Synthesis of (±)-Cylindricines A, D, and E

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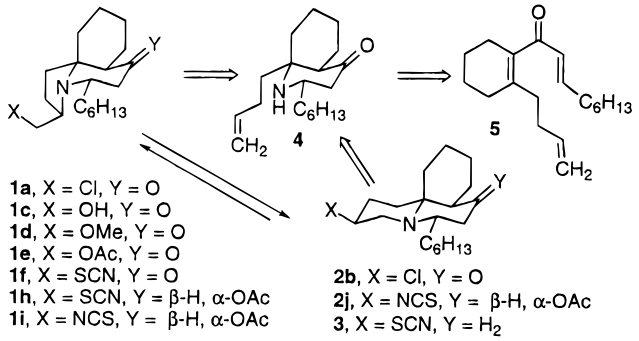
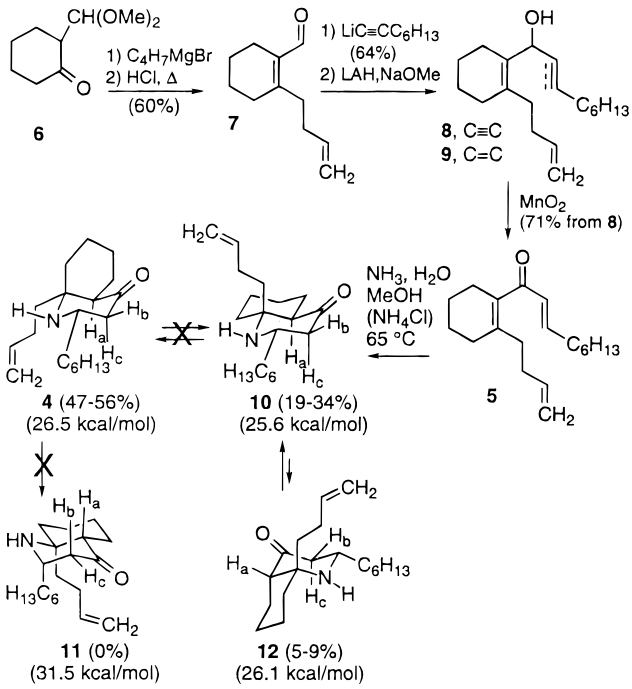
Cylindricines A−K were isolated by Blackman and co-workers from the ascidian *Clavelina cylindrica* collected in Tasmania.[1−3] The two main alkaloids, cylindricines A (**1a**) and B (**2b**), are readily interconvertible via an aziridinium ion intermediate.[1] A 30 μM solution of the 3:2 equilibrium mixture causes significant mortality in the brine shrimp bioassay.[1] Cylindricines C (**1c**), D (**1d**), E (**1e**), and F (**1f**) were isolated as minor products from these ascidians and can be prepared from the equilibrium mixture of cylindricines A and B by reaction with the appropriate nucleophile.[2] Cylindricine H (**1h**) is the acetate of the reduction product of cylindricine F (**1f**), cylindricine I (**1i**) is the analogous isothiocyanate, and cylindricine J (**2j**) is a reduced isothiocyanate analogue of cylindricine B.[3] Patil and co-workers recently isolated the more highly reduced thiocyanate fasicularin (**3**), which shows selective activity against a DNA repair-deficient organism, from the ascidian *Nephteis fasicularis* collected in Micronesia.[4]



We envisioned that cylindricines A (**1a**) and B (**2b**) could be prepared from butenylquinolinone **4** by either a radical cyclization of the *N*-chloroamine[5] or by addition of *N*-chlorosuccinimide to the alkene.[6] Addition of NH_3 to dienone **5** should provide a simple route to **4** since addition of NH_3 to propenyl 2-methyl-1-cyclohexenyl ketone afforded the comparable stereoisomer as one of two major products.[7]

Results and Discussion

Addition of 3-butenylmagnesium bromide to acetal ketone **6**[8] followed by hydrolysis of the acetal and dehydration gave 60% of cyclohexenecarboxaldehyde **7**. Other procedures based on Grignard addition to an alkoxymethylenecyclohexanone or an (alkylthio)methylenecyclohexanone were much less successful.[9] Addition of 1-octynyllithium to **7** provided 64% of propargyl alcohol **8**. Reduction with LAH/NaOMe[10] gave the unstable alcohol **9**, which underwent allylic rearrangement on chromatography. Similar rearrangement occurred on reduction with LAH without NaOMe. Oxidation of crude **9** with MnO_2 in CH_2Cl_2 afforded 71% of the requisite dienone **5**.



