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Studies directed towards the total synthesis of polyether antibiotic ionomycin: asymmetric synthesis of fragments C(24)–C(32) and C(1)–C(23)

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ABSTRACT

A convergent and stereoselective approach for the synthesis of C1–C23 and C24–C32 segments of polyether antibiotic, ionomycin has been achieved. The key steps involved in this approach are the elaboration of two advanced fragments from a common precursor using enzymatic desymmetrization to create two methyl chiral centers, desymmetrization of the bicyclic olefin to introduce two methyl and two hydroxyl chiral centers, the use of Evans auxiliary to introduce another methyl group and the creation of four chiral centers in *bis*-tetrahydrofuran ring by Sharpless asymmetric epoxidation and the regioselective opening of epoxide with methyl sulphone. The coupling of C11–C16 with C17–C23 was achieved through a Julia-Kocienski olefination and directed Aldol reaction. Oxidation of C9 alcohol facilitates the coupling of C10–C23 with C1–C9.

1. Introduction

Ionomycin (**1**, Fig. 1) is one of the important polyether antibiotics, which was isolated by Meyers and co-workers from fermentation broths of *Streptomyces congoblatus* in 1978.[1] It has the ability to chelate various inorganic cations so as to transport them across lipid membranes. Ionomycin has a unique feature that distinguishes it from all other ionophores. In particular, it chelates slectively with calcium (and other divalent) ions as a *dibasic acid* in an octahedral coordination array,[2] while other ionophores exhibit their chelating property as monobasic acids.

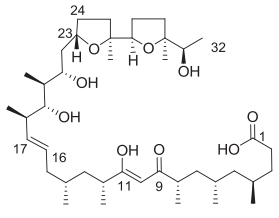

Fig. 1. Chemical structure of ionomycin (**1**).

The X-ray structure and absolute stereochemistry of calcium and cadmium complexes of ionomycin were established by Gougoutas and co-workers in 1979.[3] The main structural feature of this ionophore includes the presence of substituted bis-tetrahydrofuran ring, 14 stereogenic centers and a β-dicarbonyl moiety, which is rare in these natural products. The presence of β-dicarbonyl moiety is responsible for ionomycin's intense ultraviolet absorption at 280 nm and also provides two of the six metal ligation points. Because of its broad range of therapeutic potentials and unique structural features, ionomycin has attracted the attention of many synthetic organic chemists.

A few total syntheses[4–7] and many formal synthetic approaches[8] have been reported in the literature. The retrosynthesis of all the previously published total syntheses of ionomycin employs similar strategies. Hanessian et al.[4] and Evans[5] et al. reported the identical disconnections for the construction of ionomycin backbone but used different strategies for the synthesis of polypropionate and deoxypolypropionate fragments. Hanessian et al. used the chiron approach using L-glutamic acid and Evans et al. reported convergent asymmetric synthesis of ionomycin using chiral enolate chemistry. Lautens[6] applied ring opening strategy for the synthesis of polypropionate and deoxypolypropionate subunits, while *Trans*-tetrahydrofuran motif was prepared via Sharpless asymmetric epoxidation and $VO(acac)_2$ catalyzed epoxidation protocol. Recently, Kocienski et al.[7] reported the total synthesis of

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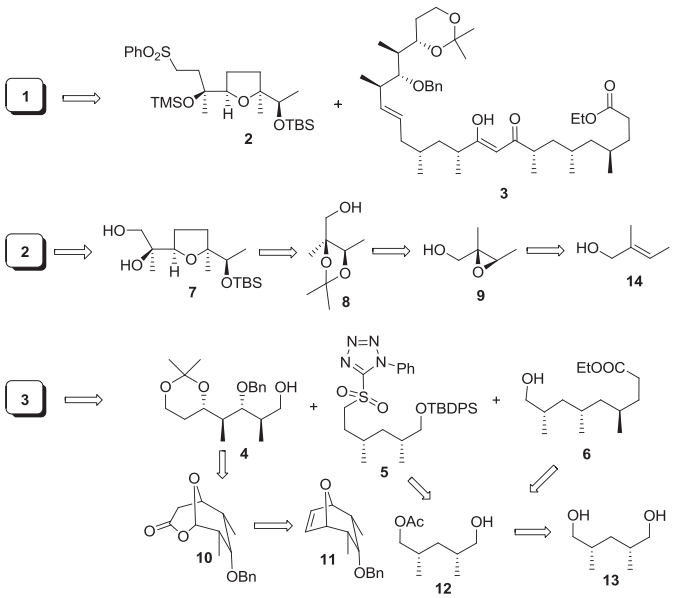
ionomycin using gold(III)-catalyzed cycloisomerization of α-hydroxyallene and rhodium-catalyzed rearrangement reaction to generate the β-diketone moiety.

Following our interest in the total synthesis of biologically active natural products by desymmetrization strategy[9,10] and inspiring biological activity combined with fascinating structural features of ionomycin (**1**), we herein report a convergent stereoselective method for the synthesis of C24–C32 (**2**) and C1–C23 (**3**) fragments of ionomycin. This method involves Sharpless asymmetric epoxidation to generate tetrahydrofuran ring, desymmetrization strategy, Evans alkylation, Julia-Kocienski olefination and directed Aldol reaction.

Retrosynthetically, ionomycin **1** (Scheme 1) can be synthesized from four key fragments, **6** (C1–C9), **5** (C11–C16), **4** (C17–C23) and **2** (C24–C32), which is similar to Lautens approach.[6] *Trans*-Tetrahydrofuran **2** was proposed to be synthesized via the Sharpless epoxidation of a suitable allylic alcohol followed by regioselective ring opening of the epoxide.



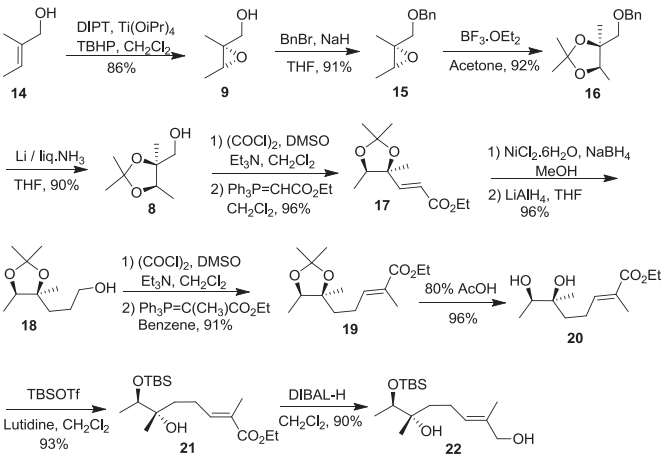
Scheme 1. Retrosynthetic analysis of C24–C32 (**2**) and C1–C23 (**3**) segments of ionomycin (**1**).

Polypropionate fragment (**4**) can be obtained through desymmetrization of bicyclic olefin developed previously by us.[9] Deoxypolypropionate segment can be achieved through a common precursor **12**, which in turn can be synthesized by desymmetrization of *meso*-diol[9k,10] and Evan's asymmetric alkylation. The three fragments could be connected through a modified Julia olefination followed by base catalyzed directed Aldol reaction, while fragment (**2**) can be coupled with fragment **4** via sulphone addition to aldehyde corresponding to alcohol fragment (**4**) to finish the total synthesis.

2. Results and discussion

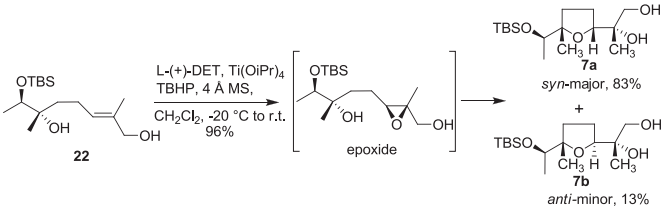
2.1. Stereoselective synthesis of C24–C32 furanoid fragment of ionomycin (2)

Accordingly, the synthesis of C24–C32 fragment (**2**) began from the readily available starting material tiglic acid. The requisite allylic alcohol **14** was prepared from tiglic acid by esterification[11] followed by reduction of the ethyl tiglate.[12] Sharpless asymmetric epoxidation of allylic alcohol **14** using D-DIPT, Ti(O*i*Pr)$_4$ and TBHP in dry CH_2Cl_2 afforded the epoxy alcohol **9** in 86% yield with 92% *ee*. The analytical data of **9** was found to be identical with the data reported in literature.[13] The free hydroxy group of **9** was protected as its benzyl ether (**15**). Stereoselective ring opening of the epoxide (**15**) with acetone in the presence of $BF_3{\cdot}OEt_2$ at 0 °C afforded the pure acetonide **16** in 92% yield.[9e,14] Debenzylation of **16** under the Birch conditions[15] using liquid ammonia and lithium metal afforded the primary alcohol **8** in 90% yield as a colorless liquid. Swern oxidation of the primary alcohol **8** followed by C_2-Wittig reaction afforded the α,β-unsaturated ester **17** in 96% yield over two steps. Reduction of double bond of the ester **17** with $NaBH_4$ and $NiCl_2.6H_2O$ in MeOH[16] afforded the saturated ester, which was further reduced with $LiAlH_4$ in THF to give the saturated alcohol **18** in 96% yield in two steps. Swern oxidation of **18** followed by a two carbon Wittig reaction resulted in the formation of α,β-unsaturated ester **19** (exclusively *E*-isomer) in 91% yield over two steps. Cleavage of the isopropylidene acetal **19** with 80% aqueous acetic acid afforded the diol **20** in 96% yield. Selective silyl protection of the secondary alcohol of **20** with TBSOTf and 2,6-lutidine in CH_2Cl_2 at 0 °C afforded the silyl ester **21** in 93% yield. Reduction of the ester **21** with DIBAL-*H* furnished the primary allylic alcohol **22** in 90% yield (Scheme 2).



Scheme 2. Synthesis of precursor **22** for key intermediate **7a**.

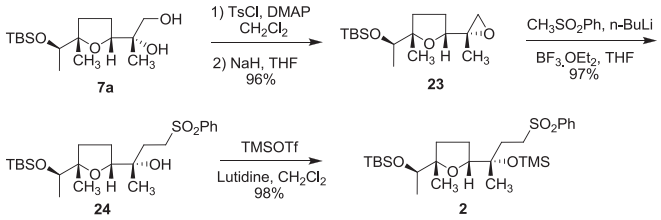
The tetrahydrofuran moiety **7** was achieved by Sharpless asymmetric epoxidation protocol[17,18] using 1 equiv of L-DET, 1 equiv of Ti(O*i*Pr)$_4$ and 2.2 equiv of TBHP in CH_2Cl_2 at −20 °C to room temperature. The corresponding product was obtained as a mixture of *syn*-diol (major **7a**, 83% yield) along with a minor *anti*-diol (**7b**, 13% yield, Scheme 3). The formation of **7a** and **7b** could be explained by intramolecular stereoselective ring opening of the epoxide with hydroxyl function catalyzed by Ti(O*i*Pr)$_4$. Both products were easily separated by column chromatography and well characterized by NMR spectrum.



Scheme 3. Synthesis of key intermediate **7a**.

Selective sulfonylation of 1,2-diol[19] followed by treatment with NaH afforded the terminal epoxide **23** in 96% yield over two steps (Scheme 4). Regioselective opening of terminal epoxide **23** with

phenylmethyl sulphone anion in the presence of $BF_3 \cdot OEt_2$ afforded the alcohol **24** in 97% yield.[18,20]

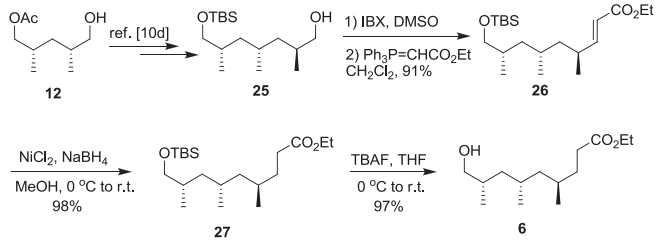


Scheme 4. Synthesis of C24–C32 furanoid fragment of ionomycin (**2**).

TMS protection of *tert*-alcohol with TMSOTf afforded the furanoid fragment (**2**, 98% yield) of ionomycin in 18 steps from tiglic alcohol in 33% yield. Analytical data of fragment **2** was found to be identical with the data reported by Lautens et al.[6]

2.2. Facile stereoselective synthesis of C1–C9 fragment (6)

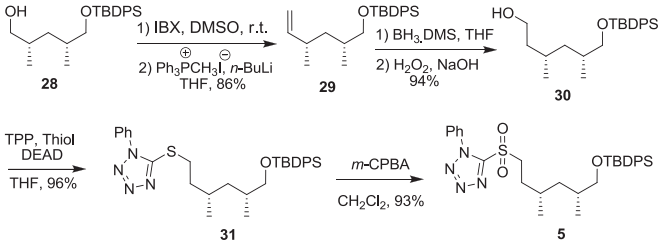
Synthesis of C1–C9 fragment **6** started from compound **25**. The synthesis of **25** was reported earlier by enzymatic desymmetrization of *meso*-diol.[10d] Alcohol **25** was subjected to oxidation followed by C_2-Wittig reaction to afford the α,β-unsaturated ester **26** in 91% for two steps. Further reduction of double bond with $NaBH_4$ and $NiCl_2.6H_2O$ in MeOH afforded the saturated ester **27** in 98% yield. Deprotection of TBS group with TBAF in THF afforded the alcohol **6** in 97% yield (Scheme 5).



