Supporting Information

Asymmetric Total Synthesis of (–)-Panacene and Correction of Its Relative Configuration

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General Information: Unless otherwise indicated, reactions were carried out under a nitrogen atmosphere in flamed-dried glassware using freshly distilled solvents. Reactions were monitored by thin layer chromatography (TLC) carried out on silica gel 60 precoated plates (0.25 mm thickness) from Silicycle using UV light as visualizing agent and/or cerium ammonium molybdate (CAM) as a developing agent. Flash column chromatography was performed using silica gel 60 (230-400 mesh) from Silicycle. ¹H and ¹³C NMR spectra were recorded using Varian AS400 spectrometer and are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (CDCl₃: δ 7.27 and 77.0 for ¹H and ¹³C respectively). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, m = multiplet, br = broad. Infrared spectra were recorded on a Bomem FTIR MB-Series. Optical rotations were measured using a 2 mL cell with 1 dm length on a Jasco DIP-360 polarimeter. High resolution mass spectra were recorded at Université de Sherbrooke on a ZAB-1F micromass spectrometer using electronic impact ionisation (70 eV). The crystal structure of compound *ent*-**9A** was determined at the laboratory of X-ray diffraction, Université de Montréal.

2-Ethyl-6-methoxybenzoic acid (7). To a solution of 2-methoxy-6-methylbenzoic acid **6**¹ (1.33 g, 8.00 mmol) in THF (135 mL) at $-78\text{ }^{\circ}\text{C}$ was added dropwise *s*-BuLi (1.28 M in cyclohexane, 16.2 mL, 20.8 mmol). The resulting orange-red solution was stirred at $-78\text{ }^{\circ}\text{C}$ for 2 h and MeI (2.00 mL, 32.1 mmol) was then added. The colorless solution was stirred 1 h at $-78\text{ }^{\circ}\text{C}$, warmed to rt and then stirred an additional 2 h before quenched with water. The aqueous layer was acidified with 10% aq. HCl and then extracted with AcOEt. The combined organic layers were dried over MgSO_4 , and concentrated under reduced pressure. Discoloration of the residue with activated carbon followed by flash column chromatography (silica gel, hexanes/AcOEt, 60/40) afforded **7** (1.35 g, 94%) as a white solid; mp $152\text{--}153\text{ }^{\circ}\text{C}$ (lit.² $149\text{ }^{\circ}\text{C}$). IR (KBr, cm^{-1}): 3100, 3013, 2983, 1694, 1584, 1267. ^1H NMR (400 MHz, CDCl_3): δ = 1.28 (t, J = 7.6 Hz, 3H), 2.78 (q, J = 7.6 Hz, 2H), 3.90 (s, 3H), 6.83 (d, J = 8.3 Hz, 1H), 6.91 (d, J = 7.6 Hz, 1H), 7.34 (t, J = 8.0 Hz, 1H), 11.79 (br s, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ = 15.5, 26.7, 56.0, 108.6, 121.2, 121.8, 131.0, 143.5, 156.4, 173.6. The ^1H NMR data of **7** are in full agreement with those reported in the literature.³

2-Ethyl-6-methoxybenzyl alcohol (7A). A solution of acid **7** (5.80 g, 32.2 mmol) in THF (100 mL) was added dropwise to a mixture of LiAlH_4 (1.83 g, 48.3 mmol) in THF (20 mL) at $0\text{ }^{\circ}\text{C}$. After hydrogen evolution ended the reaction mixture was heated under reflux for 15 h and then cooled to $0\text{ }^{\circ}\text{C}$ before quenched with the successive addition of 1.83 mL H_2O , 1.83 mL 15% aq. NaOH and 3.66 mL H_2O . The mixture was warmed to rt and stirred for an additional 1 h before filtered. The organic phase was dried over MgSO_4 and then concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, CH_2Cl_2) to afford the alcohol **7A** (4.93 g, 92%) as a white solid; mp $43\text{--}44\text{ }^{\circ}\text{C}$. IR (KBr, cm^{-1}): 3303, 2976, 2929,

1587, 1261. ^1H NMR (400 MHz, CDCl_3): δ = 1.23 (t, J = 7.6 Hz, 3H), 2.36 (br s, 1H), 2.75 (q, J = 7.6 Hz, 2H), 3.88 (s, 3H), 4.76 (s, 2H), 6.78 (d, J = 8.2 Hz, 1H), 6.85 (d, J = 7.7 Hz, 1H), 7.22 (t, J = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ = 16.2, 26.1, 55.4, 57.1, 108.1, 121.5, 126.6, 128.7, 144.0, 158.2. HRMS: m/z calcd for $\text{C}_{10}\text{H}_{14}\text{O}_2$: 166.0994; found: 166.0999.

2-Ethyl-6-methoxybenzaldehyde (8). A solution of alcohol **7A** (4.93 g, 29.6 mmol) in CH_2Cl_2 (40 mL) was added to a mixture of PCC (9.57 g, 44.4 mmol) and silica gel (9.6 g) in CH_2Cl_2 (40 mL) at rt. The reaction mixture was stirred for 3.5 h and then concentrated under reduced pressure. Flash

chromatography (silica gel, CH_2Cl_2) of the crude product adsorbed on silica gel afforded **8** (4.52 g, 93%) as a colorless oil. IR (neat, cm^{-1}): 2971, 2937, 2874, 1686, 1596, 1260. ^1H NMR (400 MHz, CDCl_3): δ = 1.21 (t, J = 7.6 Hz, 3H), 2.98 (q, J = 7.6 Hz, 2H), 3.90 (s, 3H), 6.84 (d, J = 8.4 Hz, 1H), 6.85 (d, J = 7.7 Hz, 1H), 7.42 (t, J = 8.0 Hz, 1H), 10.64 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ = 15.5, 27.0, 55.8, 109.0, 122.5, 122.8, 134.6, 148.2, 163.1, 192.2. HRMS: m/z calcd for $\text{C}_{10}\text{H}_{12}\text{O}_2$: 164.0837; found: 164.0841.

(S)-1-(2-ethyl-6-methoxyphenyl)-3-(triisopropylsilyl)prop-2-yn-1-ol (8A). Diethylzinc (1.1 M in toluene, 33.2 mL, 36.5 mmol) was added to a solution of (triisopropylsilyl)acetylene (7.39 g, 40.5 mmol) in toluene (21 mL) at rt and then heated under reflux for 5 h.

