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A concise route to the C3–C23 fragment of the macrolide palmerolide A

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Abstract—A concise route to the C3–C23 part of the macrolide palmerolide A was developed. This part features the 7,10,11-trihydroxy sector containing the 8*E*-double bond as well as the 14,16-diene subunit. The stereocenter at C-7 originated from a Noyori reduction on alkynone **8**. The substrate **16** containing an enyne was obtained via a Claisen rearrangement. The vicinal diol at C10,C11 was created by a Sharpless asymmetric dihydroxylation. After selective protecting group manipulations the propargylic alcohol was reduced with Red-Al to the *E*-alkylic alcohol **26**. The conjugated diene in the fragment **40** resulted from a Stille cross-coupling reaction between the vinylstannane derived from alkyne **30** and the vinyl iodide **39**. The latter could conveniently be prepared by an aldol/Wittig strategy.

1. Introduction

A range of natural products rely on reactive functional groups to confer biological activity.[1] Thus, epoxide functions are quite common such as in the amphidinolides[2] or fumagillin.[3] Other natural products feature an electrophilic *exo*-methylene butenolide as reactive Michael acceptor.[4] Besides these groups various natural products are known that contain an enamide terminus. Prominent examples include the benzolactone enamides.[5] It seems likely that protonation of the enamide double bond generates an electrophilic acyliminium ion.[6] Recently, the structure of a further macrolactone enamide, palmerolide A (**1**) was described by Baker et al.[7] This natural product displayed selective and strong antitumor activity (LC_{50}=18 nM) against melanoma cells (Fig. 1). It could be shown that the mode of action on a molecular level is due to the inhibition of V-ATPase, which is an important proton pump.[8] In this regard palmerolide is related to the benzolactone enamides. Due to the novel structural features and the mode of action we became interested in a total synthesis of palmerolide A. From a structural point of view the unsaturated *N*-acyldienamine side chain, five stereocenters, the unsaturated segments, and the 20-membered macrolactone pose certain challenges. As with any macrolactone, classical lactonization reactions, alkylative lactonization (cf. Mitsunobu) or any other C–C bond formation on suitable ester substrates can be considered.[9] Our retrosynthetic analysis was built upon a Horner–Wadsworth–Emmons macrocyclization of a phosphonate of type **3**. A further key disconnection at the diene generates the two fragments **4** and **5**. The *syn* stereochemistry in the enoate **4** should be available via an aldol reaction. The fragment **5** was traced back to enyne **6**.

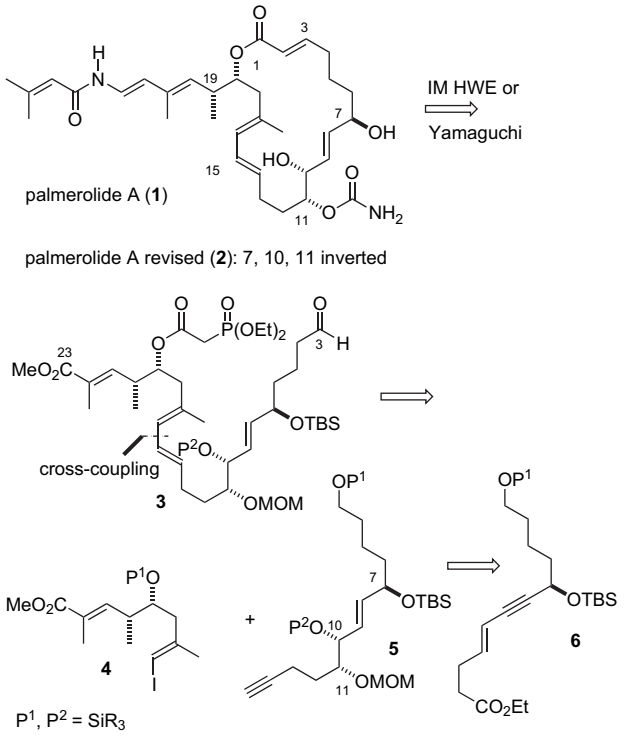

Figure 1. Original (**1**) and revised structure of palmerolide A (**2**) together with retrosynthetic considerations.

Keywords: Palmerolide; Asymmetric dihydroxylation; Claisen rearrangement; Suzuki cross-coupling; Evans aldol; Protecting groups.
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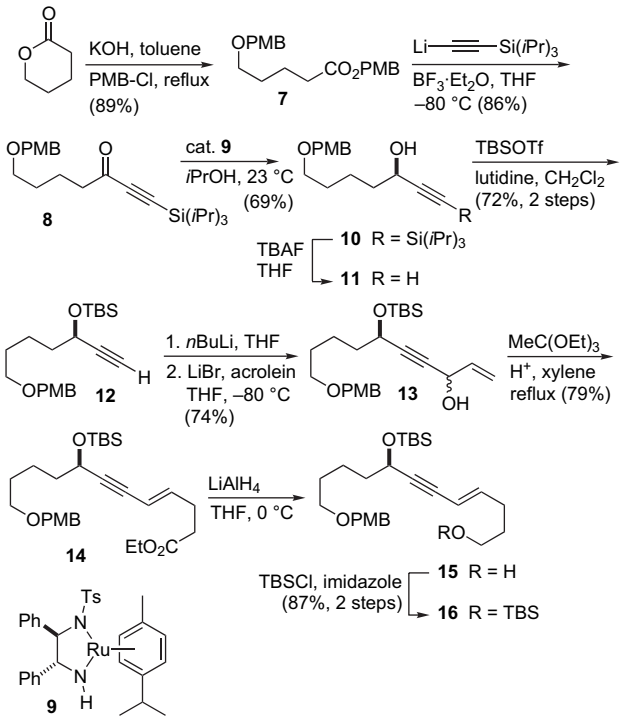
While our work was in progress the group of De Brabander published the synthesis of the proposed structure of palmerolide A.[10] Through chemical correlation they could show that the structure of palmerolide A (**1**) has to be revised to **2**. The macrocyclization was achieved by HWE olefination to an enone with the formation of the C8–C9 double bond. The stereocenter at C7 was created by a CBS reduction.[11] The two stereocenters at C10 and C11 came from D-arabitol. A further publication by Kaliappan and Gowrisankar [12] described the synthesis of the C1–C9 and C15–C21 fragments. Quite recently the Nicolaou–Chen group published the total synthesis of the originally proposed and revised structures of palmerolide A. Their synthesis relies on a ring-closing metathesis reaction to form the C8–C9 double bond.[13] In this publication we report the synthesis of the C3–C23 fragment **40** of the originally proposed structure of palmerolide A via the enyne **25** as a key intermediate.

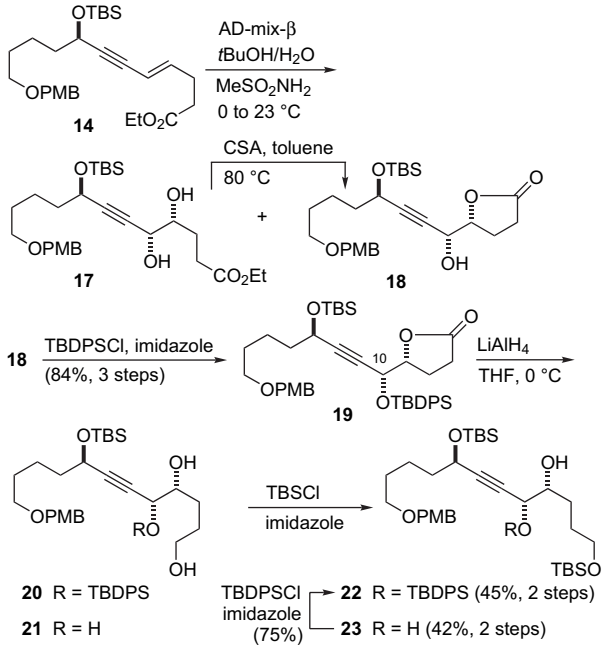
2. Results

The synthesis started with valerolactone that was opened under basic conditions and alkylated with *para*-methoxybenzyl chloride to give the ester **7** (Scheme 1). The ester **7** could be converted to the alkynone **8** by reacting it with the lithium anion of triisopropysilylacetylene in presence of $BF_3 \cdot OEt_2$.[14] At this stage a transfer hydrogenation according to Noyori using the Ru catalyst containing the (*R*,*R*)-diamine derivative **9** furnished a good yield of the propargylic alcohol **10**.[15] According to GC analysis on the derived alcohol **11** an ee-value of 98% was obtained. The absolute configuration of alcohol **11** could be supported by Mosher analysis.[16,17] Two further steps via alkynol **11** served to protect the alcohol function and to liberate the terminal alkyne giving alkyne **12**. The stage called now for extension of the carbon chain to an enyne. While this could be achieved via a cross-coupling reaction, in the case at hand a Claisen rearrangement seemed more suitable.[18] Accordingly, the anion of alkyne **12** was reacted with acrolein to give the allylic alcohol **13** as a mixture of diastereomers. A Johnson–Claisen rearrangement[19] using triethyl orthoacetate, a trace of propionic acid and heating of the mixture in xylene provided a 79% yield of 1,4-unsaturated ester **14**. Subsequently, ester reduction to the primary alcohol **15** and protection of the hydroxyl group delivered enyne **16**.



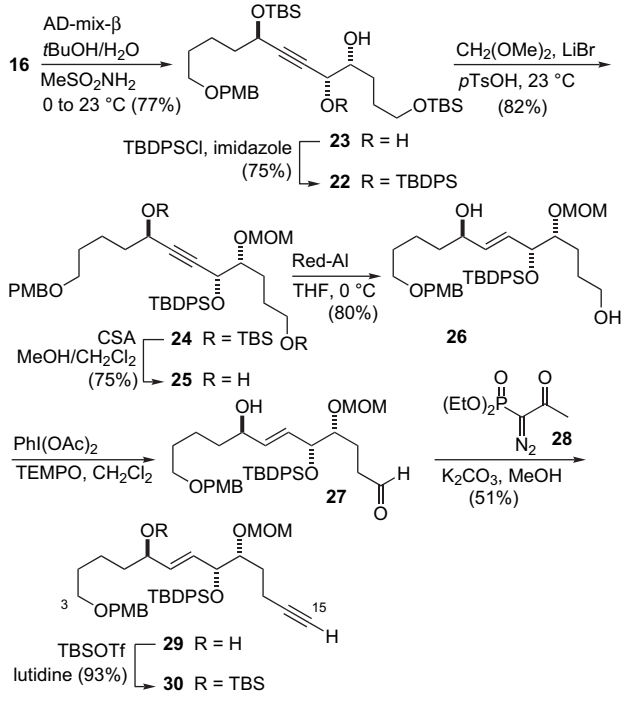
Scheme 1. Synthesis of the enyne **16** via the alkynone **8** and Johnson–Claisen rearrangement of the derived allylic alcohol **13** to the enoate **14**.

Initially the asymmetric dihydroxylation was performed on the ester **14**. The idea was to use lactonization as a means to differentiate the vicinal hydroxyl functions resulting from the dihydroxylation.[20] As it is known from the literature, the double bond of enynes can be selectively dihydroxylated.[21,22] Using $(DHQD)_2PHAL$ as the ligand, Sharpless dihydroxylation of enyne **14** generally yielded a mixture of diol **17** and butyrolactone **18** (Scheme 2). Heating of this mixture in toluene in presence of a trace of CSA converted the diol **17** to the lactone **18**. As we detected only one set of signals in the ^{13}C NMR spectrum of lactone **18**, a high diastereoselectivity for the hydroxylation reaction could be inferred. The lactone allowed for a selective protection of the 10-OH group (palmerolide numbering) as its *tert*-butyldiphenylsilyl ether **19**. Reduction of the lactone **19** with $LiAlH_4$ in THF led to diol **20**. However, this reduction was accompanied by some cleavage of the *tert*-butyldiphenylsilyl ether function yielding roughly a 3:1 mixture of **20** and **21**. Selective protection of the primary hydroxyl function, either on the mixture of **20** and **21**, or the separated compounds led to compounds **22** and **23**. We were surprised to see that treatment of the diol **23** with *tert*-butyldiphenylsilyl chloride/imidazole generated the alcohol **22** in a selective manner. It should be noted that with *tert*-butyldimethylsilyl chloride this reaction was not selective.