Heating **5** in 3:1 MeOH/concentrated NH_4OH in a sealed tube at 73 °C for 16 h gave 56% of **4**, 19% of **10**, and 6% of **12**. The pH has been shown to affect the stereochemical ratio in the formation of 4-piperidinones by double Michael addition of ammonia to dienones.[11] As expected,[11] lowering the pH favored the undesired trans isomer **10** at the expense of the desired cis isomer **4**. Reaction of **5** in MeOH containing 60 mg of NH_4Cl per mL of concentrated NH_4OH (1:13 NH_4^+/NH_3) provided 47% of **4**, 34% of **10**, and 5% of **12** while a similar reaction containing 1 g of NH_4Cl per mL of concentrated NH_4OH (1.3:1 NH_4^+/NH_3) afforded 20% of **4**, 26% of **10**, and 9% of **12**.

The structures of **4**, **10**, and **12** were established by ^1H NMR spectroscopic analysis and chemical equilibration. In all three isomers, H_c absorbs as a doublet of doublets with a large 10−12 Hz vicinal coupling constant, establishing that the hexyl side chain is equatorial. In **11**, the hexyl side chain is axial so that H_b and H_c would both have small vicinal coupling constants. In the desired isomer **4**, H_a absorbs as dd, $J = 4$, 4 Hz, establishing that H_a is equatorial on the cyclohexane ring. In the trans-fused isomer **10**, H_a absorbs as ddd, $J = 11.7$, 2.9, 0.9 Hz. The 11.7 Hz coupling constant establishes that H_a

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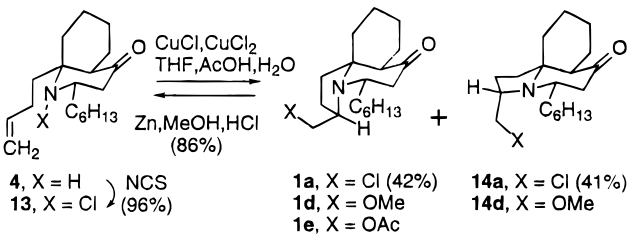
is axial on the cyclohexane ring, and the 0.9 Hz long-range coupling constant to H_c indicates that both H_a and H_c are axial on the piperidinone ring.[12] In the cis-fused isomer **12**, H_a absorbs as ddd, J = 12.0, 3.9, 0.8 Hz. The 12.0 Hz coupling constant establishes that H_a is axial on the cyclohexane ring, and the 0.8 Hz long-range coupling constant to H_b indicates that both H_a and H_b are equatorial on the piperidinone ring.[12]

Resubjection of either pure **10** or **12** to the reaction conditions for longer times afforded a 3:1 equilibrium mixture of **10** and **12** containing a trace of **4**, indicating that partial equilibration of **10** and **12** by enolization is facile. The 3:1 mixture of isomers of **10** and **12** is close to that expected from the MM2 strain energies, which are shown under the structures.[13] Attempted equilibration of **4** gave >90% recovered **4**, 6% of **10**, and no **11**. The trans isomer **11** is 5 kcal/mol less stable than **4** due to 1,3-diaxial interactions and is therefore not observed in the original reaction or equilibration. Although 2,6-dialkyl-4-piperidinones are reported to undergo equilibration by retro-Michael and Michael reactions in aqueous *tert*-butylamine at reflux,[14] we were unable to effect efficient equilibration of **10** or **12** with **4** under these or more forcing conditions. These more highly substituted quinolinones equilibrate slowly by retro-Michael and Michael reactions. Therefore, the ratio of **4** to **10** and **12** is determined in the second, kinetically-controlled, intramolecular Michael reaction.

