New Iridoids from *Asperula maximowiczii*

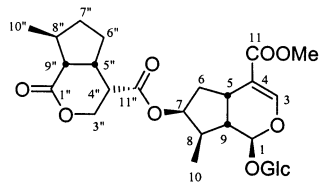
Aeri Park, Hyoung Ja Kim, Ji Sun Lee, Eun-Rhan Woo, Hokoon Park, and Yong Sup Lee*

Division of Life Sciences, Korea Institute of Science & Technology, P.O. Box 131, Cheongryang, Seoul 130-650, Korea

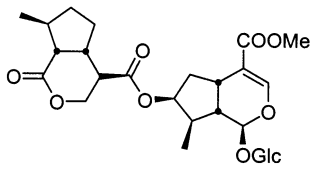
Received January 25, 2002

Three new dimeric iridoid glucosides, named asperuloides A (**1**), B (**2**), and C (**3**), were isolated from *Asperula maximowiczii*, along with the known compound picconioside II. The structures of the new compounds were determined by spectroscopic and chemical methods and by the single-crystal X-ray diffraction analysis of **1**.

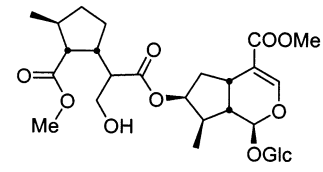
Asperula maximowiczii Komarov belongs to the family Rubiaceae, which is a perennial plant distributed on damp ground in Korea, China, and Taiwan. Flavonoids, anthraquinones, and iridoids have been isolated from the other species of the same genus (i.e., *A. odorata*, *A. oppositifolia*, and *A. tinctoria*).[1] However, phytochemical studies have not been carried out on this plant. During our search for biologically active compounds from plant sources, *A. maximowiczii* was selected for investigation. Separation and isolation of the alcoholic extract of *A. maximowiczii* collected from Kang-Won, Korea, afforded three new dimeric iridoid glucosides, named asperuloides A (**1**), B (**2**), and C (**3**), along with the known iridoid picconioside II.[2] In this paper, we report the isolation and structural determination of **1**−**3**.



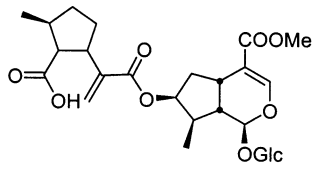
1



2



3



4

From the methanolic extract of the air-dried whole plant of *A. maximowiczi*, the CH_2Cl_2-soluble portion afforded asperuloides A, B, and C (**1**−**3**), and the EtOAc-soluble extract gave asperuloide C (**3**) and piccouioside II.

Compound **1** was obtained as colorless needles upon recrystallization from CH_2Cl_2−MeOH. Its molecular formula, $C_{27}H_{38}O_{13}$, was established by HRFABMS. The IR spectrum indicated the presence of hydroxyl (3422 cm^{-1}), ester (1718 cm^{-1}), and α,β-conjugated ester (1646 cm^{-1}) groups. The ^1H NMR spectrum showed a singlet for the 11-carbomethoxy group at 3.69 ppm, as confirmed by the signal of the olefinic H-3 at 7.43 ppm (d, $J = 1.3$ Hz), which was highly deshielded by an ester carbonyl group. Two hemiacetal proton signals at 5.24 (d, $J = 5.4$ Hz) and 4.66 ppm (d, $J = 7.9$ Hz) were assigned to H-1 and the anomeric proton of a β-D-glucopyranosyl moiety, respectively. The ^1H NMR signals for the iridoid moiety of **1** (Table 1) and loganin[3] differed only in the chemical shifts for H-7 and H-8. These signals were shifted downfield by 1.12 and 0.29 ppm in the spectrum of **1**. These chemical shift differences in H-7 and H-8 were expected, since the δ-lactone moiety is linked to C-7 of loganin.[4] In their ^{13}C NMR spectra, most of the signals for the loganin moiety of **1** (Table 2) and in loganin[3] had very similar chemical shifts to each other except for the signals at C-6, C-7, and C-8.[5] Significant differences between the spectra of **1** and loganin were the large downfield shift (+4.65 ppm) of the C-7 signal and smaller upfield shifts for C-6 and C-8 (−2.3 and −1.4 ppm) in **1** owing to an α-effect caused by acylation of the 7-hydroxy group.[6] On the basis of the $^1H-^1H$ COSY and HMQC spectral data, the remaining proton signals of the δ-lactone moiety in **1** could be assigned.

