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Facile Total Synthesis of Carbonolides by Wittig–Horner Macro-Cyclization and Stereoselective Epoxidation[1]

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Sixteen-membered dienone type macrolide aglycons, carbonolide B (1), niddanolide (5), and platenolide W_1 (6), were synthesized highly stereoselectively from D-glucose *via* Yamaguchi's esterification of two fragments, 8 (C1—C10) and 9 (C11—C16), followed by Wittig–Horner cyclization. Stereoselective epoxidation of the 16-membered dienones (34, 35) gave epoxy-enone-type macrolide aglycons, carbonolide A (2) and EOP aglycon (7).

Keywords macrolide aglycon; carbonolide; total synthesis; Yamaguchi's esterification; Wittig–Horner cyclization; stereoselective epoxidation; conformation; NOE

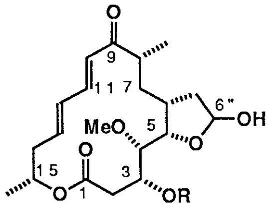
Carbonolide B (**1**) and A (**2**), leuconolide A_3 (**3**), and maridonolide II (**4**) are four representative 16-membered aglycones, differing in oxidation levels, in the largest group of macrolide antibiotics.[2] For the synthesis of these aglycons (**1**—**4**), it seems reasonable to synthesize **1** first, and then to convert **1** to **2**—**4** by stereoselective epoxidation and reduction, because a facile common methodology for the synthesis of enone and dienone type aglycons has been established through the stereoselective synthesis of 12-membered methynolide,[3] 14-membered pikronolide,[4] and 16-membered tylonolide[5] by virtue of some stereoselective reactions, MPM (4-methoxybenzyl) protection,[6] and Wittig–Horner cyclization.[3—5,7] We report here the synthesis of carbonolide B (**1**),[8] niddanolide (**5**)[9] and platenolide W_1 (**6**),[10] and their stereoselective epoxidation to carbonolide A (**2**)[11] and its homolog, EOP aglycon (**7**).[12,13]

Results and Discussion

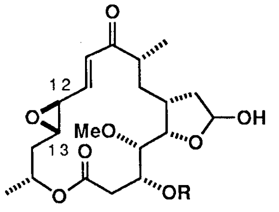
Synthesis of Niddanolide (5), Carbonolide B (1) and Platenolide W_1 (6) According to the established methodology,[3—5] our retro-synthesis can be depicted as shown in Chart 1; the esterification between two stereoselectively synthesized fragments, **8** and **9**, and subsequent Wittig–Horner cyclization are the most important steps.

The small C11—C16 fragment (**9**)[14] has only one chiral center and was easily synthesized from L(−)-malic acid *via* the known allylic alcohol (**11**).[15] The primary alcohol of **11** was first protected with an MPM group,[6] and the ketal group was removed to give the diol, whose primary alcohol was selectively tosylated and then reduced to give **12**. Deprotection of the MPM group with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ),[6] followed by oxidation with manganese dioxide gave **9**.

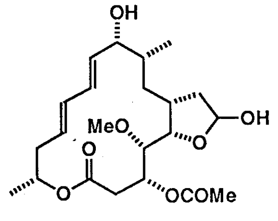
The large C1—C10 fragment (**8**) is quite similar to the C1—C10 fragment used in the synthesis of tylonolide,[5] the only difference being in the C4-substituent, and hence the methodology employed in the synthesis of tylonolide was directly applicable to the synthesis of **8**. The alcohol (**13**),[5b]



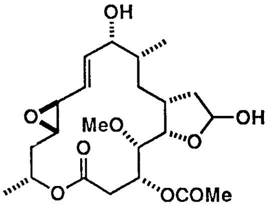
5: R=H niddanolide
1: R=COMe carbonolide B
6: R=COEt platenolide W_1



2: R=COMe carbonolide A
7: R=COEt EOP aglycon

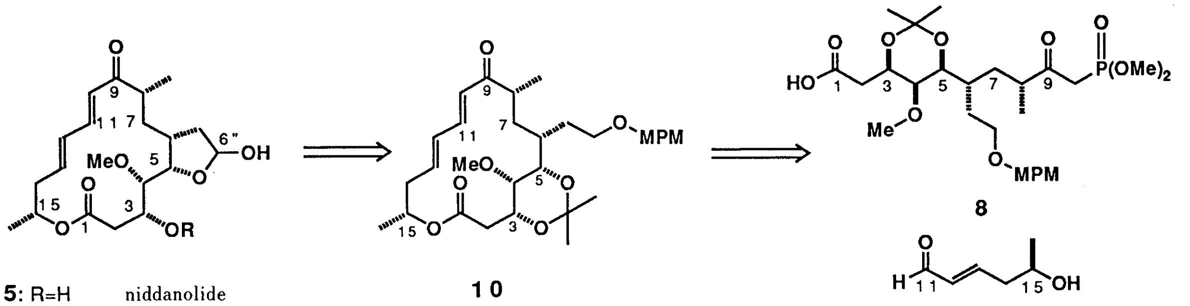


3: leuconolide A_3
(josanolide)



4: maridonolide II

Fig. 1



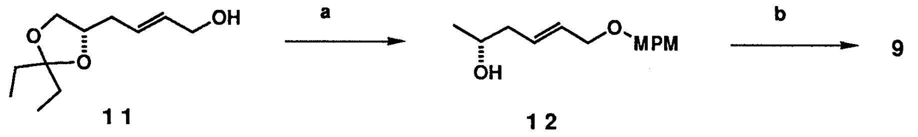
5: R=H niddanolide
1: R=COMe carbonolide B
6: R=COEt platenolide W_1

10

8

9

Chart 1



(a) 1) MPMCl, NaH, DMSO-THF (4:3) (94%); 2) 1% H_2SO_4-MeOH; TsCl, Py., CH_2Cl_2 (2 steps 70%). 3) $LiAlH_4$, ether, (92%); (b) 1) DDQ, CH_2Cl_2-H_2O; 2) MnO_2, CH_2Cl_2 (2 steps, 86%).

Chart 2

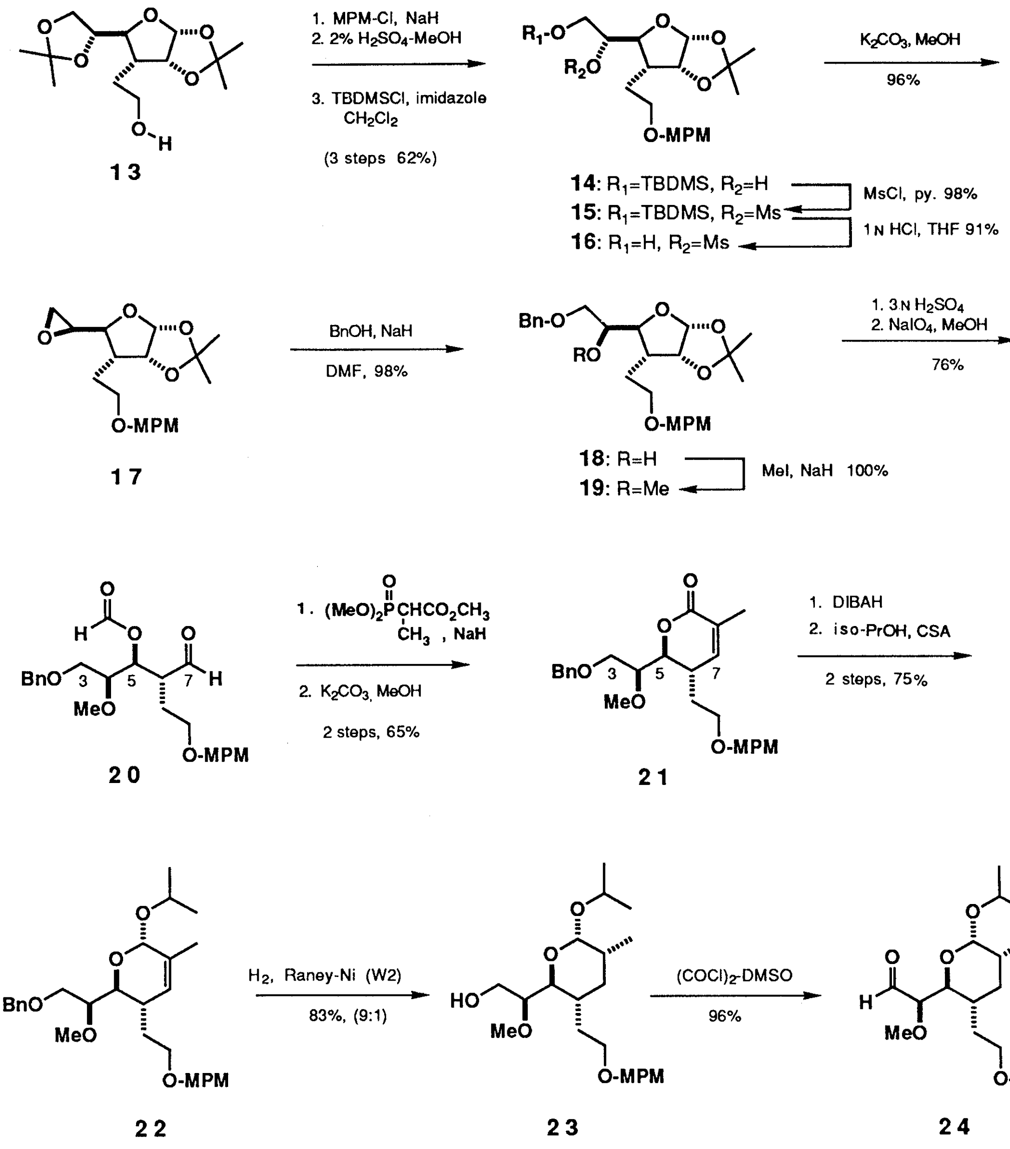


Chart 3

easily available from D-glucose, was selected as a suitable starting material, although inversion at the C5-position[16)] was required. The MPM protection of **13** and then hydrolysis of the ketal group gave the diol, whose primary alcohol was protected with a *tert*-butyldimethylsilyl (TBDMS) group to give **14**. Mesylation of the remaining secondary alcohol to **15** and subsequent removal of the TBDMS protection gave **16**, which was readily converted to the epoxide (**17**). The epoxide ring was opened with sodium benzyl alcoholate, and the resulting alcohol (**18**) was converted to the desired methoxy compound (**19**), which has three consecutive chiral centers corresponding to the C4—C6 portion of **1**—**7**.

The fourth chiral center at C8 was introduced by hydrogenation of the unsaturated lactolide (**22**) as follows. After removal of the isopropylidene group of **19** with 3 N sulfuric acid in dioxane, the resulting diol was cleaved with sodium periodate to obtain the aldehyde (**20**), which was treated with the sodium salt of trimethyl 1-phosphonopropionate at −90 °C and then potassium carbonate in methanol to yield the α,β-unsaturated lactone (**21**). Reduction of **21** with diisobutylaluminum hydride (DIBAH) followed by treatment with isopropanol in the presence of camphorsulfonic acid (CSA) gave the anomerically pure α-lactolide (**22**) in good yield. Finally selective removal of the benzyl protection[6d] and reduction of the double bond were accomplished by catalytic hydrogenation in the presence of Raney nickel (W_2) to give **23** with 9.0 : 1 selectivity at C8.[17] The Swern oxidation of **23** readily gave the aldehyde (**24**).

The final chiral center at C3 was constructed by a chelation-controlled addition of allylmetal compounds to the α-alkoxyaldehyde (**24**). When **24** was treated with allyltrimethylsilane in the presence of titanium tetrachloride,[18] the expected product (**25**) was obtained with high stereoselectivity (60 : 1), but the yield was only 22% because of unavoidable loss of the MPM group. The Grignard reaction with allymagnesium bromide at −90 °C also proceeded smoothly to give **25**, but the 3,4-*syn* selectivity was unsatisfactory (4 : 1). An excellent result, however, was obtained under Yamamoto's conditions.[19] When **24** was treated with allyltributyltin in the presence of magnesium bromide at −60 °C, the chelation-controlled addition took place almost completely stereoselectively to give **25** with 76 : 1 selectivity. The structure of **25** was confirmed after conversion to **27**. The acetal of **25** was hydrolyzed with 1 N hydrochloric acid in tetrahydrofuran (THF), and the resulting hemiacetal was reduced with calcium borohydride to give the open-chain triol (**26**). The 1,3-diol group of **26** was protected as an acetonide by treatment with 2,2-dimethoxypropane in the presence of CSA to give **27**. In the nuclear magnetic resonance (NMR) spectrum of **27**, nuclear Overhauser enhancement (NOE) of H_a and H_b from the axial methyl of isopropylidene group was observed to be 12.4 and 8.3%, respectively. Thus, the introduction of all the chiral centers required for the C1—C10 fragment (**8**) was completed.

Compound **27** was finally converted to the C1—C10 fragment (**8**) in essentially the same way as described for the synthesis of tylonolide.[5] Oxidation of the primary alcohol of **27** under Swern's conditions readily gave the aldehyde (**28**), which was treated with the lithio derivative of dimethyl methylphosphonate at −80 °C and then oxidized with pyridinium dichromate (PDC) in *N*,*N*-dimethylformamide (DMF) to give the ketophosphonate (**29**). Finally oxidation of the terminal olefin of **29** under Lemieux–von Rudloff's conditions[20] gave the carboxylic acid (C1—C10 fragment, **8**) in good yield.

Coupling between the C1—C10 (**8**) and C11—C16 (**9**) fragments proceeded smoothly under the conditions of Yamaguchi's esterification method,[21] and the resulting ester (**30**) was subjected to the Wittig–Horner cyclization under Aristoff–Nicolaou's conditions.[7] When **30** was heated with powdered potassium carbonate and 18-crown-6 in toluene at 80 °C, the cyclization was completed within 3 h to give the expected 16-membered dienone (**10**), but in modest yield (30—40%), probably because β-elimination at C2—C3 occurred concomitantly. The yield of **10** was improved to 57% by carrying out the cyclization at room temperature for a longer reaction time (15—20 h).

