

SUPPORTING INFORMATION

Total Synthesis of Clavepictines A and B. Diastereoselective Cyclization of δ -Aminoallenes

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Experimental procedures and ^1H and ^{13}C NMR spectra for synthetic (-)-clavepictine A and (+)-clavepictine B, and also key synthetic intermediates.

Experimental Section

General. All reactions were conducted under an atmosphere of dry nitrogen and in oven-dried glassware, and concentrations were performed under reduced pressure using a Büchi rotary evaporator. All solvents were purified before use. Ether, tetrahydrofuran, and toluene were distilled from sodium benzophenone ketyl. Methylene chloride was distilled from CaH_2 .

NMR spectra were measured on commercially available spectrometers: ^1H at 360 and ^{13}C at 90 MHz. The ^1H and ^{13}C NMR spectra of clavopictines A and B were also measured at 500 MHz and 125 MHz, respectively. For ^1H spectra tetramethylsilane was used as internal standard. ^{13}C NMR spectra were referenced with the δ 77.0 resonance of CDCl_3 . Low and high resolution mass spectra were measured as EI.

Melting points are uncorrected. Optical rotation were measured with a Perkin-Elmer polarimeter; concentration c is reported in g/100 mL. Analytical thin layer chromatography (TLC) was performed by using Merck 60 F₂₅₄ glass plates precoated with a 0.25-mm thickness of silical gel. Column chromatography was performed on kieselgel 60 (70-230 mesh) silical gel. Unless otherwise noted, all compounds purified by chromatography are sufficiently pure (>95% by ^1H analysis) for use in subsequent reactions. Elemental analyses were performed by Atlantic Microlab, GA.

(R)-5-[(R)-1-hydroxyethyl]-butyrolactone (15). A mixture of **14** (3 g, 17.2 mmol) and Rh on alumina (5 wt %; 0.1 g) in EtOH (30 mL) was stirred under an atmosphere of hydrogen for 6 h. The mixture was filtered through a pad of Celite, and the filter cake was rinsed with EtOH (10 mL). The combined filtrates, whose ^1H NMR indicated a 5:1 mixture of the saturated diol ester and **15**, were treated with potassium carbonate (50 mg). The resulting mixture was stirred overnight and concentrated *in vacuo*. The residue was dissolved in EtOAc (30 mL), washed with brine (2 mL), dried over Na_2SO_4 , and concentrated. Purification of the concentrate by column chromatography (1:2

hexane-EtOAc) afforded the lactone **15** (2 g, 92%) as a colorless oil: $[\alpha]_D = -58^\circ$ (*c* 1.0, CH₂Cl₂); IR(film) 3423, 1759 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 1.18 (d, *J* = 6.6 Hz, 3 H), 2.02 (m, 1 H), 2.20 (m, 1 H), 2.44-2.60 (m, 2 H), 2.95 (br s, 1 H, -OH), 3.73 (dq, *J* = 5.2, 6.6 Hz, 1 H), 4.31 (dt, *J* = 7.3, 5.2 Hz, 1 H); ¹³C NMR (90 MHz, CDCl₃) δ 18.3, 23.2, 28.5, 69.5, 81.2, 177.5.

(5R,6S)-5-Hydroxy-6-methyl-2-piperidinone (16). To a solution of **15** (4.6 g, 35.6 mmol) in CH₂Cl₂ (100 mL) were added at 0 °C methanesulfonyl chloride (5.5 mL, 71 mmol) and triethylamine (14.9 mL, 0.1 mol). The reaction mixture was stirred at 0 °C for 4 h and quenched with aqueous saturated NaHCO₃ solution. The aqueous layer was extracted with CH₂Cl₂. The combined organic extracts were washed with saturated NaHCO₃ solution, followed by brine, dried over MgSO₄, and concentrated to give the crude mesylate (8.3 g) as a white solid: mp 98-100 °C; IR (CH₂Cl₂) 1778, 1349 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 1.47 (d, *J* = 6.6 Hz, 3 H), 2.10 (m, 1 H), 2.34 (m, 1 H), 2.49-2.68 (m, 2 H), 3.10 (s, 3 H), 4.52 (dt, *J* = 7.2, 5.1 Hz, 1 H), 4.77 (dq, *J* = 6.6, 5.1 Hz, 1 H); ¹³C NMR (90 MHz, CDCl₃) δ 17.2, 24.1, 28.0, 38.9, 79.3, 80.6, 176.0.

Sodium azide (13.9 g, 0.21 mol) was added to a solution of the crude mesylate in DMF (60 mL). The resulting mixture was heated at 80 °C for 8 h, cooled, poured into water (20 mL), and extracted with EtOAc (3 x 30 mL). The combined extracts were washed with brine (5 x 10 mL), dried over MgSO₄, and concentrated *in vacuo*. Purification by column chromatography (3:1 hexane-EtOAc) afforded the azido lactone (5.1 g, 92%) as a colorless oil: $[\alpha]_D = -12.6^\circ$ (*c* 2.5, CH₂Cl₂); IR(film) 2119, 1781 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 1.29 (d, *J* = 6.7 Hz, 3 H), 2.12 (m, 1 H), 2.30 (m, 1 H), 2.59 (m, 2 H), 3.79 (dq, *J* = 6.7, 4.8 Hz, 1 H), 4.37 (dt, *J* = 7.1, 4.8 Hz, 1 H); ¹³C NMR (90 MHz, CDCl₃) δ 15.3, 22.7, 28.0, 59.4, 81.5, 176.3.

A solution of the azido lactone (5.1 g, 32.9 mmol) in EtOH (150 mL) was treated with 10% Pd/C (0.2 g). The resulting mixture was stirred under an atmosphere of hydrogen for 8

h. The mixture was filtered through a pad of Celite, and the filter cake was rinsed with EtOH. The combined filtrates were concentrated and purified by column chromatography (10:1 CH₂Cl₂-EtOH) to give the lactam **16** (3.78 g, 88%) as a white solid: mp 130-131 °C; [α]_D = -49.1° (*c* 1.0, CH₂Cl₂); IR(CH₂Cl₂) 3354 (br), 1635 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 1.35 (d, *J* = 6.5 Hz, 3 H), 1.86 (m, 1 H), 2.02 (m, 1 H), 2.35 (ddd, *J* = 18.0, 8.7, 6.6 Hz, 1 H), 2.52 (dt, *J* = 18.0, 6.2 Hz, 1 H), 2.91 (br s, 1 H, -OH), 3.37 (apparent quint, *J* = 6.5, 1.0 Hz, 1 H), 3.63 (ddd, *J* = 8.4, 6.5, 3.4 Hz, 1 H), 6.17 (br s, 1 H, NH); ¹³C NMR (90 MHz, CDCl₃) δ 10.4, 27.4, 28.3, 54.7, 69.7, 171.6; MS *m/z* 129 (M⁺, 100), 119 (39), 105 (39); HRMS (M⁺) calcd for C₆H₁₁NO₂ 129.0789, found 129.0784.

(5R,6S)-N-(Benzyloxycarbonyl)-6-methyl-5-(triisopropylsiloxy)-2-piperidinone (17). To a solution of **16** (1.93 g, 14.9 mmol) in CH₂Cl₂ (50 mL) were added sequentially at 0 °C 2,6-lutidine (2.1 mL, 30 mmol) and TIPSOTf (6.0 mL, 22.3 mmol). After the reaction mixture was stirred at rt for 3 h, it was quenched with aqueous NaHCO₃ solution and extracted with CH₂Cl₂ (3 x 50 mL). The combined organic extracts were washed sequentially with 1N HCl, aqueous saturated NaHCO₃, followed by brine, dried over MgSO₄, and concentrated *in vacuo*. The residue was purified by column chromatography (1:1 hexane-EtOAc) to give the protected lactam (3.57 g, 84%) as a white solid: mp 71-72 °C; [α]_D = -4.9° (*c* 1.2, CH₂Cl₂); ¹H NMR (360 MHz, CDCl₃) δ 1.04 (m, 21 H), 1.19 (d, *J* = 6.6 Hz, 3 H), 1.84 (m, 1 H), 1.95 (m, 1 H), 2.27 (td, *J* = 6.3, 17.6 Hz, 1 H), 2.56 (ddd, *J* = 6.3, 8.4, 17.6 Hz, 1 H), 3.42 (ddq, *J* = 2.2, 4.4, 6.6 Hz, 1 H), 3.78 (ddd, *J* = 6.8, 4.4, 2.4 Hz, 1 H), 6.45 (br s, 1 H); ¹³C NMR (90 MHz, CDCl₃) δ 12.4, 18.0, 21.0, 26.7, 27.6, 55.4, 69.9, 171.6; MS *m/z* 242 (M⁺ - C₃H₇, 100), 224 (13), 198 (18), 185 (74), 157 (14), 131 (20), 112 (14), 103 (40); HRMS(M⁺ - C₃H₇) calcd for C₁₂H₂₄NO₂Si 242.1576, found 242.1605.

To a solution of this lactam (3.2 g, 11.2 mmol) in THF (60 mL) was added slowly at -78 °C *n*-BuLi (1.6M solution in THF; 8.3 mL, 13.4 mmol). After the mixture was stirred for 30 min, a solution of benzyl chloroformate (2.4 mL, 16.8 mmol) in THF (10 mL) was added

dropwise at $-78\text{ }^{\circ}\text{C}$. The reaction mixture was then stirred for an additional 30 min, allowed to warm to $-20\text{ }^{\circ}\text{C}$, quenched with aqueous saturated NH_4Cl , and extracted with EtOAc (3 x 40 mL). The combined extracts were washed with brine and dried over MgSO_4 , and concentrated *in vacuo*. The residue was purified by column chromatography (7:1 hexane-EtOAc) to afford the Cbz-protected lactam **17** (4.61 g, 98%) as a colorless oil: IR(CH_2Cl_2) 1775, 1717 cm^{-1} ; ^1H NMR (360 MHz, CDCl_3) δ 1.01 (m, 21 H), 1.21(d, $J = 6.8\text{ Hz}$, 3 H), 1.88 (m, 1 H), 2.06 (m, 1 H), 2.42 (ddd, $J = 17.5, 7.0, 2.1\text{ Hz}$, 1 H), 2.81 (ddd, $J = 17.5, 11.6, 7.8\text{ Hz}$, 1 H), 3.98 (apparent q, $J = 2.3\text{ Hz}$, 1 H), 4.33 (dq, $J = 2.3, 6.8\text{ Hz}$, 1 H), 5.28 (AB q, $J = 13.0\text{ Hz}$, 2 H), 7.39 (m, 5 H); ^{13}C NMR (90 MHz, CDCl_3) δ 12.2, 17.8, 17.9, 19.4, 24.7, 29.5, 59.1, 68.2, 68.3, 127.9, 128.1, 128.4, 135.6, 154.4, 171.0; MS m/z 376 ($\text{M}^+ - \text{C}_3\text{H}_7$, 2), 332 (43), 242 (100), 198 (18), 185 (83), 157 (11), 131 (18); HRMS($\text{M}^+ - \text{C}_3\text{H}_7$) calcd for $\text{C}_{20}\text{H}_{30}\text{NO}_4\text{Si}$ 376.1944, found 376.1923.

Trifluoromethanesulfonic acid (2S,3R)-N-(benzyloxycarbonyl)-2-methyl-3-(triisopropylsiloxy)-1,2,3,4-tetrahydropyridin-6-yl ester (12). To a solution of **17** (4.5 g, 10.7 mmol) in THF (100 mL) was added dropwise at $-78\text{ }^{\circ}\text{C}$ LiHMDS (1 M solution in hexane; 21.4 mL). After 30 min, a solution of 2-[*N,N*-bis(trifluoromethylsulfonyl)amino]-5-chloropyridine (8.8 g, 22.5 mmol) in THF (20 mL) was added. The resulting mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 2 h. Following addition of 2 N KOH solution, the temperature was allowed to warm to $0\text{ }^{\circ}\text{C}$. The mixture was extracted with ether (3 x 50 mL). The combined extracts were washed with brine, dried over MgSO_4 , and concentrated *in vacuo*. The residue was purified by column chromatography (20:1 hexane-EtOAc) to afford the triflate **12** (5.2 g, 88%) as a colorless oil: $[\alpha]_{\text{D}} = -51.0^{\circ}$ ($c\ 0.7, \text{CH}_2\text{Cl}_2$); IR(CH_2Cl_2) 1734, 1685, 1371 cm^{-1} ; ^1H NMR (360 MHz, CDCl_3) δ 1.00 (m, 21 H), 1.10 (d, $J = 6.9\text{ Hz}$, 3 H), 2.24 (dd, $J = 18.9, 3.8\text{ Hz}$, 1 H), 2.38 (ddd, $J = 18.9, 3.8, 3.4\text{ Hz}$, 1 H), 3.94 (dd, $J = 3.4, 2.3\text{ Hz}$, 1 H), 4.61 (dq, $J = 2.3, 6.9\text{ Hz}$, 1 H), 5.16 (br s, 2 H), 5.21 (t, $J = 3.8\text{ Hz}$, 1 H); ^{13}C NMR (90 MHz, CDCl_3) δ 12.2, 13.9, 17.9, 18.0, 29.1, 57.1, 67.5, 68.5, 103.6, 116.6, 120.1, 128.2, 128.4, 135.2, 137.2, 154.4.

(2S,3R)-N-(Benzyloxycarbonyl)-6-(4-acetoxy-1-butynyl)-2-methyl-3-(triisopropylsiloxy)-1,2,3,4-tetrahydropyridine (11). To a solution of **12** (0.28 g, 0.51 mmol) in THF (5 mL) were added 3-butyn-1-ol (43 mg, 0.61 mmol), Et₃N (0.36 mL, 2.6 mmol), CuI (10 mg, 0.05 mmol) and tetrakis(triphenylphosphine) palladium(0) (61 mg, 0.05 mmol). The reaction mixture was stirred for 18 h at rt, followed by addition of aqueous saturated NH₄Cl solution. The mixture was extracted with EtOAc (2 x 5 mL). The combined organic extracts were washed with brine, dried over MgSO₄, and concentrated *in vacuo*. The residue was purified by column chromatography (5:1 hexane-EtOAc) to afford the coupling product (0.23 g, 91%) as a colorless oil: IR (film) 3476, 1703 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 1.02 (m, 21 H), 1.09 (d, *J* = 7.0 Hz, 3 H), 2.22 (dd, *J* = 19.6, 4.3 Hz, 1 H), 2.33 (dt, *J* = 19.6, 3.9 Hz, 1 H), 2.47 (t, *J* = 5.6 Hz, 2 H), 2.93 (br s, 1 H, -OH), 3.60 (m, 2 H), 3.87 (m, 1 H), 4.43 (dq, *J* = 7.0, 3.0 Hz, 1 H), 5.08 (d, A of AB q, *J* = 12.4 Hz, 1 H), 5.13 (d, B of AB q, *J* = 12.4 Hz, 1 H), 5.39 (t, *J* = 3.5 Hz, 1 H), 7.38 (m, 5 H); ¹³C NMR (90 MHz, CDCl₃) δ 12.2, 14.9, 17.9, 23.9, 29.1, 54.1, 60.8, 67.3, 67.6, 76.9, 80.0, 117.4, 118.7, 128.0, 128.3, 128.4, 136.1, 154.1.

To a solution of the enyne alcohol (0.2 g, 0.42 mmol) in CH₂Cl₂ (5 mL) were added acetic anhydride (0.2 mL, 2.1 mmol) and Et₃N (0.58 mL, 4.2 mmol). After the reaction mixture was stirred at rt for 5 h, it was quenched with aqueous NaHCO₃ solution. The aqueous layer was extracted with CH₂Cl₂. The combined organic extracts were washed with aqueous NaHCO₃ solution and brine, dried over MgSO₄, and concentrated *in vacuo*. The residue was purified by column chromatography (10:1 hexane-EtOAc) to give the acetate **11** (0.21 g, 97%): IR (film) 1743, 1699 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 0.96 (m, 21 H), 1.00 (d, *J* = 6.9 Hz, 3 H), 2.00 (s, 3 H), 2.12 (dd, *J* = 19.5, 4.1 Hz, 1 H), 2.27 (dt, *J* = 19.5, 3.8 Hz, 1 H), 2.46 (t, *J* = 7.0 Hz, 2 H), 3.91 (m, 1 H), 3.99 (t, *J* = 7.0 Hz, 2 H), 4.48 (dq, *J* = 6.9, 3.1 Hz, 1 H), 5.07 (d, A of AB q, *J* = 12.4 Hz, 1 H), 5.18 (d, B of AB q, *J* = 12.4 Hz, 1 H), 5.41 (t, *J* = 3.6 Hz, 1 H), 7.34 (m, 5 H); ¹³C NMR (90 MHz, CDCl₃) δ 12.2, 14.7, 18.0, 19.7, 20.8, 29.5, 54.0, 62.2, 67.5, 67.6, 79.2, 83.7, 118.6, 118.8, 127.8, 128.1, 128.3, 136.3, 154.7, 170.7.