The HMBC spectrum of compound **1** indicated that the carbonyl carbon signal (δ 176.0, C-1″) of the δ-lactone moiety showed a $^1H-^{13}C$ long-range correlation with the H-3″ signal. The ^{13}C NMR signal (δ 171.6, C-11″) of the other carbonyl group was correlated with the ^1H NMR signal at δ 3.23 (H-4″). These data indicated that the carbonyl groups of the ester were located at C-9″ and C-4″ of the lactone part, respectively. The proton signal pattern of this δ-lactone unit was very close to that of scaevoloside, previously isolated from *Scaevola racemigera*.[7] The conformation of the loganin portion and the configuration of iridolactone in **1** were determined by NOE observations. Signals at H-5 and H-9 were determined as being in a *cis* configuration by their NOE correlations. On irradiation at H-9, the H-5 and H-10 signals were enhanced by 5%, but enhancements of the H-8 and H-1 signals were not observed. On the basis of the assumption that H-9 has the usual β-configuration, the methyl group at C-8 and H-5 could also be assigned with a β-configuration. The irradiation of the H-9″ signal led to enhancement of both the H-5″ and H-10″ signals. As a result, H-9″ was deduced to be *cis* to H-5″ and H-8″ *trans* to H-9″. To confirm the stereo-

* To whom correspondence should be addressed. Tel: +82-2-958-5167. Fax: +82-2-958-5189. E-mail: yslee@kist.re.kr.

10.1021/np020017q CCC: $22.00
Published on Web 08/22/2002

Table 1. ^{1}H NMR Data (CD_3OD, 500 MHz) of Compounds **1**−**3**

position	1	2	3
H-1	5.24 d (5.4)	5.25 d (5.1)	5.33 d (3.8)
H-3	7.43 d (1.3)	7.41 d (1.3)	7.40 d (1.2)
H-5	3.08 dd (7.9, 7.7)	3.10 dd (7.9, 7.5)	3.10 m
H-6$_\alpha$	1.71 ddd (14.0, 8.5, 4.8)	1.73 ddd (14.4, 8.1, 5.2)	1.76 ddd (14.7, 7.2, 5.3)
H-6$_\beta$	2.29 ddd (14.5, 7.5, 1.2)	2.27 ddd (14.4, 11.8, 7.5)	2.33 ddd (14.8, 8.1, 1.6)
H-7	5.16 t (4.7)	5.16 dd (4.8, 3.9)	5.12 br t (3.8)
H-8	2.15 td (13.6, 6.9)	2.14 m	2.10 m
H-9	2.03 td (8.7, 5.5)	2.04 td (8.8, 5.1)	2.10 m
H-10	1.08 d (6.9)	1.06 d (6.9)	1.11 d (6.5)
H-1′	4.66 d (7.9)	4.65 d (7.9)	4.66 d (7.9)
H-2′	3.20 dd (9.1, 7.9)	3.19 dd (9.1, 7.9)	3.18 dd (8.0, 7.9)
H-3′	3.37 dd (9.0, 8.7)	3.36 dd (9.0, 8.7)	3.37 dd (8.9, 8.7)
H-4′	3.26 dd (9.6, 8.6)	3.28 dd (9.6, 8.6)	3.27 dd (9.6, 8.5)
H-5′	3.31 m	3.30 m	3.31 m
H-6$_\alpha$′	3.64 dd (11.9, 6.1)	3.65 dd (11.9, 6.1)	3.66 dd (11.9, 5.8)
H-6$_\beta$′	3.90 dd (11.9, 2.1)	3.89 dd (11.9, 2.1)	3.90 dd (11.9, 2.1)
H-3$_\alpha$″	4.42 m	4.38 dd (11.3, 7.6)	3.72 dd (13.9, 7.2)
H-3$_\beta$″	3.23 m	4.49 dd (11.3, 3.2)	3.83 dd (10.8, 3.7)
H-4″	2.96 m	2.65 td (7.4, 3.2)	2.60 m (11.0, 2.9)
H-5″	1.53 m	2.84 m	2.50 m
H-6″	1.93 m	1.44 m (9.7, 6.4)	1.57 m (11.1, 8.2)
H-6″	1.28 m (12.1, 6.4)	2.10 m	1.90 m (11.1, 6.7)
H-7$_\alpha$″	1.98 m	1.23 m (12.0, 6.5)	1.22 ddd (7.3, 6.3, 2.1)
H-7$_\beta$″	2.09 m	2.03 m (6.1, 1.6)	2.04 m (7.9, 1.7)
H-8″	2.52 t (10.6)	2.20 m	2.25 ddd (14.4, 7.3, 4.1)
H-9″	1.18 d (6.4)	2.54 dd (11.1, 9.2)	2.55 m
H-10″	3.69 s	1.18 d (6.6)	1.06 d (6.9)
OMe		3.66 s	3.69 s, 3.66 s

