The [3 + 2] Annulations of Cyclohexenyl Silanes and Chlorosulfonyl Isocyanate:
Application to the Total Synthesis of (±)-Peduncularine

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Supporting Information

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General. ^1H NMR and ^{13}C NMR spectra were recorded at ambient temperature using Bruker DRX 500 spectrometers. The data are reported as follows: chemical shift in ppm from internal tetramethylsilane on the δ scale, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration. High resolution mass spectra were acquired on a VG Analytical 7070E or Fisons Autospec spectrometer, and were obtained by peak matching. Microanalyses were performed by Atlantic Microlab, Atlanta, GA. Melting points are reported uncorrected. Analytical thin layer chromatography was performed on EM Reagents 0.25 mm silica gel 60-F plates. Liquid chromatography was performed using forced flow (flash chromatography) of the indicated solvent system on EM Reagents silica gel (SiO_2) 60 (230-400) mesh. All reactions were carried out under an atmosphere of nitrogen in glassware which had been flame-dried under a stream of nitrogen. Unless otherwise noted, all reagents were commercially obtained and, where appropriate, purified prior to use. Toluene, THF, Et_2O , and CH_2Cl_2 were dried by filtration through alumina according to the procedure of Grubbs.¹ Chlorosulfonyl isocyanate was purchased from Aldrich and distilled over K_2CO_3 prior to use. Cyclohex-2-enyl benzoate was prepared according to the method of DeShong,² and 1,3-cyclohexadiene oxide (**5**) was prepared according to the method of Borchardt.³ Tebbe reagent was prepared according to the method of Grubbs.⁴

I. Cyclohexenyl Silanes as Nucleophiles

(1R*,2R*)-2-tert-Butyldiphenylsilyl-cyclohex-3-enol (6).

A suspension of lithium wire (1.90 g, 0.273 mol) in 25 mL of THF at 0 °C was treated with *tert*-butyldiphenylsilyl chloride (3.23 mL, 12.4 mmol). After 4 h at 0 °C, the silyllithium solution was transferred by cannula to a cooled (−45 °C) solution of **5** (0.800 g, 8.30 mmol) in 30 mL of THF. A solution of 9:1 saturated aqueous $\text{NH}_4\text{Cl}:\text{NH}_4\text{OH}$ (60 mL) was added after 1 h at −45 °C. The biphasic mixture was allowed to warm to 23 °C, the phases were separated, and the aqueous phase was washed with 2 x 60 mL of Et_2O . The combined organic layers were dried over Na_2SO_4 , filtered, and concentrated *in vacuo*. Purification by flash chromatography (9:1 hexanes:EtOAc) provided **6** (2.24 g, 80%) as a solid: mp 106–108 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.70 (m, 2H), 7.63 (m, 2H), 7.43–7.32 (m, 6H), 5.93 (m, 1H), 5.69 (m, 1H), 4.18 (m, 1H), 2.54 (m, 1H), 2.09 (m, 1H), 1.83 (m, 1H), 1.54 (br s, 1H), 1.42 (m, 1H), 1.27 (m, 1H), 1.13 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3) δ 136.44, 136.36, 134.0, 133.8, 129.3, 129.2, 127.7, 127.5, 125.7, 125.1, 67.0, 33.7, 28.7, 28.0, 20.6, 18.9; IR (KBr) 3567, 3050, 2920, 1654 cm^{-1} ; HRMS (CI/isobutane) m/z calcd for $\text{C}_{22}\text{H}_{26}\text{Si}$ ($\text{M}-\text{H}_2\text{O}$)⁺ 318.1804, found 318.1795. Anal. Calcd for $\text{C}_{22}\text{H}_{28}\text{OSi}$: C, 78.52; H, 8.39. Found: C, 78.31; H, 8.42.

(3R*,4R*)-3-tert-Butyldiphenylsilyl-4-(tert-butyldimethylsilyloxy)cyclohex-1-ene (7a).

To a cooled (−78 °C) solution of **6** (0.205 g, 0.609 mmol) in 5 mL of CH_2Cl_2 were added 2,6-lutidine (0.138 mL, 1.19 mmol) and *tert*-butyldimethylsilyl triflate (0.164 mL, 0.713 mmol). The solution was treated with 2 mL of 5 % aqueous NaHCO_3 after 30 min at −78 °C and was allowed to warm to 23 °C. The biphasic mixture was separated and the aqueous layer was extracted with 2 x 4 mL of CH_2Cl_2 . The combined organic layers were dried over Na_2SO_4 , filtered and concentrated *in vacuo*. Purification by flash chromatography (9:1 hexanes:EtOAc) provided **7a** (0.272 g, 99%) as an oil: ^1H NMR (400 MHz, CDCl_3) δ 7.68 (m, 4H), 7.42–7.29 (m, 6H), 5.90 (m, 1H), 5.67 (m, 1H), 4.13 (m, 1H), 2.45 (m, 1H), 2.18–2.10 (m, 1H), 1.71–1.64 (m, 1H), 1.32 (m, 1H), 1.11 (s, 9H), 1.08–1.02 (m, 1H), 0.82 (s, 9H), −0.10 (s, 3H), −0.15 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 136.8, 136.6, 134.4, 134.0, 129.1, 129.0, 127.5, 127.2, 125.3, 124.9, 66.7, 34.2, 28.7, 27.4, 25.8, 19.6, 18.7, 18.0, −4.56, −4.58; IR (thin film) 3025, 2929, 1643 cm^{-1} ; HRMS (CI/isobutane) m/z calcd for $\text{C}_{28}\text{H}_{43}\text{OSi}_2$ ($\text{M}+\text{H}$)⁺ 451.2852, found 451.2869. Anal. Calcd for $\text{C}_{28}\text{H}_{42}\text{OSi}_2$: C, 74.60; H, 9.39. Found: C, 74.39; H, 9.44.

