

Saponins from the Leaves of *Aralia elata* SEEM. (Araliaceae)Setsuo SAITO,*^a Shigeya SUMITA,^a Norihiro TAMURA,^b Yoichi NAGAMURA,^c Keishi NISHIDA,^d Madoka ITO,^d and Isao ISHIGURO^dFaculty of Pharmaceutical Sciences, Josai University,^a 1-1 Keyakidai, Sakado, Saitama 350-02, Japan, Department of Chemistry, School of Dentistry, Meikai University,^b 1-1 Keyakidai, Sakado, Saitama 350-02, Japan, School of Hygiene,^c and School of Medicine,^d Fujita Gakuen Health University, Kusakake, Toyoake, Aichi 470-11, Japan. Received June 7, 1989

Eleven triterpenoidal saponins having oleanolic acid or hederagenin as the aglycone and two flavonoidal glycosides were isolated from the leaves of *Aralia elata* SEEM. (Araliaceae). The structures of four new saponins (1, 2, 3, and 4) were established to be 3-*O*- α -L-rhamnopyranosyl(1 \rightarrow 2)- α -L-arabinopyranosyl-hederagenin 28-*O*- β -D-xylopyranosyl(1 \rightarrow 6)- β -D-glucopyranosyl ester, 3-*O*- α -L-rhamnopyranosyl(1 \rightarrow 2)- α -L-arabinopyranosyl-oleanolic acid 28-*O*- β -D-xylopyranosyl(1 \rightarrow 6)- β -D-glucopyranosyl ester, 3-*O*- β -D-glucopyranosyl(1 \rightarrow 3)- α -L-rhamnopyranosyl(1 \rightarrow 2)- α -L-arabinopyranosyl-hederagenin 28-*O*- β -D-glucopyranosyl(1 \rightarrow 6)- β -D-glucopyranosyl ester, and 3-*O*- β -D-glucopyranosyl(1 \rightarrow 3)- α -L-rhamnopyranosyl(1 \rightarrow 2)- α -L-arabinopyranosyl-hederagenin, respectively, on the basis of spectroscopic and chemical evidence.

Keywords *Aralia elata*; Araliaceae; triterpenoidal saponin; hederagenin glycoside; oleanolic acid glycoside; bisdesmoside; monodesmoside

The roots and bark of *Aralia elata* SEEM. (Araliaceae) (Japanese name "taranoki") have been used as a folk medicine in Japan and China as a tonic, anti-gastric ulcer agent, and antidiabetes agent. Isolation and structural studies of various triterpenoidal saponins from *Aralia* species have been reported by the three groups as follows:

tarasaponins from the roots of *A. elata* by Shoji *et al.*,¹⁾ araloside A, B, and C from *A. mansurica* by Kochetkov *et al.*,²⁾ and saponin AC's from *A. cordata* by Kawai *et al.*³⁾ This paper describes the structural elucidation of four new triterpenoidal saponins (1-4) isolated from the leaves of *A. elata*.