Table 2. ^{13}C NMR Data (CD_3OD, 125 MHz) of Compounds **1**−**3**[a]

carbon	1	2	3
C-1	97.7 d	97.5 d	97.1 d
C-3	152.7 d	152.5 d	152.2 d
C-4	112.8 s	113.0 s	113.5 s
C-5	32.9 d	32.7 d	32.9 d
C-6	40.4 t	40.4 t	40.4 t
C-7	79.4 d	79.7 d	79.1 d
C-8	40.8 d	40.8 d	40.8 d
C-9	46.9 d	46.9 d	47.2 d
C-10	13.8 q	13.7 q	13.5 q
C-11	169.2 s	169.2 s	169.2 s
C-1′	100.2 d	100.2 d	100.1 d
C-2′	74.7 d	74.7 d	74.7 d
C-3′	78.0 d	77.9 d	78.0 d
C-4′	71.6 d	71.6 d	71.6 d
C-5′	78.4 d	78.3 d	78.3 d
C-6′	62.8 t	62.8 t	62.7 t
C-1″	176.0 s	176.3 s	177.4 s
C-3″	66.0 t	68.2 t	63.7 t
C-4″	43.2 d	46.7 d	51.7 d
C-5″	38.5 d	40.2 d	42.1 d
C-6″	28.9 t	33.3 t	32.1 t
C-7″	36.1 t	35.5 t	34.4 t
C-8″	42.8 d	40.7 d	40.0 d
C-9″	51.3 d	50.0 d	52.0 d
C-10″	19.1 q	20.0 q	21.9 q
C-11″	171.6 s	172.7 s	175.4 s
OMe	51.7 q	51.7 q	51.4 q
			51.6 q

[a] Assignments were confirmed by DEPT, ^{1}H−^{1}H COSY, HMQC, and HMBC methods.

chemistry of compound **1**, a single-crystal X-ray analysis[8] was carried out. The absolute configuration was established from data on the configuration of the anomeric proton of the β-D-glucose unit of the loganin moiety, as shown in Figure 1. The identification deduced spectroscopically was therefore fully confirmed.

Alkaline hydrolysis of compound **1** with sodium hydroxide provided two compounds, loganin[3] and compound **4**. The ^{1}H NMR spectrum of compound **4** revealed a set of new terminal ethylene signals at 6.14 and 5.54 ppm. The signals

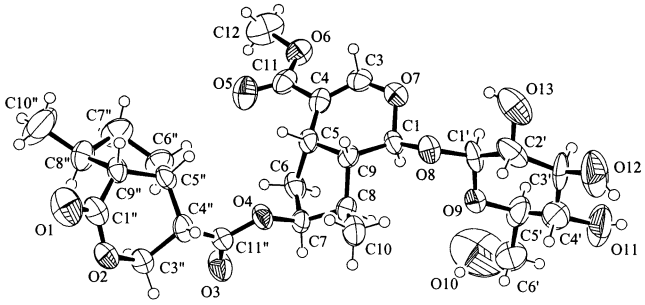


Figure 1. ORTEP drawing of compound **1**.

