Synthetic Studies of an 18-Membered Antitumor Macrolide, Tedanolide. 5. Stereoselective Synthesis of the C13—C23 Part *via* Condensation of Two Fragments, C13—C17 and C18—C21, by Taking Advantage of the 3,4-Dimethoxybenzyl Protecting Group[1)]

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An efficient and stereoselective synthesis of the C13—C23 part (8) was achieved starting from methyl (R)- and (*S*)-3-hydroxy-2-methylpropionates (9) *via* coupling of the C13—C17 aldehyde (6), prepared by Evans asymmetric aldol reaction, with the C18—C21 iodoalkene (5b) by taking advantage of the 3,4-dimethoxybenzyl protecting group.

Key words macrolide; stereoselective synthesis; Evans asymmetric aldol reaction; protecting group; Wittig reaction

Tedanolide (**1**), a highly cytotoxic 18-membered macrolide, was isolated from a Caribbean sponge, *Tedania ignis*, and its structure determined by Schmitz *et al*. in 1984.[2,3)] In contrast to many typical macrolides,[4)] the structure of **1** is unusual; having four labile aldol units, an α-epoxy alcohol and an 18-membered lactone formed between C16-primary alcohol and C1-carboxyl group, the synthesis of **1** seemed to be difficult. As part of our synthetic studies of **1** we reported in 1996 the synthesis of the 18-membered lactone (**2**),[5)] a key intermediate to **1**, *via* highly efficient macrolactonization[6)] of the corresponding seco-acid (**3**), which was designed with the aid of molecular mechanics (MM2-CONFLEX3)[7)] calculations and synthesized by condensation of four fragments, the C1—C7 (**4**), C8—C11 (**5a**), C13—C17 (**6**) and C18—C21 (**5b**),[8)] although the procedure required many improvements. In previous papers[9)] we reported improved syntheses of **4** and **5a**, and their coupling to the C1—C12 part (**7**), half the molecule **3**. Recently Masamune[10)] and Taylor[11)] reported syntheses of C3—C12 and C15—C19 portions, respectively. In this full paper we describe a synthesis of the C13—C23 part (**8**), another half of the molecule **3**, *via* coupling between **6** and **5b**. The former **6** was synthesized starting from methyl (*R*)-3-hydroxy-2-methylpropionate (**9a**) *via* **10**, which was an intermediate common to **4**, and the latter **5b** is the enantiomer of **5a**.[9)]

Synthesis of the C13—C17 Fragment (6) The double bond of **10**, synthesized from **9a**,[9)] was dihydroxylated with osmium tetroxide (OsO_4) in the presence of *N*-methylmorpholine-*N*-oxide (NMO), and then cleaved oxidatively with sodium periodate ($NaIO_4$) in the usual way to readily give a C16-aldehyde in excellent yield. The aldehyde was easily converted to **11** by reduction with lithium borohydride ($LiBH_4$), followed by silylation with *tert*-butyldimethylsilyl chloride (TBSCl). Regioselective reductive ring opening of the benzylidene acetal of **11** with diborane and triethylsilane in the presence of several Lewis acids as well as diisobutylaluminum hydride (DIBAH)[12)] was examined. Among them only DIBAH gave an acceptable result as expected, although it required improvement; thus, the primary alcohol (**12**) was isolated in 54% yield, accompanied by a by-product diol with loss of the TBS group in 30% yield. Swern oxidation of **12** readily gave the C13—C17 fragment (**6**) in almost quantitative yield. The overall yield for the 14 steps starting from **9a** to **6** was 28.7%.

A more concise and efficient synthesis of **6** was accomplished *via* Evans asymmetric aldol reaction.[13)] An excess aldehyde was usually employed to react with boron or titanium enolates of Evans acyloxazolidinones.[14)] The reactions with titanium enolates, in particular, required 2—5 eq of aldehydes in order to achieve reasonable reaction rates in good yields of Evans-*syn*-aldols.[15)] However, in the multistep synthesis of complex natural products, intermediary aldehydes are sometimes much more expensive than the Evans auxiliaries, which can also be recycled after reductive cleavage of aldol products; hence, experiments using excess titanium enolates were examined, although it was reported that excess enolate reagents, di-*n*-butylboron triflate (Bu_2BOTf)[16)] and titanium tetrachloride ($TiCl_4$),[17)] are responsible for the decrease of the Evans-*syn*-aldol formation.

When the aldehyde (**13a**), readily prepared from **9a**,[9)] was allowed to react with 1.5 eq of the titanium enolate, prepared from the Evans acyloxazolidinone (**14**)[13a)] with $TiCl_4$ and diisopropylethylanime (DIPEA), the coupling proceeded smoothly to give the desired Felkin-*syn*-Evans-*syn*-aldol (**15**) with high diastereoselectivity (>95% de), as determined by the ^{1}H-NMR of the crude product. Reduction of the crude **15** with $LiBH_4$ readily gave the diol (**16**) in 61% overall yield from **13a**.

Conversion of **16** to **6** was smoothly carried out in a manner similar to the conversion from **10** to **6**. Protection as a 3,4-dimethoxybenzylidene acetal, followed by regioselective ring opening with DIBAH to the 3,4-dimethoxybenzyl (DMPM) ether and then protection of the resulting primary alcohol with TBSCl gave **17** in excellent overall yield (92%). Dihydroxylation with OsO_4 in the presence of NMO, and subsequent oxidative cleavage with $NaIO_4$ easily gave **6**. The overall yield of this improved method for the 10 steps starting from **9a** to **6** was 50%.

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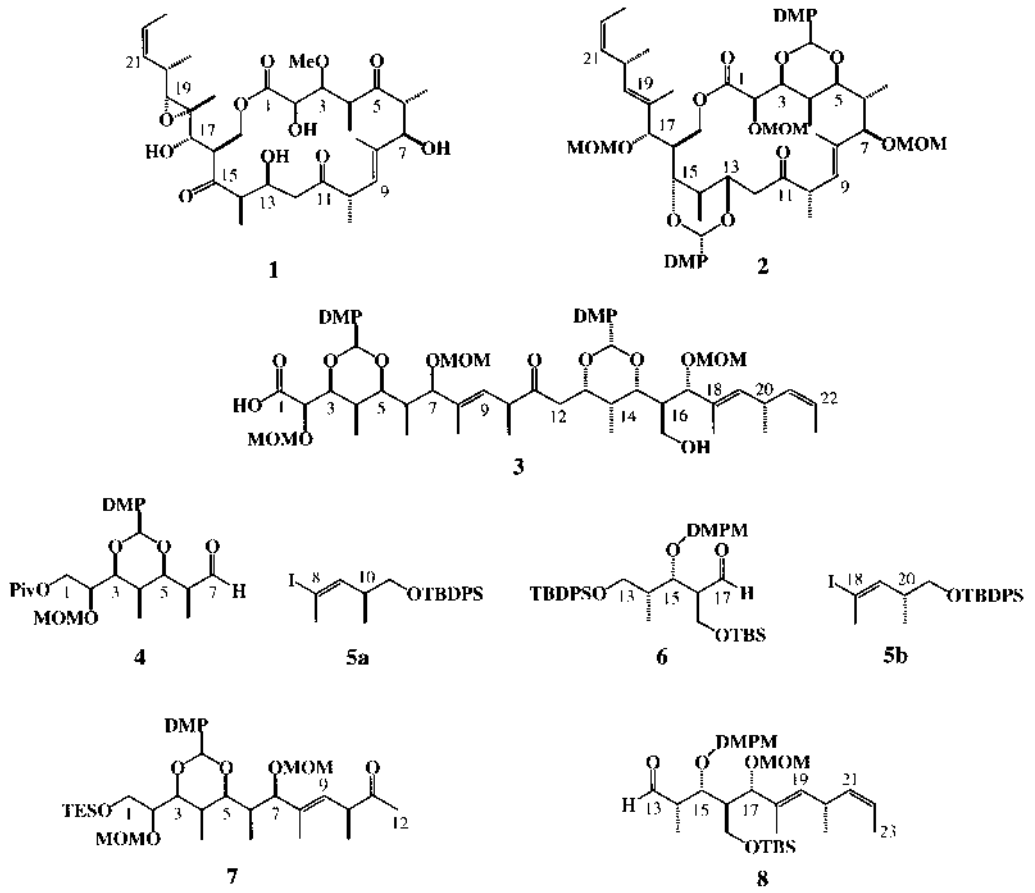
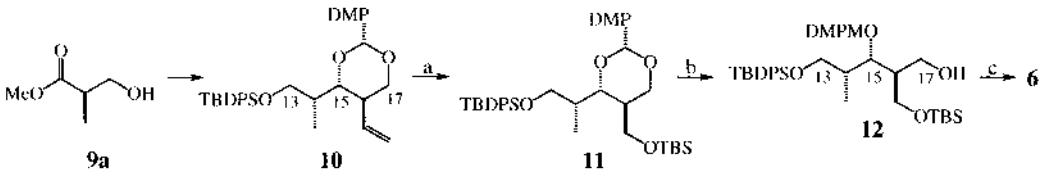
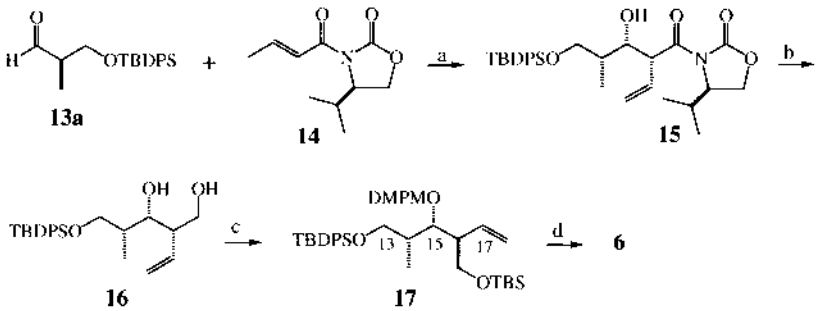


Fig. 1



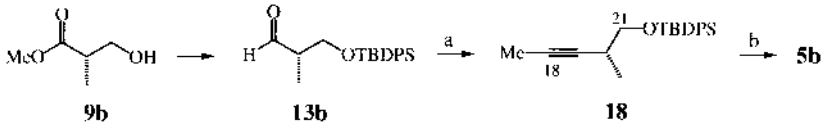
(a) 1) OsO_4, NMO, Me_2CO-H_2O, r.t. (95%); 2) $NaIO_4$, THF-H_2O, r.t. (100%); 3) $LiBH_4$, Et_2O, r.t. (93%); 4) TBSCl, imidazole, CH_2Cl_2, r.t. (100%). (b) DIBAH, CH_2Cl_2, −20°C (54%). (c) $(COCl)_2$, DMSO, iso-Pr_2EtN, CH_2Cl_2, −78°C to r.t. (98%).

Chart 1



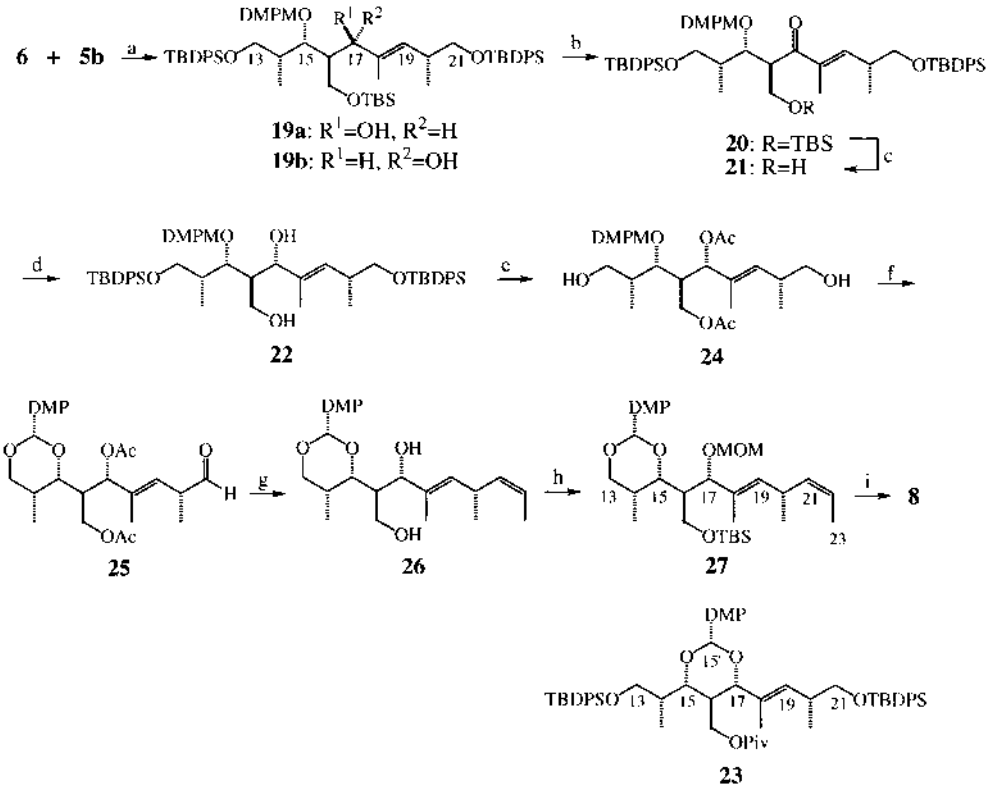
(a) $TiCl_4$, iso-Pr_2EtN, CH_2Cl_2, −78 to 0°C (70%). (b) $LiBH_4$, Et_2O-THF (2 steps, 61%). (c) 1) $DMPCH(OMe)_2$, CSA, CH_2CH_2, r.t. (99%); 2) DIBAH, toluene, −35°C (93%); 3) TBSCl, imidazole, CH_2Cl_2, 0°C (99%). (d) 1) OsO_4, NMO, acetone-H_2O, r.t. (91%); 2) $NaIO_4$, THF-H_2O, r.t. (99%).

