Flavonol glycosides from *Cardamine komarovii*

Seung Young Lee, Il Kyun Lee, and Kang Ro Lee

Abstract: Two new flavonol glycosides (**1** and **2**) were isolated from a MeOH extract of the aerial parts of *Cardamine komarovii* Nakai (Cruciferae) together with 13 known phenolic compounds (**3**–**15**). The structures of **1** and **2** were determined by spectroscopic methods including 1D and 2D NMR (COSY, HMQC, HMBC, NOESY, and TOCSY) and HR-FAB-MS data.

Key words: Cardamine komarovii, Cruciferae, flavonol glycosides.

Résumé : Les produits d'extractions des tiges de *Cardamine komarovii* Nakai, cruciféracée, par le méthanol ont permis d'isoler deux nouveaux glucosides (**1** et **2**) ainsi que 13 composés phénoliques connus (**3**–**15**). Les structures des **1** et **2** ont été déterminées par des méthodes spectroscopiques, dont la RMN 1D et 2D (« COSY », « HMQC », « HMBC », « NEOSY » et « TOSY ») et des données de spectrométrie de masse avec bombardement avec des atomes rapides et à haute résolution (SM-BAR-HR).

Mots-clés : Cardamine komarovii, cruciféracée, glucosides de flavonol.

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Introduction

Cardamine komarovii Nakai (Cruciferae) is widely distributed throughout Asia.[1] The aerial parts of this plant have been used for the treatment of respiratory diseases and hemostasis in Chinese folk medicine.[2] In Korea, this indigenous herb is an edible wild vegetable and is also used as a folk medicine for the control of blood pressure.[2] As part of our continuing search for biologically active compounds from Korean medicinal plants, we investigated the constituents of the aerial parts of *C. komarovii* and reported their cytotoxic constituents, including megastigmane,[3] and flavonoids.[4] In our ongoing search on this source, we have further isolated two new flavonol glycosides (**1** and **2**) together with 13 known phenolic compounds (**3**–**15**).

Results and discussion

The 80% MeOH extract of the aerial parts of *C. komarovii* was subjected to repeated column chromatography on silica gel to afford **1** and **2** together with **3**–**15** (Fig. 1). The identification and structural elucidation of **1** and **2** were based on 1D- and 2D-NMR and HR-FAB-MS data.

