The Development of an Enantiodivergent Strategy for the Total Synthesis of (+)- and (−)-Dragmacidin F from a Single Enantiomer of Quinic Acid

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Supporting Information

Materials and Methods. Unless stated otherwise, reactions were conducted in flame-dried glassware under an atmosphere of nitrogen using anhydrous solvents (either freshly distilled or passed through activated alumina columns). All commercially obtained reagents were used as received. Reaction temperatures were controlled using an IKAmag temperature modulator, and unless stated otherwise, reactions were performed at 23 °C. Thin-layer chromatography (TLC) was conducted with E. Merck silica gel 60 F254 pre-coated plates, (0.25 mm) and visualized using a combination of UV, anisaldehyde, ceric ammonium molybdate, and potassium permanganate staining. ICN silica gel (particle size 0.032-0.063 mm) was used for flash column chromatography. $^{1}$H NMR spectra were recorded on a Varian Mercury 300 (at 300 MHz), a Varian Inova 500 (at 500 MHz), or a Varian Inova 600 (at 600 MHz) and are reported relative to Me$_4$Si (δ 0.0). Data for $^{1}$H NMR spectra are reported as follows: chemical shift (δ ppm), multiplicity, coupling constant (Hz) and integration. $^{13}$C NMR spectra were recorded on a Varian Mercury 300 (at 75 MHz), or a Varian Inova 500 (at 125 MHz) and are reported relative to Me$_4$Si (δ 0.0). Data for $^{13}$C NMR spectra are reported in terms of chemical shift. NOESY-1D, gCOSY, and homodecoupling NMR experiments were performed on a Varian Inova 300 (at 300 MHz) or a Varian Mercury 600 (at 600 MHz). IR spectra were recorded on a Perkin Elmer Spectrum BXII spectrometer and are reported in terms of frequency of absorption (cm$^{-1}$). Optical rotations were measured with a Jasco P-1010 polarimeter. High resolution mass spectra were obtained from the California Institute of Technology Mass Spectral Facility.
# Table of Contents

## (+)-Dragmacidin F

a. \( \pi \)-Allyl reduction studies ........................................... S3  
b. Favorskii and Neber rearrangements .............................. S5

## (-)-Dragmacidin F

a. \( \pi \)-Allyl reduction studies ........................................... S8  
b. Synthesis ........................................................................ S9  
c. Oxidative cyclizations table ........................................... S15  
d. Oxidative cyclizations substrate synthesis .................. S15  
e. Oxidative cyclizations products and general procedure.... S26  
f. Completion of the synthesis ........................................... S30  
g. Comparison spectra ...................................................... S37

References ........................................................................... S38
(+)-Dragmacidin F:

Note: Supporting information for compounds: 8-11, and 27 has been previously reported as part of the (±)-dragmacidin D synthesis.\(^1\) Supporting information for compounds: 12-15, 17-19, 24-26, 28, 29, 35, 36, and 40 has been previously reported as part of the (+)-dragmacidin F synthesis.\(^2\)

Methyl Ester 20. To lactone 18\(^2\) (420 mg, 1.477 mmol) and activated oven-dried 4Å molecular sieves (100 mg) was added MeOH (15 mL). The reaction mixture was stirred at 23 °C for 5.5 h, then filtered over a short plug of Celite (EtOAc eluent). After evaporation of the reaction mixture under reduced pressure, the residue was purified by flash column chromatography (2:1 hexanes:EtOAc eluent) to afford starting material lactone 18 (82 mg, 20% yield) and siloxy diol SM1 (345 mg, 74% yield, 92% yield based on recovered starting material), which was used directly in the subsequent reaction.

To siloxy diol SM1 (80.0 mg, 0.253 mmol) in CH\(_2\)Cl\(_2\) (1.5 mL) was added Et\(_3\)N (71 \(\mu\)L, 0.506 mmol), DMAP (3 mg, 0.0253 mmol), followed by Ac\(_2\)O (31 \(\mu\)L, 0.329 mmol). The reaction mixture was stirred at 23 °C for 10 min, quenched with saturated aq. NaHCO\(_3\) (5 mL), and extracted with CH\(_2\)Cl\(_2\) (3 x 15 mL). The combined organic layers were filtered over a plug of silica gel (CH\(_2\)Cl\(_2\) eluent, then EtOAc eluent) and evaporated under reduced pressure. The crude product was purified by flash chromatography (3:1 hexanes:EtOAc eluent) to afford methyl ester 20 (89.0 mg, 98% yield) as a colorless oil. R\(_f\) 0.50 (1:1 hexanes:EtOAc); \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 5.90-5.81 (m, 1H), 4.96 (br s, 1H), 4.94 (br s, 1H), 4.91-4.89 (m, 1H), 4.67 (app. t, \(J = 3.2\) Hz, 1H), 3.74 (s, 3H), 2.38 (ddd, \(J = 12.7, 5.2, 2.2\) Hz, 1H), 2.19-2.03 (comp. m, 2H), 2.09 (s, 3H), 1.93 (app. t, \(J = 12.1\) Hz, 1H), 0.87 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); \(^1\)^13C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 173.7, 169.6, 146.3, 108.5, 76.5, 75.1, 68.0, 52.9, 42.7, 41.2, 25.8 (3C), 21.1, 18.1, -4.6, -5.2; IR (film) 3464 (br), 2954, 2932, 2858, 2888, 1739 (br), 1369, 1233 (br), 1124,
1098, 1072, 1036 cm$^{-1}$; HRMS-FAB (m/z): [M + H]$^+$ calc’d for C$_{17}$H$_{31}$O$_6$Si, 359.1890; found, 359.1900; $[\alpha]^{26}_D$ -26.61° (c 1.0, C$_6$H$_6$).

The stable chair conformer of methyl ester 20 was determined using homodecoupling NMR experiments. The coupling constant between $H_a$ and $H_b$ was measured as $J_{ab} = 10.7$ Hz.

Siloxycyclohexene 21. Methyl ester 20 (94 mg, 0.262 mmol), Pd(P(t-Bu)$_3$)$_2$ (40.2 mg, 0.0786 mmol), anhydrous $N$-methylmorpholine $N$-oxide (307 mg, 2.52 mmol), THF (5.2 mL), and freshly distilled Et$_3$SiH (1.67 mL, 10.5 mmol) were combined under a glovebox atmosphere. The reaction mixture was immediately removed from the glovebox and placed in a 70 °C oil bath. After 3.5 h, the reaction mixture was cooled to 0 °C and the volatiles were removed under reduced pressure. Saturated aq. NH$_4$Cl (15 mL) was added and the mixture was extracted with Et$_2$O (3 x 25 mL). The combined organic layers were washed with brine (15 mL), dried over MgSO$_4$, and evaporated under reduced pressure. The crude product was purified by flash chromatography (5:1 hexanes:EtOAc eluent) to afford siloxycyclohexene 21 (70 mg, 89% yield) as a pale yellow oil. R$_f$ 0.55 (2:1 hexanes:EtOAc); $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 5.49-5.42 (m, 1H), 4.62 (s, 1H), 4.18-4.12 (m, 1H), 3.76 (s, 3H), 2.45-2.38 (comp. m, 2H), 2.16-2.10 (comp. m, 2H), 1.79-1.74 (m, 3H), 0.88 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 175.3, 133.7, 120.9, 73.0, 68.7, 52.6, 38.4, 36.9, 25.9 (3C), 21.4, 18.0, -4.3, -4.7; IR (film) 3478 (br), 2955, 2858, 1740, 1451, 1253, 1217, 1111, 1065, 1037 cm$^{-1}$; HRMS-FAB (m/z): [M + H]$^+$ calc’d for C$_{15}$H$_{19}$O$_4$Si, 301.1835; found, 301.1835; $[\alpha]^{24}_D$ +77.62° (c 0.47, CHCl$_3$).
α-Bromoketone 33. To ketone 29\(^2\) (5.0 mg, 0.0061 mmol) and triethylamine (160 µL, 1.15 mmol) in CH\(_2\)Cl\(_2\) (1 mL) at 0 °C was added TMSOTf (70 µL, 0.350 mmol) dropwise over 1 min. The reaction mixture was stirred for 30 min, quenched with saturated aq. NaHCO\(_3\) (2 mL), and extracted with EtOAc (5 x 1 mL). The combined organic layers were washed with brine (1.5 mL) and dried over Na\(_2\)SO\(_4\). Evaporation of the solvent under reduced pressure afforded silyl enol ether 31 as an unstable yellow oil that was used immediately in the subsequent reaction.

To crude silyl enol ether product 31 in THF (1.5 mL) at 23 °C was added freshly recrystallized NBS (14 mg, 0.0786 mmol). The reaction mixture was stirred for 1 min, quenched with saturated aq. NaHCO\(_3\) (2 mL), and extracted with EtOAc (5 x 1 mL). The combined organic layers were washed with brine (1.5 mL), dried by passage over a plug of silica gel (EtOAc eluent), and evaporated under reduced pressure to afford the crude product. Purification by preparative thin layer chromatography (1:1 hexanes:EtOAc eluent) afforded α-bromoketone 33 (5.3 mg, 97% yield, 2 steps) as a colorless oil. 

\(R' = 0.68\) (1:1 hexanes:EtOAc); \(^1\)H NMR (300 MHz, C\(_6\)D\(_6\)) \(\delta\) 9.01 (d, \(J = 8.5\) Hz, 1H), 8.87 (s, 1H), 8.69 (s, 1H), 8.15 (s, 1H), 7.70 (d, \(J = 8.3\) Hz, 2H), 7.49 (d, \(J = 8.5\) Hz, 1H), 7.10 (s, 1H), 6.40 (d, \(J = 8.0\) Hz, 2H), 5.45 (d, \(J = 10.2\) Hz, 1H), 5.36 (d, \(J = 10.2\) Hz, 1H), 4.75 (s, 1H), 4.14-4.06 (m, 1H), 3.68 (s, 3H), 3.60-3.46 (comp. m, 3H), 3.44 (s, 3H), 2.64-2.55 (m, 1H), 2.52-2.43 (m, 1H), 1.58 (s, 3H), 0.89 (t, \(J = 8.0\) Hz, 2H), 0.78 (d, \(J = 6.6\) Hz, 3H), -0.03 (s, 9H); 
\(^13\)C NMR (125 MHz, C\(_6\)D\(_6\), 38/39 C): \(\delta\) 202.4, 185.4, 156.6, 145.5, 143.2, 136.9, 136.7, 136.6, 135.8, 133.2, 131.8, 130.5 (2C), 129.8, 129.4, 128.0, 127.3 (2C), 126.5, 121.0, 120.0, 117.7, 117.3, 82.9, 77.3, 67.0, 58.4, 54.1, 53.0, 43.4, 36.7, 35.0, 21.3, 18.4, 12.4, -1.0 (3C); IR (film): 2950, 1719, 1662, 1557, 1374, 1190, 1178, 1141, 1089; HRMS-FAB (m/z): [M + H]\(^+\) calc’d for C\(_{39}\)H\(_{43}\)Br\(_2\)N\(_4\)O\(_7\)SSi, 899.0968; found, 899.0952; [\(\alpha\)]\(^{27}\)_D +10.23° (c 0.66, C\(_6\)H\(_6\)).
The relative stereochemistry of α-bromoketone 33 was determined by NOE experiments. Medium strength NOE interactions were observed as indicated below.³

Favorskii product 34. To α-bromoketone 33 (3.0 mg, 0.0033 mmol) in THF (1.0 mL) at 23 °C was added TBAF (1.0 M in THF, 20 µL, 0.020 mmol). The reaction mixture was stirred for 15 min, quenched with 10% (w/v) aq. citric acid (1 mL), diluted with brine (500 µL) and extracted with EtOAc (5 x 1 mL). The combined organic layers were dried by passage over a plug of silica gel (EtOAc eluent, then 5:1 CH₂Cl₂:MeOH eluent), and evaporated under reduced pressure to afford the crude product. Purification by preparative thin layer chromatography (5:1 CH₂Cl₂:MeOH eluent) afforded Favorskii product 34 (1.5 mg, 66% yield) as a yellow oil. Rf 0.53 (5:1 CH₂Cl₂:MeOH); ¹H NMR (600 MHz, CD₃OD): δ 8.61 (d, J = 9.2 Hz, 1H), 8.59 (s, 1H), 8.21 (s, 1H), 7.97 (s, 1H), 7.60 (s, 1H), 7.25 (d, J = 8.2 Hz, 1H), 5.81 (d, J = 10.1 Hz, 1H), 5.76 (d, J = 10.1 Hz, 1H), 4.96 (app. d, J = 3.7 Hz, 1H), 4.24 (s, 3H), 3.65 (m, 2H), 3.42 (s, 3H), 2.98 (d, J = 14.7 Hz, 1H), 2.38 (d, J = 11.0 Hz, 1H), 2.30 (dd, J = 11.0, 4.6 Hz, 1H), 1.63 (d, J = 14.7 Hz, 1H), 1.07 (s, 3H), 0.94-0.88 (m, 2H), -0.02 (s, 9H); ¹³C NMR (125 MHz, CD₃OD): δ 193.1, 170.2, 157.1, 142.4, 142.3, 139.5, 139.1, 133.1, 131.5, 130.6, 128.4, 126.9, 125.5, 124.4, 121.9, 116.8, 115.3, 112.8, 91.3, 77.8, 67.2, 55.1, 54.1, 46.2, 45.6, 44.7, 30.9, 25.0, 18.8, -1.1 (3C); IR (film): 3288 (br), 2927, 2855, 1711, 1659, 1553, 1535, 1449, 1409, 1367, 1250, 1198, 1093; HRMS-FAB (m/z): [M + H]+ calc’d for C₃₂H₃₈BrN₄O₆Si, 683.1724; found, 683.1721; [α]²³D -26.34° (c 0.2, CH₃OH).
The relative stereochemistry of Favorskii product 34 was determined by NOE experiments. Medium strength NOE interactions were observed as indicated below.³

**Hemiaminal 39.** Details for the Neber rearrangement/deprotection sequence have already been described.² Although hemiaminal 39 is typically used in crude form, it has been observed by ¹H NMR. ¹H NMR (600 MHz, CD₃OD): δ 8.61 (d, J = 8.2 Hz, 1H), 8.52 (s, 1H), 8.24 (s, 1H), 7.94 (s, 1H), 7.60 (s, 1H), 7.25 (d, J = 9.2 Hz, 1H), 5.72 (d, J = 10.1 Hz, 1H), 5.65 (d, J = 10.1 Hz, 1H), 4.85-4.82 (m, 1H), 4.49 (s, 1H), 4.21 (s, 3H), 3.47 (s, 3H), 3.36-3.30 (m, 1H), 3.26 (dd, J = 12.8, 2.7 Hz, 1H), 2.61 (dd, J = 12.8, 2.7 Hz, 1H), 0.85 (d, J = 7.3 Hz, 3H).
(--)-Dragmacidin F:

[Chemical structure diagram]

Acetoxycyclohexene 44. A mixture of methyl ester 20 (50.0 mg, 0.140 mmol) and 10% Pd/C (1.5 mg, 0.0014 mmol) in MeOH (1.3 mL) was stirred under an H₂ atmosphere at 23 °C. After 35 min, the reaction mixture was filtered over a Celite plug (MeOH eluent) and the solvent was evaporated *in vacuo*. \(^1\)H NMR integration showed that acetoxycyclohexene 44 was formed in approximately 10% yield.

