# Supporting information

For

**Combination of asymmetric organo- and biocatalytic reactions in organic media using immobilized catalysts in different compartments**

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## CONTENTS

## 1. General Informations

All reagents and solvents were purchased from commercial sources and used without further purification, unless otherwise indicated. 3-Chlorobenzaldehyde was distilled prior to use (46°C @ 0.5 mbar). Enzymes are commercially available from evocatal GmbH (*Rhodococcus* sp., *Lactobacillus kefir* ADH). Solvents were equilibrated with water prior to use in biocatalytic reactions by vigorous stirring of the corresponding two-phase systems for at least 1h. Superabsorbent Polymer "Favor SXM 9155" is commercially available from Evonik industries, Stockhausen.

$^1$H spectra were recorded on a Bruker DRX 500 spectrometer and all chemical shift values refer to $CDCl_3$ ($\delta(^1H)$, 7.26 ppm). Indexed ($^{\#}$) signals in 'experimental procedures and analytical data' section may not be visible, depending on used NMR solvents and number of pulses. Peaks marked with an asterisk in 'NMR spectra' section refer to solvent signals.

Analytical HPLC was carried out with a SF Chromatography setup consisting of: Sampler/Injector AS-2059-SF Plus (Jasco),pressure regulator BP-2080 Plus (Jasco), detector MD-2010 Plus (Jasco), cryostat F250 (Julabo), pumps PU-2080 Plus (Jasco), line degasser DG-2080-53 (Jasco), net box LC-Net II/ADC (Jasco), column oven CO-2060 Plus (Jasco). As solvent a mixture of carbon dioxide and isopropanol was used. The enantiomeric excesses (ee) and diastereomeric ratios (dr) were determined by using a Daicel Chiralpak® column AD-H or Daicel Chiralcel® column OJ-H with the above mentioned HPLC setting. In order to safely attribute HPLC-peaks to the corresponding enantiomers or diastereomers, samples were cross-checked by either adding a racemic mixture (compare S11/12) or the opposite stereoisomers (compare S13/14). Diastereomeric ratios were double-checked *via* NMR spectroscopic data (S8/S9).

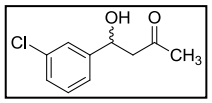
## 2. Immobilization procedure

**Preparation of the superabsorbed alcohol dehydrogenase from *Rhodococcus* sp. (Rsp-ADH) together with its cofactor $NAD^+$**

Components applied for the immobilization of the ADH from *Rhodococcus* sp. according to the protocol by JEROMIN[1] were modified as follows: a mixture consisting of 178 µL potassium phosphate buffer (pH 7, 100 mM), 15 mg $NAD^+$, 13 µL isopropanol and 190 µL ADH from *Rhodococcus* sp. (265 U/mL relative to 4'-chloro acetophenone) was stirred for 10 min prior to adding 63 mg of superabsorbent polymer Favor SXM 9155®(Evonik Industries AG). After the mixture solidified 510 µL isopropanol were added. Subsequent filtration and washing with 255 µL isopropanol, followed by 15 min drying under an airflow then gave 160 mg (60% (m/m) of water) of superabsorbed Rsp-ADH with an activity of 0.2 U/mg (which was determined *via* a photometric assay according to Jeromin).[1]

## 3. Experimental procedures and analytical data

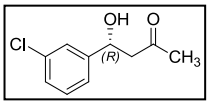
**Synthesis of *rac*-1-(3-Chlorophenyl)-1-hydroxybutan-3-one in aqueous medium as reference compound, *rac*-1**



To a solution of sodium hydroxide (8.5 mmol, 343 mg) in water (25 mL) was added acetone (10 mmol, 736 µL), followed by dropwise addition of 3-chlorobenzaldehyde (5 mmol, 702 mg). The colorless suspension is stirred at room temperature for 80 min and extracted with dichloromethane. The combined organic layers are washed with water and dried over $MgSO_4$. The crude product (yellow-colored oil) was purified by column chromatography over silica gel using chloroform:acetone (9:1, v/v) as an eluent, furnishing the product *rac*-**1** in pure form. The enantioselectivity was determined from the purified product by chiral HPLC. *rac*-**1** was obtained with a conversion of 8%, yield of 7% and <0.5% ee.

$^1$H-NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.40 (s, 1H), 7.33 – 7.22 (m, 3H), 5.16 (dd, *J* = 8.0, 4.4 Hz, 1H), 3.42[#] (bs, 1H), 2.89 – 2.83 (m, 2H), 2.23 (s, 3H). The analytical data are in accordance with those reported in reference 2. HPLC (Chiralpak® column AD-H at 40°C, $CO_2$:isopropanol 95:5, flow 1.8 mL/min, 220 nm) $t_r$=23.1 min ((*R*)-**1**), 29.0 min ((*S*)-**1**).

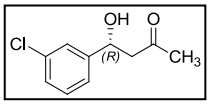
**Synthesis of (*R*)-1-(3-Chlorophenyl)-1-hydroxybutan-3-one <u>in aqueous medium using (*S*,*S*)-3</u>, (*R*)-1**



The reactions were carried out in analogy to a protocol reported in reference 2: A mixture of 3-chlorobenzaldehyde (10 mmol, 1.41 g), organocatalyst (*S*,*S*)-**5** (0.05 mmol, 18.3 mg, corresponding to a catalytic amount of 0.5 mol%) and acetone (90 mmol, 6.6 mL, 9 equivalents) in an aqueous saturated solution of NaCl (6.6 mL, corresponding to 50%(v/v)) was stirred at room temperature for 24h. The reaction mixture was extracted with dichloromethane and the organic layers were combined. After removing the solvent by evaporation (750 mbar, 50 °C), the conversion was determined from the ratio of the integral of the product signals in the $^1$H NMR-spectra in relation to the sum of integrals of substrate (aldehyde), product and side products. To isolate the product, the crude product (yellow-colored oil) was purified by column chromatography over silica gel using chloroform:acetone (9:1, v/v) as an eluent, furnishing the product (*R*)-**1** in pure form. For the isolation process, a fast workup is recommended in order to avoid dehydration of the product (*R*)-**1**. The enantioselectivity was determined from the purified product by chiral HPLC. (*R*)-**1** was obtained with a conversion of 82%, yield of 68% and 95% ee.

$^1$H-NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.37 (s, 1H), 7.30 – 7.19 (m, 3H), 5.12 (dt, *J* = 7.8, 3.8 Hz, 1H), 3.40 (d, *J* = 3.2 Hz, 1H), 2.89 – 2.80 (m, 2H), 2.20 (s, 3H). The analytical data are in accordance with those reported in reference 2. HPLC (Chiralpak® column AD-H at 40°C, $CO_2$:isopropanol 95:5, flow 1.8 mL/min, 220 nm) $t_r$=23.1 min ((*R*)-**1**), 29.0 min ((*S*)-**1**).

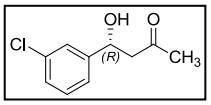
**Synthesis of (*R*)-1-(3-Chlorophenyl)-1-hydroxybutan-3-one <u>in cyclohexane using (*S*,*S*)-3</u>, (*R*)-1**



A mixture of 3-chlorobenzaldehyde (0.5 mmol, 70 mg), organocatalyst (*S*,*S*)-**5** (0.0025 mmol, 1 mg, corresponding to a catalytic amount of 0.5 mol%), 3-chloro benzoic acid (0.01 mmol, 1.5 mg, corresponding to 2 mol%) and acetone (4.5 mmol, 0.33 mL, 9 equivalents) in cyclohexane (0.33 mL, corresponding to 50%(v/v)) was stirred at 3°C for 24h. After removing the solvent by evaporation (200 mbar, 50 °C), the conversion was determined from the ratio of the integral of the product signals in the $^1$H NMR-spectra in relation to the sum of integrals of substrate (aldehyde), product and side products. The enantioselectivity was determined from the crude product by chiral HPLC. (*R*)-**1** was obtained with a conversion of 95% and 95% ee.

$^1$H-NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.37 (s, 1H), 7.30 – 7.19 (m, 3H), 5.12 (dt, *J* = 7.8, 3.8 Hz, 1H), 3.40 (d, *J* = 3.2 Hz, 1H), 2.89 – 2.80 (m, 2H), 2.20 (s, 3H). The analytical data are in accordance with those reported in reference 2. HPLC (Chiralpak® column AD-H at 40°C, $CO_2$:isopropanol 95:5, flow 1.8 mL/min, 220 nm) $t_r$=20.9 min ((*R*)-**1**), 26.0 min ((*S*)-**1**).