Chart 2



(a) 1) CBr_4, Ph_3P, CH_2Cl_2, −60°C (93%); 2) *n*-BuLi, MeI, THF, r.t. (96%). (b) Cp_2ZrHCl, C_6H_6, 45°C, then I_2 (50%).

Chart 3



(a) *tert*-BuLi, Et_2O, −78°C to −30°C (85%) (**19a** : **19b** = 7.5 : 1). (b) Dess-Martin oxid., pyridine, CH_2Cl_2, 0°C (91%). (c) PPTS, EtOH (99%). (d) $Zn(BH_4)_2$, Et_2O, 0°C (96%). (e) 1) Ac_2O, Et_3N, DMAP, CH_2Cl_2, 0°C to r.t. (96%); 2) *n*-Bu_4NF, AcOH, THF, 0°C to r.t. (100%). (f) 1) DDQ, CH_2Cl_2, −10°C (93%); 2) Dess-Martin oxid. (100%). (g) 1) $Ph_3PCH_2CH_3Br$, *tert*-BuOK, THF, −78°C to r.t.; 2) $LiAlH_4$, Et_2O, 0°C to r.t. (2 steps 74%). (h) 1) TBSCl, imidazole, CH_2Cl_2, r.t. (86%); 2) MOMCl, iso-Pr_2EtN, (100%). (i) 1) DIBAH, CH_2Cl_2, −50°C (70%); 2) Dess-Martin oxid. (99%).

Chart 4

Synthesis of the C13—C23 Part (8) *via* Coupling of 6 with the C18—C21 Fragment (5b) The synthesis of the enantiomer (**5a**) of the C18—C21 fragment (**5b**) was recently reported,[9a] and hence, **5b** was also synthesized from **9b** *via* the hydrozirconation[18] of the acetylene (**18**) in completely the same way.

For the synthesis of the C13—C23 part, coupling between **6** and **5b** was carefully examined first. The expected alcohol (**19b**) was an adduct of **5b** to **6** controlled by chelation of lithium between the C17-aldehyde and the C15-DMPM ether. When excess **5b** (1.5 eq) was lithiated with *tert*-butyllithium (*tert*-BuLi) and subjected to react with **6** at −78 °C to −30 °C, the coupling proceeded quite smoothly to give **19** in 85% yield, which was, however, a 7.5 : 1 mixture of C17-isomers; unfortunately, the major product was the undesired Cram adduct (**19a**). In order to improve the selectivity the chelating metals magnesium bromide etherate ($MgBr_2 \cdot Et_2O$) and zinc chloride ($ZnCl_2$) were added, but no improvements were observed, and hence selective reduction of the corresponding C17-ketone (**20**), readily available from **19** by Dess-Martin oxidation, was examined. Reduction of **20** with sodium borohydride ($NaBH_4$), $LiBH_4$, and lithium aluminum hydride ($LiAlH_4$) readily gave the expected C17-α-alcohol (**19b**) stereoselectively, but considerable concomitant loss of the TBS group was unavoidable, similar to the reduction of **11** with DIBAH as mentioned above. A typical reduction of **20** with $LiAlH_4$ gave a 1 : 2 mixture of **19b** and **22** in 82% yield. On treatment with pyridinium *p*-toluensulfonate (PPTS), **19b** was easily converted to **22** in 70% yield. The following procedure gave **22** much more efficiently and clearly. The ketone (**20**) was first treated with PPTS to remove the TBS group and **21** was isolated in almost quantitative yield. When **21** was treated with zinc borohydride [$Zn(BH_4)_2$],[19] a chelation-controlled reduction with complete

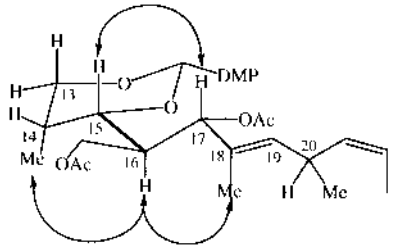


Fig. 2. NOESY Correlations and Vicinal Coupling Constants (J_{H-H}) of the Olefin, Prepared from **25**

stereoselectivity proceeded to give only **22** in 96% yield. The configuration of **22** was confirmed after conversion to **23** *via* protection of the primary alcohol with a pivaloyl (Piv) group and subsequent 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) oxidation of the DMPM ether to the 3,4-dimethoxybenzylidene acetal[20]; thus, correlations among the C15, C15′ and C17 protons in nuclear Overhauser and exchange spectroscopy (NOESY) were clearly observed.

Conventional acetylation to protect the diol of **22** followed by treatment with tetra-*n*-butylammonium fluoride (*n*-Bu_4NF) to remove the two *tert*-butyldiphenylsilyl (TBDPS) groups gave **24** with two primary alcohols at C13 and C21. The C13 alcohol was selectively protected as a benzylidene acetal again by DDQ oxidation.[20] Dess-Martin oxidation of the C21 primary alcohol readily gave the aldehyde (**25**), which was treated with a ylide prepared from ethyltriphenylphosphonium bromide and potassium *tert*-butoxide (*tert*-BuOK) to readily give the (*Z*)-olefin with excellent selectivity (15 : 1). As shown in Fig. 2, NOESY correlations and vicinal proton coupling constants (J_{H-H}) revealed that the olefin has a favorable conformation in which the *syn*-pentane interaction[21] between the C14-methyl group and the C16-substituents as well as the 1,3-allylic strain[22] to the C18-methyl group and the C19-hydrogen are minimized; hence this observed conformation is very similar to that of the C8—C17 segment, a part of the calculation model of the seco-acid (**3**) calculated by the MM2-CONFLEX method.[5,7] After the two acetyl groups of the olefin were removed by $LiAlH_4$, the primary alcohol of the resulting diol (**26**) was selectively protected with a TBS group and the remaining secondary alcohol was converted to a methoxymethyl (MOM) ether to give **27** in excellent yield. Finally, the benzylidene group was selectively reduced with DIBAH and the resulting primary alcohol was subjected to Dess-Martin oxidation to readily give the title compound (**8**). A remarkable feature of this synthesis of **8** is the advantageous use of the DMPM protecting group, which is variable by oxidation and reduction.[12,20]

The coupling between **8** and the C1—C12 part (**7**) followed by macrolactonization to the lactone (**2**) will be reported soon.

Experimental

(2*S*,3*S*,4*R*)-2-(*tert*-Butyldimethylsilyloxymethyl)-5-(*tert*-butyldiphenylsilyloxy)-1,3-[(*R*)-3,4-dimethoxybenzylidenedioxy]-4-methylpentane (11) OsO_4 (44 mg, 0.17 mmol) was added to a stirred solution of **10** (1.89 g, 3.46 mmol) and NMO (809 mg, 6.91 mmol) in acetone (15 ml) and H_2O (4 ml) at room temperature. After 20 h, saturated aqueous $NaHSO_3$ (20 ml) was added at 0 °C and the precipitated solid was removed by filtration through a Celite pad. The filtrate was concentrated *in vacuo* to remove acetone, and extracted with EtOAc. The extract was washed with brine, dried over $MgSO_4$, concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (2 : 3) to give a 1.3 : 1 mixture of diols as a colorless oil (1.91 g, 95%). IR (neat) cm^{-1}: 3400 (br), 2960, 2930, 2860, 1595, 1519, 1464, 1427, 1264, 1236, 1162, 1112, 863, 823, 759, 703. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.90 (1.3H, d, J=7.0 Hz), 0.91 (1.7 H, d, J=7.0 Hz), 1.05 (5H, s), 1.06 (4H, s), 1.50—2.50 (4H, m), 3.50—4.21 (7H, m), 3.84 (1.7H, s), 3.87 (1.3H, s), 3.88 (1.3H, s), 3.89 (1.7H, s), 4.35 (1H, m), 5.38 (0.56H, s), 5.41 (0.44H, s), 6.80—6.90 (1H, m), 6.92—7.06 (2H, m), 7.15—7.28 (2H, m), 7.29—7.50 (4H, m), 7.55—7.75 (4H, m). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 9.6, 9.7, 19.15, 19.18, 26.80, 26.82, 36.2, 37.1, 37.5, 38.9, 55.66, 55.67, 55.86, 63.0, 64.8, 65.0, 65.5, 66.6, 67.6, 69.5, 70.2, 76.4, 77.2, 100.4, 100.7, 109.0, 109.1, 110.60, 110.61, 118.57, 118.60, 127.52, 127.54, 127.59, 129.46, 129.49, 129.55, 131.5, 131.6, 133.49, 133.55, 133.59, 133.7, 135.39, 135.42, 135.43, 148.5, 148.6, 149.05, 149.11. FAB-MS *m/z* (%): 581 (M^++1, 29), 580 (M^+, 4), 523 (6.2), 357 (8.2), 337 (4.6), 307 (12), 279 (15), 239 (21), 199 (78), 167 (93), 154 (77), 135 (100). HR-MS (FAB) Calcd for $C_{33}H_{45}O_7Si$ (M^++1): 581.2935. Found: 581.2966.

A solution of $NaIO_4$ (490 mg, 2.29 mmol) in H_2O (4 ml) was added to a stirred solution of the mixture of diols (474 mg, 0.816 mmol) in tetrahydrofuran (THF) (5 ml) at 0 °C. The mixture was stirred for 1 h at room temperature, then diluted with H_2O (30 ml), and extracted with EtOAc. The extract was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to leave a crude aldehyde as a colorless oil (451 mg, 100%), which was subjected to the next reaction without purification. A part of the crude aldehyde was purified by chromatography on a silica gel column eluting with *n*-hexane–EtOAc (6 : 1). $[\alpha]_D^{25}$ −26.8° (c=1.00, $CHCl_3$). IR (neat) cm^{-1}: 3070, 2970, 2932, 2857, 1719, 1610, 1595, 1519, 1464, 1427, 1372, 1264, 1237, 1163, 1112, 1030, 861, 823, 760, 704, 613. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.95 (3H, d, J=7.0 Hz), 0.97 (9H, s), 2.05 (1H, m), 3.14 (1H, m), 3.57 (1H, dd, J=5.5, 9.8 Hz), 3.76 (1H, dd, J=9.8, 9.8 Hz), 3.85 (3H, s), 3.90 (3H, s), 4.04 (1H, dd, J=11.3, 11.3 Hz), 4.37 (1H, dd, J=4.9, 11.3 Hz), 4.46 (1H, dd, J=1.8, 10.4 Hz), 5.41 (1H, s), 6.80—6.90 (1H, m), 6.95—7.05 (2H, m), 7.20—7.45 (6H, m), 7.55—7.70 (4H, m), 9.73 (1H, d, J=2.4 Hz). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 10.18, 19.16, 26.78, 38.39, 49.23, 55.69, 55.86, 64.70, 65.99, 75.68, 100.76, 109.00, 110.61, 118.62, 127.55, 127.61, 129.53, 129.60, 130.76, 133.43, 133.44, 135.40, 135.43, 148.66, 149.34, 200.09. FAB-MS *m/z* (%): 549 (M^++1, 8.1), 307 (25), 289 (13), 269 (10), 220 (10), 219 (14), 199 (11), 197 (11), 167 (17), 166 (14), 165 (15), 155 (25), 154 (100). HR-MS (FAB) Calcd for $C_{32}H_{41}O_6Si$ (M^++1): 549.2672. Found: 549.2685.

