Stereoselective Synthesis of the C(1)−C(12) Fragments of Tedanolides − Application of a *syn*-Selective Tin(II)-Mediated Aldol Reaction and a Convertible Methoxybenzyl Protecting Group

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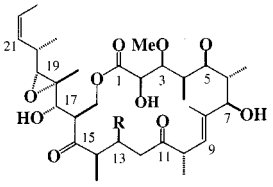
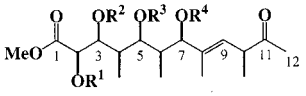
Stereoselective synthesis of two C(1)–C(12) fragments, **3** and **4**, of antitumor agents tedanolide (**1**) and 13-deoxytedanolide (**2**) was achieved by means of several regio- and/or stereoselective reactions. Ethyl ketone **14** was synthesized from methyl (*S*)-3-hydroxy-2-methylpropionate (**16a**) by way of a Weinreb amide. A highly *syn*-selective tin(II)-mediated aldol reaction between **14** and aldehyde **15**, prepared from (*R*)-propionate **16b,** proceeded smoothly, and subsequent reduction gave diol **13**, which was transformed into **3**, incorporating a C(3),C(5)-MP acetal moiety, by taking advantage of convertible MPM protecting groups. Another fragment, **4**, with C(3)-*O*-methyl and C(5)-*O*-MPM groups, was also synthesized. A crucial step was the selective transformation of C(2),C(3)-diol **21** into C(2)-*O*-TBS, C(3)-*O*-Me compound **22**.

Introduction

Tedanolide (**1**), a highly cytotoxic, 18-membered macrolide, was isolated by Schmitz and co-workers from the Caribbean sponge *Tedanis ignis* in 1984.[1] In 1991, Fusetani and co-workers isolated a related antitumor macrolide, 13-deoxytedanolide (**2**), from the Japanese sponge *Mycale adhaerens*.[2] Because of their unusual structural features and powerful biological activities, **1** and **2** have attracted considerable synthetic attention.[3] As part of our synthetic studies of **1** and **2**, we now report concise and completely stereoselective syntheses of two C(1)−C(12) fragments **3** and **4** (Figure 1), which should be practically useful for the synthesis of **1** and **2**.



Tedanolide (**1**): R = OH
13-Deoxytedanolide (**2**): R = H



3: $R^1 = R^4$ = MOM, R^2R^3 = 4-$MeOC_6H_4CH$
4: $R^1 = R^4$ = TBS, R^2 = Me, R^3 = MPM
MPM: 4-$MeOC_6H_4CH_2$

Figure 1. Tedanolide (**1**), 13-deoxytedanolide (**2**) and two C(1)−C(12) fragments (**3**, **4**)

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In macrolide synthesis, macrolactonization is usually the most crucial step, and so it is very important to design a seco-acid derivative suitable for macrolactonization. The seco-acid derivative should be designed so that its conformation is very close to that of the corresponding lactone.[4] Several years ago we designed the seco-acid **5**, with the aid of conformational analyses based on molecular mechanics calculations (MM2-CONFLEX),[5] and **5** was then synthesized by a coupling of **6** and **7** (Figure 2). When **5** was subjected to macrolactonization using the Yamaguchi method[6] at a normal substrate concentration, not under high-dilution conditions,[4] the cyclization proceeded quite smoothly and **8** was isolated in high yield.[3a,3l] However, in order to complete the synthesis of **1** and **2**, this synthetic procedure required several serious improvements. The synthesis of **6** needed too many steps, and in addition the condensation of **9** and **10** was poorly stereoselective (3.6:1) and also quite difficult to reproduce.[3f] Instead of **6**, we planned to synthesize **3** and **4** by aldol coupling of ethyl ketone **14** and aldehyde **15**.

Results and Discussion

Synthesis of 3

A retrosynthetic analysis of **3** is shown in Scheme 1. The most important steps were the *syn*-selective aldol reaction between **14** and **15** and subsequent stereoselective reduction in order to construct four consecutive asymmetric centers to give **13**. The hydroxy group of methyl (*S*)-3-hydroxy-2-methylpropionate (**16a**) was first protected with a 4-methoxybenzyl (MPM) group by treatment with MPM trichloroacetimidate,[7] and the resulting **17** was treated with *N*,*O*-dimethylhydroxylamine to give a Weinreb amide,[8] which was readily converted into ethyl ketone **14**[9] without any racemization.

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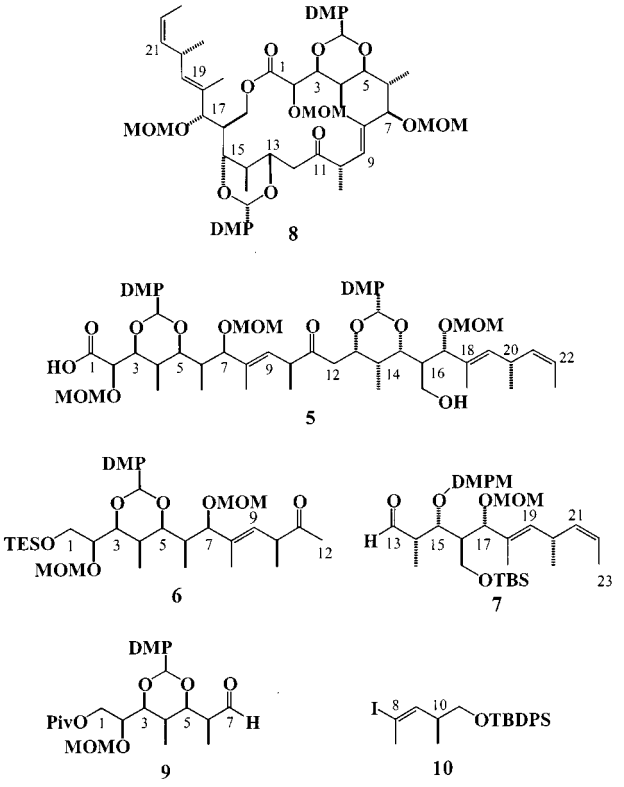
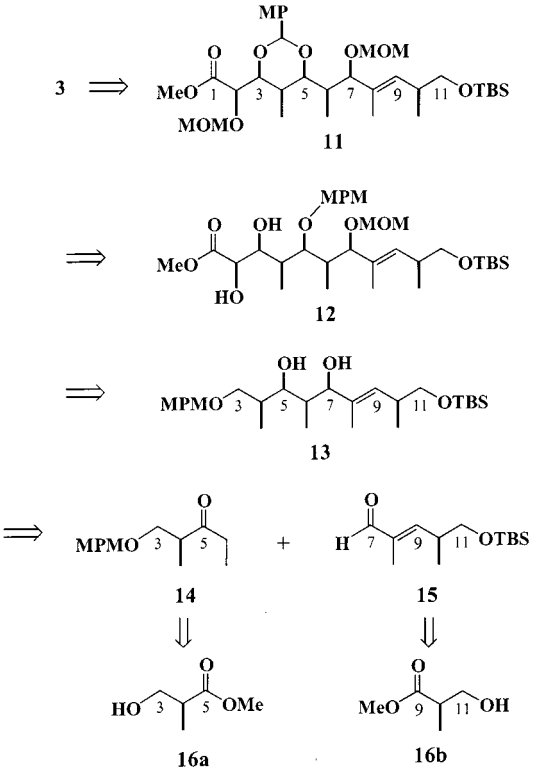
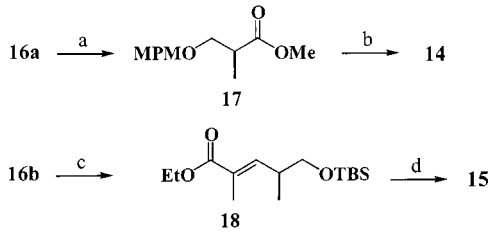


Figure 2. Lactone **8**, seco acid **5** and synthetic intermediates **6**, **7**, **9**, **10**



Scheme 1. Retrosynthesis of **3**

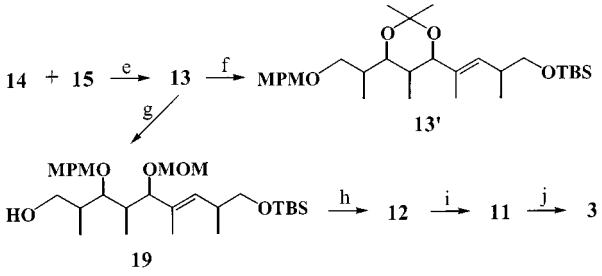
Aldehyde **15** was next synthesized by a series of conventional reactions, starting from (*R*)-propionate **16b**. After protection of the hydroxy group of **16b** with a *tert*-butyldimethylsilyl (TBS) group, the ester was reduced to an alcohol, which was oxidized to an aldehyde and then subjected to Wittig reaction to give the C(7)−C(11) ester **18**. Reduction and reoxidation of **18** readily gave aldehyde **15** in excellent yield (Scheme 2).



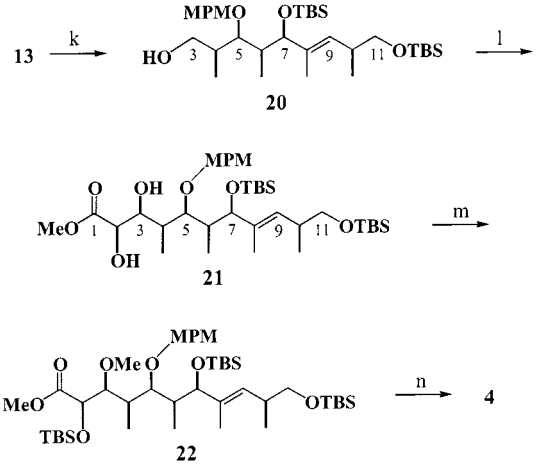
Scheme 2. (a) MPMC(=NH)CCl_3, PPTS, 92%; (b) 1) MeONHMe·HCl, *i*PrMgBr, 2) EtMgBr, 2 steps 92%; (c) 1) TBSCl, 2) $LiBH_4$, 3) Swern oxid., 4) $Ph_3P{=}C(Me)CO_2Et$ 90%; (d) 1) DIBAH, 2) Swern oxid, 2 steps 98%, 2 steps

Paterson had achieved a highly *syn*-selective aldol reaction using tin triflate [$Sn(OTf)_2$] under modified Mukaiyama conditions,[10] and this was now successfully applied to the coupling of **14** and **15**. When **14** was converted into a tin(II) (*Z*)-enolate with $Sn(OTf)_2$/Hünig's base (iPr_2NEt) at −78 °C, and **15** then gradually added dropwise, the *syn*-selective aldol reaction proceeded smoothly to give the adduct, with a selectivity of more than 20:1. This β-hydroxy ketone was immediately subjected to a stereoselective reduction with diisobutylaluminium hydride (DIBAH)[11] to give diol **13** with all the expected *syn* configurations. The stereochemistry of **13** was confirmed by conversion into acetonide **13′** and by its NMR spectrum [$J_{H5\text{-}H6}$ (ax-eq) = 1.8 Hz, $J_{H6\text{-}H7}$ (eq-ax) < 1.0 Hz].

Transformation of **13** into **11** was achieved by taking advantage of the convertible MPM protecting group. After oxidation of **13** to a 4-methoxybenzylidene (MP-CH) acetal with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ),[12] the remaining C(7)-hydroxy group was protected with a methoxymethyl (MOM) group, and the acetal was then selectively reduced with DIBAH to give **19**.[13] Dess−Martin oxidation[14] of **19**, followed by Wittig reaction, gave an α,β-unsaturated ester, and subsequent stereoselective dihydroxylation with AD-mix-α[3f,15] proceeded quite smoothly to give **12** as a single product. The construction of six consecutive asymmetric centers, all with *syn* configuration, was thus achieved. Again, DDQ oxidation of the MPM group formed an acetal, and the remaining C(2)-hydroxy group was protected as a MOM ether to give **11**. The stereochemistry of **11** was confirmed by NMR spectroscopy, including H-H COSY spectroscopy ($J_{H2\text{-}H3}$ = 9.0 Hz, $J_{H3\text{-}H4}$ = 1.7 Hz, $J_{H4\text{-}H5}$ = 1.7 Hz, $J_{H5\text{-}H6}$ = 9.9 Hz). After removal of the TBS protecting group, Dess−Martin oxidation readily gave an aldehyde, which was selectively methylated with methyllithium (MeLi), although the yield is still unsatisfactory, and further oxidation under Dess−Martin conditions finally gave the title compound **3** (Scheme 3).



Scheme 3. (e) 1) $Sn(OTf)_2$, iPr_2EtN, 2) DIBAH, 2 steps 80%; f) $(MEO)_2CMe_2$, PPTS, 89%; (g) 1) DDQ, 2) MOMCl, 3) DIBAH, 3 steps 63%; (h) 1) Dess−Martin oxid., 2) $Ph_3P{=}CHCO_2Me$, 2 steps 94%, 3) AD-mix α, 86%; (i) 1) DDQ, 2) MOMCl, 2 steps 60%; (j) TBAF, 93%, 2) Dess−Martin oxid., 3) MeLi, 2 steps 48%, 4) Dess−Martin oxid., 85%



Scheme 4. (k) 1) DDQ, 2) TBSCl, 2 steps 69%, 3) DIBAH, 90%; (l) 1) Dess−Martin oxid., 2) $Ph_3P{=}CHCO_2Me$ 2 steps 93%, 3) AD-mix α, 68%; (m) 1) TBSCl, 84%, 2) Me_3OBF_4, proton sponge, 92%; (n) 1) CSA, 85%, 2) Dess−Martin oxid., 3) MeLi, 2 steps 37%, 4) 92%

Synthesis of 4

Another C(1)−C(12) fragment (**4**) was also synthesized for two reasons: 1) it would be easier to complete the synthesis of **1** and **2** if a seco-acid derived from **4** were to form the corresponding lactone efficiently, although MM calculations gave an unfavorable prediction, and 2) the reliability of the calculations could be gauged by whether the seco-acid cyclized efficiently or not.

