CHEMISTRY
A EUROPEAN JOURNAL

DOI: 10.1002/chem.200701529

The Total Synthesis of (+)-Tedanolide—A Macrocyclic Polyketide from Marine Sponge *Tedania ignis*

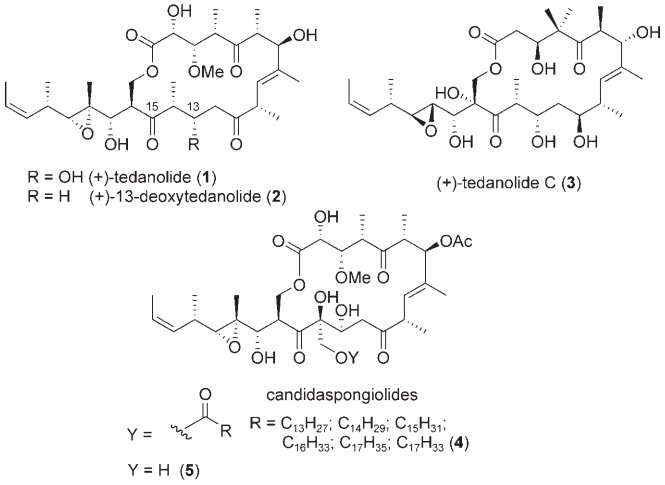
Gunnar Ehrlich, Jorma Hassfeld, Ulrike Eggert, and Markus Kalesse*[a]

Abstract: Tedanolide, which was isolated by Schmitz in 1984 from the marine sponge *Tedania ignis*, is a highly cytotoxic macrolide leading to strong growth inhibition of P338 tumor cells in bioassays. A unique structural feature of the known tedanolides is the primary hydroxyl group incorporated in the macrolactone. This unusual motif for macrolactones originated from PKS biosynthesis might arise through lactonizations others than those derived by the thioesterase reaction. First experimental data that support this hypothesis and reflect the inherent preference of PKS-induced macrolactonization were obtained during this synthesis. The inherent preference for the formation of a 14-membered macrocyclization is discussed together with the pivotal steps in the synthesis.

Keywords: aldol reactions · macrolactone · natural products · tedanolide

Introduction

Currently five members of tedanolides are known, tedanolide (**1**), 13-deoxytedanolide (**2**), tedanolide C (**3**) and candidaspongiolides (**4**, **5**). Tedanolide (**1**) was isolated by Schmitz et al.[1] in 1984 from the Caribbean sponge *Tedania ignis* and the structure as well as the absolute configuration was unambiguously assigned by X-ray analysis. It attracted very much attention due to its high cytotoxicity against tumor cell lines and was shown to arrest the growth of P338 cells in the S-phase.[1] In 1991 the isolation of a structural related compound, 13-deoxytedanolide (**2**) from the sponge *Mycale adhaerens*, exhibiting a deoxygenated position at C13, was reported by Fusetani et al.[2] Even though only limited studies on the biological profile have been performed so far, first data indicate a similar biological profile compared with tedanolide (**1**).[3] These biological tests unraveled a strong binding to the 60S subunit of ribosomes leading to an efficient inhibition of peptide elongation in eukaryotic cells.[4] As a matter of fact, 13-deoxytedanolide (**2**) is the first known macrolide binding efficiently to eukaryotic ribosomes, whereas other macrolide antibiotics such as erythromycin or carbomycin exclusively bind to procaryontic ribosomes. A third member of this family, tedanolide C (**3**) was isolated in 2005 by Ireland et al.[5] from the marine sponge *Ircinia sp.* collected near Papua New Guinea. Very recently, the group of candidaspongiolides (**4**, **5**) was isolated by McKee et al. from the sponge of the genus *Candidaspongi.*[6] A unique structural element of all these natural products is a primary alcohol which is incorporated in the macrolactone. The chemical stability of tedanolides **1** and **2** is limited by the highly acid sensitive β-hydroxy ketone moieties and the epoxide in the side chain which is prone to acid-catalyzed opening. Since its first publication by the Schmitz



[a] Dr. G. Ehrlich, Dr. J. Hassfeld, U. Eggert, Prof. Dr. M. Kalesse
Institut für Organische Chemie
Gottfried Wilhelm Leibniz Universität Hannover
Schneiderberg 1B, 30167 Hannover (Germany)
Fax: (+49) 0511-7623011
E-mail: Markus.Kalesse@oci.uni-hannover.de

Supporting information for this article is available on the WWW under http://www.chemistry.org or from the author.

group in 1984 a large variety of synthetic efforts have been put forward, leading to advanced fragment syntheses.[7] In the course of these synthetic endeavors the first total synthesis of 13-deoxytedanolide (**2**) was presented by Smith et al. in 2003,[8] aiming to provide synthetic access to compounds **1**, **2** through a unified approach. Very recently, their concept resulted in a total synthesis for tedanolide (**1**) as well.[9] Short after the first synthesis of 13-deoxytedanolide (**2**) had been completed a second total synthesis of **2** by the Roush group was published.[10] Here we describe the synthetic details that led to our total synthesis of tedanolide (**1**).[11] The key features are an aldol coupling to set up the carbon backbone and a final stage epoxidation. Additionally, it turned out that correct choice of the configuration at C15 was pivotal for the successful synthesis.

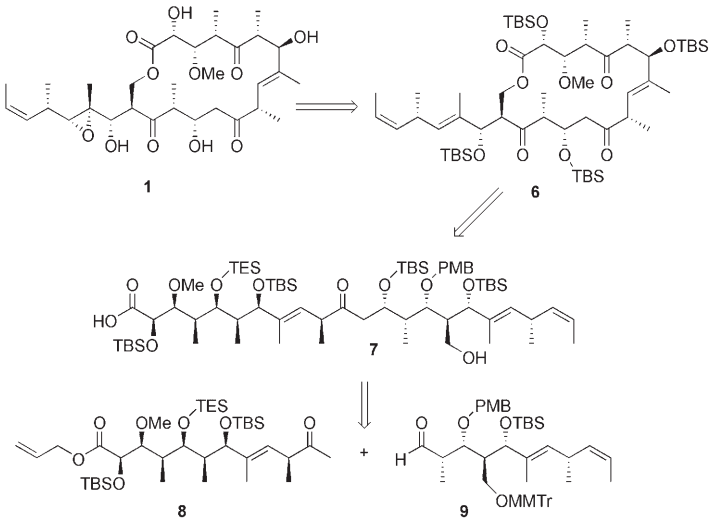
Results and Discussion

Retrosynthetic analysis: As a consequence of the labile epoxide moiety in tedanolide (**1**) we decided to introduce this functional group as the last step of the synthesis. The stereoselective epoxidation of the Δ^{18}-allylic alcohol moiety using *m*CPBA has already been demonstrated in the Smith synthesis of 13-deoxytedanolide (**2**).[8] Nevertheless, in their synthesis the second Δ^{8}-allylic alcohol was blocked through protection as the TIPS ether. Since both segments represent a pseudo-enantiomeric relationship we envisioned to use the Sharpless asymmetric epoxidation as a fall-back position in order to discriminate between both allylic alcohols as it has been successfully applied by Mulzer et al.[12] in their laulimalide synthesis. Consequently, we envisioned to perform the epoxidation after global TBS deprotection of macrolactone **6**. This triketo lactone **6** in turn is generated by a macrolactonization of hydroxy acid **7** followed by stepwise deprotection and oxidation at C5 and C15. To achieve a convergent synthesis of C1–C23 hydroxy acid **7** we decided to perform an aldol coupling of methyl ketone **8**, previously synthesized in our group,[7y] and aldehyde **9** (Scheme 1).

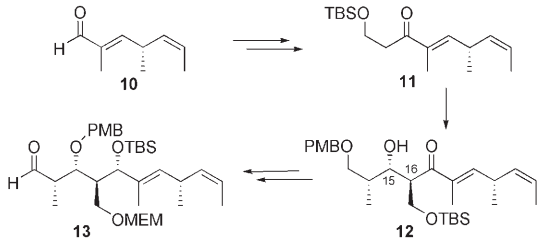
Another essential issue was the appropriate choice of orthogonal protecting groups for the C29 hydroxy group and the carboxylate. After substantial variations we found the monomethoxytrityl group (MMTr) to be ideal as a protecting group for C29 hydroxyl since its installation and chemical stability was compatible with the operations employed. Additionally, the very mild conditions for its removal, namely treatment with hexafluoroisopropanol[13] allow removal even in the presence of unprotected β-hydroxy ketones.

Synthesis of aldehyde 9: In 2005 we reported a first-generation synthesis of C13–C23 aldehyde **13**[7z] using an *anti* selective aldol coupling between C15 and C16 (Scheme 2).

This route had its drawbacks due to a relatively long number of 18 linear steps and occasionally uncontrolled migration of protecting groups. These disadvantages led to an improved synthesis to the C13–C23 aldehyde **9**, using a



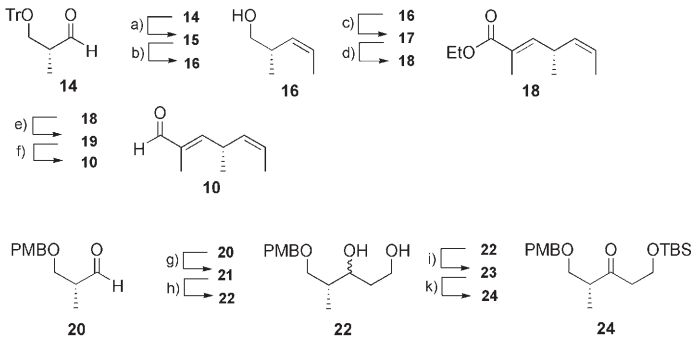
Scheme 1. Retrosynthesis of tedanolide (**1**).



Scheme 2. First-generation synthesis of **13**.

more convergent aldol coupling between C16 and C17 that parallels the fragment synthesis presented by Loh and coworkers.[7t] The synthesis starts with known trityl protected Roche aldehyde **14**.[14] Subsequent olefination with ethylidene triphenylphosphorane yielded alkene **15** with high *Z* selectivity (92:8). The acid-catalyzed cleavage of trityl ether **15** in methanol/CH_2Cl_2 turned out to be the optimal procedure and separation of the so-obtained alcohol **16** by column chromatography required careful evaporation of solvents in order to prevent significant loss of volatile **16**. On larger scale the isolation of alcohol **16** first required removal of the solvents by fractionated distillation over a Vigreux column. Then the residue was heated to 100 °C at a pressure of 1 mbar, while **16** was collected in a cooling trap at −190 °C together with some residual CH_2Cl_2. For the subsequent transformation it was not necessary to obtain **16** in pure form. Thus the solution of **16** in CH_2Cl_2 was used in the subsequent Swern oxidation[15] to generate aldehyde **17** which was directly subjected to Wittig olefination providing unsaturated ester **18**. Conversion of ester **18** to aldehyde **10** was achieved in a stepwise sequence using DIBAL-H reduction and subsequent oxidation with manganese dioxide (Scheme 3).

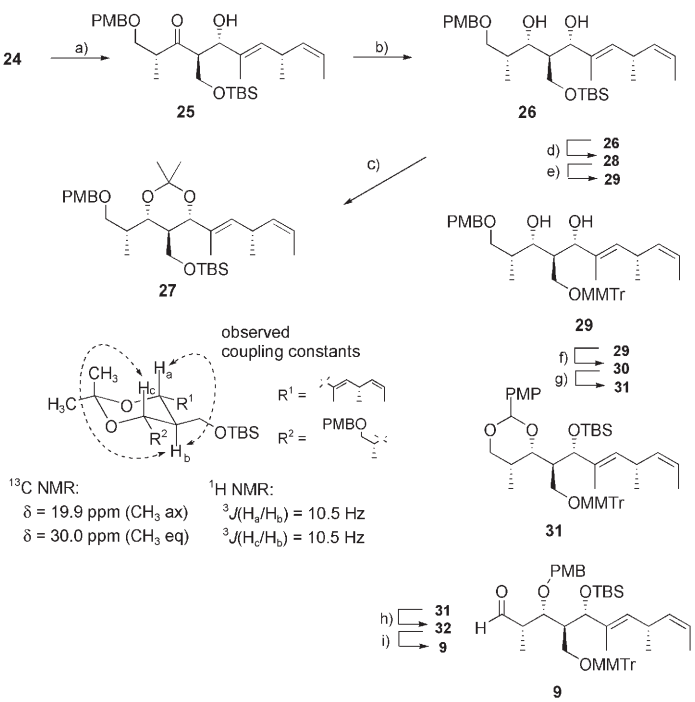
Ketone **24** was synthesized in four steps according to the route described by Loh.[7t] Therefore PMB-protected alde-



Scheme 3. Synthesis of fragments **10** and **24**: a) $EtPPh_3^+Br^-$, *n*BuLi, 85%, *Z*/*E* 92:8; b) *p*-TsOH, MeOH; c) Swern oxidation; d) $EtO_2CC(CH_3)=PPh_3$, 43% from **15**; e) DIBAL-H, 87%; f) MnO_2, 90%; g) LDA, CH_3CO_2Et, 88%; h) $LiAlH_4$, 95%; i) TBSCl, imidazole, 93%; k) Swern oxidation, 98%.

hyde **20** was subjected to an unselective acetate aldol reaction to generate hydroxy ester **21** as a 1:1 mixture of diastereomers. Reduction of **21** yielded 1,3-diol **22** and the primary hydroxy group was selectively TBS-protected. In the last step alcohol **23** was oxidized to give ketone **24** and providing enantiomerically pure material again.

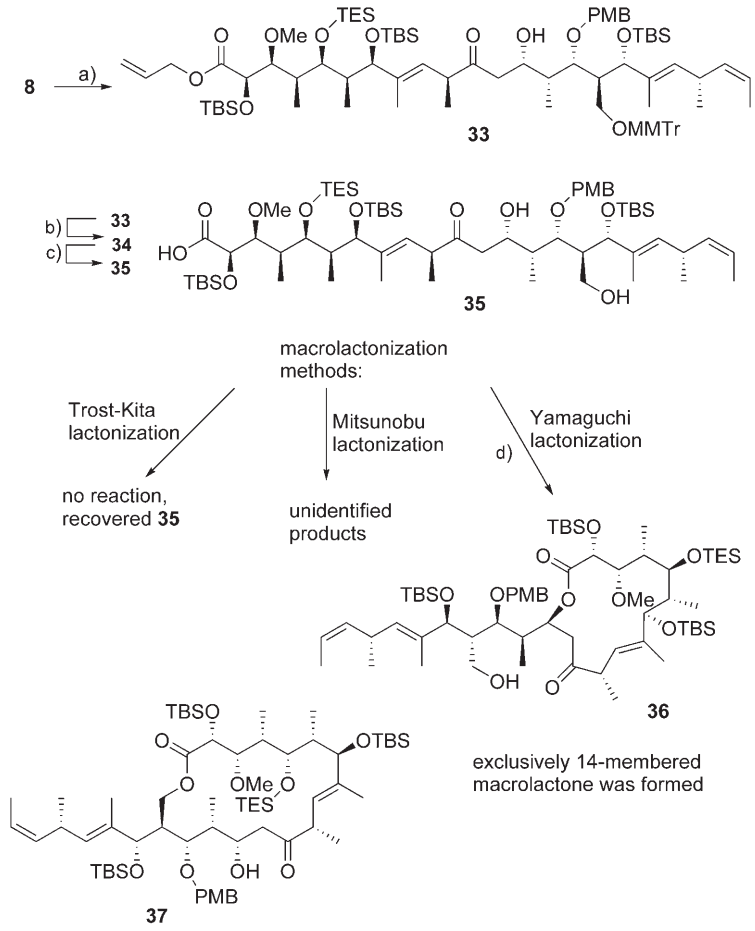
In order to set the desired *anti*-relationship between the C17 hydroxy and the C16 hydroxymethyl group we envisioned using an *anti*-selective aldol addition between compounds **10** and **24**. When ketone **24** was enolized with dicyclohexylboron chloride the (*E*)-enolate was formed predominately and the absolute configuration of both new formed stereocenters was induced by the chiral ketone **24**.[7t,16] Although the aldol addition succeeded with an acceptable yield of 68%, the diastereomeric ratio was only 2:1 in favor of the desired isomer **25**. Subsequently, hydroxy ketone **25** was reduced to avoid retro aldol reaction. In principal, both configurations at C15 can be used in the synthesis since this hydroxy group will be oxidized to the ketone during the endgame of the synthesis. Nevertheless, in fragments exhibiting an *anti*-orientation both centers would be Felkin enforcing, thus potentially enhancing the selectivity of the aldol step. Based on this analysis Roush's synthesis used the (15*R*)-configuration for the synthesis of 13-deoxytedanolide (**2**).[10] Unfortunately, the *R* configuration in combination with the presence of a carbonyl group at C5 led to the formation of a stable hemiketal that inhibited oxidation of the hydroxyl group. Based on experiences in our synthesis of callystatin[17] we realized that the inherent stereochemistry of methyl ketone **8** would be a substitute for a chiral auxiliary that would override the stereochemical preferences of the aldehyde **9**. Consequently, we decided to apply a *syn*-reduction of **25** to generate the (15*S*)-configured 1,3-*syn*-diol **26**. For this reduction the use of DIBAL-H provided exclusively *syn*-diol **26** (*dr*> 95:5) in good yields. In order to assign the configuration of diol **26** applying Rychnovsky's acetonide method[18] **26** was transformed into acetonide **27** using 2,2-dimethoxy propane. ^{1}H NMR analysis showed for all three indicative hydrogen atoms (H15, H16, H17) large coupling constants of approximately 10 Hz suggesting an axial position for these hydrogens. The ^{13}C NMR analysis unraveled two characteristic signals at δ 19.9 and 30.0 ppm indicative of axial and equatorial methyl groups in acetonide **27**. After removing the TBS group in **26** with TBAF triol **28** was obtained. This could be used for introducing the required protecting groups selectively. We focused particularly on identifying a suitable protecting group for the primary C29 alcohol which would allow selective removal prior to macrolactonization. After substantial screening of protecting groups we decided to use the monomethoxytrityl (MMTr) group,[19] which can be removed under very mild acidic conditions, required for this sensitive intermediate. The introduction of this protecting group is known to be highly selective for primary hydroxy groups and diol **29** was obtained in acceptable yield. Next, the allylic hydroxy group was protected as the TBS ether **30** and the PMB group was put on to the secondary alcohol using the sequence of oxidation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ)[20] and reductive opening of the intermediate PMP acetal[21] with DIBAL-H. Overall, a shift of the PMB group was achieved to furnish alcohol **32**. Oxidation of **32** with TPAP/NMO[22] proceeded smoothly and provided aldehyde **9** (Scheme 4).



Scheme 4. Synthesis of **9**: a) Cy_2BCl, Et_3N, then **10**, 68%, dr 2:1; b) DIBAL-H, 76%, dr >95:5; c) $(MeO)_2C(CH_3)_2$, PPTS, quant.; d) TBAF, 91%; e) MMTrCl, Et_3N, 69%; f) TBSCl, imidazole, 92%; g) DDQ, 85%; h) DIBAL-H, 81%; i) TPAP, NMO, 90%.

Aldol reaction: For the pivotal aldol coupling of methyl ketone **8** and aldehyde **9** careful screening of different bases for the enolization of **8** identified KHMDS to provide the highest selectivities for obtaining Felkin product **33**.[7y] A

preparative separation of **33** from its complex mixture of diastereomers using chromatography was not successful, but an analytically pure sample of **33** could be isolated using HPLC.[23] Next, we analyzed compound **33** for its potential to undergo macrolactonization. Based on Smith's synthesis of 13-deoxytedanolide (**2**)[8] in which an unprotected triol was successfully subjected to macrolactonization we concluded that in our case the primary hydroxy group at C29 should be subjected more readily to ring closure compared with the sterically hindered secondary C13 alcohol. So we continued the synthesis with liberating the C29 alcohol. For this conversion a very mild acid-catalyzed deprotection of monomethoxytrityl ethers using hexafluoroisopropanol had been described by Leonard and Neelima.[13] In our case hexafluoroisopropanol did cleave only the MMTr ether while all other protecting groups remained unchanged and no retro aldol products were detected. Addition of a small amount of methanol was necessary to trap the trityl cation. Gratifyingly, with the dihydroxy compound **34** it was possible to separate the minor diastereomers resulting from the aldol coupling by simple column chromatography. Next, the transformation of **34** to free carboxylic acid **35** was performed by palladium(0)-catalyzed cleavage of the allyl ester and reduction of the π-allyl palladium species with Bu_3SnH.[24] The subsequent screening of different conditions for macrolactonization started with the Mitsunobu protocol,[25] thus taking advantage of the carboxylate as the nucleophile and displacement of the primary C29 hydroxy group. Unfortunately the Mitsunobu method proved to be unsuitable for substrate **35** leading only to complex mixtures of side products. Other lactonization strategies such as Keck–Boden protocol[26] or Trost–Kita method[27] were also unsuccessful. On the other hand the Yamaguchi protocol[28] which was already employed in both syntheses of 13-deoxytedanolide (**2**) provided under high dilution conditions between 10–35% of a macrolactone and best results were obtained when freshly prepared dihydroxy acid **35** was used immediately. Even though it was expected that the desired macrolactone **37** had been formed, assignment of the alcohol incorporated in the lactone was difficult to perform. Investigations via 2D-NMR methods (HMBC, NOE) did not indicate any NMR contact between the carboxylic carbon C1 and the two possible hydrogens at H13 or H29. One argument in favor of the 14-membered lactone **36** was the chemical shift of nearly 6 ppm for H13, indicating acylation at the secondary C13 alcohol (Scheme 5).

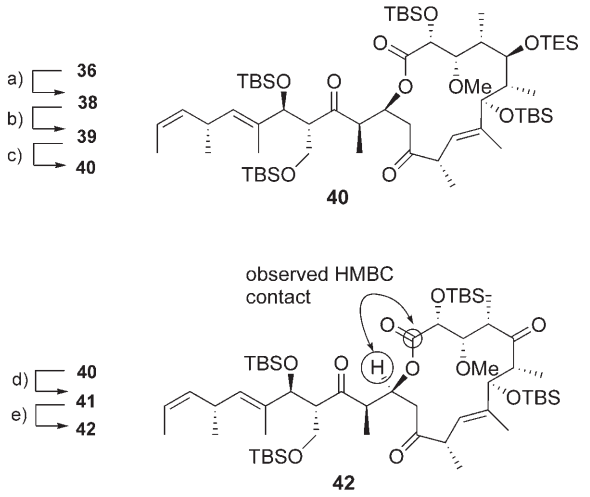


Scheme 5. Aldol coupling and lactonization: a) KHMDS, then **9**, 59%; b) $(CF_3)_2CHOH$, MeOH, 85%; c) $[Pd(PPh_3)_2Cl_2]$, Bu_3SnH; d) 2,4,6-$Cl_3C_6H_2COCl$, DMAP, iPr_2NEt, 34% over 2 steps.

As a consequence of the unknown ring size of the macrolactone we decided to carry on with the planned synthesis and hoped to elucidate the ring size at an advanced intermediate. NMR analysis at a later stage then clearly identified the prepared lactone to be the undesired 14-membered lactone **36**.

