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Supporting Information

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Supporting Information

Efficient Total Syntheses of (–)-Colombiasin A and (–)-Elisapterosin B: Application of the Cr-Catalyzed Asymmetric Quinone Diels-Alder Reaction

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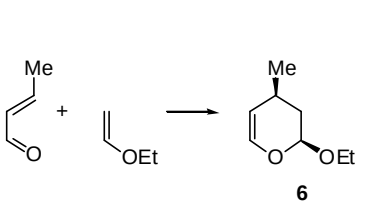
Part 1. Experimental Procedures and Analytical Data
a. General Procedures

Analytical thin-layer chromatography (TLC) was performed on silical gel 60 F_{254} precoated plates (0.25 mm thickness). Visualization was accomplished by irradiation with a UV light and/or staining with anisaldehyde, ceric ammonium molybdate (CAM), or $KMnO_4$ solutions. Flash chromatography was performed using silica gel 60 (230-400 mesh) from EM Science or Davisil (grade 643, 200-425 mesh, 150 A) from Aldrich. Proton and carbon NMR spectra were recorded on a Varian Mercury-400 (400 MHz), Inova-500 (500 MHz), or an Inova-600 (600 MHz) spectrometer. Proton chemical shifts are reported in ppm (δ) relative to tetramethylsilane (TMS) with the respective solvent resonance employed as the internal standard ($CDCl_3$, δ 7.26 ppm; C_6D_6, δ 7.16 ppm). Data are reported as follows: chemical shift (multiplicity [singlet (s), doublet (d), triplet (t), quartet (q), and multiplet (m), broad (br)], coupling constants [Hz], integration). Carbon chemical shifts are reported in ppm (δ) relative to TMS with the respective solvent resonance as the internal standard ($CDCl_3$, δ 77.0). NMR data were collected at ambient temperature. Infrared spectra were obtained as thin films between NaCl plates on a Matteson FTIR 3000. Optical rotations were measured using a 2 mL cell with a 1 dm length on a Jasco DIP 370 polarimeter. Mass spectra were obtained at the Mass Spectrometry Facilities of Harvard University (Cambridge, MA). The method of ionization is given in parentheses. Analytical HPLC was performed on a Shimadzu VP-series instrument employing a dual-wavelength UV detector (214, 254 nm) and the column specified in the individual experiment. Analytical GC analysis was performed on a Hewlett-Packard 5890 Series II gas chromatograph, equipped with an FID detector and an HP 3396 integrator, using the column specified in the experiment.

All reactions were carried out under inert atmosphere employing oven- and flame-dried glassware. Unless otherwise stated, all reagents were purchased from Aldrich, Alfa Aesar or Strem and used without further purification. All solvents were distilled from appropriate drying agents prior to use. 5 Å molecular sieves (3.2 mm pellet, Aldrich) were crushed and dried in a vacuum oven (135 °C) prior to use. Quinone **3**[†] was prepared by the literature procedures and was purified by flash chromatography before use. (Note: quinone **3** is quite volatile and prone to sublimation, even at 0 °C, and so should be chromatographed with 5% Et_2O/pentanes and be stored at -30 °C.) Catalysts **9**[‡] and **12**[§] were prepared as previously reported. 1-Bromo-1-propene (*cis:trans* = 1:1) was distilled over CaH_2; methyltriphenylphosphonium bromide was dried by heating under vacuum at 110 °C overnight; TESCl was purified by distillation over CaH_2; MeI was purified by filtration over Al_2O_3, distillation, and was stored over Cu; CS_2 was purified by distillation over CaH_2 in the dark; 2-methyl-3-buten-2-ol was purified by distillation over CaH_2; $BF_3 \cdot Et_2O$ was distilled over CaH_2 and stored over CaH_2. *All quinones were manipulated in the dark and chromatographed rapidly to minimize decomposition.*

[†] a) I.M. Godfrey, M.V. Sargent, J.A. Elix, *J.Chem. Soc. Perkins 1* **1974**, 1353-1354. b) J.R. Luly, H.Rapoport, *J. Org. Chem.* **1981**, *46*, 2745-2752.
[‡] K. Gademann, D. E. Chavez, E. N. Jacobsen, *Angew. Chem. Int. Ed.* **2002**, *41*, 3059-3061
[§] See adjoining communication: E.R. Jarvo, B.M. Lawrence, E.N. Jacobsen, *Angew. Chem. Int. Ed.*

b. Experimental Procedures and Analytical Data



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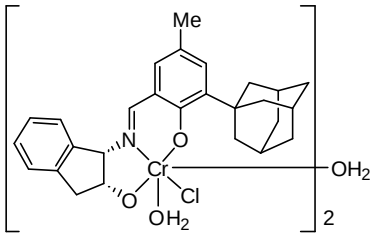
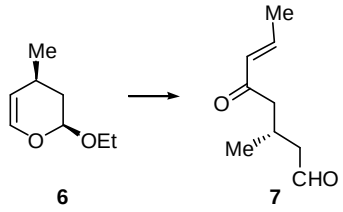


(1*S*, 2*R*)-**8**

To a solution of freshly distilled *trans*-crotonaldehyde (8.38 mL, 0.101 mol, 1.00 equiv.) and ethyl vinyl ether (96.9 mL, 1.01 mol, 10.0 equiv.) was added in one portion a mixture of dry MS 4Å (15.2 g) and (1*S*, 2*R*)-**8** (2.60 g, 2.53 mmol, 0.025 equiv. 2.5 mol%). The resulting brown mixture was kept at rt for 12 h and then diluted with 500 mL of pentane and triturated for 1h. The suspension was filtered through a plug of celite and washed three times with 100 mL of pentane. The solvent was removed by distillation (60 °C) and the resulting brown oil was distilled under reduced pressure (76-80 °C, 30 mmHg) to give a colorless oil (11.6 g, 80.5%) with spectral data that are identical to those reported in the literature. The ee of the product was determined to be 93% by the method reported in the literature.[**]



6 **7**

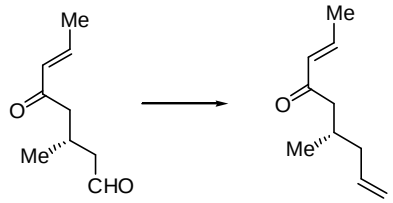
To a solution of dihydropyran **6** (2.85 g, 20.0 mmol, 1.00 equiv.) in 8 mL of THF at -78 °C was added dropwise *t*-BuLi (1.75 M in pentane, 17.2 mL, 30.1 mmol, 1.50 equiv.). After the addition was complete the yellow suspension was warmed to 0 °C at which time the solid material went into solution. The mixture was kept at this temperature for 30 minutes. This organolithium was transfered via cannula to a solution of $ZnCl_2$ (5.46 g, 40.1 mmol, 2.00 equiv., fused under vacum) in 50 mL of THF. After complete addition of the organolithium, the reaction was warmed to rt for 30 minutes. The intermediate organozinc was transferred via cannula to a solution of $Pd(PPh_3)_4$ (579 mg, 0.500 mmol, 0.0250 equiv.) and 1-bromo-1-propene (7.0 mL, 82 mmol, 4.0 equiv., *cis:trans* = 1:1) in 90 mL of THF. The yellow reaction mixture was stirred at rt for approximately 2-3 h, during which time the color changed from light yellow to orange with formation of a white precipitate.