(2R,5R,6S)-N-(Benzyloxycarbonyl)-2-(4-acetoxy-1-butynyl)-6-methyl-5-

(triisopropylsiloxy)piperidine (18). To a solution of the enyne acetate **11** (0.21 g, 0.41 mmol) in CH₂Cl₂ (20 mL) was added NaBH₃CN (0.15 g, 2.46 mmol). After the mixture was stirred for 20 min at rt, a solution of trifluoroacetic acid (0.32 mL, 4.1 mmol) in CH₂Cl₂ (3 mL) was added dropwise at -50 °C. The resulting mixture was stirred for 3 h at -20 – -15 °C and quenched with addition of aqueous saturated NaHCO₃ solution. The organic layer was separated, and the aqueous layer was extracted with CH₂Cl₂. The combined organic extracts were washed with aqueous NaHCO₃ solution, followed by brine, dried over MgSO₄, and concentrated *in vacuo*. The residue was purified by column chromatography (10:1 hexane-EtOAc) to give the piperidine **18** (0.14 g, 66%) as a colorless oil, along with the corresponding desilylated alcohol (18 mg, 12%): [α]_D = +15.0° (c 4.8, CH₂Cl₂); ¹H NMR (360 MHz, CDCl₃) δ 1.05 (m, 21 H), 1.45 (d, *J* = 7.0 Hz, 3 H), 1.68-1.99 (m, 4 H), 2.07 (s, 3 H), 2.52 (dt, *J* = 6.1, 2.0 Hz, 2 H), 3.64 (m, 1 H), 3.77 (quint, *J* = 7.0 Hz, 1 H), 4.13 (t, *J* = 6.9 Hz, 2 H), 5.01 (m, 1 H), 5.08 (d, A of AB q, *J* = 12.3 Hz, 1 H), 5.14 (d, B of AB q, *J* = 12.3 Hz, 1 H), 7.34 (m, 5 H); ¹³C NMR (90 MHz, CDCl₃) δ 12.6, 17.2, 18.1, 19.3, 20.8, 29.0, 30.4, 46.5, 56.5, 62.3, 67.0, 71.5, 80.0, 80.1, 127.9, 128.0, 128.4, 136.6, 155.7, 170.7.

(2S,3R,6S)-N-(*t*-Butyloxycarbonyl)-6-(4-hydroxybutyl)-2-methyl-3-

(triisopropylsiloxy)piperidine (9). A solution of **18** (0.58 g, 1.12 mmol) in MeOH (50 mL) was treated with K₂CO₃ (50 mg). The reaction mixture was stirred overnight at rt. After most of the solvent was removed *in vacuo*, the residue was dissolved in CH₂Cl₂ (60 mL), washed with brine, dried over MgSO₄, and concentrated *in vacuo*. Purification by column chromatography (5:1 hexane-EtOAc) afforded the alcohol (0.5 g, 94%) as a colorless oil: [α]_D = +18.6° (c 0.5, CH₂Cl₂); IR (film) 3452, 1692 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 1.14 (m, 21 H), 1.35 (d, *J* = 7.1 Hz, 3 H), 1.77 (m, 2 H), 1.93 (m, 2 H), 2.44 (dt, *J* = 6.0, 2.1 Hz, 2 H), 3.69 (t, *J* = 6.0 Hz, 2 H), 3.71 (m, 1 H), 3.97 (dq, *J* = 7.1, 5.9 Hz, 1 H), 4.74 (m, 1

H), 5.07 (d, A of AB q, $J = 12.4$ Hz, 1 H), 5.16 (d, B of AB q, $J = 12.4$ Hz, 1 H), 7.33 (m, 5 H); ^{13}C NMR (90 MHz, CDCl_3) δ 12.5, 17.0, 18.0, 18.1, 23.4, 28.3, 29.2, 45.5, 56.3, 61.1, 67.0, 70.7, 81.2, 81.3, 127.9, 128.3, 128.4, 136.6, 155.9.

A solution of the alcohol (0.49 g, 1.0 mmol) in EtOH (30 mL) was treated with 10% Pd/C (50 mg). The mixture was stirred under an atmosphere of hydrogen for 4 h. The mixture was filtered through a pad of Celite, and the filter cake was rinsed with EtOH. The combined filtrates were concentrated *in vacuo* to give the amino alcohol (0.32 g, 93%) which was used for the next step without further purification: IR (film) 3440 (br) cm^{-1} ; ^1H NMR (360 MHz, benzene- d_6) δ 1.17 (m, 21 H), 1.39-1.80 (m, 8 H), 1.61 (d, $J = 6.8$ Hz, 3 H), 1.88 (m, 1 H), 2.02 (m, 1 H), 3.18 (quint, $J = 6.8$ Hz, 1 H), 3.30 (m, 1 H), 3.79 (t, $J = 5.2$ Hz, 2 H), 3.89 (m, 1 H); ^{13}C NMR (90 MHz, CDCl_3) δ 12.4, 16.1, 18.1, 22.0, 26.4, 27.2, 32.1, 33.6, 49.5, 54.1, 62.0, 70.1.

To a solution of the amino alcohol (43 mg, 0.13 mmol) in 1:1 THF- H_2O (2 mL) were added at 0 °C di-*t*-butyl dicarbonate (43 mg, 0.19 mmol) and 6N NaOH (50 μL). The resulting mixture was stirred overnight at rt and extracted with EtOAc (3 \times 3 mL). The combined extracts were washed with brine, dried over MgSO_4 , and concentrated *in vacuo*. The residue was purified by column chromatography (5:1 hexane-EtOAc) to give the *N*-BOC amino alcohol **9** (48 mg, 84%) as a colorless oil: IR (film) 3472, 1694 cm^{-1} ; ^1H NMR (360 MHz, CDCl_3) δ 1.08 (m, 21 H), 1.27 (d, $J = 6.9$ Hz, 3 H), 1.37 (m, 1 H), 1.47 (s, 9 H), 1.55-2.95 (m, 9 H), 3.65 (t, $J = 6.2$ Hz, 2 H), 3.78 (m, 2 H), 3.89 (m, 1 H).

Ethyl 6-[(2*S*,5*R*,6*S*)-*N*-(Benzyloxycarbonyl)-6-methyl-5-(triisopropylsiloxy)piperidin-2-yl]-2(*E*)-hexenoate (8). To a solution of oxalyl chloride (31 μL , 0.36 mmol) in CH_2Cl_2 (2 mL) was added at -78 °C DMSO (32 μL , 0.45 mmol). After 15 min at -78 °C, a solution of **9** (40 mg, 0.09 mmol) in CH_2Cl_2 (0.2 mL) was added. The reaction mixture was then stirred at -78 °C for 30 min. Triethylamine (0.25 mL, 1.8 mmol) was added dropwise, and the temperature was raised to 0 °C. The reaction mixture was quenched with addition of

aqueous saturated NaHCO₃ solution, extracted with EtOAc, washed with brine, and dried over MgSO₄. Concentration *in vacuo* afforded the crude aldehyde which was used for the next step without further purification.

(Carbethoxymethylene)triphenylphosphorane (63 mg, 0.18 mmol) was added to a solution of the crude aldehyde in benzene (3 mL). The resulting mixture was refluxed for 10 h and concentrated *in vacuo*. Purification by column chromatography (20:1 hexane-EtOAc) furnished the ester **8** (39 mg, 88%) as a colorless oil: IR (film) 1720, 1695 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 1.04 (m, 21 H), 1.27 (d, *J* = 6.9 Hz, 3 H), 1.30 (t, *J* = 7.2 Hz, 3 H), 1.47 (s, 9 H), 1.56-1.99 (m, 8 H), 2.23 (m, 2 H), 3.80 (m, 2 H), 3.90 (m, 1 H), 4.21 (q, *J* = 7.2 Hz, 2 H), 5.77 (d, *J* = 15.7 Hz, 1 H), 6.93 (dt, *J* = 15.7, 6.9 Hz, 1 H).

Ethyl (4R,6S,7R,9aS)-Octahydro-6-methyl-7-(triisopropylsiloxy)-4H-quinolizin-4-yl acetate (7). To a solution of the ester **8** (16 mg, 0.03 mmol) in CH₂Cl₂ (1 mL) was added at 0 °C trifluoroacetic acid (12 μL, 0.16 mmol). After the reaction mixture was stirred at 0 °C for 3 h, triethylamine (42 mL, 0.3 mmol) was added. The resulting mixture was stirred at 0 °C for 30 min, allowed to warm to rt, and stirred for an additional 2 h. The reaction mixture was quenched with addition of aqueous saturated NaHCO₃ solution. The aqueous layer was extracted with CH₂Cl₂ (2 x 2 mL), and the combined organic extracts were washed with saturated NaHCO₃, followed by brine, dried over Na₂SO₄, and concentrated *in vacuo*. The residue was purified by column chromatography (1:1 hexane-EtOAc) to give the quinolizidine **7** (9.6 mg, 82%) as a colorless oil: IR (film) 1724 cm⁻¹; ¹H NMR (360 MHz, benzene-d₆) δ 0.89 (d, *J* = 6.8 Hz, 3 H), 1.03 (t, *J* = 7.1 Hz, 3 H), 1.20 (m, 21 H), 1.25-1.50 (m, 5 H), 1.59 (m, 3 H), 1.81 (m, 1 H), 1.92 (m, 1 H), 2.26 (tt, *J* = 11.0, 2.8 Hz, 1 H), 2.28 (dd, *J* = 14.3, 7.8 Hz, 1 H), 2.88 (dd, *J* = 14.3, 4.8 Hz, 1 H), 3.03 (dddd, *J* = 10.6, 7.8, 4.8, 2.8 Hz, 1 H), 3.31 (dq, *J* = 6.8, 2.7 Hz, 1 H), 3.79 (q, *J* = 2.7 Hz, 1 H), 4.03 (q, *J* = 7.1 Hz, 2 H); ¹³C NMR (90 MHz, benzene-d₆) δ 8.2, 12.8, 14.3, 18.4, 24.3, 27.1, 29.2, 33.8, 34.8, 40.3, 53.1, 55.2, 55.3, 60.1, 71.7, 172.4; MS *m/z* 396 (M⁺ - CH₃, 15), 324 (100), 308 (12), 280

(22), 198 (26), 150 (28); HRMS ($M^+ - CH_3$) calcd for $C_{22}H_{42}NO_3Si$ 396.2934, found 396.2958.

(R)-2-Hydroxy-4-pentyn-1-yl 2,2-dimethylpropionate (47). To a solution of (trimethylsilyl)acetylene (1.6 mL, 11.4 mmol) in THF (20 mL) was added at $-78\text{ }^\circ\text{C}$ *n*-BuLi (7.1 mL of a 1.6 M solution of THF, 11.4 mmol). After the mixture was stirred at $-78\text{ }^\circ\text{C}$ for 10 min, $BF_3 \cdot OEt_2$ (1.5 mL, 11.9 mmol) was added at $-78\text{ }^\circ\text{C}$. The resulting mixture was stirred for 10 min. A solution of (*S*)-glycidol pivalate (1.5 g, 9.5 mmol) in THF (6 mL) was then added dropwise at $-78\text{ }^\circ\text{C}$. The reaction mixture was stirred for an additional 30 min and quenched with addition of aqueous NH_4Cl solution. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. Purification by column chromatography (5:1 hexane-EtOAc) gave the trimethylsilylacetylene (2 g, 82%) as a colorless oil: $[\alpha]_D = -6.4^\circ$ (*c* 0.5, CH_2Cl_2); IR (CH_2Cl_2) 3452, 2178, 1736 cm^{-1} ; 1H NMR (360 MHz, $CDCl_3$) δ 0.13 (s, 9 H), 1.21 (s, 9 H), 2.47 (d, *J* = 6.2 Hz, 2 H), 3.97 (m, 1 H), 4.13 (m, 2 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ -0.1, 25.2, 27.0, 27.1, 38.8, 66.9, 68.2, 88.2, 101.7, 178.6.

To a solution of the trimethylsilylacetylene (2 g, 7.8 mmol) in THF (30 mL) was added at $0\text{ }^\circ\text{C}$ TBAF (8.2 mL of a 1.0 M solution in THF). After the resulting mixture was stirred for 2 h at rt, it was quenched with addition of aqueous saturated NH_4Cl solution and extracted with EtOAc (2 x 15 mL). The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. Purification by column chromatography (5:1 hexane-EtOAc) furnished the acetylene 47 (1.3 g, 90%) as a colorless oil: $[\alpha]_D = -8.5^\circ$ (*c* 0.5, CH_2Cl_2); IR(CH_2Cl_2) 3464, 3298, 2119, 1727 cm^{-1} ; 1H NMR (360 MHz, $CDCl_3$) δ 1.22 (s, 9 H), 2.07 (t, *J* = 2.7 Hz, 1 H), 2.44 (dt, *J* = 6.1, 2.3 Hz, 1 H), 4.01 (ddd, *J* = 10.6, 6.1, 4.5 Hz, 1 H), 4.18 (m, 2 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 23.7, 27.0, 38.8, 66.7, 68.1, 71.0, 79.5, 78.6.

(2R)-5-[(2S,3R)-N-(Benzyloxycarbonyl)-2-methyl-3-(triisopropylsiloxy)-1,2,3,4-

tetrahydropyridin-6-yl]-2-hydroxy-4-pentyn-1-yl 2,2-dimethylpropionate (48). To a solution of the triflate **12** (2.31 g, 4.19 mmol) in THF (40 mL) were added the acetylene **47** (0.93 g, 5.0 mmol), Et₃N (2.9 mL, 21.0 mmol), CuI (80 mg, 0.4 mmol) and tetrakis(triphenylphosphine) palladium(0) (0.48 g, 0.4 mmol). The reaction mixture was stirred overnight at rt, followed by addition of aqueous saturated NH₄Cl. The mixture was extracted with EtOAc (3 x 40 mL). The combined organic extracts were washed with brine, dried over MgSO₄, and concentrated *in vacuo*. The residue was purified by column chromatography (4:1 hexane–EtOAc) to afford the coupling product **48** (2.6 g, 81%) as a colorless oil: $[\alpha]_D = +55.0^\circ$ (*c* 1.7, CH₂Cl₂); IR (CH₂Cl₂) 3471, 1732, 1705 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 1.01 (m, 21 H), 1.03 (d, *J* = 6.9 Hz, 3 H), 1.22 (s, 9 H), 2.12 (dd, *J* = 4.1, 19.6 Hz, 1 H), 2.20 (td, *J* = 3.5, 19.6 Hz, 1 H), 2.48 (m, 2 H), 3.90 (m, 2 H), 4.05–4.16 (m, 2 H), 4.44 (m, 1 H), 5.11 (d, A of AB q, *J* = 12.3 Hz, 1 H), 5.16 (d, B of AB q, *J* = 12.3 Hz, 1 H), 5.42 (t, *J* = 3.5 Hz, 1 H), 7.35 (m, 5 H); ¹³C NMR (90 MHz, CDCl₃) δ 12.5, 14.9, 17.9, 25.1, 27.2, 29.1, 38.8, 54.1, 66.8, 67.3, 67.6, 68.1, 80.6, 84.0, 117.6, 118.6, 128.0, 128.3, 128.4, 136.1, 154.0, 178.4; MS *m/z* 585 (M⁺, 6), 498 (83), 464 (21), 450 (28), 396 (51), 348 (44), 306 (59), 264 (31), 199 (85), 131 (97), 103 (100); HRMS(M⁺) calcd for C₃₃H₅₁NO₆Si 585.3486, found 585.3514.