Removal of the MPM group by DDQ oxidation[6] proceeded smoothly and gave the primary alcohol (**31**), which was oxidized under Swern's conditions to give the aldehyde (**32**). The remaining isopropylidene group was

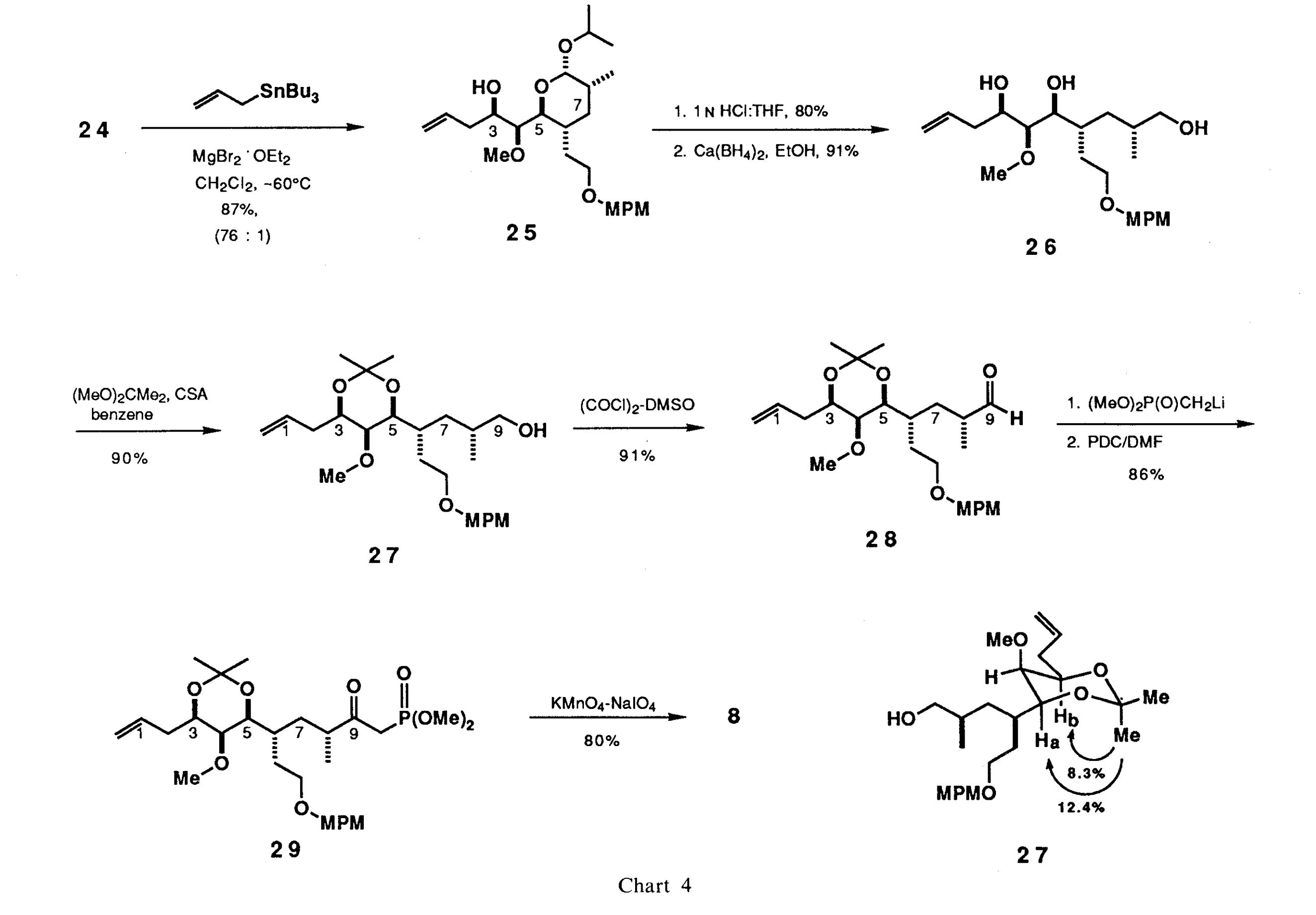
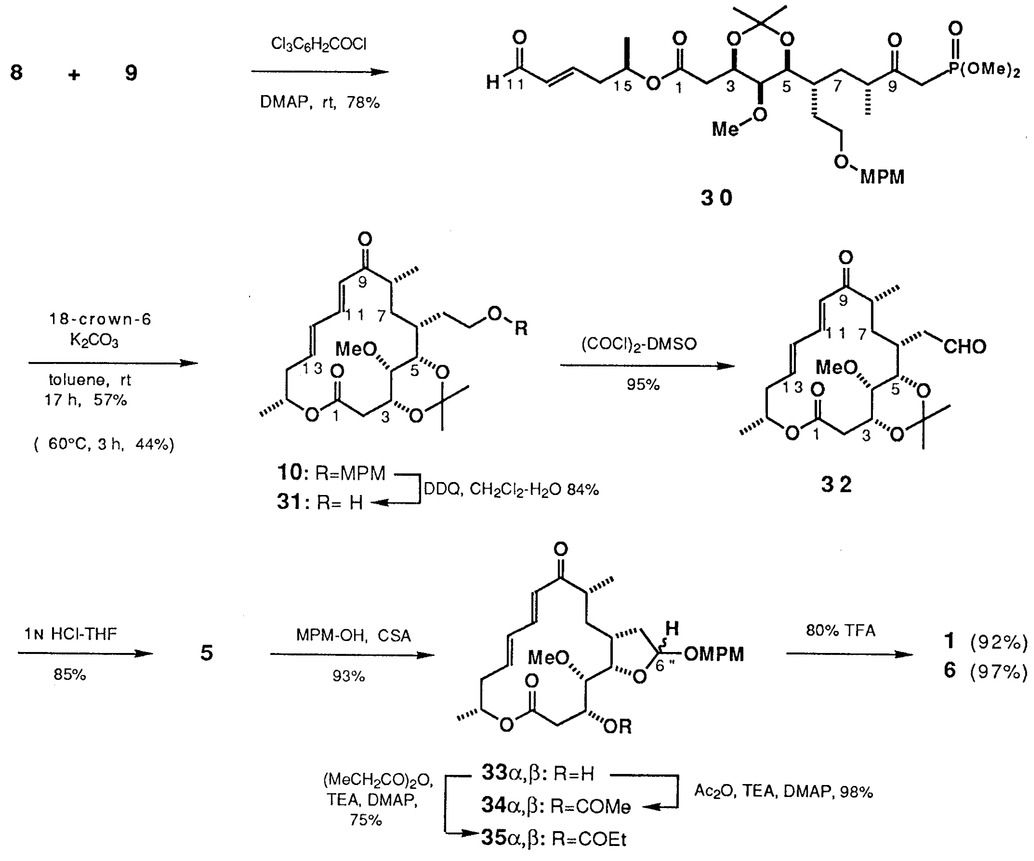


Chart 4



6"-diastereomer: 6'αH=β and 6"βH=α

Chart 5

Table I. The Matrix of ^{1}H-NOE Obtained for **33** in $CDCl_3$

NOE observed (%)

Signal irradiated

^{1}H \ ^{1}H	2a	2b	3	4	5	6	7a	7b	8	8Me	10	11	12	13	14a	14b	15
2a		38															
2b	NOE			NOE													
3				5.5	3.5	3.2	4.3						2.7	1.9		2.4	
4		4.9	5.9		2.7		5.4										
5				2.2													
6			3.2		8.1				4.9								
7a			3.2	8.6						4.4		8.1					
7b																	
8				1.6		8.1				2.7		1.6					
8Me							4.3		3.8			1.9					
10				4.3			3.2			0.9			10.8				
11														10.8			2.2
12											7.0						3.8
13											1.9	11.9					NOESY
14a														3.5		32	7.0
14b													NOE		NOE		
15														NOESY			

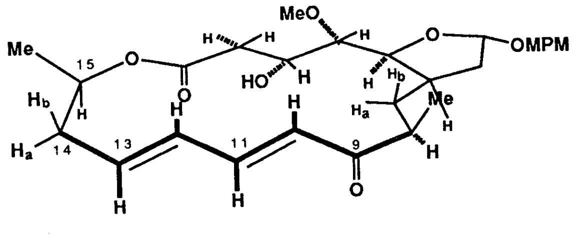
immediately removed with 1 N hydrochloric acid in THF to give niddanolide (5).[9,22] Treatment of **5** with 4-methoxybenzyl alcohol (MPMOH) in the presence of CSA gave the 4-methoxybenzyl furanoside (**33**) as a mixture of 6″-epimers (**33**α, **33**β). Acetylation of the C3 secondary alcohol followed by removal of the MPM protecting group with trifluoroacetic acid gave carbonolide B (**1**)[22] in excellent yield. Platenolide W$_1$ (**6**) was similarly obtained by *O*-propionylation of **33**.[22]

Synthesis of Carbonolide A (2) and EOP Aglycon (7) Double bonds in macro-ring compounds tend to be situated perpendicular to the plane of the rings in order to minimize transannular interactions. The two faces of a double bond are effectively differentiated and a reagent usually attacks at the less hindered peripheral face. Accordingly, formation of a stereoselective product is expected,[23] although it is quite difficult to predict which face of the double bond is peripheral.

For the synthesis of **2** and **7** from carbonolide B type compounds (such as **10**, **33**—**35**) by regio- and stereoselective epoxidation of the C12–C13 double bond,[24,25] it was essential to know the 16-membered ring conformations.

In order to analyze the conformation of **33**, all the proton signals in its 500 MHz ^{1}H-NMR spectrum were first assigned with the aid of two dimensional proton correlated spectroscopy (2D ^{1}H-COSY) experiments, and then NOE and NOE correlation spectroscopy (NOESY) spectra were taken.[26] From the results summarized in Table I, we concluded that the most probable conformation of **33** is as shown in Fig. 2, in which the C12–C13 double bond fortunately lies favorably for the selective epoxidation.[27] This conformation was confirmed by a single-crystal X-ray analysis of **34** (Fig. 3) which revealed that the conformation in the solid state is almost the same as that in solution.

When **34** and **35** were treated with *m*-chloroperbenzoic acid (MCPBA) in the presence of sodium hydrogen carbonate at room temperature, the expected epoxides, **36** and **37**, were obtained with complete stereoselectivity in 90 and 73% yields, respectively. The MPM protecting groups of **36** and **37** were removed by DDQ oxidation[6] to readily give carbonolide A (**2**) and EOP aglycon (**7**).[28]



33

Fig. 2

Experimental

All melting points were measured with a Yanaco hot-stage micro melting point apparatus and are uncorrected. Optical rotations were measured with a JASCO DIP-4 digital polarimeter. Infrared (IR) spectra were recorded in CHCl$_3$ or neat on a JASCO IRA-2 spectrometer. ^{1}H-NMR spectra were recorded in CDCl$_3$ on a JEOL FX-100, JEOL JMX GX-270, or JEOL JMS GX-500 instrument. Low- and high-resolution mass spectra (MS) were taken on a JEOL JMS HX-110 or JEOL JMS DX-303 spectrometer. Ultraviolet (UV) spectra were obtained on a Varian Cary 219 spectrophotometer using ethanol as a solvent.

6-(4-Methoxybenzyloxy)hex-4(*E*)-en-2(*R*)-ol (12) A solution of **11** (5.40 g, 18 mmol) in THF (20 ml) was added dropwise to a stirred suspension of NaH (1.0 g, 25 mmol: 60% oil suspension) in dimethyl sulfoxide (DMSO)–THF (4 : 3) solution (140 ml) under an argon atmosphere at room temperature. After 1 h, MPM chloride (3.9 g, 25 mmol) was added, and stirring was continued for 10 h. The reaction mixture was poured into cold aqueous NH$_4$Cl solution, and extracted with CH$_2$Cl$_2$. The extract was washed with brine, dried over anhydrous MgSO$_4$, and evaporated *in vacuo* to leave an oil, which was chromatographed on a silica gel column using EtOAc–hexane (1 : 5) as the eluant to give the MPM ether as a colorless oil (5.4 g, 94%). $[\alpha]_D^{16}$ +1.7° (c=2.80, MeOH). ^{1}H-NMR δ: 0.89 (6H, t, J=7.1 Hz), 1.61 (2H, q, J=7.6 Hz), 1.65 (2H, q, J=7.3 Hz), 2.20—2.40 (2H, m), 3.52 (1H, t, J=7.0 Hz), 3.77—4.09 (4H, m), 3.80 (3H, s), 4.43 (2H, s), 5.65—5.69 (2H, m), 6.87 (2H, d, J=8.4 Hz), 7.26 (2H, d, J=8.5 Hz). MS m/z (relative intensity): 320 (M$^+$, 0.6%), 291 (8.5), 135 (5.2), 129 (21.9), 121 (100), 91 (4.8), 57 (25).

A stirred ice-cold MeOH solution (80 ml) of the MPM ether (2.0 g,

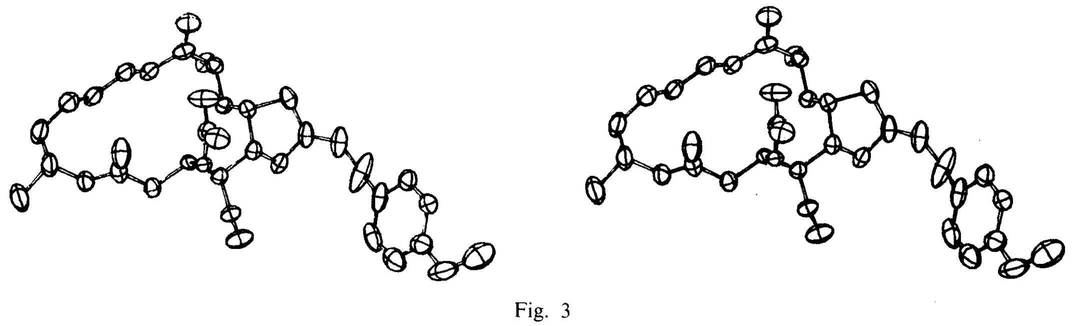
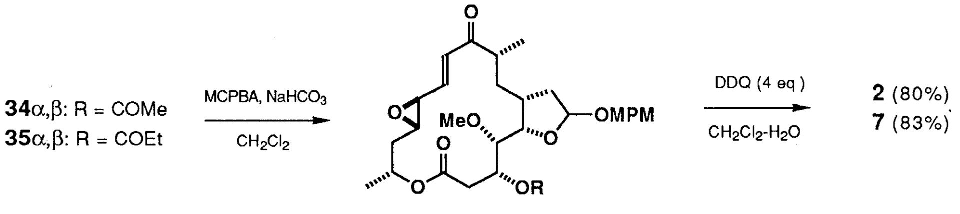


Fig. 3



36α,β: R = COMe (90%)
37α,β: R = COEt (73%)

Chart 6

6.2 mol) was treated with 2% H_2SO_4 (20 ml) and the solution was stirred for 4 h at room temperature. After neutralization with $NaHCO_3$, the reaction mixture was evaporated *in vacuo*, and the residue was extracted with CH_2Cl_2. The extract was washed with brine, dried over anhydrous $MgSO_4$, and evaporated to leave a diol as a colorless oil (1.5 g, 97%). $[\alpha]_{\mathrm{D}}^{16}$ -9.1° ($c=1.94$, MeOH). ^{1}H-NMR δ: 2.11—2.23 (4H, m), 3.42—3.72 (3H, m), 3.80 (3H, s), 3.96 (2H, dd, $J=2.7$, 1.0 Hz), 4.44 (2H, s), 5.66—5.76 (2H, m), 6.87 (2H, d, $J=8.8$ Hz). MS m/z (relative intensity): 252 (M^+, 0.64%), 251 (0.22), 221 (0.37), 176 (2.2), 137 (13.7), 121 (100), 109 (12.5), 91 (13.7), 77 (38.6). Exact MS m/z Calcd for $C_{14}H_{20}O_4$ (M^+): 252.1361. Found: 252.1366. IR ν (neat) cm^{-1}: 3550 (OH), 1650.

A solution of the diol (0.5 g, 5.19 mmol), tosyl chloride (392 mg, 1.96 mmol) and pyridine (0.24 ml, 2.94 mmol) in CH_2Cl_2 (5 ml) was stirred for 10 h at room temperature. The reaction mixture was poured into cold aqueous NH_4Cl solution, and extracted with CH_2Cl_2. The extract was successively washed with 10% HCl, saturated aqueous $NaHCO_3$, and brine, and dried over anhydrous $MgSO_4$. Concentration of the solvent gave an oil, which was chromatographed on a silica gel short column with EtOAc–hexane (1 : 2) as the eluant to give the tosylate as a colorless oil (574 mg, 72%). $[\alpha]_{\mathrm{D}}^{15}$ $+8.6^\circ$ ($c=1.30$, MeOH). ^{1}H-NMR δ: 2.10—2.30 (3H, m), 2.44 (2H, s), 3.80 (3H, s), 3.87—4.08 (4H, m), 4.41 (2H, s), 5.60—5.69 (2H, m), 6.87 (2H, d, $J=8.5$ Hz), 7.21—7.38 (4H, m), 7.79 (2H, d, $J=8.3$ Hz). MS m/z (relative intensity): 406 (M^+, 2.5%), 405 (M^+-1, 4.9), 375 (2.36), 348 (0.84), 269 (0.69), 256 (1.0), 176 (9.3), 155 (31.5), 137 (99), 121 (100), 109 (14.6), 91 (59.3). Exact MS m/z Calcd for $C_{21}H_{26}O_6S$ (M^+): 406.1450. Found: 406.1473. IR ν (neat) cm^{-1}: 3400 (OH), 1610, 1510, 1450, 1350, 1300, 1240, 1190.