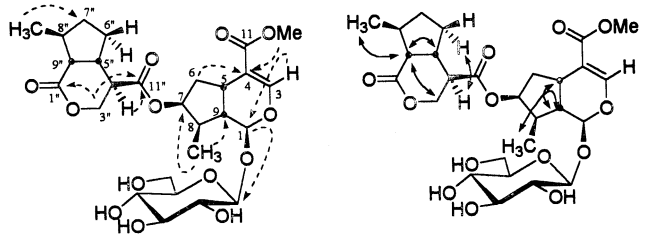


Figure 2. NOESY (↔) and HMBC (- - ->) correlations for compound **2**.

corresponding to H-3″ and H-4″ were not found, leading to the formulation of structure **4**. Loganin was identified by comparison with an authentic sample.[3]

Compound **2** was obtained as an amorphous powder and was assigned the same molecular formula, $C_{27}H_{38}O_{13}$, as that of **1**. All the signals in the ^{1}H NMR spectrum of **2** for the loganin unit and for an iridolactone moiety were in good agreement with those of **1**. However, the H-4″ signal in **2** was shifted upfield by 0.58 ppm when compound with **1**, as confirmed from the HMBC spectrum (Figure 2). Furthermore, the ^{1}H NMR spectrum of **2** exhibited an AB part of an ABX system at δ 4.38 (dd, J = 11.2, 7.5 Hz) and 4.49 (dd, J = 11.2, 3.2 Hz), indicating the presence of a methylene group in the lactone ring. The ^{1}H and ^{13}C NMR (Tables 1 and 2) spectra of **2** were very similar to those of compound **1** except for the distinct differences in the

resonances due to an iridolactone moiety. The chemical shifts of all carbons were determined by correlation with the proton chemical shifts assigned by detailed decoupling experiments. Accordingly, the ^{13}C NMR spectrum of **2** was fully assigned, as shown in Table 2. These data also supported the proposed structure **2**. The stereochemistry of compound **2** was determined by NOESY data, which showed correlations between H-9″ and H-5″ but not between H-4″ and H-5″, demonstrating a *cis* configuration for the C-11″ carbonyl group and H-5″ (Figure 2). As a result, the absolute structure of compound **2** was determined as shown.

Compound **3** was obtained as an amorphous powder, whose composition was determined to be $C_{28}H_{43}O_{14}$ by HRFABMS. Compound **3** was considered to be closely related structurally to compound **1**, since their IR and UV spectra were essentially the same. Compound **3** exhibited two distinctive signals for methoxy groups from the ^1H and ^{13}C NMR spectra. An upfield shift of the H-3″ signal was observed, indicating the opening of the lactone ring of **1** (Table 1). The configuration of the methyl ester could be proposed, since a connectivity in the HMBC spectrum was observed between H-9″ at δ 2.55 and C-1″ at δ 177.4 of the methyl ester. The correlations between H-3″ (δ 3.72 and 3.83) and C-4″ (δ 51.7), and H-3″ and C-11″ (δ 175.4), were also observed. The structure of **3** was thus established. Since compounds **1** and **2** did not decompose under any of the laboratory conditions applied or in solution of MeOH, compound **3** does not appear to be an extraction artifact.