(2R)-5-[(2R,5R,6S)-N-(Benzyloxycarbonyl)-6-methyl-5-(triisopropylsiloxy)piperidin-2-yl]-2-hydroxy-4-pentyn-1-yl 2,2-dimethylpropionate (49). To a solution of **48** (1.77 g, 3.02 mmol) in CH₂Cl₂ (150 mL) was added NaBH₃CN (1.2g, 18.12 mmol). After the mixture was stirred for 20 min at rt, a solution of trifluoroacetic acid (2.3 mL, 30 mmol) in CH₂Cl₂ (10 mL) was added dropwise at -30 °C. The resulting mixture was stirred for 3 h at -20 ~ -15 °C and quenched with addition of aqueous saturated NaHCO₃. The aqueous layer was extracted with CH₂Cl₂ (2 x 20 mL). The combined organic extracts were washed with saturated NaHCO₃ and brine, dried over MgSO₄, and concentrated *in vacuo*. The residue was purified by column chromatography (5:1 → 2:1 hexane–EtOAc) to give the

piperidine **49** (0.92 g, 52%) as a colorless oil, along with the corresponding (desilylated) alcohol (0.22 g, 17%): $[\alpha]_D = +18.9^\circ$ (c 1.77, CH_2Cl_2); IR (CH_2Cl_2) 3469, 1733, 1698 cm^{-1} ; ^1H NMR (360 MHz, CDCl_3) δ 1.01 (m, 21 H), 1.21 (s, 9 H), 1.35 (d, $J = 6.9$ Hz, 3 H) 1.74 (m, 2 H), 1.93 (m, 2 H), 2.43 (m, 2 H), 3.69 (m, 1 H), 3.96 (m, 2 H), 4.13 (d, $J = 5.2$ Hz, 2 H), 4.70 (m, 1 H), 5.07 (d, A of AB q, $J = 12.4$ Hz, 1 H), 5.18 (d, B of AB q, $J = 12.4$ Hz, 1 H), 7.38 (m, 5 H); ^{13}C NMR (90 MHz, CDCl_3) δ 12.4, 16.9, 18.0, 24.5, 27.2, 28.2, 29.1, 38.8, 45.4, 56.4, 66.9, 67.1, 68.4, 70.5, 79.8, 82.0, 127.9, 128.0, 128.4, 136.6, 155.9, 178.6; MS m/z 544 ($\text{M}^+ - \text{C}_3\text{H}_7$, 11), 526 (8), 500 (79), 442 (43), 400 (59), 356 (51), 334 (24), 226 (100), 215 (37), 186 (42), 157 (45), 131 (61); HRMS ($\text{M}^+ - \text{C}_3\text{H}_7$) calcd for $\text{C}_{30}\text{H}_{46}\text{NO}_6\text{Si}$ 544.3094, found 544.3095.

(2R)-5-[(2S,5R,6S)-N-(Allyloxycarbonyl)-6-methyl-5-(triisopropylsiloxy)piperidin-2-yl]-2-hydroxypent-1-yl 2,2-dimethylpropionate (50). A solution of the alcohol **49** (0.51 g, 0.87 mmol) in methanol (20 mL) was treated with 10% Pd/C (250 mg). The mixture was stirred under an atmosphere of hydrogen for 3 h. The mixture was filtered through a pad of Celite, and the filter cake was rinsed with 5 mL of MeOH. The combined filtrates were concentrated *in vacuo* to give, as colorless oil, the saturated amine (0.40 g) which was used immediately for the next step without further purification: $[\alpha]_D = -9.5^\circ$ (c 0.95, CH_2Cl_2); ^1H NMR (360 MHz, CDCl_3) δ 1.05 (m, 21 H), 1.13 (d, $J = 6.9$ Hz, 3 H), 1.21 (s, 9 H), 1.39–1.53 (m, 8 H), 1.60–1.67 (m, 1 H), 1.73–1.81 (m, 1 H), 2.76 (m, 1 H), 2.90 (dq, $J = 3.7, 6.9$ Hz, 1 H), 3.53 (m, 1 H), 3.84 (m, 1 H), 3.97 (dd, $J = 11.2, 6.7$ Hz, 1 H), 4.09 (dd, $J = 11.2, 3.6$ Hz, 1 H); ^{13}C NMR (90 MHz, CDCl_3) δ 12.4, 16.8, 18.1, 21.5, 27.2, 27.5, 27.9, 33.3, 35.5, 38.8, 48.9, 53.9, 68.6, 69.6, 70.6, 178.7; MS m/z 414 ($\text{M}^+ - \text{C}_3\text{H}_7$, 5), 337 (32), 324 (91), 308 (28), 294 (35), 270 (41), 242 (27), 164 (49), 150 (38), 124 (100), 110 (76), 103 (68); HRMS($\text{M}^+ - \text{C}_3\text{H}_7$) calcd for $\text{C}_{25}\text{H}_{51}\text{NO}_4\text{Si}$ 414.3040, found 414.3031.

The crude amine (0.39 g, 0.85 mmol) was dissolved in 1:1 THF/ H_2O (20 mL). Sodium carbonate (0.18 g, 1.7 mmol) and allyl chloroformate (0.14 mL, 1.3 mmol) were added sequentially at 0 °C. The reaction mixture was then stirred for 1 h at 0 °C, extracted with

CH₂Cl₂ (2 x 20 mL), dried over MgSO₄, and concentrated *in vacuo*. Purification of the concentrate by column chromatography (5:1 hexane–EtOAc) afforded the carbamate **50** (0.39 g, 82%): [α]_D = -2.5° (*c* 1.17, CH₂Cl₂); IR(CH₂Cl₂) 3468, 1730, 1693 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 1.03 (m, 21 H), 1.22 (s, 9 H), 1.26 (d, *J* = 6.9 Hz, 3 H), 1.32–1.92 (m, 10 H), 3.73 (m, 1 H), 3.87–3.90 (m, 3 H), 3.96 (dd, *J* = 11.3, 6.9 Hz, 1 H), 4.09 (dd, *J* = 11.3, 3.3 Hz, 1 H), 4.54 (m, 2 H), 5.17 (dd, *J* = 10.5, 1.2 Hz, 1 H), 5.26 (dd, *J* = 17.0, 1.2 Hz, 1 H), 5.91 (m, 1 H); ¹³C NMR (90 MHz, CDCl₃) δ 12.3, 17.8, 18.0, 22.5, 23.6, 27.2, 32.0, 33.1, 38.8, 52.5, 54.8, 65.4, 68.6, 68.9, 70.2, 116.9, 133.3, 156.2, 178.7; MS *m/z* 498 (M⁺ – C₃H₇, 40), 454 (22), 396 (100), 380 (29), 352 (70), 338 (45), 294 (51), 270 (26), 226 (78), 180 (79), 164 (54), 131 (62); HRMS(M⁺ – C₃H₇) calcd for C₂₉H₅₅NO₆Si 498.3251, found 498.3227.

(2S,5R,6S)-N-(Allyloxycarbonyl)-2-[(4R)-5-hydroxy-4-(tetrahydro-2H-pyran-2-yloxy)pentyl]-6-methyl-5-(triisopropylsiloxy)piperidine (51). To a solution of **50** (386 mg, 0.7 mmol) in CH₂Cl₂ (10 mL) was added dihydropyran (0.13 mL, 1.0 mmol) and pyridinium *p*-toluenesulfonate (18 mg, 0.07 mmol). After the reaction mixture was stirred overnight at rt, aqueous saturated NaHCO₃ was added. The aqueous layer was separated and extracted with CH₂Cl₂. The extracts were washed with brine, dried over MgSO₄, and concentrated *in vacuo*. The concentrate was purified by column chromatography (10:1 hexane–EtOAc) to give the THP ether (416 mg, 93%): [α]_D = -3.9° (*c* 1.0, CH₂Cl₂); ¹H NMR (360 MHz, CDCl₃) δ 1.05 (m, 21 H), 1.19 (1.20) (s, 9 H), 1.28 (1.29) (d, *J* = 6.6 Hz, 3 H), 1.31–2.00 (m, 16 H), 3.48 (m, 1 H), 3.69–3.97 (m, 6 H), 4.10–4.19 (m, 2 H), 4.51–4.61 (m, 2 H), 4.69 (4.76) (m, 1 H), 5.17 (dd, *J* = 10.3, 1.3 Hz, 1 H), 5.27 (dd, *J* = 17.1, 1.3 Hz, 1 H), 5.92 (m, 1 H); ¹³C NMR (90 MHz, CDCl₃) δ 12.3, 17.8, 18.1, 19.4 (19.8), 22.3 (22.7), 23.6 (23.7), 25.5, 27.2 (27.4), 30.9 (31.0), 31.4, 32.2 (32.3), 32.5, 38.8, 52.5 (52.7), 54.8, 62.1 (62.7), 65.4, 66.2 (66.6), 70.3 (70.4), 74.1 (75.0), 98.0 (98.1), 116.9, 133.4, 156.2, 178.4.

A solution of the THP ether thus obtained (410 mg, 0.65 mmol) in CH₂Cl₂ (25 mL) was treated with DIBAL (1M solution in hexane, 1.6 mL) at -78 °C. After the reaction mixture

was stirred at $-78\text{ }^{\circ}\text{C}$ for 30 min, it was quenched by slow addition of MeOH (2 mL), followed by brine (1 mL). The resulting mixture was allowed to warm to rt and diluted with ether (60 mL), followed by addition of MgSO_4 (5 g). The suspension was then stirred vigorously for 30 min and filtered through a pad of Celite. The filter cake was rinsed with ether (20 mL) and the combined filterates were concentrated *in vacuo*. Purification by column chromatography (2:1 hexane–EtOAc) gave the primary alcohol 51 (0.34 g, 96%) as a colorless oil: $[\alpha]_{\text{D}} = -1.6^{\circ}$ (c 1.43, CH_2Cl_2); IR (CH_2Cl_2) 3469, 1692 cm^{-1} ; ^1H NMR (360 MHz, CDCl_3) δ 1.14 (m, 21 H), 1.28 (d, $J = 6.6$ Hz, 3 H), 1.30–1.93 (m, 16 H), 3.42–4.04 (m, 8 H), 4.44 (4.72) (m, 1 H), 4.44–4.61 (m, 2 H), 5.17 (dd, $J = 1.4, 11.5$ Hz, 1 H), 5.27 (dd, $J = 1.4, 17.2$ Hz, 1 H), 5.91 (m, 1 H); ^{13}C NMR (90 MHz, CDCl_3) δ 12.3, 17.8, 18.0, 20.2 (21.1), 22.8, 23.8 (23.9), 25.0 (25.3), 27.3 (27.4), 31.1 (31.3), 31.5 (31.7), 32.04 (32.2), 52.5 (52.6), 54.8, 63.3 (64.0), 65.0 (66.2), 65.4, 70.3 (70.4), 77.6 (83.5), 97.7 (101.7), 116.9, 133.4, 156.3; MS m/z 498 ($\text{M}^+ - \text{C}_3\text{H}_7$, 99), 468 (16), 454 (51), 414 (39), 396 (85), 382 (31), 370 (66), 354 (100), 338 (58), 294 (66), 226 (63), 180 (55); HRMS($\text{M}^+ - \text{C}_3\text{H}_7$) calcd for $\text{C}_{29}\text{H}_{55}\text{NO}_6\text{Si}$ 498.3251, found 498.3248.98.

(2S,5R,6S)-N-(Allyloxycarbonyl)-2-[(4R)-4-hydroxy-5-hexynyl]-6-methyl-5-

(triisopropylsiloxy)piperidine (52). To solution of oxalyl chloride (0.13 mL, 1.4 mmol) in CH_2Cl_2 (10 mL) was added at $-78\text{ }^{\circ}\text{C}$ DMSO (0.12 mL, 1.75 mmol). After 20 min at $-78\text{ }^{\circ}\text{C}$, a solution of the alcohol 51 (190 mg, 0.35 mmol) in CH_2Cl_2 (3 mL) was added. The mixture was then stirred at $-78\text{ }^{\circ}\text{C}$ for 40 min. Triethylamine (1.0 mL, 7.0 mmol) was added dropwise, and the temperature was gradually raised to $0\text{ }^{\circ}\text{C}$. The reaction mixture was quenched with addition of a few drops of aqueous saturated NaHCO_3 and then diluted with hexane. The precipitates were first removed by filtration. The filtrate was washed with water and brine, dried over MgSO_4 , and concentrated *in vacuo* to afford the crude aldehyde, which was used immediately for the next step.

A solution of dimethyl (diazomethyl)phosphonate (63 mg, 0.42 mmol) in THF (5 mL)

was treated with *tert*-BuOK (0.42 mL of a 1M solution in THF) at -78 °C. After the resulting solution was stirred at -78 °C for 20 min, a solution of the crude aldehyde in THF (5 mL) was added slowly. The resulting mixture was allowed to slowly warm to 0 °C and stirred at 0 °C for an additional 8 h. After aqueous saturated NH₄Cl was added, the mixture was extracted with EtOAc (2 × 20 mL), washed with brine, and dried over MgSO₄. Concentration afforded the crude acetylene which was used for the next step without further purification.

The crude acetylene was dissolved in MeOH (10 mL), and a catalytic amount of *p*-toluenesulfonic acid was added. The mixture was then stirred at rt for 5 h, diluted with EtOAc (20 mL), washed sequentially with aqueous saturated NaHCO₃ and brine, dried over MgSO₄, and concentrated *in vacuo*. The residue was purified by column chromatography (4:1 hexane–EtOAc) gave the propargyl alcohol **52** (117 mg, 74%) as a colorless oil: $[\alpha]_D = -5.0^\circ$ (*c* 0.38, CH₂Cl₂); IR (CH₂Cl₂) 3426, 3312, 1709, 1693 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 1.08 (m, 21 H), 1.25 (d, *J* = 6.8 Hz, 3 H), 1.40–1.90 (m, 10 H), 2.44 (d, *J* = 1.9 Hz, 1 H), 3.75 (m, 1 H), 3.88 (m, 2 H), 4.38 (td, *J* = 6.4, 1.9 Hz, 1 H), 4.49–4.62 (m, 2 H), 5.27 (qd, *J* = 1.3, 10.5 Hz, 1 H), 5.28 (qd, *J* = 1.3, 17.4 Hz, 1 H), 5.92 (m, 1 H); ¹³C NMR (90 MHz, CDCl₃) δ 12.3, 17.8, 18.0, 22.1, 23.7, 27.2, 31.7, 37.3, 52.5, 54.8, 62.1, 65.5, 70.3, 72.7, 85.0, 117.0, 133.3, 156.3; MS *m/z* 408 (M⁺ – C₃H₇, 100), 382 (50), 364 (71), 354 (44), 338 (50), 324 (20), 306 (46), 254 (25), 226 (48), 180 (33); HRMS (M⁺ – C₃H₇) calcd for C₂₂H₃₈NO₄Si 408.2570, found 408.2571.

Ethyl (3R)-8-[(2S,5R,6S)-N-(Allyloxycarbonyl)-6-methyl-5-(triisopropylsiloxy)piperidin-2-yl]-3,4-octadienoate (53). A mixture of **52** (190 mg, 0.42 mmol), triethyl orthoacetate (2 mL, 11 mmol), and a catalytic amount (3 drops) of propionic acid was heated at 145 °C for 3 h, while ethanol was distilled off. The mixture was cooled and concentrated *in vacuo*. Purification by column chromatography (15:1 hexane–EtOAc) gave the allenic ester **53** (182 mg, 83%) as a colorless oil: $[\alpha]_D = -26.5^\circ$ (*c* 0.56, CH₂Cl₂); IR (CH₂Cl₂) 1968, 1745, 1702

cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 1.05 (m, 21 H), 1.25 (t, *J* = 7.1 Hz, 3 H), 1.28 (d, *J* = 6.7 Hz, 3 H), 1.37 (m, 2 H), 1.63–2.05 (m, 8 H), 2.99 (dd, *J* = 7.0, 2.8 Hz, 2 H), 3.74 (m, 1 H), 3.85 (m, 2 H), 4.13 (q, *J* = 7.1 Hz, 2 H), 4.45–4.61 (m, 2 H), 5.15–5.22 (m, 2 H), 5.18 (qd, *J* = 1.3, 10.5 Hz, 1 H), 5.27 (qd, *J* = 1.3, 17.3 Hz, 1 H), 5.92 (m, 1 H); ¹³C NMR (90 MHz, CDCl₃) δ 12.3, 14.2, 17.8, 18.0, 23.9, 26.4, 27.4, 28.5, 31.6, 35.0, 52.6, 54.8, 60.6, 65.4, 70.4, 84.1, 92.1, 116.8, 133.4, 156.2, 171.6, 204.9; MS *m/z* 521 (M⁺, 2), 478 (100), 461 (19), 446 (28), 434 (44), 418 (17), 354 (36), 304 (28), 248 (24), 226 (20), 180 (36); HRMS (M⁺ – C₃H₇) calcd for C₂₆H₄₄NO₅Si 478.2989, found 478.2972.

