Phenolic Glycosides from *Pyrola japonica*

Ju Sun KIM,[a] Sang Hee SHIM,[a] Yong Nan XU,[a] Sam Sik KANG,*[,a] Kun Ho SON,[b] Hyeun Wook CHANG,[c] Hyun Pyo KIM,[d] and KiHwan BAE[e]

[a] *Natural Products Research Institute and College of Pharmacy, Seoul National University; Seoul 110–460, Korea:* [b] *Department of Food and Nutrition, Andong National University; Andong 760–749, Korea:* [c] *College of Pharmacy, Yeungnam University; Gyongsan 712–749, Korea:* [d] *College of Pharmacy, Kangwon National University; Chuncheon 200–749, Korea: and* [e] *College of Pharmacy, Chungnam National University; Taejon 305–764, Korea.*

Received January 9, 2004; accepted February 20, 2004

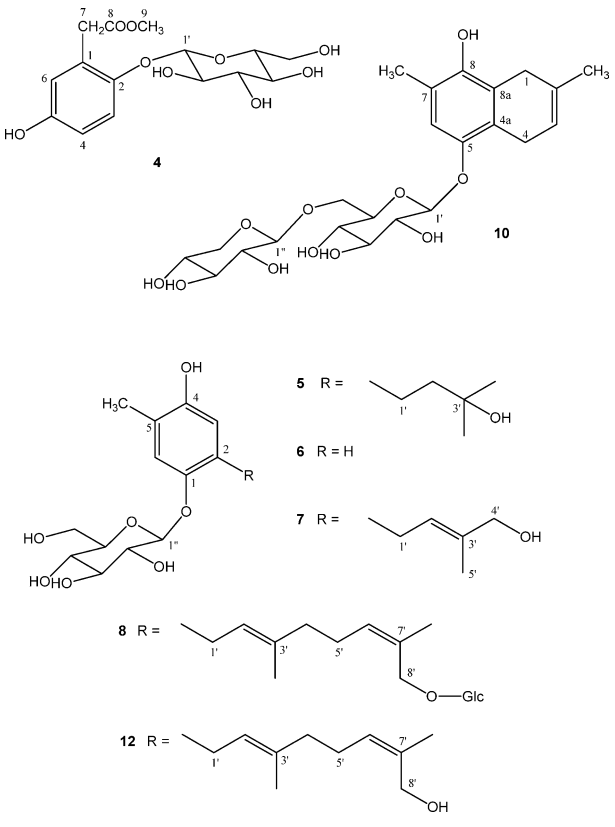
Five new phenolic glycosides, 2-β-D-glucopyranosyloxy-5-hydroxyphenylacetic acid methyl ester (4), 4-hydroxy-2-[3-hydroxy-3-methylbutyl]-5-methylphenyl β-D-glucopyranoside (5), 4-hydroxy-2-[(*E*)-4-hydroxy-3-methyl-2-butenyl]-5-methylphenyl β-D-glucopyranoside (7), 4-hydroxy-2-[(2*E*,6*Z*)-8-β-D-glucopyranosyloxy-3,7-dimethylocta-2,6-dien-1-yl]-5-methylphenyl β-D-glucopyranoside (8), and 2,7-dimethyl-1,4-dihydronaphthalene-5,8-diol 5-*O*-β-D-xylopyranosyl(1→6)-β-D-glucopyranoside (10), were isolated from the whole plants of *Pyrola japonica* (Pyrolaceae), together with androsin, (−)-syringaresinol glucoside, homoarbutin, pirolatin, hyperin, monotropein and chimaphilin.

Key words *Pyrola japonica*; Pyrolaceae; phenolic glycoside; structure elucidation

Pyrola japonica KLENZE (Pyrolaceae) is a herbaceous plant widespread in Korea, Japan and China.[1)] The leaves of this plant are utilized as a detoxicant for bites of snakes, insects, dogs, and as drugs to cure yellowish and bloody sputum.[2)] In Chinese traditional medicine, the whole plants of *P. japonica* or other *Pyrola* plants have been used as tonics, sedatives, analgesics against rheumatoid arthritis, and hemostatics.[1)] Earlier investigations of *Pyrola* plants led to the isolation of ursolic acid,[3)] an iridoid,[4)] quinones,[5,6)] flavonoids,[4,5,7)] tetralones[5)] and other phenolic glycosides.[4,8—12)] As part of our continuing search for anti-inflammatory agents from plants,[13—16)] a BuOH extract of the whole plant of *P. japonica* was subjected to a chemical investigation leading to the isolation of twelve compounds, among which five were new. The present paper deals with the isolation and identification of these compounds.

