Catalytic Enantioselective Approach to the Eudesmane Sesquiterpenoids: Total Synthesis of (+)-Carissone

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Materials and Methods. Unless otherwise stated, reactions were performed in flame-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents. Solvents were dried by passage through an activated alumina column under argon. All the starting materials were purchased from commercial sources and used as received, unless otherwise stated. Liquids and solutions were transferred via syringe or positive-pressure cannula. Brine solutions refer to saturated aqueous sodium chloride solutions. TMEDA was distilled from sodium under nitrogen prior to use. Benzenethiol was distilled under nitrogen prior to use. Previously reported methods were used to prepare (S)-t-BuPHOX ((S)-12) and (R)-t-BuPHOX ((R)-12), as well as Pd2(pmdba)3. Grubbs’ catalyst 18 was a generous gift from Materia, Inc. Rhodium was purchased from Strem as a 1 wt % loading on alumina powder in reduced form. Diazomethane was freshly prepared from Diazald® as a solution in Et2O. Manganese dioxide was purchased from Aldrich in activated form, ~85%, <5 µm, and used as received. Reaction temperatures were controlled by an IKAmag temperature modulator. Thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized by UV fluorescence quenching, anisaldehyde, or KMnO4 staining. SiliCycle® SiliaFlash® P60 Academic Silica Gel (particle size 40-63 µm; pore diameter 60 Å) was used for flash chromatography. Analytical chiral HPLC was performed with an Agilent 1100 Series HPLC utilizing a Chiralpak AD column (4.6 mm x 25 cm) obtained from Daicel Chemical Industries, Ltd. with 1 mL/min flow rate and visualization at 254 nm. Analytical chiral supercritical fluid chromatography was performed with a Berger Analytix SFC (Thar Technologies) utilizing a Chiralpak AD-H column (4.6 mm x 25 cm) obtained from Daicel Chemical Industries, Ltd. with 2 mL/min flow rate at 30 °C and visualization at 244 nm. Optical rotations were measured with a Jasco P-1010 polarimeter at 589 nm in spectrophotometric grade solvents. 1H and 13C NMR spectra were recorded on a Varian Mercury 300 (at 300 MHz and 75 MHz respectively) or a Varian Inova 500 (at 500 MHz and 126 MHz, respectively), and are reported relative to Me4Si (δ 0.0 ppm). Data for 1H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity and qualifier abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, comp = complex, br = broad, app = apparent. On occasion, an artifact appears in
the $^{13}$C NMR spectra (126 MHz) with negative phasing at $\delta$ 44.9 ppm (CDCl$_3$) or $\delta$ 45.2 ppm (C$_6$D$_6$). IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm$^{-1}$). Melting points are uncorrected. High-resolution mass spectra were obtained from the Caltech Mass Spectral Facility.

### Experimental Procedures and Tabulated Spectroscopic Data

**Vinylogous Ester SI2.** Diketone SI1 (3.000 g, 23.78 mmol, 1.0 equiv) was partially dissolved in PhH (42.5 mL, 0.56 M), and $i$-BuOH (12.75 mL, 137.9 mmol, 5.8 equiv) and $p$-TsOH•H$_2$O (226 mg, 1.19 mmol, 0.05 equiv) were added with vigorous stirring. The flask was affixed with a Dean–Stark adapter and a water-cooled condenser and warmed to reflux in a 104 °C oil bath. Upon consumption of SI1 by TLC analysis (ca. 3.5 h), the reaction was cooled to ambient temperature, diluted with Et$_2$O (50 mL), and poured into saturated aq NaHCO$_3$ (20 mL). The layers were separated and the aqueous was extracted with Et$_2$O (3 x 15 mL). The organics were combined, washed with brine, dried with Na$_2$SO$_4$, filtered, and concentrated in vacuo to afford a pale brown oil. To this oil was added PhMe (ca. 10 mL) followed by further concentration in vacuo. Purification by bulb-to-bulb distillation yielded vinylogous ester SI2 (3.988 g, 21.88 mmol, 92% yield) as a clear, colorless oil. $R_f = 0.48$ (2:1 EtOAc-hexanes); bp =135-140 °C at 0.8 torr; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 3.76 (d, $J = 6.5$ Hz, 2H), 2.54 (ddd, $J = 6.1, 1.5, 1.5$ Hz, 2H), 2.34 (t, $J = 7.1$ Hz, 2H), 2.08-1.90 (comp m, 3H), 1.72 (app t, $J = 1.5$ Hz, 3H), 0.99 (d, $J = 6.7$ Hz, 6H). All other data were consistent with reported values.

**Methyl Vinylogous Ester SI3.** To a solution of $i$-Pr$_2$NH (1.12 mL, 7.99 mmol, 1.9 equiv) in THF (26 mL, 0.15 M) at 0 °C was added dropwise a solution of $n$-BuLi (2.55 M in hexanes, 3.06 mL, 7.80 mmol, 1.85 equiv). After 15 min, a solution of vinylogous ester SI2 (765.2 mg, 4.198 mmol, 1.0 equiv) in THF (2.0 mL) was added dropwise via cannula transfer. The resulting solution was cooled to $-78$ °C and stirred for 45 min, to which a solution of MeI (485 µL, 7.80 mmol, 1.85 equiv) in THF (5.0 mL) was added over 30 min via positive-pressure cannula transfer. The cooling bath was allowed to expire over ca. 4 h and the reaction was quenched with brine (15 mL). The phases were separated and the aqueous phase was extracted with hexanes (3 x 25 mL). The combined organics were washed with brine, dried over MgSO$_4$, filtered, and concentrated in vacuo to a yellow oil. Purification by flash chromatography (4:1 → 2:1 hexanes-Et$_2$O) afforded methyl vinylogous ester SI3 (659 mg, 3.36 mmol, 80% yield) as a
pale yellow oil. \( R_f = 0.48 \) (2:1 hexanes-EtOAc); \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta \) 3.73 (ddd, \( J = 15.6, 9.2, 6.5 \) Hz, 2H), 2.61 (ddd, \( J = 17.3, 5.3, 1.2 \) Hz, 1H), 2.55-2.44 (m, 1H), 2.35-2.19 (m, 1H), 2.06 (app dq, \( J = 8.3, 4.8 \) Hz, 1H), 1.98 (app septet, \( J = 6.6 \) Hz, 1H), 1.71 (dd, \( J = 1.6, 1.6 \) Hz, 3H), 1.73-1.60 (m, 1H), 1.14 (d, \( J = 6.9 \) Hz, 3H), 0.99 (d, \( J = 6.7 \) Hz, 6H). All other data are consistent with reported values.

