Alangionosides G—M: Glycosides of Megastigmane Derivatives from the Leaves of *Alangium premnifolium*

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Phytochemical investigation of the 1-BuOH-soluble fraction of the MeOH extract of *Alangium premnifolium* resulted in the isolation of ten megastigmane glycosides, of which, two, (6*R*,9*R*)-3-oxo-α-ionol apiofuranosylglucopyranoside and roseoside with (6*S*,9*R*)-blumeol A as an aglycone were known. The structures of the eight new compounds were determined by spectroscopic methods.

Key words *Alangium premnifolium*; Alangiaceae; megastigmane glycoside; roseoside; alangionosides G—M

In continuing phytochemical studies on Okinawan plants, the constituents of *Alangium premnifolium* OHWI (Japanese name, shimaurinoki) were investigated. From the 1-BuOH-soluble fraction of the MeOH extract of leaves of the title plant, several megastigmane glycosides (alangionosides A—F and dendranthemoside A) have been isolated.[1,2] Further extensive isolation of related compounds afforded 10 megastigmane glycosides, of which seven were new compounds (named alangionosides G—M) and one was a new diastereomer of roseoside. The present paper deals with their structural determination.

Results and Discussion

Megastigmane glycosides in the 1-BuOH-soluble fraction of the MeOH extract were isolated by the following procedures. The 95% aqueous methanolic solution of the extract was partitioned with *n*-hexane, and the methanol layer was concentrated. A water suspension of the concentrate was partitioned with EtOAc and then with 1-BuOH. The 1-BuOH-soluble fraction was separated by the combination of synthetic highly porous resin (Diaion HP-20, Nippon Rensui Co., Tokyo) column, silica gel column, reversed-phase gravity column (RPCC), droplet counter-current (DCCC), and reversed-phase high-performance liquid (HPLC) or Sephadex LH-20 column chromatographies. An outline of the separation is given in Experimental.

Compound **1** was found to be a known megastigmane glycoside. By spectroscopic analysis, the structure of compound **1** was determined to be (6*R*,9*R*)-3-oxo-α-ionol β-D-apiofuranosyl(1→6)-β-D-glucopyranoside (**1**), which has been isolated from *Eriobotrya japonica*.[3,4]

The ^{13}C-NMR spectra of compounds **2** and **3** were virtually indistinguishable from each other, the largest difference being observed in the chemical shifts of the C-9 positions (only 0.3 ppm, which was within the range of experimental error). Therefore, the two compounds were considered to have the same planar "roseoside" skeleton. However, their HPLC retention times were different (t_R 47.3 and 50.8 min, respectively). Roseoside was first isolated from *Vinca rosea* by Bhakuni *et al.*,[5] and since then it has been isolated from various plant sources. However, some conflicting physical data have been reported for roseoside from different sources. Achenbach *et al.* isolated it [roseoside (I)] from *Canthium subcordatum*[6] and the roseoside (I) seemed to be identical with that isolated by Bhakuni *et al.*, as judged from the optical rotation values of their acetates. In 1988, Andersson and Lundgren claimed to have isolated roseoside (II) from *Pinus sylvestris*.[7] Although the optical rotation values

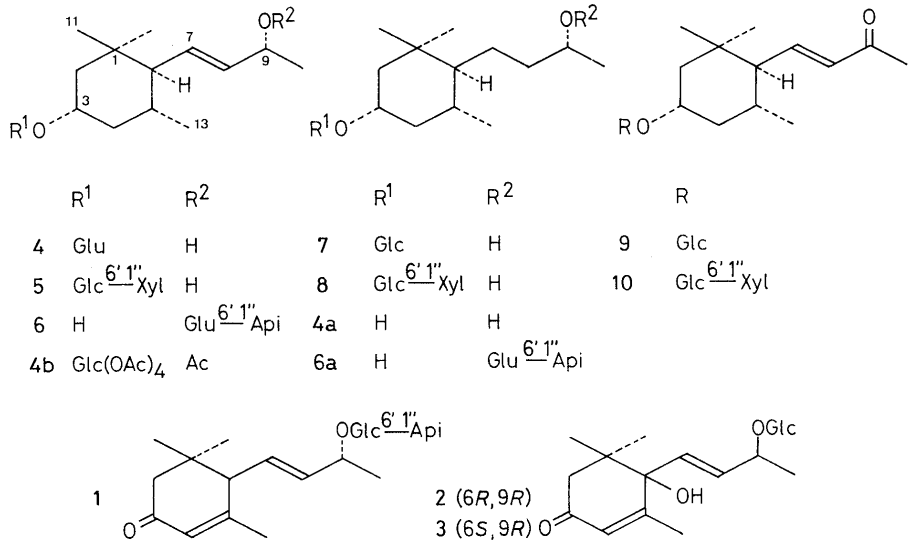

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Table 1. NMR Data for Roseosides (I and II), and Compounds **2** and **3** (400 MHz, CD_3OD)[a]

	2 (I)[b] H	**2** (II)[c] C	**2** (II)[c] H	**2** C	**2** H	**3** C	**3** H
1		42.5		42.5		42.5	
2a	2.17 (br d, 17)	50.8	2.14 (dd, 1.0, 17.0)	50.9	2.16 (d, 17.0)	50.7	2.15 (dd, 0.7, 17.0)
b	2.62 (br d, 17)		2.52 (d, 17.0)		2.51 (d, 17.0)		2.52 (d, 17.0)
3		201.2		201.3		201.2	
4	5.87 (br s)	127.3	5.86 (qd, 1.0, 1.4)	127.2	5.87 (quintet-like, 1.3)	127.2	5.87 (quintet-like, 1.3)
5		167.2		167.4		167.3	
6		80.1		80.0		80.0	
7	5.98 (br d, 15)	131.7	5.85 (br s)	131.8	5.848 (d, 1.5)	131.6	5.854 (d, 1.4)
8	5.73 (dd, 7, 15)	135.4	5.85 (br s)	135.2	5.850 (d, 3.6)	135.3	5.857 (d, 4.2)
9	4.53 (qd, 6.5, 6.5)	77.3	4.42 (m)	77.0	4.44 (qdd, 6.4, 1.5, 3.6)	77.3	4.42 (qdd, 6.4, 1.4, 4.2)
10	1.29 (d, 6.5)	21.2	1.28 (d, 6.4)	21.2	1.30 (d, 6.4)	21.2	1.29 (d, 6.4)
11	1.01 (s)	23.5	1.028 (s)	23.5	1.00 (s)	23.5	1.03 (s)
12	1.04 (s)	24.8	1.032 (s)	24.7	1.03 (s)	24.7	1.04 (s)
13	1.95 (d, 1)	19.6	1.92 (d, 1.4)	19.8	1.92 (d, 1.3)	19.6	1.92 (d, 1.3)
1′	4.28 (d, 7.5)	102.9	4.34 (d, 7.8)	102.7	4.33 (d, 7.9)	102.8	4.34 (d, 7.8)
2′	—	75.4	—	75.3	3.16 (dd, 7.9, 9.1)	75.3	3.17 (dd, 7.8, 9.2)
3′	—	78.3	—	78.1	— —	78.1	— —
4′	—	71.4	—	71.6	— —	71.7	3.26 (t, 9.5)
5′	—	78.1	—	78.0	— —	78.0	— —
6′a	3.63 (dd, 6, 12)	63.0	—	62.7	3.65 (dd, 5.3, 12.1)	62.9	3.62 (dd, 5.5, 11.7)
b	3.84 (dd, 2.5, 12)				3.82 (dd, 2.4, 12.1)		3.85 (dd, 2.2, 11.7)

