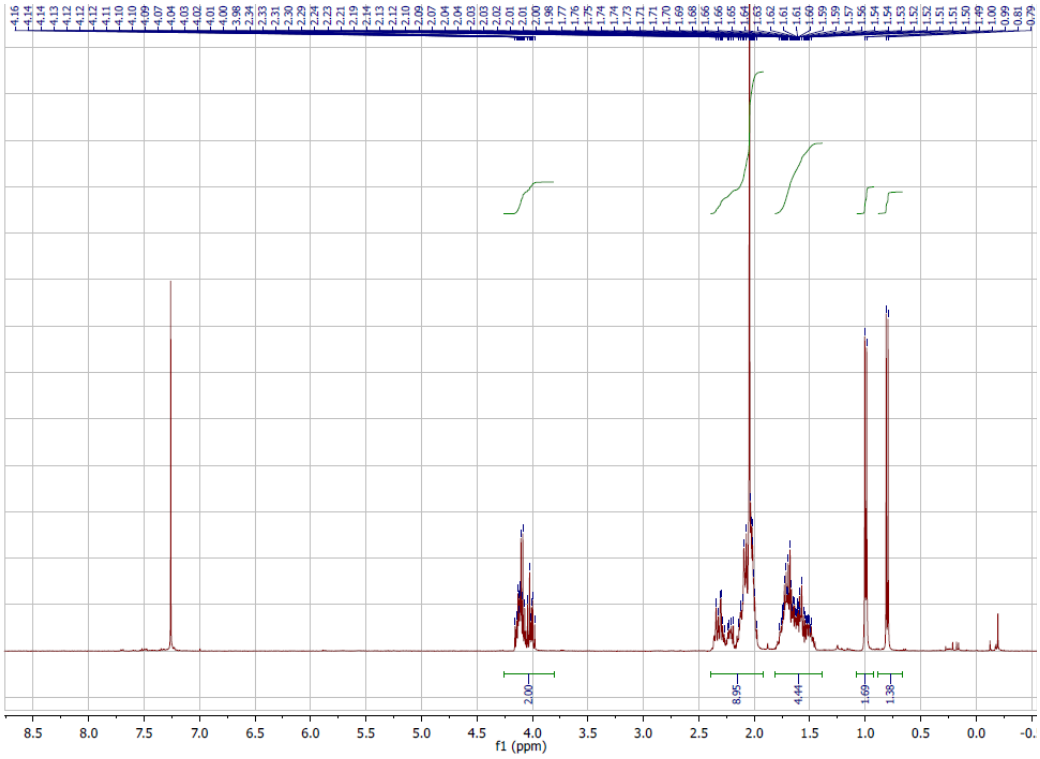
Method description : Chiralcel OD-3, Heptane/isopropanol 90/10, 1 ml/min, UV 254 nm et polarimètre

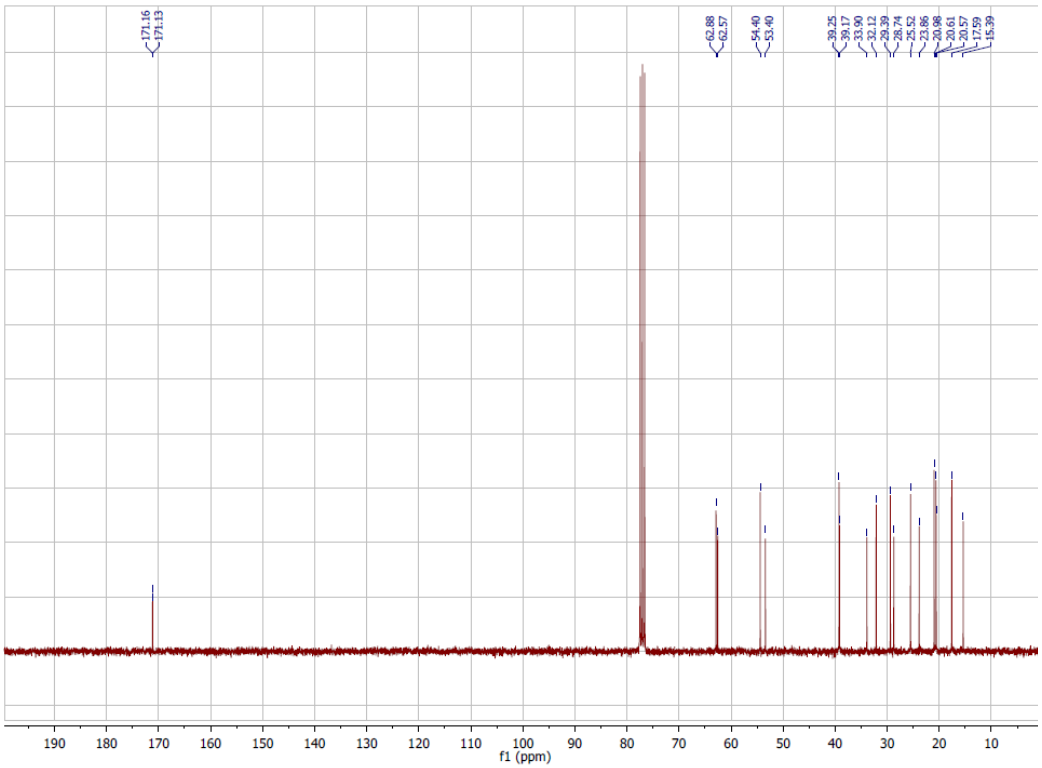



| Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 21.12 | 27727386 | 9.88 | 6.04 | 1.00 | 0.00 |
| 23.84 | 252945949 | 90.12 | 6.95 | 1.15 | 2.40 |

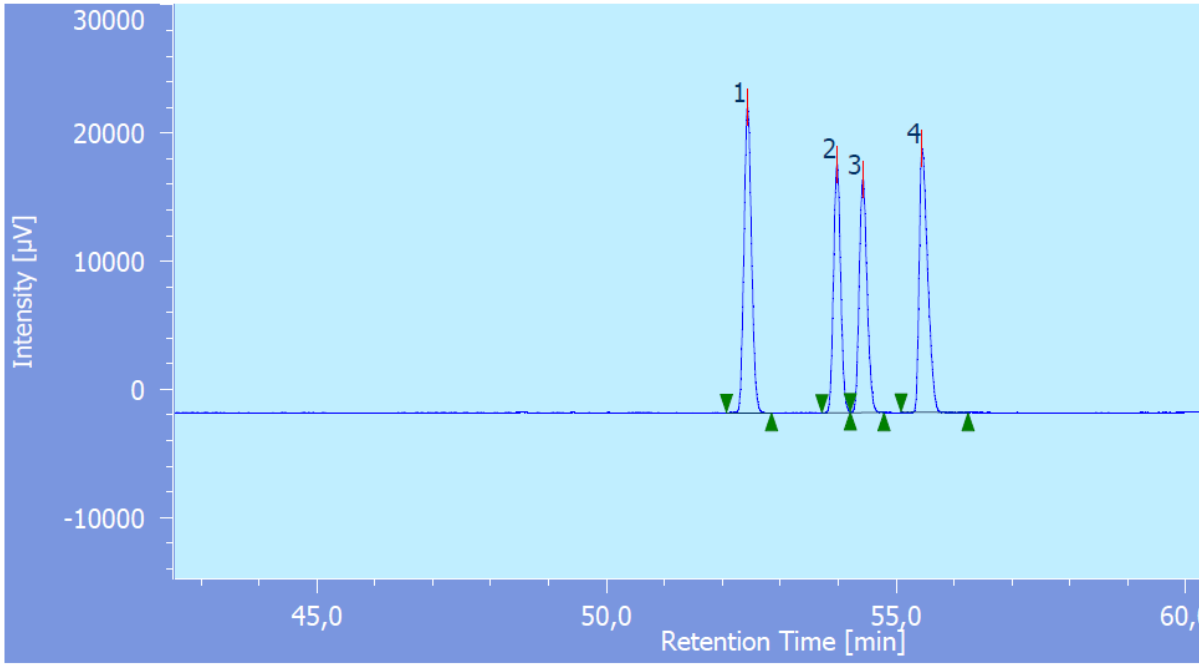
**Compound 3e**



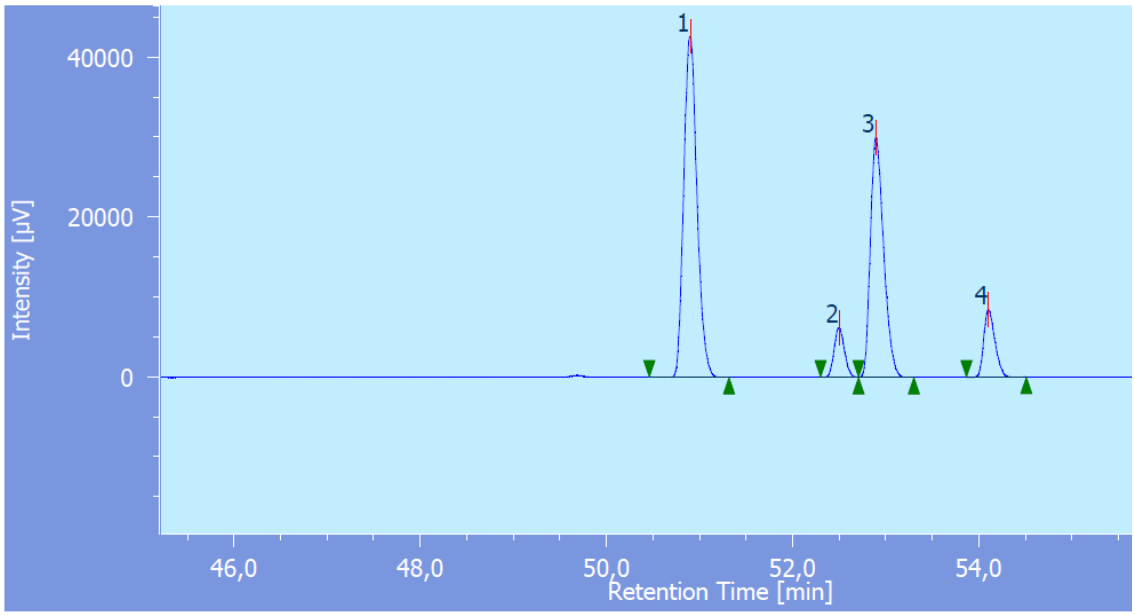



Racemate :



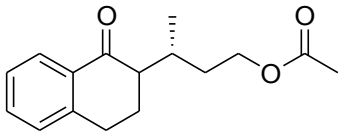

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 1 | 52.433 | 215260 | 23792 | 28.260 | 29.077 | N/A | 770933 | 6.677 | 1.116 | |
| 2 | Unknown | 1 | 53.983 | 166037 | 19353 | 21.798 | 23.652 | N/A | 907566 | 1.863 | 1.036 | |
| 3 | Unknown | 1 | 54.425 | 171358 | 18128 | 22.496 | 22.155 | N/A | 766414 | 3.935 | 1.157 | |
| 4 | Unknown | 1 | 55.442 | 209064 | 20551 | 27.446 | 25.117 | N/A | 677559 | N/A | 1.668 | |

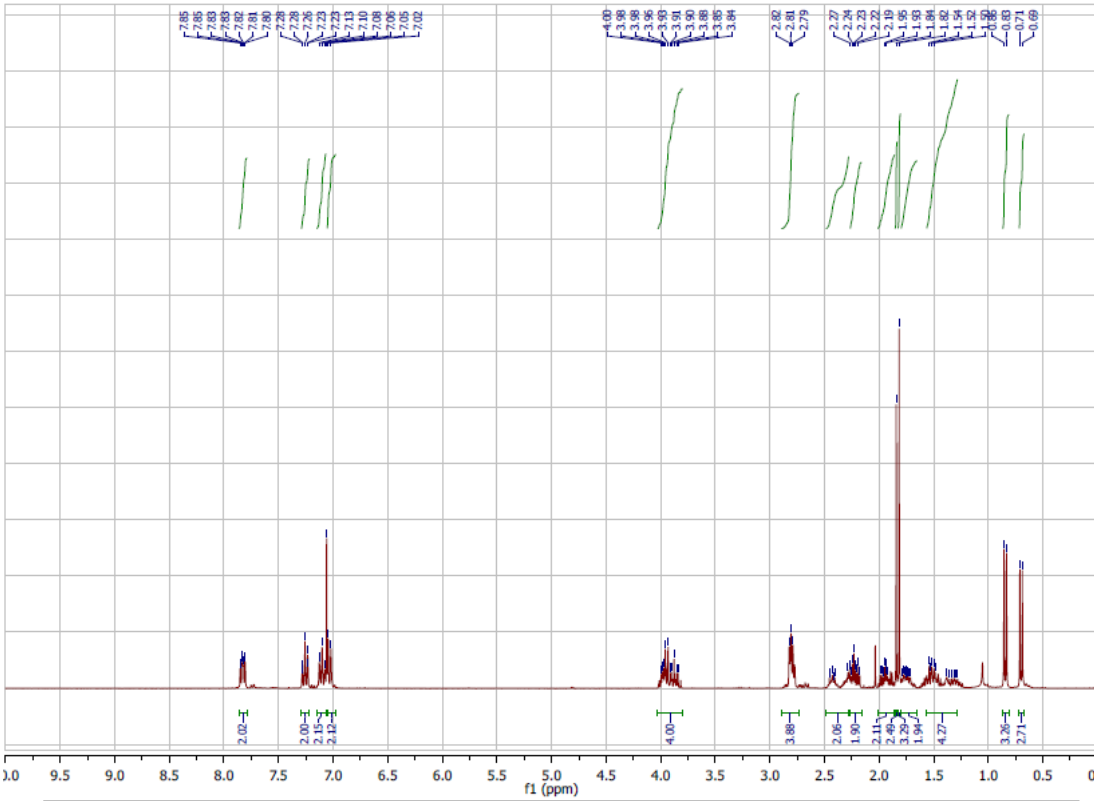
Enantioenriched :

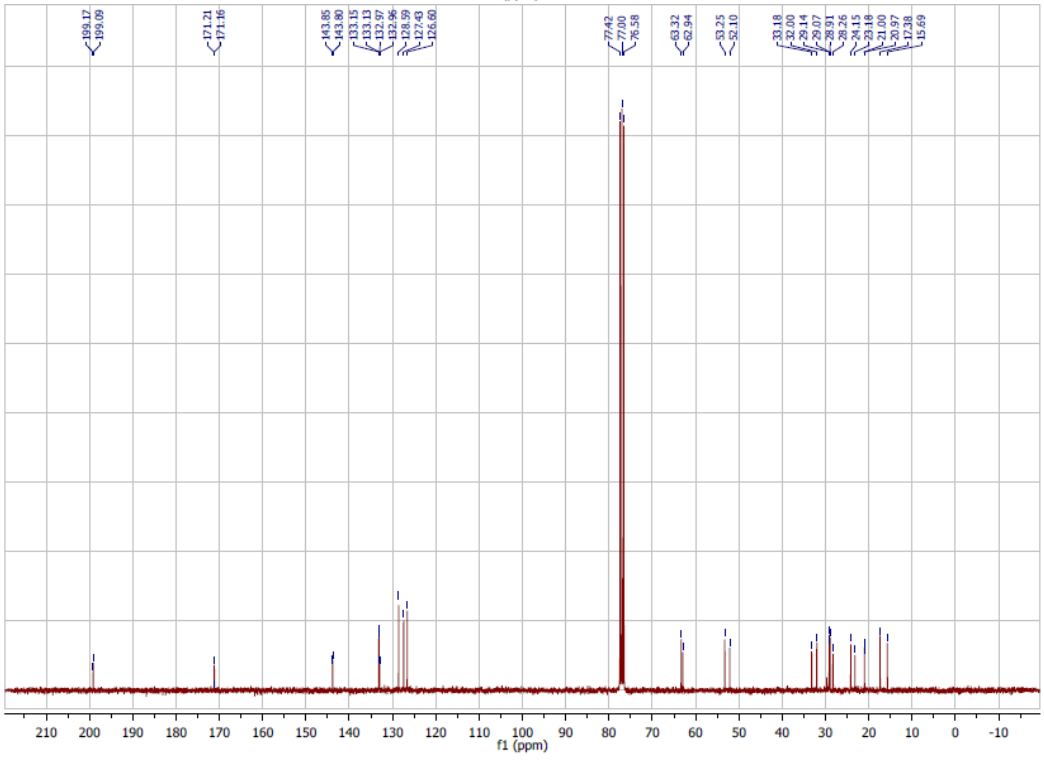



| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 1 | 50.900 | 422779 | 42665 | 50.435 | 48.856 | N/A | 610861 | 6.898 | 1.158 | |
| 2 | Unknown | 1 | 52.500 | 48115 | 6219 | 5.740 | 7.121 | N/A | 1053396 | 1.685 | 1.073 | |
| 3 | Unknown | 1 | 52.892 | 297025 | 30012 | 35.433 | 34.367 | N/A | 654431 | 5.022 | 1.350 | |
| 4 | Unknown | 1 | 54.100 | 70344 | 8432 | 8.392 | 9.656 | N/A | 958889 | N/A | 1.316 | |

**Compound 3g**

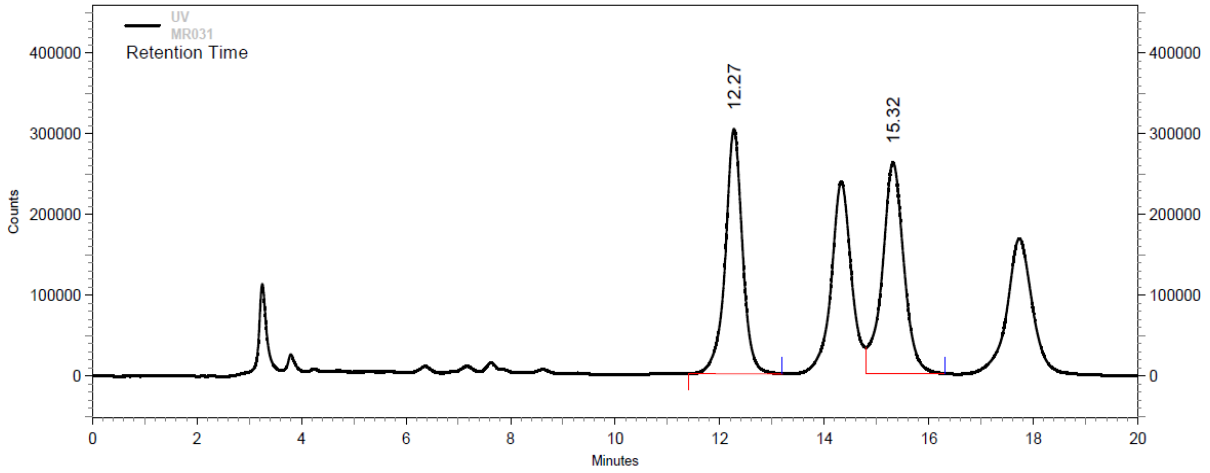






Racemate (dia 1):

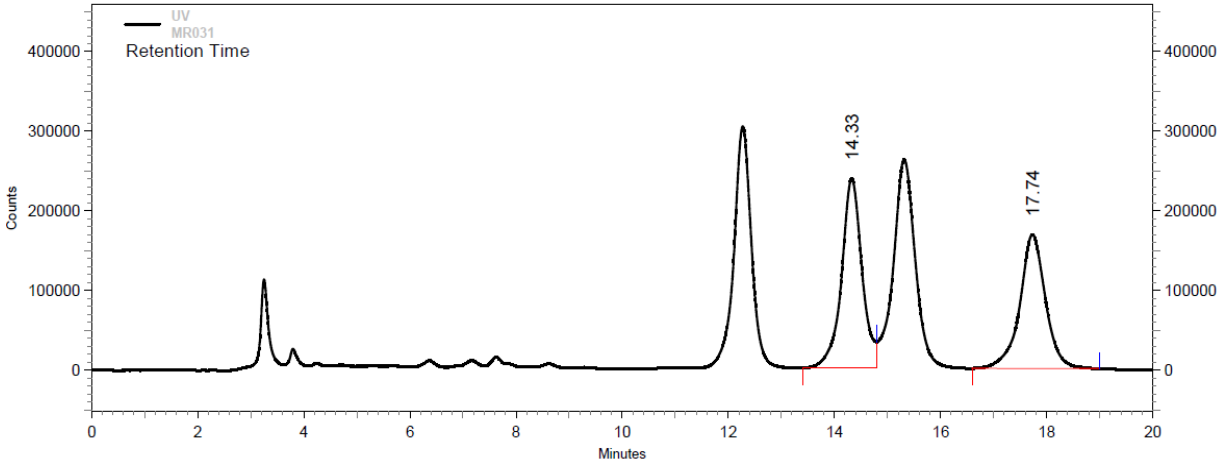
Method description : (S,S)-Whelk-O1, Heptane/isopropanol 70/30, 1 ml/min, UV 254 nm et CD254nm




| Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 12.27 | 6910419 | 48.02 | 3.09 | 1.00 | 0.00 |
| 15.32 | 7479045 | 51.98 | 4.11 | 1.33 | 4.64 |

Racemate (dia 2):

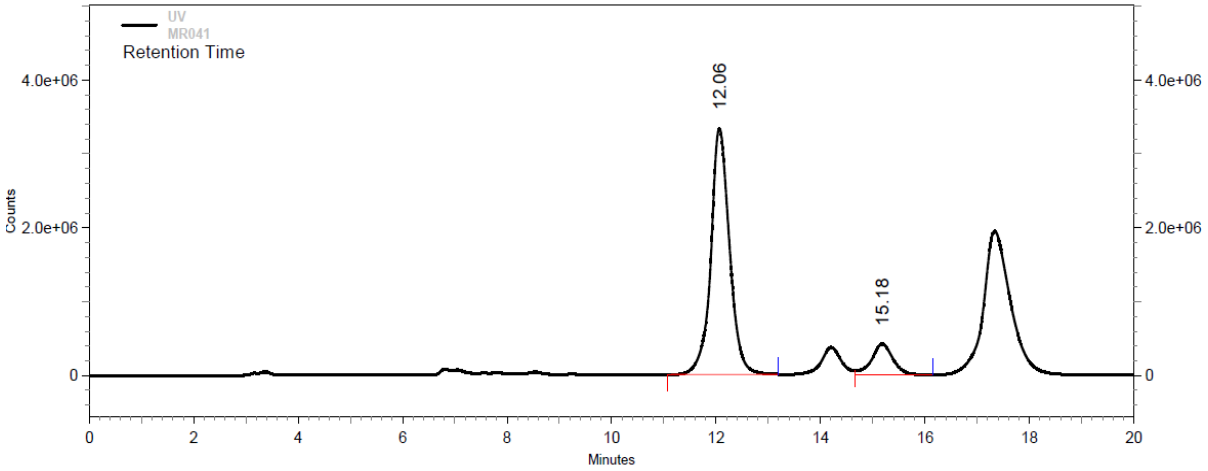
Method description : (S,S)-Whelk-O1, Heptane/isopropanol 70/30, 1 ml/min, UV 254 nm et CD254nm




| Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 14.33 | 6380642 | 52.96 | 3.78 | 1.00 | 0.00 |
| 17.74 | 5668283 | 47.04 | 4.91 | 1.30 | 4.42 |