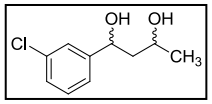
**Synthesis of (*R*)-1-(3-Chlorophenyl)-1-hydroxybutan-3-one <u>in cyclohexane using (*S*,*S*)-4</u>, (*R*)-1**



A mixture of 3-chlorobenzaldehyde (0.5 mmol, 70 mg), organocatalyst (*S*,*S*)-**4** (0.05 mmol, 78 mg, 0.63 mmol/g catalyst/support, determined *via* elemental analysis;[3] corresponding to a catalytic amount of 10 mol%), 3-chloro benzoic acid (0.01 mmol, 1.5 mg, corresponding to 2 mol%) and acetone (4.5 mmol, 0.33 mL, 9 equivalents) in cyclohexane (0.33 mL, corresponding to 50%(v/v)) was stirred at 3°C for 24h. After removing the solvent by evaporation (200 mbar, 50 °C), the conversion was determined from the ratio of the integral of the product signals in the $^1$H NMR-spectra in relation to the sum of integrals of substrate (aldehyde), product and side products. The enantioselectivity was determined from the crude product by chiral HPLC. (*R*)-**1** was obtained with a conversion of 95% and 95% ee.

$^1$H-NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.37 (s, 1H), 7.30 – 7.19 (m, 3H), 5.12 (dt, *J* = 7.8, 3.8 Hz, 1H), 3.40 (d, *J* = 3.2 Hz, 1H), 2.89 – 2.80 (m, 2H), 2.20 (s, 3H). The analytical data are in accordance with those reported in reference 2. HPLC (Chiralpak® column AD-H at 40°C, $CO_2$:isopropanol 95:5, flow 1.8 mL/min, 220 nm) $t_r$=20.9 min ((*R*)-**1**), 26.0 min ((*S*)-**1**).

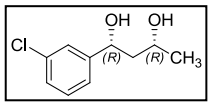
**Synthesis of *rac*-syn and *rac*-anti-(1-(3-Chlorophenyl)-1,3-butandiol (mixture of diastereomers) as reference compounds**




The synthesis of the diastereomers was performed according to a protocol given in reference 2 obtaining the diol in <10% ee. The analytical data are in accordance with those reported in reference 2.

$^1$H-NMR (400 MHz, CDCl3): δ (ppm) = 7,32 (s, 1H), 7,16-7,25 (m, 3H), 4,98 (m, 1H, H-C4-anti), 4,84-4,88 (dd, 1H, H-C4-syn, 3J = 9,3 Hz, 3J = 3,6 Hz), 3,98-4,15 (m, 2H, H-C2-anti, H-C2-syn), 3,58 (br s, 1H, OH4-syn), 3,28 (br s, 1H, OH4-anti), 2,75 (br s, 1H, OH2-syn), 2,20 (br s, 1H, OH2-anti), 1,66-1,87 (m, 2H), 1,17-1,21 (m, 3H). The analytical data are in accordance with those reported in reference 2. HPLC (Chiralcel® column OJ-H at 30°C, $CO_2$:isopropanol 97:3, flow 1.0 mL/min, 220 nm) $t_r$=43.0 min ((*S*,*S*)-**2**), 44.8 min ((*S*,*R*)-**2**), 51.3 min ((*R*,*R*)-**2**), 55.2 min ((*R*,*S*)-**2**).

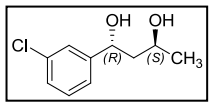
**Synthesis of (*R*,*R*)-(1-(3-Chlorophenyl)-1,3-butandiol as reference compound, (*R*,*R*)-2**




The synthesis of the diastereomers was performed according to a protocol given in reference 2 obtaining the diol in >99% ee and >35:1 dr. The analytical data are in accordance with those reported in reference 2.

$^1$H-NMR (500 MHz, CDCl3): δ (ppm) = 7.38 (s, 1H), 7.30 – 7.20 (m, 3H), 4.93 (dd, *J* = 9.9, 3.0 Hz, 1H), 4.16 (qd, *J* = 6.5, 3.6 Hz, 1H), 3.50 (s, 1H), 2.64 (s, 1H), 1.87 – 1.70 (m, 2H), 1.24 (d, *J* = 6.2 Hz, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ (ppm) = 146.66, 134.53, 129.92, 127.79, 126.05, 123.92, 74.78, 69.16, 47.22, 24.52. The analytical data are in accordance with those reported in reference 2. HPLC (Chiralcel® column OJ-H at 30°C, $CO_2$:isopropanol 97:3, flow 1.0 mL/min, 220 nm) $t_r$=44.9 min ((*S*,*R*)-**2**), 52.0 min ((*R*,*R*)-**2**).

**Synthesis of (*R*,*S*)-(1-(3-Chlorophenyl)-1,3-butandiol <u>using immobilized Rsp-ADH in organic media</u>**




To 80 mg (0.2 U/mg, corresponding to 32 U/mmol) of the superabsorbed ADH, prepared according to procedure a), was added organic solvent (7.5 mL), (*R*)-**3** (0.5 mmol, 99 mg; 95% ee) and isopropanol (190 µL, 5 equivalents). The reaction mixture is stirred with a fishclip® spinner for 24h at room temperature. The organic phase was decanted and the residue rinsed with 1 mL of the corresponding organic solvent. After removing the solvent of the combined organic layers by evaporation, the conversion was determined from the ratio of the integral of the product signals in the $^1$H NMR-spectra in relation to the integral of substrate (no side- or byproducts were detected). The enantioselectivity and diastereomeric ratio were determined from the crude product by chiral HPLC.

For any following reaction cycles, the residual superabsorber hydrogel was used according to the above mentioned protocol (addition of solvent, substrate and isopropanol) without any purification. No cofactor was added.

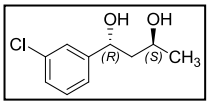
$^1$H-NMR (500 MHz, CDCl3): δ (ppm) = 7.38 (s, 1H), 7.30 – 7.21 (m, 3H), 5.05 (dd, *J* = 7.2, 3.9 Hz, 1H), 4.13 – 4.04 (m, 1H), 3.26 – 3.09 (m, 1H), 2.06 (d, *J* = 4.4 Hz, 1H), 1.95 – 1.81 (m, 2H), 1.26 (d, *J* = 6.4 Hz, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ (ppm) = 146.79, 134.53, 129.85, 127.51, 125.95, 123.83, 71.39, 65.69, 45.95, 23.84. The analytical data are in accordance with those reported in reference 2. HPLC (Chiralcel® column OJ-H at 30°C, $CO_2$:isopropanol 97:3, flow 1.0 mL/min, 220 nm) $t_r$=45.3 min ((*S*,*S*)-**2**), 54.4 min ((*R*,*S*)-**2**).

**Table S1**

| solvent | cycle | conversion [%][a] | recovery rate [%] | ee (1*R*,3*S*)-2 [%][c] |
|---|---|---|---|---|
| **isooctane** | 1 | 93 | 80 | > 99 |
| | 2 | 91 | 72 | > 99 |
| | 3 | 89 | 75 | > 99 |
| | 4 | 83 | 72 | > 99 |
| **cyclohexane** | 1 | 89 | > 95 | > 99 |
| | 2 | 86 | > 95 | > 99 |
| | 3 | 85 | > 95 | > 99 |
| | 4 | 79 | > 95 | > 99 |
| | 5[b] | 66 | > 95 | > 99 |
| **chloroform** | 1 | 46 | > 95 | > 99 |
| | 2 | 24 | > 95 | > 99 |
| | 3 | 10[c] | > 95 | > 99 |
| **ethyl acetate** | 1 | 24 | > 95 | > 99 |
| | 2 | 16[c] | 94 | > 99 |

a) product related conversion, determined from the ratio of the integral of the product signals in the $^1$H NMR-spectra, b) experiment conducted after 11d storage of the superabsorbed ADH (derived from cycle 4 *via* filtration) at 7°C under air, c) due to the low conversion rate, no further recycling experiments were conducted.

**Chemoenzymatic synthesis of (*R*,*S*)-(1-(3-Chlorophenyl)-1,3-butandiol <u>using organocatalyst (*S*,*S*)-3 and immobilized Rsp-ADH</u>**

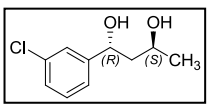



A mixture of 3-chlorobenzaldehyde (0.5 mmol, 70 mg), organocatalyst (*S*,*S*)-**5** (0.0025 mmol, 1 mg, corresponding to a catalytic amount of 0.5 mol%), 3-chloro benzoic acid (0.01 mmol, 1.5 mg, corresponding to 2 mol%) and acetone (4.5 mmol, 0.33 mL, 9 equivalents) in cyclohexane (0.33 mL, corresponding to 50%(v/v)) was stirred at 3°C for 24h. After removing the solvent by evaporation (200 mbar, 50 °C), the residue is dissolved in cyclohexane (7.5 mL) and added to 80 mg (0.2 U/mg, corresponding to 32 U/mmol) immobilized Rsp-ADH, prepared according to procedure a). After the addition of isopropanol (190 µL, 5 equivalents) the reaction mixture is stirred with a fishclip® spinner for 24h at room temperature. The organic phase was decanted and the residue rinsed with 2 mL of cyclohexane. After removing the solvent of the combined organic layers by evaporation, the conversion was determined from the ratio of the integral of the product signals in the $^1$H NMR-spectra in relation to the integral of the sum of integrals of substrate, product and side product.† The enantioselectivity and diastereomeric ratio were determined from the crude product by chiral HPLC. (*R*,*S*)-**2** was obtained with a conversion of 89%, >99% ee and >35:1 dr.