A solution of the tosylate (314 mg, 0.072 mmol) in ether (3 ml) was added to a stirred solution of $LiAlH_4$ (36 mg, 0.95 mmol) in ether (5 ml) at 0 °C under an argon atmosphere. After 40 min, H_2O (37 μl), 15% NaOH (37 μl), and H_2O (110 μl) were successively added, and the resulting precipitates were removed by filtration. After evaporation of the solvent, the residue was purified through a short silica gel column with hexane–EtOAc (3 : 1) to afford **12** as a colorless oil (167 mg, 92%). $[\alpha]_{\mathrm{D}}^{15}$ -2.3° ($c=1.12$, MeOH). ^{1}H-NMR δ: 1.20 (3H, d, $J=6.4$ Hz), 1.52 (1H, s), 2.10—2.25 (2H, d, $J=4.4$ Hz), 3.80 (3H, s), 4.44 (2H, s), 5.66—5.76 (2H, m), 6.87 (2H, d, $J=8.6$ Hz), 7.27 (2H, d, $J=8.5$ Hz). MS m/z (relative intensity): 236 (M^+, 2.2%), 213 (0.67), 205 (0.9), 176 (7.5), 137 (29.2), 121 (100), 109 (10.4), 77 (11.4). Exact MS m/z Calcd for $C_{14}H_{20}O_3$ (M^+): 236.1413. Found: 236.1399. IR ν (neat) cm^{-1}: 3350 (OH), 1650, 1520.

5(*R*)-Hydroxy-2(*E*)-hexenal (9) DDQ (237 mg, 1.0 mmol) was added to a stirred solution of **12** (206 mg, 0.87 mmol) in CH_2Cl_2 (10 ml) and H_2O (0.5 ml). After being stirred for 40 min, the reaction mixture was quenched by addition of saturated $NaHCO_3$, and extracted with EtOAc. The extract was dried ($MgSO_4$) and concentrated to leave an oil, which was chromatographed on a silica gel column (hexane : EtOAc = 2 : 1) to give the diol (90 mg, 90%) as a colorless oil.

A mixture of the above diol (90 mg, 0.9 mmol) in CH_2Cl_2 (2 ml) and active MnO_2 (740 mg) was stirred for 1 h. After filtration to remove the MnO_2, the filtrate was concentrated *in vacuo*, and the residue was chromatographed on a silica gel column (EtOAc–hexane, 1 : 1) to give **9** as a colorless oil (86 mg, 90%). $[\alpha]_{\mathrm{D}}^{15}$ -15.0° ($c=1.46$, MeOH). ^{1}H-NMR δ: 1.27 (3H, d, $J=6.2$ Hz), 1.65 (1H, s), 2.45—2.53 (2H, m), 4.04 (1H, sex, $J=6.2$ Hz), 6.19 (1H, ddt, $J=16.0$, 8.1, 1.1 Hz), 6.90 (1H, dt, $J=16.0$, 7.3 Hz), 9.53 (1H, d, $J=8.1$ Hz). IR ν (neat) cm^{-1}: 3350 (OH), 1680 (CO).

6-*O*-(*tert*-Butyldimethylsilyl)-3-deoxy-1,2-*O*-isopropylidene-3-*C*-[2-(4-methoxybenzyloxy)ethyl]-α-D-allofuranose (14) A solution of **13** (2.07 g, 7.18 mmol) in THF (12 ml) was added dropwise to a stirred suspension of NaH (560 mg, 14 mmol: 60% oil suspension) in DMF (8 ml) under an argon atmosphere at room temperature. After 2 h, MPM chloride (1.6 g, 10 mmol) was added, and stirring was continued for 2.5 h. The reaction mixture was poured into cold aqueous NH_4Cl solution, and extracted with CH_2Cl_2. The extract was washed with brine, dried over anhydrous $MgSO_4$, and evaporated *in vacuo* to leave an oil, which was chromatographed on a silica gel column using EtOAc–hexane (1 : 5) as the eluant to give the MPM ether as a colorless oil (2.83 g, 96.5%). $[\alpha]_{\mathrm{D}}^{19}$ $+52^\circ$ ($c=3.06$, $CHCl_3$). ^{1}H-NMR δ: 1.30 (3H, s), 1.34 (3H, s), 1.41 (3H, s), 1.50 (3H, s), 1.85—1.97 (1H, m), 1.99—2.05 (2H, m), 3.56—3.61 (2H, m), 3.75—3.78 (1H, m), 3.81 (3H, s), 3.90—4.10 (3H, m), 4.46 (2H, ABq, $J=4.4$ Hz), 4.57 (1H, t, $J=4.0$ Hz), 5.72 (1H, d, $J=3.5$ Hz), 6.88 (2H, d, $J=8.5$ Hz), 7.27 (2H, d, $J=8.5$ Hz).

A stirred ice-cold MeOH solution (400 ml) of the MPM ether (53 g, 0.13 mol) was treated with 2% H_2SO_4 (100 ml) and the solution was stirred for 5 h at room temperature. After neutralization with $NaHCO_3$, the reaction mixture was evaporated *in vacuo*, and the residue was extracted with CH_2Cl_2. The extract was washed with H_2O, dried over anhydrous $MgSO_4$, and evaporated to leave an oil, which was dissolved in CH_2Cl_2 (200 ml) containing imidazole (13.0 g, 191 mmol). The solution was cooled in an ice-bath, and a CH_2Cl_2 solution (50 ml) of TBDMS chloride (14 g, 93 mmol) was added dropwise. After 1 h, the reaction mixture was washed with saturated aqueous NH_4Cl solution, dried over anhydrous $MgSO_4$, and evaporated *in vacuo* to leave a colorless oil, which was chromatographed on a silica gel column with EtOAc–hexane (1 : 10) as the eluent to give the recovered MPM ether (9 g, 17%) and **14** as a colorless oil (40 g, 64%). $[\alpha]_{\mathrm{D}}^{16}$ $+44^\circ$ ($c=2.54$, $CHCl_3$). ^{1}H-NMR δ: 0.07 (6H, s), 0.89 (9H, s), 1.30 (3H, s), 1.48 (3H, s), 1.89 (1H, ddt, $J=14.0$, 11.5, 5.5 Hz), 2.04—2.13 (2H, m), 2.63 (1H, d, $J=4.0$ Hz), 3.50—3.67 (1H, m), 3.75—3.82 (2H, m), 3.80 (3H, s), 4.46 (1H, d, $J=14.5$ Hz), 4.50 (1H, d, $J=14.5$ Hz), 4.58 (1H, t, $J=3.5$ Hz), 5.72 (1H, d, $J=3.5$ Hz), 6.87 (2H, d, $J=8.5$ Hz), 7.27 (2H, d, $J=8.5$ Hz). IR ν (neat) cm^{-1}: 3450 (OH).

6-*O*-(*tert*-Butyldimethylsilyl)-3-deoxy-1,2-*O*-isopropylidene-5-*O*-methanesulfonyl-3-*C*-[2-(4-methoxybenzyloxy)ethyl]-α-D-allofuranose (15) A solution of **14** (2.46 g, 5.19 mmol) and mesyl chloride (1.18 g, 10.3 mmol) in pyridine (12 ml) was stirred for 6 h at room temperature. The reaction mixture was poured into cold aqueous NH_4Cl solution, and extracted with CH_2Cl_2. The extract was successively washed with 10% HCl, saturated aqueous $NaHCO_3$, and brine, and dried over anhydrous $MgSO_4$. Concentration of the solvent gave an oil, which was chromatographed on a silica gel short column with EtOAc–hexane (1 : 5) as the eluant to give **15** as a colorless oil (2.80 g, 97.9%). $[\alpha]_{\mathrm{D}}^{15}$ $+40^\circ$ ($c=2.30$, $CHCl_3$). ^{1}H-NMR δ: 0.07 (6H, s), 0.89 (9H, s), 1.30 (3H, s), 1.49 (3H, s), 1.92 (1H, q, $J=6.5$ Hz), 2.25 (1H, ddt, $J=10.0$, 4.5, 6.0 Hz), 3.07 (3H, s), 3.59 (2H, t, $J=6.0$ Hz), 3.80 (3H, s), 3.86 (2H, d, $J=6.0$ Hz), 4.10 (1H, dd, $J=10.0$, 4.0 Hz), 4.42 (1H, d, $J=11.5$ Hz), 4.48 (1H, d, $J=11.5$ Hz), 4.60 (1H, t, $J=4.0$ Hz), 4.71 (1H, dt, $J=4.4$, 5.5 Hz), 5.72 (1H, d, $J=4.0$ Hz), 6.87 (2H, d, $J=8.5$ Hz), 7.27 (2H, d, $J=8.5$ Hz).

3-Deoxy-1,2-*O*-isopropylidene-5-*O*-methanesulfonyl-3-*C*-[2-(4-methoxybenzyloxy)ethyl]-α-D-allofuranose (16) A solution of **15** (130 g, 0.239 mmol) in THF (500 ml) and 1 N HCl (100 ml) was stirred for 1 h at room temperature. After neutralization with $NaHCO_3$, the solution was evaporated *in vacuo*, and the residue was extracted with CH_2Cl_2. The extract was washed with brine, dried over anhydrous $MgSO_4$, and evaporated *in vacuo* to leave **16** as a colorless oil (97 g, 91%). $[\alpha]_{\mathrm{D}}^{15}$ $+40^\circ$ ($c=2.10$, $CHCl_3$). ^{1}H-NMR δ: 1.30 (3H, s), 1.49 (3H, s), 1.85 (1H, ddt, $J=14.0$, 3.0, 5.5 Hz), 1.93 (1H, dd, $J=14.0$, 5.5 Hz), 2.21 (1H, dd, $J=10.0$, 4.5 Hz), 2.40 (1H, t, $J=6.0$ Hz), 3.10 (3H, s), 3.56 (1H, ddd, $J=14.0$, 5.0, 3.0 Hz), 3.61 (1H, ddd, $J=14.0$, 5.5, 3.0 Hz), 3.81 (3H, s), 3.89 (2H, dd, $J=6.0$, 5.0 Hz), 4.11 (1H, dd, $J=10.0$, 4.0 Hz), 4.42 (1H, d, $J=11.5$ Hz), 4.47 (1H, d, $J=11.5$ Hz), 4.58 (1H, dd, $J=6.0$, 5.0 Hz), 4.77 (1H, dt, $J=4.0$, 5.0 Hz), 5.74 (1H, d, $J=4.0$ Hz), 6.88 (2H, d, $J=8.5$ Hz), 7.27 (2H, d, $J=8.5$ Hz). MS m/z (relative intensity): 348 (M^+, 0.9%), 311 (3), 228 (19), 197 (7), 121 (23), 43 (100). IR ν (neat) cm^{-1}: 3450 (OH).

6-*O*-Benzyl-3-deoxy-1,2-*O*-isopropylidene-3-*C*-[2-(4-methoxybenzyloxy)ethyl]-β-L-talofuranose (18) A stirred MeOH solution of **16** (20 g, 44.8 mmol) was treated with K_2CO_3 (7.3 g, 52.8 mmol) at room temperature. After 2 h, NH_4Cl was added to quench the reaction. The MeOH was concentrated to dryness, and the residue was dissolved in CH_2Cl_2, washed with brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo* to leave an oil, which was chromatographed on a silica gel column with EtOAc–hexane (1 : 3) as the eluant to give the epoxide (**17**) as an oil (15 g, 96%).

A DMF (5 ml) solution of benzyl alcohol (491 mg, 4.54 mmol) was added to a stirred suspension of NaH (182 mg, 4.55 mmol; 60% activity) in DMF (5 ml) under argon at room temperature. After 30 min, **17** (318 mg, 0.91 mmol) was added, and the stirring was continued for 90 min at 60 °C. The reaction mixture was cooled, poured into cooled aqueous NH_4Cl solution, and extracted with ether. The extract was washed with brine, dried over anhydrous $MgSO_4$, and evaporated *in vacuo* to leave an oil, which was chromatographed on a silica gel column with EtOAc–hexane (1 : 3) as the eluant to give **18** as a colorless oil (408 mg, 98%). $[\alpha]_{\mathrm{D}}^{15}$ $+42^\circ$ ($c=3.10$, $CHCl_3$). ^{1}H-NMR δ: 1.30 (3H, s), 1.48 (3H, s), 1.67 (1H, ddt, $J=14.0$, 10.0, 4.5 Hz), 1.88 (1H, ddt, $J=14.0$, 10.0, 6.5 Hz), 2.30 (1H, d, $J=6.5$ Hz), 2.34 (1H, tt, $J=10.5$, 4.5 Hz), 3.56 (1H, dd, $J=10.0$, 5.0 Hz), 3.58 (1H, ddd, $J=14.0$, 10.5, 4.5 Hz), 3.59 (1H, ddd, $J=14.0$, 7.0, 6.5 Hz), 3.64 (1H, dd, $J=10.0$, 7.5 Hz), 3.79 (3H, s), 3.77—3.87 (1H, m), 3.86 (1H, dd, $J=10.0$, 1.0 Hz), 4.42 (1H, d, $J=11.5$ Hz), 4.47 (1H, d, $J=11.5$ Hz), 4.54 (1H, d, $J=11.5$ Hz), 4.58 (1H, dd, $J=4.5$, 3.5 Hz), 4.59 (1H, d, $J=11.5$ Hz), 5.77 (1H, d, $J=4.0$ Hz), 6.87 (2H, d, $J=8.5$ Hz), 7.24—7.34 (7H, m). MS m/z (relative intensity): 458 (M^+, 0.5%), 309 (1.5), 279 (1.3), 173 (5), 121 (100), 91 (27.5). Exact MS m/z Calcd for $C_{26}H_{34}O_7$ (M^+):

458.2304. Found: 458.2303. IR ν (neat) cm^{-1}: 3450 (OH).

6-*O*-Benzyl-3-deoxy-1,2-*O*-isopropylidene-3-*C*-[2-(4-methoxybenzyloxy)ethyl]-5-*O*-methyl-β-L-talofuranose (19) A solution of **18** (65 g, 0.14 mol) in THF (200 ml) was added dropwise to a stirred suspension of NaH (8.5 g, 0.21 mol; 60% oil suspension) in DMSO (100 ml) and THF (100 ml) under argon at room temperature. After 2 h, iodomethane (30 g, 0.20 mol) was added, and the stirring was continued for 12 h. The reaction mixture was poured into cold aqueous NH_4Cl solution, and extracted with CH_2Cl_2. The extract was washed with brine, dried over anhydrous $MgSO_4$, and evaporated *in vacuo* to leave an oil, which was chromatographed on a silica gel short column using EtOAc–hexane (1 : 2) as the eluant to give **19** as a colorless oil (66.2 g, 100%). $[\alpha]_D^{15}$ +45° (c = 2.0, $CHCl_3$). ^{1}H-NMR δ: 1.30 (3H, s), 1.47 (3H, s), 1.68 (1H, ddt, J = 14.0, 4.0, 7.0 Hz), 1.89 (1H, ddt, J = 14.0, 10.5, 5.5 Hz), 2.31 (1H, tt, J = 10.5, 4.0 Hz), 3.45 (1H, ddd, J = 7.0, 5.0, 1.5 Hz), 3.50 (3H, s), 3.57 (1H, ddd, J = 14.0, 7.0, 5.5 Hz), 3.64 (1H, ddd, J = 14.0, 7.0, 5.5 Hz), 3.68 (1H, dd, J = 10.0, 5.0 Hz), 3.75 (1H, dd, J = 10.0, 7.0 Hz), 3.80 (3H, s), 3.91 (1H, dd, J = 10.5, 1.5 Hz), 4.42 (1H, d, J = 11.5 Hz), 4.48 (1H, d, J = 11.5 Hz), 4.56 (1H, dd, J = 4.0, 3.5 Hz), 4.55 (2H, s), 5.77 (1H, d, J = 3.5 Hz), 6.87 (2H, d, J = 8.5 Hz), 7.24—7.34 (7H, m). MS m/z (relative intensity): 472 (M^+, 0.5%), 323 (1.0), 278 (1.6), 219 (4.3), 121 (100), 91 (29). Exact MS m/z Calcd for $C_{27}H_{36}O_7$ (M^+): 472.2462. Found: 472.2482.

