

Supporting Information

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**Gold(I) as an Artificial Cyclase: Short Stereodivergent Syntheses of (–)-Epiglobulol and (–)-4 $\beta$ ,7 $\alpha$ - and (–)-4 $\alpha$ ,7 $\alpha$ -Aromadendranediols\*\***

*Javier Carreras, Madeleine Livendahl, Paul R. McGonigal, and Antonio M. Echavarren\**

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## SUPPORTING INFORMATION

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## Experimental Procedures

Unless otherwise stated, reactions were carried out under argon atmosphere in solvents dried by passing through an activated alumina column on a PureSolv™ solvent purification system (Innovative Technologies, Inc., MA). Analytical thin layer chromatography was carried out using TLC-aluminium sheets with 0.2 mm of silica gel (Merck GF234) using UV light as visualizing agent or an acidic solution of vanillin in ethanol as developing agent. Chromatography purifications were carried out using flash grade silica gel (SDS Chromatogel 60 ACC, 40-60 mm). Preparative TLC was performed on 20 cm × 20 cm silica gel plates (2.0 mm thick, catalogue number 02015, Analtech). Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator. NMR spectra were recorded at 298 K on a Bruker Avance 400 Ultrashield or a Bruker Avance 500 Ultrashield. <sup>1</sup>H and <sup>13</sup>C chemical shifts (δ) are given in ppm relative to TMS, coupling constants (J) in Hz. The solvent signals were used as references and the chemical shifts converted to the TMS scale. Mass spectra were recorded on a Waters Micromass LCT Premier (ESI), Waters Micromass GCT (EI, CI). Melting points were determined using a Büchi melting point apparatus. Optical rotations were obtained using a Jasco P-1030 polarimeter and concentrations are given in g/mL. Crystal structure determinations were carried out using a Bruker-Nonius diffractometer equipped with an APEX 2 4K CCD area detector, a FR591 rotating anode with MoKα radiation, Montel mirrors as monochromator and a Kryoflex low temperature device (T = -173 °C). Full-sphere data collection was used with ω and φ scans. Programs used: Data collection APEX-2, data reduction Bruker SAINT V.60A and absorption correction SADABS. Structure Solution and Refinement: Crystal structure solution was achieved using direct methods as implemented in SHELXTL and visualized using the program XP. Missing atoms were subsequently located from difference Fourier synthesis and added to the atom list. Least-squares refinement on F<sup>2</sup> using all measured intensities was carried out using the program SHELXTL. All non-hydrogen atoms were refined including anisotropic displacement parameters.

Gold complexes **13** and **Au-I** were purchased from Aldrich, **Au-II**,<sup>1</sup> **Au-III**,<sup>2</sup> **Au-IV**,<sup>3</sup> **Au-V**,<sup>2</sup> **Au-VI**,<sup>4</sup> **Au-VII**,<sup>4</sup> **Au-VIII**<sup>1</sup> and (1,5-cyclooctadiene)(pyridine)(tricyclohexylphosphine)iridium(I) tetrakis(3,5-bis(trifluoromethyl)phenyl)borate<sup>5</sup> were prepared according to literature procedures.

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<sup>1</sup> E. S. Smirnova, A. M. Echavarren, *Angew. Chem. Int. Ed.* **2013**, *52*, 9023-9026.

<sup>2</sup> C. H. M. Amijs, V. López-Carrillo, M. Raducan, P. Pérez-Galán, C. Ferrer, A. M. Echavarren, *J. Org. Chem.* **2008**, *73*, 7721-7730.

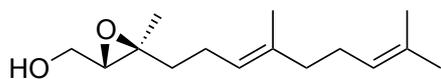
<sup>3</sup> N. Delpont, I. Escofet, P. Pérez-Galán, D. Spiegl, M. Raducan, C. Bour, R. Sinisi, A. M. Echavarren, *Catal. Sci. Technol.*, **2013**, *3*, 3007-3012

<sup>4</sup> C. Obradors, D. Leboeuf, J. Aydin, A. M. Echavarren, *Org. Lett.* **2013**, *15*, 1576-1579.

<sup>5</sup> B. Wüstenberg, A. Pfaltz, *Adv. Synth. Catal.* **2008**, *350*, 174-178.

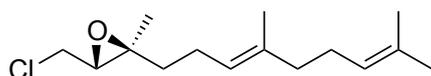
## Characterization of new compounds

### Compound 10



Epoxy alcohol **10** was prepared according to the reported procedure: Tanuwidjaja, J.; Ng, S.-S.; Jamison, T. F. *J. Am. Chem. Soc.* **2009**, *131*, 12084-12085. The ee was the previously reported, 82% (91:9). Chiral Analytical HPLC analysis was performed on a Hewlett-Packard 1200 Series HPLC equipped with DAD (diode array) detector and Chiralpack IA (250x4.6mm, 5 $\mu$ m, hexane/*iso*-propanol/ethanol 96:2:2, 1.0 mL/min): tR(2*S*, 3*S*) = 9.029 min, tR(2*R*, 3*R*) = 10.222 min. See page S-33.

### Compound 11



A stirred mixture of epoxy alcohol **10** (2.5 g, 10.3 mmol), PPh<sub>3</sub> (3.25 g, 12.4 mmol), and NaHCO<sub>3</sub> (168 mg, 10 wt.-%) in CCl<sub>4</sub> (20 mL) was heated at reflux for 6 h. After completion of the reaction, the solution was filtered through Celite and the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography (12:1 cyclohexane/AcOEt) to obtain epoxy chloride **11** (2.5 g, 94 %) as a colorless oil.

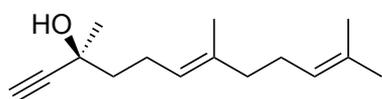
$[\alpha]_D^{25} = +7.2$  (c = 1.07, CHCl<sub>3</sub>)

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.15 - 5.03 (m, 2H), 3.68 (dd,  $J = 11.4, 5.9$  Hz, 1H), 3.45 (dd,  $J = 11.4, 7.1$  Hz, 1H), 3.04 (dd,  $J = 7.1, 5.9$  Hz, 1H), 2.16 - 2.01 (m, 4H), 2.02 - 1.93 (m, 2H), 1.80 - 1.69 (m, 1H), 1.67 (s, 3H), 1.61 (s, 3H), 1.60 (s, 3H), 1.51 - 1.39 (m, 1H), 1.32 (s, 3H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  136.1, 131.6, 124.4, 123.2, 62.3, 61.7, 42.4, 39.8, 38.4, 26.8, 25.8, 23.8, 17.8, 16.5, 16.1.

HRMS:  $m/z$  calculated for C<sub>15</sub>H<sub>26</sub>ClO [M+H]<sup>+</sup>: 257.1667, found: 257.1663.

### Compound 12



To a stirred solution of epoxy chloride **11** (2.0 g, 7.8 mmol) in dry THF (15 mL) at -40 °C was added *n*BuLi (9.4 mL, 23.4 mmol) dropwise, and the mixture was allowed to stir for an additional 2 h. The mixture was quenched with saturated NH<sub>4</sub>Cl (20 mL), and THF was removed under reduced pressure. The aqueous layer was extracted with ethyl acetate (2 x 20 mL), dried with Na<sub>2</sub>SO<sub>4</sub>, and concentrated. The residue was purified by silica gel column chromatography (9:1 cyclohexane/AcOEt) to afford propargyl alcohol derivative **12** (1.4 g, 82 %) as a colorless oil.

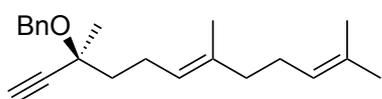
$[\alpha]_D^{25} = -10.9$  (c = 0.95, CHCl<sub>3</sub>)

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.18 (ddd,  $J = 7.9, 6.6, 1.3$  Hz, 1H), 5.08 (ddt,  $J = 8.4, 5.6, 1.5$  Hz, 1H), 2.45 (s, 1H), 2.37 - 2.25 (m, 1H), 2.24 - 2.13 (m, 2H), 2.11 - 2.03 (m, 2H), 2.02 - 1.94 (m, 2H), 1.75 - 1.70 (m, 2H), 1.68 (d,  $J = 1.0$  Hz, 3H), 1.65 (s, 3H), 1.60 (s, 3H), 1.50 (s, 3H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  136.4, 131.6, 124.3, 123.7, 87.8, 71.6, 68.4, 43.3, 39.8, 30.0, 26.8, 25.8, 23.6, 17.8, 16.2.

NMR data were in accordance with those previously reported for the racemic compound: Fürstner, A.; Hannen, P. *Chem. Eur. J.* **2006**, *12*, 3006 - 3019.

### Compound 6



Dienyne **12** (1.4 g, 6.4 mmol) was dissolved in THF (5 mL) and added slowly over a THF solution (15 mL) of NaH (305 mg, 7.6 mmol, 60% weight suspension in mineral oil) at 0 °C. The solution was kept at 0 °C for 1 h. TBAI (235 mg, 0.6 mmol) and benzyl bromide (0.91 mL, 7.6 mmol) was then added. The solution was allowed to warm to room temperature and left stirring overnight. The reaction was quenched with water

(10 mL) and AcOEt (10 mL) was added. The two phases were then separated and the organic phase was washed with brine (10 mL). The organic phase was dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated. Purification was made by column chromatography (cyclohexane to 4:1 cyclohexane/AcOEt) to obtain the product as a colorless oil (1.8 g, 91%).

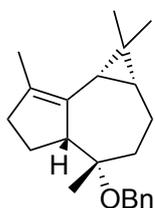
$[\alpha]_D^{25} = +2.5$  (c = 1.16, CHCl<sub>3</sub>)

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.41 - 7.31 (m, 4H), 7.30 - 7.21 (m, 1H), 5.16 (ddd, *J* = 8.5, 5.9, 1.4 Hz, 1H), 5.10 (ddt, *J* = 8.4, 5.6, 1.5 Hz, 1H), 4.68 (d, *J* = 11.1 Hz, 1H), 4.61 (d, *J* = 11.2 Hz, 1H), 2.51 (s, 1H), 2.23 (ddp, *J* = 20.5, 14.1, 7.1, 6.6 Hz, 2H), 2.07 (q, *J* = 7.5 Hz, 2H), 1.99 (dd, *J* = 9.2, 6.0 Hz, 2H), 1.89 - 1.71 (m, 2H), 1.68 (s, 3H), 1.63 (s, 3H), 1.60 (s, 3H), 1.52 (s, 3H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 139.3, 135.7, 131.5, 128.4, 127.7, 127.4, 124.5, 123.8, 85.4, 73.6, 73.6, 66.4, 41.7, 39.8, 26.9, 26.5, 25.9, 23.1, 17.8, 16.2.

NMR data were in accordance with those previously reported for the racemic compound: Jimenez-Núñez, E.; Raducan, M.; Lauterbach, T.; Molawi, K.; Solorio, C. R.; Echavarren, A. *M. Angew. Chem. Int. Ed.* **2009**, *48*, 6152 - 6155.

### Compound 7



(Acetonitrile)[(2-biphenyl)di-*tert*-butylphosphine]gold(I) hexafluoroantimonate (**13**) (40.4 mg, 0.05 mmol) was dissolved in dry CH<sub>2</sub>Cl<sub>2</sub> (10 mL) and added dropwise over a stirred solution of the diyne **6** (810 mg, 2.6 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (43 mL, 0.05 M overall volume). The reaction mixture was stirred for 5 min and quenched by drops of Et<sub>3</sub>N. The crude was concentrated in vacuo and the product **7** was purified by column chromatography (cyclohexane) as a white solid (487 mg, 60%).

M.p. = 61-62 °C

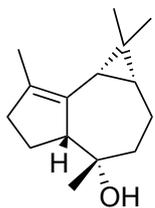
$[\alpha]_D^{25} = -11.1$  (c = 1.18, CHCl<sub>3</sub>)

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.32 (d, *J* = 4.4 Hz, 4H), 7.29 - 7.18 (m, 1H), 4.40 (d, *J* = 12.1 Hz, 1H), 4.29 (d, *J* = 12.1 Hz, 1H), 2.64 - 2.56 (m, 1H), 2.54 - 2.46 (m, 1H), 2.22 - 2.10 (m, 1H), 2.08 - 1.98 (m, 2H), 1.96 - 1.81 (m, 1H), 1.68 (s, 3H), 1.67 - 1.59 (m, 1H), 1.58 - 1.48 (m, 2H), 1.32 - 1.25 (m, 1H), 1.24 (s, 3H), 1.13 (s, 3H), 1.06 - 1.01 (m, 1H), 1.00 (s, 3H), 0.73 (ddd, *J* = 10.6, 9.4, 6.9 Hz, 1H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 140.9, 139.5, 132.8, 128.1, 126.6, 126.4, 79.2, 62.6, 61.8, 37.3, 36.5, 28.8, 26.9, 26.7, 25.7, 25.6, 21.4, 19.1, 17.7, 16.3.

NMR data were in accordance with those previously reported for the racemic compound: Jiménez-Núñez, E.; Raducan, M.; Lauterbach, T.; Molawi, K.; Solorio, C. R.; Echavarren, A. *M. Angew. Chem. Int. Ed.* **2009**, *48*, 6152 - 6155.

### Compound 14



A solution of ether **7** (433 mg, 1.39 mmol) in MeOH:THF (1:1, 4 mL) was added over a suspension of 20% Pd(OH)<sub>2</sub>/C (108 mg) in MeOH:THF (1:1, 4 mL). The compounds were hydrogenated at 23 °C and atmospheric pressure for 4 h. The reaction mixture was filtered through Celite, evaporated and purified by column chromatography (10:1 cyclohexane/AcOEt) to obtain the product as a colorless oil (243 mg, 79%).

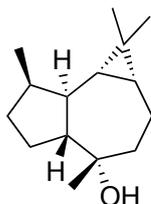
$[\alpha]_D^{25} = -57.9$  (c = 1.12, CHCl<sub>3</sub>)

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 2.68 - 2.59 (m, 1H), 2.51 - 2.35 (m, 1H), 2.15 - 1.88 (m, 3H), 1.78 - 1.71 (m, 1H), 1.68 (s, 3H), 1.68 - 1.61 (m, 1H), 1.20 (s, 3H), 1.22 - 1.15 (m, 1H), 1.11 (s, 3H), 1.03 (s, 3H), 1.01 - 0.96 (m, 1H), 0.72 (ddd, *J* = 10.8, 9.5, 6.7 Hz, 1H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 141.8, 132.3, 74.9, 60.6, 41.7, 37.1, 30.0, 28.9, 26.8, 26.3, 24.9, 21.1, 19.5, 18.2, 16.3.

NMR data were in accordance with those previously reported for the racemic compound: Jiménez-Núñez, E.; Raducan, M.; Lauterbach, T.; Molawi, K.; Solorio, C. R.; Echavarren, A. *M. Angew. Chem. Int. Ed.* **2009**, *48*, 6152 - 6155.

### Compound 3, (-)-epiglobulol



(1,5-Cyclooctadiene)(pyridine)(tricyclohexylphosphine)-iridium(I) tetrakis(3,5-bis(trifluoromethyl)phenyl)borate (98 mg, 0.03 mmol) and tricyclic **14** (100 mg, 0.45 mmol) were dissolved in dry CH<sub>2</sub>Cl<sub>2</sub> (4.5 mL, 0.1M) and placed in five tubes into a “HEL reactor” (pressure reactor) inside the glovebox. The reactor was charged with hydrogen gas (80 bar) and heated to 40 °C over 4 days. The reactor was then depressurized and the solution was filtered through a pad of silica. The product was purified through column chromatography (cyclohexane/EtOAc 10:1) to obtain (-)-epiglobulol (**3**) as a transparent oil (40 mg, 40%). See the GC analysis on page S-34.

$[\alpha]_D^{25} = -30.2$  ( $c = 0.84$ , CHCl<sub>3</sub>)

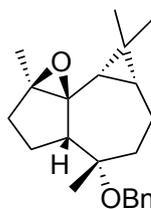
<sup>1</sup>H NMR (400 MHz, C<sub>6</sub>D<sub>6</sub>)  $\delta$  2.10 - 1.99 (m, 1H), 1.97 - 1.86 (m, 1H), 1.83 - 1.72 (m, 1H), 1.69 - 1.56 (m, 3H), 1.56 - 1.47 (m, 2H), 1.45 - 1.31 (m, 2H), 1.23 - 1.12 (m, 1H), 1.09 (s, 3H), 1.05 (s, 3H), 1.07 - 1.03 (m, 2H), 0.98 (d,  $J = 7.0$  Hz, 3H), 0.56 - 0.45 (m, 1H), 0.41 (dd,  $J = 11.0$ , 9.4 Hz, 1H).

<sup>13</sup>C NMR (101 MHz, C<sub>6</sub>D<sub>6</sub>)  $\delta$  71.6, 56.0, 43.4, 37.8, 36.2, 35.1, 31.4, 29.2, 29.0, 27.6, 26.3, 20.8, 19.6, 17.0, 16.1.

HRMS-APCI:  $m/z$  calculated for C<sub>15</sub>H<sub>26</sub>NaO [M+Na]<sup>+</sup>: 245.1876, found: 245.1882.

[Commercially available (-)-epiglobulol, CAS: 88728-58-9,  $[\alpha]_D^{26} = -34.8$  ( $c = 0.99$ , CHCl<sub>3</sub>)]

### Compound 15



To a stirred solution of **7** (250 mg, 0.81 mmol) in a mixture of CH<sub>2</sub>Cl<sub>2</sub>/acetone/water (4 mL/4 mL/2 mL), 18-crown-6 (81 mg, 0.31 mmol) and NaHCO<sub>3</sub> (1.35 g, 16 mmol) were added. The reaction mixture was cooled to 0 °C and a solution of Oxone (2.6 g) in water (4 mL) was added. After stirring for 1 h at 0 °C, the reaction mixture was diluted with saturated NaHCO<sub>3</sub> (15 mL) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (4 × 15 mL). The combined organic layers were washed with Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> 10% (20 mL), saturated NaHCO<sub>3</sub> (20 mL) and saturated NaCl (20 mL).

The organic phase was dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated. Purification was made by column chromatography (20:1 cyclohexane/AcOEt) to obtain the product as a yellow oil (134 mg, 51%).

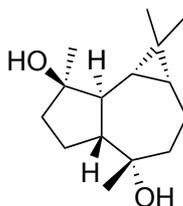
$[\alpha]_D^{26} = -47.7$  ( $c = 1.27$ , CHCl<sub>3</sub>)

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.36 - 7.19 (m, 5H), 4.35 (d,  $J = 11.5$  Hz, 1H), 4.22 (d,  $J = 11.5$  Hz, 1H), 2.21 (dd,  $J = 9.1$ , 1.3 Hz, 1H), 2.05 (ddd,  $J = 14.9$ , 6.8, 1.1 Hz, 1H), 1.90 - 1.61 (m, 5H), 1.57 - 1.40 (m, 2H), 1.38 (s, 3H), 1.24 (s, 3H), 1.03 (s, 3H), 0.98 (d,  $J = 10.1$  Hz, 1H), 0.94 (s, 3H), 0.89 (td,  $J = 9.9$ , 8.0 Hz, 1H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  139.9, 128.3, 127.0, 127.0, 79.0, 73.5, 71.7, 63.4, 57.5, 36.7, 33.4, 28.9, 28.9, 26.8, 26.1, 23.78, 19.9, 18.9, 18.9, 18.7.

