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_4Si (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_4Si (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.

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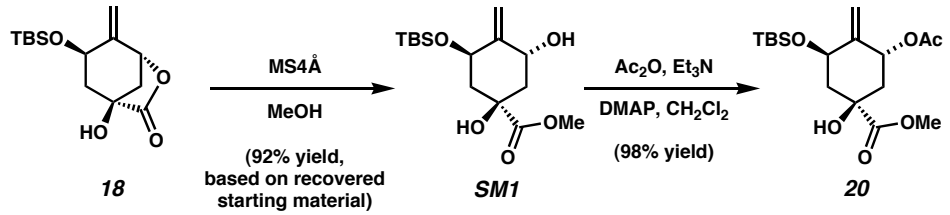
(+)-Dragmacidin F:

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]

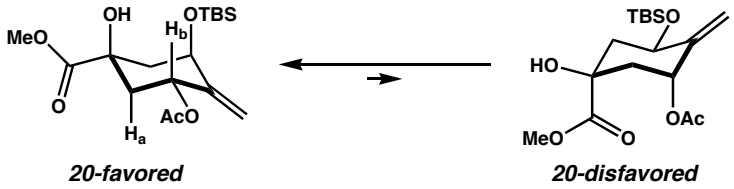


Methyl Ester 20. To lactone **18**[2] (420 mg, 1.477 mmol) and activated oven-dried 4Å molecular sieves (100 mg) was added MeOH (15 mL). The reaction mixture was stirred at 23 °C for 5.5 h, then filtered over a short plug of Celite (EtOAc eluent). After evaporation of the reaction mixture under reduced 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.

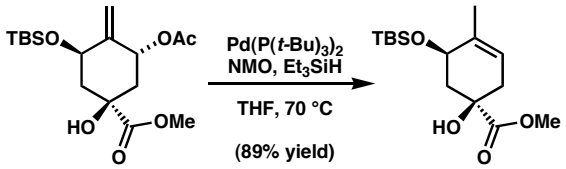
To siloxy diol **SM1** (80.0 mg, 0.253 mmol) in CH_2Cl_2 (1.5 mL) was added Et_3N (71 μL, 0.506 mmol), DMAP (3 mg, 0.0253 mmol), followed by Ac_2O (31 μL, 0.329 mmol). The reaction mixture was stirred at 23 °C for 10 min, quenched with saturated aq. $NaHCO_3$ (5 mL), and extracted with CH_2Cl_2 (3 x 15 mL). The combined organic layers were filtered over a plug of silica gel (CH_2Cl_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, $CDCl_3$): δ 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); ^{13}C NMR (75 MHz, $CDCl_3$): δ 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 $C_{17}H_{31}O_6Si$, 359.1890; found, 359.1900; $[\alpha]^{26}_D$ -26.61° (*c* 1.0, C_6H_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.

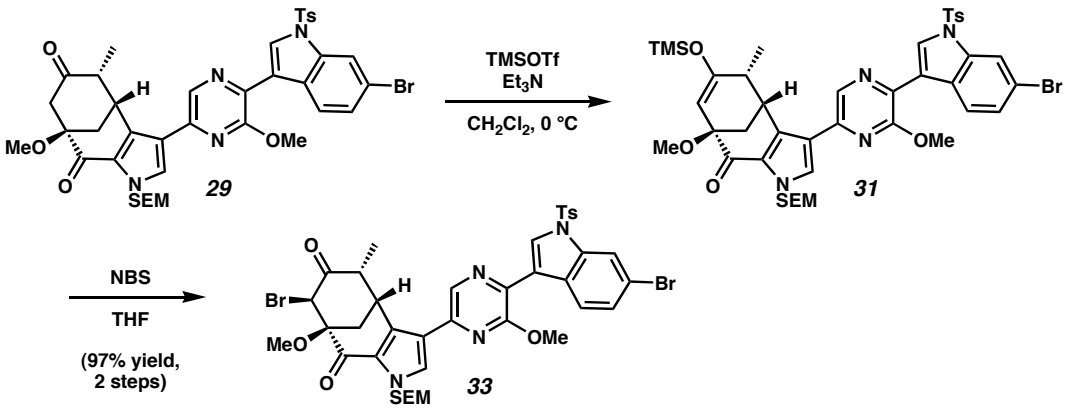


20-favored *20-disfavored*



20 *21*

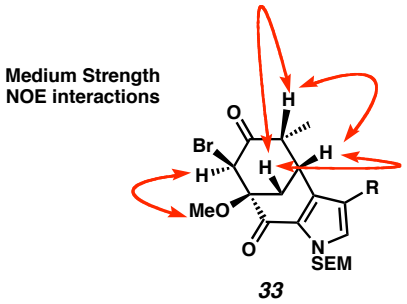
Siloxycyclohexene 21. Methyl ester **20** (94 mg, 0.262 mmol), $Pd(P(t\text{-}Bu_3)_2)$ (40.2 mg, 0.0786 mmol), anhydrous *N*-methylmorpholine *N*-oxide (307 mg, 2.52 mmol), THF (5.2 mL), and freshly distilled Et_3SiH (1.67 mL, 10.5 mmol) were combined under a glovebox atmosphere. The reaction mixture 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_4Cl (15 mL) was added and the mixture was extracted with Et_2O (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); ^1H NMR (300 MHz, $CDCl_3$): δ 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, $CDCl_3$): δ 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 $C_{15}H_{19}O_4Si$, 301.1835; found, 301.1835; $[\alpha]^{24}_D$ +77.62° (*c* 0.47, $CHCl_3$).



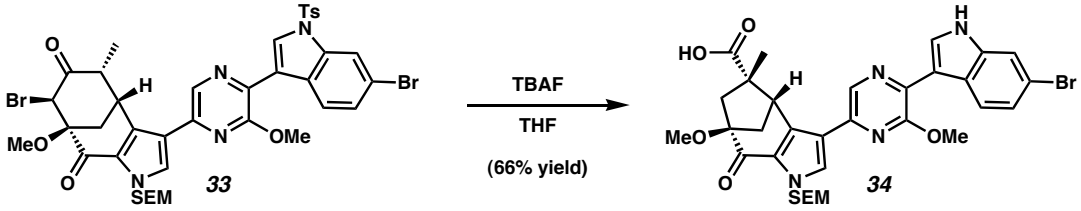
α-Bromoketone 33. To ketone **29**[2] (5.0 mg, 0.0061 mmol) and triethylamine (160 μL, 1.15 mmol) in CH_2Cl_2 (1 mL) at 0 °C was added TMSOTf (70 μL, 0.350 mmol) dropwise over 1 min. The reaction mixture was stirred for 30 min, quenched with saturated aq. $NaHCO_3$ (2 mL), and extracted with EtOAc (5 x 1 mL). The combined organic layers were washed with brine (1.5 mL) and dried over Na_2SO_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_f 0.68 (1:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, C_6D_6): δ 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_6D_6, 38/39 C): δ 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 $C_{39}H_{43}Br_2N_4O_7SSi$, 899.0968; found, 899.0952; $[\alpha]^{27}_D$ +10.23° (*c* 0.66, C_6H_6).

The relative stereochemistry of α-bromoketone **33** was determined by NOE experiments. Medium strength NOE interactions were observed as indicated below.[3]

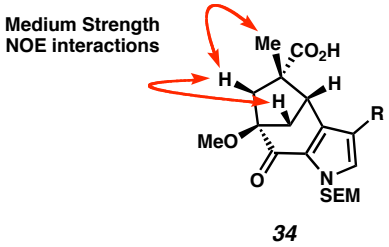


33



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 CH_2Cl_2:MeOH eluent), and evaporated under reduced pressure to afford the crude product. Purification by preparative thin layer chromatography (5:1 CH_2Cl_2:MeOH eluent) afforded Favorskii product **34** (1.5 mg, 66% yield) as a yellow oil. R_f 0.53 (5:1 CH_2Cl_2:MeOH); ^{1}H NMR (600 MHz, CD_3OD): 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); ^{13}C NMR (125 MHz, CD_3OD): 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 $C_{32}H_{38}BrN_4O_6Si$, 683.1724; found, 683.1721; $[\alpha]^{23}_D$ -26.34° (*c* 0.2, CH_3OH).