The BuOH fraction from the MeOH extract of the whole plant of *P. japonica* yielded 5 new compounds (**4**, **5**, **7**, **8**, **10**) upon column chromatographic separation, together with 7 known compounds, 5 phenolic glycosides, androsin (**2**),[17)] (−)-syringaresinol glucoside (**3**),[18)] homoarbutin (**6**),[4,10)] hyperin (**11**),[4,5,12)] pirolatin (**12**)[8,9)] together with an iridoid, monotropein (**1**)[4,7)] and a naphthoquinone, chimaphilin (**9**).[3,5,6,19)] TLC analysis of the acid hydrolysates of **4**, **5**, **7**, **8**, and **10** indicated the presence of glucose in **4**, **5**, **7**, and **8**, and glucose and xylose in **10**. The absolute configuration of the sugars was determined to be D by GC analysis of their thiazolidine derivatives.[20,21)]

Compound **4** was obtained as a whitish amorphous powder and had a protonated molecular ion peak at *m/z* 345.1188 in high-resolution (HR)-FAB-MS, in agreement with the molecular formula $C_{15}H_{20}O_9$. The absorption maxima at 223 and 288 nm in the UV spectrum, and 3464, 3372, 3293 cm^{-1} (OH) and 1508 cm^{-1} (aromatic ring) in the IR spectrum, indicated the presence of phenolic functionality. In addition, the IR spectral data of **4** suggested the presence of a carbonyl group (1715 cm^{-1}) and glycosidic C–O (1082, 1047 cm^{-1}). The ^{1}H-NMR spectrum exhibited three aromatic proton resonances at δ 6.63 (1H, br s), 6.65 (1H, dd, J=2.1, 7.2 Hz) and δ 7.06 (1H, d, J=7.2 Hz) which were indicative of a 1,2,4-trisubstituted phenyl ring. In addition, the ^{1}H-NMR spectrum showed signals assignable to a methyl ester group at δ 3.67, and two proton singlets at δ 3.69 (s), characteristic of the methylene unit of a phenylacetic acid substituent.[22,23)] The β-glucosyl protons were at δ 4.70 (d, J=7.5 Hz) for the anomeric proton, δ 3.86 (dd, J=2.1, 12.3 Hz) and 3.67 (dd, J=4.2, 12.3 Hz) for the C-6′ protons, appearing as a doublet of doublets, and between δ 3.3 to 3.4 as multiplets for the other sugar protons. They are closely related to the signals of phaseoloidin,[22,23)] except for the presence of an additional 3H singlet at δ 3.67, assignable to a methyl ester group in the former. This result was further supported by electron impact



∗ To whom correspondence should be addressed. e-mail: sskang@snu.ac.kr

(EI) mass spectrum. Although the molecular ion was not observed in the EI-MS of **4**, the fragmentation pattern of the aglycon part was identical to that of 2,5-dihydroxyphenylacetic acid methyl ester.[23] The placement of the methyl acetate, hydroxy and glucosyloxy groups at C-1, C-5 and C-2 was confirmed by analysis of the heteronuclear multiple-bond correlation (HMBC) spectrum. As shown in Table 2, both H-7 (δ_H 3.69) and H-9 (δ_H 3.67) showed HMBC correlations with the same C-8 (δ_C 174.6). Thus, the structure of **4** was determined to be 2-β-D-glucopyranosyloxy-5-hydroxyphenylacetic acid methyl ester.

Table 1. ^{13}C-NMR Data of **5**—**8** and **12** in CD_3OD (75.5 MHz)

Carbon No.	Chemical shifts (δ_C)				
	5	**6**	**7**	**8**	**12**
1	150.0	151.1	149.8	149.9	149.8
2	132.3	115.2	130.5	131.0	131.0
3	116.7	114.8	116.5	116.5	116.4
4	151.5	150.7	151.6	151.6	151.6
5	123.6	125.3	123.7	123.5	123.4
6	120.2	119.8	120.2	120.2	120.2
5-CH_3	16.1	15.2	16.1	16.1	16.1
C-1″	104.4	102.5	104.2	104.3 (102.4)[a]	104.3
C-2″	75.2	73.9	75.2	75.2 (75.1)	75.2
C-3″	78.0	76.9	78.0	78.0 (77.9)	78.0
C-4″	71.5	70.3	71.5	71.6 (71.6)	71.6
C-5″	78.1	76.9	78.3	78.3 (78.2)	78.3
C-6″	62.6	61.5	62.7	62.7 (62.7)	62.7
1′	25.7		28.7	28.8	28.7
2′	45.3		125.7	124.7	124.7[b]
3′	71.7		136.2	136.2	136.4
4′			68.9	41.0	41.1
5′			13.9	27.4	27.3
6′				131.2	128.6[b]
7′				132.6	135.7
8′				67.9	61.4
3′-CH_3	29.0			16.4	16.3
	29.4				
7′-CH_3				21.8	21.5

a) For C-8′ linked glucose moiety. *b*) Reassigned.

