Structure Elucidation of Glycosidic Antibiotics, Glykenins, from *Basidiomycetes* sp. II.[1] Absolute Structures of Unusual Polyhydroxylated C_{26}-Fatty Acids, Aglycones of Glykenins

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The structures of three aglycones of glykenins, produced by *Basidiomycetes* sp., were determined to be (2*S*,16*R*,17*S*,21*R*)-2,16,17,21-, (2*S*,17*R*,18*S*,22*R*)-2,17,18,22-, and (2*S*,17*S*,18*S*,22*R*)-2,17,18,22-tetrahydroxyhexacosanoic acids (3a—c). The absolute configurations of two of the four hydroxy groups in 3a—c were established by chiral synthesis of the degradation products (6a—c and 7a—c). Chemical transformation of 3a—c to 6,8-dioxabicyclo[3.2.1]octane derivatives (18a—c) revealed the relative and absolute configurations of the acyclic 1,2-diol moieties in 3a—c.

Keywords *Basidiomycetes* sp.; 2,16,17,21-tetrahydroxyhexacosanoic acid; 2,17,18,22-tetrahydroxyhexacosanoic acid; (5*R*)-nonan-5-olide; (2*S*)-1,2,17-heptadecanetriol; absolute configuration; 1,2-diol; dibenzoate chirality method; 6,8-dioxabicyclo[3.2.1]octane derivative

In a preceding paper[1] we reported that a strain of *Basidiomycetes* sp. produced glycosidic antibiotics, glykenins (GK), which showed inhibitory activity against gram-positive bacteria, and we described the structure determination of deacetyl glykenins (DG)- A (**1a**), B (**1b**), and C (**1c**), which form the basic structures of glykenins (Chart 1). The antibiotics contain three unusual C_{26} long-chain fatty acids (as aglycones) and trisaccharides. The aglycones have four hydroxy groups and are regio- and stereoisomers of each other. The straight chain nature of the aglycones and the presence of many hydroxy groups are major obstacles in stereochemical elucidation. But degradation to simpler fragments followed by direct correlation with chiral synthetic specimens and careful chemical transformations enabled us to determine the absolute configurations of the hydroxy groups in the fatty acids. We report here the results of detailed stereochemical studies of the aglycones of glykenins.

Isolation and Structures of Aglycone Methyl Esters A (3a), B (3b), and C (3c) The ethyl acetate extract of the culture broth of a strain of *Basidiomycetes* sp. was chromatographed on Sephadex LH-20 to give GK complex, which showed two major compounds (GK-III and IV) and five minor components (GK-I, II, V—VII) on silica gel thin layer chromatography (TLC) ($CHCl_3$: MeOH : 50% AcOH = 65 : 20 : 5). The major components, GK-III and -IV,

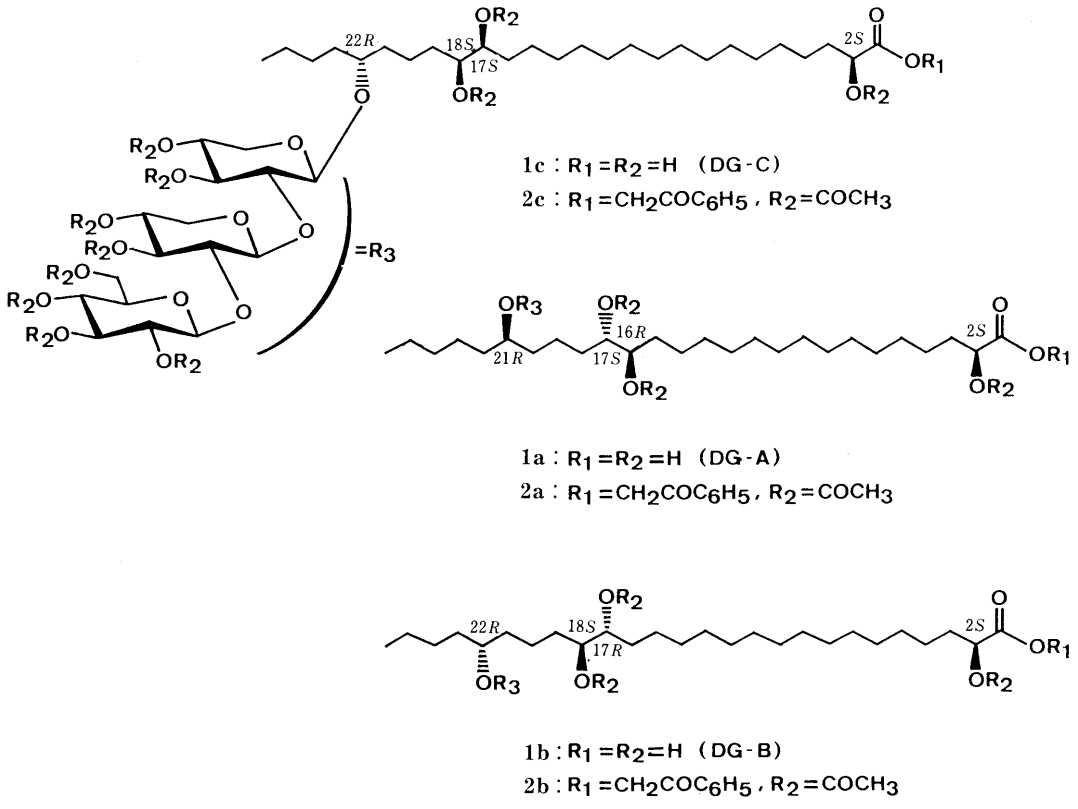


Chart 1

obtained by repeated chromatography on silica gel, had the same molecular weight of 970 [negative secondary ion mass spectrum (SIMS), m/z 969 $(M-H)^-$] and behaved like a single compound on normal and reverse-phase TLC. But high-performance liquid chromatographic (HPLC) analysis of the peracetyl phenacyl esters of GK-III and -IV gave identical chromatograms with three major peaks, indicating that both components contained three compounds (**2a**—**c**). These compounds (**2a**—**c**) were also obtained directly by preparative C_{18}-reverse-phase HPLC separation of the peracetyl phenacyl ester of a GK complex. Treatment of **2a**—**c** with NaOMe in MeOH yielded DG-A (**1a**), B (**1b**), and C (**1c**), respectively.

Hydrolysis of **2a**—**c** with 5% HCl–MeOH followed by silica gel chromatographic separation gave methyl esters of C_{26}-fatty acids (**3a**—**c**) as aglycones of glykenins.

TABLE I. Physico-Chemical Properties of **3a**, **3b**, and **3c**

Compound	**3a**	**3b**	**3c**
Appearance	White powder	White powder	White powder
Formula	$C_{27}H_{54}O_6$	$C_{27}H_{54}O_6$	$C_{27}H_{54}O_6$
CIMS (iso-C_4H_{10})	475 (MH^+)	475 (MH^+)	475 (MH^+)
(NH_3)	492 $(M+NH_4)^+$	492 $(M+NH_4)^+$	492 $(M+NH_4)^+$
UV (MeOH, nm)	End absorption	End absorption	End absorption
IR (KBr, cm^{-1})	3300, 1730	3300, 1730	3300, 1730
$[\alpha]_D^{22}$ (Py °C)	−15.8 (c=0.48)	+0.67 (c=0.37)	−17.8 (c=1.37)

The methyl esters (**3a**—**c**), having the same molecular weight of ($C_{27}H_{54}O_4$, 474), showed strong absorptions at 3300 and 1730 cm^{-1} in the infrared (IR) spectra (Table I) and gave tetraacetates on acetylation, suggesting the presence of an ester and four hydroxy groups. The proton nuclear magnetic resonance (^{1}H-NMR) spectra of **3a**—**c** were closely related and showed signals assigned to one primary methyl group, one methyl ester group, and four hydroxylated methine groups along with many methylene groups. One of the four hydroxy groups of **3a**—**c** was found to be located α to the ester groups judging from the downfield-shifted signals at 4.19 ppm (dd, J=7.8, 4.6 Hz) in **3a**, 4.19 ppm (dd, J=7.8, 4.6 Hz) in **3b**, and 4.20 ppm (dd, J=7.8, 4.6 Hz) in **3c**. Information on the locations of other hydroxy groups was obtained from mass spectral analyses of **3a**—**c**, although the molecular ions were not observed. Figure 1 shows the high-resolution electron impact mass spectra (EIMS), where the exact mass numbers of fragment ions are indicated as whole numbers. Of particular significance were two sets of fragments ions at m/z 155 ($C_{10}H_{21}O_2-H_2O$) and 283 ($C_{17}H_{33}O_4-H_2O$) in **3a**, and m/z 141 ($C_9H_{19}O_2-H_2O$) and m/z 297 ($C_{18}H_{35}O_4-H_2O$) in **3b** and **3c**, due to α-cleavage with respect to the carbon

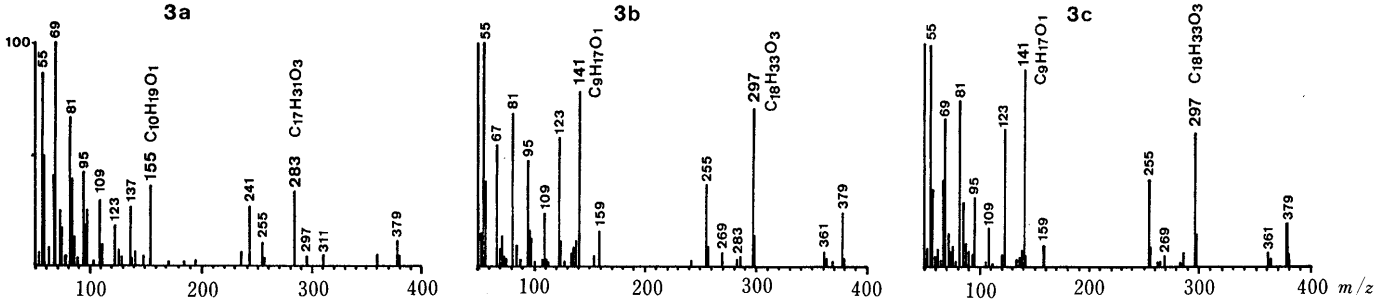


Fig. 1. Electron Impact Mass Spectra of **3a**, **3b** and **3c**
Molecular Ion Peaks of **3a**, **3b** and **3c** were not observed.