Diol **13** was converted into **21**, the C(7)-hydroxy group protected with a TBS group, by way of **20** in the same manner as described for **12**. Regioselective protection of the C(2)-hydroxy group of **21** was not an easy matter, because both the C(2)- and the C(3)-secondary hydroxy groups were rather unreactive. Prolonged treatment with excess TBS chloride gave a mixture of C(2)- and C(3)-protected compounds. When, however, **21** was treated with a large excess of TBS chloride for a relatively short period, the selectively protected product was obtained in high yield.[16] The remaining C(3)-hydroxy group was then methylated with the Meerwein reagent in the presence of 1,8-bis(dimethylamino)naphthalene (proton sponge)[17] to give a fully protected C(1)−C(11) fragment **22**. The TBS group protecting the C(11)-primary hydroxy moiety was next selectively removed by treatment with camphorsulfonic acid (CSA) at 0 °C.[18] Finally, a three-step conversion of **22**, involving Dess−Martin oxidation of the C(11)-hydroxy group, methylation of the resulting aldehyde with MeLi, and reoxidation with the Dess−Martin reagent, gave **4** (Scheme 4).

Conclusion

Two improved C(1)−C(12) fragments, **3** and **4**, of the antitumor agents tedanolide (**1**) and 13-deoxytedanolide (**2**) have been stereoselectively synthesized, starting from commercially available **16a** and **16b** by way of a common C(3)−C(11) fragment, each in twenty-three reaction steps. The synthesis of these fragments was successfully achieved by virtue of the MPM protecting groups being convertible into the MP-acetal and vice versa, and also all *syn*-selective reactions: tin(II)-mediated aldol reaction, DIBAH reduction of a β-hydroxy ketone, and dihydroxylation with AD-mix α. A new synthesis of the C(13)−C(23) fragments will be reported soon.

Experimental Section

General: Standard reagents and solvents were purified according to known procedures.[19] − TLC analyses were performed on Merck 5715, $60F_{254}$ silica gel plates. − Column chromatographic purifications were performed on Merck silica gel 7734, 70−230 mesh. − $[\alpha]_D$: JASCO DIP-1000 polarimeter. − NMR: JEOL LNM-LA 300 and 500, Varian Gemini-300. − MS: JEOL JM 303HF, JEOL MStation. − IR: JASCO FT/IR-230.

Methyl (2*S*)-3-(4-Methoxybenzyloxy)-2-methylpropanoate (17): Compound **16a** (10.0 g, 84.6 mmol) in CH_2Cl_2 (21 mL) and pyridinium *p*-toluenesulfonate (2.1 g, 8.5 mmol) were added at room temperature under Ar to a stirred solution of MPM trichloroacetimidate (2.62 g, 93.1 mmol) in CH_2Cl_2 (100 mL). After 19 h, MeOH followed by sat. aq. NH_4Cl (10 mL) was added to decompose the reagent, and the mixture was extracted with EtOAc. The extract was washed with sat. aq. NaCl, dried with $MgSO_4$, concentrated in vacuo, and chromatographed on a silica gel column, eluting with EtOAc/hexane (1:20), to give **17** (18.2 g, 92%) as a colorless oil. − R_f (EtOAc/hexane, 1:5) = 0.55. − ^1H NMR (300 MHz, $CDCl_3$): δ = 1.16 (d, *J* = 7.2 Hz, 3 H), 2.71−2.87 (m, 1 H), 3.45 (dd, *J* = 9.2, 5.9 Hz, 1 H), 3.61 (dd, *J* = 9.2, 7.3 Hz, 1 H), 3.69 (s, 3 H), 3.81 (s, 3 H), 4.56 (s, 2 H), 6.87 (d, *J* = 8.4 Hz, 2 H), 7.24 (d, *J* = 8.4 Hz, 2 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.6, 40.7, 52.3, 55.8, 72.2, 73.3, 114.3, 129.8, 130.7, 159.7, 176.0. − FAB-MS; *m*/*z* (%) = 239 (5.2) [M^+ + 1], 154 (100), 136 (73), 121 (47), 107 (23), 89 (19), 77 (18). − HR-MS (FAB): *m*/*z*: calcd. for $C_{13}H_{19}O_4$ 239.1284 [M^+ + 1]; found 239.1287.

(2*S*)-*N*-Methoxy-3-(4-methoxybenzyloxy)-*N*,2-dimethylpropanamide: *N*,*O*-dimethylhydroxylamine−HCl (3.17 g, 32.6 mmol) was added at room temperature under Ar to a stirred solution of **17** (5.0 g, 21.0 mmol) in THF (42 mL), followed by isopropylmagnesium bromide (*i*PrMgBr) (0.65 M, 97 mL, 63 mmol) at −20 °C. After 10 min, the reaction mixture was warmed to −10

°C, and stirring was continued for 30 min. Sat. aq. NH_4Cl (20 mL) was added to decompose the reagent, and the mixture was extracted with EtOAc. The extract was washed with sat. aq. NaCl, dried with $MgSO_4$, and concentrated in vacuo to give a crude Weinreb amide (5.6 g) as a colorless oil. − R_f (EtOAc/hexane, 1:1) = 0.50. − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.10 (d, J = 7.0 Hz, 3 H), 3.21 (s, 3 H), 3.21−3.31 (m, 1 H), 3.39 (dd, J = 8.9, 6.1 Hz, 1 H), 3.61 (dd, J = 8.9, 8.2 Hz, 1 H), 3.69 (s, 3 H), 3.80 (s, 3 H), 4.41 (d, J = 11.6 Hz, 1 H), 4.48 (d, J = 11.6 Hz, 1 H), 6.86 (d, J = 8.9 Hz, 2 H), 7.24 (d, J = 8.9 Hz, 2 H). − FAB-MS; *m*/*z* (%) = 268 (5.8) [M^+ + 1], 220 (5), 154 (100), 136 (100), 121 (31), 107 (33), 89 (26), 77 (24). − HR-MS (FAB): *m*/*z* calcd. for $C_{14}H_{22}O_4N$ 268.1549 [M^+ + 1]; found 268.1540.

(2*S*)-1-(4-Methoxybenzyloxy)-2-methylpentan-3-one (14): Ethylmagnesium bromide (EtMgBr) (1.02 M in THF, 41.1 mL, 42.0 mmol) was added at 0 °C to a solution of the Weinreb amide (5.6 g) in THF (102 mL). After 1 h, the reaction mixture was quenched with sat. aq. NH_4Cl (15 mL) and extracted with EtOAc. The extract was washed with sat. aq. NaCl, dried with $MgSO_4$, concentrated in vacuo, and chromatographed on a silica gel column, eluting with EtOAc/hexane (1:20), to give **14** (4.38 g, 2 steps 88%) as a colorless oil. − R_f (EtOAc/hexane, 1:5) = 0.60. − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.04 (t, J = 7.3 Hz, 3 H), 1.05 (d, J = 7.0 Hz, 3 H), 2.50 (q, J = 7.3 Hz, 2 H), 2.82−2.91(m, 1 H), 3.45 (dd, J = 7.4, 1.6 Hz, 1 H), 3.59 (dd, J = 9.2, 7.4 Hz, 1 H), 3.81(s, 3 H), 4.39 (d, J = 11.6 Hz, 1 H), 4.43 (d, J = 11.6 Hz, 1 H), 6.87 (d, J = 8.7 Hz, 2 H), 7.21 (d, J = 8.7 Hz, 2 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.5, 13.6, 35.3, 46.1, 55.2, 72.0, 72.8, 113.7, 129.2, 130.1, 159.1, 213.8. − FAB-MS; *m*/*z* (%) = 237 (5.4) [M^+ + 1], 154 (75), 137 (85), 121 (100), 107 (19), 89 (17), 77 (17). − HR-MS (FAB): *m*/*z* calcd. for $C_{14}H_{21}O_3$: 237.1491 [M^+ + 1]; found 237.1497. − $C_{14}H_{20}O_3$ (236.31): calcd. C 71.16, H 8.53; found C 70.87, H 8.62.

Methyl (2*R*)-3-[(1,1-Dimethylethyl)dimethylsilyloxy]-2-methylpropanoate: Imidazole (13.8 g, 203 mmol) and *tert*-butyldimethylsilyl chloride (TBSCl) (28.1 g, 178 mmol) were added at 0 °C under Ar to a stirred solution of **16a** (20.0 g, 169 mmol) in CH_2Cl_2 (169 mL). After 12 h at room temperature, the reaction mixture was quenched with MeOH at 0 °C, and extracted with EtOAc. The extract was washed with sat. aq. NH_4Cl and sat. aq. NaCl, dried with $MgSO_4$, and concentrated in vacuo to give crude silyl ether (39.3 g) as a colorless oil. − R_f (hexane) = 0.60. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.03 (s, 6 H), 0.87 (s, 9 H), 1.13 (d, J = 7.0 Hz, 3 H), 2.58−2.72 (m, 1 H), 3.64 (dd, J = 9.7, 6.0 Hz, 1 H), 3.67 (s, 3 H), 3.77 (dd, J = 9.7, 6.9 Hz, 1 H). − ^{13}C NMR (125 MHz, $CDCl_3$): δ = −5.5, 13.5, 18.2, 25.8, 42.5, 51.5, 65.2, 175.5. − IR (neat): $\tilde{\nu}$ = 1745, 1361, 1099 cm^{-1}.

(2*R*)-3-[(1,1-Dimethylethyl)dimethylsilyloxy]-2-methylpropanol: Lithium borohydride ($LiBH_4$) (2.18 g, 100 mmol) was added to a solution of the crude silyl ether (21.2 g) in Et_2O (91 mL), and the mixture was stirred under reflux for 5 h. The mixture was cooled to 0 °C, sat. aq. NH_4Cl was added slowly, and the quenched reaction mixture was extracted with EtOAc. The extract was washed with sat. aq. NH_4Cl and sat. aq. NaCl, dried with $MgSO_4$, and concentrated to give the crude alcohol (18.6 g) as a colorless oil. − R_f (EtOAc/hexane, 1:5) = 0.43. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.07 (s, 6 H), 0.83 (d, J = 6.8 Hz, 3 H), 0.90 (s, 9 H), 1.90−2.00 (m, 1 H), 3.54 (dd, J = 9.9, 8.2 Hz, 1 H), 3.60 (dd, J = 11.0, 7.1 Hz, 1 H), 3.61 (dd, J = 11.0, 4.3 Hz, 1 H), 3.74 (dd, J = 9.9, 4.3 Hz, 1 H). − ^{13}C NMR (125 MHz, $CDCl_3$): δ = −3.8, 13.0, 18.1, 25.6, 36.9, 68.3, 68.8. − IR (neat): $\tilde{\nu}$ = 3364 cm^{-1}.

(2*R*)-3-[(1,1-Dimethylethyl)dimethylsilyloxy]-2-methylpropanal: Dimethyl sulfoxide (DMSO) (13.9 mL, 196 mmol) was slowly added to a stirred solution of oxalyl chloride (8.5 mL, 98 mmol) in CH_2Cl_2 (80 mL) at −78 °C under N_2. After 30 min, the crude alcohol (10.0 g) in CH_2Cl_2 (18 mL) was added dropwise, and stirring was continued for 30 min. Triethylamine (41 mL, 293 mmol) was added dropwise and, after 30 min, the reaction mixture was allowed to warm to room temperature, and then quenched with sat. aq. NH_4Cl and extracted with EtOAc. The extract was washed with sat. aq. NH_4Cl and sat. aq. NaCl, dried with $MgSO_4$, and concentrated in vacuo to give the crude aldehyde (10 g) as a colorless oil. − R_f (EtOAc/hexane, 1:5) = 0.66. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.05 (s, 6 H), 0.87 (s, 9 H), 1.08 (d, J = 7.0 Hz, 3 H), 2.48−2.60 (m, 1 H), 3.80 (dd, J = 10.1, 6.3 Hz, 1 H), 3.85 (dd, J = 10.1, 5.1 Hz, 1 H), 9.73 (d, J = 1.4 Hz, 1 H). − IR (neat): $\tilde{\nu}$ = 1737 cm^{-1}.

Ethyl (2*E*,4*R*)-5-[(1,1-Dimethylethyl)dimethylsilyloxy]-2,4-dimethylpentenoate (18): [1-(Ethoxycarbonyl)ethylidene]triphenylphosphorane (26.0 g, 73.4 mmol) was added at room temperature to a stirred solution of this crude aldehyde (10.0 g) in CH_2Cl_2 (60 mL) under N_2. After 20 h, the reaction mixture was concentrated in vacuo, and chromatographed on a silica gel column, eluting with EtOAc/hexane (1:10), to give **18** (12.5 g, 4 steps 90%) as a colorless oil. − R_f (EtOAc/hexane, 1:20) = 0.57. − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.02 (s, 3 H), 0.03 (s, 3 H), 0.87 (s, 9 H), 1.00 (d, J = 6.7 Hz, 3 H), 1.28 (t, J = 7.0 Hz, 3 H), 1.85 (d, J = 1.5 Hz, 3 H), 2.64−2.74 (m, 1 H), 3.49 (dd, J = 6.4, 1.2 Hz, 2 H), 4.17 (dq, J = 7.0, 2.0 Hz, 2 H), 6.55 (dd, J = 10.1, 1.5 Hz, 1 H). − ^{13}C NMR (125 MHz, $CDCl_3$): δ = −5.4, −5.3, 12.6, 14.3, 16.2, 18.3, 25.9, 26.2, 60.4, 67.1, 127.9, 144.5, 168.3. − FAB-MS; *m*/*z* (%) = 287 (53) [M^+ + 1], 155 (58), 136 (30), 89 (30). − HR-MS (FAB): *m*/*z* calcd. for $C_{15}H_{31}O_3Si$ 287.2043 [M^+ + 1]; found 287.2021. − IR (neat): $\tilde{\nu}$ = 1730, 1658, 1387, 1098 cm^{-1}.