HRMS:  $m/z$  calculated for C<sub>22</sub>H<sub>30</sub>NaO<sub>2</sub> [M+Na]<sup>+</sup>: 349.2138, found: 349.2129.

### Compound 5, (-)-4 $\beta$ ,7 $\alpha$ -aromadendranediol



To a solution of **15** (134 mg, 0.41 mmol) in anhydrous ethylenediamine (5 mL) was added lithium (85 mg, 25% weight suspension in mineral oil) and the resulting suspension heated to 50 °C with vigorous stirring. A deep blue color rapidly developed which faded to pale yellow after heating for 5 min. After 1.5 h a pale blue color returned, the reaction mixture was allowed to cool to r.t. and quenched by dropwise addition of water (2 mL). The crude mixture was diluted with Et<sub>2</sub>O (20 mL), washed with water (2 × 15 mL) and

brine (20 mL). The organic phase was then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated. Purification was made by column chromatography (6:4 cyclohexane/AcOEt) giving the product as a white solid (76 mg, 78% (95% purity), 91% ee). Crystallization from CH<sub>2</sub>Cl<sub>2</sub>/cyclohexane increased the ee to >99% (60 mg, 61%). See the HPLC separation details on page S-36.

M.p. = 84-85 °C

$[\alpha]_D^{25} = -34.7$  (c = 1.15, CHCl<sub>3</sub>)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 2.04 (td, *J* = 10.8, 6.4 Hz, 1H), 1.93 – 1.81 (m, 1H), 1.71 – 1.62 (m, 4H), 1.61 – 1.53 (m, 2H), 1.50 (t, *J* = 10.7 Hz, 1H), 1.39 – 1.29 (m, 1H), 1.24 (s, 3H), 1.20 (s, 3H), 1.19 (s, 1H), 1.04 (s, 3H), 1.04 (s, 3H), 1.01 (s, 1H), 0.67 (ddd, *J* = 11.3, 9.6, 5.6 Hz, 1H), 0.58 (dd, *J* = 10.4, 9.6 Hz, 1H).

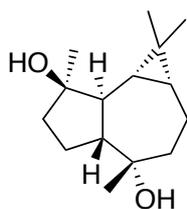
<sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 80.8, 73.1, 52.7, 46.0, 42.6, 39.8, 31.5, 29.2, 27.1, 26.1, 25.1, 23.9, 20.4, 19.2, 16.6.

HRMS: *m/z* calculated for C<sub>15</sub>H<sub>26</sub>O<sub>2</sub> [M+Na]<sup>+</sup>: 261.1825, found: 261.1832.

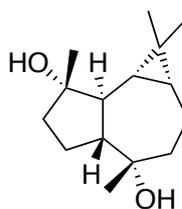
All spectral data were consistent with the previously reported literature values: [Beechan, C. M.; Djerassi, C.; Eggert, H. *Tetrahedron* **1978**, *34*, 2503  $[\alpha]_D^{20} = -35.8$  (c = 1.1, CHCl<sub>3</sub>)

Table S1. Comparison of the recorded <sup>13</sup>C NMR data of **5** with those reported in the literature for (-)-4β,7α-Aromadendranediol and (-)-4β,7β-Aromadendranediol (C. M. Beechan, C. Djerassi and H. Eggert, *Tetrahedron*, 1978, **34**, 2503–2508).

$\delta_c$ ( <b>5</b> )	$\delta_c$ (4β,7α)	$\delta_c$ (4β,7β)	$\Delta\delta$ (5–4β,7α)	$\Delta\delta$ (5–4β,7β)
16.6	16.4	16.4	0.2	0.2
19.2	19.1	19.2	0.1	0
20.4	20.1	20.9	0.3	-0.5
23.9	23.7	24.3	0.2	-0.4
25.1	24.9	25.1	0.2	0
26.1	25.8	26.9	0.3	-0.8
27.1	27.0	28.7	0.1	-1.6
29.2	29.0	30.1	0.2	-0.9
31.5	31.2	30.5	0.3	1.0
39.8	39.6	41.4	0.2	-1.6
42.6	42.4	42.8	0.2	-0.2
46.0	45.8	47.2	0.2	-1.2
52.7	52.5	56.4	0.2	-3.7
73.1	72.8	71.8	0.3	1.3
80.8	80.5	80.3	0.3	0.5

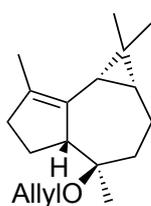


**5**, (-)-4β,7α-Aromadendranediol



(-)-4β,7β-Aromadendranediol

## Compound 8



(Acetonitrile)[(2-biphenyl)di-*tert*-butylphosphine]gold(I) hexafluoroantimonate (**13**) (45.4 mg, 0.06 mmol) was dissolved in dry CH<sub>2</sub>Cl<sub>2</sub> (10 mL) and added dropwise over a stirred solution of the dienyne **6** (913 mg, 2.9 mmol) and allylic alcohol (4.0 mL, 58.8 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (45 mL, 0.05 M overall volume). The reaction mixture was stirred for 15 min. and quenched by drops of Et<sub>3</sub>N. The crude was concentrated in vacuo and the product **8** was purified by column chromatography (50:1 cyclohexane/AcOEt) as a colorless oil (428 mg, 56%).

Compound **7** was also purified from the reaction mixture (187 mg, 21%).

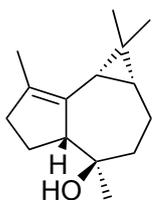
$[\alpha]_D^{25} = -46.6$  (c = 1.09, CHCl<sub>3</sub>)

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.92 (ddt,  $J = 17.1, 10.3, 5.4$  Hz, 1H), 5.26 (dq,  $J = 17.2, 1.8$  Hz, 1H), 5.09 (ddt,  $J = 10.3, 2.0, 1.4$  Hz, 1H), 4.01 - 3.80 (m, 2H), 2.83 (d,  $J = 9.1$  Hz, 1H), 2.44 - 2.29 (m, 1H), 2.12 - 1.99 (m, 2H), 1.92 - 1.82 (m, 2H), 1.77 - 1.67 (m, 2H), 1.66 (s, 3H), 1.11 (s, 3H), 1.04 - 0.98 (m, 1H), 1.00 (s, 3H), 0.96 (s, 3H), 0.92 - 0.78 (m, 1H), 0.70 (td,  $J = 9.8, 7.3$  Hz, 1H).

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  139.7, 136.8, 132.6, 115.5, 81.5, 62.1, 58.6, 38.2, 37.5, 28.8, 26.5, 25.8, 25.4, 20.1, 18.8, 18.0, 16.2.

HRMS:  $m/z$  calculated for  $\text{C}_{18}\text{H}_{28}\text{NaO}$   $[\text{M}+\text{Na}]^+$ : 283.2032, found: 283.2035.

### Compound 16



To a stirred solution of allylic alcohol **8** (390 mg, 1.5 mmol) in dry MeOH (10 mL) was added catalytic amounts of  $\text{Pd}(\text{PPh}_3)_4$  (86 mg, 0.07 mmol, 5 mol%). The slightly yellow solution was stirred for 5 min, and  $\text{K}_2\text{CO}_3$  (621 mg, 4.5 mmol) was added. The reaction mixture was stirred for 72 h at reflux. Then, the solvent was evaporated and the residue was treated with 2 M HCl (20 mL) and  $\text{CH}_2\text{Cl}_2$  (20 mL). The organic layer was washed with brine (15 mL), dried over  $\text{Na}_2\text{SO}_4$ , and concentrated in vacuo. The product was purified by column chromatography (4:1 cyclohexane/AcOEt) giving compound **16** as a white solid (236 mg, 72%).

M.p. = 81-82 °C

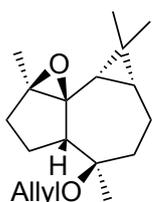
$[\alpha]_D^{25} = -33.4$  ( $c = 1.14$ ,  $\text{CHCl}_3$ )

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  2.65 - 2.55 (m, 1H), 2.43 - 2.30 (m, 1H), 2.13 - 2.00 (m, 1H), 2.00 - 1.93 (m, 2H), 1.90 - 1.79 (m, 1H), 1.70 - 1.60 (m, 4H), 1.10 (s, 3H), 1.05 - 0.97 (m, 1H), 1.00 (s, 3H), 0.95 (s, 3H), 0.92 - 0.77 (m, 1H), 0.70 (td,  $J = 9.7, 7.1$  Hz, 1H).

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  139.4, 132.4, 77.0, 62.3, 44.0, 37.2, 28.6, 26.3, 25.6, 25.4, 20.6, 20.4, 19.9, 17.8, 16.0.

NMR data were in accordance with those previously reported for the racemic compound: Jiménez-Núñez, E.; Raducan, M.; Lauterbach, T.; Molawi, K.; Solorio, C. R.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2009**, *48*, 6152 - 6155.

### Compound 17



*m*-CPBA (55 mg, 0.32 mmol) was added to a solution of **8** (75 mg, 0.29 mmol) in  $\text{CH}_2\text{Cl}_2$  (5 mL) at 0 °C. The mixture was stirred for 4h, allowing the ice bath to slowly warm to rt, during which time a colorless precipitate formed. The reaction mixture was diluted with  $\text{Et}_2\text{O}$  (30 mL), then washed with aqueous saturated  $\text{NaHCO}_3$  ( $2 \times 15$  mL), followed by brine (10 mL). The organic phase was then dried over  $\text{Na}_2\text{SO}_4$  and concentrated. Purification was made by column chromatography (4:1 cyclohexane/AcOEt) giving the product as a white solid

(66 mg, 83%).

M.p. = 56-57 °C

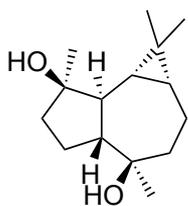
$[\alpha]_D^{26} = -90.5$  ( $c = 1.18$ ,  $\text{CHCl}_3$ )

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.87 (ddt,  $J = 17.2, 10.6, 5.4$  Hz, 1H), 5.24 (dq,  $J = 17.2, 1.8$  Hz, 1H), 5.09 (dq,  $J = 10.4, 1.5$  Hz, 1H), 3.95 - 3.81 (m, 2H), 2.59 (d,  $J = 8.5$  Hz, 1H), 2.07 - 1.93 (m, 1H), 1.90 (dd,  $J = 13.0, 1.4$  Hz, 1H), 1.82 - 1.59 (m, 4H), 1.43 (s, 3H), 1.46 - 1.39 (m, 1H), 1.20 - 1.09 (m, 1H), 1.06 (s, 3H), 1.07 - 1.04 (m, 1H), 1.02 (s, 3H), 1.00 (s, 3H), 0.96 - 0.86 (m, 1H).

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  136.2, 115.8, 78.8, 72.7, 70.8, 61.7, 53.3, 38.1, 33.1, 29.8, 29.2, 28.67, 25.2, 22.0, 21.8, 19.6, 19.3, 18.9, 18.4.

HRMS:  $m/z$  calculated for  $\text{C}_{18}\text{H}_{28}\text{NaO}_2$   $[\text{M}+\text{Na}]^+$ : 299.1982, found: 299.1987.

## Compound 4, (-)-4 $\alpha$ ,7 $\alpha$ -aromadendranediol



To a solution of **17** (30 mg, 0.11 mmol) in anhydrous ethylenediamine (2 mL) was added lithium (25 mg, 25% weight suspension in mineral oil) and the resulting suspension heated to 50 °C with vigorous stirring. A deep blue color rapidly developed which faded to pale yellow after heating for 5 min. After 1.5 h a pale blue color returned, the reaction mixture was allowed to cool to r.t. and quenched by dropwise addition of water (2 mL). The crude mixture was diluted with Et<sub>2</sub>O (30 mL), washed with water (2 × 20 mL) and brine (20 mL).

The organic phase was then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated. Purification was made by column chromatography (1:3 cyclohexane/AcOEt) giving the product as a white solid (16 mg, 62%, 76% ee). Crystallization from CH<sub>2</sub>Cl<sub>2</sub>/*c*-Hex increased the ee to >99% (11 mg, 43%). See the HPLC separation details on page S-35.

M.p. = 126-127 °C

$[\alpha]_D^{25} = -36.1$  (c = 1.06, CHCl<sub>3</sub>)

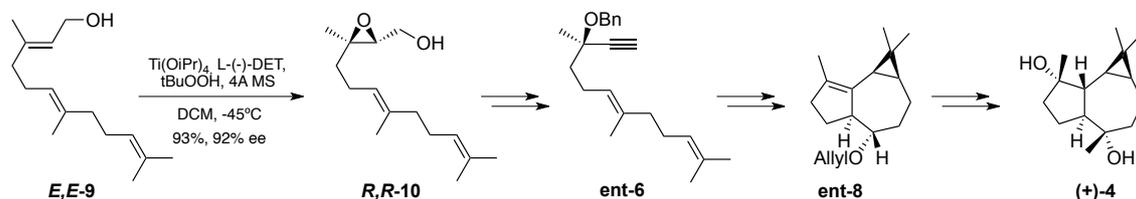
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  2.16 (td, *J* = 10.7, 4.9 Hz, 1H), 1.98 - 1.80 (m, 2H), 1.77 - 1.62 (m, 3H), 1.58 - 1.39 (m, 2H), 1.31 - 1.25 (m, 1H), 1.23 (s, 3H), 1.08 (s, 3H), 1.04 (s, 3H), 0.97 (s, 3H), 1.00 - 0.93 (m, 1H), 0.92 - 0.79 (m, 1H), 0.74 - 0.59 (m, 2H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  80.4, 75.6, 54.7, 47.7, 44.3, 40.4, 29.0, 26.3, 25.8, 25.1, 23.8, 20.5, 19.9, 19.1, 16.6.

HRMS: *m/z* calculated for C<sub>15</sub>H<sub>26</sub>O<sub>2</sub> [M+Na]<sup>+</sup>: 261.1825, found: 261.1825.

All spectral data were consistent with the previously reported literature values: [Beechan, C. M.; Djerassi, C.; Eggert, H. *Tetrahedron* **1978**, *34*, 2503  $[\alpha]_D^{20} = -39.3$  (c = 0.6, CHCl<sub>3</sub>); Simmons, B.; Abbas, M. W.; MacMillan, D. W. C. *Angew. Chem. Int. Ed.* **2009**, *48*, 4349  $[\alpha]_D^{23} = -39.0$  (c = 0.1, CHCl<sub>3</sub>)]

The synthesis of (+)-**4**, (+)-4 $\alpha$ ,7 $\alpha$ -aromadendranediol was performed following the same route described for (-)-**4**.



• **R,R-10** was prepared according to the reported procedure: J. A. Marshall, R. K. Hann, *J. Org. Chem.* **2008**, *73*, 6753–6757. HPLC separation details on page S-33 (92% ee).

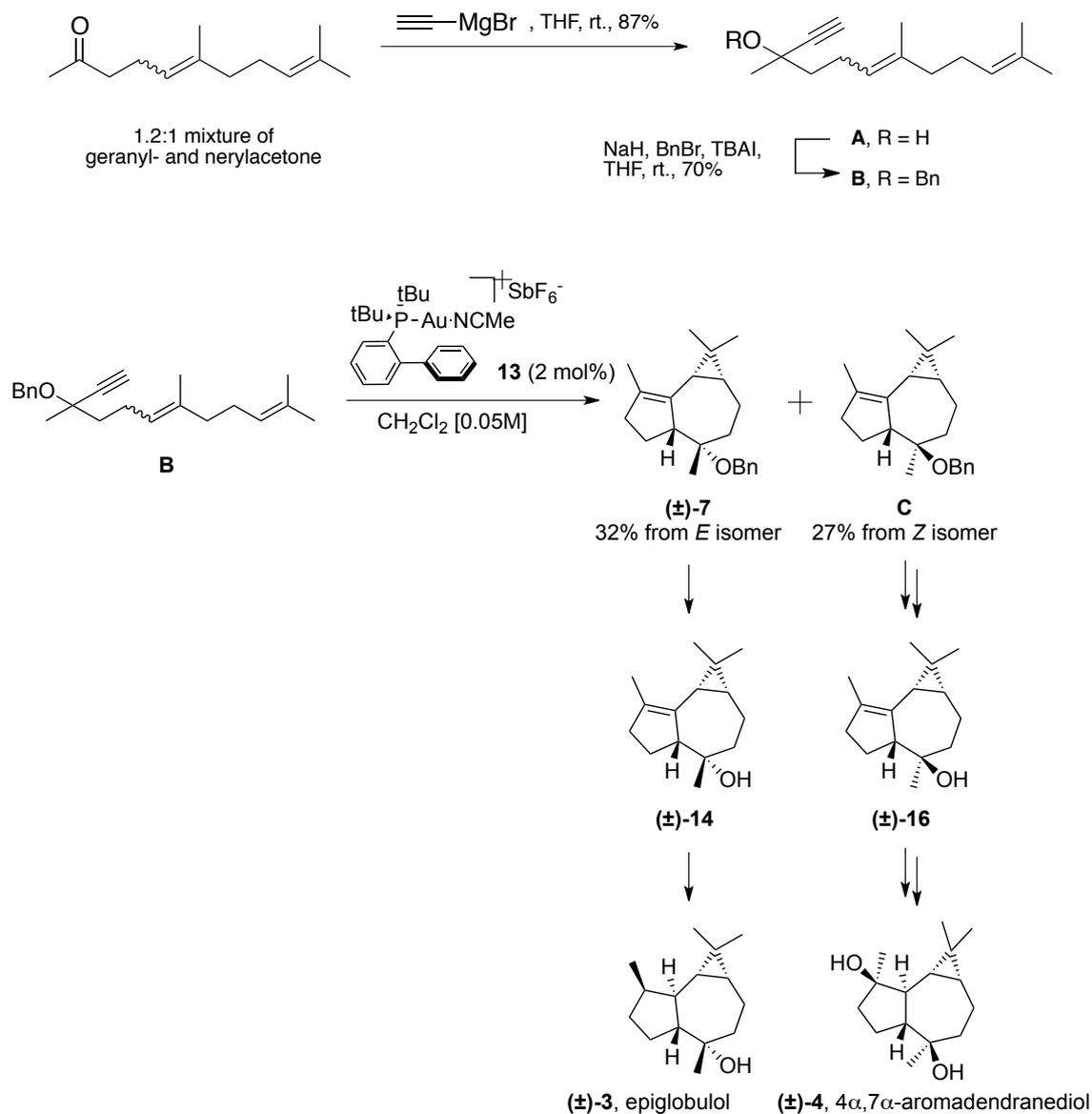
• **ent-6**:  $[\alpha]_D^{25} = -2.2$  (c = 1.11, CHCl<sub>3</sub>)

• **ent-8**:  $[\alpha]_D^{25} = +49.2$  (c = 1.21, CHCl<sub>3</sub>)

• **(+)-4**:  $[\alpha]_D^{29} = +37.0$  (c = 0.70, CHCl<sub>3</sub>)

## Syntheses of racemic **3** and **4**

The syntheses of ( $\pm$ )-**3** and ( $\pm$ )-**4** were carried out from a 1.2:1 mixture of geranyl- and nerylacetone following the route described in the next figure:



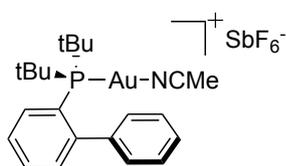
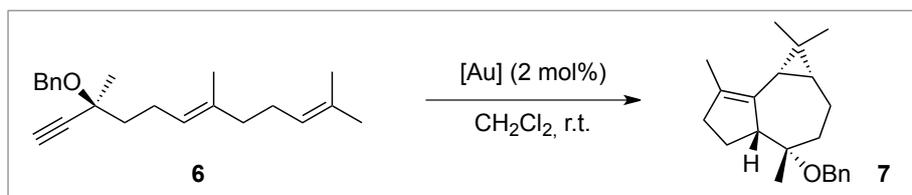
**A**: Geranyl acetone (3.4 mL, 15 mmol) (*E/Z* ratio 55:45) was dissolved in 150 mL of THF and cooled down to 0°C. Ethynylmagnesium bromide (45 mL, 0.5 M solution in THF, 22.5 mmol) was added dropwise by syringe pump over 30 min. The reaction was monitored by TLC and when the starting material had been consumed the reaction was quenched with a saturated solution of  $\text{NH}_4\text{Cl}$ . The two phases were separated and the organic phase was washed with water followed by brine. The organic phase was then dried over  $\text{Na}_2\text{SO}_4$  and concentrated. The product was purified by bulb-to-bulb distillation in a *Kugelrohr* apparatus. At a vacuum of 4 mbar the product is distilled at 160°C as a colourless oil (2.9 g, 87%).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.20-5.15 (m, 1H), 5.13-5.07 (m, 1 H), 2.45 (d, *E+Z* isomers, 1H), 2.34-1.98 (m, 7H), 1.73-1.56 (m, 12H), 1.50 (d, *E+Z* isomers, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  136.4, 131.8, 131.7, 124.5, 124.4, 124.3, 123.7, 71.6, 68.5, 68.4, 43.6, 43.3, 39.9, 32.1, 30.0, 26.8, 26.7, 25.8, 23.7, 23.6, 23.5, 17.8, 16.2.

