A Tetrahydroisoquinoline-monoterpene Glucoside and an Iridoid Glucoside from *Alangium kurzii*

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From the leaves of *Alangium kurzii*, a new tetrahydroisoquinoline-monoterpene glucoside, 6-*O*-methyl-*N*-deacetylipecosidic acid and a new iridoid glucoside, 10-*O*-benzoyladoxosidic acid, were isolated along with alangiside, demethylalangiside, 6″-*O*-β-D-glucosylhenryoside, uridine and four known flavonoid glycosides. The structures of new glucosides were determined on the basis of spectroscopic and chemical methods.

Key words *Alangium kurzii*; Alangiaceae; 6-*O*-methyl-*N*-deacetylipecosidic acid; 10-*O*-benzoyladoxosidic acid

Alangium kurzii CRAIB. (Alangiaceae) is a deciduous shrub distributed in South China and Malaya. Previous phytochemical investigation demonstrated that the plant contained a pyridine alkaloid, anabasine, and a benzoquinolizine alkaloid, ankorine.[1] The glycosidal fraction, in contrast, however, remained to be investigated. In the course of our chemical studies on the plants of Alangiaceae,[2] we have investigated the constituents of the leaves of *A. kurzii*, and isolated a tetrahydroisoquinoline-monoterpene glucoside **1** and an iridoid glucoside **2** as well as eight known compounds, alangiside (**3**),[3] demethylalangiside (**4**),[4] kaempferol-3-*O*-[2,6-di-*O*-(α-L-rhamnopyranosyl)-β-D-galactopyranoside] (**5**),[5] kaempferol-3-*O*-[2-*O*-(β-D-glucopyranosyl)-β-D-galactopyranoside] (**6**),[6] kaempferol-3-*O*-[2-*O*-(β-D-xylopyranosyl)-β-D-galactopyranoside] (**7**),[7] quercetin-3-*O*-[2-*O*-(β-D-xylopyranosyl)-β-D-galactopyranoside] (**8**),[7] 6″-*O*-β-D-glucosylhenryoside (**9**)[8] and uridine (**10**).[9] Compounds **3**—**10** were isolated for the first time from this species. We report here the structural elucidation of two new glucosides, **1** and **2**.

Compound **1** was isolated as a colorless crystalline solid, mp 203—205 °C. It showed UV maxima at 207, 228, 286 and 291sh nm, and IR bands at 3340, 1645 and 1539 cm^{-1}. ^{1}H-NMR spectrum of **1** showed a singlet for a methoxyl at δ 3.82, two singlets for aromatic protons at δ 6.68 and 6.71, a singlet for an olefinic proton at δ 7.27, signals for a terminal vinyl group at δ 5.45 (dt, J=10.5, 1.0 Hz), 5.48 (dt, J=18.0, 1.0 Hz) and 6.05 (ddd, J=18.0, 10.5, 7.5 Hz), and two acetal proton signals at δ 5.47 (d, J=8.0 Hz) and 4.75 (d, J=8.0 Hz). These spectral features as well as ^{13}C-NMR spectral data of **1** demonstrated its structural similarity to alangiside (**3**), which was also isolated from this plant material. The high resolution secondary ion mass spectrum (HR-SI-MS) of **1**, however, exhibited a strong peak at m/z 524.2125 ($[M+H]^+$) indicating a molecular formula of $C_{25}H_{33}NO_{11}$ for **1**, H_2O more than that of **3**. All these results, together with its chromatographic behavior, suggested **1** to be a hydrolysate of alangiside, *i.e.* 6-*O*-methyl-*N*-deacetylipecosidic acid. The placement of the methoxyl group at C-6 was deduced from a nuclear Overhauser enhancement and exchange spectroscopy (NOESY) interaction between a methoxyl signal at δ 3.82 and an aromatic proton at δ 6.71, which was assignable to H-5 by a cross-peak with H-4.

Final structural confirmation was obtained from the chemical correlation of **1** with alangiside (**3**) and 6-*O*-methylipecoside (**11**).[10] Conventional acetylation of **1** gave alangiside pentaacetate (**12**) and **13**, the latter of which was methylated with CH_2N_2–Et_2O to yield 6-*O*-methylipecoside pentaacetate (**14**).[10] Accordingly, the structure of **1** was elucidated as 6-*O*-methyl-*N*-deacetylipecosidic acid.

Compound **2** was isolated as a colorless amorphous powder, and was analyzed for $C_{23}H_{28}O_{11}$ from its HR-SI-MS. This revealed UV absorptions at 229 and 279sh nm and IR bands at 3413, 1702, 1637 and 1508 cm^{-1}. The ^{1}H-NMR spectrum of **2** showed a doublet at δ 7.46 (J=1.5 Hz) charac-

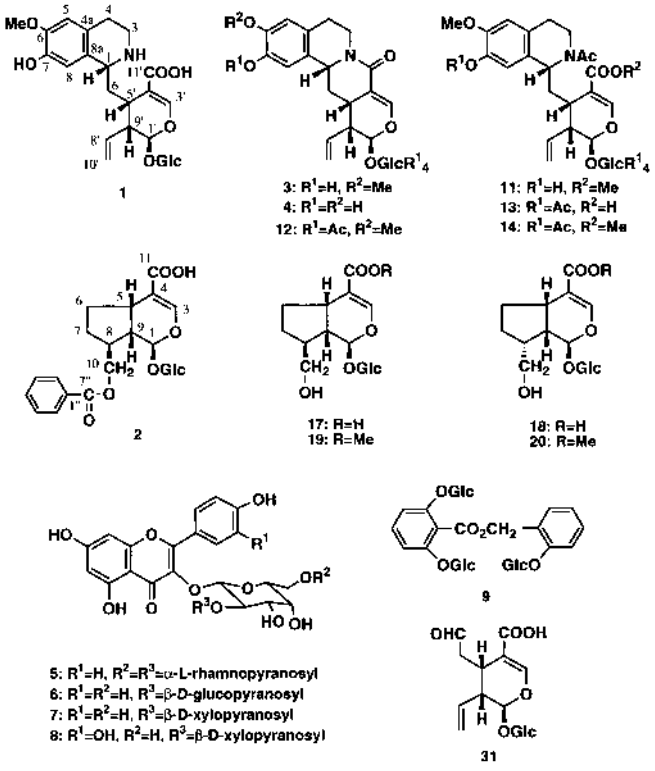

Chart 1

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Table 1. ^{13}C-NMR Spectral Data for Compounds **2**, **15**, **16**, **19**, **20**, **22**, **23**, **27** and **28**

