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New Solutions to the C-12,13 Stereoproblem of Epothilones B and D; Synthesis of a 12,13-Diol-Acetonide Epothilone B Analog

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New approaches are described to the synthesis of epothilone B and a 12,13-diol-acetonide derivative. Specifically the (12*Z*) double bond is formed quantitatively by a silicon-tethered ring-closing metathesis (RCM) reaction with 85 % selectivity. Alternatively, a direct route to the 12,13-epoxide by cyclization of a 12,13-diol has been developed.

Epothilone B (**1**)[1] shows outstanding microtubule binding affinities and cytotoxity against tumor cells and multiple drug resistant tumor cell lines.[2] The role of **1** as a potential paclitaxel successor has initiated intense interest in its synthesis, resulting in numerous total syntheses of **1** and numerous derivatives thereof.[3]

A central issue in most syntheses of epothilone B, in particular when aiming for the larger scale, has been the introduction of a 12*R*,13*R*-configured trisubstituted epoxide. The standard solution of this problem is the synthesis of the deoxy precursor, epothilone D (**2**) with a 12,13-(*Z*) double bond, which is epoxidized to give epothilone B in the last step of the sequence (Scheme 1). Alternatively, the 12,13-epoxide has been introduced with high stereocontrol relatively early, and has then been carried through the sequence to furnish **1** directly.[4]

In both variants, the key step is an aldol addition of an enolate **4** or **6** ("southern fragment") to an aldehyde **3** or **5** ("northern fragment"). We report contributions to both variations and furthermore, the synthesis of a 12,13-diol derivative **7** will be described in detail.[5]

For a stereocontrolled synthesis of the (12*Z*) double bond in a "northern fragment" such as **3** a surprisingly wide variety of approaches have been reported among which Danishefsky's *B*-alkyl Miyaura–Suzuki coupling[6] has found particularly widespread application, notwithstanding the low overall yield of 33 %.[7] Alternatively, Wittig[8] or Still–Gennari[9] carbonyl olefinations, organometallic additions to alkynols,[10] allylstannane–carbonyl addition,[11] allylic rearrangement[12] or the functionalization of nerol[3d] have also been used to solve the problem.

Our approach was to enforce the (*Z*) geometry of the 12,13-olefin by incorporating it into a relatively small ring, with a maximum ring size of 8 (Scheme 2). Hence, the lactone **10** could be envisaged as a suitable precursor of **3**. Following literature precedence,[13] **10** could be generated through a [3.3]-sigmatropic rearrangement of the ketene acetal **11**, which was to be prepared from the carbonate **12** by a Tebbe olefination or from *ortho*-acetal **13** by a Claisen–Johnson protocol.

In fact, the known aldehyde **14**[8,9] was converted into a 60:40 diastereomeric mixture of diols **15** (Scheme 3). Treatment with triphosgene furnished the cyclic carbonate **12**, again as a 60:40 mixture of isomers. However, all attempts to convert **12** into **11** with Tebbe's reagent failed. Thus, the **15a/b** mixture was heated with triethyl orthoacetate and a catalytic amount of amberlyst 15. Three products were isolated: *ortho*-acetal **13** (22 %) as a pure diastereomer and the two rearranged products **17** (10 %) and **18** (8 %) as diastereomeric mixtures with chiral centers at C-3 and C-6, respectively. The rest of the material was polymeric. Obviously, of the two diastereomers of **15**, **15b** has undergone polymerization, whereas **15a** has formed a cyclic ketal **13**, in which the two vinylic appendages and the methyl group adopt equatorial positions. The OEt substituent is axial and can easily be eliminated after protonation to form the oxonium species **16**, which adds ethanol to generate **17** and **18**, respectively (Scheme 3).

As the next possibility the formation of an eight-membered lactone by ring-closing metathesis[14] (RCM) was envisaged (Scheme 4). To avoid competition from an additional double bond, the bis-olefin **20**, readily available from the known[4b] precursor **19**, was used as the RCM substrate. However, on treatment with Grubbs' second-generation catalyst (**A**)[15] or the Grubbs–Hoveyda catalyst (**B**),[16] only the (*E*) dimer **22** was obtained in low yield. A similar result was observed with the ketone **21**, which gave the dimer **23** with both catalysts (Figure 1).

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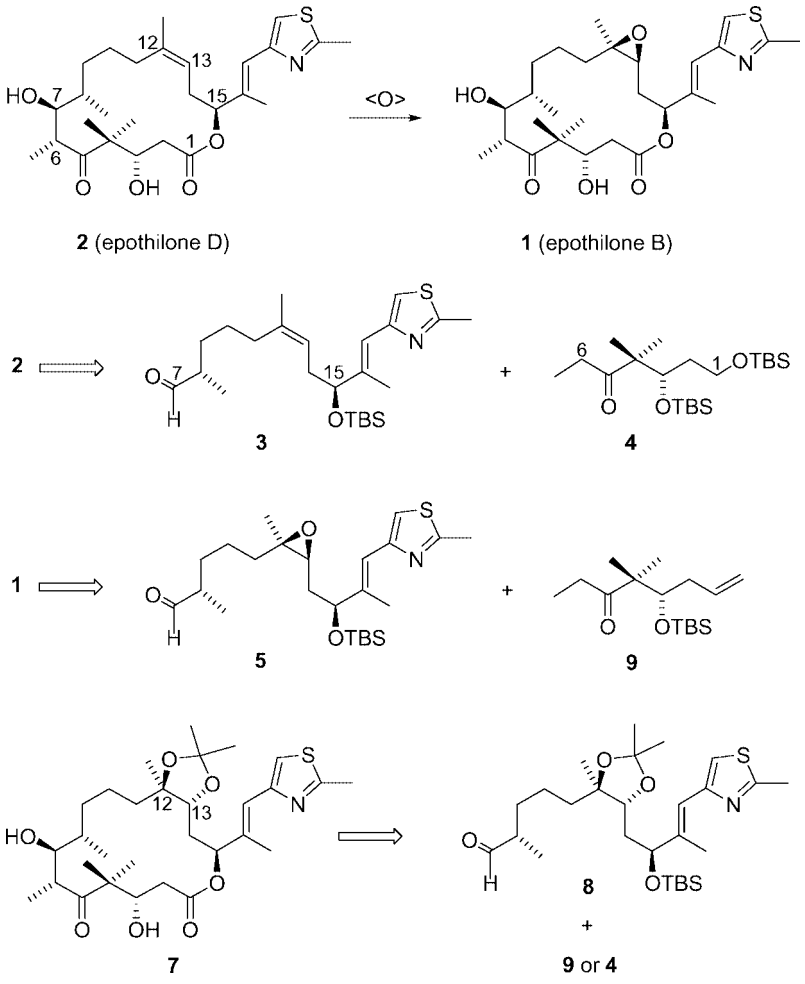
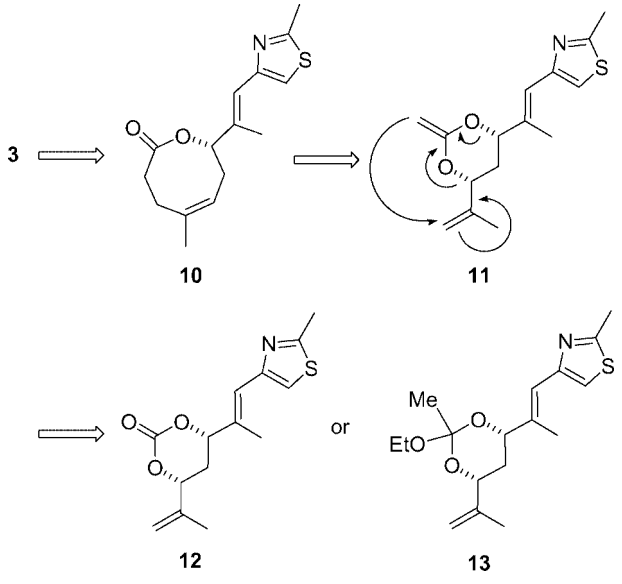
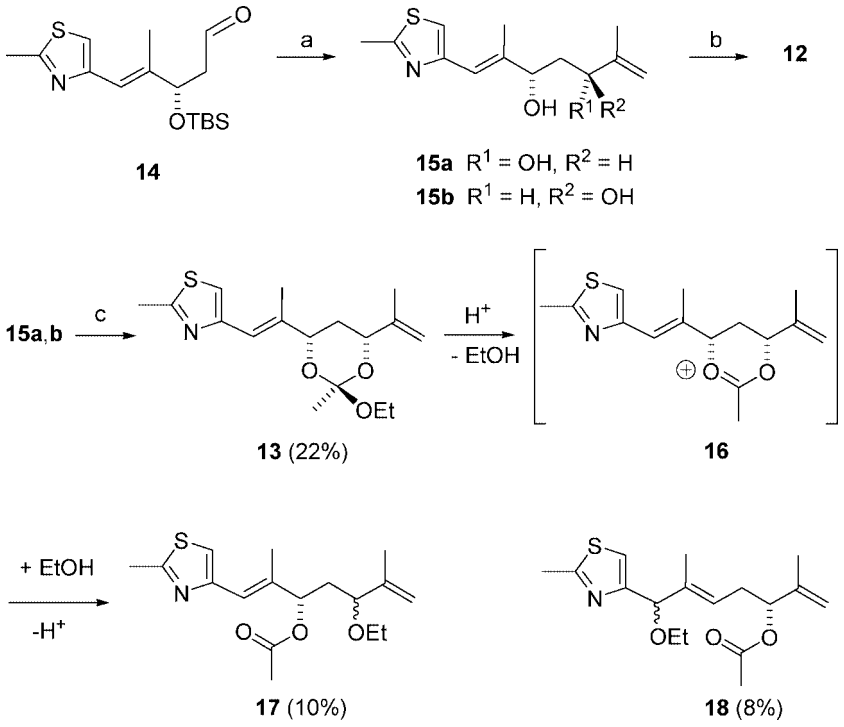


Scheme 1. Retrosynthetic considerations.

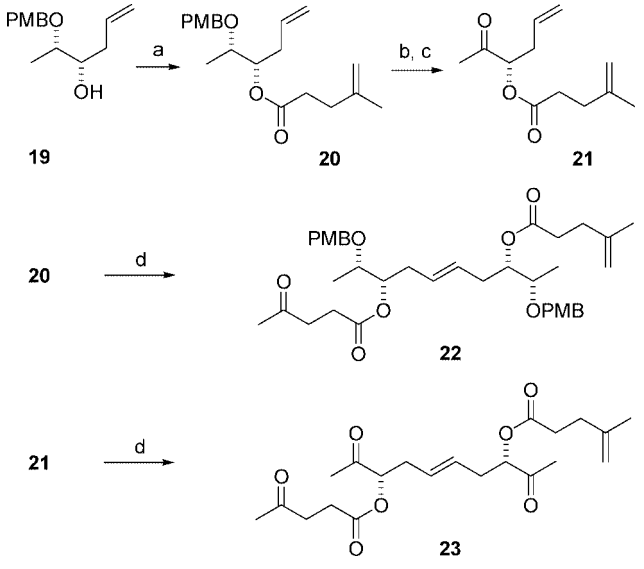


Scheme 2. Retrosynthesis of Northern fragment **3**.

We reasoned that there was too much steric hindrance in the transition state and decided to induce strain relief by using a silicon tether.[17] As silicon is bigger in size and has more polarizable soft d orbitals, its bonds are more easily distorted. On the basis of these considerations the siloxane **25** emerged as a suitable RCM substrate (Scheme 5). Compound **25** was prepared in one pot by deprotonating the alcohol **19** with *n*-butyllithium followed by addition of Me_2SiCl_2.[18] The intermediate **24** was not isolated but was treated with a THF solution of 3-methyl-3-butenol and DMAP.[19] The RCM was carried out with catalysts **A** and **B**. Both reactions gave more than 95% yield of cyclized product **26**, when the catalyst was added by syringe pump over 16 hours under reflux in dichloromethane and high dilution. The geometrical isomers were separated after conversion of the silaketal **26** into the diol **27**. The *Z*/*E* ratio was 5:1 for each catalyst. Temperature variation had no influence neither on the yield (85–90% at room temperature) nor on the selectivity (1:4–5). in contrast, catalyst addition was crucial for the yield. When the catalyst was added in one portion the yield dropped to 50%. This strong dependence of the yield on the mode of catalyst addition indicates that, for the RCM process, low catalyst concentration is of the essence. It appears that the decomposition of the catalyst is of higher order and will thus be increased with the concentration. Our findings are complementary to other re-



Scheme 3. Reagents and conditions: a) i. isopropenylmagnesium bromide, THF, 0 °C, 1 h, 97%; ii. TBAF, THF, room temp., 3 h, 97%; b) triphosgene, Et_3N, pyridine, DCM, 1 h, –78 °C to room temp., 93%; c) amberlyst 15, triethyl orthoacetate (1 equiv.), xylene, 70 °C, 1 h, 40%.



Scheme 4. Reagents and conditions: a) 4-methyl-4-pentenoic acid, EDCI, DMAP, DCM, 0 °C, 3 d, 83%; b) DDQ, DCM/H_2O, (20:1), 0.5 h, 79%; c) DMP, DCM, $NaHCO_3$, 4.5 h, 91%; d) **A** or **B** (15 mol-%), DCM, (2.6 mM), 40 °C, 16 h.

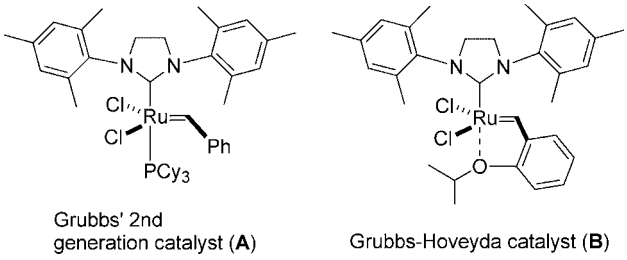
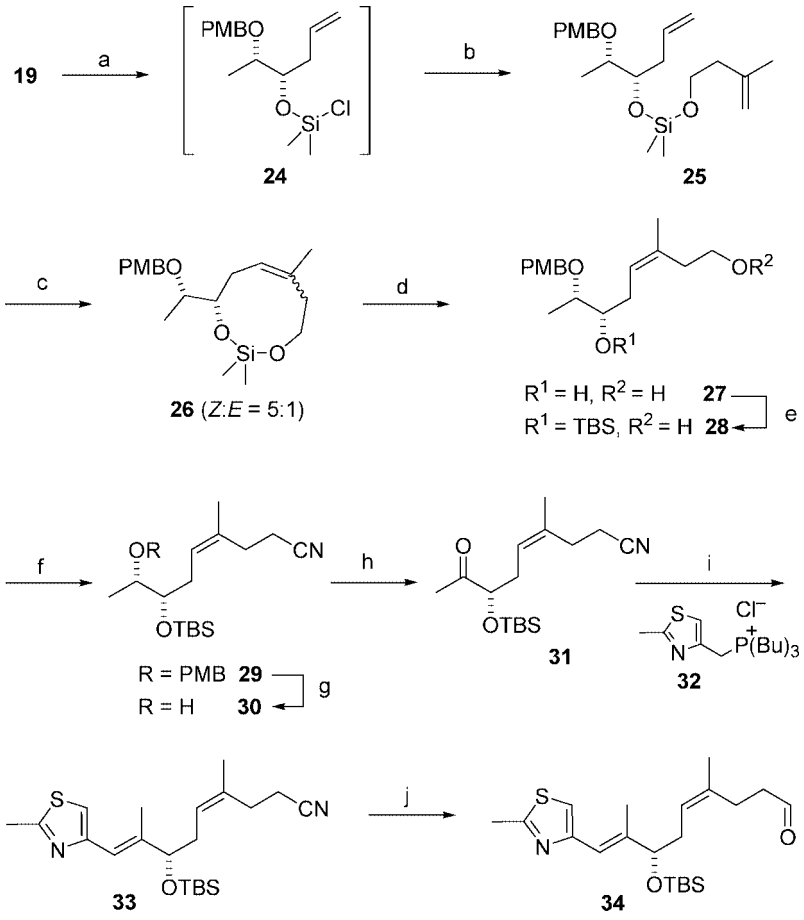


Figure 1. Structures of the catalysts **A** and **B**.

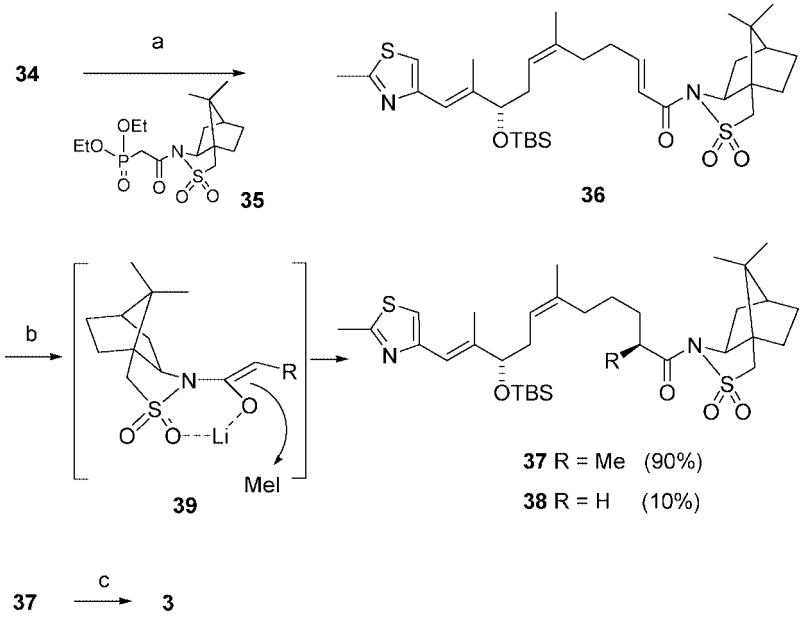
ports which state that in RCM reactions it is primarily the substrate concentration that has to be kept low.[14]

Compound (*Z*)-**27** was di-protected with TBSOTf and selectively deprotected at the primary position with HF/pyridine to give **28** in a one-pot reaction (Scheme 5). Next, a C1 chain elongation was accomplished by a Mitsunobu reaction of **28** with 2-hydroxy-2-methylpropionitrile to give nitrile **29**.[20] After PMB deprotection and Dess–Martin periodinane oxidation, the ketone **31** was obtained and then subjected to a Wittig reaction with the phosphonium salt **32**,[9b] which introduced the thiazole moiety to give the (*E*)-olefin **33**. The nitrile group was smoothly reduced to the desired aldehyde **34**. The HWE reaction of **34** with Oppolzer phosphonate **35**[21] gave pure (*E*)-enone **36** (Scheme 6). 1,4-Reduction of **36** and in situ quenching of the enolate with MeI gave the diastereomerically pure methyl compound **37** in 90% yield along with 10% of unmethylated product **38**. The last step was the reductive removal of the auxiliary with DIBALH to afford the aldehyde **3** in 90% yield. The stereoselectivity for the introduction of the methyl group from stereogenic center C8 is rationalized in terms of enolate **39**, which is alkylated from the less hindered face. in conclusion, a synthesis of the northern fragment **3** from (*S*)-methyl lactate in 14 steps and an overall yield of 18% was achieved.

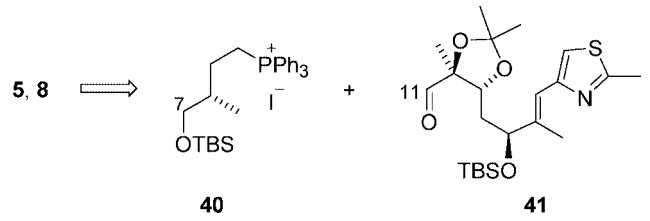
For the synthesis of the aldehydes **5** and **8**, a Wittig reaction between the aldehyde **41** and the phosphonium salt **40** was envisaged first (Scheme 7).



Scheme 5. Reagents and conditions: a) THF, –78 °C, *n*BuLi, then $SiMe_2Cl_2$, room temp.; b) 3-methyl-3-butenol, DMAP, DMF, room temp., 24 h, 84%; c) **A** or **B** (15 mol-%), DCM (2.6 mM), 40 °C, 16 h, 98%; d) i. TBAF, THF, 12 h, 84%, ii. TBSOTf, DCM, 2,6-lutidine; e) HF/pyridine, 86%; f) PPh_3, DEAD, 2-hydroxy-2-methylpropionitrile, Et_2O, 0 °C to room temp., 22 h, 89%; g) DDQ, DCM/H_2O, (20:1), 0.5 h, 91%; h) $(COCl)_2$, DCM, DMSO, Et_3N, –78 °C, 1 h, 95%; i) **32**, *n*BuLi, THF, 0 °C, 1 h, then **31**, –78 °C to –60 °C, 1 h, 94%; j) DIBAL-H, toluene, –78 °C, 2 h, 84%.



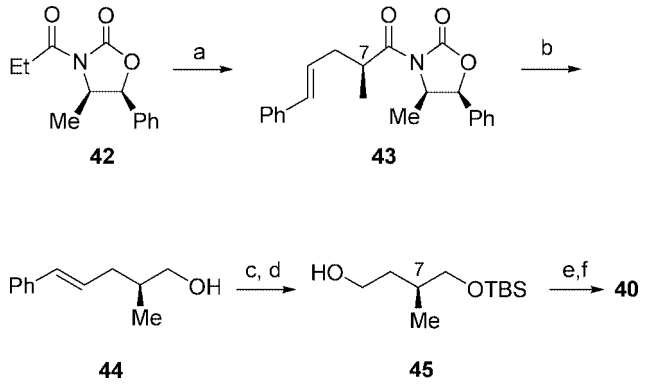
Scheme 6. Reagents and conditions: a) **35**, LiOH, THF, 0 °C, 0.5 h, 83%; b) i. L-selectride, THF, –78 °C, ii. LDA, MeI, HMPA, 16 h, room temp., 90%; c) DIBAL-H, –90 °C, DCM, 0.5 h, 90%.



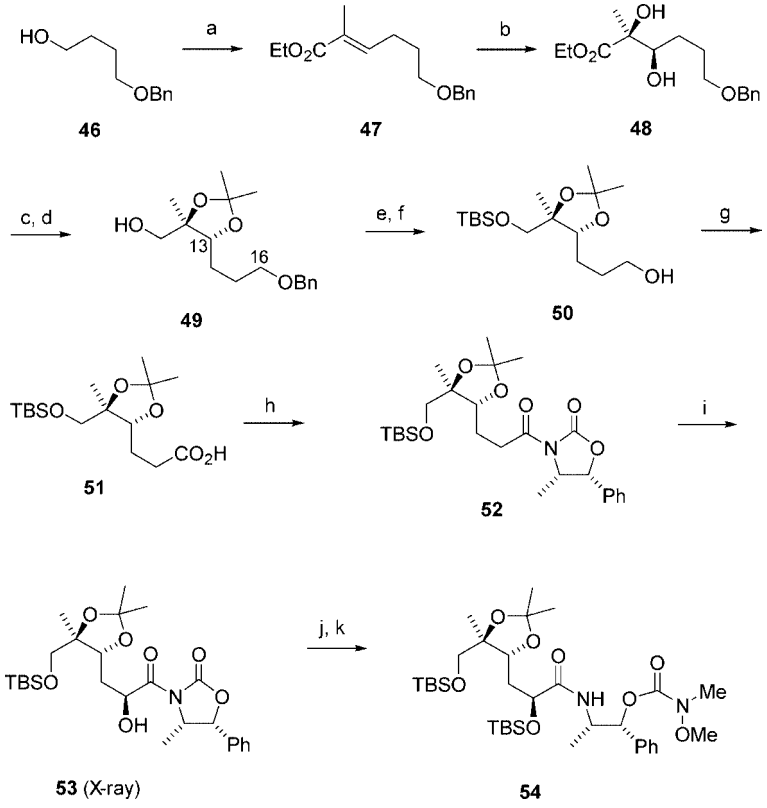
Scheme 7. Retrosynthesis of Northern fragments **5** and **8**.

As shown in Scheme 8, the phosphonium salt **40** was prepared by an alkylation of the Evans' oxazolidinone **42** with cinnamyl bromide[22] to give **43** with high stereocontrol. Reductive removal of the auxiliary gave the known alcohol **44**,[23] which after TBS protection was converted into **40**.

The attempted synthesis of the aldehyde **41** (Scheme 9) started with the monobenzylated butane-1,4-diol **46**, which was converted into the (*E*)-enoate **47**. Sharpless' AD reaction[24] proceeded with 94–96% *ee* to give **48**, which was protected as the acetonide and then reduced to the alcohol **49**. Protective-group manipulation gave **50**, which was oxidized to acid **51**. Formation of the Evans' oxazolidinone **52**



Scheme 8. Reagents and conditions: a) 1.1 equiv. NaHMDS, THF, then cinnamyl bromide, –78 °C to room temp., 4 h, 76% (> 96:4 *dr*); b) 1.2 equiv. $LiBH_4$, 1.1 equiv. H_2O, Et_2O, 0 °C to room temp., 2 h, 90%; c) TBSCl, imidazole, DMF, room temp., 3 h, 99%; d) NMO, OsO_4 (2 mol-%), THF/*t*BuOH/H_2O, room temp., 16 h; then $NaIO_4$, THF/H_2O, room temp. 3 h; then $NaBH_4$, MeOH, 0 °C, 15 min, 89%; e) 3 equiv. imidazole, 1.5 equiv. PPh_3, 1.5 equiv. I_2, Et_2O/MeCN (3:1), 0 °C, 30 min; f) 1.5 equiv. PPh_3, neat, 90 °C, 5 h, 76%.



Scheme 9. Reagents and conditions: a) i. DMSO, oxalyl chloride, –78 °C, then diisopropylethylamine; ii. 1.1 equiv. ethyl 2-(triphenylphosphoranylidene)propionate, THF, 80 °C, 4 h, 84%; b) AD-mix β, $MeSO_2NH_2$, *t*BuOH/H_2O (1:1), room temp., 12 h, 96% (>98% *ee*); c) $(MeO)_2CMe_2$, CSA, room temp., 38 h, 99%; d) 3 equiv. DIBAL-H, THF, 0 °C to room temp., 12 h, 94%; e) TBSCl, imidazole, DMF, room temp., 3 h, 99% f) Pd/C (10%), ethyl acetate, H_2 (1 bar), room temp., 28 h, 92%; g) i. Dess–Martin periodinane, pyridine, CH_2Cl_2, room temp., 4 h, ii. 5 equiv. $NaClO_2$, NaH_2PO_4, 2,3-dimethylbut-2-ene, *t*BuOH/H_2O), room temp., 50 min, 93%; h) 1.1 equiv. NEt_3, 1.0 equiv. PivCl, Et_2O, –78 to 0 °C, 1 h, then Li salt of (4*S*,5*R*)-4-methyl-5-phenyl-1,3-oxazolidinone, THF, –78 to 0 °C, 1 h, 76%. i) 1.4 equiv. NaHMDS, THF, –78 °C, 1 h, then 1.8 equiv. Davis oxaziridine, –92 °C, 5 min, then NH_4Cl, –92 °C to room temp., 10 min, 53% (> 96:4 *dr*); j) TBSOTf, 2,6-lutidine, CH_2Cl_2, room temp., 14 h, 95%; k) 4 equiv. $H_2N(OMe)MeCl$, THF, $AlMe_3$ (2 M in toluene), room temp., 45 min, 74%.