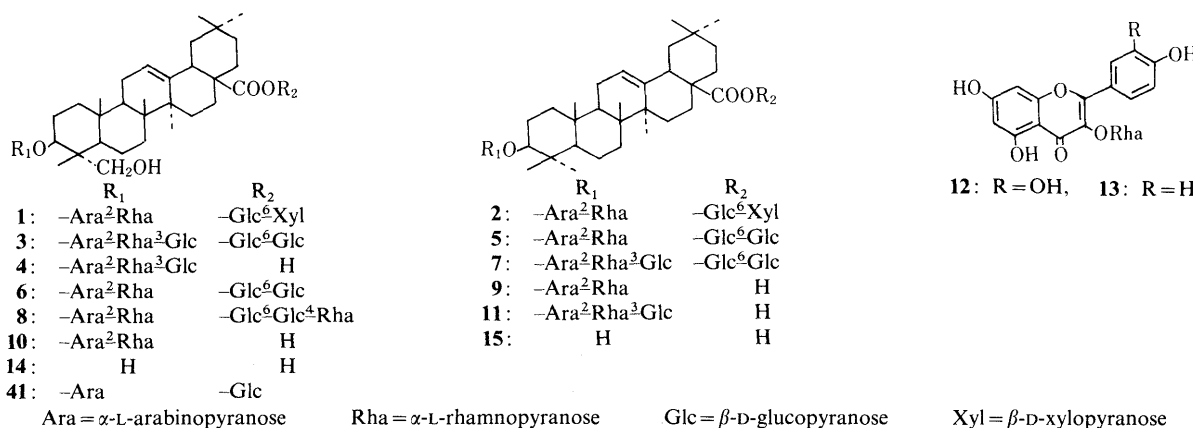


Fig. 1

TABLE I. ¹H-NMR Spectral Data for Saponins 1-4 (270 MHz, Pyridine)^{a)}

Saponin	Sugar anomeric	Vinyl (C-12)	Rha-CH ₃	CH ₃
1	6.26 (d, <i>J</i> = 7.7 Hz, Glc-1)	5.40 (br s)	1.43 (d, <i>J</i> = 5.9 Hz)	1.19, 1.16
	6.21 (s, Rha-1)			0.95, 0.95
	5.11 (d, <i>J</i> = 5.5 Hz, Ara-1)			0.88, 0.88
2	4.92 (d, <i>J</i> = 7.3 Hz, Xyl-1)	5.39 (br s)	1.57 (d, <i>J</i> = 6.2 Hz)	1.24, 1.13
	6.21 (d, <i>J</i> = 7.7 Hz, Glc-1)			1.06, 1.02
	6.16 (s, Rha-1)			0.89, 0.89
3	4.87 (d, <i>J</i> = 5.1 Hz, Ara-1)	5.41 (br s)	1.55 (d, <i>J</i> = 6.2 Hz)	0.88
	4.85 (d, <i>J</i> = 7.3 Hz, Xyl-1)			1.19, 1.16
	6.30 (s, Rha-1)			1.13, 0.99
4	6.28 (d, <i>J</i> = 8.1 Hz, Glc-1)	5.40 (br s)	1.43 (d, <i>J</i> = 5.9 Hz)	0.87, 0.87
	5.52 (d, <i>J</i> = 7.7 Hz, Glc-1)			1.19, 1.05
	5.05 (d, <i>J</i> = 7.3 Hz, Glc-1)			0.95, 0.95
	5.00 (d, <i>J</i> = 5.9 Hz, Ara-1)			0.88, 0.87
	6.15 (s, Rha-1)			
	5.39 (d, <i>J</i> = 7.7 Hz, Glc-1)			
	4.95 (d, <i>J</i> = 6.6 Hz, Ara-1)			

a) Only assignable signals are listed. Glc = β -D-glucopyranose, Rha = α -L-rhamnopyranose, Ara = α -L-arabinopyranose, Xyl = β -D-xylopyranose.