Compound **5** was obtained as a whitish amorphous powder with a molecular formula of $C_{18}H_{28}O_8$ based on (+)-HR-FAB-MS. The IR and UV spectra of **5** were closely similar to those of **4** for phenyl glycoside. The ^{1}H-NMR spectrum of **5** displayed a methyl singlet signal at δ 2.12, and two aromatic singlet signals for 1,2,4,5-tetrasubstituted phenyl moiety at δ 6.53 (H-3) and 6.92 (H-6). The β-glucosyl protons were at δ 4.68 (d, J=7.5 Hz) for the anomeric proton, 3.88 (dd, J=1.8, 12.0 Hz) and 3.69 (dd, J=5.4, 12.0 Hz) for the C-6″ protons, appearing as a doublet of doublets, and between δ 3.3 to 3.5 as multiplets for the other sugar protons. In addition, the signals at δ 1.225 (3H, s, 3′-CH_3), 1.229 (3H, s, 3′-CH_3), 1.69 (2H, m, H-2′) and 2.64 (2H, ddd, J=2.1, 7.4, 7.5 Hz, H-1′) indicated the presence of a 3-hydroxy-3-methylbutyl group.[20] In the HMBC spectrum of **5** (Table 2), a methyl proton at C-5 (δ_H 2.12, 3H, s) correlated with C-4 (δ_C 151.5), C-5 (δ_C 123.6) and C-6 (δ_C 120.2), while H-3 (δ_H 6.53), H-1′ (δ_H 2.64), H-6 (δ_H 6.92) and anomeric H (δ_H 4.68) showed HMBC correlations with C-1 (δ_C 150.0). Therefore, the structure of **5**, 4-hydroxy-2-[3-hydroxy-3-methylbutyl]-5-methylphenyl β-D-glucopyranoside, was established as shown.

Compound **7**, also identified as a phenyl glycoside, had a pseudomolecular ion $[M+Na]^+$ at m/z 393.1549 in a (+)-HR-FAB-MS compatible with a molecular formula of $C_{18}H_{26}O_8$. The gross features of its NMR spectra indicated a close structural relationship between **5** and **7**. The only difference in the ^{1}H-NMR spectrum between **5** and **7** was the presence of a 4-hydroxy-3-methyl-2-butenyl moiety[25] at δ 3.37 (2H, m, H-1′), 5.58 (1H, qt, J=1.2, 7.5 Hz, H-2′), 3.95 (2H, br s, H-4′), and 1.74 (3H, d, J=0.9 Hz, CH_3) in **7**, instead of a 3-hydroxy-3-methylbutyl group at C-2 in **5**. The cross peaks observed between the signals at δ 5.58 (H-2′) and 3.95 (H-4′), as well as between the signals at δ 3.37 (H-1′) and 1.74 (3′-CH_3) in the two dimensional nuclear Overhauser enhancement spectroscopy (NOESY) spectrum (Fig. 1), suggested an *E* configuration of the double bond of the 4-hydroxy-3-methyl-2-butenyl moiety.[25] Thus, the structure of **7** was determined to be 4-hydroxy-2-[(*E*)-4-hydroxy-3-

Table 2. Selected HMBC Correlations of Compounds **4**, **5**, **7**, **8**, and **10** in CD_3OD[a]

H	**4**	**5**	**7**[b]	**8**[b]	**10**
1					C-2, 3, 8, 4a, 8a, 2-CH_3
3	C-1, 2, 5	C-1, 4, 5, 1′			C-1, 4a
4	C-2, 5, 6				
6	C-1, 2, 4, 5, 7	C-1, 2, 4, 5-CH_3			C-5, 7, 8, 4a, 7-CH_3
7	C-1, 2, 6, 8				
2-CH_3					C-1, 2, 3
5-CH_3		C-4, 5, 6			
7-CH_3					C-6, 7, 8
9-CH_3	C-8				
1′	C-2	C-1, 2, 3, 2′	C-1, 2, 3, 2′, 3′	C-1, 3, 3′	C-5
2′		C-3′	C-1′, 4′, 5′	C-1′, 4′, 3′-CH_3	
4′		C-2′, 3′	C-2′, 3′, 5′	C-2′, 5′, 6′, 3′-CH_3	
5′		C-2′, 3′	C-2′, 3′, 4′	C-7′	
6′				7′-CH_3	C-4′, 1″
8′				C-6′, 1‴[c], 7′-CH_3	
3′-CH_3				C-2′, 3′, 4′	
7′-CH_3				C-6′, 7′, 8′	
1″		C-1	C-1	C-1	C-6′, 5′
1‴[c]				C-8′	

a) ^{1}H signal correlating with ^{13}C resonance indicated. *b*) HMBC correlations for the positions 1—6 and 5-CH_3 of **7** and **8** are the same as those of **5**. *c*) Glucose linked at C-8′ hydroxymethyl group.