a) Letters and figures in parentheses are multiplicities and coupling constants (Hz), respectively. *b*) Data taken from lit. 6 (CD_3OD, C: 62.8 MHz; H: 250 MHz), *c*) Data taken from lit. 7 (CD_3OD, C: 22.5 MHz; H: 400 MHz). —, not reported. — —, overlapped with the other signals.

were similar to those reported by Bhakuni *et al.*, some discrepancies were observed between the ^{1}H-NMR signals, especially at the H-2b, 7, 8 and 9 positions (see Table 1). Thus, these two roseosides may be diastereoisomers in the aglycone portion. The ^{1}H-NMR spectrum of the major compound **3** was essentially identical with that of the roseoside (II) isolated by Andersson and Lundgren[7] and that isolated by Nishioka *et al.* from *Zizyphus jujuba* var. *inermis*.[8] The absolute stereochemistry of the aglycone moiety was examined by Nakanishi *et al.*[9] Blumeol A, one of the possible diastereoisomers of the aglycone, which was isolated from *Podocarpus blumei* was chemically correlated with (*S*)-(+)-abscisic acid and shown to have 6*S* and 9*R* configurations. The circular dichroism (CD) spectrum of this blumeol A showed extreme values for $\Delta\varepsilon$ (nm) +9.6 (242) and −0.44° (317), which were similar to those of the compound isolated by Nishioka *et al.* [$\Delta\varepsilon$ (nm) +7.8° (240) and −0.71° (316)] and compound **3** [$\Delta\varepsilon$ (nm) +13.6°(241) and −1.15° (318)]. In contrast, the CD extreme values of the minor compound **2** [$\Delta\varepsilon$ (nm) −11.4° (241) and +0.23° (323)] were opposite to those of the aforementioned roseosides. Therefore, compound **2** ($[\alpha]_D$ −74.0°) is not identical with the compound reported by Andersson and Lundgren ($[\alpha]_D$ +112°) or that isolated by Achenbach *et al.*, and must be assigned as a third roseoside, which has (6*R*,9ξ)-blumeol A as its aglycone moiety. The absolute configuration at the 9-position of **2** must be the same as that of **3**, since the ^{13}C-NMR spectra showed that the 8-, 9- and 10-positions of **2** and **3** have essentially the same chemical shifts on β-D-glucopyranosylation. Pabst *et al.* reported the ^{13}C-NMR chemical shifts of the β-D-glucopyranoside of (9*R*)- and (9*S*)-3-oxo-α-ionol (**1**) to be δ 77.0 and 74.7, respectively.[3] Therefore, the absolute configuration of the 9-position of **2** and **3** was tentatively assigned as *R* (see Table 1). A report of the isolation of a roseoside from *Astragalus companastus* recently appeared.[10] From the reported optical rotation value and ^{13}C-NMR spectrum, this roseoside may be a fourth diastereomer, which would have 9*S* configuration [δ_C 73.2 (C-9) and 22.3 (C-10) (C_5D_5N); **3**: δ_C 76.2 (C-9) and 21.3 (C-10) (C_5D_5N)].

Alangionoside G (**4**), $[\alpha]_D$ −37.5°, was obtained as a colorless amorphous powder, whose elemental composition was determined to be $C_{19}H_{34}O_7$ from the observation of a quasi molecular ion peak in the negative FAB-MS. In addition to the signals due to the β-glucopyranosyl moiety (δ_C 102.7 and δ_H 4.35, J=8 Hz), the ^{13}C-NMR spectrum showed the presence of four methyl groups, two methylene groups, four methine groups, two of which were expected to bear electronegative substituents from their chemical shifts (δ_C 69.4 and 75.7), one quaternary carbon atom, and a disubstituted double bond (see Table 2). Two methyl groups appeared as singlets and another two as doublets in the ^{1}H-NMR spectrum, and the protons on the double bond (δ_H 5.30 and 5.45) showed a *trans* relationship (J=15 Hz). The ^{1}H–^{1}H correlation spectroscopy (COSY) spectrum unambiguously revealed all the proton spin–spin connectivities, and the correlations between protons and carbons were fully assigned from the ^{13}C–^{1}H COSY spectrum. Thus, the quaternary carbon must carry two methyl groups, and the connection of carbons 2 and 6 *via* the quaternary carbon gave the representative megastigmane skeleton.

