Stereoselective Total Synthesis of Ophiocerin C through Two Different Approaches[1])

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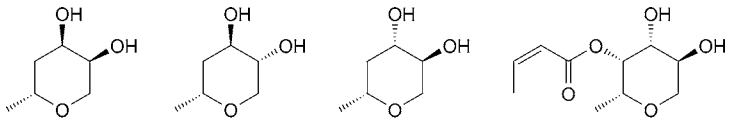
Stereoselective total synthesis of ophiocerin C has been accomplished through two different approaches starting separately from acetaldehyde and from (*R*)-propylene oxide, and *Sharpless* asymmetric dihydroxylation has been employed as the key step in both approaches.

Introduction. – The tetrahydropyran moiety is found in various natural products that possess valuable biological properties [1]. Four tetrahydropyran derivatives, ophiocerins A – D (**1** – **4**, resp.), have been isolated from the fresh water aquatic fungus *Ophiocerus unezuelense* (Magnaporthaceae) [2]. The substitution patterns of these compounds are interesting, and their synthesis is an important topic in current organic chemisty [3]. In continuation of our work [4] on the stereoselective syntheses of natural products, herein we describe the total synthesis of ophiocerin C (**3**) through two different approaches.



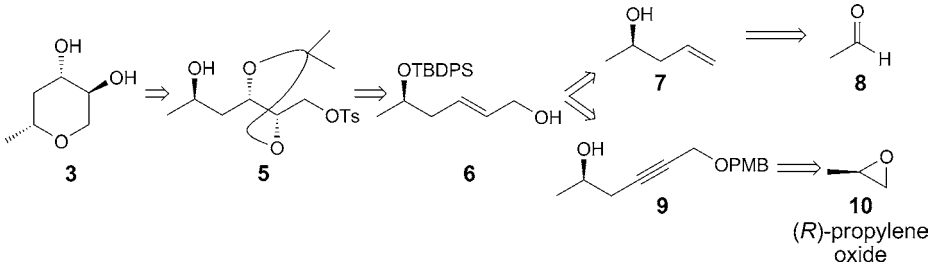
1 **2** **3** **4**

Results and Discussion. – The retrosynthetic analysis (*Scheme 1*) indicates that ophiocerin C (**3**) can be synthesized from the *p*-toluenesulfonate **5** [3g], which, in turn, can be prepared from the allylic alcohol **6**. The latter can be obtained either from the homoallylic alcohol **7**, derived from acetaldehyde (**8**) or from the homopropargyl alcohol **9**, generated from (*R*)-propylene oxide (=(*R*)-2-methyloxirane; **10**).

Acetaldehyde (**8**) was converted to the chiral homoallylic alcohol **7** as described in [5], and the OH group of the latter was protected as ^{t}BuPh$_2$Si (TBDPS) ether (→**11**) [6] by treatment with TBDPSCl and 1*H*-imidazole (*Scheme 2*). Compound **11** was subjected to *Sharpless* asymmetric dihydroxylation [7] using *AD-mix α* in ^{t}BuOH/H$_2$O 1:1 to produce the diol **12**. The diastereoisomers were not separated. The diol **12** was subsequently treated with $NaIO_4$, and the corresponding aldehyde underwent *Wittig* olefination with $Ph_3PCHCOOEt$ to form the unsaturated ester **13** [8]. Reduction of **13**

[1]) Part 76 in the series 'Synthetic Studies on Natural Products'.

Scheme 1. *Retrosynthetic Analysis*



with DIBAL afforded the common intermediate, the allylic alcohol **6**, in good yield. The reaction sequences involving **11** to **13**, and **13** to **6** have been described in [6]. However, we used *AD-mix α* for dihydroxylation of the C=C bond of **11**, though in the next step the chirality has been destroyed. The reason for using *AD-mix α* was that the reaction is pretty easy, and potassium osmate (a constituent of *AD-mix α*) is far less volatile and less unpleasant compared to OsO_4. The yield of the reaction was also high.

