Four New Glycosides from Albizziae Cortex. III[1)]

Hiroyuki HIGUCHI, Katsura FUKUI, Junei KINJO and Toshihiro NOHARA*

Faculty of Pharmaceutical Sciences, Kumamoto University, 5–1 Oe-honmachi, Kumamoto 862, Japan. *Received August 10, 1991*

Four new glycosides, together with icariside E_5 (5), were isolated from Albizziae Cortex, the dried stem bark of *Albizzia julibrissin* DURAZZ. These were determined to be 3,4,5-trimethoxyphenol 1-*O*-*β*-D-apiofuranosyl-(1→2)-*β*-D-glucopyranoside (1), vomifoliol 3′-*O*-*β*-D-apiofuranosyl-(1→6)-*β*-D-glucopyranoside (4), (+)-lyoniresinol 9′-*O*-*β*-D-glucopyranosyl-(1→4)-*β*-D-glucopyranoside (2), (+)-lyoniresinol 4, 9′-di-*O*-*β*-D-glucopyranoside (3) by spectroscopic and chemical methods.

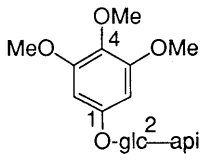
Keywords Albizziae Cortex; *Albizzia julibrissin*; Leguminosae; lignan; glycoside; lyoniresinol; vomifoliol; 3,4,5-trimethoxyphenol; icariside E_5

The dried stem bark of *Albizzia julibrissin* DURAZZ, Albizziae Cortex, is used as a tonic in China and Japan. Previous investigations reported the isolation of quercetin-3-*O*-galactoside, quercetin-3-*O*-rhamnoside,[2)] 3′,4′,7-trihydroxy flavone and α-spinasterol glucoside[3)] and some sapogenols.[4)] In the course of our studies on the constituents in leguminous plants,[1)] we had reported the isolation of 10 new aromatic glycosides, including the first examples of lignan tri- and tetra-glycosides, and syringaresinol diglucoside which appears to be responsible for the pharmacological effect as a tonic.[5)] In addition, *β*-D-apiofuranosyl-(1→2)-*β*-D-glucopyranosides of syringaresinol, 5,5′-dimethoxy-7-oxolariciresinol, glaberide I and syringic acid, which are key metabolites in a biodegradation pathway of syringaresinol, were also reported.[6)]

Now we have further obtained four new glycosides (**1**—**4**) together with a known glycoside, icariside E_5 (**5**). This paper describes the structural elucidation and identification of these compounds.

Compound **1** was obtained as a white amorphous powder, $[\alpha]_D$ −89.5° (MeOH). In the negative fast atom bombardment-mass spectrum (FAB-MS), **1** showed an $[M-H]^-$ ion at *m/z* 477. Upon acidic hydrolysis of **1**, apiose and glucose were identified by thin layer chromatography (TLC). In the ^{13}C-nuclear magnetic resonance (^{13}C-NMR) spectrum (Table I) of **1**, although the glycosidic signals were in good agreement with those of syringic acid methyl ester 4-*O*-*β*-D-apiofuranosyl-(1→2)-*β*-D-glucopyranosides, the signals due to aglycone were consistent with those of 3,4,5-trimethoxyphenol glycoside.[7)] Therefore, **1** was determined to be 3,4,5-trimethoxyphenol 1-*O*-*β*-D-apiofuranosyl-(1→2)-*β*-D-glucopyranoside.

Compounds **2**, $[\alpha]_D$ +0.4° (MeOH), and **3**, $[\alpha]_D$ −21.2° (MeOH) showed the same $[M-H]^-$ peak at *m/z* 743 in the negative FAB-MS. In the proton nuclear magnetic resonance (^{1}H-NMR) spectrum of **2**, two phenol-proton



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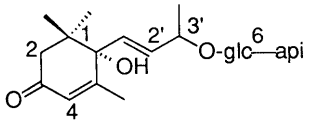

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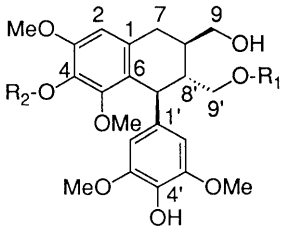

	R_1	R_2
2	4 -glc—glc	-H
3	-glc	-glc

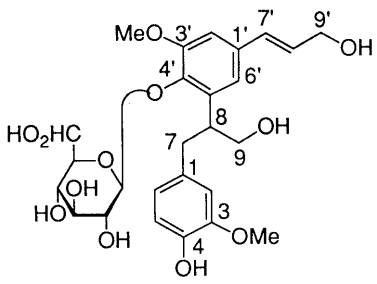

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TABLE I. ^{13}C-NMR Spectral Data for Compounds **1**—**5** (*δ*: ppm, in DMSO-d_6)

