

Synergistic Cu-amine catalysis for the enantioselective synthesis of chiral cyclohexenones

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Table of Contents

General information.....	S2
Additional results on the optimization of the dual catalyzed addition of 1 to cinnamaldehyde.....	S3
Plausible catalytic cycle for the synergistic activation.....	S4
Experimental section.....	S5
Spectras.....	S6

General information

NMR spectra were recorded on a Bruker AC 300 (300 MHz) or a Bruker AC 400 (400 MHz) spectrometer in CDCl₃ in general. Chemical shifts are given in ppm, using as internal standards the residual CHCl₃ signal for ¹H NMR ($\delta = 7.26$) and the deuterated solvent signal for ¹³C NMR ($\delta = 77.0$). Data for ¹³C 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 methanol was bought from Sigma-Aldrich (99,8% purity, ref 322415).

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 H₂SO₄, 5 mL of p-anisaldehyde and 0.5 mL of AcOH). Flash Chromatography was performed following the method of Still on 40 – 63 μ m 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 pressure ionization source (API) pneumatically assisted. Samples were ionized by positive electrospray mode as follows: electrospray tension (ISV): 5500 V; opening tension (OR): 50 V; nebulization gas pressure (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 μ m millipore membrane before use. Retention times *R_t* in minutes, retention factors $k_i = (R_{ti} - R_{t0}) / R_{t0}$ and enantioselectivity factor $\alpha = k_2 / k_1$ are given. *R_{t0}* 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).

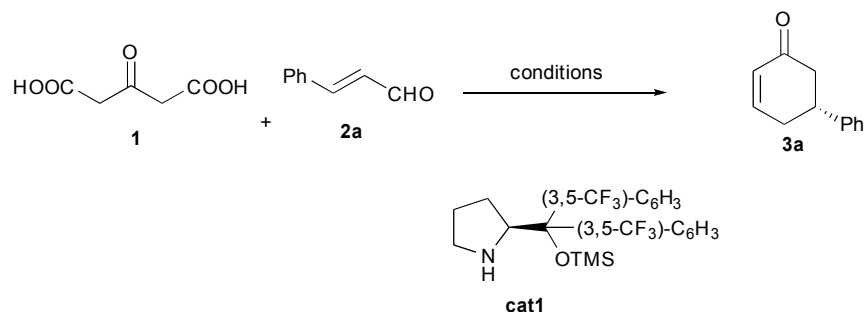
Chiral GC analysis were performed on a HP 4890 using 6 bar argon as vector. Column: 25m/0,25 mm. Chromatogram analyzed with ChromNav software.

Optical rotations were measured at 20 °C in CHCl₃ with a Anton Paar MCP 200 polarimeter with a 0.2 cm length.

All commercially available reagents were used as received except for cinnamaldehyde, distilled prior to use.

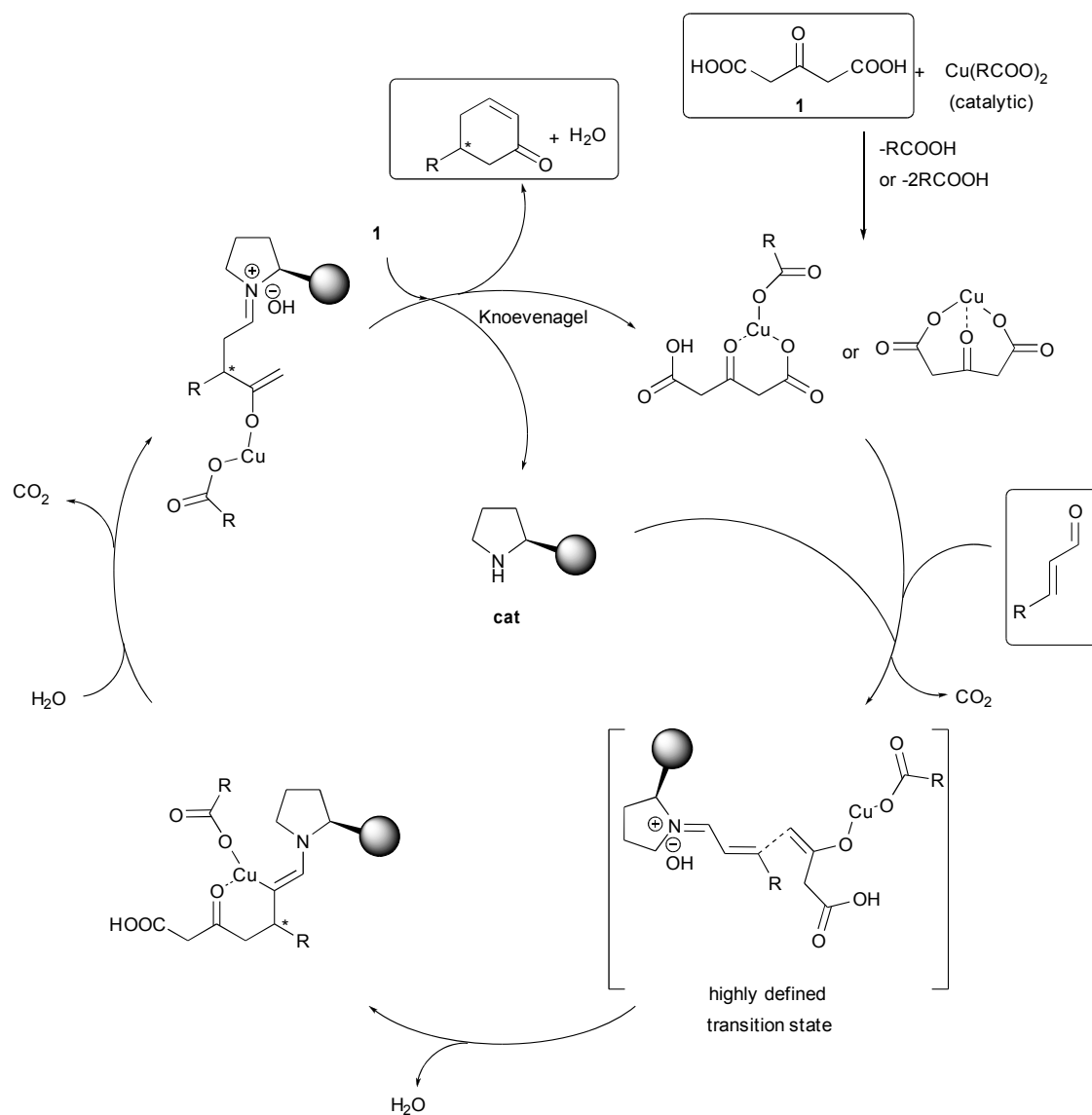
The absolute configuration of the obtained cyclohexenones was obtained by comparison of literature datas for optical rotation in compounds **3a** and **3b**. We assume the same transition state for all the aldehydes.

Additional results on the optimization of the dual catalyzed addition of 1 to cinnamaldehyde:



entry	cat	Solvent (0.25 M)	Excess reagent	Time, T°C	yield	ee
1	cat1 (15 %), Cu(OAc) ₂ (4%)	Toluene	1 (1,3 eq) added in one portion	4h, 25°C	11%	88% ee
2	cat1 (15%), Cu(OAc) ₂ (4%)	CHCl ₃	1 (1,3 eq) added in one portion	4h, 25°C	traces	-
3	cat1 (15%), Cu(OAc) ₂ (4%)	DMF	1 (1,3 eq) added in one portion	4h, 25°C	traces	-
4	cat1 (15 %), Cu(OAc) ₂ (4%)	MeOH	1 (1,3 eq) added in one portion	4h, 25°C	15%	92% ee
5	cat1 (15 %), Cu(OAc) ₂ (4%)	MeOH	2 (1,3 eq), 1 slowly added over 2h	4h, 25°C	37%	97% ee
6	cat1 (15 %), Cu(OAc) ₂ (4%)	EtOH	2 (1,3 eq), 1 slowly added over 2h	4h, 25°C	30%	96% ee
7	cat1 (15 %), Cu(OAc) ₂ (4%)	<i>i</i> PrOH	2 (1,3 eq), 1 slowly added over 2h	4h, 25°C	28%	95% ee
8	cat1 (15 %), Cu(OAc) ₂ (4%)	CF ₃ CH ₂ OH /MeOH	2 (1,3 eq), 1 slowly added over 2h	4h, 25°C	21%	89% ee
9	cat1 (15 %), Cu(OAc) ₂ (4%)	MTBE /MeOH	2 (1,3 eq), 1 slowly added over 2h	4h, 25°C	10%	95% ee
10	Cu(OAc) ₂ only (4%)	MeOH	2 (1,3 eq), 1 slowly added over 2h	4h, 25°C	No reaction	-
11	Cat1 (50 %), Cu(<i>i</i> -BuCOO) ₂ (4%)	MeOH	2 (1,3 eq), 1 slowly added over 2h	4h, 25°C	51%	96% ee

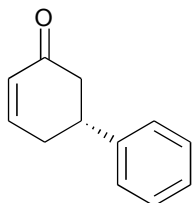
Plausible catalytic cycle for the synergistic activation:



Experimental section

General procedure for the cyclohexenone formation :

To 17.7 mg of cat 2 (0.03 mmol, 0.15 eq) in a schlenk tube under argon is added 2.8 mg of copper(ii) *i*-butyrate (0.012 mmol, 0.06 eq). 0.4 ml of dry methanol are then added before the addition of 0.32 mmol (1.6 eq) of the corresponding aldehyde. The mixture is placed at the indicated temperature (if necessary pre-heated oil bath) before the slow addition (portion wise over 2h) of 29.2 mg (0.2 mmol, 1 eq) of diacid **1** in 0.4 ml of dry methanol. After completion of the addition, the reaction is stirred at the indicated temperature for two hours more. The reaction is then filtered over silica (Et₂O), the solvent evaporated. Purification over silica gel (petroleum ether/ethyl acetate unless specified) directly yields the corresponding cyclohexenone.



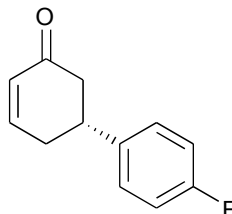
Compound **3a**: Prepared according to the general procedure using 219.3 mg of unsaturated aldehyde (1.659 mmol), 14.1 mg of copper(ii)-*i*-butyrate (0.0593 mmol), 90 mg of **cat 2** (0.1508 mmol) in 2 ml of methanol and 147.9 mg of **1** (1.012 mmol) in 2ml of methanol slowly added at 28°C: The product was isolated as a pale yellow oil after purification with diethyl ether / petroleum ether mixture. 86.9 mg (0.5046 mmol). 50% yield.

$R_f = 0.44$ (petroleum ether / ethyl acetate (7/3)). $[\alpha]_D^{20} = -56.5^\circ$ (CHCl₃, $c = 1.26$), 98% *ee*.
Literature¹: $[\alpha]_D^{20} = -39.5^\circ$ (CHCl₃, $c = 1.0$), 94% *ee*.

¹H NMR (400 MHz, CDCl₃): δ (ppm) = 2.50-2.73 (m, 2 CH₂), 3.32-3.38 (m, CH), 6.13 (dd, $J = 11.2$ and 2.2 Hz, CH=CH), 7.05 (ddd, $J = 11.0, 5.6, 2.4$ Hz, CH=CH), 7.24-7.29 (m, 2H arom), 7.33-7.37 (2H arom). ¹³C NMR (100 MHz, CDCl₃): δ (ppm) = 33.7 (CH₂), 40.9 (CH), 44.9 (CH₂), 126.7 (CH arom), 127.0 (CH arom), 128.8 (CH arom), 129.8 (CH), 143.2 (Carom), 149.5 (CH), 199.2 (CO).

GC enantiomeric excess determination: hydrodex- β -3P; 130°C for 60 minutes than 1°C/min until 220°C. rt (min) = 67.9 min; rt (maj) = 68.4 min.

Data are in accordance with the literature.¹



Compound **3b**: Prepared according to the general procedure using 29 mg of **1** and 47.6 mg of unsaturated aldehyde at 28°C: The product was isolated as a pale yellow oil. 17.9 mg (0.0941 mmol). 47% yield.

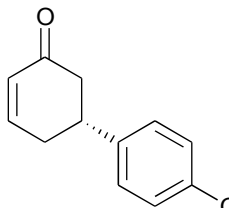
$R_f = 0.44$ (petroleum ether / ethyl acetate (7/3)). $[\alpha]_D^{20} = -48.0^\circ$ (CHCl₃, $c = 1.12$), 98% *ee*.
Literature¹: $[\alpha]_D^{20} = -29.1^\circ$ (CHCl₃, $c = 1.0$), 95% *ee*.

¹H NMR (400 MHz, CDCl₃): δ (ppm) = 2.46-2.72 (m, 2 CH₂), 3.30-3.38 (m, CH), 6.13 (dd, $J = 11.6$ and 2.4 Hz, CH=CH), 7.01-7.07 (m, 2H arom and CH=CH), 7.18-7.22 (2H arom).

¹³C NMR (75 MHz, CDCl₃): δ (ppm) = 33.8 (CH₂), 40.2 (CH), 45.0 (CH₂), 115.6 (d, $J = 21$ Hz, CH arom), 128.1 (d, $J = 7.5$ Hz, CH arom), 129.8 (CH), 138.9 (C arom), 149.2 (CH), 161.7 (d, $J = 240$ Hz, C arom), 198.8 (CO).