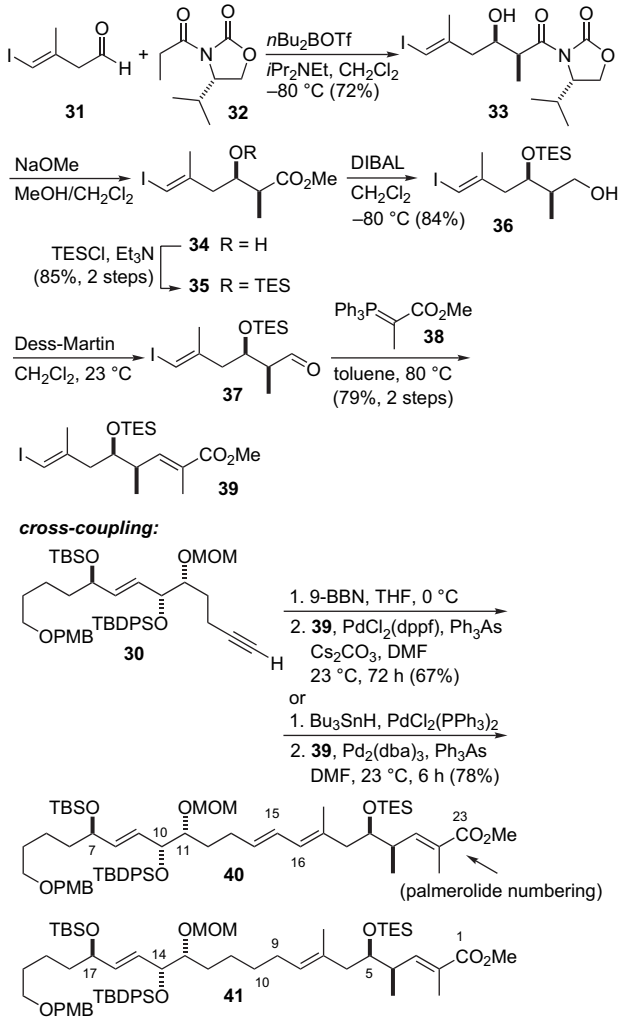
Scheme 2. Synthesis of alkyne **22** via the lactone **18**.

Based on the above results, we found it more convenient to perform the dihydroxylation not on the ester **14** but rather on the reduced derivative **16** of it. Using $(DHQD)_2PHAL$ as the ligand, Sharpless dihydroxylation of eneyne **16** provided the diol **23** in 77% yield (Scheme 3). Again, a high diastereoselectivity for the hydroxylation reaction could be concluded from the ^{13}C spectrum of diol **23**. As we had found, a selective silylation of the propargylic hydroxyl group of diol **23** to the silyl ether **22** was feasible. This allowed us to protect OH-11 of **22** with the MOM group yielding the fully protected compound **24**.[23] A subsequent treatment of compound **24** with camphorsulfonic acid (CSA) in a CH_2Cl_2/MeOH mixture removed the two *tert*-butyldimethylsilyl groups resulting in diol **25**. The free progargylic hydroxyl group of **25** allowed then for a reduction of the triple bond using Red-Al (5.5 equiv). This way the allylic alcohol **26** was obtained in 80% yield. Performing a selective oxidation of the primary alcohol function[10,24] of **26** using diacetoxyiodobenzene (2.2 equiv) and a catalytic amount of TEMPO gave rise to the hydroxy aldehyde **27**. The crude material could be converted to the alkyne **29** using the Bestmann–Ohira reagent, ketodiazophosphonate[25] **28**. The overall yield for this two-step transformation amounted to 51%. Finally, the allylic alcohol function of **29** was reprotected with *tert*-butyldimethylsilyl triflate, completing the synthesis of the C3–C15 fragment **30**.



Scheme 3. Completion of the synthesis of C3–C15 fragment **30**.

The synthesis of the C16–C23 fragment **39** relied on an Evans aldol reaction of 4-iodo-3-methyl-3-butenal[26] (**31**) with the propionyloxazolidinone[27] **32** (Scheme 4). The chiral auxiliary could be removed using NaOMe in a methanol/CH_2Cl_2 mixture[28] providing the hydroxyester **34**. This was followed by protecting the alcohol function using triethylsilyl chloride. Reduction of the ester **35** with DIBAL furnished alcohol **36** that was then oxidized to the aldehyde **37** using the Dess–Martin periodinane.[29] In a Wittig reaction



Scheme 4. Synthesis of the vinyl iodide **39** and its cross-coupling with the vinylborane, prepared in situ from the alkyne **30**, yielding the C3–C23 fragment **40** of palmerolide A. The dihydro compound **41** is formed with an excess of 9-BBN.

with phosphorane[30] **38** the enoate **39** was obtained (79% over two steps). The crucial cross-coupling reaction between the vinyl iodide **39** and a vinyl metal derivative of **30** turned out to be quite difficult. In a model study, the *tert*-butyldimethylsilyl ether of pentenol was reacted under the typical Heck conditions [$Pd(OAc)_2$, Et_3N, Cs_2CO_3, Bu_4NBr, DMF, 23 °C][31] with vinyl iodide **34**. While LC-MS analysis indicated formation of the diene, there were three signals with the correct mass. We surmised that double bond isomers were formed. Analysis by ^1H NMR did indeed show too many olefinic signals. A practical solution could be developed building upon a Suzuki cross-coupling reaction.[32] First, the alkyne **30** was reacted with 9-BBN in THF (0 °C, 36 h). Thereafter, the THF solution of the intermediate vinyl borane was added to a solution of the vinyl iodide **39** in DMF, containing $PdCl_2(dppf)$, $CsCO_3$, $AsPh_3$, and a trace of water.[33] Comparable results were obtained using the combination of $(Ph_3P)_4Pd$, and a mixture of 2 N NaOH and THF. The coupling reaction to give the key fragment **40** was complete within 72 h at room temperature. While the NMR spectrum of the tetraene **40** turned out to be quite complex, a characteristic signal appears at δ=6.16 ppm showing

coupling constants of 14.9 and 10.2 Hz, respectively. This signal was assigned to 15-H (palmerolide numbering). In order to improve the efficiency of the Suzuki cross-coupling, the hydroboration of alkyne **30** was also performed with an excess of 9-BBN (3 equiv). While the subsequent cross-coupling of the intermediate borane with **39** using the previous conditions [$PdCl_2$(dppf) (5 mol %), $AsPh_3$ (5 mol %), Cs_2CO_3 (2 equiv), trace of water, in DMF] proceeded cleanly, careful analysis of the product by NMR and LC-MS showed it to be the 9,10-dihydro derivative **41**. The formation of **41** might be explained by protonation of the initial vinyl borane with excess of 9-BBN followed by hydroboration of the resulting terminal alkene. Accordingly, we also examined the Stille cross-coupling[34] to produce **40**. Using palladium catalysis, the alkyne **30** was converted to the corresponding vinyl stannane.[35,36] Coupling of the crude stannane with vinyl iodide **39** in presence of $Pd_2(dba)_3$ (20 mol %), $AsPh_3$ (40 mol %) in DMF furnished tetraene **40** as well. Since these conditions gave **40** in higher yield and purity this is our preferred method for this case.

3. Conclusion

A convergent and efficient synthesis of the C3–C23 fragment of palmerolide A was developed. The stereocenters in the C3–C15 building block **30** were created by catalytic methods. The carbon skeleton of **30** originated from valerolactone, acetylene, acrolein, and triethyl orthoacetate. The enyne **14** was obtained via a Claisen rearrangement on the allylic alcohol **13**. A derivative of **14** was subjected to a Sharpless asymmetric dihydroxylation. Key to the synthesis was a selective silylation of the propargylic alcohol in the diol **22**. Using the free hydroxyl group at C7 allowed for a Red-Al mediated reduction of the triple bond of **25** to the *E* allyl alcohol **26**. A Stille cross-coupling reaction between the vinylstannane, generated from alkyne **30** and the vinyl iodide **39**, which was prepared via an Evans aldol strategy, delivered the C3–C23 fragment **40** of palmerolide A (**1**). While the revised structure of palmerolide A requires the enantiomer of **30**, adaption of the presented strategy should now enable the total synthesis of palmerolide A.

4. Experimental

4.1. General

^{1}H and ^{13}C NMR: Bruker Avance 400, spectra were recorded at 295 K either in $CDCl_3$ or acetone-d_6. Chemical shifts are calibrated to the residual proton and carbon resonance of the solvent: $CDCl_3$ (δH 7.25, δC 77.0 ppm); acetone-d_6 (δH 2.40, δC 29.8 ppm). HRMS (FT-ICR): Bruker Daltonic APEX 2 with electron spray ionization (ESI). Analytical LC-MS: HP 1100 Series connected with an ESI MS detector Agilent G1946C, positive mode with fragmentor voltage of 40 eV, column: Nucleosil 100–5, C-18 HD, 5 mm, 70×3 mm Machery-Nagel, eluent: NaCl solution (5 mM)/acetonitrile, gradient: 0–10–15–17–20 min with 20–80–80–99–99% acetonitrile, flow: 0.5 mL min^{-1}. Flash chromatography: J. T. Baker silica gel 43–60 μm. Thin-layer chromatography: Machery-Nagel Polygram Sil G/UV_{254}. Perkin–Elmer 341 Polarimeter, Na-lamp, 589 nm, 1 dm cuvette, 25 °C. Solvents were distilled prior to use; petroleum ether with a boiling range of 40–60 °C was used. Reactions were generally run under an argon atmosphere.

4.1.1. *para*-Methoxybenzyl-5-[(*para*-methoxybenzyl)-oxy]pentanoate (7). To a stirred solution of tetrahydro-2*H*-pyran-2-one (valerolactone, 2.2 mL, 24.14 mmol) and KOH (4.8 g, 85 mmol, 3.5 equiv) in toluene (50 mL) was added *para*-methoxybenzyl chloride[37] (16 mL, 118 mmol, 4.9 equiv) in one portion. The mixture was refluxed for 48 h (130 °C) with a Dean-Stark trap. After addition of water, the layers were separated and the aqueous layer was extracted twice with Et_2O. The combined organic layers were washed with saturated $NaHCO_3$ and NaCl solution, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash chromatography (petroleum ether/EtOAc, 10:1) to give 7.7 g (89%) of ester **7** as yellow oil. R_f=0.30 (petroleum ether/EtOAc, 5:1); ^{1}H NMR (400 MHz, acetone-d_6): δ [ppm]= 1.53–1.69 (m, 2H, 4-H), 1.69–1.79 (m, 2H, 3-H), 2.32 (t, J=7.3 Hz, 2H, 2-H), 3.41 (t, J=6.1 Hz, 2H, 5-H), 3.77 (s, 6H, CH_3O), 4.37 (s, 2H, PMB CH_2), 5.02 (s, 2H, PMB CH_2), 6.85–6.93 (m, 4H, CH_{ar}, *meta*), 7.24–7.36 (m, 4H, CH_{ar}, *ortho*); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm]=21.6 (C-3), 29.0 (C-4), 33.9 (C-2), 55.1 (OCH_3), 65.8 (PMB CH_2), 69.3 (C-5), 72.4 (PMB CH_2), 113.6 (CH_{ar}, *meta*), 113.8 (CH_{ar}, *meta*), 128.1 (C_{ar}), 129.1 (CH_{ar}, *ortho*), 129.9 (CH_{ar}, *ortho*), 130.5 (C_{ar}), 159.0 (C_{ar}, *para*), 159.5 (C_{ar}, *para*), 173.3 (C-1); HRMS (ESI): $[M+Na]^+$ calcd for $C_{21}H_{26}O_5$ 381.16725, found 381.16712.

4.1.2. 7-[(*para*-Methoxybenzyl)oxy]-1-(triisopropylsilyl)-hept-1-yn-3-one (8). To a stirred solution of ethynyl(triisopropyl)silane (7.5 mL, 33.5 mmol, 2 equiv) in THF (60 mL) at −80 °C was added *n*BuLi (13.5 mL, 1 M in hexane, 33.5 mmol, 2 equiv) dropwise. After stirring at this temperature for 45 min, a vigorously stirred solution of pentanoate **7** (6.0 g, 17.0 mmol) and $BF_3\cdot Et_2O$ (2 mL, 17 mmol) in THF (30 mL) was added slowly. After stirring for 12 h the mixture was diluted with Et_2O and treated with saturated NH_4Cl solution. The layers were separated and the aqueous layer was extracted twice with Et_2O. The combined organic layers were washed with 1 M NaOH solution, H_2O and NaCl solution, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (petroleum ether/EtOAc, 10:1) to give 5.8 g (86%) of alkynone **8** as light yellow oil. R_f=0.57 (petroleum ether/EtOAc, 5:1); ^{1}H NMR (400 MHz, acetone-d_6): δ [ppm]=1.05–1.19 (m, 21H, Si(C*H*$(CH_3)_2$)), 1.56–1.64 (m, 2H, 6-H), 1.71–1.81 (m, 2H, 5-H), 2.62 (t, J=7.3 Hz, 2H, 4-H), 3.44 (t, J=6.1 Hz, 2H, 7-H), 3.77 (s, 3H, CH_3O), 4.39 (s, 2H, PMB CH_2), 6.88 (d, J=8.7 Hz, 2H, CH_{ar}, *meta*), 7.24 (d, J=8.7 Hz, 2H, CH_{ar}, *ortho*); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm]=10.9 (Si(*C*H$(CH_3)_2$)), 18.4 (Si(CH(*C*$H_3)_2$)), 20.9 (C-5), 28.9 (C-6), 45.2 (C-4), 55.1 (CH_3O), 69.4 (C-7), 72.5 (PMB CH_2), 95.3 (C-1), 104.1 (C-2), 113.6 (CH_{ar}, *meta*), 129.1 (CH_{ar}, *ortho*), 130.5 (C_{ar}), 159.0 (C_{ar}, *para*), 187.5 (C-3); HRMS (ESI): $[M+Na]^+$ calcd for $C_{24}H_{38}O_3Si$ 425.24824, found 425.24834.

