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Synthesis of (*Z*)-Trisubstituted Olefins by Decarboxylative Grob-Type Fragmentations: Epothilone D, Discodermolide, and Peloruside A

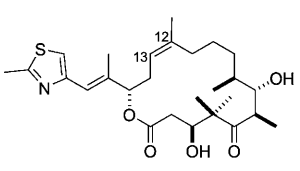
Kathrin Prantz and Johann Mulzer*[a]

Abstract: Methyl-branched (*Z*)-trisubstituted olefins are found in many polyketides with interesting biological activity, such as epothilone D (**1**), discodermolide (**3**), and peloruside A (**2**). Despite the employment of numerous different strategies, this motif has often been the weak point in total synthesis. Thus, we present a novel hydroxide-induced Grob-type fragmentation as an easy access to trisubstituted olefins. In our case, β-mesyloxy δ-lactones with three stereogenic centers were chosen whose fragmentation underlies a high stereoelectronic control. Major challenges in the syntheses were the installation of quaternary stereocenters, achieved by enzymatic desymmetrization of *meso*-diesters and by aluminium-promoted stereoselective rearrangement of chiral epoxides, respectively. Different aldol strategies were developed for the formation of the fragmentation precursors. Additionally a short survey about nucleophilic additions to aldehydes with quaternary α-centers is presented.

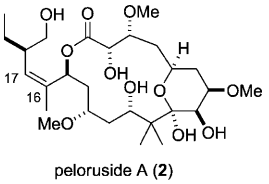
Keywords: discodermolide · epothilone D · Grob fragmentation · natural products · peloruside A · polyketides

Introduction

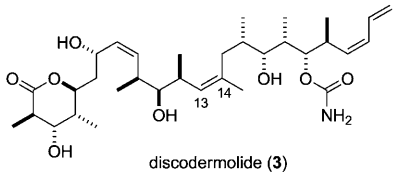
One of the major challenges for a synthetic organic chemist is the stereoselective formation of carbon–carbon bonds and carbon–carbon double bonds, respectively. Especially in polyketides, such as epothilone D (**1**), discodermolide (**3**), and peloruside A (**2**), methyl-branched (*Z*)-trisubstituted olefins are an important structural motif. These natural products are potent antitumor agents and like paclitaxel they have a stabilizing effect on microtubules. Owing to their pharmacological importance, their synthesis has been investigated intensively in the last decade. For the generation of the crucial trisubstituted (*Z*)-olefinic subunits a manifold of synthetic approaches has been devised, which rely on carbonyl olefination, olefin metathesis, alkyne functionalization, allylic rearrangements, and cross-coupling chemistry.[1] Many of these protocols show low yield and stereoselectivity, and employ toxic and/or expensive reagents. This raises the question why simple E2 eliminations and in particular the well-known Grob fragmentation has never been considered before,[2] especially as it has had an impressive revival in the synthesis of cyclic olefins.[3]



epothilone D (**1**)



peloruside A (**2**)



discodermolide (**3**)

Herein we report a novel hydroxide-induced decarboxylative Grob-type fragmentation for the stereoselective synthesis of trisubstituted double bonds.[4] This strategy utilizes δ-lactones such as **4** as fragmentation precursors that feature three stereogenic centers, one of them quaternary, with the indicated relative configuration (Scheme 1).[5] Upon hydroxide addition a tetrahedral intermediate (**5**) is generated, which undergoes fragmentation under extrusion of carbon dioxide and the mesylate to form the desired (*Z*)-olefin. Stereoelectronically, clean fragmentation can be expected if the hydroxyl anion attacks axially and the lactone adopts a chair conformation with the OMs-substituent in an equatori-

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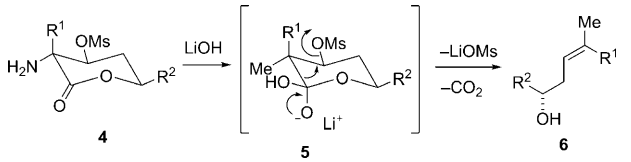
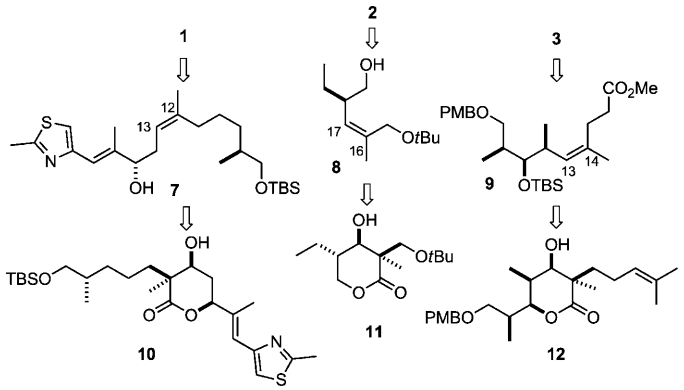


Scheme 1. Grob-type hydroxide induced fragmentation of lactone **4**. Ms = methanesulfonyl.

al position.[6] This provides an antiperiplanar arrangement of the oxygen lone pair and the bonds to be broken during the course of the reaction, which may be facilitated by introducing a bulky residue R^2 *cis* to the OMs as a conformational anchor.

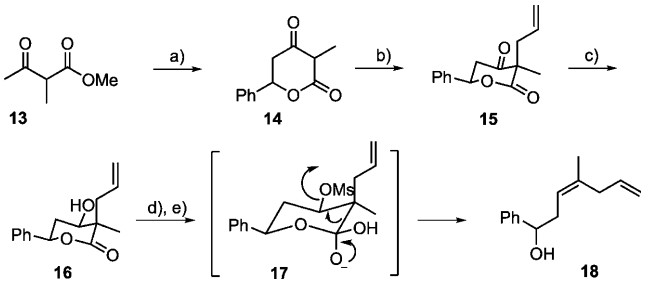
The natural compounds **1–3** can be traced back to the known precursors **7–9**, which can be gained from fragmentation precursors **10–12** (Scheme 2). As the δ-hydroxy group in **10** and **12** is homochiral, lactones **10** and **12** have to be prepared in a diastereo- *and* enantioselective manner. Thus, an additional synthetic challenge lies in the enantioselective generation of aldol-type quaternary centers, for which different strategies had to be developed.



Scheme 2. Retrosynthetic analysis. TBS = *tert*-butyldimethylsilyl, PMB = *para*-methoxybenzyl.

Results and Discussion

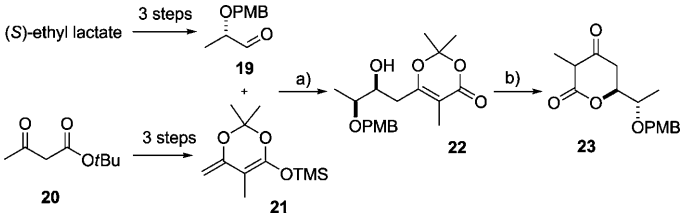
Model studies: For a proof of principle, a simplified racemic test system was used (Scheme 3). Therefore, lactone **14** was prepared by addition of the dianion of acetoacetate **13** to benzaldehyde followed by saponification. The quaternary center was introduced by a biphasic Trost–Tsuji allylation.[7] This turned out to be the only protocol mild enough for this kind of transformation, as in homogeneous organic solvents or by direct reaction of the enolate with an allyl halogenide the very base sensitive lactone **14** eliminated water to form cinnamic acid derivatives. After reduction of the β-carbonyl group, the major diastereomer **16** was isolated by column chromatography and mesylated to give **17**. Treatment with sodium hydroxide in methanol at 0 °C gave (*Z*)-olefin **18** as the only product in almost quantitative yield.



Scheme 3. Model study. a) LDA, HMPA, then PhCHO, THF, −78 °C; 1 M KOH, then HCl, 0 °C, 64% (2 steps); b) $[Pd(PPh_3)_4]$, allyl acetate, K_2CO_3, $BnEt_3NCl$, EtOAc/H_2O, 98%, d.r. 4:1; c) $NaBH_4$, MeOH, 0 °C, 97%; d) MsCl, Et_3N, Et_2O, −10 °C; e) KOH, MeOH, 0 °C, >95% (2 steps). HMPA = hexamethylphosphoramide.

Encouraged by this positive result we turned our attention to natural product synthesis, and, consequently to an enantioselective synthesis of fragmentation precursors **10–12**.

Epothilone D (first-generation approach): The first strategy towards fragmentation precursor **10** was in analogy to the test system. Therefore a Cram-chelate-controlled Mukaiyama aldol reaction was performed with enol ether **21** and known aldehyde **19**,[8] derived in three steps from (*S*)-ethyl lactate. A single diastereoisomer **22** was generated in excellent yield,[9,10] which was deprotected to form lactone **23**



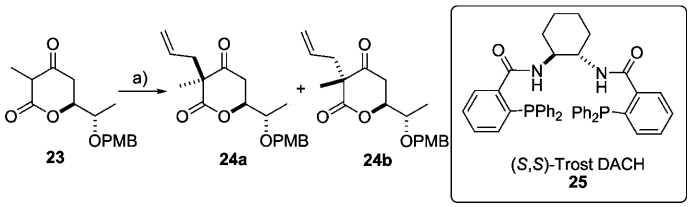
Scheme 4. Synthesis of lactone **23**. a) $MgBr_2 \cdot Et_2O$, CH_2Cl_2, −10 °C, 96%; b) K_2CO_3, methanol, RT, then HCl, quant. TMS = trimethylsilyl.

(Scheme 4).

The next objective was the introduction of the quaternary center by a diastereoselective allylic alkylation, which was first tested with allyl acetate. The biphasic "achiral" Tsuji–Trost conditions, developed for test system **14** with palladium-tetrakis(triphenylphosphane) as the catalyst, gave a 3:1-ratio of easily separable diastereoisomers **24a** and **24b** in excellent yield (Scheme 5); the relative configuration of the two diastereoisomers was determined via NOE difference spectroscopy.

Despite extensive optimizations concerning the palladium source, choice of ligands, solvent system, and bases, the best diastereomeric ratio never exceeded 7:2 in favor of **24a** (Table 1).[11]

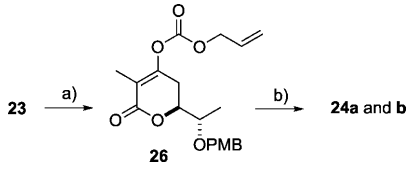
Also intramolecular allylation, as described by Trost and Stoltz, was tested (Scheme 6).[12] Therefore the potassium



Scheme 5. Tsuji–Trost allylation with allyl acetate. a) see Table 1.

Table 1. Conditions and results for Tsuji–Trost allylation with allyl acetate.

Pd/Ln*	Base	Solvent	Yield [%]	**24a/24b**
$[Pd(PPh_3)_4]$	K_2CO_3	H_2O/EtOAc	98	3:1
$[Pd_2(dba)_3]\cdot CHCl_3$, (*R*,*R*)-Trost DACH	LDA	THF	lactone opening	–
$[Pd_2(dba)_3]\cdot CHCl_3$, (*R*,*R*)-Trost DACH	LiHMDS	THF	82	1:2
$[Pd_2(dba)_3]\cdot CHCl_3$, (*R*,*R*)-Trost DACH	DBU	toluene	60	2:3
$[Pd_2(dba)_3]\cdot CHCl_3$, (*S*,*S*)-Trost DACH	LiHMDS	THF	75	3:1
$[Pd_2(dba)_3]\cdot CHCl_3$, (*S*,*S*)-Trost DACH	DBU	toluene	92	7:2



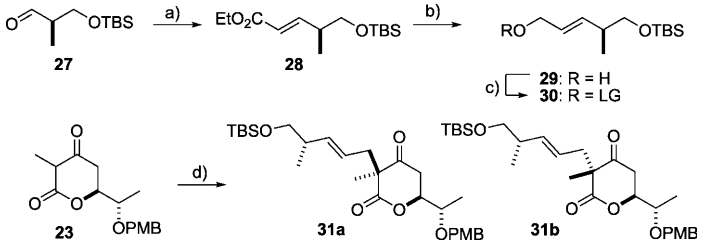
Scheme 6. Intramolecular Tsuji–Trost allylation. a) Allyl chloroformate, KO*t*Bu, THF, −78 °C, 95 %; b) $[Pd_2(dba)_3]\cdot CHCl_3$, **25**, toluene, −78 °C, 76 %, **24a/24b** 4:1. dba = dibenzylideneacetone.

enolate of **23** was trapped as allyl carbonate **26**, which could be used in the allylation without any additional base or other additives, and the diastereomeric ratio was increased to 4:1.

After this, the introduction of the quaternary center with the fully substituted allylic carbonate was tackled, and also the carbonate leaving group was varied in the optimization process. Known aldehyde **27**[13a] was olefinated by means of a Horner–Wadsworth–Emmons reaction under Masamune–Roush conditions[13b] to provide pure (*E*)-enoate **28** (Scheme 7), which was converted to a variety of allylic carbonates **30**. The allylation was performed with three achiral and two chiral catalysts. The best result is the one shown in the last row, which uses the simplest ingredients (Table 2).

The seemingly trivial task to reduce the β-ketone stereoselectively was more troublesome than expected and gave disappointing 1:1 mixtures under all conditions. Most probably the 6-sidechain was not an efficient conformational anchor. Efforts to introduce the thiazolylidene moiety earlier proved unsuccessful. Finally, carbonyl reduction and hydrogenation of the diastereomeric mixture with Adam's catalyst gave a mixture of δ-lactone-3,4-diastereomers, from which compound **33** was isolated by chromatography (Scheme 8). Mesylation and fragmentation as before delivered pure (*Z*)-olefin **34** in 91 % yield. If the diastereomeric δ -lactone mixture was used, **34** was isolated as the only olefinic product, though in correspondingly lower yield. In a simple, efficient, and high-yielding four-step endgame, olefin **34** was converted to compound **38**, which has been an important intermediate in several approaches to epothilone D and proved identical with an authentic sample in every respect.[19]

Epothilone D (second-generation approach): To achieve a higher degree of stereoselectivity, a second strategy was developed, which relies on an enzymatic desymmetrization of *meso*-malonate **39**.[14] Hydrolysis with pig liver esterase (PLE) to mono acid **40** and selective reduction of the carboxylate gave alcohol **41** (Scheme 9), a general building block whose allylic appendage can be modified in the desired manner.[15]

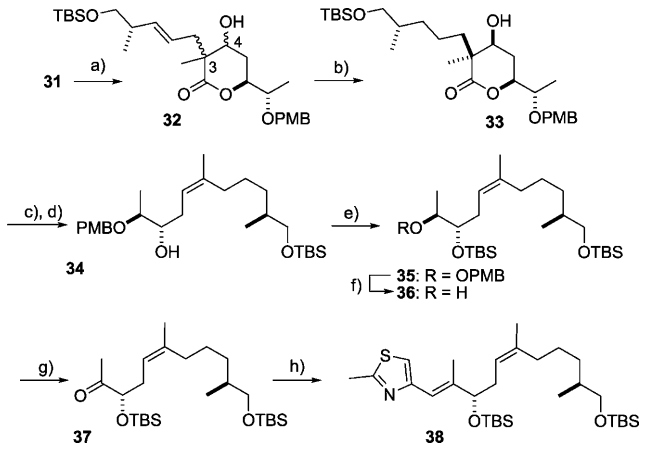


Scheme 7. Allylation with elaborated allylic carbonate **30**. a) $EtO_2CCH_2P(O)(OEt)_2$, DBU, LiCl, CH_3CN, RT, 84 %; b) DIBALH, toluene, −78 °C, 95 %; c) LG-Cl, pyridine, RT, 88 %; d) see Table 2. DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene, Troc = 2,2,2-trichloroethyl carbonate.

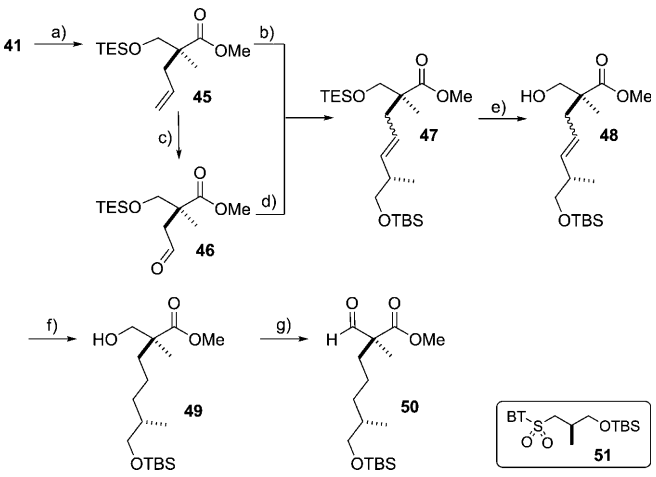
En route to our target molecule **38**, a cross metathesis of **41** with olefin **42** was investigated first, but despite variation of catalyst, solvent, reaction time, and temperature, the yield never exceeded 40 % (Scheme 10).[16] Next we tried carbonyl olefination and oxidized **41** to lactol **44**. However, neither Julia–Lythgoe nor Wittig conditions gave any reaction.[17]

Table 2. Conditions and results for Tsuji–Trost allylation with elaborated allyl carbonates.

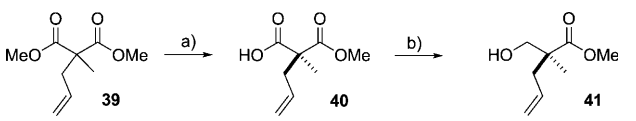
Pd/Ln*	OLG	Base	Solvent	Yield [%]	**31a/31b**
$[Pd(PPh_3)_4]$	OTroc	K_2CO_3	H_2O/EtOAc	97	3:1
$[Pd_2(dba)_3]\cdot CHCl_3$, (*R*,*R*)-Trost DACH	OTroc	DBU	toluene	60	2:3
$[Pd_2(dba)_3]\cdot CHCl_3$, (*S*,*S*)-Trost DACH	OTroc	DBU	toluene	54	3:2
$[Pd(PPh_3)_4]$	OTroc	DBU	toluene	41	3:1
$[Pd(PPh_3)_4]$	$OC(O)CH_2Cl$	DBU	toluene	17	4:1
$[Pd(PPh_3)_4]$	OC(O)OEt	DBU	toluene	34	4:1
$[Pd(PPh_3)_4]$	OC(O)OEt	–	H_2O/EtOAc	85	4:1
$[Pd(PPh_3)_4]$	OC(O)OEt	K_2CO_3	H_2O/EtOAc	97	4:1



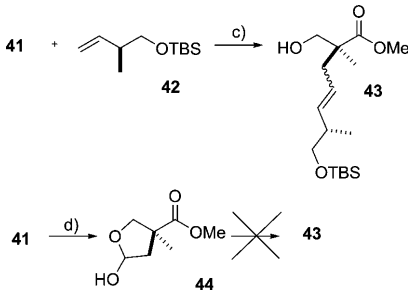
Scheme 8. Fragmentation and conversion into northern fragment **38**. a) $NaBH_4$, MeOH, 0°C, 98%; b) PtO_2, H_2, EtOAc, 1 atm, RT, quant.; chromatographic separation of diastereomers; c) MsCl, Et_3N, Et_2O, 0°C; d) KOH, methanol, 0°C, 91% (2 steps); e) TBSOTf, 2,6-lutidine, CH_2Cl_2, RT, quant.; f) DDQ, CH_2Cl_2, RT, 98%; g DMP, $NaHCO_3$, CH_2Cl_2, quant.; h) (2-methyl-thiazol-4-yl)methyltributylphosphonium chloride, *n*BuLi, THF, −78 to 60°C, 93%. DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, DMP = Dess–Martin periodinane.



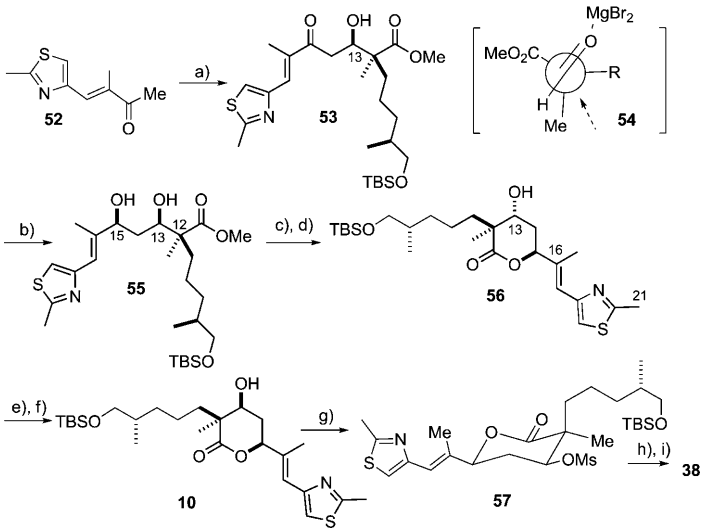
Scheme 11. Conversion of alcohol **41** into aldehyde **50**. a) TESCl, py, RT, quant; b) Grubbs–Hoveyda cat, **42**, CH_2Cl_2, reflux, 93%; c) O_3, PPh_3, PPTS, CH_2Cl_2, −78°C, quant.; d) LiHMDS, **51**, THF, −78 to −30°C, 96%; e) PPTS, MeOH, RT, 92%; f) PtO_2, H_2, EtOAc, 99%; g) DMP, CH_2Cl_2, 0°C, 91%. TES = triethylsilyl, BT = 2-benzothiazolyl, PPTS = pyridinium *p*-toluenesulfonate, HMDS = hexamethyldisilazane.



Scheme 9. Conversion of malonate **39** into alcohol **41**. a) PLE, 0.05 M KH_2PO_4, 90%; b) ClC(O)OMe, Et_3N, THF, 0°C; $NaBH_4$, MeOH, 0°C, 75%.



Scheme 10. Cross-metathesis to elongate the allyl moiety of alcohol **41**. a) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 to 0°C; b) Ph_3PCH_3, KO*t*Bu, THF, 0°C to RT, 87%; c) Grubbs–Hoveyda, CH_2Cl_2, 45°C, <40%; d) O_3, PPh_3, CH_2Cl_2, −78°C, quant.



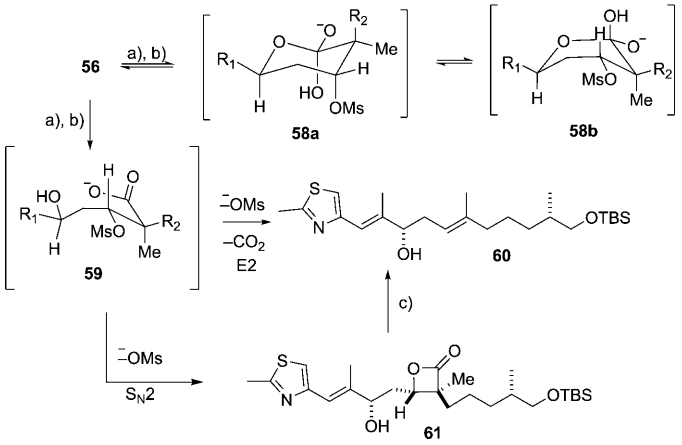
Scheme 12. Synthesis of the C7–C21 epothilone D fragment **38**. a) LiHMDS, THF, −78°C, then **50**, $MgBr_2 \cdot Et_2O$, 91%; b) catecholborane, THF, −10°C, 88%; c) LiOH, THF, 0°C; d) EDC·HCl, DMAP, CH_2Cl_2, 94% (2 steps); e) DMP, $NaHCO_3$, CH_2Cl_2, 94%; f) $NaBH_4$, MeOH, −78°C, 93%; g) MsCl, Et_3N, Et_2O, 0°C; h) LiOH, THF, 0°C, 81%; i) TBSOTf, 2,6-lutidine, CH_2Cl_2, RT, quant. EDC = 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide, DMAP = 4-(dimethylamino)pyridine.

As the free alcohol seemed to be the source of all inconvenience, it was protected as a TES-ether and indeed, both elongation strategies worked smoothly and furnished **43** in high yields (Scheme 11). From **43**, aldehyde **50** was obtained by desilylation, hydrogenation and oxidation.

Next, aldehyde **50** was activated with freshly prepared $MgBr_2 \cdot Et_2O$, and then added to the lithium enolate of ketone **52**. Adduct **53** was obtained as a single (13*R*)-diastereomer in 91% yield, presumably via a Felkin-like transition state **54** (Scheme 12). Even with stronger Lewis acids such as $TiCl_4$ or $SnCl_4$, a chelated transition state could not be enforced and without activation the reaction was sluggish and low yielding. For the substrate controlled *syn*-reduction catecholborane proved best and furnished only *syn*-dihydroxy ester **55**, whereas with $LiBH_4$, $Zn(BH_4)_2$, or $BEt_3/NaBH_4$ the selectivity was not satisfactory.[18] Saponification and lactonization led to lactone **56**. As (13*S*)-configuration was required for clean fragmentation, inversion at C13 was achieved by an oxidation–reduction sequence to give **10**. Trans-

formation to mesylate **57** set the stage for the fragmentation reaction. KOH in methanol opened the lactone to form the methyl ester, whereas LiOH, KOH, and NaOH in THF gave the desired (*Z*)-olefin **7** exclusively in about 80% yield, from which epothilone fragment **38** was obtained by silylation.

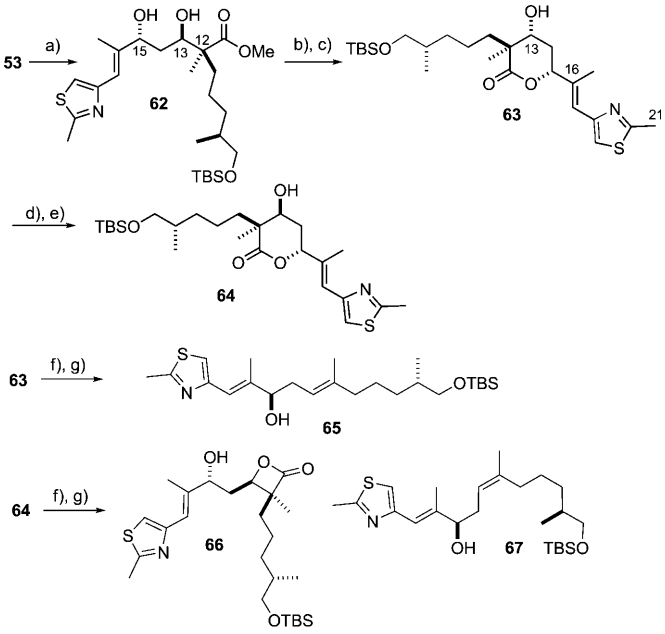
To investigate the stereoelectronic demands of the fragmentation, we turned to lactone **56** (Scheme 13). Due to the axial configuration of the 13-OH, a Grob-type fragmentation in a chair conformation (**58a**) should be impossible. On the other hand, boat conformation **58b** might stereoelectronically be suitable to undergo fragmentation, however, the species itself is energetically unfavorable. Nevertheless, olefin **60** (38%) was obtained under the usual conditions, alongside β-lactone **61** (52%). This result may be rationalized by assuming that lactone **56** under the action of base first forms carboxylate **59**, which undergoes both fragmentation to (*E*)-olefin **60** and S_N2 cyclization to β -lactone **61**.[20] On thermolysis **61** gave **60** as well, so that, overall, olefin **60** is obtained from **56** in pure (*E*)-geometry and about 80% combined yield. In effect, this result underlines the versatility of our method, as both the (*Z*)- and the (*E*)-olefin are available from lactone **56** along analogous routes.



Scheme 13. Fragmentation of lactone **56**. a) MsCl, Et_3N, Et_2O, 0°C; b) LiOH, THF, 0°C, 38% (**60**) and 52% (**61**); c) DMF, reflux, 85%.

Variation of the temperature in the fragmentation of **56** did not significantly alter the ratio of olefin and β-lactone, however, with increasing temperature the amount of the olefin was slightly enhanced. Changing the leaving group from OMs to OTs and OTf gave similar product distributions. The instability of the triflate led to slightly lower yields though.