GC enantiomeric excess determination: hydrodex- β -3P; 140°C for 60 minutes than 1°C/min until 220°C. rt (min) = 50.9 min; rt (maj) = 51.6 min.

Data are in accordance with the literature.¹



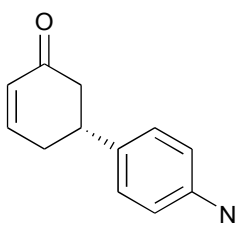
Compound **3c**: Prepared according to the general procedure using 29 mg of **1** and 52.9 mg of unsaturated aldehyde at 28°C: The product was isolated as a pale yellow oil. 19.8 mg (0.0958 mmol). 48% yield.

$R_f = 0.49$ (petroleum ether / ethyl acetate (7/3)). $[\alpha]_D^{20} = -75.1$ (CHCl_3 , $c = 1.21$), 97% *ee*.

$^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm) = 2.45-2.71 (m, 2 CH_2), 3.30-3.38 (m, CH), 6.13 (dd, $J = 11.0$ and 2.0 Hz, $\text{CH}=\text{CH}$), 7.01-7.07 (m, $\text{CH}=\text{CH}$), 7.18 (d, $J = 11.2$ Hz, 2H arom), 7.32 (d, $J = 11.2$ Hz, 2H arom). $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ (ppm) = 33.5 (CH_2), 40.3 (CH), 44.7 (CH_2), 128.8 (CH arom), 128.0 (CH arom), 129.8 (CH), 132.7 (C arom), 141.6 (CH), 149.1 (C arom), 198.6 (CO).

GC enantiomeric excess determination: hydrodex- β -3P; 140°C for 60 minutes then 1°C/min until 220°C. rt (min) = 94.1 min; rt (maj) = 94.4 min.

HRMS ESI $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{20}\text{O}_3$: 297.1485. Observed: 297.1486.



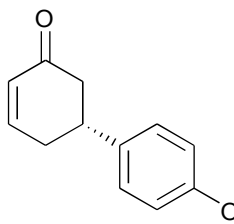
Compound **3d**: Prepared according to the general procedure using 29 mg of **1** and 56.2 mg of unsaturated aldehyde at 20°C: The product was isolated as yellow needles. 17.1 mg (0.0787 mmol). 40% yield.

$R_f = 0.22$ (petroleum ether / ethyl acetate (7/3)). $[\alpha]_D^{20} = -55.6^\circ$ (CHCl_3 , $c = 0.97$), 96% *ee*.

$^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm) = 2.53-2.71 (m, 2 CH_2), 3.46-3.52 (m, CH), 6.16 (dd, $J = 11.2$ and 2.2 Hz, $\text{CH}=\text{CH}$), 7.05 (ddd, $J = 11.2$; 5.8; 2.2 Hz; $\text{CH}=\text{CH}$), 7.41 (d, $J = 9.0$ Hz, 2H arom), 8.22 (d, $J = 9.0$ Hz, 2H arom). $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ (ppm) = 33.0 (CH_2), 40.7 (CH), 44.2 (CH_2), 124.1 (CH arom), 127.7 (CH arom), 130.0 (CH), 147.0 (C arom), 148.5 (CH), 150.3 (C arom), 197.6 (CO).

HPLC enantiomeric excess determination: Chiralpak IA, Heptane/Ethanol 40/60, 1 ml/min, DAD and CD254nm. rt (maj) = 9.5 min; rt (min) = 14.3 min.

HRMS ESI $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{12}\text{H}_{12}\text{NO}_3$: 218.0812. Observed: 218.0810.



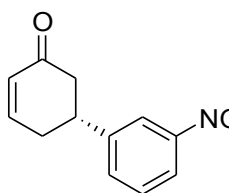
Compound **3e**: Prepared according to the general procedure using 29 mg of **1** and 51.1 mg of unsaturated aldehyde at 28°C: The product was isolated as a pale yellow oil contaminated with around 4% of starting unsaturated aldehyde. 16.8 mg (0.0831 mmol). 42% yield.

$R_f = 0.42$ (petroleum ether / ethyl acetate (7/3)). $[\alpha]_D^{20} = -55.1^\circ$ (CHCl_3 , $c = 1.04$), 96% *ee*.

$^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm) = 2.50-2.67 (m, 2 CH_2), 3.26-3.34 (m, CH), 3.80 (s, CH_3), 6.16 (dd, $J = 10.6$ and 2.4 Hz, $\text{CH}=\text{CH}$), 6.86 (d, $J = 8.6$ Hz, 2 CH arom), 6.91 (ddd, $J = 10.4$; 5.6; 2.6 Hz; $\text{CH}=\text{CH}$), 7.19 (d, $J = 8.6$ Hz, 2CH arom). $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ (ppm) = 33.9 (CH_2), 40.2 (CH), 45.2 (CH_2), 55.3 (CH_3), 114.1 (CH arom), 127.6 (CH arom), 129.7 (CH), 135.4 (C arom), 149.6 (CH), 158.5 (C arom), 199.4 (CO).

HPLC enantiomeric excess determination: Chiralpak IA, Heptane/Ethanol 80/20, 1 ml/min, DAD and polarimeter. rt (maj) = 8.9 min; rt (min) = 10.6 min.

HRMS ESI $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{13}\text{H}_{15}\text{O}_2$: 203.1067. Observed: 203.1065.



Compound **3f**: Prepared according to the general procedure using 29.2 mg of **1** and 56.7 mg of unsaturated aldehyde at 20°C: The product was isolated as yellow oil. 16.8 mg (0.0773 mmol). 39% yield.

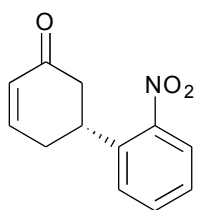
$R_f = 0.48$ (petroleum ether / ethyl acetate (1/1)). $[\alpha]_D^{20} = -38.4^\circ$ (CHCl₃, $c = 0.89$), 98% *ee*.

¹H NMR (400 MHz, CDCl₃): δ (ppm) = 2.55-2.77 (m, 2 CH₂), 3.46-3.52 (m, CH), 6.17 (dd, $J = 11.0$ and 2.4 Hz, CH=CH), 7.06 (ddd, $J = 11.0$; 5.8; 2.4 Hz; CH=CH), 7.52-7.73 (m,

2CH arom), 8.12-8.15 (m, 2CH arom). ¹³C NMR (100 MHz, CDCl₃): δ (ppm) = 33.1 (CH₂), 40.5 (CH), 44.4 (CH₂), 121.7 (CH arom), 122.2 (CH arom), 129.8 (CH), 130.0 (CH arom), 133.0 (C arom), 145.1 (C arom), 148.5 (CH), 197.7 (CO).

HPLC enantiomeric excess determination: Chiralpak IC, Heptane/Ethanol 50/50, 1 ml/min, DAD. *rt* (maj) = 13.9 min; *rt* (min) = 15.7 min.

HRMS ESI [M+H]⁺ calcd for C₁₂H₁₂NO₃: 218.0812. Observed: 218.0810.



Compound **3g**: Prepared according to the general procedure using 28.9 mg of **1** and 56.1 mg of unsaturated aldehyde at 20°C: The product was isolated as a pale yellow powder. 21.9 mg (0.1008 mmol). 51% yield.

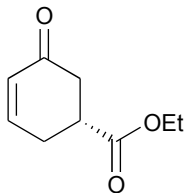
$R_f = 0.32$ (petroleum ether / ethyl acetate (7/3)). $[\alpha]_D^{20} = -4.1^\circ$ (CHCl₃, $c = 1.05$), 99% *ee*.

¹H NMR (300 MHz, CDCl₃): δ (ppm) = 2.47-2.58 (m, 1 H of CH₂), 2.70-2.81 (m, 3H of CH₂), 3.85-3.95 (m, CH), 6.13 (dd, $J = 10.0$ and 2.0 Hz, CH=CH), 7.01-7.06 (m, CH=CH), 7.39-7.64 (m, 3 CH arom), 7.81 (dd, $J = 8.0$ and 1.4 Hz, CH arom). ¹³C NMR (100 MHz, CDCl₃): δ

(ppm) = 33.1 (CH₂), 35.4 (CH), 43.9 (CH₂), 124.6 (CH arom), 127.9 (CH arom), 128.0 (CH arom), 129.7 (CH), 133.0 (CH), 136.9 (C arom), 148.8 (CH), 149.7 (C arom), 197.8 (CO).

HPLC enantiomeric excess determination: Chiralpak IE, Heptane/Ethanol 50/50, 1 ml/min, DAD and CD254nm. *rt* (maj) = 8.4 min; *rt* (min) = 10.8 min.

HRMS ESI [M+H]⁺ calcd for C₁₂H₁₂NO₃: 218.0812. Observed: 218.0812.



Compound **3h**: Prepared according to the general procedure using 29.4 mg of **1** and 41.2 mg of unsaturated aldehyde at 28°C: The product was isolated as a pale yellow oil. 9.7 mg (0.0577 mmol). 29% yield.

$R_f = 0.36$ (petroleum ether / ethyl acetate (7/3)). $[\alpha]_D^{20} = -81.03^\circ$ (CHCl₃, $c = 0.91$), 94% *ee*.

¹H NMR (400 MHz, CDCl₃): δ (ppm) = 1.26 (t, $J = 7.0$ Hz, CH₃), 2.57-2.76 (m, 2 CH₂), 3.02-3.10 (m, CH), 4.17 (q, $J = 7.0$ Hz, CH₂), 6.06 (dt, $J = 10.2$ and 2.0 Hz, CH=CH), 6.95 (ddd, $J =$

10.2; 4.6 and 3.6 Hz, CH=CH). ¹³C NMR (75 MHz, CDCl₃): δ (ppm) = 14.1 (CH₃), 28.0 (CH₂), 39.7 (CH₂), 39.8 (CH), 61.1 (CH₂), 129.8 (CH), 147.8 (CH), 172.9 (COO) 197.0 (CO).

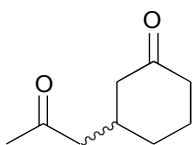
GC enantiomeric excess determination: hydrodex- β -3P; 90°C for 30 minutes then 1°C/min until 220°C. *rt* (min) = 64.7 min; *rt* (maj) = 65.0 min.

Data are in accordance with the literature.²

General procedure for the cascade addition of two molecules of **1**:

To 13.0 mg of cat **1** (0.04 mmol, 0.25 eq) in a schlenk tube under argon is added 1.8 mg of copper(ii)acetate (0.01 mmol, 0.0625 eq). 0.4 ml of dry THF are then added before the addition of 26.4 mg of cinnamaldehyde (0.20 mmol, 1.25 eq). 46.8 mg (0.32 mmol, 1.0 eq) of diacid **1** are then added all at once and the resulting mixture stirred at *rt* (22°C) for 16 hours. The reaction is then filtered over silica (Et₂O), the solvent evaporated. Purification over silica gel (petroleum ether/ethyl acetate) directly yields the corresponding cascade product in a 2.7:1 *dr* as a yellow oil. 12.1 mg (0.0525 mmol). 38% yield.

² J-M. Garnier, M. Jida, J. Ollivier, *Synlett*, **2006**, 17, 2739.



Compound **4a**: $R_f = 0.24$ (petroleum ether / ethyl acetate (7/3)).

