Glochidiolide, Isoglochidiolide, Acuminaminoside, and Glochidacuminosides A—D from the Leaves of *Glochidion acuminatum* MUELL.

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The dimeric butenolides glochidiolide and isoglochidiolide, a new glucoside of a nitrogen-containing C_8 dimer, acuminaminoside, and glucosides of C_8 compounds, designated glochidacuminosides A—D, were isolated from the leaves of *Glochidion acuminatum*. The structures of glochidionolactone and acuminaminoside were determined by X-ray analyses, and those of the remaining C_8 glucosides by NMR spectroscopic analyses, chemical conversion, and a modified Mosher's method.

Key words *Glochidion acuminatum*; Euphorbiaceae; dimeric phenylethane; alkaloidal glucoside; acuminaminoside; glochidacuminoside

In the course of studies on Okinawan resource plants, the constituents of *Glochidion acuminatum* (Euphorbiaceae) have been investigated. In a previous communication,[1)] the isolation of a structurally rare dimeric butenolide, glochidiolide (**1**) (Fig. 1), was reported. Further studies on this plant led to the isolation of isoglochidiolide (**2**), a glucoside of a nitrogen-containing dimeric phenylethane which was designated acuminaminoside (**3**), and four glucosides with C_8 aglycones (**4**—**7**), along with one known glycoside (**8**). This paper deals with the structural elucidation of the new compounds.

Results and Discussion

The compounds were isolated using several chromatographic techniques and recrystallization. The details are given in the Experimental section.

A known compound (**8**) was identified as *Z*-hex-3-en-1-ol *O*-β-D-glucopyranoside, $[\alpha]_D^{23}$ $-21.6°$ (c=0.79, MeOH)[2)] based on spectroscopic evidence.

Glochidiolide (**1**) was isolated as colorless crystals and its structure was finally elucidated by X-ray crystallographic analysis to be that shown in Fig. 1 or its enantiomer.[1)]

Isoglochidiolide (**2**) was isolated as an off-white syrup and its elemental composition was found to be the same as that of **1** by HR (high resolution)-FAB-MS. The ^{1}H- and ^{13}C-NMR spectra including ^{1}H–^{1}H correlation (COSY) and heteronuclear single-quantum correlation (HSQC) spectroscopies revealed that the basic skeleton was the same as that of **1**, and signals assignable to one (C-1′ to C-8′) of the halves were close to those of **1** (Table 1). This was also supported by the results of heteronuclear multiple-bond correlation (HMBC) spectroscopy, *i.e.*, δ_H 2.62 and 2.69 (H_2-2) crossed δ_C 87.6 (C-8′), and δ_H 1.60 and 2.97 (H_2-7′) δ_C 49.9 (C-3) (see Fig. 2). This evidence indicated that isoglochidiolide (**2**) was a stereoisomer of the other part (C-1 to C-8). The phase-sensitive nuclear Overhauser effect spectroscopy (PHNOESY) experiment (see Fig. 2) revealed that, since H-8 correlated with H-6, H-6 and H-8 were in axial positions and on the same

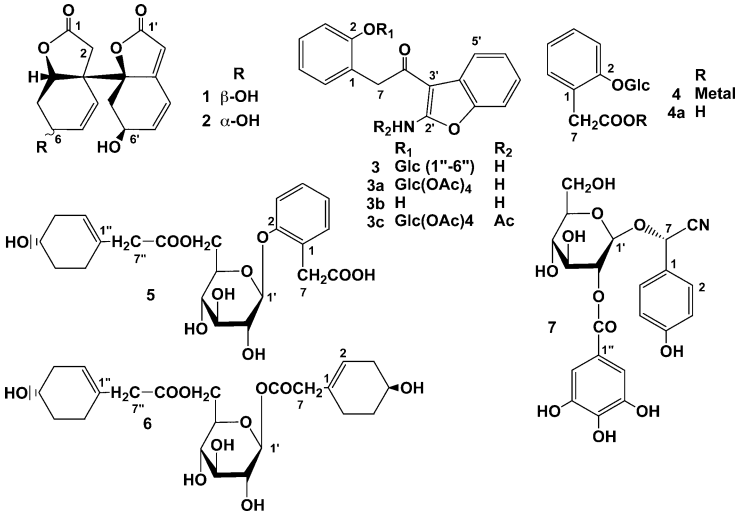

Fig. 1. Structures

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Table 1. ^{13}C-NMR Data for Glochidiolide (**1**) and Isoglochidiolide (**2**) (400 MHz, DMSO-d_6)

Carbon No.	**1**[a)]	**2**
1	173.5	173.9
2	37.1	36.4
3	47.6	49.9
4	124.9	124.7
5	134.8	136.2
6	59.8	61.7
7	33.5	36.1
8	78.0	75.9
1′	170.6	170.4
2′	113.9	113.9
3′	165.3	164.3
4′	121.7	121.7
5′	142.6	141.8
6′	63.8	63.8
7′	41.7	41.5
8′	86.9	87.6

a) Data taken from ref. 1.

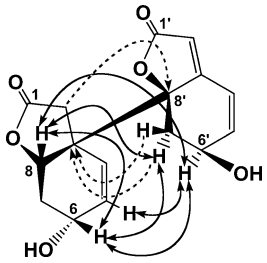

Fig. 2. Phase-sensitive NOE and HMBC Correlations of Isoglochidionolide (**2**)

Solid lines show phase-sensitive NOE correlations. Dotted lines show HMBC correlations. Arrowheads denote carbon atoms and arrow tails proton(s).

face. This was also supported by the fact that H-8 was coupled with adjacent protons with coupling constants of 10 and 2 Hz. Such a correlation was not observed in **1**. A significant correlation between H-8 and H-6′ indicated that these protons were also on the same side. Finally, H-6 and H-6′, and H-8 and H-7b′ also showed correlation. These results allowed us to establish the structure of **2** as an isomeric form of **1** regarding the stereochemistry of C-6, as shown in Fig. 1, or its enantiomer.

Acumiaminoside (**3**) was isolated as colorless needles, mp 212—215 °C (MeOH). On negative-ion FAB mass spectrometry, it exhibited a quasimolecular ion peak at *m/z* 428 ([M−H]$^-$), which corresponded to $C_{22}H_{22}O_8N$ on HR-FAB-MS. The IR and UV absorption maxima indicated the presence of an aromatic ring (s) (1595 and 1495 cm^{-1}, and 296 and 310 nm, respectively) and a ketone functional group (1654 cm^{-1}). The ^{1}H-NMR and ^{1}H–^{1}H COSY spectra indicated the presence of two sets of four aromatic protons in a series sequence, methylene protons (δ_H 4.26), and an anomeric proton (δ_H 4.94). The ^{13}C-NMR spectrum showed the presence of two disubstituted aromatic rings, one methylene, one ketone, and two sp^2 highly shielded and deshielded (δ_C 95.4, 168.3) carbon signals, together with six signals attributable to a β-glucopyranose moiety (Table 2). Acetylation of **3** with acetic anhydride and pyridine at 25 °C for 2 h afforded a tetraacetate (**3a**), while even under the stronger conditions of 60 °C for 5 h, the major product was also the

