Supporting Materials

On the Chemoselectivity of the Ruthenium Catalyzed Hydrative Diyne Cyclization: Total Synthesis of (+)-Cylindricine C, D, and E.

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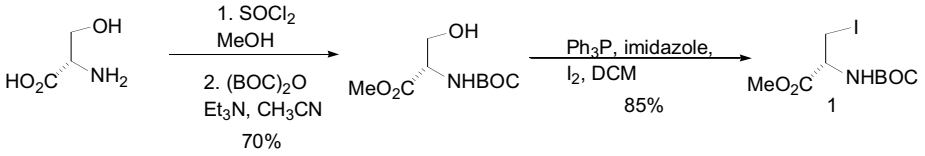
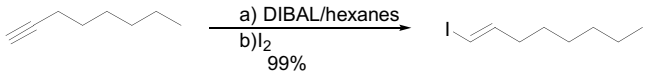


To a suspension of L-serine (25g, 0.24 mol) in MeOH(240 mL) at 0 ^{o}C was added thionyl chloride (17.3 mL, 0.24 mol) slowly, the suspension starts to dissolve during the addition, and when addition is complete, the mixture is brought to r.t. and stirred 1 hr. The stirring is then stopped, and the mixture was let stand overnight. The MeOH was then removed in vacuo, and the resulting solid was filtered, and washed with ether. The solid was then recrystallized from MeOH/ether to yield 25.4 g (70%) of a white crystallize solid (mp = 163-165 ^{o}C, lit = 163 ^{o}C; $[a]_D^{23}$ = +3.9 (c = 4.05, MeOH), lit = +3.4 (c = 4, MeOH)).

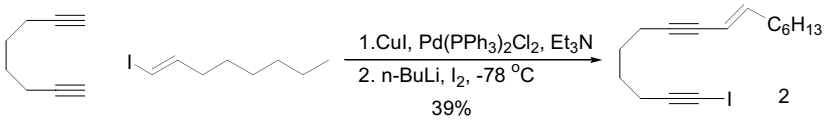
To a solution of Boc-anhydride (14 g, 64 mmol) in acetonitrile (200 mL) was added L-serine methyl ester hydrochloride salt (9.98 g, 64 mmol) and triethylamine (26.8 mL, 190 mmol) in one portion. The reaction was stirred for 6 hrs, DCM (1 L) was added, and extracted with 1 N HCl (700 mL), sat. sodium bicarbonate (100 mL). The organic layer was dried ($MgSO_4$), and the solvent was removed in vacuo, and placed under high vacuum overnight to remove the remainder of the solvent to yield Boc-serine-methylester (14 g, 99%) as a thick oil.
^{1}H NMR (400 MHz, $CDCl_3$): 5.43 (bs, 1H), 4.39 (bs, 1H), 3.95 (dq, J1 = 3.6 Hz, J2 = 11.2 Hz, 2 H), 3.78 (s, 3H), 1.45 (s, 9H).

To a solution of triphenylphosphine (20.9 g, 79.8 mmol) and imidazole (5.4 g, 79.8 mmol) in DCM (300 mL) at 0 ^{o}C was added I_2 (20.2 g, 79.8 mmol) in three portions. The solution was warmed to r.t. and stirred for 10 min, and re-cooled to 0 ^{o}C. 2 (14 g, 64 mmol) was then added in DCM (75 mL, washed with 10 mL) dropwise. The solution was stirred at this temperature for 1 hr and r.t. for 1.5 hr. The reaction mixture was then filtered through silica gel using 50/50 ether/pet. ether as eluent. The solvent was then removed in vacuo. Ether was then added to crash out the phosphine oxide, and the the mixture was filtered through celite with ether as the eluent. The solvent was again removed in vacuo, and the residue was purified on silica (10-15% ether/PE) to yield **1** (17.5 g, 84%) as an oil which solidified in the freezer.
^{1}H NMR (400 MHz, $CDCl_3$): 5.34 (broad d, 8 Hz, 1H), 4.52 (m, 1H), 3.80 (s, 3H), 3.57 (m, 2H), 1.46 (s, 9H).



To neat 1-octyne (6.7 mL, 45.4 mmol) was added DIBAL (1.0 M in hexanes, 45.4 mL) slowly so the temperature stays below 40 ^{o}C. The reaction is then heated to 50 ^{o}C for 3 hr, cooled to r.t. and the hexane is removed under vacuum. THF (20 mL) is added and the solution is cooled to –50 ^{o}C, and iodine (11.5 g, 45.4 mmol) in THF (20 mL) is slowly added. The mixture is then warmed to r.t., wherein it loses almost all of the brownish-red iodine color. The reaction is then quenched with addition of 20% sulfuric acid in a dropwise fashion. When the exotherm slows, the reaction is poured in a mixture of ice and 20 % sulfuric acid. The mixture is then extracted with pentane, and the organic extracts were extracted with sodium thiosulfate, and then sodium bicarbonate,

dried over $MgSO_4$, and the solvent was removed in vacuo. The crude product was then distilled (70 ^oC at ~1mmHg) to yield 1-iodooct-1-ene (10.8 g, 99%) as an almost clear liquid.