A solution of the crude aldehyde (450 mg, 0.819 mmol) in Et_2O (8 ml) was added dropwise to a suspension of $LiBH_4$ (27 mg, 1.24 mmol) in Et_2O (5 ml) at 0 °C and stirring was continued for 1 h at room temperature. Saturated aqueous NH_4Cl (20 ml) was added at 0 °C, and the mixture was extracted with EtOAc. The extract was washed with brine, dried over $MgSO_4$, concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (2 : 1) to give (2*R*,3*S*,4*R*)-5-(*tert*-butyldiphenylsilyloxy)-2-hydroxymethyl-1,3-[(*R*)-3,4-dimethoxybenzylidenedioxy]-4-methylpentane as a colorless oil (420 mg, 93%). $[\alpha]_D^{25}$ −27.5° (c=0.60, $CHCl_3$). IR (neat) cm^{-1}: 3490 (br), 2931, 2857, 1736, 1611, 1595, 1519, 1464, 1427, 1264, 1236, 1162, 1111, 1030, 966, 863, 823, 758, 704. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.92 (3H, d, J=7.0 Hz), 1.05 (9H, s), 1.33 (1H, br s), 2.06 (1H, m), 2.20 (1H, m), 3.52 (1H, dd, J=6.5, 11.0 Hz), 3.57 (1H, dd, J=5.5, 10.0 Hz), 3.64 (1H, dd, J=4.0, 11.0 Hz), 3.75—3.84 (2H, m), 3.84 (3H, s), 3.89 (3H, s), 4.11 (1H, m), 4.35 (1H, dd, J=4.5, 11.0 Hz), 5.40 (1H, s), 6.82—6.88 (1H, m), 6.95—7.03 (2H, m), 7.20—7.28 (2H, m), 7.32—7.45 (4H, m), 7.58—7.68 (4H, m). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 9.68, 19.06, 26.70, 36.79, 37.34, 55.56, 55.75, 60.47, 65.13, 69.55, 76.63, 100.47, 109.03, 110.51, 118.49, 127.41, 127.46, 129.36, 129.42, 131.52, 133.49, 133.61, 135.32, 148.46, 148.97. FAB-MS *m/z* (%): 551 (M^++1, 6.7), 341 (7), 308 (6), 307 (29), 289 (14), 220 (14), 219 (17), 199 (8), 167 (8), 166 (6), 165 (7), 155 (24), 154 (100). HR-MS (FAB) Calcd for $C_{32}H_{43}O_6Si$ (M^++1): 551.2829. Found: 551.2810.

TBSCl (1.56 g, 10.35 mmol) was added to a stirred solution of the above alcohol (3.80 g, 6.90 mmol) and imidazole (1.41 g, 20.71 mmol) in CH_2Cl_2 (30 ml) at 0 °C and stirring was continued for 30 min at room temperature. Saturated aqueous NH_4Cl (40 ml) was added at 0 °C, and the mixture was extracted with CH_2Cl_2. The extract was washed with brine, dried over $MgSO_4$, concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (7 : 1) to give **11** as a colorless oil (4.60 g, 100%). $[\alpha]_D^{25}$ −23.1° (c=0.61, $CHCl_3$). IR (neat) cm^{-1}: 2931, 2857, 1611, 1595, 1519, 1464, 1427, 1390, 1362, 1261, 1237, 1163, 1111, 1031, 967, 838, 704. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.07 (3H, s), 0.08 (3H, s), 0.91 (9H, s), 0.91 (3H, d, J=7.0 Hz), 1.05 (9H, s), 2.11 (1H, m), 2.19 (1H, m), 3.48 (1H, dd, J=6.4, 10.4 Hz), 3.54 (1H, dd, J=6.0, 10.1 Hz), 3.59 (1H,

J=4.4, 10.4 Hz), 3.74—3.82 (2H, m), 3.83 (3H, s), 3.89 (3H, s), 4.11 (1H, dd, J=1.7, 10.6 Hz), 4.30 (1H, dd, J=4.6, 10.6 Hz), 5.40 (1H, s), 6.80—6.87 (1H, m), 6.96—7.02 (2H, m), 7.17—7.24 (2H, m), 7.30—7.48 (4H, m), 7.58—7.68 (4H, m). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: −5.60, 9.90, 18.14, 19.20, 25.80, 26.80, 36.82, 37.60, 55.66, 55.87, 60.89, 65.26, 69.91, 77.42, 100.60, 109.14, 110.62, 118.58, 127.49, 127.55, 129.41, 129.48, 131.84, 133.69, 133.81, 135.44, 135.46, 148.60, 149.06. FAB-MS m/z (%): 665 (M^++1, 7.5), 608 (7), 607 (15), 313 (10), 309 (8), 271 (9), 269 (16), 243 (18), 239 (18), 227 (7), 225 (13), 213 (6), 211 (7), 209 (14), 199 (22), 198 (9), 197 (45), 195 (12), 185 (27), 183 (15), 171 (12), 167 (10), 166 (12), 165 (34), 151 (63), 135 (100). HR-MS (FAB) Calcd for $C_{38}H_{57}O_6Si_2$ (M^++1): 665.3693. Found: 665.3718.

(2*S*,3*S*,4*R*)-2-(*tert*-Butyldimethylsilyloxymethyl)-5-(*tert*-butyldiphenylsilyloxy)-3-(3,4-dimethoxybenzyloxy)-4-methylpentan-1-ol (12) A 0.95 M solution of DIBAH in *n*-hexane (6.08 ml, 5.78 mmol) was added dropwise to a stirred solution of **11** (1.60 g, 2.41 mmol) in CH_2Cl_2 (20 ml) at −78 °C, and the mixture was kept in a freezer for 6 h at −20 °C. After the reaction was quenched with saturated aqueous NH_4Cl (15 ml) at −20 °C, saturated aqueous Rochelle salt (30 ml) and CH_2Cl_2 (30 ml) were added, and the mixture was vigorously stirred for 2 h. The separated organic layer was dried over $MgSO_4$, concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (2 : 1) to give **12** as a colorless solid (0.87 g, 54%), which was recrystallized from *n*-pentane. mp 74—75 °C (colorless needles). $[\alpha]_D^{25}$ −1.5° (c=0.97, $CHCl_3$). IR (neat) cm^{-1}: 3502, 2960, 2930, 1518, 1469, 1362, 1264, 1157, 1111, 1034, 813, 708. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.08 (6H, s), 0.90 (9H, s), 0.91 (3H, d, J=7.0 Hz), 1.07 (9H, s), 1.87—2.04 (2H, m), 3.04 (1H, m), 3.57 (1H, dd, J=6.0, 10.0 Hz), 3.67 (1H, dd, J=7.5, 10.0 Hz), 3.69 (1H, dd, J=6.2, 10.1 Hz), 3.78 (1H, dd, J=5.0, 10.1 Hz), 3.78—3.90 (2H, m), 3.83 (3H, s), 3.87 (3H, s), 3.93 (1H, dd, J=4.0, 7.0 Hz), 4.53 (2H, s), 6.70—6.85 (3H, m), 7.30—7.49 (6H, m), 7.57—7.73 (4H, m). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: −5.62, −5.57, 11.32, 18.11, 19.18, 25.84, 26.88, 38.81, 45.06, 55.70, 55.83, 63.49, 63.84, 66.30, 74.86, 78.39, 110.90, 111.08, 120.23, 127.61, 129.60, 131.17, 133.51, 133.55, 135.49, 135.52, 148.52, 148.84. FAB-MS m/z (%): 666 (M^+, 9.5), 301 (29), 269 (13), 239 (24), 197 (96), 165 (36), 152 (100). HR-MS (FAB) Calcd for $C_{38}H_{58}O_6Si_2$ (M^+): 666.3772. Found 666.3799. *Anal*. Calcd for $C_{38}H_{58}O_6Si_2$: C, 68.42; H, 8.76. Found: C, 68.34; H, 8.73.

(2*S*,3*S*,4*R*)-2-(*tert*-Butyldimethylsilyloxymethyl)-5-(*tert*-butyldiphenylsilyloxy)-3-(3,4-dimethoxybenzyloxy)-4-methylpentanal (6) a) A solution of dimethyl sulfoxide (DMSO) (1.10 ml, 15.5 mmol) in CH_2Cl_2 (4 ml) was added to a stirred solution of $(COCl)_2$ (0.69 ml, 7.9 mmol) in CH_2Cl_2 (8 ml) at −78 °C. After 20 min, a solution of **12** (1.30 g, 1.95 mmol) in CH_2Cl_2 (16 ml) was added at the same temperature. The mixture was stirred for 20 min at −78 °C and for 30 min at −45 °C, and then diisopropylethylamine (iso-Pr_2EtN) (4.07 ml, 23.4 mmol) was added at −78 °C. Stirring was continued for 30 min at −78 °C, for 30 min at 0 °C, and for 1 h at room temperature. Saturated aqueous NH_4Cl (30 ml) was added to quench the reaction, and the mixture was extracted with EtOAc. The extract was washed with brine, dried over $MgSO_4$, concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (6 : 1) to give **6** as a colorless oil (1.27 g, 98%). $[\alpha]_D^{25}$ +11.3° (c=1.00, $CHCl_3$). IR (neat) cm^{-1}: 2931, 2857, 1724, 1592, 1517, 1465, 1427, 1262, 1112, 837, 703. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.04 (3H, s), 0.05 (3H, s), 0.87 (9H, s), 0.91 (3H, d, J=7.0 Hz), 1.08 (9H, s), 2.00 (1H, m), 2.75 (1H, m), 3.61 (1H, dd, J=10.4, 5.8 Hz), 3.67 (1H, dd, J=10.4, 7.9 Hz), 3.78 (1H, dd, J=10.4, 5.2 Hz), 3.83 (3H, s), 3.86 (3H, s), 3.88 (1H, dd, J=10.4, 6.4 Hz), 4.17 (1H, dd, J=6.6, 3.8 Hz), 4.48 (1H, d, J=11.0 Hz), 4.53 (1H, d, J=11.0 Hz), 6.72—6.82 (3H, m), 7.32—7.47 (6H, m), 7.60—7.70 (4H, m), 9.79 (1H, d, J=2.4 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: −5.61, 11.37, 18.10, 19.16, 25.75, 26.88, 38.93, 55.68, 55.81, 57.17, 60.41, 65.84, 74.31, 76.74, 110.80, 111.01, 120.05, 127.64, 129.65, 131.01, 133.38, 133.44, 135.47, 135.52, 148.48, 148.83, 203.90. FAB-MS m/z (%): 665 (M^++1, 1.6), 664 (M^+, 3.0), 663 (M^+−1, 3.8), 602 (1.9), 501 (17), 497 (6.8), 458 (7.3), 439 (4.3), 397 (3.8), 309 (10), 301 (11), 269 (39), 239 (31), 197 (85), 151 (100). HR-MS (FAB) Calcd for $C_{38}H_{57}O_6Si_2$ (M^++1): 665.3694. Found 665.3694.

b) NMO (34 mg, 291 μmol) and OsO_4 (2 mg, 8 μmol) were added to a stirred solution of **17** (97 mg, 146 μmol) in acetone–H_2O (4 : 1, 1 ml) at room temperature. After 3 h, saturated aqueous Na_2SO_3 and Et_2O were added, and the reaction mixture was stirred vigorously for 20 min and then filtered with the aid of Celite. The filtrate was washed with brine, dried over $MgSO_4$, concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (1 : 1) to give a 3 : 1 mixture of diols as a colorless oil (93 mg, 91%). IR (neat) cm^{-1}: 3464, 3071, 2954, 2930, 2857, 1517, 1464, 1262, 1111, 1031, 836, 703. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.06 (2.25H, s), 0.07 (2.25H, s), 0.08 (0.75H, s), 0.09 (0.75H, s), 0.889 (2.25H, d, J=7.0 Hz), 0.897 (6.75H, s), 0.899 (2.25H, s), 0.92 (0.75H, d, J=7.0 Hz), 1.06 (2.25H, s), 1.07 (6.75H, s), 1.83—1.88 (0.25H, m), 1.91—1.98 (0.75H, m), 1.99—2.06 (1H, m), 3.55—3.87 (6H, m), 3.82 (2.25H, s), 3.83 (0.75H, s), 3.86 (0.75H, s), 3.87 (2.25H, s), 3.92—4.11 (2H, m), 4.53 (0.75H, d, J=10.7 Hz), 4.54 (0.75H, d, J=10.7 Hz), 4.55 (0.25H, d, J=11.0 Hz), 4.57 (0.25H, d, J=11.0 Hz), 6.73—6.82 (3H, m), 7.32—7.46 (6H, m), 7.61—7.67 (4H, m). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: −5.73, −5.68, −5.63, 10.9, 11.5, 17.98, 18.02, 19.2, 25.8, 26.9, 38.3, 39.4, 44.8, 46.3, 55.68, 55.71, 55.79, 55.81, 61.4, 62.0, 64.5, 65.6, 66.2, 66.4, 71.4, 72.4, 74.7, 74.8, 77.9, 79.0, 110.9, 111.0, 111.1, 120.2, 120.3, 127.61, 127.64, 129.60, 129.62, 129.64, 129.66, 130.5, 131.1, 133.3, 133.4, 135.45, 135.46, 135.51, 135.52, 148.5, 148.6, 148.80, 148.84. FAB-MS m/z (%): 697 (M^++1, 2.6), 317 (3.0), 239 (3.7), 224 (4.0), 214 (4.7), 201 (10), 199 (25), 198 (16), 197 (100), 181 (12), 152 (37), 151 (59), 135 (30), 121 (17), 107 (18), 105 (29). HR-MS (FAB) Calcd for $C_{39}H_{61}O_7Si_2$ (M^++1): 697.3956. Found: 697.3945.