The H-3 proton (δ_H 3.87) was used as a probe to elucidate the relative structure. Since this proton is coupled with two anti-parallel axial protons on adjacent carbons with a coupling constant of 12 Hz, the hydroxy group at the 3-position must be in the equatorial orientation. Although the H-5 proton appeared as a multiplet, the splitting pattern of the H-4 axial proton (δ_H 0.90, q, J=12 Hz)

Table 2. ^{13}C-NMR Data for Alangionosides G—M (**4**—**10**), and Their Derivatives (100 MHz, CD_3OD)

Carbon	**4**		**4a**	**5**	**6**	**6a**		**7**	**8**	**9**	**10**
1	35.9		36.8	35.8	36.0	36.9		36.8	36.8	36.4	36.4
2	47.9	(−4.0)[a]	51.9	48.0	51.2	51.9		48.5	48.6	47.7	47.7
3	75.7	(+8.3)	67.4	76.0	67.4	67.5		75.8	76.0	75.4	75.7
4	43.9	(−2.6)	46.5	44.0	45.6	46.5		44.8	44.8	43.5	43.5
5	32.2		35.0	32.2	32.2	34.9		35.1	35.0	32.0	31.9
6	58.7		54.2	58.6	58.6	54.3		54.3	54.3	59.1	59.1
7	131.2		26.4	131.3	133.4	26.1		26.4	26.4	151.8	151.8
8	138.5		42.7	138.4	136.4	40.7	(−2.0)[b]	42.7	42.7	134.7	134.6
9	69.4		69.2	69.4	78.1	76.4	(+7.2)	69.2	69.2	200.8	200.8
10	24.1		23.4	24.1	21.8	20.0	(−3.4)	23.4	23.4	27.0	27.0
11	21.7		21.4	21.8	21.9	21.5		21.3	21.5	21.8	21.9
12	31.9		31.3	31.9	32.3	31.5		31.3	31.3	31.8	31.8
13	21.7		21.5	21.8	21.5	21.6		21.5	21.4	21.6	21.7
1′	102.7			102.9	102.4	102.3		102.7	102.9	102.8	103.0
2′	75.1			74.9	75.4	75.2		75.2	74.9	75.1	74.9
3′	78.1			77.9	78.1	78.1		78.2	78.0	78.1	78.0
4′	71.7			71.5	71.5	71.8		71.8	71.6	71.8	71.6
5′	77.9			76.9	76.9	76.8		77.9	76.9	77.9	77.0
6′	62.9			69.7	68.3	68.6		62.9	69.8	62.9	69.8
1″				105.5	111.0	110.9			105.5		105.6
2″				75.0	78.1	78.0			75.1		75.0
3″				77.7	80.6	80.6			77.7		77.7
4″				71.2	75.1	75.0			71.2		71.2
5″				66.9	65.7	65.8			66.9		66.9

a) $\Delta\delta_{4\ 4a}$. *b*) $\Delta\delta_{6a\ 4a}$.

required three protons to induce such a coupling pattern. Thus, the methyl group at the 5-position was placed in the equatorial direction. Finally, the coupling constant values (J=10 Hz) of H-6 (δ_H 1.31) and H-5 (δ_H 1.54) indicated that the side chain was also in the equatorial orientation. The position of the β-glucopyranose moiety was determined by comparison of the ^{13}C-NMR data for **4** and its reduced aglycone (**4a**), obtained by enzymatic hydrolysis of the reduced compound (=alangionoside J). On going from **4a** to **4**, a significant downfield shift was observed for the C-3 carbon ($\Delta\varepsilon$ +8.2) on glycosylation. Thus, the β-D-glucopyranose moiety is attached to the hydroxyl group at the 3-position. This was further confirmed by an acetylation experiment, in which H-9 shifted downfield (δ_H 4.22→5.30), whereas H-3 remained almost unchanged (δ_H 3.87→3.72) in the ^{1}H-NMR spectrum. Determination of the absolute configurations will be discussed later.

Alangionoside H (**5**), $[\alpha]_D$ −51.0°, was obtained as a white powder, whose elemental composition was determined to be $C_{24}H_{42}O_{11}$ by high-resolution FAB-MS. The ^{13}C-NMR spectrum indicated that **5** was also a glycoside of megastigmane and that the aglycone moiety was the same as that of alangionoside G (see Table 2). Gas liquid chromatography (GLC) analysis of the sugar portion revealed the presence of glucose and xylose, and ^{13}C-NMR indicated that β-xylopyranose was in the terminal position (δ_C 105.5, 75.0, 77.7, 71.2 and 66.9). A significant downfield shift (**4**→**5**, δ_C 62.9→69.7), observed at the 6-position of β-D-glucopyranose, indicated that the xylose was linked to that position. This was also confirmed by comparison of the data with those reported data for β-D-xylopyranosyl-(1→6)-β-D-glucopyranoside.[11] Therefore, the structure of alangionoside H was determined to be 6′-β-D-xylopyranosylalangionoside G (**5**), as shown in the formulae.

Alangionoside I (**6**), $[\alpha]_D$ −54.2°, was obtained as an amorphous powder, and its elemental composition was the same as that of alangionoside H (**5**). The ^{13}C-NMR signals for the sugar portion included those of the 6-glycosylated β-glucopyranose, as seen in **5**. The remaining five signals, including a singlet at δ_C 80.6 and two methylene (δ_C 65.7 and 75.1) carbons, were characteristic of the β-apiofuranose moiety. By comparison with the reported data,[1] the sugar portion was determined to be β-D-apiofuranosyl-(1→6)-β-D-glucopyranose. Although the structure of the aglycone portion, elucidated by a combination of one- and two-dimensional NMR spectroscopies, was the same as that of alangionosides G and H, the ^{13}C-NMR chemical shifts were obviously different from the common aglycone of **4** and **5** (see Table 2). The only possible explanation accounting for the ^{13}C-NMR spectrum was that the sugar portion was attached to the hydroxyl group at the 9-position: the C-9 signal was shifted downfield (δ_C 69.4→78.1) and the C-3 signal was shifted upfield (δ_C 75.7→67.4) in **6** from those of **4**. Thus, the structure of alangionoside I was determined to be **6**, as shown in the formulae.

Alangionoside J (**7**), $[\alpha]_D$ −34.5°, was obtained as an amorphous powder, whose elemental composition determined by high-resolution FAB-MS indicated that it is two mass units larger than alangionoside G (**4**). This coincided with the fact that in the ^{1}H- and ^{13}C-NMR spectra, the signals for the double bond seen in **4** were not observed, indicating that alangionoside J must be dihydroalangionoside G. To confirm this, alangionoside G was catalytically reduced with PtO_2–H_2 to give a dihydrocompound, whose physico-chemical data were indistinguishable from those of alangionoside J. Thus, the structure of alangionoside J was elucidated to be **7**, as

shown in the formulae.

Alangionoside K (**8**), $[\alpha]_D$ −53.5°, was expected to be an analogous compound to alangionoside J from the NMR data. As a similar relationship to that between alangionosides G and H in the sugar portion of the ^{13}C-NMR spectrum was observed, the structure of **8** was concluded to be 6′-*β*-D-xylopyranosylalangionoside J.