Enantioenriched (dia 1):

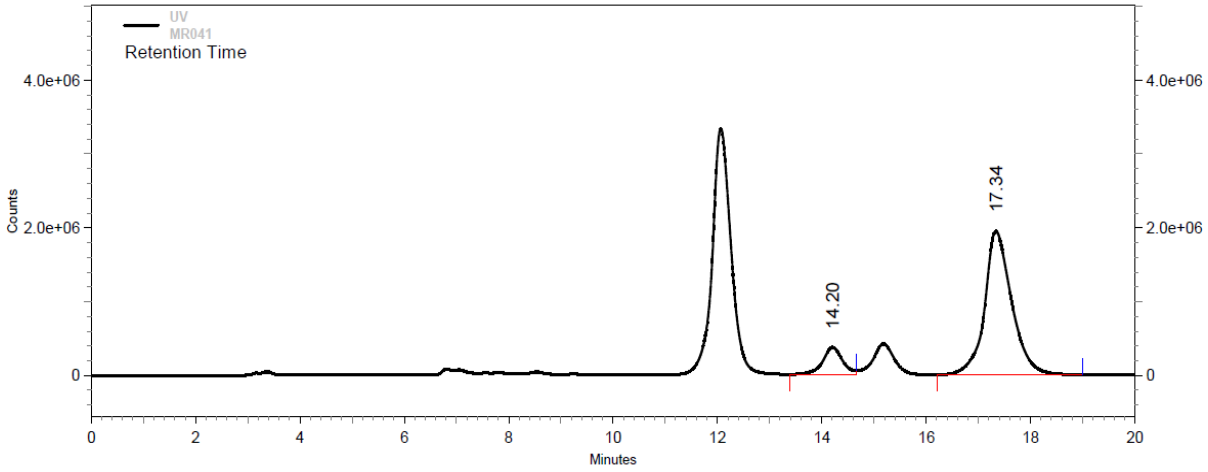
Method description : (S,S)-Whelk-O1, Heptane/isopropanol 70/30, 1 ml/min, UV 254 nm et CD254nm




| Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 12.06 | 82776724 | 87.39 | 3.02 | 1.00 | 0.00 |
| 15.18 | 11941640 | 12.61 | 4.06 | 1.34 | 4.60 |

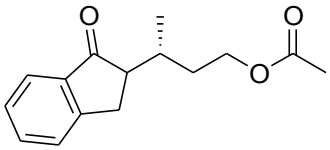
Enantioenriched (dia 2):

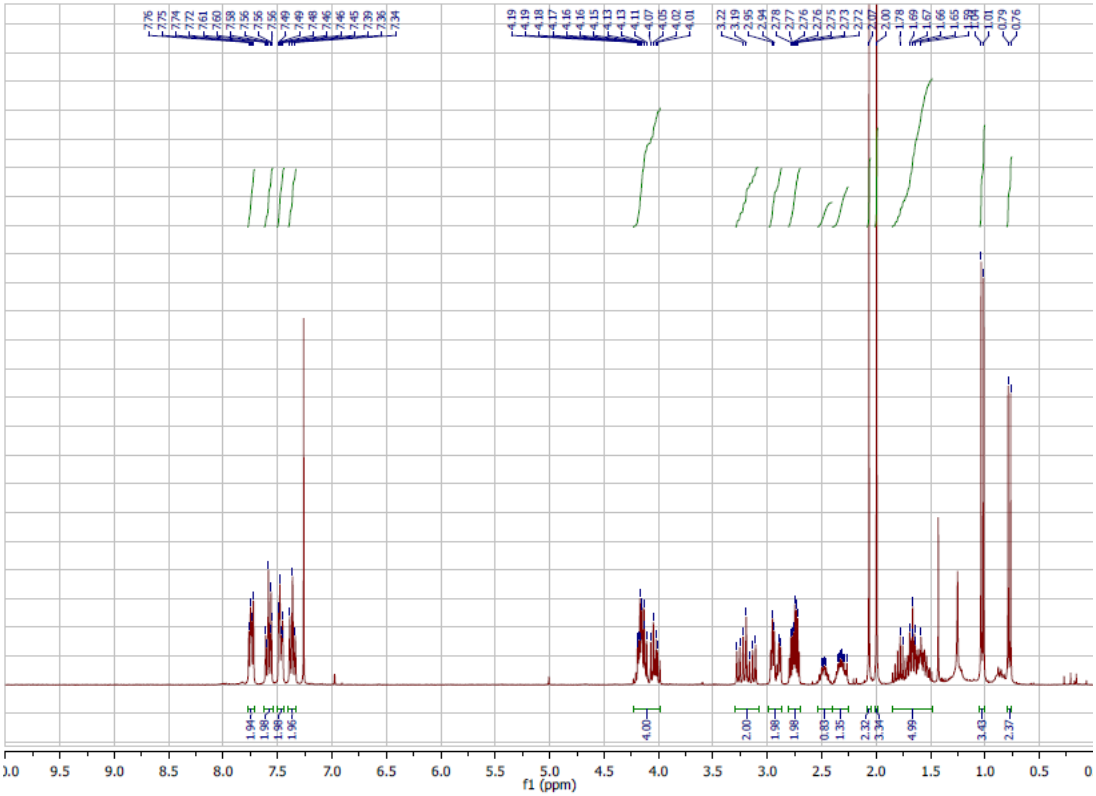
Method description : (S,S)-Whelk-O1, Heptane/isopropanol 70/30, 1 ml/min, UV 254 nm et CD254nm

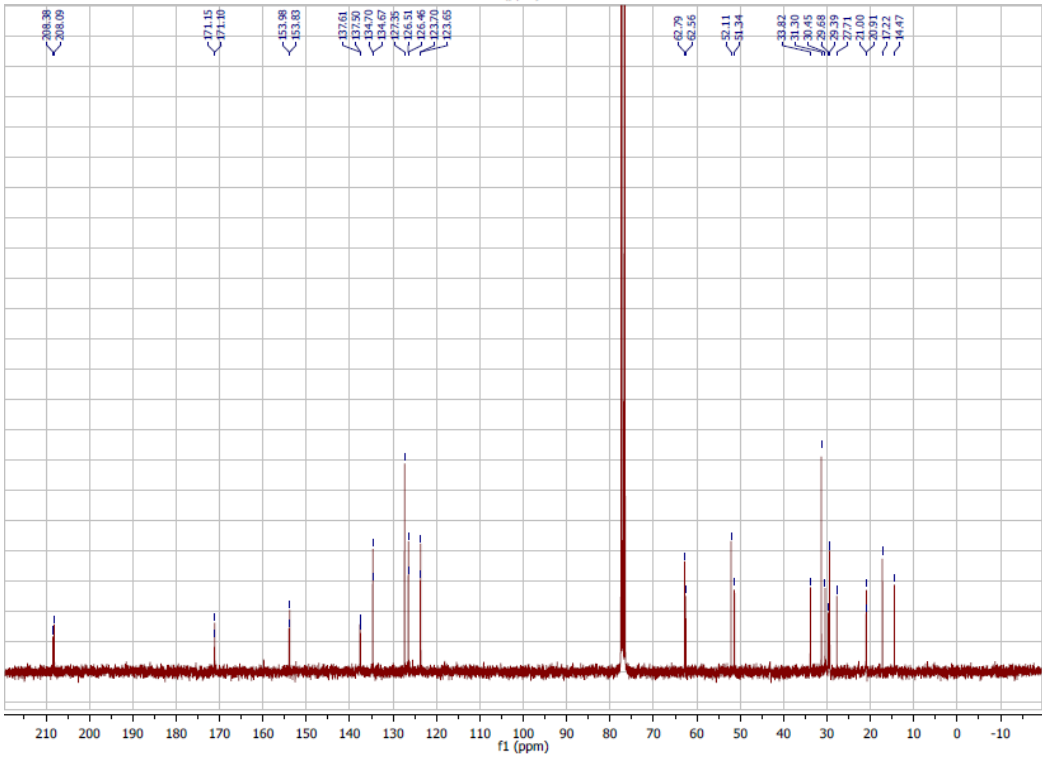



| Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 14.20 | 9562523 | 12.01 | 3.73 | 1.00 | 0.00 |
| 17.34 | 70091512 | 87.99 | 4.78 | 1.28 | 3.94 |

**Compound 3f**

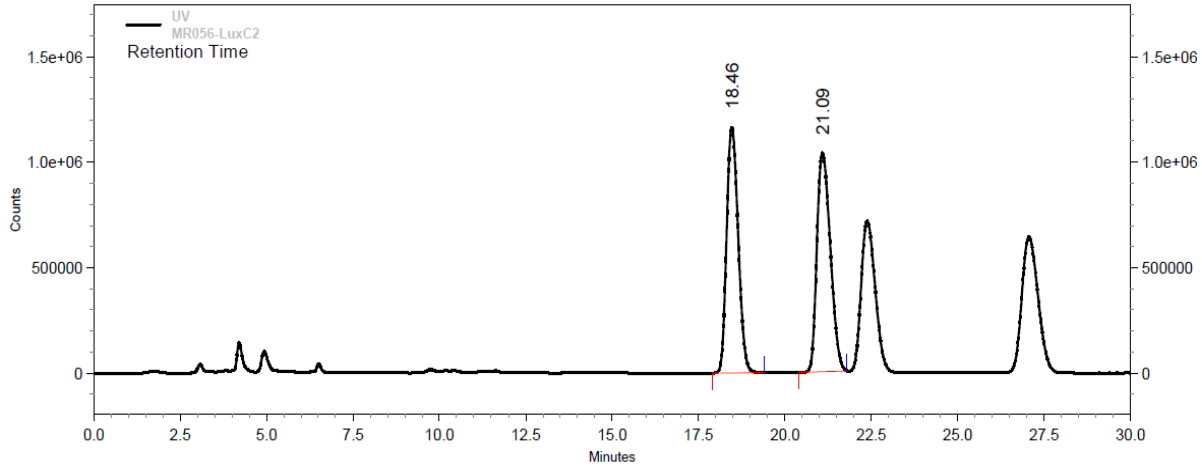






Racemate (dia 1):

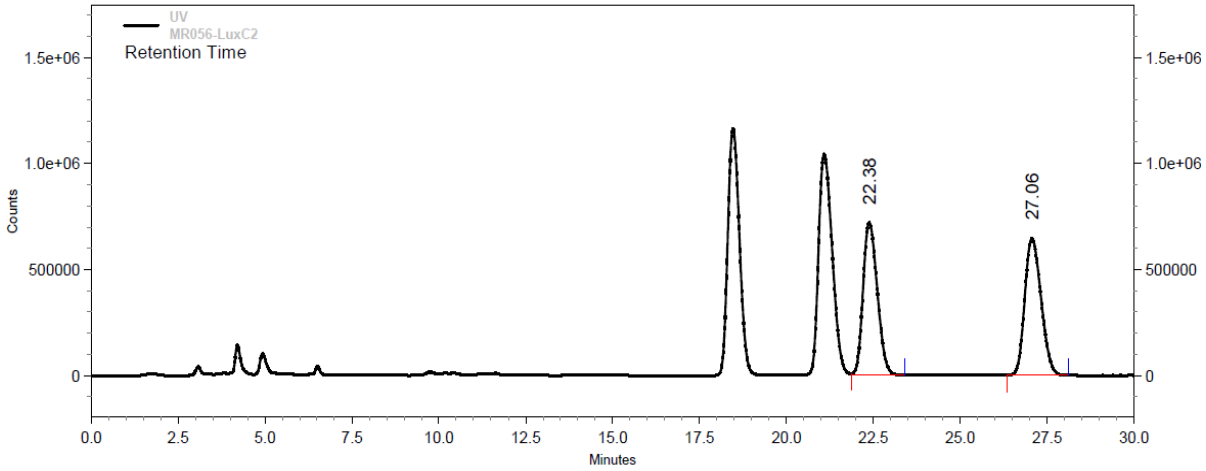
Method description : Lux-Cellulose-2, Heptane/Isopropanol 95/5, 1 ml/min, UV 254 nm et polarimetre




| Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 18.46 | 27057378 | 49.11 | 5.15 | 1.00 | 0.00 |
| 21.09 | 28036700 | 50.89 | 6.03 | 1.17 | 3.87 |

Racemate (dia 2):

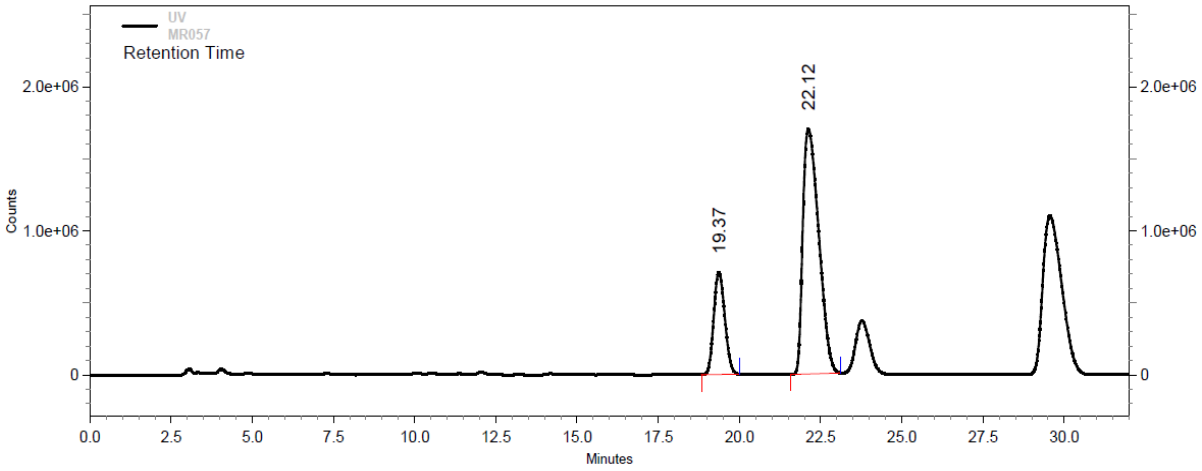
Method description : Lux-Cellulose-2, Heptane/Isopropanol 95/5, 1 ml/min, UV 254 nm et polarimetre




| Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 22.38 | 20419837 | 49.20 | 6.46 | 1.00 | 0.00 |
| 27.06 | 21081227 | 50.80 | 8.02 | 1.24 | 5.69 |

Enantioenriched (dia 1):

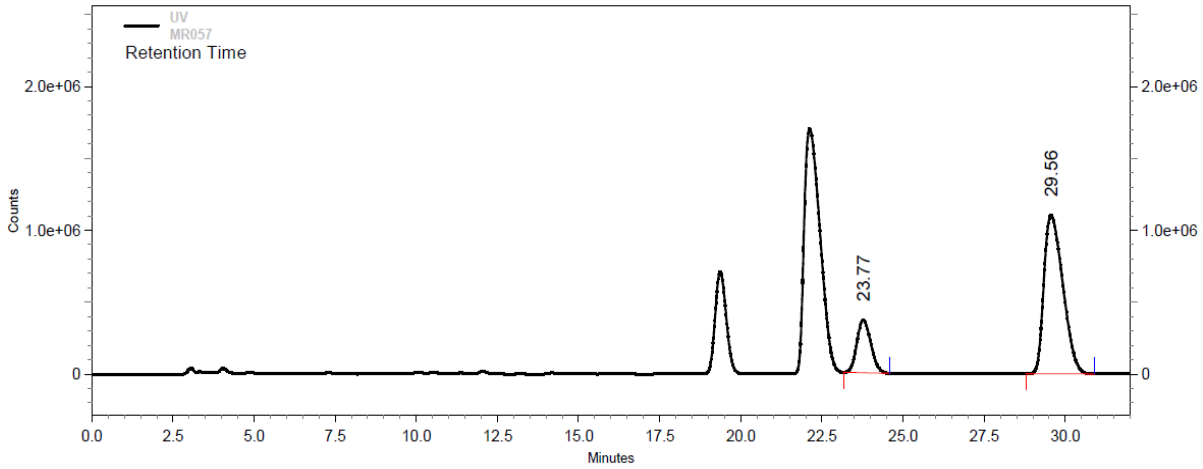
Method description : Lux-Cellulose-2, Heptane/Isopropanol 95/5, 1 ml/min, UV 254 nm et polarimetre




| Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 19.37 | 16874632 | 22.59 | 5.46 | 0.00 | 0.00 |
| 22.12 | 57838551 | 77.41 | 6.37 | 0.00 | 3.52 |

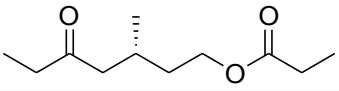
Enantioenriched (dia 2):

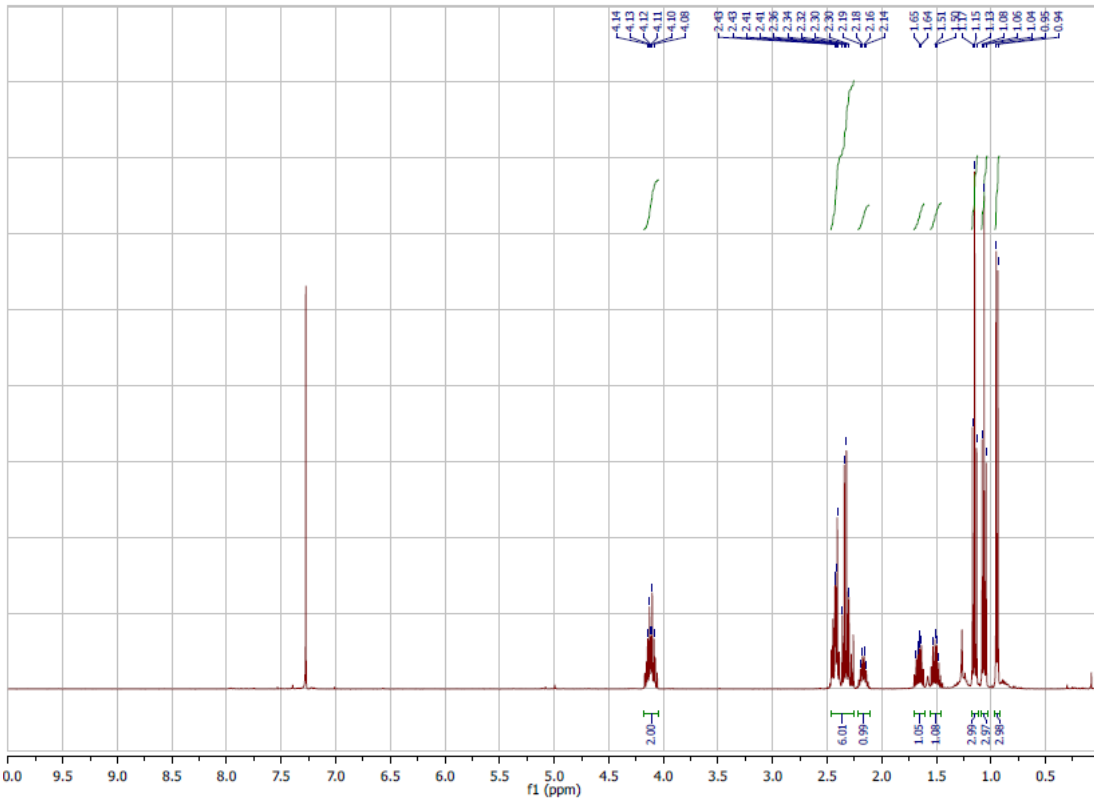
Method description : Lux-Cellulose-2, Heptane/Isopropanol 95/5, 1 ml/min, UV 254 nm et polarimetre

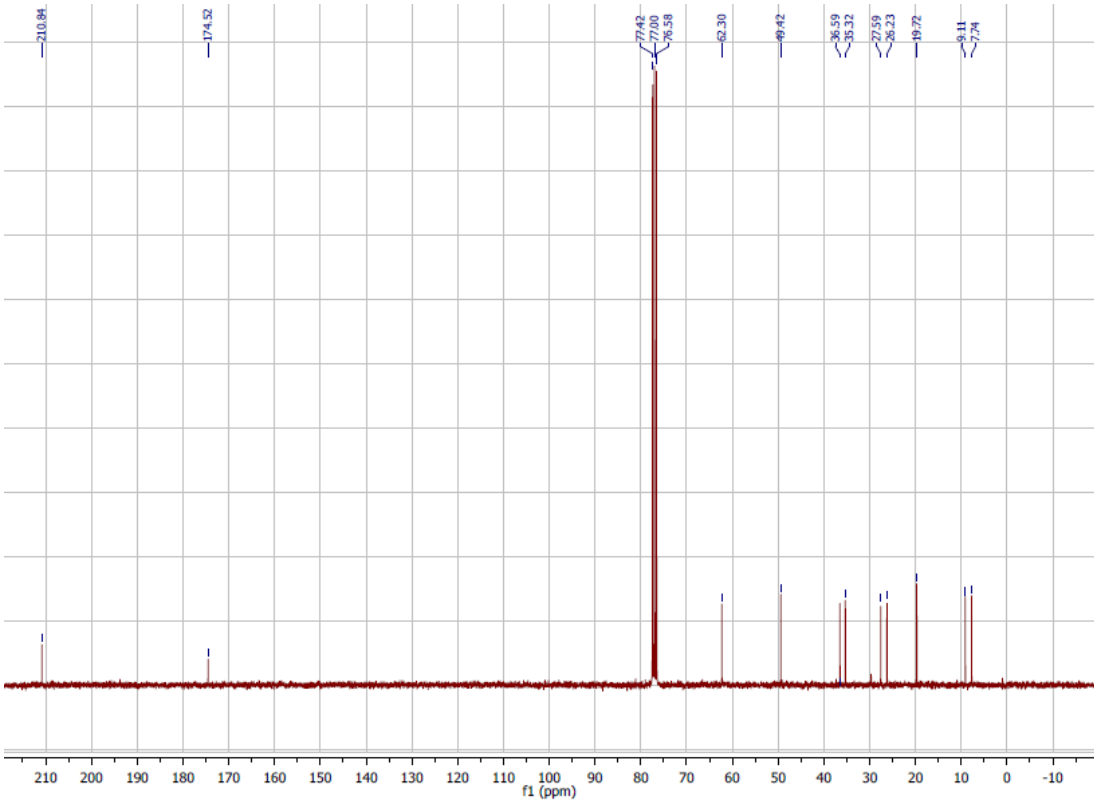



| Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 23.77 | 11026409 | 19.76 | 6.92 | 0.00 | 0.00 |
| 29.56 | 44769834 | 80.24 | 8.85 | 0.00 | 6.05 |