This result obtruded the question about the biosynthetic origin of the unusual primary lactone of the tedanolides. Since the primary alcohols in polyketides are originated after PKS biosynthesis, it is feasible to assume that the lactone of the tedanolides is preformed afterwards either from the open chain form or through transesterification from a different lactone. The formation of 14-membered lactone **36** may serve as a first chemical indication that transient lactones may be formed in the course of tedanolides biosyntheses. Protection of the remaining primary alcohol at C29 was

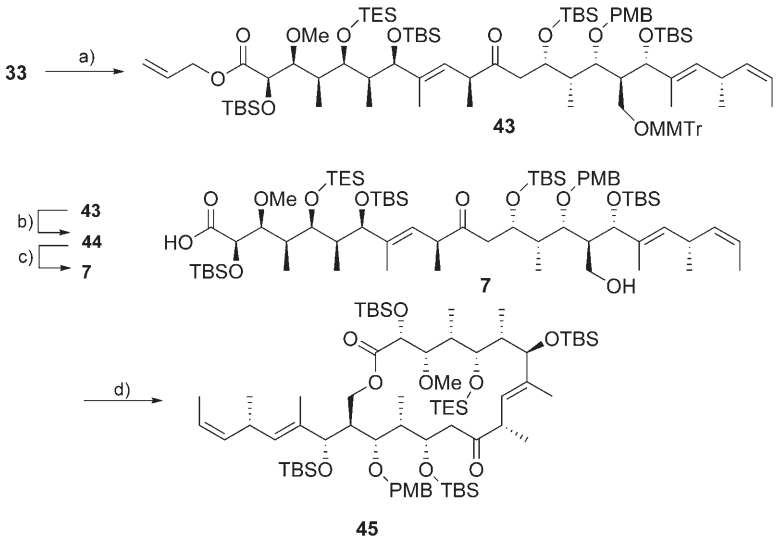
achieved with TBSCl and imidazole yielding completely protected macrolactone **38**. The next transformations required a subsequent deprotection and oxidation of the C15 and C5 hydroxy groups to install ketones at these positions. Deprotection of the PMB ether was achieved using DDQ, followed by Dess–Martin oxidation[29] to generate ketone **40**. For cleavage of the C5 TES ether in the presence of four TBS groups we decided to apply mild acidic conditions in contrast to fluoride-based desilylations. A mixture of acetic acid in water/THF (3.5:1:3.5) proved suitable for a selective removal of the TES ether. Since compound **40** shows low solubility in this very polar solvent mixture a significant amount of starting material **40** (50%) could be re-isolated after 4 d. Deprotection was followed by Dess–Martin oxidation to give lactone **42**. At this stage we were able to assign the connectivity of the macrolactone ring based on an unambiguously strong HMBC contact between carboxylic carbon C1 and H13 (Scheme 6).



Scheme 6. a) TBSCl, imidazole, 79%; b) DDQ, 83%; c) Dess–Martin oxidation, 82%; d) HOAc/THF/H_2O, 40% (95% BORSM); e) Dess–Martin oxidation, 87%.

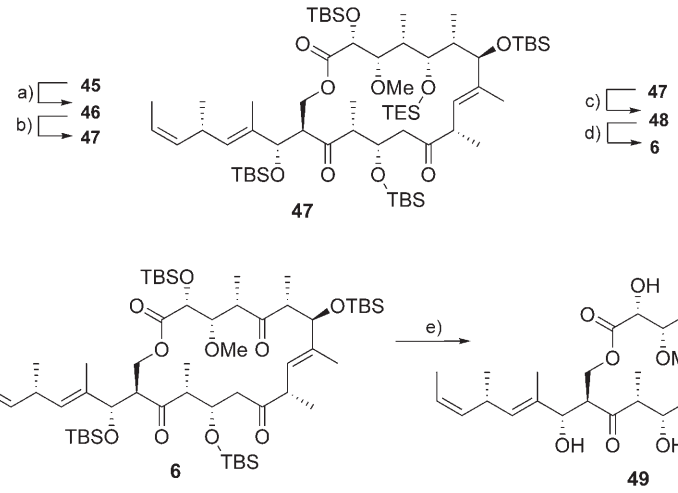
Lactonization of monohydroxy acid 7: When attempting the lactonization of dihydroxy acid **35** instead of the 18-membered lactone **37** exclusively the 14-membered isomer **36** was formed and unfortunately we were not able to change the selectivity of this lactonization. To avoid the undesired lactonization the secondary alcohol at C13 was protected with TBS triflate and 2,6-lutidine. The moderate yield of 55% in the conversion of **33** to **43** could be attributed to considerable retro aldol processes of **33**. Additionally, the MMTr-protecting group was not completely stable under these conditions as indicated by the appearance of an intensive yellow color caused by the trityl cation. Again, it was possible to start with the diastereomeric mixture of aldol products **33**. The separation of undesired isomers was achieved by simple column chromatography after acid-catalyzed removal of the MMTr ether to hydroxy ester **44**. After cleavage of the allyl ester, free carboxylic acid **7** was subjected to different lactonization methods. Interestingly, careful investigations of the Yamaguchi reaction showed that the mixed anhydride had been formed but no further lactonization was observed, consistent with the failure of generating the desired lactone **37** from compound **35** under these conditions. Gratifyingly, now the Mitsunobu protocol led to the desired macrolactone **45** in good yields (Scheme 7).

In the endgame of the synthesis the introduction of the carbonyl groups at C5 and C15 followed the line described for the 14-membered lactone, albeit the yields for the PMB deprotection of **45** were significantly lower compared to compound **38**. The maximum yield of 68% for alcohol **46** was reached when DDQ was added in small portions over a period of 4 h. The oxidation conditions for transforming the C15 hydroxy group into ketone **47** also required careful optimization. Only with high excess (10 equiv) of Dess–Martin reagent oxidation proceeded slowly in moderate yield. For the deprotection of the TES ether the use of pyridinium *p*-toluenesulfonate (PPTS) in methanol[3] was superior (16 h, 75%) to other reagents such as trifluoroacetic acid or acetic acid in THF/water. The concluding oxidation of C5 alcohol **48** to triketo lactone **6** was matched with Dess–Martin reagent in very good yield. The global deprotection of all TBS ethers was supposed to be a delicate transformation because the partially formed β-hydroxy ketone moieties were prone to retro aldol reactions.



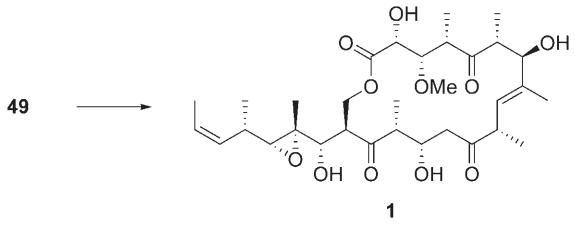
Scheme 7. Cyclization of hydroxy acid **7**: a) TBSOTf, lutidine 60%; b) $(CF_3)_2CHOH$, MeOH, 85%; c) [Pd$(PPh_3)_2Cl_2$], Bu_3SnH; d) PPh_3, DEAD, 68% over 2 steps.

For this conversion we followed the protocol established by Roush for the synthesis of 13-deoxytedanolide (**2**).[10] $3HF{\cdot}Et_3N$ was described to be only slightly acidic and a combination of this reagent and additional triethylamine proved suitable for deprotection of lactone **6**. The deprotection followed a statistical loss of TBS groups and after 4 d one defined compound with only one remaining TBS group was isolated together with 32% of completely deprotected lactone **49**. The removal of the last remaining TBS group proceeded very slowly and when the partially TBS protected compound was re-subjected to same deprotection conditions only half conversion to **49** was observed after 4 d, accompanied by side products (Scheme 8).



Scheme 8. Synthesis of tetrahydroxy lactone **49**: a) DDQ, 68%; b) Dess–Martin oxidation, 64%; c) PPTS, MeOH, 67%; d) Dess–Martin oxidation, 91%; e) $3HF{\cdot}Et_3N$, CH_3CN/Et_3N, 32%.

For the final epoxidation we intended to use unprotected lactone **49**. When **49** was treated with substoichiometric amounts of *m*CPBA at −45°C preferentially the Δ^{18} allylic alcohol was epoxidized to give tedanolide (**1**).[31] Unfortunately a separation of **49** and epoxide **1** via column chromatography was not successful, even when RP-18 silica gel was used. The only way to achieve higher purity of **1** was to increase conversion of **49** by adding three equivalents of *m*CPBA. With this excess of *m*CPBA consumption of **49** was nearly completed but competitively further epoxidation of **1** proceeded, explaining the low yield of isolated **1**. Finally a separation of **1** and over-oxidized products via simple column chromatography was possible (Scheme 9). Comparison of the NMR data of synthetic tedanolide (**1**) was identical in all respect to the data published by Schmitz.[1]



Scheme 9. Concluding epoxidation to **1**: *m*CPBA, −45°C, 3 d, 28%.

Conclusions

We have presented a convergent total synthesis of tedanolide (**1**) that provides substantial material which enables a detailed analysis of SAR data in particular probing the role of the epoxide moiety. Additionally, concluding the experimental results it materialized that subtle changes in configurations and hybridizations are reflected by dramatic changes in reactivity. It can be expected that these changes will be transmitted to the biological activity of derivatives and that cellular tests can answer the questions in connection with the prerequisites of fine-tuning the pharmacophoric parameters.

The fact that compound **35** readily generated the 14-membered macrolactone **36** is a strong indication that indeed the observed macrolactone of tedanolide (**1**) is generated at a later stage, most likely through a transesterification from a different lacton originated through catalysis by the polyketide's thioesterase. Further studies on the biological activity of analogues and the function of the epoxide moiety will be reported in due course.

Experimental Section

General methods: NMR spectra were recorded with Bruker AVS-500, AVS-400 or AM-200 spectrometers. Corresponding solvent signal served as an internal standard: for ^1H NMR spectra in $CDCl_3$—the singlet of $CHCl_3$ at δ 7.26 ppm, in C_6D_6—the singlet of C_6D_5H at δ 7.16 ppm; for ^{13}C NMR spectra in $CDCl_3$—the triplet at δ 77.00 ppm, in C_6D_6—the triplet at δ 128.40 ppm. Values of the coupling constant, *J*, are given in Hertz (Hz). High-resolution electrospray-mass spectra (HRMS-ESI) were recorded with Waters Micromass LCT spectrometer with a Lock-Spray unit. All air- and moisture sensitive reactions were performed under argon in heat gun-dried glassware. All experiments were monitored by thin layer chromatography (TLC) performed on Merck 60 F-254 (0.2 mm thick) silica gel aluminium supported plates. Spots were visualized by exposure to ultraviolet light (254 nm) or by staining with vanillin reagent (85 mL MeOH, 5 mL H_2SO_4, 10 mL AcOH, 0.5 g vanillin, cer reagent (10 g $Ce(SO_4)_2$, 25 g phosphomolybdenic acid, 80 mL H_2SO_4, H_2O to 1 L), followed by heating. Tetrahydrofuran (THF) was distilled under argon from sodium/benzophenone. Dichloromethane was distilled from calcium hydride under argon. Commercially available reagents were used as supplied. Flash chromatography was performed with J. T. Baker brand silica gel (40–60 μm, 60 Å pores). Eluents used for flash chromatography were distilled prior to use. Additional experimental procedures, ^1H and

^{13}C NMR spectra and Ortep plot of **13** are available in the Supporting Information.

(4*S*,2*Z*)-4-Methyl-5-trityloxypent-2-ene (15): Ethyltriphenylphosphonium bromide (48.5 g, 131 mmol, 1.6 equiv) was suspended in THF (150 mL) and cooled to −78 °C. Then *n*BuLi solution (49.0 mL, 123 mmol; 1.5 equiv 2.5 M in hexane) was added slowly. The orange colored suspension was warmed up and stirred for 30 min at RT while the most part of the white solids became dissolved. Then the dark red solution was cooled again to −78 °C and a solution of aldehyde **14** (27.0 g, 81.7 mmol, 1.0 equiv) in THF (150 mL) was added rapidly. After complete addition the reaction was allowed to warm up und stirring was continued for 3 h at RT. Then water was added and the organic layer was separated. The aqueous layer was extracted with ethyl acetate and the combined organic layers were dried over $MgSO_4$ and filtered. The solvent was removed under vacuum to give a brownish residue. Purification was performed by column chromatography (hexane/ethyl acetate 10:1 + 1% Et_3N) to yield alkene **15** (23.8 g, 69.5 mmol, 85%) as a highly viscous oil. $[\alpha]_D^{25} = +37.9$ ($c = 0.99$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49 (d, $J = 7.5$ Hz, 6H), 7.32 (t, $J = 7.7$ Hz, 6H), 7.25 (t, $J = 7.3$ Hz, 3H), 5.51 (dq, $J = 10.9$, 6.7 Hz, 1H), 5.25 (ddq, $J = 10.7$, 9.4, 1.5 Hz, 1H), 3.02 (dd, 1H, $J = 8.4$, 6.5 Hz, H-6), 2.94 (dd, $J = 8.3$, 7.0 Hz, 1H), 2.83 (m, 1H), 1.69 (dd, $J = 6.8$, 1.5 Hz, 3H), 1.05 ppm (d, $J = 6.7$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.5 (s, 3C), 133.9 (d), 128.8 (d, 6C), 127.6 (d, 6C), 126.8 (d, 3C), 123.9 (d), 86.2 (s), 68.1 (t), 32.4 (d), 17.9 (q), 13.1 ppm (q); IR (ATR): $\tilde{\nu}$ = 3059 (m), 3021 (m), 2059 (m), 2917 (m), 2864 (m), 1597 (w), 1491 (s), 1448 (s), 1405 (w), 1317 (w), 1221 (w), 1182 (w), 1154 (w), 1066 (s), 1033 (m), 986 (w), 896 (w), 774 (s), 763 (s), 746 (s), 705 cm^{-1} (ss); HRMS (EI): *m*/*z*: calcd for $C_{25}H_{26}O$: 342.1984 $[M]^+$, found 342.1987.

(2*S*,3*Z*)-2-Methylpent-3-ene-1-ol (16): *p*-Toluene sulfonic acid (1.0 g) was added to a solution of alkene **15** (23.5 g, 68.6 mmol) in CH_2Cl_2/methanol 2:1 (150 mL) and the yellow solution was stirred at RT for 24 h. Then sat. $NaHCO_3$ solution was added to wash out methanol and to neutralize *p*-toluene sulfonic acid, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layers were dried over $MgSO_4$ and the solvent was removed for the most part by distillation over a Vigreux column at normal pressure yielding a brownish residue. Then a cooling trap (cooled with liquid nitrogen) was connected and at a pressure of 1 mbar the residue was slowly heated to 100 °C. Alcohol **16** was collected in a cooling trap together with remaining CH_2Cl_2. The obtained solution of **16** in CH_2Cl_2 was directly used for oxidation. An analytically pure sample was prepared by column chromatography (pentane/Et_2O 2:1). $[\alpha]_D^{25} = -26.6$ ($c = 1.10$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.61 (dq, $J = 11.0$, 6.7 Hz, 1H), 5.17 (ddq, $J = 10.9$, 9.5, 1.5 Hz, 1H), 3.50 (dd, $J = 10.4$, 5.9 Hz, 1H), 3.35 (dd, $J = 10.4$, 8.1 Hz, 1H), 2.72 (m, 1H), 1.67 (dd, $J = 6.6$, 1.8 Hz, 3H), 0.96 ppm (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.0 (d), 126.1 (d), 67.6 (t), 34.3 (d), 16.7 (q), 13.1 ppm (q); IR (ATR): $\tilde{\nu}$ = 3328 (br, ss), 3010 (m), 2958 (s), 2922 (s), 2872 (s), 1453 (m), 1405 (m), 1374 (m), 1260 (w), 1222 (w), 1030 (ss), 984 (m), 947 (m), 715 cm^{-1} (ss).

(2*S*,3*Z*)-2-Methylpent-3-ene-1-al (17): DMSO (10.7 g, 138 mmol, 2.0 equiv) was added at −78 °C to a stirred solution of oxalyl chloride (13.1 g, 103 mmol, 1.5 equiv, calc. based on alkene **15**) in CH_2Cl_2 (100 mL). After 30 min a solution of alcohol **16** in CH_2Cl_2 (volume ca. 20 mL) was added and the reaction mixture was kept at −78 °C for 1 h. Then triethylamine (34.7 g, 343 mmol, 5.0 equiv) was added and the temperature was raised to RT, leading to precipitation of white solids. Water was added until solids became dissolved. The organic layer was separated and the aqueous layer was washed with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and filtered. Due to the highly volatile aldehyde **17** the filtrate was used directly without concentration under reduced pressure.

(4*S*,2*E*,5*Z*)-Ethyl 2,4-dimethylhepta-2,5-dienoate (18): $EtO_2CC(CH_3)=PPh_3$[32] (74.6 g, 206 mmol, 3.0 equiv, calcd for olefin **15**) was added to the solution of crude aldehyde **17** in CH_2Cl_2 (ca. 300 mL) and the yellow solution was stirred at RT for 24 h. Then the reaction mixture was carefully concentrated under reduced pressure. The precipitated solids were washed several times with MTB ether whereby triphenylphosphine oxide and ylide remained as solids and the ester **18** remained in solution. The yellow filtrate was concentrated again under reduced pressure to dryness and subjected to column chromatography (hexane/ethyl acetate 10:1). Ester **18** (5.38 g, 29.5 mmol, 43% over 3 steps) was isolated as a colorless liquid. $[\alpha]_D^{25} = +138.2$ ($c = 1.08$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.61 (dd, $J = 9.7$, 1.3 Hz, 1H), 5.44 (dq, $J = 10.8$, 6.7 Hz, 1H), 5.29 (ddq, $J = 10.7$, 9.1, 1.6 Hz, 1H), 4.19 (q, $J = 7.2$ Hz, 2H), 3.49 (m, 1H), 1.89 (d, $J = 1.3$ Hz, 3H), 1.65 (dd, $J = 6.7$, 1.6 Hz, 3H), 1.30 (t, $J = 7.1$ Hz, 3H), 1.09 ppm (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.4 (s), 145.6 (d), 133.2 (d), 125.8 (d), 60.4 (t), 31.5 (d), 14.3 (q), 13.0 (q), 12.4 ppm (q); IR (ATR): $\tilde{\nu}$ = 3012 (m), 2967 (s), 2929 (s), 2871 (m), 1708 (ss), 1647 (m), 1449 (m), 1390 (w), 1367 (m), 1291 (s), 1261 (s), 1229 (ss), 1146 (s), 1098 (s), 1034 (s), 989 (m), 951 (m), 750 (s), 719 cm^{-1} (s); HRMS (EI): *m*/*z*: calcd for $C_{11}H_{18}O_2$: 182.1307 $[M]^+$, found 182.1306.

(4*S*,2*E*,5*Z*)-2,4-Dimethylhepta-2,5-diene-1-ol (19): A solution of ester **18** (5.20 g, 28.5 mmol, 1.0 equiv) in THF (100 mL) was cooled to −78 °C and DIBAL-H solution (47.5 mL, 71.3 mmol, 2.5 equiv, 1.5 M in toluene) was added. After 1 h the temperature was raised to RT and sat. K/Na tartrate solution was added slowly under intensive stirring. When gas evolution ceased the reaction mixture turned gelatinous. Addition of sat. K/Na tartrate solution was continued under intensive stirring until the aluminium hydroxide gels were resolved. The reaction mixture was diluted with ethyl acetate and the organic layer was separated. The aqueous layer was extracted with ethyl acetate and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure (20 mbar). Purification by column chromatography (hexane/ethyl acetate 4:1) provided allyl alcohol **19** (3.48 g, 24.8 mmol, 87%) as a colorless liquid. $[\alpha]_D^{25} = +74.2$ ($c = 1.12$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.37 (dq, $J = 11.1$, 6.6 Hz, 1H), 5.27 (dd, $J = 8.9$, 1.1 Hz, 1H), 5.24 (ddq, $J = 10.6$, 9.1, 1.6 Hz, 1H), 3.96 (s, 2H), 3.40 (m, 1H), 1.71 (d, $J = 1.0$ Hz, 3H), 1.66 (dd, $J = 6.7$, 1.6 Hz, 3H), 1.60 (br s), 1.02 ppm (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.1 (d), 1329 (s), 130.8 (d), 121.9 (d), 68.8 (t), 30.4 (d), 21.4 (q), 13.7 (q), 12.9 ppm (q); IR (ATR): $\tilde{\nu}$ = 3299 (br, ss), 3010 (m), 2963 (s), 2921 (s), 2867 (s), 1653 (w), 1451 (s), 1402 (m), 1371 (m), 1258 (w), 1224 (w), 1068 (m), 1008 (ss), 951 (s), 855 (m), 814 (w), 719 cm^{-1} (ss); HRMS (EI): *m*/*z*: calcd for $C_9H_{15}O$: 139.1123 $[M-H]^+$, found 139.1118.

(4*S*,2*E*,5*Z*)-2,4-Dimethylhepta-2,5-diene-1-al (10): Manganese(IV)oxide (16.5 g, 190 mmol, 20 equiv) was added to a solution of alcohol **19** (1.33 g, 9.46 mmol, 1.0 equiv) in Et_2O (25 mL) and the suspension was stirred intensively for 4 h. Then the suspension was filtered over celite. The residue was washed with ethyl acetate and the combined filtrates were concentrated under reduced pressure (20 mbar). The obtained aldehyde **10** (1.18 g, 8.52 mmol, 90%) was used without further purification. An analytically pure sample was prepared by column chromatography (hexane/ethyl acetate 6:1). $[\alpha]_D^{25} = +120.8$ ($c = 0.96$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.36 (s, 1H), 6.31 (dd, $J = 9.5$, 1.1 Hz, 1H), 5.49 (dq, $J = 10.8$, 6.8 Hz, 1H), 5.31 (ddq, $J = 10.6$, 9.0, 1.6 Hz, 1H), 3.67 (m, 1H), 1.79 (d, $J = 1.1$ Hz, 3H), 1.65 (dd, $J = 6.8$, 1.7 Hz, 3H), 1.14 ppm (d, $J = 6.7$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.5 (d), 157.8 (d), 137.0 (s), 132.2 (d), 124.6 (d), 31.7 (d), 20.4 (q), 13.0 (q), 9.2 ppm (q); IR (ATR): $\tilde{\nu}$ = 3013 (m), 2967 (m), 2926 (m), 2871 (m), 2710 (w), 1686 (ss), 1638 (s), 1453 (m), 1403 (m), 1376 (m), 1355 (m), 1279 (m), 1209 (m), 1014 (s), 956 (w), 878 (w), 830 (w), 722 cm^{-1} (s); HRMS (EI): *m*/*z*: calcd for $C_9H_{13}O$: 137.0966 $[M-H]^+$, found 137.0951.