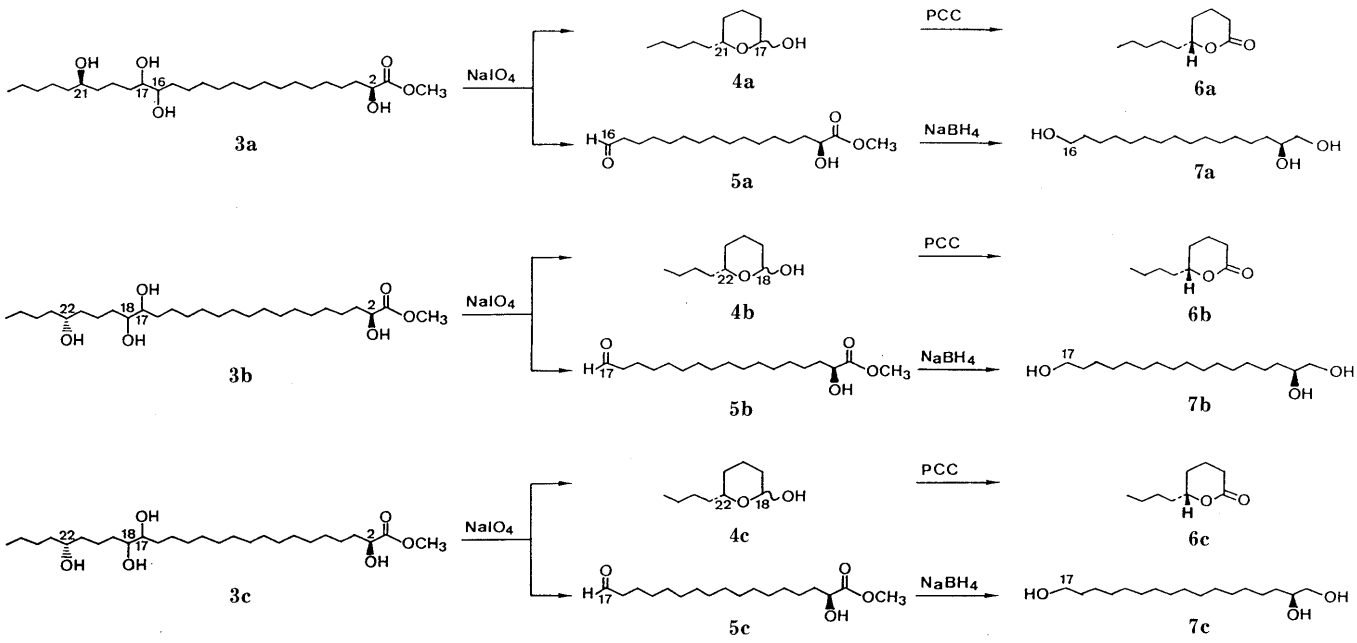


Chart 2

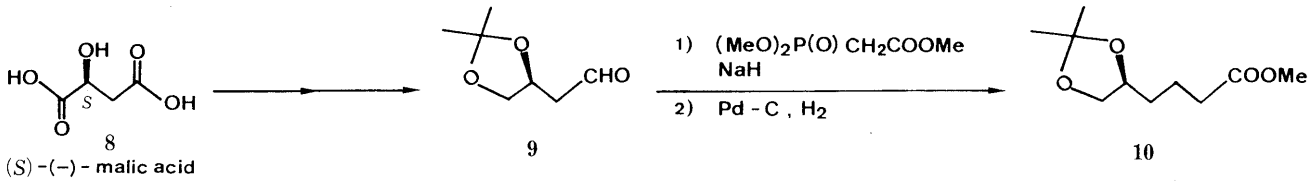
atoms carrying the hydroxy groups. The compositions of the fragment ions suggested that the two hydroxy groups were attached to C-16 and C-17 in **3a**, and C-17 and C-18 in both **3b** and **3c**. The location of another hydroxy group of **3a—c** was not so readily apparent but it was inferred from the results of chemical degradations of the aglycones.

Oxidative cleavage of the 1,2-diol moiety of **3a—c** was then undertaken. Treatment of **3a—c** with sodium metaperiodate in aqueous methanol followed by chromatographic separation of the products gave lactols (**4a—c**) and aldehydes (**5a—c**) (Chart 2). In order to confirm the structures, **4a—c** were oxidized with pyridinium chlorochromate to give lactones, **6a**: $[\alpha]_D^{23}$ +50.8° (c=0.32, $CHCl_3$), **6b**: $[\alpha]_D^{25}$ +51.4° (c=0.58, $CHCl_3$), **6c**: $[\alpha]_D^{22}$ +53.9° (c=0.65, $CHCl_3$). The chemical ionization mass spectra (CIMS) of **6a—c** showed pseudo-molecular ion peaks at m/z 171 ($C_{10}H_{18}O_2+H^+$), m/z 157 ($C_9H_{16}O_2+H^+$), and m/z 157 ($C_9H_{16}O_2+H^+$), respectively, and eventually, **6b** and **6c** were found to be identical by NMR and IR spectral comparisons. The presence of δ-lactone was confirmed by the IR and EIMS of **6a—c**, which exhibited an absorption at 1720 cm^{-1} charactaristic of a 6-membered lactone, and a base peak caused by loss of the alkyl side chain at m/z 99.

On the other hand, **5a—c** showed NMR signals at 9.76 ppm (1H, t, J=1.9 Hz), 4.19 ppm (1H, dd, J=7.3, 4.0 Hz), 3.70 ppm (3H, s), and 2.41 ppm (2H, td, J=7.3, 1.9 Hz), respectively, indicating the presence of an aldehyde, a secondary hydroxy group adjacent to an ester, a methyl ester, and a methylene group next to an aldehyde. The molecular weight ($C_{18}H_{32}O_4$, 314) of **5b** and **5c** was higher by one methylene unit than that of **5a** ($C_{17}H_{30}O_4$, 300). Reduction of **5a—c** with excess sodium borohydride in methanol yielded the C_{16}-triol (**7a**): $[\alpha]_D^{21}$ −6.39° (c=0.27, MeOH), and the C_{17}-triols (**7b**): $[\alpha]_D^{23}$ −6.87° (c=0.75, MeOH) and (**7c**): $[\alpha]_D^{21}$ −6.41° (c=0.27, MeOH), respectively. It is well documented that α-hydroxy esters are reduced to the corresponding 1,2-diols by sodium borohydride[2] and, therefore, the conversion of **5a—c** to **7a—c** confirmed the presence of α-hydroxy ester groups in **5a—c**. Combination of the lactols **4a—c** and the aldehydes **5a—c** can give only the structures **3a—c**, respectively. These results revealed that the positions of the four hydroxy groups were C-2, -16, -17, and -21 in **3a**, and C-2, -17, -18, and -22 in **3b** and **3c**.

Absolute Configurations of C-2 and C-21 in 3a, and C-2 and C-22 in 3b and 3c It was apparent that the degradation products **6a—c** and **7a—c** contained two of the four chiral centers originally present in **3a—c**. In order to determine the absolute configurations **6a—c** and **7a—c** were synthesized in optically active forms starting from (*S*)-(−)-malic acid (**8**) as shown in Charts 3 and 4, respectively. Reaction of the aldehyde (**9**), prepared from **8** in four steps,[3] with trimethyl phosphonoacetate followed by catalytic hydrogenation provided the ester (**10**). Deprotection of the acetonide groups, tosylation of the primary hydroxy group and treatment with lithium methoxide in methanol gave the epoxy ester **11**. Coupling reaction of **11** with di-*n*-propylcopperlithium and di-*n*-butylcopperlithium directly afforded (5*R*)-nonan-5-olide (**12**) $[\alpha]_D^{26}$ +50.2° (c=1.0, $CHCl_3$) and (5*R*)-decan-5-olide (**13**) $[\alpha]_D^{23}$ +48.1° (c=0.94, $CHCl_3$), respectively. IR, NMR, and MS spectral comparisons revealed that **12** is identical with the lactones **6b** and **6c**, and **13** with the lactone **6a**. Their specific rotations indicated that the absolute configurations of **6a—c** are *R*, and, therefore, those of C-21 in **3a** and C-22 in **3b** and **3c** are *R*.