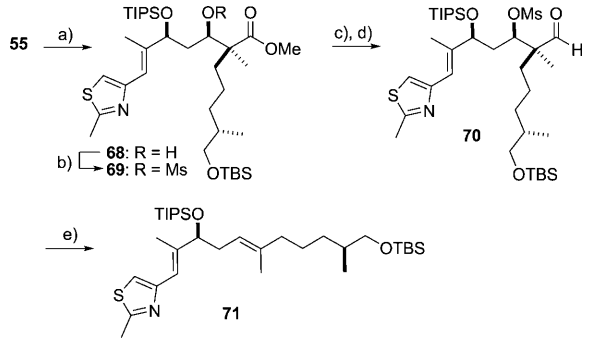
Two additional diastereoisomers can easily be gained from **53** by reducing ketone **53** to *anti*-diol **62** (Scheme 14),[21] from which lactones **63** and **64** were available by saponification and Steglich lactonization. Fragmentation of **63** via the chair transition state cleanly led to (*E*)-olefin **65**, whereas **64** gave β-lactone **66** and (*Z*)-olefin **67**, as expected. Thus four diastereomers of the northern fragment



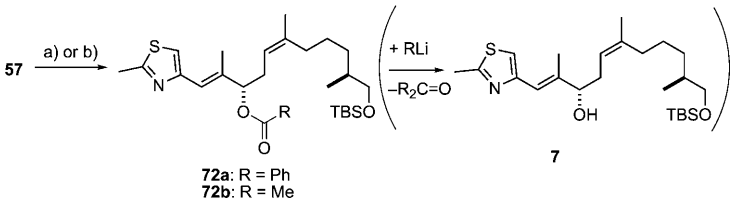
Scheme 14. Fragmentation of lactones **63** and **64**. a) $Me_4NBH(OAc)_3$, CH_3CN/AcOH, −30°C, 87%; b) LiOH, THF, 0°C; c) EDC·HCl, DMAP, CH_2Cl_2, 85% (2 steps); d) DMP, $NaHCO_3$, CH_2Cl_2, 94%; e) $NaBH_4$, MeOH, −78°C, 90%; f) MsCl, Et_3N, Et_2O, 0°C; g) LiOH, THF, 0°C, 64% (**65**), 36% (**66**), 52% (**67**).

of **1** are available from intermediate **53** using the same fragmentation protocol.

Do we need δ-lactones as fragmentation precursors or would an acyclic derivative also do? To test this possibility intermediate **55** was regioselectively protected as 15-OTIPS ether and mesylated to give **69** (Scheme 15). All attempts to convert the ester into the carboxylate either by using various hydroxides, KOTMS or the Krapcho protocol failed.[22,23] However, after reducing the ester to the aldehyde, fragmentation gave olefin **71** in excellent yield. Notwithstandingly, the lactone route appears more reliable, as inversion of the β-OH and regioselective protection of the δ-OH position might be problematic in acyclic molecules.



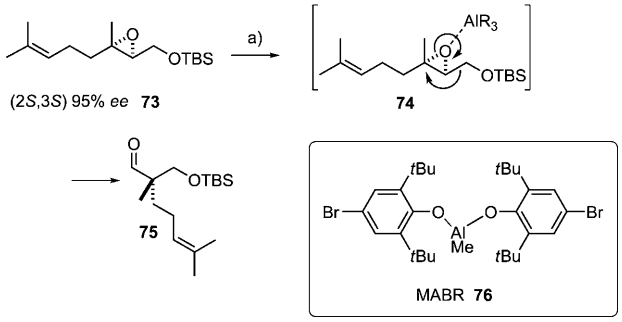
Scheme 15. Fragmentation of open chain precursor **70**. a) TIPSOTf, 2,6-lutidine, CH_2Cl_2, RT, 85%; b) MsCl, Et_3N, Et_2O, RT, 96%; c) DIBAL-H, toluene, −78°C, 87%; d) DMP, $NaHCO_3$, CH_2Cl_2, 0°C, 94%; e) LiOH, THF, 0°C, 82%. TIPS = triisopropylsilyl.



Scheme 16. Fragmentation of **57** using organolithium species. a) PhLi, THF, −78 °C, 43 % (**72a**), 20 % (**7**), b) MeLi, THF, −78 °C, 23 % (**72b**), 51 % (**7**).

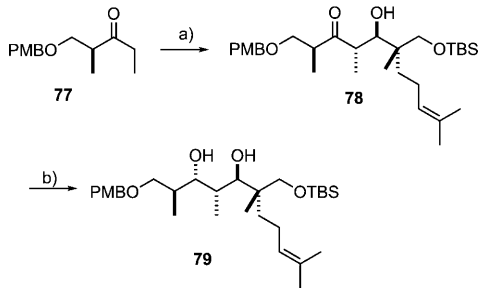
Phenyl- and methyllithium were also tested in the fragmentation of lactone **57** (Scheme 16). Both gave the (*Z*)-olefin, either in form of the carbonate **72** or the unprotected alcohol **7**. However, when fragmentation of **56** was attempted with these organolithium species, only decomposition was observed. This result again underlines the need for a chairlike transition state.

Discodermolide: In this case, the required quaternary stereocenter was generated by the organoaluminum-promoted rearrangement of OTBS-protected epoxy-geraniol (**73**) to aldehyde **74**, which was obtained under complete chirality transfer (Scheme 17).[24]



Scheme 17. Yamamoto's organoaluminum-promoted rearrangement to generate aldehyde **75**. a) MABR, CH_2Cl_2, −78 to 0 °C, quant., 95 % ee.

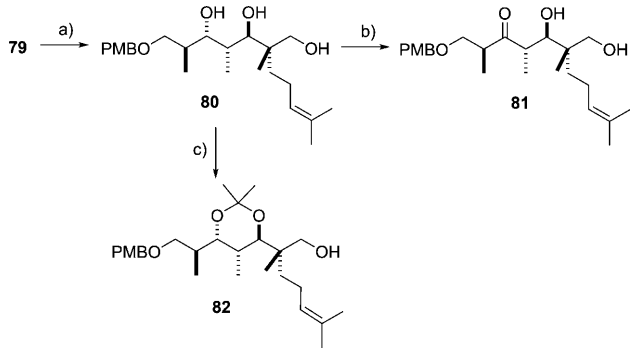
An *anti–anti*-selective Paterson aldol addition of **75** with known ethyl ketone **77**,[26] gave multigram quantities of aldol adduct **78** in good yield and excellent selectivity.



Scheme 18. Synthesis of the stereopentad **79**. a) Cy_2BCl, Et_3N, then **75**, Et_2O, −78 to 0 °C, 76 %; b) $Me_4NBH(OAc)_3$, CH_3CN/AcOH, −30 °C, 94 % (b.r.s.m.). Cy = cyclohexyl.

Evans–Carreira *anti*-reduction transformed **78** to the stereopentad **79** (Scheme 18).

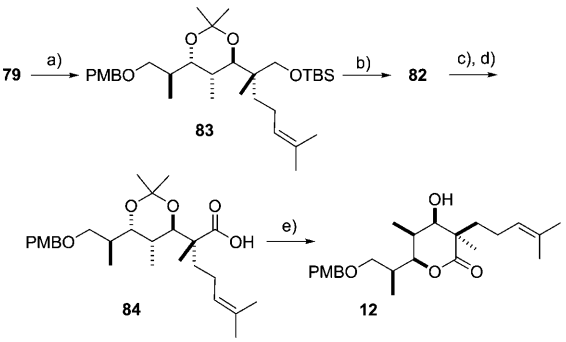
For the preparation of the δ-lactone, the primary neopentyl position in **79** had to be oxidized to the acid and then cyclized to the lactone. Thus, the TBS ether was cleaved with HF·pyridine to get triol **80**. To our surprise, the oxidation of **80** with one equivalent of DMP cleanly furnished ketone **81**, which impressively demonstrates the inaccessibility of the neopentyl position (Scheme 19). As an additional test, triol



Scheme 19. Selective oxidation of triol **80**. a) 35 % HF·py, CH_3CN, RT, 92 %; b) DMP, $NaHCO_3$, CH_2Cl_2, 0 °C, 65 %; c) 2,2-dimethoxypropane, CSA, CH_2Cl_2, RT, 88 %.

80 was converted into acetonide **82**, which again shows that the primary alcohol site is the least reactive one.

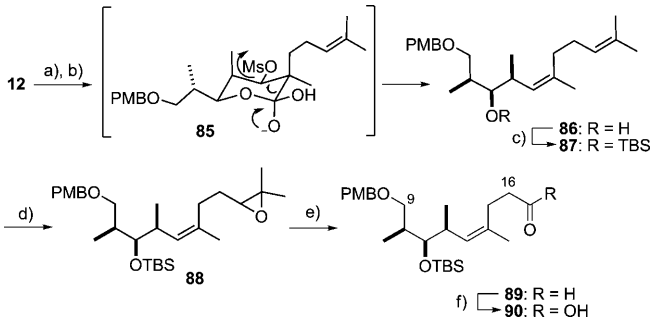
Alternatively, **82** was prepared from **79** via TBS-ether **83** (Scheme 20). A two-step oxidation of **82** led to the acid,



Scheme 20. Synthesis of the discodermolide fragmentation precursor **12**. a) 2,2-Dimethoxypropane, CSA, CH_2Cl_2, RT, 86 %; b) 35 % HF·py, CH_3CN, RT, 97 %; c) IBX, EtOAc, reflux, 86 %; d) 2-methyl-2-butene, $NaClO_2$, NaH_2PO_4, *tert*-butanol/H_2O, RT, quant.; e) CSA, CH_2Cl_2, RT, 83 %. CSA = camphorsulfonic acid, IBX = 2-iodoxybenzoic acid.

which spontaneously cyclized to lactone **12** upon treatment with CSA.

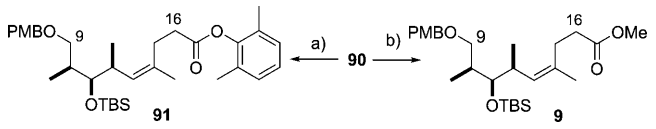
Due to severe steric hindrance, the mesylation of δ-lactone **12** required an excess of mesyl chloride and DMAP. Upon treatment with lithium hydroxide the mesylate cleanly furnished (*Z*)-olefin **86** via the chair transition state



Scheme 21. Fragmentation of **12** and conversion to acid **90**. a) MsCl, DMAP, py, CH_2Cl_2, RT; b) LiOH, THF, RT, 88% (2 steps); c) TBSOTf, 2,6-lutidine, CH_2Cl_2, RT, quant.; d) *m*CPBA, NaOAc, CH_2Cl_2, −20°C, 92%; e) $HIO_4{\cdot}2H_2O$, THF/Et_2O, 0°C, 90%; f) 2-methyl-2-butene, $NaClO_2$, NaH_2PO_4, *tert*-butyl alcohol/H_2O, RT, quant. *m*CPBA = *meta*-chloroperbenzoic acid.

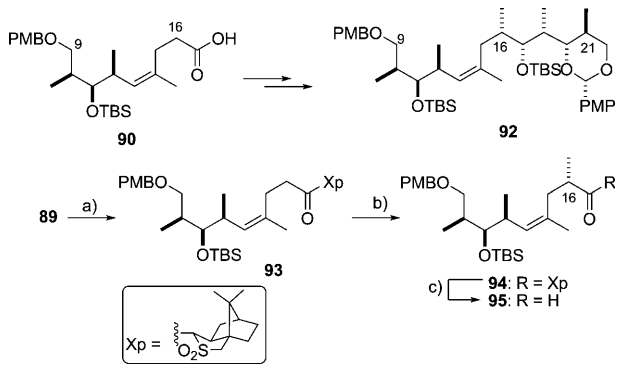
(Scheme 21). After silylation of the secondary alcohol a three-step oxidation of the terminal olefin led to acid **90**, from which the key intermediates of both Paterson's and Smith's discodermolide syntheses were prepared.

Thus, Paterson's aryl ester **91** and methyl ester **9** are available by esterification of acid **90** under Steglich conditions or treatment with diazomethane, respectively (Scheme 22).[26b]



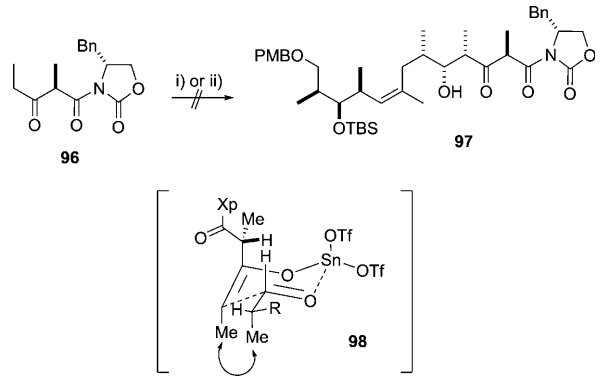
Scheme 22. Conversion into Paterson's intermediates **91** and **9**. a) 2,6-dimethylphenol, DIC, DMAP, CH_2Cl_2, RT (99%); b) CH_2N_2, MeOH, RT (quant.). DIC = *N*,*N*′-diisopropylcarbodiimide.

To intersect Smith's intermediate **92**, the C16–C21 (eastern) part of discodermolide had to be attached to **90**. First, the C16 methyl group was introduced via the Oppolzer sultam **93** (Scheme 23).[27] Then the auxiliary was removed to yield aldehyde **95**, from which the missing four contiguous stereogenic centers were to be generated by aldol strategy.



Scheme 23. Generation of aldehyde **95**. a) (1*R*)-camphore-2,10-sultam, DIC, DMAP, CH_2Cl_2, RT, 96%; b) NaHMDS, MeI, THF, −78°C, 89%; c) DIBALH, CH_2Cl_2, −100°C, 94%.

First aldolization with β-ketoimide **96** was attempted,[28,29] but even under a variety of conditions no product was observed. This is not surprising as the combination of **95** and **96** results in a mismatched transition state (**98**), with unfavorable *syn*-pentane interaction (Scheme 24).

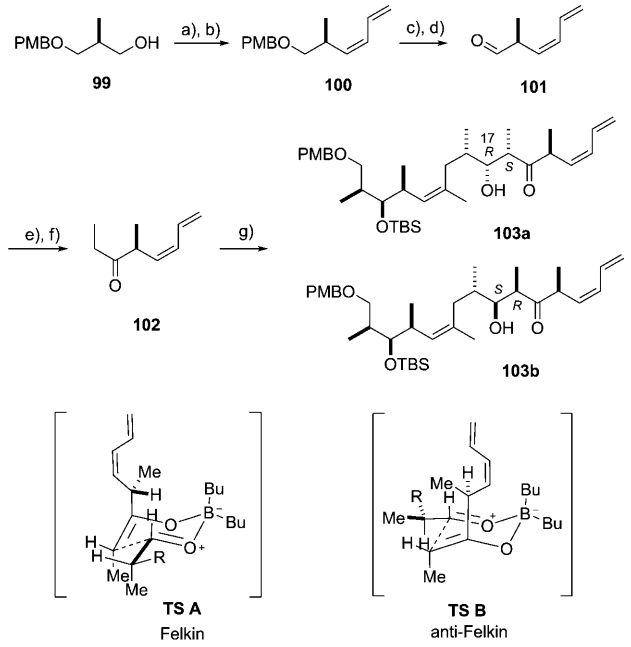


Scheme 24. Unsuccessful aldolization of aldehyde **95** with diketoimide **96**. i) Bu_2BOTf, Et_3N, then **95**, CH_2Cl_2, −78 to 0°C; or ii) $Sn(OTf)_2$, Et_3N,then **95**, CH_2Cl_2, −78 to 0°C.

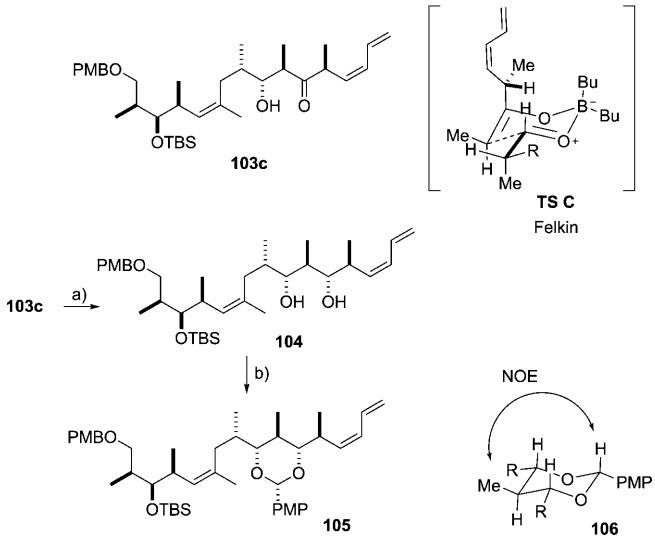
Next, ethyl ketone **102** was tried; but again we face a mismatched situation, though with considerably less steric interaction. Thus, the Nozaki–Hiyama/Peterson protocol was used to prepare (*Z*)-diene **100** from **101**, which was converted to ethyl ketone **102** (Scheme 25).[30] On trying to convert **102** into the (*Z*)-enolborinate, (−)-diisopinocampheylboron-triflate failed to react,[31a] whereas dibutylboron triflate smoothly gave an aldol adduct (**103**),[31b] which, based on literature precedence, could either be **103a** or **103b**.[31c] The latter one was more likely, because with α-chiral aldehydes, (*Z*)-enolborinates normally form *anti*-Felkin adducts via transition state **TS B**. The Felkin transition state **TS A**[26a] is destabilized by a *syn*-pentane interaction.

On determining the configurations of the newly formed stereogenic centers in **103**, C17 was shown to have the desired *R* configuration via the corresponding Mosher esters (Scheme 26).[32] For further assignments, adduct **103** was converted into acetal **105** by *syn* reduction with catecholborane and reaction with anisaldehyde dimethyl acetal. NOE signals definitely proved an 17,18-*anti*-arrangement and hence, the aldol adduct has the unexpected structure **103c!** Obviously, both transition states **TS A** and **TS B** are flawed by unfavorable interactions; the system has dodged this situation by isomerizing the initially formed (*Z*)-borinate to the (*E*)-isomer and then using the favorable Felkin transition state **TS C**.

After the convergent approaches had failed, a stepwise strategy was finally successful. Aldehyde **95** was subjected to a *syn* selective Evans' aldol addition which gave **108** with excellent selectivity (Scheme 27).[33] Silyl protection and reductive removal of the auxiliary furnished alcohol **110**,

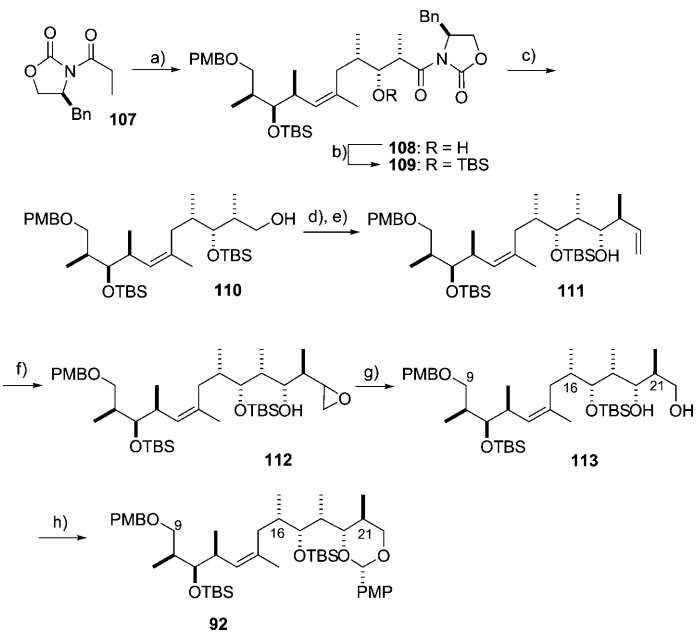


Scheme 25. Paterson-type aldol addition with ethyl ketone **102**. a) IBX, EtOAc, RT; b) $CrCl_3$, $LiAlH_4$, (1-bromoallyl)trimethylsilane, THF, 0°C to RT, then KOH, 0°C, 90% (over 2 steps); c) DDQ, CH_2Cl_2, RT, 93%; d) DMP, $NaHCO_3$, CH_2Cl_2, RT; e) EtMgBr, Et_2O, 0°C, 89%; f) DMP, $NaHCO_3$, CH_2Cl_2, RT, 99%; g) Bu_2BOTf, Et_3N, then **95**, CH_2Cl_2, −78 to 0°C, 89% (b.r.s.m.).



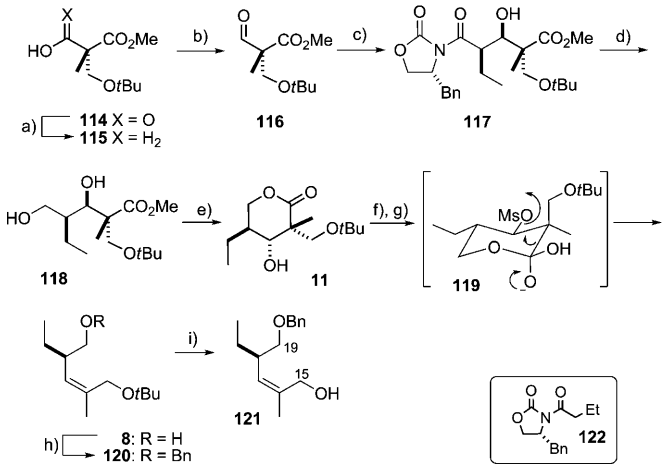
Scheme 26. Conversion to discodermolide fragment **105**. a) Catecholborane, THF, −10°C, 65%; b) $PMPCH(OMe)_2$, CSA, CH_2Cl_2, RT, 99%.

which was oxidized to the aldehyde. This compound was then used in a Roush crotylation to create the missing two stereocenters.[34] Oxidative cleavage of the terminal olefin, by a vanadium-mediated epoxidation,[35] was followed by reduction and led to the C19,21-diol **113**. Protection of the diol led to PMP-acetal **92**, whose analytical data were in full agreement with those reported by Smith and co-workres.[36]



Scheme 27. Conversion to Smith's discodermolide fragment **92**. a) Bu_2BOTf, Et_3N, then **95**, CH_2Cl_2, −78 to 0°C, 65% (99% b.r.s.m.); b) TBSOTf, 2,6-lutidine, CH_2Cl_2, RT, quant.; c) $LiBH_4$, Et_2O, MeOH, 0°C, 86%; d) IBX, DMSO, RT; e) (*R*,*R*)-diisopropyl tartrate (*E*)-crotylboronate, toluene, −78 to 0°C, 87%; f) $VO(acac)_2$, *t*BuOOH, CH_2Cl_2, 0°C, 87% (2 steps); g) $HIO_4 \cdot 2H_2O$, Et_2O/THF, 0°C, then $NaBH_4$, methanol, 0°C 51% b.r.s.m.; h) anisaldehyde dimethyl acetal, CSA, CH_2Cl_2, RT, 86%.

Peloruside A: For the synthesis of Ghosh's peloruside A intermediate **121** an enzymatic desymmetrization was used to generate the quaternary center in mono acid **114** (Scheme 28).[37] Conversion to alcohol **115** by reduction via the mixed anhydride was followed by oxidation to aldehyde



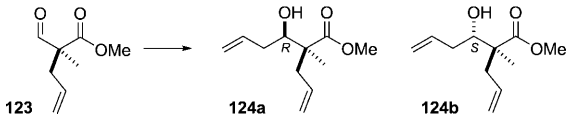
Scheme 28. Synthesis of the C15–C19 peloruside A fragment **121**. a) ClC(O)OMe, Et_3N, THF, 0°C; $NaBH_4$, MeOH, 0°C, 83%; b) IBX, DMSO, RT, 80%; c) **122**, Bu_2BOTf, Et_3N, then **116**, CH_2Cl_2, −78 to 0°C, 85%; d) $LiBH_4$, Et_2O, MeOH, 0°C, 80%; e) K_2CO_3, MeOH, RT, 1N HCl, quant.; f) MsCl, DMAP, CH_2Cl_2, RT, 99%; g) LiOH, dioxane, RT, 83%; h) BnBr, Ag_2O, TBAI, quant.; i) TFA, CH_2Cl_2, RT, 91%. TFA = trifluoroacetic acid.

116 which was used in a *syn*-selective aldol addition with oxazolidinone **122**.[38] Reductive removal of the auxiliary was optimized carefully to avoid the spontaneous cyclization of dihydroxy ester **118** to lactone **11**, which is immediately reduced to inseparable product mixtures under the conditions. Instead, base induced saponification of **118** was used to obtain δ-lactone **11**, which was mesylated and fragmented *via* the chair transition state **119** to give (*Z*)-olefin **8**. Now only a change of protecting groups was required to intercept intermediate **121**.[39,40]

Nucleophile additions to an aldehyde with quaternary α-center: When we observed the unusual behaviour of aldehyde **50** in the aldol addition, we decided to investigate this kind of substrates further. Thus, starting from aldehyde **123**, easily accessible by oxidation of alcohol **41**, a variety of allylation protocols were tested (Scheme 29, Table 3). With allyl silanes or stannanes the stereochemical outcome correlated with the nature of the Lewis acid, giving the Cram chelate product **124b** with $TiCl_4$, $SnCl_4$, and $MgBr_2{\cdot}Et_2O$ and the Felkin product **124a** with BF_3.[41] In the Brown or Roush allylation adduct **124a** was preferred, and the influence of the chiral ligand was of minor importance.[42] Thus we conclude that substrate control overruled reagent control and the chiral ligands can only modify this basic trend. The relative configuration of **124a**,**b** was verified via the corresponding β-lactones.

Table 3. Allylation of aldehyde **123**.

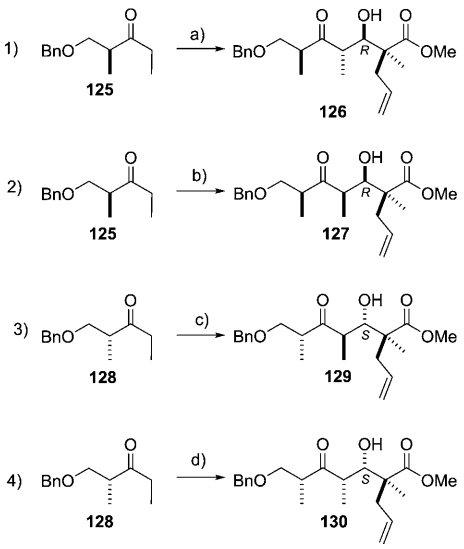
Allyl reagent	LA	Yield [%]	**124a**/**124b**
Brown allylation [(−)-Ipc]		51	3:1
Brown allylation [(+)-Ipc]		quant.	20:1
Roush allylation [L-(+)-DIPT]		69	8:1
Roush allylation [D-(−)-DIPT]		60	20:1
allytrimethylsilane	$BF_3{\cdot}Et_2O$	84	>95:5
allytrimethylsilane	$TiCl_4$	85	<5:95
allytributylstannane	$TiCl_4$	quant.	1:2
allytributylstannane	$MgBr_2{\cdot}Et_2O$	87	1:7



Scheme 29. Allylation of aldehyde **123**.

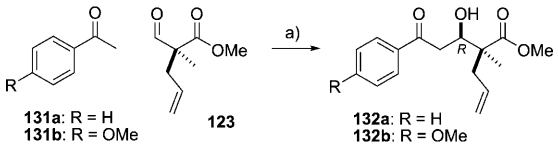
Subjecting aldehyde **123** to the Paterson aldol addition with ketones **125** and **128** (Scheme 30), cases 1) and 2) should represent the matched and 3) and 4) the mismatched combinations, assuming that **123** exerts the same stereochemical influence as in the boron-induced allylation reactions. In fact, cases 1) and 2) gave a 9:1 and 4:1 selectivity, whereas in cases 3) and 4) 1:1 mixtures were observed. This basic trend apparently corroborates our theory, although the configurations of the adducts were not rigorously proven.

