Tetrahedron 71 (2015) 709–726

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Total synthesis of zincophorin methyl ester. Stereocontrol of 1,2-induction using sterically hindered enoxysilanes

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ARTICLE INFO

Article history:
Received 19 September 2014
Received in revised form 21 November 2014
Accepted 24 November 2014
Available online 28 November 2014

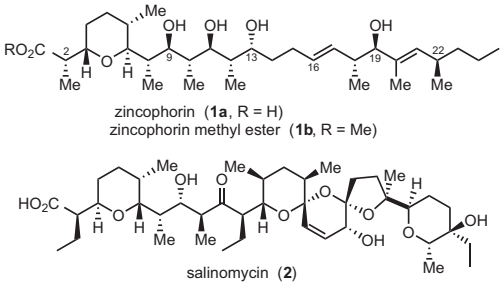
Keywords:
Total synthesis
Polyketide ionophore
Mukaiyama aldol
Radical reduction
Lewis acid

ABSTRACT

Reported herein is the total synthesis of zincophorin methyl ester, a polyketide ionophore. Of particular interest is the use of sterically hindered nucleophiles to surmount the unfavorable stereochemical outcome, leading to acetate aldol adducts, in nucleophilic addition to the aldehyde derived from propionates. The approach is based on the addition of an enoxysilane (bearing a removable phenylselenide moiety) to generate selectively Felkin–Anh adducts in a $BF_3{\cdot}OEt_2$-mediated Mukaiyama aldol reaction. Subsequent reduction of the selenide group led to the corresponding *syn*-aldol acetate motif, and this approach was applied to induce selectively the C12–C13 relationship of zincophorin.

1. Introduction

Polyketides, such as zincophorin **1** or salinomycin **2** (Scheme 1) are an important class of biologically active molecules,[1] partly because a large proportion displays ionophore properties.[2] Indeed, the pseudo-cyclic conformation adopted by their tertiary structure allows for the creation of a cavity capable of coordinating certain metal cations, in order to facilitate their transport across lipophilic membranes. This permeability can lead to a disruption of the cellular potential,[3] hence supporting why many polyketides have found commercial applications as antibiotics, antiparasitics and insecticides.[4] The scarce availability and structural complexity of these compounds have attracted numerous groups to design strategies towards their synthesis.[5] Recently, identification of the antitumoral activity of salinomycin **2** against cancer stem cells (CSCs)[6] has greatly intensified the interest of the scientific community towards polyether ionophores. Following this important discovery, several compounds of this class were investigated, as well as analogs thereof, by a derivatization of the natural product.[7] In order to increase the diversity of the compounds being evaluated and possibly identify the pharmacophores, de novo synthetic approaches also need to be considered.



Scheme 1. Representative polyketide ionophores.

The total synthesis of these molecules bearing polypropionate motifs is, however, not trivial although numerous methodologies were developed over the years to access these sequences of contiguous stereogenic centers.[8] Indeed, not all isomers can be selectively accessed by a single methodology and, more importantly, it is somewhat difficult to predict cases of mismatched double diastereoselectivity induction as the complexity of the substrate increases. To address this issue, our group has developed a robust iterative approach that allows an easily predictable elaboration of propionate units based on a Mukaiyama aldol reaction and a diastereoselective radical reduction (Scheme 2).[9] At each step, the stereochemistry (*anti* or *syn*) of the center being created is simply

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http://dx.doi.org/10.1016/j.tet.2014.11.061
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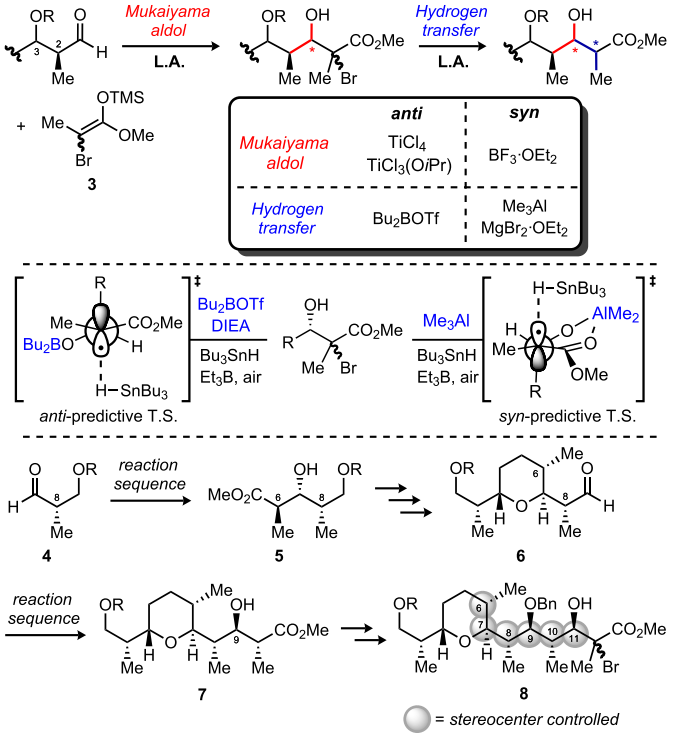


Scheme 2. Methodology for the synthesis of polypropionate motifs and application to zincophorin fragment **8**.

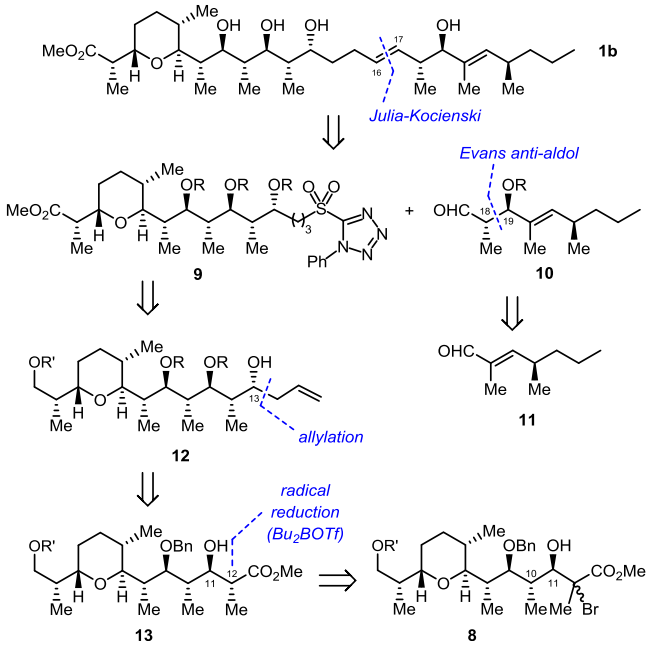
dictated by the choice of Lewis acid (L.A.). Furthermore, we have demonstrated that the reaction sequence can be used iteratively to access all 16 polypropionate stereopentads,[10] and we have applied this methodology to the synthesis of zincophorin fragment C1–C13 **8** from aldehyde **4**.[11] Recently, we have also reported a DFT analysis of the transition states for the hydrogen transfer step.[12]

Zincophorin **1a** was first isolated in 1984 from strains of *Streptomyces griseus* and its structure was confirmed by crystallographic analysis of the zinc–magnesium salt.[13] From a biological perspective, it shows a strong in vivo antibiotic activity against Gram-positive bacteria and *Clostridium welchii*, as well as for type I herpes simplex virus (HSV). The methyl ester of zincophorin **1b** was also reported active against influenza virus A/WSN, and displayed significantly less cytotoxicity than the free carboxylic acid **1a**.[14] Since its discovery, many groups have reported the synthesis of various fragments,[15] but only four total syntheses of the target were completed.[16]

Herein, we describe the total synthesis of zincophorin methyl ester **1b** by employing a sterically hindered nucleophile, bearing a phenylselenide, to introduce selectively the stereogenic center at C13. A systematic study on the aldehydes of simplified propionates revealed that an excellent stereocontrol is achieved under monodentate Lewis acid activation, and leads to the corresponding 3,4-*syn* aldol acetate motifs after cleavage of the phenylselenide group. The synthesis of zincophorin fragment C17–C25 is also presented.

2. Results and discussion

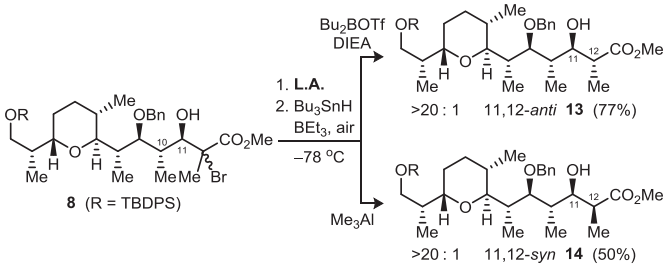
Our retrosynthetic analysis for **1b** is presented in Scheme 3. We envisioned a disconnection at the C16–C17 *trans* olefin, which could be obtained by a Julia–Kocienski coupling[17] of fragments **9** and **10**. We intended to generate the 18,19-*anti* relationship of **10** by taking advantage of the $MgCl_2$-catalyzed *anti*-aldol developed by Evans[18] on the α,β-unsaturated aldehyde **11**. The sulfone **9** could in turn arise from a functionalization of the homoallylic alcohol **12** obtained by an allylation reaction under Felkin–Anh control. Finally, the



Scheme 3. Retrosynthetic analysis of **1b**.

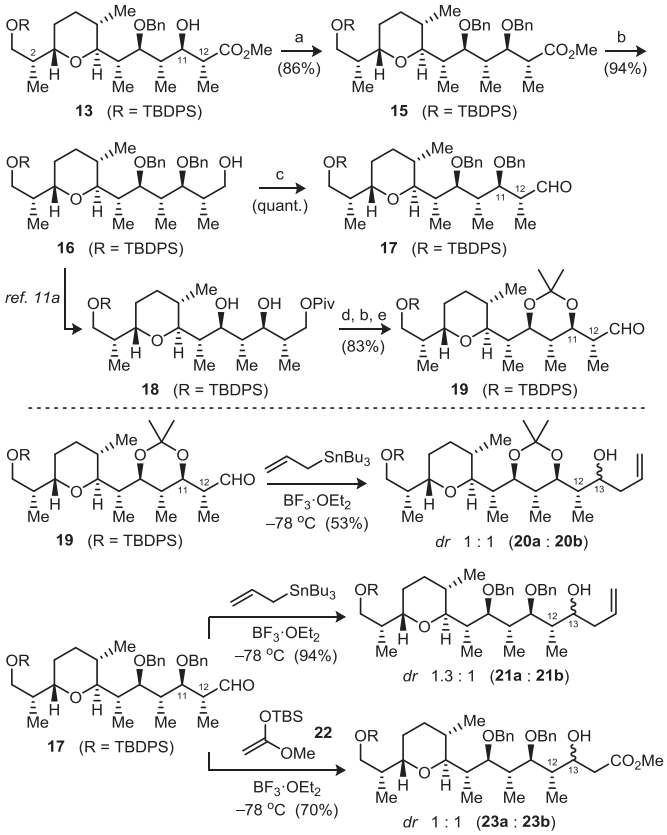
stereogenic center at C12 of **13** could be introduced by a Bu_2BOTf-mediated diastereoselective radical reduction of halide precursor **8**, previously obtained selectively via a Mukaiyama aldol reaction.[11a]

The completion of the synthesis begins with the radical reduction of 10,11-*anti* β-hydroxyester **8**.[19] As expected, the desired 11,12-*anti* product **13** or its 11,12-*syn* isomer **14** were obtained selectively following a L.A. pre-complexation, with either Bu_2BOTf or Me_3Al (Scheme 4). Having most of the polypropionate sequence completed, we decided to introduce the remaining C12–C13 *syn* relationship of zincophorin by an allylation reaction in presence of a monodentate Lewis acid. Our goal was to take advantage of the matched 1,2- and 1,3-asymmetric induction originating from the relative *anti*-relationship of substituents, on the corresponding aldehyde,[20] to favor formation of the Felkin–Anh product. Using the common precursor **16** prepared from fragment **13** (Scheme 5), two aldehyde substrates were considered, either benzyl-protected **17** or as an acetonide **19**. In both cases, a similar disappointing result was noted. Indeed, an equimolar mixture of homoallylic alcohols **20a**,**b** or **21a**,**b** were obtained with allylstannane and $BF_3{\cdot}OEt_2$, although previous reports yielded selectively the desired product on a simpler aldehyde.[20b,21]



Scheme 4. Radical reduction of β-hydroxyester **8**.

Another approach was then evaluated with enoxysilane **22** in a Mukaiyama aldol reaction of **17** using a monodentate Lewis acid, which should give the corresponding *syn* β-hydroxyester **23a**, a useful intermediate. Unfortunately, once again no diastereoselectivity was noted. These results were surprising, and the causes at the origin of this lack of stereocontrol remains unknown.

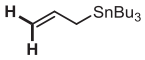
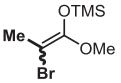
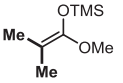
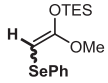
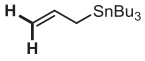
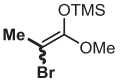
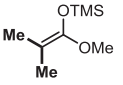
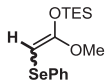


Scheme 5. Synthesis of aldehydes **17** and **19**—Reagents and conditions: (a) BnOC(NH)CCl_3, TfOH, *c*Hex/CH_2Cl_2 (2:1), 0 °C, 18 h; (b) DIBAL-H, CH_2Cl_2, −40 °C, 1 h; (c) DMP, $NaHCO_3$, CH_2Cl_2, rt, 1 h; (d) 2-methoxypropene, PPTS, CH_2Cl_2, 0 °C, 3 h; (e) $(COCl)_2$, DMSO, Et_3N, −78 °C, 1 h.

We decided to further investigate this reaction, in search of a solution to access the desired *syn* acetate motif. Simpler propionate fragments **24** and **25** were first studied (Table 1). Under the same allylation reaction conditions, substrate **24** leads to the exclusive formation of Felkin product **28a** (entry 1), while **25** affords the anti-Felkin isomer **32b** in a modest 4.9:1 ratio (entry 5).[22] This poor selectivity originates from competing 1,2- and 1,3-induction for 2,3-*syn* aldehyde **25**. The stereochemistry of the major product can be rationalized by a dominant control exerted by the β stereocenter in this case. Our solution to this problem originated from previous work by our group and others.[20b] We previously demonstrated that $BF_3{\cdot}OEt_2$-mediated Mukaiyama aldol reaction using tetrasubstituted enoxysilane **3** led to high levels of diastereoselectivity (entries 2 and 6).[10] Replacing the silylated enolate by nucleophile **26** proved to yield also the desired isomer selectively (entries 3 and 7). Clearly, the presence of substituents on the olefin increases the steric effects of the nucleophile hence, the resulting 1,2-induction and stereofacial selectivity. This observation also suggested an alternative pathway to circumvent the lack of diastereoselectivity noted when preparing **23a**. Indeed, we hypothesized that an enoxysilane bearing a bulky terminal substituent, which could eventually be removed at a later step, would also favor a reaction controlled uniquely by 1,2-induction. Based on previous studies by our group for the elaboration of tertiary centers,[23] we envisioned that the use of trisubstituted enoxysilane **27**, bearing a phenylselenide, could provide high ratios in the presence of $BF_3{\cdot}OEt_2$. To our delight, aldehydes **24** and **25** submitted to these conditions also led to excellent diastereoselectivity in favor of Felkin adducts **31a**[24] and **35a** (entries 4 and 8).

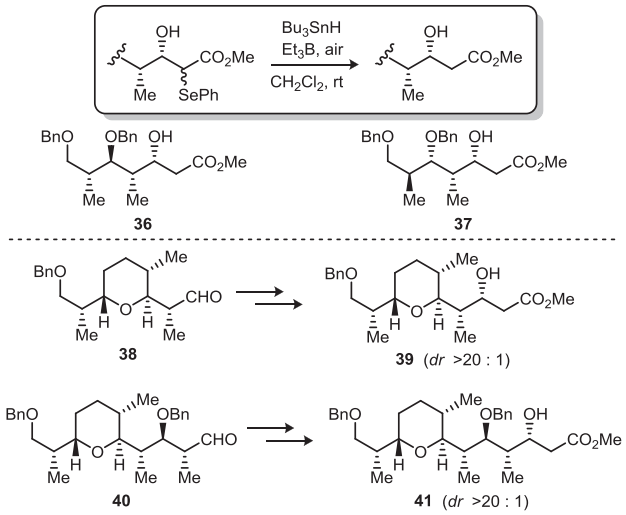
In a subsequent step, the resulting α-phenylselenide adducts were cleaved by radical reduction, to yield acetate aldol products[25] **36** and **37** from their corresponding precursors **31a** and **35a** (Scheme 6). Moreover, we demonstrated that the aldol–reduction reaction sequence can also be applied to other functionalized aldehydes in order to generate exclusively the 3,4-*syn* isomer **39** and **41** from elaborate fragments of zincophorin (**38** and **40**).[11a]

Table 1
Nucleophilic addition on aldehydes **24** and **25**

Entry	Nucleophile		Ratio[a] (product)	Yield[b] (%)
	24		**28a–31a** (Felkin) + **28b–31b** (anti-Felkin)	
1			>20:1 (**28**)	86
2		**3**	>20:1 (**29**)	84[d]
3		**26**	>20:1 (**30**)	78[c]
4		**27**	>20:1 (**31**)	92
	25		**32a–35a** (Felkin) + **32b–35b** (anti-Felkin)	
5			1:4.9 (**32**)	74
6		**3**	>20:1 (**33**)	88[d]
7		**26**	>20:1 (**34**)	61[c]
8		**27**	>20:1 (**35**)	97

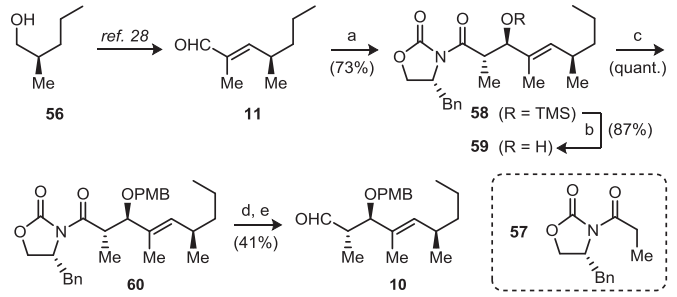
[a] Product ratios were determined by ^1H NMR analysis of the crude reaction mixture.
[b] Yields of isolated products.
[c] Yield based on recovered starting material.
[d] Reference 10.

Our next objective was to apply these conditions onto an advanced substrate of zincophorin (Scheme 7) by taking advantage of the sterical bias imposed by the nucleophile to remove possible mismatched situations. We were able to isolate the desired C12–C13 *syn* isomer **42a** with a good selectivity (*dr* 13:1) in the $BF_3{\cdot}OEt_2$-promoted Mukaiyama aldol of aldehyde **17** in the presence of enoxysilane **27**, therefore completing the introduction of the necessary stereogenic centers after reduction to the corresponding acetate aldol **23a**. Having the key motif in hand, the next challenge was to complete the synthesis of fragment **9** necessary for the coupling reaction. The aldehyde **45** was obtained easily after

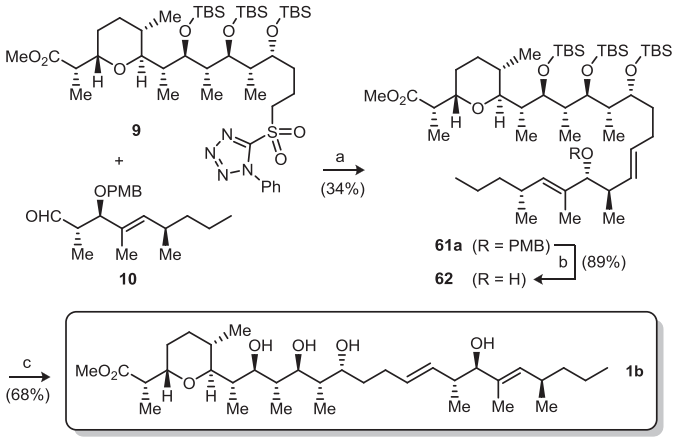


Scheme 6. Radical reduction to access acetate motifs.

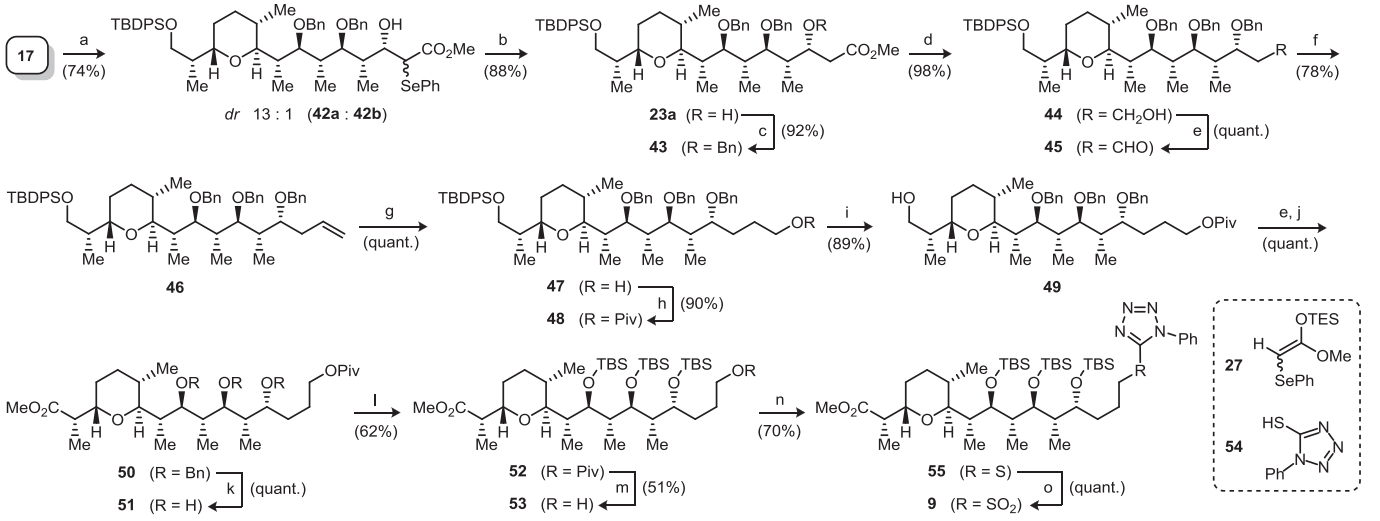
protection of the alcohol **23a**, reduction of the ester **43** and oxidation of alcohol **44** by the Dess-Martin reagent.[26] Homologation by a Wittig reaction yielded the desired terminal olefin **46** in good yield, before the subsequent hydroboration provided primary alcohol **47**, which was protected as pivaloate **48**. TBDPS group was then cleaved, and alcohol **49** oxidized to the corresponding ester **50** in three steps. Benzyl ethers were then cleaved and replaced by TBS protecting groups (**52**). Finally, the pivaloate ester was removed and the alcohol **53** submitted to a Mitsunobu reaction to yield phenyltetrazol thioether **55**, followed by a Mo(VI)-catalyzed oxidation to the desired sulfone **9** using hydrogen peroxide.[27]



Scheme 8. Synthesis of C17–C25 fragment **10**—Reagents and conditions: (a) $MgCl_2$, Et_3N, TMSCl, **57**, EtOAc, rt, 18 h; (b) TFA, MeOH, 0 °C, 1 h; (c) PMBOC(NH)CCl_3, TfOH, *c*Hex/CH_2Cl_2 (2:1), 0 °C, 18 h; (d) $LiBH_4$, MeOH, Et_2O, 0 °C, 18 h; (e) DMP, $NaHCO_3$, CH_2Cl_2, rt, 1 h.



Scheme 9. Coupling of fragments **9** and **10**—Reagents and conditions: (a) KHMDS, DME, −55 °C to −40 °C, 1.5 h; (b) DDQ, buffer pH 7, rt, 30 min; (c) TBAF, THF, rt, 68 h.



Scheme 7. Synthesis of C1–C16 fragment **9**—Reagents and conditions: (a) **27**, $BF_3{\cdot}OEt_2$, CH_2Cl_2, −78 °C, 1 h; (b) Bu_3SnH, Et_3B, air, CH_2Cl_2, rt, 18 h; (c) BnOC(NH)CCl_3, TfOH, *c*Hex/CH_2Cl_2 (2:1), 0 °C, 18 h; (d) DIBAL-H, CH_2Cl_2, −40 °C, 1 h; (e) DMP, $NaHCO_3$, CH_2Cl_2, rt, 1 h; (f) $MePPh_3Br$, *n*BuLi,; (g) 1. 9-BBN, THF, 0 °C, 6 h; 2. NaOH, H_2O_2, 0 °C to rt, 18 h; (h) PivCl, pyridine, CH_2Cl_2, rt, 18 h; (i) TBAF, THF, 0 °C to rt, 18 h; (j) 1. $NaClO_2$, NaH_2PO_4, 2-methyl-2-butene, *t*BuOH, rt, 18 h; 2. $TMSCHN_2$, MeOH/toluene (2:3), rt, 2 h; (k) H_2, Pd/C, MeOH, rt, 18 h; (l) TBSOTf, 2,6-lutidine, CH_2Cl_2, rt, 36 h; (m) K_2CO_3, MeOH, rt, 36 h; (n) DIAD, PPh_3, **54**, THF, rt, 3 h; (o) $(NH_4)_6Mo_7O_{24}{\cdot}4H_2O$, H_2O_2, EtOH, rt, 18 h.