A solution of $NaIO_4$ (136 mg, 636 μmol) in H_2O (2 ml) was added to a stirred solution of the above diol (159 mg, 228 μmol) in THF (3 ml) at 0 °C. The mixture was stirred for 1 h at room temperature, then diluted with H_2O, and extracted with Et_2O. The extract was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (6 : 1), to give **6** as a colorless oil (150 mg, 99%).

[4*R*,3(2*R*,3*S*,4*R*)]-3-(5-*tert*-Butyldiphenylsilyloxy-3-hydroxy-4-methyl-2-vinylpentanoyl)-4-isopropyl-2-oxazolidinone (15) A 1.0 M solution of $TiCl_4$ in CH_2Cl_2 (0.69 ml, 0.69 mmol) was added dropwise to a stirred solution of (*R*)-3-crotonyl-4-isopropyl-2-oxazolidinone (**14**) (136 mg, 0.69 mmol) in CH_2Cl_2 (1.5 ml) at 0 °C under argon. After 10 min, iso-Pr_2EtN (120 μl, 0.69 mmol) was added, and stirring was continued for 30 min. The mixture was cooled to −78 °C and a solution of **13a** (150 mg, 0.46 mmol) in CH_2Cl_2 (1.0 ml) was added. The reaction mixture was allowed to warm to 0 °C over 3 h and kept at 0 °C for 3 h. The reaction was quenched with MeOH and then aqueous NH_4Cl. After 20 min, the mixture was extracted with EtOAc. The extract was washed with brine, dried over $MgSO_4$, concentrated *in vacuo* to leave crude **15** as a colorless oil (299 mg), which was subjected to the next reaction without further purification. A part of crude **15** (100 mg) was purified by chromatography on a silica gel column, eluting with *n*-hexane–EtOAc (4 : 1) to give recovered **13a** (14 mg, 9%) and **15** as a colorless oil (56 mg, 70%). $[\alpha]_D^{26}$ +5.5° (c=1.00, $CHCl_3$). IR (neat) cm^{-1}: 3511 (br), 3071, 2962, 2930, 2858, 1782, 1695, 1386, 1372, 1201, 1112, 704. ^{1}H-NMR (300 MHz, $CDCl_4$) δ: 0.83 (3H, d, J=7.0 Hz), 0.90 (3H, d, J=7.0 Hz), 1.02 (3H, d, J=7.0 Hz), 1.05 (9H, s), 1.70—1.82 (1H, m), 2.26—2.39 (1H, m), 3.18 (1H, d, J=2.3 Hz), 3.65 (1H, dd, J=4.9, 10.0 Hz), 3.74 (1H, dd, J=4.6, 10.0 Hz), 4.19 (1H, dd, J=3.4, 9.3 Hz), 4.22—4.32 (2H, m), 4.44 (1H, ddd, J=3.5, 3.5, 8.0 Hz), 4.83 (1H, dd, J=6.9, 8.8 Hz), 5.32 (1H, dd, J=1.4, 10.2 Hz), 5.43 (1H, d, J=16.3 Hz), 5.97 (1H, ddd, J=8.9, 10.2, 16.3 Hz), 7.34—7.47 (6H, m), 7.63—7.72 (4H, m). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 11.77, 15.09, 18.51, 19.82, 27.46, 28.70, 38.26, 51.07, 58.75, 63.50, 68.39, 73.73, 121.41, 128.30, 130.29, 130.34, 133.63, 133.80, 134.04, 136.19, 136.27, 153.82, 173.82. FAB-MS m/z (%): 524 (M^++1, 14), 506 (3.6), 467 (5.6), 466 (16), 446 (6.2), 395 (8.7), 368 (8.4), 337 (11), 328 (9.7), 310 (8.7), 269 (26), 250 (21), 239 (28), 199 (100), 197 (57), 183 (26), 139 (23), 137 (50), 136 (24), 135 (100), 130 (41) 121 (60), 91 (23). HR-MS (FAB) Calcd for $C_{30}H_{42}NO_5Si$ (M^++1): 524.2832. Found: 524.2820.

(2*S*,3*S*,4*R*)-5-*tert*-Butyldiphenylsilyloxy-4-methyl-2-vinylpentane-1,3-diol (16) A solution of $LiBH_4$ (13 mg, 0.60 mmol) in THF (1 ml) was added dropwise to a stirred solution of the above crude **15** (199 mg) in Et_2O (8 ml) and H_2O (11 μl, 0.61 mmol) at 0 °C. After 30 min, a 1.0 M aqueous NaOH (1.8 ml) was added, and the mixture was extracted with Et_2O. The extract was washed with brine, dried over $MgSO_4$, concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (2 : 1) to give **16** as a colorless oil (74 mg, 61% from **13a**). $[\alpha]_D^{25}$ −7.8° (c=1.00, $CHCl_3$). IR (neat) cm^{-1}: 3390 (br), 3071, 2959, 2930, 2858, 1472, 1427, 1112, 1055, 823, 741, 702, 613. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.01 (3H, d, J=7.0 Hz), 1.06 (9H, s), 1.65—1.95 (3H, m), 2.30—2.41 (1H, m), 3.59 (1H, dd, J=6.8, 10.5 Hz), 3.62—3.73 (3H, m), 3.90 (1H, dd, J=5.0, 5.0 Hz), 5.15 (1H, ddd, J=1.8, 1.8, 17.2 Hz), 5.25 (1H, dd, J=1.8, 10.4 Hz), 5.91 (1H, ddd, J=9.0, 10.4, 17.2 Hz), 7.35—7.49 (6H, m), 7.62—7.72 (4H, m). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 12.06, 12.11, 19.79, 27.46, 38.66, 50.14, 64.94, 68.37, 74.66, 119.57, 128.33, 130.40, 133.61, 133.76, 136.17, 136.26, 136.95. FAB-MS m/z (%): 399 (M^++1, 6.4), 303 (6.7), 269 (11), 239 (22), 200 (23), 199 (100), 197 (62), 183 (23), 165 (18), 139 (44), 137 (74), 136 (29), 135 (100), 121 (22), 107 (22), 105 (25), 91 (33). HR-MS (FAB) Calcd for $C_{24}H_{35}O_3Si$ (M^++1): 399.2355. Found: 399.2333.

(3*S*,4*S*,5*R*)-3-(*tert*-Butyldimethylsilyloxymethyl)-6-(*tert*-butyldiphenylsilyloxy)-4-(3,4-dimethoxybenzyloxy)-5-methyl-1-hexene (17) A solution of **16** (79 mg, 198 μmol), 3,4-dimethoxybenzaldehyde dimethyl acetal [DMPCH(OMe)$_2$] (63 mg, 297 μmol) and *dl*-camphorsulfonic acid (CSA) (5 mg, 21.6 μmol) in CH_2Cl_2 (1.5 ml) was stirred at room temperature for 5 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$, and extracted with EtOAc. The extract was washed with saturated aqueous $NaHCO_3$ and brine, dried over K_2CO_3, concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (3 : 1), to give a 3,4-dimethoxybenzylidene acetal as a colorless oil (107 mg, 99%). $[\alpha]_D^{26}$ +0.5° (c=1.00, $CHCl_3$). IR (neat) cm^{-1}: 3070, 2963, 2931, 2856, 1595, 1518, 1463, 1427, 1264, 1237, 1163, 1113, 1032, 704. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.08 (9H, s), 1.17 (3H, d, J=6.7 Hz), 1.74—1.88 (1H, m), 1.93—2.01 (1H, m), 3.58—3.62 (4H, m), 3.82—3.91 (1H, m), 3.88 (3H, s), 3.90 (3H, s), 4.01—4.06 (2H, m), 4.82 (1H, dd, J=2.0, 17.4 Hz), 5.05 (1H, dd, J=2.0, 10.3 Hz), 5.51 (1H, s), 6.24 (1H, ddd, J=10.3, 10.3, 17.4 Hz), 6.86 (1H, d, J=8.6 Hz), 7.02—7.08 (2H, m), 7.34—7.49 (6H, m), 7.62—7.49 (2H, m). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 14.0, 19.3, 26.9, 37.5, 41.6, 55.8, 55.9, 64.1, 73.1, 81.0, 101.8, 109.0, 110.7, 116.9, 118.5, 127.6, 127.7, 129.6, 129.7, 131.7, 133.5, 133.7, 135.62, 135.64, 136.4, 148.7, 149.2. FAB-MS *m/z* (%): 548 (M^++2, 2.1), 547 (M^++1, 4.2), 323 (9), 239 (20), 227 (8), 200 (12), 199 (52), 198 (19), 197 (98), 183 (45), 181 (35), 166 (24), 165 (53), 151 (34), 135 (100), 105 (41), 91 (15). HR-MS (FAB) Calcd for $C_{33}H_{43}O_5Si$ (M^++1): 547.2880. Found: 547.2853.

A 0.94 M solution of DIBAH in *n*-hexane (3.1 ml, 2.91 mmol) was added dropwise to a stirred solution of the above acetal (318 mg, 0.58 mmol) in toluene (5 ml) at −35 °C under argon. After 1 h, the reaction was quenched with MeOH. Et_2O and saturated aqueous potassium sodium tartrate were added, and the mixture was vigorously stirred for 1 h. The organic layer was washed with brine, dried over Na_2SO_4, concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (3 : 1) to give an alcohol (296 mg, 93%). $[\alpha]_D^{27}$ −12.3° (c=0.98, $CHCl_3$). IR (neat) cm^{-1}: 3532, 3070, 2963, 2931, 2857, 1517, 1265, 1112, 1030, 704. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.01 (3H, d, J=7.0 Hz), 1.07 (9H, s), 1.86—1.97 (1H, m), 2.41—2.52 (1H, m), 3.49—3.58 (2H, m), 3.60—3.68 (2H, m), 3.72 (1H, dd, J=5.0, 5.0 Hz), 3.85 (3H, s), 3.87 (3H, s), 4.48 (1H, d, J=11.5 Hz), 4.51 (1H, d, J=11.5 Hz), 5.05 (1H, dd, J=1.8, 17.4 Hz), 5.15 (1H, dd, J=1.8, 10.3 Hz), 5.81 (1H, ddd, J=9.2, 10.3, 17.4 Hz), 6.77—6.88 (3H, m), 7.32—7.48 (6H, m), 7.62—7.61 (4H, m). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 12.7, 19.2, 26.9, 38.8, 49.9, 55.7, 55.8, 63.7, 66.0, 74.2, 79.6, 110.8, 111.1, 118.4, 120.2, 127.59, 127.62, 129.59, 129.63, 131.2, 133.6, 135.6, 136.4, 148.5, 148.8. FAB-MS *m/z* (%): 549 (M^++1, 0.8), 303 (1.2), 239 (3.6), 199 (16), 198 (10), 197 (22), 183 (10), 152 (11), 151 (100), 139 (21), 135 (38), 121 (13), 105 (20). HR-MS (FAB) Calcd for $C_{33}H_{45}O_5Si$ (M^++1): 549.3036. Found: 549.3064.