**Enol Carbonate 9.** To a solution of \( i\)-Pr\(_2\)NH (1.56 mL, 11.15 mmol, 1.2 equiv) in THF (85 mL, 0.11 M) at 0 °C was added a solution of \( n\)-BuLi (2.55 M in hexanes, 4.0 mL, 10.22 mmol, 1.1 equiv) dropwise. The reaction mixture was allowed to stir for 30 min and then cooled to –78 °C. A solution of ketone SI3 (1.824 g, 9.29 mmol, 1.0 equiv) in THF (10 mL) was added dropwise via cannula and stirred for 1 h. TMEDA (1.67 mL, 11.15 mmol, 1.2 equiv) was then added via syringe and the resulting solution stirred for 75 min. To this solution allyl chloroformate (1.08 mL, 10.13 mmol, 1.09 equiv) was added via syringe and the reaction mixture was stirred at –78 °C for an additional hour. The reaction was quenched with saturated aq NaHCO\(_3\) (40 mL) and H\(_2\)O (40 mL), and the flask was transferred to a 23 °C water bath and allowed to equilibrate. The phases were separated and the aqueous was extracted with Et\(_2\)O (2 x 200 mL). The combined organics were washed with brine, dried over MgSO\(_4\), and concentrated in vacuo to afford enol carbonate 9 as a yellow oil (2.472 g); \(^1\)H NMR analysis shows 9 is the major product with other impurities present. \( R_f = \) unstable to SiO\(_2\); \(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta \) 5.97 (ddd, \( J = 16.4, 10.8, 5.8 \) Hz, 1H), 5.42 (app d, \( J = 17.2 \) Hz, 1H), 5.33 (app d, \( J = 10.4 \) Hz, 1H), 4.72 (dd, \( J = 5.7, 0.8 \) Hz, 2H), 3.86 (d, \( J = 6.7 \) Hz, 2H), 2.85 (app t, \( J = 7.9 \) Hz, 2H), 2.52 (app t, \( J = 7.9 \) Hz, 2H), 2.19 (s, 3H), 1.92 (app septet, \( J = 6.7 \) Hz, 1H), 1.82 (s, 3H), 0.93 (d, \( J = 6.7 \) Hz, 6H); IR (Neat Film NaCl) 2963, 1760, 1736, 1699, 1361, 1248, 1170, 990 cm\(^{-1}\); HRMS (FAB+) \( m/z \): calc’d for C\(_{13}\)H\(_{19}\)O\(_4\) [M – C\(_3\)H\(_3\)]\(^+\) : 239.1283, found 239.1273.

This material was unstable to various purification attempts (distillation or flash chromatography using silica gel or Florisil) and storage. Aromatic carbonate \( i \) was identified as a colorless oil from this complex mixture. \( R_f = 0.51 \) (4:1 hexanes-EtOAc); \(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta \) 6.97 (d, \( J = 8.4 \) Hz, 1H), 6.65 (d, \( J = 8.4 \) Hz, 1H), 6.00 (ddd, \( J = 17.1, 10.5, 5.7 \) Hz, 1H), 5.43 (ddd, \( J = 17.2, 1.4, 1.4 \) Hz, 1H), 5.33 (ddd, \( J = 10.5, 1.2, 1.2 \) Hz, 1H), 4.75 (app dt, \( J = 5.8, 1.3 \) Hz, 2H), 3.70 (d, \( J = 6.4 \) Hz, 2H), 2.14 (s, 3H), 2.09 (s, 3H), 2.09 (app septet, \( J = 6.6 \) Hz, 1H), 1.03 (d, \( J = 6.7 \) Hz, 6H); \(^13\)C NMR (126 MHz, CDCl\(_3\)): \( \delta \) 156.3, 153.0, 148.7, 131.4, 127.7, 121.8, 119.5, 119.4, 109.1, 74.9, 69.2, 28.6, 19.5, 15.7, 9.2; IR (Neat Film NaCl) 2960, 2874, 1762, 1620, 1494, 1470, 1365, 1244, 1202, 1172, 1115, 1048, 799 cm\(^{-1}\); HRMS (FAB+) \( m/z \): calc’d for C\(_{16}\)H\(_{22}\)O\(_4\) [M\(^+\)]\(^+\) : 278.1518, found 278.1517.
(±)-β-Ketoester 10. To a −78 °C solution of t-Pr₂NH (425 µL, 3.03 mmol, 1.9 equiv) in PhMe (10 mL) was added dropwise n-BuLi (2.55 M in hexanes, 1.16 mL, 2.96 mmol, 1.85 equiv). The reaction vessel was placed in an ice/water bath and allowed to stir for 10 min, and then cooled to −78 °C. A solution of vinylogous ester S12 (291 mg, 1.60 mmol, 1.0 equiv) in PhMe (1.4 mL) was added dropwise via cannula to the reaction vessel, and the resulting solution was allowed to stir for 30 min. Allyl chloroformate (173 µL, 1.63 mmol, 1.02 equiv) was added dropwise, and the reaction vessel was allowed to warm to 23 °C over 1 h. After stirring for 4 h, the reaction was slowly quenched with aq KHSO₄ (1 N, 4 mL) and the resulting biphasic mixture was allowed to stir for 10 min. The phases were separated, and the aq phase was extracted with Et₂O (2 x 10 mL). The combined organic extracts were washed with brine (10 mL), dried over MgSO₄, filtered, and concentrated in vacuo. The isolated crude yellow oil was used in the next step without further purification.

The resulting crude yellow oil was dissolved in MeCN (5.9 mL, 0.27 M), and Cs₂CO₃ (603 mg, 1.85 mmol, 1.16 equiv), and MeI (276 µL, 4.44 mmol, 2.8 equiv) were added. The flask was affixed a water-cooled condenser and resulting suspension was warmed to reflush in an 80 °C oil bath with vigorous stirring. After 10 h, the reaction was cooled to room temperature, diluted with EtOAc (25 mL). The organics were dried with MgSO₄, filtered, and the solvent was evaporated in vacuo. Purification by flash chromatography (15:1 → 9:1 → 4:1 hexanes-EtOAc) afforded β-ketoester (±)-10 as pale yellow oil (246 mg, 55% yield over two steps). Rₐ = 0.27 (2:1 hexanes-EtOAc); ¹H NMR (500 MHz, CDCl₃): δ 5.82 (dddd, J = 17.2, 10.7, 5.4, 5.4 Hz, 1H), 5.22 (dddd, J = 17.2, 1.6, 1.6 Hz, 1H), 5.15 (dddd, J = 10.5, 1.2, 1.2 Hz, 1H), 4.56 (dddd, J = 13.5, 5.4, 1.5, 1.5 Hz, 2H), 3.72 (dddd, J = 9.2, 6.6, 3.2 Hz, 2H), 2.69-2.62 (m, 1H), 2.53-2.44 (comp m, 2H), 1.95 (app septuplet, J = 6.6 Hz, 1H), 1.85-1.80 (m, 1H), 1.70 (dd, J = 1.5, 1.5 Hz, 3H), 1.36 (s, 3H), 0.95 (dd, J = 6.7, 0.8 Hz, 6H); ¹³C NMR (126 MHz, CDCl₃): δ 195.8, 172.6, 170.3, 131.9, 117.8, 113.8, 73.9, 65.5, 51.6, 31.2, 28.8, 23.0, 20.8, 19.1, 19.0, 8.0; IR (Neat Film NaCl) 2961, 2935, 2875, 1733, 1649, 1460, 1382, 1354, 1237, 1176, 1103, 983 cm⁻¹; HRMS (FAB+) m/z: calc’d for C₁₁H₂₃O₄ [M + H]+: 281.1753, found 281.1740.

