Enantioselective Ir-catalyzed bi-directional reductive coupling

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General information

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 (δ = 7.26) and the deuterated solvent signal for ^{13}C NMR (δ = 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 THF was obtained were obtained from a Solvent Purification System M Braun SPS-800.

Thin-Layer Chromatography (TLC) were developed on silica Merck 60F254 and revealed under UV lamp (λ = 254 nm) and with universal stain: p-Anisaldehyde (prepared with 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 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 $CHCl_3$ with a Anton Paar MCP 200 polarimeter with a 0.2 cm length.

Racemic compounds were prepared bu using the racemic catalyst **Ir-cat1**.

Absolute and relative configuration were determined by comparison with optical rotation literature values on **3e**, **4a**, **4b** and **4d** assuming the same transition states for the other substrates.

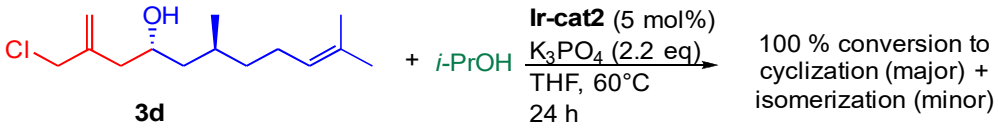
Volatile aldehydes were distilled prior to use. Otherwise, all commercially available reagents were used as received.

Additional experiments

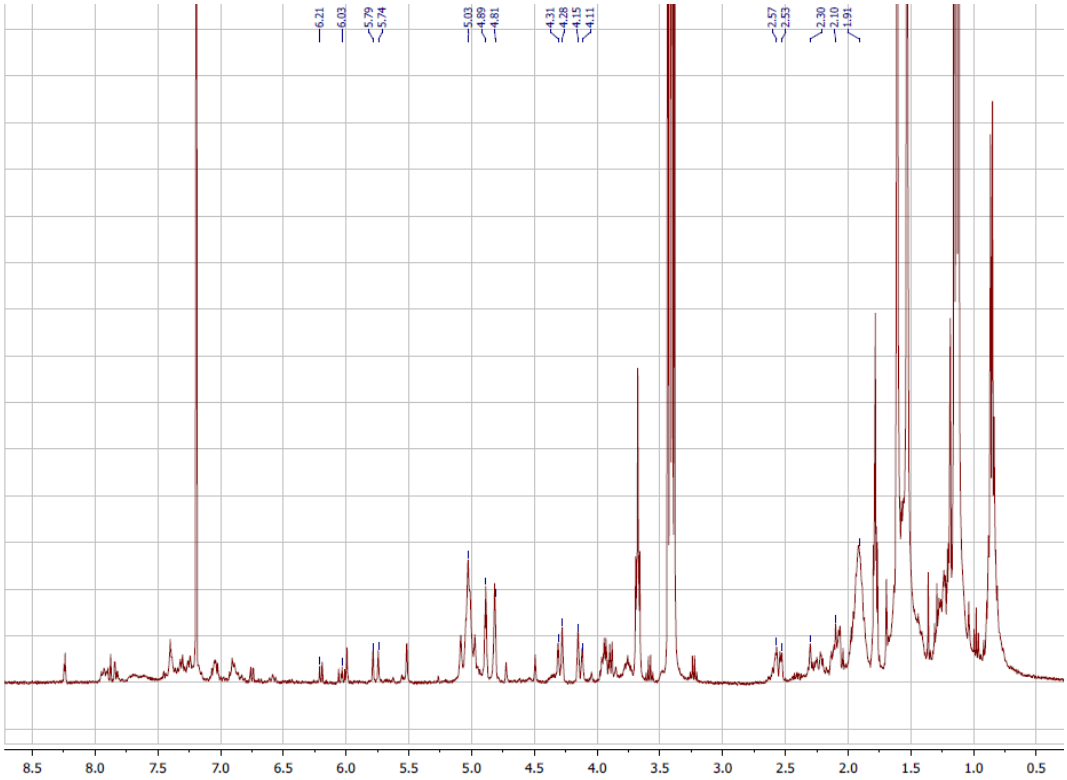
Reactivity of 3d in the absence of aldehyde:

The reaction of **3d** in the presence of isopropanol, **Ir-cat2** and K_3PO_4 and without aldehyde was performed. We choose to use **3d**, a compound with higher molecular weight to detect any volatile intermediates such as methylenetetrahydrofurans.

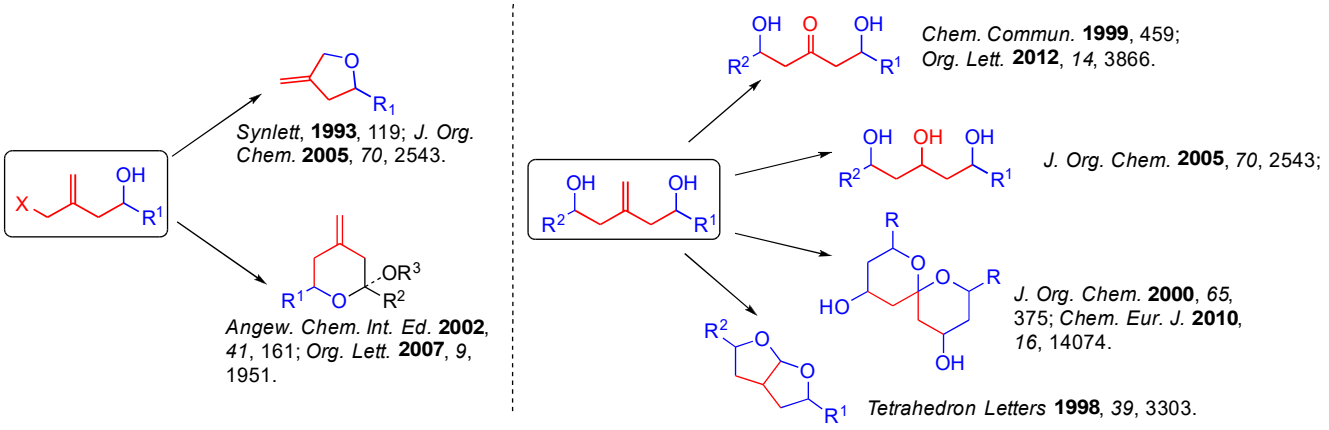
After stirring the reaction mixture for 24 hours at 60°C, **3d** was entirely converted. Notably the major pathway involved the expected cyclization to the methylenetetrahydrofurans. This result was indicative of the formation of the metal-allyl complex, which in the absence of any electrophilic pathway underwent rapid evolution.



Crude NMR after 24 h:

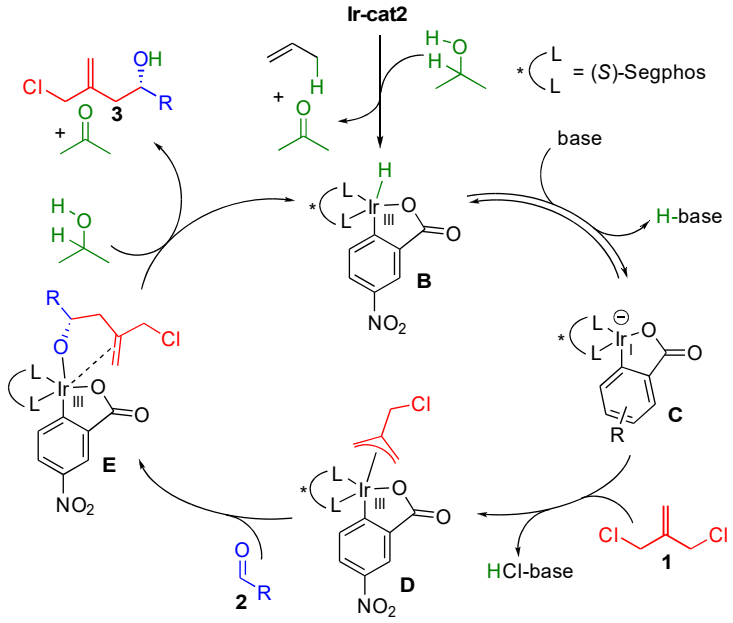


Example of literature derivatization of the obtained adducts:



Proposed mechanism

The mechanism of condensation between **1** and **2** is depicted in the following scheme, highlighting the role of the excess 2-propanol. From the initial **Ir-cat2** complex, 5 mol% of 2-propanol liberates propene and acetone forming the active catalyst **B**. Base-assisted equilibrium subsequently provides Ir(I) complex **C** able to insert the allylic chloride generating the nucleophilic Ir-π-allyl complex **D**. From **D**, stereoselective addition to the aldehyde **2** creates the new C-C bond in the σ,π-complex **E**. Then, addition of 2-propanol gives the product **3** together with acetone liberating the active complex **B**. As a result, the role of the excess 2-propanol or (**1**) used in this methodology is crucial to ensure the turn over with an appropriate kinetic limiting the decomposition of **E**.



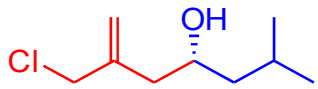
Experimental section

Procedure for the preparation of (*S*)-Ir-cat2:

(*S*)-Ir-cat2 was prepared according to a slightly modified literature procedure.[1] 134.2 mg of $[Ir(COD)Cl]_2$ (0.2 mmol), 260.8 mg of Cs_2CO_3 (0.8 mmol), 135.2 mg of 3-nitrobenzoic acid (0.8 mmol) and 247.3 mg of (S)-Segphos (0.4 mmol) are added to a schlenk tube under argon. The schlenk tube is purged with argon before addition of 4 mL of THF and the reaction mixture stirred under argon at room temperature for 1 h 20 min. 0.11 mL of allyl acetate (1 mmol) is then added, the vial rapidly sealed and stirred at 80°C for 1 h 15 min. The mixture is cooled to rt before filtration over a plug of celite (the celite is washed with dichloromethane) and the solvent evaporated. The resulting solid is filtered over 1 cm of silica (diethyl ether / dichloromethane 1/1) and the solvent evaporated. Trituration with *n*-hexanes, pipette removal of the liquid and evaporation of the solvent yields the corresponding **(*S*)-Ir-cat2** as a bright yellow powder. 366 mg, 90% yield.
The quality of the **Ir-cat2** catalyst was crucial to obtain the appropriate reactivity. Indeed, bottles of commercial **Ir-cat2** bought from Aldrich (reference RNI00091) were delivered with different aspects with colors ranging from yellow to deep brown. As a result, reactivity with this commercial catalyst considerably varied depending on the batch used. **Ir-cat3** was purified over silica gel according to known procedure.[1]

General procedure for the enantioselective mono functionalization of 1:

5.0 mg of **(*S*)-Ircat2** (0.005 mmol, 5 mol%), 43.5 mg of K_3PO_4 (0.22 mmol, 2.2 equiv) are placed in a tube under argon. 0.2 mL of THF are then added followed by 27 µL of isopropanol (0.3 mmol, 3.5 equiv); 58 µL of the bis-chloro allylic nucleophile (0.5 mmol, 5 equiv) and 1 equivalent of the aldehyde (0.1 mmol). (note, if the aldehyde is a solid, it is added simultaneously with the catalyst). The tube is then quickly sealed and the reaction mixture stirred at 60°C for the indicated time (16- 40 h). 2 ml of saturated NH_4Cl are then added and the aqueous layer is extracted by 4 times 2 ml of diethyl ether, the combined organic layers filtered over a small plug of Na_2SO_4 and silica gel and the solvent evaporated. Purification over silica gel (petroleum ether/ethyl acetate) directly yields the mono-alcohol **3**.



3a: Prepared according to the general procedure starting from 11.5 µL of isovaleraldehyde and 58 µL of **1** for 16 hours. The product was isolated as a pale oil after purification with ethyl acetate / petroleum ether mixture. 12.4 mg (0.07 mmol). 70% yield.
R_f = 0.28 (petroleum ether / ethyl acetate (9/1)). The product is obtained in 98% *ee*. $[\alpha]^{20}_D$ = -5.5° ($CHCl_3$, c = 0.7), 98% *ee*).
^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 0.93 (d, *J* = 4.5 Hz, C*H*$_3$), 0.95 (d, *J* = 4.6 Hz, C*H*$_3$), 1.28 (ddd, *J* = 13.8, 8.6, 4.4 Hz, 1H of C*H*$_2$), 1.44 (ddd, *J* = 14.0, 8.6, 5.7 Hz, 1H of C*H*$_2$), 1.52 (brs, O*H*), 1.77-1.82 (m, C*H*), 2.20 (ddd, AB, *J* = 14.6, 9.2, 1.0 Hz, 1H of C*H*$_2$), 2.43 (ddd, AB, *J* = 13.8, 5.6, 1.0 Hz, 1H of C*H*$_2$), 3.82-3.91 (m, C*H*), 4.07 (dd, AB, *J* = 11.8, 1.0 Hz, 1H of C*H*$_2$Cl), 4.13 (dd, AB, *J* = 11.6, 1.0 Hz, 1H of C*H*$_2$Cl), 5.08 (d, J = 1.0 Hz, 1H of C*H*$_2$ alkene), 5.27 (s, 1H of C*H*$_2$ alkene). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 22.1 (1 *CH*$_3$), 23.3 (1 *CH*$_3$), 24.7 (*CH*), 42.0 (*CH*$_2$), 46.5 (*CH*$_2$), 48.2 (*CH*$_2$Cl), 67.6 (*CH*(OH)), 117.3 (*CH*$_2$ alkene), 142.4 (*C* alkene).
HRMS ESI [M+Na]+ calcd for $C_9H_{17}ClONa$: 199.0860. Observed: 199.0861.
GC enantiomeric excess determination: cyclosil-b; 100°C for 0 min than 1°C/min until 220°C. rt (min) = 26.6 min; rt (maj) = 27.3 min.

[1] X. Gao, I. A. Townsend, M. J. Krische. *J. Org. Chem.* **2011**, *76*, 2350.

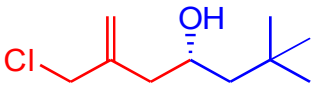
3b: Prepared on preparative scale using the following procedure: 40.7 mg of **(*S*)-Ircat2** (0.04 mmol, 2 mol%), 937.4 mg of K_3PO_4 (4.4 mmol, 2.2 equiv) are placed in a tube and the tube purged with argon. 4 mL of THF are then added, the tube placed under argon flow for 2 minutes, then kept under argon before addition of 520 µL of isopropanol (7.0 mmol, 3.5 equiv); 1.15 mL of the bis-chloro allylic nucleophile (10 mmol, 5 equiv) and 145.2 mg isobutyraldehyde. The tube is then quickly sealed and the reaction mixture stirred at 60°C for 40 h. 20 ml of saturated NH_4Cl are then added and the aqueous layer is extracted by 3 times 15 ml of diethyl ether, the combined organic layers dried over Na_2SO_4, filtered and the solvent evaporated. Purification over silica gel (petroleum ether/ethyl acetate 9/1 to 7/1) directly yields the mono-alcohol **3b** as a pale oil. 238.1 mg (1.47 mmol). 73% yield.

R_f = 0.36 (petroleum ether / ethyl acetate (9/1)). The product is obtained in 98% *ee*. $[\alpha]^{20}_D$ = -29.9° ($CHCl_3$, c = 1.0), 98% *ee*).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 0.87 (d, *J* = 6.8 Hz, 2 C*H*$_3$), 1.65-1.75 (CH), 2.17 (dd, AB, *J* = 14.5, 10.1 Hz, 1H of C*H*$_2$), 2.48 (d, AB, *J* = 13.0 Hz, 1H of C*H*$_2$), 3.50-3.60 (m, C*H*), 4.09 (d, AB, *J* = 11.5 Hz, 1H of C*H*$_2$Cl), 4.13 (d, AB, *J* = 11.5 Hz, 1H of C*H*$_2$Cl), 5.09 (s, 1H of C*H*$_2$ alkene), 5.26 (s, 1H of C*H*$_2$ alkene). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 17.4 (1 *CH*$_3$), 18.6 (1 *CH*$_3$), 33.6 (*CH*), 38.2 (*CH*$_2$), 48.1 (*CH*$_2$Cl), 74.1 (*CH*(OH)), 117.2 (*CH*$_2$ alkene), 142.8 (*C* alkene).

HRMS ESI [M+Na]+ calcd for $C_8H_{15}ClONa$: 185.0704. Observed: 185.0705.

GC enantiomeric excess determination: cyclosil-b; 90°C for 0 min than 1°C/min until 220°C. rt (min) = 26.0 min; rt (maj) = 26.3 min.



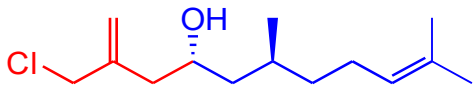
3c: Prepared according to the general procedure starting from 10.1 mg of aldehyde and 58 µL of **1** for 40 hours. The product was isolated as a pale oil after purification with ethyl acetate / petroleum ether mixture. 15.2 mg (0.08 mmol). 80% yield.

R_f = 0.58 (petroleum ether / ethyl acetate (9/1)). The product is obtained in 96% *ee*. $[\alpha]^{20}_D$ = +4.8° ($CHCl_3$, c = 0.8), 98% *ee*).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 0.97 (s, 3 C*H*$_3$), 1.39-1.49 (m, C*H*$_2$ and O*H*), 2.25 (dd, AB, *J* = 14.2, 9.2 Hz, 1H of C*H*$_2$), 2.38 (ddd, AB, *J* = 14.4, 4.0, 1.0 Hz, 1H of C*H*$_2$), 3.92-3.96 (m, C*H*), 4.09 (dd, AB, *J* = 12.2, 1.0 Hz, 1H of C*H*$_2$Cl), 4.11 (dd, AB, *J* = 12.2, 1.0 Hz, 1H of C*H*$_2$Cl), 5.07 (s, 1H of C*H*$_2$ alkene), 5.27 (s, 1H of C*H*$_2$ alkene). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 30.1 (3 *CH*$_3$), 30.2 (*C*quat), 43.5 (*CH*$_2$), 48.1 (*CH*$_2$), 50.9 (*CH*$_2$Cl), 67.2 (*CH*(OH)), 117.4 (*CH*$_2$ alkene), 142.4 (*C* alkene).

HRMS ESI [M+Na]+ calcd for $C_{10}H_{19}ClONa$: 213.1017. Observed: 213.1017.

GC enantiomeric excess determination: cyclosil-b; 100°C for 0 min than 1°C/min until 220°C. rt (min) = 28.0 min; rt (maj) = 29.5 min.



3d: Prepared according to the general procedure starting from 15.7 mg of aldehyde and 58 µL of **1** for 38 hours. The product was isolated as a pale oil after purification with ethyl acetate / petroleum ether mixture. 20.9 mg (0.085 mmol). 85% yield.

R_f = 0.51 (petroleum ether / ethyl acetate (9/1)). The product is obtained in >95:5 dr. $[\alpha]^{20}_D$ = +6.4° ($CHCl_3$, c = 0.9), 99% *ee*).

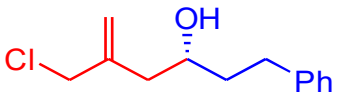
^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 0.93 (d, *J* = 6.6 Hz, C*H*$_3$), 1.17-1.53 (m, O*H* and 2 C*H*$_2$), 1.60 (s, C*H*$_3$), 1.71 (s, C*H*$_3$), 1.98-2.02 (m, C*H*$_2$), 2.23 (dd, AB, *J* = 14.4, 9.0 Hz, 1H of C*H*$_2$), 2.41 (ddd, AB, *J* = 14.2, 4.2 Hz, 1H of C*H*$_2$), 3.84-3.92 (m, C*H*), 4.09 (dd, AB, *J* = 12.0, 1.0 Hz, 1H of C*H*$_2$Cl), 4.11 (d, AB, *J* = 12.0 Hz, 1H of C*H*$_2$Cl), 5.07-5.12 (m, 1H of C*H*$_2$ alkene and C*H* alkene), 5.26 (s, 1H of C*H*$_2$ alkene). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 17.6 (*CH*$_3$), 19.2 (*CH*$_3$), 25.4 (*CH*$_2$), 25.6 (*CH*$_3$), 28.9 (*CH*), 37.7 (*CH*$_2$), 42.3 (*CH*$_2$), 44.7 (*CH*$_2$), 48.2 (*CH*$_2$Cl), 67.3 (*CH*(OH)), 117.4 (*CH*$_2$ alkene), 124.6 (*CH* alkene), 131.2 (*C* alkene), 142.4 (*C* alkene).

HRMS ESI [M+Na]+ calcd for $C_{14}H_{25}ClONa$: 267.1486. Observed: 267.1492.

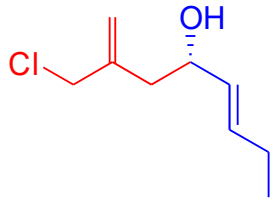
This compound was also prepared starting from the alcohol oxidation level:

4.7 mg of **(*S*)-Ircat2** (0.005 mmol, 5 mol%), 44.6 mg of K_3PO_4 (0.22 mmol, 2.2 equiv) are placed in a tube

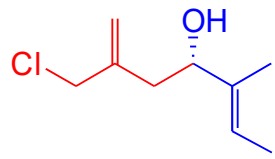
under argon. Argon is passed through the tube for 3 mintues before addition of 0.2 mL of THF, followed by 58 µL of the bis-chloro allylic nucleophile (0.5 mmol, 5 equiv) and 15.8 mg of (-)-citronellal (0.1 mmol, 1 equiv). The tube is then quickly sealed and the reaction mixture stirred at 60°C for the indicated time (22 h). 2 ml of saturated NH_4Cl are then added and the aqueous layer is extracted by 4 times 2 ml of diethyl ether, the combined organic layers filtered over a small plug of Na_2SO_4 and silica gel and the solvent evaporated. Purification over silica gel (petroleum ether/ethyl acetate) directly yields 11.9 mg of the mono-alcohol **3d** in 49% yield (0.049 mmol).



3e: Prepared according to the general procedure starting from 13.4 mg of aldehyde and 58 µL of **1** and additional 3.5 mg (0.02 mmol) of *m*-NO_2-benzoic acid for 24 hours. The product was isolated as a pale oil after purification with ethyl acetate / petroleum ether mixture. 8.4 mg (0.037 mmol). 37% yield.
R_f = 0.28 (petroleum ether / ethyl acetate (9/1)). The product is obtained in 97% *ee*. $[\alpha]^{20}_D$ = +8.4° ($CHCl_3$, c = 0.5), 97% *ee*).
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.67 (brs, OH), 1.85-1.89 (m, CH_2), 2.20 (dd, AB, *J* = 14.5, 9.0 Hz, 1H of CH_2), 2.40 (ddd, AB, *J* = 14.5, 3.7 Hz, 1H of CH_2), 2.60-2.80 (m, CH_2), 3.85-3.88 (m, C*H*), 3.98 (d, AB, *J* = 11.8 Hz, 1H of CH_2Cl), 4.02 (d, AB, *J* = 11.8 Hz, 1H of CH_2Cl), 5.12 (s, C*H* alkene), 5.31 (s, 1H of CH_2 alkene). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 32.0 (*C*H_2), 38.9 (*C*H_2), 41.6 (*C*H_2), 48.1 (*C*H_2Cl), 68.9 (*C*H(OH)), 117.6 (*C*H_2 alkene), 125.9 (*C*H arom), 128.4 (*C*H arom), 128.5 (*C*H arom), 141.8 (*C* arom), 142.4 (*C*H alkene).
Datas are in agreement with the literature.[2]

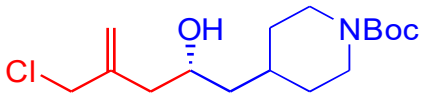


3f: Prepared according to the general procedure starting from 8.5 mg of aldehyde and 58 µL of **1** for 24 hours. The product was isolated as a pale oil after purification with ethyl acetate / petroleum ether mixture. 7.6 mg (0.043 mmol). 43% yield.
R_f = 0.30 (petroleum ether / ethyl acetate (9/1)). The product is obtained in 92% *ee*. $[\alpha]^{20}_D$ = -9.4° ($CHCl_3$, c = 0.5), 92% *ee*).
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.00 (t, *J* = 7.5 Hz, CH_3), 1.59 (d, J = 3.5 Hz, O*H*), 2.02-2.10 (m, CH_2), 2.36 (ddd, AB, *J* = 14.6, 8.4; 1.2 Hz, 1H of CH_2), 2.45 (ddd, AB, *J* = 14.6, 4.8; 1.0 Hz, 1H of CH_2), 4.07 (d, AB, *J* = 12.0 Hz, 1H of CH_2Cl), 4.13 (d, AB, *J* = 12.0 Hz, 1H of CH_2Cl), 5.08 (s, 1H of CH_2 alkene), 5.26 (s, 1H of CH_2 alkene), 5.45-5.52 (m, C*H* alkene), 5.71-5.79 (m, C*H* alkene). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 13.3 (*C*H_3), 25.1 (*C*H_2), 41.3 (*C*H_2), 48.3 (*C*H_2Cl), 70.9 (*C*H(OH)), 117.5 (*C*H_2 alkene), 130.9 (*C*H alkene), 134.1 (*C*H alkene), 141.9 (*C* alkene).
HRMS ESI [M+Na]+ calcd for $C_9H_{15}ClONa$:197.0704. Observed: 197.0704.
GC enantiomeric excess determination: cyclosil-b; 100°C for 0 min than 1°C/min until 220°C. rt (min) = 31.8 min; rt (maj) = 32.5 min.



3g: Prepared according to the general procedure starting from 12.7 mg of aldehyde (0.15 mmol) and 87 µL of **1** for 16 hours. The product was isolated as a pale oil after purification with ethyl acetate / petroleum ether mixture. 18.8 mg (0.107 mmol). 71% yield.
R_f = 0.48 (petroleum ether / ethyl acetate (9/1)). The product is obtained in 97% *ee*. $[\alpha]^{20}_D$ = -11.8° ($CHCl_3$, c = 1.0), 97% *ee*).
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.58-1.65 (m, 2 CH_3), 2.36-2.48 (m, CH_2), 4.13 (s, CH_2Cl), 4.18-4.21 (s, CH_2OH), 5.08 (s, 1H of CH_2 alkene), 5.24 (s, 1H of CH_2 alkene), 5.52 (q, *J* = 6.6 Hz, C*H* alkene). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 11.3 (*C*H_3), 13.0 (*C*H_3), 39.2 (*C*H_2), 48.1 (*C*H_2Cl), 75.6 (*C*H(OH)), 117.5 (*C*H_2 alkene), 120.9 (*C*H alkene), 137.3 (*C* alkene), 142.4 (*C* alkene).
HRMS ESI [M+Na]+ calcd for $C_9H_{15}ClONa$:197.0704. Observed: 197.0705.
GC enantiomeric excess determination: cyclosil-b; 100°C for 0 min than 1°C/min until 220°C. rt (min) = 31.7 min; rt (maj) = 32.2 min.

[2] G. E. Keck, T. Yu, M. D. McLaws, *J. Org. Chem.* **2005**, *70*, 2543.



3h: Prepared according to the general procedure starting from 22.9 mg of aldehyde and 58 µL of **1** for 16 hours. The product was isolated as a pale oil after purification with ethyl acetate / petroleum ether mixture. 19.3 mg (0.061 mmol). 61% yield.

R_f = 0.22 (petroleum ether / ethyl acetate (9/1)). The product is obtained in >90% *ee*. $[\alpha]^{20}_D$ = +4.2° ($CHCl_3$, c = 1.2), >90% *ee*).