The allylic alcohol **6** was also prepared from (*R*)-propylene oxide (=(*R*)-2-methyloxirane; **10**; *Scheme 2*). The latter was treated with the alkyne $HC{\equiv}CCH_2OPMB$ in the presence of BuLi and $BF_3 \cdot OEt_2$ to furnish the homopropargyl alcohol **9**. The free OH group of **9** was protected as TBDPS ether **14**, and the PMB group of **14** was removed with DDQ to generate the propargyl alcohol **15** [9]. Subsequent reduction of **15** with *Red-Al* afforded the intermediate allylic alcohol **6** required for further steps. A reaction analogous to **10** → **6** has been reported earlier using a different protecting group [9]. The OH group of **6** was protected as the PMB ether **16** by treatment with PMBCl and NaH. To generate the diol with required configuration, **16** was again subjected to *Sharpless* asymmetric dihydroxylation using *AD-mix α* in ^{t}BuOH/H_2O 1:1 to furnish the diol **17** along with its one minor diastereoisomer. The required major diol **17** was separated from its diastereoisomer (diastereomer ratio (dr) 93:7) and used for further steps. The two OH groups of **17** were protected by preparing the acetonide **18** by treatment with 2,2-dimethoxypropane and TsOH, and the PMB group of **18** was removed by reaction with DDQ to form the alcohol **19**. Tosylation of **19** with TsCl gave compound **20**, which, on treatment with Bu_4NF yielded the desired *p*-toluenesulfonate **5**. Finally, cyclization of **5** with ^{t}BuOK, followed by removal of the acetonide group with TsOH, afforded ophiocerin C (**3**). It should be mentioned here that the analogous reaction steps for the conversion of **6** to **5** and for the cyclization of **5** to **3** were used earlier for the synthesis of ophiocerin B (**2**) [3g]. The physical and spectroscopic properties of the synthesized ophiocerin C (**3**) were found to be identical to those reported for the naturally occurring compound [2].

In conclusion, we have described the total stereoselective synthesis of ophiocerin C (**3**) through two different approaches starting separately from a nonchiral compound, acetaldehyde (**8**) and a chiral compound, (*R*)-propylene oxide (**10**).

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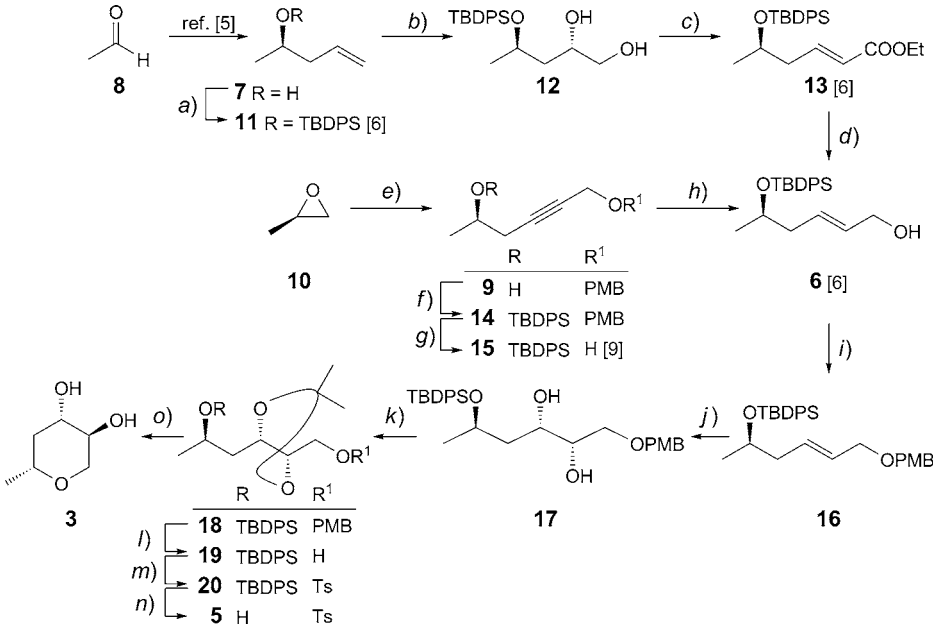
Scheme 2. *Synthesis of Ophiocerin C* (**3**)