*Alternate Procedure.* A mixture of methyl ester 20 (21.4 mg, 0.06 mmol) and 10% Pd/C (0.3 mg, 0.0003 mmol) in MeOH (1.5 mL) was cooled to 0 °C. The reaction vessel was then evacuated and back-filled with H₂ (4x). After 1 h, the reaction mixture was filtered over a Celite plug (MeOH eluent) and the solvent was evaporated *in vacuo*. \(^1\)H NMR integration showed that acetoxycyclohexene 44 was formed in approximately 3% yield.

An analytical sample of 44 was prepared via an alternate route as follows:

[Chemical structure diagram]

Acetoxycarbonate SM2. To a solution of methyl ester 20 (44.8 mg, 0.12 mmol) in THF (2 mL) was added TBAF (1.0 M in THF, 140 µL, 0.14 mmol). After 3 min of stirring, the reaction was quenched by the addition of saturated aq. NH₄Cl (2 mL). EtOAc (4 mL) was added, and the phases were partitioned. The aqueous phase was further extracted with EtOAc (2 x 2 mL). The combined organic layers were successively washed with H₂O (1 mL) and brine (1 mL), and dried over MgSO₄. The solvent was evaporated *in vacuo*, and the residue was dissolved *in vacuo*, and the mixture was heated at reflux for 2 h. After cooling to 23 °C, the crude reaction mixture was directly purified
by flash column chromatography (3:2 hexanes:EtOAc eluent) to afford pure acetoxycarbonate SM2 (16.9 mg, 45% yield, 2 steps). Rf 0.15 (1:1 hexanes:EtOAc); 1H NMR (300 MHz, CDCl3): δ 5.70-5.62 (m, 1H), 5.25 (app. d, J = 2.5 Hz, 1H), 5.19 (app. d, J = 2.5 Hz, 1H), 5.16 (dd, J = 4.1, 1.9 Hz, 1H), 3.81 (s, 3H), 2.84 (ddd, J = 13.4, 6.4, 2.7 Hz, 1H), 2.55-2.48 (m, 1H), 2.32-2.26 (m, 1H), 2.12 (s, 3H), 1.96 (dd, J = 13.3, 11.1 Hz, 1H); 13C NMR (75 MHz, CDCl3): δ 167.3, 168.3, 146.6, 140.2, 113.7, 81.6, 67.4, 53.7, 39.3, 32.7, 20.9; IR (film) 1763 (br), 1230, 1180, 1120 cm⁻¹; HRMS-FAB (m/z): [M + H]+ calc’d for C13H15O7, 271.0818; found 271.0810; [α]25D -154.53° (c 1.0, C6H6).

Acetoxycyclohexene 44. A mixture of acetoxycarbonate SM2 (18.5 mg, 0.07 mmol) and 10% Pd/C (1.4 mg, 0.001 mmol) in MeOH (1.3 mL) was cooled to 0 °C. The reaction vessel was then evacuated and back-filled with H2 (3x). After 1 hr at 0 °C, the reaction mixture was filtered over a Celite plug (MeOH eluent) and the solvent was evaporated in vacuo. The residue was purified by flash chromatography (1:1 EtOAc:hexanes eluent) to afford acetoxycyclohexene 44 (12.6 mg, 81% yield) as a colorless oil. Rf 0.46 (2:1 EtOAc:hexanes); 1H NMR (300 MHz, CDCl3): δ 5.57-5.48 (comp. m, 2H), 3.77 (s, 3H), 3.06 (br s, 1H), 2.69-2.58 (m, 1H), 2.29-2.20 (m, 1H), 2.16-1.91 (comp. m, 2H), 2.05 (s, 3H), 1.69-1.66 (m, 3H); 13C NMR (75 MHz, CDCl3): δ 176.1, 170.9, 132.7, 122.0, 73.8, 70.7, 53.2, 37.1, 35.3, 21.3, 19.2; IR (film) 3477 (br), 2953, 1736, 1239 cm⁻¹; HRMS-FAB (m/z): [M + H]+ calc’d for C12H17O5, 229.1076; found 229.1066; [α]25D -3.31° (c 0.6, CHCl3).

Anti-diol SM4. To 2-bromo SEM pyrrole2 (SM3, 4.66 g, 16.87 mmol) in THF (112 mL) at –78 °C was added n-BuLi (2.5 M in hexanes, 6.04 mL, 15.09 mmol) dropwise over 1 min. After 7 min at –78 °C, lactone 182 (1.26 g, 4.44 mmol) in THF (10 mL) was added dropwise over 1 min. The reaction vessel was immediately warmed to –42 °C, stirred for 30 min, and cooled to –78 °C. The reaction mixture was quenched with saturated aq. NH4Cl (50 mL), then warmed to 23 °C. The volatiles were removed under reduced pressure. The residue was partitioned between Et2O (125 mL) and H2O (100 mL), and the layers were separated. The
aqueous layer was further extracted with Et₂O (2 x 125 mL). The combined organic layers were washed with brine (75 mL), dried over MgSO₄, and evaporated under reduced pressure. The crude product was purified by flash chromatography (4:1 hexanes:EtOAc eluent) to afford anti-diol SM4 (1.84 g, 86% yield) as a pale yellow foam. Rf 0.48 (2:1 hexanes:EtOAc); ¹H NMR (300 MHz, C₆D₆): δ 8.11 (dd, J = 4.1, 1.7 Hz, 1H), 6.78 (app. t, J = 2.1 Hz, 1H), 6.15 (dd, J = 4.0, 2.6 Hz, 1H), 5.71 (d, J = 9.9 Hz, 1H), 5.58 (d, J = 10.2 Hz, 1H), 5.26 (s, 1H), 5.17 (app. t, J = 1.8 Hz, 1H), 4.92-4.82 (m, 1H), 4.76-4.73 (m, 1H), 4.45 (app. t, J = 3.0 Hz, 1H), 3.47 (t, J = 7.7 Hz, 2H), 2.66 (ddd, J = 12.4, 5.2, 2.5 Hz, 1H), 2.39 (dd, J = 14.4, 2.9 Hz, 1H), 2.20 (app. dt, J = 8.7, 4.8 Hz, 1H), 1.92 (app. t, J = 12.0 Hz, 1H), 0.88-0.80 (comp. m, 12H), -0.04 (s, 3H), -0.06 (s, 3H), -0.06 (s, 9H); ¹³C NMR (75 MHz, C₆D₆): δ 192.8, 151.6, 130.5, 128.6, 124.8, 109.3, 108.3, 83.0, 78.5, 76.7, 66.4, 66.2, 48.5, 42.1, 26.1 (3C), 18.4, 18.4, -0.9 (3C), -4.4, -5.1; IR (film): 3456 (br), 2953, 1637, 1406, 1250, 1091 cm⁻¹; HRMS-FAB (m/z): [M + H]⁺ calc’d for C₂₄H₄₄NO₅Si₂, 482.2758; found, 482.2751; [α]²⁸D -21.18° (c 1.0, C₆H₆).

Bis(silyl ether) 47. To a solution of anti-diol SM4 (253.1 mg, 0.53 mmol), imidazole (147.1 mg, 2.16 mmol), and DMAP (23.5 mg, 0.19 mmol) in DMF (5.0 mL), was added TBSCl (152.5 mg, 1.01 mmol). The solution was warmed to 50 °C for 70 min, cooled to 0 °C, then quenched by the addition of 10% (w/v) aq. citric acid (10 mL). Et₂O (40 mL) was added, and the layers were partitioned. The aqueous phase was further extracted with Et₂O (2 x 30 mL). The combined organic extracts were washed with brine (15 mL), dried over MgSO₄, and evaporated under reduced pressure. The crude product was purified by flash chromatography (9:1 hexanes:EtOAc eluent) to provide bis(silyl ether) 47 (296.0 mg, 95% yield) as a colorless oil that solidified under reduced pressure. Rf 0.61 (4:1 hexanes:EtOAc); ¹H NMR (300 MHz, C₆D₆): δ 8.17 (dd, J = 4.0, 1.8 Hz, 1H), 6.76 (dd, J = 2.5, 1.7 Hz, 1H), 6.14 (dd, J = 4.0, 2.6 Hz, 1H), 5.68 (d, J = 9.9 Hz, 1H), 5.62 (d, J = 10.2 Hz, 1H), 5.37 (s, 1H), 5.32 (app. t, J = 2.1 Hz, 1H), 5.22-5.14 (m, 1H), 4.77 (app. t, J = 1.9 Hz, 1H), 4.50 (app. t, J = 3.0 Hz, 1H), 3.47 (t, J = 7.8 Hz, 2H), 2.82 (ddd, J = 12.7, 5.1, 2.6 Hz, 1H), 2.45 (dd, J = 14.6, 2.8 Hz, 1H), 2.27-2.18 (comp. m, 2H),
0.99 (s, 9H), 0.88 (s, 9H), 0.82 (t, J = 7.8 Hz, 2H), 0.17 (s, 3H), 0.14 (s, 3H), -0.04 (s, 3H), -0.07 (s, 9H); \(^{13}\)C NMR (75 MHz, C\(_6\)D\(_6\), 29/30 C): δ 192.6, 151.6, 130.4, 124.5, 109.3, 108.6, 83.2, 78.5, 76.8, 67.4, 66.3, 49.3, 42.1, 26.4 (3C), 26.1 (3C), 18.9, 18.4, 18.3, -0.9 (3C), -4.3, -4.4, -4.5, -5.1; IR (film): 3464 (br), 1953, 2929, 1640, 1405, 1309, 1251, 1094 cm\(^{-1}\); HRMS-FAB (m/z): [M + H]\(^+\) calc'd for C\(_{30}\)H\(_{58}\)NO\(_5\)Si\(_3\), 596.3623; found, 596.3594; [\(\alpha\)]\(^{27}\)D -7.16° (c 1.0, C\(_6\)H\(_6\)).

The stable chair conformer of bis(silylether) 47 was determined using a combination of NOESY-1D, gCOSY, and homodecoupling NMR experiments. The coupling constant between H\(_a\) and H\(_b\) was measured as \(J_{ab} = 11.0\) Hz.

**Medium Strength NOE Interactions:**

![Diagram of chemical structure showing NOE interactions](image)

**Syn-diol 48.** To bis(silylether) 47 (113.9 mg, 0.19 mmol) in THF (10.0 mL) was added TBAF (1.0 M in THF, 195 μL, 0.20 mmol) in a dropwise fashion over 1 min. The reaction mixture was stirred for 2 min, quenched with saturated aq. NH\(_4\)Cl (15 mL), then poured into EtOAc (40 mL). The layers were partitioned and the aqueous layer was further extracted with EtOAc (2 x 40 mL). The combined organic extracts were successively washed with H\(_2\)O (15 mL) and brine (15 mL), dried over MgSO\(_4\), and evaporated under reduced pressure. The residue was purified by flash chromatography (7:1 hexanes:EtOAc eluent) to furnish syn diol 48 (87.5 mg, 95% yield) as a pale yellow oil. R\(_f\) 0.29 (4:1 hexanes:EtOAc); \(^1\)H NMR (300 MHz, C\(_6\)D\(_6\)): δ 7.09
(dd, J = 4.1, 1.4 Hz, 1H), 6.63 (dd, J = 2.3, 1.5 Hz, 1H), 5.89 (dd, J = 4.1, 2.5 Hz, 1H), 5.51-5.39 (comp. m, 4H), 5.27-5.19 (m, 1H), 5.01 (app. t, J = 2.1 Hz, 1H), 4.52-4.46 (m, 1H), 3.86 (d, J = 8.0 Hz, 1H), 3.37 (t, J = 7.7 Hz, 2H), 2.45-2.23 (comp. m, 3H), 2.04 (app. dt, J = 8.4, 4.9 Hz, 1H), 0.99 (s, 9H), 0.79 (t, J = 7.8 Hz, 2H), 0.14 (s, 3H), 0.11 (s, 3H), -0.09 (s, 9H); 13C NMR (75 MHz, C6D6): δ 191.6, 152.9, 131.4, 126.4, 124.0, 109.8, 108.5, 81.2, 78.8, 74.7, 67.4, 66.6, 49.0, 43.3, 26.4 (3C), 18.9, 18.3, -1.0 (3C), -4.5, -4.5; IR (film): 3363 (br), 2954, 1631, 1410, 1314, 1250, 1101 (br) cm⁻¹; HRMS-FAB (m/z): [M + H]⁺ calc’d for C24H44NO5Si2, 482.2758; found, 482.2780; [α]27D -27.06° (c 1.0, C6H6).