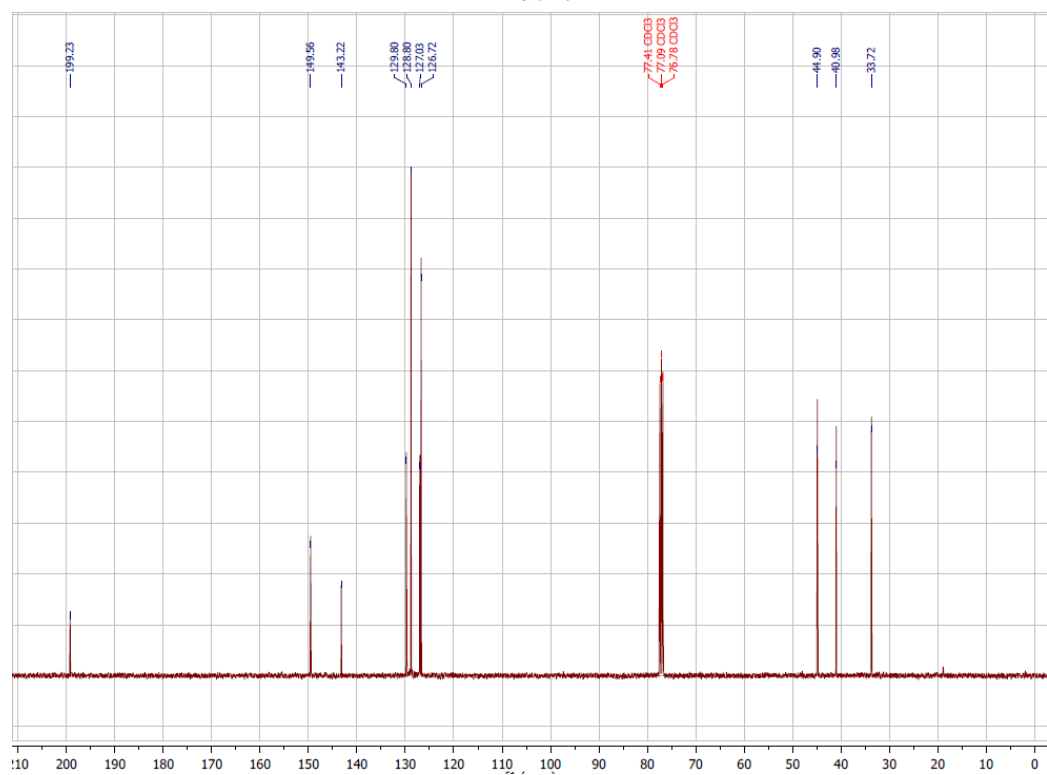
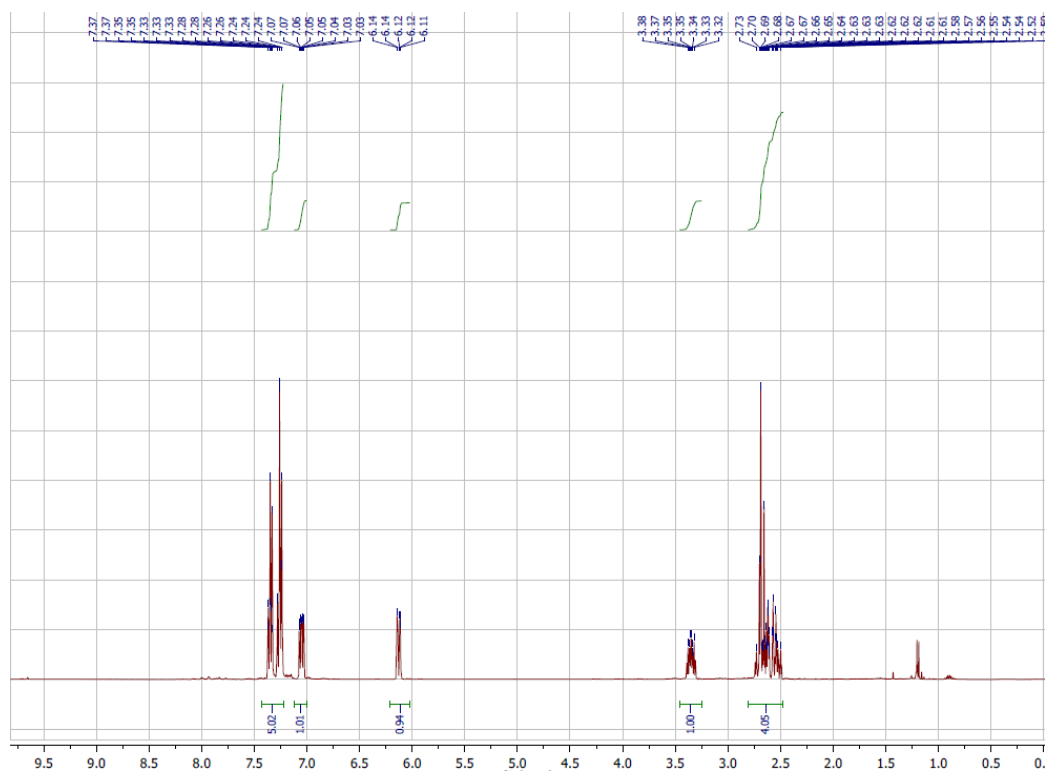
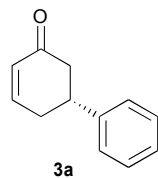
$^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm) = 1.88-1.94 (m, 1H of CH_2 , both dia), 2.05-2.24 (m, 1H of CH_2 and CH_3 , both dia), 2.42-2.67 (m, 3 CH_2 both dia), 2.70-2.76 (m, CH both dia), 2.97-3.06 (m, CH, dia mino), 3.23-3.30 (m, CH, major dia). 7.17-7.36 (m, 5H arom).

$^{13}\text{C NMR}$ (100 MHz, CDCl_3), only the major dia is described: δ (ppm) = 30.2 (CH_3), 30.5 (CH), 37.1 (CH_2), 39.9 (CH), 46.2 (CH_2), 47.4 (CH_2), 47.5 (CH_2), 126.5 (CH arom), 126.8

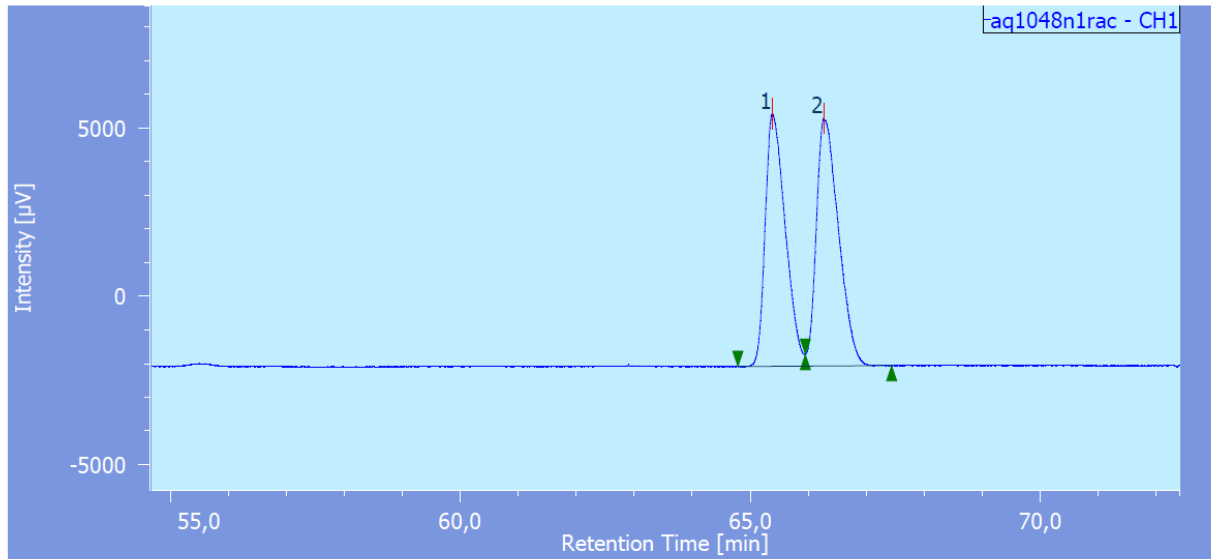
(CH arom), 128.7 (CH arom), 143.6 (C arom), 206.6 (CO), 210.7 (CO).

GC enantiomeric excess determination: hydrodex- β -3P; 140°C for 0 minutes then 1°C/min until 180°C then 30 minutes. rt (maj) = 58.7 min; rt (min) = 60.2 min. (minor dia rt = 69 min).

HRMS ESI $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{19}\text{O}_2$: 231.1380. Observed: 231.1381.

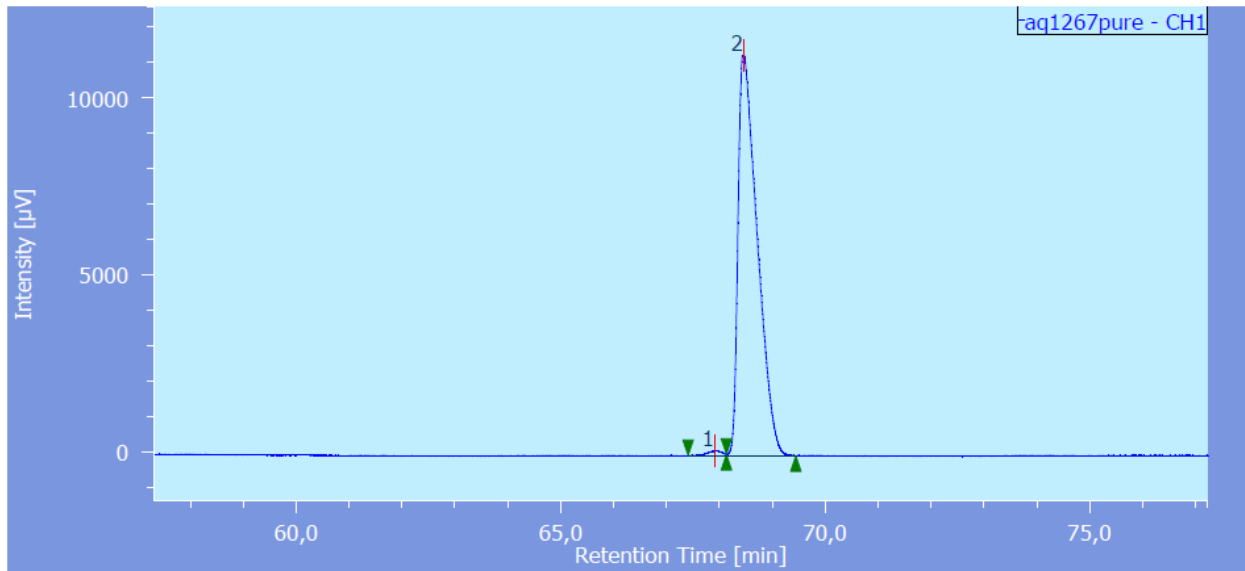


Racemate :

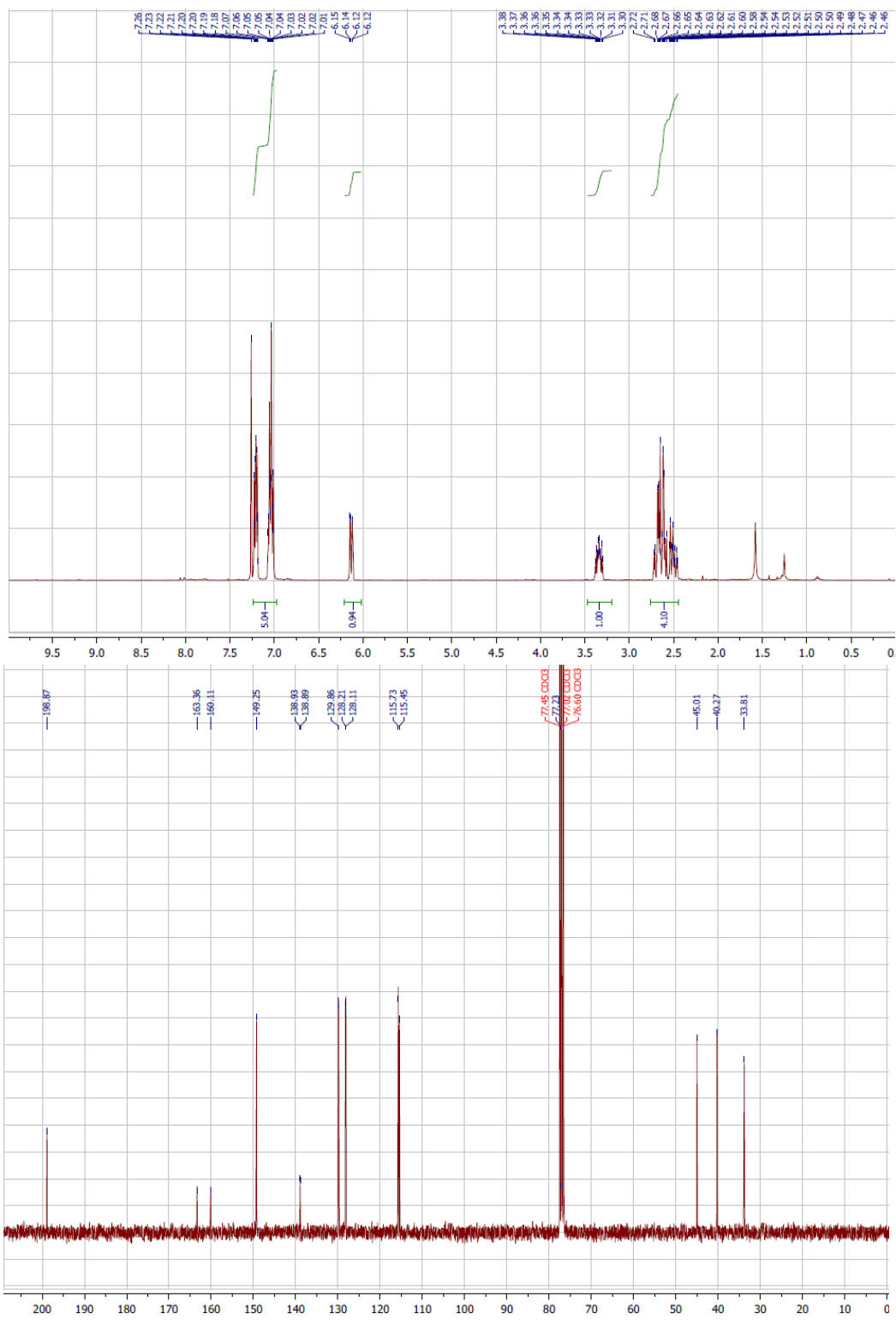
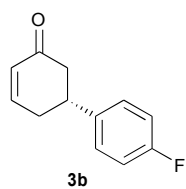