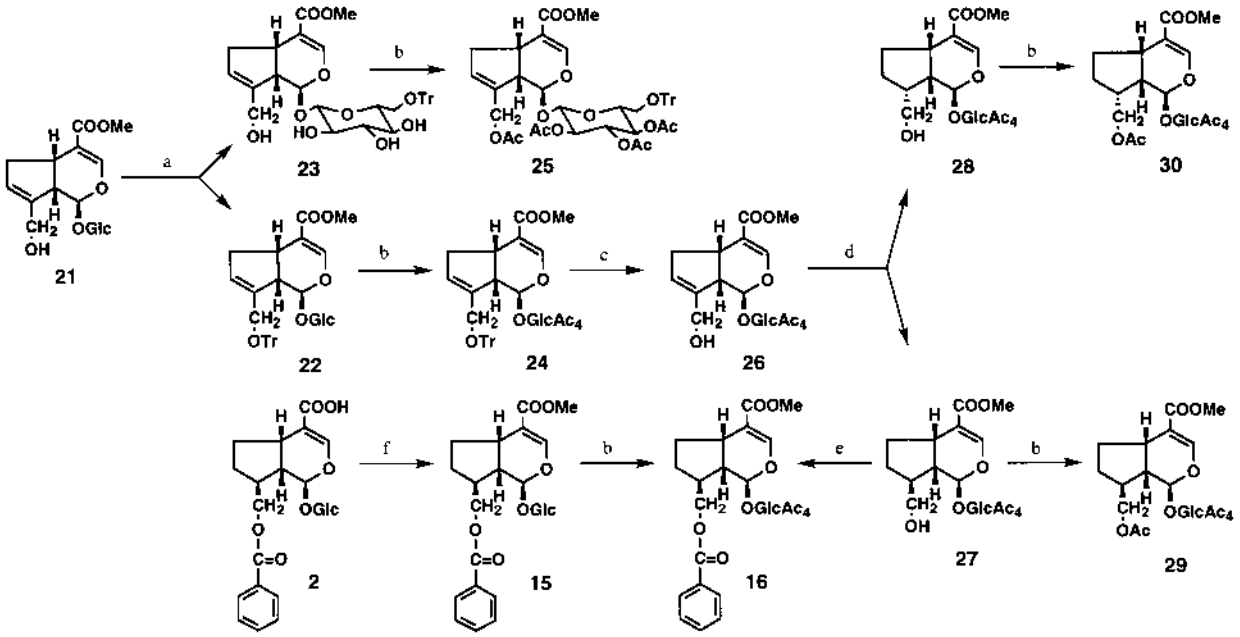
C	**2** [a,c]	**15** [b,c]	**16** [a,d,f]	**19** [e]	**20** [e]	**22** [b,d,g]	**23** [b,d,g]	**27** [a,d,f]	**28** [a,d,f]
1	98.8	98.9	95.8	98.6	96.3	96.8	97.5	96.5	94.5
3	152.9	153.5	150.6	153.2	152.9	151.5	151.7	150.8	150.5
4	112.7	111.8	111.8	111.8	112.7	111.8	111.7	111.7	112.0
5	37.0	36.8	33.8	35.0	34.4	34.3	35.8	34.5	35.1
6	33.8	33.7	31.0	32.4	31.1	38.7	39.0	31.8	31.0
7	28.9	28.8	27.2	27.8	27.0	128.5	129.6	27.4	24.9
8	41.3	41.2	39.2	43.1	44.4	140.1	142.8	42.9	45.1
9	44.5	44.9	44.1	43.7	42.2	46.6	45.0	43.7	41.0
10	69.1	69.0	67.5	65.9	63.4	62.5	61.0	66.3	62.6
11	171.5	169.5	167.2	170.7	171.1	167.8	167.6	167.4	167.4
OMe	—	51.7	51.2	52.6	52.6	51.3	51.3	51.2	51.3
1′	100.9	100.9	96.4	99.9	99.4	98.8	98.4	96.3	96.3
2′	74.6	74.6	70.6	73.6	73.5	73.1	73.3	70.8	70.8
3′	78.0	78.0	72.5	76.6	76.5	75.5	75.1	72.4	72.0
4′	71.4	71.4	68.2	70.4	70.3	69.6	70.9	68.3	68.4
5′	78.3	78.3	72.1	77.1	77.1	76.0	76.3	72.1	72.3
6′	62.7	62.7	61.7	61.5	61.5	61.7	63.0	61.7	61.4
1″	131.5	131.5	130.1						
2″, 6″	130.6	130.6	129.6						
3″, 5″	129.7	129.7	128.4						
4″	134.3	134.4	133.1						
7″	168.3	168.7	166.5						

a—*d*) Measured at *a*) 125 MHz or *b*) 75 MHz in *c*) CD_3OD or *d*) $CDCl_3$. *e*) Data taken from ref. 12. *f*) Compounds **16**, **27** and **28** showed signals of acetyl groups at δ 20.6—20.7 (CH_3) and 169.4—170.6 (CO). *g*) Compounds **22** and **23** showed signals of the trityl group at δ 113.3 (C), 143.4 (3×C) and 127.0—128.6 (15×CH) or close to those values.

teristic of an olefinic proton of the enol ether system conjugated with a carbonyl group, and signals for two acetal protons at δ 5.18 (d, J=7.5 Hz) and 4.66 (d, J=8.0 Hz), implying an iridoidic skeleton for **2**. Furthermore, it showed signals for H_2-6 and H_2-7 at δ 1.48—2.26, and acyloxy methylene signals at δ 4.29 (dd, J=11.0, 6.5 Hz) and 4.37 (dd, J=11.0, 6.5 Hz), which were assigned to H_2-10 by a sequence of correlations of H_2-10, H-8 (δ 2.52), H-9 (δ 2.09) and H-1 (δ 5.18) in the ^{1}H–^{1}H chemical shift correlation spectroscopy (COSY) spectrum, and aromatic proton signals (5H) assignable to a benzoyl group. The ^{13}C-NMR spectrum of **2** exhibited, besides the signals corresponding to a benzoyl group and a β-D-glucosyl unit, ten carbon signals including a carboxyl carbon (δ 171.5) and an oxymethylene (δ 69.1). In the ^{1}H-detected heteronuclear multiple-bond connectivity (HMBC) spectrum, interactions from H_2-10 to a carbonyl carbon (δ 168.3) were observed. The presence of a carboxyl group was confirmed by the fact that the methylation of **2** with CH_2N_2–Et_2O gave a methyl ester, **15**, which was further acetylated to a tetraacetate, **16**. These findings suggest that compound **2** possesses adoxosidic acid (**17**)[11] or its 8-epimer (**18**) as a basic skeleton, whose hydroxyl group at C-10 is benzoylated. Inspection of the chemical shifts of C-8 and C-9 in the ^{13}C-NMR spectra of **15**, adoxoside (**19**), and **20** implied the β-orientation of the oxymethylene group in **2**.[12] The configuration of C-8 was further supported by a NOESY interaction between H-8 and H-1. All these findings allowed us to formulate the structure of **2** as 10-*O*-benzoyladoxosidic acid.