**B:** Dienyne **A** (1 g, 4.6 mmol) was dissolved in THF (5 mL) and added slowly over a THF solution (10 mL) of NaH (370 mg, 9.2 mmol, 60% weight suspension in mineral oil) at 0 °C. The solution was kept at 0 °C for 1 h. TBAI (98 mg, 0.26 mmol) and benzyl bromide (0.66 mL, 5.5 mmol) was then added. The solution was allowed to warm to room temperature and left stirring overnight. The reaction was quenched with water (10 mL) and AcOEt (10 mL) was added. The two phases were then separated and the organic phase was washed with brine (10 mL). The organic phase was dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated. Purification was made by column chromatography on a ISCO Combiflash *Companion* system, with a gradient from 100% cyclohexane/0% EtOAc to 100% EtOAc over a 120g RediSep Rr Silica cartridge, giving the product as a colourless oil (1.0 g, 3.2 mmol, 70%). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.30-7.23 (m, 4H), 7.20-7.16 (m, 1 H), 5.10-5.01 (m, 2H), 4.62-4.59 (d, *J* = 11.0 Hz, 1H), 4.55-4.52 (d, *J* = 11.0 Hz, 1H), 2.43(s, *E* isomer, 1H), 2.42 (s, *Z* isomer, 1H), 2.22-2.09 (m, 2H), 1.99-1.97 (m, 3H), 1.93-1.88 (m, 1 H), 1.79-1.64 (m, 2H), 1.61 (bs, 4H), 1.53 (s, 3H), 1.46-1.44 (m, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 139.8, 135.5, 131.2, 128.5, 128.4, 127.8, 127.4, 125.3, 125.0, 124.4, 85.5, 73.8, 73.6, 66.6, 42.6, 40.2, 32.2, 27.2, 26.5, 17.8, 16.1.

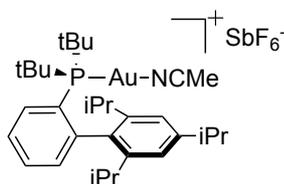
(±)-**7** and **C:** **13** (24 mg, 0.032 mmol) was dissolved in dry CH<sub>2</sub>Cl<sub>2</sub> and added dropwise over a stirred solution of the dienyne **B** (510 mg, 1.6 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (0.05 M). The reaction mixture was stirred until all starting dienyne had been consumed (TLC) and was then quenched by a 10% solution of NEt<sub>3</sub> in hexane and filtered through a pad of silica and concentrated. The two epimers were separated by column chromatography (Eluent c-Hex/EtOAc 95:5) in 59% yield (**C**, 139 mg, 27%; (±)-**7**, 164 mg, 32%). **C:** <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.34 (d, *J* = 7.3, 2H), 7.19 (t, *J* = 7.5, 2H), 7.06 (t, *J* = 7.3, 1H), 4.23 (d, *J* = 11.4, 1H), 4.15 (d, *J* = 11.4, 1H), 2.67 (m, 1 H), 2.57 (bd, *J* = 8.7, 1H), 2.32-2.25 (m, 1H), 2.12-2.06 (m, 1H), 1.99-1.82 (m, 2H), 1.70 (s, 3H), 1.68-1.61 (m, 2H), 1.43-1.38 (m, 2H), 1.14 (s, 3H), 1.14 (s, 3H), 1.11 (s, 3H), 0.75-0.68 (m, 1H). <sup>13</sup>C NMR (126 MHz, DEPTQ, CDCl<sub>3</sub>) δ 140.8, 139.7, 133.0, 128.4, 127.0, 126.8, 79.3, 63.1, 62.1, 37.5, 36.5, 28.9, 27.2, 27.1, 25.9, 25.7, 21.5, 19.4, 17.9, 16.4. HRMS: *m/z* calculated for C<sub>22</sub>H<sub>30</sub>O [M+Na]<sup>+</sup>: 333.2189, found: 333.2184.

(±)-**16:** A solution of ether **C** (840 mg, 2.7 mmol) in MeOH:THF (1:1, 5 mL) was added over a suspension of 20% Pd(OH)<sub>2</sub>/C (108 mg) in MeOH:THF (1:1, 5 mL). The compounds were hydrogenated at 23 °C and atmospheric pressure for 4 h. The reaction mixture was filtered through Celite, evaporated and purified by column chromatography (10:1 cyclohexane/AcOEt) to obtain the product as a white solid (240 mg, 41%).

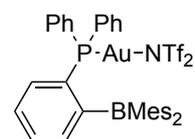
## Catalyst screening to obtain 7, 3 and 8



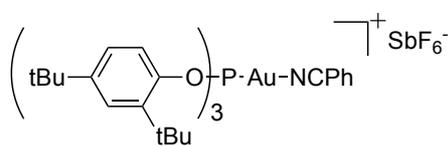
**13**, 60%



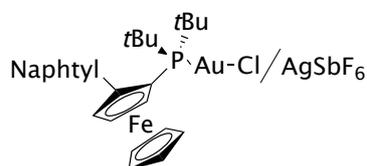
**Au-I**, 40%



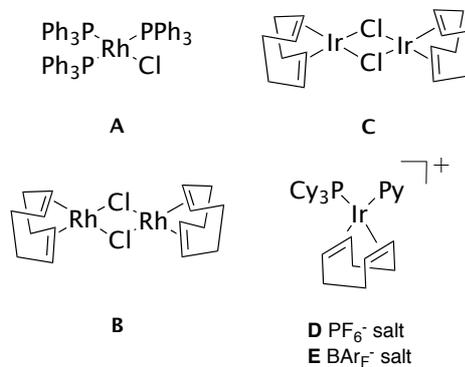
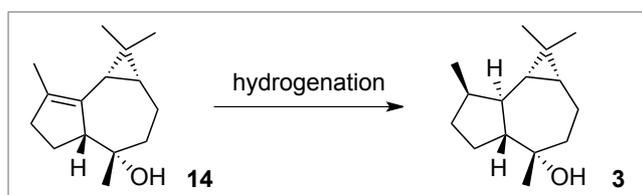
**Au-II**, 47%



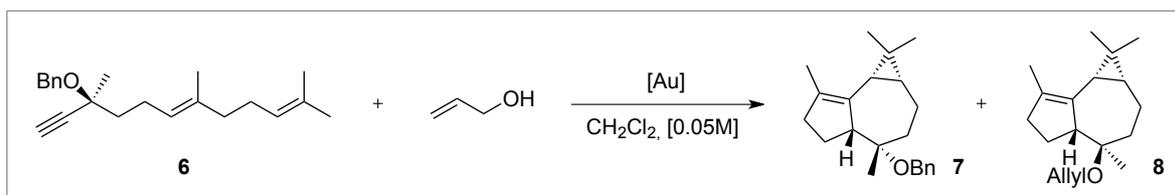
**Au-III**, 20%



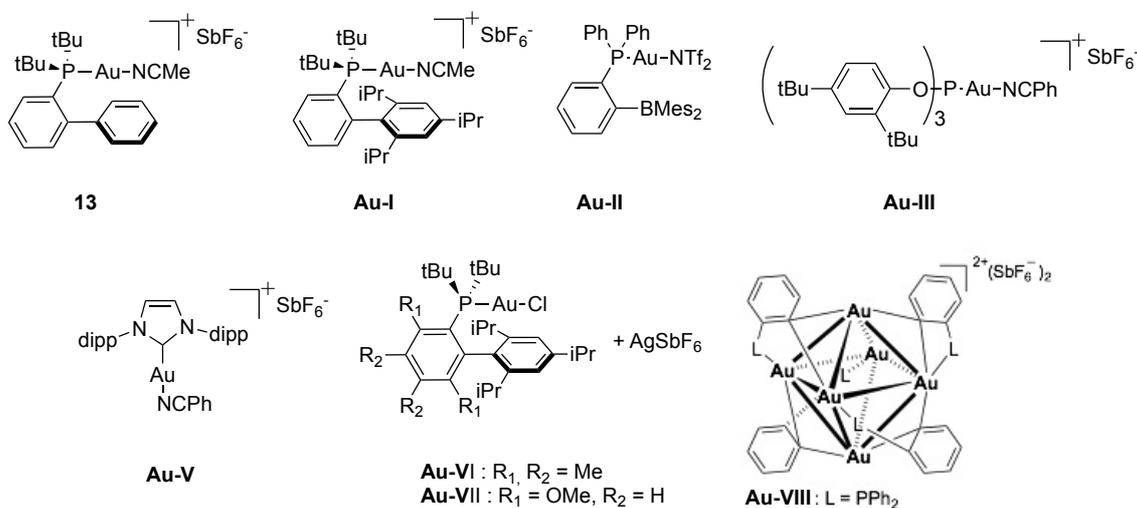
**Au-IV**, 30%



Entry	cat.	Temp. (°C)	Pressure $\text{H}_2$ (bar)	solvent	yield (%)
1	$\text{Pd(OH)}_2/\text{C}$	50	80	$\text{MeOH/THF}$	-
2	$\text{Rh/C}$	50	80	$\text{MeOH/THF}$	-
3	$\text{PtO}_2$	50	80	$\text{MeOH/THF}$	-
4	<b>A</b>	50	80	$\text{C}_2\text{H}_4\text{Cl}_2$	-
5	<b>B</b>	50	80	$\text{C}_2\text{H}_4\text{Cl}_2$	-
6	<b>C</b>	50	80	$\text{C}_2\text{H}_4\text{Cl}_2$	-
7	<b>D</b>	40	80	$\text{CH}_2\text{Cl}_2$	-
8	<b>E</b>	23	50	$\text{CH}_2\text{Cl}_2$	-
9	<b>E</b>	23	80	$\text{CH}_2\text{Cl}_2$	traces
10	<b>E</b>	40	80	$\text{CH}_2\text{Cl}_2$	40
11	<b>E</b>	50	80	$\text{C}_2\text{H}_4\text{Cl}_2$	-
12	<b>E</b>	80	80	$\text{C}_2\text{H}_4\text{Cl}_2$	-



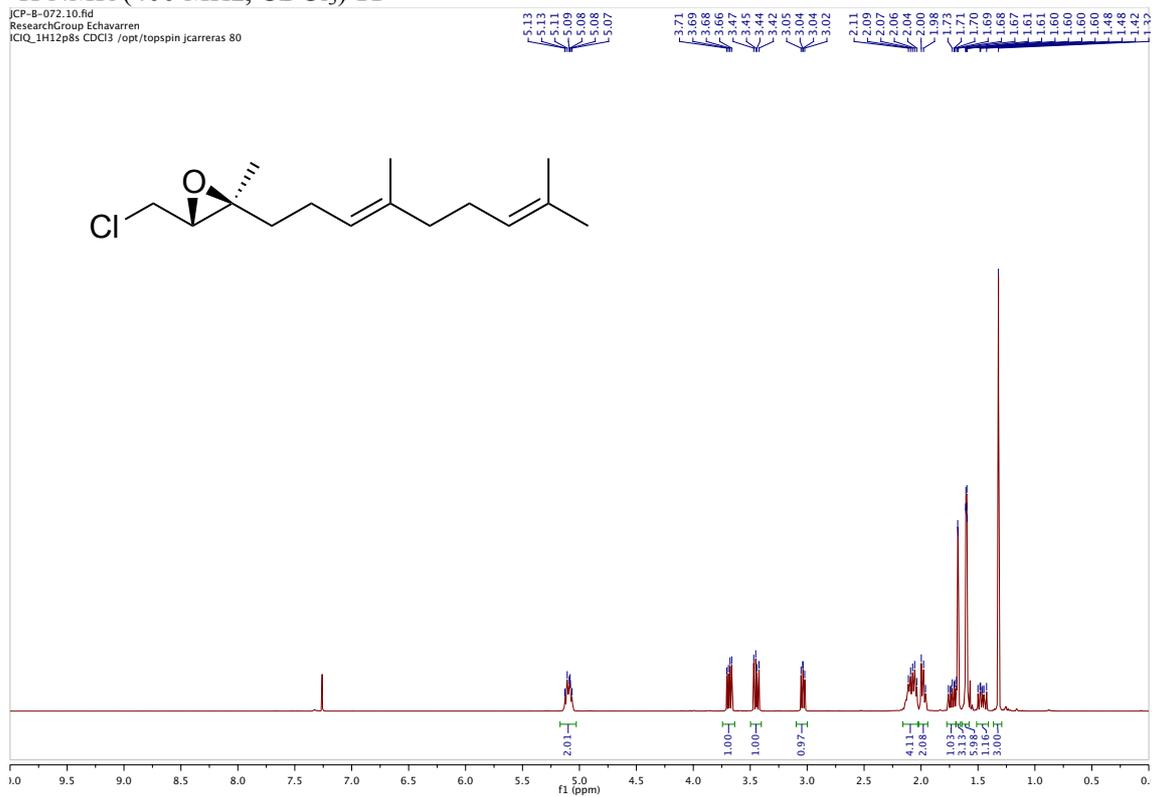
Entry	cat. (2%)	temp. (°C)	Eq. AllylOH	time (min)	Ratio 7/8 (GC-MS)	Yield (%) 7/8
1	<b>13</b>	r.t.	10	5	75/25	54/15
2	<b>13</b>	0	10	10	55/45	
3	<b>13</b>	-30	10	15	50/50	
4	<b>13</b>	-50	10	90	49/51	
5	<b>13</b>	-80	10	-	63/37	
6	<b>13</b>	-30	20	20	27/73	21/56
7	<b>13</b> (1% Au)	-30	20	30	33/67	
8	<b>13</b>	-30	30	30	21/79	
9	<b>Au-I</b>	-20	20	150	46/53	
10	<b>Au-II</b>	-30	20	20	29/71	15/43
11	<b>Au-III</b>	-20	20	120	70/30	
12	<b>Au-V</b>	-20	20	5 h.	40/60	
13	<b>Au-VI</b>	-30	20	45	65/35	
14	<b>Au-VII</b>	-30	20	45	70/30	
15	<b>Au-VIII</b>	-30 to r.t.	20	overnight	66/34	



# NMR spectra

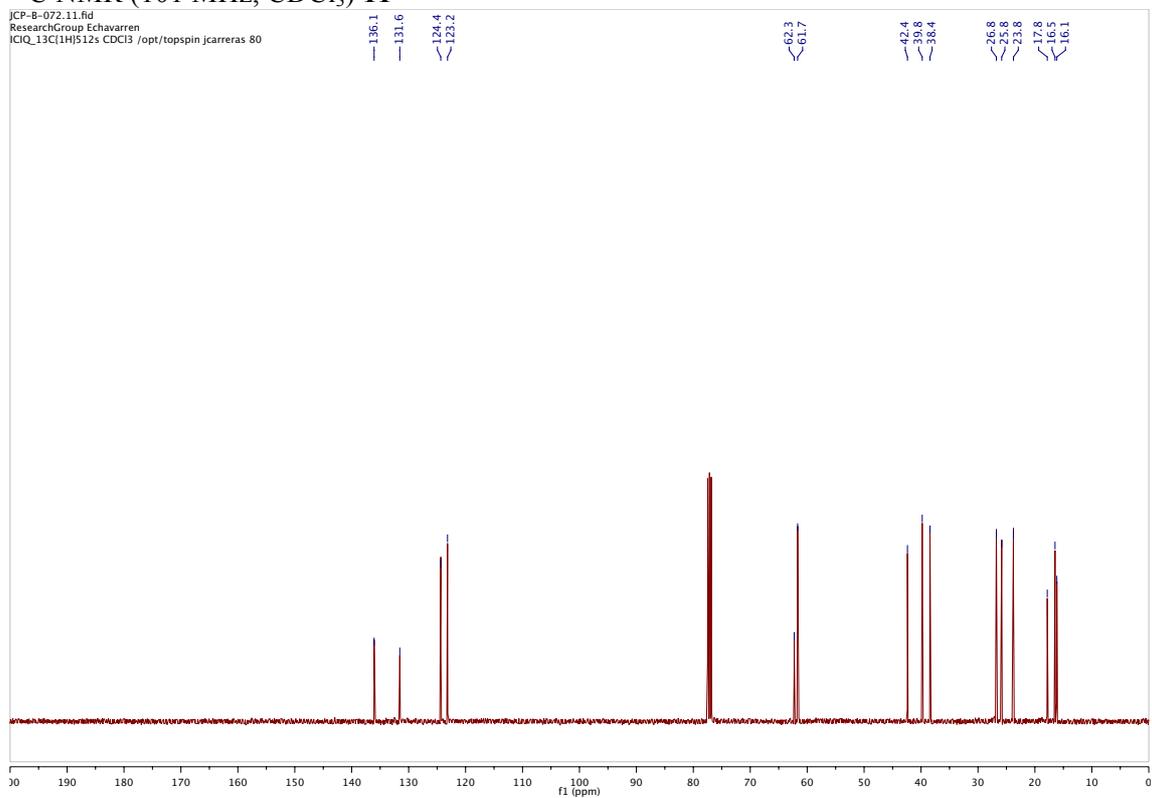
## $^1\text{H}$ NMR (400 MHz, $\text{CDCl}_3$ ) **11**

JCP-B-072.10.fid  
ResearchGroup Echavarren  
ICIQ\_1H12p8s CDCl3 /opt/topspin jcarreras 80