Vinylogous Thioester S14. To a solution of diketone S11 (2.500 g, 19.82 mmol, 1.0 equiv) in MeCN (22.0 mL, 0.9 M) was added Et₃N (3.1 mL, 22.2 mmol, 1.12 equiv), and the solution was allowed to stir for 5 min, then cooled to 0 °C. Methanesulfonyl chloride (1.63 mL, 21.0 mmol, 1.06 equiv) was added, and the reaction was warmed to 23 °C over 2 h. Stirring was continued for 5 h, and the reaction was cooled to 0 °C. Triethylamine (3.1 mL, 22.2 mmol, 1.12 equiv) was added, followed by benzenethiol (2.1 mL, 20.4 mmol, 1.03 equiv). The reaction was allowed to warm to 23 °C over 2 h and stirring was continued for 9 h. Saturated aq Na₂CO₃ (35 mL) was added, the phases were separated, and the aq phase was extracted with Et₂O (3 x 60 mL). The combined organic extracts were dried over Na₂SO₄, filtered, and the solvent was evaporated in vacuo. Purification by flash chromatography (4:1 to 2:1 hexanes-Et₂O) afforded vinylogous thioester S14 as a white crystalline solid (3.565 g, 16.33 mmol, 82% yield). Rₐ = 0.34 (1:1 hexanes-Et₂O); mp 85 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.51-7.49 (m, 2H), 7.44-7.37 (comp m, 3H), 2.38 (t, J = 6.5 Hz, 2H), 2.18 (tq, J = 6.5, 2.0 Hz, 2H), 1.97 (t, J = 2.0 Hz, 3H), 1.87 (app pentuplet, J = 6.0 Hz, 2H). All other data are consistent with reported values.
**β-Ketoester (±)-11.** To a −78 °C solution of i-Pr$_2$NH (2.63 mL, 18.78 mmol, 2.00 equiv) in PhMe (70 mL) was added dropwise n-BuLi (2.53 M in hexanes, 7.24 mL, 2.00 equiv). The reaction vessel was warmed to 0 °C, allowed to stir for 10 min, and cooled to −78 °C. A solution of vinylogous thioester SI4 (2.00 g, 9.16 mmol, 1.00 equiv) in PhMe (15 mL) was added dropwise via cannula to the reaction vessel, and the resulting solution was allowed to stir for 30 min. Allyl chloroformate (1.02 mL, 9.62 mmol, 1.05 equiv) was added dropwise and the reaction vessel was allowed to warm to 23 °C over 1 h. Stirring was continued for 4 h, then aq KHSO$_4$ (1 N, 70 mL) was added, and the resulting solution was allowed to stir for 10 min. The phases were separated, and the aq phase was extracted with Et$_2$O (3 x 30 mL). The combined organic extracts were washed with brine (1 x 30 mL), dried over Na$_2$SO$_4$, filtered, and the solvent was evaporated in vacuo. The isolated crude yellow oil was used in the next step without further purification.

To a solution of the crude yellow oil (3.32 g) in CH$_3$CN (40 mL) was added cesium carbonate (4.48 g, 13.74 mmol, 1.50 equiv), and MeI (1.71 mL, 27.48 mmol, 3.00 equiv). The resulting suspension was refluxed at 80 °C for 5 h, and then MeI (1.00 mL, 16.06 mmol, 1.75 equiv) was added. The reaction was refluxed at 80 °C for 2 h, cooled to room temperature, filtered through Celite (EtOAc eluent), dried over Na$_2$SO$_4$, filtered, and the solvent was evaporated in vacuo. Purification by flash chromatography (18% EtOAc in hexanes) afforded β-ketoester (±)-11 as a colorless oil that solidifies to a white solid over time or in a −20 °C freezer (2.26 g, 78% yield over two steps). $R_f = 0.35$ (30% EtOAc in hexanes); mp 34 °C; $^1$H NMR (300 MHz, CDCl$_3$) δ 7.51-7.35 (comp m, 5H), 5.87 (app ddt, $J = 10.5, 17.1, 5.4$ Hz, 1H), 5.27 (app ddt, $J = 17.1, 1.7, 1.8$ Hz, 1H), 5.22 (app ddt, $J = 9.9, 1.7, 1.2$ Hz, 1H), 4.65 (ddd, $J = 1.5, 1.8, 5.7, 13.5$ Hz, 1H), 4.55 (ddd, $J = 1.5, 1.8, 5.7, 13.5$ Hz, 1H), 2.41-2.32 (m, 1H), 2.16-2.06 (1H), 2.00 (t, $J = 1.8$ Hz, 3H), 1.78 (ddd, $J = 4.5, 8.1, 13.2$ Hz, 1H), 1.38 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 193.0, 172.6, 157.6, 135.6, 131.9, 129.7, 129.5, 128.9, 118.1, 65.7, 52.3, 33.1, 27.4, 20.7, 12.9; IR (Neat Film NaCl) 2936, 1733, 1656, 1580, 1314, 1254, 1238, 1174, 985, 752, 693 cm$^{-1}$; HRMS (FAB+) m/z: calc’d for C$_{18}$H$_{20}$O$_7$S [M + H]$^+$: 317.1211, found 317.1211.

**Ketone (+)-13 from enol carbonate 9.** A 1-dram vial containing a stirbar was charged with Pd$_2$(pmdba)$_3$ (4.9 mg, 0.0045 mmol, 0.025 equiv) and (S)-12 (4.4 mg, 0.0112 mmol, 0.0625 equiv), sealed with a septum, and the atmosphere was purged by three evacuate/purge cycles. To this was added PhMe (0.9 mL) and the complexation was stirred for 30 min in a 25 °C oil bath, upon which time a solution of enol carbonate 9 (50.2 mg, 0.179 mmol, 1.0 equiv) in PhMe (0.9 mL, 0.1 M total) was added via cannula. After 21.5 h at 25 °C, the reaction was diluted with Et$_2$O (2 mL), filtered through a
SiO₂ plug, and concentrated in vacuo. The filtrate was purified by flash chromatography on SiO₂ (15:1 → 4:1 hexanes-EtOAc) to afford ketone (+)-13 as a pale yellow oil (22-61% yield, 84-88% ee). Rᶠ = 0.49 (4:1 hexanes-EtOAc); ¹H NMR (500 MHz, CDCl₃) δ 5.73 (dddd, J = 16.6, 10.6, 7.4, 7.4 Hz, 1H), 5.06-5.04 (m, 1H), 5.04-5.01 (m, 1H), 3.74 (dd, J = 9.7, 6.7 Hz, 2H), 2.59-2.47 (comp m, 2H), 2.33 (dd, J = 13.7, 7.2 Hz, 1H), 2.16 (dddd, J = 13.7, 7.6, 1.0, 1.0 Hz, 1H), 1.98 (app septuplet, J = 6.6 Hz, 1H), 1.90 (dd, J = 13.3, 7.2, 5.7 Hz, 1H), 1.72-1.67 (m, 1H), 1.70 (dd, J = 1.6, 1.6 Hz, 3H), 1.06 (s, 3H), 0.99 (d, J = 6.7 Hz, 6H); ¹³C NMR (126 MHz, CDCl₃) δ 202.7, 169.5, 134.8, 117.8, 113.8, 73.8, 42.5, 41.9, 31.5, 29.0, 22.5, 22.4, 19.2, 8.0; IR (Neat Film NaCl) 3076, 2962, 2931, 1622, 1463, 1381, 1355, 1229, 1113, 1002, 915 cm⁻¹; HRMS (El⁺) m/z: calc’d for C₁₅H₂₄O₂ [M⁺]: 236.1776, found 236.1771; [α]D²⁻¹ +13.2° (c 0.20, CH₂Cl₂, 88% ee). SFC conditions: 5% IPA, AD column, tᵣ (min): major = 5.18, minor = 6.02; see graphical HPLC data on page SI 13 and SI 14.

