Supporting Information

General Procedures. All reactions were performed in flame dried round bottom or modified Schlenk (Kjeldakl shape) flasks fitted with rubber septa under a positive pressure of argon, unless otherwise indicated. Air- and moisture-sensitive liquids and solutions were transferred by syringe or canula. Where necessary (so noted), solutions were deoxygenated by alternative freeze (liquid N\textsubscript{2})/evacuation/thaw cycles (≥ three iterations). Organic solutions were concentrated by rotary evaporation at ~20 Torr. Analytical thin-layer chromatography (TLC) was carried out using 0.2 mm commercial silica gel plates (silica gel 60, F254, EMD chemical). Thin layer chromatography plates were visualized by exposure to ultraviolet light and/or exposure to an acidic solution of \textit{p}-anisaldehyde or ceric ammonium mulybdate solution followed by heating on a hot plate.

Materials. Dichloromethane, tetrahydrofuran, toluene, and benzene were purified using a Pure-Solv MD-5 Solvent Purification System (Innovative Technology). All commercial reagents were used directly, without further purification unless otherwise notes.

Instrumentation. Nuclear magnetic resonance spectra (\textsuperscript{1}H NMR and \textsuperscript{13}C NMR) were recorded with a Varian Gemini (400 MHz) or Varian (300MHz) spectrometer. Chemical shifts are reported as parts per million (ppm) downfield of tetramethylsilane and referenced relative to residual protium in NMR solvents (CHCl\textsubscript{3}: δ 7.26 ppm, C\textsubscript{6}D\textsubscript{6}H: δ 7.15 ppm: D\textsubscript{2}HCOD: δ 3.31 ppm ). Chemical shifts for carbon are reported in ppm downfield of tetramethylsilane and are referenced to the carbon resonances of the solvent (CDCl\textsubscript{3} δ 77.0, C\textsubscript{6}D\textsubscript{6} δ 128.0, D\textsubscript{2}COD: δ 44.9). Infrared spectra (IR) were recorded on a Nicolet 380 FTIR using thin film (neat). Optical rotations were measured on an ATAGO AP-300 automatic polarimeter with a path length of 100 mm. Melting points were measured on a MEL-TEMP device without correction. High-resolution mass spectra (HRMS) were obtained on a Karatos MS9 at the UT Mass Spectrometry Facility.
To a solution of p-bromophenol (1.93 g, 11.2 mmol, 1.5 eq) in CH₂Cl₂ (20 mL) at 0 °C was added a solution of AlMe₃ in hexane (1 M, 3.72 mL, 3.72 mmol, 0.5 eq) over 5 minutes, followed by stirring at 0 °C for 30 minutes, warmed to 23 °C, and stirred for 1 hour then the solution was concentrated and p-bromophenol (1.93 g, 11.2 mmol, 1.5 eq) in CH₂Cl₂ (30 mL) was added at 0 °C dropwise. After stirring for 10 minutes a solution of caryophyllene oxide (1.64 g (2.2:1 ratio of epoxides), 5.1 mmol of 4, 1 eq of 4) in CH₂Cl₂ (20 mL) was added over 30 minutes. The mixture was stirred at 0 °C for an additional 2 hours then the solvent was removed and the residue was suspended with hexane (200 mL). The organic layer was washed with 2 N HCl (50 mL), 1 NaOH (50 mL), and brine (30 mL). The organic extract was dried over MgSO₄, filtered, and concentrated to provide a viscous residue. The residue was purified by silica gel chromatography (hexane/EtOAc = 9:1 as eluent) to give 11 as a clear oil (1.37 g, yield 69% from 4. TLC Rₜ = 0.24, hexane/EtOAc = 85:15. [α]D²⁶ = 90.3°, (c 1.5, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 0.92 (s, 3H), 0.99 (s, 3H), 1.00 (s, 3H), 1.14-1.21 (m, 1H), 1.37-1.87 (m, 10H), 1.96-2.06 (m, 2H), 2.34 (ddd, J = 2.1, 3.4, 18.2 Hz, 1H), 3.49 (dd, J = 3.0, 4.6 Hz, 1H), 6.73 (d, J = 9.0 Hz, 2H), 7.28 (d, J = 9.0 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 20.8, 21.1, 26.4, 28.3, 30.3, 30.5, 34.7, 36.0, 37.5, 39.2, 40.3, 41.9, 44.8, 71.6, 80.7, 114.0, 123.2, 131.5, 154.7; FTIR: 3394, 1638, 1493, 1232 cm⁻¹; HRMS (ESI+) calculated for C₂₁H₂₉BrO₂Na 415.1249, found 415.1243.

