

# An Enantioselective Total Synthesis of Helioporins C and E

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## SUPPORTING INFORMATION

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### 1 GENERAL EXPERIMENTAL CONDITIONS

All reactions were carried out under argon in flame-dried glassware. Solids were added in a counter flow of argon. Syringes and cannulas were flushed with argon before use. Oxygen or water sensitive substances were stored and handled in a “Braun Labmaster 130” glovebox.

If not indicated differently, all chemicals were employed as purchased. **Solvents** were distilled prior to use. Tetrahydrofuran (THF), 2-methyl-tetrahydrofuran, diethylether and methy-*tert*-butylether (MTBE) were distilled from sodium/benzophenone under argon. Dichloromethane and tetrachloromethane were distilled from CaH<sub>2</sub> under argon. MeOH was distilled from Mg with I<sub>2</sub> and stored over molecular sieves 3 Å. Amines like TMEDA, NEt<sub>3</sub> or pyridine were distilled from CaH<sub>2</sub> under argon. Pentane was filtered through Alox B prior to use. Anhydrous *N,N*-dimethylformamide and anhydrous DMSO were purchased from Acros

(AeroSeal®) and stored over molecular sieves. Deuterated chloroform ( $\text{CDCl}_3$ ) was stored over molecular sieves 3 Å.

The evaporation of solvents was performed under vacuum using a *Büchi Rotavapor* RE 111 with a membrane pump. The water-bath-temperature was 40 °C if not indicated differently. The concentration of **butyllithium** solutions was determined prior to use by titration against *N*-benzylbenzamide in THF.<sup>1</sup> The concentration of purchased **Grignard reagents** was determined by titration against  $\text{I}_2$  in a 0.5 M LiCl-solution in THF at 0 °C.<sup>2</sup>

**Flash column chromatography** was performed on silica gel DAVISIL®LC60A 40-63 µm from *GRACE Davision*, silica gel 60 M 0.04-0-063 nm (230-400 mesh) ASTM from *Macherey Nagel* or Silica for Column Chromatography 0.035-0.070 nm, 60 A from *ACROS*. Reactions were monitored by analytical **thin layer chromatography** (TLC) using Merck silica gel 60 F254 aluminum plates (visualization by UV light ( $\lambda=254$  nm) or by staining with a cerium reagent followed by heating).

**Gas chromatography – mass spectrometry** (GC-MS) was performed on an *Agilent* GC 6890N gas chromatograph coupled with a HP 5973N series mass selective detector and a HP 7683 GC auto sampler using a 30-m x 0.25-mm, HP-5 MS column. The column temperature was initially held at 50 °C for 2 min, then the temperature was raised to 300 °C in a rate of 25°C/min and held for 5 min. The injector temperature was maintained at 300 °C and the injection volume was 1.0 µl in the split mode. Mass spectra were scanned from  $m/z$  35-500, the electron impact ionization energy was 70 eV.

**Mass spectra** were recorded on a MAT Incos 50 Galaxy System from *Finnigan*. The ionization energy in [eV] is given with the respective dataset. Intensities of the ratios of  $m/z$  are given relative to the intensity of the basic peak (100 %). A MAT 900 (Finnigan) mass spectrometer was used for the **high-resolution mass spectra** (HRMS).

Enantiomeric purities were determined by **chiral gas chromatography**, performed on a HP 6890 apparatus using a BGB 176 SE (30m x 0.25mm) column. The column temperature was initially held at 80 °C for 5 min, then the temperature was raised to 150 °C in a rate between 1 °C/min and 0.2 °C/min held for 5 min. Finally the temperature was held at 150 °C for 5 min.

**NMR spectra** were recorded on spectrometers from *Bruker* (AV 300 [300 MHz], DPX 300 [300 MHz], AV 400 [400 MHz], DRX 500 [500 MHz], AV 600 [600 MHz]) for  $^1\text{H}$  at room

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<sup>1</sup> A. F. Burchat, J. M. Chong, N. Nielsen, *J. Organomet. Chem.* **1997**, 542, 281.

<sup>2</sup> A. Krasovskiy, P. Knochel, *Synthesis* **2006**, 5, 890-891.

temperature using  $\text{CDCl}_3$  as a solvent. Proton shifts are reported in ppm ( $\delta$ ) downfield from TMS and were determined by reference to the residual solvent peaks ( $\text{CDCl}_3$ : 7.24 ppm). Data are reported as follows: chemical shift (multiplicity [singlet (s), doublet (d), triplet (t), quartet (q), quintet (quint.), multiplet (m)], coupling constants [Hz], integration, assignment).  $^{13}\text{C}$  NMR spectra were recorded using the APT sequence with complete proton decoupling. Multiplicities (C,  $\text{CH}_2$  or CH,  $\text{CH}_3$ ) were deduced from these spectra.  $^{13}\text{C}$  chemical shifts are reported in ppm ( $\delta$ ) relative to solvent resonance as the internal standard ( $\text{CDCl}_3$ : 77 ppm). The non-trivial assignments were effected by H,H-COSY, HMQC and HMBC spectra. **Infrared spectra** were recorded on a Paragon 100 FT IR instrument (Perkin-Elmer) at room temperature under *attenuated total reflectance* (ATR). The absorptions are given in wave numbers  $\tilde{\nu}$  [ $\text{cm}^{-1}$ ] and characterized by the abbreviations weak (w), middle (m), strong (s) or broad (br).

**CD spectra** were measured on a Jasco J-810 spectropolarimeter with the following conditions: scan speed 20 nm/min., response 1 sec, band-width 1 nm, 5 scans at 20 °C. For each compound a solution 1.5-2.4 mM in Methanol was prepared and spectra were acquired using a cell with 0.1 cm path-length length.

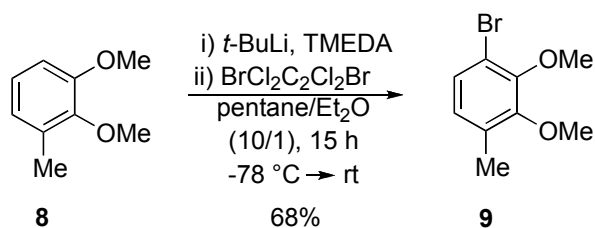
Optical rotations ( $[\alpha]_D^{20}$ ) were determined on a polarimeter *Perkin-Elmer* 343 at 20 °C in  $\text{CHCl}_3$  in a cuvette of 1 dm. The respective concentrations are given by definition in g/100 ml.

**X-ray** diffractograms were measured with a *Nonius Kappa* CCD-diffractometer. The complete dataset for full characterization of the compounds is adherent.

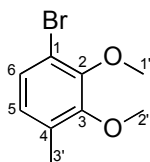
**Hydrogenations** were performed in a 50 ml pressure reactor from *Parr Instrument Company*, series 5500 (max. working pressure 200 bar). The pressure used is given in the respective experimental procedure.

## 2 EXPERIMENTAL PROCEDURES

### 1-Bromo-2,3-dimethoxy-4-methylbenzene (9)



A dried 1 l three-necked flask with a 100 ml dropping funnel was charged with 8.5 g (55.8 mmol, 1.0 equiv.) of **8** dissolved in 440 ml of pentane<sup>3</sup>/Et<sub>2</sub>O (10/1) before 11.8 ml of dry TMEDA (78.2 mmol, 1.4 equiv.) were added. The stirred mixture was cooled to -45 °C and 46.2 ml (67.0 mmol, 1.2 equiv.) of a solution of *t*-butyl lithium (1.45 M in pentane) were added dropwise over 45 min. Stirring was continued at -45 °C for 30 min. and for 3 h at 0 °C before the mixture was re-cooled to -50 °C and 36.3 g (111.6 mmol, 2.0 equiv.) of dibromotetrachloroethane, dissolved in 100 ml dry THF, were added over 1 h. The stirred mixture was allowed to warm to rt (16 h) before 170 ml of a saturated aqueous NH<sub>4</sub>Cl solution were added and the layers were separated. The aqueous layer was extracted with 100 ml of MTBE and twice with 100 ml of EtOAc. The combined organic layers were washed with saturated brine and dried with MgSO<sub>4</sub>. After filtration, the solvent was removed *in vacuo* and the crude product was purified by flash column chromatography (silica gel, CyHex/EtOAc = 100/0 → 20/1 → 10/1) to yield 8.81 g (38.1 mmol, 68%) of **9** as a yellow oil. As sample crystallized upon prolonged storage and was additionally characterized by X-ray crystallography.



**C<sub>9</sub>H<sub>11</sub>O<sub>2</sub>Br**

**M:** 231.09 g/mol.

**TLC:** R<sub>f</sub> = 0.45 (CyHex/EtOAc = 10/1).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ [ppm] = 2.20 [s, 3H, C3']; 3.83 [s, 3H, C2']; 3.86 [s, 3H, C1']; 6.77 [d, <sup>3</sup>J<sub>H,H</sub> = 8.3 Hz, 1H, C5]; 7.13 [d, <sup>3</sup>J<sub>H,H</sub> = 8.3 Hz, 1H, C6].

<sup>3</sup> Pentane was filtered through Alox B prior to use.

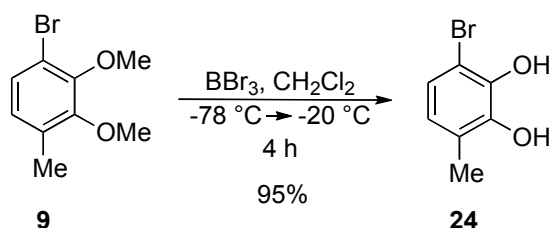
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ [ppm] = 15.6 [C(3')H<sub>3</sub>]; 60.3 [C(1')H<sub>3</sub> or C(2')H<sub>3</sub>]; 60.5 [C(1')H<sub>3</sub> or C(2')H<sub>3</sub>]; 114.6 [C1]; 126.6 [C(5)H]; 127.3 [C(6)H]; 131.9 [C4]; 150.3 [C2]; 152.4 [C3].

**IR** (ATR):  $\tilde{\nu}$  [cm<sup>-1</sup>] = 2990 (w), 2958 (m), 2934 (m), 2849 (w), 2817 (w), 1859 (w), 1728 (w), 1580 (m), 1459 (s), 1432 (s), 1399 (s), 1375 (m), 1346 (w), 1273 (s), 1230 (s), 1206 (s), 1173 (m), 1030 (m), 1081 (m), 1050 (s), 1007 (s), 920 (m), 846 (s), 796 (s), 772 (m).

**MS** (GC-MS (EI 70 eV)): m/z (%) = 51 (13), 53 (17), 63 (14), 65 (38), 77 (22), 78 (16), 91 (18), 108 (100), 121 (8), 172/175 (8/7), 187/189 (6/5), 215/217 (13/11), 230/232 [M]<sup>+</sup> (24/23).

**HR-MS** (DIP-EI 70 eV): C<sub>9</sub>H<sub>11</sub>O<sub>2</sub>Br, calculated for [M]<sup>+</sup>: 229.9942, found: 229.995 u ± <5ppm.

### 3-Bromo-6-methylbenzene-1,2-diol (**24**)



A dried 1 l three-necked flask equipped with a dropping funnel was charged with 8.81 g (38.1 mmol, 1 equiv.) of **9** and 380 ml of dry CH<sub>2</sub>Cl<sub>2</sub>. The stirred solution was cooled to -78 °C before 152.4 ml (152.4 mmol, 4 equiv.) of a BBr<sub>3</sub> solution (1 M in CH<sub>2</sub>Cl<sub>2</sub>) were added dropwise over 3 h. The mixture was stirred for additional 4 h whilst warming to -20 °C before 20 ml of H<sub>2</sub>O were carefully added. After warming to 0 °C, additional 100 ml of H<sub>2</sub>O were added and the layers were separated. The aqueous layer was extracted with 2 x 100 ml of CH<sub>2</sub>Cl<sub>2</sub> and the combined organic layers were dried with MgSO<sub>4</sub>. After filtration, the solvent was removed *in vacuo* to give 7.34 g (36.2 mmol, 95%) of the catechol **24** as red-brown oil, which proved to be sufficiently pure to be used in the next step without any purification. Only for analytical purposes a small sample of **24** was purified by flash column chromatography on silica gel (CyHex/EtOAc = 4/1 → 3/1).

**C<sub>7</sub>H<sub>7</sub>O<sub>2</sub>Br**

**M**: 203.03 g/mol.

**TLC**: R<sub>f</sub> = 0.36 (CyHex/EtOAc = 4/1), cerium-reagent.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ [ppm] = 2.21 [s, 3H, C1']; 5.49 [s, br, 2H, 2 x OH]; 6.60 [d, <sup>3</sup>J<sub>H,H</sub> = 8.4 Hz, 1H, C5]; 6.89 [d, <sup>3</sup>J<sub>H,H</sub> = 8.4 Hz, 1H, C4].

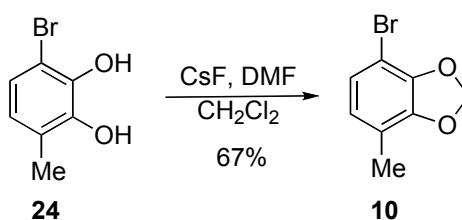
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ [ppm] = 15.3 [C(1')H<sub>3</sub>]; 106.4 [C3]; 122.0 [C(5)H]; 123.5 [C(4)H]; 124.5 [C6]; 139.5 [C2]; 142.8 [C1].

**IR** (ATR):  $\tilde{\nu}$  [ $\text{cm}^{-1}$ ] = 3455 (br, s), 3372 (br, s), 3036 (w), 2953 (w), 2923 (w), 2855 (w), 2728 (w), 2614 (w), 2464 (w), 1840 (w), 1696 (w), 1615 (m), 1584 (m), 1469 (s), 1377 (m), 1361 (s), 1289 (s), 1254 (s), 1237 (s), 1208 (s), 1188 (m), 1155 (s), 1123 (m), 1029 (s), 949 (s), 863 (s), 787 (m), 767 (m), 735 (w), 703 (m).

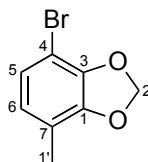
**MS** (GC-MS (EI 70 eV)):  $m/z$  (%) = 50 (11), 51 (17), 53 (15), 55 (20), 56 (23), 57 (24), 65 (18), 73 (100), 77 (23), 91 (13), 94 (14), 107 (9), 123 (39), 156 (8), 186 (4), 202/204  $[M]^+$  (40/42).

**HR-MS** (DIP-EI 70 eV):  $\text{C}_7\text{H}_7\text{O}_2\text{Br}$ , calculated for  $[M]^+$ : 201.9629, found: 201.963 u  $\pm$  <5ppm.

#### 4-Bromo-7-methylbenzo[d][1,3]dioxole (**10**)



A dried 250 ml three-necked flask equipped with a reflux condenser was charged with 21.58 g of  $\text{CsF}$  (142.04 mmol, 4 equiv.) suspended in 114 ml of dry  $\text{DMF}$ . Then 7.21 g (35.51 mmol, 1 equiv.) of **24** and 2.38 ml (37.29 mmol, 1.05 equiv.) of anhydrous  $\text{CH}_2\text{Cl}_2$  were added and the intensely stirred suspension was heated to 120 °C for 2.5 h. After cooling to rt the mixture was partitioned between 200 ml of  $\text{Et}_2\text{O}$ /MTBE (1/1) and 400 ml of  $\text{H}_2\text{O}$  and the layers were separated. The aqueous layer was extracted with 4 x 150 ml of  $\text{Et}_2\text{O}$ /MTBE (1/1). The combined organic layers were washed with  $\text{H}_2\text{O}$ , dried with  $\text{MgSO}_4$ . After filtration the solvent was removed *in vacuo* and the crude product was purified by flash column chromatography (silica gel,  $\text{CyHex}/\text{EtOAc}$  = 15/1) to yield 5.11 g (23.78 mmol, 67%) of **10** as slightly yellow oil. A small crystalline sample was obtained on prolonged standing and additionally characterized by X-ray crystallography.



$\text{C}_8\text{H}_7\text{O}_2\text{Br}$

**M**: 215.04 g/mol.

**TLC**:  $R_f$  = 0.46 ( $\text{CyHex}/\text{EtOAc}$  = 15/1).

**$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  [ppm] = 2.16 [s, 3H,  $\text{C1}'$ ]; 5.99 [s, 2H,  $\text{C2}$ ]; 6.54 [d,  $^3J_{\text{H,H}}$  = 8.4 Hz, 1H,  $\text{C6}$ ]; 6.83 [d,  $^3J_{\text{H,H}}$  = 8.4 Hz, 1H,  $\text{C5}$ ].

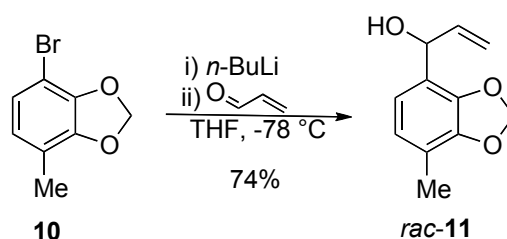
**$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  [ppm] = 14.4 [ $\text{C}(1')\text{H}_3$ ]; 97.9 [C4], 100.9 [C(2) $\text{H}_2$ ]; 118.4 [C7]; 124.4 [C(5)H]; 124.7 [C(6)H]; 144.7 [C3]; 146.1 [C2].

**IR** (ATR):  $\tilde{\nu}$  [ $\text{cm}^{-1}$ ] = 2996 (w), 2888 (w), 2773 (w), 1601 (w), 1496 (w), 1477 (m), 1448 (s), 1420 (s), 1253 (s), 1203 (s), 1175 (m), 1127 (m), 1103 (w), 1064 (s), 1030 (s), 952 (s), 932 (s), 895 (s), 776 (s).

**MS** (GC-MS (EI 70 eV)):  $m/z$  (%) = 50 (31), 51 (53), 53 (23), 65 (17), 74 (20), 75 (25), 76 (18), 77 (100), 78 (22), 79 (26), 105 (15), 107 (9), 135 (17), 213/215 [ $\text{M}]^+$  (53/57), 214/216 [ $\text{M}]^+$  (66/64).

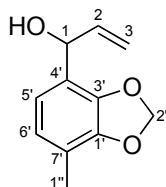
**HR-MS** (DIP-EI 70 eV):  $\text{C}_8\text{H}_7\text{O}_2\text{Br}$ , calculated for [ $\text{M}]^+$ : 213.9629, found: 213.964 u  $\pm$  <5ppm.

### 1-(7-Methylbenzo[d][1,3]dioxol-4-yl)prop-2-en-1-ol (*rac*-11)



A dried 250 ml Schlenk flask was charged with 3.78 g (17.58 mmol, 1 equiv.) of bromide **10** and 176 ml dry THF. The stirred solution was cooled to  $-78^\circ\text{C}$  before 21.1 ml (21.1 mmol, 1.2 equiv.) of *n*-butyl lithium (1.0 M in hexane) were added dropwise over 12 min. After stirring at  $-78^\circ\text{C}$  for 20 min 2.35 ml (35.16 mmol, 2 equiv.) of acrolein<sup>4</sup> were added rapidly via syringe and stirring was continued for 16 h while the mixture was slowly warming to rt. Then 20 ml of saturated aqueous  $\text{NH}_4\text{Cl}$  solution were added. After addition of additional 50 ml saturated  $\text{NH}_4\text{Cl}$  solution the layers were separated and the aqueous layer was extracted with 3 x 100 ml of MTBE. The combined organic layers were dried with  $\text{MgSO}_4$  and filtered before the solvent was removed *in vacuo*. The crude product was purified by flash column chromatography (silica gel, CyHex/EtOAc = 9/1  $\rightarrow$  7/1  $\rightarrow$  5/1  $\rightarrow$  3/1) to give 2.50 g (13.01 mmol, 74%) of *rac*-**11** as slightly yellow oil, which crystallized upon standing.

<sup>4</sup> The best yields were obtained when acrolein was refluxed over  $\text{CaSO}_4$  and distilled there from at reduced pressure prior to use.



**C<sub>11</sub>H<sub>12</sub>O<sub>3</sub>**

**M:** 192.21 g/mol.

**TLC:** R<sub>f</sub> = 0.16 (CyHex/EtOAc = 9/1).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ [ppm] = 2.19 [s, 3H, C1'']; 2.53 [s, br, 1H, OH]; 5.14-5.33 [m, 3H, C1, C3]; 5.93 [s, 2H, C2']; 6.08 [ddd, <sup>3</sup>J<sub>H,H</sub> = 17.0 Hz, <sup>3</sup>J<sub>H,H</sub> = 10.3 Hz, <sup>3</sup>J<sub>H,H</sub> = 4.5 Hz, 1H, C2]; 6.63 [d, <sup>3</sup>J<sub>H,H</sub> = 8.0 Hz, 1H, C6']; 6.72 [d, <sup>3</sup>J<sub>H,H</sub> = 8.0 Hz, 1H, C5'].