a) ^{t}BuPh$_2$SiCl (TBDPSCl), 1*H*-imidazole, cat. 4-(dimethylamino)pyridine (DMAP), CH_2Cl_2, 0° to r.t., 3 h; 90%. *b*) *AD-mix α*, $MeSO_2NH_2$, ^{t}BuOH/H_2O 1 : 1, 0°, 8 h; 82%. *c*) 1. $NaIO_4$, Et_2O/H_2O 3 : 1, r.t., 2 h; 2. Ph_3P=CHCOOEt, CH_2Cl_2, r.t., 8 h; overall yield 84%. *d*) Diisobutylaluminium hydride (DIBAL), CH_2Cl_2, −78°, 1 h; 92%. *e*) 4-Methoxybenzyl (PMB)-protected propargyl alcohol (prop-2-yn-1-ol), BuLi, $BF_3 \cdot Et_2O$, dry THF, −78°, 3 h; 85%. *f*) TBDPSCl, 1*H*-imidazole, cat. DMAP, CH_2Cl_2, 0° to r.t., 4 h; 91%. g) 2,2-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), CH_2Cl_2/H_2O 9 : 1, 0° to r.t., 30 min; 86%. *h*) *Red-Al*, dry THF, 0° to r.t., 2 h; 72%. *i*) NaH, 4-Methoxybenzyl chloride (PMBCl), dry THF, 0° to r.t., 6 h; 86%. *j*) *AD-mix α*, $MeSO_2NH_2$, ^{t}BuOH/H_2O 1 : 1, 0°, 24 h; 81%. *k*) 2,2-Dimethoxypropane, TsOH (cat.), CH_2Cl_2, r.t., 2 h; 92%. *l*) DDQ, CH_2Cl_2/H_2O 9 : 1, 0° to r.t., 30 min; 84%. *m*) TsCl, Et_3N, cat. DMAP, CH_2Cl_2, r.t., 3 h; 89%. *n*) Bu_4NF (TBAF), THF, 0° to r.t., 2 h; 85%. *o*) 1. ^{t}BuOK, Et_2O, 0°, 2 h; 2. TsOH (cat.), MeOH, r.t., 2 h; 79% (two steps).

Experimental Part

General. All commercially available reagents were used directly without further purification unless otherwise stated. The solvents used were all of AR (anal. reagent) grade and were distilled under dry N_2 where necessary. All reactions were performed in pre-dried apparatus unless otherwise stated. The progress of the reactions was monitored by anal. TLC performed on *Merck* silica-gel *60 F_{254}* plates. Yields were of purified compounds unless otherwise stated. Column chromatography (CC): silica gel 60–120 mesh (*Qingdao Marine Chemical*, P. R. China). Optical rotations: *JASCO DIP 300* digital polarimeter. NMR Spectra: *VARIAN Gemini 200* MHz spectrometer with TMS as internal standard in $CDCl_3$; δ in ppm and *J* in Hz. ESI-MS: *WATERS/MICROMASS VG-Autospec* apparatus. HR-MS: *QSTAR XL*, hybrid LC/MS/MS system (*Applied Biosystems*).

*(*tert*-Butyl)[(2*R*)-pent-4-en-2-yloxy]diphenylsilane* (**11**). To a stirred soln. of **7** (500 mg, 5.81 mmol) in dry CH_2Cl_2 (15 ml), 1*H*-imidazole (593 mg, 8.72 mmol) and cat. amount of DMAP were added at 0°, and the mixture was stirred for 20 min. Then, TBDPSCl (1.51 ml, 5.813 mmol) was added at 0°. The mixture was warmed to r.t., stirred for 3 h, and then diluted with CH_2Cl_2 (40 ml). The org. layer was

washed with brine (10 ml), dried (Na_2SO_4), and concentrated, and the residue was subjected to CC to give **11** (1.69 g, 90%). Spectroscopic data: see [6].