(2*E*,4*R*)-5-[(1,1-Dimethylethyl)dimethylsilyloxy]-2,4-dimethylpentenol: A solution of **18** (5.2 g, 18.2 mmol) in CH_2Cl_2 (21 mL) was added dropwise at −78 °C under Ar to a stirred solution of diisobutylaluminium hydride (DIBAH) (0.95 M in hexane, 40 mL, 36.4 mmol) in CH_2Cl_2 (40 mL). After 30 min, sat. aq. NH_4Cl (10 mL), sat. aq. Rochelle salt (15 mL), and EtOAc (50 mL) were added, and the mixture was stirred until it separated into two layers and then extracted with EtOAc. The extract was washed with sat. aq. NH_4Cl and sat. aq. NaCl, dried with $MgSO_4$, and concentrated in vacuo to give the crude allyl alcohol (5.2 g) as a colorless oil. − R_f (EtOAc/hexane, 1:20) = 0.57. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.04 (s, 6 H), 0.87 (s, 9 H), 0.95 (d, J = 6.6 Hz, 3 H), 1.69 (s, 3 H), 2.53−2.63 (m, 1 H), 3.37 (dd, J = 9.9, 7.3 Hz, 1 H), 3.45 (dd, J = 9.9, 6.2 Hz, 1 H), 3.99 (s, 2 H), 5.18 (d, J = 9.4 Hz, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.4, −5.3, 13.9, 17.1, 18.3, 25.9, 35.1, 67.8, 68.8, 128.9, 135.1. − FAB-MS; *m*/*z* (%) = 245 (12) [M^+ + 1], 154 (61), 136 (69), 121 (22), 89 (100). − HR-MS (FAB): *m*/*z* calcd. for $C_{13}H_{29}O_2Si$ 245.1937 [M^+ + 1]; found 245.1928.

(2*E*,4*R*)-5-[(1,1-Dimethylethyl)dimethylsilyloxy]-2,4-dimethylpentanal (15): DMSO (3.09 g, 43.6 mmol) was slowly added to a stirred solution of oxalyl chloride (1.9 mL, 22 mmol) in CH_2Cl_2 (20 mL) at −78 °C under N_2. After 30 min, this crude allyl alcohol (2.66 g, 10.9 mmol) in CH_2Cl_2 (7 mL) was added dropwise, and stirring was continued for 30 min. Triethylamine (8.9 mL, 65 mmol) was added dropwise and, after 30 min, the reaction mixture was allowed to warm to room temperature, and then quenched with sat. aq. NH_4Cl, and extracted with EtOAc. The extract was washed with sat. aq. NH_4Cl and sat. aq. NaCl, dried with $MgSO_4$, concentrated in vacuo, and chromatographed on a silica gel column, elut-

ing with EtOAc/hexane (1:20), to give **15** (2.59 g, 2 steps 98%) as a colorless oil. − R_f (EtOAc/hexane, 1:10) = 0.65. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.03 (s, 6 H), 0.04 (s, 6 H), 0.87 (s, 9 H), 1.06 (d, *J* = 6.8 Hz, 3 H), 1.77 (d, *J* = 1.5 Hz, 3 H), 2.81−2.96 (m, 1 H), 3.53 (dd, *J* = 9.9, 5.7 Hz, 1 H), 3.59 (dd, *J* = 9.9, 6.2 Hz, 1 H), 6.31 (dq, *J* = 9.7, 1.5 Hz, 1 H), 9.39 (s, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.5, −5.4, 9.4, 16.0, 25.7, 25.8, 36.5, 66.9, 139.2, 157.3, 195.5.

(2*S*,4*R*,5*R*,6*E*,8*R*)-9-[(1,1-Dimethylethyl)dimethylsilyloxy]-5-hydroxy-1-(4-methoxybenzyloxy)-2,4,6,8-tetramethyl-6-nonen-3-one: Diisopropylethylamine (2.65 mL, 15 mmol) was added at room temperature to a stirred solution of tin(II) triflate (washed with Et_2O, dried at 100 °C for 12 h, 5.29 g, 12.7 mmol) in CH_2Cl_2 (40 mL), followed at −78 °C under Ar by **14** (2.0 g, 8.46 mmol) in CH_2Cl_2 (20 mL). After 10 h, **15** (2.66 g, 11.0 mmol) in CH_2Cl_2 (5 mL) was added dropwise, and stirring was continued for 12 h. Phosphate buffer (pH = 7, 20 mL) and Et_2O (40 mL) were added, a precipitate was then removed by filtration through Celite, and the filtrate was extracted with Et_2O. The extract was washed with sat. aq. NH_4Cl and sat. aq. NaCl, dried with $MgSO_4$, and concentrated in vacuo to give the crude hydroxy ketone (4.0 g) as a colorless oil. A small proportion of the ketone was purified by chromatography on a silica gel column, eluting with EtOAc/hexane (1:20). − R_f (EtOAc/hexane, 1:7) = 0.55. − $[\alpha]_D^{30}$ = +24.9 (*c* = 2.0, $CHCl_3$). − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.02 (s, 3 H), 0.03 (s, 3 H), 0.88 (s, 9 H), 0.95 (d, *J* = 6.7 Hz, 3 H), 0.96 (d, *J* = 7.0 Hz, 3 H), 1.02 (d, *J* = 7.0 Hz, 3 H), 1.53 (s, 3 H), 2.51−2.61 (m, 1 H), 2.80−2.90 (m, 1 H), 3.11−3.22 (m, 1 H), 3.34 (dd, *J* = 9.5, 8.5 Hz, 1 H), 3.43 (dd, *J* = 8.5, 4.9 Hz, 1 H), 3.48 (dd, *J* = 9.5, 5.5 Hz, 1 H), 3.57 (dd, *J* = 8.9, 8.5 Hz, 1 H), 3.79 (s, 2 H), 4.37 (d, *J* = 11.4 Hz, 1 H), 4.41 (d, *J* = 11.4 Hz, 1 H), 4.44 (s, 1 H), 5.28 (d, *J* = 9.5 Hz, 1 H), 6.85 (d, *J* = 8.5 Hz, 2 H), 7.19 (d, *J* = 8.5 Hz, 2 H). − ^{13}C NMR (125 MHz, $CDCl_3$): δ = −5.4, −5.3, 8.2, 13.6, 14.1, 17.4, 18.4, 25.9, 35.2, 44.6, 48.6, 65.2, 67.8, 72.7, 73.1, 73.1, 113.8, 128.1, 129.3, 129.6, 133.2, 159.2, 218.2. − IR (neat): $\tilde{\nu}$ = 3490, 1710, 1613 cm^{-1}. − FAB-MS; *m*/*z* (%) = 479 (1.1) [M^+ + 1], 121 (100), 91 (8), 73 (13). − HR-MS (FAB): *m*/*z* calcd. for $C_{27}H_{47}O_5Si$ 479.3193 [M^+ + 1]; found 479.3179.

(2*S*,3*S*,4*R*,5*R*,6*E*,8*R*)-9-[(1,1-Dimethylethyl)dimethylsilyloxy]-1-(4-methoxybenzyloxy)-2,4,6,8-tetramethyl-6-nonene-3,5-diol (13): This crude hydroxy ketone (4.0 g) in THF (10 mL) was added dropwise at −78 °C under N_2 to a stirred solution of DIBAH (0.95 M in hexane, 44.5 mL, 42.3 mmol) in THF (10 mL). After 2 h, sat. aq. NH_4Cl (20 mL), sat. aq. Rochelle salt (20 mL), and EtOAc (50 mL) were added, stirring was continued for 30 min, and a precipitate was filtered off and washed with EtOAc. The filtrate was extracted with EtOAc. The extract was washed with sat. aq. NH_4Cl and sat. aq. NaCl, dried with $MgSO_4$, concentrated in vacuo, and chromatographed on a silica gel column, eluting with EtOAc/hexane (1:10), to give **13** (3.26 g, 2 steps 80%) as a colorless, viscous oil. − R_f (EtOAc/hexane, 1:3) = 0.62. − $[\alpha]_D^{30}$ = +10.8 (*c* = 2.0, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.04 (s, 6 H), 0.83 (d, *J* = 7.0 Hz, 3 H), 0.89 (s, 9 H), 0.96 (d, *J* = 6.8 Hz, 3 H), 1.05 (d, *J* = 7.0 Hz, 3 H), 1.55 (s, 3 H), 1.78−1.89 (m, 1 H), 1.90−2.01 (m, 1 H), 2.54−2.65 (m, 1 H), 3.37 (dd, *J* = 10.6, 7.5 Hz, 1 H), 3.40 (dd, *J* = 9.7, 6.4 Hz, 1 H), 3.43 (dd, *J* = 10.6, 5.6 Hz, 1 H), 3.47 (dd, *J* = 9.7, 6.1 Hz, 1 H), 3.74 (dd, *J* = 6.6, 3.5 Hz, 1 H), 3.81 (s, 1 H), 4.12 (d, *J* = 2.0 Hz, 1 H), 4.41 (s, 2 H), 5.23 (d, *J* = 9.5 Hz, 1 H), 6.86 (d, *J* = 8.6 Hz, 2 H), 7.21 (d, *J* = 8.6 Hz, 2 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.3, −5.3, 6.0, 13.4, 14.0, 17.3, 18.4, 25.9, 35.1, 36.7, 55.2, 68.0, 72.9, 73.7, 76.6, 79.5, 113.7, 127.4, 129.1, 130.1, 135.8, 159.1. − IR (neat): $\tilde{\nu}$ = 3433 cm^{-1}, 1613. − FAB-MS *m*/*z* (%) = 481 (4.9) [M^+ + 1], 154 (100), 137 (73), 121 (100), 107 (33), 89 (38). − HR-MS (FAB): *m*/*z* calcd. for $C_{27}H_{49}O_5Si$ 481.3350 [M^+ + 1]; found 481.3366.

(2*S*,3*S*,4*R*,5*R*,6*E*,8*R*)-9-[(1,1-Dimethylethyl)dimethylsilyloxy]-1-(4-methoxybenzyloxy)-3,5-(1-methylethylidenedioxy)-2,4,6,8-tetramethyl-6-nonene (13′): 2,2-Dimethoxypropane (0.06 mL, 0.5 mmol) and pyridinium *p*-toluenesulfonate (1 mg, 5 μmol) were added to a stirred solution of **13** (24 mg, 0.05 mmol) in CH_2Cl_2 (0.5 mL) under N_2. After 30 min, the reaction mixture was quenched with triethylamine, concentrated in vacuo, and chromatographed on a silica gel column, eluting with EtOAc/hexane (1:20), to give **13′** (23 mg, 89%) as a colorless oil. − R_f (EtOAc/hexane, 1:20) = 0.35. − $[\alpha]_D^{30}$ = +6.8 (*c* = 1.3, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.03 (s, 3 H), 0.04 (s, 3 H), 0.66 (d, *J* = 6.7 Hz, 3 H), 0.89 (s, 9 H), 0.95 (d, *J* = 6.4 Hz, 3 H), 1.04 (d, *J* = 6.7 Hz, 3 H), 1.40 (s, 3 H), 1.41 (s, 3 H), 1.52 (s, 3 H), 1.55−1.57 (m, 1 H), 1.77−1.86 (m, 1 H), 2.55−2.63 (m, 1 H), 3.30−3.35 (m, 2 H), 3.38 (dd, *J* = 9.8, 7.0 Hz, 1 H), 3.82 (dd, *J* = 9.8, 6.1 Hz, 1 H), 3.68 (dd, *J* = 9.8, 1.8 Hz, 1 H), 3.81 (s, 3 H), 4.14 (s, 1 H), 4.37 (d, *J* = 11.9 Hz, 1 H), 4.46 (d, *J* = 11.9 Hz, 1 H), 5.23 (d, *J* = 9.5 Hz, 1 H), 6.87 (d, *J* = 8.5 Hz, 2 H), 7.24 (d, *J* = 8.5 Hz, 2 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.4, −5.3, 5.3, 13.8, 14.8, 17.4, 18.4, 19.6, 26.0, 30.0, 35.0, 35.3, 55.2, 68.1, 72.8, 75.6, 75.7, 98.8, 113.7, 126.9, 129.1, 130.6, 132.5, 159.1. − IR (neat): $\tilde{\nu}$ = 1612 cm^{-1}. − FAB-MS; *m*/*z* (%) = 521 (1.9) [M^+ + 1], 391 (2), 154 (78), 137 (83), 121 (100), 107 (40), 89 (100), 73 (100). − HR-MS (FAB): *m*/*z* calcd. for $C_{30}H_{53}O_5Si$ 521.3663 [M^+ + 1]; found 521.3641.

(2*S*,3*S*,4*R*,5*R*,6*E*,8*R*)-9-[(1,1-Dimethylethyl)dimethylsilyloxy]-5-hydroxy-1,3-(4-methoxybenzylidenedioxy)-2,4,6,8-tetramethyl-6-nonene: DDQ (272 mg, 1.2 mmol) was added slowly at −15 °C under N_2 to a stirred mixture of molecular sieves (3 Å, 300 mg) and **13** (480 mg, 1.0 mmol) in CH_2Cl_2 (5.0 mL). After 4 h at 0 °C, sat. aq. $NaHCO_3$ (6 mL) and Et_2O (10 mL) were added, and the mixture was stirred vigorously for 20 min and then extracted with Et_2O. The extract was washed with sat. aq. $NaHCO_3$ and sat. aq. NaCl, dried with Na_2SO_4, and concentrated in vacuo to give the crude acetal (450 mg) as a colorless oil. − R_f (EtOAc/hexane, 1:5) = 0.43. − FAB-MS; *m*/*z* (%) = 479 (20) [M^+ + 1], 325 (6), 207 (26), 193 (3), 154 (100), 136 (100), 121 (82), 107 (29), 89 (63), 73 (57). − HR-MS (FAB): *m*/*z* calcd. for $C_{27}H_{47}O_5Si$ 479.3191 [M^+ + 1]; found 479.3223.