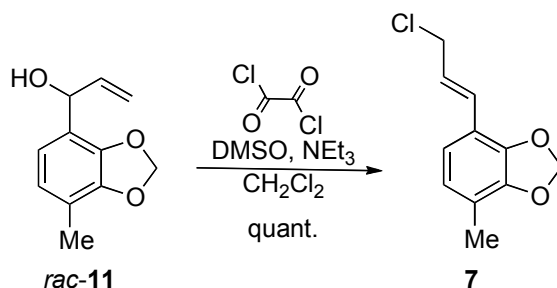
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ [ppm] = 14.6 [C(1'')H<sub>3</sub>]; 70.9 [C(1)H]; 100.9 [C(2')H<sub>2</sub>]; 115.1 [C(3)H<sub>2</sub>]; 118.7 [C7']; 119.3 [C(5')H]; 121.8 [C4']; 123.6 [C(6')H]; 138.9 [C(2)H]; 143.8 [C3']; 145.7 [C1'].

**IR** (ATR):  $\tilde{\nu}$  [cm<sup>-1</sup>] = 3366 (br, m), 3078 (w), 2971 (w), 2884 (m), 2778 (w), 2354 (w), 1866 (w), 1650 (w), 1600 (w), 1497 (m), 1429 (s), 1351 (s), 1257 (s), 1166 (m), 1081 (s), 1028 (s), 976 (s), 952 (m), 922 (s), 897 (m), 783 (s), 745 (m), 695 (w), 627 (m), 599 (m).

**MS** (GC-MS (EI 70 eV)): m/z (%) = 50 (18), 51 (48), 53 (31), 55 (64), 57 (25), 65 (26), 77 (100), 78 (26), 79 (48), 91 (47), 105 (29), 107 (86), 115 (25), 119 (17), 136 (26), 149 (28), 161 (22), 163 (23), 177 (21), 192 [M]<sup>+</sup> (62).

**HR-MS** (DIP-EI 70 eV): C<sub>11</sub>H<sub>12</sub>O<sub>3</sub>, calculated for [M]<sup>+</sup>: 192.0786, found: 192.080 u ± <5ppm.

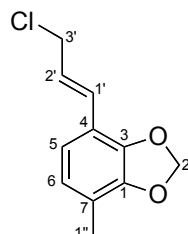
**(E)-4-(3'-Chloroprop-1'-enyl)-7-methylbenzo[d][1,3]dioxole (7)**



A dried 250 ml Schlenk flask was charged with 164 ml of dry CH<sub>2</sub>Cl<sub>2</sub> and cooled to -78 °C before 5.2 ml (61.45 mmol, 3 equiv.) of oxalyl chloride and 5.82 ml (81.94 mmol, 4 equiv.) of DMSO were added. Stirring was continued for 25 min at -78 °C before 3.94 ml (20.48 mmol, 1 equiv.) of allylic alcohol *rac*-**11**, dissolved in 40 ml dry CH<sub>2</sub>Cl<sub>2</sub>, were added via syringe within a few minutes. After 2 h at -78 °C, 17.13 ml (122.91 mmol, 6 equiv.) of anhydrous NEt<sub>3</sub>



were added and stirring was continued at -78 °C for 10 min and for 1 h at rt. The yellow reaction mixture was poured into 150 ml of ice cold aqueous HCl (1M) and the layers were separated. The aqueous layer was extracted with 3 x 70 ml of CH<sub>2</sub>Cl<sub>2</sub> and the combined organic layers were washed with 3 x 50 ml of H<sub>2</sub>O and dried with MgSO<sub>4</sub>. After filtration, the solvent removed *in vacuo* (at max. 35 °C water bath temperature)<sup>5</sup> to give 4.31 g (20.45 mmol, 100%) of **7** as an orange oil, which, due to its sensitivity towards silica and heat, was used for the next step without purification within a few days.



**C<sub>11</sub>H<sub>11</sub>O<sub>2</sub>Cl**

**M**: 210.66 g/mol.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ [ppm] = 2.21 [s, 3H, C1'']; 4.22 [d, <sup>3</sup>J<sub>H,H</sub> = 6.5 Hz, 2H, C3']; 5.98 [s, 2H, C2]; 6.52 [m, 2H, C1', C2']; 6.61 [d, <sup>3</sup>J<sub>H,H</sub> = 8.4 Hz, 1H, C6]; 6.71 [d, <sup>3</sup>J<sub>H,H</sub> = 8.4 Hz, 1H, C5].

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ [ppm] = 14.6 [C(1'')H<sub>3</sub>]; 45.9 [C(3')H<sub>2</sub>]; 100.8 [C(2)H<sub>2</sub>]; 116.2 [C7]; 118.8 [C4]; 120.7 [C(5)H]; 123.4 [C(6)H]; 126.7 [C(2')H]; 128.7 [C(1')H]; 144.5 [C3]; 145.8 [C1].

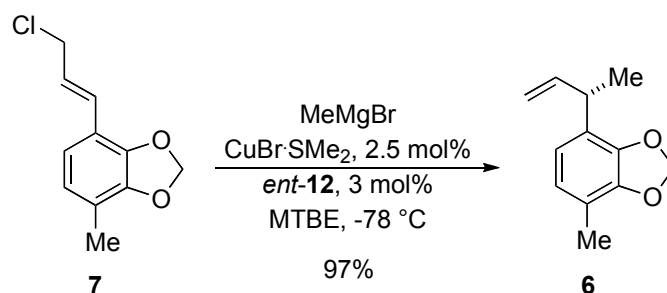
**IR** (ATR):  $\tilde{\nu}$  [cm<sup>-1</sup>] = 2946 (m), 2917 (m), 2886 (m), 2780 (w), 1710 (w), 1675 (m), 1644 (m), 1625 (m), 1586 (w), 1493 (m), 1420 (s), 1376 (w), 1356 (w), 1329 (m), 1306 (m), 1245 (s), 1216 (m), 1193 (m), 1169 (m), 1226 (s), 1103 (s), 1073 (s), 1031 (s), 966 (s), 925 (s), 787 (s), 766 (m), 666 (m).

**MS** (GC-MS (EI 70 eV)): m/z (%) = 51 (11), 63 (7), 65 (9), 77 (18), 91 (23), 105 (12), 115 (27), 117 (47), 131 (57), 145 (79), 163 (16), 175 (41), 190 [M]<sup>+</sup> (100).

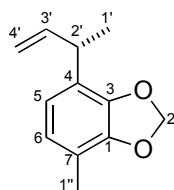
**HR-MS** (DIP-EI 70 eV): C<sub>11</sub>H<sub>11</sub>O<sub>2</sub>Cl, calculated for [M]<sup>+</sup>: 210.0447, found: 210.045 u ± <5ppm.

<sup>5</sup> At higher water temperatures decomposition of the product was observed.

**(S)-4-(But-3'-en-2'-yl)-7-methylbenzo[d][1,3]dioxole (6)**



A dried 500 ml three-necked flask was charged with 195 mg (0.23 mmol, 3 mol%) of ligand **12**, 39.3 mg (0.19 mmol, 2.5 mol%) of CuBr·SMe<sub>2</sub> and 51 ml of dry MTBE. The mixture was stirred for 30 min at rt before 1.61 g (7.64 mmol, 1 equiv.) of **7** were added. The solution was cooled to -78 °C before a solution of MeMgBr (3.7 ml, 9.17 mmol, 1.2 equiv. of a 2.5 M solution in Et<sub>2</sub>O diluted with 80 ml dry CH<sub>2</sub>Cl<sub>2</sub>) was added dropwise in two portions over 10 h by means of a syringe pump. The mixture was stirred for additional 10 h at -78 °C before the reaction was stopped by addition of 2 ml of HCl (1 M). Further 30 ml of aqueous HCl (1 M) and 50 ml of Et<sub>2</sub>O were added and the layers separated. The aqueous layer was extracted with 3 x 50 ml Et<sub>2</sub>O and the combined organic layers dried with MgSO<sub>4</sub> before the solvent was removed *in vacuo* to give 1.41 g (7.41 mmol, 97%) of pure **6** as a slightly yellow oil.



**C<sub>12</sub>H<sub>14</sub>O<sub>2</sub>**

**M**: 190.24 g/mol.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ [ppm] = 1.36 [d, <sup>3</sup>J<sub>H,H</sub> = 7.1 Hz, 3H, C1']; 2.20 [s, 3H, C1'']; 3.58 [quint., <sup>3</sup>J<sub>H,H</sub> = 6.8 Hz, 1H, C2']; 5.04 [m, 2H, C4']; 5.93 [s, 2H, C2]; 6.04 [ddd, <sup>3</sup>J<sub>H,H</sub> = 17.0 Hz, <sup>3</sup>J<sub>H,H</sub> = 10.5 Hz, <sup>3</sup>J<sub>H,H</sub> = 6.7 Hz, 1H, C3']; 6.61 [[ψ-t, <sup>3</sup>J<sub>H,H</sub> = 8.5 Hz, 2H, C5, C6].

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ [ppm] = 14.4 [C(1'')H<sub>3</sub>]; 19.4 [C(1')H<sub>3</sub>]; 37.6 [C(2')H]; 100.3 [C(2)H<sub>2</sub>]; 113.2 [C(4')H<sub>3</sub>]; 117.0 [C7]; 119.9 [C(5)H]; 123.3 [C(6)H]; 124.5 [C4]; 141.8 [C(3')H]; 144.2 [C1]; 145.2 [C3].

**[α]<sub>D</sub><sup>20</sup>**: + 3.9 (c: 1.055 g/100 ml, CHCl<sub>3</sub>).

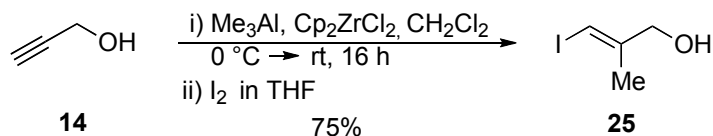
**IR** (ATR):  $\tilde{\nu}$  [cm<sup>-1</sup>] = 3073 (w), 3057 (w), 2964 (m), 2924 (m), 2873 (m), 2773 (w), 1847 (w), 1635 (m), 1597 (w), 1498 (m), 1450 (s), 1421 (s), 1368 (m), 1351 (m), 1310 (m), 1288 (m),

1245 (s), 1214 (m), 1172 (s), 1083 (s), 1066 (s), 1032 (s), 987 (s), 958 (s), 912 (s), 843 (w), 774 (s), 754 (s), 681 (w).

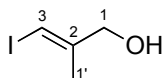
**MS** (GC-MS (EI 70 eV)):  $m/z$  (%) = 51 (22), 63 (12), 65 (17), 74 (27), 91 (37), 103 (12), 105 (19), 115 (38), 117 (58), 145 (89), 147 (17), 160 (16), 164 (23), 175 (44), 190  $[M]^+$  (100).

**HR-MS** (DIP-EI 70 eV):  $C_{12}H_{14}O_2$ , calculated for  $[M]^+$ : 190.0994, found: 190.099  $u \pm <5ppm$ .

**(E)-3-Iodo-2-methylprop-2-en-1-ol (25)**



A dried 250 ml Schlenk flask was charged with 1.96 g (6.69 mmol, 0.25 equiv.) of  $Cp_2ZrCl_2$ , and 53 ml of dry  $CH_2Cl_2$  before 40.1 ml (80.24 mmol, 3 equiv.) of a solution of  $Me_3Al$  (2 M in heptane) were added dropwise. The stirred solution was then cooled to  $0^\circ C$  before as solution of propargylic alcohol (**14**) (1.5 g, 26.75 mmol, 1 equiv.) in 21.8 ml of dry  $CH_2Cl_2$  was added dropwise over 30 min by means of a syringe pump. After stirred for 17 h under warming to rt the mixture was cooled to  $-30^\circ C$  and a solution of 8.15 g (32.1 mmol, 1.2 equiv.) of iodine in 26 ml dry of anhydrous THF was added slowly. Stirring was continued for additional 7 min at  $-30^\circ C$  before ca. 6 ml of a saturated  $NaHCO_3$  solution were carefully added (caution: heavy gas- and heat development). Then the cooling bath was removed and after the gas development had ceased another 40 ml of saturated  $NaHCO_3$  solution were added and the layers separated. The aqueous layer was extracted with 3 x 50 ml of MTBE and the combined organic layers were washed with 50 ml of saturated  $Na_2S_2O_3$  solution, dried with  $MgSO_4$ . After filtration, the solvent was removed *in vacuo* to afford the crude vinyl iodide **25**, which was purified by filtration over silica gel with (CyHex/EtOAc = 2/1) as an eluent. After careful removal of the solvents *in vacuo* 3.97 g (20.03 mmol, 75%) of **25** were obtained as a volatile oil.



**$C_4H_7IO$**

**M**: 198.00 g/mol.

**$^1H$  NMR** (300 MHz,  $CDCl_3$ ):  $\delta$  [ppm] = 1.80 [s, 3H, C1']; 2.52 [s, br, 1H, OH]; 4.06 [s, 2H, C1]; 6.22 [s, 1H, C3].

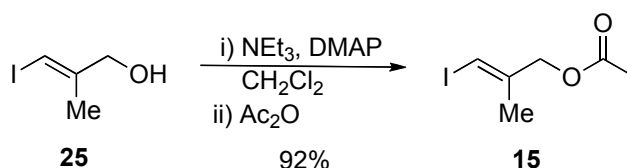
**<sup>13</sup>C-APT NMR** (75 MHz, CDCl<sub>3</sub>): δ [ppm] = 21.3 [C(1')H<sub>3</sub>]; 66.9 [C(1)H<sub>2</sub>]; 77.2 [C(3)H]; 147.1 [C2].

**IR** (ATR):  $\tilde{\nu}$  [cm<sup>-1</sup>] = 3303 (br, s), 2911 (m), 2849 (m), 1658 (w), 1619 (w), 1433 (m), 1375 (m), 1357 (m), 1274 (s), 1251 (m), 1145 (w), 1067 (s), 1009 (s), 942 (w), 829 (w), 773 (s), 665 (m).

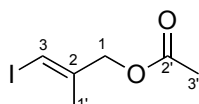
**MS** (GC-MS (EI 70 eV)): m/z (%) = 50 (12), 53 (25), 55 (48), 56 (100), 57 (27), 71 (33), 73 (13), 91 (4), 127 (5), 198 [M]<sup>+</sup> (12).

**HR-MS** (EI 70 eV): C<sub>4</sub>H<sub>7</sub>IO, calculated for [M]<sup>+</sup>: 197.9542, found: 197.954 u ± <5ppm.

### (E)-3-Iodo-2-methylallyl acetate (**15**)



A dry 250 ml Schlenk flask was charged with 3.97 g (20.03 mmol, 1 equiv.) of **25** and 116.0 ml of dry CH<sub>2</sub>Cl<sub>2</sub> before 8.33 ml (60.09 mmol, 3 equiv.) of dry NEt<sub>3</sub> and 490 mg (4.01 mmol, 20 mol%) of DMAP were added. After stirring for 30 min at rt the solution was cooled to 0 °C and 5.68 ml (60.09 mmol, 3 equiv.) of freshly distilled Ac<sub>2</sub>O were added dropwise. Stirring was continued for 16 h while the mixture was allowed to slowly warm to rt. Then 55 ml of half saturated aqueous NaHCO<sub>3</sub> solution were added after 30 min the layers were separated. The aqueous layer was extracted with 3 x 50 ml of CH<sub>2</sub>Cl<sub>2</sub> and the combined organic layers were subsequently washed with 70 ml (1M) of HCl and 70 ml of H<sub>2</sub>O and then dried with MgSO<sub>4</sub>. After removal of the solvent *in vacuo* the crude product was purified by filtration through silica gel (CyHex/EtOAc = 10/1) to give 4.41 g (18.37 mmol, 92%) of the acetate **15** as slightly yellow oil.



**C<sub>6</sub>H<sub>9</sub>IO<sub>2</sub>**

**M**: 240.04 g/mol.

**TLC**: R<sub>f</sub> = 0.50 (CyHex/EtOAc = 10/1).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ [ppm] = 1.82 [s, 3H, C1']; 2.05 [s, 3H, C3']; 4.52 [s, 2H, C1]; 6.30 [s, 1H, C3].

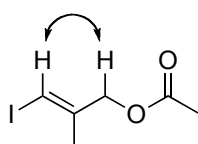
**<sup>13</sup>C-APT NMR** (75 MHz, CDCl<sub>3</sub>): δ [ppm] = 20.8 [C(3')H<sub>3</sub>]; 21.6 [C(1')H<sub>3</sub>]; 67.3 [C(1)H<sub>2</sub>]; 80.1 [C(3)H]; 142.3 [C<sub>2</sub>]; 170.3 [C<sub>2</sub>'].

**IR** (ATR):  $\tilde{\nu}$  [cm<sup>-1</sup>] = 3459 (w), 3059 (w), 2920 (w), 2860 (w), 1734 (s), 1621 (m), 1433 (m), 1374 (s), 1360 (s), 1284 (s), 1217 (s), 1151 (w), 1052 (s), 1021 (s), 979 (m), 910 (w), 841 (m), 777 (s), 720 (w), 673 (m).

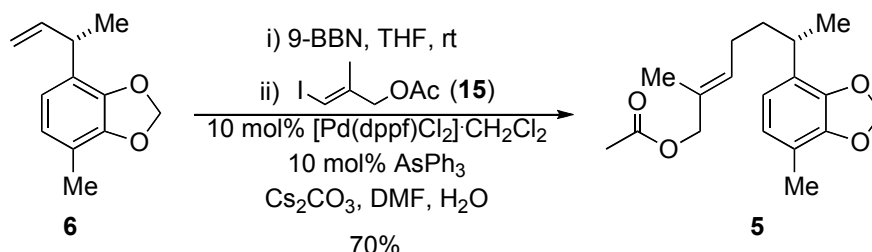
**MS** (GC-MS (EI 70 eV)): m/z (%) = 51 (12), 53 (87), 54 (33), 71 (23), 95 (4), 113 (100), 114 (9), 127 (15), 141 (5), 167 (6), 180 (12), 181 (13), 240 [M]<sup>+</sup> (11).

**HR-MS** (EI 70 eV): C<sub>6</sub>H<sub>9</sub>IO<sub>2</sub>, calculated for [M]<sup>+</sup>: 239.9647, found: 197.954 u ± <5ppm.

Double bond configuration was confirmed via a NOESY-experiment:

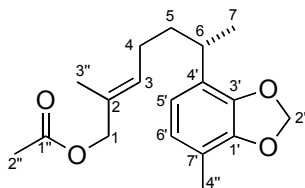


**(*S,E*)-2-Methyl-6-(7-methylbenzo[d][1,3]dioxol-4-yl)hept-2-enyl-acetate (**5**)**



A dry 50 ml flask was charged with 775 mg (4.07 mmol, 1 equiv.) of **6** which was dissolved in 32.0 ml of dry THF before 12.2 ml (6.11 mmol, 1.5 equiv.) of 9-BBN (0.5 M in THF) were added. This solution was stirred for 26 h at rt. Separately. A 100 ml two-necked flask was charged with a solution of 1.08 g (4.48 mmol, 1.1 equiv.) of the vinyl iodide **15** in 38.0 ml of dry DMF and 2.87 g (8.14 mmol, 2 eq) of Cs<sub>2</sub>CO<sub>3</sub> were added. After 15 min of stirring at rt, 126 mg (0.41 mmol, 10 mol%) of AsPh<sub>3</sub>, 300 mg (0.41 mmol, 10 mol%) of (dppf)PdCl<sub>2</sub>·CH<sub>2</sub>Cl<sub>2</sub>, and 2.7 ml (163 mmol, 40 equiv.) of H<sub>2</sub>O were added successively. The mixture was stirred for 4 h at rt, before the other solution (with the *in situ* prepared borane) was added by means of a transfer needle. The resulting combined mixture was stirred for 48 h at 40 °C (oil-bath-temperature) before it was cooled to rt, diluted with 40 ml of CHCl<sub>3</sub> and washed with 75 ml of a saturated aqueous NH<sub>4</sub>Cl solution. The aqueous layer was extracted with 3 x 30 ml of CHCl<sub>3</sub> and the combined organic layers were washed with 2 x 50 ml of H<sub>2</sub>O and dried with MgSO<sub>4</sub> before the solvents were removed *in vacuo*. The remaining oil was purified by flash-

column chromatography on silica gel (CyHex/EtOAc = 30/1) to yield 866 mg (2.84 mmol, 70%) of the coupling product **5** as an orange oil.