Aldol additions with the lithium enolates of methyl ketone **131a** and **131b** always led to the (*R*)-aldol adducts



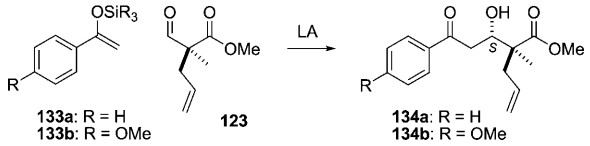
Scheme 30. Paterson aldol additions of aldehyde **123**. a) Cy_2BCl, Et_3N, then **123**, Et_2O, −78 to 0 °C, 87%, 9:1; b) Bu_2BOTf, Et_3N, then **123**, CH_2Cl_2, −78 to 0 °C, 15% (98% b.r.s.m.), 4:1; c) Cy_2BCl,Et_3N, then **123**, Et_2O, −78 to 0 °C, quant., 5:4; d) Bu_2BOTf, Et_3N, then **123**, CH_2Cl_2, −78 to 0 °C, 20% (80% b.r.s.m.), 1:1.

132a and **132b**. No reaction was observed when stronger Lewis acids like $TiCl_4$ were added to the aldehyde beforehand (Scheme 31).



Scheme 31. Aldol additions with lithium enolates to aldehyde **123**. a) LiHMDS, then **123**, THF, −78 °C, 97% **132a**, 72% **132b**.

Under Mukaiyama conditions enol ethers **133a**, **b** and aldehyde **123** formed the (*S*)-aldol adducts **134a** and **134b** in moderate to low yields, but with excellent selectivity (Scheme 32, Table 4). Short reaction times and $TiCl_4$ as the Lewis acid gave the best results.



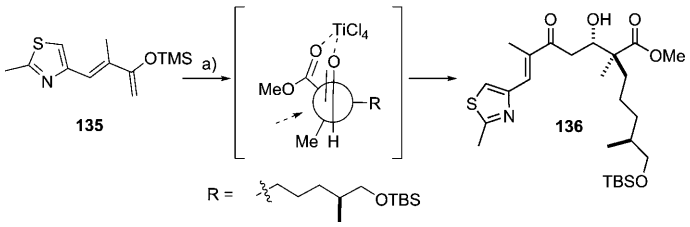
Scheme 32. Mukaiyama aldol addition.

These optimized conditions were applied to the epothilone substrates **135** and **50**. Indeed pure (*S*)-aldol adduct **136** was obtained (Scheme 33), however in too low a yield to make it a synthetically applicable step.

Aldol adducts **132a**, **b** and **134a**, **b** were converted into the δ-lactones via the corresponding *syn*- and *anti*-dihydroxy

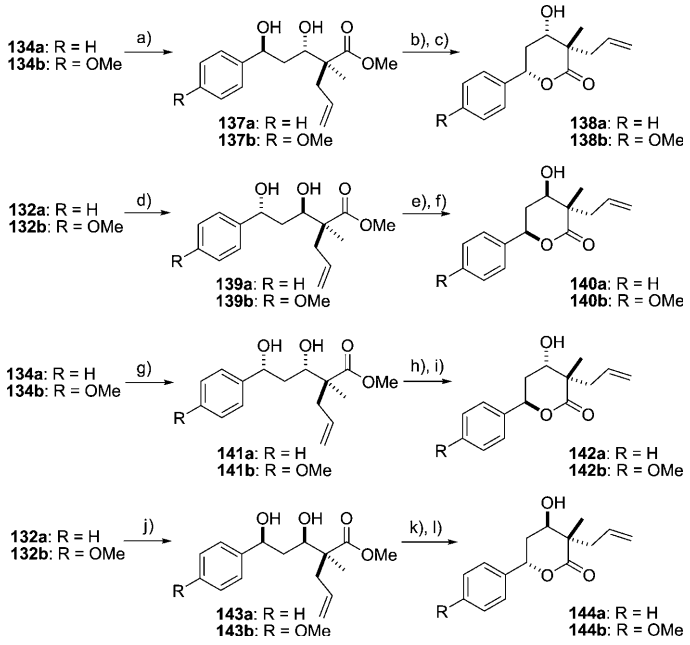
Table 4. Mukaiyama aldol addition.

R	LA	SiR_3	Yield [%]
H	$MgBr_2{\cdot}Et_2O$	TBS	no reaction
H	$TiCl_4$	TBS	35
H	$SnCl_4$	TBS	no reaction
H	$MgBr_2{\cdot}Et_2O$	TMS	no reaction
H	$SnCl_4$	TMS	no reaction
H	$TiCl_4$	TMS	42 (1 h), 34 (2.5 h)
OMe	$TiCl_4$	TMS	59

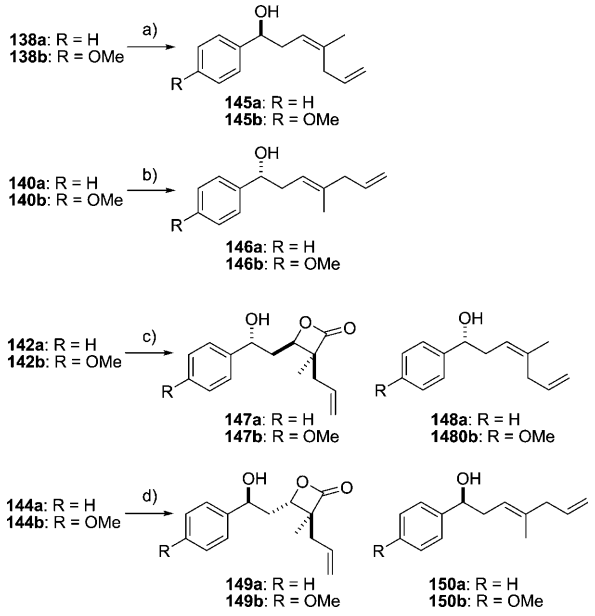


Scheme 33. Mukaiyama aldol additions of aldehyde **50**. a) **50**, $TiCl_4$, then **135**, CH_2Cl_2, −78 °C, 23 %.

esters (Scheme 34). Besides serving for configurational assignments; the lactones were employed in the established fragmentation protocol (Scheme 35).



Scheme 34. Synthesis of the δ-lactones. a) $Me_4NBH(OAc)_3$, CH_3CN/AcOH, −30 °C, 75 % **137a**, 63 % **137b**; b) LiOH, THF, 0 °C; c) EDC·HCl, DMAP, CH_2Cl_2, 75 % **138a**, 56 % **138b** (2 steps); d) $Me_4NBH(OAc)_3$, CH_3CN/AcOH, −30 °C, 95 % **139a**, 85 % **139b**; e) LiOH, THF, 0 °C; f) EDC·HCl, DMAP, CH_2Cl_2, 82 % **140a**, 91 % **140b** (2 steps); g) catecholborane, THF, −15 °C, 89 % **141a**, 88 % **141b**; h) LiOH, THF, 0 °C; i) EDC·HCl, DMAP, CH_2Cl_2, 62 % **142a**, 72 % **142b** (2 steps); j) catecholborane, THF, −15 °C, 89 % **143a**, 88 % **143b**; k) LiOH, THF, 0 °C; l) EDC·HCl, DMAP, CH_2Cl_2, 81 % **144a**, 77 % **144b** (2 steps).



Scheme 35. Fragmentations. a) i) MsCl, Et_3N, Et_2O, 0 °C; ii) LiOH, THF, 0 °C, 87 % **145a**, 74 % **145b** (2 steps); b) i) MsCl, Et_3N, Et_2O, 0 °C; ii) LiOH, THF, 0 °C, 36 % **146a**, 50 % **146b** (2 steps); c) i) MsCl, Et_3N, Et_2O, 0 °C; ii) LiOH, THF, 0 °C, 31 % **147a**, 27 % **147b**, 50 % **148a**, 28 % **148b** (2 steps); d) i) MsCl, Et_3N, Et_2O, 0 °C; ii) LiOH, THF, 0 °C, 25 % **149a**, 30 % **149b**, 9 % **150a**, 29 % **150b** (2 steps).

The *δ*-lactones **138** and **140**, derived from the *anti*-diols, fulfill all stereochemical requirements for the fragmentation via the chair transition state and thus gave only the olefins. In contrast, the *δ*-lactones **142** and **144**, derived from the *syn*-diols would bear the leaving group in axial position and thus make fragmentation via the chair transition state impossible. Indeed, they react presumably via the carboxylate, and both olefin and β-lactone are obtained.

Conclusions

In conclusion, we have shown that decarboxylative Grob fragmentation is an efficient and versatile tool for the stereoselective preparation of chirally substituted (*Z*)-trisubstituted olefins as demonstrated by the formal synthesis of epothilone D (**1**), discodermolide (**3**), and peloruside A (**2**). The synthesis starts from chiral aldehydes such as **50**, **75**, and **116**, and uses their stereogenic information for the construction of additional chiral centers on the chain. Fragmentation primarily proceeds via the chair transition state, but also acyclic fragmentation leads to olefinic products. The olefin geometry is determined by the relative configuration between the α- and β-centers and can thus be controlled by the synthesis of the fragmentation precursor. Further advantages of the approach lie in its high overall yield, stereocontrol, mild conditions and simple reagents. The method also implies high connectivity and is compatible with aldol reactions. Most steps of the sequence are rapidly performed and the intermediates do not require purification. Additionally,

we were able to show that aldehydes with stereogenic quaternary α-centers exhibit a strong substrate control on carbonyl additions.

Experimental Section

All reactions were carried out in oven-dried glassware under an argon atmosphere, unless otherwise stated. Anhydrous acetonitrile was distilled from CaH_2. Anhydrous CH_2Cl_2 (DCM) was distilled over phosphorpentoxide under argon. Anhydrous THF (tetrahydrofuran) was purchased (99.85%, water <50 ppm). Anhydrous diethyl ether was refluxed over sodium/benzophenone ketyl. Triethylamine, diisopropylamine and 2,6-lutidine were distilled from CaH_2. Hexane and ethyl acetate for chromatography were purified by distillation using a column. All other solvents were HPLC grade. Reactions were magnetically stirred and monitored by thin layer chromatography (TLC) with Merck silica gel 60-F254 plates. Flash column chromatography was performed with Merck silica gel (0.04–0.063 mm, 240–400 mesh) under pressure. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated. NMR spectra were recorded on either a Bruker Avance DRX 400 or 600 MHz spectrometer. Unless otherwise stated, all NMR spectra were measured in $CDCl_3$ solutions and referenced to the residual $CHCl_3$ signal (^{1}H, δ=7.26 ppm, ^{13}C, δ=77.00 ppm). All ^{1}H and ^{13}C shifts are given in ppm (s=singlet, d=doublet, t=triplet, q=quadruplet, m=multiplet, b=broad signal). Assignments of proton resonances were confirmed, when possible, by correlated spectroscopy. IR spectra were recorded as thin film on a silicon plate with a Perkin–Elmer 1600 FT-IR spectrometer. Optical rotations were measured on a P 341 Perkin–Elmer polarimeter at 20°C. High-resolution mass spectra (HRMS) were performed with a Finnigan MAT 8230 with a resolution of 10000. Compound names were generated using AutoNom. The Supporting Information of this paper includes experimental details for compounds **14**–**18, 24**, **26**, **28**, **29**, **39–42**, **45–52**, **80**, **81**, **99–105**, **123**, **124**, **132–150** and NMR spectra of all new compounds.

6-[(2*S*,3*S*)-2-Hydroxy-3-(4-methoxybenzyloxy)butyl]-2,2,5-trimethyl-[1,3]dioxin-4-one (22): Aldehyde **19** (800 mg, 4 mmol) in DCM (12 mL) under argon at −10°C was incubated with $MgBr_2{\cdot}Et_2O$ (2.1 g, 8 mmol) for 30 min. Silyl enol ether **21** (1420 mg, 6 mmol) in DCM (5 mL) was added and stirring continued for 1 h. A saturated NH_4Cl solution was added, layers were separated and the aqueous layer extracted with DCM. The combined DCM layers were dried over $MgSO_4$ and solvent removed under reduced pressure. Column chromatography (hexane/ethyl acetate=1:1) to yield aldol adduct **22** as pale yellow oil (1.34 mg; 96%). $[\alpha]_D^{20}$=15.8 (c=1.2, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.25 (d, J=8.6 Hz, 2H), 6.89 (d, J=8.8 Hz, 2H), 4.62 (d, J=11.1 Hz, 1H), 4.36 (d, J=11.1 Hz, 1H), 3.81 (s, 3H), 3.75–3.70 (m, 1H), 3.43 (dt, J=11.6, 6.2 Hz, 1H), 2. 53 (dd, J=14.2, 6.2 Hz, 1H), 2.44 (m, 1H), 2.35 (dd, J=14.3, 9.1 Hz, 1H), 1.84 (s, 3H), 1.64 (s, 3H), 1.63 (s, 3H), 1.24 ppm (d, J=6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=162.9, 159.4, 129.9, 113.9, 104.9, 102.3, 76.8, 72.5, 70.7, 55.3, 34.9, 25.8, 24.4, 15.5, 10.3 ppm; IR (film): $\tilde{\nu}$= 3468, 2936, 1721, 1647, 1514, 1248 cm^{-1}.HRMS (ESI): m/z: $[M]^+$ calcd for $C_{19}H_{26}O_6$: 350.1729, found: 350.1737.

(*S*)-6-[(*S*)-1-(4-Methoxybenzyloxy)ethyl]-3-methyldihydropyran-2,4-dione (23): To a solution of lactone **22** (650 mg, 1.85 mmol) in methanol (12 mL) was added K_2CO_3 (385 mg, 2.78 mmol) and the mixture was stirred overnight. The solvent was evaporated and ice and 2N HCl was added to the residue. The acidic layer was extracted with Et_2O repeatedly and the combined ethereal phases dried over $MgSO_4$. After removal of the solvent under reduced pressure lactone **23** (550 mg; quant.) was isolated as a yellow solid and used without further purification. $[\alpha]_D^{20}$=−29.5 (c=0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.23 (d, J=8.6 Hz, 2H), 6.88 (d, J=8.6 Hz, 2H), 4.64 (dt, J=8.8, 4.0 Hz, 1H), 4.58 (d, J=11.4 Hz, 1H), 4.42 (d, J=11.4 Hz, 1H), 3.80 (s, 3H), 3.70 (ddd, J=12.7, 6.4, 3.8 Hz, 1H), 3.41 (q, J=6.6 Hz, 1H), 2.72 (dd, J=18.0, 4.2 Hz, 1H), 2.60 (dd, J=18.0, 8.9 Hz, 1H), 1.31 (d, J=6.8 Hz, 3H), 1.29 ppm (d, J=6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=200.8, 169.7, 159.0, 129.8, 129.4, 113.9, 76.5, 73.8, 71.1, 55.3, 51.5, 39.4, 14.9, 8.3 ppm; IR (film): $\tilde{\nu}$= 2926, 1726, 1654, 1613, 1513, 1400, 1248, 1115 cm^{-1}. HRMS (ESI): m/z: $[M]^+$ calcd for $C_{16}H_{20}O_5$: 292.1311, found: 292.1307.

Carbonic acid (*E*)-(*S*)-5-(*tert*-butyldimethylsilanyloxy)-4-methylpent-2-enyl ester ethyl ester (30): To stirred solution of alcohol **29** (150 mg, 0.64 mmol) in pyridine (5 mL) was added ethyl chloroformate (73 μL, 0.76 mmol). The mixture was stirred at room temperature for 20 min, then quenched with brine and layers were separated. The aqueous phase was extracted with Et_2O, the combined organic solutions were washed with water, dried over $MgSO_4$, and the solvent was evaporated. Purification by column chromatography (hexane/ethyl acetate=10:1) yielded ethyl carbonate **30** (170 mg; 88%). $[\alpha]_D^{20}$=−9.2 (c=1.25, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.76 (d, J=15.5, 6.9 Hz, 1H), 5.61 (dtd, J=15.6, 6.4, 1.1 Hz, 1H), 4.57 (d, J=6.3 Hz, 2H), 4.19 (q. J=7.2 Hz, 2H), 3.49 (dd, J=9.9 6.3 Hz, 1H), 3.41 (dd, Hz, J=9.9,6.8 Hz, 1H), 2.35 (m, 1H), 1.30 (t, J=7.2 Hz, 3H), 1.00 (d, J=6.6 Hz, 3H), 0.88 (s, 9H), 0.03 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=155.0, 139.3, 123.0, 68.5, 67.6, 63.9, 39.0, 25.9, 18.3, 16.1, 14.3, −5.4 ppm; IR (film): $\tilde{\nu}$= 2956, 2930, 2857, 1747, 1258, 1105 cm^{-1}; HRMS (ESI): m/z: $[M+Na]^+$ calcd for $C_{15}H_{30}O_4SiNa$: 325.1811, found: 325.1817.

(3*S*,6*S*)-3-[(*E*)-(*S*)-5-(*tert*-Butyldimethylsilanyloxy)-4-methylpent-2-enyl]-6-[(*S*)-1-(4-methoxybenzyloxy)ethyl]-3-methyldihydropyran-2,4-dione (31): To $[Pd(PPh_3)_4]$ (87 mg, 0.075 mmol) and benzyltriethylammonium chloride (34 mg, 0.15 mmol) in degassed water (4 mL) at 0°C was added carbonate **30** (453 mg, 1.5 mmol) in ethyl acetate (3 mL) and the mixture was stirred for 15 min. A degassed suspension of **23** (650 mg, 1.8 mmol) in ethyl acetate (3 mL) was added and stirring was continued for 15 min before K_2CO_3 (270 mg, 1.95 mmol) in degassed water (2 mL) was added. After stirring for 3 h, the reaction mixture was quenched with saturated NH_4Cl solution, and phases were separated. The aqueous phase was extracted with DCM and the combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. The residue was purified by column chromatography (hexane/ethyl acetate=3:1) to afford **31** (730 mg; 97%) as a 3:1 mixture as a pale yellow oil. Minor (**31b**: $[\alpha]_D^{20}$= 38.31 (c=0.95, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.18 (d, J=8.6 Hz, 2H), 6.86 (d, J=8,6 Hz, 2H), 5.43 (dd, J=15.5, 6.9 Hz, 1H), 5.28 (dt, J=15.3, 7.5 Hz, 1H), 4.48 (d, J=11.3 Hz, 1H), 4.44 (m, 1H), 4.31 (d, J=11.6 Hz, 1H), 3.80 (s, 3H), 3.48 (m, 1H), 3.44 (dd, J=9.8, 6.1 Hz, 1H), 3.35 (dd, J=9.7, 6.9 Hz, 1H), 2.78 (dd, J=16.0, 6.2 Hz, 1H), 2.50 (dd, J=16.2, 4.5 Hz, 1H), 2.49 (m, 1H), 2.39 (dd, J=13.5, 8.2 Hz, 1H), 2.26 (m, 1H), 1.28 (d, J=6.3 Hz, 3H), 1.26 (s, 3H), 0.94 (d, J=6.8 Hz, 3H), 0.87 (s, 9H), 0.01 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ= 204.5, 174.3, 159.5, 138.7, 130.2, 128.8, 123.0, 113.8, 76.8, 74.4, 70.5, 67.8, 57.9, 55.2, 43.6, 40.6, 39.2, 25.9, 20.3, 18.3, 16.6, 15.2, −5.3, −5.4 ppm; IR (film): $\tilde{\nu}$= 2955, 2930, 1716, 1613, 1514, 1250, 1082 cm^{-1}. HRMS (ESI): m/z: $[M-C_4H_9]^+$ calcd for $C_{24}H_{35}O_6Si$: 447.2203, found: 447.2210. Major (**31a**: $[\alpha]_D^{20}$=−35.33 (c=0.3, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ= 7.23 (d, J=8.6 Hz, 2H), 6.87 (d, J=8.6 Hz, 2H), 5.44 (dd, J=15.4, 7.0 Hz, 1H), 5.32 (dt, J=14.7, 7.4 Hz, 1H), 4.58 (d, J=11.6 Hz, 1H), 4.43 (d, J=11.6 Hz, 1H), 4.42 (m, 1H), 3.80 (s, 3H), 3.69 (dd, J=6.3, 3.4 Hz, 1H), 3.66 (dd, J=6.3, 3.8 Hz, 1H), 3.43 (dd, J=9.7, 5.9 Hz, 1H), 3.31 (dd, J=9.7, 7.2 Hz, 1H), 2.68 (dd, J=15.9, 3.3 Hz, 1H), 2.64 (dd, J=13.2, 6.6 Hz, 1H), 2.49 (dd, J=15.9, 10.9 Hz, 1H), 2,45 (dd, J=13.1, 8.0 Hz, 1H), 2.22 (m, 1H), 1.37 (s, 3H), 1.26 (d, J=6.3 Hz, 3H), 0.92 (d, J=6.6 Hz, 3H), 0.87 (s, 9H), 0.01 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=206.2, 173.4, 159.4, 138.5, 129.6, 129.5, 123.3, 113.9, 75.6, 73.8, 71.0, 67.9, 56.7, 55.3, 40.7, 40.6, 39.3, 25.9, 23.0, 18.3, 16.6, 14.5, −5.3, −5.4 ppm; IR (film): $\tilde{\nu}$=2955, 2930, 1717, 1635, 1615, 1250 cm^{-1}; HRMS (ESI): m/z: $[M-C_4H_9]^+$ calcd for $C_{24}H_{35}O_6Si$: 447.2203, found: 447.2212.

(3*S*,4*S*,6*S*)-3-[(*E*)-(*S*)-5-(*tert*-Butyldimethylsilanyloxy)-4-methylpent-2-enyl]-4-hydroxy-6-[(*S*)-1-(4-methoxybenzyloxy)ethyl]-3-methyltetrahydropyran-2-one (32): To β-keto lactone **31** (220 mg, 0.44 mmol) in methanol (9 mL) at 0°C was added $NaBH_4$ (17 mg, 0.44 mmol) and the solution was stirred for 1.5 h. The reaction mixture was quenched with saturated NH_4Cl solution, the organic layer was separated, and the aqueous layer was extracted with DCM. The combined organic solutions were dried over $MgSO_4$ and the solvent was evaporated. Purification by column chromatography (hexane/ethyl acetate=3:1) yielded the reduction prod-

uct **32** (218 mg; 98%). $[\alpha]_D^{20}=23.41$ ($c=0.85$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.26$ (d, $J=8.6$ Hz, 2H), 6.87 (d, $J=8.6$ Hz, 2H), 5.47 (m, 2H), 4.63 (d, $J=11.4$ Hz, 1H), 4.43 (d, $J=11.4$ Hz, 1H), 4.42 (m, 1H), 3.82 (m, 1H), 3.80 (s, 3H), 3.56 (ddd, $J=12.6$, 6.3, 3.3 Hz, 1H), 3.46 (dd, $J=9.6$, 6.3 Hz, 1H), 3.39 (dd, $J=9.8$, 6.8 Hz, 1H), 2.55 (dd, $J=13.6$, 5.8 Hz, 1H), 2.40 (dd, $J=13.9$, 6.1 Hz, 1H), 2.29 (m,1H), 2.16 (ddd, $J=14.2$, 7.1, 4.3 Hz, 1H), 1.98 (dt, $J=14.1$, 7.1 Hz, 1H), 1.20 (d, $J=6.6$ Hz, 3H), 1.20 (s, 3H), 0.96 (d, $J=6.8$ Hz, 3H), 0.88 (s, 9H), 0.02 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=175.2$, 159.4, 137.4, 129.7, 129.4, 129.2, 124.7, 113.9, 78.3, 75.0, 70.8, 70.4, 68.0, 55.2, 47.1, 39.4, 37.4, 28.9, 25.9, 21.0, 18.3, 16.6, 14.6, −5.3, −5.4 ppm; IR (film): $\tilde{\nu}=$ 3435, 2956, 2856, 1732, 1514, 1463, 1250, 1089, 1036 cm^{-1}; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{28}H_{46}O_6$: 506.3069, found: 506.3055.

(3*S*,4*S*,6*S*)-3-[(*S*)-5-(*tert*-Butyldimethylsilanyloxy)-4-methylpentyl]-4-hydroxy-6-[(*S*)-1-(4-methoxybenzyloxy)ethyl]-3-methyltetrahydropyran-2-one (33): To β-hydroxyl lactone **32** (350 mg, 0.65 mmol) in ethyl acetate (6 mL) was added PtO_2 (12 mg, 0.07 mmol) and the resulting suspension was stirred under an atmosphere of hydrogen. After 1.5 h the reaction mixture was filtered through Celite and the filtrate was evaporated to yield **33** (350 mg; quant.) as a colorless oil. Separation by column chromatography (hexane/ethyl acetate = 10:1) yielded diastereoisomer **33** (245 mg; 70%). $[\alpha]_D^{20}=24$ ($c=0.4$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.26$ (d, $J=8.8$ Hz, 2H), 6.87 (d, $J=8.8$ Hz, 2H), 4.63 (d, $J=11.6$ Hz, 1H), 4.42 (d, $J=11.6$ Hz, 1H), 4.39 (m, 1H), 3.86 (ddd, $J=6.9$, 6.7, 4.3 Hz, 1H), 3.80 (s, 3H), 3.56 (ddd, $J=12.6$, 6.4, 3.2 Hz, 1H), 3.42 (dd, $J=9.8$, 5.8 Hz, 1H), 3.34 (dd, $J=9.8$, 6.6 Hz, 1H), 2.83 (d, $J=6.4$ Hz, 1H), 2.14 (ddd, $J=14.1$, 6.7, 4,2 Hz, 1H), 2.01 (dt, $J=14.2$, 7.6 Hz, 1H), 1.75–1.67 (m, 2H), 1.59 (m, 1H), 1.33–1.28 (m, 2H), 1.31 (d, $J=6.4$ Hz, 3H), 1.25 (s, 3H), 1.05 (m, 1H), 0,84 (d, $J=6.8$ Hz, 3H), 0.88 (s, 9H), 0.03 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=175.3$, 159.4, 129.7, 129.5, 113.9, 78.1, 74.9, 70.8, 70.7, 68.4, 55.3, 47.0, 35.6, 33.7, 33.1, 28.6, 25.9, 21.1, 18.3, 16.7, 14.6, −5.4 ppm; IR (film): $\tilde{\nu}=$ 2953, 1732, 1514, 1463, 1250, 1092 cm^{-1}; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{28}H_{48}O_6Si$: 508.3220, found:508.3224.

(*Z*)-(2*S*,3*S*,10*S*)-11-(*tert*-Butyldimethylsilanyloxy)-2-(4-methoxybenzyloxy)-6,10-dimethylundec-5-en-3-ol (34): Alcohol **33** (50 mg, 0.1 mmol) was dissolved in Et_2O (3 mL), Et_3N (0.30 mL) was added at 0°C, and the mixture was stirred for 15 min. Methanesulfonyl chloride (9 μL, 0.11 mmol) was added and stirring was continued. After 1.5 h the reaction mixture was quenched with brine, the organic layer separated, and the aqueous layer was extracted with Et_2O. The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. This yielded 80 mg of the crude mesylate which was used without further purification. To a stirred solution of the crude mesylate (70 mg, 0.1 mmol) in methanol (3 mL) at 0°C was added 1 M KOH (0.2 mL, 0.2 mmol) and the solution was stirred for 2 h. The reaction was quenched with saturated NH_4Cl solution, the organic layer separated, and the aqueous layer extracted with DCM. The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. Purification by column chromatography (hexane/ethyl acetate = 15:1) yielded **34** (42 mg; 91%) as a colorless oil. $[\alpha]_D^{20}=20$ ($c=1.9$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.26$ (d, $J=8.8$ Hz, 2H), 6.88 (d, $J=8.8$ Hz, 2H), 5.21 (t, $J=7.1$ Hz, 1H), 4.59 (d, $J=11.1$ Hz, 1H), 4.38 (d, $J=11.1$ Hz, 1H), 3.80 (s, 3H), 3.46–3.40 (m, 3H), 3.35 (dd, $J=9.8$, 6.6 Hz, 1H), 2.47 (d, $J=3.5$ Hz, 1H), 2.28–2.21 (m, 1H), 2.19–2.11 (m, 1H), 2.00 (t, $J=7.9$ Hz, 2H), 1.70 (d, $J=1.0$ Hz, 3H), 1.61–1.53 (m, 1H), 1.45–1.31 (m, 3H), 1.18 (d, $J=5.8$ Hz, 3H), 1.08–1.01 (m, 1H), 0.90 (s, 9H), 0.86 (d, $J=6.8$ Hz, 3H), 0.03 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=159.3$, 137.9, 130.5, 129.3, 120.5, 113.9, 77.3, 75.1, 70.7, 68.3, 55.3, 35.7, 33.1, 32.2, 25.9, 25.3, 23.5, 18.3, 16.7, 15.7, −5.3 ppm; IR (film): $\tilde{\nu}=$ 2929, 1726, 1514, 1249, 1180, 1093 cm^{-1}; HRMS (ESI): m/z: $[M-C_4H_9]^+$ calcd for $C_{23}H_{39}O_4Si$: 407.2617, found: 407.2610.