**Carbonate 46.** To syn diol 48 (68.2 mg, 0.14 mmol) and 1,1'-carbonyldiimidazole (37.0 mg, 0.23 mmol) in THF (2.6 mL) was added NaH (60% dispersion in mineral oil, 21.9 mg, 0.55 mmol) in one portion. The reaction was stirred for 20 min at 23 °C, then quenched by addition of saturated aq. NH₄Cl (20 mL). The reaction mixture was poured into EtOAc (30 mL), the layers were partitioned, and the aqueous layer was further extracted with EtOAc (2 x 30 mL). The combined organic extracts were successively washed with H₂O (10 mL) and brine (10 mL), dried over MgSO₄, and evaporated under reduced pressure. Purification of the residue by flash chromatography (6:1 hexanes:EtOAc eluent) afforded carbonate 46 (65.8 mg, 92% yield) as a colorless oil. Rf 0.29 (4:1 hexanes:EtOAc); ¹H NMR (300 MHz, C6D6): δ 7.91 (dd, J = 4.1, 1.7 Hz, 1H), 6.68 (dd, J = 2.8, 1.7 Hz, 1H), 6.02 (dd, J = 4.3, 2.6 Hz, 1H), 5.51 (d, J = 9.9 Hz, 1H), 5.43 (d, J = 9.9 Hz, 1H), 5.24 (app. t, J = 1.9 Hz, 1H), 4.84-4.75 (m, 1H), 4.69 (app. t, J = 1.8 Hz, 1H), 4.46 (dd, J = 3.9, 1.9 Hz, 1H), 3.39 (t, J = 7.7 Hz, 2H), 2.78 (ddd, J = 13.5, 6.1, 2.5 Hz, 1H), 2.12-1.98 (comp. m, 2H), 1.92-1.85 (m, 1H), 0.86 (s, 9H), 0.81 (t, J = 7.8 Hz, 2H), -0.07--0.08 (comp. m, 12H), -0.10 (s, 3H); ¹³C NMR (75 MHz, C6D6): δ 185.9, 147.2, 146.4, 132.1, 126.7, 125.0, 112.2, 110.3, 87.9, 80.3, 78.8, 66.8, 66.5, 46.1, 33.7, 26.2 (3C), 18.6, 18.3, -1.0 (3C), -4.7, -5.0; IR (film): 2954, 1764, 1641, 1413, 1354, 1251, 1173, 1089 cm⁻¹; HRMS-FAB (m/z): [M + H]⁺ calc’d for C25H42NO6Si2, 508.2551; found, 508.2560; [α]27D -54.78° (c 1.0, C6H6).
Pyrrolocyclohexene 42. A mixture of carbonate 46 (40.0 mg, 0.08 mmol) and 10% Pd/C (1.7 mg, 0.002 mmol) in MeOH (1.0 mL) was cooled to 0 °C. The reaction vessel was then evacuated and back-filled with H₂ (3x). After 1.75 hr at 0 °C, the reaction mixture was filtered over a Celite plug (MeOH eluent) and the solvent was evaporated in vacuo. The residue was purified by flash chromatography (9:1 hexanes:EtOAc eluent) to afford pyrrolocyclohexene 42 (33.1 mg, 90% yield) as a colorless oil. Rₜ 0.53 (4:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, C₆D₆): δ 6.94 (dd, J = 4.1, 1.4 Hz, 1H), 6.64 (dd, J = 2.6, 1.5 Hz, 1H), 5.89 (dd, J = 4.0, 2.6 Hz, 1H), 5.54 (d, J = 10.2 Hz, 1H), 5.45 (d, J = 10.2 Hz, 1H), 5.39-5.33 (m, 1H), 4.87-4.78 (m, 1H), 4.78 (s, 1H), 3.40 (t, J = 7.8 Hz, 2H), 2.97-2.85 (m, 1H), 2.48 (dd, J = 12.5, 9.8 Hz, 1H), 2.34-2.26 (m, 1H), 2.21-2.08 (m, 1H), 1.95-1.90 (m, 3H), 0.96 (s, 9H), 0.81 (t, J = 7.8 Hz, 2H), 0.06 (s, 3H), 0.03 (s, 3H), -0.08 (s, 9H); ^{13}C NMR (75 MHz, C₆D₆): δ 193.8, 138.5, 131.0, 126.4, 123.1, 120.1, 109.7, 78.8, 78.2, 69.6, 66.5, 44.7, 38.9, 26.4 (3C), 20.6, 18.6, 18.3, -1.0 (3C), -3.8, -4.5; IR (film): 3431 (br), 2954, 1634, 1414, 1250, 1089 (br) cm⁻¹; HRMS-FAB (m/z): [M + H]^+ calc’d for C₂₄H₄₄NO₄Si₂, 466.2809; found, 466.2804; [α]²⁸_D +26.19° (c 1.0, C₆H₆).

[3.3.1] Bicycle 43. To pyrrolocyclohexene 42 (40.0 mg, 0.0859 mmol) was added Pd(OAc)₂ (23.0 mg, 0.103 mmol), DMSO (14.6 µL, 0.206 mmol), t-BuOH (6.9 mL), and AcOH (1.7 mL). The mixture was heated to 60 °C for 8 h, cooled to 23 °C, and filtered over a plug of silica gel (2:1 hexanes:EtOAc eluent). The solvent was evaporated, and the product was purified by flash chromatography on silica gel (8:1 hexanes:EtOAc eluent) to afford [3.3.1] bicycle 43 contaminated with a trace amount of pyrrolocyclohexene 42. Although this material was carried on to the subsequent step without further purification, an analytical sample of 43 was obtained by flash chromatography on silica gel (12:1 hexanes:EtOAc eluent) as a colorless oil. Rₜ 0.64 (3:1
hexanes:EtOAc); $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta$ 6.64 (d, $J = 2.5$ Hz, 1H), 6.25 (d, $J = 10.2$ Hz, 1H), 5.84 (d, $J = 2.8$ Hz, 1H), 5.07 (d, $J = 9.9$ Hz, 1H), 4.79 (br s, 1H), 4.66 (br s, 1H), 4.24-4.19 (m, 1H), 4.19 (s, 1H), 3.68-3.51 (m, 2H), 3.43-3.38 (m, 1H), 2.61 (app. dt, $J = 7.3$, 3.9 Hz, 1H), 2.21-2.10 (m, 2H), 2.06-1.98 (m, 1H), 0.99-0.77 (m, 2H), 0.72 (s, 9H), -0.04 (s, 9H), -0.11 (s, 3H), -0.24 (s, 3H); $^{13}$C NMR (75 MHz, C$_6$D$_6$): $\delta$ 192.0, 148.6, 142.7, 130.5, 126.3, 113.2, 108.3, 77.0, 73.4, 73.0, 66.6, 48.5, 45.5, 40.2, 26.1 (3C), 18.4, 18.3, -1.0 (3C), -4.4, -5.1; IR (film): 3468 (br), 2951, 1648, 1422, 1250, 1094, 1062 cm$^{-1}$; HRMS-FAB ($m/z$): [M + H]$^+$ calc’d for C$_{24}$H$_{42}$NO$_4$Si$_2$, 464.2652; found, 464.2661; $\left[\alpha\right]^{27}_D +319.22 \degree$ (c 1.0, C$_6$H$_6$).

**Methyl Ether 49.** The crude mixture of 42 and 43 obtained from the previous step was dissolved in THF (1.5 mL) at 23 °C and NaH (60% dispersion in mineral oil, 17 mg, 0.429 mmol) was added. After stirring for 1 min at 23 °C, Mel was added (53 µL, 0.859 mmol). The resulting mixture was stirred for 1.5 h, quenched with saturated aq. NH$_4$Cl (1.5 mL), and extracted with Et$_2$O (4 x 1 mL). The combined organic layers were washed with brine (1 mL), dried by passage over a plug of silica gel (EtOAc eluent), and evaporated under reduced pressure. The crude product was purified by flash chromatography (10:1 hexanes:EtOAc eluent) to afford methyl ether 49 (28.2 mg, 68% yield, 2 steps) as a colorless oil. R$_f$ 0.43 (5:1 hexanes:EtOAc); $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta$ 6.62 (d, $J = 2.6$ Hz, 1H), 6.43 (d, $J = 10.3$ Hz, 1H), 5.06 (d, $J = 10.0$ Hz, 1H), 4.84 (d, $J = 1.5$ Hz, 1H), 4.69 (d, $J = 1.5$ Hz, 1H), 4.29-4.22 (m, 1H), 3.42-3.52 (m, 2H), 3.45 (app. t, $J = 2.8$ Hz, 1H), 3.39 (s, 3H), 2.79 (app. dt, $J = 7.4$, 3.8 Hz, 1H), 2.49 (app. dt, $J = 8.1$, 4.4 Hz, 1H), 1.96 (dd, $J = 13.8$, 4.7 Hz, 1H), 1.70 (dd, $J = 11.7$, 3.2 Hz, 1H), 0.96-0.82 (m, 2H), 0.73 (s, 9H), -0.06 (s, 9H), -0.11 (s, 3H), -0.23 (s, 3H); $^{13}$C NMR (75 MHz, C$_6$D$_6$): $\delta$ 189.2, 149.2, 140.9, 129.6, 128.9, 112.9, 107.6, 79.0, 77.3, 72.7, 66.6, 51.5, 46.3, 41.7, 39.9, 26.1 (3C), 18.4, 18.4, -1.0 (3C), -4.4, -5.1; IR (film): 2951, 1661, 1426, 1250, 1113, 1066; HRMS-FAB ($m/z$): [M + H]$^+$ calc’d for C$_{25}$H$_{44}$NO$_4$Si$_2$, 478.2809; found, 478.2815; $\left[\alpha\right]^{27}_D +312.37 \degree$ (c 1.0, C$_6$H$_6$).
Table 1. Pd(II)-mediated oxidative carbocyclization\(^a\)

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<th>temp [°C]</th>
<th>time</th>
<th>yield(^b)</th>
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<td>TIPSO</td>
<td>60</td>
<td>13.5 h</td>
<td>51% (63%)</td>
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<tr>
<td>2</td>
<td>HO</td>
<td>complex mixture</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>TBSO</td>
<td>no reaction</td>
<td>80</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>AcO</td>
<td>TIPSO</td>
<td>80</td>
<td>1.8 h</td>
<td>53% (66%)</td>
</tr>
<tr>
<td>5</td>
<td>TBSO</td>
<td>TIPSO</td>
<td>80</td>
<td>6.5 h</td>
<td>37% (59%)</td>
</tr>
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</table>

\(^a\) Standard Conditions: 1 equiv Pd(OAc)\(_2\), 2 equiv DMSO, \(\tau\)-BuOH:AcOH (4:1, 0.01 M). \(^b\) Isolated Yield. Number in parenthesis represents the yield based on recovered starting material. \(^c\) Trace product may have formed in this reaction, but could not be isolated. \(^d\) 20 mol% Pd(OAc)\(_2\), 40 mol% DMSO, \(\tau\)-BuOH:AcOH (4:1, 0.01 M), O\(_2\) (1 atm). \(^e\) At 80 °C, trace product formation and substantial decomposition were observed. \(^f\) Yield based on \(^1\)H NMR with internal standard.