To a solution of 11 (50 mg, 0.127 mmol, 1 eq) and 4-dimethylaminopyridine (31.1 mg, 0.254 mmol, 2 equiv.) in CH₂Cl₂ (2 mL) at 0 °C was added a solution of 3,5-dinitrobenzoyl chloride (58.6 mg, 0.254 mmol, 2eq) in CH₂Cl₂ (2 mL). The mixture was stirred at 23 °C for 4 hours, then the solution was washed with 1 N NaOH (10 mL), and 2 N HCl (10 mL). The organic layer was dried over Na₂SO₄, filtered, and concentrated. Purification by silica gel chromatography (hexane/EtOAc = 90:10 as eluent) provided the 3,5-dinitrobenzoate of 11 as a light yellow solid (58 mg, 78%). The solid was readily recrystallized from ethanol to provide crystals suitable for X-ray analysis. TLC Rₜ = 0.55, hexane/EtOAc = 80:20; Mp 177-178 °C; ¹H NMR (400 MHz, CDCl₃): δ 0.98 (s, 3H), 1.03 (s, 3H), 1.06(s, 3H), 1.32-1.37 (m, 1H), 1.47-1.54 (m, 1H), 1.58-1.76 (m, 6H), 1.89 (dd, J = 1.4, 13.3 Hz, 1H), 1.97-2.22 (m, 4H), 2.41 (ddd, J = 2.8, 9.0 and 12.0 Hz, 1H), 5.11 (t, J = 4.0 Hz, 1H), 6.79 (d, J = 9.0 Hz, 2H), 7.35 (d, J = 9.0 Hz, 2H), 9.04 (d, J = 2.1 Hz, 2H), 9.22 (t, J = 2.1 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 20.8, 21.2, 25.7, 26.9, 30.3, 31.2, 34.8, 35.8, 37.4, 38.8, 40.6, 43.2, 44.9, 79.9, 114.6, 122.4, 123.2, 129.2, 131.8, 134.1, 148.7, 154.4.
To a solution of 11 (1.23 g, 3.13 mmol, 1 eq), triethylamine (0.87 mL, 6.25 mmol, 2 eq), and 4-dimethylaminopyridine (0.382 g, 3.13 mmol, 1 eq) in CH₂Cl₂ (40 mL) at 0 °C was added the acetic anhydride (0.443 mL, 4.69 mmol, 1.5 eq). The solution was stirred at 23 °C for 20 minutes then the mixture was diluted with CH₂Cl₂ (30 mL) and washed with 2 N HCl (30 mL), 1 N NaOH (20 mL), and brine (10 mL). The organic extract was dried over MgSO₄, filtered, and concentrated. The residue was purified by silica gel chromatography (hexane/EtOAc =95:5 as eluent) to yield the acetate of 11 as colorless oil (1.14 g, 84%). TLC Rf = 0.28, hexane/EtOAc = 95:5; ¹H NMR (400 MHz, CDCl₃): δ 0.87 (s, 3H), 0.99 (s, 3H), 1.01 (s, 3H), 1.20-1.28 (m, 1H), 1.39-2.06 (m, 9H), 1.91-2.06 (m, 3H), 2.01 (s, 3H), 2.36 (dd, J = 1.3, 10.2, 11.7 Hz, 1H), 4.71 (t, J = 3.7 Hz, 1H), 6.73 (d, J = 8.9 Hz, 2H), 7.29 (d, J = 8.9 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 20.8, 21.1, 21.2, 25.7, 26.6, 30.3, 34.7, 35.9, 37.8, 38.3, 40.2, 43.1, 44.9, 73.6, 80.4, 113.8, 122.7, 131.6, 154.7, 170.6. FTIR: 1734, 1486, 1245 cm⁻¹; HRMS (ESI+), calculated for C₂₈H₃₁N₂O₇Br 586.1349, found 586.1326.

To a reaction flask charge with the acetate of 11 (0.832 g, 1.91 mmol, 1 eq) and sodium acetate (0.314 g, 3.82 mmol, 2 eq) in acetic acid (10 mL) was added bromine (0.404 mL, 7.64 mmol, 4 eq) dissolved in acetic acid (5 mL) in a single portion. The reaction was heated to 60 °C for 4 hour the reaction was diluted with hexane (100 mL) and washed with water (100 mL X 3), 1 N NaOH (20 mL X 3), and then brine (30 mL). The organic extract was dried over Na₂SO₄, filtered, and concentrated. Purification by silica gel chromatography (hexane/EtOAc = 95:5) provided 12 as colorless oil (0.902 g, 92%). TLC Rf = 0.28, hexane/EtOAc = 95:5; ¹H NMR (400 MHz, CDCl₃): δ 0.89 (s, 3H), 1.01 (s, 3H), 1.23-1.29 (m, 1H), 1.39-2.01 (m, 11H), 2.03 (s, 3H), 2.13 (m, 1H), 2.29-2.43 (m, 1H), 4.71 (t, J = 3.2 Hz, 1H), 6.78 (d, J = 8.8 Hz, 1H), 7.24 (dd, J = 2.4, 8.8 Hz, 1H), 7.65 (d, J = 2.4 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 20.8, 21.0, 21.2, 25.7, 26.7, 30.3, 30.9, 34.8, 35.8, 37.7, 38.4, 40.3, 42.4, 44.7, 73.6, 83.0, 114.0, 117.9, 122.5, 130.2, 135.4, 152.1, 170.6. FTIR: 1738, 1467, 1040, 1017 cm⁻¹; HRMS (ESI+), calculated for C₂₃H₃₀Br₂O₃Na 535.0455, found 535.0454.