#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	65,383	180178	7501	48,027	50,497	N/A	166183	1,314	1,471	
2	Unknown	1	66,267	194978	7354	51,973	49,503	N/A	140605	N/A	1,436	

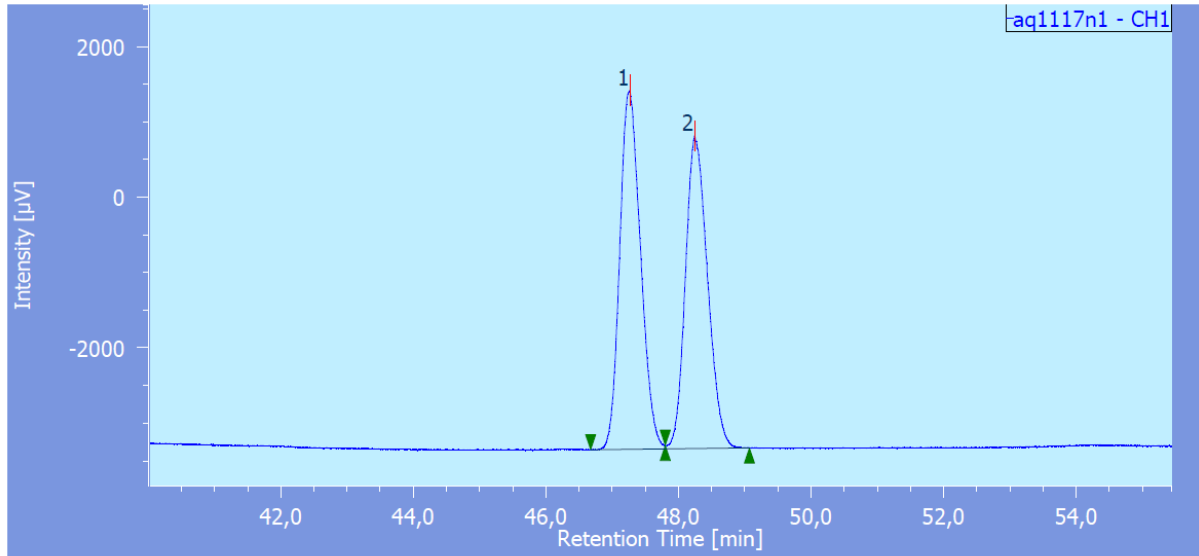
Chiral :



#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	67,917	2641	145	0,916	1,268	N/A	291022	0,938	N/A	
2	Unknown	1	68,467	285818	11314	99,084	98,732	N/A	165838	N/A	1,873	

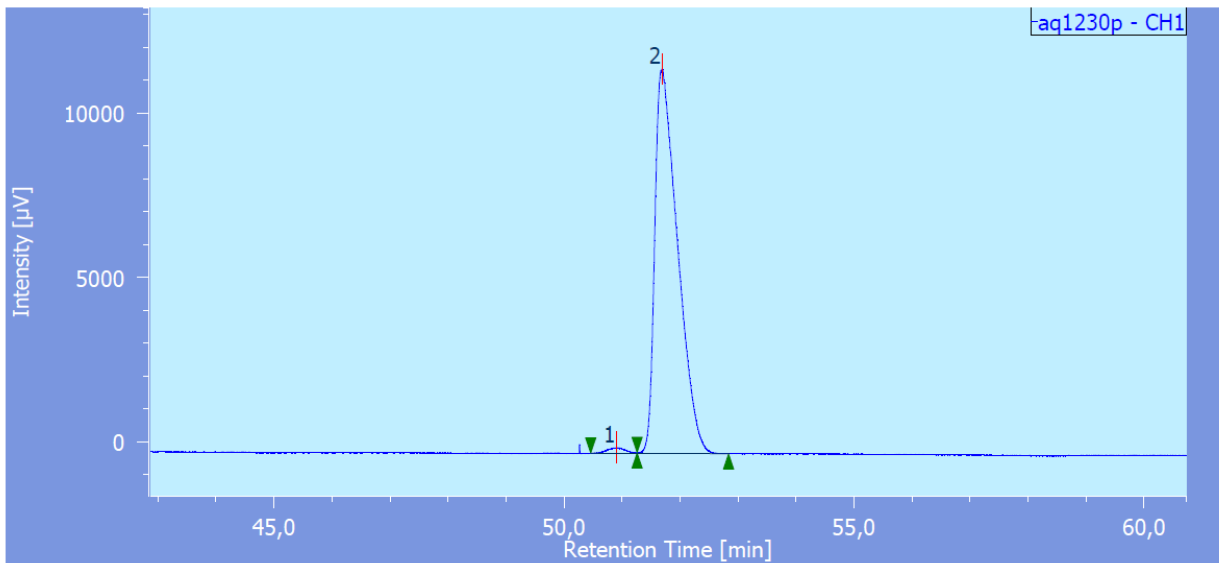


Racemate :

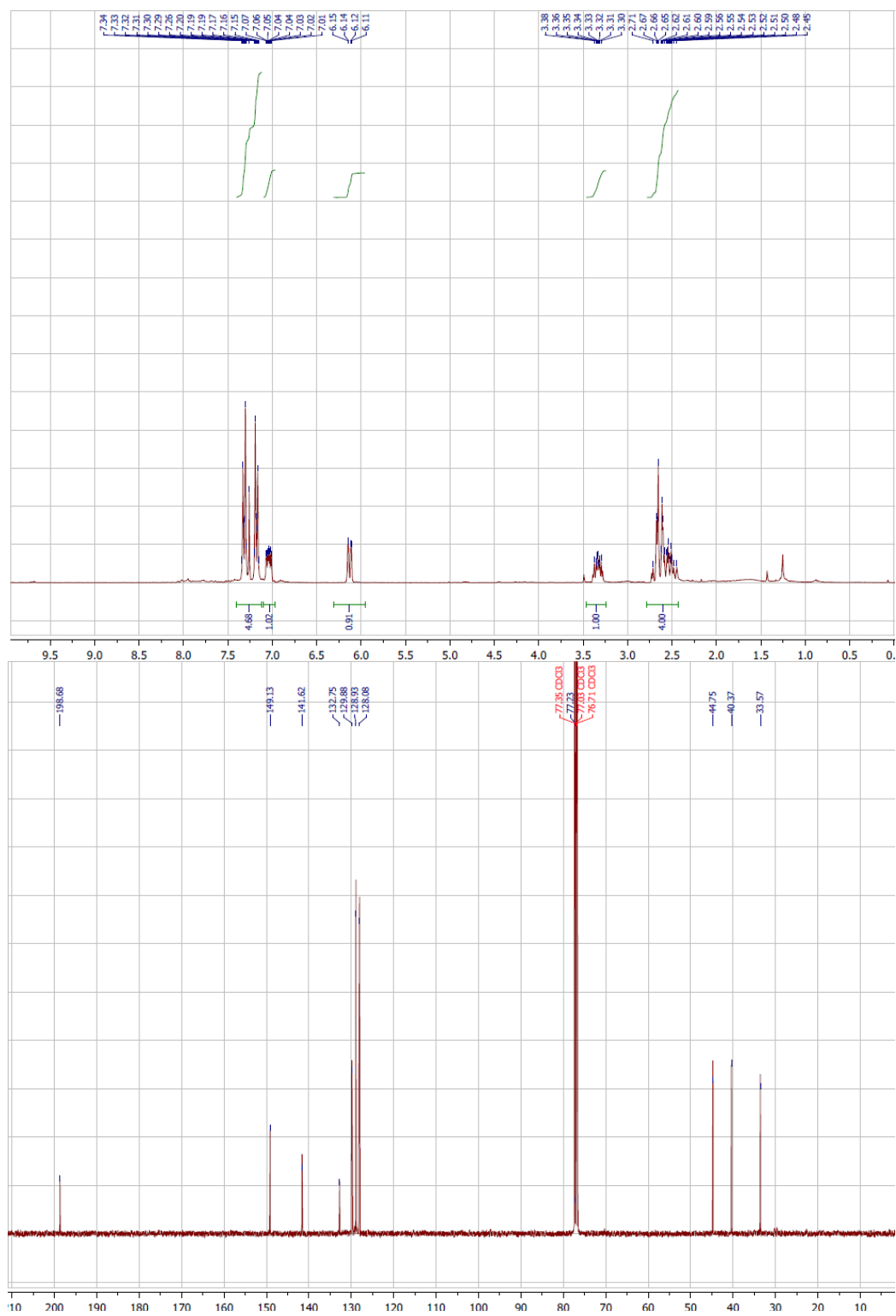
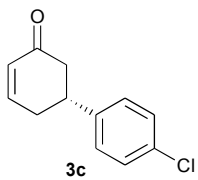


#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	47.267	103638	4765	51.893	53.469	N/A	106794	1,636	1,125	
2	Unknown	1	48.242	96077	4147	48,107	46,531	N/A	97982	N/A	1,215	

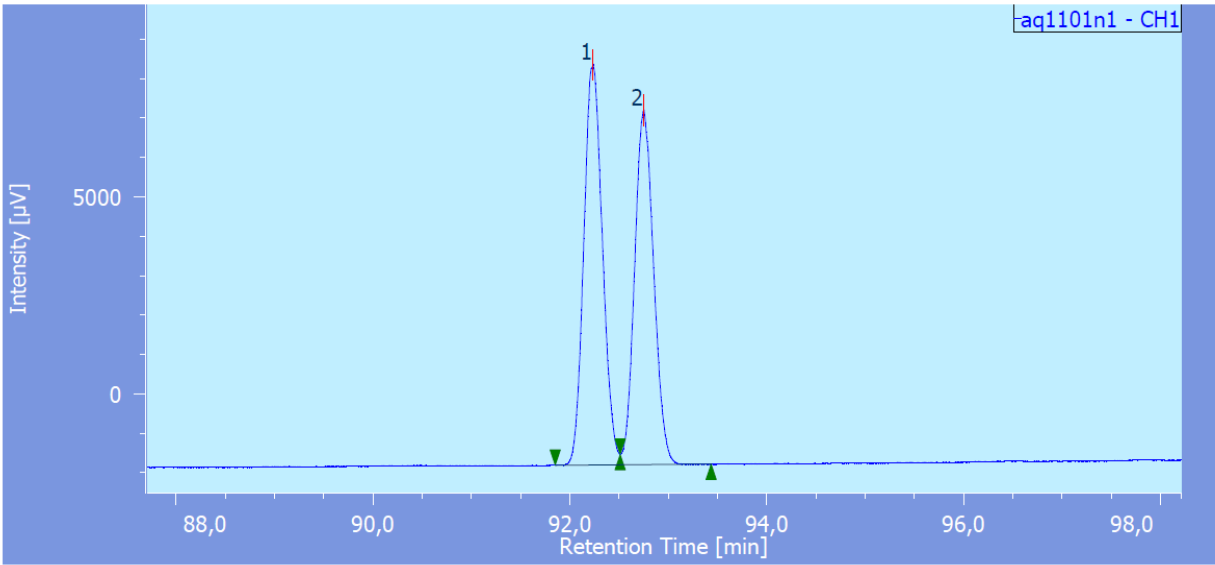
Chiral :



#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	50,900	3921	178	1,216	1,501	N/A	122918	1,202	N/A	
2	Unknown	1	51,683	318440	11695	98,784	98,499	N/A	81121	N/A	1,806	

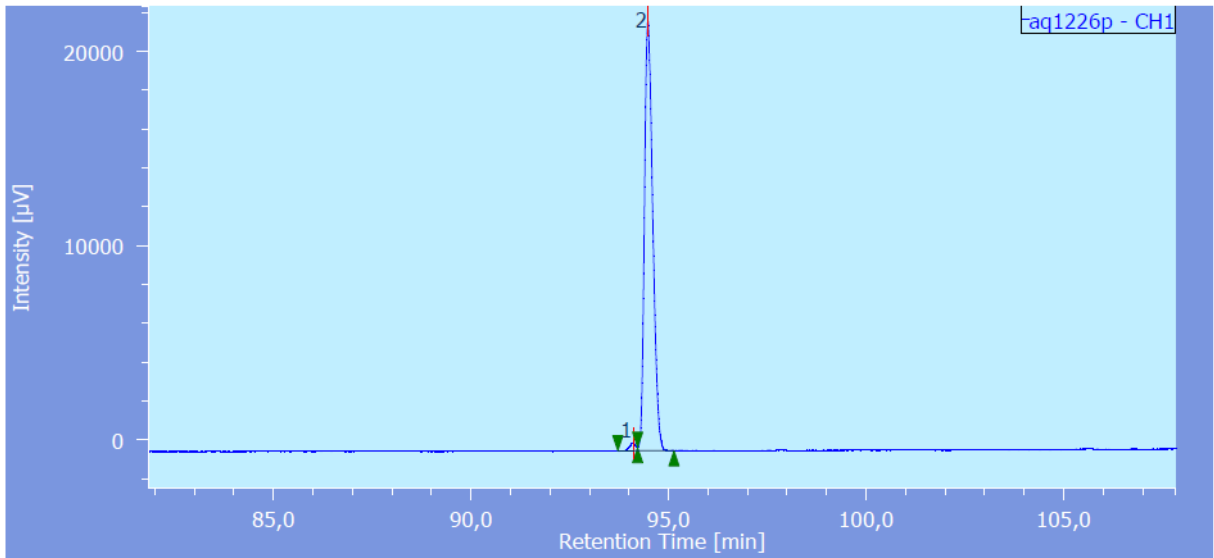


Racemate :