*(2S,4R)-4-[(*tert*-Butyl)diphenylsilyloxy]pentane-1,2-diol* (= *2*-O-*[(*tert*-Butyl)(diphenyl)silyl]-1,3-dideoxy*-D-threo-*pentitol*; **12**). To a stirred soln. of **11** (1.6 g, 4.94 mmol) in ^{t}BuOH/H_2O 1:1 (30 ml), $MeSO_2NH_2$ (50 mg, 0.51 mmol), and *AD-mix α* (6.91 g) were added at 0°, and the mixture was stirred for 8 h at the same temp. After completion, the reaction was quenched with Na_2SO_3, the mixture was stirred for another 20 min, and filtered over a *Celite* pad. The residue was extracted with AcOEt (2 × 20 ml). The combined org. layers were washed with brine (5 ml), dried (Na_2SO_4), and concentrated. The residue was purified by CC to obtain **12** (1.44 g, 82%). IR: 3407, 2960, 2931, 2858, 1108, 704. ^{1}H-NMR (200 MHz, $CDCl_3$): 7.88–7.64 (*m*, 4 H); 7.49–7.32 (*m*, 6 H); 4.22–4.01 (*m*, 2 H); 3.93 (br. *s*, 1 H); 3.59–3.33 (*m*, 2 H); 3.22 (br. *s*, 1 H); 1.81–1.63 (*m*, 2 H); 1.02 (*s*, 9 H); 1.00 (*d*, *J* = 7.0, 3 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 135.9; 134.0; 129.9; 127.8; 68.7; 68.0; 64.5; 42.1; 27.0; 22.2; 18.8. ESI-MS: 381 ([*M* + Na]$^+$). Anal. calc. for $C_{21}H_{30}O_3Si$ (358.55): C 70.35, H 8.43; found: C 70.29, H 8.41.

*Ethyl (2*E*,5*R*)-5-[[(*tert*-Butyl)(diphenyl)silyl]oxy}hex-2-enoate* (**13**). To a stirred soln. of **12** (1.3 g, 3.63 mmol) in Et_2O/H_2O 3:1 (10 ml) at 0°, $NaIO_4$ (1.55 g, 7.26 mmol) was added slowly in portions. The mixture was warmed to r.t., stirred for 2 h, and then the reaction was quenched with $NaHCO_3$ (10 ml) slowly. The org. layer was separated, washed with brine (5 ml), dried (Na_2SO_4), and concentrated. The aldehyde was used immediately for the next step. To a stirred soln. of aldehyde (1.10 g, 3.37 mmol) in dry CH_2Cl_2 (12 ml), ethyl (triphenyl-λ^5-phosphanylidene)acetate (1.40 g, 4.04 mmol) was added, and the mixture was stirred at r.t. for 8 h. It was then concentrated, and the residue was purified by CC to yield **13** (1.2 g, 84%). Spectroscopic data: see [6].

*(2*E*,5*R*)-5-[[(*tert*-Butyl)(diphenyl)silyl]oxy}hex-2-en-1-ol* (**6**). For synthetic procedure and spectroscopic data, see [6].