To a mixture of 12 (640 mg, 1.24 mmol, 1 eq), Pd(PPh₃)₄ (288 mg, 0.249 mmol, 0.2 eq), and NaOH (0.995 g, 24.9 mmol, 20 eq) was added toluene (18 mL), water (9 mL), and pinacol allylboronate 13 (4.0 mL, 16.0 mmol, 13 eq) followed by vigorous stirring (1200
rpm) at 90 °C for 55 minutes. The organic layer was separated and the aqueous layer was extracted with EtOAc (30 mL). The combined the organic extracts were combined with silica gel (1 g) and the sample was concentrated to dryness. The sample was purified by silica gel chromatography (hexane/EtOAc = 95:5 as eluent) to provide 14 as colorless oil (430 mg, 72%). TLC R_f = 0.30, hexane/EtOAc = 95:5; ¹H NMR (400 MHz, CDCl₃): δ 0.88 (s, 3H), 1.01 (s, 3H), 1.02 (s, 3H), 1.21-1.27 (m, 1H), 1.39-1.65 (m, 4H), 1.73 (dd, J = 8.0, 9.6 Hz, 1H), 1.88-1.91 (m, 5H), 1.95-2.00 (m, 1H), 2.02 (s, 3H), 2.16 (m, 1H), 2.37 (ddd, J = 1.7, 3.6, 18.2 Hz, 1H), 3.28 (d, J = 6.7 Hz, 2H), 4.70 (t, J = 3.0 Hz, 1H), 5.03-5.06 (m, 1H), 5.08-5.09 (m, 1H), 5.86-5.96 (m, 1H), 6.83 (d, J = 8.4 Hz, 1H), 6.94 (dd, J = 2.2, 8.4 Hz, 1H), 7.34 (d, J = 2.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 20.8, 21.0, 21.2, 25.7, 26.7, 30.3, 30.8, 34.8, 35.8, 37.5, 38.4, 39.0, 40.3, 42.4, 44.6, 73.8, 82.2, 116.1, 117.1, 121.7, 127.4, 133.1, 134.8, 136.9, 150.9, 170.6; FTIR: 1737, 1486, 1247 cm⁻¹; HRMS (ESI+), calculated for C₂₆H₃₅BrO₃Na 497.1665, found 497.1662.