In order to confirm the proposed structure, 10-*O*-benzoyladoxoside tetraacetate was chemically prepared from geniposide (**21**), as follows. Geniposide (**21**) was treated with 1 eq mol of trityl chloride (TrCl) in pyridine, giving two trityl ethers, **22** and **23**, in the ratio of 3 : 1. The attachment of a trityl group to the hydroxyl at C-10 in **22** and at C-6′ in **23** was determined by comparison of their ^{13}C-NMR data, where a downfield shift was observed for C-10 in **22** and for C-6′ in **23**. This was further supported by downfield shifts due to the acetylation of H_2-10 in **25** (**24**: δ 3.63, 3.78; **25**: δ 4.74, 4.88) and H_2-6′ in **24** (**24**: δ 3.88, 4.12; **25**: δ 3.10, 3.25), when **22** and **23** were acetylated to **24** and **25**, respectively. Compound **24** was heated at 80 °C in 80% AcOH to remove a trityl group, giving rise to 10-ol (**26**). Hydrogenation of **26** over Adams' catalyst afforded two stereoisomers, **27** and **28** (1 : 2). Comparative studies of their ^{13}C-NMR spectra, in which carbon signals for C-9 and C-10 of **28** were observed in a higher region than those of **27**, whereas the C-8 of **28** resonated at a lower field than that of **27**, suggested that **27** has a β-oriented substituent at C-8.[12] This assumption was supported by the fact that a NOESY correlation between H-1 and H-8 was observed in **27** but not in **28**. The stereochemistry of **27** and **28** was further confirmed by acetylation of each compound to the two known acetates **29** and **30**, respectively.[13] Finally, compound **27** was benzoylated to give 10-*O*-benzoyladoxoside tetraacetate, which was completely identical with **16** derived from **2**. Thus, the new glucoside was unequivocally assigned as 10-*O*-benzoyladoxosidic acid (**2**).

Tetrahydroisoquinoline-monoterpene glycosides such as 6-*O*-methyl-*N*-deacetylipecosidic acid (**1**) and alangiside (**3**), have so far been isolated only in species of the genera *Alangium* (Alangiaceae) and *Cephaelis* (Rubiaceae). The present work gives an additional example of the isolation of this type of glucoside from the *Alangium* species. It is also noteworthy that **1** possesses amino and carboxy groups in its structure. This is the first instance of a tetrahydroisoquinoline-monoterpene glucoside with an amino group, implying the possibility of biogenetic condensation of secologanic acid (**31**) with dopamine.



(a) TrCl, Py; (b) Ac_2O, Py; (c) 80% AcOH, 80 °C; (d) H_2/PtO_2, EtOH; (e) Benzoyl chloride, Py; (f) CH_2N_2–Et_2O, MeOH.

Chart 2

Experimental

Melting points were measured on Yanagimoto microapparatus and are uncorrected. The UV spectra were recorded on a Shimadzu UV-240 spectrophotometer and the IR spectra on a Shimadzu FT-IR-8200 spectrophotometer. The optical rotations were measured on a Jasco DIP-370 digital polarimeter. SI-MS, electron impact (EI)-MS, HR-SI-MS and HR-EI-MS were obtained with a Hitachi M-4100 mass spectrometer. Glycerol or 3-nitrobenzyl alcohol (3-NOBA) was used for SI-MS as the matrix. The NMR experiments were performed with Varian VXR-500, Varian Gemini-300 and Varian Gemini-200 spectrometers, with tetramethylsilane as an internal standard. HPLC was performed using a Waters system (510 HPLC pump, 486 Tunable absorbance detector). Thin-layer chromatography was performed on precoated Kieselgel $60F_{254}$ plates (Merck) and spots were visualized under UV light.

Isolation of Glucosides *Alangium kurzii* Craib. was collected in Xishuangbanna, Yunnan Province, People's Republic of China. A voucher specimen (KPFY-942) was deposited in the laboratory of Kobe Pharmaceutical University. The dried leaves (173 g) were extracted with hot MeOH. The MeOH extract (34.5 g) was suspended in H_2O and successively partitioned with $CHCl_3$ and *n*-BuOH, to give three fractions weighing 0.91 g ($CHCl_3$), 7.8 g (*n*-BuOH) and 16.2 g (H_2O). An aliquot (3.6 g) of the *n*-BuOH-soluble fraction was chromatographed on a Diaion HP-20 (Nippon Rensui Co., Japan) column. Elution with MeOH–H_2O mixtures with increasing MeOH content (0—50%) gave 8 fractions, B-I (H_2O), B-II (5% MeOH–H_2O), B-III (10% MeOH–H_2O), B-IV (15% MeOH–H_2O), B-V (20% MeOH–H_2O), B-VI (40% MeOH–H_2O), B-VII (45% MeOH–H_2O), and B-VIII (50% MeOH–H_2O). Fraction B-II (135 mg) was further purified by a combination of prep. TLC ($CHCl_3$–MeOH, 7 : 3) and prep. HPLC (μBondasphere 5 μC18-100 Å, MeOH–H_2O, 1 : 9), giving **10** (9.2 mg). The following fractions were also purified by prep. HPLC (μBondasphere 5 μC18-100 Å, MeOH–H_2O, 1 : 4, 3 : 17, 3 : 7, 2 : 3, 11 : 9 or MeCN–H_2O, 13 : 87) and prep. TLC ($CHCl_3$–MeOH, 7 : 3 or 6 : 4 or acetone–$CHCl_3$–H_2O, 8 : 2 : 1). Fraction B-IV (207 mg) yielded **9** (6.0 mg); fraction B-V (183 mg): **1** (31.7 mg); fraction B-VI (752 mg): **3** (13.8 mg), **4** (23.9 mg), **5** (188 mg), **6** (27.4 mg), **7** (127 mg), and **8** (13.1 mg); fraction B-VII (187 mg): **3** (64.4 mg); and fraction B-VIII (122 mg): **2** (24.5 mg). An aliquot (7.8 g) of the H_2O-soluble fraction was chromatographed on a Wakogel LP-40 C18 (Wako Pure Chemical Industries, Ltd., Osaka, Japan) column. Elution with MeOH–H_2O mixtures with increasing MeOH content (0—50%) gave 4 fractions, W-I (H_2O), W-II (10% MeOH–H_2O), W-III (30% MeOH–H_2O), and W-IV (50% MeOH–H_2O). Fractions W-II (870 mg) and W-III (618 mg) were purified by prep. HPLC (μBondasphere 5 μC18-100 Å, MeOH–H_2O, 3 : 7 and MeCN–H_2O, 13 : 87) to yield **1** (231 mg and 146 mg, respectively). Fraction W-IV was purified by prep. HPLC (μBondasphere 5 μC18-100 Å, MeOH–H_2O, 1 : 1) to yield **3** (37.3 mg).