TIPS Ether SM6 (Table 1, Entry 1). To allylic alcohol SM5\(^d\) (50.7 mg, 0.14 mmol) in CH\(_2\)Cl\(_2\) (5 mL) at 23 °C was added 2,6-lutidine (34 μL, 0.29 mmol), followed by TIPSOEt (44 μL, 0.16 mmol). After stirring 5 min, saturated aq. NH\(_4\)Cl (5 mL) was added to quench the reaction. The phases were partitioned, and the aqueous phase was extracted with CH\(_2\)Cl\(_2\) (3 x 20 mL). The combined organic extracts were washed with brine (5 mL), and dried over MgSO\(_4\). Following evaporation of the solvent in vacuo, the crude product was purified by flash chromatography (9:1 hexanes:EtOAc eluent) to provide TIPS ether SM6 (65.8 mg, 90%) as a colorless oil. R\(_f\) 0.58 (4:1 hexanes:EtOAc); \(^1\)H NMR (300 MHz, C\(_6\)D\(_6\)): δ 8.12 (dd, \(J = 3.9, 1.6\) Hz, 1H), 6.77 (dd, \(J = 2.5, 1.6\) Hz, 1H), 6.15 (dd, \(J = 3.9, 2.5\) Hz, 1H), 5.69 (d, \(J = 10.1\) Hz, 1H),
5.65 (d, \(J = 9.6\) Hz, 1H), 5.34-5.29 (m, 1H), 5.00 (s, 1H), 4.24-4.19 (m, 1H), 3.49 (t, \(J = 7.8\) Hz, 2H), 2.69-2.63 (comp. m, 2H), 2.50-2.42 (m, 1H), 2.40-2.32 (m, 1H), 1.78-1.74 (m, 3H), 1.09-0.97 (comp. m, 21H), 0.85 (t, \(J = 7.8\) Hz, 2H), -0.06 (s, 9H); \(^1\)H NMR (75 MHz, C\(_6\)D\(_6\)): \(\delta 194.1, 133.8, 130.3, 129.0, 124.7, 122.8, 109.2, 78.5, 70.5, 66.3, 39.4, 22.0, 18.7\) (3C), 18.7 (3C), 18.4 (3C), -0.9 (3C); IR (film) 3472 (br), 2947, 2868, 1639, 1413, 1310, 1249, 1084 cm\(^{-1}\); HRMS-FAB (m/z): [M + H]\(^+\) calc’d for C\(_{27}\)H\(_{50}\)NO\(_4\)Si\(_2\), 508.3278; found, 508.3273; \([\alpha]\)\(^{27}\)_D +29.49° (c 1.0, C\(_6\)H\(_6\)).

**Allylic Alcohol SM5 (Table 1, Entry 2).** To allylic silyl ether 15\(^2\) (100.0 mg, 0.21 mmol) in THF (5 mL) at 23 °C was added TBAF (1.0 M in THF, 250 µL, 0.25 mmol). After stirring 5 min, the reaction mixture was quenched by the addition of saturated aq. NH\(_4\)Cl (5 mL). The reaction was poured into Et\(_2\)O (5 mL) and H\(_2\)O (5 mL), and the phases were partitioned. The aqueous phase was extracted with Et\(_2\)O (4 x 3 mL), and the combined organic extracts were dried by passage over a plug of SiO\(_2\) gel (Et\(_2\)O eluent). The solvent was evaporated \textit{in vacuo}, and the residue was passed over another plug of SiO\(_2\) gel (Et\(_2\)O eluent) to afford allylic alcohol SM5 (72.8 mg, 96% yield) as a colorless oil. \(R_f\) 0.38 (2:1 hexanes:EtOAc); \(^1\)H NMR (300 MHz, C\(_6\)D\(_6\)): \(\delta 7.01 (dd, J = 4.1, 1.7\) Hz, 1H), 6.70 (dd, \(J = 2.5, 1.7\) Hz, 1H), 5.99 (dd, \(J = 4.1, 2.8\) Hz, 1H), 5.52 (d, \(J = 10.0\) Hz, 1H), 5.49 (d, \(J = 10.2\) Hz, 1H), 5.31-5.25 (m, 1H), 4.95 (s, 1H), 3.93-3.84 (m, 1H), 3.60 (app. d, \(J = 9.6\) Hz, 1H), 3.41 (t, \(J = 7.8\) Hz, 2H), 2.77-2.65 (m, 1H), 2.27-2.16 (comp. m, 3H), 1.93-1.89 (m, 3H), 0.82 (t, \(J = 7.7\) Hz, 2H), -0.08 (s, 9H); \(^1\)C NMR (75 MHz, C\(_6\)D\(_6\)): \(\delta 194.0, 136.2, 131.0, 126.9, 123.5, 120.0, 109.5, 78.8, 77.8, 68.1, 66.6, 41.0, 38.7, 21.7, 18.3, -1.0\) (3C); IR (film) 3388 (br), 2953, 1632, 1412, 1309, 1249, 1086 cm\(^{-1}\); HRMS-FAB (m/z): [M + H]\(^+\) calc’d for C\(_{18}\)H\(_{30}\)NO\(_4\)Si, 352.1944; found, 352.1941; \([\alpha]\)\(^{27}\)_D +31.11° (c 1.0, C\(_6\)H\(_6\)).
Methyl Ether SM7 (Table 1, Entry 3). To allylic silyl ether 15\(^2\) (55.0 mg, 0.12 mmol) in THF (2 mL) at 23 °C was added NaH (60% dispersion in mineral oil, 95.5 mg, 2.39 mmol). After stirring for 5 min, MeI (200 µL, 3.21 mmol) was added. After stirring for 30 min, saturated aq. NH\(_4\)Cl (2 mL) was added dropwise over 1 min to quench the reaction. EtOAc (1 mL) was added, and the phases were partitioned. The aqueous phase was extracted with EtOAc (2 x 1 mL), and the combined organic extracts were washed with brine (1 mL) and dried over MgSO\(_4\). After evaporation of the solvent in vacuo, the residue was purified by flash chromatography (9:1 hexanes:EtOAc eluent) to afford methyl ether SM7 (21.1 mg, 37% yield). \(R_f\) 0.53 (4:1 hexanes:EtOAc); \(^1\)H NMR (300 MHz, C\(_6\)D\(_6\)): \(\delta\) 7.76 (dd, \(J = 3.9, 1.6\) Hz, 1H), 6.69 (dd, \(J = 2.5, 1.5\) Hz, 1H), 6.08 (dd, \(J = 3.9, 2.5\) Hz, 1H), 5.64 (d, \(J = 9.6\) Hz, 1H), 5.45 (d, \(J = 10.1\) Hz, 1H), 5.35-5.30 (m, 1H), 4.52-4.43 (m, 1H), 3.45 (t, \(J = 7.8\) Hz, 2H), 3.10 (s, 3H), 2.99-2.85 (comp. m, 2H), 2.36-2.25 (m, 1H), 2.22 (dd, \(J = 12.4, 9.2\) Hz, 1H), 1.82-1.79 (m, 3H), 0.98 (s, 9H), 0.88-0.82 (m, 2H), 0.09 (s, 3H), 0.07 (s, 3H), -0.05 (s, 9H); \(^13\)C NMR (75 MHz, C\(_6\)D\(_6\), 24/25 C): \(\delta\) 193.2, 136.5, 130.0, 122.2, 120.7, 109.2, 84.6, 78.2, 70.1, 66.4, 51.7, 42.4, 35.0, 26.4 (3C), 20.3, 18.6, 18.4, -1.0 (3C), -3.7, -4.4; IR (film) 2954, 1645, 1412, 1250, 1079 cm\(^{-1}\); HRMS-FAB (m/z): [M + H]\(^+\) calc'd for C\(_{25}\)H\(_{46}\)NO\(_4\)Si\(_2\), 480.2965; found, 480.2958; [\(\alpha\)]\(^{27}\)\(_D\) +43.57° (c 1.0, C\(_6\)H\(_6\)).

Allylic Acetate SM8 (Table 1, Entries 4 and 5). To allylic alcohol SM5 (131.0 mg, 0.37 mmol) in CH\(_2\)Cl\(_2\) (7.5 mL) at 23 °C was added DMAP (68.1 mg, 0.56 mmol) followed by Ac\(_2\)O (53 µL, 0.56 mmol). After stirring for 50 min, the reaction was quenched by the addition of saturated aq. NaHCO\(_3\) (10 mL). Et\(_2\)O (30 mL) was added, the phases were partitioned, and the aqueous phase was extracted with Et\(_2\)O (3 x 30 mL). The combined organics were washed successively with H\(_2\)O (10 mL) and brine (10 mL), dried over MgSO\(_4\), and evaporated in vacuo.
Flash chromatography of the crude product (7:3 hexanes:Et₂O eluent) provided allylic acetate **SM8** (134.4 mg, 92%) as a colorless oil. R_f 0.21 (4:1 hexanes:EtOAc); ^1^H NMR (300 MHz, C₆D₆): δ 7.71 (dd, J = 3.9, 1.7 Hz, 1H), 6.76 (dd, J = 2.6, 1.8 Hz, 1H), 6.10 (dd, J = 4.0, 2.6 Hz, 1H), 5.63 (d, J = 10.2 Hz, 1H), 5.57 (d, J = 9.9 Hz, 1H), 5.50-5.45 (m, 1H), 5.32-5.26 (m, 1H), 3.45 (t, J = 7.8 Hz, 2H), 3.39 (s, 1H), 2.69-2.58 (m, 1H), 2.51-2.35 (comp. m, 2H), 2.28 (app. dt, J = 8.6, 5.0 Hz, 1H), 1.60-1.57 (comp. m, 6H), 0.84 (t, J = 7.8 Hz, 2H), -0.07 (s, 9H); ^13^C NMR (75 MHz, C₆D₆): δ 193.4, 169.9, 131.2, 130.6, 128.3, 124.6, 124.0, 109.2, 78.5, 77.6, 69.7, 66.4, 38.4, 38.3, 20.9, 20.8, 18.3, -1.0 (3C); IR (film) 3458 (br), 2924, 1734, 1641, 1314, 1372, 1247, 1085 cm⁻¹; HRMS-FAB (m/z): [M + H]^+ calc’d for C₂₀H₃₂NO₅Si, 394.2050; found, 394.2030; [α]²⁷D +22.38° (c 1.0, C₆H₆).

2-Bromo SEM Indole (SM10). To a solution of 2-bromoindole⁵ (SM9, 500.0 mg, 2.55 mmol) in THF (25 mL) cooled to 0 °C was added NaH (60% dispersion in mineral oil, 145.2 mg, 3.63 mmol). After H₂ evolution ceased (3 min), SEMCl (500.0 µL, 2.82 mmol) was added dropwise over 1 min. The reaction was stirred for 10 min, and was quenched by the addition of saturated aq. NH₄Cl (20 mL). Et₂O (50 mL) was added, the phases were partitioned, and the aqueous phase was extracted with Et₂O (2 x 75 mL). The combined organic extracts were washed with brine (15 mL) and dried over MgSO₄. After evaporation of the solvent under reduced pressure, the residue was purified by flash chromatography (9:1 hexanes:Et₂O eluent) to afford 2-bromo SEM indole (SM10, 741.3 mg, 89% yield) as a colorless oil. R_f 0.60 (4:1 hexanes:EtOAc).
Indole SM11 (Table 1, Entry 6). To 2-bromo SEM indole (SM10, 482.6 mg, 1.48 mmol) in THF (7 mL) cooled to -78 °C was added n-BuLi (2.5 M in hexanes, 590 µL, 1.48 mmol). The solution was stirred for 10 min, and was then treated dropwise over 1 min with a solution of Weinreb amide 24² (161.5 mg, 0.49 mmol) in THF (2 mL). The solution was immediately warmed to 0 °C and stirred for 30 min. The reaction was quenched at -78 °C with saturated aq. NH₄Cl (10 mL), and was allowed to thaw slowly to 23 °C. Et₂O (50 mL) was added, the phases were partitioned, and the aqueous phase was extracted with Et₂O (2 x 75 mL). The combined organic extracts were washed successively with H₂O (15 mL) and brine (15 mL), and dried over MgSO₄. Following evaporation of the solvent in vacuo, the crude product was purified by flash chromatography (19:1 hexanes:EtOAc) to furnish indole SM11 (92.2 mg, 36% yield) as a colorless oil. Rf 0.48 (4:1 hexanes:EtOAc); ¹H NMR (300 MHz, C₆D₆): δ 8.41 (s, 1H), 7.64-7.60 (m, 1H), 7.50-7.46 (m, 1H), 7.28-7.21 (m, 1H), 7.10-7.04 (m, 1H), 6.03-5.95 (m, 2H), 5.35-5.30 (m, 1H), 5.23 (s, 1H), 3.96-3.92 (m, 1H), 3.58 (t, J = 7.8 Hz, 2H), 2.77-2.57 (comp. m, 2H), 2.42-2.35 (m, 1H), 2.35-2.28 (m, 1H), 1.70-1.67 (m, 3H), 0.93-0.81 (m, 2H), 0.89 (s, 9H), 0.00 (s, 3H), -0.02 (s, 3H), -0.10 (s, 9H); ¹³C NMR (75 MHz, C₆D₆): δ 196.9, 141.0, 133.7, 132.8, 127.5, 126.8, 124.1, 122.3, 121.9, 117.8, 112.2, 79.3, 74.1, 69.9, 66.0, 39.3, 39.3, 26.2 (3C), 21.6, 18.4, 18.3, -0.9 (3C), -4.3, -4.6; IR (film) 3466 (br), 2954, 1655, 1250, 1072 cm⁻¹; HRMS-El (m/z): [M]⁺ calc’d for C₂₈H₄₅NO₄Si₂, 515.2887; found, 515.2893; [α]₂⁰ D -12.17° (c 1.0, C₆H₆).

