Supporting information

Olefin Cross-metathesis as a Tool in Natural Products Degradation. The Stereochemistry of (+)-Falcarindiol.

Anokha S. Ratnayake and Thomas Hemscheidt*

Department of Chemistry, University of Hawaii, 2545 McCarthy Mall, Honolulu, HI 96822, USA

(±)-5-Trimethylsilylpent-1-en-4-yne-3-ol **3**.
To a solution of (trimethylsilyl)acetylene (1.04 g, 1.5 mL, 10.6 mmol) in dry THF (42 mL) at –78 °C was added dropwise a solution of n-butyllithium (2.4 M in hexanes, 4.42 mL, 10.6 mmol) under a N_2 atmosphere. After the addition was complete, the solution was allowed to warm to –60 °C over a period of 15-30 min, at which point an ice-cold solution of acrolein (0.71 g, 0.85 mL, 12.7 mmol) in THF (25 mL) was introduced slowly *via* a cannula. The resulting mixture was allowed to gradually warm to 0 °C over a period of 1.5 h. After stirring for an additional 1 h at room temperature, the mixture was quenched with cold satd. NH_4Cl. The aqueous phase was extracted with Et_2O (×3), dried ($MgSO_4$) and concentrated to dryness in *vacuo*. The resulting crude oil was purified by Kugelrohr distillation (bp 85-90 °C/20 mmHg) to give 1.63 g (95% yield) of pure racemic allyl alcohol (±)-**3** as a colorless liquid. FTIR (film) 3355 (br), 2175, 1640, 1405, 1250, 1115, 1030, 985, 845, 760 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.94 (ddd, J= 17.1, 10.2, 5.4 Hz, 1H), 5.44 (dd, J= 17.1, 0.9 Hz, 1H), 5.19 (dd, J= 10.2, 0.9 Hz, 1H), 4.85 (*br*d, J= 5.4 Hz, 1H), 2.60 (*br*s, 1H), 0.16 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.9, 116.7, 104.3, 91.2, 63.6, -0.03 (3C).

(+)-5-Trimethylsilylpent-1-en-4-yne-3-ol (*S*)-**3**
To a well-stirred suspension of lipase (*Pseudomonas fluorescens*, 0.03 g, 0.15 mass equiv), ground, activated 4-Å molecular sieves (0.22 g, 1.0 mass equiv) and racemic allyl alcohol (±)-**3** (0.22 g, 1.45 mmol) in dry hexane (12 mL) was added vinyl acetate (0.53 mL, 5.8 mmol) in one portion. The suspension was allowed to stir under N_2, at room temperature for 21 h, and the course of the reaction was monitored by ^1H NMR analysis. At the end of this period, the mixture was filtered through a pad of Celite, and evaporated to dryness under reduced pressure. The crude product mixture following flash chromatography gave (*R*)-acetate (eluent: 3% Et_2O/hexane) 0.20 g (35% yield, ee > 98%) and alcohol (*S*)-**3** ((eluent: 10% Et_2O/hexane) 0.16 g (35% yield, ee > 98%) as colorless oils: (*S*)-**3** ≥95 % ee; $(\alpha)_D^{23}$ 38 (c 2.0, $CHCl_3$); for spectroscopic data see (±)-**3**.

(+)-5-bromopent-1-en-4-yne-3-ol (*S*)-**4**.
A solution of alcohol (*S*)-**3** (0.05 g, 0.32 mmol) in acetone (2 mL) was treated with N-bromosuccinimide (0.07 g, 0.39 mmol) and catalytic powdered $AgNO_3$ (0.004 g, 0.02 mmol). The reaction mixture was wrapped with aluminum foil to exclude light and stirred at room temperature for 3 h. The mixture was diluted with cold water and extracted with Et_2O (×3). The combined organic layers were dried ($MgSO_4$), concentrated to dryness *in vacuo* and subjected to flash column chromatography (silica gel, 10% Et_2O-hexane) to afford 0.03 g (55% yield) of bromo acetylene (*S*)-**4** as a clear liquid: $(\alpha)_D^{25}$ 38 (c 1.9, $CHCl_3$); FTIR (film) 3380 (br), 2215, 1640, 1405, 1265, 1120, 1015, 985, 935, 885, 800, 725 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.95 (ddd, J= 17.1, 9.9, 5.4 Hz, 1H), 5.46 (ddd, J= 17.1, 0.9, 0.9 Hz, 1H), 5.25 (ddd, J= 9.9, 0.9, 0.9 Hz, 1H), 4.90 (ddd, J= 6.3, 5.4, 0.9 Hz, 1H), 2.15 (d, J= 6.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.4, 117.2, 79.0, 64.2, 47.2.