(2*R*,3*R*/*S*)-Ethyl 3-hydroxy-1-(*p*-methoxybenzyloxy)-2-methylpentanoate (21): Diisopropylamine (8.72 g, 86.4 mmol, 1.4 equiv) was dissolved in THF (200 mL) and cooled to −78 °C. Then under stirring a solution of *n*BuLi (32.0 mL, 80.0 mmol, 1.3 equiv, 2.5 M in hexane) was slowly added and the reaction was allowed to warm up. After stirring for additional 30 min at RT the temperature was lowered to −78 °C and ethyl acetate (8.15 g, 92.5 mmol, 1.5 equiv) was added. After 30 min a solution of aldehyde **20** (12.8 g, 61.7 mmol, 1.0 equiv) in THF (20 mL) was added. The reaction was quenched after 30 min by addition of sat. NH_4Cl solution and allowed to warm up to RT. Small amounts of solids were dissolved by addition of water. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. Purification by column chromatography (hexane/ethyl acetate 1:1) yielded hydroxy

ester **21** (16.1 g, 54.3 mmol, 88%, dr 1:1) as a slightly yellow oil. $[\alpha]_D^{25} = -2.5$ ($c = 0.98$, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.27, 7.26 (d, $J = 8.5$ Hz, 2H), 6.90, 6.89 (d, $J = 8.5$ Hz, 2H), 4.46 (s, 2H), 4.23 (m, 0.5H), 4.19, 4.18 (q, $J = 7.2$ Hz, 2H), 4.01 (m, 0.5H), 3.82 (s, 3H), 3.57–3.47 (m, 2H), 2.57–2.40 (m, 2H), 1.93 (m, 1H), 1.29 (t, $J = 7.2$ Hz, 3H), 0.97, 0.95 ppm (d, $J = 7.5$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.9, 172.7, (s), 159.2 (s), 130.2, 130.0 (s), 129.2 (d, 2C), 113.8 (d, 2C), 73.4, 73.3, 73.0, 73.0, 71.8, 69.9, 60.6 (t), 55.3 (q), 39.6, 39.0, 38.3, 37.9, 14.2 (q), 13.7, 11.2 ppm (q); IR (ATR): $\tilde{\nu}$ = 3436 (br, ss), 2964 (s), 2924 (s), 2869 (m), 1734 (ss), 1718 (ss), 1448 (m), 1406 (m), 1370 (m), 1328 (m), 1270 (s), 1243 (s), 1158 (ss), 1014 (ss), 954 (m), 872 (m), 721 cm^{-1} (s); HRMS (LC-MS): m/z: calcd for $C_{15}H_{22}O_5Na$: 319.1521 $[M+Na]^+$, found 319.1524.

(2*R*,3*R*/*S*)-1-(*p*-Methoxybenzyloxy)-2-methylpentane-3,5-diol (22): A solution of hydroxy ester **21** (16.1 g, 54.1 mmol, 1.0 equiv) in THF (100 mL) was added dropwise at RT over a period of 30 min to a stirred suspension of lithium aluminum hydride (2.05 g, 54.0 mmol, 1.0 equiv) in THF (50 mL). After completion of addition the suspension was warmed to 40°C and kept at this temperature for 2 h. Then the suspension was cooled to RT and under intensive stirring sat. Na_2SO_4 solution was added dropwise until hydrogen evolution ceased. Addition of Na_2SO_4 solution was continued until precipitated aluminium hydroxides became aggregated. The organic layer was separated and the white residue was washed with ethyl acetate. The combined organic layers were directly concentrated under vacuum. After purification via column chromatography (hexane/ethyl acetate 2:1) diol **22** (13.1 g, 51.4 mmol, 95%) was obtained as a colorless oil. $[\alpha]_D^{25} = -4.2$ ($c = 1.06$, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.23 (d, $J = 8.5$ Hz, 2H), 6.88 (d, $J = 8.5$ Hz, 2H), 4.46 (d, $J = 11.6$ Hz, 1H), 4.42 (d, $J = 11.6$ Hz, 1H), 3.97 (m, 0.5H), 3.85–3.81 (m, 2H), 3.80 (s, 3H), 3.79–3.73 (m, 0.5H), 3.59 (dd, $J = 9.1$, 4.1 Hz, 0.5H), 3.51 (dd, $J = 9.1$, 4.7 Hz, 0.5H), 3.48 (dd, $J = 9.0$, 6.5 Hz, 0.5H), 3.42 (dd, $J = 9.2$, 8.0 Hz, 0.5H), 1.89 (m, 1H), 1.81–1.49 (m, 2H), 0.92, 0.85 ppm (d, $J = 7.1$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.3 (s), 129.9 (s), 129.6, 129.3 (d, 2C), 113.9, 113.8 (d, 2C), 75.1, 74.1, 73.2, 73.1, 62.2, 61.7 (t), 55.2 (q), 38.5, 38.3, 36.0, 35.0, 13.6, 11.4 ppm (q); IR (ATR): $\tilde{\nu}$ = 3313 (br, ss), 2957 (ss), 2923 (ss), 2868 (ss), 1450 (s), 1402 (s), 1370 (m), 1316 (m), 1286 (m), 1051 (ss), 987 (s), 860 (m), 720 cm^{-1} (ss); HRMS (LC-MS): m/z: calcd for $C_{14}H_{22}O_4Na$: 277.1416 $[M+Na]^+$, found 277.1426.

(2*R*,3*R*/*S*)-5-(*tert*-Butyldimethylsilyloxy)-1-(*p*-methoxybenzyloxy)-2-methylpentane-3-ol (23): Imidazole (5.25 g, 77.1 mmol, 1.5 equiv) and TBS chloride (8.52 g, 56.5 mmol, 1.1 equiv) were added in small portions to a stirred solution of diol **22** (13.1 g, 51.4 mmol, 1.0 equiv) in CH_2Cl_2 (100 mL). The suspension was stirred for 1 h at RT and sat. $NaHCO_3$ solution was added. Stirring was continued for 5 min until the precipitate was resolved. The organic layer was separated and the aqueous layer was washed with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. After purification via column chromatography (hexane/ethyl acetate 4:1) TBS-protected alcohol **23** (17.7 g, 47.9 mmol, 93%) was obtained as a colorless oil. $[\alpha]_D^{25} = -1.5$ ($c = 1.14$, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.27 (d, $J = 9.2$ Hz, 2H), 6.89 (d, $J = 8.7$ Hz, 2H), 4.46 (s, 2H), 3.91–3.83 (m), 3.82 (s, 3H), 3.76–3.70 (m, 1H), 3.56–3.48 (m, 1H), 3.52 (dd, $J = 5.5$, 4.4 Hz, 1H), 3.44 (dd, $J = 9.0$, 5.4 Hz, 1H), 1.89 (m, 1H), 1.78–1.54 (m, 2H), 0.96, 0.95 (d, $J = 7.2$ Hz, 3H), 0.92 (s, 9H), 0.09 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.1 (s), 130.4, 130.3 (s), 129.2 (d, 2C), 113.7 (d, 2C), 74.2, 72.6 (d), 73.5 (t), 72.9 (t), 62.4, 62.1 (t), 55.2 (q), 38.9, 38.7 (d), 36.3, 36.1 (t), 25.9 (q, 3C), 18.2 (s), 13.8, 11.3 (q), −5.5 ppm (q, 2C); IR (ATR): $\tilde{\nu}$ = 3493 (br, s), 2954 (ss), 2930 (ss), 2857 (ss), 1613 (m), 1513 (ss), 1464 (s), 1388 (w), 1361 (m), 1302 (w), 1248 (ss), 1173 (m), 1083 (ss), 1037 (s), 938 (w), 832 (ss), 776 (ss), 739 cm^{-1} (m); HRMS (LC-MS): m/z: calcd for $C_{20}H_{36}O_4NaSi$: 391.2281 $[M+Na]^+$, found 391.2293.

(2*R*)-5-(*tert*-Butyldimethylsilyloxy)-1-(*p*-methoxybenzyloxy)-2-methylpentane-3-one (24): Oxalyl chloride (0.85 g, 6.71 mmol, 1.5 equiv) was dissolved in CH_2Cl_2 (15 mL) and cooled to −78°C. Under stirring DMSO (0.70 g, 8.94 mmol, 1.7 equiv) was slowly added. The slightly turbid solution was stirred for further 15 min and then a solution of alcohol **23** (1.64 g, 4.47 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) was slowly added. The reaction was stirred at −78°C for 1 h and then triethylamine (2.52 g, 22.3 mmol, 5.0 equiv) was rapidly added, leading to precipitation of white salts. The suspension was allowed to warm up and water was added until all salts were resolved. The organic layer was separated and the aqueous layer was washed with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum to give ketone **24** (1.52 g, 4.14 mmol, 98%) as a slightly yellow oil, which was used without further purification. $[\alpha]_D^{25} = -8.1$ ($c = 1.15$, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.21 (d, $J = 8.5$ Hz, 2H), 6.86 (d, $J = 8.8$ Hz, 2H), 4.43 (d, $J = 11.6$ Hz, 1H), 4.39 (d, $J = 11.6$ Hz, 1H), 3.89 (dd, $J = 6.5$, 2.4 Hz, 1H), 3.87 (dd, $J = 6.3$, 2.2 Hz, 1H), 3.79 (s, 3H), 3.60 (dd, $J = 8.9$, 7.5 Hz, 1H), 3.43 (dd, $J = 9.0$, 5.6 Hz, 1H), 2.87 (m, 1H), 2.72 (dd, $J = 6.5$, 3.8 Hz, 1H), 2.68 (dd, $J = 6.1$, 3.8 Hz, 1H), 1.07 (d, $J = 6.8$ Hz, 3H), 0.87 (s, 9H), 0.04 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 211.7 (s), 159.2 (s), 130.2 (s), 129.1 (d, 2C), 113.7 (d, 2C), 72.8 (t), 71.7 (t), 58.1 (t), 55.2 (q), 47.0 (d), 44.8 (t), 25.8 (q, 3C), 18.1 (s), 13.1 (q), −5.5 ppm (q, 2C); IR (ATR): $\tilde{\nu}$ = 2954 (s), 2930 (s), 2856 (s), 1713 (ss), 1613 (m), 1587 (w), 1515 (ss), 1463 (m), 1361 (m), 1302 (w), 1247 (ss), 1211 (s), 1173 (m), 1089 (ss), 1036 (ss), 1005 (s), 917 (w), 829 (ss), 776 (ss), 664 cm^{-1} (w); HRMS (LC-MS): m/z: calcd for $C_{20}H_{34}O_4NaSi$: 389.2124 $[M+Na]^+$, found 389.2143.

(2*R*,4*R*,5*S*,6*E*,8*S*,9*Z*)-4-(*tert*-Butyldimethylsilyloxymethyl)-5-hydroxy-1-(*p*-methoxybenzyloxy)-2,6,8-trimethylundeca-6,9-diene-3-one (25): Dicyclohexylboron chloride solution (15.0 mL, 15.0 mmol, 1.9 equiv, 1.0 M in CH_2Cl_2) was diluted with Et_2O (30 mL) and cooled to −78°C. Under stirring triethylamine (1.72 g, 17.0 mmol, 2.1 equiv) was added. After 15 min a solution of ketone **24** (3.66 g, 10.0 mmol, 1.3 equiv) in Et_2O (15 mL) was slowly added. The reaction mixture was stirred for further 30 min at −78°C and then stored over night in a fridge at −5°C, leading to precipitation of white salts. Then the suspension was cooled again to −78°C and a solution of aldehyde **10** (1.10 g, 8.0 mmol, 1.0 equiv) in Et_2O (5 mL) was slowly added. The reaction mixture was stirred at −78°C for further 30 min and quenched at this temperature by addition of cold methanol (10 mL), then pH 7 buffer (5 mL) and hydrogen peroxide (30%, 5 mL) were added. The mixture was allowed to warm up and intensively stirred at RT for 1 h. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. The crude products were purified via column chromatography (hexane/ethyl acetate 4:1) to give a diastereomeric mixture of aldol product **25** (2.77 g, 5.50 mmol, 68%, dr 2:1) as a colorless oil. Both diastereomers of **25** were separated by a further chromatography (hexane/ethyl acetate 6:1). Major diastereomer (**25a**): $[\alpha]_D^{25} = +38.5$ ($c = 1.01$, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.22 (d, $J = 8.5$ Hz, 2H), 6.86 (d, $J = 6.7$ Hz, 2H), 5.32 (ddq, $J = 10.6$, 6.8, 0.6 Hz, 1H), 5.24 (d, $J = 9.0$ Hz, 1H), 5.19 (ddq, $J = 10.7$, 9.2, 1.6 Hz, 1H), 4.47 (d, $J = 11.7$ Hz, 1H), 4.42 (d, $J = 11.8$ Hz, 1H), 4.20 (d, $J = 8.0$ Hz, 1H), 3.80 (s, 3H), 3.72 (dd, $J = 9.0$, 7.2 Hz, 1H), 3.70 (dd, $J = 10.2$, 8.5 Hz, 1H), 3.52 (dd, $J = 10.1$, 5.1 Hz, 1H), 3.37 (m, 1H), 3.35 (dd, $J = 9.0$, 6.4 Hz, 1H), 3.11 (dd, $J = 8.2$, 5.1 Hz, 1H), 3.07–2.98 (m, 2H), 1.66 (d, $J = 1.3$ Hz, 3H), 1.63 (dd, $J = 6.7$, 1.7 Hz, 3H), 1.08 (d, $J = 7.0$ Hz, 3H), 1.00 (d, $J = 6.8$ Hz, 3H), 0.84 (s, 9H), −0.02 (s, 3H), −0.03 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 215.8 (s), 159.2 (s), 134.8 (d), 132.8 (d), 132.7 (s), 129.8 (s), 129.3 (d, 2C), 121.8 (d), 113.8 (d, 2C), 75.8 (d), 72.9 (t), 71.4 (t), 62.4 (t), 57.2 (d), 55.2 (q), 46.5 (d), 30.3 (d), 25.8 (q, 3C), 21.2 (q), 18.2 (s), 13.4 (q), 12.9 (q), 11.6 (q), −5.7 (q), −5.70 ppm (q); IR (ATR): $\tilde{\nu}$ = 3448 (br, m), 3054 (w), 3007 (w), 2956 (s), 2932 (s), 2858 (m), 1710 (s), 1613 (m), 1514 (s), 1464 (m), 1363 (m), 1302 (m), 1266 (s), 1250 (s), 1174 (m), 1092 (s), 1037 (m), 837 (ss), 778 (m), 741 (ss), 706 cm^{-1} (w); HRMS (LC-MS): m/z: calcd for $C_{29}H_{48}O_5NaSi$: 527.3169 $[M+Na]^+$, found 527.3159; minor isomer **25a**: $[\alpha]_D^{25} = -6.7$ ($c = 1.05$); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.24 (d, $J = 8.5$ Hz, 2H), 6.88 (d, $J = 8.5$ Hz, 2H), 5.35 (dq, $J = 11.1$, 6.7 Hz, 1H), 5.27 (d, $J = 9.9$ Hz, 1H), 5.23 (ddq, $J = 10.9$, 9.2, 1.6 Hz, 1H), 4.46 (d, $J = 11.7$ Hz, 1H), 4.41 (d, $J = 11.7$ Hz, 1H), 4.21 (d, $J = 6.7$ Hz, 1H), 3.79 (s, 3H), 3.75 (dd, $J = 10.1$, 8.2 Hz, 1H), 3.70 (dd, $J = 9.2$, 7.0 Hz, 1H), 3.60 (dd, $J = 9.9$, 5.3 Hz, 1H), 3.39 (m, 1H), 3.36 (dd, $J = 9.1$, 6.5 Hz, 1H), 3.17 (dt, $J = 7.8$, 5.4 Hz, 1H), 3.02 (m, 2H), 1.69 (d, $J = 1.1$ Hz, 3H), 1.64 (dd, $J = 6.8$, 1.6 Hz, 3H), 1.08 (d, $J = 6.9$ Hz, 3H), 1.01 (d, $J = 6.9$ Hz, 3H), 0.85 (s, 9H), 0.00 (s, 3H), −0.01 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 215.8 (s), 159.2

(s), 134.8 (d), 132.8 (s), 132.4 (d), 129.9 (s), 129.3 (d, 2C), 121.9 (d), 113.7 (d, 2C), 75.6 (d), 72.8 (t), 71.3 (t), 62.4 (t), 56.7 (d), 55.2 (q), 47.0 (d), 30.4 (d), 25.6 (q, 3C), 21.4 (q), 18.1 (s), 13.1 (q), 12.9 (q), 11.9 (q), −5.7 (q), −5.7 ppm (q); IR (ATR): $\tilde{\nu}$ = 3452 (br, m), 3054 (w), 3007 (w), 2956 (s), 2932 (s), 2858 (m), 1710 (s), 1613 (m), 1515 (s), 1464 (m), 1362 (m), 1302 (m), 1266 (s), 1250 (s), 1174 (m), 1092 (s), 1037 (m), 837 (ss), 778 (m), 741 (ss), 706 cm^{-1} (w); HRMS (LC-MS): *m*/*z*: calcd for $C_{29}H_{48}O_5NaSi$: 527.3169 [*M*+Na]$^+$, found 527.3162.

(2*R*,3*S*,4*S*,5*S*,6*E*,8*S*,9*Z*)-4-(*tert*-Butyldimethylsilyloxymethyl)-1-(*p*-methoxybenzyloxy)-2,6,8-trimethylundeca-6,9-diene-3,5-diol (26): A stirred solution of hydroxy ketone **25** (1.23 g, 2.42 mmol, 1.0 equiv) in THF (25 mL) was cooled to −78 °C and DIBAL-H solution (4.1 mL, 6.06 mmol, 2.5 equiv 1.5 M in toluene) was added. After stirring for 2 h at this temperature sat. K/Na tartrate solution was added and the reaction mixture was warmed to RT. When reaching RT the reaction mixture became solid due to precipitated aluminum hydroxides. By addition of sat. K/Na tartrate solution under intensive stirring the precipitated gels were dissolved and the organic layer was separated. The aqueous layer was extracted with ethyl acetate and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. Purification was performed via column chromatography (hexane/ethyl acetate 5:1) to give diol **26** (0.94 g, 1.85 mmol, 76 %, dr >95:5) as a colorless oil. $[\alpha]_D^{25}$ = +25.0 (*c* = 1.16, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26 (d, *J* = 8.7 Hz, 2H), 6.90 (d, *J* = 8.6 Hz, 2H), 5.35–5.26 (m, 2H), 5.22 (ddq, *J* = 10.7, 9.3, 1.5 Hz, 1H), 4.49 (d, *J* = 11.7 Hz, 1H), 4.44 (d, *J* = 11.7 Hz, 1H), 4.31 (d, *J* = 9.3 Hz, 1H), 4.25 (d, *J* = 7.0 Hz, 1H), 3.80 (s, 3H), 3.60 (dd, *J* = 9.0, 4.2 Hz, 1H), 3.54 (dd, *J* = 9.0, 4.6 Hz, 1H), 3.50 (dd, *J* = 10.4, 2.9 Hz, 1H), 3.42 (m, 1H), 3.39 (dd, *J* = 10.4, 3.4 Hz, 1H), 2.07 (m, 1H), 1.75 (m, 1H), 1.65–1.61 (m, 6H), 1.04 (d, *J* = 6.7 Hz, 6H), 0.85 (s, 9H), −0.04 (s, 3H), −0.05 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.2 (s), 135.2 (d), 134.0 (s), 133.2 (d), 130.0 (s), 129.1 (d, 2C), 121.4 (d), 113.8 (d, 2C), 79.8 (d), 76.3 (d), 75.5 (t), 73.0 (t), 61.8 (t), 55.2 (q), 44.5 (d), 35.3 (d), 30.3 (d), 25.7 (q, 3C), 21.3 (q), 18.0 (s), 12.9 (q), 11.1 (q), 10.5 (q), −5.6 (q), −5.9 ppm (q); IR (ATR): $\tilde{\nu}$ = 3380 (br, s), 2955 (s), 2928 (s), 2857 (s), 1613 (w), 1514 (s), 1463 (m), 1361 (w), 1302 (w), 1248 (ss), 1173 (w), 1100 (ss), 1038 (m), 1006 (w), 961 (m), 834 (ss), 777 (s), 725 cm^{-1} (m); HRMS (LC-MS): *m*/*z*: calcd for $C_{29}H_{50}O_5NaSi$: 529.3325 [*M*+Na]$^+$, found 529.3323.

(1′*E*,2″*R*,3′*S*,4*S*,4′*Z*,5*S*,6*S*)-5-(*tert*-Butyldimethylsilyloxymethyl)-4-(1′,3′-dimethylhexa-1′,4′-dienyl)-6-[2″-(*p*-methoxybenzyloxy)-1′-methylethyl]-2,2-dimethyl-[1,3]dioxane (27): 2,2-Dimethoxy propane (0.2 mL) and PPTS (5 mg) were added to a stirred solution of diol **26** (31 mg, 61 μmol) in acetone (1.5 mL). After 30 min the reaction was stopped by addition of sat $NaHCO_3$ solution. The organic layer was diluted with ethyl acetate and separated. The aqueous layer was washed with ethyl acetate and the combined organic layers were dried over $MgSO_4$ and filtered. The filtrate was concentrated under vacuum and purified via column chromatography (hexane/ethyl acetate 12:1). Acetonide **27** (30 mg, 55 μmol, 90 %) was obtained as a colorless oil. $[\alpha]_D^{25}$ = +31.8 (*c* = 0.83, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.27 (d, *J* = 7.9 Hz, 2H), 6.89 (d, *J* = 8.5 Hz, 2H), 5.38–5.28 (m, 2H), 5.20 (ddq, *J* = 10.7, 9.4, 1.5 Hz, 1H), 4.47 (d, *J* = 11.7 Hz, 1H), 4.42 (d, *J* = 11.6 Hz, 1H), 4.36 (d, *J* = 10.5 Hz, 1H), 4.25 (dd, *J* = 10.5, 1.6 Hz, 1H), 3.82 (s, 3H), 3.51 (dd, *J* = 10.5, 2.4 Hz, 1H), 3.50–3.39 (m, 1H), 3.46 (dd, *J* = 8.8, 7.8 Hz, 1H), 3.39 (dd, *J* = 10.4, 3.1 Hz, 1H), 3.32 (dd, *J* = 8.9, 6.8 Hz, 1H), 2.17 (m, 1H), 1.69–1.63 (m, 6H), 1.58 (m, 1H), 1.45 (s, 3H), 1.36 (s, 3H), 1.05 (d, *J* = 6.7 Hz, 3H), 0.92–0.86 (m, 3H), 0.89 (s, 9H), 0.00 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.9 (s), 135.1 (d), 134.8 (d), 131.6 (s), 131.1 (s), 129.0 (d, 2C), 121.5 (d), 113.6 (d, 2C), 97.6 (s), 76.9 (d), 73.0 (t), 72.5 (t), 68.6 (d), 59.0 (t), 55.3 (q), 38.6 (d), 34.0 (d), 30.4 (d), 30.0 (q), 25.8 (q, 3C), 21.2 (q), 19.9 (q), 18.0 (s), 12.9 (q), 11.2 (q), 9.9 (q), −5.6 (q), −5.8 ppm (q); IR (ATR): $\tilde{\nu}$ = 2954 (ss), 2929 (ss), 2856 (ss), 1728 (w), 1614 (w), 1513 (m), 1463 (m), 1379 (m), 1362 (m), 1249 (ss), 1201 (m), 1172 (m), 1138 (w), 1102 (ss), 1040 (s), 1007 (m), 834 (ss), 776 (s), 741 cm^{-1} (m); HRMS (LC-MS): *m*/*z*: calcd for $C_{32}H_{54}O_5NaSi$: 569.3638 [*M*+Na]$^+$, found 569.3631.