Table 2. ^{13}C-NMR Data for Acumiaminoside (**3**)

Carbon No.	**3**
1	126.8
2	157.4
3	117.0
4	129.3
5	123.7
6	131.7
7	43.1
8	194.5
2′	168.3
3′	95.4
4′	120.1
5′	122.8
6′	125.3
7′	110.9
8′	127.5
9′	150.8
1″	103.4
2″	75.1
3″	78.3
4″	71.5
5″	78.1
6″	62.8

tetraacetate (**3a**). The ^{1}H-NMR spectrum of **3a** in DMSO-d_6 still showed the presence of D_2O exchangeable protons at δ_H 8.20 (2H, br s), which were expected to be an amino hydrogen signal. Although NMR spectra including two-dimensional ones were carefully inspected, only partial structures could be assigned, such as that one of the aromatic rings carried a β-glucopyranose moiety on the 2-hydroxyphenyl 1-(1-oxoethyl) skeleton and the other formed a fused ring system.

Full acetylation of **3** was again attempted first with acetic anhydride and pyridine, followed by with acetyl bromide in the presence of α-pinene to give a pentaacetate (**3c**), and one of the acetyl groups obviously formed an amide bond from the rather deshielded methyl and shielded carbonyl carbons observed in the ^{13}C-NMR spectrum (δ_C 24.9, 167.1, respectively). This was also confirmed by the appearance of an amide proton at δ_H 11.01 (1H, s) in the ^{1}H-NMR spectrum. It is interesting that, as a general trend, an amino group is a more facile nucleophile than a hydroxyl group. However, the amino group in this compound was not acetylated under the usual conditions as with acetic anhydride and pyridine. This acetylation-resistant property of **3** could be explained by the reasoning that it must exist as two resonating forms due to tautomerism between amino and ketone functional groups, and this was also indicated by the IR absorption of the carbonyl double bond that appeared at 1654 cm^{-1}.

Since the entire structure could not be elucidated using spectroscopic analysis, an X-ray crystallographic method was attempted. However, the crystals of the glucoside (**3**) were not suitable for such analysis, thus it was enzymatically hydrolyzed to give glucose and an aglycone (**3b**), which gave a suitable crystal from MeOH for X-ray analysis. Its structure was determined by means of the direct method with the teXsan crystallographic package.[3)] A computer-generated perspective drawing of **3b** is shown in Fig. 3. The position of the sugar linkage has already been confirmed to be the hydroxyl group at the 2-position, and the glucose is in the D-series. As a result, acuminaminoside (**3**) was found to be the β-

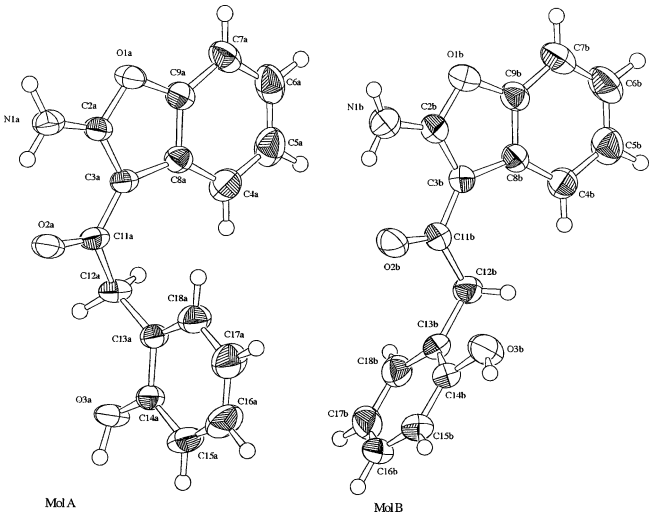

Fig. 3. Perspective ORTEP Drawing of the Aglycone (**3b**) of Acuminaminoside (**3**)

There are two independent molecules in the asymmetric unit. The molecules have X-ray crystallographic numbering.

D-glucopyranoside of a novel dimeric phenylethanic compound containing a nitrogen atom, as shown in Fig. 1.

Alkaloidal glycosides are relatively rare in nature, with the exceptions being the conjugates of iridoid glucoside and tryptamine or tyramine, and nitrogen-containing steroidal compounds. Acuminaminoside (**3**) is an alkaloidal glucoside with an unusual aglycone moiety, *i.e.*, a dimeric phenylethane skeleton.

Glochidacuminoside A (**4**) was isolated as an amorphous powder and several molecular ion peaks were observed in positive-ion mode FAB-MS, such as *m/z* 337 $[M+Na]^+$, 353 $[M+K]^+$, 359 $[M-H+Na+Na]^+$, and 375 $[M-H+K+Na]^+$. The ^{13}C-NMR spectrum indicated the presence of six signals assignable to the β-glucopyranose unit, six to the disubstituted aromatic ring, and a methylene carbon signal. However, the ^{1}H-NMR spectrum showed four peculiar aromatic proton signals at δ_H 6.95 (1H, m, split into more than eight peaks), 7.15 (1H, br s), 7.16 (1H, br s), and 7.22 (1H, br d, J=7 Hz). This is not a typical coupling pattern of a disubstituted aromatic ring. From these results, **4** was assumed to exist as a salt of several metal ions, and thus the carboxylic carbon signal collapsed and was not observed in the ^{13}C-NMR spectrum. Therefore **4** was treated with Amberlite IR-120B (H^+) to give the metal-free compound **4a**. The ^{1}H- and ^{13}C-NMR spectra clearly demonstrated that the structure of **4a** was 2-*O*-β-glucopyranoside of 2-hydroxyphenylacetic acid (Experimental and Table 3). From the sign of the optical rotation value, glucose was presumed to be in the D-series. This was later confirmed by mild alkaline hydrolysis of **5** to give **4a**.

Glochidacuminoside B (**5**) was isolated as an amorphous powder. An aliquot of **5** was treated with Amberlite IR-120B (H^+) prior to further spectroscopic analyses. Its elemental composition was determined to be $C_{22}H_{28}O_{10}$ in negative-ion HR-FAB-MS. The IR spectrum indicated the presence of an ester linkage (1735 cm^{-1}). The ^{1}H- and ^{13}C-NMR spectra indicated that the aglycone moiety was the same as that of **4a** (Table 3) with a further C_8 moiety. The carbon skeleton of the C_8 moiety consisted of four methylenes, one methine

Table 3. ^{13}C-NMR Data for Glochidacuminosides A—D (**4**—**7**) (CD_3OD, 100 MHz)