Picconioside II was identified by comparing its physical and spectral data with literature values.[2]

Experimental Section

General Experimental Procedures. Melting points were determined on a Thomas-Hoover capillary melting apparatus and are uncorrected. Optical rotations were determined on an Autopol III automatic polarimeter (Rudolph Research Co., Flanders, NJ). UV spectra were taken with a Shimazu UV 240 UV−visible recording spectrometer. IR spectra were recorded on a Perkin-Elmer 16F-PC FT-IR instrument using potassium bromide pellets. NMR spectra were recorded on a Bruker AMX-500 (500 MHz) spectrometer. $^1H-^1H$ COSY, NOE, NOESY, HMQC, and HMBC NMR spectra were obtained with the usual pulse sequences, and data processing was performed with the standard Bruker software. HRFABMS were determined on a JEOL JMS-HX 110/100A mass spectrometer. Preparative HPLC was performed on a Waters pump (model 510) with a photodiode array detector (Waters model 996) using a ChiraSper (10 mm × 250 mm, Merck) column. TLC and column chromatography were carried out on precoated silica gel F_{254} plates (Merck, art. 5715), RP-18 $F_{254}S$ plates (Merck, art. 15423), silica gel 60 (Merck, 230−400 mesh), and Lichroprep RP-18 (Merck, 40−63 μm).

Plant Material. The whole plants of *Asperula maximowiczii* were collected at Mt. Odae, Korea, in August 1994, and the species was identified by Dr. Jong Hwan Kwak at Korea Institute of Science and Technology (KIST). Voucher specimens (398-20) have been deposited in our laboratory at KIST.

Extraction and Isolation. The whole plants (697.0 g) were air-dried in the dark and then extracted with a methanol to give methanol-soluble extract. The dried extract residue (97.0 g) was suspended in water and sequentially partitioned with methylene chloride, ethyl acetate, and *n*-butanol. The methylene chloride extract was evaporated under reduced pressure to yield 30.4 g of a residue. This residue was divided into 12 fractions (DA−DL) by column chromatography on silica gel using the following solvent mixtures: CH_2Cl_2−EtOAc (75:25 → 25:75), CH_2Cl_2−MeOH (90:10 → 25:75), and a MeOH wash. Fraction DG (3.7 g) was purified by column chromatography over silica gel by elution with CH_2Cl_2−MeOH (95:5) to give three subfractions (DG1−DG3). Subfraction DG2 (802.7 mg) was further purified by column chromatography over LiChroprep RP-18 (2.5 × 30 cm) using 30% CH_3CN as eluting solvent and finally purified by preparative HPLC eluted with hexane−MeOH−*i*-PrOH (70:17:13) to afford 640.1 mg of compound **1** and 84.2 mg of compound **2**.

Fraction DH (2.3 g) was purified by column chromatography over silica gel using CH_2Cl_2−MeOH (90:10) to give six subfractions (DH1−DH6). Subfraction DH3 (382.6 mg) was further purified by column chromatography over LiChroprep RP-18 (2.5 × 30 cm) using 30% CH_3CN for elution and finally purified by preparative HPLC as described above to give 5.0 mg of compound **3**.

The EtOAc-soluble layer (2.93 g) was chromatographed on silica gel using gradient mixtures of CH_2Cl_2−MeOH (95:5 → 50:50) to give seven fractions (EA−EG). Fraction EC (165.2 mg) was purified by column chromatography over silica gel with CH_2Cl_2−MeOH (90:10) to give three fractions (EC1−EC3). Fraction EC2 was further purified by HPLC using CH_3CN-H_2O (25:75) to give an additional amount of compound **3** (3 mg). Fraction EE (501.4 mg) was purified by column chromatography over silica gel with EtOAc−MeOH (90:10 → 25:75) to give six fractions (EE1−EE6). Fraction EE2 was purified by preparative TLC on silica gel (1 mm, 20 × 20 cm, Merck), developed with CH_2Cl_2−MeOH (80:20), to afford 15.9 mg of compound **4**.

Asperuloide A (1): colorless needles from MeOH−CH_2Cl_2 (9:1); $[\alpha]^{22}_D$ −19.5° (*c* 1.52, $CHCl_3$); UV λ_{max} (MeOH) 235 (log ϵ 3.93) nm; IR (KBr) ν_{max} 3422, 2957, 1718, 1646 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 2; HRFABMS *m/z* 571.2382 $[M + H]^+$ (calcd for $C_{27}H_{39}O_{13}$, 571.2391).