Cardamoside A (**1**) was isolated as a yellowish gum with a molecular formula of $C_{48}H_{57}O_{27}$ on the basis of the $[M + H]^+$ peak at *m/z* 1065.3086 (calcd for $C_{48}H_{57}O_{27}$, 1065.3087) in the HR-FAB-MS. The IR spectrum of **1** indicated the presence of a hydroxyl group (3356 cm^{-1}), a carbonyl group (1657 cm^{-1}), and an aromatic ring (1451 cm^{-1}). The ^1H NMR spectrum of **1** showed an aglycone characterized by two doublet signals at δ 7.99 (d, J = 8.8 Hz, H-2′, 6′) and 6.89 (d, J = 8.8 Hz, H-3′, 5′), which were assigned to two aromatic protons of the B ring, with two meta-coupled doublets at δ_H 6.78 (d, J = 2.0 Hz, H-8) and 6.47 (d, J = 2.0 Hz, H-6) for the A ring. In the ^{13}C NMR spectrum, 15 carbon signals of an aglycone appeared at δ 161.0 (C-4′), 131.6 (C-2′, 6′), 115.9 (C-3′, 5′), and 121.2 (C-1′) of the B ring, as well as other signals at δ 178.2 (C-4), 163.3 (C-7), 161.6 (C-5), 158.2 (C-9), 156.8 (C-2), 134.2 (C-3), 106.5 (C-10), 100.2 (C-6), and 95.4 (C-8) of the A and C rings (Table 1). These spectral data implied that **1** was a kaempferol derivative.[5] In addition, the four anomeric protons appeared at δ 5.38, 4.15, 5.27, and 4.43 in the ^1H NMR spectrum, which showed correlations with anomeric carbons at δ 101.7, 104.2, 100.3, and 101.3 in the ^{13}C NMR spectrum by the HMQC, respectively. The characteristic coupling constant of anomeric protons at δ 5.38 (d, J = 7.8 Hz), 5.27 (d, J = 7.8 Hz) and 4.15 (d, J = 7.8 Hz) implied three β-D-glucopyranoses (Glc I, Glc II, and Glc III), and another anomeric proton at δ 4.43 (s) identified α-L-rhamnopyranose (Rha). The glycosidic position was established by an HMBC experiment, in which the long-range correlations were observed between the H-1″ (δ 5.38) of Glc I and the C-3 (δ 134.2) of aglycone, H-1‴ (δ 4.15) of Glc II and the C-4" (δ 80.9) of Glc I, H-1‴′ (δ 4.43) of Rha and the C-6″ (δ 66.7) of Glc I, and H-1⁗ (δ 5.27) of Glc III and C-7 (δ 163.3) of aglycone (Fig. 1). The ^1H and ^{13}C NMR spectra of **1** also showed *trans-p*-coumaroyl unit signals[6] (δ 7.56 (d, J = 15.6 Hz, H-7⁗), 7.55 (d, J = 8.8 Hz, H-2⁗, 6⁗), 6.79 (d, J = 8.8 Hz, H-3⁗, 5⁗), and 6.43 (d, J = 15.6 Hz, H-8⁗); δ 166.8 (C-9⁗), 160.5 (C-4⁗), 145.2 (C-7⁗), 130.9 (C-2⁗, 6⁗), 125.9 (C-1⁗), and 116.5 (C-3⁗, 5⁗)). The *trans-p*-

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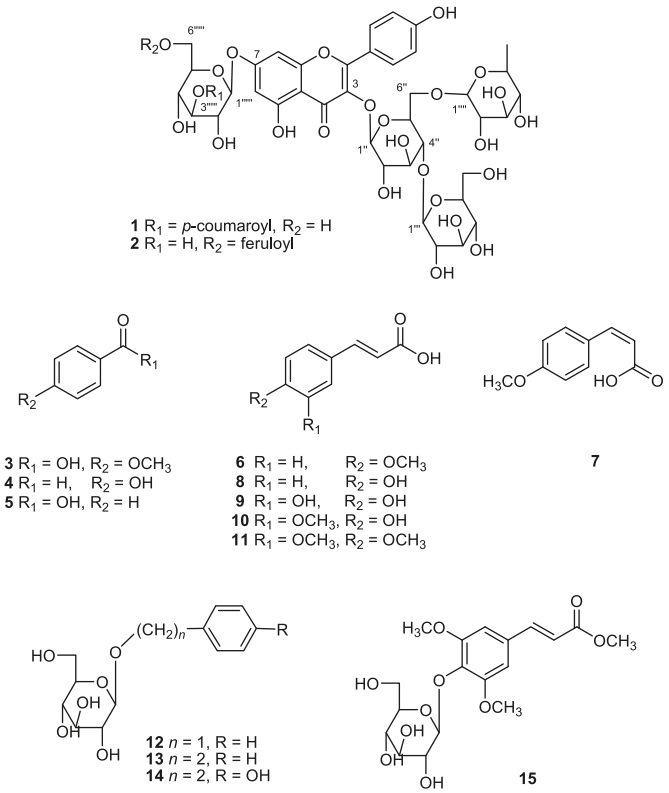
Fig. 1. Chemical structures of compounds **1**–**15**.



