A Convergent Total Synthesis of (−)-Mucocin: An Acetogenin from *Annonaceae*

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Abstract: A total synthesis of the *Annonaceous* acetogenin mucocin has been accomplished. The synthesis follows a convergent strategy, wherein at a very late stage the left part of the molecule is connected with the right part. The key reaction is the stereocontrolled addition of an organomagnesium compound **2** to the aldehyde **3**. The THP ring of mucocin is build by a 6-*endo* epoxide cyclization of an epoxyacetonide precursor (**16** → **17**). The new modular synthetic approach developed herein should be useful for the synthesis of other related natural products as well as pharmacologically interesting analogues.

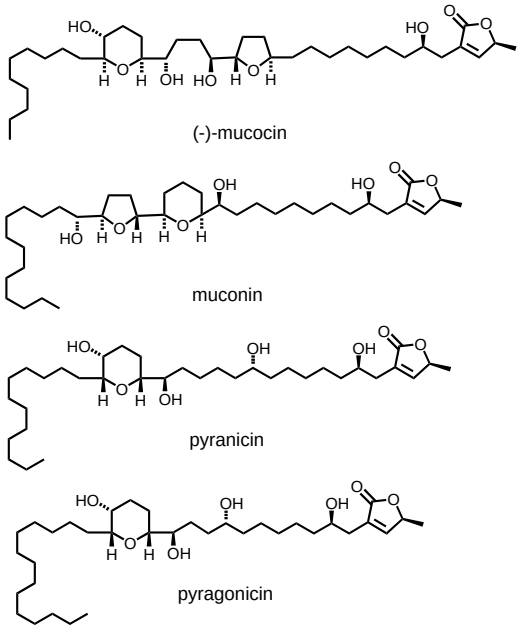
Keywords: *Annonaceous* acetogenins · antitumor agents · mucocin · natural products · total synthesis

Introduction

More than 250 acetogenins from various plant species of *Annonaceae* have been isolated and characterised.[1] This class of natural products shows potent biological properties, for example as antitumor agents, immunosuppressants or pesticides.[1] As mode of action a blockage of mitochondrial complex I (NADH-ubiquinone oxidoreductase) of mammalian and insects is discussed.[2] The membrane conformation of *Annonaceous* acetogenins and its relation to complex I inhibition has been investigated.[3] Furthermore, these compounds inhibit a NADH oxidase, that is found in the plasma membrane of tumors but not in normal cells.[4] As a consequence, the ATP level of the tumor cells decreases. This has an inhibitory effect on multiple drug resistance caused by ATP-driven transporter systems.

Common structural features of the acetogenins from *Annonaceae* are a central cyclic ether part with one left and one right side chain. A butenolide unit is located at the right terminus of the molecule. The 2,5-disubstituted tetrahydrofuran (THF) moiety is part of many acetogenins. Mono-THF, bis-THF and ter-THF substructures are known and subject to intensive synthetic efforts.[5] Within the acetogenins a group of compounds exists also bearing a THP-ring in the molecular scaffold. Representative members of that group are mucocin,[6] muconin,[7] pyranicin,[8] and pyragonicin.[8]

Mucocin was isolated from *Rollinia mucosa*.[6] The molecule shows a highly selective inhibitory effect against A-549 (lung cancer) and PACA-2 (pancreatic cancer) cell lines with a selectivity up to 10000 times that of the known antitumor agent adriamycin. Here we report in detail on a convergent total synthesis of mucocin.[9]



Results and Discussion

Our retrosynthetic analysis of mucocin leads to a disconnection at C(16)−C(17) (Scheme 1). The target structure could be constructed by addition of a THP organometallic compound **1**

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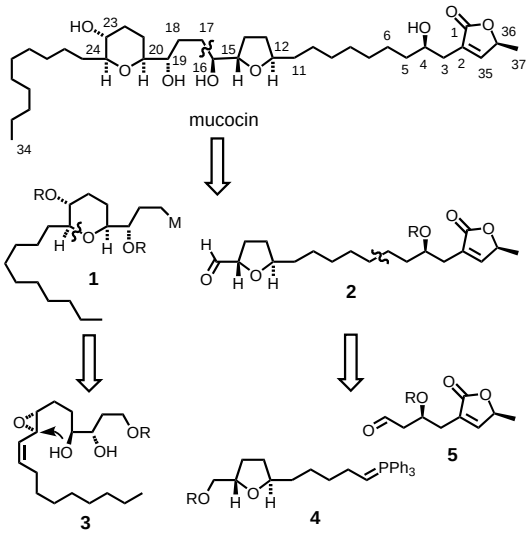
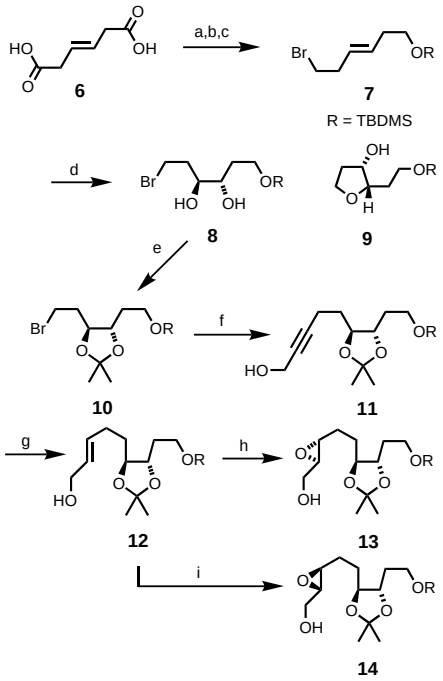


Scheme 1. Retrosynthetic analysis of mucocin.

to a THF aldehyde **2**. In this step, critical attention has to be paid to the stereocontrol as well as to the compatibility of the butenolide with the reaction conditions. For the construction of the THP-ring in **1** a double-bond directed 6-*endo* opening of the epoxide in **3** was planned. The THF aldehyde **2** was deduced from a Wittig-type reaction of the ylide **4** and the aldehyde **5**. The resulting modular strategy using three building blocks **3**, **4**, and **5** is versatile and not restricted to mucocin only.

Starting point for the synthesis of the left half of the molecule was (*E*)-dihydromuconic acid **6** (Scheme 2). Reduction of the dimethyl ester of **6** gave a diol, which was monosilylated[10] and subsequently transformed into the bromide **7**. Asymmetric dihydroxylation[11] of **7** provided the diol **8** (*ee* 86%). The diol **8** easily underwent an undesired intramolecular Williamson side reaction to the THF alcohol **9** upon evaporation of the solvent during the work up at room temperature or attempts of chromatographic purification. Therefore work up of the dihydroxylation was done below 10 °C and the crude product was directly converted into the acetonide **10**. The alkylation of **10** to **11**, followed by an (*E*)-selective reduction[12] provided the allylic alcohol **12**. The optimized solvent combination NH_3/THF/DMPU 5:5:2 was necessary for a yield of 91% in the alkylation step. The

Abstract in German: *Berichtet wird über die Totalsynthese des Annoninnaturstoffs Mucocin. Die Synthese folgt einer konvergenten Strategie, bei der auf einer sehr späten Stufe der linke Teil des Moleküls mit dem rechten verknüpft wird. Eine Schlüsselreaktion ist die stereokontrollierte Addition der Organomagnesiumverbindung* ***2*** *an den Aldehyd* ***3****. Der THP-Ring von Mucocin wird über eine 6-endo Epoxicyclisierung einer Epoxiacetonidvorstufe aufgebaut (****16*** *→* ***17****). Der hier entwickelte modulare Weg sollte nicht nur zur Synthese von strukturell verwandten Naturstoffen von Nutzen sein, sondern sich auch zur Herstellung pharmakologisch interessanter Analoga eignen.*

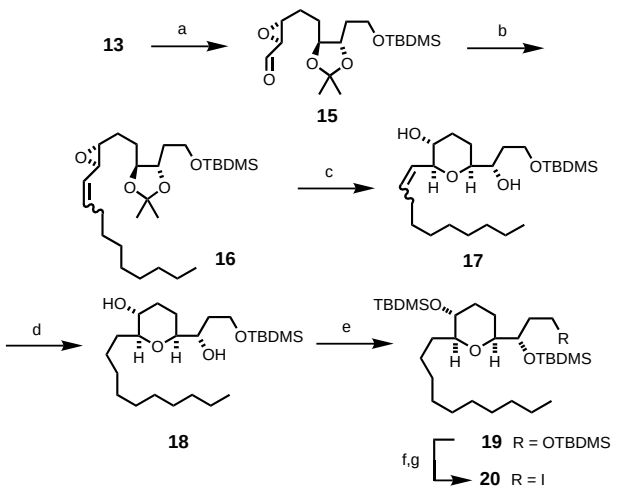


Scheme 2. a) 1) TMSCl, MeOH; 2) $LiAlH_4$, THF, 92%; b) NaH (1.0 equiv), TBDMSCl (1.0 equiv), THF, 0 °C, 1 h, 54%; c) 1) *p*-TsCl (2.0 equiv), py (10 equiv), CH_2Cl_2, 0 °C, 12 h; 2) LiBr (4.0 equiv), acetone, 12 h, 85% over two steps; d) AD-mix α, $MeSO_2NH_2$, H_2O/*t*BuOH 1:1, 0 °C → rt, 24 h; e) *p*-TsOH (5 mol%), 2,2-dimethoxypropane (4.0 equiv), CH_2Cl_2, 1 h, 92% over two steps; f) propargylic alcohol (3.0 equiv), *n*BuLi (6.0 equiv), NH_3/THF/DMPU (5:5:2), −40 °C, 6 h, 91%; g) Red-Al (2.0 equiv), THF, 0 °C, 4 h, 95%; h) TBHP (2.0 equiv), (−)-DIPT (12 mol%), $Ti(OiPr)_4$ (10 mol%), CH_2Cl_2, −20 °C, 3.5 h, 85%; i) TBHP (2.0 equiv), (+)-DIPT (12 mol%), $Ti(OiPr)_4$ (10 mol%), CH_2Cl_2, −20 °C, 3.5 h, 79%. TMS = trimethylsilyl, TBDMS = *tert*-butyldimethylsilyl, *p*-Ts = *p*-toluenesulfonyl, py = pyridine, TBHP = *tert*-butylhydroperoxide, DIPT = diisopropyltartrate.

elaboration of the THP-ring was addressed next. An 6-*endo* attack of the C(20)-oxygen on an C(23)–C(24) epoxide by an activation of the C(24) position by an C(25)–C(26) double bond was envisaged to construct the THP-ring.[13] Sharpless epoxidation[14] of the allylic alcohol **12** with (−)-diisopropyltartrate afforded the epoxy alcohol **13**. The diastereomeric epoxide **14** was also prepared in order to study the intramolecular epoxide cyclization in more detail (vide infra).

Dess–Martin oxidation[15] of **13** delivered the aldehyde **15** (Scheme 3). A Wittig reaction of **15** with the C(25)–C(34) phosphonium ylide introduced the left side chain of mucocin and provided the epoxyalkene **16** as a 1:1 *E*/*Z* mixture. THF as solvent and the addition of the ylide to a cooled solution of the aldehyde were the requirements for a 85% yield in this Wittig reaction.

With the epoxyalkene **16** in hand, the crucial cyclization to the THP ring was investigated next. This reaction (**16** → **17**) deserves further comments: Starting from an acetonide an acid catalysed intramolecular 6-*endo* attack on the alkenyl epoxide had to occur. Possible intermolecular side reactions at the epoxide and cleavage of the silyl group had to be suppressed. The weak nucleophilic protic co-solvent isopropyl alcohol allowed a clean conversion of **16** to **17**. After the selective opening of the epoxide the double bond at

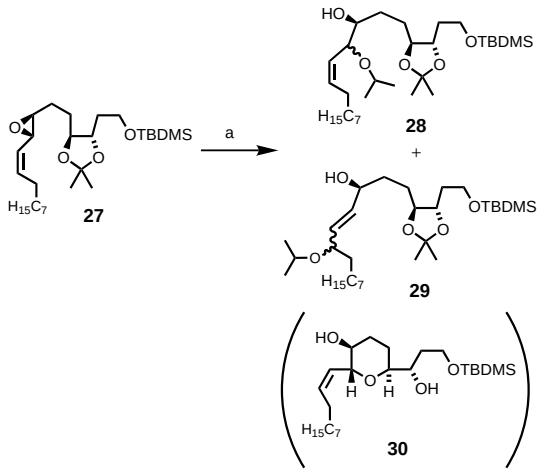


Scheme 3. a) Dess–Martin periodinane (2.0 equiv), py (10 equiv), CH_2Cl_2, 0 °C, 3 h, 89 %; b) $H_{19}C_9PPh_3Br$ (1.4 equiv), NaHMDS (1.2 equiv), THF, −78 °C, 5 min, 85 % *E*:*Z* = 1:1; c) CSA (8 mol %), CH_2Cl_2/*i*PrOH (30:1), −40 → 0 °C, 3.5 h, 89 %; d) 5 % Pt/C, 1 bar H_2, EtOAc, 0 °C, 5 h, 95 %; e) TBDMS-OTf (3.0 equiv), 2,6-lutidine (5.0 equiv), CH_2Cl_2, 0 °C, 1 h, 97 %; f) CSA (0.25 equiv), CH_2Cl_2/MeOH (2:1), 0 °C, 30 min, 74 %; g) I_2 (1.2 equiv), PPh_3 (1.1 equiv), imidazole (3.0 equiv), CH_2Cl_2, 0 °C, 3 h, 80 %. NaHMDS = sodiumhexamethyldisilazide, CSA = camphersulfonic acid.

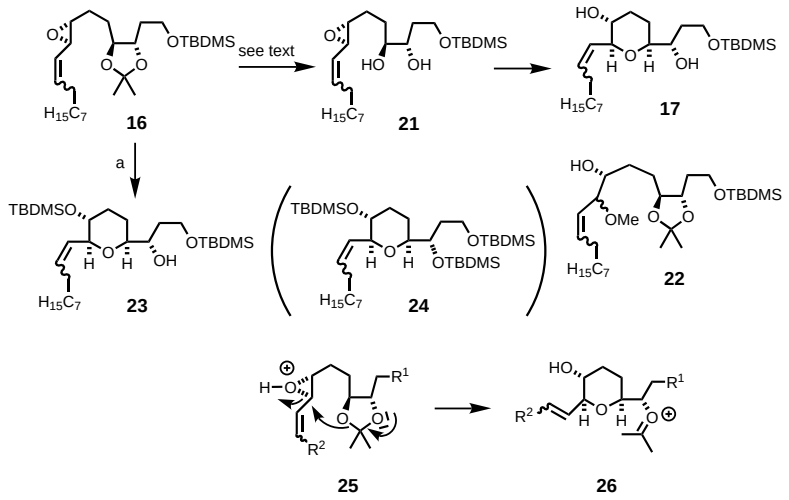
C(25)–C(26) was removed by hydrogenation(**17** → **18**). A subsequent TBDMS protection gave the bis-silyl ether **19**. Selective deprotection of the primary silyl ether followed by the conversion of the resulting alcohol into an iodide **20** provided the complete left half of mucocin.

Two mechanistic pathways are possible for the conversion of **16** to **17** (Scheme 4). First, the acetonide could be cleaved to the free diol intermediate **21** and a subsequent intramolecular attack of the OH group on the allylic position of the epoxide would give rise to the observed product. Second, the opening of the epoxide could possibly happen in a concerted manner (**25** → **26**) without the free diol **21** as an intermediate. If the epoxide opening reaction was carried out in a MeOH/CH_2Cl_2 mixture instead of *i*PrOH/CH_2Cl_2 mixture compound **22** was observed as a by-product. Silyl ether **22** results from an intermolecular attack of MeOH on the epoxide, showing the intermolecular lability of the epoxide relative to the acetonide. Examples are known in the literature[16] for the intermolecular opening of alkenyl epoxides, where a remote acetonide function is left intact. If **16** was allowed to react with an excess of TBDMS-OTf only **23**, not **24**, was observed. Herein, the TBDMS group plays the electrophilic role of the proton from **16** → **17**. The free diol cannot be an intermediate in this reaction, because it would have given rise to the formation of the tris-silyl ether **24**. All these observations favor a concerted mechanism and disfavor the occurrence of the free diol intermediate.

Furthermore the cyclisation of the diastereomeric epoxide **27** was investigated (Scheme 5). Compound **27** is accessible from the epoxy alcohol **14** along the same route as described for **16**. However, this time the *Z* olefin was isolated as the main product in the Wittig reaction. All attempts to convert **27** into the THP-derivative **30** failed. At the low temperatures used for the successful tranformation of **16** into **17**, no turnover was observed in the case of **27**. At higher temperature only **28** and **29**, products from the intermolecular attack of *i*PrOH on the epoxide were observed. Notice that the acetonide function in **28** and **29** remained intact. This leads to the conclusion, that the intramolecular opening of **16** to **17** is strongly favored, while it is not for the reaction of **27** to **30**. In addition, the observation, that the stereoisomer **27** does not form the THP product explains the whereabouts of the 7 % of the wrong enantiomer of the dihydroxylation step (**7** → **8**). This



Scheme 5. a) CSA (8 mol %), CH_2Cl_2/*i*PrOH (30:1), −60 → 20 °C, 16 h, **28**: 13 %, **29**: 23 %.



Scheme 4. A mechanistic alternative for the epoxycyclization from **16** to **17**. A two-step mechanism via the free diol (**16** → **21** → **17**) or a concerted-type mechanism (**25** → **26**). a) TBDMS-OTf, 2,6-lutidine, CH_2Cl_2, −78 → −40 °C, 61 %.

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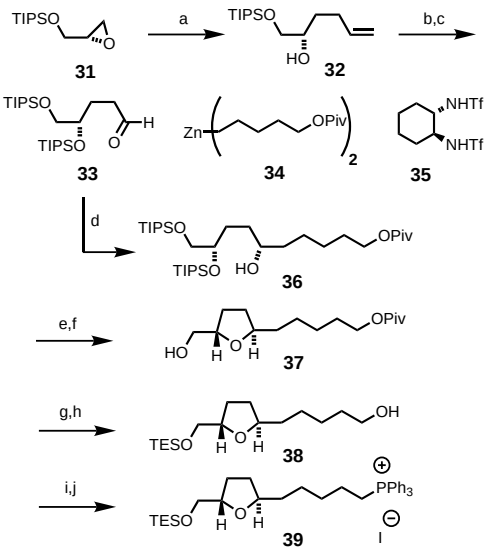
minor stereoisomer ***ent*-8** led to ***ent*-27**, which in contrast to **16** did not cyclize to a THP product. Therefore, the minor isomer from the dihydroxylation step left the synthetic way at this point.

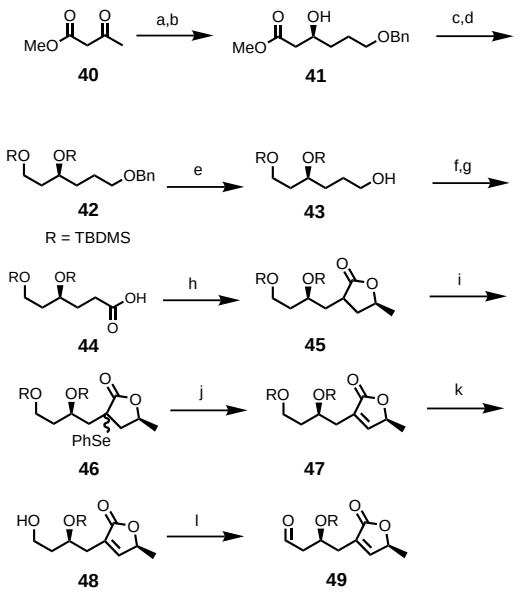
TIPS-protected (*R*)-glycidol **31** was the synthetic entrance for the preparation of the THF part of mucocin (Scheme 6). A regioselective opening of the epoxide with allyl magnesium bromide gave the homoallylic alcohol **32**. The latter was silylated and ozonized to the aldehyde **33**. Addition of the



Scheme 6. a) $H_2C{=}CHCH_2MgBr$ (5 equiv), CuI (3 mol%), THF, −30 °C, 1 h, 91%; b) TIPS-OTf (1.2 equiv), 2,6-lutidine (2.5 equiv), CH_2Cl_2, rt, 12 h, 96%; c) O_3, CH_2Cl_2, −75 °C, PPh_3 (1.0 equiv) → rt, 98%; d) **34** (1.8 equiv), **35** (0.1 equiv), $Ti(OiPr)_4$ (2.0 equiv), xylene, −25 °C, 16 h, 70% over two steps; e) *p*-TsCl (4.0 equiv), py/CH_2Cl_2 1:1, rt, 12 h, 93%; f) TBAF (3.0 equiv), THF, rt, 45 min, 95%, *trans*:*cis* = 95:5 (HPLC); g) 1) TES-Cl (1.2 equiv), imidazole (2.0 equiv), CH_2Cl_2, RT, 2 h, 86%; h) DIBAH (2.5 equiv), THF, −20 °C, 1 h, 93%; i) I_2 (1.2 equiv), PPh_3 (1.1 equiv), imidazole (3.0 equiv), CH_2Cl_2, 0 °C → RT, 1.5 h, 84%; j) PPh_3 (5.0 equiv), CH_3CN/toluene 1:1, 70 °C, 20 h. TIPS = triisopropylsilyl, TBAF = tetrabutylammoniumfluoride.

functionalized diorganozinc compound **34** to the aldehyde **33** gave the alcohol **36.** Following Knochel's protocol the chiral ligand **35** was used and a diastereoselectivity of 95:5 was achieved.[17] The use of xylene instead of toluene was beneficial. Its higher boiling point facilitated the removal of excess diethyl zinc in the preparation of **34**. After tosylation of the secondary OH group in **36** a subsequent TBAF-induced intramolecular Williamson reaction delivered the *trans*-2,5-disubstituted THF-derivative **37** together with 5% of the corresponding *cis* isomer. Both isomers, which resulted from the 95:5 stereoselectivity in the formation of **36**, were separated on the stage of **37** by chromatography. The primary OH group of **37** was protected as triethylsilyl (TES) ether and reductive cleavage of the pivalate gave compound **38**. Transformation of the alcohol into an iodide followed by reaction with triphenylphosphine provided the phosphonium salt **39**.