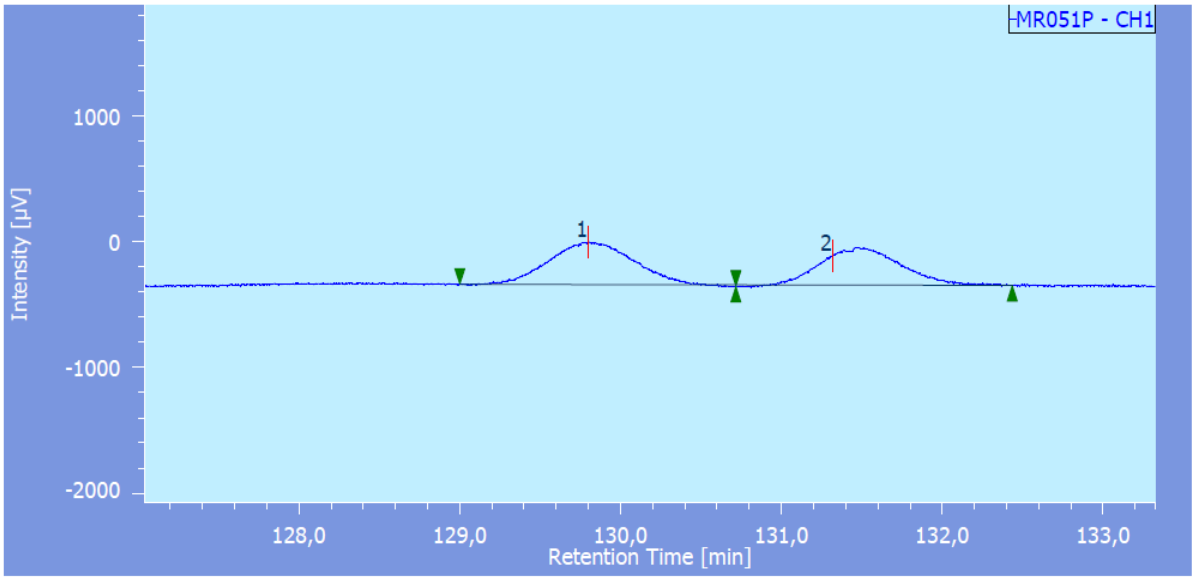
**Compound 3h**





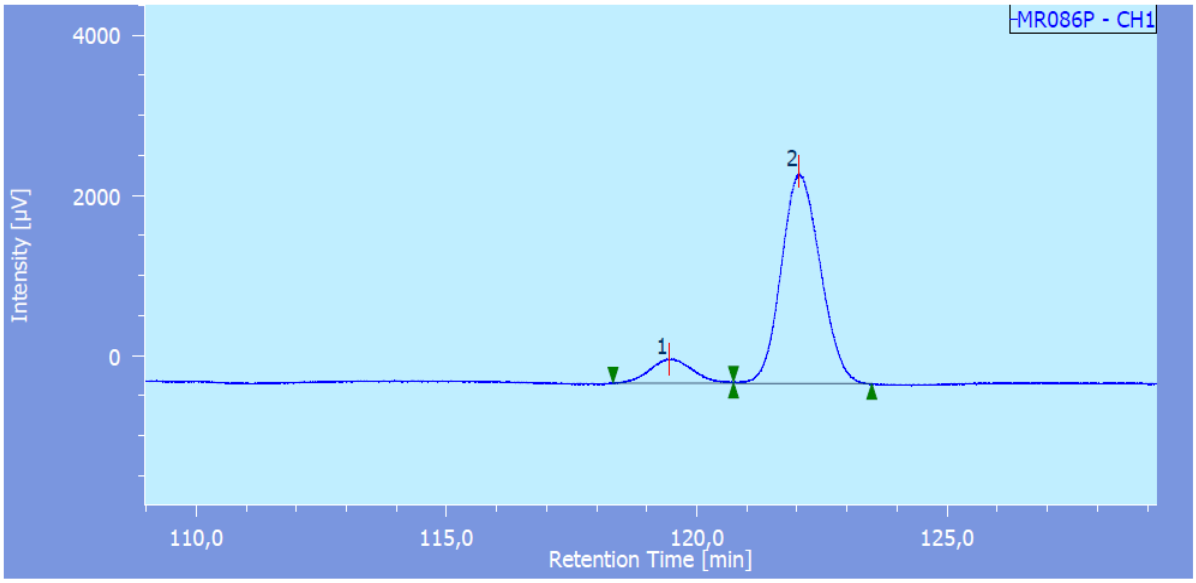



Racemate:



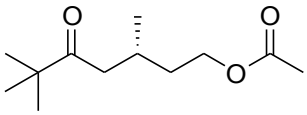

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 1 | 129,800 | 12292 | 338 | 54,501 | 59,456 | N/A | 269230 | 1,460 | 1,023 | |
| 2 | Unknown | 1 | 131,317 | 10262 | 230 | 45,499 | 40,544 | N/A | 235176 | N/A | 1,892 | |

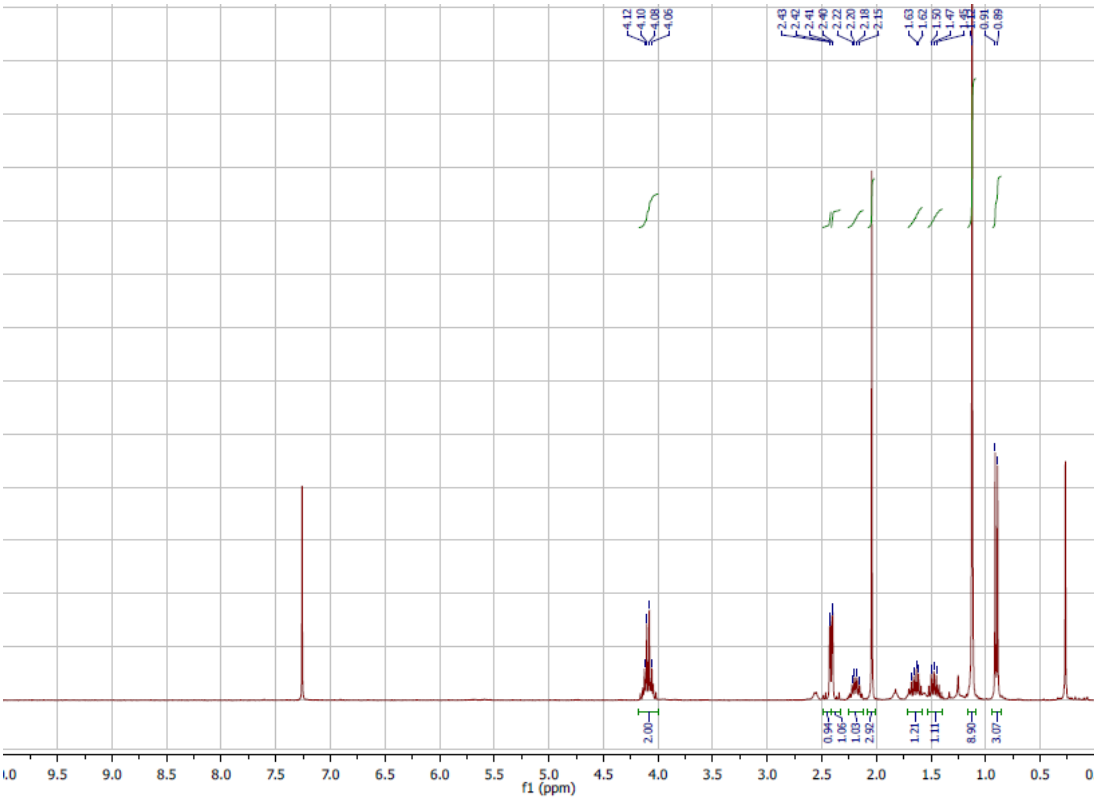
Enantioenriched:

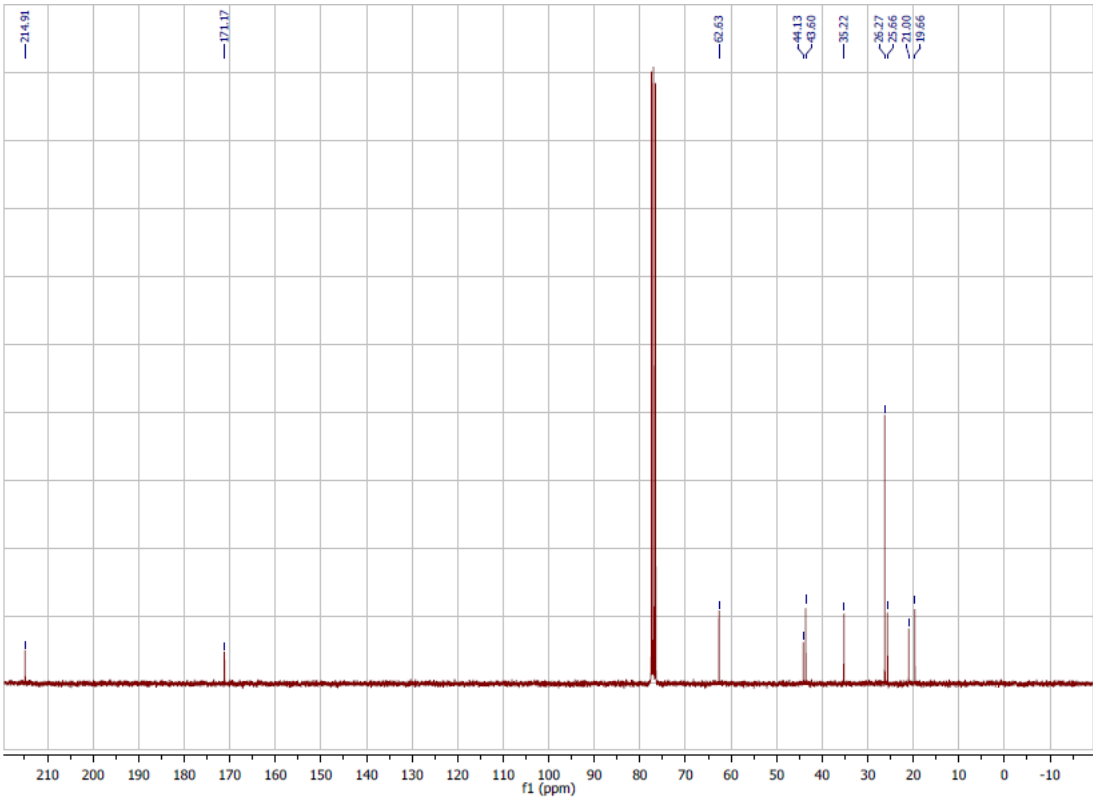



| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 1 | 119,433 | 18190 | 303 | 11,368 | 10,289 | N/A | 89796 | 1,720 | 1,199 | |
| 2 | Unknown | 1 | 122,033 | 141813 | 2643 | 88,632 | 89,711 | N/A | 115515 | N/A | 1,115 | |

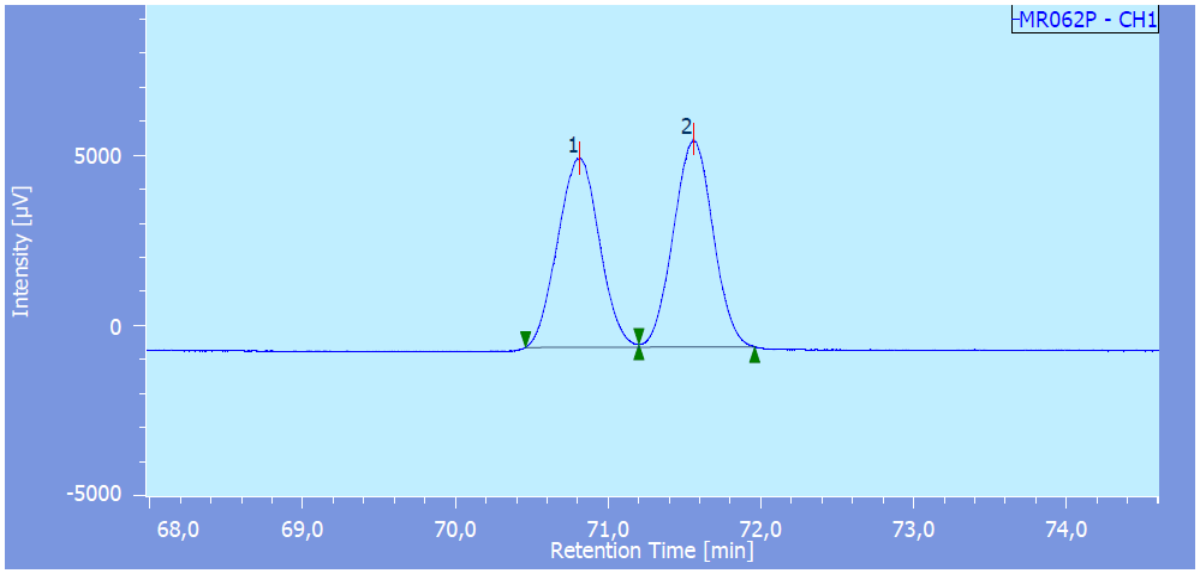
**Compound 3i**





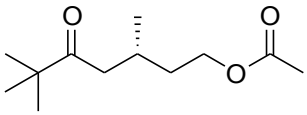


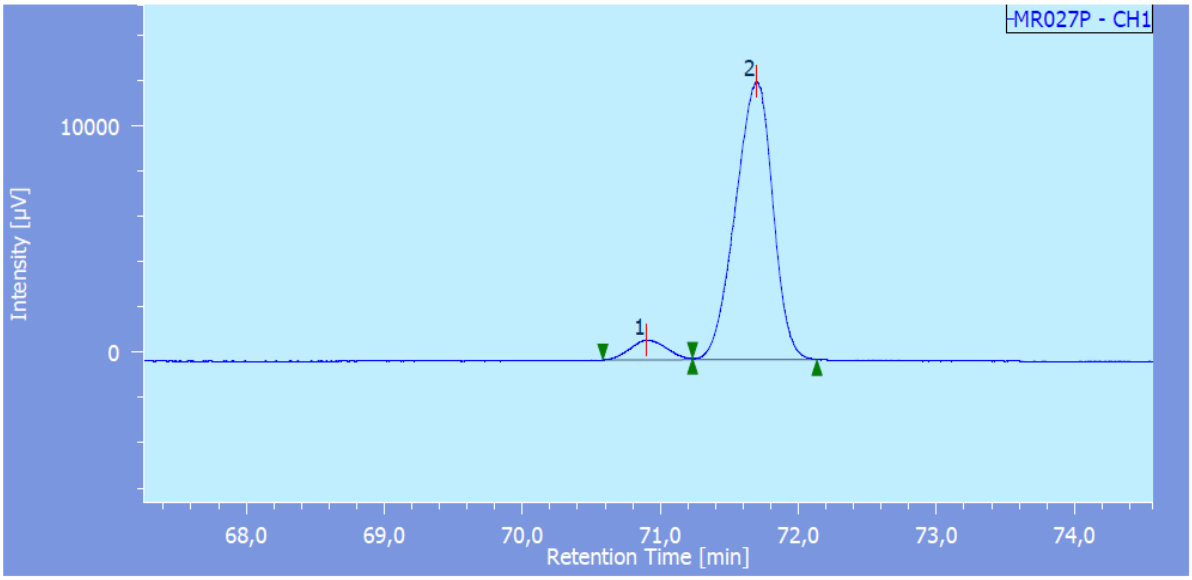
Racemate:




| # | Peak Name | CH | tR [min] | Area [µV·sec] | Height [µV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 1 | 70,817 | 105359 | 5542 | 49,056 | 47,611 | N/A | 305948 | 1,496 | 0,996 | |
| 2 | Unknown | 1 | 71,558 | 109412 | 6098 | 50,944 | 52,389 | N/A | 353142 | N/A | 1,025 | |

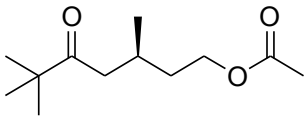
Enantioenriched (using **(*S*)-cat1**):

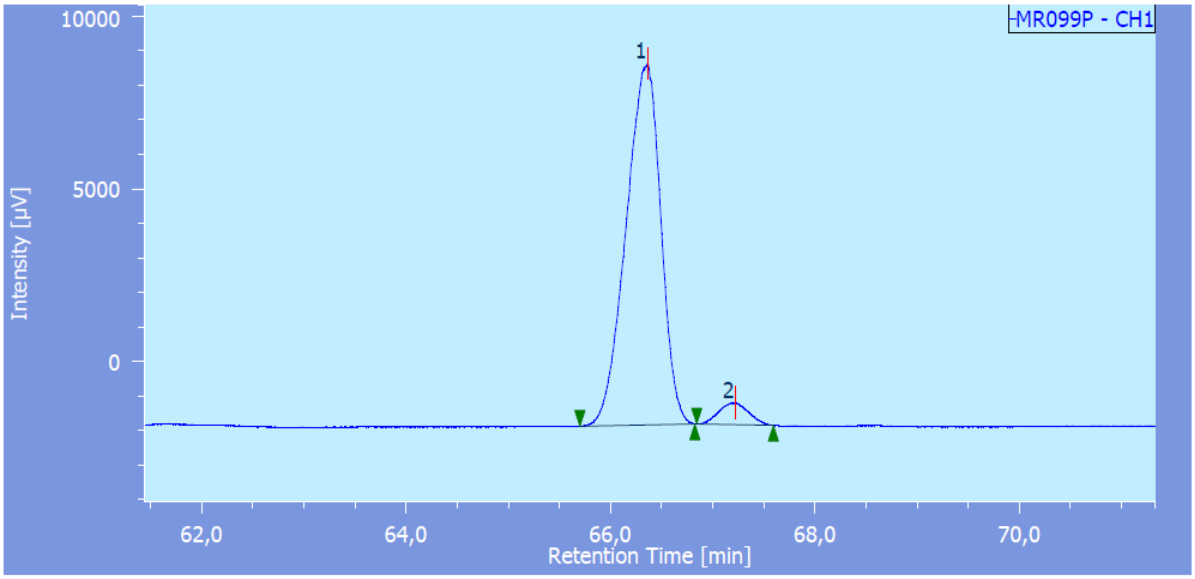



| # | Peak Name | CH | tR [min] | Area [µV·sec] | Height [µV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 1 | 70,900 | 16269 | 868 | 6,596 | 6,611 | N/A | 309467 | 1,568 | N/A | |
| 2 | Unknown | 1 | 71,692 | 230385 | 12255 | 93,404 | 93,389 | N/A | 325237 | N/A | 0,922 | |

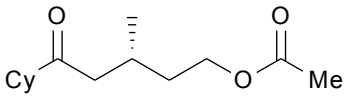
Enantioenriched (using **(*R*)-cat1**):

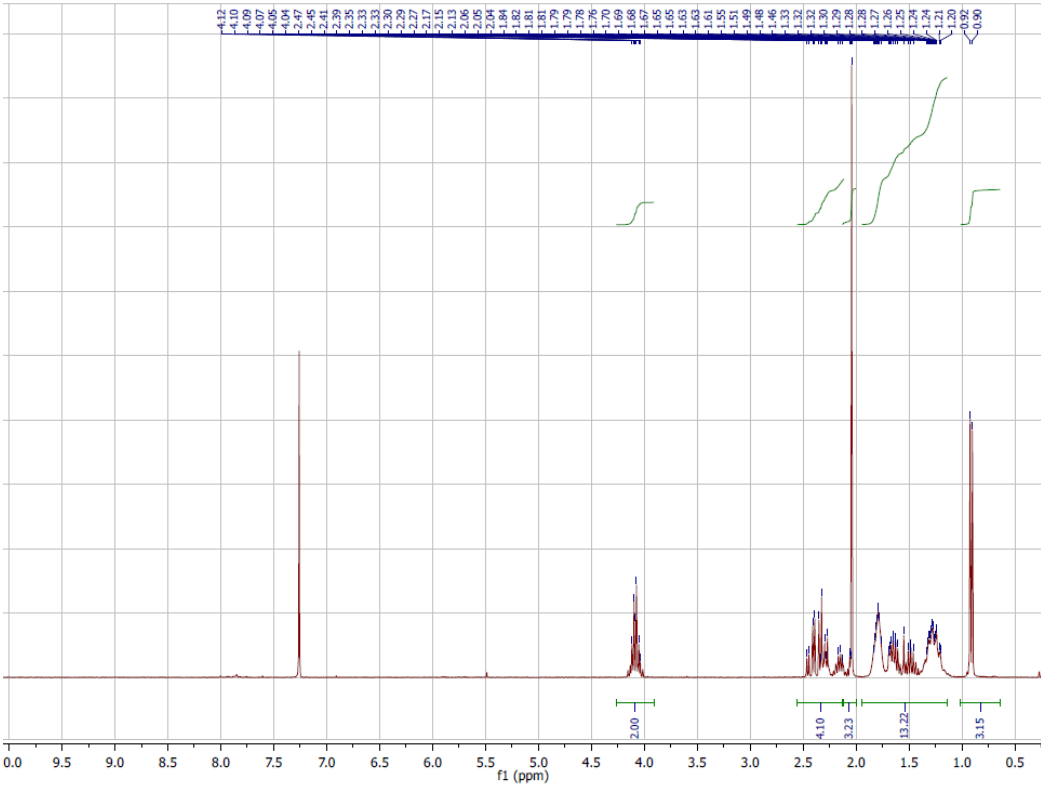


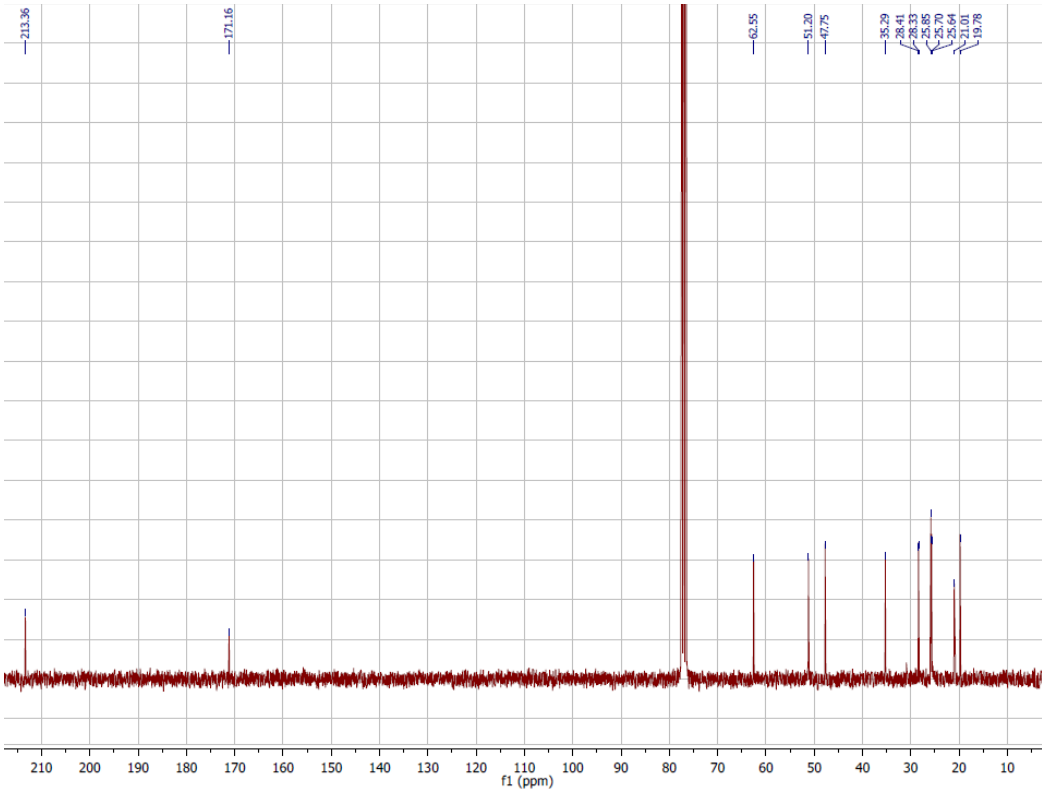



| # | Peak Name | CH | tR [min] | Area [µV·sec] | Height [µV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 1 | 66,358 | 247189 | 10457 | 95,022 | 94,245 | N/A | 175178 | 1,441 | 0,858 | |
| 2 | Unknown | 1 | 67,217 | 12950 | 639 | 4,978 | 5,755 | N/A | 230456 | N/A | 1,000 | |