The synthesis of the other fragment of zincophorin was realized using aldehyde **11**,[28] obtained from chiral alcohol **56** (Scheme 8). The C18–C19 *anti* relationship was introduced using Evans' *anti*-aldol conditions,[18] yielding product **58** selectively. Subsequent desilylation and protection of the secondary alcohol **59** with a PMB (**60**), cleavage of the auxiliary and oxidation to the aldehyde provided fragment C17–C25 **10**, whose NMR spectra (^1H and ^{13}C) were identical to those previously reported.[16d]

Coupling of fragments **9** and **10** was realized using the Julia–Kocienski conditions,[17] and led us to the selective formation of *trans* olefin **61a** (Scheme 9). Finally, cleavage of the PMB, followed by desilylation of **62** with TBAF completed the sequence leading to zincophorin methyl ester **1b**, whose spectroscopic analysis revealed to be identical to the compound reported by Cossy.[16b]

3. Conclusion

In summary, we have reported the total synthesis of zincophorin methyl ester **1b**. An important contribution of this work is the selective induction of the C13 stereocenter via a Mukaiyama aldol reaction through the use of a hindered silylated enolate. The latter bears a removable group that increases the dominance of 1,2-induction and avoids mismatch situations. In other previous reports of the target molecule, introduction of the C13 stereocenter was either accomplished on simple substrates early in the synthesis, through fragment coupling or required an important number of steps if performed on an advanced intermediate.

The synthesis of the C1–C16 fragment **9** was achieved herein using a single methodology in a linear sequence of 44 steps, with an overall yield of 0.2% from **4**. One of the most notable features of our approach is the versatility to generate all four propionate isomers from a common intermediate by only varying the nature of Lewis acid at each step. While prior total syntheses of zincophorin methyl ester required fewer steps, our methodology facilitates the access to any isomers of the natural target in the perspective of a structure-activity optimization. Work aimed at improving the efficiency by decreasing the number of steps per stereocenter (e.g., through a more convergent approach) and evaluating the generality of this methodology, to access other polyether ionophores, is currently under investigation and will be reported in due course.

4. Experimental

4.1. General comments

Silylated enol ether **27** was prepared according to a procedure previously described by our group.[9a] Experimental methods and physical characterization of products **8**, **18**, **38**, **40**[11a] as well as **24**[10] and **25**[9d] have already been reported by our group. All procedures requiring anhydrous conditions were carried out under a positive argon atmosphere (or nitrogen, for radical reductions) in oven-dried glassware using standard syringe techniques. All reaction solvents (HPLC grade) were dried using activated 4 Å molecular sieves (48 h at 180 °C under vacuum) according to the procedure described by Williams et al.[29] Crude products were purified by flash chromatography on silica gel (porosity: 60 Å, size: 40–75 μm) using HPLC-grade solvents and compressed air, or using Biotage Isolera One (v1.3.6). Chemical shifts in ppm for ^{1}H (400 or 500 MHz) and ^{13}C spectra (100 or 125 MHz) were referenced to residual solvent peak (δ_H and δ_C). For ^{1}H NMR data, the associated coupling constants (*J*, Hz), integration value and multiplicity are reported. All ratios of products were measured from crude ^{1}H spectra. Infrared spectra in cm^{-1} were recorded on a FTIR spectrophotometer (ABB Bomen, MB) on a NaCl support. Optical rotations were measured on a PerkinElmer 343 polarimeter at 25 °C from the sodium D line (589 nm) with a cell of 1.0 mL measuring 9.998 cm in length, and concentration *c* is reported in g/100 mL. Mass spectra were recorded through electrospray ionization (ESI) on a LTQ Orbitrap XL instrument (Thermo Fisher) operating at 70 eV, and coupled to an ion trapt.

4.2. General experimental procedures

4.2.1. Procedure A—protection of alcohol with benzyl ether or PMB ether. To a cooled (0 °C) solution of alcohol (1 equiv) in a solvent mixture of dry cyclohexane and CH_2Cl_2 (2:1, 0.1 M) was added successively 2,2,2-benzyltrichloroacetimidate (Bn, 1.5 equiv) or 4-methoxybenzyl 2,2,2-trichloroacetimidate (PMB, 1.5 equiv) and TfOH (0.1 equiv), followed by stirring overnight at 0 °C. The reaction mixture was treated with Et_3N (0.15 equiv), and concentrated in vacuo. The residue was solubilized in hexanes, filtered onto a pad of Celite®, washed thoroughly with hexanes and the filtrate concentrated in vacuo.

4.2.2. Procedure B—reduction of ester to primary alcohol with DIBAL-H. To a cooled (−40 °C) solution of ester (1 equiv) in dry CH_2Cl_2 (0.1 M) was added a 1 M solution of DIBAL-H in hexanes (3 equiv). The mixture was stirred for 1 h at −40 °C or until ester was completely consumed, as verified by TLC. The reaction mixture was treated first with the dropwise addition of MeOH at −40 °C until gas evolution ceased, followed by a saturated potassium sodium tartrate solution (Rochelle's salt). Mixture was stirred 1 h at rt (or until clarification of phases) followed by separation of the organic phase. The aqueous layer was extracted with Et_2O (3×) and the combined organic fractions were dried ($MgSO_4$), filtered and concentrated in vacuo.

4.2.3. Procedure C—oxidation of primary alcohol with Dess-Martin periodinane. To a solution of alcohol (1 equiv) in dry CH_2Cl_2 (0.1 M) at rt was added successively $NaHCO_3$ (10 equiv) and Dess-Martin periodinane (1.5 equiv). The reaction mixture was stirred for 1 h at rt and then concentrated in vacuo. Resulting white solid residue was digested in hexanes, filtered onto a pad of Celite®, washed thoroughly with hexanes and the filtrate concentrated in vacuo.

4.2.4. Procedure D—nucleophilic addition on aldehyde using $BF_3\cdot OEt_2$. To a cooled (−78 °C) solution of aldehyde (1 equiv) in dry CH_2Cl_2 (0.1 M) was added successively the appropriate nucleophile (2 equiv) and $BF_3\cdot OEt_2$ (1.5 equiv). After stirring for 1.5 h at −78 °C, the reaction mixture was treated with a saturated aqueous solution of NH_4Cl at −78 °C, followed by separation of the organic phase at rt. The aqueous layer was then extracted with CH_2Cl_2 (3×) and the combined organic fractions were dried ($MgSO_4$), filtered and concentrated in vacuo.

4.2.5. Procedure E—hydrogenolysis of benzyl ether with palladium. To a solution of benzyl ether (1 equiv) in MeOH (0.1 M) at rt was added 10% wt. Pd on activated carbon (0.1 equiv). Inert gas atmosphere was purged by 3 cycles of vacuum–H_2 gas before stirring reaction mixture at rt until reaction was judged completed by TLC. Mixture was then filtered onto a pad of Celite®, washed thoroughly with MeOH and the filtrate concentrated in vacuo.

4.2.6. Procedure F—radical reduction of phenylselenide. To a solution of phenylselenide in dry CH_2Cl_2 (0.1 M) at rt was added successively Bu_3SnH (2 equiv), a 1 M solution of Et_3B in CH_2Cl_2 (0.2 equiv) and air (syringe), followed by stirring overnight at rt. The mixture was treated successively with 1,4-dinitrobenzene (0.2 equiv), a saturated aqueous solution of NH_4Cl, and then concentrated in vacuo. The aqueous layer was extracted with Et_2O (3×) and combined organic fractions were washed (2×) with a saturated aqueous solution of KF and brine, then dried ($MgSO_4$), filtered and concentrated in vacuo.

4.3. (+)-(2*R*,3*R*,4*S*,5*S*,6*S*)-Methyl 5-(benzyloxy)-6-((2*S*,3*S*,6*S*)-6-((*R*)-1-((*tert*-butyldiphenylsilyl)oxy)propan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)-3-hydroxy-2,4-dimethylheptanoate (13)

To a cooled (−78 °C) solution of bromide precursors **8**[11a] (117 mg, 0.15 mmol) in dry CH_2Cl_2 (0.1 M, 1.5 mL) was added successively DIEA (1.5 equiv, 40 μL) and a 1 M solution of Bu_2BOTf in CH_2Cl_2 (1.3 equiv, 200 μL). After stirring for 1 h at −78 °C, the mixture was successively treated with Bu_3SnH (2 equiv, 82 μL), a 1 M solution of Et_3B in CH_2Cl_2 (0.2 equiv, 30 μL) and air via syringe (~3 mL). Supplementary addition of Et_3B solution and air were realized each 30 min until reaction was judged completed by TLC (3–4 h). Reaction mixture was treated with the addition of 1,4-dinitrobenzene (0.2 equiv, 5 mg) and stirring for 15 min at

−78 °C, before being treated by a saturated aqueous solution of NH_4Cl. Organic phase was separated at rt and the aqueous layer was extracted with Et_2O (3×). Combined organic fractions were washed (2×) with a saturated aqueous solution of KF and brine, then dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was solubilized in MeOH (0.1 M, 1.5 mL), cooled to 0 °C, and treated with a 35% wt. solution of H_2O_2 in water (3 equiv, 40 μL). After stirring for 2 h at 0 °C, the mixture was treated with water, diluted with Et_2O and the organic phase separated. The aqueous layer was extracted with Et_2O (3×) and the combined organic fractions were dried ($MgSO_4$), filtered, and concentrated in vacuo. ^{1}H NMR analysis of the crude product indicated a ratio >20:1 of product 11,12-*anti* (**13**): 11,12-*syn* (**14**). The residue was purified by flash chromatography on silica gel (hexanes/EtOAc, 90:10) to give 11,12-*anti* product **13** as a pale yellow oil (99.2 mg, yield=77%). R_f 0.25 (hexanes/EtOAc, 85:15); $[\alpha]_D^{25}$ +18.2 (*c* 1.69, CH_2Cl_2); $C_{42}H_{60}O_6Si$; MW 689.01 g/mol; IR (liquid film) ν_{max} 3517, 2955, 2930, 2857, 1716, 1459, 1428, 1380, 1197, 1170, 1112, 1091, 1066 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.69–7.63 (m, 4H), 7.44–7.33 (m, 6H), 7.29–7.22 (m, 3H), 7.21–7.16 (m, 2H), 4.42 (d, *J*=12.2 Hz, 1H), 4.40 (d, *J*=12.2 Hz, 1H), 3.68 (s, 3H), 3.74–3.61 (m, 4H), 3.51 (br s, 1H), 3.47 (dd, *J*=7.3, 4.2 Hz, 1H), 3.35 (dd, *J*=7.7, 3.7 Hz, 1H), 2.76 (qd, *J*=7.1, 3.5 Hz, 1H), 2.23–2.14 (m, 1H), 2.06–1.97 (m, 1H), 1.97–1.88 (m, 1H), 1.75–1.68 (m, 1H), 1.68–1.60 (m, 2H), 1.61–1.49 (m, 2H), 1.25 (d, *J*=7.1 Hz, 3H), 1.04 (s, 9H), 0.92 (d, *J*=6.9 Hz, 3H), 0.88 (d, *J*=6.9 Hz, 3H), 0.87 (d, *J*=7.0 Hz, 3H), 0.86 (d, *J*=6.4 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 176.2, 138.7, 135.89, 135.87, 134.2, 134.1, 129.65, 129.60, 128.4, 127.71, 127.69, 127.5, 127.4, 86.3, 76.6, 76.4, 74.4, 71.8, 65.9, 51.7, 42.3, 39.1, 38.1, 37.1, 30.1, 28.0, 27.1, 24.7, 19.5, 18.6, 16.6, 15.2, 13.5, 11.8 ppm; MS (ESI) *m*/*z* 227.0 (3), 360.3 (4), 689.4 (11, M+H$^+$), 706.5 (2, M+NH_4^+), 711.4 (100, M+Na$^+$), 712.4 (50), 713.4 (12); HRMS calcd for $C_{42}H_{61}O_6Si$ [M+H$^+$]: 689.4232, found: 689.4250 (2.6 ppm); calcd for $C_{42}H_{64}O_6NSi$ [M+NH_4^+]: 706.4497, found: 706.4514 (2.3 ppm); calcd for $C_{42}H_{60}O_6NaSi$ [M+Na$^+$]: 711.4051, found: 711.4072 (3.0 ppm).

4.4. (+)-(2*S*,3*R*,4*S*,5*S*,6*S*)-Methyl 5-(benzyloxy)-6-((2*S*,3*S*,6*S*)-6-((*R*)-1-((*tert*-butyldiphenylsilyl)oxy)propan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)-3-hydroxy-2,4-dimethylheptanoate (14)

To a cooled (−78 °C) solution of a mixture of bromide precursors **8**[11a] (26.6 mg, 35 μmol) in dry CH_2Cl_2 (0.1 M, 350 μL) was added a 2 M solution of Me_3Al in hexanes (2.5 equiv, 44 μL). After stirring for 1 h at −78 °C, the mixture was successively treated with Bu_3SnH (2 equiv, 19 μL), a 1 M solution of Et_3B in CH_2Cl_2 (0.2 equiv, 7 μL) and air via syringe (~1 mL). Supplementary addition of Et_3B solution and air were realized each 30 min until reaction was judged completed by TLC (3–4 h). Reaction mixture was treated with the addition of 1,4-dinitrobenzene (0.2 equiv, 2 mg) and stirring for 15 min at −78 °C. To the mixture was added MeOH dropwise until gas evolution ceased, followed by a saturated aqueous solution of potassium sodium tartrate (Rochelle's salt) and stirring overnight at rt before separation of the organic phase. The aqueous layer was extracted with Et_2O (3×) and combined organic fractions were washed (2×) with a saturated aqueous solution of KF and brine, then dried ($MgSO_4$), filtered and concentrated in vacuo. ^{1}H NMR analysis of the crude product indicated a ratio >20:1 of product 11,12-*syn* (**14**): 11,12-*anti* (**13**). The residue was purified by flash chromatography on silica gel (hexanes/EtOAc, 90:10) to give 11,12-*syn* product **14** as a colorless oil (11.9 mg, yield=50%). R_f 0.33 (hexanes/EtOAc, 85:15); $[\alpha]_D^{25}$ +26.6 (*c* 1.19, CH_2Cl_2); $C_{42}H_{60}O_6Si$; MW 689.01 g/mol; ν_{max} (liquid film) 3526, 2953, 2930, 2857, 1733, 1589, 1459, 1428, 1382, 1200, 1112, 1063 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.70–7.63 (m, 4H), 7.44–7.33 (m, 6H), 7.30–7.23 (m, 3H), 7.20–7.16 (m, 2H), 4.44 (d, *J*=11.4 Hz, 1H), 4.39 (d, *J*=11.4 Hz, 1H), 4.04 (dd, *J*=9.2, 2.9 Hz, 1H), 3.73–3.67 (m, 2H), 3.70 (s, 3H), 3.61 (dd, *J*=9.6, 4.1 Hz, 1H), 3.47 (dd, *J*=7.1, 4.5 Hz, 1H), 3.35 (dd, *J*=7.4, 3.9 Hz, 1H), 3.30 (br s, 1H), 2.60 (qd, *J*=7.0, 3.1 Hz, 1H), 2.21–2.11 (m, 1H), 1.97–1.85 (m, 2H), 1.74–1.68 (m, 1H), 1.68–1.60 (m, 1H), 1.60–1.49 (m, 2H), 1.31–1.23 (m, 1H), 1.14 (d, *J*=7.1 Hz, 3H), 1.04 (s, 9H), 0.94 (d, *J*=7.0 Hz, 3H), 0.88 (d, *J*=6.9 Hz, 3H), 0.86 (d, *J*=6.6 Hz, 3H), 0.82 (d, *J*=7.1 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 176.3, 138.5, 135.90, 135.88, 134.16, 134.15, 129.7, 129.6, 128.4, 127.72, 127.70, 127.6, 127.5, 86.6, 76.42, 74.3, 74.1, 71.8, 65.8, 51.9, 42.3, 38.4, 37.9, 37.1, 30.1, 27.1, 27.0, 24.6, 19.5, 18.6, 16.5, 13.5, 11.8, 9.2 ppm; MS (ESI) *m*/*z* 227.0 (6), 338.3 (4), 360.3 (7), 689.4 (10, M+H$^+$), 711.4 (100, M+Na$^+$), 712.4 (50); HRMS calcd for $C_{42}H_{61}O_6Si$ [M+H$^+$]: 689.4232, found: 689.4232 (−0.02 ppm); calcd for $C_{42}H_{60}O_6NaSi$ [M+Na$^+$]: 711.4051, found: 711.4057 (0.8 ppm).

4.5. (+)-(2*R*,3*R*,4*R*,5*S*,6*S*)-Methyl 3,5-bis(benzyloxy)-6-((2*S*,3*S*,6*S*)-6-((*R*)-1-((*tert*-butyldiphenylsilyl)oxy)propan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)-2,4-dimethylheptanoate (15)

Product **15** (181 mg, yield=86%) as a colorless oil was obtained from alcohol **13** (186 mg, 0.27 mmol) according to general procedure **A**, and purification by flash chromatography on silica gel (hexanes/EtOAc, 90:10). R_f 0.34 (hexanes/EtOAc, 90:10); $[\alpha]_D^{25}$ +22.1 (*c* 1.31, CH_2Cl_2); $C_{49}H_{66}O_6Si$; MW 779.13 g/mol; IR (liquid film) ν_{max} 3068, 3031, 2950, 2929, 2857, 1737, 1455, 1428, 1380, 1202, 1111, 1091, 1066 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.66–7.60 (m, 4H), 7.42–7.31 (m, 6H), 7.29–7.16 (m, 10H), 4.56 (d, *J*=11.5 Hz, 1H), 4.52 (d, *J*=11.5 Hz, 1H), 4.42 (d, *J*=11.7 Hz, 1H), 4.35 (d, *J*=11.7 Hz, 1H), 3.90 (dd, *J*=7.4, 4.8 Hz, 1H), 3.72–3.66 (m, 2H), 3.66–3.61 (m, 1H), 3.63 (s, 3H), 3.45 (dd, *J*=7.4, 3.8 Hz, 1H), 3.39 (dd, *J*=7.9, 3.4 Hz, 1H), 2.90 (qd, *J*=6.9, 4.7 Hz, 1H), 2.23–2.08 (m, 2H), 2.00–1.90 (m, 1H), 1.67–1.46 (m, 5H), 1.18 (d, *J*=7.1 Hz, 3H), 1.03 (s, 9H), 0.89 (d, *J*=7.0 Hz, 3H), 0.87 (d, *J*=6.9 Hz, 3H), 0.85 (d, *J*=7.2 Hz, 3H), 0.66 (d, *J*=6.4 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 175.5, 139.6, 139.1, 135.91, 135.86, 134.16, 134.12, 129.60, 129.58, 128.24, 128.19, 127.72, 127.68, 127.4, 127.3, 127.13, 127.09, 84.6, 82.8, 76.5, 73.8, 72.7, 71.9, 66.0, 51.6, 42.1, 37.8, 37.3, 36.5, 30.4, 27.2, 27.1, 24.9, 19.5, 18.4, 15.4, 13.6, 12.6, 11.4 ppm; MS (ESI) *m*/*z* 227.0 (2), 360.3 (7), 779.5 (16, M+H$^+$), 780.5 (9), 781.5 (2), 796.5 (3, M+NH_4^+), 801.5 (100, M+H$^+$), 802.5 (59), 803.5 (18); HRMS calcd for $C_{49}H_{67}O_6Si$ [M+H$^+$]: 779.4701, found: 779.4704 (0.3 ppm); calcd for $C_{49}H_{70}O_6NSi$ [M+NH_4^+]: 796.4967, found: 796.4970 (0.3 ppm); calcd for $C_{49}H_{66}O_6NaSi$ [M+Na$^+$]: 801.4521, found: 801.4528 (0.9 ppm).

4.6. (+)-(2*S*,3*S*,4*S*,5*S*,6*S*)-3,5-bis(Benzyloxy)-6-((2*S*,3*S*,6*S*)-6-((*R*)-1-((*tert*-butyldiphenylsilyl)oxy)propan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)-2,4-dimethylheptan-1-ol (16)

Primary alcohol **16** (26.2 mg, yield=94%) as a colorless oil was obtained from ester **15** (29.0 mg, 37 μmol) according to general procedure **B**, and purification by flash chromatography on silica gel (hexanes/EtOAc, 85:15). R_f 0.15 (hexanes/EtOAc, 85:15); $[\alpha]_D^{25}$ +28.2 (*c* 1.60, CH_2Cl_2); $C_{48}H_{66}O_5Si$; MW 751.12 g/mol; IR (liquid film) ν_{max} 3447, 3069, 3030, 2959, 2929, 2857, 1455, 1428, 1380, 1111, 1091, 1066, 1028 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.69–7.62 (m, 4H), 7.44–7.32 (m, 6H), 7.31–7.17 (m, 10H), 4.73 (d, *J*=11.4 Hz, 1H), 4.47 (d, *J*=11.4 Hz, 1H), 4.42 (s, *J*=11.6 Hz, 2H), 3.87 (dt, *J*=11.1, 3.4 Hz, 1H), 3.75–3.68 (m, 2H), 3.66 (dd, *J*=9.5, 3.9 Hz, 1H), 3.62 (dd, *J*=7.1, 3.2 Hz, 1H), 3.54 (ddd, *J*=10.8, 7.3, 4.7 Hz, 1H), 3.46 (dd, *J*=7.6, 3.7 Hz, 1H), 3.36 (dd, *J*=8.0, 3.5 Hz, 1H), 2.93 (dd, *J*=7.3, 3.9 Hz, 1H), 2.25 (ddq, *J*=3.7, 7.0, 6.9 Hz, 1H), 2.12 (ddq, *J*=3.9, 7.0, 6.9 Hz, 1H), 2.01–1.90 (m, 2H), 1.67–1.50 (m, 4H), 1.25–1.16 (m, 1H), 1.07 (d, *J*=7.1 Hz, 3H), 1.04 (s, 9H), 0.94 (d, *J*=3.1 Hz, 3H), 0.93 (d, *J*=2.9 Hz, 3H), 0.88 (d, *J*=6.8 Hz, 3H), 0.68 (d, *J*=6.5 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 139.4, 138.6, 135.90, 135.86, 134.13, 134.09, 129.66, 129.60, 128.5, 128.3, 127.72, 127.69, 127.6, 127.5, 127.2, 127.0,

86.2, 85.0, 76.4, 74.3, 73.8, 71.9, 66.0, 65.8, 37.9, 37.6, 36.6, 36.5, 30.3, 27.2, 27.1, 24.9, 19.5, 18.4, 16.8, 16.0, 13.6, 11.5 ppm; MS (ESI) *m/z* 338.3 (10), 360.3 (4), 643.4 (8), 751.5 (74, $M+H^+$), 752.5 (41), 753.5 (12), 754.5 (3), 768.5 (3, $M+NH_4^+$), 773.5 (100, $M+Na^+$), 774.5 (59), 775.5 (17), 776.5 (3); HRMS calcd for $C_{48}H_{67}O_5Si$ [$M+H^+$]: 751.4752, found: 751.4751 (−0.2 ppm); calcd for $C_{48}H_{70}O_5NSi$ [$M+NH_4^+$]: 768.5018, found: 768.5011 (−0.8 ppm); calcd for $C_{48}H_{66}O_5NaSi$ [$M+Na^+$]: 773.4572, found: 773.4571 (−0.1 ppm).

4.7. (2*R*,3*R*,4*R*,5*S*,6*S*)-3,5-bis(Benzyloxy)-6-((2*S*,3*S*,6*S*)-6-((*R*)-1-((*tert*-butyldiphenylsilyl)oxy)propan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)-2,4-dimethylheptanal (17)

Aldehyde **17** as a colorless oil was obtained from primary alcohol **16** (12.0 mg, 16 μmol) according to general procedure **C**, and was used as crude without purification. R_f 0.42 (hexanes/EtOAc, 85:15); $C_{48}H_{64}O_5Si$; MW 749.10 g/mol; IR (liquid film) ν_{max} 3069, 3031, 2959, 2929, 2857, 1701, 1686, 1588, 1455, 1363, 1264, 1239, 1112, 1092, 1027 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ_H 9.79 (d, *J*=2.3 Hz, 1H), 7.68–7.60 (m, 4H), 7.43–7.32 (m, 6H), 7.31–7.16 (m, 10H), 4.61 (d, *J*=11.6 Hz, 1H), 4.46 (d, *J*=11.6 Hz, 1H), 4.40 (d, *J*=11.6 Hz, 1H), 4.36 (d, *J*=11.6 Hz, 1H), 3.83 (dd, *J*=6.4, 2.5 Hz, 1H), 3.73–3.67 (m, 2H), 3.65 (dd, *J*=9.5, 3.9 Hz, 1H), 3.44 (dd, *J*=7.4, 3.8 Hz, 1H), 3.33 (dd, *J*=7.9, 3.6 Hz, 1H), 2.79–2.73 (m, 1H), 2.24–2.19 (m, 1H), 1.98–1.89 (m, 1H), 1.66–1.48 (m, 5H), 1.25–1.19 (m, 1H), 1.11 (d, *J*=7.0 Hz, 3H), 1.04 (s, 9H), 0.90 (d, *J*=6.8 Hz, 3H), 0.89 (d, *J*=7.1 Hz, 3H), 0.88 (d, *J*=6.6 Hz, 3H), 0.72 (d, *J*=6.4 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 205.2, 139.2, 138.7, 135.89, 135.85, 134.10, 134.06, 129.65, 129.61, 128.38, 128.30, 127.73, 127.68, 127.5, 127.4, 127.3, 127.1, 84.7, 82.4, 76.4, 74.4, 72.6, 71.9, 65.9, 48.9, 37.6, 37.4, 36.7, 30.2, 27.1, 24.9, 20.5, 19.5, 18.4, 15.3, 13.6, 12.4, 11.3 ppm; MS (ESI) *m/z* 195.1 (4), 264.9 (7), 286.9 (19), 338.3 (13), 533.3 (10), 641.4 (9), 749.5 (11, $M+H^+$), 750.5 (6), 766.5 (4, $M+NH_4^+$) 771.4 (100, $M+Na^+$), 772.4 (58), 773.4 (17); HRMS calcd for $C_{48}H_{65}O_5Si$ [$M+H^+$]: 749.4596, found: 749.4597 (0.2 ppm); calcd for $C_{48}H_{68}O_5NSi$ [$M+NH_4^+$]: 766.4861, found: 766.4847 (−1.8 ppm); calcd for $C_{48}H_{64}O_5NaSi$ [$M+Na^+$]: 771.4415, found: 771.4418 (0.4 ppm).