(2*S*,3*S*,4*R*,5*R*,6*E*,8*R*)-9-[(1,1-Dimethylethyl)dimethylsilyloxy]-1,3-(4-methoxybenzylidenedioxy)-5-methoxymethoxy-2,4,6,8-tetramethyl-6-nonene: Diisopropylethylamine (3.48 mL, 18.7 mmol) and MOMCl (0.76 mL, 9.4 mmol) were added at 0 °C to a stirred solution of this crude acetal (450 mg) in CH_2Cl_2 (10.4 mL). After 40 h at room temperature, the reaction mixture was quenched with sat. aq. NH_4Cl (2 mL), and extracted with EtOAc. The extract was washed with sat. aq. NH_4Cl and sat. aq. NaCl, dried with Na_2SO_4, and concentrated in vacuo to give the crude MOM ether (500 mg) as a colorless oil. A small proportion of the ether was purified by chromatography on a silica gel column, eluting with EtOAc/hexane (1:20). − R_f (EtOAc/hexane, 1:5) = 0.73. − $[\alpha]_D^{28}$ = +19.4 (*c* = 2.0, $CHCl_3$). − ^{1}H NMR (500 MHz, C_6D_6): δ = 0.05 (s, 6 H), 0.97 (s, 9 H), 0.98 (d, *J* = 7.0 Hz, 3 H), 1.25 (d, *J* = 6.9 Hz, 3 H), 1.29 (d, *J* = 6.7 Hz, 3 H), 1.43 (s, 3 H), 1.85−1.94 (m, 1 H), 1.95−2.02 (m, 1 H), 2.58−2.67 (m, 1 H), 3.18 (s, 3 H), 3.26 (s, 3 H), 3.38 (dd, *J* = 9.5, 6.6 Hz, 1 H), 3.43 (dd, *J* = 9.5, 6.4 Hz, 1 H), 3.92 (dd, *J* = 11.4, 1.1 Hz, 1 H), 3.94 (H, dd, *J* = 11.4, 1.4 Hz), 4.00 (dd, *J* = 9.8, 1.8 Hz, 1 H), 4.10 (s, 1 H), 4.44 (d, *J* = 6.8 Hz, 1 H), 4.69 (d, *J* = 6.8 Hz, 1 H), 5.38 (d, *J* = 9.5 Hz, 1 H), 5.53 (s, 1 H), 6.83 (d,

J = 8.6 Hz, 2 H), 7.68 (d, J = 8.6 Hz, 2 H). − ^{13}C NMR (125 MHz, C_6D_6): δ = −5.3, −5.3, 9.7, 11.7, 14.6, 17.4, 18.4, 26.0, 29.8, 35.5, 37.3, 54.7, 55.8, 68.3, 74.0, 78.4, 82.0, 95.0, 102.4, 113.7, 128.3, 129.3, 132.6, 132.6, 160.3. − IR (neat): $\tilde{\nu}$ = 1616 cm^{-1}. − FAB-MS m/z (%) = 523 (31) [M$^+$ + 1], 325 (22), 207 (46), 193 (7), 154 (100), 137 (82), 121 (91), 107 (21), 89 (51), 73 (39). − HR-MS (FAB): m/z calcd. for $C_{29}H_{51}O_6Si$ 523.3455 [M$^+$ + 1]; found 523.3443.

(2*S*,3*S*,4*R*,5*R*,6*E*,8*R*)-9-[(1,1-Dimethylethyl)dimethylsilyloxy]-3-(4-methoxybenzyloxy)-5-methoxymethoxy-2,4,6,8-tetramethyl-6-nonenol (19): DIBAH (0.95 M in hexane, 5.3 mL, 4.7 mmol) was added dropwise at −30 °C under N_2 to a stirred solution of this crude MOM ether(500 mg) in CH_2Cl_2 (10 mL). After 2 h, sat. aq. NH_4Cl, sat. aq. Rochelle salt (12 mL), and EtOAc (20 mL) were added, and stirring was continued for 30 min. A precipitate was filtered off through Celite and washed with EtOAc. The filtrate was extracted with EtOAc. The extract was washed with sat. aq. NH_4Cl and sat. aq. NaCl, dried with $MgSO_4$, concentrated in vacuo, and chromatographed on a silica gel column, eluting with Et_2O/hexane (1:5), to give **19** (330 mg, 3 steps 63%) as a colorless, viscous oil. − R_f (EtOAc/hexane, 1:5) = 0.29. − $[\alpha]_D^{29}$ = +3.3 (c = 1.9, $CHCl_3$). − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.03 (s, 6 H), 0.88 (s, 9 H), 0.93 (d, J = 7.0 Hz, 3 H), 0.94 (d, J = 6.4 Hz, 3 H), 1.11 (d, J = 6.7 Hz, 3 H), 1.54 (d, J = 1.2 Hz, 3 H), 1.90−1.99 (m, 1 H), 2.06−2.15 (m, 1 H), 2.55−2.65 (m, 1 H), 3.34 (dd, J = 9.8, 6.7 Hz, 1 H), 3.39 (s, 3 H), 3.43 (dd, J = 9.8, 7.3 Hz, 1 H), 3.80 (s, 3 H), 4.46 (d, J = 6.7 Hz, 1 H), 4.49 (d, J = 11.7 Hz, 1 H), 4.51 (d, J = 10.7 Hz, 1 H), 4.60 (d, J = 6.7 Hz, 1 H), 5.16 (d, J = 9.5 Hz, 1 H), 6.87 (d, J = 8.9 Hz, 2 H), 7.25 (d, J = 8.9 Hz, 2 H). − ^{13}C NMR (125 MHz, $CDCl_3$): δ = −5.3, −5.3, 11.0, 12.2, 12.3, 17.3, 18.4, 25.9, 35.5, 37.4, 38.0, 55.3, 55.8, 66.4, 67.9, 73.5, 81.0, 93.7, 113.7, 129.0, 131.0, 132.5, 133.8, 159.0. − IR (neat): $\tilde{\nu}$ = 3471 cm^{-1}, 1613. − FAB-MS; m/z (%) = 525 (13) [M$^+$ + 1], 325 (11), 217 (100), 207 (4), 193 (3), 181 (100), 121 (100), 107 (14), 91 (100), 73 (100). − HR-MS (FAB): m/z calcd. for $C_{29}H_{53}O_6Si$ 525.3612 [M$^+$ + 1]; found 525.3639. − $C_{29}H_{52}O_6Si$ (524.81): calcd. C 66.37, H 9.99; found C 66.44, H 10.37.

(2*S*,3*S*,4*R*,5*R*,6*E*,8*R*)-9-[(1,1-Dimethylethyl)dimethylsilyloxy]-3-(4-methoxybenzyloxy)-5-methoxymethoxy-2,4,6,8-tetramethyl-6-nonenal: Pyridine (0.12 mL, 1.43 mmol) was added at room temperature to a stirred solution of Dess−Martin periodinane (184 mg, 0.43 mmol) in CH_2Cl_2 (1.4 mL). To this solution was added **19** (150 mg, 0.29 mmol) in CH_2Cl_2 (1.5 mL), and stirring was continued for 30 min. Et_2O (3 mL), sat. aq. $NaHCO_3$ (1 mL), and sat. aq. $Na_2S_2O_3$ (1 mL) were added to decompose the reagent, and the mixture was extracted with Et_2O. The extract was washed with sat. aq. NH_4Cl and sat. aq. NaCl, dried with $MgSO_4$, and concentrated in vacuo to give the crude aldehyde (150 mg) as a colorless oil. − R_f (EtOAc/hexane, 1:5) = 0.59. − ^{1}H NMR (500 MHz, C_6D_6): δ = 0.04 (s, 3 H), 0.04 (s, 3 H), 0.93 (d, J = 6.7 Hz, 3 H), 0.95 (s, 9 H), 1.06 (d, J = 7.0 Hz, 3 H), 1.24 (d, J = 6.7 Hz, 3 H), 1.50 (d, J = 1.2 Hz, 3 H), 1.91−1.99 (m, 1 H), 2.54−2.60 (m, 1 H), 2.60−2.66 (m, 1 H), 3.21 (s, 3 H), 3.29 (s, 3 H), 3.34 (dd, J = 9.8, 6.7 Hz, 1 H), 3.43 (dd, J = 9.8, 6.7 Hz, 1 H), 3.90 (dd, J = 9.5, 4.8 Hz, 1 H), 4.05 (d, J = 7.3 Hz, 1 H), 4.39 (d, J = 6.7 Hz, 1 H), 4.44 (s, 2 H), 4.68 (d, J = 6.7 Hz, 1 H), 5.30 (d, J = 9.5 Hz, 1 H), 6.78 (d, J = 8.5 Hz, 2 H), 7.24 (d, J = 8.5 Hz, 2 H), 9.76 (d, J = 0.9 Hz, 1 H). − ^{13}C NMR (125 MHz, C_6D_6): δ = −5.2, −5.2, 9.2, 10.8, 12.4, 17.4, 18.5, 26.2, 35.8, 38.8, 49.0, 54.7, 55.7, 68.2, 73.3, 79.6, 83.0, 93.9, 114.1, 127.8, 131.2, 133.0, 133.5, 159.7, 203.3. − FAB-MS; m/z (%) = 523 (4) [M$^+$ + 1], 193 (4), 154 (52), 136 (100), 121 (100), 107 (22), 89 (32), 77 (36). − HR-MS (FAB): m/z calcd. for $C_{29}H_{51}O_6Si$ 523.3455 [M$^+$ + 1]; found 523.3475.

Methyl (2*E*,4*R*,5*R*,6*R*,7*S*,8*E*,10*R*)-11-[(1,1-Dimethylethyl)dimethylsilyloxy]-5-(4-methoxybenzyloxy)-7-methoxymethoxy-4,6,8,10-tetramethyl-8-undecenoate: (Methoxycarbonylmethylene)triphenylphosphorane (117 mg, 0.35 mmol) was added at room temperature to a stirred solution of this crude aldehyde (150 mg) in benzene (2.9 mL). After 25 h, the reaction mixture was concentrated in vacuo, and chromatographed on a silica gel column, eluting with EtOAc/hexane (1:20−1:10), to give the α,β-unsaturated ester (155 mg, 2 steps 94%) as a colorless, viscous oil. − R_f (Et_2O/CH_2Cl_2, 1:20) = 0.46; R_f (EtOAc/hexane, 1:5) = 0.59. − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.03 (s, 3 H), 0.04 (s, 3 H), 0.88 (s, 9 H), 0.93 (d, J = 6.7 Hz, 3 H), 1.04 (d, J = 6.7 Hz, 3 H), 1.12 (d, J = 6.8 Hz, 3 H), 1.57 (d, J = 1.2 Hz, 3 H), 1.84−1.89 (m, 1 H), 2.58−2.77 (m, 2 H), 3.29 (dd, J = 7.6, 2.4 Hz, 1 H), 3.37 (s, 3 H), 3.38 (dd, J = 9.0, 7.6 Hz, 1 H), 3.43 (dd, J = 9.8, 6.6 Hz, 1 H), 3.72 (s, 3 H), 3.80 (s, 3 H), 3.89 (d, J = 9.2 Hz, 1 H), 4.42 (d, J = 6.7 Hz, 1 H), 4.46 (d, J = 10.7 Hz, 1 H), 4.48 (d, J = 10.7 Hz, 1 H), 4.61 (d, J = 6.7 Hz, 1 H), 5.20 (dd, J = 9.3, 0.8 Hz, 1 H), 5.84 (dd, J = 15.7, 1.1 Hz, 1 H), 6.87 (d, J = 8.7 Hz, 2 H), 6.95 (dd, J = 8.7, 15.7 Hz, 1 H), 7.24 (d, J = 8.7 Hz, 2 H). − ^{13}C NMR (125 MHz, $CDCl_3$): δ = −5.3, −5.2, 10.3, 11.6, 15.8, 17.2, 18.4, 25.9, 35.5, 38.1, 39.9, 51.4, 55.2, 55.7, 67.9, 73.7, 82.2, 84.0, 93.1, 113.7, 120.5, 128.7, 131.0, 132.3, 135.4, 151.6, 158.9, 166.9. − FAB-MS; m/z (%) = 579 (0.4) [M$^+$ + 1], 521(0.4), 123(100), 91(8), 77(4).

Methyl (2*R*,3*S*,4*R*,5*S*,6*R*,7*S*,8*E*,10*R*)-11-[(1,1-Dimethylethyl)dimethylsilyloxy]-2,3-dihydroxy-5-(4-methoxybenzyloxy)-7-methoxymethoxy-4,6,8,10-tetramethyl-8-undecenoate (12): Methanesulfonamide (33 mg, 0.31 mmol) was added at room temperature to a stirred solution of AD-mix α (408 mg) in tBuOH/H_2O (1:1, 3.1 mL). After 10 min, this ester (180 mg, 0.31 mmol) in tBuOH/H_2O (1:1, 3.1 mL) was added at 0 °C. After 24 h, the reaction mixture was quenched with Na_2SO_3 (436 mg, 3.1 mmol), and extracted with EtOAc. The extract was washed with sat. aq. NH_4Cl and sat. aq. NaCl, dried with $MgSO_4$, concentrated in vacuo, and chromatographed on a silica gel column, eluting with EtOAc/hexane (2:3), to give **12** (164 mg, 86%) as a colorless, viscous oil. − R_f (EtOAc/hexane, 1:3) = 0.25. − $[\alpha]_D^{29}$ = +3.7 (c = 1.7, $CHCl_3$). − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.02 (s, 6 H), 0.87 (s, 9 H), 0.95 (d, J = 6.7 Hz, 3 H), 1.08 (d, J = 6.8 Hz, 6 H), 1.57 (s, 3 H), 1.95−1.99 (m, 1 H), 2.00−2.08 (m, 1 H), 2.41 (d, J = 7.6 Hz, 1 H), 2.58−2.64 (m, 1 H), 3.23 (d, J = 5.3 Hz, 1 H), 3.35 (dd, J = 9.8, 7.1 Hz, 1 H), 3.39 (s, 3 H), 3.45 (dd, J = 9.8, 6.1 Hz, 1 H), 3.51 (dd, J = 8.5, 4.2 Hz, 1 H), 3.80 (s, 6 H), 3.88 (d, J = 7.3 Hz, 1 H), 3.94 (ddd, J = 7.3, 4.8, 2.6 Hz, 1 H), 4.34 (dd, J = 5.3, 2.6 Hz, 1 H), 4.44 (d, J = 10.7 Hz, 1 H), 4.48 (d, J = 6.3 Hz, 1 H), 4.49 (d, J = 10.8 Hz, 1 H), 4.59 (d, J = 6.6 Hz, 1 H), 5.19 (d, J = 9.5 Hz, 1 H), 6.86 (d, J = 8.5 Hz, 2 H), 7.26 (d, J = 8.5 Hz, 2 H). − ^{13}C NMR (125 MHz, $CDCl_3$): δ = −5.4, −5.3, 10.0, 10.7, 12.3, 17.3, 18.3, 25.9, 35.4, 38.2, 39.4, 52.7, 55.2, 55.8, 67.8, 72.2, 73.5, 74.0, 81.0, 83.9, 93.8, 113.7, 129.0, 130.8, 132.5, 133.6, 159.1, 173.9. − IR (neat): $\tilde{\nu}$ = 3477 cm^{-1}, 1743, 1613, 1390. − FAB-MS; m/z (%) = 613 (1.3) [M$^+$ + 1], 154 (88), 136 (84), 121 (100), 107 (28), 89 (35), 73 (43). − HR-MS (FAB): m/z calcd. for $C_{32}H_{57}O_9Si$ 613.3772 [M$^+$ + 1]; found 613.3777. − $C_{32}H_{56}O_9Si$ (612.85): calcd. C 62.72, H 9.21; found C 63.04, H 9.42.