Carbon No.	**4a**	**4**	**5**	**6**[a)]	**7**
1	126.2	129.0	126.4	131.9	125.5
2	157.3	157.5	157.2	124.4	130.3
3	116.9	116.6	117.2	35.2	116.7
4	129.6	128.7	129.6	67.4	160.1
5	123.6	123.5	123.9	32.1[1)]	116.7
6	132.1	132.2	132.1	28.0[2)]	130.3
7	36.9	40.8	36.7	43.3	68.6
8	176.4	?	176.1	172.0	118.7
1′	103.3	103.7	103.4	95.6	100.0
2′	75.1	75.0	75.0	73.9	78.8
3′	78.2	78.2	77.8	77.9	76.3
4′	71.5	71.4	71.6	71.2	71.8
5′	78.0	77.8	75.5	76.2	78.8
6′	62.7	62.7	64.8	64.3	62.8
1″			132.2	132.3	140.1
2″			124.2	124.2	110.6
3″			35.2	35.2	146.6
4″			67.4	67.4	121.5
5″			32.0	32.0[1)]	146.6
6″			28.1	28.1[2)]	110.6
7″			43.5	43.5	167.7
8″			173.6	173.3	

a) Figures with same superscript may interchangeable.

with a hydroxyl group, one trisubstituted double bond, and a carboxylic carbonyl functional group. The structure was elucidated to be 4-hydroxycyclohex-1-en-1-acetic acid by means of two-dimensional NMR spectroscopy. This part was assumed to be linked with the hydroxyl group on C-6′ of glucopyranose through an ester bond. This was supported by downfield shifts of the protons on C-6′ (δ_H 4.22, 4.45) and the cross peak between carbonyl carbon (δ_C 173.6) and methylene protons (δ_H 4.22, 4.45) in the HMBC spectrum. To determine the absolute configuration of the C-4″ position, **5** was hydrolyzed under mild alkaline conditions in MeOH to give methyl esters of **5a** (=**4a**) and **5b**. The ester **5b** was further derivatized to its (*R*)-(+)- and (*S*)-(−)-α-methoxy-α-trifluoromethylphenylacetic acid (MTPA) esters (**5d** and **5e**, reapectively) to apply a modified Mosher's method.[4)] Figure 4 shows the results. Although the protons on C-5″ of **5d** and **5e** were not resolved well, based on the chemical shift ranges of H_2-5″ the signs of their ΔS–ΔR values are expected to be nrgative. From the signs of other protons, the absolute configuration of C-4″ was determined to be *S*. Glucoside **5a** was hydrolyzed with emulsin to give 2-hydroxyphenylacetic acid (**5b**) as an aglycone and D-glucose. Therefore the structure of **5** was elucidated to be 2-hydroxyphenylacetic acid 2-*O*-β-D-glucopyranoside 6′-*O*-(4*S*)-4-hydroxycyclohex-1-en-1-acetate.

Glochidacuminoside C (**6**) was isolated as an amorphous powder and its elemental composition was determined to be $C_{22}H_{32}O_{10}$ using HR-FAB mass spectrometry. The ^{13}C-NMR spectrum showed 22 signals, of which eight exhibited essentially the same chemical shifts as those of the ester moiety in **5**. Eight other signals closely resembled the aforementioned eight signals except for the carbonyl carbon at δ_C 172.0 (C-8″ at δ_C 173.3, respectively). From the anomeric carbon signal appearing at δ_C 95.6, the ester glycoside was presumed to be in the structure. This was confirmed by the HMBC spectrum, in which the anomeric proton (δ_H 5.44) crossed the carbonyl carbon at δ_C 172.0. Since mild alkaline hydrolysis

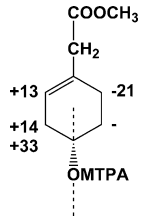

Fig. 4. Results with the Modified Mosher's Method for **5a**
The $\Delta\delta$ values are in Hz (δS–δR at 400 MHz).

of **5** furnished **5a** and D-glucose, the structure of **6** was elucidated to be β-D-glucopyranose 1′,6′-bis-*O*-(4*S*)-4-hydroxycyclohex-1-en-1-acetate.

Glochidacuminoside D (**7**) was also isolated as an amorphous powder and its elemental composition was determined to be $C_{21}H_{20}O_{11}N$ in negative-ion HR-FAB-MS. The IR spectrum showed an absorption maximum at 2255 cm^{-1}. These results indicate that **7** contains a nitrile moiety. The ^{1}H- and ^{13}C-NMR spectra showed the presence of *para*-substituted [δ_C 125.5 (s) and 160.1 (s)] and tetrasubstituted symmetrical benzene rings, a substituted β-glucopyranoside, a methine with an oxygen atom, a nitrile [δ_C 118.7 (s)], and carbonyl functional groups. The structure of the tetrasubstituted symmetrical benzene was deduced to be gallic acid based on comparison of its ^{13}C-NMR chemical shifts with those reported.[5] The acid was presumed to form an ester linkage (1704 cm^{-1}) with the hydroxyl group on C-2″ of β-glucopyranoside. This was confirmed by H–H COSY and HMBC experiments, in which a significant downfield shift of H-2′ (δ_H 4.93) was observed, and the H-2′ signal crossed with the carbonyl carbon at δ_C 167.7, respectively. Since the anomeric proton crossed the methine carbon (δ_C 68.6), the structure of **7** was elucidated to be 4-hydroxylprunasin 2′-*O*-gallate.

Experimental

General Experimental Procedures A highly porous synthetic resin (Diaion HP-20) was purchased from Mitsubishi Kagaku (Tokyo, Japan). Silica gel column chromatography (CC) was performed on silica gel 60 (E. Merck, Darmstadt, Germany) and reversed-phase [octadecyl silica gel (ODS)] open CC (RPCC) on Cosmosil 75C_{18}-OPN (Nacalai Tesque, Kyoto, Japan) [Φ=50 mm, L=25 cm, linear gradient: MeOH–H_2O (1 : 9, 1 l)→(7 : 3, 1 l), with fractions of 10 g collected]. A droplet counter-current chromatography (DCCC) apparatus (Tokyo Rikakikai, Tokyo, Japan) was equipped with 500 glass columns (Φ=2 mm, L=40 cm), and the lower and upper layers of a solvent mixture of $CHCl_3$–MeOH–H_2O–*n*-PrOH (9 : 12 : 8 : 2) were used for the stationary and mobile phases, respectively. Five-gram fractions were collected and numbered according to their order of elution with the mobile phase. HPLC was performed on ODS (Inertsil; GL Science, Tokyo, Japan; Φ=20 mm, L=250 mm), and the eluate was monitored with a UV detector at 254 nm and a reflective index monitor. β-D-Glucosidase (emulsin) was purchased from Sigma Chemical Co. (St. Louis, MO, U.S.A.). (*R*)-(+)- and (*S*)-(−)-MTPAs were from Nacalai Tesque. L-Glucose was commercially available from Kanto Chemical Co., Inc. (Tokyo, Japan).

Melting points were determined with a Yanagimoto micromelting point apparatus and are uncorrected. Optical rotations were measured on a Union Giken PM-101 digital polarimeter. IR spectra were measured on a Horiba FT-710 Fourier-transform infrared spectrophotometer and UV spectra on a JASCO V-520 UV/VIS spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were recorded on a JEOL JNM α-400 spectrometer at 400 MHz and 100 MHz, respectively, with tetramethylsilane (TMS) as an internal standard. Negative- and positive-ion HR-FAB-MS were recorded on a JEOL JMS SX-102 spectrometer.