Alangionoside L (**9**), $[\alpha]_D$ −37.5°, was also obtained as an amorphous powder. The elemental composition determined by high-resolution FAB-MS corresponded to two mass units smaller than alangionoside G. The UV absorption maximum at 229 nm and a ketone function (δ_C 200.1) observed in the ^{13}C-NMR spectrum indicated the presence of an *α*,*β*-unsaturated system in the side chain of the aglycone. The six-membered ring skeleton elucidated through one- and two-dimensional NMR spectroscopies was the same as that of the aforementioned megastigmanes. Because dichlorodicyanobenzoquinone (DDQ) oxidation of the allyl alcohol in alangionoside G afforded alangionoside L, the structure of alangionoside L was confirmed to be **9**, as shown in the formulae.

Alangionoside M (**10**), $[\alpha]_D$ −61.2°, was also obtained as an amorphous powder. For the structure determination of **10**, a similar rationale was adopted to that used in deducing the structure of alangionoside H from that of alangionoside G. Therefore, alangionoside M is 6′-*β*-D-xylopyranosylalangionoside L (**10**), as shown in the formulae.

Kasai *et al.* reported that on *β*-D-glucopyranosylation of an equatorial secondary alcohol on the cyclohexane ring, different shifts were observed at adjacent carbon atoms on ^{13}C-NMR spectroscopy, such as *ca.* 4 ppm for the pro-*S* side, but *ca.* 2 ppm for the pro-*R* side.[12] The validity of this empirical rule for the assignment of the absolute configuration of the 3-position in the megastigmane skeleton has been supported.[13,14] On going from the reduced aglycone (**4a**) to **4**, the 2-position showed an upfield shift of 4.0 ppm, whereas the 4-position showed one of 2.6 ppm (see Table 1). Thus, the 2-position was assigned as the pro-*S* equivalent side and the 4-position as the pro-*R* side. Therefore, the 3*S* configuration can be assigned to alangionoside G. The application of the rule to a secondary alcohol such as the side chain of megastigmanes was also examined.[1,14] The double bonds in alangionoside G (**4**) and alangionoside I (**6**) were catalytically reduced with PtO_2–H_2 to give structures (**7** and **6a**, respectively) which were more closely related to the compounds previously reported,[1] and enzymatic hydrolysis of **7** and **6a** gave the common aglycone. The $\Delta\delta_{7-6a}$ values in Table 2 indicate that the absolute stereochemistry of the 9-position is the same as those of alangionosides A and B, namely the *R*-configuration. Therefore, alangionoside G (**4**) has a 3*S*, 5*S*, 6*R*, 9*R* megastigmane skeleton. Since catalytic reduction and DDQ oxidation of alangionoside G gave alangionosides J (**7**) and L (**9**), respectively, all the new compounds were chemically correlated, including the absolute stereochemistry.

Experimental

The following instruments were used to obtain physical data: ^{1}H- and ^{13}C-NMR spectra, JEOL GX-400 FT-NMR spectrometer (400 and 100 MHz, respectively), with tetramethylsilane as an internal standard; specific rotation, Union Giken PM-101 digital polarimeter; mass spectra, JEOL JMS SX-102 mass spectrometer; UV spectra, Shimadzu UV-160S spectrophotometer; and CD and optical rotatory dispersion (ORD) spectra, JASCO DP-720 spectrophotometer. The following experimental conditions were used for chromatography: synthetic highly porous polymer, Diaion HP-20 (Nippon Rensui Co., Tokyo); Silica gel 60 (Merck); RPCC, Cosmosil 75C_{18}-OPN octadecyl silica (ODS) (Nacalai Tesque, Kyoto); DCCC, 500 glass columns of 2 mm inner diameter and 400 mm length (Tokyo Rikakikai, Tokyo); and reversed-phase HPLC, ODS (Inertsil, 20 mm i.d. × 250 mm; flow rate, 6 ml/min) (GL Science, Tokyo).

Isolation of Alangionosides from Leaves of *A. premnifolium* Leaves of *A. premnifolium* were collected in Nakagami-gun, Okinawa, Japan, in August, 1990. The air-dried leaves (5.72 kg) were extracted with MeOH (30 l × 3). The MeOH extract was concentrated to about 2.5 l, and then 150 ml of H_2O and an appropriate volume of MeOH were added to adjust the solution to 95% aqueous MeOH. This solution was extracted with 3 l of *n*-hexane (200 g). The concentrate was suspended in 1.5 l of H_2O, and then extracted with EtOAc (1 l × 2, 52.1 g) and 1-BuOH (1.5 l and 1 l, 139 g). The 1-BuOH-soluble fraction (138 g) was dissolved in 3 l of 20% MeOH in H_2O and then subjected to Diaion HP-20 column chromatography [i.d. = 70 mm, length = 650 mm, 20% MeOH (3 l), 40% MeOH (8 l), 60% MeOH (10 l) and 80% MeOH (10 l); fractions of 2 l being collected]. Fraction 7 (18.4 g) was separated by silica gel column chromatography ($CHCl_3$→$CHCl_3$–MeOH), RPCC (10% MeOH in H_2O→50% MeOH, linear gradient), and DCCC ($CHCl_3$–MeOH–H_2O–1-PrOH, 9 : 12 : 8 : 2). Further purification was performed by HPLC (MeOH–H_2O, isocratic) or Sephadex LH-20 (MeOH) column chromatography. Following these procedure, compounds **1** (212 mg), **2** (3.7 mg) and **3** (13.0 mg) were isolated. Fractions 8—10 (32.6 g) obtained on Diaion HP-20 column chromatography were separated in a similar manner to the above fraction to give compounds **1** (4 mg), **4** (112 mg), **5** (300 mg), **6** (30 mg), **7** (6 mg), **8** (29 mg) and **10** (23 mg). Compound **9** (32 mg) was similarly obtained from the residue of fractions 9—12 (18.7 g) obtained on Diaion HP-20 column chromatography.

(6*R*,9*R*)-3-Oxo-*α*-ionol *β*-D-Apiofuranosyl(1→6)-*β*-D-glucopyranoside (**1**): A white powder, $[\alpha]_D^{20}$ +68.6° (*c* = 0.23, MeOH).

Compound **2**: White powder, $[\alpha]_D^{22}$ −74.0° (*c* = 0.23, MeOH). UV λ_{max}^{MeOH} nm (log *ε*): 236 (3.89). ^{1}H- and ^{13}C-NMR (CD_3OD): see Table 1. CD (*c* = 0.00121, MeOH) *Δε* (*λ* nm): +7.24 (199), 0 (204), −11.4° (241), +0.23 (323). ORD (*c* = 0.00121, MeOH) [*α*] (*λ* nm): +7570° (202), +5780° (208), +6160° (216), 0° (240), −5450° (260). High-resolution FAB-MS (negative centroid) *m/z*: Found: 385.1855. Calcd for $C_{19}H_{29}O_8$ $[M-H]^-$: 385.1863. HPLC: t_R 47.3 min (MeOH–H_2O, 1 : 3).