Imidazole (85 mg, 1.25 mmol) and TBSCl (113 mg, 0.75 mmol) were added to a stirred solution of the above alcohol (273 mg, 0.50 mmol) in CH_2Cl_2 (4 ml) at 0 °C, and stirring was continued for 1 h. After the reaction was quenched with MeOH, saturated aqueous NH_4Cl was added, and the mixture was extracted with Et_2O. The extract was washed with saturated aqueous NH_4Cl and brine, dried over $MgSO_4$, concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (5 : 1), to give **17** as a colorless oil (329 mg, 99%). $[\alpha]_D^{28}$ −3.3° (c=1.00, $CHCl_3$). IR (neat) cm^{-1}: 3071, 2954, 2930, 2857, 1517, 1464, 1260, 1111, 836, 703. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.04 (6H, s), 0.89 (9H, s), 1.00 (3H, d, J=6.8 Hz), 1.06 (9H, s), 1.91—2.02 (1H, m), 2.38—2.49 (1H, m), 3.48—3.57 (2H, m), 3.62 (1H, dd, J=5.9, 10.0 Hz), 3.67 (1H, dd, J=7.6, 9.8 Hz), 3.78—3.84 (1H, m), 3.84 (3H, s), 3.87 (3H, s), 4.50 (1H, d, J=10.9 Hz), 4.55 (1H, d, J=10.9 Hz), 4.98 (1H, dd, J=2.1, 17.2 Hz), 5.04 (1H, dd, J=2.1, 10.5 Hz), 5.83 (1H, ddd, J=9.3, 10.5, 17.2 Hz), 6.77—6.88 (3H, m), 7.32—7.46 (6H, m), 7.62—7.70 (4H, m). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: −5.4, −5.3, 13.1, 18.3, 19.3, 25.9, 26.9, 39.1, 50.1, 55.7, 55.9, 64.2, 66.1, 74.4, 78.7, 110.8, 111.1, 117.3, 120.0, 127.58, 127.59, 129.5, 131.9, 133.8, 135.6, 136.9, 148.3, 148.8. FAB-MS *m/z* (%): 663 (M^++1, 3.3), 661 (2.5), 347 (4.2), 301 (5.3), 269 (8.2), 257 (8.3), 239 (15), 199 (25), 165 (21), 152 (76), 151 (100), 137 (44), 135 (80). HR-MS (FAB) Calcd for $C_{39}H_{59}O_5Si_2$ (M^++1): 663.3901. Found: 663.3925.

(2*S*)-3-(*tert*-Butyldiphenylsilyloxy)-2-methylpropanal (13b) Using the method similar to that used for the preparation of the enantiomer **13a**,[9a] **9b** was converted to **13b** in quantitative yield *via* three reactions: TBDPS protection of the hydroxy group, reduction of the ester group with $LiBH_4$ and Swern oxidation. Spectral properties of the intermediates and **13b** were in accord with those of the corresponding enantiomers.

(4*R*)-5-(*tert*-Butyldiphenylsilyloxy)-4-methyl-2-pentyne (18) By a method similar to that used for the preparation of the enantiomer of **18**,[9a] **13b** (3.7 g, 11.3 mmol) was treated with CBr_4 (5.6 g, 16.9 mmol) and Ph_3P (9.2 g, 35.1 mmol) to give (3*R*)-1,1-dibromo-4-(*tert*-butyldiphenylsilyloxy)-3-methyl-1-butene as a colorless oil (5.1 g, 93%). $[\alpha]_D^{26}$ −12.3° (c=0.82, $CHCl_3$). Spectral properties of the dibromoalkene were in accord with those of its enantiomer.

The dibromoalkene (5.1 g, 10.5 mmol) was treated with a 1.56 M hexane solution of *n*-BuLi (17 ml, 26.5 mmol) and methyl iodide (3.3 ml, 53 mmol) to give **18** (3.4 g, 96%). $[\alpha]_D^{24}$ +3.9° (c=0.84, $CHCl_3$). Spectral properties of **18** were in accord with those of its enantiomer.

(2*E*,4*R*)-5-(*tert*-Butyldiphenylsilyloxy)-2-iodo-4-methyl-2-pentene (5b) Using a method similar to that used for the preparation of the enantiomer **5a**,[9] **18** (2.6 g, 7.7 mmol) was treated with chlorobis(cyclopentadienyl)hydridozirconium (6.1 g, 23.7 mmol) and iodine (3.0 g, 11.8 mmol) to give **5b** as a pale yellow oil (1.8 g, 50%). $[\alpha]_D^{25}$ +16.3° (c=0.84, $CHCl_3$). Spectral properties of **5b** were in accord with those of the enantiomer **5a**.

(2*R*,3*E*,5*R*,6*S*,7*S*,8*R*)-6-(*tert*-Butyldimethylsilyloxymethyl)-1,9-di-(*tert*-butyldiphenylsilyloxy)-7-(3,4-dimethoxybenzyloxy)-2,4,8-trimethyl-3-nonen-5-ol (19a) and (2*R*,3*E*,5*S*,6*S*,7*S*,8*R*)-6-(*tert*-Butyldimethylsilyloxymethyl)-1,9-di-(*tert*-butyldiphenylsilyloxy)-7-(3,4-dimethoxybenzyloxy)-2,4,8-trimethyl-3-nonen-5-ol (19b) A 1.64 M solution of *tert*-BuLi in pentane (1.43 ml, 2.35 mmol) was added to a stirred solution of **5b** (497 mg, 1.07 mmol) in Et_2O (6 ml) at −78 °C. The mixture was stirred for 1 h at −78 °C and for 1 h at room temperature, then cooled again to −78 °C, and a solution of **6** (475 mg, 0.71 mmol) in Et_2O (6 ml) was added dropwise. After being stirred for 1 h at −78 °C, the reaction mixture was allowed to warm to −30 °C over 3 h, then quenched with saturated aqueous NH_4Cl (30 ml), and extracted with EtOAc. The extract was washed with brine, dried over $MgSO_4$, concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–iso-Pr_2O (3 : 2) to give a 7.5 : 1 mixture of **19a** and **19b** as a colorless oil (606 mg, 85%). **19a**: IR (neat) cm^{-1}: 3490 (br), 2930, 2857, 1591, 1517, 1465, 1427, 1390, 1362, 1262, 1111, 702. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: −0.10 (3H, s), −0.05 (3H, s), 0.80 (9H, s), 0.91 (3H, d, J=7.0 Hz), 1.05 (9H, s), 1.06 (9H, s), 1.07 (3H, d, J=7.0 Hz), 1.39 (3H, s), 1.69 (1H, m), 2.10 (1H, m), 2.65 (1H, m), 3.36 (1H, t like, J=9.6 Hz), 3.49—3.55 (2H, m), 3.57 (1H, dd, J=6.6, 9.8 Hz), 3.68 (1H, dd, J=7.0, 9.8 Hz), 3.74 (1H, dd, J=4.0, 10.4 Hz), 3.78 (3H, s), 3.86 (3H, s), 4.04 (1H, d, J=7.0 Hz), 4.21 (1H, dd, J=3.5, 8.1 Hz), 4.35 (1H, d, J=7.0 Hz), 4.54 (1H, d, J=10.7 Hz), 4.66 (1H, d, J=10.7 Hz), 5.30 (1H, d, J=9.2 Hz), 6.70—6.82 (3H, m), 7.28—7.45 (12H, m), 7.60—7.75 (8H, m). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: −5.8, −5.7, 11.2, 14.3, 17.5, 17.9, 19.17, 19.20, 25.8, 26.8, 26.9, 35.3, 38.1, 43.3, 55.7, 55.8, 60.4, 66.6, 68.5, 74.8, 74.9, 76.4, 77.2, 110.9, 111.1, 120.1, 126.3, 127.6, 129.45, 129.46, 129.49, 129.55, 131.6, 133.5, 133.6, 133.9, 134.0, 135.5, 136.5, 148.3, 148.7. FAB-MS *m/z* (%): 1003 (M^++1, 0.3), 986 (0.9), 928 (1.3), 431 (5.0), 309 (16), 269 (28), 239 (44), 197 (100).

(2*R*,3*E*,6*S*,7*S*,8*R*)-6-(*tert*-Butyldimethylsilyloxymethyl)-1,9-di-(*tert*-butyldiphenylsilyloxy)-7-(3,4-dimethoxybenzyloxy)-2,4,8-trimethyl-3-nonen-5-one (20) A solution of the mixture of **19a** and **19b** (841 mg, 0.84 mmol) in CH_2Cl_2 (15 ml) was added dropwise to a stirred suspension of the Dess-Martin periodinane (1.07 g, 2.52 mmol) and pyridine (0.39 ml, 4.82 mmol) in CH_2Cl_2 (10 ml) at 0 °C. The reaction mixture was stirred for 1 h at room temperature, cooled again to 0 °C, then quenched with saturated aqueous NH_4Cl, and extracted with CH_2Cl_2. The extract was washed with brine, dried over $MgSO_4$, concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (9 : 1) to give **20** as a colorless oil (766 mg, 91%). $[\alpha]_D^{25}$ −19.0° (c=1.00, $CHCl_3$). IR (neat) cm^{-1}: 2931, 2857, 1664, 1591, 1517, 1464, 1427, 1389, 1362, 1261, 1158, 1111, 1032, 838, 703. ^{1}H-NMR (500 MHz, C_6D_6) δ: 0.06 (3H, s), 0.08 (3H, s), 0.92 (9H, s), 0.99 (3H, d, J=6.7 Hz), 1.05 (3H, d, J=6.7 Hz), 1.14 (9H, s), 1.20 (9H, s), 1.93 (3H, d, J=0.9 Hz), 2.01 (1H, m), 2.66 (1H, m), 3.40 (3H, s), 3.43 (3H, s), 3.53 (1H, dd, J=6.0, 10.0 Hz), 3.56 (1H, dd, J=5.0, 10.0 Hz), 3.69 (1H, dd, J=6.0, 10.0 Hz), 3.78 (1H, dd, J=4.0, 9.0 Hz), 3.81 (1H, dd, J=9.5, 10.0 Hz), 4.06 (1H, dd, J=9.0, 9.0 Hz), 4.10 (1H, ddd, J=4.0, 9.0, 9.0 Hz), 4.43 (1H, d like, J=9.0 Hz), 4.51 (1H, d, J=11.0 Hz), 4.63 (1H, d, J=11.0 Hz), 6.52 (1H, d, J=8.0 Hz), 6.73—6.87 (3H, m), 7.18—7.28 (12H, m), 7.68—7.80 (8H, m). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: −5.66, −5.60, 10.02, 11.95, 16.59, 18.12, 19.19, 25.78, 26.77, 26.88, 36.47, 38.59, 50.48, 55.53, 55.78, 63.17, 66.27, 67.30, 74.57, 78.46, 110.68, 110.97, 119.90, 127.60, 127.65, 129.55, 129.57, 129.58, 129.61, 131,79, 133.48, 133.53, 133.74, 133.74, 135.48, 135.52, 135.53, 138.86, 144.31, 148.08, 148.51, 204.23. FAB-MS *m/z* (%): 1002 (M^++2, 1.0), 1001 (M^++1, 1.3), 645 (0.6), 389 (0.4), 365 (1.2), 337 (0.8), 301 (1.3), 251 (1.0), 249 (1.1), 240 (1.1), 239 (4.7), 227 (2.2), 217 (12), 199 (11), 197 (14), 183 (6.3), 165 (5.9), 152 (22), 151 (100),

137 (14), 135 (28), 106 (33), 91 (12). HR-MS (FAB) Calcd for $C_{60}H_{85}O_7Si_3$ (M^++1): 1001.5603. Found: 1001.5616.