6-*O*-Methyl-*N*-deacetylipecosidic Acid (**1**): Colorless crystalline solid, mp 203—205 °C (MeOH); $[\alpha]_D^{26}$ −144° (*c*=0.2, pyridine); $[\alpha]_D^{21}$ −124° (*c*=0.34, MeOH). UV λ_{max}^{MeOH} nm (log ε): 207 (4.51), 228 (4.18), 286 (3.56), 291sh (3.52). IR ν_{max}^{KBr} cm^{-1}: 3340, 1645, 1539. ^{1}H-NMR (500 MHz, CD_3OD) δ: 1.93 (1H, ddd, *J*=15.5, 12.0, 3.5 Hz, H-6′), 2.21 (1H, ddd, *J*=15.5, 5.0, 2.0 Hz, H-6′), 2.76 (1H, dddt, *J*=8.0, 7.5, 5.0, 1.0 Hz, H-9′), 2.84 (1H, td, *J*=5.0, 3.5 Hz, H-5′), 2.89 (1H, dt, *J*=17.0, 4.5 Hz, H-4), 2.96 (1H, dt, *J*=17.0, 8.0 Hz, H-4), 3.22 (1H, dd, *J*=9.0, 8.0 Hz, H-2″), 3.26 (1H, dd, *J*=10.0, 9.0 Hz, H-4″), 3.28—3.33 (2H, m, H_2-3), 3.31 (1H, ddd, *J*=10.0, 6.0, 2.0 Hz, H-5″), 3.39 (1H, t, *J*=9.0 Hz, H-3″), 3.65 (1H, dd, *J*=12.0, 6.0 Hz, H-6″), 3.82 (3H, s, OMe), 3.91 (1H, dd, *J*=12.0, 2.0 Hz, H-6″), 4.30 (1H, dd, *J*=12.0, 2.0 Hz, H-1), 4.75 (1H, d, *J*=8.0 Hz, H-1″), 5.45 (1H, dt, *J*=10.5, 1.0 Hz, H-10′), 5.47 (1H, d, *J*=8.0 Hz, H-1′), 5.48 (1H, dt, *J*=18.0, 1.0 Hz, H-10′), 6.05 (1H, ddd, *J*=18.0, 10.5, 7.5 Hz, H-8′), 6.68 (1H, s, H-8), 6.71 (1H, s, H-5), 7.27 (1H, s, H-3′). ^{13}C-NMR (125 MHz, CD_3OD) δ: 26.0 (C-4), 35.2 (C-5′), 38.8 (C-6′), 39.1 (C-3), 46.0 (C-9′), 56.4 (OMe), 57.6 (C-1), 62.9 (C-6″), 71.7 (C-4″), 74.8 (C-2″), 78.0 (C-3″), 78.5 (C-5″), 96.9 (C-1′), 100.2 (C-1″), 112.5 (C-5), 114.1 (C-8), 116.4 (C-4′), 120.2 (C-10′), 123.9 (C-4a), 126.0 (C-8a), 136.3 (C-8′), 147.0 (C-7), 149.1 (C-6), 150.1 (C-3′), 175.2 (C-11′). NOESY: H-1/H-8, H-1/H-5′, H-4 (δ 2.89)/H-5, H-5/OMe, H-8/H-6′ (δ 2.21), H-1′/H-9′, H-1′/H-1″. HMBC: H-1→C-3, 4a, 8, 8a, 5′, 6′, H_2-3→C-1, 4, 4a, H_2-4→C-3, 4a, 5, 8a, H-5→C-4, 4a, 6, 7, 8a, H-8→C-1, 4a, 6, 7, 8a, H-1′→C-3′, 5′, 9′, 1″, H-3′→C-1′, 4′, 5′, 11′, H-5′→C-1′, 9′, H-6′ (δ 1.93)→C-1, H-6′ (δ 2.21)→C-8a, 5′, 9′, H-8′→C-1′, H-9′→C-1′, 5′, 6′, 8′, 10′, H_2-10→C-8′, 9′, OMe→C-6. Positive ion SI-MS *m/z*: 524 $[M+H]^+$, 344, 178. Positive ion HR-SI-MS Calcd for $C_{25}H_{34}NO_{11}$: 524.2133. Found: 524.2125.

10-*O*-Benzoyladoxosidic Acid (**2**): Colorless amorphous powder, $[\alpha]_D^{24}$ −46° (*c*=1.11, MeOH). UV λ_{max}^{MeOH} nm (log ε): 229 (4.29), 279sh (3.03). IR ν_{max}^{KBr} cm^{-1}: 3413, 1702, 1637, 1508. ^{1}H-NMR (500 MHz, CD_3OD) δ: 1.48 (2H, m, H-6, 7), 1.95 (1H, m, H-7), 2.09 (1H, td, *J*=7.5, 5.0 Hz, H-9), 2.26 (1H, m, H-6), 2.52 (1H, m, H-8), 2.90 (1H, br q, *J*=7.5 Hz, H-5), 3.07 (1H, dd, *J*=9.0, 8.0 Hz, H-2′), 3.25 (1H, dd, *J*=9.5, 9.0 Hz, H-4′), 3.28 (1H, ddd, *J*=9.5, 5.5, 2.0 Hz, H-5′), 3.35 (1H, t, *J*=9.0 Hz, H-3′), 3.65 (1H, dd, *J*=12.0, 5.5 Hz, H-6′), 3.84 (1H, dd, *J*=12.0, 2.0 Hz, H-6″), 4.29 (1H, dd, *J*=11.0, 6.5 Hz, H-10), 4.37 (1H, dd, *J*=11.0, 6.5 Hz, H-10), 4.66 (1H, d, *J*=8.0 Hz, H-1′), 5.18 (1H, d, *J*=7.5 Hz, H-1), 7.46 (1H, d, *J*=1.5 Hz, H-3), 7.49 (2H, td, *J*=7.5, 1.5 Hz, H-3″, 5″), 7.61 (1H, tt, *J*=7.5, 1.5 Hz, H-4″), 8.04 (2H, dt, *J*=7.5, 1.5 Hz, H-2″, 6″). ^{13}C-NMR: Table 1. NOESY: H-1/H-