$^1$H-NMR (500 MHz, $CDCl_3$): δ (ppm) = 7.37 (s, 1H), 7.30 – 7.20 (m, 3H), 5.04 (dt, *J* = 7.0, 3.1 Hz, 1H), 4.07 (dq, *J* = 10.5, 6.5 Hz, 1H), 3.19 (d, *J* = 4.5 Hz, 1H), 2.10 (s, 1H), 1.90 – 1.84 (m, 2H), 1.26 (d, *J* = 6.3 Hz, 3H). The analytical data are in accordance with those reported in reference 2. HPLC (Chiralcel® column OJ-H at 30°C, $CO_2$:isopropanol 97:3, flow 1.0 mL/min, 220 nm) $t_r$=45.5 min ((*S*,*S*)-**2**), 54.7 min ((*R*,*S*)-**2**).

† As side product 3-chlorobenzyl alcohol can be detected due to enzymatic reduction of residual 3-chlorobenzaldehyde with a molar fraction of <5%. As a characteristic signal, a singlet at δ (ppm) = 4.68 (s, 1H) can be found.

**Chemoenzymatic synthesis of (*R*,*S*)-(1-(3-Chlorophenyl)-1,3-butandiol using <u>heterogenized organocatalyst (*S*,*S*)4 and immobilized Rsp-ADH</u>**



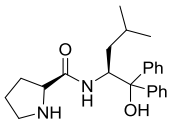

A mixture of 3-chlorobenzaldehyde (0.5 mmol, 70 mg), organocatalyst (*S*,*S*)-**6** (0.05 mmol, 78 mg, 0.63 mmol/g catalyst/support, determined *via* elemental analysis;[3] corresponding to a catalytic amount of 10 mol%), 3-chloro benzoic acid (0.01 mmol, 1.5 mg, corresponding to 2 mol%) and acetone (4.5 mmol, 0.33 mL, 9 equivalents) in cyclohexane (0.33 mL, corresponding to 50%(v/v)) was stirred at 3°C for 24h. After decantation of the organic layer and rinsing of the catalyst residue with cyclohexane (0.5 mL) the solvent was removed by evaporation (200 mbar, 50 °C). The residue is dissolved in cyclohexane (7.5 mL) and added to

80 mg (0.2 U/mg, corresponding to 32 U/mmol) immobilized Rsp-ADH, prepared according to procedure a). After the addition of isopropanol (190 µL, 5 equivalents) the reaction mixture is stirred with a fishclip® spinner for 24h at room temperature. The organic phase was decanted and the residue rinsed with 2 mL of cyclohexane. After removing the solvent of the combined organic layers by evaporation, the conversion was determined from the ratio of the integral of the product signals in the $^1$H NMR-spectra in relation to the integral of the sum of integrals of substrate, product and side product.† The enantioselectivity and diastereomeric ratio were determined from the crude product by chiral HPLC. (*R*,*S*)**2** was obtained with a conversion of 89%, >99% ee and >35:1 dr.

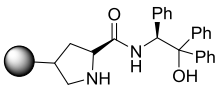
$^1$H-NMR (500 MHz, $CDCl_3$): δ (ppm) = 7.37 (s, 1H), 7.30 – 7.20 (m, 3H), 5.04 (dt, *J* = 7.0, 3.1 Hz, 1H), 4.07 (dq, *J* = 10.5, 6.5 Hz, 1H), 3.19 (d, *J* = 4.5 Hz, 1H), 2.10 (s, 1H), 1.90 – 1.84 (m, 2H), 1.26 (d, *J* = 6.3 Hz, 3H). The analytical data are in accordance with those reported in reference 2. HPLC (Chiralcel® column OJ-H at 30°C, $CO_2$:isopropanol 97:3, flow 1.0 mL/min, 220 nm) $t_r$=44.9 min ((*S*,*S*)-**2**), 53.8 min ((*R*,*S*)-**2**).

† As side product 3-chlorobenzyl alcohol can be detected due to enzymatic reduction of residual 3-chlorobenzaldehyde with a molar fraction of <5%. As a characteristic signal, a singlet at δ (ppm) = 4.68 (s, 1H) can be found.