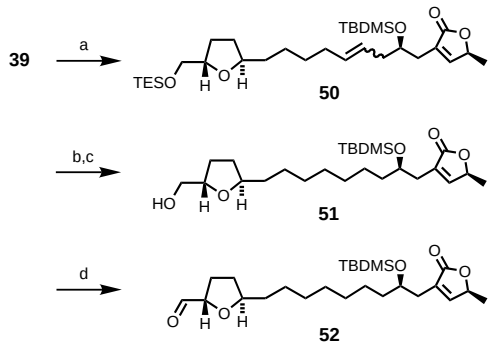
The synthesis of the butenolide aldehyde **49** is summarized in Scheme 7. Starting point was the alkylation of the dianion of the β-ketoester **40** followed by a Noyori reduction with BINAP[18] to yield the β-hydroxyester **41** containing the later



Scheme 7. a) NaH (1.5 equiv), *n*BuLi (1.5 equiv), THF, −30 → −15 °C, 15 min, then $Br(CH_2)_2OBn$ (0.85 equiv), −10 °C, 2.5 h, 72%; b) H_2 (5 bar), Ru^{II}-(*S*)-(−)-BINAP (0.6 mol%), 95 °C, 18 h, 90%, *ee* = 97% (HPLC: Chiralcel OD-H, 10% *i*PrOH in *n*-hexane, 1.0 mL min^{-1}); c) $BH_3 \cdot Me_2S$ (2.2 equiv), THF, 60 °C, 30 min, 83%; d) TBDMSCl (2.4 equiv), imidazole (3.0 equiv), DMAP (0.1 equiv), CH_2Cl_2, RT, 16 h, 88%; e) H_2 (1 atm), 10% Pd/C (5 mass%), EtOAc, 98%; f) $(COCl)_2$ (2.0 equiv), DMSO (4.0 equiv), NEt_3 (5.0 equiv), CH_2Cl_2, −78 → −40 °C, 1.5 h; g) $NaOCl_2$ (3.0 equiv), $NaH_2PO_4 \cdot 2H_2O$ (4.0 equiv), methyl-2-butene (20 equiv), *t*BuOH/H_2O 1:1, 3 h, 95% from **43;** h) 1) LDA (2.5 equiv), THF, 0 °C, 45 min, then (*S*)-(−)-propenoxide (3.0 equiv), rt, 3 h, 2) PivCl (1.1 equiv), NEt_3 (2.0 equiv), CH_2Cl_2, rt, 10 min, 73%; i) KHMDS (3.0 equiv), THF, 0 °C, 30 min, then PhSeCl (3.0 equiv), 1 h; j) MMPP (4.0 equiv), THF/MeOH 1:1, rt, 30 min, 88% from **45;** k) CSA (0.25 equiv), CH_2Cl_2/MeOH 1:1, 0 °C, 30 min, 79%; l) Dess–Martin periodinane (1.5 equiv), py (10 equiv), CH_2Cl_2, 0 °C → rt, 4.5 h, 90%. BINAP = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl, MMPP = magnesiummonoperoxophthalate.

C4-OH group of mucocin. The enantioselectivity of the reaction was determined to *ee* = 96% by chiral HPLC. The β-hydroxyester **41** was reduced to a diol which was double protected to the bis-silyl ether **42**. Hydrogenolysis of the benzyl ether function provided the alcohol **43**, which was oxidized to the carboxylic acid **44** by a two-step procedure (Swern/chlorite).[19] Treatment of dianion of **44** with (*S*)-propene oxide afforded a hydroxy carboxylic acid which was cyclized via a mixed anhydride to the butyrolactone **45**. The new stereocenter in **45** was formed with a 2:1 selectivity as determined by inspection of the ^{1}H-NMR spectra. The C(2)=C(35) double bond was introduced by selenation(**45** → **46**) and thermal *syn*-elimination of the selenium oxide. Only the endocyclic olefin **47** was formed.[20] In comparison to the selenium group the introduction of the corresponding phenyl thioether was less clean and gave a lower yield. Slightly acidic conditions were suited to deprotect the primary TBDMS group in **47**. The resulting alcohol **48** could be oxidized to the aldehyde **49** by the Dess–Martin protocol. The synthesis of the butenolide aldehyde **49** should be of interest for other acetogenin syntheses as well.

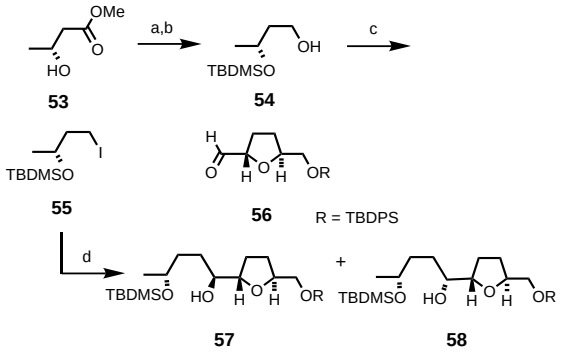
A Wittig reaction was used to connect the THF subunit **39** with the butenolide aldehyde **49** (Scheme 8). The resulting



Scheme 8. a) **39**, NaHMDS (1.0 equiv), THF, 0 °C, 30 min, then **49**, −70 °C → 0 °C, 20 min, 60 %; b) [(PPh$_3$)$_3$RhCl] (0.15 equiv), H_2 (1 atm), benzene, rt, 3 h, 95 %; c) CSA (0.08 equiv), CH_2Cl_2/MeOH 5:1, −20 °C, 10 min, 76 %; d) Dess–Martin periodinane (2.0 equiv), py (10 equiv), CH_2Cl_2, 0 °C → rt, 4.5 h, 91 %.

alkene **50** was formed as a mixture of *E*/*Z* isomers. The hydrogenation of the isolated double bond[21] of compound **50** followed by a selective cleavage of the TES ether gave the alcohol **51**. A Dess–Martin oxidation of **51** to **52** completed the synthesis of the right half of the target molecule.

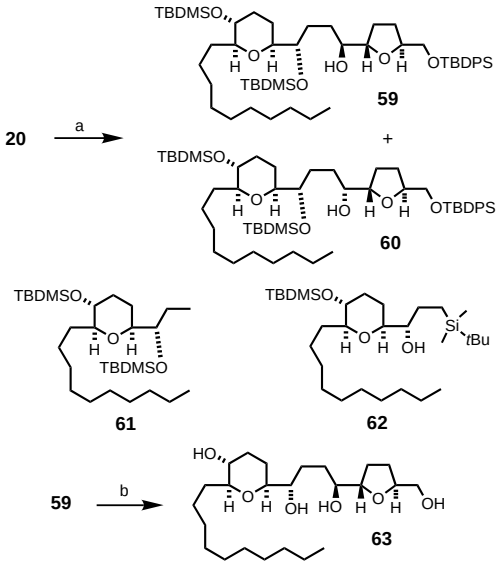
The final part of the synthesis required a coupling of the left half and the right half of the target molecule. The stereoselective coupling of an organometallic species of type **2** with the aldehyde **52** under chelation-controlled conditions should lead to the desired product. Organomagnesium compounds were known to produce the chelation-controlled product for simpler THF aldehydes. Due to the small scale of the coupling reaction (< 1 mmol) a heterogeneous Grignard-type chemistry with magnesium turnings was not very suitable. Instead a homogeneous generation of the corresponding organolithium compound followed by transmetalation to magnesium was used. The iodide **55**[22] which was available from (*R*)-β-hydroxy methyl butyrate **53** via the alcohol **54** was used as a model substrate for the left half first (Scheme 9). The iodide



Scheme 9. a) TBDMSCl, imidazole, 93 %; b) DIBAH, toluene, 81 %; c) I_2, PPh_3, CH_2Cl_2, 89 %; d) **55** (1.0 equiv), *t*BuLi (1.8 equiv), Et_2O, −105 °C, 5 min; then $MgBr_2 \cdot OEt_2$ (2.0 equiv), −100 → −25 °C, 1.5 h; → −78 °C, **56** (1.0 equiv), → −10 °C, 1.5 h, 73 %.

55 was subjected to a iodine-lithium exchange[23] in Et_2O at −100 °C and subsequently treated with a solution of magnesium bromide in Et_2O at −90 °C. Addition of the test aldehyde **56**[24] gave the two secondary alcohols **57** and **58** as coupling products with a 6:1 stereoselectivity. The major epimer **57** is the chelation-controlled product. The stereochemical assignment[25] was based on ^{13}C-NMR data (new chiral center: $\delta = 73.8$ for **57** and 72.1 for **58**).

Next, the coupling of the iodide **20**, containing the complete left half of mucocin with the test aldehyde **56** was examined (Scheme 10). It was found, that two coupling products **59** and **60** could be isolated in 50 % yield with a 4:1 diastereoselectivity. However, the precise choice of temperature and time



Scheme 10. a) **20** (1.2 equiv), *t*BuLi (2.4 equiv), Et_2O, −105 °C, 5 min; then $MgBr_2 \cdot OEt_2$ (2.4 equiv), −100 → −10 °C, 1.5 h; → −78 °C, **56** (1.0 equiv), → −10 °C, 1.5 h, 50 %; b) HF (5 equiv), CH_3CN/CH_2Cl_2, 0 °C, 6 h, 74 %.

was crucial for the success of the reaction. If the transmetallation did not take place within 5 min after the iodine-lithium exchange and if the temperature rose above −90 °C the silane **62** was obtained as the main product. The formation of **62** can be explained by retro-Brook migration[26] from the silyl group at O−C(19) to C(17). The alkane **61** was formed as side product (10–15 %) in most of the coupling reactions using the iodide **20**. The tris-silyl ether **59** was deprotected to the tetraol **63**. Compound **63** contains the complete THP/THF part of mucocin. The NMR data for the THP part matched the related data from mucocin already.

Encouraged by the results from the test coupling and equipped with experience concerning the reaction conditions the convergent final of the synthesis was addressed (Scheme 11). At −105 °C an iodine-lithium exchange in **20** could be realized followed by a transmetallation to magnesium. Addition of the aldehyde **52** and subsequent warm up to −15 °C gave the desired product **64** in 53 % yield. 34 % of unreacted aldehyde **52** was reisolated. Noteworthy, only 1.2 equivalents of iodide **20** compared with 1 equivalent of aldehyde **52** were necessary. The stereoselectivity of the reaction was 4:1 in favor of the desired epimer **64**. The synthetically undesired but pharmacologically interesting C(16) minor epimer **65** could be separated by chromatography. Cleavage of the silyl protecting groups in **64** provided (−)-mucocin ($[\alpha]_D = -12.7$, $c = 0.27$ in CH_2Cl_2) which was found to be identical with the natural occurring product in respect to the spectroscopical data. In addition, deprotection of the minor epimer **65** gave 16-*epi* mucocin.

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Conclusion

A modular strategy for the assembly of mucocin was successfully developed. A distinctive feature of this synthesis is its high convergence. New variations of mucocin with pharmacological importance should be easily available by combination of different modules. The butenolide fragment proved to be compatible with the coupling reaction. The synthetic route presented here is a new, efficient, and flexible approach to the *Annonaceous* acetogenins, a biological important class of compounds.

Experimental Section

General: All b.p.s and m.p.s are uncorrected values. IR: Biorad FTS 3000MX. NMR: Bruker AC-300, DPX-300 and AMX-600. For ^{1}H NMR, $CDCl_3$ as solvent $\delta_H = 7.24$, [D$_6$]benzene as solvent $\delta_H = 7.20$, [D$_4$]MeOH as solvent $\delta_H = 4.78$; for ^{13}C NMR, $CDCl_3$ as solvent $\delta_C = 77.0$, [D$_6$]benzene as solvent $\delta_C = 128.0$, [D$_4$]MeOH as solvent $\delta_C = 49.0$. Elemental analysis: CHN Rapid (Heraeus), CHNS-932 Analysator (Leco). HR-MS: Finnigan MAT 95. All reactions were performed under an inert atmosphere of argon in oven- or flame-dried glassware. HPLC: Rainin-Dynamax, SD-200 and SD-1, PDA1. Dry solvents: THF, Et_2O, benzene, xylene, and toluene were distilled from sodium benzophenone. Pyridine, triethylamine, and CH_2Cl_2 were distilled from CaH_2. All commercially available reagents were used without purification unless otherwise noted. 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) was performed with Merck silica gel 60 (70–200 mesh and 230–400 mesh). PE: light petroleum ether, b.p. 40–60 °C. MTBE: methyl *tert*-butyl ether. ***Θ*** nomenclature: configuration unspecified.

(*E*)-1-Bromo-6-*tert*-butyldimethylsilyloxyhex-3-ene (7)

1. Esterification of **6**: Dihydromuconic acid **6** (8.0 g, 55.5 mmol) was suspended in methanol (150 mL) at 0 °C. TMSCl (14 mL, 111 mmol) was added and the mixture was stirred for 36 h. Then methanol (50 mL) was evaporated, H_2O (100 mL) was added and the aqueous layer was extracted with Et_2O (3 × 100 mL). After washing of the combined organic layers with subsequently a sat. aq. $NaHCO_3$ solution (100 mL) and NaCl (100 mL) and drying with $MgSO_4$, the solvents were removed in vacuo. The residue was purified by distillation under reduced pressure to yield the diester (9.02 g, 52.4 mmol, 94%) as a colorless solid.

(*E*)-1,6-Dihex-3-enoic acid dimethyl ester: $R_f = 0.28$ (hexanes/MTBE 2:1); IR (film): $\tilde{\nu} = 3002, 2955, 2847, 1740, 1437, 1363, 1255, 1198, 1166, 1012, 973, 845\ cm^{-1}$; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 3.05$ (dd, $J = 1.6$, 3.8 Hz, 4H, 2,5-H$_2$), 3.64 (s, 6H, OCH_3), 5.63–5.67 (m, 2H, 3,4-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 37.5$ (C-2, C-5), 51.7 (OCH_3), 125.8 (C-3, C-4), 171.8 (C-1, C-6); $C_8H_{12}O_4$ (172.181): calcd C 55.81, H 7.03; found C 55.82, H 6.84.

2. Reduction with $LiAlH_4$: The diester (6.42 g, 37.3 mmol), dissolved in THF (50 mL), was added dropwise to a suspension of $LiAlH_4$ (4.25 g, 111.9 mmol) in THF (150 mL) at 0 °C. After stirring for 2 h at rt the reaction was quenched by slow addition of H_2O (4.2 mL), 2N NaOH (13 mL) and H_2O (4.2 mL). The suspension was refluxed for 10 min and filtered through a pad of Celite. After washing with THF, the solvents were removed in vacuo. CC (100 g silica gel, AcOEt/Et_2O 1:1) of the residue led to the diol (4.25 g, 36.6 mmol, 98%) as a colorless oil.

(*E*)-Hex-3-en-1,6-diol: $R_f = 0.20$ (AcOEt/Et_2O 1:1) IR (film): $\tilde{\nu} = 3339, 3033, 2932, 2880, 1657, 1428, 1372, 1233, 1045, 969, 861, 652\ cm^{-1}$; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.00–2.29$ (m, 4H, 2,5-H$_2$), 2.48 (s, 2H, OH), 3.59 (t, $J = 6.1$ Hz, 4H, 1,6-H$_2$), 5.41–5.49 (m, 2H, 3,4-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 35.9$ (C-2, C-5), 61.6 (C-1, C-6), 129.5 (C-3, C-4); $C_6H_{12}O_2$ (116.161): calcd C 62.04, H 10.41; found C 62.17, H 10.15.

3. Monosilylation: A solution of the diol (5.0 g, 43.0 mmol) in THF (40 mL) was added dropwise at 0 °C to a suspension of NaH (1.72 g, 60% in mineral oil, 43.0 mmol) in THF (100 mL). The mixture was stirred for 45 min at rt. TBDMSCl (6.49 g, 150.7 mmol) dissolved in THF (15 mL) was added dropwise and stirring was continued overnight. The reaction was quenched by addition of a sat. aq. sodium bicarbonate solution (100 mL). After extraction with Et_2O (4 × 75 mL), washing of the combined organic layers with a sat. aq. NaCl (2 × 40 mL) solution and drying with $MgSO_4$, the solvents were evaporated and the resulting crude oil was purified by CC (150 g silica gel, hexane/MTBE 30:1 → 2:1 → ethyl acetate) to provide (5.34 g, 23.2 mmol, 54%) of the monoprotected alcohol as a colorless oil. 24% diol (1.2 g, 10.3 mmol) was reisolated. Additionally the diprotected alcohol (2.8 g, 8.2 mmol, 19%) was obtained, which could be recycled.

(*E*)-1-*tert*-Butyldimethylsilyloxy-6-hydroxy-hex-3-ene: $R_f = 0.41$ (*n*-hexane/MTBE 2:1); IR (film): $\tilde{\nu} = 3349, 2955, 2929, 2858, 1650, 1472, 1386, 1255, 1100, 1048, 969, 836, 776, 664\ cm^{-1}$; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.02$ (s, 6H, $SiCH_3$), 0.86 (s, 9H, $SiC(CH_3)_3$), 1.79 (br s, 1H, OH), 2.16–2.25 (m, 4H, 2,5-H$_2$), 3.54–3.62 (m, 4H, 1,6-H$_2$), 5.37–5.49 (m, 2H, 3,4-H$_2$); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -5.3$ ($SiCH_3$), 18.3 [$C(CH_3)$], 25.9 [C(CH_3)], 36.0 (C-2), 36.2 (C-5), 61.8 (C-1), 62.9 (C-6), 128.0 (C-4), 130.2 (C-3); $C_{12}H_{26}O_2Si$ (230.424): calcd C 62.55, H 11.37; found: C 62.60, H 11.45.

4. Tosylation: Pyridine (37 mL) and toluenesulfonyl chloride (17.9 g, 94 mmol) were added at 0 °C to the monoprotected alcohol (10.9 g, 47 mmol) dissolved in CH_2Cl_2 (200 mL). The solution was stirred for 16 h before the reaction was quenched with H_2O (100 mL). After 2 h the aqueous phase was extracted with CH_2Cl_2 (2 × 50 mL). Washing of the combined organic layers with a sat. aq. NaCl solution (100 mL), drying with $MgSO_4$, and evaporation of the solvent led to the crude product which was treated with toluene (2 × 20 mL) and used for the following step without further purification.

5. Bromination to **7**: The crude toluene sulfonate was dissolved in acetone (300 mL) and LiBr (16 g, 188 mmol) was added. After stirring for 24 h at 25 °C the solution was quenched with water (150 mL) and extracted with hexane (3 × 60 mL). The combined organic layers were washed with a sat. aq. NaCl solution (50 mL) and dried with $MgSO_4$. The solvents were removed in vacuo. The residue was purified by CC (200 g silica gel, hexane/MTBE 40:1) to yield bromide **7** (11.8 g, 40 mmol, 85% for two steps) as a colorless oil.

(*E*)-1-Bromo-6-*tert*-butyldimethylsilyloxy-hex-3-ene (7): $R_f = 0.30$ (*n*-hexane/MTBE 40:1); IR (film): $\tilde{\nu} = 3033, 2955, 2930, 2857, 1667, 1472, 1386, 1255, 1103, 1006, 969, 940, 836, 775, 724, 662\ cm^{-1}$; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.03$ (s, 6H, $SiCH_3$), 0.87 (s, 9H, $SiC(CH_3)_3$), 2.18–2.25 (m, 2H, 5-H$_2$), 2.50–2.57 (m, 2H, 2-H$_2$), 3.34 (t, $J = 7.2$ Hz, 2H, 1-H$_2$), 3.61 (t, $J = 6.8$ Hz, 2H, 6-H$_2$), 5.39–5.60 (m, 2H, 3,4-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -5.3$ ($SiCH_3$), 18.3 [$C(CH_3)$], 25.9 [C(CH_3)], 32.6 (C-1), 36.1, 36.2 (C-2, C-5), 62.9 (C-6), 128.5 (C-3), 130.2 (C-4); $C_{12}H_{25}OSiBr$ (293.320): calcd C 49.14, H 8.59, Br 27.24; found C 49.20, H 8.53, Br 27.17.

(3*S*,4*S*)-1-Bromo-6-*tert*-butyldimethylsilyloxy-3,4-*O*-isopropyliden-hexane-3,4-diol (10): Alkene **7** (1.25 g, 4.26 mmol), AD-mix α (5.96 g) and $CH_3SO_2NH_2$ (0.41 g) were suspended in H_2O (21 mL) and *t*BuOH (21 mL) at 0 °C. After stirring for 6 h the reaction mixture was quenched with $Na_2S_2O_3$ (6.5 g). The suspension was stirred for another hour, then diluted with a half sat. aq. NH_4Cl solution (20 mL) and extracted with MTBE (3 × 20 mL). After washing of the combined organic layers with phosphate buffer (pH 7, 20 mL) and sat. aq. NaCl solution (20 mL) and drying with $MgSO_4$ the solvents were evaporated at 5 °C. The residue was instantly dissolved in CH_2Cl_2 (50 mL). Dimethoxypropane (4 mL, 26.8 mmol) and *p*-toluene sulfonic acid (30 mg, 0.14 mmol) were added at 0 °C. After 1 h the reaction mixture was quenched with a sat. aq. sodium bicarbonate solution (20 mL). After extraction with CH_2Cl_2 (3 × 20 mL), washing of the combined organic layers with sat. aq. NaCl solution (20 mL) and drying with $MgSO_4$ the solvent was removed in vacuo. The residue was purified by CC (110 g silica gel, hexane/MTBE 30:1) to yield the bromide **10** (1.44 g, 3.93 mmol, 92%) as a colorless oil. $R_f = 0.29$ (*n*-hexane/MTBE 30:1); $[\alpha]_D^{22} = -34.3$ ($c = 0.93$, $CHCl_3$) (93:7 mixture of enantiomers); IR (film): $\tilde{\nu} = 2986, 2954, 2931, 2883, 2858, 1472, 1463, 1444, 1418, 1379, 1370, 1341, 1253, 1225, 1174, 1149, 1093, 1047, 1006, 993, 971, 939, 836, 812, 776, 731, 663, 571, 517\ cm^{-1}$; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.05$ (s, 6H, $SiCH_3$), 0.88 (s, 9H, $SiC(CH_3)_3$), 1.34 (s, 3H, acetonide-CH_3), 1.37 (s, 3H, acetonide-CH_3), 1.73–1.77 (m, 2H, 5-H$_2$), 2.04–2.08 (m, 2H, 2-H$_2$), 3.46–3.54 (m, 2H, 1-H$_2$), 3.70–3.80 (m, 4H, 3,4-H, 6-H$_2$); ^{13}C NMR (75 MHz, $CDCl_3$):

$\delta = -5.4$ ($SiCH_3$), 18.3 [$C(CH_3)$], 25.9 [C(CH_3)], 27.2, 27.3 (acetonide-CH_3), 29.6 (C-1), 35.8, 36.2 (C-2, C-5), 59.7 (C-6), 77.4, 78.8 (C-3, C-4), 108.4 (acetal); $C_{15}H_{31}BrO_3Si$ (367.401): calcd C 49.04, H 8.51; found C 49.06, H 8.50.