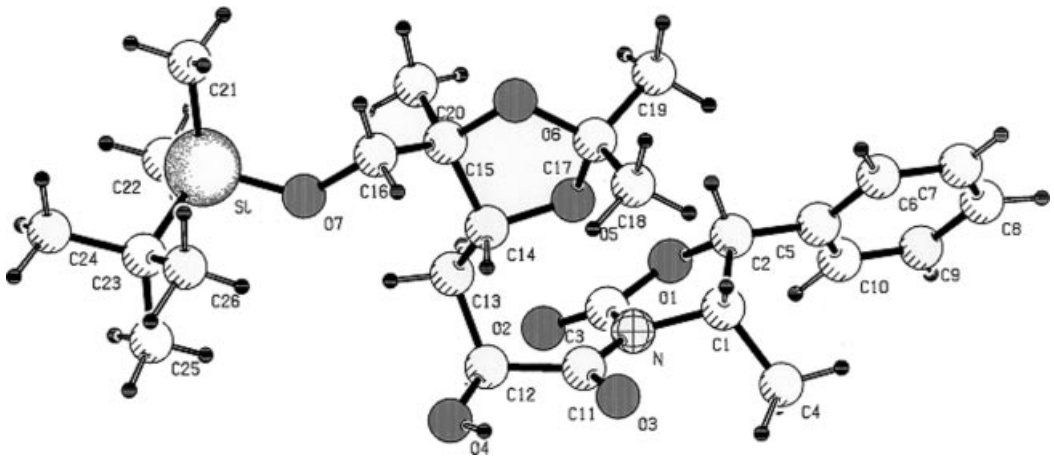
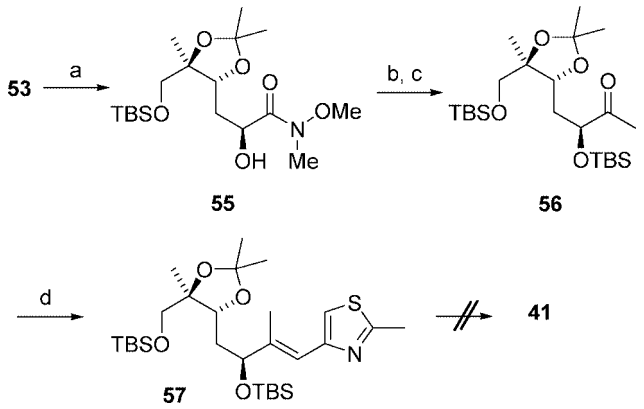


Figure 2. Crystal structure of compound **53**.

was followed by a Davis' hydroxylation[25] to form **53** whose structure was confirmed by single-crystal diffraction[26] (Figure 2).

TBS protection of the secondary alcohol prior to treatment with Weinreb's amine led to the formation of the carbamate **54**. Therefore (Scheme 10), **53** was directly converted into the Weinreb amide **55**. TBS protection, followed by addition of methyllithium, generated the methyl ketone **56**, which was subjected to a Wittig reaction furnishing the (*E*)-olefin **57**. However, all attempts to remove the primary OTBS protecting group without touching the secondary one or the acetonide failed, so that the aldehyde **41** could not be obtained. Hence, the Wittig reaction of **40** with the truncated aldehyde **58** was tried next (Scheme 11). The alcohol **49** was oxidized to the aldehyde **58** and then subjected to the envisaged Wittig reaction. Indeed, the olefin **59** was obtained as an *E*/*Z* mixture, which was hydrogenated with Pd/Al_2O_3 (Pd/C also removed the TBS group).



Scheme 10. Reagents and conditions: a) 4 equiv. $H_2N(OMe)MeCl$, 4 equiv. *i*PrMgBr, THF, –10 °C to room temp., 2 h, 80%; b) TBSOTf, 2,6-lutidine, CH_2Cl_2, room temp., 14 h, 95%; c) 1.2 equiv. MeLi, THF, –78 °C, 2.5 h, 67%; d) 2, 2 equiv. KHMDS, THF, –78 to 45 °C, 1 h, 54% (*E*/*Z*, 30:1).

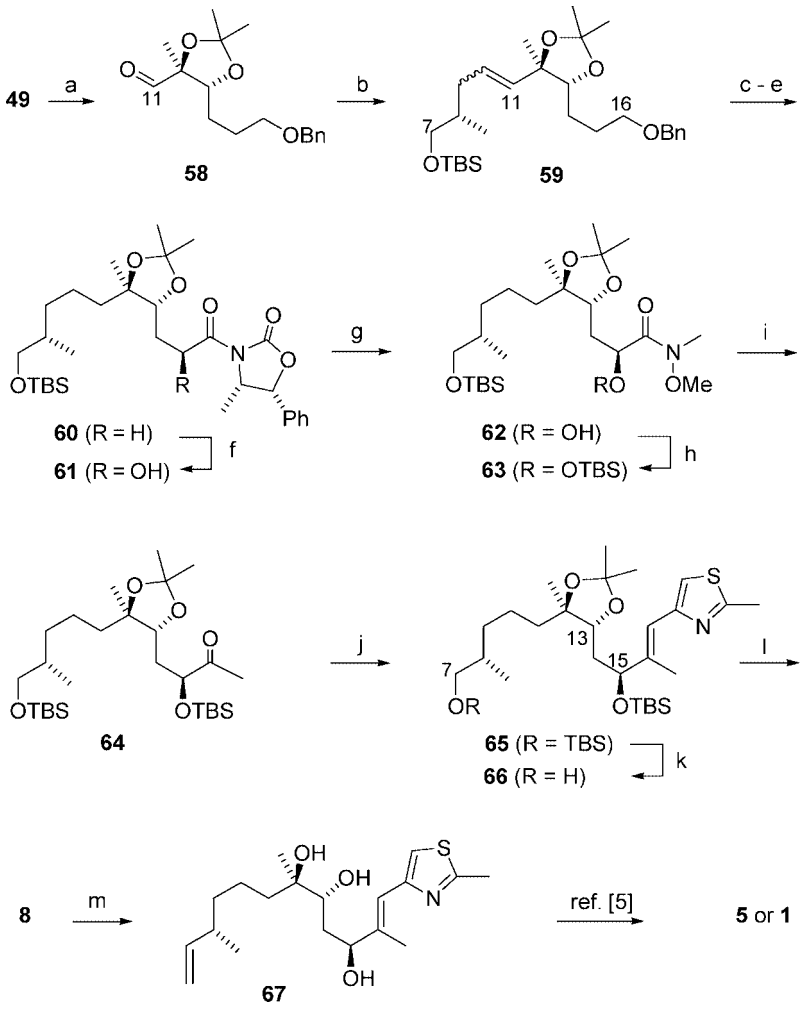
The conversion of **59** to **64** followed essentially the same protocol as described above. Wittig olefination of **64** with **32**, selective desilylation of the primary OH group and Swern oxidation led to the aldehyde **8**. For the conversion into **5**, the aldehyde **8** was methylenated and globally deprotected to give the triol **67**, whose conversion into the aldehyde **5**, and finally into **1** has been described before.[5]

For the synthesis of **7**, the aldol addition to the aldehyde **8** was performed with ketones **4** (Scheme 12) and **9** (Scheme 13). With the enolate of the ketone **4**, the aldehyde **8** gave the aldol adducts **68a** and **68b** in a ratio of 6:1 and 83% combined yield. After chromatographic separation, **68a** was converted into the alcohol **70**, which was oxidized to the acid **71**. After selective desilylation of the 15-OTBS group the *seco*-acid **72** was obtained, which was cyclized to the macrolide **73** under Yamaguchi conditions.[27] Desilylation of **73** gave **7**.

In the second approach (Scheme 13), the aldehyde **8** was treated with the enolate of the ketone **9**. This compound was preferred to the TBS-analog **6**, because it was thought that the TES group would be easier to remove than the bulkier TBS group. Aldol addition of **9** to **8** furnished the adduct **74** as the main diastereomer (6:1:1), which was separated by chromatography. After TBS protection of the 7-OH group, however, it turned out that the 15-OTBS in **75** group could not be selectively removed in the presence of the 3-OTES. Therefore, **74** was converted into the compound **76** by a desilylation–resilylation sequence. Acid **71** was obtained from **76** by oxidative cleavage of the double bond.

The epothilone derivative **7** was tested for its activity against breast tumor cells MCF-7. However, no reduction in the proliferation rate was observed.

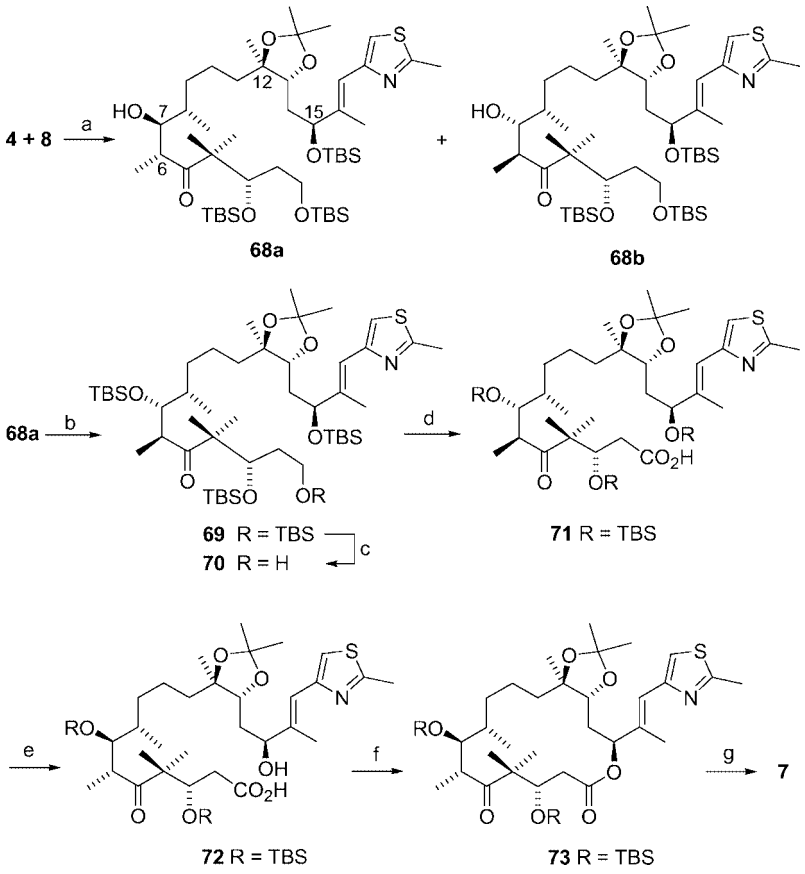
In conclusion, efficient syntheses have been presented of the aldehydes **3**, **5** and **8**, which have been used as key intermediates in the synthesis of epothilones. Specifically, the aldehyde **8** was elaborated into the novel epothilone B derivative **7**. It was demonstrated that the presence of a dioxolane ring across the 12,13 position is fatal for the antiprolific activity.



Scheme 11. Reagents and conditions: a) Dess–Martin periodinane, pyridine, CH_2Cl_2, room temp., 4 h; b) 1.1 equiv. NaHMDS, THF, 0 °C, 30 min, then **40**, 0 °C to room temp., 30 min, 87% over two steps; c) H_2, Pd/Al_2O_3 cat., EtOH, 3 bar, room temp., 36 h, 91%; d) 4 equiv. $NaIO_4$, 0.05 equiv. $RuCl_3$–H_2O, CCl_4/MeCN/H_2O (2:2:3), room temp., 80 min, 88%; e) 1.1 equiv. NEt_3, 1.0 equiv. PivCl, Et_2O, –78 to 0 °C, 1 h, then Li salt of (4*S*,5*R*)-4-methyl-5-phenyl-1,3-oxazolidinone, THF, –78 to 0 °C, 1 h, 80%; f) 1.4 equiv. NaHMDS, THF, –78 °C, 1 h, then 1.8 equiv. Davis oxaziridine, –84 °C, 5 min, then NH_4Cl, –84 °C to room temp., 10 min, 66% (> 96:4 *dr*); g) 4 equiv. $H_2N(OMe)MeCl$, 8 equiv. *i*PrMgCl, THF, –10 to 0 °C, 1 h, 94%; h) TBSOTf, 2,6-lutidine, CH_2Cl_2, 0 °C, 1 h, 97%; i) 1.1 equiv. MeLi, THF, –78 °C, 90 min, 91%; j) 5 equiv. **32**, 5 equiv. KHMDS, THF, –78 to 45 °C, 1 h, 98% (*E*/*Z*, 30:1); k) 1 equiv. CSA, CH_2Cl_2/MeOH (1:1), 0 °C, 7 h, 97%; l) 1.3 equiv. Dess–Martin periodinane, pyridine, CH_2Cl_2, 0 °C, 4 h. 97%; m) i. triphenylmethylphosphonium iodide, *n*BuLi, hexane/THF; ii. TBAF (1 M in THF), THF, room temp., 5 h; iii. EtOH, 1 M HCl, 75%.

Experimental Section

General Remarks: Solvents were purified and dried according to common procedures. Dry solvents were stored under argon over molecular sieves. All commercially available reagents were purchased in the best quality available and used without further purification. TLC was carried out with E. Merck Silica gel 60-F254 plates. The plates were usually developed with a mixture of hexane/ethyl acetate. Unless the compound was colored, UV-active spots were detected at long-wave UV (365 nm) or short-wave UV (254 nm). Most plates were additionally treated with visualization reagents. Preparative column chromatography and flash chromatography[28] were performed with Silica gel 60 from Merck (0.040–0.063 μM, 240–400 mesh). Eluents were hexanes (hex) and ethyl acetate (EE). NMR spectra were recorded with either a Bruker Avance DPX 250 MHz, a Bruker Avance DRX 400 MHz or a Bruker Avance DRX 600 MHz spectrometer. Unless otherwise stated, all NMR spectra were measured in $CDCl_3$ solutions and referenced to the residual $CDCl_3$ signal (^1H, δ = 7.26; ^{13}C, δ = 77.0 ppm) or the TMS signal (^1H, δ = 0.0; ^{13}C, δ = 0.0 ppm). The following abbreviations are used to describe spin multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, mc = centered multiplet, br = broad, dd = doublet of doublets, dt = doublet of triplets, dq = doublet of quartets, ddd = doublet of doublet of doublet, dddd = doublet of doublet of doublet of doublet etc.; other combinations derive from those listed. Coupling constants *J* are given in Hz; assignments of proton resonances were confirmed, when possible, by selective homonuclear decoupling experiments or by correlation spectroscopy. Mass spectra were measured on spectrometers from Micro Mass, Fisons Instrument and Trio200. Stated, is the kind of ionization (in most cases **E**I, **E**lectron **I**mpact; occasionally FAB, **F**ast **A**tom **B**ombardment) and electron activation energy (in eV). HRMS (**H**igh **R**esolution **M**ass **S**pectra) were taken with a Finnigan MAT 8230 with a resolution of 10000. IR spectra were recorded with a Perkin–Elmer 1600 Series FTIR spectrometer and are reported in wave numbers

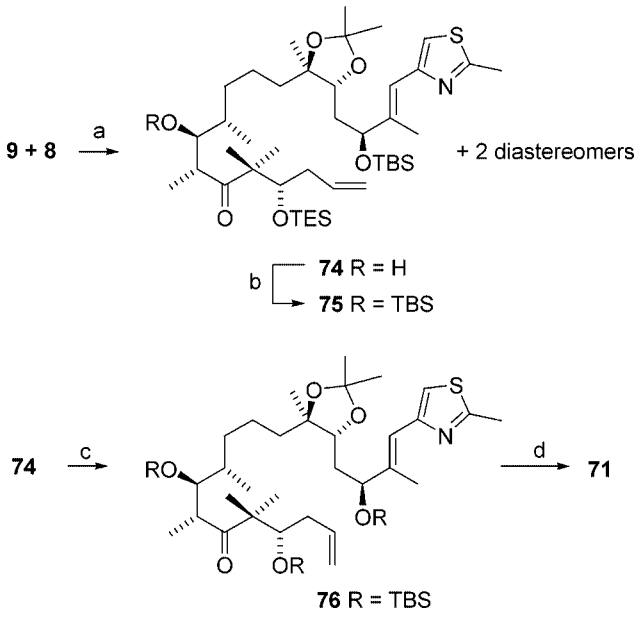


Scheme 12. Reagents and conditions: a) **4**, LDA, THF, –78 °C, 45 min, then **8**, 50 min, 73% (**68a**/**68b** = 6:1); b) TBSOTf, 2,6-lutidine, CH_2Cl_2, 0 °C, 12 h, 93%; c) CSA, CH_2Cl_2/MeOH (1:1), 0 °C, 8 h, 84%; d) i. 1.3 equiv. Dess–Martin periodinane, pyridine, CH_2Cl_2, 0 °C, 2 h, ii. 5 equiv. $NaClO_2$, NaH_2PO_4, 2,3-dimethylbut-2-ene, *t*BuOH/H_2O, room temp., 50 min, 93%; e) 7 equiv. TBAF, THF, room temp., 12 h 82%; f) 1.2 equiv. 2,4,6-trichlorobenzoyl chloride, 2 equiv. NEt_3, toluene, room temp., 2 h, then add to a solution of 10 equiv. DMAP in toluene, 110 °C, 3 h, 50% over two steps; g) 15% CF_3CO_2H in CH_2Cl_2, –18 to 0 °C, 6 h, 80%.

$\tilde{\nu}_{max}$ (cm^{-1}). All compounds were measured as a thin film on a silicon crystal plate (Si pellet). Elemental analyses were recorded on a Perkin–Elmer 240 Elemental analyser. Optical rotations were measured on a P 341 Perkin–Elmer polarimeter. The length of the measuring chamber is 1 dm and the solution is kept at 20.0 °C. The optical rotation is measured with monochromatic sodium light (589 nm).

(3*S*,5*R*/5*S*,*E*)-2,6-Dimethyl-1-(2-methylthiazol-4-yl)hepta-1,6-diene-3,5-diol (15a/15b): Aldehyde **14** (177 mg, 0.54 mmol) in THF (5 mL, 0.1 M) was cooled to 0 °C. Isopropenylmagnesium bromide (2 mL, 0.5 M in THF) was added dropwise via a syringe. The cooling bath was removed and the reaction stirred for 1 h. The reaction was diluted with diethyl ether, quenched with a saturated NH_4Cl solution, and the phases were separated and extracted with diethyl ether (3 × 25 mL). The combined organic layers were washed with brine and dried with $MgSO_4$. The solvents were removed under reduced pressure to yield the desired product 200 mg (99%) as an epimeric mixture, which was used without any further purification. A TBAF solution (2 mL, 1 M in THF) was added to the crude product and stirred for 3 h. The reaction was diluted with diethyl ether, quenched with a saturated NH_4Cl solution, the phases were separated and extracted with diethyl ether (3 × 25 mL). The combined organic layers were washed with brine and dried with $MgSO_4$. The solvents were removed under reduced pressure and the crude product was purified by column chromatography (hex/EE, 1:1) to yield 135 mg (97%) of the desired product. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.68 (s, 3 H), 1.74–1.71 (m, 1.2 H), 1.86–1.78 (m, 0.8 H), 1.95 (d, *J* = 1.26 Hz, 1.2 H), 1.96 (d, *J* = 1.26 Hz, 1.8 H), 2.62 (s, 3 H), 3.34 (s, 0.5 H), 3.63 (s, 0.5 H), 4.27 (t, *J* = 6.2 Hz, 1 H), 4.35 (t, *J* = 6.2 Hz, 1 H), 4.94 (s, 0.6 H), 4.99 (s, 0.4 H), 6.52 (s, 0.6 H), 6.57 (s, 0.4 H), 6.86 (s, 1 H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 14.8 ppm. 15.5, 19.1, 19.5, 29.3, 30.7, 73.3, 74.8, 76.6, 78.5, 110.8, 111.2, 115.8, 115.9, 118.6, 119.1, 129.2, 131.2, 142.3, 142.4, 147.6, 147.7, 153.1, 153.2, 165.1, 168.1. IR (Si, film): $\tilde{\nu}_{max}$ = 3351, 2922, 1726, 1280, 1074, 861, 547, 477 cm^{-1}.

(4*S*,6*R*,*E*)-4-[1-(2-Methylthiazol-4-yl)prop-1-en-2-yl]-6-(prop-1-en-2-yl)-1,3-dioxan-2-one (12): To a solution of the diol **15a**,**b** (100 mg, 0.4 mmol) in DCM (11 mL), pyridine (303 μL) and triethylamine (1.04 mL) were added and cooled to –78 °C. Triphosgene (152 mg, 0.5 mmol) in DCM (4 mL) was added dropwise. The solution turned yellow. Then the reaction mixture was warmed to room temp. and the solution turned deep red-purple. The reaction was quenched with a saturated NH_4Cl solution, the phases were separated, and the water phase was extracted with diethyl ether (3 × 25 mL). The combined organic layers were washed with brine and dried with $MgSO_4$. The solvents were removed under reduced pressure and the crude product was purified by column chromatography (hex/EE, 2:1) to yield 103 mg (93%) of the desired product. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.72 (s, 1.2 H), 1.75 (s, 1.8 H), 2.01–1.91 (m, 0.8 H), 2.07 (s, 3 H), 2.18–2.12 (m, 1.2 H), 2.64 (s, 3 H), 4.92–4.81 (m, 2 H), 5.08–4.97 (m, 2 H), 6.46 (s, 0.4 H), 6.53 (s, 0.6 H), 6.96 (s, 1 H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 14.4,



Scheme 13. Reagents and conditions: a) **9**, LDA, THF, –78 °C, 45 min, then **8**, 20 min, 70% (6:1:1); b) TBSOTf, 2,6-lutidine, CH_2Cl_2, room temp., 3 h; c) TBAF, THF, –18 °C, 80 min; then TBSOTf, 2,6-lutidine, CH_2Cl_2, room temp., 3 h, 81% over 3 steps; d) OsO_4 (0.05 equiv.), NMO (1 equiv.), THF, *t*BuOH, room temp., 14 h; then $NaIO_4$, H_2O, room temp., 2 h, then 5 equiv. $NaClO_2$, NaH_2PO_4, 2,3-dimethylbut-2-ene, *t*BuOH/H_2O), room temp., 50 min, 71% over 3 steps.

15.1, 17.9, 18.8, 19.6, 28.7, 31.7, 78.5, 79.9, 81.4, 83.4, 114.3, 114.8, 117.9, 118.0, 121.1, 121.9, 135.0. IR (Si, film): $\tilde{\nu}_{max}$ = 2922, 1745, 1231, 1185, 1115, 738, 546 cm^{-1}.

4-{(*E*)-2-[(2*R*,4*S*,6*R*)-2-Ethoxy-2-methyl-6-(prop-1-en-2-yl)-1,3-dioxan-4-yl]prop-1-enyl}-2-methylthiazole (13) and Byproducts 17 and 18: To a solution of diol **15a**,**b** (172 mg, 0.68 mmol) in xylene (68 mL) a catalytic amount of amberlyst 15 and triethyl orthoacetate (137 µL, 0.74 mmol) were added. The reaction was heated to 70 °C for 1 h (3 products appear on TLC). The reaction was cooled to room temp., the solvent and the amberlyst were removed and the crude mixture was separated by column chromatography (hex/EE, 3:1) to yield 48 mg (22%) of compound **13**, 21 mg (10%) of compound **17** and 18 mg (8%) of compound **18**. The yield of the three compounds could be improved by reducing the reaction temperature and elongating the reaction time. Increasing the temperature strongly favoured polymerisation. **13:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.16 (t, 7.2 Hz, 3 H), 1.56 (s, 3 H), 1.57–1.54 (m, 2 H), 1.99 (s, 3 H), 2.63 (s, 3 H), 3.85 (q, *J* = 7.2 Hz, 2 H), 4.29 (dd, m, *J* = 11.4, 2.3 Hz, 1 H), 4.35 (dd, *J* = 11.5, 2.1 Hz, 1 H), 4.80 (s, 1 H), 4.96 (s, 1 H), 6.52 (s, 1 H), 6.88 (s, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 14.5, 15.2, 15.9, 18.5, 19.6, 20.6, 30.7, 34.4, 56.8, 74.7, 75.8, 77.1, 111.6, 112.9, 116.2, 119.5, 139.4, 144.9, 153.1, 164.9 ppm. $C_{17}H_{25}NO_3S$ (323.5): calcd. C 63.13, H 7.79, N 4.33; found 63.19, H 7.92, N 4.01. **17:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.16 (t, *J* = 7.1 Hz, 3 H), 1.65 (s, 1.2 H), 1.66 (s, 1.9 H), 1.94–1.76 (m, 2 H), 1.91 (d, *J* = 1.0 Hz, 1.2 H), 1.93 (d, *J* = 1.0 Hz, 1.8 H), 2.04 (s, 3 H), 2.64 (s, 3 H), 3.28–3.19 (m, 1 H), 3.51–3.40 (m, 1 H), 3.68–3.64 (m, 1 H), 4.87 (t, *J* = 1.5 Hz, 0.6 H), 4.92 (t, *J* = 1.5 Hz, 0.4 H), 4.97 (s, 0.6 H), 4.99 (s, 0.4 H), 5.30 (t, *J* = 7.1 Hz, 0.43 H), 5.37 (dd, *J* = 9.2, 4.2 Hz, 0.67 H), 6.44 (s, 0.4 H), 6.48 (s, 0.6 H), 6.96 (s, 1 H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 13.6, 13.8, 15.5, 15.7, 18.2, 18.6, 19.6, 21.5, 21.6, 30.1, 30.7, 31.3, 37.6, 38.6, 64.1, 64.3, 74.7, 75.6, 82.2, 82.9, 112.8, 113.8, 115.9, 116.2, 121.0, 121.6, 139.6, 140.1, 143.2, 144.0, 151.9, 153.1, 164.9, 170.4, 170.5. $C_{17}H_{25}NO_3S$ (323,5): calcd. C 63,13, H 7,79, N 4,33; found C 63.22, H 8.12, N 4.10. **18:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.16 (q, *J* = 6.9 Hz, 3 H), 1.53 (s, 3 H), 1.73 (s, 3 H), 2.02 (d, *J* = 9.8 Hz, 3 H), 2.55–2.34 (m, 2 H), 2.67 (s, 3 H), 3.55–3.38 (m, 2 H), 4.82 (s, 1 H), 4.88 (s, 1 H), 4.94 (s, 1 H), 5.22 (t, *J* = 6.7 Hz, 1 H), 5.54 (dd, *J* = 13.0, 6.2 Hz, 1 H), 7.01 (dd, *J* = 2.0, 0.7 Hz, 1 H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 12.1, 12.3, 15.6, 18.7, 19.5, 19.6, 21.4, 21.5, 30.0, 30.7, 31.6, 31.8, 64.1, 64.2, 76.9, 84.0, 84.1, 113.1, 113.2, 114.3, 114.4, 124.1, 124.3, 125.9, 136.8, 136.9, 143.2, 143.3, 156.8, 165.8, 165.9, 170.5. $C_{17}H_{25}NO_3S$ (323.5): calcd. C 63.13, H 7.79, N 4.33; found 63.02, H 8.07, N 4.13.

