

Supporting Information

Desymmetrization of a *meso* allylic acetal by enantioselective conjugate elimination

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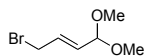
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Materials and Methods

Tetrahydrofuran (THF), toluene and diethylether (ether) were dried from sodium/benzophenone. All reagents were of reagent grade and were used as such or distilled prior to use. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck 5735 Kieselgel silica gel coated aluminium plates (60 F254) using UV light as visualizing agent and 7 % ethanolic phosphomolybdic acid, aqueous KMnO_4 or ninhydrin solution and heat as developing agents. E. Merck silica gel (60, particle size 0.040 - 0.063 mm) was used for flash chromatography. ^1H and ^{13}C NMR spectra were recorded at room temperature at 300 MHz and 75 MHz respectively and calibrated using residual undeuterated solvent as an internal reference. The solvent was deuteriochloroform, unless otherwise noted. Chemical shifts (δ) are given in parts per million (ppm) and the coupling constants (J) in hertz (Hz). The following abbreviations were used to designate the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, qt = quintet, hp = heptuplet, m = multiplet, br = broad. IR spectra were recorded by transmission on a IRTF spectrometer. Optical rotations were recorded at 20 °C on a polarimeter using the sodium D line (589 nm) and $[\alpha]_D$ are given in units of $10^{-1} \text{ deg cm}^{-2} \text{ g}^{-1}$. The mass spectra were obtained under electron impact conditions (EI) at 70 eV ionizing potential; *i*-butane (^iBuH) was used for chemical ionization (CI). Melting points (m.p.) are uncorrected and were measured using a microscope apparatus. Elemental analyses were performed with an analyser. The reference given at the end of each protocol sends back to the previous description of the same compound.

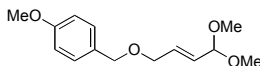
Synthesis and data of compounds 9, 10, 7 and 12

4-Bromobut-2-enal dimethyl acetal 9



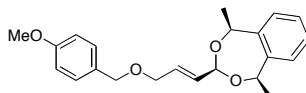
Under argon atmosphere, 1-acetoxy-1,3-butadiene **8** (1.10 g, 10.0 mmol) was dissolved in a mixture of dry THF (5 mL), methanol (5 mL) and 2,2-dimethoxypropane (10 mL). N-Bromosuccinimide (1.90 g, 10.5 mmol) was added at room temperature. The reaction mixture was stirred for 1 hour, and quenched by a solution of saturated aqueous NaHCO₃ (20 mL). The aqueous phase was extracted with diethylether (3 x 20 mL), and dried with MgSO₄. After evaporation, a dark orange oil was obtained (yield: 99%). This compound was used for the next step without further purification. R_f: 0.62 (cyclohexane/AcOEt 75:25); ¹H NMR (300 MHz) δ 3.32 (6H, s), 3.90 (2H, d, *J* = 7.5), 4.74 (1H, d, *J* = 4.5), 5.65 (1H, dd, *J* = 4.5 and 15.5), 5.96 (1H, dt *J* = 7.5 and 15.5). The NMR spectrum is identical to the one described in the literature.¹

4-(4-Methoxybenzyloxy)but-2-enal dimethyl acetal 10²



To a dispersion of KH (1.1 g, 27.5 mmol) in THF (40 mL) was slowly added a solution of *p*-methoxybenzyl alcohol (1.4 g, 10.0 mmol) in THF (20 mL). After the dihydrogen bubbling was ended, the reaction mixture was cooled to 0 °C and a solution of compound **9** (1.9 g, 10.0 mmol) in THF (20 mL) was added. After stirring at room temperature overnight, the reaction was quenched with water (15 mL) carefully. The aqueous phase was extracted with ethyl acetate (3 x 30 mL) and the resulting organic phase was dried with MgSO₄ and concentrated under vacuum. The crude product was purified by flash column chromatography on silica gel (eluent: cyclohexane/ethyl acetate 10:1) affording 1.9 g (yield: 76%) of the pure product **10** as a light yellow oil. R_f: 0.56 (cyclohexane/AcOEt 75:25); ¹H NMR (300 MHz) δ 3.25 (6H, s), 3.76 (3H, s), 3.96 (2H, d, *J* = 5.3), 4.38 (2H, s), 4.74 (1H, d, *J* = 4.8), 5.67 (1H, dd, *J* = 4.8 and 15.5), 5.88 (1H, dt, *J* = 5.3 and 15.5), 6.80 (2H, d, *J* = 8.6), 7.20 (2H, d, *J* = 8.6); ¹³C NMR (75 MHz) δ 52.9, 55.5, 69.5, 72.1, 102.7, 113.9, 128.9, 129.6, 129.8, 130.4, 131.6. IR (film) ν 2996, 2835, 1613, 1514, 1464, 1249, 1120, 1050 cm⁻¹; MS *m/z* (%) 137 (38), 121 (100). Anal. Calcd. for C₁₄H₂₀O₄: C 66.60, H 7.99. Found: C 66.64, H 7.90.