To a flask charged with 14 (330 mg, 0.694 mmol, 1 eq), borate ester 15 (997 mg, 2.78 mmol, 4 eq) and NaOH (333 mg, 8.33 mmol, 12 eq) followed by addition of toluene (7mL) and water (5 mL, sparged with argon for 5 minutes). A solution of Pd₂(dba)₃ (39.9 mg, 0.069 mmol, 0.1 eq) and t-Bu₃P (51 µL, 0.208 mmol, 0.3 eq) in toluene (3 mL) was then added. The mixture was immediately placed in a 90 °C oil bath and stirred at 1200 rpm for 30 minute (color transition of red to yellow to brown to dark brown). After cooling the mixture was diluted with EtOAc (50 mL) and water (10 mL). The layers were separated and the aqueous phase was extracted with EtOAc (20 mL). The combined organic extracts were dried over MgSO₄, filtered, and concentrated. Purification by silica gel chromatography (hexane/EtOAc = 90:10 as eluent) provided 16 as colorless oil (308 mg, 71%). TLC R_f = 0.42, hexane/EtOAc = 80:20; ¹H NMR (300 MHz, C₆D₆): δ 0.72 (s, 3H), 0.77 (t, J = 7.2 Hz, 3H), 0.82-0.87 (m, 3H), 0.91 (s, 3H), 0.99 (s, 3H), 1.03-1.60 (m, 10H), 1.66 (s, 3H), 1.68-1.82 (m, 2H), 1.88 (t, J = 9.7 Hz, 1H), 2.09 (dd, J = 8.8, 20.8 Hz, 1H), 2.90-3.12 (m, 4H), 3.21 (t, J = 8.0 Hz, 4H), 4.23 (bs, 1H), 4.91-5.03 (m, 4H), 5.82-5.96 (m, 2H), 6.87 (d, J = 8.3 Hz, 1H), 6.97 (dd, J = 1.9, 8.5 Hz, 2H), 7.20 (d, J = 1.9 Hz, 2H), 7.32 (d, J = 8.3 Hz, 1H); ¹³C NMR (75 MHz, C₆D₆): δ 13.4, 14.0, 20.6, 20.9, 24.8, 25.9, 26.7, 30.3, 30.7, 34.6, 35.8, 36.7, 38.3, 39.7, 39.9, 40.3, 41.5, 41.9, 42.0, 44.2, 73.5, 80.8, 115.5, 115.7, 122.5, 123.3, 131.9, 132.4, 132.8, 133.1, 133.3, 135.8, 136.7, 137.7, 137.8, 148.1, 151.7, 153.8, 169.5; FTIR: 1737, 1486, 1247 cm⁻¹; HRMS (EI+), calculated for C₄₀H₅₃NO₅ 627.3924, found 627.3921.
To the solution of 16 (80 mg, 0.127 mmol, 1 eq) in tetrahydrofuran (2 mL) was added LiAlH₄ solution in tetrahydrofuran (1M, 2.55 mL, 2.55 mmol, 20 eq) dropwise at 23 °C. The mixture was heated to reflux for 2 hours and then cooled to 23 °C and cautiously quenched with water (5 mL). The mixture was diluted with diethyl ether (10 mL) and 2 N HCl (5 mL). The organic layer was collected and washed with brine (20 mL). The organic phase was concentrated and the residue purified by silica gel chromatography (hexane/EtOAc = 85:15) to provide caryolanemagnolol (1) as colorless pasty oil (44 mg, 71%). TLC Rf = 0.25, hexane/EtOAc = 80:20; [α]D²⁶ = 61.6°, (c 2.1, CHCl₃); ¹H NMR (400 MHz, C₆D₆): δ 0.60 (s, 3H), 0.80 (dt, J = 4.2, 14.7 Hz, 1H), 0.88 (s, 3H), 1.08 (s, 3H), 1.12-1.41 (m, 6H), 1.44-1.59 (m, 2H), 1.64-1.82 (m, 2H), 1.91-2.03 (m, 2H), 2.16 (dd, J = 1.9, 10.2, 20.1 Hz, 1H), 2.90 (t, J = 3.0 Hz, 1H), 3.16 (d, J = 6.8 Hz, 2H), 3.24 (d, J = 6.6 Hz, 2H), 4.94-5.04 (m, 4H), 5.82 (ddt, J = 6.8, 10.1, 16.8 Hz, 1H), 5.94 (ddt, J = 6.6, 10.2, 20.1 Hz, 1H), 6.92 (d, J = 8.5 Hz, 1H, Ar-H), 6.97 (dd, J = 2.2, 8.3 Hz, 1H), 7.03 (dd, J = 2.2, 8.2 Hz, 1H), 7.19 (d, J = 2.2 Hz, 1H), 7.22 (d, J = 2.2 Hz, 1H), 7.24 (d, J = 8.2 Hz, 1H), 7.58 (s, 1H); ¹³C NMR (100 MHz, C₆D₆): δ 20.2, 20.5, 26.3, 28.4, 29.2, 30.0, 34.6, 35.3, 36.1, 38.7, 39.2, 39.41, 39.44, 39.5, 43.8, 71.0, 84.1, 115.0, 118.4, 123.7, 128.2, 128.7, 129.4, 131.3, 132.0, 133.5, 135.6, 137.2, 138.1, 149.4, 153.0; FTIR: 3361, 1638, 1491, 1209, 1045, 938, 822 cm⁻¹. MS (ESI): M+Na⁺ 509. HRMS (ESI+), calculated for C₃₃H₄₁O₃ (M–H) 485.3060, found 485.3061.

Note: reported optical rotations [α]D²³.⁵ = 11.2° synthetic material [α]D²⁶ = 61.6° see reference 2.

To a solution of 4-allylphenol (2 g, 14.9 mmol, 1 eq) and 4-dimethylamino pyridine (3.64 g, 29.8 mmol, 2 eq) in CH₂Cl₂ (40 mL) was added a solution of diethyl chlorocarbamate (3.77 ml, 29.8 mmol, 2 eq) in CH₂Cl₂ (20 mL) at 0 °C. The solution was stirred at 0 °C for 2 hours and 23 °C for 4 hours and then diluted with CH₂Cl₂ (200 mL) and washed with 1NaOH (100 mL), 2 N HCl (100 mL), and brine (50 mL). The organic extract was dried over Na₂SO₄, filtered, and concentrated. Purification of the residue by silica gel chromatography (hexane/EtOAc = 85:15 as eluent) provided the carbamate as a yellow oil (2.7 g, 78% yield). TLC Rf = 0.45, hexane/EtOAc = 80:20.