Scheme 5. Synthesis of C1–C9 fragment (**6**).

2.3. Synthesis of C11–C16 fragment (5)

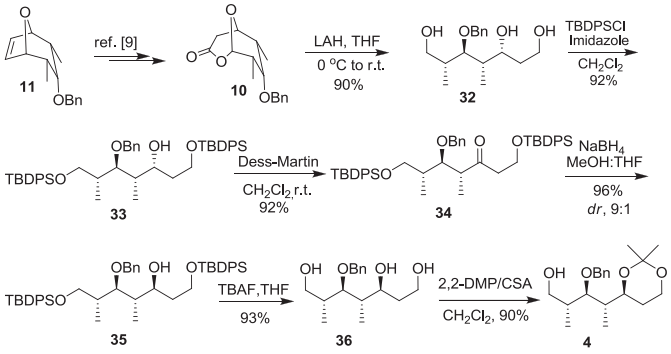
Synthesis of C11–C16 fragment began with alcohol **28**, which was synthesized from mono acetate **12**.[10] Alcohol (**28**) was subjected to IBX oxidation followed by one-carbon homologation through Wittig reaction afforded the terminal olefin **29** in 86% yield over two steps. Compound **29** was then subjected to hydroboration using $BH_3 \cdot SMe_2$ in THF followed by oxidation with alkaline H_2O_2 to furnish the primary alcohol **30** in 94% yield.[21] Alcohol **30** was converted into the sulfide **31** in 96% yield[6] under Mitsunobu conditions with thiol, (1-phenyl-1*H*-1,2,3,4-tetraazol-5-ylhydrosulfide) and a subsequent oxidation of the resulting thioester **31** with *m*-CPBA afforded the sulfone fragment **5** in 93% yield (Scheme 6).



Scheme 6. Synthesis of C11–C16 fragment (**5**).

2.4. Synthesis of C17–C23 fragment (4)

Synthesis of C17–C23 fragment **4** began with the reductive cleavage of the bicyclic lactone **10**. The key intermediate **10** was synthesized by desymmetrization of the bicyclic olefin **11**.[9] Thus treatment of **10** with $LiAlH_4$ in dry THF afforded the triol **32** in 90% yield. Selective protection of the primary alcohols with TBDPSCl and imidazole in CH_2Cl_2 afforded the di-TBDPS **33** in 92% yield (Scheme 7).



Scheme 7. Synthesis of C17–C23 fragment (**4**).

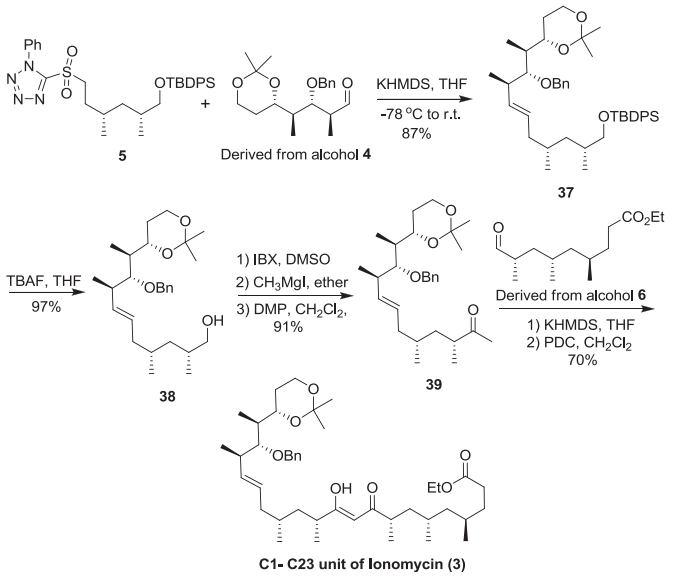
Conversion of **33** into **4** requires the inversion of configuration of the hydroxyl group at C5. As reported earlier by our group, the inversion of configuration of the hydroxyl group at C-5 of the intermediate **33** was failed employing the Mitsunobu protocol to give the required stereochemistry at C-21 of ionomycn. Therefore, we explored an alternative strategy, i.e., oxidation-reduction strategy.[9b] Accordingly, oxidation of the secondary alcohol **33** with Dess-Martin periodinane in CH_2Cl_2 afforded the corresponding ketone **34** in 92% yield. Substrate controlled reduction of the keto group of **34** with $NaBH_4$ in MeOH:THF (4:1) gave the required β-isomer **35** as a major product in 96% yield (**35**:**33**=9:1). Both isomers were separated by column chromatography and the undesired isomer **33** was again converted back to ketone **34**. The structure of major isomer **35** was confirmed by ^1H NMR spectrum in which the C5–H of **35** appeared in upfield (δ 3.94) relative to C5–H of **33** (δ 4.23) indicating an *anti* relationship between the methyl group at C-4 and OH group at C-5. Deprotection of TBDPS ether with TBAF in THF afforded the triol **36** in 93% yield. Finally, the required fragment **4** was prepared in 90% yield by treatment of triol **36** with 2,2-dimethoxypropane in the presence of a catalytic amount of camphor sulphonic acid in CH_2Cl_2 (Scheme 7).

2.5. Coupling of C1–C9 (6), C11–C16 (5) and C17–C23 (4) fragments: stereoselective synthesis of C1–C23 unit of ionomycin (3)

After successful completion of the synthesis of polypropionate fragments **6** (C1–C9), **5** (C11–C16) and **4** (C17–C23), we focused on the synthesis of C1–C23 unit of ionomycin by the coupling of fragment **5** with fragment **4** employing Julia-Kocienski olefination[22] followed by the coupling of fragment **6** by base catalyzed directed Aldol reaction.[23]

Oxidation of alcohol **4** with IBX in DMSO afforded the corresponding aldehyde, which was then subjected to Julia-Kocienski olefination with sulphone **5** using KHMDS in dry THF to give the *trans*-olefin **37** in 87% yield. The *trans*-stereochemistry of the olefin **37** was determined by its coupling constant (J=15.8 Hz). TBDPS group of **37** was selectively deprotected with TBAF to yield the alcohol **38** in 97% yield. Oxidation of the alcohol **38** to the corresponding aldehyde followed by treatment with CH_3MgI in ether at

−78 °C afforded the secondary alcohol, which was again transformed into the ketone **39** using Dess-Martin periodinane in 91% yield over three steps (Scheme 8).



Scheme 8. Synthesis of C1−C23 unit of ionomycin (**3**).

Next we attempted the coupling of ketone **39** with aldehyde derived from the alcohol **6**. Accordingly, directed Aldol reaction between ketone **39** and the aldehyde (derived from alcohol **6**) using KHMDS in THF at −78 °C gave the mixture of isomeric β-hydroxyl ketone in good yield, which was then converted into 1,3-diketone **3** (C1−C23 unit of ionomycin) using PDC on Celite[24] in 70% yield over two steps.

In summary, a concise, stereoselective and highly convergent synthetic approach has been developed for the synthesis of furanoid fragment (C24−C32) and C1−C23 unit of ionomycin. The strategy involves mainly the Sharpless asymmetric epoxidation and diastereoselective ring opening of the epoxide to construct the C24−C32 furanoid fragment, desymmetrization strategy to construct the polypropionate subunit, enzymatic desymmetrization of *meso*-diol for the deoxypolypropionate subunit, Julia-Kocienski olefination and directed Aldol reaction as key steps.

3. Experimental section

3.1. General

All reactions were carried out under inert atmosphere of argon or nitrogen using standard syringe, septa, and cannula techniques unless otherwise mentioned. Commercial reagents were used without further purification. All solvents were purified by standard techniques. Infrared (**IR**) spectra were recorded on a Perkin−Elmer 683 spectrometer using **NaCl** optics. Spectra were calibrated against the polystyrene absorption at 1610 cm^{-1}. Samples were scanned neat, in **KBr** wafers or in chloroform as a thin film. **^{1}H NMR** spectra were recorded in **$CDCl_3$** on Bruker 300, Varian Unity 500 **NMR** spectrometer. **^{13}C NMR** spectra were recorded at 75 **MHz** in **$CDCl_3$** using tetramethylsilane as a reference standard. Chemical shifts are in parts per million downfield from tetramethylsilane and coupling constants (*J*) are reported in hertz (Hertz). The following abbreviations are used to designate signal multiplicity: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad. Column chromatography was performed using silica gel (60−120 mesh) and the column was usually eluted with a mixture of ethyl acetate−petroleum ether. Visualization of the spots on **TLC** plates was achieved either by exposure to iodine vapor or **UV** light or by dipping the plates to ethanolic anisaldehyde-sulphuric acid-acetic acid or to phosphomolybdic acid-sulphuric acid solution and heating the plates at 120 °C. Mass spectra were obtained on a Finnigan **MAT1020B** or micromass **VG 70−70H** spectrometer operating at 70 **eV** using a direct inlet system. Optical rotations were recorded on PerkinElmer 241 polarimeter in 1.0 dm, 1.0 mL cells.

3.2. (*E*)-2-Methyl-2-buten-1-ol (14)

To a stirred suspension of LAH (8.5 g, 0.225 mol) in dry ether (500 mL) at 0 °C was added $AlCl_3$ (9.9 g, 0.075 mol) portion wise in the time interval of 30 min, After complete addition, the suspension was allowed to stir for another 30 min at 0 °C during, which the alane was formed. To this grey suspension at 0 °C was added a solution of ethyl tiglate (24 g, 0.187 mol) in ether (100 mL) dropwise. The mixture was allowed to stir for 1 h and then quenched with Na_2SO_4 at 0 °C and the mixture was stirred overnight. The solid was filtered through a pad of Celite and washed with ether (5×100 mL). The filtrate was then subjected to distillation using short path condenser to furnish the pure allylic alcohol **14** (13.0 g, 81%) at 140 °C at atmospheric pressure; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.45 (q, *J*=6.6, 13.2 Hz, 1H, olefinic), 3.95 (s, 2H, CH_2OH), 1.66 (s, 3H, CCH_3), 1.62 (d, *J*=6.7 Hz, 3H, $CHCH_3$), 1.32−1.43 (br s, 1H, OH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 135.2, 120.2, 68.5, 13.1, 12.9.

3.3. [(2*R*,3*R*)-2,3-Dimethyloxiran-2-yl]methanol (9)

To a 500 mL two neck round bottom flask equipped with a magnetic bar and a septum with N_2 inlet was weighed 8.5 g of 4 Å molecular sieves (dry powder). To this dry CH_2Cl_2 (200 mL) was added and the solution was then cooled to −20 °C. To this suspension was added $Ti(OiPr)_4$ (2.9 mL, 9.8 mmol) followed by D-diisopropyl tartrate (2.41 mL, 11.3 mmol) and the mixture was stirred vigorously at −20 °C for 30 min. A solution of allyl alcohol **14** (6.5 g, 75.5 mmol) in 50 mL CH_2Cl_2 was added to the above mixture and stirred for another 30 min and then TBHP (30.2 mL, 0.15 mol, 5M solution in toluene) was added at −20 °C. The mixture was then set for stirring at the same temperature for another 7 h. The mixture was filtered and the residue was washed with CH_2Cl_2. The filtrate and the washings were quenched with water (50 mL) and then subjected to stirring for 30 min at −20 °C. Then a solution of 22 mL of 20% NaOH prepared from a saturated NaCl solution was added to the above reaction mixture and the stirring was continued at rt for 12 h. The organic layers were separated, dried over anhydrous Na_2SO_4 and concentrated by distillation at atmospheric temperature to afford the crude epoxy alcohol, which was later purified on 60−120 silica column using 20% EtOAc/hexane to yield the pure product **9** (6.6 g, 86% yield). R_f=0.35 (20% EtOAc/hexane); $[\alpha]_D^{25}$ +17.8 (*c* 1.0, $CHCl_3$); IR (neat): ν 3405, 2976, 2930, 1380, 1039 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.62 (d, *J*=11.4 Hz, 1H, OCH_AH_B), 3.50 (d, *J*=11.4 Hz, 1H, OCH_AH_B), 3.11 (q, *J*=5.2 Hz, 1H, $CHCH_3$), 1.85−1.93 (br s, 1H, OH), 1.31 (d, *J*=5.2 Hz, 3H, $CHCH_3$), 1.26 (s, 3H, CCH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 65.3, 61.0, 55.8, 13.7, 13.3.

3.4. (2*R*,3*R*)-2-[(Benzyloxy)methyl]-2,3-dimethyloxirane (15)

To a stirred suspension of NaH (3.85 g, 95.5 mmol) in dry THF (200 mL) at 0 °C was added the solution of epoxy alcohol **9** (6.5 g, 63.5 mmol) in dry THF (40 mL) dropwise. After complete addition, the suspension was allowed to stir for 30 min at room temperature and again cooled to 0 °C and then benzyl bromide (8.55 mL, 70.0 mmol), followed by a catalytic amount of TBAI were added. The mixture was allowed to stir for 8 h at room temperature. After completion of reaction as indicated by TLC, the reaction was quenched with saturated solution of NH_4Cl and the organic layer was

extracted with EtOAc (3×200 mL). The combined organic layers were dried over Na_2SO_4, concentrated under reduced pressure and purified by chromatography on silica gel (EtOAc/hexane, 10%) to yield the corresponding benzyl ether **15** (11.1 g, 91% yield) as a colorless liquid. R_f=0.50 (10% EtOAc/hexane); $[\alpha]_D^{25}$ +1.2 (*c* 1.0, $CHCl_3$); IR (Neat): ν 3030, 2929, 1453, 1097, 741 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.20–7.34 (m, 5H, ArH), 4.52 (ABq, *J*=12.0 Hz, 2H, OCH_2Ph), 3.41 (s, 2H, CH_2O), 2.91 (q, *J*=5.2Hz, 1H, $CHCH_3$), 1.30 (s, 3H, CCH_3), 1.29 (d, *J*=5.2 Hz, 3H, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.9, 128.2, 127.4, 74.5, 72.9, 59.5, 56.3, 14.0, 13.5; MS (ESI): *m/z* 215 $[M+Na]^+$; HRMS: calcd for $C_{12}H_{16}O_2Na$ $[M+Na]^+$ 215.1047, found: 215.1043.