(2*S*,5*R*,6*S*)-*N*-(Allyloxycarbonyl)-2-[(4*R*,8*RS*)-8-hydroxy-4,5-tetradecadienyl]-6-methyl-5-(trisopropylsiloxy)piperidine (54). To a solution of 53 (170 mg, 0.33 mmol) in ether (5 mL) was added dropwise at -78 °C DIBAL-H (0.36 mL of a 1M solution in hexane). After the reaction mixture was stirred at -78 °C for 1 h, hexylmagnesium bromide (0.25 mL of a 2M solution in Et₂O, 0.5 mmol) was added. The resulting mixture was stirred at -78 °C for an additional 1.5 h, quenched with addition of MeOH, followed by brine, and allowed to warm to rt. Ether (35 mL) and MgSO₄ were added, and the mixture was then stirred vigorously for 20 min. The slurry was filtered through a pad of Celite, and the filter cake was rinsed with ether (10 mL). The combined filtrates were concentrated *in vacuo*. Purification by column chromatography (6:1 hexane–EtOAc) afforded the alcohol 54 (160 mg, 86%) as a colorless oil: [α]_D = -25.6° (*c* 1.1, CH₂Cl₂); IR (CH₂Cl₂) 3472, 1962, 1692, 1462 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 0.88 (t, *J* = 7.0 Hz, 3 H), 1.04 (m, 21 H), 1.29 (d, *J* = 6.6 Hz, 3 H), 1.27–2.39 (m, 22 H), 3.65 (m, 1 H), 3.75 (m, 1 H), 3.85 (m, 2 H), 4.50–4.62 (m, 2 H), 5.10 (m, 2 H), 5.17 (qd, *J* = 1.5, 10.5 Hz, 1 H), 5.28 (qd, *J* = 1.5, 17.3 Hz, 1 H), 5.92 (m, 1 H); ¹³C NMR (90 MHz, CDCl₃) δ 12.3, 14.1, 17.8, 18.1, 22.6, 23.8, 25.7, 26.4, 27.4, 28.6 (28.7), 29.4, 31.6, 31.8, 36.6 (36.7), 37.2 (37.3), 52.7, 54.8, 65.4, 70.4, 71.1 (71.3), 87.3, 91.1, 116.9, 133.4, 156.3, 205.0; MS *m/z* 563 (M⁺, 3), 520 (92), 502 (45), 476 (58), 458 (45), 418 (100), 406 (37), 354 (81), 324 (32), 226 (37), 180 (78), 136 (45); HRMS (M⁺) calcd for C₃₃H₆₁NO₄Si 563.4370, found

563.4349.

(2S,5R,6S)-6-Methyl-2-[(4R,8RS)-8-(triethylsiloxy)-4,5-tetradecadienyl]-5-

(trisopropylsiloxy)piperidine (55). A solution of **54** (155 mg, 0.27 mmol) in CH₂Cl₂ (5 mL) was treated sequentially with 2,6-lutidine (48 μL, 0.4 mmol) and TESOTf (73 μL, 0.3 mmol) at 0 °C. The mixture was stirred at rt for 3 h, quenched with addition of aqueous saturated NaHCO₃, and diluted with EtOAc (25 mL). The organic layer was washed with 1N HCl solution, saturated NaHCO₃ and brine, and dried over MgSO₄. Concentration and purification by column chromatography (15:1 hexane–EtOAc) afforded the triethylsilyl ether (170 mg, 93%) as a colorless oil: $[\alpha]_D = -19.9^\circ$ (*c* 0.75, CH₂Cl₂); IR (CH₂Cl₂) 1962, 1702 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 0.60 (q, *J* = 7.8 Hz, 6 H), 0.88 (t, *J* = 6.9 Hz, 3 H), 0.96 (t, *J* = 7.8 Hz, 9 H), 1.04 (m, 21 H), 1.29 (d, *J* = 6.8 Hz, 3 H), 1.24-2.20 (m, 22 H), 3.68 (m, 1 H), 3.75 (m, 1 H), 3.85 (m, 2 H), 4.52-4.62 (m, 2 H), 5.06 (m, 2 H), 5.18 (qd, *J* = 1.3, 10.5 Hz, 1 H), 5.29 (qd, *J* = 1.3, 15.8 Hz, 1 H), 5.93 (m, 1 H); ¹³C NMR (90 MHz, CDCl₃) δ 5.1, 6.9, 12.3, 14.1, 17.8, 18.1, 22.6, 23.9, 25.3 (25.4), 26.7, 27.5, 28.8, 29.5, 31.7 (31.9), 36.7 (36.8), 37.3 (37.5), 52.7, 54.8, 65.4, 70.4, 72.3, 87.2 (87.4), 90.3, 116.8, 133.4, 156.3, 204.7 (204.8); MS *m/z* 677 (M⁺, 1), 634 (51), 590 (21), 534 (16), 458 (21), 418 (17), 380 (19), 364 (40), 270 (26), 229 (100), 201 (43), 115 (81); HRMS (M⁺) calcd for C₃₉H₇₅NO₄Si₂ 677.5190, found 677.5200.

A solution of the triethylsilyl ether (140 mg, 0.21 mmol) in THF (5 mL) was treated with tetrakis(triphenylphosphine) palladium(0) (24 mg, 0.02 mmol) and dimedon (248 mg, 1.7 mmol). The reaction mixture was stirred at rt for 3 h, diluted with CH₂Cl₂ (20 mL), washed with 2N KOH (3 x 5 mL) and brine, and dried over MgSO₄. Concentration and purification by column chromatography (basic alumina–grade I; 40:1 hexane–EtOAc) furnished the amine **55** (107 mg, 86%) as a colorless oil: $[\alpha]_D = -23.0^\circ$ (*c* 0.53, CH₂Cl₂); IR (CH₂Cl₂) 1958, 1364 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 0.59 (q, *J* = 7.8 Hz, 6 H), 0.88 (t, *J* = 6.5 Hz, 3 H), 0.96 (t, *J* = 7.8 Hz, 9 H), 1.05 (m, 21 H), 1.13 (d, *J* = 6.9 Hz, 3 H), 1.20-1.95 (m, 18 H), 2.00 (m, 2 H), 2.15 (m, 2 H), 2.73 (m, 1 H), 2.89 (m, 1 H), 3.52 (m, 1 H), 3.69 (m, 1 H), 5.05

(m, 2 H); ^{13}C NMR (90 MHz, CDCl_3) δ 5.1, 6.9, 12.5, 14.1, 17.4, 18.2, 22.6, 25.3 (25.4), 26.0, 27.6, 27.9, 29.0, 29.5, 31.9, 34.8, 36.7 (36.8), 37.3 (37.5), 49.2, 53.8, 71.2, 72.3, 87.2 (87.4), 90.1, 204.8; MS m/z 593 (M^+ , 10), 564 (30), 550 (43), 522 (19), 508 (16), 420 (11), 390 (18), 364 (100), 270 (62), 229 (64), 201 (35), 190 (43), 115 (60); HRMS (M^+) calcd for $\text{C}_{35}\text{H}_{71}\text{NO}_2\text{Si}_2$ 593.5023, found 593.5021.

(4S,6S,7R,9aS)-Octahydro-6-methyl-4-[(1E,4RS)-4-(triethylsiloxy)-1-decenyl]-7-(triisopropylsiloxy)-4H-quinolizine (56) and **(4R,6S,7R,9aS)-Octahydro-6-methyl-4-[(1E,4RS)-4-(triethylsiloxy)-1-decenyl]-7-(triisopropylsiloxy)-4H-quinolizine (57)**. To a solution of **55** (80 mg, 0.13 mmol) in 1:1 acetone- H_2O (5 mL) was added AgNO_3 (7 mg, 0.04 mmol). The reaction mixture was stirred at rt for 18 h. After acetone was removed *in vacuo*, the residue was dissolved with CH_2Cl_2 (10 mL) and K_2CO_3 was then added. After the mixture was stirred vigorously for 10 min, the organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL). The combined organic extracts were dried over MgSO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (5:1 hexane-EtOAc) to give the quinolizidine **56** (38.4 mg, 48%), along with the epimer **57** (5.6 mg, 7%): $[\alpha]_{\text{D}} = -27.2^\circ$ (c 0.37, CH_2Cl_2); ^1H NMR (360 MHz, benzene- d_6) δ 0.72 (0.73) (q, $J = 7.9$ Hz, 6 H), 0.95 (t, $J = 8.4$ Hz, 3 H), 1.12 (1.13) (t, $J = 7.9$ Hz, 9 H), 1.21 (m, 21 H), 1.28 (t, $J = 6.7$ Hz, 3 H), 1.30–2.00 (m, 20 H), 2.44 (m, 2 H), 3.21 (m, 1 H), 3.38 (m, 1 H), 3.67 (m, 1 H), 3.85 (m, 1 H), 4.05 (m, 1 H), 5.82 (m, 2 H); ^{13}C NMR (90 MHz, CDCl_3) δ 5.1, 6.9, 12.7, 14.1, 17.1, 18.2 (18.3), 19.8, 22.6, 23.8, 25.3, 27.8, 28.8, 29.5, 29.7, 31.9, 36.6 (36.8), 40.7 (41.1), 49.6, 55.8, 56.6, 72.3 (72.4), 73.0, 127.0, 136.9 (137.0); MS m/z 593 (M^+ , 37), 578 (100), 564 (36), 550 (38), 508 (18), 420 (13), 380 (75), 364 (96), 350 (29), 324 (62), 229 (65), 115 (84); HRMS (M^+) calcd for $\text{C}_{35}\text{H}_{71}\text{NO}_2\text{Si}_2$ 593.5023, found 593.5027.

Spectral data for **57**: $[\alpha]_{\text{D}} = +8.8^\circ$ (c 0.2, CH_2Cl_2); ^1H NMR (360 MHz, benzene- d_6) δ 0.73 (q, $J = 7.9$ Hz, 6 H), 0.89 (0.90) (d, $J = 6.8$ Hz, 3 H), 0.96 (t, $J = 6.8$ Hz, 3 H), 1.11 (t, $J = 7.9$ Hz, 9 H), 1.23 (m, 21 H), 1.30–1.70 (m, 20 H), 2.31 (m, 1 H), 2.40 (m, 2 H), 2.92 (m, 1 H), 3.45 (dq, J

= 3.1, 6.8 Hz, 1 H), 3.82 (m, 2 H), 5.65–5.87 (m, 2 H); ^{13}C NMR (90 MHz, CDCl_3) δ 5.0 (5.1), 6.9, 7.9, 12.5, 14.1, 18.2, 22.6, 24.1, 25.3 (25.6), 27.2, 28.6, 29.5, 31.9, 34.2 (34.7), 36.5 (36.9), 40.5 (41.1), 52.0, 56.3, 62.0 (62.2), 71.4, 72.4 (72.6), 125.8, 136.9 (137.0).

(1E,4RS)-1-[(4S,6S,7R,9aS)-Octahydro-6-methyl-5-(triisopropylsiloxy)-4H-quinolizin-4-yl]-1-decen-4-ol (58). To solution of **56** (26 mg, 0.044 mmol) in THF (2 mL) was added at 0 °C TBAF (1M solution in THF, 90 μl). After the reaction mixture was stirred at 0 °C for 4 h, it was diluted with CH_2Cl_2 (10 mL) and washed with brine (2 x 2 mL). The aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL). The combined organic extracts were dried over MgSO_4 and concentrated *in vacuo*. Purification by column chromatography (20:1 \rightarrow 15:1 \rightarrow 10:1 CH_2Cl_2 -EtOH) afforded the alcohol **58** (21.2 mg, 81%) as a colorless oil: $[\alpha]_{\text{D}} = -22.7^\circ$ (*c* 0.37, CH_2Cl_2); IR (CH_2Cl_2) 3368 cm^{-1} ; ^1H NMR (360 MHz, benzene- d_6) δ 0.94 (t, *J* = 7.0 Hz, 3 H), 1.20 (m, 21 H), 1.21–1.54 (m, 12 H), 1.56 (1.57) (d, *J* = 6.7 Hz, 3 H), 1.57–1.92 (m, 8 H), 2.22 (m, 2 H), 3.15 (m, 1 H), 3.33 (m, 1 H), 3.48 (m, 1 H), 3.65 (m, 1 H), 4.00 (m, 1 H), 5.77 (m, 2 H); ^{13}C NMR (90 MHz, CDCl_3) δ 12.7, 14.1, 17.0 (17.1), 18.2 (18.3), 19.9, 22.6, 23.7 (23.9), 25.6, 27.7 (27.9), 28.9, 29.4, 29.5, 29.7, 31.8, 36.7, 40.7 (40.8), 49.6, 55.9, 56.4 (56.6), 70.8 (71.0), 72.9 (73.0), 126.2 (126.4), 138.6 (139.0); MS *m/z* 479 (M^+ , 15), 464 (43), 436 (11), 446 (12), 385 (39), 364 (20), 313 (37), 295 (63), 267 (39), 253 (21), 235 (24), 211 (20), 199 (100); HRMS (M^+) calcd for $\text{C}_{29}\text{H}_{57}\text{NO}_2\text{Si}$ 479.4159, found 479.4154.

Clavepictine B (1B). A solution of **58** (13 mg, 0.027 mmol) in benzene (1 mL) was treated with Martine sulfurane (90 mg, 0.135 mmol) at rt. The reaction mixture was stirred for 30 min. After the solvent was removed under reduced pressure, the residue was purified by column chromatography (2:1 hexane–EtOAc) to afford triisopropylsilyl protected clavepictine B (11 mg, 88%) as a colorless oil: $[\alpha]_{\text{D}} = -24.7^\circ$ (*c* 0.4, CH_2Cl_2); ^1H NMR (360 MHz, benzene- d_6) δ 0.95 (t, *J* = 7.0 Hz, 3 H), 1.19 (m, 21 H), 1.25 (d, *J* = 6.7 Hz, 3 H), 1.28–1.49 (m, 12 H), 1.50–1.62 (m, 2 H), 1.63–1.85 (m, 3 H), 1.90–2.15 (m, 3 H), 3.17 (m, 1

H), 3.40 (dq, $J = 3.7, 6.7$ Hz, 1 H), 3.65 (td, $J = 4.0, 3.7$ Hz, 1 H), 4.09 (m, 1 H), 5.69 (td, $J = 7.0, 15.1$ Hz, 1 H), 5.83 (dd, $J = 15.4, 6.6$ Hz, 1 H), 6.21 (dd, $J = 15.1, 10.5$ Hz, 1 H), 6.44 (dd, $J = 15.4, 10.5$ Hz, 1 H); ^{13}C NMR (90 MHz, CDCl_3) δ 12.6, 14.1, 17.2, 18.2, 18.3, 19.8, 22.6, 23.0, 28.4, 28.9, 29.4, 29.7, 31.8, 32.7, 49.7, 56.1, 57.1, 72.6, 130.3, 130.9, 133.1, 136.3; MS m/z 461 (M^+ , 73), 446 (100), 432 (19), 418 (57), 404 (17), 390 (47), 376 (31), 362 (25), 350 (15), 336 (33), 288 (27), 248 (72); HRMS (M^+) calcd for $\text{C}_{29}\text{H}_{55}\text{NOSi}$ 461.4053, found 461.4063.