(2*R*,3*R*,4*S*)-5-Benzyloxy-3-formyloxy-4-methoxy-2-[2-(4-methoxybenzyloxy)ethyl]pentanal (20) A solution of **19** in dioxane (300 ml) and 3 N H_2SO_4 (100 ml) was stirred for 48 h at room temperature. The reaction mixture was neutralized with $NaHCO_3$ and evaporated *in vacuo*. The residue was extracted with CH_2Cl_2, washed with brine, dried over anhydrous $MgSO_4$, and evaporated to leave an oil, which was chromatographed on a silica gel column using EtOAc–hexane (1 : 2) as the eluant to give recovered **19** (13.5 g, 64%) and the diol as a viscous oil (6.8 g, 36%).

An aqueous solution of $NaIO_4$ (6.8 g, 0.03 mol in 85 ml of H_2O) was added to a MeOH solution (200 ml) of the above diol at 5 °C. After 2 h, the precipitate was filtered off, and then the filtrate was concentrated *in vacuo*, and extracted with CH_2Cl_2. The extract was dried over anhydrous $MgSO_4$, and evaporated to leave **20** as a colorless oil (6.7 g, 99%), which was used for the next reaction without further purification. $[\alpha]_D^{18}$ +14° (c = 2.7, $CHCl_3$). ^{1}H-NMR δ: 1.80 (1H, dq, J = 17.5, 7.0 Hz), 1.97 (1H, ddt, J = 17.5, 10.0, 7.5 Hz), 2.76 (1H, dddd, J = 7.5, 7.0, 4.0, 3.5 Hz), 3.38 (3H, m), 3.43—3.59 (5H, m), 3.38 (3H, s), 3.79 (3H, s), 4.37 (2H, s), 4.48 (2H, s), 5.47 (1H, t, J = 3.3 Hz), 7.22 (2H, d, J = 8.8 Hz), 7.28—7.35 (5H, m), 8.12 (2H, s), 9.65 (1H, d, J = 4.0 Hz). MS m/z (relative intensity): 430 (M^+, 0.2%), 321 (0.5), 157 (6), 121 (100), 91 (46). Exact MS m/z Calcd for $C_{24}H_{30}O_7$ (M^+): 430.1992. Found: 430.2011. IR ν (neat) cm^{-1}: 1720, 1710 (CO).

(2*Z*,4*S*,5*S*,6*S*)-7-Benzyloxy-5-hydroxy-6-methoxy-4-[2-(4-methoxybenzyloxy)ethyl]-2-methylhept-2-enoic Acid δ-Lactone (21) A THF (100 ml) solution of trimethyl α-phosphonopropionate (16.2 g, 82.6 mmol) was added dropwise to a stirred suspension of NaH (8.5 g, 0.21 mol; 60% oil suspension) in THF (100 ml) under argon at 0 °C. After evolution of hydrogen had ceased, the solution was cooled to −90 °C, and a THF solution (100 ml) of **20** (11.0 g, 25.5 mmol) was added dropwise within 1 h. The reaction mixture was allowed to warm to −20 °C for 2 h, and then aqueous NH_4Cl was added in order to quench the reaction. The whole mixture was extracted with ether, and the extract was washed with brine, dried over anhydrous $MgSO_4$, and evaporated *in vacuo* to leave an oil, which was dissolved in MeOH. This solution was stirred and K_2CO_3 (3.5 g, 25 mmol) was added at 0 °C, then after 4 h, NH_4Cl was added. The reaction mixture was concentrated to dryness, and the residue was extracted with CH_2Cl_2. The extract was washed with brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo* to leave a colorless oil, which was chromatographed on a silica gel column with EtOAc–hexane (1 : 4) as the eluant to give **21** as a colorless oil (6.5 g, 58%). $[\alpha]_D^{18}$ +43° (c = 2.15, $CHCl_3$). ^{1}H-NMR δ: 1.66 (1H, ddt, J = 14.0, 8.5, 6.0 Hz), 1.87 (3H, t, J = 1.5 Hz), 1.89 (1H, ddd, J = 14.0, 6.0, 5.0 Hz), 2.91 (1H, dddd, J = 9.0, 8.5, 5.0, 1.5 Hz), 3.46 (3H, s), 3.53 (2H, t, J = 6.0 Hz), 3.57 (1H, ddd, J = 6.0, 5.5, 3.0 Hz), 3.70 (1H, dd, J = 10.0, 5.5 Hz), 3.75 (1H, dd, J = 10.0, 6.0 Hz), 3.79 (3H, s), 4.34 (1H, dd, J = 9.0, 3.0 Hz), 4.39 (1H, d, J = 11.5 Hz), 4.44 (1H, d, J = 11.5 Hz), 4.50 (1H, d, J = 11.5 Hz), 4.55 (1H, d, J = 11.5 Hz), 6.47 (1H, sex, J = 1.5 Hz), 6.86 (2H, d, J = 8.8 Hz), 7.23 (7H, d, J = 8.8 Hz). MS m/z (relative intensity): 440 (M^+, 0.9%), 349 (4), 319 (1.8), 275 (1.6), 213 (7), 121 (100), 91 (43). Exact MS m/z Calcd for $C_{26}H_{32}O_6$ (M^+): 440.2199. Found: 440.2202. IR ν (neat) cm^{-1}: 1710 (CO).

(2*S*,5*S*,6*S*)-6-[2-Benzyloxy-1(*S*)-methoxyethyl]-5,6-dihydro-2-isopropyloxy-5-[2-(4-methoxybenzyloxy)ethyl]-3-methylpyran (22) A 1 M hexane solution of DIBAH (28 ml) was added to a CH_2Cl_2 (100 ml) solution of **21** (6.2 g, 14 mmol) under argon at −80 °C. After 1 h, MeOH was added to decompose the reagent, and the reaction mixture was washed with 0.5 N HCl, 10% $NaHCO_3$ and brine, dried over $MgSO_4$, then evaporated to afford a colorless oil. This oil was dissolved in iso-PrOH (100 ml), and after addition of CSA (310 mg) the mixture was stirred for 1 h at room temperature. After addition of triethylamine (TEA) (1 ml), the reaction mixture was evaporated *in vacuo*, and the residue was chromatographed on a silica gel column with EtOAc–hexane (1 : 5) as the eluant to give **22** as a colorless oil (5.1 g, 75%). $[\alpha]_D^{19}$ +43° (c = 1.2, $CHCl_3$). ^{1}H-NMR δ: 1.14 (3H, d, J = 6.5 Hz), 1.16 (3H, d, J = 6.5 Hz), 1.48 (1H, ddt, J = 14.0, 9.0, 7.0 Hz), 1.66 (3H, t, J = 1.8 Hz), 1.79 (1H, ddt, J = 14.0, 3.5, 7.0 Hz), 2.63 (1H, t, J = 9.0 Hz), 3.50 (3H, s), 3.54 (2H, t, J = 7.0 Hz), 3.64 (1H, ddd, J = 5.5, 4.5, 1.0 Hz), 3.67 (1H, dd, J = 8.5, 4.5 Hz), 3.73 (1H, dd, J = 9.0, 1.0 Hz), 3.78 (3H, s), 3.79 (1H, dd, J = 8.5, 5.5 Hz), 3.94 (1H, heptet, J = 6.5 Hz), 4.40 (1H, d, J = 11.5 Hz), 4.45 (1H, d, J = 11.5 Hz), 4.52 (1H, d, J = 11.5 Hz), 4.56 (1H, d, J = 11.5 Hz), 4.82 (1H, s), 5.54 (1H, s), 6.86 (2H, d, J = 8.8 Hz), 7.23—7.34 (7H, m). MS m/z (relative intensity) 484 (M^+, 0.5%), 424 (0.5), 319 (1.5), 353 (1.3), 259 (10), 121 (100), 91 (28). Exact MS m/z Calcd for $C_{29}H_{40}O_6$ (M^+): 484.2824. Found: 484.2813.

2(*S*)-{2(*S*)-Isopropyloxy-5(*R*)-[2-(4-methoxybenzyloxy)ethyl-3(*R*)-methyl-6(*S*)-tetrahydropyranyl}-2-methoxyethanol (23) An EtOH solution of **22** (4.6 g, 9.4 mmol) was hydrogenated in the presence of Raney Ni W-2 (12 ml of EtOH suspension) at ordinary temperature and pressure. After 9 h, the catalyst was filtered off, and the filtrate was chromatographed on silica gel column with EtOAc–hexane (1 : 5) as the eluant to give recovered **22** (0.75 g, 6.1%) and **23** as a colorless oil (2.9 g, 77.8%). ^{1}H-NMR δ: 0.81 (3H, d, J = 7.0 Hz), 1.10 (3H, d, J = 6.2 Hz), 1.20 (3H, d, J = 6.2 Hz), 1.31—1.50 (3H, m), 1.68—1.79 (2H, m), 1.94—2.07 (1H, m), 2.80 (1H, s), 3.40—3.51 (3H, m), 3.47 (3H, s), 3.71—3.92 (4H, m), 3.80 (3H, s), 4.42 (2H, ABq, J = 5.5 Hz), 4.69 (1H, d, J = 3.3 Hz), 6.87 (2H, d, J = 8.8 Hz), 7.26 (2H, d, J = 8.8 Hz). MS m/z (relative intensity): 336 (M^+ − 60, 0.9%), 305 (1.8), 215 (1.5), 121 (100). Exact MS m/z Calcd for $C_{19}H_{28}O_5$ (M^+ − 60): 336.1937. Found: 336.1956. IR ν (neat) cm^{-1}: 3450 (OH).

2(*S*)-{2(*S*)-Isopropyloxy-5(*R*)-[2-(4-methoxybenzyloxy)ethyl]-3(*R*)-methyl-6(*S*)-tetrahydropyranyl}-2-methoxyethanal (24) Dry Me_2SO (0.75 ml, 5.26 mmol) in CH_2Cl_2 (15 ml) was added dropwise during 15 min to an efficiency stirred solution of oxalyl chloride (0.69 ml, 7.90 mmol) in dry CH_2Cl_2 (40 ml) at −90 °C, and a solution of **23** (2.08 g, 5.26 mmol) in CH_2Cl_2 (4 ml) was added to the mixture within 10 min. Stirring was continued at −90 °C for 30 min, then Et_3N (2.9 ml, 20.8 mmol) was added dropwise. The reaction mixture was allowed to warm to −70 °C (over *ca.* 1 h), and then quenched with H_2O (20 ml). The organic layer was separated, and the aqueous layer was extracted with ether (100 ml × 2). The combined extracts were washed with brine, dried over $MgSO_4$, and evaporated *in vacuo*. The residue was chromatographed on a silica gel column with hexane–EtOAc (3 : 1) as the eluant to give the aldehyde (**24**) as a colorless oil (1.99 g, 96%). ^{1}H-NMR δ: 0.79 (3H, d, J = 6.8 Hz), 1.04 (3H, d, J = 6.0 Hz), 1.12 (3H, d, J = 6.1 Hz), 1.26—2.25 (6H, m), 3.43—3.59 (2H, m), 3.51 (3H, s), 3.71—3.78 (2H, m), 3.80 (3H, s), 4.00 (2H, dd, J = 10.8, 2.9 Hz), 4.43 (2H, s), 4.60 (1H, d, J = 3.2 Hz), 6.87 (2H, d, J = 8.8 Hz), 7.25 (2H, d, J = 8.8 Hz), 9.78 (1H, d, J = 1.2 Hz). MS m/z (relative intensity): 394 (M^+, 0.5%), 334 (28.3), 225 (4.6), 213 (30.2), 199 (100), 185 (15.6), 169 (6.7), 157 (35.8), 137 (30.4), 122 (100), 121 (99), 95 (66.6). Exact m/z Calcd for $C_{22}H_{34}O_5$ (M^+): 394.2356. Found: 394.2349. Calcd for $C_{19}H_{26}O_5$ (M^+ − 60): 334.1781. Found: 334.1768. IR ν (neat) cm^{-1}: 1730 (CO).

5(*S*)-{2(*S*)-Isopropyloxy-5(*R*)-[2-(4-methoxybenzyloxy)ethyl]-3(*R*)-methyl-6(*S*)-tetrahydropyranyl}-4(*R*)-hydroxy-5-methoxypentene (25) A stirred solution of the above aldehyde **24** (1.72 g, 4.3 mmol) in dry CH_2Cl_2 (100 ml), cooled at −50 °C under nitrogen, was treated with a 1 M solution of $MgBr_2 \cdot OEt_2$ (8.6 ml, 8.6 mmol) in ether. After 10 min, allyltri-*n*-butyltin (2.76 g, 8.6 mmol) in CH_2Cl_2 (100 ml) was added. The mixture was stirred below −60 °C for 15 min, and the reaction was quenched with saturated aqueous NH_4Cl (10 ml). The cooling bath was then removed and the reaction mixture was allowed to warm to room temperature. The whole was extracted with CH_2Cl_2, and the extract was washed with brine, and dried over anhydrous $MgSO_4$. After evaporation of the solvent, the residue was chromatographed on a silica gel column with hexane–EtOAc (2 : 1) as the eluant to afford the 3,4-*anti* isomer of **25** (20 mg, 1%) and **25** as a colorless oil (1.43 g, 76%). ^{1}H-NMR δ: 0.81 (3H, d, J = 7.0 Hz), 1.09 (3H, d, J = 6.0 Hz), 1.18 (3H, d, J = 6.2 Hz), 1.28—1.42 (1H, m), 1.51 (1H, dt, J = 12.5, 4.0 Hz), 1.75—1.88 (2H, m), 1.94—2.04 (1H, m), 2.25 (1H, dt, J = 14.0, 7.0 Hz), 2.35 (1H, ddd, J = 14.0, 7.0, 5.0 Hz), 3.14 (1H, s), 3.39

(1H, dd, $J=5.0$, 0.5 Hz), 3.46—3.54 (2H, m), 3.59 (3H, s), 3.65 (2H, dd, $J=10.0$, 0.5 Hz), 3.80 (3H, s), 3.80 (1H, heptet, $J=6.0$ Hz), 4.40 (1H, d, $J=11.5$ Hz), 4.45 (1H, d, $J=11.5$ Hz), 4.69 (1H, d, $J=3.5$ Hz), 5.09 (1H, dd, $J=16.0$, 2.0 Hz), 5.11 (1H, ddd, $J=10.0$, 3.5, 1.5 Hz), 5.87 (1H, ddt, $J=16.0$, 10.0, 7.0 Hz), 6.87 (2H, d, $J=8.8$ Hz), 7.25 (2H, d, $J=8.8$ Hz). MS *m/z* (relative intensity) 436 (M^+, 0.2%), 376 (2.4), 303 (0.6), 261 (1.8), 153 (0.5), 121 (100). Exact MS *m/z* Calcd for $C_{22}H_{32}O_5$ (M^+): 376.2249. Found: 376.2252. IR ν (neat) cm^{-1}: 3400 (OH).