8, H-5/H-6 (δ 2.26), H-5/H-9, H-6 (δ 1.48)/ H-7 (δ 1.95), H-6 (δ 2.26)/H-7 (δ 1.48), H-7 (δ 1.95)/H-8. HMBC: H-1→C-1′, H-3→C-4, 11, H-5→C-3, 4, 6, H_2-6→C-5, 7, H_2-7→C-5, H-8→C-1, 5, 6, 7, 9, 10, H-9→C-1, 4, 5, 7, 8, 10, H_2-10→C-7, 8, 9, 7″, H-2″, 6″→C-1″, 7″, H-3″, 5″→C-1″. Negative ion SI-MS *m/z*: 479 $[M-H]^-$. Negative ion HR-SI-MS Calcd for $C_{23}H_{27}O_{11}$: 479.1554. Found: 479.1557.

Acetylation of 1 Compound **1** (10.8 mg) was acetylated with Ac_2O–pyridine, and the crude acetate (14.6 mg) was purified by prep. TLC ($CHCl_3$–MeOH, 19 : 1) to yield **12** (1.0 mg) and **13** (12.5 mg). Compound **12** was identified with authentic alangiside pentaacetate. **13** (6-*O*-Methylipecosidic acid pentaacetate): ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.46 (1H, ddd, J=14.0, 13.0, 4.0 Hz, H-6′), 1.86, 2.00, 2.02, 2.13, 2.24, 2.27 (18H, each s, 6×Ac), 2.42—2.63 (2H, m, H-5′, 6′), 2.74 (1H, dd, J=17.0, 3.6 Hz, H-4), 2.93 (1H, ddd, J=17.0, 12.0, 6.0 Hz, H-4), 3.32 (1H, m, H-9′), 3.56—3.80 (2H, m, H-3, 5″), 3.77 (3H, s, OMe), 3.89 (1H, dd, J=14.0, 6.0 Hz, H-3), 4.14 (1H, dd, J=12.5, 2.2 Hz, H-6″), 4.27 (1H, dd, J=12.5, 4.0 Hz, H-6″), 4.78 (1H, d, J=8.0 Hz, H-1″), 5.00 (1H, dd, J=9.0, 8.0 Hz, H-2″), 5.10 (1H, t, J=9.0 Hz, H-4″), 5.20 (1H, t, J=9.0 Hz, H-3″), 5.42 (1H, d, J=2.0 Hz, H-1′), 5.42 (1H, dd, J=6.5, 5.0 Hz, H-10′), 5.57—5.70 (3H, m, H-1, 8′, 10′), 6.59 (1H, s, H-8), 6.63 (1H, s, H-5), 7.44 (1H, d, J=1.5 Hz, H-3′).

Compound **13** (5.8 mg) was dissolved in MeOH (1 ml) and treated with CH_2N_2–Et_2O in the usual way. Purification of the crude product (6.6 mg) by prep. TLC ($CHCl_3$–MeOH, 19 : 1) gave **14** (5.9 mg) as a colorless amorphous powder, $[\alpha]_D^{26}$ −163° (c=0.35, $CHCl_3$). HR-EI-MS Calcd for $C_{38}H_{47}NO_{17}$: 789.2846. Found: 789.2865. The ^{1}H-NMR, IR, UV and EI mass spectral data for the compound were completely identical with those of authentic 6-*O*-methylipecoside pentaacetate.

Methylation of 2 Compound **2** (10.3 mg) was dissolved in MeOH and treated with CH_2N_2–Et_2O in the usual way to afford **15** (10.0 mg). **15**: Colorless amorphous powder. ^{1}H-NMR (300 MHz, CD_3OD) δ: 1.47 (2H, m, H-6, 7), 1.94 (1H, m, H-7), 2.10 (1H, td, J=7.5, 5.0 Hz, H-9), 2.25 (1H, m, H-6), 2.51 (1H, m, H-8), 2.91 (1H, br q, J=7.5 Hz, H-5), 3.07 (1H, dd, J=9.0, 8.0 Hz, H-2′), 3.26 (1H, t, J=9.0 Hz, H-4′), 3.31 (1H, m, H-5′), 3.35 (1H, t, J=9.0 Hz, H-3′), 3.65 (1H, dd, J=12.0, 5.5 Hz, H-6′), 3.71 (3H, s, COOMe), 3.84 (1H, dd, J=12.0, 2.0 Hz, H-6′), 4.28 (1H, dd, J=11.0, 6.5 Hz, H-10), 4.37 (1H, dd, J=11.0, 6.0 Hz, H-10), 4.66 (1H, d, J=8.0 Hz, H-1′), 5.19 (1H, d, J=7.5 Hz, H-1), 7.49 (1H, br s, H-3), 7.49 (2H, td, J=7.5, 1.5 Hz, H-3″, 5″), 7.61 (1H, tt, J=7.5, 1.5 Hz, H-4″), 8.04 (2H, dt, J=7.5, 1.5 Hz, H-2″, 6″). ^{13}C-NMR: Table 1.