(2*R*,3*S*,4*S*,5*S*,6*E*,8*S*,9*Z*)-4-Hydroxymethyl-1-(*p*-methoxybenzyloxy)-2,6,8-trimethylundeca-6,9-diene-3,5-diol (28): TBAF solution (2.2 mL, 2.2 mmol, 1.2 equiv, 1.0 M in THF) was added dropwise to a stirred solution of diol **26** (0.93 g, 1.83 mmol, 1.0 equiv) in THF (10 mL). The color of the solution turned to yellow. After 30 min the reaction was quenched by addition of sat $NaHCO_3$ solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. Purification via column chromatography (hexane/ethyl acetate 1:2) yielded triol **28** (0.67 g, 1.67 mmol, 91 %) as a colorless oil. $[\alpha]_D^{25}$ = +40.4 (*c* = 1.13, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.39–5.29 (m, 2H), 5.19 (ddq, *J* = 10.8, 9.2, 1.7 Hz, 1H), 4.46 (d, *J* = 11.6 Hz, 1H), 4.42 (d, *J* = 11.6 Hz, 1H), 4.27 (d, *J* = 8.9 Hz, 1H), 4.16 (dd, *J* = 9.0, 2.2 Hz, 1H), 3.79 (s, 3H), 3.59 (dd, *J* = 9.0, 4.0 Hz, 1H), 3.52 (dd, *J* = 9.0, 5.0 Hz, 1H), 3.46 (dd, *J* = 11.8, 3.8 Hz, 1H), 3.42 (dd, *J* = 11.6, 3.1 Hz, 1H), 3.43–3.38 (m, 1H), 2.05 (m, 1H), 1.77 (m, 1H), 1.68 (d, *J* = 1.3 Hz, 3H), 1.64 (dd, *J* = 6.8, 1.6 Hz, 3H), 1.03 (d, *J* = 6.8 Hz, 3H), 1.00 ppm (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.2 (s), 134.7 (s), 134.7 (d), 132.9 (d), 129.8 (s), 129.3 (d, 2C), 122.1 (d), 113.8 (d, 2C), 80.1 (d), 75.7 (d), 75.2 (t), 73.1 (t), 61.1 (t), 55.2 (q), 45.3 (d), 35.4 (d), 30.3 (d), 21.1 (q), 12.9 (q), 11.4 (q), 10.4 ppm (q); IR (ATR): $\tilde{\nu}$ = 3360 (br, ss), 2960 (s), 2919 (s), 2867 (s), 1612 (m), 1586 (m), 1513 (ss), 1454 (s), 1363 (m), 1302 (m), 1265 (s), 1247 (ss), 1174 (m), 1076 (s), 1035 (ss), 978 (m), 821 (m), 738 cm^{-1} (ss); HRMS (LC-MS): *m*/*z*: calcd for $C_{23}H_{36}O_5Na$: 415.2460 [*M*+Na]$^+$, found 415.2472.

(2*R*,3*S*,4*S*,5*S*,6*E*,8*S*,9*Z*)-1-(*p*-Methoxybenzyloxy)-4-[(*p*-methoxyphenyl)-diphenyl-methoxymethyl]-2,6,8-trimethylundeca-6,9-diene-3,5-diol (29): Triol **28** (0.67 g, 1.67 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (10 mL) and the solution was cooled to 0 °C. Then MMTr-chloride (0.57 g, 1.84 mmol, 1.1 equiv) and triethylamine (0.25 g, 2.51 mmol, 1.5 equiv) were added under stirring. After 5 min the solution was allowed to warm up to RT and the brownish solution was stirred for 2 h. Then sat. $NaHCO_3$ solution was added and the mixture was vigorously stirred for 5 min. The organic layer was separated and the aqueous layer was washed with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. Column chromatography (hexane/ethyl acetate 2:1 + 1 % Et_3N) yielded MMTr protected diol **29** (0.77 g, 1.15 mmol, 69 %) as a slightly yellow oil. $[\alpha]_D^{25}$ = +37.0 (*c* = 1.28, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 7.55 (d, *J* = 7.5 Hz, 4H), 7.39 (d, *J* = 8.8 Hz, 2H), 7.15–7.12 (m, 6H), 7.03 (t, *J* = 7.5 Hz, 3H), 6.77 (d, *J* = 8.5 Hz, 2H), 6.72 (d, *J* = 8.8 Hz, 2H), 5.35 (d, *J* = 8.9 Hz, 1H), 5.26 (dq, *J* = 10.7, 6.4 Hz, 1H), 5.19 (ddq, *J* = 10.9, 9.5, 1.0 Hz, 1H), 4.49 (d, *J* = 8.4 Hz, 1H), 4.43 (dd, *J* = 7.8, 2.1 Hz, 1H), 4.24 (s, 2H), 3.43–3.32 (m, 1H), 3.43 (dd, *J* = 8.8, 5.4 Hz, 1H), 3.38 (dd, *J* = 8.9, 4.5 Hz, 1H), 3.30 (s, 6H), 3.29 (dd, *J* = 9.7, 3.6 Hz, 1H), 3.12 (dd, *J* = 9.7, 5.6 Hz, 1H), 2.24 (m, 1H), 1.92 (m, 1H), 1.73 (s, 3H), 1.47 (dd, *J* = 6.4, 0.8 Hz, 3H), 1.07 (d, *J* = 6.9 Hz, 3H), 1.02 ppm (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 159.8 (s), 159.2 (s), 145.2 (s), 145.1 (s), 136.0 (s), 135.9 (s), 135.8 (d), 132.6 (d), 131.1 (d, 2C), 130.8 (s), 129.5 (d, 2C), 129.2 (d, 4C), 128.4 (d), 128.2 (d, 4C), 127.2 (d), 121.6 (d), 114.2 (d, 2C), 113.5 (d, 2C), 87.3 (s), 79.5 (d), 75.7 (d), 75.4 (t), 73.3 (t), 63.5 (t), 54.8 (q, 2C), 44.8 (d), 36.3 (d), 30.8 (d), 21.7 (q), 13.0 (q), 12.1 (q), 11.1 ppm (q); IR (ATR): $\tilde{\nu}$ = 3395 (br, m), 3007 (w), 2960 (m), 2931 (m), 2868 (m), 1610 (m), 1511 (s), 1447 (m), 1301 (m), 1249 (ss), 1217 (m), 1179 (m), 1076 (m), 1035 (s), 830 (m), 757 (ss), 708 cm^{-1} (m); HRMS (LC-MS): *m*/*z*: calcd for $C_{43}H_{52}O_6Na$: 687.3662 [*M*+Na]$^+$, found 687.3663.

(2*R*,3*S*,4*S*,5*S*,6*E*,8*S*,9*Z*)-5-(*tert*-Butyldimethylsilyloxy)-1-(*p*-methoxybenzyloxy)-4-[(*p*-methoxyphenyl)diphenylmethoxymethyl]-2,6,8-trimethylundeca-6,9-diene-3-ol (30): Imidazole (0.31 g, 4.60 mmol, 4.0 equiv) and TBS chloride (0.43 g, 2.88 mmol, 2.5 equiv) were added to a stirred solution of diol **29** (0.77 g, 1.15 mmol, 1.0 equiv) in CH_2Cl_2 (8 mL). After 16 h stirring at RT sat. $NaHCO_3$ solution was added. Then the organic layer was separated and the aqueous layer was washed with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. After purification via column chromatography (hexane/ethyl acetate 4:1 + 1 % Et_3N) TBS-protected diol **30** (0.83 g, 1.06 mmol, 92 %) was isolated as a colorless foam. $[\alpha]_D^{25}$ = +12.8 (*c* = 1.12, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 7.62 (d, *J* = 8.3 Hz, 4H), 7.44 (d, *J* = 8.8 Hz, 2H), 7.28 (d, *J* = 8.5 Hz, 2H), 7.19–7.14 (m, 4H), 7.04 (t, *J* = 7.2 Hz, 2H), 6.82 (d, *J* = 8.7 Hz, 2H), 6.74 (d, *J* = 8.9 Hz, 2H), 5.30 (dq,

J=10.7, 6.5 Hz, 1H), 5.18 (ddq, J=10.7, 9.2, 1.5 Hz, 1H), 5.04 (d, J=8.9 Hz, 1H), 4.59 (d, J=7.4 Hz, 1H), 4.54 (dt, J=8.0, 2.4 Hz, 1H), 4.56 (d, J=11.7 Hz, 1H), 4.52 (d, J=11.7 Hz, 1H), 3.88 (d, J=2.1 Hz, 1H), 3.81 (dd, J=8.5, 7.5 Hz, 1H), 3.51 (dd, J=8.6, 5.8 Hz, 1H), 3.37 (dd, J=9.5, 4.0 Hz, 1H), 3.32 (s, 3H), 3.31 (s, 3H), 3.15 (dd, J=9.6, 4.5 Hz, 1H), 2.38 (m, 1H), 2.32 (m, 1H), 1.65 (d, J=0.8 Hz, 3H), 1.46 (dd, J=6.7, 1.6 Hz, 3H), 1.11 (d, J=6.9 Hz, 3H), 1.02 (s, 9H), 1.03–0.98 (m, 3H), 0.20 (s, 3H), 0.09 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 159.6 (s), 159.2 (s), 145.3 (s), 145.1 (s), 136.0 (s), 135.4 (d), 135.1 (s, C-7), 132.6 (d), 131.8 (s), 131.2 (d, 2C), 129.3 (d, 2C), 129.3 (d, 2C), 129.1 (d, 2C), 128.4 (d, 2C), 128.2 (d, 2C), 128.1 (d, 2C), 127.2 (d, 2C), 122.0 (d), 114.1 (d, 2C), 113.5 (d, 2C), 87.2 (s), 80.2 (d), 74.5 (t), 73.1 (t), 71.2 (d), 62.3 (t), 54.8 (q, 2C), 46.4 (d), 36.1 (d), 30.8 (d), 26.2 (q, 3C), 21.2 (q), 18.5 (s), 13.0 (q), 11.9 (q), 11.1 (q), −3.9 (q), −4.6 ppm (q); IR (ATR): $\tilde{\nu}$ = 3502 (br, m), 3058 (w), 3003 (w), 2955 (s), 2929 (s), 2856 (m), 1611 (m), 1511 (s), 1463 (m), 1448 (m), 1362 (w), 1301 (w), 1249 (ss), 1179 (m), 1074 (s), 1036 (ss), 1003 (s), 879 (m), 834 (ss), 775 (s), 708 cm^{-1} (m); HRMS (LC-MS): m/z: calcd for $C_{49}H_{66}O_6NaSi$: 801.4526 $[M+Na]^+$, found 801.4554.

(2*S*,3*S*,4*E*,4′*S*,5′*R*,6*S*,7*Z*)-3-(*tert*-Butyldimethylsilyloxy)-1-[(*p*-methoxyphenyl)-diphenylmethoxy]-2-[2′-(*p*-methoxyphenyl)-5′-methyl-[1,3]dioxan-4′-yl]-4,6-dimethylnona-4,7-diene (31): Powdered molecular sieve (4 Å) (0.10 g) was added to a stirred solution of PMB-ether **30** (0.83 g, 1.06 mmol, 1.0 equiv) in CH_2Cl_2 (8 mL) and the suspension was stirred at RT for 30 min. Then the temperature was decreased to 0 °C and DDQ (0.29 g, 1.27 mmol, 1.2 equiv) was added in small portions. The color of the suspension changed from green to brown and stirring was continued for 2 h. Then sat. $NaHCO_3$ solution and $Na_2S_2O_5$ (50 mg) were added. After stirring for 5 min the organic layer was separated and the aqueous suspension was extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. Purification via column chromatography (hexane/ethyl acetate 6:1 + 1% Et_3N) yielded PMP acetal **31** (0.70 g, 0.90 mmol, 85%) as a colorless foam. $[\alpha]_D^{25}$ = +28.2 (c=1.04, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 7.67 (d, J=8.9 Hz, 2H), 7.64 (d, J=7.7 Hz, 4H), 7.48 (d, J=8.9 Hz, 2H), 7.22–7.15 (m, 6H), 7.06 (t, J=7.3 Hz, 1H), 7.05 (t, J=7.3 Hz, 1H), 6.95 (d, J=8.7 Hz, 2H), 6.87 (d, J=8.9 Hz, 2H), 5.50 (s, 1H), 5.38 (d, J=8.5 Hz, 2H), 5.35–5.28 (m, 2H), 4.89 (d, J=4.1 Hz, 1H), 3.88–3.80 (m, 2H), 3.77–3.71 (m, 2H), 3.32 (m, 1H), 3.31 (s, 3H), 3.25 (s, 3H), 3.00 (dd, J=9.1, 7.6 Hz, 1H), 2.81 (m, 1H), 1.72 (m, 1H), 1.59–1.55 (m, 6H), 1.47 (d, J=5.0 Hz, 3H), 1.01 (s, 9H), 0.95 (d, J=6.7 Hz, 3H), 0.11 (s, 3H), 0.10 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 160.4 (s), 159.2 (s), 145.7 (s), 145.3 (s), 136.5 (s), 135.9 (d), 133.3 (s), 132.6 (s), 132.2 (d), 130.9 (d, 2C), 129.2 (d, 2C), 129.1 (d, 2C), 128.2 (d, 2C), 128.1 (d, 2C), 127.9 (d, 2C), 127.2 (d), 127.1 (d), 122.4 (d), 113.9 (d, 2C), 113.5 (d, 2C), 102.3 (d), 87.8 (s), 81.2 (d), 75.1 (d), 74.3 (t), 62.7 (t), 54.8 (q), 54.7 (q), 48.4 (d), 31.9 (d), 30.8 (d), 26.4 (q, 3C), 21.3 (q), 18.7 (s), 13.4 (q), 13.3 (q), 12.9 (q), −4.4 (q), −4.7 ppm (q); IR (ATR): $\tilde{\nu}$ = 3060 (w), 3003 (w), 2955 (s), 2928 (s), 2855 (m), 1960 (w), 1878 (w), 1614 (m), 1510 (s), 1463 (m), 1447 (m), 1301 (m), 1249 (ss), 1179 (m), 1159 (m), 1113 (s), 1035 (ss), 1003 (s), 832 (s), 774 (m), 707 cm^{-1} (m); HRMS (LC-MS): m/z: calcd for $C_{49}H_{64}O_6NaSi$: 799.4370 $[M+Na]^+$, found 799.4390.

(2*R*,3*S*,4*S*,5*S*,6*E*,8*S*,9*Z*)-5-(*tert*-Butyldimethylsilyloxy)-3-(*p*-methoxybenzyloxy)-4-[(*p*-methoxyphenyl)diphenylmethoxymethyl]-2,6,8-trimethylundeca-6,9-diene-1-ol (32): PMP-acetal **31** (0.70 g, 0.90 mmol, 1.0 equiv) was dissolved in toluene (8 mL) and cooled under stirring to 0 °C. Then a solution of DIBAL-H (1.50 mL, 2.25 mmol, 2.5 equiv, 1.5 M in toluene) was added followed after 1 h by an additional amount of DIBAL-H solution (0.50 mL, 0.75 mmol, 0.83 equiv). The reaction was kept at 0 °C for 3 h and then sat. $NaHCO_3$ solution was added and the suspension was allowed to warm up. After reaching RT the reaction mixture became solid due to precipitated alumina gels. By addition of sat. K/Na tartrate solution and intensive stirring the precipitate was dissolved and the organic layer was separated. The aqueous layer was extracted with ethyl acetate and the combined organic layers were dried over $MgSO_4$ and filtered. After concentration the filtrate under vacuum chromatography (hexane/ethyl acetate 5:1 + 1% Et_3N) yielded alcohol **32** (0.57 g, 0.73 mmol, 81%) as a colorless foam. $[\alpha]_D^{25}$ = +14.1 (c=1.10, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 7.66 (d, J=8.4 Hz, 2H), 7.63 (d, J=8.8 Hz, 2H), 7.48 (d, J=8.8 Hz, 2H), 7.21–7.14 (m, 6H), 7.05 (t, J=7.2 Hz, 1H), 7.05 (t, J=7.0 Hz, 1H), 6.81 (d, J=8.5 Hz, 2H), 6.76 (d, J=8.8 Hz, 2H), 5.26 (dq, J=10.7, 6.7 Hz, 1H), 5.15 (ddq, J=10.7, 9.4, 1.4 Hz, 1H), 4.98 (d, J=9.2 Hz, 1H), 4.51 (d, J=11.0 Hz, 1H), 4.44 (d, J=11.0 Hz, 1H), 4.36 (d, J=8.2 Hz, 1H), 4.18 (dd, J=7.3, 1.2 Hz, 1H), 3.76 (dd, J=10.6, 4.3 Hz, 1H), 3.69 (dd, J=10.4, 6.3 Hz, 1H), 3.32–3.24 (m, 2H), 3.30 (s, 6H), 3.13 (t, J=9.2 Hz, 1H), 2.86 (m, 1H), 2.52 (m, 1H), 2.04–1.95 (br s, 1H), 1.71 (d, J=0.5 Hz, 3H), 1.36 (dd, J=6.7, 1.5 Hz, 3H), 1.17 (d, J=6.9 Hz, 3H), 0.99 (s, 9H), 0.94 (d, J=6.7 Hz, 3H), 0.13 (s, 3H), 0.05 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 159.6 (s), 159.3 (s), 145.7 (s), 145.3 (s), 136.4 (s), 135.2 (d), 134.5 (s), 132.1 (d), 132.0 (s), 131.0 (d, 2C), 129.5 (d, 2C), 129.2 (d, 2C), 129.0 (d, 2C), 128.2 (d), 128.1 (d, 2C), 127.2 (d, 2C), 127.1 (d, 2C), 121.8 (d), 114.0 (d, 2C), 113.5 (d, 2C), 87.2 (s), 80.4 (d), 78.1 (d), 74.5 (t), 66.9 (t), 63.0 (t), 54.8 (q, 2C), 44.8 (d), 39.8 (d), 30.6 (d), 26.4 (q, 3C), 21.0 (q), 18.6 (s), 15.1 (q), 12.9 (q), 12.0 (q), −3.8 (q), −4.3 ppm (q); IR (ATR): $\tilde{\nu}$ = 3458 (br, m), 3057 (w), 2954 (s), 2927 (s), 2856 (s), 1717 (w), 1611 (m), 1586 (w), 1511 (s), 1463 (m), 1447 (m), 1300 (m), 1248 (ss), 1177 (m), 1034 (ss), 880 (m), 834 (ss), 774 (s), 740 (ss), 707 cm^{-1} (s); HRMS (LC-MS): m/z: calcd for $C_{49}H_{66}O_6NaSi$: 801.4526, found 801.4551 $[M+Na]^+$.

(2*S*,3*R*,4*S*,5*S*,6*E*,8*S*,9*Z*)-5-(*tert*-Butyldimethylsilyloxy)-3-(p-methoxybenzyloxy)-4-[(*p*-methoxyphenyl)diphenylmethoxymethyl]-2,6,8-trimethylundeca-6,9-diene-1-al (9): Powdered molecular sieves (4 Å, 0.40 g) and NMO (0.165 g, 1.41 mmol, 2.5 equiv) were added to a solution of alcohol **32** (0.44 g, 0.57 mmol, 1.0 equiv) in CH_2Cl_2 (8 mL) and the suspension was stirred for 20 min at RT. Then TPAP (5 mg, 14 μmol) was added and the color turned dark green. After 30 min the suspension was directly filtered over silica gel. After concentration of the solution under vacuum, aldehyde **7** was used without further purification. For analysis purification via column chromatography (hexane/ethyl acetate 8:1 + 1% Et_3N) yielded aldehyde **9** (0.40 g, 0.51 mmol, 90%) as a white foam. $[\alpha]_D^{25}$ = +8.1 (c=1.03, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 9.72 (d, J=0.8 Hz, 1H), 7.66 (d, J=8.2 Hz, 2H), 7.63 (d, J=8.7 Hz, 2H), 7.47 (d, J=8.8 Hz, 2H), 7.20–7.14 (m, 6H), 7.04 (t, J=7.4 Hz, 2H), 6.80 (d, J=8.7 Hz, 2H), 6.75 (d, J=8.9 Hz, 2H), 5.29 (dq, J=10.9, 6.5 Hz, 1H), 5.19 (ddq, J=10.6, 9.3, 1.4 Hz, 1H), 5.09 (d, J=9.2 Hz, 1H), 4.49 (dd, J=5.2, 3.2 Hz, 1H), 4.41–4.36 (m, 3H), 3.37 (dd, J=9.3, 6.0 Hz, 1H), 3.32–3.26 (m, 1H), 3.30 (s, 6H), 3.24–3.17 (m, 2H), 2.70 (m, 1H), 1.64 (d, J=0.6 Hz, 3H), 1.40 (dd, J=6.7, 1.5 Hz, 3H), 1.20 (d, J=7.2 Hz, 3H), 0.97–0.93 (m, 3H), 0.95 (s, 9H), 0.05 (s, 3H), 0.03 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 203.4 (d), 159.8 (s), 159.3 (s), 145.6 (s), 145.2 (s), 136.3 (s), 135.2 (d), 133.9 (s), 132.1 (d), 131.3 (s), 130.9 (d, 2C), 129.6 (d, 2C), 129.2 (d, 2C), 129.0 (d, 2C), 128.2 (d, 2C), 127.2 (d), 127.2 (d), 122.1 (d), 114.0 (d, 2C), 113.6 (d, 2C), 87.4 (s), 77.2 (d), 76.1 (d), 73.3 (t), 62.5 (t), 54.8 (q, 2C), 50.3 (d), 46.1 (d), 30.7 (d), 26.3 (q, 3C), 21.2 (q), 18.5 (s), 13.0 (q), 12.6 (q), 10.4 (q), −3.9 (q), −4.6 ppm (q); IR (ATR): $\tilde{\nu}$ = 3058 (w), 2954 (s), 2929 (s), 2857 (s), 2709 (w), 1724 (s), 1611 (m), 1511 (ss), 1462 (m), 1448 (m), 1300 (m), 1249 (ss), 1178 (m), 1114 (w), 1036 (ss), 834 (ss), 775 (s), 740 (ss), 707 cm^{-1} (s); HRMS (LC-MS): m/z: calcd for $C_{49}H_{64}O_6NaSi$: 799.4370 $[M+Na]^+$, found 799.4388.