The relative stereochemistry of Favorskii product **34** was determined by NOE experiments. Medium strength NOE interactions were observed as indicated below.[3]



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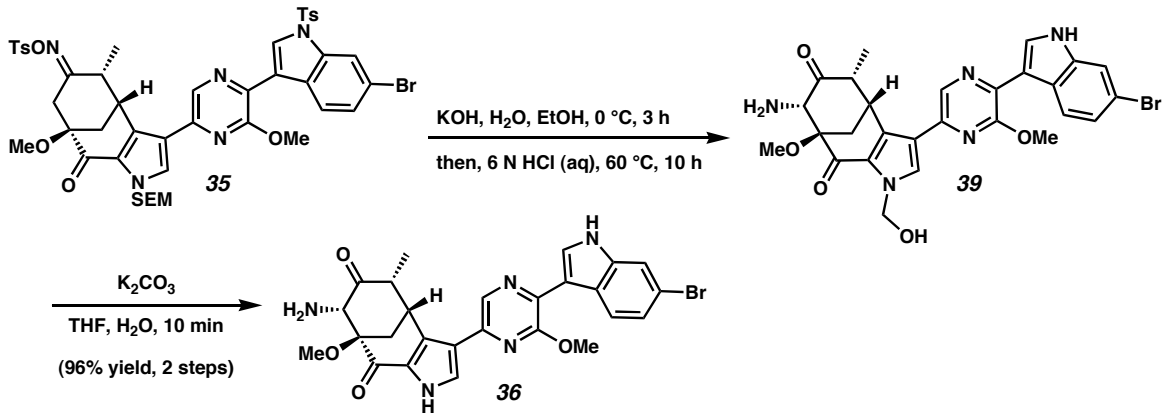
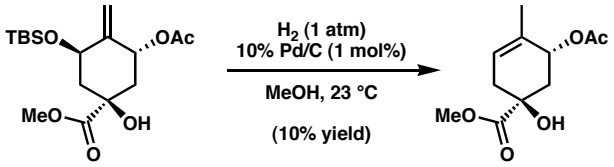


Hemiaminal 39. Details for the Neber rearrangement/deprotection sequence have already been described.[2] Although hemiaminal **39** is typically used in crude form, it has been observed by ^{1}H NMR. ^{1}H NMR (600 MHz, CD_3OD): δ 8.61 (d, J = 8.2 Hz, 1H), 8.52 (s, 1H), 8.24 (s, 1H), 7.94 (s, 1H), 7.60 (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:

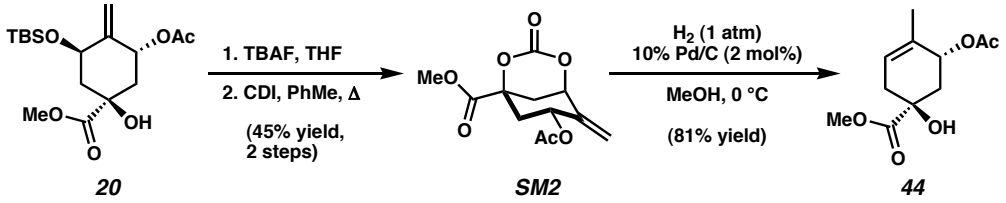


20 ***44***

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 H_2 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 H_2 (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:*

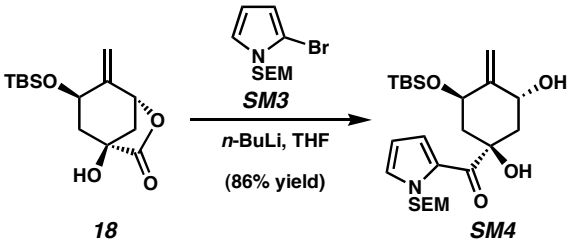


20 ***SM2*** ***44***

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. NH_4Cl (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 H_2O (1 mL) and brine (1 mL), and dried over $MgSO_4$. The solvent was evaporated *in vacuo*, and the residue was dissolved in toluene (4 mL). 1,1'-carbonyldiimidazole (82.1 mg, 0.51 mmol) was added, and the mixture was heated at reflux for 2 h. After cooling to 23 °C, the crude reaction mixture was directly purified

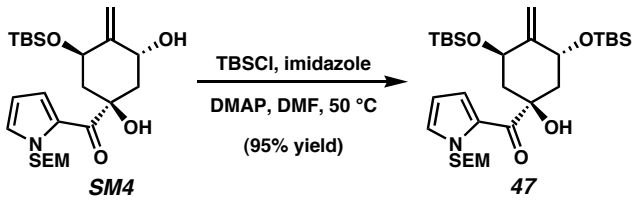
by flash column chromatography (3:2 hexanes:EtOAc eluent) to afford pure acetoxycarbonate **SM2** (16.9 mg, 45% yield, 2 steps). R_f 0.15 (1:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.70-5.62 (m, 1H), 5.25 (app. d, *J* = 2.5 Hz, 1H), 5.19 (app. d, *J* = 2.5 Hz, 1H), 5.16 (dd, *J* = 4.1, 1.9 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); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.3, 168.3, 146.6, 140.2, 113.7, 81.6, 79.5, 66.4, 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 $C_{12}H_{15}O_7$, 271.0818; found, 271.0810; $[\alpha]^{25}_D$ -154.53° (*c* 1.0, C_6H_6).

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 H_2 (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. R_f 0.46 (2:1 EtOAc:hexanes); ^{1}H NMR (300 MHz, $CDCl_3$): 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);^{13}C NMR (75 MHz, $CDCl_3$): 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 $C_{11}H_{17}O_5$, 229.1076; found 229.1066; $[\alpha]^{25}_D$ -3.31° (*c* 0.6, $CHCl_3$).



***Anti*-diol SM4**. To 2-bromo SEM pyrrole[2] (**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 **18**[2] (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. NH_4Cl (50 mL), then warmed to 23 °C. The volatiles were removed under reduced pressure. The residue was partitioned between Et_2O (125 mL) and H_2O (100 mL), and the layers were separated. The

aqueous layer was further extracted with Et_2O (2 x 125 mL). The combined organic layers were washed with brine (75 mL), dried over $MgSO_4$, 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. R_f 0.48 (2:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, C_6D_6): 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); ^{13}C NMR (75 MHz, C_6D_6): 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 $C_{24}H_{44}NO_5Si_2$, 482.2758; found, 482.2751; $[\alpha]^{28}_D$ -21.18° (*c* 1.0, C_6H_6).



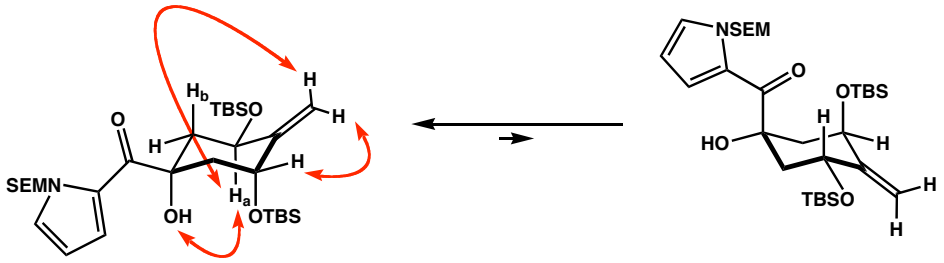
SM4 *47*

Bis(silylether) 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). Et_2O (40 mL) was added, and the layers were partitioned. The aqueous phase was further extracted with Et_2O (2 x 30 mL). The combined organic extracts were washed with brine (15 mL), dried over $MgSO_4$, and evaporated under reduced pressure. The crude product was purified by flash chromatography (9:1 hexanes:EtOAc eluent) to provide bis(silylether) **47** (296.0 mg, 95% yield) as a colorless oil that solidified under reduced pressure. R_f 0.61 (4:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, C_6D_6): 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),

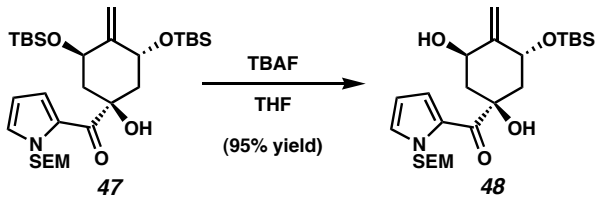
0.99 (s, 9H), 0.88 (s, 9H), 0.82 (t, J = 7.8 Hz, 2H), 0.17 (s, 3H), 0.14 (s, 3H), 0.00 (s, 3H), -0.04 (s, 3H), -0.07 (s, 9H); ^{13}C NMR (75 MHz, C_6D_6, 29/30 C): δ 192.6, 151.6, 130.4, 124.5, 109.3, 108.6, 83.2, 78.5, 76.8, 67.4, 66.3, 49.3, 42.1, 26.4 (3C), 26.1 (3C), 18.9, 18.4, 18.3, -0.9 (3C), -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 $C_{30}H_{58}NO_5Si_3$, 596.3623; found, 596.3594; $[\alpha]^{27}_D$ -7.16° (*c* 1.0, C_6H_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:[3]