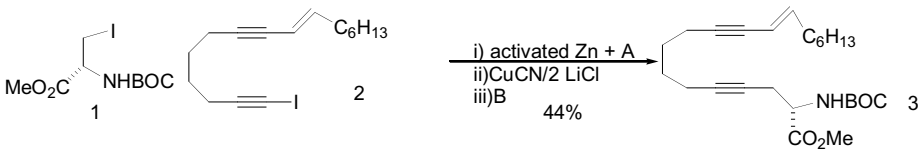


To a solution of the vinyl iodide (5g, 20.99 mmol) in triethylamine (200 mL) was added the diyne (5.6 mL, 41.99 mmol), $Pd(PPh_3)_2Cl_2$ (0.37 g, 0.55 mmol), and CuI (0.4 g, 2.1 mmol). The mixture was stirred until no vinyl iodide remained (2.5 hr), and then worked up with water and ether. The organic layer was dried over $MgSO_4$, and the solvent was removed in vacuo. The crude product was purified on silica gel (100% PE) to yield the en-diyne (1.89 g, 42%) as a mostly clear liquid.

Rf (1% Et_2O/PE): 0.4. **IR** (neat): 3311,3021, 2927, 2857, 2215, 2119, 1460, 1433, 1378, 1328, 954 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$): 6.04 (dt, J1 = 16.0 Hz, J2 = 7.0 Hz, 1H), 5.42 (dp, J1 = 16.0 Hz, J2 = 2.5 Hz, 1H), 2.30 (m, 2H), 2.21 (m, 2H), 2.07 (q, J = 7.0 Hz, 2H), 1.95 (t, J = 2.5 Hz, 1H), 1.63 (m, 4H), 1.33 (m, 2 H), 1.26 (m, 6H), 0.87 (t, J = 7.0 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): 143.9, 109.9, 88.2, 84.5, 79.8, 68.7, 33.2, 31.9, 29.0, 28.2, 28.0, 27.7, 22.9, 19.1, 18.2, 14.3.

To a solution of en-diyne (0.83 g, 3.84 mmol) in THF (10 mL) at –78 ^oC was added n-BuLi (1.56 M, 2.95 mL, 4.60 mmol). The solution was stirred for 30 min, and iodine (1.26 g, 4.98 mmol) in THF (5 mL) was added dropwise until iodine color remained. The reaction stirred for a further 30 min, quenched with sodium thiosulfate solution, and extracted with ether/PE. The organic layer was dried over $MgSO_4$, and the solvent was removed in vacuo. The crude product was purified on silica gel (100% PE) to yield the iodo-en-diyne **2** (1.20 g, 92%) as a mostly clear liquid.

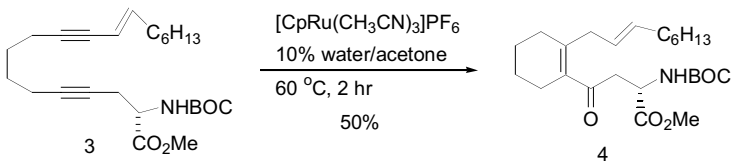
Rf (1% Et_2O/PE): 0.4. **IR** (neat): 2926, 2856, 2215, 1460, 1428, 1327, 954 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 6.05 (dt, J1 = 16.0 Hz, J2 = 7.2 Hz, 1H), 5.42 (dp, J1 = 16.0 Hz, J2 = 1.6 Hz, 1H), 2.39 (m, 2H), 2.30 (m, 2H), 2.07 (q, J = 7.0 Hz, 2H), 1.62 (m, 4H), 1.36 (m, 2 H), 1.27 (m, 6H), 0.87 (t, J = 7.0 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): 143.7, 109.6, 94.2, 87.8, 79.6, 32.9, 31.6, 28.8, 27.7, 27.5, 22.5, 20.4, 18.8, 14.1, -6.9. **HRMS** (EI, $[M]^+$) Cal'c for $C_{16}H_{23}I$: 342.0844. Found: 342.0844 (1.0), 144.0924 (28.3), 131.0851 (50.0), 91.0553 (100).