**Structures of the organocatalyst (*S*,*S*)-3 and the related heterogenized organocatalyst (*S*,*S*)-4**

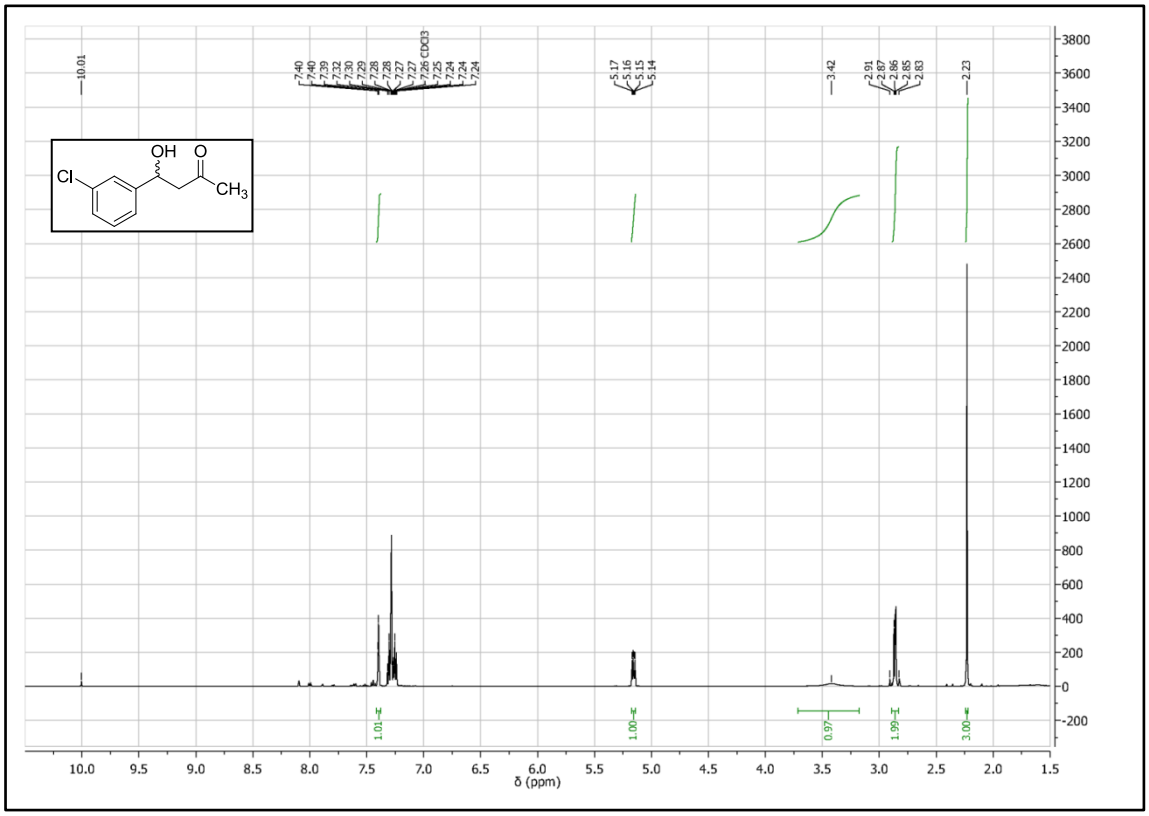


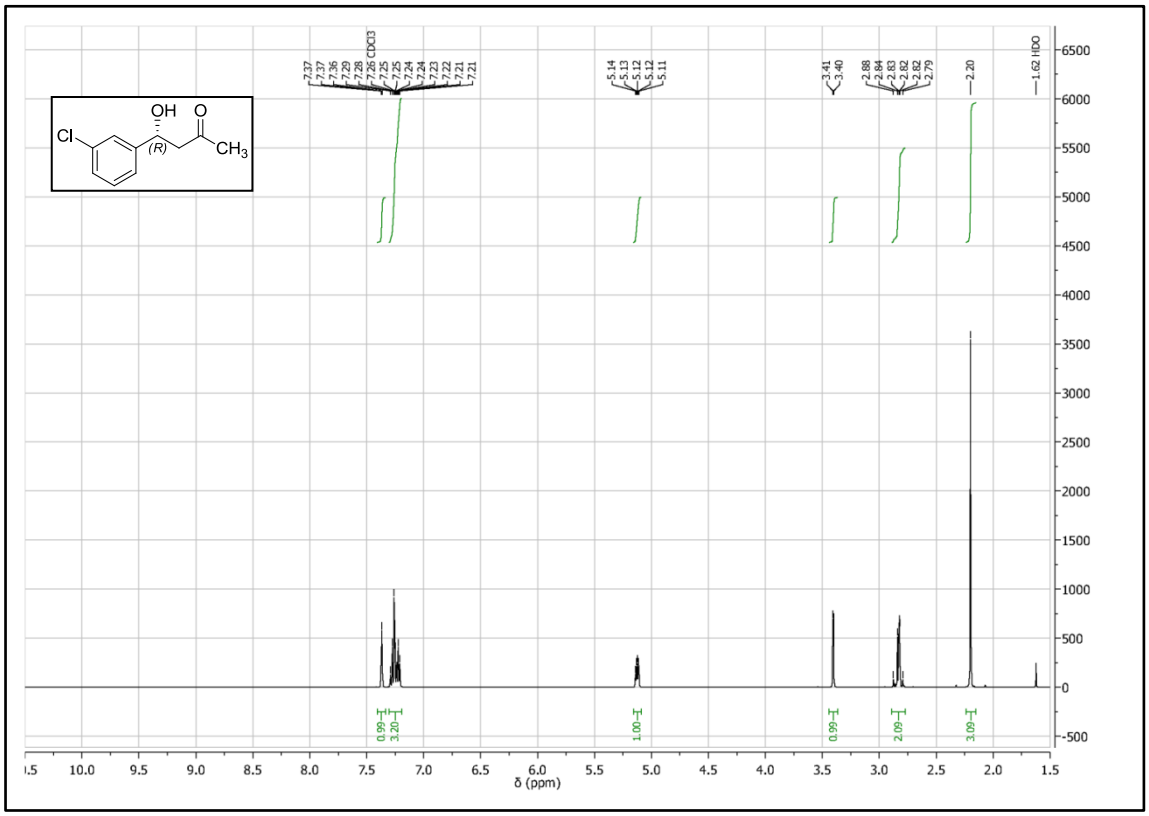
(*S*,*S*)-**3**

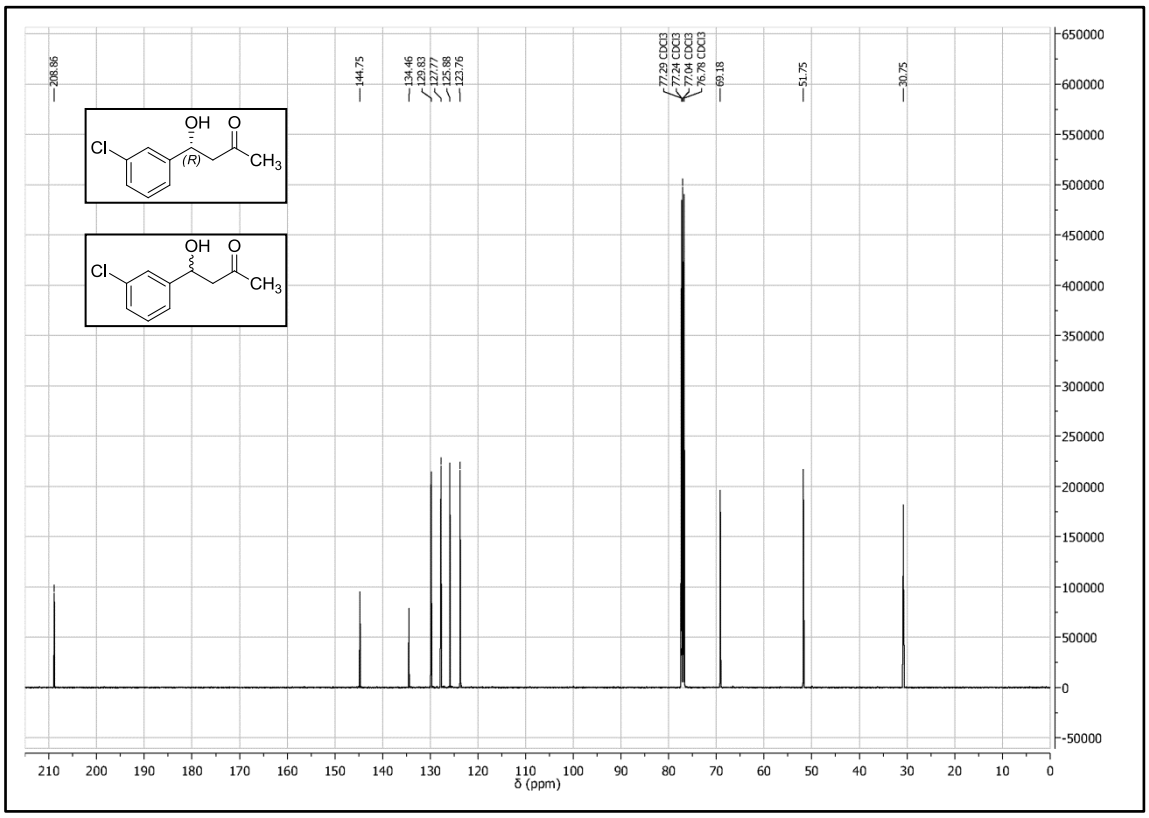


(*S*,*S*)-**4**

## 4. NMR spectra

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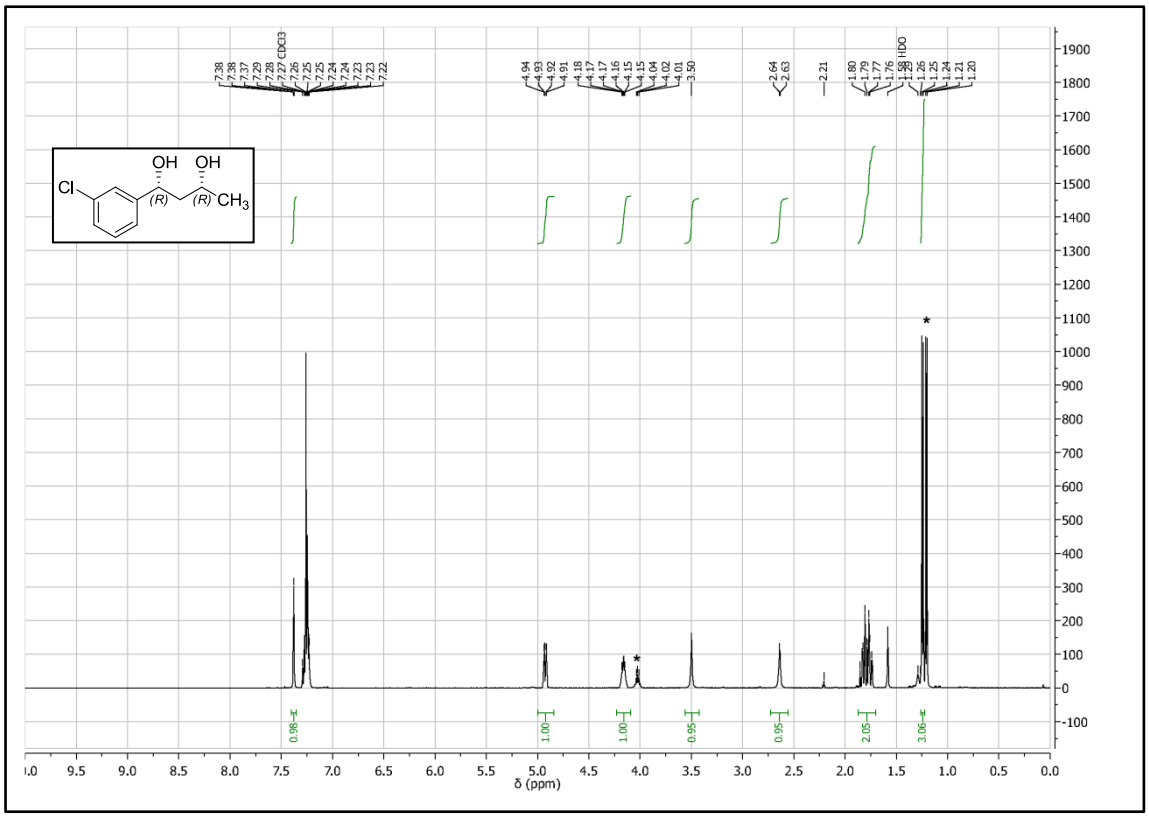