TIPS Ether SM13 (Table 1, Entry 7). To allylic alcohol SM12⁶ (48.5 mg, 0.14 mmol) in CH₂Cl₂ (5 mL) at 23 °C was added 2,6-lutidine (32 µL, 0.27 mmol), followed by TIPSOTf
(42 µL, 0.16 mmol). After stirring 5 min, saturated aq. NH₄Cl (5 mL) was added to quench the reaction. The phases were partitioned, and the aqueous phase was extracted with CH₂Cl₂ (3 x 20 mL). The combined organic extracts were washed with brine (5 mL), and dried over MgSO₄. Following evaporation of the solvent in vacuo, the crude product was purified by flash chromatography (19:1 hexanes:EtOAc → 9:1 hexanes:EtOAc eluent) to provide TIPS ether SM13 (58.5 mg, 84%) as a colorless oil. Rf 0.48 (4:1 hexanes:EtOAc); ¹H NMR (300 MHz, C₆D₆): δ 6.98 (dd, J = 4.1, 1.4 Hz, 1H), 6.64 (dd, J = 2.5, 1.6 Hz, 1H), 5.91 (dd, J = 4.1, 2.7 Hz, 1H), 5.50 (d, J = 10.0 Hz, 1H), 5.46 (d, J = 10.0 Hz, 1H), 5.39-5.33 (m, 1H), 5.07-4.98 (m, 1H), 4.79 (s, 1H), 3.39 (t, J = 7.8 Hz, 2H), 2.97-2.85 (m, 1H), 2.55-2.46 (m, 1H), 2.44-2.36 (m, 1H), 2.20-2.08 (m, 1H), 2.05-2.00 (m, 3H), 1.16-1.02 (comp. m, 21H), 0.80 (t, J = 7.8 Hz, 2H), -0.08 (s, 9H); ¹³C NMR (75 MHz, C₆D₆): δ 193.9, 139.1, 131.0, 126.3, 123.0, 119.9, 109.7, 78.8, 78.2, 70.1, 66.6, 44.9, 38.9, 20.8, 18.9 (3C), 18.8 (3C), 18.3, 13.5 (3C), -1.0 (3C); IR (film) 3431 (br), 2946, 2866, 1631, 1413, 1382, 1250, 1094 cm⁻¹; HRMS-FAB (m/z): [M + H]⁺ calc’d for C₂₇H₅₀NO₄Si₂, 508.3278; found, 508.3264; [α]₂⁷D +14.46° (c 1.0, C₆H₆).

Allylic Alcohol SM12 (Table 1, Entry 8). To carbonate 46 (41.8 mg, 0.08 mmol) in THF (1 mL) was added TBAF (1.0 M in THF, 85 µL, 0.085 mmol) at 23 °C. After stirring 3 min, the reaction was quenched by the addition of saturated aq. NH₄Cl (1 mL). EtOAc (1 mL) was added, the phases were partitioned, and the aqueous phase was extracted with EtOAc (3 x 1 mL). The combined organics were washed successively with H₂O (1 mL) and brine (1 mL), and dried over MgSO₄. The solvent was evaporated in vacuo, and the crude product was purified by flash chromatography (1:1 hexanes:EtOAc eluent) to provide hydroxycarbonate SM14 (28.7 mg, 89% yield) as a colorless oil. Rf 0.29 (1:1 hexanes:EtOAc); ¹H NMR (300 MHz, C₆D₆): δ 7.77 (dd, J = 4.1, 1.4 Hz, 1H), 6.72 (app. t, J = 2.1 Hz, 1H), 6.08 (dd, J = 4.1, 2.3 Hz, 1H), 5.48 (d, J = 10.1 Hz, 1H), 5.42 (d, J = 10.1 Hz, 1H), 5.29 (app. t, J = 1.6 Hz, 1H), 4.78-4.75 (m, 1H), 4.52-4.42 (comp. m, 2H), 3.40 (t, J = 8.0 Hz, 2H), 2.67 (ddd, J = 13.4, 6.1, 2.6 Hz, 1H), 2.47 (app. d, J = 5.5 Hz, 1H), 2.00 (dd, J = 14.4, 1.6 Hz, 1H), 1.91-1.81 (comp. m, 2H), 0.83 (t, J = 7.8 Hz,
2H), -0.07 (s, 9H); $^{13}$C NMR (75 MHz, C$_6$D$_6$): δ 185.8, 147.9, 145.9, 132.0, 126.6, 125.1, 112.2, 110.2, 88.1, 80.6, 78.7, 66.6, 65.4, 45.2, 33.4, 18.2, -1.0 (3C); IR (film) 3455 (br), 2953, 2895, 1756, 1444, 1414, 1360, 1250, 1179, 1082 (br) cm$^{-1}$; HRMS-FAB ($m/z$): [M + H]$^+$ calc'd for C$_{19}$H$_{28}$NO$_6$Si, 394.1686; found, 394.1690; $[\alpha]_{D}^{26}$ -77.69° (c 1.0, C$_6$H$_6$).

A mixture of hydroxycarbonate SM14 (34.2 mg, 0.09 mmol) and 10% Pd/C (1.5 mg, 0.001 mmol) in MeOH (1.4 mL) was cooled to 0 °C. The reaction vessel was then evacuated and back-filled with H$_2$ (3x). After 15 min at 0 °C, the reaction mixture was filtered over a Celite plug (MeOH eluent) and the solvent was evaporated in vacuo. The residue was purified by flash chromatography (3:1 hexanes:EtOAc eluent) to afford allylic alcohol SM12 (24.3 mg, 80% yield) as a colorless oil. R$_f$ 0.33 (1:1 hexanes:EtOAc); $^1$H NMR (300 MHz, C$_6$D$_6$): δ 7.19 (dd, $J$ = 4.0, 1.6 Hz, 1H), 6.69 (dd, $J$ = 2.4, 1.6 Hz, 1H), 5.98 (dd, $J$ = 4.1, 2.5 Hz, 1H), 5.50 (d, $J$ = 10.1 Hz, 1H), 5.46 (d, $J$ = 9.8 Hz, 1H), 5.27-5.21 (m, 1H), 4.45-4.34 (m, 1H), 3.99 (s, 1H), 3.41 (t, $J$ = 7.8 Hz, 2H), 2.91-2.79 (m, 1H), 2.26 (dd, $J$ = 12.9, 8.1 Hz, 1H), 2.20-2.03 (comp. m, 3H), 1.87-1.83 (m, 3H), 0.82 (t, $J$ = 7.8 Hz, 2H), -0.08 (s, 9H); $^{13}$C NMR (75 MHz, C$_6$D$_6$): δ 194.3, 137.9, 130.9, 126.9, 123.5, 119.9, 109.5, 78.7, 78.4, 68.4, 66.6, 43.9, 38.8, 19.9, 18.3, -1.0 (3C); IR (film) 3407 (br), 2953, 2920, 1629, 1412, 1309, 1250, 1081 cm$^{-1}$; HRMS-FAB ($m/z$): [M + H]$^+$ calc'd for C$_{18}$H$_{30}$NO$_4$Si, 352.1944; found, 352.1931; $[\alpha]_{D}^{25}$ +21.44° (c 1.0, C$_6$H$_6$).

Methyl Ether SM15 (Table 1, Entry 9). To allylic silyl ether 42 (10 mg, 0.02 mmol) in THF (1 mL) at 23 °C was added NaH (60% dispersion in mineral oil, 17 mg, 0.43 mmol). After stirring for 5 min, MeI (37 µL, 0.59 mmol) was added, and the reaction was stirred for 30 min. Saturated aq. NH$_4$Cl (2 mL) was added slowly to quench the reaction mixture, and Et$_2$O (1 mL) was added. The phases were partitioned, and the aqueous phase was extracted with Et$_2$O (2 x 1 mL). The combined organic extracts were dried over MgSO$_4$, evaporated in vacuo, and purified by flash chromatography (19:1 hexanes:EtOAc eluent) to afford methyl ether SM15 (4.2 mg, 41% yield). R$_f$ 0.51 (4:1 hexanes:EtOAc); $^1$H NMR (300 MHz, C$_6$D$_6$): δ 7.78 (dd, $J$ = 4.1, 1.7 Hz, 1H), 6.73 (dd, $J$ = 2.5, 1.7 Hz, 1H), 6.10 (dd, $J$ = 4.0, 2.6 Hz, 1H), 5.64 (d, $J$ = 9.9 Hz, 1H),
5.59 (d, J = 9.9 Hz, 1H), 5.29-5.23 (m, 1H), 4.62-4.53 (m, 1H), 3.47 (t, J = 2.8 Hz, 2H), 3.14 (s, 3H), 2.77 (ddd, J = 13.7, 5.4, 2.4 Hz, 1H), 2.70-2.58 (m, 1H), 2.53-2.41 (m, 1H), 2.32 (dd, J = 13.8, 9.9 Hz, 1H), 1.84-1.80 (m, 3H), 0.97 (s, 9H), 0.84 (t, J = 7.8 Hz, 2H), 0.09 (s, 6H), -0.08 (s, 9H); \(^{13}\)C NMR (75 MHz, C\(_6\)D\(_6\)): \(\delta\) 193.7, 137.6, 130.4, 129.2, 122.4, 119.8, 109.5, 85.8, 78.3, 69.6, 66.4, 52.6, 38.8, 34.9, 26.4 (3C), 20.3, 18.6, 18.3, -1.0 (3C), -3.8, -4.4; IR (film) 2953, 2930, 2857, 1644, 1412, 1250, 1078 cm\(^{-1}\); HRMS-El (m/z): [M]+ calc’d for C\(_{25}\)H\(_{45}\)NO\(_4\)Si\(_2\), 479.2887; found, 479.2887; \([\alpha]^{27}_D +7.38^\circ\) (c 0.6, C\(_6\)H\(_6\)).

**Allylic Acetate SM18 (Table 1, Entry 10).** To anti-diol SM4 (1.77 g, 3.68 mmol) in CH\(_2\)Cl\(_2\) (25 mL) at 23 °C was added Et\(_3\)N (1.28 mL, 9.19 mmol) and DMAP (45 mg, 0.368 mmol), followed by Ac\(_2\)O (451 \(\mu\)L, 4.78 mmol). The reaction mixture was stirred for 5 min, and then additional Ac\(_2\)O (125 \(\mu\)L, 1.32 mmol) was added. Stirring was continued for 5 min, and then another portion of Ac\(_2\)O (100 \(\mu\)L, 1.06 mmol) was added. After 5 min, the reaction mixture was quenched with saturated aq. NaHCO\(_3\) (15 mL). The volatile solvents were removed under reduced pressure. The residue was diluted with H\(_2\)O (30 mL) and extracted with EtOAc (3 x 70 mL). The combined organic layers were dried over MgSO\(_4\), and evaporated under reduced pressure. Subsequent filtration over a short plug of silica gel afforded the crude product, which was used immediately in the following reaction. R\(_f\) 0.63 (2:1 hexanes:EtOAc).

To the crude product in THF (25 mL) was added TBAF (1.0 M in THF, 3.85 mL, 3.85 mmol). After 2 min of stirring, the reaction was quenched by the addition of saturated aq. NH\(_4\)Cl (30 mL) and the volatile solvents were removed under reduced pressure. The residue was diluted with H\(_2\)O (50 mL) and extracted with EtOAc (3 x 60 mL). The combined organic layers were washed with brine (30 mL), dried over MgSO\(_4\), and evaporated under reduced pressure. The
crude product was purified by flash chromatography (3:2 hexanes:EtOAc eluent) to afford acetoxycyclohexene \textbf{SM16} (1.49 g, 99% yield, 2 steps) as a colorless oil. \(R_f\) 0.23 (2:1 hexanes:EtOAc).

To acetoxycyclohexene \textbf{SM16} (222 mg, 0.542 mmol) and 1,1’-carbonyldiimidazole (132 mg, 0.813 mmol) in THF (10.8 mL) at 23 °C was added NaH (60% dispersion in mineral oil, 54 mg, 1.35 mmol). After 2 min of stirring, the reaction was quenched by the addition of saturated aq. NH\(_4\)Cl (10 mL) and the volatile solvents were removed under reduced pressure. The residue was diluted with H\(_2\)O (50 mL) and extracted with EtOAc (3 x 50 mL). The combined organic layers were washed with brine (30 mL), dried over MgSO\(_4\), and evaporated under reduced pressure. The crude product was purified by flash chromatography (2:1 hexanes:EtOAc eluent) to afford acetoxycarbonate \textbf{SM17} (200.1 mg, 85% yield) as a colorless oil. \(R_f\) 0.25 (2:1 hexanes:EtOAc); \(^1\)H NMR (300 MHz, C\(_6\)D\(_6\)): \(\delta\) 7.75 (dd, \(J = 4.3, 1.5\) Hz, 1H), 6.74 (dd, \(J = 2.5, 1.7\) Hz, 1H), 6.03 (dd, \(J = 4.3, 2.6\) Hz, 1H), 5.89-5.79 (m, 1H), 5.47 (s, 2H), 4.90 (d, \(J = 2.2\) Hz, 1H), 4.54 (dd, \(J = 3.9, 1.9\) Hz, 1H), 3.40 (t, \(J = 7.8\) Hz, 1H), 2.82 (ddd, \(J = 13.4, 6.3, 2.3\) Hz, 1H), 2.03 (dd, \(J = 14.6, 1.9\) Hz, 1H), 1.95 (ddd, \(J = 14.6, 3.8, 2.4\) Hz, 1H), 1.81 (dd, \(J = 13.2, 11.3\) Hz, 1H), 1.63 (s, 3H), 0.81 (t, \(J = 7.8\) Hz, 2H), -0.08 (s, 9H); \(^{13}\)C NMR (75 MHz, C\(_6\)D\(_6\)): \(\delta\) 185.4, 168.9, 146.8, 141.6, 132.3, 126.4, 125.4, 112.6, 110.4, 87.4, 80.0, 78.7, 67.3, 66.5, 41.7, 33.3, 20.5, 18.3, -1.0 (3C); IR (film) 2953, 1764, 1643, 1413, 1356, 1234, 1177, 1129, 1086, 1048 cm\(^{-1}\); HRMS-FAB (m/z): [M + H]\(^+\) calc’d for C\(_{21}\)H\(_{30}\)NO\(_7\)Si, 436.1792; found, 436.1807; \([\alpha]_{D}^{27}\) -112.57° (c 1.0, C\(_6\)H\(_6\)).