(2*S*, 3*S*)-2-(2′-*tert*-Butyldimethylsilyloxy)-ethyl-3-hydroxy-tetrahydrofuran (9): ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.05$ (s, 6H, $SiCH_3$), 0.87 (s, 9H, $SiC(CH_3)_3$), 1.89 – 2.14 (m, 4H, 4,1′-H_2), 3.32 – 3.40 (brs, 1H, OH), 3.57 – 3.85 (m, 4H, 5,2′-H_2, 2-H), 3.98 (dt, $J = 7.5$, 7.9 Hz, 1H, 5-H_2), 4.24 – 4.26 (m, 1H, 3-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -5.6$ ($SiCH_3$), 18.2 [$C(CH_3)$], 25.8 [C(CH_3)], 31.7, 34.7 (C-4, C-1′), 60.3 (C-2′), 66.0 (C-5), 72.0 (C-3), 82.8 (C-2).

(6*S*,7*S*)-9-*tert*-Butyldimethylsilyloxy-6,7-*O*-isopropyliden-2-nonyne-1,6,7-triol (11): NH_3 (20 mL) was dried with sodium and condensed into a reaction flask at $-78\,^\circ$C. *n*BuLi (5 mL, 12.5 mmol 2.5 M in hexane) was added dropwise. Then the reaction mixture was allowed to reflux at $-33\,^\circ$C and propargylic alcohol (0.35 mL, 6 mmol), dissolved in THF (10 mL), was added. After 10 min DMPU (8 mL, distilled from CaH_2) was added slowly. After another 10 min, bromide **10** (735 mg, 2.00 mmol) dissolved in THF (10 mL) was added dropwise. The reaction mixture was refluxed for 6 h. After quenching with NH_4Cl, the NH_3 was allowed to evaporate at rt. Water (50 mL) and MTBE (30 mL) were added and the aqueous layer was extracted with MTBE (3×50 mL). The combined organic layers were washed with sat. aq. NaCl solution (40 mL), dried with $MgSO_4$, and the solvents were removed under reduced pressure. The crude product was purified by CC (30 g silica gel, hexane/MTBE 2:1) to afford the alkyne **11** (621 mg, 1.81 mmol, 91 %) as a colorless oil. $R_f = 0.22$ (*n*-hexane/MTBE 2:1); $[\alpha]_D^{22} = -28.5$ ($c = 1.02$, $CHCl_3$); IR (film): $\tilde{\nu} = 3453$, 2986, 2931, 2289, 2225, 1473, 1379, 1253, 1165, 1093, 1007, 939, 837, 777, 664, 514 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.03$ (s, 6H, $SiCH_3$), 0.86 (s, 9H, $SiC(CH_3)_3$), 1.33 (s, 3H, acetonide-CH_3), 1.34 (s, 3H, acetonide-CH_3), 1.66 – 1.80 (m, 4H, 5,8-H_2), 2.20 (d, $J = 5.8$ Hz, 1H, OH), 2.32 – 2.37 (m, 2H, 4-H_2), 3.66 – 3.78 (m, 4H, 6,7-H, 9-H_2), 4.19 (d, $J = 5.8$ Hz, 2H, 1-H_2); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -5.4$ ($SiCH_3$), 15.5 (C-4), 18.3 [$C(CH_3)$], 25.9 [C(CH_3)], 27.1, 27.2 (acetonide-CH_3), 31.7 (C-5), 35.8 (C-8), 51.1 (C-1), 59.4 (C-9), 77.2, 79.6 (C-6, C-7), 78.9, 85.4 (C-2, C-3), 108.1 (acetal); $C_{18}H_{34}O_4Si$ (342.553): calcd C 63.11, H 10.00; found C 63.07, H 9.76.

(2*E*,6*S*,7*S*)-9-*tert*-Butyldimethylsilyloxy-6,7-*O*-isopropyliden-2-nonene-1,6,7-triol (12): Red-Al (15.7 mL, 52 mmol, 3.4 M in toluene), dissolved in THF (50 mL), was added dropwise to alkyne **11** (8.90 g, 26.0 mmol) dissolved in THF (120 mL) at $0\,^\circ$C. The reaction mixture was stirred for 4 h. The reaction mixture was then cooled to $-78\,^\circ$C and water (2.5 mL) was added dropwise. After 30 min at rt the suspension was extracted with Et_2O (3×50 mL). The combined organic layers were washed with sat. aq. NaCl solution (50 mL), dried with $MgSO_4$, and the solvents were removed in vacuo. The residue was purified by CC (400 g silica gel, hexane/MTBE 2:1) to yield alkene **12** (8.51 g, 24.7 mmol, 95 %) as a colorless oil. $R_f = 0.19$ (*n*-hexane/MTBE 2:1); $[\alpha]_D^{22} = -17.0$, ($c = 1.12$, $CHCl_3$); IR (film): $\tilde{\nu} = 3413$, 2988, 2931, 2858, 1672, 1472, 1463, 1378, 1369, 1255, 1093, 1006, 970, 872, 837, 813, 777, 733, 664, 512 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.04$ (s, 6H, $SiCH_3$), 1.04 (s, 9H, $SiC(CH_3)_3$), 1.35 (s, 6H, acetonide-CH_3), 1.59 – 1.74 (m, 4H, 5,8-H_2), 2.08 – 2.27 (m, 2H, 4-H_2), 3.61 – 3.80 (m, 4H, 6,7-H, 9-H_2), 4.07 (d, $J = 4.0$ Hz, 2H, 1-H_2), 5.64 – 5.71 (m, 2H, 2,3-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -5.4$ ($SiCH_3$), 18.3 [$C(CH_3)$], 25.9 [C(CH_3)], 27.2, 27.3 (acetonide-CH_3), 28.6 (C-4), 32.0 (C-8), 36.0 (C-5), 59.9 (C-9), 63.6 (C-1), 77.6, 80.3 (C-6, C-7), 108.1 (acetal), 129.5, 132.2 (C-2, C-3); $C_{18}H_{36}O_4Si$ (344.569): calcd C 62.74, H 10.53; found C 62.93, H 10.38.

(2*R*,3*R*,6*S*,7*S*)-9-*tert*-Butyldimethylsilyloxy-2,3-epoxy-6,7-*O*-isopropyliden-nonane-1,6,7-triol (13): A suspension of powdered 4 Å molecular sieves (100 mg) in CH_2Cl_2 (10 mL) was cooled to $0\,^\circ$C. D-(−)-Diisopropyltartrate (24 mg, 0.10 mmol) and $Ti(OiPr)_4$ (25 mg, 0.087 mmol) were added sequentially. After the reaction mixture was cooled to $-25\,^\circ$C, TBHP (0.32 mL, 1.74 mmol, 5.5 M in nonane), which had been treated 15 min with molecular sieves 4 Å, was added and the resulting mixture was stirred for 25 min. During that time the allylic alcohol **12** (300 mg, 0.87 mmol) was dissolved in CH_2Cl_2 (1 mL) and dried with molecular sieves 4 Å. Then it was added to the reaction mixture and the suspension was stirred for 4 h at $-20\,^\circ$C. After quenching with NaOH (0.4 mL of a 10 % NaOH in a sat. aq. NaCl solution) and addition of Et_2O (4 mL), the mixture was allowed to warm up to $10\,^\circ$C. Stirring was maintained for an additional 10 min at $10\,^\circ$C, then $MgSO_4$ (400 mg), and Celite (50 mg) were added. After 15 min of stirring the mixture was allowed to settle and the clear solution was filtered through a pad of Celite. After washing with Et_2O, the solvents were removed in vacuo. CC (20 g silica gel, hexane/MTBE 1:1) of the residue led to the epoxide **13** (266 mg, 0.74 mmol, 85 %) as a colorless oil. $R_f = 0.23$ (*n*-hexane/MTBE 1:1); $[\alpha]_D^{22} = -13.7$ ($c = 1.01$, $CHCl_3$) *ee* (AE) > 98 % (^{1}H NMR); IR (film): $\tilde{\nu} = 3452$, 2985, 2930, 2858, 1642, 1472, 1379, 1253, 1168, 1090, 1034, 1006, 940, 837, 777, 724, 664, 512 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.02$ (s, 6H, $SiCH_3$), 0.87 (s, 9H, $SiC(CH_3)_3$), 1.33 (s, 6H, acetonide-CH_3), 1.65 – 1.75 (m, 6H, 4,5,8-H_2), 2.89 – 2.94 (m, 2H, 2,3-H), 3.59 – 3.78 (m, 6H, 6,7-H, 1,9-H_2); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -5.4$ ($SiCH_3$), 18.3 [$C(CH_3)$], 25.9 [C(CH_3)], 27.2, 27.3 (acetonide-CH_3), 28.8, 29.0 (C-4, C-5), 35.9 (C-8), 56.1, 58.2 (C-2, C-3), 59.8, 61.9 (C-1, C-9), 77.7, 80.8 (C-6, C-7), 108.2 (acetal); $C_{18}H_{36}O_5Si$ (360.569): calcd C 59.96, H 10.06; found C 60.12, H 10.17.

(2*S*,3*S*,6*S*,7*S*)-9-*tert*-Butyldimethylsilyloxy-2,3-epoxy-6,7-*O*-isopropyliden-nonane-1,6,7-triol (14): The other diastereomer was prepared on the same way as **13** with L-(+)-diisopropyl-tartrate. Yield 79 %. $R_f = 0.23$ (*n*-hexane/MTBE 1:1); $[\alpha]_D^{22} = -36.0$ ($c = 0.99$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.03$ (s, 6H, $SiCH_3$), 0.87 (s, 9H, $SiC(CH_3)_3$), 1.34 (s, 6H, acetonide-CH_3), 1.64 – 1.74 (m, 6H, 4,5,8-H_2), 2.89 – 3.01 (m, 2H, 2,3-H), 3.56 – 3.90 (m, 6H, 6,7-H, 1,9-H_2); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -5.4$ ($SiCH_3$), 18.3 [$C(CH_3)$], 25.9 [C(CH_3)], 27.2, 27.3 (acetonide-CH_3), 28.0, 28.4 (C-4, C-5), 35.9 (C-8), 55.4, 58.2 (C-2, C-3), 59.8, 61.7 (C-1, C-9), 77.6, 80.1 (C-6, C-7), 108.1 (acetal).

(2*R*,3*R*,6*S*,7*S*)-9-*tert*-Butyldimethylsilyloxy-6,7-dihydroxy-2,3-epoxy-6,7-*O*-isopropyliden-nonanal (15): The epoxide **13** (419 mg, 1.17 mmol) was dissolved in CH_2Cl_2 (10 mL) and cooled to $0\,^\circ$C. Pyridine (1.1 mL) and Dess – Martin periodinane (738 mg, 1.76 mmol) were added and the reaction mixture was stirred for 3 h. Then a sat. aq. sodium bicarbonate solution (20 mL) was added and the aqueous layer was extracted with MTBE (3×15 mL). After washing of the combined organic layers with sat. aq. NaCl solution (20 mL) and drying with $MgSO_4$, the solvents were removed in vacuo. The residue was purified at the same day by FCC (30 g silica gel, hexane/MTBE 3:1) to yield aldehyde **15** (371 mg, 1.04 mmol, 89 %) as a colorless oil. $R_f = 0.38$ (*n*-hexane/MTBE 2:1); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 0.03$ (s, 6H, $SiCH_3$), 0.87 (s, 9H, $SiC(CH_3)_3$), 1.32 (s, 3H, acetonide-CH_3), 1.33 (s, 3H, acetonide-CH_3), 1.57 – 1.85, (m, 6H, 4,5,8-H_2), 3.12 (dd, $J = 6.3$ Hz, 2.0 Hz, 1H, 2-H_2), 3.26 (dt, $J = 2.0$, 5.3 Hz, 1H, 3-H), 3.61 – 3.77 (m, 4H, 6,7-H, 9-H_2), 8.99 (d, $J = 6.3$, 1H, 1-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -5.4$ ($SiCH_3$), 18.3 [$C(CH_3)$], 25.9 [C(CH_3)], 27.2 (acetonide-CH_3), 28.5, 28.6 (C-4, C-5), 35.8 (C-8), 56.7, 59.4 (C-2, C-3), 59.7 (C-9), 77.7, 80.4 (C-6, C-7), 108.2 (acetal), 198.2 (C-1).

(3*S*,4*S*,7*R*,8*R*,9*Θ*)-1-*tert*-Butyldimethylsilyloxy-7,8-epoxy-3,4-*O*-isopropyliden-octadec-9-ene-3,4-diol (16): The phosphonium salt of nonyl bromide (4.87 g, 10.4 mmol) was dissolved in THF (25 mL) and cooled to $0\,^\circ$C. NaHMDS (8.88 mL, 8.88 mmol, 1 M in THF) was added dropwise. After stirring for 30 min the orange solution was cooled to $-78\,^\circ$C and added to a solution of cooled ($-100\,^\circ$C) aldehyde **15** (2.65 g, 7.40 mmol) in THF (25 mL) via syringe. After 5 min the reaction was quenched with H_2O. The aqueous layer was extracted with Et_2O (3×20 mL). The combined organic layers were washed with sat. aq. NaCl solution (10 mL) and phosphate buffer (pH 7, 10 mL) and dried with $MgSO_4$. The solvents were removed in vacuo. The residue was purified by CC (80 g silica gel, hexane/MTBE 10:1) to yield the vinyl epoxide **16** (2.96 g, 6.32 mmol, 85 %) as a colorless oil. $E/Z = 1:1$ (^{1}H NMR).

16: (*Z* isomer): $R_f = 0.24$ (*n*-hexane/MTBE 12:1); $[\alpha]_D^{22} = -4.4$, ($c = 1.05$, $CHCl_3$); IR (film): $\tilde{\nu} = 2984$, 2955, 2928, 2856, 1658,1463, 1378, 1368, 1252, 1168, 1091, 1006, 940, 882, 837, 777, 724, 664, 511 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 0.06$ (s, 6H, $SiCH_3$), 0.83 – 0.87 (m, 12H, $SiC(CH_3)_3$, 18-H_3), 1.21 – 1.27, 1.60 – 1.61 (m, 12H, 12,13,14,15,16,17-H_2), 1.38 (s, 6H, acetonide-CH_3), 1.70 – 1.76 (m, 6H, 2,5,6-H_2), 2.15 – 2.21 (m, 2H, 11-H_2), 2.83 – 2.86 (m, 1H, 7-H), 3.35 (dd, $J = 2.0$ Hz, 9.0 Hz, 1H, 8-H), 3.61 – 3.77 (m, 4H, 1-H_2, 3,4-H), 5.02 (dd, $J = 9.0$ Hz, 11.0 Hz, 1H, 9-H), 5.68 (dt, $J = 7.7$ Hz, 11.0 Hz, 1H, 10-H); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = -5.4$ ($SiCH_3$), 14.1 (C-18), 18.3 [$C(CH_3)$], 22.7 (C-17), 25.9 [C(CH_3)], 27.3 (acetonide-CH_3), 27.8 (C-11), 29.0, 29.1, 29.3, 29.4, 29.5, 29.6, 31.9 (C-5, C-6, C-12, C-13, C-14, C-15, C-16), 36.0 (C-2), 54.4 (C-8), 59.9 (C-7), 60.0 (C-1), 77.6, 80.6 (C-3, C-4), 108.1 (acetal), 126.8 (C-9), 136.7 (C-10); $C_{27}H_{52}O_4Si$ (468.795): calcd C 69.18, H 11.18; found C 69.21, H 10.87.

E isomer: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.06$ (s, 6H, $SiCH_3$), 0.83 – 0.87 (m, 12H, $SiC(CH_3)_3$, 18-H_3), 1.21 – 1.27, 1.60 – 1.61 (m, 12H,

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12,13,14,15,16,17-H_2), 1.38 (s, 6H, acetonide-CH_3), 1.70–1.76 (m, 6H, 2,5,6-H_2), 1.91–2.01 (m, 2H, 11-H_2), 2.83–2.86 (m, 1H, 7-H), 3.06 (dd, J = 2.3 Hz, 7.9 Hz, 1H, 8-H), 3.61–3.77 (m, 4H, 1-H_2, 3,4-H), 5.15 (dd, J = 7.9 Hz, 15.4 Hz, 1H, 9-H), 5.88 (dt, J = 6.8 Hz, 15.4 Hz, 1H, 10-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.4 ($SiCH_3$), 14.1 (C-18), 18.3 [$C(CH_3)$], 22.7 (C-17), 25.9 [$C(CH_3)$], 27.3 (acetonide-CH_3), 29.0, 29.1, 29.3, 29.4, 29.5, 29.6, 31.9 (C-5, C-6, C-12, C-13, C-14, C-15, C-16), 32.0 (C-11), 36.0 (C-2), 58.8 (C-8), 60.0 (C-1), 60.2 (C-7), 77.6, 80.6 (C-3, C-4), 108.1 (acetal), 127.3 (C-9), 136.8 (C-10).

(2*S*,3*R*,6*S*,1′*S*,1″*Θ*)-2-Decenyl-3-hydroxy-6-(3′-*tert*-butyl-dimethylsilyloxy-1′-hydroxy)-propyl-tetrahydropyran (17): Vinyl epoxide **16** (110 mg, 0.235 mmol) was dissolved in CH_2Cl_2/2-propanol (10 mL, 30:1) and cooled to −60 °C. CSA (5 mg, 0.022 mmol) was added. After 4 h (−60 °C → −15 °C) the reaction was quenched by addition of Et_3N (1 mL). The solvents were evaporated and the residue was purified by FCC (15 g silica gel, hexane/MTBE 2:1) to provide the tetrahydopyran **17** (90 mg, 0.210 mmol, 89 %) as a colorless oil. E/Z = 1:1 (^{1}H NMR). **17**: (Z isomer): R_f = 0.30 (n-hexane/MTBE 1:1); $[\alpha]_D^{25}$ = −29.9, (c = 0.85, $CHCl_3$); IR (film): $\tilde{\nu}$ = 3400, 3012, 2927, 2856, 1657, 1463, 1408, 1362, 1261, 1255, 1083, 978, 938, 872, 836, 776, 722, 666 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.05 (s, 6H, $SiCH_3$), 0.86–0.89 (m, 12H, $SiC(CH_3)_3$, 10″-H_3), 1.25–1.29, 1.30–1.38 (m, 12H, 4″, 5″, 6″, 7″, 8″, 9″-H_2), 1.49–1.52 (m, 2H, 4-H_2), 1.59–1.60 (m, 1H, 5-H_2), 1.65–1.68 (m, 2H, 2′-H_2), 1.74–1.76 (m, 1H, 5-H_2), 2.09–2.18 (m, 3H, 3″-H_2, 3-OH), 2.95 (d, J = 2.8 Hz, 1H, 1′-OH), 3.27–3.30 (m, 2H, 3,6-H), 3.65–3.67 (m, 1H, 1′-H), 3.78–3.83 (m, 2H, 3′-H_2), 3.87 (dd, J = 8.7 Hz, 9.1 Hz, 1H, 2-H), 5.36 (dd, J = 9.1 Hz, 10.7 Hz, 1H, 1″-H), 5.75–5.81 (m, 1H, 2″-H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = −5.4 ($SiCH_3$), 14.1 (C-10″), 18.3 [$C(CH_3)$], 22.7 (C-9″), 25.9 [$C(CH_3)$], 26.3 (C-4), 28.4, 29.2, 29.3, 29.4, 29.7, 30.9, 31.9 (C-3″, C-4″, C-5″, C-6″, C-7″, C-8″, C-5), 35.2 (C-2′), 60.9 (C-3′), 70.2 (C-3), 72.0 (C-1′), 78.3 (C-2), 80.1 (C-6), 127.2 (C-1″), 137.0 (C-2″); $C_{24}H_{48}O_4Si$ (428.728): calcd C 67.24, H 11.29; found C 67.41, H 11.30.

E isomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.05 (s, 6H, $SiCH_3$), 0.86–0.89 (m, 12H, $SiC(CH_3)_3$, 10″-H_3), 1.25–1.76, (m, 18H, 4,5,2′,4″,5″,6″,7″,8″,9″-H_2), 2.09–2.18 (m, 3H, 3″-H_2, 3-OH), 2.95 (s, 1H, 1′-OH), 3.27–3.30 (m, 2H, 3,6-H), 3.49–3.51 (m, 1H, 2-H), 3.65–3.67 (m, 1H, 1′-H), 3.78–3.83 (m, 2H, 3′-H_2), 5.38–5.41 (m, 1H, 1″-H), 5.80–5.85 (m, 1H, 2″-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.4 ($SiCH_3$), 14.1 (C-10″), 18.3 [$C(CH_3)$], 22.7 (C-9″), 25.9 [$C(CH_3)$], 26.3 (C-4), 28.4, 29.0, 29.2, 29.4, 29.7, 30.9, 32.4 (C-3″, C-4″, C-5″, C-6″, C-7″, C-8″, C-5), 35.2 (C-2′), 60.9 (C-3′), 71.9 (C-3), 72.0 (C-1′), 80.1 (C-6), 83.7 (C-2), 127.5 (C-1″), 136.6 (C-2″).

(2*S*,3*R*,6*S*,1′*S*)-2-Decyl-3-hydroxy-6-(3′-*tert*-butyldimethylsilyloxy-1′-hydroxy)-propyl-tetrahydropyran (18): Pt/C (90 mg, 0.023 mmol Pt, 5 % on C) was suspended in ethyl acetate (25 mL) at 0 °C. The mixture was degassed and stirred under hydrogen atmosphere (1 atm) for 5 min. Alkene **17** (1.20 g, 2.80 mmol) dissolved in ethyl acetate (5 mL) was added and the mixture was stirred vigorously for 5 h. Then the solution was filtered through a pad of silica gel, washed with ethyl acetate, and the solvent was evaporated. The residue (1.14 g, 2.65 mmol, 95 %) was a colorless oil, which was spectroscopically pure and needed no further purification. R_f = 0.27 (n-hexane/MTBE 1:1); $[\alpha]_D^{25}$ = −33.1, (c = 0.94, $CHCl_3$); IR (film): $\tilde{\nu}$ = 3410, 2926, 2856, 1466, 1388, 1361, 1256, 1094, 1006, 938, 836, 776 cm^{-1}, ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.05 (s, 6H, $SiCH_3$), 0.87–0.90 (m, 12H, $SiC(CH_3)_3$, 10″-H_3), 1.10–1.35 (m, 16H, 2″,3″,4″,5″,6″,7″,8″,9″-H_2), 1.36–1.55 (m, 4H, 1″,4,5-H_2), 1.64–1.74 (m, 3H, 2′,5-H_2), 1.78–1.82 (m, 1H, 3-OH), 2.07–2.13 (m, 1H, 4-H_2), 2.86–2.87 (m, 1H, 1′-OH), 3.00–3.06 (m, 1H, 2-H), 3.15–3.18 (m, 1H, 6-H), 3.24–3.31 (m, 1H, 3-H), 3.59–3.65 (m, 1H, 1′-H), 3.78–3.84 (m, 2H, 3′-H_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.4 ($SiCH_3$), 14.1 (C-10″), 18.3 [$C(CH_3)$], 22.7 (C-9″), 25.9 [$C(CH_3)$], 25.5, 25.6, 26.7, 29.3, 29.6, 29.7, 31.9, 32.0, 32.7 (C-4, C-5, C-1″, C-2″, C-3″, C-4″, C-5″, C-6″, C-7″, C-8″), 35.6 (C-2′), 60.6 (C-3′), 70.6 (C-3), 71.9 (C-1′), 80.1 (C-6), 82.1 (C-2); $C_{24}H_{50}O_4Si$ (430.744): calcd C 66.92, H 11.70; found C 66.76, H 11.48.