4.8. (+)-(*S*)-2-((4*S*,5*S*,6*R*)-6-((*R*)-1-((2*S*,3*S*,6*S*)-6-((*R*)-1-((*tert*-Butyldiphenylsilyl)oxy)propan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)ethyl)-2,2,5-trimethyl-1,3-dioxan-4-yl)propyl pivalate (S1)

To a cooled (0 °C) solution of diol **18** (478 mg, 0.73 mmol) in DMF (0.1 M, 7.3 mL) was added successively 2-methoxypropene (6 equiv, 410 μL) and PPTS (0.1 equiv, 17 mg). After stirring for 3 h at rt, reaction mixture was poured in a separatory funnel containing hexanes and a saturated brine solution. The aqueous layer was extracted with hexanes (3×) and combined organic fractions were washed (2×) with brine, then dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (hexanes/EtOAc, 90:10) to give acetonide-protected product **S1** as a colorless oil (0.49 g, yield=96%). R_f 0.34 (hexanes/EtOAc, 90:10); $[\alpha]_D^{25}$ +17 (*c* 0.14, $CDCl_3$); $C_{42}H_{66}O_6Si$; MW 695.06 g/mol; IR (liquid film) ν_{max} 2962, 1728, 1155, 1111 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 7.67–7.63 (m, 4H), 7.43–7.32 (m, 6H), 4.21 (dd, *J*=11.0, 5.7 Hz, 1H), 3.86 (dd, *J*=11.0, 7.3 Hz, 1H), 3.71 (dd, *J*=9.8, 5.5 Hz, 1H), 3.65 (dd, *J*=9.8, 4.7 Hz, 1H), 3.60 (td, *J*=8.2, 3.8 Hz, 1H), 3.40 (dd, *J*=7.4, 4.5 Hz, 1H), 3.32 (dd, *J*=10.0, 3.1 Hz, 1H), 3.26 (dd, *J*=10.2, 2.1 Hz, 1H), 2.15–2.05 (m, 2H), 1.94–1.85 (m, 1H), 1.83–1.76 (m, 1H), 1.72–1.59 (m, 2H), 1.55–1.47 (m, 1H), 1.42–1.30 (m, 2H), 1.23 (s, 3H), 1.20 (s, 3H), 1.19 (s, 9H), 1.05 (s, 9H), 0.98 (d, *J*=7.0 Hz, 3H), 0.97 (d, *J*=6.8 Hz, 3H), 0.95 (d, *J*=7.1 Hz, 3H), 0.88 (d, *J*=6.9 Hz, 3H), 0.77 (d, *J*=6.5 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 178.8, 135.88, 135.86, 134.26, 134.24, 129.6, 129.5, 127.66, 127.65, 97.7, 77.9, 77.5, 77.3, 70.9, 65.8, 65.6, 38.9, 38.5, 36.8, 34.1, 33.3, 30.1, 29.8, 27.4, 27.1, 26.2, 23.5, 19.5, 19.4, 18.6, 15.9, 13.9, 13.3, 13.1 ppm; MS (ESI) *m/z* 395.2 (85), 637.4 (30), 695.5 (100, $M+H^+$); HRMS calcd for $C_{42}H_{66}O_6NaSi$ [$M+Na^+$]: 717.4526, found: 717.4518 (1.2 ppm); Analysis calcd for $C_{42}H_{66}O_6Si$: C, 72.58; H, 9.57; found: C, 72.31; H, 9.70.

4.9. (+)-(*S*)-2-((4*S*,5*S*,6*R*)-6-((*R*)-1-((2*S*,3*S*,6*S*)-6-((*R*)-1-((*tert*-Butyldiphenylsilyl)oxy)propan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)ethyl)-2,2,5-trimethyl-1,3-dioxan-4-yl)propan-1-ol (S2)

Primary alcohol **S2** (413 mg, yield=98%) as a colorless oil was obtained from ester **S1** (0.48 g, 0.69 mmol) according to general procedure **B**, and purification by flash chromatography on silica gel (hexanes/EtOAc, 85:15). R_f 0.22 (hexanes/EtOAc, 80:20); $[\alpha]_D^{25}$ +18 (*c* 0.65, $CDCl_3$); $C_{37}H_{58}O_5Si$; MW 610.94 g/mol; IR (liquid film) ν_{max} 3457, 2859, 1461, 1428, 1379, 1254 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 7.68–7.63 (m, 4H), 7.44–7.31 (m, 6H), 3.94 (dd, *J*=4.0, 11.0 Hz, 1H), 3.69 (dd, *J*=6.3, 11.0 Hz, 1H), 3.66–3.57 (m, 2H), 3.51–3.43 (m, 1H), 3.43–3.31 (m, 3H), 2.88 (br s, 1H), 2.14–2.03 (m, 1H), 1.97–1.87 (m, 1H), 1.87–1.74 (m, 2H), 1.75–1.60 (m, 2H), 1.60–1.48 (m, 1H), 1.45–1.29 (m, 2H), 1.25 (s, 3H), 1.20 (s, 3H), 1.11 (d, *J*=7.0 Hz, 3H), 1.05 (s, 9H), 0.98 (d, *J*=7.0 Hz, 3H), 0.97 (d, *J*=6.8 Hz, 3H), 0.88 (d, *J*=6.9 Hz, 3H), 0.73 (d, *J*=6.5 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 135.9 (2C), 134.23, 134.19, 129.62, 129.55, 127.7 (2C), 98.1, 80.2, 77.8, 77.4, 71.1, 65.8, 63.9, 38.1, 36.8, 34.3, 34.2, 30.3, 30.0, 27.1, 26.3, 23.6, 19.5, 19.0, 18.6, 15.6, 14.1, 13.3, 13.2 ppm; MS (ESI) *m/z* 553.4 (25), 611.4 (40, $M+H^+$), 633.3 (100, $M+Na^+$); HRMS calcd for $C_{37}H_{59}O_5Si$ [$M+H^+$]: 611.4132, found: 611.4130 (0.2 ppm).

4.10. (+)-(*R*)-2-((4*R*,5*R*,6*R*)-6-((*R*)-1-((2*S*,3*S*,6*S*)-6-((*R*)-1-((*tert*-Butyldiphenylsilyl)oxy)propan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)ethyl)-2,2,5-trimethyl-1,3-dioxan-4-yl)propanal (19)

To a cooled (−78 °C) solution of oxalyl chloride (1.2 equiv, 67 μL) in dry CH_2Cl_2 (3.5 mL) was added dropwise anhydrous DMSO (2.4 equiv, 110 μL). After stirring for 5 min at −78 °C, a solution of primary alcohol **S2** (0.41 g, 0.67 mmol) in dry CH_2Cl_2 (0.2 M, 3.5 mL) was cannulated into the reaction flask, and the mixture was allowed to stir for an additional 30 min at −78 °C before addition of dry Et_3N (5 equiv, 0.47 mL). Mixture was stirred 1 h at −78 °C, before addition of a saturated aqueous solution of NH_4Cl. The aqueous layer was extracted with Et_2O (3×) and combined organic fractions were washed (2×) with brine, then dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (hexanes/EtOAc, 90:10) to give aldehyde **19** as a colorless oil (0.36 g, yield=88%). R_f 0.21 (hexanes/EtOAc, 90:10); $[\alpha]_D^{25}$ +13 (*c* 0.35, $CDCl_3$); $C_{37}H_{56}O_5Si$; MW 608.92 g/mol; IR (liquid film) ν_{max} 2858, 1725, 1379, 1202 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.73 (d, *J*=2.6 Hz, 1H), 7.68–7.63 (m, 4H), 7.44–7.33 (m, 6H), 3.71 (dd, *J*=9.7, 5.4 Hz, 1H), 3.64 (dd, *J*=9.7, 4.5 Hz, 1H), 3.62 (td, *J*=8.2, 4.2 Hz, 1H), 3.50 (dd, *J*=10.4, 2.0 Hz, 1H), 3.39–3.33 (m, 2H), 2.50 (ddq, *J*=2.3, 2.3, 6.8 Hz, 1H), 2.10–2.00 (m, 1H), 1.97–1.87 (m, 1H), 1.81–1.72 (m, 1H), 1.72–1.60 (m, 2H), 1.59–1.48 (m, 1H), 1.46–1.37 (m, 1H), 1.38–1.27 (m, 1H), 1.23 (s, 3H), 1.21 (s, 3H), 1.16 (d, *J*=7.0 Hz, 3H), 1.05 (s, 9H), 0.95 (d, *J*=6.7 Hz, 3H), 0.95 (d, *J*=7.1 Hz, 3H), 0.89 (d, *J*=6.9 Hz, 3H), 0.77 (d, *J*=6.5 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 205.2, 135.9 (2C), 134.24, 134.21, 129.6, 129.5, 127.7 (2C), 98.0, 77.7, 77.2, 76.9, 71.2, 65.8, 47.5, 37.9, 36.8, 34.3, 30.1, 30.0, 27.1, 26.4, 23.7, 19.5, 19.0, 18.6, 13.9, 13.3, 13.1, 11.9 ppm; MS (ESI) *m/z* 277.2 (100), 395.3 (50), 533.4 (50), 609.5 (70, $M+H^+$); HRMS calcd for $C_{37}H_{56}O_5NaSi$ [$M+Na^+$]: 631.3795, found: 631.3781 (2.2 ppm); Analysis calcd for $C_{37}H_{56}O_5Si$: C, 72.98; H, 9.27; found: C, 72.95; H, 9.51.

4.11. (+)-(2*S*,3*R*)-2-((4*S*,5*S*,6*R*)-6-((*R*)-1-((2*S*,3*S*,6*S*)-6-((*R*)-1-((*tert*-Butyldiphenylsilyl)oxy)propan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)ethyl)-2,2,5-trimethyl-1,3-dioxan-4-yl)hex-5-en-3-ol (20a); (+)-(2*S*,3*S*)-2-((4*S*,5*S*,6*R*)-6-((*R*)-1-((2*S*,3*S*,6*S*)-6-((*R*)-1-

((*tert*-Butyldiphenylsilyl)oxy)propan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)ethyl)-2,2,5-trimethyl-1,3-dioxan-4-yl)hex-5-en-3-ol (20b)

Homoallylic alcohols **20a** and **20b** were obtained from aldehyde **19** (0.25 g, 0.41 mmol) according to general procedure **D** using allyltributylstannane as the nucleophile. ^{1}H NMR analysis of the crude product indicated a ratio 1:1 of product 12,13-*syn* (**20a**): 12,13-*anti* (**20b**). The residue was purified by flash chromatography on silica gel (hexanes/EtOAc, 85:15) to give products **20a** (70 mg, yield=26%) and **20b** (73 mg, yield=27%) as colorless oils. **20a**; R_f 0.20 (hexanes/EtOAc, 90:10); $[\alpha]_D^{25}$ +38 (*c* 0.15, $CDCl_3$); $C_{40}H_{62}O_5Si$; MW 651.00 g/mol; IR (liquid film) ν_{max} 3484, 2960, 2859, 1460, 1428 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.68–7.63 (m, 4H), 7.43–7.33 (m, 6H), 5.89 (dddd, *J*=16.8, 10.3, 7.7, 6.1 Hz, 1H), 5.14–5.07 (m, 2H), 3.72 (dd, *J*=9.7, 5.3 Hz, 1H), 3.75–3.59 (m, 2H), 3.63 (dd, *J*=9.8, 4.5 Hz, 1H), 3.39 (dd, *J*=6.8, 5.0 Hz, 1H), 3.35–3.30 (m, 2H), 2.91 (br s, 1H), 2.47–2.39 (m, 1H), 2.21–2.10 (m, 1H), 2.10–2.00 (m, 1H), 1.96–1.88 (m, 1H), 1.88–1.73 (m, 3H), 1.71–1.60 (m, 1H), 1.55–1.47 (m, 1H), 1.46–1.28 (m, 2H), 1.25 (s, 3H), 1.20 (s, 3H), 1.05 (s, 9H), 0.97 (d, *J*=7.1 Hz, 3H), 0.95 (d, *J*=6.9 Hz, 3H), 0.94 (d, *J*=7.1 Hz, 3H), 0.89 (d, *J*=6.9 Hz, 3H), 0.77 (d, *J*=6.4 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 136.2, 135.87, 135.85, 134.25, 134.22, 129.6, 129.5, 127.67, 127.66, 117.1, 97.9, 79.8, 77.6, 77.4, 73.4, 71.1, 65.7, 39.9, 39.0, 38.1, 36.8, 35.4, 30.3, 30.0, 27.1, 26.4, 23.7, 19.5, 19.1, 18.6, 16.8, 14.0, 13.7, 13.3 ppm; MS (ESI) *m*/*z* 343.1 (60), 381.2 (52), 637.2 (65), 651.3 (60, M+H$^+$), 673.3 (100, M+Na$^+$); HRMS calcd for $C_{40}H_{62}O_5NaSi$ [M+Na$^+$]: 673.4264, found: 673.4274 (1.4 ppm). **20b**; R_f 0.33 (hexanes/EtOAc, 90:10); $[\alpha]_D^{25}$ +24 (*c* 0.20, $CDCl_3$); $C_{40}H_{62}O_5Si$; MW 651.00 g/mol; IR (liquid film) ν_{max} 3520, 3071, 2859, 1461, 1428, 1379 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.68–7.64 (m, 4H), 7.43–7.34 (m, 6H), 5.80 (dddd, *J*=16.8, 10.2, 7.7, 6.4 Hz, 1H), 5.14–5.05 (m, 2H), 4.02 (dd, *J*=7.5, 6.9 Hz, 1H), 3.71 (dd, *J*=9.7, 5.4 Hz, 1H), 3.64 (dd, *J*=9.9, 4.7 Hz, 1H), 3.66–3.58 (m, 2H), 3.40 (dd, *J*=10.4, 1.6 Hz, 1H), 3.38–3.34 (m, 2H), 2.39–2.30 (m, 1H), 2.12–2.04 (m, 2H), 1.96–1.87 (m, 1H), 1.83–1.71 (m, 2H), 1.71–1.63 (m, 1H), 1.59–1.50 (m, 2H), 1.45–1.38 (m, 1H), 1.38–1.30 (m, 1H), 1.25 (s, 3H), 1.20 (s, 3H), 1.05 (d, *J*=2.8 Hz, 9H), 1.00 (d, *J*=7.1 Hz, 3H), 0.97 (d, *J*=6.8 Hz, 3H), 0.96 (d, *J*=7.1 Hz, 3H), 0.90 (d, *J*=6.9 Hz, 3H), 0.70 (d, *J*=6.5 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 135.87, 135.86, 135.6, 134.3, 134.2, 129.62, 129.55, 127.68, 127.67, 117.0, 98.3, 81.1, 77.9, 77.2, 71.1, 69.7, 65.8, 39.3, 38.2, 37.0, 35.0, 33.6, 30.2, 30.1, 27.1, 26.3, 23.6, 19.5, 19.0, 18.7, 14.1, 13.3, 12.9, 11.0 ppm; MS (ESI) *m*/*z* 381.2 (65), 637.2 (100), 651.3 (20, M+H$^+$), 673.3 (80, M+Na$^+$); HRMS calcd for $C_{40}H_{62}O_5NaSi$ [M+Na$^+$]: 673.4264, found: 673.4260 (0.6 ppm).

4.12. (5*S*,6*S*,7*S*,8*S*,9*S*)-6,8-bis(Benzyloxy)-9-((2*S*,3*S*,6*S*)-6-((*R*)-1-((*tert*-butyldiphenylsilyl)oxy)propan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)-5,7-dimethyldec-1-en-4-ol (21a; 21b)

Homoallylic alcohols **21a** and **21b** were obtained from aldehyde **17** (12 mg, 16 μmol) according to general procedure **D** using allyltributylstannane as the nucleophile. ^{1}H NMR analysis of the crude product indicated a ratio 1.3:1 of alcohols **21a** and **21b**. The two diastereoisomers were separated by flash chromatography on silica gel (hexanes/EtOAc, 90:10) to yield **21a** (6.3 mg, yield=50% over 2 steps) and **21b** (5.6 mg, yield=44% over 2 steps) as colorless oils. **21a**; R_f 0.35 (hexanes/EtOAc, 90:10); $C_{51}H_{70}O_5Si$; MW 791.18 g/mol; IR (liquid film) ν_{max} 3503, 3069, 2962, 2929, 2857, 1456, 1428, 1380, 1112, 1092, 1065, 1028 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.69–7.61 (m, 4H), 7.42–7.31 (m, 6H), 7.28–7.17 (m, 10H), 5.76 (ddt, *J*=17.2, 10.2, 7.3 Hz, 1H), 5.05 (dd, *J*=24.8, 13.7 Hz, 2H), 4.80 (d, *J*=11.3 Hz, 1H), 4.48 (d, *J*=11.3 Hz, 1H), 4.42 (d, *J*=11.7 Hz, 1H), 4.38 (d, *J*=11.7 Hz, 1H), 4.10 (app t, *J*=7.0 Hz, 1H), 3.80 (s, 1H), 3.74–3.69 (m, 2H), 3.67–3.62 (m, 2H), 3.45 (dd, *J*=8.6, 2.4 Hz, 1H), 3.37 (dd, *J*=9.0, 2.1 Hz, 1H), 2.35–2.25 (m, 2H), 2.09–2.00 (m, 2H), 2.00–1.92 (m, 1H), 1.88–1.80 (m, 1H), 1.61–1.54 (m, 4H), 1.22–1.12 (m, 1H), 1.03 (d, *J*=6.9 Hz, 3H), 1.03 (s, 9H), 0.92 (d, *J*=7.0 Hz, 3H), 0.87 (d, *J*=7.0 Hz, 2×3H), 0.59 (d, *J*=6.4 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 139.5, 138.4, 135.92, 135.86, 135.7, 134.14, 134.10, 129.66, 129.59, 128.56, 128.3, 127.73, 127.70, 127.6, 127.23, 127.22, 127.0, 116.8, 87.3, 85.6, 76.0, 74.6, 74.5, 72.3, 70.6, 66.0, 39.4, 38.7, 37.0, 36.9, 35.9, 30.7, 27.5, 27.1, 25.4, 19.5, 18.3, 17.1, 13.8, 12.1, 11.3 ppm; MS (ESI) *m*/*z* 227.0 (6), 360.3 (5), 791.5 (25, M+H$^+$), 792.5 (25), 793.5 (5), 808.5 (3, M+NH$_4^+$), 813.5 (100, M+Na$^+$), 814.5 (60), 815.5 (17); HRMS calcd for $C_{51}H_{71}O_5Si$ [M+H$^+$]: 791.5065, found: 791.5058 (−0.9 ppm); calcd for $C_{51}H_{74}O_5NSi$ [M+NH$_4^+$]: 808.5331, found: 808.5320 (−1.4 ppm); calcd for $C_{51}H_{70}O_5NaSi$ [M+Na$^+$]: 813.4885, found: 813.4900 (1.9 ppm). **21b**; R_f 0.24 (hexanes/EtOAc, 90:10); $C_{51}H_{70}O_5Si$; MW 791.18 g/mol; IR (liquid film) ν_{max} 3462, 3070, 2959, 2929, 2857, 1496, 1455, 1428, 1382, 1111, 1091, 1065, 1028 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.67–7.61 (m, 4H), 7.42–7.31 (m, 6H), 7.26–7.18 (m, 10H), 5.92–5.83 (m, 1H), 5.07 (dd, *J*=13.0, 9.3 Hz, 2H), 4.66 (d, *J*=11.4 Hz, 1H), 4.51 (d, *J*=11.5 Hz, 1H), 4.41–4.40 (m, 2H), 3.74–3.62 (m, 4H), 3.59 (dd, *J*=6.5, 4.6 Hz, 1H), 3.46 (dd, *J*=7.1, 4.2 Hz, 1H), 3.35 (dd, *J*=7.7, 3.9 Hz, 1H), 3.14 (d, *J*=2.6 Hz, 1H), 2.41–2.35 (m, 1H), 2.25–2.20 (m, 1H), 2.19–2.14 (m, 1H), 2.12–2.04 (m, 1H), 1.99–1.90 (m, 2H), 1.67–1.55 (m, 4H), 1.24–1.14 (m, 1H), 1.03 (s, 9H), 0.96 (d, *J*=7.2 Hz, 3H), 0.91 (d, *J*=7.0 Hz, 3H), 0.88 (d, *J*=7.4 Hz, 3H), 0.87 (d, *J*=7.6 Hz, 3H), 0.68 (d, *J*=6.5 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 139.5, 138.7, 136.0, 135.90, 135.87, 134.15, 134.10, 129.65, 129.61, 128.4, 128.2, 127.72, 127.69, 127.61, 127.56, 127.18, 127.13, 117.0, 85.6, 84.8, 76.5, 74.0, 73.5, 73.2, 71.8, 66.0, 40.7, 39.0, 38.8, 37.6, 36.8, 30.2, 27.1, 27.0, 24.8, 19.5, 18.4, 15.9, 15.8, 13.6, 11.5 ppm; MS (ESI) *m*/*z* 227.0 (5), 360.3 (7), 791.5 (16, M+H$^+$), 792.5 (10), 793.5 (3), 808.5 (3, M+NH$_4^+$), 813.5 (100, M+Na$^+$), 814.5 (59), 815.5 (18), 816.5 (3); HRMS calcd for $C_{51}H_{71}O_5Si$ [M+H$^+$]: 791.5065, found: 791.5061 (−0.5 ppm); calcd for calcd for $C_{51}H_{74}O_5NSi$ [M+NH$_4^+$]: 808.5331, found: 808.5325 (−0.7 ppm); calcd for $C_{51}H_{70}O_5NaSi$ [M+Na$^+$]: 813.4885, found: 813.4903 (2.2 ppm).

4.13. (±)-(4*R*,5*S*,6*R*,7*R*)-6,8-bis(Benzyloxy)-5,7-dimethyloct-1-en-4-ol (28a)

Homoallylic alcohol **28a** was obtained from aldehyde **24**[10] (19.5 mg, 60 μmol) according to general procedure **D** using allyltributylstannane as the nucleophile. ^{1}H NMR analysis of the crude product indicated a ratio >20:1 of products 4,5-*syn* (**28a**): 4,5-*anti* (**28b**). The residue was purified by flash chromatography on silica gel (hexanes/EtOAc, 85:15) to yield **28a** as a colorless oil (18.9 mg, yield=86%).[22] R_f 0.32 (hexanes/EtOAc, 85:15); $C_{24}H_{32}O_3$; MW 368.51 g/mol; IR (liquid film) ν_{max} 3499, 2970, 2908, 2876, 1496, 1454, 1354, 1088 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.30–7.14 (m, 10H), 5.70 (dddd, *J*=6.8, 7.5, 10.2, 17.1 Hz, 1H), 5.05–4.94 (m, 2H), 4.53 (d, *J*=10.8 Hz, 1H), 4.48 (d, *J*=10.8 Hz, 1H), 4.42 (s, 2H), 3.97 (app t, *J*=7.0 Hz, 1H), 3.56 (dd, *J*=8.9, 5.0 Hz, 1H), 3.45 (td, *J*=8.6, 3.2 Hz, 2H), 3.41 (s, 1H), 2.31–2.20 (m, 1H), 2.12–1.99 (m, 2H), 1.77–1.69 (m, 1H), 1.01 (d, *J*=7.1 Hz, 3H), 0.93 (d, *J*=7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 138.6, 138.2, 135.5, 128.6, 128.5, 127.9, 127.82, 127.77, 127.69, 117.0, 87.1, 76.0, 73.3, 72.4, 69.9, 39.3, 37.0, 36.9, 15.2, 11.5 ppm; MS (ESI) *m*/*z* 369.2 (35, M+H$^+$), 391.2 (100, M+Na$^+$), 481.3 (19); HRMS calcd for $C_{24}H_{33}O_3$ [M+H$^+$]: 369.2424, found: 369.2429 (1.2 ppm); calcd for $C_{24}H_{32}O_3Na$ [M+Na$^+$]: 391.2244, found: 391.2249 (1.2 ppm).

4.14. (±)-(3*S*,4*S*,5*R*,6*R*)-Methyl 5,7-bis(benzyloxy)-3-hydroxy-2,2,4,6-tetramethylheptanoate (30a)

β-Hydroxyester **30a** was obtained from aldehyde **24** (154 mg, 0.47 mmol) according to general procedure **D** using 1-methoxy-2-methyl-1-(trimethylsiloxy)propene **26** as the nucleophile. ^{1}H NMR analysis of the crude product indicated a ratio >20:1 of product 3,4-

syn (**30a**): 3,4-*anti* (**30b**). The residue was purified by flash chromatography on silica gel (hexanes/EtOAc, 90:10) to yield unreacted aldehyde **24** (70.2 mg, yield=45%) and 3,4-*syn* product **30a** (86.1 mg, yield=43%, 78% brsm) as colorless oils. R_f 0.22 (hexanes/EtOAc, 90:10); $C_{26}H_{36}O_5$; MW 428.56 g/mol; IR (liquid film) ν_{max} 3495, 3029, 2973, 2932, 2877, 1731, 1454, 1257, 1141, 1073 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ_H 7.44–7.20 (m, 10H), 4.61 (d, *J*=11.2 Hz, 1H), 4.58 (d, *J*=11.1 Hz, 1H), 4.53 (d, *J*=12.3 Hz, 1H), 4.50 (d, *J*=12.3 Hz, 1H), 4.03 (d, *J*=3.2 Hz, 1H), 3.68 (s, 3H), 3.63 (dd, *J*=8.8, 5.4 Hz, 1H), 3.56 (dd, *J*=8.9, 3.5 Hz, 1H), 3.40 (dd, *J*=8.2, 3.3 Hz, 1H), 3.20 (d, *J*=3.3 Hz, 1H), 2.16–2.07 (m, 1H), 1.97–1.90 (m, 1H), 1.22 (s, 3H), 1.21 (s, 3H), 1.040 (d, *J*=6.6 Hz, 3H), 1.038 (d, *J*=7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 178.0, 138.6, 138.4, 128.6, 128.5, 127.91, 127.89, 127.74, 127.66, 88.1, 76.1, 74.7, 73.3, 72.2, 52.0, 46.9, 36.6, 35.3, 22.9, 22.8, 15.5, 13.3 ppm; MS (ESI) *m/z* 213.1 (4), 321.2 (4), 411.3 (17), 429.3 (86, $M+H^+$), 451.2 (100, $M+Na^+$), 519.3 (14), 541.3 (22), 879.5 (17); HRMS calcd for $C_{26}H_{37}O_5$ [$M+H^+$]: 429.2636, found: 429.2629 (−1.6 ppm); calcd for $C_{26}H_{36}O_5Na$ [$M+Na^+$]: 451.2455, found: 451.2448 (−1.6 ppm).