Acetylation of 15 Conventional acetylation of **15** (10.0 mg) and subsequent purification of the crude acetate (13.2 mg) by prep. TLC (Et_2O) yielded **16** (8.4 mg). **16**: Colorless needles, mp 180—182 °C (MeOH). $[\alpha]_D^{22}$ −52° (c=0.70, $CHCl_3$). UV λ_{max}^{EtOH} nm (log ε): 230 (4.36). IR ν_{max}^{KBr} cm^{-1}: 1742, 1700, 1641, 1367. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.49 (1H, m, H-7), 1.65 (1H, m, H-6), 1.89 (1H, m, H-7), 1.97, 2.00, 2.02, 2.05 (12H, each s, 4×Ac), 2.13 (1H, m, H-6), 2.20 (1H, td, J=7.5, 4.5 Hz, H-9), 2.34 (1H, m, H-8), 2.95 (1H, br q, J=7.5 Hz, H-5), 3.69 (1H, ddd, J=9.5, 4.5, 2.5 Hz, H-5′), 3.72 (3H, s, COOMe), 4.04 (1H, dd, J=12.0, 2.5 Hz, H-6′), 4.26 (1H, dd, J=12.0, 4.5 Hz, H-6′), 4.27 (1H, dd, J=11.0, 7.0 Hz, H-10), 4.33 (1H, dd, J=11.0, 7.0 Hz, H-10), 4.85 (1H, d, J=8.5 Hz, H-1′), 4.96 (1H, dd, J=9.5, 8.5 Hz, H-2′), 5.07 (1H, t, J=9.5 Hz, H-4′), 5.21 (1H, t, J=9.5 Hz, H-3′), 5.23 (1H, d, J=4.5 Hz, H-1), 7.39 (1H, d, J=1.0 Hz, H-3), 7.46 (2H, td, J=7.5, 1.5 Hz, H-3″, 5″), 7.57 (1H, tt, J=7.5, 1.5 Hz, H-4″), 8.03 (2H, dt, J=7.5, 1.5 Hz, H-2″, 6″). ^{13}C-NMR: Table 1. NOESY: H-1/H-8, H-5/H-9. HMBC: H-1→C-3, 9, 1′, H-3→C-1, 4, 5, 11, H-5→C-1, 4, 8, 9, H_2-6→C-4, 5, 7, 8, H-7 (δ 1.49)→C-5, 6, 8, 10, H-7 (δ 1.89)→C-5, 8, 9, H-8→C-1, 5, 7, 10, H-9→C-1, 5, 7, 8, H_2-10→C-7, 8, 9, 7″, H-2″, 6″→C-1″, 4″, 7″, H-3″, 5″→C-1″, 2″, 4″, 6″, H-4″→C-2″, 6″. Positive ion SI-MS *m/z*: 663 $[M+H]^+$. Positive ion HR-SI-MS Calcd for $C_{32}H_{39}O_{15}$: 663.2290. Found: 663.2280.

Tritylation of Geniposide (21) To a solution of geniposide (**21**) (502 mg) in pyridine (3 ml) was added TrCl (360 mg), and the mixture was stirred at room temperature overnight. After concentration, the residue was purified by column chromatography on silica gel ($CHCl_3$–MeOH), giving rise to **22** (303 mg, 37%) and **23** (117 mg, 14%). **22**: IR ν_{max}^{KBr} cm^{-1}: 3419, 1713, 1634, 1491. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.14 (1H, m, H-6), 2.74 (1H, m, H-5), 2.89 (1H, m, H-6), 3.02 (1H, m, H-9), 3.16—3.27 (4H, m, H-2′, 3′, 4′, 5′), 3.57—3.67 (2H, m, H_2-6′), 3.58 (1H, m, H-10), 3.67 (3H, s, COOMe), 3.78 (1H, d, J=13.5 Hz, H-10), 4.53 (1H, d, J=8.0 Hz, H-1′), 4.96 (1H, d, J=6.5 Hz, H-1), 5.99 (1H, m, H-7), 7.15—7.43 (15H, m, ArH), 7.44 (1H, d, J=1.0 Hz, H-3). ^{13}C-NMR: Table 1. Negative ion SI-MS *m/z*: 629 $[M-H]^-$. Negative ion HR-SI-MS Calcd for $C_{36}H_{37}O_{10}$: 629.2388. Found: 629.2373. **23**: IR ν_{max}^{KBr} cm^{-1}: 3363, 1711, 1634, 1491. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.96 (1H, m, H-6), 2.74—2.87 (2H, m, H-5, 6), 3.13 (1H, m, H-9), 3.10—3.47 (3H, m, H-2′, 3′, 4′), 3.24 (1H, dd, J=10.0, 5.0 Hz, H-6′), 3.27—3.32 (1H, m, H-5′), 3.32 (1H, m, H-6′), 3.70 (3H, s, COOMe), 4.17 (1H, d, J=13.5 Hz, H-10), 4.31 (1H, d, J=13.5 Hz, H-10), 4.74 (1H, d, J=8.0 Hz, H-1′), 5.71 (1H, m, H-7), 7.15—7.44 (15H, m, ArH), 7.46 (1H, br s, H-3). ^{13}C-NMR: Table 1.

Acetylation of 22 and 23 Compound **22** (303 mg) was acetylated with Ac_2O–pyridine, and an aliquot (21.8 mg) of the crude acetate (403 mg) was purified by prep. TLC ($CHCl_3$–MeOH, 19 : 1) to yield **24** (16.0 mg). Compound **23** was acetylated by the same procedure as described for **22** to give **25**. **24**: IR ν_{max}^{KBr} cm^{-1}: 1761, 1636, 1367. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.93, 1.96 (6H, each s, 2×Ac), 2.02 (6H, s, 2×Ac), 2.16 (1H, m, H-6), 2.83—2.88 (2H, m, H-5, 6), 3.19 (1H, m, H-9), 3.58 (1H, m, H-5′), 3.63 (1H, d, J=13.5 Hz, H-10), 3.71 (3H, s, COOMe), 3.78 (1H, d, J=13.5 Hz, H-10), 3.88 (1H, dd, J=12.0, 2.5 Hz, H-6′), 4.12 (1H, dd, J=12.0, 4.5 Hz, H-6′), 4.73 (1H, d, J=8.0 Hz, H-1′), 4.75 (1H, m, H-2′), 5.00 (1H, t, J=9.0 Hz, H-4′), 5.13 (1H, d, J=5.4 Hz, H-1), 5.15 (1H, t, J=9.0 Hz, H-3′), 5.88 (1H, m, H-7), 7.16—7.43 (15H, m, ArH), 7.47 (1H, d, J=1.0 Hz, H-3). Positive ion HR-SI-MS Calcd for $C_{44}H_{47}O_{14}$: 799.2968. Found: 799.2954. **25**: IR ν_{max}^{KBr} cm^{-1}: 1761, 1636, 1375. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.70, 1.92, 1.99, 2.02 (12H, each s, 4×Ac), 2.16 (1H, m, H-6), 2.89 (2H, m, H-5, 6), 2.90 (1H, m, H-9), 3.10 (1H, dd, J=12.0, 4.5 Hz, H-6′), 3.25 (1H, m, H-6′), 3.58 (1H, m, H-5′), 3.73 (3H, s, COOMe), 4.74 (1H, d, J=13.5 Hz, H-10), 4.88 (1H, d, J=13.5 Hz, H-10), 4.91 (1H, d, J=8.0 Hz, H-1′), 5.08 (1H, t, J=8.0 Hz, H-2′), 5.12 (1H, t, J=8.0 Hz, H-4′), 5.17 (1H, d, J=7.0 Hz, H-1), 5.17 (1H, t, J=8.0 Hz, H-3′), 5.88 (1H, m, H-7), 7.22—7.42 (15H, m, ArH), 7.48 (1H, br s, H-3).