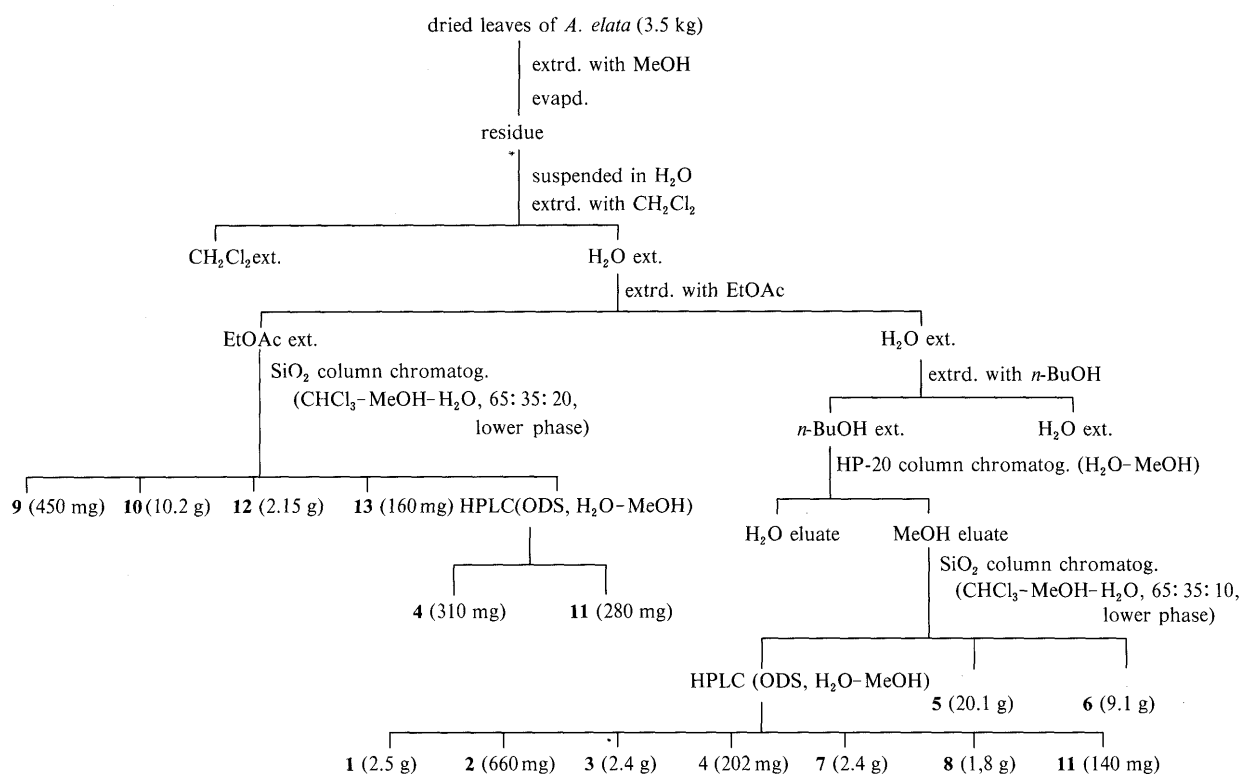


Chart 2

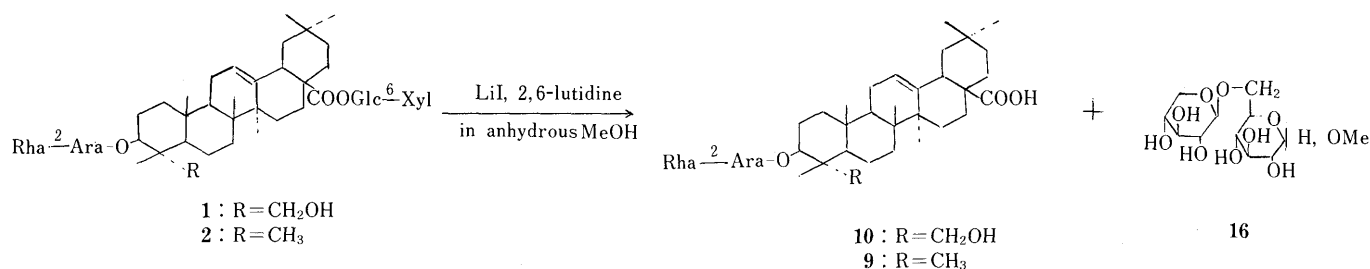


Fig. 2

Dried leaves of *A. elata* were extracted with hot MeOH, and the extracts were fractionated as shown in Chart 1. Eleven saponins (1–11) and two flavonoidal glycosides (12 and 13) were isolated by repeated column chromatography and high performance liquid chromatography (HPLC). The known saponins 5,⁴⁾ 6,⁵⁾ 7,⁶⁾ 8,⁷⁾ 9,⁸⁾ 10,⁷⁾ and 11,⁶⁾ and flavonoidal glycosides, quercetin 3-*O*- α -L-rhamnopyranoside (12)⁹⁾ and kaempferol 3-*O*- α -L-rhamnopyranoside (13),¹⁰⁾ were identified from chemical evidence and by comparison of the spectral data with published values for the compounds themselves and their derivatives.

Both saponins 1 and 2 showed the characteristic absorption band assigned to the ester group at 1740 cm⁻¹ in the infrared (IR) spectra and four anomeric protons in the ¹H-nuclear magnetic resonance (¹H-NMR) spectra (Table I). The fast atom bombardment mass spectra (FAB-MS) of 1 and 2 revealed the pseudo molecular ion at *m/z* 1083 and 1067, (M+K)⁺, respectively. On acid hydrolysis both 1 and 2 yielded the same monosaccharides, arabinose, xylose, rhamnose, and glucose (sugar ratio, 1:1:1:1, respectively) together with hederagenin (14) from 1 and oleanolic acid (15) from 2. On selective cleavage of the ester glycosidic linkage with anhydrous LiI and 2,6-lutidine in anhydrous