Methyl (2*R*,3*S*,4*R*,5*S*,6*R*,7*S*,8*E*,10*R*)-11-[(1,1-Dimethylethyl)dimethylsilyloxy]-2-hydroxy-3,5-(4-methoxybenzylidenedioxy)-7-methoxymethoxy-4,6,8,10-tetramethyl-8-undecenoate: DDQ (159 mg, 0.70 mmol) was added at −30 °C under Ar to a stirred mixture of **12** (390 mg, 0.636 mmol) and molecular sieves (3 Å, 160 mg) in CH_2Cl_2 (3.4 mL). After 30 min at −5 °C, sat. aq. $NaHCO_3$ and Et_2O (5 mL) were added, and the mixture was stirred

vigorously for 30 min and then extracted with Et_2O. The extract was washed with sat. aq. $NaHCO_3$ and sat. aq. NaCl, dried with Na_2SO_4, and concentrated in vacuo to give the crude acetal (372 mg) as a colorless viscous oil. − R_f (EtOAc/hexane, 1:3) = 0.36. − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.02 (s, 3 H), 0.03 (s, 3 H), 0.88 (s, 9 H), 0.91 (d, *J* = 6.7 Hz, 3 H), 0.94 (d, *J* = 6.7 Hz, 3 H),1.16 (d, *J* = 6.7 Hz, 3 H), 1.56 (s, 3 H), 1.90−1.94 (m, 1 H), 2.08−2.12 (m, 1 H), 2.57−2.63 (m, 1 H), 2.89 (d, *J* = 5.2 Hz, 1 H), 3.34 (s, 3 H), 3.38 (dd, *J* = 9.8, 6.8 Hz, 1 H), 3.42 (dd, *J* = 9.6, 6.4 Hz, 1 H), 3.71 (dd, *J* = 1.9, 7.4 Hz, 1 H), 3.80 (s, 3 H), 3.82 (s, 3 H), 3.97 (s, 1 H), 4.03 (dd, *J* = 6.9, 2.1 Hz, 1 H), 4.39 (dd, *J* = 6.7, 5.2 Hz, 1 H), 4.45 (d, *J* = 7.0 Hz, 1 H), 4.54 (d, *J* = 7.0 Hz, 1 H), 5.17 (d, *J* = 9.3 Hz, 1 H), 5.56 (s, 1 H), 6.89 (d, *J* = 8.7 Hz, 2 H), 7.41 (d, *J* = 8.7 Hz, 2 H).

Methyl (2*R*,3*S*,4*R*,5*S*,6*R*,7*S*,8*E*,10*R*)-11-[(1,1-Dimethylethyl)dimethylsilyloxy]-3,5-(4-methoxybenzylidenedioxy)-2,7-bis(methoxymethoxy)-4,6,8,10-tetramethyl-8-undecenoate (11): Diisopropylethylamine (2.22 mL, 12.7 mmol), tetrabutylammonium iodide (23.5 mg, 0.064 mmol), and MOMCl (0.48 mL, 6.36 mmol) were added at 0 °C under N_2 to a stirred solution of this crude acetal (372 mg) in CH_2Cl_2 (3.4 mL). After 20 h at room temperature, the reaction mixture was quenched with sat. aq. NH_4Cl (1 mL) and extracted with EtOAc. The extract was washed with sat. aq. NH_4Cl and sat. aq. NaCl, dried with Na_2SO_4, concentrated in vacuo, and chromatographed on a silica gel, eluting with EtOAc/hexane (1:10), to give **11** (250 mg, 2 steps 60%) as a colorless, viscous oil. − R_f (EtOAc/hexane, 1:3) = 0.62. − $[\alpha]_D^{29}$ = +22.0 (*c* = 2.0, $CHCl_3$). − ^{1}H NMR (500 MHz, C_6D_6): δ = 0.05 (s, 6 H), 0.96 (d, *J* = 7.8 Hz, 3 H), 0.97 (s, 9 H), 1.24 (d, *J* = 6.7 Hz, 3 H), 1.34 (s, 3 H), 1.37 (d, *J* = 6.7 Hz, 3 H), 2.00−2.07 (m, 1 H), 2.19−2.24 (m, 1 H), 2.55−2.63 (m, 1 H), 3.23 (s, 3 H), 3.26 (s, 3 H), 3.35 (s, 3 H), 3.36 (dd, *J* = 9.6, 6.8 Hz, 1 H), 3.43 (dd, *J* = 9.5, 6.5 Hz, 1 H), 3.47 (s, 3 H), 3.97 (dd, *J* = 9.9, 1.7 Hz, 1 H), 4.10 (s, 1 H), 4.39 (d, *J* = 6.6 Hz, 1 H), 4.41 (dd, *J* = 9.0, 1.7 Hz, 1 H), 4.63 (d, *J* = 9.0 Hz, 1 H), 4.64 (d, *J* = 6.9 Hz, 1 H), 4.65 (d, *J* = 7.0 Hz, 1 H), 4.70 (d, *J* = 6.9 Hz, 1 H), 5.35 (d, *J* = 9.3 Hz, 1 H), 5.61 (s, 1 H), 6.82 (d, *J* = 8.7 Hz, 2 H), 7.63 (d, *J* = 8.7 Hz, 2 H). − ^{13}C NMR (125 MHz, C_6D_6): δ = −5.4, −5.3, 10.0, 10.7, 12.3, 17.3, 18.3, 25.9, 35.4, 38.2, 39.4, 52.7, 55.2, 55.8, 67.8, 72.2, 73.5, 74.0, 81.0, 83.9, 93.8, 113.7, 129.0, 130.8, 132.5, 133.6, 159.1, 173.9. − IR (neat): $\tilde{\nu}$ = 1748 cm^{-1}, 1615, 1302. − FAB-MS; *m*/*z* (%) = 655 (14.2) [M^+ + 1], 287 (75), 207 (7), 193 (6), 181 (51), 154 (32), 135 (83), 121 (83), 107 (25), 89 (100), 77 (22). − HR-MS (FAB): *m*/*z* calcd. for $C_{34}H_{59}O_{10}Si$ 655.3875 [M^+ + 1]; found 655.3903. − $C_{34}H_{58}O_{10}Si$ (654.91): calcd. C 62.36, H 8.93; found C 62.52, H 9.28.

Methyl (2*R*,3*S*,4*R*,5*S*,6*R*,7*S*,8*E*,10*R*)-11-hydroxy-3,5-(4-methoxybenzylidenedioxy)-2,7-bis(methoxymethoxy)-4,6,8,10-tetramethyl-8-undecenoate: TBAF (1.0 M in THF, 0.53 mL, 0.53 mmol) was added at room temperature under N_2 to a stirred solution of **11** (230 mg, 0.35 mmol) in THF (3.5 mL). After 8 h, the reaction mixture was quenched with sat. aq. $NaHCO_3$ (1 mL) and extracted with EtOAc. The extract was washed with sat. aq. NH_4Cl and sat. aq. NaCl, dried with Na_2SO_4, concentrated in vacuo, and chromatographed on a silica gel column, eluting with EtOAc/hexane (2:3), to give the product (177 mg, 93%) as a colorless, viscous oil:− R_f (EtOAc/hexane, 12:3) = 0.24. − $[\alpha]_D^{29}$ = +35.5 (*c* = 2.0, $CHCl_3$). − ^{1}H NMR (500 MHz, C_6D_6): δ = 0.81 (d, *J* = 6.7 Hz, 3 H), 1.21 (d, *J* = 6.7 Hz, 3 H), 1.28 (s, 3 H), 1.35 (d, *J* = 6.7 Hz, 3 H), 1.99−2.03 (m, 1 H), 2.12−2.16 (m, 1 H), 2.40−2.47 (m, 1 H), 3.15−3.20 (m, 2 H), 3.23 (s, 3 H), 3.27 (s, 3 H), 3.31 (s, 3 H), 3.48 (s, 3 H), 3.93 (dd, *J* = 9.5, 1.2 Hz, 1 H), 4.01 (s, 1 H), 4.30 (d, *J* = 7.0 Hz, 1 H), 4.40 (dd, *J* = 9.2, 1.5 Hz, 1 H), 4.53 (d, *J* = 6.7 Hz, 1 H), 4.61 (d, *J* = 9.2 Hz, 1 H), 4.63 (d, *J* = 6.7 Hz, 1 H), 4.70 (d, *J* = 7.0 Hz, 1 H), 5.22 (d, *J* = 9.8 Hz, 1 H), 5.60 (s, 1 H), 6.83 (d, *J* = 8.5 Hz, 2 H), 7.62 (d, *J* = 8.5 Hz, 2 H). − ^{13}C NMR (125 MHz, C_6D_6): δ = 7.2, 9.8, 14.2, 17.0, 30.2, 35.5, 36.5, 51.6, 54.7, 55.7, 67.8, 78.5, 82.1, 83.2, 95.1, 97.1, 102.5, 113.7, 129.2, 132.1, 133.5, 160.4, 170.7. − IR (neat): $\tilde{\nu}$ = 3498 cm^{-1} 1745, 1615, 1348. − FAB-MS *m*/*z* (%) = 541 (9.1) [M^+ + 1], 286 (88), 154 (50), 133 (100), 121 (58), 107 (24), 89 (22), 73 (19). − HR-MS (FAB): *m*/*z* calcd. for $C_{28}H_{45}O_{10}$: 541.3013 [M^+ + 1]; found 541.2991.

Methyl (2*R*,3*S*,4*R*,5*S*,6*R*,7*S*,8*E*,10*R*)-3,5-(4-Methoxybenzylidenedioxy)-2,7-bis(methoxymethoxy)-4,6,8,10-tetramethyl-11-oxo-8-undecenoate: This compound (177 mg, 0.327 mmol) in CH_2Cl_2 (1.8 mL) was added at room temperature to a stirred solution of Dess−Martin periodinane (210 mg, 0.49 mmol) and pyridine (0.08 mL, 0.98 mmol) in CH_2Cl_2 (1.5 mL). After 30 min, Et_2O (10 mL), sat. aq. $NaHCO_3$ (1 mL), and sat. aq. $Na_2S_2O_3$ (1 mL) were added, and the mixture was extracted with Et_2O. The extract was washed with sat. aq. NH_4Cl and sat. aq. NaCl, dried with $MgSO_4$, and concentrated in vacuo to give the crude product (200 mg) as a colorless, viscous oil. − R_f (EtOAc/hexane, 2:3) = 0.50. − ^{1}H NMR (500 MHz, C_6D_6): δ = 0.88 (d, *J* = 7.0 Hz, 3 H), 1.12 (s, 3 H), 1.13 (d, *J* = 7.0 Hz, 3 H), 1.33 (d, *J* = 6.7 Hz, 3 H), 1.94−1.97 (m, 1 H), 2.16−2.17 (m, 1 H), 2.79−2.82 (m, 1 H), 3.23 (s, 3 H), 3.26 (s, 3 H), 3.29 (s, 3 H), 3.49 (s, 3 H), 3.91 (dd, *J* = 9.5, 0.9 Hz, 1 H), 3.99 (s, 1 H), 4.22 (d, *J* = 6.7 Hz, 1 H), 4.38 (dd, *J* = 9.2, 1.5 Hz, 1 H), 4.46 (d, *J* = 6.7 Hz, 1 H), 4.63 (d, *J* = 9.2 Hz, 1 H), 4.64 (d, *J* = 6.7 Hz, 1 H), 4.71 (d, *J* = 6.7 Hz, 1 H), 5.22 (d, *J* = 9.5 Hz, 1 H), 5.58 (s, 1 H), 6.83 (d, *J* = 8.5 Hz, 2 H), 7.62 (d, *J* = 8.5 Hz, 2 H), 9.20 (d, *J* = 1.5 Hz, 1 H). − ^{13}C NMR (125 MHz, C_6D_6): δ = 7.3, 9.7, 14.1, 14.3, 14.7, 30.0, 36.3, 46.0, 51.7, 54.8 55.8, 56.2, 78.1, 78.5, 82.1, 83.2, 83.3, 95.2, 97.2, 102.7, 113.8, 122.2, 132.1, 137.1, 160.6, 170.6, 199.6.