On the other hand, the absolute configurations of C-2 of **7a—c** were determined as follows. Wittig reactions of the aldehyde (**9**) with the C_{12} and C_{13}-phosphoranes prepared from **14** and **15** followed by catalytic hydrogenation and deprotection of the acetonide group yielded (2*S*)-1,2,16-hexadecanetriol (**16**) $[\alpha]_D^{22}$ −6.58° (c=0.42, MeOH) and (2*S*)-1,2,17-heptadecanetriol (**17**) $[\alpha]_D^{22}$ −6.34° (c=0.41, MeOH), respectively. Comparison of the optical and



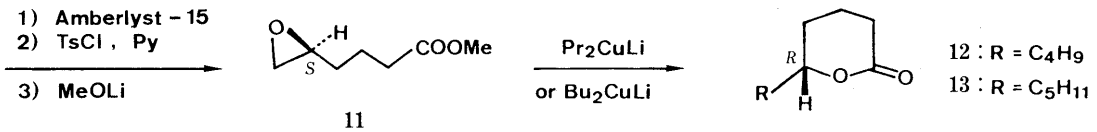


Chart 3

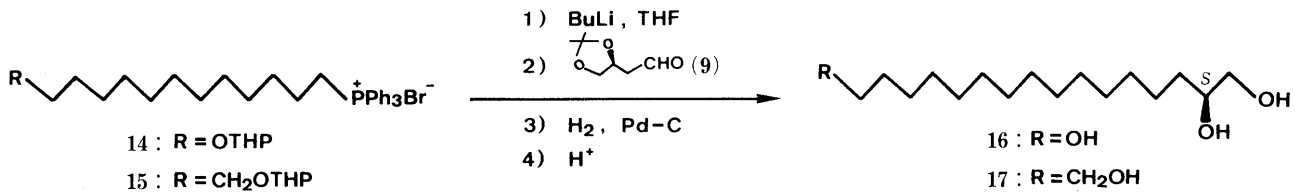
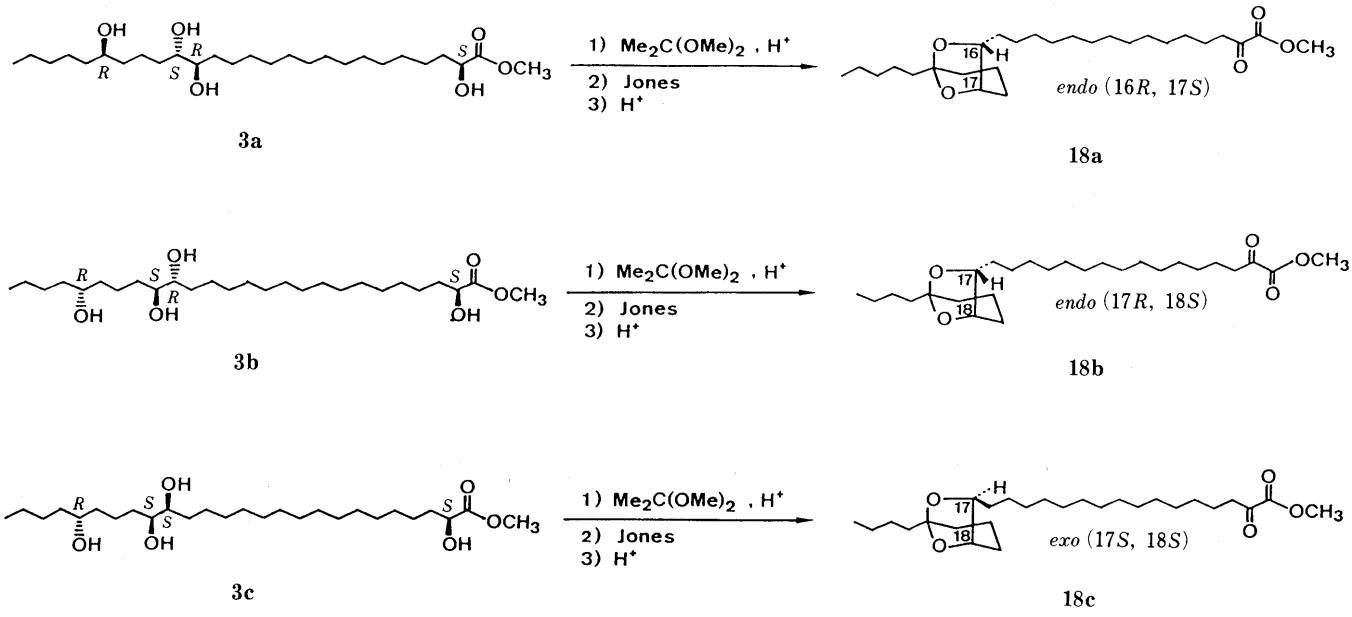


Chart 4



3a 18a

3b 18b

3c 18c

Chart 5

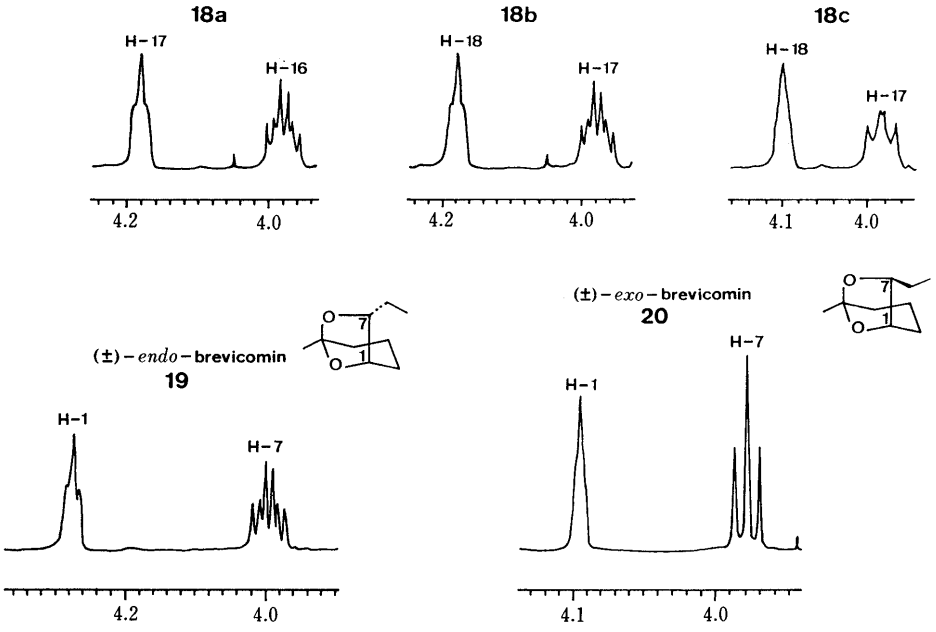


Fig. 2

spectral data of these synthetic specimens with those of the degradation products (**7a—c**) established that **7a—c** have 2*S* configuration; therefore the absolute configurations at C-2 of the aglycones (**3a—c**) are 2*S*.

Absolute Configurations of C-16 and C-17 in 3a, and C-17 and C-18 in 3b and 3c Another stereochemical problem is the configurations of the 1,2-diol moieties in the aglycones (**3a—c**). The exciton chirality method effers a general means for determining the absolute configuration of various diols, acyclic as well as cyclic.[4] Application of this method, however, is limited to *threo*-type 1,2-diols in the case of acyclic systems. In order to establish the relative configurations of the 1,2-diol moieties, **3a—c** were converted to the acetonide derivatives by treatment with 2,2-dimethoxypropane-acetone and *p*-toluenesulfonic acid (*p*-TsOH). Analyses of their ^{1}H-NMR spectra were found to be unfruitful because the signals assigned to the methine protons of the 1,3-dioxolane ring overlapped completely. But the arrays of the three hydroxy groups at C-16,17 and 21 in **3a**, and C-17,18, and 22 in **3b** and **3c** suggested that **3a—c** could be transformed into 6,8-dioxabicyclo[3.2.1]-octane derivatives, which would give information on the stereochemistry of 1,2-diol moieties.