The reaction was cooled to rt and (*R*)-BINOL (1.05 g, 3.67 mmol) in CH_2Cl_2 (180 mL) was added. The reaction mixture was stirred for 1 h before the $\text{Ti}(\text{Oi-Pr})_4$ (2.60 g, 9.15 mmol) was added and the solution stirred for an additional 1 h. To this vigorously stirred orange solution was added dropwise a solution of aldehyde **8** (1.50 g, 9.14 mmol) in dichloromethane (40

mL). The reaction was stirred 12 h and then quenched with sat. aq. NH_4Cl . The aqueous phase was extracted with CH_2Cl_2 and the combined organic layers were dried over MgSO_4 and concentrated under reduced pressure. The product was used for the next step without further purification. For characterization, a sample was purified by flash column chromatography (silica gel, hexanes/ Et_2O , 95/5) and afforded pure **8A** as a colorless oil. $[\alpha]_{\text{D}}^{22} -38.7$ (c 1.03, CHCl_3). IR (neat, cm^{-1}): 3552, 3445, 3069, 2948, 2865, 2167, 1584, 1259. ^1H NMR (400 MHz, CDCl_3): δ = 1.03 (br s, 2H), 1.24 (t, J = 7.6 Hz, 3H), 2.70 (dq, J = 15.2, 7.6 Hz, 1H), 2.78 (dq, J = 15.2, 7.6 Hz, 1H), 3.90 (s, 3H), 4.08 (d, J = 10.8 Hz, 1H), 5.64 (d, J = 10.8 Hz, 1H), 6.80 (d, J = 8.2 Hz, 1H), 6.81 (d, J = 7.8 Hz, 1H), 7.20 (t, J = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ = 11.1, 15.9, 18.5, 26.7, 55.6, 59.8, 84.3, 108.4, 109.2, 122.0, 127.5, 128.6, 142.2, 157.8. HRMS: m/z calcd for $\text{C}_{21}\text{H}_{34}\text{O}_2\text{Si}$: 346.2328; found: 346.2334.

(R)-1-(2-Ethyl-6-methoxyphenyl)prop-2-yn-1-ol (9). A solution of TBAF (1 M in THF, 11.0 mL, 11.0 mmol) was added to a solution of the crude propargyl alcohol **8A** in THF (45 mL). The reaction mixture was stirred for 30 min at rt and then H_2O was added to quench the reaction. The aqueous

phase was extracted with Et_2O . The combined organic layers were washed with H_2O and brine, dried over MgSO_4 , and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, hexanes/ CH_2Cl_2 , 50/50) to afford **9** (1.43 g, 82% for 2 steps, 96% ee) as a white solid; mp 51-52 °C. $[\alpha]_{\text{D}}^{22} -30.7$ (c 1.01, CHCl_3). IR (neat, cm^{-1}): 3541, 3435, 2963, 2846, 2115, 1583, 1259. ^1H NMR (400 MHz, CDCl_3): δ = 1.25 (t, J = 7.6 Hz, 3H), 2.48 (d, J = 2.3 Hz, 1H), 2.74 (m, 2H), 3.95 (s, 3H), 4.17 (br s, 1H), 5.67 (d, J = 2.3 Hz, 1H), 6.841 (d, J = 8.4 Hz, 1H), 6.843 (d, J = 7.8 Hz, 1H), 7.23 (t, J = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ = 15.8, 26.5, 55.8, 59.1, 71.8, 84.5, 109.6, 122.2, 126.7, 129.0, 142.3, 157.7. HRMS: m/z calcd for $\text{C}_{12}\text{H}_{14}\text{O}_2$: 190.0994; found: 190.0996. The enantiomers

were analysed by chiral HPLC using Chiralcel OD column [*i*-PrOH(containing 0.1% TFA)/hexanes, 10/90, 1 mL/min, t_R = 9.7 min (**9**), 11.2 min (*ent*-**9**), 220 and 254 nm].

(S)-1-(2-Ethyl-6-methoxyphenyl)prop-2-ynyl 4-bromo-benzoate (*ent*-9A**).** To the propargyl alcohol *ent*-**9** (23 mg, 0.12 mmol), prepared from aldehyde **8** in the same manner as **9** but using (*S*)-BINOL, in CH₂Cl₂ (1.5 mL) at rt was successively added DMAP (7 mg, 0.06 mmol), pyridine (39 μ L, 0.48 mmol)

and 4-bromobenzoyl chloride (88 mg, 0.40 mmol). The reaction mixture was stirred for 15 h, diluted with Et₂O and then washed with 1 N aq. HCl, sat. aq. NaHCO₃, H₂O and brine. The organic layer was dried over MgSO₄, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, hexanes/Et₂O, 85/15) to afford *ent*-**9A** (40 mg, 89%) as a white solid which was recrystallized from pentane for X-ray analysis (for full crystallographic data see separate cif file); mp 72-74 °C. $[\alpha]_D^{22}$ +49.3 (c 0.53, CHCl₃). IR (neat, cm⁻¹): 3290, 2968, 2861, 2126, 1725, 1589, 1260. ¹H NMR (400 MHz, CDCl₃): δ = 1.32 (t, J = 7.6 Hz, 3H), 2.60 (d, J = 2.4 Hz, 1H), 3.10 (q, J = 7.6 Hz, 2H), 3.91 (s, 3H), 6.79 (d, J = 8.3 Hz, 1H), 6.93 (d, J = 7.8 Hz, 1H), 7.30 (t, J = 8.0 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.58 (d, J = 8.4 Hz, 2H), 7.92 (d, J = 8.4 Hz, 2H). ¹³C NMR (100 MHz,

CDCl₃): δ = 15.7, 25.6, 56.1, 59.0, 74.2, 80.9, 108.7, 122.0, 122.6, 128.2, 128.8, 130.1, 131.3, 131.7, 145.6, 157.0, 164.6. HRMS: m/z calcd for C₁₉H₁₇BrO₃: 372.0361; found: 372.0356.