Roseoside II (**3**): White powder, $[\alpha]_D^{22}$ +118.8° (*c* = 0.87, MeOH).[5] ^{1}H-NMR (C_5D_5N) *δ*: 1.16, 1.26 (each 3H, each s, H_3-11, 12), 1.39 (3H, d, *J* = 7 Hz, H_3-10), 2.02 (3H, d, *J* = 1 Hz, H_3-13), 2.40 (H, d, *J* = 17 Hz, H-2a), 2.69 (H, d, *J* = 17 Hz, H-2b), 3.92 (H, ddd, *J* = 2, 6, 9 Hz, H-5′), 4.05 (H, br t, *J* = 8 Hz, H-2′), 4.17 (H, t, *J* = 9 Hz, H-4′), 4.25 (H, t, *J* = 9 Hz, H-3′), 4.30 (H, dd, *J* = 6, 12 Hz, H-6′a), 4.56 (H, dd, *J* = 2, 12 Hz, H-6′b), 4.74 (H, quintet, *J* = 7 Hz, H-9), 4.95 (H, d, *J* = 8 Hz, H-1′), 6.08 (H, s, H-4), 6.15 (H, d, *J* = 16 Hz, H-7), 6.33 (H, dd, *J* = 7, 16 Hz, H-8). ^{13}C-NMR (C_5D_5N) *δ*: 19.4 (C-11 or 12), 21.3 (C-10), 23.4 (C-12 or 11), 41.7 (C-1), 50.4 (C- 2), 63.2 (C-6′), 72.2 (C-4′), 75.4 (C-2′), 76.2 (C-9), 78.3 (C-5′), 78.7 (C-3′), 79.0 (C-6), 103.0 (C-1′), 127.0 (C-4), 131.4 (C-7), 134.9 (C-8), 163.9 (C-5), 197.6 (C-3). CD (*c* = 0.00371, MeOH) *Δε* (*λ* nm): −3.69 (203), 0 (211), +13.6 (241), −1.15 (318). ORD (*c* = 0.00371, MeOH) [*α*] (*λ* nm): −11400° (211), 0° (245), −4450° (261). ^{1}H- and ^{13}C-NMR (CD_3OD): see Table 1. HPLC: t_R 50.8 min (MeOH–H_2O, 1 : 3).

Alangionoside G (**4**): White powder, $[\alpha]_D^{20}$ −37.5° (*c* = 0.95, MeOH). ^{1}H-NMR (CD_3OD) *δ*: 0.83(3H, d, *J* = 7 Hz, H_3-13), 0.87 (3H, s, H_3-$11_{ax.}$), 0.91 (3H, s, H_3-$12_{eq.}$), 1.02 (H, q, *J* = 12 Hz, H-$4_{ax.}$), 1.16 (H, t, *J* = 12 Hz, H-$2_{ax.}$), 1.22 (3H, d, *J* = 6 Hz, H_3-10), 1.31 (H, t, *J* = 10 Hz, H-6), 1.54 (H, m, H-5), 1.85 (H, ddd, *J* = 2, 4, 12 Hz, H-$2_{eq.}$), 2.11 (H, dtd, *J* = 2, 4, 12 Hz, H-$4_{eq.}$), 3.12 (H, dd, *J* = 8, 9 Hz, H-2′), 3.66 (H, dd, *J* = 6, 12 Hz, H-6′a), 3.86 (H, dd, *J* = 2, 12 Hz, H-6′b), 3.87 (H, tt, *J* = 4, 12 Hz, H-3), 4.22 (H, dquintet, *J* = 1, 6 Hz, H-9), 4.35 (H, d, *J* = 8 Hz, H-1′), 5.30 (H, ddd, *J* = 1, 10, 15 Hz, H-7), 5.45 (H, dd, *J* = 6, 15 Hz, H-8). ^{13}C-NMR: see Table 2. High-resolution FAB-MS (negative centroid) *m/z*: Found: 373.2248. Calcd for $C_{19}H_{33}O_7$ $[M-H]^-$, 373.2227.

Alangionoside H (**5**): White powder, $[\alpha]_D^{20}$ −51.0° (*c* = 2.04, MeOH). ^{1}H-NMR (CD_3OD) *δ*: 0.83 (3H, d, *J* = 7 Hz, H_3-13), 0.88 (3H, s,

H_3-12$_{ax.}$), 0.90 (3H, s, H_3-11$_{eq.}$), 1.02 (H, q, J=12 Hz, H-4$_{ax.}$), 1.16 (H, t, J=12 Hz, H-2$_{ax.}$), 1.22 (3H, d, J=6 Hz, H_3-10), 1.31 (H, t, J=10 Hz, H-6), 1.58 (H, m, H-5), 1.84 (H, ddd, J=2, 7, 12 Hz, H-2$_{eq.}$), 2.11 (H, br d, J=12 Hz, H-4$_{eq.}$), 3.13 (H, dd, J=8, 9 Hz, H-2′), 3.18 (H, dd, J=10, 11 Hz, H-5″a), 3.20 (H, dd, J=8, 11 Hz, H-2″), 3.45 (H, m, H-5′), 3.48 (H, ddd, J=5, 8, 10 Hz, H-4″), 3.75 (H, dd, J=6, 12 Hz, H-6′a), 3.85 (H, tt, J=7, 12 Hz, H-3), 3.85 (H, dd, J=5, 11 Hz, H-5″b), 4.05 (H, dd, J=6, 12 Hz, H-6′b), 4.22 (H, dquintet, J=1, 6 Hz, H-9), 4.34 (2H, d, J=8 Hz, H-1′, H-1″), 5.30 (H, ddd, J=1, 10, 15 Hz, H-7), 5.45 (H, dd, J=6, 15 Hz, H-8). ^{13}C-NMR: see Table 2. High-resolution FAB-MS (negative centroid) m/z: Found: 505.2580. Calcd for $C_{24}H_{41}O_{11}$ $[M-H]^-$: 505.2649.