The intermediate pyran was not isolated (R_f = 0.50, 5% EtOAc/hexanes; the R_f of the starting material and this intermediate are the same). A cooled (<10 °C) aqueous solution of HCl (0.5 M, 90 mL) was added to the reaction mixture and the reaction was let stand

[**] K. Gademann, D. E. Chavez, E. N. Jacobsen, *Angew. Chem. Int. Ed.* **2002**, *41*, 3059-3061.

for 1 h and allowed to warm to rt. The mixture was extracted three times with Et_2O, washed with $NaHCO_3$(sat), dried with anhydrous $MgSO_4$ and filtered. Careful concentration under reduced pressure (the water bath of the rotary evaporator should be kept below 20 °C at all times) gave an orange oil which was chromatographed with 20% EtOAc/hexanes to give a light yellow oil (2.50 g, 80.9%). *Note: this product is somewhat volatile.*

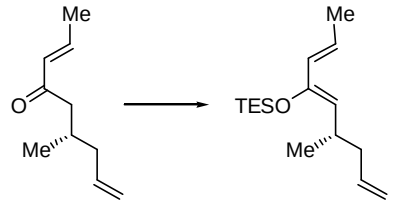
^{1}H NMR ($CDCl_3$, 600 MHz) δ 9.68 (t, *J* = 1.9 Hz, 1H), 6.81 (dq, *J* = 6.8, 15.8 Hz, 1 H), 6.05 (dd, *J* = 1.4, 15.8 Hz, 1H), 2.57 (septet, *J* = 6.7 Hz, 1H), 2.51(dd, *J* = 6.6, 15.9 Hz, 1H), 2.42 (ddd, *J* = 1.5, 6.0, 16.6 Hz, 1H), 2.41 (dd, *J* = 6.9, 15.9 Hz, 1H), 2.26 (ddd, *J* = 2.3, 7.3, 16.7 Hz, 1H), 1.84 (dd, *J* = 1.6, 6.9 Hz, 3H), 0.94 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 150 MHz) δ 201.9, 198.9, 143.0, 131.9, 50.3, 46.1, 24.3, 20.1, 18.1; **IR** (thin film) 3037, 2962, 2938, 2916, 2879, 2828, 2726, 1723, 1695, 1671, 1632; **TLC R_f** 0.25 (20% EtOAc/hexanes); **[a]$_D^{25}$** +4.57 (*c*= 1.99; $CHCl_3$); **MS** (CI^+) calc. for $C_9H_{18}O_2N$ ($M+NH_4$) 172.1338, found 172.1341.



7

Solid methyltriphenylphosphonium bromide (3.65 g, 10.2 mmol, 1.05 equiv.) was added portionwise to a suspension of KHMDS (1.94 g, 9.73 mmol, 1.00 equiv.) in 70 mL of PhMe at 0 °C. The yellow suspension was kept at 0 °C for 1 h then cooled to -78 °C. A solution of aldehyde **7** (1.50 g, 9.73 mmol, 1.00 equiv.) in 20 mL of PhMe at -78 °C was quickly transfered by cannula to the ylide. An additional 10 mL of PhMe was used to rinse any remaining aldehyde into the reaction flask. The yellow-orange suspension was slowly warmed to 0 °C over 3 hours, after which time the reaction mixture was directly purified by silica gel chromatography, eluting the toluene with pentanes then eluting the enone with 20% Et_2O/pentanes. After distillation to remove the solvent a yellow oil was obtained. The crude enone was purified by Kügelrohr distillation (200-225 °C, 30 mmHg) to provide a colorless oil (1.21 g, 81.7 %): *Note: this product is very volatile.*

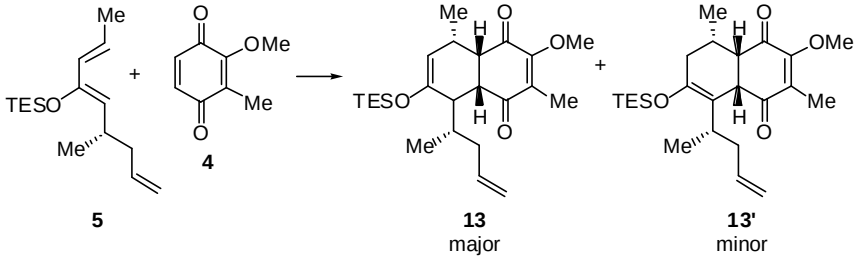
^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.80 (dq, *J* = 6.9, 15.7Hz, 1H), 6.08 (dq, *J* = 1.7, 15.8 Hz, 1H), 5.73 (m, 1H), 4.99 (s, 1H), 4.96 (d, *J* = 3.5 Hz, 1H), 2.50 (dd, *J* = 5.6, 15.5 Hz, 1H), 2.28 (dd, *J* = 8.2, 15.5 Hz, 1H), 2.09 (octet, *J* = 6.7 Hz, 1H), 2.00 (m, 1H), 1.96 (m, 1H), 1.86 (dd, *J* = 1.6, 6.9 Hz, 3H), 0.88 (d, 6.4 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 200.2, 142.3, 136.6, 132.3, 116.4, 46.5, 41.2, 29.3, 19.7, 18.1; **IR** (thin film) 3077, 3037, 2959, 2915, 2876, 1696, 1674, 1634, 1442, 1376, 1295, 1188, 971, 913; **TLC R_f** 0.35 (5% EtOAc/hexanes); **[a]$_D^{25}$** +0.76 (*c*= 1.71; $CHCl_3$); **MS** (CI^+) calc. for $C_{10}H_{20}ON$ ($M+NH_4$) 170.1545, found 170.1541.



5

Silyl enol ether formation was performed according to the literature procedure.[††] A solution of the enone in 18 mL of THF (554 mg, 3.64 mmol, 1.00 equiv., precooled to -78 °C) was added dropwise via cannula to a solution of KHMDS (1.09 g, 5.46 mmol, 1.50 equiv.) in 18 mL of THF cooled to -78 °C. The solution was kept at -78 °C for 30 min at which time TESCl (917 μL, 5.74 mmol, 1.58 equiv.) was added. The solution was stirred at -78 °C for 1 h then the reaction mixture was neutralized with $NaHCO_3$ (sat), extracted three times with EtOAc and dried over anhydrous Na_2SO_4. Filtration and evaporation under reduced pressure gave a colorless oil. *Note: this product is quite volatile.* This oil was purified by chromatography using Davisil, eluting with hexanes to give a colorless oil (871 mg, 89.8%, 90% desired isomer). Note: while diene isomers may be partially separated by chromatography, purification should be performed rapidly to prevent decomposition of the product upon prolonged exposure to silica gel. The ratio of diene isomers was determined by GC [HP-5 column (30 m, 0.32 mm I.D., 0.25 micron filter), 10 psi, temperature gradient: 0-4 min at 100 °C, ramp 15 °C/min to 200 °C, 25 °C/min to 280 °C, hold for 1.2 min. Major (desired) isomer: t_r= 7.9 min, minor isomers: t_r = 8.0, 8.05, 8.1 min. Note: if the enone starting material is not purified by distillation, a minor enone sideproduct from the olefination will carry over and will be silated to afford sideproducts. These sideproducts may be observed using the above GC assay: t_r= 14.2, 14.3, 14.4 min).

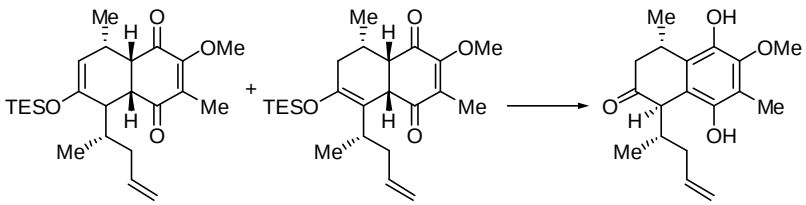
^{1}H NMR ($CDCl_3$, 600 MHz) δ 5.84 (d, *J* = 16.1 Hz, 1H), 5.77 (m, 2H), 5.00 (d, *J* = 15.8 Hz, 1H), 4.97 (d, *J* = 11.1 Hz, 1H), 4.48 (d, *J* = 9.7 Hz, 1H), 2.63 (m, 1H), 2.07 (m, 1H), 2.00 (m, 1H), 1.74 (d, *J* = 6.4 Hz, 3H), 0.99 (t, *J* = 7.9 Hz, 9H), 0.96 (d, *J* = 6.7 Hz, 3H), 0.70 (q, *J* = 8.0 Hz, 6H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 147.4, 137.2, 130.3, 123.5, 118.4, 115.6, 41.8, 30.0, 20.3, 17.6, 6.9, 5.5; **IR** (thin film) 2958, 2937, 2914, 2879, 1641, 1625, 1457, 1378, 1358, 1307, 1239, 1193, 1004, 960, 911, 739; **TLC R_f** 0.20 (hexanes); **[a]$_D^{25}$** -22.2 (*c*= 1.45; $CHCl_3$); **MS** (EI^+) calc. for $C_{16}H_{30}OSi$ (M+) 266.2066, found 266.2020.



[††] M. Arisawa, Y. Torisawa, M. Nakagawa, *Synthesis*, **1995**, 1371-1372.

A 25 mL round bottomed flask charged with 5 Å molecular sieves (174 mg) was flame-dried *in vacuo.* (1*R*,2*S*)-Catalyst **12** (835 mg, 0.33 mmol, 10 mol%), quinone **4** (505 mg, 3.33 mmol, 1.00 equiv) and toluene (3.3 mL) were added and the mixture was stirred at room temperature for 10 min, then cooled to 0 °C (for 10 min). Diene **5** (1.08 g, 3.65 mmol, 1.10 equiv., 90% desired isomer) was added dropwise via syringe pump over 2 h. Reaction progress was monitored by TLC; after 24 h all quinone **4** had been consumed. The reaction mixture was directly purified by chromatography using Davisil, eluting with 5% EtOAc/hexanes, to provide the product, an orange oil, (1.20 g, 86.4%), as a mixture of olefin isomers (**13** and **13'**).

