Total Syntheses of Squamocin A and Squamocin D, Bi-tetrahydrofuran Acetogenins from Annonaceae

Ulrich Emde[a] and Ulrich Koert*[a]

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The total syntheses of the *Annonaceous* acetogenins squamocin A and squamocin D have been achieved. The synthesis follows a modular strategy, wherein a left-side chain, the central bis-THF core and the right-side chain are assembled together. Key reactions are additions of organomagnesium compounds to bi-THF aldehydes. At the end of the synthesis the butenolide moiety was introduced. This modular synthetic approach should be useful for the synthesis of other related natural products as well as pharmacologically interesting analogs.

Introduction

The acetogenins from *Annonaceae* are a class of natural products with remarkable biological properties, e.g. as antitumor agents, immunosuppressants or pesticides.[1] More than 250 compounds from various plant species have been isolated and characterised.[1] Among them is a subclass containing a bi-THF subunit as a characteristic structural feature. Furthermore, these compounds have in common a left alkyl side chain and a right alkyl side chain. A butenolide is located at the end of the right-side chain. The bi-THF acetogenins show the most promising in vitro activity and selectivity against cancer cell lines. Studies concerned with the mode of action indicate a blockage of mitochondrial complex **I** (NADH-ubiquinone oxidoreductase).[2] The left alkyl side chain seems to be important for membrane fixation. The membrane-bound conformation of *Annonaceous* acetogenins and its relation to complex **I** inhibition has been investigated.[3] In addition, these compounds inhibit an NADH oxidase, which is overexpressed in the plasma membrane of tumors but not in normal cells.[4] The acetogenins induce a decrease of the tumor-cell ATP level, which has an inhibitory effect on multiple drug resistance caused by ATP-driven transporter systems.

Representative members of the bi-THF acetogenins with a *threo-anti-threo* configuration are squamocin A, squamocin D, squamocin G and squamocin H (Figure 1).[5] Depending on the plant source different names were given in the past for the same compound. Squamocin A[5] is synonymous to annonin I[6] and rollinicin.[7] Its relative and absolute configuration was assigned by a combination of X-ray structure analysis and spectroscopic methods.[5]–[7] Squamocin D[5] corresponds to asiminacin[8] and squamocin G[5] is known as bullatacin[9] or rolliniastatin-2.[10] Squamocin H[5] is called asimicin[11] or annonastatin.[12]

Numerous contributions highlight the importance of an efficient synthetic access to the *Annonaceous* acetogenins

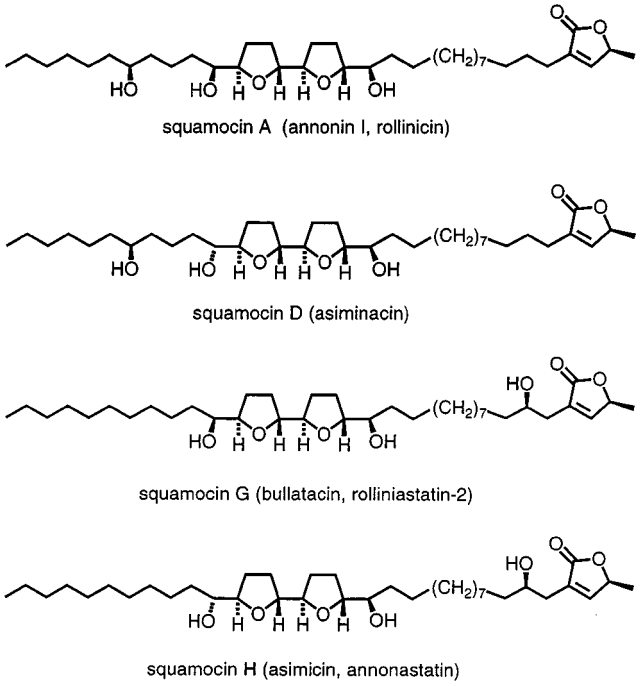

Figure 1. Structures of selected bi-THF-acetogenins

(adjacent THF-THP,[13] nonadjacent THF-THP,[14] tri-THF,[15] adjacent bi-THF,[16] nonadjacent bi-THF,[17] mono-THF,[18] other acetogenins[19]). Here we report in detail on the total syntheses of squamocin A and squamocin D.[16d]

Results and Discussion

Our retrosynthetic analysis of squamocin A and D leads to an introduction of the butenolide unit at the end of the synthesis (Scheme 1). A protected hydroxy group at C1 in **1** and **2** is a suitable precursor for the butenolide. Oxidation of the hydroxy group to the corresponding carboxylic acid and reaction with propene oxide would result in a butyrolactone. Introduction of the C2–C35 double bond could

[a] Institut für Chemie der Humboldt-Universität zu Berlin
Hessische Straße 1–2, 10115 Berlin, Germany
Fax: (internat.) + 49-(0)30/2093-7266
E-mail: koert@lyapunov.chemie.hu-berlin.de

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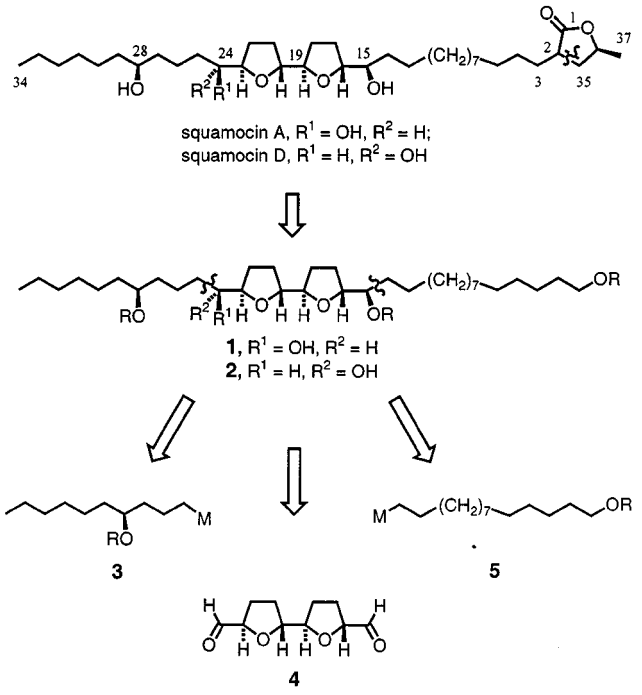
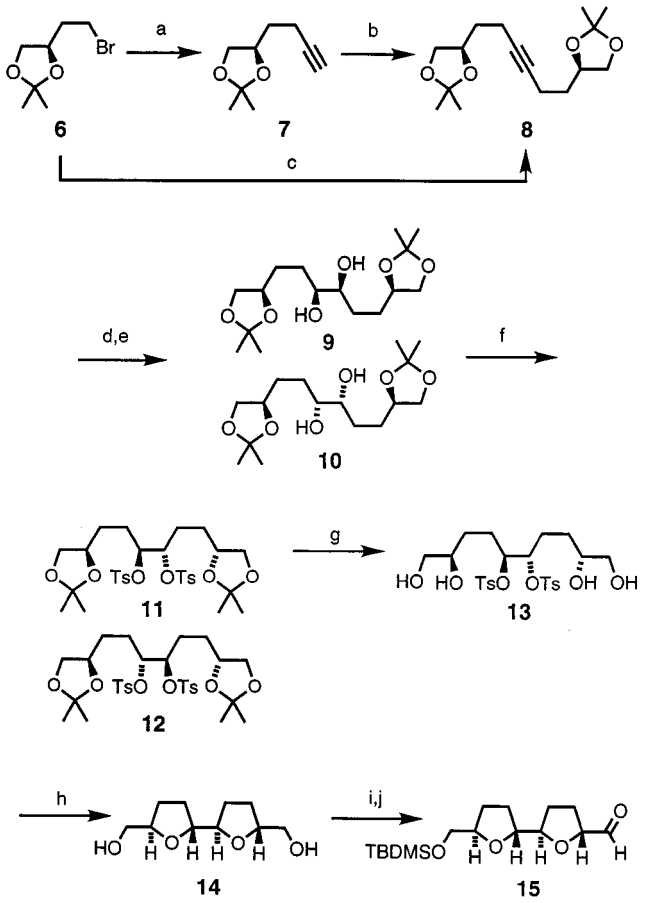


Scheme 1. Retrosynthetic analysis of squamocin A and squamocin D



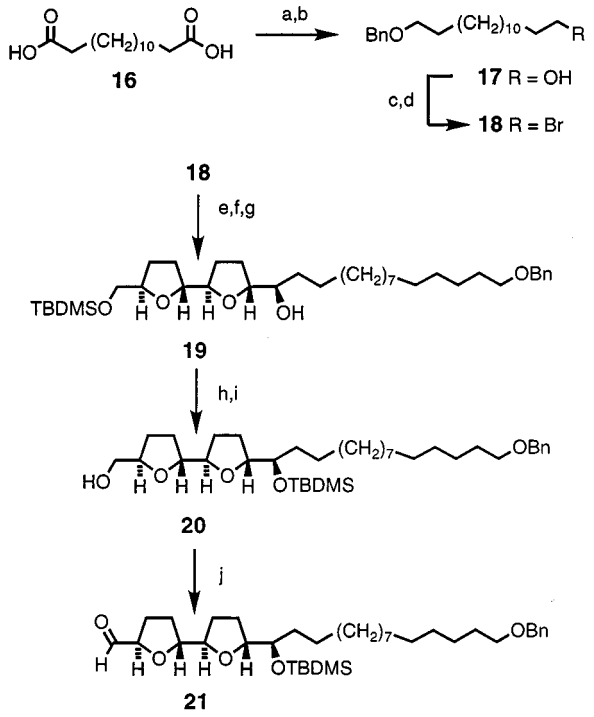
Scheme 2. (a) LiC≡CH·en, NH_3/THF (2.5:1), −33 °C, 2 h, 82%; (b) *n*BuLi, **6**, NH_3/THF/DMSO (2.5:1:1), −33 °C, 4 h, 85%; (c) LiC≡CH·en, *n*BuLi, NH_3/THF (2.5:1), −33 °C, 3 h, then *n*BuLi, with addition of DMSO as a co-solvent, **6**, −33 °C, 4 h, 45%; (d) Na, NH_3/THF (5:1), −33 °C, 4 h, 92%; (e) K_2CO_3, $K_3[Fe(CN)_6]$, $K_2OsO_4{\cdot}H_2O$, $(DHQ)_2PHAL$, $CH_3SO_2NH_2$, *t*BuOH/H_2O (1:1), 0 °C, 18 h, 91%, ds = 98:2; (f) *p*TsCl, py, CH_2Cl_2, 0 °C, 12 h, 86%; (g) HOAc/H_2O (5:1), room temp., 12 h, 99%; (h) NaH, THF, 0 °C, 4 h, 92%; (i) TBDMSCl, imidazole, CH_2Cl_2, 0 °C, 2 h, 43% and diprotected bifuran 40%; (j) $(COCl)_2$, DMSO, NEt_3, CH_2Cl_2, −60 → −40 °C, 1.5 h, 91%; TBDMS = *tert*-butyldimethylsilyl, *p*Ts = *p*-toluenesulfonyl, py = pyridine, en = ethylenediamine

then give rise to the target substructure. The next retrosynthetic steps involve the disconnection at C15−C16 and C23−C24 leading to the corresponding organometallic side chains **3** and **5** and to the dialdehyde **4**. In the synthetic sequence it would be advantageous to subsequently generate and react the two aldehyde functions. The resulting strategy has a common entry to both squamocins with a bifurcation point at the addition of the left-side chain.

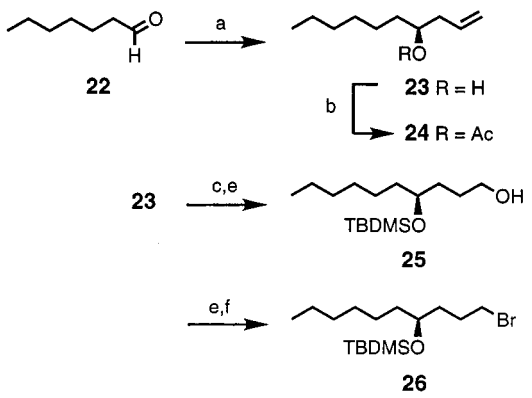
The starting point for the synthesis of the bi-THF core was bromide **6**[20] (Scheme 2). An optimized route[21,22] to the bi-THF diol **13**[23] was followed. Alkylation of bromide **6** with acetylene gave alkyne **7** in 82% yield, which was allowed to react again with the bromide **6** to yield the C_2-symmetric alkyne **8**. It was found that the solvent combination NH_3/THF/DMSO (2.5:1:1) and rapid addition of *n*BuLi were crucial for obtaining a high yield (85%) in the second alkylation step. An one-pot double alkylation of **6** to **8** was possible in 45% yield. An (*E*)-selective reduction of alkyne **8** to the corresponding alkene followed by a Sharpless dihydroxylation[24] gave, with a "self-mixed" AD-mix α, the two diastereomeric diols **9** and **10** in a ratio greater than 98:2. On using a commercially available AD-mix α, a diastereoselectivity between 90:10 and 98:2 was observed. The two diastereomers **9** and **10** were difficult to distinguish by their NMR spectra. Therefore, the selectivity was determined at the bis(tosylate) stage. Double tosylation of **9**/**10** gave the acetonide-protected bis(tosylates) **11** and **12**. Depending on the diastereoselectivity of the dihydroxylation step, varying amounts of the minor epimer **12** were chromatographically separated at this stage. Double deprotection of **11** gave the tetrahydroxy bis(tosylate) **13**. A 5-ring selective multiple Williamson reaction[21,22] of **13** gave the *trans-threo-trans* bi-THF diol **14** in 92% yield. Mono-TBDMS protection of **14** followed by Swern oxidation provided the bi-THF aldehyde **15**.

The right-side chain was prepared from the dicarboxylic acid **16** (Scheme 3). Borane reduction furnished a diol, which was monobenzylated to the monoalcohol **17**. The latter was transformed via the tosylate into the bromide **18**. Next, the Grignard reagent prepared from **18** was allowed to react with aldehyde **15**. A PCC oxidation of the resulting alcohol and a subsequent stereoselective L-selectride® reduction[25] of the ketone led to the alcohol **19**. The stereoselectivity of the L-selectride® reduction was 98:2, as determined by NMR spectroscopy. Protection of the secondary hydroxy group in **19** followed by the selective (89%) deprotection of the primary TBDMS group using CSA in CH_2Cl_2/MeOH gave the alcohol **20**. The latter could be converted into the aldehyde **21** by a Swern oxidation.

The left-side chain contains a stereogenic center at C-28. The elaboration of this partial structure (Scheme 4) was



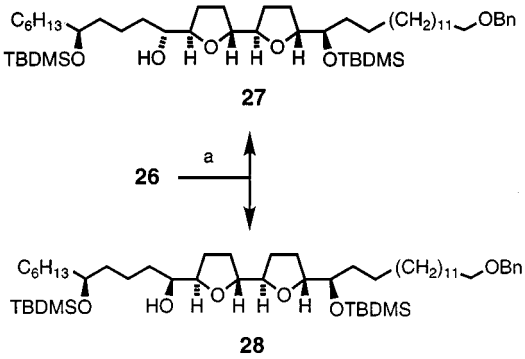
Scheme 3. (a) $BH_3{\cdot}Me_2S$, THF, room temp. → 50 °C, 4 h, 98%; (b) BnCl, KOH, 110 °C, 5 h, 61%; c) *p*TsCl, py, CH_2Cl_2, 0 °C, 12 h, 93%; (d) LiBr, THF, 0 °C → 45 °C, 5 h, 88%; (e) Mg, **18**, 1,2-dibromoethane, Et_2O, room temp. → 40 °C, 1 h, then **15**, Et_2O, −40 °C → room temp., 3 h, 76%; f) PCC, 4 Å molecular sieves, room temp., 1 h, 72%; (g) L-selectride®, THF, −100 °C → −70 °C, 2 h, 96%, ds = 98:2; (h) TBDMSCl, imidazole, CH_2Cl_2, 0 °C, 12 h, 87%; (i) CSA, CH_2Cl_2/MeOH (1:1), 2 h, −10 °C → 0 °C, 89%; (j) $(COCl)_2$, DMSO, NEt_3, CH_2Cl_2, −60 → −40 °C, 1.5 h, 90%; Bn = benzyl, PCC = pyridiniumchlorochromate, CSA = camphorsulfonic acid



Scheme 4. (a) (*R*)-BINOL, Ti(O*i*Pr)$_4$, 4 Å molecular sieves, allyltributylstannane, CH_2Cl_2, −25 °C, 5 d, 90%, *ee* 99:1 (determined by chiral GC); (b) Ac_2O, py, cat. DMAP, room temp., 36 h, 52%; (c) TBDMSCl, imidazole, CH_2Cl_2, 0 °C, 12 h, 98%; (d) 9-BBN, THF, 0 °C → room temp., 18 h, 91%; (e) *p*TsCl, py, CH_2Cl_2, 0 °C, 12 h, 82%; (f) LiBr, THF, 0 °C → 35 °C, 30 h, 93%; DMAP = 4-dimethylaminopyridine, 9-BBN = 9-borabicyclo[3.3.1]nonane, BINOL = 2,2′-dihydroxy-1,1′-binaphthyl

accomplished by an enantioselective allylation of heptanal **22** to the homoallylic alcohol **23** using Keck's procedure.[26] *R*-BINOL/Ti(O*i*Pr)$_4$ was used as the chiral Lewis acid. The enantioselectivity of the allylation was 99:1, as determined by GC analysis. In order to obtain such a high selectivity on a 30-mmol scale, it was necessary to reflux the catalyst with molecular sieves for 90 min before adding further reagents. The (*S*) configuration of the new chiral center was proven by conversion of the alcohol **23** into the acetate **24** followed by comparison of the chiroptical data for **24** and ***ent*-24**[27] {found: $[\alpha]_D^{20} = -23.5$ (c = 0.23, $CHCl_3$), ref.[27]: $[\alpha]_D^{20} = +23.7$ for ***ent*-24** (c = 1.0, $CHCl_3$)}. A TBDMS protection of **23** and a subsequent hydroboration with 9-BBN gave the primary alcohol **25**, which was then converted via its tosylate into bromide **26**.