Alangionoside I (**6**): White powder, $[\alpha]_D^{20}$ −54.2° (c=1.07, MeOH). ^{1}H-NMR (CD_3OD) δ: 0.83 (3H, d, J=7 Hz, H_3-13), 0.87 (3H, s, H_3-12$_{ax.}$), 0.90 (H, q, J=12 Hz, H-4$_{ax.}$), 0.91 (3H, s, H_3-11$_{eq.}$), 1.11 (H, t, J=12 Hz, H-2$_{ax.}$), 1.28 (3H, d, J=7 Hz, H_3-10), 1.33 (H, t, J=10 Hz, H-6), 1.54 (H, m, H-5), 1.69 (H, ddd, J=2, 4, 13 Hz, H-2$_{eq.}$), 1.97 (H, dtd, J=2, 6, 12 Hz, H-4$_{eq.}$), 3.17 (H, dd, J=8, 9 Hz, H-2′), 3.58 (2H, s, H_2-5″), 3.72 (H, tt, J=4, 11 Hz, H-3), 3.76 (H, d, J=10 Hz, H-4″a), 3.90 (H, d, J=2 Hz, H-2″), 3.92 (H, d, J=10 Hz, H-6′b), 3.96 (H, d, J=10 Hz, H-4″b), 4.32 (H, dquintet, J=1, 7 Hz, H-9), 4.33 (H, d, J=8 Hz, H-1′), 4.97 (H, d, J=2 Hz, H-1″), 5.36 (H, ddd, J=1, 10, 15 Hz, H-7), 5.52 (H, dd, J=7, 15 Hz, H-8). ^{13}C-NMR: see Table 2. High-resolution FAB-MS (negative centroid) m/z: Found: 505.2665. Calcd for $C_{24}H_{41}O_{11}$ $[M-H]^-$: 505.2649.

Alangionoside J (**7**): White powder, $[\alpha]_D^{20}$ −25.0° (c=0.40, MeOH). ^{1}H-NMR (CD_3OD) δ: 0.55 (H, ddd, J=2, 5, 11 Hz, H-6), 0.83 (3H, s, H_3-12$_{eq.}$), 0.96 (3H, s, H_3-11$_{ax.}$), 0.97 (3H, d, J=7 Hz, H_3-13), 1.03 (H, q, J=12 Hz, H-4$_{ax.}$), 1.05 (H, m, H-7a), 1.13 (H, t, J=12 Hz, H-2$_{ax.}$), 1.14 (3H, d, J=6 Hz, H_3-10), 1.4—1.6 (4H, m, H-5, -7b, -8a, -8b), 1.80 (H, ddd, J=2, 4, 12 Hz, H-2$_{eq.}$), 2.02 (H, br d, J=12 Hz, H-4$_{eq.}$), 3.11 (H, dd, J=8, 9 Hz, H-2′), 3.65 (H, dd, J=6, 12 Hz, H-6′a), *ca.* 3.65 (H, m, H-9), 3.85 (H, tt, J=4, 12 Hz, H-3), 3.85 (H, dd, J=2, 12 Hz, H-6′b), 4.33 (H, d, J=8 Hz, H-1′). ^{13}C-NMR: see Table 2. High-resolution FAB-MS (negative centroid) m/z: Found: 375.2348. Calcd for $C_{19}H_{35}O_7$ $[M-H]^-$: 375.2383.

Alangionoside K (**8**): White powder, $[\alpha]_D^{20}$ −53.5° (c=0.67, MeOH). ^{1}H-NMR (CD_3OD) δ: 0.55 (H, ddd, J=3, 5, 11 Hz, H-6), 0.84 (3H, s, H_3-12$_{eq.}$), 0.91 (3H, s, H_3-11$_{ax.}$), 0.98 (3H, d, J=7 Hz, H_3-13), 1.02 (H, q, J=12 Hz, H-4$_{ax.}$), 1.14 (H, t, J=12 Hz, H-2$_{ax.}$), 1.14 (3H, d, J=6 Hz, H_3-10), 1.4—1.6 (4H, m, H-5, -7b, -8a, -8b), 1.69 (H, ddd, J=2, 4, 13 Hz, H-2$_{eq.}$), 2.03 (H, br d, J=13 Hz, H-4$_{eq.}$), 3.12 (H, t, J=8 Hz, H-2′), 3.18 (H, dd, J=10, 12 Hz, H-5″a), 3.20 (H, dd, J=8, 9 Hz, H-2″), 3.48 (H, ddd, J=5, 9, 10 Hz, H-4″), 3.65 (H, m, H-9), 3.74 (H, dd, J=6, 12 Hz, H-6′a), 3.82 (H, tt, J=4, 12 Hz, H-3), 3.86 (H, dd, J=5, 12 Hz, H-5″b), 4.05 (H, dd, J=2, 12 Hz, H-6′b), 4.33 (H, d, J=8 Hz, H-1′ or -1″), 4.33 (H, d, J=8 Hz, H-1″ or -1′). ^{13}C-NMR: see Table 2. High-resolution FAB-MS (negative centroid) m/z: Found: 507.2830. Calcd for $C_{24}H_{43}O_{11}$ $[M-H]^-$: 507.2805.

Alangionoside L (**9**): White powder, $[\alpha]_D^{22}$ −37.5° (c=0.83, MeOH). UV λ_{max}^{MeOH} nm (log ε): 229 (4.12). ^{1}H-NMR (CD_3OD) δ: 0.83 (3H, d, J=6 Hz, H_3-13), 0.86 (3H, s, H_3-12$_{eq.}$), 0.94 (3H, s, H_3-11$_{ax.}$), 1.06 (H, q, J=12 Hz, H-4$_{ax.}$), 1.21 (H, t, J=12 Hz, H-2$_{ax.}$), 1.58 (H, t, J=10 Hz, H-6), 1.74 (H, m, H-5), 1.89 (H, ddd, J=2, 4, 12 Hz, H-2$_{eq.}$), 2.16 (H, br d, J=12 Hz, H-4$_{eq.}$), 2.26 (3H, s, H_3-10), 3.13 (H, dd, J=8, 9 Hz, H-2′), 3.35 (H, t, J=9 Hz, H-3′), 3.66 (H, dd, J=5, 12 Hz, H-6′a), 3.87 (H, br d, J=12 Hz, H-6′b), 3.92 (H, tt, J=4, 12 Hz, H-3), 4.36 (H, d, J=8 Hz, H-1′), 6.08 (H, d, J=16 Hz, H-8), 6.66 (H, dd, J=10, 16 Hz, H-7). ^{13}C-NMR: see Table 2. High-resolution FAB-MS (negative centroid) m/z: Found: 371.2056. Calcd for $C_{19}H_{31}O_7$ $[M-H]^-$: 371.2070.