3.5. (4*S*,5*R*)-4-[(Benzyloxy)methyl]-2,2,4,5-tetramethyl-1,3-dioxolane (16)

To a stirred solution of **15** (12.0 g, 62.5 mmol) in dry acetone (300 mL) at 0 °C was added $BF_3 \cdot Et_2O$ (17.1 mL, 62.5 mmol) dropwise and the reaction mixture was stirred at 0 °C for 1 h. After completion of the reaction, mixture was quenched with solid $NaHCO_3$ at 0 °C and the solvent was evaporated under reduced pressure and the residue was diluted with water and extracted with EtOAc (3×100 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification on silica gel column chromatography using 8% EtOAc/hexane afforded the compound **16** (14.3 g, 92% yield) as a pale yellow oil. R_f=0.15 (8% EtOAc/hexane); $[\alpha]_D^{25}$ −5.7 (*c* 1.2, $CHCl_3$); IR (neat): ν 2984, 2867, 1453, 1375, 1100 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.19–7.34 (m, 5H, ArH), 4.49 (s, 2H, OCH_2Ph), 3.89 (q, *J*=5.8 Hz, 1H, $CHCH_3$), 3.40 (d, *J*=9.7 Hz, 1H, OCH_AH_B), 3.18 (d, *J*=9.7 Hz, 1H, OCH_AH_B), 1.35 (s, 3H, CCH_3), 1.35 (s, 3H, CCH_3), 1.29 (s, 3H, CCH_3), 1.23 (d, *J*=6.8 Hz, 3H, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.1, 128.1, 127.3, 106.6, 81.1, 78.7, 73.1, 72.4, 28.2, 26.4, 21.4, 13.5.

3.6. [(4*S*,5*R*)-2,2,4,5-Tetramethyl-1,3-dioxolan-4-yl]methanol (8)

To a solution of compound **16** (14.0 g, 56.0 mmol) in THF (20 mL) in 250 mL 2-necked flask fitted with a septum and ammonia condenser and about 100 mL of ammonia was collected in the flask. To this clear solution at −33 °C was added lithium metal (0.784 g, 112 mmol) portion wise. After appearance of deep blue color, the reaction mixture was stirred at the same temperature for 30 min. After completion of the reaction as confirmed by TLC, the mixture was quenched with solid NH_4Cl till the blue color disappeared and the ammonia was allowed to evaporate at room temperature. The mixture was then extracted with ether (5×100 mL) and the combined organic layers were dried, concentrated under reduced pressure and then purified by chromatography on silica gel using 15% EtOAc/hexane to furnish the pure product **8** (8.0 g, 90% yield). R_f=0.25 (15% EtOAc/hexane); $[\alpha]_D^{25}$ −11.8 (*c* 1.1, $CHCl_3$); IR (neat): ν 3467, 2985, 2635, 1376, 1217, 1105, 1054, 997 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.92 (q, *J*=6.6Hz, 1H, $CHCH_3$), 3.49 (d, *J*=10.7 Hz, 1H, CH_AH_B), 3.25 (t, *J*=10.7 Hz, 1H, CH_AH_B), 1.68–1.78 (br s, 1H, OH), 1.42 (s, 3H, CCH_3), 1.36 (s, 3H, CCH_3), 1.24 (s, 3H, CCH_3), 1.22 (d, *J*=6.6 Hz, 3H, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 107.3, 81.9, 78.3, 64.9, 28.2, 26.3, 20.6, 12.7.

3.7. Ethyl (*E*)-3-[(4*S*,5*R*)-2,2,4,5-tetramethyl-1,3-dioxolan-4-yl]-2-propenoate (17)

To a solution of oxalyl chloride (6.35 mL, 75 mmol) in CH_2Cl_2 (150 mL) at −78 °C was added dimethylsulfoxide (7.6 mL, 97.5 mmol) over 20 min. The resulting mixture was stirred for another 30 min and then a solution of alcohol **8** (8.0 g, 50 mmol) in CH_2Cl_2 (40 mL) was added drop wise. The mixture was stirred for 30 min and triethylamine (42.5 mL, 300 mmol) was added dropwise. The mixture was allowed to warm to room temperature and stirred for 30 min. To the above aldehyde was added (ethoxycarbonylmethylene)triphenylphosphorane (26.1 g, 75 mmol) and the resulting mixture was stirred for 12 h at room temperature and then quenched with water and extracted with CH_2Cl_2 (3×100 mL). The combined organic layers were washed with water, brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel column chromatography using 10% EtOAc/hexane to furnish the pure **17** (10.9 g, 96% yield). R_f=0.15 (10% EtOAc/hexane); $[\alpha]_D^{25}$ +1.5 (*c* 1.2, $CHCl_3$); IR (neat): ν 2984, 2936, 1720, 1374, 1293, 1165, 993 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 6.79 (d, *J*=15.4 Hz, 1H, olefinic), 6.01 (d, *J*=15.4 Hz, 1H, olefinic), 4.18 (q, *J*=7.1 Hz, 2H, CH_2CH_3), 4.01 (q, *J*=6.4Hz, 1H, $CHCH_3$), 1.48 (s, 3H, CCH_3), 1.38 (s, 3H, CCH_3), 1.35 (s, 3H, CCH_3), 1.30 (t, *J*=7.1 Hz, 3H, CH_2CH_3), 1.21 (d, *J*=6.4 Hz, 3H, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.2, 148.8, 121.0, 107.9, 82.0, 79.9, 60.3, 27.9, 26.3, 23.8, 14.9, 14.1; MS (ESI): *m/z* 251 $[M+Na]^+$; HRMS: calcd for $C_{12}H_{20}O_4Na$ $[M+Na]^+$ 251.1259, found: 251.1266.

3.8. 3-[(4*S*,5*R*)-2,2,4,5-Tetramethyl-1,3-dioxolan-4-yl]-1-propanol (18)

To a cooled (0 °C) solution of **17** (10.5 g, 46.4 mmol) and $NiCl_2.6H_2O$ (2.19 g, 9.2 mmol) in MeOH (200 mL), was added $NaBH_4$ (4.15 g, 110.5 mmol) in small portions. During the addition of $NaBH_4$, the reaction temperature was maintained at 0 °C. After complete addition of $NaBH_4$, the mixture was stirred for 1 h at room temperature and the resulting black precipitate was filtered and then washed with MeOH. The solvent was removed under reduced pressure and then diluted with water (100 mL) and extracted with EtOAc (3×200 mL). The combined organic layers were washed with water, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford the ester.

To a stirred suspension of LAH (3.49 g, 92 mmol) in dry THF (200 mL) at 0 °C was added the above solution of ester in THF (50 mL) drop wise and the reaction mixture was allowed to stir for 30 min at 0 °C. After completion as indicated by TLC, the reaction was quenched with Na_2SO_4 at 0 °C and the mixture was stirred overnight. The solid was filtered through pad of Celite and washed with EtOAc (3×200 mL). The combined organic layers were dried over Na_2SO_4 and concentrated and purified by chromatography on silica gel (EtOAc/hexane, 30%) to yield the corresponding alcohol **18** (8.3 g, 96% yield) as a colorless liquid. R_f=0.25 (30% EtOAc/hexane); $[\alpha]_D^{25}$ −10.4 (*c* 0.65, $CHCl_3$); IR (Neat): ν 3456, 2934, 1374, 1247, 850 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.87 (q, *J*=6.4Hz, 1H, $CHCH_3$), 3.67–3.64 (m, 1H, OH), 3.62 (t, *J*=5.2 Hz, 2H, CH_2OH), 1.51–1.88 (m, 3H, $CH_AH_BCH_2$), 1.40 (s, 3H, CCH_3), 1.33 (s, 3H, CCH_3), 1.23–1.32 (m, 1H, CH_AH_B), 1.20 (s, 3H, CCH_3), 1.18 (d, *J*=6.6 Hz, 3H, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 106.6, 81.7, 79.8, 63.2, 31.2, 28.2, 26.7, 22.4, 13.5; MS (ESI): *m/z* 211 $[M+Na]^+$; HRMS: calcd for $C_{10}H_{20}O_3Na$ $[M+Na]^+$ 211.1310, found: 211.1319.

3.9. Ethyl (*E*)-2-methyl-5-[(4*S*,5*R*)-2,2,4,5-tetramethyl-1,3-dioxolan-4-yl]-2-pentenoate (19)

To a solution of oxalyl chloride (5.4 mL, 63.8 mmol) in CH_2Cl_2 (150 mL) at −78 °C was added dimethylsulfoxide (6.5 mL, 83 mmol) over 20 min. The resulting mixture was stirred for another 30 min and then a solution of alcohol **18** (8.0 g, 42.5 mmol) in CH_2Cl_2 (40 mL) was added dropwise. The mixture was stirred for 1 h and then triethylamine (35.8 mL, 255 mmol) was added dropwise. The reaction mixture was allowed to warm to room temperature and stirred for 30 min. After completion, the mixture was quenched with water (200 mL) and the aqueous phase was extracted with CH_2Cl_2 (2×200 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to get crude aldehyde.

To the above aldehyde in benzene (200 mL) was added ethyl 2-(triphenylphosphoranylidene)propanoate (23.1 g, 63.8 mmol) and the mixture was heated under reflux for 24 h. After completion, benzene was removed and the crude product was purified by silica gel column chromatography using 10% EtOAc/hexane to afford the pure unsaturated ester **19** (10.45 g, 91% yield). R_f=0.35 (10% EtOAc/hexane); $[\alpha]_D^{25}$ −4.5 (*c* 1.05, $CHCl_3$); IR (neat): *ν* 2983, 2935, 1711, 1373, 1259, 1216, 1109, 997, 519 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): *δ* 6.69 (t, *J*=8.3 Hz, 1H, olefinic), 4.13 (q, *J*=7.5Hz, 2H, CH_2CH_3), 3.84 (q, *J*=6.7Hz, 1H, $CHCH_3$), 2.28–2.47 (m, 1H, CH_AH_B), 2.10–2.28 (m, 1H, CH_AH_B), 1.84 (s, 3H, CCH_3), 1.55–1.70 (m, 1H, CH_AH_B), 1.38 (s, 3H, CCH_3), 1.33 (s, 3H, CCH_3), 1.30 (t, *J*=7.5 Hz, 3H, CH_2CH_3), 1.21 (m, 1H, CH_AH_B), 1.20 (s, 3H, CCH_3), 1.18 (d, *J*=6.0 Hz, 3H, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): *δ* 168.0, 142.2, 127.7, 106.6, 81.4, 79.7, 60.2, 33.3, 28.2, 26.7, 22.6, 22.3, 14.1, 13.3, 12.1.

3.10. Ethyl (*E*,6*S*,7*R*)-6,7-dihydroxy-2,6-dimethyl-2-octenoate (20)

Acetic acid (80%, 50 mL) was added to **19** (10.0 g, 37.0 mmol) at room temperature and reaction mixture was stirred for 12 h. The reaction mixture was quenched with saturated $NaHCO_3$ and the aqueous layer was extracted with EtOAc (5×150 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure and the residue was purified by column chromatography using 30% EtOAc/hexane to afford the pure diol **20** (8.1 g, 96% yield). R_f=0.17 (30% EtOAc/hexane); $[\alpha]_D^{25}$ +0.5 (*c* 1.05, $CHCl_3$); IR (neat): *ν* 3428, 2980, 1706, 1274, 1094 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): *δ* 6.73 (t, *J*=7.5 Hz, 1H, olefinic), 4.15 (q, *J*=6.7Hz, 2H, CH_2CH_3), 3.59 (q, *J*=6.7Hz, 1H, $CHCH_3$), 2.17–2.43 (m, 2H, CH_2), 2.16 (br s, 1H, OH), 2.04 (br s, 1H, OH), 1.84 (s, 3H, CCH_3), 1.60–1.76 (m, 1H, CH_AH_B), 1.38–1.47 (m, 1H, CH_AH_B), 1.30 (t, *J*=6.7 Hz, 3H, CH_2CH_3), 1.17 (s, 3H, CCH_3), 1.15 (d, *J*=6.0, 3H, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): *δ* 168.2, 142.3, 127.6, 74.2, 74.3, 60.4, 33.0, 23.0, 22.7, 17.3, 14.1, 12.2; MS (ESI): *m*/*z* 253 $[M+Na]^+$; HRMS: calcd for $C_{12}H_{22}O_4Na$ $[M+Na]^+$ 253.1415, found: 253.1411.