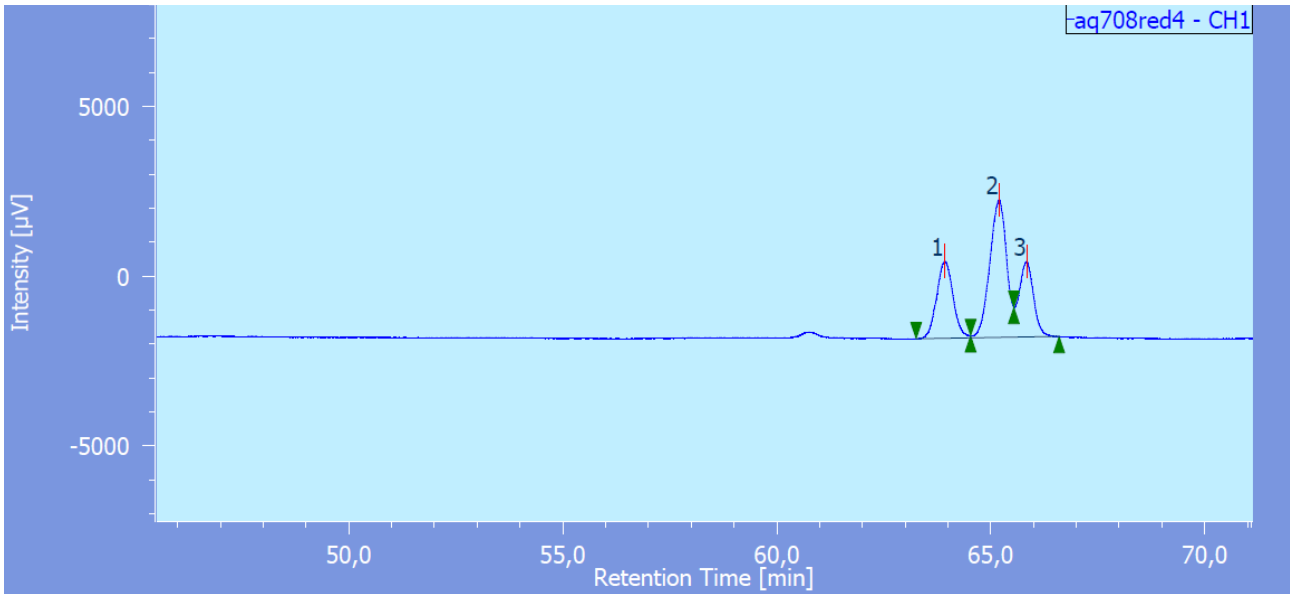
**Compound 3j**


O
O
Cy
O
Me


2.00
4.10
3.23
13.22
3.15
f1 (ppm)

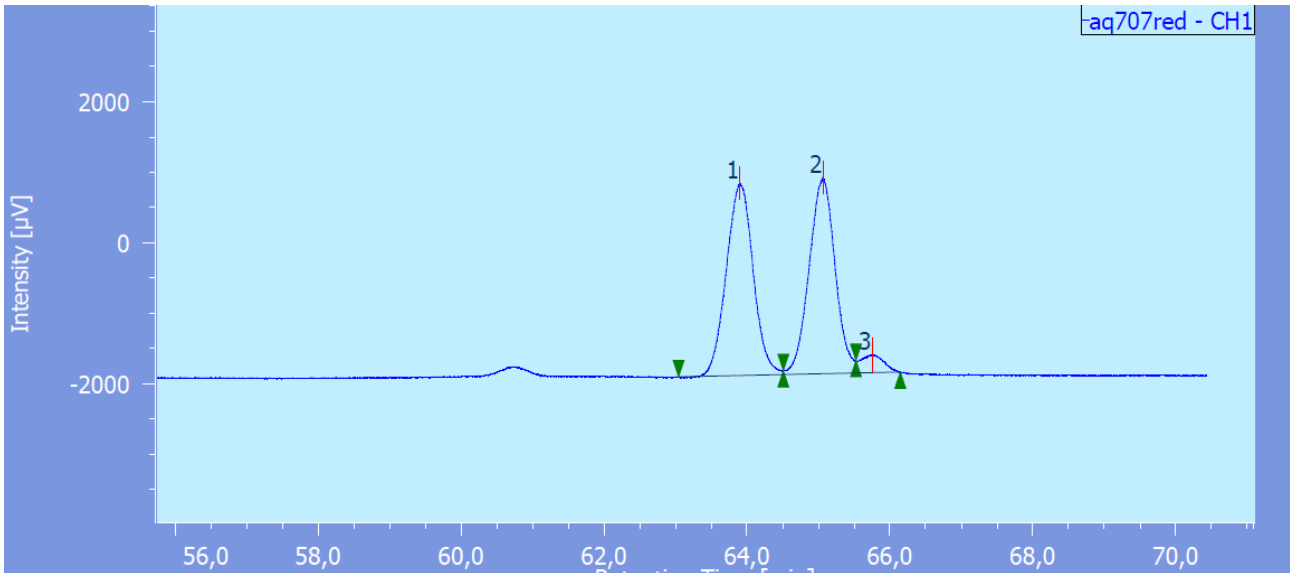

213.36
171.16
62.55
51.20
47.75
35.29
28.41
28.33
25.85
25.70
25.64
21.01
19.78
f1 (ppm)

Racemate (determined on the corresponding diol obtained by non selective reduction with $LiAlH_4$, one single diastereomers of the diol is separated):



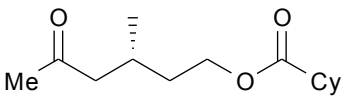

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 1 | 63.917 | 60577 | 2282 | 27.004 | 26.612 | N/A | 134913 | 1.794 | 1.074 | |
| 2 | Unknown | 1 | 65.192 | 110977 | 4059 | 49.471 | 47.343 | N/A | 127963 | 0.948 | N/A | |
| 3 | Unknown | 1 | 65.842 | 52773 | 2233 | 23.525 | 26.045 | N/A | 166369 | N/A | N/A | |

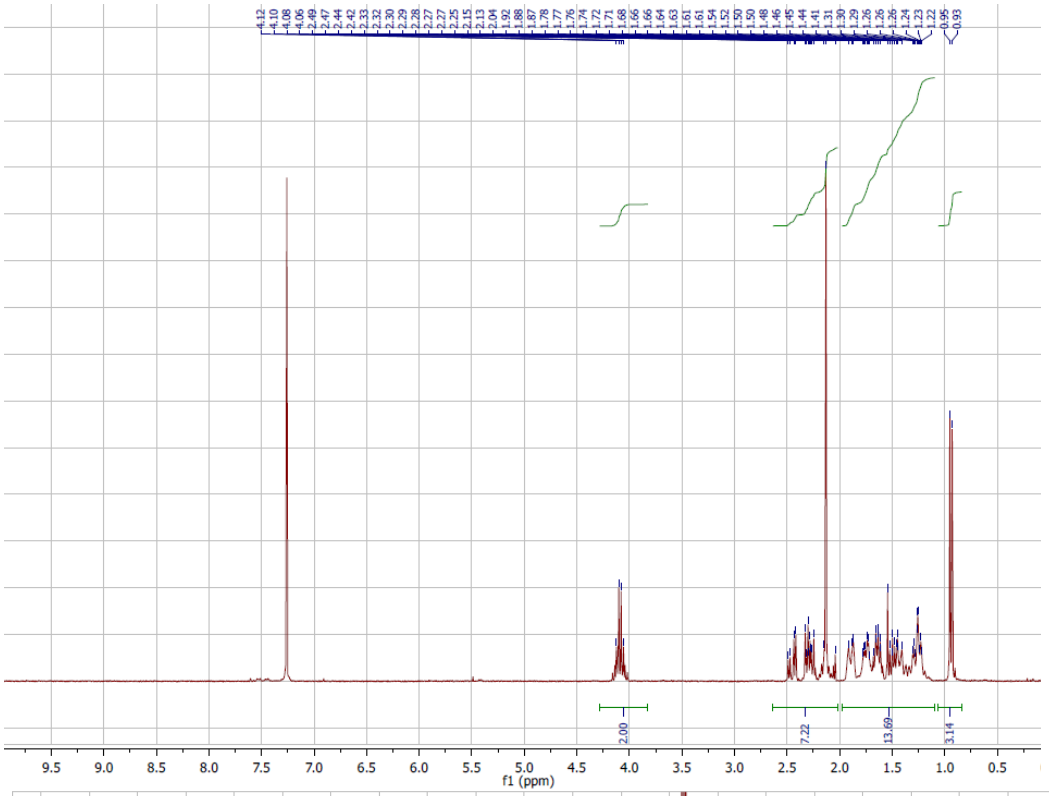
Enantioenriched (determined on the corresponding diol obtained by non selective reduction with $LiAlH_4$, one single diastereomers of the diol is separated):

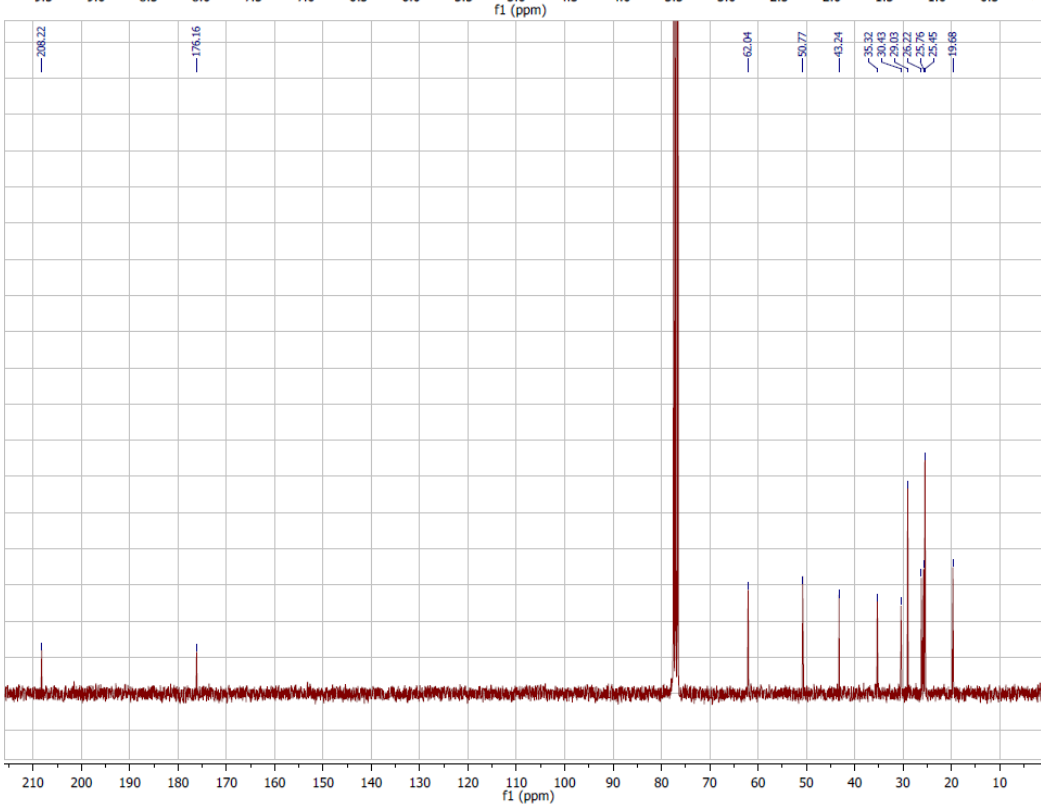



| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 1 | 63.900 | 71214 | 2726 | 48.385 | 47.304 | N/A | 139502 | 1.729 | 1.030 | |
| 2 | Unknown | 1 | 65.058 | 70201 | 2782 | 47.697 | 48.282 | N/A | 155947 | N/A | N/A | |
| 3 | Unknown | 1 | 65.750 | 5767 | 254 | 3.918 | 4.414 | N/A | N/A | N/A | N/A | |

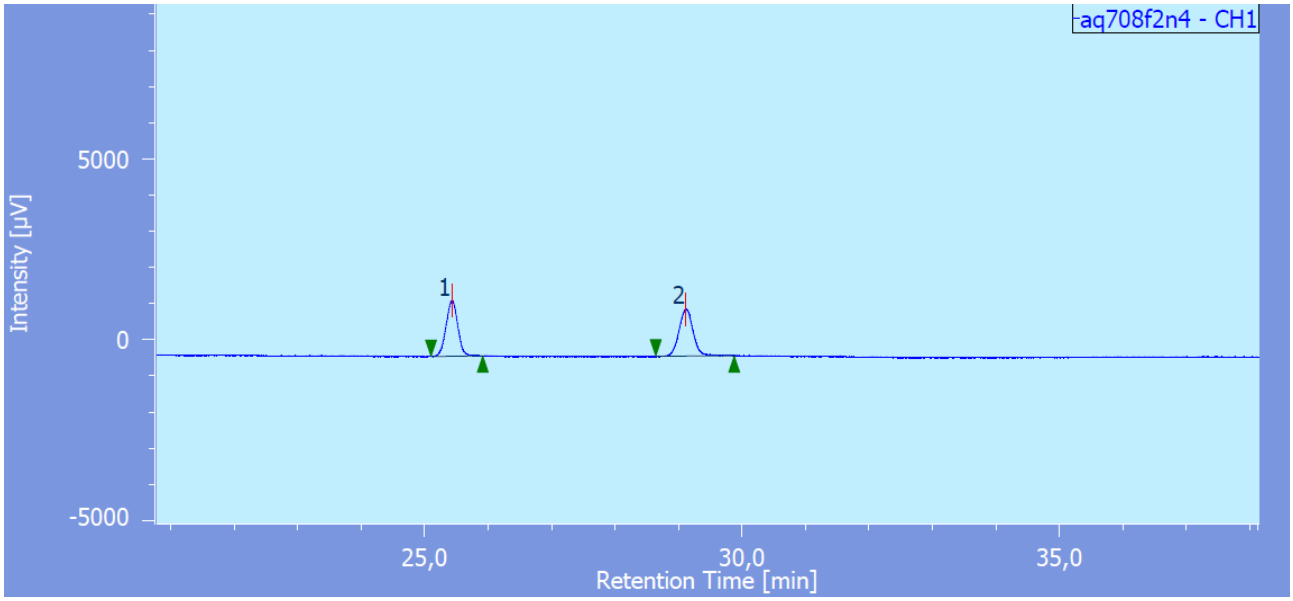
**Compound 3k**


O
O
Me
O
Cy


2.00
7.22
13.69
3.14
f1 (ppm)

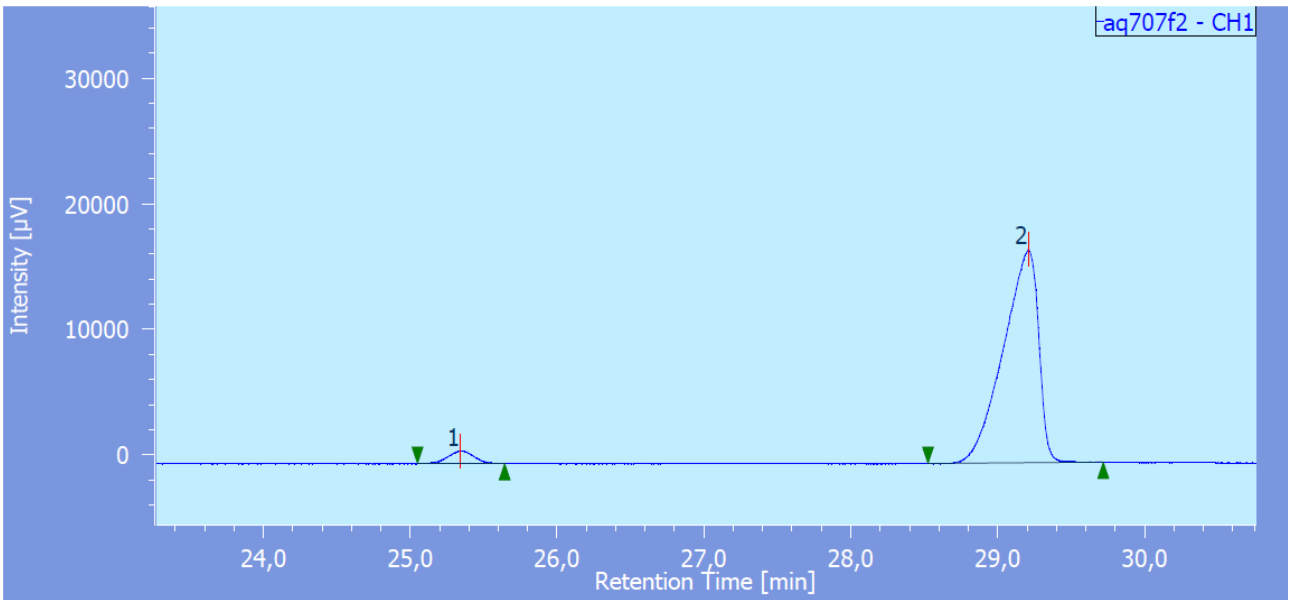

208.22
176.16
62.04
50.77
43.24
35.32
30.43
29.03
26.22
25.76
25.45
19.68
f1 (ppm)

Racemate :



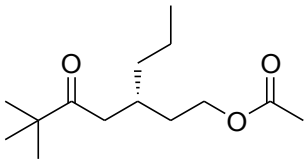

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 1 | 25.433 | 19998 | 1538 | 49.857 | 54.228 | N/A | 90264 | 10.036 | 0.997 | |
| 2 | Unknown | 1 | 29.117 | 20113 | 1298 | 50.143 | 45.772 | N/A | 85907 | N/A | 1.066 | |

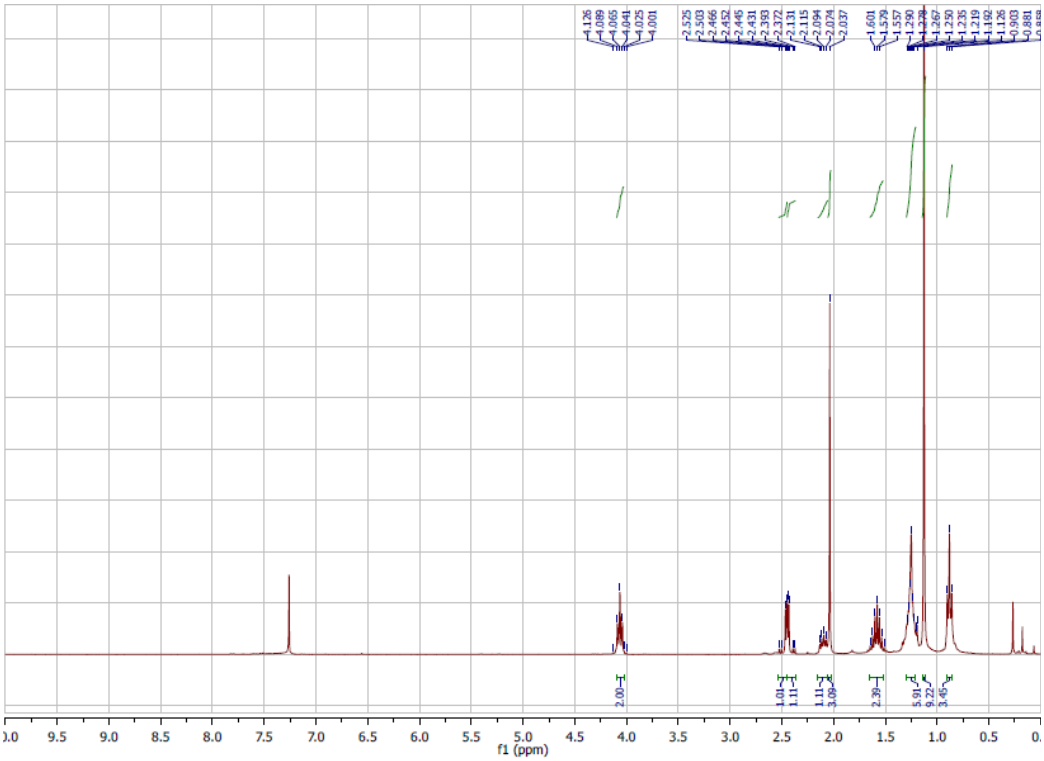
Enantioenriched :