X-ray Structure Determination of 1.[8] Suitable colorless crystals of **1** were obtained by recrystallization from MeOH−CH_2Cl_2 (9:1). The X-ray data were collected on an Enraf-Nonius CAD4 automated diffractometer equipped with a Mo X-ray tube (λ = 0.71073 Å) and a graphite crystal monochromator. The crystal (0.2 × 0.1 × 0.05 mm) belongs to the monoclinic system, space group C_2, with a = 26.144(7) Å, b = 8.704(5) Å, c = 14.209(6) Å, V = 3131(2) Å^3, Z = 4, D_{calcd} = 1.342 g/cm^3. The orientation matrix and unit cell dimensions were determined from 25 machine-centered reflections in the 2θ range from 15° to 25°. The variation of intensities was monitored by a repeated check of intensities of three reflections every 1 h during the data collection period. A direct method (SHELXS-90)[9] was employed to find all the atoms. Subsequent cycles of Fourier map and least-squares refinement were followed (SHELXL-97).[9] Absolute configuration was determined by known conformation of the anomeric proton of β-D-glucose of the loganin moiety. All non-hydrogen atoms were refined anisotropically for **1**. Hydrogen atoms were included in the structure factor calculation using a riding model. All the calculations were carried out using VAX and PC computers. The refinement converged to a final R_1 = 0.083, wR_2 = 0.2238, where $R_1 = \sum||F_o| - |F_c||/\sum|F_o|$, $wR_2 = \{\sum w(F_o^2 - F_c^2)^2/\sum wF_o^4\}^{1/2}$, for 1860 observed reflections [$I > 2\sigma(I)$] and 397 variable parameters.

Asperuloide B (2): amorphous powder; $[\alpha]^{18}_D$ −40.6° (*c* 0.38, MeOH); UV λ_{max} (MeOH) 236 (log ϵ 4.02) nm; IR (KBr) ν_{max} 3414, 2956, 1726, 1634, 1440, 1288, 1076 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 2; HRFABMS *m/z* 571.2410 $[M + H]^+$ (calcd for $C_{27}H_{39}O_{13}$, 571.2391).

Asperuloide C (3): amorphous powder; $[\alpha]^{19}_D$ −53.2° (*c* 0.063, MeOH); UV λ_{max} (MeOH) 235 (log ϵ 3.88) nm; IR (KBr) ν_{max} 3422, 2956, 1718, 1634, 1440, 1288, 1076 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 2; HRFABMS *m/z* 603.2663 $[M + H]^+$ (calcd for $C_{28}H_{43}O_{14}$, 603.2653).

Alkaline Hydrolysis of Asperuloide A (1). To a solution of compound **1** (53.2 mg) in MeOH (3 mL) was added 1 N NaOH (2 mL), and the mixture was stirred at room temperature for 12 h. The reaction mixture was neutralized by addition of Amberlite IR-120 (H^+-form). After removing the resin by filtration, the filtrate was evaporated. The residue was dissolved in 2 mL of MeOH and treated with CH_2N_2. After the reaction was completed, the solvent was evaporated in