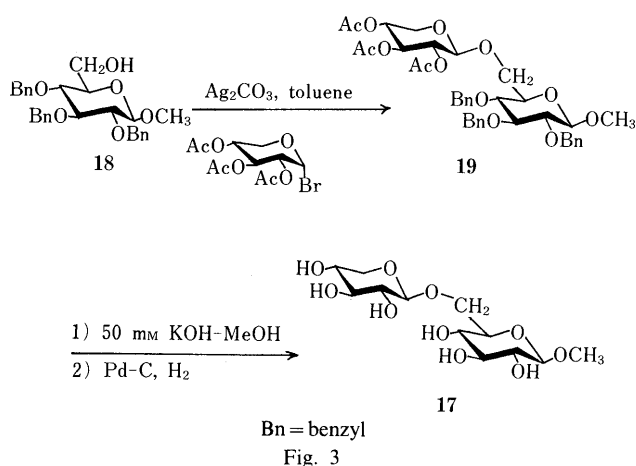
MeOH,¹¹⁾ 1 and 2 gave the same methyl glycoside (16) (an anomeric mixture), and prosapogenin 10 and 9, respectively, which suggested that 1 and 2 were bisdesmosides of 14 and 15, respectively, having four monosaccharides. The prosapogenins 10 and 9 were identical with 3-*O*- α -L-rhamnopyranosyl(1→2)- α -L-arabinopyranosyl-hederagenin and -oleanolic acid, respectively, which were isolated in this work, based on the ¹H- and ¹³C-NMR spectra and FAB-MS. The thin layer chromatography (TLC) of 16 was in accordance with that of synthetic methyl β -D-xylopyranosyl(1→6)- β -D-glucopyranoside (17) which was synthesized according to the method outlined in Fig. 3. The glycosidic oxygen linked to O-28 in 1 and 2 was determined to have the β -configuration from the coupling constant (*J* = 7.7 Hz) of the anomeric proton of the glucopyranose in the ¹H-NMR spectra of 1 and 2. These results together with the ¹³C-NMR spectra (Table II) gave the formulas of 1 and 2 as shown in Fig. 1.

Saponins 3 and 4 on acid hydrolysis, yielded the same monosaccharides, arabinose, rhamnose, and glucose. The sugar ratios, however, were different: 1:1:3 in 3 and 1:1:1 in 4, respectively. FAB-MS of 3 and 4 revealed the pseudo molecular ion at *m/z* 1275 (M+K)⁺ and 951 (M+K)⁺, respectively, and the ¹H-NMR spectra showed five and

TABLE II. ^{13}C -NMR Chemical Shifts of Sugar Moieties of Saponins 1–11 in $\text{C}_5\text{D}_5\text{N}$