coumaroyl group linkage was confirmed by an HMBC experiment, in which a correlation was observed between the H-3′′′′′ (δ 5.03) of Glc III and the C-9′′′′′′ (δ 166.8) of the *trans*-*p*-coumaroyl group as shown in Fig. 2. The downfield shift of the signals at H-3′′′′′ (δ 5.03) and C-3′′′′′ (δ 77.9), as well as concomitant upfield shifts of the adjacent carbon signals at C-2′′′′′ (δ 71.9) and C-4′′′′′ (δ 68.2), suggested that the *trans*-*p*-coumaroyl group should be placed at C-3′′′′′ of **1**.[6] Alkaline hydrolysis of compound **1** afforded *trans*-*p*-coumaric acid,[6] together with kaempferol 3-*O*-β-D-glucopyranosyl-(1′′′→4′′)-[α-L-rhamnopyranosyl(1′′′′→6′′)]-β-D-glucopyranosyl-7-*O*-β-D-glucopyranoside (**1a**), which was confirmed by comparison of its ^{1}H NMR and FAB-MS data with literature values.[4] Acid hydrolysis of **1a** yielded kaempferol and sugar residues.[4] Kaempferol was confirmed by comparison of its ^{1}H NMR and FAB-MS data with literature values.[5] The sugar residues, D-glucopyranose and L-rhamnopyranose, were identified by co-TLC with authentic sugars ($CHCl_3$–MeOH–H_2O = 6:4:1; R_f value of D-glucopyranose, 0.31 and L-rhamnopyranose, 0.60) and by GC analysis of their corresponding trimethylsilylated L-cysteine adducts.[7] Thus, the structure of **1** was determined as kaempferol 3-*O*-β-D-glucopyranosyl-(1′′′→4′′)-[α-L-rhamnopyranosyl-(1′′′′→6")]-β-D-glucopyranosyl-7-*O*-(3′′′′-*O*-*trans*-coumaroyl)-β-D-glucopyranoside and it was named cardamoside A.

Cardamoside B (**2**) was isolated as a yellowish gum. Its molecular formula was determined as $C_{49}H_{58}NaO_{28}$ from the $[M + Na]^+$ peak at *m/z* 1117.3021 (calcd for $C_{49}H_{58}NaO_{28}$, 1117.3012) in the HR-FAB-MS spectrum. The IR, UV, and ^{1}H and ^{13}C NMR spectra of **2** were similar to those of **1**. The difference in NMR spectra was the acyl moiety, that is the *trans*-*p*-coumaroyl group in **1** was replaced with the *trans*-feruloyl group[8] (δ 7.50 (d, *J* = 15.9 Hz, H-7′′′′′′), 7.21 (d, *J* = 1.8 Hz, H-2′′′′′′), 7.01 (dd, *J* = 8.8, 1.8 Hz, H-6′′′′′′), 6.74 (d, *J* = 8.8 Hz, H-5′′′′′′), 6.40 (d, *J* = 15.9 Hz, H-8′′′′′′), 3.77 (s); δ 167.2, 150.1, 148.6, 145.9, 126.2, 123.9, 116.2, 114.8, 111.7, 56.3) in **2** (Table 1). The *trans*-feruloyl group linkage was confirmed by HMBC data, in which a correlation was observed between the H-6′′′′′ (δ 4.20, 4.45) of Glc III and the C-9′′′′′′ (δ 167.2) of the *trans*-feruloyl group as shown in Fig. 2. Moreover, the downfield shift of the signals at H-6′′′′′ (δ 4.20, 4.45) and C-6′′′′′′ (δ 63.8), as well as concomitant upfield shifts of the adjacent carbon signal at C-5′′′′′ (δ 73.9), suggested that the *trans*-feruloyl group should be placed at the C-6′′′′′ of **2**.[9] Alkaline hydrolysis of compound **2** afforded *trans*-ferulic acid[8] and kaempferol 3-*O*-β-D-glucopyranosyl-(1′′′→4′′)-[α-L-rhamnopyranosyl(1′′′′→6′′)]-β-D-glucopyranosyl-7-*O*-β-D-glucopyranoside (**2a**) (same as **1a**), which was confirmed by comparison of its ^{1}H NMR and FAB-MS data with literature values.[4] Acid hydrolysis of **2a** yielded kaempferol and a sugar residue. Kaempferol was confirmed by comparison of its ^{1}H NMR, and FAB-MS data with literature values, and D-glucopyranose and L-rhamnopyranose were identified by co-TLC with authentic sugars and by GC analysis of their corresponding trimethylsilylated L-cysteine adducts.[7] Thus, the structure of **2** was determined as kaempferol 3-*O*-β-D-glucopyranosyl-(1′′′→4′′)-[α-L-rhamnopyranosyl(1′′′′→6′′)]-β-D-glucopyranosyl-7-*O*-(6′′′′′-*O*-*trans*-feruloyl)-β-D-glucopyranoside and it was named cardamoside B.