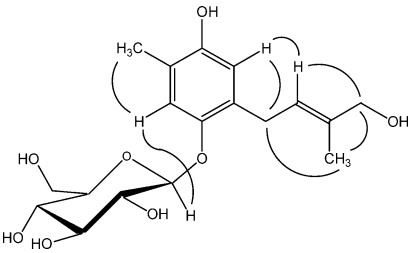


Fig. 1. Key Correlations of 4-Hydroxy-2-[(*E*)-4-hydroxy-3-methyl-2-butenyl]-5-methylphenyl *β*-D-Glucopyranoside (**7**) in NOESY Spectrum

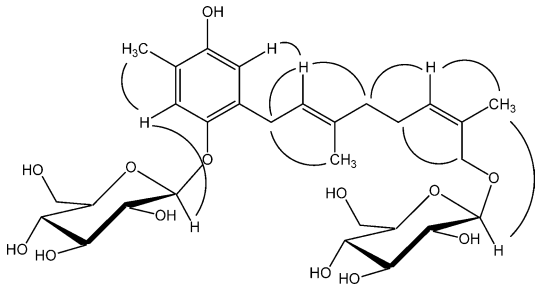


Fig. 2. Key Correlations of 4-Hydroxy-2-[(2*E*,6*Z*)-8-*β*-D-glucopyranosyl-oxy-3,7-dimethylocta-2,6-dien-1-yl]-5-methylphenyl *β*-D-Glucopyranoside (**8**) in NOESY Spectrum

methyl-2-butenyl]-5-methylphenyl *β*-D-glucopyranoside.

Compound **8** was obtained as a whitish amorphous powder and gave rise to a protonated molecular ion $[M+H]^+$ at *m/z* 601.2847 in (+)-HR-FAB-MS, compatible with a molecular formula of $C_{29}H_{44}O_{13}$. The only difference between NMRs of **8** and pirolatin (**12**)[9] was the presence of one mole of an additional glucose unit (δ_C 102.4, 75.1, 77.9, 71.6, 78.2, 62.7) in the former, and small variations in chemical shifts (C-8′: +6.5; C-7′: −3.1; C-6′: +2.6) due to a glycosidation shift.[26] Therefore, an additional glucose moiety was linked at the C-8′ position of the side-chain. In order to determine the definite linkage positions, a HMBC experiment was performed. In the HMBC spectrum of **8** (Table 2), an anomeric proton (H-1″) at δ 4.71 (d, J=7.8 Hz) correlated with C-1 (δ_C 149.9), while another anomeric proton (H-1‴) at δ 4.20 (d, J=7.8 Hz) showed HMBC correlation with the oxygenated methylene carbon (C-8′, δ_C 67.9). The NOESY experiment (Fig. 2) displayed nuclear Overhauser effect (NOE) interaction: H-2′ (δ_H 5.32)/H-4′ (δ_H 2.04), H-6′ (δ_H 5.39)/7′-CH_3 (δ_H 1.75), H-1′ (δ_H 3.33)/3′-CH_3 (δ_H 1.70), and H-5′ (δ_H 2.19)/H-8′ (δ_H 4.18; 4.33) indicated the presence of (2*E*,6*Z*)-8-hydroxy-3,7-dimethylocta-2,6-dien-1-yl moiety[9] for the side-chain. Moreover, there was also NOE interaction between H-2′ (δ_H 5.32) and H-3 (δ_H 6.53). Therefore, the structure of **8** was determined to be 4-hydroxy-2-[(2*E*,6*Z*)-8-*β*-D-glucopyranosyloxy-3,7-dimethylocta-2,6-dien-1-yl]-5-methylphenyl *β*-D-glucopyranoside.

Compound **10** showed $[M+Na]^+$ at *m/z* 507.1822 corresponding to the molecular formula $C_{23}H_{32}O_{11}$. The ^{13}C-NMR spectrum of **10** displayed signals for 23 carbons, 12 of which were assigned to the aglycon moiety; the remaining 11 must be due to one mol each of glucose and xylose units. The general NMR spectral feature of the aglycon moiety was similar to that of renifolin,[9] a characteristic glucoside of pyrolaceous plants. A comparison of the ^{13}C chemical shifts of **10** revealed that the compound differs not only with respect to the linkage position of the disaccharide moiety to the aglycon, but also the presence of additional ^{13}C signals for a set of xylose as the terminal sugar. In the HMBC spectrum (Table 2) of **10**, the anomeric proton at δ 4.30 (d, J=7.0 Hz) for the terminal xylose correlated with glucose C-6 (δ_C 68.9), while the other at δ 4.77 (d, J=7.5 Hz) for the inner glucose showed HMBC correlation with C-5 (δ_C 148.6) of aglycon. Therefore, the disaccharide moiety in **10** was linked at the C-5 hydroxyl group, instead of the glucose unit at the C-8 hydroxyl group, as in renifolin. From these data, **10** was concluded to be 2,7-dimethyl-1,4-dihydronaphthalene-5,8-diol 5-*O*-*β*-D-xylopyranosyl(1→6)-*β*-D-glucopyranoside.