Reaction of piperidinone **4** with *N*-chlorosuccinimide in CH_2Cl_2 afforded 96% of *N*-chloropiperidinone **13**[5] rather than the desired (chloromethyl)pyrrolidines **1a** and **14a** resulting from addition of Cl to the double bond.[6b] The NMR spectra of **13** showed broadening of the protons and carbons in the piperidinone ring due to slow pyramidal inversion of the nitrogen.[15] Radical cyclization of **13** by the Stella procedure[5a] using CuCl and $CuCl_2$ in 2:1:1 THF/AcOH/H_2O provided a 55:45 mixture of cylindricine A (**1a**) and *epi*-cylindricine A (**14a**), which were readily separated by flash chromatography on silica gel to provide 42% of **1a** and 41% of **14a**. As expected,[5] the radical cyclization afforded only (chloromethyl)pyrrolidines **1a** and **14a** and none of the chloropiperidine **2b** and its epimer. The ^{1}H and ^{13}C NMR spectral data of **1a** are identical to those of an authentic sample.[16] Although the radical cyclization is nonselective, the undesired isomer **14a** can be recycled by reduction with Zn dust in 7:1 MeOH/concentrated HCl to give 86% of **4**.

Since cylindricine A (**1a**) equilibrates with **2b** and is unstable toward nucleophiles, the structure was confirmed by preparation of the more stable cylindricines D (**1d**) and E (**1e**) as described by Li and Blackman.[2] Cyclization of **13** and treatment of the crude mixture of **1a** and **14a** with sodium methoxide in MeOH at 25 °C for 6 h provided 32% of **1d** and 35% of *epi*-cylindricine D



(**14d**). The ^{1}H and ^{13}C NMR spectral data of **1d** are identical to those of an authentic sample.[16] Treatment of **1a** with NaOAc in MeOH at 25 °C for 4 h yielded 91% of cylindricine E (**1e**) whose ^{13}C NMR spectrum corresponds closely to that reported.

In conclusion, the first synthesis of cylindricine A (**1a**) has been accomplished by an efficient seven-step route using a double Michael reaction to construct the quinolinone and a radical cyclization to prepare the (chloromethyl)pyrrolidine.

Experimental Section

General. NMR spectra were recorded at 300 MHz in $CDCl_3$ unless otherwise indicated. Chemical shifts are reported in δ and coupling constants in hertz. The solvent peak of C_6D_6 absorbs at δ 7.16 (H) and δ 128.4 (C). IR spectra are reported in cm^{-1}.

2-(3-Butenyl)-1-cyclohexenecarboxaldehyde (7). A solution of 3-butenylmagnesium bromide was prepared under N_2 by dropwise addition of 3.5 g (25.9 mmol) of 4-bromo-1-butene at 0 °C over 40 min to 4.1 g (169 mmol) of Mg turnings in 40 mL of dry ether. The solution was stirred for 1 h at 0 °C and then at rt for 3.5 h. The liquid layer was transferred by cannula to another flask under N_2, which was then cooled to 0 °C. 2-(Dimethoxymethyl)cyclohexanone (**6**)[8] (1.93 g, 11.2 mmol) in 25 mL of dry ether was then added over a period of 40 min. The solution was warmed to rt, stirred for 1.5 h, cooled to 0 °C, treated slowly with 200 mL of 0.1 N HCl, and extracted with ether (3 × 80 mL). The ether layers were washed with water, dried (Na_2CO_3), and concentrated to give 3.1 g of crude 2-(dimethoxymethyl)-1-(3-butenyl)cyclohexanol.

A solution of crude acetal alcohol in 30 mL of acetone was heated at reflux. To the refluxing mixture was added 0.2 mL of concentrated HCl slowly. Heating was continued for a further 2 h. After cooling, the acetone was evaporated under reduced pressure. Water (40 mL) was added to the residue, which was extracted with hexane (3 × 60 mL). The combined organic layers were dried (Na_2SO_4) and concentrated giving 1.87 g of crude **7**. Purification by flash chromatography on silica gel (94:6 hexane/EtOAc) gave 1.104 g (60%) of pure **7**: ^{1}H NMR 10.10 (1, s), 5.80 (1, ddt, J = 16.8, 10.2, 6.8), 5.05 (1, ddt, J = 16.8, 1.8, 1.6), 5.01 (1, ddt, J = 10.2, 1.8, 1.1), 2.62 (2, t, J = 7.8), 2.17−2.32 (6, m), 1.56−1.68 (4, m); ^{13}C NMR 190.8, 159.1, 136.9, 134.0, 115.8, 33.8, 32.0, 31.5, 22.2, 22.0, 21.6; IR (neat) 1665, 1629; UV (CH_3CH_2OH) λ_{max} (ϵ_{max}) = 251 (6400) nm.