(1*R,2*R**)-2-(*tert*-Butyldiphenylsilyl)cyclohex-3-enyl benzoate (7b).**

To a solution of **6** (0.503 g, 1.49 mmol) in 10 mL of pyridine and 10 mL of CH₂Cl₂ were added benzoyl chloride (0.258 mL, 2.24 mmol) and DMAP (0.018 g, 0.15 mmol). After 16 h at 23 °C, the solution was diluted with 30 mL of CH₂Cl₂ and treated with 50 mL of saturated aqueous NH₄Cl solution. The phases were separated and the aqueous phase was washed with 2 x 50 mL of CH₂Cl₂. The combined organic layers were dried over Na₂SO₄, filtered, and concentrated *in vacuo*. Purification by flash chromatography (95:5 hexanes:EtOAc) provided **7b** (0.570 g, 87%) as a solid: mp 122-123 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.98 (m, 2H), 7.75 (m, 2H), 7.59 (m, 2H), 7.52 (m, 1H), 7.45-7.30 (m, 8H), 5.87 (m, 1H), 5.70-5.66 (m, 2H), 2.87 (m, 1H), 2.15 (m, 1H), 1.74 (m, 1H), 1.62 (m, 1H), 1.23-1.15 (m, 1H), 1.19 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 166.0, 136.7, 136.6, 133.9, 132.8, 132.6, 131.0, 129.5, 129.3, 129.1, 128.2, 127.5, 127.4, 125.1, 125.0, 71.1, 29.8, 28.6, 24.5, 20.4, 18.9; IR (KBr) 3071, 2932, 1711, 1644 cm⁻¹; HRMS (CI/isobutane) *m/z* calcd for C₂₅H₂₃O₂Si (M-^tBu)⁺ 383.1467, found 383.1469.

(1*R,4*S**,5*S**,6*R**)-8-Oxo-5-*tert*-butyldiphenylsilyl-7-azabicyclo[4.2.0]oct-4-yl benzoate (10).**

To a solution of **7b** (0.056 g, 0.13 mmol) in 1.5 mL of PhCH₃ was added chlorosulfonyl isocyanate (0.080 mL, 0.92 mmol). After 6 h at 23 °C, the solution was treated with 2 mL of 25 % aqueous Na₂SO₃, and was stirred for 16 h. The phases were separated, and the aqueous phase was washed with 2 x 2 mL of PhCH₃. The combined organic layers were dried over Na₂SO₄, filtered, and concentrated *in vacuo*. Purification by flash chromatography (2:1 hexanes:EtOAc) provided **10** (0.025 g, 41%) as a solid: mp 166-168 °C; ¹H NMR (500 MHz, CDCl₃) δ 8.00 (m, 2H), 7.70-7.64 (m, 4H), 7.58 (m, 1H), 7.49-7.37 (m, 8H), 5.72 (br s, 1H), 5.66 (m, 1H), 4.19 (dd, *J* = 5.4, 2.6, 1H), 2.98 (m, 1H), 2.48 (dd, *J* = 4.8, 2.7, 1H), 1.91-1.77 (m, 3H), 1.23-1.19 (m, 1H), 1.18 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 170.5, 165.9, 136.23, 136.20, 133.4, 132.9, 132.6, 130.3, 129.8, 129.7, 129.6, 128.3, 128.03, 127.95, 71.5, 48.0, 47.1, 28.7, 28.6, 25.2, 18.9, 16.5; IR (KBr) 3262, 3071, 2933, 1752, 1718 cm⁻¹; HRMS (FAB+) *m/z* calcd for C₃₀H₃₄NO₃Si (M+H)⁺ 484.2308, found 484.2321. Anal. Calcd for C₃₀H₃₃NO₃Si: C, 74.50; H, 6.88; N, 2.90. Found: C, 74.24; H, 6.94; N, 2.74.

To a solution of **7a** (0.167 g, 0.370 mmol) in 5 mL of PhCH₃ was added chlorosulfonyl isocyanate (0.097 mL, 1.1 mmol). After 1 h at 23 °C, the solution was treated with 5 mL of 25 % aqueous Na₂SO₃ and was stirred for 16 h. The phases were separated, and the aqueous phase was washed with 2 x 5 mL of PhCH₃. The combined

organic layers were dried over Na_2SO_4 , filtered, and concentrated *in vacuo*. Purification by flash chromatography (3:1 to 1:1 hexanes:EtOAc) provided **8** (0.015 g, 8%) and **9** (0.020 g, 15%).