(2*S*,3*R*,6*S*,1′*S*)-2-Decyl-3-*tert*-butyldimethylsilyloxy-6-(1′,3′-di-*tert*-butyldimethylsilyloxy)-propyl-tetrahydropyran (19): Diol **18** (2.10 g, 4.88 mmol) was dissolved in CH_2Cl_2 (40 mL) and cooled to 0 °C. 2,6-Lutidine (2.9 mL, 25.0 mmol) and TBDMS-OTf (3.5 mL, 15 mmol) were added under stirring. After 30 min the reaction was quenched with a sat. aq. sodium bicarbonate solution (20 mL). The aqueous layer was extracted with MTBE (3 × 20 mL) and the combined organic layers were washed with a sat. aq. NaCl solution (2 × 15 mL) and dried with $MgSO_4$. After evaporation of the solvents the residue was purified by CC (80 g silica gel, hexane/CH_2Cl_2 8:1) to afford **19** (3.13 g, 4.76 mmol, 97 %) as a colorless oil. R_f = 0.28 (n-hexane/CH_2Cl_2 8:1); $[\alpha]_D^{23}$ = −39.6, (c = 0.98, $CHCl_3$); IR (film): $\tilde{\nu}$ = 2955, 2929, 2857, 1472, 1388, 1361, 1256, 1095, 1006, 873, 836, 775, 669 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.02–0.03 (br s, 18H, $SiCH_3$), 0.85–0.89 (m, 30H, $SiC(CH_3)_3$, 10″-H_3), 1.20–1.39 (m, 16H, 2″, 3″, 4″, 5″, 6″, 7″, 8″, 9″-H_2), 1.39–1.84 (m, 7H, 1″, 2′, 4,5-H_2), 1.93–2.04 (m, 1H, 4-H_2), 2.93–3.02 (m, 1H, 2-H), 3.19–3.24 (m, 2H, 3,6-H), 3.61–3.69 (m, 2H, 3′-H_2), 3.74–3.78 (m, 1H, 1′-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.8, −4.4, −4.3 ($SiCH_3$), 14.1 (C-10″), 18.2 [$C(CH_3)$], 22.7 (C-9″), 25.7, 25.9, 26.0 [$C(CH_3)$], 25.1, 25.2, 29.4, 29.7, 29.8, 31.9, 32.0 (C-4, C-5, C-1″, C-2″, C-3″, C-4″, C-5″, C-6″, C-7″, C-8″), 35.5 (C-2′), 60.1 (C-3′), 70.9, 71.1 (C-3, C-1′), 79.8 (C-6), 82.3 (C-2); HR-MS ($C_{36}H_{79}O_4Si_3$): calcd 659.5286; found 659.5280.

(2*S*,3*R*,6*S*,1′*S*)-2-Decyl-3-*tert*-butyldimethylsilyloxy-6-(1′-*tert*-butyldimethylsilyloxy-3′-iodo)-propyl-tetrahydropyran (20): *1. Monodeprotection with CSA*: Compound **19** (550 mg, 0.83 mmol) was dissolved in CH_2Cl_2 (10 mL) and MeOH (5 mL) at 0 °C. CSA (25 mg, 0.10 mmol) dissolved in MeOH (5 mL) was added under stirring. The reaction was quenched after 30 min by the addition of a sat. aq. sodium bicarbonate solution (8 mL). After extraction with MTBE (4 × 10 mL), washing of the combined organic layers with sat. aq. NaCl solution (10 mL) and drying with $MgSO_4$ the solvents were evaporated and the resulting crude oil was purified by CC (20 g silica gel, MTBE/hexane 1:5) to obtain the corresponding alcohol (332 mg, 0.61 mmol, 74 %) as a colorless oil. 14 % silyl ether **19** (80 mg, 0.12 mmol) could also be regained.

(2*S*,3*R*,6*S*,1′*S*)-2-Decyl-3-*tert*-butyl-dimethylsilyloxy-6-(1′-*tert*-butyldimethylsilyloxy-3′-hydroxy)-propyl-tetrahydropyran: R_f = 0.35 (n-hexane/MTBE 5:1); $[\alpha]_D^{23}$ = −47.5, (c = 2.26, $CHCl_3$); IR (film): $\tilde{\nu}$ = 3401, 2930, 2858, 1466, 1368, 1253, 1100, 1013, 840, 776, 672 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.04 (br s, 12H, $SiCH_3$), 0.84–0.87 (m, 21H, $SiC(CH_3)_3$, 10″-H_3), 1.21–1.49 (m, 21H, 1″,2″,3″,4″,5″,6″,7″,8″,9″,4,5-H_2), 1.54–1.74 (m, 1H, 2′-H_2), 1.76–1.91 (m, 1H, 2′-H_2), 1.93–2.05 (m, 1H, 4-H_2), 2.85 (t, 1H, 3′-OH), 3.02–3.10 (m, 1H, 2-H), 3.19–3.24 (m, 1H, 3-H), 3.25–3.34 (m, 1H, 6-H), 3.62–3.70 (m, 2H, 3′-H_2), 3.79–3.84 (m, 1H, 1′-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.8, −4.3 ($SiCH_3$), 14.1 (C-10″), 17.9, 18.0 [$C(CH_3)$], 22.7 (C-9″), 25.8, 25.9 [$C(CH_3)$], 24.5, 25.0, 29.3, 29.5, 29.6, 29.6, 29.7, 31.8, 31.9, 33.3 (C-4, C-5, C-1″, C-2″, C-3″, C-4″, C-5″, C-6″, C-7″, C-8″), 35.4 (C-2′), 60.2 (C-3′), 70.9 (C-3), 73.0 (C-1′), 80.0 (C-6), 82.7 (C-2); $C_{30}H_{64}O_4Si_2$ (545.008) calcd C 66.12, H 11.84; found C 66.17, H 11.67.

2. Iodation: Iodine (88 mg, 0.348 mmol) was added to a solution of imidazole (59 mg, 0.870 mmol) and PPh_3 (84 mg, 0.319 mmol) in CH_2Cl_2 (2 mL) at 0 °C. After stirring for 5 min, the alcohol (158 mg, 0.290 mmol) dissolved in CH_2Cl_2 (1 mL) was added slowly. The reaction mixture was stirred for 2.5 h with exclusion of light. Then it was quenched by the addition of a aqueous $Na_2S_2O_3$ solution (10 mL). The aqueous layer was extracted with MTBE (3 × 10 mL). The combined organic layers were washed with sat. aq. NaCl solution (10 mL), dried with $MgSO_4$, and the solvents were removed in vacuo. The crude product was purified by FCC (8 g silica gel, hexane/MTBE 30:1) to yield **20** (152 mg, 0.232 mmol, 80 %) as a colorless oil. R_f = 0.31 (n-hexane/CH_2Cl_2 8:1); $[\alpha]_D^{23}$ = −47.7 (c = 0.44, $CHCl_3$); IR (film): $\tilde{\nu}$ = 2929, 2857, 1466, 1367, 1253, 1098, 937, 837, 774, 672 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.03–0.07 (m, 12H, $SiCH_3$), 0.86 (m, 21H, $SiC(CH_3)_3$, 10″-H_3), 1.23–1.75 (m, 21H, 1″,2″,3″,4″,5″,6″,7″,8″,9″,4,5-H_2), 1.82–1.93 (m, 1H, 2′-H_2), 1.93–2.02 (m, 1H, 4-H_2), 2.02–2.16 (m, 1H, 2′-H_2), 2.96–3.04 (m, 1H, 2-H), 3.10–3.31 (m, 4H, 3,6-H, 3′-H_2), 3.65–3.74 (m, 1H, 1′-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.8, −4.3 ($SiCH_3$), 3.5 (C-3′), 14.1 (C-10″), 17.9, 18.0 [$C(CH_3)$], 22.7 (C-9″), 25.8, 25.9 [$C(CH_3)$], 25.0, 29.4, 29.6, 29.6, 29.7, 31.8, 31.9, 33.5 (C-4, C-5, C-1″, C-2″, C-3″, C-4″, C-5″, C-6″, C-7″, C-8″), 36.6 (C-2′), 70.9 (C-3), 74.0 (C-1′), 79.4 (C-6), 82.5 (C-2); HR-MS ($C_{30}H_{63}O_3ISi_2$): calcd 639.3126; found: 639.3122 [$M - CH_3$]$^+$.

(3*S*,4*S*,7*R*,8*Θ*,9*Θ*)-1-*tert*-Butyldimethylsilyloxy-3,4-*O*-isopropyliden-7-hydroxy-8-methoxy-octadec-9-ene-3,4-diol (22): 1:1 mixture of diastereomers at C-8; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.03 (s, 6H, $SiCH_3$), 0.88–0.97 (m, 12H, $SiC(CH_3)_3$, 18-H_3), 1.21–1.89 (m, 12H, 12,13,14,15,16,17-H_2), 1.34 (s, 6H, acetonide-CH_3), 1.63–2.07 (m, 8H, 2,5,6,11-H_2), 2.26–2.32, 2.63–2.66 (m, 1H, OH), 3.24–3.29 (m, 3H, OMe), 3.59–3.79 (m, 5H, 1-H_2, 3,4,7-H), 3.41–3.46, 3.88–3.96 (m, 1H, 8-H), 5.29–5.40 (m, 1H, 9-H), 5.64–5.79 (m, 1H, 10-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.2 ($SiCH_3$), 14.1 (C-18), 18.5

[C(CH$_3$)], 21.5 (C-17), 26.1 [C(*C*H$_3$)], 27.6 (acetonide-CH$_3$), 21.6, 23.0, 23.5, 28.3, 29.2, 29.6, 29.7, 29.9, 31.1, 32.2 (C-5, C-6, C-11, C-12, C-13, C-14, C-15, C-16), 36.0 (C-2), 56.0 (OMe), 60.0 (C-1), 73.2, 73.4 (C-7), 77.7, 81.2 (C-3, C-4), 80.8, 85.7 (C-8), 108.0 (acetal), 125.8, 136.8 (C-9, C-10).

(2*S*,3*R*,6*S*,1′*S*,1″*Θ*)-2-Decenyl-3-*tert*-butyldimethylsilyloxy-6-(3′-*tert*-butyldimethylsilyloxy-1′-hydroxy)-propyl-tetrahydropyran (23): TBDMS-OTf (44 μL, 0.192 mmol) and 2,6-lutidine (45 μL, 0.384 mmol) were dissolved in CH_2Cl_2 (0.8 mL). After 30 min vinyl epoxide **16** (30 mg, 0.064 mmol), dissolved in CH_2Cl_2 (0.3 mL), was added at −78 °C. After 1 h the reaction was quenched with phosphate buffer (pH 7, 1 mL) The aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL) and the combined organic layers were washed with a sat. aq. NaCl solution (5 mL) and dried with $MgSO_4$. After evaporation of the solvents the residue was purified by CC (2 g silica gel, hexane/MTBE 20:1) to afford **23** (21 mg, 0.039 mmol, 61 %) as a colorless oil. R_f = 0.42 (*n*-hexane/MTBE 20:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.03 – 0.04 (br s, 12H, SiCH$_3$), 0.83 – 0.87 (m, 21H, SiC(CH$_3$)$_3$, 10″-H$_3$), 1.25 – 1.38 (m, 12H, 4″, 5″, 6″, 7″, 8″, 9″-H$_2$), 1.39 – 1.79 (m, 6H, 2′,4,5-H$_2$), 2.09 – 2.18 (m, 2H, 3″-H$_2$), 2.92 (d, *J* = 2.4 Hz, 1H, 1′-OH), 3.21 – 3.36 (m, 2H, 3,6-H), 3.59 – 3.66 (m, 1H, 1′-H), 3.75 – 3.87 (m, 3H, 3′-H$_2$, 2-H), 5.26 – 5.33 (m, 1H, 1″-H), 5.55 – 5.62 (m, 1H, 2″-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.4, −4.4 (SiCH$_3$), 14.1 (C-10″), 18.3 [*C*(CH$_3$)], 22.7 (C-9″), 25.8, 25.9 [C(*C*H$_3$)], 26.4 (C-4), 28.2, 29.3, 29.5, 29.6, 31.9, 33.1 (C-3″, C-4″, C-5″, C-6″, C-7″, C-8″, C-5), 35.2 (C-2′), 60.8 (C-3′), 71.2 (C-3), 71.9 (C-1′), 78.2 (C-2), 80.0 (C-6), 128.5 (C-1″), 135.4 (C-2″); HR-MS ($C_{30}H_{62}O_4Si_2$): calcd 542.4187; found: 542.4189.

Reaction of 27 with CSA: Vinyl epoxide **27** (100 mg, 0.213 mmol) was dissolved in CH_2Cl_2 (8 mL) and 2-propanol (0.3 mL). CSA (10 mg, 0.044 mmol) was added at −60 °C. After 4 h (−60 °C → rt) no conversion was observed (TLC). After stirring for another 12 h at rt, NEt_3 (1 mL) was added. The solvents were removed in vacuo and the residue was purified by FCC (10 g silica gel, hexanes/MTBE 2:1) to provide **28** (15 mg, 0.028 mmol, 13 %) and **29** (26 mg, 0.049 mmol, 23 %) as major products.

(3*S*,4*S*,7*S*,8*Θ*,9*Z*)-1-*tert*-Butyldimethylsilyloxy-3,4-*O*-isopropyliden-7-hydroxy-8-isopropyloxy-octadec-9-ene-3,4-diol (28): (mixture of diastereomers at C-8: 2:1 ^{1}H NMR) R_f = 0.81 (*n*-hexane/MTBE 2:1); major isomer: ^{1}H NMR (300 MHz, C_6D_6): δ = 0.06 (s, 6H, SiCH$_3$), 0.88 – 0.93 (m, 3H, 18-H$_3$), 0.97 (s, 9H, SiC(CH$_3$)$_3$), 1.02 – 1.12 (m, 6H, (C*H*$_3$)$_2$CHO), 1.21 – 1.31 (m, 12H, 12,13,14,15,16,17-H$_2$), 1.40 (s, 3H, acetonide-CH$_3$), 1.41 (s, 3H, acetonide-CH$_3$), 1.63 – 2.05 (m, 8H, 2,5,6,11-H$_2$), 2.29 – 2.31 (m, 1H, OH), 3.60 – 3.66 (m, 1H, (CH$_3$)$_2$C*H*O), 3.72 – 3.90 (m, 5H, 1-H$_2$, 3,4,7-H), 4.17 – 4.20 (m, 1H, 8-H), 5.49 – 5.56 (m, 2H, 9,10-H); ^{13}C NMR (75 MHz, C_6D_6): δ = −5.2 (SiCH$_3$), 14.3 (C-18), 18.5 [*C*(CH$_3$)], 21.5 (C-17), 26.1 [C(*C*H$_3$)], 27.6 (acetonide-CH$_3$), 21.6, 23.0, 23.5, 28.3, 29.2, 29.6, 29.7, 29.9, 31.1, 32.2 (C-5, C-6, C-11, C-12, C-13, C-14, C-15, C-16, propyl-CH$_3$), 36.4 (C-2), 60.3 (C-1), 68.5 (OCHMe$_2$), 73.6 (C-7), 75.8 (C-8), 78.0, 81.2 (C-3, C-4), 108.1 (acetal), 127.9, 134.9 (C-9, C-10); minor isomer: ^{1}H NMR (300 MHz, C_6D_6): δ = 0.06 (s, 6H, SiCH$_3$), 0.88 – 0.93 (m, 3H, 18-H$_3$), 0.97 (s, 9H, SiC(CH$_3$)$_3$) 1.02 – 1.12 (m, 6H, (C*H*$_3$)$_2$CHO), 1.21 – 1.31 (m, 12H, 12,13,14,15,16,17-H$_2$), 1.40 (s, 3H, acetonide-CH$_3$), 1.41 (s, 3H, acetonide-CH$_3$), 1.63 – 2.05 (m, 8H, 2,5,6,11-H$_2$), 2.29 – 2.31 (m, 1H, OH), 3.60 – 3.66 (m, 1H, (CH$_3$)$_2$C*H*O), 3.72 – 3.90 (m, 6H, 1-H$_2$, 3,4,7,8-H), 5.49 – 5.56 (m, 2H, 9,10-H); ^{13}C NMR (75 MHz, C_6D_6): δ = −5.2 (SiCH$_3$), 14.3 (C-18), 18.5 [*C*(CH$_3$)], 21.5 (C-17), 26.1 [C(*C*H$_3$)], 27.6 (acetonide-CH$_3$), 21.6, 23.0, 23.5, 28.3, 29.2, 29.6, 29.7, 29.9, 31.1, 32.2 (C-5, C-6, C-11, C-12, C-13, C-14, C-15, C-16, propyl-CH$_3$), 36.4 (C-2), 60.3 (C-1), 68.3 (OCHMe$_2$), 73.6 (C-7), 78.0, 81.2 (C-3, C-4), 81.6 (C-8), 108.1 (acetal), 127.9, 134.9 (C-9, C-10); HR-MS ($C_{29}H_{57}O_5Si$): calcd 513.3975; found 513.3977 [*M* − CH$_3$]$^+$.

(3*S*,4*S*,7*S*,8*Θ*,9*Θ*)-1-*tert*-Butyldimethylsilyloxy-3,4-*O*-isopropyliden-7-hydroxy-10-isopropyloxy-octadec-8-ene-3,4-diol (29): R_f = 0.58 (*n*-hexane/MTBE 2:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.03 (s, 6H, SiCH$_3$), 0.82 – 0.87 (m, 12H, SiC(CH$_3$)$_3$, 18-H$_3$), 1.06 – 1.09 (m, 6H, (C*H*$_3$)$_2$CHO), 1.21 – 1.50 (m, 14H, 11,12,13,14,15,16,17-H$_2$), 1.35 (s, 6H, acetonide-CH$_3$), 1.63 – 1.81 (m, 6H, 2,5,6-H$_2$), 2.49 (s, 1H, OH), 3.48 – 3.80 (m, 6H, 1-H$_2$, 3,4,10-H, (CH$_3$)$_2$C*H*O), 4.08 – 4.19 (m, 1H, 7-H), 5.43 – 5.65 (m, 2H, 8,9-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.4 (SiCH$_3$), 14.1 (C-18), 18.3 [*C*(CH$_3$)], 22.7 (C-17), 25.9 [C(*C*H$_3$)], 27.3 (acetonide-CH$_3$), 21.6, 23.5, 25.6, 28.8, 29.3, 29.6, 29.6, 31.8, 34.4, 35.8 (C-5, C-6, C-11, C-12, C-13, C-14, C-15, C-16, propyl-CH$_3$), 36.1 (C-2), 59.8 (C-1), 68.5 (OCHMe$_2$), 72.2 (C-7), 77.3 (C-10), 77.7, 80.9 (C-3, C-4), 108.1 (acetal), 132.6, 134.0 (C-8, C-9); HR-MS ($C_{30}H_{60}O_5Si$): calcd 528.4210; found 528.4207.

(2*S*)-2,3-Epoxy-1-(triisopropylsilyloxy)propane (31): Imidazole (3.55 g, 52.2 mmol) and DMAP (530 mg, 4.34 mmol) were added to a solution of (*R*)-glycidol (3.00 mL, 43.4 mmol) in CH_2Cl_2 (75 mL). The mixture was treated with TIPSCl (10.00 g, 51.9 mmol) at 0 °C. After stirring at rt for 90 min, the reaction mixture was filtered through a pad of Celite and diluted with water (100 mL) and *n*-hexane (50 mL). The aqueous layer was extracted with *n*-hexane (2 × 30 mL). The combined organic layers were washed with water (1 × 30 mL), sat. aq. NaCl solution (2 × 30 mL) and dried with $MgSO_4$. The solvents were removed in vacuo and the residue was purified by FCC (200 g silica gel, PE/MTBE 10:1) to yield **31** (9.7 g, 97 %) as a colorless oil. R_f = 0.45 (*n*-hexane/MTBE 10:1); $[\alpha]_D^{25}$ = −3.7 (*c* = 1.0, $CHCl_3$); IR (film): $\tilde{\nu}$ = 3049 w (epoxide-CH), 2943/2866 vs (CH), 1464 s, 1384 m, 1254 m (epoxide-ROR), 1161 s, 1137 s, 1102 s, 883 s, 682 s; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.03 – 1.09 (m, 21H, TIPS), 2.64 (dd, *J* = 5.3, 2.6 Hz, 1H, 3-H$_a$), 2.75 (dd, *J* = 5.3, 4.1 Hz, 1H, 3-H$_b$), 3.06 – 3.12 (m, 1H, 2-H), 3.72 (dd, *J* = 11.7, 4.5 Hz, 1H, 1-H$_a$), 3.89 (dd, *J* = 11.5, 3.2 Hz, 1H, 1-H$_b$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.9 (Si*C*H(CH$_3$)$_2$), 17.9 (SiCH(*C*H$_3$)$_2$), 44.4 (C-1), 52.6 (C-2), 63.9 (C-3); $C_{12}H_{26}O_2Si$ (230.42): calcd C 62.55, H 11.37; found C 62.48, H 11.49.