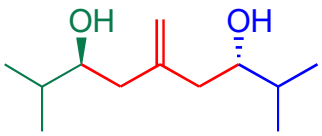
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.10-1.37 (m, 1 C*H* and CH_2), 1.45 (s, 3 CH_3), 1.59-1.75 (m, 2 CH_2), 2.22 (dd, AB, *J* = 14.0, 9.0 Hz, 1H of CH_2), 2.41 (dd, AB, *J* = 14.0, 4.6 Hz, 1H of CH_2), 2.67-2.75 (m, CH_2), 3.87-3.95 (m, C*H*), 4.04-4.12 (m, CH_2Cl and CH_2), 5.08 (s, 1H of CH_2 alkene), 5.27 (s, 1H of CH_2 alkene). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 28.4 (3 *CH*$_3$), 31.7 (*CH*$_2$), 32.6 (*CH*), 32.9 (*CH*$_2$), 42.3 (*CH*$_2$), 44.1 (*CH*$_2$), 48.1 (*CH*$_2$Cl), 66.6 (*CH*(OH)), 79.2 (*C*quat), 117.6 (*CH*$_2$ alkene), 142.1 (*C* alkene), 154.8 (*CO*).

HRMS ESI [M+Na]+ calcd for $C_{16}H_{28}NClO_3Na$: 340.1650. Observed: 340.1651.

GC enantiomeric excess determination: Hydrodex-b; 190°C for 60 min than 1°C/min until 220°C. rt (min) = 61.4 min; rt (maj) = 62.1 min.

General procedure for the step-wise enantioselective second reductive coupling:

5.1 mg of **Ir-cat2** (0.005 mmol, 5 mol%), 43.6 mg of K_3PO_4 (0.22 mmol, 2.2 equiv) are placed in a tube under argon. 0.2 mL of THF are then added followed by 27 µL of isopropanol (0.3 mmol, 3.5 equiv); 16.0 mg of **3b** (0.1 mmol, 1 equiv) and 4 equivalents of the corresponding aldehyde. The tube is then quickly sealed and the reaction mixture stirred at 50°C for 48 hours. 2 ml of saturated NH_4Cl are then added and the aqueous layer is extracted by 4 times 2 ml of diethyl ether, the combined organic layers filtered over a small plug of Na_2SO_4 and silica gel and the solvent evaporated. Purification over silica gel (petroleum ether/ethyl acetate) directly yields the bis-alcohols.



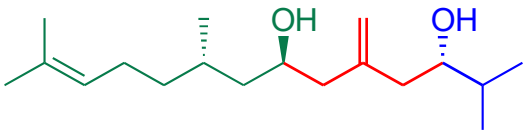
***anti*-4b**: Prepared according to the general procedure starting from 0.1 mmol (16.3 mg) of **1** and 36 µL of isobutyraldehyde. The product was isolated as a pale oil after purification with ethyl acetate / petroleum ether mixture. 11.9 mg (0.060 mmol). 60% yield.

R_f = 0.28 (petroleum ether / ethyl acetate (7/3)). The product is obtained in 96:4 *dr* and 99% *ee*. $[\alpha]^{20}_D$ = 25.1° ($CHCl_3$, c = 1.1), 99% *ee*).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 0.95 (d, *J* = 6.6 Hz, 4 CH_3), 1.66-1.73 (m, 2 C*H*), 1.99 (brs, O*H*), 2.05 (dd, *J* = 14.0; 10.5 Hz, 2 H of CH_2), 3.49 (ddd, *J* = 10.5; 5.5; 2.6 Hz, 2 C*H*); 5.02 (s, CH_2 *alkene*). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 17.8 (*CH*$_3$), 18.5 (*CH*$_3$), 33.6 (*CH*), 40.4 (*CH*$_2$), 73.7 (*CH*(OH)), 115.5 (*CH*$_2$ alkene), 144.6 (*C* alkene).

GC enantiomeric excess determination: cyclosil-b; 120°C for 0 min than 1°C/min until 220°C. Major dia: rt (maj) = 24.5 min; rt (min) = 25.1 min. Minor dia: rt = 25.3 min.

Datas are in agreement with the literature.[3]

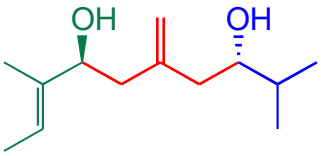


***anti*-4d**: Prepared according to the general procedure starting from 16.1 mg of **3b using (*S*)-Ircat2**. The product was isolated as a pale oil after purification with ethyl acetate / petroleum ether mixture. 19.9 mg (0.0705 mmol). 70% yield.

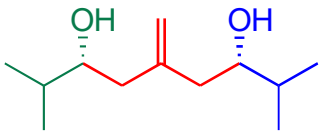
R_f = 0.20 (petroleum ether / ethyl acetate (9/1)). The product is obtained in 95:5 *dr*. $[\alpha]^{20}_D$ = -16.5° ($CHCl_3$, c = 1.1), 99% *ee*).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 0.95 (d, *J* = 6.4 Hz, CH_3), 0.98 (d, *J* = 6.7 Hz, 2 CH_3), 1.21-1.40 (m, 4 H), 1.51-1.59 (m, C*H*), 1.62 (s, CH_3), 1.69-1.74 (m, 2 H and CH_3), 2.00-2.14 (m, 5 H), 2.29-2.34 (m, 2H), 3.53 (ddd, *J* = 10.4; 5.5; 2.7 Hz, C*H*(OH)), 3.84-3.91 (m, C*H*(OH)), 5.04 (s, CH_2 *alkene*), 5.10-5.14 (m, *CH* alkene). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 17.6 (*CH*$_3$), 17.7 (*CH*$_3$), 18.5 (*CH*$_3$), 19.2 (*CH*$_3$), 25.4 (*CH*$_2$), 25.7 (*CH*), 29.0 (*CH*$_3$), 33.6 (*CH*), 37.8 (*CH*$_2$), 40.6 (*CH*$_2$), 44.5 (*CH*$_2$), 44.7 (*CH*$_2$), 66.9 (*CH*(OH)), 73.8 (*CH*(OH)), 115.5

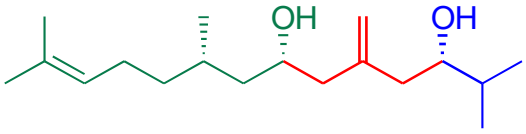
(*CH*$_2$ alkene), 124.7 (*CH* alkene), 131.2 (*C* alkene), 144.3 (*C* alkene).
HRMS ESI [M+H]+ calcd for $C_{18}H_{35}O_2$: 283.2632. Observed: 283.2631.



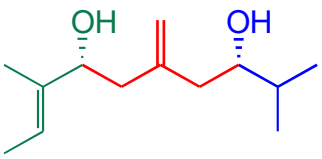
***anti*-4g**: Prepared according to the general procedure starting from 16.0 mg of **3b using (*S*)-Ircat2**. The product was isolated as a pale oil after purification with ethyl acetate / petroleum ether mixture. 13.0 mg (0.061 mmol). 61% yield.
R_f = 0.12 (petroleum ether / ethyl acetate (9/1)). The product is obtained in 95:5 dr and >99% *ee*. $[\alpha]^{20}_D$ = -25.1° ($CHCl_3$, c = 1.0), 99% *ee*).
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 0.95 (t, *J* = 7.2 Hz, 2 C*H*$_3$), 1.61-1.72 (m, 1 C*H* and 2 C*H*$_3$), 2.0 (brs, O*H*), 2.07 (dd, *J* = 14.0; 10.2 Hz, 1 H of C*H*$_2$), 2.25-2.34 (m, 2 C*H*$_2$), 3.51 (ddd, *J* = 10.6; 5.4; 2.6 Hz, C*H*(OH)), 4.15 (dd, *J* = 9.0; 4.4 Hz, C*H*(OH)), 5.02 (d, J = 6.6 Hz, C*H*$_2$), 5.54 (q, *J* = 6.6 Hz, C*H* alkene). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 11.5 (*CH*$_3$), 13.0 (*CH*$_3$), 17.8 (*CH*$_3$), 18.5 (*CH*$_3$), 33.6 (*CH*), 40.7 (*CH*$_2$), 41.8 (*CH*$_2$), 73.6 (*CH*(OH)), 76.6 (*CH*(OH)), 115.6 (*CH*$_2$ alkene), 120.5 (*CH* alkene), 137.4 (*C* alkene), 144.2 (*C* alkene).
HRMS ESI [M+Na]+ calcd for $C_{13}H_{24}O_2Na$: 235.1669. Observed: 235.1670.
GC enantiomeric excess determination: cyclosil-b; 130°C for 60 min than 1°C/min until 220°C. Major dia: rt (maj) = 66.8 min; rt (min) = 68.9 min. minor dia: 67.5 min.



***syn*-4b** (*meso*): Prepared according to the general procedure starting from 16.2 mg of **3b using (*R*)-Ircat2**. The product was isolated as a pale oil after purification with ethyl acetate / petroleum ether mixture. 8;8 mg (0.044 mmol). 44% yield.
R_f = 0.12 (petroleum ether / ethyl acetate (9/1)). The product is obtained in 93:7 *dr.*
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 0.87 (d, *J* = 6.6 Hz, 2 C*H*$_3$), 0.88 (d, *J* = 6.6 Hz, 2 C*H*$_3$), 1.60-1.65 (m, 2 C*H*), 1.86 (brs, O*H*), 2.04 (dd, *J* = 14.0; 9.8 Hz, 2 H of C*H*$_2$), 2.26 (dd, *J* = 14.2; 3.3 Hz, 2 H of C*H*$_2$), 3.44-3.50 (m, 2 C*H*(OH)); 4.94 (s, C*H*$_2$ *alkene*). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 17.3 (*CH*$_3$), 18.7 (*CH*$_3$), 35.5 (*CH*), 41.4 (*CH*$_2$), 74.8 (*CH*(OH)), 114.7 (*CH*$_2$ alkene), 145.2 (*C* alkene).
Datas are in agreement with the literature.[3]



***syn*-4d**: Prepared according to the general procedure starting from 16.4 mg of **3b using (*R*)-Ircat2**. The product was isolated as a pale oil after purification with ethyl acetate / petroleum ether mixture. 14;5 mg (0.052 mmol). 52% yield.
R_f = 0.20 (petroleum ether / ethyl acetate (9/1)). The product is obtained in 95:5 *dr.* $[\alpha]^{20}_D$ = -7;4° ($CHCl_3$, c = 0;6), 99% *ee*).
^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 0.93 (d, *J* = 6.5 Hz, C*H*$_3$), 0.98 (d, *J* = 6.6 Hz, 2 C*H*$_3$), 1.19-1.40 (m, 4 H), 1.50-1.58 (m, C*H*), 1.62 (s, C*H*$_3$), 1.68-1.73 (m, 2 H and C*H*$_3$), 1.99-2.14 (m, 5 H), 2.26-2.35 (m, 2H), 3.53 (ddd, *J* = 10.6; 5.3; 2.7 Hz, C*H*(OH)), 3.85-3.90 (m, C*H*(OH)), 5.04 (s, C*H*$_2$ *alkene*), 5.10-5.14 (m, *CH* alkene).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 17.4 (*CH*$_3$), 17.6 (*CH*$_3$), 18.7 (*CH*$_3$), 20.2 (*CH*$_3$), 25.3 (*CH*$_2$), 25.7 (*CH*), 29.3 (*CH*$_3$), 33.5 (*CH*), 36.7 (*CH*$_2$), 41.5 (*CH*$_2$), 44.8 (*CH*$_2$), 44.9 (*CH*$_2$), 68.3 (*CH*(OH)), 74.7 (*CH*(OH)), 114.9 (*CH*$_2$ alkene), 124.7 (*CH* alkene), 131.2 (*C* alkene), 144.8 (*C* alkene).
HRMS ESI [M+H]+ calcd for $C_{18}H_{35}O_2$: 283.2632. Observed: 283.2631.



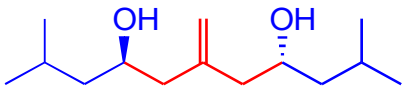
***syn*-4g**: Prepared according to the general procedure starting from 16.3 mg of **3b using (*R*)-Ircat2**. The product was isolated as a pale oil after purification with ethyl acetate / petroleum ether mixture. 13.6 mg (0.064 mmol). 64% yield.
R_f = 0.12 (petroleum ether / ethyl acetate (9/1)). The product is obtained in 95:5 dr and >90% *ee*. $[\alpha]^{20}_D$ = -4.9° ($CHCl_3$, c = 0.7), >90% *ee*).
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 0.87 (d, *J* = 4.5 Hz, C*H*$_3$), 0.89 (d, *J* = 4.6 Hz, C*H*$_3$), 1.52-1.65 (m, 1 C*H* and 2 C*H*$_3$), 1.82 (brs, O*H*), 2.01 (dd, *J* = 13.8; 10.4 Hz, 1 H of C*H*$_2$), 2.23-2.29

[3] A. G. M. Barrett, D. C. Braddock, P. D. de Koning, A. J. P. White, D. J. Williams, *J. Org. Chem.* **2000**, *65*, 375

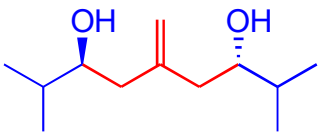
(m, 2 CH_2), 3.46 (ddd, J = 10.3; 5.5; 2.4 Hz, CH(OH)), 4.12 (dd, J = 9.3; 4.2 Hz, CH(OH)), 4.92 (d, J = 6.6 Hz, CH_2), 5.45 (q, J = 6.5 Hz, CH alkene). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 11.3 (*CH₃*), 13.0 (*CH₃*), 17.5 (*CH₃*), 18.6 (*CH₃*), 33.5 (*CH*), 41.3 (*CH₂*), 42.2 (*CH₂*), 74.4 (*CH*(OH)), 76.6 (*CH*(OH)), 114.9 (*CH₂* alkene), 120.8 (*CH* alkene), 137.4 (*C* alkene), 144.5 (*C* alkene).
HRMS ESI [M+Na]+ calcd for $C_{13}H_{24}O_2Na$: 235.1669. Observed: 235.1670.
GC enantiomeric excess determination: cyclosil-b; 130°C for 60 min than 1°C/min until 220°C. Major dia: rt (maj) = 67.4 min; rt (min) = 67.7 min. minor dia: rt = 66.8 min and 68.9 min.

General procedure for the cascade enantioselective bis-functionalization:

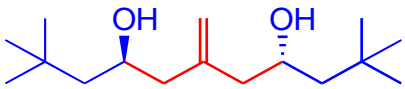
5.0 mg of **(*S*)-Ircat2** (0.005 mmol, 5 mol%), 64.9 mg of K_3PO_4 (0.3 mmol, 3.0 equiv) are placed in a tube under argon. 0.2 mL of THF are then added followed by 38 µL of isopropanol (0.5 mmol, 5.0 equiv); 12.5 mg of bis-chloro allylic nucleophile (0.1 mmol, 1 equiv) and 4 equivalents of the aldehyde (0.4 mmol). The tube is then quickly sealed and the reaction mixture stirred at 50°C for 48 hours. 2 ml of saturated NH_4Cl are then added and the aqueous layer is extracted by 4 times 2 ml of diethyl ether, the combined organic layers filtered over a small plug of Na_2SO_4 and silica gel and the solvent evaporated. Purification over silica gel (petroleum ether/ethyl acetate) directly yields the bis-alcohols.



***anti*-4a**: Prepared according to the general procedure starting from 0.5 mmol (62 mg) of **1** and 215 µL of isovaleraldehyde. The product was isolated as a pale oil after purification with ethyl acetate / petroleum ether mixture. 76.5 mg (0.335 mmol). 67% yield.
R_f = 0.24 (petroleum ether / ethyl acetate (8/2)). The product is obtained in 96:4 dr and 98% *ee*. $[\alpha]^{20}_D$ = +4.8 ($CHCl_3$, c = 0.6), 98% *ee*).
^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 0.93 (d, J = 6.6 Hz, 4 CH_3), 1.23-1.28 (m, 2 H), 1.42-1.47 (m, 2H), 1.82 (brs, O*H*), 1.74-1.81 (2 H), 2.03-2.09 (m, 2 H of CH_2 and OH), 2.27 (dd, J = 12.0 Hz, 2 H of CH_2), 3.74-3.85 (m, C*H*(OH)), 5.01 (s, CH_2 *alkene*). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 22.2 (*CH₃*), 23.1 (*CH₃*), 24.7 (*CH*), 44.5 (*CH₂*), 46.5 (*CH₂*), 67.6 (*CH*(OH)), 115.5 (*CH₂* alkene), 143.9 (*C* alkene).
GC enantiomeric excess determination: cyclosil-b; 140°C for 0 min than 1°C/min until 220°C. Major dia: rt (maj) = 23.1 min; rt (min) = 24.2 min. Minor dia: rt = 23.5 min.
Datas are in agreement with the literature.[3]



***anti*-4b**: Prepared according to the general procedure starting from 0.1 mmol (12.5 mg) of **1** and 36 µL of isobutyraldehyde. The product was isolated as a pale oil after purification with ethyl acetate / petroleum ether mixture. 12.9 mg (0.065 mmol). 65% yield.
R_f = 0.28 (petroleum ether / ethyl acetate (7/3)). The product is obtained in 97:3 dr and 99% *ee*. $[\alpha]^{20}_D$ = 25.1° ($CHCl_3$, c = 1.1), 99% *ee*).
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 0.95 (d, J = 6.6 Hz, 4 CH_3), 1.66-1.73 (m, 2 CH), 1.99 (brs, O*H*), 2.05 (dd, J = 14.0; 10.5 Hz, 2 H of CH_2), 2.30 (dd, J = 14.0; 3.6 Hz, 2 H of CH_2), 3.49 (ddd, J = 10.5; 5.5; 2.6 Hz, 2 C*H*); 5.02 (s, CH_2 *alkene*). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 17.8 (*CH₃*), 18.5 (*CH₃*), 33.6 (*CH*), 40.4 (*CH₂*), 73.7 (*CH*(OH)), 115.5 (*CH₂* alkene), 144.6 (*C* alkene).
GC enantiomeric excess determination: cyclosil-b; 120°C for 0 min than 1°C/min until 220°C. Major dia: rt (maj) = 24.5 min; rt (min) = 25.1 min. Minor dia: rt = 25.3 min.
Datas are in agreement with the literature.[3]

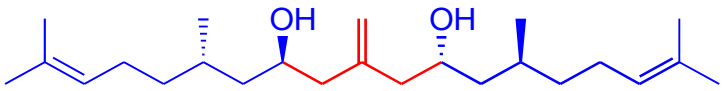


***anti*-4c**: Prepared according to the general procedure starting from 0.1 mmol (12.4 mg) of **1** and 50 µL of 3,3-dimethylbutanal. The product was isolated as a pale oil after purification with ethyl acetate / petroleum ether mixture. 17.1 mg (0.067 mmol). 67% yield.

R_f = 0.44 (petroleum ether / ethyl acetate (7/3)). The product is obtained in 94:6 *dr* and >95% *ee* as determined by Mosher ester analysis. $[\alpha]^{20}_D$ = +8.8° ($CHCl_3$, c = 0.9), >95% *ee*).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 0.96 (s, 6 C*H*$_3$), 1.35 (dd, *J* = 14.5; 2.9 Hz, 2 H of *CH*$_2$), 1.44 (dd, *J* = 14.5; 7.9 Hz, 2 H of *CH*$_2$), 2.08-2.16 (m, OH and 2 H of *CH*$_2$), 2.20 (dd, *J* = 3.5; 2.1 Hz, 2 H of C*H*$_2$), 3.85-3.92 (m, 2 C*H*); 5.00 (s, C*H*$_2$ *alkene*). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 30.1 (*CH*$_3$), 30.3 (*C*$_{quat}$), 46.0 (*CH*$_2$), 50.9 (*CH*$_2$), 66.6 (*CH*(OH)), 115.8 (*CH*$_2$ alkene), 143.8 (*C* alkene).

HRMS ESI [M+H]+ calcd for $C_{16}H_{33}O_2Na$: 257.2475. Observed: 257.2473.

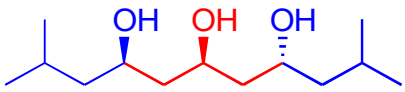


***anti*-4i**: Prepared according to the general procedure starting from 0.1 mmol (12.3 mg) of **1** and 72 µL of (*S*)-citronellal. The product was isolated as a pale oil after purification with ethyl acetate / petroleum ether mixture. 26.8 mg (0.074 mmol). 74% yield.

R_f = 0.29 (petroleum ether / ethyl acetate (9/1)). The product is obtained in >95:5 *dr*. $[\alpha]^{20}_D$ = +6.8° ($CHCl_3$, c = 1.4), >95% *ee*).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 0.91 (d, *J* = 6.6 Hz, 2 C*H*$_3$), 1.15-1.70 (m, 10 H), 1.60 (m, 2 C*H*), 1.67 (m, 2 C*H*), 1.95-2.26 (m, 10 H), 3.83-3.87 (m, 2 C*H*); 5.00 (s, C*H*$_2$ *alkene*), 5.08-5.12 (m, 2 *CH* alkene). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 17.6 (*CH*$_3$), 19.2 (*CH*$_3$), 25.4 (*CH*$_2$), 25.7 (*CH*), 29.0 (*CH*$_3$), 37.8 (*CH*$_2$), 44.7 (*CH*$_2$), 44.8 (*CH*$_2$), 66.9 (*CH*(OH)), 115.5 (*CH*$_2$ alkene), 124.7 (*CH* alkene), 131.2 (*C* alkene), 143.9 (*C* alkene).

Datas are in agreement with the literature.[3]



9a: 76.5 mg of **anti-4a** (0.33 mmol, 1 equiv) are dissolved in 15 mL of dichloromethane and cooled to -78°C. Ozone is bubbled until the solution turns blue. Air is then bubbled through the solution until the color faded. 131.0 mg of PPh3 (0.5 mmol, 1.5 equiv) are then added and the mixture stirred at room temperature for 16 hours. The organic layer is washed by 10 mL saturated $NaHCO_3$, 10 mL brine, dried over Na_2SO_4 and the solvent evaporated. Filtration over silica (petroleum ether / ethyl acetate 9/1 to 4/1) affords the ketodiol contaminated by P(O)Ph3 and engaged in the next step. The ketodiol **is** dissolved in 1.3 mL of dry THF and 0.15 mL of MeOH and cooled to 0°C under argon. 15.3 mg of $NaBH_4$ (0.39 mmol, 1.3 eq) are then added and the reaction stirred at 0°C for 30 minutes before addition of 0.1 mL of acetic acid. The reaction mixture is then stirred at room temperature for 45 min before addition of 10 mL of saturated aqueous $NaHCO_3$. The mixture is stirred for further 40 min at room temperature before extraction by 3 times 10 mL of ethyl acetate, the combined organic layers washed by 2 times 10 mL of 1M HCl, 10 mL of saturated aqueous NaCl, dried over Na_2SO_4, filtered and the solvent evaporated. Purification by recrystallization from a mixture of diethyl ether, and *n*-Hexane yields the pure triol. 59.7 mg (0.257 mmol). 78% yield over two steps.

The product is obtained in >98:2 *dr*. $[\alpha]^{20}_D$ = -90.7° (MeOH, c = 0.3)

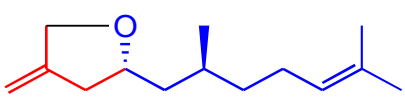
^{1}H NMR (400 MHz, MeOD): δ (ppm) = 0.93 (d, *J* = 6.6 Hz; 4 C*H*$_3$), 1.13-1.61 (m, 8 H), 1.75-1.83 (m, 2 H), 3.81-4.06 (m, 3 C*H*). ^{13}C NMR (100 MHz, MeOD): δ (ppm) = 21.0 (*CH*$_3$), 21.1 (*CH*$_3$), 22.4 (*CH*$_3$), 22.5 (*CH*$_3$), 24.0 (*CH*(CH$_3$)$_2$), 24.2 (*CH*(CH$_3$)$_2$), 44.8 (*CH*$_2$), 44.9 (*CH*$_2$), 46.7 (*CH*$_2$), 46.9 (*CH*$_2$), 65.6 (*CH*), 67.1 (*CH*), 68.0 (*CH*).

HRMS ESI [M+Na]+ calcd for $C_{13}H_{28}O_3Na$: 255.1931. Observed: 255.1928.

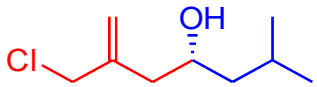
Determination of the stereoselectivity via Mosher ester formation:

To 3.6 mg of triol (0.015 mmol, 1 eq) in 0.2 ml of dry DCM were successively added 21.6 mg of (*R*)-Mosher acid (0.09 mmol, 6 eq), 1.7 mg of DMAP (0.015 mmol, 1 eq) and 18.7 mg of DCC (0.09 mmol, 6 eq). The

resulting mixture was stirred at rt for 2 hours. 6 mL of diethyl ether were then added, the organic layer washed by 2 times 3 ml saturated $NaHCO_3$, 3 mL saturated NaCl, 2 times saturated NH_4Cl, 3 mL saturated NaCl, dried over Na_2SO_4, filtered and the solvent evaporated. Filtration over a plug of silica gives the protected triol analyzed by ^{19}F NMR to determine the stereoselectivity indicating a >98:2 *dr* and >99:1 *er* on the triol.
^{19}F NMR (282 MHz, $CDCl_3$): -71.3; -70.8.