(2*S*,3*S*)-2-(4-Methoxybenzyloxy)hex-5-en-3-yl 4-Methylpent-4-enoate (20): in DCM (10 mL) 4-methyl-4-pentenoic acid (116 mg, 1.02 mmol), alcohol **19** (200 mg, 0.84 mmol) and DMAP (208 mg, 1.69 mmol) were sequentially dissolved and cooled to 0 °C. Then EDCI (195 mg, 1.02 mmol) was added, the reaction was warmed to room temp. and stirred for 3 days. The reaction was quenched with a saturated solution of NH_4Cl, the phases were separated and extracted with diethyl ether (3 × 50 mL). The combined organic phases were washed with brine and dried with $MgSO_4$. The solvent was removed under reduced pressure. The crude product was purified by column chromatography (hex/EE, 5:1) to yield 233 mg (83%) of the desired product. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.12 (d, *J* = 6.5 Hz, 3 H), 1.73 (s, 3 H), 2.36–2.28 (m, 3 H), 2.49–2.38 (m, 3 H), 3.60 (ddd, *J* = 12.5, 6.2, 4.5 Hz, 1 H), 3.80 (s, 3 H), 4.37 (d, *J* = 11.0, 1 H), 4.60 (d, *J* = 11.0 Hz, 1 H), 4.67 (s, 1 H), 4.73 (s, 1 H), 4.97–4.95 (m, 1 H), 5.06–4.98 (m, 2 H), 5.68 (ddt, *J* = 17.0, 10.0, 7.3 Hz, 1 H), 6.85 (d, *J* = 8.8 Hz, 2 H), 7.24 (d, *J* = 8.8 Hz, 2 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 15.7 ppm. 22.9, 33.0, 33.1, 34.8, 55.6, 68.5, 71.1, 74.3, 75.1, 129.7, 131.0, 134.4, 144.5, 159.6, 173.3 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2979, 1735, 1612, 1514, 1248, 1172, 1037, 772 cm^{-1}. MS (EI = 70 eV, 40 °C): *m*/*z* = 332, 276, 235, 218, 205, 195, 174, 165, 152, 137, 121, 97, 69. HRMS (EI = 70eV, 40 °C) calcd. for $C_{20}H_{28}O_4$ [M^+]: 332.1988; found for $C_{20}H_{28}O_4$: 332.1923. $[a]_D^{20}$ = +13.2 (*c* = 0.5, $CHCl_3$).

(2*S*,3*S*)-2-Hydroxyhex-5-en-3-yl 4-Methylpent-4-enoate: To a solution of ester **20** (233 mg, 0.7 mmol) in DCM/H_2O (20:1, 7 mL:350 µL) DDQ (175 mg, 0.77 mmol) was added portionwise and the reaction mixture was vigorously stirred for 30 minutes. The reaction was quenched with a saturated $NaHCO_3$ solution, $Na_2S_2O_3$ was added, and stirred for another 20 minutes. The layers were separated and the water phase was extracted with diethyl ether (3 × 50 mL). The combined organic layers were washed with brine and dried with $MgSO_4$. The solvents were removed under reduced pressure. The crude product was purified by column chromatography (hex/EE, 3:1) to yield 118 mg (79%) of the title compound. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.16 (d, *J* = 6.6 Hz, 3 H), 1.74 (s, 3 H), 1.75 (d, *J* = 6.6 Hz, 1 H), 2.35–2.28 (m, 3 H), 2.48–2.41 (m, 1 H), 2.53–2.48 (m, 2 H), 3.85–3.78 (m, 1 H), 4.70 (s, 1 H), 4.76 (s, 1 H), 4.81 (dt, *J* = 7.3, 5.1 Hz, 1 H), 5.13–5.05 (m, 2 H), 5.76 (ddt, *J* = 17.0, 10.0, 7.3 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 19.8, 22.8, 33.1, 35.7, 68.5, 68.6, 110.8, 118.4, 118.6, 131.2, 133.7, 144.5, 173.3 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 3436, 2977, 1737, 1650, 1219, 1156, 893, 772 cm^{-1}. MS (EI = 70 eV, 30 °C): *m*/*z* = 212, 194, 184, 171, 142, 114, 97, 81, 69, 57. HRMS (EI = 70 eV, 30 °C) calcd. for $C_{12}H_{20}O_3$ [M^+]: 212.1412; found for $C_{20}H_{28}O_4$: 212.1407. $[a]_D^{20}$ = +14.0 (*c* = 0.5, $CHCl_3$).

(2*S*,3*S*)-2-(4-Methoxybenzyloxy)hex-5-en-3-yl 4-Methylpent-4-enoate (21): To a solution of (2*S*,3*S*)-2-hydroxyhex-5-en-3-yl 4-methylpent-4-enoate (111 mg, 0.52 mmol) in DCM (25 mL), $NaHCO_3$ (225 mg) and Dess–Martin periodinane (444 mg, 1.05 mmol) were

added and stirred for 4.5 h at room temp. The reaction was diluted with diethyl ether and quenched with a saturated $NaHCO_3$ solution. The phases were separated and extracted with diethyl ether (3 × 50 mL). The combined organic layers were washed with brine and dried with $MgSO_4$. The solvents were removed under reduced pressure, and the crude product was purified by column chromatography to give 100 mg (91%) of the desired product. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.68 (s, 3 H), 2.08 (s, 3 H), 2.38–2.31 (m, 2 H), 2.53–2.38 (m, 4 H), 4.64 (s, 1 H), 4.69 (s, 1 H), 5.10–5.00 (m, 3 H), 5.73–5.63 (m, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 24.1, 26.9, 32.6, 32.7, 35.2, 78.2, 110.9, 119.1, 132.3, 144.2, 173.0, 205.2 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2929, 1731, 1651, 1434, 1359, 1232, 1155, 1073, 992, 892, 630 cm^{-1}.

(2*S*,3*S*,8*S*,9*S*,*E*)-2,9-Bis(4-methoxybenzyloxy)-8-(4-oxopentanoyloxy)dec-5-en-3-yl 4-Methylpent-4-enoate (22): To a refluxing solution of compound **20** (85 mg, 0.26 mmol) in degassed DCM (85 mL, 2.6 mM), a solution of Grubbs catalyst (**A**) (43 mg, 20 mol-%) in degassed DCM (20 mL) was added via a syringe pump over 16 h. The reaction was then cooled to room temp., air was bubbled through the solution to destroy the catalyst, and the solvent was removed under reduced pressure. The product was purified by column chromatography (hex/EE, 3:1) to give 15 mg (9%) of the product. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.14 (d, J = 6.3 Hz, 3 H), 1.73 (s, 3 H), 2.33–2.28 (m, 4 H), 2.48–2.44 (m, 2 H), 3.59 (ddd, J = 12.8, 6.5, 4.1 Hz, 1 H), 3.80 (s, 3 H), 4.37 (d, J = 11.0, 1 H), 4.60 (d, J = 11.0 Hz, 1 H), 4.67 (s, 1 H), 4.73 (s, 1 H), 4.91 (ddd, J = 7.4, 5.9, 4.1 Hz, 1 H), 5.01–4.97 (m, 1 H), 6.85 (d, J = 8.8 Hz, 2 H), 7.24 (d, J = 8.8 Hz, 2 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 15.7, 22.9, 33.0, 33.1, 34.8, 55.6, 68.5, 71.1, 74.3, 75.1, 129.7, 131.0, 134.4, 144.5, 159.6, 173.3 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2930, 1735, 1649, 1613, 1514, 1453, 1376, 1302, 1248, 1173, 1037, 890, 821 cm^{-1}. $[\alpha]_D^{20}$ = +13.6 (c = 0.5, $CHCl_3$).

(3*S*,8*S*,*E*)-2,9-Dioxo-8-(4-oxopentanoyloxy)dec-5-en-3-yl 4-Methylpent-4-enoate (23): in a two-necked 250 mL round-bottom flask compound **21** (50 mg, 0.24 mmol) was refluxed in degassed DCM (80 mL, 3 mM). Grubbs–Hoveyda catalyst (**B**) (23 mg, 15 mol-%) in degassed DCM (20 mL) was added via a syringe pump over 16 h. The reaction was then cooled to room temp., air was bubbled through the solution to destroy the catalyst, and the solvent was removed under reduced pressure. The product was purified by column chromatography (hex/EE, 3:1), to yield 18 mg (19%) of the product. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.68 (s, 3 H), 2.08 (s, 3 H), 2.38–2.31 (m, 2 H), 2.53–2.38 (m, 4 H), 4.64 (s, 1 H), 4.69 (s, 1 H), 4.91 (ddd, J = 7.4, 5.9, 4.1 Hz, 1 H), 5.06–5.01 (m, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 24.1, 26.9, 32.6, 32.7, 35.2, 78.2, 110.9, 119.1, 132.3, 144.2, 173.0, 205.2 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2929, 1729, 1358, 1152, 512 cm^{-1}. MS (EI = 70eV, 40 °C): m/z = 392, 279, 220, 205, 167, 149, 121, 97, 69, 55. HRMS (EI = 70eV, 40 °C) calcd. for $C_{22}H_{32}O_6$ [M^+]: 392.2199; found 392.2193. $[\alpha]_D^{20}$ = +54.5 (c = 2.35, $CHCl_3$).

[(2*S*,3*S*)-2-(4-Methoxybenzyloxy)hex-5-en-3-yloxy]dimethyl(3-methylbut-3-enyloxy)silane (25): Alcohol **19** (40 mg, 0.17 mmol) in THF (420 µL, 0.4 M) was cooled to –78 °C, and deprotonated with *n*BuLi (118 µL, 1.6 M in hexane, 0.18 mmol) for 15 minutes. Then $SiCl_2Me_2$ (102 µL, 0.85 mmol) was added and the reaction mixture was warmed to room temp. The solvents and remaining $SiCl_2Me_2$ were removed under reduced pressure, the residue was dissolved in DMF (200 µL), and a solution of 3-methyl-3-butenol (34 µL, 0.34 mmol) and imidazole (35 mg, 0.5 mmol) in DMF (400 µL) was added dropwise. The reaction mixture was stirred for 24 h at room temp., then the solvent was removed under reduced pressure, and the crude mixture was purified by column chromatography (hex/EE, 5:1 and 5% triethylamine) to yield the desired product. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.09 (s, 6 H), 1.13 (d, J = 6.3 Hz, 3 H), 1.72 (s, 3 H), 2.27–2.15 (m, 3 H), 2.42–2.35 (m, 1 H), 3.49 (ddd, J = 12.5, 6.2, 4.9 Hz, 1 H), 3.74 (t, J = 7.2 Hz, 1 H), 3.77–3.73 (m, 1 H), 3.80 (s, 3 H), 3.85–3.78 (m, 1 H), 4.44 (d, J = 11.0 Hz, 1 H), 4.55 (d, J = 11.0 Hz, 1 H), 4.68 (s, 1 H), 4.76 (s, 1 H), 4.98–5.08 (m, 2 H), 5.87(ddt, J = 17.0, 10.0, 7.0 Hz, 1 H), 6.85 (d, J = 8.6 Hz, 2 H), 7.23 (d, J = 8.5 Hz, 2 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = –0.1, 0.0, 17.0, 25.2, 39.1, 43.2, 57.7, 63.7, 73.4, 76.8, 78.9, 79.1, 114.0, 116.1, 119.1, 131.6, 133.4, 138.2 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2963, 1514, 1257, 1035, 804 cm^{-1}. MS (EI = 70 eV, 80 °C): m/z = 378, 231, 121, 91, 77. HRMS (EI = 70 eV, 80 °C) calcd. for $C_{21}H_{34}O_4Si$ [M^+]: 378.2226; found 378.1923. $[\alpha]_D^{20}$ = +10.2 (c = 0.5, $CHCl_3$).

(1*S*)-4-[(4*S*)-1-(4-Methoxybenzyloxy)ethyl]-2,2,7-trimethyl-4,5,8,9-tetrahydro-1,3,2-dioxasilonine (26): To a refluxing solution of the silane **25** (1 g, 2.6 mol) in degassed DCM (1 L, 2.6 mM), a solution of second-generation Grubbs catalyst (831 mg, 15 mol-%) in degassed DCM (40 mL) was added via a syringe pump over 16 h. The reaction was then cooled to room temp., air was bubbled through the solution to destroy the catalyst, and the solvent was removed under reduced pressure, dissolved again in hex/EE (5:1 and 5% triethylamine), and filtered (silica gel) to afford 910 mg (98%) of the desired product. ^{1}H NMR (400 MHz, $CDCl_3$): δ = –0.08 (s, 3 H), 0.04 (s, 3 H), 1.03 (d, J = 6.3 Hz, 3 H), 1.65 (s, 3 H), 1.74 (dt, J = 13.3, 2.6 Hz, 1 H), 2.00–1.93 (m, 1 H), 2.24–2.16 (m, 1 H), 2.82 (ddd, J = 13.3, 11.7, 5.2 Hz, 1 H), 3.30 (ddd, J = 12.7, 6.3, 4.5 Hz, 1 H), 3.56 (ddd, J = 8.9, 4.4, 1.5 Hz, 1 H), 3.69 (s, 3 H), 3.75 (dd, J = 11.6, 3.0 Hz, 1 H), 3.83–3.78 (m, 1 H), 4.37 (d, J = 11.0, 1 H), 4.60 (d, J = 11.0 Hz, 1 H), 5.33 (t, J = 8.2 Hz, 1 H), 6.85 (d, J = 8.6 Hz, 2 H), 7.23 (d, J = 8.5 Hz, 2 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = –1.0, 0.0, 17.5, 25.4, 33.3, 37.3, 57.9, 62.8, 73.4, 78.2, 79.3, 116.4, 127.3, 131.9, 133.8, 137.8, 161.7 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2924, 1513, 1248, 874, 772, 607 cm^{-1}. MS (EI = 70 eV, 50 °C): m/z = 350, 336, 279, 225, 180, 143, 121, 69. HRMS (EI = 70 eV, 50 °C) calcd. for $C_{19}H_{30}O_4Si$ [M^+]: 350.1913; found 350.1907. $[\alpha]_D^{20}$ = +1.6 (c = 0.25, $CHCl_3$).

(6*S*,7*S*,*Z*)-7-(4-Methoxybenzyloxy)-3-methyloct-3-ene-1,6-diol (27): Compound **26** (910 mg, 2.6 mmol) was dissolved in a solution of TBAF (10.5 mL, 1 M in THF, 4 equiv.) and stirred overnight. The reaction was diluted with Et_2O (50 mL) and quenched with a saturated NH_4Cl solution. The organic layer was separated, and the water phase was extracted with Et_2O (1 × 100 mL, 2 × 50 mL). The combined organic layers were washed with brine, dried with $MgSO_4$ and the solvents were removed under reduced pressure. The crude product was purified by column chromatography (hex/EE, 1:1) to yield 653 mg of the (*Z*)-, and 131 mg of the (*E*) olefin (86% combined yield). **(*Z*) Isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.19 (d, J = 6.1 Hz, 3 H), 1.76 (s, 3 H), 2.26–2.16 (m, 3 H), 2.48 (dt, J = 13.7, 6.8 Hz, 1 H), 3.10–2.71 (br. s, 2 H, *OH*), 3.50–3.39 (m, 3 H), 3.71–3.68 (m, 2 H), 3.80 (s, 3 H), 4.37 (d, J = 11.0, 1 H), 4.60 (d, J = 11.0 Hz, 1 H), 5.31 (t, J = 7.8 Hz, 1 H), 6.87 (d, J = 8.6 Hz, 2 H), 7.24 (d, J = 8.5 Hz, 2 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 15.6, 15.8, 23.8, 31.5, 35.2, 55.7, 60.5, 71.1, 77.1, 114.3, 124.2, 129.7 130.8, 134.9, 159.7 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 3382, 2966, 1613, 1514, 1454, 1376, 1248, 1174, 1035, 885, 584 cm^{-1}. MS (EI = 70 eV, 50 °C): m/z = 247, 135, 107, 69, 57. $[\alpha]_D^{20}$ = +3.1 (c = 2.0, $CHCl_3$). **(*E*) Isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.26 (d, J = 6.1 Hz, 3 H), 1.65 (s, 3 H), 2.30–2.16 (m, 4 H), 3.41 (dt, J = 12.4, 6.2 Hz, 1 H), 3.49 (br. s, 1 H, OH), 3.65 (t, J = 6.1 Hz, 2 H), 3.80 (s, 3 H), 4.37 (d, J = 11.0 Hz, 1 H), 4.60 (d, J = 11.0 Hz, 1 H), 5.31 (t, J = 6.8 Hz, 1 H), 6.87 (d, J = 8.6 Hz, 2 H), 7.24 (d, J = 8.5 Hz, 2 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 16.0,

16.4, 30.1, 31.5, 35.2, 55.7, 60.5, 71.2, 75.2, 77.8, 114.3, 123.9, 129.8, 130.8, 133.9, 159.7 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 3382, 2966, 1613, 1514, 1454, 1376, 1248, 1174, 1035, 885, 584 cm^{-1}.

(6*S*,7*S*,*Z*)-7-(4-Methoxybenzyloxy)-6-(*tert*-butyldimethylsilyloxy)-3-methyloct-3-en-1-ol (28): To a solution of diol **27** (653 mg, 2.22 mmol) in DCM (25 mL) 2,6-lutidine (776 μL, 6.66 mmol) and TBSOTf (1.33 mL, 5.77 mmol) were added at room temp. The reaction mixture was stirred at room temp. for 2 h, s diluted with Et_2O and quenched with aq. NH_4Cl. The organic layer was separated and the water phase extracted with Et_2O (3 × 50 mL). The combined organic layers were washed with brine and dried with $MgSO_4$. The reaction mixture was filtered through silica gel, the solvents were removed under reduced pressure. The crude product was dissolved in THF (5 mL) and HF/pyr (1 mL, 7%) was added and stirred for 4 h. Then, again HF/pyr (1 mL) was added and the mixture was stirred overnight. After ca. 40 h the reaction was diluted with Et_2O and quenched with water. The organic layer was separated and the water phase extracted with Et_2O (1 × 100 mL, 2 × 50 mL). The combined organic layers were washed with brine, and dried with $MgSO_4$. The solvents were removed under reduced pressure and the crude product was filtered through silica gel gel to give 800 mg (88%) of the desired product. ^{1}H NMR (400 MHz, $CDCl_3$): δ = –0.03 (s, 3 H), 0.00 (s, 3 H), 0.85 (s, 9 H), 1.13 (d, *J* = 6.3 Hz, 3 H), 1.71 (s, 3 H), 2.07–1.88 (br. s, 1 H, *OH*), 2.39–2.19 (m, 4 H), 3.53.3.47 (m, 1 H), 3.63 (t, *J* = 6.2 Hz, 2 H), 3.75 (ddd, *J* = 8.4, 4.2, 4.1 Hz, 1 H), 3.80 (s, 3 H), 4.37 (d, *J* = 11.0, 1 H), 4.60 (d, *J* = 11.0 Hz, 1 H), 5.31 (t, *J* = 7.5 Hz, 1 H), 6.86 (d, *J* = 8.6 Hz, 2 H), 7.24 (d, *J* = 8.5 Hz, 2 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = –4.3, –4.1, 14.0, 18.4, 24.1, 26.2, 30.1, 30.7, 35.7, 55.7, 60.9, 70.8, 74.4, 77.3, 114.1, 126.2, 129.5, 131.4, 133.2, 159.5 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 3250, 2928, 1513, 1248, 1081, 774. $[\alpha]_D^{20}$ = +3.7 (*c* = 1.0, $CHCl_3$).

(7*S*,8*S*,*Z*)-8-(4-Methoxybenzyloxy)-7-(*tert*-butyldimethylsilyloxy)-4-methylnon-4-enenitrile (29): Alcohol **28** (400 mg, 0.98 mmol) in diethyl ether (3.3 mL, 0.3 M) was cooled to 0 °C. PPh_3 (514 mg, 1.96 mmol) was added portionwise and the solution was stirred at this temperature for 10 minutes. Then DEAD (305 μL, 1.96 mmol) was added dropwise -(a precipitate was formed) – and the reaction was stirred for 20 minutes. Acetone cyanohydrin (180 μL, 1.96 mmol) was added dropwise. The reaction mixture was warmed to room temp. overnight, and stirred for another 10 h. The mixture was diluted with Et_2O/hex (1:1, 20 mL) (hydrazo ester and $OPPh_3$ precipitated) and the solvents were removed under reduced pressure. The crude product was purified by column chromatography (hex/EE, 5:1) to yield 371 mg (89%) of the desired product. ^{1}H NMR (400 MHz, $CDCl_3$): δ = –0.04 (s, 3 H), –0.01 (s, 3 H), 0.85 (s, 9 H), 1.14 (d, *J* = 6.5 Hz, 3 H), 1.79 (s, 3 H), 2.12–2.04 (m, 1 H), 2.47–2.26 (m, 5 H), 3.48 (ddd, *J* = 12.7, 6.3, 4.5 Hz, 1 H), 3.70 (ddd, *J* = 8.5, 4.6, 3.6 Hz, 1 H), 3.80 (s, 3 H), 4.37 (d, *J* = 11.0, 1 H), 4.60 (d, *J* = 11.0 Hz, 1 H), 5.34 (t, *J* = 7.2 Hz, 1 H), 6.86 (d, *J* = 8.6 Hz, 2 H), 7.25 (d, *J* = 8.5 Hz, 2 H) ppm.^{13}C NMR (100.6 MHz, $CDCl_3$): δ = –4.3, –4.2, 14.1, 16.3, 18.4, 23.4, 26.2, 27.2, 28.0, 28.0, 55.7, 74.2, 77.2, 114.1, 119.9, 126.7, 129.5, 131.4, 132.5 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2930, 1513, 1249, 1090, 836, 776 cm^{-1}. MS (EI = 70 eV, 40 °C): *m*/*z* = 350417, 360, 333, 316, 279, 252, 121, 97, 57. HRMS (EI = 70 eV, 40 °C) calcd. for $C_{20}H_{30}O_3NSi$ [M – C_4H_9]: 360.1995; found 360.1991. $[\alpha]_D^{20}$ = +7.0 (*c* = 0.5, $CHCl_3$).

(7*S*,8*S*,*Z*)-7-(*tert*-Butyldimethylsilyloxy)-8-hydroxy-4-methylnon-4-enenitrile (30): To a solution of the nitrile **29** (708 mg, 1.7 mmol) in DCM/H_2O (20:1, 21 mL) DDQ (424 mg, 1.9 mmol) was added portionwise and the reaction mixture was vigorously stirred for 30 minutes. The reaction was quenched with a saturated $NaHCO_3$ solution, $Na_2S_2O_3$ was added, and stirred for another 20 minutes. The layers were separated and the water phase was extracted with diethyl ether (3 × 50 mL). The combined organic layers were washed with brine, dried with $MgSO_4$ and the solvents were removed under reduced pressure. The crude product was purified by column chromatography (hex/EE, 3:1) to yield 459 mg (91%) of the desired product. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.04 (s, 3 H), 0.08 (s, 3 H), 0.91 (s, 9 H), 1.14 (d, *J* = 6.3 Hz, 3 H), 1.75 (s, 3 H), 2.06 (d, *J* = 7.3 Hz, 1 H), 2.46–2.28 (m, 5 H), 3.50–3.46 (m, 1 H), 3.64–3.56 (m, 1 H), 5.31 (t, *J* = 6.9 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = –5.7, –5.2, 0.0, 9.9, 14.8, 18.9, 21.9, 22.0, 22.7, 24.8, 26.6, 27.9, 29.4, 31.4, 37.7, 67.1, 67.6, 75.0, 123.3, 127.8, 129.8, 132.3 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 3630, 2958, 2930, 2858, 1724, 1560, 1460, 1381, 1258, 1088, 873, 776 cm^{-1}. MS (EI = 70 eV, 80 °C): *m*/*z* = 297, 282, 264, 252, 240, 222, 210, 173, 148, 108, 73, 57. HRMS (EI = 70 eV, 80 °C) calcd. for $C_{12}H_{22}NO_2Si$ [M – C_4H_9] 240.1429; found 240.1423. $[\alpha]_D^{20}$ = +2.06 (*c* = 1.5, $CHCl_3$).

(7*S*,4*Z*)-7-(*tert*-Butyldimethylsilyloxy)-4-methyl-8-oxonon-4-enenitrile (31): Oxalyl chloride (250 μL, 2.93 mmol/ 2 equiv.) in DCM (15 mL) was cooled to –45 °C. DMSO (454 μL, 5.87 mmol, 4 equiv.) was added dropwise. The reaction mixture was stirred at –78 °C until gas evolution ceased (ca. 30 min). Then alcohol **30** (436 mg, 1.46 mmol) in DCM (8 mL) was added dropwise via a syringe. After stirring for 1 h at –78 °C, triethylamine (1.22 mL, 8.8 mmol, 6 equiv.) was added dropwise and the reaction mixture was warmed quickly to 0 °C and was stirred for another 30 minutes at this temperature. Then the reaction was quenched with NH_4Cl (30 mL) at 0 °C, the organic layer was separated, and the water layer was extracted with DCM (2 × 100 mL). The combined organic layer were washed with brine, and dried with $MgSO_4$. The solvent was removed under reduced pressure, and the product was purified by column chromatography (hex/EE, 3:1) to yield 409 mg (95%) of the desired aldehyde, which was used immediately. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.05 (s, 6 H), 0.92 (s, 9 H), 1.69 (d, *J* = 1.0 Hz, 3 H), 2.16 (s, 3 H), 2.34–2.26 (m, 2 H), 2.47–2.37 (m, 4 H), 3.96 (dd, *J* = 6.8, 5.0 Hz, 1 H), 5.27 (t, *J* = 7.2 Hz, 1 H), ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = –4.6, –4.5, 16.3, 18.5, 23.3, 26.0, 26.1, 28.0, 33.7, 56.0, 114.7, 119.7, 123.4, 132.4, 134.4, 212.3 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2928, 2856, 1717, 1601, 1463, 1352, 1259, 1106, 924, 838, 777 cm^{-1}. MS (EI = 70 eV, 80 °C): *m*/*z* = 252, 238, 220, 194, 135, 108, 73, 57. HRMS (EI = 70 eV, 80 °C) calcd. for $C_{16}H_{29}NO_2Si$ [M^+ – C_4H_9]: 238.1263; found 238.1267. $[\alpha]_D^{20}$ = +29.0 (*c* = 0.5, $CHCl_3$).