4.15. (±)-(3*S*,4*S*,5*R*,6*R*)-Methyl 5,7-bis(benzyloxy)-3-hydroxy-4,6-dimethyl-2-(phenylselanyl)heptanoate (31a-1; 31a-2)

β-Hydroxyesters **31a-1** and **31a-2** were obtained from aldehyde **24** (50.2 mg, 0.15 mmol) according to general procedure **D** using enoxysilane **27**[9a] as the nucleophile. ^1H NMR analysis of the crude product indicated a ratio >20:1 of products 3,4-*syn* (**31a**): 3,4-*anti* (**31b**) and a mixture ~3:1 of C2-phenylselenides **31a-1** and **31a-2**. The two diastereoisomers were separated by flash chromatography on silica gel (hexanes/EtOAc, 80:20) to yield products **31a-1** and **31a-2** (76.6 mg, combined yield=92%) as pale yellow oils. The relative stereochemistry of compounds **31a-1** and **31a-2** was not determined. **31a-1**; R_f 0.21 (hexanes/EtOAc, 85:15); $C_{30}H_{36}O_5Se$; MW 555.56 g/mol; IR (liquid film) ν_{max} 3467, 3060, 3029, 2968, 2877, 1728, 1454, 1436, 1258, 1087 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ_H 7.66–7.61 (m, 2H), 7.38–7.18 (m, 13H), 4.58 (d, *J*=10.8 Hz, 1H), 4.55 (d, *J*=10.8 Hz, 1H), 4.49 (s, 2H), 4.33 (d, *J*=10.6 Hz, 1H), 3.98 (s, 1H), 3.93 (d, *J*=10.5 Hz, 1H), 3.66 (dd, *J*=8.9, 4.5 Hz, 1H), 3.54 (dd, *J*=9.0, 2.5 Hz, 1H), 3.47 (dd, *J*=9.0, 3.5 Hz, 1H), 3.45 (s, 3H), 2.15–2.06 (m, 1H), 1.90–1.80 (m, 1H), 1.11 (d, *J*=7.1 Hz, 3H), 0.98 (d, *J*=7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 171.3, 138.6, 137.9, 136.5, 129.0, 128.8, 128.6, 128.5, 128.0, 127.9, 127.8, 127.7, 127.5, 86.8, 77.4, 76.1, 73.3, 69.8, 51.8, 48.9, 37.0, 36.2, 14.7, 11.7 ppm; MS (ESI) *m/z* 195.1 (8), 338.3 (8), 449.1 (9), 539.2 (9), 557.2 (19, $M+H^+$), 579.2 (100, $M+Na^+$), 595.1 (5), 669.2 (16); HRMS calcd for $C_{30}H_{37}O_5Se$ [$M+H^+$]: 557.1801, found: 557.1800 (−0.2 ppm); calcd for $C_{30}H_{36}O_5SeNa$ [$M+Na^+$]: 579.1620, found: 579.1630 (1.7 ppm). **31a-2**; R_f 0.20 (hexanes/EtOAc, 85:15); $C_{30}H_{36}O_5Se$; MW 555.56 g/mol; IR (liquid film) ν_{max} 3457, 3065, 3021, 2963, 2882, 1732, 1454, 1436, 1270 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ_H 7.61–7.56 (m, 2H), 7.36–7.18 (m, 13H), 4.55 (d, *J*=11.4 Hz, 1H), 4.53 (d, *J*=11.5 Hz, 1H), 4.51 (s, 2H), 4.43 (d, *J*=10.7 Hz, 1H), 3.88 (s, 1H), 3.71–3.66 (m, 2H), 3.64 (s, 3H), 3.57 (dd, *J*=9.0, 2.8 Hz, 1H), 3.52 (dd, *J*=8.9, 3.4 Hz, 1H), 2.43–2.34 (m, 1H), 2.22–2.12 (m, 1H), 1.10 (d, *J*=7.0 Hz, 3H), 0.90 (d, *J*=7.1 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 172.8, 138.6, 134.0, 135.3, 129.4, 128.7, 128.6, 128.5, 128.02, 127.98, 127.90, 127.81, 127.74, 86.9, 76.2, 73.3, 72.3, 71.4, 52.4, 47.9, 36.9, 34.5, 15.2, 11.5 ppm; MS (ESI) *m/z* 182.2 (17), 227.0 (6), 337.1 (27), 365.1 (30), 391.2 (35), 421.2 (17), 457.3 (11), 539.2 (9), 579.2 (100, $M+Na^+$), 595.2 (9), 656.3 (16), 669.2 (12); HRMS calcd for $C_{30}H_{37}O_5Se$ [$M+H^+$]: 557.1801, found: 557.1806 (0.9 ppm); calcd for $C_{30}H_{36}O_5SeNa$ [$M+Na^+$]: 579.1620, found: 579.1634 (2.4 ppm).

4.16. (±)-(3*R*,4*S*,5*R*,6*R*)-Methyl 5,7-bis(benzyloxy)-3-hydroxy-4,6-dimethylheptanoate (36)

Product **36** (72.4 mg, yield=60%) as a colorless oil was obtained from a mixture of phenylselenide **31a-1**; **31a-2** (168 mg, 0.30 mmol) according to general procedure **F**, and purification by flash chromatography on silica gel (hexanes/EtOAc, 80:20). R_f 0.22 (hexanes/EtOAc, 80:20); $C_{24}H_{32}O_5$; MW 400.51 g/mol; IR (liquid film) ν_{max} 3494, 3030, 2965, 2913, 2879, 1737, 1454, 1355, 1173, 1089 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ_H 7.38–7.23 (m, 10H), 4.60 (d, *J*=10.9 Hz, 1H), 4.58 (d, *J*=10.9 Hz, 1H), 4.51 (s, 2H), 3.69 (s, 3H), 3.65 (dd, *J*=8.9, 5.0 Hz, 1H), 3.68–3.59 (m, 1H), 3.62 (s, 1H), 3.55 (dd, *J*=8.5, 3.4 Hz, 1H), 3.53 (dd, *J*=9.0, 3.7 Hz, 1H), 2.59 (dd, *J*=15.4, 8.3 Hz, 1H), 2.35 (dd, *J*=15.3, 5.4 Hz, 1H), 2.25–2.15 (m, 1H), 1.86–1.79 (m, 1H), 1.09 (d, *J*=7.1 Hz, 3H), 1.06 (d, *J*=7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 172.6, 138.6, 138.1, 128.6, 128.5, 128.0, 127.9, 127.8, 127.7, 86.6, 76.0, 73.3, 72.3, 67.3, 51.8, 39.7, 37.5, 36.8, 15.3, 11.7 ppm; MS (ESI) *m/z* 401.2 (7, $M+H^+$), 423.2 (100, $M+Na^+$), 513.3 (17), 603.3 (3), 823.4 (13); HRMS calcd for $C_{24}H_{33}O_5$ [$M+H^+$]: 401.2323, found: 401.2317 (−1.4 ppm); calcd for $C_{24}H_{32}O_5Na$ [$M+Na^+$]: 423.2142, found: 423.2134 (−1.9 ppm).

4.17. (±)-(4*R*,5*S*,6*S*,7*S*)-6,8-bis(Benzyloxy)-5,7-dimethyloct-1-en-4-ol (32a); (±)-(4*S*,5*S*,6*S*,7*S*)-6,8-bis(Benzyloxy)-5,7-dimethyloct-1-en-4-ol (32b)

Homoallylic alcohols **32a** and **32b** were obtained from aldehyde **25**[9d] (62.7 mg, 0.19 mmol) according to general procedure **D** using allyltributylstannane as the nucleophile. ^1H NMR analysis of the crude product indicated a ratio 1:4.9 of products 4,5-*syn* (**32a**): 4,5-*anti* (**32b**). The residue was purified by flash chromatography on silica gel (hexanes/EtOAc, 85:15) to yield **32a**[22] and **32b** (52.3 mg, combined yield=74%) as colorless oils. **32a**; R_f 0.29 (hexanes/EtOAc, 85:15); $C_{24}H_{32}O_3$; MW 368.51 g/mol; IR (liquid film) ν_{max} 3447, 3030, 2971, 2914, 1640, 1454, 1361, 1207 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ_H 7.36–7.25 (m, 10H), 5.84 (dddd, *J*=6.3, 8.2, 9.3, 20.0 Hz, 1H), 5.18–5.13 (m, 2H), 4.66 (d, *J*=11.5 Hz, 1H), 4.55 (d, *J*=11.5 Hz, 1H), 4.50 (d, *J*=12.0 Hz, 1H), 4.48 (d, *J*=12.1 Hz, 1H), 3.82 (dd, *J*=9.0, 1.9 Hz, 1H), 3.62–3.55 (m, 1H), 3.57 (dd, *J*=8.8, 3.7 Hz, 1H), 3.53 (dd, *J*=8.8, 5.9 Hz, 1H), 2.49–2.42 (m, 1H), 2.18–2.10 (m, 2H), 2.10–2.02 (m, 1H), 1.77–1.69 (m, 1H), 0.99 (d, *J*=6.9 Hz, 3H), 0.93 (d, *J*=7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 139.3, 138.9, 135.1, 128.5, 128.4, 127.8, 127.7, 127.6, 127.5, 118.5, 80.3, 74.0, 73.3, 73.0, 72.4, 40.07, 40.05, 37.0, 15.1, 10.6 ppm; MS (ESI) *m/z* 391.2 (100, $M+Na^+$), 481.3 (4); HRMS calcd for $C_{24}H_{32}O_3Na$ [$M+Na^+$]: 391.2244, found: 391.2242 (−0.5 ppm). **32b**; R_f 0.23 (hexanes/EtOAc, 85:15); $C_{24}H_{32}O_3$; MW 368.51 g/mol; IR (liquid film) ν_{max} 3447, 3030, 2969, 2922, 1496, 1455, 1361, 1207 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ_H 7.37–7.25 (m, 10H), 5.79 (tdd, *J*=7.0. 10.0, 17.1 Hz, 1H), 5.13–5.04 (m, 2H), 4.62 (d, *J*=11.1 Hz, 1H), 4.56 (d, *J*=11.0 Hz, 1H), 4.52 (d, *J*=12.0 Hz, 1H), 4.49 (d, *J*=12.0 Hz, 1H), 3.88–3.83 (m, 1H), 3.63 (dd, *J*=7.9, 3.3 Hz, 1H), 3.60 (dd, *J*=9.1, 5.2 Hz, 1H), 3.51 (dd, *J*=9.0, 4.3 Hz, 1H), 2.88 (d, *J*=1.7 Hz, 1H), 2.33–2.23 (m, 1H), 2.23–2.09 (m, 2H), 1.79 (dd, *J*=6.6, 3.5 Hz, 1H), 1.02 (d, *J*=7.0 Hz, 3H), 0.96 (d, *J*=7.1 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 138.6, 138.4, 135.6, 128.6, 128.5, 127.83 (2C), 127.82, 127.7, 117.4, 85.2, 74.7, 74.1, 73.4, 72.4, 39.8, 38.4, 36.8, 15.0, 7.0 ppm; MS (ESI) *m/z* 391.2 (100, $M+Na^+$), 481.3 (13); HRMS calcd for $C_{24}H_{32}O_3Na$ [$M+Na^+$]: 391.2244, found: 391.2242 (−0.5 ppm).

4.18. (±)-(3*S*,4*S*,5*S*,6*S*)-Methyl 5,7-bis(benzyloxy)-3-hydroxy-2,2,4,6-tetramethylheptanoate (34a)

β-Hydroxyester **34a** was obtained from aldehyde **25** (198 mg, 0.61 mmol) according to general procedure **D** using 1-methoxy-2-methyl-1-(trimethylsiloxy)propene **26** as the nucleophile. ^1H NMR analysis of the crude product indicated a ratio >20:1 of product 3,4-*syn* (**34a**): 3,4-*anti* (**34b**). The residue was purified by flash chromatography on silica gel (hexanes/EtOAc, 90:10) to yield unreacted aldehyde **25** (99.8 mg, yield=51%) and 3,4-*syn* product **34a** (78.5 mg, yield=30% over 2 steps, 61% brsm) as colorless oils. R_f 0.10 (hexanes/EtOAc, 90:10); $C_{26}H_{36}O_5$; MW 428.56 g/mol; IR (liquid film) ν_{max}

3527, 2974, 2948, 2878, 1731, 1454, 1364, 1256, 1141, 1090 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 7.37–7.25 (m, 10H), 4.62 (s, 2H), 4.53 (d, J=12.2 Hz, 1H), 4.50 (d, J=12.5 Hz, 1H), 3.80 (d, J=4.8 Hz, 1H), 3.69 (s, 3H), 3.56 (d, J=4.8 Hz, 2H), 3.49 (dd, J=7.2, 4.3 Hz, 1H), 3.00 (d, J=4.9 Hz, 1H), 2.15–2.04 (m, 1H), 2.04–1.94 (m, 1H), 1.23 (s, 3H), 1.15 (s, 3H), 1.04 (d, J=6.9 Hz, 3H), 0.88 (d, J=7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 178.2, 138.7, 138.6, 128.53, 128.46, 127.82, 127.81, 127.72, 127.66, 86.9, 79.2, 74.8, 73.3, 72.3, 52.0, 46.9, 36.5, 36.2, 23.1, 22.2, 15.6, 8.1 ppm; MS (ESI) m/z 321.2 (6), 411.3 (7), 429.3 (100, $M+H^+$), 451.2 (91, $M+Na^+$), 519.3 (12), 879.5 (5); HRMS calcd for $C_{26}H_{37}O_5$ [$M+H^+$]: 429.2636, found: 429.2633 (−0.7 ppm); calcd for $C_{26}H_{36}O_5Na$ [$M+Na^+$]: 451.2455, found: 451.2453 (−0.5 ppm).

4.19. (±)-(3*S*,4*S*,5*S*,6*S*)-Methyl 5,7-bis(benzyloxy)-3-hydroxy-4,6-dimethyl-2-(phenylselanyl)heptanoate (35a)

β-Hydroxyester **35a** was obtained from aldehyde **25** (203 mg, 0.62 mmol) according to general procedure **D** using enoxysilane **27**[9a] as the nucleophile. ^1H NMR analysis of the crude product indicated a ratio >20:1 of product 3,4-*syn* (**35a**): 3,4-*anti* (**35b**). The residue was purified by flash chromatography on silica gel (hexanes/EtOAc, 80:20) to yield product **35a** as a pale yellow oil (333 mg, yield=97%). The relative stereochemistry of compound **35a** was not determined. R_f 0.25 (hexanes/EtOAc, 85:15); $C_{30}H_{36}O_5Se$; MW 555.56 g/mol; IR (liquid film) ν_{max} 3504, 3061, 3029, 2968, 2879, 1717, 1454, 1089 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ_H 7.69–7.63 (m, 2H), 7.39–7.25 (m, 13H), 4.59 (d, J=11.2 Hz, 1H), 4.51 (d, J=11.2 Hz, 1H), 4.50 (d, J=12.4 Hz, 1H), 4.47 (d, J=12.4 Hz, 1H), 4.06 (dd, J=7.4, 3.7 Hz, 1H), 3.87 (d, J=7.7 Hz, 1H), 3.59–3.53 (m, 2H), 3.56 (s, 3H), 3.52 (br s, 1H), 3.50 (dd, J=9.8, 4.9 Hz, 1H), 2.17–2.08 (m, 1H), 2.04–1.97 (m, 1H), 1.05 (d, J=7.0 Hz, 3H), 1.02 (d, J=7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 172.6, 138.6, 138.4, 136.0, 129.1, 128.7 (2C), 128.50, 128.46, 127.75, 127.73, 127.72, 127.6, 83.8, 74.1, 73.2, 72.7, 72.2, 52.1, 49.6, 37.8, 36.7, 15.0, 7.9 ppm; MS (ESI) m/z 449.1 (61), 539.2 (17), 557.2 (44, $M+H^+$), 579.2 (100, $M+Na^+$), 669.2 (8), 1135.3 (35); HRMS calcd for $C_{30}H_{37}O_5Se$ [$M+H^+$]: 557.1801, found: 557.1813 (2.3 ppm); calcd for $C_{30}H_{36}O_5SeNa$ [$M+Na^+$]: 579.1620, found: 579.1637 (2.9 ppm).

4.20. (±)-(3*R*,4*S*,5*S*,6*S*)-Methyl 5,7-bis(benzyloxy)-3-hydroxy-4,6-dimethylheptanoate (37)

Product **37** (129 mg, yield=54%) as a colorless oil was obtained from phenylselenide **35a** (333 mg, 0.60 mmol) according to general procedure **F**, and purification by flash chromatography on silica gel (hexanes/EtOAc, 80:20). R_f 0.18 (hexanes/EtOAc, 80:20); $C_{24}H_{32}O_5$; MW 400.51 g/mol; IR (liquid film) ν_{max} 3512, 3063, 3030, 2965, 2916, 28,79, 1736, 1454, 1172, 1091 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ_H 7.41–7.25 (m, 10H), 4.62 (d, J=11.1 Hz, 1H), 4.57 (d, J=11.2 Hz, 1H), 4.53 (d, J=12.2 Hz, 1H), 4.50 (d, J=12.4 Hz, 1H), 4.24 (dt, J=8.6, 3.8 Hz, 1H), 3.70 (s, 3H), 3.65 (dd, J=7.3, 3.6 Hz, 1H), 3.58 (dd, J=9.0, 5.2 Hz, 1H), 3.54 (dd, J=9.1, 4.6 Hz, 1H), 3.25 (br s, 1H), 2.54 (dd, J=15.7, 8.8 Hz, 1H), 2.43 (dd, J=15.7, 4.2 Hz, 1H), 2.22–2.12 (m, 1H), 1.85–1.77 (m, 1H), 1.03 (d, J=7.0 Hz, 3H), 1.00 (d, J=7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 173.1, 138.5, 138.4, 128.53, 128.47, 127.75 (2C), 127.74, 127.7, 84.0, 74.0, 73.3, 72.3, 71.3, 51.8, 39.7, 39.2, 36.7, 15.0, 7.9 ppm; MS (ESI) m/z 401.2 (16, $M+H^+$), 423.2 (100, $M+Na^+$), 513.3 (8), 823.4 (30), 913.5 (3); HRMS calcd for $C_{24}H_{33}O_5$ [$M+H^+$]: 401.2323, found: 401.2329 (1.6 ppm); calcd for $C_{24}H_{32}O_5Na$ [$M+Na^+$]: 423.2142, found: 423.2144 (0.4 ppm).

4.21. (±)-(3*S*,4*S*)-Methyl 4-((2*S*,3*S*,6*S*)-6-((*R*)-1-(benzyloxy) propan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)-3-hydroxy-2-(phenylselanyl)pentanoate (S3)

β-Hydroxyester **S3** was obtained from aldehyde **38**[11a] (116 mg, 0.38 mmol) according to general procedure **D** using enoxysilane **27**[9a] as the nucleophile. ^1H NMR analysis of the crude product indicated a ratio >20:1 of product 3,4-*syn* (**S3**): 3,4-*anti*. The residue was purified by flash chromatography on silica gel (hexanes/EtOAc, 90:10) to yield product **S3** as a pale yellow oil (137 mg, yield=68%). R_f 0.19 (hexanes/EtOAc, 90:10); $C_{28}H_{38}O_5Se$; MW 533.56 g/mol; IR (liquid film) ν_{max} 3440, 2950, 2929, 2858, 1729, 1455, 1437, 1089, 1018 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ_H 7.70–7.66 (m, 2H), 7.41–7.24 (m, 8H), 4.58 (d, J=11.9 Hz, 1H), 4.53 (d, J=11.9 Hz, 1H), 4.14 (dd, J=9.6, 1.9 Hz, 1H), 4.11 (s, 1H), 3.97 (d, J=9.5 Hz, 1H), 3.71 (dt, J=10.2, 3.8 Hz, 1H), 3.55 (dd, J=9.1, 3.2 Hz, 1H), 3.49 (s, 3H), 3.44 (dd, J=9.1, 6.3 Hz, 1H), 3.40 (dd, J=9.4, 2.8 Hz, 1H), 2.31–2.21 (m, 1H), 1.86–1.77 (m, 1H), 1.71–1.65 (m, 2H), 1.64–1.52 (m, 2H), 1.29–1.18 (m, 1H), 0.95 (d, J=7.1 Hz, 3H), 0.93 (d, J=6.8 Hz, 3H), 0.77 (d, J=6.5 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 171.9, 138.9, 136.4, 129.0, 128.7, 128.5, 127.84, 127.81, 127.5, 80.9, 74.8, 74.4, 73.4, 72.6, 51.9, 48.7, 36.1, 32.2, 31.6, 26.9, 25.7, 17.7, 14.9, 5.6 ppm; MS (ESI) m/z 247.2 (5), 517.2 (11), 535.2 (27, $M+H^+$), 557.2 (100, $M+Na^+$), 1091.4 (41, $2M+Na^+$); HRMS calcd for $C_{28}H_{39}O_5Se$ [$M+H^+$]: 535.1957, found: 535.1953 (−0.9 ppm); calcd for $C_{28}H_{38}O_5SeNa$ [$M+Na^+$]: 557.1777, found: 557.1774 (−0.4 ppm).

4.22. (±)-(3*R*,4*S*)-Methyl 4-((2*S*,3*S*,6*S*)-6-((*R*)-1-(benzyloxy) propan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)-3-hydroxypentanoate (39)

Product **39** (72.9 mg, yield=75%) as a colorless oil was obtained from phenylselenide **S3** (137 mg, 0.26 mmol) according to general procedure **F**, and purification by flash chromatography on silica gel (hexanes/EtOAc, 80:20). R_f 0.31 (hexanes/EtOAc, 80:20); $C_{22}H_{34}O_5$; MW 378.50 g/mol; IR (liquid film) ν_{max} 3472, 2952, 2929, 2858, 1739, 1455, 1438, 1171, 1089, 1017 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ_H 7.40–7.24 (m, 5H), 4.56 (d, J=11.9 Hz, 1H), 4.51 (d, J=11.9 Hz, 1H), 4.28 (ddd, J=7.5, 5.9, 1.4 Hz, 1H), 3.76 (br s, 1H), 3.71 (s, 3H), 3.73–3.68 (m, 1H), 3.60 (dd, J=9.0, 3.2 Hz, 1H), 3.48 (dd, J=9.6, 2.7 Hz, 1H), 3.43 (dd, J=9.0, 6.7 Hz, 1H), 2.61 (dd, J=15.3, 7.9 Hz, 1H), 2.42 (dd, J=15.3, 5.8 Hz, 1H), 2.40–2.31 (m, 1H), 1.81–1.74 (m, 1H), 1.74–1.68 (m, 2H), 1.67–1.53 (m, 2H), 1.34–1.23 (m, 1H), 0.95 (d, J=7.0 Hz, 3H), 0.93 (d, J=7.3 Hz, 3H), 0.81 (d, J=6.5 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 172.6, 138.9, 128.4, 127.8, 127.5, 81.4, 74.6, 73.4, 72.7, 72.6, 51.7, 39.9, 37.1, 32.0, 31.8, 27.1, 25.8, 17.7, 15.0, 5.2 ppm; MS (ESI) m/z 289.2 (4), 379.2 (42, $M+H^+$), 401.2 (100, $M+Na^+$), 415.2 (7), 779.5 (14, $2M+Na^+$); HRMS calcd for $C_{22}H_{35}O_5$ [$M+H^+$]: 379.2479, found: 379.2486 (2.0 ppm); calcd for $C_{22}H_{34}O_5Na$ [$M+Na^+$]: 401.2298, found: 401.2303 (1.0 ppm).

4.23. (±)-(3*S*,4*S*,5*S*,6*S*)-Methyl 5-(benzyloxy)-6-((2*S*,3*S*,6*S*)-6-((*R*)-1-(benzyloxy)propan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)-3-hydroxy-4-methyl-2-(phenylselanyl)heptanoate (S4)

β-Hydroxyester **S4** was obtained from aldehyde **40**[11a] (18.3 mg, 40 μmol) according to general procedure **D** using enoxysilane **27**[9a] as the nucleophile. ^1H NMR analysis of the crude product indicated a ratio >20:1 of product 3,4-*syn* (**S4**): 3,4-*anti*. The residue was purified by flash chromatography on silica gel (hexanes/EtOAc, 85:15) to yield product **S4** as a pale yellow oil (11.4 mg, yield=40%). R_f 0.25 (hexanes/EtOAc, 85:15); $C_{28}H_{50}O_6Se$; MW 681.76 g/mol; IR (liquid film) ν_{max} 3457, 2950, 2925, 2856, 1729, 1455, 1437, 1086, 1022 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ_H 7.68–7.63 (m, 2H), 7.34–7.23 (m, 13H), 4.60 (d, J=10.9 Hz, 1H), 4.52 (d, J=10.9 Hz, 1H), 4.49 (d, J=12.7 Hz, 1H), 4.46 (d, J=12.8 Hz, 1H), 4.31 (d, J=10.4 Hz, 1H), 4.25 (s, 1H), 3.94 (d, J=10.5 Hz, 1H), 3.68 (dd, J=8.6, 3.3 Hz, 1H), 3.54 (dd, J=9.3, 4.5 Hz, 1H), 3.50 (dd, J=8.9, 2.1 Hz, 1H), 3.48–3.45 (m, 1H), 3.46 (s, 3H), 3.29 (dd, J=8.5, 7.7 Hz, 1H), 2.13–2.05 (m, 1H), 2.06–1.97 (m, 1H), 1.85–1.77 (m, 1H), 1.69–1.58 (m, 4H), 1.26–1.18 (m, 1H), 1.13 (d, J=7.1 Hz, 3H), 0.91 (d, J=6.7 Hz, 3H), 0.82 (d, J=6.4 Hz, 3H), 0.77 (d, J=7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 171.3, 138.7, 138.0, 136.5, 129.0, 128.7, 128.6, 128.4, 127.9,

127.78, 127.76, 127.60, 127.57, 87.5, 76.1, 75.7, 73.6, 73.5, 73.4, 70.0, 51.9, 48.8, 36.2, 34.7, 30.5, 29.9, 27.4, 25.6, 18.6, 14.5, 12.2, 9.7 ppm; MS (ESI) *m/z* 360.3 (7), 475.3 (7), 683.3 (5, M+H$^+$), 705.3 (100, M+Na$^+$), 719.3 (6); HRMS calcd for $C_{28}H_{51}O_6Se$ [M+H$^+$]: 683.2845, found: 683.2847 (0.2 ppm); calcd for $C_{28}H_{50}O_6SeNa$ [M+Na$^+$]: 705.2665, found: 705.2687 (3.1 ppm).