(2*R*,4*R*,5*S*,6*S*,7*R*)-6-Methoxy-4-[2-(4-methoxybenzyloxy)ethyl]-2-methyl-9-decene-1,5,7-triol (26) A solution of **25** (1.2 g, 2.76 mmol) in 1 N HCl (40 ml) and THF (120 ml) was stirred at 50 °C for 6 h. After neutralization with solid $NaHCO_3$, the reaction mixture was evaporated to dryness. CH_2Cl_2 and water were added to the residue, and the CH_2Cl_2 layer was separated. The aqueous layer was extracted with CH_2Cl_2 (30 ml × 2), and the organic layers were combined and dried over $MgSO_4$. After evaporation of the solvent, purification of the residue on a silica gel column with hexane–EtOAc (1 : 1) as the eluant afforded recovered **25** (63 mg, 5%) and a lactol as a colorless oil (857 mg, 80%).

A solution of $CaCl_2$ (726 mg, 6.54 mmol) in EtOH (50 ml) was cooled at −40 °C, and $NaBH_4$ (424 mg, 10.9 mmol) in EtOH (30 ml) was added dropwise. NaCl separated out at once as a fine solid. After 30 min, an EtOH (10 ml) solution of the above lactol (726 mg) was added to the resulting $Ca(BH_4)_2$ solution at −20 °C. The reaction mixture was stirred for 3 h at room temperature, then excess $Ca(BH_4)_2$ was decomposed by addition of 1 N HCl, and the mixture was neutralized with Na_2CO_3. After removal of the precipitates by filtration, the filtrate was concentrated *in vacuo*. The residue was extracted with CH_2Cl_2, dried over $MgSO_4$, and evaporated *in vacuo* to leave **26** as a colorless oil (783 mg, 91%). $[\alpha]_D^{22}$ +6.4° ($c=5.10$, $CHCl_3$). ^{1}H-NMR δ: 0.92 (3H, d, $J=6.4$ Hz), 1.26—1.92 (6H, m), 2.30—2.38 (2H, m), 3.20—3.70 (7H, m), 3.54 (3H, s), 3.79 (3H, s), 4.42 (2H, s), 5.05—5.18 (2H, m), 5.69—6.04 (1H, m), 6.86 (2H, d, $J=8.8$ Hz), 7.24 (2H, d, $J=8.8$ Hz). MS *m/z* (relative intensity): 396 (M^+, 0.57), 346 (0.36), 323 (0.63), 305 (1.0), 280 (6.7), 262 (6.7), 224 (8.3), 171 (18.3), 155 (33.9), 137 (42.7), 121 (100), 98 (36.4). Exact MS *m/z* Calcd for $C_{22}H_{36}O_6$ (M^+): 396.2512. Found: 396.2531. IR ν cm^{-1}: 3400 (OH).

(2*R*,4*R*,5*S*,6*S*,7*R*)-5,7-Isopropylidenedioxy-6-methoxy-4-[2-(4-methoxybenzyloxy)ethyl]-2-methyl-9-decenol (27) A benzene solution (30 ml) of 2,2-dimethoxypropane (2.4 ml), **26** (775 mg, 1.96 mmol) and CSA (23 mg) was stirred at room temperature for 2 h. Et_3N (1 ml) was added to quench the reaction and after evaporation of the solvent, the residue was chromatographed on a silica gel column (hexane–AcOEt, 2 : 1) to give the acetal **27** as a colorless oil (766 mg, 90%). $[\alpha]_D^{12}$ +10° ($c=2.70$, $CHCl_3$). ^{1}H-NMR δ: 0.88 (3H, d, $J=6.2$ Hz), 1.06—1.11 (1H, m), 1.40 (3H, s), 1.43 (3H, s), 1.46—1.61 (2H, m), 1.75—1.87 (1H, m), 1.95—2.10 (1H, m), 2.35 (1H, ddd, $J=14.0$, 7.5, 7.0 Hz), 2.42 (1H, ddd, $J=14.0$, 7.0, 6.5 Hz), 3.10 (1H, s), 3.37 (1H, dd, $J=11.5$, 4.5 Hz), 3.48 (1H, dd, $J=7.5$, 1.5 Hz), 3.53 (1H, dd, $J=13.5$, 7.5 Hz), 3.59 (1H, dd, $J=11.5$, 4.0 Hz), 3.73 (1H, dt, $J=1.5$, 7.0 Hz), 3.80 (3H, s), 4.42 (2H, s), 5.01 (1H, ddd, $J=17.0$, 3.0, 1.5 Hz), 5.07 (1H, ddd, $J=10.0$, 1.5, 1.0 Hz), 5.81 (1H, dddd, $J=17.0$, 10.0, 7.5, 6.5 Hz), 6.87 (2H, d, $J=8.5$ Hz), 7.24 (2H, d, $J=8.5$ Hz). MS *m/z* (relative intensity) 421 (M^+-15, 0.1%), 280 (1.4), 262 (1.8), 137 (11), 121 (99), 98 (100). IR ν (neat) cm^{-1}: 3350 (OH).

(2*R*,4*R*,5*S*,6*S*,7*R*)-5,7-Isopropylidenedioxy-6-methoxy-4-[2-(4-methoxybenzyloxy)ethyl]-2-methyl-9-decenal (28) A solution of DMSO (0.37 ml, 5.22 mmol) in dry CH_2Cl_2 (10 ml) was added to a stirred solution of oxalyl chloride (0.3 ml, 3.44 mmol) in dry CH_2Cl_2 (20 ml) at −70 °C. After 15 min, a CH_2Cl_2 (30 ml) solution of **27** (765 mg, 1.74 mmol) was added to the reaction mixture. Stirring was continued for 30 min at −65 °C, and then Et_3N (1.2 ml, 8.6 mmol) was added. After 30 min at −65 °C, the reaction mixture was warmed to −30 °C and then quenched with saturated aqueous NH_4Cl. After dilution with CH_2Cl_2, the CH_2Cl_2 solution was washed with brine, and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified on a silica gel column with hexane–EtOAc (2 : 1) as the eluant to afford **28** as a viscous oil (684 mg, 91%). $[\alpha]_D^{15}$ +10° ($c=2.07$, $CHCl_3$). ^{1}H-NMR δ: 1.05 (3H, d, $J=6.8$ Hz), 1.37 (6H, s), 1.26—2.65 (8H, m), 3.45—3.72 (5H, m), 3.52 (3H, s), 3.80 (3H, s), 4.41 (2H, s), 5.02—5.19 (2H, m), 5.68—6.00 (1H, m), 6.86 (2H, d, $J=8.8$ Hz), 7.24 (2H, d, $J=8.8$ Hz), 9.57 (1H, d, $J=2.0$ Hz). IR ν (neat) cm^{-1}: 1715 (CO).

Dimethyl (3*R*,5*R*,6*S*,7*S*,8*R*)-6,8-Isopropylidenedioxy-7-methoxy-5-[2-(4-methoxybenzyloxy)ethyl]-3-methyl-2-oxo-10-undecenylphophonate (29) A 1.5 M *n*-BuLi solution in hexane (3.28 ml, 4.8 mmol) was added to a stirred solution of dimethyl methylphosphonate (0.68 ml, 6.27 mmol) in THF (30 ml) at −80 °C. After 30 min, a solution of **28** (0.68 g, 1.57 mmol) in THF (30 ml) was added dropwise, and the reaction mixture was gradually warmed to −40 °C during 6 h. After the reaction had been quenched with saturated NH_4Cl solution, the whole mixture was extracted with ether, and the extract was washed with brine, dried over $MgSO_4$, and evaporated *in vacuo* to give the β-hydroxyphosphonate as a colorless oil (0.87 g, 99%).

Pyridinium dichromate (PDC) (3.5 g, 9.4 mmol) was added to a stirred solution of the β-hydroxyphosphonate (0.87 g, 1.56 mmol) in DMF (35 ml) at room temperature. After 7 h, the reaction mixture was poured into H_2O and then extracted with ether. The extract was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*, and the residue was chromatographed on a silica gel column with EtOAc to give the β-ketophosphonate (**29**) as a colorless oil (693 mg, 86.5%). $[\alpha]_D^{18}$ −6.6° ($c=1.31$, $CHCl_3$). ^{1}H-NMR δ: 1.07 (3H, d, $J=6.6$ Hz), 1.17 (1H, ddd, $J=14.0$, 8.5, 3.5 Hz), 1.40 (3H, s), 1.44 (3H, s), 1.75 (1H, ddd, $J=14.0$, 7.0, 3.0 Hz), 1.84 (1H, ddd, $J=14.0$, 7.0, 3.0 Hz), 1.95—2.05 (2H, m), 2.35—2.41 (2H, m), 3.06 (1H, t, $J=1.0$ Hz), 3.15 (2H, d, $J=22.0$ Hz), 3.45—3.55 (2H, m), 3.57 (1H, dd, $J=9.5$, 1.0 Hz), 3.52 (3H, s), 3.76 (3H, d, $J=11.0$ Hz), 3.78 (3H, d, $J=11.0$ Hz), 3.80 (3H, s), 4.40 (2H, s), 5.08 (1H, dd, $J=10.0$, 1.5 Hz), 5.13 (1H, ddd, $J=17.5$, 3.0, 1.5 Hz), 5.81 (1H, ddd, $J=17.0$, 10.0, 7.2 Hz), 6.86 (2H, d, $J=8.4$ Hz), 7.23 (2H, d, $J=8.4$ Hz). MS *m/z* (relative intensity): 556 (M^+, 0.2%), 541 (0.2), 396 (0.8), 378 (2), 275 (3), 202 (16), 180 (23), 121 (100). Exact MS *m/z* Calcd for $C_{28}H_{45}O_9$ (M^+): 556.2801. Found: 556.2815. IR ν (neat) cm^{-1}: 1720, 1705 (CO).

(3*R*,4*S*,5*S*,6*R*,8*R*)-10-Dimethoxyphosphono-3,5-isopropylidenedioxy-4-methoxy-6-[2-(4-methoxybenzyloxy)ethyl]-8-methyl-9-oxodecanoic Acid (8) A solution of **29** in acetone (30 ml), 10% aqueous $NaHCO_3$ (1.9 ml) and a 0.1 M solution of $KMnO_4$ in H_2O (1.86 ml) were added succesively to a stirred aqueous solution of $NaIO_4$ (2.0 g in 18 ml H_2O) at room temperature. After 1 h, the reaction mixture was filtered, then the filtrate was mixed with CH_2Cl_2, and the mixture was washed with aqueous NH_4Cl and brine, dried over anhydrous $MgSO_4$, and evaporated *in vacuo* to leave the carboxylic acid **8** as a colorless oil (425 mg, 80%). $[\alpha]_D^{18}$ +16° ($c=3.60$, $CHCl_3$). ^{1}H-NMR δ: 1.06 (3H, d, $J=6.6$ Hz), 1.17 (1H, ddd, $J=14.0$, 8.5, 3.5 Hz), 1.42 (3H, s), 1.43 (3H, s), 1.76 (1H, ddd, $J=14.0$, 7.0, 3.0 Hz), 1.86 (1H, ddd, $J=14.0$, 6.5, 5.0 Hz), 1.97—2.03 (1H, m), 2.68 (2H, d, $J=6.6$ Hz), 2.90—2.97 (1H, m), 3.15 (2H, d, $J=22.0$ Hz), 3.18 (1H, t, $J=1.0$ Hz), 3.50 (3H, s), 3.41—3.57 (2H, m), 3.64 (3H, d, $J=9.2$ Hz), 3.76 (3H, d, $J=11.0$ Hz), 3.78 (3H, d, $J=11.0$ Hz), 3.80 (3H, s), 4.20 (1H, dt, $J=6.6$, 1.0 Hz), 4.40 (2H, s), 5.07—5.30 (2H, m), 6.86 (2H, d, $J=8.4$ Hz), 7.22 (2H, d, $J=8.4$ Hz). MS *m/z* (relative intensity): 556 (M^+-18, 0.3%), 395 (1.7), 377 (1.8), 202 (13), 180 (21.5), 121 (100). Exact MS *m/z* Calcd for $C_{27}H_{41}O_{10}$ (M^+-18): 556.2438. Found: 556.2422. IR ν (neat) cm^{-1}: 3450 (OH), 1720, 1705 (CO).

4-Formyl-1(*R*)-methyl-3(*Z*)-butenyl (3*R*,4*S*,5*S*,6*R*,8*R*)-10-Dimethoxyphosphono-3,5-isopropylidenedioxy-4-methoxy-6-[2-(4-methoxybenzyloxy)-ethyl]-8-methyl-9-oxodecanoate (30) 2,4,6-Trichlorobenzoyl chloride (185 mg, 0.76 mmol) was added dropwise to a stirred solution of **8** (425 mg, 0.74 mmol) and Et_3N (0.105 ml, 0.76 mmol) in THF (10 ml) at room temperature. After 1 h, precipitated $Et_3N \cdot HCl$ was filtered off and the filtrate was evaporated *in vacuo* to leave an oil, which was dissolved in toluene (10 ml). To this stirred solution, a mixture of **9** (100 mg, 0.88 mmol) and DMAP (93 mg, 0.76 mmol) in toluene (10 ml) was added. After 1.5 h, the reaction mixture was diluted with ether, washed with brine and saturated $NaHCO_3$, dried ($MgSO_4$), and evaporated *in vacuo*. The residue was chromatographed on a silica gel column with hexane–EtOAc (1 : 2) to give **30** as a colorless oil (388 mg, 78%). $[\alpha]_D^{17}$ −4.8° ($c=2.92$, $CHCl_3$). ^{1}H-NMR δ: 1.06 (3H, d, $J=7.0$ Hz), 1.18 (1H, ddd, $J=14.0$, 8.5, 3.5 Hz), 1.29 (3H, d, $J=6.5$ Hz), 1.41 (6H, s), 1.67—1.91 (2H, m), 1.95—2.05 (1H, m), 2.57—2.65 (4H, m), 2.88—3.01 (1H, m), 3.14 (2H, d, $J=22.5$ Hz), 3.14 (1H, t, $J=0.5$ Hz), 3.44—3.53 (3H, m), 3.47 (3H, s), 3.63 (1H, dd, $J=9.2$, 0.5 Hz), 3.76 (3H, d, $J=11.5$ Hz), 3.77 (3H, d, $J=11.5$ Hz), 3.80 (3H, s), 4.22 (1H, ddd, $J=7.5$, 6.5, 1.5 Hz), 4.40 (2H, s), 5.13 (1H, sextet, $J=6.5$ Hz), 6.16 (1H, ddt, $J=16.0$, 7.5, 1.2 Hz), 6.77 (1H, dt, $J=16.0$, 7.5 Hz), 6.86 (1H, d, $J=8.4$ Hz), 7.23 (1H, d, $J=8.4$ Hz), 9.51 (1H, d, $J=7.5$ Hz). FI-MS *m/z* 671 (M^++1, 84%), 670 (M^+, 100), 121 (70.9). IR ν (neat) cm^{-1}: 1730, 1710, 1695 (CO).