**C<sub>18</sub>H<sub>24</sub>O<sub>4</sub>**

**M:** 304.38 g/mol.

**TLC:**  $R_f$  = 0.21 (CyHex/EtOAc = 30/1).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>):  $\delta$  [ppm] = 1.22 [d,  $^3J_{H,H}$  = 7.0 Hz, 3H, C7]; 1.56 [s, 3H, C3'']; 1.65 [m, 2H, C5]; 1.97 [m, 2H, C4]; 2.05 [s, 3H, C2'']; 2.18 [s, 3H, C4'']; 2.81 [m, 1H, C6]; 4.41 [s, 2H, C1]; 5.42 [dt,  $^3J_{H,H}$  = 7.1 Hz,  $^4J_{H,H}$  = 1.0 Hz, 1H, C3]; 5.89 [s, 2H, C2']; 6.57 [m, 2H, C5' und C6'].

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>):  $\delta$  [ppm] = 13.8 [C(3'')H<sub>3</sub>]; 14.4 [C(4'')H<sub>3</sub>]; 20.7 [C(7)H<sub>3</sub>]; 21.0 [C(2'')H<sub>3</sub>]; 25.9 [C(4)H<sub>2</sub>]; 33.9 [C(6)H]; 36.0 [C(5)H<sub>2</sub>]; 70.3 [C(1)H<sub>2</sub>]; 100.2 [C(2')H<sub>2</sub>]; 116.5 [C7']; 119.9 [C(5')H]; 123.2 [C(6')H]; 126.0 [C4']; 129.7 [C(3)H]; 129.9 [C2]; 144.3 [C3']; 145.2 [C3']; 170.9 [C1''].

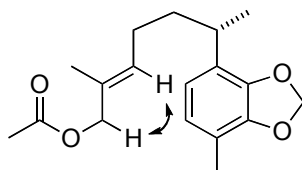
**[ $\alpha$ ]<sub>D</sub><sup>20</sup>** : + 20.2 (c: 1.09 g/100 ml, CHCl<sub>3</sub>).

**IR** (ATR):  $\tilde{\nu}$  [cm<sup>-1</sup>] = 2958 (m), 2921 (m), 2871 (m), 2776 (w), 2358 (w), 1733 (s), 1596 (w), 1498 (w), 1450 (s), 1422 (s), 1374 (s), 1355 (s), 1222 (s), 1171 (m), 1117 (m), 1074 (m), 1021 (s), 961 (s), 923 (m), 846 (m), 794 (s), 745 (m), 717 (w), 706 (w), 693 (w), 668 (w).

**MS** (GC-MS (EI 70 eV)):  $m/z$  (%) = 60 (13), 77 (23), 79 (15), 91 (17), 105 (26), 117 (18), 128 (19), 149 (17), 163 (100), 164 (32), 171 (30), 176 (18), 187 (10), 199 (14), 201 (17), 203 (26), 229 (24), 244 (76), 304 [M]<sup>+</sup> (15).

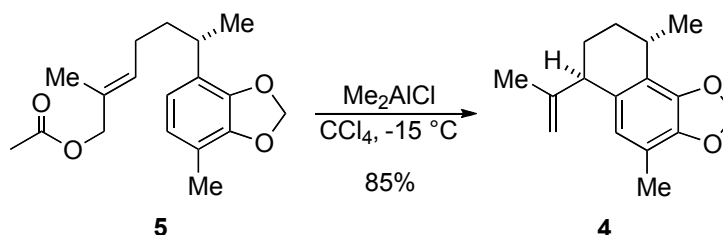
**HR-MS** (EI 70 eV): C<sub>18</sub>H<sub>24</sub>O<sub>4</sub>, calculated for [M]<sup>+</sup>: 304.1674, found: 304.167 u  $\pm$  <5ppm.

The double bond configuration was proven by a NOESY-experiment:

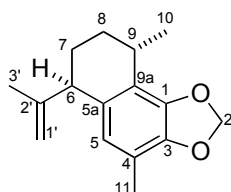


**(6*R*,9*S*)-4,9-Dimethyl-6-(prop-1-en-2-yl)-6,7,8,9-tetrahydronaphtho[1,2-*d*][1,3]dioxole**

**(4)**



A dried 250 ml Schlenk flask was charged with a solution of 838 mg (2.75 mmol, 1 equiv.) of **5** diluted 84 ml of dry  $\text{CCl}_4$ . After cooling to  $-15\text{ }^\circ\text{C}$  (ice/ $\text{NaCl}$  bath), 7.64 ml (6.86 mmol, 2.5 equiv.) of a solution of  $\text{Me}_2\text{AlCl}$  (0.9 M in heptane) were added dropwise over 20 min. by means of a syringe pump. Stirring was continued for 60 min. at  $-15\text{ }^\circ\text{C}$  before 4 ml of  $\text{H}_2\text{O}$  were added carefully and the cooling bath was removed. After the gas development had ceased, additional 30 ml of  $\text{H}_2\text{O}$  were added, the layers were separated and the aqueous layer was extracted with 3 x 40 ml of  $\text{CH}_2\text{Cl}_2$ . The combined organic layers were dried with  $\text{MgSO}_4$ , filtered and the solvent removed *in vacuo*. The crude product was purified by filtration through silica gel (CyHex/EtOAc = 25/1) to afford 575 mg (2.35 mmol, 85%) of a 4:1 diastereomeric mixture<sup>6</sup> of the calamenenes **4** and *dia*-**4** as colorless oil. The diastereomeric ratio (**4** / *dia*-**4**) was determined as 4 :1 through the integration ratios of significant  $^1\text{H}$  NMR signals of the crude product. A separation of diastereomers was not possible by flash-column chromatography. Therefore the synthesis was continued with the mixture.



**C<sub>16</sub>H<sub>20</sub>O<sub>2</sub>**

**M:** 244.33 g/mol.

**DC:**  $R_f$  = 0.63 (CyHex/EtOAc = 25/1), cerium-reagent.

**$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  [ppm] = 1.24 [d,  $^3J_{\text{H,H}}$  = 6.9 Hz, 3H, C10]; 1.41 [m, 2H, C8]; 1.67 [s, 3H, C3']; 1.81 [m, 2H, C7]; 2.14 [s, 3H, C11]; 2.95 [ddd,  $^3J_{\text{H,H}}$  = 6.4 Hz,  $^3J_{\text{H,H}}$  = 6.4 Hz,  $^3J_{\text{H,H}}$  = 6.4 Hz, H, C9]; 3.36 [t,  $^3J_{\text{H,H}}$  = 5.7 Hz, 1H, C6]; 4.44 [s, 1H, C1']; 4.85 [s, 1H, C1']; 5.89 [d,  $^3J_{\text{H,H}}$  = 14.5 Hz, 2H, C2]; 6.39 [s, 1H, C5].

<sup>6</sup> The analytical data of **4** were determined from the 4:1 mixture of diastereomers. Only the chemical shifts of the main diastereomer are given.

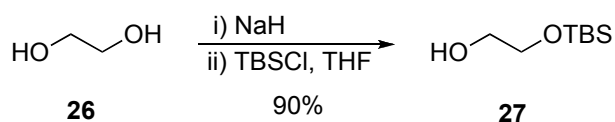
**$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  [ppm] = 14.5 [C(11) $\text{H}_3$ ]; 20.5 [C(3') $\text{H}_3$  or C(10) $\text{H}_3$ ]; 20.8 [C(10) $\text{H}_3$  or C(3') $\text{H}_3$ ]; 24.6 [C(7) $\text{H}_2$ ]; 27.9 [C(8) $\text{H}_2$ ]; 28.2 [C(9) $\text{H}$ ]; 46.5 [C(6) $\text{H}$ ]; 100.3 [C(2) $\text{H}_2$ ]; 113.4 [C(1') $\text{H}_2$ ]; 116.3 [C4]; 122.5 [C9a]; 123.8 [C(5) $\text{H}$ ]; 131.9 [C5a]; 143.2 [C3]; 143.9 [1]; 149.6 [C2'].

**IR** (ATR):  $\tilde{\nu}$  [ $\text{cm}^{-1}$ ] = 3058 (w), 2925 (s), 2860 (s), 2771 (w), 1642 (m), 1592 (w), 1483 (m), 1449 (s), 1415 (s), 1371 (m), 1324 (m), 1294 (m), 1183 (m), 1121 (s), 1102 (m), 1070 (s), 1034 (m), 961 (s), 926 (w), 890 (s), 865 (m), 800 (w), 752 (w), 630 (w).

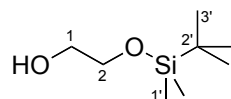
**MS** (GC-MS (EI 70 eV)):  $m/z$  (%) = 51 (10), 56 (11), 76 (11), 91 (12), 107 (6), 115 (22), 128 (32), 129 (22), 141 (12), 143 (16), 145 (15), 158 (21), 171 (33), 173 (24), 187 (17), 199 (28), 203 (63), 229 (36), 244 [ $\text{M}$ ] $^+$  (100).

**HR-MS** (EI 70 eV):  $\text{C}_{16}\text{H}_{20}\text{O}_2$ , calculated for [ $\text{M}$ ] $^+$ : 244.1463, found: 244.146 u  $\pm$  <5ppm.

## 2-(*tert*-Butyldimethylsiloxy)ethanol (**27**)



A dried 250 ml Schlenk flask was charged with 1.93 g of NaH (ca. 60 weight% in mineral oil, ca. 48.33 mmol, 1 equiv.) and stirred for 20 min with *n*-hexane, which was then pipetted off. This procedure was repeated once before the NaH was dried in the vacuum of an oil pump. The resulting dry NaH was suspended in 95 ml of dry THF before 3.0 g (48.33 mmol, 1 equiv.) ethylene glycol (**26**) were added (as quickly as gas development allowed for) and the mixture was stirred for 45 min at rt. Then 7.3 g (48.33 mmol, 1.0 equiv.) of TBSCl were added and stirring was continued for 45 min. at rt before the mixture was participated between  $\text{Et}_2\text{O}$  followed and a 10% aqueous solution of  $\text{K}_2\text{CO}_3$ . The aqueous layer was extracted with 3 x 50 ml of MTBE and the combined organic layers were washed with saturated NaCl-solution and dried with  $\text{MgSO}_4$ . After filtration and removal of the solvent *in vacuo* the remaining oil was purified by flash-column chromatography on silica gel (CyHex/EtOAc = 3/1) to give 7.71 g (43.7 mmol, 90%) of the monoprotected glycol **27** as a colorless oil



**$\text{C}_8\text{H}_{20}\text{O}_2\text{Si}$**

**M**: 176.33 g/mol.



**DC:**  $R_f = 0.34$  (CyHex/EtOAc = 3/1), cerium-reagent.

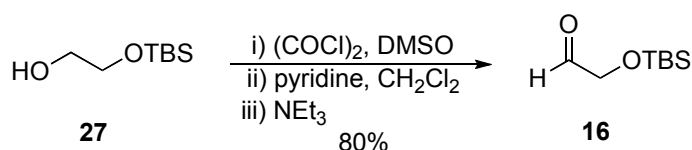
**$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  [ppm] = 0.05 [s, 6H, C1']; 0.88 [s, 9H, C3']; 2.12 [t,  $^3J_{\text{H,H}} = 5.8$  Hz, 1H, OH]; 3.63 [m, 4H, C1, C2].

**$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  [ppm] = -5.4 [C(1')H<sub>3</sub>]; 18.3 [C2']; 25.9 [C(3')H<sub>3</sub>]; 63.7 [C1 or C2]; 64.1 [C1 or C2].

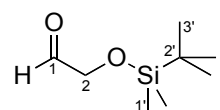
**IR** (ATR):  $\tilde{\nu}$  [ $\text{cm}^{-1}$ ] = 3374 (s, br), 2950 (m), 2927 (m), 2882 (m), 2855 (m), 2709 (w), 1652 (w), 1470 (m), 1462 (m), 1388 (w), 1360 (w), 1253 (s), 1217 (w), 1112 (s), 1056 (s), 1005 (m), 936 (s), 880 (m), 831 (s), 810 (s), 774 (s), 717 (m), 679 (w), 662 (m).

**MS / HR-MS** A mass-spectrometric analysis was not possible, since no product peak was detectable.

### 2-(*tert*-Butyldimethylsiloxy)acetaldehyde (**16**)



A dry 250 ml Schlenk flask was charged with 82 ml of  $\text{CH}_2\text{Cl}_2$ , cooled to  $-78^\circ\text{C}$  and 3.17 ml (37.43 mmol, 1.1 equiv.) of oxalyl chloride were added followed by 5.8 ml (81.67 mmol, 2.4 equiv.) of dry DMSO. After 20 min, 6 g (34.03 mmol, 1.0 equiv.) of alcohol **27** were added dropwise together with 5.48 ml (68.06 mmol, 2.0 equiv.) of dry pyridine dissolved in 34 ml of  $\text{CH}_2\text{Cl}_2$ . The mixture was stirred for 30 min at  $-78^\circ\text{C}$ , before 23.71 ml (170.15 mmol, 5.0 equiv.) of dry  $\text{NEt}_3$  were added. Stirring was continued while the mixture was allowed to warm to rt within 50 min. The solution was acidified with HCl (first 6 M, then 1 M) to pH = 4 before the layers were separated. The aqueous layer was extracted with 2 x 70 ml of  $\text{CH}_2\text{Cl}_2$  and the combined organic layers were dried with  $\text{MgSO}_4$ . After filtration and careful removal of the solvent *in vacuo*, the remaining oil was purified by flash-column chromatography on silica gel (CyHex/EtOAc = 3/1) to afford 4.77 g (27.4 mmol, 80%) of the aldehyde **16** as a light yellow oil. (Caution: the product is rather volatile).



**C<sub>8</sub>H<sub>18</sub>O<sub>2</sub>Si**

**M:** 174.31 g/mol.

**DC:**  $R_f = 0.42$  (CyHex/EtOAc = 3/1), cerium-reagent.

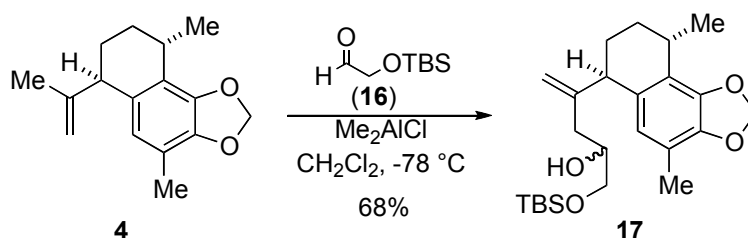
**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ [ppm] = 0.08 [s, 6H, C1']; 0.89 [s, 9H, C3']; 4.19 [s, 2H, C2]; 9.68 [s, 1H, C1].

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ [ppm] = -5.4 [C(1')H<sub>3</sub>]; 18.4 [C2']; 25.8 [C(3')H<sub>3</sub>]; 69.6 [C2]; 202.3 [C1].

**IR** (ATR):  $\tilde{\nu}$  [cm<sup>-1</sup>] = 3456 (w), 2951 (m), 2927 (m), 2884 (m), 2855 (m), 2707 (w), 1737 (s), 1471 (m), 1462 (m), 1434 (w), 1407 (w), 1388 (w), 1372 (w), 1360 (m), 1327 (w), 1252 (s), 1217 (w), 1161 (s), 1124 (s), 1042 (m), 1005 (m), 938 (m), 876 (m), 831 (s), 774 (s), 684 (m), 667 (m), 634 (w), 618 (w), 610 (w).

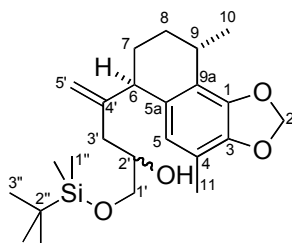
**MS / HR-MS** A mass-spectrometric analysis was not possible, since no product peak was detectable.

**1'-(*tert*-Butyldimethylsiloxy)-4'-((6*R*,9*S*)-4,9-dimethyl-6,7,8,9-tetrahydronaphtho[1,2-*d*][1,3]dioxole-6-yl)pent-4'-en-2'-ol (**17**)**



A dry Schlenk tube was charged with a solution of 533 mg (3.06 mmol, 1.3 equiv.) of aldehyde **16** in 2.75 ml of CH<sub>2</sub>Cl<sub>2</sub> and the mixture was cooled to -78 °C before 2.88 ml (2.59 mmol, 1.1 equiv.) of Me<sub>2</sub>AlCl (0.9 M solution in heptane) were added. Subsequently, 575 mg (2.35 mmol, 1.0 equiv.) of the calamenene **4**, diluted in 3 ml of dry CH<sub>2</sub>Cl<sub>2</sub>, were quickly added dropwise. The mixture was stirred for 7 h while it slowly warmed to rt. Then ca. 2 ml of an aqueous Na-/K tartrate solution (1.8 M) were added. After gas development has ceased additional 10 ml of saturated aqueous NaCl were added and the layers were separated. The aqueous layer was extracted with 5 x 10 ml of CH<sub>2</sub>Cl<sub>2</sub> and the combined organic layers were dried with MgSO<sub>4</sub>, filtered and the solvent was removed *in vacuo*. The remaining oil was purified by flash-column chromatography on silica gel (CyHex/EtOAc = 25/1 → 20/1) to give 670 mg (1.6 mmol, 68%) of **17** (colorless oil) as an unseparable mixture of diastereomers<sup>7</sup>, besides 90 mg of re-isolated starting material **4**.

<sup>7</sup> The analytical data of **17** were determined from the mixture of diastereomers. Only chemical shifts of the main diastereomer are given.



**C<sub>24</sub>H<sub>38</sub>O<sub>4</sub>Si**

**M:** 418.64 g/mol.

**DC:** R<sub>f</sub> = 0.56 (CyHex/EtOAc = 10/1), cerium-reagent.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ [ppm] = 0.07 [s, 6H, C1'']; 0.09 [s, 9H, C3'']; 1.23 [d, <sup>3</sup>J<sub>H,H</sub> = 6.7 Hz, 3H, C10]; 1.37 [m, 1H, C8]; 1.67 [m, 1H, C8]; 1.93 [m, 2H, C7]; 2.11 [s, 3H, C11]; 2.23 [m, 2H, C3']; 2.49 [m, 1H, C6]; 2.95 [m, 1H, C9]; 3.39 [m, 2H, C1', C2']; 3.63 [m, 1H, C1']; 3.87 [m, br, 1H, OH]; 4.41 [s, 1H, C5']; 4.96 [s, 1H, C5']; 5.88 [s, 1H, C2]; 5.93 [s, 1H, C2]; 6.31 [s, 1H, C5].

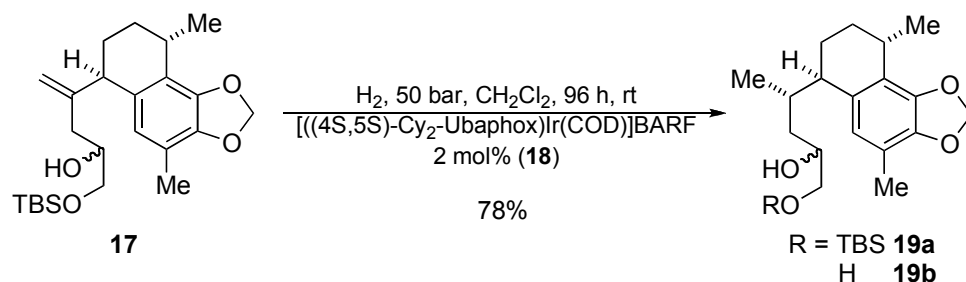
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ [ppm] = -5.3 [C(1'')H<sub>3</sub>]; 14.5 [C(11)H<sub>3</sub>]; 18.3 [C2'']; 20.7 [C(10)H<sub>3</sub>]; 23.2 [C(7)H<sub>2</sub>]; 25.8 [C(3'')H<sub>3</sub>]; 26.2 [C(8)H<sub>2</sub>]; 27.5 [C(9)H]; 38.0 [C(3')H<sub>2</sub>]; 45.0 [C(6)H]; 66.8 [C(1')H<sub>2</sub>]; 70.9 [C(2')H]; 100.4 [C(2)H<sub>2</sub>]; 114.8 [C(5')H<sub>2</sub>]; 116.4 [C4]; 122.8 [C9a]; 124.3 [C(5)H]; 131.7 [C5a]; 143.4 [C1]; 144.3 [C3]; 150.7 [C4'].