		1	2	3	4	5	6	7	8	9	10	11	41 ⁽³⁾	
3-Ara	C-1	105.6	105.4	104.6	104.8	104.6	104.0	105.1	104.3	104.6	104.1	105.2	106.5	
	C-2	75.9	75.8	75.6	75.6	75.9	75.9	75.8	76.0	75.8	75.2	75.9	73.0	
	C-3	74.7 ^{a)}	73.8	74.6	74.8	73.4	74.0	74.3	74.5	73.5	74.4	74.1	74.6	
	C-4	67.0	68.2	69.6	69.6	69.8	69.6	69.8	69.9	69.9	69.7	69.5	69.7	69.5
	C-5	64.0	64.2	66.0	66.2	64.3	65.1	65.6	65.5	64.4	65.4	65.4	66.9	
3-Rha	C-1	101.7	101.6	101.2	101.4	101.6	101.6	101.6	101.8	101.6	101.4	101.6		
	C-2	72.3 ^{b)}	72.1 ^{a)}	71.4	71.6	72.4 ^{a)}	72.4 ^{a)}	71.6	72.4 ^{a)}	72.4 ^{a)}	72.4 ^{a)}	71.4		
	C-3	72.5 ^{b)}	72.4 ^{a)}	82.7	82.8	72.2 ^{a)}	72.1 ^{a)}	83.1	72.6 ^{a)}	72.2 ^{a)}	72.1 ^{a)}	83.0		
	C-4	74.5 ^{a)}	73.7	72.6	72.8	73.9	74.1	72.9	74.2	73.9	73.9	72.8		
	C-5	69.7	69.8	69.4	69.7	68.4	69.3	69.3	69.3	69.4	69.4	69.1		
	C-6	18.5	18.4	18.3	18.4	18.5	18.4	18.5	18.7	18.4	18.4	18.4		
3-Glc	C-1			106.4	106.5			106.6				106.4		
	C-2			75.3	75.6			75.7				75.7		
	C-3			78.4 ^{a)}	78.4 ^{a)}			78.4 ^{a)}				78.4 ^{a)}		
	C-4			71.3	71.6			71.5				71.5		
	C-5			78.1 ^{a)}	78.3 ^{a)}			78.5 ^{a)}				78.3 ^{a)}		
	C-6			62.4	62.5			62.6				62.4		
28-Glc	C-1	95.6	95.4	96.3		95.6	95.6	95.7	95.8				95.7	
	C-2	73.9 ^{c)}	73.3 ^{b)}	73.7		73.8	73.8	73.8	74.1				74.0	
	C-3	78.7	78.1	78.3 ^{a)}		78.5 ^{b)}	78.6	78.8 ^{a)}	78.5 ^{b)}				79.2	
	C-4	71.0	70.9	70.6		70.7	70.7	70.9	70.9				71.0	
	C-5	77.3	77.8	77.7		77.8	77.8	77.9	78.1				78.8	
	C-6	69.2	69.0	69.2		69.2	69.2	69.2	69.3				62.2	
28-Glc (Terminal)	C-1			104.9		105.0	105.0	105.3	104.9					
	C-2			74.9		75.0	75.0	75.0	75.5					
	C-3			78.2 ^{a)}		78.2 ^{b)}	77.8	78.2	76.7					
	C-4			71.1		71.4	71.5	71.4	78.7 ^{b)}					
	C-5			78.1 ^{a)}		78.2 ^{b)}	77.8	78.2	77.1					
	C-6			62.6		62.5	62.6	62.6	61.5					
28-Xyl	C-1	104.2	104.5											
	C-2	74.1 ^{c)}	73.7 ^{b)}											
	C-3	74.7	74.5											
	C-4	70.9	70.9											
	C-5	65.5	65.8											
28-Rha	C-1								102.8					
	C-2								72.6 ^{c)}					
	C-3								72.8 ^{c)}					
	C-4								74.1					
	C-5								70.5					
	C-6								18.7					

a–c) These values may be interchangeable in each column.



three anomeric proton signals, respectively (Table I). Furthermore, the IR spectra of **3** and **4** demonstrated the characteristic bands due to the ester group at 1735 cm^{-1} and the COOH group at 1690 cm^{-1} . These findings indicated that **3** was 3,28-*O*-bisglycosidic hederagenin and **4** was 3-*O*-monoglycosidic hederagenin. The ^{13}C -NMR

chemical shifts of the sugar moieties of **4** were in close accordance with those of saponin **11** (Table II), which, together with the chemical evidence, gave the formula of **4** as shown in Fig. 1. On alkaline hydrolysis, **3** yielded **4**. Comparison of the ^1H -NMR spectra of **3** and **4** (Table I) revealed that two doublets at δ 6.28 ($J=8.1\text{ Hz}$) and 5.05 ($J=7.3\text{ Hz}$) had disappeared in the spectrum of **4**. Based on a comparison of the sugar ratios obtained from the acid hydrolysis of **3** and **4**, it was inferred that the absent anomeric protons could be assigned to two β -D-glucopyranose linked to O-28. The ^{13}C -NMR chemical shifts of the sugar moieties of **3** agreed closely with those of **7** (Table II), in which the glycosylation shifts were observed at C-2 of arabinopyranose and C-3 of rhamnopyranose which were linked to O-3 of the aglycone, and C-6 of the inner glucopyranose linked to O-28. These findings gave the formula of **3** as shown in Fig. 1.

Saponins isolated from the roots and bark of *A. elata*, *A. mandshurica*, and *A. cordata* have a glucuronic acid as one of the sugar components of the glycosides. Although saponins isolated from *A. cordata* lack arabinose as a sugar component, L-arabinose (which is also one of the sugar

components in saponin molecules isolated from the roots and bark of *A. elata* and *A. mandshurica*) forms a furanose ring. Interestingly, on the other hand, saponins isolated from the leaves of *A. elata* have no glucuronic acid as a sugar component, and arabinose contained in the saponins forms a pyranose ring.