Plant Material Leaves of *G. acuminatum* MUELL. (Euphorbiaceae) were collected in Okinawa, Japan, in August 1995, and a voucher specimen was deposited in the Herbarium of the Department of Pharmacognosy, Graduate School of Biomedical Sciences, Hiroshima University (95-GA-Okinawa-0801).

Extraction and Fractionation The air-dried leaves of *G. acuminatum* (4.76 kg) were extracted three times with MeOH. The MeOH extract was concentrated to 3.0 l and then 150 ml of H_2O was added to make a 95% aqueous solution. This solution was washed with 3.0 l of *n*-hexane and then the methanolic layer was concentrated to a viscous gum. The gummy residue was suspended in 3.0 l of H_2O and then extracted successively with 3.0 l each of EtOAc and *n*-BuOH to afford 195 g and 288 g of EtOAc- and *n*-BuOH-soluble fractions, respectively. A portion of the *n*-BuOH-soluble fraction (157 g) was subjected to highly porous synthetic resin (Diaion HP-20) CC (Mitsubishi Chemical Co., Ltd.; Φ=80 mm, L=55 cm), using H_2O–MeOH (4 : 1, 6 l), (2 : 3, 6), (3 : 2, 6 l), and (1 : 4, 6 l), and MeOH (6 l), with 2-l fractions collected. Fractions 3—5 were combined (30.2 g) and then subjected to silica gel (600 g) CC with increasing amounts of MeOH in $CHCl_3$ [$CHCl_3$ (2 l), and $CHCl_3$–MeOH (99 : 1, 3 l), (39 : 1, 3 l), (19 : 1, 3 l), (37 : 3, 3 l), (9 : 1, 6 l), (17 : 3, 6 l), (4 : 1, 6 l), (3 : 1, 6 l) and (7 : 3, 6 l)], and $CHCl_3$–MeOH–H_2O (70 : 30 : 4, 6 l), with 500-ml fractions collected. The residue of fractions 24—35 (1.17 g) was subjected to RPCC and then the residue of fractions 37—45 (217 mg) was purified by DCCC to give 50.0 mg of **2** as a syrup. The residue of fractions 52—65 (4.42 g) obtained on silica gel CC was purified by RPCC (98 mg in fractions 81—92), DCCC (53 mg in fractions 18—24), followed by HPLC with MeOH–H_2O (1 : 3) to give 10.1 mg of **7**.

The residue (52.6 g) of fractions 5—9 obtained on Diaion HP-20 CC was subjected to silica gel (1.20 kg) CC with increasing amounts of MeOH in $CHCl_3$ [$CHCl_3$ (1.0 l), $CHCl_3$–MeOH [(99 : 1, 2 l), (48 : 1, 2 l), (24 : 1, 4 l), (47 : 3, 6 l), (23 : 2, 6 l), (9 : 1, 8 l), (7 : 1, 8 l), (17 : 3, 8 l), (4 : 1, 8 l), (3 : 1, 4 l), and (7 : 3, 4 l)], and $CHCl_3$–MeOH–H_2O (70 : 30 : 4, 3 l), with 500-ml fractions collected. After evaporation of fractions 25—36, 152 mg of **1** was obtained as colorless rods. The residue (1.67 g) of fractions 51—65 was subjected to RPCC (153 mg in fractions 110—120 and 165 mg in fractions 138—152) and then DCCC to give 54.0 mg of **8** in fractions 84—102 and 28.6 mg of **6**. A further amount (95.5 mg) of **6** was also isolated in successive fractions obtained on silica gel CC. From the residue (8.57 g) of fractions 96—115, obtained on silica gel CC, 48.0 mg of **4** was isolated in a similar manner.

From the residues (8.67 g) of fractions 10 and 11, and those (12.5 g) of fractions 12 and 13 obtained on Diaion HP-20 CC, 147 mg of **5** was isolated as an amorphous powder and 216 mg of **3** as colorless needles, respectively.

Glochidiolide (1) Colorless rods, mp 210—213 °C, $[\alpha]_D^{25}$ −69.8° (*c*=0.49, DMSO). IR ν_{max} (KBr): 3400, 3050, 1750, 1725, 1625, 1450, 1420, 1355, 1290, 1265, 1195, 1055, 1020, 1050, 975, 925, 890 cm^{-1}; UV λ_{max} (MeOH): 256 (4.17) nm (log ε); ^{1}H-NMR (DMSO-d_6+two drops of D_2O) δ: 1.60 (1H, dd, *J*=13, 10 Hz, H-7′a), 1.77 (1H, ddd, *J*=14, 9, 2 Hz, H-7a), 2.26 (1H, d, *J*=17 Hz, H-2a), 2.39 (1H, dt, *J*=14, 5 Hz, H-7b), 2.48 (1H, d, *J*=17 Hz, H-2b), 2.93 (1H, dd, *J*=13, 6 Hz, H-7′b), 4.09 (1H, t, *J*=7 Hz, H-6), 4.53 (1H, ddd, *J*=9, 7, 2 Hz, H-14), 4.86 (1H, br s, H-8), 5.55 (1H, br d, *J*=10 Hz, H-4), 5.91 (1H, br d, *J*=10 Hz, H-5), 6.19 (1H, s, H-10), 6.20 (1H, dd, *J*=10, 2 Hz, H-13), 6.79 (1H, dt, *J*=10, 1 Hz, H-12). ^{13}C-NMR (DMSO-d_6): Table 1. HR-FAB-MS (negative-ion mode) *m/z*: 303.0855 $[M-H]^-$ (Calcd for $C_{16}H_{15}O_6$: 303.0868). *Anal.* Calcd for $C_{16}H_{16}O_6$: C, 63.15%; H, 5.30%. Found: C, 62.97%; H, 5.35%.

Isoglochidiolide (2) Off-white syrup, $[\alpha]_D^{23}$ +26.6° (*c*=2.33, MeOH). IR ν_{max} (film): 3350, 2952, 2929, 2856, 1734, 1721, 1667, 1514, 1457, 1172, 1006 cm^{-1}; UV λ_{max} (MeOH): 257 (3.87) nm (log ε); ^{1}H-NMR (DMSO-d_6+two drops of D_2O) δ: 1.60 (1H, dd, *J*=13, 9 Hz, H-7′a), 1.62 (1H, td, *J*=13, 10 Hz, H-7a), 2.17 (1H, td, *J*=13, 5 Hz, H-7b), 2.62 (1H, d, *J*=18 Hz, H-2a), 2.69 (1H, d, *J*=18 Hz, H-2b), 2.97 (1H, dd, *J*=14, 7 Hz, H-7′b), 4.05 (1H, br ddd, *J*=10, 4, 2 Hz, H-6), 4.44 (1H, br dd, *J*=9, 7 Hz, H-14), 4.58 (1H, dd, *J*=10, 5 Hz, H-8), 5.51 (1H, dd, *J*=10, 2 Hz, H-4), 5.91 (1H, dd, *J*=10, 2 Hz, H-5), 6.14 (1H, s, H-10), 6.17 (1H, dd, *J*=10, 2 Hz, H-13), 6.72 (1H. dd, *J*=10, 2 Hz, H-12). ^{13}C-NMR (DMSO-d_6): Table 1. HR-FAB-MS (negative-ion mode) *m/z*: 303.0838 $[M-H]^-$ (Calcd for $C_{16}H_{15}O_6$: 303.0868).