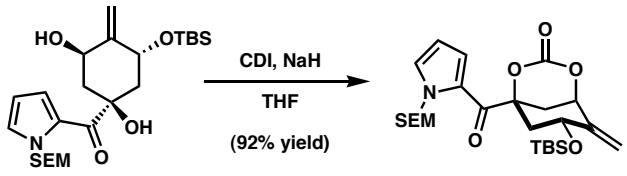
47-favored ***47-disfavored***



47 ***48***

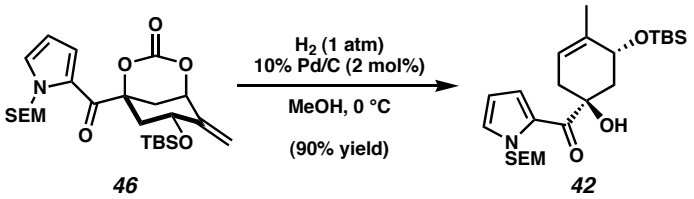
***Syn*-diol 48**. To bis(silylether) **47** (113.9 mg, 0.19 mmol) in THF (10.0 mL) was added TBAF (1.0 M in THF, 195 μL, 0.20 mmol) in a dropwise fashion over 1 min. The reaction mixture was stirred for 2 min, quenched with saturated aq. NH_4Cl (15 mL), then poured into EtOAc (40 mL). The layers were partitioned and the aqueous layer was further extracted with EtOAc (2 x 40 mL). The combined organic extracts were successively washed with H_2O (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_6D_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); ^{13}C NMR (75 MHz, C_6D_6): 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 $C_{24}H_{44}NO_5Si_2$, 482.2758; found, 482.2780; $[\alpha]^{27}_D$ -27.06° (*c* 1.0, C_6H_6).

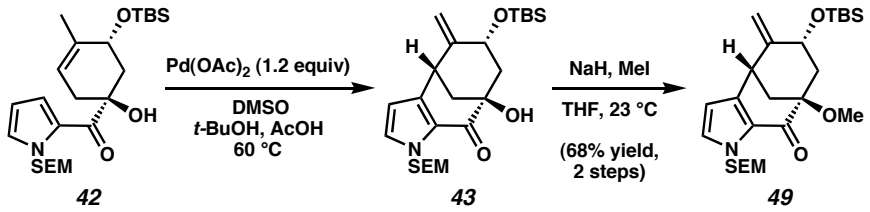


48 ***46***

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. NH_4Cl (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 H_2O (10 mL) and brine (10 mL), dried over $MgSO_4$, 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. R_f 0.29 (4:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, C_6D_6): 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); ^{13}C NMR (75 MHz, C_6D_6): 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 $C_{25}H_{42}NO_6Si_2$, 508.2551; found, 508.2560; $[\alpha]^{27}_D$ -54.78° (*c* 1.0, C_6H_6).



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 H_2 (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. R_f 0.53 (4:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, C_6D_6): 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, C_6D_6): 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 $C_{24}H_{44}NO_4Si_2$, 466.2809; found, 466.2804; $[\alpha]^{28}_D$ +26.19° (*c* 1.0, C_6H_6).

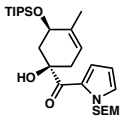
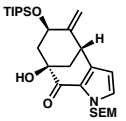
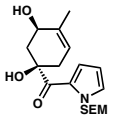
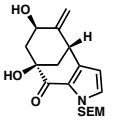
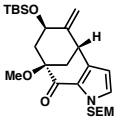
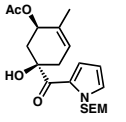
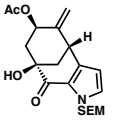
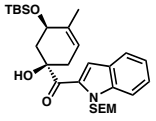
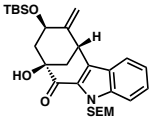


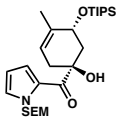
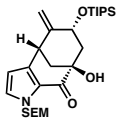
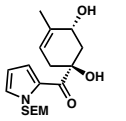
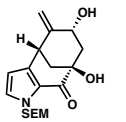
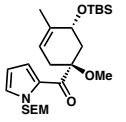
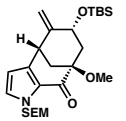
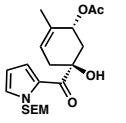
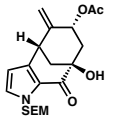
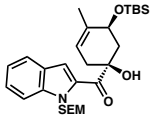
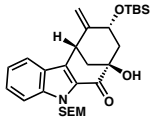
[3.3.1] Bicycle 43. To pyrrolocyclohexene **42** (40.0 mg, 0.0859 mmol) was added $Pd(OAc)_2$ (23.0 mg, 0.103 mmol), DMSO (14.6 μL, 0.206 mmol), *t*-BuOH (6.9 mL), and AcOH (1.7 mL). The mixture was heated to 60 °C for 8 h, cooled to 23 °C, and filtered over a plug of silica gel (2:1 hexanes:EtOAc eluent). 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. R_f 0.64 (3:1

hexanes:EtOAc); ^{1}H NMR (300 MHz, C_6D_6): δ 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_6D_6): δ 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 $C_{24}H_{42}NO_4Si_2$, 464.2652; found, 464.2661; $[\alpha]^{27}_D$ +319.22° (*c* 1.0, C_6H_6).

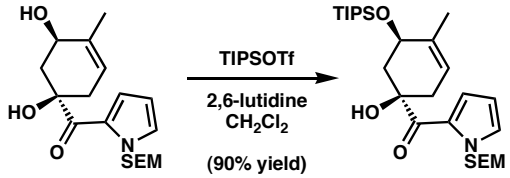
Methyl Ether 49. The crude mixture of **42** and **43** obtained from the previous step was dissolved in THF (1.5 mL) at 23 °C and NaH (60% dispersion in mineral oil, 17 mg, 0.429 mmol) was added. After stirring for 1 min at 23 °C, MeI was added (53 μL, 0.859 mmol). The resulting mixture was stirred for 1.5 h, quenched with saturated aq. NH_4Cl (1.5 mL), and extracted with Et_2O (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_6D_6): δ 6.62 (d, *J* = 2.6 Hz, 1H), 6.43 (d, *J* = 10.3 Hz, 1H), 5.86 (d, *J* = 2.6 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_6D_6): δ 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 $C_{25}H_{44}NO_4Si_2$, 478.2809; found, 478.2815; $[\alpha]^{27}_D$ +312.37° (*c* 1.0, C_6H_6).

Table 1. Pd(II)-mediated oxidative carbocyclization[a]

entry	substrate	product	temp (°C)	time	yield[b]
1			60	13.5 h	51% (63%)
2			80	*complex mixture*	
3			80	*no reaction*	
4			80	1.8 h	53% (66%)
5			80[d]	6.5 h	37% (55%)
6			80	2.5 h	49%

entry	substrate	product	temp (°C)	time	yield[b]
7			80	2.3 h	51% (70%)
8			80	*complex mixture*[c]	
9			80	*no reaction*	
10			60[e]	11 h	10%[f]
11			80	2.3 h	34%

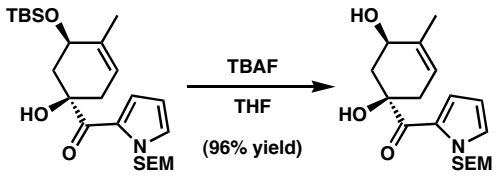
[a] Standard Conditions: 1 equiv $Pd(OAc)_2$, 2 equiv DMSO, *t*-BuOH:AcOH (4:1, 0.01 M). [b] Isolated Yield. Number in parenthesis represents the yield based on recovered starting material. [c] Trace product may have formed in this reaction, but could not be isolated. [d] 20 mol% $Pd(OAc)_2$, 40 mol% DMSO, *t*-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.