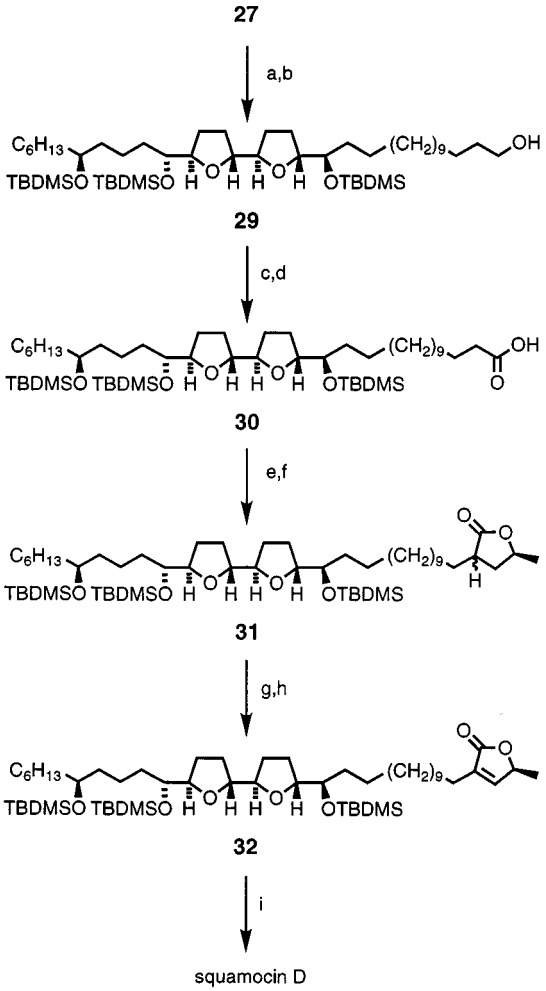
For the attachment of the left-side chain, bromide **26** was converted into the corresponding Grignard reagent (Scheme 5). Reaction of this Grignard reagent with aldehyde **21** gave the two epimers, **27** and **28**, in a 2:1 ratio. The two epimers could be separated by column chromatography. The stereochemical assignment of the two epimers was based on the ^{13}C-NMR chemical shift[6] of the new stereocenter (**27**: δ = 74.0; **28**: δ = 71.2).



Scheme 5. (a) Mg, **26**, 1,2-dibromoethane, Et_2O, room temp. → 40 °C, 1 h, then $CuBr{\cdot}Me_2S$, **21**, Et_2O, −60 °C → room temp., 12 h, 80%; separation of the two compounds by CC, ds 2:1 in favour of epimer **27**

Now that the two side chains had been attached to the bi-THF subunit, the introduction of the butenolide remained to be accomplished. For the synthesis of squamocin D, the alcohol **27** was further elaborated (Scheme 6).

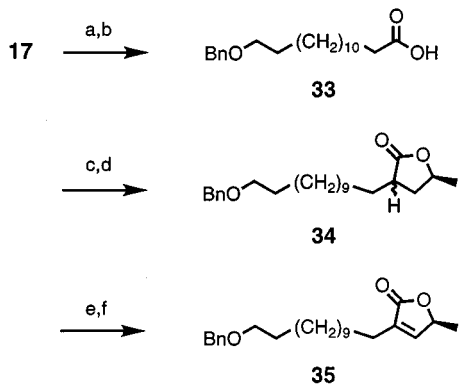
TBDMS protection followed by hydrogenolysis of the benzyl ether function provided alcohol **29**. A two-step oxidation (Swern/chlorite) of **29** gave the carboxylic acid **30**. Treatment of the dianion of **30** with (*S*)-propylene oxide[28] afforded a hydroxy carboxylic acid, which was cyclized via a mixed anhydride to the butyrolactone **31**. It was found that the addition of LiCl to the solvent was necessary for a good turnover in the reaction of the dianion with the epoxide. The dilithium salt of the carboxylic acid may form an intramolecular complex with the bi-THF moiety, resulting in a decreased reactivity of the dianion. An indication for this situation came from model studies for the introduction of the butenolide (Scheme 7). Here, the carboxylic acid **33** was converted with good turnover into the butyrolactone **34**. The addition of LiCl was not necessary in this case, where the complexing bi-THF subunit is absent. Compound **34** was transformed into the butenolide **35** by selenation and subsequent *syn* elimination of the corresponding selenium oxide.



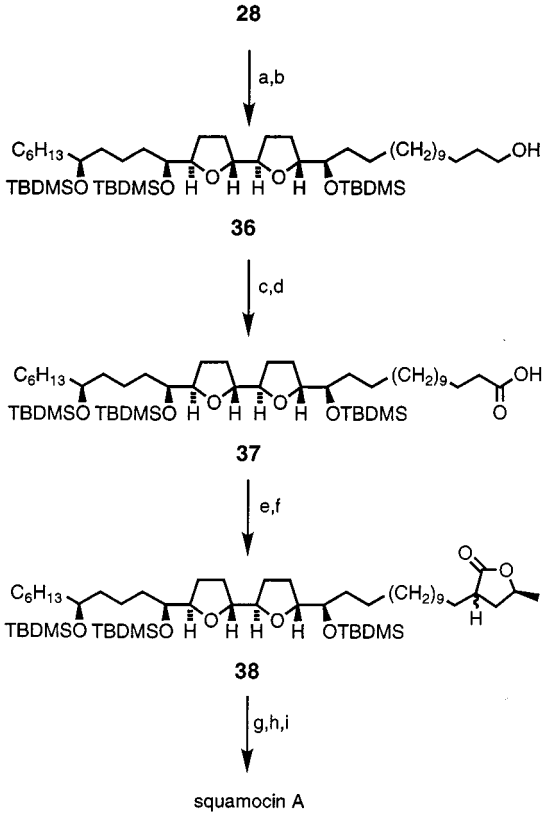
Scheme 6. (a) TBDMSOTf, 2,6-lutidine, CH_2Cl_2, −20 °C, 45 min, 91%; (b) H_2 (1 atm), 10% Pd/C, ethyl acetate/*i*PrOH (1:1), room temp., 3 h, 99%; (c) $(COCl)_2$, DMSO, NEt_3, CH_2Cl_2, −60 → −40 °C, 1.5 h; (d) $NaOCl_2$, $NaH_2PO_4{\cdot}2\ H_2O$, 2-methyl-2-butene/*t*BuOH/H_2O (1:3:5), 2.5 h, 95% from **29**; (e) LDA, THF saturated with LiCl, 0 → 20 °C, 40 min, then (*S*)-propylene oxide, 0 °C → room temp., 2.5 h; (f) PivCl, NEt_3, CH_2Cl_2, room temp., 30 min, 52% from **30**; (g) KHMDS, THF, 0 °C → room temp., 50 min, then PhSeCl, 2.5 h; (h) MMPP, THF/MeOH (1:1), room temp., 20 min, 40% from **31**; (i) 5% HF in CH_3CN, THF, room temp., 2 h, 79%; MMPP = magnesium monoperoxophthalate

The C2−C35 double bond of the natural product was introduced by the same method (Scheme 6). Selenation of **31** followed by *syn* elimination of the selenium oxide resulted in the butenolide derivative **32**. Cleavage of the silyl protecting groups in **32** provided squamocin D ($[\alpha]_D^{21} = +20$ ($c = 0.097$ in $CHCl_3$), which was found to be identical with the naturally occurring product in respect to the spectroscopic data.

On using the same reaction sequence the alcohol **28** was converted into squamocin A (Scheme 8). Compound **28** was converted via the alcohol **36** into the carboxylic acid **37**. The latter was transformed into the butyrolactone **38**. Introduction of the double bond and removal of the TBDMS protecting groups gave the target compound squamocin A.



Scheme 7. (a) $(COCl)_2$, DMSO, NEt_3, CH_2Cl_2, −60 → −40 °C, 1.5 h, 94%; (b) $NaOCl_2$, $NaH_2PO_4{\cdot}2\ H_2O$, 2-methyl-2-butene/*t*BuOH/H_2O (1:3:5), 2.5 h, 99%; (c) LDA, THF, 0 → 20 °C, 40 min, then (*S*)-propylene oxide, 0 °C → room temp., 2.5 h; (d) PivCl, NEt_3, CH_2Cl_2, room temp., 30 min, 64% from **33**; (e) KHMDS, THF, 0 °C → room temp., 50 min, then PhSeCl, 2.5 h; (f) MMPP, THF/MeOH (1:1), room temp., 20 min, 70% from **34**



Scheme 8. (a) TBDMSOTf, 2,6-lutidine, CH_2Cl_2, −20 °C, 2 h; (b) H_2 (1 atm), 10% Pd−C, ethyl acetate/*i*PrOH (1:1), room temp., 12 h, 75% from **28**; (c) $(COCl)_2$, DMSO, NEt_3, CH_2Cl_2, −60 → −40 °C, 1.5 h; (d) $NaOCl_2$, $NaH_2PO_4{\cdot}2\ H_2O$, 2-methyl-2-butene/*t*BuOH/H_2O (1:3:5), 12 h, 89% from **36**; (e) LDA, THF saturated with LiCl, room temp., 20 min, then (*S*)-propylene oxide, room temp., 12 h; (f) PivCl, NEt_3, CH_2Cl_2, room temp., 30 min, 58% from **37**; (g) LDA, THF, room temp., 30 min, then PhSeCl, 0 °C → room temp., 2.5 h; (h) MMPP, THF/MeOH (1:1), room temp., 30 min, 40% from **38**; (i) 5% HF in CH_3CN, THF, room temp., 6 h, 82%

Conclusion

A modular strategy for the assembly of squamocin A and D is presented. One noteworthy aspect is the stereodiverg-

ent step **26** → **27** + **28**, which allows the synthesis of both natural products from a common precursor. Squamocin G and squamocin H, as well as pharmacologically important analogs, should be accessible using the same strategy.

Experimental Section

General: All boiling points and melting points are uncorrected values. − IR: Perkin−Elmer FT-IR 1600, Biorad FTS 3000MX. − NMR: Bruker AC-300, DPX-300 and AMX-600. For ^{1}H NMR, $CDCl_3$ as solvent (δ_H = 7.24); for ^{13}C NMR, $CDCl_3$ as solvent (δ_C = 77.0). − Elemental analysis: CHNS-932 Analyser (Leco). − HRMS: Finnigan MAT 95. All reactions were performed under Ar in oven- or flame-dried glassware. − GC: Shimadzu GC-14A, C-R4AX. Dry solvents: THF, Et_2O, benzene, xylene and toluene were distilled from sodium benzophenone ketyl. Pyridine, triethylamine and CH_2Cl_2 were distilled from CaH_2. All commercially available reagents were used without purification unless stated otherwise. All reactions were monitored by thin-layer chromatography (TLC) carried out on Merck F-254 silica glass plates visualized with UV light and/or heat-gun treatment with 5% phosphomolybdic acid in ethanol. − Column chromatography (CC) and flash column chromatography (FCC) were performed with Merck silica gel 60 (70−200 mesh and 230−400 mesh). PE: light petroleum ether, bp 40−60 °C. MTBE: *tert*-butyl methyl ether.

(2*R*)-1,2-*O*-Isopropylidene-5-hexyne-1,2-diol (7): LiC≡CH·en complex (90%, 8.03 g, 78.5 mmol) was suspended in liquid ammonia (100 mL) at −78 °C. A solution of bromide **6** (12.63 g, 60.38 mmol) in THF (40 mL) was added quickly. The mixture was refluxed for 2 h at −33 °C. The condensed ammonia was allowed to evaporate overnight. After addition of sat. aqueous NH_4Cl (100 mL), the aqueous layer was extracted twice with MTBE (100 mL). The combined organic layers were washed with sat. aqueous NaCl (100 mL) and dried with $MgSO_4$. Removal of the solvents in vacuo and purification by CC (375 cm^3 SiO_2, PE/MTBE, 10:1) yielded alkyne **7** (7.61 g, 49.4 mmol, 82%) as a colorless liquid. − R_f = 0.43 (SiO_2, PE/MTBE, 10:1). − bp: 63 °C (14 mbar). − $[\alpha]_D^{24}$ = +7.8 (*c* = 1.89, $CHCl_3$). − IR (KBr): $\tilde{\nu}$ = 3295 s (C≡CH), 2986 s, 2937 m, 2874 w (CH), 2118 w (C≡C), 1454 s, 1380 m, 1371 m, 1246 m, 1216 m, 1156 m, 1074 s, 854 m, 638 m cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.29 (s, 3 H, acetonide-H_3), 1.34 (s, 3 H, acetonide-H_3), 1.67−1.77 (m, 2 H, 3-H_2), 1.90 (t, *J* = 2.7 Hz, 1 H, 6-H), 2.21−2.28 (m, 2 H, 4-H), 3.51 (dd, *J* = 7.9, 6.9 Hz, 1 H, 1-H′), 4.01 (dd, *J* = 7.9, 6.0 Hz, 1 H, 1-H′′), 4.10−4.16 (m, 1 H, 2-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.0 (C-4), 25.6 (acetonide-C), 26.9 (acetonide-C), 32.6 (C-3), 68.7 (C-6), 69.0 (C-1), 74.7 (C-2), 83.5 (C-5), 108.8 (acetal-C).

(2*R*,9*R*)-1,2;9,10-Di-*O*-isopropylidene-5-decyne-1,2,9,10-tetraol (8): Alkyne **7** (9.08 g, 58.9 mmol) was dissolved in liquid ammonia (100 mL) and THF (30 mL) at −78 °C. Under vigorous stirring *n*BuLi (2.4 mmol/mL, 25.0 mL, 60.0 mmol) was added as quickly as possible. After 15 min of stirring at −78 °C, the cooling bath was removed and, after another 5 min, DMSO (50 mL) was added. The solution solidified. Very rapid addition of a solution of bromide **6** (15.2 g, 72.6 mmol) in THF (20 mL) redissolved the reaction mixture immediately. The color of the solution turned to yellow-green. The mixture was refluxed for 4 h with vigorous stirring at −33 °C. The ammonia was allowed to evaporate overnight. After addition of sat. aqueous NH_4Cl (100 mL) the aqueous layer was extracted twice with MTBE (100 mL). The combined organic layers were washed with sat. aqueous NaCl (100 mL) and dried with $MgSO_4$. Removal of the solvents in vacuo and purification by CC (500 cm^3 SiO_2, PE/MTBE, 10:1) gave alkyne **8** (14.12 g, 50.0 mmol, 85%) as a colorless liquid. − R_f = 0.13 (SiO_2, PE/MTBE, 10:1). − $[\alpha]_D^{24}$ = +7.1 (*c* = 1.80, $CHCl_3$). − IR (KBr): $\tilde{\nu}$ = 2985 , 2936, 2871 s (CH), 1454 m, 1379 s, 1370 s, 1245 s, 1215 s, 1157 m, 1073 s, 855 m cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.29 (s, 6 H, acetonide-H_3), 1.34 (s, 6 H, acetonide-H_3), 1.58−1.76 (m, 4 H, 3-H_2, 8-H_2), 2.16−2.22 (m, 4 H, 4-H_2, 7-H_2), 3.50 (dd, *J* = 7.9, 6.8 Hz, 2 H, 1-H′, 10-H′), 4.00 (dd, *J* = 7.9, 6.0 Hz, 2 H, 1-H′′, 10-H′′), 4.07−4.14 (m, 2 H, 2-H, 9-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.3 (C-4, C-7), 25.7 (acetonide-C), 26.9 (acetonide-C), 33.1 (C-3, C-8), 69.1 (C-1, C-10), 74.9 (C-2, C-9), 79.6 (C-5, C-6), 108.7 (acetal-C). − $C_{16}H_{26}O_4$ (282.38): calcd. C 68.06, H 9.28; found C 67.89, H 9.01.

Alternative Preparation of (2*R*,9*R*)-1,2;9,10-Di-*O*-isopropylidene-5-decyne-1,2,9,10-tetraol (8): LiC≡CH·en complex (90%, 2.74 g, 26.8 mmol) was suspended in liquid ammonia (100 mL) at −78 °C. A solution of bromide **6** (4.08 g, 19.5 mmol) in THF (20 mL) was added quickly. The mixture was refluxed for 3 h at −33 °C. Under vigorous stirring *n*BuLi (2.5 mmol/mL, 10.0 mL, 25.0 mmol) was added as quickly as possible. The mixture was stirred for 10 min at −78 °C and the cooling bath was removed. After 5 min, DMSO (35 mL) was added and 5 min later rapid addition of a solution of bromide **6** (6.19 g, 29.6 mmol) in THF (20 mL) followed. The mixture was refluxed for 4 h with vigorous stirring at −33 °C. The condensed ammonia was allowed to evaporate overnight. After addition of sat. aqueous NH_4Cl (75 mL) the aqueous layer was extracted twice with MTBE (75 mL). The combined organic layers were washed with sat. aqueous NaCl (75 mL) and dried with $MgSO_4$. After purification by CC (300 cm^3 SiO_2, PE/MTBE, 10:1) alkyne **8** (2.48 g, 8.79 mmol, 45%) was obtained as a colorless liquid.

(2*R*,5*S*,6*S*,9*R*)-1,2;9,10-Di-*O*-isopropylidenedecane-1,2,5,6,9,10-hexaol (9). − 1. Reduction of the Alkyne: Na (2.92 g, 127.1 mmol) was dissolved in liquid ammonia (100 mL) at −78 °C (the typical dark-blue color appeared). A solution of alkyne **8** (13.01 g, 46.08 mmol) in THF (20 mL) was added. The mixture was refluxed with vigorous stirring for 4 h at −33 °C. The condensed ammonia evaporated overnight. Under argon at 0 °C the mixture was treated dropwise with 2-propanol (50 mL) and then with sat. aqueous NH_4Cl (100 mL). The aqueous layer was extracted twice with MTBE (100 mL). The combined organic layers were washed with sat. aqueous NaCl (75 mL) and dried with $MgSO_4$. Purification by CC (350 cm^3 SiO_2, PE/MTBE, 10:1 and 5:1) afforded the alkene (11.99 g, 42.22 mmol, 92%) as a colorless liquid.

(2*R*,5*E*,9*R*)-1,2;9,10-Di-*O*-isopropylidene-5-decene-1,2,9,10-tetraol: R_f = 0.41 (SiO_2, PE/MTBE, 5:1). − $[\alpha]_D^{22}$ = −23.2 (*c* = 1.07, $CHCl_3$). − IR (KBr): $\tilde{\nu}$ = 2985, 2935, 2867 s (CH), 1620 w (C=C), 1378 s, 1369 s, 1248 s, 1216 s, 1157 m, 1066 s, 971 w (*trans*-C=C), 857 m cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.28 (s, 6 H, acetonide-H_3), 1.33 (s, 6 H, acetonide-H_3), 1.46−1.51 (m, 2 H, 3-H′, 8-H′), 1.61−1.66 (m, 2 H, 3-H′′, 8-H′′), 1.95−2.05 (m, 4 H, 4-H_2, 7-H_2), 3.43 (t, *J* = 7.2 Hz, 2 H, 1-H′, 10-H′), 3.93−4.03 (m, 4 H, 1-H′′, 2-H, 9-H, 10-H′′), 5.37 (dt, *J* = 3.5, 2.0 Hz, 2 H, 5-H, 6-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.7 (acetonide-C), 26.9 (acetonide-C), 28.7 (C-4, C-7), 33.3 (C-3, C-8), 69.3 (C-1, C-10), 75.5 (C-2, C-9), 108.5 (acetal-C), 129.8 (C-5, C-6). − $C_{16}H_{28}O_4$ (284.40): calcd. C 67.57, H 9.92; found C 67.63, H 9.84.