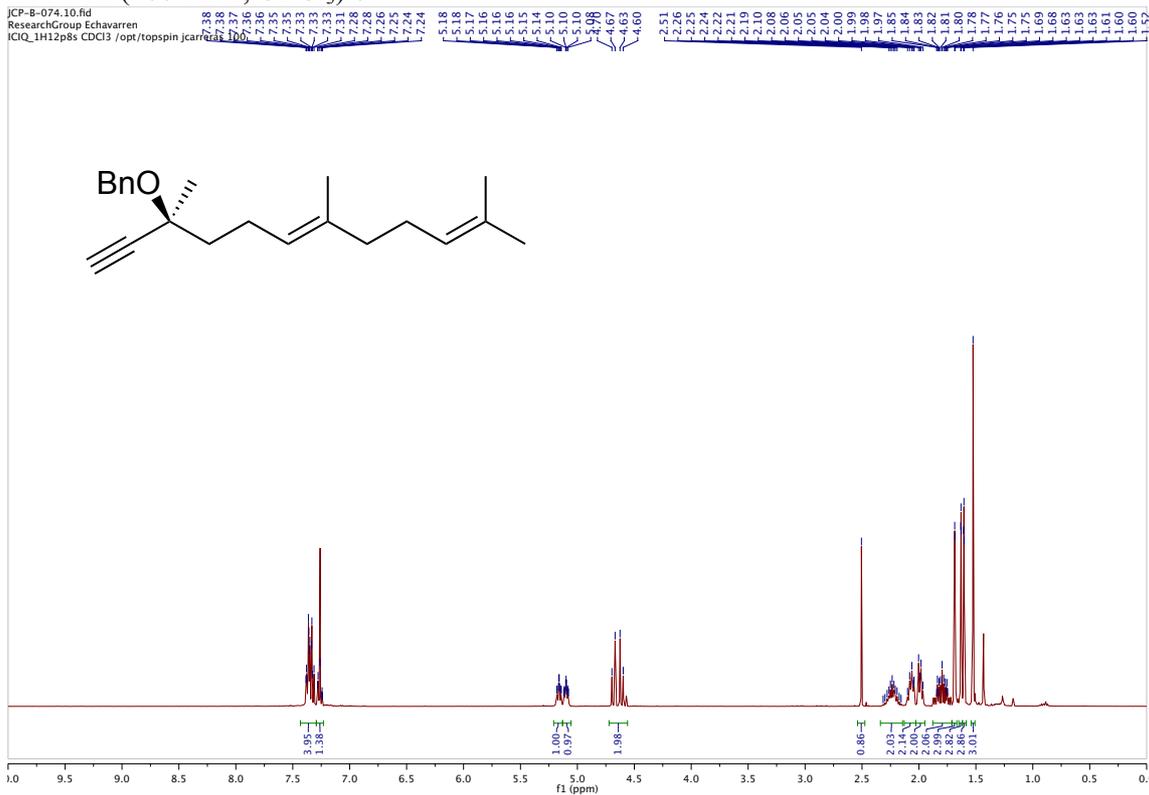
## $^{13}\text{C}$ NMR (101 MHz, $\text{CDCl}_3$ ) **11**

JCP-B-072.11.fid  
ResearchGroup Echavarren  
ICIQ\_13C1H512s CDCl3 /opt/topspin jcarreras 80

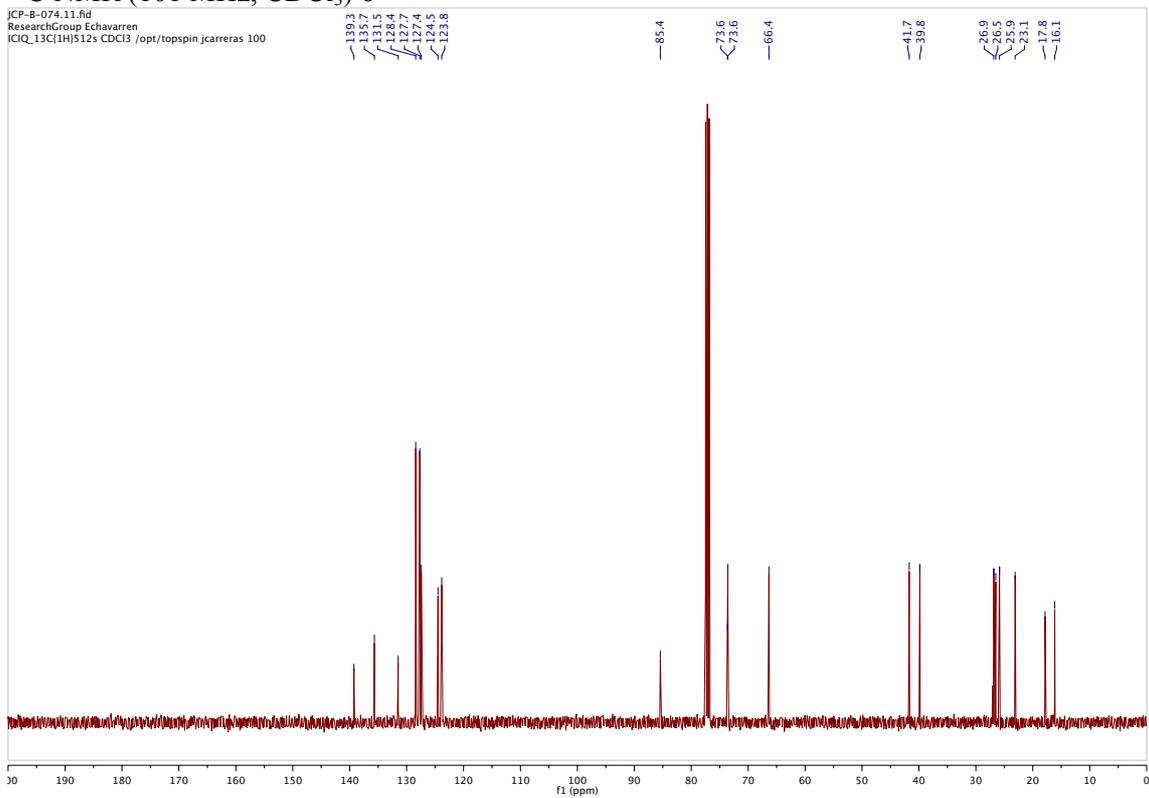




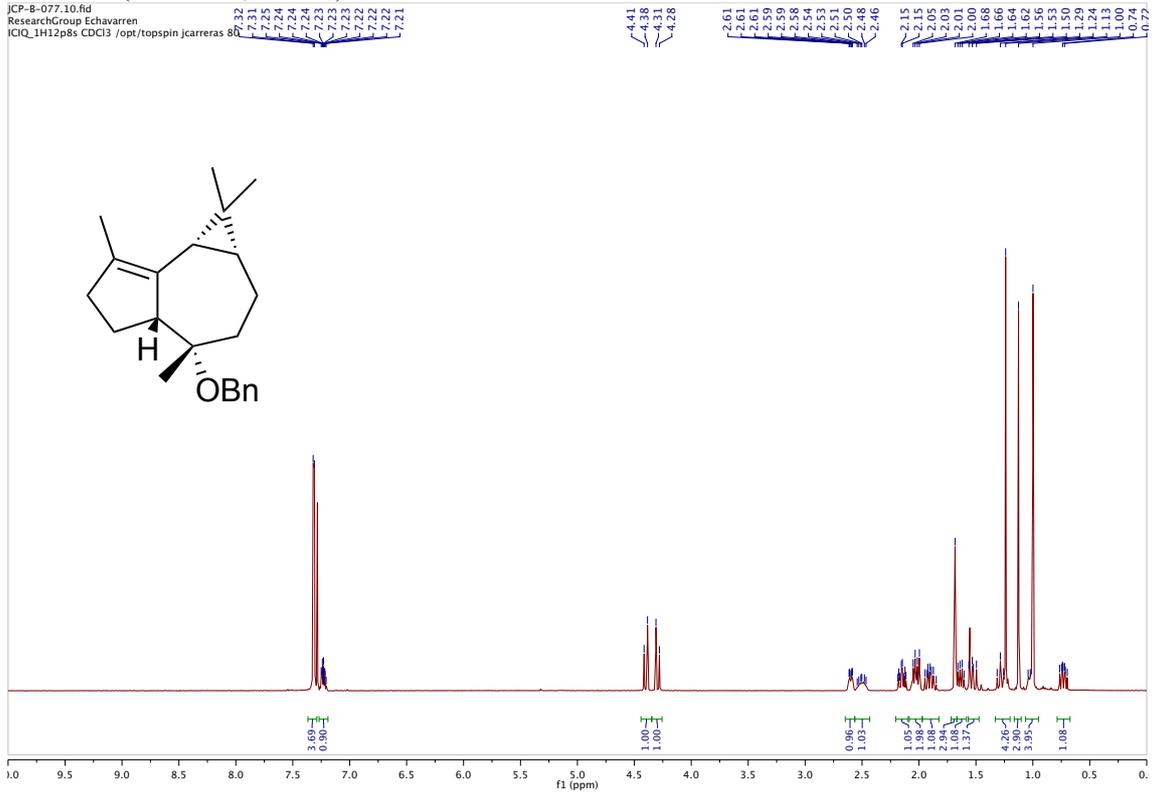
# <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) 6



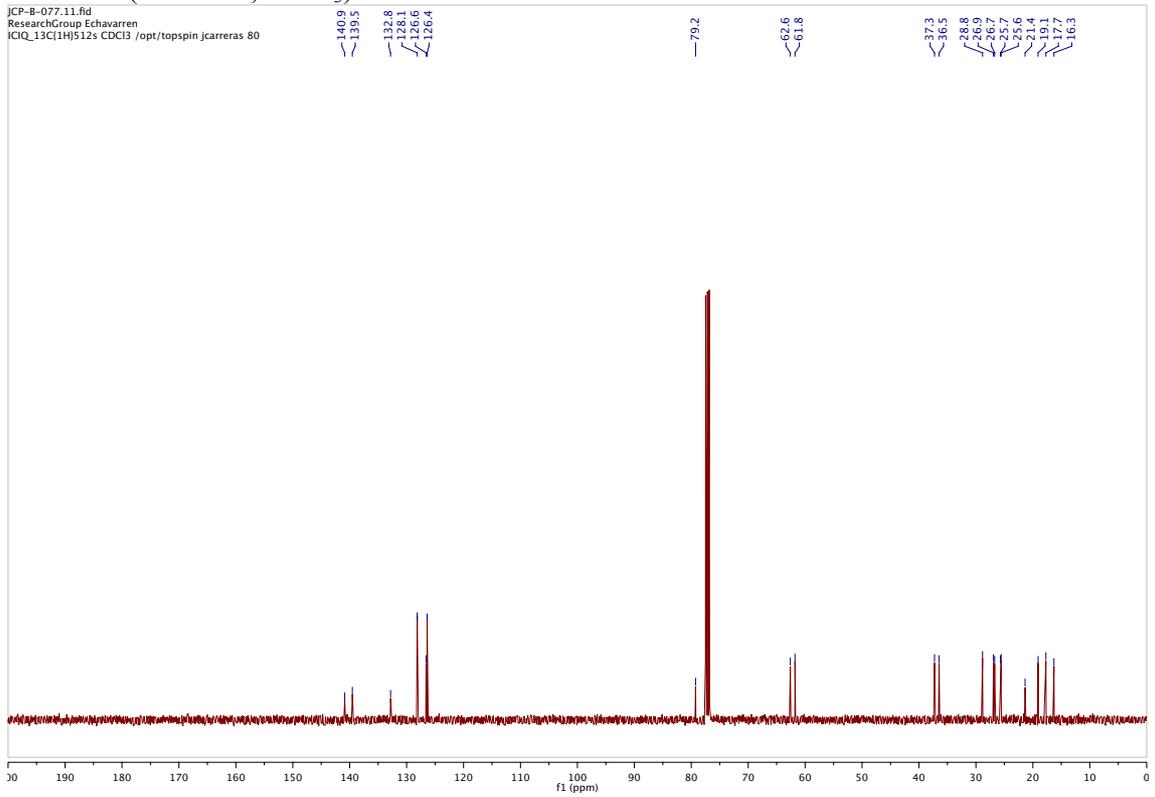
# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) 6



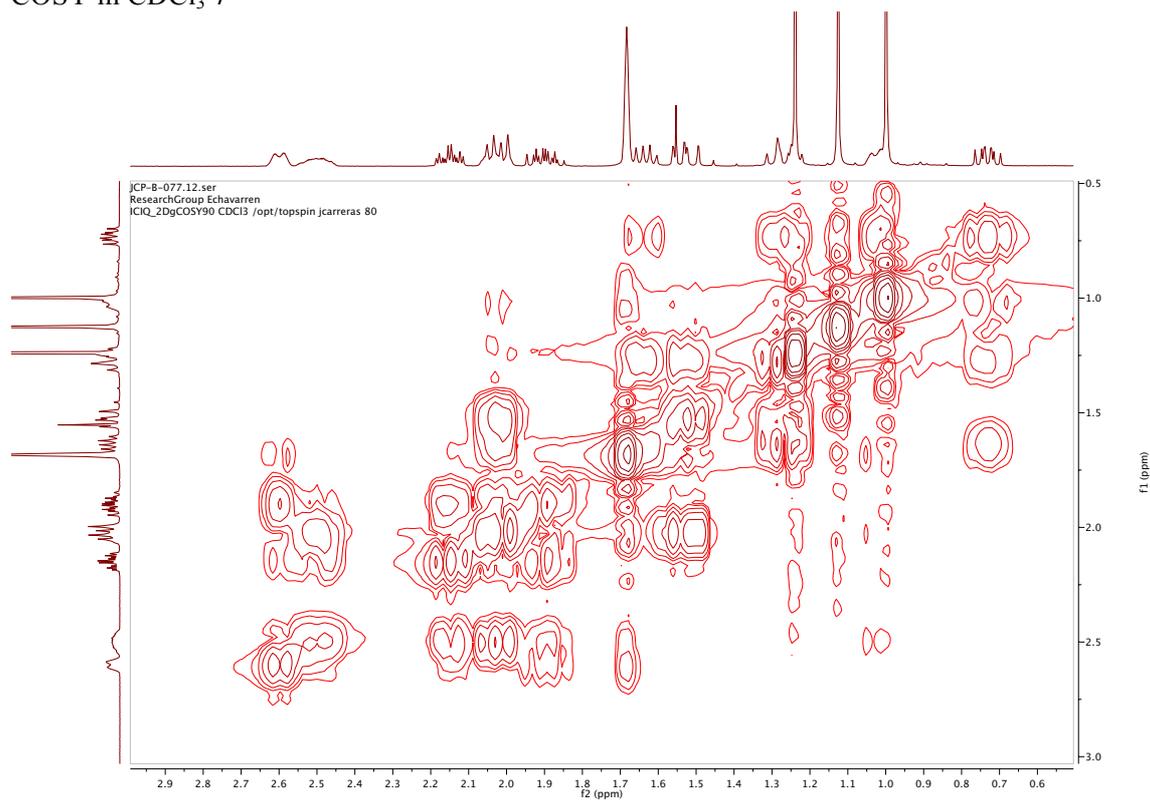
# <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) 7



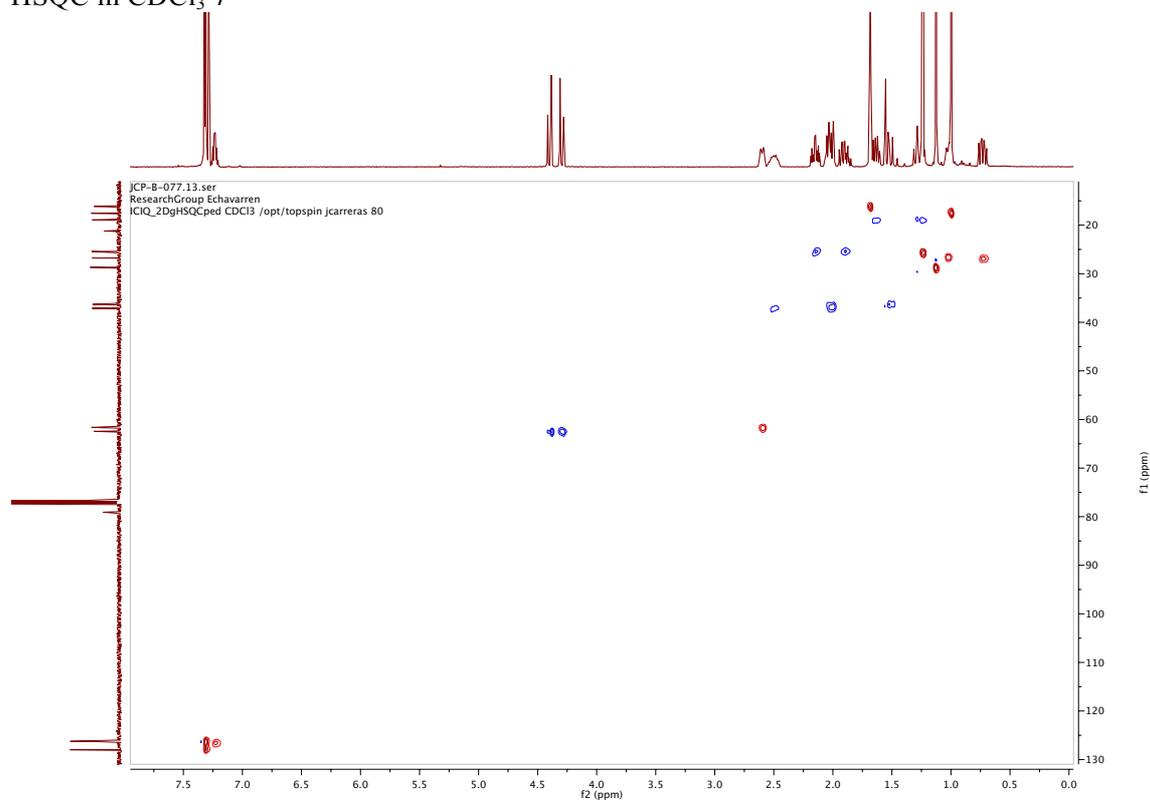
# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) 7