To THF (40 mL) under argon at –78 °C was added s-BuLi (1.21 M, 12.75 mL, 15.4 mmol, 1.2 eq) followed by TMEDA (2.33 mL, 15.4 mmol, 1.2 eq) providing a light yellow solution. After 30 minutes, a solution of the carbamate prepared above (3 g, 12.9 mmol) in THF (10 mL) was added over 10 minutes. The yellow solution was stirred for 2 hours at –78
°C then trimethyl borate (2.87 mL, 25.7 mmol, 2 eq) was added followed by warming to 23 °C over 1 hour (color fade upon addition of trimethyl borate). A solution of 0.1 N HCl (100 mL) was added and the aqueous phase was extracted with ether (20 mL X 3). The combined organic extracts were dried over Na₂SO₄, filtered, and concentrated. The oily residue was dissolved in methanol (40 mL) and pinacol (4.56 g, 38.6 mmol, 3 eq) was added as a solid. The solution was stirred at 23 °C for 1 hour and the mixture was concentrated. The viscous residue was dissolved in EtOAc (30 mL) and washed with water (20 mL X 3). The organic phase was dried over Na₂SO₄, filtered, and concentrated. Silica gel chromatography (hexane/EtOAc = 90:10 as eluent) yielded the borate 15 as colorless oil (3.8 g, 82% yield). TLC Rf = 0.37, hexane/EtOAc = 80:20; ¹HNMR (300 MHz, CDCl₃): δ 1.19 (t, J = 7.0 Hz, 3H), 1.28 (t, J = 7.0 Hz, 3H), 1.30 (s, 12H), 3.37 (q, J = 7.2 Hz, 2H), 3.37 (d, J = 8.0 Hz, 2H), 3.50 (q, J = 7.2 Hz, 2H), 5.03-5.09 (m, 2H), 5.95 (ddt, J = 6.7, 10.1, 16.8 Hz, 1H), 6.99 (d, J = 8.3 Hz, 1H, 7.24 (d, J = 2.3, 8.3 Hz, 1H), 7.57 (d, J = 2.3 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 13.4, 14.1, 24.9, 39.5, 41.6, 41.9, 83.4, 115.7, 122.2, 132.3, 136.2, 136.3, 137.5, 154.5, 154.9; FTIR: 1720, 1510 cm⁻¹; HRMS (Cl+), calculated for C₂₀H₃₁O₄NB 360.2348, found 360.2346.

To a solution of (β)-caryophyllene (2.27 g (90%), 10 mmol, 1 eq) in acetonitrile (50 mL) and dimethoxymethane (100 mL) was added a buffer solution (100 mL, 0.05 M Na₂B₄O₇•10 H₂O in 4X10⁻⁴ M Na₂(EDTA)), n-Bu₄HSO₄ (140 mg, 0.4 mmol, 0.04 eq), LT-Shi catalyst 10 (2.58 g, 10 mmol, 1 eq), and cooled to 0 °C. Addition of Oxone® (8.5 g, 13.8 mmol, 1.38 eq) in buffer aqueous solution (65 mL, 4X10⁻⁴ M Na₂EDTA aqueous solution) and K₂CO₃ aqueous solution (9.3 g, 67.3 mmol, 6.73 eq in water (65 mL)) in separate syringes over 1.5 hours using a syringe pump. After complete addition, the reaction mixture was extracted with hexane (100 mL X 3). The combined organic extracts were washed with brine (50 mL), dried over Na₂SO₄, filtered and concentrated. The crude oil was purified by silica gel chromatography (hexane/EtOAc = 95:5 as eluent) to give a light yellow oil, 1.64 g, yield 74%. TLC Rf = 0.24, Hex/EA = 95:5. ¹H NMR showed a 2.2:1 ratio of diastereomers 4 and 5 respectively with the desired epoxide as the major isomer. NMR data matches that reported.

To a solution of (β)-caryophyllene (5.6 g (90%), 24.7 mmol, 1 eq) in CH₂Cl₂ (30 mL) under argon at 0 °C was added m-CPBA (4.51 g, 25.9 mmol, 1.05 eq) in CH₂Cl₂ (30 mL) over 30 minutes via syringe pump, the reaction mixture became heterogeneous after 15
minutes. After stirring for an additional hour at 0 °C the mixture was filtered through cotton. The filtrate was concentrated, diluted with hexane (40 mL), and washed with 1N NaOH (30 mL X 2). The organic extract was dried over Na₂SO₄, filtered, and concentrated. Purification by silica gel chromatography (hexane/EtOAc = 95:5 as eluent) provided a colorless oil (4.5 g, 83%). TLC Rf = 0.24, Hex/EA = 95:5. ¹H NMR showed a 1:5 ratio of diastereomers 4 and 5 respectively. NMR data matches that reported.

To a solution of β-caryophyllene β-oxide (recrystallized from benzene)³ (5 g, 21.6 mmol, 1 eq) and p-bromophenol (11.9 g, 64.7 mmol, 3 eq) in CH₂Cl₂ (80 ml) at 0 °C was added a solution of diphenylphosphate (2.70 g, 10.8 mmol, 0.5 eq) in CH₂Cl₂ (20 ml) over 30 minutes. The gray solution was stirred at 0 °C for 4 hours then the solvent was removed under vacuum. The residue was diluted with hexane (300 mL) and washed with 1 M NaOH (50 mL X 3). The organic layer was washed with brine (10 mL) and dried over Na₂SO₄, filtered, and concentrated. The residue was purified by silica gel chromatography (hexane/EtOAc = 90:10 as eluent) to give 3.08 g of 17 as a white solid (yield 35%). TLC Rf: 0.34 hexane/EtOAc = 85:15; Mp 114-116 °C; [α]d²⁶ = 93.1°, (c 1.7, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 0.94 (s, 3H), 0.95 (s, 3H), 0.96-1.04 (m, 2H), 1.06 (s, 3H), 1.09-1.21 (m, 1H), 1.32-1.43 (m, 3H), 1.48-1.68 (m, 6H), 1.79 (dt, J = 4.7, 13.6 Hz, 1H), 1.85 (dd, J = 5.4, 12.7 Hz, 1H), 1.98-2.07 (m, 1H), 3.34 (bs, 1H), 4.19 (dd, J = 5.4, 7.9 Hz, 1H), 6.76 (d, J = 9.0 Hz, 2H), 7.33 (d, J = 9.0 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 20.9, 25.7, 26.6, 27.2, 28.3, 31.6, 33.1, 34.7, 36.0, 38.3, 43.8, 45.3, 50.0, 74.9, 86.5, 112.3, 117.5, 132.1, 158.1; FTIR: 3416, 1486, 1243 cm⁻¹; HRMS (ESI+), calculated for C₂₁H₂₈BrO (M–H₂O) 375.1323, found 375.1318.