Removal of the Trityl Group of 24 A solution of **24** (403 mg) in 80% HOAc (26 ml) was heated at 80 °C for 40 min. The reaction mixture was diluted with ice-water and extracted with $CHCl_3$. The $CHCl_3$ layer was washed successively with 5% $NaHCO_3$ aq. solution and brine, dried and concentrated *in vacuo*. The residue (288 mg) was subjected to prep. TLC ($CHCl_3$–MeOH, 19 : 1), giving **26** (211 mg, 76%). **26**: IR ν_{max}^{KBr} cm^{-1}: 3566, 1766, 1636, 1373. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.02 (6H, s, 2×Ac), 2.03, 2.08 (6H, each s, 2×Ac), 2.28 (2H, m, H-6, 9), 2.78 (1H, br q, J=7.5 Hz, H-5), 2.69—3.78 (1H, m, H-6), 3.69—3.78 (1H, m, H-5′), 3.73 (3H, s, COOMe), 4.15 (1H, dd, J=12.0, 2.0 Hz, H-6′), 4.25 (2H, s-like, H_2-10), 4.31 (1H, dd, J=12.0, 4.5 Hz, H-6′), 4.91 (1H, d, J=8.0 Hz, H-1′), 5.02 (1H, d, J=6.6 Hz, H-1), 5.03 (1H, dd, J=9.0, 8.0 Hz, H-2′), 5.11 (1H, t, J=9.0 Hz, H-4′), 5.26 (1H, t, J=9.0 Hz, H-3′), 5.82 (1H, m, H-7), 7.44 (1H, br s, H-3). Positive ion SI-MS *m/z*: 557 $[M+H]^+$. Positive ion HR-SI-MS Calcd for $C_{25}H_{33}O_{14}$: 557.1871. Found: 557.1876.

Catalytic Hydrogenation of 26 A solution of compound **26** (211 mg) in EtOH (7.0 ml) was hydrogenated at room temperature over PtO_2 (40 mg). After completion of the H_2 uptake, the catalyst was filtered off and the filtrate was concentrated *in vacuo*. The residue (231 mg) was purified by prep. HPLC (MeOH–H_2O, 47 : 53) to give **27** (48.9 mg, 23%) and **28** (105 mg, 50%). **27**: IR ν_{max}^{KBr} cm^{-1}: 3480, 1759, 1636. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.32 (1H, m, H-7), 1.47 (1H, m, H-6), 1.81 (1H, m, H-7), 1.98, 2.01, 2.03, 2.10 (12H, each s, 4×Ac), 2.00 (1H, m, H-9), 2.06 (1H, m, H-8), 2.13 (1H, m, H-6), 2.84 (1H, br q, J=7.5 Hz, H-5), 3.56 (1H, dd, J=10.5, 7.5 Hz, H-10), 3.63 (1H, dd, J=10.5, 7.5 Hz, H-10), 3.71 (3H, s, COOMe), 3.74 (1H, ddd, J=10.0, 4.5, 2.0 Hz, H-5′), 4.17 (1H, dd, J=12.0, 2.0 Hz, H-6′), 4.28 (1H, dd, J=12.0, 4.5 Hz, H-6′), 4.90 (1H, d, J=8.0 Hz, H-1′), 5.01 (1H, dd, J=9.5, 8.0 Hz, H-2′), 5.09 (1H, d, J=6.0 Hz, H-1), 5.12 (1H, dd, J=10.0, 9.5 Hz, H-4′), 5.24 (1H, t, J=9.5 Hz, H-3′), 7.39 (1H, d, J=1.5 Hz, H-3). ^{13}C-NMR: Table 1. NOESY: H-1/H-8, H-5/H-6 (δ 2.13), H-5/H-9, H-6 (δ 2.13)/H-7 (δ 1.81), H-7 (δ 1.81)/H-8. HMBC: H-1→C-3, 5, 1′, H-3→C-1, 4, 5, H-5→C-1, 3, 4, 6, 7, 8, 9, H_2-6→C-4, 5, 7, 8, 9, H-7 (δ 1.32)→C-8, 9, 10, H-7 (δ 1.81)→C-8, H-8→C-1, 7, 9, 10, H-9→C-1, 4, 5, 6, 8, 10, H_2-10→C-7, 8, 9, OMe→C-11. Positive ion SI-MS *m/z*: 559 $[M+H]^+$. Positive ion HR-SI-MS Calcd for $C_{25}H_{35}O_{14}$: 559.2028. Found: 559.2026. **28**: IR ν_{max}^{KBr} cm^{-1}: 3566, 1759, 1639. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.41 (1H, m, H-7), 1.43 (1H, m, H-6), 1.78 (1H, m, H-7), 2.02, 2.03, 2.04, 2.09 (12H, each s, 4×Ac), 2.20—2.28 (1H, m, H-6), 2.20 (1H, m, H-9), 2.46 (1H, m, H-8), 2.89 (1H, br q, J=7.5 Hz, H-5), 3.64 (1H, dd, J=11.0, 5.0 Hz, H-10), 3.72 (3H, s, COOMe), 3.72 (1H, dd, J=11.0, 4.0 Hz, H-10), 3.75 (1H, ddd, J=9.5, 4.0, 3.0 Hz, H-5′), 4.22 (1H, dd, J=12.0, 4.0 Hz, H-6′), 4.25 (1H, dd, J=12.0, 3.0 Hz, H-6′), 5.00 (1H, d, J=8.0 Hz, H-1′), 5.04 (1H, dd, J=9.5, 8.0 Hz, H-2′), 5.12 (1H, t, J=9.5 Hz, H-4′), 5.21 (1H, d, J=7.5 Hz, H-1), 5.29 (1H, t, J=9.5 Hz, H-3′), 7.38 (1H, d, J=1.0 Hz, H-3). ^{13}C-NMR: Table 1. NOESY: H-5/H-6 (δ 1.43), H-5/H-8, H-5/H-9, H-7 (δ 1.78)/H-8, H-8/H-9. HMBC: H-1→C-3, 5, 1′, H-3→C-1, 4, 11, H-5→C-1, 4, 6, 9, H-6 (δ 2.20—2.28)→C-5, 9, H-7 (δ 1.78)→C-5, 9, H-8→C-1, H-9→C-1, 5, 6, 7, 8, H_2-10→C-7, 8, 9, OMe→C-11. Positive ion SI-MS *m/z*: 559 $[M+H]^+$.