2. Dihydroxylation: K_2CO_3 (17.51 g, 126.7 mmol), $K_3[Fe(CN)_6]$ (41.72 g, 126.7 mmol), $K_2OsO_4{\cdot}2\ H_2O$ (73 mg, 0.2 mmol) and $(DHQ)_2PHAL$ (362 mg, 0.5 mmol) were dissolved in *t*BuOH

(215 mL) and H_2O (215 mL). After addition of $MeSO_2NH_2$ (4.12 g, 43.28 mmol), the mixture was cooled to 0 °C. A yellow-red precipitate appeared. The mixture was charged with the alkene (11.99 g, 42.16 mmol) and stirred for 18 h. Addition of $Na_2S_2O_3$ (62.1 g) stopped the reaction. The aqueous layer was extracted three times with ethyl acetate (150 mL). The combined organic layers were washed separately with 2 M NaOH (150 mL), sat. aqueous $NaHCO_3$ (200 mL) and sat. aqueous NaCl (100 mL) and dried with $MgSO_4$. Removal of the solvents and purification by CC (600 cm^3 SiO_2, ethyl acetate/PE, 3:1) gave diol **9** (12.26 g, 38.52 mmol, 91%, ds 98:2) as colorless crystals. − R_f = 0.18 (SiO_2, ethyl acetate/PE, 3:1). − M.p. 85 °C. − $[a]_D^{23}$ = −28.2 (*c* = 0.33, $CHCl_3$). − IR (KBr): $\tilde{\nu}$ = 3402 bs, 3286 s (OH), 2986, 2944, 2868 s (CH), 1400 s, 1370 s, 1219 s, 1158 m, 1113 m, 1064 s, 860 m cm^{-1}. − ^1H NMR (300 MHz, $CDCl_3$): δ = 1.33 (s, 6 H, acetonide-H_3), 1.39 (s, 6 H, acetonide-H_3), 1.47−1.61 (m, 2 H, 3-H′, 8-H′), 1.63−1.77 (m, 6 H, 3-H′′, 8-H′′, 4-H_2, 7-H_2), 2.70 (d, *J* = 4.4 Hz, 2 H, OH), 3.42−3.53 (m, 4 H, 1-H′, 2-H, 9-H, 10-H′), 4.01−4.10 (m, 4 H, 1-H′′, 5-H, 6-H, 10-H′′). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.7 (acetonide-CH_3), 26.9 (acetonide-CH_3), 29.5 (C-4, C-7), 29.9 (C-3, C-8), 69.5 (C-1, C-10), 74.1 (C-2, C-9), 76.2 (C-5, C-6), 109.0 (acetal-C). − $C_{16}H_{30}O_6$ (318.41): calcd. C 60.36, H 9.50; found C 60.06, H 9.40.

5,6-Bis-*p*-toluenesulfonate 11 of (2*R*,5*S*,6*S*,9*R*)-1,2;9,10-Di-*O*-isopropylidenedecane-1,2,9,10-tetraol and 5,6-Bis-*p*-toluenesulfonate 12 of (*all-R*)-1,2;9,10-Di-*O*-isopropylidenedecane-1,2,9,10-tetraol: Diol **9/10** (12.09 g, 37.96 mmol) was dissolved in CH_2Cl_2 (150 mL). Pyridine (60.0 mL, 743 mmol) and *p*TsCl (56.70 g, 297.4 mmol) were added at 0 °C. The solution was stirred overnight. Sat. aqueous $NaHCO_3$ (35 mL) was added to destroy excess *p*TsCl and the mixture was stirred for 1 h. The mixture was treated with H_2O (50 mL) and acidified with 1 M HCl (pH = 3−4). The aqueous phase was extracted twice with CH_2Cl_2 (100 mL). The combined organic layers were washed with sat. aqueous $NaHCO_3$ (200 mL) and sat. aqueous NaCl (100 mL) and dried with $MgSO_4$. Removal of the solvents in vacuo and purification by CC (1100 cm^3 SiO_2, PE/MTBE, 1:1) gave ditosylate **11** (20.53 g, 32.75 mol, 86%) as a colorless oil, which later partially crystallized. ***Note:*** Depending on the diastereoselectivity of the previous reaction (AD reaction), in some cases the minor diastereomer **12** was also obtained.

11: R_f = 0.32 (SiO_2, PE/MTBE, 1:1). − m.p.: 70 °C. − $[a]_D^{24}$ = −31.7 (*c* = 0.63, $CHCl_3$). − IR (KBr): $\tilde{\nu}$ = 2987 m, 2935 w, 2889 w (CH), 1598 w (aryl), 1399 m, 1357 s (SO_2), 1190 s, 1176 s (SO_2), 928 m, 911 m, 882 m, 818 m, 677 m, 666 s, 552 s cm^{-1}. − ^1H NMR (300 MHz, $CDCl_3$): δ = 1.04−1.18 (m, 2 H, 3-H′, 8-H′), 1.22−1.52 (m, 4 H, 3-H′′, 4-H′, 7-H′, 8-H′′), 1.26 (s, 6 H, acetonide-H_3), 1.31 (s, 6 H, acetonide-H_3), 1.71−1.84 (m, 2 H, 4-H′′, 7-H′′), 2.43 (s, 6 H, tosyl-CH_3), 3.28 (t, *J* = 6.8 Hz, 2 H, 1-H′, 10-H′), 3.77−3.92 (m, 4 H, 1-H′′, 2-H, 9-H, 10-H′′), 4.55 (d, *J* = 10.6 Hz, 2 H, 5-H, 6-H), 7.33 (d, *J* = 8.3 Hz, 4 H, tosyl-H), 7.76 (d, *J* = 8.3 Hz, 4 H, tosyl-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.6 (tosyl-CH_3), 24.8 (C-4, C-7), 25.5 (acetonide-CH_3), 26.8 (acetonide-CH_3), 29.2 (C-3, C-8), 68.9 (C-1, C-10), 75.1 (C-2, C-9), 80.6 (C-5, C-6), 108.9 (acetal-C), 128.1, 129.9, 133.0, 145.2 (tosyl-C). − $C_{30}H_{42}O_{10}S_2$ (626.77): calcd. C 57.49, H 6.75; found C 57.37, H 6.76.

12: R_f = 0.18 (SiO_2, PE/MTBE, 1:1). − $[a]_D^{24}$ = +29.7 (*c* = 0.37, $CHCl_3$). − IR (film): $\tilde{\nu}$ = 3020 w, 2985 w, 2935 w, 2875 w (CH), 1598 w (aryl), 1454 w, 1369 s (SO_2), 1216 m, 1177 s (SO_2), 1096 w, 1058 w, 910 w, 869 w, 817 w, 757 s, 669 m, 615 w cm^{-1}. − ^1H NMR (300 MHz, $CDCl_3$): δ = 1.05−1.18 (m, 4 H, 3-H_2, 8-H_2), 1.28 (s, 6 H, acetonide-H_3), 1.32 (s, 6 H, acetonide-H_3), 1.58−1.74 (m, 4 H, 4-H_2, 7-H_2), 2.44 (s, 6 H, tosyl-CH_3), 3.25−3.33 (m, 2 H, 1-H′, 10-H′), 3.77−3.90 (m, 4 H, 1-H′′, 2-H, 9-H, 10-H′′), 4.58−4.67 (m, 2 H, 5-H, 6-H), 7.34 (d, *J* = 8.3 Hz, 4 H, tosyl-H), 7.78 (d, *J* = 8.3 Hz, 4 H, tosyl-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.7 (tosyl-CH_3), 25.0 (C-4, C-7), 25.6 (acetonide-CH_3), 26.9 (acetonide-CH_3), 29.1 (C-3, C-8), 69.1 (C-1, C-10), 74.9 (C-2, C-9), 80.0 (C-5, C-6), 108.9 (acetal-C), 128.2, 129.0, 133.0, 145.2 (tosyl-C). − HRMS (EI): calcd. 611.1985 $(M - CH_3)^+$; found 611.1984.

5,6-Bis-*p*-toluenesulfonate 13 of (2*R*,5*S*,6*S*,9*R*)-Decane-1,2,9,10-tetraol: Bis(tosylate) **11** (20.45 g, 32.63 mmol) was dissolved in conc. HOAc (250 mL) and H_2O (50 mL). The solution was stirred for 12 h. After treatment with H_2O (50 mL), the solvents were removed in vacuo. The residue was treated three times with toluene (75 mL) and the solvents were, in each case, removed in vacuo. The crude product, tetraol **13** (17.77 g, 32.50 mmol, 99%), was obtained as a colorless, viscous oil. − R_f = 0.14 (SiO_2, $CHCl_3$/MeOH, 10:1). − ^1H NMR (300 MHz, $CDCl_3$): δ = 0.98−1.17 (m, 2 H, 3-H′, 8-H′), 1.18−1.34 (m, 2 H, 3-H′′, 8-H′′), 1.45−1.63 (m, 2 H, 4-H′, 7-H′), 1.73−1.91 (m, 2 H, 4-H′′, 7-H′′), 2.41 (s, 6 H, tosyl-CH_3), 3.22−3.34 (m, 2 H, 1-H′, 10-H′), 3.35−3.75 (m, 4 H, 1-H′′, 2-H, 9-H, 10-H′′), 4.61 (m, 2 H, 5-H, 6-H), 7.31 (d, *J* = 7.9 Hz, 4 H, tosyl-H), 7.73 (d, *J* = 8.3 Hz, 4 H, tosyl-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.7 (tosyl-CH_3), 25.3 (C-4, C-7), 28.3 (C-3, C-8), 66.2 (C-1, C-10), 71.6 (C-2, C-9), 81.0 (C-5, C-6), 128.1, 129.9, 132.9, 145.3 (tosyl-C).

(*all-R*)-5,5′-Bis(hydroxymethyl)octahydro-2,2′-bifuran (14): Tetraol **13** (4.00 g, 7.31 mmol) was dissolved in THF (80 mL). At 0 °C NaH (95%, 0.97 g, 40.33 mmol) was added. The mixture was stirred for 4 h at 0 °C. Under argon at 0 °C HOAc (100%, 2.8 mL, 44.3 mmol) in THF (100 mL) was added cautiously. The mixture solidified. Treatment with THF (100 mL) redissolved the residue. The solvents were removed in vacuo. The residue was treated three times with toluene (75 mL) and the solvents were, in each case, removed in vacuo. Purification by CC (200 cm^3 SiO_2, $CHCl_3$/MeOH, 10:1) afforded bi-THF diol **14** (1.36 g, 6.73 mmol, 92%) as a colorless, viscous oil. − R_f = 0.25 (SiO_2, $CHCl_3$/MeOH, 10:1). − $[a]_D^{23}$ = −16.6 (*c* = 0.79, $CHCl_3$). − IR (film): $\tilde{\nu}$ = 3373 bs (OH), 2931 m, 2872 m (CH), 1457 w, 1382 w, 1327 w, 1194 w, 1043 s, 969 w, 938 w, 883 w, 617 w cm^{-1}. − ^1H NMR (300 MHz, $CDCl_3$): δ = 1.48−2.10 (m, 8 H, 3-H_2, 4-H_2, 3′-H_2, 4′-H_2), 2.89 (br. s, 2 H, OH), 3.40−3.51 (m, 2 H, 1′′-H′, 1′′′-H′), 3.61−3.76 (m, 2 H, 1′′-H′′, 1′′′-H′′), 3.79−3.91 (m, 2 H, 2-H, 2′-H), 4.04−4.15 (m, 2 H, 5-H, 5′-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.3 (C-3, C-3′), 28.8 (C-4, C-4′), 64.5 (C-1′′, C-1′′′), 80.1 (C-5, C-5′), 82.3 (C-2, C-2′). − HRMS (EI): calcd. 202.1205 (M^+); found 202.1208.

(*all-R*)-[5′-(5′′-(*tert*-Butyldimethylsilyloxy)methyltetrahydrofuran-2′′-yl)tetrahydrofuran-2′-yl]carbaldehyde (15). − 1. TBDMS Protection: To a solution of bi-THF diol **14** (6.19 g, 30.60 mmol) in CH_2Cl_2 (200 mL) at 0 °C was added imidazole (17.0 g, 249 mmol) and TBDMSCl (50% in toluene, 9.68 g, 32.1 mmol). The mixture was stirred for 2 h at room temp. The reaction was quenched with sat. aqueous NH_4Cl (100 mL). The aqueous layer was extracted twice with CH_2Cl_2 (75 mL). The combined organic layers were washed with sat. aqueous NaCl (100 mL) and dried with $MgSO_4$. Removal of the solvents and purification by CC (300 cm^3 SiO_2, PE/MTBE, 1:1) afforded bis-TBDMS-protected bifuran (4.33 g, 10.1 mmol, 33%, yield based on conversion: 40%) and the desired mono-TBDMS-protected alcohol (3.45 g, 10.9 mmol, 36%, yield based on conversion: 43%) as colorless liquids. The combined aqueous layers were extracted three times with $CHCl_3$/2-propanol (2:1) (100 mL). The combined organic layers were dried with $MgSO_4$. Removal of the solvents and purification of the residue by CC (150

cm^3 SiO_2, $CHCl_3$/MeOH, 10:1) was performed to reisolate bi-THF diol **14** (1.06 g, 5.22 mmol).

(*all-R*)-[5′-(5′′-(*tert*-Butyldimethylsilyloxy)methyltetrahydrofuran-2′′-yl)tetrahydrofuran-2′-yl]methanol: R_f = 0.15 (SiO_2, PE/MTBE, 1:1). − $[a]_D^{23}$ = +2.8 (c = 0.89, $CHCl_3$). − IR (film): $\tilde{\nu}$ = 3416 bm (OH), 2952, 2929, 2858 m (CH), 1636 m, 1471 m, 1387 w, 1254 w, 1065 m, 909 s, 837 m, 734 s, 650 m cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = −0.03 (s, 6 H, $SiCH_3$), 0.82 [s, 9 H, $SiC(CH_3)_3$], 1.47−1.77 (m, 4 H, 3′-H′, 4′-H′, 3′′-H′, 4′′-H′), 1.84−2.01 (m, 4 H, 3′-H′′, 4′-H′′, 3′′-H′′, 4′′-H′′), 2.41 (br. s, 1 H, OH), 3.37−3.54 (m, 2 H, 1-H′, 1′′′-H′), 3.57−3.66 (m, 2 H, 1-H′′, 1′′′-H′′), 3.78−3.88 (m, 2 H, 5′-H, 2′′-H), 3.95−4.11 (m, 2 H, 2′-H, 5′′-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.4 ($SiCH_3$), 18.2 [Si*C*$(CH_3)_3$], 25.8 [SiC(*C*$H_3)_3$], 27.4, 28.27, 28.32, 28.6 (C-3′, C-4′, C-3′′, C-4′′), 64.5 (C-1), 65.7 (C-1′′′), 79.75, 79.77 (C-2′, C-5′′), 82.06, 82.12 (C-5′, C-2′′). − HRMS (EI): calcd. 301.1835 (M − $CH_3)^+$; found 301.1839. − $C_{16}H_{32}O_4Si$ (316.51): calcd. C 60.72, H 10.19; found C 60.29, H 10.28.

(*all-R*)-5,5′-Bis(*tert*-butyldimethylsilyloxy)methyloctahydro-2,2′-bifuran: R_f = 0.75 (SiO_2, PE/MTBE, 1:1). − $[a]_D^{21}$ = +13.1 (c = 1.73, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 6 H, $SiCH_3$), 0.84 [s, 9 H, $SiC(CH_3)_3$], 1.54−1.76 (m, 4 H, 3-H′, 4-H′, 3′-H′, 4′-H′) 1.84−2.03 (m, 4 H, 3-H′′, 4-H′′, 3′-H′′, 4′-H′′), 3.44−3.53 (m, 2 H, C*H*′OTBDMS), 3.61−3.68 (m, 2 H, C*H*′′OTBDMS), 3.81−3.89 (m, 2 H, 2-H, 2′-H), 3.94−4.07 (m, 2 H, 5-H, 5′-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.4 ($SiCH_3$), 17.9 [Si*C*$(CH_3)_3$], 25.9 [SiC(*C*$H_3)_3$], 28.2 (C-4, C-4′), 28.5 (C-3, C-3′), 65.8 (*C*H_2OTBDMS), 79.7 (C-5, C-5′), 81.9 (C-2, C-2′). − $C_{22}H_{46}O_4Si_2$ (430.78): calcd. C 61.34, H 10.76; found C 61.14, H 10.41.

2. Swern Oxidation: $(COCl)_2$ (360 μL, 4.13 mmol) was dissolved in CH_2Cl_2 (20 mL). The solution was cooled to −60 °C and DMSO (710 μL, 10.0 mmol) dissolved in CH_2Cl_2 (3 mL) was added. At −50 °C a solution of the bi-THF monoalcohol (522 mg, 1.65 mmol) in CH_2Cl_2 (3 mL) was added. After 45 min at −45 °C, the mixture was treated with Et_3N (2.05 mL, 14.7 mmol). After 5 min, the temperature was allowed to rise to 0 °C and H_2O (10 mL) was added to stop the reaction. The aqueous layer was extracted twice with CH_2Cl_2 (15 mL). The combined organic layers were washed with sat. aqueous NaCl (15 mL) and dried with $MgSO_4$. Removal of the solvents in vacuo and purification by CC (150 cm^3 SiO_2, PE/MTBE, 1:1) yielded aldehyde **15** (471 mg, 1.50 mmol, 91%) as a liquid. − R_f = 0.25 (SiO_2, PE/MTBE, 1:1). − $[a]_D^{21}$ = +25.4 (c = 1.32, $CHCl_3$). − IR (film): $\tilde{\nu}$ = 3030 w, 2970 m, 2872 s (CH), 2719 w, 1733 s (C=O), 1496 w, 1454 w, 1365 w, 1314 w, 1273 w, 1202 w, 1070 s, 938 w, 883 w, 819 w, 739 m, 699 m, 609 w cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.02 (s, 6 H, $SiCH_3$), 0.86 [s, 9 H, $SiC(CH_3)_3$], 1.56−1.82 (m, 3 H, 4′-H′, 3′′-H′, 4′′-H′), 1.89−2.05 (m, 4 H, 3′-H′, 4′-H′′, 3′′-H′′, 4′′-H′′), 2.17−2.30 (m, 1 H, 3′-H′′), 3.45−3.72 (m, 2 H, 1′′′-H_2), 3.78−4.16 (m, 3 H, 5′-H, 2′′-H, 5′′-H), 4.28−4.38 (m, 1 H, 2′-H), 9.66 (d, J = 1.9 Hz, 1 H, CHO). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.3 ($SiCH_3$), 18.3 [Si*C*$(CH_3)_3$], 25.9 [SiC(*C*$H_3)_3$], 27.4 (C-3′), 27.9, 28.3, 28.4 (C-4′, C-3′′, C-4′′), 65.8 (C-1′′′), 80.0 (C-5′′), 81.7 (C-2′′), 83.3 (C-2′), 83.4 (C-5′), 203.0 (CHO). − HRMS (EI): calcd. 315.1992 (M + H)$^+$; found 315.1995.

14-Benzyloxytetradecanol (17). − 1. Reduction: Dicarboxylic acid **16** (15.0 g, 58.1 mmol) was dissolved in THF (300 mL). BH_3·Me_2S complex (10 mmol/mL in THF, 13.9 mL, 139 mmol) was added and the solution was stirred for 4 h at 50 °C. Cautious treatment with MeOH (200 mL) at 0 °C stopped the reaction. The solvents were removed in vacuo. This procedure was repeated twice. The residue was crystallized from MTBE and yielded the desired diol (13.1 g, 57.0 mmol, 98%) as colorless crystals.