(2*S*)-(1-Triisopropylsilyloxy)-hex-5-en-2-ol (32): For the preparation of the Grignard reagent, a solution of allyl bromide (15.7 g, 130 mmol) in THF (100 mL) was added dropwise at 0 °C to flame-dried magnesium (4.1 g, 170 mmol) in THF (50 mL) to which 1,2-dibromoethane (2 drops) was added before. The mixture was stirred at 0 °C for additional 30 min. After that the grey suspension was cooled to −30 °C and solid copper iodide (742 mg, 3.9 mmol) was added. The color of the suspension turned to light green. At −30 °C a solution of TIPS-glycidol **31** (6.06 g, 26.3 mmol) in THF (40 mL) was added. The temperature was allowed to rise to −10 °C during another hour of stirring. At 0 °C half sat. aq. NH_4Cl solution (40 mL) was added. The mixture was filtered through a pad of Celite, diluted with MTBE (80 mL), and water (80 mL). The aqueous layer was extracted with MTBE (3 × 30 mL) and the combined organic layers were washed with sat. aq. NaCl solution (2 × 40 mL) and dried with $MgSO_4$. The solvents were removed in vacuo and the residue was purified by CC (180 g silica gel, PE/MTBE 10:1) to yield **32** (6.55 g, 91 %) as a colorless liquid. R_f = 0.32 (*n*-hexane/MTBE 10:1); $[\alpha]_D^{22}$ = 4.5 (*c* = 1.0, $CHCl_3$); IR (film): $\tilde{\nu}$ = 3576/3444 br (OH), 3077 w (=CH$_2$), 2943/2866 s (CH), 1641 m (C=C), 1463 s, 1116 s, 1068 m, 882 m; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 – 0.18 (m, 21H, TIPS), 1.40 – 1.60 (m, 2H, 4-H), 2.04 – 2.28 (m, 2H, 3-H), 2.52 (br s, 1H, OH), 3.43 – 3.51 (m, 1H, 2-H), 3.62 – 3.72 (m, 2H, 1-H), 4.91 – 5.05 (m, 2H, 6-H), 5.74 – 5.88 (m, 1H, 5-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.9 (Si*C*H(CH$_3$)$_2$), 17.9 (SiCH(*C*H$_3$)$_2$), 29.8 (C-4), 32.0 (C-3), 67.4 (C-1), 71.4 (C-2), 114.7 (C-6), 138.4 (C-5); $C_{15}H_{32}O_2Si$ (272.50): calcd C 60.11, H 11.84; found C 60.27, H 10.86.

(4*S*)-4,5-Bis(triisopropylsilyloxy)-pentanal (33): *1. TIPS-protection*: A solution of the secondary alcohol **32** (6.70 g, 24.6 mmol) and 2,6-lutidine (7.2 mL, 61.5 mmol) in CH_2Cl_2 (100 mL) was treated with TIPS-OTf (9.04 g, 29.5 mmol) at 0 °C. The solution was stirred at rt for 2.5 h, then sat. aq. NH_4Cl solution (100 mL) was added. The aqueous layer was extracted with MTBE (3 × 30 mL) and the combined organic layers were washed with sat. aq. NaCl solution (2 × 30 mL) and dried with $MgSO_4$. The solvents were removed in vacuo and the residue was purified by CC (100 g silica gel, PE) to afford the desired product (9.97 g, 96 %) as a colorless oil.

(2*S*)-1,2-Bis(triisopropylsilyloxy)-hex-5-ene: R_f = 0.75 (*n*-hexane/MTBE 10:1); $[\alpha]_D^{23}$ = −24.9 (*c* = 1.0, $CHCl_3$); IR (film): $\tilde{\nu}$ = 3077 w (=CH$_2$), 2943/2867 s (CH), 1642 w (C=C), 1464 m, 1384/1366 w (*t*Bu), 1122 m, 882 m, 681 m; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.00 – 1.11 (m, 42H, 2 × TIPS), 1.51 – 1.84 (m, 2H, 3-H$_2$), 2.11 – 2.23 (m, 2H, 4-H$_2$), 3.50 (dd, *J* = 9.4, 7.9 Hz, 1H, 1-H$_a$), 3.71 (dd, *J* = 9.4, 4.9 Hz, 1H, 1-H$_b$), 3.83 – 3.92 (m, 1H, 2-H), 4.89 – 5.05 (m, 2H, 6-H$_2$), 5.77 – 5.91 (m, 1H, 5-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.0, 12.6 (2 × Si*C*H(CH$_3$)$_2$), 18.0, 18.2 (2 × SiCH(*C*H$_3$)$_2$), 28.5 (C-4), 33.6 (C-3), 66.7 (C-1), 72.5 (C-2), 114.0 (C-6), 139.3 (C-5); $C_{24}H_{52}O_2$ (428.84): calcd C 67.22, H 12.22; found C 67.29, H 12.48.

2. Ozonolysis: Ozone (Fischer OZ 503, 100 L O_2 h^{-1}) was bubbled through a solution of (2*S*)-1,2-bis(triisopropylsilyloxy)-hex-5-ene (3.0 g, 7.0 mmol) in CH_2Cl_2 (120 mL) at −75 °C until the color began to turn blue. The excess of ozone was removed by bubbling argon through the solution. PPh_3 (1.84 g, 7.0 mmol) was added at −75 °C and the mixture was stirred at rt for 1 h. The solution was concentrated in vacuo and the residue was purified by FCC (200 g silica gel, PE/CH_2Cl_2 4:1) to yield aldehyde **33** (2.96 g, 98 %) as a colorless oil. R_f = 0.36 (*n*-hexane/MTBE 20:1); $[\alpha]_D^{25}$ = −23.1 (*c* = 1.0,

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$CHCl_3$); IR (film): $\tilde{\nu}$ = 2942/2866 s (CH), 2724 w (aldehyde-CH), 1731 s (C=O), 1463 m, 1157 s, 1120 m, 1013 m, 883 m, 681 m; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.00–1.07 (m, 42H, 2 × TIPS), 1.84–2.07 (m, 2H, 3-H_2), 2.43–2.63 (m, 2H, 2-H_2), 3.41–3.49 (m, 1H, 5-H_a), 3.72 (dd, J = 9.6, 4.7 Hz, 1H, 5-H_b), 3.89–3.97 (m, 1H, 4-H), 9.78 (t, J = 1.9 Hz, 1H, 1-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.9, 12.5 (2 × Si*C*H(CH_3)$_2$), 17.9, 18.1 (2 × SiCH(*C*H_3)$_2$), 26.5 (C-2), 38.6 (C-3), 66.0 (C-5), 71.4 (C-4), 203.0 (C-1); $C_{23}H_{50}O_3Si_2$ (430.81): calcd C 64.12, H 11.70; found C 64.19, H 11.64.

(6*S*,9*S*)-6-Hydroxy-9,10-bis(triisopropylsilyloxy)decyl pivalate (36): *1. Preparation of the dialkylzinc reagent* **34**: Diethylzinc (4.6 mL, 45 mmol) was added to 5-iodopentylpivalate (8.94 g, 30 mmol) and CuI (85 mg, 0.45 mmol) at rt. The mixture was stirred at 50 °C for 26 h. The black precipitate was allowed to settle and the solution was transferred to another flask via a PTFE tube. Xylene (4 mL) was used as rinsing liquid. The xylene and the excess of diethylzinc were condensed off at 40 °C and reduced pressure (ca. 0.1 mbar). After 18 h more xylene (4 mL) was added and evaporated again to make the removal of $ZnEt_2$ as complete as possible.

2. Preparation of the catalyst: Ti(O*i*Pr)$_4$ (4.8 mL, 16 mmol), the chiral diamine **35** (303 mg, 0.8 mmol), and xylene (5 mL) were stirred at 50 °C for 30 min.

3. Reaction with aldehyde **33**: The catalyst suspension was cooled to −40 °C and the prepared dialkylzinc **34** was added through a PTFE tube. Xylene was used to wash any residual **34** into the reaction flask. The reaction mixture was stirred at −40 °C for 5 min, then a solution of aldehyde **33** (3.45 g, 8.0 mmol) in xylene (5 mL) was added. The color of the mixture turned to light green. It was allowed to warm up to −25 °C and was stirred at this temperature for 18 h. The reaction mixture was allowed to warm up to 0 °C and water (5 mL), sat. aq. NH_4Cl solution (40 mL), and MTBE (40 mL) were added. The mixture was filtered through a pad of Celite. The aqueous layer was extracted with MTBE (3 × 30 mL) and the combined organic layers were washed with sat. aq. NaCl solution (2 × 40 mL) and dried with $MgSO_4$. The solvents were evaporated in vacuo and the residue was purified by FCC (180 g silica gel, gradient PE/MTBE 20:1 → MTBE) to obtain **36** (3.52 g, 70%) as a colorless liquid. R_f = 0.12 (*n*-hexane/MTBE 10:1); IR (film): $\tilde{\nu}$ = 3446 br w (OH), 2842/2866 s (CH), 1731 m (C=O), 1463 m, 1284/1366 w (*t*Bu), 1285 m, 1157 m, 1066 m, 882 m, 680 m; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.99–1.07 (m, 42H, 2 × TIPS), 1.16 (s, 9H, *t*Bu), 1.28–1.77 (m, 12H, 3,4,6,7,8,9-H_2), 3.50–3.59 (m, 2H, 1-H_2), 3.66–3.74 (m, 1H, 5-H), 3.86–3.96 (m, 1H, 2-H), 4.02 (t, J = 6.4 Hz, 2H, 10-H_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.9, 12.4 (2 × Si*C*H(CH_3)$_2$), 18.0, 18.1 (2 × SiCH(*C*H_3)$_2$), 25.4, 26.1, 28.6, 30.5, 31.8, 37.3 (C-3,4,6–9), 27.2 (C(*C*H_3)$_3$), 38.7 (*C*(CH_3)$_3$), 64.4 (C-10), 65.8 (C-1), 72.1 (C-5), 72.5 (C-2), 178.6 (*C*OO*t*Bu); $C_{33}H_{70}O_5Si_2$ (603.08): calcd C 65.72, H 11.70; found C 65.85, H 11.61.

5-[(2′*R*,5′*S*)-5′-(Hydroxymethyl)-tetrahydrofuran-2′-yl]-pentyl pivalate (37): *1. Tosylation*: A solution of the secondary alcohol **36** (3.37 g, 5.59 mmol) in CH_2Cl_2 (20 mL) and pyridine (20 mL) was treated with tosyl chloride (4.26 g, 22.4 mmol) at 0 °C. The solution was stirred at rt for 15 h, then sat. aq. NH_4Cl solution (40 mL) and MTBE (40 mL) were added. The aqueous layer was extracted with MTBE (3 × 10 mL). The combined organic layers were washed with 0.2 M HCl (2 × 10 mL), sat. aq. $NaHCO_3$ solution (3 × 10 mL), sat. aq. NaCl solution (2 × 20 mL), and dried with $MgSO_4$. The solvents were evaporated and the residue was filtered through silica gel (70 g, PE/MTBE 10:1) to afford tosylate (3.73 g, 88%) as a colorless oil.

(6*S*,9*S*)-6-(*p*-Toluenesulfonyloxy)-9,10-bis(triisopropyl-silyloxy)decyl pivalate: R_f = 0.26 (*n*-hexane/MTBE 10:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.96–1.04 (m, 42H, 2 × TIPS), 1.16 (s, 9H, *t*Bu), 1.19–1.74 (m, 12H, 3,4,6,7,8,9-H_2), 2.40 (s, 3H, Ar-CH_3), 3.36 (dd, J = 9.4, 8.7 Hz, 1H, 1-H_a), 3.62 (dd, J = 9.4, 4.9 Hz, 1H, 1-H_b), 3.70–3.80 (m, 1H, 2-H), 3.96 (t, J = 6.4 Hz, 2H, 10-H_2), 4.48–4.58 (m, 1H, 5-H), 7.27 (d, J = 8.1 Hz, 2H, Ar-H), 7.75 (d, J = 8.1 Hz, 2H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.8, 12.4 (2 × Si*C*H(CH_3)$_2$), 17.9, 18.0, 18.1 (2 × SiCH(*C*H_3)$_2$), 21.6 (Ar-CH_3), 24.2, 25.7, 28.3, 28.4, 29.3, 34.0 (C-3,4,6–9), 27.2 (C(*C*H_3)$_3$), 38.7 (*C*(CH_3)$_3$), 64.2 (C-10), 66.1 (C-1), 72.0 (C-2), 72.5 (C-5), 84.5 (C-5), 127.6, 129.6, 134.7, 144.2 (Ar), 178.5 (*C*OO*t*Bu).

Compound **37**: *2. Deprotection and ring closure*: A solution of the tosylate (2.51 g, 3.31 mmol) in THF (20 mL) was treated with a solution of TBAF (3.15 g, 10.0 mmol) in THF (7 mL) at rt. The reaction mixture was stirred for 1 h, then sat. NH_4Cl solution (10 mL), water (10 mL) and MTBE (20 mL) were added. The aqueous layer was extracted with MTBE (2 × 10 mL) and the combined organic layers were washed with sat. aq. NaCl solution (2 × 15 mL) and dried with $MgSO_4$. The solvents were removed in vacuo and the residue was purified by CC (45 g silica gel, PE/MTBE 1:2) to yield the THF alcohol **37** (834 mg, 93%) as a colorless oil. The C-5 epimers were separated by preparative HPLC (Rainin Si 60, 41.4 × 250 mm, *n*-hexane/*i*PrOH 96:4, 40 mL min^{-1}). **37**: R_f = 0.19 (*n*-hexane/MTBE 1:1); HPLC: t_R = 24.7 min (Superspher Si 60, *n*-hexane/*i*PrOH 96:4, 1.0 mL min^{-1}); $[\alpha]_D^{23}$ = 5.3 (c = 1.0, $CHCl_3$); IR (film): $\tilde{\nu}$ = 3437 br m (OH), 2934/2865 s (CH), 1728 s (C=O), 1541/1480 m, 1398/1366 w (*t*Bu), 1285 s, 1159 s, 1038 s; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.14 (s, 9H, *t*Bu), 1.23–1.68, 1.85–2.03 (m, 12H, 3′,4′,2,3,4,5-H_2), 2.25 (br s, 1H, OH), 3.43 (dd, J = 11.5, 6.2 Hz, 1H, 1″-H_a), 3.57 (dd, J = 11.7, 3.4 Hz, 1H, 1″-H_b), 3.83–3.93 (m, 1H, 2′-H), 3.96–4.09 (m, 1H, 5′-H), 4.00 (t, J = 6.6 Hz, 2H, 1-H_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.8, 26.0, 27.5, 28.5, 32.0, 35.5 (C-3′,4′,2–5), 27.1 (C(*C*H_3)$_3$), 38.7 (*C*(CH_3)$_3$), 64.2 (C-1), 65.0 (C-1″), 78.9 (C-5′), 79.2 (C-2′), 178.6 (*C*OO*t*Bu); $C_{15}H_{28}O_4$ (272.38): calcd C 66.14, H 10.36; found C 65.69, H 10.04.

5-[(2′*R*,5′*S*)-5′-(Triethylsilyloxymethyl)-tetrahydrofuran-2′-yl]-pentan-1-ol (38): *1. TES-protection*: Imidazole (222 mg, 3.70 mmol) and powdered molecular sieves (4 Å, 50 mg) were added to a solution of the alcohol **37** (505 mg, 1.85 mmol) in CH_2Cl_2 (20 mL). The mixture was treated with TESCl (0.37 mL, 2.22 mmol) at 0 °C. After stirring at rt for 2 h, the reaction mixture was filtered through a pad of Celite and diluted with MTBE (20 mL), phosphate buffer solution (10 mL) and water (5 mL). The aqueous layer was extracted with MTBE (3 × 7 mL) and the combined organic layers were washed with sat. aq. NaCl solution (2 × 20 mL) and dried with $MgSO_4$. The solvents were evaporated and the residue was purified by CC (25 g silica gel, PE/MTBE 2:1) to yield the protected alcohol (617 mg, 86%) as a colorless liquid.

5-[(2′*R*,5′*S*)-5′-(Triethylsilyloxymethyl)-tetrahydrofuran-2′-yl]-pentyl pivalate: R_f = 0.67 (*n*-hexane/MTBE 1:1); $[\alpha]_D^{25}$ = −3.8 (c = 1.0, $CHCl_3$); IR (film): $\tilde{\nu}$ = 2930/2875/2856 s (CH), 1760 s (C=O); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.51–0.63 (m, 6H, 3 × SiCH_2CH$_3$), 0.87–0.98 (m, 9H, 3 × SiCH$_2$C*H*$_3$), 1.16 (s, 9H, *t*Bu), 1.21–1.76 (m, 10H, 5 × alkyl-CH_2), 1.88–2.02 (m, 2H, alkyl-CH_2), 3.50 (dd, J = 10.4, 5.5 Hz, 1H, 1″-H_a), 3.60 (dd, J = 10.4, 5.1 Hz, 1H, 1″-H_b), 3.83–3.93 (m, 1H, 2′-H), 3.97–4.06 (m, 1H, 5′-H), 4.01 (t, J = 6.6 Hz, 2H, 1-H_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 4.4 (Si*C*H$_2$CH$_3$)$_3$, 6.7 (SiCH$_2$*C*H$_3$)$_3$, 25.9, 26.1, 28.3, 28.6, 31.8, 35.7 (C-3′,4′,2–5), 27.2 (C(*C*H_3)$_3$), 38.7 (*C*(CH_3)$_3$), 64.3 (C-1), 65.7 (C-1″), 79.0 (C-5′), 79.3 (C-2′), 178.6 (*C*OO*t*Bu); $C_{21}H_{42}O_4Si$ (386.64): calcd C 65.23, H 10.95; found C 64.98, H 10.85.

2. Cleavage of the pivalate: A solution of the pivalate (510 mg, 1.32 mmol) in THF (15 mL) was treated with DIBAH (3.30 mL, 3.30 mmol, 1 M in hexanes) at −40 °C. The reaction mixture was allowed to warm up to −15 °C during 1 h. The reaction was quenched by addition of MeOH (1.5 mL), sat. aq. $NaHCO_3$ solution (4 mL) and ethyl acetate (15 mL). The mixture was stirred for 30 min at rt, then solid Na_2SO_4 (10 g) was added and the mixture was stirred vigorously for 1 h. The mixture was filtered through a pad of Celite and the solvents were removed in vacuo. The crude product was purified by CC (25 g silica gel, PE/MTBE 2:1) to obtain alcohol **38** (373 mg, 93%) as a colorless oil. R_f = 0.33 (*n*-hexane/MTBE 1:1); $[\alpha]_D^{25}$ = −4.1 (c = 1.0, $CHCl_3$); IR (film): $\tilde{\nu}$ = 3407 (OH), 2935/2877 s (CH), 1008 w, 743 w; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.57 (q, J = 7.4 Hz, 6H, 3 × SiCH_2CH$_3$), 0.92 (t, J = 7.7 Hz, 9H, 3 × SiCH$_2$C*H*$_3$), 1.22–1.76 (m, 11H, OH, 5 × alkyl-CH_2), 1.90–2.02 (m, 2H, alkyl-CH_2), 3.50 (dd, J = 10.4, 5.5 Hz, 1H, 1″-H_a), 3.56–3.64 (m, 3H, 1″-H_b, 1-H_2), 3.83–3.94 (m, 1H, 2′-H), 3.97–4.07 (m, 1H, 5′-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 4.4 (Si*C*H$_2$CH$_3$)$_3$, 6.7 (SiCH$_2$*C*H$_3$)$_3$, 25.8, 26.0, 28.3, 31.8, 32.7, 35.7 (C-3′,4′,2–5), 62.9 (C-1), 65.7 (C-1″), 79.0 (C-5′), 79.4 (C-2′); $C_{16}H_{34}O_3Si$ (302.52): calcd C 63.52, H 11.33; found C 63.37, H 11.06.

Phosphonium salt 39: *1. Iodation*: To a solution of imidazole (271 mg, 3.98 mmol) and PPh_3 (383 mg, 1.46 mmol) in CH_2Cl_2 (15 mL) was added at 0 °C first a solution of iodine (404 mg, 1.59 mmol) in CH_2Cl_2 (7 mL) and then a solution of alcohol **38** (401 mg, 1.33 mmol) in CH_2Cl_2 (3 mL). The reaction mixture was stirred at rt for 1.5 h, then $Na_2S_2O_3$ solution (5% in water, 30 mL) was added and the mixture was stirred until the brown color disappeared. The phases were separated and the aqueous layer was extracted with MTBE (3 × 15 mL). The combined organic layers were washed with sat. aq. NaCl solution (2 × 20 mL) and dried with $MgSO_4$. The

solvents were evaporated in vacuo and the residue was purified by CC (45 g silica gel, PE/MTBE 1:1) to yield the iodide (460 mg, 84 %) as a colorless oil.

(2*R*,5*S*)-2-(5′-Iodopentyl)-5-(triethylsilyloxymethyl)-tetrahydrofuran: $R_f = 0.79$ (*n*-hexane/MTBE 1:1); IR (film): $\tilde{\nu} = 2953/2935$ s (CH), 2911 m, 2875 s, 1460 w, 1088 m, 1005 m, 800 w, 744/728 s; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.51 - 0.63$ (m, 6H, 3 × SiCH_2CH$_3$), 0.93 (t, $J = 7.9$ Hz, 9H, 3 × SiCH$_2$CH_3), 1.20 – 1.86 (m, 10H, 5 × alkyl-CH$_2$), 1.89 – 2.03 (m, 2H, alkyl-CH$_2$), 3.16 (t, $J = 7.0$ Hz, 2H, 5′-H$_2$), 3.47 – 3.55 (m, 1H, 1″-H$_a$), 3.55 – 3.63 (m, 1H, 1″-H$_b$), 3.82 – 3.94 (m, 1H, 2-H), 3.97 – 4.07 (m, 1H, 5-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 4.4$ (SiCH_2CH$_3$)$_3$, 6.7 (SiCH$_2$$CH_3$)$_3$, 7.1 (C-5′), 25.2, 28.3, 30.6, 31.8, 33.5, 35.6 (C-3,4,1′-4′), 65.7 (C-1″), 79.0 (C-5), 79.3 (C-2); HR-MS (EI): $C_{16}H_{33}IO_2Si$ calcd 411.1216; found 411.1212 $[M-H]^+$.

2. Preparation of the triphenyl-phosphonium salt **39**: The iodide (205 mg, 0.50 mmol) and PPh_3 (656 mg, 2.5 mmol) were dissolved in toluene (3 mL) and CH_3CN (5 mL). The solution was stirred at 70 °C for 24 h. The mixture was concentrated in vacuo and washed with Et_2O several times until the rinsing liquid was free of PPh_3 (checked by TLC). The phosphonium salt **39** was dried in vacuo (ca. 0.1 mbar) and was introduced in the Wittig reaction without further purification.