1-[(*Z*)-(1*S*,2*S*,9*S*)-2,10-Bis-(*tert*-butyldimethylsilanyloxy)-1,5,9-trimethyldec-4-enyloxymethyl]-4-methoxybenzene (35): To a stirred solution of alcohol **34** (150 mg, 0.32 mmol) in DCM (4 mL) was added 2,6-lutidine (58 μL, 0.48 mmol) and TBSOTf (92 μL, 0.38 mmol). After 1 h the reaction was quenched with saturated NH_4Cl solution and extracted with DCM. The combined organic solutions were dried over $MgSO_4$ and the solvent was evaporated. Purification by column chromatography (hexane/ethyl acetate = 20:1) yielded the protected triole **35** (185 mg; quant.) as a colorless oil. $[\alpha]_D^{20}=-2.66$ ($c=1.2$, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.25$ (d, $J=8.5$ Hz, 2H), 6.86 (d, $J=8.5$ Hz, 2H), 5.15 (t, $J=7.3$ Hz, 1H), 4.51 (d, $J=11.6$ Hz, 1H), 4.44 (d, $J=11.6$ Hz, 1H), 3.80 (s, 3H), 3.69–3.65 (m, 1H), 3.47–3,44 (m, 1H), 3.44 (dd, $J=11.9$, 6.1 Hz, 1H), 3.34 (dd, $J=9.7$, 6.7 Hz, 1H), 2.31–2.23 (m, 1H), 2.12–1.93 (m, 3H), 1.67 (s, 3H), 1.61–1.54 (m, 1H), 1.42–1.28 (m, 3H), 1.12 (d, $J=6.32$ Hz, 3H), 1.08–1.00 (m, 1H), 0.89 (s, 9H), 0.86 (s, 9H), 0.86 (d, $J=6.7$ Hz, 3H), 0.03 (s, 6H), 0.00 (s, 3H), −0.02 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=159.1$, 136.5, 131.3, 129.1, 122.3, 113.8, 77.0, 74.4, 70.6, 68.4, 55.3, 35.8, 33.2, 32.3, 29.9, 25.9, 25.8, 25.5, 23.5, 18.1, 16.7, 14.1, −4.5, −4.6 −5.3 ppm; IR (film): $\tilde{\nu}=$2856, 1513, 1472, 1249, 1249, 1093 cm^{-1}; HRMS (ESI): m/z: $[M-C_4H_9]^+$ calcd for $C_{29}H_{53}O_4Si_2$: 521.3482, found: 521.3489.

(*Z*)-(2*S*,3*S*,10*S*)-3,11-Bis-(*tert*-butyldimethylsilanyloxy)-6,10-dimethylundec-5-en-2-ol (36): To a stirred solution of triprotected triol **35** (85 mg, 0.14 mmol) in DCM (2 mL) with water (0.5 mL) was added DDQ (37 mg, 0.16 mmol) in small portions and the mixture was stirred vigorously for 20 min. The reaction was quenched with saturated $NaHCO_3$ solution, the organic layer separated and the aqueous solution extracted with DCM. The combined organic solutions were dried over $MgSO_4$, the solvent was evaporated, and the residue was purified by column chromatography (hexane/ethyl acetate = 20:1) to yield **36** (63 mg; 98%). $[\alpha]_D^{20}=11.8$ ($c=1.05$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=5.13$ (t, $J=7.2$ Hz, 1H), 3.66–3.58 (m, 1H), 3.42 (m, 1H), 3.43 (dd, $J=9.7$, 5.9 Hz, 1H), 3.36 (dd, $J=9.8$, 6.6 Hz, 1H), 2,34–2,27 (m, 1H), 2.17 (d, $J=6.6$ Hz, 1H), 2.17–2.11 (m, 1H), 2,05–1.95 (m, 2H), 1.68 (d, $J=1.0$ Hz, 3H), 1.62–1.54 (m, 1H), 1.45–1,27 (m, 3H), 1.12 (d, $J=6.3$ Hz, 3H), 1.08–1.01 (m, 1H), 0.91 (s, 9H), 0.89 (s, 9H), 0.87 (d, $J=6.8$ Hz, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.03 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=137.7$, 120.3, 76.7, 68.7, 68.3, 35.7, 33.2, 32.4, 32.2, 25.9, 25.8, 25.4, 23.5, 19.9, 18.1, 16.7, −4.1, −4.7, −5.3 ppm; IR (film): $\tilde{\nu}=$ 2929, 2857, 1472, 1256, 1094 cm^{-1}; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{25}H_{54}O_3Si_2$: 458.3612, found: 458.3618.

(*Z*)-(3*S*,10*S*)-3,11-Bis-(*tert*-butyldimethylsilanyloxy)-6,10-dimethylundec-5-en-2-one (37): To a stirred solution of alcohol **36** (40 mg, 0.087 mmol) in DCM (2 mL) was added DMP (74 mg, 0.17 mmol) and the suspension was stirred for 1.5 h. The reaction was quenched with saturated $NaHCO_3$ solution, the organic layer was separated, and the aqueous layer was extracted with DCM. The combined organic solutions were dried over $MgSO_4$, the solvent was evaporated, and the residue was purified by column chromatography (hexane/ethyl acetate = 20:1) to yield ketone **37** (39 mg; quant.). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=5.11$ (t, $J=7.3$ Hz, 1H), 3.97 (dd, $J=6.8$, 5.6 Hz, 1H), 3.43 (dd, $J=9.8$, 5.8 Hz, 1H), 3.35 (dd, $J=9.7$, 6.4 Hz, 1H), 2.38–2.22 (m, 2H), 2.15 (s, 3H), 2.04–1.91 (m, 2H), 1.68 (d, $J=1.0$ Hz, 3H), 1.61–1.53 (m, 1H), 1.39–1.27 (m, 3H), 1.08–1.00 (m, 1H), 0.91 (s, 9H), 0.89 (s, 9H), 0.86 (d, $J=6.6$ Hz, 3H), 0.05 (s, 3H), 0.04 (s, 3H), 0.03 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=212.0$, 138.6, 119.0, 79.2, 68.3, 35.7, 33.4, 33.1, 32.2, 25.9, 25.7, 25.4, 25.3, 23.5, 16.7, 14.1, −4.9, −5.0, −5.3 ; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{25}H_{52}O_3Si_2$: 456.3455, found: 456.3461.

4-[(1*E*,5*Z*)-(3*S*,10*S*)-3,11-Bis-(*tert*-butyldimethylsilanyloxy)-2,6,10-trimethylundeca-1,5-dienyl]-2-methylthiazole (38): To a stirred solution of (2-methyl-thiazol-4-yl)methyltributylphosphonium chloride (115 mg, 0.33 mmol) in THF (1 mL) at 0°C was added *n*BuLi (130 μL, 2.5 M in hexane, 0.33 mmol) to form a bright red solution, which was stirred for 1 h. The mixture was cooled to −78°C and ketone **37** (15 mg, 0.033 mmol) in THF (0.50 mmol) was added. The cooling bath was removed and the mixture stirred at 60°C for 1.5 h. After cooling down to room temperature, the reaction was quenched with saturated NH_4Cl solution, the organic layer separated and the aqueous layer was extracted with Et_2O. The combined organic solutions were dried over $MgSO_4$ and the solvent was evaporated. The crude product was purified by column chromatography (hexane/ethyl acetate = 20:1) to yield northern fragment **38** (17 mg; 93%). $[\alpha]_D^{20}=2.1$ ($c=0.7$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=6.91$ (s, 1H), 6.45 (s, 1H), 5.13 (t, $J=6.8$ Hz, 1H), 4.08 (t, $J=6.4$ Hz, 1H), 3.44 (dd, $J=9.8$, 5.8 Hz, 1H), 3.34 (dd, $J=9.8$, 6.6 Hz, 1H), 2.71 (s, 3H), 2.29–2.20 (m, 2H), 2.05–1.94 (m, 2H), 2.00 (d, $J=1.3$ Hz,

3H), 1.66 (d, $J=1.3$ Hz, 3H), 1.61–1.53 (m, 1H), 1.45–1.28 (m, 3H), 1.08–1.00 (m, 1H), 0.89 (s, 18H), 0.86 (d, $J=6.6$ Hz, 3H), 0.05 (s, 3H), 0.03 (s, 6H), 0.00 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=164.3$, 153.3, 142.6, 136.9, 121.4, 118.7, 114.9, 79.1, 68.4, 35.8, 35.3, 33.2, 32.3, 25.9, 25.8, 25.4, 23.5, 19.2, 16.7, 13.9, −4.6, −4.9, −5.3 ppm; IR (film): $\tilde{\nu}=$ 2929, 1472, 1257, 1090 cm^{-1}; HRMS (ESI): *m/z*: $[M]^+$ calcd for $C_{30}H_{57}O_2Si_2NS$: 551.3849, found: 551.3635.

(*E*)-(2*S*,3*R*)-2-[(*S*)-5-(*tert*-Butyldimethylsilanyloxy)-4-methylpentyl]-3-hydroxy-2,6-dimethyl-7-(2-methylthiazol-4-yl)-5-oxo-hept-6-enoic acid methyl ester (53): LiHMDS (0.66 mL, 1 M in THF, 0.66 mmol) was added to methyl ketone 52 (120 mg, 0.66 mmol) in THF (8 mL) at −78 °C under argon. After 1 h a solution of aldehyde **50** (219 mg, 0.66 mmol) premixed with $MgBr_2{\cdot}Et_2O$ (342 mg, 1.32 mmol) in THF (6 mL) at 0 °C for 1 h was slowly added by using a canula. After 3.5 h a saturated NH_4Cl solution was added and the aqueous phase was extracted with DCM. The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. Column chromatography (hexane/ethyl acetate = 3:1) yielded the aldol adduct **53** (312 mg; 92 %) as a colorless oil. $[\alpha]_D^{20}=26.15$ ($c=1.3$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.51$ (s, 1H), 7.38 (s, 1H), 4.34–4.30 (m, 1H), 3.69 (s, 3H), 3.42 (dd, $J=9.9$, 5.8 Hz, 1H), 3.35 (dd, $J=9.9$, 6.6 Hz, 1H), 3.33 (d, $J=3.5$ Hz, 1H), 2.92–2.89 (m, 2H), 2.75 (s, 3H), 2.23 (d, $J=1.00$ Hz, 3H), 1.84–1.77 (m, 1H), 1.60–1.50 (m, 2H), 1.42–1.32 (m, 2H), 1.23–1.17 (m, 1H), 1.20 (s, 3H), 1.08–1.02 (m, 1H), 0.89 (s, 9H), 0.85 (d, $J=6.6$ Hz, 3H), 0.03 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=202.6$, 176.3, 165.5, 151.6, 137.2, 131.2, 121.9, 71.6, 68.3, 51.7, 50.4, 39.8, 36.9, 35.5, 33.5, 25.9, 21.9, 19.3, 18.4, 16.6, 16.5, 13.2, −5.4 ppm; IR (film): $\tilde{\nu}=$ 3436, 2953, 1722, 1652, 1628, 1250, 1087 cm^{-1}. HRMS (ESI): *m/z*: $[M]^+$ calcd for $C_{26}H_{45}O_5NSSi$: 511.2788, found: 511.2776.

(*E*)-(2*S*,3*R*,5*R*)-2-[(*S*)-5-(*tert*-Butyldimethylsilanyloxy)-4-methylpentyl]-3,5-dihydroxy-2,6-dimethyl-7-(2-methylthiazol-4-yl)-hept-6-enoic acid methyl ester (55): To a solution of **53** (950 mg, 1.90 mmol) in THF (20 mL) at −10 °C under argon was added catecholborane (0.99 mL, 9.5 mmol) and stirred for 5 h. A saturated solution of potassium-sodium-tartrate was added and the mixture was stirred for 1 h. The layers were separated and the aqueous layer was extracted with DCM. The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. Column chromatography (hexane/ethyl acetate = 1:1) yielded dihydroxy ester **55** (835 mg; 88 %) as a colorless oil. $[\alpha]_D^{20}=-0.4$ ($c=0.5$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=6.97$ (s, 1H), 6.60 (s, 1H), 4.40 (dd, $J=9.2$, 2.9 Hz, 1H), 4.02 (dd, $J=9.9$, 1.6 Hz, 1H), 3.68 (s, 3H), 3.41 (dd, $J=9.9$, 5.8 Hz, 1H), 3.34 (dd, $J=9.7$, 6.4 Hz, 1H), 2.75 (s, 3H), 2.01 (d, $J=1.0$ Hz, 3H), 1.80–1.66 (m, 2H), 1.63–1.52 (m, 2H), 1.50–1.43 (m, 1H), 1.39–1.20 (m, 3H), 1.15 (s, 3H), 1.07–0.97 (m, 1H), 0.88 (s, 9H), 0.84 (d, $J=6.6$ Hz, 3H), 0.03 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=176.9$, 165.3, 151.8, 142.8, 118.1, 115.7, 78.3, 76.3, 68.4, 51.8, 50.9, 36.9, 36.1, 35.5, 33.6, 25.9, 22.0, 18.8, 18.4, 16.9, 16.6, 14.4, −5.4 ppm; IR (film): $\tilde{\nu}=$ 2952, 1731, 1090, 837 cm^{-1}; HRMS (ESI): *m/z*: $[M]^+$ calcd for $C_{26}H_{47}O_5NSSi$: 513.2945, found: 513.2936.

(3*S*,4*R*,6*S*)-3-[(*S*)-5-(*tert*-Butyldimethylsilanyloxy)-4-methylpentyl]-4-hydroxy-3-methyl-6-[(*E*)-1-methyl-2-(2-methylthiazol-4-yl)-vinyl]tetrahydropyran-2-one (56): LiOH (2.4 mL, 1 M in water, 2.4 mmol) was added to ester **55** (400 mg, 0.78 mmol) in THF (10 mL) at 0 °C and the mixture was stirred vigorously for 4 h. Brine was added and the aqueous layer was acidified with 1N HCl and extracted with DCM. The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. The residue was dissolved in DCM (8 mL) and EDC·HCl (227 mg, 1.17 mmol) and DMAP (190 mg, 1.56 mmol) were added. After 4 h brine was added and the aqueous layer was extracted with DCM. The combined DCM phases were dried over $MgSO_4$ and the solvent was evaporated. Column chromatography yielded lactone **56** (350 mg; 94 %) as a colorless oil. $[\alpha]_D^{20}=-0.54$ ($c=1.4$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=6.99$ (s, 1H), 6.56 (s, 1H), 5.21 (dd, $J=10.9$, 3.9 Hz, 1H), 4.01 (dd, $J=4.5$, 2.0 Hz, 1H), 3.40 (dd, $J=9.9$, 6.2 Hz, 1H), 3.36 (dd, $J=9.9$, 6.2 Hz, 1H), 2.73 (s, 3H), 2.27 (ddd, $J=14.1$, 11.1, 2.0 Hz, 1H) 2.11 (d, $J=0.9$ Hz, 3H), 2.04 (dt, $J=14.3$, 4.5 Hz, 1H), 1.68–1.50 (m, 3H), 1.43–1.25 (m, 3H), 1.34 (s, 3H), 1.09–0.99 (m, 1H), 0.88 (s, 9H), 0.84 (d, $J=6.6$ Hz, 3H), 0,02 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=176.1$, 165.0, 152.1, 137.3, 119.9, 116.7, 80.6, 70.4, 68.2, 47.1, 38.7, 35.5, 33.5, 31.4, 25.9, 21.4, 19.2, 19.1, 18.3, 16.6, 14.4, −5.4 ppm; IR (film): $\tilde{\nu}=$ 2952, 1710, 1250, 1086 cm^{-1}; HRMS (ESI): *m/z*: $[M]^+$ calcd for $C_{25}H_{43}O_4NSSi$: 481.2682, found: 481.2669.

(3*S*,4*S*,6*S*)-3-[(*S*)-5-(*tert*-Butyl-dimethylsilanyloxy)-4-methylpentyl]-4-hydroxy-3-methyl-6-[(*E*)-1-methyl-2-(2-methylthiazol-4-yl)vinyl]tetrahydropyran-2-one (10): Dess–Martin-periodinane (229 mg, 0.54 mmol) was added portionwise to a suspension of alcohol **56** (90 mg, 0.18 mmol) and $NaHCO_3$ (45 mg, 0.54 mmol) in DCM (3 mL) at 0 °C under argon. After 4 h water was added, the layers were separated and the aqueous layer was extracted with DCM. The combined DCM phases were dried over $MgSO_4$ and the solvent was evaporated. Column chromatography (hexane/ethyl acetate = 3:1) yielded the ketone (85 mg; 94 %) as colorless oil. $[\alpha]_D^{20}=-23.4$ ($c=1.0$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.04$ (s, 1H), 6.61 (s, 1H), 4.97 (dd, $J=11.9$, 2.3 Hz, 1H), 3.37 (dd, $J=9.8$, 6.0 Hz, 1H), 3.33 (dd, $J=9.8$, 6.0 Hz, 1H), 2.83 (dd, $J=16.3$, 2.7 Hz, 1H), 2.75–2.68 (m, 1H), 2.71 (s, 3H), 2.17 (d, $J=1.0$ Hz, 3H), 2.01–1.81 (m, 2H), 1.57–1.49 (m, 1H), 1.46 (s, 1H), 1.40–1.17 (m, 3H), 1.07–1.00 (m, 1H), 0.88 (s, 9H), 0.81 (d, $J=6.84$ Hz, 3H), 0.02 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=206.6$, 173.6, 165.1, 151.7, 134.2, 122.0, 117.7, 78.2, 68.2, 56.4, 44.2, 38.4, 35.3, 33.3, 25.9, 23.6, 22.9, 19.3, 18.3, 16.5, 13.9, −5.4 ppm; IR (film): $\tilde{\nu}=$ 2928, 1751, 1718, 1257, 1140, 1093 cm^{-1}. HRMS (ESI): *m/z*: $[M-C_4H_9]^+$ calcd for $C_{21}H_{32}O_4NSSi$: 422.1821, found: 422.1833. Sodium borohydride (13 mg, 0.3 mmol) was added to the keto lactone (150 mg, 0.3 mmol) in methanol (4 mL) at −78 °C. After 5 h brine was added, the mixture was warmed to room temperature and extracted with DCM. The combined DCM layers were dried over $MgSO_4$ and the solvent was evaporated. Column chromatography (hexane/ethyl acetate = 1:1) yielded lactone **10** (140 mg, 93 %) as a colorless oil. $[\alpha]_D^{20}=-11.45$ ($c=2$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.00$ (s, 1H), 6.55 (s, 1H), 4.75 (dd, $J=11.3$, 4.1 Hz, 1H), 4.02 (dd, $J=11.3$, 4.1 Hz, 1H), 3.42 (dd, $J=9.7$, 5.9 Hz, 1H), 3.36 (dd, $J=9.7$, 6.4 Hz, 1H), 2.71 (s, 3H), 2.27–2.18 (m, 1H) 2.10 (d, $J=1.0$ Hz, 3H), 2.13–2.06(m, 1H), 1.75–1.55 (m, 3H), 1.48–1.26 (m, 3H), 1.37 (s, 3H), 1.11–1.01 (m, 1H), 0.88 (s, 9H), 0.86 (d, $J=6.8$ Hz, 3H), 0.03 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=175.3$, 165.0, 152.0, 136.5, 120.6, 116.9, 81.2, 72.5, 68.3, 47.7, 35.6, 33.7, 33.0, 32.7, 25.9, 21.8, 20.9, 19.2, 18.3, 16.6, 14.0, −5.4 ppm; IR (film): $\tilde{\nu}=$ 3420, 2954, 1727, 1250, 1127, 1078 cm^{-1}; HRMS (ESI): *m/z*: $[M]^+$ calcd for $C_{25}H_{43}O_4NSSi$: 481.2682, found: 481.2676.

(1*E*,5*Z*)-(3*S*,10*S*)-11-(*tert*-Butyldimethylsilanyloxy)-2,6,10-trimethyl-1-(2-methylthiazol-4-yl)-undeca-1,5-dien-3-ol (7): To a solution of β-hydroxy lactone **10** (25 mg, 0.05 mmol) in 10:1 Et_2O/Et_3N (1 mL) at 0 °C under argon was added MsCl (6 μL, 0.07 mmol). After 1.5 h brine was added and the aqueous layer was extracted with Et_2O. The combined ethereal layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was taken up in THF (1 mL) and LiOH (0.15 mL, 1 M in water, 0.15 mmol) was added at 0 °C. After 1 h TLC showed completion of the reaction, and a saturated NH_4Cl solution was added, the layers were separated and the aqueous phase was extracted with DCM. The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. Column chromatography (hexane/ethyl acetate = 3:1) yielded di-olefin **7** (17.5 mg; 81 %) as a colorless oil. $[\alpha]_D^{20}=-8.2$ ($c=0.5$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=6.94$ (s, 1H), 6.56 (s, 1H), 5.16 (t, $J=7.1$ Hz, 1H), 4.14 (t, $J=6.3$ Hz, 1H), 3.43 (dd, $J=9.5$, 5.4 Hz, 1H), 3.35 (dd, $J=9.8$, 6.6 Hz, 1H), 2.71 (s, 3H), 2.35 (t, $J=6.6$ Hz, 2H), 2.05 (d, $J=1.3$ Hz, 3H), 2.03 (t, $J=6.9$ Hz, 2H), 1.71 (d, $J=1.3$ Hz, 3H), 1.62–1.54 (m, 1H), 1.44–1.31 (m, 3H), 1.10–1.01 (m, 1H), 0.89 (s, 9H), 0.86 (d, $J=6.8$ Hz, 3H), 0.02 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=164.5$, 152.9, 141.7, 139.5, 120.1, 118.8, 115.4, 77.2, 68.3, 65.8, 35.7, 34.1, 33.1, 32.3, 26.0, 25.5, 19.2, 18.4, 16.7, 15.2, 14.5, −5.3 ppm; IR (film): $\tilde{\nu}=$ 3390, 2955, 2928, 1256, 1093 cm^{-1}; HRMS (ESI): *m/z*: $[M]^+$ calcd for $C_{24}H_{43}O_2NSSi$: 437.2784, found: 437.2779.

4-[(1*E*,5*Z*)-(3*S*,10*S*)-3,11-Bis-(*tert*-butyldimethylsilanyloxy)-2,6,10-trimethylundeca-1,5-dienyl]-2-methylthiazole (38): To a stirred solution of alcohol **13** (15 mg, 0.034 mmol) in DCM (1 mL) was added 2,6-lutidine (9 μL, 0.051 mmol) and TBSOTf (10 μL, 0.041 mmol). After 1 h the reaction was quenched with saturated NH_4Cl solution and extracted with DCM. The combined organic extracts were dried over $MgSO_4$ and the

solvent was evaporated. Purification by column chromatography (hexane/ethyl acetate = 20:1) yielded **38** (16 mg; 85%) as a colorless oil. The experimental data were identical with the literature data. $[\alpha]_D^{20} = 3.5$ ($c = 1.1$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.91$ (s, 1H), 6.45 (s, 1H), 5.13 (t, $J = 7.1$ Hz, 1H), 4.08 (t, $J = 6.7$ Hz, 1H), 3.44 (dd, $J = 9.7$, 5.8 Hz, 1H), 3.34 (dd, $J = 9.7$, 6.7 Hz, 1H), 2.71 (s, 3H), 2.30–2.20 (m, 2H), 2.04–1.95 (m, 2H), 2.00 (d, $J = 1.2$ Hz, 3H), 1.66 (d, $J = 1.2$ Hz, 3H), 1.61–1.53 (m, 1H), 1.43–1.28 (m, 3H), 1.08–1.00 (m, 1H), 0.89 (s, 18H), 0.86 (d, $J = 6.56$ Hz, 3H), 0.05 (s, 3H), 0.03 (s, 6H), 0.00 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 164.3$, 153.3, 142.6, 136.9, 121.4, 118.7, 114.9, 79.1, 68.4, 35.8, 35.3, 33.2, 32.3, 25.9, 25.8, 25.4, 23.5, 19.2, 18.4, 18.2, 16.7, 13.9, −4.6, −4.9, −5.3 ppm; IR (film): $\tilde{\nu} = 2955$, 2929, 1471, 1256, 1091 cm^{-1}; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{30}H_{57}O_2Si_2NS$: 551.3849, found: 551.3635.

(1*E*,5*E*)-(3*S*,10*S*)-11-(*tert*-Butyldimethylsilanyloxy)-2,6,10-trimethyl-1-(2-methylthiazol-4-yl)-undeca-1,5-dien-3-ol (60) and (3*S*,4*S*)-3-[(*S*)-5-(*tert*-butyldimethylsilanyloxy)-4-methylpentyl]-4-[(*E*)-(*S*)-2-hydroxy-3-methyl-4-(2-methylthiazol-4-yl)-but-3-enyl]-3-methyloxetan-2-one (61): To a solution of β-hydroxy lactone 56 (25 mg, 0.05 mmol) in 10:1 Et_2O/Et_3N (1 mL) at 0 °C under argon was added MsCl (6 μL, 0.07 mmol). After 1.5 h brine was added and the aqueous layer was extracted with Et_2O. The combined ethereal layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was taken up in THF (1 mL) and LiOH (0.15 mL, 1 M in water, 0.15 mmol) was added at 0 °C. After 2 h TLC showed completion of the reaction and a saturated NH_4Cl solution was added, the layers were separated and the aqueous phase was extracted with DCM. The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. Column chromatography (hexane/ethyl acetate = 5:1) yielded di-olefin **60** (8 mg; (38%) and β-lactone **61** (12 mg; 52%). **60**: $[\alpha]_D^{20} = -9.06$ ($c = 0.85$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.94$ (s, 1H), 6.56 (s, 1H), 5.17 (t, $J = 7.2$ Hz, 1H), 4.16 (t, $J = 6.3$ Hz, 1H), 3.42 (dd, $J = 9.7$, 5.9 Hz, 1H), 3.34 (dd, $J = 9.7$, 6.1 Hz, 1H), 2.71 (s, 3H), 2.36 (t, $J = 6.8$ Hz, 2H), 2.06 (d, $J = 1.3$ Hz, 3H), 2.00 (t, $J = 7.3$ Hz, 2H), 1.78 (d, $J = 3.3$ Hz, 1H), 1.64 (s, 3H), 1.60–1.53 (m, 1H), 1.46–1.30 (m, 3H), 1.06–1.00 (m, 1H), 0.89 (s, 9H), 0.85 (d, $J = 6.8$ Hz, 3H), 0.03 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 164.6$, 153.0, 141.7, 139.4, 119.5, 118.9, 115.4, 77.2, 68.4, 40.2, 35.7, 34.4, 32.9, 26.0, 25.4, 19.2, 18.3, 16.7, 16.2, 14.5, −5.3 ppm; IR (film): $\tilde{\nu} = 2954$, 2928, 1471, 1255, 1092 cm^{-1}; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{24}H_{43}O_2NSSi$: 437.2784, found: 437.2785. **61**: $[\alpha]_D^{20} = -25.9$ ($c = 1.35$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.96$ (s, 1H), 6.06 (s, 1H), 4.66 (dd, $J = 9.3$, 3.3 Hz, 1H), 4.36 (dt, $J = 8.9$, 3.3 Hz, 1H), 3.43–3.36 (m, 2H), 2.71 (s, 3H), 2.07 (d, $J = 3.3$ Hz, 1H), 2.06 (d, $J = 1.0$ Hz, 3H), 2.00–1.86 (m, 2H), 1.74–1.67 (m, 2H), 1.62–1.56 (m, 2H), 1.49–1.34 (m, 3H), 1.26 (s, 3H), 1.14–1.05 (m, 1H), 0.89 (s, 9H), 0.86 (d, $J = 6.8$ Hz, 3H), 0.03 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 175.0$, 164.8, 152.5, 141.5, 119.0, 116.1, 78.4, 73.6, 68.2, 57.4, 36.4, 36.1, 35.6, 33.3, 25.9, 21.7, 19.2, 18.3, 16.6, 14.8, 14.4, −5.4 ppm; IR (film): $\tilde{\nu} = 2954$, 2528, 1820, 1094 cm^{-1}; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{25}H_{43}O_4NSSi$: 481.2682, found: 481.2672.