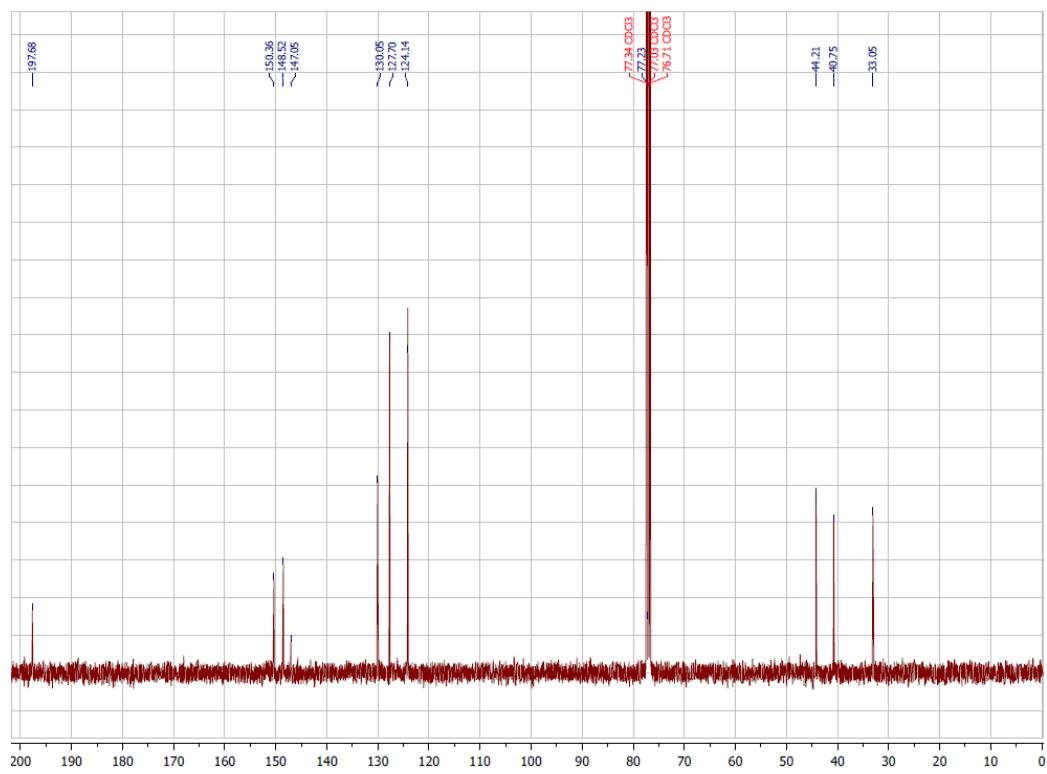
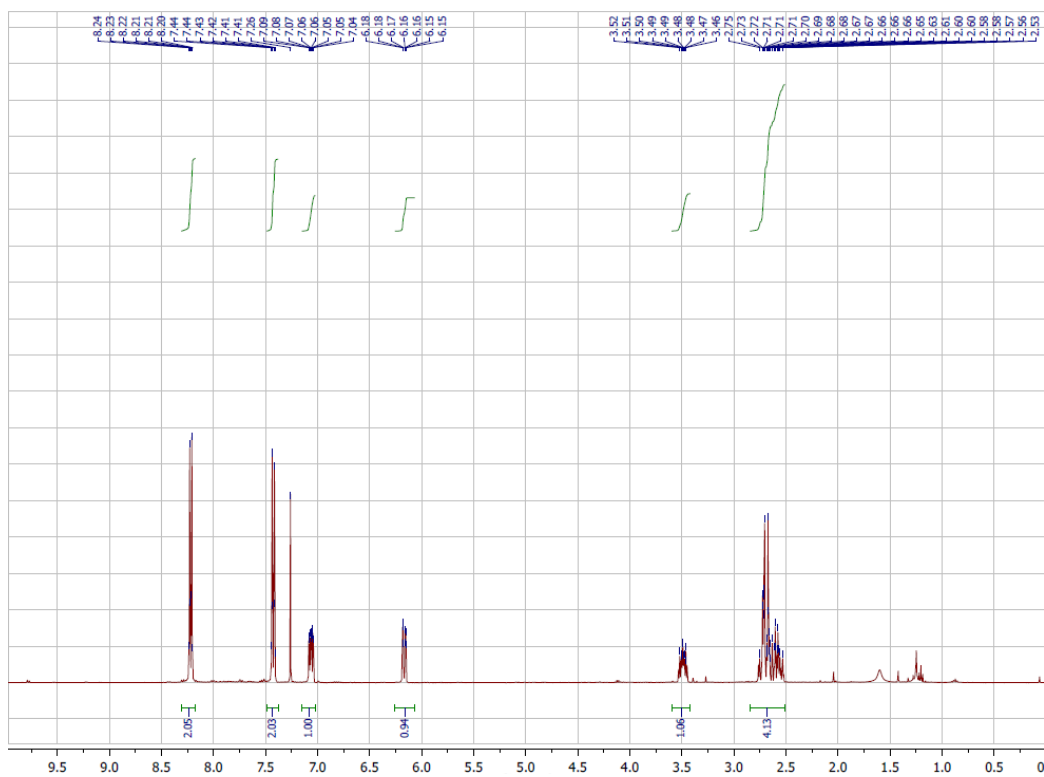
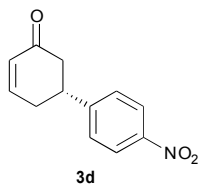


#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	92.233	133836	10154	52.522	53.025	N/A	1104238	1.460	1.094	
2	Unknown	1	92.750	120981	8995	47.478	46.975	N/A	1070520	N/A	1.085	

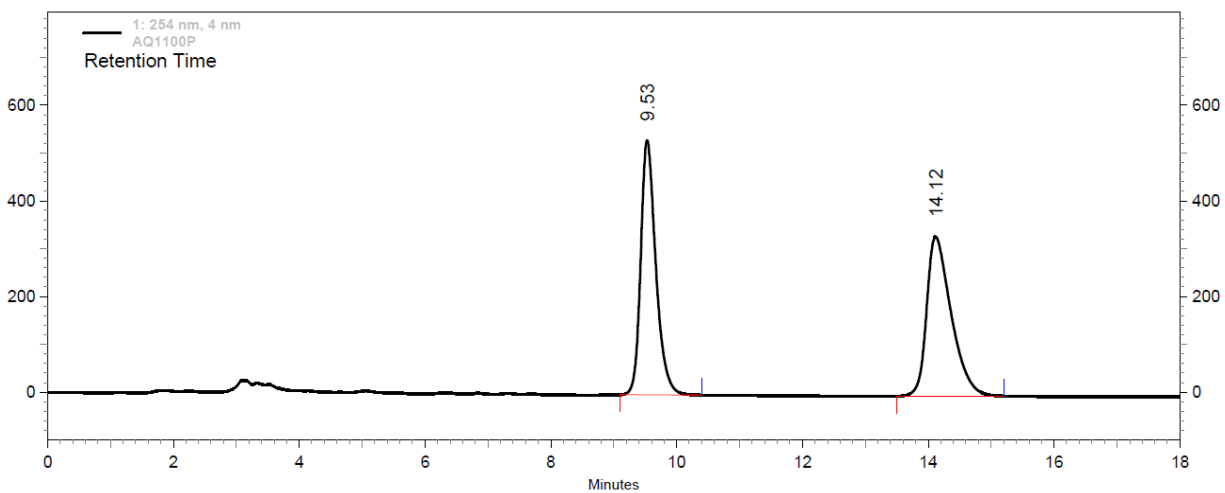
Chiral :



#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	94.100	4609	406	1.408	1.804	N/A	1339917	1.057	N/A	
2	Unknown	1	94.475	322851	22118	98.592	98.196	N/A	958401	N/A	1.295	



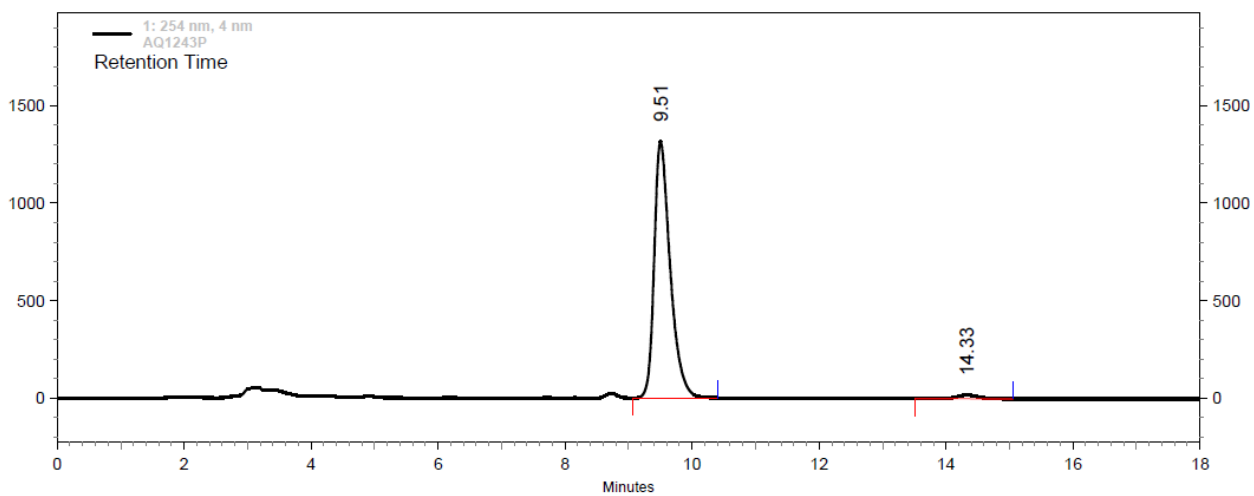
Racemate :



Retention Time	Area	Area %	Capacity factor	Relative RT	Resolution (USP)
9.53	35482158	49.62	2.18	1.00	0.00
14.12	36031476	50.38	3.71	1.70	8.00

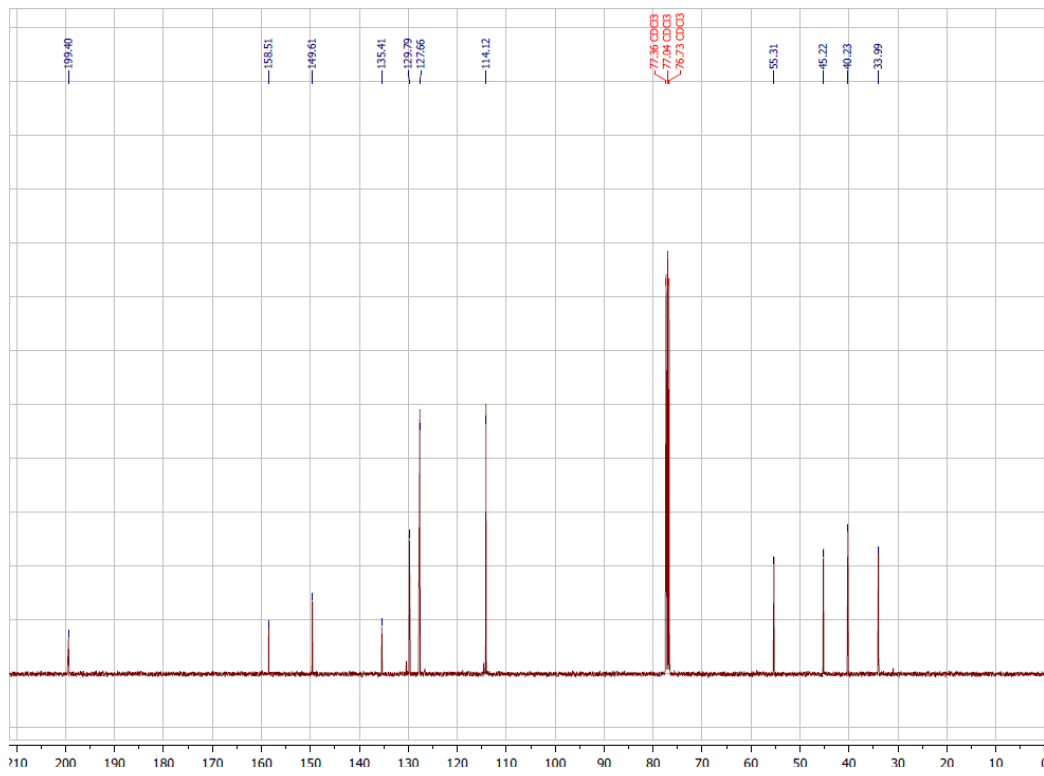
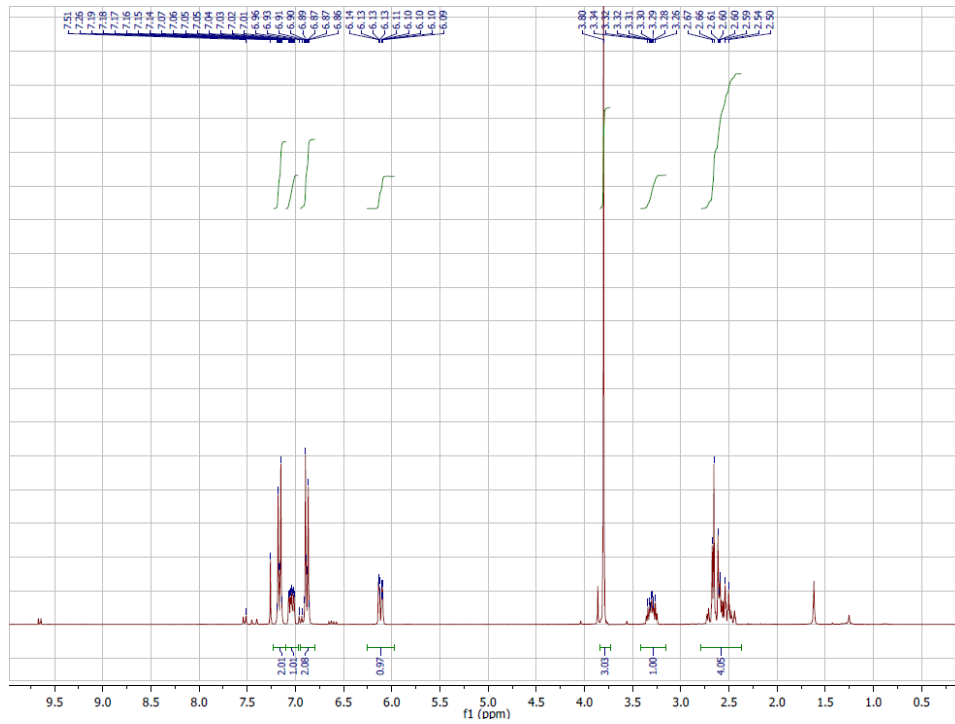
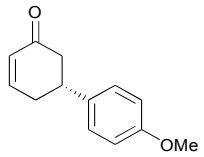
Totals	71513634	100.00			
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Chiral :