4.1.3. (3*R*)-7-[(*para*-Methoxybenzyl)oxy]-1-(triisopropylsilyl)hept-1-yn-3-ol (10). To a stirred solution of alkynone **8** (5.0 g, 12.4 mmol) in propan-2-ol (135 mL) the complex RuCl[(*R*,*R*)-NTsCH(Ph)CH(Ph)NH_2(η^6-cymene) (**9**)

(95 mg, catalytic amount), dissolved in a minimal amount of CH_2Cl_2 (0.7 mL), was added. The mixture was stirred at room temperature for 5 h. The solvent was removed and the brown residue purified by flash chromatography (petroleum ether/EtOAc, 9:1) to give 3.5 g (69%) of propargylic alcohol **10** as brown oil. Some starting material (1.5 g, 3.8 mmol) could be recovered. R_f=0.38 (petroleum ether/EtOAc, 5:1); $[\alpha]_D^{20}$ −1.6 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, acetone-d_6): δ [ppm]=1.02–1.07 (m, 21H, Si(C*H*(CH_3)$_2$)), 1.50–1.77 (m, 6H, 4-H, 5-H, 6-H), 1.94 (s, 1H, OH), 3.43 (t, *J*=6.4 Hz, 2H, 7-H), 3.78 (s, 3H, CH_3O), 4.36 (t, *J*=6.5 Hz, 1H, 3-H), 4.41 (s, 2H, PMB CH_2), 6.86 (d, *J*=8.7 Hz, 2H, CH_{ar}, *meta*), 7.24 (d, *J*=8.4 Hz, 2H, CH_{ar}, *ortho*); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm]=11.1 (Si(*C*H(CH$_3$)$_2$)), 18.6 (Si(CH(*C*H$_3$)$_2$)), 21.9 (C-5), 29.3 (C-6), 37.7 (C-4), 55.3 (CH_3O), 62.9 (C-3), 69.9 (C-7), 72.5 (PMB CH_2), 85.5 (C-1), 108.7 (C-2), 113.7 (CH_{ar}, *meta*), 129.2 (CH_{ar}, *ortho*), 130.7 (C_{ar}), 159.1 (C_{ar}, *para*); HRMS (ESI): [M+Na]$^+$ calcd for $C_{24}H_{40}O_3Si$ 427.26389, found 427.26373.

4.1.4. (3*R*)-7-[(*para*-Methoxybenzyl)oxy]hept-1-yn-3-ol (11). To a stirred solution of propargylic alcohol **10** (3.45 g, 8.53 mmol) in THF (25 mL) was added TBAF (9.7 mL, 1 M in THF, 9.7 mmol, 1.13 equiv). After stirring for 3 h at room temperature the reaction was quenched with saturated $NaHCO_3$ solution. The layers were separated and the aqueous layer was extracted twice with Et_2O. The combined organic layers were washed with saturated NaCl solution, dried over $MgSO_4$, filtered, and concentrated to give 3.6 g of crude product as yellow oil. The residue was used without further purification. GC analysis of **11** (fused silica column, 30% Lipodex E in PS255, 0.13 μm film, 80 °C, isothermal, carrier gas 50 kPa H_2) indicated an ee of 98%. An analytical amount was purified by flash chromatography (petroleum ether/EtOAc, 5:1). R_f=0.13 (petroleum ether/EtOAc, 5:1); $[\alpha]_D^{20}$ +2.7 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, acetone-d_6): δ [ppm]=1.47–1.75 (m, 6H, 4-H, 5-H, 6-H), 2.25 (s, 1H, OH), 2.43 (d, *J*=2.0 Hz, 1H, 1-H), 3.43 (t, *J*=6.5 Hz, 2H, 7-H), 3.78 (s, 3H, CH_3O), 4.29–4.36 (m, 1H, 3-H), 4.41 (s, 2H, PMB CH_2), 6.86 (d, *J*=8.4 Hz, 2H, CH_{ar}, *meta*), 7.24 (d, *J*=8.4 Hz, 2H, CH_{ar}, *ortho*); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm]=21.8 (C-5), 29.2 (C-6), 37.3 (C-4), 55.2 (CH_3O), 62.1 (C-3), 69.8 (C-7), 72.5 (PMB CH_2), 72.9 (C-1), 84.9 (C-2), 113.7 (CH_{ar}, *meta*), 129.2 (CH_{ar}, *ortho*), 130.5 (C_{ar}), 159.1 (C_{ar}, *para*); HRMS (ESI): [M+Na]$^+$ calcd for $C_{15}H_{20}O_3$ 271.13047, found 271.13080.

4.1.5. (3*R*)-3-{[*tert*-Butyl(dimethyl)silyl]oxy}-7-[(*para*-methoxybenzyl)oxy]-hept-1-yne (12). To a stirred solution of hept-1-yn-3-ol **11** (2 g crude, max. 5 mmol) in CH_2Cl_2 (31 mL) was added 2,6-lutidine (1.83 mL, 15 mmol, 3 equiv). After cooling to 0 °C, TBSOTf (1.3 mL, 5.48 mmol, 1.1 equiv) was added dropwise and the mixture was stirred for 20 min at this temperature. The mixture was diluted with CH_2Cl_2 and the organic layer was washed with H_2O, 1 N HCl, and saturated $NaHCO_3$ solution, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 10:1) to give 2.1 g (72%, over 2 steps) of silyl ether **12** as colorless oil. R_f=0.68 (petroleum ether/EtOAc, 5:1); $[\alpha]_D^{20}$ +32.0 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, acetone-d_6): δ [ppm]=0.12 (s, 3H, Si(CH$_3$)$_2$), 0.14 (s, 3H, Si(CH$_3$)$_2$), 0.90 (s, 9H, C(CH$_3$)$_3$), 1.47–1.74 (m, 6H, 4-H, 5-H, 6-H), 2.86–2.92 (m, 1H, 1-H), 3.43 (t, *J*=6.1 Hz, 2H, 7-H), 3.76 (s, 3H, CH_3O), 4.39 (s, 2H, PMB CH_2), 4.40–4.44 (m, 1H, 3-H), 6.87 (d, *J*=8.7 Hz, 2H, CH_{ar}, *meta*), 7.25 (d, *J*=8.4 Hz, 2H, CH_{ar}, *ortho*); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm]=−5.1 (Si(CH$_3$)$_2$), −4.6 (Si(CH$_3$)$_2$), 18.2 (*C*(CH$_3$)$_3$), 21.8 (C-5), 25.8 (C(*C*H$_3$)$_3$), 29.4 (C-6), 38.3 (C-4), 55.2 (CH_3O), 62.7 (C-3), 70.0 (C-7), 72.0 (C-1), 72.5 (PMB CH_2), 85.6 (C-2), 113.7 (CH_{ar}, *meta*), 129.2 (CH_{ar}, *ortho*), 130.7 (C_{ar}), 159.0 (C_{ar}, *para*); HRMS (ESI): [M+Na]$^+$ calcd for $C_{21}H_{34}O_3Si$ 385.21694, found 385.21671.

4.1.6. (6*R*)-6-{[*tert*-Butyl(dimethyl)silyl]oxy}-10-[(*para*-methoxybenzyl)oxy]dec-1-en-4-yne-3-ol (13). A solution of alkyne **12** (3.38 g, 9.31 mmol) in THF (45 mL) was treated at −80 °C with *n*BuLi (8.2 mL, 1 M in hexane, 20.48 mmol, 2.2 equiv). The mixture was stirred for 30 min, then warmed to room temperature. Now, LiBr (650 mg, 7.45 mmol, 0.8 equiv) was added and the mixture stirred until the LiBr was dissolved. It was then cooled to −80 °C before acrolein (1.44 mL, 20.48 mmol, 2.2 equiv) in THF (15 mL) was slowly added over a period of 30 min. After additional stirring for 2 h at −80 °C the reaction was quenched by addition of aqueous NH_4Cl solution and the mixture warmed to room temperature. The layers were separated and the aqueous layer was extracted twice with Et_2O. The combined organic layers were washed with saturated NaCl solution, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (petroleum ether/EtOAc, 10:1) to give 2.88 g (74%) of the allylic alcohol **13** as light yellow oil. R_f=0.38 (petroleum ether/EtOAc, 5:1); $[\alpha]_D^{20}$ +28.4 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm]=0.08, 0.11 (2s, 3H each, Si(CH$_3$)$_2$), 0.88 (s, 9H, C(CH$_3$)$_3$), 1.38–1.76 (m, 6H, 7-H, 8-H, 9-H), 2.03 (s, 1H, OH), 3.43 (t, *J*=6.5 Hz, 2H, 10-H), 3.79 (s, 3H, CH_3O), 4.38 (t, *J*=6.0 Hz, 1H, 6-H), 4.42 (s, 2H, PMB CH_2), 4.82–4.92 (m, 1H, 3-H), 5.19 (d, *J*=10.2 Hz, 1H, 1-H), 5.42 (d, *J*=17.0 Hz, 1H, 1-H), 5.86–6.00 (m, 1H, 2-H), 6.86 (d, *J*=8.7 Hz, 2H, CH_{ar}, *meta*), 7.25 (d, *J*=8.4 Hz, 2H, CH_{ar}, *ortho*); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm]=−5.0 (Si(CH$_3$)$_2$), −4.5 (Si(CH$_3$)$_2$), 18.2 (*C*(CH$_3$)$_3$), 21.9 (C-8), 25.8 (C(*C*H$_3$)$_3$), 29.3 (C-9), 38.2 (C-7), 55.2 (CH_3O), 62.8 (C-6), 63.1 (C-3), 69.8 (C-10), 72.5 (PMB CH_2), 82.6 (C-4), 88.1 (C-5), 113.7 (CH_{ar}, *meta*), 116.3 (C-1), 129.2 (CH_{ar}, *ortho*), 130.6 (C_{ar}), 136.9 (C-2), 159.1 (C_{ar}, *para*); HRMS (ESI): [M+Na]$^+$ calcd for $C_{24}H_{38}O_4Si$ 441.24316, found 441.24239.

4.1.7. Ethyl-(4*E*,8*R*)-8-{[*tert*-butyl(dimethyl)silyl]oxy}-12-[(*para*-methoxybenzyl)oxy]dodec-4-en-6-ynoate (14). A mixture of alcohol **13** (2.0 g, 5.0 mmol), triethylorthoacetate (4.6 mL, 25 mmol, 5 equiv), and propionic acid (3 drops) in xylene (25 mL) was refluxed (150 °C) for 2 h. After cooling, the mixture was concentrated under reduced pressure and the residue purified by flash chromatography (petroleum ether/EtOAc, 15:1) to give 1.9 g (79%) of 1,4-unsaturated ester **14** as light yellow oil. R_f=0.65 (petroleum ether/EtOAc, 5:1); $[\alpha]_D^{20}$ +22.0 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm]=0.08, 0.10 (2s, 3H each, Si(CH$_3$)$_2$), 0.88 (s, 9H, C(C*H*$_3$)$_3$), 1.23 (t, *J*=7.1 Hz, 3H, C*H*$_3$CH$_2$O), 1.36–1.75 (m, 6H, 9-H, 10-H, 11-H), 2.32–2.45 (m, 4H, 2-H, 3-H), 3.42 (t, *J*=6.6 Hz, 2H, 12-H), 3.78 (s, 3H,

CH_3O), 4.11 (q, J=7.1 Hz, 2H, CH_3CH_2O), 4.36–4.45 (m, 3H, 8-H, PMB CH_2), 5.51 (d, J=16.0 Hz, 1H, 5-H), 5.99–6.11 (m, 1H, 4-H), 6.85 (d, J=8.7 Hz, 2H, CH_{ar}, *meta*), 7.20 (d, J=8.7 Hz, 2H, CH_{ar}, *ortho*); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm]=−5.1 ($Si(CH_3)_2$), −4.5 ($Si(CH_3)_2$), 14.2 (OCH_2CH_3), 18.2 ($C(CH_3)_3$), 21.9 (C-10), 25.8 ($C(CH_3)_3$), 28.1 (C-3), 29.3 (C-11), 33.3 (C-2), 38.4 (C-9), 55.2 (CH_3O), 60.4 (C-8), 63.3 (OCH_2CH_3), 69.9 (C-12), 72.5 (PMB CH_2), 82.4 (C-6), 90.2 (C-7), 110.6 (C-5), 113.7 (CH_{ar}, *meta*), 129.1 (CH_{ar}, *ortho*), 130.7 (C_{ar}), 141.6 (C-4), 159.0 (C_{ar}, *para*), 172.5 (C-1); HRMS (ESI): $[M+Na]^+$ calcd for $C_{28}H_{44}O_5Si$ 511.28502, found 511.28510.