Methyl (3*S*)-6-(benzyloxy)-3-hydroxyhexanoate (41): *1. Alkylation*: Sodium hydride (80 % in mineral oil, 4.5 g, 150 mmol) was suspended in THF (200 mL) and cooled to − 30 °C (internal temperature). The *β*-ketoester **40** (13.9 g, 120 mmol) dissolved in THF (50 mL) was added dropwise, keeping the temperature below − 25 °C and stirred for 15 min. Then *n*-butyllithium (68.8 mL, 2.18 M in hexane, 150 mmol) was added ($T < 25$ °C). After 15 min stirring, *O*-benzyl-2-bromoethanol (21.5 g, 100 mmol), diluted with THF (50 mL), was added dropwise ($T < 10$ °C). The mixture was stirred for 2 h ($T < 0$ °C) and then kept at − 25 °C for further 15 h. The reaction was quenched by the addition of conc. HCl (30 mL), MTBE (150 mL) and water (50 mL). The aqueous layer was extracted with MTBE (3 × 50 mL). The combined organic layers were washed with sat. aq. $NaHCO_3$ solution (2 × 50 mL) and sat. aq. NaCl solution (2 × 50 mL) and were dried with $MgSO_4$. The solvents were removed in vacuo and the residue was purified by FCC (350 g silica gel, gradient PE/MTBE 8:1 to 1:2) to yield the desired *β*-keto ester (18.0 g, 72 %) as a pale yellow oil.

Methyl 6-(benzyloxy)-3-oxohexanoate: $R_f = 0.40$ (*n*-hexane/MTBE 1:1); IR (film): $\tilde{\nu} = 2953/2862$ s (CH), 1747/1716 s (C=O), 1453 m, 1437 m, 1322 m, 1261 m, 1104 m (COC), 739/699 m (Ar); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.90$ (quint, $J = 6.2$ Hz, 2H, 5-H$_2$), 2.64 (t, $J = 6.6$ Hz, 2H, 4-H$_2$), 3.44 (s, 2H, 2-H$_2$), 3.48 (t, $J = 6.0$ Hz, 2H, 6-H$_2$), 3.70 (s, 3H, OCH$_3$), 4.35 (s, 2H, OCH_2Ph), 7.25 – 7.36 (m, 5H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 23.6$ (C-5), 39.7 (C-4), 48.9 (C-2), 52.2 (OCH$_3$), 68.9 (C-6), 72.8 (OCH_2Ph), 126.9, 127.5, 127.6, 128.3, 128.4, 138.2 (Ph), 167.6 (C-1), 202.4 (C-3); $C_{14}H_{18}O_4$ (250.29): calcd C 67.18, H 7.25; found C 67.13, H 7.34.

2. Asymmetric hydrogenation: For the preparation of the catalyst complex $[RuCl_2(PhH)_2]_2$ (94.3 mg, 0.145 mmol) and (*S*)-(−)-BINAP (200 mg, 0.32 mmol) were dissolved in DMF (5 mL) and stirred at 110 °C for 20 min. A solution of 6-benzyloxy-3-oxo-hexanoic acid methylester (12.0 g, 47.9 mmol) in degassed methanol (20 mL) was added to the catalyst solution and this mixture was transferred to the hydrogenation reactor (Premex) through a PTFE tube. The solution was treated with 4.5 bar hydrogen at 95 °C and vigorous stirring for 18 h. After cooling to rt the dark red solution was concentrated in vacuo and purified by FCC (400 g silica gel, PE/MTBE 3:1 to 1:3) to afford *β*-hydroxy ester **41** (10.58 g, 88 %) as a pale yellow liquid. The enantioselectivity was determined by chiral HPLC and found to be 98:2 favoring the desired isomer. $R_f = 0.25$ (*n*-hexane/MTBE 1:1); HPLC: t_R (*S* enantiomer) = 14.2 min, t_R (*R* enantiomer) = 10.6 min (Chiralcel OD-H, *n*-hexane/*i*PrOH 90:10, 1.0 mL min^{-1}); $[\alpha]_D^{22} = 23.7$ (96:4 mixture of the enantiomers, $c = 1.0$, $CHCl_3$); IR (film): $\tilde{\nu} = 3444$ br (OH), 2950/2858 m (CH), 1737 vs (C=O), 1438 m, 1201 m, 1166 m, 1098 s, 739/699 m; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.41 - 1.60$ (m, 2H, 5-H$_2$), 1.60 – 1.79 (m, 2H, 4-H$_2$), 2.36 – 2.43 (m, 2H, 2-H$_2$), 3.26 (d, $J = 3.4$ Hz, 1H, OH), 3.43 (t, $J = 6.0$ Hz, 2H, 6-H$_2$), 3.62 (s, 3H, OCH$_3$), 3.91 – 4.00 (m, 1H, 3-H), 4.43 (s, 2H, OCH_2Ph), 7.17 – 7.29 (m, 5H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 25.8$ (C-5), 33.6 (C-4), 41.3 (C-2), 51.2 (OCH$_3$), 67.7 (C-3), 70.1 (C-6), 72.9 (OCH_2Ph), 127.5, 2 × 127.6, 2 × 128.3, 138.2 (Ph), 173.1 (C-1); $C_{14}H_{20}O_4$ (252.31): calcd C 66.65, H 7.99; found C 66.66, H 7.79.

(3*S*)-1,3-Bis(*tert*-butyldimethylsilyloxy)-6-benzyloxy-hexane (42): *1. Ester reduction*: In a two-necked flask equipped with a Claisen bridge, methyl ester **41** (1.0 g, 4.0 mmol) in THF (10 mL) was treated at rt with borane/dimethyl sulfide complex (0.9 mL, 8.8 mmol). Dimethyl sulfide was distilled off at 60 °C with a light argon flow. After 30 min the Claisen bridge was removed. The mixture was cooled to 0 °C and water (8 mL) was added carefully. After addition of solid K_2CO_3 (500 mg) and MTBE (10 mL) the phases were separated. The aqueous layer was extracted with MTBE (2 × 20 mL) and the combined organic layers were washed with sat. aq. NaCl solution (2 × 15 mL) and dried with $MgSO_4$. The solvents were removed in vacuo and the residue was purified by FCC (60 g silica gel, MTBE) to yield the benzyl protected triol (740 mg, 83 %) as a colorless liquid.

(3*S*)-6-(Benzyloxy)hexane-1,3-diol: $R_f = 0.16$ (MTBE); $[\alpha]_D^{19} = -6.6$ ($c = 1.1$, $CHCl_3$); IR (film): $\tilde{\nu} = 3382$ s (OH), 3087/3063/3030 w, 2941/2861 s (CH), 1453 m, 1363 m, 1204 m, 1098 s, 734/698 m; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.45 - 1.80$ (m, 6H, 2,4,5-H$_2$), 3.40 – 3.55 (m, 4H, 1-H$_2$, 2 × OH), 3.60 – 3.70 (m, 3H, 3-H, 6-H$_2$), 4.50 (s, 2H, OCH_2Ph), 7.20 – 7.37 (m, 5H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 26.0$ (C-5), 34.9 (C-4), 38.3 (C-2), 61.3 (C-1), 70.4 (C-3), 71.4 (C-6), 72.9 (OCH_2Ph), 127.6, 127.7, 128.3, 137.9 (Ph); $C_{13}H_{20}O_3$ (224.30): calcd C 69.61, H 8.99; found C 69.51, H 9.18.

2. TBDMS-protection: Imidazole (1.00 g, 14.7 mmol), DMAP (60 mg, 0.49 mmol), and powdered molecular sieves (4 Å, 50 mg) were added to a solution of the unprotected diol (1.10 g, 4.90 mmol) in CH_2Cl_2 (20 mL). The mixture was treated with TBDMSCl (3.56 g, 11.8 mmol, 50 % in toluene) at 0 °C. After stirring at rt for 16 h, the reaction mixture was filtered through a pad of Celite and diluted with MTBE (30 mL) and half sat. aq. NH_4Cl solution (30 mL). The aqueous layer was extracted with MTBE (3 × 15 mL) and the combined organic layers were washed with sat. aq. NH_4Cl solution (20 mL), sat. aq. NaCl solution (20 mL) and dried with $MgSO_4$. The solvents were removed in vacuo and the product was purified by FCC (100 g silica gel, PE/MTBE 2:1) to yield the fully protected triol **42** (1.96 g, 88 %) as a colorless liquid. $R_f = 0.50$ (*n*-hexane/MTBE 10:1); $[\alpha]_D^{20} = 8.6$ ($c = 2.0$, $CHCl_3$); IR (film): $\tilde{\nu} = 2954/2929/2857$ s, 1472 m, 1361 w, 1256 m, 1099 s, 836 s, 775 s, 734/697 w; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.03$ (s, 12H, 4 × SiCH$_3$), 0.87 (s, 18H, 2 × SiC(CH$_3$)$_3$), 1.41 – 1.57 (m, 2H, 5-H$_2$), 1.57 – 1.72 (m, 4H, 2,4-H$_2$), 3.45 (t, $J = 6.4$ Hz, 2H, 1-H$_2$), 3.65 (t, $J = 6.6$ Hz, 2H, 6-H$_2$), 3.84 (quint, $J = 5.6$ Hz, 1H, 3-H), 4.49 (s, 2H, OCH_2Ph), 7.24 – 7.35 (m, 5H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -5.3$ (2 × SiCH_3), − 4.6, − 4.4 (2 × SiCH_3), 18.1, 18.3 (2 × Si(C(CH$_3$)$_3$), 25.4 (C-5), 25.9, 25.9 (2 × Si(C(CH_3)$_3$), 33.9 (C-4), 40.9 (C-2), 59.9 (C-1), 69.1 (C-3), 70.6 (C-6), 72.8 (OCH_2Ph), 127.4, 127.6, 128.3, 138.7 (Ph); $C_{25}H_{48}O_3Si_2$ (452.82): calcd C 66.31, H 10.68; found C 66.34, H 10.48.

(4*S*)-4,6-Bis(*tert*-butyldimethylsilyloxy)-hexan-1-ol (43): 10 % Pd on activated carbon (ca. 0.4 mol %) (120 mg) was suspended in ethyl acetate (75 mL, HPLC grade). The mixture was degassed and stirred under a hydrogen atmosphere for 15 min. A solution of the benzyl ether **42** (13.0 g, 28.7 mmol) in ethyl acetate (20 mL) was added and the mixture was vigorously stirred at rt for 20 h under hydrogen atmosphere (1 atm). The suspension was filtered through a pad of Celite and the solvent was removed in vacuo to yield **43** (10.1 g, 97 %) as a colorless oil. The product required no further purification. $R_f = 0.38$ (*n*-hexane/MTBE 2:1); $[\alpha]_D^{22} = 9.5$ ($c = 1.0$, $CHCl_3$); IR (film): $\tilde{\nu} = 3348$ br (OH), 2954/2858 s (CH), 1463 w, 1339 w, 1255 m, 1096 m, 1054 m, 836 m, 774 w; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.02$ (s, 6H, 2 × SiCH$_3$), 0.04 (s, 6H, 2 × SiCH$_3$), 0.87 (s, 18H, 2 × SiC(CH$_3$)$_3$), 1.50 – 1.76 (m, 6H, 2,3,5-H$_2$), 2.09 (br s, 1H, OH), 3.56 – 3.68 (m, 4H, 1,6-H$_2$), 3.91 (quint, $J = 5.7$ Hz, 1H, 4-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -5.3$ (2 × SiCH_3), − 4.7, − 4.5 (2 × SiCH_3), 18.1, 18.2 (2 × SiC(CH$_3$)$_3$), 25.9, 25.9 (2 × SiC(CH_3)$_3$), 28.1 (C-2), 33.7 (C-3), 39.5 (C-5), 59.8 (C-6), 63.1 (C-1), 69.0 (C-4); $C_{18}H_{42}O_3Si_2$ (362.70): calcd C 59.61, H 11.67; found C 59.55, H 11.61.

(4*S*)-4,6-Bis(*tert*-butyldimethylsilyloxy)-hexanoic acid (44): *1. Swern oxidation*: DMSO (9.86 mL, 139 mmol) was added at − 75 °C to a solution of oxalyl chloride (6.07 mL, 69.6 mmol) in CH_2Cl_2 (200 mL). After 15 min stirring, a solution of the alcohol **43** (10.1 g, 27.8 mmol) in CH_2Cl_2 (20 mL) was added dropwise at − 70 °C. After stirring for 20 min, NEt_3 (27 mL, 195 mmol) was added dropwise at − 50 °C. The mixture was stirred at − 50 °C for 30 min and at 0 °C for 60 min. The reaction was quenched by the addition of water (100 mL). The phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with water (2 × 30 mL) and dried with $MgSO_4$. The solvent was removed in vacuo and the residue was filtered by FCC (100 g silica gel, PE/MTBE 2:1) to yield the aldehyde (9.75 g, 97 %) as a yellow oil which was oxidized to the carboxylic acid immediately.

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(4*S*)-4,6-Bis(*tert*-butyldimethylsilyloxy)-hexanal: $R_f = 0.62$ (*n*-hexane/MTBE 2:1); $[\alpha]_D^{23} = 4.1$ ($c = 0.56$, $CHCl_3$); IR (film): $\tilde{\nu} = 2956/2930$ s (CH), 2889 m/2858 s (CH), 2822/2712 w (aldehyde-CH), 1730 s (C=O), 1473 m, 1389/1361 w (*t*Bu), 1257 s, 1099 s, 1048 m, 836 s, 775 s; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.00-0.04$ (m, 12H, $2 \times SiCH_3$), 0.84–0.88 (m, 18H, $2 \times SiC(CH_3)_3$), 1.51–1.92 (m, 4H, 3,5-H_2), 2.47 (dt, $J = 7.5$, 1.5 Hz, 2H, 2-H_2), 3.63 (t, $J = 6.4$ Hz, 2H, 6-H_2), 3.88 (quint, $J = 5.5$ Hz, 1H, 4-H), 9.76 (t, $J = 1.5$ Hz, 1H, 1-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -5.4$ ($2 \times SiCH_3$), −4.6, −4.5 ($2 \times SiCH_3$), 18.0, 18.2 ($2 \times Si(C(CH_3)_3$), 25.8, 25.9 ($2 \times Si(C(CH_3)_3$), 29.2 (C-5), 39.6 (C-3), 39.8 (C-2), 59.6 (C-6), 68.2 (C-4), 202.5 (C-1).

2. Chlorite oxidation: A solution of the aldehyde (9.75 g, 27 mmol) in *t*BuOH (100 mL, p.A.) and 2-methyl-2-butene (25 mL) was treated with a solution of $NaClO_2$ (purity 80%, 9.4 g, 83.4 mmol) and $NaHPO_4 \times 2H_2O$ (17.3 g, 111 mmol) in water (120 mL) at 0 °C. The mixture was stirred vigorously at rt for 2 h, then the phases were separated. The aqueous layer was extracted with MTBE (2×30 mL) and the combined organic layers were washed with sat. aq. NaCl solution (2×40 mL) and dried with $MgSO_4$. The solvents were evaporated and the residue was purified by CC (100 g silica gel, $CHCl_3$/MeOH 19:1) to afford the carboxylic acid **44** (9.84 g, 97%) as a colorless oil. $R_f = 0.25$ ($CHCl_3$/MeOH 19:1); $[\alpha]_D^{21} = 1.6$ ($c = 1.0$, $CHCl_3$); IR (film): $\tilde{\nu} = 2956/2930/2858$ m, 1712 m (C=O), 1473 w, 1257 w, 1098 w, 836 w, 775 w; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.00-0.04$ (m, 12H, $2 \times SiCH_3$), 0.84–0.88 (m, 18H, $2 \times SiC(CH_3)_3$), 1.51–1.92 (m, 4H, 3,5-H_2), 2.40 (t, $J = 7.7$ Hz, 2H, 2-H_2), 3.63 (t, $J = 6.4$ Hz, 2H, 6-H_2), 3.88 (quint, $J = 5.7$ Hz, 1H, 4-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -5.4$ ($2 \times SiCH_3$), −4.6 ($2 \times SiCH_3$), 18.0, 18.2 ($2 \times SiC(CH_3)_3$), 25.8, 25.9 ($2 \times SiC(CH_3)_3$), 29.6 (C-5), 31.7 (C-3), 39.8 (C-2), 59.6 (C-6), 68.2 (C-4), 179.7 (C-1); $C_{18}H_{40}O_4Si_2$ (376.68): calcd C 57.40, H 10.70; found C 57.19, H 10.24.

(3*Θ*,5*S*)-3-[(2′*S*)-2′,4′-Bis(*tert*-butyldimethylsilyloxy)-butyl]-5-methyl-dihydrofuran-2(3*H*)-one (45): A solution of diisopropylamine (4.34 mL, 31.9 mmol) in THF (90 mL) was treated with *n*-butyllithium (10.6 mL, 2.5 M in hexanes, 26.6 mmol). The temperature was allowed to rise to 0 °C during 30 min. At 0 °C a solution of the carboxylic acid **44** in THF (20 mL) was added dropwise. The dark yellow solution was stirred for 40 min at 0 °C. Then a solution of (*S*)-propylene oxide in THF (10 mL) was added. The cooling bath was removed and the mixture was stirred at rt for 3 h. The reaction was quenched by the addition of sat. aq. NH_4Cl solution (20 mL), water (20 mL) and MTBE (30 mL). The aqueous layer was extracted with MTBE (2×30 mL), acidified to pH 3 with HCl (2 M), and extracted with MTBE (2×20 mL) again. The combined organic layers were washed with a sat. aq. NaCl solution (3×40 mL) and dried with $MgSO_4$. The mixture was concentrated in vacuo and redissolved in CH_2Cl_2 (50 mL). At 0 °C NEt_3 (2.9 mL, 21.2 mmol) and pivaloyl chloride (1.4 g, 11.7 mmol) were added. The mixture was stirred at rt for 30 min. The reaction was quenched by addition of water (40 mL), the phases were separated and the aqueous layer was extracted with MTBE (3×20 mL). The combined organic layers were washed with sat. aq. NaCl solution (2×30 mL) and dried with $MgSO_4$. The solvents were removed under reduced pressure and the residue was purified by FCC (120 g silica gel, PE/MTBE 5:1) to afford a 2:1 mixture (^{1}H NMR) of the epimeric lactones **45** (2.94 g, 67%) as a colorless oil. $R_f = 0.63$ (*n*-hexane/MTBE 1:1); IR (film): $\tilde{\nu} = 2956/2930$ s (CH), 2896/2886 m, 2858 s, 1774 s (C=O), 1257 m, 836 m, 775 s; ^{1}H NMR (300 MHz, $CDCl_3$): major epimer: $\delta = 0.00-0.06$ (m, 12H, $2 \times SiCH_3$), 0.86 (s, 18H, $2 \times SiC(CH_3)_3$), 1.33 (d, $J = 6.4$ Hz, CH_3), 1.42–1.82 (m, 4H, 1′-H_2, 3′-H_2), 1.98–2.15 (m, 2H, 4-H_2), 2.65–2.85 (m, 1H, 3-H), 3.56–3.71 (m, 2H, 4′-H_2), 3.96–4.07 (m, 1H, 2′-H), 4.57–4.69 (m, 1H, 5-H); minor epimer: $\delta =$ 0.00–0.06 (m, 12H, $2 \times SiCH_3$), 0.86 (s, 18H, $2 \times SiC(CH_3)_3$), 1.39 (d, $J =$ 6.4 Hz, CH_3), 1.42–1.82 (m, 4H, 1′-H_2, 3′-H_2), 1.98–2.15 (m, 2H, 4-H_2), 2.44–2.55 (m, 1H, 3-H), 3.56–3.71 (m, 2H, 4′-H_2), 3.87–3.97 (m, 1H, 2′-H), 4.37–4.50 (m, 1H, 5-H); ^{13}C NMR (75 MHz, $CDCl_3$): major epimer: $\delta = -5.4$ ($2 \times SiCH_3$), −4.6, −4.5 ($2 \times SiCH_3$), 18.0, 18.2 ($2 \times Si(C(CH_3)_3$), 21.0 (CH_3), 25.8 ($2 \times Si(C(CH_3)_3$), 35.5 (C-3), 36.3 (C-4), 38.5 (C-1′), 40.3 (C-3′), 59.4 (C-4′), 67.7 (C-2′), 74.6 (C-5), 179.3 (C-2); minor epimer: $\delta =$ −5.4 ($2 \times SiCH_3$), −4.6, −4.5 ($2 \times SiCH_3$), 18.0, 18.2 ($2 \times SiC(CH_3)_3$), 20.9 (CH_3), 25.8 ($2 \times SiC(CH_3)_3$), 37.7, 38.0, 38.2 (C-3,4,1′), 40.0 (C-3′), 59.4 (C-4′), 67.4 (C-2′), 75.2 (C-5), 179.4 (C-2); $C_{21}H_{44}O_4Si_2$ (416.74): calcd C 60.52, H 10.64; found C 60.63, H 10.48.

(5*S*)-3-[(2′*S*)-2′,4′-Bis(*tert*-butyldimethylsilyloxy)-butyl]-5-methylfuran-2(5*H*)-one (47): A solution of lactone **45** (1.72 g, 4.12 mmol) in THF (40 mL) was treated with a suspension of KHMDS (2.46 g, 12.4 mmol) in THF (15 mL) at −20 °C. The yellow mixture was warmed up to 0 °C and stirred for 30 min. A solution of PhSeCl (2.36 g, 12.4 mmol) in THF (10 mL) was added and the reaction mixture was stirred at 0 °C for 1 h and additional 20 min at rt. The reaction was quenched by the addition of phosphate buffer solution (1 M, pH 7) (30 mL), water (30 mL) and MTBE (30 mL). The aqueous layer was extracted with MTBE (3×20 mL) and the combined organic layers were washed with sat. aq. NaCl solution ($2 \times$ 30 mL) and dried with $MgSO_4$. The mixture was concentrated in vacuo and the crude selenium compound **46** was redissolved in THF/MeOH (20 mL/20 mL). At 0 °C MMPP (purity 85%, 9.5 g, 16.5 mmol) was added. The solution was stirred at rt for 20 min, then phosphate buffer solution (1 M, pH 7) (15 mL), water (25 mL), and MTBE (40 mL) were added. The aqueous layer was extracted with MTBE (2×20 mL) and CH_2Cl_2 (15 mL). The combined organic layers were washed with sat. aq. NaCl solution ($2 \times$ 30 mL) and dried with $MgSO_4$. The solvents were removed in vacuo and the residue was purified by FCC (60 g silica gel, PE/MTBE 5:1) to yield the unsaturated lactone **47** (1.51 g, 87%) as a colorless liquid. $R_f = 0.20$ (*n*-hexane/MTBE 5:1); $[\alpha]_D^{22} = 31.7$ ($c = 1.0$, $CHCl_3$); IR (film): $\tilde{\nu} = 2956/2930$ s (CH), 2858 m, 2762 s (C=O), 1473 m, 1257 m, 1097 s, 1030 m, 837 s, 775 s; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.00-0.06$ (m, 12H, $2 \times SiCH_3$), 0.83–0.88 (m, 18H, $2 \times SiC(CH_3)_3$), 1.38 (d, $J = 6.8$ Hz, CH_3), 1.58–1.68 (m, 2H, 3′-H_2), 2.42–2.47 (m, 2H, 1′-H_2), 3.58–3.72 (m, 2H, 4′-H_2), 4.05–4.15 (m, 1H, 2′-H), 4.93–5.02 (m, 1H, 5-H), 7.10–7.13 (m, 1H, 4-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -5.4$ ($2 \times SiCH_3$), −4.7, −4.5 ($2 \times SiCH_3$), 18.0, 18.2 ($2 \times SiC(CH_3)_3$), 19.0 (CH_3), 25.8, 25.9 ($2 \times SiC(CH_3)_3$), 32.9 (C-1′), 39.6 (C-3′), 59.5 (C-4′), 67.3 (C-2′), 77.5 (C-5), 130.6 (C-3), 151.5 (C-4), 174.0 (C-2); $C_{21}H_{42}O_4Si_2$ (414.73): calcd C 60.82, H 10.21; found C 60.57, H 10.15.