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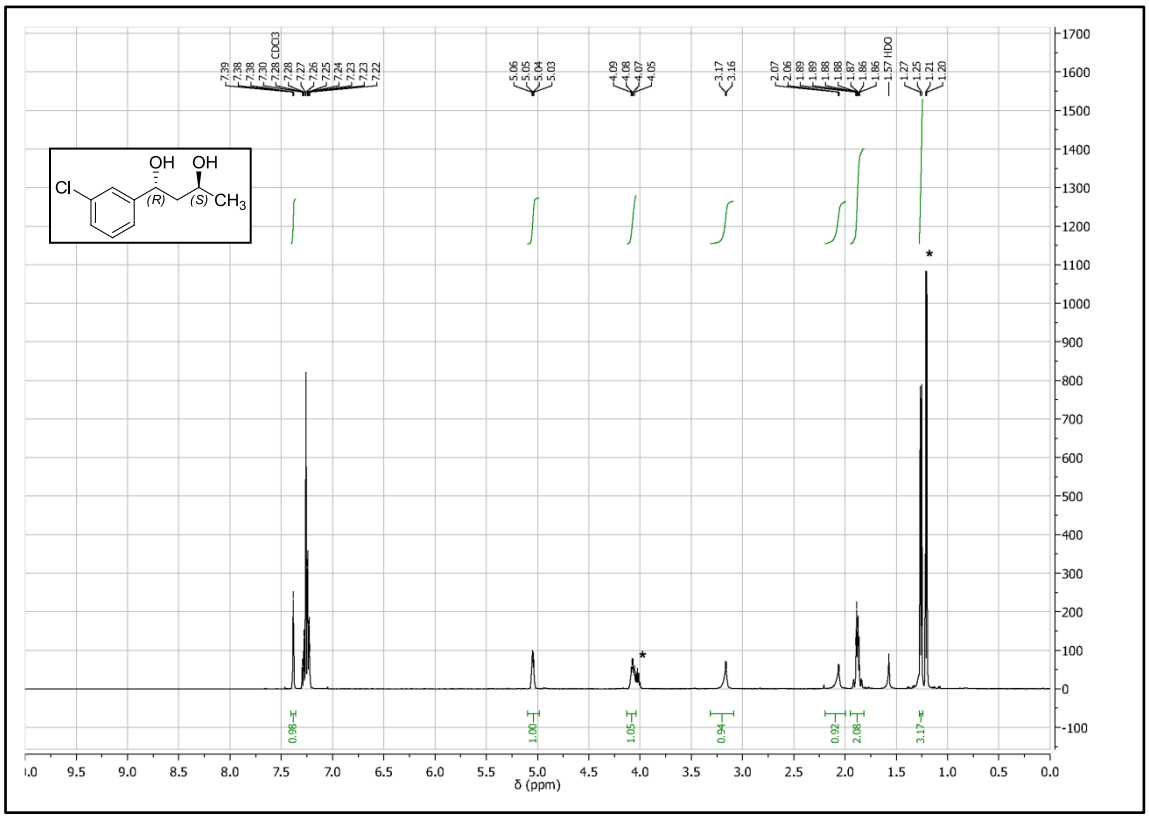
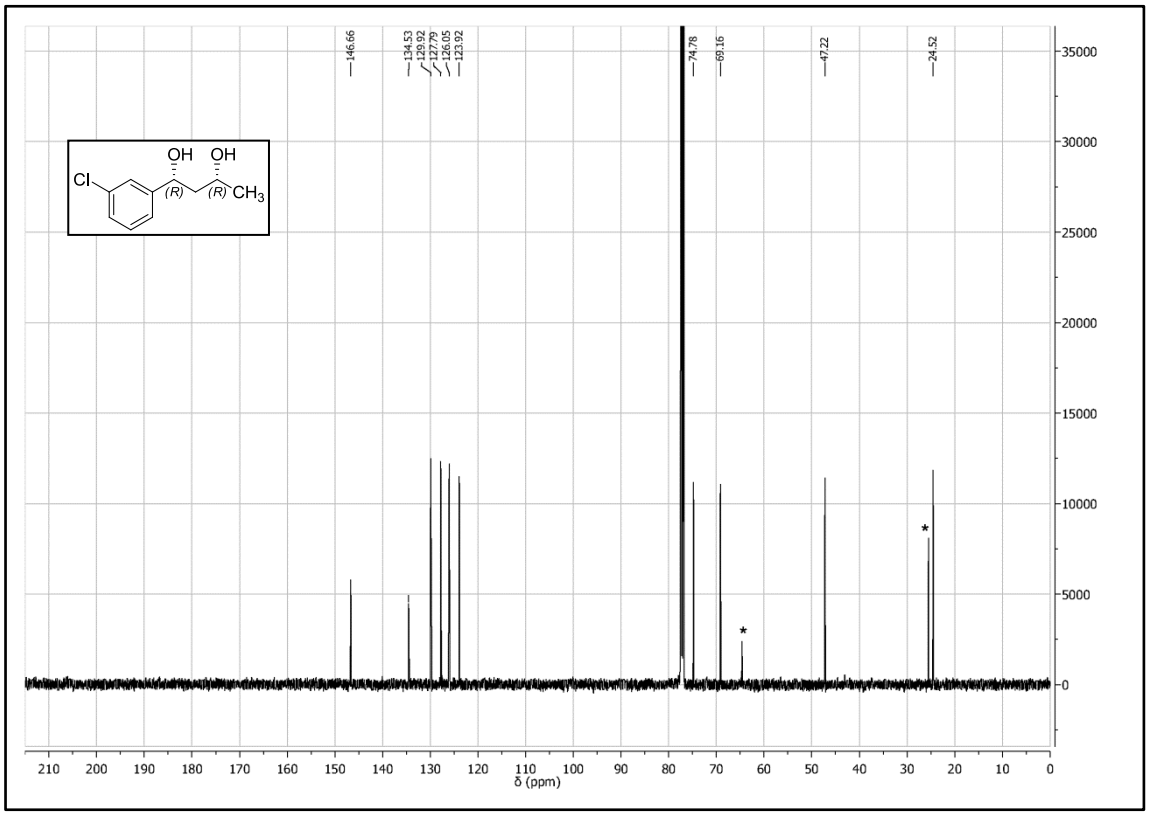
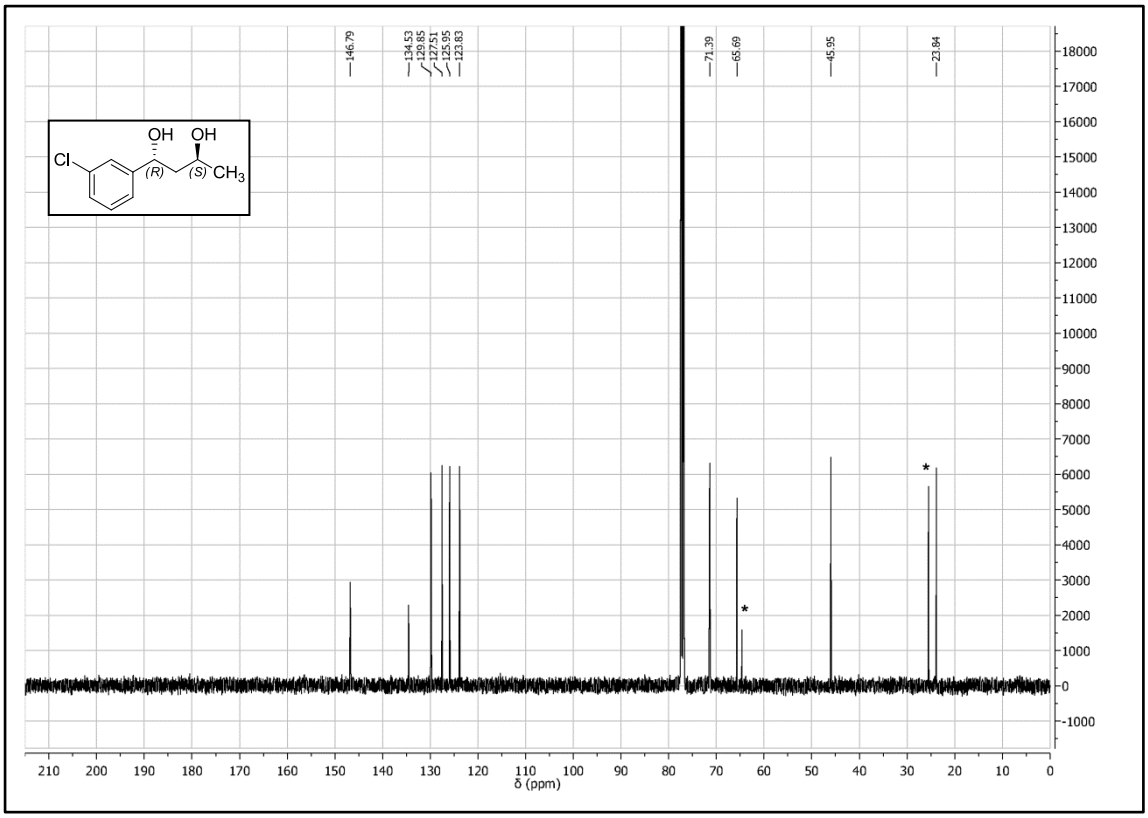
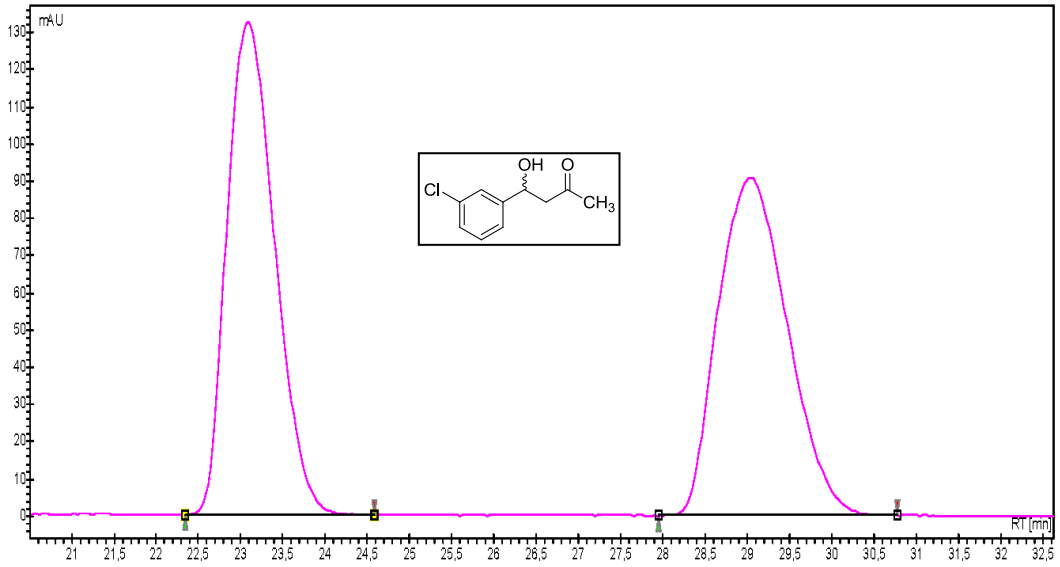
2.64
2.63
2.21
1.80
1.79
1.77
1.76
1.38 HDO
1.26
1.25
1.24
1.21
1.20
OH
OH
Cl
(R)
(R)
CH3
0.98
1.00
1.00
0.95
0.95
2.05
3.06
δ (ppm)