**Ketone (+)-13 from β-ketoester (±)-10.** A 2-dram vial containing a stir bar was charged with Pd₂(pmdba)₃ (10.6 mg, 0.00968 mmol, 0.025 equiv) and (S)-12 (9.4 mg, 0.0242 mmol, 0.0625 equiv). This was connected to a 1-dram vial containing a stir bar and β-ketoester (±)-10 (108.6 mg, 0.387 mmol, 1.0 equiv) via a cannula, and PhMe (3.9 mL, 0.1 M) was added to the vial containing the Pd/L and immediately immersed in liquid N₂. The vials were rigorously degassed by three freeze-pump-thaw cycles and warmed to 23 °C. After complexation for 30 min (purple → orange color change), the catalyst solution was transferred to the substrate via cannula and immersed in an 80 °C oil bath. The reaction immediately turned yellow in color. After 23 h the reaction was cooled to ambient temperature, diluted with Et₂O (4 mL), and filtered through a small SiO₂ plug. The filtrate was concentrated and purified by flash chromatography as above to afford ketone (+)-13 as a colorless oil (78.5 mg, 0.332 mmol, 86% yield, 75% ee).

**Ketone (+)-14 from β-ketoester (±)-11.** The reaction was performed exactly as described for enol carbonate 9 using β-ketoester (±)-11 (41.8 mg, 0.132 mmol, 1.0 equiv). After complexation of the metal for 30 min at 25 °C, a solution of the substrate was added and the reaction was warmed to 50 °C in an oil bath. After 23 h, the reaction was cooled to room temperature, diluted with Et₂O, and filtered through a SiO₂ plug. The filtrate was concentrated and purified by flash chromatography (15:1 → 9:1 hexanes-EtOAc) to afford ketone (+)-14 as a colorless oil (31.0 mg, 0.114 mmol, 86% yield, 92% ee). Rᶠ = 0.35 (9:1 hexanes-EtOAc); ¹H NMR (300 MHz, CDCl₃) δ 7.52-7.48 (m, 2H), 7.43-7.35 (comp m, 3H), 5.68 (dddd, J = 16.6, 10.4, 7.6, 7.6 Hz, 1H), 5.03 (dddd, J = 9.9, 2.4, 0.9, 0.6 Hz, 1H), 5.01 (dddd, J = 17.4, 2.4, 1.5, 1.2 Hz, 1H), 2.32 (app ddt, J = 13.8, 7.2, 1.2 Hz), 2.19-2.10 (comp m, 3H), 1.96 (app t, J = 1.8 Hz, 3H), 1.81 (ddd, 13.5, 6.4, 6.4 Hz, 1H), 1.66-1.56 (m, 1H), 1.04 (s, 3H); ¹³C NMR (75 MHz,
Scale up of ketone (−)-14 from β-ketoester (±)-11. In a glove box, a flask containing a stirbar was charged with Pd₂(pmdba)₃ (493.1 mg, 0.045 mmol, 0.025 equiv) and ligand (R)-12 (435.9 mg, 1.125 mmol, 0.0625 equiv). The solids were dissolved in PhMe (150 mL) and stirred for 45 min (purple → orange color change). To this was added a solution of β-ketoester (±)-11 (5.6956 g, 18.00 mmol, 1.0 equiv) in PhMe (30 mL, 0.1 M total). The flask was transferred out of the glove box, placed under an argon atmosphere, and warmed in a 50 °C oil bath (orange → yellow color change). After 66 h, the reaction was cooled to room temperature and concentrated in vacuo. Purification by flash chromatography (as above, dry load onto SiO₂) afforded ketone (−)-14 as a pale yellow oil (4.184 g, 15.36 mmol, 85% yield, 92% ee) and recovered β-ketoester (±)-11 (500.5 mg, 1.582 mmol, 9% yield). 

Methoxy vinylogous ester (−)-15. A 3-neck flask equipped with water-cooled reflux condenser was charged with dry MeOH (33.7 mL, 0.26 M), cooled in an ice/water bath, hexanes-washed Na₀ (1.047 g, 45.5 mmol, 5.2 equiv) was added and the bath was removed. The contents were stirred at 23 °C until all Na₀ was dissolved. A solution of ketone (−)-14 (2.3991 g, 8.81 mmol, 1.0 equiv) in MeOH (10 mL) was added dropwise via cannula to the generated NaOMe and the resulting solution was heated in an oil bath at 70 °C. Upon consumption of (−)-14 by TLC analysis (4:1 hexanes-EtOAc), the reaction mixture was cooled to ambient temperature and transferred to a separate flask with EtO and concentrated in vacuo to a viscous yellow slurry. This was dissolved in saturated aq NaHCO₃ (150 mL), stirred for ca. 20 min, and extracted with EtO (3 x 100 mL). The organics were dried over Na₂SO₄, filtered, and concentrated in vacuo to a yellow oil. Purification by flash chromatography (15:1 → 6:1 hexanes-EtOAc) afforded ketone (−)-15 as a colorless oil that solidifies in a −20 °C freezer to an off-white semi-solid (1.5241 g, 7.845 mmol, 89% yield). Rᵣ = 0.40 (4:1 hexanes-EtOAc); ¹H NMR (500 MHz, CDCl₃): δ 5.74 (dddd, J = 16.8, 10.5, 7.5, 5.7 Hz, 1H), 5.07-5.05 (m, 1H), 5.05-5.02 (m, 1H), 3.80 (s, 3H), 2.62-2.49 (comp m, 2H), 2.33 (dd, J = 13.7, 7.2 Hz, 1H), 2.17 (dddd, J = 13.8, 7.6, 1.0, 1.0 Hz, 1H), 1.92 (dd, J = 13.4, 7.2, 5.8 Hz, 1H), 1.72 (dd, J = 13.4, 6.7, 5.6 Hz, 1H), 1.68 (dd, J = 1.6, 1.6 Hz, 3H), 1.06 (s, 3H); ¹³C NMR (126 MHz, CDCl₃): δ 202.6, 169.6, 134.8, 117.9, 113.2, 55.0, 42.5, 41.9, 31.4, 22.4, 21.8, 7.9; IR (Neat
Supporting Information for Levine, Krout, and Stoltz; Total Synthesis of (+)-Carissone

Film NaCl) 2929, 1620, 1461, 1375, 1356, 1234, 1154, 1116, 999, 916 cm⁻¹; HRMS (EI⁺) m/z: calc’d for C₁₂H₁₈O₂ [M⁺]: 194.1307, found 194.1310; [α]D²²²⁻¹⁰.₆⁹ (c 1.26, CH₂Cl₂, 92% ee).