Analyses of ^{1}H–^{1}H correlation spectroscopy (COSY), distortionless enhancement by polarization transfer (DEPT), heteronuclear multiple-quantum correlation (HMQC) and HMBC data, furnished the complete ^{1}H- and ^{13}C-NMR assignments for the known compounds. From these results, the ^{13}C-NMR data for homoarbutin (**6**) and its isomer, isohomoarbutin,[27] are reported for the first time, while the data published previously in the literature[9] require revision for pirolatin (**12**).

Experimental

General Experimental Procedures The optical rotations were determined on a JASCO P-1020 polarimeter. The IR spectra were obtained on a JASCO FT/IR-5300 spectrometer. The EI-MS was performed on a Hewlett Packard 5989B mass spectrometer. The FAB mass spectrum was obtained in a 3-nitrobenzyl alcohol matrix in positive ion mode on a JEOL-700 spectrometer. The NMR spectra were measured on a Varian Gemmi 2000 instrument (300 MHz) or a Bruker AM-500 (500 MHz), and the chemical shifts were referenced to TMS. GC analysis was performed as previously described[21] using a 5890 Series II$^+$ gas chromatograph. The TLC was performed on silica gel 60F_{254} (Merck).

Plant Material The whole plants of *P. japonica* were purchased at Kyungdong crude drug market in February, 2002. The botanical identification was made by one of the authors, Prof. K.-H. Bae. A voucher specimen (CNU 1584) was deposited in the Herbarium of the College of Pharmacy, Chungnam National University.

Extraction and Isolation The powdered whole plants (2 kg) of *P. japonica* were extracted five times, with MeOH under reflux, to give an extract (650 g). The MeOH extract was suspended in water and successively partitioned with *n*-hexane, dichloromethane, ethyl acetate and *n*-butanol to yield 34.3, 24.1, 117.9, 105.9 and 338 g fractions, respectively. A portion of the *n*-butanol fraction (100 g) was subjected to Sephadex LH-20 column chromatography with H_2O containing increasing amounts of MeOH (0, 30, 50, 70, 100%), as the eluent, to furnish fourteen fractions (B-01—B-14). Fraction B-03 was crystallized from MeOH to afford **1** (840 mg). Fractions B-02, B-03 and B-04 (14.3 g) underwent silica gel column chromatography [$CHCl_3$–MeOH–H_2O (13 : 7 : 2)] to yield fractions 5, 19 and 20 (B-02-01—05, B-03-01—19 and B-04-01—20), respectively. Fraction B-02-04 was crystallized from MeOH to afford **1** (350 mg). Fractions B-03-11 and 12 were further purified by crystallization from MeOH to yield **2** (46 mg). Fraction B-04-05 (40 mg) was further purified by silica gel column [EtOAc and then EtOAc saturated with water] to yield seven fractions (B-04-05-01—07). Fraction B-04-05-04 was crystallized from EtOAc saturated with H_2O to yield **2** (15 mg). Fractions B-04-04 and B-05-09 were combined (90 mg), then further purified on a silica gel column [EtOAc and then EtOAc saturated with H_2O] to yield **3** (3 mg). Fraction B-04-09 (0.42 g) was chromatographed over silica gel [EtOAc and then EtOAc saturated with water] to afford nine fractions (B-04-09-01—09). Fraction B-04-09-01 (40 mg) was further purified on a silica gel column [$CHCl_3$–MeOH–H_2O (7 : 1 : 0.5)] to yield eight fractions, among which fraction B-04-09-01-02 was crystallized from $CHCl_3$–MeOH–H_2O (7 : 1 : 0.5) to yield **4** (5 mg). Fraction B-04-09-02 (230 mg) was treated in the same way as B-04-09-01, yielding eight fractions (B-04-09-02-01—08). Fraction B-04-09-02-04 was applied to an RP_{18} column [50% MeOH] to afford ten fractions (B-04-09-02-04-01—10). Fraction B-04-09-02-04-07 was crystallized from MeOH to yield **5** (52 mg). Fraction B-04-09-02-04-05 was crystallized from $CHCl_3$–MeOH–H_2O