(*S,S*)-1,9-decadiene-4,6-diyne-3,8-diol **2**.
To an ice-cold solution of 70% aqueous $EtNH_2$ (0.060 mL) and catalytic CuCl (0.002 g, 0.02 mmol) in MeOH (0.074 mL, degassed with Ar) was added $NH_2OH.HCl$ (0.007 g, 0.11 mmol)

dissolved in water (0.026 mL). To the above mixture at 0 °C was added a solution of bromo acetylene (*S*)-**4** (0.052 g, 0.32 mmol) in MeOH (0.65 mL). After the addition was complete, the reaction mixture was removed from the ice-bath and stirred at room temperature overnight. The solution was diluted with cold water and extracted with Et_2O. The organic layers were dried ($MgSO_4$), concentrated under reduced pressure and the resulting crude residue was purified on silica gel (20%-30% EtOAc-hexane) to yield 0.011 g (40% yield) of symmetrical dimer (*S*,*S*)-**2** as a white crystalline solid: $[\alpha]_D^{24}$ 102 (c 0.38, $CHCl_3$); mp 77-78 °C; FTIR (film) 3320 (br), 2355, 2145, 1635, 1405, 1260, 1115, 1015, 985, 935, 865 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.95 (ddd, J= 17.1, 10.2, 5.4 Hz, 2H), 5.48 (ddd, J= 17.1, 0.9, 0.9 Hz, 2H), 5.27 (ddd, J= 10.2, 0.9, 0.9 Hz, 2H), 4.95 (*br*m, 2H), 2.03 (d, J= 4.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.9 (2C), 117.7 (2C), 78.6 (2C), 70.3 (2C), 63.7 (2C).

Degradation of (+)-**1** to **2**.