A solution of triisopropylsilyl protected clavепictine B (11.7 mg, 0.025 mmol) in THF (0.5 mL) was treated at 0 °C with 1.0 M tetrabutylammonium fluoride (50 μl). The reaction mixture was stirred at rt for 3 h, diluted with CH_2Cl_2 (5 mL), and washed with brine (2 x 0.5 mL). The aqueous layer was extracted with CH_2Cl_2 (2 x 2 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by the preparative TLC (10:1 CH_2Cl_2 -MeOH) to afford clavепictine B (**1B**) (6.5 mg, 95%) as a white solid: mp 68-69 °C (lit.¹ mp 70-72 °C); $[\alpha]_{\text{D}} = +24.8^\circ$ (c 0.25, CH_2Cl_2) [lit.¹ $[\alpha]_{\text{D}} = +27.1^\circ$ (c 0.03, CH_2Cl_2); lit.⁴ $[\alpha]_{\text{D}} = +25.7^\circ$ (c 0.61, CH_2Cl_2)]; ^1H NMR (360 MHz, pyridine- d_5) δ 0.82 (t, $J = 7.0$ Hz, 3 H), 1.12-1.28 (m, 7 H), 1.29-1.47 (m, 3 H), 1.32 (d, $J = 6.6$ Hz, 3 H), 1.42 (m, 1 H), 1.53 (m, 2 H), 1.64 (m, 1 H), 1.68 (m, 1 H), 1.84 (m, 2 H), 1.93 (m, 1 H), 2.04 (br q, $J = 7.1$ Hz, 2 H), 3.13 (m, 1 H), 3.32 (apparent quintet, $J = 6.5$ Hz, 1 H), 3.62 (m, 1 H), 4.04 (q, $J = 6.4$ Hz, 1 H), 5.66 (dt, $J = 15.0, 6.2$ Hz, 1 H), 5.72 (br s, 1 H, -OH), 5.88 (dd, $J = 15.5, 6.4$ Hz, 1 H), 6.23 (dd, $J = 15.0, 10.5$ Hz, 1 H), 6.39 (dd, $J = 15.5, 10.5$ Hz, 1 H); ^{13}C NMR (90 MHz, CDCl_3) δ 14.1, 14.3, 19.2, 22.6, 25.9, 27.1, 28.9, 29.3, 29.7, 31.7, 31.9, 32.7, 47.1, 59.0, 61.1, 70.5, 129.9, 133.9, 134.4; ^{13}C NMR (90 MHz, pyridine- d_5) δ 14.2, 16.7, 20.6, 22.8, 26.2, 28.1, 28.3, 29.1, 29.3, 29.7, 31.9, 32.9, 49.5, 56.8, 57.4, 71.9, 130.9, 131.3, 133.0, 137.0; MS m/z 305 (M^+ , 10), 290 (27), 260 (100), 216 (33), 234 (17), 150 (33); HRMS (M^+) calcd for $\text{C}_{20}\text{H}_{35}\text{NO}$ 305.2718, found 305.2736.

Clavепictine A (1A). To a solution of clavепictine B (**1B**) (6 mg, 0.02 mmol) in pyridine (0.2 mL) was added acetic anhydride (19 μl , 0.2 mmol). The reaction mixture was stirred

for 15 h at rt. After the solvent was evaporated *in vacuo*, the residue was dissolved in EtOAc (2 mL), washed with aqueous saturated NaHCO₃ solution, followed by brine, dried over Na₂SO₄, and concentrated *in vacuo*. The residue was purified by the preparative TLC (10:1 EtOAc-EtOH) to afford clavopictine A (**1A**) (5.1 mg, 74%) as a colorless oil: $[\alpha]_D = -70.2^\circ$ (*c* 0.2, CH₂Cl₂) [lit.¹ $[\alpha]_D = -75.6^\circ$ (*c* 0.7, CH₂Cl₂); lit.⁴ $[\alpha]_D = -74.5^\circ$ (*c* 0.55, CH₂Cl₂)]; IR (CH₂Cl₂) 2927, 1736, 1457, 1375, 1245 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 0.88 (t, *J* = 6.4 Hz, 3 H), 1.09 (m, 1 H), 1.15 (d, *J* = 7.0 Hz, 3 H), 1.21-1.34 (m, 8 H), 1.38 (m, 2 H), 1.67 (m, 4 H), 1.77 (m, 1 H), 1.88-2.03 (m, 2 H), 2.05 (br q, *J* = 6.9 Hz, 2 H), 2.08 (s, 3 H), 3.25 (m, 1 H), 3.38 (br q, *J* = 7.0 Hz, 1 H), 3.77 (br t, *J* = 8.2 Hz, 1 H), 4.63 (m, 1 H), 5.46 (dd, *J* = 14.3, 7.4 Hz, 1 H), 5.58 (dt, *J* = 14.1, 6.9 Hz, 1 H), 6.06 (apparent quintet, *J* = 12.3 Hz, 2 H); ¹³C NMR (90 MHz, CDCl₃) δ 14.1, 17.1, 19.7, 20.7, 21.6, 22.6, 25.7, 28.9, 29.3, 29.7, 29.9, 31.7, 32.6, 49.0, 52.9, 58.1, 73.3, 130.0, 131.0, 133.6, 136.0, 170.3; MS *m/z* 347 (M⁺, 7), 332 (15), 288 (25), 260 (100); HRMS (M⁺) calcd for C₂₂H₃₇NO₂ 347.2824, found 347.2850.

(2S,3R)-N-(*t*-Butyloxycarbonyl)-2-methyl-3-(triisopropylsiloxy)piperidine (62). To a solution of the piperidone **61** (0.7 g, 2.45 mmol) in THF (30 mL) was added BH₃ (4.9 mL of a 1 M solution in THF) at rt. The resulting mixture was heated at reflux for 10 h and then cooled to 0 °C. The mixture was treated with 3N HCl (15 mL). After stirring for 2 h at rt, the mixture was adjusted to pH 12 with 2N NaOH. Di-*t*-butyl dicarbonate (0.64 g, 2.9 mmol) in THF (5 mL) was added at 0 °C. The resulting mixture was then stirred overnight at rt and extracted with EtOAc (2 x 20 mL). The extracts were washed with brine, dried over MgSO₄, and concentrated *in vacuo*. The residue was purified by column chromatography (30:1 hexane-EtOAc) to give the *N*-BOC piperidine **62** (0.65 g, 72%) as a colorless oil: $[\alpha]_D = +6.1^\circ$ (*c* 0.95, CH₂Cl₂); IR (film) 1696, 1419 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 1.15 (m, 24 H), 1.33 (m, 1 H), 1.45 (s, 9 H), 1.65 (m, 2 H), 1.94 (m, 1 H), 2.77 (dt, *J* = 13.2, 3.0 Hz, 1 H), 3.78 (m, 1 H), 3.99 (br d, *J* = 13.2 Hz, 1 H), 4.27 (dd, *J* = 6.5, 2.7 Hz, 1 H); ¹³C NMR (90 MHz, CDCl₃) δ 12.3, 14.7, 18.1, 19.2, 26.8, 28.4, 38.1, 53.2, 69.1, 78.8,

155.3; MS m/z 328 ($M^+ - C_3H_7$, 9), 272 (100), 228 (69), 131 (26); HRMS ($M^+ - C_3H_7$) calcd for $C_{17}H_{34}NO_3Si$ 328.2307, found 328.2289.

Ethyl (2R,3S)-2,3-dihydroxydecanoate (64). To a well-stirred mixture of (DHQ)-PHAL (0.1 g, 0.13 mmol), potassium ferricyanide (13.4 g, 40.7 mmol), potassium carbonate (5.6 g, 40.7 mmol), potassium osmate(VI) dihydrate (10 mg, 0.027 mmol), and $CH_3SO_2NH_2$ (1.3 g, 13.6 mmol) in a 1:1 *t*-BuOH- H_2O (150 mL) was added at 0 °C ethyl (*E*)-2-decenoate (2.7 g, 13.6 mmol). The reaction mixture was stirred at 0 °C for 24 h. Solid Na_2SO_3 (10.2 g) was added at 0 °C, and the mixture was stirred for an additional 1 h. The aqueous phase was separated and extracted with CH_2Cl_2 (3 x 100 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo* to afford a pale yellow oil. Purification by column chromatography (1:1 hexane-EtOAc) gave the diol **64** (2.78 g, 88%) as a waxy oil which solidified upon cooling: mp 43-45 °C; $[\alpha]_D = -11.1^\circ$ (*c* 1.0, CH_2Cl_2); IR (CH_2Cl_2) 3452, 1747 cm^{-1} ; 1H NMR (360 MHz, $CDCl_3$) δ 0.88 (t, $J = 6.8$ Hz, 3 H), 1.30 (m, 9 H), 1.32 (t, $J = 7.0$ Hz, 3 H), 1.48 (m, 1 H), 1.62 (m, 2 H), 1.99 (br s, 1 H, -OH), 3.06 (br s, 1 H, -OH), 3.87 (dt, $J = 6.8, 2.0$ Hz, 1 H), 4.07 (d, $J = 2.0$ Hz, 1 H), 4.29 (q, $J = 7.0$ Hz, 2 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 14.0, 14.1, 22.6, 25.7, 29.2, 29.4, 31.8, 33.8, 62.1, 72.5, 73.0, 173.7.

Ethyl (2R,3S)-2-hydroxy-3-(triisopropylsiloxy)decanoate (65). To a solution of diol **64** (2.9 g, 12.5 mmol) in CH_2Cl_2 (50 mL) were added sequentially at 0 °C 2,6-lutidine (2.2 mL, 18.8 mmol) and TIPSOTf (3.3 mL, 12.5 mmol). The reaction mixture was stirred at 0 °C for 1h and quenched with addition of aqueous saturated $NaHCO_3$ solution. The organic layer was washed with 1N HCl solution, aqueous saturated $NaHCO_3$ solution and brine, and dried over $MgSO_4$. Concentration and purification by column chromatography (30:1 hexane-EtOAc) afforded the TIPS mono-protected alcohol **65** (3.6 g, 74 %) as a colorless oil: 1H NMR (360 MHz, $CDCl_3$) δ 0.90 (t, $J = 6.2$ Hz, 3 H), 1.07 (m, 21 H), 1.30 (t, $J = 6.8$ Hz, 3H), 1.21-1.40 (m, 10 H), 1.65 (m, 1 H), 1.86 (m, 1 H), 2.89 (m, 1 H, -OH), 4.09 (m, 1 H), 4.17

(m, 2 H), 4.26 (m, 1 H).

(3S,4S)-4-(Triisopropylsiloxy)-1-undecyn-3-ol (66). To a solution of **65** (3.1 g, 8.0 mmol) in CH_2Cl_2 (20 mL) were added dihydropyran (1.5 mL, 16.0 mmol) and PPTS (0.2 g, 0.8 mmol). After the reaction mixture was stirred for 8 h at rt, it was quenched with addition of aqueous saturated NaHCO_3 solution. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 . The combined organic extracts were washed with brine, dried over MgSO_4 , and concentrated *in vacuo*. Purification by column chromatography (30:1 hexane-EtOAc) gave the diprotected ester (3.4 g, 90%) as a colorless oil: $[\alpha]_D = +9.4^\circ$ (*c* 1.0, CH_2Cl_2); IR (film) 1742, 1455 cm^{-1} ; ^1H NMR (360 MHz, CDCl_3) δ 0.87 (t, *J* = 6.9 Hz, 3 H), 1.06 (m, 21 H), 1.25 (t, *J* = 6.9 Hz, 3H), 1.16-1.34 (m, 10 H), 1.40 (m, 2 H), 1.52 (m, 3 H), 1.72 (m, 2 H), 1.83 (m, 1 H), 3.41 (m, 0.5 H), 3.50 (m, 0.5 H), 3.87 (m, 1 H), 3.93 (d, *J* = 6.7 Hz, 0.5 H), 4.08 (m, 0.5 H), 4.17 (m, 2.5 H), 4.32 (d, *J* = 3.8 Hz, 0.5 H), 4.66 (m, 1 H); ^{13}C NMR (90 MHz, CDCl_3) δ 12.8, (12.9), 14.1, 14.2, 18.1, 18.9, (19.0), 22.6, 24.2, (25.3), 25.4, (25.5), 29.2, (29.3), 29.8, (29.9), 30.3, 31.8, 33.6, (33.7), 60.4, (60.5), 62.1, (62.3), 73.2, (73.9), 76.9, (82.1), (97.2), 100.6, (171.5), 171.7.

To a solution of this ester (3.4 g, 7.2 mmol) in CH_2Cl_2 (40 mL) was added at -78°C DIBAL (15.8 mL of a 1 M solution in hexane). After the mixture was stirred for 10 min at -78°C , it was warmed to 0°C and quenched with addition of MeOH, followed by brine. Ether and MgSO_4 were added, and the mixture was then stirred vigorously for 20 min. The slurry was filtered through a pad of Celite, and the filter cake was rinsed with EtOH. The combined filtrates were concentrated. Purification by column chromatography (7:1 hexane-EtOAc) afforded the corresponding alcohol (2.78 g, 90%) as a colorless oil: $[\alpha]_D = -14.9^\circ$ (*c* 1.85, CH_2Cl_2); IR (film) 3457, 2939, 1460, 1065 cm^{-1} ; ^1H NMR (360 MHz, CDCl_3) δ 0.88 (t, *J* = 7.0 Hz, 3 H), 1.07 (m, 21 H), 1.20-1.41 (m, 11 H), 1.51 (m, 5 H), 1.79 (m, 2 H), 3.52 (m, 1 H), 3.69-3.91 (m, 4 H), 4.01 (m, 0.5 H), 4.08 (m, 0.5 H), 4.50 (m, 0.5 H), 4.77 (m, 0.5 H); ^{13}C NMR (90 MHz, CDCl_3) δ 12.7, (12.8), 14.1, 18.1, (18.2), 20.0, (20.8), 22.6, 25.1, (25.4), 25.7,

(26.4), 29.2, 29.8, (29.9), 30.9, (31.5), 31.8, 32.4, (32.9), 61.7, (62.5), 63.1, (64.7), 73.3, (74.3), 80.5, (85.3), 100.0, (101.4); MS m/z 329 ($M^+ - C_5H_9O_2$, 1), 285 (100), 234 (59), 157 (74); HRMS ($M^+ - C_5H_9O_2$) calcd for $C_{19}H_{41}OSi$ 329.2875, found 329.2853.

To a solution of oxalyl chloride (1.16 mL, 12.9 mmol) in CH_2Cl_2 (50 mL) was added at -78 °C DMSO (1.83 mL, 25.8 mmol) in CH_2Cl_2 (5 mL). After 10 min at -78 °C, a solution of this primary alcohol (2.78 g, 6.45 mmol) in CH_2Cl_2 (5 mL) was added. The mixture was stirred at -78 °C for 30 min. Triethylamine (5.4 mL, 38.7 mmol) was added dropwise, and the temperature was slowly raised to 0 °C. The reaction mixture was quenched with aqueous saturated $NaHCO_3$ and then diluted with hexane (60 mL). After the precipitates were first removed by filtration, the filtrate was washed with water and brine, dried over $MgSO_4$, and concentrated *in vacuo* to afford the crude aldehyde (2.9 g) which was used for the next step without further purification.

To a solution of carbon tetrabromide (4.27 g, 12.9 mmol) was added at 0 °C triphenylphosphine (6.76 g, 25.8 mmol). After stirring for 20 min at rt, the mixture was cooled to 0 °C, and the crude aldehyde in CH_2Cl_2 (10 mL) was added dropwise. The mixture was warmed to rt and stirred for an additional 2 h. The solvent was removed *in vacuo*, and the residue was purified by column chromatography (40:1 hexane-EtOAc) to give the dibromoolefin (3.0 g, 80%) as a colorless oil. Spectral data for one diastereomer: IR (film) 1618, 1465 cm^{-1} ; 1H NMR (360 MHz, $CDCl_3$) δ 0.89 (t, $J = 6.9$ Hz, 3 H), 1.08 (m, 21 H), 1.21-1.35 (m, 10 H), 1.42 (m, 2 H), 1.53 (m, 3 H), 1.70 (m, 1 H), 1.79 (m, 2 H), 3.51 (m, 1 H), 3.86 (m, 1 H), 3.98 (m, 1 H), 4.45 (dd, $J = 8.8, 4.2$ Hz, 1 H), 4.66 (t, $J = 3.5$ Hz, 1 H), 6.51 (d, $J = 8.8$ Hz, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 12.9, 14.1, 18.1, 18.2, 19.5, 22.7, 25.5, 29.2, 29.9, 30.6, 31.8, 33.6, 62.5, 74.0, 77.4, 92.6, 96.1, 137.3; MS m/z 483 ($M^+ - C_5H_9O_2$, 6), 457 (22), 285 (95), 243 (55), 157 (100); HRMS ($M^+ - C_5H_9O_2$) calcd for $C_{20}H_{39}OSiBr^{81}Br$ 483.1116, found 483.1094.