Acuminaminoside (3) Colorless needles (MeOH), mp 212—215 °C, $[\alpha]_D^{28}$ −33.3° (*c*=0.75, MeOH). IR ν_{max} (KBr): 3316, 1654, 1595, 1495, 1254, 1077, 999, 747 cm^{-1}. UV λ_{max} (MeOH): 214 (4.26), 236 (4.00), 256 (4.04), 296 (3.99), 310 (4.01) nm (log ε). ^{1}H-NMR (CD_3OD, 400 MHz) δ: 3.35 (1H, t, *J*=9 Hz, H-4″), 3.41 (1H, dd, *J*=9, 8 Hz, H-2″), 3.41 (1H, ddd, *J*=10, 6, 2 Hz, H-5″), 3.46 (1H, t, *J*=9 Hz, H-3″), 3.69 (1H, dd, *J*=12, 6 Hz, H-6″a), 3.88 (1H, dd, *J*=12, 2 Hz, H-6″b), 4.26 (2H, s, H_2-7), 4.94 (1H, d. *J*=8 Hz, H-1″), 6.97 (1H, m, H-5), 7.06 (1H, td, *J*=8, 1 Hz, H-5′), 7.18 (1H, td, *J*=8, 2 Hz, H-6′), 7.22—7.25 (4H, m, H-3, 4, 6 and 7′), 7.58 (1H, dd, *J*=8, 1 Hz, H-4′). ^{1}H-NMR (DMSO-d_6, 400 MHz) δ: 8.33 (2H, br s,

exchangeable with D_2O, –N$\underline{H}_2$). ^{13}C-NMR (CD_3OD, 100 MHz): Table 2. HR-FAB-MS (negative-ion mode) *m/z*: 428.1326 $[M-H]^-$ (Calcd for $C_{22}H_{22}O_8N$: 428.1345).

Glochidacuminoside A (4a) Amorphous powder, $[\alpha]_D^{20}$ −39.2° (*c*= 0.26, MeOH). IR ν_{max} (KBr): 3405, 2925, 1715, 1495, 1455, 1405, 1240, 1075, 1045, 760 cm^{-1}. UV λ_{max} (MeOH): 206 (3.88), 269 (3.14) nm (log ε). ^{1}H-NMR (CD_3OD, 400 MHz) δ: 3.39—3.48 (3H, m, H-3′, 4′, 5′), 3.49 (1H, dd, *J*=9, 8 Hz, H-2′), 3.67 (1H, d, *J*=15 Hz, H-7a), 3.70 (1H, dd, *J*=12, 5 Hz, H-6′a), 3.71 (1H, d, *J*=15 Hz, H-7b), 3.88 (1H, dd, *J*=12, 2 Hz, H-6′b), 4.88 (1H, d, *J*=8 Hz, H-1′), 6.99 (1H, td, *J*=8, 2 Hz, H-5), 7.17—7.23 (3H, m, H-3, 4, 6). ^{13}C-NMR (CD_3OD, 100 MHz): Table 3. HR-FAB-MS (negative-ion mode) *m/z*: 313.0913 $[M-H]^-$ (Calcd for $C_{14}H_{17}O_8$: 313.0923).

Glochidacuminoside B (5) Amorphous powder, $[\alpha]_D^{23}$ −48.0° (*c*=0.85, MeOH). IR ν_{max} (film): 3384, 2923, 2841, 1735, 1494, 1240, 1074 cm^{-1}. UV λ_{max} (MeOH): 215 (3.78), 269 (3.11), 274 (3.06) nm (log ε). ^{1}H-NMR (CD_3OD, 400 MHz) δ: 1.57 (1H, dddd, *J*=15, 12, 10, 7 Hz, H-5″a), 1.83 (1H, m, H-5″b), 1.95 (1H, m, H-3a″), 2.11 (2H, br s, H2-6″), 2.30 (1H, br d, *J*=16 Hz, H-3b″), 2.99 (2H, s, H_2-7″), 3.39 (1H, t, *J*=10 Hz, H-4′), 3.46 (1H, t, *J*=10 Hz, H-3′), 3.49 (1H, dd, *J*=10, 8 Hz, H-2′), 3.60 (1H, ddd, *J*=10, 6, 2 Hz, H-5′), 3.66 (1H, d, *J*=16 Hz, H-7a), 3.75 (1H, d, *J*=16 Hz, H-7b), 3.80 (1H, dddd, *J*=10, 8, 5, 3 Hz, H-4″), 4.22 (1H, dd, *J*=12, 6 Hz, H-6′a), 4.45 (1H, dd, *J*=12, 2 Hz, H-6′b), 4.85 (1H, d, *J*=8 Hz, H-1′), 5.44 (1H, br s, H-2″), 7.02 (1H, td, *J*=8, 2 Hz, H-5), 7.14 (1H, dd, *J*=8, 2 Hz, H-3), 7.23 (1H, td, *J*=8, 2 Hz, H-4), 7.23 (1H, dd, *J*=8, 2 Hz, H-6). ^{13}C-NMR (CD_3OD, 100 MHz): Table 3. HR-FAB-MS (negative-ion mode) *m/z*: 451.1604 $[M-H]^-$ (Calcd for $C_{22}H_{27}O_{10}$: 451.1632).

Glochidacuminoside C (6) Amorphous powder, $[\alpha]_D^{26}$ −25.8° (*c*=1.91, MeOH). IR ν_{max} (film): 3366, 2923, 2841, 1735, 1166, 1071, 1022 cm^{-1}. ^{1}H-NMR (CD_3OD, 400 MHz) δ: 1.61 (2H, m, H-5a and 5″a), 1.87 (2H, m, H-5b and 5″b), 1.97 (2H, m, H-3 and 3a″), 2.11 (4H, br s, H_2-6 and 6″), 2.30 (2H, br d, *J*=16 Hz, H-3b and 3b″), 2.99 (2H, s, H_2-7″), 3.06 (2H, s, H_2-7), 3.28—3.34 (2H, m, H-2′ and 4′), 3.39 (1H, t, *J*=10 Hz, H-3′), 3.60 (1H, ddd, *J*=10, 6, 2 Hz, H-5′), 3.83 (2H, m, H-4 and 4″), 4.20 (1H, dd, *J*=12, 6 Hz, H-6′a), 4.41 (1H, dd, *J*=12, 2 Hz, H-6′b), 5.44 (1H, d, *J*=8 Hz, H-1′), 5.44 (1H, br s, H-2″), 5.49 (1H, br s, H-2). ^{13}C-NMR (CD_3OD, 100 MHz): Table 3. HR-FAB-MS (negative-ion mode) *m/z*: 455.1914 $[M-H]^-$ (Calcd for $C_{22}H_{31}O_{10}$: 455.1917).