*(2*R*)-6-[(4-Methoxybenzyl)oxy]hex-4-yn-2-ol* (**9**). To a stirred soln. of PMB-protected propargyl alcohol (= prop-2-yn-1-ol; 3.33 g, 18.96 mmol) in dry THF (2 × 20 ml), BuLi (1.6M in hexane, 16.16 ml, 25.86 mmol) was added under N_2 at −78°, and the mixture was stirred for 30 min. The mixture was sequentially treated with $BF_3 \cdot OEt_2$ (2.55 ml, 20.68 mmol) and a soln. of *(*R*)-2-methyloxirane* **10** (1.2 ml, 17.24 mmol) in dry THF at 10-min intervals and stirred for 3 h at the same temp. The reaction was quenched with sat. aq. NH_4Cl (30 ml). The resulting mixture was diluted with AcOEt (2 × 20 ml), washed with H_2O (20 ml) and brine (10 ml), dried (Na_2SO_4), and concentrated. The residue was purified by CC to obtain **9** (3.43 g, 85%). $[\alpha]_D^{27} = -5.8$ (*c* = 1.0, $CHCl_3$). IR: 3446, 2931, 2859, 1513, 1248, 1073. ^{1}H-NMR (200 MHz, $CDCl_3$): 7.30 (*d*, *J* = 8.0, 2 H); 6.88 (*d*, *J* = 8.0, 2 H); 4.52 (*s*, 2 H); 4.12 (*s*, 2 H); 3.93 (*m*, 1 H); 3.80 (*s*, 3 H); 2.49–2.23 (*m*, 3 H); 1.24 (*d*, *J* = 7.0, 3 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 159.4; 129.6; 129.5; 113.2; 83.0; 78.1; 71.0; 65.9; 57.1; 55.2; 29.2; 22.1. ESI-MS: 257 ([*M* + Na]$^+$). Anal. calc. for $C_{14}H_{18}O_3$ (234.29): C 71.77, H 7.74; found: C 71.70, H 7.69.

*(*tert*-Butyl)({(2*R*)-6-[(4-methoxybenzyl)oxy]hex-4-yn-2-yl}oxy)diphenylsilane* (**14**). Compound **14** was prepared as described for **11**. Yield: 6.27 g (91%). $[\alpha]_D^{27} = +12.1$ (*c* = 2.0, $CHCl_3$). IR: 3447, 2958, 2931, 2857, 1108, 703. ^{1}H-NMR (200 MHz, $CDCl_3$): 7.74–7.65 (*m*, 4 H); 7.48–7.32 (*m*, 6 H); 7.26 (*d*, *J* = 8.0, 2 H); 6.89 (*d*, *J* = 8.0, 2 H); 4.49 (*s*, 2 H); 4.09 (*s*, 2 H); 3. 98 (*m*, 1 H); 3.80 (*s*, 3 H); 2.45–2.24 (*m*, 2 H); 1.21 (*d*, *J* = 7.0, 3 H); 1.05 (*s*, 9 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 159.2; 136.1; 136.0; 134.2; 129.8; 128.7; 113.4; 84.0; 77.9; 71.2; 68.8; 57.2; 55.0; 29.4; 27.3; 23.2; 19.1. ESI-MS: 495 ([*M* + Na]$^+$). Anal. calc. for $C_{30}H_{36}O_3Si$ (472.69): C 76.23, H 7.68; found: C 76.20, H 7.64.

*(5*R*)-5-[[(*tert*-Butyl)(diphenyl)silyl]oxy}hex-2-yn-1-ol* (**15**). To a stirred soln. of **14** (6.0 g, 12.71 mmol) in CH_2Cl_2/H_2O 9:1 (40 ml), DDQ (3.46 g, 15.25 mmol) was added at 0°, and the soln. was stirred for 20 min at r.t. The reaction was quenched with sat. $NaHCO_3$ soln. (20 ml), and the mixture was extracted with CH_2Cl_2 (2 × 20 ml), and washed with H_2O (20 ml) and brine (10 ml). The combined org. layers were dried (Na_2SO_4), concentrated, and purified by CC to obtain **15** (3.84 g, 86%). Spectroscopic data: see [9].

*(2*E*,5*R*)-5-[[(*tert*-Butyl)(diphenyl)silyl]oxy}hex-2-en-1-ol* (**6**). For synthetic procedure and spectroscopic data see ref. [9].