4.1.8. (4*E*,8*R*)-8-{[*tert*-Butyl(dimethyl)silyl]oxy}-12-[(*para*-methoxybenzyl)oxy]dodec-4-en-6-yn-1-ol (15). To a stirred suspension of $LiAlH_4$ (29 mg, 0.737 mmol, 1.2 equiv) in THF (2 mL) at 0 °C was added dropwise a solution of ester **14** (300 mg, 0.614 mmol) in THF (5 mL). After being stirred for 10 min, the reaction was quenched by addition of H_2O (0.03 mL), 1 M NaOH (0.03 mL), and H_2O (0.1 mL). After filtration the solvent was evaporated. The crude product was used without further purification. R_f= 0.08 (petroleum ether/EtOAc, 6:1); $[\alpha]_D^{20}$ +26.1 (*c* 1.00, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ [ppm]=0.09, 0.11 (2s, 3H each, $Si(CH_3)_2$), 0.89 (s, 9H, $C(CH_3)_3$), 1.41–1.78 (m, 8H, 2-H, 9-H, 10-H, 11-H), 2.13–2.23 (m, 2H, 3-H), 3.43 (t, J=6.5 Hz, 2H, 12-H), 3.62 (t, J=6.4 Hz, 2H, 1-H), 3.79 (s, 3H, CH_3O), 4.37–4.48 (m, 3H, 8-H, PMB CH_2), 5.46–5.55 (m, 1.40 Hz, 1H, 5-H), 6.01–6.14 (m, 1H, 4-H), 6.86 (d, J=8.7 Hz, 2H, CH_{ar}, *meta*), 7.24 (d, J=8.7 Hz, 2H, CH_{ar}, *ortho*); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm]=−5.0 ($Si(CH_3)_2$), −4.5 ($Si(CH_3)_2$), 18.2 ($C(CH_3)_3$), 22.0 (C-10), 25.8 ($C(CH_3)_3$), 29.3 (C-3), 29.4 (C-11), 31.5 (C-2), 38.5 (C-9), 55.2 (CH_3O), 62.0 (C-8), 63.3 (C-1), 70.0 (C-12), 72.5 (PMB CH_2), 82.7 (C-6), 89.7 (C-7), 109.9 (C-5), 113.7 (CH_{ar}, *meta*), 129.2 (CH_{ar}, *ortho*), 130.7 (C_{ar}), 143.4 (C-4), 159.0 (C_{ar}, *para*); HRMS (ESI): $[M+Na]^+$ calcd for $C_{26}H_{42}O_4Si$ 469.27446, found 469.27487.

4.1.9. (4*E*,8*R*)-1,8-Di-{[*tert*-butyl(dimethyl)silyl]oxy}-12-[(*para*-methoxybenzyl)oxy]dodec-4-en-6-yne (16). To a stirred solution of alcohol **15** (253 mg crude, max. 0.614 mmol) in DMF (6 mL) were added imidazole (64 mg, 0.960 mmol, 1.5 equiv) and DMAP (cat.). At 0 °C TBSCl (110 mg, 0.737 mmol, 1.2 equiv) was added and the mixture stirred for 3 h before it was diluted with Et_2O. Then H_2O was added and after separation of the layers, the organic layer was washed with saturated NaCl solution, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 10:1) to give 300 mg (87%, over 2 steps) of silyl ether **16** as yellow oil. R_f=0.70 (petroleum ether/EtOAc, 6:1); $[\alpha]_D^{20}$ +18.9 (*c* 1.00, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ [ppm]=0.03 (s, 6H, 1-$OSi(CH_3)_2$), 0.09, 0.11 (2s, 3H each, $Si(CH_3)_2$), 0.88 (s, 9H, 1-$OSi(CH_3)_2C(CH_3)_3$), 0.89 (s, 9H, 8-$OSi(CH_3)_2C(CH_3)_3$), 1.39–1.75 (m, 8H, 2-H, 9-H, 10-H, 11-H), 2.10–2.20 (m, 2H, 3-H), 3.43 (t, J=6.6 Hz, 2H, 12-H), 3.59 (t, J=6.2 Hz, 2H, 1-H), 3.79 (s, 3H, CH_3O), 4.38–4.46 (m, 3H, 8-H, PMB CH_2), 5.43–5.52 (m, 1H, 5-H), 6.02–6.14 (m, 1H, 4-H), 6.86 (d, J=8.7 Hz, 2H, CH_{ar}, *meta*), 7.25 (d, J=8.4 Hz, 2H, CH_{ar}, *ortho*); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm]=−5.3 (1-$OSi(CH_3)_2$), −5.0 (8-$OSi(CH_3)_2$, −4.5 (8-$OSi(CH_3)_2$), 18.3 (1-$OSi(CH_3)_2C(CH_3)_3$), 18.3 (8-$OSi(CH_3)_2C(CH_3)_3$), 22.0 (C-10), 25.8 (1-$OSi(CH_3)_2C(CH_3)_3$), 25.9 (8-$OSi(CH_3)_2C(CH_3)_3$), 29.4 (C-3), 29.4 (C-11), 31.7 (C-2), 38.5 (C-9), 55.3 (CH_3O), 62.2 (C-8), 63.3 (C-1), 70.0 (C-12), 72.5 (PMB CH_2), 82.8 (C-6), 89.5 (C-7), 109.5 (C-5), 113.7 (CH_{ar}, *meta*), 129.2 (CH_{ar}, *ortho*), 130.7 (C_{ar}), 143.9 (C-4), 159.1 (C_{ar}, *para*); HRMS (ESI): $[M+Na]^+$ calcd for $C_{32}H_{56}O_4Si_2$ 583.36093, found 583.35994.

4.1.10. Ethyl (4*R*,5*R*,8*R*)-8-{[*tert*-butyl(dimethyl)silyl]-oxy}-4,5-dihydroxy-12-[(*para*-methoxybenzyl)oxy]dodec-6-ynoate (17) and (5′*R*)-5′-{(1*R*,4*R*)-4-{[*tert*-butyl(dimethyl)silyl]oxy}-1-hydroxy-8-[(*para*-methoxybenzyl)oxy]-oct-2-ynyl}dihydrofuran-2′(3*H*)-one (18). $(DHQD)_2PHAL$ (30.9 mg, cat.), $K_3Fe(CN)_6$ (3.9 g, 11.5 mmol, 3 equiv), K_2CO_3 (1.6 g, 11.5 mmol, 3 equiv), and $K_2OsO_2(OH)_4$ (7 mg, cat.) were dissolved in a 1:1 mixture of water (20 mL) and *tert*-butyl alcohol (20 mL). $MeSO_2NH_2$ (374 mg, 3.9 mmol, 1 equiv) was added and the vigorously stirred solution was cooled to 0 °C. At this point unsaturated ester **14** (1.9 g, 3.9 mmol) was added in one portion and the mixture allowed to warm to room temperature within 4 h. Stirring was continued for 10 h before the reaction was quenched by addition of solid Na_2SO_3 (5.6 g). The solution was extracted twice with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue, a mixture of ester and lactone, was used in the following step without further purification.

To a stirred solution of dihydroxy ester **17** (crude, max. 3.9 mmol) in toluene (135 mL) was added CSA (100 mg, cat.) and the mixture was stirred at 80 °C for 6 h. After cooling, the mixture was treated with solid $CaCO_3$ (220 mg). After filtration, the solution was concentrated in vacuo and the residue, lactone **18**, was used without further purification. R_f=0.15 (petroleum ether/EtOAc, 5:1); ^1H NMR (400 MHz, $CDCl_3$): δ [ppm]=0.07, 0.10 (2s, 3H each, $Si(CH_3)_2$), 0.88 (s, 9H, $SiC(CH_3)_3$), 1.37–1.70 (m, 6H, 5-H, 6-H, 7-H), 2.06–2.35 (m, 2H, 4′-H), 2.40–2.60 (m, 2H, 3′-H), 3.43 (t, J=6.4 Hz, 2H, 8-H), 3.79 (s, 3H, CH_3O), 4.36 (t, J=6.2 Hz, 1H, 4-H), 4.41 (s, 2H, PMB CH_2), 4.42–4.57 (m, 2H, 1-H, 5′-H), 6.86 (d, J=8.7 Hz, 2H, CH_{ar}, *meta*), 7.24 (d, J=8.4 Hz, 2H, CH_{ar}, *ortho*); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm]=−5.1 ($Si(CH_3)_2$), −4.6 ($Si(CH_3)_2$), 18.2 ($SiC(CH_3)_3$), 21.8 (C-4′), 23.4 (C-6), 25.7 ($SiC(CH_3)_3$), 28.1 (C-3′), 29.3 (C-7), 38.1 (C-5), 55.3 (CH_3O), 62.7 (C-4), 64.7 (C-1), 69.8 (C-8), 72.5 (PMB CH_2), 80.0 (C-2), 81.4 (C-5′), 88.9 (C-3), 113.7 (CH_{ar}, *meta*), 129.3 (CH_{ar}, *ortho*), 130.6 (C_{ar}), 159.1 (C_{ar}, *para*), 176.6 (C-2′).

4.1.11. (5′*R*)-5′-{(1*R*,4*R*)-4-{[*tert*-Butyl(dimethyl)silyl]-oxy}-1-{[*tert*-butyl(diphenyl)silyl]oxy}-8-[(*para*-methoxybenzyl)oxy]oct-2-ynyl}dihydrofuran-2′(3*H*)-one (19). To a stirred solution of lactone **18** (1.73 g crude, max. 3.635 mmol, 1 equiv) in CH_2Cl_2 (22 mL) was added imidazole (727 mg, 5.2 mmol, 3 equiv). At 0 °C TBDPSCl (1.4 mL, 2.6 mmol, 1.5 equiv) was added and the mixture stirred for 4 h. This was followed by the addition of saturated NaCl solution and separation of the layers. The aqueous layer was extracted twice with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 8:1) to give 2.19 g (84%, over 3

steps) of silyl ether **19** as light yellow oil. R_f=0.60 (petroleum ether/EtOAc, 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm]= 0.04, 0.05 (2s, 3H each, $Si(CH_3)_2$), 0.85 (s, 9H, $Si(CH_3)_2C(CH_3)_3$), 1.06 (s, 9H, $Si(Ph)_2C(CH_3)_3$), 1.20–1.60 (m, 6H, 5-H, 6-H, 7-H), 2.18–2.35 (m, 2H, 4′-H), 2.36–2.67 (m, 2H, 3′-H), 3.38 (t, J=6.4 Hz, 2H, 8-H), 3.77 (s, 3H, CH_3O), 4.19 (t, J=6.2 Hz, 1H, 4-H), 4.40 (s, 2H, PMB CH_2), 4.41–4.54 (m, 2H, 1-H, 5′-H), 6.85 (d, J=8.7 Hz, 2H, CH_{ar}, *meta*), 7.24 (d, J=8.4 Hz, 2H, CH_{ar}, *ortho*), 7.30–7.45 (m, 6H, phenyl), 7.60–7.73 (m, 4H, phenyl); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm]=−5.2 ($Si(CH_3)_2$), −4.6 ($Si(CH_3)_2$), 18.1 ($Si(CH_3)_2C(CH_3)_3$), 19.3 ($Si(Ph)_2C(CH_3)_3$), 21.8 (C-6), 22.6 (C-4′), 25.7 ($Si(CH_3)_2C(CH_3)_3$), 26.8 ($Si(Ph)_2C(CH_3)_3$), 27.9 (C-3′), 29.3 (C-7), 38.0 (C-5), 55.2 (CH_3O), 62.6 (C-4), 65.5 (C-1), 69.9 (C-8), 72.5 (PMB CH_2), 80.3 (C-2), 80.6 (C-5′), 88.7 (C-3), 113.7 (CH_{ar}, *meta*), 127.5 (phenyl), 127.8 (phenyl), 129.2 (CH_{ar}, *ortho*), 129.8 (phenyl), 130.0 (phenyl), 130.7 (CH_{ar}), 132.6 (phenyl), 132.8 (phenyl), 135.7 (phenyl), 135.9 (phenyl), 159.0 (C_{ar}, *para*), 176.7 (C-2′).