(R)-1-(2-Ethyl-6-methoxyphenyl)prop-2-en-1-ol (9B). To the propargyl alcohol **9** (1.39 g, 7.31 mmol) in methanol (30 mL) was successively added quinoline (30 μ L, 0.25 mmol) and Lindlar catalyst (30 mg). The reaction mixture was stirred at rt under hydrogen atmosphere for 18 h and then filtered through a pad of Celite. The solution was concentrated under reduced pressure and the residue was purified by flash column chromatography (silica gel, hexanes/CH₂Cl₂, 50/50 to 0/100) to afford **9B** (1.36 g, 97%) as a light yellow oil. $[\alpha]_D^{22}$ -24.1 (c 1.02, CHCl₃). IR (neat, cm⁻¹): 3546, 3440, 3078, 2967, 2838, 1599, 1582, 1414, 1235. ¹H NMR (400 MHz, CDCl₃): δ = 1.23 (t, J = 7.6 Hz, 3H), 2.69 (m, 2H), 3.86 (s, 3H), 4.05 (d, J = 10.8 Hz, 1H), 5.10 (dt, J = 10.4, 1.6 Hz, 1H), 5.16 (dt, J = 17.2, 1.6 Hz, 1H), 5.41 (dd, J = 10.8, 5.6 Hz, 1H), 6.25 (ddd, J = 17.2, 10.4, 5.6 Hz, 1H), 6.80 (d, J = 8.2 Hz, 1H), 6.84 (d, J = 7.7 Hz, 1H), 7.20 (t, J = 8.0 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ = 15.7, 26.3, 55.4, 71.2, 109.2, 114.1, 122.1, 127.8, 128.3, 140.3, 142.7, 157.6. HRMS: m/z calcd for C₁₂H₁₆O₂: 192.1150; found: 192.1154.

5

(R)-3-Ethyl-2-(1-hydroxyallyl)phenol (5). To a solution of diphenylphosphine (3.00 mL, 17.24 mmol) in THF (20 mL) at 0 °C was added dropwise *n*-BuLi (2.5 M in hexanes, 7.20 mL, 18.0 mmol). The resulting red solution of lithium diphenylphosphide was allowed to warm to

rt over 45 min and then cannulated to a solution of the allylic alcohol **9B** (1.092 g, 5.680 mmol) in THF (30 mL) at rt. The mixture was stirred for an additional 1 h and then heated under reflux for 5 h. It was then cooled to rt and poured in a buffer pH 7 to quench the reaction. The aqueous layer was extracted with AcOEt, and the combined organic layers were washed with brine, dried over MgSO₄, and concentrated under reduced pressure. The residue was purified by flash column chromatography (Et₃N neutralised silica gel, hexanes/AcOEt, 90/10 to 85/15) to afford **5** (863 mg, 85%) as a light yellow oil. $[\alpha]_D^{22}$ –15.0 (c 1.02, MeOH). IR (neat, cm⁻¹): 3308, 3079, 2968, 2881, 1614, 1585, 1258. ¹H NMR (400 MHz, acetone-d₆ ref is 2.04): δ = 1.16 (t, *J* = 7.6 Hz, 3H), 2.55 (dq, *J* = 15.2, 7.6 Hz, 1H), 2.63 (dq, *J* = 15.2, 7.6 Hz, 1H), 5.09 (dt, *J* = 10.4, 1.6 Hz, 1H), 5.20 (dt, *J* = 17.2, 1.6 Hz, 1H), 5.66 (dt, *J* = 5.5, 1.6 Hz, 1H), 6.12 (ddd, *J* = 17.2, 10.4, 5.5 Hz, 1H), 6.61 (d, *J* = 8.1 Hz, 1H), 6.66 (d, *J* = 7.6 Hz, 1H), 7.04 (t, *J* = 7.8 Hz, 1H). ¹³C NMR (100 MHz, acetone-d₆ ref CO is 206.5): δ = 16.2, 26.6, 72.5, 115.2, 115.8, 121.0, 125.3, 129.5, 139.9, 142.8, 158.0. HRMS: *m/z* calcd for C₁₁H₁₄O₂: 178.0994; found: 178.0997.

10

Lactone 10. To a solution of diol **5** (50 mg, 0.28 mmol) and *N*-methylmorpholine (92 μL, 0.84 mmol) in THF (3 mL) under a CO atmosphere was added a solution of palladium acetate (94 mg, 0.42 mmol) in THF (7 mL). The mixture was stirred 15 h and then filtered

through a pad of Celite. The solution was concentrated under reduced pressure and the residue was purified by flash column chromatography (silica gel, hexanes/AcOEt, 80/20) to afford **10**

(33 mg, 58%) as a white solid; mp 93-95 °C. $[\alpha]_D^{22}$ -132 (c 0.76, CHCl₃). IR (neat, cm⁻¹): 2978, 2922, 1774, 1598, 1184. ¹H NMR (400 MHz, CDCl₃): δ = 1.30 (t, J = 7.6 Hz, 3H), 2.76 (q, J = 7.6 Hz, 2H), 2.99 (dd, J = 19.0, 2.0 Hz, 1H), 3.06 (dd, J = 19.0, 6.6 Hz, 1H), 5.36 (dt, J = 6.4, 2.0 Hz, 1H), 6.06 (d, J = 6.2 Hz, 1H), 6.72 (d, J = 8.1 Hz, 1H), 6.84 (d, J = 7.6 Hz, 1H), 7.28 (t, J = 7.9 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ = 14.8, 25.6, 35.4, 80.7, 82.7, 107.8, 120.9, 121.6, 132.1, 143.7, 160.6, 174.9. HRMS: m/z calcd for C₁₂H₁₂O₃: 204.0786; found: 204.0785.

(2S,3S)-4-Ethyl-2,3-dihydro-2-(2-hydroxyethyl)benzofuran-3-ol

(10A). A solution of lactone **10** (9.0 mg, 0.044 mmol) in THF (1 mL) was added dropwise to a mixture of LiAlH₄ (5 mg, 0.13 mmol) in THF (0.5 mL) at 0 °C. The reaction was allowed to warm to rt and stirred an additional 1 h before quenched by adding 5 μ L H₂O, 5 μ L 15% NaOH and 15 μ L H₂O. The mixture was stirred for 45 min and then filtered through a pad of Celite. The solution was concentrated under reduced pressure and the residue was purified by flash column chromatography (silica gel, hexanes/AcOEt, 50/50) to afford the diol **10A** (7.7 mg, 86%) as a white solid; mp 62-63 °C. $[\alpha]_D^{22}$ -22.4 (c 0.37, CHCl₃). IR (neat, cm⁻¹): 3333, 2965, 2933, 2877, 1598, 1454, 1253. ¹H NMR (400 MHz, CDCl₃): δ = 1.29 (t, J = 7.6 Hz, 3H), 2.21 (m, 2H), 2.61 (br s, 2H), 2.76 (m, 2H), 3.80 (ddd, J = 10.4, 9.0, 3.7 Hz, 1H), 3.93 (ddd, J = 10.4, 5.6, 4.4 Hz, 1H), 4.49 (td, J = 7.9, 6.0 Hz, 1H), 5.16 (d, J = 5.7 Hz, 1H), 6.68 (d, J = 8.0 Hz, 1H), 6.79 (d, J = 7.6 Hz, 1H), 7.19 (t, J = 7.8 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ = 15.0, 25.2, 30.5, 59.5, 71.3, 85.9, 107.5, 120.4, 126.8, 130.6, 143.1, 159.3. HRMS: m/z calcd for C₁₂H₁₆O₃: 208.1099; found: 208.1102.