(1R*,4S*,5S*,8S*)-4-tert-Butyldimethylsilyloxy-8-tert-butyldiphenylsilyl-6-azabicyclo[3.2.1]octan-7-one (8).

mp 76-78 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.71-7.66 (m, 4H), 7.46-7.30 (m, 6H), 5.83 (br s, 1H), 3.83 (d, $J = 4.3$, 1H), 3.63 (td, $J = 7.6$, 1.1, 1H), 2.70 (m, 1H), 2.61 (m, 1H), 1.46-1.27 (m, 4H), 1.09 (s, 9H), 0.74 (s, 9H), -0.21 (s, 3H), -0.25 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 181.8, 136.8, 133.3, 129.7, 127.83, 127.80, 66.3, 61.5, 42.0, 31.5, 28.2, 28.1, 25.6, 21.4, 19.0, 17.6, -4.8, -4.9; IR (KBr) 3214, 3072, 2932, 1700 cm^{-1} ; HRMS (CI/isobutane) m/z calcd for $\text{C}_{29}\text{H}_{43}\text{NO}_2\text{Si}_2$ (M^+) 493.2832, found 493.2813. Anal. Calcd for $\text{C}_{29}\text{H}_{43}\text{NO}_2\text{Si}_2$: C, 70.53; H, 8.78; N, 2.84. Found: C, 70.23; H, 8.76; N, 2.74.

(1R*,6R*)-4-tert-Butyldiphenylsilyl-7-azabicyclo[4.2.0]oct-4-en-8-one (9).

mp 102-104 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.55-7.49 (m, 4H), 7.43-7.33 (m, 6H), 6.33 (dd, $J = 4.6$, 2.6, 1H), 5.97 (br s, 1H), 4.04 (t, $J = 4.9$, 1H), 3.52 (m, 1H), 2.36-2.24 (m, 2H), 2.10 (m, 1H), 1.67-1.59 (m, 1H), 1.14 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3) δ 171.5, 144.5, 139.4, 136.2, 136.1, 133.9, 133.8, 129.33, 129.30, 127.8, 127.7, 49.8, 44.5, 28.8, 26.0, 22.6, 18.5; IR (KBr) 3254, 3048, 2930, 1748 cm^{-1} ; HRMS (CI/isobutane) m/z calcd for $\text{C}_{23}\text{H}_{28}\text{NOSi}$ ($\text{M}+\text{H}^+$) 362.1940, found 362.1953. Anal. Calcd for $\text{C}_{23}\text{H}_{27}\text{NOSi}$: C, 76.41; H, 7.53; N, 3.87. Found: C, 76.22; H, 7.87; N, 3.74.

2-(tert-Butyldiphenylsilyl)cyclohex-3-enone (A).

To a solution of **6** (0.060 g, 0.18 mmol) in 3 mL of CH_2Cl_2 was added Dess-Martin periodinane (0.091 g, 0.21 mmol). After 2.5 h, the reaction mixture was diluted with 15 mL of Et_2O and the heterogeneous mixture was filtered. The organic phase was concentrated *in vacuo* and was immediately purified by flash chromatography (95:5 hexanes:EtOAc) to provide **A** (0.048 g, 80%) as a solid: mp 108-110 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.73 (m, 2H), 7.54 (m, 2H), 7.45-7.34 (m, 6H), 5.75 (m, 1H), 5.58-5.28 (m, 1H), 3.69 (m, 1H), 2.21-2.10 (m, 2H), 1.93-1.83 (m, 2H), 1.15 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3) δ 210.7, 136.9, 136.4, 132.8, 131.6, 129.7, 129.4, 127.6, 127.4, 125.9, 124.5, 44.4, 38.4, 28.1, 26.0, 19.6; IR (KBr) 3043, 2933, 1681, 1652 cm^{-1} ; HRMS (FAB+) m/z calcd for $\text{C}_{22}\text{H}_{26}\text{OSiNa}$ ($\text{M}+\text{Na}^+$) 357.1651, found 357.1636. Anal. Calcd for $\text{C}_{22}\text{H}_{26}\text{OSi}$: C, 78.99; H, 7.83. Found: C, 78.76; H, 7.86.

(1R*,2S*)-2-(tert-Butyldiphenylsilyl)cyclohex-3-enol (14).