### COSY in CDCl<sub>3</sub> 7

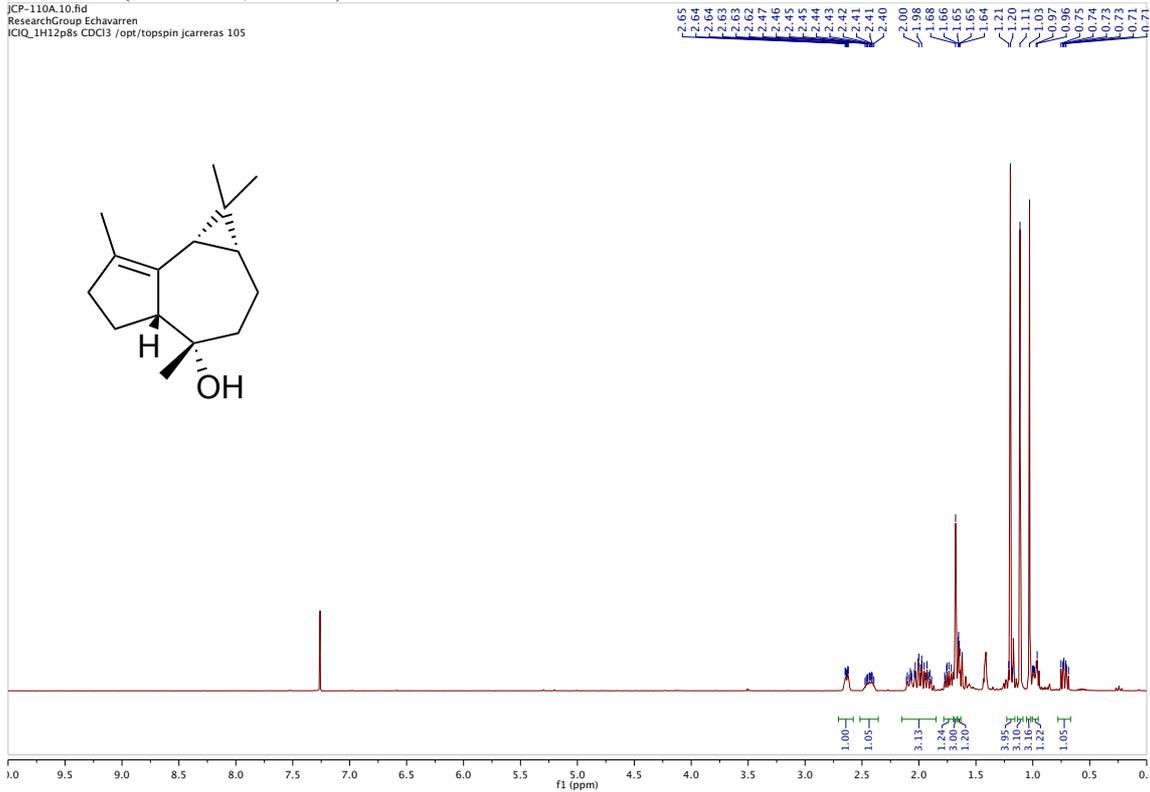


### HSQC in CDCl<sub>3</sub> 7



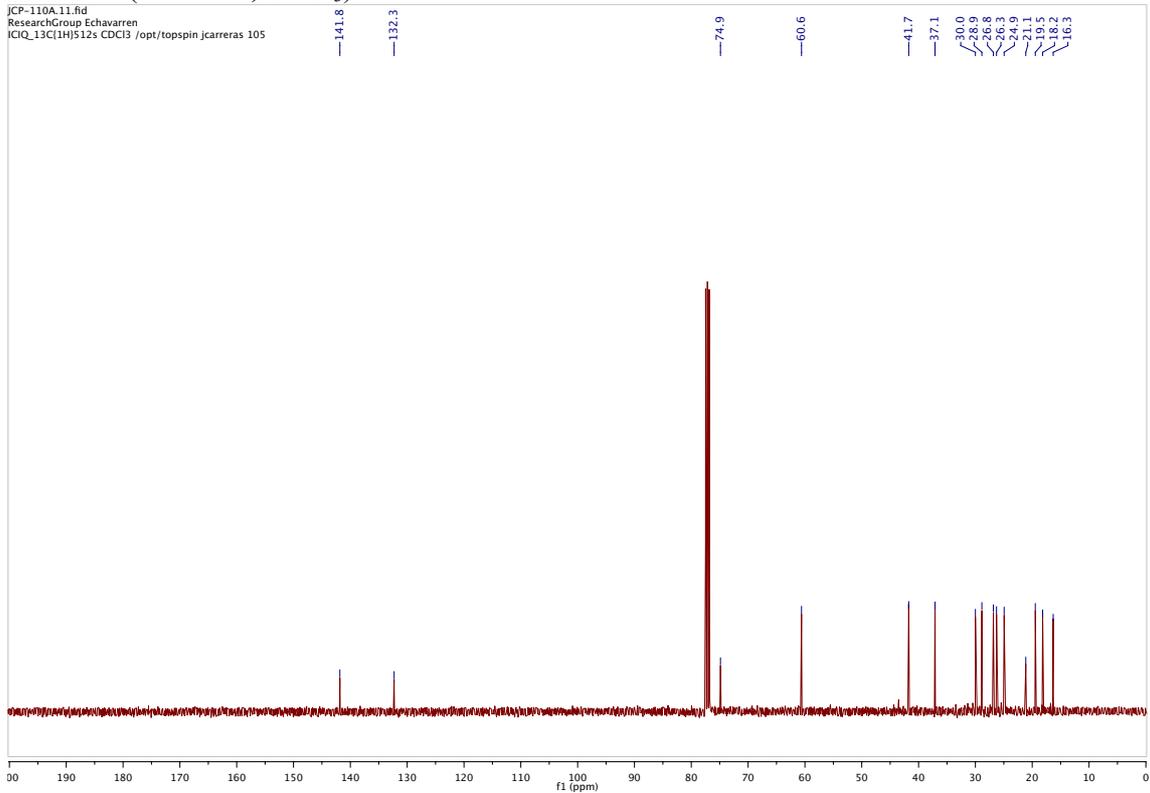
# <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) **14**

JCP-110A.10.fid  
ResearchGroup Echavarren  
ICIQ\_1H12p8s CDCl<sub>3</sub> /opt/topspin jcarreras 105

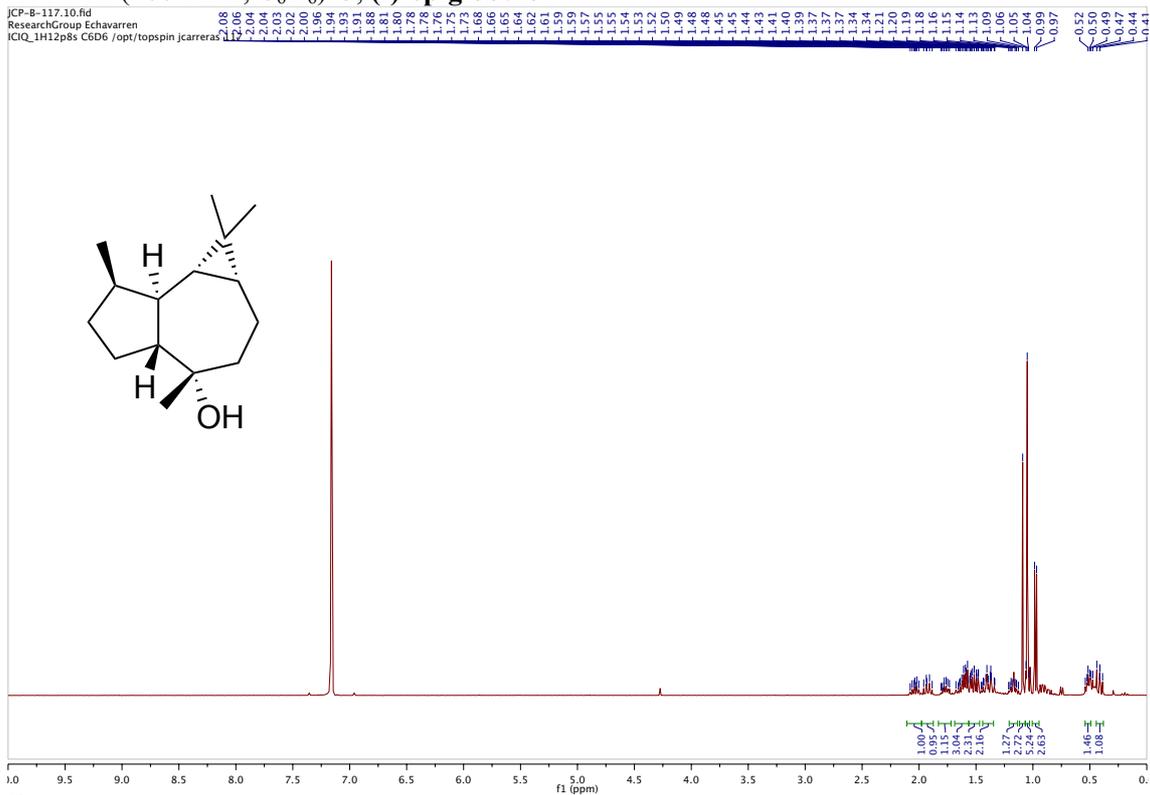


# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) **14**

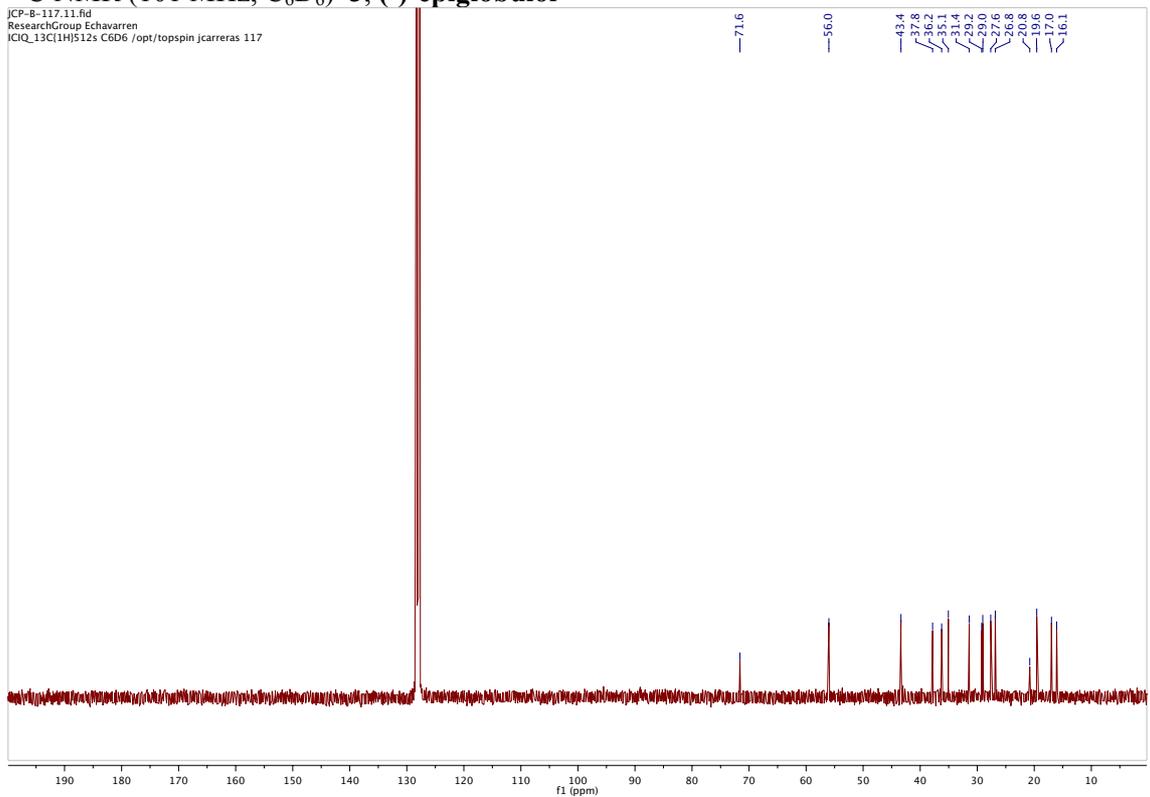
JCP-110A.11.fid  
ResearchGroup Echavarren  
ICIQ\_13C(1H)512s CDCl<sub>3</sub> /opt/topspin jcarreras 105



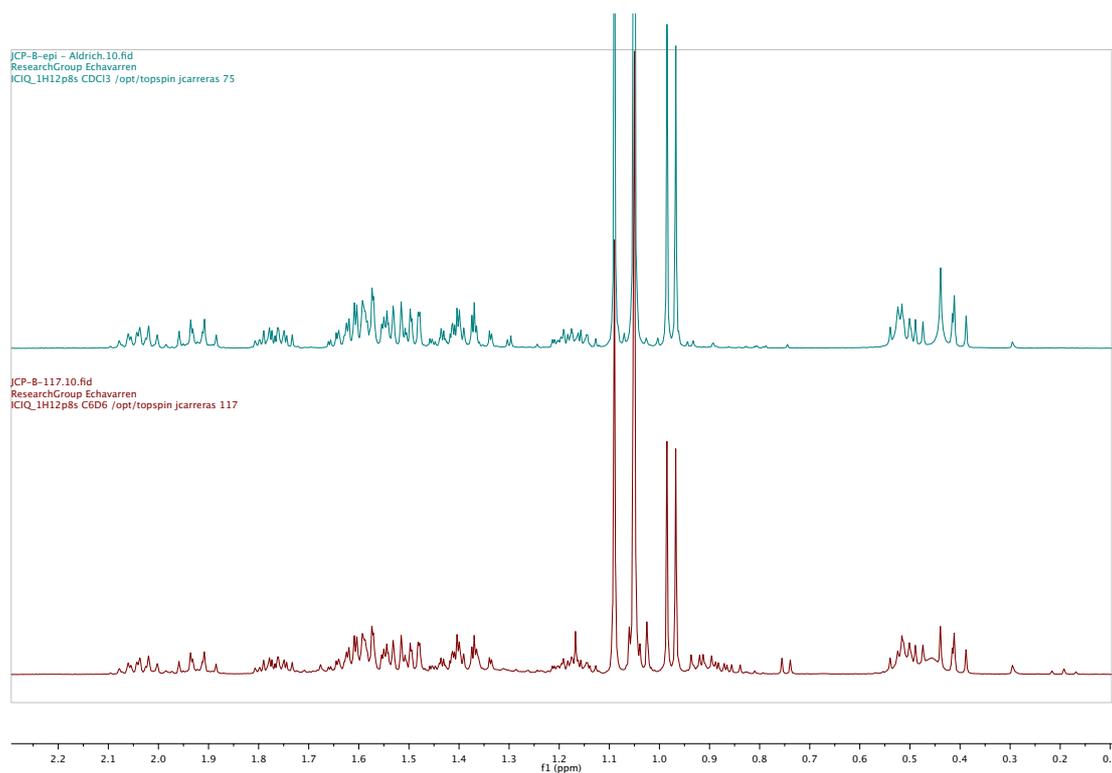
# <sup>1</sup>H NMR (400 MHz, C<sub>6</sub>D<sub>6</sub>) 3, (-)-epiglobulol



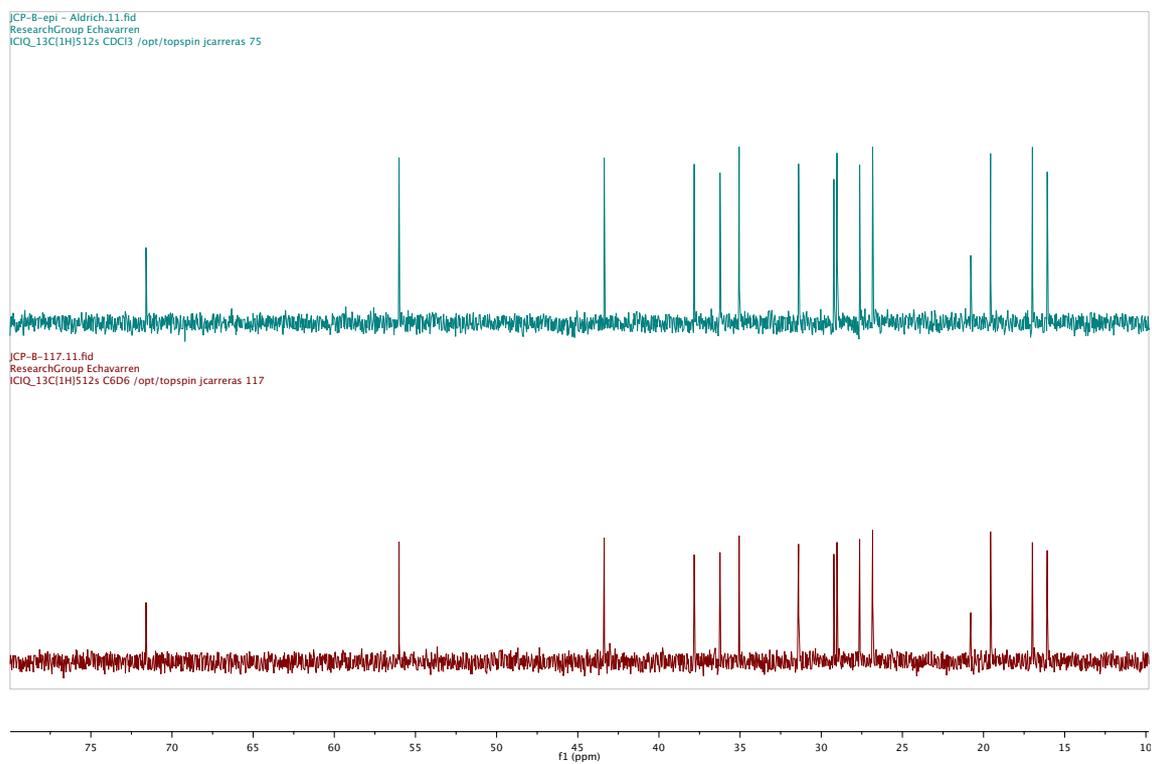
# <sup>13</sup>C NMR (101 MHz, C<sub>6</sub>D<sub>6</sub>) 3, (-)-epiglobulol



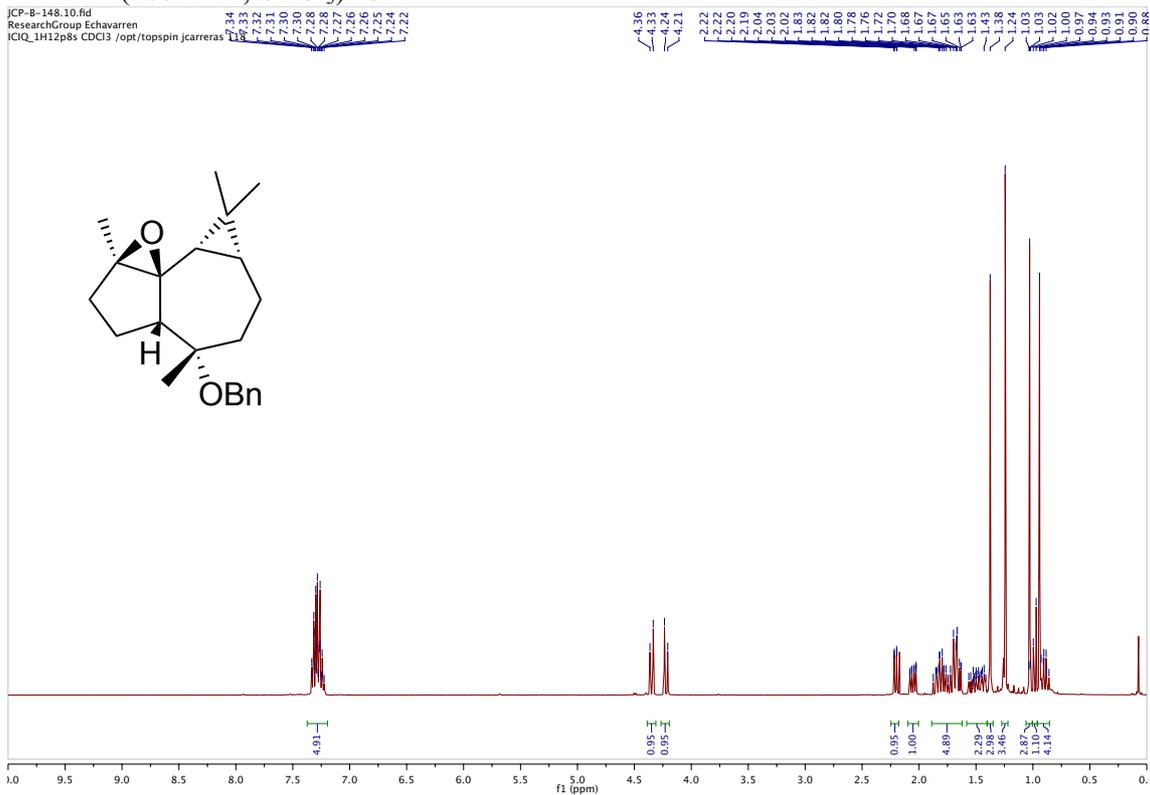
# $^1\text{H}$ NMR comparative with comercial available (-)-epiglobulol and **3**