To a solution of the dibromoolefin (2.8 g, 4.8 mmol) in THF (40 mL) was added at -78 °C *n*-BuLi (6.6 mL of a 1.6 M solution in hexane, 10.6 mmol). The resulting mixture was

slowly warmed to 0 °C. After the mixture was stirred at 0 °C for 1 h, it was quenched by addition of aqueous saturated NH₄Cl solution. The organic layer was separated, and the aqueous layer was extracted with EtOAc (2 x 20 mL). The combined organic extracts were washed with brine, dried over MgSO₄, and concentrated to give the crude propagyl ether which was used for the next step without further purification.

This compound was dissolved in MeOH (30 mL), and a catalytic amount of *p*-TsOH·H₂O (20 mg) was added. The mixture was then stirred overnight at rt and quenched with addition of solid NaHCO₃. Most of the solvent was evaporated *in vacuo*. The residue was dissolved in EtOAc (30 mL), washed with aqueous saturated NaHCO₃ solution, followed by brine, dried over MgSO₄, and concentrated *in vacuo*. Purification by column chromatography (30:1 hexane-EtOAc) gave the propagyl alcohol **66** (1.2 g, 73%) as a colorless oil: $[\alpha]_D = +5.7^\circ$ (*c* 2.1, CH₂Cl₂); IR (film) 3446, 3303, 2115 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 0.88 (t, *J* = 6.9 Hz, 3 H), 1.09 (m, 21 H), 1.20-1.43 (m, 10 H), 1.58 (m, 1 H), 1.69 (m, 1 H), 2.39 (d, *J* = 1.3 Hz, 1 H), 2.62 (br s, 1 H, -OH), 3.92 (ddd, *J* = 7.8, 4.1, 3.5 Hz, 1H), 4.27 (m, 1 H); ¹³C NMR (90 MHz, CDCl₃) δ 12.7, 14.0, 18.1, 18.2, 22.6, 24.9, 29.2, 29.8, 31.7, 33.9, 64.3, 73.0, 75.5, 83.8; MS *m/z* 297 (M⁺ - C₃H₇, 17), 285 (30), 271 (37), 157 (50), 131 (100), 115 (47); HRMS (M⁺ - C₃H₇) calcd for C₁₇H₃₃O₂Si 297.2249, found 297.2240.

Ethyl (3R,6S)-6-(triisopropylsiloxy)-3,4-tridecadienoate (67). A mixture of **66** (1.0 g, 2.94 mmol), triethyl orthoacetate (5 mL), and a catalytic amount (5 drops) of propionic acid was heated at 145 °C for 6 h, while ethanol was distilled off. The reaction mixture was concentrated *in vacuo* and purified by column chromatography (40:1 hexane-EtOAc) to provide the allenic ester **67** (0.86 g, 71 %) as a colorless oil: $[\alpha]_D = -21.5^\circ$ (*c* 0.65, CH₂Cl₂); IR (film) 1962, 1737 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 0.88 (t, *J* = 6.9 Hz, 3 H), 1.07 (m, 21 H), 1.27 (t, *J* = 7.1 Hz, 3 H), 1.19-1.40 (m, 10 H), 1.68 (m, 2 H), 3.05 (dd, *J* = 7.2, 5.5 Hz, 2 H), 4.05 (q, *J* = 7.1 Hz, 2 H), 4.25 (m, 1 H), 5.18 (m, 1 H), 5.29 (m, 1 H); ¹³C NMR (90 MHz, CDCl₃) δ 12.4, 14.1, 14.2, 18.1, 22.7, 24.9, 29.3, 29.6, 31.8, 34.4, 37.0, 60.8, 71.2, 85.2, 96.7, 171.4,

203.5; MS m/z 367 ($M^+ - C_3H_7$, 100), 321 (28), 293 (40), 157 (26), 131 (42); HRMS ($M^+ - C_3H_7$) calcd for $C_{21}H_{39}O_3Si$ 367.2668, found 367.2671.

(3R,6S)-6-(Triisopropylsiloxy)-3,4-tridecadien-1-ol (68). To a solution of **67** (0.81 g, 1.97 mmol) in CH_2Cl_2 (30 mL) was added at $-78\text{ }^\circ C$ DIBAL (4.3 mL of a 1 M solution in hexane), and the resulting mixture was warmed slowly to $0\text{ }^\circ C$. After 10 min, the mixture was quenched by addition of MeOH, followed by brine, and allowed to warm to rt. Ether (50 mL) and $MgSO_4$ were added, and the mixture was then stirred vigorously for 20 min. The slurry was filtered through a pad of Celite, and the filter cake was rinsed with ether. The combined filtrates were concentrated and purified by column chromatography (15:1 hexane-EtOAc) to provide the alcohol **68** (0.65 g, 89%) as a colorless oil: $[\alpha]_D = -9.7^\circ$ (c 0.35, CH_2Cl_2); IR (film) 3334, 1962 cm^{-1} ; 1H NMR (360 MHz, $CDCl_3$) δ 0.90 (t, $J = 6.9$ Hz, 3 H), 1.08 (m, 21 H), 1.22-1.48 (m, 10 H), 1.67 (m, 2 H), 2.29 (m, 2 H), 3.70 (m, 2 H), 4.31 (m, 1 H), 5.20 (m, 2 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 12.4, 14.1, 18.1, 22.6, 24.7, 29.3, 29.6, 31.8, 31.9, 39.0, 61.5, 71.0, 89.2, 96.6, 203.1; MS m/z 325 ($M^+ - C_3H_7$, 60), 269 (30), 157 (50), 131 (100); HRMS ($M^+ - C_3H_7$) calcd for $C_{19}H_{37}O_2Si$ 325.2563, found 325.2584.

(3R,6S)-1-Bromo-6-(triisopropylsiloxy)-3,4-tridecadiene (69). To a solution of alcohol **68** (0.62 g, 1.68 mmol) in CH_2Cl_2 (20 mL) were sequentially added at $-23\text{ }^\circ C$ triphenylphosphine (0.88 g, 3.36 mmol) and *N*-bromosuccinimide (0.6 g, 3.36 mmol). The mixture was stirred at $-23\text{ }^\circ C$ for 10 min and allowed to warm to rt. After stirring for an additional 1 h, the mixture was quenched with MeOH, and the solvent was evaporated *in vacuo*. The residue was purified by column chromatography (hexane) to give the bromide **69** (0.68 g, 94%) as a colorless oil: IR (film) 1963 cm^{-1} ; 1H NMR (360 MHz, $CDCl_3$) δ 0.88 (t, $J = 7.0$ Hz, 3 H), 1.06 (m, 21 H), 1.20-1.39 (m, 10 H), 1.56 (m, 2 H), 2.57 (m, 2 H), 3.40 (t, $J = 6.6$ Hz, 2 H), 4.27 (ddd, $J = 12.2, 7.1, 2.0$ Hz, 1 H), 5.27 (m, 2 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 12.4, 14.1, 18.1, 22.7, 24.9, 29.3, 29.6, 31.8, 32.7, 32.3, 39.1, 71.6, 89.5,

96.9, 203.2; MS m/z 389 ($M^+ - C_3H_7$, 100), 285 (6), 165 (24), 149 (19); HRMS ($M^+ - C_3H_7$) calcd for $C_{19}H_{36}OSi^{81}Br$ 389.1698, found 389.1718.

(3R,6S)-1-Cyano-6-(triisopropylsiloxy)-3,4-tridecadiene (70). A mixture of the bromide **69** (0.68 g, 1.58 mmol) and NaCN (93 mg, 1.9 mmol) in DMSO (4 mL) was heated at 50 °C for 2 h. After cooling, the reaction mixture was diluted with EtOAc (20 mL), washed with brine (3 x 5 mL), and dried over $MgSO_4$. Concentration and purification by column chromatography (20:1 hexane-EtOAc) gave the nitrile **70** (0.54 g, 90%) as a colorless oil: $[\alpha]_D = -52.9^\circ$ (c 0.95, CH_2Cl_2); IR (film) 2243, 1962 cm^{-1} ; 1H NMR (360 MHz, $CDCl_3$) δ 0.89 (t, $J = 7.0$ Hz, 3 H), 1.17 (m, 21 H), 1.20-1.39 (m, 10 H), 1.57 (m, 2 H), 2.35 (m, 2 H), 2.43 (m, 2 H), 4.30 (ddd, $J = 11.9, 6.8, 1.6$ Hz, 1 H), 5.20 (m, 2 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 12.4, 14.1, 17.0, 18.1, 22.6, 24.7, 24.8, 29.3, 29.6, 31.8, 39.0, 71.2, 89.2, 98.3, 119.1, 202.7; MS m/z 334 ($M^+ - C_3H_7$, 100), 292 (24), 204 (99), 131 (16); HRMS ($M^+ - C_3H_7$) calcd for $C_{20}H_{36}NOSi$ 334.2566, found 334.2547.

(4R,7S)-7-(Triisopropylsiloxy)-4,5-tetradecadien-1-al (71). To a solution of the nitrile **70** (0.53 g, 1.4 mmol) in CH_2Cl_2 (20 mL) was added at -78 °C DIBAL (1.54 mL of a 1 M solution in hexane). The mixture was stirred at -78 °C for 1 h, quenched by addition of H_2O (2 mL) in SiO_2 (1.2 g), and stirred for 15 min at rt. The resulting suspension was filtered through a pad of Celite, and the filter cake was rinsed with EtOAc. The combined filtrates were concentrated and the residue was purified by column chromatography (30:1 hexane-EtOAc) to give the allenic aldehyde **71** (0.51 g, 95%) which was used immediately for the next step: 1H NMR (360 MHz, $CDCl_3$) δ 0.87 (t, $J = 6.9$ Hz, 3 H), 1.10 (m, 21 H), 1.30 (m, 10 H), 1.57 (m, 2 H), 2.33 (td, $J = 7.1, 5.0$ Hz, 2 H), 2.56 (t, $J = 7.1$ Hz, 2 H), 4.24 (m, 1 H), 5.18 (m, 2 H), 9.78 (s, 1 H).

(2R,5R,6S)-1-(*t*-Butyloxycarbonyl)-2-[(1S,4R,7S)-1-hydroxy-7-(triisopropylsiloxy)-4,5-

tetradecadien-1-yl]-6-methyl-5-(triisopropylsiloxy)piperidine (72), (2R,5R,6S)-1-(*t*-butyloxycarbonyl)-2-[(1R,4R,7S)-1-hydroxy-7-(triisopropylsiloxy)-4,5-tetradecadien-1-yl]-6-methyl-5-(triisopropylsiloxy)piperidine (73), and (2S,3R,6R,7R)-2-methyl-8-oxa-3-(triisopropylsiloxy)-7-[(3R,6S)-7-(triisopropylsiloxy)-3,4-tridecadien-1-yl]-1-azabicyclo[4.3.0]nonan-9-one (74). To a 0.5 M solution of the piperidine 62 (0.4 g, 1.08 mmol) in ether at -78 °C was added *N,N,N',N'*-tetramethylethylenediamine (0.51 g, 1.3 mmol), followed by *sec*-BuLi (0.84 mL of a 1.55 M solution in cyclohexane, 1.3 mmol). The mixture was slowly warmed to -20 °C, stirred for 10 min at -20 °C, and then re-cooled to -78 °C. Aldehyde 71 (0.53 g, 1.39 mmol) in ether (0.5 mL) was added dropwise. The resulting mixture was slowly warmed to -20 °C, stirred for 10 min, and then quenched by addition of aqueous saturated NH₄Cl solution. After the mixture was warmed to rt, the organic layer was separated. The aqueous layer was extracted with EtOAc (2 x 5 mL). The combined organic extracts were washed with brine, dried over MgSO₄, and concentrated *in vacuo*. The residue was purified by column chromatography (10:1 hexane-EtOAc) to give an inseparable mixture of 72 and 73 (0.68 g) which was admixed with recovered starting material 62, along with the oxazolidinone 74 (51 mg, 7%); the ¹H NMR analysis of the crude mixture indicated that the ratio of 72:73:62 was 3:1:1, respectively.

Spectral data for the oxazolidinone 74: $[\alpha]_D = -7.1^\circ$ (*c* 0.5, CH₂Cl₂); IR (film) 2939, 1962, 1753 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 0.88 (t, *J* = 6.8 Hz, 3 H), 1.05 (m, 42 H), 1.12 (d, *J* = 7.1 Hz, 3 H), 1.27 (m, 10 H), 1.58 (m, 4 H), 1.70-1.98 (m, 4 H), 2.04-2.28 (m, 2 H), 3.35 (ddd, *J* = 10.6, 6.4, 3.4 Hz, 1 H), 3.84 (m, 1 H), 3.99 (q, *J* = 7.1 Hz, 1 H), 4.08 (ddd, *J* = 7.6, 6.4, 4.8 Hz, 1 H), 4.24 (m, 1 H), 5.15 (m, 2 H); ¹³C NMR (90 MHz, CDCl₃) δ 12.2, 12.4, 14.1, 15.0, 18.0, 18.1, 22.6, 24.1, 24.2, 24.9, 25.8, 29.3, 29.6, 31.8, 34.1, 29.1, 52.4, 55.5, 68.0, 71.7, 80.3, 91.0, 96.8, 156.8, 202.2; MS *m/z* 634 (M⁺ - C₃H₇, 100), 590 (5), 460 (35), 416 (13), 296 (16), 186 (14); HRMS (M⁺ - C₃H₇) calcd for C₃₆H₆₈NO₄Si₂ 634.4687, found 634.4686. Anal. Calcd for C₃₉H₇₅NO₄Si₂: C, 69.07; H 11.15; N, 2.07. Found: C, 69.36; H 11.22; N, 2.08.

(1*S*,4*R*,7*S*)-1-[(2*R*,5*R*,6*S*)-1-(*t*-Butyloxycarbonyl)-6-methyl-5-(triisopropylsiloxy)piperidin-2-yl]-7-(triisopropylsiloxy)-4,5-tetradecadien-1-yl 3-trifluoromethylbenzoate (76) and (1*R*,4*R*,7*S*)-1-[(2*R*,5*R*,6*S*)-1-(*t*-Butyloxycarbonyl)-6-methyl-5-(triisopropylsiloxy)piperidin-2-yl]-7-(triisopropylsiloxy)-4,5-tetradecadien-1-yl 3-trifluoromethylbenzoate (77). To a solution of an inseparable diastereomeric mixture of 72 and 73 (0.55 g) containing 62 (ca 20%) in CH₂Cl₂ (10 mL) were added pyridine (0.59 mL, 7.3 mmol), 4-dimethylaminopyridine (2 mg, 0.016 mmol), and 3-(trifluoromethyl)benzoyl chloride (0.56 mL, 3.7 mmol). After the reaction mixture was stirred at rt for 18 h, it was quenched with H₂O and extracted with EtOAc (20 mL). The organic extracts were washed successively with 1N HCl solution, aqueous NaHCO₃ solution, followed by brine, and dried over MgSO₄. Concentration and purification by column chromatography (40:1 hexane-EtOAc) afforded 76 (0.43 g) and 77 (0.13 g), along with recovered 62 (46 mg).

Spectral data for 76: $[\alpha]_D = -40^\circ$ (*c* 1.35, CH₂Cl₂); IR (film) 1962, 1726, 1698 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 0.86 (t, *J* = 6.9 Hz, 3 H), 0.97 (m, 21 H), 1.01 (m, 1 H), 1.08 (m, 21 H), 1.19-1.29 (m, 10 H), 1.31 (d, *J* = 7.0 Hz, 3 H), 1.50 (s, 9 H), 1.62 (m, 2 H), 1.71-1.95 (m, 5 H), 2.06 (m, 2 H), 3.70 (dq, *J* = 7.0, 5.3 Hz, 1 H), 3.88 (m, 1 H), 3.99 (m, 1 H), 4.16 (m, 1 H), 5.04 (m, 2 H), 5.82 (dt, *J* = 8.6, 3.5 Hz, 1 H), 7.58 (t, *J* = 7.8 Hz, 1 H), 7.81 (d, *J* = 7.8 Hz, 1H), 7.83 (d, *J* = 7.8 Hz, 1 H), 8.31 (s, 1 H); ¹³C NMR (90 MHz, CDCl₃) δ 12.3, 12.4, 14.1, 17.5, 18.0, 18.1, 21.4, 22.6, 24.9, 28.3, 28.5, 29.3, 29.6, 31.4, 31.8, 39.0, 55.0, 55.6, 70.5, 71.8, 80.0, 91.4, 96.0, 116.6, 126.6, 129.0, 129.4, 130.9, 131.2, 131.4, 132.8, 156.3, 164.8, 202.3.