SM5 ***SM6***

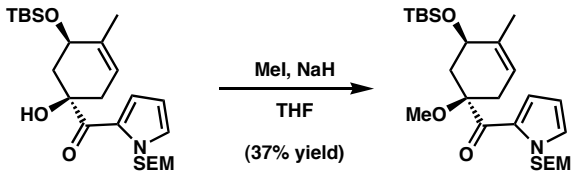
TIPS Ether SM6 (Table 1, Entry 1). To allylic alcohol **SM5**[4] (50.7 mg, 0.14 mmol) in CH_2Cl_2 (5 mL) at 23 °C was added 2,6-lutidine (34 μL, 0.29 mmol), followed by TIPSOTf (44 μL, 0.16 mmol). After stirring 5 min, saturated aq. NH_4Cl (5 mL) was added to quench the reaction. The phases were partitioned, and the aqueous phase was extracted with CH_2Cl_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_6D_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); ^{13}C NMR (75 MHz, C_6D_6): δ 194.1, 133.8, 130.3, 129.0, 124.7, 122.8, 109.2, 78.9, 78.5, 70.5, 66.3, 39.6, 39.4, 22.0, 18.7 (3C), 18.7 (3C), 18.4, 13.3 (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 $C_{27}H_{50}NO_4Si_2$, 508.3278; found, 508.3273; $[\alpha]^{27}_D$ +29.49° (*c* 1.0, C_6H_6).



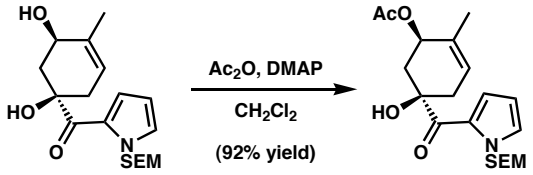
15 ***SM5***

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_4Cl (5 mL). The reaction was poured into Et_2O (5 mL) and H_2O (5 mL), and the phases were partitioned. The aqueous phase was extracted with Et_2O (4 x 3 mL), and the combined organic extracts were dried by passage over a plug of SiO_2 gel (Et_2O eluent). The solvent was evaporated *in vacuo*, and the residue was passed over another plug of SiO_2 gel (Et_2O 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_6D_6): δ 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); ^{13}C NMR (75 MHz, C_6D_6): δ 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 $C_{18}H_{30}NO_4Si$, 352.1944; found, 352.1941; $[\alpha]^{27}_D$ +31.11° (*c* 1.0, C_6H_6).



15 ***SM7***

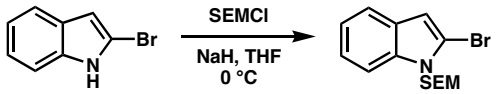
Methyl Ether SM7 (Table 1, Entry 3). To allylic silyl ether **15**[2] (55.0 mg, 0.12 mmol) in THF (2 mL) at 23 °C was added NaH (60% dispersion in mineral oil, 95.5 mg, 2.39 mmol). After stirring for 5 min, MeI (200 μL, 3.21 mmol) was added. After stirring for 30 min, saturated aq. NH_4Cl (2 mL) was 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_6D_6): δ 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_6D_6, 24/25 C): δ 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 $C_{25}H_{46}NO_4Si_2$, 480.2965; found, 480.2958; $[\alpha]^{27}_D$ +43.57° (*c* 1.0, C_6H_6).



SM5 ***SM8***

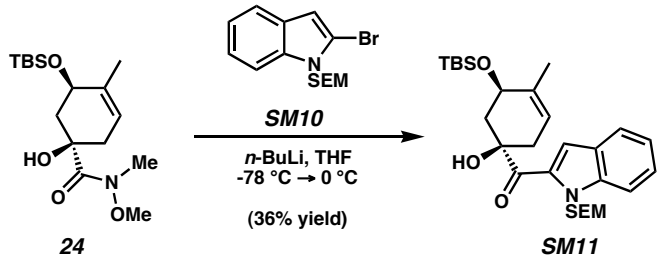
Allylic Acetate SM8 (Table 1, Entries 4 and 5). To allylic alcohol **SM5** (131.0 mg, 0.37 mmol) in CH_2Cl_2 (7.5 mL) at 23 °C was added DMAP (68.1 mg, 0.56 mmol) followed by Ac_2O (53 μL, 0.56 mmol). After stirring for 50 min, the reaction was quenched by the addition of saturated aq. $NaHCO_3$ (10 mL). Et_2O (30 mL) was added, the phases were partitioned, and the aqueous phase was extracted with Et_2O (3 x 30 mL). The combined organics were washed successively with H_2O (10 mL) and brine (10 mL), dried over $MgSO_4$, and evaporated *in vacuo*.

Flash chromatography of the crude product (7:3 hexanes:Et_2O 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, C_6D_6): 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, C_6D_6): 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 $C_{20}H_{32}NO_5Si$, 394.2050; found, 394.2030; $[\alpha]^{27}_D$ +22.38° (*c* 1.0, C_6H_6).

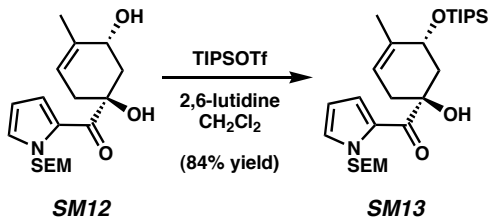


SM9 **(89% yield)** ***SM10***

2-Bromo SEM Indole (SM10). To a solution of 2-bromoindole[5] (**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 H_2 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. NH_4Cl (20 mL). Et_2O (50 mL) was added, the phases were partitioned, and the aqueous phase was extracted with Et_2O (2 x 75 mL). The combined organic extracts were washed with brine (15 mL) and dried over $MgSO_4$. After evaporation of the solvent under reduced pressure, the residue was purified by flash chromatography (9:1 hexanes:Et_2O 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).

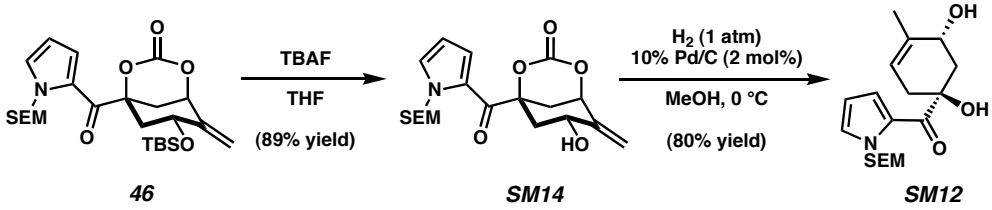


Indole SM11 (Table 1, Entry 6). To 2-bromo SEM indole (**SM10**, 482.6 mg, 1.48 mmol) in THF (7 mL) cooled to -78 °C was added *n*-BuLi (2.5 M in hexanes, 590 μL, 1.48 mmol). The solution was stirred for 10 min, and was then treated dropwise over 1 min with a solution of Weinreb amide **24**[2] (161.5 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. NH_4Cl (10 mL), and was allowed to thaw slowly to 23 °C. Et_2O (50 mL) was added, the phases were partitioned, and the aqueous phase was extracted with Et_2O (2 x 75 mL). The combined organic extracts were washed successively with H_2O (15 mL) and brine (15 mL), and dried over $MgSO_4$. 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. R_f 0.48 (4:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, C_6D_6): 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); ^{13}C NMR (75 MHz, C_6D_6): 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-EI (*m/z*): $[M]^+$ calc'd for $C_{28}H_{45}NO_4Si_2$, 515.2887; found, 515.2893; $[\alpha]^{27}_D$ -12.17° (*c* 1.0, C_6H_6).



TIPS Ether SM13 (Table 1, Entry 7). To allylic alcohol **SM12**[6] (48.5 mg, 0.14 mmol) in CH_2Cl_2 (5 mL) at 23 °C was added 2,6-lutidine (32 μL, 0.27 mmol), followed by TIPSOTf

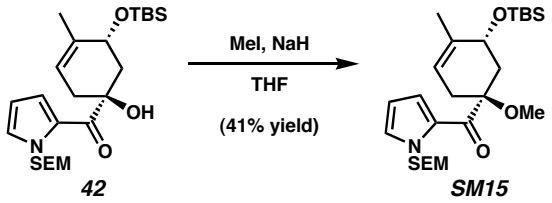
(42 μL, 0.16 mmol). After stirring 5 min, saturated aq. NH_4Cl (5 mL) was added to quench the reaction. The phases were partitioned, and the aqueous phase was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic extracts were washed with brine (5 mL), and dried over $MgSO_4$. Following evaporation of the solvent *in vacuo*, the crude product was purified by flash chromatography (19:1 hexanes:EtOAc → 9:1 hexanes:EtOAc eluent) to provide TIPS ether **SM13** (58.5 mg, 84%) as a colorless oil. R_f 0.48 (4:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, C_6D_6): 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); ^{13}C NMR (75 MHz, C_6D_6): 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 $C_{27}H_{50}NO_4Si_2$, 508.3278; found, 508.3264; $[\alpha]^{27}_D$ +14.46° (*c* 1.0, C_6H_6).