OH
OH
Cl
(R)
(S)
CH3
δ (ppm)


OH
OH
Cl
(R)
(R)
CH3
δ (ppm)

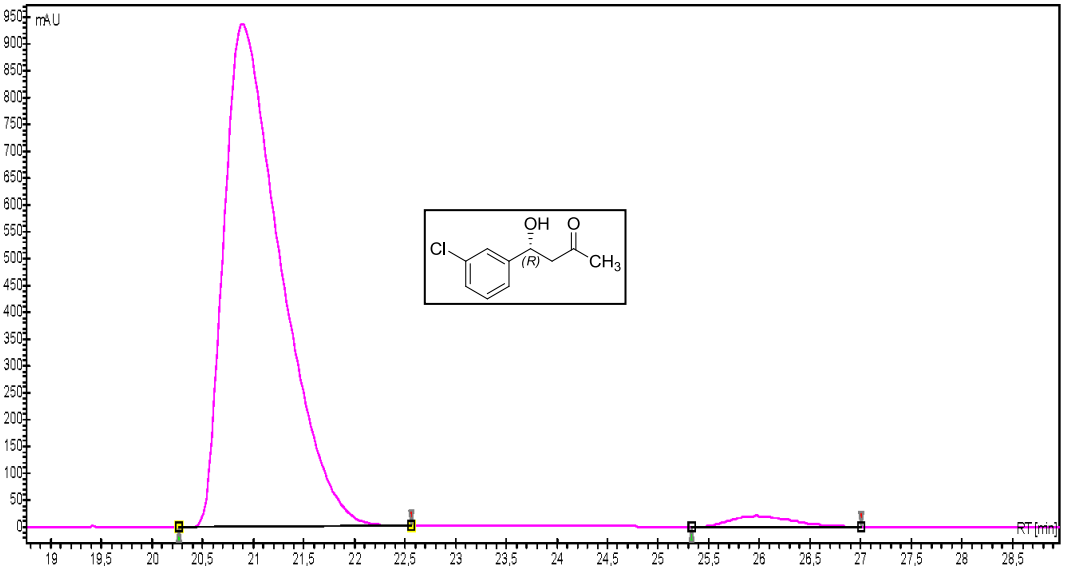

146.79
134.53
129.85
127.51
125.95
123.63
71.39
65.69
45.95
23.84
OH
OH
Cl
(R)
(S)
CH3
δ (ppm)

## 5. HPL Chromatograms



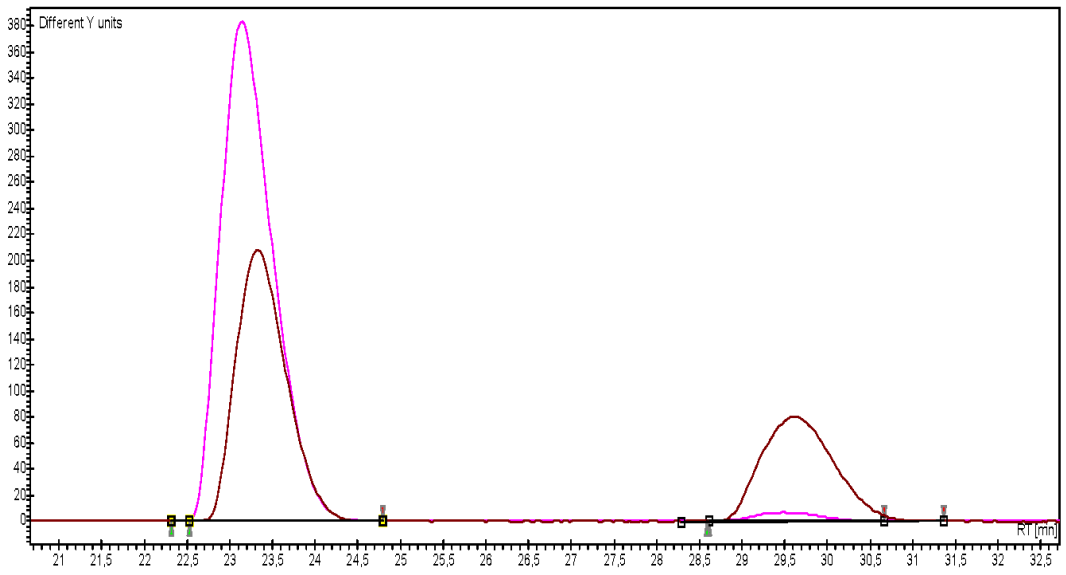

**Peak results :**

| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | (R)-1 | 23,09 | 49,96 | 132,4 | 86,5 | 49,964 |
| 2 | (S)-1 | 29,04 | 50,04 | 90,8 | 86,6 | 50,036 |
| | | | | | | |
| Total | | | 100,00 | 223,3 | 173,1 | 100,000 |



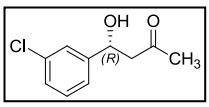

**Peak results :**

| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | (R)-1 | 20,88 | 97,75 | 937,6 | 611,2 | 97,754 |
| 2 | (S)-1 | 25,97 | 2,25 | 20,4 | 14,0 | 2,246 |
| | | | | | | |
| Total | | | 100,00 | 958,1 | 625,2 | 100,000 |

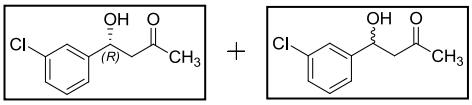


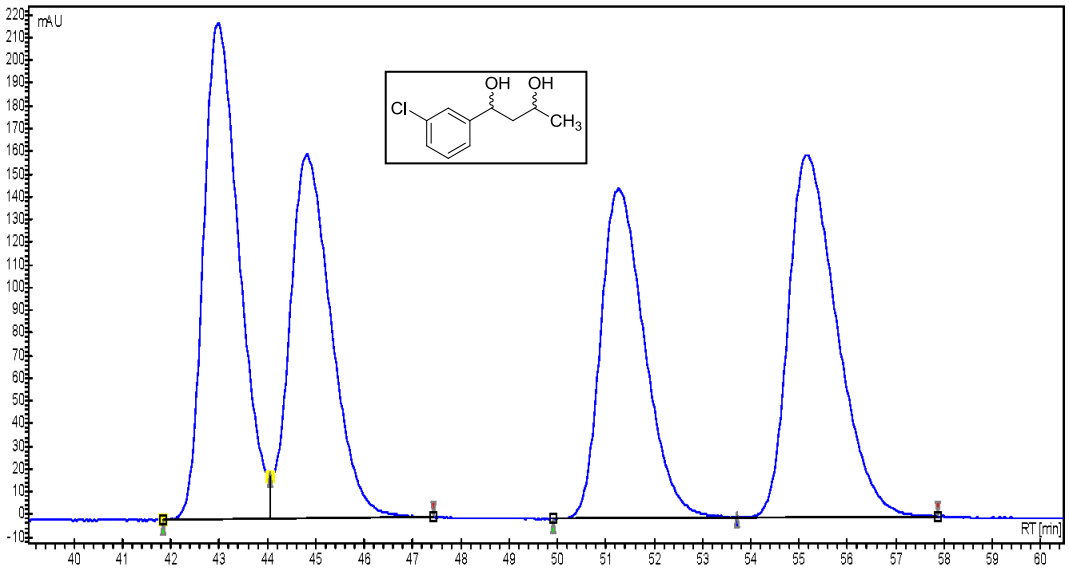

**Peak results :**

| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | (R)-1 | 23,14 | 97,84 | 383,9 | 274,3 | 97,840 |
| 2 | (S)-1 | 29,46 | 2,16 | 6,6 | 6,1 | 2,160 |