8d: 5.2 mg of **(*S*)-Ircat2** (0.005 mmol, 5 mol%), 44.2 mg of K_3PO_4 (0.22 mmol, 2.2 equiv) are placed in a tube under argon. 0.2 mL of THF are then added followed by 27 µL of isopropanol (0.3 mmol, 3.5 equiv); 58 µL of the bis-chloro allylic nucleophile (0.5 mmol, 5 equiv) and 15.6 mg of (*S*)-citronellal (0.1 mmol, 1 equiv). The tube is then quickly sealed and the reaction mixture stirred at 60°C for the 42 hours. 16.4 mg of NaH (0.4 mmol, 4 equiv, 60% in mineral oil) are then added, the reaction stirred under argon for further 2 hours and 30 minutes. 3 ml of saturated NH_4Cl are then added and the aqueous layer is extracted by 4 times 3 ml of diethyl ether, the combined organic layers filtered over a small plug of Na_2SO_4 and silica gel and the solvent evaporated. Purification over silica gel (petroleum ether/diethyl ether) directly yields the furan **8d** as a pale oil. 16.2 mg (0.073 mmol). 73% yield over two steps.
R_f = 0.72 (petroleum ether / ethyl acetate (95/5)). The product is obtained in 95:5 *dr* and 95% purity. $[\alpha]^{20}_D$ = -26.9° ($CHCl_3$, c = 1.2), >95% *ee*).
^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 0.86 (d, *J* = 6.3 Hz, C*H*$_3$), 1.10-1.28 (m, 3 H), 1.53 (m, C*H*$_3$), 1.60-1.61 (m, 1 H and *CH*$_3$), 1.85-1.96 (m, C*H*$_2$), 2.10 (ddd, *J* = 15.6, 8.6, 2.6 Hz, 1 H of C*H*$_2$), 2.55 (ddt, *J* = 15.6, 5.8, 2.6 Hz, 1 H of C*H*$_2$), 3.92-3.96 (m, C*H*), 4.15 (dd, AB, *J* = 9.8, 2.6 Hz, 1 H of C*H*$_2$), 4.30 (d, AB, *J* = 9.8, 1 H of C*H*$_2$), 4.82 (t, *J* = 1.2 Hz, 1 H of alkene), 4.89 (t, *J* = 1.0 Hz, 1 H of alkene), 5.09 (t, *J* = 1.8 Hz, 1 H of alkene).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 17.6 (*CH*$_3$), 19.4 (*CH*$_3$), 25.4 (*CH*$_2$), 25.7 (*CH*), 29.7 (*CH*$_3$), 37.6 (*CH*$_2$), 39.4 (*CH*$_2$), 42.5 (*CH*$_2$), 70.6 (*CH*$_2$), 77.9 (*CH*), 103.8 (*CH*$_2$ alkene), 124.7 (*CH* alkene), 131.1 (*C* alkene), 148.6 (*C* alkene).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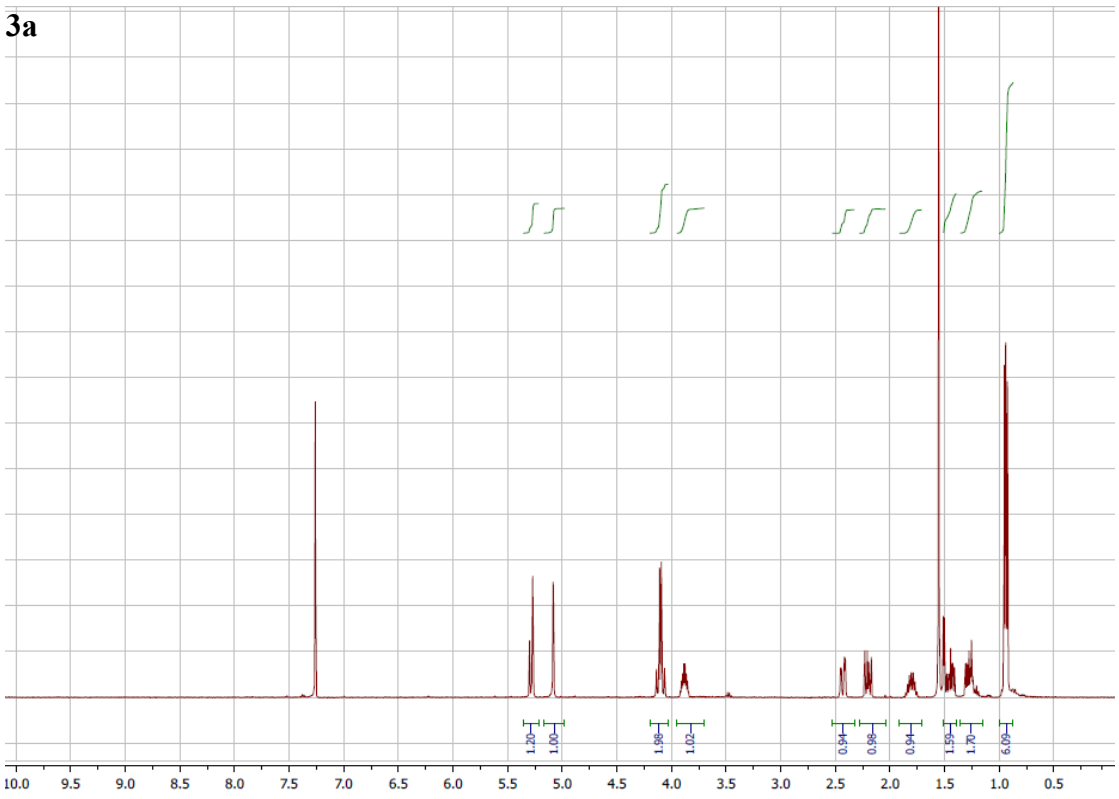
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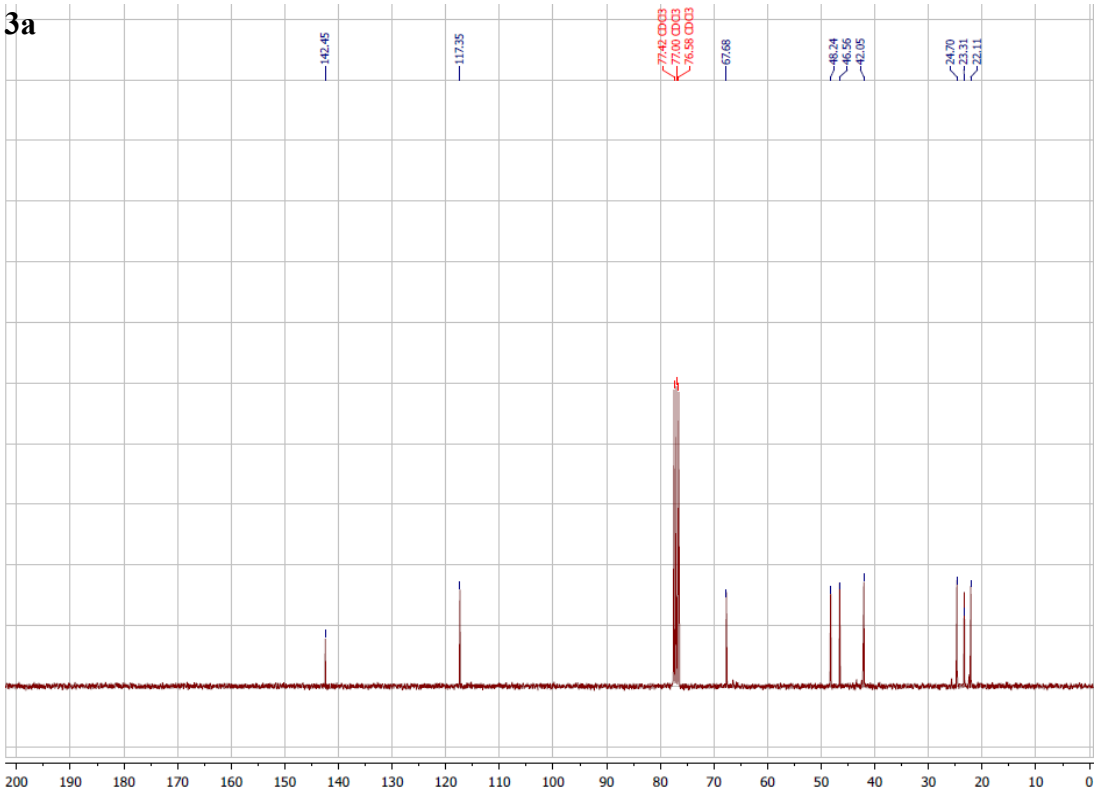
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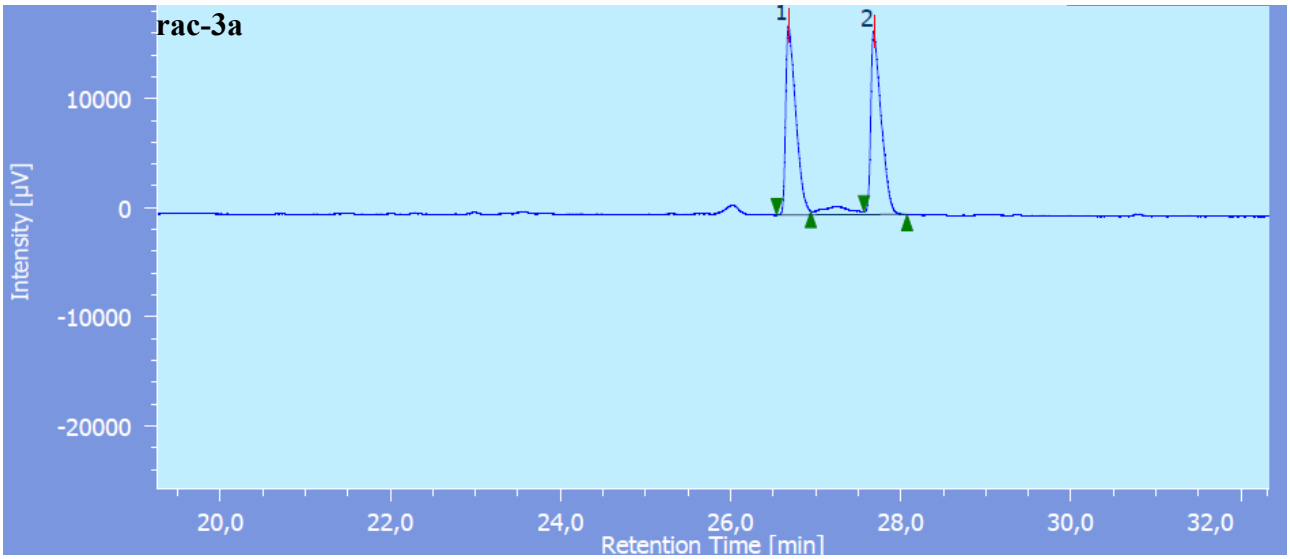

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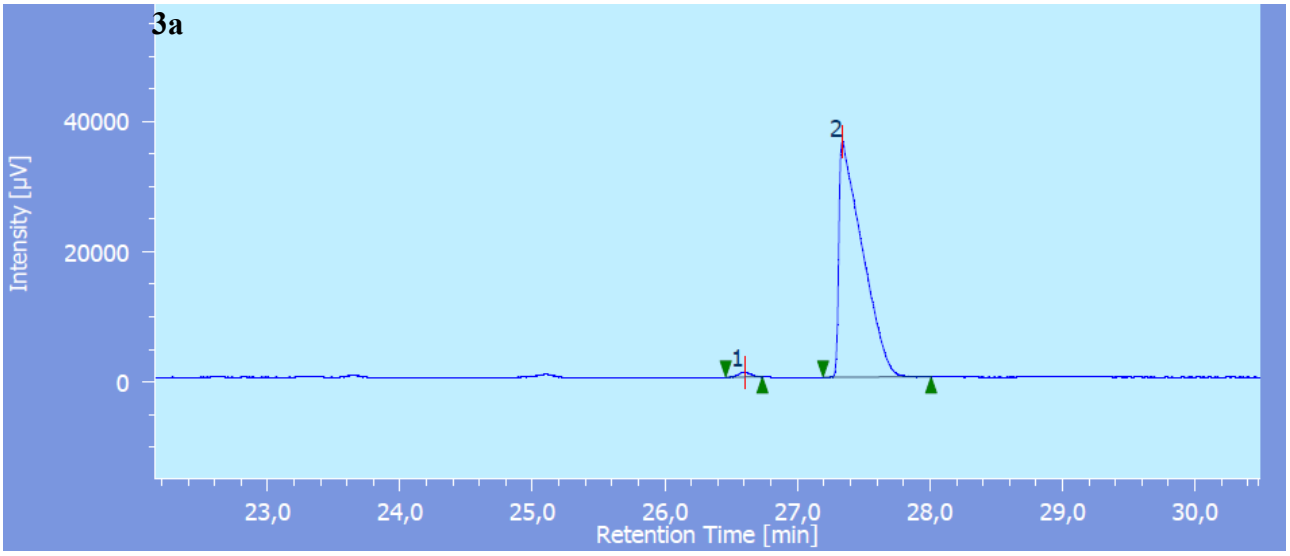

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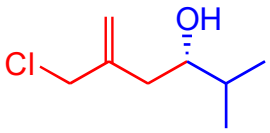
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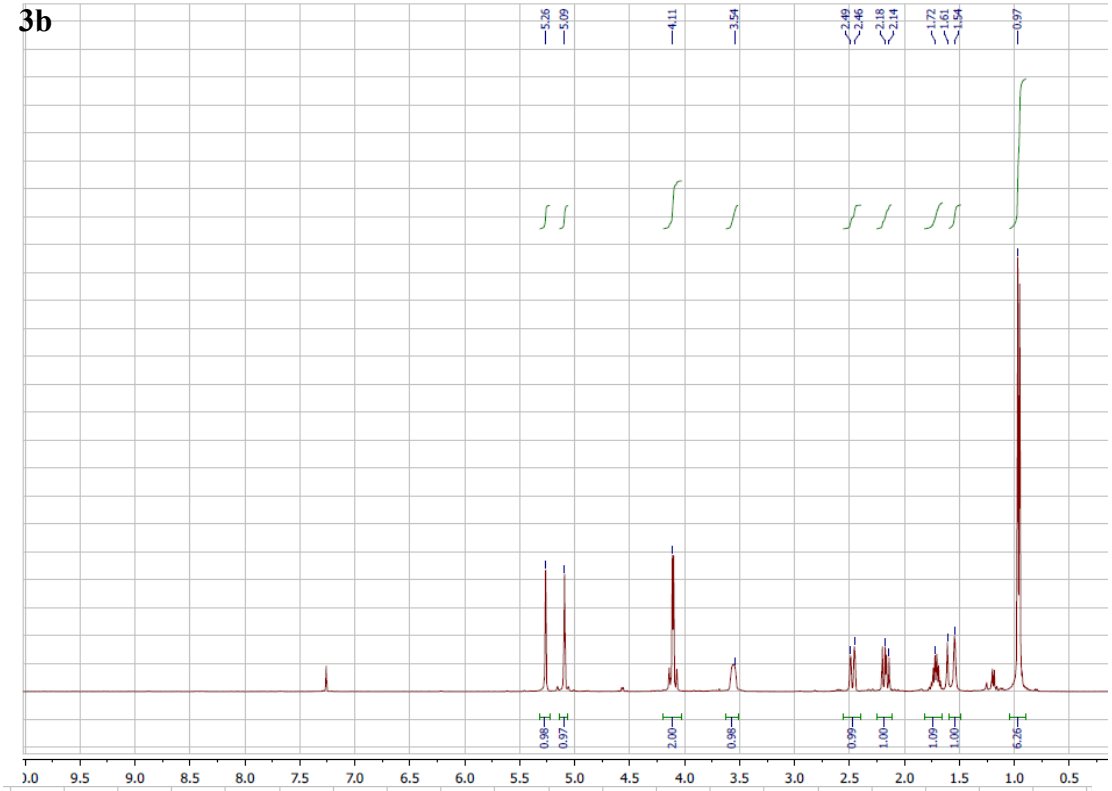
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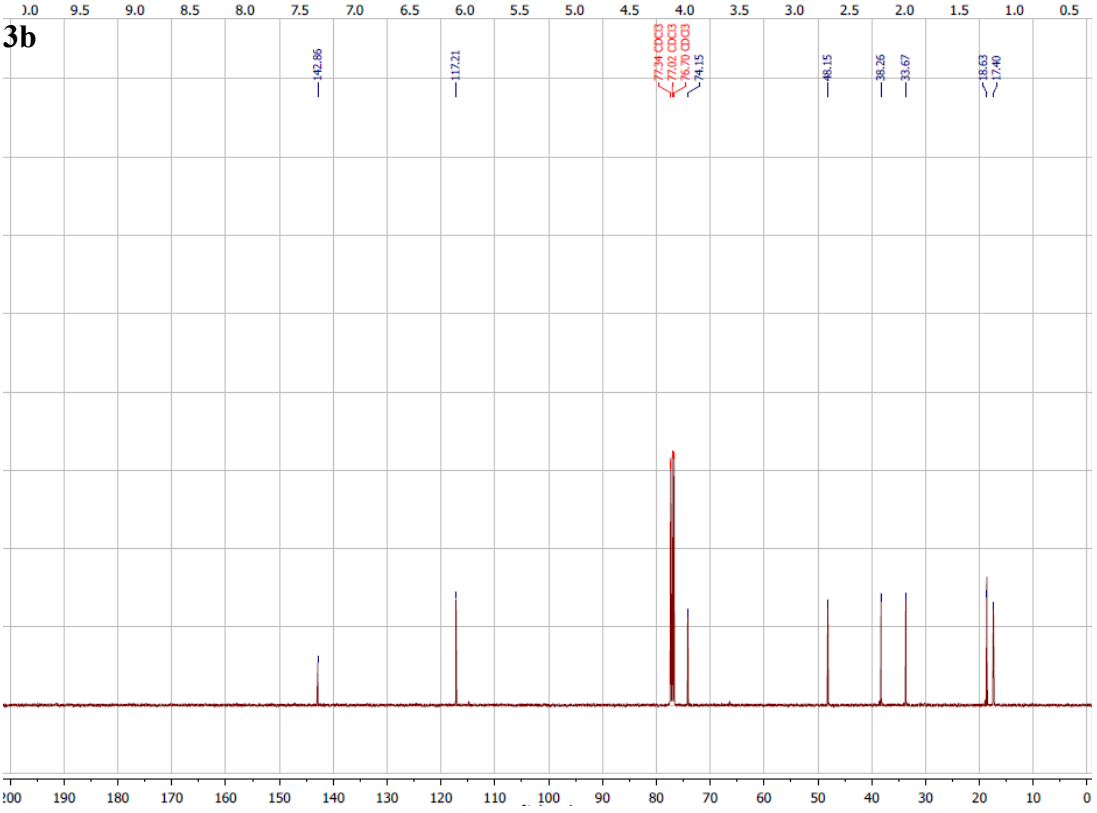
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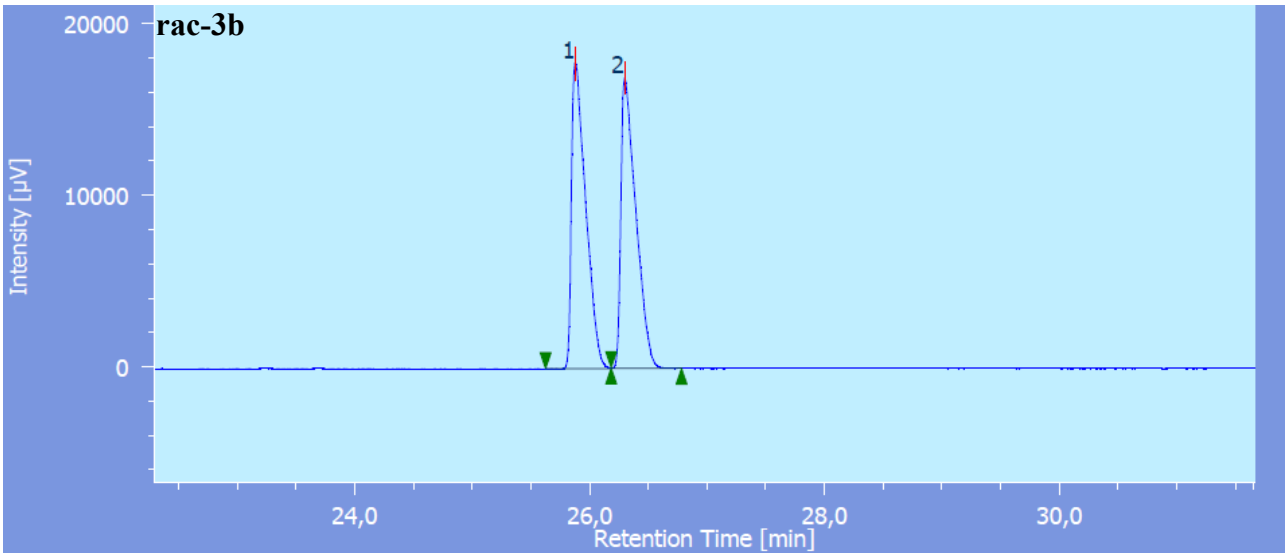

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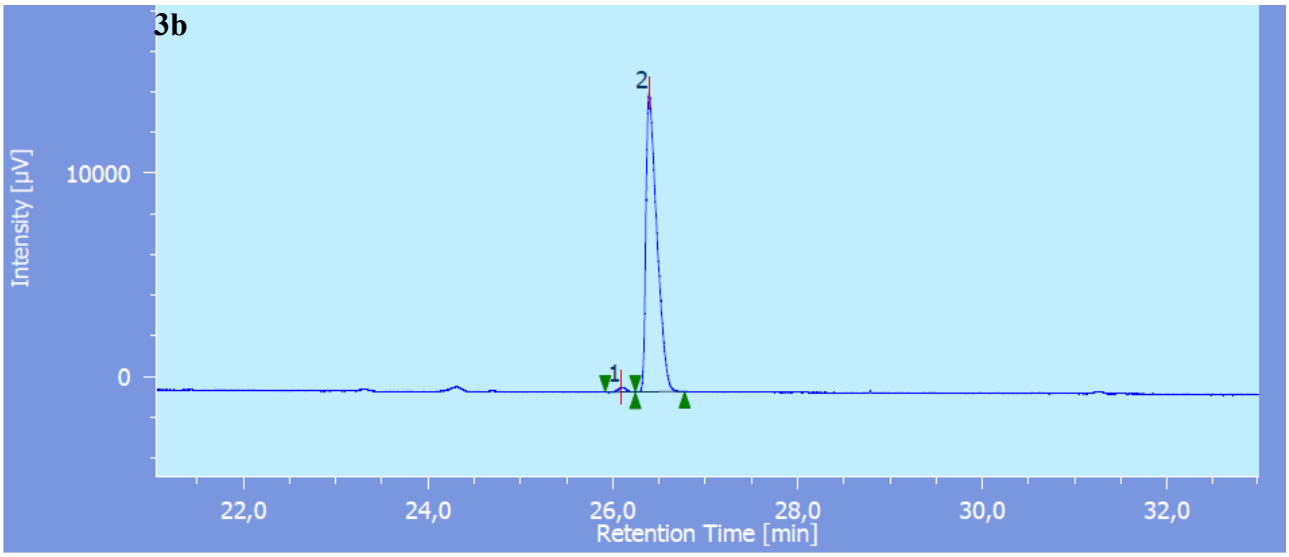

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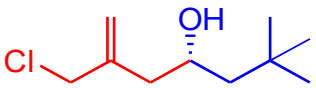
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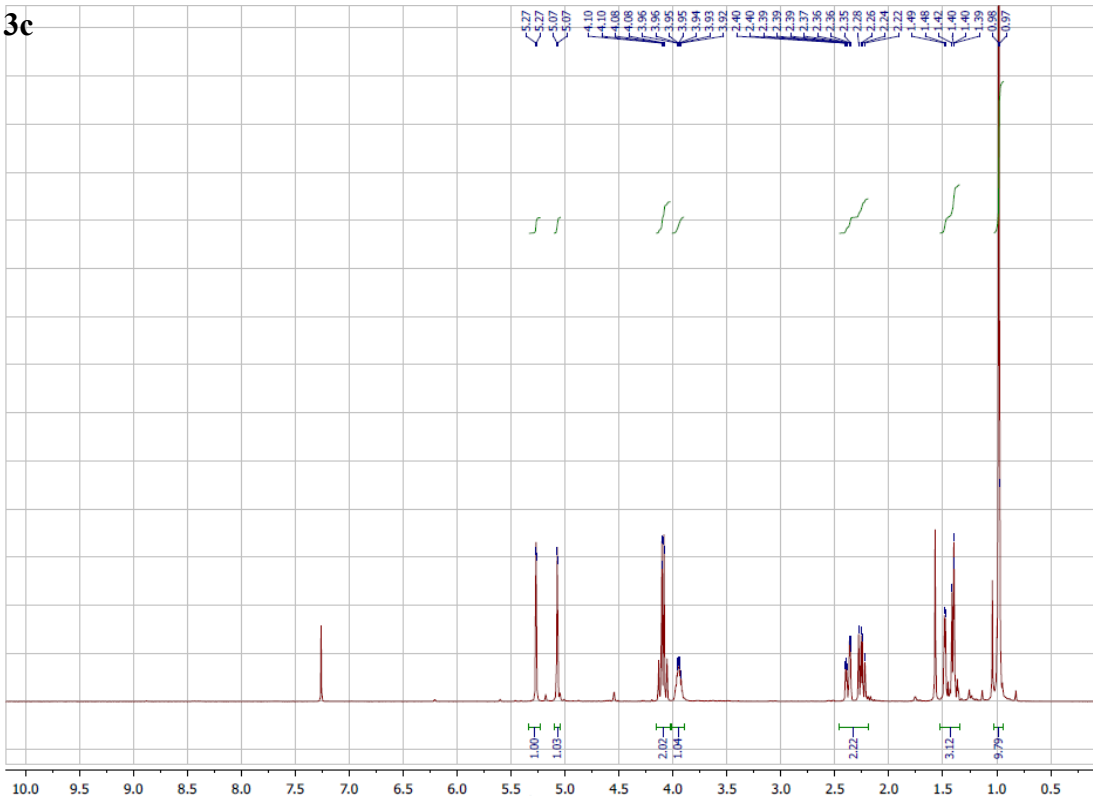
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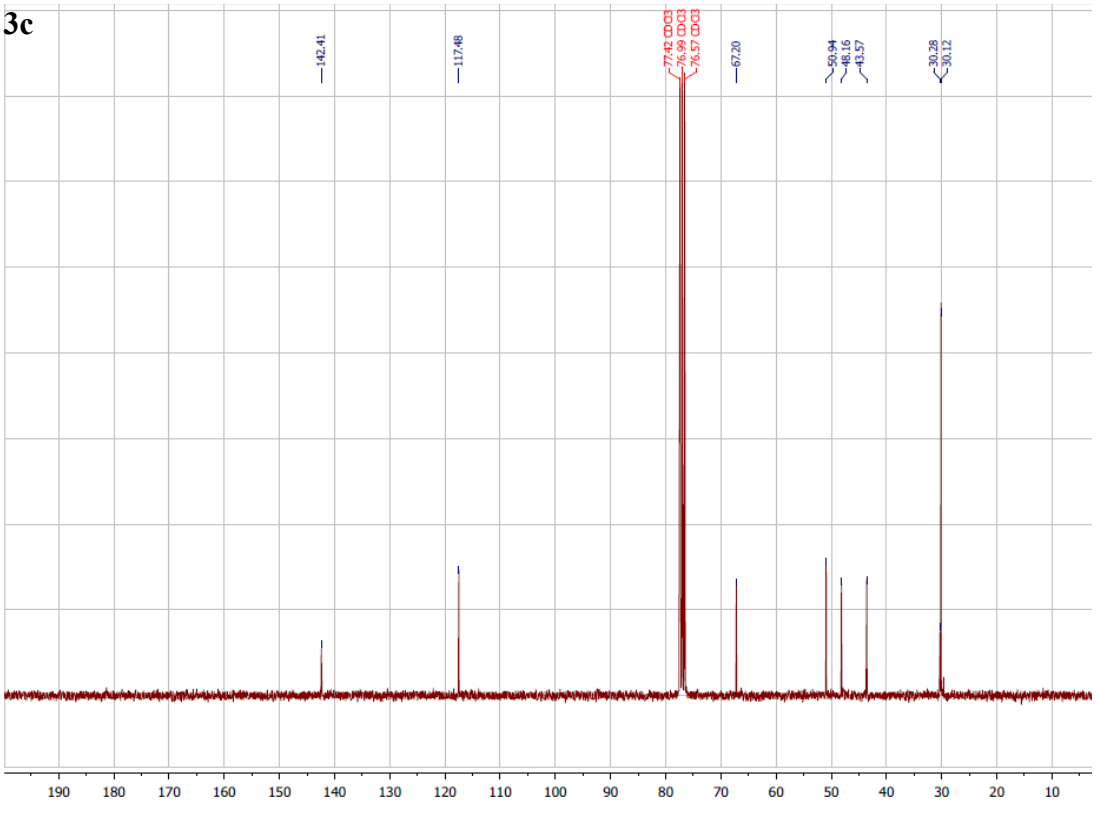
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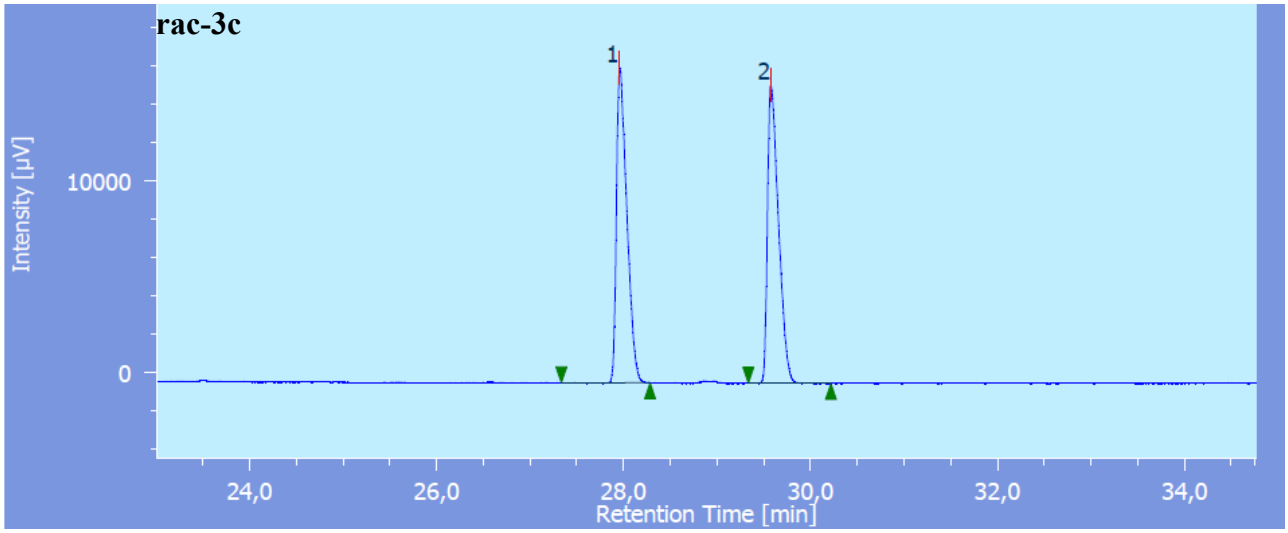