Alangionoside M (**10**): White powder, $[\alpha]_D^{20}$ −61.2° (c=1.37, MeOH). UV λ_{max}^{MeOH} nm (log ε): 229 (4.13). ^{1}H-NMR (CD_3OD) δ: 0.84 (3H, d, J=6 Hz, H_3-13), 0.89 (3H, s, H_3-12$_{eq.}$), 0.95 (3H, s, H_3-11$_{ax.}$), 1.06 (H, q, J=12 Hz, H-4$_{ax.}$), 1.21 (H, t, J=12 Hz, H-2$_{ax.}$), 1.58 (H, t, J=10 Hz, H-6), 1.77 (H, m, H-5), 1.87 (H, ddd, J=2, 4, 12 Hz, H-2$_{eq.}$), 2.17 (H, dtd, J=2, 4, 12 Hz, H-4$_{eq.}$), 2.26 (3H, s, H_3-10), 3.14 (H, dd, J=8, 9 Hz, H-2′), 3.19 (H, dd, J=10, 11 Hz, H- 5″a), 3.21 (H, dd, J=8, 9 Hz, H-2″), 3.34 (H, t, J=9 Hz, H-3′), 3.46 (H, ddd, J=2, 6, 9 Hz, H-5′), 3.49 (H, ddd, J=5, 9, 10 Hz, H-4″), 3.75 (H, dd, J=6, 12 Hz, H-6′a), 3.87 (H, dd, J=5, 11 Hz, H-5″b), 3.90 (H, tt, J=4, 12 Hz, H-3), 4.06 (H, dd, J=2, 12 Hz, H-6′b), 4.35 (2H, d, J=8 Hz, H-1′, -1″), 6.08 (H, d, J=16 Hz, H-8), 6.67 (H, dd, J=10, 16 Hz, H-7). ^{13}C-NMR: see Table 2. High-resolution FAB-MS (negative centroid) m/z: Found: 503.2526. Calcd for $C_{24}H_{39}O_{11}$ $[M-H]^-$: 503.2492.

Catalytic Hydrogenation of Alangionoside G (4) to Dihydroalangionoside G [=Alangionoside J (7)] An ethanol solution (10 ml) of alangionoside G (30 mg) was hydrogenated with PtO_2 (8 mg) under an H_2 atmosphere. At the end of absorption of H_2, the catalyst was removed by filtration and the residue of the ethanol solution was purified by DCCC to give 19 mg (63%) of dihydroalangionoside G (in fractions 78—90). An amorphous powder, $[\alpha]_D^{22}$ −20.3° (c=1.26, MeOH). The spectroscopic data were essentially indistinguishable from those of alangionoside J (**7**).

Catalytic Hydrogenation of Alangionoside I (6) An ethanol solution (10 ml) of alangionoside I (16 mg) was reduced with PtO_2 (10 mg) and H_2. A similar work-up to that described for dihydroalangionoside G gave 14 mg (88%) of dihydroalangionoside I (**6a**) (in fractions 47—58). An amorphous powder, $[\alpha]_D^{22}$ −33.1° (c=0.97, MeOH). ^{1}H-NMR (CD_3OD) δ: 0.52 (H, ddd, J=2, 5, 11 Hz, H-6), 0.83 (3H, s, H_3-12$_{eq.}$), 0.90 (H, q, J=12 Hz, H-4$_{ax.}$), 0.95 (H, 3H, s, H_3-11$_{ax.}$), 0.98 (3H, d, J=6 Hz, H_3-13), 1.08 (H, t, J=12 Hz, H-2$_{ax.}$), *ca.* 1.08 (H, m, H-7a), 1.17 (3H, d, J=6 Hz, H_3-10), 1.45 (H, m, H-5), 1.52—1.60 (3H, m, H-7b, -8a, -8b), 1.63 (H, ddd, J=3, 4, 12 Hz, H-2$_{eq.}$), 1.88 (H, m, H-4$_{eq.}$), 3.14 (H, dd, J=8, 9 Hz, H-2′), 3.27 (H, t, J=9 Hz, H-4′), 3.34 (2H, s, H_2-5″), 3.59 (H, dd, J=6, 11 Hz, H-6′a), 3.69 (H, tt, J=4, 11 Hz, H-3), 3.75 (H, d, J=10 Hz, H-4″a), 3.79 (H, sextet, J=6 Hz, H-9), 3.89 (H, d, J=2 Hz, H-2″), 3.94 (H, d, J=10 Hz, H-4″b), 3.95 (H, dd, J=2, 11 Hz, H-6′b), 4.30 (H, d, J=8 Hz, H-1′), 5.01 (H, d, J=2 Hz, H-1″). ^{13}C-NMR: see Table 2. High-resolution FAB-MS (negative centroid) m/z: Found: 507.2808. Calcd for $C_{24}H_{43}O_{11}$ $[M-H]^-$: 507.2805.

Enzymatic Hydrolysis of Dihydroalangionoside G (=Alangionoside J) (7) Dihydroalangionoside G (15 mg) was treated with an equal amount of emulsin at 37 °C for 3 h in 1.5 ml of H_2O. After the reaction mixture had been evaporated, the resultant materials were separated by silica gel column chromatography [i.d.=15 mm, length=20 cm, C_6H_6–$CHCl_3$ (3:7, 100 ml), C_6H_6–$CHCl_3$ (1:9, 100 ml), $CHCl_3$ (100 ml), $CHCl_3$–MeOH (9:1, 100 ml) and $CHCl_3$–MeOH (7:3, 300 ml); fractions of 15 g being collected] to give 3.0 mg (33%) of the aglycone (**4a**) in fractions 30—32 and 5.2 mg (68%) of glucose in fractions 44—49: Aglycone, colorless syrup, $[\alpha]_D^{20}$ −21.0° (c=0.20, MeOH). ^{1}H-NMR (CD_3OD) δ: 0.52 (H, ddd, J=3, 5, 11 Hz, H-6), 0.83 (3H, s, H_3-12$_{eq.}$), 0.90 (H, q, J=12 Hz, H-4$_{ax.}$), 0.95 (3H, s, H_3-11$_{ax.}$), 0.97 (3H, d, J=7 Hz, H_3-13), 1.03 (H, m, H-7a), 1.08 (H, t, J=12 Hz, H-2$_{ax.}$), 1.14 (3H, d, J=6 Hz, H_3-10), 1.40—1.60 (4H, m, H-5, -7b, -8a, -8b), 1.64 (H, ddd, J=3, 4, 12 Hz, H-2$_{eq.}$), 1.89 (H, br d, J=12 Hz, H-4$_{eq.}$), 3.65 (H, m, H-9), 3.69 (H, tt, J=4, 12 Hz, H-3). ^{13}C-NMR: see Table 2. EI-MS m/z (rel. int. %): 214 (0.4) $[M]^+$, 196 (20.8), 178 (11.4), 163 (35.0), 155 (27.0), 137 (75.2) ($C_{10}H_{17}$), 123 (60.0) (C_9H_{15}), 85 (100). High-resolution EI-MS m/z: Found: 214.1908. Calcd for $C_{13}H_{26}O_2$ $[M]^+$, 214.1933. Found: 196.1844. Calcd for $C_{13}H_{24}O$ $[M-H_2O]^+$, 196.1827. Found: 178.1737. Calcd for $C_{13}H_{22}$ $[M-H_2O\times2]^+$, 178.1721. D-Glucose, white powder, $[\alpha]_D^{19}$ +40.4° (c=0.35, H_2O, after being dissolved in H_2O for 24 h).