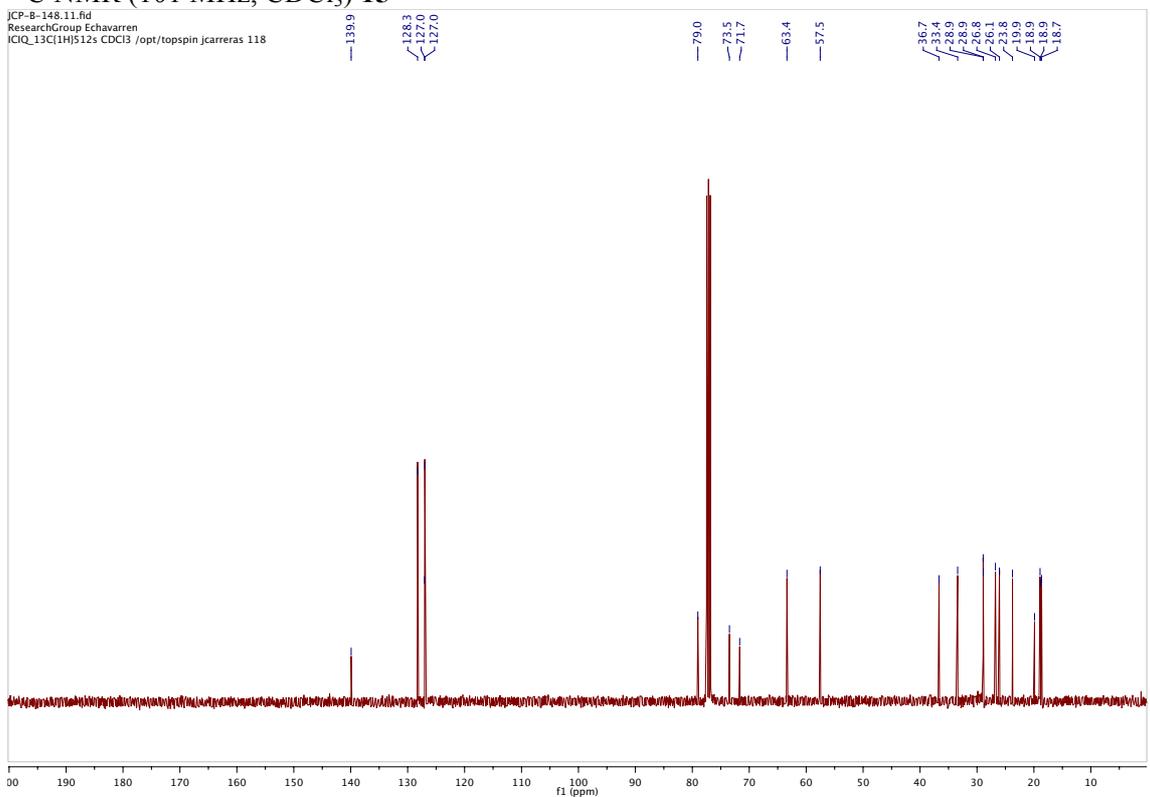
# $^{13}\text{C}$ NMR comparative with comercial available (-)-epiglobulol and **3**



# <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) 15



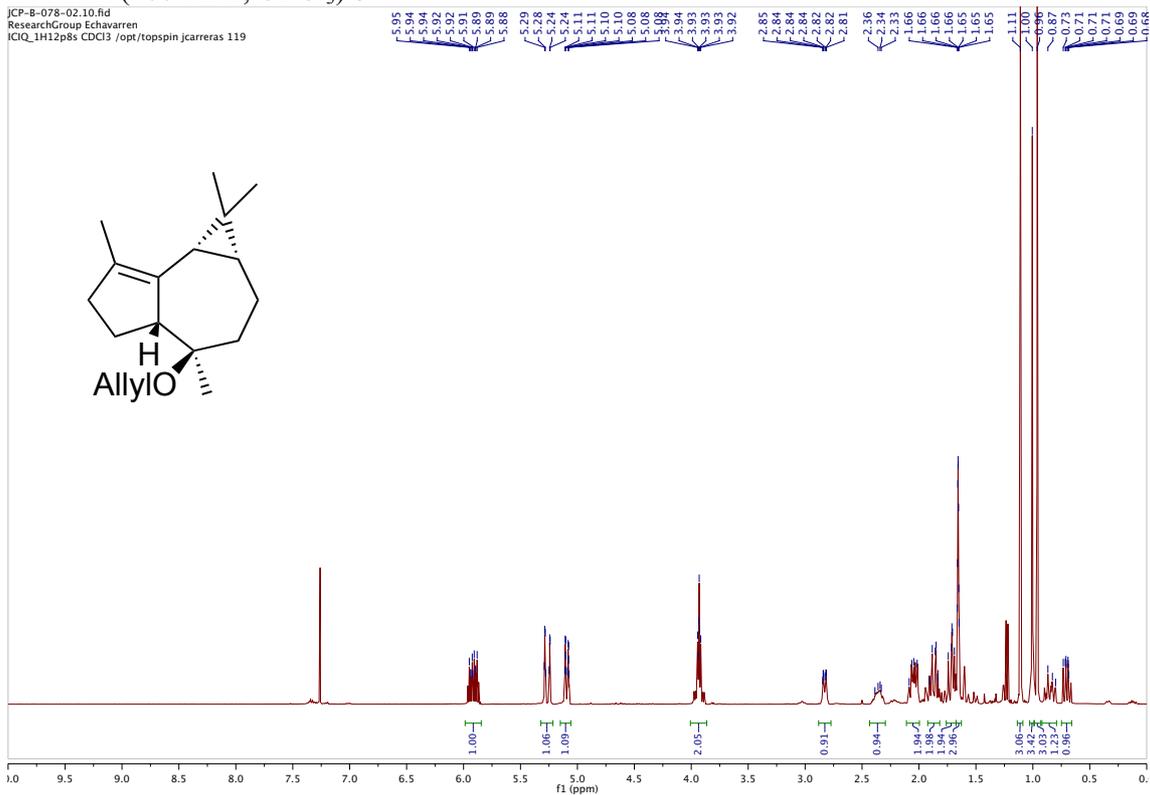
# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) 15





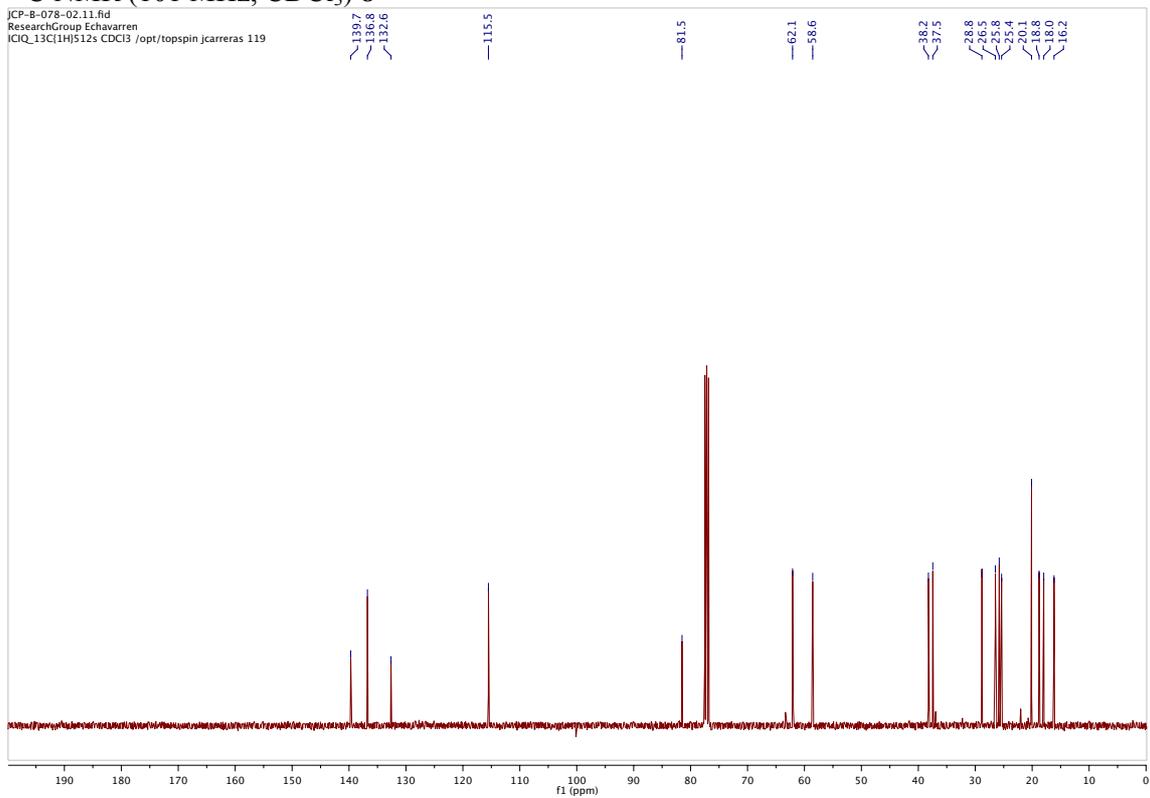
# <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) **8**

JCP-B-078-02.10.fid  
ResearchGroup Echavarren  
C1Q\_1H12p8s CDCl3 /opt/topspin jcarreras 119



# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) **8**

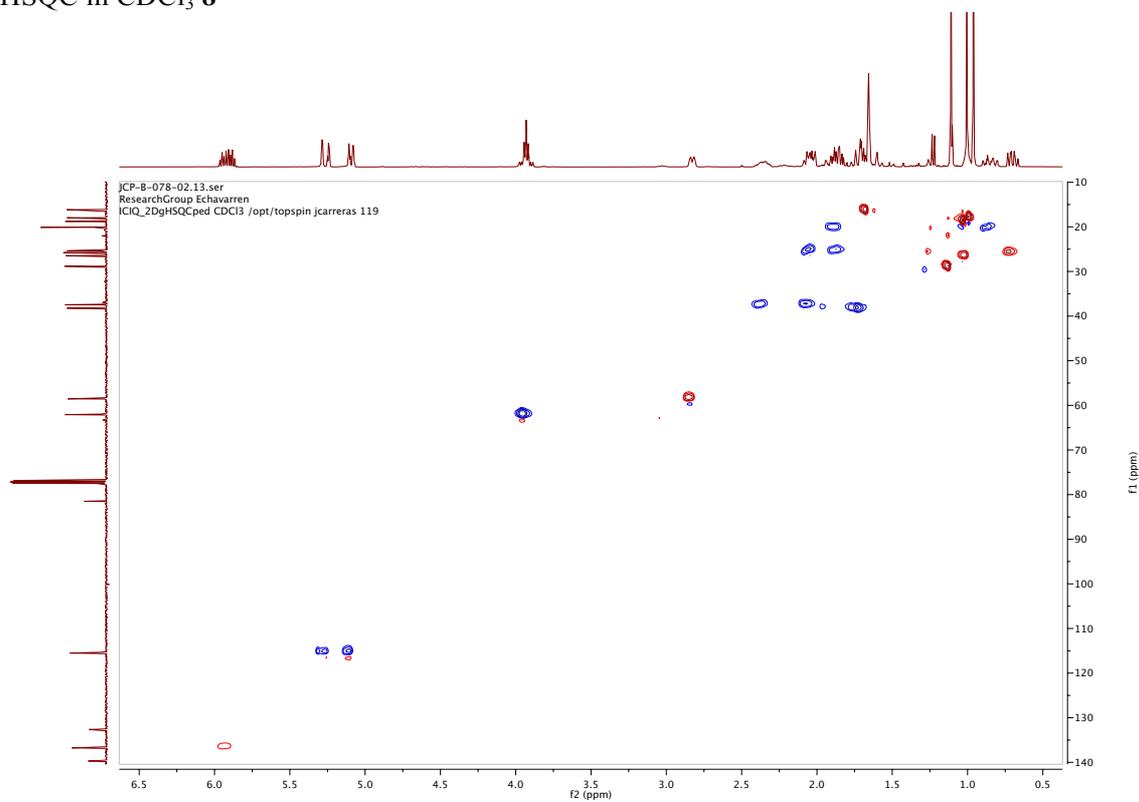
JCP-B-078-02.11.fid  
ResearchGroup Echavarren  
C1Q\_13C1H1512s CDCl3 /opt/topspin jcarreras 119



### COSY in CDCl<sub>3</sub> 8

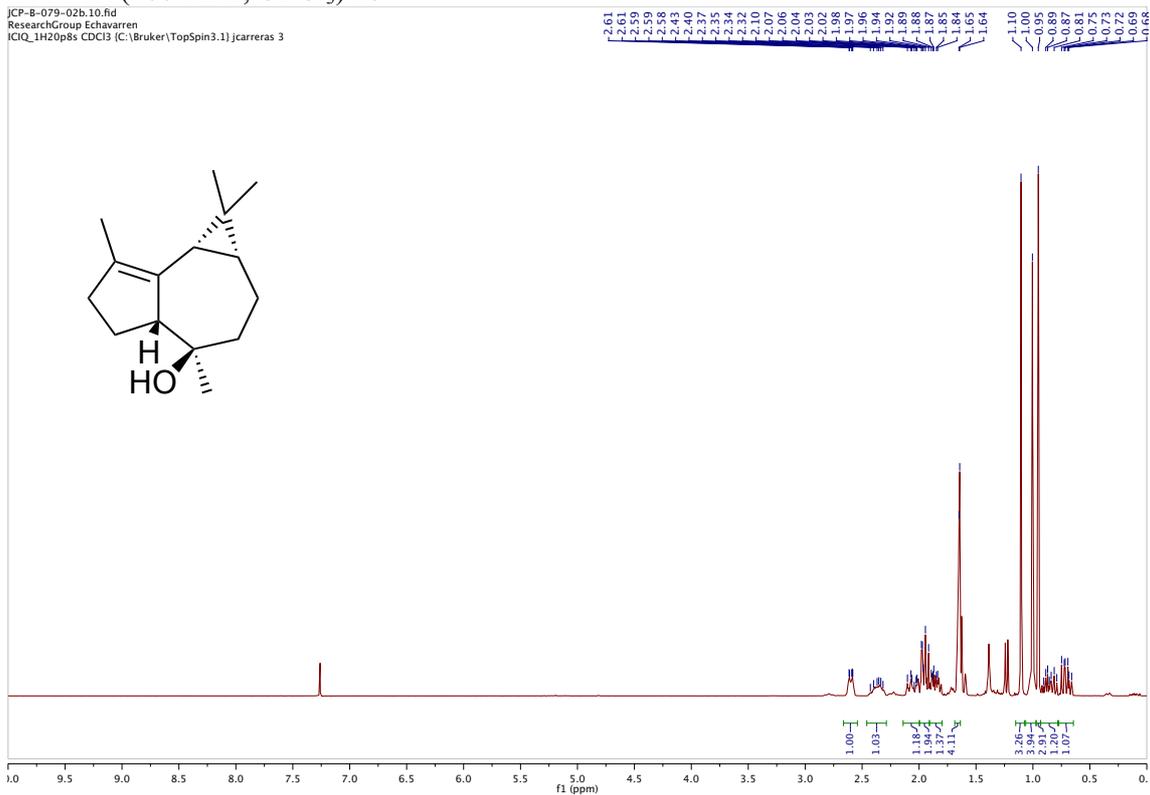


### HSQC in CDCl<sub>3</sub> 8



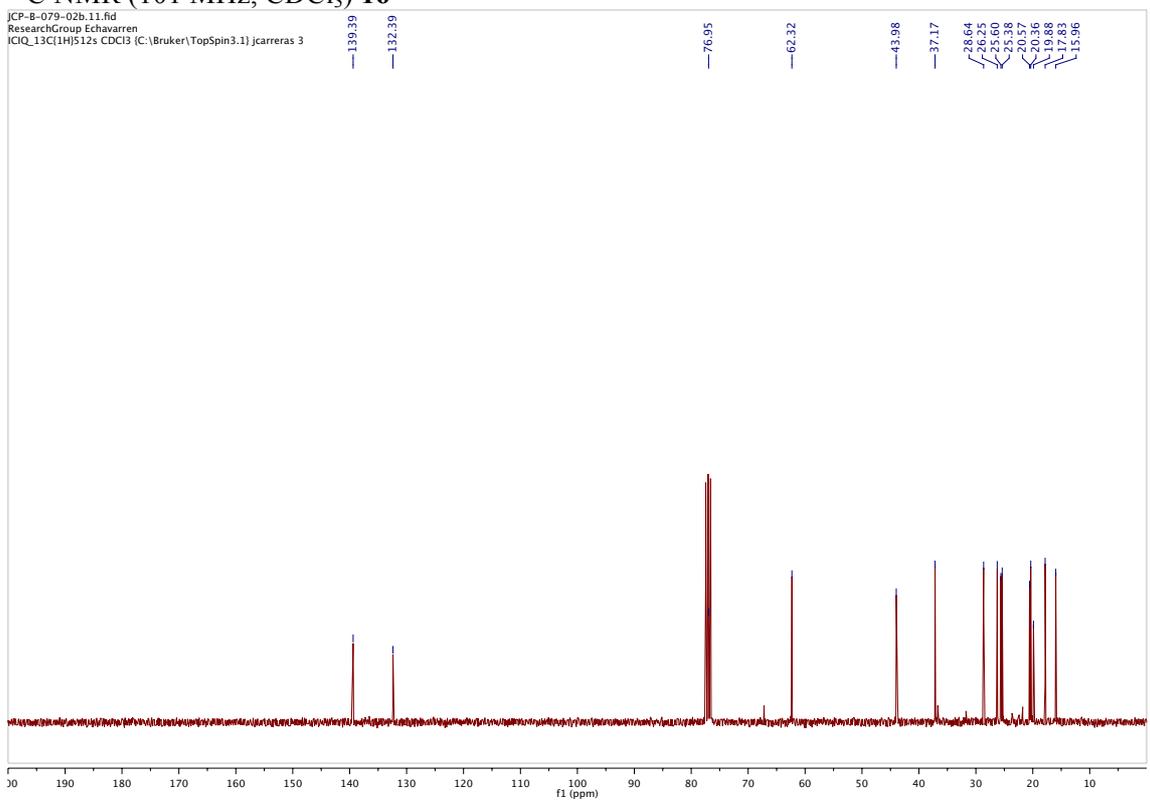
# <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) 16

JCP-B-079-02b.10.fid  
ResearchGroup Echavarren  
C1Q\_1H20p8s CDCl3 (C:\Bruker\TopSpin3.1)jcarreras 3