^{1}H NMR ($CDCl_3$, 600 MHz) δ 5.77 (m, 1H, major), 5.69 (m, 1H, minor), 4.97 (overlapping m and d, 3 H, major and minor), 4.91 (d, *J* = 10.3 Hz, 1H, minor), 4.49 (t, *J* = 2.8 Hz, 1H, major), 3.96 (s, 3H, major), 3.93 (s, 3H, minor), 3.56 (dt, *J* = 2.3, 5.6 Hz, 1H, minor), 3.28 (dd, *J* = 4.1, 5.9 Hz, 1H, major), 3.15 (dd, *J* = 5.9, 8.5 Hz, 1H, major), 2.82 (dd, *J* = 3.2, 5.6 Hz, 1H, minor), 2.76 (m, 1H, major), 2.73 (q, *J* = 7.4 Hz, 1H, minor), 2.62 (br d, *J* = 13.8 Hz, 1H, major), 2.41 (m, 1H, major), 2.25 (m, 2H, minor), 2.18 (m, 2H, minor), 2.06 (m, 2H, major and minor), 1.94 (s, 3H, minor), 1.88 (s, 3H, major), 1.75 (dt, *J* = 9.0, 13.7 Hz, 1H, major), 1.12 (d, *J* = 7.0 Hz, 3H, minor), 0.98 (t, *J* = 8.0 Hz, 9 H, major), 0.97 (t, *J* = 7.9 Hz, 9 H, minor), 0.91 (d, *J* = 7.0 Hz, 3H, minor), 0.87 (d, *J* = 7.3 Hz, 3H, major), 0.79 (d, *J* = 7.0 Hz, 3H, major), 0.71 (q, *J* = 7.7 Hz, 3H, major), 0.70 (q, *J* = 8.0 Hz, 3H, major), 0.66 (q, *J* = 7.9 Hz, 6H, minor); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 201.1 (minor), 198.6 (major), 197.4 (major), 195.3 (minor), 159.3 (major), 158.6 (minor), 152.1 (major), 146.1 (minor), 138.3 (minor), 137.7 (major), 135.3 (major), 133.2 (minor), 116.4 (minor), 115.6 (major), 114.8 (minor), 104.8 (major), 59.9 (minor), 59.6 (major), 52.4 (minor), 51.6 (major), 50.3 (minor), 49.2 (major), 44.6 (major), 42.6 (major), 38.1 (minor), 36.4 (minor), 32.9 (minor), 32.0 (minor), 30.8 (major), 30.6 (major), 19.8 (major), 18.0 (minor), 17.9 (minor), 17.5 (major), 10.0 (minor), 9.6 (major), 6.6 (major), 5.7 (minor), 4.9 (major and minor); **IR** (thin film) 2958, 2914, 2878, 1681, 1638, 1607, 1459, 1374, 1310, 1241, 1195, 1139, 1006, 744; **TLC R_f** 0.35 (5% EtOAc/hexanes); **[α]$_D^{25}$** +6.381 (*c*= 5.055; $CHCl_3$); **MS** (ES^+) calc. for $C_{24}H_{39}O_4Si$ (M+H) 419.2617, found 419.2606.

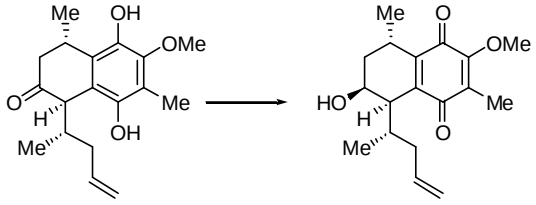


13 **13'** **14**

Concentrated HCl (5.9 mL) was added dropwise to a cooled (0 °C) solution of **13** and **13'** (620 mg, 1.48 mmol, 1.00 equiv.) in 5.9 mL of MeOH. The reaction was allowed to warm to rt and stirred for 9 h. The heterogeneous reaction mixture was poured into 10 mL of H_2O, extracted five times with CH_2Cl_2 and dried over anhydrous Na_2SO_4.

Filtration and evaporation under reduced pressure gave a yellowish solid that is somewhat air sensitive. This solid was thus reduced without purification. Ketone **14** could be crystallized from EtOAc/hexanes to afford material (as white needles) that was analytically pure (see characterization below). Single crystals suitable for x-ray crystallography were obtained by slow evaporation of a solution in EtOAc over hexanes (solvents were degassed and crystalization was performed under an atmosphere of argon). See Part 2 for full details.

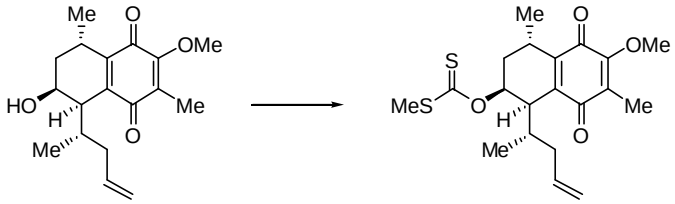
^{1}H NMR ($CDCl_3$, 600 MHz) δ 5.89 (m, 1H), 5.37 (s, 1H), 5.15 (d, *J* = 16.4 Hz, 1H), 5.08 (d, *J* = 10.2 Hz, 1H), 4.21 (s, 1H), 3.77 (s, 3H), 3.75 (quintet, *J* = 7.2 Hz, 1H), 3.57 (d, *J* = 4.4 Hz, 1H), 2.89 (dd, *J* = 7.1, 13.3 Hz, 1H), 2.51 (m, 1H), 2.39 (d, *J* = 13.5 Hz, 1H), 2.33 (dt, *J* = 6.8, 13.8 Hz, 1H), 2.17 (s, 3H), 1.96 (dt, *J* = 7.2, 14.4 Hz, 1H), 1.10 (d, *J* = 7.0 Hz, 3H), 0.80 (d, *J* = 7.3 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 211.2, 144.6, 143.7, 139.6, 137.4, 126.2, 120.3, 116.8, 114.9, 61.1, 51.7, 46.8, 39.3, 35.9, 31.0, 22.7, 17.0, 9.2; **IR** (thin film) 3346, 3081, 2958, 2933, 2865, 2836, 1693, 1642, 1613; **TLC R_f** 0.45 (30% EtOAc/hexanes); **[a]$_D^{25}$** -30.5 (*c*= 0.75; $CHCl_3$); **MS** (ES^+) calc. for $C_{18}H_{25}O_4$ (M+H) 305.1753, found 305.1750; **m.p.** 215-217 °C (dec.).



14 **15**

To a solution of crude ketone **14** in 14.8 mL of degassed MeOH was added $CeCl_3 \cdot 7H_20$ (608 mg, 1.63 mmol, 1.10 equiv.) and after complete dissolution (5-10 min.) the reaction was cooled to -78 °C. $NaBH_4$ (280 mg, 7.40 mmol, 5.00 equiv.) was added in three portions to this solution and the reaction was stirred at -78 °C for 1 hour. The septum was removed (allowing the reaction to stir under air) and the solution was warmed to rt. After complete oxidation of the hydroquinone as judged by TLC (after approximately 2-3 hours) the brown solution was neutralized with $NaHCO_3$ (sat), extracted five times with CH_2Cl_2 and dried over anhydrous Na_2SO_4. Filtration and evaporation under reduced pressure gave a red oil that was chromatographed using Davisil, eluting with 20% EtOAc/hexanes to afford alcohol **15** as a bright yellow oil (338 mg, 75.0%, >95% pure).