To a cooled ($-78\text{ }^{\circ}\text{C}$) solution of ketone A (0.248 g, 0.740 mmol) in 25 mL of Et_2O was added solid LiAlH_4 (0.084 g, 2.2 mmol) in one portion. The reaction mixture was warmed to $23\text{ }^{\circ}\text{C}$ and stirred for 1 h. A solution of saturated aqueous Na_2SO_4 was added dropwise to the cooled ($0\text{ }^{\circ}\text{C}$) reaction mixture until hydrogen evolution ceased. The suspension was warmed to $23\text{ }^{\circ}\text{C}$, dried over solid Na_2SO_4 , and filtered. The filtrate was concentrated *in vacuo*. Purification by flash chromatography (95:5 hexanes:EtOAc) provided **14** (0.222 g, 89%) as a solid: mp $86\text{--}87\text{ }^{\circ}\text{C}$; ^1H NMR (500 MHz, CDCl_3) δ 7.73 (m, 2H), 7.60 (m, 2H), 7.40–7.29 (m, 6H), 5.82 (m, 1H), 5.71 (m, 1H), 4.25 (m, 1H), 2.72 (m, 1H), 2.22–2.14 (m, 1H), 2.04–1.97 (m, 1H), 1.83–1.79 (m, 1H), 1.64–1.54 (m, 1H), 1.29 (d, $J = 7.0$, 1H), 1.14 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3) δ 136.9, 136.6, 135.5, 135.2, 129.6, 129.4, 128.0, 127.9, 126.2, 126.0, 66.9, 31.7, 30.2, 29.4, 19.8, 19.1; IR (KBr) 3553, 3049, 2922, 1655 cm^{-1} ; HRMS (FAB+) m/z calcd for $\text{C}_{22}\text{H}_{28}\text{OSiNa}$ ($\text{M}+\text{Na}$) $^+$ 359.1807, found 359.1808.

(3R*,4S*)-3-tert-Butylphenylsilyl-4-(tert-butyldimethylsilyloxy)cyclohexene (15a).

To a cooled ($-45\text{ }^{\circ}\text{C}$) solution of **14** (0.603 g, 1.79 mmol) in 20 mL of CH_2Cl_2 were added 2,6-lutidine (0.417 mL, 3.58 mmol) and *tert*-butyldimethylsilyl triflate (0.535 mL, 2.33 mmol). The mixture was treated with an additional 1 equiv (0.417 mL) of 2,6-lutidine and 0.4 equiv (0.165 mL) of *tert*-butyldimethylsilyl triflate after 8 h at $-45\text{ }^{\circ}\text{C}$. The reaction mixture was warmed to $0\text{ }^{\circ}\text{C}$ over 2 h and then treated with 20 mL of 5 % aqueous NaHCO_3 . The biphasic mixture was allowed to warm to $23\text{ }^{\circ}\text{C}$, then the layers were separated, and the aqueous layer was washed with 2 x 4 mL of CH_2Cl_2 . The combined organic layers were dried over Na_2SO_4 , filtered, and concentrated *in vacuo*. Purification by flash chromatography (98:2 hexanes:EtOAc) provided **15a** (0.600 g, 74%) as an oil: ^1H NMR (500 MHz, CDCl_3) δ 7.85 (m, 2H), 7.67 (m, 2H), 7.37–7.29 (m, 6H), 5.92 (m, 1H), 5.69 (m, 1H), 4.23 (m, 1H), 2.78 (m, 1H), 2.18 (m, 1H), 1.99 (m, 1H), 1.58 (m, 2H), 1.03 (s, 9H), 0.61 (s, 9H), -0.27 (s, 3H), -0.61 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 137.3, 136.2, 135.0, 134.6, 128.7, 128.6, 127.2, 127.0, 126.6, 125.1, 68.9, 31.8, 30.6, 29.1, 25.9, 21.8, 19.0, 18.2, -5.0, -5.1; IR (thin film) 3071, 2929, 1643 cm^{-1} ; HRMS (CI/isobutane) m/z calcd for $\text{C}_{28}\text{H}_{43}\text{OSi}_2$ ($\text{M}+\text{H}$) $^+$ 451.2852, found 451.2853.

(1R*,2S*)-2-tert-Butylphenylsilyl-cyclohex-3-enyl acetate (15b).

To a cooled ($-45\text{ }^{\circ}\text{C}$) solution of **14** (0.246 g, 0.731 mmol) in 9 mL of acetic anhydride was added a solution of $\text{Sc}(\text{OTf})_3$ (0.007 g, 0.02 mmol) in 1 mL of CH_3CN . After 2 h at $-45\text{ }^{\circ}\text{C}$, the reaction mixture was treated with 12 mL of saturated aqueous NaHCO_3 and was allowed to warm to $23\text{ }^{\circ}\text{C}$. The mixture was diluted with 20 mL

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of Et₂O. The biphasic mixture was separated and the organic layer was washed with 3 x 20 mL of saturated aqueous NaHCO₃, dried over Na₂SO₄, filtered and concentrated *in vacuo*. Purification by flash chromatography (95:5 hexanes:EtOAc) provided **15b** (0.243 g, 88%) as an oil: ¹H NMR (500 MHz, CDCl₃) δ 7.69-7.59 (m, 4H), 7.42-7.30 (m, 6H), 5.89 (m, 1H), 5.75 (m, 1H), 5.06 (m, 1H), 2.75 (m, 1H), 2.10-1.97 (m, 3H), 1.60-1.53 (m, 1H), 1.40 (s, 3H), 1.10 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 170.2, 136.4, 135.7, 134.7, 134.5, 129.0, 128.9, 127.4, 127.2, 125.9, 125.3, 70.4, 29.2, 28.9, 26.3, 20.6, 19.9, 18.7; IR (thin film) 3072, 2931, 1738, 1640 cm⁻¹; HRMS (ESI) *m/z* calcd for C₂₄H₃₀O₂SiNa (M+Na)⁺ 401.1913, found 401.1925.