*(*tert*-Butyl)({(2*R*,4*E*)-6-[(4-methoxybenzyl)oxy]hex-4-en-2-yl}oxy)diphenylsilane* (**16**). Compound **6** (2.5 g, 7.06 mmol) in dry THF (5 ml) was added to a suspension of NaH (310 mg, 7.76 mmol) in THF (20 ml) under N_2 at 0°, and the mixture was stirred for 30 min. Then, a soln. of PMBCl (1.14 g, 8.47 mmol)

was added, and the mixture was stirred for 6 h at r.t. The reaction was quenched with sat. aq. NH_4Cl (10 ml) soln., and the mixture was extracted with AcOEt (2 × 20 ml). The org. layer was washed with H_2O (10 ml) and brine (5 ml), dried (Na_2SO_4), evaporated, and purified by CC to obtain **16** (2.88 g, 86%). $[\alpha]_D^{27} = -10.2$ ($c = 0.5$, $CHCl_3$). IR: 3450, 2931, 2856, 1512, 1246, 1106, 703. ^{1}H-NMR (200 MHz, $CDCl_3$): 7.73–7.65 (*m*, 4 H); 7.48–7.32 (*m*, 6 H); 7.31–7.23 (*m*, 2 H); 6.92–6.82 (*m*, 2 H); 5.70–5.49 (*m*, 2 H); 4.51–4.38 (*m*, 4 H); 3.90 (*m*, 1 H); 3.81 (*s*, 3 H); 2.28–2.14 (*m*, 2 H); 1.09 (*d*, $J = 7.0$, 3 H); 1.03 (*s*, 9 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 159.4; 136.1; 134.8; 129.2; 129.0; 128.8; 127.3; 127.1; 113.3; 71.2; 70.3; 68.4; 55.2; 42.1; 27.2; 22.2; 19.0. ESI-MS: 497 ($[M + Na]^+$). Anal. calc. for $C_{30}H_{38}O_3Si$ (474.71): C 75.90, H 8.07; found: C 75.88, H 8.02.

5-O-*[(*tert-*Butyl)(diphenyl)silyl]-4,6-dideoxy-1*-O-*(4-methoxybenzyl)*-D-xylo-*hexitol* (**17**). Compound **17** was prepared as described for **12**. Yield: 2.34 g, 81%. $[\alpha]_D^{27} = -1.4$ ($c = 0.4$, $CHCl_3$). IR: 3448, 2929, 2857, 1632, 1108, 766. ^{1}H-NMR (200 MHz, $CDCl_3$): 7.75–7.68 (*m*, 4 H); 7.47–7.33 (*m*, 6 H); 7.22 (*d*, $J = 8.0$, 2 H); 6.88 (*d*, $J = 8.0$, 2 H); 4.50–4.44 (*m*, 2 H); 4.23–4.01 (*m*, 2 H); 3.80 (*s*, 3 H); 3.58–3.46 (*m*, 3 H); 1.84–1.78 (*m*, 2 H); 1.08 (*s*, 9 H); 1.02 (*d*, $J = 7.0$, 3 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 136.2; 134.9; 130.0; 129.8; 129.6; 127.5; 114.2; 73.1; 71.7; 70.2; 69.1; 68.8; 54.8; 40.7; 26.3; 19.6. ESI-MS: 531 ($[M + Na]^+$). Anal. calc. for $C_{30}H_{40}O_5Si$ (508.72): C 70.83, H 7.93; found: C 70.76, H 7.90.