(*E*)-(2*S*,3*R*,5*R*)-2-[(*S*)-5-(*tert*-Butyldimethylsilanyloxy)-4-methylpentyl]-3,5-dihydroxy-2,6-dimethyl-7-(2-methylthiazol-4-yl)-hept-6-enoic acid methyl ester (62): To a solution of tetramethylammonium triacetoxyboron hydride (1.06 g, 3.88 mmol) in acetonitrile (7 mL) and acetic acid (5 mL) at −30 °C was slowly added a solution of **53** (260 mg, 0.48 mmol) in acetonitrile (5 mL). After the mixture had been stirred for 9 h, a saturated solution of $NaHCO_3$ and solid $NaHCO_3$ was added very carefully till gas evolution ceased. The aqueous layer was extracted with DCM, the combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. Column chromatography (hexane/ethyl acetate = 1:1) yielded dihydroxy ester **62** (242 mg; 97%) as colorless oil. $[\alpha]_D^{20} = 14.6$ ($c = 0.5$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.93$ (s, 1H), 6.67 (s, 1H), 4.45 (dd, $J = 6.4$, 2.9 Hz, 1H), 4.00 (dd, $J = 10.2$, 1.1 Hz, 1H), 3.67 (s, 3H), 3.40 (dd, $J = 9.7$, 5.9 Hz, 1H), 3.34 (dd, $J = 9.7$, 6.3 Hz, 1H), 2.70 (s, 3H), 1.99 (d, $J = 0.8$ Hz, 3H), 1.81–1.63 (m, 3H), 1.60–1.52 (m, 1H), 1.46–1.37 (m, 1H), 1.36–1.23 (m, 2H), 1.15 (s, 3H), 1.16–0.98 (m, 2H), 0.88 (s, 9H), 0.83 (d, $J = 6.6$ Hz, 3H), 0.02 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 177.1$, 164.6, 153.0, 141.9, 118.0, 115.4, 74.4, 73.0, 68.3, 51.8, 50.6, 36.0, 35.8, 35.5, 33.6, 25.9, 21.9, 19.2, 18.4, 17.3, 16.6, 15.4, −5.4 ppm; IR (film): $\tilde{\nu} = 3400$, 2952, 2989, 1731, 1256, 1091 cm^{-1}; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{26}H_{47}O_5NSSi$: 513.2944, found: 513.2953.

(3*S*,4*R*,6*R*)-3-[(*S*)-5-(*tert*-Butyldimethylsilanyloxy)-4-methylpentyl]-4-hydroxy-3-methyl-6-[(*E*)-1-methyl-2-(2-methylthiazol-4-yl)vinyl]tetrahydropyran-2-one (63): LiOH (1.5 mL, 1 M in water, 1.5 mmol) was added to ester **62** (240 mg, 0.47 mmol) in THF (5 mL) at 0 °C and vigorously stirred for 4 h. Brine was added, the aqueous layer was acidified with 1N HCl and was extracted with DCM. The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. The residue was taken up in DCM (5 mL) and EDC·HCl (136 mg, 0.7 mmol) and DMAP (116 mg, 0.94 mmol) were added. After 3 h, brine was added and the aqueous layer was extracted with DCM, the combined DCM phases were dried over $MgSO_4$ and the solvent was evaporated. Column chromatography (hexane/ethyl acetate = 1:1) yielded lactone **63** (192 mg; 85%) as colorless oil. $[\alpha]_D^{20} = -6.6$ ($c = 2$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.00$ (s, 1H), 6.56 (s, 1H), 4.74 (dd, $J = 9.6$, 5.8 Hz, 1H), 4.20 (dd, $J = 8.5$, 6.9 Hz, 1H), 3.42 (dd, $J = 9.8$, 6.2 Hz, 1H), 3.38 (dd, $J = 9.8$, 6.2 Hz, 1H), 2.71 (s, 3H), 2.16–2.09 (m, 2H), 2.10 (d, $J = 1.0$ Hz, 3H), 1.85 (ddd, $J = 13.7$, 11.1, 4.9 Hz, 1H), 1 63 (ddd, $J = 13.8$, 11.1, 5.5 Hz, 1H), 1.59–1.54 (m, 1H), 1.45–1.26 (m, 3H), 1.29 (s, 3H), 1.26–1.17 (m, 1H), 0.89 (s, 9H), 0.86 (d, $J = 6.8$ Hz, 3H), 0.04 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 176.0$, 165.0, 152.1, 136.4, 120.8, 116.9, 81.0, 68.4, 67.8, 48.7, 36.3, 35.7, 33.6, 33.3, 25.9, 22.3, 19.2, 16.7, 14.1, −5.4 ppm; IR (film): $\tilde{\nu} = 2953$, 2928, 2856, 1712, 1250, 1087 cm^{-1}; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{25}H_{43}O_4NSSi$: 481.2682, found: 481.2671.

(3*S*,4*S*,6*R*)-3-[(*S*)-5-(*tert*-Butyldimethylsilanyloxy)-4-methylpentyl]-4-hydroxy-3-methyl-6-[(*E*)-1-methyl-2-(2-methylthiazol-4-yl)vinyl]tetrahydropyran-2-one (64): Dess–Martin periodinane (178 mg, 0.42 mmol) was added portionwise to a suspension of alcohol **63** (70 mg, 0.14 mmol) and $NaHCO_3$ (35 mg, 0.42 mmol) in DCM (2 mL) at 0 °C under argon. After 4 h, water was added, layers were separated, and the aqueous layer was extracted with DCM. The combined DCM phases were dried over $MgSO_4$ and the solvent was evaporated. Column chromatography (hexane/ethyl acetate = 3:1) yielded the ketone (66 mg; 94%) as a colorless oil. $[\alpha]_D^{20} = 6.89$ ($c = 1.2$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.03$ (s, 1H), 6.60 (s, 1H), 5.01 (dd, $J = 11.1$, 3.0 Hz, 1H), 3.41–3.34 (m, 2H), 2.87 (dd, $J = 16.2$, 11.1 Hz, 1H), 2.77 (dd, $J = 16.2$, 3.3 Hz, 1H), 2.72 (s, 3H), 2,17 (d, $J = 1.3$ Hz, 3H), 1.99 (ddd, $J = 13.2$, 11.9, 4.5 Hz, 1H), 1.73 (ddd, $J = 12.9$, 12.9, 3.7 Hz, 1H), 1.60–1.52 (m, 2H), 1.42 (s, 1H), 1.43–1.17 (m, 3H), 1.10–1.02 (m, 1H), 0.89 (s, 9H), 0.84 (d, $J = 6.8$ Hz, 3H), 0.03 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 205.9$, 173.7, 165.1, 151.8, 134.4, 121.9, 117.8, 78.0, 68.1, 57.0, 42.2, 37.6, 35.4, 33.1, 26.0, 22.7, 22.1, 19.3, 18.3, 16.6, 14.0, −5.4 ppm; IR (film): $\tilde{\nu} = 2953$, 2928, 1749, 1716, 1256, 1090 cm^{-1}; HRMS (ESI): m/z: $[M-CH_3]^+$ calcd for $C_{24}H_{38}O_4NSSi$: 464.2281, found: 464.2279 . Sodium boron hydride (1.5 mg, 0.041 mmol) was added to the keto lactone (20 mg, 0.041 mmol) in methanol (1 mL) at −78 °C. After 4 h, brine was added, the mixture was warmed to room temperature, and the aqueous phase was extracted with DCM. The combined DCM layers were dried over $MgSO_4$ and the solvent was evaporated. Column chromatography (hexane/ethyl acetate = 1:1) yielded lactone **64** (18 mg; 90%) as a colorless oil. $[\alpha]_D^{20}$ 3.8 ($c = 1.1$, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.99$ (s, 1H), 6.58 (s, 1H), 5.23 (dd, $J = 11.6$, 3.8 Hz, 1H), 4.02 (dd, $J = 4.0$, 2.0 Hz, 1H), 3.47–3.36 (m, 2H), 2.72 (s, 3H), 2.24 (ddd, $J = 14.0$, 11.4, 2.2 Hz, 1H), 2.10 (d, $J = 0.8$ Hz, 3H), 2.02 (ddd, $J = 14.0$, 4.6, 3.8 Hz, 1H), 1.68–1.51 (m, 3H), 1.41–1.24 (m, 3H), 1.34 (s, 3H), 1.08–1.01 (m, 1H), 0.89 (s, 9H), 0.87 (d, $J = 6.4$ Hz, 3H), 0.05 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 176.6$, 165.0, 152.5, 136.8, 120.1, 116.7, 80.6, 70.5, 68.3, 47.2, 38.8, 35.6, 33.7, 31.4, 25.8, 21.6, 20.2, 19.1, 18.7, 16.9, 14.2, −5.3 ppm; IR (film): $\tilde{\nu} = 3400$, 2928, 1712, 1462, 1251, 1182, 1088 cm^{-1}; HRMS (ESI): m/z: $[M-C_4H_9]^+$ calcd for $C_{21}H_{34}O_4NSSi$: 424.1978, found: 424.1985.

(1*E*,5*E*)-(3*R*,10*S*)-11-(*tert*-Butyldimethylsilanyloxy)-2,6,10-trimethyl-1-(2-methylthiazol-4-yl)-undeca-1,5-dien-3-ol (65): To a solution of β-hydroxy lactone **63** (25 mg, 0.05 mmol) in 10:1 Et_2O:Et_3N (1 mL) at 0 °C under argon was added MsCl (6 μL, 0.075 mmol). After 2 h, brine was added and the aqueous layer was extracted with Et_2O. The combined ethereal layers were dried over $MgSO_4$ and the solvent was removed

under reduced pressure. The residue was taken up in THF (1 mL), and LiOH (0.15 mL, 1 M in water, 0.15 mmol) was added at 0 °C. After 2 h, TLC showed completion of the reaction and a saturated NH_4Cl solution was added, the layers were separated, and the aqueous phase was extracted with DCM. The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. Column chromatography (hexane/ethyl acetate = 3:1) yielded the di-olefin **65** (14 mg; 64 %). $[\alpha]_D^{20} = 5.1$ ($c = 1.0$, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.94$ (s, 1H), 6.56 (s, 1H), 5.17 (t, $J = 7.3$ Hz, 1H), 4.16 (t, $J = 6.3$ Hz, 1H), 3.42 (dd, $J = 9.7$, 5.9 Hz, 1H), 3.34 (dd, $J = 9.7$, 6.7 Hz, 1H), 2.71 (s, 3H), 2.36 (t, $J = 6.8$ Hz, 2H), 2.06 (s, 3H), 1.99 (t, $J = 6.8$ Hz, 2H), 1.64 (s, 3H), 1.61–1.53 (m, 1H), 1.46–1.23 (m, 3H), 1.06–0.96 (m, 1H), 0.89 (s, 9H), 0.85 (d, $J = 6.6$ Hz, 3H), 0.03 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 164.7$, 153.0, 141.7, 139.3, 119.5, 118.9, 115.4, 77.2, 68.4, 40.2, 35.7, 34.4, 32.8, 29.7, 26.0, 25.4, 19.2, 16.7, 16.3, 14.4, −5.3 ppm; IR (film): $\tilde{\nu} =$ 2928, 2357, 1255, 1091 cm^{-1}; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{24}H_{43}O_2NSSi$: 437.2784, found: 437.2776.

(1*E*,5*Z*)-(3*R*,10*S*)-11-(*tert*-Butyldimethylsilanyloxy)-2,6,10-trimethyl-1-(2-methylthiazol-4-yl)-undeca-1,5-dien-3-ol (67) and (3*S*,4*R*)-3-[(*S*)-5-(*tert*-Butyldimethylsilanyloxy)-4-methylpentyl]-4-[(*E*)-(*R*)-2-hydroxy-3-methyl-4-(2-methylthiazol-4-yl)-but-3-enyl]-3-methyloxetan-2-one (66): To a solution of β-hydroxy lactone **64** (18 mg, 0.035 mmol) in 10:1 Et_2O:Et_3N (1 mL) at 0 °C under argon was added MsCl (4 μL, 0.05 mmol). After 1.5 h, brine was added and the aqueous layer was extracted with Et_2O. The combined ethereal layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was taken up in THF (1 mL) and LiOH (0.15 mL, 1 M in water, 0.15 mmol) was added at room temperature. After 2.5 h, TLC showed completion of the reaction and a saturated NH_4Cl solution was added, the layers were separated and the aqueous phase was extracted with DCM. The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. Column chromatography (hexane/ethyl acetate = 5:1) yielded di-olefin **67** (8 mg; 52 %) and β-lactone **66** (6 mg; 36 %). **67**: $[\alpha]_D^{20}$ 1.73 ($c =$ 0.75, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.94$ (s, 1H), 6.56 (s, 1H), 5.17 (t, $J = 7.2$ Hz, 1H), 4.14 (dt, $J = 6.6$, 2.7 Hz, 1H), 3.43 (dd, $J = 9.8$, 5.8 Hz, 1H), 3.36 (dd, $J = 9.8$, 6.5 Hz, 1H), 2.71 (s, 3H), 2.35 (t, $J =$ 6.9 Hz, 2H), 2.05 (d, $J = 1.3$ Hz, 3H), 2.09–1.97 (m, 2H), 1.71 (d, $J =$ 1.0 Hz, 1H), 1.61–1.53 (m, 1H), 1.46–1.26 (m, 3H), 1.09–1.00 (m, 1H), 0.89 (s, 9H), 0.86 (d, $J = 6.6$ Hz, 3H), 0.03 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 172.5$, 164.6, 153.0, 141.7, 139.5, 120.15, 118.9, 115.4, 77.3, 68.3, 40.2, 35.7, 34.1, 33.1, 32.3, 26.0, 25.4, 23.6, 22.7, 19.2, 18.3, 16.7, 14.5, −5.3 ppm; IR (film): $\tilde{\nu} =$ 2955, 2929, 1472, 1256, 1093 cm^{-1}; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{24}H_{43}O_2NSSi$: 437.2784, found: 437.2783. **66**: $[\alpha]_D^{20} = 14.4$ ($c = 0.5$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.96$ (s, 1H), 6.00 (s, 1H), 4.57 (dd, $J = 8.5$, 4.4 Hz, 1H), 4.37 (dd, $J = 8.5$, 4.4 Hz, 1H), 3.41 (dd, $J = 9.9$, 5.9 Hz, 1H), 3.37 (dd, $J = 9.7$, 6.2 Hz, 1H), 2.71 (s, 3H), 2.07 (s, 3H), 2.00–1.94 (m, 2H), 1.76–1.54 (m, 3H), 1.49–1.25 (m, 3H), 1.43 (s, 3H), 1.12–1.04 (m, 1H), 0.88 (s, 9H), 0.86 (d, $J = 6.8$ Hz, 3H), 0.03 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 174.8$, 164.9, 152.5, 141.4, 119.0, 116.1, 80.7, 73.7, 56.8, 35.9, 35.5, 33.6, 25.9, 21.5, 19.6, 19.1, 18.3, 16.6, 14.4, −5.4 ppm; IR (film): $\tilde{\nu} =$ 2953, 1820, 1175, 1093 cm^{-1}. HRMS (ESI): m/z: $[M]^+$ calcd for $C_{25}H_{43}O_4NSSi$: 481.2682, found: 481.2688.

(*E*)-(2*S*,3*R*,5*S*)-2-[(*S*)-5-(*tert*-Butyldimethylsilanyloxy)-4-methylpentyl]-3-hydroxy-2,6-dimethyl-7-(2-methylthiazol-4-yl)-5-triisopropylsilanyloxy-hept-6-enoic acid methyl ester (68): To a stirred solution of dihydroxy ester **53** (110 mg, 0.22 mmol) in DCM (4 mL) was added 2,6-lutidine (58 μL, 0.48 mmol) and TIPSOTf (68 μL, 0.24 mmol). After 1.5 h, the reaction was quenched with saturated NH_4Cl solution and the aqueous layer was extracted with DCM. The combined organic solutions were dried over $MgSO_4$ and the solvent was evaporated. Purification by column chromatography (hexane/ethyl acetate = 10:1) yielded **68** (125 mg; 85 %) as a colorless oil. $[\alpha]_D^{20} = -0.22$ ($c = 0.9$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.95$ (s, 1H), 6.52 (s, 1H), 4.55 (t, $J = 6.8$ Hz, 1H), 3.79 (dd, $J = 9.7$, 3.9 Hz, 1H), 3.65 (s, 3H), 3.39 (dd, $J = 9.6$, 5.8 Hz, 1H), 3,32 (dd, $J = 9.6$, 6.4 Hz, 1H), 2.75 (d, $J = 3.7$ Hz, 1H), 2.71 (s, 3H), 1.99 (d, $J = 1.0$ Hz, 3H), 1.78–1.66 (m, 2H), 1.61–1.50 (m, 2H), 1.48–1.40 (m, 1H), 1.36–1.21 (m, 3H), 1.12 (s, 3H), 1.06 (s, 21H), 1.07–0.97 (m, 1H), 0.88 (s, 9H), 0.82 (d, $J = 6.6$ Hz, 3H), 0.02 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 176.8$, 168.4, 152.9, 141.3, 120.1, 115.4, 78.3, 73.6, 68.4, 51.7, 50.9, 40.5, 39.0, 36.5, 35.5, 33.5, 25.9, 22.0, 19.2, 18.1, 16.5, 13.6, 12.5, −0.4, −5.4 ppm; IR (film): $\tilde{\nu} =$ 2948, 2865, 1734, 1465, 1256, 1088 cm^{-1}; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{25}H_{43}O_4NSSi_2$: 481.2682, found: 481.2688.

(*E*)-(2*S*,3*R*,5*S*)-2-[(*S*)-5-(*tert*-Butyldimethylsilanyloxy)-4-methylpentyl]-3-methanesulfonyloxy-2,6-dimethyl-7-(2-methylthiazol-4-yl)-5-triisopropylsilanyloxy-hept-6-enoic acid methyl ester (69): To alcohol **68** (95 mg, 0.14 mmol) in 10:1 Et_2O:Et_3N (3 mL) at room temperature was added mesyl chloride (38 μL, 0.42 mmol) and the reaction was stirred for 2 h. Brine was added, the layers were separated and the aqueous layer extracted with Et_2O. The ethereal layers were dried over $MgSO_4$ and solvent was evaporated. Column chromatography (hexane/ethyl acetate = 5:1) yielded **69** (100 mg; 96 %) as a colorless oil. $[\alpha]_D^{20} = 14.27$ ($c = 0.55$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.97$ (s, 1H), 6.63 (s, 1H), 4.84 (t, $J = 8.8$ Hz, 1H), 4.59 (dd, $J = 10.7$, 3.7 Hz, 1H), 3.61 (s, 3H), 3.38 (dd, $J = 9.7$, 5.9 Hz, 1H), 3.31 (dd, $J = 9.8$, 6.3 Hz, 1H), 3.05 (s, 3H), 2.71 (s,3H), 2.03–1.94 (m, 1H), 1.98 (d, $J = 1.0$ Hz, 3H), 1.84–1.74 (m, 2H), 1.56–1.48 (m, 2H), 1.46–1.23 (m, 3H), 1.17 (s, 3H), 1.05 (s, 21H), 1.07–0.97 (m, 1H), 0.87 (s, 9H), 0.81 (d, $J = 6.6$ Hz, 3H), 0.01 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 175.4$, 164.2, 153.8, 144.9, 138.8, 121.9, 116.2, 83.3, 79.9, 75.2, 68.4, 63.1, 52.1, 51.5, 36.7, 35.6, 33.4, 32.8, 25.9, 19.4, 18.1, 16.7, 15.9, 12.2, −5.4 ppm; IR (film): $\tilde{\nu} =$ 2951, 2865, 1736, 1340, 1174 cm^{-1}; HRMS (ESI): m/z: $[M+Na]^+$ calcd for $C_{36}H_{69}O_7NS_2Si_2Na$: 770.3952, found: 770.3968.

Methanesulfonic acid (1*R*,2*S*,6*S*)-7-(*tert*-butyldimethylsilanyloxy)-2-formyl-2,6-dimethyl-1-[(*E*)-(*S*)-3-methyl-4-(2-methylthiazol-4-yl)-2-triisopropylsilanyloxybut-3-enyl]heptyl ester (70): To ester **69** (90 mg, 0.12 mmol) in toluene (2 mL) at −78 °C was slowly added DIBALH (0.1 mL, 1.5 M in toluene, 0.14 mmol). After the reaction mixure had been stirred for 3 h, the reaction mixture was quenched by the addition of methanol, potassium sodium tartrate solution was added and stirring was continued for 2 h. The layers were separated and the aqueous layer was extracted with DCM, the combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. Column chromatography (hexane : ethyl acetate = 10:1) yielded the alcohol (75 mg; 87 %) as a colorless oil. $[\alpha]_D^{20} = 20.17$ ($c = 1.2$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta =$ 6.94 (s, 1H), 6.64 (s, 1H), 4.70 (d, $J = 7.6$ Hz, 1H), 4.66 (dd, $J = 10.3$, 3.8 Hz, 1H), 3.57 (d, $J = 11.9$ Hz, 1H), 3.42 (dd, $J = 9.8$, 6.0 Hz, 1H), 3.34 (dd, $J = 9.8$, 6.4 Hz, 1H), 3.33 (d, $J = 12.6$ Hz, 1H), 3.07 (s, 3H), 2.70 (s, 3H), 2.07 (m, 1H), 2.02 (s, 3H), 1.91 (ddd, $J = 15.4$, 8.7, 3.9 Hz, 1H), 1.56 (m, 1H), 1.40–1.19 (m, 5H), 1.07 (s, 3H), 1.05 (s, 21H), 0.99 (m, 1H), 0.89 (s, 9H), 0.84 (d, $J = 6.8$ Hz, 3H), 0.03 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 164.4$, 152.9, 139.3, 121.9, 116.1, 83.9, 75.4, 68.3, 66.5, 42.4, 38.6, 37.4, 35.6, 34.3, 32.8, 25.9, 20.7, 19.4, 19.2, 18.1, 18.0, 16.6, 12.2, −5.4 ppm; IR (film): $\tilde{\nu} =$ 3368, 2944, 2893, 2865, 1464, 1334, 1171, 1083, 1062 cm^{-1}; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{35}H_{69}O_6NS_2Si_2$: 719.4105, found: 719.4112. Dess–Martin periodinane (87 mg, 0.21 mmol) was added portionwise to a suspension of the alcohol (50 mg, 0.07 mmol) and $NaHCO_3$ (52 mg, 0.63 mmol) in DCM (3 mL) at 0 °C under argon. After 2 h, water was added, layers were separated and the aqueous layer was extracted with DCM. The combined DCM phases were dried over $MgSO_4$ and the solvent was evaporated. Column chromatography (hexane/ethyl acetate = 3:1) yielded aldehyde **70** (47 mg; 94 %) as colorless oil. $[\alpha]_D^{20} = 23.58$ ($c = 0.95$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta =$ 9.46 (s, 1H), 6.98 (s, 1H), 6.65 (s, 1H), 4.78 (dd, $J = 5.8$, 4.5 Hz, 1H), 4.62 (dd, $J = 7.8$, 6.3 Hz, 1H), 3.37 (dd, $J = 9.9$, 6.2 Hz, 1H), 3.32 (dd, $J = 9.7$, 6.2 Hz, 1H), 3.03 (s, 3H), 2.70 (s, 3H), 2.02 (s,3H), 1.95 (dd, $J = 6.8$, 5.6 Hz, 2H), 1.71 (dq, $J = 12.9$, 4.6 Hz, 1H), 1.52 (m, 1H), 1.46–1.32 (m, 4H), 1.27–1.14 (m, 2H), 1.08 (s, 3H), 1.04 (s, 21H), 0.88 (s, 9H), 0.80 (d, $J = 6.8$ Hz, 3H), 0.02 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta =$ 203.2, 164.3, 153.0, 138.6, 122.4, 116.5, 81.6, 75.2, 68.2, 53.5, 38.9, 37.9, 35.5, 33.8, 32.4, 25.9, 21.2, 19.3, 18.1, 17.9, 16.6, 16.0, 12.5, 12.2, −5.4 ppm; IR (film): $\tilde{\nu} =$2945, 2865, 1731, 1463, 1339, 1174, 1085, 1064 cm^{-1}; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{35}H_{67}O_6NS_2Si_2$: 717.3948, found: 717.3943.

4-[(1*E*,5*E*)-(3*S*,10*S*)-11-(*tert*-Butyldimethylsilanyloxy)-2,6,10-trimethyl-3-triisopropylsilanyloxyundeca-1,5-dienyl]-2-methylthiazole (71): To aldehyde **70** (25 mg, 0.035 mmol) in THF (1 mL) was added LiOH (0.1 mL, 1 M in water, 0.1 mmol) at 0 °C. After 6 h, a saturated NH_4Cl solution was

added, the layers were separated and the aqueous layer was extracted with DCM. The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. Column chromatography (hexane/ethyl acetate = 10:1) yielded olefin **71** (17 mg; 82%) as a colorless oil. $[\alpha]_D^{20} = 8.12$ ($c = 0.85$, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 6.90$ (s, 1H), 6.43 (s, 1H), 5.09 (t, $J = 7.2$ Hz, 1H), 4.24 (t, $J = 6.6$ Hz, 1H), 3.40 (dd, $J = 9.8$, 6.0 Hz, 1H), 3.30 (dd, $J = 9.8$, 6.8 Hz, 1H), 2.70 (s, 3H), 2.38–2.34 (m, 1H), 2.33–2.28 (m, 1H), 2.00 (d, $J = 1.1$ Hz, 3H), 1.94–1.88 (m, 2H), 1.57 (s, 3H), 1.52 (m, 1H), 1.39–1.35 (m, 1H), 1.32–1.25 (m, 3H), 1.06 (s, 11H), 1.04 (s, 10H), 1.00–0.95 (m, 1H), 0.88 (s, 9H), 0.81 (d, $J = 6.8$ Hz, 3H), 0.02 ppm (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 164.1$, 153.2, 142.2, 136.8, 120.2, 119.1, 114.7, 78.8, 68.4, 40.2, 35.7, 35.6, 32.9, 29.7, 25.9, 25.4, 19.2, 18.3, 18.1, 18.0, 16.7, 16.2, 12.4, −5.3 ppm; IR (film): $\tilde{\nu} =$ 2928, 2864, 1463, 1255, 1091, 1064 cm^{-1}. HRMS (ESI): m/z: $[M]^+$ calcd for $C_{33}H_{63}O_2NSSi_2$: 593.4118, found: 593.4125.