Glochidacuminoside D (7) Amorphous powder, $[\alpha]_D^{28}$ −72.8° (*c*=0.67, MeOH). IR ν_{max} (film): 3365, 2932, 2255, 1704, 1613, 1517, 1452, 1351, 1231, 1075, 1037, 765 cm^{-1}. UV λ_{max} (MeOH): 223 (4.19), 275 (3.98) nm (log ε). ^{1}H-NMR (CD_3OD, 400 MHz) δ: 3.46 (1H, t, *J*=9 Hz, H-4′), 3.73 (1H, t, *J*=9 Hz, H-3′), 3.74 (1H, dd, *J*=12, 5 Hz, H-6′a), 3.97 (1H, dd, *J*=12, 2 Hz, H-6′b), 4.91 (1H, d, *J*=8 Hz, H-1′), 4.93 (1H, dd, *J*=9, 8 Hz, H-2′), 5.84 (1H, s, H-7), 6.72 (2H, d, *J*=9 Hz, H-3 and 5), 7.13 (2H, s, H-2″ and 6″), 7.22 (2H, d, *J*=9 Hz, H-2 and 6). ^{13}C-NMR (CD_3OD, 100 MHz): Table 3. HR-FAB-MS (negative-ion mode) *m/z*: 462.1008 $[M-H]^-$ (Calcd for $C_{21}H_{20}O_{11}N$: 462.1038).

Acuminaminoside Tetraacetate (3a) Acuminaminoside (3, 30 mg) was acetylated with a mixture of acetic anhydride (0.5 ml) and pyridine (0.5 ml) at 25 °C for 4 h. The usual workup gave 38 mg (90%) of the tetraacetate (**3a**) as an amorphous powder. **3a**: ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 1.85, 1.94, 2.00, 2.02 (each 3H, each s, C$\underline{H}_3$CO– ×4), 3.82 (1H, ddd, *J*=10, 6, 2 Hz, H-5″), 4.12 (1H, dd, *J*=12, 2 Hz, H-6′a), 4.13 (1H, d, *J*=17 Hz, H-7a), 4.24 (1H, d, *J*=17 Hz, H-7b), 4.26 (1H, dd, *J*=12, 6 Hz, H-6″b), 5.10—5.15 (2H, m) and 5.20—5.28 (1H, m) (H-2″, 3″ and 4″), 5.25 (1H, d, *J*=8 Hz, H-1″), 7.04—7.13 (3H, m), 7.18—7.27 (4H, m), 7.53 (1H, d, *J*=8 Hz) (aromatic protons). ^{1}H-NMR (DMSO-d_6, 400 MHz) δ: 1.80, 1.91, 1.99, 2.00 (each 3H, each s, CH_3CO–×4), 8.20 (2H, br s, exchangeable with D_2O, –NH_2). ^{13}C-NMR ($CDCl_3$, 100 MHz) δ: 20.3, 20.5, 20.6 (×2) (C$\underline{H}_3$CO– ×4), 42.1 (C-7), 62.0 (C-6″), 68.5, 71.2, 72.0, 72.9 (C-2″, 3″, 4″ and 5″), 95.0 (C-3′), 99.5 (C-1″), 110.2 (d), 116.0 (d), 118.9 (d), 121.8 (d), 123.6 (d), 124.4 (d), 125.5 (s), 126.2 (s), 128.3 (d), 131.4 (d), 149.3 (C-9′), 155.1 (C-2), 165.2 (C-2′), 169.1, 169.4, 170.2, 170.6 ($CH_3\underline{C}O$– ×4), 192.1 (C-8); HR-FAB-MS (negative-ion mode) *m/z*: 596.1745 $[M-H]^-$ (Calcd for $C_{30}H_{30}O_{12}N$: 596.1768).

Acuminaminoside Pentaacetate (3b) Acuminaminoside (**3**) (35 mg) was first acetylated as above and then further acetylated with acetyl bromide (10 μl) and α-pinene (20 μl) in 2 ml of dried CH_2Cl_2 at 25 °C for 4 h. The reaction mixture was washed successively with 2 ml of each of H_2O, 5% $NaHCO_3$, and brine and dried with the addition of Na_2SO_4. The pentaacetate was purified by preparative TLC (developed with benzene : acetone, 4 : 1, and eluted with $CHCl_3$: MeOH, 9 : 1) to give 35.8 mg (95%) of **3b**. Amorphous powder, $[\alpha]_D^{22}$ −5.9° (*c*=2.39, $CDCl_3$). IR ν_{max} (KBr): 3483, 1755, 1647, 1597, 1568, 1464, 1371, 1228, 1041, 985, 754 cm^{-1}. UV λ_{max} (MeOH): 216 (4.23), 239 (4.20), 275 (3.92), 280sh (3.89), 315 (3.97) nm (log ε). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 1.85, 1.91, 1.99, 2.02 (each 3H, each s, CH_3CO– ×4), 2.31 (3H, s, C$\underline{H}_3$CONH–), 3.84 (1H, ddd, *J*=10, 5, 2 Hz, H-5″), 4.12 (1H, dd, *J*=12, 2 Hz, H-6″a), 4.23 (1H, d, *J*=17 Hz, H-7a), 4.26 (1H, dd, *J*=12, 5 Hz, H-6″b), 4.38 (1H, d, *J*=7 Hz, H-7b), 5.11 (1H, dd, *J*=9, 8 Hz, H-2″), 5.14 (1H, d, *J*=8 Hz, H-1″), 5.19 (1H, t, *J*=9 Hz, H-4″), 5.26 (1H, t, *J*=9 Hz, H-3″), 7.08—7.11 (2H, m), 7.19 (1H, dd, *J*=8, 2 Hz, H-6′), 7.29—7.31 (2H, m), 7.37 (1H, td, *J*=8, 2 Hz), 7.57 (1H, d, *J*=8 Hz), 7.40 (1H, dd, *J*=8, 2 Hz) (aromatic protons), 11.01 (1H, br s, $CH_3CON\underline{H}$–). ^{13}C-NMR ($CDCl_3$, 100 MHz) δ: 20.38, 20.43, 20.54 (×2) (C$\underline{H}_3$CO– ×4), 24.9 (C$\underline{H}_3$CONH–), 43.1 (C-7), 62.0 (C-6″), 68.4, 71.2, 72.0, 72.7 (C-2″, 3″, 4″ and 5″), 99.2 (C-1″), 99.7 (C-3′), 111.8 (d), 115.6 (d), 120.0 (d), 123.5 (d), 123.6 (s), 123.9 (d), 124.2 (s), 125.0 (d), 128.8 (d), 131.5 (d), 150.7 (C-9′), 154.9 (C-2), 157.0 (C-2′), 167.1 ($CH_3\underline{C}ONH$–), 169.0, 169.3, 170.1, 170.4 (CH_3CO– ×4), 194.6 (C-8); HR-FAB-MS (negative-ion mode) *m/z*: 638.1860 $[M-H]^-$ (Calcd for $C_{32}H_{32}O_{13}N$: 638.1874).