1,14-Tetradecanediol: R_f = 0.17 (SiO_2, PE/MTBE, 1:1). − m.p.: 81 °C. − IR (KBr): $\tilde{\nu}$ = 3414 bs (OH), 2923 s, 2848 s (CH), 1661 m, 1558 m, 1480 w, 1462 w, 1400 w, 1357 w, 1333 w, 1212 w, 1052 m, 1017 m, 972 w, 728 w, 616 bm cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25−1.29 (m, 20 H, 3-H_2 to 12-H_2), 1.50−1.59 (m, 4 H, 2-H_2, 13-H_2), 3.62 (t, J = 6.6 Hz, 4 H, 1-H_2, 14-H_2). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.7 (C-7, C-8), 29.4 (C-6, C-9), 29.5 (C-5, C-10), 29.6 (C-3,C-4,C-11,C-12), 32.8 (C-2, C-13), 63.1 (C-1, C-14). − $C_{14}H_{30}O_2$ (230.39): calcd. C 72.99, H 13.12; found C 73.16, H 12.90.

2. Monoprotection: A mixture of diol (22.2 g, 96.4 mmol), BnCl (11.1 mL, 96.4 mmol) and powdered KOH (5.4 g, 96.4 mmol) was stirred for 5 h at 110 °C. Treatment with ice/water (300 mL) and $CHCl_3$ (400 mL) stopped the reaction. The aqueous layer was extracted twice with $CHCl_3$ (200 mL). The combined organic layers were washed with sat. aqueous NaCl (250 mL) and dried with $MgSO_4$. Removal of the solvents in vacuo and purification by CC (800 cm^3 SiO_2, PE/MTBE, 5:1, 1:1 and MTBE) yielded alcohol **17** (12.4 g, 38.8 mmol, 61% based on turnover) as colorless crystals. − R_f = 0.48 (SiO_2, PE/MTBE, 1:1). − M.p.: 41 °C. − IR (KBr): $\tilde{\nu}$ = 3428 bm, 3371 bm (OH), 3066 w, 2920 s, 2848 s (CH), 1469 m, 1454 m, 1400 w, 1369 w, 1356 w, 1117 m, 1094 w, 1060 m, 1028 w, 1004 w, 983 w, 757 w, 736 m, 722 w, 702 w, 696 w cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.24−1.33 (m, 20 H, 3-H_2 to 12-H_2), 1.52−1.62 (m, 5 H, 2-H_2, 13-H_2 and OH), 3.44 (t, J = 6.6 Hz, 2 H, 14-H_2), 3.61 (t, J = 6.6 Hz, 2 H, 1-H_2), 4.48 (s, 2 H, PhCH_2O), 7.25−7.33 (m, 5 H, phenyl-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.7, 26.2, 29.41, 29.47, 29.57, 29.61 (C-3 to C-12), 29.8 (C-13), 32.8 (C-2), 63.1 (C-1), 70.5 (C-14), 72.8 (Ph*C*H_2O), 127.4, 127.6, 128.3, 138.7 (phenyl-C). − $C_{21}H_{36}O_2$ (320.51): calcd. C 78.70, H 11.32; found C 78.58, H 11.05.

14-Benzyloxytetradecane Bromide (18). − 1. Tosylation: To a solution of alcohol **17** (4.4 g, 13.7 mmol) in CH_2Cl_2 (100 mL) was added pyridine (6.0 mL, 74.2 mmol). The mixture was treated with *p*TsCl (4.5 g, 23.7 mmol) at 0 °C. The reaction mixture was stirred overnight. H_2O (50 mL) was added to destroy excess *p*TsCl at 0 °C and the mixture was stirred for 1 h. The aqueous layer was extracted twice with MTBE (75 mL). The combined organic layers were washed with 2 M HCl (100 mL), sat. aqueous $NaHCO_3$ (200 mL) and sat. aqueous NaCl (100 mL) and dried with $MgSO_4$. Removal of the solvents in vacuo afforded the crude tosylate (6.0 g, 12.7 mmol, 93%, R_f = 0.36 [SiO_2, PE/MTBE, 5:1] as colorless crystals.

2. Bromination: To a solution of the crude tosylate (6.0 g, 12.7 mmol) in THF (200 mL) was added LiBr (9.0 g, 105 mmol) at 0 °C. The mixture was stirred for 5 h at 50 °C. Treatment with H_2O (100 mL) stopped the reaction. The aqueous layer was extracted twice with MTBE (75 mL). The combined organic layers were washed with sat. aqueous NaCl (100 mL) and dried with $MgSO_4$. Removal of the solvents and purification by CC (250 cm^3 SiO_2, PE/MTBE, 10:1) yielded bromide **18** (4.3 g, 11.2 mmol, 88%) as colorless crystals. − R_f = 0.73 (SiO_2, PE/MTBE, 5:1). − M.p.: 31 °C. − IR (KBr): $\tilde{\nu}$ = 3030 w, 2921 s, 2851 s (CH), 1641 w, 1497 w, 1468 w, 1455 w, 1400 w, 1367 w, 1356 w, 1206 w, 1125 m, 1107 m, 1076 w, 1029 w, 1017 w, 992 w, 972 w, 906 w, 739 m, 697 m cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.18−1.35 (m, 20 H, 3-H_2 to 12-H_2), 1.50−1.55 (m, 2 H, 13-H_2), 1.73−1.78 (m, 2 H, 2-H_2), 3.33 (t, J = 7.0 Hz, 2 H, 1-H_2), 3.39 (t, J = 6.6 Hz, 2 H, 14-H_2), 4.41

(s, 2 H, PhCH_2O), 7.17−7.25 (m, 5 H, phenyl-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.2, 28.2, 28.8, 29.42, 29.47, 29.51, 29.57, 29.60 (C-3 to C-12), 29.8 (C-13), 32.8 (C-2), 34.0 (C-1), 70.5 (C-14), 72.8 (Ph*C*H_2O), 127.4, 127.6, 128.3, 138.7 (phenyl-C). − $C_{21}H_{35}BrO$ (383.41): calcd. C 65.79, H 9.20, Br 20.84; found C 65.80, H 8.93, Br 21.00.

(*all-R*)-1-[5′-(5′′-(*tert*-Butyldimethylsilyloxy)methyltetrahydrofuran-2′′-yl)tetrahydrofuran-2′-yl]-15-benzyloxypentadecan-1-ol (19). − 1. Grignard Reaction and Oxidation: A three-necked flask (100 mL), equipped with a dropping funnel, a reflux condenser and a magnetic stirring bar, was flame-dried in vacuo and, after cooling to 20 °C, flushed with argon. The flask was charged with Mg (1.44 g, 59.2 mmol) and the same drying procedure was repeated. Et_2O (5 mL) was added and the mixture was stirred vigorously. The dropping funnel was charged with a solution of bromide **18** (5.13 g, 13.4 mmol) in Et_2O (30 mL) and 1,2-dibromoethane (250 µL, 2.90 mmol). 7 mL of the solution was added quickly to the vigorously stirred mixture. After warming the mixture slightly with a heat gun, the Grignard reaction started. The remaining bromide solution was added over 20 min and the mixture was stirred for 1 h at 35 °C. The Grignard solution was transferred by cannula into a Schlenk flask (100 mL) and was cooled to −40 °C. A precipitate that could be stirred was obtained. A solution of aldehyde **15** (832 mg, 2.65 mmol) in Et_2O (8 mL) was added dropwise. Over 3 h the reaction mixture was stirred and the temperature was allowed to rise to room temp. Addition of sat. aqueous NH_4Cl (25 mL) and Et_2O (25 mL) stopped the reaction. The aqueous layer was extracted twice with Et_2O (25 mL). The combined organic layers were washed with sat. aqueous NaCl (50 mL) and dried with $MgSO_4$. Removal of the solvents in vacuo and purification by CC (250 cm^3 SiO_2, PE/MTBE, 3:1, 2:1) afforded a mixture (1:1 by ^{13}C NMR) of the epimeric alcohols [1.25 g, 2.02 mmol, 76%, R_f = 0.56 and 0.59 (SiO_2, PE/MTBE, 1:1)] as a colorless liquid. The epimeric alcohols (1.23 g, 1.98 mmol) were dissolved in CH_2Cl_2 (20 mL). Molecular sieves (4 Å, 1.37 g) and PCC (1.30 g, 6.02 mmol) were added. The mixture was stirred for 1 h at room temp., then diluted with MTBE (50 mL) and filtered through a pad of Celite. The solvents were removed in vacuo. Purification by CC (200 cm^3 SiO_2, PE/MTBE, 4:1, 2:1) gave the desired ketone (879 mg, 1.43 mmol, 72%) as a colorless liquid.

(*all-R*)-1-[5′-(5′′-(*tert*-Butyldimethylsilyloxy)methyltetrahydrofuran-2′′-yl)-tetrahydrofuran-2′-yl]-15-benzyloxypentadecan-1-one: R_f = 0.42 (SiO_2, PE/MTBE, 4:1). − $[\alpha]_D^{22}$ = +20.4 (*c* = 0.26, $CHCl_3$). − IR (film): $\tilde{\nu}$ = 2927, 2855 cm^{-1} s (CH), 1717 m (C=O), 1461 m, 1363 w, 1254 w, 1098 bm, 839 m, 777 w, 736 w, 697 w. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.03 (s, 6 H, $SiCH_3$), 0.87 [s, 9 H, $SiC(CH_3)_3$], 1.20−2.10 (m, 34 H, 2-H_2 to 14-H_2, 3′-H_2, 4′-H_2, 3′′-H_2, 4′′-H_2), 3.42 (t, *J* = 6.5 Hz, 2 H, 15-H_2), 3.50−3.70 (m, 2 H, 1′′′-H_2), 3.80−4.00 (m, 4 H, 2′-H, 5′-H, 2′′-H, 5′′-H), 4.48 (s, 2 H, PhCH_2O), 7.22−7.33 (m, 5 H, phenyl-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.3 ($SiCH_3$), 18.3 [Si*C*$(CH_3)_3$], 25.9 [SiC(*C*$H_3)_3$], 23.1, 26.2, 28.0, 28.4, 29.3, 29.5, 29.6, 29.8, 38.1 (C-2 to C-14, C-3′, C-4′, C-3′′, C-4′′), 65.9 (C-1′′′), 70.5 (C-15), 72.8 (Ph*C*H_2O), 80.0, 81.6, 83.0, 83.9 (C-2′, C-5′, C-2′′, C-5′′), 127.4, 127.6, 128.3, 138.7 (phenyl-C), 212.9 (C-1). − HRMS (EI): calcd. 616.4523 $(M)^+$; found 616.4527.

2. Reduction: To a solution of the ketone (879 mg, 1.43 mmol) in THF (20 mL) at −100 °C was added L-selectride® (1 mol/L in THF, 3.0 mL, 3.0 mmol), which had been precooled at −78 °C. The mixture was stirred for 2 h. During that period the temperature was allowed to rise to −70 °C. At 0 °C, 2 M NaOH (10 mL) and 30% H_2O_2 (10 mL) were added carefully. The mixture was stirred for 1 h and then treated with H_2O (50 mL) and MTBE (50 mL). The aqueous layer was extracted twice with MTBE (50 mL). The combined organic layers were washed with sat. aqueous $NaHCO_3$ (75 mL) and sat. aqueous NaCl (75 mL) and dried with $MgSO_4$. Removal of the solvents and purification by CC (150 cm^3 SiO_2, PE/MTBE, 3:1) afforded alcohol **19** (850 mg, 1.37 mmol, 96%) as a colorless oil. The stereoselectivity was determined to be better than 98:2 by ^{13}C-NMR analysis. − R_f = 0.27 (SiO_2, PE/MTBE, 3:1). − $[\alpha]_D^{22}$ = +8.2 (*c* = 0.96, $CHCl_3$). − IR (film): $\tilde{\nu}$ = 3450 bm (OH), 2926, 2854 s (CH), 1463 w, 1360 w, 1251 w, 1102 m, 1070 w, 836 m, 776 w, 734 w, 697 w cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.03 (s, 6 H, $SiCH_3$), 0.87 [s, 9 H, $SiC(CH_3)_3$], 1.21−1.42 (m, 26 H, 2-H_2 to 14-H_2), 1.53−1.66 (m, 4 H, 3′-H′, 4′-H′, 3′′-H′, 4′′-H′), 1.88−2.04 (m, 4 H, 3′-H′′, 4′-H′′, 3′′-H′′, 4′′-H′′), 2.33 (br. s, 1 H, OH), 3.33−3.39 (m, 1 H, 1-H), 3.44 (t, *J* = 7.2 Hz, 2 H, 15-H_2), 3.55 (dd, *J* = 4.6, 9.4 Hz, 1 H, 1′′′-H′), 3.66 (dd, *J* = 4.6, 9.4 Hz, 1 H, 1′′′-H′′), 3.77−3.91 (m, 3 H, 2′-H, 5′-H, 2′′-H), 4.01−4.10 (m, 1 H, 5′′-H), 4.48 (s, 2 H, PhCH_2O), 7.22−7.33 (m, 5 H, phenyl-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.3 ($SiCH_3$), 18.3 [Si*C*$(CH_3)_3$], 25.9 [SiC(*C*$H_3)_3$], 25.6, 26.2, 28.31, 28.33, 28.5, 28.9, 29.46, 29.58, 29.60, 29.63, 29.72, 29.75, 33.5 (C-2 to C-14, C-3′, C-4′, C-3′′, C-4′′), 65.8 (C-1′′′), 70.5 (C-15), 72.8 (Ph*C*H_2O), 74.0 (C-1), 79.9 (C-5′′), 81.9, 82.0 (C-5′, C-2′′), 82.9 (C-2′), 127.4, 127.6, 128.3, 138.7 (phenyl-C). − HRMS (EI): calcd. 619.4758 $(M + H)^+$; found 619.4759.

(*all-R*)-[5′-(5′′-(1′′′-*tert*-Butyldimethylsilyloxy-15′′′-benzyloxypentadec-1′′′-yl)tetrahydrofuran-2′′-yl)tetrahydrofuran-2′-yl]-methanol (20): − 1. TBDMS Protection: To a solution of alcohol **19** (737 mg, 1.19 mmol) in CH_2Cl_2 (25 mL) at 0 °C was added imidazole (795 mg, 11.7 mmol) and TBDMSCl (50% in toluene, 1.65 g, 5.46 mmol). The mixture was stirred overnight at room temp. The reaction was quenched with sat. aqueous NH_4Cl (25 mL). The aqueous layer was extracted twice with CH_2Cl_2 (25 mL). The combined organic layers were washed with sat. aqueous NaCl (20 mL) and dried with $MgSO_4$. Removal of the solvents in vacuo and purification by CC (150 cm^3 SiO_2, PE/MTBE, 20:1) afforded bis-TBDMS-protected diol (753 mg, 1.03 mmol, 87%) as a colorless liquid.

(*all-R*)-1-[5′-(5′′-(*tert*-Butyldimethylsilyloxy)methyltetrahydrofuran-2′′-yl)tetrahydrofuran-2′-yl]-1-*tert*-butyldimethylsilyloxy-15-benzyloxypentadecane: R_f = 0.36 (PE/MTBE, 20:1). − $[\alpha]_D^{22}$ = +18.6 (*c* = 0.37, $CHCl_3$). − IR (film): $\tilde{\nu}$ = 2927, 2855 s (CH), 1462 w, 1361 w, 1252 m, 1100 m, 1005 w, 939 w, 836 m, 776 m, 733 w, 697 w cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.02, 0.025, 0.03 (3 × s, 12 H, $SiCH_3$), 0.86, 0.87 [2 × s, 18 H, $SiC(CH_3)_3$], 1.19−1.52 (m, 26 H, 2-H_2 to 14-H_2), 1.53−1.74 (m, 4 H, 3′-H′, 4′-H′, 3′′-H′, 4′′-H′), 1.78−2.04 (m, 4 H, 3′-H′′, 4′-H′′, 3′′-H′′, 4′′-H′′), 3.44 (t, *J* = 6.8 Hz, 2 H, 15-H_2), 3.52 (dd, *J* = 5.9, 10.4 Hz, 1 H, 1′′′-H′), 3.60−3.69 (m, 2 H, 1-H, 1′′′-H′′), 3.81−4.08 (m, 4 H, 2′-H, 5′-H, 2′′-H, 5′′-H), 4.48 (s, 2 H, PhCH_2O), 7.22−7.33 (m, 5 H, phenyl-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.3, −4.6, −4.3 ($SiCH_3$), 18.2, 18.3 [Si*C*$(CH_3)_3$], 25.91, 25.94 [SiC(*C*$H_3)_3$], 26.2, 26.9, 28.2, 28.43, 28.45, 29.48, 29.60, 29.65, 29.67, 29.8, 29.9, 32.1 (C-2 to C-14, C-3′, C-4′, C-3′′, C-4′′), 65.9 (C-1′′′), 70.5 (C-15), 72.8 (Ph*C*H_2O), 74.6 (C-1), 79.8 (C-5′′), 81.8, 81.9 (C-5′, C-2′′), 82.1 (C-2′), 127.4, 127.6, 128.3, 138.7 (phenyl-C). − $C_{43}H_{80}O_5Si_2$ (733.27): calcd. C 70.43, H 11.00; found C 70.39, H 10.83.

2. Monodeprotection: Bis-TBDMS-protected diol (685 mg, 934 µmol) was dissolved in CH_2Cl_2 (10 mL) and MeOH (2 mL). At −10 °C, CSA (22 mg, 95 µmol) was added. The mixture was stirred for 2 h. During that period the temperature was allowed to rise to

0 °C. When a TLC spot of the dideprotected side product started to appear, the mixture was treated with phosphate buffer solution (pH = 7, 10 mL) to stop the reaction. The aqueous layer was extracted twice with CH_2Cl_2 (25 mL). The combined organic layers were dried with $MgSO_4$. Removal of the solvents in vacuo and purification by CC (150 cm^3 SiO_2, PE/MTBE, 5:1, 4:1, 1:1) afforded reisolated bis-TBDMS-protected diol (250 mg, 341 μmol) and primary alcohol **20** (327 mg, 528 μmol, 57%, yield based on turnover: 89%) as a colorless viscous oil. In the refrigerator (−30 °C) alcohol **20** solidified to a colorless wax. − R_f = 0.22 (SiO_2, PE/MTBE, 2:1). − M.p.: 20− 25 °C. − $[\alpha]_D^{22}$ = +8.9 (*c* = 0.70, $CHCl_3$). − IR (film): $\tilde{\nu}$ = 3453 bm (OH), 3030 w, 2926, 2854 s (CH), 1463 m, 1361 w, 1251 m, 1102 s, 1070 w, 836 s, 776 m, 734 w, 697 w cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.03 (s, 3 H, $SiCH_3$), 0.04 (s, 3 H, $SiCH_3$), 0.86 [s, 9 H, $SiC(CH_3)_3$], 1.20−1.51 (m, 26 H, 2′′′-H_2 to 14′′′-H_2), 1.53−1.76 (m, 4 H, 3′-H′, 4′-H′, 3′′-H′, 4′′-H′), 1.83−2.00 (m, 4 H, 3′-H′′, 4′-H′′, 3′′-H′′, 4′′-H′′), 3.41−3.50 (m, 3 H, 15′′′-H_2, 1-H′), 3.61−3.71 (m, 2 H, 1′′′-H, 1-H′′), 3.81−3.99 (m, 3 H, 5′-H, 2′′-H, 5′′-H), 4.05−4.15 (m, 1 H, 2′-H), 4.48 (s, 2 H, PhCH_2O), 7.22−7.34 (m, 5 H, phenyl-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.7, −4.3 ($SiCH_3$), 18.2 [Si*C*$(CH_3)_3$], 25.9 [SiC(*C*$H_3)_3$], 26.2, 26.9, 27.4, 28.6, 28.7, 29.47, 29.59, 29.63, 29.75, 29.9, 32.1 (C-2′′′ to C-14′′′, C-3′, C-4′, C-3′′, C-4′′), 64.6 (C-1), 70.5 (C-15′′′), 72.8 (Ph*C*H_2O), 74.5 (C-1′′′), 79.7 (C-2′), 82.0, 82.1, 82.2 (C-5′, C-2′′, C-5′′), 127.4, 127.6, 128.3, 138.7 (phenyl-C). − HRMS (EI): calcd. 562.4054 $(M - C_4H_8)^+$; found 562.4055. − $C_{37}H_{66}O_5Si$ (619.01): calcd. C 71.79, H 10.75; found C 71.60, H 11.04.