2-(3-Butenyl)-α-(1-octynyl)-1-cyclohexenemethanol (8). *n*-BuLi (2.5 M, 5 mL, 12.5 mmol) was added slowly to a solution of 1-octyne (1.4 g, 12.7 mmol) in 20 mL of THF at −78 °C. The mixture was warmed to rt for 20 min, and DMPU (2 mL) was added to the mixture, which was then cooled to −78 °C. Aldehyde **7** (1.057 g, 6.4 mmol) in 10 mL of THF was added slowly to the mixture, which then was stirred at rt for 14 h. The mixture was treated with saturated NH_4Cl (20 mL). The organic layer was separated, and the aqueous layer was extracted with ether (3 × 40 mL). The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure to give 1.56 g of crude **8**. Flash chromatography on silica gel (9:1 hexane/EtOAc) gave pure **8** (1.12 g, 64%): ^{1}H NMR 5.82 (1, ddt, J = 17.1, 10.1, 7.2), 5.31 (1, br s), 5.02 (1, dd, J = 17.1, 2.0), 4.97 (1, dd, J = 10.1, 2.0), 2.32−2.08 (6, m), 2.21 (2, dt, J = 2.1, 7.0), 2.06−1.97 (2, m), 1.76−1.28 (12, m), 0.89 (3, t, J = 6.6); ^{13}C NMR 138.4, 133.9, 130.8, 114.7, 85.6, 80.1, 61.5, 32.9, 32.5, 31.3, 30.1, 28.6, 28.5, 23.5, 22.9, 22.8, 22.5,

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(16) We thank Prof. Blackman for copies of the ^{1}H and ^{13}C NMR spectra of cylindricines A, B, and D.

18.8, 14.0; IR (neat) 3458. Anal. Calcd for $C_{19}H_{30}O$: C, 83.21; H, 10.94. Found: C, 83.09; H, 10.84.

1-(2-(3-Butenyl)-1-cyclohexenyl)-2(*E*)-nonen-1-one (5). A solution of **8** (1.09 g, 3.98 mmol), 6.3 mL of a 1 M solution of $LiAlH_4$ in THF (6.3 mmol), and suspended NaOMe (680 mg, 12.6 mmol) in 40 mL of THF was refluxed for 45 min and then quenched with water (60 mL). The solution was extracted with ether (3 × 60 mL), and the combined organic layers were dried (Na_2CO_3) and concentrated under reduced pressure to give 1.67 g of crude **9**.

Crude **9** was dissolved in 50 mL of CH_2Cl_2, and 3.5 g of MnO_2 (85% activated, 34.2 mmol) was added. The solution was stirred for 12 h, and an additional 6.6 g of MnO_2 (85% activated, 64.5 mmol) was added. After being stirred for 36 h, the mixture was filtered through a bed of Celite 521. The residue was washed with CH_2Cl_2 (3 × 20 mL). The combined filtrates were concentrated under reduced pressure. Flash chromatography of the residue on silica gel (9:1 hexane/EtOAc) provided 772 mg (71%) of **5**: ^{1}H NMR 6.79 (1, dt, J = 15.8, 6.9), 6.13 (1, dt, J = 15.8, 1.4), 5.74 (1, ddt, J = 10.2, 17.0, 6.3), 4.97 (1, ddt, J = 17.0, 1.7, 0.9), 4.92 (1, ddt, J = 10.2, 1.7, 0.9), 2.24 (2, ddt, J = 1.4, 6.9, 6.9), 2.18−2.03 (8, m), 1.62−1.68 (4, m), 1.46 (2, tt, J = 7.1, 7.1), 1.35−1.25 (6, m), 0.89 (3, t, J = 6.8); ^{13}C NMR 200.8, 150.3, 138.2, 137.5, 133.6, 130.5, 114.5, 34.2, 32.5, 32.3, 31.5, 28.8, 28.6, 28.0, 27.3, 22.5, 22.5, 22.2, 14.0; IR (neat) 1651, 1618; UV (CH_3CH_2OH) λ_{max} (ϵ_{max}) = 228 (11 900) nm.