Acrylate SI6.⁶ To a solution of acrylate SI5 (4.7012 g, 36.19 mmol, 1.0 equiv) and TBSCI (6.00 g, 39.8 mmol, 1.1 equiv) in CH₂Cl₂ (72 mL, 0.5 M) at 0 °C was added Et₃N (15.1 mL, 108.6 mmol, 3.0 equiv) and DMAP (442 mg, 3.62 mmol, 0.1 equiv). The reaction was allowed to stir for 30 min, at which point the cooling bath was removed and the contents warmed to 23 °C and stirred overnight. The reaction mixture was filtered into a separatory funnel and washed with 1N HCl (70 mL), saturated aq NaHCO₃ (100 mL), and brine (100 mL). The organics were dried over MgSO₄, filtered, and concentrated in vacuo to afford ester SI6 as a colorless oil (8.806 g). The material was used in the next step without purification. Rf = 0.63 (6:1 hexanes-EtOAc); ¹H NMR (300 MHz, CDCl₃): δ 6.25 (dd, J = 2.0, 2.0 Hz, 1H), 5.90 (dd, J = 2.0, 2.0 Hz, 1H), 4.37 (dd, J = 2.1, 2.1 Hz, 2H), 4.21 (q, J = 7.1 Hz, 2H), 1.30 (t, J = 7.1 Hz, 3H), 0.92 (s, 9H), 0.08 (s, 6H).

Allylic Alcohol SI7.⁶ To a solution of crude ester alcohol SI6 (8.806 g, 36.03 mmol, 1.0 equiv) in THF (144 mL, 0.25 M) cooled to −78 °C was added dropwise DiBAI (neat, 14.1 mL, 79.3 mmol, 2.2 equiv) over 15 min. The resulting solution was stirred at −78 °C until complete consumption by TLC analysis (4:1 hexanes-EtOAc), at which point the excess DiBAI was quenched with dry EtOAc (4 mL). The resulting solution was stirred for 10 min at −78 °C, then warmed to 0 °C and aged for 30 min. A solution of Rochelle’s salt (75 mL, 1 M) was then added slowly with vigorous stirring. The cooling bath was removed and the contents were vigorously stirred until two homogeneous layers appeared (several hours). The phases were separated and the aqueous was extracted with Et₂O (3 x 75 mL), the combined organics were washed with brine (2 x 100 mL), dried over MgSO₄, filtered, and concentrated in vacuo to afford SI7 as a cloudy colorless oil (7.29 g). The crude material was used in the next reaction without purification. Rf = 0.19 (4:1 hexanes-EtOAc); ¹H NMR (300 MHz, CDCl₃): δ 5.10 (s, 1H), 5.08 (s, 1H), 4.24 (s, 2H), 4.17 (d, J = 5.5 Hz, 2H), 1.95 (t, J = 6.0 Hz, 1H), 0.91 (s, 9H), 0.09 (s, 6H).

Allylic Bromide 16.⁸ To a solution of crude allylic alcohol SI7 (7.29 g, 36.04 mmol, 1.0 equiv) in CH₂Cl₂ (120 mL, 0.3 M) cooled to 0 °C was added CBr₄ (17.942, 54.1 mmol, 1.5 equiv) and PPh₃ (11.331 g, 43.2 mmol, 1.2 equiv). The reaction mixture was stirred at 0 °C until consumption by TLC analysis (4:1 hexanes-EtOAc; required ca. 30 min). The reaction was then quenched slowly with saturated aq NaHCO₃ (40 mL) and warmed to ambient temperature while stirring. The phases were separated and the aqueous was extracted with EtOAc (3 x 50 mL). The combined organics were washed with brine, dried over MgSO₄, filtered, and concentrated in vacuo to a yellow oil containing a Ph₃PO precipitate. This material was dry loaded on SiO₂ and purified by flash chromatography (24:1 → 15:1 → 3:1 hexanes-Et₂O). Fractions containing the desired product were repurified by flash chromatography on SiO₂ (49:1 → 24:1 hexanes-acetone) to afford allylic bromide 16 as a pale yellow oil (5.4251 g, 20.45 mmol, 57% yield over 3 steps). Rf = 0.48 (24:1 hexanes-Et₂O); ¹H NMR (300 MHz, CDCl₃): δ 5.26-5.25 (m, 1H), 5.23 (ddd, J = 1.4, 1.4, 1.4 Hz, 1H), 4.27 (dd, J = 1.4, 1.4 Hz, 2H), 4.01 (s, 2H), 0.92 (s, 9H), 0.10 (s, 6H). All other data are consistent with reported values.
**Triolefin (−)-17.** To a flask containing Mg⁰ turnings (125.4 mg, 5.16 mmol, 3.0 equiv) was added Et₂O (30 mL) and a chip of I₂. The contents were stirred for 25 min at 23 °C and then cooled to 0 °C. Allylic bromide 16 (1.141 g, 4.30 mmol, 2.5 equiv) was dissolved in Et₂O (5 mL) and transferred via cannula to the Mg/Et₂O and stirred for 30 min at 0 °C, then warmed to 23 °C over 30 min. A solution of ketone (−)-15 (333.5 mg, 1.72 mmol, 1.0 equiv) in THF (5 mL) and transferred dropwise to the allylmagnesium bromide via cannula, followed by washings to total 35 mL of THF. Upon consumption of ketone (−)-15 by TLC analysis (4:1 hexanes-ethyl acetate), the reaction was quenched slowly with aq ammonium chloride (50 mL) and stirred until complete dissolution of Mg⁰. The phases were separated and the aqueous phase was extracted with ethyl acetate (3 x 50 mL). The combined organics were washed with brine, dried over MgSO₄, filtered, and concentrated to a pale yellow oil. Purification by flash chromatography (9:1 → 4:1 hexanes-Et₂O, dry load onto SiO₂) afforded the desired triolefin (−)-17 as a colorless oil (563.4 mg, 1.616 mmol, 94% yield). Rf = 0.62 (4:1 hexanes-Et₂O); ¹H NMR (500 MHz, C₆D₆): δ 5.54 (ddd, J = 17.6, 10.3, 7.3, 7.3 Hz, 1H), 5.06 (dd, J = 3.2, 1.7 Hz, 1H), 4.97 (ddd, J = 10.3, 2.2, 1.2 Hz, 1H), 4.92 (ddd, J = 16.9, 2.4, 1.2, 1.2 Hz, 1H), 4.56 (d, J = 1.2 Hz, 2H), 3.95 (s, 2H), 2.75 (dd, J = 17.1, 17.1 Hz, 2H), 2.36 (ddd, J = 17.1, 17.1, 10.3, 5.1 Hz, 1H), 2.33 (ddd, J = 17.1, 17.1, 7.1, 5.4 Hz, 1H), 2.01 (ddd, J = 13.9, 13.9, 13.9, 7.6 Hz, 2H), 1.89 (s, 3H), 1.60 (ddd, J = 13.4, 6.8, 5.1 Hz, 1H), 1.41 (ddd, J = 13.4, 10.0, 5.1 Hz, 1H), 0.98 (s, 9H), 0.87 (s, 3H), 0.06 (s, 6H); ¹³C NMR (126 MHz, C₆D₆): δ 196.6, 158.9, 144.4, 134.5, 134.3, 118.0, 110.3, 67.1, 43.2, 39.2, 34.2, 33.9, 33.2, 32.6, 26.1, 23.9, 18.5, 12.5, 5.2; IR (Neat Film NaCl) 3078, 2930, 2857, 1668, 1610, 1463, 1337, 1081, 1005, 912, 836, 776 cm⁻¹; HRMS (EI⁺) m/z: calc’d for C₂₁H₃₆O₂Si [M⁺]: 348.2485, found 348.2499; [α]D²¹.⁰ −37.3° (c 1.11, CH₂Cl₂, 92% ee).