Spectral data for 77: $[\alpha]_D = -41.2^\circ$ (*c* 6.59, CH₂Cl₂); IR (film) 1964, 1727, 1697 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 0.87 (t, *J* = 6.5 Hz, 3 H), 1.01 (m, 21 H), 1.05 (m, 21 H), 1.24 (m, 10 H), 1.28 (s, 9 H), 1.39 (d, *J* = 6.9 Hz, 3 H), 1.48-1.75 (m, 6 H), 1.82 (m, 2 H), 2.14 (m, 2 H), 3.22 (dq, *J* = 8.1, 6.9 Hz, 1 H), 3.97 (m, 1 H), 4.21 (m, 2 H), 5.11 (m, 2 H), 5.49 (m, 1 H), 7.54 (t, *J* = 7.8 Hz, 1 H), 7.77 (d, *J* = 7.8 Hz, 1H), 8.25 (d, *J* = 7.8 Hz, 1 H), 8.30 (s, 1 H); ¹³C NMR (90

MHz, CDCl₃) δ 12.4, 12.5, 14.1, 17.1, 18.1, 21.3, 22.6, 24.8, 24.9, 28.2, 29.3, 29.6, 30.4, 31.1, 31.8, 39.1, 54.6, 57.4, 71.2, 71.8, 73.9, 79.7, 91.0, 96.3, 126.7, 128.9, 129.2, 130.7, 131.1, 131.4, 133.1, 156.7, 164.9, 202.6.

(1S,4R,7S)-1-[(2R,5R,6S)-6-Methyl-5-(triisopropylsiloxy)piperidin-2-yl]-7-

(triisopropylsiloxy)-4,5-tetradecadien-1-yl 3-trifluoromethylbenzoate (78). To a solution of the carbamate **76** (68 mg, 0.07 mmol) in CH₂Cl₂ (2 mL) were added at 0 °C 2,6-lutidine (43 μL, 0.37 mmol) and TMSOTf (40 μL, 0.22 mmol). After the reaction mixture was stirred at 0 °C for 1h, it was quenched by addition of aqueous saturated NaHCO₃ solution and diluted with EtOAc (10 mL). The organic layer was washed with aqueous NaHCO₃ solution, followed by brine, and dried over MgSO₄. Concentration and purification by column chromatography (5:1 hexane-EtOAc) afforded the amine **78** (55 mg, 95%) as a colorless oil: [α]_D = -24.4° (c 0.55, CH₂Cl₂); IR (film) 2936, 1962, 1724, 1461, 1247 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 0.95 (t, *J* = 6.9 Hz, 3 H), 1.09 (m, 21 H), 1.15 (d, *J* = 7.0 Hz, 3 H), 1.18 (m, 21 H), 1.34 (m, 8 H), 1.50 (m, 3 H), 1.71-2.13 (m, 7 H), 2.20 (m, 2 H), 2.94 (ddd, *J* = 9.5, 6.2, 3.2 Hz, 1 H), 3.02 (dq, *J* = 7.0, 3.4 Hz, 1 H), 3.47 (m, 1 H), 4.40 (m, 1 H), 5.23 (m, 1 H), 5.33 (m, 1 H), 5.58 (m, 1 H), 6.99 (dt, *J* = 14.1, 7.7 Hz, 1 H), 7.40 (dd, *J* = 14.1, 7.7 Hz, 1H), 8.21 (d, *J* = 7.7 Hz, 1 H), 8.61 (s, 1 H); ¹³C NMR (90 MHz, CDCl₃) δ 12.3, 12.4, 14.1, 16.6, 18.1, 21.9, 22.6, 24.9, 27.1, 29.3, 29.6, 31.1, 31.8, 39.1, 51.4, 54.5, 69.7, 71.9, 77.4, 91.2, 96.4, 125.2, 126.6, 129.0, 129.4, 130.9, 131.2, 132.9, 164.9, 202.4.

(1R,4R,7S)-1-[(2R,5R,6S)-6-Methyl-5-(triisopropylsiloxy)piperidin-2-yl]-7-

(triisopropylsiloxy)-4,5-tetradecadien-1-yl 3-trifluoromethylbenzoate (79). The identical experimental procedure, as described for the preparation of **78**, was followed to convert **77** (0.12 g, 0.13 mmol) to **79** (98 mg, 92%), which was obtained as a colorless oil: [α]_D = -40.3° (c 0.95, CH₂Cl₂); IR (film) 2934, 1963, 1726, 1466, 1247 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 0.94 (t, *J* = 6.8 Hz, 3 H), 1.03 (m, 21 H), 1.10 (d, *J* = 7.1 Hz, 3 H), 1.21 (m, 21 H), 1.33

(m, 10 H), 1.55 (m, 2 H), 1.66 (m, 2 H), 1.78 (m, 3 H), 1.98 (m, 1 H), 2.20 (m, 2 H), 2.82 (ddd, $J = 10.6, 3.4, 2.9$ Hz, 1 H), 3.13 (dq, $J = 7.1, 2.3$ Hz, 1 H), 3.50 (m, 1 H), 4.46 (br q, $J = 6.3$ Hz, 1 H), 5.23 (m, 1 H), 5.33 (m, 1 H), 5.48 (m, 1 H), 6.96 (dd, $J = 14.1, 7.7$ Hz, 1 H), 7.40 (dd, $J = 14.1, 7.7$ Hz, 1H), 8.21 (d, $J = 7.7$ Hz, 1 H), 8.59 (s, 1 H); ^{13}C NMR (90 MHz, CDCl_3) δ 12.3, 12.4, 14.1, 16.6, 18.0, 22.6, 24.1, 25.0, 27.4, 29.3, 29.6, 31.2, 31.8, 39.1, 51.5, 54.3, 69.6, 71.8, 76.6, 91.0, 96.3, 126.5, 129.0, 129.4, 130.9, 131.2, 131.3, 132.8, 164.9, 202.4; MS m/z 823 (M^+ , 1), 762 (15), 590 (40), 534 (21), 460 (16), 348 (66), 173 (100), 131 (82); HRMS (M^+) calcd for $\text{C}_{46}\text{H}_{80}\text{NO}_4\text{F}_3\text{Si}_2$ 823.5578, found 823.5598.

(1S,4S,6S,7R,9aR)-Octahydro-6-methyl-4-[(1E,3S)-3-(triisopropylsiloxy)-1-decenyl]-7-(triisopropylsiloxy)-4H-quinolizin-1-yl 3-trifluoromethylbenzoate (80). To a solution of the aminoallene **78** (0.3 g, 0.36 mmol) in 5:1 acetone- H_2O (12 mL) was added AgNO_3 (30 mg, 0.18 mmol). The reaction mixture was stirred at rt for 48 h. After acetone was removed *in vacuo*, the residue was dissolved in EtOAc (15 mL). The aqueous layer was separated and extracted with EtOAc (2 x 5 mL). The combined organic extracts were washed with aqueous saturated NaHCO_3 solution, followed by brine, dried over MgSO_4 , and concentrated *in vacuo*. Purification by column chromatography (30:1 hexane-EtOAc) afforded the quinolizidine **80** (0.28 g, 94%) as a colorless oil: $[\alpha]_{\text{D}} = +11.7^\circ$ (c 0.35, CH_2Cl_2); IR (film) 1725, 1463 cm^{-1} ; ^1H NMR (360 MHz, CDCl_3) δ 0.84 (t, $J = 6.8$ Hz, 3 H), 1.07 (m, 42 H), 1.17 (d, $J = 6.2$ Hz, 3 H), 1.29 (m, 10 H), 1.41-1.73 (m, 5 H), 1.80 (m, 3 H), 1.97 (m, 1 H), 2.05 (m, 1 H), 2.98 (dq, $J = 6.8, 6.2$ Hz, 1 H), 3.23 (m, 1 H), 3.48 (ddd, $J = 8.5, 6.2, 2.3$ Hz, 1 H), 3.38 (m, 1 H), 4.24 (m, 1 H), 5.39 (ddd, $J = 9.2, 9.0, 4.6$ Hz, 1H), 5.62 (m, 2 H), 7.57 (t, $J = 7.8$ Hz, 1 H), 7.81 (d, $J = 7.8$ Hz, 1H), 8.20 (d, $J = 7.8$ Hz, 1 H), 8.26 (s, 1 H); ^{13}C NMR (90 MHz, CDCl_3) δ 12.5, 12.8, 14.1, 16.6, 18.1, 18.2, 18.3, 22.5, 22.6, 23.4, 25.1, 26.1, 29.2, 29.4, 29.6, 31.8, 38.6, 52.7, 53.7, 56.8, 69.5, 73.8, 74.1, 126.4, 126.5, 129.0, 129.3, 130.8, 131.2, 131.6, 132.7, 134.3, 164.7; MS m/z 823 (M^+ , 10), 808 (30), 780 (39), 634 (61), 610 (83), 538 (48), 460 (54), 348 (66), 190 (65), 173 (100); HRMS (M^+) calcd for $\text{C}_{46}\text{H}_{80}\text{NO}_4\text{F}_3\text{Si}_2$ 823.5578, found 823.5548.

Anal. Calcd for $C_{46}H_{80}NO_4F_3Si_2$: C, 67.03; H 9.78; N, 1.70. Found: C, 66.94; H 9.96; N, 1.71.

(1R,4S,6S,7R,9aR)-Octahydro-6-methyl-4-[(1E,3S)-3-(triisopropylsiloxy)-1-decenyl]-7-(triisopropylsiloxy)-4H-quinolizin-1-yl 3-trifluoromethylbenzoate (81). The identical experimental procedure, as described for the preparation of **80**, was applied to **79** (85 mg, 0.1 mmol) to afford **81** (77 mg, 91%) as a colorless oil: $[\alpha]_D = -40.3^\circ$ (c 0.95, CH_2Cl_2); IR (film) 2941, 1726, 1464, 1254 cm^{-1} ; 1H NMR (360 MHz, $CDCl_3$) δ 0.88 (t, $J = 6.9$ Hz, 3 H), 1.06 (m, 42 H), 1.08 (d, $J = 6.9$ Hz, 3 H), 1.22-1.47 (m, 12 H), 1.55 (m, 2 H), 1.68-1.91 (m, 5 H), 2.10 (m, 1 H), 3.45 (m, 2 H), 3.71 (br d, $J = 2.1$ Hz, 1 H), 4.01 (ddd, $J = 10.2, 6.6, 3.5$ Hz, 1 H), 4.19 (br q, $J = 5.4$ Hz, 1 H), 5.14 (ddd, $J = 10.7, 5.3, 4.3$ Hz, 1 H), 5.53 (dd, $J = 15.7, 6.7$ Hz, 1 H), 5.66 (dd, $J = 15.7, 6.3$ Hz, 1 H), 7.58 (t, $J = 7.8$ Hz, 1 H), 7.81 (d, $J = 7.8$ Hz, 1H), 8.23 (d, $J = 7.8$ Hz, 1 H), 8.30 (s, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 12.5, 12.7, 14.1, 15.4, 17.7, 18.1, 18.3, 18.4, 22.7, 24.9, 25.1, 29.0, 29.4, 29.7, 30.6, 31.9, 38.4, 52.2, 55.5, 56.6, 72.1, 73.4, 74.4, 126.5, 129.0, 129.3, 130.8, 131.2, 131.6, 132.8, 134.1, 134.3, 164.5; MS m/z 823 (M^+ , 3), 808 (7), 634 (54), 590 (31), 534 (32), 460 (43), 348 (50), 190 (77), 173 (100); HRMS (M^+) calcd for $C_{46}H_{80}NO_4F_3Si_2$ 823.5578, found 823.5550. Anal. Calcd for $C_{46}H_{80}NO_4F_3Si_2$: C, 67.03; H 9.78; N, 1.70. Found: C, 67.22; H 9.88; N, 1.75.

(1S,4S,6S,7R,9aR)-Octahydro-6-methyl-4-[(1E,3S)-3-(triisopropylsiloxy)-1-decenyl]-7-(triisopropylsiloxy)-4H-quinolizin-1-ol (82). To a solution of the quinolizidine **80** (0.29 g, 0.35 mmol) in CH_2Cl_2 (10 mL) was added at $-78^\circ C$ DIBAL (0.77 mL of a 1 M solution in hexane). After the reaction mixture was stirred at $-78^\circ C$ for 1 h, it was quenched with careful addition of MeOH, followed by brine. The resulting mixture was allowed to warm to rt; ether (20 mL) and $MgSO_4$ were added. The resulting suspension was then stirred vigorously for 30 min and filtered through a pad of Celite. The filter cake was rinsed with ether, and the combined filtrates were concentrated *in vacuo*. Purification by column chromatography (10:1 \rightarrow 5:1 hexane-EtOAc) gave the alcohol **82** (0.2 g, 86%) as

a colorless oil: $[\alpha]_D = -25.5^\circ$ (c 1.2, CH_2Cl_2); IR (film) 3406, 1463 cm^{-1} ; ^1H NMR (360 MHz, CDCl_3) δ 0.87 (t, $J = 6.9$ Hz, 3 H), 1.05 (m, 42 H), 1.08 (d, $J = 6.9$ Hz, 3 H), 1.19-1.37 (m, 10 H), 1.47-1.67 (m, 5 H), 1.75 (m, 2 H), 1.83 (m, 1 H), 2.12 (m, 1 H), 2.20 (m, 1 H), 2.98 (ddd, $J = 7.1, 6.9, 3.6$ Hz, 1 H), 3.19 (dq, $J = 6.9, 3.6$ Hz, 1 H), 3.61 (ddd, $J = 5.2, 3.6, 3.2$ Hz, 1 H), 3.74 (m, 1 H), 3.88 (m, 1 H), 4.18 (br q, $J = 5.2$ Hz, 1 H), 5.54 (d, $J = 17.0$ Hz, 1 H), 5.62 (d, $J = 17.0$ Hz, 1 H); ^{13}C NMR (90 MHz, CDCl_3) δ 12.5, 12.7, 14.1, 17.4, 18.1, 18.2, 18.3, 20.1, 22.7, 25.0, 26.1, 27.6, 29.4, 29.7, 31.8, 38.5, 55.0, 56.1, 56.4, 67.2, 72.9, 73.6, 133.7, 134.1; MS m/z 651 (M^+ , 26), 636 (73), 608 (46), 552 (26), 478 (33), 366 (60), 131 (100); HRMS (M^+) calcd for $\text{C}_{38}\text{H}_{77}\text{NO}_3\text{Si}_2$ 651.5442, found 651.5431.

(1R,4S,6S,7R,9aR)-Octahydro-6-methyl-4-[(1E,3S)-3-(triisopropylsiloxy)-1-decenyl]-7-(triisopropylsiloxy)-4H-quinolizin-1-ol (83). As described for the preparation of 82, DIBAL-H reduction of 81 (0.1 g, 0.12 mmol) gave 83 (67 mg, 86%) as a white solid: mp 83-84 $^\circ\text{C}$; $[\alpha]_D = -13.1^\circ$ (c 0.7, CH_2Cl_2); IR (film) 3320, 1460 cm^{-1} ; ^1H NMR (360 MHz, CDCl_3) δ 0.87 (t, $J = 6.4$ Hz, 3 H), 1.03 (d, $J = 7.1$ Hz, 3 H), 1.06 (m, 42 H), 1.19-1.35 (m, 11 H), 1.49-1.88 (m, 8 H), 2.00 (m, 1 H), 3.27 (ddd, $J = 12.1, 3.9, 3.6$ Hz, 1 H), 3.32 (dq, $J = 7.1, 1.1$ Hz, 1 H), 3.69 (m, 1 H), 3.73 (m, 1 H), 3.80 (ddd, $J = 9.4, 6.4, 3.4$ Hz, 1 H), 4.18 (dd, $J = 12.1, 5.3$ Hz, 1 H), 5.58 (dd, $J = 15.8, 5.3$ Hz, 1 H), 5.64 (dd, $J = 15.8, 6.5$ Hz, 1 H); ^{13}C NMR (90 MHz, CDCl_3) δ 12.5, 12.6, 14.1, 14.4, 17.6, 18.1, 18.2, 18.3, 22.7, 24.9, 28.0, 28.1, 29.4, 29.7, 31.5, 31.8, 38.4, 54.2, 56.7, 57.1, 70.4, 72.0, 73.3, 133.7, 134.1; MS m/z 651 (M^+ , 1), 493 (11), 286 (30), 131 (96), 105 (100); HRMS (M^+) calcd for $\text{C}_{38}\text{H}_{77}\text{NO}_3\text{Si}_2$ 651.5442, found 651.5442.