(2α,4aα,8aα)-, (2α,4aα,8a*β*)-, and (2α,4a*β*,8a*β*)-8a-(3-Butenyl)-2-hexyloctahydro-4(1*H*)-quinolinone (4, 10, and 12). NH_4Cl (440 mg, 8.2 mmol) and 7.2 mL of concentrated ammonium hydroxide were added to a solution of **5** (500 mg, 1.82 mmol) in 42 mL of MeOH at rt in a resealable tube. The tube was sealed, and the reaction mixture was heated to 76 °C. After 16 h of stirring, the solution was cooled to rt, removed from the reaction tube, and concentrated under reduced pressure. The resulting oily solid was diluted with 1:1 (v/v) EtOAc and saturated aqueous Na_2CO_3 (40 mL). The layers were separated, and the organic layer was washed with saturated aqueous Na_2CO_3 (1 × 10 mL). The combined aqueous layers were extracted with EtOAc (2 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure to give a quantitative yield of crude quinolinones. Flash chromatography on silica gel (9:1 hexane/EtOAc) provided **12** (26 mg, 5%), followed by **4** (247 mg, 47%) and **10** (180 mg, 34%).

Data for 4: ^{1}H NMR 5.87 (1, ddt, J = 16.9, 10.2, 6.6), 5.07 (1, br d, J = 16.9), 4.99 (1, br d, J = 10.2), 3.12 (1, dddd, J = 11.5, 2.7, 6.0, 6.0), 2.37 (1, dd, J = 13.5, 2.7), 2.25 (1, dd, J = 4.0, 4.0), 2.05−2.21 (2, m), 1.96 (1, dd, J = 13.5, 11.5), 1.87−1.20 (20, m), 0.88 (3, t, J = 6.5); ^{13}C NMR 210.9, 138.8, 114.6, 58.1, 53.8, 49.9, 48.8, 37.8, 37.6, 31.7, 31.6, 29.2, 27.2, 25.6, 22.6, 22.5, 21.4, 21.1, 14.0; IR (neat) 3318, 1709.

Data for 10: ^{1}H NMR 5.79 (1, ddt, J = 17.1, 10.2, 6.6), 5.01 (1, dd, J = 17.1, 1.2), 4.94 (1, dd, J = 10.2, 1.2), 3.02 (1, dddd, J = 12.0, 3.6, 5.7, 5.7), 2.35 (1, dd, J = 13.4, 3.6), 2.30 (1, ddd, J = 11.7, 2.9, 0.9), 2.08 (1, ddd, J = 13.4, 12.0, 0.9), 1.12−1.93 (22, m), 0.89 (3, t, J = 6.5); ^{13}C NMR 210.4, 138.3, 114.4, 60.3, 58.5, 51.3, 48.8, 37.5, 35.8, 31.6, 29.2, 26.0, 26.0, 25.7, 24.9, 22.5, 21.5, 20.1, 13.9; IR (neat) 3307, 1709.

Data for 12: ^{1}H NMR 5.79 (1, ddt, J = 17.1, 10.2, 6.7), 4.99 (1, ddt, J = 17.1, 1.8, 1.6), 4.93 (1, ddt, J = 10.2, 1.8, 1.2), 2.95 (1, dddd, J = 10.5, 4.2, 7.4, 7.4), 2.21 (1, dd, J = 10.5, 14.7), 2.13 (1, ddd, J = 4.2, 14.7, 0.8), 2.07 (1, ddd, J = 3.9, 12.0, 0.8), 1.13−2.04 (22, m), 0.89 (3, t, J = 6.9); ^{13}C NMR 214.5, 138.6, 114.4, 58.2, 54.9, 50.5, 44.0, 38.0, 37.6, 35.7, 31.8, 29.4, 27.0, 26.4, 25.7, 25.4, 22.6, 20.9, 14.1; IR (neat) 3332, 1704.

(2α,4aα,8aα)-8a-(3-Butenyl)-1-chloro-2-hexyloctahydro-4(1*H*)-quinolinone (13). Amine **4** (120 mg, 0.41 mmol) and *N*-chlorosuccinimide (150 mg, 1.10 mmol) were dissolved in 12 mL of CH_2Cl_2 at rt, and the solution was stirred for 18 h. The solution was concentrated under reduced pressure. Flash chromatography of the residue on silica gel (94:6 hexane/EtOAc) gave 130 mg (96%) of **13**: ^{1}H NMR 5.88 (1, ddt, J = 17.3, 10.2, 6.9), 5.07 (1, br d, J = 17.3), 4.97 (1, br d, J = 10.2), 3.54 (1, br), 2.64−2.55 (3, br), 2.27−2.19 (3, br), 2.06−1.59 (3, m), 1.47−1.24 (16, m), 0.88 (3, t, J = 6.3); ^{13}C NMR 208.7, 138.9, 114.4, 69.6, 59.7 (br), 50.3, 43.1 (br), 35.1, 34.1, 31.7, 30.2 (br), 29.7, 29.0, 26.3, 25.1 (br), 23.1, 22.8, 21.1, 14.1; IR (neat) 1711.