syn 3-[3-(4-Methoxybenzyloxy)propenyl]-1,5-dimethyl-benzo[*e*]-[1,3]dioxepane 7.

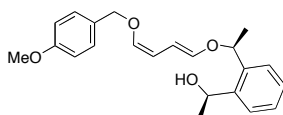


A catalytic amount of camphorsulfonic acid (CSA) was added, under argon atmosphere, to a solution of compound **10** (252 mg, 1.0 mmol) and *meso* 1,2-bis(1-hydroxyethyl)benzene **11** (250 mg, 1.5 mmol) in dichloromethane (5 mL). The reaction mixture was stirred at room temperature for 4 hours and quenched with a saturated solution of sodium bicarbonate (5 mL). The aqueous phase was extracted with dichloromethane (3 x 7 mL) and the resulting organic layers were dried with MgSO₄. After evaporation under reduced pressure, the residue was purified by flash column chromatography on silica gel (eluent: cyclohexane/ethyl acetate 8:1) affording 284 mg (yield: 82%) of the pure product **7** as a colorless oil. R_f: 0.33 (cyclohexane/AcOEt 75:25); ¹H NMR (300 MHz) δ 1.66 (6H, d, *J* = 6.4), 3.76 (3H, s), 3.97 (2H, d, *J* = 5.3), 4.40 (2H, s), 5.12 (2H, q, *J* = 6.4), 5.58 (1H, d, *J* = 4.2), 5.76 (1H, ddt, *J* = 1.3, 4.2 and 15.8), 5.96 (1H, dt, *J* = 5.3 and 15.8), 6.79 (2H, d, *J* = 8.6), 7.19-7.35 (6H, m); ¹³C NMR (75 MHz) δ 18.9, 20.6, 54.7, 56.6, 72.4, 74.5, 107.2, 109.7, 113.0, 115.2, 124.4, 126.4, 126.9, 128.0, 128.7, 129.2, 129.6, 130.7, 142.5, 160.2; MS *m/z* (%) 354 [M⁺] (1), 147 (17), 133 (67), 121 (100). HRMS (ESI): calcd. for C₂₂H₂₆NaO₄ *m/z* 377.1729. Found: 377.1732.

(1) Gaonac'h, O.; Maddaluno, J.; Chauvin, J.; Duhamel, L. *J. Org. Chem.* **1991**, *56*, 4045-4048.

(2) Bataille, C.; Bégin, G.; Guillam, A.; Lemiègre, L.; Lys, C.; Maddaluno, J.; Toupet, L. *J. Org. Chem.* **2002**, *67*, 8054-8062.