A mixture of acetoxycarbonate \textbf{SM17} (734 mg, 1.69 mmol) and 10% Pd/C (36 mg, 0.03 mmol) in MeOH (17 mL) was cooled to 0 °C. The reaction vessel was then evacuated and back-filled with H\(_2\) (3x). After 20 min at 0 °C, the reaction mixture was filtered over a Celite plug (MeOH eluent) and the solvent was evaporated in vacuo. The residue was purified by flash chromatography (3:1 hexanes:EtOAc eluent) to afford allylic acetate \textbf{SM18} (625 mg, 94% yield). \(R_f\) 0.56 (2:1 hexanes:EtOAc); \(^1\)H NMR (300 MHz, C\(_6\)D\(_6\)): \(\delta\) 7.05 (dd, \(J = 4.3, 1.5\) Hz, 1H), 6.69 (dd, \(J = 2.2, 1.4\) Hz, 1H), 6.07-5.98 (m, 1H), 5.95 (dd, \(J = 3.9, 2.8\) Hz, 1H), 5.53 (d, \(J = 9.9\) Hz, 1H), 5.47 (d, \(J = 9.9\) Hz, 1H), 5.36-5.30 (m, 1H), 4.09 (br s, 1H), 3.42 (t, \(J = 7.8\) Hz, 2H), 2.80 (ddd, \(J = 18.0, 5.2, 2.6\) Hz, 1H), 2.43 (ddd, \(J = 12.6, 6.1, 1.7\) Hz, 1H), 2.34 (dd, \(J = 12.4, 9.6\) Hz, 1H), 2.17-2.06 (m, 1H), 1.72-1.69 (m, 3H), 1.68 (s, 3H), 0.82 (t, \(J = 7.8\) Hz, 2H), -0.08 (s, 9H); \(^{13}\)C NMR (75 MHz, C\(_6\)D\(_6\)): \(\delta\) 193.3, 170.4, 133.8, 130.9, 126.9, 123.1, 122.7, 109.5, 78.7, 78.3,
Following evaporation of the solvent (15 mL). The combined organic extracts were washed with brine (15 mL) and dried over MgSO$_4$ (2 x 50 mL). The combined organic extracts were washed with brine (15 mL) and dried over MgSO$_4$. Following evaporation of the solvent in vacuo, the crude product was purified by flash chromatography (9:1 hexanes:EtOAc) to afford anti-diol SM19 (108.9 mg, 72% yield) as a pale yellow foam.

**Indole SM23 (Table 1, Entry 11).** To 2-bromo SEM indole (SM10, 345.0 mg, 1.06 mmol) in THF (7 mL) cooled to -78 °C was added n-BuLi (2.5 M in hexanes, 380 µL, 0.95 mmol) dropwise over 1 min. The reaction was stirred for 7 min, and then a solution of lactone 18 (80.8 mg, 0.28 mmol) in THF (1 mL) was added dropwise over 2 min. The solution was warmed to -42 °C, and stirred for 1 h. The reaction was quenched at -78 °C by the addition of saturated aq. NH$_4$Cl (3 mL), and was allowed to thaw slowly to 23 °C. Et$_2$O (50 mL) and H$_2$O (10 mL) were added, the phases were partitioned, and the aqueous phase was extracted with Et$_2$O (2 x 50 mL). The combined organic extracts were washed with brine (15 mL) and dried over MgSO$_4$. Following evaporation of the solvent in vacuo, the crude product was purified by flash chromatography (9:1 hexanes:EtOAc) to afford anti-diol SM19 (108.9 mg, 72% yield) as a pale yellow foam.

To anti-diol SM19 (762.8 mg, 1.43 mmol) in CH$_2$Cl$_2$ (20 mL) at 23 °C was added 2,6-lutidine (360 µL, 3.09 mmol). The solution was treated with TBSOTf (480 µL, 2.09 mmol), and was stirred for 10 min. The reaction was quenched by the addition of saturated aq. NH$_4$Cl (50 mL). The phases were partitioned, and the aqueous phase was extracted with CH$_2$Cl$_2$ (4 x 50 mL). The combined organic extracts were washed with brine (15 mL) and dried over MgSO$_4$. Following evaporation of the solvent in vacuo, the crude product was purified by flash chromatography (9:1 hexanes:EtOAc) to afford anti-diol SM19 (108.9 mg, 72% yield) as a pale yellow foam.
chromatography (9:1 hexanes:EtOAc eluent) to afford bis(silylether) SM20 (859.6 mg, 93% yield) as a white solid. Rf 0.48 (4:1 hexanes:EtOAc).

To bis(silylether) SM20 (859.6 mg, 1.33 mmol) in THF (34 mL) at 23 °C was added TBAF (1.0 M in THF, 1.40 mL, 1.40 mmol) in a dropwise fashion over 1 min. After stirring 5 min, the reaction was quenched by the addition of saturated aq. NH₄Cl (50 mL). Et₂O (50 mL) was added, the phases were partitioned, and the aqueous phase was extracted with Et₂O (75 mL x 2). The combined organics were washed with brine (25 mL), dried over MgSO₄, and evaporated under reduced pressure. The residue was purified by flash chromatography (9:1 hexanes:EtOAc → 4:1 hexanes:EtOAc eluent) to afford syn-diol SM21 (687.1 mg, 97% yield) as a pale yellow foam. Rf 0.28 (4:1 hexanes:EtOAc).

To syn-diol SM21 (687.1 mg, 1.29 mmol) in THF (30 mL) at 23 °C was added NaH (60% dispersion in mineral oil, 167.0 mg, 4.18 mmol). When H₂ evolution ceased (3 min), 1,1'-carbonyldiimidazole (331.3 mg, 2.04 mmol) was added in one portion. The reaction was quenched after 30 min of stirring with saturated aq. NH₄Cl (50 mL). Et₂O (50 mL) was added, the phases were partitioned, and the aqueous phase was extracted with Et₂O (75 mL x 2). The combined organics were washed with brine (25 mL), dried over MgSO₄, and evaporated under reduced pressure. The residue was purified by flash chromatography (9:1 hexanes:EtOAc eluent) to afford indolocarbonate SM22 (668.9 mg, 93% yield) as a white foam. Rf 0.37 (4:1 hexanes:EtOAc); ¹H NMR (300 MHz, C₆D₆): δ 8.24 (d, J = 0.8 Hz, 1H), 7.45 (app. dt, J = 4.5, 2.8 Hz, 1H), 7.38-7.34 (m, 1H), 7.24-7.18 (m, 1H), 7.03-6.97 (m, 1H), 5.86 (d, J = 10.6 Hz, 1H), 5.77 (d, J = 10.4 Hz, 1H), 5.26 (dd, J = 2.0, 1.5 Hz, 1H), 4.88-4.79 (m, 1H), 4.74 (app. t, J = 1.7 Hz, 1H), 4.54 (dd, J = 3.9, 2.0 Hz, 1H), 3.51-3.44 (m, 2H), 2.86 (ddd, J = 13.5, 6.0, 2.3 Hz, 1H), 2.11-1.92 (comp. m, 3H), 0.87 (s, 9H), 0.80 (t, J = 7.7 Hz, 2H), -0.05 (s, 3H), -0.07 (s, 3H), -0.12 (s, 9H); ¹³C NMR (75 MHz, C₆D₆): δ 188.9, 147.0, 146.2, 141.5, 130.7, 127.9, 127.3, 124.7, 122.4, 118.2, 112.5, 111.9, 88.3, 80.2, 74.1, 66.7, 66.2, 46.1, 33.6, 26.2 (3C), 18.6, 18.3, -1.0 (3C), -4.7, -4.9; IR (film) 2954, 1765, 1656, 1355, 1170, 1086 cm⁻¹; HRMS-El (m/z): [M]⁺ calc’d for C₂₉H₄₃NO₆Si₂, 557.2629; found, 557.2632; [α]23D -34.29 (c 1.0, C₆H₆).

A mixture of indolocarbonate SM22 (230.2 mg, 0.41 mmol) and 10% Pd/C (8.8 mg, 0.008 mmol) in MeOH (10 mL) was cooled to 0 °C. The reaction vessel was then evacuated and back-filled with H₂ (3x). After 4 hr at 0 °C, the reaction mixture was filtered over a Celite plug (MeOH eluent) and the solvent was evaporated in vacuo. The residue was purified by flash
chromatography (9:1 hexanes:EtOAc eluent) to afford indole SM23 (192.2 mg, 90% yield) as a pale yellow oil. Rf 0.48 (4:1 hexanes:EtOAc); 1H NMR (300 MHz, C6D6): δ 7.43-7.42 (m, 1H), 7.42-7.39 (m, 1H), 7.39-7.37 (m, 1H), 7.24-7.17 (m, 1H), 7.07-7.01 (m, 1H), 5.90 (d, J = 10.6 Hz, 1H), 5.82 (d, J = 10.6 Hz, 1H), 5.41-5.35 (m, 1H), 4.87-4.77 (m, 1H), 4.29 (s, 1H), 3.51 (t, J = 7.8 Hz, 1H), 3.03-2.92 (m, 1H), 2.66-2.57 (m, 1H), 2.43-2.35 (m, 1H), 2.23-2.11 (m, 1H), 1.95-1.92 (m, 3H), 0.96 (s, 9H), 0.82 (t, J = 7.8 Hz, 2H), 0.08 (s, 3H), 0.06 (s, 3H), -0.12 (s, 9H); 13C NMR (75 MHz, C6D6): δ 197.1, 141.0, 138.7, 130.7, 127.4, 127.0, 124.0, 119.9, 116.1, 112.2, 79.3, 74.2, 69.5, 66.2, 44.4, 38.8, 26.4 (3C), 20.6, 18.6, 18.3, -1.0 (3C), -3.8, -4.5; IR (film) 3449 (br), 2954, 1643, 1249, 1092 cm⁻¹; HRMS-ESI (m/z): [M]+ calc’d for C28H45NO4Si2, 515.2887; found, 515.2875; [α]27 D -27.67° (c 1.0, C6H6).

Representative Procedure for Oxidative Cyclizations (Table 1, Entry 6 is used as an example):

To indole SM11 (23.5 mg, 0.05 mmol) was added Pd(OAc)2 (10.2 mg, 0.05 mmol), DMSO (6.5 µL, 0.09 mmol), t-BuOH (3.6 mL), and AcOH (0.9 mL). The mixture was heated at 80 °C for 2.5 h, cooled to 23 °C, and filtered over a plug of silica gel (EtOAc eluent). The solvent was evaporated, and the crude product was purified by flash chromatography on silica gel (19:1 hexanes:EtOAc eluent) to afford pure [3.3.1] bicycle.

Entry 1. Purified by preparative thin-layer chromatography (4:1 hexanes:EtOAc eluent). Rf 0.29 (4:1 hexanes:EtOAc); 1H NMR (300 MHz, C6D6): δ 6.54 (d, J = 2.7 Hz, 1H), 5.78 (d, J = 2.7 Hz, 1H), 5.52 (d, J = 10.1 Hz, 1H), 5.41 (app. t, J = 2.1 Hz, 1H), 5.32 (d, J = 10.1 Hz, 1H), 5.02 (app. t, J = 2.3 Hz, 1H), 4.38-4.29 (m, 1H), 4.25 (s, 1H), 3.59-3.45 (comp. m, 3H), 2.50-2.38 (comp. m, 2H), 2.21-2.04 (comp. m, 2H), 1.09-0.78 (comp. m, 23H), -0.01 (s, 9H); 13C NMR (75 MHz, C6D6): δ 191.5, 149.6, 141.7, 131.8, 125.6, 108.5, 107.5, 76.9, 75.9, 68.6, 66.5, 49.2, 40.7, 18.6 (3C) 18.2, 13.1 (3C), -0.9 (3C); IR (film) 3478 (br), 2954, 2867, 1650, 1100, 1080 cm⁻¹; HRMS-ESI (m/z): [M]+ calc’d for C27H47NO4Si2, 505.3044; found, 505.3041; [α]27 D -207.44° (c 0.6, C6H6).

Entries 4 and 5. Purified by preparative thin-layer chromatography (4:1 CH2Cl2:Et2O eluent). Note: Entry 5 was performed in a round-bottom flask fitted with reflux condenser and an O2
balloon. R$_f$ 0.56 (4:1 CH$_2$Cl$_2$:Et$_2$O); $^1$H NMR (300 MHz, C$_6$D$_6$): δ 6.52 (d, $J = 2.7$ Hz, 1H), 5.76 (d, $J = 2.7$ Hz, 1H), 5.51-5.41 (m, 1H), 5.46 (d, $J = 10.4$ Hz, 1H), 5.27 (d, $J = 10.4$ Hz, 1H), 4.93 (app. t, $J = 1.7$ Hz, 1H), 4.91-4.88 (m, 1H), 4.35 (s, 1H), 3.56 (t, $J = 7.7$ Hz, 2H), 3.47 (app. t, $J = 3.1$ Hz, 1H), 2.49-2.36 (comp. m, 2H), 2.17-2.09 (m, 1H), 1.94 (app. t, $J = 12.0$ Hz, 1H), 1.55 (s, 3H), 0.96-0.86 (m, 2H), -0.01 (s, 9H); $^{13}$C NMR (75 MHz, C$_6$D$_6$): δ 190.6, 169.2, 145.5, 141.0, 132.4, 125.4, 108.6, 106.8, 76.8, 75.4, 69.0, 66.5, 45.3, 44.5, 40.9, 20.6, 18.2, -0.9 (3C); IR (film) 3469 (br), 2952, 1743, 1651, 1237, 1093, 1037 cm$^{-1}$; HRMS-FAB (m/z): [M+H]$^+$ calc’d for C$_{20}$H$_{30}$NO$_5$Si, 392.1893; found, 392.1886; [α]$^{27}$D = -389.72° (c 0.6, C$_6$H$_6$).