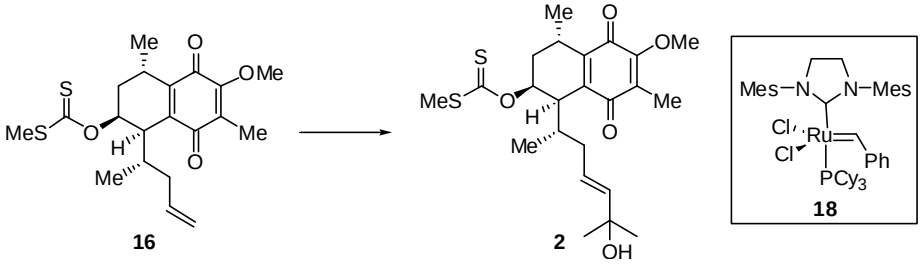
^{1}H NMR ($CDCl_3$, 600 MHz) δ 5.65 (m, 1H), 4.90 (d, *J* = 4.1 Hz, 1H), 4.87 (d, *J* = 11.7 Hz, 1H), 4.07 (m, 1H), 3.96 (s, 3H), 3.08 (m, 2H), 1.92 (overlapping s and m, 6H), 1.59 (m, 2H), 1.15 (d, *J* = 7.3 Hz, 3H), 1.11 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 188.3, 182.9, 155.6, 144.2, 143.2, 138.1, 128.6, 115.7, 66.8, 60.8, 42.6, 39.9, 33.7, 32.5, 28.4, 21.9, 21.6, 8.9; **IR** (thin film) 3503, 3499, 3481, 2964, 2937, 2876, 1651, 1608; **TLC R_f** 0.30 (20% EtOAc/hexanes); **[a]$_D^{25}$** +97.6 (*c*= 1.46; $CHCl_3$); **MS** (ES^+) calc. for $C_{18}H_{25}O_4$ (M+H) 305.1753, found 305.1744.



15 **16**

To a solution of **15** (149 mg, 0.49 mmol, 1.00 equiv.) in THF (5 mL) was added NaH, in three portions (94.0 mg, 2.45 mmol, 5.00 equiv., 60% dispersion in oil). The reaction was stirred at rt for 0.5 h. CS_2 (935 µL, 15.5 mmol, 31.0 equiv.) was added dropwise and the reaction was stirred for an additional 0.5 h, after which time MeI (777 µL, 12.5 mmol, 25.0 equiv.) was added dropwise, and the reaction mixture was stirred in the dark for 9 h. The yellow-brown solution was neutralized with $NaHCO_3$ (sat), extracted three times with EtOAc, and dried over anhydrous Na_2SO_4. Filtration and evaporation under reduced pressure gave a red oil. This oil was purified by chromatography using Davisil, eluting with 5% EtOAc/hexanes to afford xanthate **16** as a bright yellow oil (162.0 mg, 83.9%). *Note:* purification should be performed rapidly to prevent decomposition of the product upon prolonged exposure to silica gel. The thiocarbonate may be formed as a minor biproduct (<5%) upon prolonged exposure to adventitious water, however, this impurity may be easily separated from the more stable cyclized **17**.

^{1}H NMR ($CDCl_3$, 600 MHz) δ 5.92 (ddd, *J* = 3.4, 5.3, 12.7 Hz, 1H), 5.69 (m, 1H), 4.94 (s, 1H), 4.91 (d, *J* = 7.6 Hz, 1H), 3.98 (s, 3H), 3.44 (m, 1H), 3.18 (quintet, *J* = 6.7 Hz, 1H), 2.58 (s, 3H), 2.17 (dt, *J* = 6.4, 12.8 Hz, 1H), 1.99 (m, 1H), 1.94 (s, 3H), 1.84 (br d, *J* = 12.9 Hz, 1H), 1.69 (m, 1H), 1.23 (d, *J* = 7.0 Hz, 3H), 1.08 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 215.1, 187.8, 182.6, 155.6, 144.2, 142.1, 137.8, 128.8, 116.0, 79.0, 60.8, 39.9, 39.5, 34.2, 30.3, 28.5, 21.5, 20.5, 19.0, 8.9; **IR** (thin film) 2965, 2936, 1650, 1610, 1294, 1221; **TLC R_f** 0.3 (5% EtOAc/hexanes); **[α]$_D^{25}$** +78.4 (*c*= 3.65; $CHCl_3$); **MS** (ES^+) calc. for $C_{20}H_{27}O_4S_2$ (M+H) 395.1351, found 395.1351.

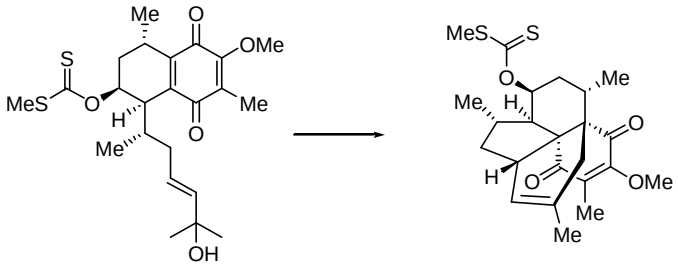


16 **2** **18**

To a solution of terminal olefin **16** (128 mg, 0.320 mmol, 1.00 equiv.) in CH_2Cl_2 (160 µL) was added 2-methyl-3-buten-2-ol (169 µL, 1.62 mmol, 5.00 equiv.) and Grubbs' second generation catalyst **18** (28 mg, 33 µmol, 0.10 equiv.). The red reaction mixture was stirred at rt for 24 h then directly purified by chromatography using Davisil, eluting with 30% EtOAc/hexanes to yield **2**, as a bright yellow oil (127 mg, 86.5%). *Note:* purification should be performed rapidly to prevent decomposition of the product upon prolonged exposure to silica gel. The thiocarbonate may form as a minor biproduct

(<5%) upon prolonged exposure to adventitious water, however, this impurity may be easily separated from the more stable cyclized **17**.

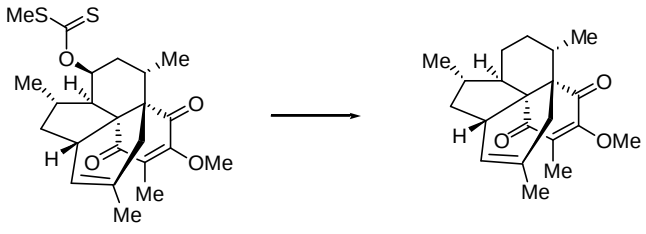
^{1}H NMR ($CDCl_3$, 600 MHz) δ 5.92 (ddd, *J* = 3.5, 5.6, 12.9 Hz, 1H), 5.51 (m, 2H), 3.97 (s, 3H), 3.43 (br m, 1H), 3.16 (quintet, *J* = 6.7 Hz, 1H), 2.57 (s, 3H), 2.17 (dt, *J* = 6.3, 13.0 Hz, 1H), 1.92 (overlapping s and m, 5H), 1.82 (br d, *J* = 12.6 Hz, 1H), 1.65 (m, 1H), 1.25 (s, 3H), 1.24 (s, 3H), 1.21 (d, *J* = 7.0 Hz, 3H), 1.05 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 215.1, 187.7, 182.6, 155.6, 144.2, 142.0, 139.6, 128.7, 126.1, 78.9, 70.4, 60.8, 39.3, 38.2, 34.5, 30.3, 29.8, 29.7, 28.4, 21.5, 20.4, 19.0, 8.9; **IR** (thin film) 3453, 2968, 2932, 2875, 1649, 1609, 1451, 1374, 1293, 1222, 1058; **TLC R_f** 0.40 (30% EtOAc/hexanes); **[a]$_D^{25}$** +65.8 (*c*= 0.35; $CHCl_3$); **MS** (ES^+) calc. for $C_{23}H_{36}O_5S_2N$ ($M+NH_4$) 470.2035, found 470.2037.



2 **17**

To a solution of the tertiary alcohol **2** (56.2 mg, 0.124 mmol, 1.00 equiv.) in benzene (2.5 mL) was added anhydrous $MgSO_4$ (374 mg, 3.11 mmol, 25.0 equiv.) and the reaction mixture was stirred and heated to vigorous reflux for 3 h. The mixture was cooled to room temperature and filtered through celite, washing with benzene. Purification by silica gel chromatography, eluting with benzene afforded **17**, an off-white solid (41.5 mg, 76.9%, R_f = 0.40, benzene).

Spectral data (^{1}H, ^{13}C NMR) matched those reported in the literature.[‡‡] $[\alpha]_D^{25}$ -113 (c=3.8, $CDCl_3$); literature $[\alpha]_D^{25}$ (Nicolaou and coworkers) -90.3 (c=3.6, $CDCl_3$).