Thirteen other known compounds obtained in this investigation were identified as *p*-anisic acid (**3**),[10] *p*-hydroxybenzaldehyde (**4**),[11] benzoic acid (**5**),[8] 4-methoxy-*trans*-cinnamic acid (**6**),[12] 4-methoxy-*cis*-cinnamic acid (**7**),[13] *p*-coumaric acid (**8**),[6] caffeic acid (**9**),[6] ferulic acid (**10**),[8] 3,4-dimethoxycinnamic acid (**11**),[14] benzyl glucopyranoside (**12**),[15] phenylethyl glucopyranoside (**13**),[15] *p*-hydroxy phenylethyl glucopyranoside (**14**),[15] and *p*-*trans*-sinaposyl glucopyranoside (**15**),[16] by comparing their spectroscopic data with those in the literature (Fig. 1). The known compounds **3**–**15** are reported from this plant source for the first time.

Experimental

General experimental procedures

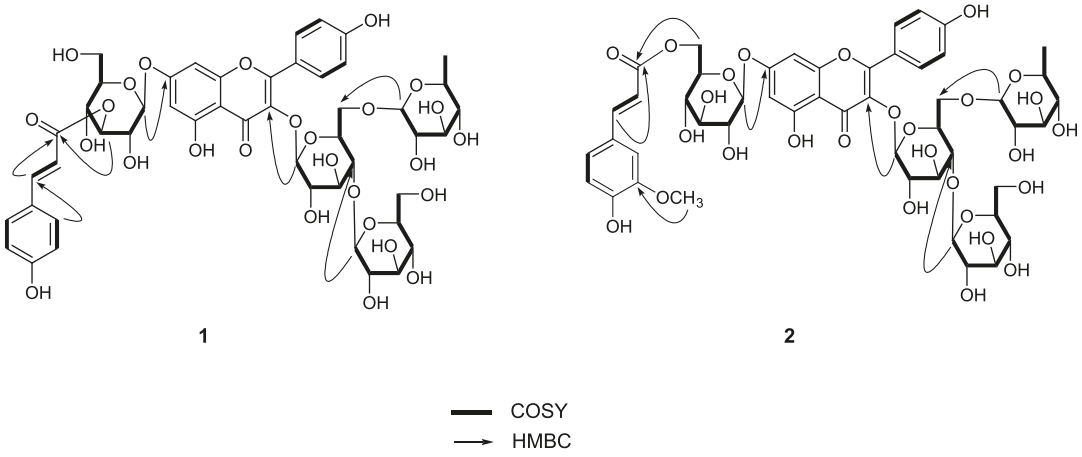
IR spectra were recorded on a Bruker IFS-66/S FT-IR spectrometer. FAB and HR-FAB mass spectra were obtained on a JEOL JMS700 mass spectrometer. NMR spectra, including ^{1}H–^{1}H COSY, HSQC, HMBC, NOESY, and TOCSY experiments, were recorded on a Varian Unity Inova 500 NMR spectrometer operating at 500 MHz (^{1}H) and 125 MHz (^{13}C), with chemical shifts given in ppm (δ). Preparative HPLC was conducted using a Gilson 306 pump with a Shodex refractive index detector. Chromatographic separation was performed on an Apollo Silica 5 μm column (250 × 10 mm i.d.) or an Optimapak ODS-A (250 × 10 mm i.d.). Gas chromatography was carried out using a ZB-1MS capillary column (30 cm × 0.25 mm × 0.25 μm, Zebron); column temperature, 230 °C; injection temperature, 250 °C; and carrier gas, He. Silica gel 60 (Merck, 70–230 mesh and 230–400 mesh) and RP-C_{18} silica gel (Merck, 230–400 mesh) were used for column chromatography. The packing material for molecular sieve column chromatography was Sephadex LH-20 (Pharmacia Co.). Merck precoated silica gel F_{254} plates and RP-18 F_{254s}