4.1.12. (4*R*,5*R*,8*R*)-8-{[*tert*-Butyl(dimethyl)silyl]oxy}-5-{[*tert*-butyl(diphenyl)silyl]oxy}-12-[(*para*-methoxybenzyl)oxy]dodec-6-yne-1,4-diol (20) and (4*R*,5*R*,8*R*)-8-{[*tert*-butyl(dimethyl)silyl]oxy}-12-[(*para*-methoxybenzyl)-oxy]dodec-6-yne-1,4,5-triol (21). A suspension of $LiAlH_4$ (80 mg, 2.1 mmol, 1.5 equiv) in THF (15 mL) was cooled to 0 °C and a solution of lactone **19** (1.0 g, 1.4 mmol, 1 equiv) in THF (20 mL) was added dropwise. The mixture was stirred for 15 min. This was followed by the addition of saturated NH_4Cl solution and separation of the layers. The aqueous layer was extracted twice with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude mixture of diol **20** and triol **21** was used in the following step without further purification. R_f (**20**)=0.15 (petroleum ether/EtOAc, 3:1); R_f (**21**)=0.01 (petroleum ether/EtOAc, 3:1).

4.1.13. (4*R*,5*R*,8*R*)-1,8-Di-{[*tert*-butyl(dimethyl)silyl]-oxy}-5-{[*tert*-butyl(diphenyl)silyl]oxy}-12-[(*para*-methoxybenzyl)oxy]dodec-6-yne-4-ol (22).

4.1.13.1. By selective silylation of the primary alcohol function of diol 20. A crude mixture of diol **20** and triol **21** (1.0 g, max. 1.4 mmol) was dissolved in DMF (13 mL) followed by the addition of imidazole (145 mg, 2.1 mmol, 1.5 equiv) and DMAP (cat.). At 0 °C TBSCl (250 mg, 1.55 mmol, 1.1 equiv) was added and the mixture was stirred for 1 h at room temperature before it was diluted with Et_2O. Now, H_2O was added and after separation of the layers, the organic layer was washed with saturated NaCl solution, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 9:1) to give 525 mg (45%, over 2 steps) of alcohol **22** and 350 mg (42%, over 2 steps) of diol **23** as light yellow oils.

4.1.13.2. By selective silylation of diol 23. To a stirred solution of diol **23** (1.18 g, 2 mmol) in CH_2Cl_2 (10 mL) was added imidazole (405 mg, 6.0 mmol, 3 equiv). After cooling to 0 °C TBDPSCl (0.58 mL, 2.2 mmol, 1.1 equiv) was added and the mixture stirred for 3 h. This was followed by the addition of saturated NaCl solution and separation of the layers. The aqueous layer was extracted twice with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 15:1) to give 1.25 g (75%) of alcohol **22** as light yellow oil. R_f=0.53 (petroleum ether/EtOAc, 6:1); $[\alpha]_D^{20}$ −10.3 (c 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm]= 0.02 (s, 6H, 1-$OSi(CH_3)_2$), 0.03 (s, 6H, 8-$OSi(CH_3)_2$), 0.84 (s, 9H, 1-$OSi(CH_3)_2C(CH_3)_3$), 0.88 (s, 9H, 8-$OSi(CH_3)_2C(CH_3)_3$), 1.06 (s, 9H, $OSi(Ph)_2C(CH_3)_3$), 1.17–1.91 (m, 10H, 2-H, 3-H, 9-H, 10-H, 11-H), 2.64 (s, 1H, OH), 3.36 (t, J=6.7 Hz, 2H, 12-H), 3.57–3.64 (m, 3H, 1-H, 4-H), 3.79 (s, 3H, CH_3O), 4.11 (t, J=5.6 Hz, 1H, 8-H), 4.27 (d, J=6.4 Hz, 1H, 5-H), 4.42 (s, 2H, PMB CH_2), 6.87 (d, J=8.7 Hz, 2H, CH_{ar}, *meta*), 7.25 (d, J=8.7 Hz, 2H, CH_{ar}, *ortho*), 7.29–7.45 (m, 6H, phenyl), 7.63–7.76 (m, 4H, phenyl); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm]=−5.3 (1-$OSi(CH_3)_2$), −5.1 (8-$OSi(CH_3)_2$), −4.5 (8-$OSi(CH_3)_2$), 18.1 (1-$OSi(CH_3)_2C(CH_3)_3$), 18.3 (8-$OSi(CH_3)_2C(CH_3)_3$), 19.3 ($OSi(Ph)_2C(CH_3)_3$), 21.8 (C-10), 25.7 (8-$OSi(CH_3)_2C(CH_3)_3$), 26.0 (1-$OSi(CH_3)_2C(CH_3)_3$), 26.9 ($OSi(Ph)_2C(CH_3)_3$), 28.8 (C-11), 29.1 (C-2), 29.3 (C-3), 38.0 (C-9), 55.2 (CH_3O), 62.6 (C-8), 63.3 (C-1), 68.1 (C-5), 70.0 (C-12), 72.5 (PMB CH_2), 74.8 (C-4), 82.0 (C-6), 88.5 (C-7), 113.7 (CH_{ar}, *meta*), 127.4 (phenyl), 127.7 (phenyl), 129.2 (CH_{ar}, *ortho*), 129.6 (phenyl), 129.9 (phenyl), 130.7 (C_{ar}), 133.0 (phenyl), 133.3 (phenyl), 135.8 (phenyl), 136.0 (phenyl), 159.1 (C_{ar}, *para*); HRMS (ESI): $[M+Na]^+$ calcd for $C_{48}H_{76}O_6Si_3$ 855.48419, found 855.48473.

4.1.14. (4*R*,5*R*,8*R*)-1,8-Di-{[*tert*-butyl(dimethyl)silyl]-oxy}-12-[(*para*-methoxybenzyl)oxy]dodec-6-yne-4,5-diol (23). $(DHQD)_2PHAL$ (4.3 mg, cat.), $K_3Fe(CN)_6$ (532 mg, 1.6 mmol, 3 equiv), K_2CO_3 (226 mg, 1.6 mmol, 3 equiv), and $K_2OsO_2(OH)_4$ (1 mg, cat.) were dissolved in a 1:1 mixture of water (3 mL) and *tert*-butyl alcohol (3 mL). $MeSO_2NH_2$ (52 mg, 0.54 mmol, 1 equiv) was added and the vigorously stirred solution was cooled to 0 °C. At this point the enyne **16** (300 mg, 0.53 mmol) was added in one portion and the mixture allowed to warm to room temperature within 4 h. Stirring was continued for 10 h before the reaction was quenched by addition of solid Na_2SO_3 (770 mg). The solution was extracted twice with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 6:1) to give 243 mg (77%) of diol **23** as light yellow oil. R_f=0.25 (petroleum ether/EtOAc, 6:1); $[\alpha]_D^{20}$ +20.2 (c 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm]=0.06 (s, 6H, 1-$OSi(CH_3)_2$), 0.08, 0.11 (2s, 3H each, $Si(CH_3)_2$), 0.88 (s, 9H, 1-$OSi(CH_3)_2C(CH_3)_3$), 0.89 (s, 9H, 8-$OSi(CH_3)_2C(CH_3)_3$), 1.34–1.92 (m, 10H, 2-H, 3-H, 9-H, 10-H, 11-H), 3.42 (t, J=6.5 Hz, 2H, 12-H), 3.52–3.73 (m, 3H, 4-H, 1-H), 3.79 (s, 3H, CH_3O), 4.16 (d, J=6.9 Hz, 1H, 5-H), 4.35 (t, J=5.7 Hz, 1H, 8-H), 4.41 (s, 2H, PMB CH_2), 6.86 (d, J=8.7 Hz, 2H, CH_{ar}, *meta*), 7.24 (d, J=8.4 Hz, 2H, CH_{ar}, *ortho*); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm]=−5.4 (1-$OSi(CH_3)_2$), −5.0 (8-$OSi(CH_3)_2$), −4.5 (8-$OSi(CH_3)_2$), 18.2 (1-$OSi(CH_3)_2C(CH_3)_3$), 18.3 (8-$OSi(CH_3)_2C(CH_3)_3$), 21.9 (C-10), 25.8 (8-$OSi(CH_3)_2C(CH_3)_3$), 25.9 (1-$OSi(CH_3)_2C(CH_3)_3$), 28.9 (C-11), 29.3 (C-2), 30.3 (C-3), 38.2 (C-9), 55.2 (CH_3O), 62.8 (C-8), 63.5 (C-1), 66.3 (C-5), 69.9 (C-12), 72.5 (PMB CH_2), 74.6 (C-4), 82.2 (C-6), 87.8 (C-7), 113.7 (CH_{ar}, *meta*), 129.2 (CH_{ar}, *ortho*), 130.6 (C_{ar}), 159.1 (C_{ar}, *para*); HRMS

(ESI): $[M+Na]^+$ calcd for $C_{32}H_{58}O_6Si_2$ 617.36641, found 617.36628.

4.1.15. (4*R*,5*R*,8*R*)-1,8-Di-{[*tert*-butyl(dimethyl)silyl]-oxy}-5-{[*tert*-butyl(diphenyl)silyl]oxy}-12-[(*para*-methoxybenzyl)oxy]-4-(methoxymethoxy)dodec-6-yne (24). To a stirred solution of 6-yne-4-ol **22** (1.2 g, 1.44 mmol) in $CH_2(OCH_3)_2$ (22 mL), were added LiBr (46 mg, 0.4 equiv) and *para*-toluenesulfonic acid (46 mg, 0.2 equiv) at room temperature and followed by stirring of the mixture for 4 days. The mixture was treated with saturated NaCl solution and extracted twice with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 10:1) to give 1.03 g (82%) of MOM ether **24** as light yellow oil. R_f=0.60 (petroleum ether/EtOAc, 6:1); $[\alpha]_D^{20}$ −4.0 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm]=0.03 (s, 6H, 1-OSi$(CH_3)_2$), 0.04 (s, 6H, 8-OSi$(CH_3)_2$), 0.84 (s, 9H, 1-OSi$(CH_3)_2$C$(CH_3)_3$), 0.89 (s, 9H, 8-OSi$(CH_3)_2$C$(CH_3)_3$), 1.05 (s, 9H, OSi$(Ph)_2$C$(CH_3)_3$), 1.18–2.01 (m, 10H, 2-H, 3-H, 9-H, 10-H, 11-H), 3.20 (s, 3H, CH_3OCH_2O), 3.31–3.46 (m, 3H, 4-H, 12-H), 3.53–3.69 (m, 2H, 1-H), 3.79 (s, 3H, CH_3O), 4.14–4.26 (m, 1H, 8-H), 4.34–4.55 (m, 5H, 5-H, CH_3OCH_2O, PMB CH_2), 6.86 (d, *J*=8.7 Hz, 2H, CH_{ar}, *meta*), 7.25 (d, *J*=8.4 Hz, 2H, CH_{ar}, *ortho*), 7.29–7.45 (m, 6H, phenyl), 7.61–7.75 (m, 4H, phenyl); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm]=−5.3 (1-OSi$(CH_3)_2$), −4.5 (8-OSi$(CH_3)_2$), 18.1 (1-OSi$(CH_3)_2C(CH_3)_3$), 18.3 (8-OSi$(CH_3)_2C(CH_3)_3$), 19.2 (OSi$(Ph)_2C(CH_3)_3$), 21.8 (C-10), 25.8 (8-OSi$(CH_3)_2$C$(CH_3)_3$), 26.0 (1-OSi$(CH_3)_2$C$(CH_3)_3$), 26.9 (OSi$(Ph)_2$C$(CH_3)_3$), 27.0 (C-11), 29.2 (C-3), 29.4 (C-2), 38.2 (C-9), 55.2 (CH_3O PMB), 55.5 (CH_3OCH_2), 62.7 (C-8), 63.3 (C-1), 66.2 (C-5), 70.0 (C-12), 72.5 (PMB CH_2), 80.8 (C-4), 82.3 (C-6), 87.6 (C-7), 96.9 (CH_3OCH_2O), 113.7 (CH_{ar}, *meta*), 127.4 (phenyl), 127.6 (phenyl), 129.1 (CH_{ar}, *ortho*), 129.5 (phenyl), 129.8 (phenyl), 130.7 (C_{ar}), 133.3 (phenyl), 133.4 (phenyl), 135.8 (phenyl), 135.9 (phenyl), 159.4 (C_{ar}, *para*); HRMS (ESI): $[M+Na]^+$ calcd for $C_{50}H_{80}O_7Si_3$ 899.51041, found 899.51123.