**Cyclohexene (−)-19.** Triolefin (−)-17 (280.1 mg, 0.804 mmol, 1.0 equiv) was dissolved in PhH (16 mL, 0.05 M) and sparged with N₂ for 15 min. Grubbs’ catalyst 18 (20.5 mg, 0.0241 mmol, 0.03 equiv) was added to the solution, and the flask was placed in a 40 °C oil bath. Upon consumption by TLC analysis (3:1 hexanes-Et₂O), the reaction was cooled to ambient temperature and ethyl vinyl ether (8 mL) was added to the solution. After stirring for ca. 30 min, the solution was concentrated in vacuo. Purification via flash chromatography (9:1 → 4:1 hexanes-Et₂O) afforded cyclohexene (−)-19 as a colorless oil (256.3 mg, 0.800 mmol, 99% yield). Rf = 0.30 (3:1 hexanes-Et₂O); ¹H NMR (500 MHz, C₆D₆): δ 5.58 (ddd, J = 5.4, 1.5, 1.5, 1.5 Hz, 1H), 3.93 (d, J = 1.2 Hz, 1H), 2.86 (d, J = 22.0 Hz, 1H), 2.60 (d, J = 21.7 Hz, 1H), 2.32-2.29 (comp m, 2H), 1.87 (d, J = 1.2 Hz, 3H), 1.83 (dd, J = 16.9, 2.0 Hz, 1H), 1.61 (dd, J = 16.9, 6.1 Hz, 1H), 1.45-1.35 (comp m, 2H), 0.99 (s, 9H), 0.85 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H); ¹³C NMR (126 MHz, C₆D₆): δ 196.4, 157.4, 135.1, 129.5, 119.5, 66.7, 39.6, 36.4, 35.1, 34.3, 29.7, 26.1,
Enone (+)-SI8. Cyclohexene (-)-19 (25.0 mg, 78.0 μmol, 1.0 equiv) was dissolved in MeOH (3.1 mL, 25 mM), and Rh/Al₂O₃ catalyst (40.1 mg, 3.90 μmol, 0.05 equiv) was added with vigorous stirring. The vial was placed under an atmosphere of hydrogen via a balloon and stirred at 26 °C. Upon consumption by TLC (3:1 hexanes-Et₂O, developed thrice), the solids were filtered over Celite washing with EtOAc and concentrated in vacuo. Purification via flash chromatography (9:1 hexanes-Et₂O) afforded the desired enone (+)-SI8 as a colorless oil (14.8 mg, 45.9 μmol, 59% yield, 10:1 dr). R_f = 0.36 (3:1 hexanes-Et₂O, developed twice); ¹H NMR (500 MHz, C₆D₆, major diastereomer): δ 3.33 (dd, J = 14.0, 9.8, 5.1 Hz, 2H), 2.63 (ddd, J = 14.7, 1.7, 1.7 Hz, 1H), 2.38-2.26 (comp m, 2H), 1.96 (s, 3H), 1.68 (dd, J = 13.7, 13.7 Hz, 1H), 1.44 (ddd, J = 13.4, 13.4, 3.7 Hz, 1H), 1.42-1.39 (m, 1H), 1.31-1.23 (comp m, 2H), 1.08 (ddd, J = 14.2, 14.2, 3.6 Hz, 1H), 0.99 (s, 9H), 0.84 (s, 3H), 0.06 (s, 6H); ¹³C NMR (126 MHz, C₆D₆): δ 197.0, 160.0, 129.2, 68.1, 41.6, 41.5, 37.7, 36.0, 34.1, 30.9, 26.1, 24.7, 22.2, 18.5, 11.2, -5.2 (2C); IR (Neat Film NaCl) 2928, 2857, 1668, 1615, 1463, 1305, 1257, 1158, 1098 cm⁻¹; HRMS (FAB+) m/z: calcd for C₁₉H₃₅O₃Si [M + H⁺]: 323.2406, found 323.2402; [α]D⁺⁰.³⁷ +73.0° (c 0.53, CH₂Cl₂, 92% ee).

Alcohol (+)-20. Enone (+)-SI8 (40.3 mg, 0.125 mmol, 1.0 equiv) was dissolved in THF (2.5 mL, 50 mM) and aq HCl (1N, 1.0 mL) was added with vigorous stirring. Upon consumption by TLC (2:1 hexanes-EtOAc), brine was added, the layers were separated, and the aqueous was extracted with Et₂O (3 x 4 mL). The combined organics were washed with saturated aq NaHCO₃, this aq was back extracted with Et₂O (2 x 5 mL), and the organics were dried over MgSO₄, filtered, and concentrated in vacuo. Purification via flash chromatography (2:1 → 1:1 hexanes-EtOAc) afforded alcohol (+)-20 as a colorless oil (24.5 mg, 0.118 mmol, 94% yield, 10:1 d.r.). R_f = 0.37 (1:1 hexanes-EtOAc); ¹H NMR (500 MHz, C₆D₆, major diastereomer): δ 3.12 (d, J = 5.5 Hz, 2H), 2.52 (ddd, J = 14.6, 1.9, 1.9 Hz, 1H), 2.37-2.24 (comp m, 2H), 1.92 (dd, J = 1.3, 1.3 Hz, 3H), 1.52 (ddd, J = 13.1, 13.1, 3.1 Hz, 1H), 1.43 (ddd, J = 13.4, 13.4, 5.3 Hz, 1H), 1.36-1.33 (m, 1H), 1.29-1.21 (comp m, 3H), 1.17-1.09 (m, 1H), 1.03 (ddd, J = 12.9, 12.9, 3.3 Hz, 1H), 0.79 (s, 3H), 0.74 (br s, 1H); ¹³C NMR (126 MHz, C₆D₆): δ 197.2, 160.1, 129.1, 67.7, 41.5, 41.4, 37.7, 35.9, 34.1, 30.8, 24.6, 22.2, 11.3; IR (Neat Film NaCl) 3418 (br), 2924, 1660, 1652, 1608, 1453, 1352, 1150, 1083, 1013 cm⁻¹; HRMS (EI+) m/z: calcd for C₁₃H₂₀O₂ [M⁺]: 208.1463, found 208.1463; [α]D⁺²³ +120.9° (c 0.35, CH₂Cl₂, 92% ee).
Ester (+)-21. Alcohol (+)-20 (24.5 mg, 0.118 mmol, 1.0 equiv) was dissolved in CH₂Cl₂ (2.4 mL, 50 mM) and cooled in an ice/water bath. To this solution was added Dess–Martin periodinane (69.8 mg, 0.165 mmol, 1.4 equiv), and after 5 min the bath was removed and the reaction was stirred at room temperature. Upon completion by TLC analysis (2:1 hexanes-EtOAc), the reaction was diluted with 1:1 hexanes-Et₂O (4 mL) and filtered through a small silica gel plug. Heptanes (5 mL) were added and the filtrate was concentrated in vacuo to a white solid. Purification by filtration through a silica gel plug (3:1 → 1:1 hexanes-Et₂O) afforded a colorless oil (22.3 mg) that was used in the next step.