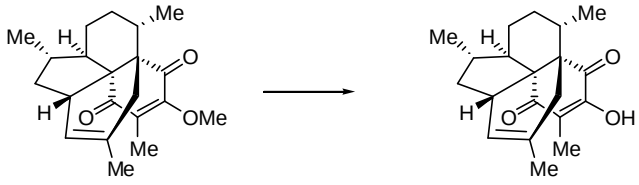
17

The deoxygenation was performed according to the following procedure, a modification of that reported by Nicolaou. To a solution of xanthate **17** (26.2 mg, 60.0 μmol, 1.00

[‡‡] a) K. C. Nicolaou, G. Vassilikogiannakis, W. Magerlein, R. Kranich, *Angew. Chem. Int. Ed.* **2001**, *40*, 2482-2486; *Angew. Chem.* **2001**, *113*, 2543-2547. b) K. C. Nicolaou, G. Vassilikogiannakis, W. Magerlein, R. Kranich, *Chem. Eur. J.* 2001, 7, 5359-5371.

equiv.) in PhMe (4.3 mL) in a Smith Process Vial™ (2-5 mL, Personal Chemistry), was added *n*-Bu_3SnH (81 µL, 0.30 mmol, 5.00 equiv.) and a freshly-made solution of AIBN (81 µL, 6.0 µmol, 0.10 equiv., in PhMe (10 mg /mL)). The mixture was degassed by bubbling argon through it for 30 min. The reaction flask was then sealed and immersed into a 110 °C oil bath with high stirring for 30 min. After cooling, the reaction mixture was concentrated and the tin byproducts were removed by silica gel chromatography, eluted with hexanes and the desired product was eluted with 5% EtOAc/hexanes. This afforded *O*-methyl-colombiasin A as a yellowish oil (>90% pure as judged by ^1H NMR) that was used directly without further purification.

Purification of a sample by silica gel chromatography, eluting with 5% EtOAc/hexanes afforded analytically pure material for characterization. Spectral data (^1H, ^{13}C NMR) matched those reported in the literature.[‡‡,§§] $[\alpha]_D^{25}$ -213 (c=0.49, $CDCl_3$); literature $[\alpha]_D^{25}$ (Nicolaou and coworkers) -168.2 (c=1.1, $CDCl_3$).



(-)-Colombiasin A

The demethylation was performed according to the following procedure, a modification of that reported by Rychnovsky.[§§] *O*-Methyl-colombiasin A was dissolved in CH_2Cl_2 (1.2 mL), cooled to 0 °C, and *N*,*N*-dimethylaniline (46 µL, 0.36 mmol, 6.00 equiv.) and solid $AlCl_3$ (40 mg, 0.30 mmol, 5.00 equiv.) were added. The orange solution was warmed to rt to furnish a deep green solution that was stirred for 30 min. The solution was diluted with CH_2Cl_2, acidified with 1 N HCl, extracted three times with CH_2Cl_2 and the combined organic phases were dried over anhydrous Na_2SO_4. Filtration and concentration under reduced pressure gave a light brown product that was dissolved in a minimal amount of $CHCl_3$ and applied to silica gel chromatography, eluting with 10% EtOAc/hexanes, to yield (–)-colombiasin A as a yellowish film (12.6 mg, 66.5% over two steps from **17**).

Spectral data were in agreement with those reported in the literature and are reported below. ^1H spectra for synthetic and natural (–)-colombiasin A are shown below, and ^1H and ^{13}C spectra and $[\alpha]_D^{25}$ values for synthetic and natural colombiasin A are tabulated below. Representative nOe's that confirm the relative stereochemistry of our synthetic material are also shown below. While our optical rotation differs from that of natural and synthetic material prepared by other groups, we believe that the spectral data and X-ray crystal structure of intermediate **14** confirm our structural assignment. We suggest that a minor impurity may strongly influence the value of the optical rotation.

[§§] A. I. Kim, S. D. Rychnovsky, *Angew. Chem. Int. Ed.* **2003**, *42*, 1267-1270

^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.90 (s, 1H), 5.68 (br s, 1H), 3.05 (br m, 1H), 2.41 (br d, *J* = 18.7 Hz, 1H), 2.13 (dt, *J* = 11.8, 9.0 Hz, 1H), 1.96-1.92 (m, 2H), 1.91 (br d, *J* = 18.7 Hz, 1H), 1.91 (s, 3H), 1.88-1.81 (m, 3H), 1.58 (m, 1H), 1.57 (br s, 3H), 1.37 (d, *J* = 7.0 Hz, 3H), 1.35-1.25 (m, 2H), 0.81 (d, *J* = 7.3 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 202.6, 199.6, 149.5, 128.9, 123.8, 120.3, 64.0, 51.6, 48.2, 39.5, 38.7, 36.3, 33.6, 33.5, 31.8, 31.1, 22.8, 22.1, 17.7, 9.8; **IR** (thin film) 3383, 2961, 2929, 2878, 1668, 1451, 1381, 1344; **TLC R_f** 0.45 (10% EtOAc/hexanes); **MS** (ES^+) calc. for $C_{20}H_{30}O_3N$ ($M+NH_4$) 332.2226, found 332.2231.

$[\alpha]_D^{25}$ -158 (c=0.1, $CHCl_3$);
literature $[\alpha]_D^{25}$ (natural material, Rodriguez and coworkers[***]) -55.3 (c=0.9, $CHCl_3$); literature $[\alpha]_D^{25}$ (synthetic material, Nicolaou and coworkers[‡‡b]) -61.0 (c=0.1, $CHCl_3$); literature $[\alpha]_D^{25}$ (synthetic material, Harrowven and coworkers[†††]) -58.7 (c=0.15, $CHCl_3$).

Table SI-1. Comparison of ^{1}H and ^{13}C NMR spectral data for natural and synthetic (–)-colombiasin A.

^{13}C NMR	
Rodriguez (75 MHz) (Natural material)	**Jacobsen (100 MHz) (Present work)**
202.6	202.6
199.6	199.6
149.5	149.5
128.9	128.9
123.9	123.8
120.4	120.3
64.0	64.0
51.6	51.6
48.2	48.2
39.5	39.5
38.7	38.7
36.3	36.3
33.6	33.6
33.5	33.5
31.8	31.8
31.1	31.1
22.8	22.8
22.1	22.1
17.7	17.7
9.7	9.8

^{1}H NMR	
Rodriguez (300 MHz) (Natural material)	**Jacobsen (600 MHz) (Present work)**
0.81 (d, *J* = 7.3 Hz, 3H)	0.81 (d, *J* = 7.3 Hz, 3H)
1.25 (m, 1H)	1.35-1.25 (m, 2H)
1.30 (m, 1H)	
1.37 (d, *J* = 7.0 Hz, 3H)	1.37 (d, *J* = 7.0 Hz, 3H)
1.57 (br s, 3H)	1.57 (br s, 3H)
1.59 (m, 1H)	1.58 (m, 1H)
1.82 (m, 1H)	1.88-1.81 (m, 3H)
1.83 (m, 1H)	
1.86 (m, 1H)	
1.90 (s, 3H)	1.91 (s, 3H)
1.91 (br d, *J* = 18.5 Hz, 1H)	1.91 (br d, *J* = 18.7 Hz, 1H)
1.93 (m, 1H)	1.96-1.92 (m, 2H)
1.93 (m, 1H)	
2.13 (ddd, *J* = 11.7, 9.0, 2.5 Hz, 1H)	2.13 (dt, *J* = 11.8, 9.0 Hz, 1H)
2.41 (br d, *J* = 18.5 Hz, 1H)	2.41 (br d, *J* = 18.7 Hz, 1H)
3.05 (br m, 1H)	3.05 (br m, 1H)
5.68 (br s, 1H)	5.68 (br s, 1H)
6.91 (br s, 1H)	6.90 (s, 1H)

[***] A. D. Rodríguez, C. Ramirez, *Org. Lett.* **2000**, *2*, 507-510.
[†††] D. C. Harrowven, D. D. Pascoe, D. Demurtas, H. O. Bourne, *Angew. Chem. Int. Ed.* **2005**, *44*, 1221-1222.