5-O-*[(*tert-*Butyl)(diphenyl)silyl]-4,6-dideoxy-1*-O-*(4-methoxybenzyl)-2,3*-O-*(1-methylethylidene)*-D-xylo-*hexitol* (**18**). To a stirred soln. of **17** (2.2 g, 4.33 mmol) in CH_2Cl_2 (20 ml), $Me_2C(OMe)_2$ (0.63 ml, 5.19 mmol) and TsOH (cat.) were added, and the mixture was stirred at r.t. for 2 h. The reaction was then quenched with sat. aq. $NaHCO_3$ (20 ml). The aq. layer was extracted with CH_2Cl_2 (30 ml), and the combined org. layers were dried (Na_2SO_4) and concentrated. The residue was purified by CC to furnish **18** (2.18 g, 92%). $[\alpha]_D^{27} = +2.9$ ($c = 0.5$, $CHCl_3$). IR: 3449, 2929, 2855, 1246, 1105, 768, 702. ^{1}H-NMR (200 MHz, $CDCl_3$): 7.72–7.63 (*m*, 4 H); 7.44–7.21 (*m*, 8 H); 6.89 (*d*, $J = 8.0$, 2 H); 4.54–4.42 (*m*, 2 H); 4.14–3.98 (*m*, 2 H); 3.82 (*s*, 3 H); 3.71 (*m*, 1 H); 3.51–3.44 (*m*, 2 H); 1.81–1.70 (*m*, 2 H); 1.38 (*s*, 3 H); 1.22 (*s*, 3 H); 1.08 (*d*, $J = 8.0$, 3 H); 1.05 (*s*, 9 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 136.0; 129.5; 129.3; 129.0; 127.6; 127.2; 113.8; 108.3; 80.4; 75.8; 73.3; 70.4; 67.5; 55.2; 43.5; 27.6; 24.7; 23.0; 19.2. ESI-MS: 571 ($[M + Na]^+$). Anal. calc. for $C_{33}H_{44}O_5Si$ (548.78): C 72.22, H 8.08; found: C 72.19, H 8.05.

5-O-*[(*tert-*Butyl)(diphenyl)silyl]-4,6-dideoxy-2,3*-O-*(1-methylethylidene)*-D-xylo-*hexitol* (**19**). Compound **19** was prepared as described for **15**. Yield: 1.31 g (84%). $[\alpha]_D^{27} = -6.2$ ($c = 1.0$, $CHCl_3$). IR: 3448, 2932, 2858, 1107, 703. ^{1}H-NMR (200 MHz, $CDCl_3$): 7.86–7.63 (*m*, 4 H); 7.46–7.38 (*m*, 6 H); 4.10 (*m*, 1 H); 3.82 (*m*, 1 H); 3.72 (*m*, 1 H); 3.58 (*m*, 1 H); 1.71–1.52 (*m*, 2 H); 1.38 (*s*, 3 H); 1.30 (*s*, 3 H); 1.09 (*d*, $J = 7.0$, 3 H); 1.02 (*s*, 9 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 136.2; 134.9; 129.9; 127.8; 108.8; 81.9; 73.8; 67.2; 61.6; 42.9; 27.1; 24.3; 22.5; 19.1. ESI-MS: 451 ($[M + Na]^+$). Anal. calc. for $C_{25}H_{36}O_4Si$ (428.64): C 70.05, H 8.47; found: C 70.03, H 8.41.

5-O-*[(*tert-*Butyl)(diphenyl)silyl]-4,6-dideoxy-2,3*-O-*(1-methylethylidene)-1*-O-*[(4-methylphenyl)-sulfonyl]*-D-xylo-*hexitol* (**20**). To a stirred soln. of **19** (1.2 g, 2.80 mmol) in CH_2Cl_2 (15 ml), Et_3N (0.58 ml, 4.20 mmol) and DMAP (34 mg, 0.28 mmol) were added at r.t., and the mixture was stirred for 10 min. TsCl (639 mg, 3.36 mmol) was then added, and stirring was continued at r.t. for 3 h. The reaction was quenched with sat. aq. NH_4Cl (3 ml), and the mixture was extracted with CH_2Cl_2 (30 ml). The combined org. layers were washed with H_2O (10 ml) and brine (5 ml), then dried (Na_2SO_4), and concentrated. The residue was purified by CC to obtain **20** (1.45 g, 89%). $[\alpha]_D^{27} = -6.5$ ($c = 0.4$, $CHCl_3$). IR: 3449, 2928, 2856, 1369, 1178, 1106, 770, 703. ^{1}H-NMR (200 MHz, $CDCl_3$): 7.84–7.62 (*m*, 6 H); 7.48–7.30 (*m*, 8 H); 4.11–3.95 (*m*, 4 H); 3.67 (*m*, 1 H); 2.45 (*s*, 3 H); 1.61–1.50 (*m*, 2 H); 1.28 (*s*, 3 H); 1.22 (*s*, 3 H); 1.07 (*d*, $J = 7.0$, 3 H); 1.02 (*s*, 9 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 145.2; 136.4; 135.0; 133.2; 129.4; 129.1; 128.0; 127.8; 127.7; 109.9; 78.5; 74.1; 43.9; 29.6; 27.0; 24.2; 22.8; 18.9. ESI-MS: 605 ($[M + Na]^+$). Anal. calc. for $C_{32}H_{42}O_6SSi$ (582.82): C 65.94, H 7.26; found: C 65.89, H 7.22.