Methyl (2*R*,3*S*,4*R*,5*S*,6*R*,7*S*,8*E*,10*R*)-11-Hydroxy-3,5-(4-methoxybenzylidenedioxy)-2,7-bis(methoxymethoxy)-4,6,8,10-tetramethyl-8-dodecenoate: Methyllithium (MeLi) (1.19 M in Et_2O, 0.33 mL, 0.39 mmol) was added at −78 °C to a stirred solution of this crude compound (200 mg) in Et_2O (6.6 mL). After 30 min, additional MeLi (0.1 mL, 0.13 mmol) was added, and stirring was continued for 30 min. The reaction mixture was quenched with sat. aq. NH_4Cl and extracted with Et_2O. The extract was washed with sat. aq. NH_4Cl and sat. aq. NaCl, dried with Na_2SO_4, concentrated in vacuo, and chromatographed on a silica gel column, eluting with EtOAc/hexane (1:3), to give a 1:2.6 diastereomeric mixture of secondary hydroxy compounds (73 mg, 2 steps 40%) and the recovered starting material (29 mg, 16%).

Methyl (2*R*,3*S*,4*R*,5*S*,6*R*,7*S*,8*E*,10*R*)-3,5-(4-Methoxybenzylidenedioxy)-2,7-bis(methoxymethoxy)-4,6,8,10-tetramethyl-11-oxo-8-dodecenoate (3): The mixture of hydroxy compounds (73 mg, 0.132 mmol) was oxidized with Dess−Martin periodinane (85 mg, 0.198 mmol) as described above, and chromatographed on a silica gel column, eluting with EtOAc/hexane (1:5), to give **3** (62 mg, 85%) as a colorless, viscous oil. − R_f (EtOAc/hexane, 2:3) = 0.54. − $[\alpha]_D^{21}$ = +69.6 (*c* = 2.0, $CHCl_3$). − ^{1}H NMR (500 MHz, C_6D_6): δ = 1.00 (d, *J* = 6.7 Hz, 3 H), 1.14 (d, *J* = 6.7 Hz, 3 H), 1.18 (s, 3 H), 1.34 (d, *J* = 6.7 Hz, 3 H), 1.71 (s, 3 H), 1.93−1.98 (m, 1 H), 2.15−2.19 (m, 1 H), 2.99−3.06 (m, 1 H), 3.23 (s, 3 H), 3.27 (s, 3 H), 3.29 (s, 3 H), 3.49 (s, 3 H), 3.90 (dd, *J* = 9.8, 1.8 Hz, 1 H), 3.99 (s, 1 H), 4.21 (d, *J* = 7.0 Hz, 1 H), 4.38 (dd, *J* = 9.2, 1.5 Hz, 1 H), 4.42 (d, *J* = 6.7 Hz, 1 H), 4.62 (d, *J* = 9.2 Hz, 1 H), 4.64 (d, *J* = 6.7 Hz, 1 H), 4.71 (d, *J* = 7.0 Hz, 1 H), 5.35 (d, *J* = 9.8 Hz, 1 H), 5.89 (s, 1 H), 6.83 (d, *J* = 8.9 Hz, 2 H), 7.62 (d, *J* = 8.9 Hz, 2 H). − ^{13}C NMR (125 MHz, C_6D_6): δ = 7.2, 9.6, 14.3, 16.4, 27.4,

29.4, 36.3, 46.6, 51.7, 54.7, 55.7, 56.1, 78.0, 78.5, 82.0, 83.2, 95.0, 97.1, 102.6, 113.7, 128.3, 131.8, 132.0, 160.5, 170.6, 207.5. − FAB-MS; *m/z* (%) = 553 (5.6) [M^+ + 1], 307 (57), 289 (30), 219 (23), 154 (100), 136 (100), 121 (16), 107 (34), 89 (31), 77 (28). − HR-MS (FAB): *m/z* calcd. for $C_{29}H_{45}O_{10}$ 553.3013 [M^+ + 1]; found 553.2995.

(2*S*,3*R*,4*S*,5*R*,7*S*,6*E*,8*R*)-5,9-Bis[(1,1-dimethylethyl)-dimethylsilyloxy]-3,5-(4-methoxybenzylidenedioxy)-2,4,6,8-tetramethyl-6-nonene: Compound **13** (16.8 mg, 34.9 mmol) was oxidized with DDQ as described above to give the crude acetal (16.7 g), which was dissolved in dimethylformamide (263 mL). Imidazole (11.9 g, 175 mmol) and TBSCl (15.8 g, 104 mmol) were added at 0 °C under N_2. After having been stirred at room temperature for 5 d, the reaction mixture was quenched with sat. aq. NH_4Cl (10 mL) and extracted with EtOAc. The extract was washed with sat. aq. NH_4Cl and sat. aq. NaCl, dried with Na_2SO_4, concentrated in vacuo, and chromatographed on a silica gel column, eluting with EtOAc/hexane (1:20), to give the bis(TBS) ether (14.5 g, 2 steps 69%) as a colorless oil. − R_f (EtOAc/hexane, 1:5) = 0.88. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = −0.01 (s, 3 H), 0.01 (s, 3 H), 0.5 (s, 3 H), 0.05 (s, 3 H), 0.90 (s, 3 H), 0.91 (d, *J* = 6.1 Hz, 3 H), 0.94 (s, 9 H), 0.96 (d, *J* = 6.7 Hz, 3 H), 1.21 (d, *J* = 6.9 Hz, 3 H), 1.59 (s, 3 H), 1.68−1.80 (m, 2 H), 2.54−2.60 (m, 1 H), 3.34 (dd, *J* = 9.8, 7.7 Hz, 1 H), 3.48 (dd, *J* = 9.8, 6.0 Hz, 1 H), 3.76 (dd, *J* = 9.3, 1.8 Hz, 1 H), 3.80 (s, 3 H), 3.99 (s, 1 H), 4.02 (2 H, dm, *J* = 1.8 Hz), 5.21 (d, *J* = 9.6 Hz, 1 H), 5.44 (s, 1 H), 6.88 (d, *J* = 8.7 Hz, 2 H), 7.42 (d, *J* = 8.7 Hz, 2 H). − FAB-MS *m/z* (%) = 595 [M^+ + 1, 0.1), 359 (9), 123 (100), 74 (46). − HR-MS (FAB): *m/z* calcd. for $C_{33}H_{63}O_5Si_2$ 595.4214 [M^+ + 1]; found 595.4203.

(2*S*,3*R*,4*S*,5*R*,7*S*,6*E*,8*R*)-5,9-Bis[(1,1-dimethylethyl)dimethylsilyloxy]-3-(4-methoxybenzyloxy)-2,4,6,8-tetramethyl-6-nonenol (20): DIBAH (0.95 M in hexane, 240 mL, 228 mmol) was added dropwise at −30 °C under N_2 to a stirred solution of the bis(TBS) ether (25.2 g, 42.5 mmol) in CH_2Cl_2 (300 mL). After 3 h, sat. aq. NH_4Cl (100 mL), sat. aq. NH_4Cl (100 mL), sat. aq. Rochelle salt (100 mL), and EtOAc (500 mL) were added, and stirring was continued for 30 min. A precipitate was filtered off through Celite and the filtrate was extracted with EtOAc. The extract was washed with sat. aq. NaCl, dried with $MgSO_4$, concentrated in vacuo, and chromatographed on a silica gel column, eluting with EtOAc/hexane (1:10), to give **20** (12.0 g, 47%) as a colorless, viscous oil. − R_f (EtOAc/hexane, 1:10) = 0.21. − $[\alpha]_D^{22}$ = −13.1 (*c* = 2.0, $CHCl_3$). − ^{1}H NMR (500 MHz, $CDCl_3$): δ = −0.04 (s, 3 H), 0.04 (s, 3 H), 0.04 (s, 3 H), 0.05 (s, 3 H), 0.88 (d, *J* = 6.4 Hz, 3 H), 0.89 (s, 9 H), 0.90 (s, 9 H), 0.91 (d, *J* = 6.7 Hz, 3 H), 1.05 (d, *J* = 6.7 Hz, 3 H), 1.54 (s, 3 H), 1.78−1.84 (m, 1 H), 2.02−2.09 (m, 1 H), 2.51−2.57 (m, 1 H), 3.33 (dd, *J* = 9.8, 6.7 Hz, 1 H), 3.43 (dd, *J* = 9.8, 6.1 Hz, 1 H), 3.43−3.45 (m, 1 H), 3.52 (dd, *J* = 10.7, 5.5 Hz, 1 H), 3.68 (dd, *J* = 10.7, 7.3 Hz, 1 H), 3.80 (d, *J* = 7.0 Hz, 1 H), 3.81 (s, 3 H), 4.43 (d, *J* = 11.7 Hz, 1 H), 4.51 (d, *J* = 11.7 Hz, 1 H), 4.93 (d, *J* = 9.2 Hz, 1 H), 6.88 (d, *J* = 8.5 Hz, 2 H), 7.25 (d, *J* = 8.5 Hz, 2 H). − ^{13}C NMR (125 MHz, $CDCl_3$): δ = −5.3, −5.3, −4.9, −4.3, 11.3, 11.7, 12.5, 16.9, 18.2, 18.4, 25.9, 26.0, 35.4, 38.2, 38.7, 55.3, 66.4, 68.0, 72.9, 80.9, 81.3, 113.8, 129.0, 131.2, 131.4, 136.6, 159.1. − IR (neat): $\tilde{\nu}$ = 3448 cm^{-1}, 1614. − FAB-MS; *m/z* (%) = 595 (0.1) [M^+ + 1], 359 (9), 123 (100), 74 (46). − HR-MS (FAB): *m/z* calcd. for $C_{33}H_{63}O_5Si_2$ 595.4214 [M^+ + 1]; found 595.4203.

Methyl (2*E*,4*R*,5*S*,6*R*,7*S*,8*E*,10*R*)-7,11-Bis[(1,1-dimethylethyl)dimethylsilyloxy]-5-(4-methoxybenzyloxy)-4,6,8,10-tetramethyl-2,8-undecadienoate: Compound **20** (1.0 g, 1.68 mmol) in CH_2Cl_2 (6.2 mL) was added to a stirred mixture of Dess−Martin periodinane (1.07 g, 2.52 mmol) and $NaHCO_3$ (1.41 g, 16.8 mmol) in CH_2Cl_2 (5 mL). After 20 min, Et_2O (3 mL), sat. aq. $NaHCO_3$ (10 mL), and sat. aq. $Na_2S_2O_3$ (10 mL) were added, and the mixture was extracted with Et_2O. The extract was washed with sat. aq. NH_4Cl and sat. aq. NaCl, dried with $MgSO_4$, and concentrated in vacuo to give the crude aldehyde (1.13 g). (methoxycarbonylmethylene)-triphenylphosphorane (1.69 g, 5.05 mmol) was added at room temperature to a stirred solution of the crude aldehyde (1.13 g) in benzene (8.4 mL). After 18 h, the reaction mixture was concentrated in vacuo, and chromatographed on a silica gel column, eluting with EtOAc/hexane (1:20), to give the α,β-unsaturated ester (1.02 g, 2 steps 93%) as a colorless, viscous oil. − R_f (EtOAc/hexane, 1:3) = 0.47. − $[\alpha]_D^{23}$ = −5.4 (*c* = 2.0, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = −0.03 (s, 3 H), −0.04 (s, 3 H), 0.02 (s, 6 H), 0.86 (s, 9 H), 0.90 (s, 9 H), 0.91 (d, *J* = 5.9 Hz, 3 H), 0.95 (d, *J* = 6.7 Hz, 3 H), 1.10 (d, *J* = 6.8 Hz, 3 H), 1.52 (s, 3 H), 1.69−1.73 (m, 1 H), 2.55−2.71 (m, 2 H), 3.23 (1 H, dm, *J* = 5.5 Hz), 3.33 (dd, *J* = 9.7, 7.2 Hz, 1 H), 3.43 (dd, *J* = 9.7, 6.2 Hz, 1 H), 3.73 (s, 3 H), 3.81 (s, 3 H), 3.85 (d, *J* = 9.2 Hz, 1 H), 4.44 (d, *J* = 11.3 Hz, 1 H), 4.51 (d, *J* = 11.3 Hz, 1 H), 4.96 (d, *J* = 8.5 Hz, 1 H), 5.81 (d, *J* = 15.8 Hz, 1 H), 6.88 (d, *J* = 8.6 Hz, 2 H), 6.94 (dd, *J* = 15.8, 8.1 Hz, 1 H), 7.24 (d, *J* = 8.6 Hz, 2 H). − ^{13}C NMR (125 MHz, $CDCl_3$): δ = −5.3, −5.3, −4.9, −4.4, 10.4, 11.2, 16.0, 18.2, 18.4, 25.9, 26.0, 35.3, 39.7, 40.1, 51.4, 55.2, 68.0, 73.5, 81.3, 82.2, 113.7, 120.3, 128.6, 131.3, 132.0, 136.6, 151.7, 159.0, 167.0. − IR (neat): $\tilde{\nu}$ = 1728 cm^{-1}, 1613, 1462, 1175. − FAB-MS; *m/z*: (%) 649 (0.2) [M^+ + 1], 359 (14), 227 (4), 187 (6), 149 (5), 123 (100), 90 (16), 74 (39). − HR-MS (FAB): *m/z* calcd. for $C_{36}H_{65}O_6Si_2$ 649.4320 [M^+ + 1]; found 649.4596.