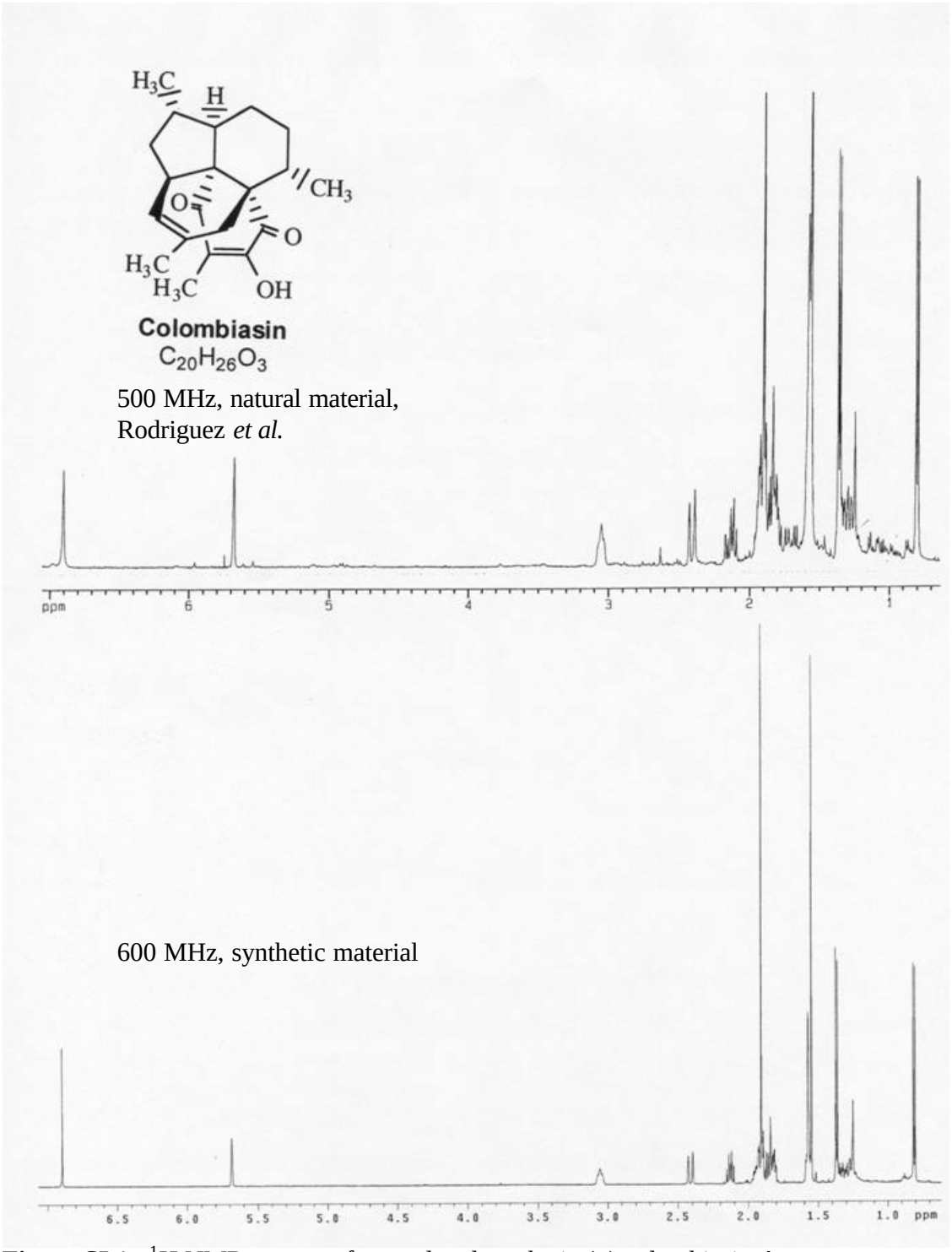


Figure SI-1. ^{1}H NMR spectra of natural and synthetic (–)-colombiasin A.

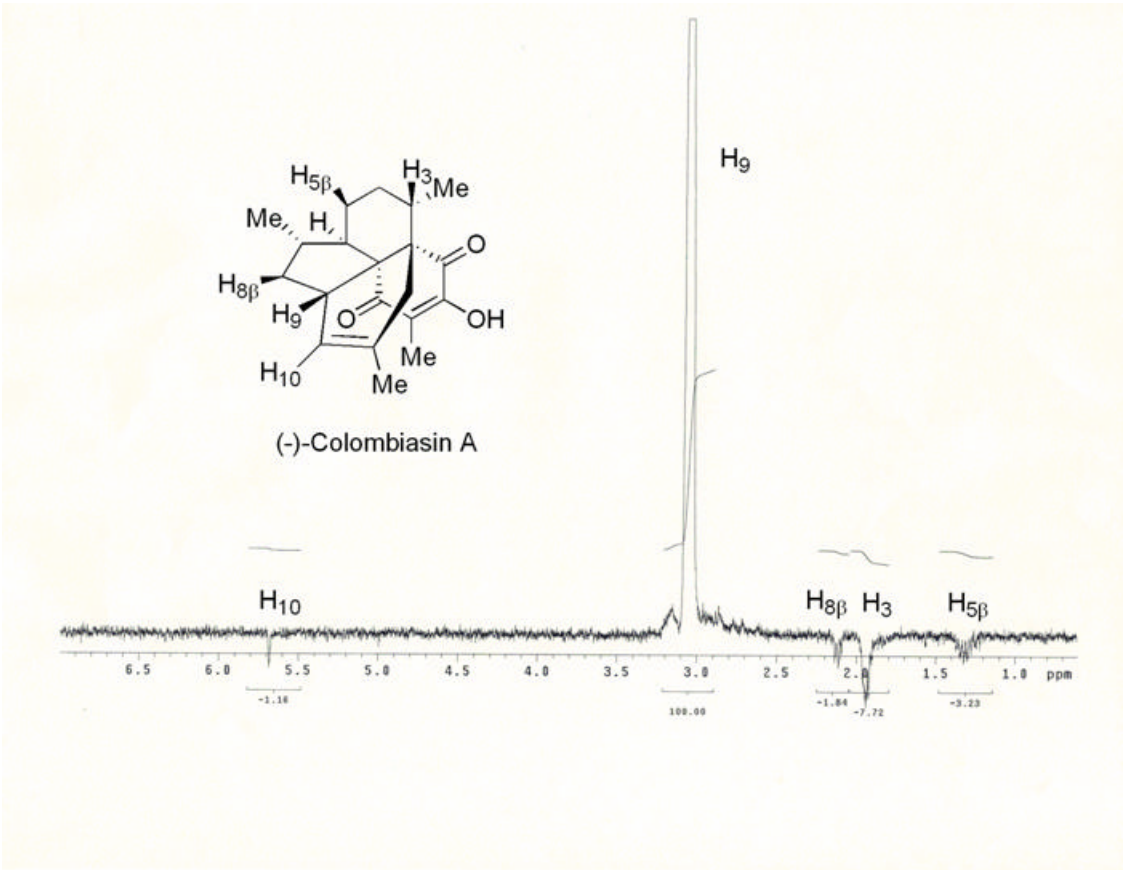
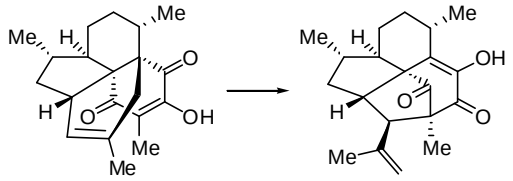


Figure SI-2. 1-D nOe spectrum of synthetic (–)-colombiasin A, irradiating at 3.05 ppm (H_9).



(-)-Colombiasin A (-)-Elisapterosin B

To a solution of (–)-colombiasin A (3.1 mg, 9.9 μmol, 1.0 equiv.) in CH_2Cl_2 (0.99 mL) cooled to 0 °C was added freshly distilled $BF_3 \cdot Et_2O$ (25 uL, 0.20 mmol, 20 equiv.). The reaction was warmed to r.t. and stirred for 3 h. The solution was diluted with CH_2Cl_2, neutralized with $NaHCO_3$ (sat), extracted five times with CH_2Cl_2 and the combined organic phases were dried over anhydrous Na_2SO_4. Filtration and concentration under reduced pressure gave an off-white solid that was purified by silica gel chromatography, eluting with benzene, to yield (–)-elisapterosin B as a white solid (2.9 mg, 94%). *Note: the use of freshly distilled $BF_3 \cdot Et_2O$ that has been stored over CaH_2 is critical to prevent formation of biproducts such as iso-colombiasin.*[‡‡‡]

Spectral data were in agreement with those reported in the literature and are reported below. ^{1}H spectra for synthetic and natural (–)-elisapterosin B are shown below, and ^{1}H and ^{13}C spectra and $[\alpha]_D^{25}$ values for synthetic and natural elisapterosin B are tabulated below. Representative nOe's that confirm the relative stereochemistry of our synthetic material are also shown below. While our optical rotation differs from that of natural and synthetic material prepared by other groups, we believe that the spectral data and X-ray crystal structure of intermediate **14** confirm our structural assignment and suggest that a minor impurity may strongly influence the value of the optical rotation.