The resulting material was dissolved in t-BuOH (1.7 mL), to which 2-methyl-2-butene (85 µL, 0.80 mmol, 7.4 equiv) was added with stirring. To this was added a solution of NaH₂PO₄·H₂O (103 mg, 0.746 mmol, 6.9 equiv) and NaClO₂ (89.9 mg, 0.995 mmol, 9.2 equiv) in water (850 µL) over ca. 5 min. Upon consumption by TLC analysis (1:1 hexanes-EtOAc), the t-BuOH was removed on a rotovap, water (2 mL) was added to this slurry, and 1 N HCl was added dropwise until pH < 3. The resulting aq was extracted with Et₂O (4 x 4 mL), a stir bar was added and the extract was cooled in an ice/water bath. A fresh solution of CH₂N₂ in Et₂O (5 mL) was added and the bath was allowed to expire. After the solution was colorless it was dried over MgSO₄, filtered, and concentrated in vacuo. Purification via flash chromatography (3:1 → 2:1 hexanes-Et₂O) afforded ester (+)-21 as a colorless oil that solidifies to a white solid over time or in a −20 °C freezer (24.4 mg, 0.103 mmol, 87% yield over two steps). The diastereomers are separable by flash chromatography with 3:1 hexanes-Et₂O. Rₕ = 0.59 (1:1 hexanes-EtOAc); mp = 46-48 °C; ¹H NMR (500 MHz, C₆D₆, major diastereomer): δ 3.38 (s, 3H), 2.83-2.76 (m, 1H), 2.30-2.09 (comp m, 4H), 1.82 (m, 3H), 1.66-1.62 (comp m, 2H), 1.32 (ddd, J = 13.6, 13.6, 4.9 Hz, 1H), 1.17 (ddd, J = 13.2, 3.9, 3.9 Hz, 1H), 1.12 (ddd, J = 13.5, 2.8, 2.8 Hz, 1H), 0.91-0.85 (m, 1H, 0.72 (s, 3H); ¹³C NMR (126 MHz, C₆D₆): δ 196.8, 174.7, 157.7, 129.9, 51.3, 43.5, 40.9, 37.4, 35.4, 34.0, 29.9, 24.7, 21.9, 11.2; IR (Neat Film NaCl) 2949, 1733, 1668, 1613, 1435, 1350, 1301, 1256, 1190, 1173, 1024, 914 cm⁻¹; HRMS (FAB⁺) m/z: calc’d for C₁₄H₂₁O₃ [M + H]⁺: 237.1491, found 237.1493; [α]D²⁰ +64.0° (c 0.56, CH₂Cl₂, 92% ee).

Diol (+)-22.⁹ To a solution of ester (+)-21 (10.1 mg, 42.7 µmol, 1.0 equiv) in MeOH (1.7 mL, 25 mM) was added CeCl₃·7H₂O (47.8 mg, 128 µmol, 3.0 equiv), followed by cooling to ca. −45 °C in a MeCN/CO₂(s) bath. Solid NaBH₄ (3.2 mg, 85.5 µmol, 2.0 equiv) was added, and upon consumption by TLC analysis (1:1 hexanes-EtOAc), acetone (5 drops) was added, followed by brine (1 mL) and EtOAc (1 mL). The suspension was warmed to room temperature, the aq was extracted with EtOAc (2 x 4 mL),
dried over MgSO₄, filtered, and concentrated *in vacuo* to a colorless film (9.1 mg). This material was used directly in the subsequent reaction.

The resulting material was dissolved in THF (1.5 mL, 25 mM) and cooled in an ice/water bath. A solution of MeMgBr (71 µL, 2.7 M in THF, 191 µmol, 5 equiv) was added and the bath was removed after 5 min. Upon consumption by TLC analysis (1:1 hexanes-EtOAc), the reaction was cooled in an ice/water bath, and MeOH (200 µL), brine (1 mL), saturated aq NH₄Cl (1 mL), and EtOAc (2 mL) were added. The aq layer was extracted with EtOAc (2 x 4 mL), dried over MgSO₄, filtered, and concentrated *in vacuo*. Purification via flash chromatography (2:1 hexanes-EtOAc) afforded diol (+)-22 as a colorless film that solidifies over time to an off-white solid (7.4 mg, 31.0 µmol, 73% yield over two steps, > 20:1 dr). 

R<sub>f</sub> = 0.30 (1:1 hexanes-EtOAc); mp = 123-126 °C; <sup>1</sup>H NMR (500 MHz, CDCl₃): δ 4.03 (app t, <i>J</i> = 6.6 Hz, 1H), 2.60 (app dt, <i>J</i> = 13.5, 2.8 Hz, 1H), 1.94-1.88 (m, 1H), 1.73 (s, 3H), 1.71-1.23 (comp m, 11H), 1.21 (s, 6H), 1.08 (s, 3H); <sup>13</sup>C NMR (126 MHz, CDCl₃): δ 139.7, 126.9, 72.9, 71.7, 50.7, 41.7, 36.2, 35.3, 29.0, 27.4, 27.0, 26.9, 24.8, 23.2, 15.2; IR (Neat Film NaCl) 3366 (br), 2934, 2863, 1455, 1374, 1277, 1138, 1076, 1014, 922, 734 cm⁻¹; HRMS (FAB+) <i>m/z</i>: calc’ed for C₁₅H₂₆O₂ [M]<sup>+</sup>: 238.1933, found 238.1921; [α]<sub>D</sub><sup>21.6</sup> +21.6° (c 0.34, MeOH, 92% ee).

(+)-Carissone (1).<sup>9b</sup> To a solution of diol (+)-22 (3.1 mg, 13.0 µmol, 1.0 equiv) in CH₂Cl₂ (520 µL, 25 mM) was added oven-dried 4ÅMS (15 mg), followed by MnO₂ (13.3 mg, 130 µmol, 10 equiv). Upon consumption by TLC (1:1 hexanes-EtOAc), the reaction was diluted with Et₂O (2 mL) and filtered through a small plug of silica gel, washing with Et₂O. This was concentrated *in vacuo* to afford (+)-carissone (1) as a colorless film (3.1 mg, 131 µmol, 100% yield). R<sub>f</sub> = 0.34 (1:1 hexanes-EtOAc); <sup>1</sup>H NMR (500 MHz, CDCl₃): δ 2.86 (app dt, <i>J</i> = 14.4, 2.6 Hz, 1H), 2.51 (ddd, <i>J</i> = 16.9, 13.3, 6.4 Hz, 1H), 2.39 (app dt, <i>J</i> = 16.8, 3.8 Hz, 1H), 1.90 (app t, <i>J</i> = 13.9 Hz, 1H), 1.82-1.69 (comp m, 4H), 1.78 (s, 3H), 1.55-1.36 (comp m, 3H), 1.26 (s, 3H), 1.25 (s, 3H), 1.20 (s, 3H); <sup>13</sup>C NMR (126 MHz, CDCl₃): δ 199.1, 162.6, 128.8, 49.6, 41.9, 37.3, 35.8, 33.7, 28.7, 27.5, 26.7, 22.5, 22.4, 10.9; IR (Neat Film NaCl) 3448 (br), 2970, 2935, 1652, 1568, 1452, 1353, 1300, 1212, 1189, 1149, 1014, 918, 817 cm⁻¹; HRMS (FAB+) <i>m/z</i>: calc’ed for C₁₅H₂₅O₂ [M + H]<sup>+</sup>: 237.1855, found 237.1844; [α]<sub>D</sub><sup>23.1</sup> +119.6° (c 0.31, CHCl₃, 92% ee); lit. [α]<sub>D</sub><sup>22</sup> +138.7° (c 0.163, CHCl₃).
Chiral SFC and HPLC Data