(7*S*,4*Z*,8*E*)-7-(*tert*-Butyldimethylsilyloxy)-4,8-dimethyl-9-(2-methylthiazol-4-yl)nona-4,8-dienenitrile (33): A solution of the phosphonium salt **32** (960 mg, 2.7 mmol) in THF (7 mL) was cooled to 0 °C. *n*BuLi (1.75 mL, 1.6 M in hexane, 2.8 mmol) was added dropwise and the solution was stirred at 0 °C for 1 h (deep red solution). The ice bath was removed and the mixture was cooled to –78 °C. Then ketone **31** (200 mg, 0.67 mmol) in THF (5 mL) was added slowly to the red solution over 5 min. The cooling bath was removed and the reaction stirred for 1 h at 60 °C, cooled to room temp., and quenched with a saturated NH_4Cl solution. The organic phase was separated and the water phase was extracted with diethyl ether (3 × 50 mL). The combined organic phases were washed with brine, dried with $MgSO_4$ and the solvent was removed under reduced pressure. The product was purified by column chromatography (hex/EE, 5:1) to yield 510 mg (94%) as a single (*E*) isomer. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.00 (s, 3 H), 0.04 (s, 3 H), 0.88 (s, 9 H), 1.72 (d, *J* = 1.2 Hz, 3 H), 2.00 (d, *J* = 1.2 Hz, 3 H), 2.47–2.20 (m, 6 H), 2.71 (s, 3 H), 4.14–4.09 (m, 1 H), 5.32 (t, *J* = 7.4 Hz, 1 H), 6.46 (s, 1 H), δ = 6.92 (s, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = –4.5, –4.3, 14.2, 16.3, 18.6, 19.6, 23.3, 26.2, 28.2, 35.8,

39.1, 55.7, 78.8, 114.5, 115.6, 119.3, 119.7, 119.9, 125.7, 128.2, 130.9, 133.0, 142.5, 153.5 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2954, 2928, 2855, 1725, 1513, 1461, 1252, 1183, 1074, 945, 836, 776 cm^{-1}. MS (EI = 70 eV, 50 °C): *m*/*z* = 390, 375, 350, 333, 308, 282, 259, 231, 205, 147, 121, 73, 57. HRMS (EI = 70 eV, 50 °C) calcd. for $C_{20}H_{31}N_2OSi$ [$M^+ - CH_3$]: 390.1926; found 390.1918. $[\alpha]_D^{20}$ = +3.4 (*c* = 1.0, $CHCl_3$). $C_{21}H_{34}N_2OSSi$ (390.7): calcd. C 64.56, H 8.77, N 7.17; found C 64.29, H 8.92, N 7.01.

(7*S*,4*Z*,8*E*)-7-(*tert*-Butyldimethylsilyloxy)-4,8-dimethyl-9-(2-methylthiazol-4-yl)nona-4,8-dienal (34): A solution of **33** (300 mg, 0.77 mmol) in toluene (7 mL) was cooled to –78 °C. DIBAL-H (1.8 mL, 1 M in toluene, 1.85 mmol) was added dropwise, and stirred for 2 h at –78 °C. The reaction mixture was then warmed to room temp. and quenched with a saturated NH_4Cl solution. The organic phase was separated and the water phase was extracted with diethyl ether (3 × 50 mL). The combined organic layers were washed with brine (1 × 50 mL, 1 × 25 mL), dried with $MgSO_4$, and the solvents were removed under reduced pressure. The crude product was purified by column chromatography (hex/EE, 5:1) to yield 220 mg (84%) of the desired product. ^{1}H NMR (400 MHz, $CDCl_3$): δ = –0.01 (s, 3 H), 0.02 (s, 3 H), 0.88 (s, 9 H), 1.68 (d, *J* = 1.2 Hz, 3 H), 1.99 (d, *J* = 1.2 Hz, 3 H), 2.40–2.19 (m, 4 H), 2.50–2.45 (m, 2 H), 2.70 (s, 3 H), 4.05 (dd, *J* = 6.3, 6.1 Hz, 1 H), 5.20 (t, *J* = 6.8 Hz, 1 H), 6.46 (s, 1 H), 6.92 (s, 1 H), 9.76 (t, *J* = 1.8 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, CDCl3): δ = –4.5, –4.3, 14.4, 18.6, 19.6, 23.6, 24.1, 24.9, 26.2, 35.8, 39.1, 42.7, 55.7, 79.1, 115.5, 119.2, 123.6, 128.2, 134.8, 142.7, 153.5, 202.6 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2956, 2928, 2856, 2348, 1726, 1460, 1255, 1182, 1074, 940, 836, 776. $[\alpha]_D^{20}$ = +3.06 (*c* = 0.5, $CHCl_3$).

(1*R*)-*N*-[(9*S*,2*E*,6*Z*,10*E*)-9-(*tert*-Butyldimethylsilyloxy)-11-(2-methylthiazol-4-yl)undeca-2,6,10-trienoyl]bornan-10,2-sultam (36): To a solution of *n*BuLi (600 μL, 1.6 M in hexane, 0.96 mmol) in diethyl ether (5 mL) a mixture of THF/H_2O (4:1, 160 μL) was added at 0 °C and stirred for 5 minutes. Phosphonate **35** (1.1 mmol, 433 mg) in THF (1.6 mL) was added and the reaction was stirred for 5 minutes. Then a solution of aldehyde 122 (235 mg, 0.6 mmol) in THF (800 μL) was added and stirred for 30 minutes. The reaction mixture was diluted with diethyl ether and quenched with a saturated NH_4Cl solution. The phases were separated and extracted with diethyl ether (2 × 25 mL). The combined organic layers were washed with brine, and dried with $MgSO_4$. The solvent was removed under reduced pressure, and filtered off through silica gel to yield 313 mg (83%) of the desired product. ^{1}H NMR (400 MHz, $CDCl_3$): δ = –0.01 (s, 3 H), 0.02 (s, 3 H), 0.88 (s, 9 H), 0.97 (s, 3 H), 1.17 (s, 3 H), 1.44–1.33 (m, 6 H), 1.68 (d, *J* = 1.0 Hz, 3 H), 1.92–1.83 (m, 3 H), 1.99 (d, *J* = 1.0 Hz, 3 H), 2.36–2.15 (m, 4 H), 2.70 (s, 3 H), 3.42 (d, *J* = 13.5 Hz, 1 H), 3.48 (d, *J* = 13.5 Hz, 1 H), 3.92 (dd, *J* = 7.3, 5.1 Hz, 1 H), 4.08 (t, *J* = 6.2 Hz, 1 H), 5.18 (t, *J* = 7.1 Hz, 1 H), 6.46 (s, 1 H), 6.56 (dt, *J* = 14.8, 1.2 Hz, 1 H), 6.92 (s, 1 H), 7.06 (dt, *J* = 15.0, 6.9 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = –4.5, –4.3, 14.3, 14.4, 18.6, 19.6, 20.3, 26.2, 26.9, 31.5, 33.3, 35.7, 39.0, 45.1, 48.2, 48.8, 53.6, 65.5, 79.1, 115.4, 121.3, 123.2, 135.4, 142.8, 153.6, 164.4, 164.6 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2957, 2929, 2856, 1727, 1682, 1640, 1461, 1374, 1334, 1267, 1250, 1218, 1165, 1134, 1072, 996, 940, 837, 776, 544. $[\alpha]_D^{20}$ = +16.0 (*c* = 0.25, $CHCl_3$). $C_{33}H_{52}N_2O_4S_2Si$ (633.0): calcd. C 62.62, H 8.28, N 4.43; found C 62.29, H 8.53, N 4.78.

(1*R*)-*N*-[(2*S*,9*S*,6*Z*,10*E*)-9-(*tert*-Butyldimethylsilyloxy)-2-methyl-11-(2-methylthiazol-4-yl)undeca-6,10-dienoyl]bornan-10,2-sultam (37): A solution of **36** (164 mg, 0.25 mmol) in THF (2.5 mL) was cooled to –90 °C and L-selectride (1 M in THF) (410 μL, 0.41 mmol) was added dropwise. Within 15 minutes the reaction was warmed to –60 °C and stirred for 45 minutes at this temperature. The reaction was cooled to –78 °C and a solution of LDA (0.3 mmol/1.2 equiv.) in THF (200 μL) was added and stirred for 15 minutes. Then sequentially HMPT (270 μL, 1.5 mmol) and MeI (200 μL, 3 mmol) were added dropwise. The reaction was warmed to room temp. overnight, diluted with diethyl ether and quenched with a saturated NH_4Cl solution. The phases were extracted with diethyl ether (3 × 25 mL). The combined organic layers were washed with brine, dried with $MgSO_4$ and the solvent was removed under reduced pressure. The products were separated by column chromatography (hex/EE, 3:1) or better by HPLC to yield 146 mg (90%) of the desired product **37** and 10% of the by-product **38**. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.00 (s, 3 H), 0.04 (s, 3 H), 0.88 (s, 9 H), 0.99 (s, 3 H), 1.15 (s, 3 H), 1.18 (d, *J* = 6.8 Hz, 3 H), 1.45–1.25 (m, 6 H), 1.64 (d, *J* = 1.0 Hz, 3 H), 1.79–1.63 (m, 2 H), 1.90–1.81 (m, 3 H), 1.99 (d, *J* = 1.26 Hz, 3 H), 2.08–1.85 (m, 2 H), 2.24 (dd, *J* = 12.8, 7.0 Hz, 2 H), 2.69 (s, 3 H), 3.08–3.00, (m, 1 H), 3.42 (d, *J* = 13.5 Hz, 1 H), 3.48 (d, *J* = 13.5 Hz, 1 H), 3.88 (t, *J* = 6.2 Hz, 1 H), 4.07 (t, *J* = 6.4 Hz, 1 H), 5.13 (t, *J* = 7.0 Hz, 1 H), 6.44 (s, 1 H), 6.91 (s, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = –4.5, –4.3, 14.3, 14.4, 18.6, 19.5, 19.6, 20.3, 21.2, 26.0, 26.2, 26.8, 33.0, 33.2, 35.6, 39.1, 40.7, 45.0, 48.1, 48.6, 53.6, 65.5, 77.7, 79.4, 115.3, 119.0, 122.1, 143.0, 164.6, 176.6, ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2957, 2856, 1698, 1461, 1389, 1334, 1249, 1132, 1064, 940, 836, 775, 544 cm^{-1}. MS (EI = 70 eV, 170 °C): *m*/*z* = 648, 633, 591, 517, 282, 73. HRMS (EI = 70 eV, 170 °C) calcd. for $C_{34}H_{56}N_2O_4S_2Si$: [M^+]: 648.3451; found 648.3468. $[\alpha]_D^{20}$ = +49.4 (*c* = 1.5, $CHCl_3$). **38:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = –0.02 (s, 3 H), 0.03 (s, 3 H), 0.87 (s, 9 H), 0.95 (s, 3 H), 1.14 (s, 3 H), 1.45–1.23 (m, 6 H), 1.65 (d, *J* = 1.0 Hz, 3 H), 1.68–1.60 (m, 2 H), 1.94–1.84 (m, 3 H), 1.98 (d, *J* = 1.26 Hz, 3 H), 2.14–1.96 (m, 2 H), 2.29–2.18 (m, 2 H), 2.69 (s, 3 H), 2.76–2.62 (m, 2 H), 3.42 (d, *J* = 13.5 Hz, 1 H), 3.48 (d, *J* = 13.5 Hz, 1 H), 3.85 (dd, *J* = 7.3, 5.3 Hz, 1 H), 4.07 (t, *J* = 6.4 Hz, 1 H), 5.13 (t, *J* = 7.1 Hz, 1 H), 6.44 (s, 1 H), 6.91 (s, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = –4.5, –4.3, 14.3, 14.4, 18.6, 19.6, 20.2, 21.2, 24.9, 26.2, 26.8, 27.8, 32.1, 35.7, 35.9, 39.1, 45.0, 48.1, 48.7, 53.4, 65.6, 79.4, 115.3, 119.0, 122.2, 136.7, 142.9, 153.7, 164.6, 172.2 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2959, 2930, 2390, 1729, 1461, 1271, 1133, 1072, 862, 838, 772, 614, 543 cm^{-1}. MS (EI = 70 eV, 160 °C): *m*/*z* = 634, 619, 577, 282, 73. HRMS (EI = 70 eV, 160 °C) calcd. for $C_{33}H_{54}N_2O_4S_2Si$ [M^+]: 634.3294; found 634.3276. $[\alpha]_D^{20}$ = +9.9 (*c* = 1.0, $CHCl_3$).

(2*S*,6*Z*,9*S*,10*E*)-9-(*tert*-Butyldimethylsilyloxy)-2,6,10-trimethyl-11-(2-methylthiazol-4-yl)undeca-6,10-dienal (3): A solution of **37** (47 mg, 0.072 mmol) in DCM (1.4 mL, 50 mM) was cooled to –90 °C. DIBAL-H (71 μL, 0.072 mmol) was added dropwise and the solution was warmed to –80 °C within 45 min. Again DIBAL-H (71 μL, 0.072 mmol) was added and stirred for 30 min. The reaction was quenched with a few drops MeOH and a saturated NH_4Cl solution. $MgSO_4$ was added, and the reaction mixture was stirred for 2 h at room temp. Then the product was filtered, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (hex/EE, 3:1) to yield 28 mg (90%) of the desired product. ^{1}H NMR (400 MHz, $CDCl_3$): δ = –0.02 (s, 3 H), 0.02 (s, 3 H), 0.88 (s, 9 H), 1.08 (d, *J* = 7.1 Hz, 3 H), 1.33–1.25 (m, 2 H), 1.66 (d, *J* = 1.26 Hz, 3 H), 1.75–1.60 (m, 2 H), 1.99 (d, *J* = 1.26 Hz, 3 H), 2.09–1.97 (m, 2 H), 2.36–2.19 (m, 3 H), 2.70 (s, 3 H), 4.08 (t, *J* = 6.2 Hz, 1 H), 5.16 (t, *J* = 7.0 Hz, 1 H), 6.45 (s, 1 H), 6.91 (s, 1 H), 9.60 (d, *J* = 2.0 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = –4.5, –4.3, 13.7, 14.3, 14.4, 18.6, 19.6, 25.6, 26.2, 30.7, 35.8, 46.6, 79.3, 115.4, 119.1, 122.5, 136.5, 142.8, 153.6, 164.7, 205.5 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2930, 2857, 1727, 1461, 1256, 1074, 837, 776 cm^{-1}. MS (EI = 70 eV, 80 °C): *m*/*z* =

435, 420, 407, 390, 378, 350, 338, 308, 282, 149, 105, 57. HRMS (EI = 70 eV, 80 °C) calcd. for $C_{20}H_{32}NO_2SSi$ (-C_4H_9): 378.1923; found 378.1931. $[\alpha]_D^{20}$ = +10.0 (*c* = 0.75, $CHCl_3$).

(4*R*,5*S*)-4-Methyl-3-[(*S*,*E*)-2-methyl-5-phenylpent-4-enoyl]-5-phenyloxazolidin-2-one (43): Oxazolidinone **42** (5.705 g, 24.46 mmol) in THF (70 mL) was treated dropwise at –78 °C for 10 min with NaHMDS (1 M in THF, 26.9 mL, 26.9 mmol) and stirred for 60 minutes. Then 3-bromo-1-phenyl-1-propene (7.4 g, 37.5 mmol, 1.5 equiv.) in THF (10 mL) was added dropwise over 10 min. The mixture was warmed to –20 °C over 4 h, and then stirred for 1 h at 0 °C. The mixture was quenched with aq. NH_4Cl and extracted with diethyl ether. The combined organic phase was washed with aq. $NaHCO_3$, dried with $MgSO_4$ and concentrated in vacuo. Chromatography (hex/EE, 10:1) furnished 6.182 g (17.69 mmol) of **43** (R_f 0.48) and 275 mg (0.787 mmol) of the (2*R*) diastereomer (R_f 0.56) as colorless oils. The total yield is 76%, and the diastereomeric ratio is 96:4. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.85 (d, *J* = 6.4 Hz, 3 H), 1.28 (d, *J* = 6.9 Hz, 3 H), 2.42 (dquint, *J* = 6.9, 0.9 Hz, 1 H), 2.67 (dquint, *J* = 6.9, 0.9 Hz, 1 H), 4.03 (sext, *J* = 6.9 Hz, 1 H), 4.81 (quint, *J* = 6.6 Hz, 1 H), 5.67 (d, *J* = 7.5 Hz, 1 H), 6.25 (dt, *J* = 15.8, 7.3 Hz, 1 H), 6.45 (d, *J* = 16.0 Hz, 1 H), 7.46–7.18 (m, 10 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 14.64, 16.64, 37.44, 37.65, 54.82, 78.74, 125.66, 126.08, 126.97, 127.11, 128.47, 128.65, 128.71, 132.35, 133.39, 137.33, 152.77, 176.33 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2971, 1781 s1702, 1456, 1344, 1237, 1196, 1109, 960, 896, 739 cm^{-1}. MS (EI = 70 eV, 90 °C): *m*/*z* = 349 [M$^+$, 3], 289 (1), 234 (8), 233 (58) [M–*t*BuSi(CH_3)$_2$], 206 (2), 163 (11), 117 (12), 116 (17), 107 (100), 105 (10). HRMS calcd. for $C_{22}H_{23}NO_3$ [M$^+$]: 349.1678; found 349.1687. $[\alpha]_D^{20}$ = +74.6 (*c* = 1.0, $CHCl_3$). $C_{22}H_{23}NO_3$ (349.2): calcd. C 75.62, H 6.63, N 4.01; found C 74.31, H 6.27, N 3.93. **(2*R*) Diastereomer:** ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.47–7.20 (m, 10 H), 6.48 (d, *J* = 16.0 Hz, 1 H), 6.25 (dt, *J* = 15.8, 7.3 Hz, 1 H), 5.54 (d, *J* = 7.3 Hz, 1 H), 4.74 (quint, *J* = 7.0 Hz, 1 H), 3.97 (sext, *J* = 6.9 Hz, 1 H), 2.65 (dquint, *J* = 7.3, 1.2 Hz, 1 H), 2.40 (dquint, *J* = 6.9, 1.2 Hz, 1 H), 1.28 (d, *J* = 6.9 Hz, 3 H), =0.92 (d, *J* = 6.4 Hz, 3 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 176.20, 152.77, 137.31, 133.31, 132.26, 128.70, 128.65, 128.54, 127.23, 127.20, 126.07, 125.64, 78.84, 54.92, 38.01, 38.01, 16.95, 14.44 ppm. IR (Si, film): $\tilde{\nu}$ = 2972, 2934, 1781, 1702, 1493, 1456, 1346, 1238, 1195, 1115, 962, 898, 741, 697 cm^{-1}. MS (EI = 70 eV, 150 °C): *m*/*z* = 351 (3), 350 (21), 349 (75) [M$^+$], 233 (3) [M–*t*BuSiMe_2], 232 (10), 214 (15), 206 (13), 178 (16), 172 (50), 171 (15), 159 (24), 145 (28), 144 (100).

(2*S*,4*E*)-2-Methyl-5-phenyl-4-penten-1-ol (44): (2*S*) Diastereomer **43** (6.167 g, 17.65 mmol) in diethyl ether (250 mL) was treated with H_2O (0.35 mL, 19.4 mmol, 1.1 equiv.). At 0 °C $LiBH_4$ (0.46 g, 20 mmol) in THF (20 mL) was added dropwise over 10 minutes. The mixture was stirred at room temp. for 2 h and a white precipitate is formed. For workup, NaOH (1 N, 20 mL) was added and the precipitate is dissolved on stirring for 20 minutes. The mixture was diluted with 100 mL H_2O (100 mL) and the aqueous phase was extracted with diethyl ether. The ethereal layer was washed with aq. NaCl, dried with $MgSO_4$ and evaporated under reduced pressure to give, after chromatography (hex/EE, 7:1) 2.812 g (15.95 mmol, 90%) of alcohol **44** as a colorless oil. The analytical data are in accordance with those described. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.98 (d, *J* = 6.9 Hz, 3 H), 1.39 (br. s, OH), 1.83 (mc, 1 H), 2.11 (dquint, *J* = 7.3, 1.1 Hz, 1 H), 2.28–2.41 (m, 1 H), 3.54 (mc, 2 H), 6.22 (dt, *J* = 15.8, 7.1 Hz, 1 H), 6.44 (d, *J* = 15.8 Hz, 1 H), 7.15–7.38 (m, 5 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 16.47, 36.14, 36.91, 67.87, 125.97, 126.96, 128.49, 127.74, 131.44, 137.64 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 3333b, 2957, 2925, 1107, 1030, 965, 892, 740, 692 cm^{-1}. MS (EI = 70 eV, 40 °C): *m*/*z* = 177 (15), 176 (85) [M$^+$], 158 (9), 145 (27), 143 (7), 130(29), 129 (84), 128 (33), 118 (50), 117 (100), 104 (80). $[\alpha]_D^{20}$ = –12.9 (*c* = 1.0, EtOH). $C_{12}H_{16}O$ (176.25): calcd. C 81.77, H 9.15; found C 81.77, H 8.93.

(*S*,*E*)-*tert*-Butyldimethyl(2-methyl-5-phenylpent-4-enyloxy)silane: Alcohol **44** (2.796 g, 15.86 mmol) in 80 mL DMF (80 mL) was treated at 0 °C with imidazole (2.05 g, 30 mmol, 1.9 equiv.) and TBSCl (3.12 g, 20.7 mmol, 1.3 equiv.) and stirred for 3 h at room temp. Then hexane (100 mL), aq. $NaHCO_3$ (100 mL) and water (180 mL) were added and the aqueous phase was extracted with diethyl ether. The organic layer was washed with H_2O, dried with MgSO4 and concentrated under reduced pressure. Chromatography of the residue (hex/EE, 20:1) gave TBS ether 45 (4.561 g, 15.70 mmol, 99%) as a colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.07 (s, 6 H), 0.93 (s, 9 H), 0.94 (d, 3 H), 1.78 (mc, 1 H), 2.03 (mc, 1 H), 2.37 (mc, 1 H), 3.48 (d, *J* = 6.2 Hz, 2 H), 6.23 (dt, *J* = 15.8, 7.1 Hz, 1 H), 6.41 (d, *J* = 15.8 Hz, 1 H), 7.16–7.39 (m, 5 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.35, 16.50, 18.35, 25.96, 36.19, 36.79, 67.76, 125.94, 126.79, 128.11, 128.46, 129.34, 131.11, 137.93 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2956, 2927, 2856, 1256, 1105, 964, 739, 692 cm^{-1}. MS (EI = 70 eV, 80 °C): *m*/*z* = 275 (3) [M–CH_3], 235 (6), 234 (22), 233 (100) [M–*t*Bu], 203 (10), 158 (48), 157 (13), 143 (18), 129 (57), 117 (42), 115 (72). $[\alpha]_D^{20}$ = +2.1 (*c* = 1.0, $CHCl_3$). $C_{18}H_{30}OSi$ (290.52): calcd. C 74.42, H 10.41; found C 74.68, H 10.43.

(*S*)-4-(*tert*-Butyldimethylsilyloxy)-3-methylbutan-1-ol (45): (*S*,*E*)-*tert*-Butyldimethyl(2-methyl-5-phenylpent-4-enyloxy)silane (4.545 g, 5.54 mmol) in THF/*t*BuOH/H_2O (10:10:1, 110 mL) was treated at 0 °C with NMO (50% in H_2O, 4.8 M, 3.9 mL, 18.7 mmol, 1.2 equiv.) and OsO_4. (100 mg/mL in *t*BuOH, 0.74 mL, 0.02 equiv.). The dark mixture was warmed to room temp. and stirred overnight (16 h). $Na_2S_2O_3$. (20% in H_2O, 100 mL) was added and the mixture was stirred for 15 min, diluted with water and then extracted with Et_2O. The organic phase was washed with H_2O, dried with $MgSO_4$ and evaporated under reduced pressure. The resulting yellow oil was dissolved in THF (140 mL), water (15 mL) and aq. $NaHCO_3$ (15 mL). Dropwise additions of $NaIO_4$ (7.34 g, 34.3 mmol, in 50 mL H_2O) at 0 °C formed a white voluminous precipitate, which was dissolved after addition of of THF/H_2O (1:1, 40 mL). After 3 h at room temp. water (500 mL) was added, and the aqueous layer was extracted with diethyl ether. The organic layer was washed with water, dried with $MgSO_4$ and evaporated under reduced pressure. The crude aldehyde was dissolved in 150 mL abs. MeOH (150 mL) and treated in portions with $NaBH_4$ (2.06 g, 54.6 mmol, 3.5 equiv.) at 0 °C for 15 min. Aq. NH_4Cl was added and the mixture was diluted with water (200 mL) and CH_2Cl_2 (200 mL) and stirred for 1 h at room temp. The organic layer was washed with brine, dried with $MgSO_4$ and evaporated under reduced pressure to give after chromatography (hex/EE, 7:1) the alcohol (3.046 g, 13.95 mmol, 89%) as a colorless, mobile oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.05 (s, 6 H), 0.88 (d, *J* = 6.9 Hz, 3 H), 0.89 (s, 9 H), 1.46–1.67 (m, 2 H), 1.68–1.83 (m, 1 H), 2.58 (tb, OH), 3.41 (dd, *J* = 9.8, 7.0 Hz, 1 H), 3.51 (dd, *J* = 9.8, 4.8 Hz, 1 H), 3.55–3.76 (m, 2 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.51, –5.46, 17.28, 18.29, 25.88, 33.89, 37.97, 61.12, 68.76 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 3356, 2956, 2926, 2858, 1472, 1256, 1102, 836, 775, 669 cm^{-1}. MS (EI = 70 eV, 70 °C): *m*/*z* = 162 (3), 161 (16) [M–*t*Bu], 143 (3), 119 (3), 115 (9), 106 (12), 105 (98), 75 (100). $[\alpha]_D^{20}$ = –9.0 (*c* = 1.1, $CHCl_3$). $C_{11}H_{26}O_2$ (218.41): calcd. C 60.49, H 12.00; found C 60.79, H 12.21.

(*S*)-[4-(*tert*-Butyldimethylsilyloxy)-3-methylbutyl]triphenylphosphonium Iodide (40): The alcohol obtained above (1.498 g, 6.859 mmol) in Et_2O/MeCN (3:1, 40 mL) was treated in succession

at 0 °C with imidazole (1.4 g, 20 mmol, 3 equiv.), triphenylphosphane (2.73 g, 10.5 mmol, 1.5 equiv.) and iodine (2.66 g, 10.5 mmol, 1.5 equiv.), whereupon an orange yellow solution and a colorless precipitate were formed. The mixture was stirred for 30 min at 0 °C, quenched with satd. aq. $Na_2S_2O_3$ (30 mL) and diluted with water. The aqueous phase was extracted with diethyl ether, and the combined organic phases were dried with $MgSO_4$ and evaporated under reduced pressure. Chromatography (hex/EE, 20:1) furnished the alkyl iodide (2.093 g, 93%) as a colorless oil which was heated with triphenylphosphane (2.70 g, 10.5 mmol, 1.5 equiv.) to 90 °C for 5 h. Chromatography (CH_2Cl_2 with 2% MeOH) furnished **40** (3.089 g, 76%) as a slightly yellow foam (m.p. 40–44 °C). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.09 (s, 6 H), 0.76 (s, 9 H), 0.96 (d, J = 6.6 Hz, 3 H), 1.35–1.54 (mc, 1 H), 1.71–1.89 (mc, 1 H), 1.98–2.22 (mc, 1 H), 3.36 (dd, J = 10.3, 6.4 Hz, 1 H), 3.40–3.59 (mc, 1 H), 3.65 (dd, J = 10.3, 4.1 Hz, 1 H), 3.72–3.93 (mc, 1 H), 7.63–7.87 (m, 15 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.59, –5.49, 16.66, 18.01, 20.58, 21.39, 25.73, 28.83, 35.60, 35.84, 66.80, 117.30, 118.67, 130.37, 130.57, 133.45, 133.60, 135.01, 135.06 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2956, 2856, 1587, 1484, 1471, 1438, 1251, 1112, 920, 837, 738, 690, 610 cm^{-1}. MS (FI = 25 keV, 3 μA, 150 °C): m/z = 465 (13), 464 (38), 463 (100) [M–I$^-$], 289 (4), 262 (6). $[\alpha]_D^{20}$ = –9.2 (c = 1.0, $CHCl_3$).