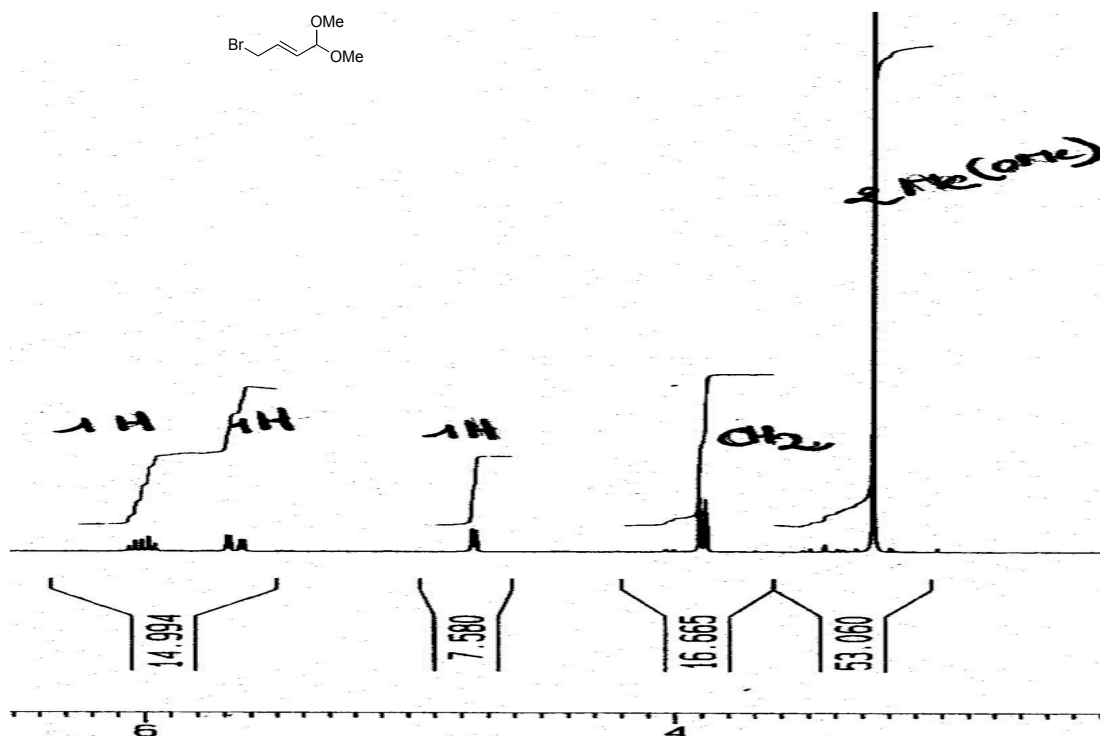
Typical procedure for the enantioselective δ -elimination: from **7** to **12**