Reduction of 20 with $LiAlH_4$ A solution of **20** (524 mg, 0.52 mmol) in THF (5 ml) was added to a stirred suspension of $LiAlH_4$ (38 mg, 1.00 mmol) in THF (5 ml) at −50 °C. After 10 min, the reaction mixture was allowed to warm to −30 °C over 10 min, then quenched with EtOAc (1 ml) and then ice (10 g), and extracted with EtOAc. The extract was washed with brine, dried over $MgSO_4$, concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (3 : 1) to give **19b** (118 mg, 26%) and **22** (228 mg, 56%) as colorless oils. **19b**: $[\alpha]_D^{25}$ +10.4° (c=1.00, $CHCl_3$). IR (neat) cm^{-1}: 3470, 2930, 2857, 1735, 1591, 1517, 1464, 1427, 1263, 1112, 939, 835, 703. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: −0.17 (3H, s), −0.10 (3H, s), 0.80 (9H, s), 0.92 (3H, d, J=7.0 Hz), 1.05 (9H, s), 1.06 (9H, s), 1.07 (3H, d, J=7.0 Hz), 1.51 (3H, d, J=1.2 Hz), 1.85 (1H, m), 2.07 (1H, m), 2.62 (1H, m), 3.28—3.37 (3H, m), 3.51—3.56 (2H, m), 3.62 (1H, dd, J=7.5, 10.0 Hz), 3.78 (3H, s), 3.85 (3H, s), 4.04 (1H, dd, J=3.5, 7.0 Hz), 4.20 (1H, d, J=9.0 Hz), 4.47 (1H, d, J=10.5 Hz), 4.61 (1H, d, J=10.5 Hz), 5.13 (1H, d, J=9.0 Hz), 6.70—6.76 (3H, m), 7.28—7.43 (12H, m), 7.58—7.70 (8H, m). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: −5.65, −5.62, 11.12, 11.55, 17.41, 18.00, 19.18, 19.22, 25.83, 26.87, 26.92, 35.27, 40.37, 45.65, 55.74, 55.83, 62.51, 66.54, 68.13, 74.73, 77.87, 81.12, 110.95, 111.16, 120.39, 127.55, 127.61, 129.46, 129.49, 129.56, 129.58, 130.14, 130.65, 133.51, 133.58, 133.89, 133.94, 135.50, 135.53, 135.57, 136.06, 148.59, 148.83. FAB-MS *m/z* (%): 1004 (M^++2, 0.6), 1003 (M^++1, 0.7), 986 (1.2), 985 (1.6), 835 (1.5), 563 (1.3), 539 (2.2), 431 (2.6), 377 (5.4), 321 (5.8), 309 (6.9), 271 (7.0), 269 (18), 257 (7.5), 251 (7.5), 249 (7.9), 239 (23), 227 (12), 217 (24), 199 (61), 198 (16), 197 (79), 195 (16), 183 (28), 181(21), 165 (30), 152 (99), 151 (100), 137 (81), 135 (100), 121 (59), 106 (30), 91 (63). HR-MS (FAB) Calcd for $C_{60}H_{87}O_7Si_3$ (M^++1): 1003.5760. Found: 1003.5771.

(2*R*,3*E*,6*S*,7*S*,8*R*)-1,9-Di-(*tert*-butyldiphenylsilyloxy)-6-hydroxymethyl-7-(3,4-dimethoxybenzyloxy)-2,4,8-trimethyl-3-nonen-5-one (21) PPTS (0.7 mg, 2.8 μmol) was added to a stirred solution of **20** (5.6 mg, 5.6 μmol) in absolute EtOH (0.5 ml) at room temperature. The reaction mixture was stirred 6 h at 50—55°C, then quenched with saturated aqueous $NaHCO_3$, and extracted with EtOAc. The extract was washed with brine, dried over $MgSO_4$, concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (4 : 1), to give **21** as a colorless oil (5.0 mg, 99%). $[\alpha]_D^{28}$ −9.8° (c=0.99, $CHCl_3$). IR (neat) cm^{-1}: 3521, 3071, 2958, 2931, 2858, 1661, 1516, 1463, 1427, 1265, 1112, 1032, 703. ^{1}H-NMR (500 MHz, C_6D_6) δ: 0.93 (3H, d, J=8.0 Hz), 0.99 (3H, d, J=6.5 Hz), 1.17 (9H, s), 1.26 (9H, s), 1.89 (3H, s), 2.13—2.22 (1H, m), 2.36—2.41 (1H, m), 2.59—2.70 (1H, m), 3.43 (3H, s), 3.47 (3H, s), 3.53 (1H, dd, J=6.0, 10.0 Hz), 3.56 (1H, dd, J=5.5, 10.0 Hz), 3.63—3.70 (1H, m), 3.74 (1H, dd, J=6.0, 10.0 Hz), 3.75—3.83 (2H, m), 3.88 (1H, dd, J=9.5, 10.0 Hz), 4.57 (1H, d, J=11.0 Hz), 4.60 (1H, d, J=11.0 Hz), 4.68 (1H, dd, J=1.5, 9.0 Hz), 6.55 (1H, d, J=8.0 Hz), 6.75—6.85 (3H, m), 7.20—7.40 (12H, m), 7.70—7.90 (8H, m). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 10.0, 11.9, 16.5, 19.17, 19.20, 26.76, 26.80, 26.83, 26.86, 36.5, 37.9, 48.8, 55.5, 55.8, 61.7, 66.1, 67.1, 74.4, 77.9, 110.6, 110.9, 119.9, 127.61, 127.63, 127.65, 127.66, 129.56, 129.60, 129.62, 129.66, 131.4, 133.4, 133.6, 133.7, 135.47, 135.52, 135.53, 135.60, 138.1, 145.8, 148.1, 148.5, 206.2. FAB-MS *m/z* (%): 888 (M^++2, 1.0), 887 (M^++1, 1.4), 365 (2.6), 301 (2.8), 269 (4.6), 239 (10), 199 (29), 197 (35), 183 (13), 165 (13), 152 (39), 151 (100), 137 (29), 135 (70), 121 (18), 105 (10), 91 (16). HR-MS (FAB) Calcd for $C_{54}H_{71}O_7Si_2$ (M^++1): 887.4738. Found: 887.4760.

(2*R*,3*E*,5*S*,6*S*,7*S*,8*R*)-1,9-Di-(*tert*-butyldiphenylsilyloxy)-6-hydroxymethyl-7-(3,4-dimethoxybenzylosy)-2,4,8-trimethyl-3-nonen-5-ol (22) a) PPTS (1.00 g, 3.98 mmol) was added to a stirred solution of **19b** (330 mg, 0.33 mmol) in MeOH (5 ml) at room temperature. The reaction mixture was stirred for 2 h at 50 °C, then quenched with saturated aqueous $NaHCO_3$, and extracted with EtOAc. The extract was washed with brine, dried over $MgSO_4$, concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (3 : 1) to give **22** as a colorless oil (205 mg, 70%). $[\alpha]_D^{25}$ +16.1° (c=1.04, $CHCl_3$). IR (neat) cm^{-1}: 3470 (br), 2930, 2858, 1738, 1591, 1516, 1464, 1427, 1389, 1362, 1265, 1240, 1158, 1112, 939, 823, 807, 742, 703. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.89 (3H, d, J=6.7 Hz), 0.96 (3H, d, J=6.7 Hz), 1.06 (9H, s), 1.07 (9H, s), 1.65 (3H, d, J=1.2 Hz), 1.96—2.04 (2H, m), 2.64 (1H, m), 3.34 (1H, dd, J=4.4, 11.8 Hz), 3.46 (1H, dd, J=4.3, 11.8 Hz), 3.48 (2H, d, J=6.4 Hz), 3.59 (1H, dd, J=5.8, 10.1 Hz), 3.63 (1H, dd, J=8.5, 10.1 Hz), 3.82 (3H, s), 3.85 (3H, s), 4.09 (1H, d, J=9.2 Hz), 4.15 (1H, dd, J=2.1, 7.6 Hz), 4.54 (1H, d, J=10.7 Hz), 4.62 (1H, d, J=10.7 Hz), 5.28 (1H, d, J=9.2 Hz), 6.76—6.83 (3H, m), 7.33—7.45 (12H, m), 7.63—7.69 (8H, m). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 10.72, 11.49, 16.98, 19.15, 19.17, 26.85, 26.87, 34.96, 39.00, 46.05, 55.77, 55.82, 61.94, 66.50, 68.83, 74.80, 78.76, 80.03, 110.97, 111.31, 120.54, 127.59, 127.60, 127.63, 129.58, 129.64, 130.52, 131.30, 133.49, 133.59, 133.64, 133.70, 135.54, 135.55, 136.68, 148.68, 148.84. FAB-MS *m/z* (%): 889 (M^++1, 1.8), 871 (7.0), 377 (11), 309 (11), 269 (32), 239 (43), 152 (100), 121 (44). HR-MS (FAB) Calcd for $C_{54}H_{72}O_7Si_2$ (M^+): 888.4816. Found: 888.4821.

b) A solution of **21** (94 mg, 0.10 mmol) in Et_2O (2 ml) was added to a 0.08 M solution of $Zn(BH_4)_2$ in Et_2O (4.0 ml, 0.32 mmol) at 0 °C. After 7 h, saturated aqueous NH_4Cl was added, and the mixture was extracted with Et_2O. The extract was washed with brine, dried over Na_2SO_4, concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (2 : 1) to give **22** as a colorless oil (90 mg, 96%).

(2*R*,3*E*,5*S*,6*S*,7*S*,8*R*)-1,9-Di-(*tert*-butyldiphenylsilyloxy)-5,7-[(*S*)-3,4-dimethoxybenzylidenedioxy]-2,4,8-trimethyl-6-pivaloyloxymethyl-3-nonene (23) Et_3N (23 μl, 165 μmol), 4-dimethylaminopyridine (DMAP) (catalytic amount), and pivaloyl chloride (PivCl) (10 μl, 81.2 μmol) were successively added to a stirred solution of **22** (35.5 mg, 39.9 μmol) in CH_2Cl_2 (1.0 ml) at 0 °C. After 1.5 h, MeOH was added to quench the reaction. The mixture was concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (3 : 1) to give a pivaloate as a colorless oil (34.0 mg, 87.5%).

DDQ (10 mg, 44 μmol) was added to a stirred solution of the pivaloate (34 mg, 34.9 μmol) in CH_2Cl_2 (2 ml) at −10 °C. After being stirred for 1 h at −5 °C, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ and extracted with Et_2O. The extract was washed with brine, dried over Na_2SO_4, concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (5 : 1) to give **23** as a colorless oil (34.0 mg, 100%). ^{1}H-NMR (400 MHz, C_6H_6) δ: 0.90 (3H, d, J=7.0 Hz), 1.05 (3H, d, J=6.5 Hz), 1.14 (9H, s), 1.18 (9H, s), 1.19 (9H, s), 1.70 (3H, d, J=1.0 Hz), 2.08—2.16 (1H, m), 2.16—2.26 (1H, m), 2.65—2.77 (1H, m), 3.36 (3H, s), 3.38 (3H, s), 3.52 (1H, dd, J=7.5, 10.0 Hz), 3.64 (1H, dd, J=6.0, 9.0 Hz), 3.66 (1H, dd, J=6.0, 9.0 Hz), 3.95—4.04 (3H, m), 4.35 (1H, d, J=10.5 Hz), 4.46 (1H, dd, J=2.0, 10.5 Hz), 5.33 (1H, dd, J=1.0, 9.0 Hz), 5.75 (1H, s), 6.62 (1H, d, J=8.0 Hz), 7.16—7.30 (14H, m), 7.74—7.84 (8H, m).