(*2R*)-2-((*2S,3S*)-4-Ethyl-2,3-dihydro-3-hydroxybenzo-furan-2-yl)ethyl 3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (**10B**). To the diol **10A** (7.7 mg, 0.037 mmol) in CH₂Cl₂ (1 mL) was successively added EDC (43 mg, 0.22 mmol), (*R*)-Mosher's acid (32 mg, 0.14 mmol) and

DMAP (1 mg, 0.008 mmol). The reaction mixture was stirred for 6.5 h and then quenched with H₂O and extracted with Et₂O. The combined organic layers were washed with sat. aq. NaHCO₃ and brine, dried over MgSO₄, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, hexanes/AcOEt, 80/20) to afford a colorless oil as an inseparable mixture of diastereomers **10B**:**10C** (14.6 mg, 93%) in a 98:2 ratio (ratio of crude product was identical). $[\alpha]_D^{22} +10.4$ (c 0.73, CHCl₃). IR (neat, cm⁻¹): 3288, 2968, 2938, 2851, 1750, 1598, 1251, 1170. ¹H NMR (400 MHz, CDCl₃): δ = 1.29 (t, *J* = 7.6 Hz, 3H), 2.33 (m, 2H), 2.75 (m, 2H), 3.57 (q, *J* = 1.2 Hz, 3H), 4.40 (ddd, *J* = 7.2, 6.6, 5.7 Hz, 1H), 4.58 (ddd, *J* = 11.1, 7.3, 6.7 Hz, 1H), 4.67 (dt, *J* = 11.1, 5.7 Hz, 1H), 5.06 (d, *J* = 5.7 Hz, 1H), 6.68 (d, *J* = 8.0 Hz, 1H), 6.80 (d, *J* = 7.6 Hz, 1H), 7.21 (t, *J* = 7.8 Hz, 1H), 7.41 (m, 3H), 7.54 (m, 2H). ¹³C NMR (100 MHz, CDCl₃): δ = 15.1, 25.3, 27.4, 55.4 (q, *J* = 1.5 Hz), 63.7, 71.3, 83.2, 84.6 (q, *J* = 27.6 Hz), 107.8, 120.6, 123.3 (q, *J* = 287 Hz), 126.9, 127.3 (q, *J* = 1.3 Hz), 128.5, 129.7, 130.9, 132.1, 142.8, 159.4, 166.5. HRMS: *m/z* calcd for C₂₂H₂₃F₃O₅: 424.1497; found: 424.1493.

(*2R*)-2-((*2R,3R*)-4-Ethyl-2,3-dihydro-3-hydroxybenzo-furan-2-yl)ethyl 3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (**10C**). ¹H NMR (400 MHz, CDCl₃): δ = 1.27 (t, *J* = 7.6 Hz, 3H), 2.33 (m, 2H), 2.70 (m, 2H), 3.59 (q, *J* = 1.2 Hz, 3H), 4.33 (ddd, *J* = 7.5, 6.4, 5.7 Hz, 1H), 4.61

(m, 2H), 4.91 (d, $J = 5.7$ Hz, 1H), 6.67 (d, $J = 8.1$ Hz, 1H), 6.79 (d, $J = 7.6$ Hz, 1H), 7.20 (t, $J = 7.8$ Hz, 1H), 7.37 (m, 3H), 7.51 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3): $\delta = 15.1, 25.2, 27.4, 55.6$ (q, $J = 1.7$ Hz), 63.8, 71.2, 83.6, 84.6 (q, $J = 27.5$ Hz), 107.7, 120.5, 123.2 (q, $J = 287$ Hz), 126.8, 127.2 (q, $J = 1.3$ Hz), 128.5, 129.7, 130.9, 132.2, 142.9, 159.3, 166.4.

Acetates 11. To a solution of lactone **10** (646 mg, 3.16 mmol) in CH_2Cl_2 (30 mL) at -78°C was added dropwise DIBAL (1 M in CH_2Cl_2 , 4.00 mL). The reaction was stirred 1 h at -78°C and then acetic anhydride (1.50 mL, 15.82 mmol), pyridine (1.02 mL, 12.66 mmol) and DMAP (580 mg, 4.75 mmol) were added. The solution was warmed to rt and then stirred an additional 1 h. The reaction was quenched with sat. aq. NH_4Cl and extracted with CH_2Cl_2 . The combined organic layers were washed with sat. aq. NaHCO_3 and brine, dried over MgSO_4 and then concentrated under reduced pressure to afford acetates **11** in quantitative yield (784 mg). ^1H NMR spectrum of the mixture revealed a 2:1 ratio of β - and α -**11** which were pure enough to be use in the next step without further purification. A sample was purified for analytical purposes by flash column chromatography (Et_3N neutralised silica gel, hexanes/ AcOEt , 90/10) to afford the β - and α -anomers of acetate **11** in isomerically pure form.

Acetate β -11 was obtained as a white solid; mp $51\text{--}52^\circ\text{C}$. $R_f = 0.30$ (hexanes/ AcOEt , 90/10). $[\alpha]_D^{22} -130$ (c 0.57, MeOH). IR (neat, cm^{-1}): 3049, 2968, 2932, 2876, 1752, 1600, 1243. ^1H NMR (400 MHz, acetone- d_6 ref is 2.04): $\delta = 1.22$ (t, $J = 7.6$ Hz, 3H), 2.01 (s, 3H), 2.39 (dddd, $J = 14.6, 5.4, 4.0, 0.4$ Hz, 1H), 2.64 (ddd, $J = 14.6, 7.8, 1.4$ Hz, 1H), 2.69 (m, 2H), 5.43 (dddd, $J = 7.8, 6.4, 4.0, 0.5$ Hz, 1H), 5.84 (d, $J = 6.4$ Hz, 1H), 6.33 (dddd, $J = 5.4, 1.4, 0.6, 0.5$ Hz, 1H), 6.62 (dm, $J = 8.1$ Hz, 1H), 6.77 (ddd, $J = 8.3, 1.4, 0.6$ Hz, 1H), 7.20

(t, $J = 8.0$ Hz, 1H). ^{13}C NMR (100 MHz, acetone- d_6 ref CO is 206.5): $\delta = 15.8, 21.5, 26.6, 41.5, 84.2, 85.9, 99.5, 108.7, 121.2, 125.2, 132.2, 144.2, 161.5, 170.5$. HRMS: m/z calcd for $\text{C}_{14}\text{H}_{16}\text{O}_4$: 248.1048; found: 248.1053.