To a solution of compound 17 (2.6 g, 6.38 mmol, 1 eq) and 4-dimethylaminopyridine (0.78 g, 6.38 mmol, 1 eq) in CH₂Cl₂ (40 mL) at 0 °C was added triethylamine (1.21 mL, 12.8 mmol, 2 eq) and acetic anhydride (1.78 mL, 12.8 mmol, 2 eq). Subsequently, acetic anhydride (1.21 mL, 12.8 mmol, 2 eq) was added dropwise over 10 minutes. The solution was stirred at 0 °C for 1 hour then diluted with CH₂Cl₂ (100 mL) washed with 1 N NaOH (30 mL), 2 N HCl (30 mL) and brine (20 mL). The organic layer was dried over Na₂SO₄, filtered, and concentrated. The residue was purifed by silica gel chromatography (hexane/EtOAc = 95:5) to provide the acetate of 17 as colorless oil (2.50 g yield 87%). TLC Rf = 0.32, hexane/EtOAc = 95:5; ¹H NMR (400 MHz, CDCl₃): δ 0.85 (s, 3H), 0.94 (s, 3H), 1.05 (s, 3H), 1.09 (d, J = 12.6 Hz, 1H), 1.21-1.28 (m, 1H), 1.33-1.74 (m, 9H), 1.85 (d, J = 5.4, 12.8 Hz, 1H), 1.93-1.99 (m, 1H), 2.02 (s, 3H), 4.20 (dd, J = 1.9, 7.4 Hz, 1H), 4.57 (b, 1H), 6.77 (d, J = 9.0 Hz, 2H), 7.34 (d, J = 9.0 Hz, 2H); ¹³C NMR (100 MHz,
CDCl₃: δ 20.8, 21.3, 24.1, 25.8, 27.8, 28.1, 31.7, 32.8, 33.6, 36.9, 38.5, 43.7, 45.3, 50.0, 86.5, 112.4, 117.6, 132.1, 157.9, 170.8; FTIR: 1733, 1486 cm⁻¹; HRMS (ESI+), calculated for C₂₃H₃₁BrO₃Na 457.1356, found 457.1349.

To a solution of the acetate of 17 (2.00 g, 4.45 mmol, 1 eq) and sodium acetate (0.73 g, 8.9 mmol, 2 eq) in acetic acid (30 mL) was added a solution of bromine (0.918 mL, 17.8 mmol, 4 eq) in acetic acid (10 mL) over 1 minute. The flask was stirred at 60 °C for 4 hours the mixture was diluted with hexane (200 mL) and washed with water (100 mL X 3), 1 N NaOH (3 X 100 mL), and brine (50 mL). The organic layer was dried over Na₂SO₄, filtered, and concentrated. Purification by silica gel chromatography (hexane/EtOAc = 95:5 as eluent) gave 18 as colorless oil (2.01 g, 85%). TLC Rf = 0.32, hexane/EtOAc = 95:5; ¹H NMR (400 MHz, CDCl₃): δ 0.87 (s, 3H), 0.96 (s, 3H), 1.08 (s, 3H), 1.10 (d, J = 13.2 Hz, 1H), 1.24-1.31 (m, 1H), 1.35-1.48 (m, 1H), 1.53-1.85 (m, 7H), 1.88 (dd, J = 5.3, 13.0 Hz, 1H), 1.96-2.01 (m, 1H), 2.03 (s, 3H), 4.21 (dd, J = 0.9, 6.5 Hz, 1H), 4.58 (bs, 1H), 6.73 (d, J = 8.9 Hz, 1H), 7.32 (dd, J = 2.4, 8.8 Hz, 1H), 7.64 (d, J = 2.4 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 20.8, 21.3, 24.3, 25.9, 27.9, 28.1, 31.8, 32.8, 33.6, 36.8, 39.0, 43.7, 45.9, 49.9, 87.9, 112.3, 114.0, 115.4, 130.9, 135.5, 154.4, 170.8; FTIR: 1735, 1246, 1042 cm⁻¹; HRMS (ESI+), calculated for C₂₃H₃₀Br₂O₃Na 535.0455, found 535.0454.