(7 : 1 : 0.5) to yield **4** (5 mg). Fraction B-04-11 (4.6 g) was further purified on a silica gel column [EtOAc, EtOAc saturated with H_2O, EtOAc saturated with H_2O–MeOH (3% and then 5%)] to give ten fractions (B-04-11-01—10). Fraction B-04-11-02 was crystallized from CH_2Cl_2–MeOH to yield **6** (107 mg). Fraction B-04-11-06 (0.9 g) was treated in the same way as B-04-09-01, yielding 16 fractions (B-04-11-01—16). Fraction B-04-11-06-13 was crystallized from MeOH to yield **7** (153 mg). Fraction B-04-13 (0.68 g) was further purified on a silica gel column [EtOAc, EtOAc saturated with H_2O, EtOAc saturated with H_2O–MeOH (1, 5, 10 and 50%)] to yield 13 fractions (B-04-13-01—13). Fraction B-04-13-09 was applied to an RP_{18} column [50% MeOH] to afford 8 fractions (B-04-13-09-01—08). Fraction B-04-13-09-06 was crystallized from MeOH to yield **8** (17 mg). Fraction B-06 (1.0 g) was applied to an RP_{18} column [70% MeOH] to afford 5 fractions (B-06-01—05). Fraction B-06-01 (0.3 g) was further purified on a silica gel column [$CHCl_3$–MeOH–H_2O (7 : 3 : 1)] to yield 20 fractions (B-06-01-01—20). Fraction B-06-01-13 (50 mg) was subjected to an RP_{18} column [50% MeOH] to yield 10 fractions (B-06-01-13-01—10). Fraction B-06-01-13-05 was crystallized from MeOH to yield **10** (17 mg). Fraction B-08 (4.4 g) underwent silica gel chromatography [EtOAc, EtOAc–H_2O (100 : 1), EtOAc saturated with H_2O, and then EtOAc saturated with H_2O–MeOH (1% and then 50%)] to afford 15 fractions (B-08-01—15). Fraction B-08-05 (560 mg) was separated by column chromatography [$CHCl_3$–MeOH–H_2O (7 : 1 : 0.5)] to afford **12** (82 mg). Fraction B-08-01 (80 mg) was applied to a silica gel column [hexane–$CHCl_3$ (1 : 1), $CHCl_3$, $CHCl_3$–MeOH (1% and then 5%)] to afford 12 fractions (B-08-01-01—12). Fractions B-08-01-03 and 04 were combined and crystallized from MeOH to give **9** (13 mg). Fraction B-12 was crystallized from MeOH to give **11** (17 mg). The seven known compounds, monotropein (**1**),[4,7] androsin (**2**),[17] (−)-syringaresinol monoglucoside (**3**),[18] homoarbutin (**6**),[4,10] chimaphilin (**9**),[5,6] hyperin (**11**),[4,5] and pirolatin (**12**)[8,9] were identified by comparison of their physical and spectral data with those previously reported.

Compound **4**: mp 180—182 °C. $[\alpha]_D^{31}$ −37.9° (c=0.3, MeOH). UV λ_{max} (MeOH) nm (log ε): 223 (3.78), 288 (3.40). IR (KBr) cm^{-1}: 3464, 3372, 3293 (OH), 1715 (C=O), 1508, 1460, 1441, 1356, 1318, 1235, 1082, 1047. ^{1}H-NMR (CD_3OD, 300 MHz) δ: see text. ^{13}C-NMR (CD_3OD, 75.5 MHz) δ: 174.6 (C-8), 153.9 (C-5), 150.4 (C-2), 127.1 (C-1), 119.1 (C-3), 118.3 (C-6), 115.8 (C-4), 104.4 (C-1′), 78.1 (C-5′), 78.0 (C-3′), 75.0 (C-2′), 71.4 (C-4′), 62.6 (C-6′), 52.5 (9-CH_3), 36.5 (C-7). EI-MS m/z (rel. int., %): [M^+ missing], 182 [M−162]$^+$ (68.6), 150 (100), 122 (54.5), 92 (16.5). HR-FAB-MS m/z: 345.1188 (Calcd for $C_{15}H_{20}O_9$+H: 345.1186).

Compound **5**: mp 100—105 °C. $[\alpha]_D^{31}$ −36.4° (c=0.1, MeOH). UV λ_{max} (MeOH) nm (log ε): 218 (4.12), 287 (3.73). IR (KBr) cm^{-1}: 3409 (OH), 1510, 1460, 1414, 1200, 1073, 1040. ^{1}H-NMR (CD_3OD, 300 MHz) δ: see text. ^{13}C-NMR (CD_3OD, 75.5 MHz) δ: Table 1. HR-FAB-MS m/z: 373.1862 (Calcd for $C_{18}H_{28}O_8$+H: 373.1862).