α -11

Acetate α -11 was obtained as a white solid; mp 42-43 °C. $R_f = 0.16$ (hexanes/AcOEt, 90/10). $[\alpha]_D^{22} +60.0$ (c 0.63, MeOH). IR (neat, cm^{-1}): 2968, 2937, 2877, 1751, 1599, 1234. ^1H NMR (400 MHz, acetone- d_6 ref is 2.04): $\delta = 1.19$ (t, $J = 7.6$ Hz, 3H), 1.39 (s,

3H), 2.45 (m, 2H), 2.67 (q, $J = 7.6$ Hz, 2H), 5.38 (m, 1H), 5.90 (d, $J = 6.4$ Hz, 1H), 6.31 (m, 1H), 6.60 (d, $J = 8.0$ Hz, 1H), 6.71 (d, $J = 7.6$ Hz, 1H), 7.16 (t, $J = 7.8$ Hz, 1H). ^{13}C NMR (100 MHz, acetone- d_6 ref CO is 206.5): $\delta = 15.9, 20.9, 26.5, 40.6, 85.1, 85.3, 99.3, 108.1, 120.9, 126.8, 131.7, 143.9, 161.6, 170.3$. HRMS: m/z calcd for $\text{C}_{14}\text{H}_{16}\text{O}_4$: 248.1048; found: 248.1053.

12

Nitrile 12. To a solution of the crude mixture of acetates **11** (784 mg, 3.16 mmol) in THF (63 mL) at rt was added Et_2AlCN (1 M in toluene, 4.75 mL). The reaction mixture was stirred for 2 h and then H_2O was added to quench the reaction. The aqueous phase was extracted with

Et_2O and the combined organic layers were washed with brine, dried over MgSO_4 and then concentrated under reduced pressure. ^1H NMR spectrum of the residue revealed a 17:1 ratio of **12** and α -**12**, which were separated by flash column chromatography (silica gel, hexanes/AcOEt, 90/10 to 80/20) to afford isomerically pure **12** (598 mg, 88%) and its α -anomer (α -**12**, 35 mg, 5%). **Nitrile 12** was obtained as a white solid; mp 53-54 °C. $R_f = 0.65$ (hexanes/AcOEt, 70/30). $[\alpha]_D^{22} -15.1$ (c 0.72, CHCl_3). IR (neat, cm^{-1}): 3049, 2969, 2876, 2257, 1578, 1242. ^1H NMR (400 MHz, CDCl_3): $\delta = 1.29$ (t, $J = 7.6$ Hz, 3H), 2.56 (ddd, $J = 13.7, 9.2, 6.1$ Hz, 1H), 2.71 (dddd, $J = 13.7, 5.8, 1.5, 0.5$ Hz, 1H), 2.75 (m, 2H), 4.46 (dd, $J =$

9.2, 5.8 Hz, 1H), 5.36 (ddt, $J = 6.0, 1.5, 0.5$ Hz, 1H), 5.88 (d, $J = 5.9$ Hz, 1H), 6.66 (d, $J = 8.1$ Hz, 1H), 6.82 (dm, $J = 7.6$ Hz, 1H), 7.24 (t, $J = 7.9$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): $\delta = 14.9, 25.5, 39.8, 64.1, 83.6, 84.7, 107.4, 117.6, 120.9, 121.8, 131.6, 143.6, 160.5$. HRMS: m/z calcd for $\text{C}_{13}\text{H}_{13}\text{NO}_2$: 215.0946; found: 215.0941.

Nitrile α -12 was obtained as a white solid, mp 78-79 °C. $R_f = 0.29$ (hexanes/AcOEt, 70/30). $[\alpha]_D^{22} -51.0$ (c 0.52, CHCl_3). IR (neat, cm^{-1}): 3049, 2968, 2872, 1598, 1249. ^1H NMR (400 MHz, CDCl_3): $\delta = 1.31$ (t, $J = 7.6$ Hz, 3H), 2.55 (ddd, $J = 14.2, 8.2, 6.0$ Hz, 1H), 2.77 (m, 3H), 4.90 (dd, $J = 8.2, 1.3$ Hz, 1H), 5.37 (dt, $J = 6.0, 0.6$ Hz, 1H), 5.88 (d, $J = 5.9$ Hz, 1H), 6.72 (d, $J = 8.1$ Hz, 1H), 6.83 (d, $J = 7.6$ Hz, 1H), 7.27 (t, $J = 7.8$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): $\delta = 14.9, 25.6, 39.4, 64.7, 2 \times 84.7, 107.6, 118.2, 120.8, 122.3, 131.8, 143.4, 160.7$. HRMS: m/z calcd for $\text{C}_{13}\text{H}_{13}\text{NO}_2$: 215.0946; found: 215.0944.

Aldehyde 3. To a solution of the nitrile **12** (16.0 mg, 0.074 mmol) in toluene (0.5 mL) at -78 °C was added DIBAL (1 M in toluene, 112 μL , 0.112 mmol). The reaction was stirred for 1 h and then 15% aq. tartaric acid was added. The mixture was allowed to warm to rt and then stirred for an additional 1 h before the aqueous layer was extracted with AcOEt. The combined organic layers were washed with sat. aq. NaHCO_3 and brine, dried over MgSO_4 and concentrated under reduced pressure. As this aldehyde is prone to decomposition, it was immediately used for the next step without further purification. Analytical data were obtained from purification of a sample of the crude residue. Colorless oil. ^1H NMR (400 MHz, CDCl_3): $\delta = 1.29$ (t, $J = 7.6$ Hz, 3H), 2.15 (ddd, $J = 13.6, 10.8, 5.8$ Hz, 1H), 2.56 (ddt, $J = 13.6, 5.5, 0.6$ Hz, 1H), 2.78 (m, 2H), 4.19 (dddd, $J = 10.8, 5.5, 1.8, 0.4$ Hz, 1H), 5.32 (tm, $J = 5.8$ Hz, 1H), 5.90 (d, $J = 5.8$ Hz, 1H), 6.66 (dm, $J = 8.1$ Hz, 1H), 6.80 (ddd, $J = 7.6, 1.3, 0.6$ Hz, 1H),