	1	2	3	4	5
C-1	153.9	128.3	134.3	41.0	132.2
C-2	94.3	106.6	108.1	49.4	113.2
C-3	153.0	146.4	150.9	197.9	148.3
C-4	132.4	137.7	136.8	125.0	146.1
C-5	153.0	146.8	151.4	164.2	116.0
C-6	94.3	124.7	125.4	78.0	122.2
C-7		32.3	32.3	24.1 (C-1-Me)	39.1
C-8		39.0	39.2	23.1 (C-1-Me)	42.2
C-9		63.9	64.0	19.1 (C-5-Me)	66.6
C-1′		132.2	133.4	130.5	135.0
C-2′		105.8	105.7	133.0	108.5
C-3′		147.4	147.6	74.0	152.9
C-4′		137.2	137.4	20.7 (C-3′-Me)	145.0
C-5′		147.4	147.6		139.6
C-6′		105.8	105.7		118.5
C-7′		40.5	40.5		130.9
C-8′		44.3	43.6		129.6
C-9′		69.8	70.1		62.9
OMe	55.5 (C-3, 5)	55.6 (C-3)	56.3 (C-3)		55.9
	60.0 (C-4)	58.8 (C-5)	60.3 (C-5)		55.7
		56.0 (C-3′, 5′)	56.1 (C-3′, 5′)		
Glc-1	99.7	103.1	103.1	100.6	105.6
Glc-2	77.2	73.2	74.3	73.7	76.2
Glc-3	75.4	74.7	76.8	76.7	78.4
Glc-4	70.3	80.5	70.1	70.0	71.0
Glc-5	77.0	75.2	77.3	75.9	78.2
Glc-6	60.7	60.4	61.2	67.5	62.3
Api-1	108.4			109.3	
Api-2	76.0			75.5	
Api-3	79.2			78.9	
Api-4	73.9			73.3	
Api-5	64.5			63.3	
Glc′ C-1		103.1	103.1		
Glc′ C-2		73.1	73.5		
Glc′ C-3		76.3	76.5		
Glc′ C-4		69.9	70.0		
Glc′ C-5		76.7	77.0		
Glc′ C-6		60.9	60.9		

signals were observed, whereas only one phenol-proton was present in **3**. Both were hydrolyzed enzymatically to yield the same aglycones (**2a**), $[\alpha]_D$ +38° (MeOH) and **3a**, $[\alpha]_D$ +39° (MeOH), respectively. They were identified as (+)-lyoniresinol[8] based on electron impact (EI)-MS (*m/z* 420) and ^{1}H-NMR spectra. In the ^{13}C-NMR spectrum (Table I), the signals of **2** were in accord with those of lyoniresinol 9′-*β*-D-glucopyranoside[7] except for a downfield shift at C-4 and upfield shifts at C-3 and 5 of the glucose moiety, along with the occurrence of an additional glucosyl unit. Therefore, the structure of **2** was established as (+)-lyoniresinol 9′-*O*-*β*-D-glucopyranosyl-(1→4)-*β*-D-glucopyranoside. On the other hand, **3** showed signals assignable to two terminal *β*-D-glucopyranosyl units in the ^{13}C-NMR spectrum. Since the signals due to C-3 and -5 in the aglycone moiety appeared in the downfield in contrast with those of **2**, the structure of **3** was concluded to be (+)-lyoniresinol 4,9′-bis-*O*-*β*-D-glucopyranoside. Thus, **2** and **3** are new glycosides of (+)-lyoniresinol.

Compound **4**, $[\alpha]_D$ +15° (MeOH), showed an $[M-H]^-$ peak at *m/z* 517 in negative FAB-MS. In the infrared (IR) spectrum, **4** showed the absorptions due to hydroxy (3440 cm^{-1}) and carbonyl (1650 cm^{-1}) groups. In the ^{13}C-NMR spectrum of **4** (Table I), the signals in the aglycone and sugar units were in good agreement with those of vomifoliol 3′-*β*-D-glucopyranoside,[9] except for a downfield shift at C-6 and an upfield shift at C-5 of the glucose moiety, together with the appearance of one additional pentosyl unit. The signals due to the pentosyl unit were identical to those of the *β*-D-apiofuranosyl moiety. Since **4** provided the aglycone (**4a**) identified as vomifoliol upon enzymatic hydrolysis,[9] the structure of **4** was elucidated as vomifoliol 3′-*O*-*β*-D-apiofuranosyl-(1→6)-*β*-D-glucopyranoside.