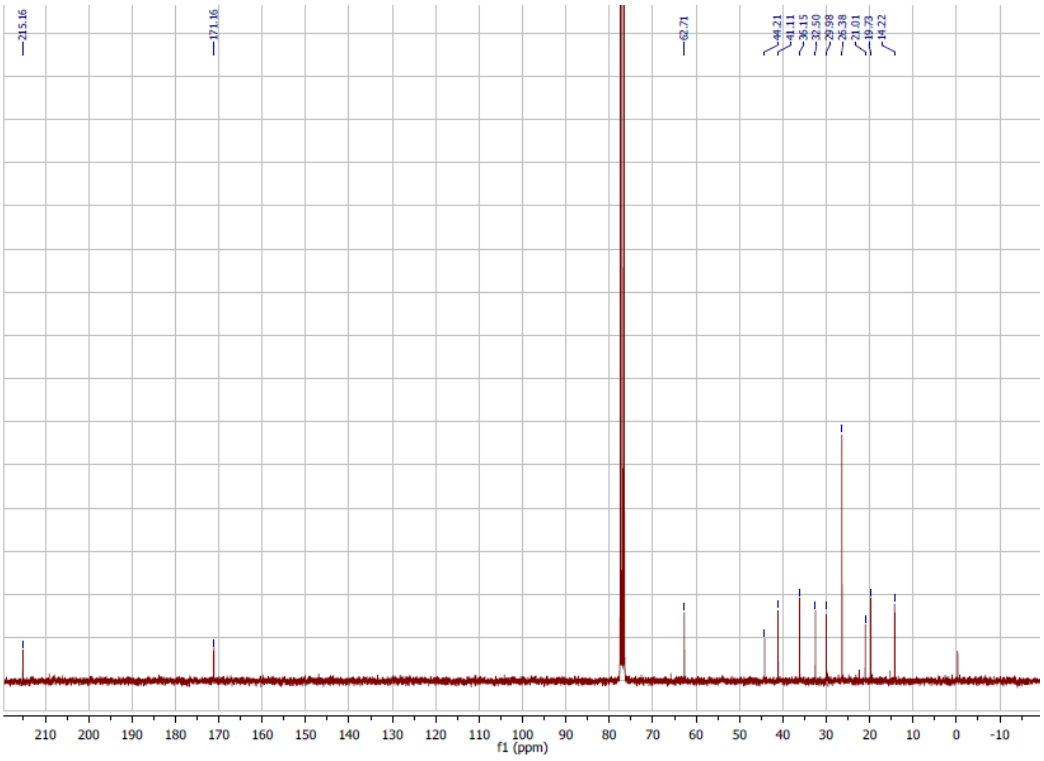



| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 1 | 25.342 | 12173 | 988 | 4.131 | 5.488 | N/A | 95875 | 10.054 | 1.012 | |
| 2 | Unknown | 1 | 29.208 | 282480 | 17018 | 95.869 | 94.512 | N/A | 69278 | N/A | 0.690 | |

**Compound 3l**



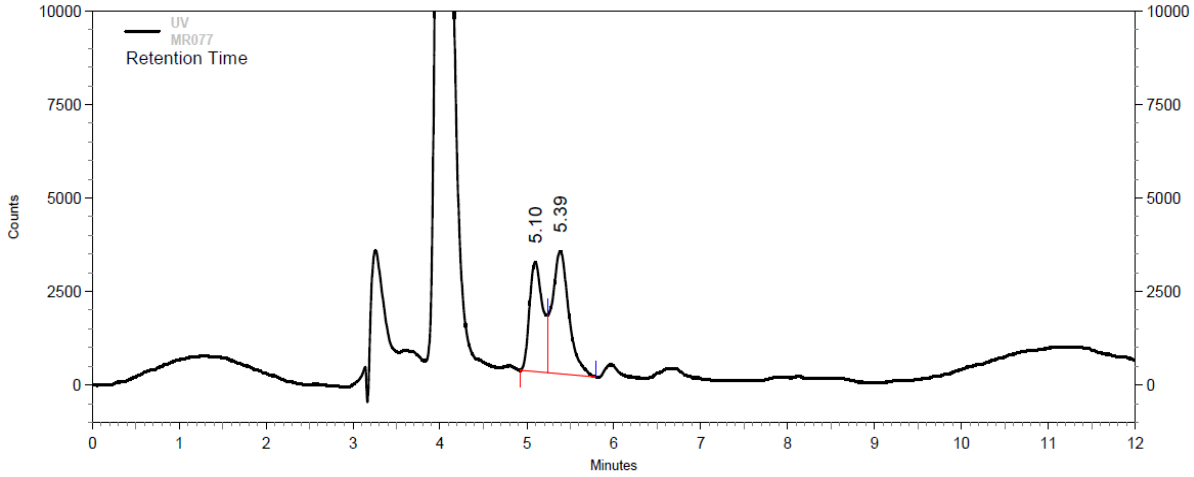




The compound containing a poor chromophore was separated on two different chiral columns. These two columns gave the same results in terms of enantiocontrol (ee > 90%).

Racemate (column 1):

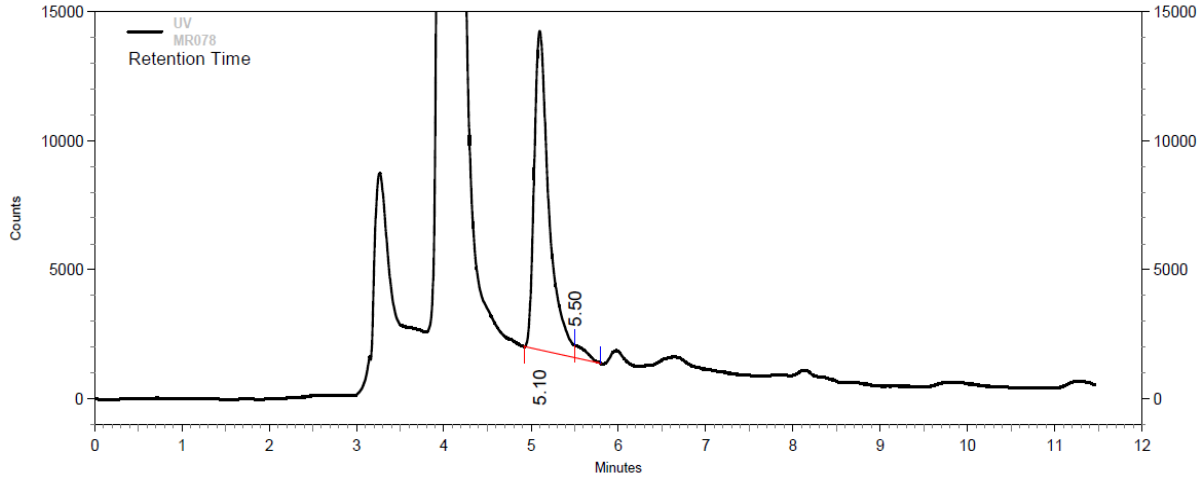
Method description : Chiralpak AZ-H, Heptane/Isopropanol 95/5, 1 ml/min, UV 310 nm




| UV Results Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 5.10 | 31447 | 42.05 | 0.70 | 0.00 | 0.00 |
| 5.39 | 43336 | 57.95 | 0.80 | 0.00 | 0.87 |

Enantionenriched (column 1):

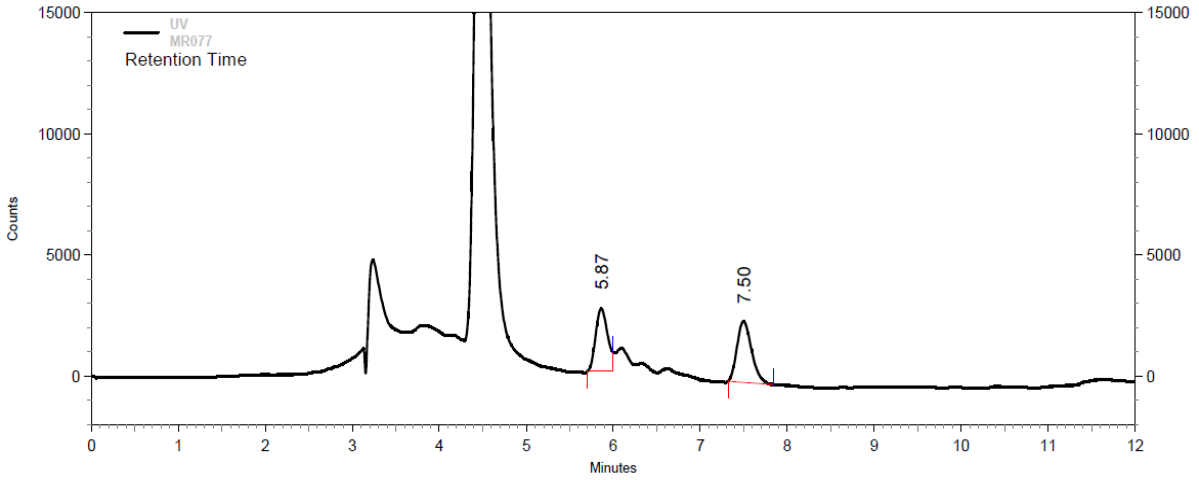
Method description : Chiralpak AZ-H, Heptane/Isopropanol 95/5, 1 ml/min, UV 310 nm




| UV Results Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 5.10 | 145240 | 96.92 | 0.70 | 0.00 | 0.00 |
| 5.50 | 4612 | 3.08 | 0.83 | 0.00 | 0.00 |

Racemate (column 2):

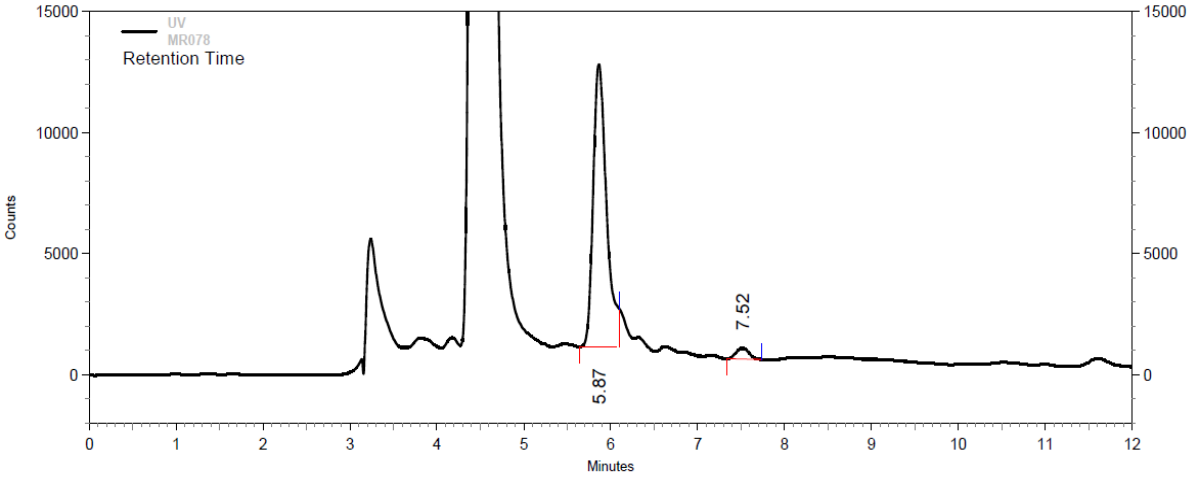
Method description : Lux-Amylose-2, Heptane/Isopropanol 95/5, 1 ml/min, UV 310 nm




| UV Results Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 5.87 | 25079 | 46.01 | 0.96 | 0.00 | 0.00 |
| 7.50 | 29426 | 53.99 | 1.50 | 0.00 | 0.00 |

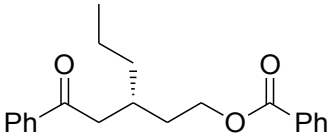
Enantionenriched (column 2):

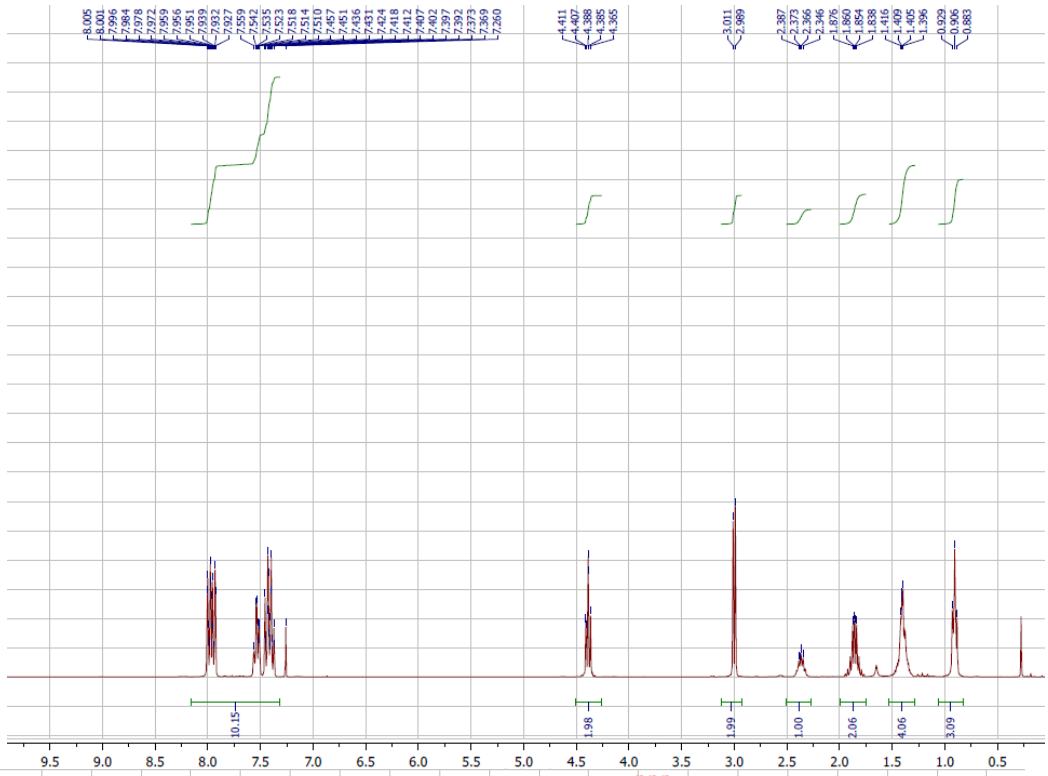
Method description : Lux-Amylose-2, Heptane/Isopropanol 95/5, 1 ml/min, UV 310 nm

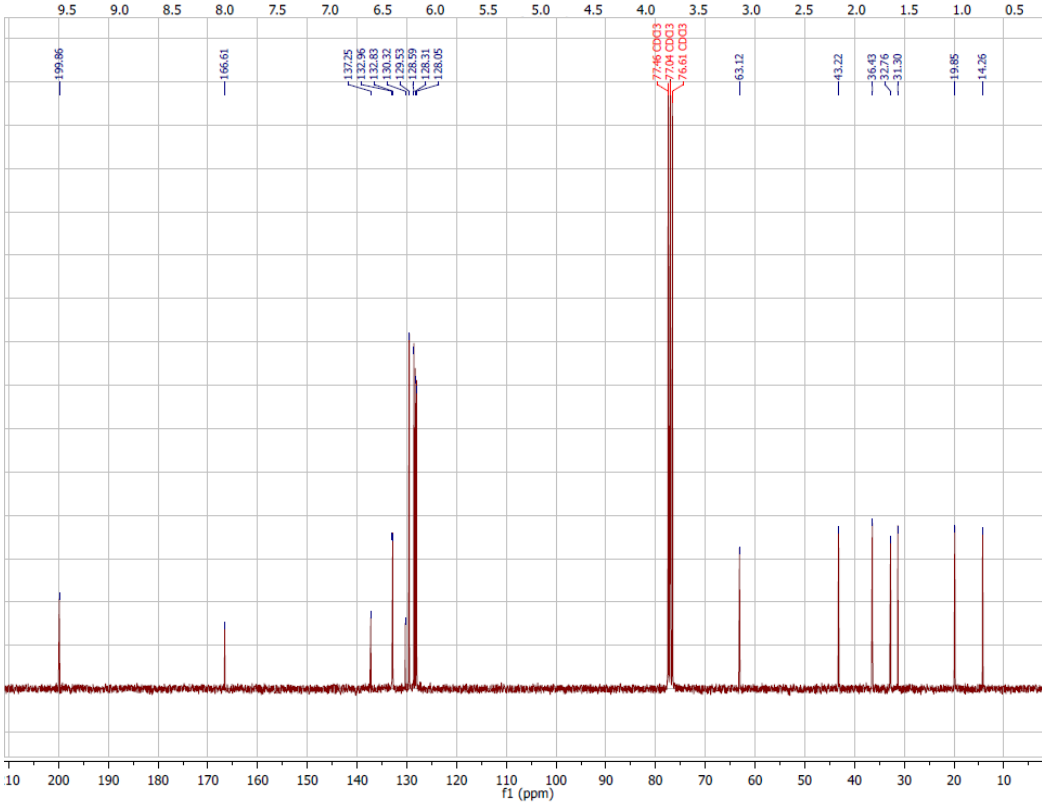



| UV Results Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 5.87 | 124130 | 96.43 | 0.96 | 0.00 | 0.00 |
| 7.52 | 4593 | 3.57 | 1.51 | 0.00 | 6.10 |

**Compound 3m**

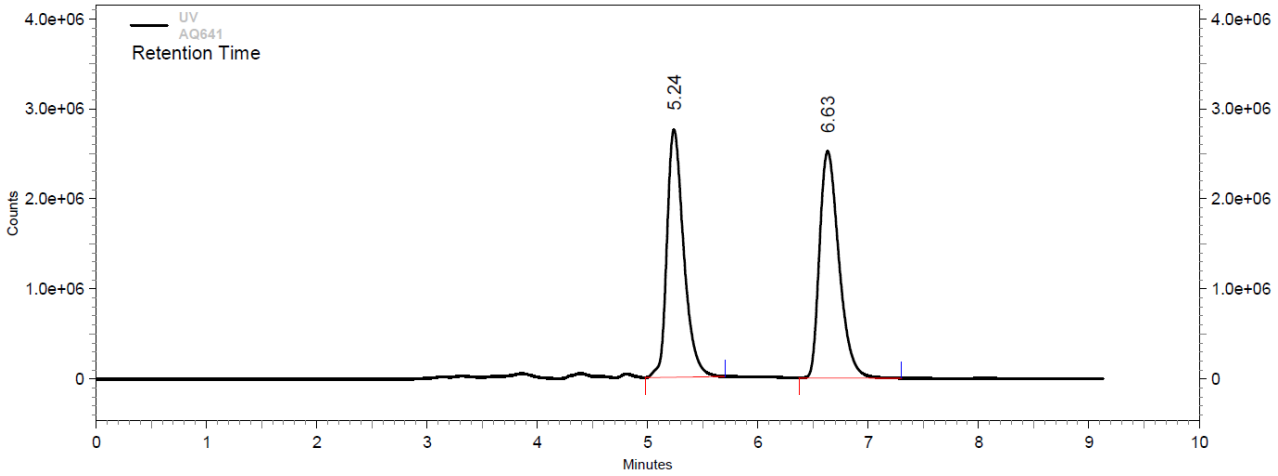




Racemate :

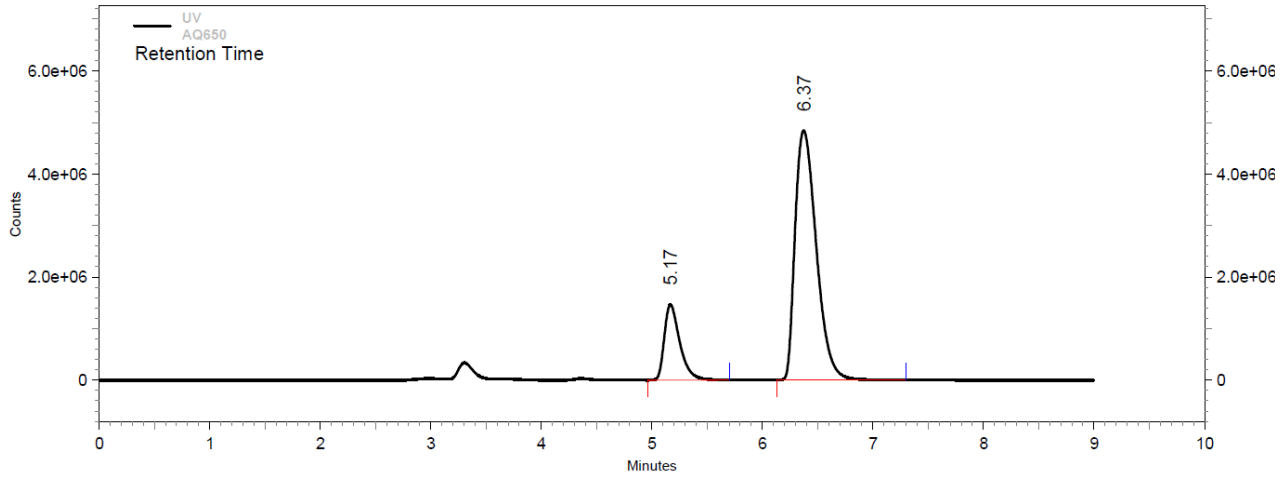
Method description : Chiralcel OD-3, Heptane/Ethanol 90/10, 1 ml/min, UV 254 nm et polarimetre




| Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 5.24 | 29163072 | 48.72 | 0.75 | 1.00 | 0.00 |
| 6.63 | 30692572 | 51.28 | 1.21 | 1.62 | 4.69 |

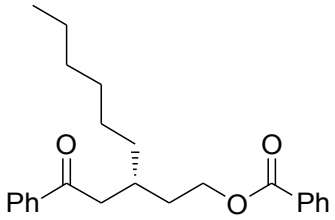
Enantioenriched :

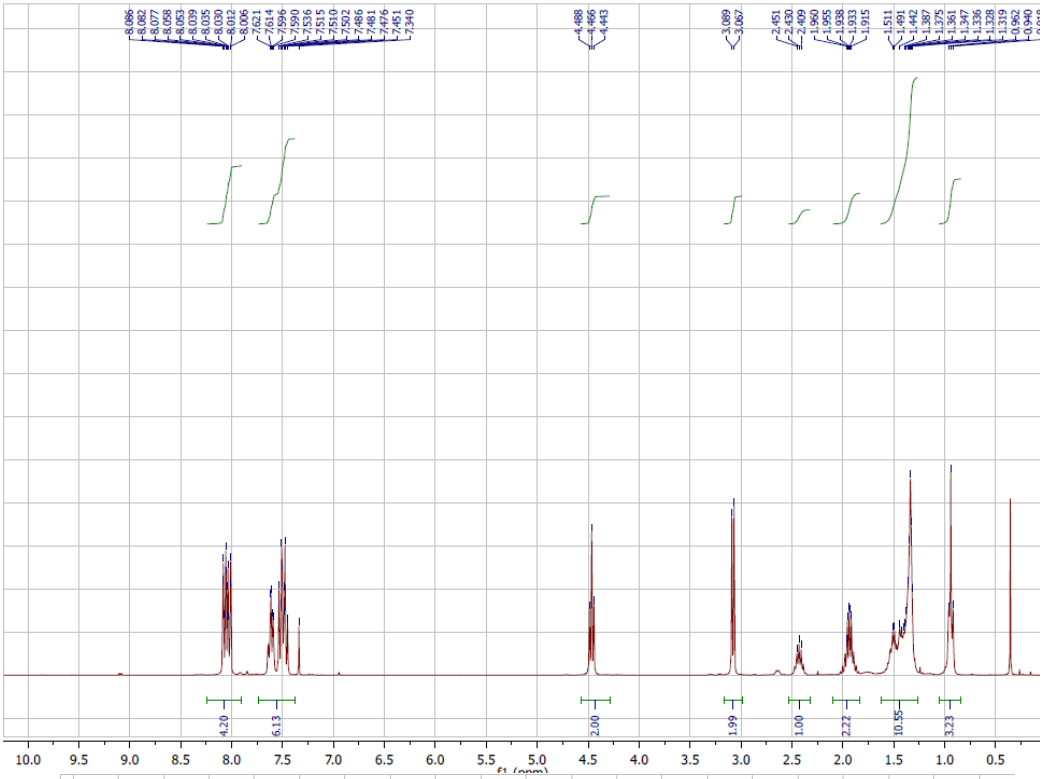
Method description : Chiralcel OD-3, Heptane/Ethanol 90/10, 1 ml/min, UV 254 nm et polarimetre