(1R*,4S*,5R*,8R*)-4-tert-Butyldimethylsilyloxy-8-tert-butyldiphenylsilyl-6-azabicyclo[3.2.1]octan-7-one (16).

To a solution of **15a** (0.057 g, 0.13 mmol) in 2 mL of benzene was added chlorosulfonyl isocyanate (0.033 mL, 0.38 mmol). After 16 h at 23 °C, the solution was treated with 3 mL of 25 % aqueous Na₂SO₃, and was stirred for 16 h. The phases were separated, and the aqueous phase was washed with 2 x 3 mL of benzene. The combined organic layers were dried over Na₂SO₄, filtered, and concentrated *in vacuo*. Purification by flash chromatography (1:1 hexanes:EtOAc) provided **16** (0.010 g, 16%) as an oil which solidified on standing: ¹H NMR (500 MHz, CDCl₃) δ 7.85 (m, 2H), 7.61 (m, 2H), 7.43-7.31 (m, 6H), 5.69 (br s, 1H), 4.07 (m, 1H), 3.79 (m, 1H), 2.59 (m, 1H), 2.40 (m, 1H), 1.80 (m, 1H), 1.33-1.26 (m, 2H), 1.21 (m, 1H), 1.04 (s, 9H), 0.75 (s, 9H), -0.12 (s, 3H), -0.49 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 182.5, 137.6, 136.8, 135.3, 134.2, 129.6, 129.3, 127.6, 127.5, 67.6, 60.3, 41.9, 30.0, 28.7, 26.6, 26.5, 19.6, 19.5, 19.2, -5.3, -5.5; IR (thin film) 3194, 3071, 2923, 1694 cm⁻¹; HRMS (FAB) *m/z* calcd for C₂₉H₄₃NO₂Si₂Na (M+Na)⁺ 516.2730, found 516.2726.

3-Dimethyl(diphenylmethyl)silyl-1,4-cyclohexadiene (19b).

To a cooled (-78 °C) solution of 1,4-cyclohexadiene (0.055 mL, 0.60 mmol) in 1 mL of THF were added *s*-BuLi (0.625 mL, 0.96 M in cyclohexane, 0.60 mmol) and TMEDA (0.100 mL, 0.60 mmol). The yellow solution was warmed to -45 °C, and after 2.5 h was treated with (Ph₂CH)Me₂SiCl²⁷ (0.160 g, 0.61 mmol) in 1 mL of THF. After 10 min at -45 °C, the solution was treated with 6 mL of saturated aqueous NH₄Cl and warmed to 23 °C. The organic phase was diluted with 3 mL of Et₂O, separated from the aqueous phase, and washed with 6 mL of brine. The combined organic phases were dried over Na₂SO₄, filtered and concentrated *in vacuo*. Purification by flash chromatography (hexanes) provided **19b** as an oil (0.139 g, 76%): ¹H NMR (500 MHz, CDCl₃) δ 7.25 (m, 8H), 7.12 (m, 2H), 5.53-5.48 (m, 4H), 3.67 (s, 1H), 2.69-2.56 (m, 2H), 2.25 (m, 1H), 0.08 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 142.3, 128.7, 128.4, 125.8, 125.2, 122.0, 43.6, 29.5, 26.3, -5.5; IR (thin film) 3023, 2819, 1665, 1622, 1600 cm⁻¹; HRMS (CI/isobutane) *m/z* calcd for C₂₁H₂₄Si (M)⁺ 304.1647, found 304.1647. Anal. Calcd for C₂₁H₂₄Si: C, 82.83; H, 7.94. Found: C, 82.83; H, 7.87.

(1R*,5R*,8R*)-8-Dimethyl(diphenylmethyl)silyl-6-azabicyclo[3.2.1]oct-3-en-7-one (20b).

To a cooled (-78°C) solution of **19b** (0.030 g, 0.099 mmol) in 1.5 mL of CH_2Cl_2 was added chlorosulfonyl isocyanate (0.020 mL, 0.23 mmol). The solution was warmed to -40°C and stirred for 24 h. The solution was treated with 2 mL of 25 % aqueous Na_2SO_3 , then was warmed to 23°C and stirred for 16 h. The organic phase was separated from the aqueous phase, dried over Na_2SO_4 , filtered and concentrated *in vacuo*. Purification by flash chromatography (1:1 EtOAc:hexanes) provided **20b** and **21b** (0.026 g, 76%) in an 82 : 18 ratio as determined from ^1H NMR spectroscopy. Recrystallization provided a pure sample of **20b** as a white solid: mp $154\text{--}156^\circ\text{C}$; ^1H NMR (500 MHz, CDCl_3) δ 7.27 (m, 8H), 7.15 (m, 2H), 6.14 (br s, 1H), 6.04 (m, 1H), 5.59 (m, 1H), 3.54 (s, 1H), 3.25 (t, $J = 4.1$, 1H), 2.23 (m, 2H), 1.86 (t, $J = 3.8$, 1H), 0.15 (s, 3H), 0.13 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 182.4, 142.01, 141.95, 131.5, 128.7, 128.6, 128.52, 128.47, 125.6, 51.2, 45.7, 41.7, 34.8, 27.0, -2.7, -2.8; IR (KBr) 3168, 3021, 2961, 1734, 1716, 1700, 1684, 1676, 1670, 1653 cm^{-1} ; HRMS (CI/isobutane) m/z calcd for $\text{C}_{22}\text{H}_{26}\text{NOSi}$ ($\text{M}+\text{H}^+$) 348.1784, found 348.1779. Anal. Calcd for $\text{C}_{22}\text{H}_{25}\text{NOSi}$: C, 76.03; H, 7.25; N, 4.03. Found: C, 75.80; H, 7.24; N, 4.01.