Experimental

General Procedure All melting points were measured on a Yanagimoto micro melting point apparatus and are uncorrected. ¹H- and ¹³C-NMR spectra were obtained with a JEOL JNM-GX 270 FT NMR spectrometer at 270 and 67.8 MHz, respectively, and chemical shifts were given in ppm with tetramethylsilane as an internal standard. Electron impact- (EI-) and FAB-MS were recorded on a JEOL JMS-DX 300 mass spectrometer. Optical rotations were measured with a JASCO J-20A spectropolarimeter. Gas liquid chromatography (GLC) was run on a Shimadzu GC-9A with a flame ionization detector using a glass column (2.0 m × 4 mm) packed with 3% ECNSS-M (column temperature, gradient from 150 up to 190 °C; H₂ 60 ml/min, N₂ 80 ml/min). A Shimadzu LC-6A liquid chromatograph was employed for analytical HPLC, and was further equipped with an SSC-6310 autoinjector and an SSC-6320 fraction collector (Senshu Sci. Co., Ltd.) for preparative HPLC using ODS-H-4251 (250 mm × 10 mm). Thin-layer chromatograms utilized Kieselgel HF₂₅₄ (Merck), and spots were detected by spraying with dilute H₂SO₄ followed by heating at 80 °C for 20 min. Column chromatograms were prepared with Wakogel C-200 and Diaion HP-20.

Extraction and Separation of Glycosides Dried leaves (3.5 kg) of *A. elata*, collected in June, 1987, at Hiki-gun, Saitama Prefecture, were extracted and separated as described in Chart 1.

Saponin 1 White powder, mp 209–213 °C, $[\alpha]_D^{18} - 5.7^\circ$ ($c=0.88$, MeOH). IR $\nu_{\max}^{\text{Nujol}} \text{cm}^{-1}$: 1740. FAB-MS m/z : 1083 (M+K)⁺. Anal. Calcd for C₅₂H₈₄O₂₁·H₂O: C, 58.74; H, 8.15. Found: C, 58.75; H, 8.10.

Saponin 2 White powder, mp 208–212 °C, $[\alpha]_D^{18} - 12.7^\circ$ ($c=0.86$, MeOH). IR $\nu_{\max}^{\text{Nujol}} \text{cm}^{-1}$: 1740. FAB-MS m/z : 1067 (M+K)⁺. Anal. Calcd for C₅₂H₈₄O₂₀·3H₂O: C, 57.65; H, 8.37. Found: C, 57.74; H, 8.07.

Saponin 3 Colorless needles (*n*-BuOH), mp 219–221 °C, $[\alpha]_D^{20} - 6.9^\circ$ ($c=1.44$, MeOH). IR $\nu_{\max}^{\text{Nujol}} \text{cm}^{-1}$: 1735. FAB-MS m/z : 1275 (M+K)⁺. Anal. Calcd for C₅₉H₉₆O₂₇·3H₂O: C, 54.87; H, 7.96. Found: C, 54.86; H, 7.99.

Saponin 4 White powder, mp 240–245 °C, $[\alpha]_D^{25} + 7.6^\circ$ ($c=1.34$, pyridine). IR $\nu_{\max}^{\text{Nujol}} 1690 \text{cm}^{-1}$. FAB-MS m/z : 951 (M+K)⁺. Anal. Calcd for C₄₇H₇₆O₁₇·5/2H₂O: C, 58.92; H, 8.52. Found: C, 58.67; H, 8.64.

Acid Hydrolysis of 1–4 Compound **1** (10 mg) was refluxed with 5 ml of 1 N H₂SO₄ in 1,4-dioxane–H₂O (3:1) for 5 h. The reaction mixture was diluted with H₂O (10 ml) and extracted with AcOEt (10 ml × 3). The combined AcOEt extracts were evaporated to give **14** (4.3 mg, 95.1%). The H₂O layer was neutralized with saturated aqueous Ba (CO₃)₂ solution, and centrifuged to provide a solution which was evaporated to give a syrup. The syrup was reacted with NaBH₄ and acetylated. The acetylated mixture was subjected to GLC, which revealed four peaks for the derivatives of arabinose, xylose, rhamnose, and glucose (1:1:1:1, respectively). Acid hydrolyses of **2**, **3**, and **4** were performed by the same method as for **1**, and the sugar components of each saponin were confirmed by the same method as for **1**. The results are summarized Table III.