(2*R*,3*S*,4*R*,5*R*,6*S*,7*R*,8*E*,10*S*,13*S*,14*R*,15*S*,16*S*,17*S*,18*E*,20*S*,21*Z*)-Allyl-2,7,17-tris-(*tert*-butyldimethylsilyloxy)-13-hydroxy-3-methoxy-15-(*p*-methoxybenzyloxy)-16-[(*p*-methoxyphenyl)-diphenylmethoxymethyl]-4,6,8,10,14,18,20-heptamethyl-11-oxo-5-triethylsilyloxytricosa-8,18,21-trienoate (33): A solution of KHMDS (1.40 mL, 0.69 mmol, 1.45 equiv, 0.5 M in toluene) was slowly added at −78 °C to a stirred solution of ketone **8** (388 mg, 0.53 mmol, 1.1 equiv) in THF (14 mL). After 1 h a solution of aldehyde **9** (0.33 g, 0.43 mmol, 1.0 equiv) in THF (4 mL) was slowly added. Then the reaction was stirred for further 30 min at −78 °C and was quenched by addition of sat. NH_4Cl solution and warmed up to RT. To dissolve precipitated NH_4Cl a small amount of water was added, and the organic layer was separated. The aqueous layer was extracted with ethyl acetate. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. The crude product was purified by two consecutive column chromatography. After the first chromatography (hexane/ethyl acetate 20:1 + 1% Et_3N) ketone **8** (57 mg, 78 μmol) was reisolated. The other fractions were purified again (hexane/ethyl acetate 8:1 + 1% Et_3N) to give a diastereomeric mixture of aldol product **33** (384 mg, 0.26 mmol, 59%) as a colorless oil. An analytical sample of

diastereomerically pure **33** was obtained after semipreparative HPLC (eluent MeOH 100%, Merck licrospher 100 RP-18 column, detection via UV absorption at 250 nm). $[\alpha]_D^{25} = +21.1$ ($c = 1.10$, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 7.72 (d, $J = 7.4$ Hz, 2H), 7.68 (d, $J = 7.4$ Hz, 2H), 7.52 (d, $J = 8.8$ Hz, 2H), 7.25–7.19 (m, 6H), 7.07 (t, $J = 7.3$ Hz, 1H), 7.06 (t, $J = 7.3$ Hz, 1H), 6.83 (d, $J = 8.7$ Hz, 2H), 6.79 (d, $J = 8.8$ Hz, 2H), 5.78 (ddt, $J = 16.9$, 10.6, 6.1 Hz, 1H), 5.70 (d, $J = 9.0$ Hz, 1H), 5.27 (dq, $J = 10.7$, 6.6 Hz, 1H), 5.20–5.11 (m, 1H), 5.14 (dd, $J = 17.1$, 1.4 Hz, 1H), 5.06–4.99 (m, 1H), 5.01 (dd, $J = 10.4$, 1.3 Hz, 1H), 4.71 (d, $J = 9.3$ Hz, 1H), 4.57 (d, $J = 10.5$ Hz, 1H), 4.55 (d, $J = 6.8$ Hz, 1H), 4.49–4.39 (m, 5H), 4.12 (d, $J = 10.0$ Hz, 1H), 3.79 (d, $J = 8.3$ Hz, 1H), 3.66 (dd, $J = 7.0$, 0.9 Hz, 1H), 3.63 (s, 3H), 3.51–3.48 (s, 1H), 3.38 (dd, $J = 9.2$, 7.0 Hz, 1H), 3.35–3.26 (m, 2H), 3.33 (s, 3H), 3.32 (s, 3H), 3.13 (t, $J = 9.2$ Hz, 1H), 2.93–2.84 (m, 2H), 2.61 (dd, $J = 16.9$, 2.9 Hz, 1H), 2.53 (m, 1H), 2.11 (m, 1H), 2.00 (m, 1H), 1.75 (d, $J = 0.2$ Hz, 3H), 1.71 (d, $J = 0.2$ Hz, 3H), 1.38 (dd, $J = 6.7$, 1.5 Hz, 3H), 1.29 (d, $J = 7.0$ Hz, 3H), 1.26 (d, $J = 6.9$ Hz, 6H), 1.15 (t, $J = 7.9$ Hz, 9H), 1.15 (d, $J = 6.9$ Hz, 3H), 1.03 (s, 18H), 1.02 (s, 9H), 0.97 (d, $J = 6.7$ Hz, 3H), 0.87–0.79 (m, 6H), 0.21 (s, 3H), 0.18 (s, 3H), 0.16 (s, 6H), 0.11 (s, 3H), 0.07 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 211.6 (s), 171.6 (s), 159.7 (s), 159.3 (s), 145.8 (s), 145.3 (s), 139.3 (s), 136.4 (s), 135.2 (d), 134.6 (s), 132.3 (d), 132.2 (d), 131.8 (s), 131.1 (d, 2C), 129.7 (d, 2C), 129.2 (d, 2C), 129.1 (d, 2C), 128.4 (d, 2C), 128.3 (d), 128.2 (d, 2C), 127.2 (d, 2C), 121.8 (d), 119.0 (t), 114.0 (d, 2C), 113.5 (d, 2C), 87.2 (s), 83.1 (d), 81.4 (d), 80.5 (d), 78.2 (d), 76.6 (d), 74.6 (t), 74.4 (d), 69.7 (d), 65.6 (t), 63.0 (t), 61.1 (q), 54.8 (q, 2C), 46.8 (t), 46.5 (d), 44.5 (d), 41.8 (d), 40.3 (d, 2C), 30.7 (d), 26.5 (q), 26.2 (q), 26.1 (q), 21.0 (q), 18.6 (s, 3C), 17.0 (q), 12.9 (q), 12.1 (q), 12.0 (q), 11.7 (q), 10.7 (q), 10.6 (q), 7.7 (q), 6.6 (t, 3C), −3.8 (q), −3.9 (q), −4.2 (q), −4.5 (q), −4.7 (q), −4.8 ppm (q); IR (ATR): $\tilde{\nu}$ = 2954 (s), 2930 (s), 2881 (m), 2857 (m), 1740 (m), 1715 (m), 1611 (w), 1511 (m), 1462 (m), 1361 (w), 1300 (w), 1249 (ss), 1106 (s), 1036 (ss), 1005 (s), 834 (ss), 774 (ss), 726 (m), 708 cm^{-1} (m); HRMS (LC-MS): m/z: calcd for $C_{87}H_{140}O_{13}NaSi_4$: 1527.9269 $[M+Na]^+$, found 1527.9273.

(2*R*,3*S*,4*R*,5*R*,6*S*,7*R*,8*E*,10*S*,13*S*,14*R*,15*S*,16*S*,17*S*,18*E*,20*S*,21*Z*)-Allyl-2,7,17-tris-(*tert*-butyldimethylsilyloxy)-13-hydroxy-16-hydroxymethyl-3-methoxy-15-(*p*-methoxybenzyloxy)-4,6,8,10,14,-18,20-heptamethyl-11-oxo-5-triethylsilyloxytricosa-8,18,21-trienoate (34): The diastereomeric mixture of aldol products **33** (384 mg, 0.26 mmol) was dissolved in CH_2Cl_2 (2 mL) and hexafluoroisopropanol (3 mL) was added. After stirring for a few min an intensive orange color appeared. After 10 min methanol was added dropwise until a slight yellow color remained and stirring was continued for 16 h at RT. Then sat. $NaHCO_3$ solution was added and the organic layer was diluted with CH_2Cl_2 and separated. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layers were dried over $MgSO_4$ and filtered. After removing the solvent under vacuum the diastereomeric mixture of diols could be easily separated via column chromatography (hexane/ethyl acetate 10:1 + 1% Et_3N) to yield major diastereomer **34** (213 mg, 0.17 mmol, 68%) as a colorless oil. $[\alpha]_D^{25} = +29.1$ ($c = 0.66$, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 7.30 (d, $J = 8.5$ Hz, 2H), 6.82 (d, $J = 8.4$ Hz, 2H), 5.77 (ddt, $J = 17.0$, 10.6 Hz, 6.1 Hz, 1H), 5.71 (d, $J = 9.7$ Hz, 1H), 5.37 (dq, $J = 10.3$, 6.7 Hz, 1H), 5.32–5.26 (m, 2H), 5.15 (dd, $J = 17.2$, 1.4 Hz, 1H), 5.01 (dd, $J = 10.3$, 1.0 Hz, 1H), 4.65 (d, $J = 11.0$ Hz, 1H), 4.54 (d, $J = 6.9$ Hz, 1H), 4.51–4.41 (m, 3H), 4.50 (d, $J = 10.8$ Hz, 1H), 4.24–4.18 (m, 2H), 4.11 (d, $J = 9.9$ Hz, 1H), 3.85–3.75 (m, 1H), 3.77 (d, $J = 8.5$ Hz, 1H), 3.68–3.62 (m, 1H), 3.65 (d, $J = 6.9$ Hz, 1H), 3.59 (s, 3H), 3.44–3.35 (m, 2H), 3.32 (s, 3H), 2.76 (dd, $J = 16.7$, 8.9 Hz, 1H), 2.58–2.49 (m, 1H), 2.50 (dd, $J = 16.8$, 3.2 Hz, 1H), 2.27 (m, 1H), 2.10 (m, 1H), 2.00 (m, 1H), 1.73 (s, 3H), 1.69 (s, 3H), 1.56 (dd, $J = 6.4$, 1.1 Hz, 1H), 1.26 (d, $J = 6.8$ Hz, 3H), 1.24 (d, $J = 7.3$ Hz, 3H), 1.23 (d, $J = 6.9$ Hz, 3H), 1.18–1.12 (m, 3H), 1.15 (t, $J = 7.8$ Hz, 9H), 1.08 (d, $J = 6.8$ Hz, 3H), 1.05 (s, 9H), 1.03 (s, 9H), 1.02 (s, 9H), 0.83 (q, $J = 7.7$ Hz, 6H), 0.21 (s, 3H), 0.19 (s, 3H), 0.17 (s, 3H), 0.15 (s, 3H), 0.11 (s, 3H), 0.09 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 211.1 (s), 171.6 (s), 159.9 (s), 139.3 (s), 135.1 (d), 134.8 (s), 132.4 (d), 132.2 (d), 130.9 (s), 128.7 (d, 2C), 128.2 (d), 122.6 (d), 119.0 (t), 114.3 (d, 2C), 83.1 (d), 81.6 (d), 81.4 (d), 78.0 (d), 76.5 (d), 74.4 (d), 72.4 (t), 71.4 (d), 65.6 (t), 61.7 (t), 61.1 (q), 54.8 (q), 46.6 (d), 46.6 (t), 46.5 (d), 40.3 (d, 2C), 39.9 (d), 30.8 (d), 26.4 (q, 3C), 26.2 (q, 3C), 26.1 (q, 3C), 21.2 (q), 18.6 (s, 3C), 17.1 (q), 13.2 (q), 12.4 (q), 12.0 (q), 11.7 (q), 10.6 (q), 9.5 (q), 7.7 (q, 3C), 6.6 (t, 3C), −3.9 (s), −4.0 (s), −4.5 (s), −4.7 (s), −4.7 (s), −4.8 ppm (s); IR (ATR): $\tilde{\nu}$ = 3494 (br, m), 2954 (ss), 2929 (ss), 2884 (s), 2857 (s), 1738 (m), 1716 (m), 1613 (w), 1514 (m), 1462 (m), 1361 (w), 1250 (ss), 1173 (w), 1108 (s), 1038 (ss), 1006 (s), 836 (ss), 776 (ss), 738 cm^{-1} (ss); HRMS (LC-MS): m/z: calcd for $C_{67}H_{124}O_{12}NaSi_4$: 1255.8068 $[M+Na]^+$, found 1255.8048.

(1′*R*,2′*S*,3*R*,3′*S*,4*S*,4′*S*,5*S*,5′*E*,6*R*,7*S*,7′*S*,8*R*,8′*Z*,9*E*,11*S*,14*S*)-3,8-Bis-(*tert*-butyldimethylsilyloxy)-14-[4′-(*tert*-butyldimethylsilyloxy)-3′-hydroxymethyl-2′-(*p*-methoxybenzyloxy)-1′,5′,7′-trimethyldeca-5,8-dienyl]-4-methoxy-5,7,9,11-tetramethyl-6-triethylsilyloxy-oxacyclotetradec-9-ene-2,12-dione (36)

a) Cleavage of allyl ester 34: $[Pd(PPh_3)_2Cl_2]$ (5 mg, 7 μmol) and tri-*n*-butyltin hydride (0.24 mL, 0.91 mmol, 6.0 equiv) were added to a solution of allyl ester **34** (188 mg, 0.15 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL). The color of the solution rapidly changed to dark red and gas evolution occurred. After 20 min sat. $NaHCO_3$ solution was added. The aqueous layer was separated and the organic layer was washed with brine and sat. NH_4Cl solution. The combined aqueous layers were washed again with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and filtered. The brownish filtrate of **35** was carefully concentrated under vacuum at 20°C and used immediately without further purification.

b) Yamaguchi lactonization: Crude dihydroxy acid **35** was diluted with CH_2Cl_2 (50 mL) and diisopropylamine (1.2 mL, solution in CH_2Cl_2, c = 0.5 M, 0.60 mmol, 4.0 equiv), DMAP (1.5 mL, solution in CH_2Cl_2, c = 0.1 M, 0.15 mmol, 1.0 equiv) and 2,4,6-trichlorobenzoyl chloride (1.5 mL, solution in CH_2Cl_2, c = 0.2 M, 0.30 mmol, 2.0 equiv) were added. The reaction mixture was stirred for 3 h at RT and then sat. $NaHCO_3$ solution was added. The organic layer was separated and the aqueous layer was washed with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. After purification via column chromatography (hexane/ethyl acetate 15:1) macrolactone **36** (61 mg, 52 μmol, 34% over 2 steps) was obtained as a colorless oil. $[\alpha]_D^{25} = +66.8$ ($c = 0.84$, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 7.44 (d, $J = 8.5$ Hz, 2H), 6.85 (d, $J = 8.5$ Hz, 2H), 5.71 (m, 1H), 5.57 (d, $J = 9.6$ Hz, 1H), 5.38 (dq, $J = 10.8$, 6.4 Hz, 1H), 5.33–5.28 (m, 2H), 4.78 (d, $J = 10.9$ Hz, 1H), 4.74 (d, $J = 10.6$ Hz, 1H), 4.46 (d, $J = 4.8$ Hz, 1H), 4.42 (d, $J = 6.8$ Hz, 1H), 4.06 (d, $J = 7.9$ Hz, 1H), 3.98 (dd, $J = 5.5$, 2.0 Hz, 1H), 3.82 (t, $J = 4.3$ Hz, 1H), 3.75 (dd, $J = 10.6$, 7.2 Hz, 1H), 3.69–3.65 (m, 2H), 3.59 (s, 3H), 3.39 (m, 1H), 3.31 (s, 3H), 3.21 (m, 1H), 2.97 (dd, $J = 17.1$, 6.5 Hz, 1H), 2.72 (m, 1H), 2.52–2.45 (m, 2H), 2.08 (m, 1H), 1.92 (m, 1H), 1.75 (s, 3H), 1.69 (s, 3H), 1.56 (dd, $J = 6.5$, 1.0 Hz, 3H), 1.36 (d, $J = 6.8$ Hz, 3H), 1.33 (d, $J = 7.2$ Hz, 3H), 1.29 (d, $J = 6.8$ Hz, 3H), 1.22 (d, $J = 6.8$ Hz, 3H), 1.12 (t, $J = 8.0$ Hz, 9H), 1.08–1.03 (m, 3H), 1.06 (s, 9H), 1.04 (s, 9H), 1.01 (s, 9H), 0.81 (q, $J = 8.0$ Hz, 6H), 0.26 (s, 3H), 0.20 (s, 3H), 0.17 (s, 3H), 0.17 (s, 3H), 0.10 (s, 3H), 0.07 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 207.1 (s), 172.8 (s), 159.8 (s), 141.4 (s), 135.2 (d), 135.0 (s), 132.1 (d), 131.6 (s), 129.8 (d, 2C), 127.9 (d), 122.5 (d), 114.2 (d, 2C), 84.9 (d), 81.3 (d), 79.0 (d), 77.9 (d), 77.7 (d), 75.9 (d), 74.4 (d), 73.9 (t), 62.1 (t), 59.9 (q), 54.8 (q), 46.6 (t), 46.6 (d), 46.5 (d), 45.0 (d), 43.2 (d), 42.3 (d), 30.8 (d), 26.5 (q, 3C), 26.2 (q, 3C), 26.2 (q, 3C), 21.3 (q), 18.6 (s, 3C), 15.6 (q), 15.2 (q), 13.2 (q), 12.7 (q), 11.7 (q), 11.5 (q), 10.7 (q), 7.6 (q, 3C), 6.0 (t, 3C), −3.9 (q), −4.0 (q), −4.0 (q), −4.4 (q), −4.5 (q), −4.6 ppm (q); IR (ATR): $\tilde{\nu}$ = 3520 (w), 2954 (s), 2928 (s), 2856 (s), 1740 (m), 1721 (m), 1514 (w), 1462 (m), 1386 (w), 1302 (w), 1249 (s), 1151 (m), 1111 (s), 1039 (ss), 1005 (s), 835 (ss), 775 (ss), 724 (m), 672 cm^{-1} (w); HRMS (LC-MS): m/z: calcd for $C_{64}H_{118}O_{11}NaSi_4$: 1197.7649 $[M+Na]^+$, found 1197.7607.

(1′*R*,2′*S*,3*R*,3′*S*,4*S*,4′*S*,5*S*,5′*E*,6*R*,7*S*,7′*S*,8*R*,8′*Z*,9*E*,11*S*,14*S*)-3,8-Bis-(*tert*-butyldimethylsilyloxy)-14-[4′-(*tert*-butyldimethylsilyloxy)-3′-(*tert*-butyldimethylsilyloxymethyl)-2′-(*p*-methoxybenzyloxy)-1′,5′,7′-trimethyldeca-5,8-dienyl]-4-methoxy-5,7,9,11-tetramethyl-6-triethylsilyloxyoxacyclotetradec-9-ene-2,12-dione (38): Imidazole (45 mg, 0.66 mmol, 30 equiv) and TBS-chloride (30 mg, 0.20 mmol, 9.0 equiv) were added to a solution of hydroxy macrolactone **36** (25.7 mg, 21.9 μmol, 1.0 equiv) in CH_2Cl_2 (1 mL). After 1 h sat. $NaHCO_3$ solution was added. The organic layer was diluted with CH_2Cl_2 and separated, the aqueous layer was washed with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. After purification via column chromatography

(hexane/ethyl acetate 50:1) TBS-protected macrolactone **38** (22.3 mg, 17.3 μmol, 79%) was obtained as a colorless oil. $[\alpha]_D^{25}=+46.1$ ($c=0.90$, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 7.52 (d, $J=8.5$ Hz, 2H), 6.86 (d, $J=8.5$ Hz, 2H), 5.65 (d, $J=9.2$ Hz, 1H), 5.59 (ddd, $J=7.7$, 6.1, 1.7 Hz, 1H), 5.52 (d, $J=8.9$ Hz, 1H), 5.46–5.38, (m, 2H), 4.84 (d, $J=10.6$ Hz, 1H), 4.74 (d, $J=10.9$ Hz, 1H), 4.67 (d, $J=3.4$ Hz, 1H), 4.50 (d, $J=5.5$ Hz, 1H), 4.12–4.07 (m, 1H), 4.11 (d, $J=7.5$ Hz, 1H), 3.97–3.92 (m, 2H), 3.83 (t, $J=4.6$ Hz, 1H), 3.73 (dd, $J=5.5$, 3.4 Hz, 1H), 3.61 (s, 3H), 3.48 (m, 1H), 3.35 (m, 1H), 3.31 (s, 3H), 3.02 (dd, $J=17.4$, 5.8 Hz, 1H), 2.79–2.71 (m, 2H), 2.40 (m, 1H), 2.13 (m, 1H), 2.02 (m, 1H), 1.81 (s, 3H), 1.71 (s, 3H), 1.60 (d, $J=5.1$ Hz, 3H), 1.35 (d, $J=7.5$ Hz, 3H), 1.32 (d, $J=6.8$ Hz, 1H), 1.31 (d, $J=7.2$ Hz, 3H), 1.29 (d, $J=6.5$ Hz, 3H), 1.14 (d, $J=6.8$ Hz, 3H), 1.12 (t, $J=7.9$ Hz, 9H), 1.06 (s, 9H), 1.03 (s, 18H), 1.00 (s, 9H), 0.81 (q, $J=8.0$ Hz, 6H), 0.22 (s, 3H), 0.19 (s, 3H), 0.17 (s, 3H), 0.15 (s, 3H), 0.14 (s, 6H), 0.13 (s, 3H), 0.06 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 207.4 (s), 172.1 (s), 159.8 (s), 141.6 (s), 135.6 (d), 134.8 (s), 131.7 (s), 131.1 (d), 129.8 (d, 2C), 127.9 (d), 122.2 (d), 114.2 (d, 2C), 85.3 (d), 81.3 (d), 78.2 (d), 77.0 (d), 76.4 (d), 75.5 (d, 2C), 72.7 (t), 60.9 (t), 60.2 (q), 54.8 (q), 47.9 (d), 46.9 (d), 46.8 (t), 45.3 (d), 42.1 (d), 41.8 (d), 30.9 (d), 26.5 (q, 3C), 26.3 (q, 3C), 26.2 (q, 3C), 26.2 (q, 3C), 21.8 (q), 18.7 (s), 18.6 (s, 2C), 18.5 (s), 16.0 (q), 14.9 (q), 14.1 (q), 13.2 (q), 12.2 (q), 11.6 (q), 11.0 (q), 7.7 (q, 3C), 6.0 (t, 3C), 5.1 (q), −3.8 (q), −4.1 (q), −4.2 (q), −4.6 (q), −4.6 (q), −4.7 (q), −5.0 ppm (q); IR (ATR): $\tilde{\nu}$ = 2954 (s), 2929 (s), 2884 (s), 2857 (s), 1742 (m), 1721 (m), 1614 (w), 1514 (m), 1463 (m), 1250 (s), 1152 (m), 1111 (s), 1041 (s), 1005 (s), 836 (ss), 776 (ss), 724 (m), 671 cm^{-1} (w); HRMS (LC-MS): *m/z*: calcd for $C_{70}H_{136}NO_{11}Si_5$: 1306.8960 $[M+NH_4]^+$, found 1306.8948.