Benzoic acid (*Z*)-(1*S*,8*S*)-9-(*tert*-butyldimethylsilanyloxy)-4,8-dimethyl-1-[(*E*)-1-methyl-2-(2-methylthiazol-4-yl)vinyl]non-3-enyl ester (72a): To a solution of β-hydroxy lactone **57** (30 mg, 0.06 mmol) in 10:1 Et_2O: Et_3N (1.5 mL) at 0°C under argon was added MsCl (17 μL, 0.09 mmol). After 1 h, brine was added and the aqueous layer was extracted with Et_2O. The combined ethereal layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was taken up in THF (1 mL) and PhLi (0.18 mL, 1 M in dibutyl ether, 0.18 mmol) was added at −78°C under argon. After 3 h, a saturated NH_4Cl solution was added, the layers were separated and the aqueous layer was extracted with DCM. The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. Column chromatography (hexane/ethyl acetate = 3:1) yielded **72a** (14 mg; 43%) and free alcohol **7** (5 mg; 19%). $[\alpha]_D^{20} = 5.2$ ($c = 0.25$, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 8.07$ (m, 2H), 7.55 (m, 1H), 7.44 (m, 2H), 6.95 (s, 1H), 6.60 (s, 1H), 5.47 (t, $J = 6.8$ Hz, 1H), 5.15 (t, $J = 6.6$ Hz, 1H), 3.43 (dd, $J = 9.6$, 5.8 Hz, 1H), 3.34 (dd, $J = 9.6$, 6.6 Hz, 1H), 2.70 (s, 3H), 2.64–2.59 (m, 1H), 2.54–2.50 (m, 1H), 2.15 (d, $J = 1.5$ Hz, 3H), 2.07–1.98 (m, 2H), 1.66 (d, $J = 1.1$ Hz, 3H), 1.56 (m, 1H), 1.42–1.24 (m, 3H), 1.07–1.02 (m, 1H), 0.88 (s, 9H), 0.85 (d, $J = 6.8$ Hz, 3H), 0.03 ppm (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 165.7$, 164.5, 152.6, 138.6, 137.6, 132.8, 130.6, 129.7, 128.3, 120.6, 119.3, 116.2, 79.6, 68.3, 35.8, 33.1, 32.3, 31.8, 25.9, 25.4, 23.5, 22.6, 19.2, 16.7, 14.9, −5.3 ppm; IR (film): $\tilde{\nu} =$ 2955, 2360, 2343, 1718, 1654, 1458, 1271 cm^{-1}; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{31}H_{47}O_3SiNS$: 541.3046, found: 541.3055.

Acetic acid (*Z*)-(1*S*,8*S*)-9-(*tert*-butyldimethylsilanyloxy)-4,8-dimethyl-1-[(*E*)-1-methyl-2-(2-methylthiazol-4-yl)vinyl]non-3-enyl ester (72b): To a solution of β-hydroxy lactone **57** (18 mg, 0.036 mmol) in 10:1 Et_2O:NEt_3 (1 mL) at 0°C under argon was added MsCl (4 μL, 0.052 mmol). After 1 h, brine was added and the aqueous layer was extracted with Et_2O. The combined ethereal layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was taken up in THF (1 mL) and MeLi (36 μL, 1.6 M in diethyl ether, 0.054 mmol) was added at −78°C. After 5 h, a saturated NH_4Cl solution was added, layers were separated and the aqueous layer was extracted with DCM. The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. Column chromatography (hexane/ethyl acetate = 3:1) yielded **72b** (4 mg; 23%) and free alcohol **7** (8 mg; 51%). $[\alpha]_D^{20} = -12$ ($c = 0.1$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.94$ (s, 1H), 6.51 (s, 1H), 5.23 (t, $J = 6.8$ Hz, 1H), 5.07 (t, $J = 6.8$ Hz, 1H), 3.44 (dd, $J = 9.8$, 6.0 Hz, 1H), 3.35 (dd, $J = 9.6$, 6.6 Hz, 1H), 2.70 (s, 3H), 2.49–2.34 (m, 2H), 2.08 (d, $J = 1.2$ Hz, 3H), 2.06 (s, 3H), 2.00 (t, $J = 7.0$ Hz, 2H), 1.67 (d, $J = 1.2$ Hz, 3H), 1.57 (m, 1H), 1.42–1.32 (m, 3H), 1.05 (m, 1H), 0.89 (s, 9H), 0.86 (d, $J = 6.5$ Hz, 3H), 0.03 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.2$, 164.5, 152.7, 138.5, 137.6, 120.5, 119.3, 116.1, 78.9, 68.3, 35.7, 33.1, 32.3, 31.7, 29.7, 25.9, 25.4, 23.5, 21.2, 19.2, 18.3, 16.7, 14.9, −5.3 ppm; IR (film): $\tilde{\nu} =$ 2929, 1508, 1458, 1238; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{26}H_{45}O_3SiNS$: 479.2889, found: 479.2899.

(2*S*,4*S*,5*R*,6*S*)-6-(*tert*-Butyldimethylsilanyloxymethyl)-5-hydroxy-1-(4-methoxybenzyloxy)-2,4,6,10-tetramethylundec-9-en-3-one (78): To a solution of chlorodicyclohexylborane (55 mL, 1 M in hexane, 54.6 mmol) in diethyl ether (200 mL) at 0°C under argon atmosphere was added triethylamine (8 mL, 58.2 mmol). After 15 min, a solution of (*R*)-1-(4-methoxy-benzyloxy)-2-methyl-pentan-3-one (**77**) (8.60 g, 36.4 mmol) in diethyl ether (50 mL) was added dropwise. Stirring was continued for 1 h and then the mixture was cooled to −78°C and a solution of (*S*)-2-(*tert*-butyldimethylsilanyloxymethyl)-2,6-dimethyl-hept-5-enal (**75**) (11.38 g, 40 mmol) in diethyl ether (70 mL) was added over 25 min. After the addition was complete the reaction was kept at −78°C for 3 h, then it was warmed to 0°C for 15 min and pH 7 buffer solution (500 mL), methanol (100 mL), and H_2O_2 (50 mL, 30% aqueous) were added. After the mixture had been stirred for 1.5 h at room temperature, it was extracted with DCM, the combined organic layers were dried over $MgSO_4$, and the solvent was evaporated. The crude aldol product was purified by column chromatography (hexane/ethyl acetate = 50:1 to 10:1) to yield **77** (14.30 g; 75%) as a pale yellow oil. At smaller scales (5 mmol) was the yield quantitative. $[\alpha]_D^{20} = 16.23$ ($c = 1.4$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.21$ (d, $J = 8.6$ Hz, 2H), 6.86 (d, $J = 8.6$ Hz, 2H), 5.07 (bt, $J = 7.1$ Hz, 1H), 4.43 (d, $J = 11.4$ Hz, 1H), 4.39 (d, $J = 11.4$ Hz, 1H), 3.98 (d, $J = 8.1$ Hz, 1H (OH)), 3.80 (s, 3H), 3.62–3.55 (m, 3H), 3.44–3.37 (m, 2H), 3.09–3.00 (m, 2H), 1.97–1.88 (m, 2H), 1.67 (s, 3H), 1.59 (s, 3H), 1.45–1.37 (m, 1H), 1.26–1.18 (m, 1H), 1.21 (d, $J = 7.1$ Hz, 3H), 1.07 (d, $J = 7.3$ Hz, 3H), 0.89 (s, 9H), 0.77 (s, 3H), 0.06 (s, 3H), 0.05 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 219.0$, 159.2, 131.3, 130.1, 129.2, 124.9, 113.8, 79.9, 73.0, 72.0, 67.9, 55.3, 47.5, 45.5, 42.5, 35.0, 25.9, 22.1, 18.2, 16.7, 13.6, −5.6 ppm; IR (film): $\tilde{\nu} =$ 3474, 2931, 1696, 1613, 1514, 1463, 1249, 1092 cm^{-1}; HRMS (ESI): m/z: $[M+Na]^+$ calcd for $C_{30}H_{52}O_5SiNa$: 543.3482, found: 543.3476.

(2*S*,3*S*,4*R*,5*R*,6*S*)-6-(*tert*-Butyldimethylsilanyloxymethyl)-1-(4-methoxybenzyloxy)-2,4,6,10-tetramethylundec-9-ene-3,5-diol (79): To a solution of tetramethylammonium triacetoxyboron hydride (17.07 g, 102.9 mmol) in 1:1 acetonitrile: acetic acid (120 mL) at −30°C was slowly added a solution of **78** (6.70 g, 12.86 mmol) in acetonitrile (30 mL). After the reaction had been stirred for 7 h, the reaction was kept in the freezer (−25°C) for 96 h, then a saturated solution of $NaHCO_3$ and solid $NaHCO_3$ was added very carefully until the gas evolution ceased. The aqueous layer was extracted with DCM, the combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. Column chromatography (hexane/ethyl acetate = 1:1) yielded dihydroxy ester **79** (4.30 g, 64%) and the precursor **78** (2.01 g, 30%). $[\alpha]_D^{20} = 10.72$ ($c = 0.97$, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.25$ (d, $J = 8.7$ Hz, 2H), 6.86 (d, $J = 8.7$ Hz, 2H), 5.07 (bt, $J = 7.0$ Hz, 1H), 4.46 (d, $J = 11.3$ Hz, 1H), 4.43 (d, $J = 11.3$ Hz, 1H), 3.86 (d, $J = 9.8$ Hz, 1H), 3.80 (s, 3H), 3.65–3.60 (m, 2H), 3.57 (m, 1H), 3.49–3.40 (m, 2H), 1.98–1.87 (m, 4H), 1.68 (s, 3H), 1.60 (s, 3H), 1.45–1.40 (m, 1H), 1.33–1.25 (m, 1H), 1.04 (d, $J = 7.0$ Hz, 3H), 0.90 (s, 3H), 0.89 (s, 9H), 0.86 (d, $J = 6.8$ Hz, 3H), 0.06 (s, 3H), 0.05 ppm (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.0$, 131.3, 130.5, 129.2, 124.7, 113.7, 82.4, 74.8, 74.3, 70.2, 55.2, 41.7, 36.3, 35.5, 25.8, 22.0, 18.0, 17.7, 13.8, 13.4, −5.7, −5.8 ppm; IR (film): $\tilde{\nu} =$ 3447, 2930, 2856, 1513, 1406, 1249, 1094 cm^{-1}; HRMS (ESI): m/z: $[M+Na]^+$ calcd for $C_{30}H_{54}O_5SiNa$: 545.3638, found: 545.3632; $[\alpha]_D$ −2.98 ($c = 1.5$, CH_2Cl_2).

***tert*-Butyl-((*S*)-2-{(4*R*,5*R*,6*S*)-6-[(*S*)-2-(4-methoxybenzyloxy)-1-methylethyl]-2,2,5-trimethyl-[1,3]dioxan-4-yl}-2,6-dimethylhept-5-enyloxy)dimethylsilane (83)**: To a stirred solution of **79** (2.50 g, 4.75 mmol) in DCM (50 mL) at room temperature under argon was added 2,2-dimethoxypropane (2.25 mL, 14.25 mmol) followed by CSA (110 mg, 0.47 mmol). After 2 h, brine was added and the aqueous layer was extracted with DCM, the combined DCM layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. Column chromatography (hexane/ethyl acetate = 10:1) yielded acetonide **83** (2.30 g, 86%) as a colorless oil. $[\alpha]_D^{20} = 6.9$ ($c = 0.86$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.25$ (d, $J = 8.6$ Hz, 2H), 6.87 (d, $J = 8.6$ Hz, 2H), 5.08 (bt, $J = 6.6$ Hz, 1H), 4.45–4.38 (m, 2H), 3.80 (s, 3H), 3.56 (dd, $J = 8.8$, 3.0 Hz, 1H), 3.48 (dd, $J = 10.4$, 2.8 Hz, 1H), 3.46 (d, $J = 9.4$ Hz, 1H), 3.40–3.32 (m, 3H), 1.99–1.89 (m, 3H), 1.84–1.76 (m, 1H), 1.68 (s, 3H), 1.60 (s, 3H), 1.36–1.18 (m, 2H), 1.29 (s, 3H), 1.22 (s, 3H), 0.92 (d, $J = 6.6$ Hz, 3H), 0.88 (s, 12H), 0.80 (s, 3H), 0.03 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 159.0$, 131.1, 129.1, 125.3, 113.7, 99.9, 76.9, 72.8, 72.5, 70.5, 65.2, 55.3, 41.9, 33.8, 32.7, 32.0, 25.9, 23.5, 22.0, 18.2, 17.6, 16.1, 13.4, 13.3, −5.5, −5.6 ppm; IR (film): $\tilde{\nu} =$ 2932, 1614, 1513, 1458, 1376, 1248, 1098 cm^{-1}; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{33}H_{58}O_5Si$: 562.4054, found: 562.4049.

(*S*)-2-{(4*R*,5*R*,6*S*)-6-[(*S*)-2-(4-Methoxybenzyloxy)-1-methylethyl]-2,2,5-trimethyl-[1,3]dioxan-4-yl}-2,6-dimethyl-hept-5-en-1-ol (82): To a stirred

solution of silyl ether **83** (1.20 g, 2.07 mmol) in acetonitrile (8 mL) and pyridine (3 mL) in a plastic vessel was added HF·py (2 mL, 70%) and the mixture was then stirred overnight. HF·py (1 mL, 70%) was added and stirred for another 5 h, the reaction was quenched by addition of saturated $NaHCO_3$ solution and DCM was added. The aqueous layer was extracted with DCM, and the combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. Column chromatography (hexane/ethyl acetate = 5:1) yielded free alcohol **82** (900 mg; 97%) as a colorless oil. $[\alpha]_D^{20} = 10.72$ ($c = 0.97$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.25$ (d, $J = 8.6$ Hz, 2H), 6.87 (d, $J = 8.6$ Hz, 2H), 5.11 (bt, $J = 6.9$ Hz, 1H), 4.41 (s, 2H), 3.80 (s, 3H), 3.72 (dd, $J = 11.4$, 3.8 Hz, 1H), 3.59 (dd, $J = 10.7$, 3.4 Hz, 1H), 3.53 (dd, $J = 8.7$, 2.9 Hz, 1H), 3.39–3.32 (m, 3H), 2.01–1.94 (m, 3H), 1.86–1.79 (m, 1H), 1.69 (s, 3H), 1.61 (s, 3H), 1.53–1.38 (m, 2H), 1.33 (s, 3H), 1.27 (s, 3H), 0.95 (d, $J = 6.8$ Hz, 3H), 0.92 (d, $J = 6.6$ Hz, 3H), 0.81 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 159.0$, 131.4, 130.9, 129.2, 124.7, 113.7, 100.6, 81.9, 72.9, 72.1, 70.6, 68.6, 55.3, 40.8, 34.8, 33.7, 32.5, 25.7, 23.2, 21.9, 17.0, 13.4, 13.2 ppm; IR (film): $\tilde{\nu} =$ 3509, 2967, 2933, 1513, 1377, 1247, 1085, 1038 cm^{-1}; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{27}H_{44}O_5$: 448.3189, found: 448.3192.

(*R*)-2-[(4*R*,5*R*,6*S*)-6-[(*S*)-2-(4-Methoxybenzyloxy)-1-methylethyl]-2,2,5-trimethyl-[1,3]dioxan-4-yl]-2,6-dimethyl-hept-5-enoic acid (84): To a solution of alcohol **83** (2.1 g, 4.68 mmol) in ethyl acetate (40 mL) was added IBX (2.62 g, 9.35 mmol). The mixture was heated under reflux for 2 h, then the white precipitate was filtered off and the solvent was removed under reduced pressure. Column chromatography (hexane/ethyl acetate = 10:1) yielded the aldehyde (1.78 g; 86%) as colorless oil. $[\alpha]_D^{20} = 4.56$ ($c = 1.36$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 9.54$ (s, 1H), 7.24 (d, $J = 8.6$ Hz, 2H), 6.87 (d, $J = 8.6$ Hz, 2H), 5,03 (tt, $J = 7.0$, 1.3 Hz, 1H), 4.40 (s, 2H), 3.80 (s, 3H), 3.54–3.49 (m, 3H), 3.36 (dd, $J = 8.7$, 6.2 Hz, 1H), 1.98–1.85 (m, 2H), 1.83–1.71 (m, 2H), 1.67 (s, 3H), 1.64–1.46 (m, 2H), 1.57 (s, 3H), 1.31 (s, 3H), 1.22 (s, 3H), 1.06 (s, 3H), 0.94 (d, $J = 6.6$ Hz, 3H), 0.91 ppm (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 206.1$, 159.0, 132.3, 130.9, 129.2, 123.7, 113.7, 100.5, 78.3, 72.9, 72.0, 70.1, 55.3, 53.3, 33.6, 32.8, 32.6, 25.7, 25.3, 23.2, 22.2, 17.7, 13.6, 13.2, 13.0 ppm; IR (film): $\tilde{\nu} =$ 2969, 2935, 1726, 1515, 1456, 1378, 1247, 1096, 1037 cm^{-1}; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{27}H_{42}O_5$: 446.3032, found: 446.3028. To a solution of the aldehyde (1.65 g, 3.69 mmol) in *tert*-butyl alcohol (25 mL) with 2-methyl-2-butene (5 mL) was added dropwise a solution of $NaClO_2$ (4 950 mg, 55 mmol) and NaH_2PO_4 (4.95 g) in water (15 mL). After 3 h, 0.01N NaOH was added and the aqueous layer was extracted with diethyl ether, 1N HCl was added until pH 2 was reached and the aqueous layer was extracted with DCM. The organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. Column chromatography (hexane/ethyl acetate = 1:1) yielded acid **84** (1.71 g; quant.). $[\alpha]_D^{20} = 14.26$ ($c = 1.36$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.24$ (d, $J = 8.6$ Hz, 2H), 6.87 (d, $J = 8.6$ Hz, 2H), 5.06 (bt, $J = 6.9$ Hz, 1H), 4.41 (s, 2H), 3.80 (s, 3H), 3.56 (dd, $J = 10.7$, 3.4 Hz, 1H), 3.49 (dd, $J = 8.6$, 2.8 Hz, 1H), 3.48 (d, $J = 6.1$ Hz, 1H), 3.37 (dd, $J = 8.6$, 6.1 Hz, 1H), 2.08–1.96 (m, 3H), 1.89–1.70 (m, 1H), 1.67 (s, 3H), 1.59 (s, 3H), 1.48–1.38 (m, 2H), 1.34 (s, 3H), 1.30 (s, 3H), 1.19 (s, 3H), 0.97 (d, $J = 6.6$ Hz, 3H), 0.91 ppm (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 178.4$, 159.0, 132.4, 130.9, 129.1, 123.4, 113.7, 101.5, 79.1, 72.9, 71.9, 70.6, 55.3, 50.8, 35.9, 33.9, 33.6, 25.6, 25.2, 23.3, 22.7, 17.6, 16.5, 13.6, 13.2, 13.0 ppm; IR (film): $\tilde{\nu} =$ 2981, 2935, 1701, 1513, 1226 cm^{-1}; HRMS (ESI): m/z: $[M+Na]^+$ calcd for $C_{27}H_{42}O_6Na$: 485.2879, found: 485.2896.

(3*R*,4*R*,5*S*,6*S*)-4-Hydroxy-6-[(*S*)-2-(4-methoxybenzyloxy)-1-methylethyl]-3,5-dimethyl-3-(4-methylpent-3-enyl)tetrahydropyran-2-one (12): To a stirred solution of acid **84** (1.66 mg, 3.5 mmol) in DCM (35 mL) at room temperature under argon was added CSA (783 mg, 3.5 mmol) and the mixture was stirred for 6 h. Brine was added and the aqueous layer was extracted with DCM. The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. Column chromatography (hexane/ethyl acetate = 3:1) yielded lactone **12** (1.175 g, 83%) as a colorless oil. $[\alpha]_D^{20} = -23.5$ ($c = 0.92$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta =$ 7.23 (d, $J = 8.6$ Hz, 2H), 6.86 (d, $J = 8.6$ Hz, 2H), 5.01 (bt, $J = 7.2$ Hz, 1H), 4.45 (d, $J = 11.4$ Hz, 1H), 4.36 (d, $J = 11.4$ Hz, 1H), 4.18 (dd, $J = 7.7$, 4.4 Hz, 1H), 3.79 (s, 3H), 3.73 (d, $J = 4.0$ Hz, 1H), 3.62 (dd, $J = 8.8$, 6.1 Hz, 1H), 3.60 (m, 1H), 3.49 (dd, $J = 8.9$, 4.7 Hz, 1H), 2.42–2.29 (m, 2H), 2.07–1.97 (m, 3H), 1.69–1.59 (m, 1H), 1.66 (s, 3H), 1.58 (s, 3H), 1.31 (s, 3H), 1.08 (d, $J = 7.1$ Hz, 3H), 0.96 ppm (d, $J = 7.1$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 176.1$, 159.3, 131.7, 129.9, 129.6, 124.3, 113.7, 81.3, 76.0, 72.9, 71.6, 55.2, 46.5, 34.4, 34.1, 33.8, 25.8, 25.6, 22.8, 15.9, 8.8 ppm; IR (film): $\tilde{\nu} =$ 3435, 2968, 1706, 1513, 1248, 1102 cm^{-1}; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{24}H_{36}O_5$: 404.2563, found: 404.2559.

(*Z*)-(2*S*,3*R*,4*S*)-1-(4-Methoxybenzyloxy)-2,4,6,10-tetramethylundeca-5,9-dien-3-ol (86): To lactone **12** (450 mg, 1.05 mmol) in 1:1 DCM:pyridine (10 mL) at room temperature under argon atmosphere was added methanesulfonyl chloride (0.25 mL, 3.15 mmol) and DMAP (136 mg, 1.05 mmol). After 3 h, brine was added, the layers were separated and the aqueous layer extracted with DCM. The combined organic phases were dried over $MgSO_4$ and the solvent was evaporated. The residue was dissolved in THF (10 mL) and LiOH (3.15 mL, 1M in water, 3.15 mmol) was added. After 2 h, the reaction was quenched with saturated NH_4Cl solution and the aqueous layer was extracted with DCM. The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. Column chromatography (hexane/ethyl acetate = 3:1) yielded olefin **86** (333 mg, 88%). $[\alpha]_D^{20} = 18.42$ ($c = 1.14$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.23$ (d, $J = 8.6$ Hz, 2H), 6.87 (d, $J = 8.6$ Hz, 2H), 5.10 (m, 2H), 4.46–4.39 (m, 2H), 3.80 (s, 3H), 3.59 (dd, $J = 9.1$, 4.0 Hz, 1H), 3.41 (dd, $J = 9.1$, 6.3 Hz, 1H), 3.30–3.23 (m, 1H + 1H (OH)), 2.53–2.44 (m, 1H), 2.08–1.94 (m, 4H), 1.93–1.86 (m, 2H), 1.68 (s, 6H), 1.61 (s, 3H), 0.96 ppm (d, $J = 6.8$ Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 159.3$, 134.0, 129.9, 129.3, 129.1, 124.3, 113.8, 80.4, 74.5, 73.2, 55.3, 35.7, 35.6, 32.2, 26.6, 25.7, 23.4, 22.6, 15.4, 14.8 ppm; IR (film): $\tilde{\nu} =$ 3503, 2930, 1513, 1248, 1083, 1037 cm^{-1}; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{23}H_{36}O_3$: 360.2664, found: 360.2671.

***tert*-Butyl-{(*Z*)-(1*R*,2*S*)-1-[(*S*)-2-(4-methoxybenzyloxy)-1-methylethyl]-2,4,8-trimethylnona-3,7-dienyloxy}dimethylsilane (87)**: To a stirred solution of alcohol **86** (240 mg, 0.65 mmol) in DCM (6 mL) was added 2,6-lutidine (120 μL, 0.98 mmol) and TBSOTf (160 μL, 0.72 mmol). After 1 h, the reaction was quenched with saturated NH_4Cl solution and extracted with DCM. The combined organic solutions were dried over $MgSO_4$ and the solvent was evaporated. Purification by column chromatography (hexane/ethyl acetate = 10:1) yielded protected diol **87** (320 mg; quant.) as a colorless oil. $[\alpha]_D^{20} = 6.64$ ($c = 1.28$, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.24$ (d, $J = 8.6$ Hz, 2H), 6.86 (d, $J = 8.6$ Hz, 2H), 5.10 (t, $J = 6.1$ Hz, 1H), 4.98 (d, $J = 9.8$ Hz, 1H), 4.39 (s, 2H), 3.80 (s, 3H), 3.51 (dd, $J = 9.1$, 4.8 Hz, 1H), 3.39 (t, $J = 5.3$ Hz, 1H), 3.20 (t, $J = 8.7$ Hz, 1H), 2.59–2.50 (m, 1H), 2.12–1.91 (m, 5H), 1.68 (s, 3H), 1.65 (s, 3H), 1.60 (s, 3H), 0.96 (d, $J = 6.8$ Hz, 3H), 0.89 (d, $J = 6.1$ Hz, 3H), 0.89 (s, 9H), 0.02 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 159.0$, 133.3, 131.5, 130.2, 129.1, 124.1, 113.7, 78.6, 72.7, 72.6, 55.3, 38.5, 35.5, 32.2, 26.6, 26.1, 25.7, 23.3, 18.4, 17.6, 16.9, 14.8, −3.8, −3.9 ppm; IR (film): $\tilde{\nu} =$ 2957, 2929, 1462, 1249, 1083, 1040 cm^{-1}; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{29}H_{50}O_3Si$: 474.3529, found: 474.3532.

***tert*-Butyl-{(*Z*)-(1*R*,2*S*)-6-dimethyloxiranyl-1-[(*S*)-2-(4-methoxybenzyloxy)-1-methylethyl]-2,4-dimethylhex-3-enyloxy}dimethylsilane (88)**: To a stirred solution of **87** (320 mg, 0.65 mmol) in DCM (7 mL) at −20°C NaOAc (60 mg, 0.68 mmol) and *m*CPBA (168 mg, 80 wt%, 0.68 mmol) was added. The mixture was warmed to 0°C over 2 h and saturated $NaHCO_3$ solution was added. The organic layer was separated and the aqueous layer was extracted with DCM. The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. Column chromatography (hexane/ethyl acetate = 10:1) yielded epoxide **88** (293 mg, 92%) as a 1:1 mixture of diastereoisomers. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.24$ (d, $J = 8.4$ Hz, 2H), 6.87 (d, $J = 8.4$ Hz, 2H), 5.03 (d, $J = 9.8$ Hz, 1H), 4.39 (s, 2H), 3.80 (s, 3H), 3.51 (dd, $J = 8.8$, 4.8 Hz, 1H), 3.40 (t, $J = 5.4$ Hz, 1H), 3.21 (t, $J = 8.6$ Hz, 1H), 2.68 (t, $J = 6.2$ Hz, 1H) or 2.67 (t, $J = 6.2$ Hz, 1H), 2.60–2.54 (m, 1H), 2.30–2.16 (m, 2H), 2.10–1.93 (m, 3H), 1.66 (s, 3H), 1.64–1.53 (m, 3H), 1.30 (s, 3H), 1.26 (s, 3H), 0.96 (d, $J = 6.8$ Hz, 3H), 0.90 (d, $J = 6.9$ Hz, 3H), 0.89 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 159.0$, 132.5, 130.9, 130.8/130.7, 129.1/129.0, 113.7, 78.6, 72.6, 72.5/72.4, 64.1/64.0, 58.3/58.2, 55.3, 38.4, 36.5/36.4, 35.6/35.5, 28.8, 27.6/27.5, 26.2, 24.9/24.8, 23.3, 18.7/18.6, 18.4, 17.0/16.9, 14.9/14.8, −3.8, −3.9 ppm; IR (film): $\tilde{\nu} =$ 2952, 1612, 1513,

1458, 1376, 1248, 1037 cm^{-1}. HRMS (ESI): m/z: $[M-C_4H_9]^+$ calcd for $C_{25}H_{41}O_4Si$: 433.2774, found: 433.2768.