Reaction of 1 with LiI and 2,6-Lutidine in Anhydrous MeOH 2,6-Lutidine (1 ml) and LiI (10 mg) were added to a solution of **1** (50 mg) in anhydrous MeOH (5 ml), and the mixture was refluxed for 16 h under argon. The reaction mixture was diluted with H₂O (30 ml) and extracted with AcOEt (10 ml × 3). The combined AcOEt extracts were evaporated to afford a residue which was chromatographed on silica gel and eluted with a solution of CHCl₃–MeOH–H₂O (65:35:20, lower layer) to give **10** (28.1 mg, 78%). The H₂O layer was evaporated to afford a residue which was subjected to column chromatography (20% MeOH–CHCl₃) to give **16** (9.9 mg, 63%), which was identical with synthetic methyl β-D-xylopyranosyl(1→6)-β-D-glucopyranoside **17** by TLC and GLC.

Reaction of 2 with LiI and 2,6-Lutidine in Anhydrous MeOH 2,6-Lutidine (1 ml) and LiI (15 mg) were added to a solution of **2** (65 mg) in anhydrous MeOH (5 ml), and the mixture was refluxed for 20 h under argon. The reaction mixture was treated by the same method as for **1** to give **9** (37.6 mg, 81%) and **16** (12 mg, 58%).

Alkaline Hydrolysis of 3 A solution of **3** (100 mg) in 10 ml of 1 N KOH in H₂O–MeOH (1:1) was stirred at 60 °C for 2 d. The reaction mixture was neutralized with AcOH and evaporated to afford a residue which was subjected to column chromatography to give compound **4** (a white

TABLE III. Products Obtained on Acid Hydrolysis of Saponins 1–4

Saponin	Products	
	Aglycon	Sugars (molar ratios)
1	14	Arabinose (1), xylose (1), rhamnose (1), glucose (1)
2	15	Arabinose (1), xylose (1), rhamnose (1), glucose (1)
3	14	Arabinose (1), rhamnose (1), glucose (3)
4	14	Arabinose (1), rhamnose (1), glucose (1)

powder, 21 mg, 28%). Compound **4** was identical with the authentic saponin, which was isolated in this study, based on TLC and ¹³C-NMR.

Methyl 2,3,4-Tri-O-acetyl-β-D-xylopyranosyl(1→6)-2,3,4-tri-O-benzyl-β-D-glucopyranoside (19) 2,3,4-Tri-O-acetyl-α-D-xylopyranosyl bromide (4.3 g) and Ag₂CO₃ (5.6 g) were added to a solution of methyl 2,3,4-tri-O-benzyl-β-D-glucopyranoside (**18**) (1 g) in toluene (30 ml) and the mixture was stirred overnight. The mixture was then poured into ice-water (100 ml), and extracted with CH₂Cl₂ (100 ml × 3). The combined extracts were washed successively with saturated aqueous NaHCO₃ and H₂O, dried over Na₂SO₄, filtered, and evaporated. The resultant residue was subjected to column chromatography (benzene–acetone, gradient up to 20% acetone) to obtain **19** (oil, 670 mg, 43%). EI-MS m/z (%): 690 (trace, M⁺ – MeOH), 631 (4, M⁺ – CH₂C₆H₅), 525 (3), 493 (5), 431 (5), 409 (5), 259 (68). Anal. Calcd for C₃₉H₄₆O₁₃: C, 64.81; H, 6.42. Found: C, 64.67; H, 6.50.

Methyl β-D-Xylopyranosyl(1→6)-β-D-glucopyranoside (17) A solution of **19** (600 mg) in 50 mM NaOH–MeOH (10 ml) was allowed to stand overnight. The reaction mixture was neutralized with AcOH, and evaporated to afford a residue. The residue was dissolved in MeOH (50 ml), and 10% Pd–C (50 mg) was added. The mixture was stirred for 20 h under hydrogen at atmospheric pressure. The catalyst was removed by filtration and washed with MeOH, and the solution was concentrated under reduced pressure to give **17** (a white powder, 154 mg, 57%). FAB-MS m/z (%): 365 (M+K)⁺. ¹³C-NMR (*d*₅-pyridine) δ : 105.8 (Xyl-1), 101.3 (Glc-1), 78.2 (Glc-3), 75.3 (Glc-5), 74.4 (Xyl-3), 73.6 (Xyl-2), 72.8 (Glc-2), 71.9 (Glc-4), 71.1 (Glc-6), 70.7 (Xyl-4), 67.0 (Xyl-5), 55.2 (OCH₃). Anal. Calcd for C₁₂H₂₂O₁₀·H₂O: C, 41.86; H, 7.03. Found: C, 41.58; H, 7.09.

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