To solution of Zn dust (198 mg, 3.03 mmol) under argon in THF (1 mL) was added dibromoethane (13 µL, 0.15 mmol). The mixture was heated to reflux, cooled to r.t. 3 times, and then trimethylsilylchloride (12 µL, 0.09 mmol) was added, and the mixture was stirred for 30 min. **1** (0.5 g, 1.52 mmol) in THF (2 mL, wash with 1 mL) was added

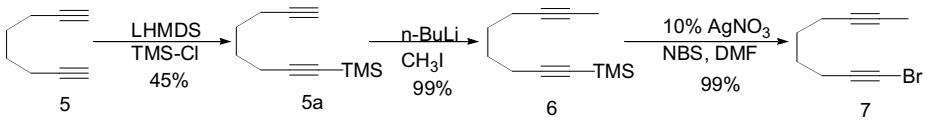
to this heterogeneous mixture. The reaction was heated to 40 °C for 3 hr (all **1** gone in NMR), and cooled to r.t., and the excess Zn was allowed to settle. In a separate flask, CuCN(0.14g, 1.52 mmol) and LiCl (0.13 g, 3.03 mmol) were dissolved in THF (1 mL) at r.t., and then cooled to –10 °C, and the solution of the alkyl zinc iodide was added slowly. The mixture was allowed to warm to 0 °C and stirring was continued for 10 min. After cooling to –78 °C, **2** (0.36 g, 1.06 mmol) in THF (2 mL, wash with 1 mL) was added dropwise. The reaction was stirred at this temperature for 20 hr, quenched with ammonium chloride solution, and extracted with ether. The organic layer was dried over $MgSO_4$, and the solvent was removed in vacuo. The crude product was purified on silica gel (20% ether/PE) to yield **3** (0.194 g, 44%) as a thick oil.

Rf (25% Et_2O/PE): 0.4. **IR** (neat): 3200, 2927, 2858, 1745, 1720, 1501, 1439, 1366, 1252, 1215, 1166, 1060, 1021, 954 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$): 6.06 (dt, J1 = 16.0 Hz, J2 = 7.0 Hz, 1H), 5.46 (dt, J1 = 16.0 Hz, J2 = 1.5 Hz, 1H), 5.31 (bd, J = 8.5 Hz, 1H), 4.45 (m, J = 4.5 Hz, 1H), 3.79 (s, 3H), 2.75 (dm, J = 15 Hz, 1H), 2.66 (dm, J = 17 Hz, 1H), 2.32 (m, 2H), 2.18 (m, 2H), 2.10 (q, J = 7.0 Hz, 2H), 1.29 (m, 2H), 1.48 (s, 9H), 1.37 (m, 2H), 1.29 (m, 6H), 0.89 (t, J = 7.0 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): 171.5, 155.1, 143.6, 109.6, 88.2, 83.4, 80.3, 79.7, 74.2, 52.7, 52.5, 33.2, 31.9, 29.0, 28.6, 28.1, 28.0, 23.4, 22.8, 19.1, 18.5, 14.3. **LRMS** (EI, $[M]^+$) Cal'c for $C_{25}H_{39}NO_4$: 417.6. Found: 417.6. $[\alpha]_D^{23}$ = +36.9 (c = 1.08, CH_2Cl_2).



To a test tube containing diyne **3** (50 mg, 0.119 mmol), 1.2 mL acetone, and 0.12 mL of H_2O was added $[CpRu(CH_3CN)_3]PF_6$ **11** (5.2 mg, 0.0119 mmol) under argon. The resulting yellow-orange solution was then sealed and stirred in an oil bath maintained at 60 °C for 14 hours (diyne still remained) and filtered through a pad of silica gel with Et_2O as the eluent. The solvent was then removed in vacuo to yield a yellow oil which was further purified by silica gel chromatography (20% ether/PE) to yield the cyclized product (25 mg, 50%).

Rf (20% Et_2O/PE): 0.25. **IR** (neat): 3441, 3372, 2927, 2856, 1749, 1715, 1605, 1495, 1437, 1392, 1366, 1344, 1288, 1248, 1210, 1168, 1065, 1025, 970, 907, 861, 826, 779, 760, 724 cm^{-1}. **^{1}H NMR** (500 MHz, C_6D_6): 5.81 (bd, J = 9 Hz, 1H), 5.55 (m, 1H), 5.45 (m, 1H), 4.74 (m, J = 4 Hz, 1H), 3.29 (s, 3H), 3.12 (s, 1H), 3.05 (dd, J1 = 18 Hz, J2 = 4 Hz, 1H), 2.90 (d, J = 6.5 Hz, 2 H), 2.80 (dd, J1 = 18 Hz, J2 = 4 Hz, 1H)1.97 (q, J = 7 Hz, 2H), 1.86 (m, 2H), 1.80 (m, 2H), 1.41 (s, 9H), 1.31 (m, 4 H), 1.21 (m, 6 H), 0.87 (t, J = 7 Hz, 3H). **^{13}C NMR** (125 MHz, C_6D_6): 202.8, 172.1, 155.7, 144.7, 132.4, 132.3, 128.3, 79.4, 51.9, 50.1, 43.7, 38.9, 32.9, 32.0, 30.4, 29.9, 29.2, 28.3, 26.5, 23.0, 22.3, 22.214.3. **Anal** Cal'c for $C_{25}H_{41}NO_5$: C, 68.93; H, 9.49; N, 3.22; Found: C, 69.13; H, 9.37. $[\alpha]_D^{23}$ = +40.11 (c = 0.55, CH_2Cl_2).