4.24. (±)-(3*R*,4*S*,5*S*,6*S*)-Methyl 5-(benzyloxy)-6-((2*S*,3*S*,6*S*)-6-((*R*)-1-(benzyloxy)propan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)-3-hydroxy-4-methylheptanoate (41)

Product **41** (6.8 mg, yield=38%) as a colorless oil was obtained from phenylselenide **S4** (23 mg, 33 μmol) according to general procedure **F**, and purification by flash chromatography on silica gel (hexanes/EtOAc, 85:15). R_f 0.20 (hexanes/EtOAc, 85:15); $C_{32}H_{46}O_6$; MW 526.70 g/mol; IR (liquid film) ν_{max} 3489, 2952, 2925, 1737, 1454, 1380, 1172, 1084, 1020 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.33–7.24 (m, 10H), 4.62 (d, *J*=10.8 Hz, 1H), 4.55–4.51 (m, 1H), 4.50 (d, *J*=12.1 Hz, 1H), 4.48 (d, *J*=12.1 Hz, 1H), 3.81 (s, 1H), 3.72 (dd, *J*=8.6, 3.3 Hz, 1H), 3.74–3.64 (m, 1H), 3.69 (s, 3H), 3.57 (dt, *J*=9.4, 4.9 Hz, 1H), 3.52 (dd, *J*=8.8, 2.3 Hz, 1H), 3.50 (dd, *J*=9.0, 2.1 Hz, 1H), 3.32 (dd, *J*=8.5, 7.7 Hz, 1H), 2.59 (dd, *J*=15.0, 8.2 Hz, 1H), 2.34 (dd, *J*=14.9, 5.4 Hz, 1H), 2.17–2.10 (m, 2H), 1.84–1.76 (m, 1H), 1.73–1.60 (m, 4H), 1.33–1.22 (m, 1H), 1.11 (d, *J*=7.2 Hz, 3H), 0.93 (d, *J*=6.8 Hz, 3H), 0.86 (d, *J*=7.0 Hz, 3H), 0.85 (d, *J*=6.4 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 172.5, 138.7, 138.2, 128.6, 128.4, 127.9, 127.8, 127.60, 127.59, 87.3, 75.92, 75.86, 73.52, 73.45, 73.35, 67.4, 51.8, 39.9, 37.7, 37.3, 34.7, 30.6, 27.3, 25.5, 18.6, 14.4, 12.2, 10.4 ppm; MS (ESI) *m/z* 527.3 (9, M+H$^+$), 549.3 (100, M+Na$^+$), 639.4 (12); HRMS calcd for $C_{32}H_{47}O_6$ [M+H$^+$]: 527.3367, found: 527.3370 (0.5 ppm); calcd for $C_{32}H_{46}O_6Na$ [M+Na$^+$]: 549.3187, found: 549.3192 (1.0 ppm).

4.25. (3*S*,4*S*,5*S*,6*S*,7*S*,8*S*)-Methyl 5,7-bis(benzyloxy)-8-((2*S*,3*S*,6*S*)-6-((*R*)-1-((*tert*-butyldiphenylsilyl)oxy)propan-2-yl)-3-methyltetrahydro-2H-pyran-2-yl)-3-hydroxy-4,6-dimethyl-2-(phenylselanyl)nonanoate (42a)

β-Hydroxyester **42a** was obtained from crude aldehyde **17** (52 mg, 69 μmol) according to general procedure **D** using enoxysilane **27**[9a] as the nucleophile. ^{1}H NMR analysis of the crude product indicated a ratio 13:1 of product 12,13-*syn* (**42a**): 12,13-*anti* (**42b**).[19] The major diastereoisomer was separated by flash chromatography on silica gel (hexanes/EtOAc, 90:10) to yield an inseparable mixture (~9:1) of C14-phenylselenide **42a** as a colorless oil (50 mg, yield=74% over 2 steps). The relative stereochemistry of compound **42a** was not determined. R_f 0.13 (hexanes/EtOAc, 95:5); $C_{57}H_{74}O_7SeSi$; MW 978.24 g/mol; IR (liquid film) ν_{max} 3461, 3068, 2951, 2929, 2857, 1728, 1455, 1428, 1381, 1092, 1065, 1027 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.71–7.61 (m, 6H), 7.42–7.12 (m, 19H), 4.84 (d, *J*=11.4 Hz, 1H), 4.48 (d, *J*=11.4 Hz, 1H), 4.42 (d, *J*=11.8 Hz, 1H), 4.34 (d, *J*=11.9 Hz, 1H), 4.28 (s, 1H), 3.88 (d, *J*=10.6 Hz, 1H), 3.76–3.70 (m, 2H), 3.66–3.59 (m, 2H), 3.45 (s, 3H), 3.46–3.41 (m, 1H), 3.35 (dd, *J*=9.0, 1.2 Hz, 1H), 2.26–2.17 (m, 1H), 2.10–2.00 (m, 1H), 2.00–1.91 (m, 1H), 1.84 (d, *J*=7.1 Hz, 1H), 1.62–1.50 (m, 4H), 1.33–1.24 (m, 1H), 1.20–1.11 (m, 1H), 1.07 (d, *J*=7.1 Hz, 3H), 1.03 (s, 9H), 0.91 (d, *J*=7.0 Hz, 3H), 0.87 (d, *J*=6.8 Hz, 3H), 0.80 (d, *J*=7.2 Hz, 3H), 0.54 (d, *J*=6.4 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 171.4, 139.5, 138.1, 136.9, 135.89, 135.85, 134.2, 134.0, 129.69, 129.67, 128.94, 128.89, 128.6, 128.3, 127.73, 127.72, 127.69, 127.17, 127.16, 127.15, 126.8, 87.6, 86.1, 75.9, 74.8, 74.6, 72.3, 69.8, 65.9, 51.8, 48.2, 38.9, 36.7, 36.3, 35.6, 30.8, 27.5, 27.1, 25.4, 19.5, 18.2, 17.3, 13.8, 12.1, 11.4 ppm; MS (ESI) *m/z* 193.6 (18), 261.1 (23), 300.9 (8), 338.3 (100), 360.3 (92), 408.3 (21), 457.3 (14), 480.9 (5), 536.6 (11), 594.0 (12), 979.4 (10, M+H$^+$), 1001.4 (59, M+Na$^+$); HRMS calcd for $C_{57}H_{75}O_7SeSi$ [M+H$^+$]: 979.4442, found: 979.4440 (−0.2 ppm); calcd for $C_{57}H_{74}O_7SeSiNa$ [M+Na$^+$]: 1001.4261, found: 1001.4258 (−0.3 ppm).

4.26. (3*R*,4*S*,5*S*,6*S*,7*S*,8*S*)-Methyl 5,7-bis(benzyloxy)-8-((2*S*,3*S*,6*S*)-6-((*R*)-1-((*tert*-butyldiphenylsilyl)oxy)propan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)-3-hydroxy-4,6-dimethylnonanoate (23a)

Product **23a** (37.2 mg, yield=88%) as a colorless oil was obtained from phenylselenide **42a** (49.9 mg, 51 μmol) according to general procedure **F**, and purification by flash chromatography on silica gel (hexanes/EtOAc, 85:15). *Note*: Reaction was repeated from a larger scale of crude aldehyde **17** (721 mg, 0.96 mmol), providing 12,13-*syn* product **23a** with similar results (514 mg, yield=65% over 3 steps). R_f 0.22 (hexanes/EtOAc, 85:15); $C_{51}H_{70}O_7Si$; MW 823.18 g/mol; IR (liquid film) ν_{max} 3489, 3069, 3030, 2957, 2928, 2857, 1739, 1457, 1428, 1379, 1171, 1092, 1016 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.73–7.65 (m, 4H), 7.48–7.35 (m, 6H), 7.33–7.21 (m, 10H), 4.84 (d, *J*=11.3 Hz, 1H), 4.59 (app t, *J*=6.8 Hz, 1H), 4.51 (d, *J*=11.3 Hz, 1H), 4.46 (d, *J*=11.6 Hz, 1H), 4.42 (d, *J*=11.6 Hz, 1H), 3.87 (br s, 1H), 3.79–3.73 (m, 2H), 3.71 (s, 3H), 3.73–3.67 (m, 2H), 3.50 (dd, *J*=8.3, 2.5 Hz, 1H), 3.43 (dd, *J*=8.7, 2.2 Hz, 1H), 2.59 (dd, *J*=15.1, 8.0 Hz, 1H), 2.40–2.34 (m, 1H), 2.30 (dd, *J*=15.2, 5.9 Hz, 1H), 2.13–2.05 (m, 1H), 2.05–1.96 (m, 1H), 1.96–1.89 (m, 1H), 1.72–1.59 (m, 4H), 1.27–1.16 (m, 1H), 1.072 (d, *J*=6.8 Hz, 3H), 1.070 (s, 9H), 0.97 (d, *J*=6.8 Hz, 3H), 0.97 (d, *J*=7.5 Hz, 3H), 0.92 (d, *J*=6.8 Hz, 3H), 0.65 (d, *J*=6.4 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 172.4, 139.4, 138.2, 135.88, 135.83, 134.09, 134.01, 129.64, 129.62, 128.5, 128.2, 127.71, 127.70, 127.69, 127.3, 127.2, 127.0, 87.0, 85.6, 76.0, 74.6, 74.4, 72.2, 67.9, 66.0, 51.7, 39.8, 38.5, 37.5, 36.9, 36.0, 30.6, 27.4, 27.1, 25.3, 19.5, 18.3, 17.7, 16.9, 12.2, 11.4 ppm; MS (ESI) *m/z* 179.0 (10), 338.3 (14), 360.3 (17), 625.2 (5), 823.5 (21, M+H$^+$), 824.5 (12), 825.4 (4), 845.5 (100, M+Na$^+$), 846.5 (60), 847.5 (18), 848.5 (4); HRMS calcd for $C_{51}H_{71}O_7Si$ [M+H$^+$]: 823.4969, found: 823.4960 (−0.5 ppm); calcd for $C_{51}H_{70}O_7NaSi$ [M+Na$^+$]: 845.4783, found: 845.4796 (1.5 ppm).

4.27. (3*S*,4*S*,5*S*,6*S*,7*S*,8*S*)-Methyl 5,7-bis(benzyloxy)-8-((2*S*,3*S*,6*S*)-6-((*R*)-1-((*tert*-butyldiphenylsilyl)oxy)propan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)-3-hydroxy-4,6-dimethylnonanoate (23b)

β-Hydroxyesters **23a** and **23b** were obtained from aldehyde **17** (22.5 mg, 30 μmol) according to general procedure **D** using 1(*tert*-butyldimethylsilyloxy)-1-methoxyethene **22** as the nucleophile. ^{1}H NMR analysis of the crude product indicated a ratio ~1:1 of alcohols 12,13-*syn* (**23a**): 12,13-*anti* (**23b**). The two diastereoisomers were separated by flash chromatography on silica gel (hexanes/EtOAc, 85:15) to yield products **23a** and **23b** as colorless oils (combined yield; 17.2 mg, 70% over 2 steps). **23b**; R_f 0.17 (hexanes/EtOAc, 85:15); $C_{51}H_{70}O_7Si$; MW 823.18 g/mol; IR (liquid film) ν_{max} 3499, 3068, 3031, 2929, 2857, 1737, 1456, 1428, 1380, 1171, 1111, 1092, 1066 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.67–7.60 (m, 4H), 7.42–7.32 (m, 6H), 7.26–7.17 (m, 10H), 4.67 (d, *J*=11.7 Hz, 1H), 4.48 (d, *J*=11.6 Hz, 1H), 4.41–4.40 (m, 2H), 4.23–4.17 (m, 1H), 3.92 (br s, 1H), 3.69 (s, 3H), 3.71–3.66 (m, 2H), 3.64 (dd, *J*=9.5, 3.9 Hz, 1H), 3.58 (dd, *J*=6.8, 4.4 Hz, 1H), 3.45 (dd, *J*=7.2, 4.0 Hz, 1H), 3.35 (dd, *J*=7.8, 3.7 Hz, 1H), 2.60 (dd, *J*=15.7, 2.7 Hz, 1H), 2.35 (dd, *J*=15.8, 10.0 Hz, 1H), 2.24–2.18 (m, 1H), 2.16–2.09 (m, 1H), 2.05–1.97 (m, 1H), 1.97–1.89 (m, 1H), 1.63–1.45 (m, 4H), 1.24–1.17 (m, 1H), 1.03 (s, 9H), 0.96 (d, *J*=7.2 Hz, 3H), 0.899 (d, *J*=6.9 Hz, 3H), 0.897 (d, *J*=7.1 Hz, 3H), 0.87 (d, *J*=6.8 Hz, 3H), 0.66 (d, *J*=6.4 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 173.9, 139.5, 138.8, 135.90, 135.87, 134.15, 134.10, 129.65, 129.62, 128.4, 128.3, 127.72, 127.69, 127.52, 127.47, 127.2, 127.1, 84.9, 84.3, 76.5, 74.1, 73.4, 71.8, 69.9, 66.0, 51.8, 40.7, 39.0, 38.2, 37.7, 36.7, 30.3, 27.9, 27.1, 24.8, 19.5, 18.4, 16.0, 14.5, 14.3, 11.5 ppm; MS (ESI) *m/z* 192.9 (4), 227.0 (8), 338.3 (14), 360.3 (21), 755.4 (6), 823.5 (12, M+H$^+$), 824.5 (7), 825.5 (2), 840.5 (3, M+NH$_4^+$), 845.5 (100, M+Na$^+$), 846.5 (63), 847.5 (21), 848.5 (5), 935.5 (4);

HRMS calcd for $C_{51}H_{71}O_7Si$ [M+H$^+$]: 823.4969, found: 823.4955 (−1.0 ppm); calcd for $C_{51}H_{74}O_7NSi$ [M+NH$_4^+$]: 840.5229, found: 840.5220 (−1.0 ppm); calcd for $C_{51}H_{70}O_7NaSi$ [M+Na$^+$]: 845.4783, found: 845.4792 (1.1 ppm).

4.28. (3*R*,4*S*,5*S*,6*S*,7*S*,8*S*)-Methyl 3,5,7-tris(benzyloxy)-8-((2*S*,3*S*,6*S*)-6-((*R*)-1-(*tert*-butyldiphenylsilyloxy)propan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)-4,6-dimethylnonanoate (43)

Product **43** (451 mg, yield=92%) as a colorless oil was obtained from primary alcohol **23a** (443 mg, 0.54 mmol) according to general procedure **A**, and purification by flash chromatography on silica gel (hexanes/EtOAc, 90:10). R_f 0.29 (hexanes/EtOAc, 90:10); $C_{58}H_{76}O_7Si$; MW 913.31 g/mol; IR (liquid film) ν_{max} 3069, 3029, 2954, 2929, 2857, 1737, 1496, 1454, 1428, 1378, 1361, 1112, 1066, 1028 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.67–7.61 (m, 4H), 7.41–7.32 (m, 8H), 7.26–7.17 (m, 13H), 4.61 (d, *J*=11.7 Hz, 1H), 4.46 (d, *J*=11.5 Hz, 1H), 4.44 (d, *J*=11.7 Hz, 1H), 4.43 (d, *J*=11.8 Hz, 1H), 4.42 (d, *J*=11.6 Hz, 1H), 4.40 (d, *J*=11.4 Hz, 1H), 4.28 (ddd, *J*=7.7, 5.5, 2.3 Hz, 1H), 3.70–3.57 (m, 4H), 3.59 (s, 3H), 3.47 (app t, *J*=6.0 Hz, 1H), 3.42 (app t, *J*=6.0 Hz, 1H), 2.66 (dd, *J*=15.0, 7.4 Hz, 1H), 2.43 (dd, *J*=15.1, 5.5 Hz, 1H), 2.34–2.27 (m, 1H), 2.27–2.20 (m, 1H), 1.98–1.91 (m, 1H), 1.90–1.83 (m, 1H), 1.77–1.68 (m, 1H), 1.67–1.59 (m, 1H), 1.54–1.47 (m, 1H), 1.44–1.36 (m, 1H), 1.31–1.23 (m, 1H), 1.04 (s, 9H), 1.02 (d, *J*=7.1 Hz, 3H), 0.97 (d, *J*=6.8 Hz, 3H), 0.96 (d, *J*=6.9 Hz, 3H), 0.87 (d, *J*=6.9 Hz, 3H), 0.81 (d, *J*=6.8 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 172.7, 139.44, 139.41, 139.2, 135.9 (2C), 134.16, 134.14, 129.63, 129.61, 128.30, 128.27, 128.25, 127.70, 127.68, 127.49, 127.44, 127.31, 127.24, 127.21, 127.17, 84.2, 83.4, 77.7, 76.3, 73.5, 73.2, 72.2, 70.8, 65.9, 51.7, 40.8, 39.0, 38.5, 38.0, 36.6, 29.4, 27.1, 26.3, 23.7, 19.5, 18.5, 15.5, 13.2, 12.4, 12.3 ppm; MS (ESI) *m*/*z* 227.0 (24), 338.3 (50), 408.3 (15), 675.7 (8), 913.5 (19, M+H$^+$), 930.6 (5, M+NH$_4^+$), 935.5 (100, M+Na$^+$), 1012.6 (13); HRMS calcd for $C_{58}H_{77}O_7Si$ [M+H$^+$]: 913.5433, found: 913.5409 (−2.6 ppm); calcd for $C_{58}H_{80}O_7NSi$ [M+NH$_4^+$]: 930.5699, found: 930.5671 (−2.9 ppm); calcd for $C_{58}H_{76}O_7NaSi$ [M+Na$^+$]: 935.5253, found: 935.5234 (−2.0 ppm).

4.29. (3*R*,4*S*,5*S*,6*S*,7*S*,8*S*)-3,5,7-tris(Benzyloxy)-8-((2*S*,3*S*,6*S*)-6-((*R*)-1-(*tert*-butyldiphenylsilyloxy)propan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)-4,6-dimethylnonan-1-ol (44)

Alcohol **44** (879 mg, yield=98%) as a colorless oil was obtained from ester **43** (934 mg, 1.0 mmol) according to general procedure **B**, and purification by flash chromatography on silica gel (hexanes/EtOAc, 75:25). R_f 0.14 (hexanes/EtOAc, 80:20); $C_{57}H_{76}O_6Si$; MW 885.30 g/mol; IR (liquid film) ν_{max} 3435, 3067, 3030, 2958, 2930, 2857, 1496, 1454, 1428, 1378, 1111, 1091, 1066, 1028 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.68–7.61 (m, 4H), 7.41–7.32 (m, 7H), 7.26–7.18 (m, 14H), 4.62 (d, *J*=11.6 Hz, 1H), 4.51 (d, *J*=11.4 Hz, 1H), 4.45 (d, *J*=11.5 Hz, 1H), 4.42 (d, *J*=11.4 Hz, 1H), 4.41 (d, *J*=11.6 Hz, 1H), 4.40 (d, *J*=11.6 Hz, 1H), 3.86 (ddd, *J*=7.7, 6.0, 2.6 Hz, 1H), 3.72–3.52 (m, 7H), 3.49 (app t, *J*=5.8 Hz, 1H), 3.43 (app t, *J*=5.9 Hz, 1H), 2.35–2.27 (m, 1H), 2.27–2.20 (m, 1H), 2.00–1.92 (m, 1H), 1.92–1.84 (m, 1H), 1.84–1.79 (m, 1H), 1.79–1.72 (m, 1H), 1.70–1.60 (m, 2H), 1.54–1.49 (m, 1H), 1.47–1.38 (m, 1H), 1.34–1.24 (m, 1H), 1.04 (s, 9H), 1.03 (d, *J*=7.1 Hz, 3H), 0.99 (d, *J*=6.9 Hz, 3H), 0.95 (d, *J*=7.1 Hz, 3H), 0.87 (d, *J*=6.8 Hz, 3H), 0.84 (d, *J*=6.7 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 139.5, 139.3, 139.2, 135.88, 135.87, 134.16, 134.15, 129.63, 129.60, 128.42, 128.33, 128.28, 127.70, 127.68, 127.66, 127.62, 127.5, 127.3, 127.22, 127.18, 84.4, 83.4, 77.8, 77.6, 73.5, 73.1, 72.1, 70.9, 65.9, 60.9, 40.5, 38.4, 37.9, 36.7, 36.0, 29.5, 27.1, 26.4, 23.8, 19.5, 18.5, 15.6, 13.3, 12.6, 12.3 ppm; MS (ESI) *m*/*z* 192.8 (9), 228.2 (7), 338.3 (100), 360.3 (73), 408.3 (18), 675.7 (18), 697.7 (8), 885.5 (26, M+H$^+$), 902.6 (7, M+NH$_4^+$), 907.5 (88, M+Na$^+$), 997.6 (11); HRMS calcd for $C_{57}H_{77}O_6Si$ [M+H$^+$]: 885.5484, found: 885.5464 (−2.2 ppm); calcd for $C_{57}H_{80}O_6NSi$ [M+NH$_4^+$]: 902.5749, found: 902.5730 (−2.2 ppm); calcd for $C_{57}H_{76}O_6NaSi$ [M+Na$^+$]: 907.5303, found: 907.5293 (−1.2 ppm).

4.30. (3*R*,4*S*,5*S*,6*S*,7*S*,8*S*)-3,5,7-tris(Benzyloxy)-8-((2*S*,3*S*,6*S*)-6-((*R*)-1-(*tert*-butyldiphenylsilyloxy)propan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)-4,6-dimethylnonanal (45)

Aldehyde **45** as a colorless oil was obtained from alcohol **44** (857 mg, 0.97 mmol) according to general procedure **C**, and was used as crude without purification. R_f 0.53 (hexanes/EtOAc, 80:20); $C_{57}H_{74}O_6Si$; MW 883.28 g/mol; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 9.65 (t, *J*=2.2 Hz, 1H), 7.67–7.61 (m, 4H), 7.41–7.32 (m, 7H), 7.26–7.15 (m, 14H), 4.63 (d, *J*=11.7 Hz, 1H), 4.50 (d, *J*=11.3 Hz, 1H), 4.41 (d, *J*=11.8 Hz, 1H), 4.41 (d, *J*=11.4 Hz, 1H), 4.39 (d, *J*=10.1 Hz, 1H), 4.37 (d, *J*=11.5 Hz, 1H), 4.34–4.29 (m, 1H), 3.71–3.59 (m, 4H), 3.48 (dd, *J*=6.5, 5.2 Hz, 1H), 3.42 (app t, *J*=5.9 Hz, 1H), 2.71 (ddd, *J*=16.3, 7.3, 2.5 Hz, 1H), 2.45 (ddd, *J*=16.3, 5.1, 1.9 Hz, 1H), 2.37–2.29 (m, 1H), 2.28–2.20 (m, 1H), 1.98–1.91 (m, 1H), 1.91–1.83 (m, 1H), 1.79–1.71 (m, 1H), 1.71–1.62 (m, 1H), 1.53–1.48 (m, 1H), 1.44–1.36 (m, 1H), 1.33–1.27 (m, 1H), 1.05 (s, 9H), 1.00 (d, *J*=8.0 Hz, 3H), 0.99 (d, *J*=7.4 Hz, 3H), 0.97 (d, *J*=7.2 Hz, 3H), 0.87 (d, *J*=6.9 Hz, 3H), 0.85 (d, *J*=6.8 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 201.8, 139.30, 139.28, 138.83, 135.87, 135.86, 134.15, 134.13, 129.64, 129.61, 128.39, 128.37, 128.29, 127.70, 127.68, 127.54, 127.50, 127.47, 127.36, 127.32, 127.27, 84.3, 83.5, 77.8, 74.3, 73.5, 73.3, 72.0, 70.7, 65.8, 48.4, 41.3, 38.7, 38.0, 36.4, 29.9, 29.3, 27.1, 26.2, 23.6, 19.5, 18.5, 15.6, 13.2, 12.5 ppm.