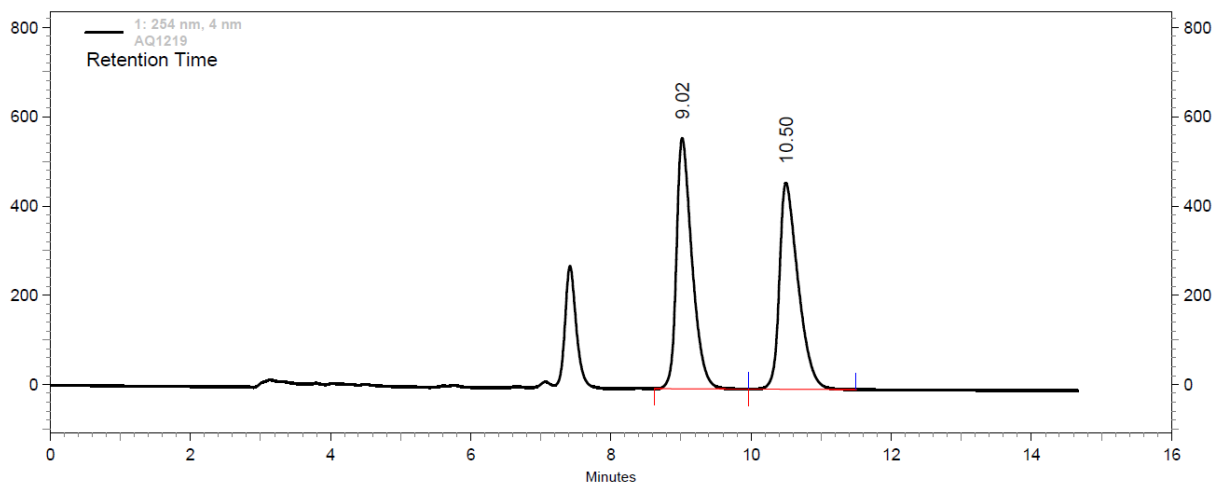


Retention Time	Area	Area %	Capacity factor	Relative RT	Resolution (USP)
9.51	92093476	98.08	2.17	1.00	0.00
14.33	1800738	1.92	3.78	1.74	9.02

Totals	93894214	100.00			
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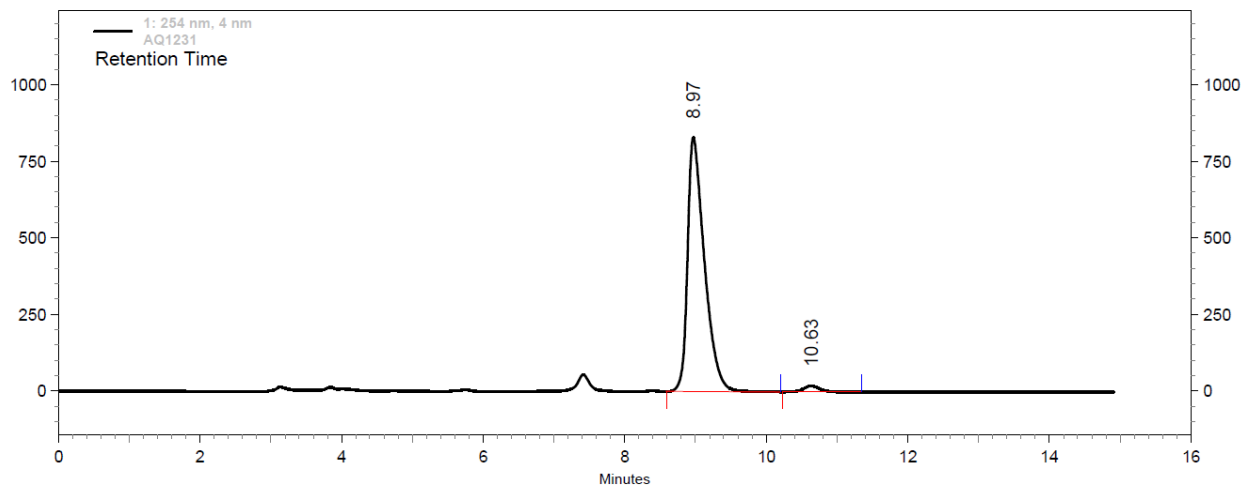


Racemate :

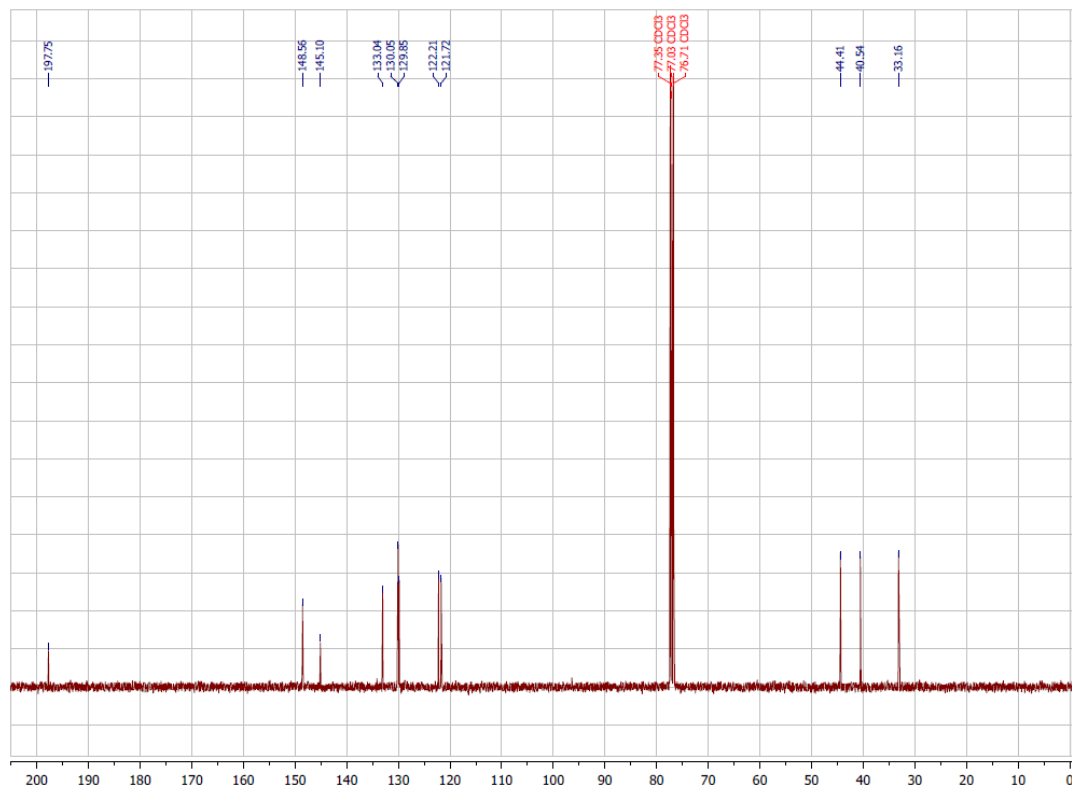
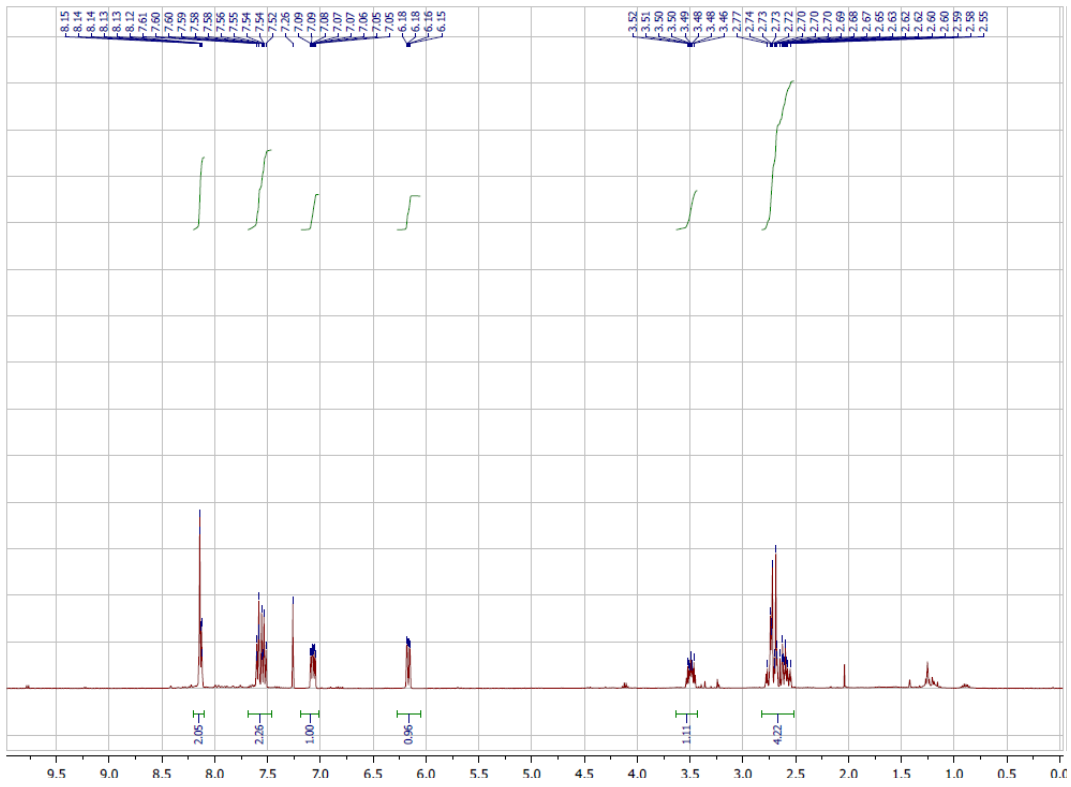
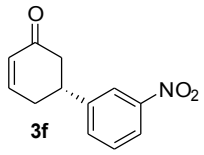


Retention Time	Area	Area %	Capacity factor	Relative RT	Resolution (USP)
9.02	34798763	50.38	2.01	0.00	0.00
10.50	34279396	49.62	2.50	0.00	3.30
Totals	69078159	100.00			

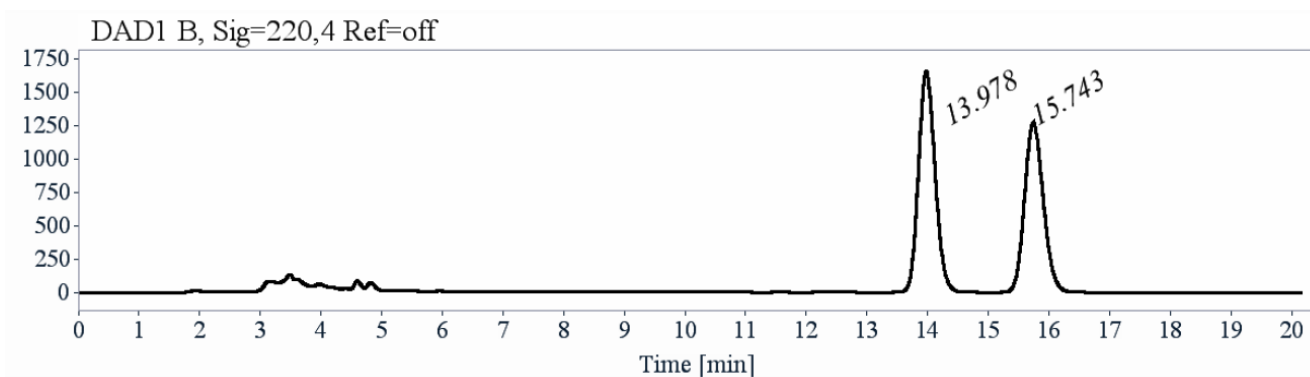
Chiral :