(*Z*)-(6*S*,7*R*,8*S*)-7-(*tert*-Butyldimethylsilanyloxy)-9-(4-methoxybenzyloxy)-4,6,8-trimethyl-non-4-enal (89): To a stirred solution of epoxide **88** (190 mg, 0.38 mmol) in diethyl ether (3 mL) at 0 °C was added dropwise a solution of $HIO_4 \cdot 2H_2O$ (97 mg, 0.42 mmol) in THF (2 mL). The mixture was stirred for 2.5 h and then a saturated $NaHCO_3$ solution was added. The organic layer was separated and the aqueous layer was extracted with DCM. The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. Column chromatography (hexane/ethyl acetate = 10:1) yielded aldehyde **89** (155 mg; 90 %) as colorless oil. $[\alpha]_D^{20} = 2.2$ ($c = 1.00$, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 9.70$ (t, $J =$ 1.6 Hz, 1H), 7.24 (d, $J = 8.6$ Hz, 2H), 6.87 (d, $J = 8.8$ Hz, 2H), 5.03 (d, $J =$ 9.8 Hz, 1H), 4.39 (s, 2H), 3.80 (s, 3H), 3.50 (dd, $J = 9.1$, 5.1 Hz, 1H), 3.39 (dd, $J = 6.1$, 4.3 Hz, 1H), 3.20 (dd, $J = 9.2$, 7.8 Hz, 1H), 2.60–2.53 (m, 1H), 2.47–2.33 (m, 2H), 2.26–2.17 (m, 1H), 2.01–1.93 (m, 1H), 1.63 (s, 3H), 0.96 (d, $J = 7.1$ Hz, 3H), 0.90 (d, $J = 5.3$ Hz, 3H), 0.89 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 202.1$, 159.0, 132.5, 131.4, 131.4, 130.7, 129.1, 113.7, 78.7, 72.7, 72.4, 55.3, 42.2, 38.3, 35.8, 28.8, 27.5, 26.2, 24.4, 23.1, 18.4, 17.3, 15.1, −3.8, −3.9 ppm; IR (film): $\tilde{\nu} =$ 2958, 2930, 2856, 1725, 1513, 1249, 1089, 1037 cm^{-1}; HRMS (ESI): m/z: $[M-C_4H_9]^+$ calcd for $C_{22}H_{35}O_4Si$: 391.2305, found: 391.2308.

(*Z*)-(6*S*,7*R*,8*S*)-7-(*tert*-Butyldimethylsilanyloxy)-9-(4-methoxybenzyloxy)-4,6,8-trimethylnon-4-enoic acid (90): To a solution of aldehyde **87** (155 mg, 0.34 mmol) in *tert*-butyl alcohol (3 mL) with 2-methyl-2-butene (0.5 mL) was added dropwise a solution of $NaClO_2$ (465 mg, 5.2 mmol) and NaH_2PO_4 (465 mg) in water (2 mL). After 3 h, 0.01N NaOH was added and the aqueous layer was extracted with diethyl ether. 1N HCl was added until pH 2 was reached and the aqueous layer was extracted with DCM. The organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude acid **90** (160 mg), which was directly used for the following reaction. ^{1}H NMR (400 MHz, C_6D_6): $\delta = 7.27$ (d, $J = 8.6$ Hz, 2H), 6.82 (d, $J = 8.6$ Hz, 2H), 5.11 (d, $J =$ 10.1 Hz, 1H), 4.40 (d, $J = 2.0$ Hz, 2H), 3.60 (dd, $J = 9.1$, 5.3 Hz, 1H), 3.53 (dd, $J = 6.3$, 4.3 Hz, 1H), 3.33 (s, 3H), 3.32 (m, 1H), 2.81–2.72 (m, 1H), 2.37–2.20 (m, 4H), 2.18–2.11 (m, 1H), 1.53 (d, $J = 1.3$ Hz, 3H), 1.08 (d, $J = 7.1$ Hz, 3H), 1.04 (d, $J = 6.6$ Hz, 3H), 1.01 (s, 9H), 0.10 ppm (s, 6H); ^{13}C NMR (100 MHz, C_6D_6): $\delta = 179.1$, 159.7, 132.1, 131.8, 131.2, 129.6, 114.1, 79.1, 73.0, 72.6, 54.8, 39.0, 36.0, 32.7, 27.6, 26.4, 22.9, 18.7, 17.5, 15.4, −3.6, −3.7 ppm.

(*Z*)-(6*S*,7*R*,8*S*)-7-(*tert*-Butyldimethylsilyloxy)-9-(4-methoxybenzyloxy)-4,6,8-trimethylnon-4-enoic acid methyl ester (9): Crude acid **90** (10 mg, 0.022 mmol) in methanol (1 mL) was treated with diazomethane (0.5 mL, ca. 0.1 M in Et_2O) until the solution remained yellow. Acetic acid was added to quench excess diazomethane until the solution was colorless. The solvent was removed under educed pressure and purification by column chromatography (hexane/ethyl acetate = 10:1) yielded methyl ester **9** (11 mg; quant.). $[\alpha]_D^{20} = 2.20$ ($c = 0.5$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CHCl_3$): $\delta = 7.24$ (d, $J = 8.6$ Hz, 2H), 6.87 (d, $J = 8.6$ Hz, 2H), 5.02 (d, $J =$ 9.8 Hz, 1H), 4.39 (s, 2H), 3.80 (s, 3H), 3.66 (s, 3H), 3.50 (dd, $J = 9.1$, 4.8 Hz, 1H), 3.39 (dd, $J = 5.9$, 4.7 Hz, 1H), 3.20 (t, $J = 8.6$ Hz, 1H), 2.61–2.52 (m, 1H), 2.43–2.33 (m, 3H), 2.29–2.20 (m, 1H), 2.02–1.93 (m, 1H), 1.64 (d, $J = 1.3$ Hz, 3H), 0.96 (d, $J = 6.8$ Hz, 3H), 0,89 (d, $J = 6.1$ Hz, 3H), 0.89 (s, 9H), 0.02 ppm (s, 6H); ^{13}C NMR (100 MHz, $CHCl_3$): $\delta = 173.7$, 159.0, 131.5, 131,4, 131.0, 129.2, 113.7, 78.6, 72.6, 72.5, 55.3, 51.5, 38.4, 35.7, 32.7, 27.4, 26.1, 22.9, 18.4, 17.2, 14.9, −3.8, −3.9 ppm; IR (film): $\tilde{\nu} =$ 2957, 1741, 1513, 1249, 1087, 1038 cm^{-1}; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{27}H_{46}O_5Si$: 478.3115, found: 478.3107.

(*Z*)-(6*S*,7*R*,8*S*)-7-(*tert*-Butyldimethylsilanyloxy)-9-(4-methoxybenzyloxy)-4,6,8-trimethylnon-4-enoic acid 2,6-dimethylphenyl ester (91): To acid **90** (5 mg, 0.01 mmol) in DCM (1 mL) at room temperature under argon was added 2,6-dimethylphenol (2 mg, 0.015 mmol) followed by DMAP (1.5 mg, 0.011 mmol) and DIC (2 μL, 0.011 mmol) and the mixture was stirred for 18 h. Brine was added and the organic layer was separated. The aqueous layer was extracted with DCM and the combined organic phases were dried over $MgSO_4$ and the solvent was evaporated. Purification by column chromatography (hexane/ethyl acetate = 20:1) yielded aromatic ester **91** (6 mg; 99 %). $[\alpha]_D^{20} = 10.4$ ($c = 0.25$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CHCl_3$): $\delta = 7.23$ (d, $J = 8.6$ Hz, 2H), 7.05 (s, 3H), 6.85 (d, $J =$ 8.6 Hz, 2H), 5.09 (d, $J = 9.6$ Hz, 1H), 4.41 (d, $J = 11.4$ Hz, 1H), 4.37 (d, $J = 11.4$ Hz, 1H), 3.78 (s, 3H), 3.51 (dd, $J = 9.1$, 5.1 Hz, 1H), 3.42 (t, $J =$ 5.1 Hz, 1H), 3.21 (dd, $J = 8.9$, 8.2 Hz, 1H), 2.68–2.55 (m, 4H), 2.44–2.36 (m, 1H), 2.12 (s, 6H), 2.02–1.95 (m, 1H), 1.64 (d, $J = 1.2$ Hz, 3H), 0.97 (d, $J = 6.8$ Hz, 3H), 0.92 (d, $J = 6.6$ Hz, 3H), 0.89 (s, 9H), 0.04 (s, 3H), 0.03 ppm (s, 3H); ^{13}C NMR (100 MHz, $CHCl_3$): $\delta = 171.0$, 159.0, 148.2, 131.8, 131.3, 131.0, 129.1, 128.6, 125.8, 113.7, 78.6, 72.6, 72.5, 55.3, 38.4, 35.7, 32.6, 27.5, 26.2, 23.0, 18.4, 16.9, 16.3, 14.9, −3.8, −3.9 ppm; IR (film): $\tilde{\nu} =$ 2928, 1757, 1249 cm^{-1}; HRMS (ESI): m/z: $[M-C_4H_9]^+$ calcd for $C_{30}H_{43}O_5Si$: 511.2880, found: 511.2875.

(*Z*)-(6*S*,7*R*,8*S*)-*N*-[7-(*tert*-Butyldimethylsilanyloxy)-9-(4-methoxybenzyloxy)-4,6,8-trimethylnon-4-enoyl]-(1′*R*)-bornan-2′,10′-sultam (93): To a stirred solution of crude acid **90** (60 mg, 0.13 mmol), DMAP (16 mg, 0.13 mmol) and (1*R*)-camphore-2,10-sultam (29 mg, 0.13 mmol) in DCM (2 mL) under argon at room temperature was slowly added DIC (23 μL. 0.14 mmol). The mixture was stirred for 2 h, brine was added, and the layers were separated. The aqueous layer was extracted with DCM and the combined organic phases were dried over $MgSO_4$ and the solvent was evaporated. Purification by column chromatography (hexane/ethyl acetate = 3:1) yielded *N*-acyl sultam **93** (83 mg; 96 %). $[\alpha]_D^{20} = 34.95$ ($c = 1.58$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CHCl_3$): $\delta = 7.25$ (d, $J = 8.8$ Hz, 2H), 6.86 (d, $J = 8.8$ Hz, 2H), 5,03 (d, $J = 9.3$ Hz, 1H), 4.39 (s, 2H), 3.85 (dd, $J = 7.6$, 5.5 Hz, 1H), 3.80 (s, 3H), 3.51 (dd, $J = 9.3$, 5.1 Hz, 1H), 3.48 (d, $J =$ 13.9 Hz, 1H), 3.41 (d, $J = 13.4$ Hz, 1H), 3.39 (t, $J = 5.3$ Hz, 1H), 3.19 (t, $J = 8.7$ Hz, 1H), 2.82–2.69 (m, 2H), 2.64–2.55 (m, 1H), 2.53–2.46 (m, 1H), 2.32–2.20 (m, 1H), 2.15–2.02 (m, 2H), 1.99–1.84 (m, 4H), 1.65 (d, $J = 1.3$ Hz, 3H), 1.43–1.25 (m, 3H), 1.15 (s, 3H), 0.97 (s, 3H), 0.96 (d, $J =$ 7.1 Hz, 3H), 0.89 (d, $J = 6.8$ Hz, 3H), 0.88 (s, 9H), 0.01 ppm (s, 6H); ^{13}C NMR (100 MHz, $CHCl_3$): $\delta = 171.5$, 159.0, 131.3, 131.1, 129.1, 113.7, 78.5, 72.6, 72.5, 65.2, 55.3, 52.9, 48.4, 47.7, 44.7, 38.6, 38.5, 35.4, 34.0, 32.9, 26.9, 26.5, 26.2, 23.0, 20.9, 19.9, 18.4, 16.8, 14.7, −3.8, −3.9 ppm; IR (film): $\tilde{\nu} =$ 2958, 2855, 1698, 1513, 1461, 1332, 1248, 1212, 1171, 1133, 1085 cm^{-1}. HRMS (ESI): m/z: $[M+Na]^+$ calcd for $C_{36}H_{59}O_6SNSiNa$: 684.3730, found: 684.3736.

(*Z*)-(2*S*,6*S*,7*R*,8*S*)-*N*-[7-(*tert*-Butyldimethylsilanyloxy)-9-(4-methoxybenzyloxy)-2,4,6,8-tetramethylnon-4-enoyl]-(1′*R*)-bornan-2′,10′-sultam (94): To *N*-acyl sultam **93** (35 mg, 0.05 mmol) in THF (1 mL) at −78 °C was slowly added NaHMDS (55 μL, 1 M in THF, 0.055 mmol) and the solution was stirred for 1 h. MeI (9 μL, 0.1 mmol) was added and stirring was continued for 1.5 h. The reaction was quenched by the addition of a saturated NH_4Cl solution and the layers were separated. The aqueous layer was extracted with DCM and the combined organic phases were dried over $MgSO_4$ and the solvent was evaporated. Purification by column chromatography (hexane/ethyl acetate = 5:1) yielded α-methylated *N*-acyl sultam **94** (30 mg; 89 %). $[\alpha]_D^{20} = 55.3$ ($c = 1.00$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CHCl_3$): $\delta = 7.25$ (d, $J = 8.6$ Hz, 2H), 6.86 (d, $J = 8.6$ Hz, 2H), 5.09 (d, $J =$ 9.9 Hz, 1H), 4.39 (d, $J = 1.8$ Hz, 2H), 3.87 (t, $J = 6.3$ Hz, 1H), 3.80 (s, 3H), 3.49 (dd, $J = 14.8$, 9.7 Hz, 1H), 3.49 (d, $J = 13.6$ Hz, 1H), 3.42 (d, $J =$ 13.6 Hz, 1H), 3.40 (t, $J = 5.2$ Hz, 1H), 3.19 (t, $J = 8.7$ Hz, 1H), 2.65–2.56 (m, 1H), 2.40 (dd, $J = 13.5$, 9.5 Hz, 1H), 2.23 (dd, $J = 13.2$, 4.8 Hz, 1H), 2.08–1.93 (m, 3H), 1.91–1.79 (m, 3H), 1.64 (s, 3H), 1.44–1.23 (m, 3H), 1.16 (s, 3H), 1.12 (d, $J = 6.8$ Hz, 3H), 0.97 (s, 3H), 0.96 (d, $J = 6.8$ Hz, 3H), 0.90 (d, $J = 7.1$ Hz, 3H), 0.88 (s, 9H), 0.02 (s, 3H), 0.01 ppm (s, 3H); ^{13}C NMR (100 MHz, $CHCl_3$): $\delta = 176.0$, 159.0, 132.8, 131.1, 130.2, 129.1, 113.7, 78.5, 72.7, 72.5, 65.2, 55.3, 53.2, 48.3, 47.7, 44.6, 38.6, 38.4, 37.9, 35.5, 34.2, 32.9, 29.5, 26.4, 26.2, 23.0, 20.9, 19.9, 18.4, 17.8, 16.9, 14.7, −3.8, −3.9 ppm; IR (film): $\tilde{\nu} =$ 2959, 1696, 1513, 1332, 1248, 1132, 1036 cm^{-1}; HRMS (ESI): m/z: $[M+Na]^+$ calcd for $C_{37}H_{61}O_6SNSiNa$: 698.3887, found: 698.3902.

(*Z*)-(2*S*,6*S*,7*R*,8*S*)-7-(*tert*-Butyldimethylsilanyloxy)-9-(4-methoxybenzyloxy)-2,4,6,8-tetramethylnon-4-enal (95): To *N*-acyl sultam **94** (65 mg, 0.092 mmol) in DCM (2 mL) at −100 °C was slowly added DIBALH (62 μL, 1.5 M in toluene, 0.92 mmol) and the mixture was stirred for 1 h. A second equivalent of DIBALH (62 μL, 1.5 M in toluene, 0.92 mmol) was added and stirring was continued for 1 h, after which time the temperature reached −65 °C. The reaction was quenched by the addition of a small amount of methanol, and potassium sodium tartrate was added and

stirred vigorously at room temperature for 2 h. The layers were separated and the aqueous layer was extracted with DCM. The combined organic phases were dried over $MgSO_4$ and the solvent was evaporated. Purification by column chromatography (hexane/ethyl acetate = 10:1) yielded aldehyde **95** (40 mg; 94%). $[\alpha]_D^{20} = 3.92$ ($c = 1.30$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 9.61$ (d, $J = 1.5$ Hz, 1H), 7.24 (d, $J = 8.8$ Hz, 2H), 6.87 (d, $J = 8.8$ Hz, 2H), 5.12 (d, $J = 10.6$ Hz, 1H), 4.39 (s, 2H), 3.80 (s, 3H), 3.48 (dd, $J = 9.1$, 5.0 Hz, 1H), 3.38 (dd, $J = 5.8$, 4.8 Hz, 1H), 3.19 (dd, $J = 8.8$, 8.1 Hz, 1H), 2.57–2.43 (m, 2H), 2.22 (dd, $J = 13.9$, 5.8 Hz, 1H), 2.16 (dd, $J = 13.8$, 9.6 Hz, 1H), 2.26–2.17 (m, 1H), 2.00–1.88 (m, 1H), 1.63 (d, $J = 1.2$ Hz, 3H), 1.00 (d, $J = 6.8$ Hz, 3H), 0.94 (d, $J = 6.8$ Hz, 3H), 0.90 (d, $J = 6.8$ Hz, 3H), 0.89 (s, 9H), 0.03 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 204.5$, 158.6, 134.0, 133.0, 130.9, 129.3, 113.8, 78.5, 72.7, 72.4, 57.6, 55.2, 44.5, 38.4, 35.7, 32.6, 26.8, 23.3, 17.1, 14.9, 13.0, −4.1, −4.2 ppm; IR (film): $\tilde{\nu} =$ 2958, 2930, 2856, 1727, 1513, 1472, 1462, 1249, 1091, 1037 cm^{-1}; HRMS (ESI): *m/z*: $[M]^+$ calcd for $C_{27}H_{46}O_4Si$: 462.3165, found: 462.3171.

(*S*)-4-Benzyl-3-[(*Z*)-(2*S*,3*R*,4*S*,8*S*,9*R*,10*S*)-9-(*tert*-butyldimethylsilanyloxy)-3-hydroxy-11-(4-methoxybenzyloxy)-2,4,6,8,10-pentamethylundec-6-enoyl]oxazolidin-2-one (108): To a stirred solution of acyloxazolidinone **107** (17 mg, 0.071 mmol) in DCM (0.7 mL) at −78 °C under argon was slowly added dibutylboron triflate (74 μL, 1 M in DCM, 0.074 mmol) followed by triethylamine (12 μL, 0.081 mmol) and stirring was continued for 10 min. The reaction mixture was warmed to 0 °C for 1 h and then recooled to −78 °C. Aldehyde **95** (29 mg, 0.062 mmol) in DCM (0.5 mL) was added dropwise. After 1 h the reaction mixture was warmed to 0 °C and stirred for 1.5 h. A pH 7 buffer solution (2 mL), methanol (1 mL), and H_2O_2 (0.1 mL, 30% aqueous) were added and the mixture was stirred for 1 h at room temperature. Layers were separated and the aqueous layer was extracted with DCM, the combined organic layers were dried over $MgSO_4$, and the solvent was evaporated. The crude aldol product was purified by column chromatography (hexane/ethyl acetate = 5:1 to 3:1) to yield aldol adduct **108** (28 mg; 65%) and aldehyde 95 (10 mg; 34%). $[\alpha]_D^{20} = 32.2$ ($c = 0.45$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.36$–7.28 (m, 4H), 7.24–7.19 (m, 3H), 6.86 (d, $J = 8.5$ Hz, 2H), 5.05 (d, $J = 10.0$ Hz, 1H), 4.67 (ddt, $J = 9.5$, 6.9, 3.43 Hz, 1H), 4.44 (d, $J = 11.5$ Hz, 1H), 4.38 (d, $J = 11.5$ Hz, 1H), 4.18 (m, 2H), 3,94 (m, 1H), 3.80 (s, 3H), 3.65 (dd, $J = 10.0$, 5.0 Hz, 1H), 3.58 (dd, $J = 9.3$, 4.7 Hz, 1H), 3.35 (dd, $J = 6.6$, 3.6 Hz, 1H), 3.24 (dd, $J = 13.3$, 3.3 Hz, 1H), 3.20–3.16 (m, 2H), 2.77 (dd, $J = 13.3$, 9.5 Hz, 1H), 2.64 (dt, $J = 9.9$, 6.7 Hz, 1H), 2.10 (dd, $J = 13.3$, 6.7 Hz, 1H), 1.98–1.86 (m, 2H), 1.77 (m, 1H), 1.63 (d, $J = 1.0$ Hz, 3H), 1.20 (d, $J = 6.7$ Hz, 3H), 0.94 (d, $J = 7.0$ Hz, 3H), 0.89 (d, $J = 6.2$ Hz, 3H), 0.88 (s, 9H), 0.88 (d, $J = 6.3$ Hz, 3H), 0.04 (s, 3H), 0.02 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 177.0$, 159.1, 152.8, 135.1, 132.0, 131.8, 130.7, 129.4, 128.9, 127.4, 113.7, 79.1, 74.0, 72.7, 72.5, 65.9, 55.3, 55.1, 40.5, 38.2, 37.7, 35.9, 35.8, 33.4, 29.2, 26.2, 23.1, 18.4, 17.3, 15.6, 14.4, 12.7, −3.7, −3.8 ppm; IR (film): $\tilde{\nu} =$ 2928, 1781, 1701, 1512, 1458, 1388, 1248, 1080 cm^{-1}; HRMS (ESI): *m/z*: $[M]^+$ calcd for $C_{40}H_{61}NO_7Si$: 695.4217, found: 695.4225.

(*S*)-4-Benzyl-3-[(*Z*)-(2*S*,3*R*,4*S*,8*S*,9*R*,10*S*)-3,9-bis-(*tert*-butyldimethylsilanyloxy)-11-(4-methoxybenzyloxy)-2,4,6,8,10-pentamethylundec-6-enoyl]-oxazolidin-2-one (109): To a stirred solution of alcohol **108** (14 mg, 0.019 mmol) in DCM (1 mL) was added 2,6-lutidine (4 μL, 0.029 mmol) and TBSOTf (5 μL, 0.023 mmol). After 1 h, the reaction was quenched with saturated NH_4Cl solution and extracted with DCM. The combined organic solutions were dried over $MgSO_4$ and the solvent was evaporated. Purification by column chromatography (hexane/ethyl acetate = 5:1) yielded **109** (16 mg; quant.) as a colorless oil. $[\alpha]_D^{20} = 48$ ($c = 0.6$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.35$–7.27 (m, 3H), 7.24–7.19 (m, 4H), 6.86 (d, $J = 8.5$ Hz, 2H), 5.02 (d, $J = 10.0$ Hz, 1H), 4.65–4.59 (m, 1H), 4.41 (d, $J = 11.5$ Hz, 1H), 4.36 (d, $J = 11.8$ Hz, 1H), 4.16 (d, $J = 5.0$ Hz, 2H), 3.98 (m, 2H), 3.80 (s, 3H), 3.49 (dd, $J = 9.2$, 4.9 Hz, 1H), 3.37 (dd, $J = 6.0$, 4.9 Hz, 1H), 3.26 (dd, $J = 13.3$, 3.3 Hz, 1H), 3.21 (t, $J = 8.9$ Hz, 1H), 2.75 (dd, $J = 13.3$, 9.5 Hz, 1H), 2.51 (m, 1H), 2.21 (t, $J = 12.4$ Hz, 1H), 1.96 (m, 1H), 1.86 (m, 1H), 1.75 (m, 1H), 1.57 (s, 3H), 1.24 (d, $J = 6.3$ Hz, 3H), 0.95 (d, $J = 7.0$ Hz, 3H), 0.93 (s, 9H), 0.88 (d, $J = 6.5$ Hz, 3H), 0.88 (s, 9H), 0.74 (d, $J = 6.8$ Hz, 3H), 0.09 (s, 3H), 0.06 (s, 3H), 0.01 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 176.0$, 159.0, 152.8, 135.3, 131.2, 129.5, 129.1, 128.9, 127.4, 113.7, 78.5, 76.9, 72.7, 72.5, 65.9, 55.6, 55.3, 41.6, 38.7, 37.7, 36.5, 35.5, 26.1, 25.7, 23.1, 18.4, 17.0, 14.5, 14.4, 14.0, −3.5, −3.8, −4.0 ppm; IR (film): $\tilde{\nu} =$ 2930, 1784, 1698, 1514, 1463, 1385, 1249, 1040 cm^{-1}. HRMS (ESI): *m/z*: $[M+Na]^+$ calcd for $C_{46}H_{75}NO_7Si_2Na$: 832.4980, found: 832.4987.

(*Z*)-(2*R*,3*R*,4*S*,8*S*,9*R*,10*S*)-3,9-Bis-(*tert*-butyldimethylsilanyloxy)-11-(4-methoxybenzyloxy)-2,4,6,8,10-pentamethyl-undec-6-en-1-ol (110): To **109** (18 mg, 0.022 mmol) in diethyl ether (0.5 mL) with methanol (10 μL) at 0 °C was slowly added $LiBH_4$ (12 μL, 2 M in THF, 0. 024 mmol). After 1.5 h, the reaction was quenched by the addition of brine and the layers were separated. The aqueous layer was extracted with DCM and the combined organic layers were dried over $MgSO_4$. After evaporation of the solvent, purification by column chromatography (hexane/ethyl acetate = 5:1) yielded **110** (12 mg; 86%). $[\alpha]_D^{20} = 1.81$ ($c = 0.55$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.24$ (d, $J = 8.8$ Hz, 2H), 6.86 (d, $J = 8.8$ Hz, 2H), 5.02 (d, $J = 10.0$ Hz, 1H), 4.40 (d, $J = 11.5$ Hz, 1H), 4.36 (d, $J = 11.5$ Hz, 1H), 3.80 (s, 3H), 3.60 (m, 2H), 3.49–3.43 (m, 2H), 3.38 (dd, $J = 6.2$, 4.6 Hz, 1H), 3.21 (t, $J = 8.8$ Hz, 1H), 2.51 (m, 1H), 2.16 (t, $J = 12.0$ Hz, 1H), 1.99–1.88 (m, 2H), 1.83 (m, 1H), 1.77 (m, 1H), 1.59 (s, 3H), 0.94 (d, $J = 7.0$ Hz, 3H), 0.91 (d, $J = 6.5$ Hz, 3H), 0.92 (s, 9H), 0.89 (s, 9H), 0.88 (d, $J = 8.1$ Hz, 3H), 0.79 (d, $J = 6.8$ Hz, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.03 (s, 3H), 0.02 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 159.0$, 131.9, 131.5, 131.1, 129.1, 113.7, 78.5, 77.8, 72.6, 72.5, 66.4, 55.3, 39.4, 38.5, 36.6, 35.6, 34.5, 26.1, 26.0, 23.1, 18.4, 18.3, 17.0, 15.0, 14.8, 12.3, −3.8, −3.9, −4.1 ppm; IR (film): $\tilde{\nu} =$ 2929, 2856, 1613, 1513, 1462, 1250, 1039 cm^{-1}; HRMS (ESI): *m/z*: $[M+Na]^+$ calcd for $C_{36}H_{68}O_5Si_2Na$: 636.4605, found: 636.4598.