6″-Dihydro-6″-*O*-(4-methoxybenzyl)-3,5-*O*-isopropylideneniddanolide (10) K_2CO_3 (47 mg, 0.34 mmol) was added to the solution of **30** (38.0 mg, 0.056 mmol) and 18-crown-6 (180 mg, 0.684 mmol) in toluene (57 ml), and the reaction mixture was stirred vigorously at room temperature. After 17 h, the reaction mixture was quenched by addition of saturated NH_4Cl (10 ml), and the mixture was poured into ether (20 ml). The organic layer was washed with saturated KCl, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was chromatographed on a silica gel column with hexane–EtOAc (3 : 1) to give **10** as a colorless oil (17.6 mg, 57%). $[\alpha]_D^{19}$ +1.8° ($c=2.19$, $CHCl_3$). ^{1}H-NMR δ: 1.15 (3H, d, $J=7.0$ Hz), 1.31 (3H, d, *J*=6.2 Hz), 1.36 (3H, s), 1.37—1.50 (2H, m), 1.40 (3H, s), 1.62—1.73 (1H, m), 2.00 (1H, dt, *J*=14.3, 8.3 Hz), 2.15 (1H, ddt, *J*=14.0, 5.5, 7.0 Hz), 2.31 (1H, ddd, *J*=14.0, 10.5, 9.5 Hz), 2.46 (1H, dd, *J*=14.5, 4.5 Hz), 2.50 (1H, ddd, *J*=14.5, 4.5, 2.8 Hz), 2.60—2.70 (1H, m), 2.71 (1H, dd, *J*=14.5, 8.5 Hz), 2.92 (1H, dd, *J*=1.5, 1.0 Hz), 3.427 (1H, ddd, *J*=13.5, 6.0, 2.0 Hz), 3.431 (1H, ddd, *J*=13.5, 6.0, 2.0 Hz), 3.56 (3H, s), 3.76 (1H, dd, *J*=4.0, 1.0 Hz), 3.81 (3H, s), 4.11 (1H, ddd, *J*=8.5, 4.5, 1.5 Hz), 4.40 (2H, s), 5.16 (1H, ddq, *J*=10.5, 2.8, 6.2 Hz), 6.04 (1H, ddd, *J*=15.0, 6.3, 4.5 Hz), 6.18 (1H, dd, *J*=15.5, 10.0 Hz), 6.35 (1H, d, *J*=15.5 Hz), 6.88 (2H, d, *J*=8.8 Hz), 6.96 (1H, dd, *J*=15.5, 10.0 Hz), 7.24 (2H, d, *J*=8.8 Hz). MS *m/z* (relative intensity): 544 (M^+, 0.2%), 408 (0.3), 318 (4), 249 (4), 234 (4), 150 (11), 121 (100). Exact MS *m/z* Calcd for $C_{31}H_{44}O_8$ (M^+): 544.3037. Found: 544.3053. IR ν (neat) cm^{-1}: 1720, 1675 (CO).

(6″-Dihydro-3,5-*O*-isopropylidene)niddanolide (31) DDQ (33 mg, 0.15 mmol) was added to a stirred solution of **10** (39.6 mg, 0.073 mmol) in CH_2Cl_2 (1 ml) and H_2O (0.05 ml). Stirring was continued for 1 h, then the reaction mixture was quenched by addition of saturated $NaHCO_3$, and the mixture was extracted with EtOAc. The extract was dried ($MgSO_4$) and concentrated to leave an oil, which was purified on a silica gel column with hexane–EtOAc (1 : 1) to give **31** as a colorless oil (26 mg, 84%). $[\alpha]_D^{21}$ +14.4° (*c*=1.38, $CHCl_3$). ^{1}H-NMR δ: 1.19 (3H, d, *J*=7.0 Hz), 1.32 (3H, d, *J*=6.2 Hz), 1.43 (6H, s), 1.35—1.79 (4H, m), 1.98—2.10 (3H, m), 2.23—2.38 (1H, m), 2.44—2.55 (3H, m), 2.64—2.75 (2H, m), 3.53—3.61 (1H, m), 3.57 (3H, s), 3.66—3.72 (1H, m), 3.79 (1H, dd, *J*=4.0, 1.1 Hz), 4.12 (1H, dq, *J*=4.4, 1.5 Hz), 5.10—5.21 (1H, m), 6.04 (1H, ddd, *J*=15.0, 6.3, 4.5 Hz), 6.18 (1H, dd, *J*=15.5, 10.0 Hz), 6.35 (1H, d, *J*=15.5 Hz), 7.03 (1H, dd, *J*=15.5, 10.0 Hz). MS *m/z* (relative intensity): 424 (M^+, 0.4%), 409 (5), 334 (5), 250 (24), 233 (55), 150 (79), 121 (100). Exact MS *m/z* Calcd for $C_{23}H_{36}O_7$ (M^+): 424.2461. Found: 424.2466. IR ν (neat) cm^{-1}: 3400 (OH), 1720, 1670 (CO).

(3,5-*O*-Isopropylidene)niddanolide (32) Dry Me_2SO (0.24 ml, 3.39 mmol) in dry CH_2Cl_2 (1 ml) was added dropwise during 15 min to an efficiently stirred solution of oxalyl chloride (0.15 ml, 1.7 mmol) in dry CH_2Cl_2 (1 ml), cooled to below −78 °C under an argon atmosphere. After 15 min at −78 °C, a solution of **31** (0.36 g, 0.85 mmol) was added to the mixture during 10 min. Stirring was continued at −78 °C for 30 min, then Et_3N (0.7 ml, 5 mmol) was added dropwise, and after removal of the cooling bath, the reaction mixture was allowed to warm to room temperature (over *ca.* 1 h). Then H_2O (20 ml) was added, the organic layer was separated, and the aqueous layer was extracted with ether (30 ml × 2). The combined extracts were washed with brine, dried over $MgSO_4$, and evaporated *in vacuo*. The residue was chromatographed on a silica gel column with hexane–EtOAc (2 : 1) as the eluant to give the aldehyde **32** (0.34 g, 95%) as a colorless oil. $[\alpha]_D^{17.5}$ −1.6° (*c*=1.50, $CHCl_3$). ^{1}H-NMR δ: 1.19 (3H, d, *J*=6.8 Hz), 1.32 (3H, d, *J*=6.3 Hz), 1.33 (3H, s), 1.37 (1H, ddd, *J*=15.0, 9.8, 3.4 Hz), 1.39 (3H, s), 1.87 (1H, ddd, *J*=14.6, 10.3, 6.8 Hz), 2.24 (1H, ddd, *J*=17.1, 7.8, 2.0 Hz), 2.32 (1H, dt, *J*=14.6, 4.4 Hz), 2.39—2.47 (1H, m), 2.49 (1H, dd, *J*=14.6, 3.9 Hz), 2.4 (1H, ddd, *J*=14.6, 4.9, 2.9 Hz), 2.72 (1H, dd, *J*=15.1, 7.8 Hz), 2.74 (1H, m), 2.91 (1H, s), 3.07 (1H, ddd, *J*=17.6, 5.4, 1.5 Hz), 3.52 (3H, s), 3.87 (1H, dd, *J*=4.9, 0.5 Hz), 4.15 (1H, ddd, *J*=7.8, 3.9, 1.5 Hz), 5.22 (1H, ddq, *J*=9.3, 2.9, 6.3 Hz), 6.10 (1H, ddd, *J*=15.6, 10.3, 4.9 Hz), 6.19 (1H, dd, *J*=15.6, 10.3 Hz), 6.26 (1H, d, *J*=15.6 Hz), 7.01 (1H, dd, *J*=15.6, 10.3 Hz), 9.70 (1H, dd, *J*=2.0, 1.7 Hz). MS *m/z* (relative intensity): 407 ($M^+ - 15$, 8.6%), 364 (5.5), 248 (24), 150 (93), 121 (100), 71 (84.5). Exact MS *m/z* Calcd for $C_{22}H_{31}O_7$ ($M^+ - 15$): 407.2070. Found: 407.2080. IR ν ($CHCl_3$) cm^{-1}: 1740 (shoulder), 1720, 1680 (CO).

Niddanolide Hemiacetal (5) A solution of **31** (0.34 g, 0.80 mmol) in 1 N HCl (2 ml) and THF (10 ml) was stirred at room temperature for 6 h. After neutralization with solid $NaHCO_3$, the reaction mixture was evaporated to dryness. CH_2Cl_2 (20 ml) and water (10 ml) were added to the residue, and the CH_2Cl_2 layer was separated. The aqueous layer was extracted with CH_2Cl_2, and the combined extracts were dried over $MgSO_4$. After evaporation of the solvent, purification of the residue on a silica gel column with hexane–EtOAc (1 : 1) as the eluant afforded **5** as colorless fine needles (256 mg, 85%), mp 188—189 °C. $[\alpha]_D^{16.5}$ +13.3° (*c*=1.07, $CHCl_3$). ^{1}H-NMR δ: 1.20 (0.34H, d, *J*=7.0 Hz), 1.21 (0.66H, d, *J*=7.0 Hz), 1.30 (3H, s), 1.33 (3H, s), 1.50—1.75 (2H, m), 1.80—2.00 (1H, m), 2.10 (1H, dd, *J*=13.0, 6.0 Hz), 2.18 (1H, dd, *J*=16.0, 1.5 Hz), 2.20—2.70 (2H, m), 2.80 (0.66H, dd, *J*=16.0, 8.5 Hz), 2.84 (0.34H, dd, *J*=16.0, 11.0 Hz), 3.31 (0.34H, dd, *J*=6.5, 1.0 Hz), 3.47—3.59 (1H, m), 3.52 (2H, s), 3.55 (1H, s), 3.65 (0.66H, dt, *J*=11.5, 1.5 Hz), 3.89 (0.66H, s), 3.95 (0.34H, s), 4.13 (1H, dd, *J*=7.0, 5.5 Hz), 4.40 (1H, dd, *J*=9.0, 3.5 Hz), 5.24 (1H, ddq, *J*=18.0, 3.0, 7.0 Hz), 5.46 (0.34H, dt, *J*=6.5, 2.0 Hz), 5.57 (0.66H, t, *J*=4.5 Hz), 6.00—6.20 (2H, m), 6.30 (0.34H, d, *J*=15.5 Hz), 6.34 (0.66H, d, *J*=15.5 Hz), 7.08 (0.34H, dd, *J*=15.5, 9.5 Hz), 7.16 (0.66H, dd, *J*=15.5, 9.5 Hz). MS *m/z* (relative intensity): 382 (M^+, 6%), 364 (10), 231 (16.5), 150 (94), 121 (100). Exact MS *m/z* Calcd for $C_{20}H_{30}O_7$ (M^+): 382.1992. Found: 382.1999. *Anal.* Calcd for $C_{20}H_{30}O_7$: C, 62.81; H, 7.91. Found: C, 62.65; H, 7.91. IR ν (neat) cm^{-1}: 3500 (OH), 1705, 1675 (CO). UV $\lambda_{max}^{ethanol}$ nm (log ε): 274 (4.28).

Niddanolide 4-Methoxybenzylacetal (33α, β) A solution of **5** (120 mg, 0.314 mmol) in CH_2Cl_2 (2 ml) was treated with 4-methoxybenzyl (MPM) alcohol (164 mg, 1.19 mmol) and CSA (7.3 mg, 10 mol%) at room temperature for 3 h. After neutralization with TEA (0.1 ml), the reaction mixture was concentrated *in vacuo*, and the residue was purified on a silica gel column with hexane–EtOAc (2 : 1) as the eluant to give **33β** as colorless prisms (97.5 mg, 62%), mp 161.5—163 °C. $[\alpha]_D^{24}$ +57.8° (*c*=0.95, $CHCl_3$). ^{1}H-NMR δ: 1.19 (3H, d, *J*=6.8 Hz), 1.32 (3H, d, *J*=6.2 Hz), 1.56 (1H, dd, *J*=14.5, 11.5 Hz), 1.90—2.05 (3H, m), 2.07 (1H, dd, *J*=16.2, 2.0 Hz), 2.16 (1H, ddd, *J*=14.2, 13.0, 9.5 Hz), 2.44 (1H, ddq, *J*=9.5, 2.5, 6.8 Hz), 2.54 (1H, ddd, *J*=13.0, 4.0, 2.5 Hz), 2.87 (1H, dd, *J*=16.5, 11.0 Hz), 3.06 (1H, dd, *J*=9.0, 1.0 Hz), 3.58 (3H, s), 3.67 (1H, dt, *J*=10.5, 1.5 Hz), 3.79 (3H, s), 4.34 (1H, dd, *J*=9.0, 3.0 Hz), 4.42 (1H, d, *J*=11.5 Hz), 4.70 (1H, d, *J*=11.5 Hz), 5.23 (1H, ddq, *J*=13.0, 2.5, 6.2 Hz), 5.24 (1H, dd, *J*=5.5, 3.5 Hz), 6.07 (1H, ddd, *J*=15.0, 9.5, 4.0 Hz), 6.15 (1H, dd, *J*=15.0, 9.5 Hz), 6.34 (1H, d, *J*=15.0 Hz), 6.84—6.89 (2H, m), 7.16 (1H, dd, *J*=15.0, 9.5 Hz), 7.24—7.29 (2H, m). MS *m/z* (relative intensity): 502 (M^+, 0.4%), 470 (0.2), 381 (1.4), 366 (2.5), 249 (4.2), 231 (11.2), 187 (2.2), 150 (5.0), 121 (100), 109 (6.0). Exact MS *m/z* Calcd for $C_{28}H_{38}O_8$ (M^+): 502.2567. Found: 502.2605. *Anal.* Calcd for $C_{28}H_{38}O_8$: C, 66.91; H, 7.62. Found: C, 66.78; H, 7.82. IR ν (neat) cm^{-1}: 3600 (OH), 1735, 1710, 1665 (CO), 1615, 1580, 1450, 1290, 1200, 1140. UV $\lambda_{max}^{ethanol}$ nm (log ε): 274 (4.34).

Continued elution provided **33α** as colorless prisms (49.5 mg, 31%), mp 141—142 °C. $[\alpha]_D^{27}$ +8.5° (*c*=1.3, $CHCl_3$). ^{1}H-NMR δ: 1.21 (3H, d, *J*=7.0 Hz), 1.32 (3H, d, *J*=6.5 Hz), 1.54 (1H, dd, *J*=12.0, 2.5 Hz), 1.77 (1H, ddd, *J*=12.0, 7.0, 5.0 Hz), 1.85 (1H, d, *J*=13.5 Hz), 1.91 (1H, ddd, *J*=13.0, 12.0, 2.5 Hz), 2.06—2.24 (1H, m), 2.16 (1H, dd, *J*=16.1, 1.5 Hz), 2.44 (1H, ddq, *J*=13.5, 2.5, 7.0 Hz), 2.53 (1H, dt, *J*=12.5, 3.0 Hz), 2.86 (1H, dd, *J*=16.1, 11.0 Hz), 3.08 (1H, d, *J*=9.5 Hz), 3.57 (3H, s), 3.65 (1H, d, *J*=11.0 Hz), 3.81 (3H, s), 4.13 (1H, dd, *J*=9.5, 4.0 Hz), 4.42 (1H, d, *J*=11.5 Hz), 4.72 (1H, d, *J*=11.5 Hz), 5.19 (1H, d, *J*=6.0 Hz), 5.21 (1H, m), 6.05 (1H, ddd, *J*=15.0, 10.0, 4.5 Hz), 6.14 (1H, dd, *J*=15.0, 10.0 Hz), 6.38 (1H, d, *J*=15.0 Hz), 6.84—6.90 (2H, m), 7.15 (1H, dd, *J*=15.0, 9.5 Hz), 7.21—7.28 (2H, m). MS *m/z* (relative intensity): 502 (M^+, 0.04%), 470 (0.1), 381 (0.8), 366 (5.2), 316 (2.3), 231 (7.7), 187 (2.7), 150 (8.1), 121 (100), 109 (7.7). Exact MS *m/z* Calcd for $C_{28}H_{38}O_8$ (M^+): 502.2567. Found: 502.2541. *Anal.* Calcd for $C_{28}H_{38}O_8$: C, 66.91; H, 7.62. Found: C, 66.72; H, 7.81. IR ν (neat) cm^{-1}: 3450 (OH), 1700, 1680 (CO), 1635 (C=C).