Compound **5** was identified with icariside E$_5$.[10]

Experimental

The instruments and reagents used in this study were the same as described in the previous paper.[6]

Extraction and Isolation Albizziae Cortex was purchased from Uchida Wakanyaku Co., Ltd., Tokyo. Albizziae Cortex (2.0 kg) was extracted with MeOH twice under reflux. The combined extract (126 g) was concentrated and partitioned with 1-BuOH and H_2O. The aqueous portion (51 g) was subjected to Bondapak C_{18} column chromatography using 0→100% MeOH to give fractions 1 to 4. Fractions 1—3 were further separated by MCI gel CHP 20P (0→100% MeOH), Sephadex LH-20 (0→100% MeOH) and silica gel ($CHCl_3$–MeOH–H_2O=8:2:0.2→7:3:0.5) to provide compounds **1** (0.004%), **2** (0.002%), **3** (0.004%), **4** (0.004%) and **5** (0.005%).

Compound **1**: A white amorphous powder, $[\alpha]_D^{25}$ −89.5° (*c*=0.10, MeOH), ultraviolet (UV) λ_{max} (MeOH) nm (log ε): 275 (2.25). Negative FAB-MS: *m/z* 477 $[M-H]^-$. ^{1}H-NMR (in DMSO-d_6): 6.37 (2H, s, H-2, 6), 5.36 (1H, s, api H-1), 4.81 (1H, d, *J*=7.7 Hz, glc H-1), 3.73 (6H, s, 3, 5-OMe), 3.59 (3H, s, 4-OMe). ^{13}C-NMR: Table I.

Solvolysis of 1 A solution of **1** in 1 N HCl/MeOH was heated under reflux for 30 min and the reaction mixture was neutralized by 3% KOH/MeOH. After filtration and evaporation *in vacuo*, the residue taken in a small amount of $CHCl_3$–MeOH was analyzed by TLC ($CHCl_3$–MeOH–H_2O (8:2:0.2)). Methylapioside (*Rf* 0.37); methylglucoside (*Rf* 0.14).

Compound **2**: A white amorphous powder, $[\alpha]_D^{25}$ +0.4° (*c*=0.47, MeOH). UV λ_{max} (MeOH) nm (log ε): 277 (3.74). Negative FAB-MS: *m/z* 743 $[M-H]^-$. ^{1}H-NMR (in DMSO-d_6): 6.54 (1H, s, H-2), 6.33 (2H, s, H-2′, 6′), 3.76 (3H, s, 3-OMe), 3.28 (3H, s, 5-OMe), 3.64 (6H, s, 3′,5′-OMe), 8.17 (1H, br s, 4-OH), 7.98 (1H, br s, 4′-OH). ^{13}C-NMR: Table I.

Compound **3**: A white amorphous powder, $[\alpha]_D^{25}$ −21.2° (*c*=0.12, MeOH). UV λ_{max} (MeOH) nm (log ε): 274 (3.48). Negative FAB-MS: *m/z* 743 $[M-H]^-$. ^{1}H-NMR (in DMSO-d_6): 6.63 (1H, s, H-2), 6.28 (2H, s, H-2′, 6′), 3.77 (3H, s, 3-OMe), 3.43 (3H, s, 5-OMe), 3.63 (6H, s, 3′, 5′-OMe), 8.01 (1H, br s, 4′-OH). ^{13}C-NMR: Table I.

Enzymatic Hydrolysis of 2 and 3 A mixture of **2** (14 mg) and hesperidinase (20 mg) in citrate–phosphate buffer (pH 5.0) was incubated at 37 °C for 5 d. After filtration the reaction mixture was subjected to MCI gel CHP 20P. The MeOH eluate was separated by silica gel to give **2a** (5 mg), a white amorphous powder. $[\alpha]_D^{25}$ +38.0° (*c*=0.20, MeOH). UV λ_{max} (MeOH) nm (log ε): 281 (3.35). EI-MS: *m/z* 420 $[M]^+$. ^{1}H-NMR (in $CDCl_3$): 6.46 (1H, s, H-2), 6.35 (2H, s, H-2′, 6′), 5.34 (2H, br s, 4,4′-OH), 4.03 (1H, d, *J*=7.3 Hz, H-7′), 3.89 (3H, s, 3-OMe), 3.31 (3H, s, 5-OMe), 3.81 (6H, s, 3′, 5′-OMe).