^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.07 (s, 1H), 4.87 (s, 1H), 4.67 (s, 1H), 3.21 (m, 1H), 2.43 (dt, *J* = 11.9, 6.0 Hz, 1H), 2.28 (m, 1H), 2.28 (br d, *J* = 5.6 Hz, 1H), 2.14 (dt, *J* = 12.2, 6.1 Hz, 1H), 1.99 (m, 1H), 1.80-1.75 (m, 2H), 1.63 (br s, 3H), 1.55-1.51 (m, 1H), 1.50-1.44 (m, 1H), 1.42 (s, 3H), 1.15 (d, *J* = 7.0 Hz, 3H), 1.04 (d, *J* = 6.4 Hz, 3H), 0.84 (q, *J* = 12.1 Hz, 1H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 203.8, 193.0, 146.1, 142.6, 141.4, 114.7, 70.1, 61.5, 55.8, 55.0, 42.9, 41.6, 40.2, 28.4, 24.2, 22.8, 19.2, 18.1, 17.7, 13.3; **IR** (thin film) 2271, 2950, 2933, 2870, 2360, 2341, 1757, 1660, 1618, 1453, 1385, 1365, 1043; **TLC R_f** 0.35 (benzene); **MS** (EI^+) calc. for $C_{20}H_{26}O_3$ (M+) 314.1882, found 314.1878.

$[\alpha]_D^{25}$ -180 (c=0.1, $CHCl_3$);
literature $[\alpha]_D^{25}$ (natural material, Rodriguez and coworkers[§§§,§§]) -29.8 (c=0.44, $CHCl_3$);
literature $[\alpha]_D^{25}$ (synthetic material, Rychnovsky and coworkers[§§]) -31.5 (c=0.16, $CHCl_3$);
literature $[\alpha]_D^{25}$ (synthetic material, Harrowven and coworkers[†††]) -33.8 (c=0.10, $CHCl_3$).

[‡‡‡] For characterization of iso-colombiasin, see reference 6b.
[§§§] A. D. Rodríguez, C. Ramirez, I. I. Rodríguez, C. L. Barnes, *J. Org. Chem.* **2000**, *65*, 1390-1398. The $[\alpha]_D^{25}$ reported for (–)-elisapterosin was corrected in reference 7.

Table SI-2. Comparison of ^{1}H and ^{13}C NMR spectral data for natural and synthetic (–)-elisapterosin B.

^{13}C NMR	
Rodriguez (75 MHz) (Natural material)	**Jacobsen (100 MHz) (Present work)**
203.8	203.8
193.0	193.0
146.1	146.1
142.5	142.6
141.5	141.4
114.7	114.7
70.1	70.1
61.5	61.5
55.7	55.8
54.9	55.0
42.9	42.9
41.5	41.6
40.1	40.2
28.4	28.4
24.2	24.2
22.7	22.8
19.2	19.2
18.1	18.1
17.6	17.7
13.3	13.3

^{1}H NMR	
Rodriguez (300 MHz) (Natural material)	**Jacobsen (600 MHz) (Present work)**
0.84 (q, *J* = 11.9 Hz, 1H)	0.84 (q, *J* = 12.1 Hz, 1H)
1.03 (d, *J* = 6.4 Hz, 3H)	1.04 (d, *J* = 6.4 Hz, 3H)
1.14 (d, *J* = 7.1 Hz, 3H)	1.15 (*d*, *J* = 7.0 Hz, 3H)
1.41 (s, 3H)	1.42 (s, 3H)
1.50 (m, 1H)	1.50-1.44 (m, 1H)
1.53 (m, 1H)	1.55-1.51 (m, 1H)
1.63 (br s, 3H)	1.63 (br s, 3H)
1.68 (m, 1H)	1.80-1.75 (m, 2H)
1.77 (m, 1H)	
1.98 (m, 1H)	1.99 (m, 1H)
2.14 (dt, *J* = 11.9, 5.7 Hz, 1H)	2.14 (dt, *J* = 12.2, 6.1 Hz, 1H)
2.28 (br d, *J* = 5.7 Hz, 1H)	2.28 (br d, *J* = 5.6 Hz, 1H)
2.28 (m, 1H)	2.28 (m, 1H)
2.42 (dt, *J* = 11.9, 5.7 Hz, 1H)	2.43 (dt, *J* = 11.9, 6.0 Hz, 1H)
3.20 (m, 1H)	3.21 (m, 1H)
4.67 (br s, 1H)	4.67 (s, 1H)
4.86 (br s, 1H)	4.87 (s, 1H)
6.10 (s, 1H)	6.07 (s, 1H)

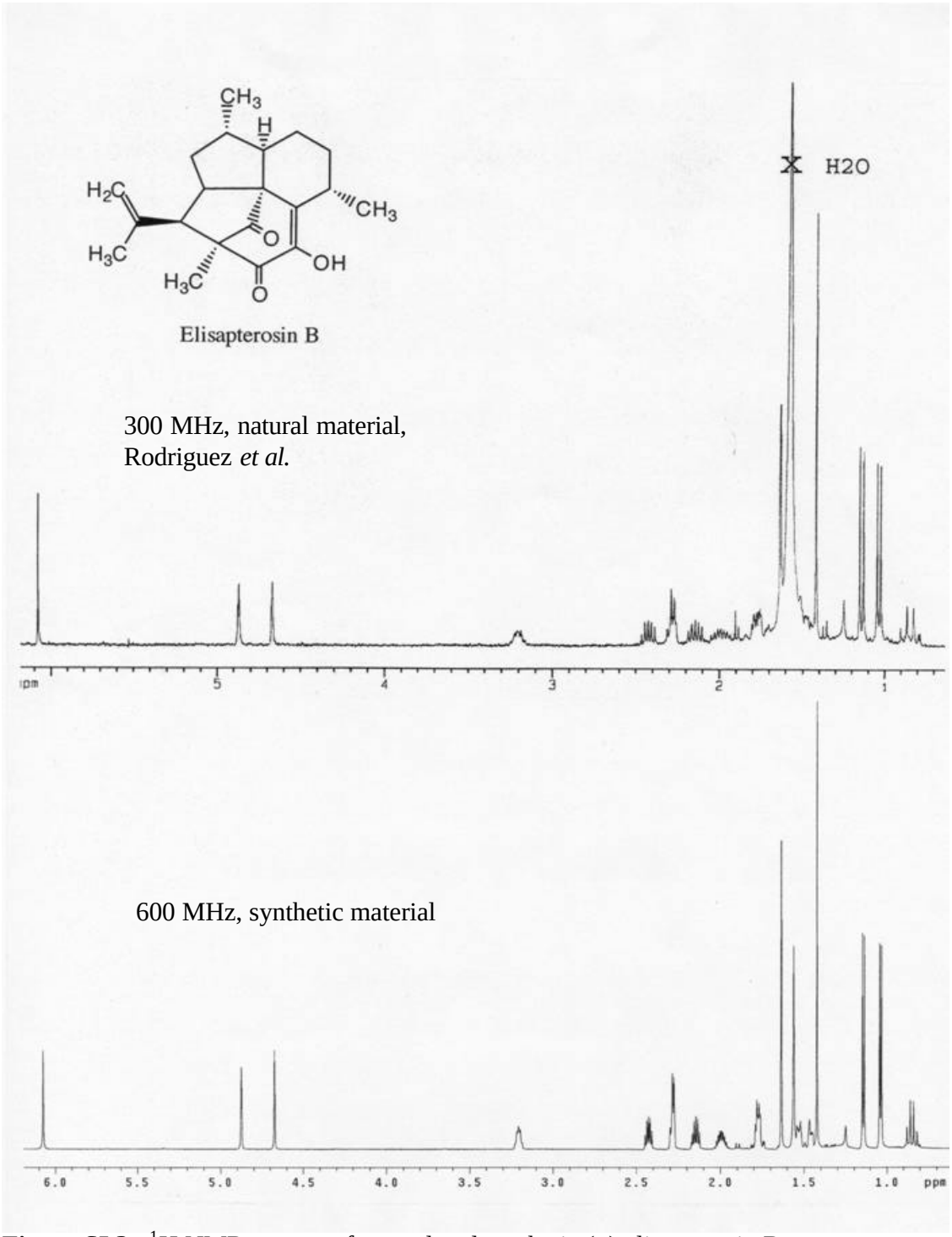


Figure SI-3. ^{1}H NMR spectra of natural and synthetic (–)-elisapterosin B.