Methyl (2*R*,3*S*,4*R*,5*S*,6*R*,7*S*,8*E*,10*R*)-7,11-Bis[(1,1-dimethylethyl)-dimethylsilyloxy]-2,3-dihydroxy-5-(4-methoxybenzyloxy)-4,6,8,10-tetramethyl-8-undecenoate (21): Methanesulfonamide (411 mg, 4.38 mmol) was added at room temperature to a stirred solution of AD-mix α (5.16 g) in *t*BuOH/H_2O (1:1, 88 mL). After 10 min, this ester (2.84 g, 4.38 mmol) in *t*BuOH (5 mL) was added at 0 °C, and stirring was continued for 60 h. The reaction mixture was quenched with Na_2SO_3 (5.54 g, 43.8 mmol), and extracted with EtOAc. The extract was washed with sat. aq. NH_4Cl and sat. aq. NaCl, dried with $MgSO_4$, concentrated in vacuo, and chromatographed on a silica gel column, eluting with EtOAc/hexane (1:5), to give **21** (2.02 g, 68%) as a colorless, viscous oil. − R_f (EtOAc/hexane, 1:3) = 0.47. − $[\alpha]_D^{21}$ = −2.9 (*c* = 1.8, $CHCl_3$). − ^{1}H NMR (500 MHz, $CDCl_3$): δ = −0.03 (s, 3 H), 0.03 (s, 6 H), 0.04 (s, 3 H), 0.88 (s, 9 H), 0.89 (s, 9 H), 0.94 (d, *J* = 6.4 Hz, 3 H), 1.03 (d, *J* = 7.0 Hz, 3 H), 1.05 (d, *J* = 7.0 Hz, 3 H), 1.56 (s, 3 H), 1.83−1.86 (m, 1 H), 1.99−2.05 (m, 1 H), 2.31−2.39 (1 H, br, OH), 2.52−2.58 (m, 1 H), 2.97−3.07 (1 H, br, OH), 3.29 (dd, *J* = 9.5, 8.2 Hz, 1 H), 3.44 (dd, *J* = 4.0, 4.0 Hz, 1 H), 3.62 (dd, *J* = 9.5, 5.2 Hz, 1 H), 3.80 (s, 3 H), 3.84 (d, *J* = 8.0 Hz, 1 H), 3.88−3.93 (m, 1 H), 4.32 (s, 1 H), 4.42 (d, *J* = 11.6 Hz, 1 H), 4.45 (d, *J* = 11.6 Hz, 1 H), 5.00 (d, *J* = 9.5 Hz, 1 H), 6.87 (d, *J* = 8.5 Hz, 2 H), 7.25 (d, *J* = 8.5 Hz, 2 H). − ^{13}C NMR (125 MHz, $CDCl_3$): δ = −5.4, −5.0, −4.3, 10.6, 10.9, 11.7, 16.9, 18.2, 18.4, 25.9, 25.9, 35.3, 39.7, 52.8, 55.2, 55.2, 67.7, 72.5, 73.0, 73.9, 80.8, 81.5, 113.7, 128.9, 131.0, 131.3, 136.6, 159.0, 174.1. − IR (neat): $\tilde{\nu}$ = 3473 cm^{-1}, 1613, 1248. − FAB-MS; *m/z* (%) = 683 (0.2) [M^+ + 1], 359 (15), 155 (1), 136 (2), 123 (100). − HR-MS (FAB): *m/z* calcd. for $C_{36}H_{67}O_8Si_2$ 683.4375 [M^+ + 1]; found 683.4376. − $C_{36}H_{66}O_8Si_2$ (683.08): calcd. C 63.30, H 9.74; found C 63.16, H 10.09.

Methyl (2*R*,3*S*,4*R*,5*S*,6*R*,7*S*,8*E*,10*R*)-2,7,11-Tris[(1,1-dimethylethyl)-dimethylsilyloxy]-3-hydroxy-5-(4-methoxybenzyloxy)-4,6,8,10-tetramethyl-8-undecenoate: Imidazole (50 mg, 0.73 mmol) and TBSCl (55 mg, 0.365 mmol) were added at 0 °C under Ar to a stirred solu-

tion of **21** (80 mg, 0.117 mmol) in dimethylformamide (0.78 mL). After 5 h, the reaction mixture was quenched with sat. aq. NH_4Cl (1 mL) and extracted with EtOAc/hexane (1:5). The extract was washed with sat. aq. NaCl, dried with $MgSO_4$, concentrated in vacuo, and chromatographed on a silica gel column, eluting with EtOAc/hexane (1:10), to give the monohydroxy compound (81 mg, 84%) as a colorless, viscous oil. − R_f (EtOAc/hexane, 1:10) = 0.50. − $[\alpha]_D^{22}$ = −9.0 (*c* = 1.9, $CHCl_3$). − ^{1}H NMR (500 MHz, $CDCl_3$,H-H COSY): δ = −0.04 (s, 3 H), 0.03 (s, 6 H), 0.03 (s, 3 H), 0.10 (s, 6 H), 0.88 (s, 9 H), 0.89 (s, 9 H), 0.93 (s, 9 H), 0.96 (d, *J* = 6.7 Hz, 3 H, C10-Me), 0.98 (d, *J* = 6.7 Hz, 3 H, C6-Me), 1.02 (d, *J* = 6.9 Hz, 3 H, C4-Me), 1.59 (s, 3 H, C8-Me), 1.80−1.93 (m, 2 H, H4+H6), 2.42 (*J* = 3.0 Hz, C3-OH), 2.52−2.61 (m, 1 H, H10), 3.28 (dd, *J* = 9.6, 8.1 Hz, 1 H, H11a), 3.34 (1 H, dm, *J* = 7.9 Hz, H5), 3.48 (dd, *J* = 9.6, 5.3 Hz, 1 H, H11b), 3.71 (s, 3 H), 3.75−3.79 (m, 1 H, H3), 3.80 (s, 3 H), 3.89 (d, *J* = 9.5 Hz, 1 H, H7), 4.15 (1 H,d, *J* = 7.3 Hz, H2), 4.48 (s, 2 H), 4.96 (d, *J* = 9.3 Hz, 1 H, H9), 6.87 (d, *J* = 8.5 Hz, 2 H), 7.24 (d, *J* = 8.5 Hz, 2 H). − ^{13}C NMR (125 MHz, $CDCl_3$): δ = −5.3, −5.0, −4.9, −4.3. 9.9, 10.1, 11.0, 16.8, 18.2, 18.3, 18.4, 25.7, 25.9, 26.0, 35.3, 37.9, 39.3, 52.0, 55.2, 67.8, 72.7, 73.7, 75.0, 81.3, 81.8, 113.7, 128.9, 131.7, 131.7, 137.2, 158.8, 172.2. − IR (neat): $\tilde{\nu}$ = 3583 cm^{-1}, 1613, 1513, 1361. − FAB-MS; *m*/*z* (%) = 797 (0.1) [M^+ + 1], 149 (5), 123 (100), 90 (13), 74 (42). − HR-MS (FAB): *m*/*z* calcd. for $C_{42}H_{81}O_8Si_3$ 797.5239 [M^+ + 1]; found 797.5225.

Methyl (2*R*,3*S*,4*R*,5*S*,6*R*,7*S*,8*E*,10*R*)-2,7,11-Tris[(1,1-dimethylethyl)-dimethylsilyloxy]-3-methoxy-5-(4-methoxybenzyloxy)4,6,8,10-tetramethyl-8-undecenoate (22): Proton sponge (70.9 mg, 0.33 mmol) and trimethyloxonium tetrafluoroborate (48.9 mg, 0.33 mmol) were added at 0 °C under Ar to a stirred solution of this monohydroxy compound (43.9 mg, 0.055 mmol) in CH_2Cl_2 (1.1 mL). After 25 h at room temperature, additional proton sponge (23.6 mg, 0.11 mmol) and borate (16.3 mg, 0.11 mmol) were added, and stirring was continued for 15 h. The reaction mixture was quenched with sat. aq. $NaHCO_3$, and extracted with EtOAc/hexane (1:5). The extract was washed with sat. aq. NaCl, dried with $MgSO_4$, concentrated in vacuo, and chromatographed on a silica gel column, eluting with EtOAc/hexane (1:40), to give **22** (41.3 mg, 92%) as a colorless, viscous oil. − R_f (EtOAc/hexane, 1:10) = 0.55. − $[\alpha]_D^{20}$ = −5.0 (*c* = 2.0, $CHCl_3$). − ^{1}H NMR (500 MHz, $CDCl_3$, H-H COSY): δ = −0.06 (s, 3 H), 0.02 (s, 3 H), 0.03 (s, 3 H), 0.03 (s, 3 H), 0.08 (s, 3 H), 0.10 (s, 3 H), 0.87 (s, 9 H), 0.88 (s, 9 H), 0.91 (s, 9 H), 0.92 (d, *J* = 7.3 Hz, 3 H, C10-Me), 0.94 (d, *J* = 6.7 Hz, 3 H, C6-Me), 0.98 (d, *J* = 7.0 Hz, 3 H, C4-Me), 1.61 (s, 3 H, C8-Me), 1.77−1.83 (m, 2 H, H4+H6), 2.50−2.59 (m, 1 H, H10), 3.20 (dd, *J* = 8.5, 0.6 Hz, 1 H, H5), 3.26 (dd, *J* = 9.8, 7.9 Hz, 1 H, H11a), 3.33 (dd, *J* = 7.3, 0.9 Hz, 1 H, H3), 3.47 (dd, *J* = 9.8, 5.5 Hz, 1 H, H11b), 3.52 (s, 3 H), 3.71 (s, 3 H), 3.80 (s, 3 H), 3.91 (d, *J* = 9.5 Hz, 1 H, H7), 4.31 (d, *J* = 7.3 Hz, 1 H, H2), 4.41 (d, *J* = 11.6 Hz, 1 H), 4.54 (d, *J* = 11.6 Hz, 1 H), 4.94 (d, *J* = 9.2 Hz, 1 H, H9), 6.87 (d, *J* = 8.5 Hz, 2 H), 7.23 (d, *J* = 8.5 Hz, 2 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.3, −5.2, −5.1, −4.9, −4.4, 9.9, 10.3, 11.2, 13.7, 18.2, 18.2, 18.4, 25.7, 25.9, 26.0, 35.4, 38.5, 40.1, 51.8, 55.3, 61.1, 67.7, 73.7, 75.6, 80.9, 81.6, 83.1, 113.6, 128.2, 131.8, 131.68, 136.9, 158.7, 172.3. − IR (neat): $\tilde{\nu}$ = 1748 cm^{-1}, 1513, 1248. − FAB-MS; *m*/*z* (%) = 811 (0.1) [M^+ + 1], 187 (6), 149 (4), 123 (100), 90 (16), 74 (49). − HR-MS (FAB): *m*/*z* calcd. for $C_{43}H_{83}O_8Si_3$ 811.53958 [M^+ + 1]; found 811.5378. − $C_{43}H_{82}O_8Si_3$ (811.37): calcd. C 63.65, H 10.19; found C 63.70, H 10.17.

Methyl (2*R*,3*S*,4*R*,5*S*,6*R*,7*S*,8*E*,10*R*)-2,7-Bis[(1,1-dimethylethyl)dimethylsilyloxy]-11-hydroxy-3-methoxy-5-(4-methoxybenzyloxy)-4,6,8,10-tetramethyl-8-undecenoate: 10-Camphorsulfonic acid (CSA) (165 mg, 0.71 mmol) was added at 0 °C under Ar to a stirred solution of **22** (577 mg, 0.71 mmol) in CH_2Cl_2/MeOH (1:1, 14.2 mL). After 3 h, the reaction mixture was quenched with sat. aq. $NaHCO_3$ (1 mL) and extracted with Et_2O. The extract was washed with sat. aq. NaCl, dried with $MgSO_4$, concentrated in vacuo, and chromatographed on a silica gel column, eluting with EtOAc/hexane (1:5−1:3), to give the primary hydroxy compound (420 mg, 85%) as a colorless, viscous oil. − R_f (EtOAc/hexane, 1:5) = 0.27. − $[\alpha]_D^{22}$ = −9.0 (*c* = 2.0, $CHCl_3$). − ^{1}H NMR (500 MHz, $CDCl_3$): δ = −0.05 (s, 3 H), 0.04 (s, 3 H), 0.07 (s, 3 H), 0.09 (s, 3 H), 0.87 (s, 9 H), 0.90 (s, 9 H), 0.91 (d, *J* = 5.2 Hz, 3 H), 0.95 (d, *J* = 6.7 Hz, 3 H), 0.97 (d, *J* = 7.0 Hz, 3 H), 1.62 (d, *J* = 0.9 Hz, 3 H), 1.79−1.86 (m, 2 H), 2.58−2.65 (m, 1 H), 3.21 (dd, *J* = 7.0, 1.5 Hz, 1 H), 3.33 (dd, *J* = 8.2, 1.2 Hz, 1 H), 3.35 (dd, *J* = 10.4, 7.3 Hz, 1 H), 3.43 (dd, *J* = 10.4, 6.4 Hz, 1 H), 3.52 (s, 3 H), 3.81 (s, 3 H), 3.81 (s, 3 H), 3.90 (d, *J* = 9.8 Hz, 1 H), 4.32 (d, *J* = 7.0 Hz, 1 H), 4.40 (d, *J* = 11.6 Hz, 1 H), 4.55 (d, *J* = 11.6 Hz, 1 H), 4.87 (dd, *J* = 9.5, 0.6 Hz, 1 H), 6.88 (d, *J* = 8.5 Hz, 2 H), 7.24 (d, *J* = 8.5 Hz, 2 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.2, −5.2, −4.9, −4.4, 10.3, 10.3, 11.3, 16.3, 18.2, 18.2, 25.7, 25.8, 35.2, 38.2, 40.0, 51.8, 55.2, 61.0, 67.7, 73.3, 75.4, 81.0, 81.5, 83.2, 113.7, 128.3, 131.5, 131.6, 138.3, 158.8, 172.3. − IR (neat): $\tilde{\nu}$ = 3478 cm^{-1}, 1745, 1513, 1248, 1039. − FAB-MS *m*/*z* (%) = 697 (0.1) [M^+ + 1]), 245 (18), 123 (100), 90 (5), 74 (36). − HR-MS (FAB): *m*/*z* calcd. for $C_{37}H_{69}O_8Si_2$ 697.4531 [M^+ + 1]; found 697.5300.