To a solution of 1,7-octadiyne (13.27 mL, 100 mmol) in THF (150 mL) at –78 ^{o}C was added LHMDS (1.0 M, 100 mmol). The solution was stirred for 30 min, and TMS-Cl was added slowly. The reaction was warmed to r.t., stirred for 2 hr, quenched with water, and worked up with ether and 1 N HCl. The organic layer was dried over $MgSO_4$, and the solvent was removed in vacuo. The crude product was distilled through a column of packed glass beads (bath temp = 114 ^{o}C, b.p. 54 ^{o}C at 1mmHg) to give 7.8 g (45%) of the product **5a** as a clear liquid.

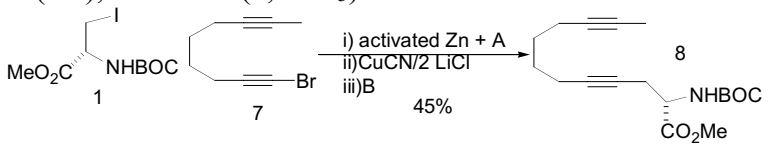
^{1}H NMR (400 MHz, $CDCl_3$): 2.23 (m, 4 H), 1.94 (t, J = 2.8 Hz, 1H), 1.63 (m, 4H), 0.14 (s, 9H).

To a solution of **5a** (7.6 g, 42.6 mmol) in THF (200 mL) at –78 ^{o}C was added n-BuLi (2.5 M, 63.9 mmol). The solution was stirred for 1 hr, and methyl iodide (5.3 mL, 85.2 mmol) was added, and the reaction was warmed slowly to r.t., and stirred for an additional 3 hr. The mixture was then cooled to 0 ^{o}C, and quenched with water, and worked up with ether. The organic layer was dried over $MgSO_4$, and the solvent was removed in vacuo. The crude product was distilled (bp = 104 ^{o}C at 40 mmHg) to give 8.1 g (99%) of the product **6** as a clear liquid.

^{1}H NMR (300 MHz, $CDCl_3$): 2.24 (t, J = 6.6 Hz, 2H), 2.14 (m, 2H), 1.78 (t, J = 2.4 Hz, 3H), 1.59 (m, 4 H), 0.14 (s, 9 H).

To a solution of **6** (1g, 5.19 mmol) in DMF (30 mL) at r.t. was added NBS (1.38 g, 7.79 mmol) and ground silver nitrate (88 mg, 0.52 mmol). The solution was stirred for 3 hr, cooled to 0 ^{o}C, and worked up with $Na_2S_2O_3$ (aq), ether/PE. The organic layer was extracted with water (5 X) and sodium chloride (aq) (2 X). The organic layer was then dried over $MgSO_4$, and the solvent was removed in vacuo to yield **7** (1.03 g, 99%) as a light yellow oil.

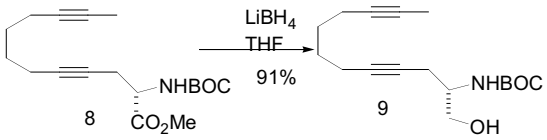
Rf (20% Et_2O/PE): 0.8. **IR** (neat): 2942, 2918, 2858, 2216, 2170, 1718, 1695, 1460, 1431, 1328, 1170, 844 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 2.20 (t, J = 6.8 Hz, 2H), 2.13 (m, 2H), 1.75 (t, J = 2.4 Hz, 3H), 1.56 (m, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$): 80.0, 78.7, 75.8, 37.9, 28.0, 27.4, 19.2, 18.2, 3.5. **HRMS** (EI, $[M-Br]^{+}$) Cal'c for C_9H_{11}: 119.0860. Found: 119.0958 (8.4), 182.9799 (1, -CH_3).



To solution of Zn dust (0.56 g, 8.5 mmol) under argon in THF (2 mL) was added dibromoethane (37 µL, 0.42 mmol). The mixture was heated to reflux, cooled to r.t. 3 times, and then trimethylsilylchloride (31 µL, 0.25 mmol) was added, and the mixture

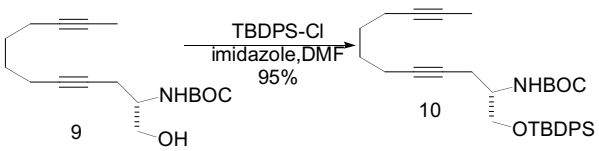
was stirred for 30 min. **1** (1.4 g, 4.25 mmol) in THF (5 mL, wash with 1 mL) was added to this heterogeneous mixture. The reaction was heated to 40 °C for 3 hr (all A gone in NMR), and cooled to r.t., and the excess Zn was allowed to settle. In a separate flask, CuCN (0.38 g, 4.25 mmol) and LiCl (0.36, 8.5 mmol) were dissolved in THF (4 mL) at r.t., and then cooled to –10 °C, and the solution of the alkyl zinc iodide was added slowly. The mixture was allowed to warm to 0 °C and stirring was continued for 10 min. After cooling to –78 °C, **7** (0.76 g, 3.83 mmol) in THF (4 mL, wash with 1 mL) was added dropwise. The reaction was stirred at this temperature for 20 hr and –50 °C for 24 hr, quenched with ammonium chloride solution, and extracted with ether. The organic layer was dried over $MgSO_4$, and the solvent was removed in vacuo. The crude product was purified on silica gel (10% ether/PE) to yield **8** (0.54 g, 44%) as a thick oil.