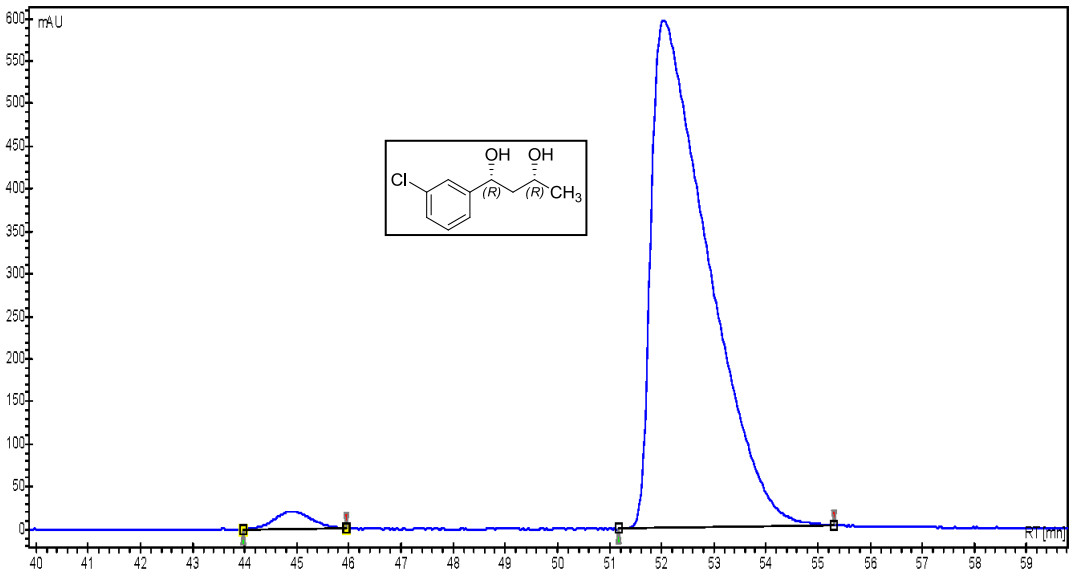

| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | (R)-1 | 23,33 | 64,10 | 208,3 | 143,0 | 64,102 |
| 2 | (S)-1 | 29,60 | 35,90 | 80,9 | 80,1 | 35,898 |
| | | | | | | |
| Total | | | 100,00 | 289,1 | 223,0 | 100,000 |





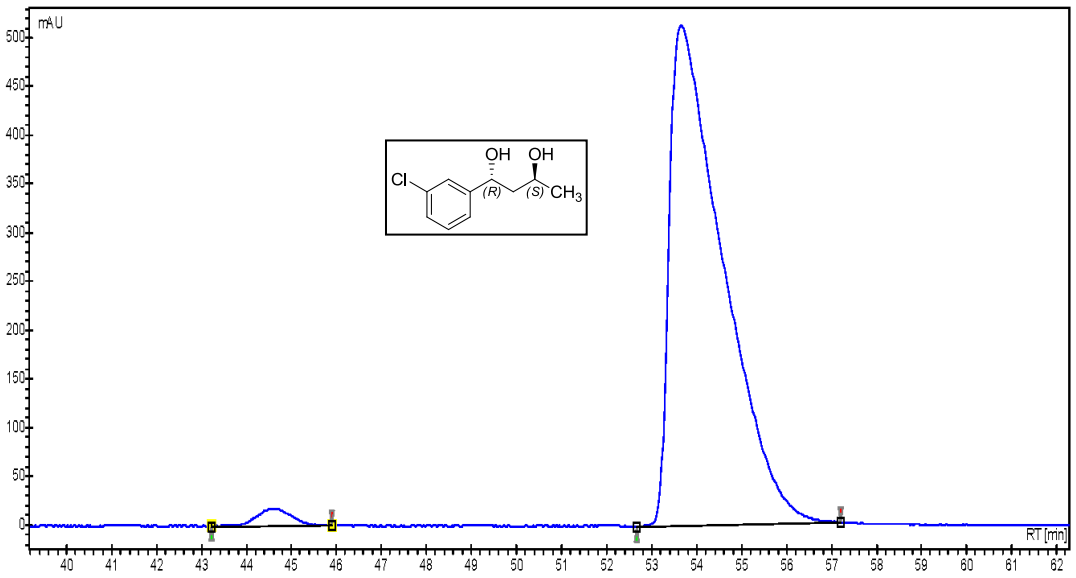

**Peak results :**

| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | (S,S)-2 | 42,98 | 27,39 | 218,7 | 187,1 | 27,391 |
| 2 | (S,R)-2 | 44,82 | 23,27 | 160,4 | 158,9 | 23,269 |
| 3 | (R,R)-2 | 51,25 | 22,22 | 145,4 | 151,8 | 22,218 |
| 4 | (R,S)-2 | 55,17 | 27,12 | 159,6 | 185,3 | 27,123 |
| | | | | | | |
| Total | | | 100,00 | 684,0 | 683,0 | 100,000 |



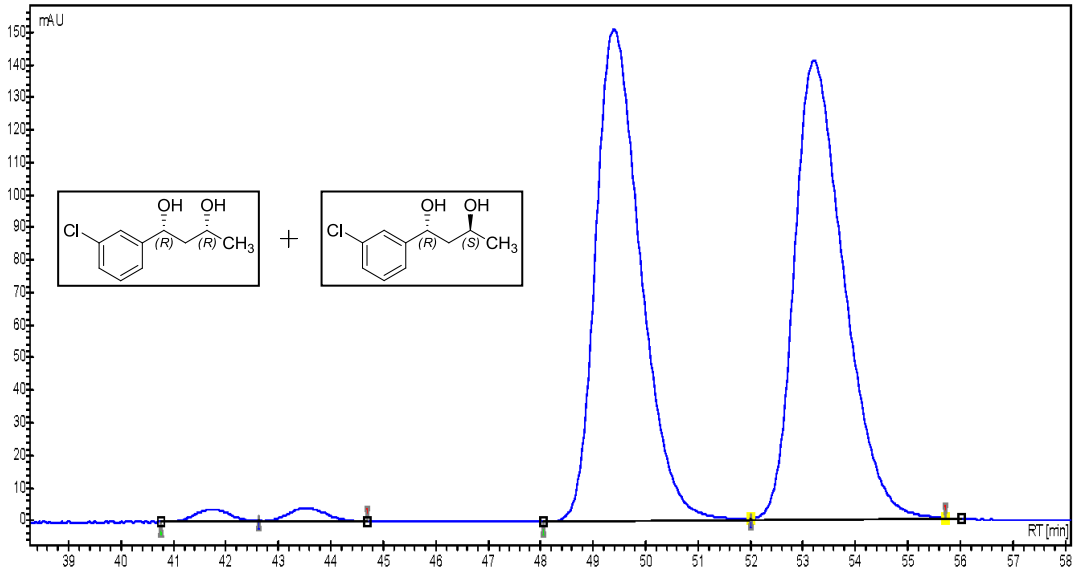

**Peak results :**

| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | (S,R)-2 | 44,90 | 2,13 | 19,9 | 16,3 | 2,126 |
| 2 | (R,R)-2 | 52,02 | 97,87 | 596,7 | 750,5 | 97,874 |
| | | | | | | |
| Total | | | 100,00 | 616,6 | 766,8 | 100,000 |



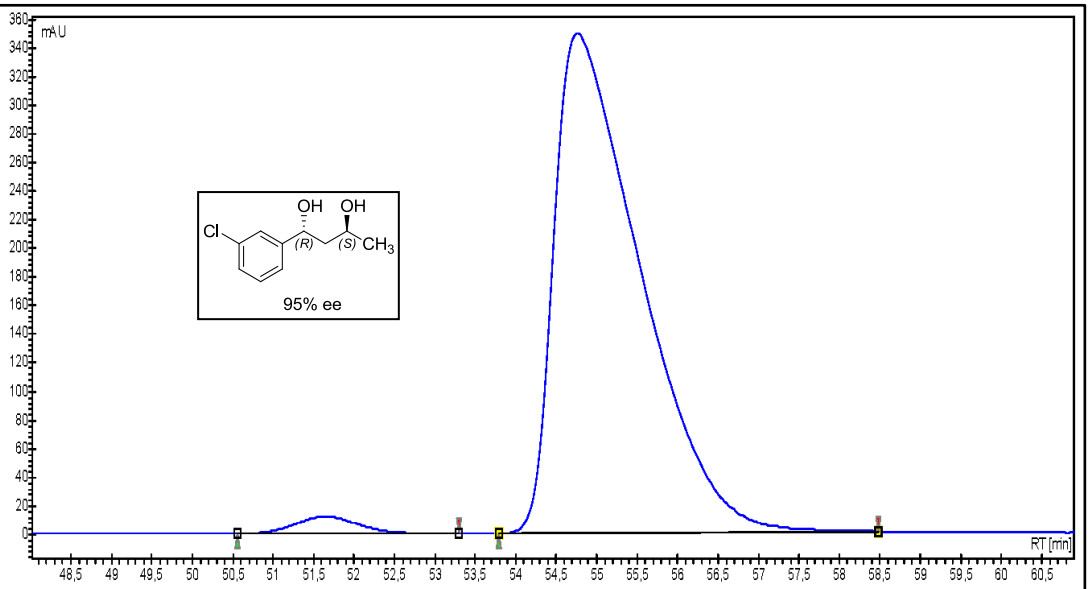

**Peak results :**

| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | (S,S)-2 | 44,61 | 2,28 | 18,3 | 16,4 | 2,280 |
| 2 | (R,S)-2 | 53,65 | 97,72 | 512,5 | 703,5 | 97,720 |
| | | | | | | |
| Total | | | 100,00 | 530,8 | 719,9 | 100,000 |