**IR** (ATR):  $\tilde{\nu}$  [cm<sup>-1</sup>] = 3568 (w), 3453 (br, w), 2925 (s), 2855 (s), 1737 (w), 1638 (w), 1461 (s), 1416 (s), 1371 (w), 1359 (m), 1333 (w), 1296 (m), 1251 (s), 1208 (w), 1183 (m), 1119 (s), 1070 (s), 1034 (s), 1005 (m), 962 (s), 937 (w), 903 (m), 834 (s), 813 (m), 776 (s), 668 (w).

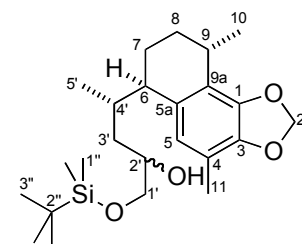
**MS** (GC-MS (EI 70 eV)): m/z (%) = 55 (32), 57 (28), 73 (32), 75 (100), 77 (31), 91 (30), 97 (41), 115 (34), 117 (39), 127 (25), 141 (23), 165 (25), 185 (13), 199 (22), 203 (22), 207 (68), 113 (39), 225 (15), 243 (21), 255 (16), 269 (16), 281 (15), 355 (12), 418 [M]<sup>+</sup> (10).

**HR-MS** (EI 70 eV): C<sub>24</sub>H<sub>38</sub>O<sub>4</sub>Si, calculated for [M]<sup>+</sup>: 480.2539, found: 418.254 u ± <5ppm.

**(S)-1'-(*tert*-Butyldimethylsilyloxy)-4'-((6*R*,9*S*)-4,9-dimethyl-6,7,8,9-tetrahydronaphtho[1,2-*d*][1,3]dioxole-6-yl)pentan-2'-ol (**19a**)**



A small dry glass vessel equipped with a rubber septum and a magnetic stirring bar was set under argon and charged with 670 mg (1.6 mmol, 1 equiv.) of olefin **17**, 55 mg (32  $\mu\text{mol}$ , 2 mol%) of [((4*S*,5*S*)-Cy<sub>2</sub>-ubaphox)Ir(COD)]BARF (**18**) and 17.5 ml of dry and degassed CH<sub>2</sub>Cl<sub>2</sub>. Then, hydrogen gas was bubbled through the solution for some minutes, which changed its color from orange to yellow. Under argon, the solution was transferred into a pressure reactor, which was then flushed with 3 x 30 bar of H<sub>2</sub> before a pressure of 50 bar was adjusted and the mixture was stirred for 96 h at rt. The hydrogen pressure was then released, the solution transferred into a round bottom flask and the solvent was removed *in vacuo* to leave behind a slightly brown oil. Purification by flash-column chromatography on silica gel (CyHex/EtOAc = 25/1  $\rightarrow$  10/1  $\rightarrow$  3/1  $\rightarrow$  0/1) afforded 254 mg (604  $\mu\text{mol}$ , 38%) of the hydrogenated product **19a** and 196 mg (640  $\mu\text{mol}$ , 40%) of its desilylated derivative **19b** as inseparable mixture of diastereomers.<sup>8</sup>



**C<sub>24</sub>H<sub>40</sub>O<sub>4</sub>Si**

**M:** 420.66 g/mol.

**DC:** R<sub>f</sub> = 0.11 (CyHex/EtOAc = 25/1), cerium-reagent.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>):  $\delta$  [ppm] = 0.07 [s, 6H, C1'']; 0.73 [d, <sup>3</sup>J<sub>H,H</sub> = 6.8 Hz, 3H, C5']; 0.90 [s, 9H, C3'']; 1.20 [d, <sup>3</sup>J<sub>H,H</sub> = 7.0 Hz, 3H, C10]; 1.43 [m, 4H, C3', C4', C7]; 1.72 [m, 2H, C8]; 1.96 [m, 1H, C7]; 2.16 [s, 3H, C11]; 2.39 [m, 1H, C6]; 2.62 [m, 1H, C2']; 2.90 [m, 1H, C9]; 3.38 [m,

<sup>8</sup> The analytical data of **19a** were determined from the mixture. Only chemical shifts of the main diastereomers (with respect to C9) are given.

1H, C1']; 3.61 [m, 1H, C1']; 3.74 [m, 1H, OH]; 5.85 [d,  $^4J_{H,H} = 1.4$  Hz, 1H, C2]; 5.91 [d,  $^4J_{H,H} = 1.4$  Hz, 1H, C2]; 6.55 [s, 1H, C5].

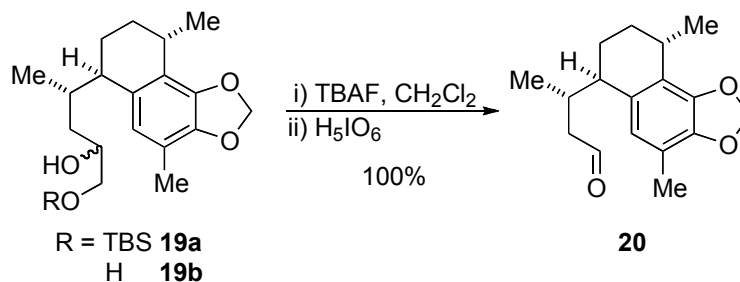
**$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  [ppm] = -5.3 [C(1'')H<sub>3</sub>]; 14.7 [C(11)H<sub>3</sub>]; 15.0 [C(5')H<sub>3</sub>]; 18.3 [C2'']; 20.9 [C(7)H<sub>7</sub>]; 21.0 [C(10)H<sub>3</sub>]; 25.9 [C(3'')H<sub>3</sub>]; 28.6 [C(9)H]; 29.5 [C(8)H<sub>2</sub>]; 33.5 [C(4')H]; 37.9 [C(3')H<sub>2</sub>]; 42.1 [C(6)H]; 68.0 [C(1')H<sub>2</sub>]; 69.9 [C(2')H]; 100.1 [C(2)H<sub>2</sub>]; 116.0 [C4]; 122.5 [C(5)H]; 123.0 [C9a]; 133.3 [C5a]; 143.1 [C3]; 144.5 [C1].

**IR** (ATR):  $\tilde{\nu}$  [ $\text{cm}^{-1}$ ] = 3566 (w), 3460 (br, w), 2946 (s), 2925 (s), 2853 (s), 1730 (w), 1646 (w), 1593 (w), 1460 (m), 1416 (s), 1373 (m), 1360 (m), 1323 (m), 1286 (m), 1251 (s), 1186 (w), 1106 (s), 1072 (s), 1030 (m), 1003 (m), 964 (m), 890 (w), 835 (s), 813 (m), 776 (s), 666 (w).

**MS** (GC-MS (EI 70 eV)):  $m/z$  (%) = 53 (10), 55 (24), 57 (19), 73 (17), 75 (75), 77 (21), 91 (22), 106 (11), 115 (20), 128 (21), 141 (14), 145 (12), 157 (19), 165 (13), 173 (17), 188 (9), 203 (100), 206 (23), 230 (11), 255 (16), 270 (19), 271 (23), 288 (6), 347 (3), 420 [ $\text{M}]^+$  (3).

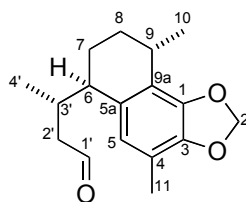
**HR-MS** (EI 70 eV):  $\text{C}_{24}\text{H}_{40}\text{O}_4\text{Si}$ , calculated for [ $\text{M}]^+$ : 420.2696, found: 420.269  $\text{u} \pm <5\text{ppm}$ .

**(S)-3'-((6R,9S)-4,9-Dimethyl-6,7,8,9-tetrahydronaphtho[1,2-d][1,3]dioxol-6-yl)butanal**  
**(20)**



A dried Schlenk flask was charged with 269 mg (640  $\mu\text{mol}$ , 1 equiv.) of a mixture of the alcohols **19a** and **19b** dissolved in 8.1 ml of dry  $\text{CH}_2\text{Cl}_2$ . Then 0.77 ml (768  $\mu\text{mol}$ , 1.2 equiv.) of a TBAF-solution (1.0 M in THF) were added and the mixture was stirred for 5.5 h at rt before 175 mg (768  $\mu\text{mol}$ , 1.2 equiv.) of  $\text{H}_5\text{IO}_6$  were added and (intense) stirring was continued for additional 2.5 h at rt. After partition between  $\text{H}_2\text{O}$  and  $\text{CH}_2\text{Cl}_2$  the layers were separated and the aqueous layer was extracted with 3 x 20 ml of  $\text{CH}_2\text{Cl}_2$ . The combined organic layers were dried with  $\text{MgSO}_4$ , filtered and the solvent was removed *in vacuo*. The remaining solid was treated with ice cold MTBE, the TBAF precipitate was filtered off and washed with ice cold MTBE. The combined filtrates were concentrated *in vacuo* to give a light brown oil, which was purified by filtration on celite (CyHex/EtOAc = 10/1) to afford 175 mg (640  $\mu\text{mol}$ , 100%)

of aldehyde **20** as an inseparable 4:1 mixture of diastereomers.<sup>9</sup> At this stage the diastereoselectivity of the ratio of the previous hydrogenation step could be determined as being  $\geq 95 : 5$  by means of GC-MS/FID.



**C<sub>17</sub>H<sub>22</sub>O<sub>3</sub>**

**M:** 274.35 g/mol.

**DC:** R<sub>f</sub> = 0.32 (CyHex/EtOAc = 10/1), cerium-reagent.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ [ppm] = 0.88 [d, <sup>3</sup>J<sub>H,H</sub> = 6.1 Hz, 3H, C4']; 1.25 [d, <sup>3</sup>J<sub>H,H</sub> = 6.8 Hz, 3H, C10]; 1.38 [m, 1H, C7]; 1.63 [m, 1H, C8]; 1.76 [m, 1H, C8]; 1.98 [m, 1H, C7]; 2.17 [s, 3H, C11]; 2.32 [dt, <sup>3</sup>J<sub>H,H</sub> = 5.4 Hz, <sup>3</sup>J<sub>H,H</sub> = 7.9 Hz, 1H, C3']; 2.52 [m, 3H, C6, C2']; 2.93 [m, 1H, C9]; 5.85 [s, 1H, C2]; 5.93 [s, 1H, C2]; 6.46 [s, 1H, C5]; 9.66 [s, 1H, C1'].

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ [ppm] = 14.6 [C(11)H<sub>3</sub>]; 16.7 [C(4')H<sub>3</sub>]; 20.7 [C(7)H<sub>2</sub>]; 21.1 [C(10)H<sub>3</sub>]; 27.2 [C(8)H<sub>2</sub>]; 28.0 [C(9)H]; 32.3 [C(3')H]; 41.7 [C(6)H]; 49.7 [C(2')H<sub>2</sub>]; 100.3 [C(2)H<sub>2</sub>]; 116.0 [C4]; 122.7 [C9a]; 123.2 [C(5)H]; 132.1 [C5a]; 143.5 [C3]; 144.8 [C1]; 202.9 [C1'].

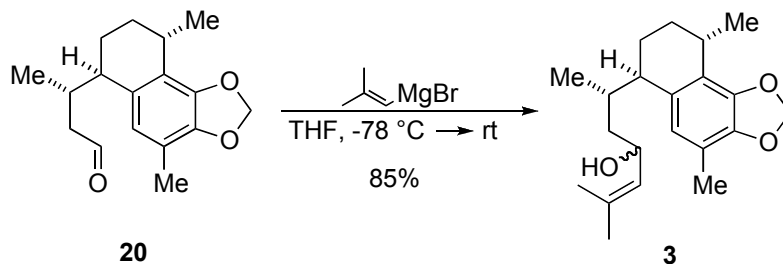
**IR** (ATR):  $\tilde{\nu}$  [cm<sup>-1</sup>] = 2925 (m), 2870 (m), 2715 (w), 1719 (s), 1648 (w), 1595 (w), 1459 (m), 1415 (s), 1376 (m), 1327 (m), 1279 (m), 1187 (m), 1126 (m), 1085 (s), 1069 (s), 1023 (m), 962 (s), 926 (w), 893 (w), 857 (w), 804 (w), 780 (w), 759 (w), 668 (w).

**MS** (GC-MS (EI 70 eV)): m/z (%) = 51 (12), 53 (10), 76 (18), 91 (19), 106 (10), 115 (28), 127 (14), 128 (34), 129 (22), 141 (21), 152 (23), 165 (25), 173 (37), 199 (52), 203 (100), 114 (21), 116 (20), 228 (39), 241 (48), 256 (51), 274 [M]<sup>+</sup> (11).

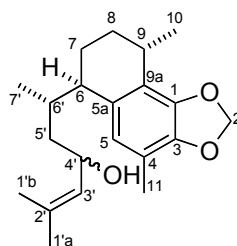
**HR-MS** (EI 70 eV): C<sub>8</sub>H<sub>18</sub>O<sub>2</sub>Si, calculated for [M]<sup>+</sup>: 274.1569, found: 274.157 u ± <5ppm.

<sup>9</sup> The analytical data of **20** were determined from the 4:1 mixture of diastereomers. Only chemical shifts of the main diastereomer are given.

**(S)-6'-((6R,9S)-4,9-Dimethyl-6,7,8,9-tetrahydronaphtho[1,2-d][1,3]dioxol-6-yl)-2'-methyl-hept-2'-en-4'-ol (3)**



In a dried Schlenk tube 175 mg (640  $\mu\text{mol}$ , 1 equiv.) of aldehyde **20** were dissolved in 7 ml of dry THF, cooled to  $-78\text{ }^\circ\text{C}$  and 2.6 ml (1.28 mmol, 2 equiv.) of a solution of *iso*-butenylmagnesium bromide (0.5 M in THF) were added dropwise by means of a syringe pump over 40 min. The mixture was stirred for 18 h (slowly warming to rt), before the reaction was quenched with ca. 10 ml of a saturated aqueous  $\text{NH}_4\text{Cl}$  solution. Water was added until the precipitate just dissolved and the mixture was transferred with MTBE into a separation funnel. The aqueous layer was extracted with 3 x 30 ml of MTBE and the combined organic layers were dried with  $\text{MgSO}_4$ , filtered and the solvent removed *in vacuo*. The crude product was filtered through celite (CyHex/EtOAc = 10/1) to give 179 mg (541  $\mu\text{mol}$ , 85%) of the allylic alcohol **3** as an inseparable mixture of diastereomers<sup>10</sup> (1:1 with respect to C4'; 4:1 with respect to C9). For analytical purposes, a small portion of the product was purified by flash-column chromatography on silica gel (CyHex/EtOAc = 10/1  $\rightarrow$  5/1).



**C<sub>21</sub>H<sub>30</sub>O<sub>3</sub>**

**M:** 330.46 g/mol.

**DC:**  $R_f$  = 0.13 (CyHex/EtOAc = 10/1).

**<sup>1</sup>H NMR** (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  [ppm] = 0.72 [dd,  $^3J_{\text{H,H}}$  = 6.8 Hz,  $^4J_{\text{H,H}}$  = 1.5 Hz, 3H, C7']; 1.24 [d,  $^3J_{\text{H,H}}$  = 6.9 Hz, 3H, C10]; 1.36 [m, 2H, C7]; 1.54 [m, 2H, C5']; 1.69 [s, 3H, C1'b]; 1.73 [s, 3H, C1'a]; 1.95 [m, 2H, C8]; 2.08/2.19 [m, 1H, C6']; 2.16 [s, 3H, C11]; 2.64 [m, 1H, C6]; 2.91 [m,

<sup>10</sup> The analytical data of **3** were determined from the mixture of diastereomers. Only chemical shifts of the main diastereomer are given.

1H, C9]; 4.44 [m, 1H, C4']; 5.17 [dd,  $^3J_{\text{H,H}} = 7.6 \text{ Hz}$ ,  $^3J_{\text{H,H}} = 7.6 \text{ Hz}$ , 1H, C3']; 5.85 [s, 1H, C2]; 5.92 [s, 1H, C2]; 6.50 [s, 1H, C5].

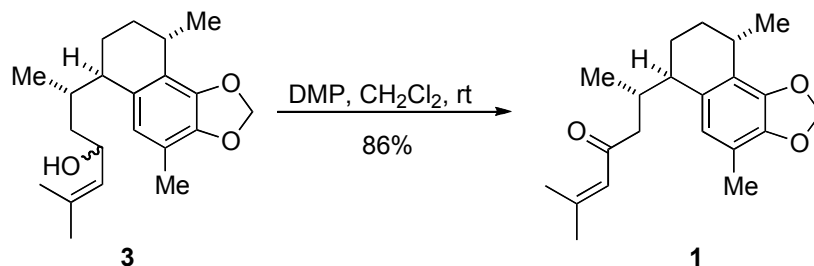
**$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  [ppm] = 14.7 [C(11) $\text{H}_3$ ]; 16.2 [C(7') $\text{H}_3$ ]; 18.2 [C(1'b) $\text{H}_3$ ]; 20.6/20.7 [C(7) $\text{H}_2$ ]; 21.0 [C(10) $\text{H}_3$ ]; 25.8 [C(1'a) $\text{H}_3$ ]; 28.5 [C(9) $\text{H}$ ]; 29.5/29.6 [C(8) $\text{H}_2$ ]; 33.9/34.2 [C(6') $\text{H}$ ]; 40.8/41.2 [C(6) $\text{H}$ ]; 43.2/43.3 [C(5') $\text{H}_2$ ]; 66.8/67.2 [C(4') $\text{H}$ ]; 100.2 [C(2) $\text{H}_2$ ]; 116.0 [C4]; 122.4 [C(5) $\text{H}$ ]; 123.1 [C9a]; 128.5/128.7 [C(3') $\text{H}$ ]; 133.4 [C5a]; 133.4 [C5a]; 134.8 [C2']; 143.1 [C3]; 144.6 [C1].

**IR** (ATR):  $\tilde{\nu}$  [ $\text{cm}^{-1}$ ] = 3362 (br, w), 2922 (s), 2868 (s), 1717 (w), 1670 (w), 1647 (w), 1595 (w), 1446 (s), 1416 (s), 1375 (s), 1327 (m), 1288 (m), 1188 (m), 1119 (m), 1071 (s), 1032 (s), 964 (s), 926 (w), 896 (w), 857 (w), 733 (w), 668 (w).

**MS** (GC-MS (EI 70 eV)):  $m/z$  (%) = 41 (18), 55 (6), 77 (6), 91 (7), 115 (17), 128 (19), 129 (14), 145 (12), 165 (11), 173 (22), 188 (19), 199 (23), 203 (100), 204 (20), 213 (19), 230 (92), 231 (15), 241 (25), 255 (22), 256 (28), 257 (16), 297 (35), 312 (49), 330 [ $\text{M}]^+$  (4).

**HR-MS** (EI 70 eV):  $\text{C}_{21}\text{H}_{30}\text{O}_3$ , calculated for [ $\text{M}]^+$ : 330.2195, found: 330.218  $\pm$  <5ppm.

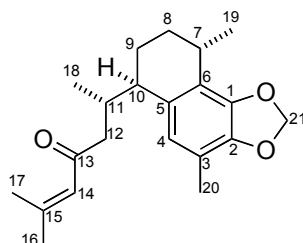
### Helioporin C (1)



A dried GC vial was charged with 7 mg of alcohol **3** (21.1  $\mu\text{mol}$ , 1 equiv.) dissolved in 0.47 ml of dry  $\text{CH}_2\text{Cl}_2$ . Then 5.1  $\mu\text{l}$  (63.3  $\mu\text{mol}$ , 3 equiv.) of dry pyridine were added followed by 9.9 mg (23.3  $\mu\text{mol}$ , 1.1 equiv.) of the *Dess-Martin* periodinane. The mixture was stirred for 2 h at rt before the solvent was removed *in vacuo* and the residue was taken up in CyHex/EtOAc (10/1). The suspension was filtered through a small pipette filled with  $\text{MgSO}_4$  with CyHex/EtOAc (10/1) as an eluent. After removal of the solvent *in vacuo* the crude product was filtered through a plug of celite with CyHex/EtOAc (7/1) to afford 6 mg (18.3  $\mu\text{mol}$ , 86%) of helioporphin C (**1**) as a 4:1 mixture of diastereomers<sup>11</sup>.

<sup>11</sup> The analytical data of **1** were determined from the 4:1 mixture of diastereomers. Only chemical shifts of the main diastereomer are given.