(5*S*)-3-[(2′*S*)-2′-(*tert*-Butyldimethylsilyloxy)-4′-hydroxy-butyl]-5-methylfuran-2(5*H*)-one (48): At 0 °C a solution of CSA (188 mg, 0.81 mmol) in MeOH (20 mL) was added to a solution of the protected alcohol **47** (1.35 g, 3.26 mmol) in CH_2Cl_2 (20 mL). The mixture was stirred at 0 °C for 30 min, then phosphate buffer solution (1 M, pH 7) (5 mL) and water (10 mL) were added. The aqueous layer was extracted with MTBE (4×10 mL) and the combined organic layers were washed with sat. aq. $NaHCO_3$ solution (pH 8, 10 mL), H_2O (10 mL), sat. aq. NaCl solution (2×15 mL), and dried with $MgSO_4$. The solvents were evaporated in vacuo and the residue was purified by FCC (60 g silica gel, PE/MTBE 1:2) to yield the primary alcohol **48** (772 mg, 79%) as a colorless liquid. 11% starting material **47** (155 mg) was recovered. $R_f = 0.16$ (*n*-hexane/MTBE 1:2); $[\alpha]_D^{22} = 40.5$ ($c = 1.3$, $CHCl_3$); IR (film): $\tilde{\nu} = 3443$ br (OH), 2955/2931 s, 2887/2858 m, 1752 s (C=O), 1256 m, 1085 m, 1028 m, 837 m, 776 m; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.05$ (s, 3H, $SiCH_3$), 0.08 (s, 3H, $SiCH_3$), 0.86 (s, 9H, $SiC(CH_3)_3$), 1.39 (d, $J = 6.8$ Hz, CH_3), 1.59–1.81 (m, 2H, 3′-H_2), 2.21 (br s, OH), 2.42–2.58 (m, 2H, 1′-H_2), 3.66–3.84 (m, 2H, 4′-H_2), 4.14–4.24 (m, 1H, 2′-H), 4.95–5.04 (m, 1H, 5-H), 7.09–7.13 (m, 1H, 4-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -4.8$, −4.5 ($2 \times SiCH_3$), 17.9 ($SiC(CH_3)_3$), 18.9 (CH_3), 25.8 ($SiC(CH_3)_3$), 32.9 (C-1′), 38.1 (C-3′), 59.7 (C-4′), 68.9 (C-2′), 77.6 (C-5), 130.4 (C-3), 151.9 (C-4), 173.9 (C-2); $C_{15}H_{28}O_4Si$ (300.47): calcd C 59.96, H 9.39; found C 59.86, H 9.01.

(3*S*)-3-(*tert*-Butyldimethylsilyloxy)-4-[(5′*S*)-5′-methyl-2′-oxo-2′,5′-dihydrofuran-3′-yl]-butanal (49): Dess–Martin periodinane (2.12 g, 5.0 mmol) was added to a solution of alcohol **48** (500 mg, 1.66 mmol) in CH_2Cl_2 (20 mL) and pyridine (1.34 mL, 16.6 mmol). The solution was stirred at rt for 4.5 h, then phosphate buffer solution (1 M, pH 7, 15 mL) and water (10 mL) were added. The aqueous layer was extracted with MTBE (3×15 mL) and the combined organic layers were washed with sat. aq. NaCl solution ($2 \times$ 20 mL) and dried with $MgSO_4$. The solution was concentrated in vacuo and the residue was purified by FCC (40 g silica gel, PE/MTBE 1:1) to afford aldehyde **49** (446 mg, 90%) as a colorless oil. $R_f = 0.30$ (*n*-hexane/MTBE 1:1); $[\alpha]_D^{23} = 27.8$ ($c = 0.36$, $CHCl_3$); IR (film): $\tilde{\nu} = 2956/2932$ s (CH), 2858 m, 1755/1728 s (C=O), 1405 m, 1085 m, 938 m; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.03-0.07$ (m, 6H, $2 \times SiCH_3$), 0.81–0.86 (m, 9H, $SiC(CH_3)_3$), 1.40 (d, $J = 6.8$ Hz, 3H, CH_3), 2.43–2.61 (m, 4H, 2,4-H_2), 4.45–4.55 (m, 1H, 3-H), 4.95–5.05 (m, 1H, 5′-H), 7.11–7.16 (m, 1H, 4′-H), 9.77 (t, $J = 2.3$ Hz, 1H, 1-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -4.8$, −4.6 ($2 \times SiCH_3$), 17.9 ($Si(C(CH_3)_3$), 18.7 (CH_3), 25.6 ($Si(C(CH_3)_3$), 33.4 (C-4), 50.2 (C-2), 65.9 (C-3), 77.6 (C-5′), 129.7 (C-3′), 152.4 (C-4′), 173.6 (C-2′), 201.2 (C-1); $C_{15}H_{26}O_4Si$ (298.45): calcd C 60.37, H 8.78; found C 60.33, H 9.11.

(5*S*)-3-{(2′*R*,4′*Θ*)-2′-*tert*-Butyldimethylsilyloxy-9′-[(2″*R*,5″S)-5″-(triethylsilyloxy)methyl-tetrahydrofuran-2″-yl}-non-4′-enyl]-5-methylfuran-2(5*H*)-one (50): The phosphonium salt **39** was dissolved in THF (5 mL) and

treated with NaHMDS (0.4 mL 1M in THF, 0.4 mmol) at 0 °C. The orange solution was stirred at 0 °C for 30 min, then it was cooled to −70 °C and a solution of aldehyde **49** (120 mg, 0.4 mmol) in THF (3 mL) was added dropwise. The cooling bath was replaced by an ice bath and the now light brown-yellow solution was stirred 20 min at 0 °C. The reaction was quenched by the addition of phosphate buffer solution (1M, pH 7, 7 mL). The mixture was diluted with MTBE (10 mL) and water (8 mL). The aqueous layer was extracted with MTBE (3 × 7 mL) and the combined organic layers were washed with sat. aq. NaCl solution (2 × 10 mL) and dried with $MgSO_4$. The solvents were removed in vacuo and the residue was purified by FCC (35 g silica gel, PE/MTBE 2:1) to yield olefin **50** (138 mg, 60 %) as a colorless oil. $R_f = 0.65$ (*n*-hexane/MTBE 1:1); IR (film): $\tilde{\nu} = 2954/2929$ s (CH), 2876/2857 m (CH), 1767 m (C=O), 1462 w, 1377/1361 w (*t*Bu), 1252 w, 1083 m, 1005 w, 837 w, 776 w; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = -0.01$ (s, 3H, $SiCH_3$), 0.03 (s, 3H, $SiCH_3$), 0.58 (q, $J = 8.0$ Hz, 6H, 3 × $SiCH_2CH_3$), 0.85 (s, 9H, $SiC(CH_3)_3$), 0.93 (t, $J = 8.1$ Hz, 9H, 3 × $SiCH_2CH_3$), 1.39 (d, $J = 7.2$ Hz, 3H, CH_3), 1.22–1.76 (m, 8H, 4 × alkyl-CH_2), 1.90–2.04 (m, 4H, 2 × alkyl-CH_2), 2.09–2.48 (m, 4H, 2 × alkyl-CH_2), 3.50 (dd, $J = 10.4$, 5.5 Hz, 1H, 1‴-H_a), 3.60 (dd, $J = 10.4$, 5.1 Hz, 1H, 1‴-H_b), 3.82–3.93 (m, 1H, 2″-H), 3.93–4.08 (m, 2H, 4-H, 5″-H), 4.98 (dq, $J = 6.7$, 1.0 Hz, 1H, 5-H), 5.27–5.53 (m, 2H, 4′-H, 5′-H), 7.09 (d, $J = 1.5$ Hz, 1H, 4-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -4.6$, −4.4 (2 × $SiCH_3$), 4.4 (2 × $SiCH_2CH_3$), 6.7 (2 × $SiCH_2CH_3$), 18.0 ($SiC(CH_3)_3$), 18.9 (CH_3), 25.8 ($SiC(CH_3)_3$), 26.0, 27.5, 28.3, 29.7, 31.8, 32.6, 35.1, 35.7 (C-1′,3′,6′-9′,3″,4″), 66.7 (C-1‴), 70.0 (C-2′), 77.2 (C-5), 79.0 (C-5″), 79.4 (C-2″), 124.8 (C-5′), 130.9 (C-3), 132.1 (C-4′), 151.5 (C-4), 173.9 (C-2); $C_{31}H_{58}O_5Si_2$ (566.96): calcd C 65.67, H 10.31; found C 66.11, H 10.19; HR-MS (EI): calcd 567.3901; found 567.3902 $[M+H]^+$.

(5*S*)-3-{(2′*R*)-*tert*-Butyldimethylsilyloxy-9′-[(2″*R*,5″*S*)-5″-(hydroxymethyl)-tetrahydrofuran-2″-yl]-nonyl}-5-methylfuran-2(5*H*)-one (51): *1. Wilkinson hydrogenation*: A solution of $[(PPh_3)_3RhCl]$ (85 mg, 0.09 mmol) in benzene (4 mL, spectroscopy grade) was degassed and stirred under hydrogen atmosphere for 15 min. A solution of olefin **50** (340 mg, 0.60 mmol) in benzene (2 mL) was added and the mixture was stirred under hydrogen atmosphere (1 atm) for 3 h at rt. The solution was concentrated in vacuo and the residue was purified by FCC (18 g silica gel, cyclohexane/MTBE 2:1) to yield the desired compound (325 mg, 95 %) as a light brown oil.

(5*S*)-3-{(2′*R*)-*tert*-Butyldimethylsilyloxy-9′-{(2″*R*,5″*S*)-5″-[(triethylsilyloxy)methyl]-tetrahydrofuran-2″-yl}-nonyl}-5-methyl-furan-2(5*H*)-one: $R_f = 0.55$ (silica gel treated with 1M $AgNO_3$, *n*-hexane/MTBE 2:1); $[\alpha]_D^{22} = 5.6$ ($c = 1.1$, $CHCl_3$); IR (film): $\tilde{\nu} = 2953/2930$ s (CH), 2876/2857 m (CH), 1766 s (C=O), 1463 w, 1385 w, 1253 w, 1084 m, 1005 w, 836 w; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = -0.01$– −0.06 (m, 6H, 2 × $SiCH_3$), 0.58 (q, $J = 7.9$ Hz, 6H, 3 × $SiCH_2CH_3$), 0.85 (s, 9H, $SiC(CH_3)_3$), 0.93 (t, $J = 7.9$ Hz, 9H, 3 × $SiCH_2CH_3$), 1.39 (d, $J = 7.2$ Hz, 3H, CH_3), 1.15–1.75 (m, 16H, 8 × alkyl-CH_2), 1.90–2.03 (m, 2H, alkyl-CH_2), 2.37–2.43 (m, 2H, 1′-H_2), 3.50 (dd, $J = 10.4$, 5.5 Hz, 1H, 1‴-H_a), 3.61 (dd, $J = 10.6$, 4.9 Hz, 1H, 1‴-H_b), 3.61–3.97 (m, 2H, 12-H, 2′-H), 3.97–4.07 (m, 1H, 5″-H), 4.98 (dq, $J = 6.7$, 1.4 Hz, 1H, 5-H), 7.09 (d, $J = 1.1$ Hz, 1H, 4-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -4.5$ (2 × $SiCH_3$), 4.4 (2 × $SiCH_2CH_3$), 6.7 (2 × $SiCH_2CH_3$), 18.0 ($SiC(CH_3)_3$), 19.0 (CH_3), 25.9 ($SiC(CH_3)_3$), 25.1, 26.2, 27.0, 28.3, 29.5, 29.6, 31.8, 32.7, 35.8, 36.9 (C-1′,3′-9′,3″,4″), 65.8 (C-1‴), 70.1 (C-2′), 77.4 (C-5), 79.0 (C-5″), 79.5 (C-2″), 130.8 (C-3), 151.4 (C-4), 174.0 (C-2); HR-MS (EI): $C_{31}H_{60}O_5Si_2$ calcd 569.4058; found 569.4055 $[M+H]^+$.

2. TES-deprotection: At −20 °C a solution of CSA (10 mg, 43 μmol) in MeOH (1 mL) was added to a solution of the protected alcohol (307 mg, 540 μmol) in CH_2Cl_2 (5 mL). The mixture was stirred at −20 °C for 10 min, then phosphate buffer solution (1M, pH 7, 3 mL) and water (2 mL) were added. The aqueous layer was extracted with MTBE (4 × 5 mL) and the combined organic layers were washed with sat. aq. NaCl solution (2 × 7 mL) and dried with $MgSO_4$. The solvents were evaporated in vacuo and the residue was purified by FCC (15 g silica gel, MTBE) to yield the primary alcohol **51** (187 mg, 76 %) as a light orange liquid. $R_f = 0.44$ (MTBE); $[\alpha]_D^{20} = 3.5$ ($c = 0.6$, $CHCl_3$); IR (film): $\tilde{\nu} = 3433$ br (OH), 2929 s (CH), 2857 m (CH), 1757 m (C=O), 1462 w, 1377 w, 1361 w, 1254 w, 1196 w, 1976 m, 836 m, 775 w; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = -0.04$ (s, 3H, $SiCH_3$), −0.01 (s, 3H, $SiCH_3$), 0.81 (s, 9H, $SiC(CH_3)_3$), 1.36 (d, $J = 6.8$ Hz, 3H, CH_3), 1.14–1.69 (m, 16H, 8 × alkyl-CH_2), 1.84–2.03 (m, 2H, alkyl-CH_2), 1.36 (br s, 1H, OH), 2.36 (d, $J = 5.3$ Hz, 2H, 1′-H_2), 3.37–3.48 (m, 1H, 1‴-H_a), 3.51–3.62 (m, 1H, 1‴-H_b), 3.81–3.95 (m, 2H, 2″-H, 2′-H), 3.99–4.09 (m, 1H, 5″-H), 4.90–5.00 (m, 1H, 5-H), 7.04–7.09 (m, 1H, 4-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -4.6$ (2 × $SiCH_3$), 17.9 ($SiC(CH_3)_3$), 18.9 (CH_3), 25.8 ($SiC(CH_3)_3$), 25.0, 26.1, 27.4, 29.4, 29.5 (2 ×), 31.9, 32.6, 35.6, 36.8 (C-1′,3′-9′,3″,4″), 64.9 (C-1‴), 70.1 (C-2′), 77.4 (C-5), 78.8 (C-5″), 79.4 (C-2″), 130.7 (C-3), 151.5 (C-4), 174.0 (C-2); HR-MS (EI): $C_{25}H_{46}O_5Si$ calcd 455.3193; found 455.3191 $[M+H]^+$.

(2*S*,5*R*)-5-{(8′*R*)-8′-*tert*-Butyldimethylsilyloxy-9′-[(5″*S*)-5″-methyl-2″-oxo-2″,5″-dihydrofuran-3″-yl]nonyl}-tetrahydrofuran-2-carbaldehyde (52): Dess–Martin periodinane (145 mg, 340 μmol) was added to a solution of alcohol **51** (78 mg, 170 μmol) in CH_2Cl_2 (6 mL) and pyridine (0.14 mL, 1.7 mmol). The solution was allowed to warm up to rt and was stirred for 4.5 h, then phosphate buffer solution (1M, pH 7, 5 mL), water (3 mL) and MTBE (6 mL) were added. The aqueous layer was extracted with MTBE (4 × 7 mL) and the combined organic layers were washed with sat. aq. NaCl solution (2 × 10 mL) and dried with $MgSO_4$. The solution was concentrated in vacuo and the residue was purified by FCC (8 g silica gel, PE/MTBE 1:2) to afford aldehyde **52** (70 mg, 91 %) as a colorless oil. $R_f = 0.38$ (*n*-hexane/MTBE 1:2); IR (film): $\tilde{\nu} = 2930/2857$ s (CH), 1757 s (C=O), 1405 w, 1255 w, 1076 m, 837 m, 776 w; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = -0.02$ (s, 3H, $SiCH_3$), 0.00 (s, 3H, $SiCH_3$), 0.83 (s, 9H, $SiC(CH_3)_3$), 1.37 (d, $J = 6.8$ Hz, 3H, CH_3), 1.15–2.21 (m, 18H, 1′-7′,3,4-CH_2), 2.37 (d, $J = 5.6$ Hz, 2H, 9′-H_2), 3.84–4.01 (m, 2H, 5-H, 8′-H), 4.24–4.31 (m, 1H, 2-H), 4.96 (dq, $J = 6.8$, 0.9 Hz, 1H, 5″-H), 7.05–7.10 (m, 1H, 4″-H), 9.61 (d, $J = 1.9$ Hz, 1H, CHO); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -4.5$ (2 × $SiCH_3$), 18.0 ($SiC(CH_3)_3$), 18. 9 (CH_3), 25.8 ($SiC(CH_3)_3$), 25.0, 26.0, 27.1, 29.4, 29.5, 29.5, 31.1, 32.6, 35.3, 36.9 (C-3,4,1′-7′,9′), 70.1 (C-8′), 77.4 (C-5″), 81.2 (C-2), 82.3 (C-5), 130.7 (C-3″), 151.5 (C-4″), 174.0 (C-2″), 203.2 (CHO); HR-MS (EI): $C_{25}H_{44}O_5Si$ calcd 452.2958; found 452.2959 $[M]^+$.

(2*S*,5*S*,1″*R*,4″*R*)-*tert*-Butyldiphenylsilyloxymethyl-5-(1″-hydroxy-4″-*tert*-butyldimethylsilyloxy)-pentyl-tetrahydrofuran (57): *t*BuLi (0.35 mL, 0.59 mmol, 1.68M in pentane) was added to a solution of iodide **55** (101 mg, 0.32 mmol) in Et_2O (7 mL) at −105 °C. After 10 min magnesium bromide etherate (0.27 mL, 0.64 mmol, 2.35M in Et_2O) was added and the solution was stirred for 1.5 h (−100 °C → −25 °C). Then the mixture was cooled to −78 °C and a solution of aldehyde **56** (118 mg, 0.32 mmol) in Et_2O (2 mL) was added. The solution was allowed to warm up to −10 °C during 1.5 h. The reaction was quenched by the addition of water (2 mL). The mixture was diluted with water (5 mL) and MTBE (10 mL). The aqueous layer was extracted with MTBE (3 × 5 mL) and the combined organic layers were washed with a sat. aq. NaCl solution (5 mL) and dried with $MgSO_4$. The solvents were removed in vacuo and the residue was purified by FCC (20 g silica gel, PE/MTBE 5:1) to yield the coupling products **57** and **58** (131 mg, 0.235 mmol, 73 %) as colorless oils. The diastereomers could be separated by FCC (6:1 mixture): **57** (major isomer, chelate product): $R_f = 0.46$ (*n*-hexane/MTBE 5:1); **58** (minor isomer): $R_f = 0.33$ (*n*-hexane/MTBE 5:1); **57** (major isomer): ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.05$ (s, 6H, $SiCH_3$), 0.89 (s, 9H, $SiC(CH_3)_3$), 1.06 (s, 9H, $SiC(CH_3)_3$), 1.13–1.19 (m, 3H, 5″-H_3), 1.45–1.54 (m, 2H, 2″-H_2), 1.60–1.72 (m, 2H, 3″-H_2), 1.77–1.90 (m, 2H, 3,4-H_2), 1.91–2.51 (m, 2H, 3,4-H_2), 2.40 (m, 1H, 1″-OH), 3.33–3.44 (m, 1H, 1″-H), 3.62–3.71 (m, 2H, 1′-H_2), 3.79–3.90 (m, 2H, 4″, 5-H), 4.08–4.17 (m, 1H, 2-H), 7.37–7.40 (m, 6H, SiPh), 7.67–7.71 (m, 4H, SiPh); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -4.7$, −4.4 ($SiCH_3$), 18.1, 19.2 [$SiC(CH_3)$], 23.7 (C-5″), 25.9, 26.7 [$C(CH_3)$], 28.2, 28.4 (C-3, C-4), 29.2 (C-2″), 35.2 (C-3″), 66.4 (C-1′), 68.3 (C-4″), 73.8 (C-1″), 79.5 (C-2), 82.6 (C-5), 127.6, 129.6, 133.6, 135.6 (SiPh); HR-MS ($C_{32}H_{52}O_4Si_2$): calcd 499.2700; found 499.2698 $[M - C_4H_9]^+$. **58** (minor isomer): ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.05$ (s, 6H, $SiCH_3$), 0.89 (s, 9H, $SiC(CH_3)_3$), 1.05 (s, 9H, $SiC(CH_3)_3$), 1.13–1.19 (m, 3H, 5″-H_3), 1.42–2.14 (m, 8H, 2″,3″,3,4-H_2), 2.51 (d, $J = 2.4$ Hz, 1H, 1″-OH), 3.67–3.76 (m, 3H, 1″-H, 1′-H_2), 3.79–3.89 (m, 2H, 4″, 5-H), 4.08–4.18 (m, 1H, 2-H), 7.37–7.40 (m, 6H, SiPh), 7.67–7.72 (m, 4H, SiPh); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -4.7$, −4.4 ($SiCH_3$), 18.1, 19.2 [$SiC(CH_3)$], 23.7 (C-5″), 25.9, 26.7 [$C(CH_3)$], 28.2, 28.3 (C-3, C-4), 29.2 (C-2″), 35.2 (C-3″), 66.0 (C-1′), 67.6 (C-4″), 72.1 (C-1″), 79.9 (C-2), 83.4 (C-5), 127.6, 129.6, 133.6, 135.6 (SiPh).