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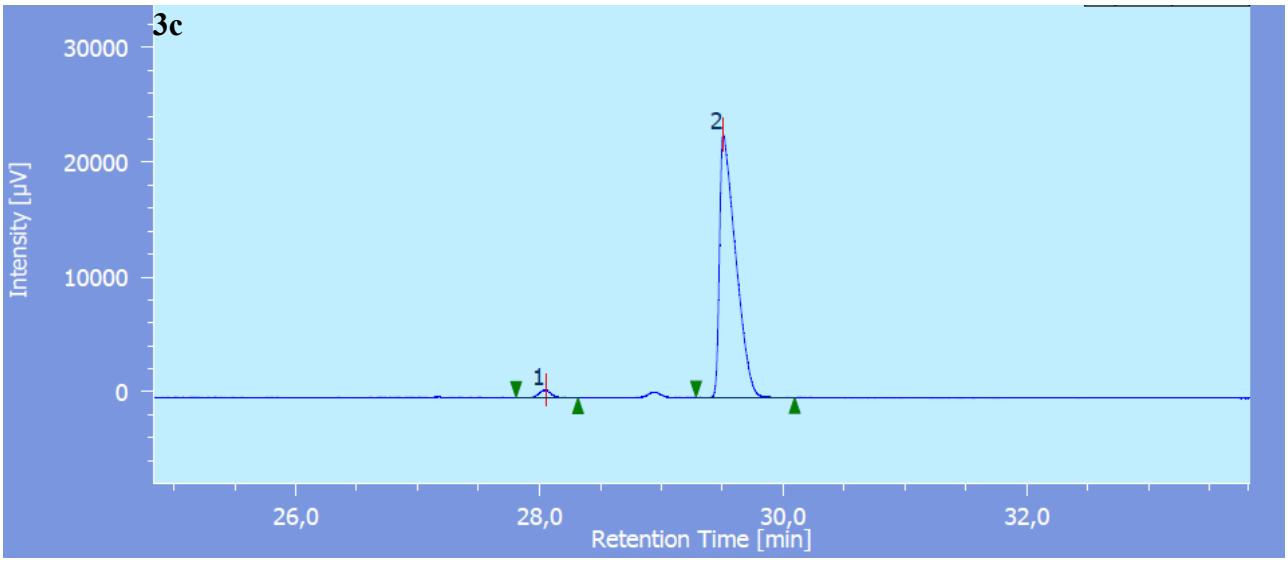

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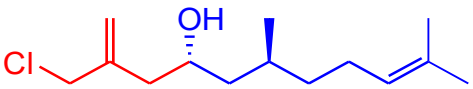

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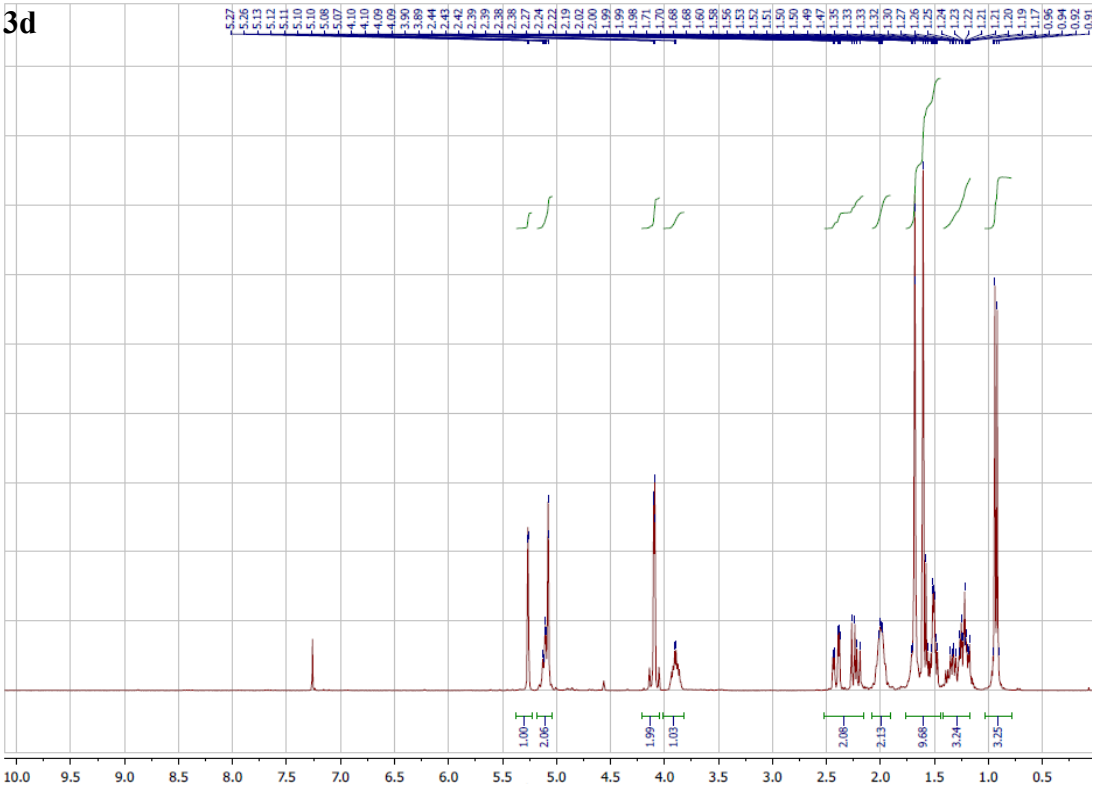

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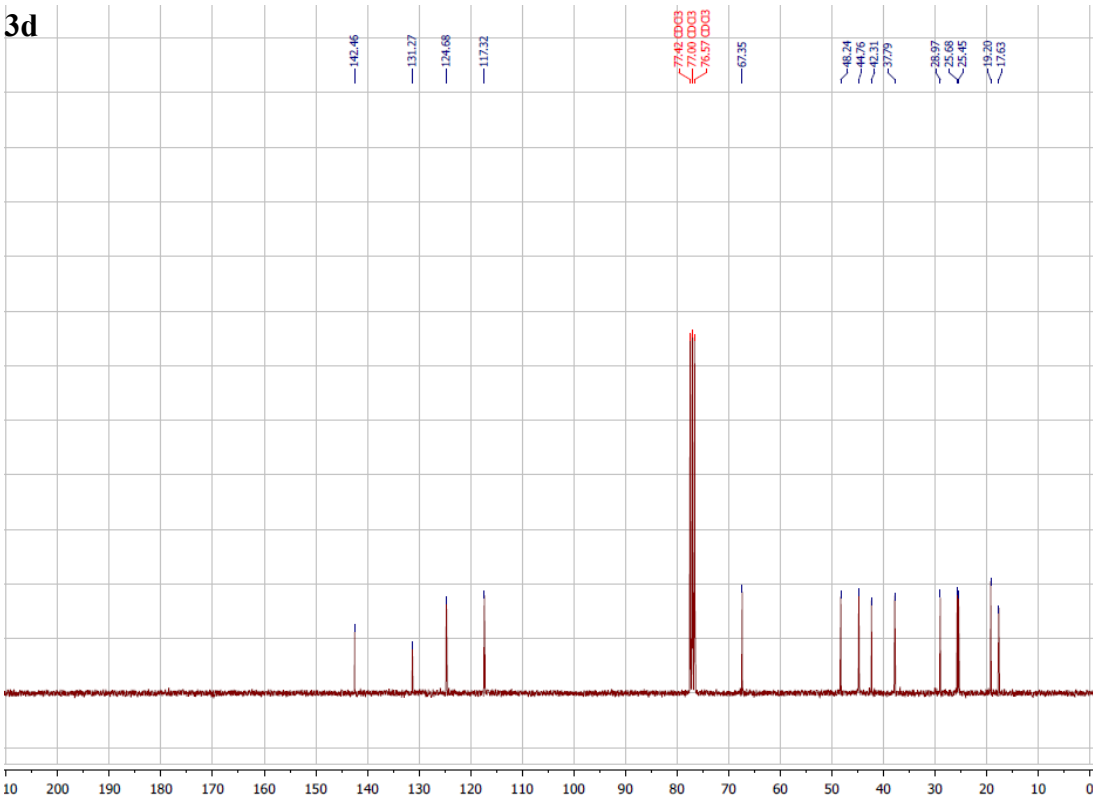

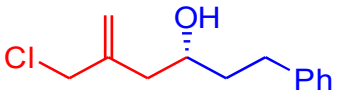
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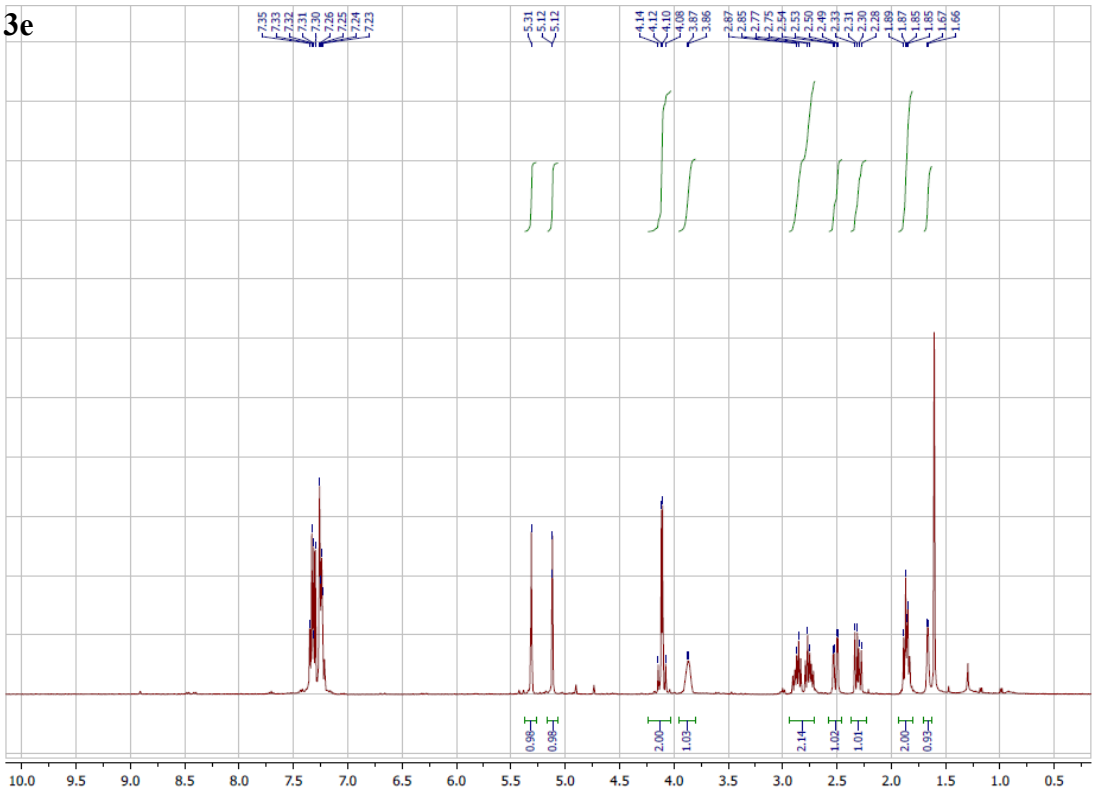
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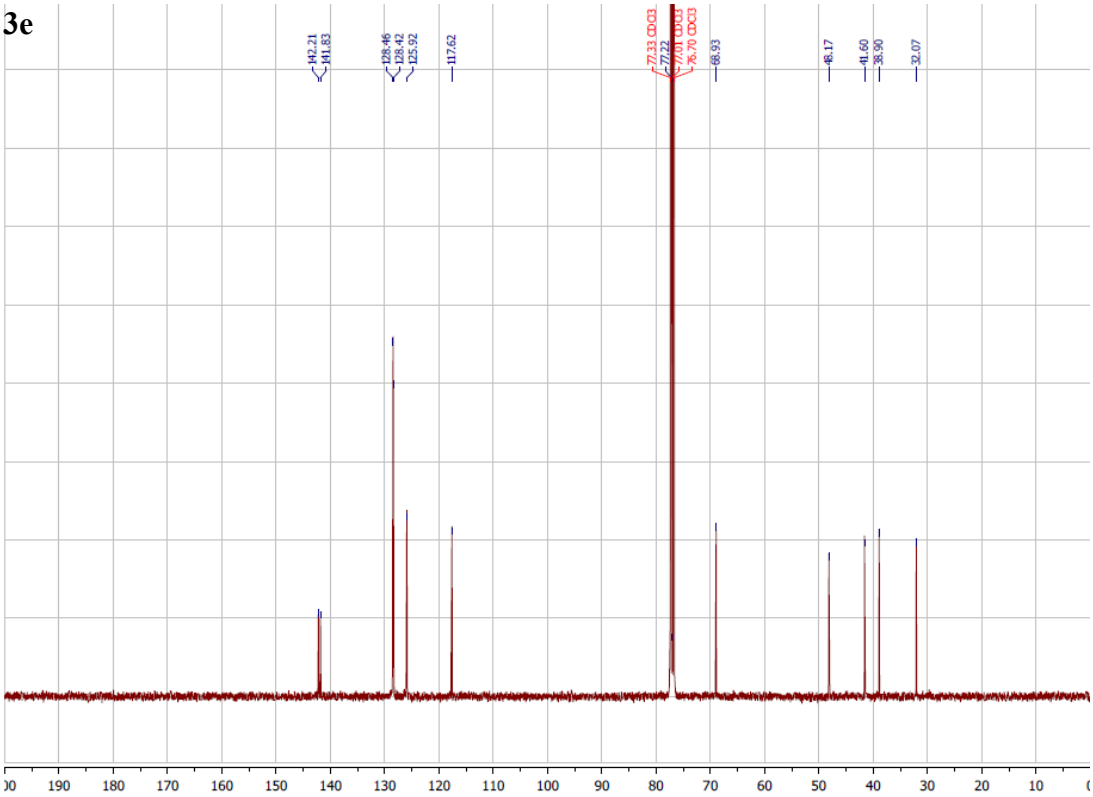
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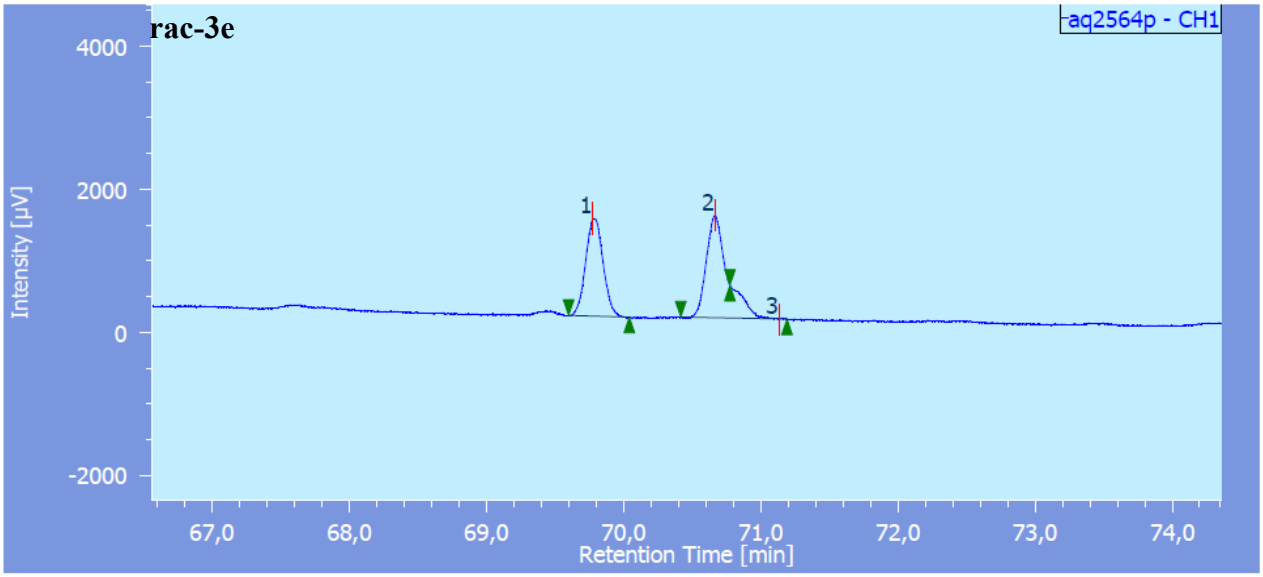

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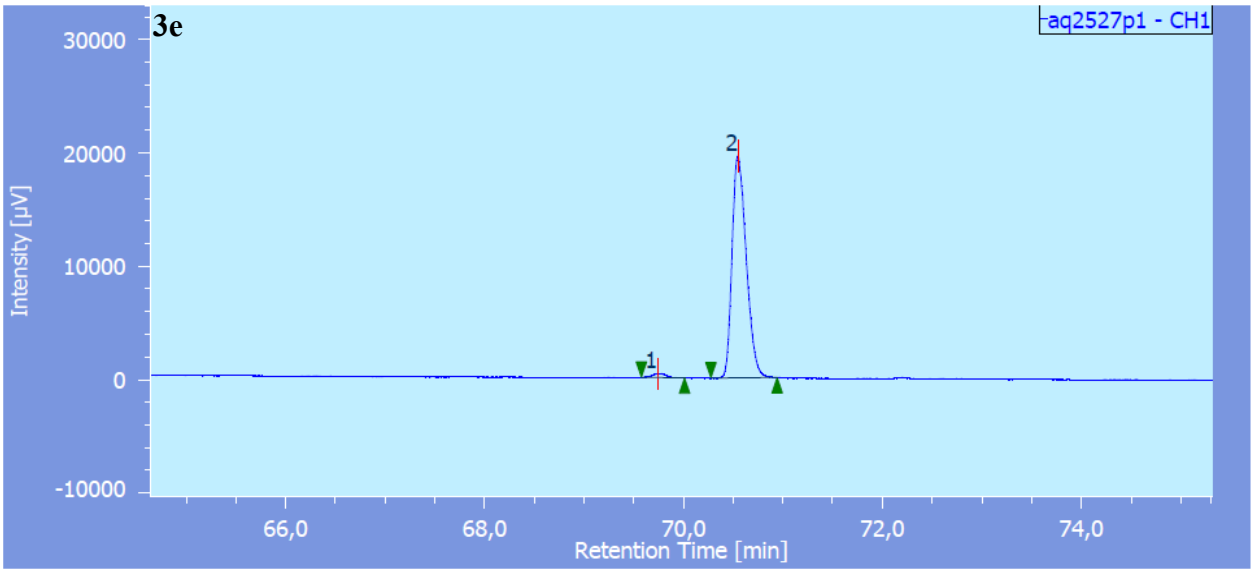

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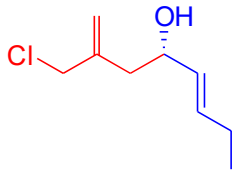

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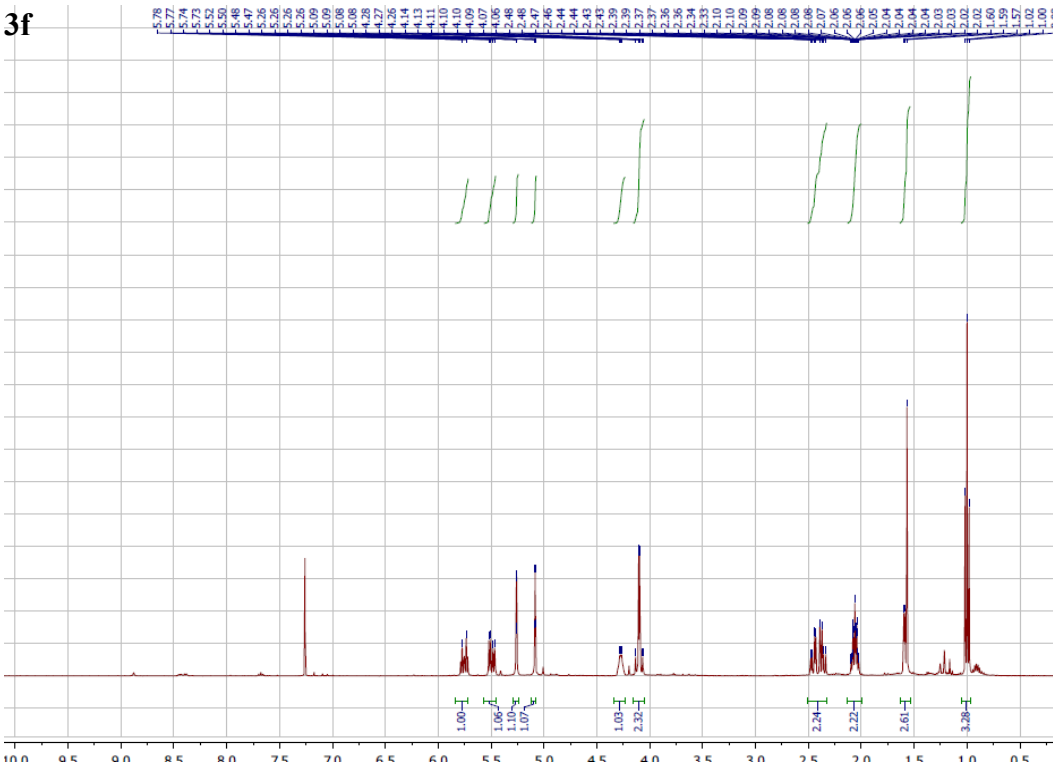

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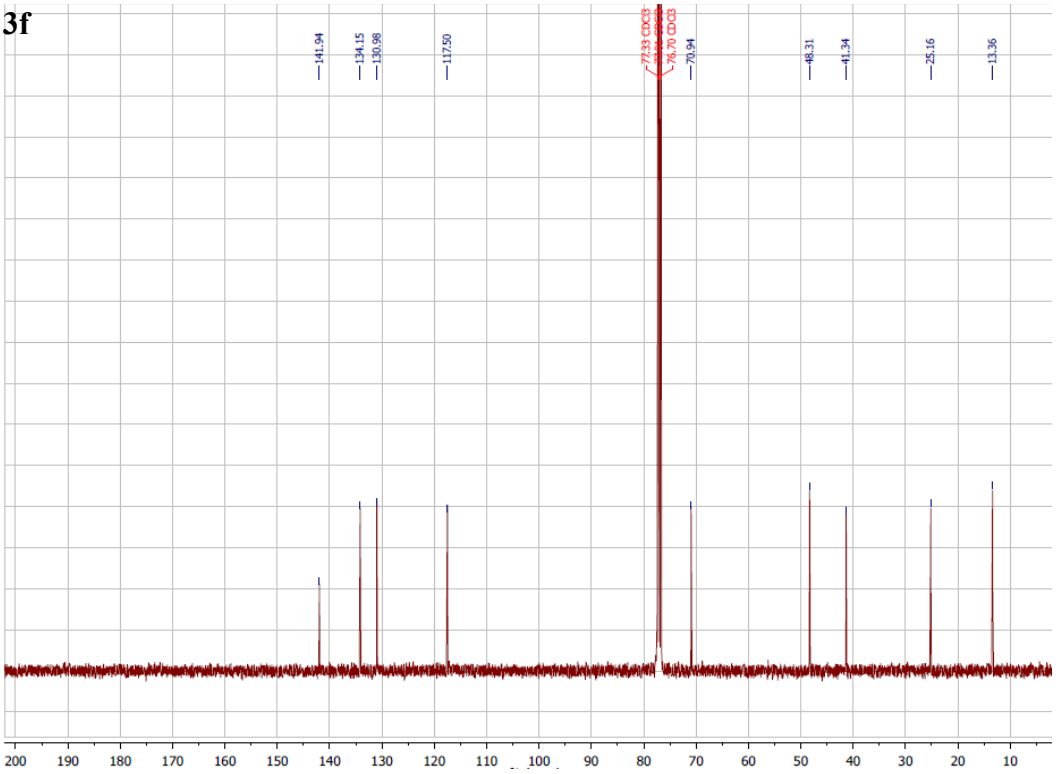