7.22 (t, $J = 7.9$ Hz, 1H), 9.72 (d, $J = 1.8$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): $\delta = 14.9$, 25.5, 35.9, 80.8, 83.5, 85.4, 107.2, 120.6, 122.8, 131.2, 143.5, 160.6, 200.0. The ^1H NMR data are in perfect agreement with those reported in the literature.^{4,5}

TMS-13

Alcohol TMS-13. $\text{Zn}(\text{OTf})_2$ (61 mg, 0.17 mmol) was charged in a flask and dried at 120 °C in vacuo (1 mmHg) for 20 h. After the flask was cooled and the pressure released, (1*S*,2*R*)-(+)-*N*-methyl-ephedrine (32 mg, 0.18 mmol), CH_2Cl_2 (165 μL) and Et_3N (25 μL , 0.18 mmol) were added. The reaction mixture was stirred 3.5 h at rt then (trimethylsilyl)acetylene (21 μL , 0.15 mmol) was added. After stirring for an additional 30 min, a solution of aldehyde **3** (0.074 mmol) in CH_2Cl_2 (200 μL) was added. The mixture was stirred for 40 h and then sat. aq. NH_4Cl was added to quench the reaction. The aqueous phase was extracted with AcOEt and the combined organic layers were washed with brine, dried over MgSO_4 and concentrated under reduced pressure. The ^1H NMR spectrum of the residue revealed a 11:1 ratio of **TMS-13** and **TMS-14**. These alcohols were inseparable by flash column chromatography (silica gel, hexanes/ Et_2O , 90/10 to 80/20) and were obtained as a 11:1 mixture (colorless oil, 10.8 mg, 46%). $[\alpha]_{\text{D}}^{22} -88.1$ (c 0.54, CHCl_3).

Spectral data for **TMS-13**: IR (neat, cm^{-1}) 3445, 2963, 2928, 2892, 2176, 1597, 1454, 1251. ^1H NMR (400 MHz, CDCl_3): $\delta = 0.17$ (s, 9H), 1.27 (t, $J = 7.6$ Hz, 3H), 2.31 (br d, $J = 3.6$ Hz, 1H), 2.32 (ddd, $J = 13.9$, 10.0, 6.0 Hz, 1H), 2.38 (dd, $J = 13.9$, 5.4 Hz, 1H), 2.75 (m, 2H), 4.01 (ddd, $J = 10.0$, 5.4, 3.6 Hz, 1H), 4.61 (t, $J = 3.6$ Hz, 1H), 5.31 (t, $J = 6.0$ Hz, 1H), 5.84 (d, $J = 6.0$ Hz, 1H), 6.66 (d, $J = 8.0$ Hz, 1H), 6.78 (d, $J = 7.6$ Hz, 1H), 7.20 (t, $J = 7.9$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): $\delta = -0.3$, 15.0, 25.5, 34.2, 62.8, 79.3, 83.1, 86.2, 91.2, 102.4, 107.1, 120.3, 123.5, 130.8, 143.4, 160.7.

TMS-14

Alcohol TMS-14. Zn(OTf)₂ (61 mg, 0.17 mmol) was charged in a flask and dried at 120 °C in vacuo (1 mmHg) for 20 h. After the flask was cooled and the pressure released, (1*R*,2*S*)-(-)-*N*-methylephedrine (32 mg, 0.18 mmol), CH₂Cl₂ (165 μL) and Et₃N (25 μL, 0.18 mmol) were added. The reaction mixture was stirred 3.5 h at rt then (trimethylsilyl)acetylene (21 μL, 0.15 mmol) was added. After stirring for an additional 30 min, a solution of aldehyde **3** (0.074 mmol) in CH₂Cl₂ (200 μL) was added. The mixture was stirred for 40 h and then sat. aq. NH₄Cl was added to quench the reaction. The aqueous phase was extracted with AcOEt and the combined organic layers were washed with brine, dried over MgSO₄ and concentrated under reduced pressure. The ¹H NMR spectrum of the residue revealed a 11:1 ratio of **TMS-14** and **TMS-13**. These alcohols were inseparable by flash column chromatography (silica gel, hexanes/Et₂O, 90/10 to 80/20) and were obtained as a 11:1 mixture (white solid, 13.7 mg, 59%); mp 67-68 °C. [α]_D²² -89.2 (c 0.50, CHCl₃).

Spectral data for **TMS-14**: IR (neat, cm⁻¹) 3451, 2963, 2934, 2897, 2175, 1597, 1455, 1251. ¹H NMR (400 MHz, CDCl₃): δ = 0.16 (s, 9H), 1.28 (t, *J* = 7.6 Hz, 3H), 2.11 (ddd, *J* = 13.7, 10.5, 6.0 Hz, 1H), 2.33 (br d, *J* = 5.4 Hz, 1H), 2.36 (dd, *J* = 13.7, 5.1 Hz, 1H), 2.75 (q, *J* = 7.6 Hz, 2H), 3.93 (ddd, *J* = 10.5, 5.4, 5.1 Hz, 1H), 4.36 (t, *J* = 5.4 Hz, 1H), 5.29 (t, *J* = 6.0 Hz, 1H), 5.84 (d, *J* = 6.0 Hz, 1H), 6.66 (d, *J* = 8.0 Hz, 1H), 6.78 (d, *J* = 7.6 Hz, 1H), 7.20 (t, *J* = 7.9 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ = -0.3, 15.3, 25.7, 36.6, 64.5, 79.7, 83.0, 86.0, 90.8, 103.0, 107.0, 120.5, 123.3, 130.8, 143.6, 160.7.

Propargyl alcohol 13. A solution of TBAF (1 M in THF, 40 μ L) was added to a solution of silylated propargyl alcohol **TMS-13** (10.6 mg, 0.0335 mmol) in THF (0.5 mL). The mixture was stirred for 30 min at rt and then H₂O was added to quench the

reaction. The aqueous phase was extracted with Et₂O and the combined organic layers were washed with brine, dried over MgSO₄ and concentrated under reduced pressure. The ¹H NMR spectrum of the residue revealed a 11:1 ratio of **13** and **14**. These alcohols were inseparable by flash column chromatography (silica gel, hexanes/Et₂O, 70/30) and were obtained as a 11:1 mixture (white solid, 7.5 mg, 92%); mp 96-97 °C. [α]_D²² -72.3 (c 0.37, CHCl₃).