3.11. Ethyl (*E*,6*S*,7*R*)-7-[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy-6-hydroxy-2,6-dimethyl-2-octenoate (21)

tert-Butyldimethylsilyltrifluoromethane sulfonate (TBSOTf, 5.4 mL, 23.9 mmol) was added drop wise to a cooled solution (0 °C) of diol **20** (5.0 g, 21.7 mmol) and 2,6-lutidine (5.0 mL, 43.4 mmol) in dry CH_2Cl_2 (100 mL). After 10 min, the reaction mixture was diluted with CH_2Cl_2 (50 mL) and quenched with water and extracted with CH_2Cl_2 (2×50 mL). The organic layer was dried over Na_2SO_4, concentrated in vacuo and the residue was purified by column chromatography using 10% EtOAc/hexane to afford the pure compound **21** (6.9 g, 93% yield). R_f=0.22 (10% EtOAc/hexane); $[\alpha]_D^{25}$ −5.0 (*c* 1.15, $CHCl_3$); IR (neat): *ν* 2955, 2933, 2858, 1709, 1254, 1099, 834 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): *δ* 6.71 (t, *J*=5.9 Hz, 1H, olefinic), 4.16 (q, *J*=6.9Hz, 2H, CH_2CH_3), 3.61 (q, *J*=6.9Hz, 1H, $CHCH_3$), 2.29–2.40 (m, 1H, CH_AH_B), 2.13–2.24 (m, 1H, CH_AH_B), 2.20 (br s, 1H, OH), 1.84 (s, 3H, CCH_3), 1.58–1.67 (m, 1H, CH_AH_B), 1.36–1.45 (m, 1H, CH_AH_B), 1.30 (t, *J*=6.9 Hz, 3H, CH_2CH_3), 1.11 (d, *J*=5.9 Hz, 3H, $CHCH_3$), 1.10 (s, 3H, CCH_3), 0.91 (s, 9H, $(CH_3)_3C$), 0.09 (s, 6H, $(CH_3)_2Si$); ^{13}C NMR (75 MHz, $CDCl_3$): *δ* 168.1, 142.5, 127.6, 75.2, 74.0, 60.3, 34.5, 25.7, 22.9, 22.8, 17.9, 14.2, 12.2, −4.1, −5.0; MS (ESI): *m*/*z* 367 $[M+Na]^+$; HRMS: calcd for $C_{18}H_{36}O_4NaSi$ $[M+Na]^+$ 367.2280, found: 367.2273.

3.12. (*E*,6*S*,7*R*)-7-[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy-2,6-dimethyl-2-octene-1,6-diol (22)

To a cooled (0 °C) solution of **21** (6.8 g, 19.7 mmol) in dry CH_2Cl_2 (80 mL) was added DIBAL-H (43.4 mL, 43.4 mmol, 1M solution in toluene) slowly over 15 min. The resulting mixture was allowed to stir for 30 min at 0 °C, before being quenched with sodium potassium tartarate solution (40 mL). The mixture was then stirred at room temperature until it becomes clear solution. The aqueous layer was extracted with CH_2Cl_2 (3×50 mL) and the combined organic layers were dried over Na_2SO_4, concentrated in vacuo and then purified by column chromatography using 16% EtOAc/hexanes to afford the pure **22** (5.3 g, 90% yield) as light yellow oil. R_f=0.34 (16% EtOAc/hexane); $[\alpha]_D^{25}$ −4.9 (*c* 0.8, $CHCl_3$); IR (neat): *ν* 3378, 2954, 2858, 1254, 1100 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): *δ* 5.38 (t, *J*=6.9 Hz, 1H, olefinic), 3.95 (s, 2H, CH_2OH), 3.59 (q, *J*=6.9Hz, 1H, $CHCH_3$), 2.12–2.23 (m, 1H, CH_AH_B), 2.02–2.09 (m, 1H, CH_AH_B), 2.0 (br s, 1H, OH), 1.67 (s, 3H, CCH_3), 1.49–1.57 (m, 1H, CH_AH_B), 1.30–1.38 (m, 1H, CH_AH_B), 1.10 (d, *J*=5.9, 3H, $CHCH_3$), 1.09 (s, 3H, CCH_3), 0.91 (s, 9H, $(CH_3)_3C$), 0.09 (s, 6H, $(CH_3)_2Si$); ^{13}C NMR (75 MHz, $CDCl_3$): *δ* 134.6, 126.3, 75.1, 74.2, 68.7, 35.8, 25.7, 23.1, 21.7, 20.7, 17.9, 13.3, −4.1, −5.0; MS (ESI): *m*/*z* 325 $[M+Na]^+$.

3.13. (2*S*)-2-[(2*R*,5*S*)-5-((1*R*)-1-[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxyethyl)-5-methyltetrahydro-2-furanyl]propane-1,2-diol (7a)

To a 100 mL two neck round bottom flask equipped with a magnetic bar and a septum with N_2 inlet was weighed 1.9 g of 4 Å molecular sieves (dry powder). To this was added dry CH_2Cl_2 (50 mL) and the solution was then cooled to −20 °C. To the above suspension was added $Ti(OiPr)_4$ (5.1 mL, 17.2 mmol) followed by L-diethyl tartrate (2.9 mL, 17.2 mmol) and the mixture was stirred vigorously at −20 °C for 30 min. A solution of allyl alcohol **22** (5.2 g, 17.2 mmol) in 20 mL CH_2Cl_2 was added to the above reaction mixture and stirred for another 30 min and then TBHP (10.5 mL, 37.8 mmol, 3.6M solution in toluene) was added at −20 °C. The resulting mixture was then set for stirring at the same temperature for 1 h and then at room temperature for another 2 h. The reaction mixture was filtered and the residue was washed with CH_2Cl_2. The filtrate and the washings were quenched with water (100 mL) at 0 °C and then stirred for another 30 min. After, which a solution of 17 mL of 20% NaOH solution prepared from a satd NaCl was added to the reaction mixture and the stirring was continued at rt for 12 h. The organic layers were separated, dried over anhydrous Na_2SO_4 and concentrated in vacuo and then purified by column chromatography using 20% EtOAc/hexane to afford the pure **7a** (4.5 g, 83% yield, R_f=0.15 (20% EtOAc/hexane)) along with another diastereoisomer **7b** (711 mg, 13%, R_f=0.25 (20% EtOAc/hexane) as a colorless liquid; $[\alpha]_D^{25}$ −7.4 (*c* 1.0, $CHCl_3$); IR (neat): *ν* 3442, 2955, 2932, 2859, 1638, 1465, 1253, 1100, 833, 774 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): *δ* 3.89 (t, *J*=6.9 Hz, 1H, OCH), 3.61 (q, *J*=6.9Hz, 1H, $CHCH_3$), 3.58 (d, *J*=10.8 Hz, 1H, CH_AH_B), 3.33 (d, *J*=10.8 Hz, 1H, CH_AH_B), 2.46 (br s, 1H, OH), 2.23 (br s, 1H, OH), 1.74–1.99 (m, 3H, CH_2, H_AH_B), 1.56–1.63 (m, 1H, CH_AH_B), 1.12 (d, *J*=5.9 Hz, 3H, $CHCH_3$), 1.11 (s, 3H, CCH_3), 1.10 (s, 3H, CCH_3), 0.88 (s, 9H, $(CH_3)_3C$), 0.07 (s, 3H, CH_3Si), 0.06 (s, 3H, CH_3Si); ^{13}C NMR (75 MHz, $CDCl_3$): *δ* 85.8, 83.4, 73.1, 67.4, 34.6, 26.1, 25.8, 21.0, 20.2, 18.7, 17.9, −4.0, −4.6; MS (ESI): *m*/*z* 341 $[M+Na]^+$; HRMS: calcd for $C_{16}H_{34}O_4NaSi$ $[M+Na]^+$ 341.2124, found: 341.2113.

3.14. *tert*-Butyl(dimethyl)[((1*R*)-1-(2*S*,5*R*)-2-methyl-5-[(2*S*)-2-methyloxiran-2-yl]tetrahydro-2-furanylethyl)oxy]silane (23)

To a stirred solution of the diol **7a** (4.4 g, 13.8 mmol), triethylamine (3.8 mL, 27.6 mmol) in dry CH_2Cl_2 (50 mL) at 0 °C was added *p*-toluenesulfonyl chloride (3.15 g, 16.6 mmol), DMAP (336 mg, 2.7 mmol) and dibutyltin oxide (669 mg, 2.7 mmol). The resulting mixture was stirred at 0 °C for 1 h. After complete conversion as indicated by TLC, the mixture was quenched with water (20 mL), extracted with CH_2Cl_2 (3×50 mL) and the combined organic layers

were dried over Na_2SO_4 and concentrated in vacuo to afford the tosylate.

To a solution of crude tosylate in dry THF (60 mL) at 0 °C was added NaH (1.1 g, 27.6 mmol). The resulting mixture was stirred at room temperature for 3–4 h. The mixture was quenched with water (20 mL), extracted with EtOAc (3×50 mL) and the combined organic layers were dried over Na_2SO_4, concentrated in vacuo and then purified by column chromatography using 8% EtOAc/hexanes to afford the pure product **23** (3.9 g, 96% yield) as colorless liquid. R_f=0.3 (8% EtOAc/hexane); $[\alpha]_D^{25}$ −7.4 (*c* 0.7, $CHCl_3$); IR (neat): *ν* 2956, 2858, 1465, 1253, 1099 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): *δ* 3.84 (t, *J*=7.1 Hz, 1H, OCH), 3.58 (q, *J*=5.9 Hz, 1H, $CHCH_3$), 2.60 (d, *J*=4.7 Hz, 1H, CH_AH_B), 2.52 (d, *J*=4.7 Hz, 1H, CH_AH_B), 1.93–2.0 (m, 1H, CH_AH_B), 1.80–1.88 (m, 1H, CH_AH_B), 1.65–1.73 (m, 1H, CH_AH_B), 1.55–1.64 (m, 1H, CH_AH_B), 1.31 (s, 3H, CCH_3), 1.13 (d, *J*=5.9 Hz, 3H, $CHCH_3$), 1.10 (s, 3H, CCH_3), 0.88 (s, 9H, $(CH_3)_3C$), 0.06 (s, 3H, CH_3Si), 0.05 (s, 3H, CH_3Si); ^{13}C NMR (75 MHz, $CDCl_3$): *δ* 86.0, 80.5, 72.6, 57.2, 52.3, 35.4, 26.7, 25.7, 19.6, 18.2, 17.8, 17.5, −4.0, −4.9; MS (ESI): *m/z* 323 $[M+Na]^+$; HRMS: calcd for $C_{16}H_{32}O_3NaSi$ $[M+Na]^+$ 323.2018, found: 323.2006.

3.15. (2*S*)-2-[(2*R*,5*S*)-5-((1*R*)-1-[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxyethyl)-5-methyltetrahydro-2-furanyl]-4-(phenylsulfonyl)butan-2-ol (24)

To a well-stirred solution of methyl phenyl sulphone (2.57 g, 16.5 mmol) in anhydrous THF (20 mL) at −78 °C was added *n*-butyl lithium (10.3 mL, 16.5 mmol, 1.6M solution in hexanes) dropwise and stirred for 30 min at the same temperature. $BF_3\cdot Et_2O$ (0.93 mL, 7.2 mmol) was added to the above mixture and allowed to stir for 10 min and then a solution of epoxide **23** (2.0 g, 6.6 mmol) in dry THF (15 mL) was added dropwise at −78 °C. The mixture was stirred for 4 h at −78 °C and then warm to room temperature. After completion, the reaction mixture was quenched with saturated NH_4Cl and the product was extracted with EtOAc (3×50 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4 was and then purified by column chromatography (EtOAc/hexane, 5%) to afford the pure product **24** (2.94 g, 97% yield) as a pale yellow liquid. R_f=0.15 (5% EtOAc/hexane); $[\alpha]_D^{25}$ −8.7 (*c* 0.55, $CHCl_3$); IR (neat): *ν* 3508, 2928, 2856, 1308, 834 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): *δ* 7.90 (d, *J*=7.1 Hz, 2H, ArH), 7.53–7.70 (m, 3H, ArH), 3.75 (t, *J*=7.1 Hz, 1H, $CHCH_2$), 3.56 (q, *J*=6.2 Hz, 1H, $CHCH_3$), 3.29 (dt, *J*=4.5, 13.5 Hz, 1H, $CH_AH_BSO_2$), 3.11 (dt, *J*=4.5, 13.5 Hz, 1H, $CH_AH_BSO_2$), 2.22 (br s, 1H, OH), 1.53–2.01 (m, 6H, 3×CH_2), 1.11 (s, 3H, CCH_3), 1.09 (s, 3H, CCH_3), 1.06 (d, *J*=6.2 Hz, 3H, $CHCH_3$), 0.87 (s, 9H, $(CH_3)_3C$), 0.07 (s, 3H, CH_3Si), 0.04 (s, 3H, CH_3Si); ^{13}C NMR (75 MHz, $CDCl_3$): *δ* 139.1, 133.6, 129.2, 127.9, 84.8, 84.1, 72.9, 72.0, 51.5, 34.2, 29.5, 25.7, 25.4, 23.6, 20.4, 18.7, 17.8, −4.1, −4.5; MS (ESI): *m/z* 479 $[M+Na]^+$; HRMS: calcd for $C_{23}H_{40}O_5NaSiS$ $[M+Na]^+$ 479.2263, found: 479.2256.