Compound **7**: mp 121—123 °C. $[\alpha]_D^{19}$ −27.2° (c=0.13, EtOH). UV λ_{max} (EtOH) nm (log ε): 288 (3.89). IR (KBr) cm^{-1}: 3389 (OH), 1514, 1460 (aromatic C=C), 1080 (glycosidic C–O). ^{1}H-NMR (500 MHz, CD_3OD) δ: 6.91 (1H, br s, H-6), 6.52 (1H, s, H-3), 5.58 (1H, qt, J=1.2, 7.5 Hz, H-2′), 4.72 (1H, d, J=7.8 Hz, H-1″), 3.95 (2H, br s, H-4′), 3.87 (1H, dd, J=1.8, 12.0 Hz, H-6″b), 3.69 (1H, dd, J=5.1, 12.0 Hz, H-6″a), 3.37 (2H, m, H-1′), 2.12 (3H, s, 5-CH_3), 1.74 (3H, d, J=0.9 Hz, H-5′). ^{13}C-NMR (CD_3OD, 75.5 MHz) δ: Table 1. HR-FAB-MS m/z: 393.1549 (Calcd for $C_{18}H_{26}O_8$+Na: 393.1525).

Compound **8**: mp 106—111 °C. $[\alpha]_D^{31}$ −29.4° (c=0.1, MeOH). UV λ_{max} (MeOH) nm (log ε): 287 (3.71). IR (KBr) cm^{-1}: 3393 (OH), 1638, 1508, 1412, 1197, 1074, 1040. ^{1}H-NMR (CD_3OD, 300 MHz) δ: 6.91 (1H, s, H-6), 6.53 (1H, s, H-3), 5.39 (1H, br t, J=7.5 Hz, H-6′), 5.32 (1H, dt, J=1.5, 7.5 Hz, H-2′), 4.71 (1H, d, J=7.8 Hz, H-1″), 4.33 (1H, d, J=11.7 Hz, H-8′b), 4.20 (1H, d, J=7.8 Hz, H-1‴), 4.18 (1H, d, J=11.7 Hz, H-8′a), 3.33 (2H, m, H-1′), 2.19 (2H, m, H-5′), 2.12 (3H, s, 5-CH_3), 2.04 (2H, m, H-4′), 1.75 (3H, d, J=1.2 Hz, 7′-CH_3), 1.70 (3H, br s, 3′-CH_3). ^{13}C-NMR (CD_3OD, 75.5 MHz) δ: Table 1. HR-FAB-MS m/z: 601.2847 (Calcd for $C_{29}H_{44}O_{13}$+H: 601.2860).

Compound **10**: mp 215—217 °C. $[\alpha]_D^{26}$ −33.9° (c=0.13, MeOH). UV λ_{max} (MeOH) nm (log ε): 283 (3.35). IR (KBr) cm^{-1}: 3410 (OH), 1638, 1483, 1460 (aromatic C=C), 1163, 1047 (glycosidic C–O). ^{1}H-NMR (500 MHz, CD_3OD) δ: 6.83 (1H, s, H-6), 5.59 (1H, m, H-3), 4.77 (1H, d, J=7.5 Hz, H-1′), 4.30 (1H, d, J=7.0 Hz, H-1″), 4.09 (1H, dd, J=2.5, 12.0 Hz, H-6′b), 3.86 (1H, dd, J=5.0, 11.5 Hz, H-5″b), 3.81 (1H, dd, J=6.0, 12.0 Hz, H-6′a), 3.34 (2H, overlap, H-4), 3.28 (1H, t, J=9.0 Hz, H-3′), 3.21 (1H, dd, J=7.5, 9.0 Hz, H-2″), 3.16 (2H, m, H-1), 3.15 (1H, dd, J=10.0, 11.5 Hz, H-5″a), 2.23 (3H, s, 7-CH_3), 1.82 (3H, d, J=1.0 Hz, 2-CH_3). ^{13}C-NMR (CD_3OD, 125.8 MHz) δ: 148.6 (C-5), 147.2 (C-8), 130.2 (C-2), 123.2 (C-8a), 122.9 (C-4a), 122.3 (C-7), 118.2 (C-3), 115.4 (C-6), 104.2 (C-1″), 102.6 (C-1′), 77.0 (C-3″), 76.4 (C-3′), 76.0 (C-5′), 73.9 (C-2′), 73.8 (C-2″), 70.4 (C-4″), 70.0 (C-4′), 68.9 (C-6′), 65.7 (C-5″), 29.3 (C-1), 25.2 (C-4), 22.4 (2-CH_3), 15.5 (7-CH_3). HR-FAB-MS m/z: 507.1822 (Calcd for $C_{23}H_{32}O_{11}$+Na: 507.1842).

Sugar Analysis A solution of each new compound (**4**, **5**, **7**, **8**, or **10**) (1 mg) in 2 N HCl–dioxane (1 : 1, 2 ml) was heated at 100 °C for 1 h. The reaction mixture was neutralized with Ag_2CO_3, filtered and then concentrated to dryness *in vacuo* to give a residue. The residue was treated with L-cysteine methyl ester hydrochloride (1 mg) in pyridine (0.2 ml) at 60 °C for 1 h. The solution was treated with *N*,*O*-bis(trimethylsilyl)trifluoroacetamide (0.05 ml) at 60 °C for 1 h. The supernatant was applied to GC as described previously.[21] D-Glucose from **4**, **5**, **7** and **8** and D-xylose and D-glucose from **10** were identified.