(*all-R*)-[5′-(5′′-(1′′′-*tert*-Butyldimethylsilyloxy-15′′′-benzyloxypentadec-1′′′-yl)tetrahydrofuran-2′′-yl)tetrahydrofuran-2′-yl]carbaldehyde (21): $(COCl)_2$ (170 μL, 1.95 mmol) was dissolved in CH_2Cl_2 (5 mL). The solution was cooled to −60 °C and DMSO (340 μL, 4.79 mmol) dissolved in CH_2Cl_2 (3 mL) was added. At −50 °C, a solution of alcohol **20** (475 mg, 767 μmol) in CH_2Cl_2 (3 mL) was added. After 45 min at −45 °C, the mixture was treated with Et_3N (1.00 mL, 7.18 mmol). After 5 min, the reaction mixture was allowed to warm up to 0 °C and H_2O (10 mL) was added to stop the reaction. The aqueous layer was extracted twice with CH_2Cl_2 (10 mL). The combined organic layers were washed with sat. aqueous NaCl (10 mL) and dried with $MgSO_4$. Removal of the solvents and purification by CC (75 cm^3 SiO_2, PE/MTBE, 3:1, 1:1) yielded aldehyde **21** (424 mg, 687 μmol, 90%) as a colorless liquid. − R_f = 0.17 (SiO_2, PE/MTBE, 3:1). − $[\alpha]_D^{21}$ = +23.3 (*c* = 0.51, $CHCl_3$). − IR (film): $\tilde{\nu}$ = 2926, 2854 s (CH), 1733 (C=O), 1463 m, 1361 w, 1252 w, 1102 s, 836 m, 776 m, 734 w, 697 w cm^-. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.03 (s, 3 H, $SiCH_3$), 0.04 (s, 3 H, $SiCH_3$), 0.86 [s, 9 H, $SiC(CH_3)_3$], 1.20−2.25 (m, 34 H, 2′′′-H_2 to 14′′′-H_2, 3′-H_2, 4′-H_2, 3′′-H_2, 4′′-H_2), 3.44 (t, *J* = 6.6 Hz, 2 H, 15′′′-H_2), 3.58−3.66 (m, 1 H, 1′′′-H), 3.84−4.04 (m, 3 H, 5′-H, 2′′-H, 5′′-H), 4.28−4.35 (m, 1 H, 2′-H), 4.48 (s, 2 H, PhCH_2O), 7.21−7.33 (m, 5 H, phenyl-H), 9.65 (d, *J* = 6.3 Hz, 1 H, CHO). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.6, −4.3 ($SiCH_3$), 18.2 [Si*C*$(CH_3)_3$], 25.9 [SiC(*C*$H_3)_3$], 25.8, 26.2, 27.1, 27.4, 27.8, 28.5, 29.45, 29.57, 29.60, 29.73, 29.84, 32.4 (C-2′′′ to C-14′′′, C-3′, C-4′, C-3′′, C-4′′), 70.5 (C-15′′′), 72.8 (Ph*C*H_2O), 74.6 (C-1′′′), 81.3, 82.4, 83.2, 83.3 (C-2′, C-5′, C-2′′, C-5′′), 127.4, 127.6, 128.3, 138.7 (phenyl-C), 202.9 (C-1). − HRMS (EI): calcd. 560.3897 $(M - C_4H_8)^+$; found 560.3894.

(4*S*)-1-Decen-4-ol (23): (*R*)-BINOL (1.75 g, 6.12 mmol) was dissolved in CH_2Cl_2 (50 mL). Molecular sieves (4 Å, 17.83 g), which had been rinsed out with CH_2Cl_2 (10 mL), and Ti(O*i*Pr)$_4$ (1.80 mL, 6.10 mmol) were added. The orange-red suspension was refluxed for 90 min. After cooling down to room temp. the mixture was charged with heptanal (**22**) (4.30 mL, 30.8 mmol) and stirred for 1 h. At −78 °C allyltributylstannane (10.5 mL, 33.9 mmol) was added. The suspension was stirred for 30 min at −78 °C and the flask was allowed to stand at −25 °C for 5 d. The reaction was quenched by adding sat. aqueous $NaHCO_3$ (50 mL) and stirred for 1 h. The reaction mixture was filtered through a pad of Celite and the pad was washed with H_2O (50 mL) and CH_2Cl_2 (50 mL). The aqueous layer was extracted twice with CH_2Cl_2 (50 mL). The combined organic layers were washed with sat. aqueous NaCl (50 mL) and dried with $MgSO_4$. Removal of the solvents in vacuo and purification by CC (600 cm^3 SiO_2, PE/MTBE, 10:1) yielded heptanal (365 mg, 3.20 mmol) and the alcohol **23** (3.90 g, 25.0 mmol, 81%, yield based on turnover: 90%) as a colorless liquid. The enantioselectivity was determined by chiral GC and found to be 99:1 in favor of the desired isomer. ***Note:*** The reaction was although done with 0.1 equiv. (*R*)-BINOL and 0.1 equiv. Ti(O*i*Pr)$_4$. Use of heptanal (1.61 g, 14.1 mmol) afforded alcohol **23** (1.48 g, 9.48 mmol, 68%, yield based on conversion: 85%) with an enantioselectivity of 99:1 determined by chiral GC. − R_f = 0.19 (SiO_2, PE/MTBE, 10:1). − GC: R_t [(*S*) enantiomer)]: 8.08 min, R_t [(*R*) enantiomer)]: 8.50 min [chiral column β-3p, 25 m, temperature program: start temp.: 95 °C (hold for 12 min), end temp.: 180 °C (hold for 5 min), heating rate: 10 °C/min, pressure: H_2 (0.5 kg/cm^2)]. − $[\alpha]_D^{25}$ = −9.1 (*c* = 0.72, $CHCl_3$). − IR (film): $\tilde{\nu}$ = 3356 bs (OH), 3077 w, 2956, 2929, 2857 s (CH), 1641 m (C=C), 1466 m, 1436 m, 1378 w, 1341 w, 1228 w, 1125 m, 1069 m, 1036 m, 994 m, 912 s, 877 s, 724 w, 666 w cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85 (t, *J* = 6.8 Hz, 3 H, 10-H_3), 1.18−1.48 (m, 10 H, 5-H_2 to 9-H_2), 1.70 (br. s, 1 H, OH), 2.04−2.16 (m, 1 H, 3-H′), 2.21−2.31 (m, 1 H, 3-H′′), 3.54−3.66 (m, 1 H, 4-H), 5.04−5.13 (m, 2 H, 1-H_2), 5.71−5.87 (m, 1 H, 2-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0 (C-10), 22.6 (C-9), 25.6, 29.3, 31.8 (C-6, C-7, C-8), 36.8 (C-5), 41.9 (C-3), 70.6 (C-4), 117.9 (C-1), 134.9 (C-2). − $C_{10}H_{20}O$ (156.27): calcd. C 76.86, H 12.90; found C 76.59, H 12.72.

(4*S*)-4-Acetoxy-1-decene (24): To a solution of alcohol **23** (144 mg, 920 μmol) in CH_2Cl_2 (4 mL) was added pyridine (270 μL, 3.34 mmol), DMAP (7 mg, 57 μmol) and Ac_2O (205 μL, 2.17 mmol). The mixture was stirred for 36 h at room temp. The solvents were removed in vacuo and the residue was purified by CC (25 cm^3 SiO_2, PE) to afford acetate **24** (92 mg, 474 μmol, 52%) as a colorless liquid. R_f = 0.48 (SiO_2, PE/MTBE, 20:1). − $[\alpha]_D^{20}$ = −23.5 (*c* = 0.23, $CHCl_3$). − IR (film): $\tilde{\nu}$ = 3079 cm^{-1} w, 2955, 2930, 2858 s (CH), 1740 s (C=O), 1642 w (C=C), 1466 w, 1437 w, 1373 m, 1240 s, 1128 w, 1023 m, 994 w, 915 w, 830 w, 724 w, 666 w. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 6.7 Hz, 3 H, 3-H_3), 1.18−1.33 (m, 8 H) and 1.44−1.56 (m, 2 H, 5-H_2 to 9-H_2), 1.99 (s, 3 H, acetate-CH_3), 2.21−2.30 (m, 2 H, 3-H_2), 4.88 (quint, *J* = 6.2 Hz, 1 H, 4-H), 4.98−5.07 (m, 2 H, 1-H_2), 5.63−5.78 (m, 1 H, 2-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0 (C-10), 21.2 (acetate-CH_3), 22.5 (C-9), 25.2, 29.1, 31.7 (C-6, C-7, C-8), 33.5 (C-5), 38.6 (C-3), 73.3 (C-4), 117.5 (C-1), 133.8 (C-2), 170.7 (C=O). − $C_{12}H_{22}O_2$ (198.31): calcd. C 72.68, H 11.18; found C 72.59, H 10.97.

(4*S*)-4-*tert*-Butyldimethylsilyloxy-1-decanol (25). − 1. TBDMS Protection: To a solution of alcohol **23** (3.21 g, 20.6 mmol) in CH_2Cl_2 (75 mL) at 0 °C was added imidazole (12.59 g, 185 mmol) and TBDMSCl (50% in toluene, 18.2 g, 60.5 mmol). The mixture was stirred overnight at room temp. The reaction was quenched with sat. aqueous NH_4Cl (100 mL) and the aqueous layer was extracted twice with CH_2Cl_2 (50 mL). The combined organic layers were washed with sat. aqueous NaCl (50 mL) and dried with $MgSO_4$.

Removal of the solvents in vacuo and purification by CC (350 cm^3 SiO_2, PE) afforded the TBDMS-protected alkene (5.43 g, 20.1 mmol, 98%) as a colorless liquid.

(4*S*)-4-*tert*-Butyldimethylsilyloxy-1-decene: R_f = 0.49 (SiO_2, PE). − $[a]_D^{26}$ = −14.8 (*c* = 1.26, $CHCl_3$). − IR (film): $\tilde{\nu}$ = 3077 w, 2956, 2929, 2857 s (CH), 1641 m, 1472 m, 1463 m, 1434 w, 1388 w, 1361 m, 1255 s, 1127 m, 1070 m, 1005 m, 938 m, 912 s, 836 s, 809 m, 773 s, 722 w, 666 w cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.03 (s, 6 H, $SiCH_3$), 0.82−0.89 [m, 12 H, 10-H_3, $SiC(CH_3)_3$], 1.17−1.47 (m, 10 H, 5-H_2 to 9-H_2), 2.11−2.23 (m, 2 H, 3-H_2), 3.66 (quint, *J* = 5.6 Hz, 1 H, 4-H), 4.97−5.05 (m, 2 H, 1-H_2), 5.72−5.87 (m, 1 H, 2-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.5, −4.4 ($SiCH_3$), 14.1 (C-10), 18.2 [Si*C*$(CH_3)_3$], 22.6 (C-9), 25.9 [SiC(*C*$H_3)_3$], 25.3, 29.5, 31.9 (C-6, C-7, C-8), 36.8 (C-5), 42.0 (C-3), 72.0 (C-4), 116.5 (C-1), 135.5 (C-2). − $C_{16}H_{34}OSi$ (270.53): calcd. C 71.04, H 12.67; found C 71.29, H 12.47.

2. Hydroboration: The alkene (5.65 g, 20.90 mmol) was dissolved in THF (80 mL) and cooled to 0 °C. 9-BBN (0.5 mmol/mL in THF, 54.3 mL, 26.9 mmol) was added dropwise. The mixture was stirred for 18 h at room temp. At 0 °C first 2 M NaOH (50 mL) and then 30% H_2O_2 (50 mL) was added slowly. The mixture was stirred for 5 h. During that period the temperature was allowed to rise to room temp. After addition of sat. aqueous NH_4Cl (75 mL) the aqueous layer was extracted twice with MTBE (50 mL). The combined organic layers were washed with sat. aqueous NaCl (50 mL) and dried with $MgSO_4$. Removal of the solvents in vacuo and purification by CC (500 cm^3 SiO_2, PE/MTBE, 5:1) afforded alcohol **25** (5.47 g, 19.0 mmol, 91%) as a colorless liquid. R_f = 0.24 (SiO_2, PE/MTBE, 5:1). − $[a]_D^{24}$ = +4.0 (*c* = 2.12, $CHCl_3$). − IR (film): $\tilde{\nu}$ = 3331 bs (OH), 2929 s, 2857 s (CH), 1472 m, 1463 m, 1407 w, 1377 w, 1360 m, 1255 s, 1127 m, 1058 s, 1005 m, 939 m, 906 m, 835 s, 811 m, 714 s, 722 w, 666 w cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.03 (s, 6 H, $SiCH_3$), 0.82−0.89 [m, 12 H, 10-H_3, $SiC(CH_3)_3$], 1.17−1.33 (m, 8 H, 6-H_2 to 9-H_2), 1.36−1.67 (m, 6 H, 2-H_2, 3-H_2, 5-H_2), 2.23 (br. s, 1 H, OH), 3.50−3.74 (m, 3 H, 1-H_2, 4-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.5 ($SiCH_3$), 14.1 (C-10), 18.1 [Si*C*$(CH_3)_3$], 22.6 (C-9), 25.9 [SiC(*C*$H_3)_3$], 25.4, 29.5, 31.8 (C-6, C-7, C-8), 28.1 (C-2), 33.4 (C-3), 36.5 (C-5), 63.2 (C-1), 72.1 (C-4). − $C_{16}H_{36}O_2Si$ (288.55): calcd. C 66.60, H 12.57; found C 66.47, H 12.32.

(4*S*)-4-*tert*-Butyldimethylsilyloxy-1-decyl Bromide (26). − 1. Tosylation: To an ice-cooled solution of the alcohol **25** (5.38 g, 18.6 mmol) in CH_2Cl_2 (120 mL) was added pyridine (7.5 mL, 93.0 mmol). To this solution was added *p*TsCl (8.86 g, 46.5 mmol) at 0 °C. The reaction mixture was stirred overnight. Sat. aqueous $NaHCO_3$ (50 mL) was added to destroy excess *p*TsCl at 0 °C and the mixture was stirred for 1 h. The aqueous layer was extracted twice with MTBE (80 mL). The combined organic layers were washed with sat. aqueous NH_4Cl (80 mL) and sat. aqueous NaCl (80 mL) and dried with $MgSO_4$. Removal of the solvents in vacuo and purification by CC (300 cm^3 SiO_2, PE/MTBE, 10:1) afforded the desired tosylate (6.75 g, 15.3 mmol, 82%) as a colorless liquid. **(4*S*)-4-*tert*-Butyldimethylsilyloxy-1-decyl-*p*-toluenesulfonate:** R_f = 0.39 (SiO_2, PE/MTBE, 10:1). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = −0.04 (s, 3 H, $SiCH_3$), −0.02 (s, 3 H, $SiCH_3$), 0.82−0.89 [m, 12 H, 10-H_3, $SiC(CH_3)_3$], 1.17−1.45 (m, 12 H, 3-H_2, 5-H_2 to 9-H_2), 1.59−1.73 (m, 2 H, 2-H_2), 2.42 (s, 3 H, tosyl-CH_3), 3.50−3.59 (m, 1 H, 4-H), 4.01 (t, *J* = 6.6 Hz, 2 H, 1-H_2), 7.32 (d, *J* = 7.9 Hz, 2 H, tosyl-H), 7.76 (d, *J* = 8.3 Hz, 2 H, tosyl-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.6 ($SiCH_3$), −4.4 ($SiCH_3$), 14.1 (C-10), 18.0 [Si*C*$(CH_3)_3$], 21.6 (tosyl-CH_3), 22.6 (C-9), 24.7 (C-2), 25.8 [SiC(*C*$H_3)_3$], 25.1, 29.4, 31.8 (C-6, C-7, C-8), 32.5 (C-3), 37.0 (C-5), 71.1 (C-1), 71.4 (C-4), 127.9, 129.8, 133.2, 144.6 (tosyl-C). − **2. Bromination:** To a solution of the tosylate (3.95 g, 8.92 mmol) in THF (100 mL) was added LiBr (2.40 g, 27.74 mmol) at 0 °C. The mixture was stirred for 32 h at 35 °C. Treatment with H_2O (100 mL) and MTBE (100 mL) stopped the reaction. The aqueous layer was extracted twice with MTBE (75 mL). The combined organic layers were washed with sat. aqueous NaCl (100 mL) and dried with $MgSO_4$. Removal of the solvents in vacuo and purification by CC (100 cm^3 SiO_2, PE) yielded bromide **26** (2.91 g, 8.29 mmol, 93%) as a colorless liquid. R_f = 0.23 (SiO_2, PE). − $[a]_D^{22}$ = +2.7 (*c* = 1.18, $CHCl_3$). − IR (film): $\tilde{\nu}$ = 2955, 2929, 2856 cm^{-1} s (CH), 1462 m, 1377 w, 1360 w, 1255 m, 1133 m, 1099 m, 1005 w, 939 w, 835 m, 774 s, 665 m. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.02 (s, 6 H, $SiCH_3$), 0.84−0.88 [m, 12 H, 10-H_3, $SiC(CH_3)_3$], 1.18−1.34 (m, 8 H, 6-H_2 to 9-H_2), 1.35−1.45 (m, 6 H, 5-H_2), 1.46−1.63 (m, 2 H, 3-H_2), 1.82−1.95 (m, 2 H, 2-H_2), 3.39 (t, *J* = 6.8 Hz, 2 H, 1-H_2), 3.50−3.74 (quint, *J* = 5.6 Hz, 1 H, 4-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.5, −4.4 ($SiCH_3$), 14.1 (C-10), 18.1 [Si*C*$(CH_3)_3$], 25.9 [SiC(*C*$H_3)_3$], 28.6 (C-2), 22.6, 25.2, 29.5, 31.9 (C-6, C-7, C-8, C-9), 34.4 (C-1), 35.4 (C-3), 37.1 (C-5), 71.5 (C-4). − $C_{16}H_{35}BrOSi$ (351.44): calcd. C 54.68, H 10.04, Br 22.74; found C 54.93, H 9.86, Br 22.73.