Retention Time	Area	Area %	Capacity factor	Relative RT	Resolution (USP)
8.97	54943571	97.83	1.99	0.00	0.00
10.63	1219578	2.17	2.54	0.00	3.96
Totals	56163149	100.00			



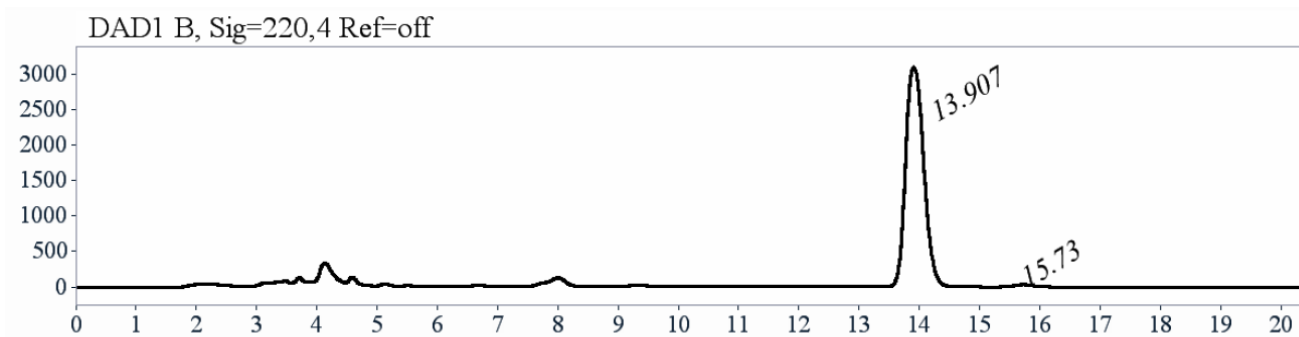
Racemate:



Signal: DAD1 B, Sig=220,4 Ref=off

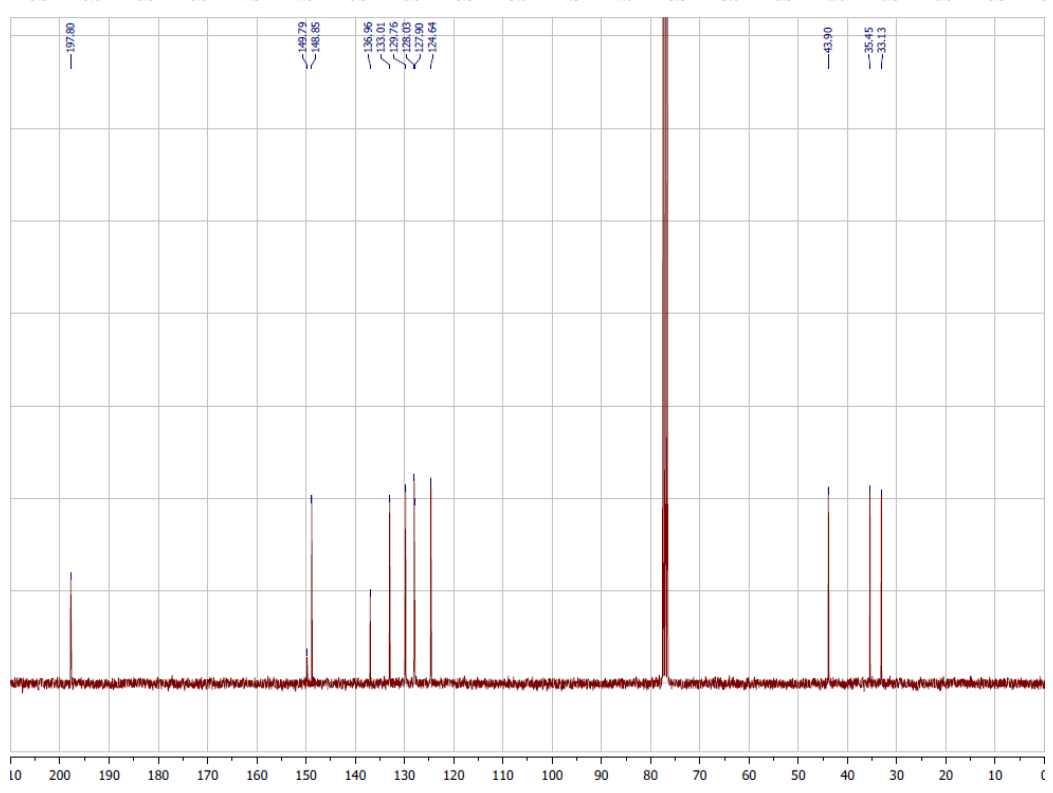
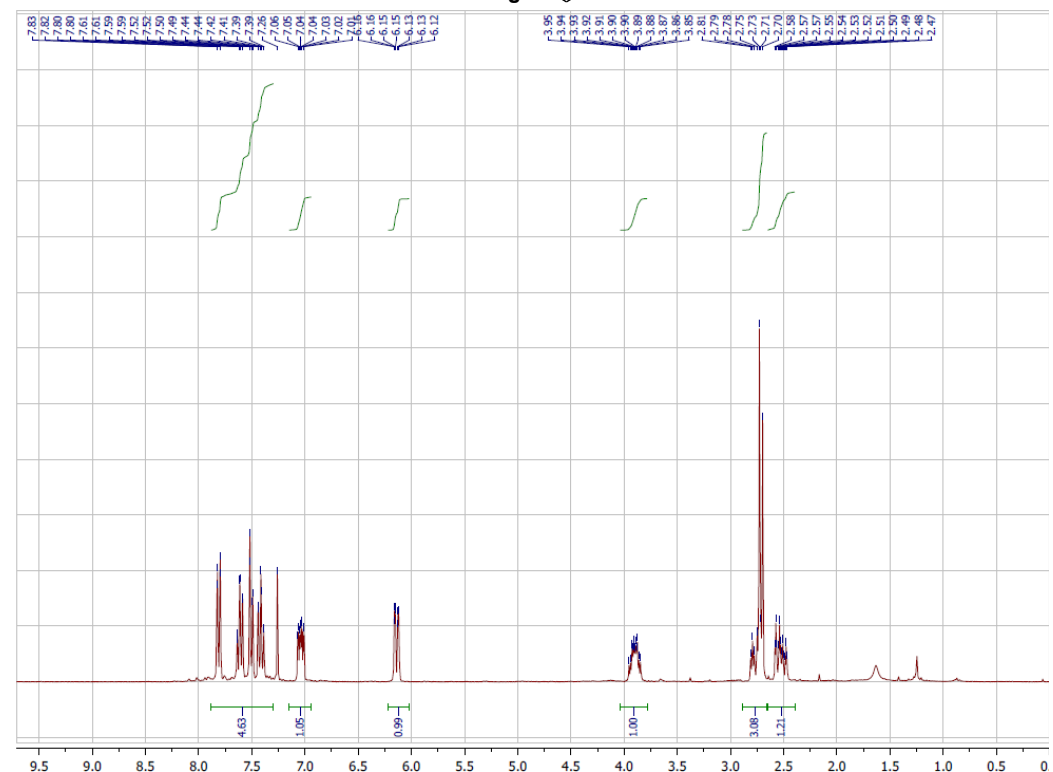
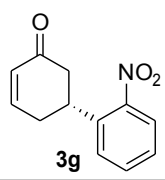
RT [min]	Area	Area%	Capacity Factor	Enantioselectivity	Resolution (USP)
13.98	31531	53.40	3.74		
15.74	27513	46.60	4.34	1.16	3.30
Sum	59043	100.00			

Chiral:

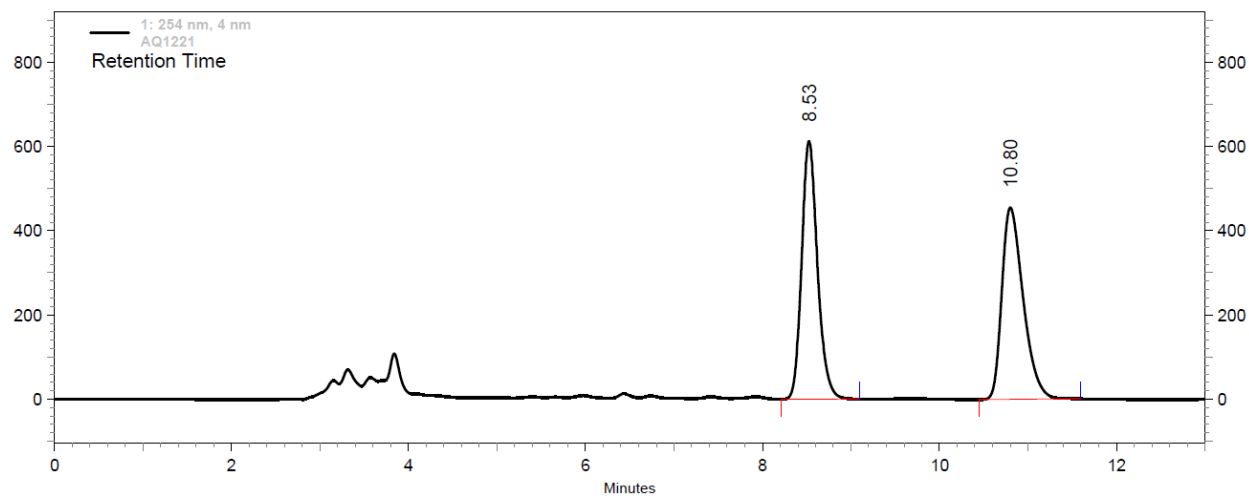


Signal: DAD1 B, Sig=220,4 Ref=off

RT [min]	Area	Area%	Capacity Factor	Enantioselectivity	Resolution (USP)
13.91	64773	98.94	3.71		
15.73	695	1.06	4.33	1.17	3.37
Sum	65468	100.00			

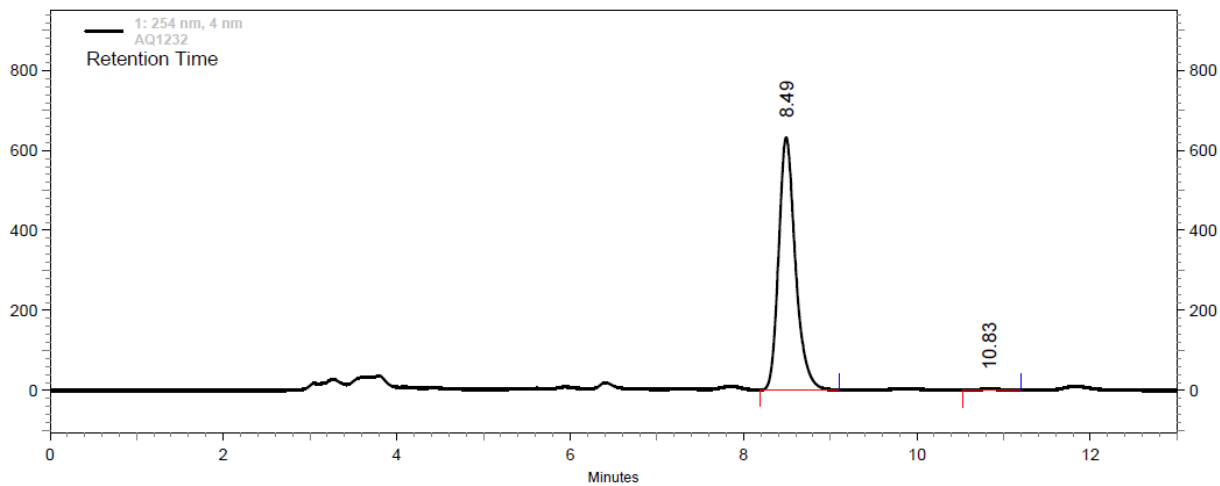


Racemate :

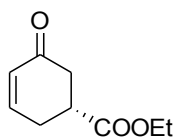


Retention Time	Area	Area %	Capacity factor	Relative RT	Resolution (USP)
8.53	30584854	50.14	1.84	0.00	0.00
10.80	30414807	49.86	2.60	1.00	5.90
Totals	60999661	100.00			