Table 1. ^{1}H and ^{13}C NMR spectral data of compounds **1** and **2** in DMSO-d_6.

	1		**2**	
Position	^{1}H (*J*)	^{13}C	^{1}H (*J*)	^{13}C
Flavonol				
2		156.8		156.6
3		134.2		134.1
4		178.2		178.2
5		161.6		161.8
6	6.47 d (2.0 Hz)	100.2	6.51 d (2.0 Hz)	99.7
7		163.3		163.4
8	6.78 d (2.0 Hz)	95.4	6.71 d (2.0 Hz)	95.7
9		158.2		158.4
10		106.5		106.4
1′		121.2		121.3
2′	7.99 d (8.8 Hz)	131.6	7.97 d (8.8 Hz)	131.6
3′	6.89 d (8.8 Hz)	115.9	6.86 d (8.8 Hz)	115.9
4′		161.0		161.0
5′	6.89 d (8.8 Hz)	115.9	6.86 d (8.8 Hz)	115.9
6′	7.99 d (8.8 Hz)	131.6	7.97 d (8.8 Hz)	131.6
Glc I				
1″	5.38 d (7.8 Hz)	101.7	5.38 d (7.8 Hz)	101.7
2″	3.24 m	74.6	3.21 m	74.5
3″	3.39 m	75.3	3.38 m	75.3
4″	3.34 m	80.9	3.34 m	80.9
5″	3.42 m	74.5	3.44 m	74.5
6″	3.77, 3.48 m	66.7	3.74, 3.45 m	66.7
Glc II				
1‴	4.15 d (7.8 Hz)	104.2	4.14 d (7.9 Hz)	104.2
2‴	2.96 m	73.9	2.95 m	73.8
3‴	3.12 m	77.1	3.12 m	77.2
4‴	3.06 m	70.7	3.06 m	70.7
5‴	3.17 m	77.5	3.17 m	77.5
6‴	3.70, 3.42 m	61.8	3.69, 3.41 m	61.8
Rha				
1⁗	4.43 s	101.3	4.40 s	101.3
2⁗	3.44 m	71.1	3.45 m	71.1
3⁗	3.32 m	71.4	3.30 m	71.4
4⁗	3.09 m	72.5	3.06 m	72.5
5⁗	3.38 m	68.9	3.24 m	68.9
6⁗	0.94 d (5.9 Hz)	18.4	0.91 d (6.1 Hz)	18.4
Glc III				
1′′′′′	5.27 d (7.8 Hz)	100.3	5.12 d (7.5 Hz)	100.1
2′′′′′	3.49 m	71.9	3.25 m	73.5
3′′′′′	5.03 d (9.0 Hz)	77.9	3.23m	77.3
4′′′′′	3,45 m	68.2	3,19 m	70.1
5′′′′′	3.59 m	77.6	3.70 m	73.9
6′′′′′	3.70, 3.52 m	61.0	4.20, 4.45 m	63.8
Acyl				
1′′′′′′		125.9		126.2
2′′′′′′	7.55 d (8.8 Hz)	130.9	7.21 d (1.8 Hz)	111.7
3′′′′′′	6.79 d (8.8 Hz)	116.5		148.6
4′′′′′′		160.5		150.1
5′′′′′′	6.79 d (8.8 Hz)	116.5	6.74 d (8.8 Hz)	116.2
6′′′′′′	7.55 d (8.8 Hz)	130.9	7.01 dd (8.8, 1.8 Hz)	123.9
7′′′′′′	7.56 d (15.6 Hz)	145.2	7.50 d (15.9 Hz)	145.9
8′′′′′′	6.43 d (15.6 Hz)	115.5	6.40 d (15.9 Hz)	114.8
9′′′′′′		166.8		167.2
OCH_3			3.77 s	56.3