4.31. (+)-*tert*-Butyl-((*R*)-2-((2*S*,5*S*,6*S*)-5-methyl-6-((2*S*,3*S*,4*S*,5*S*,6*S*,7*R*)-3,5,7-tris(benzyloxy)-4,6-dimethyldec-9-en-2-yl)tetrahydro-2*H*-pyran-2-yl)propoxy)diphenylsilane (46)

To a cooled (0 °C) solution of methyltriphenylphosphonium bromide (3.1 equiv, 1.08 g) in dry THF (0.1 M, 10 mL) was added a 2.5 M solution of *n*BuLi in hexanes (3 equiv, 1.17 mL), and the mixture was stirred for 40 min at 0 °C. To the mixture was added a solution of crude aldehyde **45** (863 mg, 0.98 mmol) in dry THF (0.1 M, 10 mL) and the mixture was stirred at 0 °C for 18 h or until starting material was completely consumed, as verified by TLC (hexanes/EtOAc, 80:20). Reaction mixture was then treated dropwise with a saturated aqueous solution of NH_4Cl at 0 °C, followed by separation of the organic phase at rt. The aqueous layer was extracted with Et_2O (3×) and the combined organic fractions were washed with a saturated brine solution, then dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (hexanes/EtOAc, 95:5) to yield homoallylic product **46** as a pale yellow oil (661 mg, yield=78% over 2 steps). R_f 0.40 (hexanes/EtOAc, 95:5); $[\alpha]_D^{25}$ +4.6 (*c* 0.50, CH_2Cl_2); $C_{58}H_{76}O_5Si$; MW: 881.31 g/mol; IR (liquid film) ν_{max} 3068, 3029, 2959, 2929, 2857, 1495, 1454, 1427, 1111, 1092, 1067, 1028 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.57–7.51 (m, 4H), 7.32–7.21 (m, 8H), 7.15–7.08 (m, 13H), 5.61 (ddt, *J*=17.2, 10.2, 7.1 Hz, 1H), 4.88 (ddd, *J*=13.7, 11.1, 1.1 Hz, 2H), 4.46 (d, *J*=11.4 Hz, 1H), 4.44 (d, *J*=11.3 Hz, 1H), 4.36 (s, 2H), 4.29 (d, *J*=11.7 Hz, 1H), 4.22 (d, *J*=11.7 Hz, 1H), 3.72–3.67 (m, 1H), 3.60–3.48 (m, 4H), 3.37 (dd, *J*=6.6, 5.1 Hz, 1H), 3.34 (app t, *J*=5.9 Hz, 1H), 2.38–2.30 (m, 1H), 2.28–2.19 (m, 1H), 2.16–2.06 (m, 2H), 1.91–1.83 (m, 1H), 1.80–1.71 (m, 1H), 1.69–1.61 (m, 1H), 1.59–1.50 (m, 1H), 1.43–1.36 (m, 1H), 1.32–1.17 (m, 2H), 0.94 (s, 9H), 0.91 (d, *J*=7.0 Hz, 3H), 0.88 (d, *J*=6.9 Hz, 3H), 0.85 (d, *J*=7.2 Hz, 3H), 0.77 (d, *J*=6.6 Hz, 3H), 0.75 (d, *J*=6.4 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 139.64, 139.58, 139.50, 135.87, 135.86, 135.7, 134.2, 134.0, 129.61, 129.58, 128.30, 128.24, 128.21, 127.69, 127.67, 127.46, 127.42, 127.23, 127.21, 127.15, 127.12, 116.8, 84.0, 83.2, 78.5, 78.0, 73.2, 73.1, 71.5, 70.7, 65.9, 39.6, 38.8, 38.2, 37.1, 36.4, 30.5, 29.3, 27.1, 26.2, 19.5, 18.5, 15.3, 13.2, 12.5, 11.6 ppm; MS (ESI) *m*/*z*

192.8 (6), 228.2 (9), 338.3 (61), 411.4 (7), 675.7 (13), 881.5 (100, $M+H^+$), 898.6 (8, $M+NH_4^+$), 903.5 (5, $M+Na^+$), 971.6 (6), 988.6 (5); HRMS calcd for $C_{58}H_{77}O_5Si$ [$M+H^+$]: 881.5535, found: 881.5529 (−0.7 ppm); calcd for $C_{58}H_{80}O_5NSi$ [$M+NH_4^+$]: 898.5800, found: 898.5782 (−2.0 ppm); calcd for $C_{58}H_{76}O_5NaSi$ [$M+Na^+$]: 903.5354, found: 903.5337 (−1.9 ppm).

4.32. (+)-(4*R*,5*S*,6*S*,7*S*,8*S*,9*S*)-4,6,8-tris(Benzyloxy)-9-((2*S*,3*S*,6*S*)-6-((*R*)-1-((*tert*-butyldiphenylsilyl)oxy)propan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)-5,7-dimethyldecan-1-ol (47)

To a cooled (0 °C) solution of homoallylic product **46** (11.5 mg, 13 μmol) in dry THF (0.1 M, 13 μL) was added dropwise a 0.5 M solution of 9-BBN in THF (3 equiv, 78 μL), turning the pale yellow solution to colorless. After stirring for 6 h at 0 °C, the reaction mixture was treated successively at 0 °C with MeOH (40 μL), a 3 M solution of NaOH (25 μL) and a 35% wt. solution of H_2O_2 in water (15 μL). The mixture was stirred and allowed to warm overnight from 0 °C to rt before addition of a saturated brine solution and dilution with Et_2O (1 mL). The aqueous layer was then extracted with Et_2O (3×), and the combined organic fractions were dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (hexanes/EtOAc, 95:5) to yield product **47** (12.8 mg, quantitative yield) as a colorless oil. *Note*: Reaction was repeated on a larger scale of homoallylic olefin **46** (150–200 mg) with similar results. R_f 0.20 (hexanes/EtOAc, 80:20); $[\alpha]_D^{25}$ +0.9 (*c* 1.28, CH_2Cl_2); $C_{58}H_{78}O_6Si$; MW 899.32 g/mol; IR (liquid film) ν_{max} 3408, 3066, 3029, 2929, 2857, 1496, 1454, 1426, 1378, 1111, 1091, 1066, 1028 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ_H 7.67–7.61 (m, 4H), 7.42–7.31 (m, 7H), 7.27–7.18 (m, 14H), 4.59 (d, *J*=11.8 Hz, 1H), 4.51 (d, *J*=11.6 Hz, 1H), 4.46 (d, *J*=11.9 Hz, 1H), 4.46 (d, *J*=11.8 Hz, 1H), 4.40 (d, *J*=11.7 Hz, 1H), 4.35 (d, *J*=11.7 Hz, 1H), 3.71–3.64 (m, 3H), 3.64–3.58 (m, 2H), 3.53–3.42 (m, 5H), 2.39–2.29 (m, 1H), 2.25–2.18 (m, 1H), 2.02–1.94 (m, 1H), 1.90–1.82 (m, 1H), 1.82–1.74 (m, 1H), 1.71–1.62 (m, 2H), 1.51–1.35 (m, 4H), 1.34–1.25 (m, 2H), 1.04 (s, 9H), 1.00 (d, *J*=7.1 Hz, 3H), 0.99 (d, *J*=7.1 Hz, 3H), 0.97 (d, *J*=7.4 Hz, 3H), 0.88 (d, *J*=6.9 Hz, 3H), 0.87 (d, *J*=6.8 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 139.62, 139.60, 139.58, 135.88, 135.87, 134.23, 134.22, 129.63, 129.60, 128.33, 128.30, 128.24, 127.70, 127.68, 127.49, 127.48, 127.29, 127.24, 127.16, 127.11, 84.2, 83.8, 78.8, 78.0, 77.4, 73.3, 71.6, 70.8, 65.9, 63.2, 40.0, 39.0, 38.1, 36.5, 35.0, 29.4, 28.9, 27.6, 27.1, 22.9, 19.5, 18.5, 15.8, 13.2, 12.7, 11.9 ppm; MS (ESI) *m*/*z* 195.1 (13), 338.3 (9), 791.5 (5), 899.6 (100, $M+H^+$), 916.6 (14, $M+NH_4^+$), 921.5 (57, $M+Na^+$); HRMS calcd for $C_{58}H_{79}O_6Si$ [$M+H^+$]: 899.5640, found: 899.5654 (1.5 ppm); calcd for $C_{58}H_{82}O_6NSi$ [$M+NH_4^+$]: 916.5906, found: 916.5896 (−1.0 ppm); calcd for $C_{58}H_{78}O_6NaSi$ [$M+Na^+$]: 921.5460, found: 921.5465 (0.6 ppm).

4.33. (+)-(4*R*,5*S*,6*S*,7*S*,8*S*,9*S*)-4,6,8-tris(Benzyloxy)-9-((2*S*,3*S*,6*S*)-6-((*R*)-1-((*tert*-butyldiphenylsilyl)oxy)propan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)-5,7-dimethyldecyl pivalate (48)

To a cooled (0 °C) solution of alcohol **47** (468 mg, 0.52 mmol) in dry CH_2Cl_2 (0.2 M, 2.6 mL) was added successively pyridine (5 equiv, 210 μL) and pivaloyl chloride (2.5 equiv, 160 μL). After stirring for 18 h at rt, the opaque white mixture was treated with a saturated aqueous solution of NH_4Cl and concentrated in vacuo. The resulting white paste was extracted with Et_2O (3×), and the combined organic fractions were washed with a saturated brine solution, then dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (hexanes/EtOAc, 90:10) to yield product **48** as a colorless oil (461 mg, yield=90%). R_f 0.36 (hexanes/EtOAc, 90:10); $[\alpha]_D^{25}$ +1.4 (*c* 1.60, CH_2Cl_2); $C_{63}H_{86}O_7Si$; MW 983.44 g/mol; IR (liquid film) ν_{max} 3068, 3029, 2958, 2930, 2857, 1727, 1454, 1428, 1363, 1284, 1155, 1111, 1067, 1028 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ_H 7.67–7.62 (m, 5H), 7.41–7.32 (m, 7H), 7.25–7.20 (m, 13H), 4.59 (d, *J*=11.7 Hz, 1H), 4.50 (d, *J*=11.4 Hz, 1H), 4.45 (d, *J*=11.6 Hz, 1H), 4.44 (d, *J*=11.5 Hz, 1H), 4.38 (d, *J*=11.7 Hz, 1H), 4.32 (d, *J*=11.7 Hz, 1H), 3.98–3.91 (m, 2H), 3.72–3.58 (m, 5H), 3.51–3.43 (m, 2H), 2.40–2.32 (m, 1H), 2.24–2.17 (m, 1H), 1.96–1.89 (m, 1H), 1.89–1.82 (m, 1H), 1.82–1.75 (m, 1H), 1.71–1.62 (m, 2H), 1.53–1.43 (m, 4H), 1.39–1.27 (m, 2H), 1.18 (s, 9H), 1.04 (s, 9H), 0.99 (d, *J*=6.8 Hz, 3H), 0.98 (d, *J*=7.2 Hz, 3H), 0.97 (d, *J*=7.6 Hz, 3H), 0.88 (d, *J*=6.4 Hz, 3H), 0.87 (d, *J*=6.5 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 178.7, 139.55, 139.54, 139.4, 135.88, 135.87, 134.16 (2C), 129.62, 129.59, 128.32, 128.30, 128.24, 127.69, 127.67, 127.5, 127.4, 127.27, 127.23, 127.17, 127.16, 84.0, 83.4, 78.6, 78.1, 73.2, 73.1, 71.5, 70.6, 65.8, 64.5, 39.9, 39.0, 38.8, 38.1, 36.3, 30.1, 29.9, 29.2, 28.8, 27.4, 27.1, 23.4, 19.5, 18.5, 15.5, 13.1, 12.6, 11.7 ppm; MS (ESI) *m*/*z* 195.1 (8), 338.3 (16), 983.6 (100, $M+H^+$), 1000.6 (41, $M+NH_4^+$), 1005.6 (20, $M+Na^+$), 1082.7 (36); HRMS calcd for $C_{63}H_{87}O_7Si$ [$M+H^+$]: 983.6216, found: 983.6208 (−0.7 ppm); calcd for $C_{63}H_{90}O_7NSi$ [$M+NH_4^+$]: 1000.6481, found: 1000.6463 (−1.8 ppm); calcd for $C_{63}H_{86}O_7NaSi$ [$M+Na^+$]: 1005.6035, found: 1005.6016 (−1.9 ppm).

4.34. (−)-(4*R*,5*S*,6*S*,7*S*,8*S*,9*S*)-4,6,8-tris(Benzyloxy)-9-((2*S*,3*S*,6*S*)-6-((*R*)-1-hydroxypropan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)-5,7-dimethyldecyl pivalate (49)

To a cooled (0 °C) solution of TBDPS ether **48** (390 mg, 0.40 mmol) in dry THF (0.1 M, 2.1 mL) was added dropwise a 1 M solution of TBAF in THF (1.5 equiv, 310 μL), followed by stirring overnight at rt. The reaction mixture was then treated with a saturated aqueous solution of NH_4Cl, and concentrated in vacuo. The aqueous layer was extracted with Et_2O (3×) and combined organic fractions were dried ($MgSO_4$), filtered and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (hexanes/EtOAc, 85:15) to give primary alcohol **49** as a colorless oil (264 mg, yield=89%). R_f 0.17 (hexanes/EtOAc, 85:15); $[\alpha]_D^{25}$ −8.0 (*c* 0.70, CH_2Cl_2); $C_{47}H_{68}O_7$; MW 745.04 g/mol; IR (liquid film) ν_{max} 3435, 2957, 2928, 2873, 1727, 1455, 1376, 1284, 1157, 1090, 1067 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ_H 7.32–7.19 (m, 15H), 4.64 (d, *J*=11.8 Hz, 1H), 4.59 (d, *J*=12.0 Hz, 1H), 4.58 (d, *J*=11.7 Hz, 1H), 4.44 (d, *J*=11.8 Hz, 1H), 4.41 (d, *J*=11.8 Hz, 1H), 4.25 (d, *J*=11.8 Hz, 1H), 3.99–3.91 (m, 2H), 3.76–3.72 (m, 1H), 3.66 (dd, *J*=8.4, 2.9 Hz, 1H), 3.63–3.59 (m, 1H), 3.56–3.52 (m, 3H), 3.50–3.44 (m, 1H), 3.38–3.34 (m, 1H), 2.36–2.27 (m, 2H), 1.95–1.85 (m, 2H), 1.85–1.76 (m, 1H), 1.72–1.64 (m, 2H), 1.62–1.55 (m, 2H), 1.52–1.43 (m, 3H), 1.40–1.32 (m, 1H), 1.18 (s, 9H), 1.11 (d, *J*=7.0 Hz, 3H), 1.02 (d, *J*=7.2 Hz, 3H), 0.98 (d, *J*=7.0 Hz, 3H), 0.95 (d, *J*=6.8 Hz, 3H), 0.78 (d, *J*=6.9 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 178.7, 139.55, 139.54, 139.4, 128.35, 128.33, 128.32, 127.64, 127.61, 127.34, 127.31, 127.28, 127.27, 84.2, 78.4, 77.8, 77.4, 76.6, 73.5, 72.9, 71.4, 68.4, 64.5, 39.9, 38.9, 38.3, 38.1, 35.6, 29.9, 29.6, 28.3, 27.4, 25.8, 25.5, 25.4, 18.7, 14.0, 13.3, 11.2 ppm; MS (ESI) *m*/*z* 338.3 (12), 360.3 (8), 745.5 (47, $M+H^+$), 762.5 (5, $M+NH_4^+$), 767.5 (100, $M+Na^+$), 790.6 (50), 844.6 (8), 857.5 (13), 880.6 (6); HRMS calcd for $C_{47}H_{69}O_7$ [$M+H^+$]: 745.5038, found: 745.5034 (−0.5 ppm); calcd for $C_{47}H_{72}O_7N$ [$M+NH_4^+$]: 762.5303, found: 762.5291 (−1.6 ppm); calcd for $C_{47}H_{68}O_7Na$ [$M+Na^+$]: 767.4857, found: 767.4866 (1.2 ppm).

4.35. (4*R*,5*S*,6*S*,7*S*,8*S*,9*S*)-4,6,8-tris(Benzyloxy)-5,7-dimethyl-9-((2*S*,3*S*,6*S*)-3-methyl-6-((*S*)-1-oxopropan-2-yl)tetrahydro-2*H*-pyran-2-yl)decyl pivalate (S5)

Aldehyde **S5** as a colorless oil was obtained from alcohol **49** (30 mg, 40 μmol) according to general procedure **C**, and was used as crude without purification. R_f 0.24 (hexanes/EtOAc, 90:10); $C_{47}H_{66}O_7$; MW 743.02 g/mol; ^1H NMR (500 MHz, $CDCl_3$) δ_H 9.74 (d, *J*=2.8 Hz, 1H), 7.34–7.21 (m, 15H), 4.62 (d, *J*=12.5 Hz, 1H), 4.61 (s, 2H), 4.46 (d, *J*=11.7 Hz, 1H), 4.45 (d, *J*=11.6 Hz, 1H), 4.35 (d, *J*=11.7 Hz, 1H), 4.00–3.95 (m, 2H), 3.87–3.81 (m, 1H), 3.73–3.69 (m, 1H), 3.64 (dd, *J*=7.0, 4.7 Hz, 1H), 3.59 (app t, *J*=5.9 Hz, 1H), 3.54 (dd,

J=6.6, 5.4 Hz, 1H), 2.62–2.53 (m, 1H), 2.33–2.23 (m, 2H), 1.99–1.91 (m, 1H), 1.84–1.76 (m, 1H), 1.75–1.66 (m, 2H), 1.55–1.37 (m, 6H), 1.20 (s, 9H), 1.04 (d, J=7.0 Hz, 3H), 1.03 (d, J=7.1 Hz, 3H), 1.03 (d, J=6.8 Hz, 3H), 0.98 (d, J=7.0 Hz, 3H), 0.91 (d, J=6.8 Hz, 3H) ppm.

4.36. (4*R*,5*S*,6*S*,7*S*,8*S*,9*S*)-4,6,8-tris(Benzyloxy)-9-((2*S*,3*S*,6*S*)-6-((*S*)-1-methoxy-1-oxopropan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)-5,7-dimethyldecyl pivalate (50)

Crude aldehyde **S5** (40 μmol) was solubilized in *tert*-butyl alcohol (0.05 M, 0.8 mL) and a 2 M solution of 2-methyl-2-butene in THF (40 equiv, 0.8 mL). To the mixture was added dropwise (over 5 min) a solution of $NaClO_2$ (2 equiv, 10 mg) and NaH_2PO_4 (8 equiv, 45 mg) solubilized in deionized water (0.4 mL). After stirring for 18 h at rt, the resulting pale yellow mixture was concentrated in vacuo and the residue was diluted with H_2O (1 mL) and Et_2O (3 mL). The aqueous layer was acidified to pH 3 with a 6 N aqueous solution of HCl (few drops) and was extracted with Et_2O (3×). The combined organic fractions were dried ($MgSO_4$), filtered and then concentrated in vacuo to yield the carboxylic acid used as crude in the next step. The crude carboxylic acid was solubilized in a mixture of MeOH and toluene (2:3, 0.1 M, 0.4 mL). The mixture was treated dropwise with a 2 M solution of trimethylsilyldiazomethane in Et_2O (2 equiv, 40 μL). After stirring for 2 h at rt, the resulting pale yellow mixture was concentrated in vacuo and the residue was purified by flash chromatography on silica gel (hexanes/EtOAc, 85:15) to yield product **50** as a colorless oil (31 mg, quantitative yield). R_f 0.21 (hexanes/EtOAc, 90:10); $C_{48}H_{68}O_8$; MW 773.05 g/mol; IR (liquid film) ν_{max} 2954, 2931, 2873, 1729, 1496, 1455, 1376, 1284, 1160, 1091, 1067 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ_H 7.33–7.19 (m, 15H), 4.65 (d, J=11.6 Hz, 1H), 4.59 (d, J=11.8 Hz, 1H), 4.53 (d, J=11.4 Hz, 1H), 4.44 (d, J=11.8 Hz, 1H), 4.37 (d, J=11.6 Hz, 1H), 4.28 (d, J=11.8 Hz, 1H), 3.96–3.92 (m, 2H), 3.78–3.73 (m, 1H), 3.72–3.68 (m, 1H), 3.65 (s, 3H), 3.66–3.62 (m, 1H), 3.55 (dd, J=8.2, 3.8 Hz, 1H), 3.49 (dd, J=7.8, 4.3 Hz, 1H), 2.62–2.54 (m, 1H), 2.42–2.33 (m, 1H), 2.28–2.20 (m, 1H), 1.96–1.89 (m, 1H), 1.89–1.82 (m, 1H), 1.76–1.65 (m, 2H), 1.52–1.41 (m, 5H), 1.39–1.33 (m, 1H), 1.18 (s, 9H), 1.07 (d, J=7.1 Hz, 3H), 1.02 (d, J=7.1 Hz, 3H), 1.01 (d, J=7.0 Hz, 3H), 0.97 (d, J=6.8 Hz, 3H), 0.96 (d, J=6.6 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 178.7, 176.1, 139.54, 139.53, 139.49, 128.33, 128.32, 128.29, 127.5, 127.4, 127.27, 127.26, 127.23, 127.22, 83.7, 83.4, 78.9, 78.5, 77.4, 72.9, 71.9, 71.4, 64.5, 51.8, 44.9, 39.9, 38.9, 38.2, 36.0, 29.9, 28.7, 28.5, 27.4, 25.5, 25.3, 23.6, 18.5, 13.6, 12.7, 11.4 ppm; MS (ESI) m/z 227.0 (10), 301.1 (5), 773.5 (10, $M+H^+$), 790.5 (2, $M+NH_4^+$), 795.5 (100, $M+Na^+$), 796.5 (55), 885.5 (14); HRMS calcd for $C_{48}H_{69}O_8$ [$M+H^+$]: 773.4987, found: 773.4967 (−2.5 ppm); calcd for $C_{48}H_{72}O_8N$ [$M+NH_4^+$]: 790.5252, found: 790.5232 (−2.6 ppm); calcd for $C_{48}H_{68}O_8Na$ [$M+Na^+$]: 795.4806, found: 795.4804 (−0.4 ppm).

4.37. (4*R*,5*S*,6*S*,7*S*,8*S*,9*S*)-4,6,8-Trihydroxy-9-((2*S*,3*S*,6*S*)-6-((*S*)-1-methoxy-1-oxopropan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)-5,7-dimethyldecyl pivalate (51)

Triol **51** as a colorless oil was obtained from tris-benzyl product **50** (31 mg, 40 μmol) according to general procedure **E**, and was used as crude without purification. R_f <0.05 (hexanes/EtOAc, 85:15); $C_{27}H_{50}O_8$; MW 502.68 g/mol; IR (liquid film) ν_{max} 3421, 3365, 2958, 2934, 2874, 1728, 1459, 1439, 1381, 1284, 1161, 1121, 1083 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ_H 4.42 (d, J=7.9 Hz, 1H), 4.20 (s, 1H), 4.16–4.04 (m, 4H), 3.71 (s, 3H), 3.72–3.68 (m, 1H), 3.64 (dd, J=8.8, 1.6 Hz, 1H), 3.44 (td, J=8.6, 3.0 Hz, 1H), 3.11 (dq, J=10.7, 7.0 Hz, 1H), 2.08–1.98 (m, 2H), 1.88–1.76 (m, 1H), 1.78–1.58 (m, 8H), 1.42–1.35 (m, 1H), 1.28–1.21 (m, 1H), 1.19 (s, 9H), 1.08 (d, J=7.1 Hz, 3H), 1.08 (d, J=7.1 Hz, 3H), 1.06 (d, J=7.2 Hz, 3H), 0.83 (d, J=6.5 Hz, 3H), 0.68 (d, J=6.8 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 178.8, 175.5, 84.2, 83.9, 76.4, 74.7, 70.1, 64.7, 52.5, 40.1, 38.9, 38.4, 37.2, 34.4, 31.7, 31.3, 27.4, 26.6, 25.6, 25.1, 18.0, 14.8, 13.6, 11.5, 11.3 ppm; MS (ESI) m/z 227.0 (6), 360.3 (10), 503.4 (13, $M+H^+$), 525.3 (100, $M+Na^+$), 551.3 (3); HRMS calcd for $C_{27}H_{51}O_8$ [$M+H^+$]: 503.3578, found: 503.3591 (2.5 ppm); calcd for $C_{27}H_{50}O_8Na$ [$M+Na^+$]: 525.3398, found: 525.3419 (4.0 ppm).

4.38. (+)-(4*R*,5*S*,6*S*,7*R*,8*R*,9*R*)-4,6,8-tris(*tert*-Butyldimethylsilyloxy)-9-((2*S*,3*S*,6*S*)-6-((*S*)-1-methoxy-1-oxopropan-2-yl)-3-methyltetrahydro-2*H*-pyran-2-yl)-5,7-dimethyldecyl pivalate (52)

To a cooled (0 °C) solution of crude triol **51** (40 μmol) in dry CH_2Cl_2 (0.1 M, 0.4 mL) was added successively 2,6-lutidine (40 equiv, 190 μL) and TBSOTf (20 equiv, 190 μL). The reaction mixture was stirred for 36 h at rt or until alcohol was completely consumed, as verified by TLC (hexanes/EtOAc, 95:5). The reaction mixture was treated with a saturated aqueous solution of NH_4Cl, followed by separation of the organic phase at rt. The aqueous layer was then extracted with CH_2Cl_2 (3×), and the combined organic fractions were dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (hexanes/EtOAc, 95:5) to yield **52** as a pale yellow oil (21 mg, 62% over 2 steps). R_f 0.45 (hexanes/EtOAc, 95:5); $[\alpha]_D^{25}$ +0.5 (c 2.17, CH_2Cl_2); $C_{45}H_{92}O_8Si_3$; MW 845.46 g/mol; IR (liquid film) ν_{max} 2956, 2931, 2858, 1733, 1472, 1463, 1376, 1284, 1257, 1160, 1052 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ_H 4.08–3.98 (m, 2H), 3.98–3.93 (m, 1H), 3.92–3.84 (m, 2H), 3.68 (s, 3H), 3.68–3.62 (m, 1H), 3.57 (app d, J=9.3 Hz, 1H), 2.51 (dq, J=7.1, 7.1 Hz, 1H), 2.25–2.17 (m, 1H), 2.01–1.92 (m, 1H), 1.91–1.76 (m, 2H), 1.71–1.64 (m, 1H), 1.62–1.53 (m, 4H), 1.49–1.41 (m, 3H), 1.19 (s, 9H), 1.08 (d, J=7.0 Hz, 3H), 1.07 (d, J=6.5 Hz, 3H), 0.94 (d, J=6.9 Hz, 3H), 0.91 (s, 9H), 0.87 (s, 2×9H), 0.85 (d, J=7.0 Hz, 3H), 0.85 (d, J=7.4 Hz, 3H), 0.12 (s, 3H), 0.11 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 178.7, 175.9, 79.7, 74.1, 72.03, 72.02, 71.2, 64.8, 51.7, 45.7, 39.6, 38.88, 38.87, 33.07, 30.11, 29.1, 27.8, 27.36, 26.35, 26.27, 26.24, 25.3, 24.5, 23.9, 23.2, 18.7, 18.53, 18.46, 18.41, 13.2, 11.9, −3.0, −3.3, −3.5, −3.7, −3.85, −3.87 ppm; MS (ESI) m/z 227.0 (13), 390.3 (21), 393.1 (7), 498.9 (4), 566.9 (4), 634.9 (3), 753.5 (4), 845.6 (2, $M+H^+$), 862.6 (3, $M+NH_4^+$), 867.6 (100, $M+Na^+$), 944.7 (5); HRMS calcd for $C_{45}H_{93}O_8Si_3$ [$M+H^+$]: 845.6173, found: 845.6190 (2.1 ppm); calcd for $C_{45}H_{96}O_8NSi_3$ [$M+NH_4^+$]: 862.6438, found: 862.6454 (1.8 ppm); calcd for $C_{45}H_{92}O_8NaSi_3$ [$M+Na^+$]: 867.5992, found: 867.6014 (2.5 ppm).