4-(Benzyloxy)-1-butanol (46): 1.4-Butanediol (17.8 mL, 200 mmol) in THF (30 mL) was added dropwise at 0 °C to a stirred suspension of sodium hydride (60%, 3.2 g). After stirring for 30 min NBu_4I (80 mg) was added. Benzyl bromide (9.7 mL, 82 mmol) in THF (20 mL) was added dropwise at 0 °C. After stirring at room temp. for 14 h water (100 mL) was added and the aqueous phase was extracted with diethyl ether. The ether layer was washed with brine, dried with $MgSO_4$ and concentrated under reduced pressure to give after chromatography (hex/EE, 2:1) **46** (13.29 g, 92%) as a colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.62–1.76 (mc, 4 H), 2.24 (mc, OH), 3.55 (t, J = 5.8 Hz, 2 H), 3.67 (t, J = 5.9 Hz, 2 H), 4.52 (s, 2 H), 7.25–7.36 (m, 5 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 27.09, 30.55, 63.12, 70.75, 73.47, 128.06, 128.12, 128.82, 138.60 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 3385, 3062, 3029, 2938, 2864, 1718, 1453, 1364, 1276, 1107, 738, 610 cm^{-1}. MS (EI = 70 eV, 150 °C): m/z = 180 (8) [M$^+$], 162 (4), 137 (9), 133 (2), 120 (4), 108 (33), 107 (BnO, 97), 92 (42), 91 (Bn, 100), 79 (28), 71 (24), 65 (21).

Ethyl (*E*)-6-Benzyloxy-2-methylhex-2-enoate (47): Oxalyl chloride (4.8 mL, 55 mmol) in CH_2Cl_2 (100 mL) was treated with DMSO (8.9 mL, 125 mmol) at –78 °C versetzt and stirred for 15 min. 46 (9.01 g, 50 mmol) in CH_2Cl_2 (40 mL) was added dropwise and the mixture was stirred for 30 min at –78 °C and then treated with *N*-ethyl-diisopropylamine (43 mL, 250 mmol). Over 30 min, the mixture was warmed to –60 °C and diluted with water (500 mL) at 0 °C. The mixture was extracted with diethyl ether, and the ether layer was washed with 2 N HCl, aq. $NaHCO_3$ and brine, dried with $MgSO_4$ and concentrated under reduced pressure to give the aldehyde which was dissolved in THF (200 mL) and treated in small portions with ethyl 2-(triphenylphosphoranylidene)propionate (19.9 g, 55 mmol) and stirred for 4 h at 80 °C. The mixture was quenchend with water (200 mL) and the organic layer was washed with brine, dried with $MgSO_4$ and concentrated under reduced pressure to give after chromatography (hex/EE, 7:1) followed by HPLC (hex/EE, 10:1) (*E*)-**47** (11.021 g, 84%) as a colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.32 (t, J = 7.0 Hz, 3 H), 1.79 (mc, 2 H), 1.86 (d, J = 1.0 Hz, 3 H), 2.31 (dd, J = 7.0, 15.6 Hz, 2 H), 3.52 (t, J = 6.5 Hz, 2 H), 4.22 (q, J = 7.0, 14.6 Hz, 2 H), 4.53 (s, 2 H), 6.78 (dt, J = 1.5, 7.5 Hz, 1 H), 7.28–7.4 (m, 5 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 12.31, 14.27, 25.37, 28.67, 60.38, 69.52, 72.96, 127.53, 127.59, 128.35, 128.31, 138.47, 141.42, 168.18 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2937, 2859, 1709, 1650 m, 1453, 1366, 1266, 1195, 1098, 903, 739 cm^{-1}. MS (EI = 70 eV, 30 °C): m/z = 262 (2) [M], 217 (7) [M–OEt], 203 (7.7), 189 (17) [M–CO_2Et], 171 (21) [M–CH_2Ph], 156 (37), 143 (38), 128 (13), 113 (24), 91 (100). $C_{16}H_{22}O_3$ (262.35): calcd. C 73.25, H 8.45, N 4.01; found C 73.27, H 8.48.

Ethyl (2*S*,3*R*)-6-Benzyloxy-2,3-dihydroxy-2-methylhexanoate (48): A suspension of AD-Mix β (35 g) and methanesulfonamide (2,38 g) in *tert*-butyl alcohol (100 mL) and water (125 mL) was stirred at 0 °C for 5 min, and then treated with **47** (5.247 g, 20.0 mmol) in *tert*-butyl alcohol (25 mL) at room temp. for 14 h. For workup, Na_2SO_3 (37.5 g) was added at 0 °C and the mixture was stirred for 30 min at room temp. The aqueous phase was extracted with EE and the organic layer was washed with NaOH (1 M), then with water, dried with $MgSO_4$ and evaporated under reduced pressure. Chromatography (hex/EE, 2:1) furnished **48** (5.661 g, 96%) with an *ee* of 94% according to HPLC. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.33 (t. J = 7.3 Hz, 3 H), 1.36 (s, 3 H), 1.49–1.63 und 1.74–1.95 (m), 2.67 (d, J = 7.8 Hz, 1 H), 3.40 (s, 1 H), 3.56 (t, J = 5.7 Hz, 2 H), 3.78 (ddd, J = 10.0, 7.8, 2.0 Hz, 1 H), 4.29 (dq, J = 7.3, 0.9 Hz, 2 H), 4.55 (s. 2 H), 7.26–7.40 (m, 5 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 14.12, 21.68, 26.20, 27.60, 62.05, 70.27, 73.02, 75.24, 76.49, 127.61, 127.68, 128.37, 138.21 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 3490, 2938, 2861, 1732, 1453, 1366, 1258, 1102, 1021, 739. MS (EI = 70 eV, 90 °C): m/z = 296 (3) [M], 223 (7) [M–EtO$_2$C], 205 (2) [M–*t*Bu], 172 (36), 126 (39), 118 (78), 115 (21), 113 (22), 107 (15), 91 (100). $[\alpha]_D^{20}$ = +24.2 (c = 1.1, $CHCl_3$). $C_{16}H_{24}O_5$ (296.36): calcd. C 64.84, H 8.16; found C 65.07; H 8.41.

Ethyl (4*S*,5*R*)-5-[3-(Benzyloxy)propyl]-2,2,4-trimethyl-1,3-dioxolane-4-carboxylate: Diol **48** (5.639 g, 19.03 mmol) in 2,2-dimethoxypropane (80 mL) was stirred with CSA (100 mg) at room temp. for 14 h. CSA (50 mg) was added and the mixture was stirred for additional 24 h. The reaction was quenched with aq. $NaHCO_3$, and extracted with diethyl ether. The organic phase was washed with brine and dried with $MgSO_4$ to give after chromatography (hex/EE, 7:1) the acetonide (6.329 g, 99%) as a colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.28 (t, J = 7.3 Hz, 3 H), 1.32 (s, 3 H), 1.38 (s, 3 H), 1.46 (s, 3 H), 1.63–1.92 (m, 4 H), 3.48–3.56 (m, 2 H), 4.21 (dq, J = 7.3, 1.1 Hz, 2 H), 4.16–4.23 (m, 1 H), 4.51 (s, 2 H), 7.26–7.36 (m, 5 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 14.09, 19.75, 25.47, 26.48, 26.92, 28.25, 61.30, 69.90, 72.83, 80.04, 82.52, 108.80, 127.48, 127.56, 1218.32, 138.58, 173.28 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2987, 2938, 2858, 1732, 1454, 1373, 1264, 1109, 1007, 738 cm^{-1} MS (EI = 70 eV, 50 °C): m/z = 336 (12) [M], 321 (11) [M–CH_3], 263 (11) [M–CO_2Et], 205 (10), 172 (15), 171 (24), 161 (30), 158 (15), 113 (16), 91 (100), 87 (25). $[\alpha]_D^{20}$ = +8.3 (c = 1.1, $CHCl_3$). $C_{19}H_{28}O_5$ (336.43): calcd. C 67.81, H 8.39; found C 67.59, H 8.14.

{(4*R*,5*R*)-5-[3-(Benzyloxy)propyl]-2,2,4-trimethyl-1,3-dioxolan-4-yl}methanol (49): Ethyl (4*S*,5*R*)-5-[3-(benzyloxy)propyl]-2,2,4-trimethyl-1,3-dioxolane-4-carboxylate (6.580 g, 19.65 mmol) in THF (150 mL) was treated with DIBAH (1 M in hexane, 60 mL, 60 mmol) at 0 °C. After 10 min the mixture was warmed to room temp. and stirred for 14 h. After recooling to 0 °C aq. 1 M KNa tartrate (250 mL) and ether (50 mL) were added and the mixture was stirred for 90 min at room temp. The organic layer was washed with brine, dried with $MgSO_4$ and concentrated under reduced pressure. Chromatography (hex/EE, 4:1) furnished **49** (5.417 g, 94%) as a colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.08 (s, 3 H), 1.38 (s, 3 H), 1.47 (s, 3 H), 1.52–1.98 (m, 4 H), 2.06 (dd, J = 9.1, 3.9 Hz, 1 H), 3.41 (dd, J = 11.9, 9.1 Hz, 1 H), 3.55 (mc, 3 H), 4.07 (dd, J = 8.7, 3.9 Hz, 1 H), 4.53 (s, 2 H), 7.25–7.38 (m, 5 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 18.77, 26.20, 26.74,

27.10, 28.71, 65.58, 69.98, 72.86, 77.76, 82.66, 127.52, 127.62, 128.34, 138.52 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 3453, 2984, 2935, 2864, 1454, 1373, 1213, 1105, 738 cm^{-1}. MS (EI = 70 eV, 70 °C): *m*/*z* = 294 (1) [M], 280 (1), 279 (19) [M–CH_3], 263 (4), 236 (4), 205 (4),145 (2), 129 (10), 112 (19), 91 (100). HRMS calcd. for $C_{16}H_{23}O_4$ [M–CH_3] 279.159; found 279.160. $[\alpha]_D^{20}$ = +4.5 (*c* = 1.1, $CHCl_3$). $C_{17}H_{26}O_4$ (294.39): calcd. C 69.36, H 8.90; found C 69.13, H 8.89.

({(4*R*,5*R*)-5-[3-(Benzyloxy)propyl]-2,2,4-trimethyl-1,3-dioxolan-4-yl}methoxy)(*tert*-butyl)dimethylsilane: Alcohol **49** (4.816 g,16.36 mmol) in DMF (45 mL) was treated with imidazole (2.38 g, 35 mmol, 2.1 equiv.) and TBSCl (2.86 g, 19 mmol, 1.2 equiv.) at 0 °C and the mixture was stirred at room temp. for 12 h. Hexane (200 mL) and aq. $NaHCO_3$ was added, and the aqueous phase was extracted with diethyl ether. The organic layer was washed with brine, dried with $MgSO_4$ and concentrated under reduced pressure. Chromatography (hex/EE, 20:1) furnished **50** (6.598 g, 99%) as a colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.08 (s, 6 H), 0.92 (s, 9 H), 1.10 (s, 3 H), 1.35 (s, 3 H), 1.45 (s, 3 H), 1.57–1.90 (m, 4 H), 3.55 (mc, 4 H), 4.01 (dd, *J* = 7.8, 4.8 Hz, 1 H), 4.54 (s, 2 H), 7.26–7.39 (m, 5 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.63, –5.44, 18.26, 19.01, 25.88, 26.72, 26.90, 27.36, 28.71, 68.34, 70.17, 72.78, 80.03, 82.04, 106.81, 127.44, 127.56, 128.29, 138.68 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2928, 2856, 1106, 882, 776, 738 cm^{-1}. MS (FD = 7 kV, 35 °C): *m*/*z* = 408 (2) [M], 393 (3) [M–CH_3], 375 (1), 353 (8), 352 (26), 351 (100) [M–Bu], 263 (12). $[\alpha]_D^{20}$ = +1.1 (*c* = 1.1, $CHCl_3$). $C_{23}H_{40}O_4Si$, (408.65): calcd. C 67.60, H 9.87; found C 67.40, H 9.58.

3-{(4*R*,5*R*)-5-[(*tert*-Butyldimethylsilyloxy)methyl]-2,2,5-trimethyl-1,3-dioxolan-4-yl}propan-1-ol (50): The TBS ether (see above) (6.636 g, 16.24 mmol) in ethyl acetate (80 mL) was hydrogenated over Pd/C (ca. 50% H_2O, 150 mg) with hydrogen (1 bar) at room temp. for 14 h. Additional catalyst (50 mg) was added and the hydrogenation was continued for another 14 h. The mixture was filtered through celite and the filtrate was concentrated under reduced pressure to give after chromatography (hex/EE, 4:1) alcohol **50** (4.784 g, 92%) as a colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.05 (s, 6 H), 0.88 (s, 9 H), 1.07 (s, 3 H), 1.34 (s, 3 H), 1.44 (s, 3 H), 1.47–1.80 (m, 4 H), 2.21 (t, *J* = 5.7 Hz, OH), 3.49 (d, *J* = 10.3 Hz, 1 H), 3.57 (d, *J* = 10.3 Hz, 1 H), 3.62–3.74 (m, 2 H), 3.99 (dd, *J* = 9.6, 2.7 Hz, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.65, –5.47, 18.25, 18.95, 25.85, 26.70, 27.10, 28.64, 30.61, 62.74, 68.36, 80.44, 82.12, 106.98 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 3424, 2934, 2858, 1106, 1007, 851, 669 cm^{-1}. MS (FD = 7 kV, 3 mA, 32 °C): *m*/*z* = 304 (12), 303 (38) [M–CH_3], 263 (5), 262 (10), 261 (100) [M–*t*Bu] 260 (7), 203 (28) [M–TBS], 173 (43), 145 (4), 133 (1), 57 (20). $[\alpha]_D^{20}$ = +1.3 (*c* = 1.1, $CHCl_3$). $C_{16}H_{34}O_4Si$ (318.52): calcd. C 60.33, H 10.76; found C 60.44; H 10.52.

3-{(4*R*,5*R*)-5-[(*tert*-Butyldimethylsilyloxy)methyl]-2,2,5-trimethyl-1,3-dioxolan-4-yl}propanoic Acid (51): Alcohol **50** (4.141 g, 13.00 mmol) in CH_2Cl_2 (200 mL) and pyridine (10 mL) was treated at 0 °C with Dess–Martin periodinane (6.5 g, 15.3 mmol, 1.2 equiv.). The mixture was stirred at room temp. for 2 h and then quenched with aq. $Na_2S_2O_3$/$NaHCO_3$. After 10 min the mixture was diluted with water and extracted with CH_2Cl_2. The organic layer was dried with $MgSO_4$ and concentrated under reduced pressure. The residue was filtered through silica gel (hex/EE, 4:1), and the crude aldehyde was dissolved in *tert*-butyl alcohol (260 mL) and 2.3-dimethyl-2-butene (20 mL). A solution of NaH_2PO_4 (7 g) and $NaClO_2$ (80%, 7 g) in water (70 mL) was added dropwise. The mixture was stirred at room temp. for 90 min and then quenched with aq. NH_4Cl. The aqueous phase was extracted with CH_2Cl_2, and the organic layer was washed with brine, dried with $MgSO_4$ and concentrated under reduced pressure. Chromatography (hex/EE, 7:1→1:1) furnished acid **51** (4.009 g, 93%) as a viscous oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.05 (s, 6 H), 0.89 (s, 9 H), 1.10 (s, 3 H), 1.32 (s, 3 H), 1.42 (s, 3 H), 1.60–1.91 (m, 2 H), 2.55 (mc, 2 H), 3.51 (d, *J* = 10.3 Hz, 1 H), 3.58 (d, *J* = 10.3 Hz, 1 H), 3.98 (dd, *J* = 8.5, 4.6 Hz, 1 H), 9.1 (br. s, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.67, –5.50, 18.26, 19.05, 25.39, 25.86, 26.77, 28.65, 31.49, 68.43, 79.43, 82.02, 107.24, 178.77 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 3096, 2986, 2934, 2859, 1713, 1377, 1258, 1216, 1105, 1005, 850, 778 cm^{-1}. MS (FD, 7 kV, 3 mA, 25 °C): *m*/*z* = 334 (1), 333 ,(2) [M^+], 322 (1), 317 (1) [M–CH_3], 308 (2), 294 (4), 280 (8), 276 (22), 275 (100) [M–*t*Bu], 266 (8), 259 (15). $[\alpha]_D^{20}$ = +12.5 (*c* = 1.0, $CHCl_3$). $C_{16}H_{32}O_5Si$ (332.51): calcd. C 57.79, H 9.70; found C 58.65; H 9.41.

(4*S*,5*R*)-3-(3-{(4*R*,5*R*)-5-[(*tert*-Butyldimethylsilyloxy)methyl]-2,2,5-trimethyl-1,3-dioxolan-4-yl}propanoyl)-4-methyl-5-phenyloxazolidin-2-one (52): Acid **51** (4.453 g, 13.39 mmol) in diethyl ether (100 mL) was treated dropwise at –78 °C with triethylamine (2.1 mL, 15 mmol, 1.1 equiv.) and pivaloyl chloride (1.67 mL, 13.5 mmol). A voluminous white precipitate was formed and the mixture was slowly warmed to –30 °C and stirred for 30 min in a separate flask, (4*S*,5*R*)-4-methyl-5-phenyl-1,3-oxazolidin-2-one (2.48 g, 14.0 mmol) in THF (15 mL) was treated with *n*BuLi (1.6 M in THF, 8.8 mL, 14 mmol) at –78 °C and stirred for 15 min. This solution was added at –78 °C through a double needle to the mixture prepared above. After 30 min the mixture was warmed to 0 °C and stirred for 2.5 h. Aq. NH_4Cl was added at 0 °C and the aqueous phase was extracted with diethyl ether. The organic phase was washed with brine, dried with $MgSO_4$ and concentrated under reduced pressure. Chromatography (hex/EE, 7:1) furnished **52** (4.971 g, 76%) which was crystallized from hexane/ether (m.p. 114–116 °C). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.06 (s, 6 H), 0.89 (d, *J* = 6.4 Hz, 3 H), 0.90 (s, 9 H), 1.11 (s, 3 H), 1.34 (s, 3 H), 1.42 (s, 3 H), 1.82–1.87 (m, 2 H), 3.13 (mc, 2 H), 3.52 (d, *J* = 10.0 Hz, 1 H), 3.58 (d, *J* = 10.0 Hz, 1 H), 4.03 (dd, *J* = 8.7, 4.8 Hz, 1 H), 4.76 (quint, *J* ≈ 7.0 Hz, 1 H), 5.66 (d, *J* = 7.3 Hz, 1 H), 7.28–7.48 (m, 5 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.63, –5.44, 14.47, 18.28, 19.06, 25.13, 25.90, 26.81, 28.70, 33.35, 54.78, 68.45, 78.97, 79.39, 82.03, 107.15, 125.64, 128.70, 128.75, 133.40, 152.98, 172.60 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2856, 1786, 1697, 1106, 859 cm^{-1}. MS (EI = 70 eV, 120 °C): *m*/*z* = 477 (11), 476 (31) [M^+–CH_3], 435 (20), 434 (68) [M^+–*t*Bu], 417 (18), 416 (56), 377 (19), 476 (73), 346 (39), 332 (19), 301 (13), 289 (20), 288 (100), 252 (30), 245 (26), 244 (72). $C_{26}H_{41N}O_6Si$ (491.69): calcd. C 63.51, H 8.40, N 2.85; found C 63.44; H 8.25, N 3.11.

(4*S*,5*R*)-3-[(*S*)-3-{(4*R*,5*R*)-5-[(*tert*-Butyldimethylsilyloxy)methyl]-2,2,5-trimethyl-1,3-dioxolan-4-yl}-2-hydroxypropanoyl]-4-methyl-5-phenyloxazolidin-2-one (53): NaHMDS (1 M in THF, 3.75 mL, 3.75 mmol, 1.25 equiv.) in THF (10 mL) was treated at –78 °C with oxazolidinone **52** (1.475 g, 3.00 mmol) in THF (10 mL). The mixture was stirred for 60 min, then cooled to –92 °C and treated dropwise with Davis oxaziridine (1.18 g, 4.5 mmol, 1.5 equiv.) in THF (5 mL). After 8 min aq. NH_4Cl was added and the mixture was slowly warmed to room temp. The aqueous phase was extracted with diethyl ether and the organic layer was washed with aq. $NaHCO_3$, Na_2SO_3 and brine. The combined organic layers were dried with $MgSO_4$ and concentrated under reduced pressure. Chromatography (hex/EE, 7:1) followed by HPLC (supersphere, hex/EE, 9:1) furnished **53** (0.801 g, 53%) as colorless crystals which were recrystallized from hex/EE (mp 133–135 °C) and subjected to X-ray single crystal diffraction. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.07 (s, 6 H), 0.91 (s, 9 H), 0.97 (d, *J* = 6.6 Hz, 3 H), 1.07 (s, 3 H), 1.33 (s, 3 H), 1.43 (s, 3 H), 2.05–2.18 (m, 2 H), 3.53 (d, *J* = 10.3 Hz,

1 H), 3.58 (d, J = 10.1 Hz, 1 H), 3.77 (d, J = 5.7 Hz, OH), 4.21 (dd, J = 8.9, 3.4 Hz, 1 H), 4.64 (quint, $J \approx$ 6.8 Hz, 1 H), 5.30 (q, 1 H), 5.68 (d, J = 7.08 Hz, 1 H), 7.25–7.47 (m, 5 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.72, –5.50, 14.46, 18.25, 18.96, 25.87, 26.60, 28.76, 34.26, 55.96, 67.94, 68.87, 75.70, 80.03, 82.09, 107.12, 125.57, 128.78, 128.92, 132.80, 152.80, 174.26 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 3507, 2934, 2857, 1787, 1697 s, 1548, 1257, 1106, 837, 769, 738 cm^{-1}. MS (FI = 7 kV, 3 mA, 120 °C): m/z = 509 (3), 508 (13) [MH$^+$], 492 (5) [M–CH_3], 452 (7), 451 (23), 450 (100) [M–tBu]. HRMS calcd. for $C_{25}H_{38}NO_7Si$ [M–CH_3]: 492.2418; found 492.2403 $[\alpha]_D^{20}$ = –13.4 (c = 1.0, $CHCl_3$). **Crystal Data:** Formula $C_{26}H_{41}NO_7Si$, molecular. weight = 507.71, crystal dimensions 0.46 × 0.65 × 0.70 mm, crystal system orthorhombic, space group $P2_12_12_1$, space group no. 19, a = 12.1943(9) A, b = 13.403(2), c = 17.625(2), V = 2880.5(5) A^3, Z = 4, $D_{calcd.}$ = 1.171 g/cm^3, linear absorption coeff. 1.2 cm, radiation Mo-K, scan range sphere (2 theta)$_{max}$ 63.6, resolution 0.67 A, number of reflections measured 49782, number of independent reflections 8709, reflections used with $I > 0.8510$, number of variables 480, $R(F)$ = 0.055, $wR(F)$ = 0.037, S = 0.81. A single crystal was measured on a SIEMENS SMART diffractometer at a temperature of about –138 °C. Repeatedly measured reflections remained stable. An empirical absorption correction using program SADABS gave an effective transmission range from 0.840 to 1.000. Equivalent reflections were averaged. Bijvoet pairs of reflections were not averaged. $R(I)$ internal = 0.039. The structure was determined by direct methods using program SHELXS. The H atoms were taken from a difference Fourier synthesis and were refined with isotropic thermal parameters. The non-H atoms were refined with anisotropic thermal parameters. The structure was refined on F values using weighting scheme: $w(F) = 4F^2/[2\sigma(F^2) + (0.03F^2)^2]$. The final difference density was between –0.21 and +0.28 e/Å. A refinement of the Flack x parameter gave x = 0.06(10) and confirmed the absolute configuration of the structure. The calculations were performed with the SMART, SHELX and MolEN program systems.

(4*S*,5*R*)-3-[(*S*)-2-(*tert*-Butyldimethylsilyloxy)-3-{(4*R*,5*R*)-5-[(*tert*-butyldimethylsilyloxy)methyl]-2,2,5-trimethyl-1,3-dioxolan-4-yl}propanoyl]-4-methyl-5-phenyloxazolidin-2-one: Alcohol **53** (0.243 g, 0.48 mmol) in CH_2Cl_2 (3 mL) was treated with 2,6-lutidine (100 μL, 0.9 mmol) and TBSOTf (0.14 mL, 0.6 mmol) and stirred for 14 h at room temp. CH_2Cl_2, and aq. $NaHCO_3$ were added and the aqueous phase was extracted with diethyl ether. The organic phase was washed with brine, dried with $MgSO_4$ and concentrated under reduced pressure to give after chromatography (hex/EE, 10:1) the disilyl ether (0.284 g, 95%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.06 (s, 9 H), 0.10 (s, 3 H), 0.94 (s, 9 H), 0.96 (s. 9 H), 0.95 (d, J = 6.9 Hz, 3 H), 1.05 (s, 3 H), 1.31 (s, 3 H), 1.41 (s, 3 H), 1.91 (ddd, J = 14.6, 4.8, 1.6 Hz, 1 H), 2.13 (ddd, J = 14.6, 10.3, 4.3 Hz, 1 H), 3.51 (d, J = 10.3 Hz, 1 H), 3.57 (d, J = 10.3 Hz, 1 H), 4.25 (dd, J = 10.3, 1.6 Hz, 1 H), 4.60 (quint, J = 6.8 Hz, 1 H), 5.53 (t, J = 4.6 Hz, 1 H), 5.64 (d, J = 7.1 Hz, 1 H), 7.27–7.46 (m, 5 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.60, –5.41, –5.17, –4.78, 14.49, 18.34, 18.86, 25.86, 25.99, 26.56, 28.80, 35.80, 55.80, 67.85, 69.61, 75.65, 79.76, 82.10, 106.94, 125.62, 128.73, 128.77, 133.21, 153.00, 172.93 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2955, 2931, 2857, 1783, 1720, 1459, 1368, 1343, 1252, 1109, 838, 778, 610 cm^{-1}. MS (FI = 7 kV, 3 mA, 110 °C): m/z = 622 (1) [M], 566 (18), 565 (39), 564 (100) [M–tBu]. $[\alpha]_D^{20}$ = –18.6 (c = 0.8, $CHCl_3$). $C_{32}H_{55}NO_7Si_2$ (621.95): calcd. C 61.80, H 8.91, N 2.25; found C 61.86, H 8.64, N 2.51.