Rf (30% Et_2O/PE): 0.3. **IR** (neat): 3378, 2977, 2934, 2862, 2232, 1748, 1715, 1504, 1436, 1392, 1366, 1249, 1217, 1060, 1021, 859, 778 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$): 5.27 (bd, J = 8.5 Hz, 1H), 4.41 (ddd, J = 4.5 Hz, 1H), 2.69 (dm, J = 17 Hz, 1H), 2.62 (dm, J = 17 Hz, 1H), 2.12 (m, 4H), 1.75 (t, J = 2.5 Hz, 3H), 1.53 (m, 4H), 1.44 (s, 9H). **^{13}C NMR** (125 MHz, $CDCl_3$): 171.6, 155.2, 83.5, 80.1, 78.8, 75.7, 74.2, 52.5, 52.3, 28.3, 28.0, 27.9, 23.2, 18.2, 3.5. **Anal** Cal'c for $C_{18}H_{27}NO_4$: C, 67.26; H, 8.47. Found: C, 67.39; H, 8.39. $[\alpha]_D^{24}$ = +41.48 (c = 1.1, CH_2Cl_2).



To a solution of **8** (147 mg, 0.45 mmol) in THF (5 mL) at 0 °C was added $LiBH_4$ (15 mg, 0.69 mmol). The solution was allowed to warm to r.t., and stirred for 20 hr, cooled to 0 °C, and quenched with NH_4Cl (aq). The mixture was extracted with ether, dried over $MgSO_4$, and the solvent was removed in vacuo. The crude product was purified on silica (60 % ether/PE) to yield **9** (120 mg, 91 %).

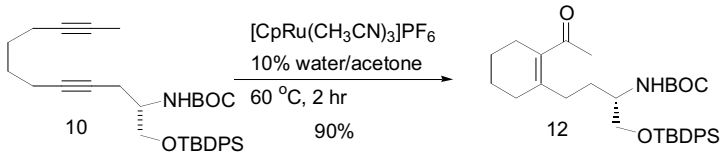
Rf (30% Et_2O/Pet. Ether): 0.1. mp = 41-43 °C**. IR** (neat): 3429, 2977, 2934, 2863, 1693, 1505, 1457, 1432, 1392, 1366, 1249, 1169, 1058, 873, 780 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 4.94 (bs, 1H), 3.61-3,10 (m, 3H), 2.68 (bs, 1H), 2.39 (m, 2H), 2.09 (m, 4H), 1.73 (t, J = 2.4 Hz, 3H), 1.52 (m, 4H), 1.40 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$): 156.0, 82.7, 79.8, 78.8, 75.8, 75.7, 64.3, 51.0, 28.4, 28.1, 27.9, 21.5, 18.3, 18.2, 3.5. **HRMS** (EI, $[M\text{-}CH_2OH]^+$) Cal'c for $C_{16}H_{24}NO_2$: 262.1807. Found: 262.1812 (0.8), 160.0974 (16.1), 145.1014 (10.2), 104.0350 (22.7). **LRMS** (CI, $[M+H]^+$) Cal'c for $C_{17}H_{28}NO_3$: 294.4. Found: 294.4 $[\alpha]_D^{25}$ = 30.19 (c = 0.36, CH_2Cl_2).



To a solution of **9** (0.55 g, 1.87 mmol) in DMF (2 mL) was added imidazole (0.51 g, 7.49 mmol) and TBDPS-Cl (0.98 mL, 3.75 mmol). The reaction was stirred 3 hr, at which point the sm had disappeared, quenched with water and extracted with ether. The organic

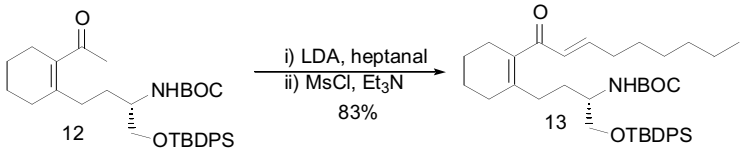
layer was then extracted with water (5X) and NaCl (aq) (2X), dried over $MgSO_4$, and the solvent was removed in vacuo. The crude product was purified on silica (10 % ether/PE) to yield **10** (0.93 g, 95%).