**C<sub>21</sub>H<sub>28</sub>O<sub>3</sub>**

**M:** 328.44 g/mol.

**DC:** R<sub>f</sub> = 0.4 (CyHex/EtOAc = 10/1).

**<sup>1</sup>H NMR** (600 MHz, CDCl<sub>3</sub>): δ [ppm] = 0.75 [d, <sup>3</sup>J<sub>H,H</sub> = 6.5 Hz, 3H, C18]; 1.21 [d, <sup>3</sup>J<sub>H,H</sub> = 6.5 Hz, 3H, C19]; 1.36 [m, 1H, C8]; 1.59 [m, 1H, C9]; 1.75 [m, 1H, C9]; 1.86 [s, 3H, C16]; 1.99 [m, 1H, C8]; 2.11 [s, 3H, C17]; 2.16 [s, 3H, C20]; 2.30 [m, 1H, C12]; 2.52 [m, 2H, C12 und C11]; 2.55 [ψ-t, <sup>3</sup>J<sub>H,H</sub> = 5.4 Hz, 1H, C10]; 2.91 [ddq, <sup>3</sup>J<sub>H,H</sub> = 6.5 Hz, <sup>3</sup>J<sub>H,H</sub> = 6.5 Hz, <sup>3</sup>J<sub>H,H</sub> = 6.5 Hz, 1H, C7]; 5.85 [d, <sup>1</sup>J<sub>H,H</sub> = 1.5 Hz, 1H, C21]; 5.91 [d, <sup>2</sup>J<sub>H,H</sub> = 1.5 Hz, 1H, C21]; 6.03 [t, <sup>4</sup>J<sub>H,H</sub> = 1.0 Hz, 1H, C14]; 6.52 [s, 1H, C4].

**<sup>13</sup>C NMR** (150 MHz, CDCl<sub>3</sub>): δ [ppm] = 14.6 [C(20)H<sub>3</sub>]; 16.3 [C(18)H<sub>3</sub>]; 20.6 [C(17)H<sub>3</sub>]; 20.9 [C(9)H<sub>2</sub>]; 21.1 [C(19)H<sub>3</sub>]; 27.7 [C(16)H<sub>3</sub>]; 28.2 [C(7)H]; 28.6 [C(8)H<sub>2</sub>]; 34.1 [C(11)H]; 41.4 [C(10)H]; 50.1 [C(12)H<sub>2</sub>]; 100.3 [C(21)H<sub>2</sub>]; 116.0 [C3]; 122.9 [C6]; 123.1 [C(4)H]; 124.2 [C(14)H]; 132.9 [C5]; 143.3 [C2]; 144.6 [C1]; 154.9 [C15]; 201.1 [C13].

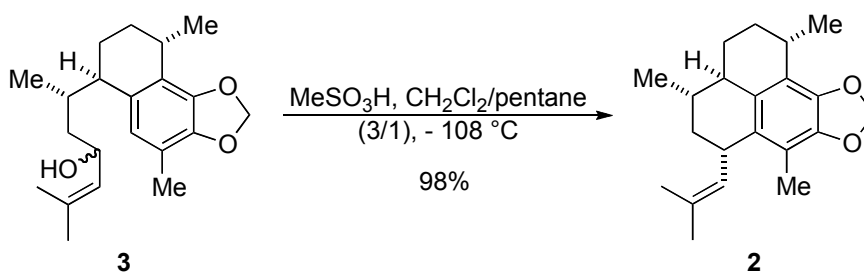
**IR** (ATR):  $\tilde{\nu}$  [cm<sup>-1</sup>] = 2953 (s), 2925 (s), 2866 (s), 1726 (w), 1683 (s), 1616 (s), 1440 (s), 1417 (s), 1373 (m), 1326 (m), 1280 (m), 1186 (w), 1116 (m), 1074 (s), 1033 (s), 964 (s), 926 (w), 890 (w), 856 (w), 816 (w), 733 (w), 703 (w).

**MS** (GC-MS (EI 70 eV)): m/z (%) = 39 (3), 41 (3), 55 (5), 83 (11), 105 (4), 115 (7), 128 (10), 129 (10), 145 (11), 157 (6), 158 (7), 185 (8), 188 (9), 203 (36), 215 (22), 230 (100), 231 (30), 255 (2), 295 (3), 310 (84), 328 [M]<sup>+</sup> (4).

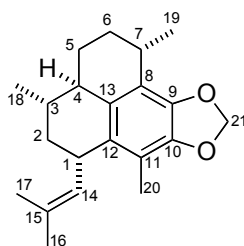
**HR-MS** (EI 70 eV): C<sub>21</sub>H<sub>28</sub>O<sub>3</sub>, calculated for [M]<sup>+</sup>: 328.2039, found: 328.203 u ± <5ppm.

The analytical data of the main diastereomer are in full agreement with the data published by Higa for helioporphin C (**1**).<sup>1</sup>

## Heliopoin E (2)



A dried Schlenk tube was charged with 85 mg (257  $\mu\text{mol}$ , 1 equiv.) of alcohol **3** (4:1 mixture of diastereomers) dissolved in 8 ml of  $\text{CH}_2\text{Cl}_2$ /pentane (3/1). The solution was cooled to  $-108\text{ }^{\circ}\text{C}$  (THF/ $\text{N}_2$ -bath) and 7  $\mu\text{l}$  (103  $\mu\text{mol}$ , 0.5 equiv.) of  $\text{MeSO}_3\text{H}$  dissolved in 1 ml of  $\text{CH}_2\text{Cl}_2$  were added slowly. The mixture was stirred for 7 h at  $-108\text{ }^{\circ}\text{C}$  before the reaction was quenched by addition of  $\text{H}_2\text{O}$  and the cooling bath was removed. After 30 min, the layers were separated and the aqueous layer was extracted with 3 x 20 ml of  $\text{CH}_2\text{Cl}_2$ . The combined organic layers were filtered through  $\text{MgSO}_4$  and the solvent was removed *in vacuo* to afford 79 mg (253  $\mu\text{mol}$ , 98%) of **2/epi-2** as a yellow oil. By means of  $^1\text{H}$  NMR of the crude product the ratio of the C1 epimers (**2** / *epi-2*) was determined to be 3:1.<sup>12</sup>



**C<sub>21</sub>H<sub>28</sub>O<sub>2</sub>**

**M:** 312.45 g/mol.

**DC:**  $R_f = 0.6$  (CyHex/EtOAc = 10/1), cerium-reagent.

**$^1\text{H}$  NMR** (600 MHz,  $\text{CDCl}_3$ ):  $\delta$  [ppm] = 1.01 [d, 3H,  $^3J_{\text{H,H}} = 5.9\text{ Hz}$ , C18]; 1.02 [m, 1H, C5]; 1.18 [m, 1H, C2]; 1.21 [m, 1H, C3]; 1.26 [m, 1H, C6]; 1.30 [d, 3H,  $^3J_{\text{H,H}} = 6.8\text{ Hz}$ , C19]; 1.66 [s, 3H, C16]; 1.72 [s, 3H, C17]; 1.99 [m, 1H, C2]; 2.03 [s, 3H, C20]; 2.06 [m, 2H, C4, C6]; 2.11 [m, 1H, C5]; 2.97 [ddq,  $^3J_{\text{H,H}} = 6.9\text{ Hz}$ ,  $^3J_{\text{H,H}} = 10.1\text{ Hz}$ ,  $^3J_{\text{H,H}} = 6.9\text{ Hz}$ , 1H, C7]; 3.72 [ddd,  $^3J_{\text{H,H}} = 7.8\text{ Hz}$ ,  $^3J_{\text{H,H}} = 7.8\text{ Hz}$ ,  $^3J_{\text{H,H}} = 8.6\text{ Hz}$ , 1H, C1]; 4.95 [dt,  $^3J_{\text{H,H}} = 9.3\text{ Hz}$ ,  $^4J_{\text{H,H}} = 1.1\text{ Hz}$ , 1H, C14]; 5.84 [s, 1H, C21]; 5.90 [s, 1H, C21].

**$^{13}\text{C}$  NMR** (150 MHz,  $\text{CDCl}_3$ ):  $\delta$  [ppm] = 11.9 [C(20) $\text{H}_3$ ]; 17.6 [C(17) $\text{H}_3$ ]; 19.7 [C(18) $\text{H}_3$ ]; 21.9 [C(19) $\text{H}_3$ ]; 25.4 [C(16) $\text{H}_3$ ]; 28.1 [C(5) $\text{H}_2$ ]; 29.9 [C(7) $\text{H}$ ]; 32.4 [C(6) $\text{H}_2$ ]; 34.4 [C(3) $\text{H}$ ];

<sup>12</sup> The analytical data of **2** were determined from the obtained 12:4:3:1 mixture of diastereomers. Only chemical shifts of the main diastereomer are given.

36.6 [C(1)H]; 40.2 [C(2)H<sub>2</sub>]; 44.8 [C(4)H]; 99.9 [C(21)H<sub>2</sub>]; 116.0 [C11]; 121.0 [C12]; 128.6 [C15]; 131.1 [C(14)H]; 131.6 [C8]; 132.2 [C13]; 143.0 [C10]; 144.2 [C9].

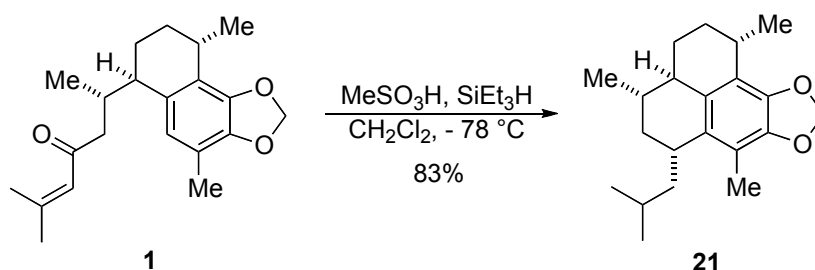
**IR** (ATR):  $\tilde{\nu}$  [cm<sup>-1</sup>] = 2949 (s), 2921 (s), 2865 (s), 1729 (m), 1684 (m), 1617 (m), 1445 (s), 1418 (s), 1374 (s), 1326 (m), 1279 (m), 1255 (w), 1190 (m), 1114 (s), 1083 (s), 1030 (s), 962 (s), 896 (w), 838 (m), 807 (w), 775 (w), 759 (w), 739 (w), 701 (w), 667 (w).

**MS** (GC-MS (EI 70 eV)): m/z (%) = 39 (5), 41 (10), 75 (4), 91 (6), 107 (3), 115 (7), 128 (9), 143 (6), 152 (8), 153 (8), 165 (11), 183 (7), 199 (37), 214 (16), 207 (7), 241 (80), 242 (13), 256 (100), 257 (28), 297 (6), 312 [M]<sup>+</sup> (26).

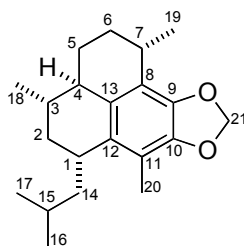
**HR-MS** (EI 70 eV): C<sub>21</sub>H<sub>28</sub>O<sub>2</sub>, calculated for [M]<sup>+</sup>: 312.2089, found: 312.208 ± <5ppm.

The analytical data of the main diastereomer are in full agreement with the data published by Higa for heliopirin E (**2**).<sup>1</sup>

### Dihydro-heliopirin E (**21**)



A dried GC vial was charged with 5 mg (15.2 μmol, 1 equiv.) of heliopirin C (**1**) (4:1 mixture of diastereomers) dissolved in 0.33 ml of dry CH<sub>2</sub>Cl<sub>2</sub> and the solution was cooled to -78 °C before 2.5 μl (38.1 μmol, 2.5 equiv.) of MeSO<sub>3</sub>H, dissolved in 0.1 ml of dry CH<sub>2</sub>Cl<sub>2</sub> (0.38 M stock solution) were added. After 30 min of stirring at -78 °C a solution of 5.3 μl (33.4 μmol, 2.2 Äq.) of SiEt<sub>3</sub>H in 0.1 ml of dry CH<sub>2</sub>Cl<sub>2</sub> (0.33 M stock solution) was injected and the mixture was stirred for additional 2 h at -78 °C. The reaction was quenched by addition of a small amount of H<sub>2</sub>O and the cooling bath was removed. After 1 h CH<sub>2</sub>Cl<sub>2</sub> and H<sub>2</sub>O were added, the layers were separated and the aqueous layer was extracted with 5 x 1 ml of CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layers were dried with MgSO<sub>4</sub>, filtered and the solvent was removed *in vacuo* to give 4.2 mg (12.6 μmol, 83%) of dihydro-heliopirin E (**21**) as a colorless oil as 4:1 diastereomeric mixture. The diastereoselectivity regarding C1 was determined as > 95:5 in favor of **21** by GC-FID.



**C<sub>21</sub>H<sub>30</sub>O<sub>2</sub>**

**M:** 314.46 g/mol.

**DC:** R<sub>f</sub> = 0.64 (CyHex/EtOAc = 10/1), cerium-reagent.

**<sup>1</sup>H NMR** (600 MHz, CDCl<sub>3</sub>): δ [ppm] = 0.85 [d, 3H, <sup>3</sup>J<sub>H,H</sub> = 6.7 Hz, C16 or C17]; 0.96 [d, 3H, <sup>3</sup>J<sub>H,H</sub> = 6.5 Hz, C16 or C17]; 0.98 [d, 3H, <sup>3</sup>J<sub>H,H</sub> = 5.9 Hz, C18]; 1.01 [d, 1H, <sup>3</sup>J<sub>H,H</sub> = 6.3 Hz, C5]; 1.14 [m, 2H, C2 und C3]; 1.22 [m, 2H, C14]; 1.24 [m, 1H, C6]; 1.28 [d, 3H, <sup>3</sup>J<sub>H,H</sub> = 6.7 Hz, C19]; 1.77 [m, 1H, C15]; 2.05 [m, 4H, C2, C4, C5, C6]; 2.13 [s, 3H, C20]; 2.88 [m, 1H, C7]; 3.07 [m, 1H, C1]; 5.81 [s, 1H, <sup>2</sup>J<sub>H,H</sub> = 1.5 Hz, C21]; 5.88 [s, 1H, <sup>2</sup>J<sub>H,H</sub> = 1.5 Hz, C21].

**<sup>13</sup>C NMR** (150 MHz, CDCl<sub>3</sub>): δ [ppm] = 11.6 [C(20)H<sub>3</sub>]; 19.9 [C(18)H<sub>3</sub>]; 20.8 [C(16 or 17)H<sub>3</sub>]; 21.3 [C(19)H<sub>3</sub>]; 24.3 [C(16 or 17)H<sub>3</sub>]; 25.1 [C(15)H]; 28.2 [C(5)H<sub>2</sub>]; 30.3 [C(7)H]; 32.2 [C(6)H<sub>2</sub>]; 32.3 [C(1)H]; 35.8 [C(3)H]; 38.2 [C(2)H<sub>2</sub>]; 43.1 [C(4)H]; 49.0 [C(14)H<sub>2</sub>]; 99.8 [C(21)H<sub>2</sub>]; 114.4 [C(11)]; 121.0 [C(8)]; 132.4 [C(13)]; 134.0 [C(12)]; 142.3 [C(9)]; 143.9 [C(10)].

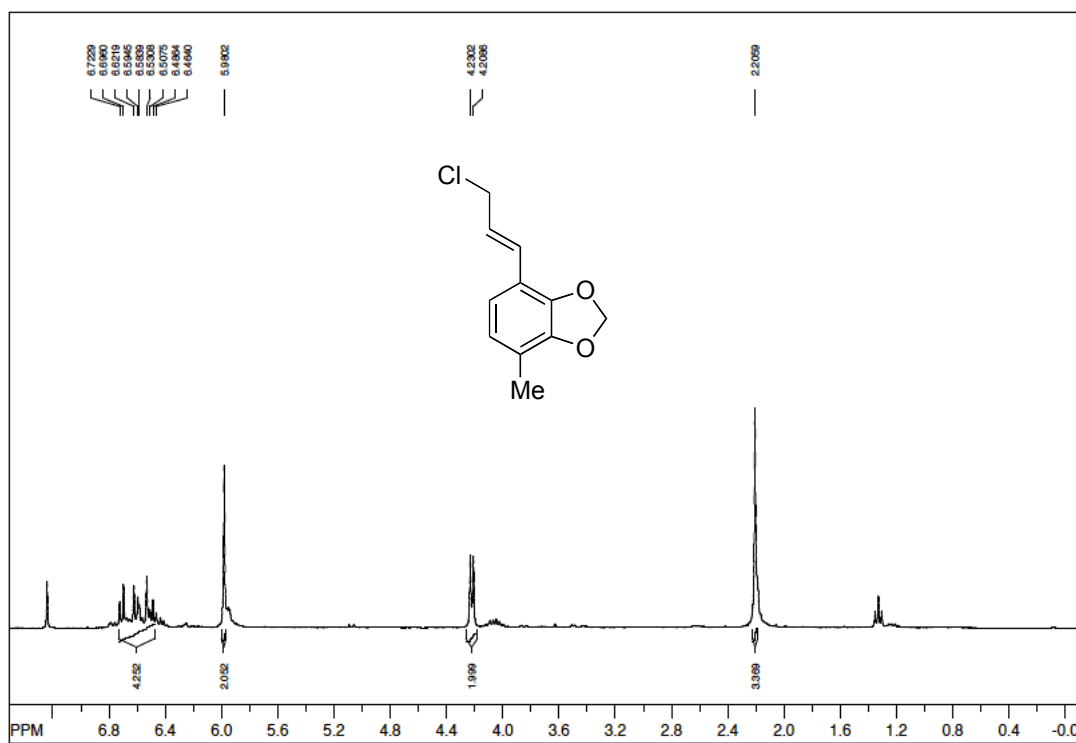
**IR** (ATR):  $\tilde{\nu}$  [cm<sup>-1</sup>] = 2949 (s), 2921 (s), 2864 (s), 2357 (w), 1733 (w), 1713 (w), 1602 (w), 1457 (s), 1419 (s), 1372 (m), 1364 (m), 1323 (m), 1284 (m), 1194 (w), 1138 (m), 1122 (m), 1110 (m), 1086 (s), 1070 (m), 1028 (w), 973 (w), 959 (m), 905 (w), 798 (w), 762 (w), 739 (w), 667 (w).

**MS** (GC-MS (EI 70 eV)): m/z (%) = 41 (5), 43 (3), 76 (2), 91 (3), 128 (4), 141 (4), 153 (3), 168 (3), 183 (6), 199 (10), 212 (5), 227 (7), 242 (4), 257 (100), 258 (18), 314 [M]<sup>+</sup> (14).

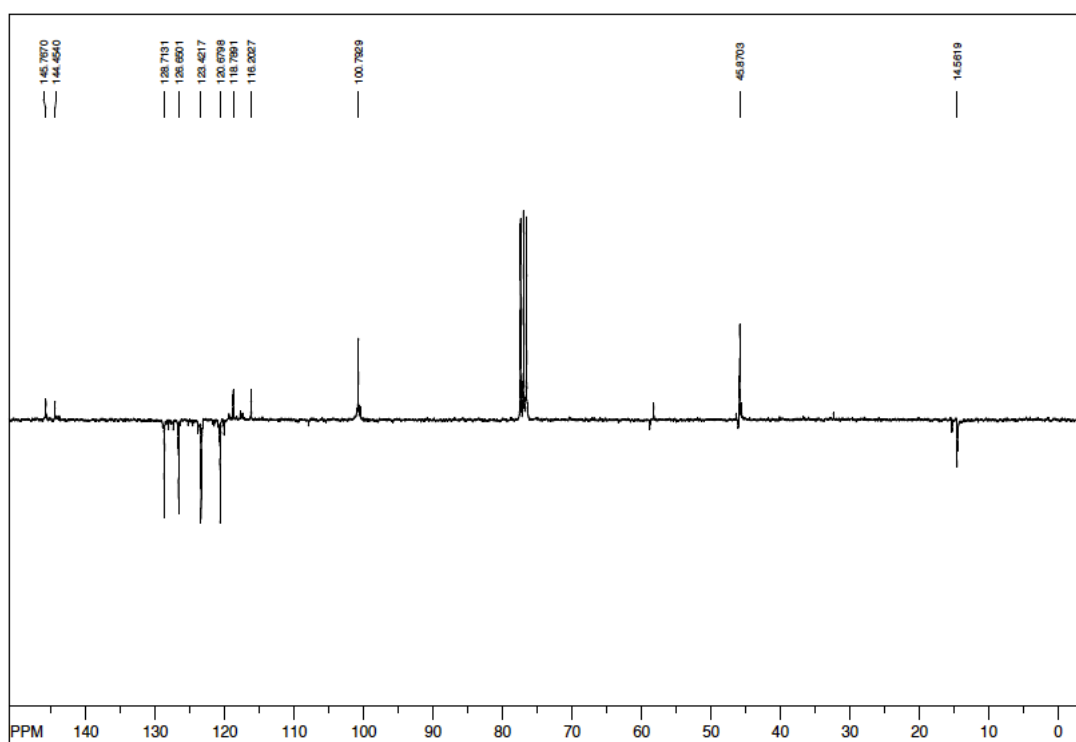
**HR-MS** (EI 70 eV): C<sub>8</sub>H<sub>18</sub>O<sub>2</sub>Si, calculated for [M]<sup>+</sup>: 314.2245, found: 314.224 u ± <5ppm.