Note: NMR data were obtained at 500 MHz for ^{1}H and 125 MHz for ^{13}C.

Fig. 2. Key ^{1}H–^{1}H COSY and HMBC correlations of **1** and **2**.



plates were used for TLC. Spots were detected on TLC under UV light or by heating after spraying with 10% H_2SO_4 in C_2H_5OH (*v*/*v*).

Plant material

The aerial parts of *C. komarovii* were collected at Goseung-gun in Gangwon-Do province, Korea, in August 2008, and the plants were identified by one of the authors (K.R.L.). A voucher specimen (SKKU 2008-11) has been deposited in the herbarium of the School of Pharmacy, Sungkyunkwan University, Suwon, Korea.

Extraction and Isolation

The aerial parts of *C. komarovii* (1.7 kg) were extracted using 80% aqueous MeOH at room temperature. The solvent was evaporated under reduced pressure to give a crude extract (120 g). The crude extract was dissolved in distilled water (800 mL) and successively extracted with *n*-hexane, $CHCl_3$, EtOAc, and *n*-BuOH to provide *n*-hexane (12 g), $CHCl_3$ (13 g), EtOAc (3 g), and *n*-BuOH (26 g) extracts. The $CHCl_3$-soluble fraction (13 g) was subjected to normal-phase column chromatography (CC) over a silica gel using $CHCl_3$/MeOH of increasing polarity (40:1 to 1:1) to give seven fractions (C1–C7). Fraction C3 (1.0 g) was isolated by Sephadex LH-20 chromatography (80% MeOH) and was purified with a silica gel preparatory HPLC with a solvent system of *n*-hexane/EtOAc (15:1) to yield **3** (5 mg). Fraction C3 (2.0 g) was isolated by Sephadex LH-20 chromatography (80% MeOH) and was subjected to reversed-phase CC over a RP-C_{18} silica gel using MeOH/H_2O (9:1) to provide four subfractions (C31–C34). Subfraction C32 (70 mg) was separated by preparative normal-phase HPLC using a solvent system of $CHCl_3$/MeOH (20:1) to obtain **4** (5 mg), **5** (4 mg), **6** (6 mg), and **7** (5 mg). Fraction C4 (2.5 g) was isolated by Sephadex LH-20 chromatography (80% MeOH) and was purified with a RP-C_{18} HPLC with a solvent system of MeOH/H_2O (1:1) to yield **8** (4 mg), **9** (4 mg), **10** (4 mg), and **11** (7 mg). The *n*-BuOH soluble fraction (26 g) was subjected to CC over HP-20 resin using 100% H_2O and 100% MeOH to give two fractions (B1 – 100% H_2O and B2 – 100% MeOH). Fraction B2 (9.7 g) was subjected to normal-phase CC over a silica gel using $CHCl_3$/MeOH/H_2O (10:4:0.5) to give 14 fractions (B21–B214). Fraction B22 (120 mg) was purified by preparative RP-C_{18} HPLC using a solvent system of MeOH/H_2O (2:3) to afford **15** (5 mg). Fraction B22 (500 mg) was isolated by Sephadex LH-20 chromatography (90% MeOH) and was purified over a silica gel CC using MeCN/H_2O (1:4) to yield **12** (3 mg), **13** (9 mg), and **14** (11 mg). Fraction B212 (500 mg) was isolated by Sephadex LH-20 chromatography (70% MeOH) and was purified over a silica gel CC using MeOH/H_2O (1:4) to yield **1** (13 mg), and **2** (15 mg).