(1′*S*,2′*S*,3*R*,3′*S*,4*S*,4′*S*,5*S*,5′*E*,6*R*,7*S*,7′*S*,8*R*,8′*Z*,9*E*,11*S*,14*S*)-3,8-Bis-(*tert*-butyldimethylsilyloxy)-14-[4′-(*tert*-butyldimethylsilyloxy)-3′-(*tert*-butyldimethylsilyloxymethyl)-2′-hydroxy-1′,5′,7′-trimethyldeca-5,8-dienyl]-4-methoxy-5,7,9,11-tetramethyl-6-triethylsilyloxy-oxacyclotetradec-9-ene-2,12-dione (39): Water (0.1 mL) was added to a solution of PMB ether **38** (11.2 mg, 8.7 μmol, 1.0 equiv) in CH_2Cl_2 (1 mL) and under intensive stirring at 0°C DDQ (2.5 mg, 10.5 μmol, 1.2 equiv) was added. Stirring was continued for 2 h and sat $NaHCO_3$ solution and $Na_2S_2O_5$ (5 mg) were added. The organic layer was diluted with CH_2Cl_2 and separated, while the aqueous layer was washed with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. After chromatography (hexane/ethyl acetate 50:1) alcohol **39** (8.5 mg, 7.3 μmol, 83%) was obtained as a colorless oil. $[\alpha]_D^{25}=+45.2$ ($c=0.85$, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 5.76 (dt, $J=7.1$, 2.8 Hz, 1H), 5.60 (d, $J=9.3$ Hz, 1H), 5.42–5.29 (m, 3H), 4.56 (d, $J=8.2$ Hz, 1H), 4.37 (d, $J=5.0$ Hz, 1H), 4.24 (d, $J=7.9$ Hz, 1H), 4.14 (s, 1H), 4.08 (d, $J=8.2$ Hz, 1H), 3.82 (t, $J=3.8$ Hz, 1H), 3.71 (t, $J=4.5$ Hz, 1H), 3.60 (s, 3H), 3.57 (dd, $J=6.8$, 3.7 Hz, 1H), 3.46 (dd, $J=10.3$, 3.7 Hz, 1H), 3.39 (m, 1H), 3.29 (m, 1H), 3.18 (dd, $J=17.1$, 7.2 Hz, 1H), 2.92 (dd, $J=17.2$, 2.8 Hz, 1H), 2.49 (m, 1H), 2.04 (m, 1H), 1.98 (m, 1H), 1.88 (m, 1H), 1.80 (s, 3H), 1.65 (s, 3H), 1.56 (d, $J=5.3$ Hz, 3H), 1.32 (d, $J=7.2$ Hz, 3H), 1.30 (d, $J=6.8$ Hz, 3H), 1.29 (d, $J=7.0$ Hz, 3H), 1.21 (d, $J=6.8$ Hz, 3H), 1.13 (t, $J=8.0$ Hz, 9H), 1.08 (s, 9H), 1.05 (d, $J=6.8$ Hz, 3H), 1.01 (s, 27H), 0.82 (q, $J=7.9$ Hz, 6H), 0.28 (s, 3H), 0.22 (s, 3H), 0.21 (s, 3H), 0.18 (s, 3H), 0.11 (s, 3H), 0.10 (s, 3H), 0.09 (s, 3H), 0.07 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 207.8 (s), 172.2 (s), 140.8 (s), 135.2 (d), 134.7 (s), 133.3 (d), 128.1 (d), 122.4 (d), 84.5 (d), 81.4 (d), 80.9 (d), 76.7 (d), 76.2 (d), 75.6 (d), 71.3 (d), 61.5 (t), 60.0 (q), 46.8 (d), 46.6 (d), 45.2 (t), 45.1 (d), 44.1 (d), 39.7 (d), 30.9 (d), 26.3 (q), 26.2 (q, 3C), 21.2 (q), 18.7 (s), 18.6 (s), 18.5 (s), 18.4 (s), 15.7 (q), 14.7 (q), 13.2 (q), 11.8 (q, 2C), 10.8 (q), 10.5 (q), 7.7 (q, 3C), 6.1 (t, 3C), −3.8 (q), −3.9 (q), −4.0 (q), −4.3 (q), −4.6 (q), −4.8 (q), −5.3 ppm (q, 2C); IR (ATR): $\tilde{\nu}$ = 3498 (w), 2954 (s), 2928 (ss), 2856 (s), 1743 (m), 1721 (m), 1462 (m), 1407 (w), 1387 (w), 1253 (s), 1151 (m), 1100 (s), 1043 (s), 1005 (s), 835 (ss), 776 (ss), 725 (m), 672 cm^{-1} (w); HRMS (LC-MS): *m/z*: calcd for $C_{62}H_{124}O_{10}NaSi_5$: 1193.8097 $[M+Na]^+$, found 1193.7958.

(1′*R*,3*R*,3′*R*,4*S*,4′*S*,5*S*,5′*E*,6*R*,7*S*,7′*S*,8*R*,8′*Z*,9*E*,11*S*,14*S*)-3,8-Bis-(*tert*-butyldimethylsilyloxy)-14-[4′-(*tert*-butyldimethylsilyloxy)-3′-(*tert*-butyldimethylsilyloxymethyl)-2′-oxo-1′,5′,7′-trimethyldeca-5,8-dienyl]-4-methoxy-5,7,9,11-tetramethyl-6-triethylsilyloxyoxacyclotetradec-9-ene-2,12-dione (40): A sat. solution of Dess–Martin reagent in CH_2Cl_2 (0.1 mL) was added to a solution of alcohol **39** (8.5 mg, 7.3 μmol) in CH_2Cl_2 (1 mL), and the turbid solution was stirred for 1 h at RT. Then sat. $NaHCO_3$ solution and $Na_2S_2O_3$ (30 mg) were added. Intensive stirring was continued until the organic layer became clear. The organic layer was diluted with CH_2Cl_2 and separated. The aqueous layer was washed with CH_2Cl_2 and the combined organic layers were dried over $MgSO_4$ and filtered. After removing the solvent under vacuum the residue was purified via column chromatography (hexane/ethyl acetate 50:1) to give diketo lactone **40** (7.0 mg, 6.0 μmol, 82%) as a colorless oil. $[\alpha]_D^{25}=+87.1$ ($c=1.61$, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 6.00 (dt, $J=7.6$, 2.1 Hz, 1H), 5.53 (dd, $J=9.5$, 0.7 Hz, 1H), 5.35 (dq, $J=10.8$, 6.8 Hz, 1H), 5.20 (ddq, $J=10.8$, 9.3, 1.5 Hz, 1H), 5.08 (d, $J=8.9$ Hz, 1H), 4.39 (d, $J=8.9$ Hz, 1H), 4.34 (d, $J=5.0$ Hz, 1H), 4.05 (d, $J=8.2$ Hz, 1H), 3.79 (t, $J=3.7$ Hz, 1H), 3.68 (dd, $J=16.1$, 9.4 Hz, 1H), 3.66 (t, $J=4.3$ Hz, 1H), 3.57 (s, 3H), 3.51 (dd, $J=9.9$, 5.0 Hz, 1H), 3.38–3.25 (m, 3H), 3.21 (qui, $J=7.3$ Hz, 1H), 3.01 (dd, $J=17.3$, 7.8 Hz, 1H), 2.73 (dd, $J=17.2$, 2.3 Hz, 1H), 2.00 (m, 1H), 1.85–1.79 (m, 1H), 1.81 (d, $J=0.8$ Hz, 3H), 1.67 (d, $J=0.9$ Hz, 1H), 1.57 (dd, $J=6.7$, 1.7 Hz, 3H), 1.44 (d, $J=7.4$ Hz, 3H), 1.30 (d, $J=7.0$ Hz, 3H), 1.26 (d, $J=7.0$ Hz, 3H), 1.16 (d, $J=7.7$ Hz, 3H), 1.13 (t, $J=8.0$ Hz, 9H), 1.08 (s, 9H), 1.01 (s, 9H), 1.00–0.97 (m), 0.98 (s), 0.95 (s, 9H), 0.82 (q, $J=7.9$ Hz, 6H), 0.33 (s, 3H), 0.25 (s, 3H), 0.17 (s, 3H), 0.13 (s, 3H), 0.12 (s, 3H), 0.12 (s, 3H), 0.07 (s, 3H), 0.06 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 211.4 (s), 206.5 (s), 172.1 (s), 140.8 (s), 135.2 (d), 133.4 (s), 133.3 (d), 128.1 (d), 122.1 (d), 84.4 (d), 81.4 (d), 77.6 (d), 76.7 (d), 76.1 (d), 72.7 (d), 64.4 (t), 59.9 (q), 56.6 (d), 52.9 (d), 46.4 (d), 46.1 (t), 45.1 (d), 44.3 (d), 30.7 (d), 26.3 (q, 3C), 26.3 (q, 3C), 26.2 (q, 3C), 26.2 (q, 3C), 21.0 (q), 18.7 (s), 18.7 (s), 18.6 (s), 18.5 (s), 15.7 (q), 14.4 (q), 13.2 (q), 12.3 (q), 11.9 (q), 11.3 (q), 10.6 (q), 7.7 (q, 3C), 6.1 (t, 3C), −3.9 (q), −3.9 (q), −4.3 (q), −4.4 (q), −4.4 (q), −4.6 (q), −5.2 (q), −5.3 ppm (q); IR (ATR): $\tilde{\nu}$ = 2955 (s), 2929 (ss), 2885 (m), 2857 (s), 1747 (m), 1720 (m), 1471 (m), 1463 (m), 1387 (w), 1362 (w), 1253 (s), 1146 (m), 1105 (m), 1048 (s), 1006 (m), 836 (ss), 777 (ss), 725 cm^{-1} (m); HRMS (LC-MS): *m/z*: calcd for $C_{62}H_{126}NO_{10}Si_5$: 1184.8228 $[M+NH_4]^+$, found 1184.8191.

(1′*R*,2′*S*,3*R*,3′*S*,4*S*,4′*S*,5*R*,5′*E*,6*R*,7*S*,7′*S*,8*R*,8′*Z*,9*E*,11*S*,14*S*)-3,8-Bis-(*tert*-butyldimethylsilyloxy)-14-[4′-(*tert*-butyldimethylsilyloxy)-3′-(*tert*-butyldimethylsilyloxymethyl)-2′-oxo-1′,5′,7′-trimethyldeca-5,8-dienyl]-6-hydroxy-4-methoxy-5,7,9,11-tetramethyloxacyclotetradec-9-ene-2,12-dione (41): TES ether **40** (19.3 mg, 16.5 μmol) was dissolved in a mixture of HOAc/THF/H_2O (3.5:3.5:1, 3 mL) and some drops of CH_2Cl_2 were added to improve solubility of the TES ether. The solution was stirred for 5 d at RT and then sat $NaHCO_3$ solution was added carefully. After the gas evolution ceased, the organic layer was diluted with ethyl acetate and separated. The aqueous layer was extracted with ethyl acetate and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. After column chromatography (hexane/ethyl acetate 25:1) alcohol **41** (7.0 mg, 6.6 μmol, 40%, 95% borsm) was obtained as a white solid as well as reisolated TES ether **40** (10.8 mg, 9.2 μmol, 56%). $[\alpha]_D^{25}=+127.3$ ($c=0.62$, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 5.97 (q, $J=4.8$ Hz, 1H), 5.36 (dq, $J=10.9$, 6.7 Hz, 1H), 5.28–5.20 (m, 2H), 5.15 (d, $J=9.2$ Hz, 1H), 4.58 (d, $J=5.9$ Hz, 1H), 4.44 (d, $J=8.4$ Hz, 1H), 4.13 (d, $J=9.9$ Hz, 1H), 3.76–3.71 (m, 2H), 3.59 (dd, $J=9.9$, 5.3 Hz, 1H), 3.41–3.30 (m, 4H), 3.24–3.15 (m, 2H), 3.22 (s, 3H), 3.07 (dd, $J=18.8$, 4.1 Hz, 1H), 2.54 (dd, $J=18.7$, 5.5 Hz, 1H), 1.96 (m, 1H), 1.83–1.73 (m), 1.80 (d, $J=0.9$ Hz, 3H), 1.75 (d, $J=0.8$ Hz, 3H), 1.57 (dd, $J=6.8$, 1.6 Hz, 1H), 1.41 (d, $J=6.8$ Hz, 3H), 1.39 (d, $J=6.4$ Hz, 3H), 1.37 (d, $J=6.5$ Hz, 3H), 1.16 (d, $J=6.5$ Hz, 3H), 1.02–0.98 (m, 3H), 1.01 (s, 9H), 0.99 (s, 18H), 0.98 (s, 9H), 0.25 (s, 3H), 0.17 (s, 3H), 0.16 (s, 3H), 0.16 (s, 6H), 0.11 (s, 3H), 0.10 (s, 3H), 0.02 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 210.7 (s), 205.5 (s), 173.3 (s), 140.0 (s), 135.2 (d), 133.6 (s), 133.1 (d), 128.5 (d), 122.1 (d), 86.9 (d), 82.2 (d), 77.7 (d), 72.8 (d), 70.5 (d), 67.5 (d), 63.8 (t), 58.6 (q), 56.6 (d), 51.7 (d), 46.3 (d), 44.4 (t), 44.4 (d), 43.1 (d), 30.8 (d), 26.4 (q, 3C), 26.3 (q, 3C), 26.2 (q, 3C), 26.0 (q, 3C), 21.1 (q), 18.7 (s), 18.6 (s), 18.5 (s), 18.5 (s), 15.0 (q), 13.2 (q), 12.4 (q), 11.6 (q, 2C), 11.6 (q), 10.5 (q), −4.1 (q), −4.3 (q), −4.4 (q), −4.6 (q), −4.7 (q), −5.5 (q), −5.3 (q), −5.4 ppm (q); IR (ATR): $\tilde{\nu}$ = 3521 (w), 2955 (s), 2929 (s), 2857 (s), 1722 (s), 1463 (m), 1408 (w), 1388 (w), 1361 (w), 1252 (s), 1205 (w), 1127 (m), 1098 (m), 1050 (s), 1005 (m), 835 (ss), 776 cm^{-1} (ss); HRMS (LC-MS): *m/z*: calcd for $C_{56}H_{108}O_{10}NaSi_4$: 1075.6917 $[M+Na]^+$, found 1075.6917.

(1′*R*,2′*S*,3*R*,3′*S*,4*S*,4′*S*,5*S*,5′*E*,7*R*,7′*S*,8*R*,8′*Z*,9*E*,11*S*,14*S*)-3,8-Bis-(*tert*-butyldimethylsilyloxy)-14-[4′-(*tert*-butyldimethylsilyloxy)-3′-(*tert*-butyldimethylsilyloxymethyl)-2′oxo-1′,5′,7′-trimethyldeca-5,8-dienyl]-4-methoxy-5,7,9,11-tetramethyloxacyclotetradec-9-ene-2,6,12-trione (42): Alcohol **41** (6.1 mg, 5.8 μmol) was dissolved in CH_2Cl_2 (1 mL) and a sat. solution of Dess–Martin-periodinane in CH_2Cl_2 (0.1 mL) was added. The turbid solution was stirred for 6 h at RT and sat. $NaHCO_3$ solution and $Na_2S_2O_3$ (30 mg) were added. Stirring was kept on until the organic layer became clear. The organic layer was diluted with CH_2Cl_2 and separated, the aqueous layer was washed with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. Purification via column chromatography (hexane/ethyl acetate 25:1) yielded triketone **42** (5.3 mg, 5.0 μmol, 87%) as a white solid. $[\alpha]_D^{25} = +108.8$ ($c = 0.51$, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 6.14 (dt, J = 9.0, 1.0 Hz, 1H), 5.35 (dq, J = 10.5, 6.5 Hz, 1H), 5.19 (ddq, J = 10.7, 9.2, 1.8 Hz, 1H), 5.11 (d, J = 9.8 Hz, 1H), 5.06 (d, J = 9.2 Hz, 1H), 4.39 (d, J = 9.2 Hz, 1H), 4.35 (d, J = 9.3 Hz, 1H), 4.26 (d, J = 9.5 Hz, 2H), 3.68 (t, J = 9.8 Hz, 1H), 3.63 (s, 3H), 3.49 (dd, J = 9.9, 4.8 Hz, 1H), 3.40 (m, 1H), 3.34–3.22 (m, 3H), 3.17–3.08 (m, 1H), 3.16 (dd, J = 19.2, 9.3 Hz, 1H), 2.97 (dd, J = 19.1, 1.5 Hz, 1H), 2.37 (dq, J = 7.5, 0.8 Hz, 1H), 1.84 (d, J = 1.0 Hz, 3H), 1.66 (d, J = 0.9 Hz, 3H), 1.57 (dd, J = 6.8, 1.6 Hz, 3H), 1.47 (d, J = 7.4 Hz, 3H), 1.31 (d, J = 7.4 Hz, 3H), 1.20 (d, J = 6.7 Hz, 3H), 1.08 (s, 9H), 0.99–0.94 (m, 6H), 0.98 (s, 9H), 0.95 (s, 18H), 0.26 (s, 3H), 0.22 (s, 3H), 0.14 (s, 3H), 0.11 (s, 6H), 0.06 (s, 6H), −0.05 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 212.1 (s), 211.9 (s), 104.8 (s), 171.3 (s), 137.9 (s), 135.2 (d), 133.4 (d), 133.4 (s), 128.4 (d), 122.0 (d), 80.9 (d), 78.6 (d), 77.6 (d), 75.5 (d), 71.7 (d), 64.7 (t), 61.7 (q), 56.4 (d), 51.8 (d), 50.4 (d), 47.4 (d), 46.5 (t), 45.2 (d), 30.7 (d), 26.3 (q, 3C), 26.2 (q, 3C), 26.2 (q, 3C), 26.1 (q, 3C), 21.0 (q), 18.7 (s), 18.7 (s), 18.6 (s), 18.4 (s), 16.4 (q), 15.5 (q), 13.2 (q), 13.0 (q), 11.2 (q), 11.1 (q), 9.7 (q), −4.4 (q), −4.5 (q), −4.5 (q), −4.6 (q), −4.7 (q), −4.9 (q), −5.2 (q), −5.3 ppm (q); IR (ATR): $\tilde{\nu}$ = 2955 (m), 2929 (s), 2857 (m), 1766 (w), 1727 (m), 1713 (m), 1462 (m), 1388 (w), 1362 (w), 1254 (s), 1145 (m), 1114 (m), 1082 (s), 1053 (s), 989 (m), 878 (w), 835 (ss), 777 cm^{-1} (ss); HRMS (LC-MS): m/z: calcd for $C_{56}H_{106}O_{10}NaSi_4$: 1073.6761 $[M+Na]^+$, found 1073.6743.

(2*R*,3*S*,4*R*,5*R*,6*S*,7*R*,8*E*,10*S*,13*S*,14*S*,15*S*,16*S*,17*S*,18*E*,20*S*,21*Z*)-Allyl-2,7,13,17-tetrakis-(*tert*-butyldimethylsilyloxy)-3-methoxy-15-(*p*-methoxybenzyloxy)-16-[(*p*-methoxyphenyl)-diphenylmethoxymethyl]-4,6,8,10,14,18,20-heptamethyl-11-oxo-5-triethylsilyloxytricosa-8,18,21-trienoate (43): 2,6-Lutidine (48 μL, 0.41 mmol, 10 equiv) und TBS triflate (47 μL, 0.21 mmol, 5.0 equiv) were added at 0°C to a solution of aldol product **33** (62 mg, 41 μmol, 1.0 equiv) in CH_2Cl_2 (5 mL). During the addition of TBS triflate the solution rapidly turned to intensive orange color. After stirring for 4 h sat. $NaHCO_3$ solution was added and the solution turned colorless. The organic layer was separated and the aqueous layer was washed with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and filtered. The solvent was removed under vacuum and purification via column chromatography (hexane/ethyl acetate 20:1 + 1% Et_3N) yielded TBS protected aldol product **43** (37 mg, 23 μmol, 55%) as a colorless oil. $[\alpha]_D^{25} = +29.0°$ ($c = 1.38$, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 7.71 (d, J = 7.3 Hz, 2H), 7.69 (d, J = 7.0 Hz, 2H), 7.51 (d, J = 8.8 Hz, 2H), 7.26–7.20 (m, 4H), 7.17–7.12 (m, 2H), 7.09 (t, J = 7.3 Hz, 1H), 7.08 (t, J = 7.3 Hz, 1H), 6.82 (d, J = 8.7 Hz, 2H), 6.77 (d, J = 8.9 Hz, 2H), 5.83–5.72 (m, 2H), 5.33–5.16 (m, 3H), 5.15 (dd, J = 17.1, 1.4 Hz, 1H), 5.01 (dd, J = 10.4, 1.2 Hz, 1H), 4.73 (m, 1H), 4.77 (d, J = 10.5 Hz, 1H), 4.72 (d, J = 10.5 Hz, 1H), 4.56 (d, J = 6.9 Hz, 1H), 4.54 (d, J = 6.5 Hz, 1H), 5.33–5.16 (m, 2H), 4.20 (dd, J = 7.5, 2.6 Hz, 1H), 4.13 (d, J = 9.5 Hz, 1H), 3.82–3.74 (m, 1H), 3.76 (d, J = 8.4 Hz, 1H), 3.71 (dd, J = 6.9, 1.0 Hz, 1H), 3.60 (s, 3H), 3.40–3.26 (m, 3H), 3.34 (s, 6H), 3.09 (dd, J = 16.3, 8.1 Hz, 1H), 2.90 (m, 1H), 2.67 (dd, J = 16.3, 4.5 Hz, 1H), 2.33 (m, 1H), 2.13 (m, 1H), 1.99 (m, 1H), 1.75 (s, 3H), 1.73 (s, 3H), 1.44 (dd, J = 6.8, 0.8 Hz, 3H), 1.33 (d, J = 6.8 Hz, 3H), 1.26 (d, J = 6.4 Hz, 3H), 1.25 (d, J = 6.9 Hz, 3H), 1.21 (d, J = 7.0 Hz, 3H), 1.16 (t, J = 7.8 Hz, 9H), 1.13 (s, 9H), 1.05 (s, 9H), 1.04 (s, 18H), 0.98 (d, J = 6.8 Hz, 3H), 0.83 (q, J = 8.0 Hz, 6H), 0.38 (s, 3H), 0.34 (s, 3H), 0.28 (s, 3H), 0.21 (s, 3H), 0.20 (s, 3H), 0.19 (s, 3H), 0.17 (s, 3H), 0.13 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 208.9 (s), 171.6 (s), 159.5 (s), 159.3 (s), 245.9 (s), 145.3 (s), 139.3 (s), 136.4 (s), 135.6 (s), 135.5 (d), 132.1 (d, 2C), 131.3 (d, 2C), 129.5 (d, 2C), 129.4 (d, 2C), 129.3 (d, 2C), 128.2 (d, 2C), 128.1 (d, 2C), 127.7 (d), 127.2 (d), 127.1 (d), 121.9 (d), 119.1 (t), 113.8 (d), 113.5 (d), 87.5 (s), 83.0 (d), 81.3 (d), 79.5 (d), 76.9 (d), 76.6 (d), 74.8 (t), 74.7 (d), 70.7 (d), 65.6 (t), 62.9 (t), 61.0 (q), 54.8 (q, 2C), 48.3 (d), 47.8 (d), 47.1 (d), 42.1 (d), 40.4 (d), 40.1 (d), 30.7 (d), 26.6 (q, 3C), 26.5 (q, 3C), 26.3 (q, 3C), 26.2 (q, 3C), 21.4 (q), 18.7 (s), 18.6 (s, 2C), 18.5 (s), 17.3 (q), 13.5 (q), 13.0 (q), 12.1 (q), 11.7 (q), 10.9 (q), 10.6 (q), 7.8 (q, 3C), 6.7 (t, 3C), −3.4 (q), −3.5 (q), −3.8 (q), −3.9 (q), −4.1 (q), −4.5 (q), −4.6 (q), −4.8 ppm (q); IR (ATR): $\tilde{\nu}$ = 2955 (s), 2930 (s), 2881 (m), 2857 (m), 1740 (m), 1715 (m), 1611 (w), 1511 (m), 1461 (m), 1361 (w), 1300 (w), 1248 (ss), 1106 (s), 1034 (ss), 1008 (s), 834 (ss), 776 (ss), 726 (m), 709 cm^{-1} (m); HRMS (LC-MS): m/z: calcd for $C_{93}H_{158}NO_{13}Si_5$: 1637.0580 $[M+NH_4]^+$, found 1637.0571