(3α,5*β*,7a*β*,11a*R)- and (3*β*,5*β*,7a*β*,11a*R**)-3-(Chloromethyl)-5-hexyloctahydro-1*H*-pyrrolo[2,1-*j*]quinolin-7(7a*H*)-one (Cylindricine A (1a) and *epi*-Cylindricine A (14a)).** A solution of **13** (18.0 mg, 0.056 mmol) in 1.0 mL of THF was cooled to 0 °C (under N_2) and treated over 10 min with a solution of CuCl (5 mg, 0.05 mmol) and $CuCl_2$ (27 mg, 0.19 mmol) in 1.6 mL of THF/AcOH/H_2O (2:1:1) (solvents were purged with N_2 to remove dissolved oxygen). The solution was stirred at 0 °C for 40 min and concentrated under reduced pressure. Flash chromatography of the residue on silica gel containing 0.8 g of Na_2SO_4 on top (97:3 hexane/EtOAc) provided 7.4 mg (41%) of **14a** followed by 7.6 mg (42%) of **1a**.

Data for 1a: ^{1}H NMR (C_6D_6) 3.37 (1, dd, J = 10.5, 2.6), 3.20 (1, dddd, J = 9.5, 9.5, 2.6, 2.6), 2.98 (1, dd, J = 10.5, 9.5), 3.03−2.94 (1, m), 2.35 (1, br d, J = 12.6), 2.09 (1, dd, J = 12.9, 2.1), 1.77−1.01 (23, m), 0.89 (3, t, J = 7.1); ^{13}C NMR (C_6D_6) 208.5, 70.5, 58.6, 55.3, 51.1, 49.8, 43.4, 36.5, 35.6, 35.1, 32.5, 29.9, 27.5, 27.5, 25.0, 23.6, 23.3, 22.6, 14.6; IR (neat) 1707. The ^{1}H and ^{13}C NMR spectral data are identical to those reported,[1] except that the literature data were referenced to C_6D_6 at δ 7.40 and δ 128.7.

Data for 14a: ^{1}H NMR (C_6D_6) 3.37 (1, dd, J = 10.0, 2.2), 3.08−3.01 (1, m), 2.94 (1, dd, J = 10.0, 10.0), 2.87−2.78 (1, m), 2.40 (1, br d, J = 12.0), 2.37 (1, dd, J = 15.2, 3.4), 1.90 (1, br s), 1.60 (1, dd, J = 15.2, 9.6), 1.78−0.94 (21, m), 0.91 (3, t, J = 6.6); ^{13}C NMR (C_6D_6) 208.5, 67.1, 60.0, 57.9, 52.8, 49.7, 47.9, 37.2, 32.7, 32.6, 30.2, 28.4, 27.1, 26.8, 24.4, 24.0, 23.4, 22.0, 14.7; IR (neat) 1707.

Recycling 14a. A solution of **14a** (7.0 mg, 0.022 mmol) in 0.7 mL of MeOH was added to a mixture of concentrated HCl (12.1 M, 0.7 mL) and 4.5 mL of MeOH. Zinc dust (740 mg, 11.4 mmol) was added to the solution, and H_2 liberation started. The mixture was stirred for 4 h, more zinc dust (690 mg, 10.6 mmol) was added, and the mixture was stirred for another 12 h. Workup was accomplished by adding saturated Na_2CO_3 solution (5 mL) and CH_2Cl_2 (10 mL) to the solution, which was then filtered through a Celite 521 bed. The residue was washed with CH_2Cl_2 (3 × 10 mL), the organic layer was separated from the combined filtrates, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure to give 10.2 mg of crude **4**. Flash chromatography on silica gel (96:4 hexane/EtOAc) gave 5.4 mg (86%) of pure **4**.