Treatment of the acetonide derivatives of **3a—c** with Jones reagent and then *p*-TsOH in MeOH yielded the bicyclic ketals (**18a—c**) as expected (Chart 5). In the ^{1}H-NMR spectra, the H-16, and H-17 signals of **18a** appeared at 3.98 ppm (ddd, J=7.1, 4.6, 3.9 Hz) and 4.18 ppm (t, J=4.6 Hz), and the H-17 and H-18 signals of **18b** at 3.98 ppm (ddd, J=7.1, 4.6, 3.9 Hz) and 4.18 ppm (t, J=4.6 Hz), respectively. In the case of **18c** the signal assigned to H-17 was observed at 3.98 ppm (dd, J=7.3,

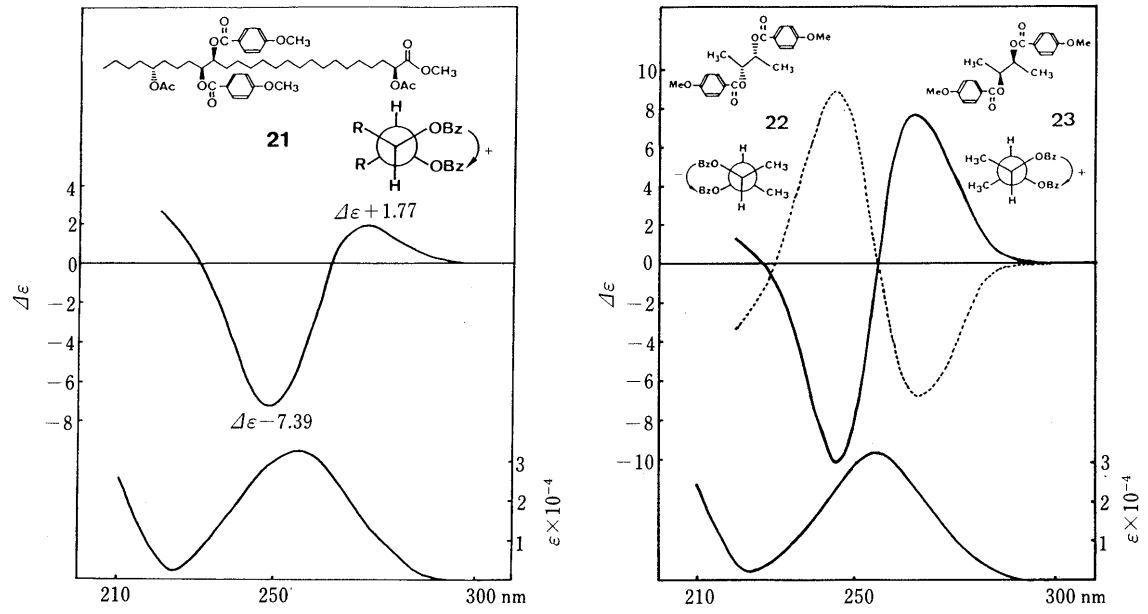


Fig. 3

TABLE II. Comparison of Specific Rotation of Bicyclic Acetals and Brevicomins

Brevicomin	Bicyclic acetal
(+)-*endo*(1*S*,7*R*) $[\alpha]_D^{25} = +96.6°$ ($c=0.98$, Et_2O) $[\phi] = +150.7°$	**18a** *endo*(16*R*,17*S*) $[\alpha]_D^{25} = +36.9°$ ($c=0.17$, Et_2O) $[\phi] = +166.8°$
(−)-*endo*(1*R*,7*S*) $[\alpha]_D^{25} = -93.1°$ ($c=1.01$, Et_2O) $[\phi] = -145.2°$	**18b** *endo*(17*R*,18*S*) $[\alpha]_D^{23} = +35.4°$ ($c=0.17$, Et_2O) $[\phi] = +160.0°$
(−)-*exo*(1*S*,7*S*) $[\alpha]_D^{25} = -80.3°$ ($c=2.23$, Et_2O) $[\phi] = -125.3°$	**18c** *exo*(17*S*,18*S*) $[\alpha]_D^{23} = -36.1°$ ($c=0.38$, Et_2O) $[\phi] = -163.2°$
(+)-*exo*(1*R*,7*R*) $[\alpha]_D^{25} = +80.9°$ ($c=2.18$, Et_2O) $[\phi] = +126.2°$	

5.6 Hz), and that of H-18 at 4.10 (br s), indicating that there is no coupling between H-17 and H-18, so that the side chain at C-17 has *exo* orientation.[5] Therefore, **18a** and **18b** are *endo* derivatives. The 6,8-dioxabicyclo[3.2.1]octane structure of **18a—c** was reminiscent of breviomin,[6] a pheromone of western pine beetle. The relative stereochemistries stated above were confirmed by comparison of the ^{1}H-NMR spectra of **18a—c** with those of racemic *endo*- and *exo*-brevicomines (**19** and **20**) prepared from *E* and *Z*-1-bromo-3-hexene in five steps[7] (Fig. 2). These ^{1}H-NMR results led unambiguously to the relative configurations of the 1,2-diol moieties (*erythro* for **3a** and **3b**, and *threo* for **3c**).

The spatial disposition of the *threo*-diol in **3c** is suited for stereochemical analysis by the dibenzoate chirality method.[4] The di-*p*-methoxybenzoate derivative (**21**) was prepared from the acetonide of **3c** by acetylation, deketalization, and then *p*-methoxybenzoylation. It is appropriate to mention here that the signs of Cotton effects obtained from acyclic dibenzoates depends upon their conformation, which could be determined by ^{1}H-NMR analysis. But in the present case, it was impossible to clarify the conformation because the protons geminal to the benzoate groups had the same chemical shift (5.32 ppm, 2H, m). Therefore, we decided to correlate the Cotton effect of **21** with those of (2*R*,3*R*)-(−)- and (2*S*,3*S*)-(+)-butanediol di-*p*-methoxybenzoates (**22** and **23**). As shown in Fig. 3, **21** displayed a positively split circular dichroic (CD) spectrum [273 nm ($\Delta\varepsilon+1.77$), 249 nm ($\Delta\varepsilon-7.39$)]. Since the signs of the Cotton effects of **22** and **23** predicted from their absolute

configurations were in good accordance with those obtained from the CD curves, it is reasonable to consider that the conformations of **21** and **23** are essentially the same. Accordingly, the absolute configurations of C-17 and C-18 in **3c** were established to be 17*S* and 18*S*. The dibenzoate chirality method was not applicable to the *erythro*-diols (**3a** and **3b**).

The absolute stereochemistry of the 1,2-diol moieties of **3a** and **3b** was established by comparison of the molecular rotations of **18a** and **18b** with those of optically active synthetic brevicomins[8] (Table II). The optical data revealed that the absolute configurations of the 1,2-diol moieties are 16*R* and 17*S* in **3a**, and 17*R* and 18*S* in **3b**. The absolute configuration of **18c** determined by the CD method also agreed well with the result obtained from the molecular rotation.

In conclusion, on the basis of the degradations and chemical transformations described above, the structures of three aglycones (**3a**—**c**) of glykenins were determined to be (2*S*,16*R*,17*S*,21*R*)-2,16,17,21-, (2*S*,17*R*,18*S*,22*R*)-2,17,18,22-, and (2*S*,17*S*,18*S*,22*R*)-2,17,18,22-tetrahydroxyhexacosanoic acids, respectively. It is interesting that the aglycones of glykenins are unusual C_{26} long-chain fatty acids, in which hydroxylation occurs at various sites in the chain and three of the four hydroxyl groups are regio- and stereoisomeric to each other.

Experimental

Optical rotations were measured on a JASCO DIP-181 digital polarimeter. IR spectra were recorded on a Hitachi 215 spectrometer, and ultraviolet (UV) spectra were measured on a Hitachi 200-10 spectrophotometer. NMR spectra were recorded on JEOL JNM-FX100 (100 MHz for ^{1}H-NMR and 25 MHz for ^{13}C-NMR), JNM-GX270 (270 MHz for ^{1}H-NMR), and JNM-GX400 (400 MHz for ^{1}H-NMR and 100 MHz for ^{13}C-NMR) spectrometers, and chemical shifts are given in ppm (δ) scale with tetramethylsilane as an internal standard. Mass spectra (MS) were taken on a Shimadzu GC-MS QP-1000 or Hitachi M-80 spectrometer. Column chromatographic separations were carried out using Sephadex LH-20 (Pharmacia) or Silica gel 60 (Nacalai). Analytical TLC was performed on precoated Silica gel 60 plates (Merck, Art. 5715) and RP-18F_{254s} (Merck, Art. 15685). High performance liquid chromatography was performed on a JASCO Trirotar-V using a Develosil ODS column. CD spectra were measured on a JASCO J-20 spectrometer.

Isolation of Glykenins The fermentation of the *Basidiomycetes* sp. was carried out at 30 °C for 10—14 d with aeration. The production medium consisted of glucose 40 g, glutamine 3 g, $MgSO_4 \cdot 7H_2O$ 0.5 g, $Na_2HPO_4 \cdot 12H_2O$ 1 g, KH_2PO_4 0.6 g, and thiamine 200 μg (pH 6.6). The fermentation broth was extracted with AcOEt (3—4 times) and the organic layer was concentrated to give a brown oil. The LH-20 column chromatography of the oil (4.95 g) gave GK complex (3.34 g), which (1 g) was purified by repetitive silica gel column chromatography using $CHCl_3$: MeOH : 50% AcOH ((i) 65 : 15 : 5, (ii) 65 : 10 : 5, (iii) 65 : 5 : 5) to give GK-III (15 mg) and GK-IV (75 mg).

GK-III: Amorphous powder. UV λ_{max}^{MeOH} nm: end absorption. IR ν_{max}^{KBr} cm^{-1}: 3600—3200, 1735. SIMS (positive) *m/z*: 993 $(M+Na)^+$. SIMS (negative) *m/z*: 969 $(M-H)^-$.

GK-IV: Amorphous powder. UV λ_{max}^{MeOH} nm: end absorption. IR ν_{max}^{KBr} cm^{-1}: 3600—3200, 1735. SIMS (positive) *m/z*: 993 $(M+Na)^+$. SIMS (negative) *m/z*: 969 $(M-H)^-$.