3.16. *t*ert-Butyl(dimethyl)[(1*R*)-1-((2*S*,5*R*)-2-methyl-5-(1*S*)-1-methyl-3-(phenylsulfonyl)-1-[(1,1,1-trimethylsilyl)oxy]propyltetrahydro-2-furanyl)ethyl]oxysilane (2)

To a stirred solution of alcohol **24** (1.8 g, 3.9 mmol) and 2,6-lutidine (1.0 mL, 8.58 mmol) in dry CH_2Cl_2 (20 mL) at −15 °C was added trimethylsilyl trifluoromethanesulfonate (TMSOTf, 0.80 mL, 4.3 mmol) dropwise. After 10 min, the mixture was diluted with CH_2Cl_2 (20 mL) and quenched with water and extracted with CH_2Cl_2 (2×40 mL). The organic layer was dried and concentrated in vacuo and the residue was purified by column chromatography using 20% EtOAc/hexane to afford the pure compound **2** (2.0 g, 98% yield). R_f=0.5 (20% EtOAc/hexane); $[\alpha]_D^{25}$ −8.3 (*c* 1.0, $CHCl_3$); IR (neat): *ν* 2956, 2857, 1252, 1093, 836 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): *δ* 7.90 (d, *J*=7.5 Hz, 2H, ArH), 7.53–7.70 (m, 3H, ArH), 3.66 (t, *J*=6.7 Hz, 1H, OCH), 3.43 (q, *J*=6.0 Hz, 1H, $CHCH_3$), 3.21 (dd, *J*=6.7, 9.0 Hz, 2H, CH_2SO_2), 1.52–2.02 (m, 6H, 3×CH_2), 1.09 (s, 3H, CCH_3), 1.03 (s, 3H, CCH_3), 1.01 (d, *J*=6.0 Hz, 3H, $CHCH_3$), 0.87 (s, 9H, $(CH_3)_3C$), 0.05 (s, 3H, CH_3Si), 0.03 (s, 9H, $(CH_3)_3Si$), 0.01 (s, 3H, CH_3Si); ^{13}C NMR (75 MHz, $CDCl_3$): *δ* 139.0, 133.4, 129.1, 128.0, 85.6, 82.7, 75.6, 73.3, 51.8, 35.8, 32.5, 26.1, 25.7, 22.9, 18.8, 18.3, 17.8, 2.2, −3.9, −4.9.

3.17. Ethyl (*E*,4*S*,6*S*,8*S*)-9-[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy-4,6,8-trimethyl-2-nonenoate (26)

To a stirred solution of IBX (2.9 g, 10.4 mmol) in DMSO (8 mL) at 25 °C, was slowly added a solution of alcohol **25** (2.0 g, 6.94 mmol) in CH_2Cl_2 (20 mL). The resulting mixture was stirred at 25 °C for 3 h. The solid was filtered and was washed with ether. The filtrate was diluted with ether, washed with saturated aqueous $NaHCO_3$ solution followed by water, brine and dried over Na_2SO_4. The solvent was removed under reduced pressure to furnish the crude aldehyde. To a solution of aldehyde in CH_2Cl_2 (40 mL) was added (ethoxycarbonylmethylene)triphenylphosphorane (6.38 g, 18.3 mmol) and the resulting mixture was stirred for 12 h at room temperature and then quenched with water and extracted with CH_2Cl_2 (3×100 mL). The combined organic layers were washed with water, followed by brine, dried over anhydrous Na_2SO_4 and concentrated in vacuo. The crude product was purified by silica gel column chromatography (1:19 EtOAc/hexane) to afford the **26** in (2.24 g, 91%) yield as colorless oil. R_f=0.45 (5% EtOAc/hexane); $[\alpha]_D^{25}$ +11.9 (*c* 1.0, $CHCl_3$); IR (neat): *ν* 2957, 2857, 1723, 1256, 838 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): *δ* 6.86 (dd, *J*=7.7, 15.6 Hz, 1H, olefinic), 5.77 (d, *J*=15.6 Hz, 1H, olefinic), 4.21 (q, *J*=7.1Hz, 2H, CH_2CH_3), 3.44 (dd, *J*=5.2, 9.6 Hz, 1H, OCH_AH_B), 3.33 (dd, *J*=6.2, 9.6 Hz, 1H, OCH_AH_B), 2.31–2.49 (m, 1H, CH), 1.46–1.73 (m, 2H, 2×CH), 1.33 (t, *J*=7.1 Hz, 3H, CH_2CH_3), 1.07–1.33 (m, 4H, 2×CH_2), 1.05 (d, *J*=6.6 Hz, 3H, $CHCH_3$), 0.85–0.95 (m, 15H, 2×CH_3, $(CH_3)_3C$), 0.03 (s, 6H, $(CH_3)_2Si$); ^{13}C NMR (75 MHz, $CDCl_3$): *δ* 166.9, 155.1, 119.1, 68.1, 60.0, 43.4, 41.3, 33.9, 33.1, 27.7, 25.9, 20.4, 18.9, 18.3, 17.7, 14.2, −5.4; MS (ESI): *m/z* 379 $[M+Na]^+$; HRMS: calcd for $C_{20}H_{40}O_3NaSi$ $[M+Na]^+$ 379.2644, found: 379.2640.

3.18. Ethyl (4*R*,6*S*,8*S*)-9-[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy-4,6,8-trimethylnonanoate (27)

To a cooled solution of **26** (2.2 g, 6.17 mmol) and $NiCl_2.6H_2O$ (292 mg, 1.23 mmol) in MeOH (30 mL), was added $NaBH_4$ (562 mg, 14.8 mmol) in small portions at 0 °C. After complete addition of $NaBH_4$, the mixture was stirred for 1 h at room temperature. The black precipitate formed was filtered and washed with MeOH. The solvent was removed under reduced pressure and the residue was diluted with water (40 mL) and extracted with ethyl acetate (2×50 mL). The combined organic layers were washed with water, brine and dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure and purification by silica gel column chromatography using ethyl acetate and hexane (1:19) afforded the pure compound **27** (2.16 g, 98% yield) as a colorless liquid. R_f=0.15 (5% EtOAc/hexane); $[\alpha]_D^{25}$ −14.3 (*c* 1.25, $CHCl_3$); IR (neat): *ν* 2957, 2929, 1723, 1256, 839 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 4.13 (q, *J*=7.3Hz, 2H, CH_2CH_3), 3.44 (dd, *J*=5.1, 9.5 Hz, 1H, OCH_AH_B), 3.34 (dd, *J*=6.5, 9.5 Hz, 1H, OCH_AH_B), 2.22–2.31 (m, 2H, CH_2CO), 1.41–1.72 (m, 6H, alkyl chain), 1.27 (t, *J*=7.3 Hz, 3H, CH_2CH_3), 1.20 (m, 1H, alkyl chain), 0.95–1.13 (m, 2H, alkyl chain), 0.88 (s, 9H, $(CH_3)_3C$), 0.87 (d, *J*=7.3 Hz, 3H, $CHCH_3$), 0.86 (d, *J*=7.3 Hz, 3H, $CHCH_3$), 0.84 (d, *J*=6.6 Hz, 3H, $CHCH_3$), 0.02 (s, 6H, $(CH_3)_2Si$); ^{13}C NMR (75 MHz, $CDCl_3$): *δ* 174.0, 68.3, 60.1, 44.0, 41.9, 33.0, 32.1, 29.7, 27.3, 25.9, 20.1, 18.9, 18.3, 17.3, 14.2, −5.3; MS (ESI): *m/z* 376 $(M+NH_4)^+$; HRMS: calcd for $C_{20}H_{42}O_3NaSi$ $[M+Na]^+$ 381.2800, found: 381.2810.

3.19. Ethyl (4*R*,6*S*,8*S*)-9-hydroxy-4,6,8-trimethylnonanoate (6)

To a stirred solution of silyl ether **27** (4.2 g, 11.7 mmol) in dry THF (30 mL) at 0 °C was added drop wise a solution of TBAF (17.5 mL, 17.5 mmol) in THF. The resulting mixture was allowed to warm to rt and stirred for 12 h. The reaction mixture was then quenched with water and extracted with ethyl acetate (2×100 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure and the crude product was purified by silica gel column chromatography (1.5:8.5, EtOAc/hexane) to afford the pure product **6** (2.76 g, 97% yield) as a colorless liquid. R_f=0.22 (15% EtOAc/hexane); $[\alpha]_D^{25}$ −17.0 (*c* 1.05, $CHCl_3$); IR (neat): ν 3442, 2957, 2873, 1735, 1460, 1376, 1176, 1036 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.15 (q, *J*=7.5Hz, 2H, CH_2CH_3), 3.34–3.51 (m, 2H, OCH_2), 2.32 (t, *J*=7.5 Hz, 2H, CH_2CO), 1.43–1.75 (m, 5H, alkyl chain), 1.29–1.43 (m, 2H, alkyl chain), 1.28 (t, *J*=7.5 Hz, 3H, CH_2CH_3), 0.98–1.17 (m, 2H, alkyl chain), 0.93 (d, *J*=6.7 Hz, 3H, $CHCH_3$), 0.87 (d, *J*=6.7 Hz, 6H, 2×$CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.1, 68.0, 60.1, 44.0, 41.4, 32.8, 32.6, 31.9, 29.5, 27.2, 20.2, 19.0, 17.1, 14.1; MS (ESI): *m*/*z* 245 $(M+H)^+$; HRMS: calcd for $C_{14}H_{28}O_3Na$ $[M+Na]^+$ 267.1936, found: 267.1947.

3.20. *tert*-Butyl[(2*R*,4*S*)-2,4-dimethyl-5-hexenyl]oxy-diphenylsilane (29)

To a stirred solution of IBX (1.98 g, 7.08 mmol) in DMSO (10 mL) was added dropwise a solution of alcohol **28** (1.75 g, 4.72 mmol) in CH_2Cl_2 (25 mL). The resulting mixture was stirred at rt for 3 h. The solid was filtered through a pad of Celite and washed with ether. The filtrate was washed with saturated aqueous $NaHCO_3$ solution, water, brine and dried over Na_2SO_4. The solvent was removed under reduced pressure and then the residue was purified by flash column chromatography (1:9, EtOAc/hexane) to furnish the crude aldehyde. To a stirred suspension of methyl(triphenyl)phosphonium iodide (7.62 g, 18.8 mmol) in dry THF (100 mL) at −78 °C was added n-BuLi (5.87 mL, 1.6 M in hexanes, 9.4 mmol) dropwise and the resulting mixture was stirred for 30 min at the same temperature. A solution of aldehyde in THF was slowly added to the above reaction mixture and the mixture was stirred for 1 h at −78 °C, then warmed to room temperature and stirred for another 6 h. The reaction mixture was quenched with saturated NH_4Cl solution at 0 °C and then extracted with EtOAc (3×100 mL). The combined organic layers were washed with water, brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography (1:9 EtOAc/hexane) to afford the compound **29** (1.48 g, 86% yield). R_f=0.25 (10% EtOAc/hexane); $[\alpha]_D^{25}$ +4.1 (*c* 1.25, $CHCl_3$); IR (neat): ν 3071, 2958, 2929, 2859, 1640, 1466, 1426, 1109, 910, 702, 504 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.62 (d, *J*=7.5 Hz, 4H, ArH), 7.27–7.43 (m, 6H, ArH), 5.48–5.63 (m, 1H, olefinic), 4.77–4.97 (m, 2H, olefinic), 3.34–3.50 (m, 2H, OCH_2), 2.07–2.25 (m, 1H, $CHCH_3$), 1.59–1.76 (m, 1H, $CHCH_3$), 1.30–1.46 (m, 2H, CH_2), 1.04 (s, 9H, $(CH_3)_3C$), 0.97 (d, *J*=6.7 Hz, 3H, $CHCH_3$), 0.91 (d, *J*=6.7 Hz, 3H, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.6, 135.6, 134.0, 129.4, 127.5, 112.5, 69.2, 40.3, 35.4, 33.3, 26.8, 21.3, 19.3, 16.7.

3.21. (3*S*,5*R*)-6-[1-(*tert*-Butyl)-1,1-diphenylsilyl]oxy-3,5-dimethylhexan-1-ol (30)

To a stirred solution of alkene **29** (1.4 g, 3.82 mmol) in dry THF (15 mL) at 0 °C was added borane-dimethyl sulfide complex (2M solution in THF, 2.1 mL, 4.2 mmol) dropwise and the resulting mixture was stirred at room temperature for 4 h. After complete conversion of the starting material as indicated by TLC, the mixture was cooled to 0 °C, and then treated with 1 M NaOH solution (76 mL) followed by 30% H_2O_2 (25 mL) solution. The resulting mixture was warmed to room temperature and then allowed to stir for 3 h. The mixture was quenched with $NaHCO_3$ solution and extracted with EtOAc (3×50 mL). Removal of the solvent followed by purification on silica gel column chromatography (20% EtOAc/hexane) gave the desired product **30** (1.37 g, 94% yield) as a viscous liquid. R_f=0.15 (20% EtOAc/hexane); $[\alpha]_D^{25}$ +4.5 (*c* 1.0, $CHCl_3$); IR (neat): ν 3351, 2929, 1427, 822, 740 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.64 (d, *J*=7.5 Hz, 2H, ArH), 7.63 (d, *J*=7.5 Hz, 2H, ArH), 7.28–7.43 (m, 6H, ArH), 3.52–3.70 (m, 2H, OCH_2), 3.36–3.52 (m, 2H, OCH_2), 1.14–1.79 (m, 6H, 2×CH, 2×CH_2), 1.05 (s, 9H, $(CH_3)_3C$), 0.95 (d, *J*=6.7 Hz, 3H, $CHCH_3$), 0.86 (d, *J*=6.0 Hz, 3H, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 135.6, 133.9, 129.4, 127.5, 68.7, 61.0, 41.1, 39.7, 33.0, 26.9, 26.8, 20.2, 19.2, 17.6; MS (ESI): *m*/*z* 407 $[M+Na]^+$; HRMS: calcd for $C_{24}H_{36}O_2NaSi$ $[M+Na]^+$ 407.2382, found: 407.2400.