4.39. (+)-(*S*)-Methyl 2-((2*S*,5*S*,6*S*)-5-methyl-6-((2*R*,3*R*,4*R*,5*S*,6*S*,7*R*)-3,5,7-tris(*tert*-butyldimethylsilyloxy)-10-hydroxy-4,6-dimethyldecan-2-yl)tetrahydro-2*H*-pyran-2-yl)propanoate (53)

To a cooled (0 °C) solution of pivaloyl ester **52** (43.2 mg, 51 μmol) in MeOH (0.1 M, 0.5 mL) was added K_2CO_3 (1.2 equiv, 8.5 mg). After stirring for 36 h at rt, the reaction mixture was treated with water (1 mL) and diluted with EtOAc (3 mL). The aqueous layer was then extracted with EtOAc (3×), and the combined organic fractions were dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (hexanes/EtOAc, 90:10) to yield starting material **52** (14.9 mg, yield=31%) and product **53** (19.7 mg, yield=51%, 78% brsm) as colorless oils. R_f 0.28 (CH_2Cl_2/EtOAc, 95:5); $[\alpha]_D^{25}$ +1.4 (c 1.36, CH_2Cl_2); $C_{40}H_{84}O_7Si_3$; MW 761.35 g/mol; IR (liquid film) ν_{max} 3456, 2953, 2929, 2857, 1742, 1472, 1462, 1376, 1256, 1053 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ_H 3.99–3.95 (m, 1H), 3.92–3.86 (m, 2H), 3.68 (s, 3H), 3.69–3.64 (m, 2H), 3.64–3.60 (m, 2H), 3.55 (app d, J=8.7 Hz, 1H), 2.52 (dq, J=7.4, 7.4 Hz, 1H), 2.25–2.15 (m, 1H), 2.00–1.92 (m, 1H), 1.92–1.86 (m, 1H), 1.86–1.77 (m, 1H), 1.77–1.70 (m, 1H), 1.61–1.39 (m, 7H), 1.08 (d, J=6.9 Hz, 3H), 1.07 (d, J=7.0 Hz, 3H), 0.94 (d, J=7.0 Hz, 3H), 0.91 (s, 9H), 0.88 (s, 9H), 0.88 (s, 9H), 0.87 (d, J=7.1 Hz, 3H), 0.85 (d, J=7.4 Hz, 3H), 0.11 (s, 2×3H), 0.10 (s, 3H), 0.09 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 176.1, 79.8, 77.7,

76.8, 74.4, 71.4, 63.5, 51.9, 42.4, 33.0, 30.0, 28.6, 27.8, 26.43, 26.40, 26.37, 26.35, 26.32, 26.30, 25.4, 23.2, 18.88, 18.85, 18.61, 18.55, 18.53, 18.52, 13.3, −3.2, −3.45, −3.55, −3.65, −3.8 (2C) ppm; MS (ESI) *m/z* 193.0 (12), 338.3 (14), 360.3 (35), 497.4 (6), 595.5 (6), 669.5 (18), 761.6 (2, M+H$^+$), 783.5 (100, M+Na$^+$), 860.7 (7); HRMS calcd for $C_{40}H_{85}O_7Si_3$ [M+H$^+$]: 761.5598, found: 761.5610 (1.6 ppm); calcd for $C_{40}H_{84}O_7NaSi_3$ [M+Na$^+$]: 783.5417, found: 783.5432 (1.9 ppm).

4.40. (−)-(*S*)-Methyl 2-((2*S*,5*S*,6*S*)-5-methyl-6-((2*R*,3*R*,4*R*,5*S*,6*S*,7*R*)-3,5,7-tris(*tert*-butyldimethylsilyloxy)-4,6-dimethyl-10-(1-phenyl-1*H*-tetrazol-5-ylthio)decan-2-yl)tetrahydro-2*H*-pyran-2-yl)propanoate (55)

To a cooled (0 °C) solution of PPh_3 (1.4 equiv, 7.7 mg) and 1-phenyl-1*H*-tetrazole-5-thiol **54** (1.5 equiv, 5.5 mg) in dry THF (0.05 M, 220 μL) was added dropwise DIAD (1.5 equiv, 6.2 μL). The resulting yellow mixture was stirred for 10 min at 0 °C before dropwise addition of primary alcohol **53** (16.0 mg, 21 μmol) in dry THF (0.05 M, 220 μL) and stirring for 3 h at rt The reaction mixture was then treated with water (1 mL) and diluted with Et_2O (3 mL). The aqueous layer was extracted with Et_2O (3×) and the combined organic fractions were washed with a saturated brine solution, then dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (hexanes/EtOAc, 90:10) to yield product **55** as a colorless oil (13.6 mg, yield=70%). R_f 0.39 (hexanes/EtOAc, 90:10); $[\alpha]_D^{25}$ −1.0 (*c* 1.36, CH_2Cl_2); $C_{47}H_{88}N_4O_6SSi_3$; MW 921.55 g/mol; IR (liquid film) ν_{max} 2953, 2930, 2886, 2857, 1741, 1501, 1462, 1387, 1253, 1052 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.60–7.51 (m, 5H), 3.93 (dt, *J*=6.7, 4.1 Hz, 1H), 3.88 (dd, *J*=7.5, 3.4 Hz, 1H), 3.84 (dd, *J*=8.4, 3.7 Hz, 1H), 3.67 (s, 3H), 3.69–3.62 (m, 1H), 3.55 (dd, *J*=9.6, 1.1 Hz, 1H), 3.45–3.35 (m, 2H), 2.51 (dq, *J*=7.0, 7.0 Hz, 1H), 2.24–2.16 (m, 1H), 1.94 (ddq, *J*=3.7, 7.3, 7.3 Hz, 1H), 1.89–1.73 (m, 4H), 1.70–1.62 (m, 3H), 1.49–1.40 (m, 3H), 1.08 (d, *J*=7.1 Hz, 3H), 1.06 (d, *J*=7.1 Hz, 3H), 0.92 (d, *J*=7.1 Hz, 3H), 0.91 (s, 9H), 0.852 (s, 9H), 0.849 (s, 9H), 0.845 (d, *J*=7.2 Hz, 3H), 0.82 (d, *J*=7.4 Hz, 3H), 0.11 (s, 3H), 0.09 (s, 3H), 0.07 (s, 3H), 0.05 (s, 3H), 0.034 (s, 3H), 0.027 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 175.9, 154.5, 133.9, 130.2, 129.9, 124.0, 79.6, 77.4, 74.1, 71.9, 71.2, 51.7, 45.7, 43.9, 39.7, 35.7, 33.9, 27.8, 26.3, 26.22, 26.21, 25.5, 25.3, 24.7, 23.2, 18.7, 18.5, 18.43, 18.38, 13.2, 12.2, 11.0, 10.2, −3.0, −3.3, −3.6, −3.7, −3.8, −3.9 ppm; MS (ESI) *m/z* 247.0 (7), 338.3 (6), 515.4 (56), 614.5 (42), 657.4 (81), 789.5 (29), 921.6 (79, M+H$^+$), 938.6 (15, M+NH$_4^+$), 943.6 (26, M+Na$^+$), 1020.7 (100); HRMS calcd for $C_{47}H_{89}N_4O_6SSi_3$ [M+H$^+$]: 921.5805, found: 921.5804 (−0.1 ppm); calcd for $C_{47}H_{92}N_5O_6SSi_3$ [M+NH$_4^+$]: 938.6071, found: 938.6066 (−0.4 ppm); calcd for $C_{47}H_{88}N_4O_6NaSSi_3$ [M+Na$^+$]: 943.5625, found: 943.5620 (−0.5 ppm).

4.41. (+)-(*S*)-Methyl 2-((2*S*,5*S*,6*S*)-5-methyl-6-((2*R*,3*R*,4*R*,5*S*,6*S*,7*R*)-3,5,7-tris(*tert*-butyldimethylsilyloxy)-4,6-dimethyl-10-(1-phenyl-1*H*-tetrazol-5-ylsulfonyl)decan-2-yl) tetrahydro-2*H*-pyran-2-yl)propanoate (9)

Oxidation reagent was prepared at 0 °C by the dropwise addition of a 35% wt. solution of H_2O_2 in water (10 equiv, 17 μL) to $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ (0.3 equiv, 5.5 mg) forming a bright yellow solution. The mixture was added dropwise to a cooled (0 °C) solution of sulfide **55** (13.6 mg, 15 μmol) in 95% EtOH (0.1 M, 200 μL) and was stirred for 18 h at rt, resulting in the formation of a yellow precipitate. The reaction mixture was then treated with water (1 mL) and diluted with EtOAc (3 mL). The aqueous layer was extracted with EtOAc (3×) and the combined organic fractions were washed with a saturated brine solution, then dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (hexanes/EtOAc, 90:10) to yield sulfone **9** as a colorless oil (14.9 mg, quantitative yield). R_f 0.38 (hexanes/EtOAc, 90:10); $[\alpha]_D^{25}$ +0.5 (*c* 1.12, CH_2Cl_2); $C_{47}H_{88}N_4O_8SSi_3$; MW 953.55 g/mol; IR (liquid film) ν_{max} 2954, 2930, 2886, 2857, 1741, 1498, 1463, 1344, 1257, 1152, 1050 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.71–7.67 (m, 2H), 7.65–7.57 (m, 3H), 3.93 (dd, *J*=10.2, 4.9 Hz, 1H), 3.90 (dd, *J*=7.3, 3.3 Hz, 1H), 3.84 (dd, *J*=8.3, 3.4 Hz, 1H), 3.73 (app t, *J*=7.9 Hz, 2H), 3.67 (s, 3H), 3.69–3.62 (m, 1H), 3.56 (dd, *J*=9.8, 1.2 Hz, 1H), 2.52 (dq, *J*=7.2, 7.2 Hz, 1H), 2.26–2.17 (m, 1H), 2.03–1.90 (m, 3H), 1.89–1.77 (m, 2H), 1.76–1.65 (m, 3H), 1.50–1.40 (m, 3H), 1.08 (d, *J*=6.9 Hz, 3H), 1.07 (d, *J*=6.8 Hz, 3H), 0.93 (d, *J*=6.9 Hz, 3H), 0.91 (s, 9H), 0.86 (s, 9H), 0.88–0.85 (m, 3H), 0.85 (s, 9H), 0.84 (d, *J*=7.1 Hz, 3H), 0.12 (s, 3H), 0.10 (s, 3H), 0.09 (s, 3H), 0.06 (s, 3H), 0.05 (s, 2×3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 175.9, 153.6, 133.2, 131.6, 129.9, 125.2, 79.7, 74.8, 74.2, 71.6, 71.3, 56.4, 51.7, 45.6, 44.0, 39.7, 35.3, 27.8, 26.3, 26.21, 26.18 (2C), 25.3, 23.2, 18.7, 18.6, 18.39, 18.36, 17.8, 13.2, 12.7, 11.0, 10.3, −3.1, −3.4, −3.66, −3.71, −3.81, −3.82 ppm; MS (ESI) *m/z* 189.0 (11), 247.0 (15), 262.0 (11), 338.3 (20), 515.4 (61), 532.4 (37), 588.5 (10), 614.5 (100), 953.6 (11, M+H$^+$), 970.6 (14, M+NH$_4^+$), 975.5 (7, M+Na$^+$), 1020.7 (10), 1052.7 (26); HRMS calcd for $C_{47}H_{89}N_4O_8SSi_3$ [M+H$^+$]: 953.5703, found: 953.5676 (−2.8 ppm); calcd for $C_{47}H_{92}N_5O_8SSi_3$ [M+NH$_4^+$]: 970.5969, found: 970.5942 (−2.8 ppm); calcd for $C_{47}H_{88}N_4O_8NaSSi_3$ [M+Na$^+$]: 975.5523, found: 975.5496 (−2.7 ppm).

4.42. (−)-(*R*)-4-Benzyl-3-((2*S*,3*R*,6*R*,*E*)-2,4,6-trimethyl-3-((trimethylsilyl)oxy)non-4-enoyl)oxazolidin-2-one (58)

To a solution of crude aldehyde **11**[28] (1.50 g, 11 mmol) in dry EtOAc (0.25 M, 40 mL) at rt was added successively (*R*)-4-benzyl-3-propionyloxazolidin-2-one **57** (1.2 equiv, 2.99 g), dried $MgCl_2$ (0.2 equiv, 204 mg), Et_3N (2.4 equiv, 3.6 mL) and TMSCl (2 equiv, 2.7 mL). The pale orange mixture was stirred for 18 h at rt before filtration onto a pad of Celite® (conditioned with Et_2O) and washing with Et_2O (2×15 mL). Filtrate was concentrated in vacuo to yield **58** as an orange oil (3.48 g, yield=73% over 2 steps). R_f 0.27 (hexanes/EtOAc, 85:15); $[\alpha]_D^{25}$ −42 (*c* 1.4, $CDCl_3$); $C_{25}H_{39}NO_4Si$; MW 445.67 g/mol; IR (liquid film) ν_{max} 2958, 1784, 1669, 1386, 1212 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.37–7.24 (m, 5H), 5.16 (ddd, *J*=9.5, 2.4, 1.4 Hz, 1H), 4.72 (ddt, *J*=9.6, 7.8, 3.3 Hz, 1H), 4.29 (d, *J*=9.6 Hz, 1H), 4.20–4.08 (m, 3H), 3.33 (dd, *J*=13.4, 3.3 Hz, 1H), 2.71 (dd, *J*=13.4, 9.7 Hz, 1H), 2.48–2.35 (m, 1H), 1.62 (d, *J*=1.3 Hz, 3H), 1.31–1.17 (m, 4H), 0.96 (d, *J*=6.8 Hz, 2×3H), 0.90–0.84 (m, 3H), 0.05 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 176.8, 153.4, 136.8, 135.7, 133.3, 129.6, 129.1, 127.4, 82.6, 65.8, 55.3, 41.6, 39.9, 38.2, 32.0, 20.9, 20.7, 14.5, 14.3, 10.6, 0.4 ppm; MS (ESI) *m/z* 356.2 (80), 396.2 (75, M−TMS+Na$^+$), 468.2 (8, M+Na$^+$); HRMS calcd for $C_{22}H_{31}NO_4Na$ [M−TMS+Na$^+$]: 396.2151, found: 396.2137 (3.5 ppm); Analysis calcd for $C_{25}H_{39}NO_4Si$: C, 67.37; H, 8.82; N, 3.14; found: C, 67.16; H, 9.17; N, 3.11.

4.43. (−)-(*R*)-4-Benzyl-3-((2*S*,3*R*,6*R*,*E*)-3-hydroxy-2,4,6-trimethylnon-4-enoyl)oxazolidin-2-one (59)

To a cooled (0 °C) solution of silylated aldol adduct **58** (3.48 g, 7.8 mmol) in MeOH (0.1 M, 80 mL) was added TFA (1 drop). After stirring for 1 h at 0 °C, the mixture was concentrated in vacuo and TFA was co-evaporated with toluene (3×5 mL). The pale yellow residue was then purified by flash chromatography on silica gel (hexanes/EtOAc, 80:20) to yield alcohol **59** as a colorless oil (2.53 g, yield=87%). R_f 0.26 (hexanes/EtOAc, 75:25); $[\alpha]_D^{25}$ −70 (*c* 0.28, $CDCl_3$); $C_{22}H_{31}NO_4$; MW 373.49 g/mol; IR (liquid film) ν_{max} 3510, 2957, 2871, 1780, 1698, 1388, 1212, 1012 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.36–7.24 (m, 5H), 5.24 (dq, *J*=9.6, 1.3 Hz, 1H), 4.70 (dtd, *J*=3.2, 6.6, 7.1 Hz, 1H), 4.24–4.06 (m, 4H), 3.33 (dd, *J*=3.4, 13.5 Hz, 1H), 2.80 (dd, *J*=9.4, 13.5 Hz, 1H), 2.52 (br s, 1H), 2.47–2.36 (m, 1H), 1.68 (d, *J*=1.3 Hz, 3H), 1.33–1.18 (m, 4H), 1.05 (d, *J*=6.5 Hz, 3H), 0.95 (d, *J*=6.7 Hz, 3H), 0.89–0.85 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 176.9, 154.0, 136.9, 135.5, 132.8, 129.7, 129.1, 127.4, 81.9, 66.2, 55.8, 40.8, 39.9, 37.9, 32.1, 21.0, 20.8, 14.9, 14.3, 10.9 ppm; MS (ESI) *m/z* 356.1 (100, M+H$^+$−H$_2$O), 396.2 (45, M+Na$^+$); HRMS calcd for $C_{22}H_{31}NO_4Na$

[M+Na$^+$]: 396.2151, found: 396.2153 (0.6 ppm); Analysis calcd for $C_{22}H_{31}NO_4$: C, 70.75; H, 8.37; N, 3.75; found: C, 70.85; H, 8.57; N, 3.72.

4.44. (−)-(*R*)-4-Benzyl-3-((2*S*,3*R*,6*R*,*E*)-3-(4-methoxybenzyloxy)-2,4,6-trimethylnon-4-enoyl)oxazolidin-2-one (60)

PMB ether **60** (75 mg, quantitative yield) as a colorless oil was obtained from primary alcohol **59** (52 mg, 0.14 mmol) according to general procedure **A**, and purification by flash chromatography on silica gel (hexanes/EtOAc, 85:15). R_f 0.29 (hexanes/EtOAc, 85:15); $[\alpha]_D^{25}$ −21.5 (*c* 2.96, $CDCl_3$); $C_{30}H_{39}NO_5$; MW 493.63 g/mol; IR (liquid film) ν_{max} 2956, 2929, 2870, 1781, 1699, 1613, 1514, 1455, 1386, 1248, 1212, 1068 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.29–7.21 (m, 3H), 7.16 (d, *J*=8.6 Hz, 2H), 7.14–7.11 (m, 2H), 6.76 (d, *J*=8.6 Hz, 2H), 5.26 (d, *J*=9.6 Hz, 1H), 4.67 (ddt, *J*=7.9, 7.0, 3.3 Hz, 1H), 4.35 (d, *J*=11.1 Hz, 1H), 4.25 (dq, *J*=9.9, 6.9 Hz, 1H), 4.10 (app t, *J*=8.7 Hz, 1H), 4.10 (d, *J*=11.2 Hz, 1H), 4.00 (dd, *J*=9.0, 3.3 Hz, 1H), 3.94 (d, *J*=10.1 Hz, 1H), 3.70 (s, 3H), 3.17 (dd, *J*=13.6, 3.2 Hz, 1H), 2.54–2.45 (m, 1H), 2.37 (dd, *J*=13.6, 9.9 Hz, 1H), 1.67 (s, 3H), 1.35–1.20 (m, 4H), 1.00 (d, *J*=6.8 Hz, 2×3H), 0.89 (t, *J*=6.3 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 176.9, 159.1, 153.4, 139.7, 135.9, 130.9, 130.2, 129.7, 129.5, 128.9, 127.2, 113.6, 89.2, 69.8, 65.8, 55.31, 55.29, 39.8, 39.6, 37.7, 32.3, 21.4, 20.9, 14.3, 14.2, 10.7 ppm; MS (ESI) *m*/*z* 356.2 (36), 494.3 (8, M+H$^+$), 511.3 (5, M+NH$_4^+$), 516.3 (100, M+Na$^+$), 567.4 (7), 593.4 (16), 1009.6 (73); HRMS calcd for $C_{30}H_{40}NO_5$ [M+H$^+$]: 494.2901, found: 494.2903 (0.4 ppm); calcd for $C_{30}H_{43}N_2O_5$ [M+NH$_4^+$]: 511.3166, found: 511.3168 (0.4 ppm); calcd for $C_{30}H_{39}NO_5Na$ [M+Na$^+$]: 516.2720, found: 516.2731 (2.1 ppm).

4.45. (+)-(2*R*,3*R*,6*R*,*E*)-3-(4-Methoxybenzyloxy)-2,4,6-trimethylnon-4-en-1-ol (S6)

To a cooled (0 °C) solution of product **60** (358 mg, 0.725 mmol) in dry Et_2O (0.1 M, 7.2 mL) was added successively MeOH (4 equiv, 120 μL) and a 2 M solution of $LiBH_4$ in THF (4 equiv, 1.5 mL). After stirring for 18 h at 0 °C, the mixture was treated with a 1 N solution of HCl at 0 °C, followed by separation of the organic phase at rt. The aqueous layer was extracted with Et_2O (3×) and the combined organic fractions were washed with a saturated brine solution, then dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (hexanes/EtOAc, 75:25) to yield product **S6** as a colorless oil (117 mg, yield=50%). R_f 0.31 (hexanes/EtOAc, 80:20); $[\alpha]_D^{25}$ +32.4 (*c* 1.16, CH_2Cl_2); $C_{20}H_{32}O_3$; MW 320.24 g/mol; IR (liquid film) ν_{max} 3447, 2957, 2927, 2870, 1613, 1514, 1456, 1302, 1248, 1173, 1037 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.22 (d, *J*=8.6 Hz, 2H), 6.87 (d, *J*=8.7 Hz, 2H), 5.11 (d, *J*=9.6 Hz, 1H), 4.42 (d, *J*=11.4 Hz, 1H), 4.16 (d, *J*=11.5 Hz, 1H), 3.80 (s, 3H), 3.57 (d, *J*=5.9 Hz, 2H), 3.46 (d, *J*=9.7 Hz, 1H), 3.40 (br s, 1H), 2.53–2.42 (m, 1H), 2.02–1.93 (m, 1H), 1.60 (d, *J*=1.2 Hz, 3H), 1.33–1.18 (m, 4H), 1.01 (d, *J*=6.7 Hz, 3H), 0.87 (t, *J*=6.8 Hz, 3H), 0.66 (d, *J*=7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 159.3, 138.6, 130.7, 130.4, 129.7, 114.0, 91.9, 69.1, 68.8, 55.4, 39.8, 37.1, 32.1, 21.5, 20.9, 14.3, 14.0, 10.8 ppm; MS (ESI) *m*/*z* 303.2 (3), 321.2 (1, M+H$^+$), 343.2 (100, M+Na$^+$), 344.2 (21); HRMS calcd for $C_{20}H_{33}O_3$ [M+H$^+$]: 321.2424, found: 321.2419 (−1.5 ppm); calcd for $C_{20}H_{32}O_3Na$ [M+Na$^+$]: 343.2244, found: 343.2239 (−1.4 ppm).

4.46. (+)-(2*S*,3*R*,6*R*,*E*)-3-(4-Methoxybenzyloxy)-2,4,6-trimethylnon-4-enal (10)

Aldehyde **10** (54 mg, yield=81%) as a colorless oil was obtained from alcohol **S6** (68 mg, 0.21 mmol) according to general procedure **C**, and purification by flash chromatography on silica gel (hexanes/EtOAc, 90:10). ^{1}H and ^{13}C NMR chemical shift were identical to those previously reported for the same compound by Leighton et al.[16d] R_f 0.66 (hexanes/EtOAc, 80:20); $[\alpha]_D^{25}$ +32.3 (*c* 4.13, $CDCl_3$); $C_{20}H_{30}O_3$; MW 318.45 g/mol; IR (liquid film) ν_{max} 2957, 2927, 2870, 1729, 1613, 1513, 1456, 1302, 1248, 1173, 1064, 1036 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 9.68 (d, *J*=2.8 Hz, 1H), 7.18 (d, *J*=8.2 Hz, 2H), 6.86 (d, *J*=8.3 Hz, 2H), 5.18 (d, *J*=9.6 Hz, 1H), 4.42 (d, *J*=11.6 Hz, 1H), 4.15 (d, *J*=11.6 Hz, 1H), 3.80 (s, 3H), 3.71 (d, *J*=10.0 Hz, 1H), 2.65–2.57 (m, 1H), 2.53–2.43 (m, 1H), 1.60 (d, *J*=1.3 Hz, 3H), 1.34–1.17 (m, 4H), 1.02 (d, *J*=6.6 Hz, 3H), 0.87 (t, *J*=6.3 Hz, 3H), 0.84 (d, *J*=7.1 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 205.2, 159.3, 139.5, 130.4, 129.7, 129.4, 113.9, 85.7, 69.2, 55.4, 48.3, 39.8, 32.3, 21.4, 20.9, 14.3, 11.0, 10.7 ppm; MS (ESI) *m*/*z* 193.4 (2), 301.2 (5), 319.2 (2, M+H$^+$), 341.2 (35, M+Na$^+$), 342.2 (21), 373.2 (100), 403.2 (8), 493.3 (6), 723.5 (6); HRMS calcd for $C_{20}H_{31}O_3$ [M+H$^+$]: 319.2268, found: 319.2271 (1.0 ppm); calcd for $C_{20}H_{30}O_3Na$ [M+Na$^+$]: 341.2087, found: 341.2092 (1.5 ppm).