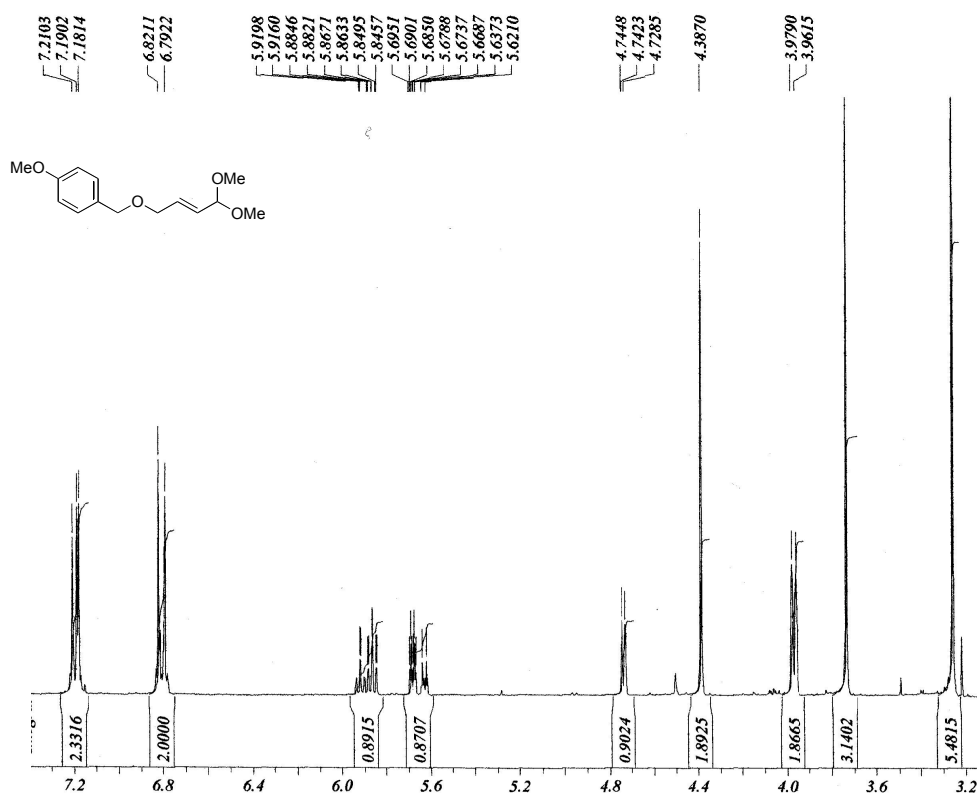
*s*BuLi (1.3 mol.L⁻¹ in cyclohexane, 40 μ L, 0.052 mmol) was added dropwise at -78 °C and under argon atmosphere, to a solution of (-)-sparteine (12 mg, 0.051 mmol) in Et₂O (2 mL). After 10 minutes, a solution of compound **7** (9.0 mg, 0.025 mmol) in Et₂O (1 mL) was introduced and the resulting mixture was stirred for 3 hours at -78 °C. The reaction was quenched with a saturated aqueous NaHCO₃ solution (2 mL) and the aqueous layer was extracted with diethylether (3 x 3 mL). The resulting organic phase was dried with MgSO₄, and evaporated under reduced pressure. The residue was purified by preparative thin layer chromatography (eluent: cyclohexane/AcOEt 3:1) affording 7.1 mg (yield: 72%, *ee* 64%) of the desired product **12** as a colorless oil. R_f: 0.67 (cyclohexane/AcOEt 50:50); ¹H NMR (300 MHz) δ 1.43 (3H, d, *J* = 6.4), 1.50 (3H, d, *J* = 6.4), 1.60-1.75 (1H, br s), 3.76 (3H, s), 4.70 (2H, s), 4.88 (1H, dd, *J* = 6.0 and 11.5), 5.22-5.29 (2H, m), 5.83 (1H, d, *J* = 6.0), 5.88 (1H, dd, *J* = 11.5 and 12.0), 6.33 (1H, d, *J* = 12.0), 6.87 (2H, d, *J* = 8.4), 7.10-7.30 (6H, m). HPLC analyses: Chiralpak OD* (25 cm x 4.6 mm); eluent: heptane/*isopropanol* 90:10 (v/v); flow rate: 1.0 mL/min; temperature: 25 °C; monitored at UV at 230 nm. (+)-Enantiomer: retention time: 21.0 min. [α]_D = +0.062 (*c* 0.72, CHCl₃). HRMS: calcd for C₂₂H₂₆NaO₄ *m/z* 377.1729. Found: 377.1728. (-)-Enantiomer: retention time: 8.9 min. [α]_D = -0.030 (*c* 0.46, CHCl₃). HRMS (ESI): calcd for C₂₂H₂₆NaO₄ *m/z* 377.1729. Found: 377.1736.