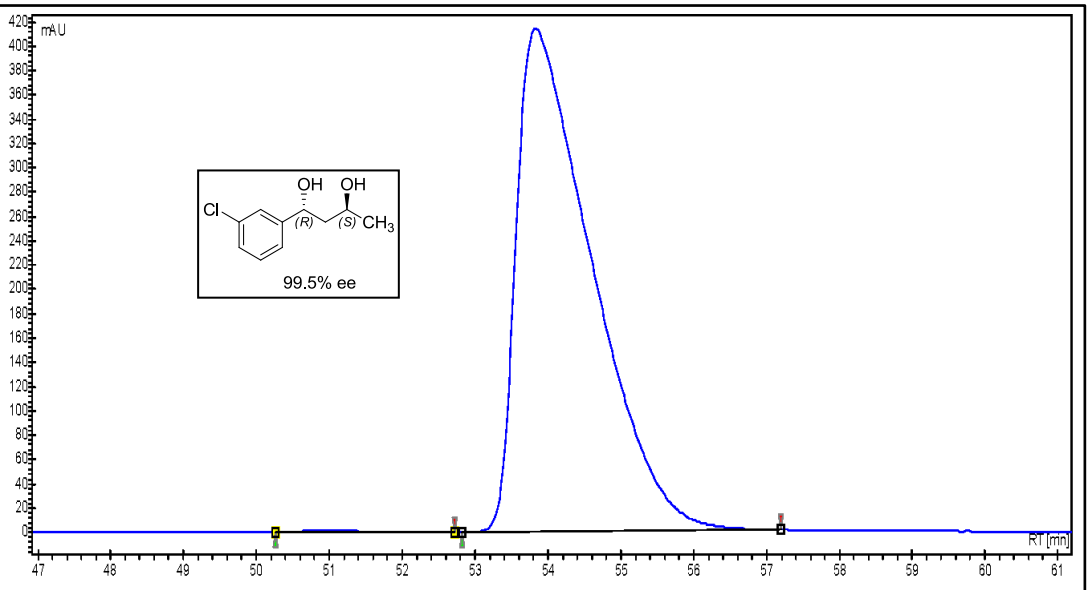

**Peak results :**

| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | (S,S)-2 | 41,73 | 1,01 | 3,9 | 3,2 | 1,009 |
| 2 | (S,R)-2 | 43,54 | 1,17 | 4,3 | 3,7 | 1,171 |
| 3 | (R,R)-2 | 49,38 | 48,11 | 151,0 | 150,4 | 48,110 |
| 4 | (R,S)-2 | 53,20 | 49,71 | 140,8 | 155,4 | 49,710 |
| | | | | | | |
| Total | | | 100,00 | 300,1 | 312,6 | 100,000 |



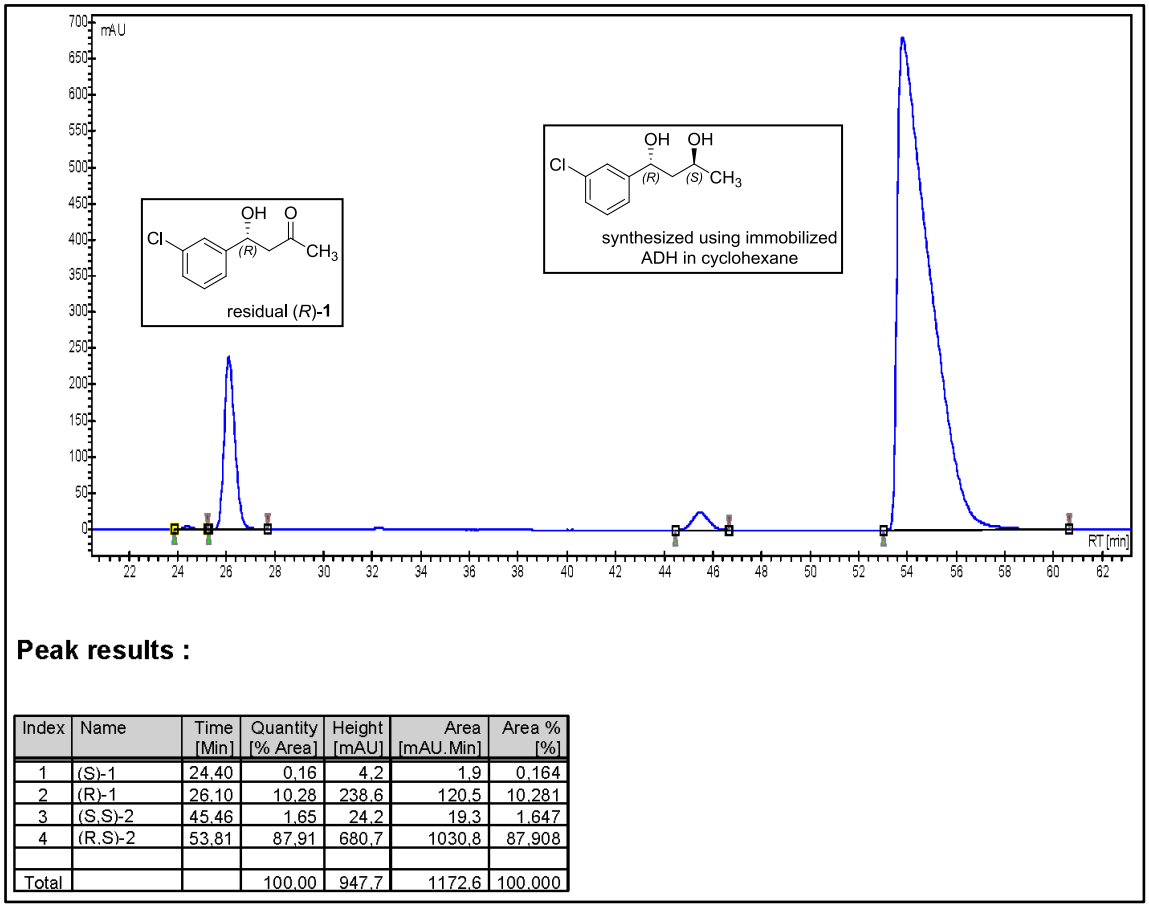

**Peak results :**

| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | (R,R)-2 | 51,65 | 2,46 | 11,9 | 10,9 | 2,459 |
| 2 | (R,S)-2 | 54,77 | 97,54 | 348,7 | 430,6 | 97,541 |
| | | | | | | |
| Total | | | 100,00 | 360,6 | 441,4 | 100,000 |




**Peak results :**

| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | (R,R)-2 | 51,01 | 0,24 | 1,5 | 1,2 | 0,241 |
| 2 | (R,S)-2 | 53,84 | 99,76 | 414,1 | 497,1 | 99,759 |
| | | | | | | |
| Total | | | 100,00 | 415,6 | 498,3 | 100,000 |




**Peak results :**

| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | (S)-1 | 24,40 | 0,16 | 4,2 | 1,9 | 0,164 |
| 2 | (R)-1 | 26,10 | 10,28 | 238,6 | 120,5 | 10,281 |
| 3 | (S,S)-2 | 45,46 | 1,65 | 24,2 | 19,3 | 1,647 |
| 4 | (R,S)-2 | 53,81 | 87,91 | 680,7 | 1030,8 | 87,908 |
| | | | | | | |
| Total | | | 100,00 | 947,7 | 1172,6 | 100,000 |

## 6. References

(1) Jeromin, G. E. *Biotechnol. Lett.* **2009**, 31, 1717-1721.

(2) Rulli, G.; Duangdee, N.; Baer, K.; Hummel, W.; Berkessel, A.; Gröger, H. *Angew. Chem.* **2011**, 123, 8092-8095; *Angew. Chem. Int. Ed.* **2011**, 50, 7944-7947.

(3) Rulli, G.; Fredriksen, K. A.; Duangdee, N.; Bonge-Hansen, T.; Berkessel, A.; Gröger, H. *Synthesis* **2013**, 45, 2512-2519.