Spectral data for alcohol **13**: IR (neat, cm⁻¹) 3372, 3270, 2965, 2926, 2872, 2125, 1592, 1452, 1234. ¹H NMR (400 MHz, CDCl₃): δ = 1.27 (t, J = 7.6 Hz, 3H), 2.31 (ddd, J = 13.8, 10.2, 5.8 Hz, 1H), 2.38 (br s, 1H), 2.40 (dd, J = 13.8, 5.0 Hz, 1H), 2.47 (d, J = 2.2 Hz, 1H), 2.76 (m, 2H), 4.02 (ddd, J = 10.2, 5.0, 3.3 Hz, 1H), 4.62 (dd, J = 3.3, 2.2 Hz, 1H), 5.31 (t, J = 5.8 Hz, 1H), 5.85 (d, J = 5.8 Hz, 1H), 6.66 (d, J = 7.8 Hz, 1H), 6.78 (d, J = 7.8 Hz, 1H), 7.20 (t, J = 7.8 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ = 15.0, 25.5, 34.3, 62.4, 74.4, 79.1, 80.9, 83.1, 86.2, 107.1, 120.4, 123.4, 130.9, 143.4, 160.7. The ¹H NMR data are in perfect agreement with those reported in the literature.⁴

Propargyl alcohol 14. A solution of TBAF (1 M in THF, 90 μ L) was added to a solution of silylated propargyl alcohol **TMS-14** (23.4 mg, 0.0739 mmol) in THF (1 mL). The solution was stirred for 30 min at rt and then H₂O was added to quench the reaction.

The aqueous phase was extracted with Et₂O and the combined organic layers were washed with brine, dried over MgSO₄ and concentrated under reduced pressure. The ¹H NMR spectrum of the residue revealed a 11:1 ratio of **14** and **13**. These alcohols were inseparable by

flash column chromatography (silica gel, hexanes/Et₂O, 70/30) and were obtained as a 11:1 mixture (colorless oil, 16.7 mg, 93%). $[\alpha]_D^{22} -83.4$ (c 0.41, CHCl₃).

Spectral data for alcohol **14**: IR (neat, cm⁻¹): 3432, 3282, 2968, 2936, 2878, 2118, 1596, 1454, 1236. ¹H NMR (400 MHz, CDCl₃): δ = 1.28 (t, J = 7.6 Hz, 3H), 2.12 (ddd, J = 13.8, 10.6, 6.0 Hz, 1H), 2.41 (dd, J = 13.8, 5.3 Hz, 1H), 2.46 (d, J = 2.2 Hz, 1H), 2.49 (br s, 1H), 2.75 (q, J = 7.6 Hz, 2H), 3.95 (dt, J = 10.6, 5.3 Hz, 1H), 4.40 (dd, J = 5.3, 2.2 Hz, 1H), 5.30 (t, J = 6.0 Hz, 1H), 5.83 (d, J = 6.0 Hz, 1H), 6.66 (d, J = 8.1 Hz, 1H), 6.78 (d, J = 7.6 Hz, 1H), 7.20 (t, J = 7.8 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ = 15.1, 25.5, 36.4, 63.8, 74.0, 79.4, 81.6, 83.0, 86.0, 107.0, 120.4, 123.2, 130.8, 143.5, 160.7. The ¹H NMR data are in perfect agreement with those reported in the literature.⁴

Trisilate 15. To a solution of propargyl alcohol **13** (7.2 mg, 0.029 mmol) in CH₂Cl₂ (0.5 mL) at rt was successively added DMAP (11 mg, 0.090 mmol) and 2,4,6-triisopropylbenzenesulphonyl chloride (18 mg, 0.060 mmol). The reaction mixture was stirred 1 h and then diluted with Et₂O and filtered through a pad of Celite. The residue was purified by flash column chromatography (silica gel, hexanes/AcOEt, 100/0 to 98/2) to afford isomerically pure **15** (12.7 mg, 84%) as a colorless oil. R_f = 0.13 (hexanes/AcOEt, 95/5). $[\alpha]_D^{22} -13.6$ (c 0.39, CHCl₃). IR (neat, cm⁻¹): 3283, 2962, 2932, 2877, 2126, 1599, 1454, 1178. ¹H NMR (400 MHz, CDCl₃): δ = 1.25 (t, J = 7.6 Hz, 3H), 1.26 (d, J = 6.8 Hz, 6H), 1.27 (d, J = 6.8 Hz, 6H), 1.28 (d, J = 6.8 Hz, 6H), 2.25 (ddd, J = 13.8, 9.8, 6.0 Hz, 1H), 2.29 (d, J = 2.3 Hz, 1H), 2.43 (dd, J = 13.8, 5.3 Hz, 1H), 2.72 (m, 2H), 2.91 (sept, J = 6.8 Hz, 1H), 4.09 (ddd, J = 9.8, 5.3, 3.6 Hz, 1H), 4.14 (sept, J = 6.8 Hz, 2H), 5.27 (t, J = 6.0 Hz, 1H), 5.33 (dd, J = 3.6, 2.3 Hz, 1H), 5.79 (d, J = 6.0 Hz, 1H), 6.63 (d, J = 8.0 Hz, 1H), 6.77 (d, J = 7.6 Hz, 1H), 7.17 (s, 2H), 7.19 (t, J = 7.8 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ = 14.9, 23.6, 24.6,

24.7, 25.5, 29.7, 34.2, 35.7, 70.0, 76.3, 77.2, 78.1, 83.3, 85.6, 107.1, 120.4, 123.3, 123.6, 130.7, 130.9, 143.5, 150.7, 153.8, 160.6. HRMS: m/z calcd for $C_{30}H_{38}SO_5$: 510.2440; found: 510.2436.

Trisilate 16. To a solution of propargyl alcohol **14** (16.4 mg, 0.067 mmol) in CH_2Cl_2 (1 mL) at rt was successively added DMAP (25 mg, 0.21 mmol) and 2,4,6-triisopropylbenzenesulphonyl chloride (41 mg, 0.14 mmol). The reaction mixture was stirred 1 h and then diluted with Et_2O and filtered through a pad of Celite. The residue was purified by flash column chromatography (silica gel, hexanes/ $AcOEt$, 100/0 to 98/2) to afford isomerically pure **16** (28.9 mg, 84%) as a colorless oil. R_f = 0.10 (hexanes/ $AcOEt$, 95/5). $[\alpha]_D^{22}$ -32.4 (c 1.00, $CHCl_3$). IR (neat, cm^{-1}): 3278, 2962, 2930, 2871, 2126, 1599, 1454, 1179. 1H NMR (400 MHz, $CDCl_3$): δ = 1.23 (t, J = 7.6 Hz, 3H), 1.25 (d, J = 6.8 Hz, 6H), 1.26 (d, J = 6.8 Hz, 6H), 1.27 (d, J = 6.8 Hz, 6H), 2.27 (ddd, J = 13.8, 9.7, 6.0 Hz, 1H), 2.34 (d, J = 2.2 Hz, 1H), 2.44 (dd, J = 13.8, 5.4 Hz, 1H), 2.71 (q, J = 7.6 Hz, 2H), 2.91 (sept, J = 6.8 Hz, 1H), 4.09 (m, 1H), 4.12 (sept, J = 6.8 Hz, 2H), 5.30 (t, J = 6.0 Hz, 1H), 5.32 (dd, J = 5.0, 2.2 Hz, 1H), 5.81 (d, J = 6.0 Hz, 1H), 6.63 (d, J = 8.1 Hz, 1H), 6.76 (d, J = 7.6 Hz, 1H), 7.16 (s, 2H), 7.19 (t, J = 7.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.9, 23.6, 24.5, 24.7, 25.5, 29.6, 34.2, 36.3, 70.0, 76.5, 77.236, 77.244, 83.2, 85.8, 107.1, 120.4, 123.2, 123.6, 130.4, 130.9, 143.5, 150.7, 153.8, 160.5. HRMS: m/z calcd for $C_{30}H_{38}SO_5$: 510.2440; found: 510.2436.