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. NH_4Cl (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 H_2O (1 mL) and brine (1 mL), and dried over $MgSO_4$. 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. R_f 0.29 (1:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, C_6D_6): 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_6D_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, 1644, 1414, 1360, 1250, 1179, 1082 (br) cm^{-1}; HRMS-FAB (*m/z*): $[M + H]^+$ calc'd for $C_{19}H_{28}NO_6Si$, 394.1686; found, 394.1690; $[\alpha]^{26}_D$ -77.69° (*c* 1.0, C_6H_6).

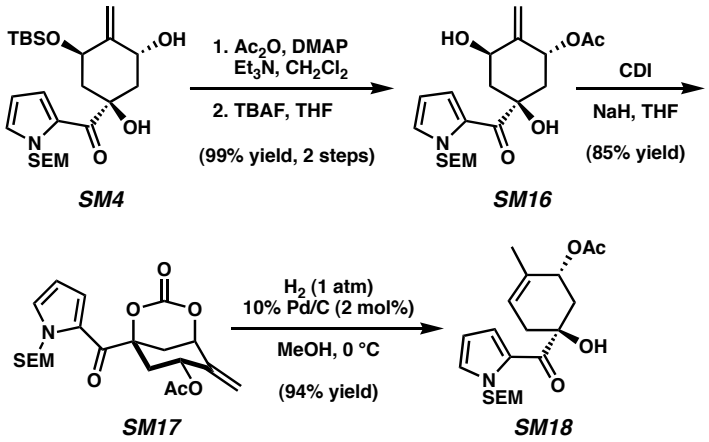
A mixture of hydroxycarbonate **SM14** (34.2 mg, 0.09 mmol) and 10% Pd/C (1.5 mg, 0.001 mmol) in MeOH (1.4 mL) was cooled to 0 °C. The reaction vessel was then evacuated and back-filled with H_2 (3x). After 15 min at 0 °C, the reaction mixture was filtered over a Celite plug (MeOH eluent) and the solvent 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_6D_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_6D_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 $C_{18}H_{30}NO_4Si$, 352.1944; found, 352.1931; $[\alpha]^{25}_D$ +21.44° (*c* 1.0, C_6H_6).



42 *SM15*

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_4Cl (2 mL) was added slowly to quench the reaction mixture, and Et_2O (1 mL) was added. The phases were partitioned, and the aqueous phase was extracted with Et_2O (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_6D_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_6D_6): δ 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-EI (*m/z*): $[M]^+$ calc'd for $C_{25}H_{45}NO_4Si_2$, 479.2887; found, 479.2887; $[\alpha]^{27}_D$ +7.38° (*c* 0.6, C_6H_6).



Allylic Acetate SM18 (Table 1, Entry 10). To *anti*-diol **SM4** (1.77 g, 3.68 mmol) in CH_2Cl_2 (25 mL) at 23 °C was added Et_3N (1.28 mL, 9.19 mmol) and DMAP (45 mg, 0.368 mmol), followed by Ac_2O (451 μL, 4.78 mmol). The reaction mixture was stirred for 5 min, and then additional Ac_2O (125 μL, 1.32 mmol) was added. Stirring was continued for 5 min, and then another portion of Ac_2O (100 μL, 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_2O (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).

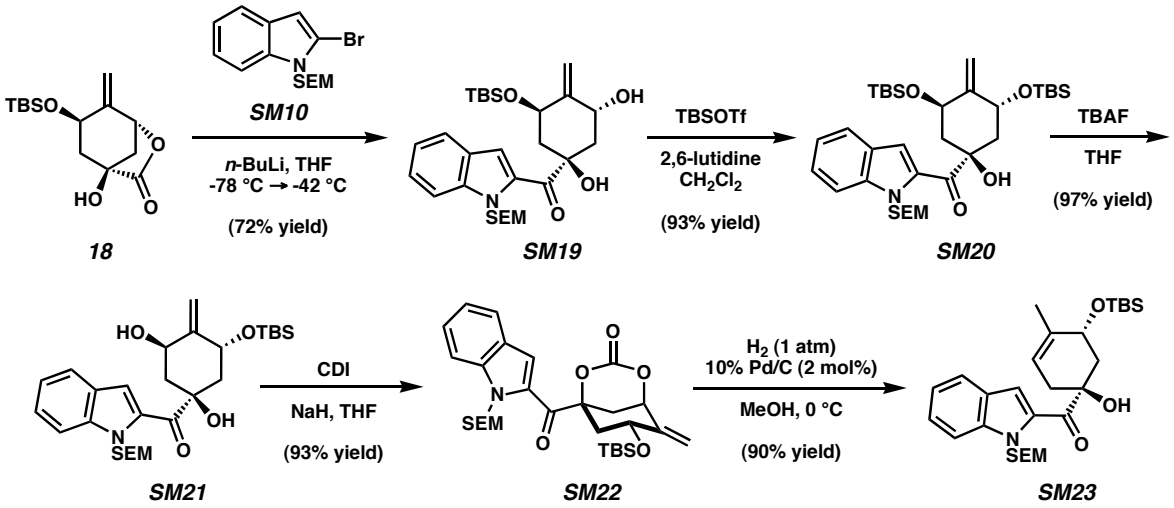
To the crude product in THF (25 mL) was added TBAF (1.0 M in THF, 3.85 mL, 3.85 mmol). After 2 min of stirring, the reaction was quenched by the addition of saturated aq. NH_4Cl (30 mL) and the volatile solvents were removed under reduced pressure. The residue was diluted with H_2O (50 mL) and extracted 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 **SM16** (1.49 g, 99% yield, 2 steps) as a colorless oil. R_f 0.23 (2:1 hexanes:EtOAc).

To acetoxycyclohexene **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_4Cl (10 mL) and the volatile solvents were removed under reduced pressure. The residue was diluted with H_2O (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 **SM17** (200.1 mg, 85% yield) as a colorless oil. R_f 0.25 (2:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, C_6D_6): δ 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), 4.73 (d, *J* = 1.9 Hz, 1H), 4.54 (dd, *J* = 3.9, 1.9 Hz, 1H), 3.40 (t, *J* = 7.8 Hz, 2H), 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_6D_6): δ 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, 1106, 1086, 1048 cm^{-1}; HRMS-FAB (*m/z*): $[M + H]^+$ calc'd for $C_{21}H_{30}NO_7Si$, 436.1792; found, 436.1807; $[\alpha]^{27}_D$ -112.57° (*c* 1.0, C_6H_6).

A mixture of acetoxycarbonate **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 **SM18** (625 mg, 94% yield). R_f 0.56 (2:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, C_6D_6): δ 7.05 (dd, *J* = 4.1, 1.7 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_6D_6): δ 193.3, 170.4, 133.8, 130.9, 126.9, 123.1, 122.7, 109.5, 78.7, 78.3,

71.9, 66.6, 39.6, 38.2, 21.0, 19.4, 18.3, -1.0 (3C); IR (film) 3438 (br), 2951, 1735, 1717, 1636, 1413, 1370, 1241, 1082, 1024 cm^{-1}; HRMS-FAB (*m/z*): $[M + H]^+$ calc'd for $C_{20}H_{32}NO_5Si$, 394.2050; found, 394.2031; $[\alpha]^{27}_D$ -9.91° (*c* 1.0, C_6H_6).



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**[2] (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_4Cl (3 mL), and was allowed to thaw slowly to 23 °C. Et_2O (50 mL) and H_2O (10 mL) were added, the phases were partitioned, and the aqueous phase was extracted with Et_2O (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. R_f 0.40 (4:1 hexanes:EtOAc).

To *anti*-diol **SM19** (762.8 mg, 1.43 mmol) in CH_2Cl_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_4Cl (50 mL). The phases were partitioned, and the aqueous phase was extracted with CH_2Cl_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 eluent) to afford bis(silylether) **SM20** (859.6 mg, 93% yield) as a white solid. R_f 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. NH_4Cl (50 mL). Et_2O (50 mL) was added, the phases were partitioned, and the aqueous phase was extracted with Et_2O (75 mL x 2). The combined organics were washed with brine (25 mL), dried over $MgSO_4$, 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. R_f 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 H_2 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. NH_4Cl (50 mL). Et_2O (50 mL) was added, the phases were partitioned, and the aqueous phase was extracted with Et_2O (75 mL x 2). The combined organics were washed with brine (25 mL), dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified by flash chromatography (9:1 hexanes:EtOAc eluent) to furnish indolocarbonate **SM22** (668.9 mg, 93% yield) as a white foam. R_f 0.37 (4:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, C_6D_6): 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); ^{13}C NMR (75 MHz, C_6D_6): 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-EI (*m/z*): $[M]^+$ calc'd for $C_{29}H_{43}NO_6Si_2$, 557.2629; found, 557.2632; $[\alpha]^{23}_D$ -34.29 (*c* 1.0, C_6H_6).