(1*R*,5*S*,2′*R*,5′*R*,2″*R*,5″*R*,1‴*R*)-1-[5′-(5″-(1‴-*tert*-Butyldimethylsilyloxy-15‴-benzyloxypentadec-1‴-yl)tetrahydrofuran-2″-yl)tetrahydrofuran-2′-yl]-5-(*tert*-butyldimethylsilyloxy)-undecan-1-ol (27) and (1*S*,5*S*,2′*R*,5′*R*,2″*R*,5″*R*,1‴*R*)-1-[5′-(5″-(1‴-*tert*-Butyldimethylsilyloxy-15‴-benzyloxypentadec-1‴-yl)-tetrahydrofuran-2″-yl)tetrahydrofuran-2′-yl]-5-(*tert*-butyldimethylsiloxy)undecan-1-ol (28): A three-necked flask (100 mL), equipped with a dropping funnel, a reflux condenser and a magnetic stirring bar, was carefully flame-dried in vacuo and, after cooling to 20 °C, flushed with argon. The flask was charged with Mg (984 mg, 40.5 mmol) and the drying procedure was repeated twice. Dry, oxygen-free Et_2O (5 mL) was added and the mixture was stirred vigorously. The dropping funnel was charged with a solution of bromide **26** (1.61 g, 4.59 mmol) in Et_2O (25 mL) and 1,2-dibromoethane (70 μL, 812 μmol). 7 mL of the solution was added quickly to the vigorously stirred mixture. After slight warming with a heat gun the Grignard reaction started. The remaining bromide solution was added over 10 min and the mixture was stirred for an additional 1 h at 35 °C. The Grignard solution was transferred by cannula into a Schlenk flask (50 mL), diluted with Et_2O (10 mL) and cooled to −60 °C. A precipitate that could be stirred was obtained. The flask was charged with CuBr·Me_2S (75 mg, 365 μmol) and the mixture stirred for 15 min at −60 °C. A solution of aldehyde **21** (424 mg, 687 μmol) in Et_2O (7 mL) was added. The reaction mixture was stirred overnight. During that period the temperature was allowed to rise to room temp. Addition of sat. aqueous NH_4Cl (25 mL) and MTBE (25 mL) stopped the reaction. The aqueous layer was extracted twice with MTBE (25 mL). The combined organic layers were washed with sat. aqueous NaCl (50 mL) and dried with $MgSO_4$. The solvents were removed in vacuo. Purification by CC (250 cm^3 SiO_2, PE/MTBE, 5:1, 3:1) afforded reisolated aldehyde **21** (61 mg, 99 μmol) and the separated epimeric alcohols **27** (276 mg, 310 μmol) and **28** (141 mg, 159 μmol) (stereoselectivity ca. 2:1, 68%; yield based on conversion: 80%) as viscous oils.

27: R_f = 0.58 (SiO_2, PE/MTBE, 3:1). − $[a]_D^{18}$ = +9.8 (*c* = 0.40, $CHCl_3$). − IR (film): $\tilde{\nu}$ = 3410 bm (OH), 2928, 2856 s (CH), 1463 m, 1377 w, 1254 w, 1069 m, 836 m, 774 w, 733 w, 698 w cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.02, 0.03, 0.06 (3 × s, 12 H, $SiCH_3$), 0.80−0.89 [m, 21 H, 11-H_3, $SiC(CH_3)_3$], 1.19−1.46 (m, 42 H, 2‴-H_2 to 14‴-H_2, 2-H_2 to 4-H_2, 6-H_2 to 10-H_2), 1.55−1.71

(m, 4 H, 3′-H′, 4′-H′, 3′′-H′, 4′′-H′), 1.82−1.98 (m, 4 H, 3′-H′′, 4′-H′′, 3′′-H′′, 4′′-H′′), 2.42 (d, J = 3.8 Hz, 1 H, OH), 3.30−3.39 (m, 1 H, 1-H), 3.44 (t, J = 6.6 Hz, 2 H, 15′′′-H_2), 3.54−3.61 (m, 2 H, 5-H, 1′′′-H), 3.74−3.93 (m, 4 H, 2′-H, 5′-H, 2′′-H, 5′′-H), 4.48 (s, 2 H, PhCH_2O), 7.23−7.33 (m, 5 H, phenyl-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.7, −4.43, −4.38, −4.2 ($SiCH_3$), 14.1 (C-11), 18.1, 18.3 [SiC(CH_3)$_3$], 25.9, 26.0 [SiC(CH$_3$)$_3$], 21.6 (C-3), 22.6 (C-10), 25.3, 25.8, 26.2, 27.0, 27.4, 28.4, 28.7, 28.8, 29.49, 29.51, 29.63, 29.65, 29.76, 29.86, 31.9 (C-3′′′ to C-14′′′, C-3′, C-4′, C-3′′, C-4′′, C-7 to C-9), 32.5, 33.7 (C-2′′′, C-2), 37.1, 37.3 (C-4, C-6), 70.5 (C-15′′′), 72.4 (C-5), 72.8 (PhCH$_2$O), 74.0 (C-1), 74.9 (C-1′′′), 81.6, 81.7, 82.5, 82.8 (C-2′, C-5′, C-2′′, C-5′′), 127.4, 127.6, 128.3, 138.7 (phenyl-C). − HRMS (EI): calcd. 870.6953 (M − H_2O)$^+$; found 870.6955.

28: R_f = 0.45 (SiO_2, PE/MTBE, 3:1). − $[\alpha]_D^{19}$ = +17.0 (c = 0.50, $CHCl_3$). − IR (film): ṽ = 3412 bm (OH), 2928, 2855 s (CH), 1460 m, 1377 w, 1254 w, 1187 w, 1069 m, 836 m, 774 w, 733 w, 698 w cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.01, 0.02, 0.04 (3 × s, 12 H, $SiCH_3$), 0.83−0.88 [m, 21 H, 11-H_3, SiC(CH_3)$_3$], 1.19−1.48 (m, 42 H, 2′′′-H_2 to 14′′′-H_2, 2-H_2 to 4-H_2, 6-H_2 to 10-H_2), 1.55−1.69 (m, 4 H, 3′-H′, 4′-H′, 3′′-H′, 4′′-H′), 1.76−1.99 (m, 4 H, 3′-H′′, 4′-H′′, 3′′-H′′, 4′′-H′′), 2.11 (br. s, 1 H, OH), 3.44 (t, J = 6.6 Hz, 2 H, 15′′′-H_2), 3.57−3.69 (m, 2 H, 5-H, 1′′′-H), 3.79−3.99 (m, 5 H, 1-H, 2′-H, 5′-H, 2′′-H, 5′′-H), 4.48 (s, 2 H, PhCH_2O), 7.23−7.33 (m, 5 H, phenyl-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.6, −4.44, −4.41, −4.3 ($SiCH_3$), 14.1 (C-11), 18.1, 18.2 [SiC(CH_3)$_3$], 25.9 [SiC(CH$_3$)$_3$], 21.7 (C-3), 22.6 (C-10), 24.5, 25.3, 25.87, 26.01, 26.2, 26.8, 28.5, 28.7, 29.49, 29.51, 29.63, 29.66, 29.76, 29.9, 31.9 (C-3′′′ to C-14′′′, C-3′, C-4′, C-3′′, C-4′′, C-7 to C-9), 32.0, 32.6 (C-2, C-2′′′), 37.0, 37.1 (C-4, C-2), 70.52 (C-15′′′), 71.2 (C-1), 72.2 (C-5), 72.8 (PhCH$_2$O), 74.5 (C-1′′′), 82.2, 82.3, 82.4, 82.5 (C-2′, C-5′, C-2′′, C-5′′), 127.4, 127.6, 128.3, 138.7 (phenyl-C). − HRMS (EI): calcd. 832.6432 (M − C_4H_8)$^+$; found 832.6437.

(15*R*,2′*R*,5′*R*,2′′*R*,5′′*R*,1′′′*R*,5′′′*S*)-15-[5′-(5′′-(5′′′-(*tert*-Butyldimethylsilyloxy)undec-1′′′-yl)-tetrahydrofuran-2′′-yl)tetrahydrofuran-2′-yl]-15-(*tert*-butyldimethylsilyloxy)pentadecan-1-ol (29): − **1. TBDMS Protection:** To a solution of alcohol **27** (231 mg, 260 μmol) in CH_2Cl_2 (10 mL) at −20 °C was added 2,6-lutidine (250 μL, 2.15 mmol) and TBDMSOTf (140 μL, 610 μmol). The mixture was stirred for 45 min at −20 °C. The reaction was quenched with sat. aqueous NH_4Cl (10 mL). The aqueous layer was extracted twice with CH_2Cl_2 (10 mL). The combined organic layers were washed with sat. aqueous NaCl (10 mL) and dried with $MgSO_4$. The solvents were removed in vacuo. Purification by CC (100 cm^3 SiO_2, PE/MTBE, 20:1) afforded the *all*-TBDMS-protected benzyl ether (237 mg, 236 μmol, 91%) as a colorless liquid.

(1*R*,2′*R*,5′*R*,2′′*R*,5′′*R*,1′′′*R*,5′′′*S*)-1-[5′-(5′′-(1′′′,5′′′-Bis(*tert*-butyldimethylsilyloxy)undec-1′′′-yl)tetrahydrofuran-2′′-yl)tetrahydrofuran-2′-yl]-1-*tert*-butyldimethylsilyloxy-15-benzyloxypentadecane: R_f = 0.50 (SiO_2, PE/MTBE, 20:1). − $[\alpha]_D^{20}$ = +26.1 (c = 0.33, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.01, 0.02, 0.03, 0.04 (4 × s, 18 H, $SiCH_3$), 0.81−0.88 [m, 21 H, 11′′′-H_3, SiC(CH_3)$_3$], 1.17−1.70 (m, 46 H, 2-H_2 to 14-H_2, 3′-H′, 4′-H′, 3′′-H′, 4′′-H′, 2′′′-H_2 to 4′′′-H_2, 6′′′-H_2 to 10′′′-H_2), 1.80−1.95 (m, 4 H, 3′-H′′, 4′-H′′, 3′′-H′′, 4′′-H′′), 3.44 (t, J = 6.6 Hz, 2 H, 15-H_2), 3.55−3.65 (m, 3 H, 1-H, 1′′′-H, 5′′′-H), 3.82−3.93 (m, 4 H, 2′-H, 5′-H, 2′′-H, 5′′-H), 4.48 (s, 2 H, PhCH_2O), 7.23−7.33 (m, 5 H, phenyl-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.6, −4.46, −4.37, −4.2 ($SiCH_3$), 14.1 (C-11′′′), 18.2 [SiC(CH_3)$_3$], 26.0 [SiC(CH$_3$)$_3$], 21.6 (C-3′′′), 22.6 (C-10′′′), 25.2, 25.8, 26.2, 27.0, 27.4, 28.4, 28.6, 28.8, 29.50, 29.55, 29.62, 29.67, 29.77, 29.9, 31.9 (C-3 to C-14, C-3′, C-4′, C-3′′, C-4′′, C-7′′′ to C-9′′′), 32.5, 33.7 (C-2, C-2′′′), 37.0, 37.2 (C-4′′′, C-6′′′), 70.5 (C-15), 72.4 (C-5′′′), 72.8 (PhCH$_2$O), 74.8 (C-1′′′), 74.9 (C-1), 81.5, 81.6, 82.2, 82.3 (C-2′, C-5′, C-2′′, C-5′′), 127.4, 127.6, 128.3, 138.7 (phenyl-C). − HRMS(EI): calcd. 1001.7845 (M − H)$^+$; found 1001.7835.

2. Deprotection: The *all*-TBDMS-protected benzyl ether (213 mg, 212 μmol) was dissolved in ethyl acetate (5 mL) and *i*PrOH (5 mL). After adding Pd (10% on activated carbon, 22.7 mg) the mixture was evacuated and filled with H_2 (1 bar). This procedure was repeated four times. The mixture was stirred for 3 h at room temp. The reaction mixture was filtered through a pad of Celite and the pad was washed with CH_2Cl_2 (25 mL). Removal of the solvents and purification by CC (75 cm^3 SiO_2, PE/MTBE, 10:1, 5:1) afforded alcohol **29** (193 mg, 211 μmol, 99%) as a colorless oil. − R_f = 0.18 (SiO_2, PE/MTBE, 10:1). − $[\alpha]_D^{18}$ = +18.0 (c = 0.35, $CHCl_3$). − IR (film): ṽ = 3359 bm (OH), 2954 m, 2928 s, 2856 s (CH), 1472 w, 1463 w, 1254 m, 1094 m, 1005 w, 835 s, 774 m cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.01, 0.02, 0.04 (3 × s, 18 H, $SiCH_3$), 0.82−0.89 [m, 21 H, 11′′′-H_3, SiC(CH_3)$_3$], 1.19−1.76 (m, 46 H, 2-H_2 to 14-H_2, 3′-H′, 4′-H′, 3′′-H′, 4′′-H′, 2′′′-H_2 to 4′′′-H_2, 6′′′-H_2 to 10′′′-H_2), 1.79−1.90 (m, 4 H, 3′-H′′, 4′-H′′, 3′′-H′′, 4′′-H′′), 3.55−3.65 (m, 5 H, 1-H_2, 15-H, 1′′′-H, 5′′′-H), 3.81−3.96 (m, 4 H, 2′-H, 5′-H, 2′′-H, 5′′-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.62, −4.59, −4.45, −4.38, −4.23 ($SiCH_3$), 14.1 (C-11′′′), 18.1, 18.2 [SiC(CH_3)$_3$], 25.9, 26.0 [SiC(CH$_3$)$_3$], 21.8 (C-3′′′), 22.6 (C-10′′′), 25.2, 25.8, 25.87, 27.1, 27.2, 28.4, 29.4, 29.54, 29.59, 29.61, 29.64, 29.9, 31.9 (C-3 to C-13, C-3′, C-4′, C-3′′, C-4′′, C-7′′′ to C-9′′′), 32.4, 32.7 (C-14, C-2′′′), 32.8 (C-2), 37.0, 37.6 (C-4′′′, C-6′′′), 63.1 (C-1), 72.4 (C-5′′′), 74.76 (C-1′′′), 74.83 (C-15), 81.53, 81.58, 82.17, 82.19 (C-2′, C-5′, C-2′′, C-5′′). − HRMS (EI): calcd. 856.6828 (M − C_4H_8)$^+$; found 856.6829.

(15*R*,2′*R*,5′*R*,2′′*R*,5′′*R*,1′′′*R*,5′′′*S*)-15-[5′-(5′′-(1′′′,5′′′-Bis(*tert*-butyldimethylsilyloxy)undec-1′′′-yl)tetrahydrofuran-2′′-yl)tetrahydrofuran-2′-yl]-15-(*tert*-butyldimethylsilyloxy)pentadecanoic Acid (30): $(COCl)_2$ (50 μL, 585 μmol) was dissolved in CH_2Cl_2 (2 mL). The solution was cooled to −60 °C and DMSO (100 μL, 1.37 mmol) dissolved in CH_2Cl_2 (3 mL) was added. At −50 °C, a solution of alcohol **29** (174 mg, 190 μmol) in CH_2Cl_2 (5 mL) was added. After 45 min at −45 °C, the mixture was treated with Et_3N (325 μL, 2.33 mmol). After 5 min the temperature was allowed to rise to 0 °C and H_2O (5 mL) was added to stop the reaction. The aqueous layer was extracted three times with CH_2Cl_2 (5 mL). The combined organic layers were washed with sat. aqueous NaCl (10 mL) and dried with $MgSO_4$. Removal of the solvents afforded the crude aldehyde (R_f = 0.73; SiO_2, PE/MTBE, 5:1), which was dissolved in *t*BuOH (3 mL) and 2-methyl-2-butene (1 mL). The mixture was treated with a solution of $NaClO_2$ (80%, 137 mg, 1.2 mmol) and NaH_2PO_4·2 H_2O (255 mg, 1.6 mmol) in H_2O (5 mL) at 0 °C. The mixture was stirred vigorously at room temp. for 2 h 30 min. MTBE (10 mL) and H_2O (10 mL) were added. The aqueous layer was extracted three times with MTBE (20 mL). The combined organic layers were dried with $MgSO_4$ and the solvents removed in vacuo. Purification by CC (75 cm^3 SiO_2, PE/MTBE, 3:1, MTBE) yielded acid **30** (168 mg, 181 μmol, 95% over two steps) as a colorless oil. − R_f = 0.38 (SiO_2, PE/MTBE, 3:1). − $[\alpha]_D^{20}$ = +15.8 (c = 0.38, $CHCl_3$). − IR (film): ṽ = 3366 bm (OH), 2928, 2856 s (CH), 1711 m (C=O), 1463 w, 1360 w, 1254 m, 1096 m, 1071 w, 1005 w, 836 m, 774 m cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.01, 0.02, 0.04 (3 × s, 18 H, $SiCH_3$), 0.82−0.89 [m, 21 H, 11′′′-H_3, SiC(CH_3)$_3$], 1.19−1.75 (m, 44 H, 3-H_2 to 14-H_2, 3′-H′, 4′-H′, 3′′-H′, 4′′-H′, 2′′′-H_2 to 4′′′-H_2, 6′′′-H_2 to 10′′′-H_2), 1.79−1.93

(m, 4 H, 3′-H′′, 4′-H′′, 3′′-H′′, 4′′-H′′), 2.32 (t, J = 7.5 Hz, 2-H_2), 3.55−3.64 (m, 3 H, 15-H, 1′′′-H, 5′′′-H), 3.81−3.96 (m, 4 H, 2′-H, 5′-H, 2′′-H, 5′′-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.61, −4.58, −4.45, −4.37, −4.22 ($SiCH_3$), 14.1 (C-11′′′), 18.1, 18.2 [Si*C*$(CH_3)_3$], 26.0 [SiC(*C*$H_3)_3$], 21.8 (C-3′′′), 22.7 (C-10′′′), 24.7, 25.2, 25.9, 27.0, 27.1, 27.2, 28.4, 29.1, 29.2, 29.4, 29.55, 29.60, 29.63, 29.9, 31.9 (C-3 to C-13, C-3′, C-4′, C-3′′, C-4′′, C-7′′′ to C-9′′′), 32.4, 32.7 (C-14, C-2′′′), 33.9 (C-2), 37.0, 37.6 (C-4′′′, C-6′′′), 72.4 (C-5′′′), 74.76 (C-1′′′), 74.84 (C-15), 81.54, 81.59, 82.17, 82.20 (C-2′, C-5′, C-2′′, C-5′′), 178.87 (C-1). − HRMS (EI): calcd. 926.7246 $(M)^+$; found 926.7258.