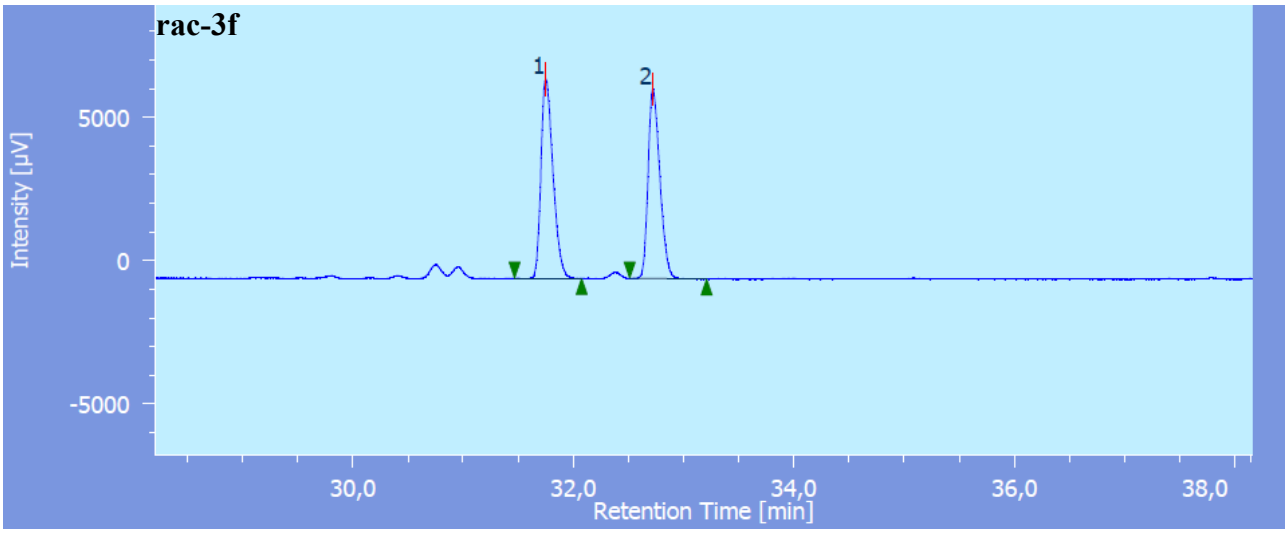

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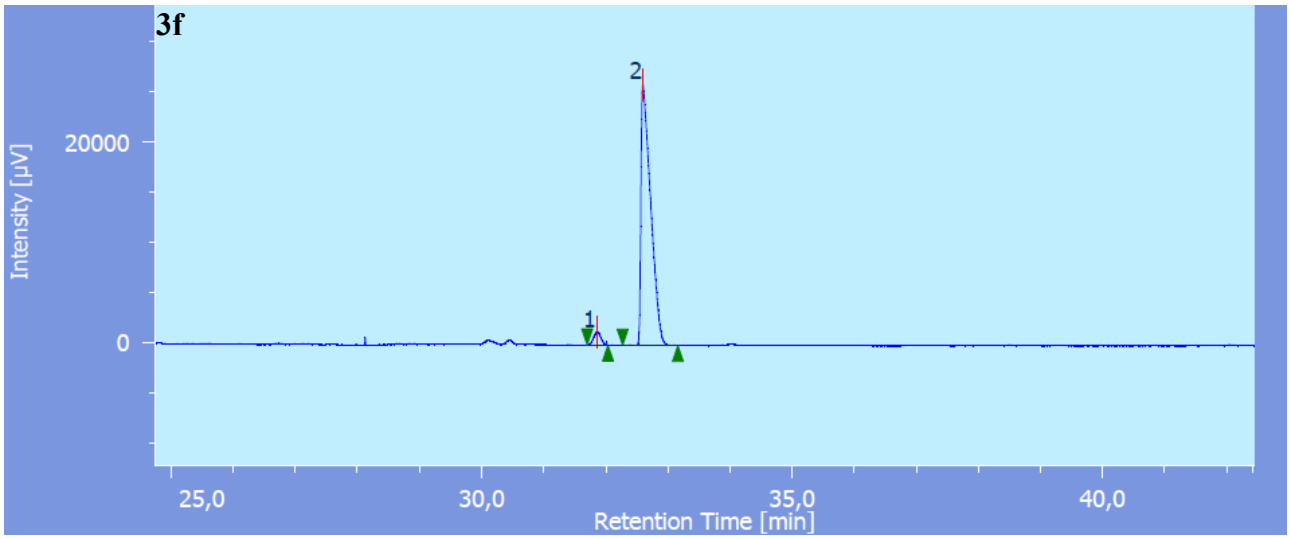

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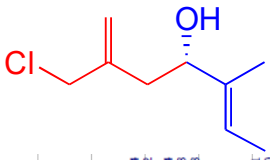
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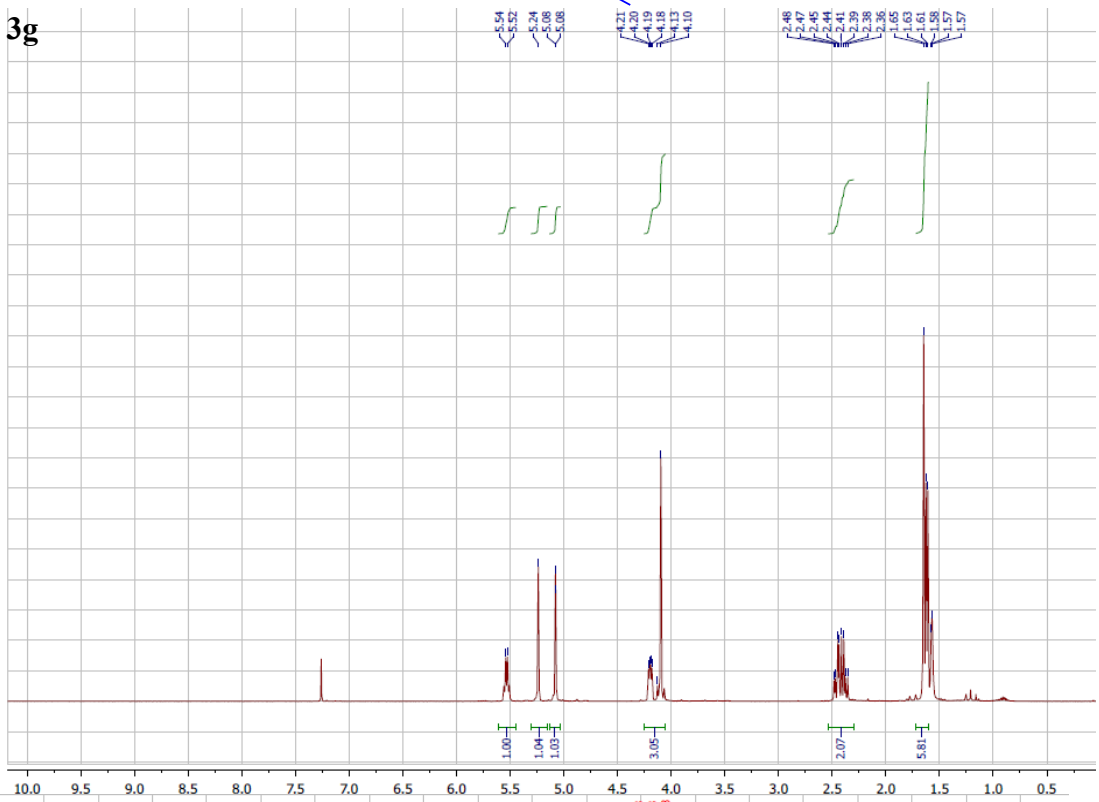
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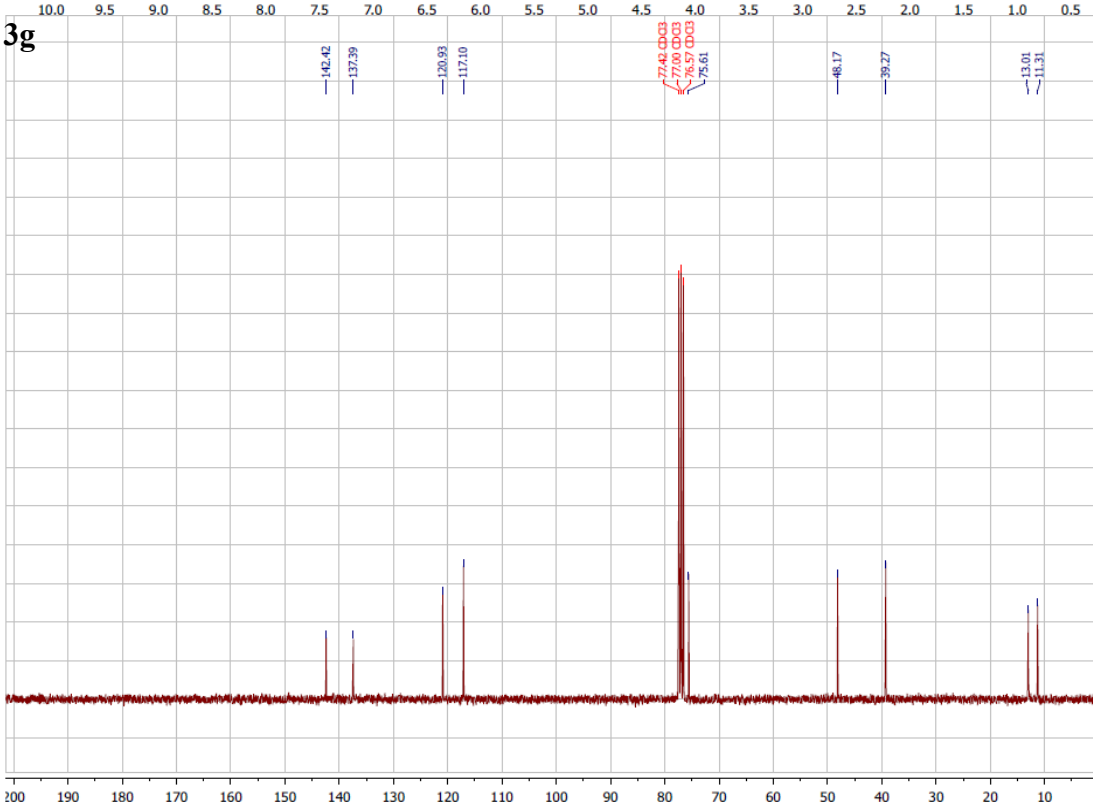
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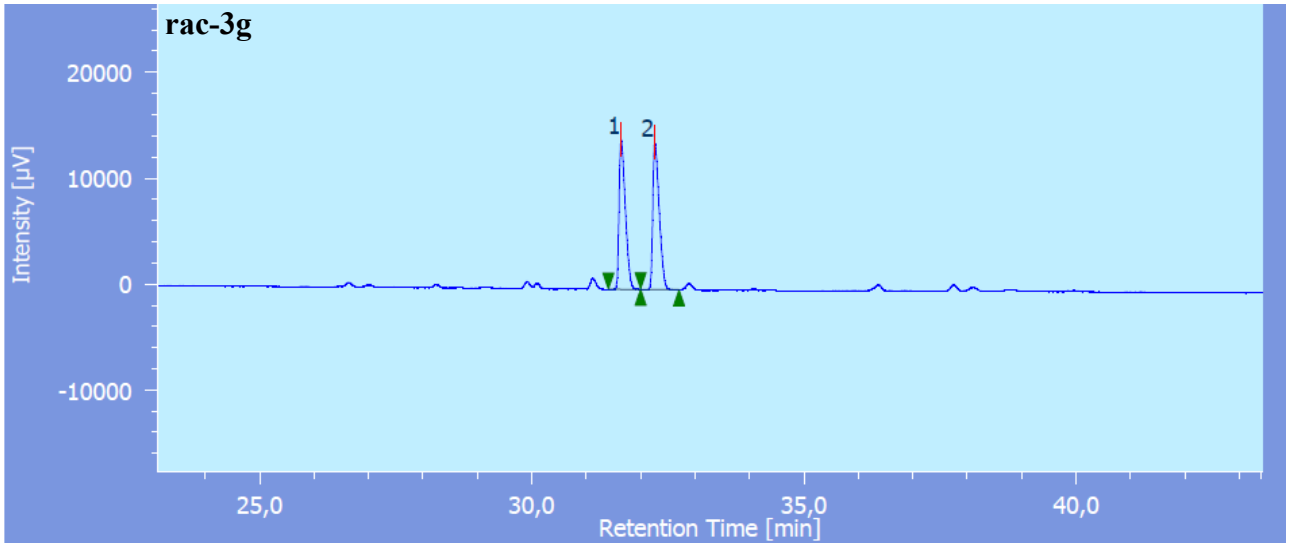
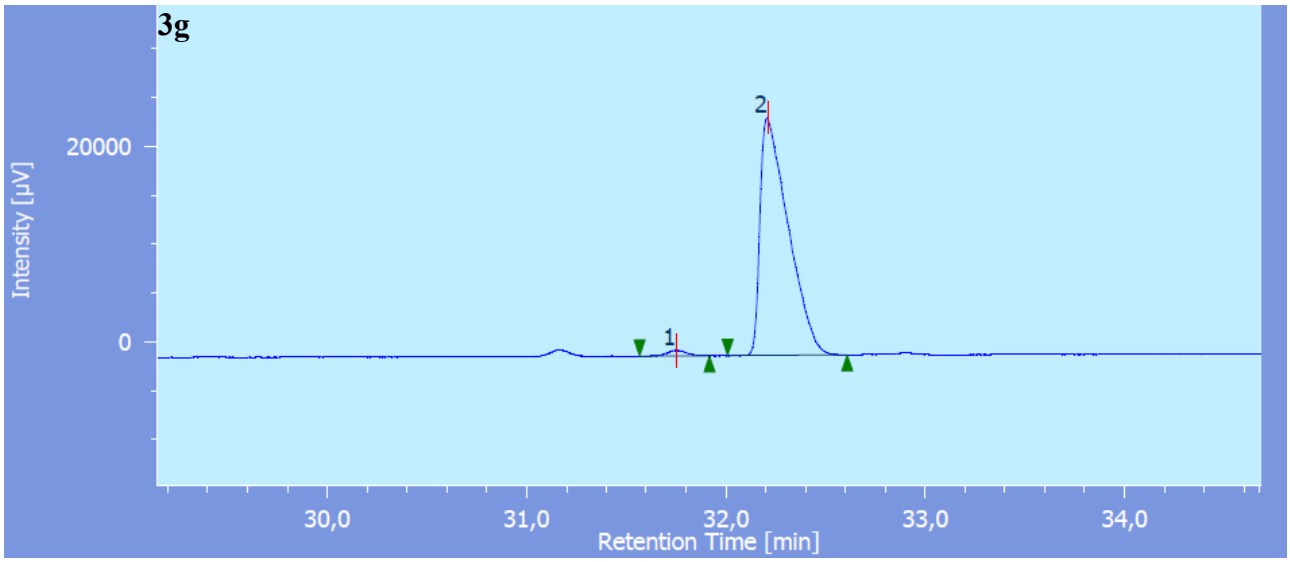
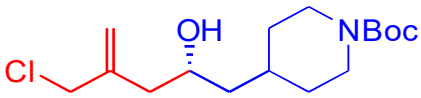
20
10



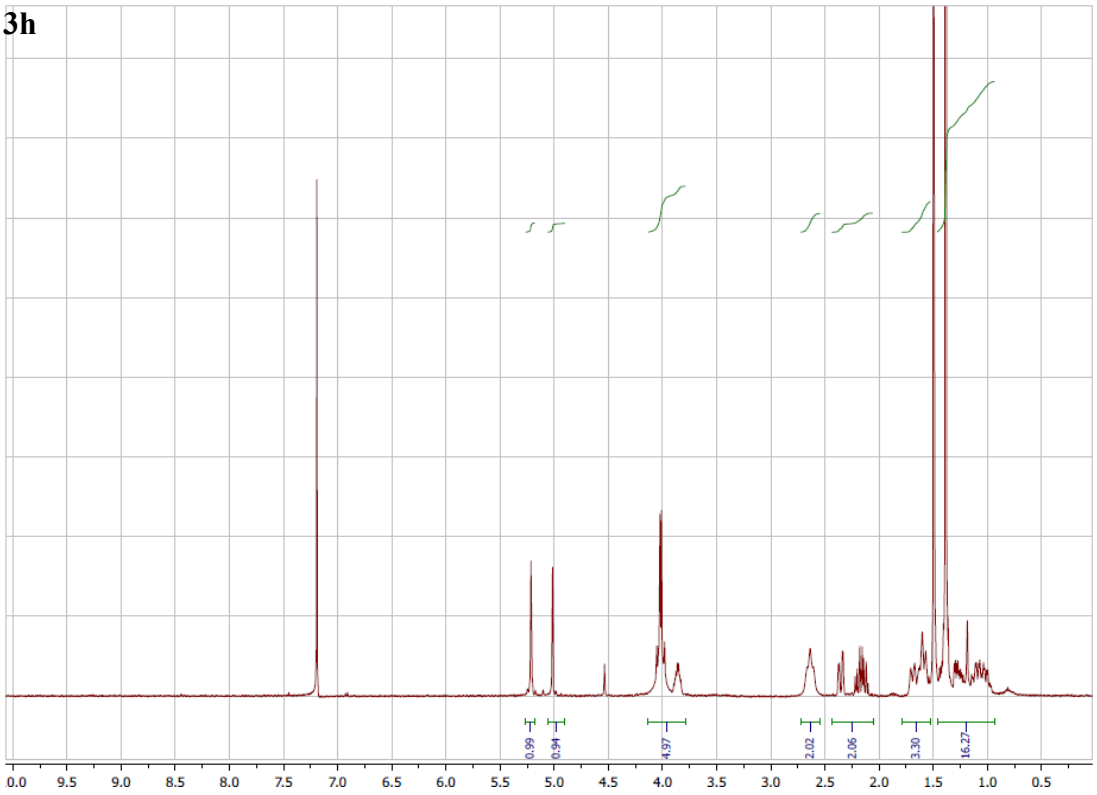
#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	31,642	112998	14137	50,039	50,421	N/A	359443	2,907	1,625	
2	Unknown	1	32,258	112819	13900	49,961	49,579	N/A	362555	N/A	1,715	



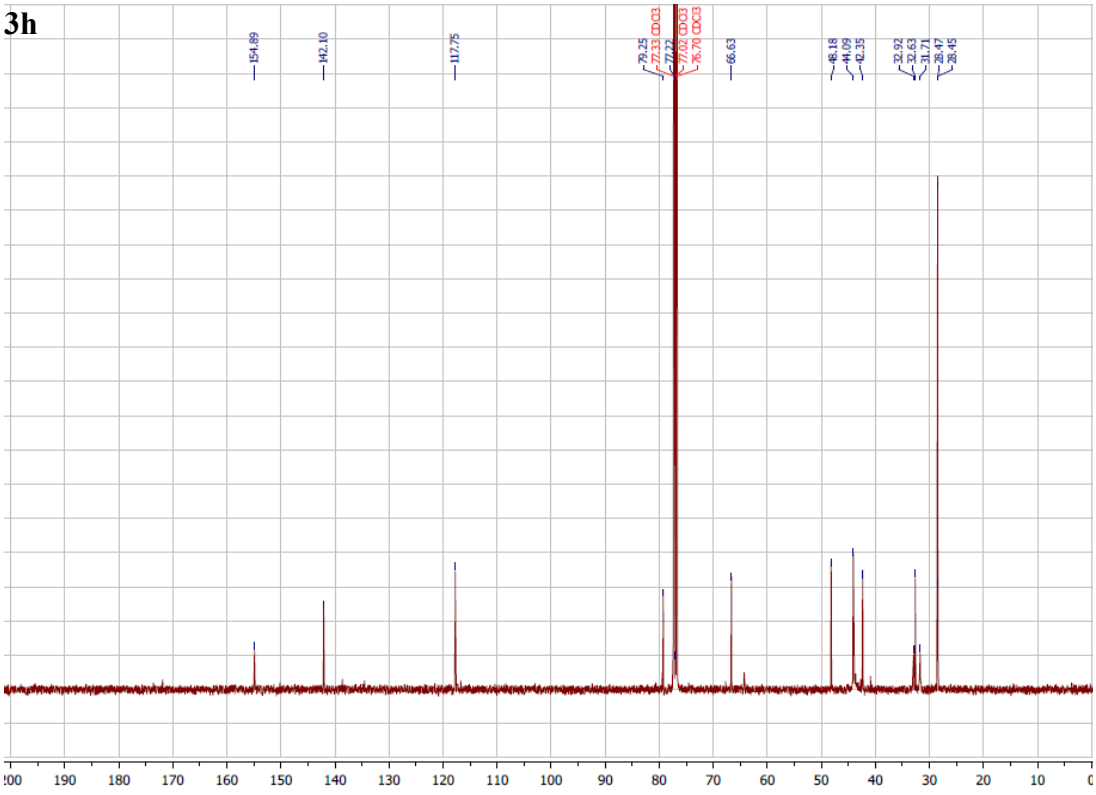
#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	31,750	3748	560	1,553	2,247	N/A	506210	2,084	1,071	
2	Unknown	1	32,208	237502	24343	98,447	97,753	N/A	240877	N/A	2,223	


OH
NBoc
Cl

3h


0.99
0.94
4.97
2.02
2.06
3.30
16.27
0.0 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

3h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79.25
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77.22
77.02 CDCl3
76.70 CDCl3
66.63
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44.09
42.35
32.92
32.63
31.71
28.47
28.45
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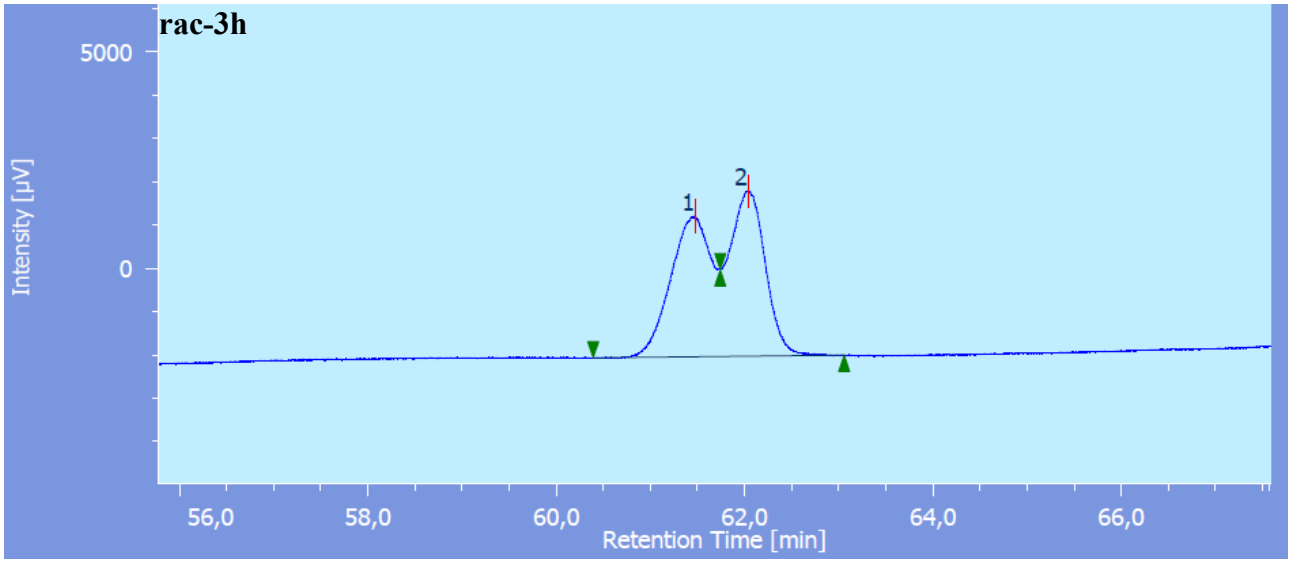
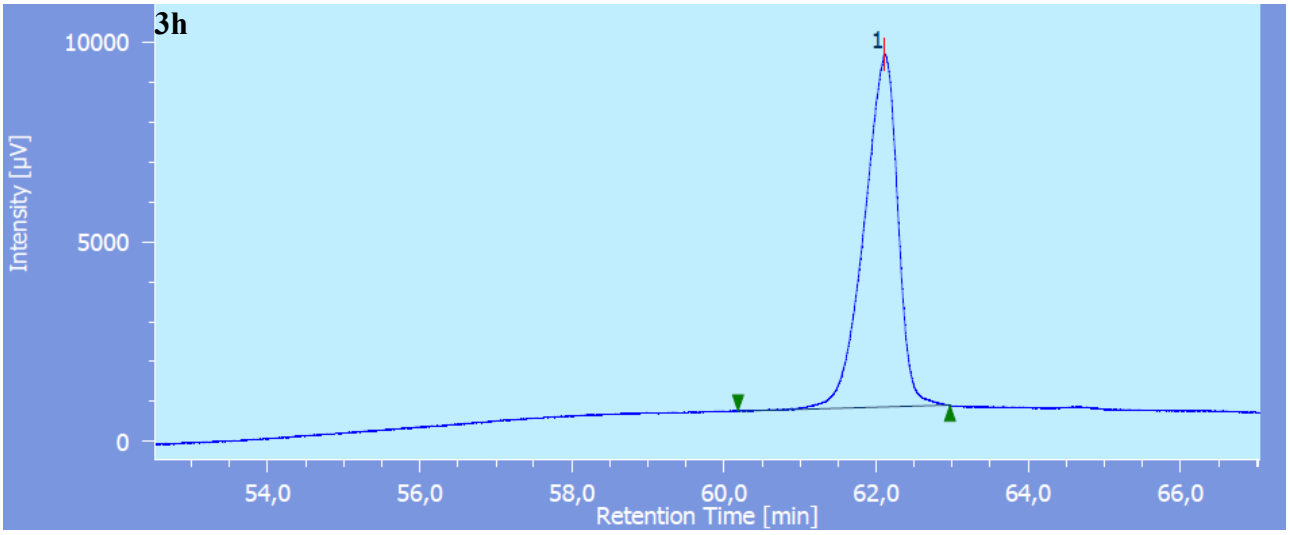
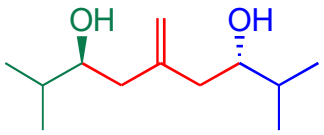


#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	61,475	98642	3250	49,405	46,046	N/A	N/A	N/A	N/A	
2	Unknown	1	62,033	101017	3809	50,595	53,954	N/A	N/A	N/A	N/A	