### 3 NMR SPECTRA

(*E*)-4-(3'-Chloroprop-1'-enyl)-7-methylbenzo[d][1,3]dioxole (**7**)

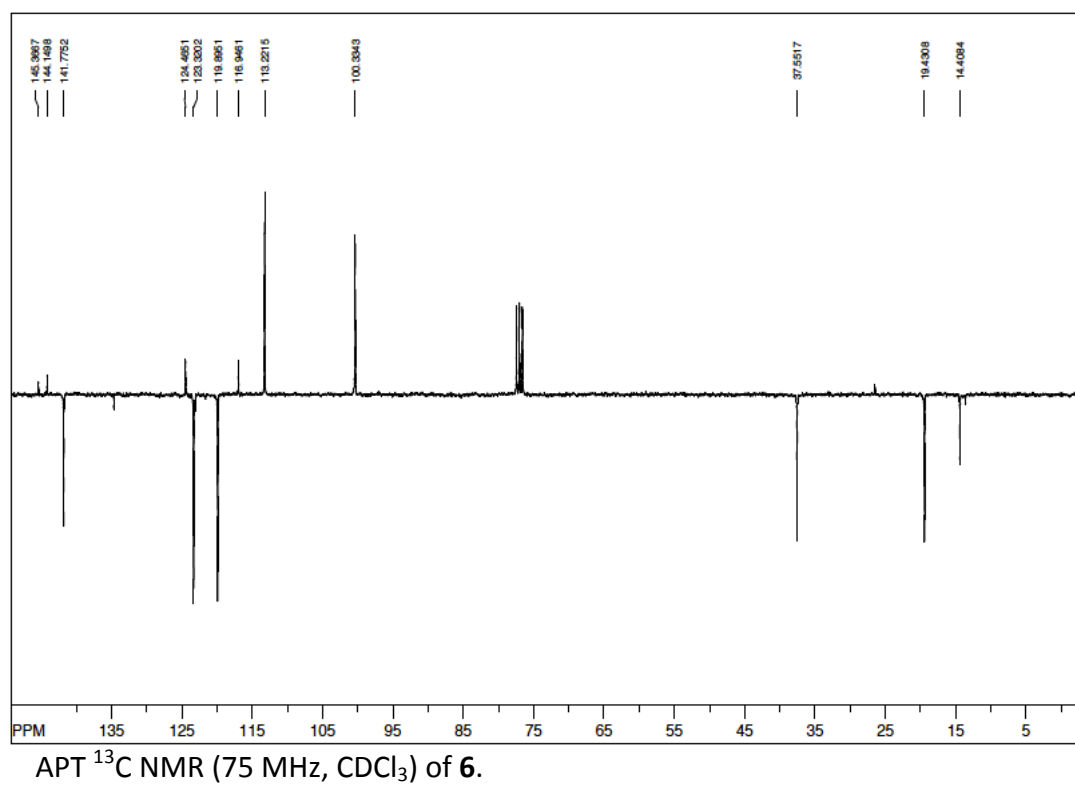
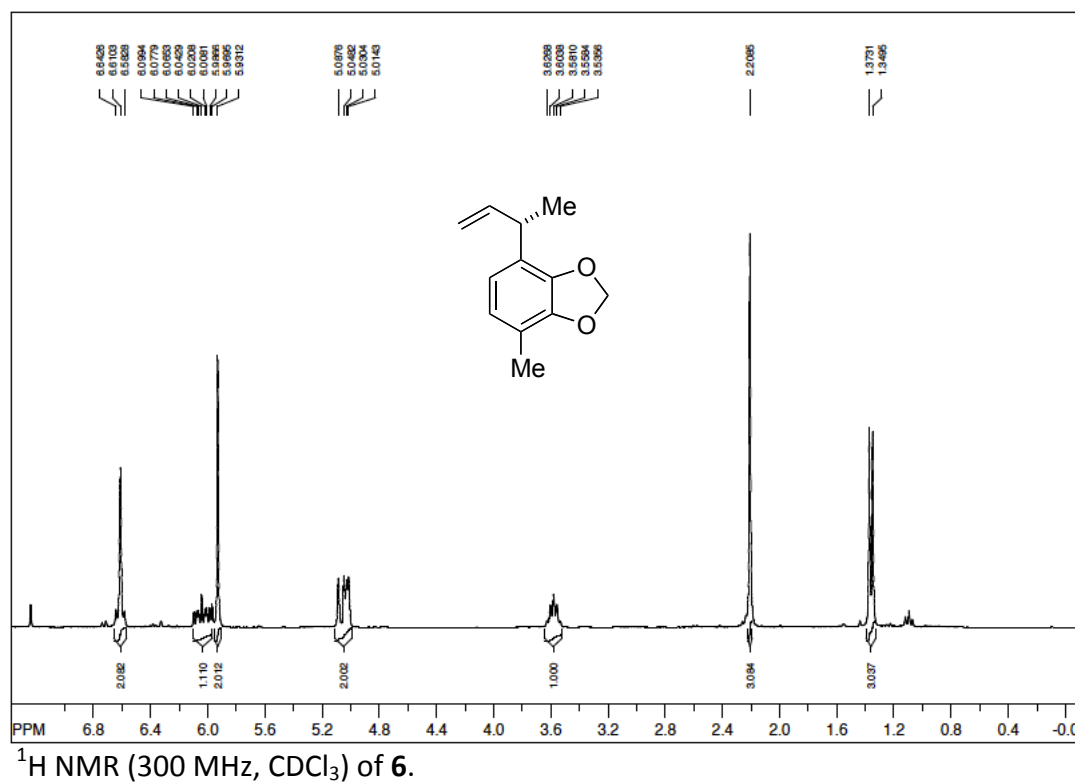


<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) of **7**.

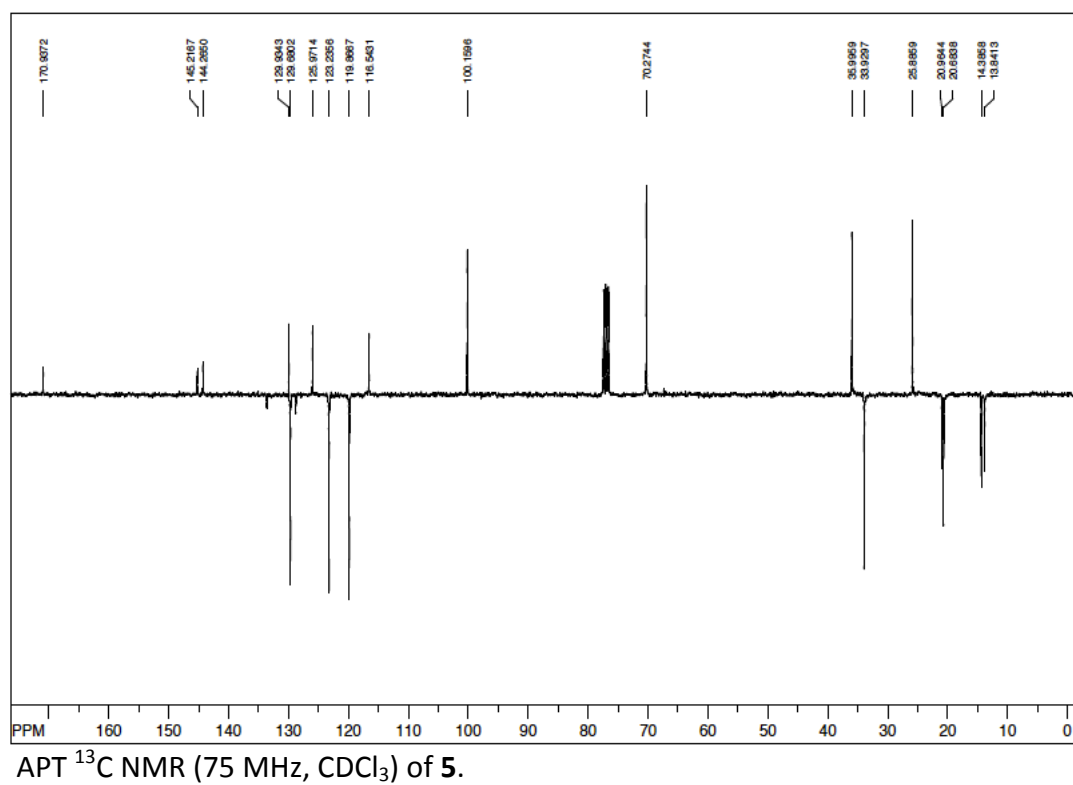
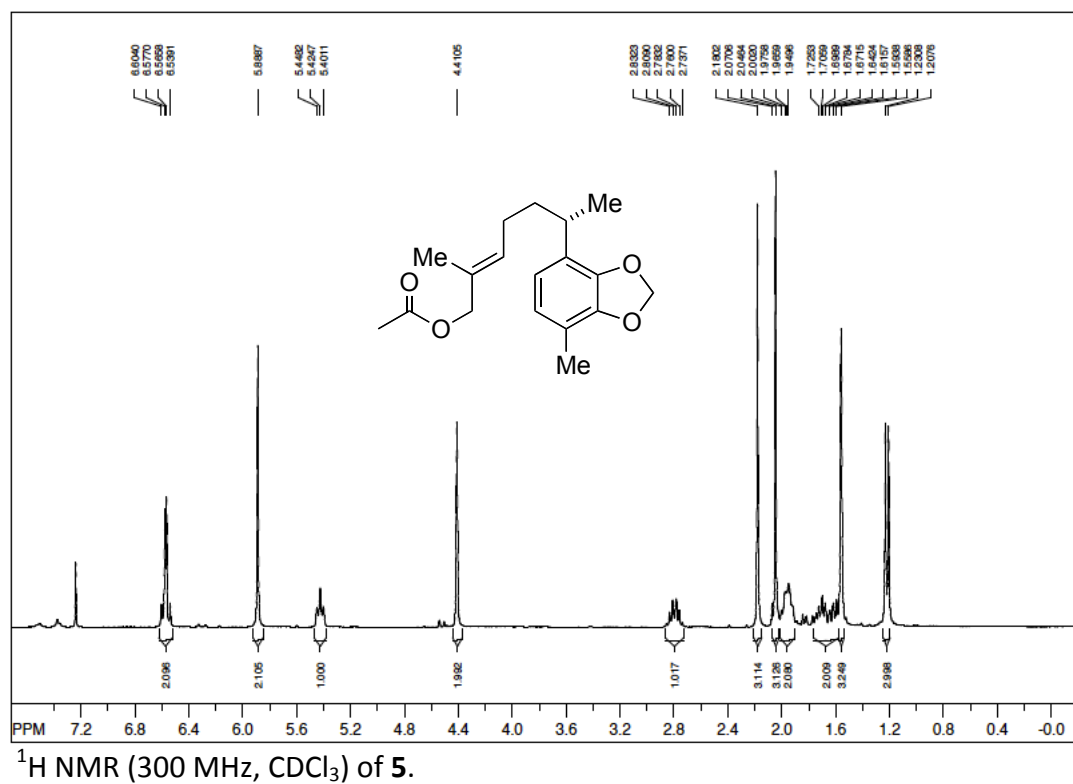


APT <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) of **7**.

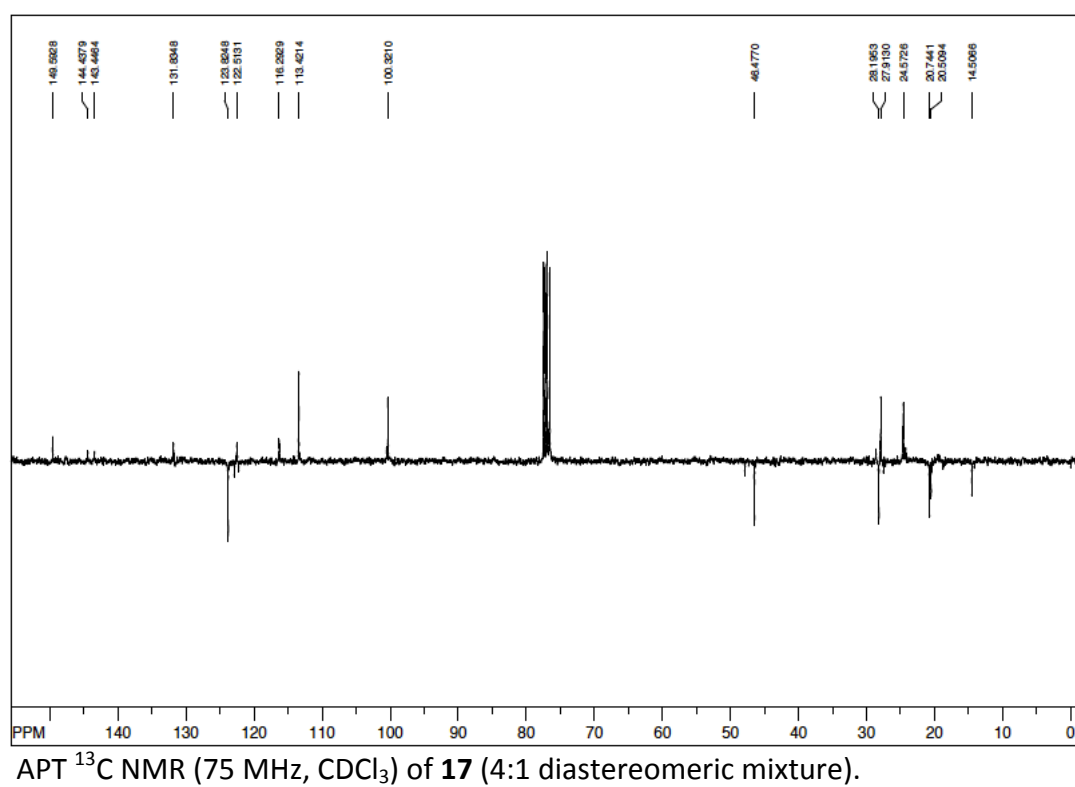
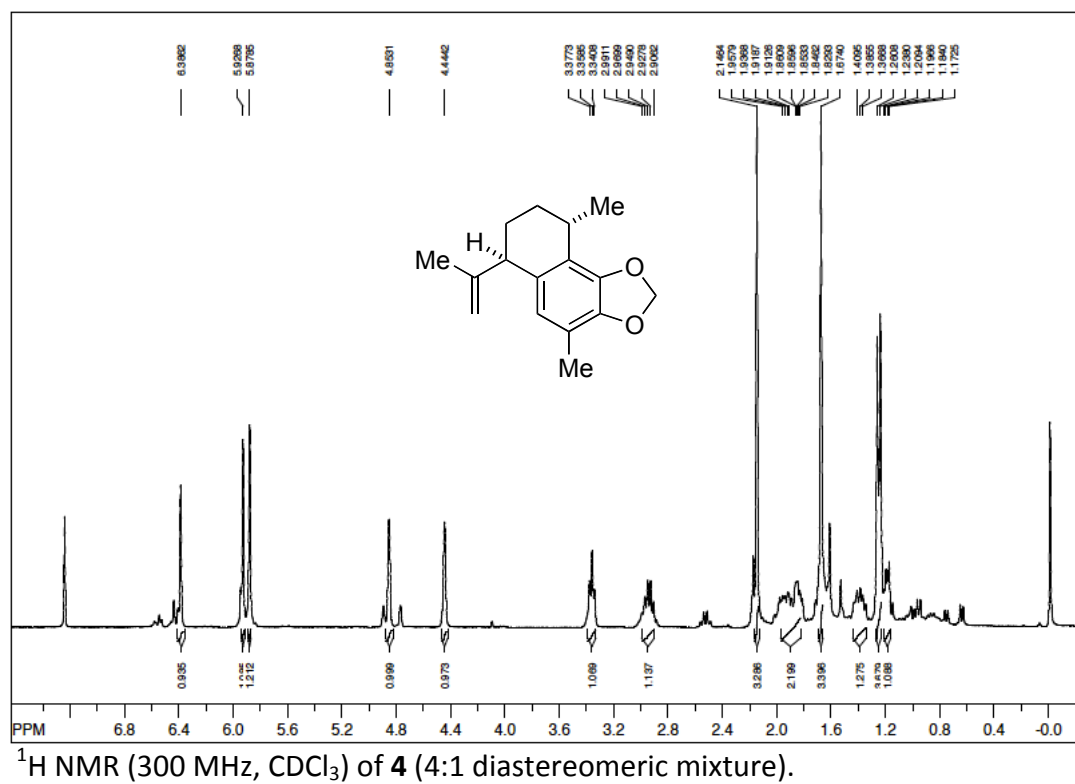
(S)-4-(But-3'-en-2'-yl)-7-methylbenzo[d][1,3]dioxole (**6**)



(*S,E*)-2-methyl-6-(7-methylbenzo[*d*][1,3]dioxole-4-yl)hept-2-enyl-acetat (**5**)

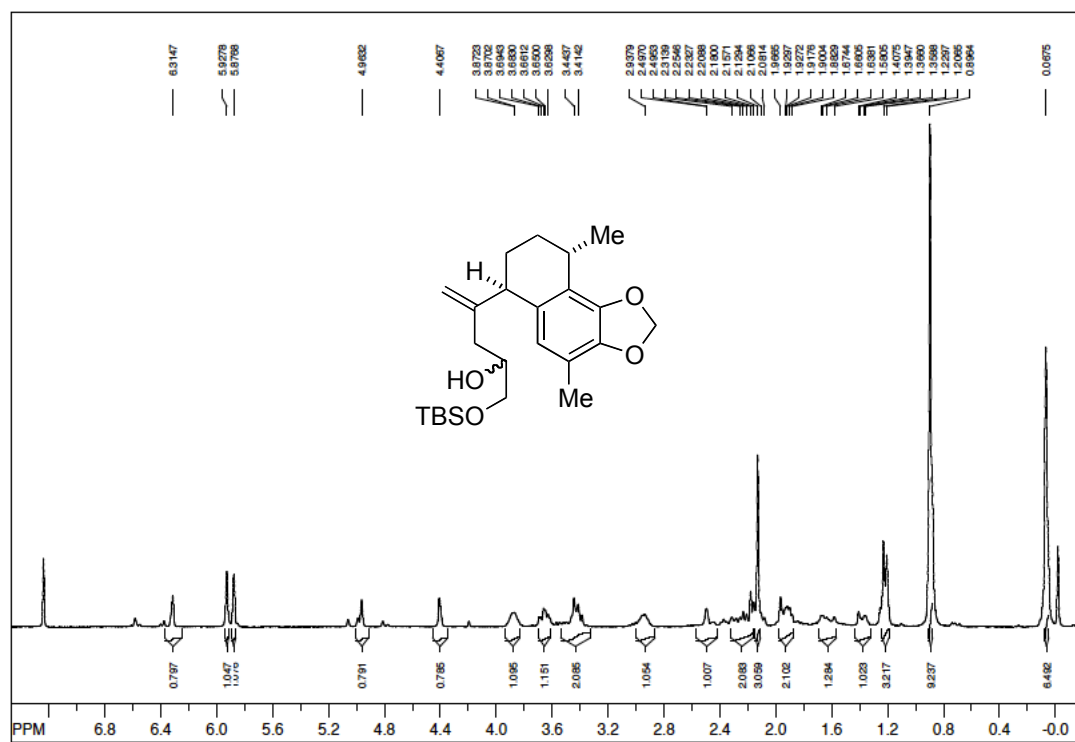


(6*R*,9*S*)-4,9-Dimethyl-6-(prop-1-en-2-yl)-6,7,8,9-tetrahydronaphtho[1,2-*d*][1,3]dioxole (**4**)