(3*Θ*,5*S*,13′*R*,2′′*R*,5′′*R*,2′′′*R*,5′′′*R*,1′′′′*R*,5′′′′*S*)-3-[13′-(5′′-(5′′′-(1′′′′,5′′′′-Bis(*tert*-butyldimethylsilyloxy)undec-1′′′′-yl)tetrahydrofuran-2′′′-yl)tetrahydrofuran-2′′-yl)-13′-(*tert*-butyldimethylsilyloxy)tridec-1-yl]-5-methyldihydrofuran-2(3*H*)-one (31): To a freshly prepared solution of LDA (2.0 mmol/mL in THF, 1.45 mL, 2.9 mmol) was added LiCl (previously dried for 15 h at 150 °C under reduced pressure; 64 mg, 1.51 mmol) and the mixture was stirred for 30 min at room temp. A 10-mL flask was charged with carboxylic acid **30** (28.5 mg, 30.7 μmol), cooled to 0 °C and the previously prepared LDA solution (sat. with LiCl, 2.0 mmol/mL in THF, 200 μL, 400 μmol) was added dropwise. The yellow solution was stirred for 20 min at room temp. (*S*)-propylene oxide (100 μL, 1.42 mmol) was then added. The mixture was stirred overnight at room temp. The reaction was quenched with sat. aqueous NH_4Cl (2 mL). The aqueous layer was extracted three times with MTBE (10 mL). The combined organic layers were dried with $MgSO_4$. The solvents were removed in vacuo and the residue was redissolved in CH_2Cl_2 (750 μL). Et_3N (100 μL, 717 μmol) and PivCl (50 μL, 406 μmol) were added at 0 °C. The mixture was stirred for 30 min at room temp. The reaction was quenched with sat. aqueous NH_4Cl (1 mL). The aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were dried with $MgSO_4$ and the solvents were removed in vacuo. Purification by CC (20 cm^3 SiO_2, *n*-hexane/MTBE, 5:1) afforded lactone **31** (mixture of C-3 epimers, 15.8 mg, 16.3 μmol, 53% over two steps) as a colorless oil. − R_f = 0.40 and 0.44 (SiO_2, PE/MTBE, 5:1). − IR (film): $\tilde{\nu}$ = 2928, 2856 s (CH), 1775 m (C=O), 1465 m, 1385 w, 1253 m, 1096 m, 1071 w, 836 m, 774 m cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.01, 0.02, 0.04, 0.05 (4 × s, 18 H, $SiCH_3$), 0.84−0.88 [m, 21 H, 11′′′′-H_3, SiC$(CH_3)_3$], 1.19−1.48 and 1.57−1.73 (2 × m, 44 H, 1′-H_2 to 12′-H_2, 3′′-H′, 4′′-H′, 3′′′-H′, 4′′′-H′, 2′′′′-H_2 to 4′′′′-H_2, 6′′′′-H_2 to 10′′′′-H_2, 4-H_2 epimers) with 1.34 and 1.39 (2 × d, J = 6.2 Hz, 3 H, CH_3-lactone epimers), 1.77−1.89 (m, 4 H, 3′′-H′′, 4′′-H′′, 3′′′-H′′, 4′′′-H′′), 1.98−2.09 and 2.40−2.62 (2 × m, 1 H, 3-H epimers), 3.54−3.64 (m, 3 H, 13′-H, 1′′′′-H, 5′′′′-H), 3.80−3.96 (m, 4 H, 2′′-H, 5′′-H, 2′′′-H, 5′′′-H), 4.39−4.49 and 4.58−4.68 (2 × m, 1 H, 5-H epimers). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.63, −4.61, −4.46, −4.38, −4.24 ($SiCH_3$), 14.1 (C-11′′′′), 18.11, 18.18, 18.21 [Si*C*$(CH_3)_3$], 25.94, 25.96 [SiC(*C*$H_3)_3$], 21.0, 21.2 (CH_3-lactone), 21.8 (C-3′′′′), 22.6 (C-10′′′′), 25.2, 25.9, 27.1, 27.2, 27.4, 28.3, 29.3, 29.44, 29.49, 29.53, 29.56, 29.62, 29.9, 30.7, 31.9, 32.3, 32.7, 35.1 (C-1′ to C-12′, C-3′′, C-4′′, C-3′′′, C-4′′′, C-2′′′′, C-7′′′′ to C-9′′′′, C-2), 37.0, 37.6 (C-4′′′′, C-6′′′′), 39.3, 41.5 (C-3), 72.4 (C-5′′′′), 74.7, 74.8 (C-13′, C-1′′′′), 74.9, 75.0 (C-5), 81.55, 81.59, 82.16, 82.19 (C-2′′, C-5′′, C-2′′′, C-5′′′), 179.1, 179.4 (C-1). − HRMS (EI): calcd. 910.6933 $(M - C_4H_8)^+$; found 910.6919.

(5*S*,13′*R*,2′′*R*,5′′*R*,2′′′*R*,5′′′*R*,1′′′′*R*,5′′′′*S*)-3-[13′-(5′′-(5′′′-(1′′′′,5′′′′-Bis(*tert*-butyldimethylsilyloxy)undec-1′′′′-yl)tetrahydrofuran-2′′′-yl)tetrahydrofuran-2′′-yl)-13′-(*tert*-butyldimethylsilyloxy)tridec-1-yl]-5-methylfuran-2(5*H*)-one (32): KHMDS (95%, 53 mg, 252 μmol) was dissolved in THF (200 μL). A mixture of the lactone **31** (19.2 mg, 19.8 μmol) dissolved in THF (300 μL) was added at 0 °C. The mixture was stirred for 30 min at 0 °C and 20 min at room temp. A solution of PhSeCl (107 mg, 559 μmol) in THF (400 μL) was added. The mixture was stirred for 1 h at 0 °C and 1 h 30 min at room temp. The reaction was quenched by adding phosphate buffer (pH = 7, 2 mL) and MTBE (3 mL). The aqueous layer was extracted four times with MTBE (10 mL). The combined organic layers were dried with $MgSO_4$ and the solvents were removed in vacuo. Purification by CC (75 cm^3 SiO_2, *n*-hexane/MTBE, 8:1, 6:1) yielded the selenyllactone (C-3 epimers; R_f = 0.24 and 0.26; SiO_2, *n*-hexane/MTBE, 8:1), which was dissolved in THF (500 μL) and MeOH (500 μL). At 0 °C, MMPP (85%, 40 mg, 69 μmol) was added. The yellow mixture was stirred for 20 min at room temp. The yellow color disappeared. The reaction was quenched by addition of phosphate buffer (pH = 7, 1 mL), sat. aqueous NH_4Cl (1 mL) and MTBE (3 mL). The aqueous layer was extracted four times with MTBE (10 mL). The combined organic layers were dried with $MgSO_4$ and the solvents were removed in vacuo. Purification by CC (30 cm^3 SiO_2, *n*-hexane/MTBE, 6:1) yielded the α,β-unsaturated lactone **32** (7.7 mg, 8.0 μmol, 40% over two steps) as a colorless oil. − R_f = 0.23 (SiO_2, *n*-hexane/MTBE, 5:1). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.01, 0.02, 0.04 (3 × s, 18 H, $SiCH_3$), 0.82−0.89 [m, 21 H, 11′′′′-H_3, SiC$(CH_3)_3$], 1.19−1.45 and 1.59−1.72 (2 × m, 42 H, 2′-H_2 to 12′-H_2, 3′′-H′, 4′′-H′, 3′′′-H′, 4′′′-H′, 2′′′′-H_2 to 4′′′′-H_2, 6′′′′-H_2 to 10′′′′-H_2) with 1.38 (d, J = 6.8 Hz, 3 H, CH_3-lactone), 1.79−1.90 (m, 4 H, 3′′-H′′, 4′′-H′′, 3′′′-H′′, 4′′′-H′′), 2.24 (t, J = 7.2 Hz, 2 H, 1′-H_2), 3.55−3.64 (m, 3 H, 13′-H, 1′′′′-H, 5′′′′-H), 3.81−3.96 (m, 4 H, 2′′-H, 5′′-H, 2′′′-H, 5′′′-H), 4.97 (dd, J = 7.2, 1.5 Hz, 1 H, 5-H), 6.96 (d, J = 1.5 Hz, 1 H, 4-H). − ^{13}C NMR (75 MHz; $CDCl_3$): δ = −4.62, −4.59, −4.45, −4.37, −4.22 ($SiCH_3$), 14.1 (C-11′′′′), 18.1, 18.20, 18.22 [Si*C*$(CH_3)_3$], 19.2 (CH_3-lactone), 25.95, 25.97 [SiC(*C*$H_3)_3$], 21.8 (C-3′′′′), 22.6 (C-10′′′′), 25.2, 25.9, 27.1, 27.2, 27.4, 28.4, 29.2, 29.3, 29.5, 29.6, 29.9, 31.9, 32.4, 32.7 (C-1′ to C-12′, C-3′′, C-4′′, C-3′′′, C4′′′, C-2′′′′, C-7′′′′ to C-9′′′′), 37.0, 37.6 (C-4′′′′, C-6′′′′), 72.4 (C-5′′′′), 74.76, 74.83 (C-13′, C-1′′′′), 77.4 (C-5), 81.55, 81.59, 82.17, 82.20 (C-2′′, C-5′′, C-2′′′, C-5′′′), 134.4 (C-3), 148.8 (C-4), 173.9 (C-2).

Squamocin D (Asiminacin): Unsaturated lactone **32** (7.7 mg, 8.0 μmol) was dissolved in THF (1 mL). HF (5% in MeCN, 2.0 mL, 5.0 mmol) was added and the mixture was stirred for 2 h at room temp. The reaction was quenched with sat. aqueous $NaHCO_3$ (3 mL) and CH_2Cl_2 (2 mL). The aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were dried with $MgSO_4$. Removal of the solvents in vacuo and purification by CC (10 cm^3 SiO_2, MTBE, MTBE/MeOH, 100:1, 20:1, $CHCl_3$/MeOH, 10:1) afforded squamocin D (3.9 mg, 6.3 μmol, 79%) as a colorless solid. − R_f = 0.29 (MTBE/MeOH, 100:1). − $[\alpha]_D^{21}$ = +20 (c = 0.095, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, J = 6.4 Hz, 3 H, 34-CH_3), 1.21−1.69 (m, 42 H, 4-H_2 to 14-H_2, 17-H′, 18-H′, 21-H′, 22-H′, 25-H_2 to 27-H_2, 29-H_2 to 33-H_2), 1.38 (d, J = 6.8 Hz, 3 H, 37-H_3), 1.91−2.01 (m, 4 H, 17-H′′, 18-H′′, 21-H′′, 22-H′′), 2.24 (tt, J = 7.9, 1.5 Hz, 3-H_2), 3.33−3.42 (m, 2 H, 15-H, 24-H), 3.55−3.60 (m, 1 H, 28-H), 3.78−3.89 (m, 4 H, 16-H, 19-H, 20-H, 23-H), 4.97 (qq, J = 6.8, 1.5 Hz, 1 H, 36-H), 6.96 (q, J = 1.5 Hz, 1 H, 35-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 (C-34), 19.2 (C-37), 21.7 (C-26), 22.6 (C-33), 25.2 (C-3), 25.64, 25.65, 27.40, 28.40, 28.93, 28.96, 29.1−29.7 signal overlap, 29.72, 31.8 (C-4 to C-13, C-17, C-18, C-21, C-22, C-30 to C-32), 33.3, 33.5 (C-14, C-25), 37.32, 37.54 (C-27, C-29), 71.8 (C-28), 73.9, 74.1 (C-15, C-24), 77.4 (C-36), 81.76, 81.83 (C-19, C-20), 83.0, 83.2 (C-16, C-23), 134.4 (C-2), 148.8 (C-

35), 173.9 (C=O). − HRMS (EI): calcd. 604.4703 $(M - H_2O)^+$; found 604.4705.

14-Benzyloxytetradecanoic Acid (33): 1. Swern Oxidation: $(COCl)_2$ (770 μL, 8.83 mmol) was dissolved in CH_2Cl_2 (20 mL). The solution was cooled to −60 °C and DMSO (1.50 mL, 21.1 mmol) dissolved in CH_2Cl_2 (2 mL) was added. At −55 °C, a solution of alcohol **17** (1.10 g, 3.45 mmol) in CH_2Cl_2 (20 mL) was added. After 45 min at −50 °C, the mixture was treated with Et_3N (4.50 mL, 32.3 mmol). After 5 min, the temperature was allowed to rise to 0 °C and H_2O (50 mL) was added to stop the reaction. The aqueous layer was extracted twice with CH_2Cl_2 (50 mL). The combined organic layers were washed with 1 M HCl (50 mL), sat. aqueous $NaHCO_3$ (50 mL) and sat. aqueous NaCl (50 mL) and dried with $MgSO_4$. After evaporation of the solvents, the crude aldehyde (1.06 g, 3.31 mmol, 94%) was obtained as a yellow liquid.

14-Benzyloxytetradecanal: R_f = 0.60 (PE/MTBE, 5:1). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.22−1.40 (m, 18 H, 4-H_2 to 12-H_2), 1.52−1.67 (m, 4 H, 3-H_2, 13-H_2), 2.39 (dt, J = 7.5, 1.9 Hz, 2 H, 2-H_2), 3.44 (t, J = 6.8 Hz, 2 H, 14-H_2), 4.48 (s, 2 H, PhCH_2O), 7.21−7.30 (m, 5 H, phenyl-H), 9.73 (t, J = 1.9 Hz, 1 H, CHO). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.1, 26.2, 29.1, 29.3, 29.37, 29.45, 29.52, 29.54, 29.56 (C-3 to C-12), 29.8 (C-13), 43.9 (C-2), 70.5 (C-14), 72.8 (PhCH$_2$O), 127.4, 127.6, 128.3, 138.7 (phenyl-C), 202.9 (CHO).

2. Chlorite Oxidation: A solution of the aldehyde (1.06 g, 3.31 mmol) in *t*BuOH (25 mL) and 2-methyl-2-butene (10.0 mL) was treated with a mixture of $NaClO_2$ (80%, 1.19 g, 10.5 mmol) and $NaH_2PO_4{\cdot}2\ H_2O$ (2.18 g, 14.0 mmol) in H_2O (25 mL) at 0 °C. The mixture was stirred vigorously at room temp. for 5 h. MTBE (50 mL) and H_2O (50 mL) were added and the phases were separated. The aqueous layer was extracted twice with MTBE (50 mL). The combined organic layers were washed with sat. aqueous NaCl (75 mL) and dried with $MgSO_4$. Purification by CC (200 cm^3 SiO_2, PE/MTBE, 3:1) yielded acid **33** (1.09 g, 3.27 mmol, 99%) as colorless crystals. − R_f = (PE/MTBE, 3:1). − M.p.: 49 °C. − IR (KBr): $\tilde{\nu}$ = 3438 bw (OH), 3029 w, 2916, 2849 s (CH), 2793 w, 2677 w, 1703 s (C=O), 1496 w, 1471 w, 1463 w, 1454 w, 1360 w, 1321 w, 1302 m, 1255 w, 1207 w, 1188 w, 1103 m, 1046 w, 1026 w, 992 w, 944 w, 913 w, 748 m, 698 m cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.20−1.39 (bm, 18 H, 4-H_2 to 12-H_2), 1.53−1.67 (m, 4 H, 3-H_2, 13-H_2), 2.32 (t, J = 7.6 Hz, 2 H, 2-H_2), 3.45 (t, J = 6.6 Hz, 2 H, 14-H_2), 4.49 (s, 2 H, PhCH_2O), 7.22−7.34 (m, 5 H, phenyl-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.7, 26.2, 29.0, 29.2, 29.39, 29.45, 29.51, 29.54 (C-3 to C-12), 29.7 (C-13), 34.0 (C-2), 70.5 (C-14), 72.8 (PhCH$_2$O), 127.4, 127.6, 128.3, 138.6 (phenyl-C), 179.5 (COOH). − $C_{21}H_{34}O_3$ (334.50): calcd. C 75.41, H 10.24; found C 75.35, H 10.25.

(3*Θ*,5*S*)-3-(12′-Benzyloxydodecyl)-5-methyldihydrofuran-2(3*H*)-one (34): A solution of diisopropylamine (280 μL, 2.00 mmol) in THF (5 mL) was treated with *n*BuLi (2.51 mmol/mL in *n*-hexane, 600 μL, 1.51 mmol) at −40 °C. The temperature was allowed to rise to 0 °C during 20 min. At 0 °C a solution of carboxylic acid **33** (190 mg, 569 μmol) in THF (5 mL) was added dropwise. The yellow solution was stirred for 45 min at 0 °C. (*S*)-Propylene oxide (500 μL, 7.14 mmol) was then added. The mixture was stirred 15 min at 0 °C and for a further 2 h at room temp. The reaction was quenched with sat. aqueous NH_4Cl (10 mL). The aqueous layer was extracted twice with MTBE (25 mL). The combined organic layers were washed with sat. aqueous NaCl (25 mL) and dried with $MgSO_4$. The solvents were removed in vacuo and the residue was redissolved in CH_2Cl_2 (3 mL). Et_3N (180 μL, 1.29 mmol) and PivCl (100 μL, 812 μmol) were added at 0 °C. The mixture was stirred for 45 min at room temp. The reaction was quenched with sat. aqueous NH_4Cl (15 mL). The aqueous layer was extracted twice with CH_2Cl_2 (25 mL). The combined organic layers were washed with sat. aqueous NaCl (25 mL) and dried with $MgSO_4$. Purification by CC (100 cm^3 SiO_2, PE/MTBE, 3:1) afforded a mixture of the epimeric lactones **34** (138 mg, 367 μmol, 64%) as a colorless wax. − R_f = 0.39 and 0.42 (PE/MTBE, 3:1). − M.p.: 20−25 °C. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21−2.10 (m, 24 H, 1′-H_2 to 11′-H_2, 4-H_2) with 1.34 and 1.39 (2 × d, J = 6.4 Hz, 3 H, CH_3 epimers), 2.39−2.63 (m, 1 H, 3-H epimers), 3.44 (t, J = 6.8 Hz, 2 H, 12′-H_2), 4.48 (s, 2 H, PhCH_2O), 4.57−4.68 (m, 1 H, 5-H), 7.23−7.33 (m, 5 H, phenyl-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.0, 21.2 (CH_3 epimers), 26.2, 27.3, 29.3, 29.39, 29.44, 29.50, 29.53, 29.7, 30.3, 30.7 (C-1′ to C-11′), 35.0, 37.0 (C-4), 39.3, 41.5 (C-3), 70.5 (C-12′), 72.8 (PhCH$_2$O), 74.9, 75.0 (C-5), 127.4, 127.6, 128.3, 138.7 (phenyl-C), 179.1, 179.4 (C-2).