3.22. 1-(*tert*-Butyl)-1,1-diphenylsilyl(2*R*,4*S*)-2,4-dimethyl-6-[(1-phenyl-1*H*-1,2,3,4-tetraazol-5-yl)sulfanyl]hexyl ether (31)

To a cooled (0 °C) solution of alcohol **30** (1.3 g, 3.38 mmol), PPh_3 (1.32 g, 5.07 mmol), and thiol (843 mg, 4.73 mmol) in 30 mL THF was added diethyl azodicarboxylate (0.85 mL, 5.4 mmol) dropwise. The reaction mixture was stirred for 2 h before being quenched with saturated aqueous $NaHCO_3$ solution, and extracted with EtOAc (3×50 mL). The organic layers were combined and dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified on silica gel column chromatography (10% EtOAc/hexane) to afford the desired product **31** (1.76 g, 96% yield) as a viscous liquid. R_f=0.35 (10% EtOAc/hexane); $[\alpha]_D^{25}$ +10.5 (*c* 0.55, $CHCl_3$); IR (neat): ν 2957, 2858, 1499, 1387, 1108, 822, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.44–7.67 (m, 10H, ArH), 7.27–7.43 (m, 5H, ArH), 3.23–3.53 (m, 4H, 2×CH_2), 1.37–1.89 (m, 6H, 2×CH, 2×CH_2), 1.03 (s, 9H, $(CH_3)_3C$), 0.94 (d, *J*=6.4 Hz, 6H, 2×$CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 154.3, 135.5, 133.9, 129.9, 129.7, 129.4, 127.5, 123.7, 68.6, 40.7, 35.9, 33.0, 31.2, 29.6, 26.8, 19.7, 19.2, 17.6; MS (ESI): *m*/*z* 567 $[M+Na]^+$; HRMS: calcd for $C_{31}H_{40}N_4ONaSiS$ $[M+Na]^+$ 567.2589, found: 567.2586.

3.23. (3*S*,5*R*)-6-[1-(*tert*-Butyl)-1,1-diphenylsilyl]oxy-3,5-dimethylhexyl(1-phenyl-1*H*-1,2,3,4-tetraazol-5-yl) sulfone (5)

To a stirred solution of sulphide **31** (1.7 g, 3.1 mmol) in CH_2Cl_2 (25 mL) at 0 °C was added *m*CPBA (1.61 g, 9.3 mmol). The reaction mixture was allowed to stir for 12 h at room temperature. After completion of the reaction as indicated by TLC, the mixture was quenched with aqueous $NaHCO_3$ and the organic layer was extracted with CH_2Cl_2 (3×30 mL). The combined organic layers were dried over Na_2SO_4, concentrated under reduced pressure and purified by chromatography on silica gel (5%, EtOAc/hexane) to yield the corresponding sulphone **5** (1.66 g, 93% yield) as a colorless liquid. R_f=0.55 (5% EtOAc/hexane); $[\alpha]_D^{25}$ +5.6 (*c* 0.65, $CHCl_3$); IR (Neat): ν 2957, 2857, 1341, 1152, 1109 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.54–7.77 (m, 9H, ArH), 7.28–7.47 (m, 6H, ArH), 3.53–3.77 (m, 2H, CH_2), 3.46 (dd, *J*=3.0, 5.2 Hz, 2H, CH_2), 1.82–2.0 (m, 1H, alkyl chain), 1.56–1.82 (m, 3H, alkyl chain), 1.22–1.49 (m, 2H, alkyl chain), 1.04 (s, 9H, $(CH_3)_3C$), 0.95 (d, *J*=6.0 Hz, 3H, $CHCH_3$), 0.94 (d, *J*=6.7 Hz, 3H, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.4, 135.5, 134.7, 133.8, 133.0, 131.3, 129.6, 129.5, 127.5, 125.0, 68.5, 54.0, 40.3, 32.9, 29.3, 28.1, 26.8, 19.6, 19.2, 17.5; MS (ESI): *m*/*z* 599 $[M+Na]^+$; HRMS: calcd for $C_{31}H_{40}N_4O_3NaSiS$ $[M+Na]^+$ 599.2488, found: 599.2483.

3.24. (3*R*,4*S*,5*R*,6*R*)-5-(Benzyloxy)-4,6-dimethylheptane-1,3,7-triol (32)

To an ice cooled suspension of LAH (1.03 g, 27.1 mmol) in dry THF (50 mL) was added a solution of lactone **10** (5.0 gm, 18.1 mmol)

in THF (25 mL) under nitrogen atmosphere. The reaction mixture was stirred for 1 h at room temperature. After completion of the reaction, it was quenched with saturated ammonium chloride solution and the precipitate formed was filtered off on a pad of Celite using EtOAc. The filtrate was dried over anhydrous Na_2SO_4 and concentrated in vacuo to afford the triol **32** (4.5 g, 90% yield) as a colorless viscous liquid; $[\alpha]_D^{25}$ +9.3 (*c* 0.95, $CHCl_3$); IR (Neat): ν 3414, 2937, 2881, 1679, 754 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.26–7.38 (m, 5H, ArH), 4.67 (s, 2H, CH_2Ph), 4.17–4.26 (m, 1H, OCH), 3.70–3.80 (m, 3H, OCH_2, OCH), 3.66 (dd, *J*=4.5, 10.5 Hz, 1H, OCH_AH_B), 3.51 (dd, *J*=3.7, 7.5 Hz, 1H, OCH_AH_B), 1.94–2.07 (m, 1H, $CHCH_3$), 1.78–1.92 (m, 1H, $CHCH_3$), 1.64–1.76 (m, 1H, CH_AH_B), 1.32–1.42 (m, 1H, CH_AH_B), 1.10 (d, *J*=6.7 Hz, 3H, $CHCH_3$), 1.0 (d, *J*=6.7 Hz, 3H, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.5, 128.5, 128.0, 127.8, 88.0, 76.0, 70.3, 64.9, 61.6, 39.1, 37.7, 36.5, 14.9, 11.7; MS (ESI): *m*/*z* 305 $[M+Na]^+$; HRMS: calcd for $C_{16}H_{26}O_4Na$ $[M+Na]^+$ 305.1728, found: 305.1728.

3.25. (3*R*,4*S*,5*R*,6*R*)-5-(Benzyloxy)-1,7-di[1-(*tert*-butyl)-1,1-diphenylsilyl]oxy-4,6-dimethylheptan-3-ol (33)

To a stirred solution of triol **32** (4.4 g, 15.6 mmol) and imidazole (3.18 g, 46.8 mmol) in dry CH_2Cl_2 (50 mL) at 0 °C was added TBDPSCl (3.87 mL, 34.3 mmol) dropwise. The reaction mixture was brought to rt and stirred for 2 h. After completion of the reaction as indicated by TLC, it was quenched by NH_4Cl solution and extracted with CH_2Cl_2 (3×50 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by silica gel column chromatography (10%, EtOAc/hexanes) to afford the pure disilyl ether **33** (10.9 g, 93% yield) as viscous liquid. R_f=0.3 (10% EtOAc/hexane); $[\alpha]_D^{25}$ +8.3 (*c* 1.0, $CHCl_3$); IR (neat): ν 3425 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.57–7.72 (m, 8H, ArH), 7.27–7.42 (m, 14H, ArH), 7.18–7.24 (m, 2H, ArH), 7.06–7.11 (m, 1H, ArH), 4.55 (ABq, *J*=11.0 Hz, 2H, CH_2Ph), 4.17–4.23 (m, 1H, OCH), 3.67–3.80 (m, 4H, 2×OCH_2), 3.49 (dd, *J*=4.0, 7.0 Hz, 1H, OCH), 3.18 (br, s, 1H, OH), 1.98–2.10 (m, 1H, CH_3CH), 1.81–1.86 (m, 1H, CH_3CH), 1.69–1.79 (m, 1H, CH_AH_B), 1.34–1.47 (m, 1H, CH_AH_B), 1.06 (s, 9H, $(CH_3)_3C$), 1.03 (s, 9H, $(CH_3)_3C$), 1.02 (d, *J*=6.0 Hz, 3H, $CHCH_3$), 1.0 (d, *J*=6.0 Hz, 3H, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.1, 135.7, 135.5, 134.7, 133.7, 133.6, 129.5, 128.3, 127.6, 86.2, 75.6, 67.8, 65.4, 61.8, 38.5, 38.3, 37.5, 26.9, 26.8, 19.2, 19.1, 14.8, 11.6; MS (ESI): *m*/*z* 781 $[M+Na]^+$; HRMS: calcd for $C_{48}H_{62}O_4NaSi_2$ $[M+Na]^+$ 781.4084, found: 781.4062.

3.26. (4*R*,5*R*,6*R*)-5-(Benzyloxy)-1,7-di[1-(*tert*-butyl)-1,1-diphenylsilyl]oxy-4,6-dimethylheptan-3-one (34)

Dess-Martin periodinane (8.22 g, 19.3 mmol) was added to an ice-cooled solution of disilyl ether **33** (10.5 g, 13.8 mmol) in CH_2Cl_2 (80 mL) under N_2 atmosphere. After stirring for 10 min, it was brought to room temperature and the stirring was continued for another 3 h. The reaction mixture was diluted with ether and the precipitate was filtered on a pad of Celite using ether as solvent. The filterate was washed with aqueous $NaHCO_3$ followed by brine solution, and dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel column chromatography (8%, EtOAc/hexanes) to afford the pure keto compound **34** (9.5 g, 92% yield) as viscous liquid. R_f=0.25 (8% EtOAc/hexane); $[\alpha]_D^{25}$ −17.8 (*c* 1.0, $CHCl_3$); IR (neat): ν 1740 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.53–7.74 (m, 8H, ArH), 7.03–7.47 (m, 17H, ArH), 4.32–4.48 (m, 2H, CH_2Ph), 3.53–3.99 (m, 5H, 2×OCH_2, OCH), 2.90–3.08 (m, 1H, CHCO), 2.62–2.79 (m, 1H, CH_AH_B), 2.47–2.62 (m, 1H, CH_AH_B), 1.89–2.07 (m, 1H, $CHCH_3$), 1.06 (s, 9H, $(CH_3)_3C$), 1.02 (d, *J*=6.0 Hz, 3H, $CHCH_3$), 0.98 (s, 9H, $(CH_3)_3C$), 0.96 (d, *J*=6.0 Hz, 3H, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 212.4, 138.5, 135.6, 135.5, 133.6, 129.5, 128.1, 127.6, 127.4, 127.3, 83.8, 74.4, 65.1, 59.2, 49.0, 46.1, 38.0, 26.9, 26.7, 19.2, 19.0, 14.9, 13.1; MS (ESI): *m*/*z* 779 $[M+Na]^+$; HRMS: calcd for $C_{48}H_{60}O_4NaSi_2$ $[M+Na]^+$ 779.3927, found: 779.3937.

3.27. 5-(Benzyloxy)-1,7-di[1-(*tert*-butyl)-1,1-diphenylsilyl] oxy-(3*S*,4*S*,5*R*,6*R*)-4,6-dimethylheptan-3-ol (35)

To a stirred solution of keto compound **34** (5.0 g, 6.61 mmol) in MeOH-THF (4:1, 60 mL) at 0 °C was added $NaBH_4$ (376 mg, 9.91 mmol) portion wise. The mixture was brought to room temperature and the stirring was continued for 1 h. After completion of the reaction, it was quenched with Na_2SO_4 solution (10 mL) at 0 °C. The solvent was evaporated and the residue was extracted with EtOAc. The combined organic layers were washed with brine, and dried over Na_2SO_4. The solvent was evaporated to dryness and the residue was purified by silica gel column chromatography to afford the desired products **35** (4.35 g, 87% yield, R_f=0.22 (10% EtOAc/hexane)) along with another diastereoisomer **33** (450 mg, 9% yield, R_f=0.3 (10% EtOAc/hexane)) as viscous liquid; $[\alpha]_D^{25}$ −1.4 (*c* 1.0, $CHCl_3$); IR (neat): ν 3445 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.58–7.67 (m, 8H, ArH), 7.27–7.40 (m, 14H, ArH), 7.16–7.22 (m, 2H, ArH), 7.07–7.13 (m, 1H, ArH), 4.50 (ABq, *J*=11.0 Hz, 2H, CH_2Ph), 3.94 (t, *J*=8.0 Hz, 1H, OCH), 3.80–3.87 (m, 1H, OCH), 3.71–3.80 (m, 2H, OCH_2), 3.68 (dd, *J*=7.0, 10.0 Hz, 1H, OCH_AH_B), 3.42 (t, *J*=6.0 Hz, 1H, OCH_AH_B), 3.30 (br s, 1H, OH), 1.95–2.05 (m, 1H, CH_3CH), 1.84–1.92 (m, 1H, CH_3CH), 1.69–1.79 (m, 1H, CH_AH_B), 1.49–1.63 (m, 1H, CH_AH_B), 1.06 (s, 9H, $(CH_3)_3C$), 1.04 (s, 9H, $(CH_3)_3C$), 1.03 (d, *J*=7.0 Hz, 3H, $CHCH_3$), 0.90 (d, *J*=7.0 Hz, 3H, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.5, 135.6, 135.5, 133.8, 133.3, 129.6, 129.5, 128.2, 127.6, 127.5, 127.4, 127.3, 84.9, 74.4, 72.0, 65.5, 63.0, 40.8, 39.1, 35.3, 26.9, 26.8, 19.2, 19.0, 14.8, 13.6; MS (ESI): *m*/*z* 781 $[M+Na]^+$; HRMS: calcd for $C_{48}H_{62}O_4NaSi_2$ $[M+Na]^+$ 781.4084, found: 781.4062.