**Entry 6.** Purified by flash chromatography (19:1 hexanes:EtOAc eluent). R$_f$ 0.33 (4:1 hexanes:EtOAc); $^1$H NMR (300 MHz, C$_6$D$_6$): δ 7.52-7.46 (m, 1H), 7.37-7.32 (m, 1H), 7.20-7.14 (m, 1H), 7.05-6.97 (m, 1H), 5.97 (d, $J = 10.9$ Hz, 1H), 5.73 (d, $J = 10.9$ Hz, 1H), 5.39 (app. t, $J = 2.1$ Hz, 1H), 5.11 (app. t, $J = 2.0$ Hz, 1H), 4.24-4.15 (m, 1H), 4.18 (s, 1H), 3.85 (app. t, $J = 3.2$ Hz, 1H), 3.69-3.52 (m, 2H), 2.47 (app. dt, $J = 7.5$, 3.9 Hz, 1H), 2.40-2.31 (m, 1H), 2.29-2.22 (m, 1H), 2.11 (app. t, $J = 11.8$ Hz, 1H), 1.01-0.77 (m, 2H), 0.83 (s, 9H), -0.05 (s, 9H), -0.17 (s, 3H), -0.24 (s, 3H); $^{13}$C NMR (75 MHz, C$_6$D$_6$, 27/28 C): δ 194.9, 148.1, 141.6, 133.8, 129.1, 125.0, 122.2, 122.1, 112.6, 108.3, 76.5, 73.6, 68.3, 66.1, 48.6, 45.4, 38.7, 26.2 (3C), 18.7, 18.2, -0.9 (3C), -4.5, -4.8; IR (film) 3485, 2953, 1657, 1250, 1106, 1073 cm$^{-1}$; HRMS-FAB (m/z): [M]$^+$ calc’d for C$_{28}$H$_{43}$NO$_4$Si$_2$, 513.2731; found, 513.2719; [α]$^{27}$D = -281.78° (c 0.3, C$_6$H$_6$).

**Entry 7.** Purified by preparative thin-layer chromatography (9:1 CH$_2$Cl$_2$:Et$_2$O eluent). R$_f$ 0.48 (4:1 hexanes:EtOAc); R$_f$ 0.65 (4:1 Et$_2$O:CH$_2$Cl$_2$); $^1$H NMR (300 MHz, C$_6$D$_6$): δ 6.62 (d, $J = 2.7$ Hz, 1H), 6.26 (d, $J = 10.1$ Hz, 1H), 5.86 (d, $J = 2.7$ Hz, 1H), 5.06 (d, $J = 10.1$ Hz, 1H), 4.84 (app. d, $J = 1.6$ Hz, 1H), 4.73 (app. d, $J = 1.6$ Hz, 1H), 4.39-4.33 (m, 1H), 4.24 (s, 1H), 3.67-3.50 (m, 2H), 3.42 (app. t, $J = 3.1$ Hz, 1H), 2.62 (app. dt, $J = 7.4$, 4.1 Hz, 1H), 2.30 (app. dt, $J = 8.1$, 4.7 Hz, 1H), 2.15 (dd, $J = 11.8$, 3.1 Hz, 1H), 2.06 (dd, $J = 14.0$, 4.9 Hz, 1H), 0.98-0.71 (comp. m, 23H), -0.04 (s, 9H); $^{13}$C NMR (75 MHz, C$_6$D$_6$): δ 192.0, 148.3, 142.6, 130.6, 126.1, 113.8, 108.6, 77.0, 73.5, 72.9, 66.6, 48.6, 45.9, 40.3, 18.6 (3C), 18.6 (3C), 18.2, 12.8 (3C), -1.0 (3C); IR (film) 3475 (br), 2945, 1648, 1094, 1057 cm$^{-1}$; HRMS-EI (m/z): [M]$^+$ calc’d for C$_{27}$H$_{47}$NO$_4$Si$_2$, 505.3044; found, 505.3040; [α]$^{23}$D = +253.79° (c 0.7, C$_6$H$_6$).
**Entry 10.** A 10% yield of SM24 was obtained based on $^1$H NMR integration relative to an internal standard. An analytical sample of SM24 was prepared as follows:

![Reaction Scheme](image)

**[3.3.1] Bicycle SM24.** To 43 (10.4 mg, 0.02 mmol) in THF (1 mL) was added TBAF (1.0 M in THF, 75 μL, 0.075 mmol) dropwise over 1 min at 23 °C. After 23 h, the reaction was quenched by the addition of saturated aq. NH$_4$Cl (1 mL). The aqueous layer was extracted with EtOAc (4 x 1 mL), and the combined organics were dried over MgSO$_4$ and evaporated *in vacuo*. Purification of the crude product by preparative thin-layer chromatography (1:1 hexanes:EtOAc eluent) afforded the crude diol, which was used in the subsequent reaction. $R_f$ 0.09 (7:3 hexanes:EtOAc).

To a vial containing the crude diol in CH$_2$Cl$_2$ (1.1 mL) was added DMAP (2.2 mg, 0.02 mmol) and Et$_3$N (31 μL, 0.22 mmol), followed by Ac$_2$O (31 μL, 0.33 mmol). The vial was sealed and heated at 50 °C for 40 min. The reaction was allowed to cool to 23 °C, and saturated aq. NaHCO$_3$ (1 mL) was added. The aqueous layer was extracted with EtOAc (4 x 1 mL), and the combined organics were dried over MgSO$_4$ and evaporated *in vacuo*. Purification of the residue by preparative thin-layer chromatography (7:3 hexanes:EtOAc) afforded [3.3.1] bicycle SM24 (4.1 mg, 47% yield, 2 steps) as a colorless oil. $R_f$ 0.22 (7:3 hexanes:EtOAc); $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta$ 6.53 (d, $J = 2.3$ Hz, 1H), 5.73 (d, $J = 2.3$ Hz, 1H), 5.53 (d, $J = 10.1$ Hz, 1H), 5.49-5.45 (m, 1H), 5.39 (d, $J = 10.1$ Hz, 1H), 5.12 (d, $J = 1.4$ Hz, 1H), 4.92 (d, $J = 1.8$ Hz, 1H), 4.20 (s, 1H), 3.67-3.52 (m, 2H), 3.33-3.29 (m, 1H), 2.50 (app. dt, $J = 7.7$, 4.0 Hz, 1H), 2.12 (ddd, $J = 14.7$, 2.7, 1.8 Hz, 1H), 2.04 (dd, $J = 12.1$, 3.0 Hz, 1H), 1.96 (dd, $J = 14.7$, 5.5 Hz, 1H), 1.35 (s, 3H), 0.91-0.85 (m, 2H), -0.04 (s, 9H); $^{13}$C NMR (125 MHz, C$_6$D$_6$): $\delta$ 191.4, 169.0, 143.6, 142.3, 131.2, 126.1, 117.5, 108.2, 76.8, 73.1, 72.9, 66.7, 44.5, 44.0, 40.0, 20.8, 18.3, -1.0 (3C); IR (film) 3471 (br), 2951, 1738, 1650, 1231, 1094 cm$^{-1}$; HRMS-EI ($m/z$): [M]$^+$ calc’d for C$_{20}$H$_{29}$NO$_5$Si, 391.1815; found, 391.1800; [$\alpha$]$^{24}_D$ +396.32° (c 0.5, C$_6$H$_6$).
**Entry 11.** Purified by preparative thin-layer chromatography (4:1 hexanes:EtOAc eluent). R<sub>f</sub> 0.55 (4:1 hexanes:EtOAc); <sup>1</sup>H NMR (300 MHz, C<sub>6</sub>D<sub>6</sub>): δ 7.51-7.48 (m, 1H), 7.48-7.46 (m, 1H), 7.27-7.21 (m, 1H), 7.08-7.02 (m, 1H), 6.63 (d, J = 10.7 Hz, 1H), 5.59 (d, J = 10.7 Hz, 1H), 4.89 (app. d, J = 1.4 Hz, 1H), 4.68 (app. d, J = 1.7 Hz, 1H), 4.20-4.15 (m, 1H), 4.13 (s, 1H), 3.79-3.58 (comp. m, 3H), 2.69 (app. dt, J = 7.6, 4.0 Hz, 1H), 2.23 (dd, J = 11.8, 3.0 Hz, 1H), 2.20-2.12 (m, 1H), 2.09-2.01 (m, 1H), 1.03-0.79 (m, 2H), 0.51 (s, 9H), -0.07 (s, 9H), -0.25 (s, 3H), -0.69 (s, 3H); <sup>13</sup>C NMR (125 MHz, C<sub>6</sub>D<sub>6</sub>, 27/28 C): δ 195.3, 147.4, 141.4, 134.7, 129.8, 127.8, 127.8, 121.8, 121.6, 113.8, 112.4, 74.1, 73.7, 72.9, 66.2, 48.6, 45.2, 38.1, 25.7 (3C), 18.2, 18.1, -1.0 (3C), -5.0, -5.3; IR (film) 3475 (br), 2951, 1656, 1250, 1061 cm<sup>-1</sup>; HRMS EI (m/z): [M]<sup>+</sup> calc’d for C<sub>28</sub>H<sub>43</sub>NO<sub>4</sub>Si<sub>2</sub>, 513.2731; found, 513.2730; [α]<sup>24</sup>D +216.18° (c 0.25, C<sub>6</sub>H<sub>6</sub>).

For entries 2 and 8, small quantities of enone SM25 was observed. An authentic sample was prepared as follows:

**Enone SM25.** To allylic alcohol SM5 (11.4 mg, 0.032 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (1 mL) was added Dess-Martin Periodinane (31.4 mg, 0.074 mmol). After stirring for 20 min, a solution of saturated Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>: saturated NaHCO<sub>3</sub> (1:1, 1 mL) was added to quench the reaction. The phases were partitioned, and the aqueous phase was extracted with Et<sub>2</sub>O (1 x 4 mL). The combined organics were dried by passage over a plug of SiO<sub>2</sub>, and the solvent was evaporated in vacuo. The residue was purified by preparative thin layer chromatography (1:1 hexanes:EtOAc eluent) to furnish enone SM25 (11.4 mg, 99% yield) as a pale yellow oil. R<sub>f</sub> 0.40 (2:1 hexanes:EtOAc); <sup>1</sup>H NMR (300 MHz, C<sub>6</sub>D<sub>6</sub>): δ 7.03 (dd, J = 4.1, 1.4 Hz, 1H), 6.68 (dd, J = 2.5, 1.6 Hz, 1H), 5.97 (dd, J = 4.1, 2.7 Hz, 1H), 5.92-5.87 (m, 1H), 5.48 (d, J = 9.6 Hz, 1H), 5.43 (d, J = 9.6 Hz, 1H), 3.40 (t, J = 7.8 Hz, 2H), 3.25 (s, 1H), 2.98 (d, J = 16.0 Hz, 1H), 2.83-2.73 (m, 1H), 2.66 (dd, J = 16.3, 1.6 Hz, 1H), 2.25-2.14 (m, 1H), 1.84-1.81 (m, 3H), 0.82 (t, J = 7.8 Hz, 2H), -0.08 (s, 9H); <sup>13</sup>C NMR (75 MHz, C<sub>6</sub>D<sub>6</sub>): δ 195.2, 191.4, 138.9, 135.8, 131.1, 126.7, 123.5, 109.5, 80.3, 78.7, 66.6, 49.5, 38.4, 18.3, 16.4, -1.0 (3C); IR (film) 3424 (br), 2951, 1667, 1639, 1412, 1249, 1085.
Reduced Bicycle 52. Methyl ether 49 (23 mg, 0.0479 mmol), 10% Pd/C (15 mg, 0.014 mmol), and EtOAc (2.5 mL) were combined, and the reaction vessel was evacuated and back-filled with H₂ (1 atm). The reaction mixture was stirred under H₂ for 5 min, then filtered over a plug of silica gel topped with Celite (EtOAc eluent) to afford reduced bicycle 52 as a colorless oil (23 mg, 99% yield). Rᶠ 0.28 (5:1 hexanes:EtOAc); ¹H NMR (300 MHz, C₆D₆): δ 6.64 (d, J = 2.5 Hz, 1H), 6.52 (d, J = 10.2 Hz, 1H) 5.83 (d, J = 2.5 Hz, 1H), 5.05 (d, J = 10.2 Hz, 1H), 3.71-3.51 (comp. m, 3H), 3.42 (s, 3H), 2.78 (app. dt, J = 7.4, 3.9 Hz, 1H), 2.60 (app. q, J = 3.1 Hz, 1H), 2.40 (app. dt, J = 8.1, 4.6 Hz, 1H), 1.81 (dd, J = 13.8, 4.4 Hz, 1H), 1.58 (dd, J = 11.4, 2.9 Hz, 1H), 1.42-1.53 (m, 1H), 0.99-0.81 (m, 2H), 0.87 (d, J = 7.2 Hz, 3H), 0.72 (s, 9H), -0.06 (s, 9H), -0.10 (s, 3H), -0.21 (s, 3H); ¹³C NMR (75 MHz, C₆D₆, 24/25 C): δ 189.3, 140.3, 129.1, 109.2, 79.2, 77.2, 71.5, 66.5, 51.2, 45.4, 41.9, 38.3, 36.8, 26.1 (3C), 18.4, 18.4, 17.1, -1.0 (3C), -4.4, -5.0; IR (film): 2952, 1660, 1497, 1425, 1251, 1118, 1100, 1042 cm⁻¹; HRMS-FAB (m/z): [M + H]⁺ calc’d for C₂₅H₄₆NO₄Si₂, 480.2965; found, 480.2955; [α]²⁵_D +220.84° (c 1.0, C₆H₆).
Pyrazine 50. To silyl ether 52 (10.0 mg, 0.0208 mmol) in THF (2 mL) at 0 °C was added freshly recrystallized NBS (4.8 mg, 0.0271 mmol) in THF (200 µL). After 10 min at 0 °C, the reaction mixture was warmed to 23 °C, stirred for 40 min, then cooled to 0 °C. The reaction was quenched with saturated aq. Na2S2O3 (1.5 mL), diluted with H2O (1 mL) and extracted with EtOAc (5 x 1 mL). The combined organic layers were washed with brine (1 mL), dried by passage over a plug of silica gel (EtOAc eluent), and evaporated under reduced pressure to afford the crude product. Further purification by preparative thin layer chromatography (4:1 hexanes:EtOAc eluent) afforded bromide SM26 (8.5 mg, 73% yield) as a colorless oil. \( R_f \) 0.4 (5:1 hexanes:EtOAc).