Enzymatic Hydrolysis of Acuminaminoside (3) to Its Aglycone (3c) Acuminaminoside (**3**, 34 mg) was hydrolyzed with hesperidinase at 37 °C for 24 h. The resulting hydrolysate was separated by silica gel column chromatography to give an aglycone (**3c**), which was crystallized from MeOH (6.7 mg, 33%), and 8.4 mg of D-glucose. Aglycone (**3c**): Colorless prisms (MeOH), mp 171—173 °C. ^{1}H-NMR (CD_3OD, 400 MHz) δ: 4.12 (2H, s, H_2-7), 6.76 (1H, td, *J*=8, 1 Hz, H-5), 6.83 (1H, dd, *J*=8, 1 Hz, H-3), 7.06 (1H, td, *J*=8, 1 Hz, H-5′), 7.05—7.10 (2H, m, H-4 and 6), 7.17 (1H, td, *J*=8, 1 Hz, H-6′), 7.23 (1H, ddd, *J*=8, 2, 1 Hz, H-7′), 7.56 (1H, ddd, *J*=8, 2, 1 Hz. H-4′). ^{13}C-NMR (CD_3OD, 100 MHz) δ: 43.0 (C-7), 95.3 (C-3′), 110.9 (C-7′), 116.4 (C-3), 119.9 (C-4′), 120.7 (C-5), 122.8 (C-5′), 123.4 (C-1), 125.2 (C-6′), 127.6 (C-8′), 129.1 (C-4), 131.5 (C-6), 150.8 (C-9′), 156.8 (C-2), 168.4 (C-2′), 194.8 (C-8). HR-FAB-MS (negative-ion mode) *m/z*: 266.0837 $[M-H]^-$ (Calcd for $C_{16}H_{12}O_3N$: 266.0817). D-Glucose: $[\alpha]_D^{28}$ +39.2° (*c*=0.67, H_2O, 24 h after being dissolved in the solvent).

X-Ray Analysis of 1 The crystal used for data collection was a colorless rod (0.3 mm×0.3 mm×0.4 mm). All data were obtained on a Rigaku AFC-5S automated four-circle diffractometer with graphite-monochromated Mo$K\alpha$ radiation. Unit cell parameters were determined by least-squares refinement of the optimized setting of 21 reflections. The intensities were measured using an $\omega/2\theta$ scan up to 45°. Three standard reflections were monitored for every 150 measurements. The data were corrected for Lorentz and polarization factors. Absorption was applied and decay correction was not applied. Of the 1407 reflections collected, 1161 unique reflections with $I>3.0\sigma(I)$ were used for structure determination and refinement. The structure was solved using a direct method with the teXan crystallographic software package.[3] All non-H atoms were found in a Fourier map. The refinement of atomic parameters was carried out by means of full-matrix least-squares refinement using anisotropic temperature factors for all non-H atoms. All H atoms, except for those attached to O atoms, were located geometrically and refined. The H atoms attached to O atoms were found in a difference Fourier map and refined isotropically. The minimum and maximum peaks in the final difference Fourier map were −0.19 and 0.25 e Å^{-3}, respectively. The final refinement converged with R_1=0.049, R_w=0.056 for 198 parameters. Atomic scattering factors were taken from the "International Tables for X-ray Crystallography."[6] Crystal data: **1**: $C_{16}H_{16}O_6$, M_r= 304.30, monoclinic, space group $P2_1$, *a*=5.835(5) Å, *b*=14.649(8) Å, *c*= 8.136(7) Å, β=97.80(7)°, *V*=691.1(8) Å^3, *Z*=2, D_C=1.462 Mgm^3, *F*(000)= 320, μ(Mo$K\alpha$)=1.05 cm^{-1}.

X-Ray Analysis of 3b The crystal used for data collection was a colorless prism (0.2 mm×0.2 mm×0.2 mm). All data were obtained on a Rigaku AFC-5S automated four-circle diffractometer with graphite-monochromated Mo$K\alpha$ radiation. Unit cell parameters were determined by least-squares refinement of the optimized setting of 25 reflections in the range of 12.5°< θ<14.3°. The intensities were measured using an $\omega/2\theta$ scan up to 55°. Three standard reflections were monitored for every 150 measurements. The data were corrected for Lorentz and polarization factors. Correction of secondary extinction was applied (coefficient=0.75773×10^{-5}). Absorption (Ψ-scan,[7] transmission factor=0.941—1.000) and decay (−0.897% decline) corrections were also applied. Of the 6264 reflections collected, 6260 unique reflections were used for structure determination and refinement. The structure was solved using a direct method with the teXan crystallographic software package.[3] All non-H atoms were found in a Fourier map. The refinement of atomic parameters was carried out by means of full-matrix least-squares refinement using anisotropic temperature factors for all non-H atoms. All H atoms, except for those attached to N and O atoms, were located geometrically and refined. The H atoms attached to N and O atoms were found in a difference Fourier map and refined isotropically. The

final refinement converged with $R_1=0.038$, $R_w=0.121$ for 386 parameters. Atomic scattering factors were taken from the "International Tables for X-ray Crystallography."[6] Crystal data **3b**: $C_{16}H_{13}O_3N$, $M_r=267.28$, triclinic, space group P_1, $a=11.457(1)$ Å, $b=12.163(2)$ Å, $c=10.625(1)$ Å, $\alpha=111.18(1)°$, $\beta=99.201(9)°$, $\gamma=70.373(9)°$, $V=1299.1(3)$ Å^3, $Z=4$, $D_C=1.366$ Mgm^{-3}, $F(000)=560$, $\mu(\mathrm{Mo}K\alpha)=0.951$ cm^{-1}.

Mild Alkaline Hydrolysis of Glochidacuminoside B (5) Glochidacuminoside B (**5**) (39.4 mg) was treated with 1 ml of 0.1 M NaOH in MeOH at 25 °C for 30 min. The reaction mixture was diluted with 4 ml of H_2O and then extracted with 4 ml and 2 ml of $CHCl_3$ twice. The combined organic layer was washed with 1 ml of brine and then treated with Amberlite IR-120B (H^+). After being dried over Na_2SO_4, the organic solvent was evaporated to give the methyl ester (**5a**) as a syrup (12.0 mg, 81%). The aqueous layer was neutralized with Amberlite IR-120B (H^+) to yield **5b** (25.2 mg, 91%). Methyl ester (**5a**): Colorless syrup, $[\alpha]_D^{23}$ −23.8° ($c=0.80$, $CHCl_3$). IR ν_{max} (film): 3421, 2925, 2842, 1739, 1437, 1337, 1261, 1157, 1073, 1053 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 1.69 (1H, dddd, $J=15$, 12, 10, 6 Hz, H-5a), 1.87 (1H, m, H-5b), 2.04 (1H, v br d, $J=17$ Hz, H-3a), 2.11—2.21 (2H, m, H_2-6), 2.38 (1H, br d, $J=17$ Hz, H-3b), 2.98 (2H, s, H_2-7), 3.68 (3H, s, –$COOCH_3$), 3.96 (1H, dddd, $J=10$, 8, 5, 3 Hz, H-4), 5.46 (1H, br s, H-2). ^{13}C-NMR ($CDCl_3$, 100 MHz) δ: 26.5 (C-6), 30.8 (C-5), 34.4 (C-3), 42.7 (C-7), 51.8 (–$COOCH_3$), 66.4 (C-4), 122.8 (C-2), 140.0 (C-1), 172.2 (C-8). HR-FAB-MS (negative-ion mode) *m/z*: 169.0683 $[M-H]^-$ (Calcd for $C_9H_{13}O_3$: 169.0865). **5b**: All physical data were essentially the same as those for the natural **4a**.