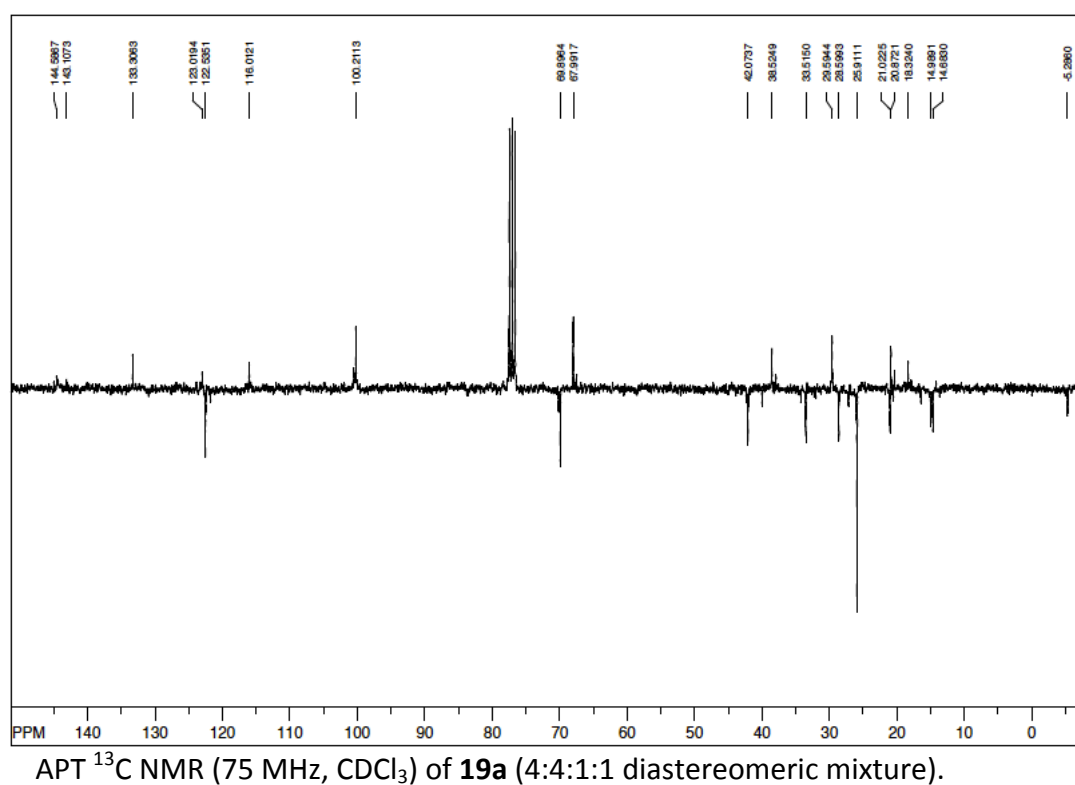
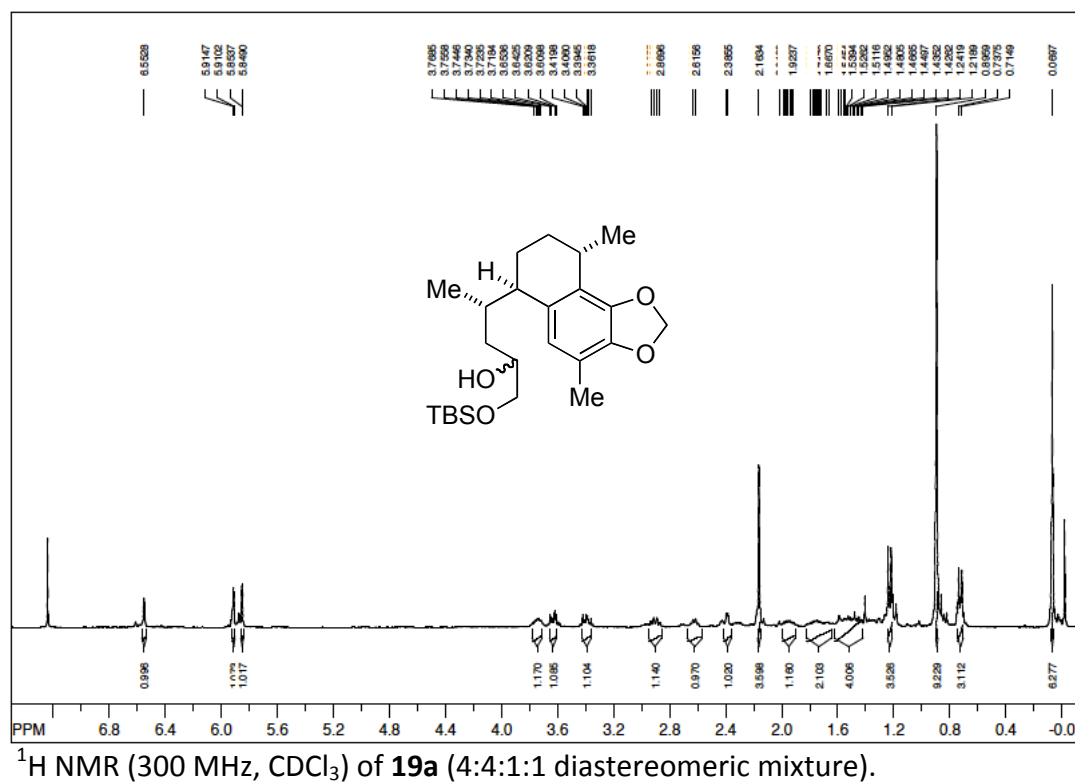




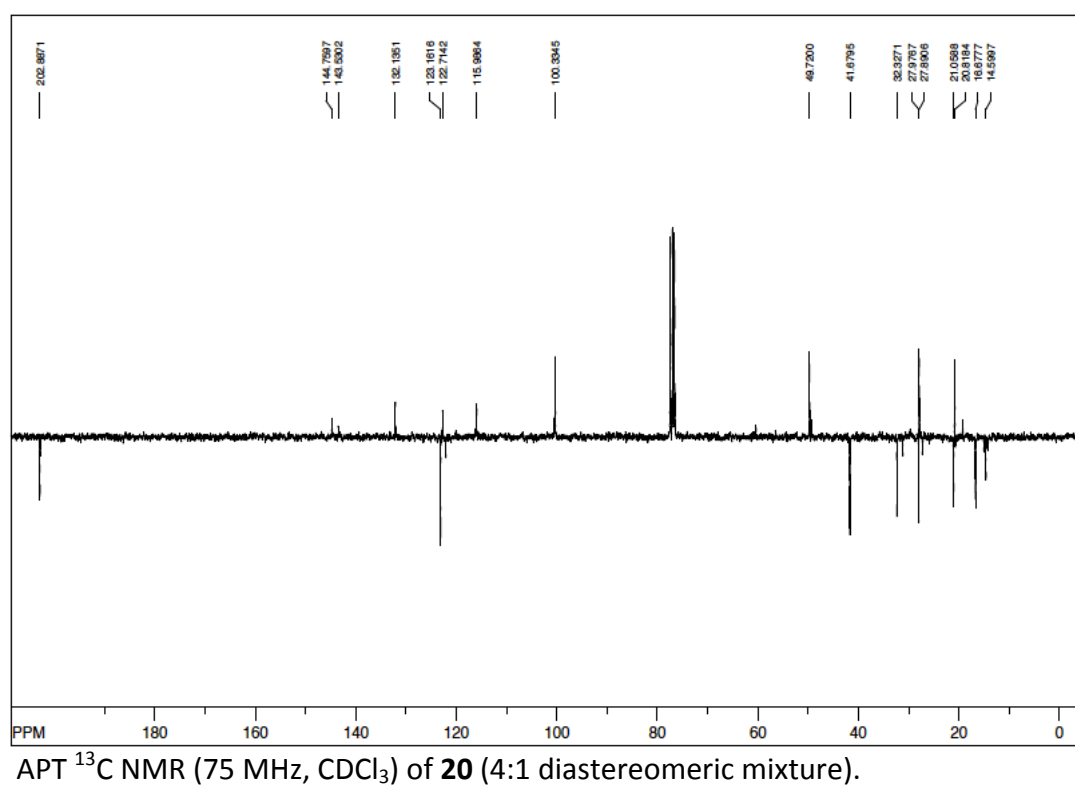
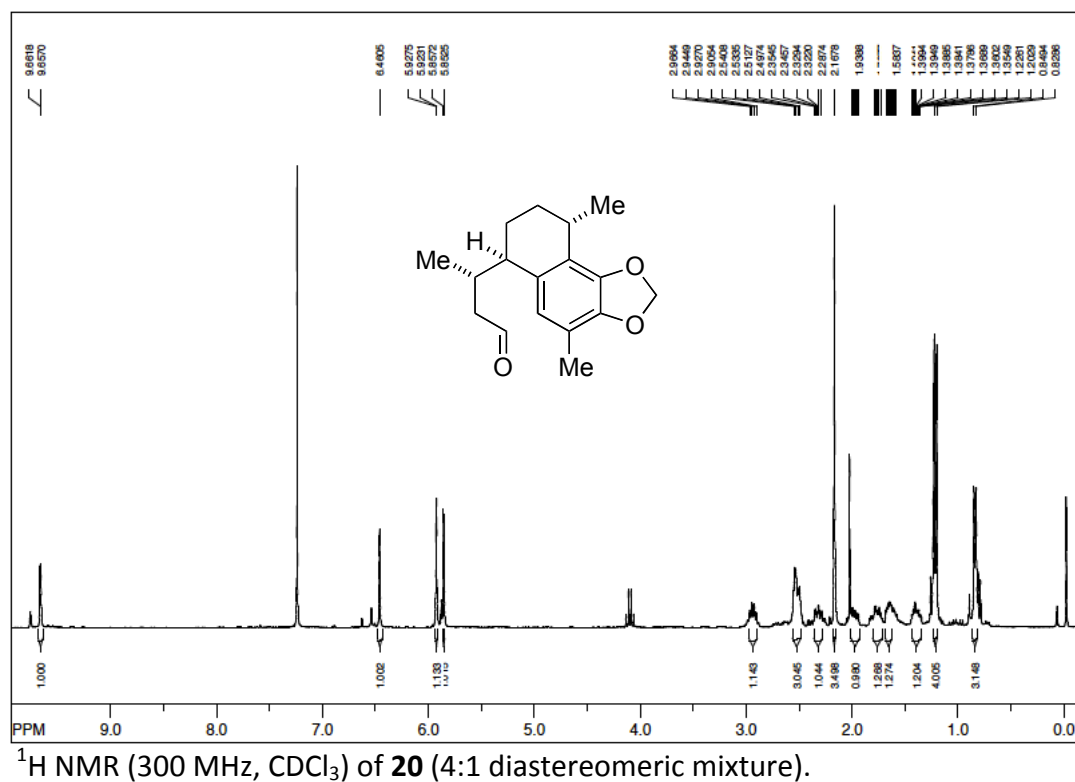
1-(*tert*-Butyldimethylsiloxy)-4-((6*R*,9*S*)-4,9-dimethyl-6,7,8,9-tetrahydronaphtho[1,2-*d*][1,3]dioxol-6-yl)pent-4-en-2-ol (**17**)



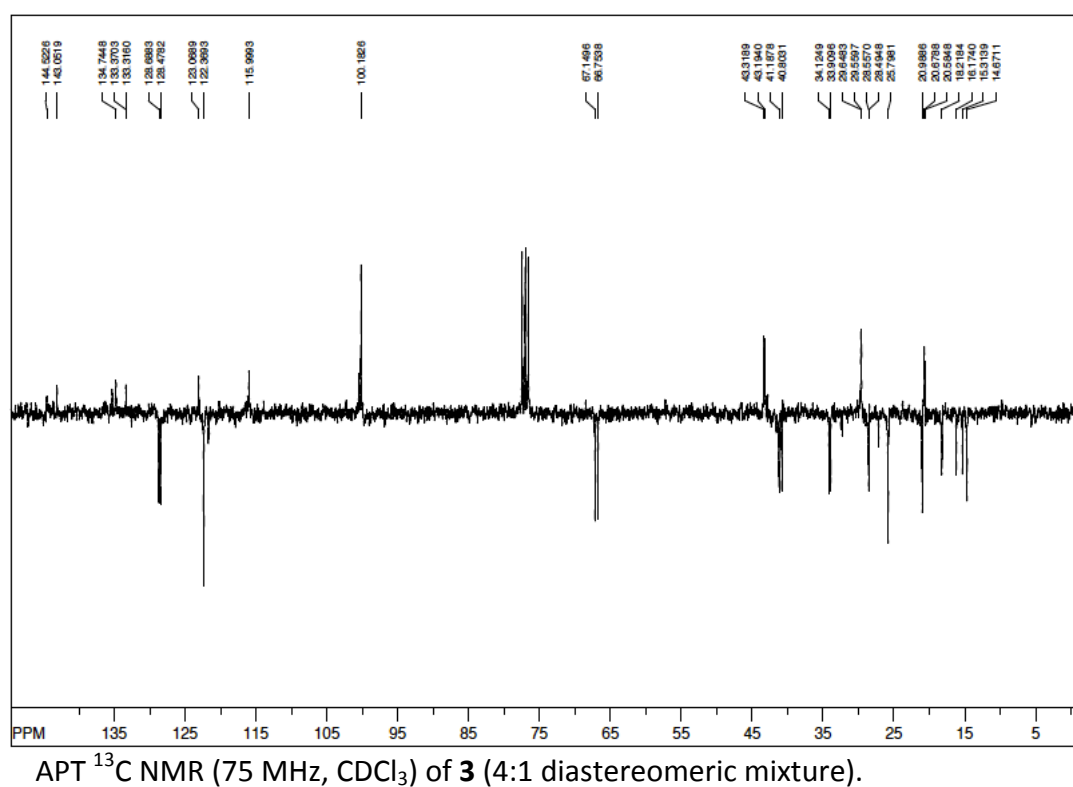
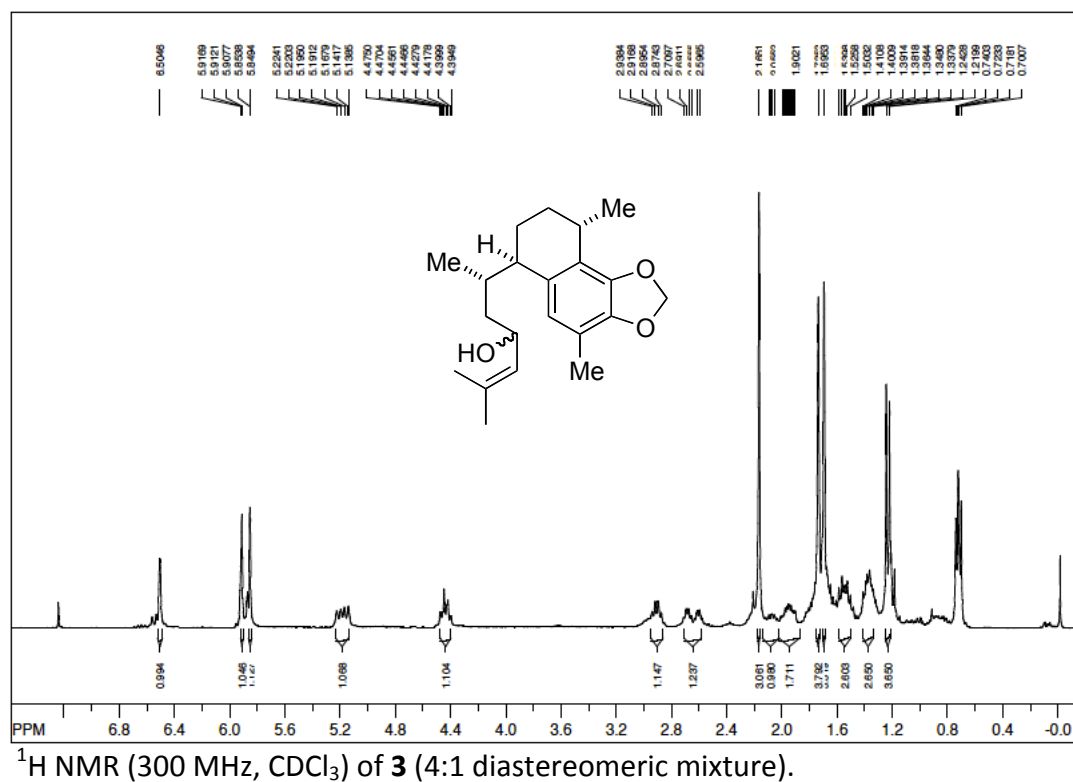
(*S*)-1-(*tert*-Butyldimethylsilyloxy)-4-((6*R*,9*S*)-4,9-dimethyl-6,7,8,9-tetrahydronaphtho[1,2-*d*][1,3]dioxol-6-yl)pentan-2-ol (**19a**)



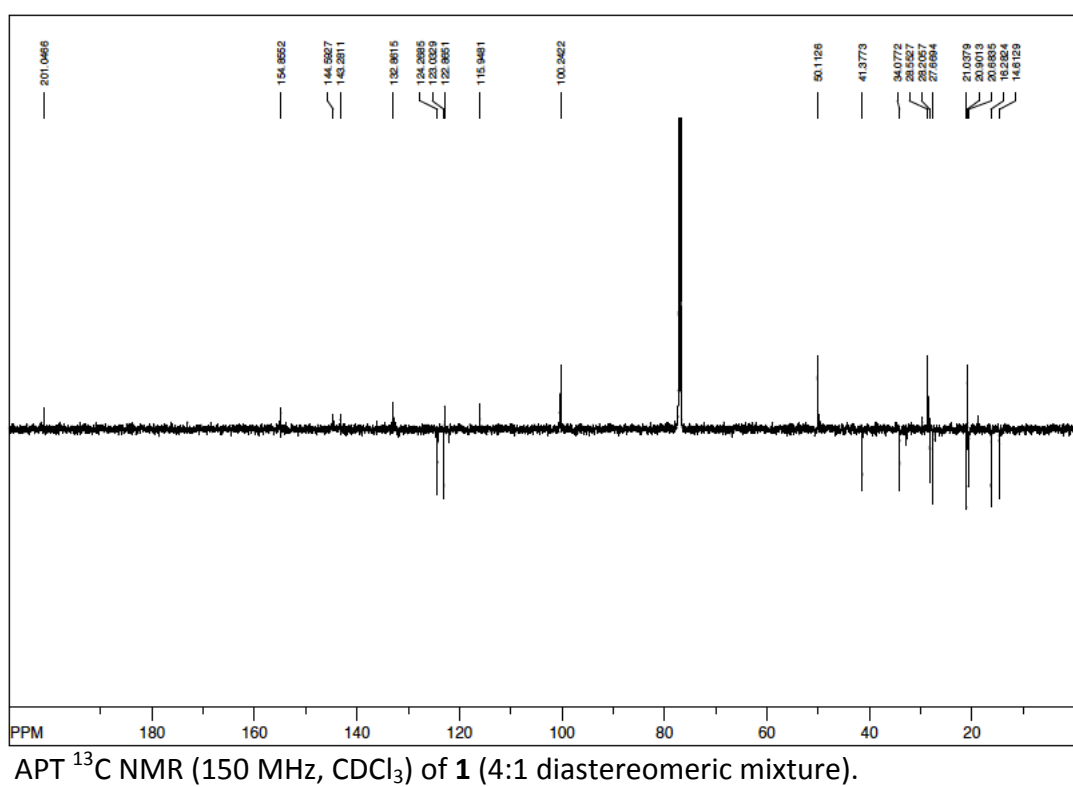
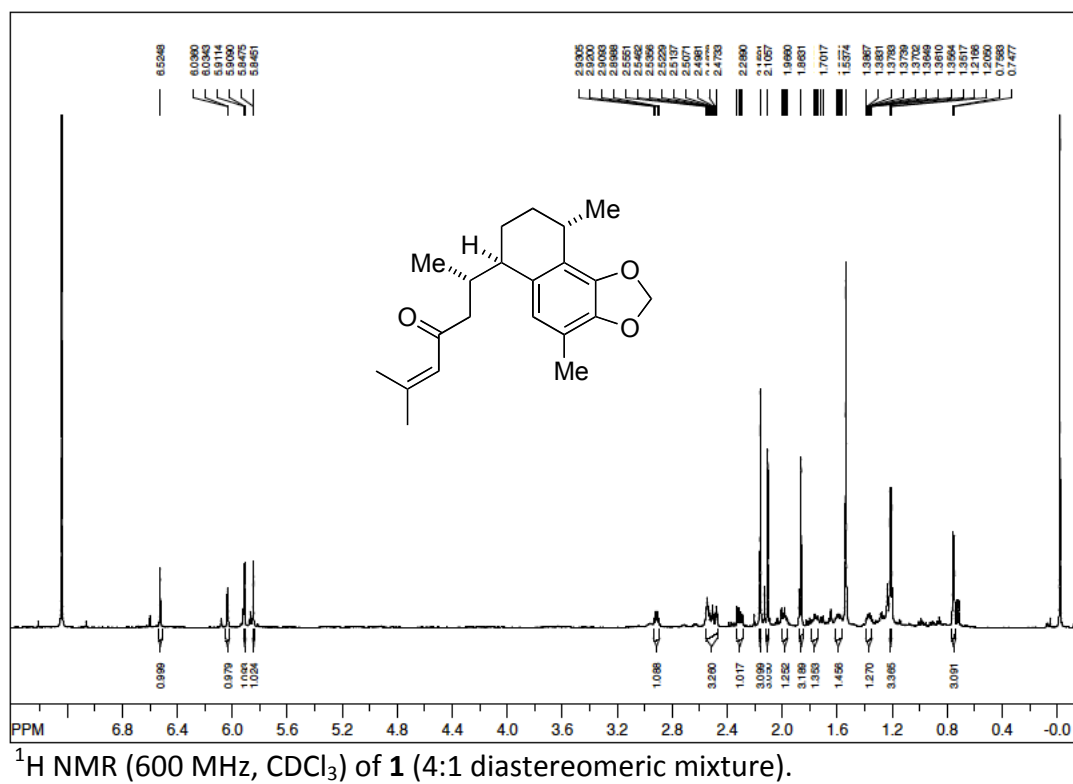
(S)-3-((6R,9S)-4,9-Dimethyl-6,7,8,9-tetrahydronaphtho[1,2-d][1,3]dioxol-6-yl)butanal (**20**)