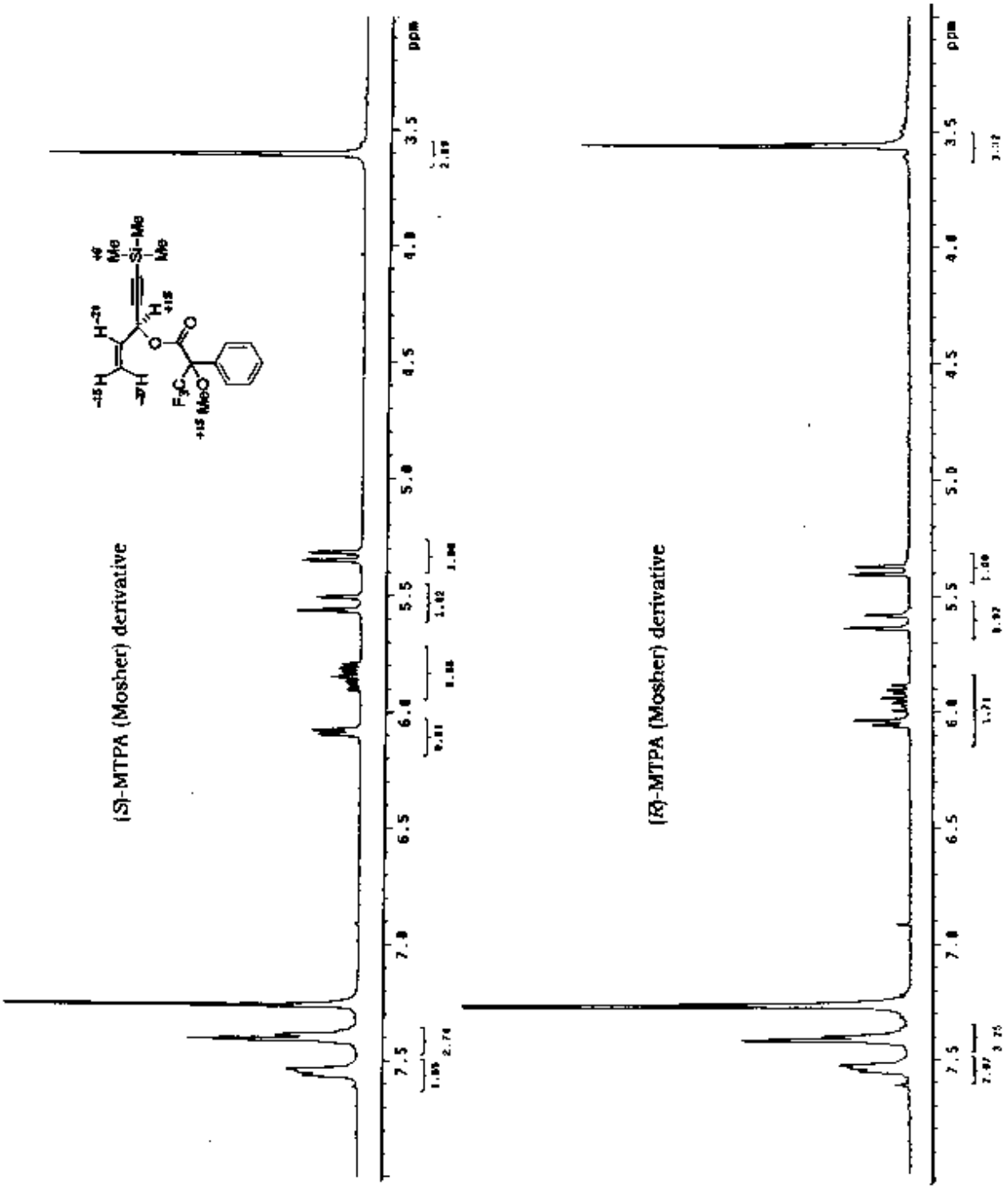
A solution of second-generation Grubbs' catalyst (0.011 g, 0.013 mmol, 10 mol%) in degassed anhydrous CH_2Cl_2 (45.5 mL) at room temperature was stirred vigorously under an atmosphere of ethylene gas. After bubbling a steady stream of ethylene gas for 15 min, a solution of (+)-**1** (0.035 g, 0.13 mmol) in degassed CH_2Cl_2 (70 mL) under ethylene gas was added slowly *via* a cannula to the above reaction flask at room temperature. Progress of the reaction was monitored by TLC analysis. After stirring overnight (16 h), the solvent was removed in *vacuo* and the residue was purified by flash column chromatography (silica gel, 20-30% EtOAc-hexane) to afford the symmetrical dimer **2**-(meso) as a slightly brown solid. The crude solid was re-crystallized in Et_2O-hexane to give 0.018 g (81% yield) of pure product as white crystalline material: $[\alpha]_D^{23}$ 5 (c 0.7, $CHCl_3$); mp 49-51 °C; FTIR (film) 3300 (br), 2360, 2145, 1640, 1400, 1325, 1260, 1115, 1015, 985, 930, 865 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.94 (ddd, J= 17.0, 10.1, 5.4 Hz, 2H), 5.48 (d, J= 17.0 Hz, 2H), 5.27 (d, J= 10.1 Hz, 2H), 4.95 (d, J= 5.4 Hz, 2H), 2.36 (*br*s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.6 (2C), 117.5 (2C), 78.3 (2C), 70.1 (2C), 63.4 (2C).

General procedure for the preparation of MTPA-esters:

A 0.01 M solution of alcohol product in anhydrous CH_2Cl_2 at 0 °C was treated successively with 2,6-lutidine (8 mol equiv), MTPA-Cl (4 mol equiv per OH) and DMAP (1 mol equiv per OH) under N_2. The mixture was allowed to stir at room temperature for 15 h and treated with 3(N,N-dimethylamino)propylamine (0.3 mol equiv over acid chloride). After stirring for an additional 10 min, the solvent was removed *in vacuo*. The residue was dissolved in a minimum amount of CH_2Cl_2 and applied to a silica gel column (5% Et_2O-hexane) to afford pure ester in 85-90% yield:

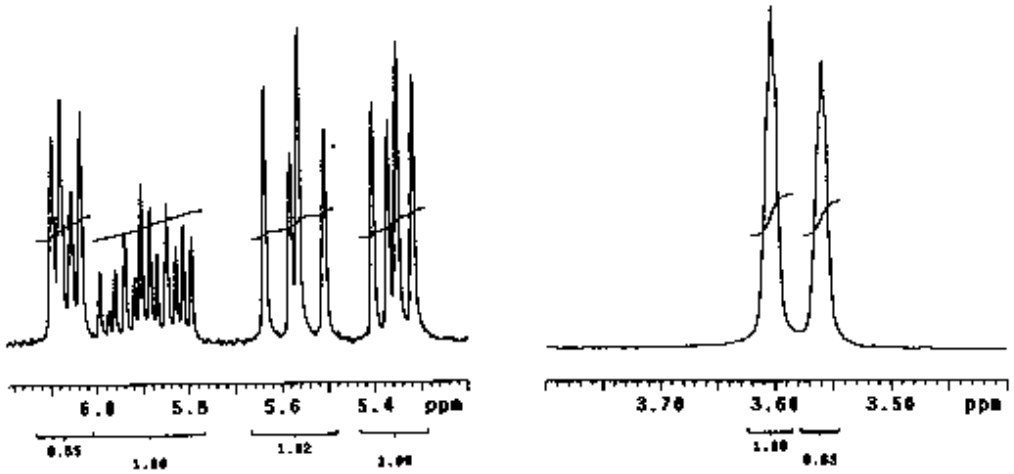
(+)-(3*R*,8*S*)-**1**-(*S*)-MTPA-*bis*-ester: ^1H NMR (500 MHz, $CDCl_3$) 7.52-7.50 (m, 5H), 7.41-7.38 (m, 5H), 6.40 (d, J= 9.0 Hz, 1H), 6.09 (d, J= 5.4 Hz, 1H), 5.92 (m, 1H), 5.73 (*br*m, 1H), 5.60 (d, J= 16.5 Hz, 1H), 5.46 (m, 1H), 5.43 (d, J= 10.5 Hz, 1H), 3.63 (s, 3H), 3.58 (s, 3H), 2.15 (m, 2H), 1.45-1.17 (m, 10H), 0.88 (t, J= 6.9 Hz, 1H). (+)-(3*R*,8*S*)-**1**-(*R*)-MTPA-*bis*-ester: ^1H NMR (500 MHz, $CDCl_3$) δ 7.52-7.49 (m, 5H), 7.41-7.39 (m, 5H), 6.35 (d, J= 8.6 Hz, 1H), 6.11 (d, J= 5.8

Hz, 1H), 5.82 (ddd, J= 16.9, 10.2, 5.8 Hz, 1H), 5.77 (m, 1H), 5.55 (m, 1H), 5.52 (d, J= 16.9 Hz, 1H), 5.37 (d, J= 10.2 Hz, 1H), 3.60 (s, 3H), 3.57 (s, 3H), 2.17 (m, 2H), 1.40-1.24 (m, 10H), 0.87 (t, J= 7.1 Hz, 1H).

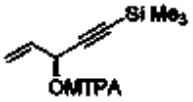


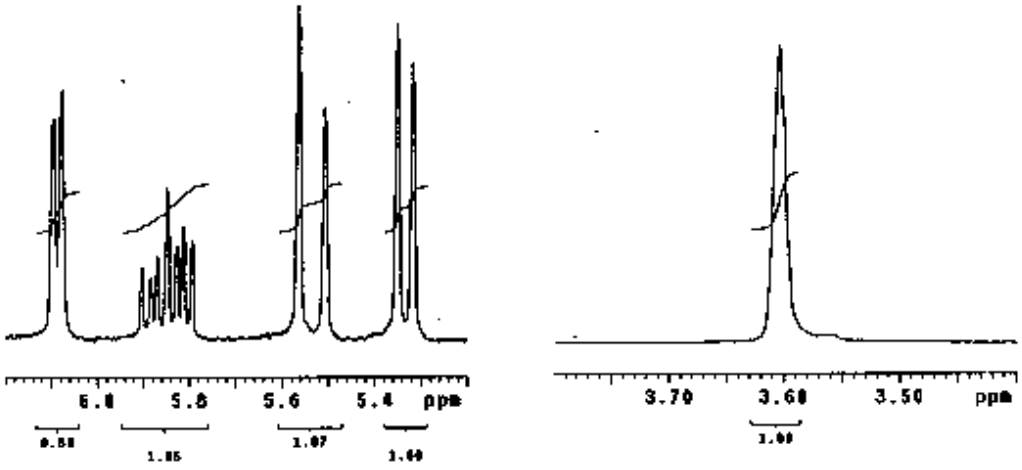
Δδ Values ($\Delta\delta = \delta_S - \delta_R$) measured in Hertz (300 MHz, $CDCl_3$).