(*Z*)-(3*S*,4*S*,5*R*,6*R*,7*S*,11*S*,12*R*,13*S*)-6,12-Bis-(*tert*-butyldimethylsilanyloxy)-14-(4-methoxybenzyloxy)-3,5,7,9,11,13-hexamethyltetradeca-1,9-dien-4-ol (111): To alcohol **110** (10 mg, 0.015 mmol) in DMSO (0.5 mL) at room temperature under argon was added IBX (9 mg, 0.031 mmol) and the mixture was stirred for 2 h. Water and diethyl ether were added and the phases were separated. The aqueous layer was extracted with diethyl ether and the combined ethereal layers were dried over $MgSO_4$. After evaporation of the solvent the crude aldehyde was used without further purification. To (*E*)-(*R*,*R*)-crotyl boronate (0.5 mL, 0.3 M in toluene, 0.15 mmol) at −78 °C was very slowly added the aldehyde (9 mg, 0.015 mmol) in toluene (0.5 mL). The mixture was kept at −78 °C overnight and then 1 N NaOH was added and the mixture was stirred for 45 min at 0 °C. The layers were separated and the aqueous layer was extracted with DCM. The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. Purification by column chromatography (hexane/ethyl acetate = 10:1) yielded olefin **111** (9 mg; 87%) as a single diastereoisomer. $[\alpha]_D^{20} = 12$ ($c = 0.4$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.24$ (d, $J = 8.6$ Hz, 2H), 6.86 (d, $J = 8.6$ Hz, 2H), 5.79–5.69 (m, 1H), 5.15–5.09 (m, 2H), 5.02 (d, $J = 10.1$ Hz, 1H), 4.40 (d, $J = 11.6$ Hz, 1H), 4.36 (d, $J = 11.6$ Hz, 1H), 3.80 (s, 3H), 3.64 (dd, $J = 5.6$, 3.3 Hz, 1H), 3.48 (dd, $J = 9.1$, 4.5 Hz, 1H), 3.39 (dd, $J = 5.7$, 5.1 Hz, 1H), 3.31 (dt, $J = 7.3$, 3.7 Hz, 1H), 3.21 (t, $J = 8.8$ Hz, 1H), 2.52 (m, 1H), 2.29 (dd, $J = 14.6$, 7.5 Hz, 1H), 2.22 (t, $J = 12.1$ Hz, 1H), 1.99–1.87 (m, 2H), 1.83–1.77 (m, 2H), 1.60 (s, 3H), 0.99 (d, $J = 6.8$ Hz, 3H), 0.95 (d, $J = 7.3$ Hz, 3H), 0.93 (d, $J = 7.0$ Hz, 3H), 0.92 (s, 9H), 0.89 (s, 9H), 0.89 (d, $J = 8.1$ Hz, 3H), 0.75 (d, $J = 6.8$ Hz, 3H), 0.09 (s, 6H), 0.03 (s, 3H), 0.02 ppm (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.1$, 141.3, 132.1, 131.4, 131.0, 129.1, 116.4, 113.7, 78.8, 78.5, 75.8, 72.6, 72.5, 55.3, 42.4, 38.6, 37.9, 36.2, 35.6, 35.1, 26.2, 26.1, 23.2, 18.5, 18.4, 16.9, 16.7, 14.6, 13.5, 9.4, −3.3, −3.7, −3.9 ppm; IR (film): $\tilde{\nu} =$ 2958, 2930, 2856, 1514, 1463, 1250, 1079, 1040 cm^{-1}; HRMS (ESI): *m/z*: $[M]^+$ calcd for $C_{40}H_{74}O_5Si_2$: 690.5075 , found: 690.5081.

(*Z*)-(2*R*,3*S*,4*R*,5*R*,6*S*,10*S*,11*R*,12*S*)-5,11-Bis-(*tert*-butyldimethylsilanyloxy)-13-(4-methoxybenzyloxy)-4,6,8,10,12-pentamethyl-2-oxiranyltridec-8-en-3-ol (112): To olefin **111** (9 mg, 0.013 mmol) in DCM (0.5 mL) was added $[VO(acac)_2]$ (0.2 mg, 5 mol%) at 0 °C followed by *t*BuOOH (5 μL, 5.5 M in decane, 0.026 mmol). The reaction mixture was kept overnight at 0 °C. A saturated $Na_2S_2O_3$ solution was added and the layers were separated. The aqueous phase was extracted with DCM and the combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. Column chromatography (hexane/ethyl acetate = 5:1) yielded epoxide **112** (8 mg; 87%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.24$

(d, J=8.6 Hz, 2H), 6.86 (d, J=8.6 Hz, 2H), 5.03 (d, J=10.4 Hz, 1H), 4.40 (d, J=11.6 Hz, 1H), 4.36 (d, J=11.6 Hz, 1H), 3.80 (s, 3H), 3.68 (dd, J=6.1, 3.0 Hz, 1H), 3.64 (dt, J=8.2, 2.8 Hz, 1H), 3.49 (dd, J=9.1, 4.8 Hz, 1H), 3.40 (t, J=5.6 Hz, 1H), 3.21 (t, J=8.7 Hz, 1H), 2.92 (ddd, J=7.8, 4.0, 2.8 Hz, 1H), 2.75 (t, J=4.4 Hz, 1H), 2.53 (m, 1H), 2.48 (dd, J=4.8, 2.7 Hz, 1H), 2.40 (d, J=3.0 Hz, 1H (OH)), 2.27 (t, J=12.2 Hz, 1H), 2.00–1.93 (m, 2H), 1.84–1.78 (m, 2H), 1.62 (s, 3H), 0.97 (d, J=6.8 Hz, 3H), 0.95 (d, J=6.8 Hz, 3H), 0.92 (s, 9H), 0.89 (s, 12H), 0.86 (d, J=6.3 Hz, 3H), 0.75 (d, J=6.8 Hz, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.03 (s, 3H), 0.02 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=159.0, 132.1, 131.3, 131.1, 129.1, 113.7, 78.7, 78.5, 77.1, 72.6, 72.5, 55.8, 55.3, 45.1, 4.0, 38.6, 38.2, 36.2, 35.6, 34.9, 26.2, 26.1, 23.2, 18.5, 18.4, 16.9, 14.6, 14.1, 13.3, 12.9, 9,2, −3.3, −3.7, −3.9 ppm; IR (film): $\tilde{\nu}$= 2929, 1513, 1462, 1250, 1039 cm^{-1}; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{40}H_{74}O_6Si_2$: 706.5024, found: 706.5029.

(*Z*)-(2*S*,3*S*,4*R*,5*R*,6*S*,10*S*,11*R*,12*S*)-5,11-Bis-(*tert*-butyldimethylsilanyloxy)-13-(4-methoxybenzyloxy)-2,4,6,8,10,12-hexamethyltridec-8-ene-1,3-diol (113): To epoxide **112** (7 mg, 0.0099 mmol) in Et_2O/THF 1/1 (1 mL) at 0 °C was added $HIO_4{\cdot}2H_2O$ (3 mg, 0.0014 mmol) and the mixture was stirred for 16 h at 0 °C. A saturated $NaHCO_3$ solution was added and diluted with DCM, the layers were separated, and the aqueous layer was extracted with DCM. The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. The residue was taken up in methanol (1 mL) and $NaBH_4$ was added at 0 °C. After 30 min, brine was added and DCM, the layers were separated and the aqueous layer was extracted with DCM. The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. Column chromatography (hexane : ethyl acetate=3:1) yielded alcohol **113** (2 mg; 29%, 51% b.r.s.m.) and epoxide **112** (3 mg). $[\alpha]_D^{20}$=4 (c=0.1, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$): δ=7.24 (d, J=8.6 Hz, 2H), 6.86 (d, J=8.6 Hz, 2H), 5.04 (d, J=10.2 Hz, 1H), 4.39 (d, J=11.7 Hz, 1H), 4.37 (d, J=11.7 Hz, 1H), 3.80 (s, 3H), 3.68 (t, J=3.9 Hz, 1H), 3.66 (m, 2H), 3.54 (dd, J=9.4, 0.1 Hz, 1H), 3.49 (dd, J=9.1, 4.5 Hz, 1H), 3.38 (dd, J=6.0, 4.9 Hz, 1H), 3.21 (t, J=8.7 Hz, 1H), 2.53 (m, 1H), 2.20 (t, J=12.3 Hz, 1H), 1.97 (m, 1H), 1.91 (m, 1H), 1.88–1.83 (m, 2H), 1.60 (s, 3H), 0.95 (d, J=6.8 Hz, 6H), 0.91 (d, J=9.5 Hz, 3H), 0.92 (s, 9H), 0.88 (s, 9H), 0.79 (d, J=6.8 Hz, 3H), 0.76 (d, J=6.8 Hz, 3H), 0.12 (s, 3H), 0.11 (s, 3H), 0.03 (s, 3H), 0.02 ppm (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=159.8, 131.8, 129.1, 116.1, 113.7, 81.4, 80.4, 78.5, 72.6, 68.8, 55.3, 38.5, 37.6, 37.2, 36.9, 35.7, 35.0, 26.2, 26.1, 23.2, 16.8, 14.8, 14.5, 13.7, 9.8, 8.2, −3.3, −3.8, −4.6 ppm; IR (film): $\tilde{\nu}$= 3325, 2928, 2855, 1513, 1466, 1364, 1248, 1098, 1039 cm^{-1}; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{39}H_{74}O_6Si_2$: 694.5024, found: 694.5018.

(2*S*,4*S*,5*S*)-4-[(*Z*)-(1*R*,2*R*,3*S*,7*S*,8*R*,9*S*)-2,8-Bis-(*tert*-butyldimethylsilanyloxy)-10-(4-methoxybenzyloxy)-1,3,5,7,9-pentamethyl-dec-5-enyl]-2-(4-methoxyphenyl)-5-methyl[1,3]dioxane (92): To diol **111** (1 mg, 0.0014 mmol) in DCM (0.5 mL) was added anisaldehyde dimethyl acetal (1 μL, 0.0056 mmol) and CSA (cat.) at room temperature under argon. The mixture was stirred for 1.5 h. Brine was added and the mixture was diluted with DCM. The layers were separated and the aqueous layer was extracted with DCM. The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. Column chromatography (hexane/ethyl acetate=15:1) yielded acetal **92** (1 mg; 86%) as a colorless oil. Data were in every aspect identical with the literature data. $[\alpha]_D^{20}$=24 (c=0.05, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ=7.37 (d, J=8.7 Hz, 2H), 7.23 (d, J=8.6 Hz, 2H), 6.87 (d, J=8.6 Hz, 2H), 6.85 (d, J=8.7 Hz, 2H), 5.38 (s, 1H), 5.01 (d, J=10.2 Hz, 1H), 4.39 (d, J=11.7 Hz, 1H), 4.35 (d, J=11.7 Hz, 1H), 4.10 (dd, J=10.9, 4.5 Hz, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 3.61 (dd, J=7.0, 1.7 Hz, 1H), 3.51 (dd, J=9.8, 1.9 Hz, 1H), 3.48 (t, J=11.1 Hz, 1H), 3.47 (dd, J=9.1, 4.9 Hz, 1H), 3.38 (dd, J=5.8, 4.7 Hz, 1H), 3.19 (t, J=8.9 Hz, 1H), 2.51 (m, 1H), 2.32 (t, J=12.1 Hz, 1H), 2.05 (m, 1H), 1.99–1.94 (m, 2H), 1.88 (m, 1H), 1.67 (d, J=11.7 Hz, 1H), 1.55 (s, 3H), 1.01 (d, J=7.2 Hz, 3H), 0.94 (d, J=6.8 Hz, 3H), 0.91 (s, 9H), 0.89 (d, J=6.9 Hz, 3H), 0.88 (s, 9H), 0.74 (d, J=6.8 Hz, 3H), 0.73 (d, J=6.4 Hz, 3H), 0.03 (s, 3H), 0.018 (s, 3H), 0.014 (s, 3H), 0.012 ppm (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=159.7, 159.0, 131.9, 131.5, 129.0, 127.3, 113.7, 113.4, 101.0, 83.3, 78.42, 78.40, 73.3, 72.6, 72.5, 55.3, 55.2, 38.7, 38.2, 37.6, 35.6, 33.6, 30.8, 26.2, 26.1, 23.1, 18.43, 18.39, 17.0, 14.6, 12.5, 12.1, 10.9, −3.6, −3.7, −3.8, −3.9 ppm; IR (film): $\tilde{\nu}$= 2929, 1514, 1470, 1242, 830 cm^{-1}; HRMS (ESI): m/z: $[M]^+$ calcd for $C_{47}H_{80}O_7Si_2$: 812.5443, found: 812.5449.

(*S*)-2-*tert*-Butoxymethyl-3-hydroxy-2-methylpropionic acid methyl ester (115): To a solution of (*R*)-2-*tert*-butoxymethyl-2-methylmalonic acid monomethyl ester (**114**) (1.20 g, 5.5 mmol) in THF (15 mL) at 0 °C under an argon atmosphere, was added Et_3N (0.84 mL, 6.05 mmol) followed by methyl chloroformate (0.47 mL, 6.05 mmol). After 10 min at 0 °C, the reaction mixture was warmed to room temperature and stirred for 45 min. The white precipitate was filtered off, washed with Et_2O, and concentrated. To the residue was added MeOH (15 mL) and the mixture was cooled to 0 °C. $NaBH_4$ (416 mg, 11 mmol) was added portionwise. After 1 h, the reaction was quenched with a saturated solution of NH_4Cl, and extracted with DCM. The organic extracts were dried over $MgSO_4$ and the organic solvent was removed under reduced pressure. Column chromatography (hexane/ethyl acetate=3:1) gave alcohol **115** (934 mg; 83%). $[\alpha]_D^{20}$=2.00 (c=1.3, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ=3.80 (dd, J=10.9, 5.4 Hz, 1H), 3.74–3.69 (m, 2H), 3.71 (s, 3H), 3.36 (d, J=8.6 Hz, 1H), 2.92 (dd, J=7.6, 5.6 Hz, 1H (OH)), 1.16 (s, 9H), 1.15 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=175.8, 73.4, 67.7, 66.4, 51.9, 48.6, 27.5, 18.0, 14.0 ppm; IR (film): $\tilde{\nu}$= 3467, 2975, 1732, 1364, 1234, 1197, 1084, 1049 cm^{-1}; HRMS (ESI): m/z: $[M-CH_3]^+$ calcd for $C_9H_{17}O_4$: 189.1127, found: 189.1129.

(*R*)-2-*tert*-Butoxymethyl-2-methyl-3-oxopropionic acid methyl ester (116): To a stirred solution of alcohol **115** (3.50 g, 17.13 mmol) in dimethyl sulfoxide (50 mL) was added IBX (9.40 g, 34.26 mmol) and stirring was continued for 2.5 h. Water and diethyl ether were added and the organic layer was separated. The aqueous layer was extracted with diethyl ether and the combined ethereal phases were dried over $MgSO_4$ and the solvent was evaporated. Column chromatography (hexane/ethyl acetate=5:1) yielded aldehyde **116** (2.80 g; 80%) as a colorless oil. $[\alpha]_D^{20}$=0.86 (c=1.4, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ=9.79 (s, 1H), 3.80 (d, J=8.6 Hz, 1H), 3.75 (s, 3H), 3.52 (d, J=8.3 Hz, 1H), 1.30 (s, 3H), 1.14 ppm (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=199.8, 171.8, 73.4, 65.0, 58.1, 52.3, 27.2, 15.0 ppm; IR (film): $\tilde{\nu}$= 1724, 1455, 1237, 1195, 1087 cm^{-1}; HRMS (ESI): m/z: $[M-CH_3]^+$ calcd for $C_9H_{15}O_4$: 187.0970, found: 187.0973.

(2*R*,3*R*,4*R*)-4-((*R*)-4-Benzyl-2-oxooxazolidine-3-carbonyl)-2-*tert*-butoxymethyl-3-hydroxy-2-methylhexanoic acid methyl ester (117): To a stirred solution of (*R*)-4-benzyl-3-butyryl-oxazolidin-2-one (**122**) (612 mg, 2.47 mmol) in DCM (3 mL) at −78 °C under argon was slowly added dibutylboron triflate (3.2 mL, 1 M in DCM, 3.2 mmol) followed by triethylamine (0.48 mL, 3.45 mmol) and stirring was continued for 30 min. The reaction mixture was warmed to 0 °C for 1 h and then recooled to −78 °C. Aldehyde **116** (500 mg, 2.47 mmol) in DCM (1 mL) was added dropwise. After 30 min the reaction mixture was warmed to 0 °C and stirred for 3 h. A pH 7 buffer solution (10 mL), methanol (3 mL), and H_2O_2 (3 mL, 30% aqueous) were added and the mixture was stirred for 2 h at room temperature. The layers were separated and the aqueous layer was extracted with DCM, and the combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. The crude aldol product was purified by column chromatography (hexane/ethyl acetate=10:1 to 3:1) to yield **117** (950 mg; 85%) as a pale yellow oil. $[\alpha]_D^{20}$=−38.47 (c=1.24, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.35–7.21 (m, 5H), 4.60–4.54 (m, 1H), 4.23–4.07 (m, 4H), 3.87 (d, J=9.0 Hz, 1H), 3.77 (d, J=10.3 Hz, 1H), 3.64 (s, 3H), 3.43 (d, J=9.0 Hz, 1H), 3.33 (dd, J=13.2, 3.1 Hz, 1H), 2.68 (dd, J=13.3, 10.3 Hz, 1H), 1.97–1.83 (m, 2H), 1.39 (s, 3H), 1.19 (s, 9H), 0.98 ppm (t, J=7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=175.7, 174.9, 153.3, 135.6, 129.3, 128.9, 127.3, 76.3, 74.0, 65.9, 65.7, 63.8, 55.9, 52.0, 49.5, 46.4, 38.1, 27.2, 23,4, 19.3, 10.7 ppm; IR (film): $\tilde{\nu}$= 2974, 1781, 1718, 1387, 1208, 1072 cm^{-1}; HRMS (ESI): m/z: $[M+Na]^+$ calcd for $C_{24}H_{35}O_7Na$: 472.2311, found: 472.2323.

(2*R*,3*R*,4*S*)-2-*tert*-Butoxymethyl-3-hydroxy-4-hydroxymethyl-2-methylhexanoic acid methyl ester (118): To aldol adduct **117** (440 mg, 0.98 mmol) in diethyl ether (10 mL) and methanol (20 μL) at 0 °C was slowly added $LiBH_4$ (21 mg, 0.98 mmol). After 30 min the reaction was quenched by the addition of saturated NH_4Cl solution and the layers were separated. The aqueous layer was extracted with DCM and the combined organic layers were dried over $MgSO_4$. After evaporation of

the solvent, the crude diol was purified by column chromatography (hexane/ethyl acetate = 3:1) to yield **118** (215 mg; 80%) as a colorless oil. $[\alpha]_D^{20} = 19.90$ ($c = 0.97$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.99$ (dd, $J = 8.3$, 2.0 Hz, 1H), 3.90 (d, $J = 8.6$ Hz, 1H (OH)), 3.76–3.66 (m, 2H), 3.70 (s, 3H), 3.64 (d, $J = 8.7$ Hz, 1H), 3.54 (d, $J = 8.7$ Hz, 1H), 1.53–1.39 (m, 2H), 1.36–1.27 (m, 1H), 1.23 (s, 3H), 1.14 (s, 9H), 0.94 ppm (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 176.9$, 77.6, 73.5, 66.6, 64.6, 60.3, 52.0, 49.9, 43.3, 27.2, 18.1, 16.7, 12.1 ppm; IR (film): $\tilde{\nu} = 3435$, 3974, 1728, 1364, 1234, 1197, 1141, 1079, 1046 cm^{-1}; HRMS (ESI): *m/z*: $[M+Na]^+$ calcd for $C_{14}H_{28}O_5Na$: 299.1834, found: 299.1832.

(3*R*,4*R*,5*S*)-3-*tert*-Butoxymethyl-5-ethyl-4-hydroxy-3-methyltetrahydropyran-2-one (11): To a stirred solution of ester **118** (180 mg, 0.65 mmol) in methanol (8 mL) was added K_2CO_3 (180 mg, 1.3 mmol) and stirring was continued for 3 h. The mixture was diluted with water, acidified with 1N HCl, and extracted with DCM. After drying the organic layers over $MgSO_4$, the solvent was removed to yield lactone **11** (159 mg; quant.) as white crystals, which was directly used in the following fragmentation. For analytical purposes a small sample was purified by column chromatography (hexane/ethyl acetate = 3:1). $[\alpha]_D^{20} = 11.56$ ($c = 1.15$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 4.37$ (dd, $J = 11.49$, 4.67 Hz, 1H), 3.88 (t, $J = 10.99$ Hz, 1H), 3.83 (d, $J = 8.84$ Hz, 1H), 3.67 (d, $J = 7.83$ Hz, 1H (OH)), 3.56 (d, $J = 8.59$ Hz, 1H), 3.49 (dd, $J = 9.22$, 8.21 Hz, 1H), 2.07–1.97 (m, 2H), 1.87–1.77 (m, 1H), 1.36 (s, 3H), 1.29–1.20 (m, 1H), 1.19 (s, 9H), 0.97 ppm (t, $J = 7.45$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 175.2$, 77.2, 74.5, 69.1, 66.9, 48.2, 41.6, 27.2, 22.0, 21.6, 11.2 ppm; IR (film): $\tilde{\nu} = 3503$, 2973, 1701, 1364, 1237, 1198, 1147, 1089 cm^{-1}; HRMS (ESI): *m/z*: $[M]^+$ calcd for $C_{13}H_{24}O_4$: 229.1440, found: 229.1442.

Methanesulfonic acid (3*R*,4*R*,5*S*)-3-*tert*-butoxymethyl-5-ethyl-3-methyl-2-oxotetrahydropyran-4-yl ester (119): To lactone **11** (160 mg, 0.64 mmol) in DCM (6 mL) and pyridine (0.6 mL) at room temperature under an argon atmosphere was added mesyl chloride (99 μL, 1.28 mmol) and DMAP (cat.). After 1 h, brine was added, the layers were separated, and the aqueous layer was extracted with DCM. The combined organic phases were dried over $MgSO_4$ and the solvent was evaporated. Column chromatography (hexane/ethyl acetate = 3:1) yielded mesylate **119** (205 mg; 99%). $[\alpha]_D^{20} = 44.58$ ($c = 1.2$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 4.66$ (d, $J = 9.8$ Hz, 1H), 4.45 (dd, $J = 11.6$, 5.3 Hz, 1H), 3.88 (t, $J = 11.2$ Hz, 1H), 3.63 (d, $J = 8.3$ Hz, 1H), 3.54 (d, $J = 8.3$ Hz, 1H), 3.11 (s, 3H), 2.88–2.78 (m, 1H), 1.83–1.72 (m, 1H), 1.37 (s, 3H), 1.28–1.18 (m, 1H), 1.16 (s, 9H), 0.96 ppm (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 174.0$, 85.2, 73.6, 68.6, 66.4, 48.7, 38.8, 38.4, 27.2, 21.9, 21.5, 10.8 ppm; IR (film): $\tilde{\nu} = 2974$, 1732, 1339, 1177, 1093 cm^{-1}; HRMS (ESI): *m/z*: $[M-CH_3]^+$ calcd for $C_{13}H_{23}O_6S$: 307.1215, found: 307.1211.

(*Z*)-(*R*)-5-*tert*-Butoxy-2-ethyl-4-methyl-pent-3-en-1-ol (8): Mesylate **119** (200 mg, 0.6 mmol) was dissolved in dioxane (8 mL) and LiOH (1.8 mL, 1M in water, 1.8 mmol) was added. After 1.5 h the reaction was quenched with saturated NH_4Cl solution and the aqueous layer was extracted with DCM. The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. Column chromatography (hexane/ethyl acetate = 5:1) yielded olefin **8** (110 mg; 83%). $[\alpha]_D^{20} = 32.66$ ($c = 0.65$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 5.07$ (d, $J = 10.1$ Hz, 1H), 3.98 (d, $J = 9.3$ Hz, 1H), 3.63 (d, $J = 8.3$ Hz, 1H), 3.57 (ddd, $J = 10.2$, 6.7, 3.9 Hz, 1H), 3.21 (t, $J = 9.8$ Hz, 1H), 2.87 (dd, $J = 7.2$, 2.6 Hz, 1H (OH)), 2.47–2.38 (m, 1H), 1.82 (s, 3H),1.42–1.33 (m, 1H), 1.27–1.12 (m, 2H), 1.23 (s, 9H), 0.87 ppm (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 136.1$, 131.8, 73.6, 65.9, 60.8, 43.0, 27.4, 24.9, 23.2, 11.8 ppm; IR (film): $\tilde{\nu} = 3629$, 2970, 1653, 2559, 1056 cm^{-1}; HRMS (ESI): *m/z*: $[M-H]^+$ calcd for $C_{12}H_{23}O_2$: 199.1698, found: 199.1703.

(*Z*)-(*R*)-5-*tert*-Butoxy-2-ethyl-4-methylpent-3-enyloxymethyl)benzene (120): To a stirred solution of alcohol **8** (15 mg, 0.07 mmol) in benzylbromide (0.3 mL) was added tetrabutylammonium iodide (2 mg, 0.007 mmol) and after 10 min silver(I) oxide (32 mg, 0.14 mmol) was added. After 24 h the mixture was filtered over celite, washed with diethyl ether, and the solvent was evaporated. Purification by column chromatography (hexane/ethyl acetate = 40:1) yielded benzyl ether **120** (21 mg; quant.) as a colorless oil. $[\alpha]_D^{20} = -37.07$ ($c = 0.75$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.33$ (m, 4H), 7.28 (m, 1H), 5.05 (d, $J = 9.6$ Hz, 1H), 4.49 (s, 2H), 3.88 (s, 2H), 3.36 (dd, $J = 9.2$, 5.9 Hz, 1H), 3.31 (dd, $J = 9.2$, 7.2 Hz, 1H), 2.59 (m, 1H), 1.78 (s, 3H), 1.68–1.60 (m, 1H), 1.26–1.17 (m, 1H), 1.21 (s, 9H), 0.86 ppm (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 138.8$, 135.2, 129.2, 128.3, 127.5, 127.4, 74.1, 72.9, 61.0, 39.8, 27.6, 25.2, 21.9, 11.6 ppm; IR (film): $\tilde{\nu} = 2970$, 1454, 1362, 1197, 1058, 1021 cm^{-1}; HRMS (ESI): *m/z*: $[M]^+$ calcd for $C_{19}H_{30}O_2$: 290.2246, found: 290.2251.

(*Z*)-(*R*)-4-Benzyloxymethyl-2-methyl-hex-2-en-1-ol (121): To a solution of **120** (21 mg, 0.07 mmol) in DCM (1 mL) at room temperature was added TFA (50 μL) and the mixture was stirred for 16 h. The reaction mixture was diluted with water and the layers were separated. The aqueous layer was extracted with DCM and the combined organic phases were dried over $MgSO_4$. Purification by column chromatography (hexane/ethyl acetate = 40:1) yielded alcohol **121** (15 mg; 92%) as a colorless oil. The experimental data were identical with the literature data. $[\alpha]_D^{20} = -38.8$ ($c = 0.25$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.36$–7.27 (m, 5H), 5.29 (d, $J = 10.1$ Hz, 1H), 4.94 (d, $J = 11.9$ Hz, 1H), 4.80 (d, $J = 12.4$ Hz, 1H), 4.48 (s, 2H), 3.38 (dd, $J = 9.2$, 5.9 Hz, 1H), 3.28 (dd, $J = 9.2$, 6.9 Hz, 1H), 2.57 (m, 1H), 1.81 (d, $J = 1.5$ Hz, 3H), 1.61–1.55 (m, 1H), 1.23–1.16 (m, 1H), 0.84 ppm (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 158.3$, 138.5, 134.9, 129.3, 128.3, 127.5, 127.4, 73.5, 73.0, 67.0, 40.4, 24.8, 21.2, 11.5 ppm; IR (film): $\tilde{\nu} = 2963$, 2895, 1785, 1454, 1364, 1222, 1167 cm^{-1}. HRMS (ESI): *m/z*: $[M]^+$ calcd for $C_{15}H_{22}O_2$: 234.1620, found: 234.1917.

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