To a flask charged with substrate 18 (0.4875 g, 0.948 mmol, 1 eq), NaOH (0.758 g, 17.0 mmol, 18 eq), and tetrakis(triphenylphosphine)palladium (0.219 g, 0.190 mmol, 0.2 eq) under argon was added toluene (10 mL), water (5 mL, sparged with argon for 5 minutes), and allyl pinacol borate 13 (3.05 mL, 15.17 mmol, 16 eq). The biphasic mixture was stirred at 1200 rpm at 90 °C for 50 minutes where upon TLC (hexane/EtOAc = 97:3) showed full conversion. Then the mixture was cooled to 23 °C and extracted with EtOAc (50 mL). The organic layer was washed with brine (50 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel chromatography (hexane/EtOAc = 97:3 as eluent) to provide 19 as colorless oil (0.316 g, yield 70%). TLC Rf = 0.33, hexane/EtOAc = 95:5; ¹H NMR (400 MHz, CDCl₃): δ 0.87 (s, 3H), 0.95 (s, 3H), 1.09 (s, 3H), 1.10 (d, J = 7.2 Hz, 1H), 1.25-1.48 (m, 4H), 1.53-1.78 (m, 5H), 1.88 (dd, J = 5.3, 12.9 Hz, 2H), 1.96-2.01 (m, 1H), 2.03 (s, 3H), 3.29 (d, J = 6.7 Hz, 2H), 4.22 (dd, J = 5.4, 7.0 Hz, 1H), 4.58 (b, 1H), 5.04-5.07 (m, 1H), 5.07-5.09 (m, 1H), 5.86-5.96 (m, 1H), 6.79 (d, J = 8.4 Hz, 1H), 7.03 (dd, J = 2.2, 8.3 Hz, 1H), 7.35 (d, J = 2.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 20.8, 21.3, 24.2, 25.8, 27.9, 28.1, 31.8, 32.8, 33.6, 36.8, 38.8, 38.9, 43.9, 45.7, 49.9, 87.7, 113.0, 114.4, 116.0, 128.2, 133.2, 133.3, 137.1, 153.5, 170.9; FTIR: 1735, 1246 cm⁻¹; HRMS (ESI+), calculated for C₂₆H₃₅Br₃O₃Na 497.1665, found 497.1662.
To a flask charged with 19 (200 mg, 0.421 mmol, 1 eq), the borate 15 (604 mg, 1.683 mmol, 4 eq), and NaOH (202 mg, 5.05 mmol, 12 eq) under argon was added toluene (6 mL), water (4 mL, sparged with argon for 5 minutes) and a solution of Pd(dba)$_2$ (24.2 mg, 0.042 mmol, 0.1 eq), and t-Bu$_3$P (31 µL, 0.126 mmol, 0.3 eq) solution in toluene (2 mL, stirring for 10 minutes before addition). The mixture was immediately placed in a 90 °C oil bath and stirred at 1200 rpm for 30 minutes (red to yellow to brown to dark brown color sequence) then the reaction was diluted with EtOAc (30 mL) and water (10 mL). The phases were separated and the aqueous phase was extracted with EtOAc (20 mL). The combined organic extracts were dried over MgSO$_4$, filtered, and concentrated. Silica gel chromatography (hexane/EtOAc = 90:10 as eluent) provided 20 as colorless pasty oil (196 mg, 74%).

**TLC R$_f$ = 0.40, hexane/EtOAc = 80:20;**

**$^1$H NMR (400 MHz, C$_6$D$_6$):** δ 0.70 (s, 3H), 0.81 (s, 3H), 0.86 (s, 3H), 0.71-0.90 (m, 8H), 0.95-1.24 (m, 5H), 1.44 (d, $J$ = 12.7 Hz, 1H), 1.50-1.70 (m, 5H), 1.80 (s, 3H), 2.91 (d, $J$ = 5.4 Hz, 2H), 3.00 (d, $J$ = 5.6 Hz, 2H), 3.18 (t, $J$ = 7.5 Hz, 4H), 4.01 (dd, $J$ = 5.8, 15.6 Hz, 1H), 4.68 (b, 1H), 4.93-5.02 (m, 4H), 5.80-6.00 (m, 2H), 6.85 (d, $J$ = 8.4 Hz, 1H), 6.92 (dd, $J$ = 2.3, 8.3 Hz, 1H), 7.01 (dd, $J$ = 2.3, 8.3 Hz, 1H), 7.16 (d, $J$ = 2.1 Hz, 1H, Ar-H), 7.20 (d, $J$ = 2.3 Hz, 1H, Ar-H), 7.31 (d, $J$ = 8.3 Hz, 1H, Ar-H);

**$^{13}$C NMR (100 MHz, C$_6$D$_6$):** δ 13.1, 13.7, 18.1, 20.6, 24.2, 25.5, 27.8, 28.0, 31.4, 32.7, 33.3, 36.6, 38.2, 39.4, 39.6, 41.3, 41.7, 43.7, 45.4, 49.7, 76.3, 87.2, 115.0, 115.1, 115.4, 122.9, 129.1, 131.7, 131.8, 132.1, 135.7, 137.4, 137.8, 148.0, 153.5, 154.7, 169.4; FTIR: 1720, 1246, cm$^{-1}$; HRMS (CI+), calculated for C$_{40}$H$_{54}$O$_5$N$_6$ 628.4002, found 628.3986.