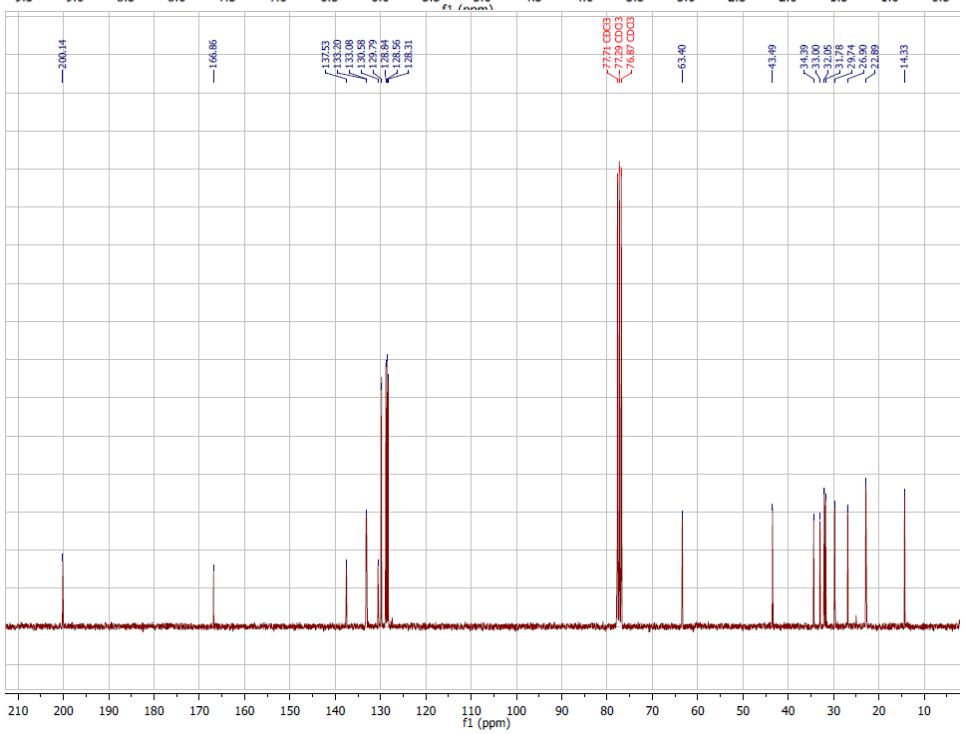



| Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 5.17 | 14156231 | 17.98 | 0.72 | 1.00 | 0.00 |
| 6.37 | 64562701 | 82.02 | 1.12 | 0.00 | 4.00 |

**Compound 3n**

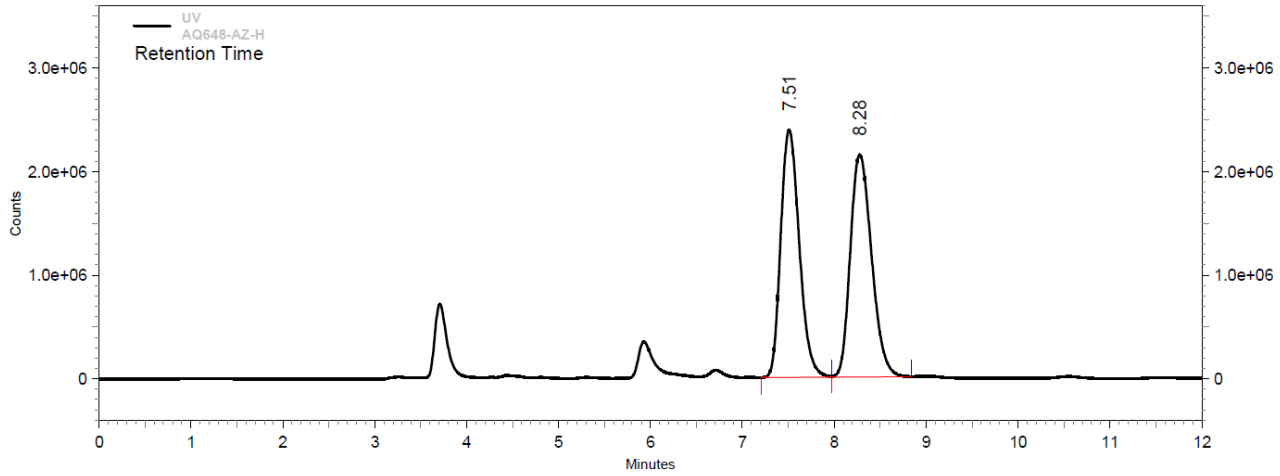

O
O
Ph
O
Ph


8.086
8.082
8.077
8.068
8.065
8.039
8.035
8.030
8.012
8.006
7.621
7.614
7.596
7.590
7.556
7.515
7.510
7.502
7.486
7.481
7.476
7.451
7.340
4.488
4.466
4.443
3.089
3.067
2.451
2.430
2.409
1.960
1.955
1.938
1.933
1.915
1.511
1.491
1.442
1.387
1.375
1.361
1.347
1.336
1.328
1.319
0.962
0.940
4.20
6.13
2.00
1.99
1.00
2.22
10.55
3.23
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5


200.14
166.86
137.53
133.20
131.68
130.58
129.79
128.84
128.56
128.31
77.71 CDCl3
77.29 CDCl3
76.87 CDCl3
63.40
43.49
34.39
33.00
32.05
31.78
29.74
26.90
22.89
14.33
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

Racemate :

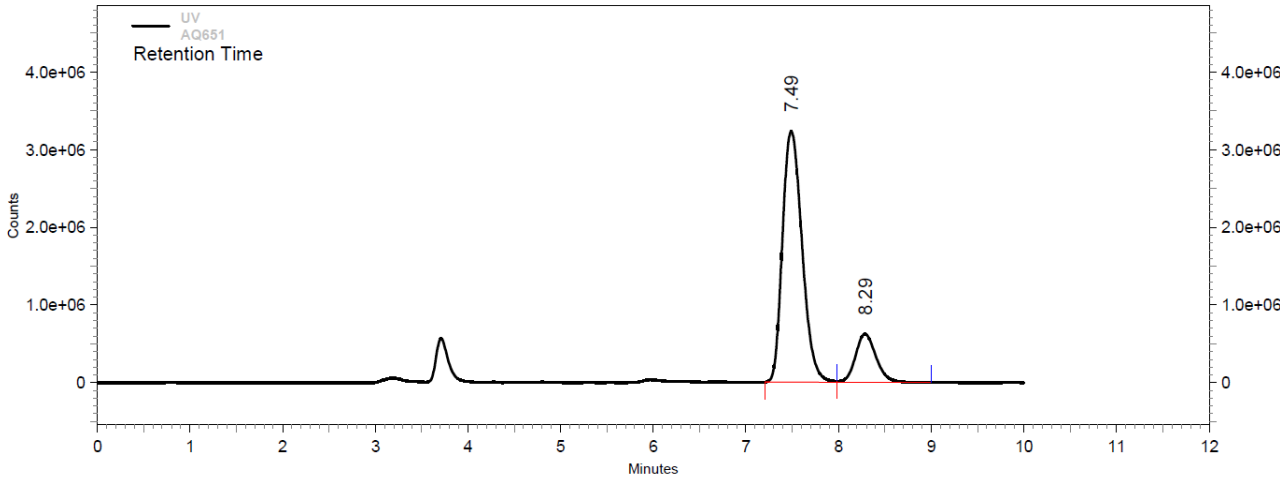
Method description : Chiralpak AZ-H, Heptane/Ethanol 90/10, 1 ml/min, UV 254 nm et polarimetre




| Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 7.51 | 33563352 | 49.25 | 1.50 | 1.00 | 0.00 |
| 8.28 | 34590111 | 50.75 | 1.76 | 1.17 | 1.92 |

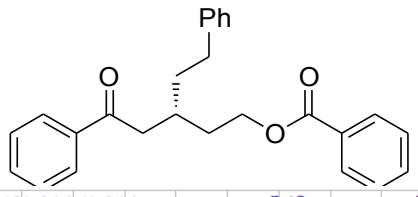
Enantioenriched :

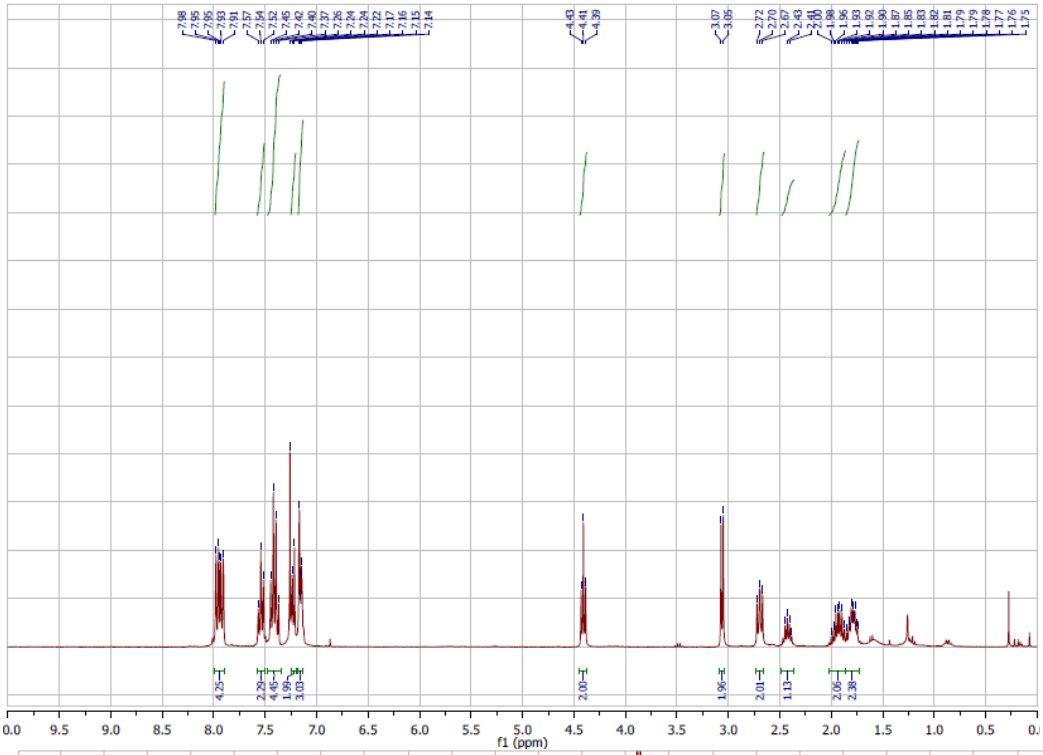
Method description : Chiralpak AZ-H, Heptane/Ethanol 90/10, 1 ml/min, UV 254 nm et polarimetre

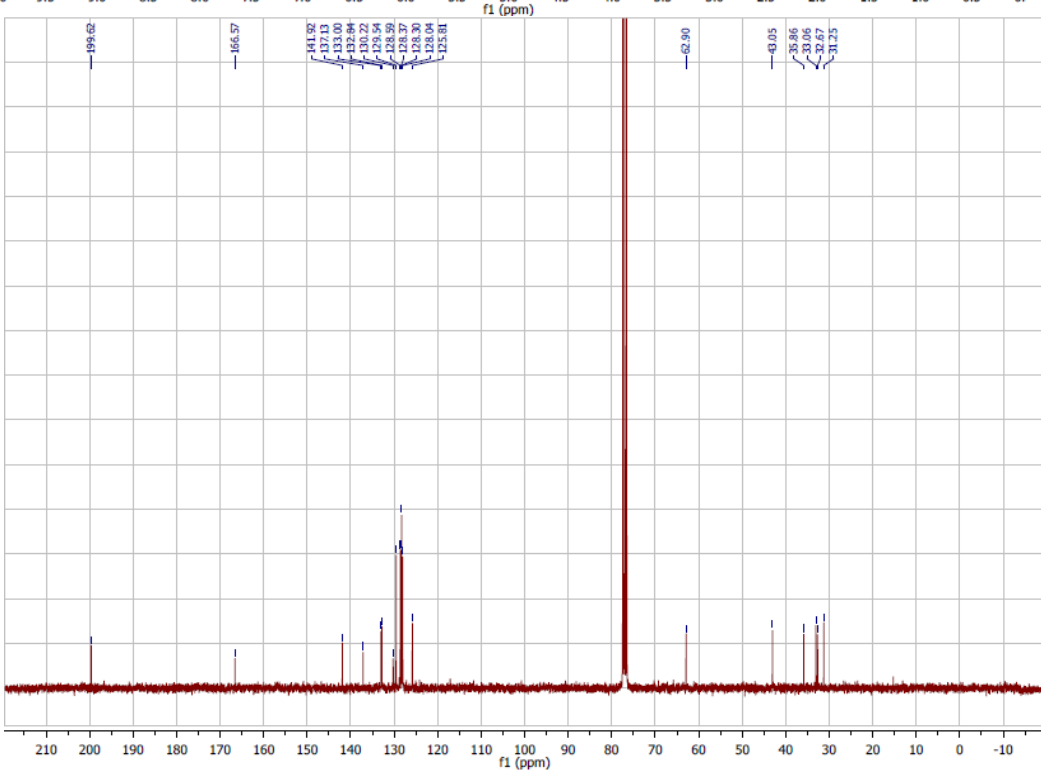



| Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 7.49 | 47531955 | 83.29 | 1.50 | 1.00 | 0.00 |
| 8.29 | 9535471 | 16.71 | 1.76 | 1.18 | 2.01 |

**Compound 3o**

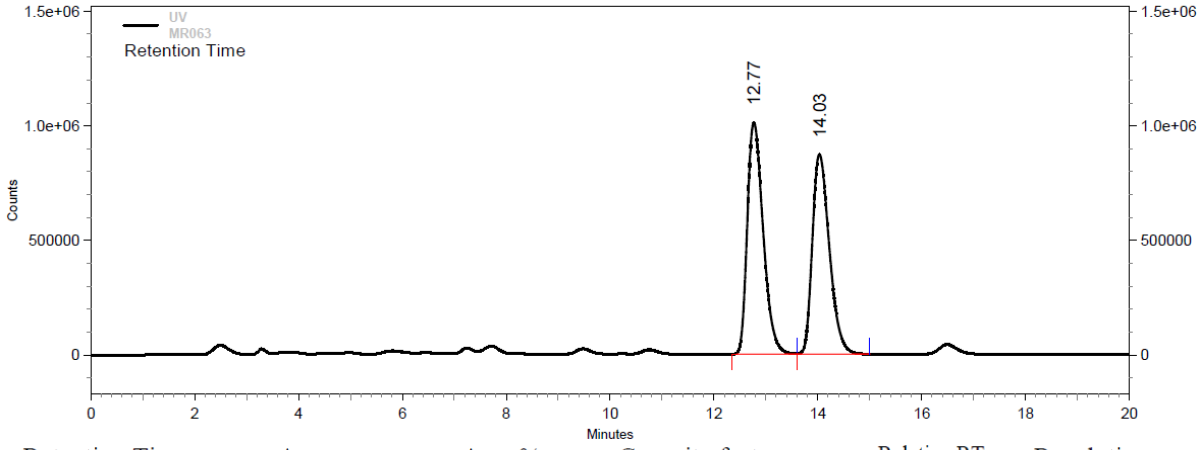


Racemate:

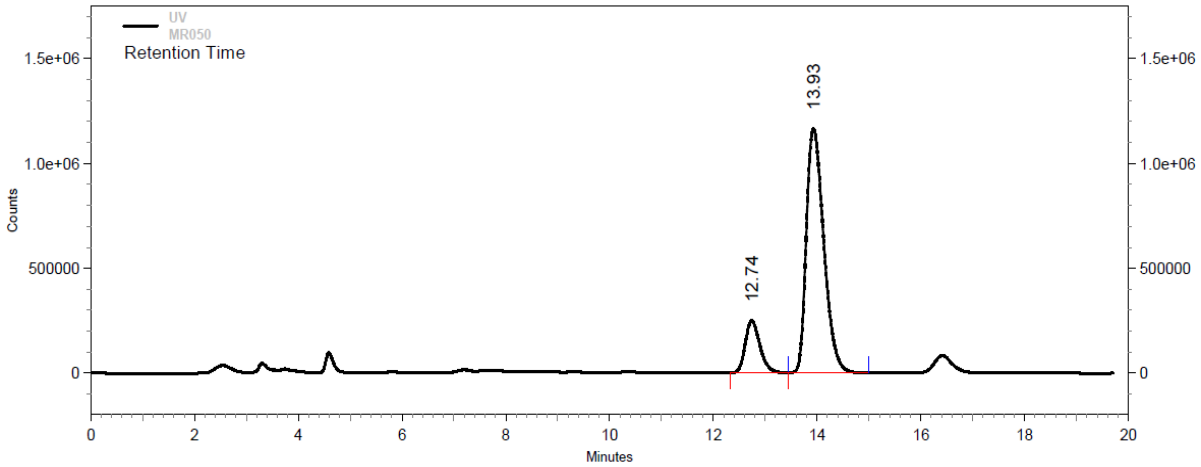
Method description : Lux-Cellulose-4, Heptane/Isopropanol 95/5, 1 ml/min, UV 254 nm et polarimetre




| Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 12.77 | 21469290 | 51.92 | 3.26 | 1.00 | 0.00 |
| 14.03 | 19882722 | 48.08 | 3.68 | 1.13 | 2.17 |

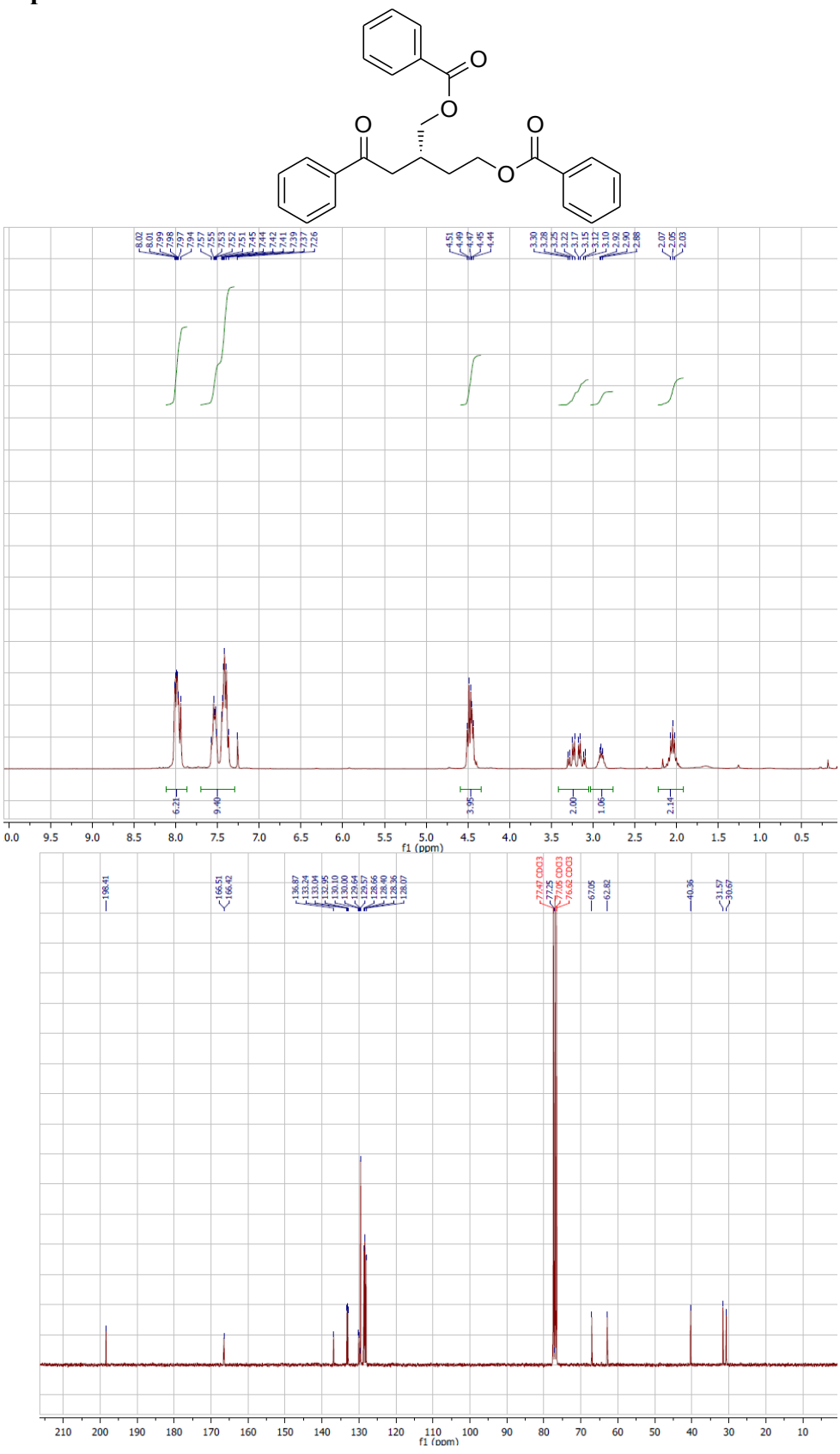
Enantioenriched:

Method description : Lux-Cellulose-4, Heptane/Isopropanol 95/5, 1 ml/min, UV 254 nm et polarimetre

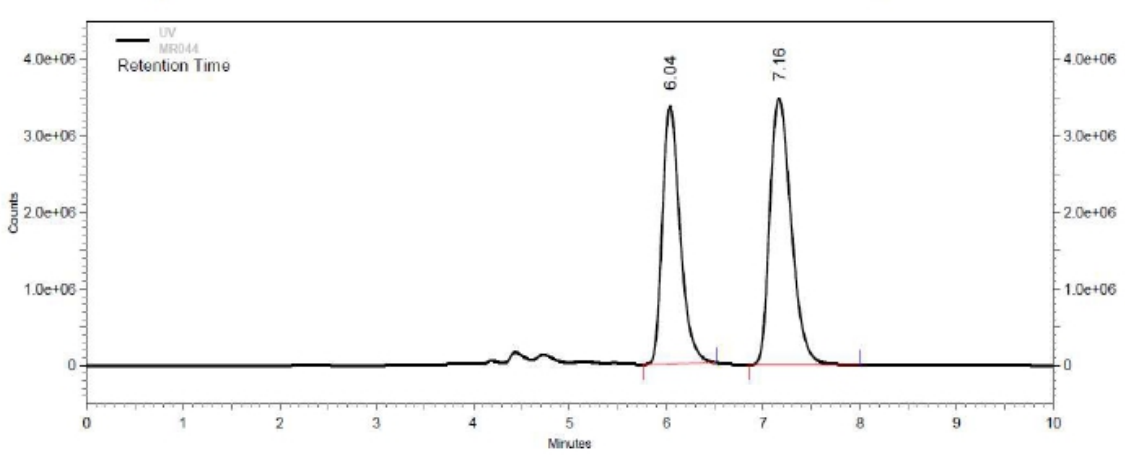



| Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 12.74 | 4895312 | 15.27 | 3.25 | 1.00 | 0.00 |
| 13.93 | 27152600 | 84.73 | 3.64 | 1.12 | 2.09 |