(2*R*,3*E*,5*S*,6*S*,7*S*,8*R*)-5-Acetoxy-6-acetoxymethyl-7-(3,4-dimethoxybenzyloxy)-2,4,8-trimethyl-3-nonene-1,9-diol (24) Et_3N (2.22 ml, 15.9 mmol), DMAP (10 mg, 82 μmol) and Ac_2O (0.75 ml, 7.98 mmol) were added successively to a stirred solution of **22** (709 mg, 797 μmol) in CH_2Cl_2 (10 ml) at 0 °C under argon. After 10.5 h, MeOH was added to quench the reaction. The reaction mixture was diluted with Et_2O, washed with saturated aqueous NH_4Cl and brine, dried over Na_2SO_4, concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (3 : 1), to give a diacetate as a colorless oil (744 mg, 96%). $[\alpha]_D^{21}$ −8.0° (c=1.65, $CHCl_3$). IR (neat) cm^{-1}: 2950, 2875, 1740, 1515, 1260, 1230, 1110, 705. ^{1}H-NMR (500 MHz, C_6D_6) δ: 1.08 (3H, d, J=7.0 Hz), 1.10 (3H, d, J=7.0 Hz), 1.23 (9H, s), 1.24 (9H, s), 1.65 (3H, s), 1.66 (3H, s), 1.71 (3H, s), 2.17—2.28 (1H, m), 2.60—2.80 (2H, m), 3.46 (3H, s), 3.52 (1H , dd, J=8.0, 9.5 Hz), 3.63—3.70 (1H, m), 3.64 (3H, s), 3.76 (1H, dd, J=6.0, 10.0 Hz), 3.84 (1H, dd, J=7.0, 10.0 Hz), 4.07 (1H, t, J=4.5 Hz), 4.19 (1H, dd, J=6.0, 11.0 Hz), 4.27 (1H, dd, J=5.0, 11.0 Hz), 4.62 (1H, d, J=11.0 Hz), 4.76 (1H, d, J=11.0 Hz), 5.49 (1H, d, J=9.5 Hz), 5.72 (1H, d, J=9.0 Hz), 6.60—6.70 (1H, m), 6.90—7.10 (2H, m), 7.20—7.40 (12H, m), 7.75—7.90 (8H, m). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 12.41, 12.96, 17.56, 19.61, 19.67, 21.01, 21.57, 27.23, 27.31, 35.53, 39.23, 42.22, 56.13, 56.62, 63.33, 66.84, 68.24, 73.96, 77.75, 77.88, 111.19, 111.26, 120.06, 128.01, 128.06, 129.95, 130.04, 131.96, 132.39, 132.43, 133.93, 134.05, 134.13, 134.23, 135.87, 135.91, 135.95, 148.67, 149.24, 169.80, 170.83. FAB-MS *m/z* (%): 973 (M^++1, 4.9), 972 (M^+, 4.4), 915 (28), 795 (11), 389 (18), 309 (57), 269 (63), 165 (85), 121 (100). HR-MS (FAB) Calcd for $C_{58}H_{77}O_9Si_2$ (M^++1): 973.5106. Found: 973.5158.

AcOH (262 μl, 4.58 mmol) and a 1.0 M solution of tetra-*n*-butylammonium fluoride (*n*-Bu_4NF) (2.3 ml, 2.3 mmol) in THF were added to a stirred solution of the diacetate (744 mg, 764 μmol) in THF (10 ml) at 0 °C. The solution was stirred for 6 d at room temperature, then diluted with Et_2O, washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with CH_2Cl_2–MeOH (15:1), to give **24** as a colorless oil (380 mg, 100%). $[\alpha]_D^{22}$ −28.0 ° (c=1.08, $CHCl_3$). IR (neat) cm^{-1}: 3500, 2950, 2875, 1735, 1520, 1460, 1370, 1235, 1030, 735. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.89 (3H, d, J=6.5 Hz), 0.91 (3H, d, J=6.5 Hz), 1.65 (3H, s), 1.60—1.80 (2H, br), 1.90—2.05 (1H, m), 2.010 (3H, s), 2.016 (3H, s), 2.47—2.55 (1H, m), 2.55—2.67 (1H, m), 3.26 (1H, dd, J=8.5, 10.5 Hz), 3.40—3.54 (3H, m), 3.80 (1H, t, J=4.0 Hz), 3.86 (3H, s), 3.89 (3H, s), 3.96 (1H, dd, J=6.0, 11.5

Hz), 4.28 (1H, dd, *J*=4.0, 11.5 Hz), 4.44 (1H, d, *J*=11.5 Hz), 4.57 (1H, d, *J*=11.5 Hz), 5.22 (1H, d, *J*=9.5 Hz), 5.30 (1H, d, *J*=9.5 Hz), 6.80—6.95 (3H, m). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 12.41, 12.65, 16.89, 21.20, 21.55, 35.64, 38.28, 41.76, 56.20, 56.27, 62.91, 66.47, 67.88, 73.43, 77.84, 78.35, 111.26, 111.78, 120.63, 131.45, 133.27, 133.79, 149.00, 149.36, 170.30, 171.38. EI-MS *m/z* (%): 496 (M^+, 3.2), 211 (6.4), 166 (13), 151 (100), 107 (12), 99 (13). HR-MS Calcd for $C_{26}H_{40}O_9$ (M^+): 496.2673. Found: 496.2668.

(2*R*,3*E*,5*S*,6*S*,7*S*,8*R*)-5-Acetoxy-6-acetoxymethyl-7,9-[(*S*)-3,4-dimethoxybenzylidenedioxy)-2,4,8-trimethyl-3-nonenal (25) DDQ (220 mg, 969 μmol) was added to a stirred solution of **24** (380 mg, 764 μmol) in CH_2Cl_2 (14 ml) at −10 °C under argon. After 35 min, saturated aqueous $NaHCO_3$ was added to quench the reaction, and the reaction mixture was extracted with Et_2O. The extract was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (1 : 3), to give a 3,4-dimethoxybenzylidene acetal as a colorless oil (353 mg, 93%). $[\alpha]_D^{22}$ +18.1° (*c*=1.25, $CHCl_3$). IR (neat) cm^{-1}: 3500, 2975, 2875, 1740, 1520, 1260, 1240, 1030, 735. ^{1}H-NMR (500 MHz, C_6D_6) δ: 0.83 (3H, d, *J*=6.5 Hz), 1.31 (3H, d, *J*=7.0 Hz), 1.28—1.38 (1H, m), 1.53 (3H, s), 1.70 (3H, s), 1.75 (3H, s), 1.80—1.95 (1H, br), 2.35—2.44 (1H, m), 2.48—2.60 (1H, m), 3.23 (1H, dd, *J*=8.0, 10.5 Hz), 3.37—3.43 (1H, m), 3.40 (3H, s) 3.56 (3H, s), 3.75—3.87 (2H, m), 3.99 (1H, dd, *J*=3.5, 12.0 Hz), 4.19 (1H, dd, *J*=1.5, 10.0 Hz), 4.23 (1H, dd, *J*=3.5, 12.0 Hz), 5.39 (1H, d, *J*=9.5 Hz), 5.51 (1H, s), 6.00 (1H, d, *J*=7.5 Hz), 6.64 (1H, d, *J*=8.0 Hz), 7.20—7.40 (2H, m). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 11.83, 13.07, 16.84, 21.16, 21.48, 30.67, 35.47, 41.57, 56.18, 56.27, 61.76, 67.92, 74.15, 78.36, 80.17, 102.85, 109.73, 110.97, 119.37, 131.71, 132.99, 133.29, 149.10, 149.78, 170.47, 171.51. EI-MS *m/z* (%): 494 (M^+, 18), 322 (8.6), 237 (56), 182 (15), 166 (91), 151 (81), 43 (100). HR-MS Calcd for $C_{26}H_{38}O_9$ (M^+): 494.2516. Found: 494.2491.

A solution of the above acetal (353 mg, 714 μmol) in CH_2Cl_2 (5 ml) was added to a stirred solution of the Dess-Martin periodinane (606 mg, 1.43 mmol) and pyridine (0.29 ml, 3.59 mmol) in CH_2Cl_2 (10 ml) at room temperature. After 30 min, saturated aqueous $NaHCO_3$ and saturated aqueous $Na_2S_2O_3$ were added to quench the reaction, and the reaction mixture was extracted with Et_2O. The extract was washed with brine, dried over Na_2SO_4, concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (2 : 3), to give **25** as a pale yellow oil (352 mg, 100%). IR (neat) cm^{-1}: 2975, 2950, 2850, 1740, 1525, 1465, 1370, 1240, 1165, 1030, 735. ^{1}H-NMR (500 MHz, C_6D_6) δ: 0.88 (3H, d, *J*=7.0 Hz), 0.97 (3H, d, *J*=6.5 Hz), 1.25—1.35 (1H, m), 1.54 (3H, s), 1.58 (3H, s), 1.77 (3H, s), 2.40—2.50 (1H, m), 2.80—2.90 (1H, m), 3.40 (3H, s), 3.57 (3H, s), 3.75—3.85 (2H, m), 4.04 (1H, dd, *J*=4.5, 12.0 Hz), 4.08 (1H, dd, *J*=2.0, 10.0 Hz), 4.17 (1H, dd, *J*=4.0, 12.0 Hz), 5.42 (1H, d, *J*=9.0 Hz), 5.50 (1H, s), 6.02 (1H, d, *J*=6.5 Hz), 6.64 (1H, d, *J*=8.0 Hz), 7.25—7.35 (2H, m), 9.26 (1H, d, *J*=1.0 Hz).

(2*Z*,4*S*,5*E*,7*S*,8*S*,9*S*,10*R*)-9,11-[(*S*)-3,4-Dimethoxybenzylidenedioxy]-8-hydroxymethyl-4,6,10-trimethyl-2,5-undecadien-7-ol (26) A 1.0 M solution of *tert*-BuOK in THF (3.2 ml, 3.2 mmol) was added dropwise to a suspension of ethyltriphenylphosphonium bromide (1.33 g, 3.58 mmol) in THF (15 ml) at 0 °C under argon. After 1 h, the reaction mixture was cooled to −78 °C, and a solution of **25** (352 mg, 714 μmol) in THF (5 ml) was added dropwise. The reaction mixture was allowed to warm to room temperature, and the stirring was continued for 38 h. The reaction was quenched with saturated aqueous NH_4Cl, and the reaction mixture was extracted with Et_2O. The extract was washed with saturated aqueous NH_4Cl and brine, dried over Na_2SO_4, and concentrated *in vacuo*, to leave a crude oil of (2*Z*,4*S*,5*E*,7*S*,8*S*,9*S*,10*R*)-7-acetoxy-8-acetoxymethyl-9,11-[(*S*)-3,4-dimethoxybenzylidenedioxy]-4,6,10-trimethyl-2,5-undecadiene (1.1 g), a part of which was purified by chromatography on a silica gel column, eluting with *n*-hexane–EtOAc (1 : 1). ^{1}H-NMR (500 MHz, C_6D_6) δ: 1.01 (3H, d, *J*=7.0 Hz), 1.23 (3H, d, *J*=6.5 Hz), 1.25—1.35 (1H, m), 1.57 (3H, s), 1.59 (3H, dd, *J*=1.5, 7.0 Hz), 1.69 (3H, d, *J*=1.0 Hz), 1.74 (3H, s), 2.40—2.50 (1H, m), 3.33—3.45 (1H, m), 3.40 (3H, s), 3.57 (3H, s), 3.79 (1H, dd, *J*=2.0, 11.0 Hz), 3.83 (1H, dd, *J*=1.0, 11.0 Hz), 4.02 (1H, dd, *J*=4.0, 12.0 Hz), 4.10 (1H, dd, *J*=1.0, 10.0 Hz), 4.19 (1H, dd, *J*=3.5, 12.0 Hz), 5.29 (1H, ddd, *J*=1.5, 9.0, 10.5 Hz), 5.40 (1H, dq, *J*=10.5, 7.0 Hz), 5.50 (1H, s), 5.56 (1H, dd, *J*=1.0, 9.0 Hz), 6.06 (1H, d, *J*=7.0 Hz), 6.63 (1H, d, *J*=8.0 Hz), 7.25—7.40 (2H, m).

A solution of crude diacetate (1.1 g) in ether (10 ml) was added dropwise to a stirred suspension of $LiAlH_4$ (68 mg, 1.79 mmol) in Et_2O (2 ml) at 0 °C under argon. After 3 h, MeOH was added to quench the reaction. After the reaction mixture was diluted with Et_2O, H_2O (70 μl), 15% NaOH (70 μl) and H_2O (210 μl) were added successively with vigorous stirring, and then insoluble materials were removed by filtration through a Celite pad and washed with Et_2O. The filtrate was concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (1 : 1), to give **26** as a colorless oil (221 mg, 74%). $[\alpha]_D^{19}$ +97.7° (*c*=1.10, $CHCl_3$). IR (neat) cm^{-1}: 3450, 2950, 2850, 1610, 1595, 1520, 1460, 1260, 1235, 1160, 1030, 860, 810, 730. ^{1}H-NMR (500 MHz, C_6D_6) δ: 1.08 (3H, d, *J*=6.5 Hz), 1.22 (3H, d, *J*=7.0 Hz), 1.50—1.60 (1H, m), 1.60 (3H, d, *J*=6.0 Hz), 1.82 (3H, s), 2.03—2.13 (1H, m), 2.50—2.70 (1H, br), 3.43 (3H, s), 3.40—3.60 (3H, m), 3.53 (3H, s), 3.84 (2H, s), 4.28 (1H, d, *J*=10.0 Hz), 4.40—4.50 (1H, br), 4.69 (1H, d, *J*=7.5 Hz), 5.30—5.45 (2H, m), 5.50 (1H, s), 5.51 (1H, d, *J*=8.5 Hz), 6.64 (1H, d, *J*=8.0 Hz), 7.20—7.30 (2H, m). ^{13}C-NMR (125 MHz, C_6D_6) δ: 11.62, 12.13, 13.07, 21.43, 30.52, 30.70, 45.23, 55.54, 55.61, 59.99, 73.90, 79.82, 82.02, 102.36, 110.38, 111.82, 118.91, 122.07, 128.29, 131.87, 132.59, 135.62, 149.89, 150.47. EI-MS *m/z* (%): 420 (M^+, 2.0), 402 (1.9), 333 (1.6), 212 (4.0), 185 (23), 166 (100), 151 (24), 97 (50). HR-MS Calcd for $C_{24}H_{36}O_6$ (M^+): 420.2512. Found: 420.2530.