4,6-Dideoxy-2,3-O-*(1-methylethylidene)-1*-O-*[(4-methylphenyl)sulfonyl]*-D-xylo-*hexitol* (**5**). To a stirred soln. of **20** (1.0 g, 1.71 mmol) in dry THF (10 ml), 1M soln. of Bu_4NF (5.15 ml, 5.15 mmol) in THF was added at 0°, and the mixture was stirred for 2 h at r.t. The reaction was quenched with sat. aq. NH_4Cl (15 ml), and the mixture was extracted with CH_2Cl_2 (30 ml). The combined org. layers were washed with H_2O (10 ml) and brine (5 ml), dried (Na_2SO_4), and concentrated. The residue was purified by CC to obtain **5** (0.5 g, 85%). $[\alpha]_D^{27} = +2.0$ ($c = 0.2$, $CHCl_3$). IR: 3443, 2926, 1456, 1178, 780. ^{1}H-NMR (200 MHz, $CDCl_3$): 7.80 (*d*, $J = 8.0$, 2 H); 7.38 (*d*, $J = 8.0$, 2 H); 4.18–4.03 (*m*, 4 H); 4.00 (*m*, 1 H); 3.85

(*m*, 1 H); 2.42 (*s*, 3 H); 1.74–1.62 (*m*, 2 H); 1.39 (*s*, 3 H); 1.32 (*s*, 3 H); 1.23 (*d*, $J = 7.0$, 3 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 143.3; 130.7; 128.1; 126.0; 107.6; 76.5; 73.6; 67.2; 63.3; 39.2; 25.2; 24.4; 22.1; 21.6; 19.9. ESI-MS: 367 ($[M + Na]^+$). Anal. calc. for $C_{16}H_{24}O_6S$ (344.42): C 55.80, H 7.02; found: C 55.78, H 7.0.

Ophiocerin C (=*1,5-Anhydro-4,6-dideoxy*-D-xylo-*hexitol*; **3**). To a soln. of **5** (100 mg, 0.3 mmol) in dry Et_2O (2 ml) was added to a stirred suspension of ^{t}BuOK (71.6 mg, 0.63 mmol) in dry Et_2O (5 ml) at 0°, and the mixture was stirred for 2 h at 0°. The reaction was quenched with sat. aq. NH_4Cl (5 ml), and the mixture was extracted with Et_2O (10 ml). The combined org. layers were washed with H_2O and brine and then treated with TsOH (10 mg) and MeOH (5 ml) with stirring at r.t. for 2 h. The reaction was quenched with sat. aq. $NaHCO_3$ soln., and the solvents (MeOH and Et_2O) were evaporated under reduced pressure. The residue was extracted with CH_2Cl_2 (2 × 20 ml), and the combined org. layers were washed with H_2O and brine, then dried (Na_2SO_4), and concentrated. The residue was purified by CC to obtain **3** (30 mg, 79% over two steps). White solid. M.p. 82–83°. Spectroscopic data: see [3f].

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