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 H_2 (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. R_f 0.48 (4:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, C_6D_6): 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, 2H), 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); ^{13}C NMR (75 MHz, C_6D_6): δ 197.1, 141.0, 138.7, 130.7, 127.4, 127.0, 124.0, 122.3, 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-EI (*m/z*): $[M]^+$ calc'd for $C_{28}H_{45}NO_4Si_2$, 515.2887; found, 515.2875; $[\alpha]^{27}_D$ -27.67° (*c* 1.0, C_6H_6).

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). R_f 0.29 (4:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, C_6D_6): 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); ^{13}C NMR (75 MHz, C_6D_6): 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) 18.6 (3C), 18.2, 13.1 (3C), -0.9 (3C); IR (film) 3478 (br), 2946, 2867, 1650, 1100, 1080 cm^{-1}; HRMS-EI (*m/z*): $[M]^+$ calc'd for $C_{27}H_{47}NO_4Si_2$, 505.3044; found, 505.3041; $[\alpha]^{27}_D$ -207.44° (*c* 0.6, C_6H_6).

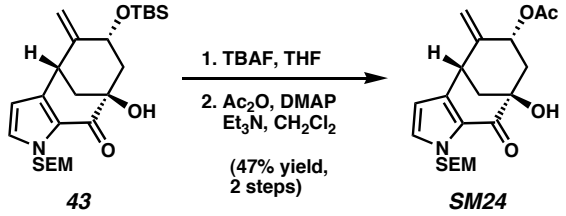
Entries 4 and 5. Purified by preparative thin-layer chromatography (4:1 CH_2Cl_2:Et_2O eluent). *Note:* Entry 5 was performed in a round-bottom flask fitted with reflux condenser and an O_2

balloon. R_f 0.56 (4:1 CH_2Cl_2:Et_2O); ^{1}H NMR (300 MHz, C_6D_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_6D_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 $C_{20}H_{30}NO_5Si$, 392.1893; found, 392.1886; $[\alpha]^{27}_D$ -389.72° (*c* 0.6, C_6H_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_6D_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_6D_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 $C_{28}H_{43}NO_4Si_2$, 513.2731; found, 513.2719; $[\alpha]^{27}_D$ -281.78° (*c* 0.3, C_6H_6).

Entry 7. Purified by preparative thin-layer chromatography (9:1 CH_2Cl_2:Et_2O eluent). R_f 0.48 (4:1 hexanes:EtOAc); R_f 0.65 (4:1 Et_2O:CH_2Cl_2); ^{1}H NMR (300 MHz, C_6D_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_6D_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 $C_{27}H_{47}NO_4Si_2$, 505.3044; found, 505.3040; $[\alpha]^{23}_D$ +253.79° (*c* 0.7, C_6H_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:



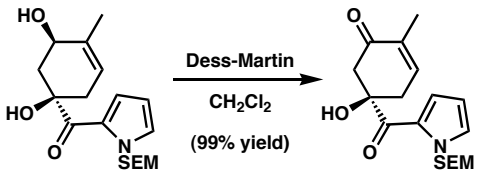
43 ***SM24***

[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_4Cl (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_2Cl_2 (1.1 mL) was added DMAP (2.2 mg, 0.02 mmol) and Et_3N (31 μL, 0.22 mmol), followed by Ac_2O (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_6D_6): δ 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_6D_6): δ 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 $C_{20}H_{29}NO_5Si$, 391.1815; found, 391.1800; $[\alpha]^{24}_D$ +396.32° (*c* 0.5, C_6H_6).

Entry 11. Purified by preparative thin-layer chromatography (4:1 hexanes:EtOAc eluent). R_f 0.55 (4:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, C_6D_6): 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); ^{13}C NMR (125 MHz, C_6D_6, 27/28 C): δ 195.3, 147.4, 141.4, 134.7, 129.8, 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^{-1}; HRMS-EI (*m/z*): $[M]^+$ calc'd for $C_{28}H_{43}NO_4Si_2$, 513.2731; found, 513.2730; $[\alpha]^{24}_D$ +216.18° (*c* 0.25, C_6H_6).

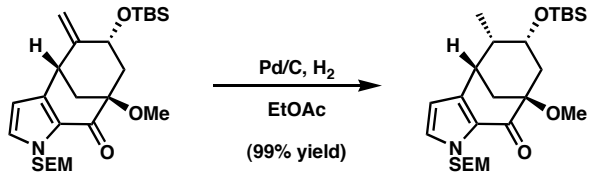
*For entries 2 and 8, small quantities of enone **SM25** was observed. An authentic sample was prepared as follows:*



SM5 ***SM25***

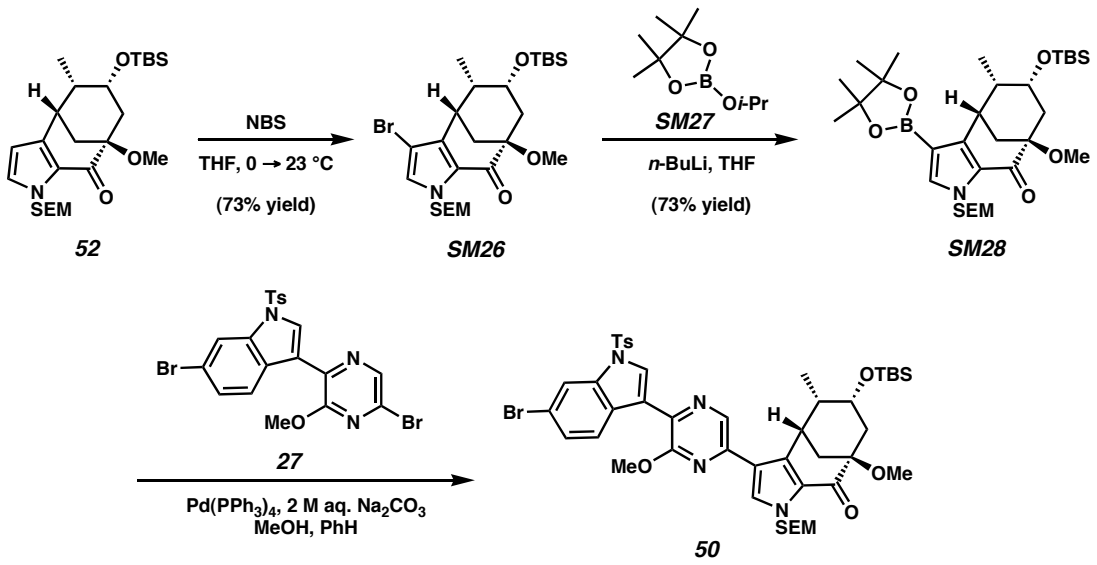
Enone SM25. To allylic alcohol **SM5** (11.4 mg, 0.032 mmol) in CH_2Cl_2 (1 mL) was added Dess-Martin Periodinane (31.4 mg, 0.074 mmol). After stirring for 20 min, a solution of saturated $Na_2S_2O_3$: saturated $NaHCO_3$ (1:1, 1 mL) was added to quench the reaction. The phases were partitioned, and the aqueous phase was extracted with Et_2O (1 x 4 mL). The combined organics were dried by passage over a plug of SiO_2, 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_f 0.40 (2:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, C_6D_6): 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); ^{13}C NMR (75 MHz, C_6D_6): 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), 2953, 1677, 1639, 1412, 1249, 1085

cm^{-1}; HRMS-FAB (*m/z*): $[M + H]^+$ calc'd for $C_{18}H_{28}NO_4Si$, 350.1788; found, 350.1784; $[\alpha]^{27}_D$ -21.94° (*c* 1.0, C_6H_6).



49 ***52***

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 H_2 (1 atm). The reaction mixture was stirred under H_2 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). R_f 0.28 (5:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, C_6D_6): 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); ^{13}C NMR (75 MHz, C_6D_6, 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 $C_{25}H_{46}NO_4Si_2$, 480.2965; found, 480.2955; $[\alpha]^{25}_D$ +220.84° (*c* 1.0, C_6H_6).