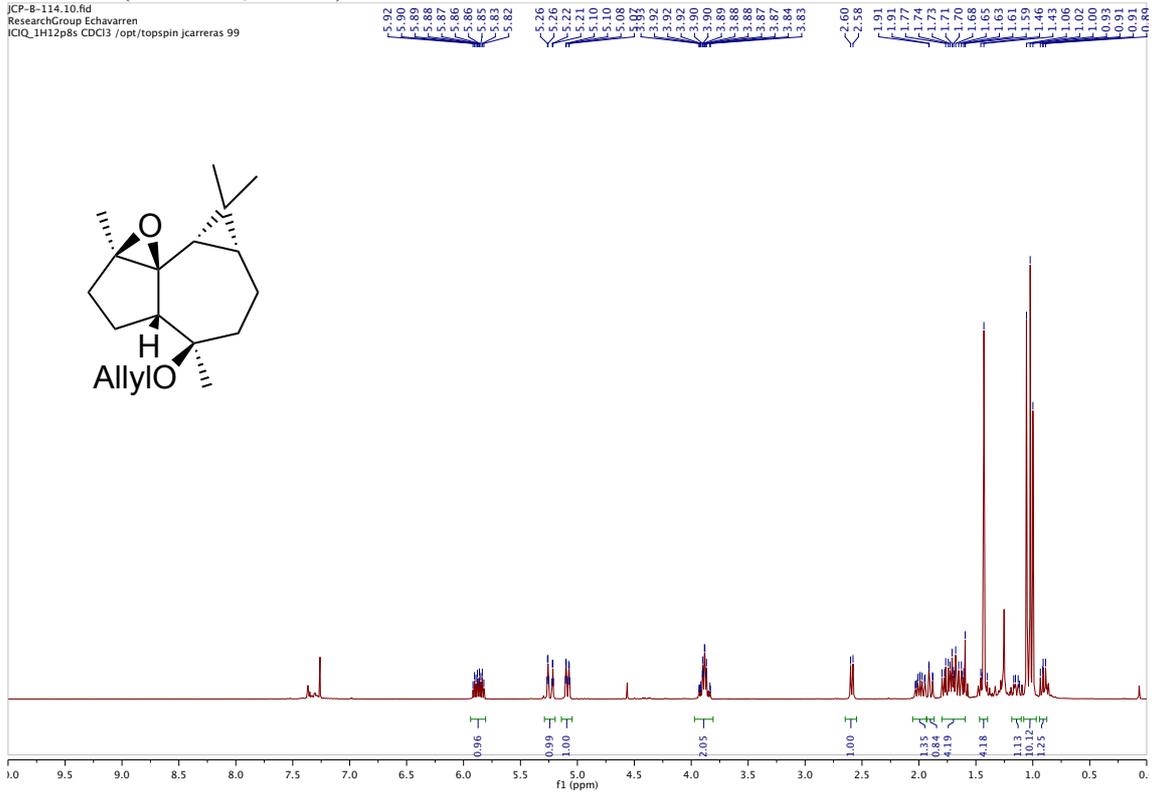
# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) 16

JCP-B-079-02b.11.fid  
ResearchGroup Echavarren  
C1Q\_13C1H512s CDCl3 (C:\Bruker\TopSpin3.1)jcarreras 3



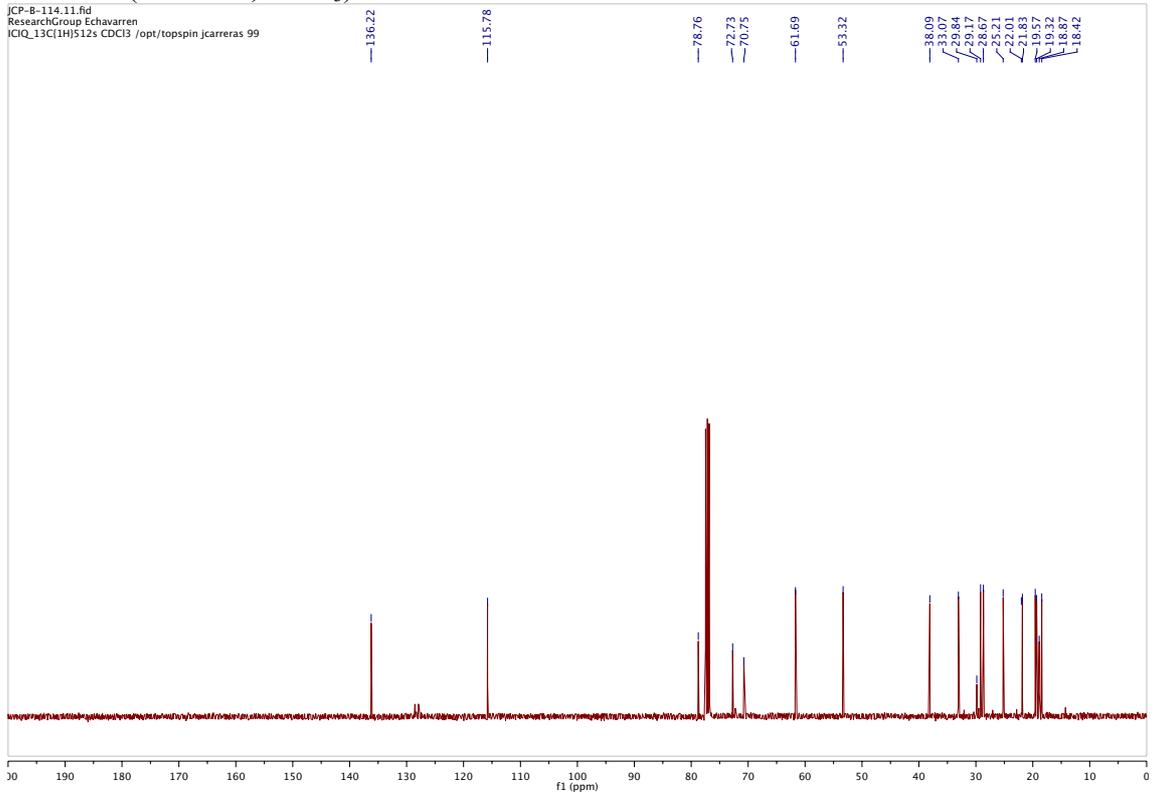
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) **17**

JCP-B-114.10.fid  
ResearchGroup Echavarren  
ICIQ\_1H12p8s CDCl3 /opt/topspin jcarreras 99



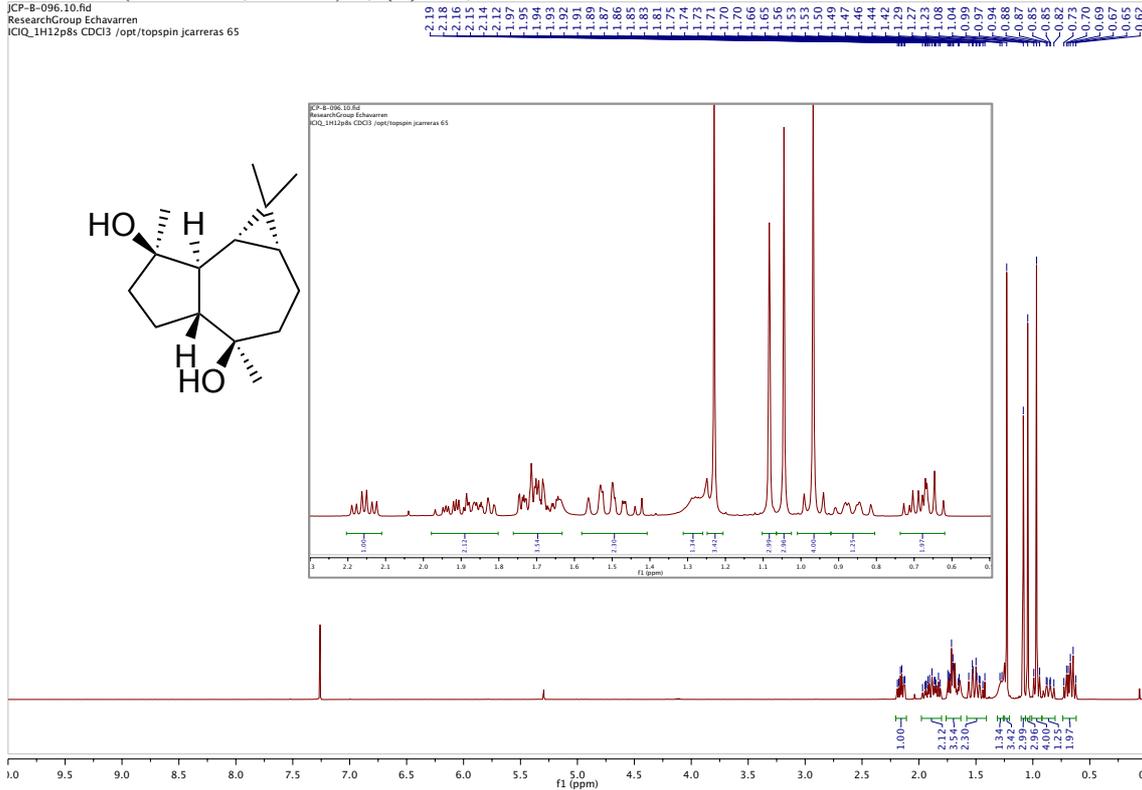
<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) **17**

JCP-B-114.11.fid  
ResearchGroup Echavarren  
ICIQ\_13C(1H)512s CDCl3 /opt/topspin jcarreras 99



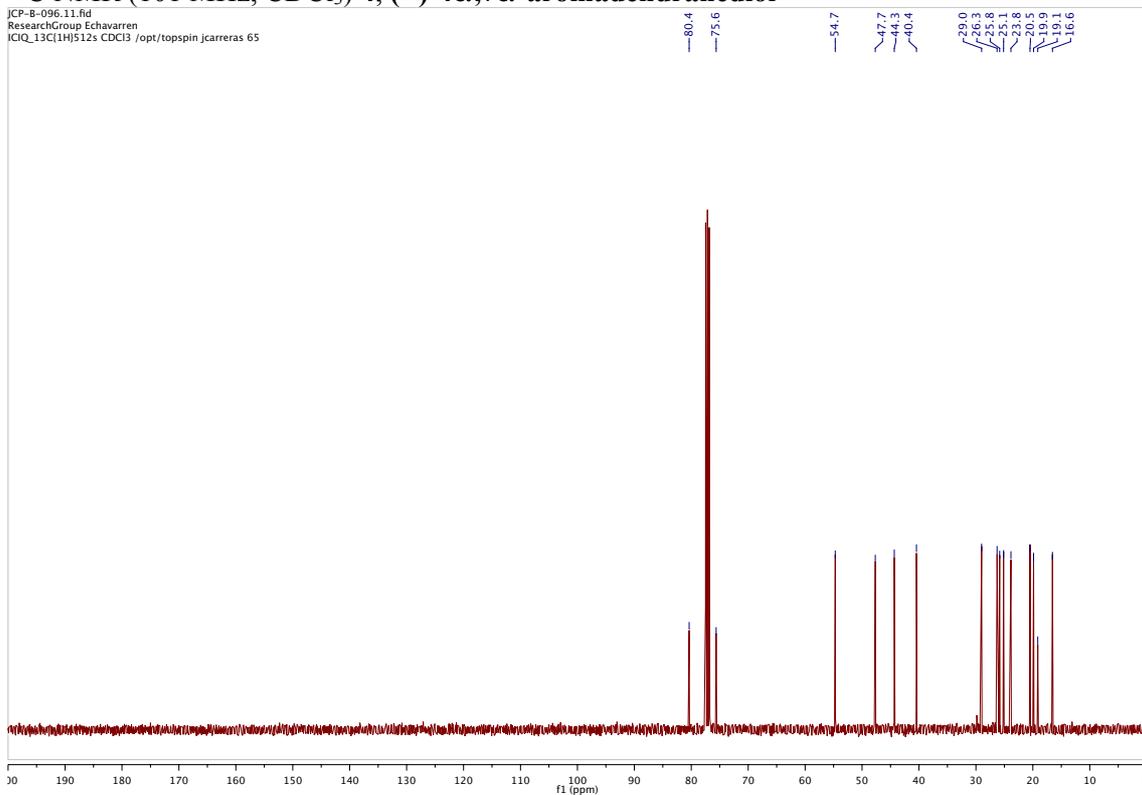
# <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) 4, (-)-4 $\alpha$ ,7 $\alpha$ -aromadendranediol

JCP-B-096.10.fid  
ResearchGroup Echavarren  
ICIQ\_1H12p8s CDCl3 /opt/topspin jcarreras 65

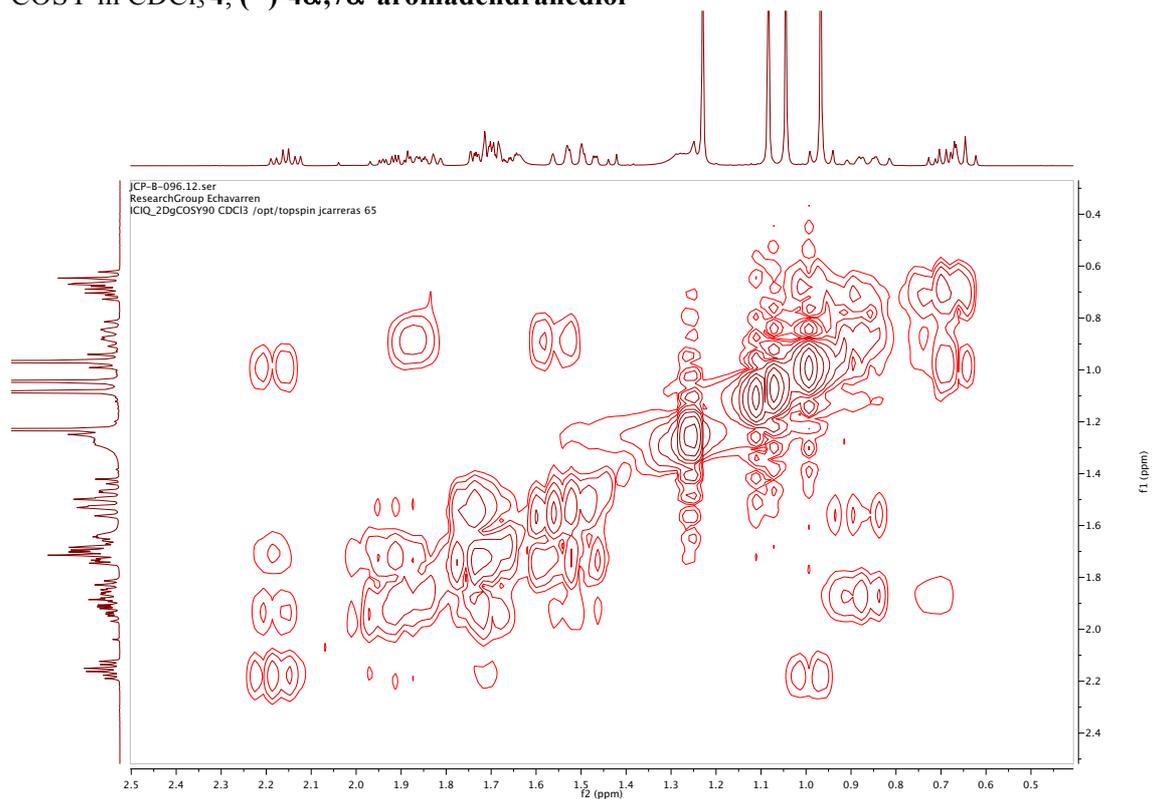


# <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) 4, (-)-4 $\alpha$ ,7 $\alpha$ -aromadendranediol

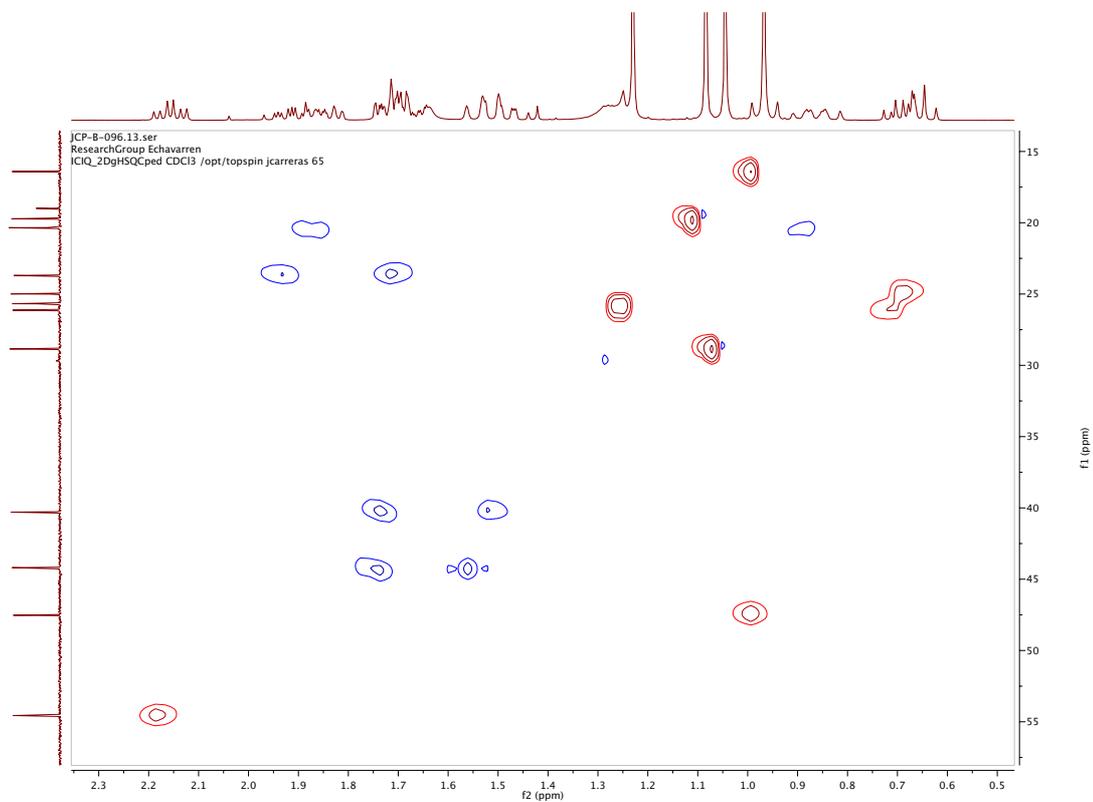
JCP-B-096.11.fid  
ResearchGroup Echavarren  
ICIQ\_13C1H512s CDCl3 /opt/topspin jcarreras 65



COSY in CDCl<sub>3</sub> 4, (-)-4 $\alpha$ ,7 $\alpha$ -aromadendranediol



HSQC in CDCl<sub>3</sub> 4, (-)-4 $\alpha$ ,7 $\alpha$ -aromadendranediol



## X-ray structure analyses

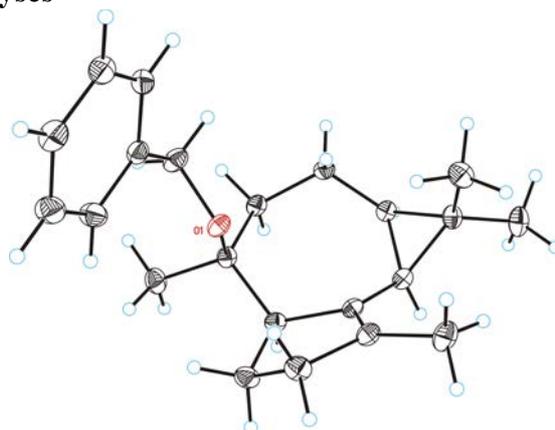


Table 1. Crystal data and structure refinement for (±)-7.