Enzymatic Hydrolysis of 5b The glucoside (**5b**, 25.2 mg) derived from **5** was hydrolyzed by emulsin (10 mg) in 3 ml of H_2O at 37 °C for 4 h. The reaction mixture was extracted with 2 ml of EtOAc twice to give 2-hydroxyphenylacetic acid (**5c**), which was recrystallized from $CHCl_3$ as colorless plates (10.6 mg, 87%). The aqueous layer was evaporated to dryness and the residue was triturated with MeOH. After evaporation of MeOH, the residue was dissolved in H_2O and then treated with a Sep-Pak C_{18} cartridge to gave 10.5 mg (73%) of D-glucose. 2-Hydroxyphenylacetic acid (**5c**): colorless plates ($CHCl_3$), mp 146—148 °C. ^{1}H-NMR (CD_3OD, 400 MHz) δ: 3.58 (2H, s, H_2-7), 6.75—6.79 (2H, m), 7.05—7.11 (2H, m) (aromatic protons). ^{13}C-NMR (CD_3OD, 100 MHz): 36.6 (C-7), 116.1 (C-3), 120.5 (C-5), 122.9 (C-1), 129.3 (C-4), 132.1 (C-6), 156.8 (C-2), 176.3 (C-8). HR-FAB-MS (negative-ion mode) *m/z*: 151.0394 $[M-H]^-$ (Calcd for $C_8H_7O_3$: 151.0395). D-Glucose: $[\alpha]_D^{23}$ +50.0° ($c=0.70$, H_2O, 24 h after being dissolved in the solvent).

(*R*)- and (*S*)-MTPA Esters of 5a A solution of **5a** (3.0 mg) in 1 ml of dehydrated CH_2Cl_2 was reacted with (*R*)-MTPA (45 mg) in the presence of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC) (39 mg) and *N*,*N*′-dimethylaminopyridine (DMAP) (21 mg), and the mixture was occasionally stirred, at 25 °C for 1 h. After the addition of 1 ml of CH_2Cl_2, the solution was successively washed with H_2O (1 ml), 5% HCl (1 ml), $NaHCO_3$-saturated H_2O (1 ml), and brine (1 ml). The organic layer was dried over Na_2SO_4 and then evaporated under reduced pressure. The residue was purified by preparative TLC [silica gel (0.50 mm thickness, Merck), applied for 18 cm, developed with *n*-hexane–EtOAc (4 : 1) for 9 cm and eluted with $CHCl_3$–MeOH (9 : 1)] to furnish the (*S*)-MTPA ester, **5d** (4.8 mg, 71%). Through a similar procedure, **5e** (4.9 mg, 72%) was prepared from **5a** (3.0 mg) using (*S*)-MTPA (42 mg), EDC (39 mg), and DMAP (19 mg). (*R*)-MTPA ester (**5d**): colorless syrup. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 1.86—1.94 (1H, m, H-5a), 1.94—2.03 (1H, m, H-5b), 2.04 (1H, br d, $J=17$ Hz, H-3a), 2.17 (1H, v br d, $J=17$ Hz, H-3a), 2.19 (2H, t-like, $J=7$ Hz, H_2-6), 2.45 (1H, br d, $J=17$ Hz, H-3b), 2.96 (2H, s, Hz-7), 3.54 (3H, br s, –OCH_3), 3.66 (3H, s, –$COOCH_3$), 5.28 (1H, dddd, $J=10$, 8, 5, 3 Hz, H-4), 5.44 (1H, br s, H-2), 7.26—7.41 (3H, m), 7.52—7.53 (2H, m) (aromatic protons). HR-FAB-MS (positive-ion mode) *m/z*: 409.1259 $[M+Na]^+$ (+NaI) (Calcd for $C_{19}H_{21}O_5F_3Na$: 409.1239). (*S*)-MTPA ester (**5e**): colorless syrup. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 1.84—1.93 (2H, m, H-5a and 5b), 1.87 (1H, m, H-5b), 2.04 (1H, br d, $J=17$ Hz, H-3a), 2.13 (2H, t-like, $J=7$ Hz, H_2-6), 2.27 (1H, br d, $J=17$ Hz, H-3a), 2.48 (1H, br d, $J=17$ Hz, H-3b), 2.97 (2H, s, H_2-7), 3.55 (3H, s, –OCH_3), 3.64 (3H, s, –$COOCH_3$), 5.29 (1H, dddd, $J=10$, 8, 5, 3 Hz, H-4), 5.47 (1H, br s, H-2), 7.26—7.40 (3H), 7.52—7.54 (2H) (aromatic protons). HR-FAB-MS (positive-ion mode) *m/z*: 409.1241 $[M+Na]^+$ (+NaI) (Calcd for $C_{19}H_{21}O_5F_3Na$: 409.1239).

Mild Alkaline Hydrolysis of Glochidacuminoside C (6) Compound **6** (25.0 mg) was similarly treated with 0.1 M NaOH in MeOH (0.5 ml) as for **5** at 20 °C for 1 h. The reaction mixture was diluted with H_2O (4 ml), neutralized with Amberlite IR-120B (H^+), and then extracted twice with EtOAc (2 ml×2). Evaporation of the organic layer afforded 10.9 mg (59%) of the methyl ester (**6a**) (=**5a**). After the aqueous layer had been evaporated, the residue was redissolved in H_2O and then purified with a Sep-Pak C_{18} cartridge to give 6.8 mg (65%) of D-glucose. Methyl ester **6a** (=**5a**): $[\alpha]_D^{25}$ −19.2° ($c=0.73$, $CHCl_3$). D-Glucose: $[\alpha]_D^{25}$ +33.1° ($c=0.45$, H_2O, 24 h after being dissolved in the solvent).

Determination of the Absolute Structure of the Glucose Obtained on Hydrolysis of 7 About 2 mg of **7** was hydrolyzed with 2 N H_2SO_4 in a water-bath. The hydrolyzate was neutralized with a mixed bed resin (MB-3) and then dried. The residue was treated with cysteine methyl ester in pyridine to yield thiazolidine derivatives according to the reported procedure,[8,9] and the resultant derivatives were analyzed on silica gel TLC (*Rf* 0.52 and 0.48, $CHCl_3$–MeOH–H_2O, 15 : 6 : 1). Authentic thiazolidine derivatives were obtained from D- and L-glucoses.

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