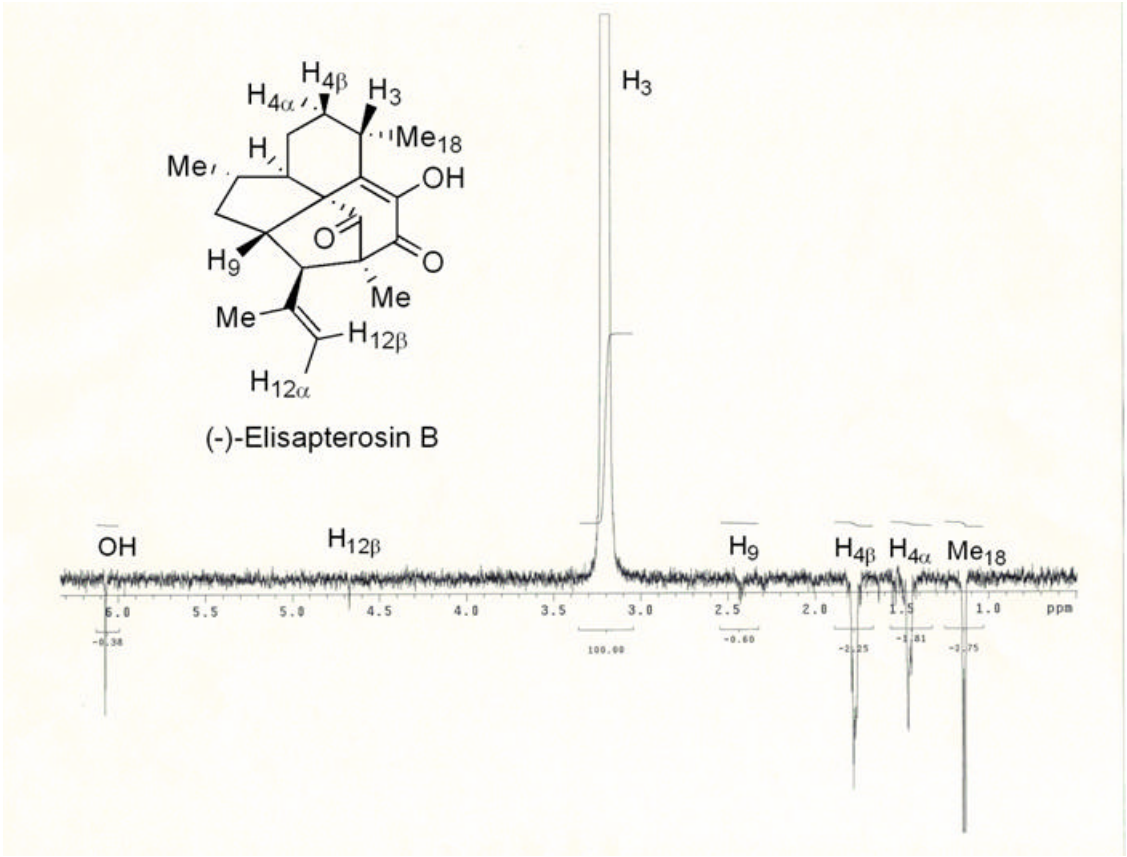
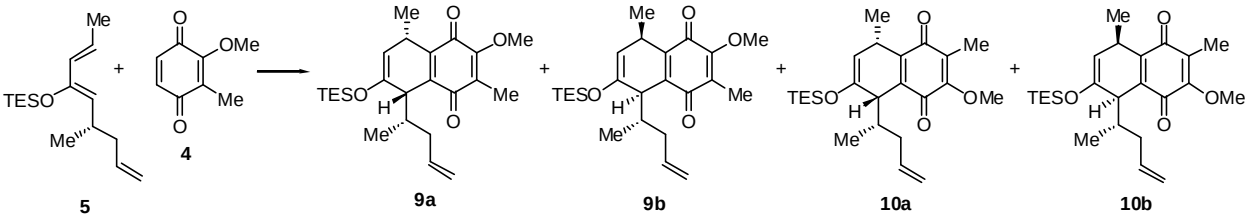


Figure SI-4. 1-D nOe spectrum of synthetic (–)-elisapterosin B, irradiating at 3.21 ppm (H_3).

c. Quinone Diels-Alder Reaction of 4 and 5 followed by Oxidation to Determine Diastereo- and Regioselectivity



The procedure for the DA reaction of **4** and **5** described above was followed, employing 1.5 equiv. of diene **5**. Upon complete consumption of quinone **4** (as judged by TLC), the reaction mixture was diluted to 0.1 M ([cycloadduct]), the reaction was cooled to 0 ^{o}C, Co(salen) (2.5 mol%) was added, and O_2 was bubbled through the solution for 10 minutes. While constantly bubbling O_2 through the reaction, a solution of DBU (1 equiv., 0.2 M in toluene) was added over 30 minutes using a syringe pump, after which time the reaction mixture was *immediately* applied to silica gel chromatography (0-1-2% EtOAc/hexanes). This afforded the desired product as a bright yellow oil (87% yield).

The *dr* and regioselectivity of the product were determined by chiral HPLC analysis [(*S*,*S*)-Whelk-O (Regis) in tandem with YMC-Pack Diol-NP (YMC, Inc.), prewash 5% EtOH/hexanes, 0.6 mL/min, for 5 min, preequilibrate 0.01% *i*-PrOH/hexanes, 0.6 mL/min, for 20 min, run 0.01% *i*-PrOH/hexanes, 0.6 mL/min. Major diastereomer (**9a**): t_r= 15.6 min; minor regioisomers (**10a** and **10b**): t_r=17.2 and 18.3 min; minor diastereomer (**9b**): t_r = 20.8 min].

^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.71 (m, 1H), 4.97 (m, 2H), 4.88 (d, *J* = 4.8 Hz, 1H), 4.00 (s, 3H), 3.48 (m, 1H), 3.38 (m, 1H), 2.19 (m, 1H), 1.94 (s, 3H), 1.81 (m, 2H), 1.25 (d, 6.9 Hz, 3H), 1.03 (d, *J* = 6.2 Hz, 3H), 0.97 (t, *J* = 8.0 Hz, 9H), 0.69 (q, *J* = 7.9 Hz, 6H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 187.8, 182.5, 155.4, 149.7, 142.8, 142.6, 137.9, 128.5, 115.8, 105.9, 60.8, 43.9, 38.0, 37.1, 30.6, 22.4, 19.0, 8.8, 6.7, 5.0; **IR** (thin film) 3074, 2958, 2938, 2914, 2878, 1680, 1651, 1612; **TLC R_f** 0.3 (5% EtOAc/hexanes); **[**a**]$_D^{25}$** -54.6 (*c*= 0.52; CH_2Cl_2); **MS** (ES^+) calc. for $C_{24}H_{37}O_4Si$ (M+H) 417.2461, found 417.2457.

Part 2. X-ray Crystallographic Data for Ketone 14

Data were collected using a Bruker SMART CCD (charge coupled device) based diffractometer equipped with an Oxford Cryostream low-temperature apparatus operating at 193 K. A suitable crystal was chosen and mounted on a glass fiber using grease. Data were measured using omega scans of 0.3° per frame for 30 seconds, such that a hemisphere was collected. A total of 1271 frames were collected with a maximum resolution of 0.76 Å. The first 50 frames were recollected at the end of data collection to monitor for decay. Cell parameters were retrieved using SMART[****] software and refined using SAINT on all observed reflections. Data reduction was performed using the SAINT software[††††] which corrects for Lp and decay. The structures are solved by the direct method using the SHELXS-97[‡‡‡] program and refined by least squares method on F^2, SHELXL-97,[§§§§] incorporated in SHELXTL-PC V 6.10.[*****] The structure was solved in the space group $P2_12_12_1$ (# 19) by analysis of systematic absences. All non-hydrogen atoms are refined anisotropically. Hydrogens were calculated by geometrical methods and refined as a riding model. Disodered group refined to 50%. The crystal used for the diffraction study showed no decomposition during data collection. All drawing are done at 50% ellipsoids.

[a] Obtained with graphite monochromated Mo Kα (*l* = 0.71073 Å) radiation. [b]$R1 = \Sigma||F_o| - |F_d||/\Sigma|F_o|$. [c]$wR_2 = \{\Sigma[w(F_o^2 - F_c^2)^2/\{\Sigma[w(F_o^2)^2]\}^{1/2}$.

[****] SMART V 5.625 (NT) *Software for the CCD Detector System*; Bruker Analytical X-ray Systems, Madison, WI (2001).

[††††] SAINT V 6.22 (NT) *Software for the CCD Detector System* Bruker Analytical X-ray Systems, Madison, WI (2001).

[‡‡‡] Sheldrick, G. M. SHELXS-90, *Program for the Solution of Crystal Structure*, University of Göttingen, Germany, 1990.

[§§§§] Sheldrick, G. M. SHELXL-97, *Program for the Refinement of Crystal Structure*, University of Göttingen, Germany, 1997.

[*****] SHELXTL 6.1 (PC-Version), *Program library for Structure Solution and Molecular Graphics*; Bruker Analytical X-ray Systems, Madison, WI (2000).