#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	62,108	270921	8829	100,000	100,000	N/A	98818	N/A	0,812	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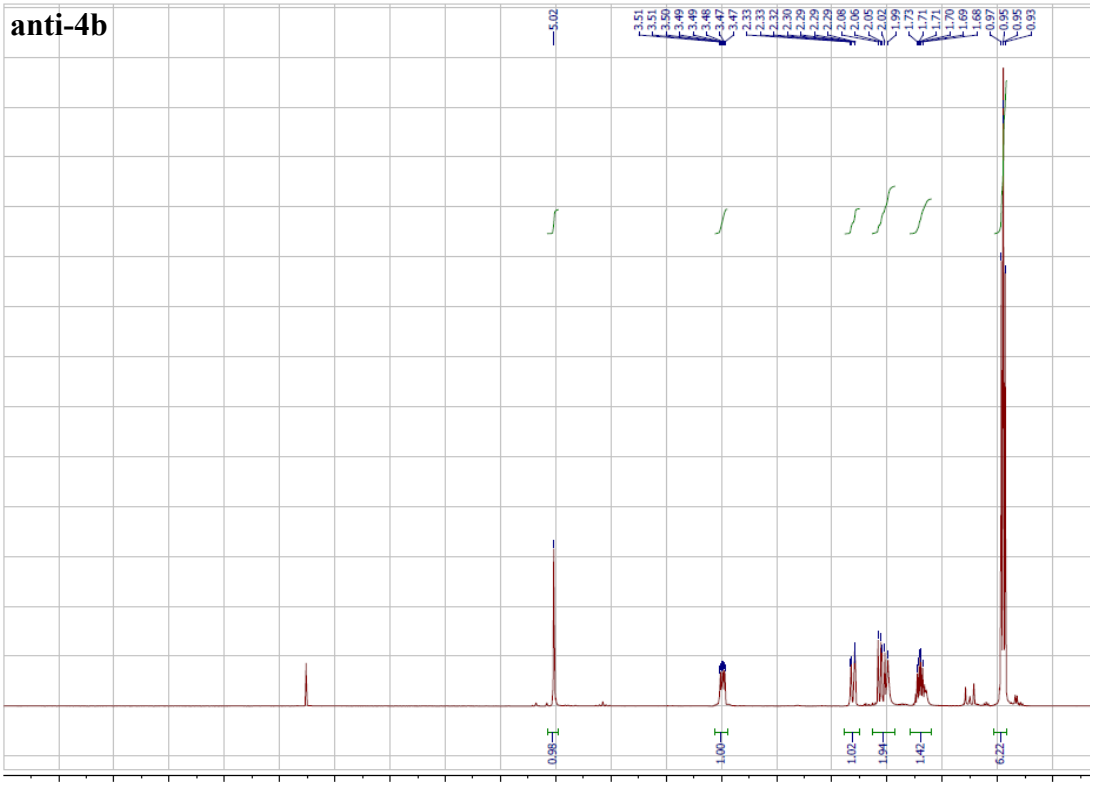
OH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5.02
3.51
3.51
3.50
3.49
3.49
3.48
3.47
3.47
2.33
2.33
2.32
2.30
2.29
2.29
2.29
2.08
2.06
2.05
2.02
1.99
1.73
1.71
1.71
1.70
1.69
1.69
1.07
0.95
0.95
0.93
0.98
1.00
1.02
1.94
1.42
6.22
9.5
9.0
8.5
8.0
7.5
7.0
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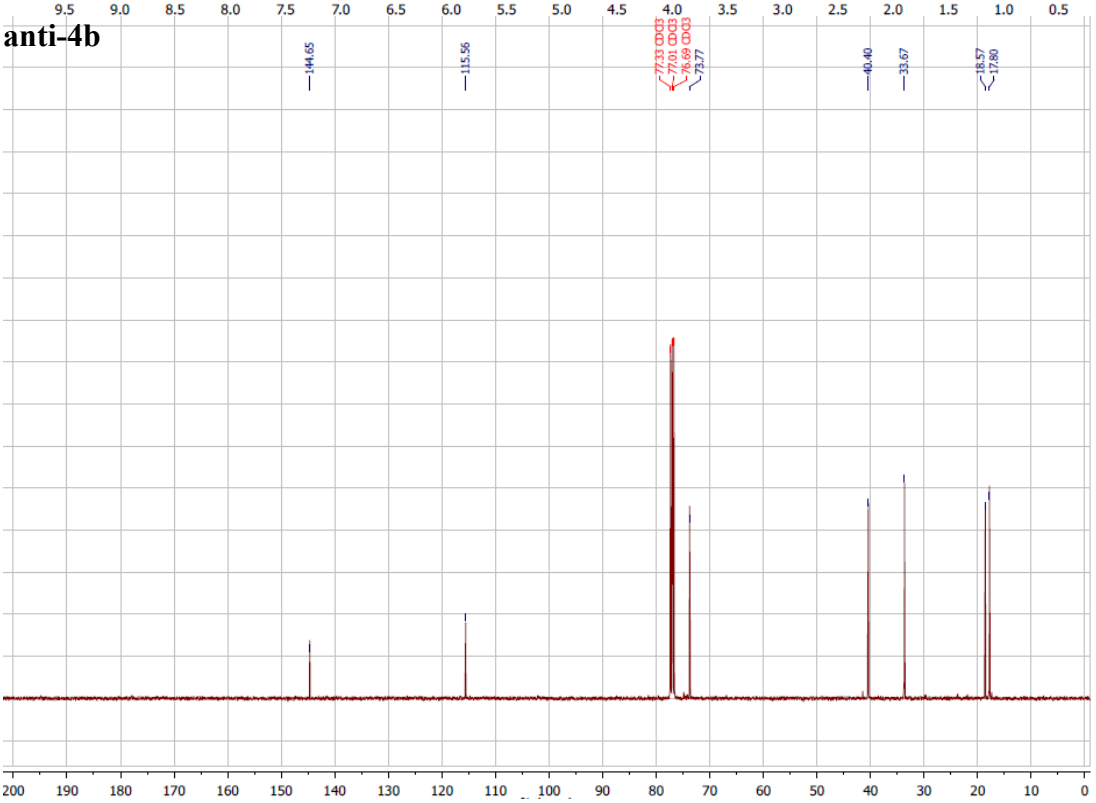
0.5


anti-4b
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77.01
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73.77
40.40
33.67
18.57
17.80
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150
140
130
120
110
100
90
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70
60
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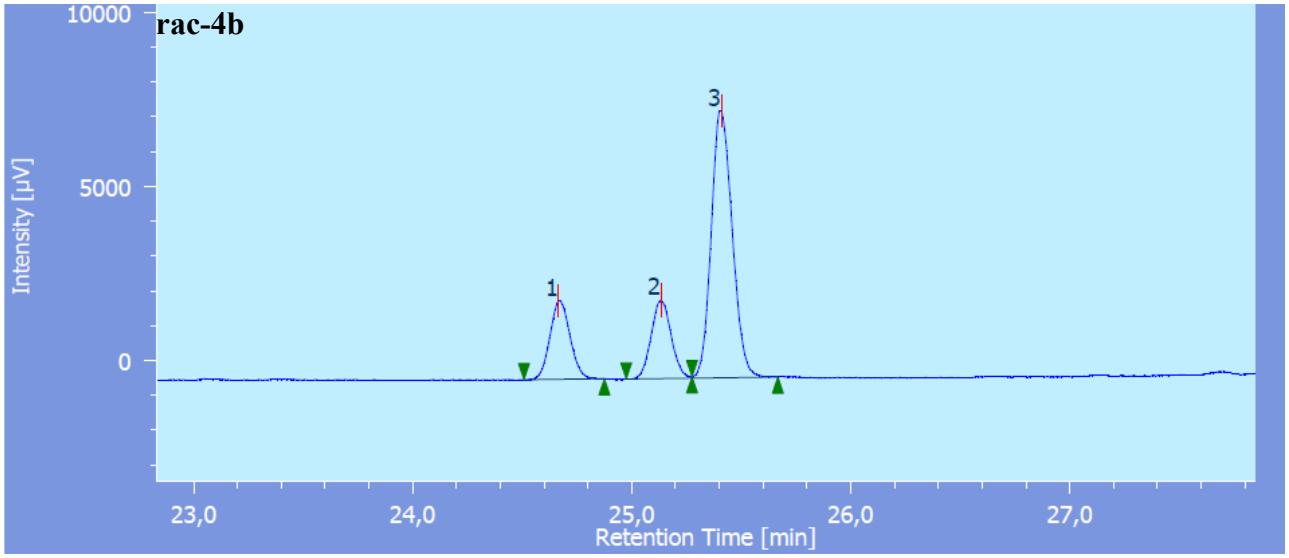
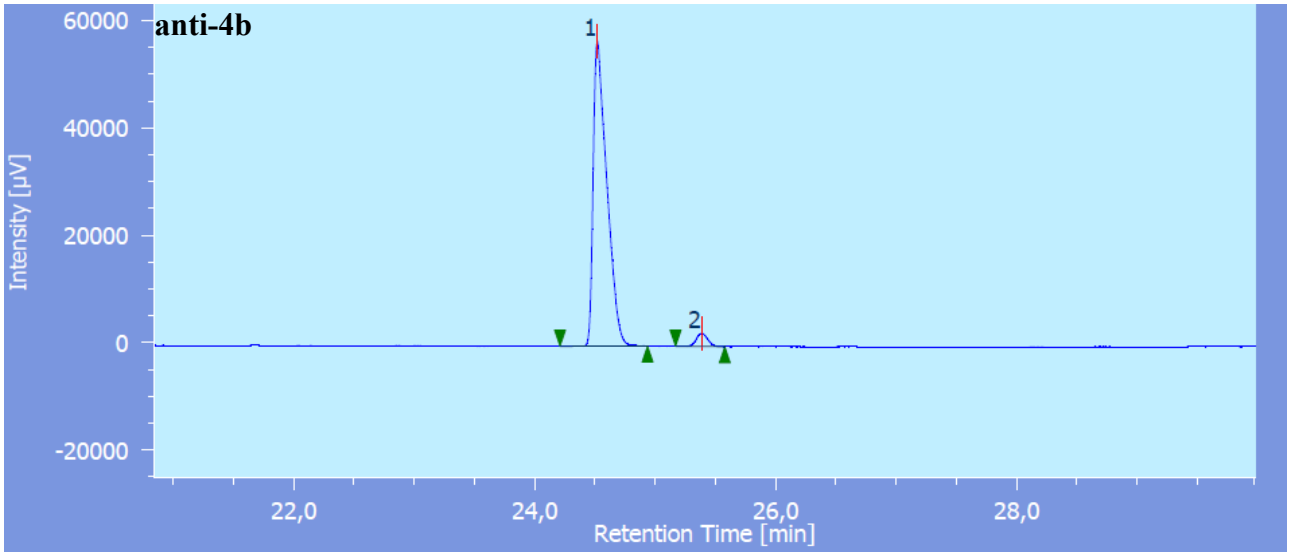
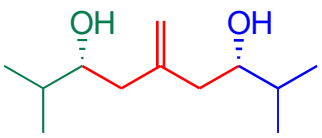
30
20
10
0

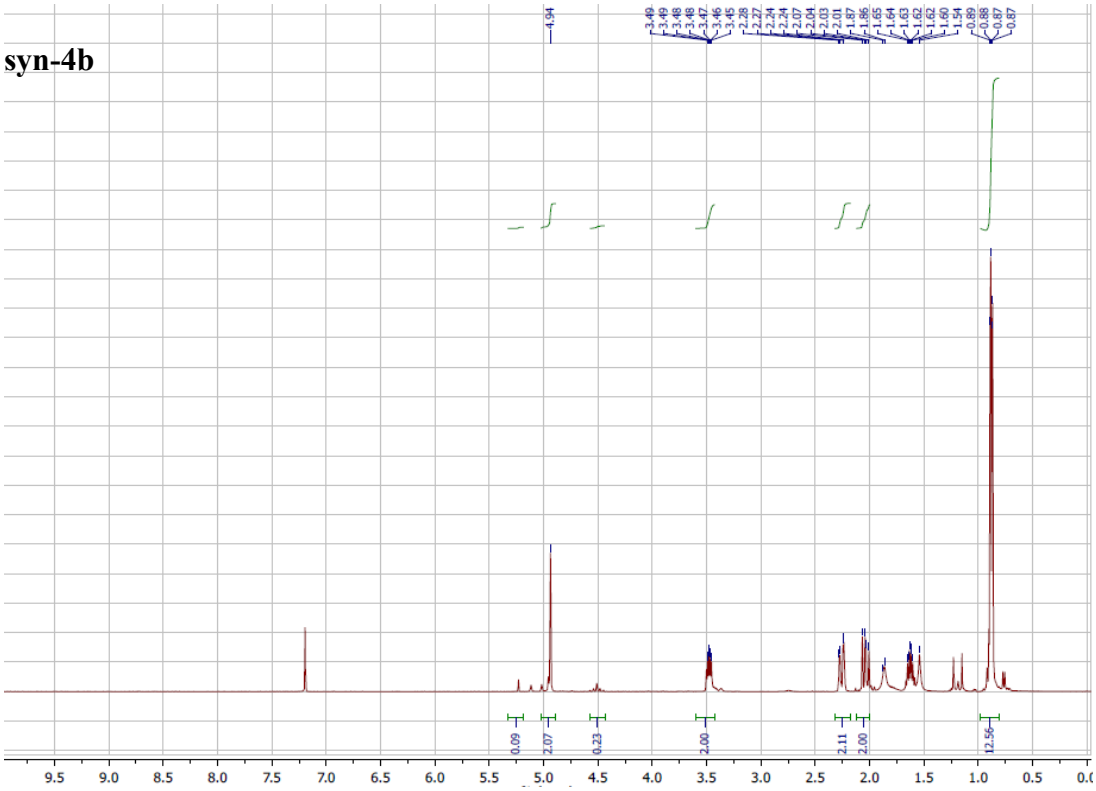




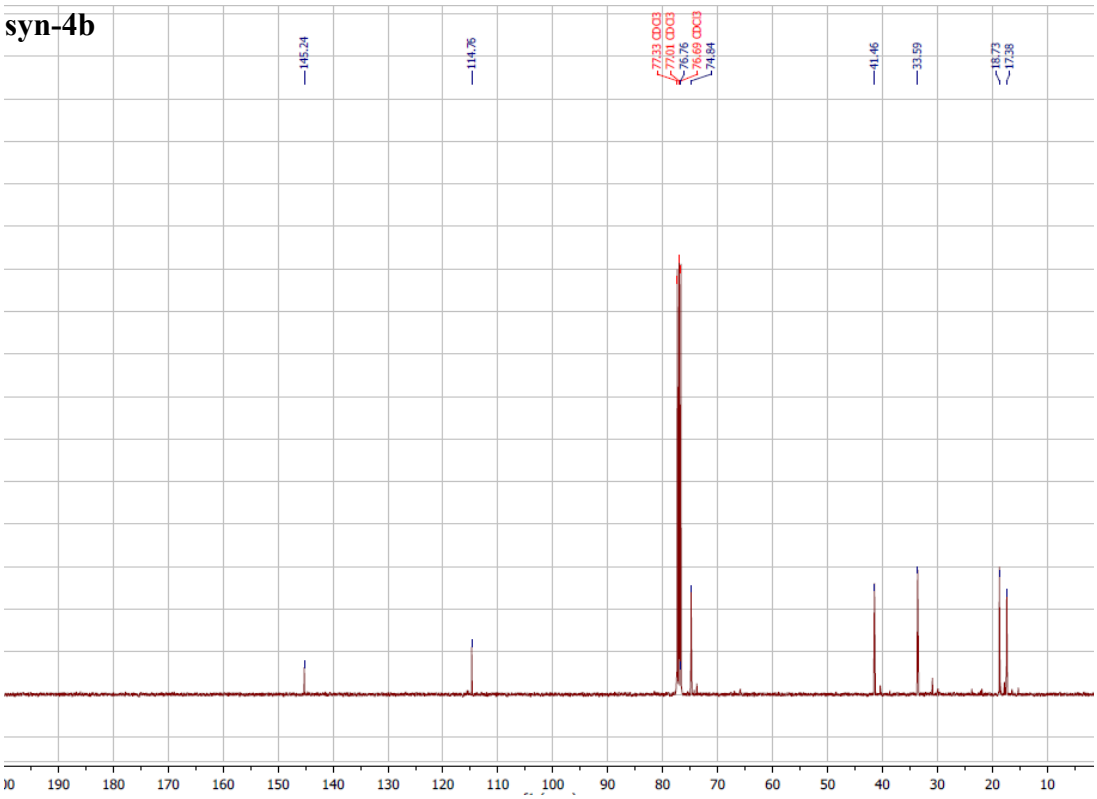
#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	24,517	445503	56800	96,559	95,905	N/A	218395	4,537	1,933	
2	Unknown	1	25,383	15877	2425	3,441	4,095	N/A	343853	N/A	1,091	

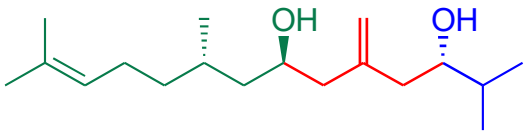


syn-4b

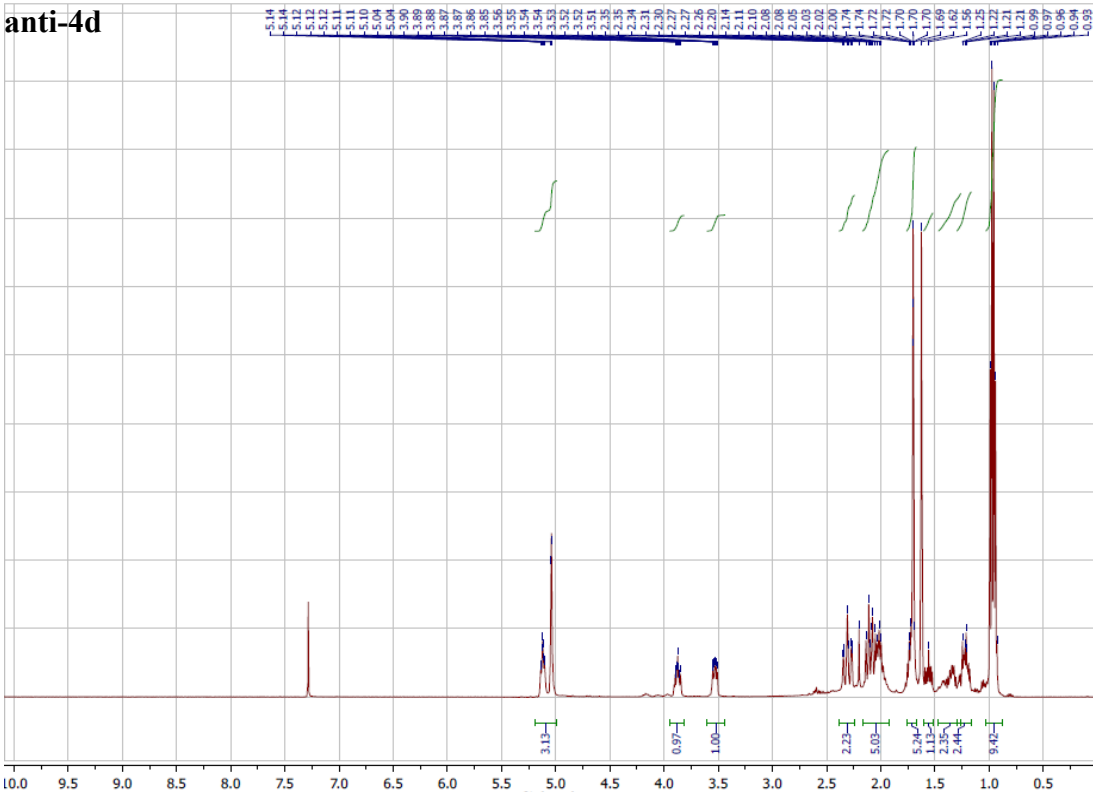


syn-4b

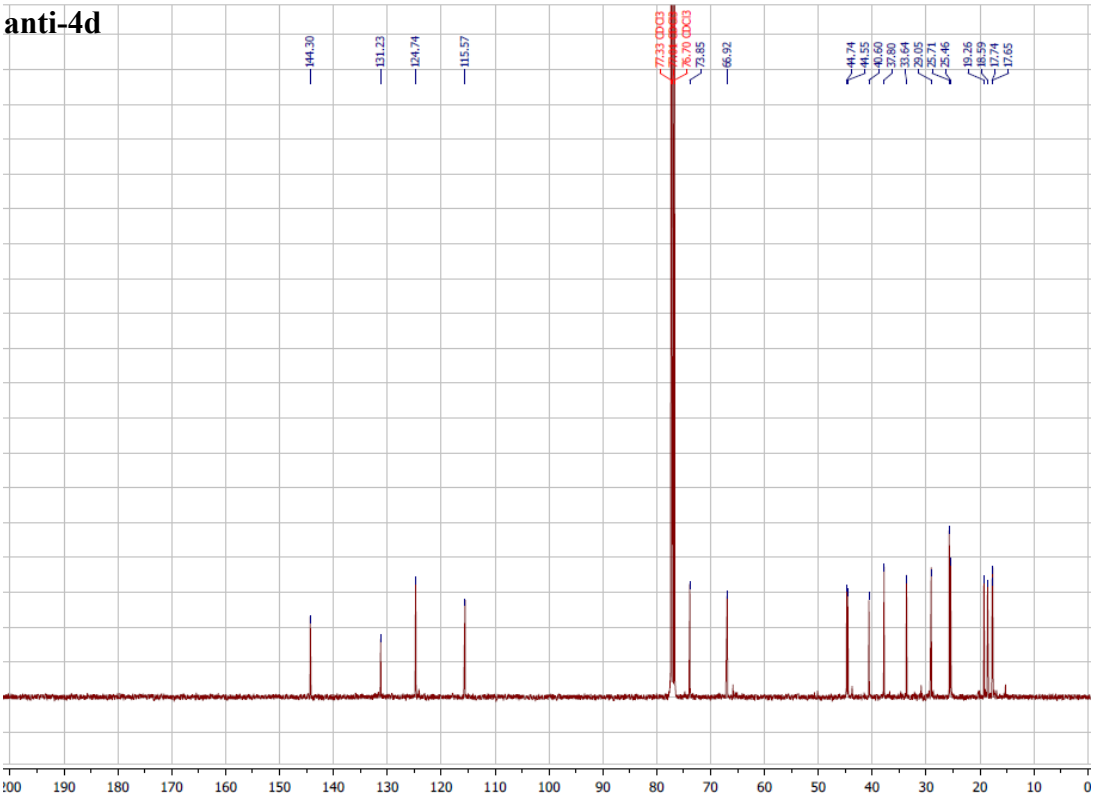


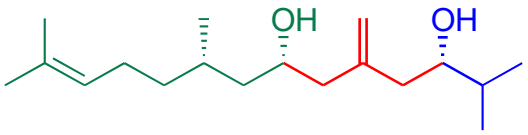


anti-4d



anti-4d

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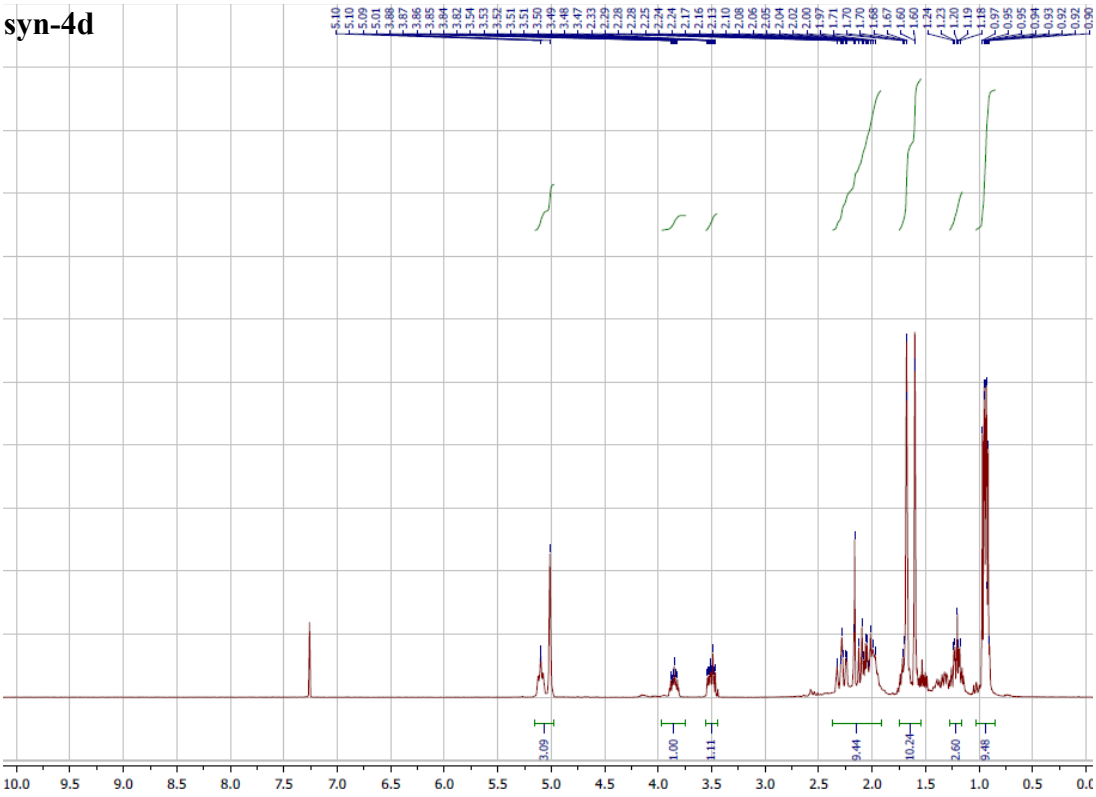
OH

syn-4d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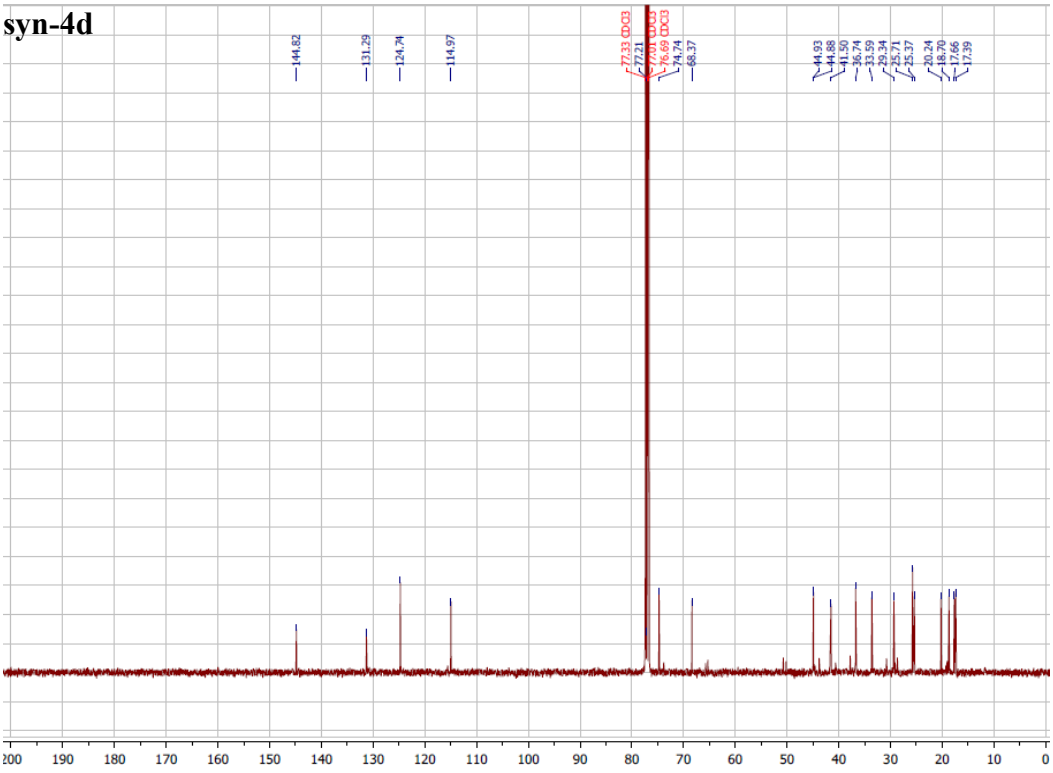
1.00
1.11
9.44
10.24
2.60
9.48
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5

syn-4d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124.74
114.97
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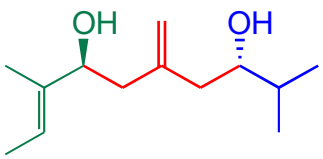
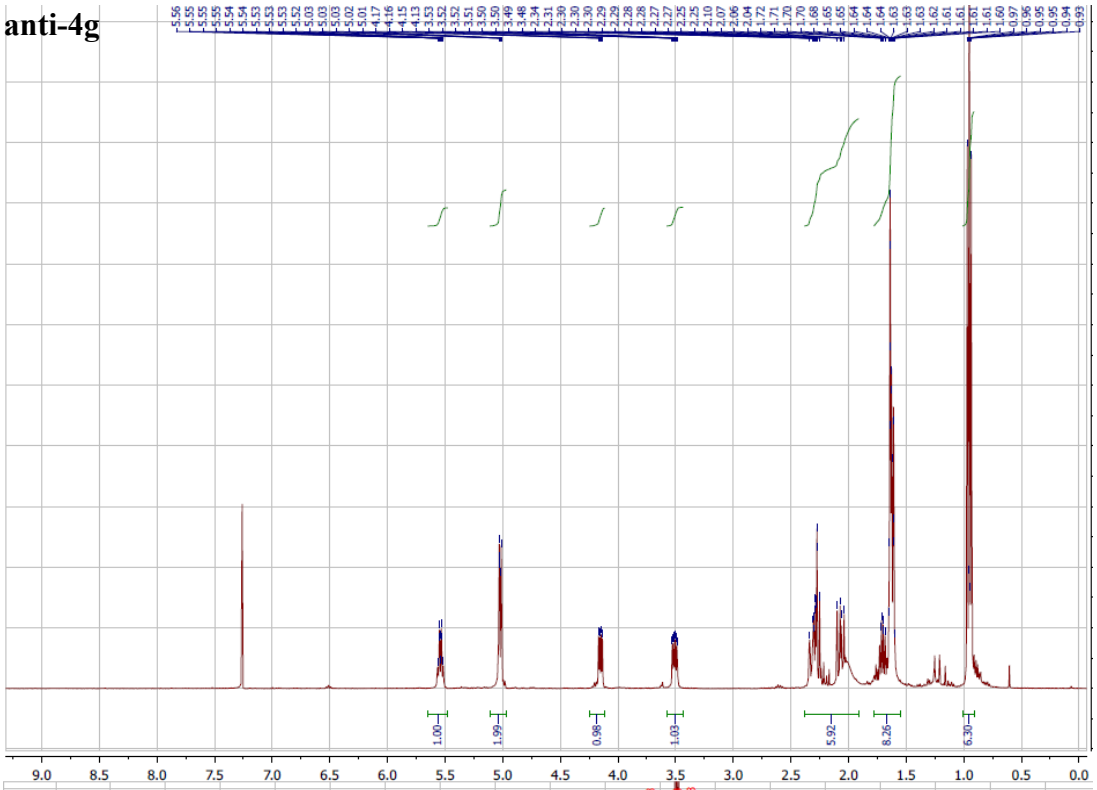
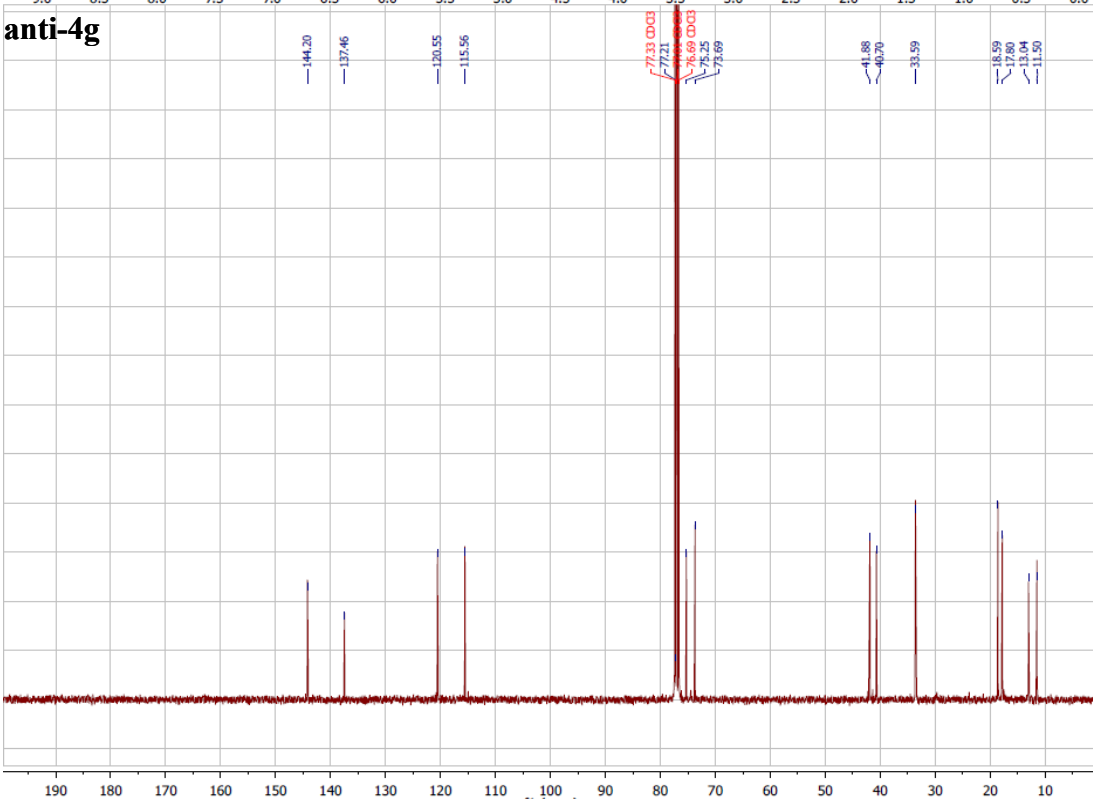
77.21
77.00 CDCl3
76.69 CDCl3
74.74
68.37
44.93
44.88
41.50
36.74
33.59
29.34
25.71
25.37
20.24
18.70
17.66
17.39
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