The Peracetyl Phenacyl Esters (2a—c) A solution of 1% NaOH in MeOH (11.5 ml) was added to an MeOH solution (7 ml) of GK complex (1.4 g). The reaction mixture was stirred for 3 h at room temperature and then the solvent was removed *in vacuo*. The residue was dissolved in *N*,*N*-dimethylformamide (10 ml), and dicyclohexyl 18-crown-6 (1.07 g, 2 mmol) and phenacyl bromide (0.86 g, 3 mmol) were added to the solution. The mixture was stirred for 5 h, then the solvent was evaporated off *in vacuo*. The residue was chromatographed on silica gel using $CHCl_3$: MeOH : H_2O (65 : 15 : 5) to give the phenacyl esters (756 mg). The phenacyl esters (756 mg) were dissolved in acetic anhydride (6 ml) and pyridine (7 ml). This solution was allowed to stand then chromatographed on Sephadex LH-20 (MeOH) to give the peracetyl phenacyl esters (1.06 g). The preparative ODS-HPLC (CH_3CN : MeOH : H_2O = 9.0 : 0.5 : 0.5) separation of the esters afforded **2a** (345 mg), **2b** (197 mg), and **2c** (485 mg). The ^{1}H- and ^{13}C-NMR spectral data are summarized in Table III. The

TABLE III. ^{1}H and ^{13}C Spectral Data for **2a**, **2b**, and **2c**

Position		^{13}C-NMR (100 MHz, $CDCl_3$)			^{1}H-NMR (400 MHz, $CDCl_3$) (Hz)		
		2a	**2b**	**2c**	**2a**	**2b**	**2c**
Aglycone	1	170.0	170.0	170.0			
	2	72.3	72.4	72.4	5.12 (m)	5.10 (dd, 8.1, 4.6)	5.09 (m)
	16	74.2	—	—	4.99[a] (m)		
	17	74.2	74.2	73.7[a]	5.01[a] (m)	4.96[a] (m)	4.98[a] (m)
	18	—	74.2	74.0[a]		4.99[a] (m)	5.01[a] (m)
	21	79.6	—	—	3.55 (m)		
	22	—	79.6	79.3		3.55 (m)	3.55 (m)
Xylose-1	1	100.9	100.9	100.8	4.43 (d, 7.1)	4.44 (d, 6.8)	4.44 (d, 6.8)
	2	76.9	76.9	76.9	3.58 (dd, 9.0, 7.1)	3.59 (dd, 9.2, 6.8)	3.59 (dd, 9.0, 6.8)
	3	74.3	74.3	74.2	5.15 (t, 9.0)	5.16 (t, 9.2)	5.16 (t, 9.0)
	4	70.0	70.0	70.1	4.86 (m)	4.87 (m)	4.88 (m)
	5	62.3	62.3	62.3	3.38 (dd, 11.7, 9.3)	3.38 (dd, 11.6, 9.0)	3.39 (dd, 11.7, 9.0),
					3.95 (dd, 11.7, 5.6)	3.95 (dd, 11.6, 5.3)	3.97 (dd, 11.7, 5.4)
Xylose-2	1	101.2	101.2	101.2	4.63 (d, 6.4)	4.63 (d, 6.4)	4.64 (d, 6.4)
	2	77.9	77.9	77.9	3.51 (dd, 8.8, 6.4)	3.51 (dd, 8.9, 6.4)	3.52 (dd, 8.8, 6.4)
	3	73.5	73.4	73.4	5.07 (t, 8.8)	5.07 (t, 8.9)	5.07 (t, 8.8)
	4	69.8	69.8	69.9	4.83 (m)	4.83 (m)	4.84 (m)
	5	61.9	61.9	61.9	3.32 (dd, 12.7, 7.8),	3.33 (dd, 12.8, 7.6),	3.33 (dd, 12.5, 7.6),
					4.05 (dd, 12.7, 5.1)	4.05 (dd, 12.8, 5.0)	4.05 (dd, 12.5, 5.1)
Glucose	1	101.1	101.1	101.1	4.54 (d, 8.1)	4.55 (d, 8.1)	4.55 (d, 8.1)
	2	70.9	70.9	70.9	4.95 (dd, 9.3, 8.1)	4.95 (dd, 9.5, 8.1)	4.95 (dd, 9.5, 8.1)
	3	73.2	72.2	73.2	5.11 (t, 9.3)	5.11 (t, 9.5)	5.11 (t, 9.5)
	4	68.2	68.2	68.3	5.18 (t, 9.3)	5.19 (t, 9.5)	5.18 (t, 9.5)
	5	71.9	71.9	71.9	3.62 (m)	3.62 (ddd, 9.8, 3.8, 2.3)	3.64 (ddd, 9.5, 3.9, 2.2)
	6	61.4	61.9	61.4	4.22 (dd, 12.2, 3.7),	4.22 (dd, 12.2, 3.7),	4.23 (dd, 12.2, 3.9),
					4.36 (dd, 12.2, 1.9)	4.37 (dd, 12.2, 1.9)	4.35 (dd, 12.2, 2.2)

a) May be interchanged.

assignments of the signals of **2a—c** were carried out on the basis of ^1H–^1H, ^{13}C–^1H and long range ^{13}C–^1H COSY spectra.

2a: Oil. $[\alpha]_D^{20}$ +0.37° (c=0.7, MeOH). SIMS (positive) m/z: 1489 $(M+Na)^+$. UV λ_{max}^{MeOH} nm: 242. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1750, 1365, 1240.

2b: Oil. $[\alpha]_D^{20}$ −0.08° (c=0.8, MeOH). SIMS (positive) m/z: 1489 $(M+Na)^+$. UV λ_{max}^{MeOH} nm: 242. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1750, 1365, 1240.

2c: Oil. $[\alpha]_D^{20}$ −1.49° (c=0.4, MeOH). SIMS (positive) m/z: 1489 $(M+Na)^+$. UV λ_{max}^{MeOH} nm: 242. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1750, 1365, 1240.

Methanolysis of 2a—c The aglycone **2a** (320 mg) was hydrolyzed with 5% HCl–MeOH (8 ml) for 5 h under reflux. After cooling, the reaction mixture was neutralized with Ag_2CO_3 and filtered. The filtrate was evaporated *in vacuo* and the residue was subjected to column chromatography on silica gel using $CHCl_3$: MeOH : H_2O ((i) 65 : 15 : 5 (ii) 65 : 5 : 5) to give **3a** (142 mg).

In the same manner **2b** (180 mg) and **2c** (405 mg) were hydrolyzed to give **3b** (88 mg) and **3c** (198 mg), respectively.

3a: White powder. $[\alpha]_D^{22}$ −15.8° (c=0.48, pyridine). CIMS (iso-C_4H_{10}) m/z: 475 (MH^+). CIMS (NH_3) m/z: 492 $(M+NH_4)^+$. UV λ_{max}^{MeOH} nm: end absorption. IR ν_{max}^{KBr} cm^{-1}: 3300, 1730. ^{1}H-NMR (CD_3OD, 400 MHz) δ: 0.93 (3H, t, J=7.1 Hz), 1.30—1.70 (m), 3.70 (3H, s), 3.35 (2H, m), 3.51 (1H, m), 4.19 (1H, dd, J=7.8, 4.6 Hz).

3b: White powder. $[\alpha]_D^{22}$ +0.67° (c=0.37, pyridine). CIMS (iso-C_4H_{10}) m/z: 475 (MH^+). CIMS (NH_3) m/z: 492 $(M+NH_4)^+$. UV λ_{max}^{MeOH} nm: end absorption. IR ν_{max}^{KBr} cm^{-1}: 3300, 1730. ^{1}H-NMR (CD_3OD, 400 MHz) δ: 0.92 (3H, t, J=7.1 Hz), 1.30—1.70 (m), 3.35 (2H, m), 3.51 (1H, m), 3.71 (3H, s), 4.19 (1H, dd, J=7.8, 4.6 Hz).

3c: White powder. $[\alpha]_D^{22}$ −17.8° (c=1.37, pyridine). CIMS (iso-C_4H_{10}) m/z: 475 (MH^+). CIMS (NH_3) m/z: 492 $(M+NH_4)^+$. UV λ_{max}^{MeOH} nm: end absorption. IR ν_{max}^{KBr} cm^{-1}: 3300, 1730. ^{1}H-NMR (CD_3OD, 400 MHz) δ: 0.92 (3H, t, J=7.1 Hz), 1.30—1.70 (m), 3.34 (2H, m), 3.50 (1H, m), 3.71 (3H, s), 4.20 (1H, dd, J=7.8, 4.6 Hz).

Acetylation of 3a—c The aglycone (**3a**, 8 mg) was dissolved in pyridine (1 mg) and acetic anhydride (0.5 mg), and the solution was allowed to stand overnight at room temperature, then concentrated to dryness under reduced pressure. Sephadex LH-20 column chromatography (MeOH) of the residue gave the tetraacetate of **3a** (12 mg).

In the same manner, **3b** (5 mg) and **3c** (10 mg) were acetylated to give the tetraacetates of **3b** (9 mg) and **3c** (13 mg), respectively.

Tetraacetate of **3a**: Oil. UV λ_{max}^{MeOH} nm: end absorption. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1730. CIMS (iso-C_4H_{10}) m/z: 643 (MH^+). CIMS (NH_3) m/z: 660 $(M+NH_4)^+$. ^{1}H-NMR ($CDCl_3$, 100 MHz) δ: 0.93 (3H, t, J=7.1 Hz), 1.32 (m), 2.08 (6H, s), 2.15 (6H, a), 3.77 (3H, s), 4.91—5.28 (4H, m).