II. Total Synthesis of Peduncularine

The installation of the C-7 side chain from *N,O*-acetal proceeded to give the carbamate **26** that appeared to be a single stereoisomer. This material gave one peak in the GCMS, although two compounds (presumably rotamers) were evident in the ^1H NMR spectrum (this data is included). To determine whether carbamate **26** was two conformational stereoisomers (rotamers) or two diastereoisomers, the carbamate moiety was removed. The resulting amine was found to be a single compound by ^1H NMR spectroscopy (this data is included as well). Consequently, the carbamate **26** was determined to be a single diastereomer.

(1R*,5R*,7R*,8R*)-7-Allyl-8-dimethylphenylsilyl-6-azabicyclo[3.2.1]oct-3-ene (B).

A solution of **26** (3.33 g, 7.78 mmol) in 70 mL of CH_3CN was treated with $n\text{-Bu}_4\text{NF}$ (10.3 mL, 10 mmol, 1.0 M in THF) and was heated to 65°C for 3 h. Upon cooling to 23°C , the reaction mixture was diluted with 200 mL of CH_2Cl_2 and was treated with 200 mL of H_2O . The organic layer was separated from the aqueous layer, and it was dried over Na_2SO_4 , filtered, and concentrated *in vacuo*. Purification by flash chromatography (90:10:1 CH_2Cl_2 :MeOH: NEt_3) provided **B**, an oil (1.86 g, 84%), as a single stereoisomer as determined by analysis of a ^1H NMR spectrum (this spectrum is included): ^1H NMR (500 MHz, CDCl_3) δ 7.51 (m, 2H), 7.33 (m, 3H), 5.93

(m, 1H), 5.77 (ddt, $J = 17.1, 10.2, 6.8$, 1H), 5.44 (m, 1H), 5.03 (m, 2H), 3.52 (dd, $J = 5.6, 3.5$, 1H), 3.02 (t, $J = 7.0, 1H$), 2.32 (m, 1H), 2.20-2.05 (m, 4H), 1.89 (m, 1H), 1.36 (t, $J = 3.9$, 1H), 0.35 (s, 3H), 0.32 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 139.4, 136.2, 133.4, 132.2, 128.7, 127.6, 126.8, 116.2, 64.3, 55.3, 41.5, 40.9, 34.9, 32.7, -1.6, -2.3; IR (thin film) 3383, 3022, 2898, 1639, 1615 cm^{-1} ; HRMS (CI/ammonia) m/z calcd for $\text{C}_{18}\text{H}_{26}\text{NSi}(\text{M}+\text{H})^+$ 284.1834, found 284.1837.

Peduncularine (1).

More detailed analytical data for the natural product is included below. On the following pages, tabulated ^1H and ^{13}C NMR spectra are included to compare the synthetic material to information reported for the natural product.^{6,7} mp 145-147 $^\circ\text{C}$; ^1H NMR (500 MHz, CDCl_3) δ 7.98 (br s, 1H, NH), 7.61 (d, $J = 7.9$, 1H, H-4'), 7.36 (d, $J = 8.1$, 1H, H-7'), 7.20 (t, $J = 7.5$, 1H, H-6'), 7.12 (t, $J = 7.5$, 1H, H-5'), 6.99 (s, 1H, H-2'), 5.95 (ddt, $J = 9.3, 5.2, 2.0$, 1H, H-4), 5.69 (dt, $J = 9.3, 2.8$, 1H, H-3), 4.95 (s, 1H, H-9), 4.82 (s, 1H, H-9), 3.84 (d, $J = 5.0$, 1H, H-5), 3.00 (septet, $J = 6.2$, 1H, H-10), 2.95 (d, $J = 15.4$, 1H, H-13), 2.89 (d, $J = 11.3$, 1H, H-7), 2.71 (dd, $J = 14.7, 11.4$, 1H, H-13), 2.50 (br d, $J = 4.1$, 1H, H-1), 2.46 (ddt, $J = 17.6, 4.6, 2.4$, 1H, H-2), 2.07 (ddt, $J = 17.6, 3.3, 1.7$, 1H, H-2), 1.31 (d, $J = 6.3$, 3H, $(\text{CH}_3)_2\text{CH}$), 1.17 (d, $J = 6.1$, 3H, $(\text{CH}_3)_2\text{CH}$); ^{13}C NMR (125 MHz, CDCl_3) δ 150.1 (C-8), 136.2 (C-7a'), 130.6 (C-4), 128.4 (C-3), 127.8 (C-3a'), 122.0 (C-6'), 121.3 (C-2'), 119.3 (C-5'), 119.0 (C-4'), 115.0 (C-3'), 111.0 (C-7'), 101.4 (C-9), 69.8 (C-7), 60.4 (C-5), 50.9 (C-10), 45.9 (C-1), 40.1 (C-2), 34.2 (C-13), 23.6 (CH_3), 22.7 (CH_3); IR (KBr) 3416, 2969, 1684, 1626 cm^{-1} ; HRMS (CI/ammonia) m/z calcd for $\text{C}_{20}\text{H}_{24}\text{N}_2(\text{M})^+$ 292.1939, found 292.1938.