(1*R*,2*S*)-2-[(*S*)-2-(*tert*-Butyldimethylsilyloxy)-3-{(4*R*,5*R*)-5-[(*tert*-butyldimethylsilyloxy)methyl]-2,2,5-trimethyl-1,3-dioxolan-4-yl}propanamido]-1-phenylpropyl Methoxy(methyl)carbamate (54): A suspension of *N*,O-dimethylhydroxylamine hydrochloride (43 mg, 0.44 mmol, 4 equiv.) in THF (3 mL) was treated dropwise at 0 °C with $AlMe_3$ (2 M in toluene, 0.17 mL, 0.33 mmol) and stirred at room temp. for 45 min. The oxazolidinone disilyl ether prepared above (67 mg, 0.11 mmol) in THF (2 mL) was added dropwise at –15 °C. The mixture was warmed to room temp. and stirred for 14 h. Aq. KNa tartrate (1 M) was added at 0 °C and the aqueous phase was extracted with diethyl ether. The organic phase was washed with brine, dried with $MgSO_4$, concentrated under reduced pressure and chromatographed (hex/EE, 4:1) to give **54** (54 mg, 74%) as a colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.03 (s, 3 H), 0.04 (s, 3 H), 0.05 (s, 3 H), 0.09 (s, 3 H), 0.088 (s, 9 H), 0.92 (s, 9 H), 1.04 (s, 3 H), 1.10 (d, J = 6.6 Hz, 3 H), 1.26 (s, 3 H), 1.35 (s, 3 H), 1.83 (ddd, J = 14.2, 7.1, 2.1 Hz, 1 H), 2.02 (ddd, J = 14.2, 10.7, 3.2 Hz, 1 H), 3.15 (s, 3 H), 3.51 (s, 2 H), 3.74 (s, 3 H), 4.21–4.30 (m, 2 H), 4.38–4.48 (mc, 1 H), 5.88 (d, J = 3.9 Hz, 1 H), 6.74 (d, J = 9.1 Hz, 1 H), 7.24–7.36 (m, 5 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.60, –5.40, –5.33, –5.04, 14.47, 17.94, 18.33, 19.00, 25.78, 25.94, 26.70, 28.66, 35.30, 35.58, 48.44, 61.73, 68.42, 71.09, 75.96, 79.31, 81.67, 107.06, 126.17, 127.95, 128.44, 137.69, 156.19, 172.85 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 3425, 2934, 2857, 1720, 1685, 1508, 1460, 1377, 1256, 1107, 840 m, 780, 610 cm^{-1}. MS (FI = 7 kV, 3 mA, 120 °C): m/z = 684 (6), 683 (44) [M], 627 (8), 626 (36), 625 (100) [M–tBu], 523 (4), 267 (20).

(*S*)-3-{(4*R*,5*R*)-5-[(*tert*-Butyldimethylsilyloxy)methyl]-2,2,5-trimethyl-1,3-dioxolan-4-yl}-2-hydroxy-*N*-methoxy-*N*-methylpropanamide (55): Oxazolidinone **53** (0.233 g, 0.459 mmol) in THF (2 mL) was added to a suspension of *N*,O-dimethylhydroxylamine hydrochloride (0.20 g, 2.0 mmol, 4.3 equiv.) in THF (4 mL) and the mixture was treated with isopropylmagnesium bromide (2 M in Et_2O, 1.0 mL) at –15 °C. The mixture was stirred for 30 min at –15 °C and then for 90 min at room temp. Additional 100 mg of of *N*,O-dimethylhydroxylamine hydrochloride and 0.5 mL of *i*PrMgCl were added and the mixture was stirred for 15 min at 0 °C. Then the reaction was quenched with aq. NH_4Cl and the mixture was extracted with diethyl ether. The organic phase was washed with brine, dried with $MgSO_4$ and concentrated under reduced pressure to give after chromatography (hex/EE, 4:1) Weinreb amide **55** (0.144 g, 80%) as a colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.04 (s, 6 H), 0.87 (s, 9 H), 1.05 (s, 3 H), 1.29 (s, 3 H), 1.38 (s, 3 H),1.85–2.05 (m, 2 H), 3.20 (s, 3 H), 3.46–3.60 (m, 2 H), 3.52 (d, J = 5.3 Hz, OH), 3.69 (s, 3 H), 4.14 (dd, J = 9.1, 3.6 Hz, 1 H), 4.55 (m, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.72, –5.52, 18.25, 18.90, 25.85, 26.55, 28.57, 32.95, 34.71, 61.28, 67.09, 68.17, 76.29, 82.04, 107.13, 174.43 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 3451, 2934, 2858, 1665, 1493, 1371, 1257, 1105, 1001, 839, 778 cm^{-1}. MS (FI = 7 kV, 3 mA, 25 °C): m/z = 392 [M$^+$, 8], 376 (1) [M–CH_3], 335 (27), 334 (100) [M–tBu], 245 (17). HRMS calcd. for $C_{17}H_{34}NO_6Si$ 376.2155 [M – CH_3]; found 376.2141. $[\alpha]_D^{20}$ = –19.5 (c = 1.0, $CHCl_3$).

(*S*)-2-(*tert*-Butyldimethylsilyloxy)-3-{(4*R*,5*R*)-5-[(*tert*-butyldimethylsilyloxy)methyl]-2,2,5-trimethyl-1,3-dioxolan-4-yl}-*N*-methoxy-*N*-methylpropanamide: Weinreb amide **55** (52 mg, 0.133 mmol) in CH_2Cl_2 (3 mL) was treated at 0 °C with 2,6-lutidine (30 μL, 0.3 mmol, 2.2 equiv.) and TBSOTf (40 μL, 0.17 mmol, 1.3 equiv.) and stirred for 14 h at room temp. Workup as described for the preparation of **54** followed by chromatography (hex/EE, 7:1) furnished the silyl ether (63 mg, 93%) as a colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.03 (s, 6 H), 0.07 (s, 6 H), 0.87 (s, 9 H), 0.88 (s, 9 H), 1.04 (s, 3 H), 1.27 (s, 3 H), 1.39 (s, 3 H), 1.84 (ddd, J = 13.7, 10.5, 5.0 Hz, 1 H), 1.99 (ddd, J = 13.7, 7.8, 2.1 Hz, 1 H), 3.19 (s, 3 H), 3.44 (d, J = 10.5 Hz, 1 H), 3.52 (d, J = 10.5 Hz, 1 H), 3.70 (s, 3 H), 3.93 (dd, J = 10.5, 2.3 Hz, 1 H), 4.74 (dd, J =

7.8, 5.0 Hz, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.68, –5.48, –4.98, –4.72, 18.20, 18.26, 18.93, 25.79, 25.88, 26.68, 28.73, 35.68, 61.23, 67.41, 75.88, 82.40, 107.12 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2934, 2858, 1682, 1463, 1372, 1255, 1107, 1003, 841, 778 cm^{-1}. MS (EI = 70 eV, 30 °C): *m*/*z* = 491 (3) [M$^+$–CH_3], 450 (8), 449 (18), 448 (35) [M–*t*Bu], 390 (21), 302 (29), 299 (11), 298 (49), 218 (15), 201 (12), 115 (20), 73 (100). HRMS calcd. for $C_{23}H_{48}NO_6Si_2$ 490.3020 [M – CH_3]; found 490.3042. $[\alpha]_D^{20}$ = +4.8 (*c* = 1.0, $CHCl_3$).

(*S*)-3-(*tert*-Butyldimethylsilyloxy)-4-{(4*R*,5*R*)-5-[(*tert*-butyldimethylsilyloxy)methyl]-2,2,5-trimethyl-1,3-dioxolan-4-yl}butan-2-one (56): The TBS ether prepared above (59 mg, 0.117 mmol) in THF (3 mL) was treated at –78 °C with MeLi (1.6 M in Et_2O, 85 μL, 0.14 mmol, 1.2 equiv.). The mixture was stirred for 45 min and then treated with another 80 μL of MeLi and stirred for 2 h at –78 °C. Then the mixture was poured into an icecold mixture of aq. NH_4Cl and Et_2O (3:1). The aqueous layer was extracted with diethyl ether and the organic phase was washed with brine, dried with $MgSO_4$ and concentrated under reduced pressure. Chromatography (hex/EE, 7:1) furnished the ketone **56** (36 mg, 67%) as a colorless oil along with of mono-desilylated material (10 mg). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.040 (s, 3 H), 0.042 (s, 3 H), 0.072 (s, 3 H), 0.084 (s, 3 H), 0.88 (s, 9 H), 0.93 (s, 9 H), 1.04 (s, 3 H), 1.29 (s, 3 H), 1.36 (s, 3 H), 1.79 (ddd, *J* = 13.9, 7.3, 2.3 Hz, 1 H), 1.93 (ddd, *J* = 13.9, 10.5, 3.4 Hz, 1 H), 2.19 (s, 3 H), 3.51 (s, 2 H), 4.16 (m, 2 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.62, –5.43, –5.11, –4.87, 18.06, 18.32, 19.03, 25.76, 25.93, 26.58, 28.57, 35.69, 68.57, 75.88, 76.44, 81.56, 107.14, 212.46 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2956, 2932, 2858, 1720, 1463, 1378, 1257, 1216, 1106, 838, 778, 671 cm^{-1}. MS (FI = 7 kV, 3 mA, 40 °C): *m*/*z* = 445 (<1) [M–CH_3], 406 (1), 405 (7), 404 (26), 403 (100) [M–*t*Bu]. HRMS: calcd. for $C_{22}H_{45}O_5Si_2$ 445.2805 [M–CH_3]; found 445.2819. $[\alpha]_D^{20}$ = +0.6 (*c* = 1.0, $CHCl_3$).

4-[(*S*,*E*)-3-(*tert*-Butyldimethylsilyloxy)-4-{(4*R*,5*R*)-5-[(*tert*-butyldimethylsilyloxy)methyl]-2,2,5-trimethyl-1,3-dioxolan-4-yl}-2-methylbut-1-enyl]-2-methylthiazole (57): Phosphonium salt **32** (0.233 g, 0.66 mmol, 2.1 equiv.) in dry THF (2 mL) was cooled to –78 °C and treated dropwise with KHMDS (0.12 g, 0.60 mmol, in 1 mL THF). After 5 min the mixture was warmed to room temp. to dissolve the white suspension. After recooling to –78 °C, the ketone **56** (0.146 g, 0.317 mmol) in THF (1.5 mL) was added. The reaction was warmed to 40 °C and the stirred for 1 h at 40 °C. The orange-red solution was quenched with aq. NH_4Cl and the aqueous phase was extracted with diethyl ether. The organic phase was washed with aq. $NaHCO_3$ and brine, dried with $MgSO_4$ and concentrated under reduced pressure. Chromatography (hex/EE, 20:1) furnished **57** (92 mg, 54%) along with unreacted ketone **56** (57 mg, 0.123 mmol) and the (*Z*) olefin (3 mg) as colorless oils. **(*E*)-Isomer (*E*)-57:** ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.00 (s, 6 H), 0.02 (s, 3 H), 0.09 (s, 3 H), 0.82 (s, 9 H), 0.89 (s, 9 H), 1.05 (s, 3 H), 1.24 (s, 3 H), 1.42 (s, 3 H), 1.63–1.72 (m, 2 H), 1.99 (d, *J* = 1.1 Hz, 3 H), 2.70 (s, 3 H), 3.43 (d, *J* = 10.3 Hz, 1 H), 3.49 (d, *J* = 10.3 Hz, 1 H), 3.86 (dd, *J* = 9.1, 3.4 Hz, 1 H), 4.37 (dd, *J* = 8.2, 5.9 Hz, 1 H), 6.48 (s, 1 H), 6.90 (s, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.69, –5.49, –4.90, –4.60, 13.03, 18.18, 19.19, 25.81, 25.86, 26.61, 28.70, 36.69, 67.85, 76.77, 77.18, 81.83, 106.93, 115.08, 120.05, 141.00, 153.23, 164.10 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2956, 2931, 2857, 1377, 1256, 1104, 837, 776 cm^{-1}. MS (FI = 7 keV, 3 mA, 115 °C): *m*/*z* = 557 (11), 556 (41), 555 (100) [M$^+$], 553 (<1), 498 (1) [M–*t*Bu], 272 (1). 254 (1), 184 (<1), 168 (1), 85 (1). HRMS: calcd. for $C_{26}H_{53}NO_4SSi_2$: 555.3234 [M$^+$]; found 555.3251. $[\alpha]_D^{20}$ = +37.0 (*c* = 1.0, $CHCl_3$). $C_{26}H_{53}NO_4SSi_2$ (555.96): calcd. C 60.49, H 9.61, N 2.52; S 5.77; found C 60.74; H 9.66, N 2.47; S 5.44. **(*Z*)-Isomer (*Z*)-57:** ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.01 (s, 3 H), 0.05 (s, 3 H), 0.06 (s, 3 H), 0.09 (s, 3 H), 0.90 (s, 9 H), 0.91 (s, 9 H), 1.04 (s, 3 H), 1.33 (s, 3 H), 1.43 (s, 3 H), 1.61–1.82 (m, 2 H), 2.02 (s, 3 H), 2.71 (s, 3 H), 3.54 (s, 2 H), 4.09 (d, *J* = 8.9 Hz, 1 H), 4.38 (d, *J* = 11.0 Hz, 1 H), 6.51 (s, 1 H), 6.90 (s, 1 H) ppm.

((*S*)-5-{(4*R*,5*R*)-5-[3-(Benzyloxy)propyl]-2,2,4-trimethyl-1,3-dioxolan-4-yl}-2-methylpent-4-enyloxy)(*tert*-butyl)dimethylsilane (59): Alcohol **49** (1.472 g, 5.00 mmol) in. CH_2Cl_2 (80 mL) was treated with pyridine (4 mL) and Dess–Martin periodinane (2.54 g, 6.0 mmol, 1.2 equiv.) and stirred for 4 h at 0 °C. Aq. $Na_2S_2O_3$/$NaHCO_3$ (1:1) was added and the mixture was stirred for 10 min. The aqueous phase was extracted with diethyl ether and the organic phase was washed with brine, dried with $MgSO_4$ and concentrated under reduced pressure to give after chromatography (hex/EE, 4:1) aldehyde **58** (1.411 g, 97%) as a colorless oil, which was used immediately for the Wittig reaction. Thus phosphonium salt **40** (2.994 g, 5.07 mmol) in THF (20 mL) was treated dropwise with NaHMDS (1 M in THF, 5.6 mL, 5.6 mmol, 1.1 equiv.) at 0 °C. The dark orange solution was stirred for 30 min at 0 °C; aldehyde **58** in THF (3 mL) was added dropwise and the mixture was stirred for 30 min at room temp. Aq. NH_4Cl was added at 0 °C; the aqueous phase was extracted with diethyl ether and the organic phase was washed with brine, dried with $MgSO_4$ and concentrated under reduced pressure to give after chromatography (hex/EE, 10:1) olefin **59** (2.078 g, 87%) as an *E*/*Z* mixture, which was used for the next step without separation. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.04 (s, 6 H), 0.89 (d, *J* = 6.6 Hz, 3 H), 0.90 (s, 9 H), 1.20 (s, 3 H), 1.34 (s, 3 H), 1.43 (s, 3 H), 1.54–1.93 (m, 5 H), 2.11–2.25 (m, 1 H), 2.35–2.48 (m, 1 H), 3.35–3.60 (m, 4 H), 3.82 (t, *J* = 6.2 Hz, 1 H), 4.51 (s, 2 H), 5.26–5.49 (m, 2 H), 7.22–7.36 (m, 5 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.34, 16.59, 18.35, 22.61, 25.96, 26.01, 26.58, 27.23, 28.74, 31.78, 36.69, 68.20, 70.03, 72.86, 77.20, 82.72, 107.23, 127.49, 127.60, 128.33, 130.66, 132.07, 138.63 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2956, 2856, 1455, 1369, 1255, 1105, 737, 697 cm^{-1}. MS (EI = 70 eV, 120 °C): *m*/*z* = 477 (0.2) [M$^+$], 461 (0.4) [M–CH_3], 362 (9), 361 (23) [M–*t*Bu], 299 (16), 298 (26), 241 (32), 227 (17), 211 (18), 185 (22), 171 (20), 159 (29), 153 (29), 91 (100). $[\alpha]_D^{20}$ = +2.6 (*c* = 1.0, $CHCl_3$). $C_{28}H_{48}O_4Si$, (476.76): calcd. C 70.54, H 10.15; found C 70.26; H 9.94.

3-{(4*R*,5*R*)-5-[(*S*)-5-(*tert*-Butyldimethylsilyloxy)-4-methylpent-1-enyl]-2,2,5-trimethyl-1,3-dioxolan-4-yl}propan-1-ol: Olefin **59** (1.161 g, 2.435 mmol) in ethanol (110 mL) was treated with Pd/Al_2O_3 (ca. 50% H_2O, 120 mg) and hydrogenated under 3 bar of hydrogen at room temp. for 14 h. Another 80 mg of the catalyst were added and the hydrogenation was continued for another 14 h. The mixture was filtered through celite, and the filtrate was concentrated under reduced pressure. Chromatography (hex/EE, 7:1) furnished the saturated compound (0.861 g, 91%) as acolorless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.03 (s, 6 H), 0.88 (d, *J* = 6.9 Hz, 3 H), 0.89 (s, 9 H), 1.07 (s, 3 H), 1.33 (s, 3 H), 1.34–1.65 (m, 9 H), 1.43 (s, 3 H), 1.68–1.80 (m, 2 H), 2.19 (t, *J* = 5.1 Hz, OH), 3.33–3.50 (m, 2 H), 3.65–3.77 (m, 3 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.40, –5.34, 16.68, 18.31, 21.11, 21.28, 25.92, 26.54, 26.89, 28.62, 30.56, 33.68, 35.63, 39.59, 62.55, 68.25, 82.22, 82.49, 106.58 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 3424, 2935, 2902, 2857, 1471, 1372, 1252, 1216, 1178, 1100, 1006, 837, 610 cm^{-1}. MS (EI = 70 eV, 25 °C): *m*/*z* = 373 (24) [M–CH_3], 313 (17), 273 (41), 259 (21), 185 (14), 181 (33), 163 (39), 115 (58), 75 (100). $[\alpha]_D^{20}$ = +1.0 (*c* = 1.1, $CHCl_3$). $C_{21}H_{44}O_4Si$, (388.66): calcd. C 64.90, H 11.41; found C 64.66; H 11.36.

3-{(4*R*,5*R*)-5-[(*S*)-5-(*tert*-Butyldimethylsilyloxy)-4-methylpent-1-enyl]-2,2,5-trimethyl-1,3-dioxolan-4-yl}propanoic Acid: The hydrogenation product from above (0.861 g, 2.22 mmol) in CCl_4/MeCN/

H_2O (2:2:3, 10 mL) was treated with $NaIO_4$ (1.9 g, 8.9 mmol, 4 equiv.) for 5 min at room temp. $RuCl_3 \cdot H_2O$ (25 mg, 0.05 equiv.) was added and the dark brown mixture was stirred for 80 min at room temp., and then diluted with H_2O and CH_2Cl_2. The aqueous phase was extracted with diethyl ether and the organic phase was washed with brine, dried with $MgSO_4$ and concentrated under reduced pressure. Chromatography (hex/EE, 4:1 → 2:1) furnished the carboxylic acid (0.784 g, 88%) as a colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.03 (s, 6 H), 0.86 (d, 3 H), 0.89 (s, 9 H), 1.08 (s, 3 H), 1.23–1.70 (m, 7 H), 1.31 (s, 3 H), 1.41 (s, 3 H), 1.71–1.85 (m, 2 H), 2.38–2.71 (mc, 2 H), 3.35 (dd, *J* = 9.6, 6.4 Hz, 1 H), 3.43 (dd, *J* = 9.8, 5.9 Hz, 1 H), 3.68–3.77 (dd, *J* = 9.1, 3.8 Hz, 1 H), 10.4–11.4 (br. s, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.36, 16.68, 18.34, 21.18, 21.31, 24.84, 25.95, 26.95, 28.66, 31.53, 33.69, 35.65, 39.72, 68.31, 81.07, 82.34, 106.89, 179.01 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2956, 2934, 2856, 1712, 1460, 1376, 1255, 1107, 876, 775, 610 cm^{-1}. MS (EI = 70 eV, 110 °C): *m*/*z* = 401 (3) [M$^+$], 389 (13), 388 (17), 387 (42) [M – CH_3], 345 (1) [M – *t*Bu], 329 (13), 328 (11), 327 (15), 289 (11), 288 (16), 287 (M – TBS, 32), 271 (15), 270 (23), 269 (100). HRMS: calcd. for $C_{20}H_{39}NO_5Si$: 387.2567 [M – CH_3]; found 387.2579. $[\alpha]_D^{20}$ = +9.3 (*c* = 1.1, $CHCl_3$).

(4*S*,5*R*)-3-(3-{(4*R*,5*R*)-5-[(*S*)-5-(*tert*-Butyldimethylsilyloxy)-4-methylpentyl]-2,2,5-trimethyl-1,3-dioxolan-4-yl}propanoyl)-4-methyl-5-phenyloxazolidin-2-one (60): The carboxylic acid from above (0.784 g, 1.95 mmol) in Et_2O (15 mL) was treated at –78 °C with NEt_3 (0.30 mL, 2.2 mmol, 1.1 equiv.) and pivaloyl chloride (0.25 mL, 2.0 mmol, 1.02 equiv.) and a voluminous white precipitate was formed. The mixture was stirred for 60 min at –30 °C and recooled to –78 °C. (4*S*,5*R*)-4-Methyl-5-phenyl-1,3-oxazolidin-2-one (0.354 g, 2.00 mmol, 1.02 equiv.) was dissolved in THF (3 mL) and deprotonated with *n*BuLi (1.4 M in THF, 1.4 mL, 2 mmol) for 10 min at –78 °C. This solution was added dropwise to the mixture prepared previously. The reaction mixture was warmed to 0 °C and then stirred for 1 h. Aq. NH_4Cl was added at 0 °C and the aqueous phase was extracted with diethyl ether. The combined organic phases were washed with brine, dried with $MgSO_4$ and concentrated under reduced pressure. Chromatography (hex/EE, 10:1) furnished oxazolidinone **60** (0.872 g, 80%) as a colorless viscous oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = –0.03 (s, 6 H), 0.85–0.92 (m, 6 H), 0.88 (s, 9 H), 1.09 (s, 3 H), 1.31 (s, 3 H), 1.31–1.67 (m, 10 H), 1.67–1.96 (m, 2 H), 2.95–3.09 (m, 1 H), 3.18–3.30 (m, 1 H), 3.31–3.51 (mc, 2 H), 3.80 (dd, *J* = 9.8, 3.0 Hz, 1 H), 4.75 (quint, *J* = ca. 6.8 Hz, 1 H), 5.66 (d, *J* = 7.3 Hz, 1 H), 7.25–7.45 (m, 5 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.39, 14.45, 16.69, 18.31, 21.16, 21.35, 24.52, 25.93, 26.99, 28.70, 33.23, 33.70, 35.66, 39.75, 54.74, 68.23, 78.96, 80.97, 82.29, 106.73, 125.61, 128.67, 128.73, 133.34, 152.93, 172.55 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2900, 2856, 1787, 1703, 1458, 1370, 1348, 1109, 837, 774, 610 cm^{-1}. MS (EI = 70 eV, 80 °C): *m*/*z* = 548 (3), 547 (7), 546 (12) [M – CH_3], 505 (10) 504 (14) [M – *t*Bu], 446 (8) [M – TBS], 402 (13), 385 (8), 354 (11), 303 (12), 99 (100). HRMS: calcd. for $C_{30}H_{48}NO_6Si$: 546.3251 [M – CH_3]; found 546.3272. $[\alpha]_D^{20}$ = –14.4 (*c* = 1.1, $CHCl_3$). $C_{31}H_{51}NO_6Si$,(561.83): calcd. C 66.27, H 9.15, N 2.49; found C 65.97, H 8.88, N 2.55.

(4*S*,5*R*)-3-[(*S*)-3-{(4*R*,5*R*)-5-[(*S*)-5-(*tert*-butyldimethylsilyloxy)-4-methylpentyl]-2,2,5-trimethyl-1,3-dioxolan-4-yl}-2-hydroxypropanoyl]-4-methyl-5-phenyloxazolidin-2-one (61): Oxazolidinone **60** (0.255 g (0.40 mmol) was hydroxylated with Davis'oxaziridine (0.19 g, 0.72 mmol, 1.8 equiv.) as described for the preparation of **53** to furnish after chromatography (hex/EE, 10:1) and HPLC (supersphere, hex/EE, 7:1) **61** (0.147 g, 0.254 mmol) along with the (2*R*) diastereomer (6 mg) as colorless oils. Total yield 66%, *dr* = 96:4. **Main Diastereomer 61:** ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.03 (s, 6 H), 0.88 (d, *J* = 6.8, 3 H), 0.89 (s, 9 H), 0.98 (d, *J* = 6.6 Hz, 3 H), 1.07 (s, 3 H), 1.31 (s, 3 H), 1.31–1.66 (m, 7 H), 1.41 (s, 3 H), 1.95 (ddd, *J* = 14.7, 4.6, 1.8 Hz, 1 H), 2.09 (m, 1 H), 3.36 (dd, *J* = 9.8, 6.4 Hz, 1 H), 3.50 (dd, *J* = 9.8, 5.9 Hz, 1 H), 3.83 (d, *J* = 5.5 Hz, OH), 3.95 (dd, *J* = 9.8, 1.8 Hz, 1 H), 4.65 (quint, *J* = 6.7 Hz, 1 H), 5.28 (m, 1 H), 5.71 (d, *J* = 7.1 Hz, 1 H), 7.27–7.48 (m, 5 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.36, 14.48, 16.70, 18.35, 21.14, 21.27, 25.97, 26.86, 28.81, 33.66, 33.75, 35.67, 39.38, 55.99, 68.30, 68.81, 77.26, 80.12, 82.45, 106.76, 125.59, 128.81, 128.97, 132.79, 152.89, 174.14 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 3507, 2934, 2900, 2856, 1790, 1700, 1458, 1368, 1349, 1295, 1255, 1218, 1200, 1149, 1103, 770, 699, 610 cm^{-1}. MS (EI = 70 eV, 120 °C): *m*/*z* = 564 (15), 563 (33), 562 (34) [M – CH_3], 523 (13), 522 (33), 521 (46), 520 (100) [M – *t*Bu], 502 (27), 471 (33), 462 (35) [M – TBS], 444 (38), 413 (44). HRMS: calcd. for $C_{28}H_{48}NO_7Si$,: 562.3200 [M – CH_3]; found 562.3221. $[\alpha]_D^{20}$ = –10.0 (*c* = 1.1, $CHCl_3$). $C_{31}H_{51}NO_7Si$, (577.82): calcd. C 64.44, H 8.90, N 2.42; found C 64.21; H 9.12, N 2.39. **Minor Diastereomer:** ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.03 (s, 6 H), 0.86 (d, *J* = 6.6 Hz, 3 H), 0.89 (s, 9 H), 0.91 (d, *J* = 6.6, 3 H), 1.09 (s, 3 H), 1.25–1.63 (m, 7 H), 1.34 (2, 3 H), 1.41 (s, 3 H), 1.83 (ddd, *J* = 13.9, 7.5, 1.6 Hz, 1 H), 2.05 (mc, 1 H), 3.34 (dd, *J* = 9.8, 6.4 Hz, 1 H), 3.43 (dd, *J* = 9.8, 5.9 Hz, 1 H), 3.64 (d, *J* = 9.1 Hz, 1 H), 4.02 (d, *J* = 10.6, 1.7 Hz, 1 H), 4.81 (quint, *J* = 6.9 Hz, 1 H), 5.26 (mc, 1 H), 5.76 (d, *J* = 7.3 Hz, 1 H), 7.26–7.48 (m, 5 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.40, 14.41, 16.63, 18.23, 21.19, 21.30, 25.91, 26.92, 28.63, 33.62, 33.83, 35.63, 39.41, 54.80, 68.24, 69.11, 77.94, 79.93. 82.24, 107.12, 125.54, 128.75, 128.91, 132.95, 152.86, 173.96 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 3509, 2934, 2900, 2856, 1787, 1702, 1459, 1370, 1251, 1199, 1106, 1031, 610 cm^{-1}. MS (FI = 7 kV, 3 mA, 110 °C): *m*/*z* = 579 (12), 578 (15) [M$^+$], 563 (4), 562 (11) [M – CH_3], 524 (4), 522 (19), 521 (57), 520 (100) [M – *t*Bu], 492 (2), 267 (7), 115 (6), 57 (23).