(4S,6S,7R,9aR)-Octahydro-6-methyl-4-[(1E,3S)-3-(triisopropylsiloxy)-1-decenyl]-4H-quinolizin-7-ol (86). A solution of the α -alcohol 83 (45 mg, 0.069 mmol) in pyridine (0.5 mL) was treated at 0 $^\circ\text{C}$ with methanesulfonyl chloride (32 mg, 0.28 mmol). After the resulting mixture was stirred at 0 $^\circ\text{C}$ for 6 h, it was diluted with anhydrous ether (3 mL). The precipitates were removed by filtration, and the filter cake was rinsed with cold

ether. The combined filtrates were concentrated to give the crude unstable mesylate **85** which was used immediately for the next step.

To a solution of crude **85** in anhydrous ether (5 mL) was added at -20 °C LAH (51 mg, 1.38 mmol). The resulting mixture was warmed to rt, stirred for 4 h, and quenched at 0 °C by careful addition of MeOH, followed by brine. Ether (5 mL) and MgSO₄ were added, and the suspension was stirred vigorously for 20 min. The slurry was filtered, and the filter cake was rinsed with ether. The combined filtrates were concentrated *in vacuo*. Purification by column chromatography (1:2 hexane-EtOAc) gave the alcohol **86** (29 mg, 88%) as a colorless oil: $[\alpha]_D = +18.3^\circ$ (*c* 0.75, CH₂Cl₂); IR (film) 3426, 1451 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 0.87 (t, *J* = 7.0 Hz, 3 H), 1.05 (m, 21 H), 1.09 (d, *J* = 6.8 Hz, 3 H), 1.20-1.30 (m, 11 H), 1.31-1.65 (m, 9 H), 1.75 (m, 2 H), 2.30 (br s, 1 H, -OH), 3.01 (m, 2 H), 3.48 (m, 1H), 3.55 (ddd, *J* = 7.9, 3.8, 3.7 Hz, 1 H), 4.22 (dd, *J* = 12.1, 6.4 Hz, 1 H), 5.47 (dd, *J* = 15.6, 6.4 Hz, 1 H), 5.92 (dd, *J* = 15.6, 7.9 Hz, 1 H); ¹³C NMR (90 MHz, CDCl₃) δ 12.5, 14.1, 14.6, 18.1, 19.2, 22.6, 24.9, 26.2, 26.7, 29.3, 29.6, 31.8, 32.3, 32.8, 38.7, 47.3, 58.7, 60.3, 70.7, 73.2, 132.7, 133.3; MS *m/z* 479 (M⁺, 9), 464 (57), 434 (98), 194 (61), 150 (100); HRMS (M⁺) calcd for C₂₉H₅₇NO₂Si 479.4158, found 479.4145.

Conversion 82 to 83. To a solution of oxalyl chloride (13 μ L, 0.15 mmol) in CH₂Cl₂ (1 mL) was added at -78 °C DMSO (13 μ L, 0.19 mmol). After 10 min at -78 °C, a solution of the β -alcohol **82** (24 mg, 0.037 mmol) in CH₂Cl₂ (0.5 mL) was added. The mixture was stirred at -78 °C for 20 min. Triethylamine (60 μ L, 0.44 mmol) was then added dropwise. After the temperature was gradually raised to 0 °C, the reaction mixture was quenched by addition of H₂O (1 drop) and then diluted with hexane (5 mL). The precipitates were first removed by filtration, and the filtrate was washed with water, followed by brine, dried over MgSO₄, and concentrated *in vacuo* to afford the crude ketone which was used immediately for the next step.

A solution of the crude ketone in THF (0.5 mL) was added at 0 °C to a solution of

sodium borohydride (7 mg, 0.18 mmol) in MeOH (1.5 mL). The resulting mixture was allowed to slowly warm to rt and stirred for an additional 10 min. The reaction mixture was quenched by addition of aqueous saturated NH₄Cl solution. After most of MeOH was evaporated *in vacuo*, the residue was dissolved in EtOAc (5 mL), washed with water, followed by brine, dried over MgSO₄, and concentrated *in vacuo*. The residue was purified by column chromatography (2:1 hexane-EtOAc) to afford the α -alcohol **83** (21 mg, 87%).

(4S,6S,7R,9aR)-Octahydro-6-methyl-4-[(1E,3S)-3-(triisopropylsiloxy)-1-decenyl]-4H-quinolizin-7-yl acetate (87). To a solution of **86** (26 mg, 0.054 mmol) in pyridine (0.5 mL) were added acetic anhydride (56 mg, 0.54 mmol) and 4-(dimethylamino)pyridine (0.3 mg). The reaction mixture was stirred for 3 h at rt. After the solvents were evaporated *in vacuo*, the residue was dissolved in EtOAc (5 mL), washed with aqueous saturated NaHCO₃ solution and brine, dried over MgSO₄, and concentrated *in vacuo*. The residue was purified by column chromatography (5:1 hexane-EtOAc) to afford the acetate **87** (28 mg, 99%) as a colorless oil: $[\alpha]_D = -55.5^\circ$ (*c* 0.45, CH₂Cl₂); IR (film) 1737, 1460 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 0.86 (t, *J* = 6.5 Hz, 3 H), 1.03 (m, 21 H), 1.12 (d, *J* = 7.1 Hz, 3 H), 1.18-1.35 (m, 12 H), 1.43-1.62 (m, 7 H), 1.79 (m, 1 H), 1.91 (m, 2 H), 2.07 (s, 3 H), 3.22 (m, 1 H), 3.40 (dq, *J* = 7.1, 2.1 Hz, 1H), 3.78 (ddd, *J* = 10.1, 7.5, 2.6 Hz, 1 H), 4.16 (ddd, *J* = 7.0, 4.8, 2.5 Hz, 1 H), 4.65 (m, 1 H), 5.38 (dd, *J* = 15.5, 7.5 Hz, 1 H), 5.51 (dd, *J* = 15.5, 7.0 Hz, 1 H); ¹³C NMR (90 MHz, CDCl₃) δ 12.4, 14.1, 17.2, 18.1, 19.6, 20.8, 21.6, 22.6, 24.8, 25.7, 29.3, 29.6, 30.1, 31.8, 32.8, 38.6, 49.1, 53.0, 57.5, 73.3, 73.7, 134.6, 135.0, 170.1; MS *m/z* 478 (M⁺ - C₃H₇, 22), 461 (15), 434 (100), 260 (27), 176 (51); HRMS (M⁺ - C₃H₇) calcd for C₂₈H₅₂NO₃Si 478.3716, found 478.3698.

(4S,6S,7R,9aR)-Octahydro-6-methyl-4-[(1E,3S)-3-hydroxy-1-decenyl]-4H-quinolizin-7-yl

acetate (88). To a solution of **87** (45 mg, 0.086 mmol) in CH₃CN (2 mL) was added at 0 °C 48% aqueous HF (0.1 mL). After the reaction mixture was stirred for 3h at rt, it was quenched by addition of solid NaHCO₃ (0.1 g). After gas evolution ceased, the mixture was extracted with CH₂Cl₂ (3 x 5 mL). The combined extracts were dried over Na₂SO₄ and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc) to give the allylic alcohol **88** (26 mg, 82%) as a colorless oil: [α]_D = -46.4° (*c* 0.55, CH₂Cl₂); IR (film) 3423, 1736 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 0.86 (t, *J* = 6.9 Hz, 3 H), 1.12 (m, 1 H), 1.18 (d, *J* = 7.0 Hz, 3 H), 1.21-1.39 (m, 11 H), 1.45 (m, 1 H), 1.50-1.70 (m, 6 H), 1.78 (m, 1 H), 2.00 (m, 2 H), 2.08 (s, 3 H), 3.27 (m, 1 H), 3.47 (dq, *J* = 7.0, 1.6 Hz, 1H), 3.79 (m, 1 H), 4.06 (m, 1 H), 4.58 (m, 1 H), 5.53 (m, 2H); ¹³C NMR (90 MHz, CDCl₃) δ 14.0, 17.0, 19.5, 20.5, 21.7, 22.6, 25.4, 25.5, 29.2, 29.4, 29.8, 31.8, 32.8, 37.0, 49.3, 53.0, 58.1, 72.9, 73.3, 134.5, 135.5, 170.7; MS *m/z* 350 (M⁺ - CH₃, 33), 288 (29), 260 (56), 176 (56), 123 (100); HRMS (M⁺ - CH₃) calcd for C₂₁H₃₆NO₃ 350.2696, found 350.2679.

Clavepictine A (1A). A solution of *N*-phenylthiophthalimide (15 mg, 0.06 mmol) in benzene (0.3 mL) was treated with tri-*n*-butylphosphine (13 mg, 0.06 mmol) at rt. After stirring for 10 min, a solution of alcohol **88** (17 mg, 0.047 mmol) in benzene (0.1 mL) was added. The reaction mixture was stirred for 2 h at rt. The solvent was evaporated *in vacuo*. The residue was purified by preparative TLC (EtOAc) to give the phenyl thioether (14 mg, 75%) as a colorless oil: [α]_D = -15.8° (*c* 0.6, CH₂Cl₂); IR (film) 1734, 1583 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 0.88 (t, *J* = 6.9 Hz, 3 H), 0.94 (m, 1 H), 1.07 (d, *J* = 7.0 Hz, 3 H), 1.18-1.34 (m, 11 H), 1.35-1.47 (m, 4 H), 1.56 (m, 2 H), 1.70 (m, 2 H), 1.87 (m, 2 H), 2.05 (s, 3 H), 2.99 (m, 1 H), 3.23 (dq, *J* = 7.0, 2.9 Hz, 1H), 3.62 (m, 2 H), 3.57 (br q, *J* = 3.5 Hz, 1 H), 5.12 (dd, *J* = 15.5, 7.3 Hz, 1 H), 5.28 (dd, *J* = 15.5, 9.2 Hz, 1 H), 7.24 (m, 3 H), 7.36 (m, 2 H); ¹³C NMR (90 MHz, CDCl₃) δ 14.1, 17.0, 19.4, 21.2, 21.5, 22.6, 25.6, 27.4, 29.2, 29.4, 29.7, 31.5, 31.8, 34.5, 48.8, 51.6, 52.8, 57.3, 73.4, 126.8, 128.5, 131.3, 132.8, 134.8, 136.9, 170.1; MS *m/z* 442 (M⁺ - CH₃, 5), 370 (76), 348 (42), 288 (100), 260 (61), 176 (30), 150 (47); HRMS (M⁺ - CH₃)

calcd for $C_{27}H_{40}NO_2S$ 442.2780, found 442.2798.

Oxone (21 mg, 0.034 mmol) was added at 0 °C to a solution of this phenyl thioether (13 mg, 0.028 mmol) in 1:1 EtOH-H₂O (1 mL). After the resulting mixture was stirred at 0 °C for 15 min, it was quenched with addition of solid NaHCO₃. After an additional 10 min, the mixture was extracted with EtOAc (3 X 3 mL). The combined extracts were washed with aqueous saturated NaHCO₃ solution, followed by brine, dried over Na₂SO₄, and concentrated to give the crude sulfoxide (15 mg) which was used for the next step without further purification.

A solution of the crude sulfoxide and triethylamine (10 mg, 0.1 mmol) in THF (1.5 mL) was heated at 80 °C (bath temperature) for 24 h. After the solvent was evaporated *in vacuo*, the residue was dissolved with EtOAc (5 mL), washed with brine, dried over Na₂SO₄, and concentrated to give crude clavepictine A. The ¹H NMR of the crude product indicated that the ratio of **1A** and its Z isomer was 7:1, respectively. The preparative TLC (9:1:1 EtOAc-EtOH-hexane) afforded **1A** (7 mg, 72%).

Clavepictine B (**1B**) was obtained in quantitative yield by hydrolysis of **1A** with K₂CO₃ in MeOH.

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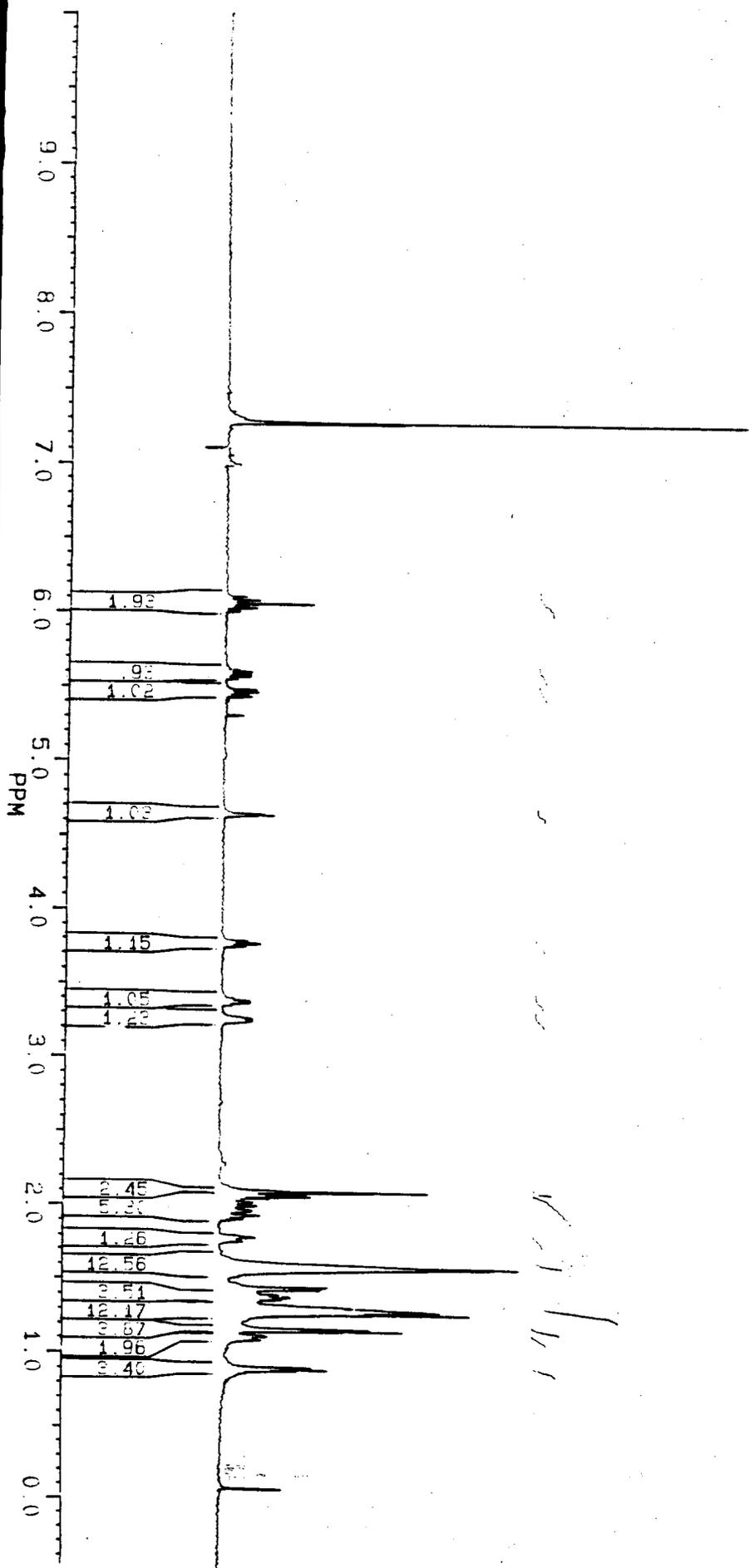
SUPPORTING INFORMATION

Total Synthesis of Clavepictines A and B. Diastereoselective Cyclization of δ -Aminoallenes

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^1H and ^{13}C NMR spectra of synthetic (-)-clavepictine A and (+)-clavepictine B, and also key synthetic intermediates.



Clavepicine A (1A)