To bromide SM26 (12.7 mg, 0.0227 mmol) and 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (SM27, 190 µL, 0.932 mmol) in THF (2.3 mL) at -78 °C was added \( n \)-BuLi (2.5 M in hexanes, 273 µL, 0.682 mmol) dropwise over 1 min. After stirring for 10 min at -78 °C, the reaction mixture was quenched with saturated aq. NH₄Cl (1.5 mL), warmed to 23 °C, diluted with H₂O (1 mL) and extracted with EtOAc (5 x 1 mL). The combined organic layers were washed with brine (1 mL), dried by passage over a plug of silica gel (EtOAc eluent), and evaporated under reduced pressure to afford the crude product. Further purification by preparative thin layer chromatography (4:1 hexanes:EtOAc eluent) afforded boronic ester SM28 (10.1 mg, 73% yield) as a colorless oil. \( R_f \) 0.38 (5:1 hexanes:EtOAc).

A vial charged with bromopyrazine 27 (12.4 mg, 0.0231 mmol), boronic ester SM28 (10.0 mg, 0.0165 mmol), and tetrakis(triphenylphosphine)palladium(0) (2.9 mg, 0.00248 mmol),
was evacuated and purged with \( \text{N}_2 \). Deoxygenated benzene (330 \( \mu \text{L} \)), deoxygenated methanol (65 \( \mu \text{L} \)), and deoxygenated 2 M aq. \( \text{Na}_2\text{CO}_3 \) (28 \( \mu \text{L} \)) were then added. The reaction vessel was sealed, heated to 50 °C for 82 h, cooled to 23 °C, then quenched by the addition of \( \text{Na}_2\text{SO}_4 \) (100 mg). Following filtration over a pad of silica gel (1:1 hexanes:EtOAc eluent) to afford pyrazine 50 (4.4 mg, 28% yield) as a yellow foam. \( R_f \) 0.44 (2:1 hexanes:EtOAc); \( \text{IR} \) (film): 2951, 1661, 1556, 1376, 1345, 1335, 1291, 1279, 1274 (2C), 1267, 1208, 1198, 1180, 1172, 79.0, 77.8, 72.1, 67.1, 53.9, 51.4, 45.4, 41.7, 39.8, 34.6, 26.2 (3C), 21.3, 18.6, 18.5, 17.3, -1.0 (3C), -4.4, -5.0; \( \text{IR} \) (film): 2951, 1661, 1556, 1376, 1250, 1178, 1141, 1090, 1011 cm\(^{-1}\); HRMS-FAB (m/z): [M]\(^+\) calc’d for \( \text{C}_{45}\text{H}_{59}\text{BrN}_{4}\text{O}_7\text{Si}_2 \), 934.2826; found, 934.2872; \([\alpha]_{20}^\text{D} \) -91.02° (c 0.57, \( \text{C}_6\text{H}_6 \)).

**Ketone 54.** To methyl ether 49 (120 mg, 0.25 mmol) in THF (12.5 mL) was added TBAF (1.0 M in THF, 750 \( \mu \text{L} \), 0.75 mmol). The reaction mixture was stirred for 4 h, quenched with saturated aq. \( \text{NH}_4\text{Cl} \) (10 mL), diluted with \( \text{H}_2\text{O} \) (5 mL), and extracted with EtOAc (3 x 25 mL). The combined organic extracts were washed with brine (15 mL), dried over \( \text{MgSO}_4 \), and evaporated under reduced pressure. The residue was purified by flash chromatography (1:1 hexanes:EtOAc eluent) to furnish allylic alcohol 53 (86 mg, 95% yield) as a pale yellow oil. \( R_f \)
Allylic alcohol 53 (44.0 mg, 0.121 mmol) and freshly prepared Rh(nbd)(dppe)BF₄ (8.6 mg, 0.0121 mmol)⁷ were combined under a glovebox atmosphere. The reaction vessel was carefully sealed, and removed from the glovebox. CH₂Cl₂ (12.0 mL) was added, and a balloon of H₂ (1 atm) was applied without purging. After 3 h of stirring, the reaction mixture was filtered over a plug of silica gel (CH₂Cl₂, then 2:1 hexanes:EtOAc eluent) to afford ketone 54 (43.0 mg, 98% yield) as a colorless oil.

Alternate Procedure. To allylic alcohol 53 (10.6 mg, 0.029 mmol) in CH₂Cl₂ (1.5 mL) at 23 °C was added Dess-Martin periodinane (50.0 mg, 0.118 mmol). The mixture was stirred for 10 min, quenched with a solution of saturated aq. NaHCO₃ and saturated aq. Na₂S₂O₅ (1:1, 2 mL), stirred for 10 min, and extracted with EtOAc (4 x 1 mL). The combined organic layers were washed with brine (1 mL), dried by passage over a plug of silica gel (EtOAc eluent), and evaporated under reduced pressure to afford the crude oxidized product, which was used in the subsequent reaction. Rf 0.31 (2:1, hexanes:EtOAc).

A flask containing the crude oxidized product and 10% Pd/C (10 mg, 0.0094 mmol) in EtOH (2.0 mL) at 23 °C was evacuated and back-filled with H₂ (3x). After 20 min, the reaction mixture was filtered over a Celite plug (EtOAc eluent) and the solvent was evaporated in vacuo. The residue was dissolved in EtOAc (2 mL), and then filtered over a short plug of silica gel (EtOAc eluent). After evaporation of solvent under reduced pressure, the crude material was further purified by preparative thin layer chromatography (2:1 hexanes:EtOAc) to afford ketone 54 (9.9 mg, 93% yield, 2 steps) as a colorless oil. Rf 0.30 (2:1 hexanes:EtOAc); ¹H NMR (300 MHz, C₆D₆): δ 6.53 (d, J = 2.5 Hz, 1H), 5.66 (d, J = 2.5 Hz, 1H), 5.50 (d, J = 10.5 Hz, 1H), 5.36 (d, J = 10.2 Hz, 1H), 3.57-3.38 (m, 2H), 3.34 (s, 3H), 2.98 (dd, J = 14.3, 2.5 Hz, 1H), 2.70-2.64...
(m, 1H), 2.57-2.47 (m, 1H), 2.43 (d, J = 14.3 Hz, 1H), 2.11-1.99 (m, 1H), 1.69 (dd, J = 12.2, 2.6 Hz, 1H), 0.95 (d, J = 6.6 Hz, 3H), 0.84 (t, J = 8.0 Hz, 2H), -0.03 (s, 9H); $^{13}$C NMR (125 MHz, C$_6$D$_6$): δ 205.7, 187.9, 137.5, 131.1, 126.6, 109.7, 82.9, 76.8, 66.4, 52.7, 52.3, 48.1, 41.0, 37.7, 18.3, 13.0, -1.0 (3C); IR (film): 2952, 2931, 1716, 1660, 1421, 1123, 1097, 1076 cm$^{-1}$; HRMS-FAB (m/z): [M + H]$^+$ - H$_2$ calc’d for C$_{19}$H$_{28}$NO$_4$Si, 362.1788; found, 362.1778; [α]$^2$D$_{27}$ +163.23° (c 1.0, C$_6$H$_6$).

**Boronic Ester 55.** A flask wrapped in aluminum foil at 23 °C was charged with ketone 54 (25 mg, 0.0689 mmol), THF (5 mL) and freshly recrystallized NBS (37.5 mg, 0.211 mmol). The reaction vessel was placed in a 40 °C oil bath, stirred for 15 min, then cooled to 0 °C. The reaction was quenched with saturated aq. Na$_2$S$_2$O$_3$ (10 mL), diluted with H$_2$O (5 mL) and extracted with Et$_2$O (3 x 20 mL). The combined organic layers were washed with brine (15 mL), dried over MgSO$_4$, and evaporated under reduced pressure to afford the crude product. Further purification by flash column chromatography (3:1 hexanes:EtOAc eluent) afforded bromide SM29 (29.9 mg, 98% yield) as a colorless oil. R$_f$ 0.45 (2:1 hexanes:EtOAc).

To bromide SM29 (27 mg, 0.061 mmol) and 2-isoproxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (SM27, 510 µL, 2.5 mmol) in THF (7 mL) at -78 °C was added n-BuLi (2.5 M in hexanes, 730 µL, 0.183 mmol) dropwise over 3 min. After stirring for an additional 10 min at -78 °C, the reaction mixture was quenched with saturated aq. NH$_4$Cl (7 mL), warmed to 23 °C, diluted with H$_2$O (10 mL) and extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine (15 mL), dried over MgSO$_4$ and evaporated under reduced pressure to afford the crude product. Further purification by flash column chromatography (3:1 hexanes:EtOAc eluent) afforded boronic ester 55 (22 mg, 74% yield) as a colorless oil. R$_f$ 0.42 (2:1 hexanes:EtOAc); $^1$H NMR (300 MHz, C$_6$D$_6$): δ 7.37 (s, 1H), 5.46 (d, J = 10.2 Hz, 1H), 5.33 (d, J = 10.2 Hz, 1H), 3.77-3.72 (m, 1H), 3.49-3.38 (m, 2H), 3.31 (s, 3H), 3.03 (dd, J = 14.0, 2.8 Hz, 1H), 2.61-2.53 (m, 1H), 2.47 (d, J = 13.8 Hz, 1H), 2.36-2.25 (m, 1H), 1.78 (dd, J = 12.4, 3.0
Hz, 1H), 1.24 (d, 1H), 1.12 (s, 12H), 0.84-0.77 (m, 2H), -0.05 (s, 9H); $^{13}$C NMR (125 MHz, C$_6$D$_6$, 23/25 C): δ 206.4, 188.3, 144.6, 140.0, 83.6 (2C), 83.1, 77.1, 66.5, 52.9, 52.3, 49.0, 41.4, 37.1, 25.3 (2C), 25.2 (2C), 18.3, 13.0, -0.9 (3C); IR (film) 2977, 2951, 1718, 1664, 1543, 1399, 1322, 1263, 1145, 1092, 1074; HRMS-FAB (m/z): [M + H]$^+$ calc’d for C$_{25}$H$_{41}$NO$_6$SiB, 490.2796; found, 490.2800; $[\alpha]^{29}_D +50.77^\circ$ (c 0.4, C$_6$H$_6$).

**Pyrazine (–)-29.** A vial charged with bromopyrazine 27 (29.6 mg, 0.055 mmol), boronic ester 55 (18 mg, 0.0368 mmol), and tetrakis(triphenylphosphine)palladium(0) (6.4 mg, 0.0055 mmol), was evacuated and purged with N$_2$. Deoxygenated benzene (735 µL), deoxygenated methanol (150 µL), and deoxygenated 2 M aq. Na$_2$CO$_3$ (61 µL) were then added. The reaction vessel was sealed, heated to 50 °C for 72 h, cooled to 23 °C, then quenched by the addition of Na$_2$SO$_4$ (200 mg). Following filtration over a pad of silica gel (3:1 EtOAc:hexanes eluent) and evaporation to dryness under reduced pressure, the residue was purified by flash column chromatography (2:1 → 1:1 hexanes:EtOAc eluent) to afford pyrazine (–)-29 (26.8 mg, 89% yield) as a yellow foam. $R_s$, $^1$H NMR, $^{13}$C NMR, HRMS, and IR characterization data for (–)-29 have been previously reported.$^2$ $[\alpha]^{27}_D -72.92^\circ$ (c 1.0, CHCl$_3$).

(–)-Dragmacidin F (7). Pyrazine (–)-29 was converted to (–)-dragmacidin F (7) by previously described methods.$^2$ $^1$H NMR, $^{13}$C NMR, HRMS, and IR characterization data for
(+)-7 have been previously reported.\(^2\) \([\alpha]^{29}_D -148.33^\circ\) \((c 0.20, \text{MeOH})\). For comparison, natural 
(−)-dragmacidin F (7): \([\alpha]^{25}_D -159^\circ\) \((c 0.40, \text{MeOH})\).\(^8\)
References:

4 The synthesis of SM5 is described in Table 1, Entry 2.
6 The synthesis of SM12 is described in Table 1, Entry 8.