III. References

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- (6) Dragar, C.; Bick, I. R. C. *Phytochemistry* **1992**, *31*, 3601-3603.
- (7) Klaver, W. J.; Hiemstra, H.; Speckamp, W. N. *J. Am. Chem. Soc.* **1989**, *111*, 2588-2595.

IV. Tables of Peduncularine Spectral Data

Tabulated ^1H and ^{13}C NMR spectra are included to compare the synthetic material to information reported for the natural product:

^1H no. ^a	Current Synthesis In ppm, 500 MHz, CDCl_3	Natural Peduncularine ^b In ppm, 300 MHz, CDCl_3
NH	7.98 (br s, 1H)	8.93 (br s, 1H)
H4'	7.61 (d, $J = 7.9$, 1H)	7.61 (d, $J = 7.7$, 1H)
H7'	7.36 (d, $J = 8.1$, 1H)	7.36 (d, $J = 8.0$, 1H)
H6'	7.20 (t, $J = 7.5$, 1H)	7.18 (t, $J = 7.9$, 1H)
H5'	7.12 (t, $J = 7.5$, 1H)	7.10 (t, $J = 8.0$, 1H)
H2'	6.99 (s, 1H)	6.99 (s, 1H)
H4	5.95 (ddt, $J = 9.3, 5.2, 2.0$, 1H)	5.93 (ddt, $J = 9.3, 5.3, 2.0$, 1H)
H3	5.69 (dt, $J = 9.3, 2.8$, 1H)	5.70 (dt, $J = 9.4, 3.1$, 1H)
H9a	4.95 (s, 1H)	4.97 (s, 1H)
H9b	4.82 (s, 1H)	4.85 (s, 1H)
H5	3.84 (d, $J = 5.0$, 1H)	3.83 (d, $J = 5.3$, 1H)
H10	3.00 (septet, $J = 6.2$, 1H)	3.03 (septet, $J = 6.3$, 1H)
H13a	2.95 (d, $J = 15.4$, 1H)	2.97 (dd, $J = 16.5, 2.5$, 1H)
H7	2.89 (d, $J = 11.3$, 1H)	2.92 (dd, $J = 13.3, 2.6$, 1H)
H13b	2.71 (dd, $J = 14.7, 11.4$, 1H)	2.70 (dd, $J = 13.8, 10.6$, 1H)
H1	2.50 (br d, $J = 4.1$, 1H)	2.53 (br d, $J = 4.8$, 1H)
H2a	2.46 (ddt, $J = 17.6, 4.6, 2.4$, 1H)	2.44 (ddt, $J = 17.8, 4.9, 2.5$, 1H)
H2b	2.07 (ddt, $J = 17.6, 3.3, 1.7$, 1H)	2.04 (ddt, $J = 17.8, 3.6, 1.6$, 1H)
H12	1.31 (d, $J = 6.3$, 3H)	1.33 (d, $J = 6.4$, 3H)
H11	1.17 (d, $J = 6.1$, 3H)	1.17 (d, $J = 6.2$, 3H)

a) Proton assignments from COSY and NOE experiments (ref. b).

b) Dragar, C.; Bick, I. R. C. *Phytochemistry*, **1992**, *31*, 3601-3603.