(*S*)-3-{(4*R*,5*R*)-5-[(*S*)-5-(*tert*-Butyldimethylsilyloxy)-4-methylpentyl]-2,2,5-trimethyl-1,3-dioxolan-4-yl}-2-hydroxy-*N*-methoxy-*N*-methylpropanamide (62): Oxazolidinone **61** (0.357 g, 0.618 mmol) in THF (5 mL) was converted into the Weinreb amide with *N*,O-dimethylhydroxylamine hydrochloride (0.24 g, 2.4 mmol, 3.9 equiv.) as described for the transformation of **53** into **55**. Chromatography (hex/EE, 4:1) furnished 0.269 g (94%) of the amide **62** as a colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.02 (s, 6 H), 0.86 (d, *J* = 6.8 Hz, 3 H), 0.87 (s, 9 H), 1.05 (s, 3 H), 1.27 (s, 3 H), 1.31–1.73 (m, 7 H), 1.37 (s, 3 H), 1.81 (ddd, *J* = 14.4, 4.3, 2.9 Hz, 1 H), 2.02 (mc, 1 H), 3.22 (s, 3 H), 3.34 (dd, *J* = 9.8, 6.4 Hz, 1 H), 3.43 (dd, *J* = 9.8, 5.9 Hz, 1 H), 3.61 (d, *J* = 6.2 Hz, OH), 3.72 (s, 3 H), 3.92 (dd, *J* = 9.4, 2.9 Hz, 1 H), 4.52 (dd, *J* = 10.3, 5.7 Hz, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.39, 16.67, 18.32, 21.16, 21.26, 25.94, 26.74, 28.60, 29.65, 33.03, 33.66, 34.15, 35.66, 39.49, 61.34, 66.97, 68.28, 82.27, 106.71, 174.24 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 3474, 2934, 2856, 1666, 1463, 1374, 1256, 1105, 738, 610 cm^{-1}. MS (EI = 70 eV, 150 °C): *m*/*z* = 448 (3), 447 (9), 446 (29) [M – CH_3], 404 8 (6) [M – *t*Bu], 388 (9), 368 (5), 348 (9), 347 (26), 346 (100) [M – TBS], 329 (10), 328 (42), 285 (7), 254 (11), 213 (16), 188 (2). HRMS: calcd. for $C_{22}H_{44}NO_6Si$,$_2$: 446.2938 [M – CH_3]; found 446.2950. $[\alpha]_D^{20}$ = –19.7 (*c* = 1.0, $CHCl_3$). $C_{23}H_{47}NO_6Si$, (461.71): calcd. C 59.83, H 10.26, N 3.03; found C 59.60; H 10.05, N 3.04.

(*S*)-2-(*tert*-Butyldimethylsilyloxy)-3-{(4*R*,5*R*)-5-[(*S*)-5-(*tert*-butyldimethylsilyloxy)-4-methylpentyl]-2,2,5-trimethyl-1,3-dioxolan-4-yl}-*N*-methoxy-*N*-methylpropanamide (63): Weinreb amide **62** (0.269 g, 0.583 mmol) in CH_2Cl_2 (10 mL) was converted into the TBS ether as described for **55**. Chromatography (hex/EE, 10:1) furnished the silyl ether **63** (0.324 g, 97%) as a colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.02 (s, 6 H), 0.08 (s, 6 H), 0.85 (d, *J* = 6.6 Hz, 3 H), 0.88 (s, 9 H), 0.89 (s, 9 H), 1.05 (s, 3 H), 1.25 (s, 3 H), 1.22–1.71

(m, 7 H), 1.38 (s, 3 H), 1.77–2.00 (m, 2 H), 3.21 (s, 3 H), 3.33 (dd, J = 9.8, 6.4 Hz 1 H), 3.43 (dd, J = 9.8, 5.9 Hz, 1 H), 3.65 (d, J = 2.75 Hz, 1 H), 3.71 (s, 3 H), 4.74 (dd, J = 7.5, 5.3 Hz, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.36, –4.94, –4.62, 16.66, 18.21, 18.34, 21.11, 21.34, 25.80, 25.96, 26.85, 28.72, 33.70, 35.19, 35.72, 39.50, 61.33, 68.39, 78.16, 82.41, 106.70 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2934, 2856, 1680, 1472, 1374, 1105, 999, 837, 777, 610 cm^{-1}. MS (EI = 70 eV, 100 °C): m/z = 561 (4), 560 (12) [M–CH_3], 520 (20), 519 (53), 518 (100) [M–tBu], 502 (4), 500 (3), 462 (5), 461 (1), 460 (38) [M–TBS], 442 (7), 429 (7). HRMS: calcd. for $C_{28}H_{58}NO_6Si_2$: 560.3803 [M–CH_3]; found 560.3805. $[\alpha]_D^{20}$ = +2.8 (c = 1.0, $CHCl_3$).

(*S*)-3-(*tert*-Butyldimethylsilyloxy)-4-{(4*R*,5*R*)-5-[(*S*)-5-(*tert*-butyldimethylsilyloxy)-4-methylpentyl]-2,2,5-trimethyl-1,3-dioxolan-4-yl}butan-2-one (64): Weinreb amide **63** (0.323 g, 0.561 mmol) in THF (8 mL) was converted into the methyl ketone as described for the synthesis of **56**. Chromatography (hex/EE, 10:1) furnished the ketone **64** (0.272 g, 91%) as a colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.03 (s, 6 H), 0.08 (s, 6 H), 0.87 (d, J = 6.6 Hz, 3 H), 0.89 (s, 9 H), 0.94 (s, 9 H), 1.03 (s, 3 H), 1.28 (s, 3 H), 1.30–1.59 (m, 7 H), 1.35 (s, 3 H), 1.65 (ddd, J = 14.2, 7.1, 1.6 Hz, 1 H), 1.94 (ddd, J = 14.0, 10.5, 3.0 Hz, 1 H), 2.20 (s, 3 H), 3.34 (dd, J = 9.8, 6.4 Hz, 1 H), 3.44 (dd, J = 9.8, 5.9 Hz, 1 H), 3.98 (dd, J = 10.5, 1.6 Hz, 1 H), 4.18 (dd, J = 7.1, 3.0 Hz, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.35, –5.07, –4.87, 16.68, 18.04, 18.36, 21.30, 21.43, 25.72, 25.97, 26.08, 26.70, 28.59, 33.75, 35.27, 35.81, 39.46, 68.38, 76.20, 76.50, 81.94, 106.77, 212.29 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2934, 2857, 1720, 1463, 1375, 1256, 1213 m, 1108, 837, 777, 739, 610 cm^{-1}. MS (EI = 70 eV, 100 °C): m/z = 516 (2), 515 (6) [M–CH_3], 457(6), 455 (9), 430 (3), 429 (9), 417 (14), 416 (44), 415 (100) [M–TBS], 397 (5), 323 (5), 305 (4), 283 (42). HRMS: calcd. for $C_{27}H_{55}O_5Si_2$: 515.3588 [M–CH_3]; found 515.3586. $[\alpha]_D^{20}$ = –0.8 (c = 1.1, $CHCl_3$).

4-[(*S*,*E*)-3-(*tert*-Butyldimethylsilyloxy)-4-{(4*R*,5*R*)-5-[(*S*)-5-(*tert*-butyldimethylsilyloxy)-4-methylpentyl]-2,2,5-trimethyl-1,3-dioxolan-4-yl}-2-methylbut-1-enyl]-2-methylthiazole (65): The Wittig reaction of the ketone **64** (0.271 g, 0.51 mmol) with **32** (0.892 g, 2.55 mmol, 5 equiv.) was performed as described for **56**. After purification by columnn chromatography (hex/EE, 20:1) olefin **65** was obtained (0.313 g, 98%; E/Z = 30:1). **(*E*)-65:** ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.02 (s, 6 H), 0.03 (s, 3 H), 0.09 (s, 3 H), 0.82 (d, J = 6.6 Hz, 3 H), 0.88 (s, 9 H), 0.90 (s, 9 H), 1.06 (s, 3 H), 1.22 (s, 3 H), 1.22–1.68 (m, 8 H), 1.40 (s, 3 H), 1.73–1.87 (m, 1 H), 2.00 (d, J = 1.0 Hz, 3 H), 2.70 (s, 3 H), 3.32 (dd, J = 9.8, 6.4 Hz, 1 H), 3.42 (dd, J = 9.8, 5.9 Hz, 1 H), 3.62 (dd, J = 9.8, 2.5 Hz, 1 H), 4.36 (dd, J = 8.2, 5.5 Hz, 1 H), 6.48 (s, 1 H), 6.91 (s, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.36, –4.95, –4.61, 13.13, 16.61, 18.16, 18.33, 19.21, 21.34, 21.38, 25.85, 25.95, 26.73, 28.66, 33.72, 35.71, 36.21, 39.51, 68.32, 76.95, 78.64, 82.03, 106.49, 115.23, 120.05, 140.86, 153.13, 164.27 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2928, 2856, 1462, 1374, 1252, 1104, 836, 776, 610 cm^{-1}. MS (EI = 70 eV, 100 °C): m/z = 627 (7), 626 (16) [M$^+$], 613 (2), 612 (2), 611 (9) [M–CH_3], 569 (17) [M–tBu], 552 (5), 537 (81), 511 (52) [M–TBS], 510 (67), 283 (42), 43 (100). HRMS: calcd. for $C_{33}H_{63}NO_4SSi_2$: 625.4016 [M$^+$]; found 625.3984. $[\alpha]_D^{20}$ = +16.1 (c = 1.0, $CHCl_3$). **(*Z*)-65:** ^{1}H NMR (250 MHz, $CDCl_3$): δ = –0.10 (s, 3 H), –0.09 (s, 3 H), 0.03 (s, 6 H), 0.84 (s, 9 H), 0.86–0.90 (m, 12 H), 1.09 (s, 3 H), 1.16 (s, 3 H), 1.24–1.60 (m, 7 H), 1.42 (s, 3 H), 1.65–1.76 (m, 1 H), 1.80–1.95 (m, 1 H), 1.85 (d, J = 1.4 Hz, 3 H), 2.67 (s, 3 H), 3.34 (dd, J = 9.8, 6.4 Hz, 1 H), 3.43 (dd, J = 9.8, 5.9 Hz, 1 H), 3.67 (dd, J = 9.1, 2.5 Hz, 1 H), 5.55 (dd, J = 8.4, 5.9 Hz, 1 H), 6.38 (s, 1 H), 7.24 (s, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.35, –5.15, –4.87, 16.68, 17.64, 18.12, 18.36, 19.07, 21.23, 21.40, 25.82, 25.96, 26.68, 28.77, 33.78, 35.78, 39.54, 68.01, 68.35, 77.21, 78.64, 82.32, 106.58, 115.48, 121.29, 141.37, 151.98, 164.08 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2934, 2856, 1462, 1375, 1107, 880, 610 cm^{-1}. MS (EI = 70 eV, 110 °C): m/z = 628 (4), 627 (8), 626 [M$^+$, 15], 610 (3) [M–CH_3], 569 (4), 568 (7) [M–tBu], 567 (2), 552 (2), 513 (4), 512 (17), 511 (37), 510 (100) [M–TBS]. HRMS: calcd. for $C_{33}H_{63}NO_4SSi_2$: 625.4016 [M$^+$]; found 625.4027.

(*S*)-5-{(4*R*,5*R*)-5-[(*S*,*E*)-2-(*tert*-Butyldimethylsilyloxy)-3-methyl-4-(2-methylthiazol-4-yl)but-3-enyl]-2,2,4-trimethyl-1,3-dioxolan-4-yl}-2-methylpentan-1-ol (66): For mono-desilylation, olefin **65** (0.303 g, 0.484 mmol) in CH_2Cl_2/MeOH (1:1, 10 mL) was treated with CSA (0.112 g, 1 equiv.) at 0 °C for 7 h. Satd. aq. $NaHCO_3$ and CH_2Cl_2 were added, and the aqueous phase was extracted with diethyl ether. The combined organic phases were washed with brine, dried with $MgSO_4$ and concentrated under reduced pressure to give after chromatography (hex/EE, 4:1) alcohol **66** (0.241 g, 97%) as a colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.03 (s, 3 H), 0.09 (s, 3 H), 0.87 (d, J = 6.9 Hz, 3 H), 0.90 (s, 9 H), 1.07 (s, 3 H), 1.23 (s, 3 H), 1.29–1.50 (m, 5 H), 1.41 (s, 3 H), 1.52–1.68 (m, 4 H), 1.74–1.87 (m, 1 H), 2.00 (d, J = 1.1 Hz, 3 H), 2.71 (s, 3 H), 3.42 (mc, 2 H), 3.64 (dd, J = 9.8, 2.3 Hz, 1 H), 4.35 (dd, J = 8.5, 5.3 Hz, 1 H), 6.47 (s, 1 H), 6.92 (s, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –4.94, –4.62, 13.19, 16.61, 18.16, 19.17, 21.13, 21.48, 25.85, 26.73, 28.65, 33.58, 35.47, 36.24, 37.95, 39.08, 67.94, 76.93, 78.42, 82.01, 106.55, 115.32, 119.95, 141.00, 153.09, 164.53 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 3450, 2934, 2856, 1459, 1375, 1251, 1107, 887, 776, 738, 610 cm^{-1}. MS (EI = 70 eV, 110 °C): m/z = 512 (2), 511 (4) [M$^+$], 496 (5) [M–CH_3], 453 (5) [M–tBu], 436 (2), 398 (6), 397 (17), 396 (49), 379 (10), 364 (2), 321 (13), 282 (100). HRMS: calcd. for $C_{27}H_{49}NO_4SSi$ 511.3152 [M$^+$]; found 511.3173. $[\alpha]_D^{20}$ = +20.7 (c = 1.2, $CHCl_3$).

(3*S*,5*R*,6*R*,10*S*,*E*)-2,6,10-Trimethyl-1-(2-methylthiazol-4-yl)dodeca-1,11-diene-3,5,6-triol (67): Alcohol **66** (0.240 g, 0.469 mmol) in CH_2Cl_2 (12 mL) was treated at 0 °C with pyridine (1 mL) and Dess–Martin periodinane (0.258 g, 0.61 mmol, 1.3 equiv.) and stirred for 4 h at room temp. For workup, aq. $Na_2S_2O_3$/$NaHCO_3$ (1:1, 20 mL) was added and the aqueous phase was extracted with two 10 mL portions of ether. The combined organic phases were washed with brine, dried with $MgSO_4$ and concentrated under reduced pressure to give crude aldehyde **8** (204 mg), which was used without further purification. in a separate flask, methyl-triphenylphosphonium chloride (312 mg, 1.0 mmol) in diethyl ether (5 mL) was deprotonated with nBuLi (1 M in hexane, 1.5 mL) at –40 °C for 1 h. The solution was decanted from lithium chloride and then added dropwise at –40 °C to the aldehyde in diethyl ether (2 mL). The mixture was stirred at 0 °C for 30 min and the solvent was removed under reduced pressure. After chromatography (hex/EE 3:1) the olefin (180 mg) was dissolved in in a solution of TBAF (2 mL, 1 M in THF, 5 equiv.) and stirred overnight. The reaction was diluted with Et_2O (50 mL) and quenched with a satd. NH_4Cl solution. After extraction of the aq. phase with ether, the combined organic phases were washed with brine, dried with $MgSO_4$ and concentrated under reduced pressure. The residue was diluted with ethanol (5 mL) and treated with 1 N HCl (3 mL). This mixture was stirred for 12 h at 25 °C. After addition of ice water (20 mL) and neutralization with saturated aqueous $NaHCO_3$ solution (20 mL), the aqueous phase was extracted with EE (2×20 mL) and ether (2×20 mL). The combined organic phases were then washed with brine (20 mL), dried ($MgSO_4$) and concentrated. The crude mixture was purified by flash column chromatography (hex/EE, 1:2) to provide triol **67** (110 mg, 75% over 4 steps) as a colorless oil, whose spectroscopic data and optical rotation were congruent with those described previously.[5]

(3*S*,6*R*,7*S*,8*S*)-1,3-Bis(*tert*-butyldimethylsilyloxy)-11-{(4*R*,5*R*)-5-[(S,E)-2-(*tert*-butyldimethylsilyloxy)-3-methyl-4-(2-methylthiazol-4-yl)but-3-enyl]-2,2,4-trimethyl-1,3-dioxolan-4-yl}-7-hydroxy-4,4,6,8-tetramethylundecan-5-one (68): The aldol addition of ketone **4** (0.185 g, 0.46 mmol) in THF (2 mL) to crude aldehyde **8** (0.117 g, 0.23 mmol) in THF (1 mL) was performed as described for ketone **9** to give the aldol adducts **70a** (126 mg) and **70b** (20 mg) after HPLC (supersphere, hex/EE, 8:1). Total yield was 70%, and the diastereomeric ratio was 6:1. **Main Diastereomer (68):** ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.02 (s, 3 H), 0.03 (s, 6 H), 0.07 (s, 3 H), 0.08 (s, 3 H), 0.10 (s, 3 H), 0.79 (d, J = 6.9 Hz, 3 H), 0.81–1.85 (m, 14 H), 0.88 (s, 9 H), 0.89 (s, 9 H), 0.90 (s, 9 H), 1.05 (s, 3 H), 1.08 (s, 3 H), 1.20 (s, 3 H), 1.21 (s, 3 H), 1.40 (s, 3 H), 1.99 (d, J = 1.1 Hz, 3 H), 2.70 (s, 3 H), 3.23–3.32 (m, 2 H), 3.47 (s, 1 H), 3.55–3.72 (m, 3 H), 3.90 (dd, J = 7.3, 3.0 Hz, 1 H), 4.35 (dd, J = 8.5, 5.5 Hz, 1 H), 6.48 (s, 1 H), 6.92 (s, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.28, –4.92, –4.60, –4.07, –3.76, 9.56, 13.11, 15.28, 18.17, 18.26, 18.33, 19.21, 20.50, 21.18, 21.25, 22.87, 25.86, 25.93, 26.09, 26.74, 28.66, 33.41, 35.55, 36.22, 37.86, 39.60, 41.26, 53.98, 60.48, 74.15, 74.96, 76.97, 78.90, 82.05, 106.53, 115.25, 120.07, 140.89, 153.10, 164.29, 222.37 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2957, 2933, 2857, 1685, 1375, 11256, 1105, 996, 837, 776, 610 cm^{-1}. MS (FI = 7 kV, 2 mA, 140 °C): m/z = 913 (4), 912 (28) [M], 911 (12), 603 (3), 533(6), 520 (7), 519 (7), 511 (18), 510 (43), 509 (100) [aldehyde], 463 (6), 404 (9), 403 (22), 402 (60) [ketone], 345 (17). $[\alpha]_D^{20}$ = –20.4 (c = 1.1, $CHCl_3$). **Minor Diastereomer:** ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.03 (s, 9 H), 0.06 (s, 3 H), 0.09 (s, 3 H), 0.10 (s, 3 H), 0.85–1.70 (m, 16 H), 0.87 (s, 9 H), 0.88 (s, 9 H), 0.89 (s, 9 H), 0.94 (d, J = 6.4 Hz, 3 H), 1.07 (s, 3 H), 1.20 (s, 3 H), 1.22 (s, 3 H), 1.40 (s, 3 H), 1.73–1.88 (m, 1 H), 2.00 (d, J = 1.0 Hz, 3 H), 2.70 (s, 3 H), 3.21–3.40 (m, 3 H), 3.51–3.70 (m, 3 H), 3.89 (dd, J = 7.3, 3.0 Hz, 1 H), 4.35 (dd, J = 8.5, 5.5 Hz, 1 H), 6.48 (s, 1 H), 6.91 (s, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.28, –4.94, –4.61, –4.05, –3.75, 10.39, 13.13,14.40, 18.16, 18.26, 18.32, 19.21, 20.30, 21.14, 21.35, 23.12, 25.85, 25.93, 26.22, 26.73, 28.63, 33.27, 35.52, 36.16, 37.92, 39.35, 41.48, 53.95, 60.55, 74.09, 75.04, 76.94, 78.71, 81.91, 106.61, 115.28, 120.07, 140.82, 153.09, 164.42, 221.83 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2930, 1686, 1472, 1375, 1256, 1105, 837, 776, 610 cm^{-1}. MS (FI = 7 kV, 2 mA, 120 °C): m/z = 915 (1), 914 (4), 913 (13), 912 (18) [M], 911 (24), 855 (1) [M – tBu], 854 (1), 513 (1), 512 (2), 511 (12), 510 (46), 509 (100) [aldehyde], 494 (2), 404 (8), 403 (30), 402 (89) [ketone], 345 (22). $[\alpha]_D^{20}$ = –4.0 (c = 1.6, $CHCl_3$).

(3*S*,6*R*,7*S*,8*S*)-1,3,7-Tris(*tert*-butyldimethylsilyloxy)-11-{(4*R*,5*R*)-5-[(*S*,*E*)-2-(*tert*-butyldimethylsilyloxy)-3-methyl-4-(2-methylthiazol-4-yl)but-3-enyl]-2,2,4-trimethyl-1,3-dioxolan-4-yl}-4,4,6,8-tetramethylundecan-5-one (69): Aldol adduct **68** (0.120 g, 0.131 mmol) in CH_2Cl_2 (8 mL) was treated with 2,6-lutidine (80 µL, 0.69 mmol, 5.2 equiv.) and TBSOTf (80 µL, 0.36 mmol, 2.8 equiv.) at room temp. The mixture was stirred for 14 h and then quenched with satd. aq. $NaHCO_3$ (10 mL). The aqueous phase was extracted with diethyl ether, and the combined organic phases were washed with brine, dried with $MgSO_4$ concentrated under reduced pressure and chromatographed (hex/EE, 10:1) to give **69** (126 mg, 93%) as a colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.01 (s, 3 H), 0.03 (s, 9 H), 0.04 (s, 6 H), 0.06 (s, 3 H), 0.09 (s, 3 H), 0.83–1.68 (m, 18 H), 0.86 (s, 9 H), 0.88 (s, 9 H), 0.89 (s, 18 H), 1.01 (s, 3 H), 1.05 (s, 3 H), 1.21 (s, 3 H), 1.40 (s, 3 H), 1.72–1.87 (m, 2 H), 1.99 (d, J = 0.9 Hz, 3 H), 2.70 (s, 3 H), 3.05–3.17 (mc, 1 H), 3.53–3.70 (m, 3 H), 3.74 (dd, J = 6.4, 1.8 Hz, 1 H), 3.88 (dd, J = 7.3, 3.0 Hz, 1 H), 4.35 (dd, J = 8.6, 5.5 Hz, 1 H), 6.48 (s, 1 H), 6.91 (s, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.27, –5.24, –4.93, –4.60, –3.98, –3.79, –3.69, –2.96, 13.08, 15.05, 17.37, 18.17, 18.28, 18.33, 18.51, 19.22, 19.40, 21.33, 22.11, 24.51, 25.86, 25.95, 26.11, 26.23, 26.27, 28.65, 31.61, 36.12, 38.11, 39.13, 39.60, 45.00, 53.65, 60.96, 74.02, 76.97, 77.32, 78.60, 81.91, 106.55, 115.24, 120.10, 140.80, 153.13, 164.32, 218.09 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2933, 2857, 1685 s, 1577, 1459, 1417, 1295, 1112, 877, 822, 740, 610 cm^{-1}. MS (FI = 7 keV, 2 mA, 140 °C): m/z = 1031 (3), 1030 (11), 1029 (18), 1028 (84), 1027 (100) [M], 1026 (63), 1011 (2) [M–CH_3], 972 (7), 971 (15), 970 (38), 969 (55) [M–tBu], 912 (6), 911 (9) [M–TBS], 303 (23). $[\alpha]_D^{20}$ = –3.0 (c = 0.8, $CHCl_3$).

(3*S*,6*R*,7*S*,8*S*)-3,7-Bis(*tert*-butyldimethylsilyloxy)-11-{(4*R*,*5R*)-5-[(*S*,*E*)-2-(*tert*-butyldimethylsilyloxy)-3-methyl-4-(2-methylthiazol-4-yl)but-3-enyl]-2,2,4-trimethyl-1,3-dioxolan-4-yl}-1-hydroxy-4,4,6,8-tetramethylundecan-5-one (70): TBS ether **71** (0.123 g, 0.120 mmol) in CH_2Cl_2/MeOH (1:1, 4 mL) was stirred with CSA (28 mg, 1 equiv.) for 8 h at 0 °C. The reaction was quenched with satd. aq. $NaHCO_3$ and the aqueous phase was extraceted with CH_2Cl_2 and the organic phase was washed with brine, dried with $MgSO_4$ and chromatographed (hex/EE, 4:1) to furnish alcohol **72** (92 mg, 84%) as a colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.02 (s, 3 H), 0.05 (m, 9 H), 0.08 (s, 3 H), 0.09 (s, 3 H), 0.89 (m, 27 H), 1.00–1.46 (m, 17 H), 1.04 (s, 3 H), 1.19 (s, 3 H), 1.20 (s, 3 H), 1.39 (s, 3 H), 1.53–1.65 (m, 3 H), 1.72–1.86 (m, 1 H), 1.98 (d, J = 0.9 Hz, 3 H), 2.69 (s, 3 H), 3.02–3.15 (mc, 1 H), 3.56–3.67 (m, 3 H), 3.77 (dd, J = 6.9, 1.6 hz, 1 H), 4.04 (dd, J = 5.7, 4.6 Hz, 1 H), 4.35 (dd, J = 8.2, 5.5 Hz, 1 H), 6.47 (s, 1 H), 6.90 (s, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –4.96, –4.63, –3.94, –3.79, –3.70, 13.08, 15.50, 17.50, 17.81, 18.14, 18.24, 18.48, 19.18, 21.37, 22.04, 24.93, 25.83, 26.02, 26.20, 26.69, 28.61, 31.40, 36.07, 38.32, 38.92, 39.49, 45.00, 53.74, 60.16, 73.09, 76.93, 77.36, 78.46, 81.90, 106.52, 115.22, 120.05, 140.79, 153.07, 164.34, 219.36 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2957, 2934, 2886, 2856, 1686, 1459, 1375, 1256, 1106, 775, 610 cm^{-1}. MS (FI = 7 kV, 2 mA, 140 °C): m/z = 915 (11), 914 (8), 913 (51), 912 (57) [M], 911 (100), 854 (8) [M–tBu], 662 (9), 658 (16), 655 (30), 598 (4), 509 (6), 418 (7), 392 (10), 391 (46), 281 (15). $[\alpha]_D^{20}$ = +0.2 (c = 1.0, $CHCl_3$).