Rf (40% Et_2O/Pet. Ether): 0.6. **IR** (neat): 3439, 3058, 2931, 2858, 1718, 1494, 1428, 1391, 1365, 1245, 1171, 1113, 823, 740, 702 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 7.65 (m, 4H), 7.37 (m, 6H), 4.79 (bd, J = 8.8 Hz, 1H), 3.83 (bs, 1H), 3.78 (m, 1H), 3.65 (m, 1H), 2.52 (m, 2 H), 2.10 (m, 4H), 1.74 (t, J = 2.4 Hz, 3H), 1.51 (m, 4H), 1.43 (s, 9H), 1.05 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$): 155.3, 135.6, 133.2, 129.7, 127.7, 82.1,79.3, 78.8, 76.1, 75.7, 64.0, 50.7, 28.4, 28.1, 28.0, 26.9, 21.6, 19.4, 18.4, 18.3, 3.5. **HRMS** (EI, $[M-(t\text{-}Bu)_2]^+$) Cal'c for $C_{25}H_{28}NO_3Si$: 418.1830. Found: 418.1810 (40.0), 342.1530 (10.2), 199.0571 (100). **LRMS** (CI, $[M+H]^+$) Cal'c for $C_{33}H_{46}NO_3Si$: 532.4. Found: 532.4 $[\alpha]_D^{25}$ = 3.66 (c = 1.9, CH_2Cl_2).



To a test tube containing **10** (0.93 g, 1.75 mmol), 17.5 mL acetone, and 1.75 mL of H_2O was added $[CpRu(CH_3CN)_3]PF_6$ **11** (38 mg, 0.087 mmol) under argon. The resulting yellow-orange solution was then sealed and stirred in an oil bath maintained at 60 °C for 2 hours until all starting material was consumed as judged by TLC and filtered through a pad of silica gel with Et_2O as the eluent. The solvent was then removed *in vacuo* to yield a yellow oil (crude product showed ~20:1 chemoselectivity) which was further purified by silica gel chromatography (20% ether/PE) to yield **12** (0.86 g, 90%).

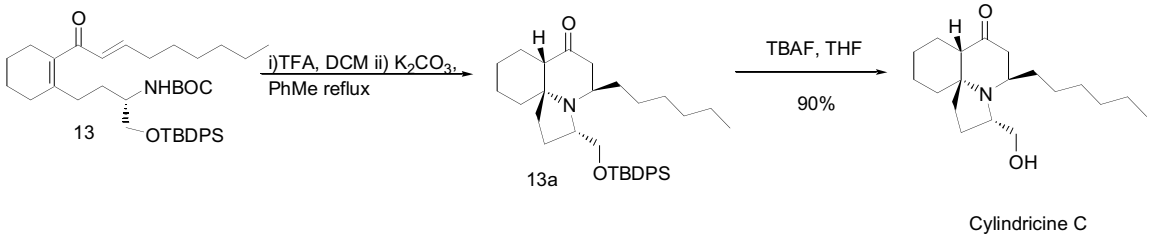
Rf (50% Et_2O/Pet. Ether): 0.65. **IR** (neat): 3356, 3058, 2931, 2858, 1714, 1682, 1600, 1499, 1451, 1428, 1390, 1364, 1274, 1231,1172, 1112, 823, 740, 702 cm^{-1}. **^{1}H NMR** (400 MHz, C_6D_6): 7.77 (m, 4H), 7.24 (m, 6H), 5.03 (bd, J = 8.4 Hz, 1H), 3.93 (m, 1H), 3.71 (m, 2H), 2.46 (m, 1H), 2.11 (m, 1H), 1.87 (s, 3H), 1.85 (m, 4H), 1.78 (m, 1H), 1.63 (m, 1H), 1.48 (s, 9H), 1.31 (m, 4H), 1.17 (s, 9H). **^{13}C NMR** (100 MHz, C_6D_6): 201.8, 155.8, 144.8, 136.0, 134.0, 133.9, 133.1, 129.9, 128.1, 78.4, 66.1, 52.7, 31.9, 31.0, 30.7, 29.1, 28.5, 27.1, 27.0, 22.5, 22.4, 19.5. **HRMS** (EI, $[M-(t\text{-}Bu)_2]^+$) Cal'c for $C_{25}H_{20}NO_4Si$: 436.1944. Found: 436.1933 (24.2), 374.1945 (15.1). **LRMS** (CI, $[M+H]^+$) Cal'c for $C_{33}H_{48}NO_4Si$: 550.5. Found: 550.5. $[\alpha]_D^{25}$ = -18.78 (c = 3.2, CH_2Cl_2).