Protected mucocin fragment without butenolide 59: Iodide **20** (230 mg, 0.35 mmol) was dissolved in Et_2O (10 mL) at −105 °C. *t*BuLi (0.40 mL, 0.67 mmol, 1.68M in pentane) and, after 10 min, magnesium bromide etherate (0.29 mL, 0.68 mmol, 2.3M in Et_2O) were added and the solution was allowed to warm up to −10 °C during 1.5 h. Then the mixture was cooled to −78 °C and a solution of aldehyde **56** (104 mg, 0.28 mmol) in

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Et_2O (2 mL) was added. The mixture was stirred for 1.5 h (−78 °C → −10 °C). The reaction was quenched by the addition of sat. aq. sodium bicarbonate solution (10 mL). The aqueous layer was extracted with MTBE (3 × 5 mL) and the combined organic layers were washed with sat. aq. NaCl solution (5 mL) and dried with $MgSO_4$. The solvents were removed in vacuo and the residue was purified by FCC (100 g silica gel, PE/MTBE 10:1) to yield the coupling products **59** and **60** (124 mg, 0.139 mmol, 50 %) as colorless oils. The diasteromers could be separated by FCC (4.5:1 mixture): **59** (major isomer, chelate product): $R_f = 0.34$ (*n*-hexane/MTBE 10:1); **60** (minor isomer): $R_f = 0.31$ (*n*-hexane/MTBE 10:1); **59** (major isomer): ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.05$ (s, 12H, $Si(CH_3)$), 0.88 (m, 21H, $SiC(CH_3)_3$, 34-H_3), 1.06 (s, 9H, $SiC(CH_3)_3$), 1.31–2.10 (m, 30H, 13, 14, 17, 18, 21, 22, 25, 26, 27, 28, 29, 30, 31, 32, 33-H_2), 2.39 (m, 1H, 16-OH), 2.99–3.04 (m, 1H, 24-H), 3.21–3.30 (m, 2H, 20-H, 23-H), 3.31–3.40 (m, 1H, 16-H) 3.61–3.70 (m, 3H, 11-H_2, 19-H), 3.78–3.86 (m, 1H, 15-H), 4.07–4.16 (m, 1H, 12-H), 7.37–7.40 (m, 6H, SiPh), 7.67–7.71 (m, 4H, SiPh); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -4.8$, −4.6, −4.4, −4.0 ($SiCH_3$), 14.1 (C-34), 18.0, 18.2, 19.2 ($SiC(CH_3)_3$), 25.8, 25.9, ($SiC(CH_3)_3$), 22.7, 25.1, 26.8, 28.3, 28.4, 29.1, 29.3, 29.6, 29.7, 29.8, 31.9, 33.5 (C-13, 14, 17, 18, 21, 22, 25–33), 66.4 (C-11), 71.0 (C-23), 74.1 (C-19), 74.5 (C-16), 79.5 (C-12), 80.0 (C-20), 82.4 (C-24), 82.8 (C-15), 127.6, 129.6, 133.6, 135.6 (SiPh); **60** (minor isomer): ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.05$ (s, 12H, $Si(CH_3)$), 0.88 (m, 21H, $SiC(CH_3)_3$, 34-H_3), 1.06 (s, 9H, $SiC(CH_3)_3$), 1.31–2.10 (m, 30H, 13,14,17,18,21,22,25,26,27,28,29,30,31,32,33-H_2), 2.43 (m, 1H, 16-OH), 2.97–3.04 (m, 1H, 24-H), 3.19–3.27 (m, 2H, 20,23-H), 3.61–3.74 (m, 4H, 11-H_2, 16,19-H), 3.78–3.90 (m, 1H, 15-H), 4.09–4.16 (m, 1H, 12-H), 7.37–7.40 (m, 6H, SiPh), 7.67–7.71 (m, 4H, SiPh); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -4.8$, −4.6, −4.4, −4.0 ($SiCH_3$), 14.1 (C-34), 18.0, 18.2, 19.2 ($SiC(CH_3)_3$), 25.8, 25.9, ($SiC(CH_3)_3$), 22.7, 25.1, 25.2, 26.8, 28.2, 29.1, 29.4, 29.6, 29.6, 29.7, 29.8, 31.9, 33.5, (C-13, 14, 17, 18, 21, 22, 25–33), 66.6 (C-11), 70.9 (C-23), 72.4 (C-16), 74.4 (C-19), 79.8 (C-12), 80.0 (C-20), 82.3 (C-24), 82.4 (C-15), 127.6, 129.6, 133.6, 135.6 (SiPh).

(2*S*,3*R*,6*S*,1′*S*)-2-Decyl-3-*tert*-butyldimethylsilyloxy-6-(1′-*tert*-butyldimethylsilyloxy)-propyl-tetrahydropyran (61): ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.03$ (s, 12H, $SiCH_3$), 0.86–0.87 (m, 21H, $SiC(CH_3)_3$, 10″-H_3), 1.23–1.77 (m, 25H, 1″,2″,3″,4″,5″,6″,7″,8″,9″,2′,3′,4,5-H_2), 1.93–2.02 (m, 1H, 4-H_2), 2.96–3.04 (m, 1H, 2-H), 3.17–3.26 (m, 2H, 3,6-H), 3.43–3.55 (m, 1H, 1′-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -4.7$, −4.6, −4.4, −4.0 ($SiCH_3$), 10.1 (C-3′), 14.1 (C-10″), 17.9, 18.2 [$C(CH_3)$], 22.7 (C-9″), 25.8, 25.9 [$C(CH_3)$], 25.0, 25.2, 25.4, 26.0, 29.4, 29.7, 29.7, 29.8, 31.9, 33.6 (C-4, C-5, C-2′, C-1″, C-2″, C-3″, C-4″, C-5″, C-6″, C-7″, C-8″), 71.1 (C-3), 75.5 (C-1′), 79.9 (C-6), 82.4 (C-2); HR-MS ($C_{30}H_{64}O_3Si_2$): calcd 471.3690; found 471.3689 [$M - t$Bu]$^+$.

(2*S*,3*R*,6*S*,1′*S*)-2-Decyl-3-*tert*-butyldimethylsilyloxy-6-(1′-hydroxy-3′-*tert*-butyldimethylsilyl)-propyl-tetrahydropyran (62): ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.01$ (s, 6H, $SiCH_3$), 0.03 (s, 12H, $SiCH_3$), 0.33–0.75 (m, 2H, 3′-H_2), 0.85–0.87 (m, 21H, $SiC(CH_3)_3$, 10″-H_3), 1.23–1.77 (m, 23H, 1″,2″,3″,4″,5″,6″,7″,8″,9″,2′,4,5-H_2), 1.93–2.02 (m, 1H, 4-H_2), 2.48–2.53 (m, 1H, OH), 2.96–3.04 (m, 1H, 2-H), 3.17–3.33 (m, 3H, 3,6,1′-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -6.6$, −6.3, −4.7, −4.0 ($SiCH_3$), 7.5 (C-3′), 14.1 (C-10″), 16.2, 18.2 [$SiC(CH_3)$], 22.7 (C-9″), 25.5, 25.8 [$SiC(CH_3)$], 25.2, 25.4, 26.6, 27.1, 27.6, 29.4, 29.7, 29.7, 31.9, 32.0, 33.2 (C-4, C-5, C-2′, C-1″, C-2″, C-3″, C-4″, C-5″, C-6″, C-7″, C-8″), 71.3 (C-3), 76.1 (C-1′), 79.2 (C-6), 82.2 (C-2); HR-MS ($C_{30}H_{64}O_3Si_2$): calcd 471.3690; found 471.3682 [$M - t$Bu]$^+$.

Mucocin fragment without butenolide 63: Compound **59** (73 mg, 0.082 mmol) was dissolved in THF (5 mL) and treated with HF (1 mL, 5 % in CH_3CN) at 0 °C. After 6 h the reaction was quenched by addition of sat. aq. NH_4Cl solution (5 mL). The aqueous phase was extracted with ethyl acetate (4 × 10 mL). Washing of the combined organic layers with sat. aq. NaCl solution (5 mL), drying with $MgSO_4$, evaporation of the solvent and purification by FCC (1 g silica gel, MTBE/acetone 1:1) provided **63** (26 mg, 0.061 mmol, 74 %) as a colorless oil. $R_f = 0.43$ (acetone/MTBE 1:1); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.85$ (t, 3H, 34-H_3), 1.21–2.10 (m, 30H, 13,14,17,18,21,22,25,26,27,28,29,30,31,32,33-H_2), 2.30–2.60 (brs, 1H, OH), 2.77–2.94 (brs, 2H, OH), 2.98–3.05 (m, 1H, 24-H), 3.08–3.20 (m, 1H, 20-H), 3.21–3.28 (m, 1H, 23-H), 3.36–3.54 (m, 3H, 11-H_2, 16,19-H), 3.61–3.68 (m, 1H, 11-H_2), 3.78–3.86 (m, 1H, 15-H), 4.07–4.15 (m, 1H, 12-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 14.1$ (C-34), 22.7, 25.5, 26.9, 27.8, 28.5, 28.7, 28.9, 29.3, 29.6, 29.7, 31.9, 32.0, 32.6 (C-13, 14, 17, 18, 21, 22, 25–33), 64.8 (C-11), 70.5 (C-23), 73.5 (C-19), 73.8 (C-16), 79.7 (C-12), 80.1 (C-20), 82.0 (C-24), 82.9 (C-15); HR-MS ($C_{24}H_{47}O_6$): calcd 431.3373; found 431.3369.

4,19,23-*O*-Tris(*tert*-butyldimethylsilyl)-mucocin (64) and 16-*epi*-4,19,23-*O*-tris(*tert*-butyldimethylsilyl)-mucocin (65): In a 10 mL Schlenk tube a solution of iodide **20** (200 mg, 0.305 mmol) in Et_2O (5 mL) was cooled to −105 °C and treated with *tert*-butyllithium (0.37 mL, 1.482 M in pentane, 0.559 mmol). After 4 min at −100 °C $MgBr_2 \cdot Et_2O$ (0.2 mL, 0.61 mmol) was added. The reaction mixture was allowed to warm up to −35 °C during 1.5 h. Then the mixture was cooled to −78 °C and a solution of aldehyde **52** (113 mg, 0.25 mmol) in Et_2O (2 mL) was added. The solution was allowed to warm up to −15 °C during 1.5 h. The reaction was quenched by the addition of phosphate buffer solution (1M, pH 7, 2 mL). The mixture was diluted with water (5 mL) and MTBE (10 mL). The aqueous layer was extracted with MTBE (5 × 5 mL) and the combined organic layers were washed with sat. aq. NaCl solution (2 × 6 mL) and dried with $MgSO_4$. The solvents were removed in vacuo and the residue was purified by FCC (20 g silica gel, gradient PE/MTBE 3:1 → MTBE) to yield the coupling products **64** and **65** (136 mg, 56 %) as a colorless oil and to recover unconsumed aldehyde **52** (33 mg, 34 %). The 4:1 mixture (HPLC) of the C-16 epimers were separated by preparative HPLC (Rainin Si 60, 21.4 mm × 250 mm, *n*-hexane/*i*PrOH 99:1, 20 mL min^{-1}). Major isomer **64**: $R_f = 0.30$ (*n*-hexane/MTBE 2:1); HPLC: $t_R = 10.34$ min (Rainin Si 60, *n*-hexane/*i*PrOH 99:1, 1.0 mL min^{-1}); $[\alpha]_D^{22} = -19.2$ ($c = 0.60$, $CHCl_3$); IR (film): $\tilde{\nu} = 3123$ brs (OH), 2929 s (CH), 2856 s, 1760 m (C=O), 1255 w, 1095 m, 836 m, 776 m; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.02$ (brs, 18H, 6 × $SiCH_3$), 0.85 (brs, 30H, 3 × $SiC(CH_3)_3$, 34-H_3), 1.39 (d, $J = 6.8$ Hz, 3H, 37-H_3), 1.15–2.04 (m, 44H, alkyl), 2.40 (d, $J = 5.3$ Hz, 2H, 3-H_2), 2.43 (d, $J = 2.7$ Hz, 1H, OH), 2.98 (m, 1H, 24-H), 3.14–3.27 (m, 2H, 20-H, 23-H), 3.27–3.38 (m, 1H, 16-H), 3.62 (dt, $J = 10.5$, 5.3 Hz, 1H, 19-H), 3.75 (dt, $J = 14.2$, 6.7 Hz, 1H, 15-H), 3.79–3.88 (m, 1H, 12-H), 3.89–3.94 (m, 1H, 4-H), 4.98 (dq, $J = 6.8$, 1.1 Hz, 1H, 36-H), 7.09 (d, $J = 1.1$ Hz, 1H, 35-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -4.8$, −4.6, −4.5, −4.4, −4.0 ($SiCH_3$), 14.1 (C-34), 17.9, 18.0, 18.2 (3 × $SiC(CH_3)_3$), 19.0 (C-35), 25.8, 25.85, 25.9 (3 × $SiC(CH_3)_3$), 22.7, 25.1, 25.6, 26.2, 28.4, 28.7, 28.8, 29.3, 29.5, 29.6, 29.7, 29.8, 31.9, 32.4, 32.7, 33.5, 35.7, 36.9 (C-3,5–11,13,14,17,18,21,22,25–33), 70.1 (C-4), 71.0 (C-23), 74.1 (C-19), 74.6 (C-16), 77.4 (C-36), 79.2 (C-12), 79.9 (C-20), 82.0 (C-15), 82.4 (C-24), 130.8 (C-2), 151.5 (C-35), 174.0 (C-1); HR-MS (EI): $C_{55}H_{108}O_8Si_3$ calcd 981.7430; found 981.7441 [M+H]$^+$; minor isomer **65**: $R_f = 0.30$ (*n*-hexane/MTBE 2:1); HPLC: $t_R = 13.66$ min (Rainin Si 60, *n*-hexane/*i*PrOH 99:1, 1.0 mL min^{-1}); $[\alpha]_D^{22} = -21.7$ ($c = 0.18$, $CHCl_3$); IR (film): $\tilde{\nu} = 3127$ brs (OH), 2929 m (CH), 2857 w, 1760 w (C=O), 1255 w, 1096 m, 836 w, 775 w; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.00–0.06$ (m, 18H, 6 × $Si(CH_3)$), 0.82–0.90 (m, 30H, 3 × $SiC(CH_3)_3$, 34-H_3), 1.39 (d, $J = 6.8$ Hz, 3H, 37-H_3), 1.18–2.09 (m, 44H, alkyl), 2.37–2.43 (m, 3H, 3-H_2, OH), 2.94–3.04 (m, 1H, 24-H), 3.16–3.27 (m, 2H, 20,23-H), 3.57–3.73 (m, 2H, 16, 19-H), 3.80–3.97 (m, 3H, 4,12,15-H), 4.94–5.04 (m, 1H, 36-H), 7.10 (d, $J = 1.5$ Hz, 1H, 35-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -4.8$, −4.6, −4.5, −4.3, −4.0 (6 $SiCH_3$), 14.1 (C-34), 18.0, 18.0, 18.2 (3 × $SiC(CH_3)_3$), 19.0 (C-35), 25.8, 25.9, 25.9 (3 × $SiC(CH_3)_3$), 22.7, 25.1, 25.1, 25.3, 25.5, 26.1, 29.0, 29.1, 29.4, 29.5, 29.6, 29.7, 29.7, 29.8, 31.9, 32.3, 32.7, 33.5, 36.1, 37.0 (C-3,5–11,13,14,17,18,21,22,25–33), 70.2 (C-4), 70.9 (C-23), 72.6 (C-16), 74.3 (C-19), 77.2 (C-36), 80.0, 80.1 (C-12, C-20), 81.4 (C-15), 82.4 (C-24), 130.9 (C-2), 151.5 (C-35), 174.0 (C-1); HR-MS (EI): $C_{55}H_{108}O_8Si_3$ calcd 981.7430; found 981.7443 [M+H]$^+$.

(−)-Mucocin: A solution of tris-silyl ether **64** (22 mg, 24.4 μmol) in CH_2Cl_2 (1 mL) was treated with HF/acetonitrile (0.4 mL, ca. 0.12 mmol, 5 % HF in CH_3CN). The mixture was stirred at rt for 1 h, then phosphate buffer solution (1M, pH 7, 1 mL) and water (1 mL) were added. The aqueous layer was extracted with $CHCl_3$/*i*PrOH 1:1 (6 × 5 mL) and the combined organic layers were dried with $MgSO_4$. The solvents were removed in vacuo and the residue was purified by FCC (8 g silica gel, hexane/MTBE 2:1 then $CHCl_3$/MeOH 10:1) to afford (−)-mucocin (13 mg, 91 %) as a colorless oil. $R_f = 0.36$ ($CHCl_3$/MeOH 10:1); HPLC: $t_R = 8.9$ min (Rainin Si 60, *n*-hexane/*i*PrOH 70:30, 1.5 mL min^{-1}); $[\alpha]_D^{25} = -12.7$, $[\alpha]_{578}^{25} = -13.1$, $[\alpha]_{546}^{25} = -14.9$, $[\alpha]_{436}^{25} = -26.5$, $[\alpha]_{365}^{25} = -40.3$ ($c = 0.27$, CH_2Cl_2); IR (film): $\tilde{\nu} = 3124$ brs (OH), 2926 s (CH), 2854 w, 1740 w (C=O), 1094 w, 1072 w; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.85$ (t, $J = 6.8$ Hz, 3H, 34-H_3), 1.41 (d, $J = 6.8$ Hz, 3H, 37-H_3), 1.13–1.75 (m, 41H, alkyl), 1.76–1.88 (m, 1H), 1.89–2.05 (m, 2H, 13,14-H_2), 2.05–2.14 (m, 1H, 22-H_2), 2.30 (brs, 1H, OH), 2.37 (dd, $J = 15.1$, 8.3 Hz, 1H, 3-H_2), 2.50 (d, $J = 15.1$ Hz, 1H, 3-H_2), 2.71 (brs, 1H, OH), 2.84 (brs, 1H, OH), 3.02 (dt, $J = 8.8$, 2.2 Hz, 1H, 24-H), 3.08–3.18 (m, 1H,

20-H), 3.18–3.32 (m, 1H, 23-H), 3.34–3.52 (m, 2H, 16,19-H), 3.67–3.95 (m, 3H, 4,12,15-H), 5.04 (dq, $J = 6.8$, 1.5 Hz, 1H, 36-H), 7.16 (d, $J = 1.5$ Hz, 1H, 35-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 14.11$ (C-34), 19.10 (C-35), 22.67, 25.47, 25.52, 26.15, 26.90, 28.33, 28.69, 28.76, 29.32, 29.40, 29.45, 29.53, 29.63, 29.72, 31.89, 31.96, 32.39, 32.62, 33.34, 35.58, 37.37 (C-3,5–11,13,14,17,18,21,22,25–33), 69.95 (C-4), 70.55 (C-23), 73.48 (C-19), 73.77 (C-16), 77.97 (C-36), 79.30 (C-12), 80.14 (C-20), 81.90 (C-15), 82.00 (C-24), 131.17 (C-2), 151.80 (C-35), 174.61 (C-1); HR-MS (EI): $C_{37}H_{66}O_8$ calcd 639.4836; found 639.4838 $[M+H]^+$.

16-*epi*-Mucocin: A solution of tris-silyl ether **65** (9 mg, 9.17 μmol) in CH_2Cl_2 (1 mL) was treated with HF/acetonitrile (0.20 mL, ca. 0.06 mmol, 5% HF in CH_3CN). The mixture was stirred at rt for 2 h, then phosphate buffer solution (1M, pH 7, 1 mL) and water (1 mL) were added. The aqueous layer was extracted with $CHCl_3$/*i*PrOH 1:1 (6×5 mL) and the combined organic layers were dried with $MgSO_4$. The solvents were removed in vacuo and the residue was purified by FCC (8 g silica gel, hexane/MTBE 1:2, then $CHCl_3$/MeOH 10:1) to afford 16-*epi*-mucocin (4 mg, 75%) as a colorless oil. $R_f = 0.36$; $[\alpha]_D^{25} = -4.5$ ($c = 0.09$, $CHCl_3$); IR (film): $\tilde{\nu} = 3411/3140$ br m (OH), 2926 s (CH), 2855 m, 1745 w (C=O), 1094 w, 1082 w; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.86$ (t, $J = 6.8$ Hz, 3H, 34-H_3), 1.43 (d, $J = 6.8$ Hz, 3H, 37-H_3), 1.13–1.65 (m, 41H, alkyl), 1.76–1.88 (m, 1H), 1.89–2.05 (m, 2H, 13,14-H_2), 1.98–2.14 (m, 1H, 22-H_2), 2.25 (br s, 1H, OH), 2.37 (dd, $J = 15.1$, 8.3 Hz, 1H, 3-H_2), 2.52 (d, $J = 15.1$ Hz, 1H, 3-H_2), 2.79 (br s, 1H, OH), 2.98–3.07 (m, 1H, 24-H), 3.08–3.17 (m, 1H, 20-H), 3.18–3.31 (m, 1H, 23-H), 3.39–3.50 (m, 2H, 19-H), 3.69–3.72 (m, 1H, 16-H), 3.75–3.98 (m, 3H, 4,12,15-H), 5.04 (dq, $J = 6.8$, 1.5 Hz, 1H, 36-H), 7.16 (d, $J = 1.5$ Hz, 1H, 35-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 14.11$ (C-34), 19.11 (C-35), 22.68, 25.46, 25.54, 25.71, 26.11, 26.97, 27.01, 28.86, 29.32, 29.42, 29.48, 29.58, 29.62, 29.72, 31.91, 31.96, 32.23, 32.58, 33.37, 35.99, 37.39 (C-3,5–11,13,14,17,18,21,22,25–33), 69.97 (C-4), 70.53 (C-23), 72.51 (C-16), 74.15 (C-19), 77.97 (C-36), 80.08 (C-12), 80.21 (C-20), 81.47 (C-15), 81.99 (C-24), 131.17 (C-2), 151.79 (C-35), 174.60 (C-1); HR-MS (EI): $C_{37}H_{66}O_8$ calcd 620.4652; found 620.4659 $[M - H_2O]^+$.

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