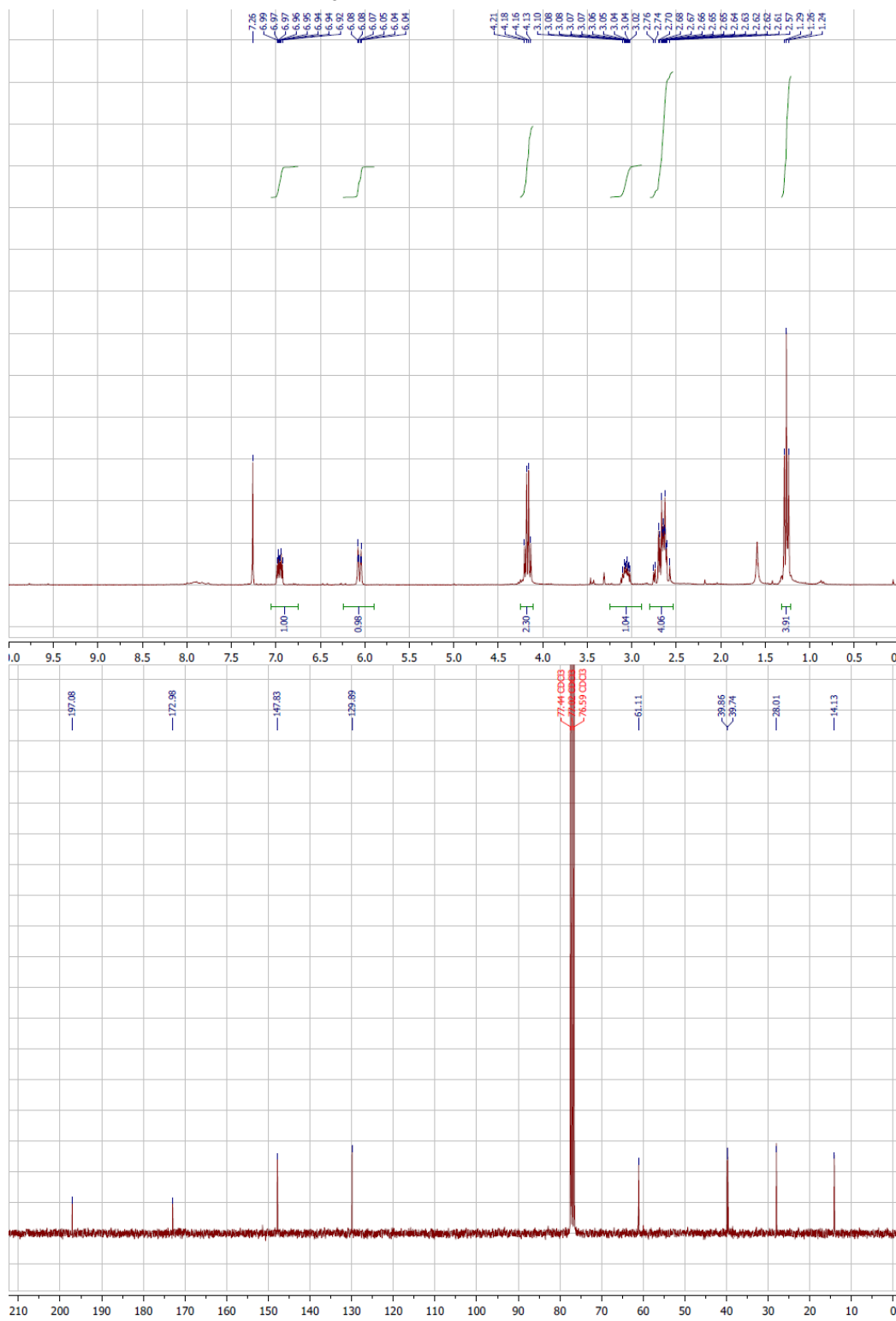
Chiral :



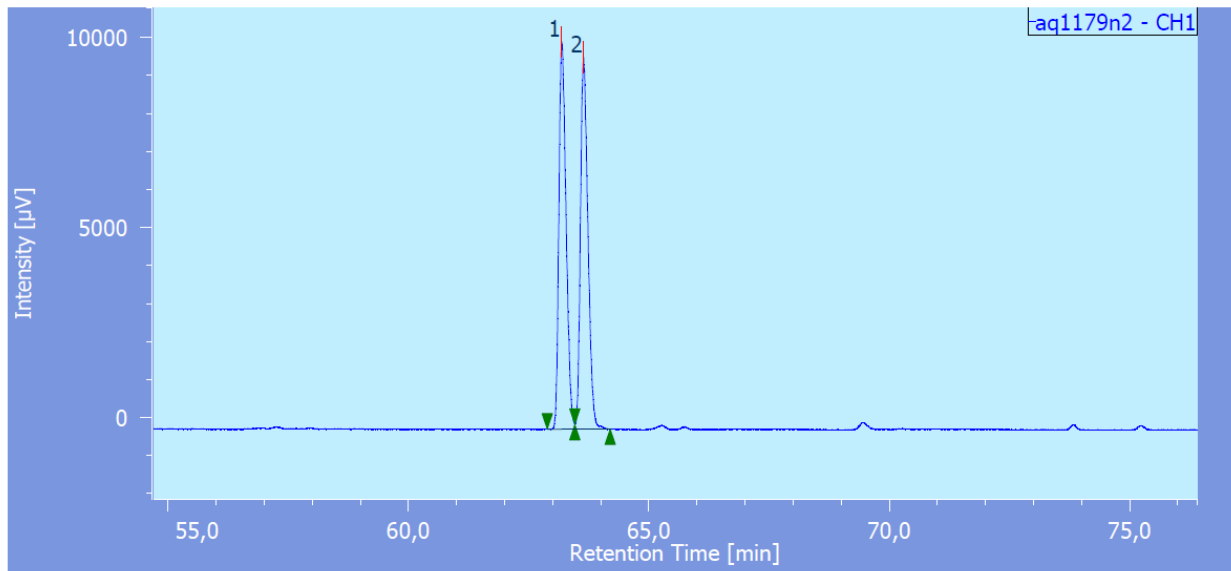
Retention Time	Area	Area %	Capacity factor	Relative RT	Resolution (USP)
8.49	34144867	99.39	1.83	0.00	0.00
10.83	208337	0.61	2.61	1.00	6.18
Totals	34353204	100.00			



3h

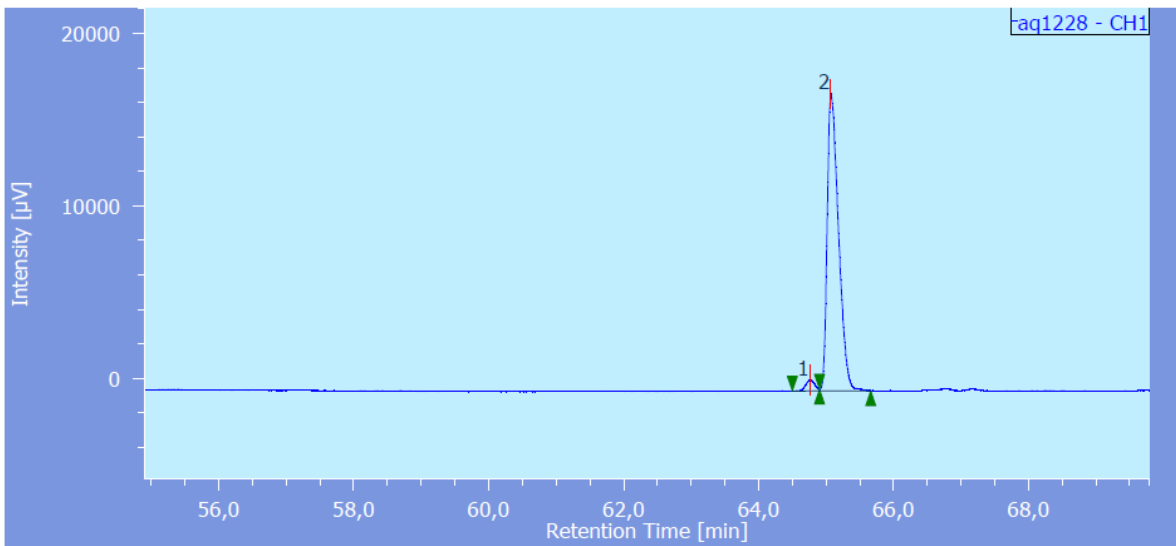


Racemate :



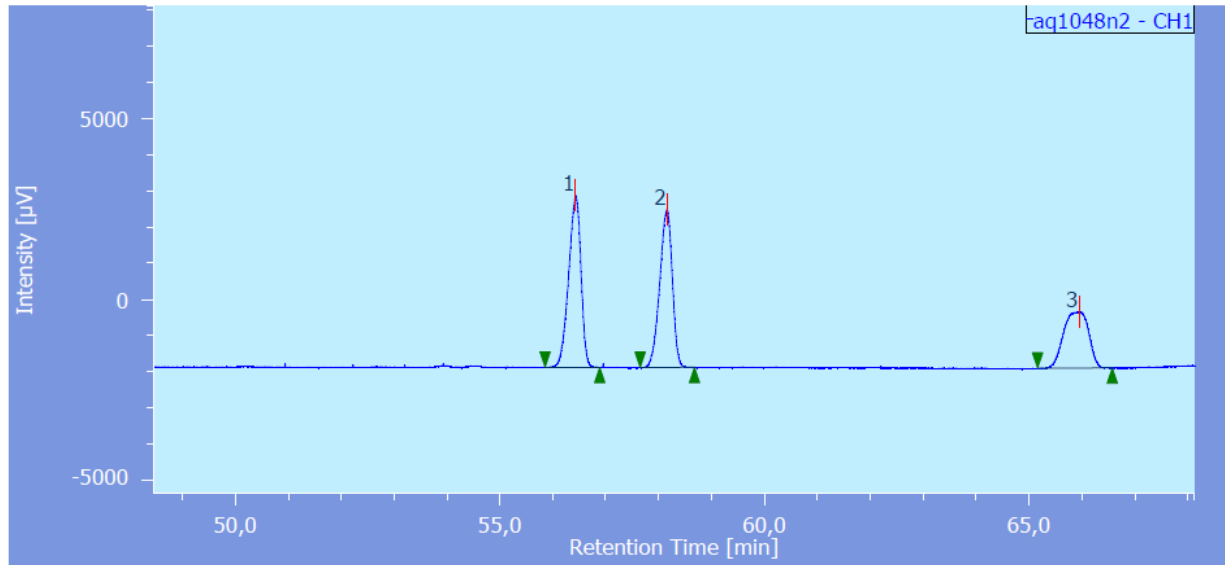
#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	63.183	106143	10184	50.131	51.030	N/A	831281	1.636	1.355	
2	Unknown	1	63.642	105589	9773	49.869	48.970	N/A	800399	N/A	1.286	

Chiral :



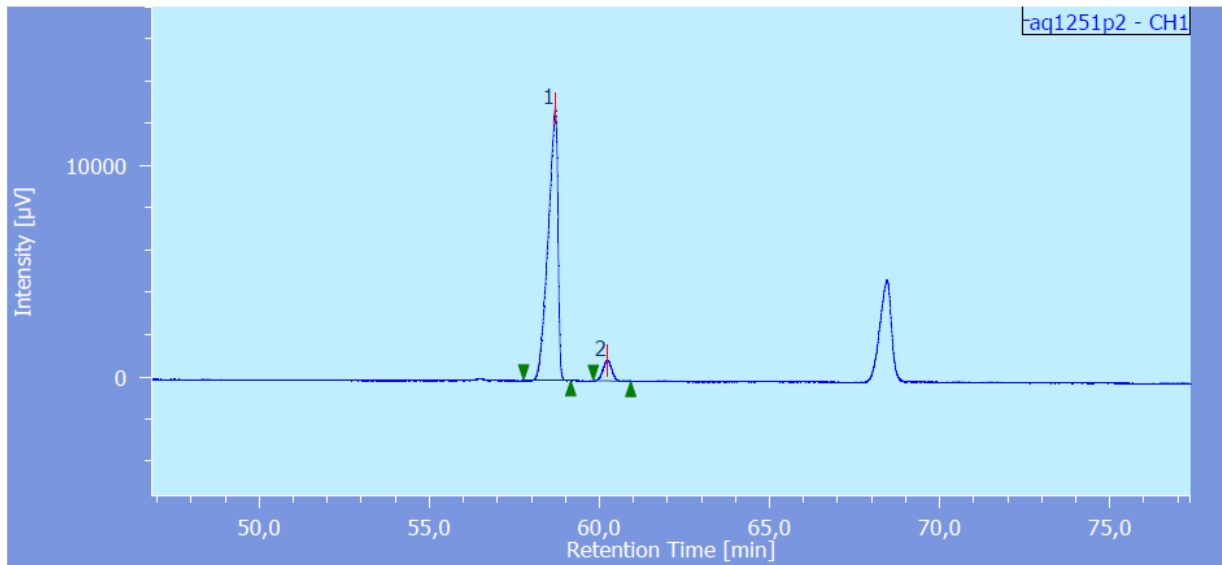
#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	64.758	5954	637	2.882	3.569	N/A	1058172	1.108	N/A	
2	Unknown	1	65.067	200640	17209	97.118	96.431	N/A	721473	N/A	1.675	

Racemate :



#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	56,425	76358	4754	38,293	44,567	N/A	278771	4,013	0,874	
2	Unknown	1	58,158	71729	4352	35,972	40,795	N/A	281352	11,527	0,868	
3	Unknown	1	65,942	51316	1561	25,735	14,638	N/A	83020	N/A	0,857	

Chiral :



#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	58,708	256412	12863	93,667	93,037	N/A	195401	3,039	0,662	
2	Unknown	1	60,242	17335	963	6,333	6,963	N/A	251329	N/A	0,963	