3.28. (3*S*,4*S*,5*R*,6*R*)-5-(Benzyloxy)-4,6-dimethylheptane-1,3,7-triol (36)

To a cooled (0 °C), solution of disilylether **35** (4.3 g, 5.67 mmol) in THF (15 mL) was added TBAF (17.0 mL, 17.0 mmol, 1 M solution in THF) under nitrogen. After 15 min, the resulting mixture was brought to rt and stirred for another 5 h. The reaction mixture was quenched with ammonium chloride solution, extracted with EtOAc, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography (EtOAc) to afford the triol **36** (1.48 g, 93% yield) as a viscous liquid. R_f=0.35 (EtOAc); $[\alpha]_D^{25}$ −5.7 (*c* 0.65, $CHCl_3$); IR (neat): ν 3444, 2937, 2881, 1457 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.26–7.39 (m, 5H, ArH), 4.55–4.70 (m, 2H, CH_2Ph), 3.53–3.94 (m, 5H, 2×OCH, OCH_2, OCH_AH_B), 3.48 (t, *J*=5.4 Hz, 1H, OCH_AH_B), 2.32–3.0 (br s, 3H, 3×OH), 1.88–2.08 (m, 2H, 2×$CHCH_3$), 1.52–1.84 (m, 2H, CH_2), 1.09 (d, *J*=7.1 Hz, 3H, $CHCH_3$), 0.93 (d, *J*=6.9 Hz, 3H, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.5, 128.5, 128.0, 127.9, 88.0, 75.0, 74.0, 65.2, 61.6, 41.9, 38.1, 35.0, 15.5, 14.0; MS (ESI): *m*/*z* 305 $[M+Na]^+$; HRMS: calcd for $C_{16}H_{26}O_4Na$ $[M+Na]^+$ 305.1728, found: 305.1728.

3.29. (2*R*,3*R*,4*R*)-3-(Benzyloxy)-4-[(4*S*)-2,2-dimethyl-1,3-dioxan-4-yl]-2-methylpentan-1-ol (4)

To a stirred solution of triol **36** (3.0 g, 10.6 mmol) and 2,2-dimethoxypropane (2.63 mL, 21.2 mmol) in dry CH_2Cl_2 (40 mL) at 0 °C was added a catalytic amount of CSA (232 mg, 1.0 mmol), and stirred at room temperature for 5 h. After completion of the reaction, it was quenched with saturated aqueous $NaHCO_3$ solution, extracted with CH_2Cl_2 and the combined organic layers were washed with water, brine, and dried over Na_2SO_4. Removal of the solvent in vacuo followed by purification on silica gel column

chromatography (15% EtOAc/hexanes) afforded the pure compound **4** (3.07 g, 90% yield). R_f=0.3 (15% EtOAc/hexane); $[\alpha]_D^{25}$ +14.7 (*c* 0.65, $CHCl_3$); IR (neat): ν 3469, 1379, 1038, 769, 575 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.22–7.40 (m, 5H, ArH), 4.61 (ABq, *J*=11.3 Hz, 2H, CH_2Ph), 3.74–3.95 (m, 3H, 2×OCH, OCH_AH_B), 3.41–3.67 (m, 3H, OCH_2, OCH_AH_B), 2.58 (br s, 1H, OH), 1.84–2.07 (m, 2H, 2×$CHCH_3$), 1.49–1.65 (m, 1H, CH_AH_B), 1.41–1.47 (m, 1H, CH_AH_B), 1.38 (s, 3H, CCH_3), 1.35 (s, 3H, CCH_3), 0.99 (d, *J*=7.5 Hz, 3H, $CHCH_3$), 0.96 (d, *J*=7.5 Hz, 3H, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.0, 128.4, 127.8, 127.7, 98.0, 84.5, 73.2, 69.5, 66.5, 59.9, 40.8, 36.3, 29.9, 28.7, 19.0, 15.7, 11.0; MS (ESI): *m*/*z* 345 $[M+Na]^+$; HRMS: calcd for $C_{19}H_{30}O_4Na$ $[M+Na]^+$ 345.2041, found: 345.2048.

3.30. (2*R*,4*R*,6*E*,8*R*,9*R*,10*R*)-9-(Benzyloxy)-10-[(4*S*)-2,2-dimethyl-1,3-dioxan-4-yl]-2,4,8-trimethyl-6-undecenyloxy)(*tert*-butyl)diphenylsilane (37)

To a stirred solution of IBX (313 mg, 1.12 mmol) in DMSO (2 mL) at rt was added drop wise a solution of alcohol **4** (240 mg, 0.74 mmol) in CH_2Cl_2 (8 mL). The resulting mixture was stirred for 3 h at the same temperature. The solid was filtered through a pad of Celite and washed with ether. The filtrate was washed with saturated aqueous $NaHCO_3$ solution, water, brine and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (1:9, EtOAc/hexane, R_f=0.15) to furnish the crude aldehyde (230 mg, 0.71 mmol), which was used for the Julia olefination without further purification.

To a solution of azeotropically dried sulfone **5** (576 mg, 1.0 mmol) in dry THF (10 mL) at −78 °C was added KHMDS (2.0 mL, 0.5M solution in toluene, 1.0 mmol) and the mixture was stirred for 30 min. To this, a solution of the above aldehyde (azeotropically dried with benzene) in dry THF (10 mL) was added via cannula and the reaction mixture was slowly warm to room temperature and stirred for 12 h. The reaction was quenched with NH_4Cl solution. The aqueous phase was extracted with EtOAc (3×15 mL), and the combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (5%, EtOAc/hexanes) to give the *trans*-olefin **37** (413 mg, 87% yield) as a colorless liquid. R_f=0.25 (5% EtOAc/hexane); $[\alpha]_D^{25}$ −3.0 (*c* 0.9, $CHCl_3$); IR (neat): ν 2958, 2929, 2861, 1377, 1103 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.57–7.75 (m, 5H, ArH), 7.20–7.45 (m, 10H, ArH), 5.54 (dd, *J*=8.3, 15.8 Hz, 1H, olefinic), 5.24–5.38 (m, 1H, olefinic), 4.57 (ABq, *J*=11.3 Hz, 2H, CH_2Ph), 3.92–4.02 (m, 1H, OCH), 3.66–3.84 (m, 2H, OCH, OCH_AH_B), 3.50 (dd, *J*=5.2, 9.0 Hz, 1H, OCH_AH_B), 3.39 (dd, *J*=6.7, 9.8 Hz, 1H, OCH_AH_B), 3.24 (dd, *J*=3.7, 6.7 Hz, 1H, OCH_AH_B), 2.32–2.48 (m, 1H, $CHCH_3$), 1.42–2.05 (m, 6H, 2×CH_2, 2×$CHCH_3$), 1.32 (s, 3H, CCH_3), 1.25 (s, 3H, CCH_3), 1.14–1.41 (m, 3H, CH_2, $CHCH_3$), 1.06 (d, *J*=6.7 Hz, 3H, $CHCH_3$), 1.04 (s, 9H, $(CH_3)_3C$), 0.93 (d, *J*=6.7 Hz, 3H, $CHCH_3$), 0.84 (d, *J*=6.7 Hz, 3H, $CHCH_3$), 0.81 (d, *J*=6.7 Hz, 3H, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.0, 135.5, 134.7, 134.0, 133.8, 129.4, 128.4, 128.2, 127.5, 127.3, 98.1, 84.2, 73.7, 69.4, 68.8, 60.0, 40.6, 40.5, 39.9, 39.4, 33.1, 30.5, 29.9, 29.6, 26.8, 20.1, 17.7, 11.1.

3.31. (2*R*,4*R*,6*E*,8*R*,9*R*,10*R*)-9-(Benzyloxy)-10-[(4*S*)-2,2-dimethyl-1,3-dioxan-4-yl]-2,4,8-trimethyl-6-undecen-1-ol (38)

To a stirred solution of silyl ether **37** (400 mg, 0.59 mmol) in dry THF (5 mL) at 0 °C was added drop wise a solution of TBAF (0.9 mL, 0.9 mmol) in THF. The resulting mixture was allowed to stir for 12 h at rt upon completion, the mixture was then quenched with water and extracted with ethyl acetate (3×10 mL). The combined organic extracts were dried over Na_2SO_4, concentrated under reduced pressure and the crude was purified by silica gel column chromatography (1:9, EtOAc/hexane) to afford the pure alcohol **38** (247 mg, 97% yield) as a viscous liquid. R_f=0.15 (10% EtOAc/hexane); $[\alpha]_D^{25}$ −12.1 (*c* 1.35, $CHCl_3$); IR (neat): ν 3461, 1339, 1031, 835 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.26–7.39 (m, 5H, ArH), 5.57 (dd, *J*=8.8, 15.3 Hz, 1H, olefinic), 5.36–5.45 (m, 1H, olefinic), 4.58 (ABq, *J*=11.3 Hz, 2H, CH_2Ph), 4.05–4.15 (m, 1H, OCH), 3.71–3.82 (m, 2H, OCH, OCH_AH_B), 3.45 (dd, *J*=4.8, 10.5 Hz, 1H, OCH_AH_B), 3.35 (dd, *J*=6.4, 10.5 Hz, 1H, OCH_AH_B), 3.24 (dd, *J*=3.2, 7.2 Hz, 1H, OCH_AH_B), 2.41–2.50 (m, 1H, $CHCH_3$), 1.81–2.02 (m, 5H, CH_2, 2×$CHCH_3$, CH_AH_B), 1.51–1.76 (m, 4H, CH_2, $CHCH_3$, CH_AH_B), 1.40 (s, 3H, CCH_3), 1.36 (s, 3H, CCH_3), 1.12 (d, *J*=7.2 Hz, 3H, $CHCH_3$), 0.91 (d, *J*=7.2 Hz, 3H, $CHCH_3$), 0.89 (d, *J*=7.2 Hz, 3H, $CHCH_3$), 0.87 (d, *J*=7.2 Hz, 3H, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.9, 133.6, 128.2, 128.1, 127.6, 127.4, 98.2, 84.2, 74.0, 69.3, 68.1, 59.9, 40.6, 39.9, 39.5, 39.2, 33.1, 29.8, 26.7, 25.5, 20.5, 19.4, 19.2, 17.1, 10.9; MS (ESI): *m*/*z* 455 $[M+Na]^+$.

3.32. (3*R*,5*R*,7*E*,9*R*,10*R*,11*R*)-10-(Benzyloxy)-11-[(4*S*)-2,2-dimethyl-1,3-dioxan-4-yl]-3,5,9-trimethyl-7-dodecen-2-one (39)

To a stirred solution of IBX (145 mg, 0.52 mmol) in DMSO (2 mL) at rt was added a solution of alcohol **38** (150 mg, 0.34 mmol) in CH_2Cl_2 (8 mL). The resulting mixture was stirred for 3 h at the same temperature. The solid was filtered through a pad of Celite and washed with ether. The filtrate was washed with saturated aqueous $NaHCO_3$ solution, water, brine and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (5%, EtOAc/hexane) to furnish the crude aldehyde, which was used for the Grignard reaction without further purification.

To a stirred solution of above aldehyde in dry ether (10 mL) at −78 °C was added freshly prepared CH_3MgI (0.3 mL, 2 M in ether, 0.6 mmol) and reaction was allowed to stir at the same temperature for 1 h. After complete conversion of the starting material as indicated by TLC, the mixture was quenched with NH4Cl solution and extracted with EtOAc (3×15 mL). Removal of the solvent followed by purification on silica gel column chromatography (10% EtOAc/hexane, R_f=0.15) gave the isomeric alcohol, which was used for the oxidation reaction.

To a stirred solution of the above alcohol in dry CH_2Cl_2 (5 mL) at 0 °C was added Dess-Martin periodinane (288 mg, 0.68 mmol) under N_2 atmosphere. After stirring for 10 min, it was brought to room temperature and the stirring was continued for another 3 h. The mixture was diluted with ether and the precipitate was filtered on a pad of Celite using ether as a solvent. The filterate was washed with water, $NaHCO_3$, dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel column chromatography (7%, EtOAc/hexane) to afford the pure keto compound **39** (137 mg, 91% yield over three steps) as a colorless liquid. R_f=0.10 (7% EtOAc/hexane); $[\alpha]_D^{25}$ −10.2 (*c* 0.5, $CHCl_3$); IR (neat): ν 2960, 2925, 1713, 1459, 1374, 1175, 1106, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.26–7.39 (m, 5H, ArH), 5.60 (dd, *J*=8.3, 15.4 Hz, 1H, olefinic), 5.30–5.44 (m, 1H, olefinic), 4.55 (ABq, *J*=11.5 Hz, 2H, CH_2Ph), 4.01–4.11 (m, 1H, OCH), 3.74–3.88 (m, 2H, OCH, OCH_AH_B), 3.28 (dd, *J*=3.5, 7.5 Hz, 1H, OCH_AH_B), 2.39–2.68 (m, 2H, 2×$CHCH_3$), 2.01 (s, 3H, CH_3CO), 1.79–2.05 (m, 3H, $CHCH_3$, CH_2), 1.59–1.76 (m, 2H, $CHCH_3$, CH_AH_B), 1.41 (s, 3H, CCH_3), 1.36 (s, 3H, CCH_3), 1.19–1.36 (m, 3H, CH_AH_B, CH_2), 1.12 (d, *J*=6.9 Hz, 3H, $CHCH_3$), 1.08 (d, *J*=6.9 Hz, 3H, $CHCH_3$), 0.87 (d, *J*=6.9 Hz, 3H, $CHCH_3$), 0.86 (d, *J*=6.9 Hz, 3H, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 212.9, 138.9, 134.2, 128.2, 127.8, 127.5, 127.3, 98.0, 84.1, 73.7, 69.3, 59.9, 44.9, 40.6, 39.9, 39.8, 39.4, 30.9, 29.9, 29.6, 27.0, 19.7, 19.3, 19.1, 17.0, 11.0; MS (ESI): *m*/*z*

467 $[M+Na]^+$; HRMS: calcd for $C_{28}H_{44}O_4Na$ $[M+Na]^+$ 467.3137, found: 467.3127.