Methyl (2*R*,3*S*,4*R*,5*S*,6*R*,7*S*,8*E*,10*R*)-2,7-Bis[(1,1-dimethylethyl)dimethylsilyloxy]-3-methoxy-5-(4-methoxybenzyloxy)-4,6,8,10-tetramethyl-11-oxo-8-undecenoate: This primary hydroxy compound (347 mg, 0.498 mmol) in CH_2Cl_2 (3.0 mL) was added at room temperature to a stirred mixture of Dess−Martin periodinane (321 mg, 0.747 mmol) and $NaHCO_3$ (418 mg, 4.98 mmol) in CH_2Cl_2 (2.0 mL). After 30 min, Et_2O (10 mL), sat. aq. $NaHCO_3$ (1 mL), and sat. aq. $Na_2S_2O_3$ (1 mL) were added, and the mixture was extracted with Et_2O. The extract was washed with sat. aq. NH_4Cl and sat. aq. NaCl, dried with $MgSO_4$, and concentrated in vacuo to give the crude aldehyde (370 mg) as a colorless, viscous oil. − R_f (EtOAc/hexane, 1:5) = 0.66. − ^{1}H NMR (500 MHz, $CDCl_3$): δ = −0.08(s, 3 H), 0.03 (s, 3 H), 0.08 (s, 3 H), 0.09 (s, 3 H), 0.86 (s, 9 H), 0.90 (s, 3 H), 0.95 (d, *J* = 6.7 Hz, 3 H), 0.97 (d, *J* = 7.0 Hz, 3 H), 1.09 (d, *J* = 7.0 Hz, 3 H), 1.65 (s, 3 H), 1.78−1.84 (m, 2 H), 3.19 (dd, *J* = 7.9, 0.6 Hz, 1 H), 3.22−3.29 (m, 1 H), 3.30 (dd, *J* = 7.0, 1.5 Hz, 1 H), 3.51 (s, 3 H), 3.71 (s, 3 H), 3.81 (s, 3 H), 3.90 (d, *J* = 9.8 Hz, 1 H), 4.31 (d, *J* = 7.0 Hz, 1 H), 4.32 (d, *J* = 11.9 Hz, 1 H), 4.59 (d, *J* = 11.9 Hz, 1 H), 4.79 (d, *J* = 9.5 Hz, 1 H), 6.86 (d, *J* = 8.5 Hz, 2 H), 7.22 (d, *J* = 8.5 Hz, 2 H), 9.48 (d, *J* = 1.5 Hz, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.2, −5.1, −4.9, −4.5, 9.9, 10.2, 11.6, 13.5, 18.2, 18.3, 25.7, 25.8, 38.3, 40.2, 46.2, 51.8, 55.3, 61.0, 73.3, 75.3, 80.7, 81.0, 83.2, 113.7, 124.6, 128.3, 131.7, 141.7, 158.8, 172.3, 200.7. − FAB-MS; *m*/*z* (%) = 709 (5.6) [M^+ + 1], 307 (57), 289 (30), 219 (23), 154 (100), 136 (100), 121 (16), 107 (34), 89 (31), 77 (28). − HR-MS (FAB): *m*/*z* calcd. for $C_{37}H_{67}O_8Si_2$ 695.43745 [M^+ + 1]; found 709.2995.

Methyl (2*R*,3*S*,4*R*,5*S*,6*R*,7*S*,8*E*,10*R*)-2,7-Bis[(1,1-dimethylethyl)dimethylsilyloxy]-11-hydroxy-3-methoxy-5-(4-methoxybenzyloxy)-4,6,8,10-tetramethyl-8-dodecenoate: MeLi (1.14 M in Et_2O, 0.66 mL, 0.747 mmol) was added at −78 °C under Ar to this crude compound (370 mg) in Et_2O (10 mL). After 1 h, the solution was allowed to warm to −50 °C, and stirred for 1 h. The reaction mixture was quenched with sat. aq. NH_4Cl (1 mL) and extracted with Et_2O. The extract was washed with sat. aq. NH_4Cl and sat. aq. NaCl, dried with Na_2SO_4, concentrated in vacuo, and chromatographed on a silica gel column, eluting with EtOAc/hexane (1:5−1:3), to

give the recovered starting material (24 mg, 7%) and a mixture (4.8:1) of secondary hydroxy compounds (119 g, 2 steps 34%) as a colorless, viscous oil. − R_f (EtOAc/hexane, 1:5) = 0.26. − ^{1}H NMR (500 MHz, $CDCl_3$): δ = −0.05 (s, 3 H), 0.04 (s, 3 H), 0.07 (s, 3 H), 0.08 (s, 3 H), 0.87 (s, 9 H), 0.90 (s, 3 H), 0.90−0.91 (m, 3 H), 0.95 (d, J = 7.0 Hz, 3 H), 0.96 (d, J = 6.4 Hz, 3 H), 1.15 (d, J = 6.4 Hz, 3 H), 1.62 (s, 3 H), 1.82−1.87 (m, 2 H), 2.40−2.45 (m, 1 H), 3.22 (dd, J = 8.2, 0.9 Hz, 1 H), 3.35 (dd, J = 7.0, 1.5 Hz, 1 H), 3.51 (s, 3 H), 3.71 (s, 3 H), 3.81 (s, 3 H), 3.93 (d, J = 10.1 Hz, 1 H), 4.32 (d, J = 7.0 Hz, 1 H), 4.44 (d, J = 11.0 Hz, 1 H), 4.54 (d, J = 11.0 Hz, 1 H), 5.01 (d, J = 9.2 Hz, 1 H), 6.87 (d, J = 8.5 Hz, 2 H), 7.23 (d, J = 8.5 Hz, 2 H). − FAB-MS m/z (%) = 709 (5.6) [M^+ + 1], 307 (57), 289 (30), 219 (23), 154 (100), 136 (100), 121 (16), 107 (34), 89 (31), 77 (28). − HR-MS (FAB): m/z calcd. for $C_{38}H_{71}O_8Si_2$ 711.46875 [M^+ + 1]; found 709.2995.

Methyl (2*R*,3*S*,4*R*,5*S*,6*R*,7*S*,8*E*,10*R*)-2,7-Bis[(1,1-dimethylethyl)dimethylsilyloxy]-3-methoxy-5-(4-methoxybenzyloxy)-4,6,8,10-tetramethyl-11-oxo-8-dodecenoate (4): The mixture of secondary hydroxy compounds (119 mg) in CH_2Cl_2 (0.8 mL) was oxidized with Dess−Martin periodinane (108 mg, 0.25 mmol) and $NaHCO_3$ (140 mg, in CH_2Cl_2 (0.8 mL) at room temperature for 1 h. Workup as described above gave **4** (110 mg, 92%) as a colorless, viscous oil. − R_f (EtOAc/hexane, 1:5) = 048. − $[\alpha]_D^{21}$ = +61.8 (c = 2.0, $CHCl_3$). − ^{1}H NMR (500 MHz, $CDCl_3$): δ = −0.08 (s, 3 H), 0.02 (s, 3 H), 0.07 (s, 3 H), 0.09 (s, 3 H), 0.86 (s, 9 H), 0.90 (s, 9 H), 0.95 (d, J = 7.0 Hz, 3 H), 0.96 (d, J = 7.0 Hz, 3 H), 1.09 (d, J = 7.0 Hz, 3 H), 1.67 (s, 3 H), 1.81−1.88 (m, 2 H), 2.12 (s, 3 H), 3.15 (dd, J = 8.2, 0.6 Hz, 1 H), 3.34 (dd, J = 7.0, 0.8 Hz, 1 H), 3.38−3.42 (m, 1 H), 3.51 (s, 3 H), 3.71 (s, 3 H), 3.80 (s, 3 H), 3.91 (d, J = 9.8 Hz, 1 H), 4.33 (d, J = 7.0 Hz, 1 H), 4.34 (d, J = 11.3 Hz, 1 H), 4.54 (d, J = 11.3 Hz, 1 H), 4.99 (d, J = 9.8 Hz, 1 H), 6.87 (d, J = 8.5 Hz, 2 H), 7.22 (d, J = 8.5 Hz, 2 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.2, −5.2, 4.9, −4.4, 9.9, 10.4, 11.4, 15.9, 18.2, 18.2, 25.7, 25.8, 28.3, 38.2, 40.1, 46.7, 51.8, 55.2, 60.9, 73.5, 75.2, 80.9, 81.0, 83.0, 113.7, 127.7, 128.3, 131.5, 139.8, 158.8, 172.3, 209.0. − IR (neat): $\tilde{\nu}$ = 1767 cm^{-1}, 1716, 1513, 1249, 1042. − FAB-MS; m/z (%) = 709 (5.6) [M^+ + 1], 307 (57), 289 (30), 219 (23), 154 (100), 136 (100), 121 (16), 107 (34), 89 (31), 77 (28). − HR-MS (FAB): m/z calcd. for $C_{38}H_{69}O_8Si_2$ 709.4531 [M^+ + 1]; found 709.2995.

[1] F. J. Schmitz, S. P. Gunasekera, G. Yalamanchili, M. B. Hossain, D. van der Helm, *J. Am. Chem. Soc.* **1984**, *106*, 7251−7252.

[2] N. Fusetani, T. Sugawara, S. Matsunaga, J. Horita, *J. Org. Chem.* **1991**, *56*, 4971−4974.

[3] [3a] T. Matsushima, K. Horita, N. Nakajima, O. Yonemitsu, *Tetrahedron Lett.* **1996**, *37*, 385−388. − [3b] T. Matsuhima, M. Mori, N. Nakajima, H. Maeda, J. Uenishi, O. Yonemitsu, *Chem. Pharm. Bull.* **1998**, *46*, 1335−1336. − [3c] J.-F. Liu, A. Abiko, Z. Pei, D. C. Buske, S. Masamune, *Tetrahedron Lett.* **1998**, *39*, 1873−1876. − [3d] R. E. Taylor, J. P. Ciavarri, B. R. Hearn, *Tetrahedron Lett.* **1998**, *39*, 9361−9364. − [3e] W. R. Roush, G. C. Lane, *Org. Lett.* **1999**, *1*, 95−98. − [3f] T. Matsushima, M. Mori, B.-Z. Zheng, H. Maeda, N. Nakajima, J. Uenishi, O Yonemitsu, *Chem. Pharm. Bull.* **1999**, *47*, 308−321. − [3g] M. E. Jung, U. Karama, R. Marquez, *J. Org. Chem.* **1999**, *64*, 663−665. − [3h] T. Matsushima, B.-Z. Zheng, H. Maeda, N. Nakajima, J. Uenishi, O. Yonemitsu, *Synlett* **1999**, 780−782. − [3i] A. B. Smith III, S. A. Lodies, *Org. Lett.* **1999**, *1*, 1249−1252. − [3j] B.-Z. Zheng, H. Maeda, M. Mori, S. Kusaka, O. Yonemisu, T. Matsushima, N. Nakajima, J. Uenishi, *Chem. Pharm. Bull.* **1999**, *47*, 1288−1296. − [3k] M. E. Jung, R. Marquez, *Tetrahedron Lett.* **1999**, *40*, 3129−3132. − [3l] T. Matsushima, N. Nakajima, B.-Z. Zheng, O. Yonemitsu, *Chem. Pharm. Bull.* **2000**, *48*, 855−860. − [3m] M. E. Jung, C. P. Lee, *Org. Lett.* **2001**, *3*, 333−336.

[4] [4a] M. Hikota, H. Tone, K. Horita, O. Yonemitsu, *J. Org. Chem.* **1990**, *55*, 7−9. − [4b] M. Hikota, H. Tone, K. Horita, O. Yonemitsu, *Tetrahedron* **1990**, *46*, 4613−4628. − [4c] M. Hikota, Y. Sakurai, K. Horita, O. Yonemitsu, *Tetrahedron Lett.* **1990**, *31*, 6367−6370.

[5] [5a] H. Goto, E. Osawa, *Tetrahedron Lett.* **1992**, *33*, 1343−1346. − [5b] H. Goto, E. Osawa, *J. Chem. Soc., Perkin Trans. 2* **1993**, 187−198. − [5c] H. Goto, E. Osawa, M. Yamato, *Tetrahedron* **1993**, *49*, 387−396.

[6] J. Inanaga, K. Hirata, H. Saeki, T. Katsuki, M. Yamaguchi, *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1989−1993.

[7] N. Nakajima, K. Horita, R. Abe, O. Yonemitsu, *Tetrahedron Lett.* **1988**, *29*, 4139−4142.

[8] J. M. Williams, R. B. Jobson, N. Yasuda, G. Marchesini, U.-H. Dolling, E. J. J. Grabowski, *Tetrahedron Lett.* **1995**, *36*, 5461−5464.

[9] C. S. Lee, C. J. Forsyth, *Tetrahedron Lett.* **1996**, *37*, 6449−6452.

[10] I. Paterson, R. D. Norcross, R. A. Ward, P. Romea, M. A. Lister, *J. Am. Chem. Soc.* **1994**, *116*, 11287−11314.

[11] S. Kiyooka, H. Kuroda, Y. Shimasaki, *Tetrahedron Lett.* **1986**, *27*, 3009−3012.

[12] Y. Oikawa, T. Yoshioka, O. Yonemitsu, *Tetrahedron Lett.* **1982**, *23*, 889−892.

[13] S. Takano, M. Akiyama, K. Ogasawara, *Chem. Pharm. Bull.* **1984**, *32*, 791−794.

[14] D. B. Dess, J. C. Martin, *J. Org. Chem.* **1983**, *48*, 4155−4156.

[15] K. B. Sharpless, W. Amberg, Y. L. Bennani, G. A. Crispino, J. Hartung, K.-S. Jeong, H.-L. Kwong, K. Morikawa, Z.-M. Wang, D. Xu, X.-L. Zhang, *J. Org. Chem.* **1992**, *57*, 2768−2771.

[16] J. N. Denis, A. E. Greene, *J. Org. Chem.* **1990**, *55*, 1957−1959.

[17] J. S. Panek, R. T. Beresis, C. A. Celatka, *J. Org. Chem.* **1996**, *61*, 6495−6496.

[18] J. Mulzer, A. Mantoulidis, E. Ohler, *J. Org. Chem.* **2000**, *65*, 7456−7467.

[19] W. L. F. Armarego, D. D. Perrin, *Purification of Laboratory Chemicals*, 4th ed., Pergamon Press, Butterworth-Heinemann, Oxford, **1997**.

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