Acknowledgements This work was supported by the grant (PF0320302-00) from the Plant Diversity Research Center of the 21st century Frontier Research Program funded by the Ministry of Science and Technology of Korea.

References and Notes

1) Bae K.-H., "Medicinal Plants of Korea," Kyo-Hak Publishing Co., Ltd., Seoul, 2000.
2) Perry L. M., "Medicinal Plants of East and Southeast Asia: Attributed Properties and Uses," The MIT Press, Cambridge, 1980.
3) Kosuge T., Yokota M., Sugiyama K., Mure T., Yamazawa H., Yamamoto T., *Chem. Pharm. Bull.*, **33**, 5355—5357 (1985).
4) Bergeron C., Marston A., Antus S., Gauthier R., Hostettmann K., *Phytochemistry*, **49**, 233—236 (1998).
5) Kagawa K., Tokura K., Uchida K., Kakushi H., Shike T., Nakai H., *Chem. Pharm. Bull.*, **40**, 2083—2087 (1992).
6) Lee S.-M., An R.-B., Min B.-S., Na M.-K., Lee C.-H., Kang S.-J., Maeng H.-Y., Bae K.-H., *Arch. Pharm. Res.*, **24**, 522—523 (2001).
7) Inouye H., Arai T., *Chem. Pharm. Bull.*, **12**, 533—539 (1964).
8) Inouye H., Tokura K., Tobita S., *Chem. Ber.*, **101**, 4057—4065 (1968).
9) Inouye H., Inoue K., *Phytochemistry*, **24**, 1857—1859 (1985).
10) Thieme H., *Pharmazie*, **25**, 129 (1970).
11) Yazaki K., Shida S., Okuda T., *Phytochemistry*, **28**, 607—609 (1989).
12) Averett J. E., Bohm B. A., *Phytochemistry*, **25**, 1995—1996 (1986).
13) Moon T. C., Murakami M., Kudo I., Son K. H., Kim H. P., Kang S. S., Chang H. W. *Inflammation Res.*, **48**, 621—625 (1999).
14) Kang S. S., Kim J. S., Son K. H., Kim H. P., Chang H. W., *Chem. Pharm. Bull.*, **49**, 321—323 (2001).
15) Kwak W.-J., Han C. K., Son K. H., Chang H. W., Kang S. S., Park B. K., Kim H. P., *Planta Medica*, **68**, 316—321 (2002).
16) Kwak W.-J., Han C. K., Chang H. W., Kim H. P., Kang S. S., Son K. H., *Chem. Pharm. Bull.*, **51**, 333—335 (2003).
17) De Rosa S., De Giulio A., Tommonaro G., *Phytochemistry*, **42**, 1031—1034 (1996).
18) Chiba K., Yamazaki M., Umegaki E., Li M.-R., Xu Z.-W., Terada S., Taka M., Naoi N., Mohri T., *Biol. Pharm. Bull.*, **25**, 791—793 (2002).
19) Inouye H., *Yakugaku Zasshi*, **76**, 976—977 (1956).
20) Hara S., Okabe H., Mihashi K., *Chem. Pharm. Bull.*, **35**, 501—506 (1987).
21) Kang S. S., Kim J. S., Kim Y. H., Choi J. S., *J. Nat. Prod.*, **60**, 1060—1062 (1997).
22) Barua A. K., Chakrabarty M., Datta P. K., Ray S., *Phytochemistry*, **27**, 3259—3261 (1988).
23) Dai J., Kardono L. B. S., Tsauri S., Padmawinata K., Pezzuto J. M., Kinghorn A. D., *Phytochemistry*, **30**, 3749—3752 (1991).
24) Nomura T., Fukai T., Katayanagi M., *Chem. Pharm. Bull.*, **26**, 1453—1458 (1978).
25) Herath W., Ferreira D., Khan S. I., Khan I. A., *Chem. Pharm. Bull.*, **51**, 1237—1240 (2003).
26) Seo S., Tomita Y., Tori K., Yoshimura Y., *J. Am. Chem. Soc.*, **100**, 3331—3339 (1978).
27) Isohomoarbutin could be identified as a mixture of homoarbutin. ^{13}C-NMR data were determined as follows: δ_C 149.5, 129.4, 117.0, 152.3, 112.7, 117.5 (C-1—C-6), 15.5 (CH_3), 102.9, 73.9, 77.1, 70.3, 76.9, 61.5 (Glc C-1—C-6).