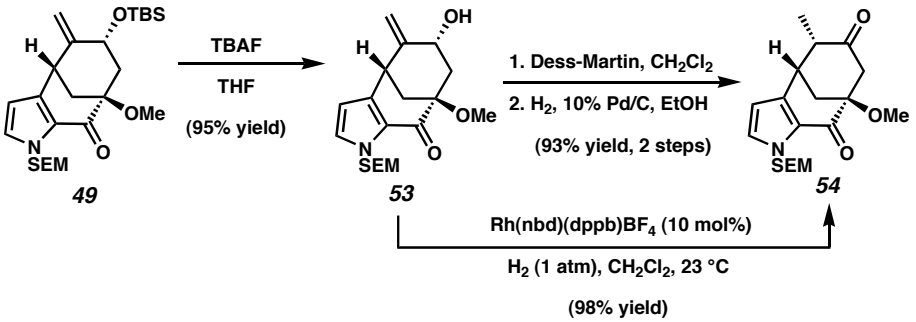


Pyrazine 50. To silyl ether **52** (10.0 mg, 0.0208 mmol) in THF (2 mL) at 0 °C was added freshly recrystallized NBS (4.8 mg, 0.0271 mmol) in THF (200 μL). After 10 min at 0 °C, the reaction mixture was warmed to 23 °C, stirred for 40 min, then cooled to 0 °C. The reaction was quenched with saturated aq. $Na_2S_2O_3$ (1.5 mL), diluted with H_2O (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. NH_4Cl (1.5 mL), warmed to 23 °C, diluted with H_2O (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 N_2. Deoxygenated benzene (330 μL), deoxygenated methanol (65 μL), and deoxygenated 2 M aq. Na_2CO_3 (28 μL) 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 Na_2SO_4 (100 mg). Following filtration over a pad of silica gel (1:1 hexanes:EtOAc eluent) and evaporation to dryness under reduced pressure, the residue was purified by preparative thin layer chromatography (2:1 hexanes:EtOAc eluent) to afford pyrazine **50** (4.4 mg, 28% yield) as a yellow foam. R_f 0.44 (2:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, C_6D_6): δ 9.02 (d, *J* = 8.8 Hz, 1H), 8.85 (s, 1H), 8.69 (d, *J* = 2.0 Hz, 1H), 8.35 (s, 1H), 7.71-7.68 (m, 2H), 7.48 (dd, *J* = 8.8 Hz, 2.0 Hz, 1H), 7.26 (s, 1H), 6.57 (d, *J* = 10.3 Hz, 1H), 6.40 (d, *J* = 8.3 Hz, 2H), 5.16 (d, *J* = 10.3 Hz, 1H), 3.92 (d, *J* = 3.4 Hz, 1H), 3.74 (s, 3H), 3.73-3.58 (comp. m, 3H), 3.45 (s, 3H), 2.91 (app. dt, *J* = 7.3, 3.6 Hz, 1H), 2.44 (app. t, *J* = 7.1 Hz, 1H), 1.86 (dd, *J* = 13.9, 4.2 Hz, 1H), 1.74 (dd, *J* = 11.7, 2.9 Hz, 1H), 1.64-1.55 (comp. m, 4H), 1.02-0.86 (m, 2H), 0.75 (s, 9H), 0.68 (d, *J* = 6.8 Hz, 3H), -0.05 (s, 9H), -0.09 (s, 3H), -0.23 (s, 3H); ^{13}C NMR (125 MHz, C_6D_6): δ 190.4, 156.7, 145.4, 145.0, 138.6, 136.7, 135.9, 135.8, 133.4, 131.0, 130.4 (2C), 129.5, 129.5, 129.1, 127.9, 127.4 (2C), 126.7, 120.8, 119.8, 118.0, 117.2, 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; IR (film): 2951, 1661, 1556, 1376, 1250, 1178, 1141, 1090, 1011 cm^{-1}; HRMS-FAB (*m/z*): $[M]^+$ calc'd for $C_{45}H_{59}BrN_4O_7SSi_2$, 934.2826; found, 934.2872; $[\alpha]^{20}_D$ -91.02° (*c* 0.57, C_6H_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 μL, 0.75 mmol). The reaction mixture was stirred for 4 h, quenched with saturated aq. NH_4Cl (10 mL), diluted with H_2O (5 mL), and extracted with EtOAc (3 x 25 mL). The combined organic extracts were washed with brine (15 mL), dried over $MgSO_4$, 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

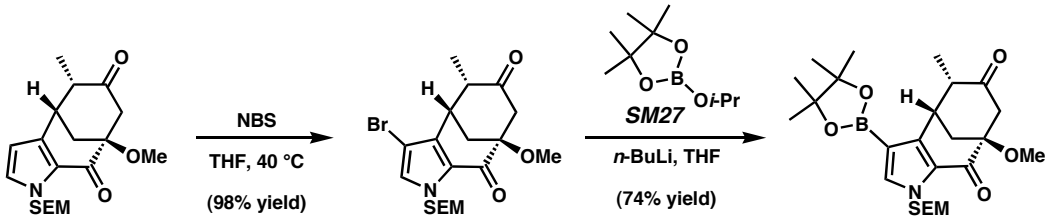
0.12 (2:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, C_6D_6): δ 6.60 (d, *J* = 2.8 Hz, 1H), 5.81 (d, *J* = 2.8 Hz, 1H), 5.64 (d, *J* = 10.2 Hz, 1H), 5.58 (d, *J* = 10.2 Hz, 1H), 4.80 (d, *J* = 1.7 Hz, 1H), 4.64 (d, *J* = 1.7 Hz, 1H), 4.15-4.09 (m, 1H), 3.68-3.59 (m, 2H), 3.42 (t, *J* = 3.2 Hz, 1H), 3.36 (s, 3H), 2.72 (app. dt, *J* = 7.4, 3.9 Hz, 1H), 2.58 (app. dt, *J* = 8.1, 4.9 Hz, 1H), 1.89 (dd, *J* = 14.2, 5.1 Hz, 1H), 1.65 (dd, *J* = 11.6, 3.0 Hz, 1H), 0.97-0.88 (m, 2H), 0.59 (d, *J* = 3.9 Hz, 1H), -0.03 (s, 9H); ^{13}C NMR (75 MHz, C_6D_6, 18/19 C): δ 189.4, 149.4, 140.6, 130.4, 113.8, 107.4, 78.9, 76.7, 72.0, 66.2, 51.6, 44.3, 41.1, 39.5, 18.4, -0.9 (3C); IR (film): 3460 (br), 2951, 1659, 1424, 1248, 1111, 1023 cm^{-1}; HRMS-FAB (*m/z*): $[M + H]^+$ calc'd for $C_{19}H_{30}NO_4Si$, 364.1944; found, 364.1942; $[\alpha]^{24}_D$ +330.71° (*c* 1.0, C_6H_6).

Allylic alcohol **53** (44.0 mg, 0.121 mmol) and freshly prepared Rh(nbd)(dppb)BF_4 (8.6 mg, 0.0121 mmol)[7] were combined under a glovebox atmosphere. The reaction vessel was carefully sealed, and removed from the glovebox. CH_2Cl_2 (12.0 mL) was added, and a balloon of H_2 (1 atm) was applied without purging. After 3 h of stirring, the reaction mixture was filtered over a plug of silica gel (CH_2Cl_2, 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 CH_2Cl_2 (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. $NaHCO_3$ and saturated aq. $Na_2S_2O_3$ (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. R_f 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 H_2 (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. R_f 0.30 (2:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, C_6D_6): 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_6D_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 $C_{19}H_{28}NO_4Si$, 362.1788; found, 362.1778; $[\alpha]^{27}_D$ +163.23° (*c* 1.0, C_6H_6).