**Compound 3p**



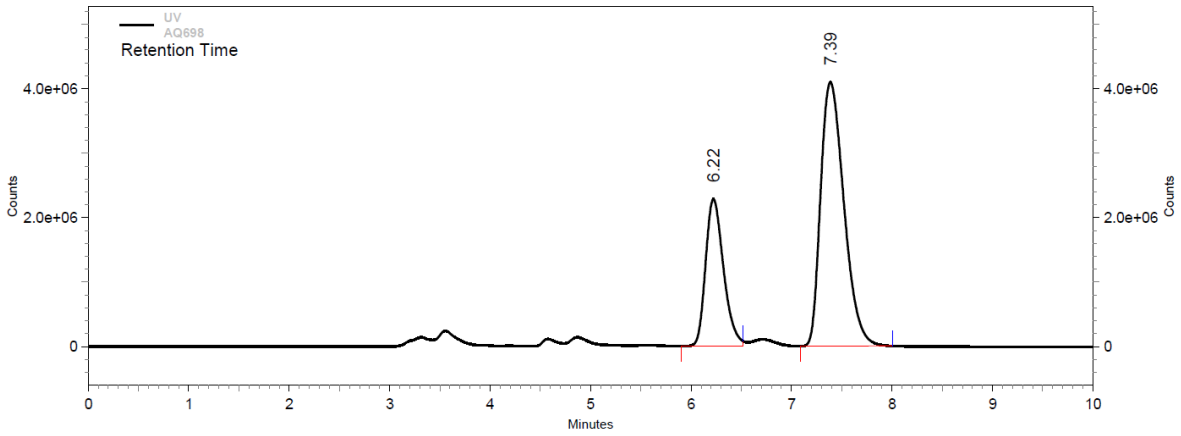
Racemate:




| Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 6.04 | 42777656 | 44.37 | 1.01 | 1.00 | 0.00 |
| 7.16 | 53627691 | 55.63 | 1.39 | 1.37 | 3.05 |

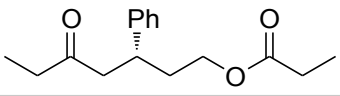
Enantioenriched:

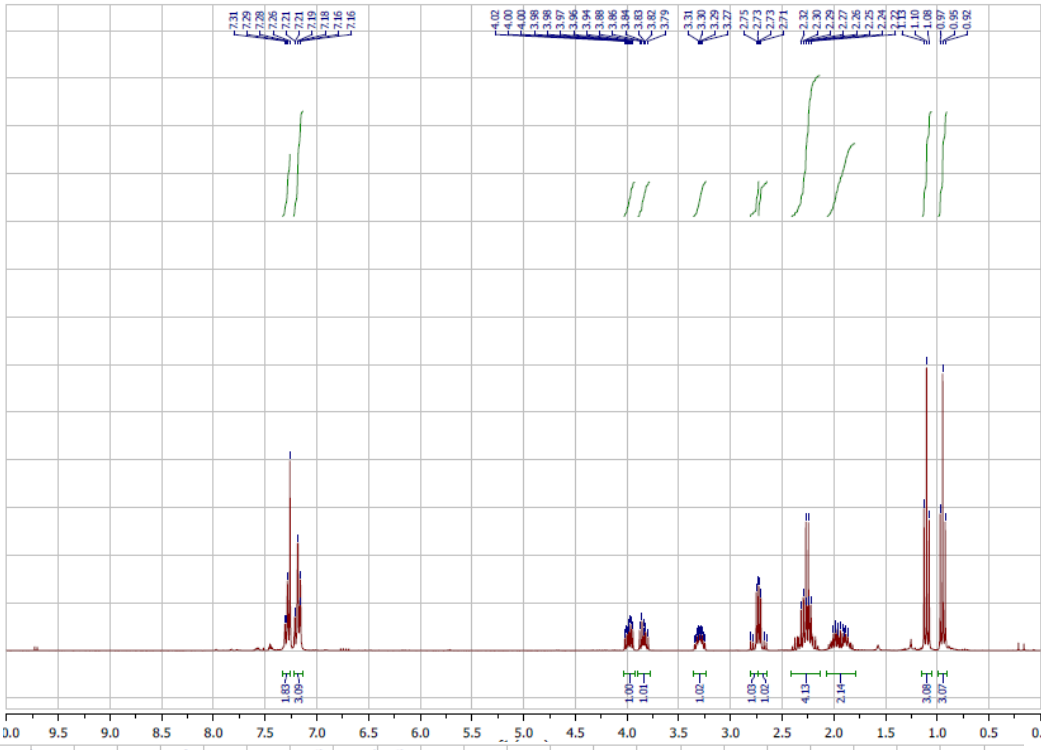
Method description : Chiralcel OD-3, Heptane/ethanol 50/50, 1 ml/min, UV 254 nm et polarimetre

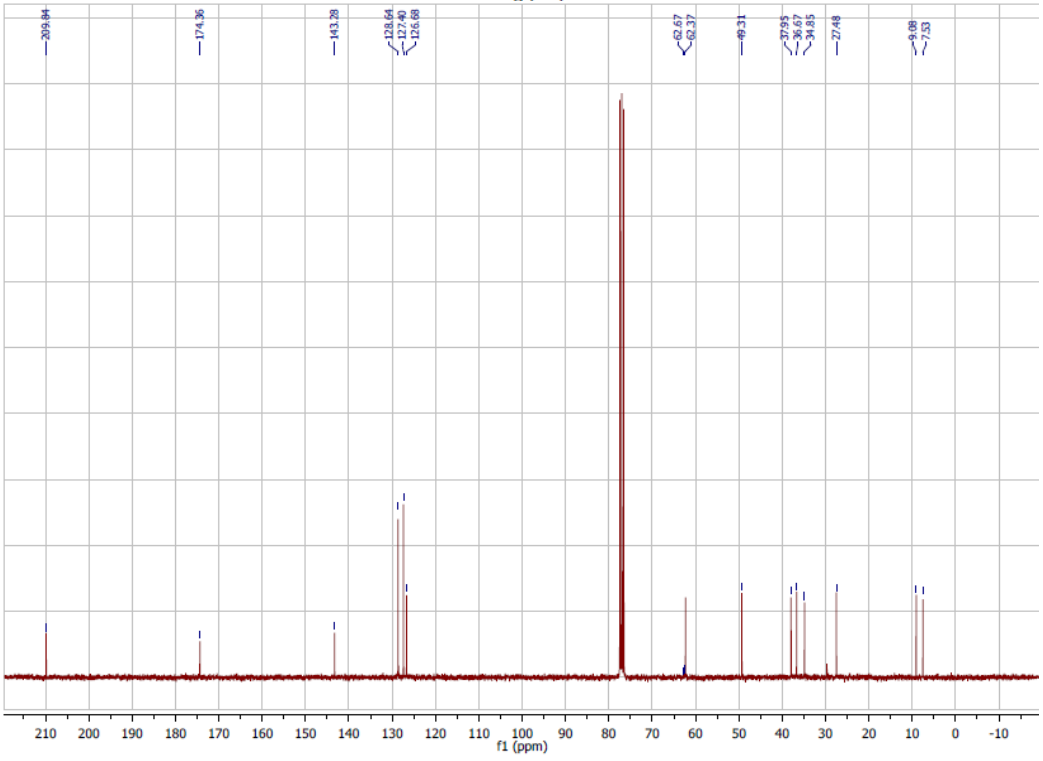



| Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 6.22 | 28262684 | 29.97 | 1.07 | 0.00 | 0.00 |
| 7.39 | 66039451 | 70.03 | 1.46 | 0.00 | 3.08 |

**Compound 3q**

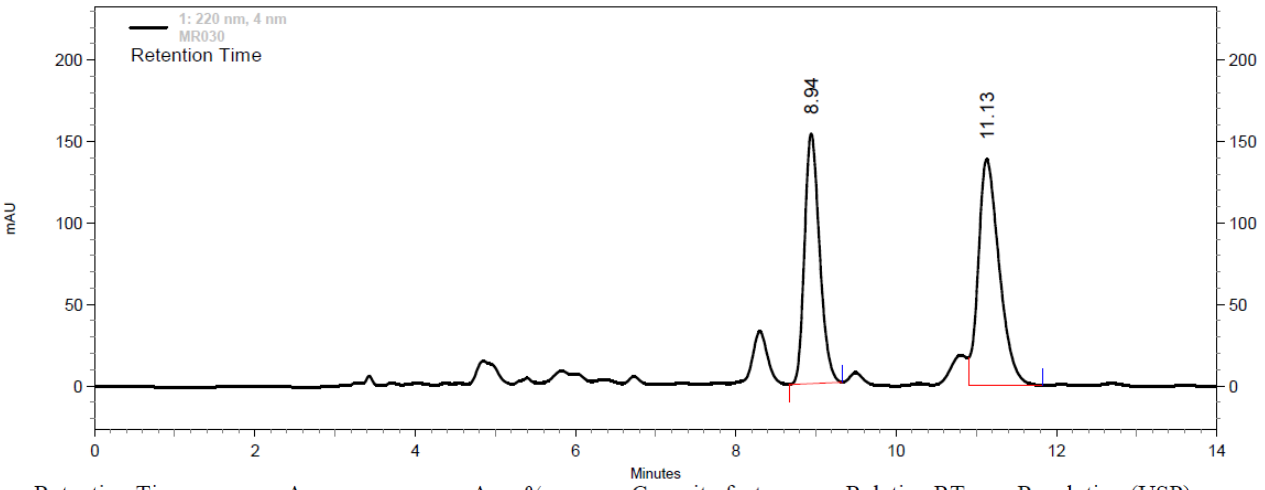




Racemate:

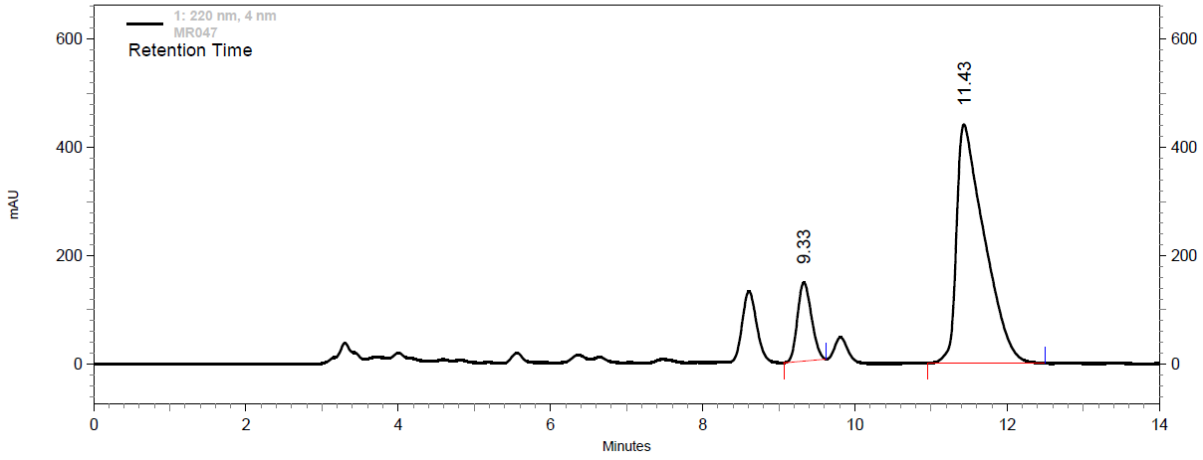
Method description : Chiralpak IF, Hexane/Ethanol 95/5, 1 ml/min, DAD and CD 254nm




| Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 8.94 | 7974901 | 44.30 | 1.98 | 1.00 | 0.00 |
| 11.13 | 10026210 | 55.70 | 2.71 | 1.37 | 5.32 |

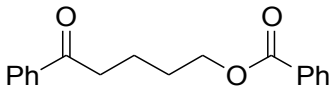
Enantioenriched:

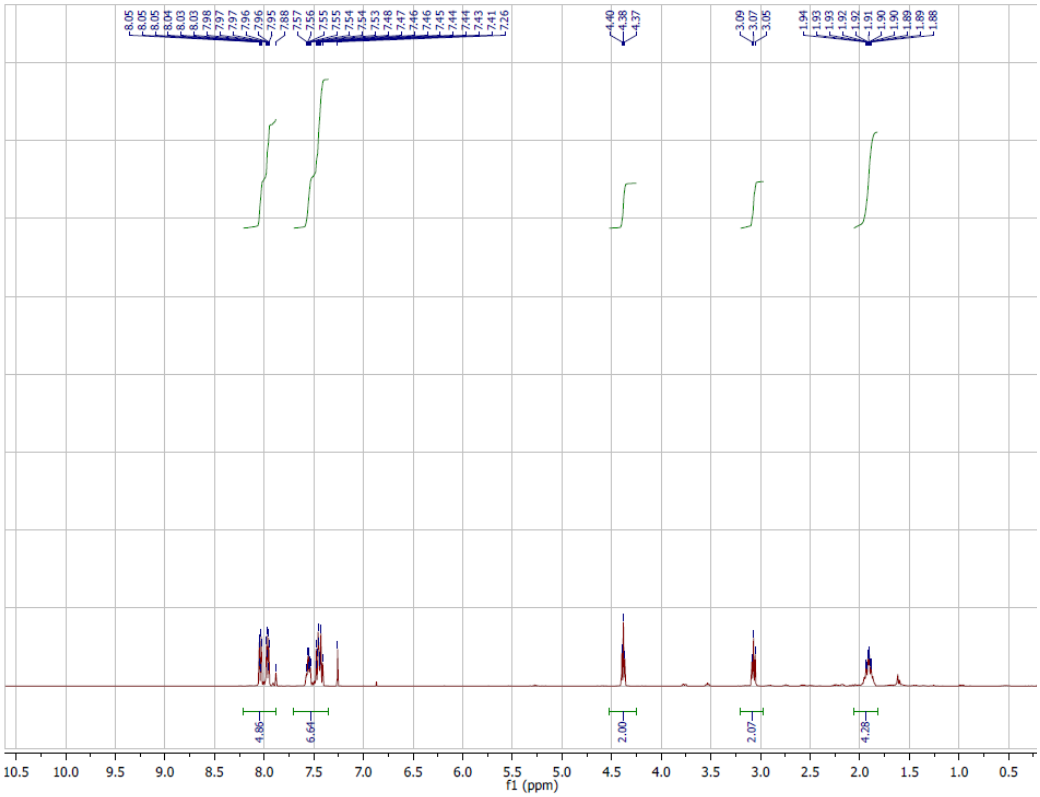
Method description : Chiralpak IF, Hexane/Ethanol 95/5, 1 ml/min, DAD and CD 254nm

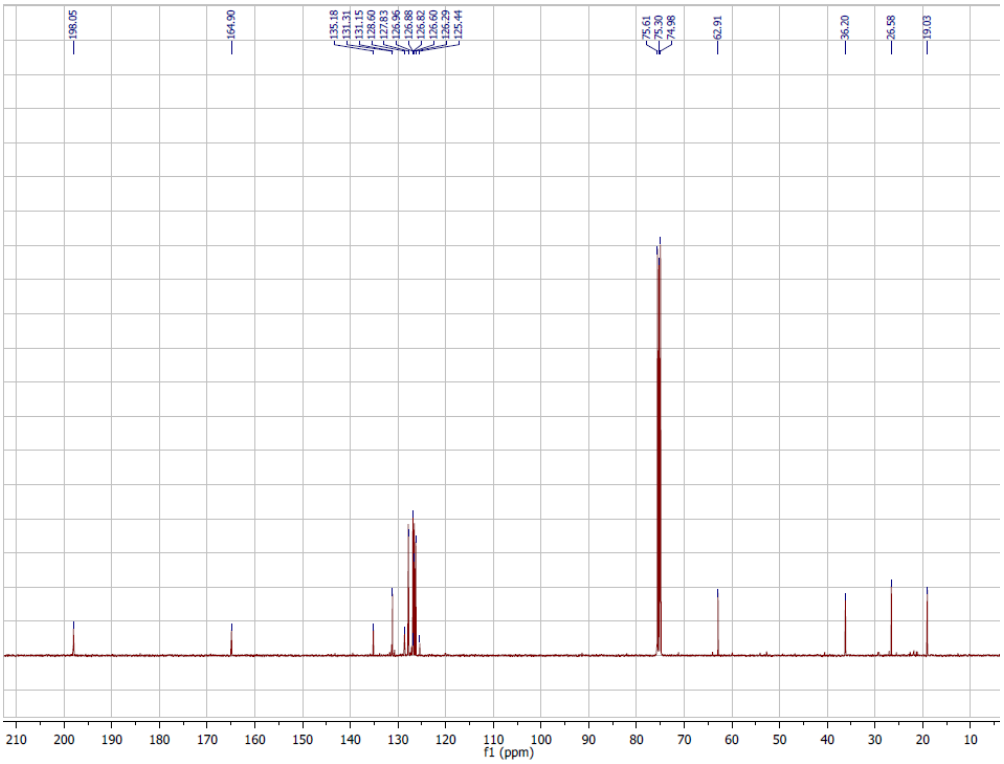



| Retention Time | Area | Area % | Capacity factor | Relative RT | Resolution (USP) |
|---|---|---|---|---|---|
| 9.33 | 7430579 | 14.26 | 2.11 | 0.00 | 0.00 |
| 11.43 | 44683774 | 85.74 | 2.81 | 0.00 | 4.01 |

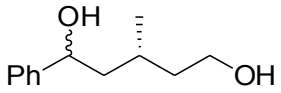
**Compound 3r**

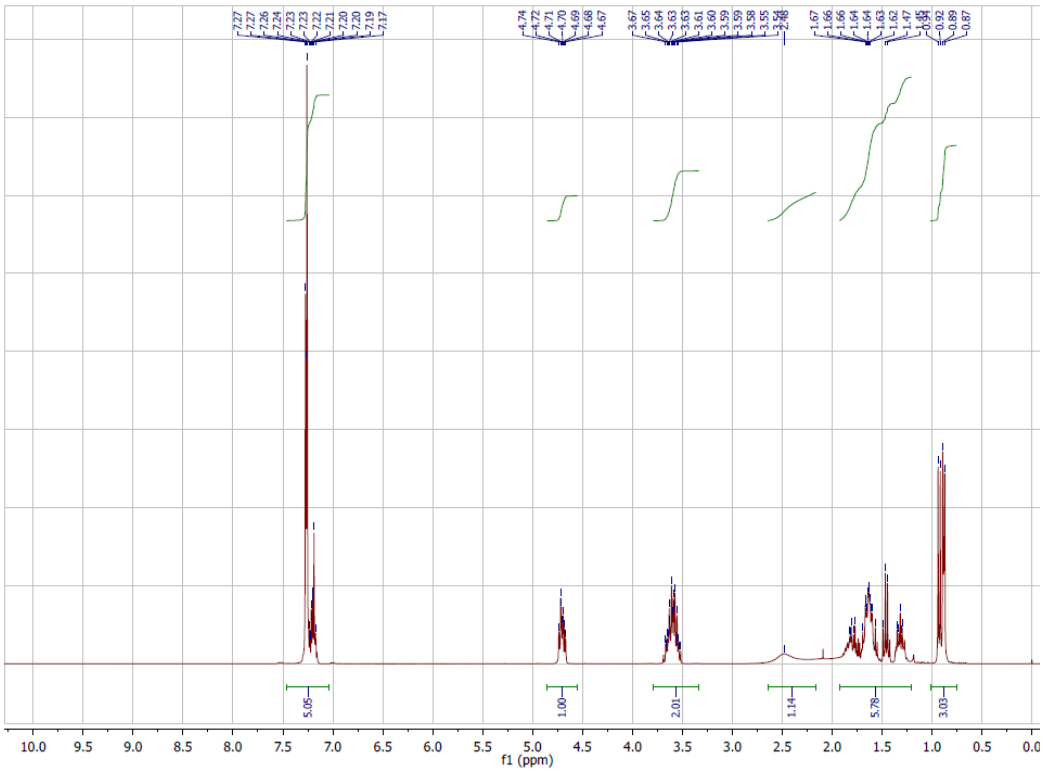

O
O
Ph
O
Ph

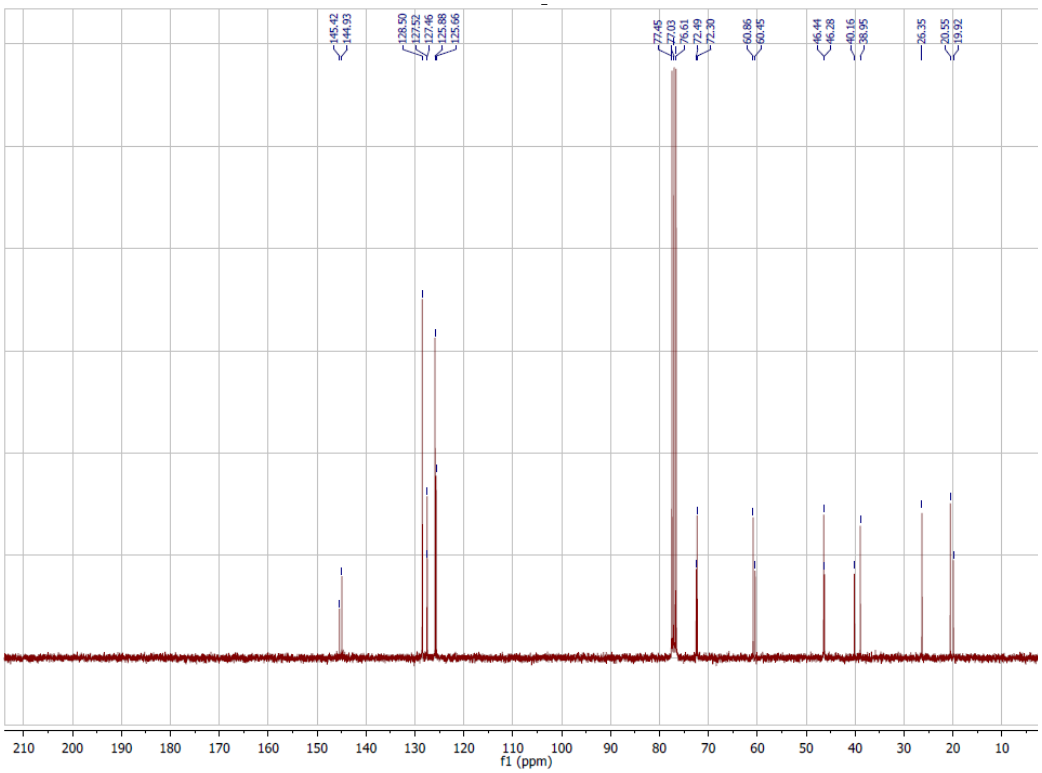

8.05
8.05
8.05
8.04
8.03
8.03
7.98
7.97
7.97
7.96
7.96
7.95
7.88
7.57
7.56
7.55
7.55
7.54
7.54
7.53
7.48
7.47
7.47
7.46
7.46
7.45
7.44
7.44
7.43
7.41
7.26
4.40
4.38
4.37
3.09
3.07
3.05
1.94
1.93
1.93
1.92
1.92
1.91
1.90
1.90
1.89
1.89
1.88
4.86
6.64
2.00
2.07
4.28
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