Enzymatic Hydrolysis of Dihydroalangionoside I (6a) Hydrolysis of dihydroalangionoside I (13 mg) was initiated with 25 mg of crude hesperidinase in 1 ml of H_2O at 37 °C, and then 25 and 20 mg portions of the enzyme were added at 15 and 20 h, respectively. After 40 h, a similar work-up to that described for dihydroalangionoside G gave 4.7 mg (85%) of the aglycone (**4a**). Aglycone, colorless syrup, $[\alpha]_D^{20}$ −14.4° (c=0.31, MeOH). Other physico-chemical properties were essentially the same as those of the aglycone of dihydroalangionoside G.

DDQ Oxidation of Alangionoside G (4) to Alangionoside L (9) Alangionoside G (11 mg) was oxidized with DDQ (25 mg) in 2 ml of dry dioxane at 70 °C for 20 h. The oxidation product was purified by silica gel column chromatography [i.d.=15 mm, length=20 cm, $CHCl_3$ (100 ml), $CHCl_3$–MeOH (19:1, 100 ml), $CHCl_3$–MeOH (9:1, 100 ml), $CHCl_3$–MeOH (17:3, 100 ml) and $CHCl_3$–MeOH (4:1, 100 ml); fractions of 15 g being collected] to give 6.8 mg of 9-oxoalangionoside G from fractions 28—31 (62%). A white powder, $[\alpha]_D^{20}$ −39.7° (c=0.45, MeOH). UV λ_{max}^{MeOH} nm (log ε): 229 (4.15). The spectroscopic data were essentially indistinguishable from those of alangionoside L (**9**).

Alangionoside G Pentaacetate (4b) Alangionoside G (**4**) (15 mg) was acetylated with a mixture of acetic anhydride (250 μl) and pyridine (250 μl) at 25 °C for 15 h. The reagents were removed under a stream of N_2 and then the residue was purified by preparative TLC (16 mg, 70%) [precoated silica gel plate (0.5 mm thickness, 20 cm width ×10 cm, developed for 9 cm with C_6H_6:$(CH_3)_2CO$=4:1 and eluted with $CHCl_3$:MeOH=9:1]. Colorless needles (EtOH), mp 95—98 °C, $[\alpha]_D^{18}$

$+35.0°$ ($c=1.09$, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.79 (3H, d, $J=7$ Hz, H_3-13), 0.83 (3H, s, H_3-$11_{ax.}$), 0.84 (3H, s, H_3-$12_{eq.}$), 1.03 (H, q, $J=12$ Hz, H-$4_{ax.}$), 1.08 (H, t, $J=12$ Hz, H-$2_{ax.}$), 1.28 (H, t, $J=9$ Hz, H-6), 1.30 (3H, d, $J=6$ Hz, H_3-10), 1.49 (H, m, H-5), 1.67 (H, ddd, $J=2$, 4, 12 Hz, H-$2_{eq.}$), 2.00, 2.026, 2.028, 2.04, 2.08 (3H each, each s, Ac × 5), 3.69 (H, ddd, $J=2$, 5, 10 Hz, H-5′), 3.72 (H, tt, $J=5$, 11 Hz, H-3), 4.13 (H, dd, $J=2$, 12 Hz, H-6′a), 4.26 (H, dd, $J=5$, 12 Hz, H- 6′b), 4.57 (H, d, $J=8$ Hz, H-1′), 4.94 (H, dd, $J=8$, 10 Hz, H-2′), 5.07 (H, t, $J=10$ Hz, H-4′), 5.20 (H, t, $J=10$ Hz, H-3′), 5.30 (H, quintet, $J=6$ Hz, H-9), 5.34 (H, dd, $J=9$, 15 Hz, H-7), 5.40 (H, dd, $J=6$, 15 Hz, H-8), the H-$4_{eq.}$ signal was in the envelopes of acetyl signals. ^{13}C-NMR ($CDCl_3$) δ: 20.60, 20.62, 20.65, 20.71, 20.76, 21.02, 21.31, 21.42 ($\underline{C}H_3CO-$ × 5, C-10, C-11 and C-13), 30.8 (C-12), 31.2 (C-5), 34.8 (C-1), 42.2 (C- 4), 46.8 (C-2), 56.9 (C-6), 62.2 (C-6′), 68.6 (C-4′), 71.2, 71.5, 71.7 (C-9, C-2′ and C-3′), 72.8 (C-5′), 75.9 (C-3), 99.7 (C-1′), 132.6, 133.3 (C-7 and C-8), 169.2, 169.4, 170.3 × 2, 170.7 ($CH_3\underline{C}O-$ × 5). High-resolution FAB-MS (negative centroid) m/z: Found: 583.2745. Calcd for $C_{29}H_{43}O_{12}$ $[M-H]^-$: 583.2755. EI-MS m/z (%): 524 (M^+-AcOH, 1), 464 (M^+-AcOH × 2, 0.2), 404 (M^+-AcOH × 3, 0.1), 331 [Glu(OAc)$_4$ oxonium ion, 33], 177 [M^+-Glu(OAc)$_4$O$-$AcOH, 26], 169 (62), 94 (59), 43 (100).

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