Carbonolide B 4-Methoxybenzylacetal (34α, β) A solution of **33β** (31 mg, 0.062 mmol) in a mixture of acetic anhydride (18 μl), Et_3N (77 μl), DMAP (1 mg), and CH_2Cl_2 (2 ml) was allowed to stand at room temperature for 3 h. The reaction mixture was diluted with CH_2Cl_2 and washed with saturated aqueous NH_4Cl, and brine, and dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue was chromatographed on a silica gel column with AcOEt–hexane (1 : 2) as the eluant to give **34β** as colorless prisms (33.0 mg, 98%), mp 148.5—149 °C. **34β**: $[\alpha]_D^{24}$ +93.8° (*c*=0.82, $CHCl_3$). ^{1}H-NMR δ: 1.19 (3H, d, *J*=7.0 Hz), 1.28 (3H, d, *J*=6.5 Hz), 1.88—1.96 (1H, m), 2.03 (3H, ddd, *J*=11.0, 10.0, 5.2 Hz), 2.07 (3H, s), 2.19 (1H, ddd, *J*=13.2, 10.0, 5.2 Hz), 2.20 (1H, dd, *J*=14.5, 1.5 Hz), 2.51 (1H, dt, *J*=13.0, 3.7 Hz), 2.55 (1H, ddq, *J*=9.5, 2.8, 6.5 Hz), 2.97 (1H, dd, *J*=14.5, 11.5 Hz), 3.21 (1H, dd, *J*=9.0, 1.5 Hz), 3.61 (3H, s), 3.80 (3H, s), 3.96 (1H, dd, *J*=9.2, 3.5 Hz), 4.42 (1H, d, *J*=11.5 Hz), 4.68 (1H, d, *J*=11.5 Hz), 5.01 (1H, ddq, *J*=9.5, 2.8, 6.5 Hz), 5.06 (1H, dt, *J*=11.5, 1.5 Hz), 5.32 (1H, dd, *J*=6.0, 4.0 Hz), 6.07 (1H, ddd, *J*=15.0, 10.0, 4.0 Hz), 6.08 (1H, dd, *J*=15.0, 10.0 Hz), 6.31 (1H, d, *J*=15.5 Hz), 6.85—6.88 (2H, m), 7.25—7.28 (2H, m), 7.29 (1H, dd, *J*=15.5, 10.0 Hz). MS *m/z* (relative intensity): 544 (M^+, 0.2%), 423 (4.0), 408 (5.6), 249 (4.8), 231 (8.8), 121 (100). Exact MS *m/z* Calcd for $C_{30}H_{40}O_9$ (M^+): 544.2673. Found: 544.2661.

Similarly, **33α** (21 mg, 0.042 mmol) gave **34α** as a colorless oil (22.5 mg, 99%). **34α**: $[\alpha]_D^{24}$ +18.2° (*c*=0.85, $CHCl_3$). ^{1}H-NMR δ: 1.20 (3H, d, *J*=7.0 Hz), 1.27 (3H, d, *J*=6.5 Hz), 1.57 (1H, t, *J*=10.5 Hz), 1.83—1.86 (1H, m), 1.91 (1H, d, *J*=13.5 Hz), 1.99—2.10 (2H, m), 2.05 (3H, s), 2.185 (1H, ddd, *J*=13.5, 11.5, 8.5 Hz), 2.193 (1H, dd, *J*=15.0, 1.5 Hz), 2.52 (1H, dt, *J*=13.5, 3.8 Hz), 2.47—2.60 (1H, m), 2.97 (1H, dd, *J*=15.0, 11.0 Hz), 3.22 (1H, dd, *J*=9.5, 1.0 Hz), 3.59 (3H, s), 3.74 (1H, dd, *J*=9.7, 3.3 Hz), 3.81 (3H, s), 4.41 (1H, d, *J*=11.5 Hz), 4.69 (1H, d, *J*=11.5 Hz), 5.00 (1H, ddq, *J*=9.5, 3.0, 6.5 Hz), 5.03 (1H, dt, *J*=11.0, 1.0 Hz), 5.15 (1H, d,

J=6.0 Hz), 6.05 (1H, ddd, J=15.5, 10.5, 4.5 Hz), 6.18 (1H, dd, J=15.0, 10.0 Hz), 6.36 (1H, d, J=15.0 Hz), 6.85—6.88 (2H, m), 7.22—7.25 (2H, m), 7.26 (1H, dd, J=15.5, 10.0 Hz). MS m/z (relative intensity): 502 (M^+-32, 0.1%), 423 (1.0), 408 (4.0), 231 (6.7), 121 (100). IR ν (neat) cm^{-1}: 1740, 1730, 1680 (CO), 1630, 1600 (C=C).

Platenolide W$_1$ 4-Methoxybenzylacetal (35α,β) A solution of **33β** (11 mg, 0.022 mmol) in a mixture of propionic anhydride (16 μl), Et_3N (46 μl) and CH_2Cl_2 (2 ml) was allowed to stand at room temperature for 3 h. The reaction mixture was diluted with CH_2Cl_2 and washed with saturated aqueous NH_4Cl, and brine, and dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue was chromatographed on a silica gel column with AcOEt–hexane (1 : 2) as the eluant to give **35β** as a colorless oil (9.5 mg, 78%). **35β**: $[\alpha]_D^{21.5}$ +80.5° (c=0.38, $CHCl_3$). ^{1}H-NMR δ: 1.12 (3H, d, J=7.5 Hz), 1.18 (3H, d, J=7.0 Hz), 1.28 (3H, d, J=6.0 Hz), 1.60 (1H, dd, J=14.0, 9.0 Hz), 1.85—2.00 (1H, m), 2.07 (1H, dd, J=13.0, 6.0 Hz), 2.20 (1H, ddd, J=13.0, 10.5, 9.5 Hz), 2.21 (1H, dd, J=15.0, 1.5 Hz), 2.35 (1H, q, J=7.5 Hz), 2.36 (1H, q, J=7.5 Hz), 2.53—2.66 (1H, m), 2.96 (1H, dd, J=15.0, 11.0 Hz), 3.21 (1H, dd, J=9.5, 1.0 Hz), 3.581 (1H, m), 3.60 (3H, s), 3.80 (3H, s), 3.96 (1H, dd, J=9.5, 3.5 Hz), 4.42 (1H, d, J=11.5 Hz), 4.68 (1H, d, J=11.5 Hz), 4.99 (1H, m), 5.08 (1H, d, J=11.0 Hz), 5.21 (1H, dd, J=5.5, 4.2 Hz), 6.07 (1H, ddd, J=15.0, 9.5, 4.0 Hz), 6.19 (1H, dd, J=15.0, 10.0 Hz), 6.30 (1H, d, J=15.5 Hz), 6.86—6.88 (2H, m), 7.22—7.24 (2H, m), 7.29 (1H, dd, J=15.5, 10.0 Hz). MS m/z (relative intensity): 558 (M^+, 0.4%), 442 (4.7), 231 (10), 189 (5.7), 121 (100), 57 (12.8). Exact MS m/z Calcd for $C_{31}H_{42}O_6$ (M^+): 558.2829. Found: 558.2839. IR ν (neat) cm^{-1}: 1735, 1720, 1685 (CO), 1635 (C=C).

Similarly, **33α** (12.3 mg, 0.024 mmol) gave **35α** as a colorless oil (10.3 mg, 75%). **35α**: $[\alpha]_D^{21.5}$ +15.6° (c=0.41, $CHCl_3$). ^{1}H-NMR δ: 1.11 (3H, d, J=7.5 Hz), 1.20 (3H, d, J=7.5 Hz), 1.28 (3H, d, J=6.5 Hz), 1.55—1.64 (1H, m), 1.65—1.75 (1H, m), 1.82—1.88 (1H, m), 1.92 (1H, d, J=13.6 Hz), 2.04 (1H, m), 2.19 (1H, dd, J=15.0, 1.0 Hz), 2.32 (1H, q, J=7.5 Hz), 2.33 (1H, q, J=7.5 Hz), 2.51 (1H, dt, J=13.0, 3.5 Hz), 2.47—2.60 (1H, m), 2.97 (1H, dd, J=15.0, 11.5 Hz), 3.21 (1H, dd, J=9.5, 1.0 Hz), 3.581 (1H, dd, J=8.5, 2.5 Hz), 3.584 (3H, s), 3.73 (1H, dd, J=9.5, 3.0 Hz), 3.80 (3H, s), 4.40 (1H, d, J=11.5 Hz), 4.68 (1H, d, J=11.5 Hz), 4.97 (1H, m), 5.04 (1H, d, J=11.0 Hz), 5.14 (1H, d, J=6.0 Hz), 6.06 (1H, ddd, J=15.5, 9.5, 4.5 Hz), 6.18 (1H, dd, J=15.0, 10.0 Hz), 6.36 (1H, d, J=15.5 Hz), 6.86—6.88 (2H, m), 7.22—7.24 (2H, m), 7.27 (1H, dd, J=15.5, 10.0 Hz). MS m/z (relative intensity): 558 (M^+, 0.4%), 526 (0.42), 442 (0.42), 437 (6.0), 396 (5.3), 348 (14.9), 231 (44.2), 189 (36), 121 (100), 57 (99). Exact MS m/z Calcd for $C_{31}H_{42}O_9$ (M^+): 558.2829. Found: 558.2848. IR ν (neat) cm^{-1}: 1730, 1680 (CO), 1635 (C=C).

Carbonolide B Hemiacetal (1) A solution of **34α,β** (18.8 mg, 0.035 mmol) in trifluoroacetic acid (0.8 ml) and water (0.2 ml) was stirred at 0 °C for 15 min. After neutralization with saturated aqueous $NaHCO_3$, the reaction mixture was extracted with AcOEt three times, and the combined extracts were washed with brine, and dried over $MgSO_4$. After evaporation of the solvent, purification of the residue on a silica gel column with hexane–EtOAc (1 : 2) as the eluant afforded **1** as an amorphous solid (13.5 mg, 92%), mp 86—87.5 °C. $[\alpha]_D^{19}$ +44° (c=0.8, $CHCl_3$). ^{1}H-NMR δ: 1.21 (0.75H, d, J=7.0 Hz), 1.27 (0.25H, d, J=7.0 Hz), 1.29 (1H, d, J=6.5 Hz), 1.87 (1H, dd, J=13.0, 5.5 Hz), 1.94—2.03 (1H, m), 2.06 (0.25H, s), 2.08 (0.75H, s), 2.09—2.15 (1H, m), 2.20 (2H, d, J=14.0 Hz), 2.25—2.35 (1H, m), 2.51 (1H, ddd, J=14.0, 3.5, 2.8 Hz), 2.53—2.65 (1H, m), 2.89 (0.25H, dd, J=15.0, 11.0 Hz), 2.95 (0.75H, dd, J=15.0, 11.0 Hz), 3.17 (0.75H, d, J=9.5 Hz), 3.24 (0.25H, dd, J=8.0, 1.0 Hz), 3.55 (0.7H, s), 3.57 (0.3H, s), 3.78 (0.3H, dd, J=7.5, 4.5 Hz), 4.03 (0.67H, dd, J=9.5, 3.2 Hz), 4.55—5.09 (1H, m), 5.04 (0.7H, d, J=10.5 Hz), 5.15 (0.3H, ddd, J=10.5, 2.5, 1.0 Hz), 5.44 (0.3H, dd, J=6.2, 1.8 Hz), 5.57 (0.7H, t, J=5.0 Hz), 6.10 (1H, d, J=15.0 Hz), 6.18 (1H, d, J=15.0 Hz), 6.33 (1H, d, J=15.5 Hz), 7.22 (0.3H, dd, J=15.5, 10.0 Hz), 7.28 (0.7H, dd, J=15.5, 10.0 Hz). MS m/z (relative intensity): 424 (M^+, 3%), 406 (3.4), 248 (6.4), 231 (8.5), 175 (6.4), 150 (20), 121 (56), 98 (30), 71 (43), 43 (100). Exact MS m/z Calcd for $C_{22}H_{32}O_8$ (M^+): 424.2088. Found: 424.2098. IR ν (neat) cm^{-1}: 3425, 1740, 1730, 1680, 1640, 1600, 1450, 1370, 1310, 1240, 1120.

Platenolide W$_1$ Hemiacetal (6) A solution of **35α,β** (9.1 mg, 0.016 mmol) in trifluoroacetic acid (0.8 ml) and water (0.2 ml) was stirred at 0°C for 15 min. After neutralization with saturated aqueous $NaHCO_3$, the reaction mixture was extracted with AcOEt three times, and the combined extracts were washed with brine and dried over $MgSO_4$. After evaporation of the solvent, purification of the residue on a silica gel column with hexane–EtOAc (1 : 2) as the eluant afforded **6** as an amorphous solid (6.8 mg, 97%), mp 84.5—86 °C. $[\alpha]_D^{19}$ +41.5° (c=0.68, $CHCl_3$). ^{1}H-NMR δ: 1.12 (0.9H, d, J=7.5 Hz), 1.13 (2.1H, d, J=7.5 Hz), 1.20 (3H, d, J=7.0 Hz), 1.26 (0.9H, d, J=6.0 Hz), 1.28 (2.1H, d, J=6.0 Hz), 1.55—1.75 (2H, m), 1.80—1.89 (1H, m), 1.95—2.05 (1H, m), 2.10—2.16 (0.3H, m), 2.21 (1H, dd, J=13.5, 2.0 Hz), 2.45 (2H, dq, J=2.5, 7.5 Hz), 2.51 (1H, ddd, J=13.5, 4.7, 3.0 Hz), 2.60 (0.7H, dt, J=6.5, 2.5 Hz), 2.63 (0.3H, t, J=6.2 Hz), 2.88 (0.3H, dd, J=15.5, 9.5 Hz), 2.94 (0.7H, dd, J=15.0, 11.5 Hz), 3.18 (0.7H, dd, J=9.5, 1.2 Hz), 3.27 (0.3H, dd, J=7.5, 3.0 Hz), 3.55 (2H, s), 3.57 (1H, s), 3.79 (0.3H, dd, J=7.5, 5.0 Hz), 4.02 (0.7H, dd, J=9.5, 3.5 Hz), 4.93—5.06 (1H, m), 5.05 (0.7H, dt, J=11.2, 1.8 Hz), 5.18 (0.3H, ddd, J=9.5, 3.5, 2.0 Hz), 5.43 (0.3H, dd, J=6.5, 1.5 Hz), 5.56 (0.7H, t, J=5.0 Hz), 6.08 (1H, ddd, J=15.5, 10.0, 4.5 Hz), 6.19 (1H, dd, J=15.5, 9.5 Hz), 6.31 (1H, d, J=15.5 Hz), 7.21 (0.3H, dd, J=15.5, 10.0 Hz), 7.35 (0.7H, dd, J=15.5, 10.0 Hz). MS m/z (relative intensity): 438 (M^+, 6.4%), 420 (10), 248 (11), 231 (19), 189 (10.6), 150 (35), 121 (72), 57 (100). Exact MS m/z Calcd for $C_{23}H_{32}O_8$ (M^+): 438.2254. Found: 438.2229. IR ν (neat) cm^{-1}: 1735, 1680, 1640.