Tetraacetate of **3b**: Oil. UV λ_{max}^{MeOH} nm: end absorption. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1730. CIMS (iso-C_4H_{10}) m/z: 643 (MH^+). CIMS (NH_3) m/z: 660 $(M+NH_4)^+$. ^{1}H-NMR ($CDCl_3$, 100 MHz) δ: 0.92 (3H, t, J=7.08 Hz), 1.32 (m), 2.08 (6H, s), 2.15 (6H, s), 3.77 (3H, s), 4.91—5.29 (4H, m).

Tetraacetate of **3c**: Oil. UV λ_{max}^{MeOH} nm: end absorption. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1730. CIMS (iso-C_4H_{10}) m/z: 643 (MH^+). CIMS (NH_3) m/z: 660 $(M+NH_4)^+$. ^{1}H-NMR ($CDCl_3$, 100 MHz) δ: 0.92 (3H, t, J=7.08 Hz), 1.32 (m), 2.07 (6H, s), 2.15 (6H, s), 3.77 (3H, s), 4.91—5.28 (4H, m).

Periodate Oxidation of 3a—c i) A mixture of **3a** (91 mg) and $NaIO_4$ (123 mg) in MeOH (3 ml) and H_2O (1 ml) was stirred for 3 h and then concentrated to dryness. The residue was chromatographed on silica gel using AcOEt : *n*-hexane (2 : 8) to afford **4a** (10.5 mg) and **5a** (27 mg).

4a: IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 3400. CIMS (iso-C_4H_{10}) m/z: 173 (MH^+). CIMS (NH_3) m/z: 190 $(M+NH_4)^+$. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 0.89 (3H, t, J=7.1 Hz), 1.10—1.91 (m), 2.38 (1H, br s), 2.86 (1H, br s), 3.39 (1H, m), 3.90 (1H, m), 4.69 (1H, d, J=9.2 Hz), 5.30 (1H, s).

5a: IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500, 1730. CIMS (iso-C_4H_{10}) m/z: 283$(MH^+ - H_2O)$. CIMS (NH_3) m/z: 318 $(M+NH_4)^+$. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 1.25—1.77 (m), 2.41 (2H, td, J=7.3, 1.9 Hz), 3.70 (3H, s), 4.19 (1H, dd, J=7.3, 4.0 Hz), 9.76 (1H, t, J=1.9 Hz).

ii) **3b** (42 mg) was treated with $NaIO_4$ (56.8 mg) in the same way to give **4b** (11.5 mg) and **5b** (23 mg).

4b: IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 3400. CIMS (iso-C_4H_{10}) m/z: 159 (MH^+). CIMS (NH_3) m/z: 186 $(M+NH_4)^+$. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 0.90 (3H, t, J=7.1 Hz), 1.10—1.91 (m), 2.37 (1H, br s), 2.86 (1H, br s), 3.39 (1H, m), 3.91 (1H, m), 4.69 (1H, d, J=9.2 Hz), 5.30 (1H, s).

5b: IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500, 1730. CIMS (iso-C_4H_{10}) m/z: 297 $(MH^+ - H_2O)$. CIMS (NH_3) m/z: 332 $(M+NH_4)^+$. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 1.25—1.78 (m), 2.41 (2H, td, J=7.3, 1.9 Hz), 3.70 (3H, s), 4.19 (1H, dd, J=7.3, 4.0 Hz), 9.76 (1H, t, J=1.9 Hz).

iii) **3c** (77 mg) was treated with $NaIO_4$ (104.6 mg) in the same way to give **4c** (15.8 mg) and **5c** (45 mg).

4c: IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 3400, CIMS (iso-C_4H_{10}) m/z: 159 (MH^+), CIMS (NH_3) m/z: 186 $(M+NH_4)^+$, ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 0.90 (3H, t, J=7.1 Hz), 1.10—1.91 (m), 2.37 (1H, br s), 2.86 (1H, br s), 3.39 (1H, m), 3.92 (1H, m), 4.68 (1H, d, J=9.2 Hz), 5.30 (1H, s).

5c: IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500, 1730. CIMS (iso-C_4H_{10}) m/z: 297 $(MH^+ - H_2O)$. CIMS (NH_3) m/z: 332 $(M+NH_4)^+$. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 1.24—1.78 (m), 2.41 (2H, td, J=7.3, 1.9 Hz), 3.70 (3H, s), 4.19 (1H, dd, J=7.3, 4.0 Hz), 9.76 (1H, t, J=1.9 Hz).

Pyridinium Chlorochromate (PCC) Oxidation of 4a—c A solution of **4a** (8.7 mg) in CH_2Cl_2 (1 ml) was added to a stirred solution of pyridinium chlorochromate (PCC, 21.7 mg) in CH_2Cl_2 (1 ml) and the reaction mixture was stirred for 4 h at room temperature. The mixture was diluted with ether and filtered through a Florisil column with ether. The filtrate was concentrated *in vacuo* and the residue was purified by silica gel column chromatography using benzene : acetone (9 : 1) to give **6a** (5.4 mg). In the same manner, **4b** (11 mg) and **4c** (15.8 mg) were oxidized with PCC to give **6b** (7.0 mg) and **6c** (9.4 mg), respectively.

6a: Oil. $[\alpha]_D^{23}$ +50.8° (c=0.32, $CHCl_3$). UV λ_{max}^{MeOH} nm: end absorption. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720. CIMS (iso-C_4H_{10}) m/z: 171 (MH^+). CIMS (NH_3) m/z: 171 (MH^+). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 0.19 (3H, t, J=7.2 Hz), 1.25—1.94 (m), 2.44 (1H, m), 2.57 (1H, m), 4.29 (1H, m).

6b: Oil. $[\alpha]_D^{25}$ +51.4° (c=0.58, $CHCl_3$). UV λ_{max}^{MeOH} nm: end absorption. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720. CIMS (iso-C_4H_{10}) m/z: 157 (MH^+). CIMS (NH_3) m/z: 157 (MH^+). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 0.19 (3H, t, J=7.2 Hz), 1.25—1.94 (m), 2.44 (1H, m), 2.57 (1H, m), 4.29 (1H, m).

6c: Oil. $[\alpha]_D^{22}$ +53.9° (c=0.65, $CHCl_3$). UV λ_{max}^{MeOH} nm: end absorption. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720. CIMS (iso-C_4H_{10}) m/z: 157 (MH^+). CIMS (NH_3) m/z: 157 (MH^+). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 0.19 (3H, t, J=7.2 Hz), 1.25—1.94 (m), 2.44 (1H, m), 2.57 (1H, m), 4.29 (1H, m).

Sodium Borohydride Reduction of 5a—c Sodium borohydride ($NaBH_4$, 50 mg) was added to a stirred solution of **5a** (17 mg) in MeOH (2 ml). The reaction mixture was stirred for 2 h at room temperature and then concentrated to dryness. The residue was chromatographed on silica gel using $CHCl_3$: MeOH (9 : 1) to give **7a** (3.5 mg). In the same way, **5b** (20 mg) and **5c** (30.2 mg) were reduced with $NaBH_4$ to give **7b** (11 mg) and **7c** (9.9 mg), respectively.

7a: White amorphous powder. $[\alpha]_D^{21}$ −6.39° (c=0.27, MeOH). IR ν_{max}^{KBr} cm^{-1}: 3350, CIMS (iso-C_4H_{10}) m/z: 257 $(MH^+ - H_2O)$. CIMS (NH_3) m/z: 275 (MH^+), 292 $(M+NH_4)^+$. ^{1}H-NMR (CD_3OD, 400 MHz) δ: 1.29—1.54 (m), 3.41 (1H, dd, J=11.1, 6.7 Hz), 3.46 (1H, dd, J=11.1, 4.4 Hz), 3.53 (2H, t, J=6.7 Hz), 3.56 (1H, m).

7b: White amorphous powder. $[\alpha]_D^{23}$ −6.87° (c=0.75, MeOH). IR ν_{max}^{KBr} cm^{-1}: 3350. CIMS (iso-C_4H_{10}) m/z: 271 $(MH^+ - H_2O)$. CIMS (NH_3) m/z: 289 (MH^+), 306 $(M+NH_4)^+$. ^{1}H-NMR (CD_3OD, 400 MHz) δ: 1.29—1.54 (m), 3.41 (1H, dd, J=11.1, 6.7 Hz), 3.46 (1H, dd, J=11.1, 4.4 Hz), 3.53 (2H, t, J=6.7 Hz), 3.56 (1H, m).

7c: White amorphous powder. $[\alpha]_D^{21}$ −6.41° (c=0.27, MeOH). IR ν_{max}^{KBr} cm^{-1}: 3350. CIMS (iso-C_4H_{10}) m/z: 271 $(MH^+ - H_2O)$. CIMS (NH_3) m/z: 289 (MH^+), 306 $(M+NH_4)^+$. ^{1}H-NMR (CD_3OD, 400 MHz) δ: 1.29—1.54 (m), 3.41 (1H, dd, J=11.1, 6.7 Hz), 3.46 (1H, dd, J=11.1, 4.4 Hz), 3.53 (2H, t, J=6.7 Hz), 3.56 (1H, m).