Cardamoside A (1)

Yellowish gum. UV (MeOH) λ_{max} (log ε): 317 (4.1), 267 (3.8). IR (KBr, cm^{-1}) ν_{max}: 3356, 2941, 2832, 1657, 1602, 1451, 1167, 1032, 802, 670. ^{1}H NMR (DMSO-d_6, 500 MHz) and ^{13}C NMR (DMSO-d_6, 125 MHz): see Table 1. HR-FAB-MS *m*/*z*: 1065.3086 $[M + H]^+$ (calcd for $C_{48}H_{57}O_{27}$, 1065.3087).

Cardamoside B (2)

Yellowish gum. UV (MeOH) λ_{max} (log ε): 323 (4.0), 267 (3.9). IR (KBr, cm^{-1}) ν_{max}: 3355, 2947, 2832, 1452, 1032, 797, 670. ^{1}H NMR (DMSO-d_6, 500 MHz) and ^{13}C NMR (DMSO-d_6, 125 MHz): see Table 1. HR-FAB-MS *m*/*z*: 1117.3021 $[M + Na]^+$ (calcd for $C_{49}H_{58}NaO_{28}$, 1117.3012).

Alkaline hydrolysis of 1 and 2

Compounds **1** (10 mg) in 0.05 mol/L KOH (2 mL) was stirred at room temperature for 2 h. The hydrolysate was extracted with $CHCl_3$, and the $CHCl_3$ extract was evaporated in vacuo. The $CHCl_3$ extract was purified using HPLC (Optimapak ODS-A, 250 × 10 mm; mobile phase, 40% MeOH; detector, RI; and flow rate, 2.0 mL/min) to yield *trans-p*-coumaric acid (1.2 mg) and **1a** (7 mg). Compound **2** (10 mg) was treated using the same method to give **2a** (=**1a**) (6.5 mg) and *trans*-ferulic acid (1.3 mg).

1a (**2a**): yellowish gum. ^{1}H NMR (DMSO-d_6, 500 MHz) δ: 7.95 (d, J = 8.8 Hz, H-2′,6′), 6.87 (d, J = 8.8 Hz, H-3′,5′), 6.73 (d, J = 2.0 Hz, H-8), 6.44 (d, J = 2.0 Hz, H-6), 5.37 (d, J = 7.8 Hz, Glc I), 5.06 (d, J = 7.8 Hz, Glc III), 4.43 (s, Rha), 4.16 (d, J = 7.8 Hz, Glc II). FAB-MS *m*/*z*: 917 $[M - H]^-$.

Acid hydrolysis of 1a and 2a

Compounds **1a** (=**2a)** (5 mg) was heated in an ampoule with 1 mL of aq. 1.5 mol/L HCl at 80 °C for 2 h. After cooling, the reaction mixture was extracted with EtOAc. The EtOAc solvent was evaporated in vacuo, and the residue was purified by HPLC (Optimapak ODS-A, 250 × 10 mm; mobile phase, 50% MeOH; detector, RI; and flow rate, 2.0 mL/min) to yield kaempferol (1.5 mg). The structure was identified by ^{1}H NMR and MS spectral analysis.