¹ H no. ^a	Current Synthesis In ppm, 500 MHz CDCl ₃ / 20 μL 40%NaOD/D ₂ O	Hiemstra and Speckamp ^c In ppm, 600 MHz CDCl ₃ / 15 μL 40%NaOD/D ₂ O
H4'	7.61 (d, <i>J</i> = 7.9, 1H)	7.59 (d, <i>J</i> = 7.9, 1H)
H7'	7.36 (d, <i>J</i> = 8.1, 1H)	7.34 (d, <i>J</i> = 8.1, 1H)
H6'	7.20 (td, <i>J</i> = 7.5, 1.0, 1H)	7.18 (t, <i>J</i> = 7.5, 1H)
H5'	7.12 (td, <i>J</i> = 7.5, 0.8, 1H)	7.10 (t, <i>J</i> = 7.5, 1H)
H2'	6.98 (s, 1H)	6.96 (s, 1H)
H4	5.95 (ddt, <i>J</i> = 9.2, 5.1, 2.0, 1H)	5.94 (ddt, <i>J</i> = 9.3, 5.2, 2.0, 1H)
H3	5.69 (dt, <i>J</i> = 9.3, 3.0, 1H)	5.67 (dt, <i>J</i> = 9.3, 3.2, 1H)
H9a	4.95 (s, 1H)	4.94 (s, 1H)
H9b	4.82 (s, 1H)	4.80 (s, 1H)
H5	3.84 (d, <i>J</i> = 5.2, 1H)	3.83 (d, <i>J</i> = 5.2, 1H)
H10	3.00 (septet, <i>J</i> = 6.3, 1H)	2.99 (septet, <i>J</i> = 6.3, 1H)
H13a	2.96 (dd, <i>J</i> = 14.9, 1.6, 1H)	2.93 (dd, <i>J</i> = 15.0, 2.9, 1H)
H7	2.89 (dd, <i>J</i> = 11.2, 2.6, 1H)	2.87 (dd, <i>J</i> = 11.3, 2.8, 1H)
H13b	2.70 (dd, <i>J</i> = 14.8, 11.3, 1H)	2.69 (dd, <i>J</i> = 14.9, 11.3, 1H)
H1	2.50 (br d, <i>J</i> = 4.6, 1H)	2.49 (br d, <i>J</i> = 4.7, 1H)
H2a	2.46 (ddt, <i>J</i> = 17.6, 4.6, 2.5, 1H)	2.44 (ddt, <i>J</i> = 17.6, 4.8, 2.5, 1H)
H2b	2.07 (ddt, <i>J</i> = 17.6, 3.5, 1.8, 1H)	2.06 (ddt, <i>J</i> = 17.6, 3.6, 1.8, 1H)
H12	1.31 (d, <i>J</i> = 6.4, 3H)	1.30 (d, <i>J</i> = 6.4, 3H)
H11	1.17 (d, <i>J</i> = 6.2, 3H)	1.17 (d, <i>J</i> = 6.2, 3H)

c) Klaver, W. J.; Hiemstra, H.; Speckamp, W. N. *J. Am. Chem. Soc.* **1989**, *111*, 2588-2595.

Carbon Number ^a	Current Synthesis	Natural Peduncularine ^b
	In ppm, 125 MHz CDCl ₃	In ppm, 75 MHz CDCl ₃
C-8	150.1	149.9
C-7a'	136.2	136.0
C-4	130.6	130.3
C-3	128.4	128.6
C-3a'	127.8	127.6
C-6'	122.0	121.9
C-2'	121.3	121.3
C-5'	119.3	119.1
C-4'	119.0	119.0
C-3'	115.0	114.7
C-7'	111.0	111.0
C-9	101.4	101.4
C-7	69.8	69.8
C-5	60.4	60.5
C-10	50.9	50.9
C-1	45.9	45.7
C-2	40.1	40.1
C-13	34.2	34.0
C-12	23.6	23.5
C-11	22.7	22.5

a) Carbon assignments from DEPT and HETCOR experiments (ref. b).

b) Dragar, C.; Bick, I. R. C. *Phytochemistry*, **1992**, *31*, 3601-3603.

c) Klaver, W. J.; Hiemstra, H.; Speckamp, W. N. *J. Am. Chem. Soc.* **1989**, *111*, 2588-2595.

Supporting Information: C.W. Roberson and K.A. Woerpel

Carbon Number ^a	Current Synthesis In ppm, 125 MHz CDCl ₃ / 20 μ L 40%NaOD/D ₂ O	Natural Peduncularine ^c In ppm, 75 MHz CDCl ₃ / 15 μ L 40%NaOD/D ₂ O
C-8	150.1	150.2
C-7a'	136.0	136.4
C-4	130.6	130.8
C-3	128.5	128.3
C-3a'	127.8	128.0
C-6'	122.0	122.0
C-2'	121.2	121.1
C-5'	119.3	119.3
C-4'	119.1	119.1
C-3'	115.0	115.3
C-7'	111.0	111.0
C-9	101.4	101.2
C-7	69.8	69.8
C-5	60.4	60.5
C-10	50.9	50.9
C-1	45.9	46.0
C-2	40.1	40.2
C-13	34.2	34.3
C-12	23.6	23.7
C-11	22.7	22.8

c) Klaver, W. J.; Hiemstra, H.; Speckamp, W. N. *J. Am. Chem. Soc.* **1989**, *111*, 2588-2595.

V. Additional Spectra

Data Source:
D:\Xcalibur\Data\05010002_204333.RAW

Date: 05/01/01 9:30 PM

Page 1

UCI Mass Spec Facility

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Comments:	croberso			
Run Time (min):	39.97	Scans:	2402	Low Mass (m/z): 49.60 High Mass (m/z): 650.40
Vial:	66	Inj Vol (uL):	1.00	Samp Vol: 0.00 Samp Wt: 0.00
ISTD Amt:	0.000	Dil Factor:	0.00	Revision: 1.1
Inst Method:	C:\Xcalibur\methods\50-10-270-20.meth		Proc Method: C:\Xcalibur\methods\chro_spec	

Qualitative Peaks

RT: 0.00 - 42.99 SM: 3B

NL:
1.38EB
TIC MS
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