(2*Z*,4*S*,5*E*,7*S*,8*S*,9*S*,10*R*)-8-(*tert*-Butyldimethylsilyloxymethyl)-9,11-[(S)-3,4-dimethoxybenzylidenedioxy]-7-methoxymethoxy-4,6,10-trimethyl-2,5-undecadiene (27) Imidazole (82 mg, 1.20 mmol) and TBSCl (103 mg, 683 μmol) were added to a stirred solution of **26** (221 mg, 525 μmol) in CH_2Cl_2 (5 ml) at room temperature under argon. The solution was stirred for 3 d, then MeOH and saturated aqueous NH_4Cl were added to quench the reaction, and the reaction mixture was extracted with Et_2O. The extract was washed with saturated aqueous NH_4Cl and brine, dried over Na_2SO_4, concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (7 : 2), to give (2*Z*,4*S*,5*E*,7*S*,8*S*,9*S*,10*R*)-8-(*tert*-butyldimethylsilyloxymethyl)-9,11-[(*S*)-3,4-dimethoxybenzylidenedioxy]-4,6,10-trimethyl-2,5-undecadien-7-ol as a colorless oil (241 mg, 86%). $[\alpha]_D^{22}$ +72° (*c*=0.96, $CHCl_3$). IR (neat) cm^{-1}: 3500, 2950, 2850, 1520, 1460, 1260, 1165, 1030, 835. ^{1}H-NMR (500 MHz, C_6D_6) δ: 0.02 (3H, s), 0.08 (3H, s), 1.01 (9H, s), 1.11 (3H, d, *J*=6.5 Hz), 1.29 (3H, d, *J*=7.0 Hz), 1.62 (3H, d, *J*=5.0 Hz), 1.68—1.75 (1H, m), 1.84 (3H, s), 2.00—2.10 (1H, m), 3.37 (3H, s), 3.47 (2H, d, *J*=3.0 Hz), 3.49 (3H, s), 3.45—3.55 (1H, m), 3.88 (1H, dd, *J*=1.0, 10.5 Hz), 3.92 (1H, dd, *J*=1.5, 10.5 Hz), 4.46 (1H, dd, *J*=1.0, 9.5 Hz), 4.56 (1H, s), 4.76 (1H, d, *J*=8.5 Hz), 5.37—5.47 (2H, m), 5.51 (1H, s), 5.54 (1H, d, *J*=9.0 Hz), 6.58 (1H, d, *J*=8.0 Hz), 7.20—7.30 (2H, m). ^{13}C-NMR (125 MHz, C_6D_6) δ: −5.31, −4.83, 12.10, 12.28, 13.54, 18.78, 22.15, 26.38, 26.50, 31.30, 31.38, 44.84, 55.92, 55.97, 61.19, 74.37, 80.76, 84.09, 103.02, 110.67, 112.28, 119.24, 122.08, 128.80, 132.09, 133.55, 135.36, 136.50, 150.55, 151.09. EI-MS *m/z* (%): 534 (M^+, 2.5), 299 (5.5), 223 (16), 166 (76), 151 (53), 137 (32), 121 (22), 75 (100). HR-MS Calcd for $C_{30}H_{50}O_6Si$ (M^+): 534.3376. Found: 534.3392.

Iso-Pr_2EtN (1.57 ml, 9.0 mmol) and chloromethyl methyl ether (MOMCl) (355 μl, 4.5 mmol) were added to a stirred solution of the above alcohol (273 mg, 510 μmol) in CH_2Cl_2 (2 ml) at room temperature under argon. The solution was stirred for 7 d, and then the reaction was quenched with NaOH. The reaction mixture was diluted with Et_2O, washed with saturated aqueous NH_4Cl and brine, dried over Na_2SO_4, concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (3 : 1), to give **27** as a colorless oil (296 mg, 100%). $[\alpha]_D^{23}$ +20.6° (*c*=1.07, $CHCl_3$). IR (neat) cm^{-1}: 2950, 2850, 1520, 1460, 1265, 1165, 1100, 1030, 840. ^{1}H-NMR (500 MHz, C_6D_6) δ: 0.13 (3H, s), 0.14 (3H, s), 1.02 (9H, s), 1.05 (3H, d, *J*=7.0 Hz), 1.50 (3H, d, *J*=7.0 Hz), 1.64 (3H, d, *J*=5.0 Hz), 1.75 (3H, d, *J*=1.0 Hz), 1.80—1.90 (1H, m), 2.50—2.58 (1H, m), 3.16 (3H, s), 3.42 (3H, s), 3.45—3.53 (1H, m), 3.56 (3H, s), 3.78 (1H, dd, *J*=5.5, 10.5 Hz), 3.90—4.00 (2H, m), 4.00 (1H, dd, *J*=1.5, 10.0 Hz), 4.07 (1H, dd, *J*=3.5, 10.5 Hz), 4.53 (1H, d, *J*=6.5 Hz), 4.67 (1H, d, *J*=6.5 Hz), 4.76 (1H, d, *J*=5.0 Hz), 5.35—5.45 (2H, m), 5.59 (1H, d, *J*=9.0 Hz), 5.62 (1H, s), 6.68 (1H, d, *J*=8.0 Hz), 7.35—7.45 (2H, m). ^{13}C-NMR (125 MHz, C_6D_6) δ: −4.97, −4.88, 13.11, 13.55, 13.71, 18.90, 22.07, 26.65, 31.39, 31.94, 48.34, 55.93, 56.03, 56.07, 60.76, 74.79, 79.76, 80.96, 95.04, 103.00, 111.42, 112.37, 119.63, 122.62, 131.39, 133.33, 135.14, 136.31, 150.52, 150.95. EI-MS *m/z* (%): 578 (M^+, 1.2), 533 (0.9), 367 (2.5), 237 (6.3), 183 (25), 166 (33), 151 (56), 89 (37), 45 (100). HR-MS Calcd for $C_{32}H_{54}O_7Si$ (M^+): 578.3641. Found: 578.3644.

(2*S*,3*S*,4*S*,5*S*,6*E*,8*S*,9*Z*)-4-(*tert*-Butyldimethylsilyloxymethyl)-3-(3,4-dimethoxybenzyloxy)-5-methoxymethoxy-2,6,8-trimethyl-6,9-undecadienal (8) A solution of **27** (145 mg, 250 μmol) in CH_2Cl_2 (2 ml) was added dropwise to a stirred 0.93 M solution of DIBAH in *n*-hexane (1.0 ml, 0.93 mmol) diluted with CH_2Cl_2 (1 ml) at −50 °C under argon. The solution was stirred for 13.5 h, and then MeOH was added to quench the reaction. The reaction mixture was diluted with Et_2O, mixed with saturated aqueous potassium sodium tartrate, and stirred vigorously for 1 h. The separated organic layer was washed with brine, dried over Na_2SO_4, concentrated *in vacuo*, and

chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (3 : 1), to give the recovered starting material (16 mg, 11%) and (2*R*,3*S*,4*S*,5*S*,6*E*,8*S*,9*Z*)-4-(*tert*-butyldimethylsilyloxymethyl)-3-(3,4-dimethoxybenzyloxy)-5-methoxymethoxy-2,6,8-trimethyl-6,9-undecadien-1-ol as a colorless oil (102 mg, 70%). $[\alpha]_D^{20}$ +16° (c=0.57, $CHCl_3$). IR (neat) cm^{-1}: 3450, 2925, 2850, 1510, 1460, 1255, 1025. ^{1}H-NMR (500 MHz, C_6D_6) δ: 0.13 (3H, s), 0.16 (3H, s), 1.02 (3H, d, J=7.0 Hz), 1.04 (9H, s), 1.20 (3H, d, J=7.0 Hz), 1.61 (3H, dd, J=1.5, 6.5 Hz), 1.70 (3H, s), 2.35 (1H, br), 2.50—2.65 (2H, m), 3.30 (3H, s), 3.38—3.48 (1H, m), 3.44 (3H, s), 3.61 (3H, s), 3.62 (1H, dd, J=5.5, 10.0 Hz), 3.66 (1H, dd, J=8.0, 10.0 Hz), 3.74 (1H, dd, J=6.0, 10.0 Hz), 3.84 (1H, dd, J=3.0, 10.0 Hz), 4.12 (1H, dd, J=2.0, 7.0 Hz), 4.47 (1H, d, J=9.5 Hz), 4.49 (1H, d, J=6.5 Hz), 4.68 (1H, d, J=6.5 Hz), 4.72 (1H, d, J=11.0 Hz), 4.78 (1H, d, J=11.0 Hz), 5.28 (1H, ddd, J=1.5, 9.5, 10.5 Hz), 5.30—5.45 (2H, m), 6.67 (1H, d, J=8.0 Hz), 6.95—7.10 (2H, m). ^{13}C-NMR (125 MHz, C_6D_6) δ: −4.81, −4.73, 12.11, 13.55, 15.49, 18.95, 21.95, 26.69, 30.66, 31.33, 40.37, 45.61, 56.15, 56.65, 62.69, 66.99, 75.04, 81.07, 81.15, 94.20, 112.75, 120.61, 122.44, 128.79, 131.74, 133.46, 135.76, 135.96, 150.77, 151.15. EI-MS (*m/z*, %): 580 (M^+, 1.9), 373 (2.2), 226 (5.2), 211 (22), 151 (100), 89 (8.6), 69 (12). HR-MS Calcd for $C_{32}H_{56}O_7Si$ (M^+): 580.3796. Found: 580.3768.

A solution of the above primary alcohol (49 mg, 84 μmol) in CH_2Cl_2 (1 ml) was added dropwise to a stirred solution of the Dess-Martin periodinane (72 mg, 169 μmol) and pyridine (69 μl, 853 μmol) in CH_2Cl_2 (2 ml) at room temperature. The solution was stirred for 19 h, then saturated aqueous $NaHCO_3$ and saturated aqueous $Na_2S_2O_3$ were added to quench the reaction, and the reaction mixture was extracted with Et_2O. The extract was washed with brine, dried over Na_2SO_4, concentrated *in vacuo*, and chromatographed on a silica gel column, eluting with *n*-hexane–EtOAc (2 : 1), to give **8** as a pale yellow oil (49 mg, 100%). IR (neat) cm^{-1}: 2950, 1725, 1520, 1465, 1260, 1155, 1085, 1030, 840. ^{1}H-NMR (500 MHz, C_6D_6) δ: 0.12 (3H, s), 0.13 (3H, s), 1.01 (3H, d, J=6.5 Hz), 1.03 (9H, s), 1.30 (3H, d, J=7.0 Hz), 1.60 (3H, dd, J=1.5, 7.0 Hz), 1.63 (3H, s), 2.35—2.50 (1H, m), 3.15—3.25 (1H, m), 3.27 (3H, s), 3.43 (3H, s), 3.35—3.50 (1H, m), 3.59 (3H, s), 3.72 (2H, d, J=6.5 Hz), 4.40 (1H, d, J=8.5 Hz), 4.45 (1H, d, J=6.0 Hz), 4.46 (1H, d, J=6.0 Hz), 4.58 (1H, d, J=11.0 Hz), 4.65 (1H, d, J=4.0 Hz), 4.66 (1H, d, J=11.0 Hz), 5.26 (1H, ddd, J=1.5, 9.0, 10.5 Hz), 5.33 (1H, d, J=9.0 Hz), 5.35—5.45 (1H, m), 6.65 (1H, d, J=8.0 Hz), 6.90—7.00 (2H, m), 9.85 (1H, s). FAB-MS *m/z* (%): 579 (M^++1, 5.1), 578 (M^+, 4.6), 349 (13), 253 (23), 211 (42), 165 (37), 152 (100), 137 (53), 115 (30), 89 (68). HR-MS Calcd for $C_{32}H_{54}O_7Si$ (M^+): 578.3639. Found: 578.3642.

References and Notes

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