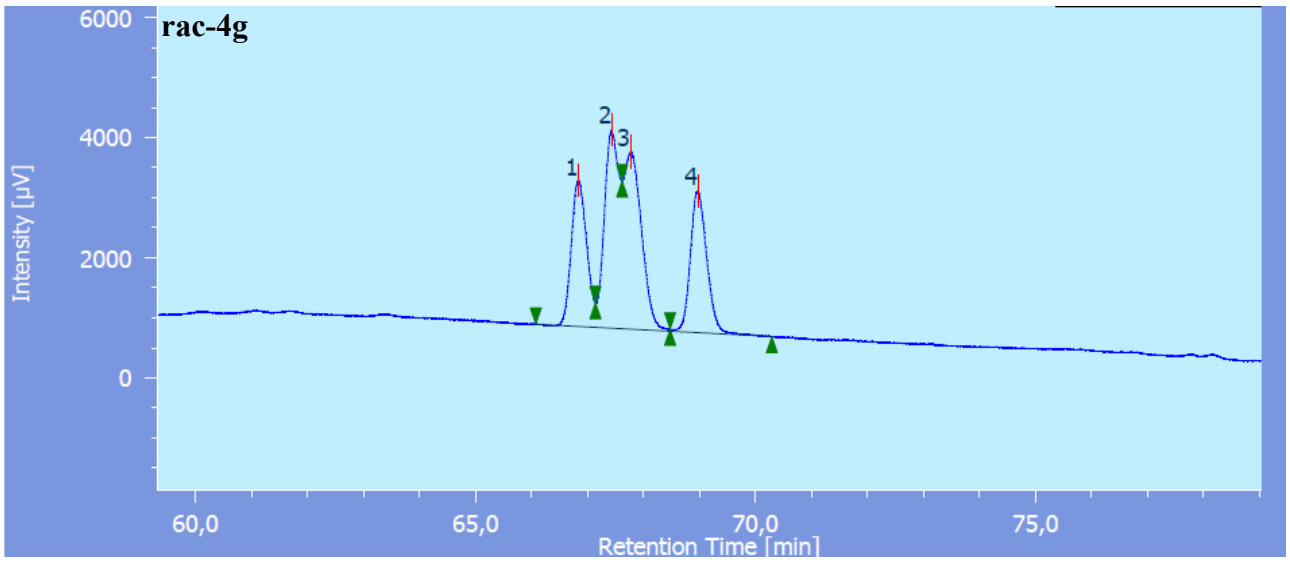


anti-4g

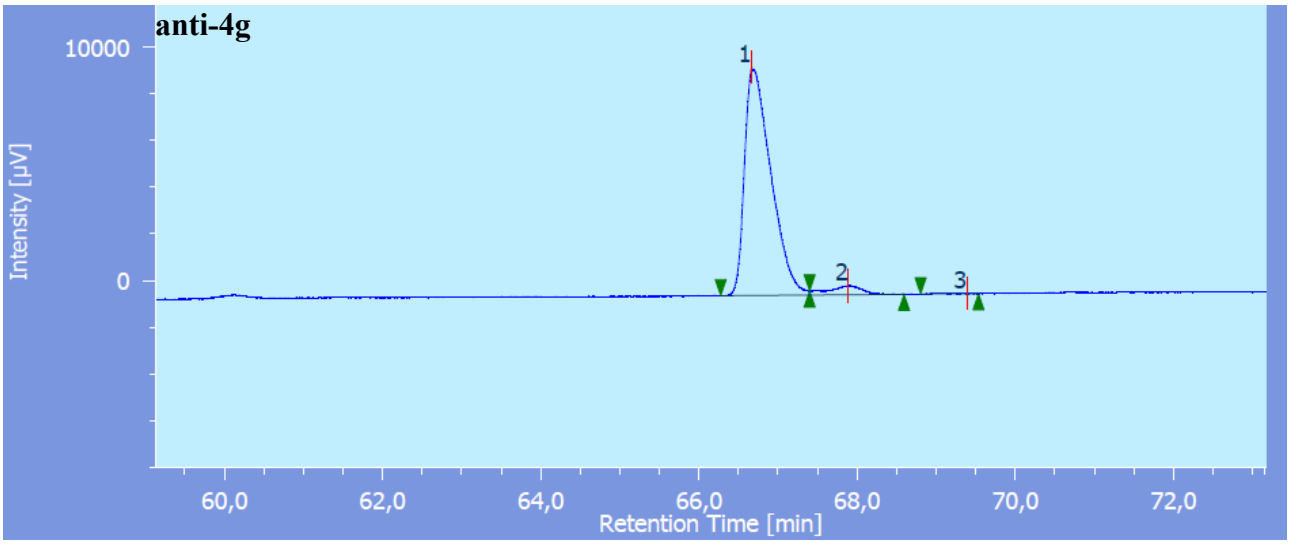


anti-4g

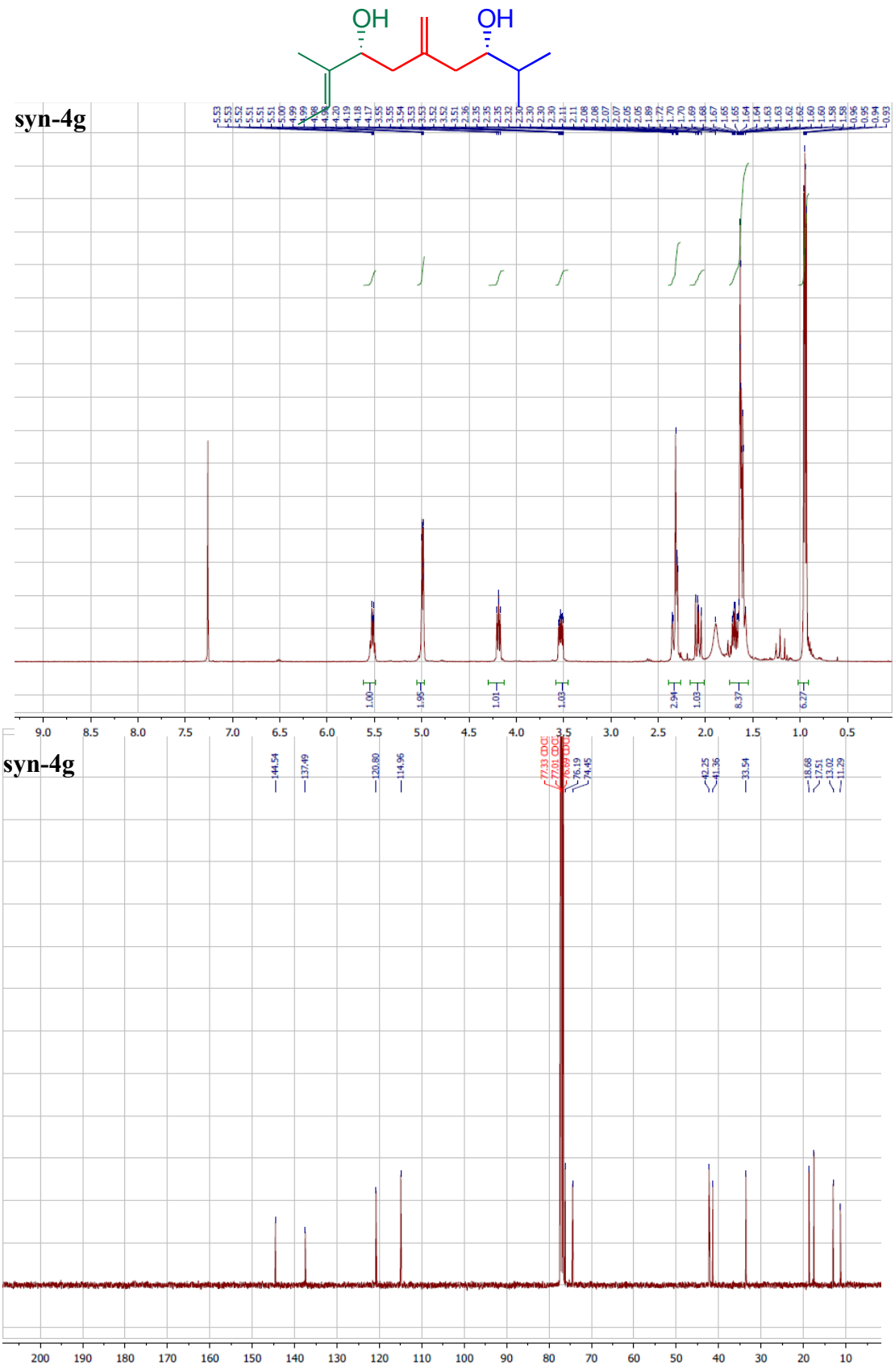


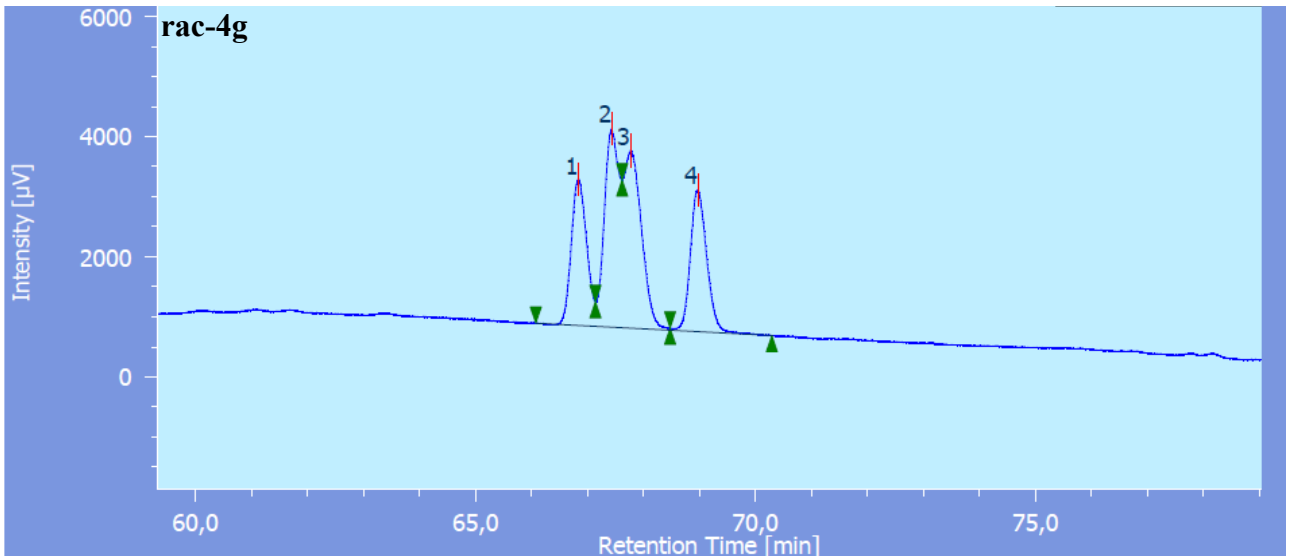


#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	66,842	46388	2433	20,917	22,008	N/A	271434	N/A	N/A	
2	Unknown	1	67,433	61812	3306	27,872	29,909	N/A	N/A	N/A	N/A	
3	Unknown	1	67,767	65583	2954	29,573	26,723	N/A	N/A	N/A	N/A	
4	Unknown	1	68,967	47984	2361	21,637	21,360	N/A	275332	N/A	1,176	

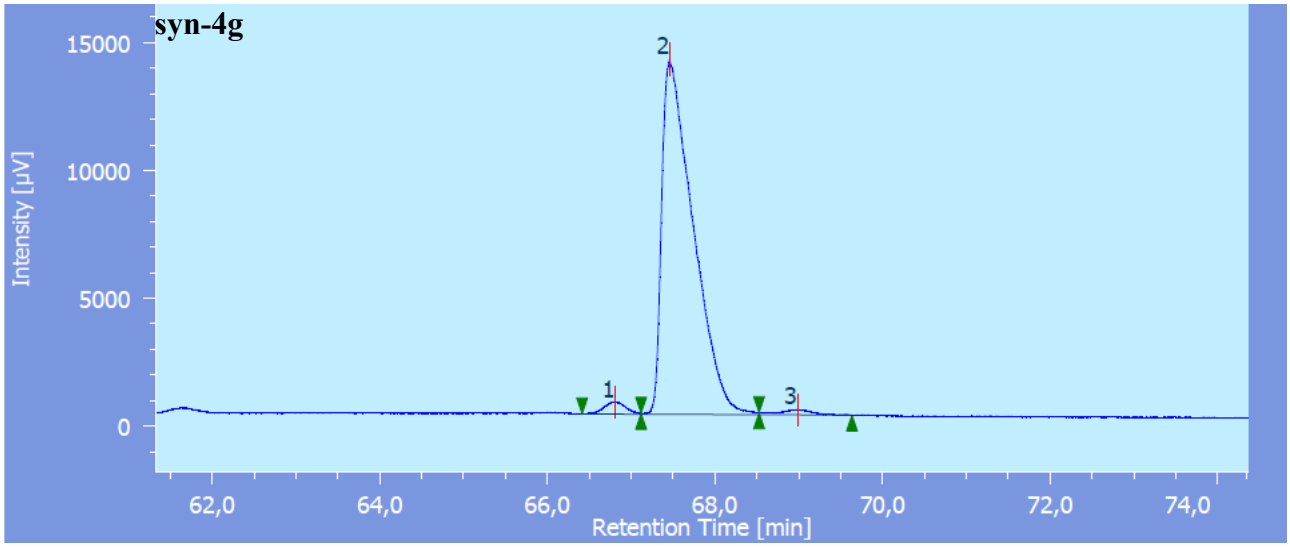


#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	66,667	225207	9759	95,045	96,057	N/A	193186	1,820	1,880	
2	Unknown	1	67,892	11583	388	4,888	3,820	N/A	133478	1,858	N/A	
3	Unknown	1	69,392	158	13	0,067	0,123	N/A	100546	N/A	0,636	

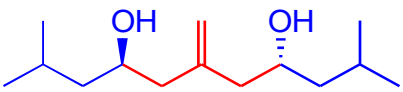

OH
OH
syn-4g
syn-4g



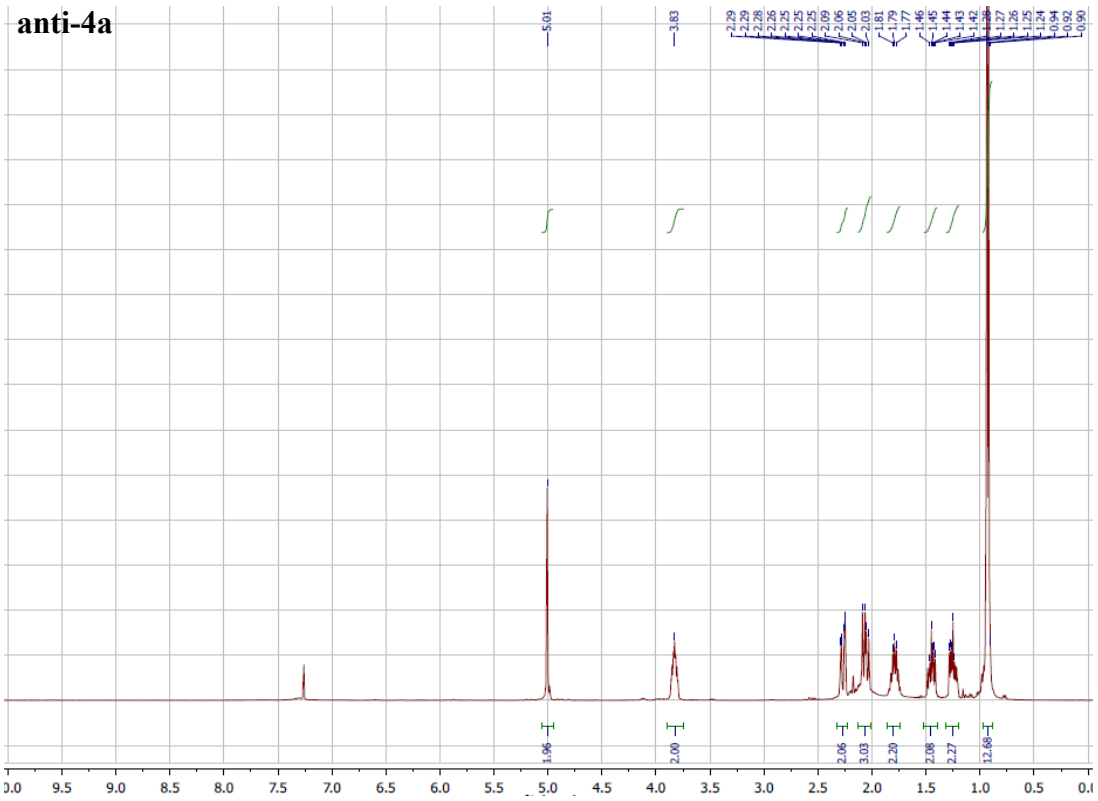
#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	66,842	46388	2433	20,917	22,008	N/A	271434	N/A	N/A	
2	Unknown	1	67,433	61812	3306	27,872	29,909	N/A	N/A	N/A	N/A	
3	Unknown	1	67,767	65583	2954	29,573	26,723	N/A	N/A	N/A	N/A	
4	Unknown	1	68,967	47984	2361	21,637	21,360	N/A	275332	N/A	1,176	



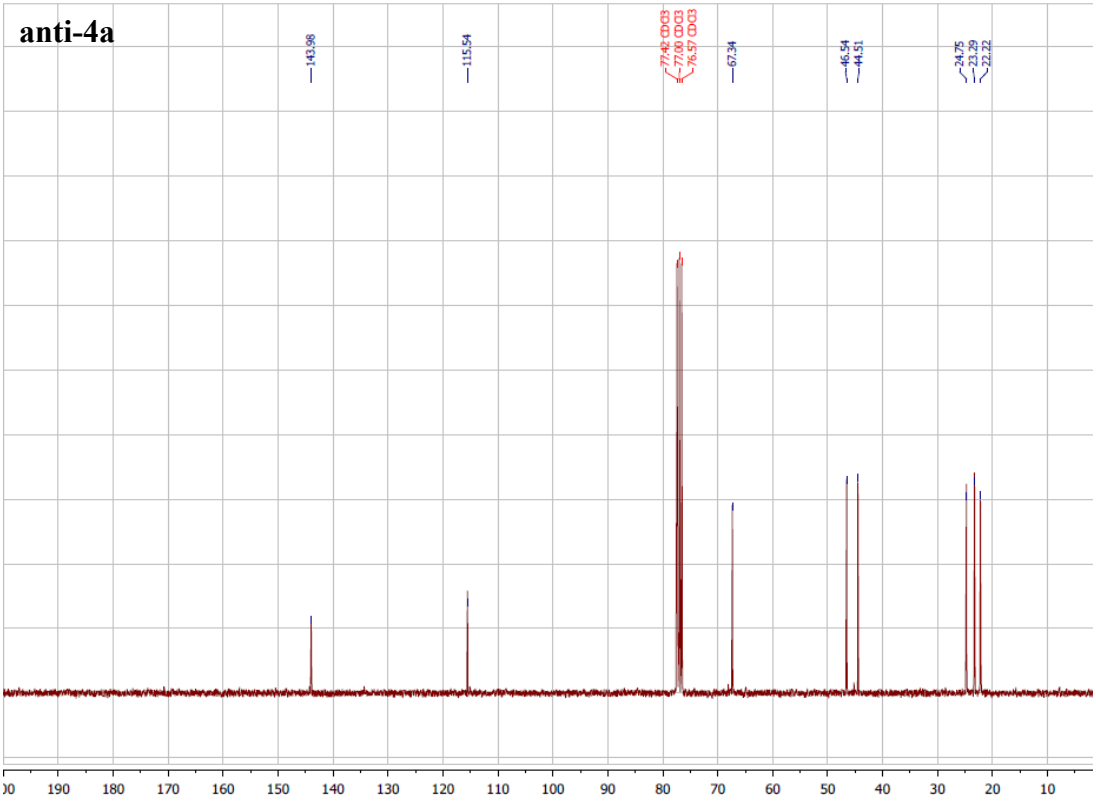
#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	66,817	8543	476	2,290	3,272	N/A	316556	1,104	N/A	
2	Unknown	1	67,458	358998	13866	96,251	95,356	N/A	152859	2,291	2,354	
3	Unknown	1	68,983	5441	200	1,459	1,372	N/A	183196	N/A	N/A	