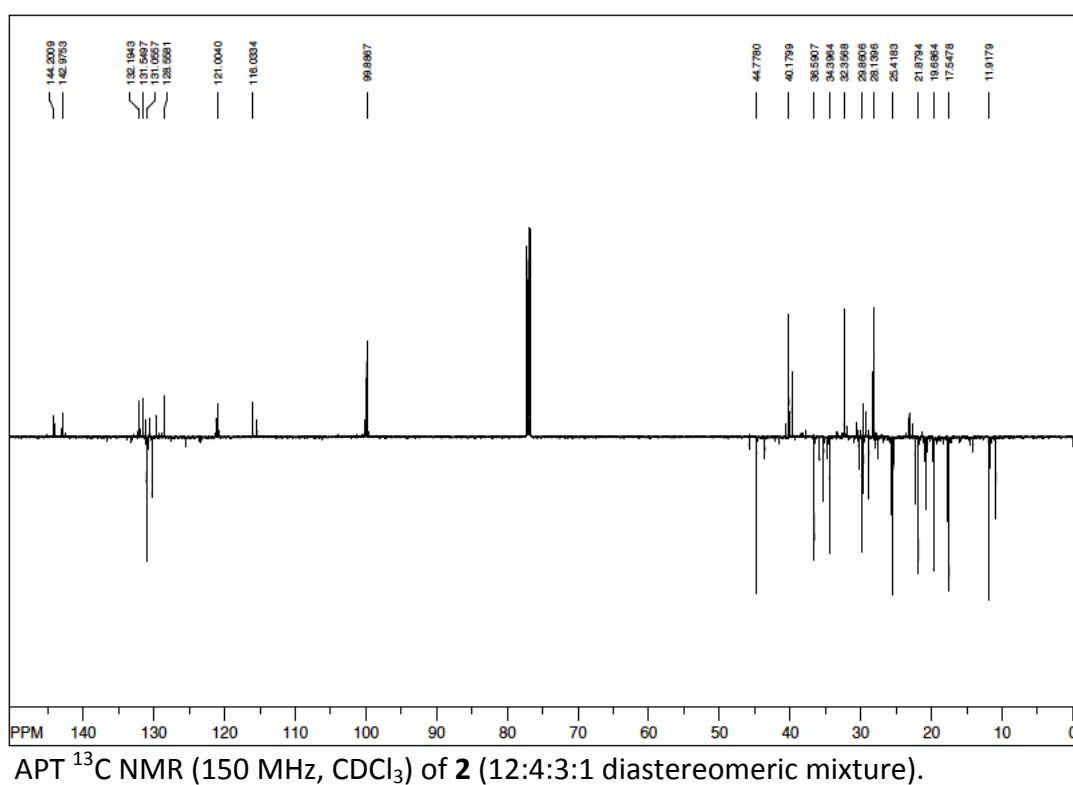
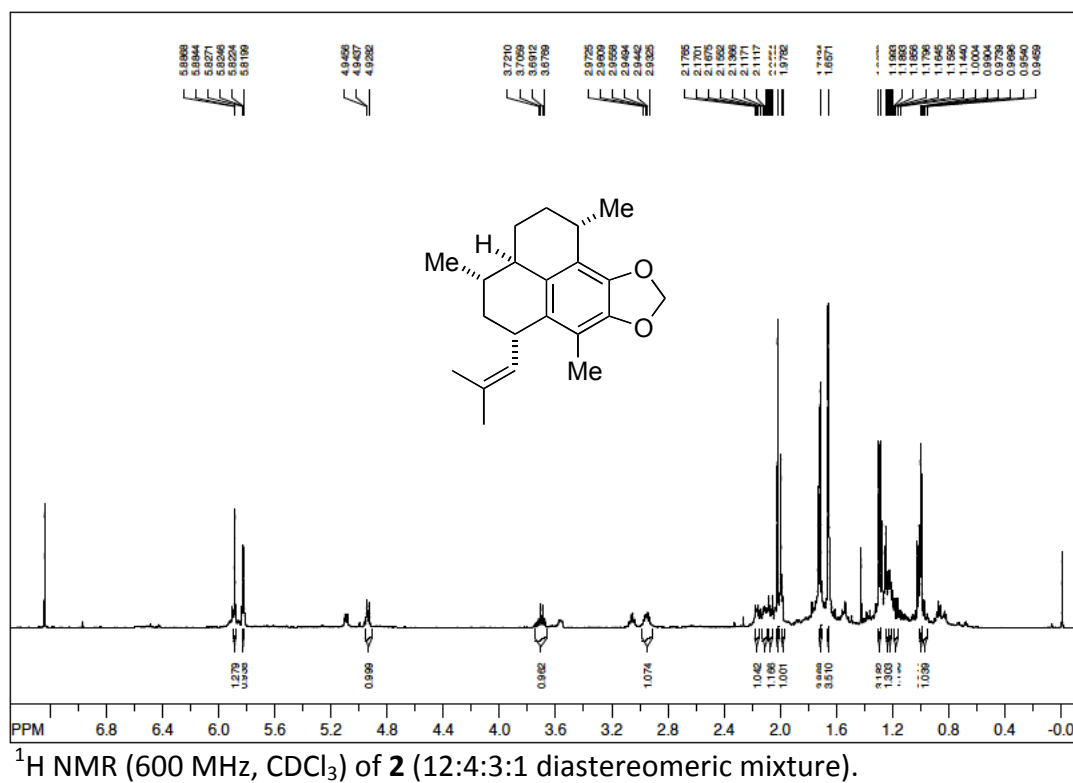
(S)-6-((6R,9S)-4,9-Dimethyl-6,7,8,9-tetrahydronaphtho[1,2-d][1,3]dioxol-6-yl)-2-methyl-hept-2-en-4-ol (**3**)



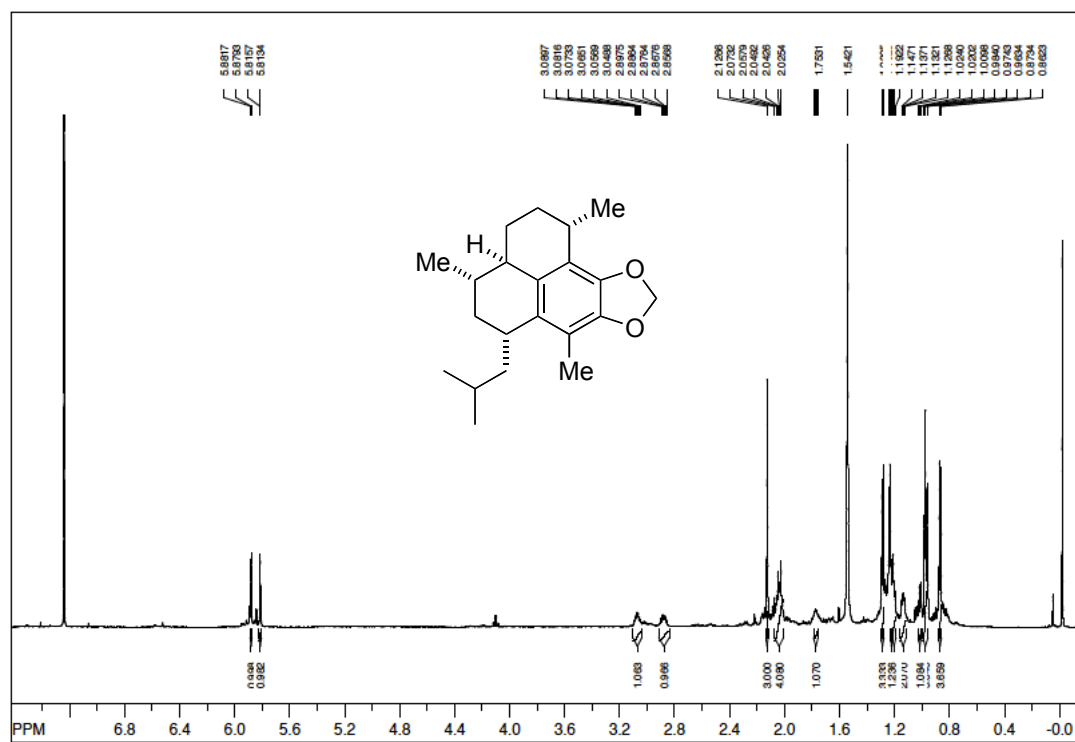
# Heliopirin C (**1**)



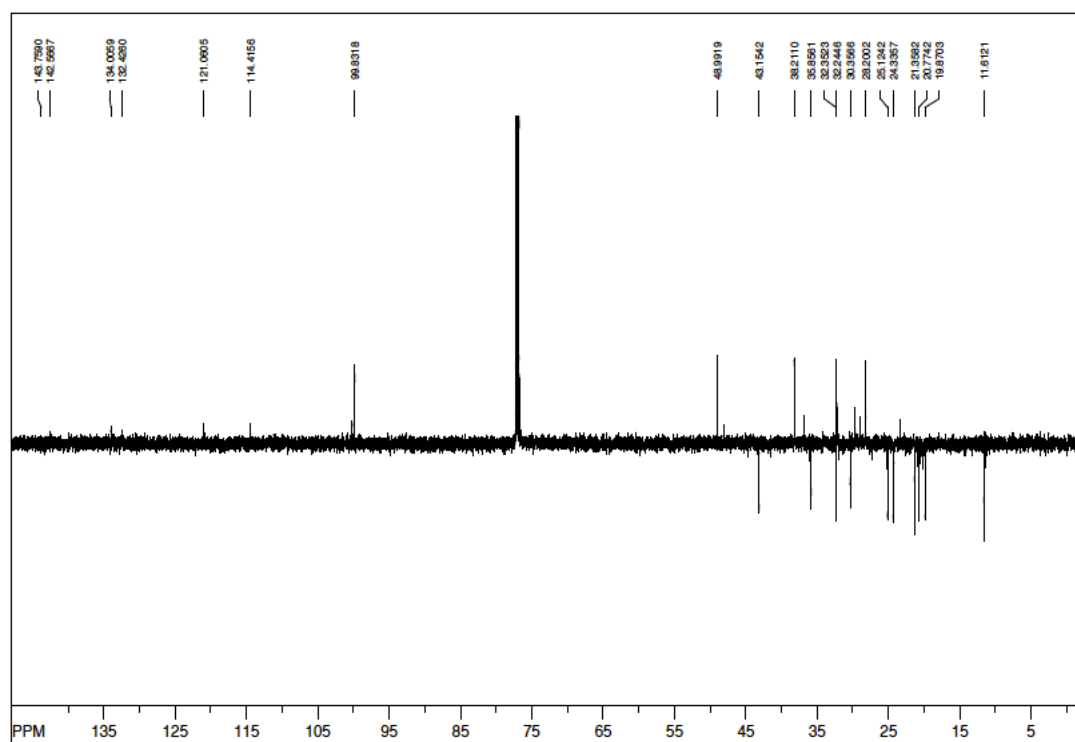
# Helioparin E (**2**)



Dihydro-helioporin E (**21**)



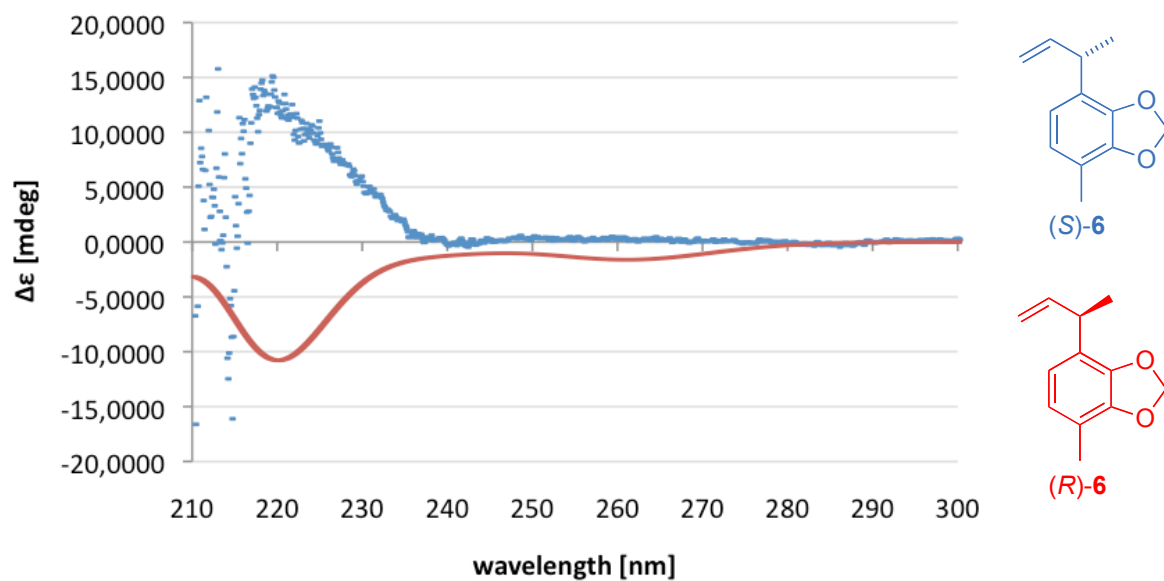
<sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) of **21** (4:1 diastereomeric mixture).



APT <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) of **21** (4:1 diastereomeric mixture).

#### 4 CD SPECTRUM OF COMPOUND 6

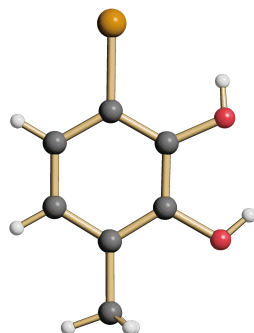
Comparison of experimental spectrum (blue) of the synthesized product (S)-**6** measured in MeOH with the spectrum (red) calculated for the enantiomer (R)-**6**.





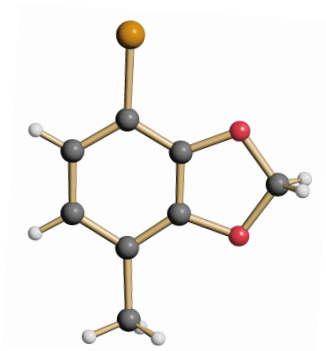
## 5 X-RAY CRYSTAL DATA

X-ray crystal data of compound **9**



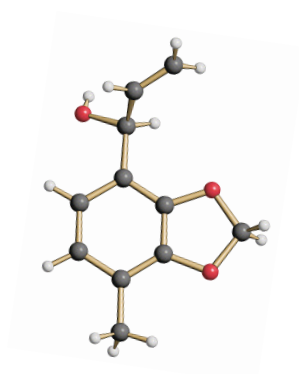
Identification code	wilo487
Empirical formula	C7 H7 Br O2
Moiety formula	C7 H7 Br O2
Formula weight	203.04
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, P21cn
Unit cell dimensions	a = 3.96750(10) Å      alpha = 90 deg. b = 9.4906(3) Å      beta = 90 deg. c = 19.1045(5) Å      gamma = 90 deg.
Volume	719.36(3) Å <sup>3</sup>
Z, Calculated density	4, 1.875 Mg/m <sup>3</sup>
Absorption coefficient	5.644 mm <sup>-1</sup>
F(000)	400
Crystal size	.2 x .04 x .02 mm
Theta range for data collection	2.13 to 27.00 deg.
Limiting indices	-5 ≤ h ≤ 5, -12 ≤ k ≤ 12, -24 ≤ l ≤ 24
Reflections collected / unique	5869 / 1555 [R(int) = 0.0232]
Reflection observed [I > 2σ(I)]	1452
Completeness to theta = 27.00	100.0 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F <sup>2</sup>
Data / restraints / parameters	1555 / 1 / 92
Goodness-of-fit on F <sup>2</sup>	1.097
Final R indices [I > 2σ(I)]	R1 = 0.0195, wR2 = 0.0528
R indices (all data)	R1 = 0.0222, wR2 = 0.0536
Absolute structure parameter	0.014(13)
Largest diff. peak and hole	0.377 and -0.256 e.Å <sup>-3</sup>

# X-ray crystal data of compound **10**



Identification code	wilo491-vor
Empirical formula	C <sub>8</sub> H <sub>7</sub> Br O <sub>2</sub>
Moiety formula	C <sub>8</sub> H <sub>7</sub> Br O <sub>2</sub>
Formula weight	215.05
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, P2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub>
Unit cell dimensions	a = 4.1168(3) Å      alpha = 90 deg. b = 13.513(2) Å      beta = 90 deg. c = 13.837(2) Å      gamma = 90 deg.
Volume	769.76(17) Å <sup>3</sup>
Z, Calculated density	4, 1.856 Mg/m <sup>3</sup>
Absorption coefficient	5.280 mm <sup>-1</sup>
F(000)	424
Crystal size	.3 x .03 x .03 mm
Theta range for data collection	2.11 to 26.98 deg.
Limiting indices	-5 ≤ h ≤ 3, -17 ≤ k ≤ 9, -13 ≤ l ≤ 17
Reflections collected / unique	2986 / 1604 [R(int) = 0.0347]
Reflection observed [I > 2σ(I)]	1371
Completeness to theta = 26.98	99.3 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F <sup>2</sup>
Data / restraints / parameters	1604 / 0 / 101
Goodness-of-fit on F <sup>2</sup>	1.037
Final R indices [I > 2σ(I)]	R <sub>1</sub> = 0.0438, wR <sub>2</sub> = 0.1077
R indices (all data)	R <sub>1</sub> = 0.0571, wR <sub>2</sub> = 0.1124
Absolute structure parameter	0.08(2)
Largest diff. peak and hole	1.040 and -0.647 e.Å <sup>-3</sup>

# X-ray crystal data of compound *rac*-**11**



Identification code	wilo532
Empirical formula	C <sub>11</sub> H <sub>12</sub> O <sub>3</sub>
Moiety formula	C <sub>11</sub> H <sub>12</sub> O <sub>3</sub>
Formula weight	192.21
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2 <sub>1</sub> /c
Unit cell dimensions	a = 11.0992(12) Å      alpha = 90 deg. b = 4.7398(2) Å      beta = 110.813(5) deg. c = 19.2922(18) Å      gamma = 90 deg.
Volume	948.69(14) Å <sup>3</sup>
Z, Calculated density	4, 1.346 Mg/m <sup>3</sup>
Absorption coefficient	0.098 mm <sup>-1</sup>
F(000)	408
Crystal size	.8 x .1 x .05 mm
Theta range for data collection	1.96 to 26.99 deg.
Limiting indices	-11 ≤ h ≤ 14, -5 ≤ k ≤ 4, -24 ≤ l ≤ 16
Reflections collected / unique	4316 / 1987 [R(int) = 0.0797]
Reflection observed [I > 2σ(I)]	1327
Completeness to theta = 26.99	96.2 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F <sup>2</sup>
Data / restraints / parameters	1987 / 0 / 136
Goodness-of-fit on F <sup>2</sup>	1.011
Final R indices [I > 2σ(I)]	R <sub>1</sub> = 0.0382, wR <sub>2</sub> = 0.0969
R indices (all data)	R <sub>1</sub> = 0.1044, wR <sub>2</sub> = 0.1048
Largest diff. peak and hole	0.233 and -0.199 e.Å <sup>-3</sup>