(2*R*,3*S*,4*S*,5*R*,6*S*,7*R*,8*E*,10*S*,13*S*,14*S*,15*S*,16*S*,17*S*,18*E*,20*S*,21*Z*)-Allyl-2,7,13,17-tetrakis-(*tert*-butyldimethylsilyloxy)-16-hydroxymethyl-3-methoxy-15-(*p*-methoxybenzyloxy)-4,6,8,10,14,18,20-heptamethyl-11-oxo-5-triethylsilyloxytricosa-8–18–21-trienoate (44): MMTr ether **43** (28.0 mg, 17.3 μmol) was dissolved in a mixture of CH_2Cl_2 (0.5 mL) and hexafluoroisopropanol (0.5 mL). After a short period the stirred solution changed from colorless to an intensive orange color. After 10 min methanol was added dropwise until a slight yellow color remained, and the solution was stirred for 16 h at RT. Subsequently sat. $NaHCO_3$ solution was added, then the organic layer was diluted with CH_2Cl_2 and separated. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layers were dried over $MgSO_4$ and filtered. After removing the solvent under vacuum column chromatography (hexane/ethyl acetate 25:1 + 1% Et_3N) provided alcohol **44** (20.0 mg, 14.8 μmol, 85%) as a colorless oil. $[\alpha]_D^{25} = +51.0$ ($c = 1.01$, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 7.38 (d, J = 8.5 Hz, 2H), 6.85 (d, J = 8.7 Hz, 2H), 5.77 (ddt, J = 17.0, 10.5, 6.0 Hz, 1H), 5.72 (d, J = 8.3 Hz, 1H), 5.37 (dq, J = 10.8, 6.7 Hz, 1H), 5.31–5.24 (m, 2H), 5.15 (dd, J = 17.2, 1.4 Hz, 1H), 5.01 (dd, J = 10.4, 1.1 Hz, 1H), 4.69 (d, J = 10.7 Hz, 1H), 4.65 (d, J = 10.8 Hz, 1H), 4.60–4.55 (m, 1H), 4.56 (d, J = 6.9 Hz, 1H), 4.52–4.40 (m, 3H), 4.13 (d, J = 9.7 Hz, 1H), 3.86 (dd, J = 8.2, 1.3 Hz, 1H), 3.77–3.68 (m, 1H), 3.76 (d, J = 7.5 Hz, 1H), 3.70 (dd, J = 7.0, 0.9 Hz, 1H), 3.60–3.57 (m, 1H), 3.64 (s, 3H), 3.41 (m, 1H), 3.36 (m, 1H), 3.31 (s, 3H), 3.04 (dd, J = 16.5, 8.7 Hz, 1H), 2.56 (dd, J = 16.4, 4.1 Hz, 1H), 2.45–2.36 (m, 2H), 2.13 (m, 1H), 1.99 (m, 1H), 1.88 (d, J = 0.6 Hz, 3H), 1.76 (d, J = 0.6 Hz, 3H), 1.57 (dd, J = 6.7, 1.5 Hz, 3H), 1.34 (d, J = 6.9 Hz, 3H), 1.26 (d, J = 6.7 Hz, 3H), 1.25 (d, J = 6.8 Hz, 3H), 1.24 (d, J = 6.7 Hz, 3H), 1.16 (t, J = 8.1 Hz, 9H), 1.08 (s, 9H), 1.05–1.02 (m, 3H), 1.04 (s, 9H), 1.04 (s, 18H), 0.83 (q, J = 8.0 Hz, 6H), 0.31 (s, 3H), 0.26 (s, 3H), 0.22 (s, 3H), 0.21 (s, 3H), 0.19 (s, 3H), 0.17 (s, 3H), 0.14 (s, 3H), 0.15 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 208.5 (s), 171.6 (s), 159.8 (s), 139.4 (s), 136.1 (s), 135.3 (d), 132.5 (d), 132.1 (d), 131.9 (s), 129.8 (d, 2C), 128.0 (d), 122.4 (d), 119.1 (t), 114.1 (d, 2C), 83.0 (d), 81.4 (d), 81.3 (d), 78.9 (d), 76.6 (d), 74.9 (t), 74.6 (d), 69.8 (d), 65.6 (t), 63.7 (t), 61.0 (q), 54.8 (q), 48.4 (d), 47.7 (d), 47.0 (d), 43.1 (d), 40.3 (d), 40.1 (d), 30.8 (d), 26.5 (q, 3C), 26.4 (q, 3C), 26.2 (q, 3C), 26.1 (q), 21.1 (q), 18.7 (s), 18.6 (s), 18.6 (s), 18.5 (s), 17.2 (q), 13.2 (q), 12.5 (q), 12.1 (q), 11.7 (q), 10.6 (q), 9.8 (q), 7.7 (q, 3C), 6.6 (t, 3C), −3.6 (q), −3.8 (q), −4.0 (q), −4.1 (q), −4.2 (q), −4.5 (q), −4.6 (q), −4.8 ppm (q); IR (ATR): $\tilde{\nu}$ = 3502 (br, w), 2954 (s), 2930 (s), 2884 (m), 2857 (m), 1741 (w), 1741 (w), 1614 (w), 1514 (w), 1462 (m), 1361 (w), 1249 (s), 1105 (m), 1037 (ss), 1005 (s), 938 (w), 869 (m), 835 (ss), 775 (ss), 727 cm^{-1} (m); HRMS (LC-MS): m/z: calcd for $C_{73}H_{138}O_{12}NaSi_5$: 1369.8932 $[M+Na]^+$, found 1369.8929.

(1′*S*,2′*E*,3*R*,4*S*,4′*S*,5*S*,5′*Z*,6*R*,7*S*,8*R*,9*E*,11*S*,14*S*,15*S*,16*S*,17*S*)-3,8,14-Tris-(*tert*-butyldimethylsilyloxy)-17-[1′-(*tert*-butyldimethylsilyloxy)-2′,4′-dimethylhepta-2′,5′-dienyl]-4-methoxy-16-[*p*-methoxybenzyloxy)-5,7,9,11,15-pentamethyl-6-triethylsilyloxy-oxacyclooctadec-9-ene-2,12-dione (45)

a) Cleavage of allyl ester 44: $[Pd(PPh_3)_2Cl_2]$ (3.0 mg, 4 μmol) and Bu_3SnH (68 μL, 0.26 mmol, 6.0 equiv) were added to a stirred solution of hydroxy allylester **44** (58 mg, 43 μmol, 1.0 equiv) in CH_2Cl_2 (6 mL). The color of the solution rapidly changed from yellow to dark red and gas evolution occurred. After 15 min the reaction mixture was diluted with CH_2Cl_2 and transferred into sat. $NaHCO_3$ solution. The organic layer was separated and washed with sat. NH_4Cl solution and brine. The combined aqueous layers were additionally extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and filtered. After concentration

under vacuum the crude hydroxy acid **7** was obtained as a grey residue which was used without further purification.

b) Mitsunobu lactonization: PPh_3 (0.113 g, 0.43 mmol, 10 equiv) and DEAD (67 μL, 0.43 mmol 10 equiv) were dissolved in toluene (5 mL). After stirring for 30 min a slight yellow color remained. The crude hydroxy acid **7** was dissolved in toluene (3 mL) and slowly added to the solution. After 5 h the reaction was quenched by adding water. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. After drying the combined organic layers with $MgSO_4$ and filtration the solvents were evaporated under vacuum to give a brown oil. A mixture of hexane/ethyl acetate (50:1, 1 mL) was added and under continuous stirring CuCl was added in portions leading to precipitation of Ph_3PO and complexation of PPh_3. After 30 min the resulting clear solution was directly subjected to column chromatography (hexane/ethyl acetate 50:1). Macrolactone **45** (38 mg, 29 μmol, 68 %) was obtained as a colorless oil. $[\alpha]_D^{25} = +41.0$ ($c = 0.83$, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 7.47 (d, $J = 8.5$ Hz, 2H), 6.90 (d, $J = 8.5$ Hz, 2H), 5.47 (d, $J = 8.9$ Hz, 1H), 5.36 (dq, $J = 10.8$, 6.5 Hz, 1H), 5.30–5.22 (m, 2H), 4.78 (d, $J = 10.9$ Hz, 1H), 4.65 (d, $J = 10.9$ Hz, 1H), 4.64 (d, $J = 7.5$ Hz, 1H), 4.55–4.50 (m, 3H), 4.23 (t, $J = 10.8$ Hz, 1H), 4.00 (d, $J = 10.2$ Hz, 1H), 3.75 (d, $J = 2.0$ Hz, 1H), 3.69 (t, $J = 4.8$ Hz, 1H), 3.63 (dd, $J = 7.9$, 2.4 Hz, 1H), 3.45 (s, 3H), 3.44–3.34 (m, 2H), 3.32 (s, 3H), 2.89–2.83 (m, 2H′), 2.64 (m, 1H), 2.45 (m, 1H), 2.17 (m, 1H), 2.06 (m, 1H), 1.80 (s, 3H), 1.78 (s, 3H), 1.59 (dd, $J = 6.7$, 1.6 Hz, 3H), 1.32 (d, $J = 7.2$ Hz, 3H), 1.28 (d, $J = 6.8$ Hz, 3H), 1.24 (d, $J = 6.8$ Hz, 6H), 1.14 (t, $J = 7.7$ Hz, 9H), 1.13 (s, 9H), 1.05 (s, 9H), 1.02 (s, 9H), 1.01–0.98 (m, 1H), 1.00 (s, 9H), 0.79 (d, 6H), 0.40 (s, 3H), 0.36 (s, 3H), 0.28 (s, 3H), 0.22 (s, 3H), 0.19 (s, 3H), 0.18 (s, 3H), 0.10 (s, 3H), 0.08 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 208.3 (s), 172.7 (s), 159.9 (s), 141.5 (s), 135.2 (d), 134.5 (s), 133.9 (d), 131.4 (s), 129.5 (d, 2C), 127.7 (d), 122.4 (d), 114.3 (d, 2C), 84.4 (d), 82.1 (d), 79.8 (d), 77.7 (d), 74.9 (t), 74.6 (d), 72.4 (d), 72.0 (d), 65.5 (t), 60.3 (q), 54.8 (q), 48.5 (d), 47.4 (d), 46.6 (t), 44.8 (d), 43.2 (d), 43.1 (d), 30.8 (d), 26.7 (q, 2C), 26.4 (q), 26.1 (q), 21.1 (q), 19.3 (s), 18.7 (s), 18.6 (s), 18.5 (s), 16.4 (q), 13.2 (q), 12.4 (q, 2C), 12.1 (q, 2C), 10.6 (q), 7.7 (q, 3C), 6.5 (t, 3C), −2.8 (q), −3.6 (q, 3C), −3.9 (q), −4.1 (q), −4.2 (q), −4.6 ppm (q); IR (ATR): $\tilde{\nu}$ = 2955 (s), 2930 (s), 2883 (m), 2857 (m), 1758 (m), 1715 (m), 1614 (w), 1514 (m), 1462 (m), 1388 (w), 1361 (w), 1249 (ss), 1153 (m), 1099 (s), 1042 (ss), 1006 (s), 955 (w), 880 (w), 835 (ss), 776 (ss), 725 cm^{-1} (m); HRMS (LC-MS): m/z: calcd for $C_{70}H_{132}O_{11}NaSi_5$: 1311.8514 $[M+Na]^+$, found 1311.8518.

(1′*S*,2′*E*,3*R*,4*S*,4′*S*,5*S*,5′*Z*,6*R*,7*S*,8*R*,9*E*,11*S*,14*S*,15*S*,16*S*,17*S*)-3,8,14-Tris-(*tert*-butyldimethylsilyloxy)-17-[1′-(*tert*-butyldimethylsilyloxy)-2′,4′-dimethylhepta-2′,5′-dienyl]-16-hydroxy-4-methoxy-5,7,9,11,15-pentamethyl-6-triethylsilyloxyoxacyclooctadec-9-ene-2,12-dione (46): Water (0.4 mL) was added to a solution of PMB-ether **45** (38.0 mg, 29.5 μmol, 1.0 equiv) in CH_2Cl_2 (4 mL). After cooling to 0 °C DDQ (8.0 mg, 35.3 μmol, 1.2 equiv) was added and the solution was stirred vigorously. After 2 h an additional portion of DDQ (0.7 mg, 3.1 μmol, 0.5 equiv) was added. After 4 h the reaction was stopped by addition of sat. $NaHCO_3$ solution and $Na_2S_2O_5$ (10 mg). The organic layer was diluted with CH_2Cl_2 and separated. The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and filtered. After removing the solvents under vacuum purification via column chromatography (hexane/CH_2Cl_2 2:1) provided alcohol **46** as a colorless oil (23.5 mg, 20.1 μmol, 68 %). $[\alpha]_D^{25} = +25.4$ ($c = 0.65$, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 5.45–5.33 (m, 4H), 4.74 (m, 1H), 4.61 (d, $J = 9.3$ Hz, 1H), 4.54 (d, $J = 5.1$ Hz, 1H), 4.41 (s, 1H), 4.22–4.16 (m, 2H), 4.10 (dd, $J = 11.9$, 1.5 Hz, 1H), 4.02 (d, $J = 10.3$ Hz, 1H), 3.89 (d, $J = 6.1$ Hz, 1H), 3.82 (t, $J = 4.3$ Hz, 1H), 3.52 (s, 3H), 3.37 (m, 2H), 2.95 (dd, $J = 17.4$, 6.7 Hz, 1H), 2.85 (dd, $J = 17.3$, 3.0 Hz, 1H), 2.12–1.93 (m, 4H), 1.93 (s, 3H), 1.58–1.56 (m, 6H), 1.29 (d, $J = 6.8$ Hz, 3H), 1.25 (d, $J = 7.0$ Hz, 3H), 1.20 (d, $J = 6.8$ Hz, 3H), 1.17 (t, $J = 8.1$ Hz, 9H), 1.07 (d, $J = 6.5$ Hz, 3H), 1.08–1.06 (m, 3H), 1.07 (s, 9H), 1.05 (s, 9H), 1.03 (s, 9H), 0.97 (s, 9H), 0.79 (q, $J = 8.0$ Hz, 6H), 0.40 (s, 3H), 0.31 (s, 3H), 0.27 (s, 3H), 0.20 (s, 9H), 0.10 (s, 3H), 0.07 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 207.5 (s), 172.3 (s), 141.6 (s), 135.0 (d), 134.5 (d), 133.6 (s), 128.1 (d), 123.1 (d), 83.1 (d), 81.8 (d), 81.6 (d), 74.7 (d), 74.3 (d), 73.7 (d), 72.1 (d), 63.3 (t), 59.8 (q), 47.2 (d), 46.8 (t), 44.8 (d), 41.6 (d), 41.3 (d), 40.8 (d), 30.9 (d), 26.8 (q, 3C), 26.3 (q, 3C), 26.2 (q, 3C), 26.0 (q, 3C), 21.1 (q), 18.8 (s), 18.8 (s), 18.6 (s), 18.3 (s), 16.7 (q), 13.2 (q), 12.2 (q), 11.4 (q), 11.3 (q, 2C), 8.9 (q), 7.7 (q, 3C), 6.5 (t, 3C), −3.5 (q), −3.6 (q), −3.9 (q), −4.1 (q), −4.1 (q), −4.5 (q), −4.6 (q), −4.9 ppm (q); IR (ATR): $\tilde{\nu}$ = 3491 (br, w), 2955 (s), 2930 (s), 2884 (m), 2858 (s), 1753 (m), 1718 (m), 1463 (m), 1409 (w), 1383 (m), 1362 (m), 1252 (s), 1104 (s), 1042 (s), 1005 (s), 938 (w), 836 (ss), 776 (ss), 726 (m), 673 cm^{-1} (w); HRMS (LC-MS): m/z: calcd for $C_{64}H_{124}O_{10}NaSi_5$: 1191.7939 $[M+Na]^+$, found 1191.7937.

(1′*S*,2′*E*,3*R*,4*S*,4′*S*,5*S*,5′*Z*,6*R*,7*S*,8*R*,9*E*,11*S*,14*S*,15*R*,17*R*)-3,8,14-Tris-(*tert*-butyldimethylsilyloxy)-17-[1′-(*tert*-butyldimethylsilyloxy)-2′,4′-dimethylhepta-2′,5′-dienyl]-4-methoxy-5,7,9,11,15-pentamethyl-6-triethylsilyloxyoxacyclooctadec-9-ene-2,12,16-trione (47): Dess–Martin-periodinane (40 mg, 94 μmol, 5 equiv) was added to a stirred solution of alcohol **46** (22.0 mg, 18.8 μmol) in CH_2Cl_2 (2 mL). After 2 h an additional portion of Dess–Martin-periodinane (40 mg, 94 μmol, 5 equiv) was added and stirring of the suspension was continued for 4 h. If the reaction showed no complete conversion the reaction time could be prolonged. The reaction was quenched by addition of sat. $NaHCO_3$ solution and $Na_2S_2O_3$ (0.10 g) and stirring was continued until the turbid organic layer became clear. The organic layer was diluted with CH_2Cl_2 and separated. The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. After purification via column chromatography (hexane/CH_2Cl_2 2:1) diketone **47** was obtained as a colorless oil (14.1 mg, 12.1 μmol, 64 %). $[\alpha]_D^{25} = +48.7$ ($c = 0.86$, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 5.43–5.34 (m, 2H), 5.22 (ddq, $J = 10.4$, 9.0, 1.5 Hz, 1H), 5.09 (d, $J = 9.2$ Hz, 1H), 4.79 (dd, $J = 10.2$, 5.5 Hz, 1H), 4.55 (d, $J = 4.4$ Hz, 1H), 4.37 (d, $J = 9.6$ Hz, 1H), 4.34 (dd, $J = 11.1$, 3.9 Hz, 1H), 4.08 (t, $J = 10.9$ Hz, 1H), 3.97 (d, $J = 9.9$ Hz, 1H), 3.77 (d, $J = 2.4$ Hz, 1H), 3.63–3.55 (m, 2H), 3.50–3.41 (m, 1H), 3.44 (s, 3H), 3.34 (m, 1H), 3.19 (m, 1H), 2.86 (dd, $J = 16.2$, 4.3 Hz, 1H), 2.71 (dd, $J = 16.2$, 6.0 Hz, 1H), 1.94 (m, 1H), 1.87 (m, 1H), 1.76 (s, 3H), 1.72 (s, 3H), 1.60 (dd, $J = 6.8$, 1.7 Hz, 3H), 1.45 (d, $J = 7.5$ Hz, 3H), 1.25–1.20 (m, 9H), 1.11 (t, $J = 7.9$ Hz, 9H), 1.06 (s, 9H), 1.06 (s, 9H), 1.01 (s, 9H), 0.97 (d, $J = 6.8$ Hz, 3H), 0.96 (s, 9H), 0.78 (q, $J = 8.0$ Hz, 6H), 0.36 (s, 3H), 0.30 (s, 3H), 0.25 (s, 3H), 0.17 (s, 6H), 0.13 (s, 3H), 0.07 (s, 3H), 0.06 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 213.2 (s), 208.0 (s), 172.0 (s), 141.3 (s), 134.7 (d), 134.6 (d), 132.8 (s), 128.0 (d), 123.1 (d), 84.5 (d), 82.0 (d), 78.8 (d), 75.4 (d), 73.4 (d), 69.2 (d), 65.5 (t), 60.6 (q), 55.3 (d), 53.6 (d), 47.9 (d), 46.7 (d), 43.9 (d), 43.1 (d), 30.7 (d), 26.6 (q, 3C), 26.4 (q, 3C), 26.3 (q, 3C), 26.2 (q, 3C), 20.7 (q), 18.9 (s), 18.7 (s), 18.6 (s), 18.5 (s), 16.2 (q, C-14), 13.3 (q), 12.4 (q), 12.1 (q), 11.9 (q), 10.9 (q), 10.1 (q), 7.7 (q, 3C), 6.5 (t, 3C), −3.6 (q), −3.8 (q), −3.9 (q), −4.0 (q), −4.2 (q), −4.3 (q), −4.4 (q), −4.6 ppm (q); IR (ATR): $\tilde{\nu}$ = 2955 (s), 2930 (s), 2884 (m), 2858 (m), 1742 (w), 1716 (m), 1462 (m), 1388 (w), 1361 (w), 1252 (s), 1147 (m), 1099 (s), 1062 (s), 1005 (s), 836 (ss), 776 (ss), 730 cm^{-1} (m); HRMS (LC-MS): m/z: calcd for $C_{62}H_{122}O_{10}NaSi_5$: 1189.7782 $[M+Na]^+$, found 1189.7788.

(1′*S*,2′*E*,3*R*,4*S*,4′*S*,5*R*,5′*Z*,6*R*,7*S*,8*R*,9*E*,11*S*,14*S*,15*R*,17*R*)-3,8,14-Tris-(*tert*-butyldimethylsilyloxy)-17-[1′-(*tert*-butyldimethylsilyloxy)-2′,4′-dimethylhepta-2′,5′-dienyl]-6-hydroxy-4-methoxy-5,7,9,11,15-pentamethyloxacyclooctadec-9-ene-2,12,16-trione (48): TES ether **47** (14.1 mg, 12.1 μmol) was dissolved in a mixture of MeOH (1.5 mL) and CH_2Cl_2 (0.3 mL). Then PPTS (5 mg) was added and the clear solution was stirred at RT for 16 h. Under continued stirring sat. $NaHCO_3$ solution was carefully added and the organic layer was diluted with CH_2Cl_2 and separated. The aqueous layer was washed with CH_2Cl_2 and the combined organic layers were dried over $MgSO_4$ and filtered. After concentration under vacuum purification was performed via column chromatography (hexane/ethyl acetate 25:1) to provide alcohol **48** (8.4 mg, 8.0 μmol, 67 %) as a colorless oil. $[\alpha]_D^{25} = +111.6$ ($c = 0.58$, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 5.43 (dq, $J = 10.4$, 6.8 Hz, 1H), 5.25 (ddq, $J = 10.7$, 9.0, 1.7 Hz, 1H), 5.15 (d, $J = 10.2$ Hz, 1H), 5.13 (d, $J = 9.0$ Hz, 1H), 4.76 (ddd, $J = 7.6$, 5.2, 3.9 Hz, 1H), 4.46 (dd, $J = 10.6$, 3.6 Hz, 1H), 4.44 (d, $J = 6.0$ Hz, 1H), 4.36 (d, $J = 9.5$ Hz, 1H), 4.00 (t, $J = 11.1$ Hz, 1H), 3.91 (d, $J = 9.8$ Hz, 1H), 3.74 (t, $J = 1.6$ Hz, 1H), 3.62 (t, $J = 5.5$ Hz, 1H), 3.56 (ddd, $J = 11.0$, 9.9, 3.6 Hz, 1H), 3.49–3.42 (m, 1H), 3.44 (s, 3H), 3.39–3.25 (m, 2H), 2.88 (dd, $J = 16.0$, 3.8 Hz, 1H), 2.61 (dd, $J = 16.0$, 5.5 Hz, 1H), 2.12 (d, $J = 3.8$ Hz, 1H), 1.76–1.69 (m, 2H), 1.72 (d, $J = 0.9$ Hz, 3H), 1.65–1.61 (m, 6H), 1.41 (d, $J = 7.3$ Hz, 3H), 1.24 (d, $J = 6.8$ Hz, 3H), 1.22 (d, $J = 6.7$ Hz, 3H), 1.15 (d, $J = 7.0$ Hz, 3H), 1.03 (s, 18H), 0.99–0.96 (m, 3H), 0.98 (s, 9H), 0.94 (s,

9H), 0.31 (s, 3H), 0.28 (s, 3H), 0.24 (s, 3H), 0.18 (s, 3H), 0.09 (s, 3H), 0.06 (s, 3H), 0.03 (s, 3H), −0.03 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 213.5 (s), 207.8 (s), 171.1 (s), 140.5 (s), 134.9 (d), 134.5 (d), 132.6 (s), 128.2 (d), 123.4 (d), 87.6 (d), 83.1 (d), 78.5 (d), 75.9 (d), 72.5 (d), 71.2 (d), 64.9 (t), 61.0 (q), 56.3 (d), 54.0 (d), 49.4 (t), 46.6 (d), 43.6 (d), 40.9 (d), 30.7 (d), 26.5 (q, 3C), 26.2 (q, 3C), 26.1 (q, 6C), 20.8 (q), 18.7 (s), 18.6 (s), 18.5 (s), 18.4 (s), 15.2 (q), 14.2 (q), 13.3 (q), 11.5 (q), 11.3 (q), 10.8 (q), 8.8 (q), −3.6 (q), −4.1 (q), −4.2 (q), −4.2 (q), −4.3 (q), −4.5 (q), −4.5 (q), −4.8 ppm (q); IR(ATR): $\tilde{\nu}$ = 3548 (br, w), 2956 (s), 2930 (s), 2857 (s), 1747 (w), 1716 (m), 1463 (m), 1389 (w), 1361 (w), 1253 (s), 1150 (m), 1065 (s), 1004 (s), 836 (ss), 777 cm^{-1} (ss); HRMS (LC-MS): *m*/*z*: calcd for $C_{56}H_{108}O_{10}NaSi_4$: 1075.6917 [*M*+Na]$^+$, found 1075.6929.