Methyl (5*S*)-5,6-*O*-Isopropylidene-5,6-dihydroxyhexanoate (10) Trimethyl phosphonoacetate (2.62 g) was added to a suspension of NaH (50% in mineral oil, 1.25 g) in dry tetrahydrofuran (THF) (20 ml) at room temperature under nitrogen, and the mixture was stirred for 30 min. Then a solution of (3*S*)-3,4-*o*-isopropylidene-3,4-dihydroxybutanal (**9**, 3.75 g) in dry THF (10 ml) was added dropwise and the whole was stirred for 12 h at room temperature. The reaction mixture was extracted with ether, washed with water and brine, and dried ($MgSO_4$), and the solvent was removed *in vacuo*. Bulb-to-bulb distillation (120 °C, 2 mmHg) of the oily residue gave 4.6 g of the unsaturated ester.

The ester (4.6 g) was dissolved in ethyl acetate (15 ml) and hydrogenated in the presence of 10% Pd–C (200 mg) for 5 h at room temperature. The catalyst was filtered off and the filtrate was concentrated to dryness. Bulb-to-bulb distillate at 80 °C (1 mmHg) gave the ester (**10**, 4.55 g). $[\alpha]_D^{23}$ +15.6° (c=0.25, $CHCl_3$). EIMS m/z: 187 $(M^+ - CH_3)$. IR ν_{max}^{film} cm^{-1}: 1730. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.35 (3H, s), 1.40 (3H, s), 1.52—1.81 (2H), 2.37 (2H, t, J=7.1 Hz), 3.52 (1H, t, J=7.3 Hz), 3.67 (3H, s), 4.04 (1H, dd, J=7.3, 5.9 Hz), 4.09 (1H, m).

Methyl (5*S*)-5,6-Epoxyhexanoate (11) The ester (**10**, 2.2 g) was dissolved in MeOH (50 ml) and Amberlyst-15 was added to the solution. The mixture was stirred for 12 h at room temperature and filtered. The filtrate was concentrated to dryness to give the diol-ester (1.8 g).

The hydroxy ester (826 mg) was dissolved in 4 ml of pyridine, and *p*-toluenesulfonyl chloride (970 mg) was added at 0 °C. The mixture was stirred at 0 °C for 4 h, allowed to stand at 5 °C for 9 h, diluted with ether

and filtered to remove precipitates. The filtrate was concentrated to dryness. The oily residue was purified by flash chromatography on silica gel (AcOEt : *n*-hexane = 1 : 1) to give the tosyl ester (960 mg).

The tosyl ester (720 mg) was dissolved in methanol (10 ml). A solution of lithium methoxide in methanol, prepared from 1.6 M BuLi (1.43 ml) and methanol (5 ml), was added and the mixture was stirred for 10 min. After removal of the solvent, the residue was flash-chromatographed on silica gel (AcOEt : *n*-hexane = 3 : 7) to give the epoxy ester (**11**, 251 mg). bp 105 °C (13 mmHg, bulb-to-bulb distillation). $[\alpha]_D^{24}$ −16.02° (c = 0.58, $CHCl_3$). CIMS (iso-C_4H_{10}) m/z: 145 (MH^+). IR ν_{max}^{film} cm^{-1}: 1740. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 1.49—1.87 (4H), 2.39 (2H, t, J = 7.0 Hz), 2.48 (1H, dd, J = 5.0, 2.7 Hz), 2.75 (1H, dd, J = 5.0, 4.0 Hz), 2.92 (1H, m), 3.68 (3H, s).

(5*R*)-Nonan-5-olide (12) A solution of **11** (100 mg) in ether (3 ml) was added to a stirred solution of dipropylcopperlithium [prepared from 0.5 M PrLi (9.7 ml) and CuI (530 mg) in dry ether (3 ml)] at −40 °C under argon and the mixture was stirred for 20 min at the same temperature. The reaction mixture was quenched with aqueous NH_4Cl and extracted with ethyl acetate. The extract was washed with aqueous NH_4Cl and NaCl, dried ($MgSO_4$), and concentrated to dryness. The residue was purified by flash chromatography on silica gel (AcOEt : *n*-hexane = 1.5 : 8.5) to give **12** (86.4 mg). bp 90 °C (4 mmHg, bulb-to-bulb distillation). $[\alpha]_D^{26}$ +50.2° (c = 1.0, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720. EIMS m/z: 99 ($M^+ - C_4H_9$). CIMS (iso-C_4H_{10}) m/z: 157 (MH^+). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.92 (3H, t, J = 7.1 Hz), 1.30—1.96 (10H), 2.44 (1H, ddd, J = 17.6, 8.8, 7.1 Hz), 2.58 (1H, dddd, J = 17.6, 7.2, 5.1, 1.4 Hz), 4.28 (1H, dddd, J = 12.5, 7.7, 4.9, 2.8 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 13.9, 18.5, 22.5, 27.0, 27.8, 29.5, 35.5, 80.5, 171.9.

(5*S*)-Decan-5-olide (13) The lactone (**13**, 20 mg) was prepared from the epoxide (**11**, 50 mg) and dibutylcopperlithium in the same manner as in the case of (**12**). bp 88 °C (2 mmHg, bulb-to-bulb distillation); $[\alpha]_D^{23}$ +48.1° (c = 0.94, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720. CIMS (iso-C_4H_{10}) m/z: 171 (MH^+). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.90 (3H, t, J = 7.1 Hz), 1.27—1.95 (12H), 2.44 (1H, ddd, J = 17.6, 8.8, 7.1 Hz), 2.57 (1H, dddd, J = 17.6, 7.2, 5.1, 1.4 Hz), 4.27 (1H, dddd, J = 12.5, 7.7, 4.9, 2.8 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 13.9, 18.5, 22.5, 24.6, 27.8, 29.4, 31.6, 35.8, 80.5, 171.9.

(2*S*)-1,2,16-Hexadecanetriol (16) A solution of the phosphonium bromide (**14**, 226 mg) [prepared from 12-bromododecanol tetrahydropyranyl ether and triphenylphosphine in acetonitrile (reflux, 20 h)] in dry THF (5 ml) was treated with 1.6 M BuLi (0.23 ml) and the mixture was stirred for 20 min at room temperature under nitrogen.

A solution of (3*S*)-3,4-*o*-isopropylidene-3,4-dihydroxybutanal (**9**, 53 mg) in dry THF (2 ml) was added, and the mixture was stirred for 30 min at room temperature, then extracted with ethyl acetate. The extract was washed with brine, dried ($MgSO_4$), and concentrated to dryness. Flash chromatography on silica gel (EtOAc : *n*-hexane = 1 : 9) gave 50 mg of an oil. The oil (43 mg) was dissolved in ethyl acetate and catalytically hydrogenated in the presence of 5% Pd–C (10 mg). The catalyst was filtered off and the filtrate was concentrated to give 43 mg of the product. This product (40 mg) was dissolved in methanol (2 ml) and one drop of 6 N HCl was added. The solution was allowed to stand for 3 h at room temperature, then the solvent was removed and the residue was purified by flash chromatography on silica gel (MeOH : $CHCl_3$ = 8 : 92) to give the triol (**16**, 26 mg). $[\alpha]_D^{22}$ −6.58° (c = 0.42, MeOH). IR ν_{max}^{KBr} cm^{-1}: 3350. CIMS (NH_3) m/z: 275 (MH^+), 297 $(M+NH_4)^+$. ^{1}H-NMR (400 MHz, CD_3OD) δ: 1.29—1.54 (methylene protons), 3.41 (1H, dd, J = 11.1, 6.7 Hz), 3.46 (1H, dd, J = 11.1, 4.4 Hz), 3.53 (2H, t, J = 6.7 Hz), 3.56 (1H, m).

(2*S*)-1,2,17-Heptadecanetriol (17) In the same manner as in the case of **16**, Wittig reaction of **15** (100 mg) and (3*S*)-3,4-*o*-isopropylidene-3,4-dihydroxybutanal (**9**, 83 mg) followed by catalytic hydrogenation and acid treatment gave the triol (**17**, 12 mg). $[\alpha]_D^{22}$ −6.34° (c = 0.41, MeOH). IR ν_{max}^{KBr} cm^{-1}: 3350. CIMS (NH_3) m/z: 289 (MH^+), 306 $(M+NH_4)^+$. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.29—1.54 (methylene protons), 3.41 (1H, dd, J = 11.1, 6.7 Hz), 3.46 (1H, dd, J = 11.1, 4.4 Hz), 3.53 (2H, t, J = 6.7 Hz), 3.56 (1H, m).

The Acetonides of 3a—c The aglycone (**3a**) (15.9 mg) was dissolved in acetone (2 ml) containing 2 mg of *p*-TsOH and 2,2-dimethoxypropane (0.3 mg) and stirred for 3.5 h at room temperature. The reaction mixture was neutralized with powdered $NaHCO_3$ and filtered through a short column of Na_2SO_4. The filtrate was concentrated *in vacuo* and the residue were chromatographed on a silica gel column using AcOEt : *n*-hexane (2 : 8) to give **3a**-acetonide (11.8 mg). In the same manner **3b** (17 mg) and **3c** (32 mg) were converted to **3b**-acetonide (15.1 mg) and **3c**-acetonide (23.2 mg), respectively.