4.1.16. (4*R*,5*R*,8*R*)-5-{[*tert*-Butyl(diphenyl)silyl]oxy}-12-[(*para*-methoxybenzyl)oxy]-4-(methoxymethoxy)dodec-6-yne-1,8-diol (25). The fully protected dodec-6-yne derivative **24** (930 mg, 1.06 mmol) was dissolved in a 1:1 mixture of methanol (8 mL) and CH_2Cl_2 (8 mL). CSA (cat.) was added and the mixture stirred at room temperature for 4 h. The reaction was quenched with saturated $NaHCO_3$ solution and the mixture extracted twice with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 1:3) to give 470 mg (69%) of diol **25** as light yellow oil. R_f=0.37 (petroleum ether/EtOAc, 1:3); $[\alpha]_D^{20}$ −22.5 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm]=1.05 (s, 9H, Si$(Ph)_2$C$(CH_3)_3$), 1.27–1.80 (m, 10H, 2-H, 3-H, 9-H, 10-H, 11-H), 3.27 (s, 3H, CH_3OCH_2O), 3.39 (t, *J*=6.6 Hz, 2H, 12-H), 3.50–3.58 (m, 1H, 4-H), 3.62 (t, *J*=5.7 Hz, 2H, 1-H), 3.79 (s, 3H, CH_3O), 4.01–4.18 (m, 1H, 8-H), 4.41 (s, 2H, PMB CH_2), 4.46–4.66 (m, 3H, 5-H, CH_3OCH_2O), 6.86 (d, *J*=8.7 Hz, 2H, CH_{ar}, *meta*), 7.24 (d, *J*=7.1 Hz, 2H, CH_{ar}, *ortho*), 7.30–7.49 (m, 6H, phenyl), 7.63–7.78 (m, 4H, phenyl); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm]=19.2 (OSi$(Ph)_2C(CH_3)_3$), 21.8 (C-10), 26.8 (OSi$(Ph)_2$C$(CH_3)_3$), 27.0 (C-3), 28.7 (C-11), 29.3 (C-2), 37.1 (C-9), 55.3 (CH_3O PMB), 55.7 (CH_3OCH_2), 62.1 (C-8), 62.8 (C-1), 66.4 (C-5), 69.9 (C-12), 72.6 (PMB CH_2), 80.6 (C-4), 83.3 (C-7), 87.6 (C-6), 97.1 (CH_3OCH_2O), 113.8 (CH_{ar}, *meta*), 127.4 (phenyl), 127.7 (phenyl), 129.3 (CH_{ar}, *ortho*), 129.7 (phenyl), 129.9 (phenyl), 130.6 (C_{ar}), 133.0 (phenyl), 133.7 (phenyl), 135.8 (phenyl), 136.1 (phenyl), 159.1 (C_{ar}, *para*); HRMS (ESI): $[M+Na]^+$ calcd for $C_{38}H_{52}O_7Si$ 671.33745, found 671.33814.

4.1.17. (4*R*,5*R*,6*E*,8*R*)-5-{[*tert*-Butyl(diphenyl)silyl]oxy}-12-[(*para*-methoxybenzyl)oxy]-4-(methoxymethoxy)dodec-6-ene-1,8-diol (26). To a stirred solution of alkynediol **25** (470 mg, 0.72 mmol) in THF (25 mL) was added at 0 °C a solution of Red-Al (1.2 mL, 65% in toluene, 4.0 mmol, 5.5 equiv). The mixture was allowed to warm to room temperature and stirring was continued for 12 h. After being quenched with 1 N HCl, the mixture was extracted twice with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 1:3) to give 375 mg (80%) of allylic alcohol **26** as light yellow oil. R_f=0.20 (petroleum ether/EtOAc, 1:3); $[\alpha]_D^{20}$ +8.7 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm]=1.06 (s, 9H, Si$(Ph)_2$C$(CH_3)_3$), 1.17–1.69 (m, 10H, 2-H, 3-H, 9-H, 10-H, 11-H), 3.23 (s, 3H, CH_3OCH_2O), 3.32–3.43 (m, 3H, 4-H, 12-H), 3.56 (t, *J*=6.2 Hz, 2H, 1-H), 3.79 (s, 3H, CH_3O), 3.88–3.99 (m, 1H, 8-H), 4.30–4.49 (m, 5H, 5-H, CH_3OCH_2O, PMB CH_2), 5.40–5.53 (m, 1H, 6-H), 5.54–5.66 (m, 1H, 7-H), 6.86 (d, *J*=8.7 Hz, 2H, CH_{ar}, *meta*), 7.24 (d, *J*=8.4 Hz, 2H, CH_{ar}, *ortho*), 7.29–7.48 (m, 6H, phenyl), 7.57–7.71 (m, 4H, phenyl); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm]=19.3 (Si$(Ph)_2C(CH_3)_3$), 22.0 (C-10), 26.1 (C-11), 27.0 (Si$(Ph)_2$C$(CH_3)_3$), 29.0 (C-3), 29.6 (C-2), 36.6 (C-9), 55.2 (CH_3O PMB), 55.7 (CH_3OCH_2O), 62.8 (C-1), 69.9 (C-12), 72.2 (C-8), 72.5 (PMB CH_2), 74.4 (C-5), 81.3 (C-4), 97.0 (CH_3OCH_2O), 113.7 (CH_{ar}, *meta*), 127.5 (phenyl), 127.6 (phenyl), 128.8 (CH_{ar}, *ortho*), 129.3 (C-6), 129.7 (phenyl), 129.8 (phenyl), 130.6 (C_{ar}), 133.7 (phenyl), 133.9 (phenyl), 135.3 (C-7), 135.9 (phenyl), 135.9 (phenyl), 159.1 (C_{ar}, *para*); HRMS (ESI): $[M+Na]^+$ calcd for $C_{38}H_{54}O_7Si$ 673.35310, found 673.35320.

4.1.18. (4*R*,5*R*,6*E*,8*R*)-5-{[*tert*-Butyl(diphenyl)silyl]oxy}-8-hydroxy-12-[(*para*-methoxybenzyl)oxy]-4-(methoxymethoxy)dodec-6-enal (27). To a stirred solution of 1,8-diol **26** (50 mg, 0.077 mmol) in CH_2Cl_2 (5 mL) was added a solid mixture of $PhI(OAc)_2$ (55 mg, 0.17 mmol, 2.2 equiv) and TEMPO (3 mg, 0.017 mmol, 0.22 equiv). After stirring at air for 6 h, TLC showed complete conversion to the aldehyde. The reaction was quenched with 10% $Na_2S_2O_3$ solution and the product was extracted twice with CH_2Cl_2. The combined organic layers were washed with $NaHCO_3$ solution and water, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was used without further purification. An analytical sample was subjected to flash chromatography (petroleum ether/EtOAc, 1.5:1). R_f=0.48 (petroleum ether/EtOAc, 1:2); ^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm]=1.07 (s, 9H, Si$(Ph)_2$C$(CH_3)_3$), 1.17–1.70 (m, 8H, 3-H, 9-H, 10-H, 11-H), 2.36–2.56 (m, 2H, 2-H), 3.21 (s, 3H, CH_3OCH_2O), 3.27–3.36 (m, 1H, 4-H), 3.40 (t, *J*=6.6 Hz, 2H, 12-H), 3.79 (s, 3H, CH_3O PMB), 3.91–4.00 (m, 1H, 8-H), 4.29–4.39 (m, 3H, 5-H, CH_3OCH_2O), 4.41 (s, 2H, PMB CH_2), 5.43–5.73 (m, 2H, 6-H, 7-H), 6.86 (d, *J*=8.7 Hz, 2H, CH_{ar},

meta), 7.24 (d, J=6.9 Hz, 2H, CH_{ar}, *ortho*), 7.29–7.47 (m, 6H, phenyl), 7.58–7.71 (m, 4H, phenyl), 9.70 (s, 1H, 1-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm]=19.3 ($OSi(Ph)_2$-$C(CH_3)_3$), 22.1 (C-10), 22.3 (C-3), 27.0 ($OSi(Ph)_2C(CH_3)_3$), 29.6 (C-11), 36.7 (C-9), 40.5 (C-2), 55.3 (CH_3O PMB), 55.7 (CH_3OCH_2O), 70.0 (C-12), 72.1 (C-8), 72.5 (PMB CH_2), 74.0 (C-4), 80.6 (C-5), 97.1 (CH_3OCH_2O), 113.7 (CH_{ar}, *meta*), 127.5 (phenyl), 127.7 (phenyl), 128.2 (C-6), 129.2 (CH_{ar}, *ortho*), 129.7 (phenyl), 129.9 (phenyl), 130.7 (C_{ar}), 133.6 (phenyl), 133.8 (phenyl), 135.5 (C-7), 135.9 (phenyl), 135.9 (phenyl), 159.1 (C_{ar}, *para*), 202.3 (C-1).

4.1.19. (5*R*,6*E*,8*R*,9*R*)-8-{[*tert*-Butyl(diphenyl)silyl]oxy}-1-[(*para*-methoxybenzyl)oxy]-9-(methoxymethoxy)tridec-6-en-12-yn-5-ol (29). Diethyl-1-diazo-2-oxopropylphosphonate (**28**) (25 mg, 0.12 mmol, 1.5 equiv) was added to a stirred solution of hydroxy aldehyde **27** (max. 0.077 mmol, 1 equiv, crude) and K_2CO_3 (20 mg, 2 equiv) and stirring was continued for 12 h. The reaction mixture was diluted with Et_2O and washed with $NaHCO_3$ solution. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 1.5:1) to give 25 mg (51%, over 2 steps) of alkynol **29** as light yellow oil. R_f=0.60 (petroleum ether/EtOAc, 1:1); $[\alpha]_D^{20}$ +8.1 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm]=1.07 (s, 9H, $Si(Ph)_2C(CH_3)_3$), 1.16–1.70 (m, 8H, 2-H, 3-H, 4-H, 10-H), 1.90 (s, 1H, 13-H), 2.12–2.36 (m, 2H, 11-H), 3.21 (s, 3H, CH_3OCH_2O), 3.39 (t, J=6.6 Hz, 2H, 1-H), 3.49–3.56 (m, 1H, 9-H), 3.78 (s, 3H, CH_3O PMB), 3.89–4.02 (m, 1H, 5-H), 4.32–4.47 (m, 5H, 8-H, CH_3OCH_2O, PMB CH_2), 5.47–5.57 (m, 1H, 7-H), 5.58–5.67 (m, 1H, 6-H), 6.86 (d, J=8.4 Hz, 2H, CH_{ar}, *meta*), 7.21–7.27 (m, 2H, CH_{ar}, *ortho*), 7.29–7.47 (m, 6H, phenyl), 7.58–7.72 (m, 4H, phenyl); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm]=14.6 (C-11), 19.0 ($OSi(Ph)_2C(CH_3)_3$), 21.8 (C-3), 26.7 ($OSi(Ph)_2C(CH_3)_3$), 28.2 (C-2), 29.3 (C-10), 36.4 (C-4), 55.0 (CH_3O PMB), 55.4 (CH_3OCH_2O), 68.3 (C-13), 69.7 (C-1), 71.8 (C-5), 72.2 (PMB CH_2), 73.4 (C-8), 79.5 (C-9), 83.8 (C-12), 96.8 (CH_3O-CH_2O), 113.5 (CH_{ar}, *meta*), 127.2 (phenyl), 127.3 (phenyl), 128.2 (C-7), 128.9 (CH_{ar}, *ortho*), 129.4 (phenyl), 129.5 (phenyl), 130.4 (C_{ar}), 133.3 (phenyl), 133.6 (phenyl), 135.0 (C-6), 135.6 (phenyl), 135.7 (phenyl), 158.8 (C_{ar}, *para*); HRMS (ESI): $[M+Na]^+$ calcd for $C_{39}H_{52}O_6Si$ 667.34254, found 667.34281.

4.1.20. (5*R*,6*R*,7*E*,9*R*)-9-{[*tert*-Butyl(dimethyl)silyl]oxy}-6-{[*tert*-butyl(diphenyl)silyl]oxy}-13-[(*para*-methoxybenzyl)oxy]-5-(methoxymethoxy)tridec-7-en-1-yne (30). To a stirred solution of alkynol **29** (77 mg, 0.12 mmol) in CH_2Cl_2 (1 mL), 2,6-lutidine (47 μL, 0.36 mmol, 3 equiv) was added. At 0 °C TBSOTf (42 μL, 0.18 mmol, 1.5 equiv) was added dropwise and the mixture stirred for 40 min. The mixture was diluted with CH_2Cl_2 and the organic layer washed with H_2O, 1 N HCl, and saturated $NaHCO_3$ solution, dried over $MgSO_4$ and filtered. The filtrate was concentrated in vacuo and the residue purified by flash chromatography (petroleum ether/EtOAc, 10:1) to give 85 mg (93%) of alkyne **30** as colorless oil. R_f=0.48 (petroleum ether/EtOAc, 10:1); $[\alpha]_D^{20}$ +7.4 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm]=0.00, 0.02 (2s, 3H each, $Si(CH_3)_2$), 0.86 (s, 9H, $Si(CH_3)_2C(CH_3)_3$), 1.07 (s, 9H, $Si(Ph)_2C(CH_3)_3$), 1.14–1.67 (m, 8H, 4-H, 10-H, 11-H, 12-H), 1.88 (t, J=2.5 Hz, 1H, 1-H), 2.07–2.33 (m, 2H, 3-H), 3.17 (s, 3H, CH_3OCH_2O), 3.32–3.45 (m, 3H, 5-H, 13-H), 3.79 (s, 3H, CH_3O PMB), 4.01–4.11 (m, 1H, 9-H), 4.22–4.32 (m, 2H, CH_3OCH_2O), 4.33–4.38 (m, 1H, 6-H), 4.42 (s, 2H, PMB CH_2), 5.53–5.68 (m, 2H, 7-H, 8-H), 6.86 (d, J=8.7 Hz, 2H, CH_{ar}, *meta*), 7.22–7.28 (m, 2H, CH_{ar}, *ortho*), 7.29–7.46 (m, 6H, phenyl), 7.56–7.73 (m, 4H, phenyl); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm]=−4.9 ($Si(CH_3)_2$), −4.4 ($Si(CH_3)_2$), 14.9 (C-3), 18.2 ($Si(CH_3)_2C(CH_3)_3$), 19.3 ($Si(Ph)_2C(CH_3)_3$), 21.9 (C-11), 25.9 ($Si(CH_3)_2C(CH_3)_3$), 27.1 ($Si(Ph)_2C(CH_3)_3$), 28.4 (C-12), 29.8 (C-4), 38.2 (C-10), 55.3 (CH_3O PMB), 55.5 (CH_3OCH_2O), 68.4 (C-1), 70.2 (C-13), 72.5 (C-9), 73.0 (PMP CH_2), 73.6 (C-6), 79.9 (C-5), 84.3 (C-2), 97.0 (CH_3O-CH_2O), 113.7 (CH_{ar}, *meta*), 127.2 (C-7), 127.5 (phenyl), 127.6 (phenyl), 129.2 (CH_{ar}, *ortho*), 129.6 (phenyl), 129.8 (phenyl), 130.8 (C_{ar}), 133.7 (phenyl), 133.9 (phenyl), 135.6 (C-8), 135.9 (phenyl), 136.0 (phenyl), 159.1 (C_{ar}, *para*); HRMS (ESI): $[M+Na]^+$ calcd for $C_{45}H_{66}O_6Si_2$ 781.42901, found 781.43091.