(±)-3-(*S*)-MTPA ester



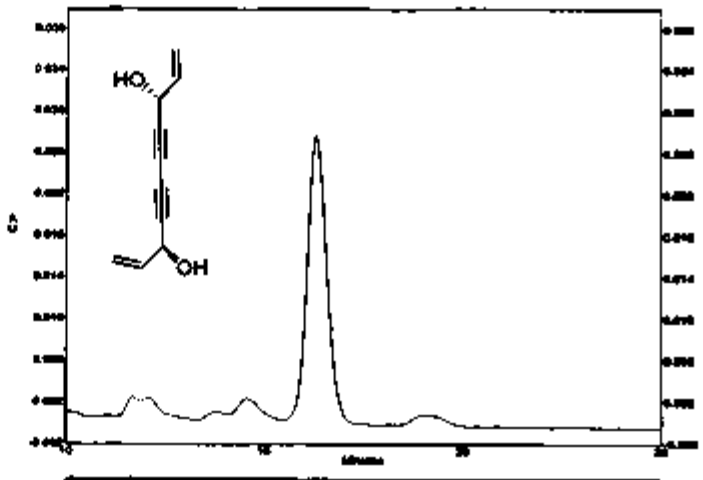
(+)-3-(*S*)-MTPA ester



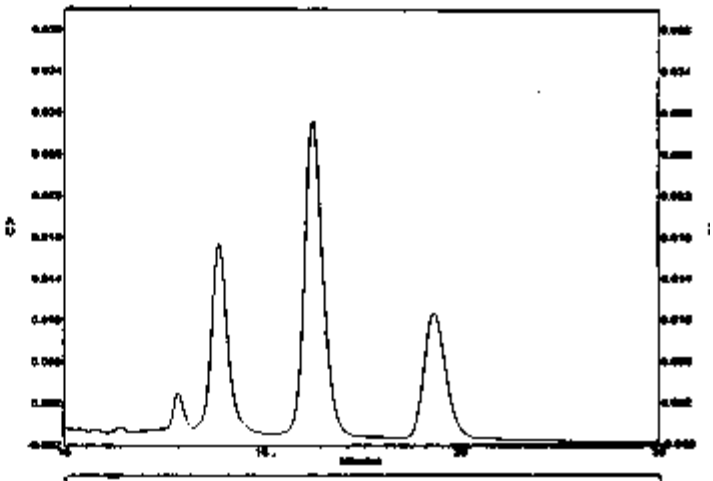


(*S*)-MTPA (Mosher) derivatives of **3** (300 MHz, $CDCl_3$).

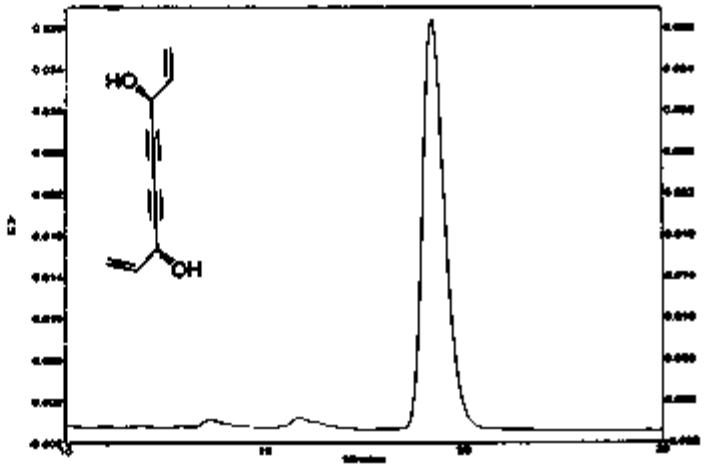
2 (meso)
retention time (min)- 16.28 (R,S)



Synthetic (±)-**2** (racemic)
retention times (min)- 13.90 (R,R)
16.27 (R,S)
19.33 (S,S)



Synthetic (+)-**2** (chiral)
retention time (min)- 19.22 (S,S)



HPLC (chiral) Chiralcel OD (250×4.6 mm), 23 °C, λ=254 nm,
15% iPrOH-hexane, 1 mL/min