(5*S*)-3-(12′-Benzyloxydodecyl)-5-methylfuran-2(5*H*)-one (35): KHMDS (95%, 105 mg, 528 μmol) was dissolved in THF (0.5 mL). A solution of lactone **34** (38.8 mg, 104 μmol) in THF (0.5 mL) was added at 0 °C. The mixture was stirred for 30 min at 0 °C and 20 min at room temp. A solution of PhSeCl (164 mg, 856 μmol) in THF (1 mL) was added. The mixture was stirred for 2 h at room temp. The reaction was quenched by adding phosphate buffer (pH = 7, 5 mL), sat. aqueous NH_4Cl (5 mL) and MTBE (10 mL). The aqueous layer was extracted twice with MTBE (25 mL). The combined organic layers were washed with sat. aqueous NaCl (50 mL) and dried with $MgSO_4$. Purification by CC (50 cm^3 SiO_2, PE/MTBE, 5:1) yielded the epimeric selenyllactones, which were dissolved in THF (2 mL) and MeOH (2 mL). At 0 °C, MMPP (85%, 506 mg, 870 μmol) was added. The yellow mixture was stirred for 1 h at room temp. The reaction was quenched by addition of sat. aqueous NH_4Cl (5 mL) and MTBE (10 mL). The aqueous layer was extracted twice with MTBE (25 mL). The combined organic layers were washed with sat. aqueous NaCl (15 mL) and dried with $MgSO_4$. Purification by CC (30 cm^3 SiO_2, PE/MTBE, 3:1) yielded the unsaturated lactone **35** (27.2 mg, 73.0 μmol, 70%) as a colorless wax. R_f = 0.31 (PE/MTBE, 3:1). − M.p.: 20−25 °C. − $[\alpha]_D^{20}$ = +12.0 (c = 0.25, $CHCl_3$). − IR (KBr): $\tilde{\nu}$ = 2926, 2854 cm^{-1} s (CH), 1756 s (C=O), 1650 w (C=C), 1454 w, 1362 w, 1318 w, 1100 m, 1027 w, 858 w, 736 w, 671 w. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.22−1.64 (m, 20 H) with 1.38 (d, J = 6.8 Hz, 3 H, CH_3-lactone) and 2.20−2.28 (m, 2 H) (1′-H_2 to 11′-H_2), 3.44 (t, J = 6.6 Hz, 2 H, 12′-H_2), 4.48 (s, 2 H, PhCH_2O), 4.92−5.01 (m, 1 H, 4-H), 6.96 (dd, J = 3.4, 1.7 Hz, 1 H, 3-H), 7.22−7.33 (m, 5 H, phenyl-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.2 (CH_3), 25.1, 26.2, 27.4, 29.2, 29.27, 29.45, 29.47, 29.52, 29.54, 29.8 (C-1′ to C-11′), 70.5 (C-12′), 72.8 (PhCH$_2$O), 77.4 (C-5), 127.4, 127.6, 128.3 (phenyl-C), 134.2 (C-3), 138.7 (phenyl-C), 148.8 (C-4), 173.9 (C-2). − $C_{24}H_{36}O_3$ (372.55): calcd. C 77.38, H 9.74; found C 77.13, H 9.72.

(15*R*,2′*R*,5′*R*,2′′*R*,5′′*R*,1′′′*S*,5′′′*S*)-15-[5′-(5′′-(1′′′,5′′′-Bis(*tert*-butyldimethylsilyloxy)undec-1′′′-yl-tetrahydrofuran-2′′-yl)tetrahydrofuran-2′-yl]-15-(*tert*-butyldimethylsilyloxy)pentadecan-1-ol (36): To a solution of alcohol **28** (130 mg, 146 μmol) in CH_2Cl_2 (10 mL) at −20 °C were added 2,6-lutidine (220 μL, 1.89 mmol) and TBDMSOTf (120 μL, 523 μmol). The mixture was stirred for 2 h at −20 °C. The reaction was quenched with sat. aqueous NH_4Cl (10 mL). The aqueous layer was extracted twice with CH_2Cl_2 (10 mL). The combined organic layers were washed with sat. aqueous NaCl (10 mL) and dried with $MgSO_4$. Removal of the solvents in vacuo and purification by CC (75 cm^3 SiO_2, PE/MTBE,

20:1) afforded the *all*-TBDMS protected benzyl ether (R_f = 0.43; PE/MTBE, 20:1; 131 mg, 131 μmol, 90%) as a colorless liquid, which was redissolved in ethyl acetate (5 mL) and *i*PrOH (5 mL). After adding Pd (10% on activated carbon, 15.7 mg), the flask was evacuated and filled with H_2 (1 bar). The procedure was repeated four times. The reaction mixture was then stirred overnight at room temp., filtered through a pad of Celite and washed with CH_2Cl_2 (25 mL). Removal of the solvents and purification by CC (30 cm^3 SiO_2, PE/MTBE, 5:1) afforded the primary alcohol **36** (100 mg, 109 μmol, 75% over two steps) as a colorless oil. − R_f = 0.22 (PE/MTBE, 5:1). − $[a]_D^{21}$ = +12.4 (c = 0.34, $CHCl_3$). − IR (film): $\tilde{\nu}$ = 3387 cm^{-1} bm (OH), 2952, 2928, 2856 s (CH), 1462 w, 1253 m, 1070 m, 836 m, 775 m. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.01, 0.02, 0.04 (3 × s, 18 H, $SiCH_3$), 0.82−0.89 [m, 21 H, 11‴-H_3, $SiC(CH_3)_3$], 1.19−1.45 and 1.49−1.71 (2 × m, 46 H, 2-H_2 to 14-H_2, 3′-H′, 4′-H′, 3″-H′, 4″-H′, 2‴-H_2 to 4‴-H_2, 6‴-H_2 to 10‴-H_2), 1.76−1.91 (m, 4 H, 3′-H″, 4′-H″, 3″-H″, 4″-H″), 3.55−3.65 (m, 4 H, 1-H_2, 15-H, 5‴-H), 3.71−3.77 (m, 1 H, 1‴-H), 3.79−3.94 (m, 4 H, 2′-H, 5′-H, 2″-H, 5″-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.7, −4.5, −4.45, −4.38, −4.2 ($SiCH_3$), 14.1 (C-11‴), 18.12, 18.15, 18.24 [Si*C*$(CH_3)_3$], 25.93, 25.98 [SiC(*C*$H_3)_3$], 21.1 (C-3‴), 22.6 (C-10‴), 25.3, 25.7, 25.9, 26.1, 27.2, 28.4, 29.4, 29.5, 29.62, 29.64, 29.9, 31.9 (C-3 to C-13, C-3′, C-4′, C-3″, C-4″, C-7‴ to C-9‴), 32.4, 32.8 (C-14, C-2‴), 35.1 (C-2), 37.0, 37.5 (C-4‴, C-6‴), 63.1 (C-1), 72.2 (C-5‴), 73.7 (C-1‴), 74.8 (C-15), 81.36, 81.43, 82.17, 82.20 (C-2′, C-5′, C-2″, C-5″). − HRMS (EI): calcd. 855.6750 (M − C_4H_9)$^+$; found 855.6749.

(15*R*,2′*R*,5′*R*,2″*R*,5″*R*,1‴*S*,5‴*S*)-15-[5′-(5″-(1‴,5‴-Bis(*tert*-butyldimethylsilyloxy)undec-1‴-yl)tetrahydrofuran-2″-yl)tetrahydrofuran-2′-yl]-15-(*tert*-butyldimethylsilyloxy)pentadecanoic Acid (37): $(COCl)_2$ (50 μL, 550 μmol) was dissolved in CH_2Cl_2 (2 mL). The solution was cooled to −60 °C and DMSO (90 μL, 1.30 mmol), dissolved in CH_2Cl_2 (1 mL), was added. At −50 °C a solution of alcohol **36** (99 mg, 108 μmol) in CH_2Cl_2 (2 mL) was added. After 45 min at −45 °C, the mixture was treated with Et_3N (300 μL, 2.15 mmol). After 5 min, the temperature was allowed to rise to 0 °C and H_2O (5 mL) was added to stop the reaction. The aqueous layer was extracted three times with CH_2Cl_2 (5 mL). The combined organic layers were washed with sat. aqueous NaCl (10 mL) and dried with $MgSO_4$. Removal of the solvents afforded the crude aldehyde (R_f = 0.83; PE/MTBE, 3:1), which was dissolved in *t*BuOH (3 mL) and 2-methyl-2-butene (1 mL). The mixture was treated with a solution of $NaClO_2$ (80%, 95 mg, 840 μmol) and NaH_2PO_4·2 H_2O (190 mg, 1.22 mmol) in H_2O (5 mL) at 0 °C. The mixture was stirred vigorously at room temp. overnight. MTBE (10 mL) and H_2O (10 mL) were added and the layers were separated. The aqueous layer was extracted three times with MTBE (20 mL). The combined organic layers were dried with $MgSO_4$ and the solvents were removed in vacuo. Purification by CC (50 cm^3 SiO_2, *n*-hexane/MTBE, 5:1, MTBE) yielded acid **37** (89 mg, 96 μmol, 89% over two steps) as a colorless oil. − R_f = 0.29 (PE/MTBE, 3:1). − $[a]_D^{20}$ = +11.4 (c = 0.90, $CHCl_3$). − IR (film): $\tilde{\nu}$ = 2928, 2856 s (CH), 1712 m (C=O), 1472 w, 1463 w, 1362 w, 1254 m, 1096 m, 1072 w, 1005 w, 836 m, 774 m, 723 w, 663 w cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.01, 0.03, 0.04 (3 × s, 18 H, $SiCH_3$), 0.82−0.94 [m, 21 H, 11‴-H_3, $SiC(CH_3)_3$], 1.18−1.48 and 1.56−1.74 (2 × m, 44 H, 3-H_2 to 14-H_2, 3′-H′, 4′-H′, 3″-H′, 4″-H′, 2‴-H_2 to 4‴-H_2, 6‴-H_2 to 10‴-H_2), 1.77−1.93 (m, 4 H, 3′-H″, 4′-H″, 3″-H″, 4″-H″), 2.32 (t, J = 7.5 Hz, 2-H_2), 3.55−3.66 (m, 2 H, 15-H, 5‴-H), 3.72−3.78 (m, 1 H, 1‴-H), 3.80−3.95 (m, 4 H, 2′-H, 5′-H, 2″-H, 5″-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.7, −4.52, −4.46, −4.39, −4.2 ($SiCH_3$), 14.1 (C-11‴), 18.11, 18.14, 18.22 [Si*C*$(CH_3)_3$], 25.92, 25.97 [SiC(*C*$H_3)_3$], 21.1 (C-3‴), 22.6 (C-10‴), 24.7, 25.3, 25.9, 27.2, 28.41, 28.45, 29.1, 29.2, 29.4, 29.51, 29.55, 29.6, 29.9, 31.9 (C-3 to C-13, C-3′, C-4′, C-3″, C-4″, C-7‴ to C-9‴), 32.3, 35.1 (C-14, C-2‴), 34.0 (C-2), 37.0, 37.4 (C-4‴, C-6‴), 72.2 (C-5‴), 73.6 (C-1‴), 74.7 (C-15), 81.36, 81.42, 82.15, 82.18 (C-2′, C-5′, C-2″, C-5″), broad C=O signal not seen. − HRMS(EI): calcd. 851.6437 (M − C_4H_9. − H_2O)$^+$; found 851.6439.

(3*Θ*,5*S*,13′*R*,2‴*R*,5‴*R*,2⁗*R*,5⁗*R*,1⁗⁗*S*,5⁗⁗*S*)-3-[13′-(5″-(5‴-(1⁗⁗,5⁗⁗-Bis(*tert*-butyldimethylsilyloxy)undec-1⁗⁗-yl)tetrahydrofuran-2‴-yl)tetrahydrofuran-2″-yl)-13′-(*tert*-butyldimethylsilyloxy)tridec-1-yl]-5-methyldihydrofuran-2(3*H*)-one (38): To a freshly prepared solution of LDA in THF (2.0 mmol/mL, 1.45 mL, 2.9 mmol) was added LiCl (previously dried for 15 h at 150 °C under reduced pressure, 64 mg, 1.51 mmol) and the mixture was stirred for 30 min at room temp. A 10-mL flask was charged with carboxylic acid **37** (25.0 mg, 26.9 μmol), cooled to 0 °C and the previously prepared LDA solution in THF (sat. with LiCl, 2.0 mmol/mL, 200 μL, 400 μmol) was added dropwise. The yellow solution was stirred for 20 min at room temp. (*S*)-Propylene oxide (250 μL, 3.57 mmol) was added. The mixture was stirred overnight at room temp. The reaction was quenched with sat. aqueous NH_4Cl (2 mL). The aqueous layer was extracted three times with MTBE (10 mL). The combined organic layers were dried with $MgSO_4$. The solvents were removed in vacuo and the residue was redissolved in CH_2Cl_2 (750 μL). Et_3N (100 μL, 717 μmol) and PivCl (50 μL, 406 μmol) were added at 0 °C. The mixture was stirred for 30 min at room temp. The reaction was quenched with sat. aqueous NH_4Cl (1 mL). The aqueous layer was extracted three times with CH_2Cl_2 (15 mL). The combined organic layers were dried with $MgSO_4$ and the solvents were removed in vacuo. Purification by CC (20 cm^3 SiO_2, *n*-hexane/MTBE, 5:1) afforded lactone **38** (epimeric mixture at C-3, 15.1 mg, 15.6 μmol, 58% over two steps) as a colorless oil. R_f = 0.20 and 0.25 (PE/MTBE, 5:1). − IR (film): $\tilde{\nu}$ = 2928, 2856 s (CH), 1777 m (C=O), 1462 m, 1361 w, 1253 m, 1096 m, 1070 w, 1006 w, 836 m, 774 m, 725 w cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.00, 0.01, 0.03, 0.04 (4 × s, 18 H, $SiCH_3$), 0.83−0.89 [m, 21 H, 11⁗⁗-H_3, $SiC(CH_3)_3$], 1.20−1.49 and 1.58−1.73 (2 × m, 44 H, 1′-H_2 to 12′-H_2, 3‴-H′, 4‴-H′, 3⁗⁗-H′, 4⁗⁗-H′, 2⁗⁗⁗-H_2 to 4⁗⁗⁗-H_2, 6⁗⁗⁗-H_2 to 10⁗⁗⁗-H_2, 35-H_2 epimers) with 1.34, 1.38 (2 × d, J = 6.3 Hz, 3 H, CH_3-lactone epimers), 1.77−1.90 (m, 4 H, 3‴-H″, 4‴-H″, 3⁗⁗-H″, 4⁗⁗-H″), 2.02−2.61 (m, 1 H, 3-H epimers), 3.54−3.65 (m, 2 H, 13′-H, 5⁗⁗⁗-H), 3.70−3.77 (m, 1 H, 1⁗⁗⁗-H), 3.80−3.95 (m, 4 H, 2‴-H, 5‴-H, 2⁗⁗⁗-H, 5⁗⁗⁗-H), 4.19−4.66 (m, 1 H, 5-H epimers). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.6, −4.4, −4.3, −4.2 ($SiCH_3$), 14.1 (C-11⁗⁗), 18.1, 18.2, 18.25 [Si*C*$(CH_3)_3$], 25.95, 26.0 [SiC(*C*$H_3)_3$], 21.0, 21.1, 21.2 (CH_3-lactone epimers, C-3⁗⁗), 22.6 (C-10⁗⁗), 24.6, 25.2, 25.9, 27.2, 28.4, 28.5, 29.0−29.7 signal overlap, 29.9, 30.8, 31.9, 32.3, 32.7, 35.1 (C-1′ to C-12′, C-3‴, C-4‴, C-3⁗⁗, C-4⁗⁗, C-2⁗⁗⁗, C-7⁗⁗⁗ to C-9⁗⁗⁗, C-2 epimers), 37.0, 37.5 (C-4⁗⁗⁗, C-6⁗⁗⁗), 39.3, 41.5 (C-3 epimers), 72.2 (C-5⁗⁗⁗), 73.6 (C-1⁗⁗⁗), 74.8 (C-13′), 74.9, 75.0 (C-5 epimers), 81.3, 81.4, 82.15, 82.2 (C-2‴, C-5‴, C-2⁗⁗⁗, C-5⁗⁗⁗), 179.1, 179.4 (C-2 epimers). − HRMS(EI): calcd. 909.6855 (M − C_4H_9)$^+$; found 909.6839.

Squamocin A (Annonin I, Rollinicin): − 1. Introduction of the Double Bond: To a solution of lactone **38** (8.5 mg, 8.8 μmol) in THF (300 μL) was added freshly prepared LDA (2.0 mmol/mL, 350 μL, 700 μmol) at 0 °C. The mixture was stirred at room temp. for 30 min. PhSeCl (250 mg, 1.31 mmol) was added at 0 °C. The mixture was stirred for 1 h at 0 °C and 1 h 30 min at room temp. The reaction was quenched by adding phosphate buffer (pH = 7,

2 mL) and MTBE (3 mL). The aqueous layer was extracted four times with MTBE (10 mL). The combined organic layers were dried with $MgSO_4$. The solvents were removed and the residue was redissolved in THF (500 µL) and MeOH (500 µL). At 0 °C, MMPP (85%, 30 mg, 59 µmol) was added. The yellow mixture was stirred for 30 min at room temp. The reaction were quenched by addition of phosphate buffer (pH = 7, 1 mL), sat. aqueous NH_4Cl (1 mL) and MTBE (3 mL). The aqueous layer was extracted four times with MTBE (10 mL). The combined organic layers were dried with $MgSO_4$ and the solvents were removed in vacuo. Purification by CC (20 cm^3 SiO_2, *n*-hexane/MTBE, 6:1) yielded the corresponding butenolide (3.4 mg, 3.5 µmol, 40% over two steps) as a colorless oil (R_f = 0.45, PE/MTBE, 4:1).

2. Deprotection: The protected squamocin A (3.4 mg, 3.5 µmol) was dissolved in THF (1 mL). HF (5% in MeCN, 1.0 mL, 2.5 mmol) was added and the mixture was stirred for 6 h at room temp. The reaction was quenched with sat. aqueous $NaHCO_3$ (1 mL) and $CHCl_3$ (1 mL). The aqueous layer was extracted three times with CH_2Cl_2 (10 mL). The combined organic layers were dried with $MgSO_4$. Removal of the solvents in vacuo and purification by CC (5 cm^3 SiO_2, $CHCl_3$ → $CHCl_3$/MeOH, 10:1) afforded squamocin A (1.8 mg, 2.9 µmol, 82%) as a colorless solid. R_f = 0.44 (MTBE/MeOH, 20:1). − $[\alpha]_D^{22}$ = +15 (*c* = 0.080, $CHCl_3$). − IR (KBr): $\tilde{\nu}$ = 3450 bs (OH), 2923 m, 2852 m, 1752 (C=O), 1654 (C=C), 1507 m, 1399 w, 1047 m, 809 w, 669 m cm^{-1}. − ^1H NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 6.8 Hz, 3 H, 34-H_3), 1.22−1.68 (m, 42 H, 4-H_2 to 14-H_2, 17-H′, 18-H′, 21-H′, 22-H′, 25-H_2 to 27-H_2, 29-H_2 to 33-H_2), 1.38 (d, *J* = 6.8 Hz, 3 H, 37-H_3), 1.91−2.02 (m, 4 H, 17-H′′, 18-H′′, 21-H′′, 22-H′′), 2.24 (t, *J* = 7.2 Hz, 3-H_2), 3.33−3.42 (m, 1 H, 15-H), 3.55−3.66 (m, 2 H, 24-H, 28-H), 3.79−3.94 (m, 4 H, 16-H, 19-H, 20-H, 23-H), 4.97 (qq, *J* = 6.8, 1.9 Hz, 1 H, 36-H), 6.96 (q, *J* = 1.5 Hz, 1 H, 35-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 (C-34), 19.2 (C-37), 22.0 (C-26), 22.6 (C-33), 25.2 (C-3), 24.8, 25.63, 25.66, 27.4, 28.4, 28.9, 29.1−29.7 signal overlap, 29.72, 31.8 (C-4 to C-13, C-17, C-18, C-21, C-22, C-30 to C-32), 32.5 (C-25), 33.4 (C-14), 37.3, 37.5 (C-27, C-29), 71.4 (C-24), 71.8 (C-28), 74.1 (C-15), 77.4 (C-36), 82.3, 82.5, 82.8, 83.3 (C-16, C-19, C-20, C-23), 134.3 (C-2), 148.8 (C-35), 173.9 (C=O). − HRMS (EI): calcd. 623.4887 $(M + H)^+$; found 623.4897.

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