Determination of the sugars of compounds 1 and 2

The sugar residues (each ~2.0 mg) obtained from the hydrolysis of **1** and **2** were dissolved in anhydrous pyridine (0.1 mL) and L-cysteine methyl ester hydrochloride (2 mg) was subsequently added. The mixture was stirred at 60 °C for 1.5 h. After the reaction mixture was dried in vacuo, the residue was trimethylsilylated with 1-trimethylsilylimidazole (0.1 mL) for 2 h. The mixture was partitioned between *n*-hexane and H_20 (0.3 mL each), and the organic layer (1 μL) was analyzed by GC–MS. Identification of D-glucopyranose, and L-rhamnopyranose for **1** and **2** were detected in each case by co-injection of the hydrolysate with standard silylated samples, giving single peaks at D-glucopyranose (10.11 min) and L-rhamnopyranose (5.54 min) for **1**, and at D-glucopyranose (10.19 min) and L-rhamnopyranose (5.49 min) for **2**. Retention times of authentic samples treated in the same way with 1-trimethylsilylimidazole in pyridine, were D-glucopyranose (10.14 min) and L-rhamnopyranose (5.51 min).

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References

(1) Lee T. B.; *Coloured Flora of Korea;* Hyang-Moon publishing Co.: Korea, 2003; p 433.
(2) Ahan, D. K.; *Illustrated Book of Korean Medicinal Herbs;* Koy-Hak Publishing Co.: Korea, 1998; p 400.
(3) Lee, I. K.; Kim, K. H.; Lee, S. Y.; Choi, S. U.; Lee, K. R. *Chem. Pharm. Bull. (Tokyo)* **2011**, *59* (6), 773. doi:10.1248/cpb.59.773.
(4) Lee, I. K.; Jeong, E.-K.; Choi, S. U.; Hong, J. K.; Lee, K. R. *Heterocycles* **2011**, *83* (11), 2615. doi:10.3987/COM-11-12330.
(5) Budzianowski, J. *Phytochemistry* **1991**, *30* (5), 1679. doi:10.1016/0031-9422(91)84233-I.
(6) Liu, H.; Orjala, J.; Sticher, O.; Rali, T. *J. Nat. Prod.* **1999**, *62* (1), 70. doi:10.1021/np980179f.
(7) Jiang, W.; Li, W.; Han, L.; Liu, L.; Zhang, Q.; Zhang, S.; Nikaido, T.; Koike, K. *J. Nat. Prod.* **2006**, *69* (11), 1577. doi:10.1021/np060195+.
(8) Young, H. S.; Kim, M. S.; Park, H. J.; Chung, H. Y.; Choi, J. S. *Arch. Pharm. Res.* **1992**, *15* (4), 322. doi:10.1007/BF02974106.
(9) Weckerle, B.; Michel, K.; Balazs, B.; Schreier, P.; Toth, G. *Phytochemistry* **2001**, *57* (4), 547. doi:10.1016/S0031-9422(01)00059-0.
(10) Sy, L. K.; Brown, G. D. *J. Nat. Prod.* **1998**, *61* (8), 987. doi:10.1021/np9800553.
(11) Bouaicha, N.; Amade, P.; Puel, D.; Roussakis, C. *J. Nat. Prod.* **1994**, *57* (10), 1455. doi:10.1021/np50112a019.
(12) Rahman, M. A. A.; Moon, S. S. *Arch. Pharm. Res.* **2007**, *30* (11), 1374. doi:10.1007/BF02977359.
(13) Lu, W.; Yamaoka, Y.; Taniguchi, Y.; Kitamura, T.; Takaki, K.; Fujiwara, Y. J. *Organomet. Chem.* **1999**, *580* (2), 290. doi:10.1016/S0022-328X(98)01160-7.
(14) Jung, W. Y.; Ma, E. S. *Yakhak Hoechi* **2003**, *47*, 1.
(15) Schwab, W.; Schreier, P. *Phytochemistry* **1988**, *27* (6), 1813. doi:10.1016/0031-9422(88)80450-3.
(16) Park, S. Y.; Kim, J. S.; Lee, S. Y.; Bae, K. H.; Kang, S. S. *Nat. Prod. Sci.* **2008**, *14*, 281.