(3*S*,6*R*,7*S*,8*S*)-3,7-Bis(*tert*-butyldimethylsilyloxy)-11-{(4R,5R)-5-[(*S*,*E*)-2-(*tert*-butyldimethylsilyloxy)-3-methyl-4-(2-methylthiazol-4-yl)but-3-enyl]-2,2,4-trimethyl-1,3-dioxolan-4-yl}-4,4,6,8-tetramethyl-5-oxoundecanoic Acid (71): Olefin **76** (see below) (0.037 g, 0.041 mmol) was dissolved in THF/tBuOH (1:1, 4 mL) at 0 °C and was treated with OsO_4 (10 mg/mL in tBuOH, 50 µL, 0.05 equiv.) and NMO (0.21 mL, 0.042 mmol, 0.2 M in H_2O). The mixture was stirred at room temp. for 14 h, quenched with aq. $Na_2S_2O_3$, diluted with water and extracted with diethyl ether. The combined organic phases were washed with brine, dried with $MgSO_4$ and filtered through silica gel (hex/EE, 4:1) to give the crude diol which was dissolved in ethanol (3 mL). Water (1 mL) and $NaIO_4$ (24 mg, 2.2 equiv.) were added and the mixture was stirred at room temp. for 2 h. The flaky residue was dissolved by adding water. The mixture was extracted with diethyl ether, and the organic phase was dried with $MgSO_4$ and filtered through silica gel (hex/EE, 4:1). The resulting crude aldehyde was dissolved in tBuOH (1.5 mL) and 2.3-dimethyl-2-butene (1.5 mL) and was treated dropwise with a mixture of NaH_2PO_4 (26 mg) and $NaClO_2$ (26 mg) in water (1.5 mL). The reaction mixture was stirred at room temp. for 90 min. Satd. aq. NH_4Cl was added and the mixture was extracted with CH_2Cl_2. The combined organic phases were washed with brine, dried with $MgSO_4$ concentrated under reduced pressure and chromatographed (hex/EE, 7:1→4:1) to give the acid **73** (27 mg, 71%) as a colorless oil.

Alternatively alcohol **70** (0.086 g, 0.094 mmol) in CH_2Cl_2 (10 mL) at 0 °C was treated with pyridine (0.2 mL) and Dess–Martin

periodinane (50 mg, 0.12 mmol, 1.3 equiv.) for 2 h. Aq. $Na_2S_2O_3$/$NaHCO_3$ (1:1) was added and the mixture was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried with $MgSO_4$ concentrated under reduced pressure and chromatographed (hex/EE, 7:1) to give the crude aldehyde which was oxidized as described above to give **71** (81 mg, 93%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.02 (s, 3 H), 0.04 (s, 3 H), 0.06 (s, 3 H), 0.07 (s, 3 H), 0.09 (s, 3 H), 0.10 (s, 3 H), 0.88 (s, 9 H), 0.89 (s, 18 H), 0.98–1.65 (m, 14 H), 1.12 (s, 3 H), 1.19 (s, 3 H), 1.23 (s, 3 H), 1.25 (s, 3 H), 1.40 (s, 3 H), 1.78–1.91 (m, 1 H), 1.97 (d, J = 0.7 Hz, 3 H), 2.31 (d, J = 16.7, 6.6 Hz, 1 H), 2.50 (d, J = 16.7, 3.4 Hz, 1 H), 2.71 (s, 3 H), 3.05–3.17 (mc, 1 H), 3.67 (d, J = 9.1, 2.3 Hz, 1 H), 3.77 (d, J = 6.4, 1.6 Hz, 1 H), 4.30–4.40 (m, 2 H), 6.56 (s, 1 H), 6.92 (s, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –4.94, –4.61, –4.14, –3.88, –3.75, 13.21, 15.84, 17.28, 18.17, 18.22, 18.48, 18.85, 19.23, 21.15, 22.03, 23.63, 25.83, 26.03, 26.19, 26.73, 28.63, 29.68, 31.58, 36.47, 39.01, 39.83, 44.93, 53.60, 73.40, 76.20, 77.30, 79.23, 82.15, 106.58, 114.99, 119.60, 141.65, 152.74, 165.02, 175.33, 218.06 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2957, 2934, 2856, 1715, 1463, 1376, 1257, 1106, 776, 610 cm^{-1}. MS (FI = 7 kV, 3 mA, 160 °C): m/z = 929 (1), 928 (4), 927 (23), 926 (34) [M], 833 (1), 773 (1), 466 (1), 208 (1), 153 (15), 93 (21), 61 (100). $[\alpha]_D^{20}$ = –7.3 (c = 2.1, $CHCl_3$).

(3*S*,6*R*,7*S*,8*S*)-3,7-Bis(*tert*-butyldimethylsilyloxy)-11-{(4*R*,5*R*)-5-[(*S*,*E*)-2-hydroxy-3-methyl-4-(2-methylthiazol-4-yl)but-3-enyl]-2,2,4-trimethyl-1,3-dioxolan-4-yl}-4,4,6,8-tetramethyl-5-oxoundecanoic Acid (72): Acid **71** (26 mg, 0.028 mmol) in THF (3 mL) was treated with TBAF (1 M in THF, 0.2 mL, 7 equiv.) at room temp. for 20 h. The mixture was quenched with satd. aq. NH_4Cl, diluted with water and extracted with diethyl ether. The ether layer was washed with $KHSO_4$ (0.1 M) and brine, dried with $MgSO_4$, and chromatographed (hex/EE, 1:1) to give the *seco* acid **72** (19 mg, 82%), which was lactonized without further purification. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0,05 (s, 3 H), 0.06 (s, 3 H), 0.10 (s, 3 H), 0.14 (s, 3 H), 0.89 (s, 9 H), 0.90 (s, 9 H), 1.01–1.90 (m, 13 H), 1.09 (s, 3 H), 1.16 (s, 3 H), 1.22 (s, 3 H), 1.26 (s, 3 H), 1.36 (s, 3 H), 1.45 (s, 3 H), 2.02 (d, J = 1.1 Hz, 3 H), 2.33 (dd, J = 16.7, 7.3 Hz, 1 H), 2.54 (dd, J = 16.7, 3.0 Hz, 1 H), 2.69 (s, 3 H), 3.10–3.23 (mc, 1 H), 3.81 (d, J = 6.6 Hz, 1 H), 3.99 (dd, J = 9.6, 2.7 Hz, 1 H), 4.29 (dd, J = 7.1, 2.9 Hz, 1 H), 4.44 (dd, J = 9.3, 2.7 Hz, 1 H), 6.75 (s, 1 H), 6.97 (s, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –4.59, –3.95, –3.78, –3.63, 13.92, 16.59, 17.83, 18.32, 18.44, 18.51, 19.12, 20.92, 21.83, 23.74, 26.11, 26.21, 27.06, 28.59, 29.69, 31.15, 36.23, 38.42, 39.43, 45.28, 53.57, 72.85, 77.20, 77.62, 82.40, 82.94, 107.55, 114.96, 119.09, 142.32, 152.18, 165.51, 174.19, 218.32 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2957, 2934, 2856, 1715, 1462, 1376 1106, 879, 610 cm^{-1}. MS (FI = 7 kV, 3 mA,160 °C): m/z = 817 (2), 812 (100) [M], 754 (3), 610 (1), 153 (5), 93 (25). $[\alpha]_D^{20}$ = –5.3 (c = 0.4, $CHCl_3$).

Lactone 73: A solution of NEt_3 (80 μL, 0.55 mmol) and 2,4,6-trichlorobenzoyl chloride (51 μL, 0.33 mmol) in toluene (1 mL) was prepared. 0.1 mL of this solution was added to the acid **72** (19 mg) in toluene (1.5 mL) at room temp. The mixture was stirred for 2 h, and the colorless residue was dissolved by adding another 1.5 mL of toluene. This solution was added dropwise to DMAP (35 mg, 10 equiv.) in toluene (7 mL) at 110 °C via syringe pump over 2 h. After the addition was completed the mixture was stirred for 1 h at 110 °C, cooled to room temp. and quenched with sat aq. NH_4Cl. Water was added and the mixture was extracted with diethyl ether. The combined organic phases were washed with brine, dried with $MgSO_4$ concentrated under reduced pressure. Column chromatography (hex/EE, 10:1) furnished the macrolactone **73** (11 mg, 50%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.05 (s, 3 H), 0.06 (s, 3 H), 0.08 (s, 3 H), 0.16 (s, 3 H), 0.87 (s, 9 H), 0.90 (s, 9 H), 0.93 (d, J = 6.8 Hz, 3 H), 1.06 (d, J = 6.8 Hz, 3 H), 1.08 (s, 3 H), 1.13 (s, 3 H), 1.20 (s, 3 H), 1.21–1.57 (m, 9 H), 1.34 (s, 3 H), 1.80 (dt, J = 12.9, 6.1 Hz, 1 H), 2.03 (s, 3 H), 2.03–2.08 (m, 2 H), 2.65 (dd, J = 15.9, 8.9 Hz, 1 H), 2.70 (s, 3 H), 2.89 (dd, J = 15.8, 3.4 Hz, 1 H), 3.02 (dt, J = 9.1, 6.8 Hz, 1 H), 3.96–4.01 (m, 2 H), 4.12 (dd, J = 8.7, 3.1 Hz, 1 H), 5.52 (br. s, 1 H), 6.45 (s, 1 H), 6.91 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = –4.87, –4.15, –3.72, –3.57, 14.09, 16.63, 17.68, 18.49, 18.54, 19.12, 19.19, 19.97, 22.00, 24.26, 26.10, 26.23, 26.45, 28.57, 29.69, 33.26, 37.40, 39.98, 42.61, 47.59, 53.19, 74.66, 76.22, 77.20, 78.33, 82.21, 105.71, 115.13, 117.57, 136.74, 152.59, 164.22, 169.90, 214.94 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2925, 2854, 1745, 1698, 1461, 1375, 1255, 1105, 775, 610 cm^{-1}. MS (FI = 7 kV, 3 mA, 130 °C): m/z = 796 (2), 795 (30), 794 (79) [M], 793 (100), 737 (5) [M–tBu], 520 (3). HRMS calcd. for $C_{42}H_{75}NO_7SSi_2$ [M$^+$] 793.4803; found 793.4831. $[\alpha]_D^{20}$ = –40.4 (c = 0.5, $CHCl_3$).

Epothilone Derivative 7: Macrolide **73** (11.1 mg, 0.014 mmol) was treated at –18 °C with TFA (15% in CH_2Cl_2, 0.4 mL) for 80 min. Another 1 mL of the TFA solution was added and stirring was continued for 30 min. The reaction was quenched with aq. $NaHCO_3$, diluted with water and extracted with CH_2Cl_2. The combined organic phases were dried with $MgSO_4$ and chromatographed (hex/EE, 1:1) to give monosilylated and unsilylated material. The monosilyl ether was desilylated with TFA as described above. The total yield of **7** was 6.4 mg (80%) as a waxy solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.98 (d, J = 7.1 Hz, 3 H), 1.08 (s, 3 H), 1.10 (s, 3 H), 1.12 (s, 3 H), 1.14 (d J = 6.8 Hz, 3 H), 1.18–1.42 (m, 4 H), 1.34 (s, 3 H), 1.43 (s, 3 H), 1.55–1.67 (m, 3 H), 1.91 (ddd, J = 15.7, 3.3, 1.8 Hz, 1 H), 1.99 (s, 3 H), 2.10 (ddd, J = 15.7, 7.8, 4.0 Hz, 1 H), 2.45–2.59 (m, 3 H), 2.68 (s, 3 H), 3.28 (dq, 6.8, 5.8, 1 H), 3.57 (br. s, 1 H), 3.72 (t, J = 4.0 Hz, 1 H), 3.99 (dd, J = 7.8, 1.5 Hz, 1 H), 4.15 (dd, J = 10.7, 2.6 Hz, 1 H), 5.47 (tb, 1 H), 6.57 (s, 1 H), 6.92 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.58, 16.73, 16.92, 18.97, 19.07, 20.83, 21.17, 21.58, 26.48, 28.55, 31.16, 32.77, 36.05, 38.88, 40.30, 43.41, 53.15, 71.74, 74.14, 75.33, 76.21, 77.21, 106.14, 114.94, 117.43, 137.00, 152.24, 164.55, 169.69, 219.76 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2958, 2935, 2925, 1734, 1684, 1508, 1375, 1106, 958, 900, 737, 610 cm^{-1}. MS (EI = 70 eV, 180 °C): m/z = 568 (<1), 567 (3), 566 (9), 565 (27) [M], 552 (1), 551 (4), 550 (12) [M–CH_3], 509 (3), 508 (8), 507 (23) [M], 493 (5), 492 (4), 491 (7), 490 (18), 450 (5), 435 (8), 417 (3), 378 (13), 352 (7), 336 (21), 320 (34), 302 (12), 252 (14), 234 (16), 164 (88), 43 (100). HRMS calcd. for $C_{30}H_{47}NO_7S$ [M$^+$] 565.3073; found 565.3081. $[\alpha]_D^{20}$ = –37.6 (c = 0.6, $CHCl_3$).

(4*S*,7*R*,8*S*,9*S*)-12-{(4*R*,5*R*)-5-[(*S*,*E*)-2-(*tert*-butyldimethylsilyloxy)-3-methyl-4-(2-methylthiazol-4-yl)but-3-enyl]-2,2,4-trimethyl-1,3-dioxolan-4-yl}-8-hydroxy-5,5,7,9-tetramethyl-4-(triethylsilyloxy)-dodec-1-en-6-one (74): A 0.3 M solution of LDA in THF (6.5 mL) was prepared from 0.35 mL (2.5 mmol) DIPA and 1.1 mL (2.4 mmol) of *n*BuLi (2.2 M in hexane) at –20 °C (30 min). The LDA solution was added dropwise to the ketone **9** (0.199 g, 0.70 mmol) in THF (2 mL) at –78 °C. The mixture was stirred at –78 °C for 20 min, warmed to –30 °C and stirred for additional 60 min. The resulting enolate solution was recooled to –78 °C and treated dropwise with crude aldehyde **8** (200 mg, 0.39 mmol) (prepared from alcohol **66** as described above). After 50 min at –78 °C the reaction was quenched with satd. aq. NH_4Cl and warmed to room temp. Water (20 mL) was added and the aqueous phase was extracted with diethyl ether. The combined organic phases were washed with brine, dried with $MgSO_4$ concentrated under reduced pressure and chromatographed (hex/EE, 10:1) to furnish a mixture of aldol adducts which was separated by HPLC (Supersphere, hex/EE, 10:1) to give adduct **74** (0.204 g) along with two additional aldol adducts (39 and 35 mg). Total yield was 89% and the dia-

stereomeric ratio was 5.8:1.1:1.0. **Major Diasteromer 74:** ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.02 (s, 3 H), 0.08 (s, 3 H), 0.62 (q, J = 8.0 Hz, 6 H), 0.79 (d, J = 6.9 Hz, 3 H), 0.84–1.86 (m, 9 H), 0.89 (s, 9 H), 0.96 (t, J = 7.8 Hz, 9 H), 1.02 (d, J = 6.9 Hz, 3 H), 1.05 (s, 3 H), 1.13 (s, 3 H), 1.16 (s, 3 H), 1.21 (s, 3 H), 1.39 (s, 3 H), 1.99 (d, J = 1.1 Hz, 3 H), 2.02–2.17 (m, 2 H), 2.70 (s, 3 H), 3.20–3.31 (m, 2 H), 3.46 (s, 1 H), 3.60 (dd, J = 9.8, 2.3 Hz, 1 H), 3.93 (dd, J = 7.1, 3.9 Hz, 1 H), 4.35 (dd, J = 8.4, 5.5 Hz, 1 H), 4.96–5.08 (m, 2 H), 5.70–5.87 (m, 1 H), 6.48 (s, 1 H), 6.92 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = –4.94, –4.61, 5.46, 7.01, 9.71, 13.10, 15.27, 18.17, 19.21, 19.48, 21.17, 21.20, 22.76, 25.85, 26.73, 28.66, 33.38, 35.48, 36.20, 39.23, 39.59, 41.15, 54.28, 74.93, 76.97, 77.08, 78.91, 82.04, 106.53, 115.26, 116.92, 120.07, 136.13, 140.87, 153.09, 164.31, 222.47 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2957, 1684, 1461, 1375, 1252, 1180, 1104, 998, 738, 610 cm^{-1}. MS (EI = 70 eV, 180 °C): m/z = 796 (<1), 795 (4), 794 (2) [M$^+$], 793 (5), 510 (40), 509 (100) [aldehyde], 285 (8), 284 (44) [ketone]. HRMS: calcd. for $C_{43}H_{79}NO_6SSi_2$ [M$^+$] 793.5167; found 793.5135. $[\alpha]_D^{20}$ = –6.8 (c = 0.9, $CHCl_3$). $C_{43}H_{79}NO_6SSi_2$ (794.32): calcd. C 65.02, H 10.02, N 1.76; S, 4.04; found C 64.94, H 10.33, N 1.74; S, 3.51. **Minor Diastereomer I:** ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.03 (s, 3 H), 0.09 (s, 3 H), 0.60 (q, J = 7.5 Hz, 6 H), 0.90–1.68 (m, 23 H), 0.90 (s, 9 H), 1.07 (s, 3 H), 1.14 (s, 6 H), 1.22 (s, 3 H), 1.40 (s, 3 H), 1.74–1.88 (m, 1 H), 2.00 (d, J = 1.1 Hz, 3 H), 2.01–2.21 (m, 2 H), 2.70 (s, 3 H), 3.22 (qd, J = 6.9, 2.1 Hz, 1 H), 3.40 (dd, J = 8.0, 1.6 Hz, 1 H), 3.49 (s, 1 H), 3.62 (dd, J = 9.8, 2.3 Hz, 1 H), 3.95 (dd, J = 7.1, 4.1 Hz, 1 H), 4.36 (dd, J = 8.4, 5.2 Hz, 1 H), 4.98–5.08 (m, 2 H), 5.68–5.87 (m, 1 H), 6.48 (s, 1 H), 6.91 (s, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –4.94, –4.62, 5.47, 7.03, 10.69, 13.16, 15.47, 18.16, 19.20, 19.77, 21.25, 21.30, 22.72, 25.84, 26.74, 28.64, 33.24, 35.42, 36.22, 39.23, 39.35, 41.40, 54.12, 75.02, 76.76, 76.93, 78.65, 81.90, 106.59, 115.28, 116.89, 120.05, 136.15, 140.84, 153.10, 164.41 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2956, 1458, 1375, 1255, 1107, 888, 817, 739, 611 cm^{-1}. MS (FI = 7 kV, 3 mA, 130 °C): m/z = 794 (1) [M$^+$], 793 (6), 511 (14), 510 (31), 509 (100) [aldehyde], 285 (4), 284 (40) [ketone], 255 (15), 243 (4). **Minor Diastereomer II:** ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.03 (s, 3 H), 0.09 (s, 3 H), 0.61 (q, J = 7.3 Hz, 6 H), 0.91–1.69 (m, 23 H), 0.90 (s, 9 H), 1.07 (s, 3 H), 1.11 (s, 3 H), 1.17 (s, 3 H), 1.23 (s, 3 H), 1.41 (s, 3 H), 1.74–1.88 (m, 1 H), 2.00 (d, J = 1.1 Hz, 3 H), 2.03–2.17 (m, 2 H), 2.71 (s, 3 H), 3.20–3.36 (m, 3 H), 3.62 (dd, J = 9.8, 2.1 Hz, 1 H), 3.92 (dd, J = 7.3, 3.9 Hz, 1 H), 4.36 (dd, J = 8.5, 5.3 Hz, 1 H), 4.97–5.08 (m, 2 H), 5.70–5.88 (m, 1 H), 6.48 (s, 1 H), 6.91 (s, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –4.94, –4.61, 5.49, 7.03, 10.58, 13.13, 15.41, 18.17, 19.22, 19.41, 21.17, 21.39, 22.98, 25.85, 26.73, 28.64, 33.38, 35.50, 36.20, 39.24, 39.32, 41.53, 54.20, 75.10, 76.94, 77.05, 78.65, 81.91, 106.61, 115.28, 116.88, 120.06, 136.20, 140.84, 153.11, 164.42 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2956, 1687, 1460, 1375, 1252, 1178, 1106, 976, 888, 837, 739, 610 cm^{-1}. MS (FI = 7 kV, 3 mA, 130 °C): m/z = 795 (1), 794 (1) [M$^+$], 793 (6), 511 (13), 510 (37), 509 (100) [aldehyde], 285 (6), 284 (44) [ketone], 255 (16), 243 (3).

(4*S*,7*R*,8*S*,9*S*)-8-(*tert*-Butyldimethylsilyloxy)-12-{(4*R*,5*R*)-5-[(S,E)-2-(*tert*-butyldimethylsilyloxy)-3-methyl-4-(2-methylthiazol-4-yl)but-3-enyl]-2,2,4-trimethyl-1,3-dioxolan-4-yl}-5,5,7,9-tetramethyl-4-(triethylsilyloxy)dodec-1-en-6-one (75): Aldol adduct **74** (26 mg, 0.033 mmol) in CH_2Cl_2 (4 mL) was treated with 2,6-lutidine (18 µL, 4 equiv.) and TBSOTf (18 µL, 2 equiv.). The mixture was stirred for 3 h at room temp. and then quenched with satd. aq. $NaHCO_3$ (10 mL). The aqueous phase was extracted with diethyl ether, and the combined organic phases were washed with brine, dried with $MgSO_4$ concentrated under reduced pressure. Column chromatography (hex/EE, 10:1) gave **69** (28 mg, 94%) as a colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.02 (s, 3 H), 0.05 (s, 3 H), 0.06 (s, 3 H), 0.09 (s, 3 H), 0.60 (q, J = 8.0 Hz, 6 H), 0.85–1.47 (m, 19 H), 0.89 (s, 18 H), 0.94 (t, J = 7.8 Hz, 9 H), 1.19 (s, 3 H), 1.20 (s, 3 H), 1.39 (s, 3 H), 1.55–1.63 (m, 1 H), 1.73–1.88 (m, 1 H), 1.99 (d, J = 0.9 Hz, 3 H), 2.05–2.19 (m, 2 H), 2.70 (s, 3 H), 3.10 (mc, 1 H), 3.59 (dd, J = 10.0, 2.3 hz, 1 H), 3.75 (dd, J = 6.6, 1.8 Hz, 1 H), 3.94 (dd, J = 7.3, 3.4 Hz, 1 H), 4.35 (dd, J = 8.4, 5.5 Hz, 1 H), 4.92–5.07 (m, 2 H), 5.70–5.89 (m, 1 H), 6.48 (s, 1 H), 6.90 (s, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –4.94, –4.61, –3.79, –3.67, 5.51, 7.03, 13.07, 15.20, 17.45, 18.17, 18.51, 18.80, 19.21, 21.34, 22.19, 24.43, 25.85, 26.23, 26.71, 28.64, 31.50, 36.12, 39.03, 39.27, 39.59, 45.11, 53.76, 76.97, 77.05, 77.45, 78.59, 81.92, 106.55, 115.24, 116.49, 120.10, 136.66, 140.80, 153.12, 164.33, 218.40 ppm. IR (Si, film): $\tilde{\nu}_{max}$ = 2956, 2934, 2856, 1694, 1373, 1253, 1105, 986, 836, 775 m, 738, 610 cm^{-1}. MS (FI = 7 kV, 3 mA, 135 °C): m/z = 910 (30), 909 (28), 908 (100), 907 (31), 894 (2), 851 (4), 774 (3), 653(5), 382 (2), 283 (2), 185 (14). $[\alpha]_D^{20}$ = –4.7 (c = 0.9, $CHCl_3$).

(4*S*,7*R*,8*S*,9*S*)-4,8-Bis(*tert*-butyldimethylsilyloxy)-12-{(4*R*,5*R*)-5-[(*S*,*E*)-2-(*tert*-butyldimethylsilyloxy)-3-methyl-4-(2-methylthiazol-4-yl)but-3-enyl]-2,2,4-trimethyl-1,3-dioxolan-4-yl}-5,5,7,9-tetramethyldodec-1-en-6-one (76): In analogy to the procedure above, aldol product **74** (52 mg, 0.066 mmol) in dry CH_2Cl_2 (5 mL) was treated with 2,6-lutidine (60 µL) und 60 µL TBSOTf. After work-up and concentration in vacuo the crude product **75** was dissolved in THF (5 mL) and cooled to –18 °C. TBAF (80 µL, 1 M in THF, 1.2 equiv.) was added dropwise and the mixture was stirred for 80 min at –18 °C. After addition of satd. NH_4Cl (5 mL), the aqueous phase was extracted with diethyl ether, and the combined organic phases were washed with brine, dried with $MgSO_4$ concentrated under reduced pressure. Purification by chromatography (hex/EE, 7:1) gave compound **75** (6 mg) and the TES-deprotected product (44 mg). The latter was dissolved in dry CH_2Cl_2 (5 mL) and treated with 80 µL 2,6-Lutidin und 80 µL TBSOTf. After 3 h at room temp. and standard work-up the product was purified by chromatography (hex/EE, 10:1) to give compound **76** as a colorless oil (48 mg, 81%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.02 (s, 3 H), 0.04 (s, 3 H), 0.05 (s, 6 H), 0.06 (s, 3 H), 0.09 (s, 3 H), 0.82–0.95 (m, 3 H), 0.89 (s, 9 H), 0.90 (s, 18 H), 0.99–1.47 (m, 13 H), 1.04 (s, 3 H), 1.05 (s, 3 H), 1.20 (s, 3 H), 1.40 (s, 3 H), 1.58–1.67 (m, 1 H), 1.74–1.87 (m, 1 H), 1.99 (d, J = 1.1, 3 H), 2.02–2.17 (m, 2 H), 2.70 (s, 3 H), 3.09 (m, 1 H), 3.69 (dd, J = 10.0, 2.3, 1 H), 3.77 (dd, J = 6.6, 1.8, 1 H), 3.97 (dd, J = 6.6, 4.1, 1 H), 4.35 (dd, J = 8.4, 5.5, 1 H), 4.93–5.04 (m, 2 H), 5.70–5.90 (m, 1 H), 6.48 (s, 1 H), 6.91 (s, 1 H). ^{13}C NMR (63 MHz, $CDCl_3$): δ = –4.92, –4.56, –3.97, –3.77, –3.66, –3.31, 13.09, 15.31, 17.49, 18.18, 18.54, 19.23, 21.36, 22.11, 24.95, 25.86, 26.10, 26.24, 26.73, 28.65, 29.70, 31.50, 36.12, 39.02, 39.60, 45.07, 53.94, 76.28, 77.45, 78.58, 81.93, 106.56, 115.25, 116.29, 120.11, 136.78, 140.80, 153.13, 164.24, 218.47. IR (Si): $\tilde{\nu}$ = 2957 m, 2928 s, 2856 s, 1695 m, 1472 m, 1374 m, 1256 m, 1216 w, 1180 w, 1106 s, 986 m, 886 w, 837 w, 775 m, 738 w, 671 w, 610 s. MS (FI = 7 kV, 2 mA, 150 °C): m/z = 912 (6), 911 (12), 910 (40), 909 (84), 908 (100) [M], 897 (4), 851 (14) [M – tBu], 710 (2), 653 (4), 637 (3). $[\alpha]_{365}^{20}$ = +12.0 (c = 1.0, $CHCl_3$).

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