198.05
164.90
135.18
133.31
133.15
128.60
127.83
126.96
126.88
126.82
126.60
126.29
125.44
75.61
75.30
74.98
62.91
36.20
26.58
19.03
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

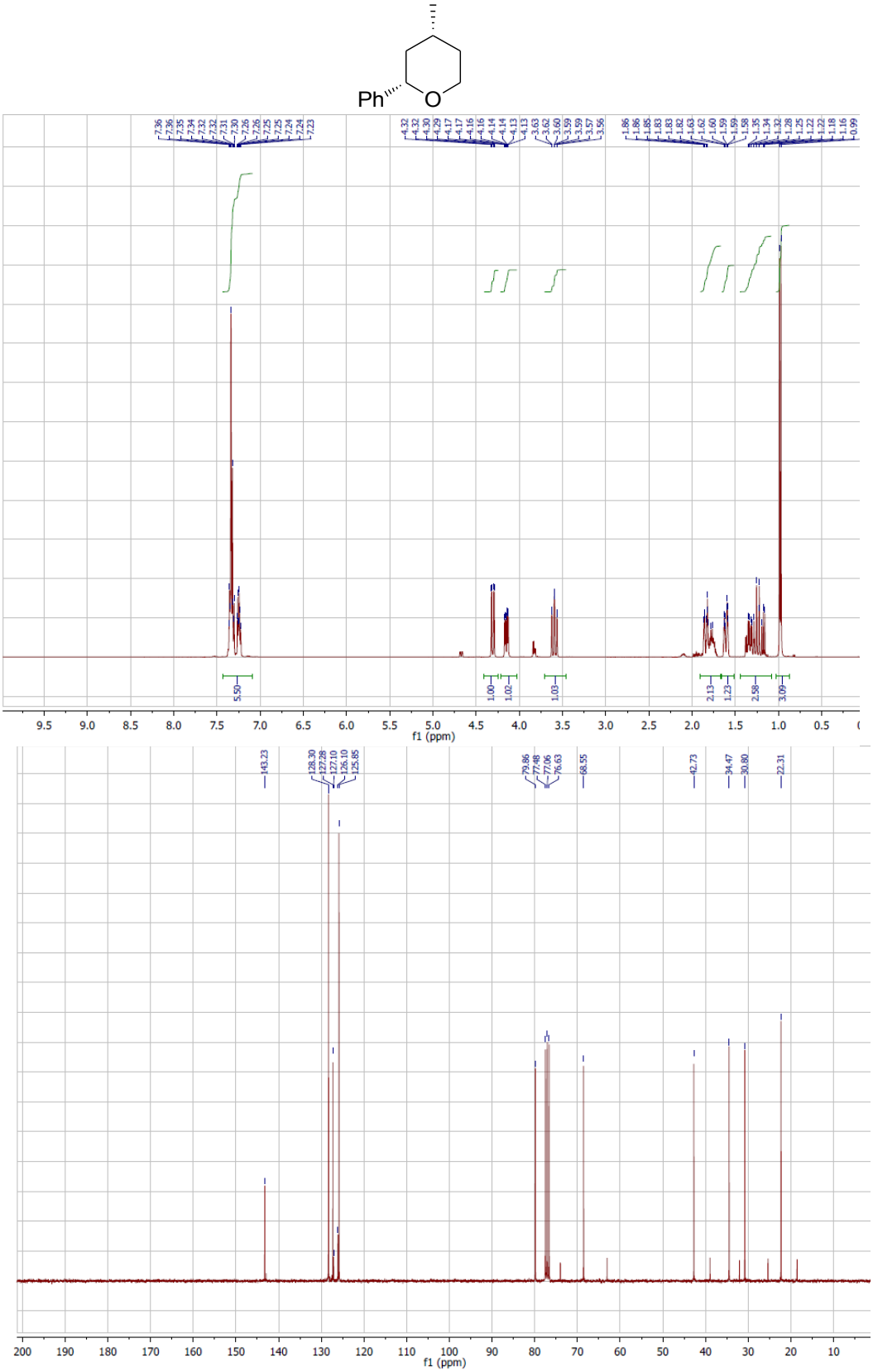
**Compound 4-prec**



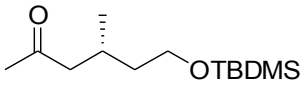



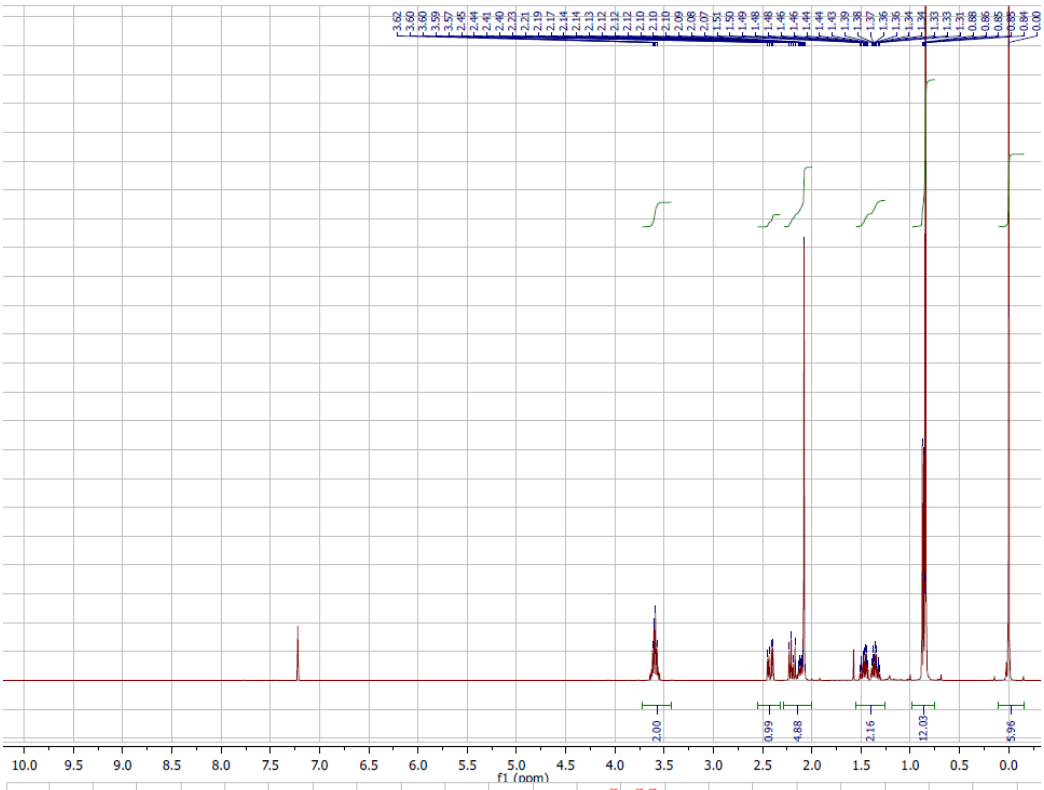



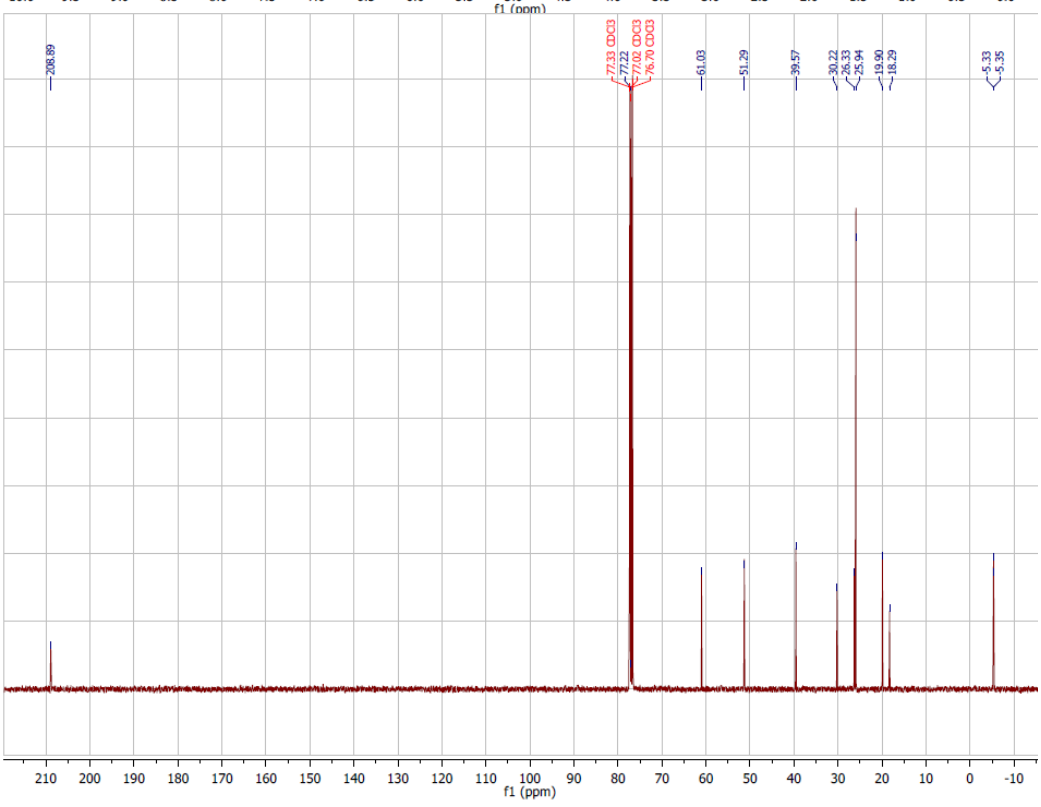
**Compound 4 (10:1 *dr*)**



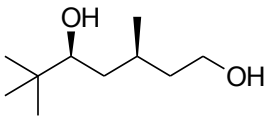
**Compound 5**

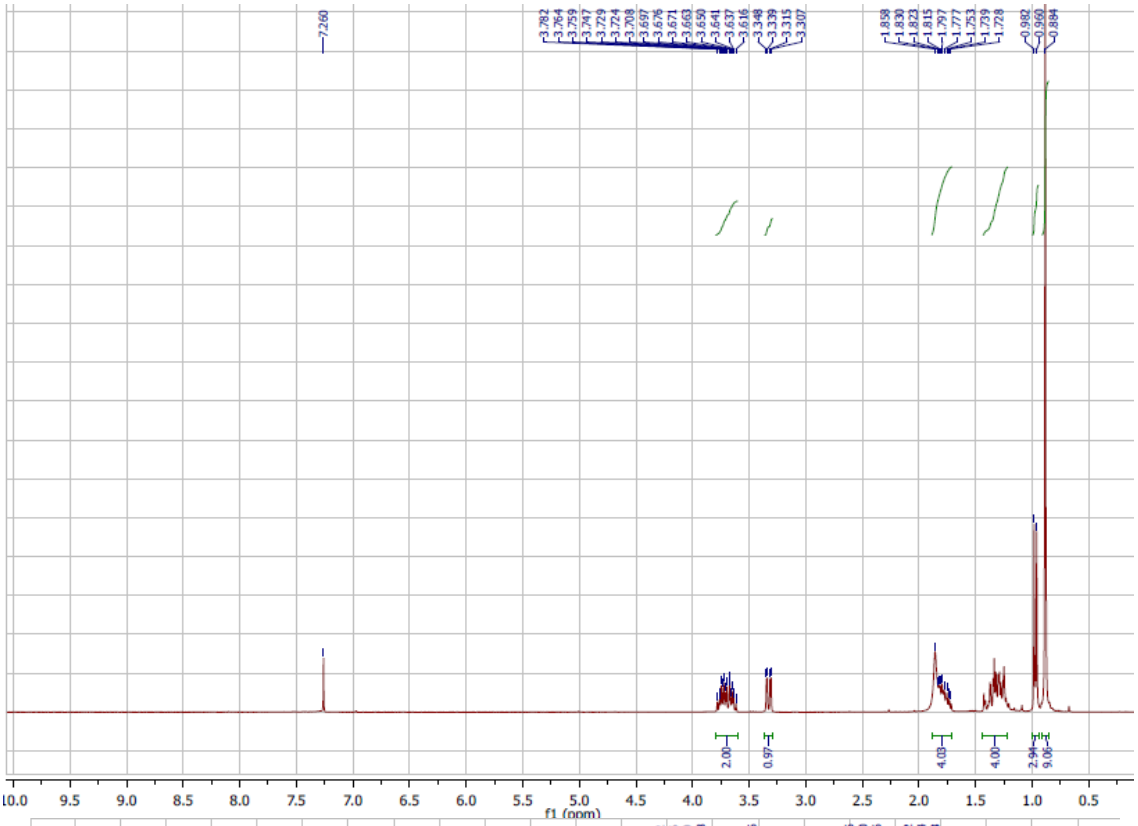

O
OTBDMS

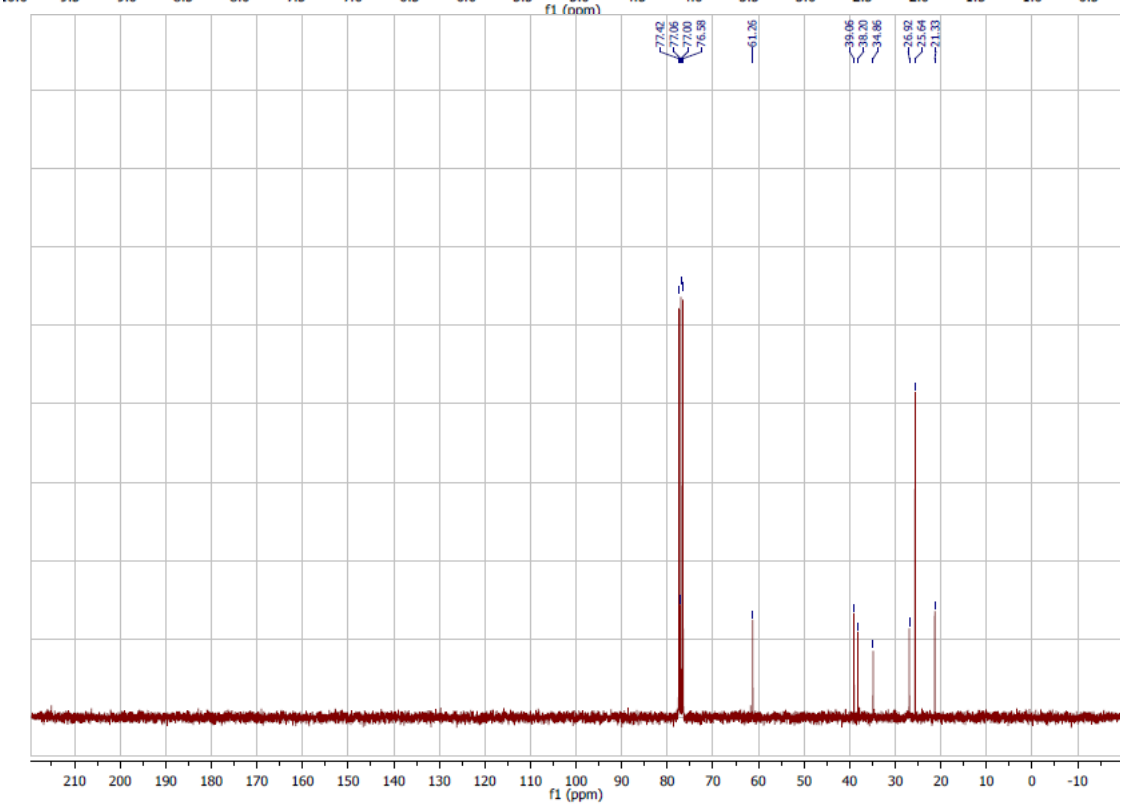

f1 (ppm)


208.89
77.33 CDCl3
77.22
77.02 CDCl3
76.70 CDCl3
61.03
51.29
39.57
30.22
26.33
25.94
19.90
18.29
-5.33
-5.35
f1 (ppm)

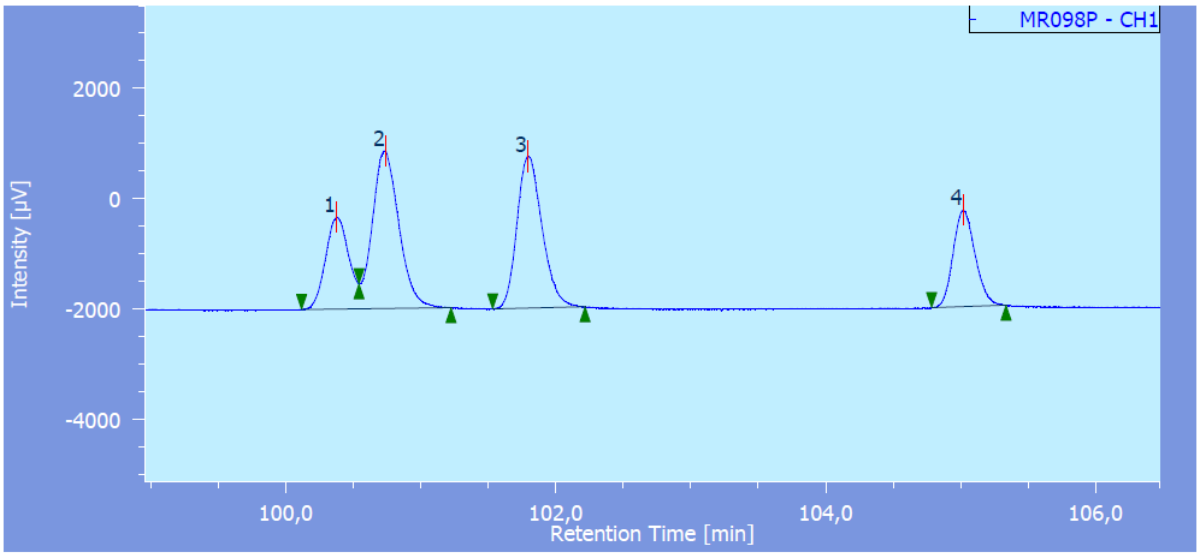
**Compound 6**


OH
OH


7.260
3.782
3.764
3.759
3.747
3.729
3.724
3.708
3.697
3.676
3.671
3.663
3.650
3.641
3.637
3.616
3.348
3.339
3.315
3.307
1.858
1.830
1.823
1.815
1.797
1.777
1.753
1.739
1.728
0.982
0.960
0.894
2.00
0.97
4.08
4.00
2.94
9.06
f1 (ppm)

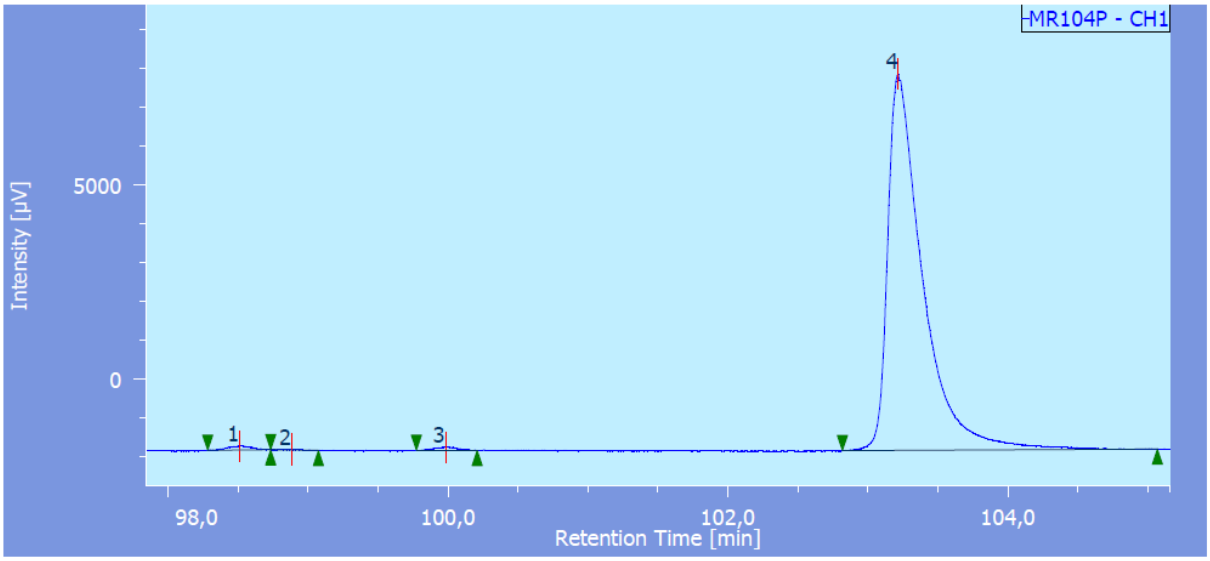

77.42
77.06
77.00
76.58
61.26
39.06
38.20
34.86
26.92
25.64
21.33
f1 (ppm)

Racemate (68:32 *dr*):




| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 1 | 100,375 | 19934 | 1665 | 17,431 | 18,489 | N/A | 1501487 | 1,079 | N/A | |
| 2 | Unknown | 1 | 100,742 | 39247 | 2852 | 34,321 | 31,667 | N/A | 1295279 | 3,041 | N/A | |
| 3 | Unknown | 1 | 101,792 | 35497 | 2744 | 31,041 | 30,470 | N/A | 1447785 | 10,156 | 1,251 | |
| 4 | Unknown | 1 | 105,017 | 19677 | 1745 | 17,207 | 19,373 | N/A | 1981620 | N/A | 1,172 | |

Enantioenriched:




| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 1 | 98,517 | 1218 | 100 | 0,716 | 1,008 | N/A | 1291539 | 1,173 | 0,912 | |
| 2 | Unknown | 1 | 98,883 | 138 | 18 | 0,081 | 0,179 | N/A | 1998559 | 3,559 | 1,542 | |
| 3 | Unknown | 1 | 99,983 | 1013 | 80 | 0,595 | 0,814 | N/A | 1383334 | 8,663 | 1,082 | |
| 4 | Unknown | 1 | 103,217 | 167795 | 9684 | 98,608 | 97,999 | N/A | 1021743 | N/A | 2,106 | |