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Area Percent Report

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Use Multiplier x Dilution Factor with ISIDs

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Totals : 1.4508664 1353.43664

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*** End of Report ***
## Supporting Information for Levine, Krout, and Stoltz; Total Synthesis of (+)-Carissone

### NMR Spectroscopy Data

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### NMR Spectra

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  - **5% IPA, 2 mL/min, 30 °C, 244 nm**

### Area Percent Report

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(modified after loading)

IPA-Z1S9C1TRIC 20 μm

Area Percent Report

Sorted By : Signal
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Dilution : 1.00000

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Peak RectTime Type Width Area Height Area % %
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Results obtained with enhanced integrator!

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<td>10/12/2008 11:29:26 PM by ACJ</td>
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</tr>
</tbody>
</table>

**Area Percent Report**

<table>
<thead>
<tr>
<th>Sorted By</th>
<th>Signal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiplier:</td>
<td>1.0000</td>
</tr>
<tr>
<td>Dilution:</td>
<td>1.0000</td>
</tr>
</tbody>
</table>

**Signal 1: WVD1 A, Wavelength=254 nm, TT**

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<tr>
<th>Peak RetTime Width Area Height Area</th>
<th>#</th>
<th>[min]</th>
<th>[min]</th>
<th>mAU</th>
<th>mAU</th>
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</thead>
<tbody>
<tr>
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<td>7.243</td>
<td>0.1847</td>
<td>7951.59325</td>
<td>717.50653</td>
<td>95.9365</td>
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<tr>
<td>2</td>
<td>9.479</td>
<td>0.2664</td>
<td>336.79871</td>
<td>21.07134</td>
<td>4.0635</td>
</tr>
</tbody>
</table>

| Totals: | 0260.39197 | 738.57037 |

Results obtained with enhanced integrator!

*** End of Report ***
4% EtOH, AD column

Injection Date : 10/2/2008 10:39:58 AM   Seq. Line : 4
Sample Name : srl1-243 mixA   Location : Vial 2
Acq. Operator : mike k   Inj Volume : 5 µl

Act. Method : C:\HPCHEM3\METHODS\AD-E0H30.M
Analysis Method : C:\HPCHEM3\METHODS\AD.EOH30.M
Last changed : 10/12/2008 11:12:47 PM by ACJ
(modified after loading)

HPLC, Chiralpak AD
4% EtOH, 1 mL/min
254 nm

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: UV/Vis A, Wavelength=254 nm, TT

Peak RetTime Type Width Area Height Area
# [min] [min] nAU %s [nAU] %
-----|------|--|--------|--------|-----|------|--|---------|------|--------|------|
1  7.060 MM 0.1893 387.7554  34.13640 4.1710
2  9.078 MM 0.2518 8906.74707 589.68390 95.8290

Totals : 9296.50266  623.02050

Results obtained with enhanced integrator!

*** End of Report ***
$^1$H and $^{13}$C NMR Spectra

$^1$H NMR spectrum of enol carbonate 9 (500 MHz, CDCl$_3$)
$^1$H NMR spectrum of aromatic carbonate $i$ (500 MHz, CDCl$_3$)
$^{13}$C NMR spectrum of aromatic carbonate $i$ (126 MHz, CDCl$_3$)
$^1$H NMR spectrum of β-ketoester (±)-10 (500 MHz, CDCl$_3$)
Supporting Information for Levine, Krout, and Stoltz; Total Synthesis of (+)-Carissone

$^{13}$C NMR spectrum of β-ketoester (±)-10 (126 MHz, CDCl$_3$)
$^1$H NMR spectrum of vinylogous ester (+)-13 (500 MHz, CDCl$_3$)
$^{13}$C NMR spectrum of vinylogous ester (+)-13 (126 MHz, CDCl$_3$)
$^1$H NMR spectrum of $\beta$-ketoester (±)-11 (300 MHz, CDCl$_3$)
$^{13}$C NMR spectrum of β-ketoester (±)-11 (75 MHz, CDCl₃)
$^1$H NMR spectrum of vinylogous thioester (+)-14 (300 MHz, CDCl$_3$)
$^{13}$C NMR spectrum of vinylogous thioester (+)-14 (75 MHz, CDCl$_3$)
$^1$H NMR spectrum of vinylogous ester (-)-15 (500 MHz, CDCl$_3$)
$^{13}$C NMR spectrum of vinylogous ester (−)-15 (126 MHz, CDCl$_3$)
$^1$H NMR spectrum of bis-olefin (−)-17 (500 MHz, C$_6$D$_6$)
$^{13}$C NMR spectrum of bis-olefin (-)-17 (126 MHz, C$_6$D$_6$)
$^{1}$H NMR spectrum of cyclohexene $(-)-19$ (500 MHz, C$_6$D$_6$)
Supporting Information for Levine, Krout, and Stoltz; Total Synthesis of (+)-Carissone

SI 34

$^{13}$C NMR spectrum of cyclohexene (–)-19 (126 MHz, C,D₆)

O O

T B

(-19)
$^1$H NMR spectrum of enone (+)-SI8 (500 MHz, C$_6$D$_6$)
$^{13}$C NMR spectrum of enone (+)-SI8 (126 MHz, C$_6$D$_6$)
$^{1}$H NMR spectrum of alcohol (+)-20 (500 MHz, C$_6$D$_6$)
13C NMR spectrum of alcohol (+)-20 (126 MHz, C₆D₆)
$^1$H NMR spectrum of ester (+)-21 (500 MHz, C$_6$D$_6$)
\( ^{13}\text{C} \) NMR spectrum of ester (\( + \))-21 (126 MHz, \( \text{C}_6\text{D}_6 \))
$^1$H NMR spectrum of diol (+)-22 (500 MHz, CDCl$_3$)
Supporting Information for Levine, Krout, and Stoltz; Total Synthesis of (+)-Carissone

$^{13}$C NMR spectrum of diol (+)-22 (126 MHz, CDCl$_3$)
H NMR spectrum of (+)-carissone (1) (500 MHz, CDCl$_3$)
$^{13}$C NMR spectrum of (+)-carissone (1) (126 MHz, CDCl$_3$)
References