To a solution of **12** (313 mg, 0.569 mmol) in THF (10 mL)at –78 °C was added LDA (0.59 M, 2.9 mL, 1.70 mmol). The solution was stirred for 30 min, and heptanal (0.317 mL, 2.27 mmol) was added dropwise. The reaction was stirred a further 4 hr, quenched with NH_4Cl (aq), and worked up with ether. The organic layer was dried over $MgSO_4$,

and the solvent was removed in vacuo. The crude product (mostly β-hydroxy ketone with some amount of eliminated product) was taken up in DCM (8 mL), and cooled to 0 ^{o}C. Triethylamine (0.79 mL, 5.7 mmol) in one portion, and MsCl (0.22 mL, 2.85 mmol) dropwise, were added. After 15 min at this temperature, the solution was warmed to r,t. and stirred until the β-hydroxy ketone starting material disappeared (by TLC) (20 hr). The reaction was then worked up with water and ether, the organic layer was dried over $MgSO_4$, and the solvent was removed in vacuo. The crude product was purified on silica gel (20 % ether/PE) to yield **13** (302 mg, 83 %).

Rf (20% Et_2O/Pet. Ether): 0.25. **IR** (neat): 3363, 3058, 2958, 2930, 2857, 1715, 1648, 1497, 1461, 1428, 1390, 1364, 1279, 1247, 1174, 1113, 1070, 975, 823, 740, 702 cm^{-1}. **^{1}H NMR** (500 MHz, C_6D_6): 7.75 (m, 4H), 7.24 (m, 6H), 6.84 (dt, J1 = 15.5 Hz, J2 = 7.0 Hz, 1H), 6.21 (d, J = 15.5 Hz, 1H), 4.83 (d, J = 9 Hz, 1H), 3.86 (m, 1H) 3.63 (m, 2H), 2.27 (m, 1H), 2.15 (m, 2H), 2.06 (m, 1H), 1.93 (m, 3H), 1.8 (m, 2H), 1.63 (m, 1H), 1.47 (s, 9H), 1.43 (m, 4H), 1.22 (m, 2H) 1.15 (s, 9H), 1.14 (m, 4H), 0.88 (t, J = 7.0 Hz, 3H). **^{13}C NMR** (125 MHz, C_6D_6): 197.9, 155.6, 148.5, 139.2, 136.0, 133.8, 130.5, 129.9, 128.3, 128.1, 78.4, 65.9, 52.6, 32.6, 31.8, 30.5, 29.3, 29.2, 28.5, 28.3, 27.5, 27.1, 22.9, 22.8, 22.6, 19.5, 14.2. **LRMS** (EI, $[M]^+$) Cal'c for $C_{40}H_{59}NO_4Si$: 645.42. Found: 645.42. $[\alpha]_D^{25}$ = -9.88 (c = 1.2, CH_2Cl_2).

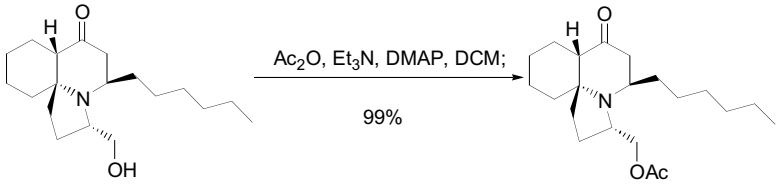


To a solution of **13** (14 mg, 0.0216 mmol) in DCM (0.2 mL) was added TFA (0.2 mL) dropwise. After 1 hr the excess TFA and DCM were removed in vacuo. The residue was then taken up in DCM (5 mL), and the solution was then extracted with 2M NaOH (10 mL). The organic layer was taken off, dried, and the solvent removed in vacuo to give a mixture of uncyclized and cyclized amines (12 mg). The crude mixture of amines was then taken up in toluene (1 mL) and potassium carbonate was added (50 mg). The reaction was then refluxed until only trace amount of uncyclized product remained (68 hr). The crude mixture was then directly submitted to column chromatography on silica (20% ether/PE with 2% Et_3N) to yield **13a** (11 mg, 90%).

Rf (20% Et_2O/Pet. Ether): 0.4. **IR** (neat): 2930, 2856, 1717, 1589, 1462, 1446, 1427, 1389, 1357, 1265, 1195, 1112, 1075, 823, 739, 701 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 7.64 (m, 4H), 7.36 (m, 6H), 3.71 (dd, J1 = 9.5 Hz, J2 = 4.0 Hz, 1H), 3.44 (m, 1H), 3.25 (t, J = 9.5 Hz, 1H), 3.14 (m, 1H), 2.60 (dd, J1 = 11.2 Hz, J2 = 3.2 Hz, 1H), 2.13 (m, 2H), 1.98-1.03 (m, 22H), 1.02 (s, 9H), 0.82 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): 213.6, 135.7, 134.0, 133.9, 129.7, 129.6, 127.7, 70.4, 68.3, 60.3, 54.7, 54.1, 41.5, 40.7, 33.4, 31.8, 31.5, 29.3, 28.4, 27.3, 26.9, 25.0, 24.2, 22.7, 22.6, 19.3, 14.1. $[\alpha]_D^{25}$ = -63.30 (c =0.9, CH_2Cl_2).