(3α,5*β*,7a*β*,11a*R)- and (3*β*,5*β*,7a*β*,11a*R**)-5-Hexyloctahydro-3-(methoxymethyl)-1*H*-pyrrolo[2,1-*j*]quinolin-7(7a*H*)-one (Cylindricine D (1d) and *epi*-Cylindricine D (14d)). 13** (18 mg, 0.056 mmol) was treated by the same procedure as above to provide 19 mg of crude **1a** and **14a**. The crude mixture was dissolved in 4 mL of dry methanol, and NaOMe (10 mg, 0.19 mmol) was added to the solution at rt. The mixture was stirred at rt for 6 h. After removal of the solvent under reduced pressure, water (5 mL) was added and the solution was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure to give 16 mg of crude **1d** and **14d**. Purification by flash chromatography on silica gel (97:3 hexane/EtOAc) gave 6.3 mg (35%) of **14d** followed by 5.7 mg (32%) of **1d**.

Data for 1d: ^{1}H NMR (C_6D_6) 3.34 (1, dd, J = 9.1, 3.0), 3.33−3.28 (1, m), 3.18 (3, s), 3.18−3.10 (1, m), 3.00 (1, dd, J = 9.1, 9.2), 2.40 (1, br d, J = 13.5), 2.15 (1, dd, J = 12.6, 2.2), 1.96−0.93 (23, m), 0.89 (3, t, J = 6.9); ^{13}C NMR (C_6D_6) 209.1, 79.0, 70.1, 59.1, 56.2, 55.8, 51.3, 43.5, 36.7, 35.8, 35.5, 32.5, 30.1, 27.7, 27.3, 25.2, 23.7, 23.4, 22.8, 14.7; IR (neat) 1707, 1113. The ^{1}H and ^{13}C NMR spectral data are identical to those reported,[2] except that the literature data were referenced to C_6D_6 at δ 7.40 and δ 128.7 and the H_6 absorption at δ 2.40 was not reported.

Data for 14d: ^{1}H NMR (C_6D_6) 3.37 (1, dd, J = 8.7, 3.2), 3.16 (3, s), 3.24−3.08 (1, m), 3.00 (1, dd, J = 8.7, 8.7), 3.00−2.92 (1, m), 2.47 (1, dd, J = 15.0, 3.3), 2.52−2.42 (1, m), 2.11 (1, br s), 1.90−1.75 (4, m), 1.71−1.00 (18, m), 0.91 (3, t, J = 6.8); ^{13}C NMR (C_6D_6) 209.2, 79.2, 66.6, 59.2, 58.0, 57.8, 53.3, 48.2, 37.3, 33.5, 32.6, 30.3, 28.3, 27.5, 26.9, 24.5, 24.1, 23.4, 22.2, 14.7; IR 1706, 1110.

(3α,5*β*,7a*β*,11a*R)-3-(Acetoxymethyl)-5-hexyloctahydro-1*H*-pyrrolo[2,1-*j*]quinolin-7(7a*H*)-one (Cylindricine E (1e)).** A solution of **1a** (7.8 mg, 0.024 mmol) in 1.5 mL of MeOH was treated with sodium acetate (8 mg, 0.098 mmol) at rt, and the mixture was stirred at rt for 4 h. After removal of the solvent under reduced pressure, water (5 mL) was added and the solution was extracted with CH_2Cl_2 (3 × 5 mL). The combined

organic layers were dried (Na_2SO_4) and concentrated under reduced pressure to give 10.8 mg of crude **1e**. Purification by flash chromatography on silica gel (97:3 hexane/EtOAc) gave 7.6 mg (91%) of pure **1e**: ^{1}H NMR ($CDCl_3$) 4.12 (1, dd, J = 10.5, 3.4), 3.68 (1, dd, J = 10.5, 8.7), 3.55−3.45 (1, m), 3.28−3.16 (1, m), 2.28−2.14 (3, m), 2.07 (3, s), 1.84−1.04 (22, m), 0.88 (3, t, J = 6.0); ^{13}C NMR ($CDCl_3$) 211.0, 171.0, 70.0, 68.6, 55.2, 54.5, 51.1, 42.9, 36.0, 34.9 (2 C), 31.8, 29.3, 27.1, 26.4, 24.4, 22.9, 22.6, 21.9, 21.0, 14.0; IR (neat) 1747, 1707, 1227. The ^{13}C NMR spectral data are identical to those reported,[2] except that (1) the literature data are at ≈0.8 δ larger chemical shift than our data and (2) Li and Blackman reported two absorptions at δ 21.8 and we observed one at δ 21.0 and another at δ 29.3.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for most compounds (22 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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