4.47. (−)-(*S*)-Methyl 2-((2*S*,5*S*,6*S*)-5-methyl-6-((2*R*,3*R*,4*R*,5*S*,6*S*,7*R*,10*E*,12*R*,13*R*,14*E*,16*R*)-3,5,7-tris(*tert*-butyldimethylsilyloxy)-13-(4-methoxybenzyloxy)-4,6,12,14,16-pentamethylnonadeca-10,14-dien-2-yl)tetrahydro-2*H*-pyran-2-yl)propanoate (61a)

To a cooled (−55 °C) solution of sulfone **9** (25.5 mg, 27 μmol) in anhydrous DME (0.05 M, 540 μL) was added a 0.5 M solution of KHMDS in toluene (1.1 equiv, 59 μL), followed immediately with a 0.5 M solution of aldehyde **10** in anhydrous DME (1.2 equiv, 64 μL). The reaction was stirred for 1 h at −55 °C, then 30 min at −40 °C before the mixture was treated with a saturated aqueous solution of NH_4Cl at −40 °C. After separation of the organic phase at rt, the aqueous layer was extracted with 20% EtOAc/hexanes and the combined organic fractions were dried ($MgSO_4$), filtered and concentrated in vacuo. ^{1}H NMR analysis of the crude product indicated a ratio 9:1 of isomers *E* (**61a**): *Z* (**61b**). The residue was purified by flash chromatography on silica gel (hexanes/EtOAc, 95:5 to 90:10) to yield sulfone **9** (6.2 mg, yield=24%), aldehyde **10** (3.7 mg, yield=43%) and an inseparable mixture of product **61a**,**b** (9.5 mg, yield=34%, 45% brsm) as colorless oils. R_f 0.60 (hexanes/EtOAc, 90:10); $[\alpha]_D^{25}$ −3.6 (*c* 0.93, $CDCl_3$); $C_{60}H_{112}O_8Si_3$; MW 1045.78 g/mol; IR (liquid film) ν_{max} 2955, 2929, 2857, 1742, 1513, 1459, 1375, 1249, 1171 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.21 (d, *J*=8.5 Hz, 2H$_a$+2H$_b$), 6.84 (d, *J*=8.6 Hz, 2H$_a$+2H$_b$), 5.44–5.34 (m, 2H$_a$+2H$_b$), 5.04 (d, *J*=9.5 Hz, 1H$_a$+1H$_b$), 4.412 (d, *J*=12.2 Hz, 1H$_b$), 4.406 (d, *J*=11.8 Hz, 1H$_a$), 4.26–4.18 (m, 1H$_a$+1H$_b$), 4.14 (d, *J*=11.9 Hz, 1H$_a$), 4.13 (d, *J*=12.1 Hz, 1H$_b$), 3.98–3.92 (m, 1H$_a$+1H$_b$), 3.92–3.85 (m, 2H$_a$+2H$_b$), 3.80 (s, 3H$_b$), 3.79 (s, 3H$_a$), 3.67 (s, 3H$_a$+3H$_b$), 3.57 (d, *J*=9.6 Hz, 1H$_a$+1H$_b$), 3.24 (d, *J*=8.7 Hz, 1H$_b$), 3.23 (d, *J*=9.1 Hz, 1H$_a$), 2.70–2.60 (m, 1H$_b$), 2.55–2.49 (m, 1H$_a$+1H$_b$), 2.49–2.41 (m, 1H$_a$+1H$_b$), 2.35–2.28 (m, 1H$_a$), 2.24–2.18 (m, 1H$_a$+1H$_b$), 2.06–1.93 (m, 3H$_a$+3H$_b$), 1.92–1.77 (m, 2H$_a$+2H$_b$), 1.76–1.66 (m, 2H$_a$+2H$_b$), 1.56 (s, 3H$_a$), 1.55 (s, 3H$_b$), 1.47–1.40 (m, 4H$_a$+4H$_b$), 1.37–1.15 (m, 7H$_a$+7H$_b$), 1.08 (d, *J*=7.3 Hz, 3H$_a$+3H$_b$), 1.07 (d, *J*=7.5 Hz, 3H$_a$+3H$_b$), 0.99 (d, *J*=6.6 Hz, 3H$_a$+3H$_b$), 0.94 (d, *J*=6.8 Hz, 3H$_a$), 0.93 (d, *J*=7.3 Hz, 3H$_b$), 0.92 (s, 9H$_a$), 0.913 (d, *J*=7.0 Hz, 3H$_a$+3H$_b$), 0.912 (s, 9H$_b$), 0.89 (s, 2×9H$_a$), 0.88 (s, 9H$_b$), 0.87 (s, 9H$_b$), 0.85 (d, *J*=7.1 Hz, 3H$_a$+3H$_b$), 0.79 (d, *J*=6.9 Hz, 3H$_a$), 0.75 (d, *J*=6.9 Hz, 3H$_b$), 0.12 (s, 3H$_a$+3H$_b$), 0.11 (s, 3H$_a$+3H$_b$), 0.09 (s, 3H$_a$), 0.09 (s, 3H$_a$+3H$_b$), 0.08 (s, 3H$_b$), 0.07 (s, 3H$_a$), 0.05 (s, 3H$_a$+3H$_b$), 0.04 (s, 3H$_b$) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 175.9, 159.0, 137.6, 134.0, 131.5, 131.0, 129.4, 129.0, 113.7, 89.3, 79.7, 74.1, 72.5, 71.2, 69.2, 68.3, 55.4, 51.7, 39.9, 39.0, 38.9, 32.1, 30.5, 29.1, 27.9, 26.4, 26.34, 26.31, 25.28, 23.9, 23.1, 21.61, 21.58, 20.9, 18.7, 18.52, 18.45, 18.1, 17.5, 14.4, 14.2, 13.2, 11.7, 11.23, 11.17, 11.12, −3.0, −3.2, −3.5, −3.6, −3.8, −3.9 ppm; MS (ESI) *m*/*z* 159.0 (7), 227.0 (19), 250.2 (5), 338.3 (10), 360.3 (100), 413.3 (53), 441.3 (9), 566.9 (4), 697.7 (7), 750.6 (10), 803.5 (3), 1067.8 (9, M+Na$^+$), 1117.4 (5); HRMS calcd for $C_{60}H_{112}O_8NaSi_3$ [M+Na$^+$]: 1067.7557, found: 1067.7586 (2.7 ppm).

4.48. (+)-(*S*)-Methyl 2-((2*S*,5*S*,6*S*)-5-methyl-6-((2*R*,3*R*,4*R*,5*S*,6*S*,7*R*,10*E*,12*R*,13*R*,14*E*,16*R*)-3,5,7-tris(*tert*-butyldimethylsilyloxy)-13-hydroxy-4,6,12,14,16-pentamethylnonadeca-10,14-dien-2-yl)tetrahydro-2*H*-pyran-2-yl)propanoate (62)

To a solution of PMB ether **61a,b** (9.5 mg, 9 μmol) in a solvent mixture of CH_2Cl_2 and sodium phosphate buffer pH 7 (10:1, 0.02 M, 450 μL) at rt, was added DDQ (4 equiv, 8.2 mg) in 2 portions over 10 min. After stirring for 30 min at rt, the aqueous layer was extracted with 20% EtOAc/hexanes and the combined organic fractions were washed with a saturated $NaHCO_3$ solution, then dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (hexanes/EtOAc, 95:5) to yield C19-alcohol **62** as a colorless oil (7.5 mg, yield=89%). R_f 0.31 (hexanes/EtOAc, 95:5); $[\alpha]_D^{25}$ +3.8 (*c* 0.53, $CDCl_3$); $C_{52}H_{104}O_7Si_3$; MW: 925.63 g/mol; IR (liquid film) ν_{max} 3549, 2956, 2929, 2857, 1743, 1463, 1378, 1256, 1168, 1051 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ_H 5.63–5.54 (m, 1H), 5.31–5.17 (m, 1H), 5.17–5.10 (m, 1H), 3.97–3.92 (m, 1H), 3.92–3.84 (m, 2H), 3.68 (s, 3H), 3.69–3.62 (m, 2H), 3.59–3.52 (m, 2H), 2.55–2.47 (m, 1H), 2.46–2.36 (m, 1H), 2.25–2.18 (m, 2H), 2.06–1.99 (m, 1H), 1.99–1.92 (m, 1H), 1.91–1.86 (m, 1H), 1.84–1.78 (m, 1H), 1.75–1.66 (m, 2H), 1.59 (s, 3H), 1.48–1.42 (m, 4H), 1.30–1.17 (m, 8H), 1.08 (d, *J*=7.0 Hz, 3H), 1.07 (d, *J*=7.0 Hz, 3H), 0.94 (d, *J*=6.6 Hz, 3H), 0.94 (d, *J*=6.9 Hz, 3H), 0.91 (s, 9H), 0.89–0.87 (m, 3H), 0.88 (s, 9H), 0.88 (s, 9H), 0.86 (d, *J*=7.2 Hz, 3H), 0.84 (d, *J*=6.6 Hz, 3H), 0.12 (s, 3H), 0.11 (s, 3H), 0.10 (s, 3H), 0.08 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 175.9, 136.2, 133.4, 133.1, 132.8, 82.8, 82.0, 79.7, 74.2, 72.3, 71.2, 51.7, 41.5, 40.0, 36.7, 36.0, 32.0, 30.5, 29.9, 29.1, 27.9, 26.4, 26.30, 26.28, 25.3, 23.9, 23.2, 20.8, 18.7, 18.53, 18.49, 18.4, 17.6, 17.5, 14.4, 13.2, 11.9, 11.1, 11.0, 10.9, −3.0, −3.3, −3.5, −3.6, −3.8, −3.9 ppm; MS (ESI) *m/z* 227.0 (3), 360.3 (4), 413.3 (8), 511.4 (5), 643.5 (6), 833.6 (4), 925.7 (4, $M+H^+$), 942.7 (4, $M+NH_4^+$), 947.7 (100, $M+Na^+$); HRMS calcd for $C_{52}H_{105}O_7Si_3$ [$M+H^+$]: 925.7163, found: 925.7149 (−1.5 ppm); calcd for $C_{52}H_{108}O_7NSi_3$ [$M+NH_4^+$]: 942.7428, found: 942.7415 (−1.4 ppm); calcd for $C_{52}H_{104}O_7Si_3Na$ [$M+Na^+$]: 947.6982, found: 947.6993 (1.2 ppm).

4.49. (*S*)-Methyl 2-((2*S*,5*S*,6*S*)-5-methyl-6-((2*S*,3*S*,4*S*,5*S*,6*S*,7*R*,10*E*,12*R*,13*R*,14*E*,16*R*)-3,5,7,13-tetrahydroxy-4,6,12,14,16-pentamethylnonadeca-10,14-dien-2-yl)tetrahydro-2*H*-pyran-2-yl)propanoate (1b)

Following a reported procedure,[30] the tris-TBS ether **62** (7.5 mg, 8 μmol) was solubilized in dry THF (0.05 M, 160 μL) and was treated with a 1 M solution of TBAF in THF (8 equiv, 49 μL). After stirring for 68 h at rt (or until all starting material was consumed), the mixture was treated with $CaCO_3$ (25 mg), DOWEX® 50WX8 100–200 mesh (80 mg, used as supplied) and MeOH (1 mL). The suspension was stirred for 18 h at rt and then filtered onto a pad of Celite®, washed with MeOH thoroughly (~20 mL). The filtrate was concentrated in vacuo and the pale yellow residue was purified by flash chromatography on silica gel (hexanes/EtOAc, 60:40) to yield zincophorin methyl ester **1b** (3.2 mg, yield=68%) as a colorless oil. ^1H chemical shift were identical to those previously reported for the same compound by Cossy et al.[16b] R_f 0.49 (hexanes/EtOAc, 60:40); $C_{34}H_{62}O_7$; MW: 582.85 g/mol; ^1H NMR (500 MHz, $CDCl_3$) δ_H 5.93 (s, 1H), 5.61 (app dt, *J*=15.4, 6.9 Hz, 1H), 5.34 (dd, *J*=15.3, 8.8 Hz, 1H), 5.11 (d, *J*=9.9 Hz, 1H), 4.43 (d, *J*=8.2 Hz, 1H), 4.12–4.06 (m, 3H), 3.76 (d, *J*=9.7 Hz, 1H), 3.72 (s, 3H), 3.63 (dd, *J*=8.8, 1.6 Hz, 1H), 3.55 (d, *J*=9.0 Hz, 1H), 3.43 (app dt, *J*=10.5, 2.2 Hz, 1H), 3.23 (dq, *J*=10.8, 6.9 Hz, 1H), 2.45–2.37 (m, 1H), 2.26–2.17 (m, 3H), 2.12 (d, *J*=1.8 Hz, 1H), 2.06–1.96 (m, 2H), 1.79–1.67 (m, 4H), 1.60 (d, *J*=1.1 Hz, 3H), 1.38–1.15 (m, 6H), 1.10 (d, *J*=7.1 Hz, 3H), 1.08 (d, *J*=7.0 Hz, 3H), 1.06 (d, *J*=7.5 Hz, 3H), 0.93 (d, *J*=6.6 Hz, 3H), 0.90–0.85 (m, 5H), 0.84 (d, *J*=6.8 Hz, 3H), 0.82 (d, *J*=6.5 Hz, 3H), 0.66 (d, *J*=6.8 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 175.7, 134.8, 133.6, 133.42, 133.37, 84.6, 84.2, 82.0, 76.2, 74.7, 69.2, 52.6, 42.0, 41.2, 40.1, 38.5, 37.6, 34.6, 34.1, 32.0, 31.8, 29.9, 26.4, 25.2, 21.2, 20.8, 17.9, 17.6, 15.0, 14.4, 13.4, 11.44, 11.37, 10.9 ppm; MS (ESI) *m/z* 193.3 (4), 227.0 (7), 296.2 (3), 338.3 (3), 360.3 (11), 413.3 (4), 565.4 (7), 583.5 (12, $M+H^+$), 605.4 (100, $M+Na^+$), 606.4 (37); HRMS calcd for $C_{34}H_{63}O_7$ [$M+H^+$]: 583.4568, found: 583.4559 (−1.6 ppm); calcd for $C_{34}H_{62}O_7Na$ [$M+Na^+$]: 605.4388, found: 605.4389 (0.2 ppm).

Acknowledgements

The authors wish to express their gratitude to the Natural Sciences and Engineering Research Council of Canada (EG #1504) for its financial support. Fellowship support (B2) from Fonds Québécois de la Recherche sur la Nature et les Technologies (FQRNT) to F.G. is also gratefully acknowledged.

Supplementary data

Supplementary data (experimental procedures, spectroscopic data, copies of ^1H and ^{13}C spectra for all reported compounds) related to this article can be found at http://dx.doi.org/10.1016/j.tet.2014.11.061.

References and notes

1. (a) O'Hagan, D. *Nat. Prod. Rep.* **1992**, *9*, 447–479; (b) Koskinen, A. M. P.; Karisalmi, K. *Chem. Soc. Rev.* **2005**, *34*, 677–690.
2. (a) Dutton, C. J.; Banks, B. J.; Cooper, C. B. *Nat. Prod. Rep.* **1995**, *12*, 165–181; (b) Kevin, D. A., II; Meujo, D. A. F.; Hamann, M. T. *Expert Opin. Drug Disc.* **2009**, *4*, 109–146.
3. Pressman, B. C. *Annu. Rev. Biochem.* **1976**, *45*, 501–530.
4. Hertweck, C. *Angew. Chem., Int. Ed.* **2009**, *48*, 4688–4716.
5. (a) Norcross, R. D.; Paterson, I. *Chem. Rev.* **1995**, *95*, 2041–2114; (b) Faul, M. M.; Huff, B. E. *Chem. Rev.* **2000**, *100*, 2407–2473.
6. Gupta, P. B.; Onder, T. T.; Jiang, G. Z.; Tao, K.; Kuperwasser, C.; Weinberg, R. A.; Lander, E. S. *Cell* **2009**, *138*, 645–659.
7. (a) Huczyński, A.; Stefanska, J.; Przybylski, P.; Brzezinski, B.; Bartl, F. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 2585–2589; (b) Huczyński, A. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 7002–7010; (c) Huczyński, A.; Janczak, J.; Antoszczak, M.; Wietrzyk, J.; Maj, E.; Brzezinski, B. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 7146–7150; (d) Łowicki, D.; Huczyński, A. *Biomed. Res. Int.* **2013**, *742149*, 1–14; (e) Huang, X. L.; Borgström, B.; Månsson, L.; Persson, L.; Oredsson, S.; Hegardt, C.; Strand, D. *ACS Chem. Biol.* **2014**, *9*, 1587–1594.
8. (a) Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc.* **1981**, *103*, 2127–2129; (b) Miyashita, M.; Hoshino, M.; Yoshikoshi, A. *J. Org. Chem.* **1991**, *56*, 6483–6485; (c) Lautens, M.; Chiu, P.; Ma, S. H.; Rovis, T. *J. Am. Chem. Soc.* **1995**, *117*, 532–533; (d) Yadav, J. S.; Rao, C. S.; Chandrasekhar, S.; Rao, A. V. R. *Tetrahedron Lett.* **1995**, *36*, 7717–7720; (e) Masse, C. E.; Panek, J. S. *Chem. Rev.* **1995**, *95*, 1293–1316; (f) Jain, N. F.; Takenaka, N.; Panek, J. S. *J. Am. Chem. Soc.* **1996**, *118*, 12475–12476; (g) Hanessian, S.; Gai, Y. H.; Wang, W. G. *Tetrahedron Lett.* **1996**, *37*, 7473–7476; (h) Marshall, J. A. *Chem. Rev.* **1996**, *96*, 31–47; (i) Marshall, J. A. *Chem. Rev.* **2000**, *100*, 3163–3185; (j) Arjona, O.; Menchaca, R.; Plumet, J. *J. Org. Chem.* **2001**, *66*, 2400–2413; (k) Cossy, J.; Blanchard, N.; Meyer, C. *Org. Lett.* **2001**, *3*, 2567–2569; (l) Cowden, C. J.; Paterson, I. Asymmetric Aldol Reactions Using Boron Enolates In. *Organic Reactions*; Paquette, L. A., Ed.; John Wiley & Sons, Inc.: New York, NY, 1997; Vol. 51, pp 1–200; (m) Lachance, H.; Hall, D. G. Allylboration of Carbonyl Compounds In. *Organic Reactions*; Denmark, S. E., Ed.; John Wiley & Sons, Inc.: New York, NY, 2008; Vol. 73, pp 1–574; (n) Hackman, B. M.; Lombardi, P. J.; Leighton, J. L. *Org. Lett.* **2004**, *6*, 4375–4377; (o) Ward, D. E. *Chem. Commun.* **2011**, 11375–11393; For a review of several methodologies, see: (p) Schetter, B.; Mahrwald, R. *Angew. Chem., Int. Ed.* **2006**, *45*, 7506–7525; (q) Li, J.; Menche, D. *Synthesis* **2009**, *14*, 2293–2315.
9. (a) Guindon, Y.; Houde, K.; Prévost, M.; Cardinal-David, B.; Landry, S. R.; Daoust, B.; Bencheqroun, M.; Guérin, B. *J. Am. Chem. Soc.* **2001**, *123*, 8496–8501 and references therein; (b) Guindon, Y.; Prévost, M.; Mochirian, P.; Guérin, B. *Org. Lett.* **2002**, *4*, 1019–1022; (c) Mochirian, P.; Cardinal-David, B.; Guérin, B.; Prévost, M.; Guindon, Y. *Tetrahedron Lett.* **2002**, *43*, 7067–7071; (d) Guindon, Y.; Brazeau, J.-F. *Org. Lett.* **2004**, *6*, 2599–2602.
10. Brazeau, J.-F.; Mochirian, P.; Prévost, M.; Guindon, Y. *J. Org. Chem.* **2009**, *74*, 64–74.
11. (a) Mochirian, P.; Godin, F.; Katsoulis, I.; Fontaine, I.; Brazeau, J.-F.; Guindon, Y. *J. Org. Chem.* **2011**, *76*, 7654–7676; For an alternative synthesis of **6**, see: (b) Godin, F.; Katsoulis, I.; Fiola-Masson, E.; Dhambri, S.; Mochirian, P.; Guindon, Y. *Synthesis* **2012**, *44*, 474–488.
12. (a) Godin, F.; Prévost, M.; Gorelsky, S. I.; Mochirian, P.; Nguyen, M.; Viens, F.; Guindon, Y. *Chem.—Eur. J.* **2013**, *19*, 9308–9318; (b) Godin, F.; Duplessis, M.; Buonomano, C.; Trinh, T.; Houde, K.; Chapdelaine, D.; Rodrigue, J.; Boutros, A.; Guindon, Y. *Org. Chem. Front.* **2014**, *1*, 974–982.

13. (a) Brooks, H. A.; Gardner, D.; Poyser, J. P.; King, T. J. *J. Antibiot.* **1984**, *37*, 1501–1504; (b) Gräfe, U.; Schade, W.; Roth, M.; Radics, L.; Incze, M.; Ujszaszy, K. *J. Antibiot.* **1984**, *37*, 836–846.
14. (a) Graefe, U. *Germany Patent DD231* **1986**, *793* (A1); (b) Tonew, E.; Tonew, M.; Graefe, U.; Zopel, P. *Pharmazie* **1988**, *43*, 717–719.
15. (a) Mulzer, J.; Schollhorn, B. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1476–1478; (b) Cywin, C. L.; Kallmerten, J. *Tetrahedron Lett.* **1993**, *34*, 1103–1106; (c) Booysen, J. F.; Holzapfel, C. W. *Synth. Commun.* **1995**, *25*, 1473–1488; (d) Chemler, S. R.; Roush, W. R. *J. Org. Chem.* **1998**, *63*, 3800–3801; (e) Marshall, J. A.; Palovich, M. R. *J. Org. Chem.* **1998**, *63*, 3701–3705; (f) Guindon, Y.; Murtagh, L.; Caron, V.; Landry, S. R.; Jung, G.; Bencheqroun, M.; Faucher, A.-M.; Guérin, B. *J. Org. Chem.* **2001**, *66*, 5427–5437; (g) Song, Z. L.; Hsung, R. P.; Lu, T.; Lohse, A. G. *J. Org. Chem.* **2007**, *72*, 9722–9731; (h) Sabitha, G.; Srinivas, R.; Yadav, J. S. *Synthesis* **2011**, *9*, 1484–1488; (i) Cooksey, J. P. *Org. Biomol. Chem.* **2013**, *11*, 5117–5126.
16. (a) Danishefsky, S. J.; Selnick, H. G.; Zelle, R. E.; Deninno, M. P. *J. Am. Chem. Soc.* **1988**, *110*, 4368–4378; (b) Defosseux, M.; Blanchard, N.; Meyer, C.; Cossy, J. *J. Org. Chem.* **2004**, *69*, 4626–4647; (c) Komatsu, K.; Tanino, K.; Miyashita, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 4341–4345; (d) Harrison, T. J.; Ho, S.; Leighton, J. L. *J. Am. Chem. Soc.* **2011**, *133*, 7308–7311; For a review, see: (e) Song, Z. L.; Lohse, A. G.; Hsung, R. P. *Nat. Prod. Rep.* **2009**, *26*, 560–571.
17. (a) Baudin, J. B.; Hareau, G.; Julia, S. A.; Ruel, O. *Tetrahedron Lett.* **1991**, *32*, 1175–1178; (b) Blakemore, P. R.; Cole, W. J.; Kocieński, P. J.; Morley, A. *Synlett* **1998**, 26–28; For a review, see: (c) Blakemore, P. R. *J. Chem. Soc., Perkin Trans. 1* **2002**, *23*, 2563–2585.
18. Evans, D. A.; Tedrow, J. S.; Shaw, J. T.; Downey, C. W. *J. Am. Chem. Soc.* **2002**, *124*, 392–393.
19. Numbering of atoms throughout article was attributed according to that of zincophorin **1a**.
20. (a) Evans, D. A.; Dart, M. J.; Duffy, J. L.; Yang, M. G.; Livingston, A. B. *J. Am. Chem. Soc.* **1995**, *117*, 6619–6620; (b) Evans, D. A.; Dart, M. J.; Duffy, J. L.; Yang, M. G. *J. Am. Chem. Soc.* **1996**, *118*, 4322–4343.
21. Pattenden, G.; Gonzalez, M. A.; Little, P. B.; Millan, D. S.; Plowright, A. T.; Tornos, J. A.; Ye, T. *Org. Biomol. Chem.* **2003**, *1*, 4173–4208.
22. See Supplementary data for proof-of-structure details.
23. (a) Cardinal-David, B.; Guérin, B.; Guindon, Y. *J. Org. Chem.* **2005**, *70*, 776–784; (b) Cardinal-David, B.; Brazeau, J.-F.; Katsoulis, I. A.; Guindon, Y. *Curr. Org. Chem.* **2006**, *10*, 1939–1961.
24. A mixture (~3:1) of C2-phenylselenides **31a-1** and **31a-2** was isolated. See Experimental section for details.
25. For a review of the methodologies, see: Romea, P.; Urpí, F. Stereoselective Acetate Aldol Reactions In *Modern Methods in Stereoselective Aldol Reactions*; Mahrwald, R., Ed.; Wiley-VCH Verlag GmbH & Co.: Weinheim, Germany, 2013; pp 1–81.
26. Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277–7287.
27. Jeyakumar, K.; Chakravarthy, R. D.; Chand, D. K. *Catal. Commun.* **2009**, *10*, 1948–1951.
28. Lister, T.; Perkins, M. V. *Aust. J. Chem.* **2004**, *57*, 787–797.
29. Bradley, D.; Williams, G.; Lawton, M. *J. Org. Chem.* **2010**, *75*, 8351–8354.
30. Kaburagi, Y.; Kishi, Y. *Org. Lett.* **2007**, *9*, 723–726.