4.1.21. (4*S*)-3-[(2*S*,3′*R*,5′*E*)-3′-Hydroxy-6′-iodo-2′,5′-dimethyl-5-hexenoyl]-4-isopropyl-1,3-oxazolidin-2-one (33). To a solution of (3*E*)-4-iodo-3-methyl-3-buten-1-ol[26] (2.02 g, 9.54 mmol) in CH_2Cl_2 (50 mL) was added $NaHCO_3$ (4.00 g, 47.70 mmol, 5 equiv) followed by Dess–Martin periodinane (15% in CH_2Cl_2, 21.78 mL, 10.49 mmol, 1.1 equiv) at room temperature. After 20 min, a 1:1:1 solution (50 mL) of saturated $Na_2S_2O_3$ solution, saturated $NaHCO_3$ solution, and water was added and the mixture stirred vigorously for 30 min. The aqueous layer was extracted twice with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. To the resulting oil Et_2O was added, the white solid formed was filtered and the filtrate was concentrated again. The crude aldehyde **31** was used for the aldol reaction without further purification. To a solution of 4-isopropyl-3-propionyl-1,3-oxazolidin-2-one[27] (**32**) (1.59 g, 8.59 mmol, 0.9 equiv) in CH_2Cl_2 (17 mL) was added di-*n*-butylboryl triflate (1 M in CH_2Cl_2, 9.54 mL, 9.54 mmol, 1.0 equiv) at 0 °C. The resulting brown solution was stirred for 10 min, then *i*Pr_2NEt (1.78 mL, 10.49 mmol, 1.1 equiv) was added, resulting in a color change from red to light yellow. The mixture was stirred for 1 h at 0 °C and cooled to −80 °C. Now, a solution of the above aldehyde **31** in CH_2Cl_2 (3 mL) was added and stirring was continued for 1 h at −80 °C. The reaction mixture was allowed to warm to 0 °C over 30 min and stirred for 30 min at this temperature. The reaction was quenched with pH 7 phosphate buffer (10 mL), MeOH (35 mL), finally treated with a mixture of MeOH/H_2O_2 (2:1, 35 mL), allowed to warm to room temperature and stirred for 1 h. Most of the organic solvents were removed by rotary evaporation and the aqueous layer was extracted twice with diethyl ether. The combined extracts were washed with saturated $NaHCO_3$ solution, saturated NaCl solution, dried over $NaSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (petroleum ether/ethyl acetate, 3:1) to afford the aldol product **33** (2.48 g, 72% over two steps) as a light yellow oil. R_f=0. 36 (petroleum ether/EtOAc, 3:1); $[\alpha]_D^{20}$ +50.2 (*c* 1.02, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm]=0.85 (d, J=7.1 Hz, 3H, $CH(CH_3)_2$), 0.90 (d, J=7.1 Hz, 3H, $CH(CH_3)_2$), 1.25 (d, J=7.1 Hz, 3H, 2′-CH_3), 1.86 (d, J=0.8 Hz, 3H, 5′-CH_3), 2.24–2.37 (m, 2H, 4′-H, $CH(CH_3)_2$), 2.39–2.49 (m, 1H, 4′-H), 2.77 (br s, 1H, OH), 3.71–3.80 (m, 1H, 2′-H), 4.05–4.13 (m, 1H, 3′-H),

4.19 (dd, J=9.1, 3.0 Hz, 1H, 5-H), 4.28 (t, J=8.7 Hz, 1H, 5-H), 4.44 (dt, J=3.4, 8.4 Hz, 1H, 4-H), 6.02 (s, 1H, H-6′); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm]=11.6 (2′-CH_3), 14.6 (CH(CH_3)$_2$), 17.9 (CH(CH_3)$_2$), 24.0 (5′-CH_3), 28.3 ($CH(CH_3)_2$), 42.1 (C-2′), 44.1 (C-4′), 58.2 (C-4), 63.3 (C-5), 69.0 (C-3′), 77.4 (C-6′), 144.7 (C-5′), 153.5 (C-2), 176.9 (C-1′); HRMS (ESI): [M+Na]$^+$ calcd for $C_{14}H_{22}INO_4$ 418.04857, found 418.04898.

4.1.22. Methyl (2*S*,3*R*,5*E*)-3-hydroxy-6-iodo-2,5-dimethyl-5-hexenoate (34). To a solution of aldol product **33** (1.38 g, 3.48 mmol) in CH_2Cl_2 (30 mL) at −30 °C was added dropwise NaOMe (0.5 M in MeOH, 8.35 mL, 4.18 mmol, 1.2 equiv). The reaction mixture was allowed to warm to 0 °C and stirred for 10 min at this temperature before saturated NH_4Cl (9 mL) solution was added. The aqueous layer was extracted twice with CH_2Cl_2 and the combined organic layers were dried over $NaSO_4$, filtered, and concentrated in vacuo to afford 1.35 g of the crude product. The residue was used for the next reaction without further purification. For analytical purposes a small amount was purified by flash chromatography (petroleum ether/ethyl acetate, 4:1). R_f=0. 27 (petroleum ether/EtOAc, 4:1); $[\alpha]_D^{20}$ +20.4 (c 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm]= 1.18 (d, J=7.1 Hz, 3H, CH_3C-2), 1.85 (s, 3H, 5-CH_3), 2.24–2.41 (m, 2H, 4-H), 2.43–2.58 (m, 1H, 2-H, OH), 3.68 (s, 3H, OCH_3), 4.00–4.08 (m, 1H, 3-H), 6.01 (s, 1H, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm]=10.9 (2-CH_3), 23.9 (5-CH_3), 43.9 (C-2), 43.9(C-4), 51.9 (OCH_3), 69.2 (C-3), 77.5 (C-6), 144.4 (C-5), 176.0 (C-1); HRMS (ESI): [M+Na]$^+$ calcd for $C_9H_{15}IO_3$ 320.99581, found 320.99586.

4.1.23. Methyl (2*S*,3*R*,5*E*)-6-iodo-2,5-dimethyl-3-[(triethylsilyl)oxy]-5-hexenoate (35). After cooling a solution of crude hydroxyester **34** in CH_2Cl_2 (22 mL) to 0 °C, Et_3N (1.45 mL, 10.44 mmol, 3.0 equiv) was added. A catalytic amount of DMAP was added and the reaction mixture was stirred for 10 min before triethylsilyl chloride (1.17 mL, 6.96 mmol, 2.0 equiv) was added dropwise. The reaction mixture was allowed to warm to room temperature. After 20 h the reaction was quenched with water. The aquous layer was extracted twice with diethyl ether and the combined organic layers were washed with saturated NaCl solution, dried over $NaSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (petroleum ether/EtOAc, 20:1) to afford silyl ether **35** (1.22 g, 85% over two steps) as a colorless oil. R_f=0. 45 (petroleum ether/ethyl acetate, 20:1); $[\alpha]_D^{20}$ +14.2 (c 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm]=0.55 (q, J=8.1 Hz, 6H, CH_3CH_2Si), 0.93 (t, J=7.9 Hz, 9H, CH_3CH_2Si), 1.12 (d, J=6.9 Hz, 3H, 2-CH_3), 1.85 (d, J=0.9 Hz, 3H, 5-CH_3), 2.38 (d, J=6.6 Hz, 2H, 4-H), 2.40–2.46 (m, 1H, 2-H), 3.66 (s, 3H, OCH_3), 4.22 (dt, J=6.6, 4.5 Hz, 1H, 3-H), 5.95–5.97 (m, 1H, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm]= 5.0 (CH_3CH_2Si), 6.8 (CH_3CH_2Si), 10.8 (2-CH_3), 24.1 (5-CH_3), 44.6 (C-4), 45.8 (C-2), 51.6 (OCH_3), 70.9 (C-3), 78.1 (C-6), 144.4 (C-5), 175.2 (C-1); HRMS (ESI): [M+Na]$^+$ calcd for $C_{15}H_{29}IO_3Si$ 435.08229, found 435.08235.

4.1.24. (2*R*,3*R*,5*E*)-6-Iodo-2,5-dimethyl-3-[(triethylsilyl)oxy]-5-hexen-1-ol (36). To a solution of ester **35** (1.22 g, 2.96 mmol) in CH_2Cl_2 (30 mL) at −80 °C was added DIBAL (1 M in hexane, 8.88 mL, 8.88 mmol, 3.0 equiv) in a dropwise fashion. After 1.5 h the reaction was quenched with saturated Na, K-tartrate solution and the mixture stirred vigorously at room temperature for 1 h. The aqueous layer was extracted twice with CH_2Cl_2 and the combined organic layers were dried over $NaSO_4$, filtered, and concentrated in vacuo. Flash chromatography (petroleum ether/EtOAc, 10:1) of the residue provided hexenol **36** (0.96 g, 84%) as a colorless oil. R_f=0. 38 (petroleum ether/ethyl acetate, 10:1); $[\alpha]_D^{20}$ +6.0 (c 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm]=0.57 (q, J=7.6 Hz, 6H, CH_3CH_2Si), 0.81 (d, J= 6.9 Hz, 3H, 2-CH_3), 0.94 (t, J=8.8 Hz, 9H, CH_3CH_2Si), 1.83 (d, J=0.9 Hz, 3H, 5-CH_3), 1.84–1.93 (m, 1H, 2-H), 2.38 (dd, J=6.6, 0.6 Hz, 2H, 4-H), 2.46–2.51 (m, 1H, OH), 3.48–3.56 (m, 1H, 1-H), 3.59–3.68 (m, 1H, 1-H), 3.96 (dt, J=6.7, 2.9 Hz, 1H, 3-H), 5.92–5.99 (m, 1H, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm]=5.0 (CH_3CH_2Si), 6.9 (CH_3CH_2Si), 11.4 (2-CH_3), 24.1 (5-CH_3), 39.6 (C-2), 43.1 (C-4), 65.7 (C-1), 72.9 (C-3), 77.7 (C-6), 144.5 (C-5); HRMS (ESI): [M+Na]$^+$ calcd for $C_{14}H_{29}IO_2Si$ 407.08737, found 407.08736.

4.1.25. (2*S*,5*E*)-6-Iodo-2,5-dimethyl-3-[(triethylsilyl)oxy]-5-hexenal (37). To a solution of alcohol **36** (0.32 g, 0.84 mmol) in CH_2Cl_2 (16 mL) was added $NaHCO_3$ (0.25 g, 2.95 mmol, 3.5 equiv) at room temperature, followed by Dess–Martin periodinane (15% in CH_2Cl_2, 2.00 mL, 0.96 mmol, 1.1 equiv). After 30 min, saturated $Na_2S_2O_3$ solution (8 mL) was added and the mixture was stirred vigorously for 30 min. The aqueous layer was extracted twice with CH_2Cl_2 and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. To the resulting oil was added Et_2O, the white solid formed was filtered off, and the filtrate concentrated in vacuo. The crude aldehyde **37** was used for the subsequent Wittig reaction without further purification. For analytical purposes a small amount was purified by flash chromatography (petroleum ether/EtOAc, 12:1). R_f=0.56 (petroleum ether/ethyl acetate 12:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm]=0.55 (q, J= 7.9 Hz, 6H, CH_3CH_2Si), 0.92 (t, J=7.9 Hz, 9H, CH_3CH_2Si), 1.08 (d, J=7.1 Hz, 3H, 2-CH_3), 1.85 (d, J=1.0 Hz, 3H, 5-CH_3), 2.31–2.46 (m, 3H, 2-H, 4-H), 4.30 (dt, J=6.7, 3.3 Hz 1H, 3-H), 5.96–6.01 (m, 1H, 6-H), 9.73 (s, 1H, 1-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm]=5.0 (CH_3CH_2Si), 6.8 (CH_3CH_2Si), 7.5 (2-CH_3), 24.2 (5-CH_3), 44.9 (C-4), 51.0 (C-2), 69.6 (C-3), 78.4 (C-6), 144.4 (C-5), 204.6 (C-1).