Carbonolide A 4-Methoxybenzylacetal (36) MCPBA (27 mg, 0.16 mmol; 85% purity) and $NaHCO_3$ (10 mg) were added to a stirred solution of **34β** (24 mg, 0.044 mmol) in CH_2Cl_2 (2 ml) at room temperature. After 8 h, the reaction mixture was poured into saturated aqueous NH_4Cl solution and extracted with CH_2Cl_2. The extract was washed with brine, dried over $MgSO_4$, and evaporated *in vacuo* to leave an oil, which was chromatographed on a silica gel column with EtOAc–hexane (1 : 2) as the eluant to give the epoxide (**36β**) as a colorless viscous oil (22.2 mg, 90%). **36β**: $[\alpha]_D^{12}$ +52.1° (c=1.12, $CHCl_3$). ^{1}H-NMR δ: 1.23 (3H, d, J=7.0 Hz), 1.28 (3H, d, J=6.2 Hz), 1.35 (1H, dd, J=10.7, 6.9 Hz), 1.38 (1H, ddd, J=14.3, 12.1, 9.0 Hz), 1.54 (1H, t, J=12.2 Hz), 1.71 (1H, m), 1.88 (1H, m), 1.91 (1H, ddd, J=6.2, 4.6, 0.7 Hz), 2.01 (3H, s), 2.03 (1H, m), 2.29 (1H, dt, J=14.0, 2.3 Hz), 2.30 (1H, dd, J=13.0, 2.7 Hz), 2.48 (1H, ddq, J=11.3, 3.5, 7.0 Hz), 2.98 (1H, dd, J=13.0, 12.0 Hz), 3.14 (1H, dt, J=9.8, 1.8 Hz), 3.20 (1H, dd, J=9.2, 1.8 Hz), 3.22 (1H, dd, J=9.8, 1.4 Hz), 3.63 (3H, s), 3.80 (3H, s), 4.02 (1H, dd, J=9.3, 3.7 Hz), 4.44 (1H, d, J=11.5 Hz), 4.69 (1H, d, J=11.5 Hz), 4.93 (1H, ddq, J=12.1, 2.7, 6.1 Hz), 4.98 (1H, ddd, J=11.7, 2.2, 1.7 Hz), 5.23 (1H, dd, J=5.5, 4.5 Hz), 6.61 (1H, dd, J=16.0, 9.5 Hz), 6.74 (1H, d, J=16.0 Hz), 6.86—6.89 (2H, m), 7.25—7.28 (2H, m). MS m/z (relative intensity): 560 (M^+, 0.56%), 528 (0.43), 439 (3.6), 424 (0.7), 248 (1.9), 175 (16), 163 (5.2), 143 (5.2), 121 (100), 109 (7.3). Exact MS m/z Calcd for $C_{30}H_{40}O_{10}$ (M^+): 560.2621. Found: 560.2602. IR ν (neat) cm^{-1}: 1730, 1690, 1630, 1615.

Similarly, **34α** (14 mg, 0.02 mmol) gave **36α** as a colorless viscous oil (12.0 mg, 83%). **36α**: ^{1}H-NMR δ: 1.23 (3H, d, J=7.0 Hz), 1.28 (3H, d, J=6.2 Hz), 1.40 (1H, dt, J=12.5, 2.5 Hz), 1.46 (1H, t, J=12.5 Hz), 1.89—2.10 (3H, m), 1.99 (3H, s), 2.30 (1H, m), 2.31 (1H, dd, J=13.0, 2.2 Hz), 2.50 (1H, m), 2.97 (1H, dd, J=12.5, 12.0 Hz), 3.16 (1H, dt, J=9.8, 1.8 Hz), 3.21 (1H, dd, J=9.2, 1.8 Hz), 3.24 (1H, dd, J=9.8, 0.5 Hz), 3.61 (3H, s), 3.81 (1H, dd, J=9.0, 4.0 Hz), 3.81 (3H, s), 4.42 (1H, d, J=11.5 Hz), 4.70 (1H, d, J=11.5 Hz), 4.93 (1H, ddq, J=12.0, 3.0, 6.5 Hz), 4.99 (1H, dt, J=11.7, 2.2, 1.7 Hz), 5.16 (1H, d, J=5.5 Hz), 6.58 (1H, dd, J=15.5, 8.8 Hz), 6.77 (1H, d, J=15.5 Hz), 6.86—6.89 (2H, m), 7.22—7.25 (2H, m). MS m/z (relative intensity): 560 (M^+, 4.4%), 528 (1.6), 439 (15), 423 (5.2), 175 (19), 121 (100). Exact MS m/z Calcd for $C_{30}H_{40}O_{10}$ (M^+): 560.2621. Found: 560.2629. UV $\lambda_{max}^{ethanol}$ nm (log ε): 224 (4.08).

EOP Aglycon 4-Methoxybenzylacetal (37β) MCPBA (10.7 mg, 0.06 mmol; 85% purity) and $NaHCO_3$ (6 mg) were added to a stirred solution of **35β** (8 mg, 0.014 mmol) in CH_2Cl_2 (1 ml) at room temperature. After 9 h, the reaction mixture was diluted with CH_2Cl_2, washed with saturated aqueous $NaHCO_3$ and brine, and dried over $MgSO_4$. The solvent was removed *in vacuo* to leave an oil, which was chromatographed on a silica gel column with AcOEt–hexane (1 : 2) as the eluant to give the epoxide (**37β**) as an oil (6.0 mg, 73%). **37β**: $[\alpha]_D^{21.5}$ +52.0° (c=0.70, $CHCl_3$). ^{1}H-NMR δ: 1.06 (3H, t, J=7.2 Hz), 1.22 (3H, d, J=7.0 Hz), 1.27 (3H, d, J=6.5 Hz), 1.34 (1H, dd, J=11.5, 7.0 Hz), 1.40 (1H, ddd, J=14.2, 12.0, 10.0 Hz), 1.63—1.74 (1H, m), 1.85—1.95 (1H, m), 2.06 (1H, dd, J=14.0, 6.0 Hz), 2.28 (1H, q, J=7.2 Hz), 2.29 (1H, q, J=7.2 Hz), 2.31 (1H, dd, J=12.5, 2.3 Hz), 2.31—2.42 (1H, m), 2.97 (1H, dd, J=12.5, 11.5 Hz), 3.19 (1H, dd, J=9.0, 2.0 Hz), 3.22 (1H, dd, J=9.2, 2.0 Hz), 3.24 (1H, dd, J=9.5, 1.4 Hz), 3.63 (3H, s), 3.80 (3H, s), 4.02 (1H, dd, J=9.5, 3.5 Hz), 4.43 (1H, d, J=11.0 Hz), 4.68 (1H, d, J=11.0 Hz), 4.90 (1H, ddq, J=12.5, 3.0, 6.5 Hz), 5.02 (1H, ddd, J=10.5, 3.0, 1.5 Hz), 5.25 (1H, dd, J=6.0, 4.5 Hz), 6.61 (1H, dd, J=15.5, 8.5 Hz), 6.74 (1H, d, J=15.5 Hz), 6.86—6.89 (2H, m), 7.24—7.28 (2H, m). MS m/z (relative intensity): 574 (M^+, 0.35%) 542 (0.21), 500 (0.15), 453 (3.3), 437 (1.5), 420 (0.72), 247 (2.7), 189 (15.6), 157 (4.6), 137 (6.7), 121 (100), 109 (10.4), 57 (19). Exact MS m/z Calcd for $C_{31}H_{42}O_{10}$ (M^+): 574.2778. Found: 574.2766. IR ν (neat) cm^{-1}: 1740, 1730, 1695 (CO), 1635, 1620 (C=C).

Carbonolide A Hemiacetal (2) DDQ (37 mg, 0.156 mmol) was added to a stirred solution of **36α,β** (22.6 mg, 0.04 mmol) in a mixture of CH_2Cl_2

and H_2O (20 : 1, 1.0 ml) at room temperature. After 1 h, the reaction mixture was poured into aqueous $NaHCO_3$ solution and extracted with CH_2Cl_2. The extract was washed with brine, dried over anhydrous $MgSO_4$, and evaporated *in vacuo* to leave an oil, which was chromatograhed on a silica gel column using EtOAc–hexane (1 : 1) as the eluant to give **2** as an amorphous solid (14.0 mg, 80%), mp 82.5—84 °C. $[\alpha]_D^{19}$ +15° (c=0.81, $CHCl_3$). ^{1}H-NMR δ: 1.25 (3H, d, J=7.0 Hz), 1.28 (3H, d, J=7.3 Hz), 1.36—1.43 (1H, m), 1.70—1.76 (0.7H, m), 1.77—1.84 (0.7H, m), 1.82 (1H, dd, J=6.0, 4.5 Hz), 1.83 (0.3H, dd, J=6.0, 4.5 Hz), 1.87 (0.3H, dd, J=6.0, 4.5 Hz), 2.00 (0.3H, s), 2.02 (0.7H, s), 2.12 (0.3H, dd, J=13.5, 5.5 Hz), 2.13 (0.7H, dd, J=13.5, 5.5 Hz), 2.30 (0.7H, dd, J=13.0, 2.8 Hz), 2.37 (0.3H, dd, J=8.0, 3.5 Hz), 2.45—2.63 (1H, m), 2.93 (0.3H, dd, J=13.0, 10.5 Hz), 2.94 (0.7H, dd, J=12.5, 11.7 Hz), 3.14 (0.3H, dt, J=13.0, 10.5 Hz), 3.20 (0.7H, dd, J=9.0, 1.5 Hz), 3.22 (0.7H, dd, J=9.0, 2.0 Hz), 3.27 (0.3H, dd, J=9.0, 2.0 Hz), 3.57 (0.7H, s), 3.60 (0.3H, s), 3.74 (0.3H, dd, J=9.0, 4.5 Hz), 3.78 (0.7H, dd, J=9.0, 4.5 Hz), 4.09 (0.7H, dd, J=9.5, 4.0 Hz), 4.11 (0.3H, t, J=7.0 Hz), 4.90—5.05 (1H, m), 4.98 (1H, ddd, J=10.5, 2.5, 1.5 Hz), 5.48 (0.3H, dd, J=6.0, 1.5 Hz), 5.59 (0.7H, dd, J=6.0, 4.0 Hz), 6.58 (0.3H, dd, J=16.0, 9.0 Hz), 6.60 (0.7H, dd, J=16.0, 9.0 Hz), 6.75 (0.3H, d, J=16.0 Hz), 6.76 (0.7H, d, J=16.0 Hz). MS m/z (relative intensity): 440 (M^+, 2.6%), 422 (4.5), 380 (5.2), 368 (4.2), 256 (24), 236 (21), 216 (99), 171 (32), 149 (61), 57 (100). Exact MS m/z Calcd for $C_{22}H_{32}O_9$ (M^+): 440.2047. Found: 440.2069. IR ν (neat) cm^{-1}: 1735, 1705, 1680.

EOP Aglycon Hemiacetal (7) DDQ (7 mg, 0.03 mmol) was added to a stirred solution of **37**α,β (6.0 mg, 0.01 mmol) in a mixture of CH_2Cl_2 and H_2O (20 : 1, 0.5 ml) at room temperature. After 50 min, the reaction mixture was poured into aqueous $NaHCO_3$ solution, and extracted with CH_2Cl_2. The extract was washed with brine, dried over anhydrous $MgSO_4$, and evaporated *in vacuo* to leave an oil, which was chromatographed on a silica gel column using EtOAc–hexane (2 : 1) as the eluant to give **7** as an amorphous solid (3.9 mg, 83%), mp 75—76 °C. $[\alpha]_D^{18.5}$ +12.6° (c=0.31, $CHCl_3$). ^{1}H-NMR δ: 1.07 (2.1H, t, J=7.0 Hz), 1.16 (0.9H, t, J=7.0 Hz), 1.25 (3H, d, J=7.3 Hz), 1.27 (3H, d, J=6.3 Hz), 1.40 (1H, dt, J=11.5, 2.0 Hz), 1.52 (1H, t, J=13.0 Hz), 1.61—1.74 (1H, m), 1.79—1.91 (1H, m), 2.13 (1H, dd, J=13.0, 6.0 Hz), 2.29 (1H, q, J=7.0 Hz), 2.30 (1H, q, J=7.0 Hz), 2.47—2.66 (1H, m), 2.91 (0.3H, dd, J=13.2, 11.2 Hz), 2.95 (0.7H, t, J=13.2 Hz), 3.11—3.27 (2H, m), 3.56 (2.1H, s), 3.59 (0.9H, s), 3.78 (0.3H, dd, J=9.0, 5.0 Hz), 4.10 (1H, dd, J=10.0, 4.0 Hz), 4.20—4.30 (0.3H, m), 4.47 (0.3H, J=9.5, 8.5 Hz), 4.86—4.98 (1H, m), 4.99 (0.7H, ddd, J=11.5, 3.0, 1.5 Hz), 5.06 (0.3H, ddd, J=11.5, 3.0, 2.5 Hz), 5.48 (0.3H, dd, J=5.5, 0.5 Hz), 5.58 (0.7H, dd, J=5.5, 4.0 Hz), 6.59 (0.3H, dd, J=15.5, 8.5 Hz), 6.62 (0.7H, dd, J=15.5, 8.5 Hz), 6.69 (0.7H, d, J=15.5 Hz), 6.70 (0.3H, d, J=15.5 Hz). MS m/z (relative intensity): 436 (M^+, 3.1%), 380 (3.5), 265 (1.7), 253 (2.3), 247 (4.4), 203 (4.4), 189 (8.5), 177 (4.6), 161 (8.3), 149 (11), 139 (8.3), 121 (21), 108 (73), 98 (72), 95 (31), 81 (31), 71 (57), 57 (100), 44 (85). Exact MS m/z Calcd for $C_{23}H_{32}O_8$: 436.2097. Found: 436.2079. IR ν (neat) cm^{-1}: 1740, 1705, 1680, 1625.

Crystal Structure of 34β Colorless prisms of **34**β were mounted on a Rigaku AFC-5 diffractometer and exposed to graphite monochromated Cu K_α radiation. The unit cell parameters are a=19.259(5)A, b=15.370(5)A, and c=10.022(3)A in space group $p2_12_12_1$ (z=4). Of the 2821 reflections measured with a $2\theta/\omega$ scan, 2274 were independently observed at the level of $F \geq 3(F)$. The structure was solved by MULTAN78[29] and refined by using the block-diagonal least-squares method with anisotropic temperature factors for non-hydrogen atoms. All hydrogen atoms were located from the difference Fourier map and refined with isotropic temperature factors. The final R factor was 0.056. Calculations were carried out with the DIRECT-SEARCH program system.[30] Four tables consisting of atomic fractional coordinates, bond lengths, and bond angles have been deposited as supplementary materials.

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