In the same way as described above, **3** gave **3a** (3 mg), a white amorphous powder, $[\alpha]_D^{25}$ +39.0° (*c*=0.12, MeOH). UV λ_{max} (MeOH) nm (log ε): 280 (3.30). EI-MS: *m/z* 420 $[M]^+$. ^{1}H-NMR (in $CDCl_3$): 6.45 (1H, s, H-2), 6.33 (2H, s, H-2′, 6′), 5.33 (2H, br s, 4, 4′-OH), 4.00 (1H, d, *J*=7.3 Hz, H-7′), 3.90 (3H, s, 3-OMe), 3.31 (3H, s, 5-OMe), 3.81 (6H, s, 3′, 5′-OMe).

Compound **4**: A white amorphous powder, $[\alpha]_D^{25}$ +15.0° (*c*=0.14, MeOH). IR (KBr): 3440 (ν_{O-H}) cm^{-1}, 1650 ($\nu_{C=O}$) cm^{-1}. UV λ_{max} (MeOH) nm (log ε): 237 (3.99). Negative FAB-MS: *m/z* 517 $[M-H]^-$, ^{1}H-NMR (in DMSO-d_6): 5.78 (1H, s, H-4), 5.73 (2H, m, H-1′, 2′), 5.00 (1H, s, api H-1), 4.33 (1H, qui, *J*=6.2 Hz, H-3′), 4.20 (1H, d, *J*=8.1 Hz, glc H-1), 2.39 (1H, d, *J*=16.9 Hz, H-2eq), 2.05 (1H, d, *J*=16.9 Hz, H-2ax), 1.81 (3H, s, 5-Me), 1.19 (3H, d, *J*=6.2 Hz, 3′-Me), 0.94, 0.92 (each 3H, s, 1-Me×2). ^{13}C-NMR: Table I.

Enzymatic Hydrolysis of 4 A solution of **4** (10 mg) and glycosidases from *Turbo cornutus* in citrate–phosphate buffer (pH 5.0) was incubated at 37 °C for 5 d, and after filtration the reaction mixture was separated as above to give **4a** (3 mg), a white amorphous powder. $[\alpha]_D^{25}$ +137° (*c*=0.14, MeOH).

Compound **5**: A white amorphous powder, $[\alpha]_D^{20}$ −117.7° (*c*=0.55, MeOH). UV λ_{max} (MeOH) nm (log ε): 203 (4.51), 217 (4.34), 259 (3.96). Negative FAB-MS: *m/z* 521 $[M-H]^-$. ^{1}H-NMR (in DMSO-d_6): 6.89—7.39 (5H, m, H-2, 5, 6, 2′, 6′), 6.64 (1H, dt, *J*=15.8, 5.1 Hz, H-8′), 5.48 (1H, d, *J*=7.0 Hz, glc H-1), 4.59 (2H, br d, *J*=5.1 Hz, H_2-9′), 3.66, 3.65 (each 3H, s, 3, 3′-OMe). ^{13}C-NMR: Table I.

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References and Notes

1) Part 29 in the series of Studies on Leguminous Plants.
2) M. Kaneta, H. Hikichi, S. Endo and N. Sugiyama, *Agric. Biol. Chem.*, **44**, 1407 (1980).
3) P. Chamsuksai, J. S. Choi and W. S. Woo, *Arch. Pharm. Res.*, **4**, 129 (1981).
4) Y. Y. You, W. S. Woo, J. S. Choi and S. S. Kang, *Arch. Pharm. Res.*, **5**, 33 (1982); S. S. Kang and W. S. Woo, *ibid.*, **6**, 25 (1983); W. S. Woo and S. S. Kang, *J. Nat. Prod.*, **47**, 547 (1984).
5) J. Kinjo, K. Fukui, H. Higuchi and T. Nohara, *Chem. Pharm. Bull.*, **39**, 1623 (1991).
6) J. Kinjo, H. Higuchi, K. Fukui and T. Nohara, *Chem. Pharm. Bull.*, **39**, 2952 (1991).
7) M. Miyamura, T. Nohara, T. Tomimatsu and I. Nishioka, *Phytochemistry*, **22**, 215 (1983).
8) M. Ogawa and Y. Ogihara, *Chem. Pharm. Bull.*, **24**, 2102 (1976); G. Dada, A. Corbani, P. Manitto, G. Speranza and L. Lunazzi, *J. Nat. Prod.*, **52**, 1327 (1989).
9) N. Okamura, A. Yagi and I. Nishioka, *Chem. Pharm. Bull.*, **29**, 3507 (1981); R. G. Powell and C. R. Smith, *J. Nat. Prod.*, **44**, 86 (1981).
10) T. Miyase, A. Ueno, N. Takizawa, H. Kobayashi and H. Oguchi, *Phytochemistry*, **28**, 3483 (1989).