Positive ion HR-SI-MS Calcd for $C_{25}H_{35}O_{14}$: 559.2028. Found: 559.2024.

Acetylation of 27 Compound **27** (7.7 mg) was acetylated in the usual way and the resulting crude product (8.2 mg) was purified by prep. TLC (Et_2O) to yield **29** (6.7 mg, 80%) as colorless needles, mp 141—142 °C (EtOH). $[\alpha]_D^{26}$ −58° (c=0.34, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 1751, 1705, 1636. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.37 (1H, m, H-7), 1.61 (1H, m, H-6), 1.80 (1H, m , H-7), 1.94, 2.01, 2.03, 2.06, 2.09 (15H, each s, 5×Ac), 2.06—2.09 (2H, m, H-6, 9), 2.19 (1H, m, H-8), 2.89 (1H, br q, J=7.5 Hz, H-5), 3.71 (3H, s, COOMe), 3.73 (1H, ddd, J=9.5, 4.5, 2.5 Hz, H-5′), 4.02 (1H, dd, J=11.5, 6.5 Hz, H-10), 4.06 (1H, dd, J=11.5, 6.5 Hz, H-10), 4.16 (1H, dd, J=12.0, 2.5 Hz, H-6′), 4.26 (1H, dd, J=12.0, 4.5 Hz, H-6′), 4.86 (1H, d, J=8.0 Hz, H-1′), 4.99 (1H, dd, J=9.5, 8.0 Hz, H-2′), 5.10 (1H, t, J=9.5 Hz, H-4′), 5.18 (1H, d, J=4.0 Hz, H-1), 5.23 (1H, t, J=9.5 Hz, H-3′), 7.37 (1H, d, J=1.5 Hz, H-3). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 20.3, 20.6 (×2), 20.7, 20.9 (5×CO<u>Me</u>), 27.1 (C-7), 31.0 (C-6), 33.7 (C-5), 38.9 (C-8), 44.1 (C-9), 51.2 (OMe), 61.7 (C-6′), 67.1 (C-10), 68.3 (C-4′), 70.7 (C-2′), 72.2 (C-3′), 72.5 (C-5′), 95.6 (C-1), 96.2 (C-1′), 111.8 (C-4), 150.5 (C-3), 167.2 (C-11), 169.1, 169.4, 170.2, 170.6, 171.1 (5×<u>C</u>OMe). Positive ion SI-MS m/z: 601 $[M+H]^+$, 331. Positive ion HR-SI-MS Calcd for $C_{27}H_{37}O_{15}$: 601.2134. Found: 601.2139.

Acetylation of 28 Compound **28** (10.2 mg) was acetylated as usual and the resulting crude product (10.1 mg) was purified by prep. TLC (Et_2O) to yield **30** (9.5 mg, 88%) as colorless needles, mp 113—115 °C (EtOH). $[\alpha]_D^{29}$ −55° (c=0.55, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 1759, 1709, 1638. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.40 (1H, m, H-7), 1.63 (1H, m, H-6), 1.83 (1H, m, H-7), 1.95, 2.01, 2.03, 2.06, 2.10 (15H, each s, 5×Ac), 2.08 (1H, m, H-6), 2.40 (1H, m, H-9), 2.48 (1H, m, H-8), 2.92 (1H, br td, J=8.0, 5.0 Hz, H-5), 3.71 (3H, s, COOMe), 3.71 (1H, ddd, J=9.5, 4.0, 3.0 Hz, H-5′), 4.02 (1H, dd, J=11.0, 7.5 Hz, H-10), 4.21 (1H, dd, J=12.0, 3.0 Hz, H-6′), 4.22 (1H, dd, J=11.0, 7.5 Hz, H-10), 4.23 (1H, dd, J=12.0, 4.0 Hz, H-6′), 4.87 (1H, d, J=8.5 Hz, H-1′), 4.98 (1H, dd, J=9.5, 8.5 Hz, H-2′), 5.11 (1H, t, J=9.5 Hz, H-4′), 5.22 (1H, t, J=9.5 Hz, H-3′), 5.31 (1H, d, J=5.0 Hz, H-1), 7.37 (1H, d, J=1.0 Hz, H-3). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 20.3, 20.6 (×2), 20.7, 21.0 (5×CO<u>Me</u>), 27.2 (C-7), 30.6 (C-6), 33.3 (C-5), 40.3 (C-8), 41.6 (C-9), 51.2 (OMe), 61.6 (C-6′), 65.1 (C-10), 68.3 (C-4′), 70.7 (C-2′), 72.2 (C-3′), 72.5 (C-5′), 93.9 (C-1), 95.9 (C-1′), 112.5 (C-4), 150.5 (C-3), 167.1 (C-11), 169.1, 169.4, 170.2, 170.6, 170.9 (5×<u>C</u>OMe). Positive ion SI-MS m/z: 601 $[M+H]^+$, 331. Positive ion HR-SI-MS Calcd for $C_{27}H_{37}O_{15}$: 601.2134. Found: 601.2136.

Benzoylation of 27 A mixture of **27** (3.5 mg), benzoyl chloride (0.1 ml) and pyridine (0.3 ml) was allowed to stand at room temperature overnight. The conventional workup of the reaction mixture afforded a crude residue, which was subjected to prep. TLC (Et_2O) to yield **16** (4.4 mg, 100%) as colorless needles, mp 180—182 °C (MeOH). $[\alpha]_D^{26}$ −51° (c=0.25, $CHCl_3$). Positive ion HR-SI-MS Calcd for $C_{32}H_{39}O_{15}$: 663.2290. Found: 663.2297. The ^{1}H-NMR, IR and SI-MS data for the compound were completely identical with those of **16** derived from **2**.

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