3a-Acetonide: Oil. $[\alpha]_D^{24}$ +4.65° (c = 0.98, $CHCl_3$). UV λ_{max}^{MeOH} nm: end absorption. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500, 1730. CIMS (iso-C_4H_{10}) m/z: 515 (MH^+). CIMS (NH_3) m/z: 515 (MH^+). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 0.90 (3H, t, J = 5.9 Hz), 1.25—1.80 (m), 1.35 (3H, s), 1.44 (3H, s), 3.61 (1H, m), 4.03 (2H, m), 4.19 (1H, dd, J = 7.8, 4.6 Hz), 3.78 (3H, s).

3b-Acetonide: Oil. $[\alpha]_D^{24}$ +4.15° (c = 1.15, $CHCl_3$). UV λ_{max}^{MeOH} nm: end absorption. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500, 1730. CIMS (iso-C_4H_{10}) m/z: 439 ($MH^+ - 76$). CIMS (NH_3) m/z: 515 (MH^+). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 0.91 (3H, t, J = 5.9 Hz), 1.22—1.82 (m), 1.33 (3H, s), 1.43 (3H, s), 3.61 (1H, m), 3.79 (3H, s), 4.03 (2H, m), 4.19 (1H, dd, J = 7.8, 4.6 Hz).

3c-Acetonide: Oil. $[\alpha]_D^{24}$ −12.6° (c = 1.45, $CHCl_3$). UV λ_{max}^{MeOH} nm: end absorption. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500, 1730. CIMS (iso-C_4H_{10}) m/z: 439 ($MH^+ - 76$). CIMS (NH_3) m/z: 515 (MH^+). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 0.90 (3H, t, J = 5.9 Hz), 1.25—1.80 (m), 1.37 (6H, s), 3.59 (3H, m), 3.78 (3H, s), 4.19 (1H, m).

The Bicyclic Acetals 18a—c A solution of **3a**-acetonide (11.8 mg) in acetone (2 ml) was cooled to 0 °C and two drops of Jones' reagent were added. The reaction mixture was stirred for 1.5 h and quenched with isopropanol. The solution was neutralized with saturated aqueous $NaHCO_3$ and passed through a short Celite column. The filtrate was concentrated to give an oily residue. The residue was dissolved in MeOH and *p*-TsOH (2 mg) was added. The reaction mixture was stirred for 1.5 h, neutralized with saturated aqueous $NaHCO_3$, and passed through a Celite column, and the filtrate was concentrated *in vacuo*. The residue was chromatographed on silica gel column using AcOEt : *n*-hexane (1 : 9) to give the **18a** (2.5 mg). In the same manner, **3b**-acetonide (15.1 mg) and **3c**-acetonide (12.1 mg) were converted **18b** (2.5 mg) and **18c** (5.5 mg), respectively.

18a: Oil. $[\alpha]_D^{25}$ +36.9° (c = 0.17, Et_2O). UV λ_{max}^{MeOH} nm: end absorption. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720. CIMS (iso-C_4H_{10}) m/z: 453 (MH^+). CIMS (NH_3) m/z: 470 $(M+NH_4)^+$, 453 (MH^+). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 0.90 (3H, t, J = 7.08 Hz), 1.22—1.85 (m), 2.83 (2H, t, J = 7.1 Hz), 3.87 (3H, s), 3.98 (1H, ddd, J = 7.1, 4.6, 3.9 Hz), 4.18 (1H, t, J = 4.6 Hz).

18b: Oil. $[\alpha]_D^{23}$ +35.4° (c = 0.17, Et_2O). UV λ_{max}^{MeOH} nm: end absorption. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720. CIMS (iso-C_4H_{10}) m/z: 453 (MH^+). CIMS (NH_3) m/z: 470 $(M+NH_4)^+$, 453 (MH^+). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 0.90 (3H, t, J = 7.1 Hz), 1.22—1.85 (m), 2.83 (2H, t, J = 7.1 Hz), 3.87 (3H, s), 3.98 (1H, ddd, J = 7.1, 4.6, 3.9 Hz), 4.20 (1H, t, J = 4.6 Hz).

18c: Oil. $[\alpha]_D^{23}$ −36.1° (c = 0.38, Et_2O). UV λ_{max}^{MeOH} nm: end absorption. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720. CIMS (iso-C_4H_{10}) m/z: 453 (MH^+). CIMS (NH_3) m/z: 470 $(M+NH_4)$, 453 (MH^+). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 0.91 (3H, t, J = 7.1 Hz), 1.26—1.92 (m), 2.83 (2H, t, J = 7.1 Hz), 3.79 (3H, s), 3.98 (1H, dd, J = 7.3, 5.6 Hz), 4.10 (1H, br s).

The Di-*p*-methoxybenzoate (21) The **3c**-acetonide (25.6 mg) was dissolved in pyridine (2 ml) and acetic anhydride (1.5 ml) and the reaction mixture was allowed to stand at room temperature overnight. The solvents were removed *in vacuo* and the residue was chromatographed on a silica gel column using AcOEt : *n*-hexane (2 : 8) to give the diacetate of **3c**-acetonide (26.2 mg).

The diacetate (23.8 mg) was dissolved in MeOH (2 ml) and *p*-TsOH (5 mg) was added. The reaction mixture was stirred for 5 h and then neutralized with saturated aqueous $NaHCO_3$. After filtration of the mixture the filtrate was evaporated *in vacuo*. The residue was chromatographed on a silica gel column using AcOEt : *n*-Hexane (3 : 7) to give the diol (17.1 mg).

The diol (15.4 mg) was dissolved in CH_2Cl_2 (2 ml) and to this solution were added 4-dimethylaminopyridine (24 mg) and *p*-methoxybenzoyl chloride (18 μl). The reaction mixture was stirred for 6 d at room temperature. After filtration of the mixture the filtrate was concentrated *in vacuo*. The residue was chromatographed on a silica gel column using AcOEt : *n*-hexane (2 : 8) to give the di-*p*-methoxybenzoate (**21**, 15.6 mg).

21: Oil. $[\alpha]_D^{24}$ −33.3° (c = 1.0, $CHCl_3$). UV λ_{max}^{MeOH} nm: 264. CD (c = 6.17 × 10^{-5} M, EtOH): 273 nm ($\Delta\varepsilon$ +1.77), 249 nm ($\Delta\varepsilon$ −7.39). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1705, 1735. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 0.85 (3H, t, J = 7.1 Hz), 1.17—1.85 (m), 1.95 (3H, s), 2.14 (3H, s), 3.75 (3H, s), 3.86 (6H, s), 4.79 (1H, q, J = 7.1 Hz), 4.98 (1H, t, J = 6.6 Hz), 5.33 (2H, m), 6.90 (4H, d, J = 8.6 Hz), 7.99 (4H, d, J = 8.6 Hz). CIMS (iso-C_4H_{10}) m/z: 827 (MH^+). CIMS (NH_3) m/z: 844 $(M+NH_4)^+$.

(2*R*,3*R*)-(−)-Butane-2,3-diol Di-*p*-methoxybenzoate (22) 4-Dimethylaminopyridine (56.9 mg) and *p*-methoxybenzoyl chloride (30 μl) were added to a solution of (2*R*,3*R*)-(−)-2,3-butane-2,3-diol (14 mg) in CH_2Cl_2 (5 ml). The reaction mixture was stirred for 5 h and concentrated *in vacuo*. The residue was chromatographed on a silica gel column using AcOEt : *n*-hexane (1 : 9) to give **22** (21 mg).

22: Oil. $[\alpha]_D^{24}$ −12.4° (c = 0.15, $CHCl_3$). EIMS m/z: 358 (M^+), 135. UV λ_{max}^{MeOH} nm: 255. CD (c = 2.23 × 10^{-5} M, EtOH): 245 nm ($\Delta\varepsilon$ +8.90), 265 nm

($\Delta\varepsilon -6.79$). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 1.39 (6H, d, $J=6.4$ Hz), 3.84 (6H, s), 5.32 (2H, m), 6.89 (4H, d, $J=8.8$ Hz), 7.99 (4H, d, $J=8.8$ Hz).

(2*S*,3*S*)-(+)-Butane-2,3-diol Di-*p*-methoxybenzoate (23) In the same manner as in the case of **22**, (2*S*,3*S*)-(+)-butane-2,3-diol (30 mg) was *p*-methoxybenzoylated using 4-dimethylaminopyridine (138 mg) and *p*-methoxybenzoyl chloride (121 μl) to give **23** (105 mg).

23: Oil. $[\alpha]_D^{24}$ +18.1° ($c=0.31$, $CHCl_3$). EIMS *m/z*: 358 (M^+), 135. UV λ_{max}^{MeOH} nm: 255. CD ($c=5.59\times10^{-5}$ M, EtOH): 265 nm ($\Delta\varepsilon +7.61$), 245 nm ($\Delta\varepsilon -10.38$). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 1.39 (6H, d, $J=6.1$ Hz), 3.85 (6H, s), 5.32 (2H, m), 6.90 (4H, d, $J=9.0$ Hz), 7.99 (4H, d, $J=9.0$ Hz).

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