(1′*S*,2′*E*,3*R*,4*S*,4′*S*,5*S*,5′*Z*,7*R*,8*R*,9*E*,11*S*,14*S*,15*R*,17*R*)-(3,8,14-Tris-(*tert*-butyldimethylsilyloxy)-17-[1′-(*tert*-butyldimethylsilyloxy)-2′,4′-dimethylhepta-2′,5′-dienyl]-4-methoxy-5,7,9,11,15-pentamethyloxacyclooctadec-9-ene-2,6,12,16-tetraone (6): The Dess–Martin-reagent (20 mg, 47 μmol) was added to a stirred solution of alcohol **48** (6.0 mg, 5.7 μmol) in CH_2Cl_2 (1.5 mL). After stirring for 30 min at RT the oxidation was completed and sat. $NaHCO_3$ solution and $Na_2S_2O_3$ (0.10 g) were added. Stirring was continued until the organic layer became clear. Then the organic layer was diluted with CH_2Cl_2 and separated. The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. After purification via column chromatography (hexane/ethyl acetate 25:1) triketone **6** (5.5 mg, 5.2 μmol, 91%) was obtained as a colorless oil. $[\alpha]_D^{25}$ = +111.6 (*c* = 0.58, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 5.39 (dq, *J* = 10.8, 6.7 Hz, 1H), 5.32 (dd, *J* = 9.7, 0.5 Hz, 1H), 5.21 (ddq, *J* = 10.6, 8.9, 1.7 Hz, 1H), 5.02 (d, *J* = 9.6 Hz, 1H), 4.92 (q, *J* = 5.0 Hz, 1H), 4.50 (t, *J* = 11.1 Hz, 1H), 4.30 (d, *J* = 4.1 Hz, 1H), 4.22–4.17 (m, 2H), 4.04–3.99 (m, 2H), 3.79 (ddd, *J* = 11.3, 9.9, 3.1 Hz, 1H), 3.47 (s, 3H), 3.37 (dq, *J* = 7.1, 5.5 Hz, 1H), 3.28 (m, 1H), 3.20–3.09 (m, 2H), 2.99 (dq, *J* = 6.8, 6.7 Hz, 1H), 2.76 (dd, *J* = 18.3, 4.3 Hz, 1H), 2.61 (dd, *J* = 18.1, 5.5 Hz, 1H), 1.68 (d, *J* = 1.0 Hz, 3H), 1.59 (d, *J* = 0.7 Hz, 3H), 1.57 (dd, *J* = 6.8, 1.7 Hz, 3H), 1.30 (d, *J* = 6.8 Hz, 3H), 1.28 (d, *J* = 6.8 Hz, 3H), 1.23 (d, *J* = 6.8 Hz, 3H), 1.15 (d, *J* = 6.8 Hz, 3H), 1.12 (s, 9H), 1.11 (s, 9H), 0.96–0.91 (m, 3H), 0.94 (s, 18H), 0.40 (s, 3H), 0.39 (s, 3H), 0.38 (s, 3H), 0.33 (s, 3H), 0.06 (s, 3H), 0.08 (s, 3H), −0.01 (s, 3H), −0.07 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 213.7 (s), 213.5 (s), 208.1 (s), 171.3 (s), 138.1 (s), 134.7 (d), 134.5 (d), 132.8 (s), 129.3 (d), 123.1 (d), 82.3 (d), 80.8 (d), 79.3 (d), 75.9 (d), 70.4 (d), 65.2 (t), 60.7 (q), 55.8 (d), 54.1 (d), 50.0 (d), 48.9 (d), 47.8 (t), 46.5 (d), 30.7 (d), 26.7 (q, 3C), 26.5 (q, 3C), 26.1 (q, 3C), 26.0 (q, 3C), 20.7 (q), 19.2 (s), 18.8 (s), 18.4 (s), 18.4 (s), 15.5 (q), 15.3 (q), 13.4 (q), 13.3 (q), 12.9 (q), 11.0 (q), 10.7 (q), −3.3 (q), −3.8 (q), −4.0 (q), −4.2 (q), −4.2 (q), −4.6 (q), −4–6 (q), −5.0 ppm (q); IR (ATR): $\tilde{\nu}$ = 2956 (s), 2930 (s), 2896 (m), 2857 (s), 1761 (m), 1708 (s), 1462 (m), 1389 (w), 1362 (w), 1253 (s), 1162 (s), 1102 (m), 1068 (ss), 1004 (s), 885 (w), 837 (ss), 777 (ss), 719 cm^{-1} (w); HRMS (LC-MS): *m*/*z*: calcd for $C_{56}H_{106}O_{10}NaSi_4$: 1073.6761 [*M*+Na]$^+$, found 1073.6721.

(1′*S*,2′*E*,3*R*,4*S*,4′*S*,5*S*,5′*Z*,7*R*,8*R*,9*E*,11*S*,14*S*,15*R*,17*R*)-3,8,14-Trihydroxy-17-(1′-hydroxy-2′,4′-dimethylhepta-2′,5′-dienyl)-4-methoxy-5,7,9,11,15-pentamethyloxacyclooctadec-9-ene-2,6,12,16-tetraone (49): $HF{\cdot}NEt_3$ (1.1 mL) was added followed by triethylamine (1.2 mL) to a solution of triketone **6** (10.8 mg, 10.3 μmol) in dry acetonitrile (2.5 mL) in a Nalgene vessel. Stirring was continued for 5 d at RT. After this period the reaction mixture was diluted with ethyl acetate and carefully transferred into sat. $NaHCO_3$ solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. Purification via column chromatography (CH_2Cl_2/methanol 20:1) yielded completely deprotected macrolactone **49** (2.1 mg, 3.5 μmol, 32%) as a colorless oil and a partially deprotected macrolactone with one remaining TBS group (2.3 mg, 3.2 μmol, 30%). $[\alpha]_D^{25}$ = +72.3 (*c* = 0.16, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 5.52 (dd, *J* = 9.5, 0.9 Hz, 1H), 5.35 (dq, *J* = 10.4, 6.9 Hz, 1H), 5.20 (ddq, *J* = 10.7, 9.0, 1.6 Hz, 1H), 5.02 (d, *J* = 9.2 Hz, 1H), 4.52 (m, 1H), 4.43 (t, *J* = 11.2 Hz, 1H), 4.14 (dd, *J* = 10.5, 4.0 Hz, 1H), 3.97 (dd, *J* = 9.0, 1.4 Hz, 1H), 3.97–3.93 (m, 1H), 3.92 (dd, *J* = 9.3, 3.6 Hz, 1H), 3.75 (dd, *J* = 9.1, 1.4 Hz, 1H), 3.67 (ddd, *J* = 11.7, 9.1, 4.0 Hz, 1H), 3.44 (d, *J* = 3.6 Hz, 1H), 3.28 (m, 1H), 3.16–3.07 (m, 1H), 3.12 (s, 3H), 3.04 (dq, *J* = 9.3, 7.0 Hz, 1H), 2.95 (dq, *J* = 8.8, 7.3 Hz, 1H), 2.92 (dq, *J* = 10.0, 7.0 Hz, 1H), 2.78 (d, *J* = 9.2 Hz, 1H), 2.64 (dd, *J* = 17.4, 9.4 Hz, 1H), 2.94 (dd, *J* = 17.4, 2.6 Hz, 1H), 1.60 (d, *J* = 1.0 Hz, 3H), 1.55 (dd, *J* = 6.8, 1.6 Hz, 3H), 1.49 (d, *J* = 1.1 Hz, 3H), 1.27 (d, *J* = 7.0 Hz, 3H), 1.17 (d, *J* = 6.9 Hz, 3H), 1.00 (d, *J* = 7.2 Hz, 3H), 0.98 (d, *J* = 7.0 Hz, 3H), 0.95 ppm (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6): δ = 215.2 (s), 214.4 (s), 212.2 (s), 172.2 (s), 137.3 (s), 134.7 (d), 133.9 (d), 133.3 (s), 129.3 (d), 122.8 (d), 84.0 (d), 79.4 (d), 78.0 (d), 71.6 (d), 69.1 (d), 65.6 (t), 60.3 (q), 54.0 (d), 52.9 (d), 50.1 (d), 48.4 (d), 45.8 (t), 45.6 (d), 30.7 (d), 21.3 (q), 16.6 (q), 15.4 (q), 14.6 (q), 13.2 (q), 11.8 (q), 10.8 (q), 10.2 ppm (q); IR (ATR): $\tilde{\nu}$ = 3467 (brs), 2957 (s), 2924 (ss), 2854 (s), 1739 (s), 1707 (ss), 1458 (s), 1376 (m), 1273 (s), 1203 (w), 1123 (m), 1084 (m), 995 (m), 860 (w), 722 cm^{-1} (w); HRMS (LC-MS): *m*/*z*: calcd for $C_{32}H_{50}O_{10}Na$: 617.3302 [*M*+Na]$^+$, found 617.3306.

(+)-Tedanolide (1): $NaHCO_3$ (1.0 mg) and *m*CPBA (0.7 mg, 4.2 μmol) were added to a cooled solution (−40 °C) of completely deprotected macrolactone **49** (2.1 mg, 3.5 mmol) in CH_2Cl_2 (0.4 mL). After 24 h the temperature was raised to −30 °C and an additional equivalent of *m*CPBA (0.6 mg, 3.5 μmol) was added. The reaction progress was monitored by reversed phase TLC (RP-18 F_{254S}, MeOH/H_2O 3:1) and showed complete consumption of all starting material after 2–3 d. The reaction mixture was diluted with CH_2Cl_2 and then transferred into sat. $NaHCO_3$ solution. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. After drying over $MgSO_4$ the solution was filtered and concentrated under vacuum. Purification via column chromatography (hexane/ethyl acetate 1:1) gave (+)-tedanolide (**1**) (0.6 mg, 1.0 μmol, 28%) as a colorless oil. $[\alpha]_D^{25}$ = +14.0 (*c* = 0.05, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.47 (dd, *J* = 8.5, 1.0 Hz, 1H), 5.46 (dq, *J* = 10.8, 6.8 Hz, 1H), 5.23 (ddq, *J* = 10.6, 10.4, 1.7 Hz, 1H), 4.31 (m, 1H), 4.26 (dd, *J* = 10.6, 4.1 Hz, 1H), 4.12 (t, *J* = 11.1 Hz, 1H), 4.11 (dd, *J* = 7.5, 1.0 Hz, 1H), 3.89 (dd, *J* = 7.9, 0.7 Hz, 1H), 3.68 (dd, *J* = 8.5, 1.4 Hz, 1H), 3.54 (ddd, *J* = 11.6, 9.4, 3.9 Hz, 1H), 3.44–3.37 (m, 1H), 3.30 (s, 3H), 3.24 (dd, *J* = 9.4, 3.6 Hz, 1H), 3.07–3.00 (m, 3H), 2.76 (d, *J* = 8.5 Hz, 1H), 2.61 (d, *J* = 9.2 Hz, 1H), 2.57 (dd, *J* = 16.7, 9.2 Hz, 1H), 2.47 (dd, *J* = 17.0, 3.1 Hz, 1H), 2.48–2.40 (m, 1H), 2.14 (d, *J* = 4.1 Hz, 1H), 1.62 (d, *J* = 1.4 Hz, 3H), 1.61 (dd, *J* = 8.2, 1.4 Hz, 3H), 1.39 (s, 3H), 1.28 (d, *J* = 7.2 Hz, 3H), 1.23 (d, *J* = 7.2 Hz, 3H), 1.12 (d, *J* = 6.5 Hz, 3H), 1.11 (d, *J* = 7.2 Hz, 3H), 1.09 ppm (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 215.6 (s), 214.2 (s), 212.8 (s), 171.4 (s), 136.3 (s), 130.0 (d), 129.3 (s), 125.2 (d), 83.0 (d), 79.6 (d), 77.0 (d), 71.2 (d), 68.3 (d), 66.7 (d), 63.9 (t), 62.8 (s), 60.5 (q), 53.3 (d), 52.0 (d), 49.6 (d), 48.3 (d), 45.5 (d), 44.8 (t), 31.1 (d), 18.5 (q), 16.6 (q), 15.3 (q), 14.3 (q), 13.4 (q), 11.4 (q), 10.6 (q), 10.2 ppm (q); HRMS (LC-MS): *m*/*z*: calcd for $C_{32}H_{50}O_{11}Na$: 633.3251 [*M*+Na]$^+$, found 633.3244.

Acknowledgements

This work was supported by the DFG (KA 913/9-1, KA 913/9-2). The authors thank Myriam Roy (Taylor group, University of Notre Dame) for helpful discussions.

[1] F. J. Schmitz, S. P. Gunasekera, G. Yalamanchili, M. B. Hossain, D. van der Helm, *J. Am. Chem. Soc.* **1984**, *106*, 7251.
[2] N. Fusetani, T. Sugawara, S. Matsunaga, H. Hirota, *J. Org. Chem.* **1991**, *56*, 4971.
[3] S. Nishimura, S. Matsunaga, M. Yoshida, H. Hirota, S. Yokoyama, N. Fusetani, *Bioorg. Med. Chem.* **2005**, *13*, 449.
[4] S. Nishimaura, S. Matsunaga, M. Yoshida, Y. Nakao, H. Hirota, N. Fusetani, *Bioorg. Med. Chem.* **2005**, *13*, 455.
[5] C. Chevallier, T. S. Bugni, X. Feng, M. K. Harper, A. M. Orendt, C. M. Ireland, *J. Org. Chem.* **2006**, *71*, 2510.
[6] T. L. Meragelman, R. H. Willis, G. M. Woldemichael, A. Heaton, P. T. Murphy, K. M. Snader, D. J. Newman, R. van Soest, M. R. Boyd, J. H. Cardellina, T. McKee, *J. Nat. Prod.* **2007**, *70*, 1133.
[7] a) O. Yonemitsu, *J. Synth. Org. Chem.* **1994**, *52*, 946; b) T. Matsushima, K. Horita, N. Nakajima, O. Yonemitsu, *Tetrahedron Lett.* **1996**,

37, 385; c) T. Matsushima, M. Mori, N. Nakajima, H. Maeda, J. Uenishi, O. Yonemitsu, *Chem. Pharm. Bull.* **1998**, *46*, 1335; d) J.-F. Liu, A. Abiko, Z. Pei, D. C. Buske, S. Masamune, *Tetrahedron Lett.* **1998**, *39*, 1873; e) R. E. Taylor, J. P. Ciavarri, B. R. Hearn, *Tetrahedron Lett.* **1998**, *39*, 9361; f) T. Matsushima, M. Mori, B.-Z. Zheng, H. Maeda, N. Nakajima, J.-I. Uenishi, O. Yonemitsu, *Chem. Pharm. Bull.* **1999**, *47*, 308; g) T. Matsushima, B.-Z. Zheng, H. Maeda, N. Nakajima, J. Uenishi, O. Yonemitsu, *Synlett* **1999**, 780; h) B.-Z. Zheng, H. Maeda, M. Mori, S. Kusak, O. Yonemitsu, T. Matsushima, N. Nakajima, J.-I. Uenishi, *Chem. Pharm. Bull.* **1999**, *47*, 1288; i) M. E. Jung, R. Marquez, *Tetrahedron Lett.* **1999**, *40*, 3129; j) W. R. Roush, G. C. Lane, *Org. Lett.* **1999**, *1*, 95; k) M. E. Jung, U. Karama, R. Marquez, *J. Org. Chem.* **1999**, *64*, 663; l) A. B. Smith III, S. A. Lodise, *Org. Lett.* **1999**, *1*, 1249; m) M. E. Jung, C. P. Lee, *Tetrahedron Lett.* **2000**, *41*, 9719; n) H. Matsushima, Nakajima, B.-Z. Zheng, O. Yonemitsu, *Chem. Pharm. Bull.* **2000**, *48*, 855; o) B.-Z. Zheng, M. Yamauchi, H. Dei, S. Kusaka, K. Matsui, O. Yonemitsu, *Tetrahedron Lett.* **2000**, *41*, 6441; p) B.-Z. Zheng, M. Yamauchi, H. Dei, O. Yonemitsu, *Chem. Pharm. Bull.* **2000**, *48*, 1761; q) M. E. Jung, R. Marquez, *Org. Lett.* **2000**, *2*, 1669; r) M. E. Jung, C. P. Lee, *Org. Lett.* **2001**, *3*, 333; s) T.-P. Loh, L.-C. Feng, *Tetrahedron Lett.* **2001**, *42*, 6001; t) T.-P. Loh, L.-C. Feng, *Tetrahedron Lett.* **2001**, *42*, 3223; u) K. Matsui, B.-Z. Zheng, S.-I. Kusaka, M. Kuroda, K. Yoshimoto, H. Yamada, O. Yonemitsu, *Eur. J. Org. Chem.* **2001**, 3615; v) B. R. Hearn, J. P. Ciavarri, R. E. Taylor, *Org. Lett.* **2002**, *4*, 2953; w) J. Hassfeld, M. Kalesse, *Synlett* **2002**, 2007; x) W. R. Roush, J. S. Newcom, *Org. Lett.* **2002**, *4*, 4739; y) J. Hassfeld, U. Eggert, M. Kalesse, *Synthesis* **2005**, 1183; z) G. Ehrlich, M. Kalesse, *Synlett* **2005**, 655; aa) Y. Iwata, K. Tanino, M. Miyashita, *Org. Lett.* **2005**, *7*, 2341; ab) C.-M. Wong, T.-P. Loh, *Tetrahedron Lett.* **2006**, *47*, 4485; ac) V. K. Nyavanandi, S. Nanduri, R. V. Dev, A. Naidu, J. Iqbal, *Tetrahedron Lett.* **2006**, *47*, 6667; ad) M. E. Jung, D. Yoo, *Org. Lett.* **2007**, *9*, 3543.

[8] A. B. Smith III, C. M. Adams, S. A. L. Barbosa, P. Degnan, *J. Am. Chem. Soc.* **2003**, *125*, 350; A. B. Smith III, C. M. Adams, S. A. L. Barbosa, P. Degnan, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 12042.

[9] A. B. Smith III, D. Lee, *J. Am. Chem. Soc.* **2007**, *129*, 10957.

[10] L. D. Julian, J. S. Newcom, W. R. Roush, *J. Am. Chem. Soc.* **2005**, *127*, 6186.

[11] G. Ehrlich, J. Hassfeld, U. Eggert, M. Kalesse, *J. Am. Chem. Soc.* **2006**, *128*, 14038.

[12] J. Mulzer, E. Öhler, *Angew. Chem.* **2001**, *113*, 3961; *Angew. Chem. Int. Ed.* **2001**, *40*, 3842.

[13] N. J. Leonard, Neelima, *Tetrahedron Lett.* **1995**, *36*, 7833.

[14] J. Mulzer, S. Dupre, J. Buschmann, P. Luger, *Angew. Chem.* **1993**, *105*, 1538; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1452.

[15] A. J. Mancuso, D. Swern, *Synthesis* **1981**, 165.

[16] I. Paterson, R. D. Tillyer, *J. Org. Chem.* **1993**, *58*, 4182.

[17] M. Kalesse, M. Quitschalle, C. P. Khandavalli, *Chem. Eur. J.* **2003**, *9*, 1129.

[18] a) S. D. Rychnovsky, D. J. Skalitzky, *Tetrahedron Lett.* **1990**, *31*, 945; b) S. D. Rychnovsky, B. N. Rogers, G. Yang, *J. Org. Chem.* **1993**, *58*, 3511; c) S. D. Rychnovsky, B. N. Rogers, T. I. Richardson, *Acc. Chem. Res.* **1998**, *31*, 9.

[19] M. Smith, D. H. Rammler, I. H. Goldberg, H. G. Khorana, *J. Am. Chem. Soc.* **1962**, *84*, 430.

[20] Y. Oikawa, T. Yoshioka, O. Yonemitsu, *Tetrahedron Lett.* **1982**, *23*, 889.

[21] S. Takano, N. Akiyama, K. Ogasawara, *Chem. Pharm. Bull.* **1984**, *32*, 791.

[22] S. V. Ley, J. Norman, W. P. Griffith, S. P. Marsden, *Synthesis* **1994**, 639.

[23] For semipreparative separation of **33** via HPLC a Merck LiChrospher 100 RP-18 column and methanol as eluent were used. Detection was performed via UV absorption at 250 nm.

[24] O. Dangles, F. Guibé, G. Bavaloine, *J. Org. Chem.* **1987**, *52*, 4984.

[25] O. Mitsunobu, *Synthesis* **1981**, 1.

[26] E. P. Boden, Keck, G. E. *J. Org. Chem.* **1985**, *50*, 2394.

[27] a) Y. Kita, H. Maeda, K. Omori, T. Okuno, Y. Tamura, *Synlett* **1993**, 273; b) Y. Kita, H. Maeda, K. Omori, T. Okuno, Y. Tamura, *J. Chem. Soc. Perkin Trans. 1* **1993**, 2999; c) B. M. Trost, J. D. Chisholm, *Org. Lett.* **2002**, *4*, 3743.

[28] N. Nakajima, K. Horita, R. Abe, O. Yonemitsu, *Tetrahedron Lett.* **1988**, *29*, 4139.

[29] D. B. Dess, J. C. Martin, *J. Org. Chem.* **1983**, *48*, 4155.

[30] C. Pakrash, S. Saleh, I. A. Blair, *Tetrahedron Lett.* **1989**, *30*, 19.

[31] K. N. Fleming, R. E. Taylor, *Angew. Chem.* **2004**, *116*, 1760; *Angew. Chem. Int. Ed.* **2004**, *43*, 1728.

[32] The ylide was prepared according to: H.-J. Bestmann, H. Hartung, *Chem. Ber.* **1966**, *99*, 1198.

Received: September 27, 2007
Published online: December 28, 2007