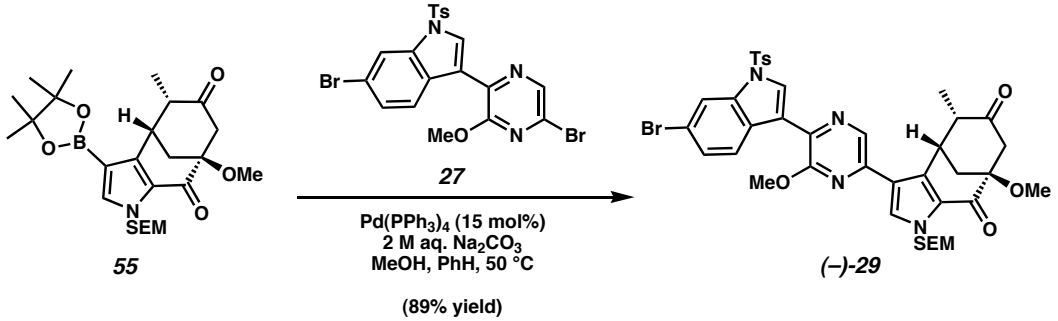


54 *SM29* *55*

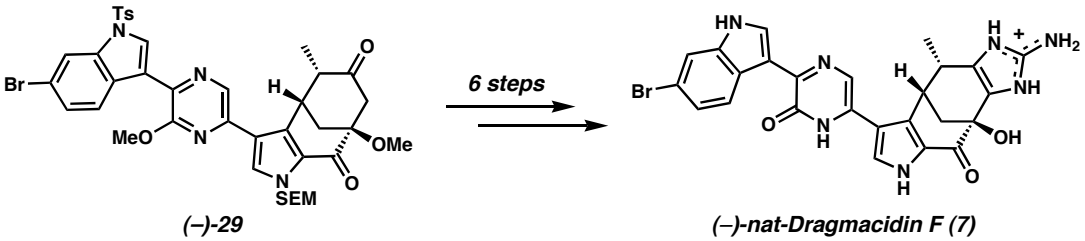
Boronic Ester 55. A flask wrapped in aluminum foil at 23 °C was charged with ketone **54** (25 mg, 0.0689 mmol), THF (5 mL) and freshly recrystallized NBS (37.5 mg, 0.211 mmol). The reaction vessel was placed in a 40 °C oil bath, stirred for 15 min, then cooled to 0 °C. The reaction was quenched with saturated aq. $Na_2S_2O_3$ (10 mL), diluted with H_2O (5 mL) and extracted with Et_2O (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-isopropoxy-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_4Cl (7 mL), warmed to 23 °C, diluted with H_2O (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_6D_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, J = 6.6 Hz, 3H), 1.12 (s, 12H), 0.84-0.77 (m, 2H), -0.05 (s, 9H); ^{13}C NMR (125 MHz, C_6D_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 $C_{25}H_{41}NO_6SiB$, 490.2796; found, 490.2800; $[\alpha]^{29}_D$ +50.77° (*c* 0.4, C_6H_6).

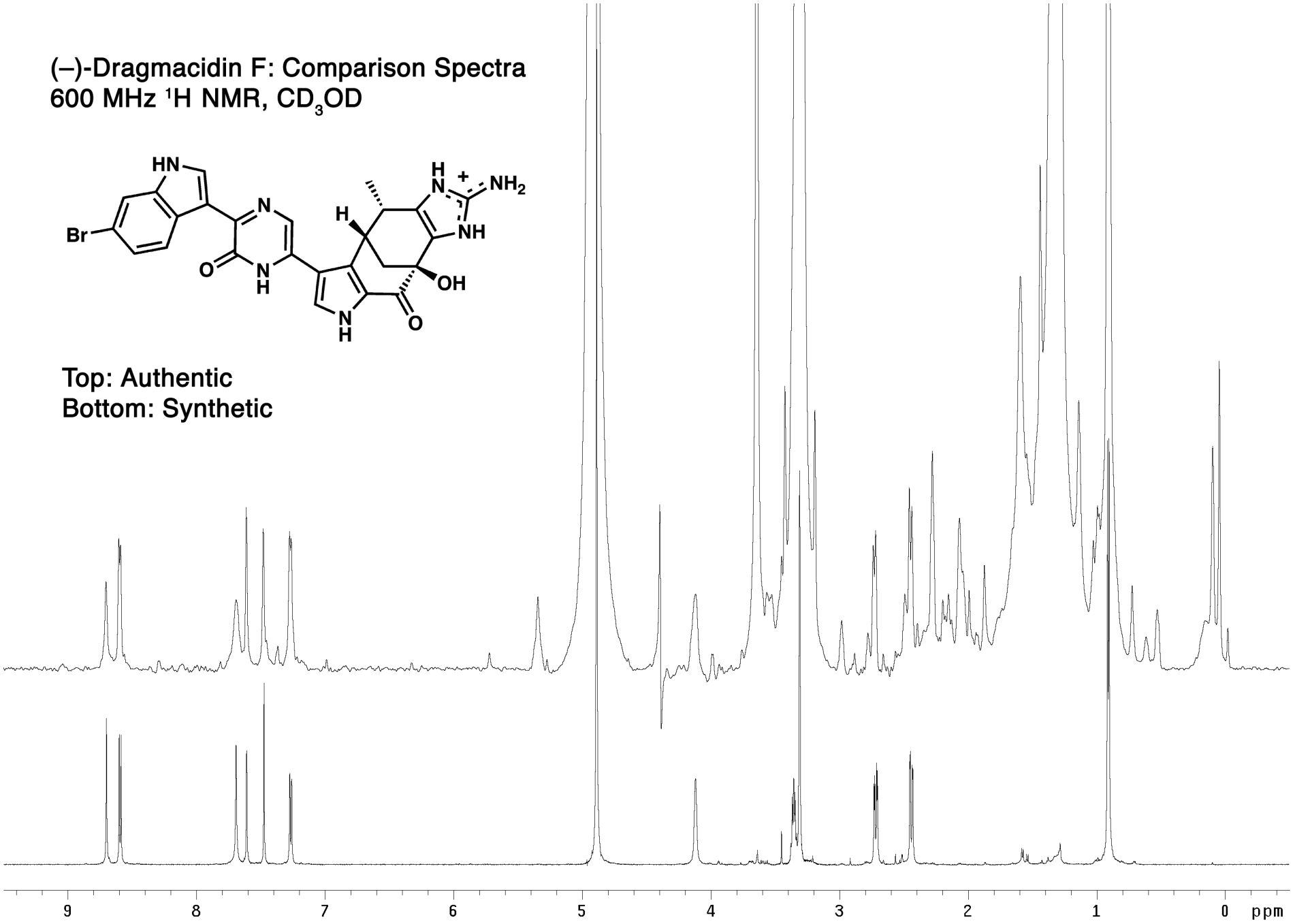


Pyrazine (–)-29. A vial charged with bromopyrazine **27** (29.6 mg, 0.055 mmol), boronic ester **55** (18 mg, 0.0368 mmol), and tetrakis(triphenylphosphine)palladium(0) (6.4 mg, 0.0055 mmol), was evacuated and purged with N_2. Deoxygenated benzene (735 μL), deoxygenated methanol (150 μL), and deoxygenated 2 M aq. Na_2CO_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_2SO_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_f, ^{1}H NMR, ^{13}C NMR, HRMS, and IR characterization data for (+)-**29** have been previously reported.[2] $[\alpha]^{27}_D$ -72.92° (*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° (*c* 0.20, MeOH). For comparison, natural (–)-dragmacidin F (**7**): $[\alpha]^{25}_{D}$ –159° (*c* 0.40, MeOH).[8]


(–)-Dragmacidin F: Comparison Spectra
600 MHz ¹H NMR, CD3OD
HN
Br
N
O
N
H
H
N
+
H
NH2
NH
OH
N
H
O
Top: Authentic
Bottom: Synthetic
9
8
7
6
5
4
3
2
1
0
ppm

References:

[1] Garg, N. K.; Sarpong, R.; Stoltz, B. M. *J. Am. Chem. Soc.* **2002**, *124*, 13179-13184.
[2] Garg, N. K.; Caspi, D. D.; Stoltz, B. M. *J. Am. Chem. Soc.* **2004**, *126*, 9552-9553.
[3] Claridge, T. D. W. in *High-Resolution NMR Techniques in Organic Chemistry*; Pergamon: Amsterdam, 1999; pp 320-326.
[4] The synthesis of **SM5** is described in Table 1, Entry 2.
[5] a) Liu, Y.; Gribble, G. W. *J. Nat. Prod.* **2002**, *65*, 748-749. b) Bergman, J.; Venemalm, L. *J. Org. Chem.* **1992**, *57*, 2495-2497.
[6] The synthesis of **SM12** is described in Table 1, Entry 8.
[7] Brown, J. M. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 190-203.
[8] Cutignano, A.; Bifulco, G.; Bruno, I.; Casapullo, A.; Gomez-Paloma, L.; Riccio, R. *Tetrahedron* **2000**, *56,* 3743-3748.