3.33. Ethyl (4*R*,6*S*,8*S*,9*Z*,12*R*,14*R*,16*E*,18*R*,19*R*,20*R*)-19-(benzyloxy)-20-[(4*S*)-2,2-dimethyl-1,3-dioxan-4-yl]-9-hydroxy-4,6,8,12,14,18-hexamethyl-11-oxo-9,16-henicosadienoate (3)

To a stirred solution of IBX (68 mg, 0.24 mmol) in DMSO (1 mL) at rt, was added drop wise a solution of alcohol **6** (40 mg, 0.16 mmol) in CH_2Cl_2 (5 mL). The resulting mixture was stirred for 2 h at the same temperature. The solid was filtered through a pad of Celite and washed with ether. The filtrate was washed with saturated aqueous $NaHCO_3$ solution, water, brine and dried over Na_2SO_4. The solvent was removed under reduced pressure to furnish the crude aldehyde, which was used for the aldol reaction without further purification.

To a solution of azeotropically dried methyl ketone **39** (60 mg, 0.13 mmol) in dry THF (2 mL) at −78 °C was added KHMDS (0.26 mL, 0.5M solution in toluene, 0.13 mmol) and the mixture was stirred for 30 min. To this, a solution of the above aldehyde (azeotropically dried with benzene) in dry THF (1.5 mL) was added via cannula and the resulting mixture was stirred for 4 h at the same temperature. The reaction was quenched with NH_4Cl solution and the aqueous phase was extracted with EtOAc (3×5 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (10%, EtOAc/hexanes) to give the isomeric β-hydroxy ketone, which was used for the PDC oxidation reaction without further purification.

To a stirred solution of above β-hydroxy ketone and Celite (75 mg) in dry CH_2Cl_2 (3 mL) at 0 °C was added PDC (188 mg, 0.5 mmol). After stirring for 10 min it was brought to room temperature and the stirring was continued for another 12 h. The solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography (5%, EtOAc/hexane) to afford the pure diketo compound **3** (64 mg, 70% yield for three steps) as pale yellow liquid. R_f=0.15 (5% EtOAc/hexane); $[\alpha]_D^{25}$ −7.9 (*c* 0.7, $CHCl_3$); IR (neat): ν 2923, 2853, 1736, 1628, 1461, 1375, 1174, 1097, 970, 757 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.27–7.41 (m, 5H, ArH), 5.58 (dd, *J*=8.3, 15.1 Hz, 1H, olefinic), 5.46 (s, 1H, olefinic), 5.27–5.42 (m, 1H, olefinic), 4.56 (ABq, *J*=11.3 Hz, 2H, CH_2Ph), 4.15 (q, *J*=7.5 Hz, 2H, CH_2CH_3), 3.99–4.07 (m, 1H, OCH), 3.68–3.89 (m, 2H, OCH, OCH_AH_B), 3.28 (dd, *J*=3.7, 6.7 Hz, 1H, OCH_AH_B), 1.77–2.55 (m, 7H, 2×CH_2, 3×$CHCH_3$), 1.41 (s, 3H, CCH_3), 1.36 (s, 3H, CCH_3), 1.26 (t, *J*=7.5 Hz, 3H, CH_2CH_3), 1.13 (d, *J*=6.7 Hz, 3H, $CHCH_3$), 1.12 (d, *J*=6.7 Hz, 3H, $CHCH_3$), 1.01–1.76 (m, 14H, alkyl chain), 0.78–0.93 (m, 15H, alkyl chain); ^{13}C NMR (75 MHz, $CDCl_3$): δ 198.8, 198.3, 173.9, 139.1, 134.3, 128.2, 127.9, 127.6, 127.3, 98.1, 97.1, 84.2, 73.7, 69.4, 60.1, 60.0, 44.3, 44.1, 42.4, 41.0, 40.6, 40.3, 40.1, 39.4, 30.9, 30.4, 29.9, 27.9, 27.2, 26.6, 22.6, 19.5, 19.4, 19.3, 19.2, 18.9, 18.8, 18.3, 14.2, 11.1; MS (ESI): *m*/*z* 707 $[M+Na]^+$; HRMS: calcd for $C_{42}H_{68}O_7Na$ $[M+Na]^+$ 707.4862, found: 707.4872.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2015.08.011.

References and notes

1. (a) Liu, C. M.; Herrnann, T. E. *J. Biol. Chem.* **1978**, *253*, 5892; (b) Liu, W.-C.; Smith-Slusarchyk, D.; Astle, G.; Trejo, W. H.; Brown, W. E.; Meyers, E. *J. Antibiot.* **1978**, *31*, 815.
2. Westley, J. W. *Adv. Appl. Microb.* **1977**, *22*, 177.
3. Toeplitz, B. K.; Cohen, A. I.; Funke, P. T.; Parker, W. L.; Gougoutas, J. Z. *J. Am. Chem. Soc.* **1979**, *101*, 3344.
4. Hanessian, S.; Cooke, N. G.; DeHoff, B.; Sakito, Y. *J. Am.Chem. Soc.* **1990**, *112*, 5276.
5. Evans, D. A.; Dow, R. L.; Shih, T. L.; Takacs, J. M.; Zahler, R. *J. Am. Chem. Soc.* **1990**, *112*, 5290.
6. Lautens, M.; Coulucci, J. T.; Hiebert, S.; Smith, N. D.; Bouchain, G. *Org. Lett.* **2002**, *4*, 1879.
7. Gao, Z.; Li, Y.; Cooksey, J. P.; Snaddon, T. N.; Schunk, S.; Viseux, E. M. E.; McAteer, S. M.; Kocienski, P. J. *Angew. Chem., Int. Ed.* **2009**, *48*, 5022.
8. (a) Wuts, P. G. M.; Dcosta, R.; Butler, W. *J. Org. Chem.* **1984**, *49*, 2582; (b) Spino, C.; Weiler, L. *Tetrahedron Lett.* **1987**, *28*, 731; (c) Nicoll-Griffith, D. A.; Weiler, L. *Tetrahedron* **1991**, *47*, 2733; (d) Taschner, M. J.; Chen, Q. Z. *Bioorg. Med. Chem. Lett.* **1991**, *1*, 535; (e) Emde, H.; Langels, A.; Noltemeyer, M.; Bruckner, R. *Tetrahedron Lett.* **1994**, *35*, 7609; (f) Guindon, Y.; Yoakim, C.; Gorys, V.; Ogilvie, W. W.; Delorme, D.; Renaud, J.; Robinson, G.; Lavallee, J. F.; Slassi, A.; Jung, G.; Rancourt, J.; Durkin, K.; Liotta, D. *J. Org. Chem.* **1994**, *59*, 1166; (g) Hu, T. Q.; Weiler, L. *Can. J. Chem.* **1994**, *72*, 1500; (h) Montana, A. M.; Garcia, F.; Grima, P. M. *Tetrahedron Lett.* **1999**, *40*, 1375; (i) Spino, C.; Allan, M. *Can. J. Chem.* **2004**, *82*, 177; (j) Novak, T.; Tan, Z.; Liang, B.; Negishi, E. *J. Am. Chem. Soc.* **2005**, *127*, 2838; (k) Marshall, J. A.; Mikowski, A. M. *Org. Lett.* **2006**, *8*, 4375.
9. (a) Yadav, J. S.; Srinivas Rao, C.; Chandrasekhar, S.; Rama Rao, A. V. *Tetrahedron Lett.* **1995**, *36*, 7717; (b) Yadav, J. S.; Abraham, S.; Muralidhar Reddy, M.; Sabitha, G.; Ravi Sankar, A.; Kunwar, A. C. *Tetrahedron Lett.* **2001**, *42*, 4713; (c) Yadav, J. S.; Ahmed, M. M. *Tetrahedron Lett.* **2002**, *43*, 7147; (d) Yadav, J. S.; Srinivas, R.; Sathaiah, K. *Tetrahedron Lett.* **2006**, *47*, 1603; (e) Yadav, J. S.; Pratap, T. V.; Rajender, V. *J. Org. Chem.* **2007**, *72*, 5882; (f) Yadav, J. S.; Rajender, V. *Eur. J. Org. Chem.* **2010**, 2148; (g) Yadav, J. S.; Rajender, V.; Rao, G. *Org. Lett.* **2010**, *12*, 348; (h) Yadav, J. S.; Rao, K. V. R.; Ravinder, K.; Reddy, B. V. S. *Eur. J. Org. Chem.* **2011**, 58; (i) Yadav, J. S.; Yadagiri, K.; Madhuri, Ch; Sabitha, G. *Tetrahedron Lett.* **2011**, *52*, 4269; (j) Yadav, J. S.; Srinivas, E.; Kumar, C. K. S.; Ghamdi, A. K. *Synthesis* **2012**, *44*, 628; (k) Yadav, J. S.; Singh, V. K.; Srihari, P. *Org. Lett.* **2014**, *16*, 836.
10. (a) Yadav, J. S.; Yadav, N. N.; Rao, T. S.; Reddy, B. V. S.; Ghamdi, A. A. K. A. *Eur. J. Org. Chem.* **2011**, 4603; (b) Yadav, J. S.; Rao, T. S.; Yadav, N. N.; Rao, K. V. R.; Reddy, B. V. S.; Ghamdi, A. K. *Synthesis* **2012**, *44*, 788; (c) Yadav, J. S.; Sengupta, S.; Yadav, N. N.; Chary, D. N.; Ghamdi, A. K. *Tetrahedron Lett.* **2012**, *53*, 5952; (d) Yadav, J. S.; Yadav, N. N. *RSC Adv.* **2013**, *3*, 4024; (e) Yadav, J. S.; Chary, D. N.; Yadav, N. N.; Sengupta, S.; Reddy, B. V. S. *Helv. Chim. Acta* **2013**, *96*, 1968.
11. Duke, R. K.; Chebib, M.; Hibbs, D. E.; Mewett, K. N.; Johnston, G. A. R. *Tetrahedron Asymmentry* **2004**, 1745.
12. Martin, T.; Rodriguez, C. M.; Martin, V. S. *Tetrahedron: Asymmentry* **1995**, 1151.
13. Toyota, M.; Hirota, M.; Nishikawa, Y.; Fukumoto, K.; Ihara, M. *J. Org. Chem.* **1998**, *63*, 5895.
14. Colvin, E. W.; Robertson, A. D.; Wakharkar, S. *J. Chem. Soc., Chem. Commun.* **1983**, 312.
15. Phillips, K. D.; Zemlicka, J.; Horowitz, J. P. *Carbohydr. Res.* **1973**, *30*, 281.
16. Satoh, T.; Nanba, K.; Suzuki, S. *Chem. Pharm. Bull.* **1971**, *19*, 817.
17. (a) Wuts, P. G. M.; D'Costa, R.; Butler, W. *J. Org. Chem.* **1984**, *49*, 2582; (b) Gao, Z.; Li, Y.; Cooksey, J. P.; Snaddon, T. N.; Schunk, S.; Viseux, E. M. E.; McAteer, S. M.; Kocienski, P. J. *Angew. Chem., Int. Ed.* **2009**, *48*, 5022.
18. Gao, Y.; Nan, F.; Xu, X. *Tetrahedron Lett.* **2000**, *41*, 4811.
19. (a) Bucher, B.; Curran, D. P. *Tetrahedron Lett.* **2000**, *41*, 9617; (b) Martinelli, M. J.; Nayyar, N. K.; Moher, E. D.; Dhokte, U. P.; Pawlak, J. M.; Vaidyanathan, R. *Org. Lett.* **1999**, *1*, 447.
20. (a) Ni, C.; Li, Y.; Hu, J. *J. Org. Chem.* **2006**, *71*, 6829; (b) Miyaoka, H.; Shida, H.; Yamada, N.; Mitome, H.; Yamada, Y. *Tetrahedron Lett.* **2002**, *43*, 2227.
21. Marshall, J. A.; Mikowski, A. M. *Org. Lett.* **2006**, *8*, 4375.
22. (a) Blakemore, P. R. *J. Chem. Soc., Perkin Trans.* **2002**, *1*, 2563; (b) Blakemore, P. R.; Cole, W. J.; Kocienski, P. J.; Morley, A. *Synlett* **1998**, 26.
23. (a) Evans, D. A.; Bender, S. L.; Morris, J. *J. Am. Chem. Soc.* **1988**, *110*, 2506; (b) Hangyou, M.; Ishiyama, H.; Takahashi, Y.; Kobayashi, J. *Org. Lett.* **2009**, *11*, 5046.
24. Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, *16*, 2647.