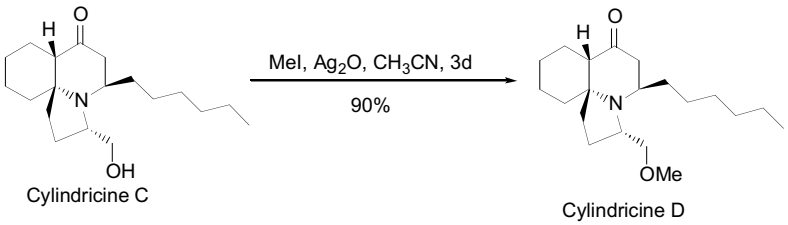
To a solution of **13a** (12 mg, 0.022 mmol) in THF (1 mL) was added TBAF (1.0 M, 0.07 mL, 0.066 mmol). The reaction was stirred until 1 had disappeared by TLC (4 hr), and purified directly on silica gel (70% ether/PE with 2% Et_3N) to yield 2 (7 mg, 99%), which matched the literature data for cyclindricine C (except the rotation had the opposite sign as the enantiomer Molander synthesized).

Rf (50% Et_2O/Pet. Ether): 0.15. **IR** (neat): 3448, 2925, 2856, 1704, 1450, 1381, 1351, 1329, 1148, 1079, 1027, 975, 923, 880 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$): 3.51 (m, 2H), 3.40 (m, 1H), 3.26 (m, 1H), 2.87 (bs, 1H), 2.28 (t, J = 13 Hz, 2H), 2.20 (dd, J1 = 13.25 Hz, J2 = 2.5 Hz, 2H), 2.10 (dd, J1 = 12.2 Hz, J2 = 8.0 Hz, 1H), 1.80 (dd, J1 = 12.2 Hz, J2 = 8.5 Hz, 1H), 1.7 – 1.17 (m, 19H), 0.85 (t, J = 7.0 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): 210.6, 70.7, 66.4, 56.6, 55.4, 50.3, 42.6, 36.5, 36.0, 35.2, 31.7, 29.4, 28.8, 27.2, 24.3, 22.8, 22.6, 21.9, 14.1 $[\alpha]_D^{25}$ = 60.82 (c =0.4, CH_2Cl_2). Lit: $[\alpha]_D^{25}$ = -64 (c =0.2, CH_2Cl_2).



To a solution of cylindricine C (2.4 mg, 0.0078 mmol) in DCM (0.5 mL) at 0 ^oC was added Et_3N (11 µL, 0.078 mmol), DMAP (0.1 mg, 0.1 eq.), and acetic anhydride (4 µL, 0.039 mmol). The solution was then warmed to r.t. and stirred 1 hr. The reaction was then partitioned between ether and water and the organic layer was extracted off, dried, and the solvent was removed in vacuo. The crude product was then purified on silica gel (20% ether/pet. ether with 2% Et_3N) to yield cylindricine E (2.7 mg, 99%).

Rf (50% Et_2O/Pet. Ether): 0.45. **IR** (neat): 2932, 2858, 1741, 1704, 1596, 1446, 1378, 1220, 1030 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$): 4.09 (dd, J1 = 10.5 Hz, J2 = 3.0 Hz, 1H), 3.65 (dd, J1 = 10.5 Hz, J2 = 9.0 Hz, 1H), 3.48 (m, 1H), 3.19 (m, 1H), 2.19 (m, 4H), 2.06 (m, 1H), 2.05 (s, 3H), 1.74 (m, 2H), 1.63-1.58 (m, 3H), 1.44 (m, 2H), 1.32-1.22 (m, 13H), 0.85 (t, J = 7.0 Hz, 3H). $[\alpha]_D^{25}$ = 28.67 (c =0.13, CH_2Cl_2).



To a solution of cylindricine C (2 mg, 0.0065 mmol) in acetonitrile (0.5 mL) was added silver oxide (30 mg, 20 eq.) and methyl iodide (16 µL, 40 eq.). The reaction was stirred for 3 days wherein all starting material disappeared. The

mixture was then filtered through celite, and the celite was washed with ether, and the solvent was removed in vacuo. The crude product was then purified on silica (10% ether/PE with 2% Et_3N) to yield cylindricine D (1.9 mg, 90%).

Rf (50% Et_2O/Pet. Ether): 0.3. **IR** (neat): 2926, 2854, 1707, 1453, 1381, 1331, 1258, 114 cm^{-1}. **^{1}H NMR** (500 MHz, C_6D_6): 3.35-3.29 (m, 2H), 3.17 (s, 3H), 3.12 (m, 1H), 3.00 (t, J = 8.5 Hz, 1H), 2.40 (dm, J = 12.5 Hz, 1H), 2.14 (dd, J 1 = 12.5 Hz, J2 = 2.0 Hz, 1H), 1.86 (m, 3H), 1.75 (m, 2H), 1.65-1.53 (m, 4H), 1.47-1.19 (m, 14 H), 0.89 (t, J = 7.0 Hz, 3H). $[\alpha]_D^{25}$ = 21.5 (c =0.08, CH_2Cl_2).