Empirical formula	C <sub>22</sub> H <sub>30</sub> O	
Formula weight	310.46	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 8.9044(4) Å	α = 82.296(2) °
	b = 9.3413(4) Å	β = 82.864(2) °
	c = 10.7520(5) Å	γ = 88.700(2) °
Volume	879.38(7) Å <sup>3</sup>	
Z	2	
Density (calculated)	1.172 Mg/m <sup>3</sup>	
Absorption coefficient	0.069 mm <sup>-1</sup>	
F(000)	340	
Crystal size	0.40 x 0.20 x 0.15 mm <sup>3</sup>	
Theta range for data collection	1.93 to 41.23 °	
Index ranges	-16 ≤ h ≤ 16, -17 ≤ k ≤ 16, -19 ≤ l ≤ 19	
Reflections collected	39501	
Independent reflections	10469 [R(int) = 0.0435]	
Completeness to theta = 41.23 °	0.891 %	
Absorption correction	Empirical	
Max. and min. transmission	0.9897 and 0.9729	
Refinement method	Full-matrix least-squares on F <sup>2</sup>	
Data / restraints / parameters	10469 / 0 / 212	
Goodness-of-fit on F <sup>2</sup>	1.031	
Final R indices [I > 2σ(I)]	R1 = 0.0449, wR2 = 0.1204	
R indices (all data)	R1 = 0.0608, wR2 = 0.1322	
Largest diff. peak and hole	0.709 and -0.264 e.Å <sup>-3</sup>	

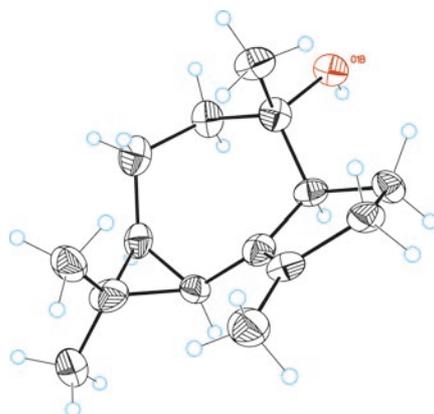


Table 2. Crystal data and structure refinement for (±)-16.

Empirical formula	C <sub>15</sub> H <sub>24</sub> O	
Formula weight	220.34	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 6.8966(4) Å	α = 90.00 °
	b = 46.307(3) Å	β = 98.017(2) °
	c = 12.7309(8) Å	γ = 90.00 °
Volume	4026.1(4) Å <sup>3</sup>	
Z	12	
Density (calculated)	1.091 Mg/m <sup>3</sup>	
Absorption coefficient	0.066 mm <sup>-1</sup>	
F(000)	1464	
Crystal size	0.20 x 0.10 x 0.10 mm <sup>3</sup>	
Theta range for data collection	1.62 to 28.98 °	
Index ranges	-9 ≤ h ≤ 7, -61 ≤ k ≤ 45, -16 ≤ l ≤ 16	
Reflections collected	24804	
Independent reflections	13158 [R(int) = 0.0427]	
Completeness to theta = 28.98 °	81.8%	
Absorption correction	Empirical	
Max. and min. transmission	0.9935 and 0.9870	
Refinement method	Full-matrix least-squares on F <sup>2</sup>	
Data / restraints / parameters	13158 / 1713 / 1187	
Goodness-of-fit on F <sup>2</sup>	1.111	
Final R indices [I > 2σ(I)]	R1 = 0.0659, wR2 = 0.1717	
R indices (all data)	R1 = 0.0885, wR2 = 0.1953	
Flack parameter	x = 0.8(19)	
Largest diff. peak and hole	0.318 and -0.289 e.Å <sup>-3</sup>	

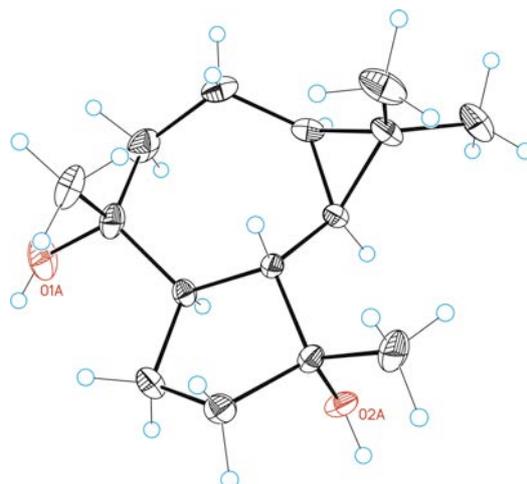


Table 3. Crystal data and structure refinement for (-)-4.

Empirical formula	C <sub>15</sub> H <sub>26</sub> O <sub>2</sub>	
Formula weight	238.36	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2	
Unit cell dimensions	a = 14.0814(6) Å	α = 90.00 °
	b = 19.3046(8) Å	β = 90.00 °
	c = 10.5513(4) Å	γ = 90.00 °
Volume	2868.2(2) Å <sup>3</sup>	
Z	8	
Density (calculated)	1.104 Mg/m <sup>3</sup>	
Absorption coefficient	0.071 mm <sup>-1</sup>	
F(000)	1056	
Crystal size	0.40 x 0.40 x 0.30 mm <sup>3</sup>	
Theta range for data collection	1.79 to 54.28 °	
Index ranges	-24 ≤ h ≤ 29, -42 ≤ k ≤ 43, -18 ≤ l ≤ 24	
Reflections collected	109373	
Independent reflections	33206 [R(int) = 0.0290]	
Completeness to theta = 28.98 °	94.2%	
Absorption correction	Empirical	
Max. and min. transmission	0.9791 and 0.9722	
Refinement method	Full-matrix least-squares on F <sup>2</sup>	
Data / restraints / parameters	33206 / 0 / 319	
Goodness-of-fit on F <sup>2</sup>	1.036	
Final R indices [I > 2σ(I)]	R1 = 0.0394, wR2 = 0.1009	
R indices (all data)	R1 = 0.0527, wR2 = 0.1092	
Flack parameter	x = 0.0(2)	
Hooft parameter	y = -0.03(10)	
Largest diff. peak and hole	0.399 and -0.240 e.Å <sup>-3</sup>	

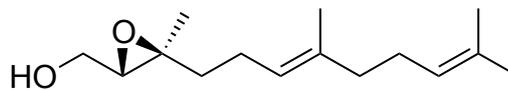
## HPLC analysis

### HPLC separation of 10.

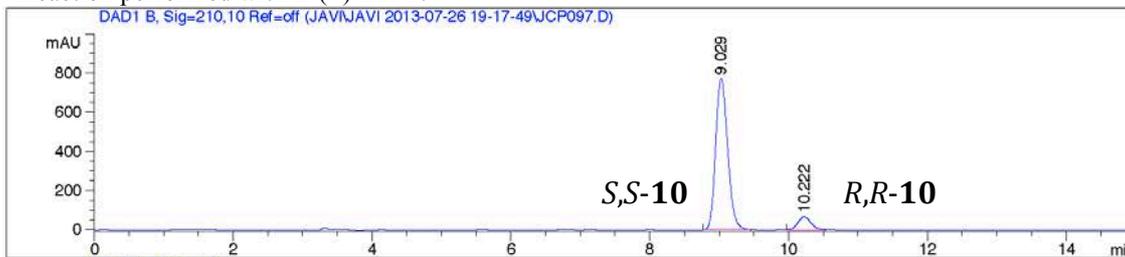
Hewlett-Packard 1200 Series HPLC equipped with DAD (diode array) detector IA

Sample Info : Hexane:IPA:EtOH (96:2:2) 1 mL/min

Chiralpack IA, 5 $\mu$ L



- Reaction performed with L-(+)-DIPT:



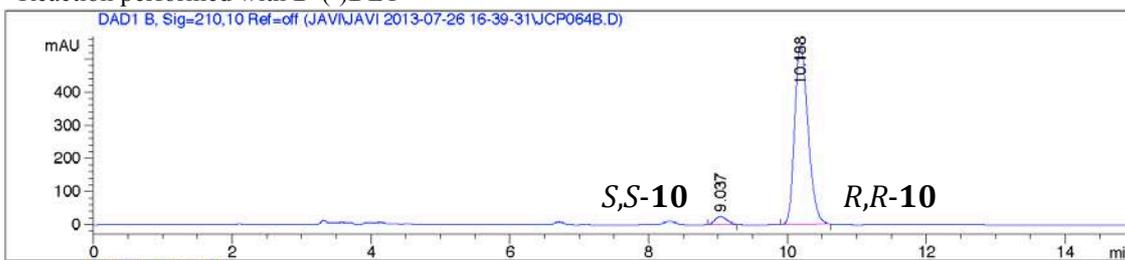
#### Area Percent Report

```
=====  
Sorted By           :      Signal  
Multiplier          :      1.0000  
Dilution            :      1.0000  
Use Multiplier & Dilution Factor with ISTDs  
Signal 1: DAD1 B, Sig=210,10 Ref=off  
=====
```

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.029	MM	0.1993	9208.02930	769.99188	91.3264
2	10.222	MM	0.2189	874.51666	66.58943	8.6736

```
Totals :                      1.00825e4  836.58131  
=====
```

- Reaction performed with D-(-)DET



#### Area Percent Report

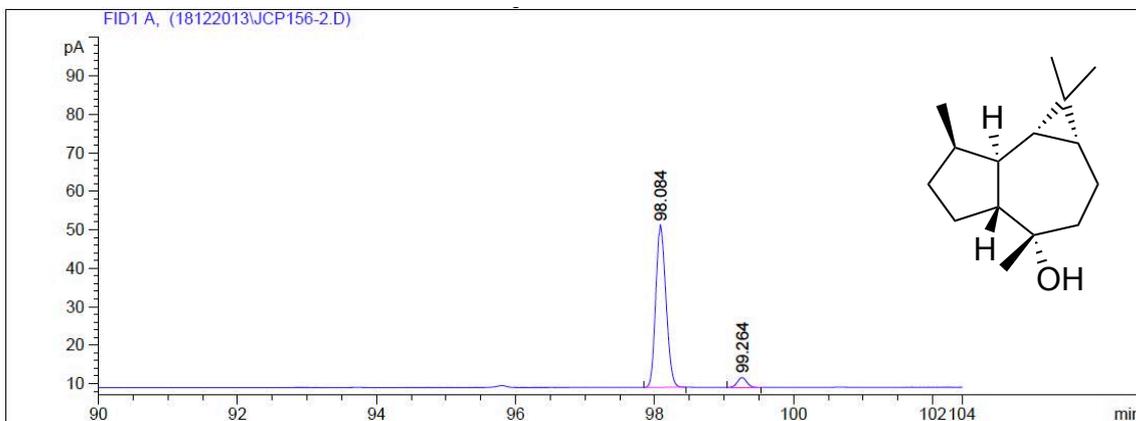
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=====  
Sorted By           :      Signal  
Multiplier          :      1.0000  
Dilution            :      1.0000  
Use Multiplier & Dilution Factor with ISTDs  
Signal 1: DAD1 B, Sig=210,10 Ref=off  
=====
```

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.037	MM	0.1943	298.22714	25.58510	3.9534
2	10.188	MM	0.2236	7245.38721	539.99695	96.0466

```
Totals :                      7543.61435  565.58205  
=====
```

### GC separation of 3.

Agilent GC 6890N equipped with FID detector, HP-Chiral-20B 30mx0.25mm, 0.25µm  
T inj/aux 240 °C, Spilt 20:1 (1µL), 1.5 mL/min  
50 -240 °C (30')/1° Cmin-1  
Sample in DCM



#### Area Percent Report

Sorted By : Signal  
Multiplier : 1.0000  
Dilution : 1.0000  
Use Multiplier & Dilution Factor with ISTDs

Signal 1: FID1 A,

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	98.084	BB	0.1248	428.99451	42.14342	<b>94.78482</b>
2	99.264	BB	0.1158	23.60382	2.50862	<b>5.21518</b>

Totals : 452.59833 44.65204

Results obtained with enhanced integrator!

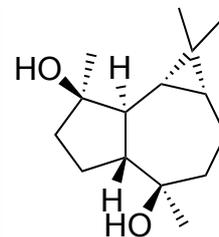
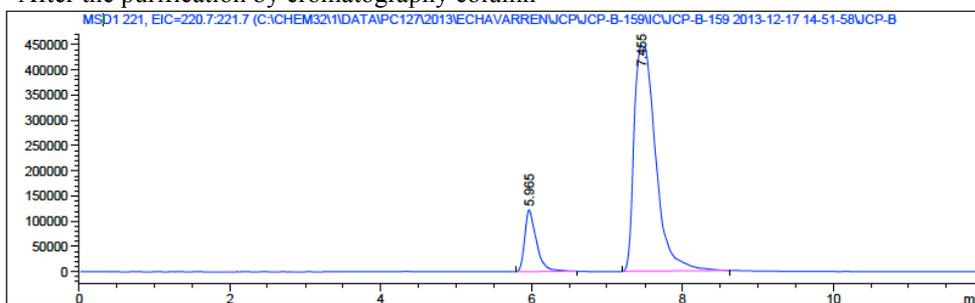
### HPLC separation of 4.

Agilent 1200 Series HPLC equipped with Quadrupole LC/MS 6130 detector (APCI)

Sample Info : Hexane:EtOH (85:15) 1 mL/min

Chiralpack IC, 5 $\mu$ L

- After the purification by chromatography column



Area Percent Report

```

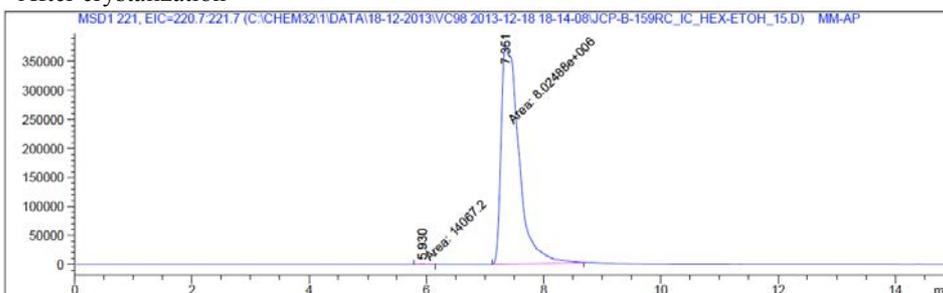
=====
Sorted By           :      Signal
Multiplier          :      1.0000
Dilution            :      1.0000
Use Multiplier & Dilution Factor with ISTDs
Signal 1: MSD1 221, EIC=220.7:221.7
  
```

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.965	BB	0.1512	1.33389e6	1.23024e5	12.9722
2	7.455	BB	0.2731	8.94879e6	4.48743e5	87.0278

```

Totals :                               1.02827e7    5.71767e5
=====
  
```

- After crystallization



Area Percent Report

```

=====
Sorted By           :      Signal
Multiplier          :      1.0000
Dilution            :      1.0000
Use Multiplier & Dilution Factor with ISTDs
Signal 1: MSD1 221, EIC=220.7:221.7
  
```

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.930	MM	0.1827	1.40672e4	1283.58118	<b>0.1750</b>
2	7.351	MM	0.3516	8.02488e6	3.80360e5	<b>99.8250</b>

```

Totals :                               8.03895e6    3.81644e5
=====
  
```

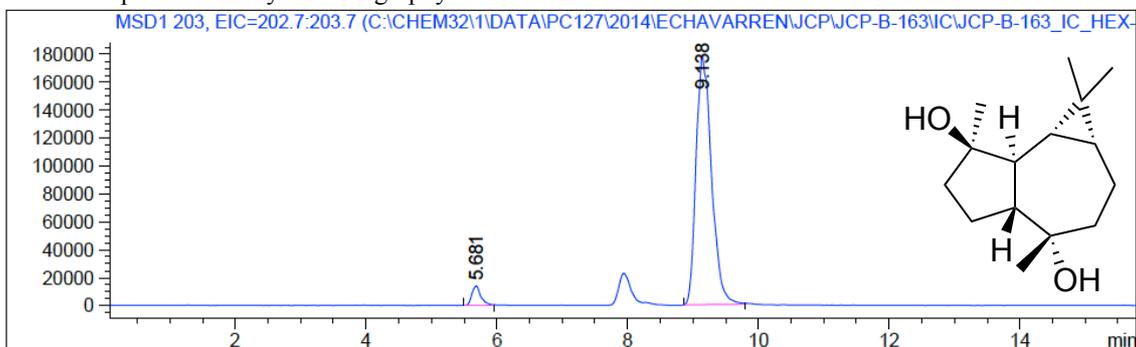
### HPLC separation of 5.

Agilent 1200 Series HPLC equipped with Quadrupole LC/MS 6130 detector (APCI)

Sample Info : Hexane:iPrOH (95:5) 1 mL/min

Chiralpack IC, 5 $\mu$ L (Sample in DCM)

- After the purification by chromatography column



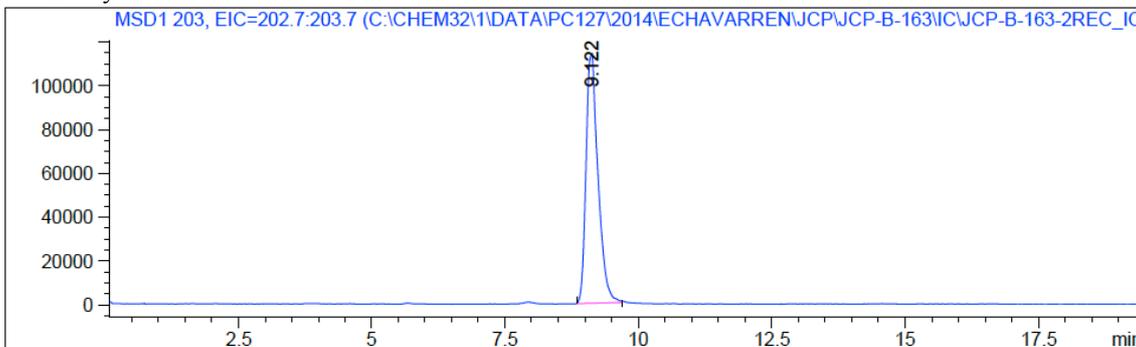
Area Percent Report

Sorted By : Signal  
Multiplier : 1.0000  
Dilution : 1.0000  
Use Multiplier & Dilution Factor with ISTDs  
Signal 1: MSD1 203, EIC=202.7:203.7

Peak #	RetTime [min]	Type	Width [min]	Area	Height	Area %
1	5.681	BB	0.1444	1.31159e5	1.39009e4	4.2694
2	9.138	BB	0.2055	2.94089e6	1.79816e5	95.7306

Totals : 3.07205e6 1.93717e5

- After crystallization



Area Percent Report

Sorted By : Signal  
Multiplier : 1.0000  
Dilution : 1.0000  
Use Multiplier & Dilution Factor with ISTDs  
Signal 1: MSD1 203, EIC=202.7:203.7

Peak #	RetTime [min]	Type	Width [min]	Area	Height	Area %
1	9.122	BB	0.2254	1.78535e6	1.14857e5	100.0000

Totals : 1.78535e6 1.14857e5