¹H and ¹³C NMR spectra of compounds **9**, **10**, **7** and **12**

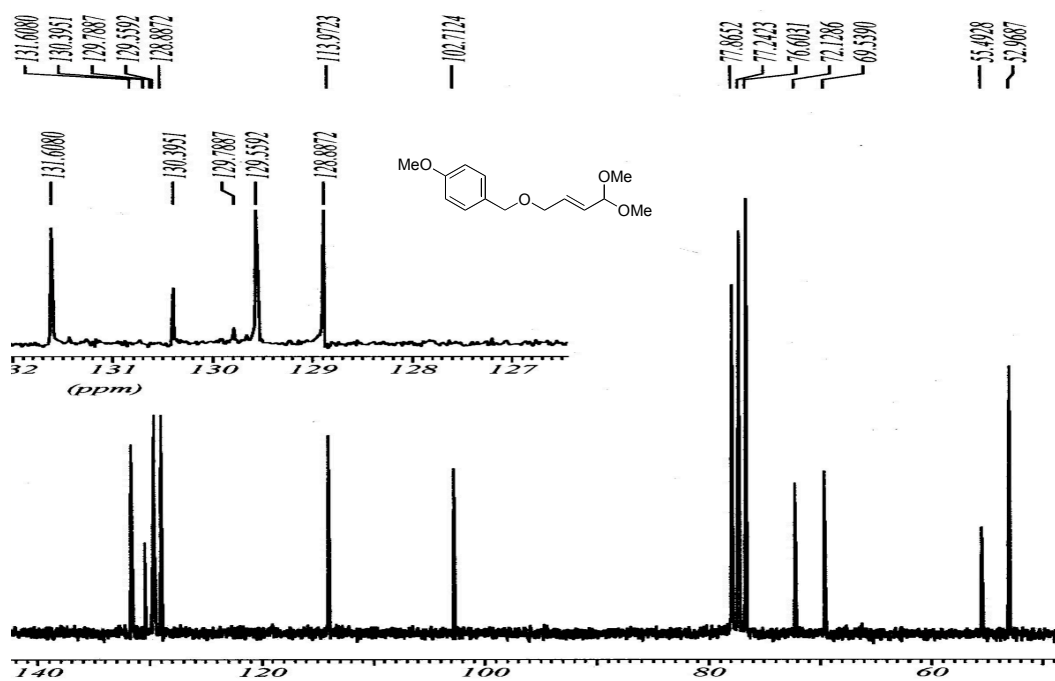
¹H NMR (CDCl₃, 300 MHz) of **9**



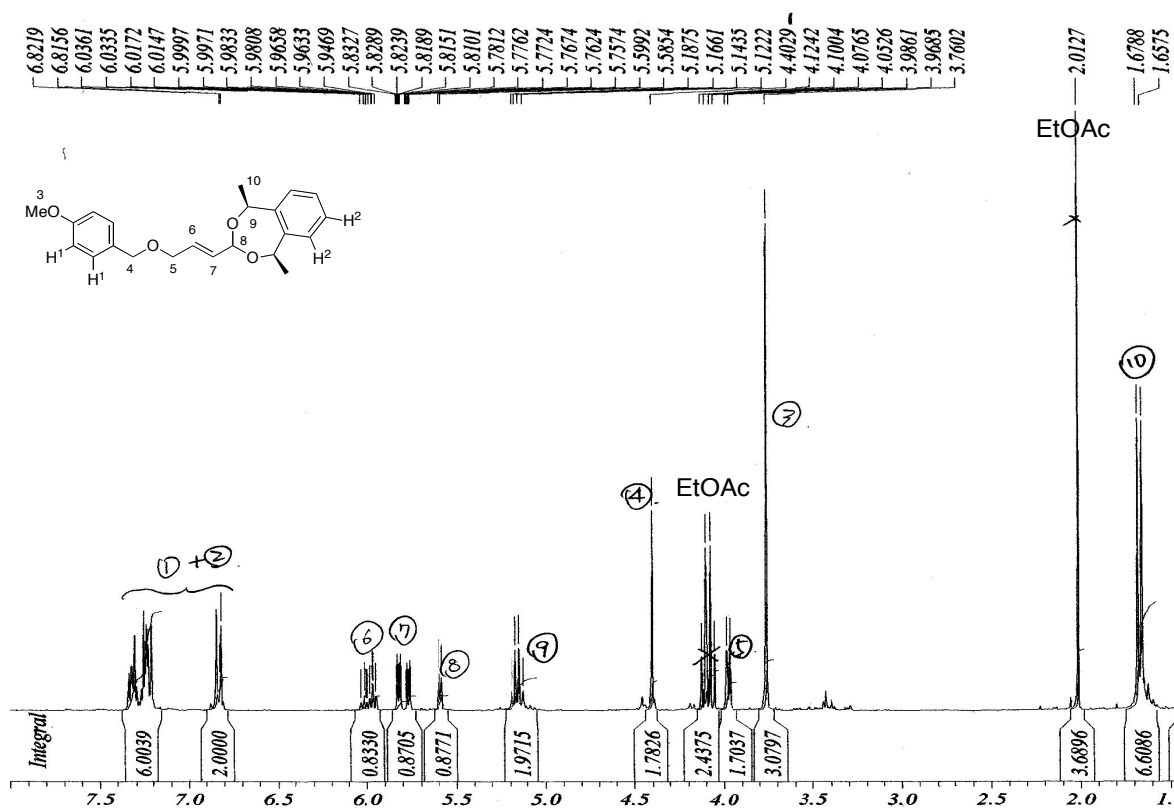
¹H NMR (CDCl₃, 300 MHz) of **10**



¹³C NMR (CDCl₃, 75 MHz) of **10**



¹H NMR (CDCl₃, 300 MHz) of 7



¹H NMR (CDCl₃, 300 MHz) of 12