(+)-1-*epi*-Panacene (1). LiBr (86 mg, 0.99 mmol) was charged in a flask and dried at 200 °C in vacuo (1 mmHg) for 24 h. After the flask was cooled and the pressure released, CuBr (142 mg, 0.990 mmol) and THF (4 mL) were added. The mixture was stirred until the bromides dissolve completely. A portion of the resulting homogenous solution of LiCuBr₂ (0.25 M in THF, 305 μ L, 0.076 mmol)⁶ was added to a solution of trisylate **15** (7.8 mg, 0.015 mmol) in THF (0.25 mL) at rt. The reaction mixture was heated under reflux for 5 h and then cooled to rt before quenched with sat. NH₄Cl. The aqueous phase was extracted with Et₂O and the combined organic layers were dried over MgSO₄ and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, hexanes/AcOEt, 90/10) to afford a mixture of products consisting of **1**, its 1-epimer (*ent*-**2**) and propargyl bromides. Isomerically pure **1** (3.1 mg, 66%) was obtained as a colorless oil by semi-preparative HPLC using a Partisil 10 column (AcOEt/hexanes, 2/98, 3 mL/min, t_R = 76 min, 280 nm). $[\alpha]_D^{22}$ +166 (c 0.16, MeOH), +138 (c 0.16, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ = 1.28 (t, J = 7.6 Hz, CH₃), 2.02 (ddd, J = 13.6, 10.3, 5.9 Hz, β -H-5), 2.46 (dd, J = 13.6, 4.7 Hz, α -H-5), 2.74 (dq, J = 15.2, 7.6 Hz, H-14), 2.78 (dq, J = 15.2, 7.6 Hz, H-14), 4.37 (dddd, J = 10.3, 6.3, 4.7, 1.6 Hz, H-4), 5.29 (t, J = 5.9 Hz, H-6), 5.50 (br t, J = 6.3, 5.7 Hz, H-3), 5.81 (d, J = 5.9 Hz, H-7), 6.06 (dd, J = 5.7, 1.6 Hz, H-1), 6.64 (d, J = 8.1 Hz, H-10), 6.78 (dd, J = 7.6, 0.6 Hz, H-12), 7.19 (t, J = 7.8 Hz, H-11). ¹³C NMR (100 MHz, CDCl₃): δ = 14.8, 25.4, 40.4, 73.2, 73.8 (J_{C-H} = 210.9 Hz), 82.5, 86.0, 99.8 (J_{C-H} = 168.0 Hz), 107.0, 120.4, 123.2, 130.9, 143.5, 160.8, 202.2.

Small amounts of *ent*-**2** (*ca.* 3%) and the isomeric propargyl bromides (*ca.* 7%) were also obtained from this reaction.

(-)-**Panacene** (*ent-2*). LiBr (86 mg, 0.99 mmol) was charged in a flask and dried at 200 °C in vacuo (1 mmHg) for 24 h. After the flask was cooled and the pressure released, CuBr (142 mg, 0.990 mmol) and THF (4 mL) were added. The mixture was stirred until the bromides

dissolve completely. A portion of the resulting homogenous solution of LiCuBr₂ (0.25 M in THF, 780 μ L, 0.195 mmol) was added to a solution of trisylate **16** (20.0 mg, 0.039 mmol) in THF (0.5 mL) at rt. The reaction mixture was heated under reflux for 5 h and then cooled to rt before quenched with sat. NH₄Cl. The aqueous phase was extracted with Et₂O and the combined organic layers were dried over MgSO₄ and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, hexanes/AcOEt, 90/10) to afford a mixture of products consisting of *ent-2*, its 1-epimer (**1**) and propargyl bromides. Isomerically pure *ent-2* (7.8 mg, 65%) was obtained as a colorless oil by semi-preparative HPLC using a Partisil 10 column (AcOEt/hexanes, 2/98, 3 mL/min, t_R = 65 min, 280 nm). ($[\alpha]_D^{22}$ -340 (c 0.20, MeOH), -319 (c 0.20, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ = 1.27 (t, J = 7.6 Hz, CH₃), 2.02 (ddd, J = 13.6, 10.3, 5.9 Hz, β -H-5), 2.48 (dd, J = 13.6, 4.7 Hz, α -H-5), 2.74 (dq, J = 15.2, 7.6 Hz, H-14), 2.78 (dq, J = 15.2, 7.6 Hz, H-14), 4.37 (dddd, J = 10.3, 6.7, 4.7, 1.5 Hz, H-4), 5.30 (t, J = 5.9 Hz, H-6), 5.46 (dd, J = 6.7, 5.7 Hz, H-3), 5.81 (d, J = 6.0 Hz, H-7), 6.07 (dd, J = 5.7, 1.5 Hz, H-1), 6.64 (d, J = 8.0 Hz, H-10), 6.78 (dd, J = 7.6, 0.7 Hz, H-12), 7.19 (t, J = 7.8 Hz, H-11). ¹³C NMR (100 MHz, CDCl₃): δ = 14.8, 25.4, 40.5, 73.6, 73.8 (J_{C-H} = 210.9 Hz), 82.5, 86.0, 99.6 (J_{C-H} = 168.0 Hz), 107.0, 120.4, 123.2, 130.9, 143.5, 160.8, 202.3.

Small amounts of **1** (0.7 mg, 6%) and the isomeric propargyl bromides (1.0 mg, 8%) were also isolated.

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