To the solution of 20 (100 mg, 0.159 mmol, 1 eq) in tetrahydrofuran (4 mL) was added LiAlH$_4$ solution in tetrahydrofuran (1M, 3.19 mL, 3.19 mmol, 20 eq) dropwise at 23°C. The mixture was heated to reflux for 2 hours and then cooled to 23 °C and excess LiAlH$_4$ was carefully quenched !! with water (10 mL). The mixture diluted with Et$_2$O (40 mL) and 2N HCl (20 mL). The organic layer was collected and washed with brine (10 mL). The concentrated organic phase was purified by silica gel chromatography with hexane/EtOAc = 85:15 to provide the clovanemagnolol 2 as colorless oil (57 mg, 73%).

**TLC R$_f$ = 0.22, hexane/EtOAc = 80:20;**

**$[^{26}]$$\alpha$$_D$$ ^{(c = 1.5, CHCl_3;}} = 96.0^\circ,$**

**$^1$H NMR (400 MHz, C$_6$D$_6$):** δ 0.64 (s, 3H), 0.70 (d, $J$ = 12.8 Hz, 1H), 0.83 (s, 3H), 0.83 (m, 1H), 0.92 (s, 3H), 0.98-1.18 (m, 4H), 1.26 (dd, $J$ = 5.5, 11.4 Hz, 1H), 1.35 (m, 1H), 1.50-1.71 (m, 4H), 1.79 (dt, $J$ = 3.7, 13.3 Hz, 1H, Ar-H));
1H), 3.04 (s, 1H), 3.18 (d, J = 6.8 Hz, 2H), 3.23 (d, J = 6.6 Hz, 2H), 4.10 (dd, J = 5.7, 8.5 Hz, 1H), 4.96-5.01 (m, 3H), 5.03 (dd, J = 1.7, 3.4 Hz, 1H), 5.81-5.98 (m, 2H), 6.58 (b, 1H), 6.94 (d, J = 8.4 Hz, 1H), 7.02 (dd, J = 2.3, 8.2 Hz, 1H), 7.04 (dd, J = 2.3, 8.4 Hz, 1H), 7.16 (d, J = 2.3 Hz, 1H), 7.17 (d, J = 2.3 Hz, 1H), 7.19 (d, J = 8.3 Hz, 1H); 13C NMR (100 MHz, C6D6): δ 20.6, 25.1, 26.5, 26.7, 28.3, 30.9, 32.8, 34.4, 35.4, 37.4, 39.3, 39.4, 44.2, 45.0, 49.9, 74.3, 89.4, 115.0, 115.4, 115.9, 117.4, 127.1, 128.9, 129.2, 129.4, 131.2, 131.8, 132.5, 133.8, 137.4, 138.0, 152.8, 154.2; FTIR: 3394, 1638, 1232, 822 cm

Note: reported optical rotations [α]D25 = 21.0° synthetic material [α]D26 = 96.0° see reference 2.

To a solution of β-caryophyllene α-oxide 4 (40 mg, 2.2:1 ratio of α-oxide 4 to β-oxide 5, 0.125 mmol of 4, 1 eq of 4) and magnolol (8) (49.3 mg, 0.185 mmol, 1.5 equiv.) in dichloromethane (2 mL) at 23 °C was added a solution of diphenylphosphate (15.4 mg, 0.062 mmol, 0.5 eq) in dichloromethane (1 mL) over 3 minutes. Then the orange solution was stirred at 38 °C for 2.5 hours the solvent was removed and the residue was diluted with hexane (50 mL). The hexane solution was washed with phosphate buffer (pH 7.4, 2 X 10 mL) and 1 N NaOH (3 X 10 mL (to recover the magnolol)). The organic layer was washed with brine (10 mL) and dried over Na2SO4. The solution was concentrated and the residue purified by silica gel chromatography (hexane/EtOAc = 85:15 as eluent) to yield a mixture of clovanemagnolol 1 and caryolanemagnolol 2. The mixture was purified by a second round of silica gel chromatography (100% dichloromethane as eluent) to provide pure caryolanemagnolol 2 as colorless oil (9.1 mg, 15% yield).
To a solution of recrystallized β-caryophyllene β-oxide 5 (60 mg, 0.259 mmol, 1 eq) and magnolol (8) (103 mg, 0.388 mmol, 1.5 eq) in dichloromethane (2 mL) was added a solution of diphenylphosphate (32.4 mg, 0.129 mmol, 0.5 eq) in dichloromethane (1 mL) over 3 minutes. The orange solution was stirred at 38 °C for 2.5 hours then the solvent was removed. The residue was diluted with hexane (50 mL) and washed with phosphate buffer (pH 7.4, 2 X 10 mL) and 1 M NaOH (3 X 10 mL (to recover the magnolol)). The organic layer was washed with brine (10 mL) and dried over Na₂SO₄ and then concentrated. The residue was purified by silica gel chromatography (hexane/EtOAc = 85:15 as eluent) to yield 12 mg of clovanemagnolol (2) a colorless oil (12 mg, 9.5% yield).

References:
Spectra of Isolated and Synthetic Caryolanemagnolol

Isolated caryolanemagnolol (1)

Synthetic caryolanemagnolol (1)