vacuo. The resulting mixture was purified by preparative TLC (precoated silica gel F_{254} plates (20 × 20 cm, 1 mm, Merck, art. 13895, CH_2Cl_2−MeOH, 85:15) to afford loganin (5.5 mg), identical to an authentic sample,[3] and compound **4** (32.9 mg) as an amorphous powder: $[\alpha]^{24}_D$ −49.0° (*c* 0.083, MeOH); IR (KBr) ν_{max} 3422, 2956, 1708, 1632, 1440, 1288, 1160, 1076 cm^{-1}; ^1H NMR (CD_3OD, 300 MHz) δ 1.02 (3H, d, J = 6.7 Hz, H-10″), 1.04 (3H, d, J = 5.5 Hz, H-10), 1.21 (1H, m, H-7″), 1.69 (1H, m, H-6), 1.76 (2H, m, H-6″), 2.01 (1H, m, H-7″), 2.05 (1H, m, H-9), 2.09 (1H, m, H-8), 2.26 (1H, ddd, J = 14.8, 8.0, 1.3 Hz, H-6), 2.36 (1H, m, H-8″), 2.65 (1H, dd, J = 9.1, 5.9 Hz, H-9″), 3.04 (1H, q, J = 7.7 Hz, H-5), 3.14 (1H, dd, J = 8.9, 7.9 Hz, H-2′), 3.23 (1H, m, H-5′), 3.24 (1H, m, H-3′), 3.30 (1H, m, H-5″), 3.33 (1H, m, H-4′), 3.58 (1H, dd, J = 11.9, 5.7 Hz, H-6′), 3.62 (3H, s, OMe), 3.83 (1H, dd, J = 11.8, 1.8 Hz, H-6′), 4.59 (1H, d, J = 7.8 Hz, H-1′), 5.11 (1H, dd, J = 4.3, 4.0 Hz, H-7), 5.25 (1H, d, J = 4.2 Hz, H-1), 5.54 (1H, s, H-3″), 6.14 (1H, s, H-3″), 7.36 (1H, d, J = 1.0 Hz, H-3); ^{13}C NMR (CD_3OD, 75 MHz) δ 14.1 (C-10), 21.8 (C-10″), 31.5 (C-6″), 32.8 (C-5), 35.0 (C-7″), 38.8 (C-8″), 40.6 (C-6), 41.4 (C-8), 45.2 (C-5″), 47.5 (C-9), 52.1 (OMe), 57.0 (C-9″), 63.1 (C-6′), 71.9 (C-4′), 75.1 (C-2′), 78.3 (C-3′), 78.7 (C-5′), 79.6 (C-7), 97.7 (C-1), 100.5 (C-1′), 113.6 (C-4″), 125.0 (C-3″),143.2 (C-4), 152.9 (C-3), 168.5 (C-11″), 169.8 (C-11), 178.6 (C-1″); HRFABMS *m*/*z* 571.2394 $[M + H]^+$ (calcd for $C_{27}H_{39}O_{13}$, 571.2391).

Acknowledgment. The authors are grateful to Eun Jung Bang for NMR at Korea Basic Science Institute (KSBI) and Dr. Kwan Mook Kim for measurements of X-ray crystallographic analysis at KIST. This work was supported by grants from the Ministry of Science and Technology, Korea (2N23260).

Supporting Information Available: Details of crystal data for compound **1**. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Corrigan, D.; Timoney, R. F.; Donnelly, D. M. X. *Phytochemistry* **1978**, *17*, 1131−1133.
(2) Damtoft, S.; Franzyk, H.; Jensen, S. R. *Phytochemistry* **1997**, *45*, 743−750.
(3) Müller, A. A.; Weigend, M. *Phytochemistry* **1998**, *49*, 131−135.
(4) Jesen, S. R.; Lyse-Petersen, S. E.; Nielsen, B. J. *Phytochemistry* **1979**, *18*, 273−277.
(5) Damtoft, S.; Jensen, S. R.; Nielsen, B. J. *Phytochemistry* **1981**, *20*, 2717−2732.
(6) (a) Chaudhuri, R. K.; Afifi-Yazar, F. Ü.; Sticher, O. *Tetrahedron* **1980**, *36*, 2317−2326. (b) Bonini, C.; Davini, E.; Iavarone, C.; Trogolo, C. *Phytochemistry* **1981**, *20*, 1587−1590.
(7) Skaltsounis, A. L.; Tillequin, F.; Koch, M.; Pusset, J.; Chauvière, G. *Planta Med*. **1989**, *55*, 191−192.
(8) Crystallographic data for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre (deposition number CCDC 185135). Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0)1223-336033 or e-mail: depodit@ccdc.cam.ac.uk).
(9) (a) Sheldrick, G. M. *SHELXS-90*: *A Program for Structure Determination*; University of Göttingen: Göttingen, Germany, 1997. (b) Sheldrick, G. M. *SHELXL-97*: *A Program for Structure Refinement*; University of Göttingen: Göttingen, Germany, 1997.

NP020017Q