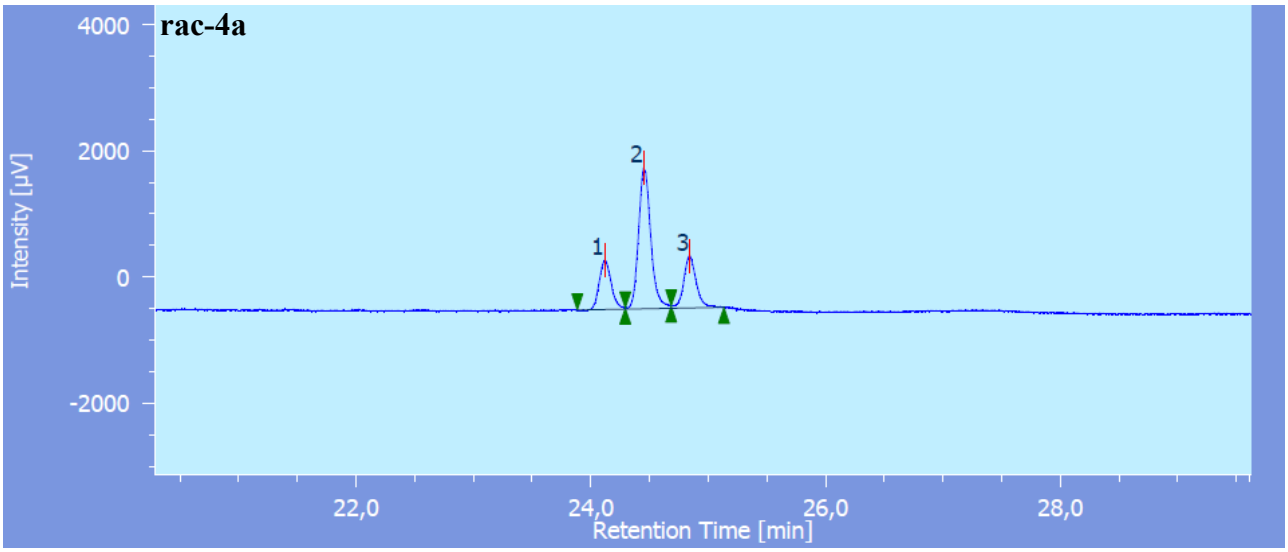


anti-4a

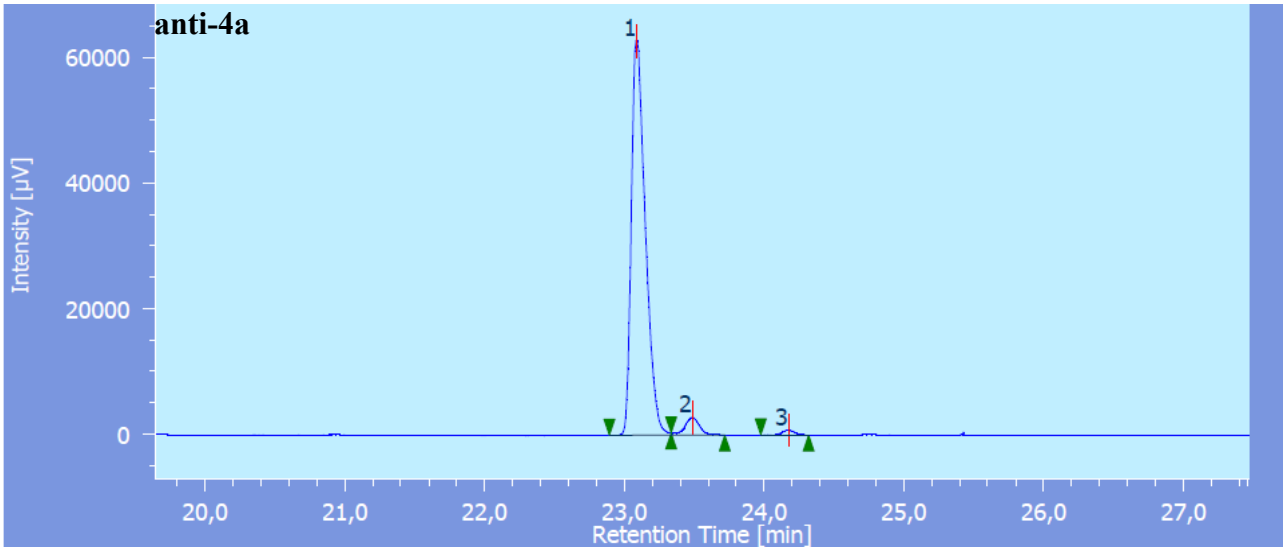


anti-4a

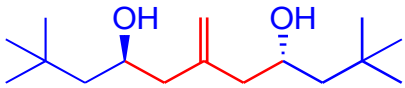




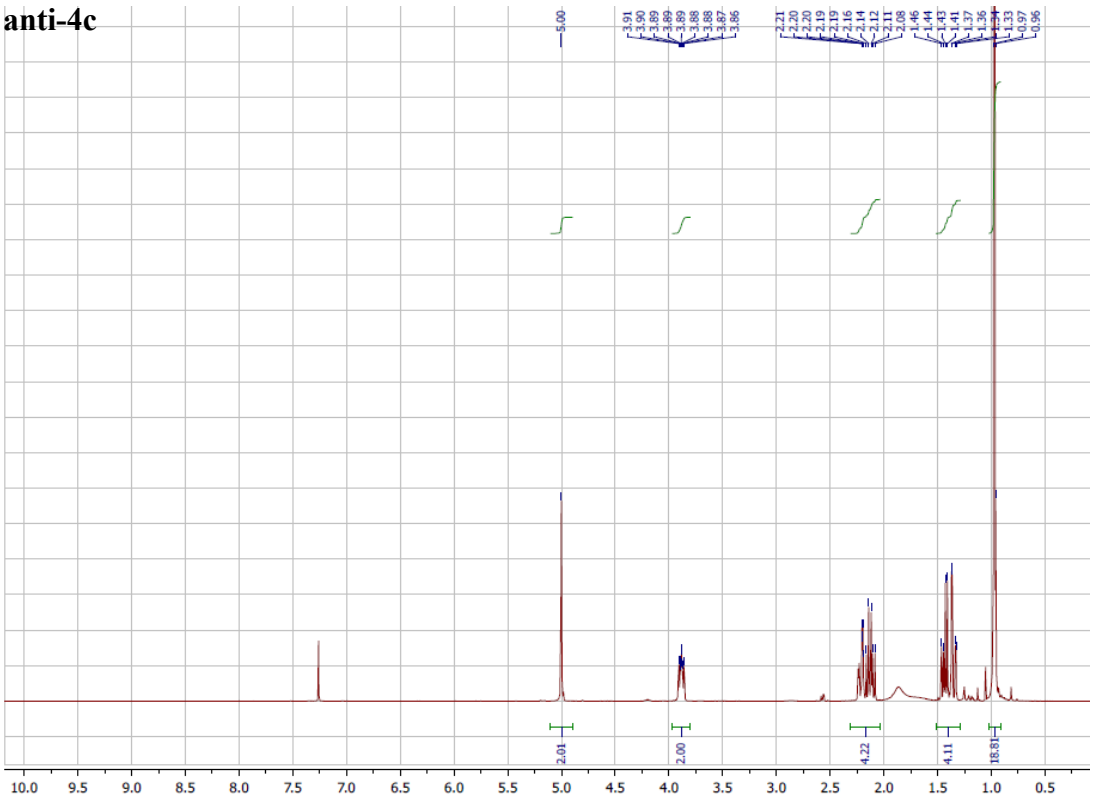
#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	24,117	5506	779	19,903	20,339	N/A	272526	1,824	1,242	
2	Unknown	1	24,450	16096	2228	58,186	58,187	N/A	289922	2,156	1,248	
3	Unknown	1	24,842	6061	822	21,910	21,474	N/A	295942	N/A	1,057	



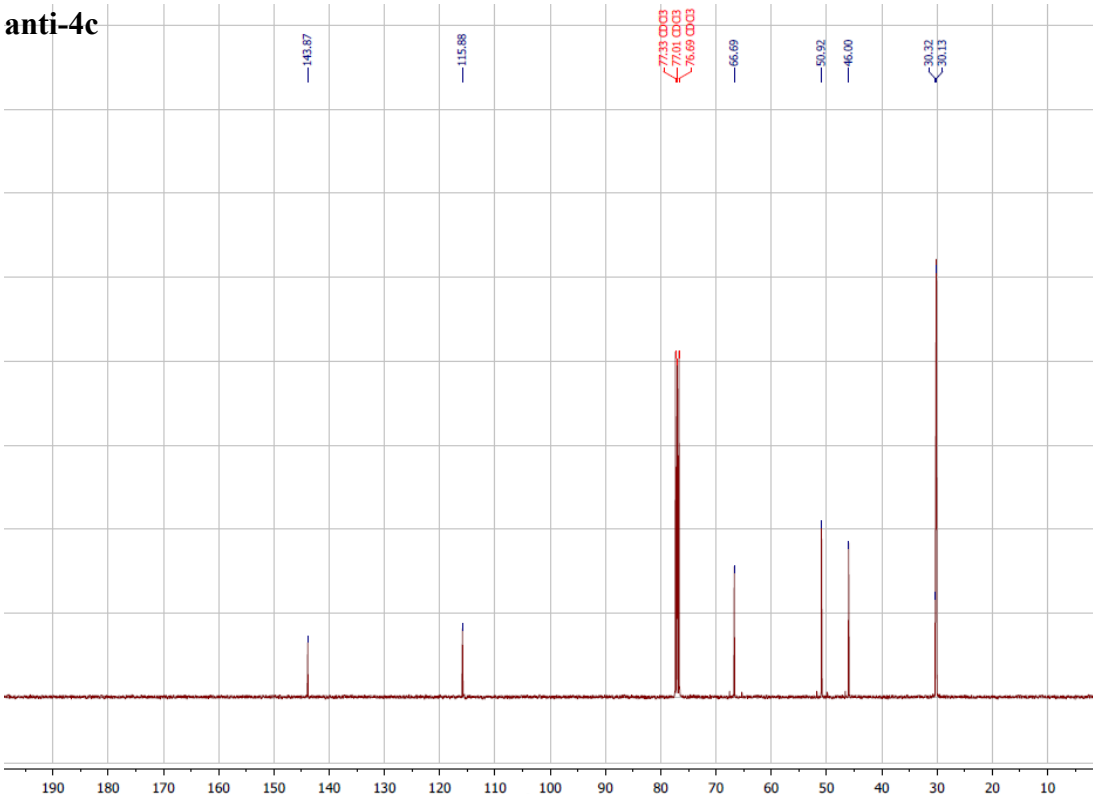
#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	23,092	438713	62747	94,595	94,650	N/A	255273	2,147	1,407	
2	Unknown	1	23,483	20367	2783	4,391	4,198	N/A	263670	4,001	N/A	
3	Unknown	1	24,175	4701	764	1,014	1,152	N/A	348710	N/A	1,036	



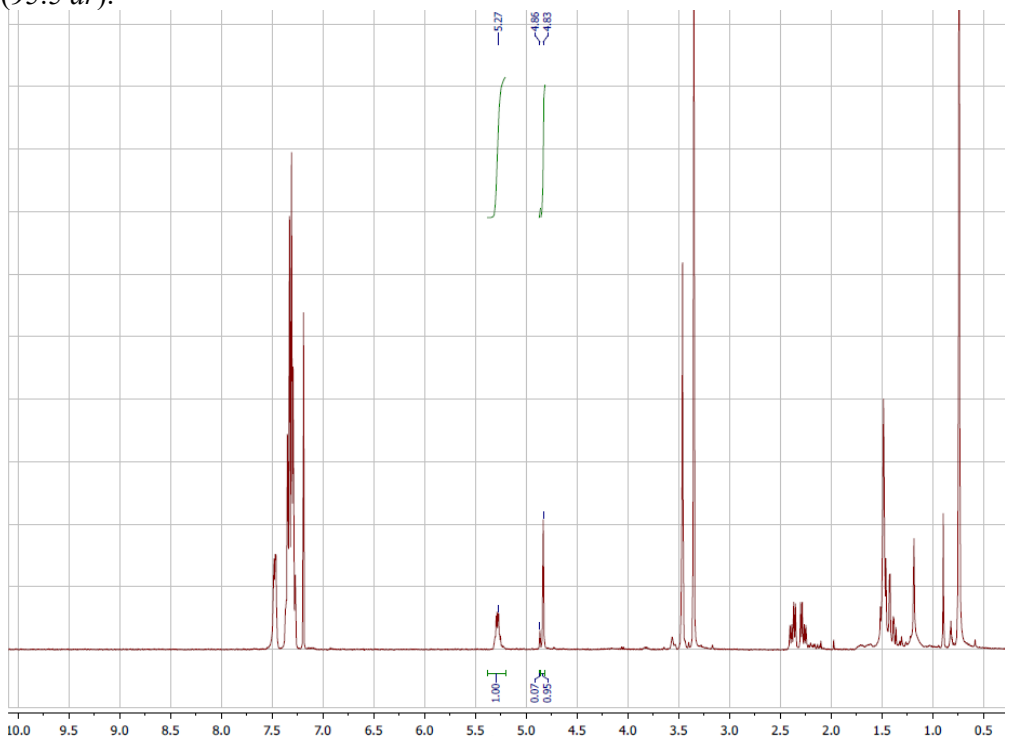
anti-4c

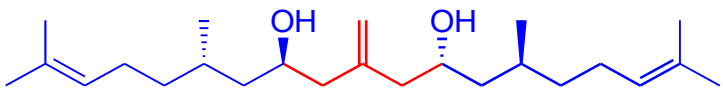


anti-4c

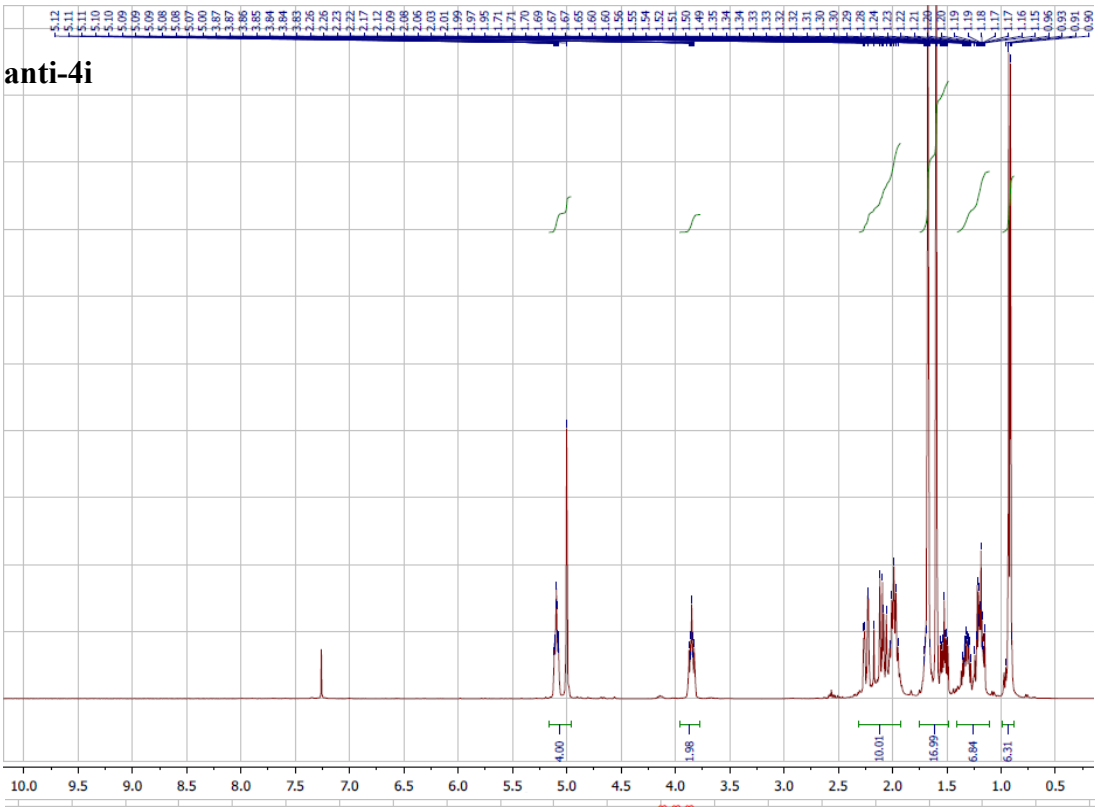


Mosher ester (95:5 *dr*):

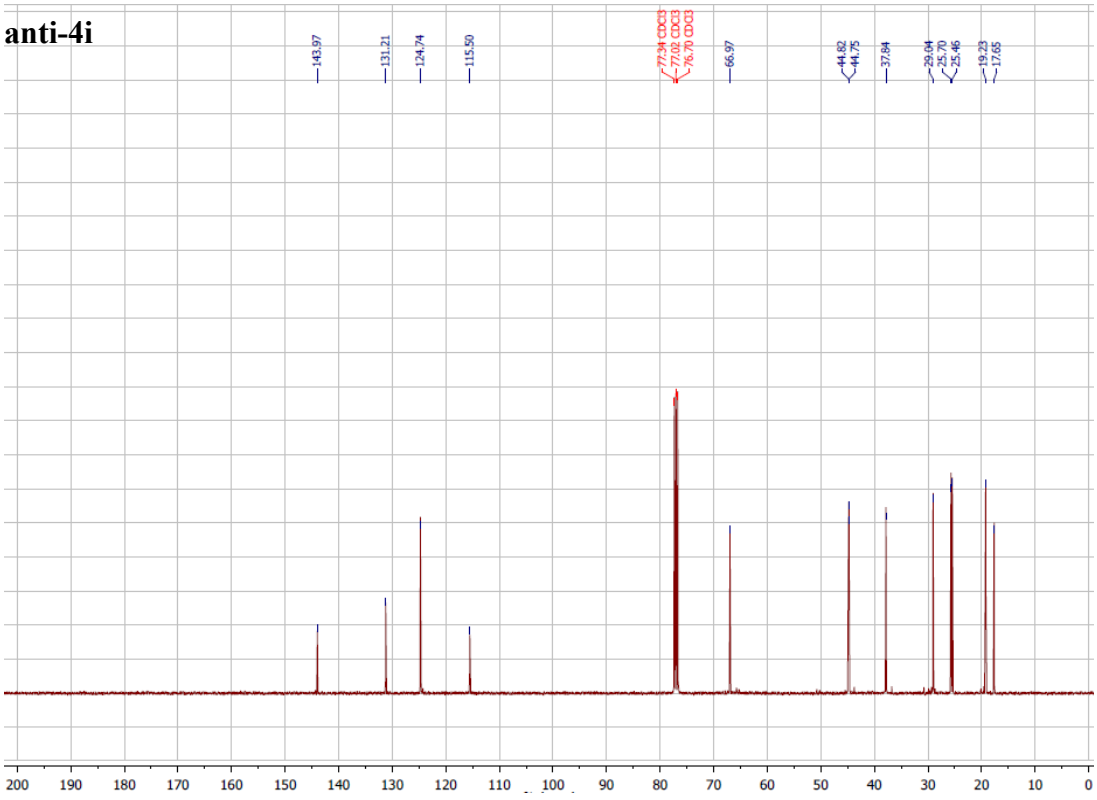


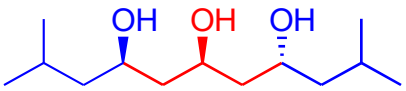


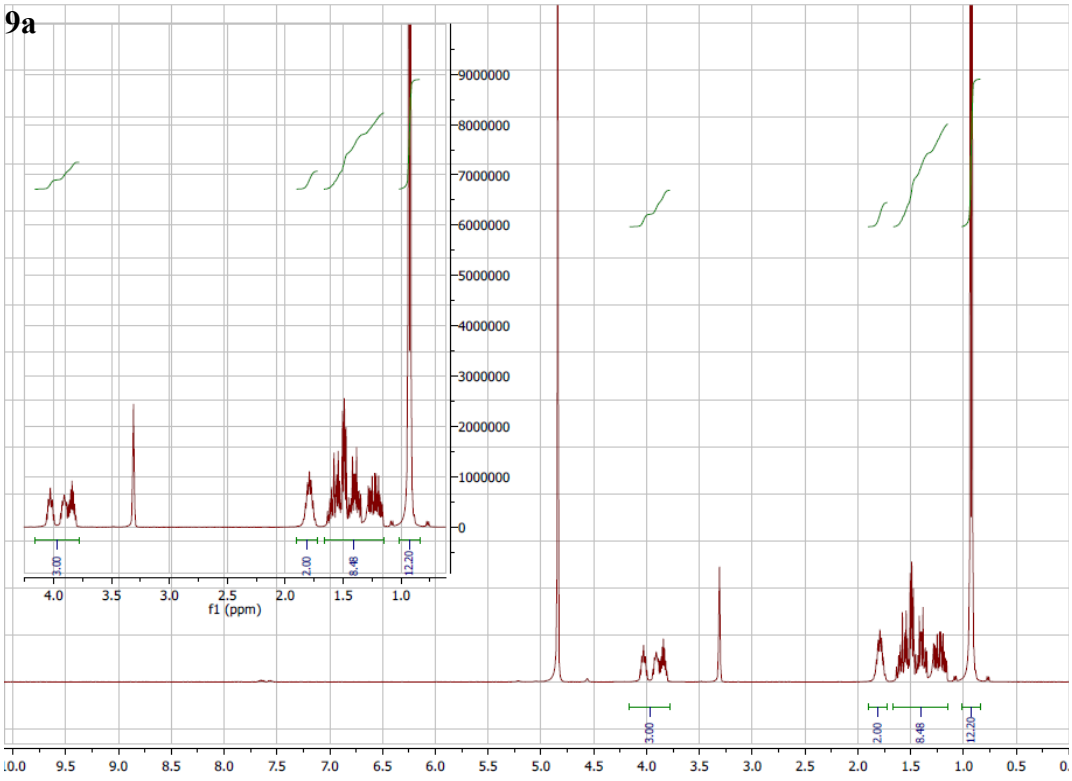
anti-4i

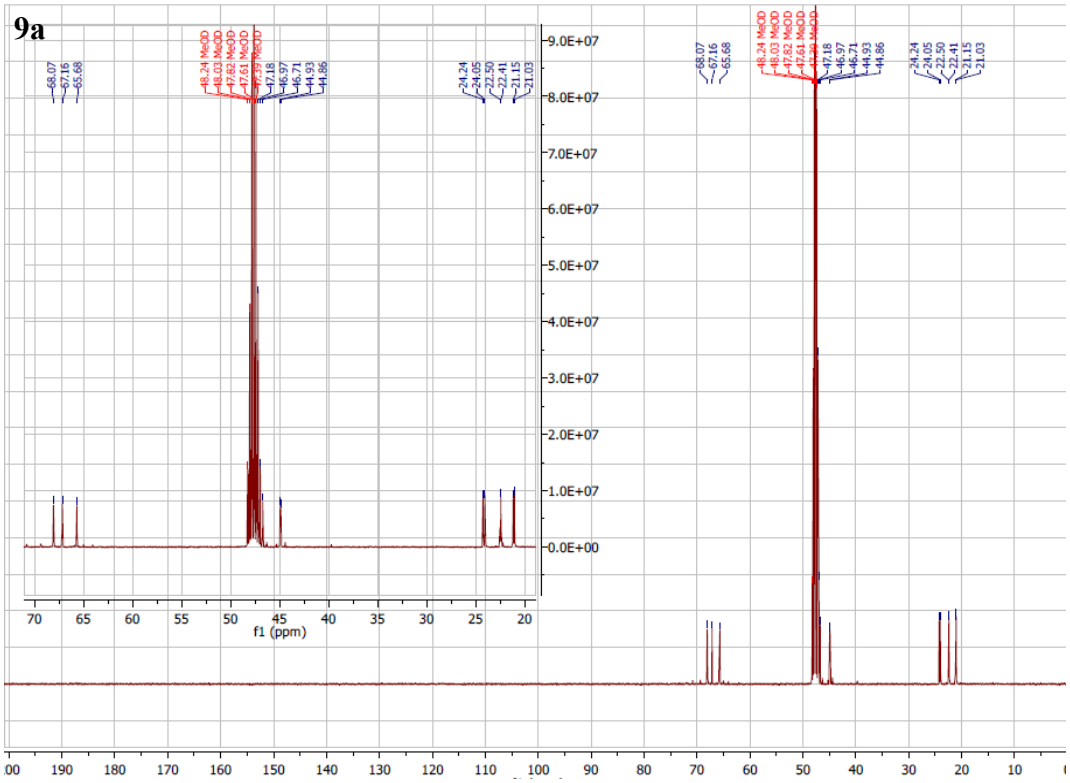


anti-4i




OH
OH
OH


9a
f1 (ppm)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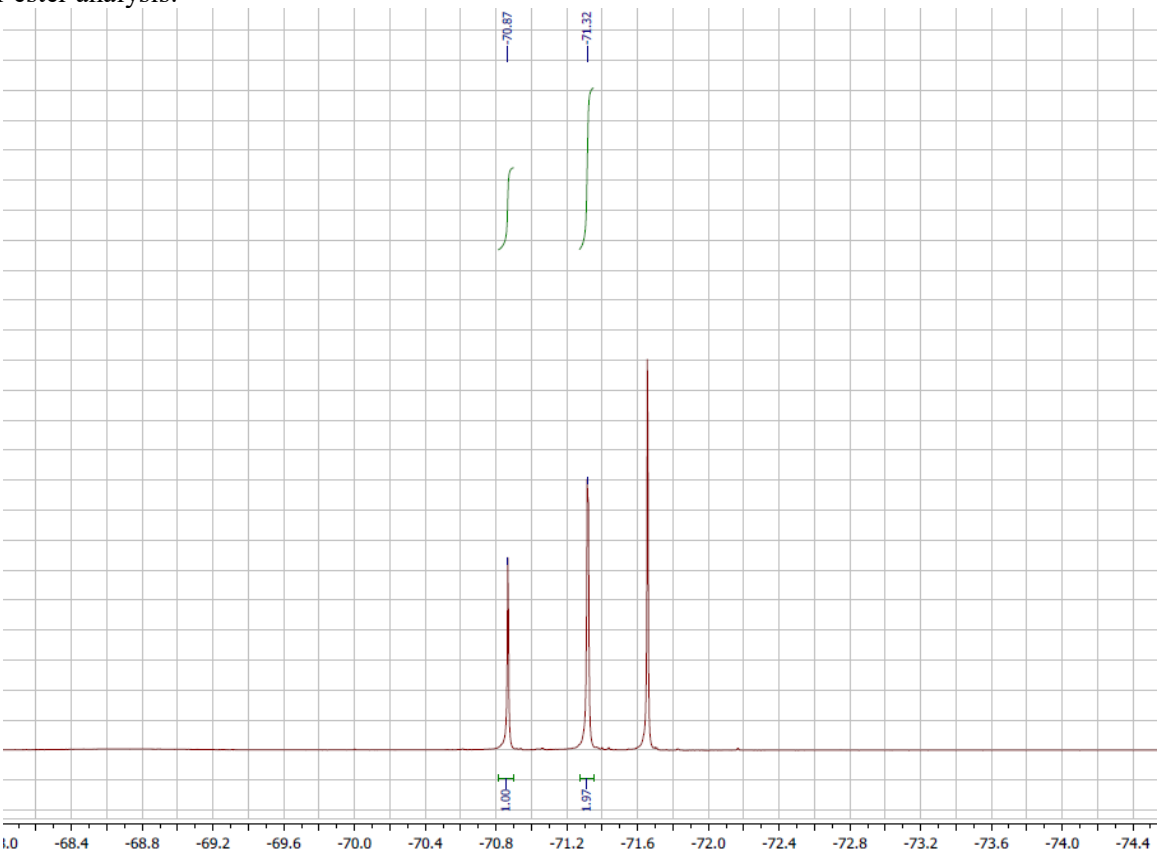
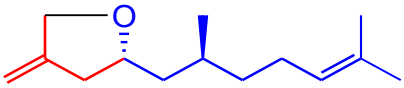
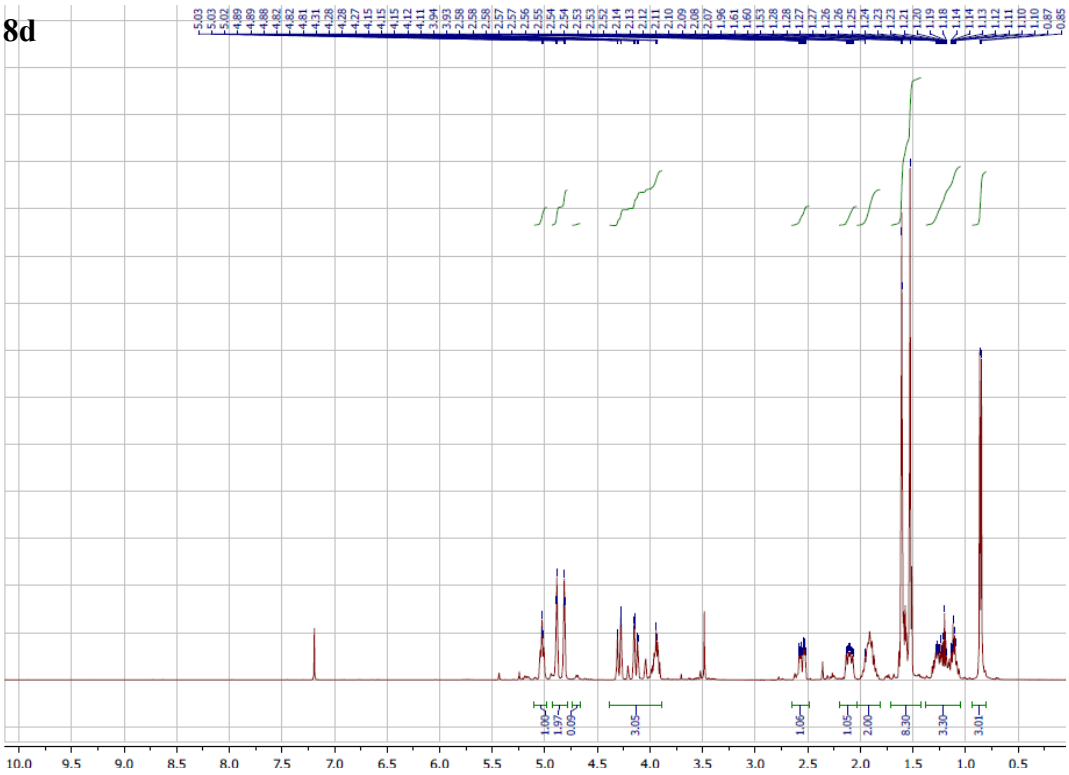
f1 (ppm)

Mosher ester analysis:





8d



8d