4.1.26. Methyl (2*E*,4*R*,5*R*,7*E*)-8-iodo-2,4,7-trimethyl-5-[(triethylsilyl)oxy]-2,7-octadienoate (39). (Methoxycarbonyl)ethylidenetriphenylphosphorane[30] **38** (0.50 g, 1.43 mmol, 1.7 equiv) was added to a solution of aldehyde **37** in toluene (10 mL). The reaction mixture was stirred for 5 h at 80 °C, cooled to room temperature, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (petroleum ether/EtOAc, 20:1) to afford dienoate **39** (0.30 g, 79% over two steps) as a colorless oil. R_f=0. 47 (petroleum ether/ethyl acetate, 20:1); $[\alpha]_D^{20}$ +28.4 (c 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm]= 0.56 (q, J=7.9 Hz, 6H, CH_3CH_2Si), 0.94 (t, J=7.9 Hz, 9H, CH_3CH_2Si), 0.98 (d, J=6.9 Hz, 3H, 4-CH_3), 1.82 (m, 6H, 2-CH_3, 7-CH_3), 2.27–2.41 (m, 2H, 6-H), 2.46–2.57 (m, 1H, 4-H), 3.69–3.74 (m, 4H, OCH_3, 5-H), 5.90–5.93 (m, 1H, 8-H), 6.60–6.65 (m, 1H, 3-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ [ppm]=5.1 (CH_3CH_2Si), 6.9 (CH_3CH_2Si), 12.7 (2-CH_3),

14.6 (4-CH_3), 24.4 (7-CH_3), 38.6 (C-4), 45.4 (C-6), 51.7 (OCH_3), 73.5 (C-5), 77.9 (C-8), 127.0 (C-2), 144.5 (C-7), 144.8 (C-3), 168.6 (C-1); HRMS (ESI): $[M+Na]^+$ calcd for $C_{18}H_{33}IO_3Si$ 475.11359, found 475.11377.

4.1.27. Methyl (2*E*,4*R*,5*R*,7*E*,9*E*,13*R*,14*R*,15*E*,17*R*)-17-{[*tert*-butyl(dimethyl)silyl]oxy}-14-{[*tert*-butyl(diphenyl)-silyl]oxy}-21-[(*para*-methoxybenzyl)oxy]-13-(methoxy-methoxy)-2,4,7-trimethyl-5-[(triethylsilyl)oxy]henicosa-2,7,9,15-tetraenoate (40).

4.1.27.1. Via Suzuki coupling. To a stirred solution of enyne **30** (10 mg, 0.013 mmol, 1 equiv) in THF (0.15 mL) was added 9-BBN (34 μL, 0.5 M in THF, 0.017 mmol, 1.3 equiv) at 0 °C. After stirring for 36 h at room temperature the vinyl borane solution was used in the following coupling step without further purification. To a stirred solution of dienoate **39** (8 mg, 0.017 mmol, 1.3 equiv) in DMF (0.2 mL) were added $AsPh_3$ (0.3 mg, 5 mol %), $PdCl_2$(dppf) (0.8 mg, 5 mol %), Cs_2CO_3 (14 mg, 0.034 mmol, 2 equiv), and 2 drops of water at room temperature. After addition of the vinyl borane solution stirring was continued for 72 h at room temperature. The reaction was quenched with saturated NH_4Cl solution and the aqueous layer extracted twice with EtOAc. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (petroleum ether/EtOAc, 12:1) to afford 9 mg (67% over 2 steps) of coupling product **40** as colorless oil. According to LC-MS this compound contains the 9,10-dihydro derivative as a by-product. The dihydro compound **41** was the only product when 9-BBN was used in excess (3 equiv).

4.1.27.2. Via Stille coupling. To a stirred solution of alkyne **30** (10 mg, 0.013 mmol, 1 equiv) in THF (0.15 mL) was added $PdCl_2(PPh_3)_2$ (0.17 mg, 200 μmol, 15 mol %) at room temperature. Thereafter, Bu_3SnH (10 μL, 0.038 mmol, 3 equiv) was added dropwise. After stirring for 10 min at room temperature TLC showed complete conversion to the vinylstannane. After evaporation of volatiles the residue can be used in the following coupling step without further purification. To a stirred solution of vinyl iodide **39** (5.5 mg, 0.012 mmol, 1.2 equiv) and the stannane (10 mg, 0.01 mmol, 1 equiv) in DMF (0.2 mL) were added $AsPh_3$ (1.3 mg, 0.4 equiv) and $Pd_2(dba)_3$ (2 mg, 0.2 equiv) at room temperature. Stirring was continued for 6 h. For the work-up, water was added and the mixture extracted with diethyl ether (2×10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 20:1) to give 8 mg (78%) of coupling product **40**.

Compound **40**: R_f=0.43 (petroleum ether/EtOAc, 10:1); $[\alpha]_D^{20}$ +41.0 (*c* 0.47, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ [ppm]=−0.01, 0.01 (2s, 3H each, $Si(CH_3)_2$), 0.57 (q, *J*=8.1 Hz, 6H, CH_3CH_2Si), 0.84 (s, 9H, $Si(CH_3)_2C(CH_3)_3$), 0.86 (t, *J*=2.2 Hz, 9H, CH_3CH_2Si), 0.99 (d, *J*=6.9 Hz, 3H, 4-CH_3), 1.05 (s, 9H, $Si(Ph)_2C(CH_3)_3$), 1.25–1.62 (m, 8H, 12-,18-,19-,20-H), 1.72 (s, 3H, 7-CH_3), 1.78–1.80 (m, 3H, 2-CH_3), 1.95–2.38 (m, 4H, 6-, 11-H), 2.48–2.59 (m, 1H, 4-H), 3.12–3.25 (m, 4H, 13-H, CH_3OCH_2O), 3.38 (t, *J*=6.7 Hz, 2H, 21-H), 3.72 (s, 3H, OCH_3), 3.74–3.77 (m, 1H, 5-H), 3.79 (s, 3H, PMB OCH_3), 3.98–4.07 (m, 1H, 17-H), 4.17–4.36 (m, 3H, 14-H, CH_3OCH_2O), 4.41 (s, 2H, PMB CH_2), 5.44–5.66 (m, 3H, 10-, 15-, 16-H), 5.72–5.79 (m, 1H, 8-H), 6.16 (dd, *J*=14.9, 10.9 Hz, 1H, 9-H), 6.71 (d, *J*=10.2 Hz, 1H, 3-H), 6.86 (d, *J*=8.7 Hz, 2H, CH_{ar}, *meta*), 7.24 (d, *J*=6.4 Hz, 2H, CH_{ar}, *para*), 7.29–7.45 (m, 6H, phenyl), 7.56–7.71 (m, 4H, phenyl); ^{13}C NMR (400 MHz, $CDCl_3$): δ [ppm]=−4.8 (17-OSi$(CH_3)_2$), −4.3 (17-OSi$(CH_3)_2$), 5.1 ($SiCH_2CH_3$), 6.9 ($SiCH_2CH_3$), 12.6 (2-CH_3), 13.6 (4-CH_3), 17.0 (7-CH_3), 18.2 (17-OSi$C(CH_3)_3$), 18.6 (14-OSi$C(CH_3)_3$), 19.4 (C-11), 21.9 (C-19), 25.9 (17-OSiC($CH_3)_3$), 27.1 (14-OSiC($CH_3)_3$), 29.7 (C-12), 29.8 (C-20), 37.9 (C-18), 38.2 (C-4), 46.0 (C-6), 51.6 (OCH_3, ester), 55.3 (PMB CH_3), 55.5 (MOM CH_3), 70.2 (C-21), 72.5 (PMB CH_2), 73.1 (C-17), 73.7 (C-5), 74.0 (C-14), 81.8 (C-13), 96.9 (MOM CH_2), 113.8 (PMB, *meta*), 126.3 (C-2), 126.7 (C-9), 127.5 (phenyl), 127.5 (C-15), 127.6 (phenyl), 128.0 (C-8), 129.2 (PMB, *ortho*), 129.6 (phenyl), 129.7 (phenyl), 130.9 (PMB), 131.5 (C-7), 132.9 (C-10), 133.8 (phenyl), 134.1 (phenyl), 135.5 (C-16), 135.9 (phenyl), 135.9 (phenyl), 146.1 (C-3), 159.1 (PMB, *para*), 168.8 (C-1); HRMS (ESI): $[M+Na]^+$ calcd for $C_{63}H_{100}O_9Si_3$ 1107.65674, found 1107.65705.

Compound **41**: R_f=0.45 (petroleum ether/EtOAc, 10:1); $[\alpha]_D^{20}$ +64.5 (*c* 1.00, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ [ppm]=−0.01, 0.01 (2s, 3H each, $Si(CH_3)_2$), 0.57 (q, *J*=8.1 Hz, 6H, CH_3CH_2Si), 0.86 (s, 9H, $Si(CH_3)_2C(CH_3)_3$), 0.89–0.96 (m, 9H, CH_3CH_2Si), 0.97 (m, 3H, 4-CH_3), 1.05 (s, 9H, $Si(Ph)_2C(CH_3)_3$), 1.15–1.71 (m, 15H, 7-CH_3, 10-,11-,12-,18-,19-,20-H), 1.80 (s, 3H, 2-CH_3), 1.88–1.99 (m, 2H, 9-H), 2.06–2.25 (m, 2H, 6-H), 2.48–2.61 (m, 1H, 4-H), 3.12–3.23 (m, 4H, 13-H, CH_3OCH_2O), 3.39 (t, *J*=6.7 Hz, 2H, 21-H), 3.68–3.76 (m, 4H, OCH_3, 5-H), 3.79 (s, 3H, PMB OCH_3), 4.01–4.09 (m, 1H, 17-H), 4.20–4.36 (m, 3H, 14-H, CH_3OCH_2O), 4.41 (s, 2H, PMB CH_2), 5.16 (t, *J*=6.6 Hz, 1H, H-8), 5.48–5.67 (m, 2H, 15-,16-H), 6.73 (d, *J*=10.2 Hz, 1H, 3-H), 6.86 (d, *J*=8.7 Hz, 2H, CH_{ar}, *meta*), 7.25 (d, *J*=8.7 Hz, 2H, CH_{ar}, *para*), 7.29–7.45 (m, 6H, phenyl), 7.56–7.71 (m, 4H, phenyl); ^{13}C NMR (400 MHz, $CDCl_3$): δ [ppm]=−4.9 (17-OSi$(CH_3)_2$), −4.4 (17-OSi$(CH_3)_2$), 5.1 ($SiCH_2CH_3$), 6.9 ($SiCH_2CH3$), 12.5 (2-CH_3), 13.4 (4-CH_3), 16.5 (7-CH_3), 18.2 (17-OSi$C(CH_3)_3$), 19.3 (14-OSi$C(CH_3)_3$), 21.9 (C-19), 25.6 (C-11), 25.9 (17-OSiC($CH_3)_3$), 27.0 (14-OSiC($CH_3)_3$), 28.1 (C-9), 29.3 (C-10), 29.8 (C-12, C-20), 37.6 (C-18), 38.1 (C-4), 45.8 (C-6), 51.6 (OCH_3, ester), 55.2 (PMB CH_3), 55.4 (MOM CH_3), 70.2 (C-21), 72.5 (PMB CH_2), 73.1 (C-17), 73.5 (C-5), 74.0 (C-14), 81.2 (C-13), 96.8 (MOM CH_2), 113.7 (PMB, *meta*), 126.0 (C-2), 127.4 (phenyl), 127.6 (phenyl), 127.6 (C-15), 128.1 (C-8), 129.2 (PMB, *ortho*), 129.6 (phenyl), 129.7 (phenyl), 130.8 (PMB), 131.4 (C-7), 133.8 (phenyl), 134.1 (phenyl), 135.2 (C-16), 135.9 (phenyl), 146.4 (C-3), 159.1 (PMB, *para*), 168.8 (C-1). HRMS: $[M+Na]^+$ calcd for $C_{63}H_{102}O_9Si_3$ 1109.7239, found 1109.7403.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2007.10.028.

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